

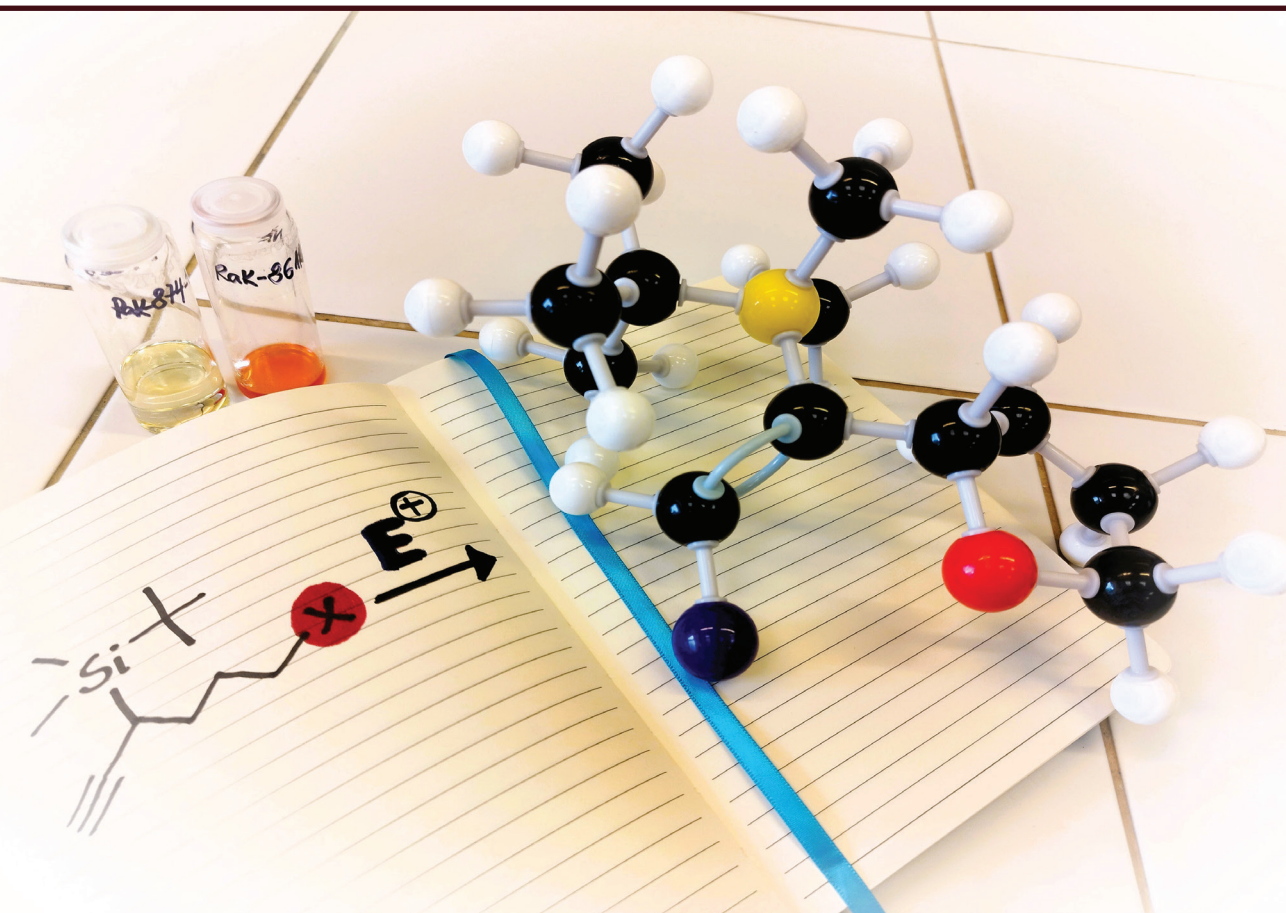
Rasma Kronkalne

**SILILGRUPAS 1,2-NOBĪDE PROPARGILSILĀNOS KĀ JAUNA
METODOLOĢIJA HETEROCIKLU UN AIZVIETOTU OLEFĪNU
SINTĒZEI**

Promocijas darbs

**1,2-SILYL SHIFT IN PROPARGYL SILANES
AS A NOVEL METHODOLOGY FOR THE SYNTHESIS
OF HETEROCYCLES AND SUBSTITUTED OLEFINS**

Doctoral Thesis



RĪGAS TEHNISKĀ UNIVERSITĀTE

Dabaszinātņu un tehnoloģiju fakultāte
Ķīmijas un ķīmijas tehnoloģijas institūts

RIGA TECHNICAL UNIVERSITY

Faculty of Natural Sciences and Technology
Institute of Chemistry and Chemical Technology

Rasma Kronkalne

Doktora studiju programmas “Ķīmija, materiālzinātne un tehnoloģijas” doktorante
Doctoral Student of the Study Programme “Chemistry, Materials Science and Engineering”

SILILGRUPAS 1,2-NOBĪDE PROPARGILSILĀNOS KĀ JAUNA METODOLOĢIJA HETEROCIKLU UN AIZVIETOTU OLEFĪNU SINTĒZEI

Promocijas darbs

1,2-SILYL SHIFT IN PROPARGYL SILANES AS A NOVEL METHODOLOGY FOR THE SYNTHESIS OF HETEROCYCLES AND SUBSTITUTED OLEFINS

Doctoral Thesis

Zinātniskais vadītājs / Scientific supervisor

Profesors *Dr. chem.* / Professor Dr. chem.

MĀRIS TURKS

RTU Izdevniecība / RTU Press

Rīga 2026 / Riga 2026

Kroņkalne, R. Sililgrupas 1,2-nobīde propargilsilānos kā jauna metodoloģija heterociklu un aizvietotu olefinu sintēzei. Promocijas darbs. Rīga: RTU Izdevniecība, 2026. – 221 lpp.

Kroņkalne, R. 1,2-Silyl Shift in Propargyl Silanes as a Novel Methodology for the Synthesis of Heterocycles and Substituted Olefins. Doctoral Thesis. Riga: RTU Press, 2026. 221 p.

Publicēts saskaņā ar RTU promocijas padomes “RTU P-01” 2026. gada 10. jūnija lēmumu, protokols Nr. 86.

Published in accordance with the decision of the RTU Promotion Council “P-01” of 10 June 2026, Minutes No. 86.

Vāka attēla autore Rasma Kroņkalne.

Cover image by Rasma Kroņkalne.

PROMOCIJAS DARBS IZVIRZĪTS ZINĀTNES DOKTORA GRĀDA IEGŪŠANAI RĪGAS TEHNISKAJĀ UNIVERSITĀTĒ

Promocijas darbs zinātnes doktora (*Ph. D.*) grāda iegūšanai tiek publiski aizstāvēts 2026. gada 23. septembrī plkst. 14.00 Rīgas Tehniskās universitātes Dabaszinātņu un tehnoloģiju fakultātē, Rīgā, Paula Valdena ielā 3/7, 272. auditorijā.

OFICIĀLIE RECENZENTI

Asociētais profesors *Dr. chem.* Eduards Baķis,
Latvijas Universitāte, Latvija

Profesore *Ph. D.* Maria Asuncion Barbero Perez,
Valjadolidas Universitāte, Spānija

Profesors *Dr. sc.* Dean Marković,
Rijekas Universitāte, Horvātija

APSTIPRINĀJUMS

Apstiprinu, ka esmu izstrādājusi šo promocijas darbu, kas iesniegts izskatīšanai Rīgas Tehniskajā universitātē zinātnes doktora (*Ph. D.*) grāda iegūšanai. Promocijas darbs zinātniskā grāda iegūšanai nav iesniegts nevienā citā universitātē.

Rasma Kronkalne

(*paraksts*)

Datums

Promocijas darbs sagatavots kā tematiski vienotu zinātnisko publikāciju kopa ar kopsavilkumu latviešu un angļu valodā. Tajā ietvertas trīs oriģinālpublikācijas *SCI* žurnālos, viens apskatraksts, viens sagatavošanā esošais manuskripts un nepublicētie rezultāti. Publikācijas zinātniskajos žurnālos uzrakstītas angļu valodā.

SATURS

LIETOTIE SAĪSINĀJUMI	6
PROMOCIJAS DARBA VISPĀRĒJS RAKSTUROJUMS.....	7
Tēmas aktualitāte.....	7
Pētījuma mērķis un uzdevumi	9
Zinātniskā novitāte un galvenie rezultāti.....	10
Darba struktūra un apjoms.....	11
Darba aprobācija un publikācijas.....	11
PROMOCIJAS DARBA GALVENIE REZULTĀTI	15
1.1. Propargilsilānu heterociklizācija, iekšējam <i>O-/N-/S</i> -nukleofilam reaģējot ar β -silīcija stabilizētu alilkatjonu.....	16
1.2. Propargilsilānu heterociklizācija arēniem kā iekšējiem <i>C</i> -nukleofiliem, reaģējot ar β -silīcija stabilizētu alilkatjonu.....	21
1.3. Arilētu heterociklu un diēnu sintēze reakcijā ar diaril- λ^3 -jodāniem vara katalīzes apstākļos	29
1.4. Ritera tipa reakcija ar β -silīcija stabilizētu alilkatjonu.....	37
SECINĀJUMI	45
LITERATŪRAS SARAKSTS	47
PATEICĪBAS.....	52
PIELIKUMI / APPENDICES.....	103

- I pielikums: Krontkalne, R.; Beļunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.*, **2023**, 88 (19), 13857-13870. <https://doi.org/10.1021/acs.joc.3c01481>
- II pielikums: Ubaidullajevs, A.; Krontkalne, R.; Mishnev, A.; Turks, M. Synthesis of Substituted Chromanes and Tetrahydroquinolines *via* Tandem 1,2-Silyl Shift – Friedel–Crafts cyclization. *J. Org. Chem.*, **2026**, 91 (17), 5785–5810. <https://doi.org/10.1021/acs.joc.5c03136>
- III pielikums: Krontkalne, R.; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. *Beilstein J. Org. Chem.*, **2025**, 21, 1984-1994. <https://doi.org/10.3762/bjoc.21.154>
- IV pielikums: Krontkalne, R.; Turks, M. Recent Advances in Intramolecular C-N Bond Formation for Pyrrolidine Synthesis. *ChemistryOpen*, **2026**, 15 (6), e70182. <https://doi.org/10.1002/open.70182>

- V pielikums: Kronkalne, R.; Turks, M. Eksperimentālās procedūras 1,3-oksazinān-2-ona atvasinājuma un tā izejvielu sintēzei. (*Nepublicētie rezultāti*)
- VI pielikums: Turka, S.; Kronkalne, R.; Rogaļevs, R.; Puriņš, M.; Mishnev, A.; Turks, M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives. (*Nepublicētais manuskripts*)
- VII pielikums: Kronkalne, R.; Turks, M. Sintēzes procedūras un raksturojumi jodētiem hromānu atvasinājumiem. (*Nepublicētie rezultāti*)

LIETOTIE SAĪSINĀJUMI

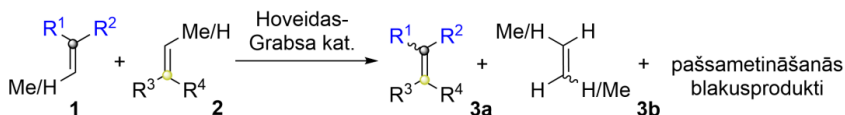
Ac	acetil-
Ar	aril-
B:	bāze
Boc	<i>t</i> -butiloksikarbonil-
Bu	butil-
Bz	benzoil-
Cbz	benziloksikarbonil-
DBU	1,8-diazabicklo(5.4.0)undec-7-ēns
DCE	1,2-dihlorekāns
DCM	dihlormetāns
DIAD	diizopropilazodikarboksilāts
DMAP	<i>N,N</i> -Dimetilpyridīn-4-amine
DMF	<i>N,N</i> -dimetilformamīds
ECAC	etil-2-(3,4-dihlorfenil)diazēn-1-karboksilāts
Et	etil-
Hal	halogēns
HFIP	1,1,1,3,3,3-heksafluorpropan-2-ols
KMR	kodolu magnētiskā rezonanse
Me	metil-
Mes	mezil-
Ms	metilsulfonil-
NBS	<i>N</i> -bromsukcinimīds
NCS	<i>N</i> -hlorsukcinimīds
NIS	<i>N</i> -jodsukcinimīds
PCC	piridīnija hlorkromāts
Ph	fenil-
Pr	propil-
Py	piridīns
Ns	<i>p</i> -nitrobenzolsulfonil-, nozil-
Su	sukcinimīds
TEMPO	(2,2,6,6-tetrametilpiperidīn-1-il)oksil
TFE	2,2,2-trifluoetān-1-ols
Tf	trifluometānsulfonil-
THF	oksolāns
Ts	4-metilbenzolsulfonil-
XPhos	dicikloheksil[2',4',6'-tris(propān-2-il)[1,1'-bifenil]-2-il]fosfāns

PROMOCIJAS DARBA VISPĀRĒJS RAKSTUROJUMS

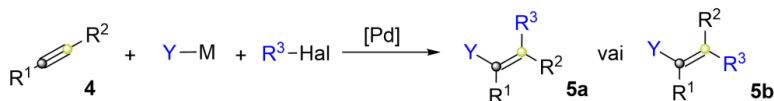
Tēmas aktualitāte

Alkēni ir izplatīta karbofunkcionālo savienojumu klase – tie kā struktūrelementi ir plaši sastopami gan dabasvielās, gan sintētiskajos savienojumos.^[1–3] Alkēni kalpo kā prekursori neskaitāmām organiskajām pārvērtībām, kas ļauj iegūt plašu vērtīgu produktu spektru.^[4, 5] Alkēnu ģeometrija un to aizvietotāji tieši ietekmē produktu īpašības, kas ir nozīmīgs faktors gan bioaktīvos savienojumos, gan polimēros, gan asimetriskās katalīzes substrātos.^[6] Neskatoties uz to, trīs- un čtraizvietotu olefīnu stereoselektīva iegūšana pat 21. gadsimtā mēdz būt izaicinoša.^[7] (*E/Z*)-selektivitāti bieži nosaka relatīvais aizvietotāju izmērs.^[8] (*E*)-izomēru tipiski iegūst kā termodinamisko produktu, taču enerģētiski neizdevīgāko (*Z*)-alkēnu sintēze ir problemātiskāka. Turklāt daudzu klasisko alkēnu sintēzes metožu, piemēram, Vitiga (*Wittig*) reakcijas, Žiliā-Kočiņska (*Julia-Kocienski*) olefinēšanas u. c., piemērotība stereoselektīvai trīs- un čtraizvietotu alkēnu sintēzei ir ierobežota.^[6, 9] Tas motivē alternatīvu olefīnu sintēzes, piemēram, olefīnu metatēzes^[10–12] stratēģiju attīstību (1. shēma). Augsti funkcionalizētu alkēnu sintēzei izmanto arī pārvērtību rindas, kas apvieno alkīnu hidrometalēšanu, karbometalēšanu vai halogēnborēšanu ar šķērssametinašanās reakcijām,^[13–16] kā arī pārejas metālu katalizētu alkīnu hidroalkilēšanu.^[6] Diemžēl šīs metodes bieži vien nav pietiekami stereoselektīvas.^[6] Tāpat aktuāls mērķis ir arī masas efektivitātes paaugstināšana trīs- un čtraizvietotu olefīnu sintēzē.^[17]

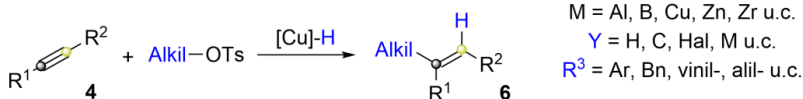
A) Olefīnu metatēze



B) Alkīnu 1,2-difunkcionalizēšana



C) Alkīnu hidroalkilēšana

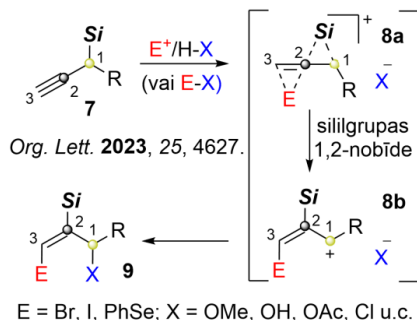


1. shēma. Mūsdienīgās stratēģijas stereoselektīvai augsti funkcionalizētu olefīnu sintēzei.

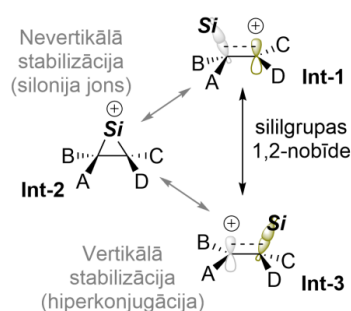
Darba autores un kolēģu zinātniskajā grupā nesen tika demonstrēta jauna pieeja stereoselektīvai trīsaizvietotu olefīnu **9** sintēzei, izmantojot propargilsilānu **7** 1,3-

difunkcionalizāciju (2. shēma).^[18, 19] Šī pieeja tika balstīta propargilsistēmas aktivēšanā ar ārējiem elektrofilēm (Hal^+ , RSe^+), kam sekoja sililgrupas 1,2-migrācija.^[19] Daudzos gadījumos β -sililkarbēnija jona kā iespējamā starpsavienojuma veidošanos veicina nevertikālā stabilizācija (**Int-2**), kas sekmē sililgrupas migrāciju un izraisa stabilākā alilkatjona veidošanos.^[20, 21] Šie β -silīcija stabilizētie alilkatjoni **8b** tālāk kalpoja kā būvbloki trīsaizvietotu alkēna fragmentu ievadīšanai molekulā **9** ar augstu stereoselektivitāti.^[19]

d) Alkīnu 1,3-difunkcionalizēšana



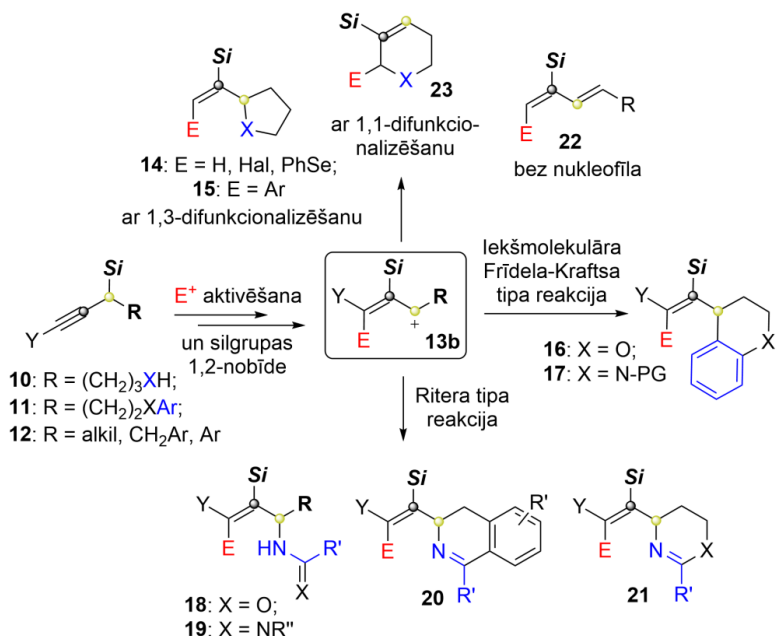
Karbēnija jonu stabilizēšana ar β -silīciju:



2. shēma. Alkīnu difunkcionalizēšana ar sililgrupas 1,2-migrāciju.

Lai gan sintētiskās metodes, kas ietver sililgrupas 1,2-nobīdi, ir pazīstamas jau kopš 20. gadsimta 80. gadiem, piemēri to lietojumam stereodefinētu alkēnu, kas satur trīs vai vairāk aizvietotājus, sintēzē joprojām ir ierobežoti. Silīcija pārgrupēšanās koncepcija heterociklisko struktūru sintēzei arī ir salīdzinoši maz pētīta.^[20, 21] Heterociklu nozīmība organiskajā ķīmijā ir nenoliedzama. Statistika rāda, ka lielākā daļa moderno zāļu vielu un agroķīmijas vielu satur vismaz vienu heterociklisku struktūrfragmentu.^[22] Piemēram, 2019. gadā vismaz pusi no jaunajām ASV Pārtikas un zāļu pārvaldes (FDA) apstiprinātajām zāļu vielām veidoja heterociklu atvasinājumi.^[23, 24] Tas veicina interesi par jaunu un efektīvu sintētisko stratēģiju izstrādi funkcionālētu heterociklisko struktūru sintēzei, arvien vairāk paplašinot iegūstamo sintētisko atvasinājumu daudzveidību.^[25, 26]

Ņemot vērā to, ka silīcija pārgrupēšanās propargilsilānos ir relatīvi maz izpētīta tēma organiskajā ķīmijā,^[20, 21] kā arī nepieciešamību pēc jaunu metožu izstrādes stereodefinētu augsti funkcionālētu olefinu un mazmolekulāro heterociklu sintēzei, tika nolemts attīstīt tālāk propargilsilānu 1,3-difunkcionalizācijas konceptu heterociklisku struktūru, kas satur stereodefinētu olefinu sānu virkni, sintēzei (3. shēma).



3. shēma. Vispārējais koncepts heterociklu un augsti funkcionālizētu C=C saiti saturošu savienojumu sintēzei no propargilsilāniem **10-12**.

Pētījuma mērķis un uzdevumi

Promocijas darba mērķis ir izstrādāt jaunu organiskās sintēzes metodoloģiju piesātinātu un daļēji piesātinātu heterociklu, kas sānu ķēdē satur stereokīmiski definētu augsti funkcionālizētu dubultsaiti, ieguvei. To plānots panākt, ar elektrofilu aktivējot propargilsilānus, kas sililgrupas 1,2-nobīdes rezultātā dod alilkatjonu vai tā ekvivalentu. Tam seko iekšējā O-, N-, S- vai C-nukleofila uzbrukums, kā rezultātā tiek iegūti cikliski produkti. Papildus tiks apskatīts propargilsilānu lietojums Ritera tipa reakcijas apstākļos, kur kā primārais nukleofils ar β-silīcija stabilizētu karbkatjonu reaģē nitrils, bet iegūtais nitrīlija jons tiek dzēsts ar iekšējiem un ārējiem nukleofiliem, lai iegūtu stereokīmiski definētus, alilamīna fragmentu saturošus produktus.

Darba mērķa īstenošanai definēti vairāki uzdevumi.

- 1) Izpētīt literatūrā zināmās metodes piesātinātu heterociklu ieguvei iekšmolekulāras ciklizācijas ceļā, identificējot līdzšinējo metožu priekšrocības un trūkumus, un apkopot tās apskatraksta veidā.
- 2) Piedalīties kopprojektā par metodes izstrādi pieclocēkļu heterociklu **14** – tetrahydrofurānu (X = O), pirolidīnu (X = N-PG) un tiolānu (X = S) – sintēzei no

propargilsilāniem **10**, kas ietver elektrofilu inducētu sililgrupas 1,2-nobīdi reaģētspējīgu, β -silīcija stabilizētu alilkatjonu **13b** veidošanai ar sekojošu cikla saslēgšanu, veidojot C-Het saiti iekšmolekulāra *O*-, *N*-, vai *S*-nukleofila uzbrukuma rezultātā.

- 3) Piedalīties kopprojektā par propargilsilānu heterociklizācijas metodes pielāgošanu Frīdela-Kraftsa (*Friedel-Crafts*) tipa reakcijai, kur β -silīcija stabilizēts alilkatjons **13b** iekšmolekulāri reaģē ar arilsistēmām (*C*-nukleofīls), veidojot bicikliskus daļēji piesātinātus heterociklus **17**. Veikt iegūto tetrahidrohinolīnu **17** ($X = N-PG$) un to skābekļa analogu **16** ($X = O$) tālākās modifikācijas, kas demonstrētu iegūto produktu sintētisko lietojumu.
- 4) Piedalīties kopprojektā par diaril- λ^3 -jodānu kā formālu *C*-elektrofilu izmantošanu propargilsilānu **10** un **12** aktivēšanai vara katalīzes apstākļos arilētu heterociklisko produktu **15** un **23**, kā arī arilētu silidiēnu **22** sintēzei.
- 5) Pētīt sililgrupas 1,2-nobīdes izraisīšanu propargilsilānos **10-12** Ritera (*Ritter*) tipa reakcijas apstākļos dažādu aciklisko **18-19** ($X = O, N-PG$) un ciklisko **20-21** produktu sintēzei, kas satur augsti funkcionalizētu $C=C$ saiti.

Zinātniskā novitāte un galvenie rezultāti

Veikto pētījumu rezultātā ir izstrādāta sintētiskā metodoloģija piesātinātu un daļēji piesātinātu heterociklu sintēzei no propargilsilāniem, ievadot sistēmā augsti funkcionalizētu alkēnu sānu virkni. Šīs pārvērtības pamatā ir β -silīcija stabilizētu alilkatjonu ģenerēšana caur sililgrupas 1,2-nobīdi, ko izraisa propargilsilānu trīskāršās saites aktivēšana ar spēcīgiem elektrofilu. *In situ* ģenerētos alilkatjonus dzēšot ar iekšējiem nukleofīliem, tika iegūta virkne heterociklisku struktūru – tetrahidrofurāni, pirolidīni, tiolāni, tetrahidrohinolīni u. c.

Lai īstenotu tetrahidrofurānu, pirolidīnu un tiolānu sintēzi, no komerciāli pieejamā heks-5-īn-1-ola tika iegūti iekšmolekulārā *O*-, *N*-, un *S*-nukleofīlu saturoši propargilsilāni. Iegūtās iekšējo nukleofīlu saturošās izejvielas tālāk tika aktivētas spēcīgu elektrofilu (H^+ , Hal^+ , RSe^+) klātbūtnē, izraisot sililgrupas 1,2-nobīdes – heterociklizācijas pārvērtību virkni, kurā cikla saslēgšana, veidojot C-Het saiti, notiek, iekšmolekulāram nukleofīlam uzbrūkot β -silīcija stabilizētam alilkatjonam. Iegūtie produkti satur vienus no izplatītākajiem heterocikliskajiem struktūrelementiem (tetrahidrofurāna, pirolidīna vai tiolāna cikls) zāļvielās, kā arī augsti funkcionalizētus alkēnu struktūrfragmentus ar izcilu (*E*)-selektivitāti.

Biciklisku, daļēji piesātinātu heterociklu – tetrahidrohinolīnu – sintēzei propargilsilānu heterociklizācijas koncepts tika pielāgots iekšmolekulārai Frīdela-Kraftsa tipa reakcijai, kur sililgrupas 1,2-nobīdes rezultātā radītais alilkatjons tiek iekšmolekulāri dzēsts ar elektroniem

bagātu arilsistēmu, kas šajā reakcijā kalpo kā C-nukleofils. Lai nodrošinātu šo pārvērtību, propargilsilāna struktūrā caur slāpekļa tiltiņu tika ievadīta arilgrupa. Funkcionalizēti arilamīda atvasinājumi tika iegūti no komerciālā pent-4-īn-1-ola. Iegūto biciklisko heterociklu sānu ķēdē tika ievadīti augsti funkcionālizētu alkēnu fragmenti ar (Z)-selektivitāti.

Diaril- λ^3 -jodānu kā formālu C-elektrofila avotu izmantošana vara katalīzes apstākļos tika attīstīta propargilsilānu arilēšanas-heterociklizācijas reakciju virknei, kurā tika iegūti sānu ķēdē arilēti tetrahidrofurāna, pirolidīna un tetrahidropiridīna atvasinājumi. Šī metode sniedz efektīvu pieeju ar stīrilgrupu funkcionālizētu heterociklu iegūšanai, saīsinot kopējo sintētisko soļu skaitu, salīdzinot ar iepriekš zināmajām pieejām.

Ar elektrofilu aktivējot propargilsilānus Ritera tipa reakcijas apstākļos, tika iegūti dihidroizohinolīna un tetrahidropirimidīna atvasinājumi, kā arī acikliski produkti – amidīni un alilamīdi, kas satur augsti funkcionālizētu C=C saiti. No entropijas viedokļa propargilsilānu pārvērtības Ritera tipa apstākļos ir īpaši komplicētas – daudzkomponentu reakcijā tika panākta secīga četru jaunu kovalento saišu veidošanās vienā stadijā, kas tika izmantotas dažādu komplicētu struktūru iegūšanai no vienkāršām izejvielām.

Darba struktūra un apjoms

Promocijas darbs sagatavots kā tematiski vienotu zinātnisko publikāciju kopa, kas veltīta pētījumiem par propargilsilānu izmantošanu mazmolekulāro heterociklu, kas satur augsti funkcionālizētu olefīnu sānu virkni, sintēzei, izmantojot sililgrupas 1,2-nobīdi β -silīcija stabilizētu alilkatjonu starpsavienojumu ģenerēšanai. Šis darbs ietver vienu apskatrakstu un trīs oriģinālpublikācijas *SCI* žurnālos, vienu sagatavošanā esošo manuskriptu, kā arī npublicētos rezultātus.

Darba aprobācija un publikācijas

Promocijas darba galvenie rezultāti publicēti trīs zinātniskajos oriģinālrakstos. Promocijas darba izstrādes laikā sagatavots viens apskatraksts. Par pētījumu rezultātiem ziņots 20 zinātniskajās konferencēs.

Zinātniskās publikācijas

1. **Kronkalne, R.**; Beļunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.*, **2023**, *88* (19), 13857–13870. Available from: <https://doi.org/10.1021/acs.joc.3c01481>.

2. **Kroņkalne, R.**; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. *Beilstein J. Org. Chem.*, **2025**, *21*, 1984–1994. Available from: <https://doi.org/10.3762/bjoc.21.154>.
3. Ubaidullajevs, A.; **Kroņkalne, R.**; Mishnev, A.; Turks, M. Synthesis and of Substituted Chromanes and Tetrahydroquinolines *via* Tandem 1,2-Silyl Shift – Friedel–Crafts Cyclization. *J. Org. Chem.* **2026**, *91* (17), 5785–5810. Available from: <https://doi.org/10.1021/acs.joc.5c03136>.
4. **Kroņkalne, R.**; Turks, M. Recent Advances in Intramolecular C-N Bond Formation for Pyrrolidine Synthesis. *ChemistryOpen*, **2026**, *15* (6), e70182. Available from: <https://doi.org/10.1002/open.70182>.
5. Turka, S.; **Kroņkalne, R.**; Rogaļevs, R.; Puriņš, M.; Mishnev, A.; Turks, M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives. (*Nepublicētais manuskripts*).

Pētījumu rezultāti prezentēti 20 zinātniskajās konferencēs.

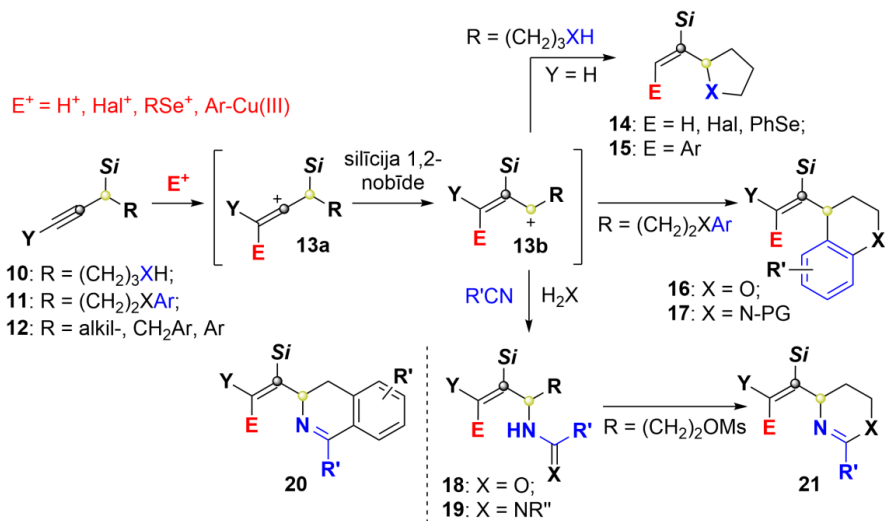
1. **Kroņkalne, R.**; Ubaidullajevs, A.; Turks, M. Synthesis of Fused Heterocycles by a Novel Cascade 1,2-Silyl Shift – Friedel-Crafts Cyclization. In: *Balticum Organicum Syntheticum 2026: Program and Abstract Book*, Estonia, Tallinn, June 28 – July 1, **2026**. Tallinn: 2026.
2. **Kroņkalne, R.**; Beļunieks, R.; Sebris, A.; Turks, M. Copper-Catalyzed Arylation and Subsequent Cyclization of Terminally Functionalized Propargyl Silanes. In: *83rd International Scientific Conference of the University of Latvia 2025, Chemistry Section and Section of Institute of Chemical Physics: Book of Abstracts*, Latvia, Riga, February 14, **2025**. Riga: University of Latvia, 2025, p. 40. ISBN 978-9934-36-369-6. Available from: <https://doi.org/10.22364/iscul.83.cs.ba>
3. **Kroņkalne, R.**; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Copper-Catalyzed Arylation of Propargyl Silanes with Iodanes Featuring 1,2-Silyl Shift and Cascade Cyclization. In: *ISySyCat: International Symposium on Synthesis and Catalysis 2025: Book of Abstracts*, Portugal, Coimbra, September 2–5, **2025**. Coimbra: 2025, p. 206. ISBN 978-989-95050-9-4
4. **Kroņkalne, R.**; Turks, M. Copper-Catalyzed Arylation of Propargyl Silanes with Iodanes Featuring the 1,2-Silyl Shift. In: *Paul Walden 14th Symposium on Organic Chemistry: Program and Abstract Book*, Latvia, Riga, September 25–26, **2025**. Riga: 2025, p. 63.

5. Rogaļevs, R.; Turka, S.; **Kronkalne, R.**; Ubaidullajevs, A.; Puriņš, M.; Turks, M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives. In: *International Symposium on Synthesis and Catalysis (ISySyCat 2025): Book of Abstracts*, Portugal, Coimbra, September 2–5, **2025**. Coimbra: 2025, p. 200.
6. Ubaidullajevs, A.; **Kronkalne, R.**; Turks, M. Synthesis of Substituted Chromanes via Tandem 1,2-silyl shift – Friedel–Crafts Cyclization. In: *82nd International Scientific Conference of the University of Latvia: Organic Chemistry Session*, Latvia, Riga, March 15, **2024**. Riga: 2024, p. 8.
7. Ubaidullajevs, A.; **Kronkalne, R.**; Turks, M. Synthesis of Vinyl Chromanes from Propargyl Silanes via Tandem Electrophilic Activation – 1,2-Silyl Shift – Friedel–Crafts Cyclization. In: *24th Tetrahedron Symposium*, France, Montpellier, June 18–21, **2024**. Montpellier: 2024.
8. Ubaidullajevs, A.; **Kronkalne, R.**; Gercāns, K.; Mishnev, A.; Turks, M. Synthesis of Fused Heterocycles by a Novel 1,2-Silyl Shift – Friedel–Crafts Domino Process. In: *29th International Society of Heterocyclic Chemistry Congress: Program*, Portugal, Aveiro, July 21–26, **2024**. Aveiro: 2024, p. 5.
9. Ubaidullajevs, A.; **Kronkalne, R.**; Gercāns, K.; Turks, M. Synthesis of Fused Heterocycles via Cascade 1,2-Silyl Shift – Friedel–Crafts Cyclization. In: *Balticum Organicum Syntheticum 2024: Program and Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 157.
10. **Kronkalne, R.**; Ubaidullajevs, A.; Beļunieks, R.; Turks, M. Expanding the Possibilities for Heterocycle Synthesis by Propargyl Silane Cyclization via the 1,2-Silyl Shift. In: *Balticum Organicum Syntheticum 2024: Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 79.
11. **Kronkalne, R.**; Ubaidullajevs, A.; Beļunieks, R.; Turks, M. Inducing 1,2-Silyl Migration in Propargyl Silanes for the Synthesis of 5- and 6-Membered Heterocycles. In: *24th Tetrahedron Symposium*, France, Montpellier, June 18–21, **2024**. Montpellier: 2024.
12. Sebris, A.; Beļunieks, R.; **Kronkalne, R.**; Turks, M. Copper-Catalyzed Arylation of Propargyl Silanes with Consequent Internal Cyclization. In: *Balticum Organicum Syntheticum 2024: Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 139.
13. Turks, M.; **Kronkalne, R.**; Ubaidullajevs, A.; Beļunieks, R.; Sebris, A.; Puriņš, M.; Rogaļevs, R. One, Two, Three, Go: Novel Applications of 1,2-Silyl Shift for 1,3-Difunctionalization of Propargyl Silanes. In: *Balticum Organicum Syntheticum 2024: Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 156.

14. Turks, M.; Beļunieks, R.; **Kronkalne, R.**; Ubaidullajevs, A.; Līpiņa, R. Synthesis of Allylic Systems and Heterocycles with Highly Functionalized Olefin Side Chain from Propargyl Silanes via 1,2-Silyl Shift. In: *International Symposium on Synthesis and Catalysis 2023: Program and Abstract Book*, Portugal, Evora, September 5–8, **2023**. Evora: 2023, p. 16.
15. **Kronkalne, R.**; Beļunieks, R.; Turks, M. Electrophile-Induced 1,2-Silyl Migration in Propargyl Silanes: a Pathway towards Saturated Heterocycles. In: *13th Paul Walden Symposium on Organic Chemistry: Program and Abstract Book*, Latvia, Riga, September 14–15, **2023**. Riga: 2023, p. 45.
16. **Kronkalne, R.**; Ubaidullajevs, A.; Beļunieks, R.; Turks, M. Electrophile-Induced 1,2-Silyl Shift in Terminally Functionalized Propargyl Silanes for the Synthesis of Small Heterocycles. In: *International Symposium on Synthesis and Catalysis 2023: Book of Abstracts*, Portugal, Evora, September 5–8, **2023**. Evora: 2023, p. 244.
17. **Kronkalne, R.**; Beļunieks, R.; Ubaidullajevs, A.; Turks, M. Use of Terminally Functionalized Propargyl Silanes for the Synthesis of Various 5-Membered Heterocycles via 1,2-Silyl Migration. In: *81st International Scientific Conference of the University of Latvia: Organic Chemistry Session*, Latvia, Riga, March 17, **2023**. Riga: 2023, p. 14.
18. Turks, M.; Beļunieks, R.; **Kronkalne, R.**; Puriņš, M.; Līpiņa, R.; Ubaidullajevs, A.; Rogaļevs, R. Synthesis of Allylic Systems or Heterocycles with Highly Functionalized Olefin Side Chain from Propargyl Silanes via 1,2-Silyl Migration. In: *ACS Fall 2023 – Sessions*, United States of America, San Francisco, August 13–17, **2023**. San Francisco: 2023, p. 3915259.
19. Ubaidullajevs, A.; **Kronkalne, R.**; Turks, M. Tandem 1,2-silyl shift – Friedel–Crafts Synthetic Approach to Substituted Vinyl Chromanes. In: *13th Paul Walden Symposium: Program and Abstracts*, Latvia, Riga, September 14–15, **2023**. Riga: 2023, p. 35.
20. **Kronkalne, R.**; Beļunieks, R.; Turks, M. Heterocyclization of Terminally Functionalized C6-Chain Containing Propargyl Silanes via 1,2-Silyl Shift. In: *Materials Science and Applied Chemistry 2022: Programme and Abstract Book*, Latvia, Riga, October 21, **2022**. Riga: 2022, p. 4.

PROMOCIJAS DARBA GALVENIE REZULTĀTI

Propargilsilānu heterociklizācijas koncepts balstās β -silīcija stabilizētu karbkatjonu ģenerēšanā, spēcīgam elektrofilam (E^+) pievienojoties trīskāršajai saitei. Sākotnēji ģenerētais vinilkatjons **13a** 1,2-sililmigrācijas rezultātā pārgrupējas par stabilāko alilkatjonu **13b**, kuru dzēšot ar iekšējiem nukleofīliem (heteroatomiem vai $C(sp^2)$) rodas cikliskas struktūras ar funkcionalizētu alkēnu sānu ķēdi (4. shēma).



4. shēma. Galvenie pētījuma virzieni heterociklu sintēzei no propargilsilāniem **10-12**.

Šajā promocijas darbā tiek apskatīta:

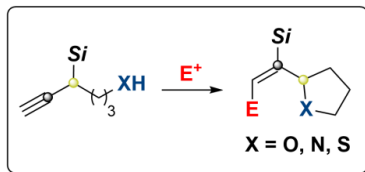
a) pieclocēkļu heterociklu **14** sintēze, ar elektrofilu ierosinot silīcija 1,2-nobīdes-heterociklizācijas reakciju kaskādā propargilsilānos, kas funkcionalizēti ar iekšējiem *O*-, *N*- vai *S*-nukleofīliem;

b) iekšmolekulāra Frīdela-Kraftsa tipa reakcija tetrahidrohinolīnu **17** ($X = N-PG$) sintēzei, kā arī to tālākās sintētiskās modifikācijas, apskatot arī to struktūranalogu **16** ($X = O$) modifēšanas iespējas;

c) vara katalizētas arilēšanas-heterociklizēšanas reakcijas, izmantojot diaril- λ^3 -jodānus kā formālus Ar^+ sintonus ($E^+ = Ar-Cu(III)$);

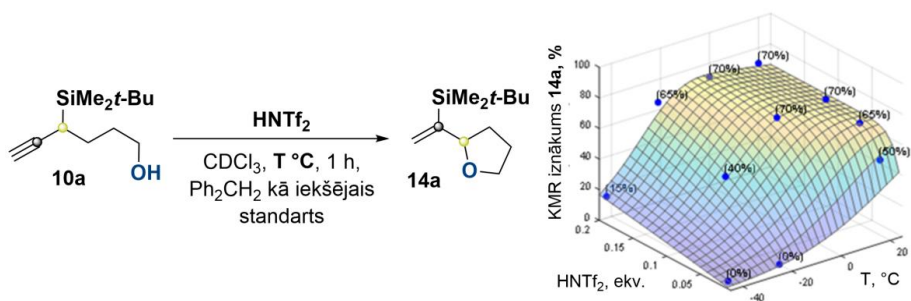
d) Ritera tipa reakcijas funkcionalizētu alilamīnu **18** ($X = O$), amidīnu **19** ($X = NR''$), dihidroizohinolīnu **20** un tetrahidropirimidīnu **21** ($X = N-PG$) sintēzei.

1.1. Propargilsilānu heterociklizācija, iekšējam *O*-/*N*-/*S*-nukleofilam reaģējot ar β -silīcija stabilizētu alilkatjonu



Iepriekšējos pētījumos tika demonstrēts, ka elektrofilu (Brensteda skābes vai Hal^+) aktivācijas apstākļos propargilsilāni var darboties kā reaģētspējīgi alilkatjona sintoni, kurus var izmantot silildiēnu vai indēnu,^[18] 1,3-funkcionalizētu olefinu,^[19] sulfolēnu^[27] un citu vērtīgu produktu sintēzē.^[28] Šī darba mērķis bija paplašināt propargilsilānu lietojuma konceptu, pielāgojot to mazmolekulāro heterociklu sintēzei. Šim nolūkam autore kopā ar Rūdolfu Beļāunieku un Artjomu Ubaidullajevu izstrādāja metodoloģiju dažādu pieclocēkļu heterociklu sintēzei, kur heterociklizācija tika panākta, iekšmolekulāri dzēšot no propargilsilāniem ģenerētos β -silīcija stabilizētos alilkatjonus ar nukleofiliem heteroatomiem (*O*, *N*, *S*).^[29] Iegūtie rezultāti tika daļēji apspriesti R. Beļāunieka promocijas darbā.^[30]

Par stratēģisko izejvielu tetrahidrofurānu sintēzei tika izvēlēts 4-(*tert*-butildimetilsilil)heks-5-īn-1-ols **10a**, kas tika iegūts no *O*-sililēta komerciālā heks-5-īn-1-ola pēc Vanga (*Wang*) aprakstītās retro-Brūka (*Brook*) pārgrupēšanās procedūras.^[31] Tālāka propargilsilāna **10a** aktivēšana ar Brensteda skābēm (HNTf_2 vai TfOH) deva heterociklizācijas produktu **14a**.

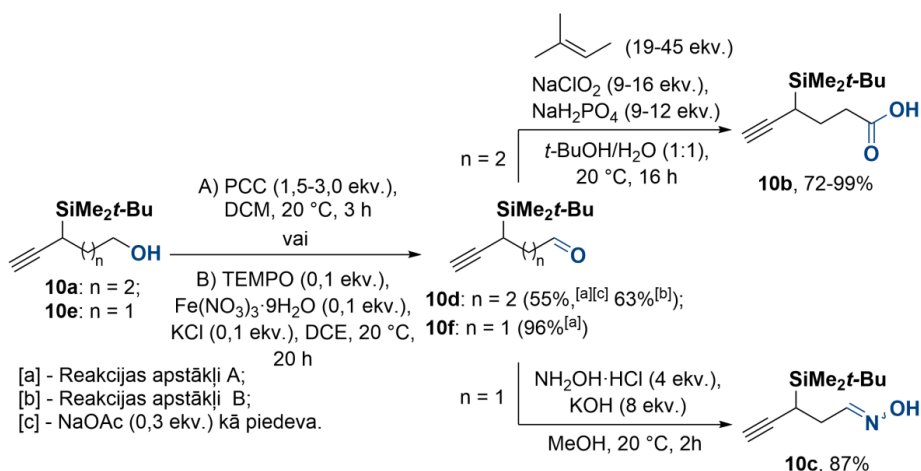


5. shēma. Apstākļu optimizācija Brensteda skābes katalizētai propargilsilāna **10a** heterociklizācijai.

Galvenie secinājumi no reakcijas apstākļu optimizācijas Brensteda skābes katalizētai pārvērtībai **10a**→**14a** bija šādi: 1) optimālā reakcijas temperatūra bija 0–20 °C; 2) optimālais skābes katalizatora daudzums bija 10–20 mol%; 3) šķīdinātāju izvēli noteica to nivelējošais

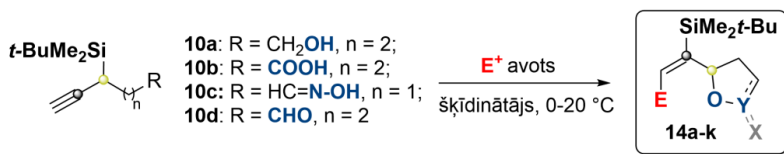
efekts, kur aprotiskajos šķīdinātājos CDCl_3 un CD_2Cl_2 tika iegūti augstākie iznākumi (**14a**, 70 % KMR, bet benzolā- d_6 un CD_3NO_2 iznākumi bija zemāki (attiecīgi 65 % un 50 % **14a**); 4) optimālajos reakcijas apstākļos (0,2 ekv. H^+ , CDCl_3 , 0 °C, 1 h) HNTf_2 un TfOH deva līdzīgi labus iznākumus (70 % KMR), savukārt ar konc. H_2SO_4 reakcija nenotika. Detalizēta skābes katalizatora daudzuma (HNTf_2 , ekv.) un temperatūras ietekme uz tetrahidrofurāna **14a** sintēzes iznākumu grafiski attēlota 5. shēmā.

Citi skābekļa nukleofīlu saturoši propargilsilāni **10b-f** tika iegūti, modificējot spirtu **10a** un tā C5-ķēdi saturošo analogu **10e**, kā tas redzams 6. shēmā. Spirts **10e** tika pagatavots pēc analogiskas procedūras C6-ķēdi saturošajam spirtam **10a**, izmantojot komerciāli pieejamo pent-4-īn-1-olu.^[31]

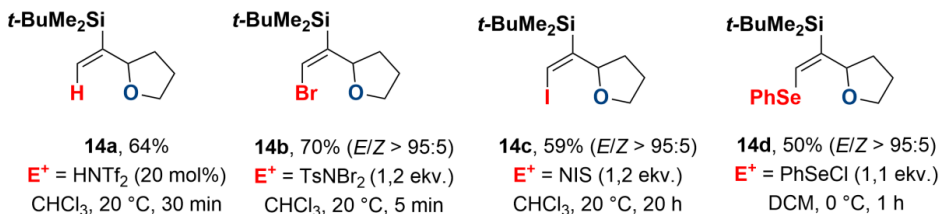


6. shēma. Iekšējo skābekļa nukleofīlu saturošu propargilsilānu **10b-f** iegūšana.

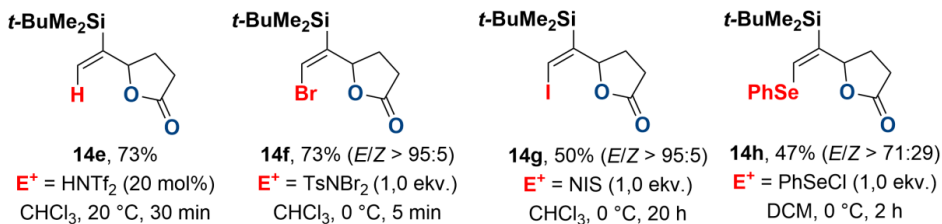
Optimizētajos apstākļos tika veikta iekšējo skābekļa nukleofīlu saturošu propargilsilānu **10a-d** ciklizēšana (7. shēma). Sililgrupas 1,2-nobīdes inducēšanai izmantojot elektrofilos halogenēšanas reaģentus (TsNBr_2 , NBS, NIS) vai elektrofilo selēna ievadīšanas reaģentu PhSeCl , tika iegūti heterocikli ar trīsaizvietotu alkēnu sānu virknē. No spirta **10a** iegūto tetrahidrofurānu **14a-d** iznākumi bija 50–70 % robežās, savukārt karbonskābe **10b** ciklizējās par laktona atvasinājumiem **14e-h** ar iznākumiem 47–73 % robežās. Oksīms **10c** deva 4,5-dihidroizoksazola atvasinājumus **14i-j** (29–32 % iznākumi), savukārt aldehīds **10d**, ciklizējoties ar NBS ūdens klātbūtnē, deva hemiacetālu **14k** (30 % iznākums).



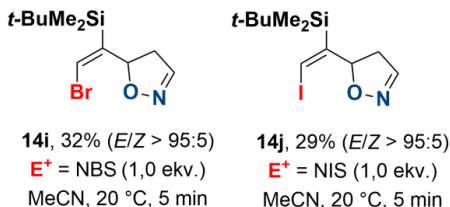
No spirta **10a** (R = CH₂OH, n = 2):



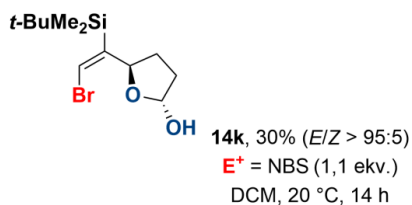
No karbonskābes **10b** (R = COOH, n = 2):



No oksīma **10c** (R = HC=N-OH, n = 1):



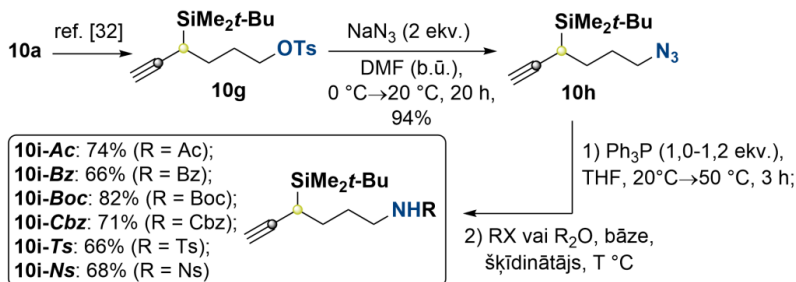
No aldehīda **10d** (R = CHO, n = 2):



7. shēma. Iekšējo skābekļa nukleofilu saturošu propargilsilānu **10a-d** heterociklizēšana.

Spirtu saturošais propargilsilāns **10a** tālāk tika modificēts par slāpekļa nukleofilu saturošām izejvielām (1. tabula). Tozīlāts **10g** tika iegūts pēc literatūrā aprakstītās metodes.^[32] Sekojoša azidēšana, azīda **10h** reducēšana Štaudingera (*Staudinger*) apstākļos un *N*-aizsarggrupas uzlikšana deva amīdus **10i-Ac** un **10i-Bz**, karbamātus **10i-Boc** un **10i-Cbz**, kā arī sulfonamīdus **10i-Ts** un **10i-Ns**.

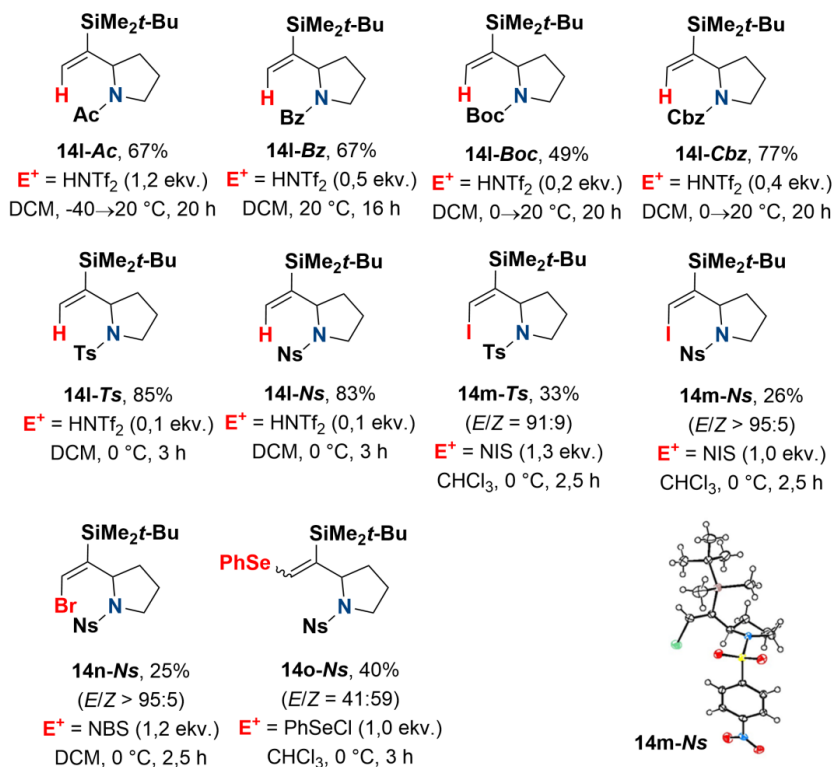
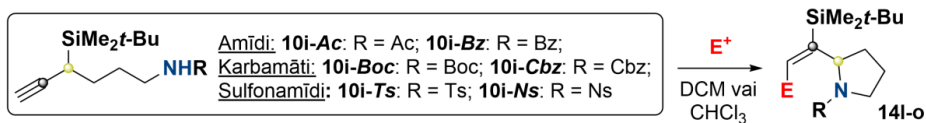
Ar iekšējo slāpekļa nukleofilu funkcionalizētu propargilsilānu **10i** sintēze



Nr. p. k.	RX/R ₂ O (ekv.)	Bāze/piedeva (ekv.)	Šķīdinātājs	T (°C)	t (h)	Produkta iznākums
1.	Ac ₂ O (2,0)	DMAP (0,5)	Py	0–20	16	10i-Ac , 74 %
2.	Bz ₂ O (2,0)	DMAP (1,0)	DMF	60	22	10i-Bz , 66 %
3.	Boc ₂ O (1,2)	NaHCO ₃ (3,0)	THF/H ₂ O (1:1)	0–20	14	10i-Boc , 82 % ^[a]
4.	Cbz-OSu (1,2)	NaHCO ₃ (2,7)	MeCN/H ₂ O (1:1)	0–20	16	10i-Cbz , 71 %
5.	TsCl (2,0)	Et ₃ N (5,0)	DCM	0–20	6	10i-Ts , 66 %
6.	NsCl (2,0)	Et ₃ N (5,0)	DCM	0–20	6	10i-Ns , 68 %

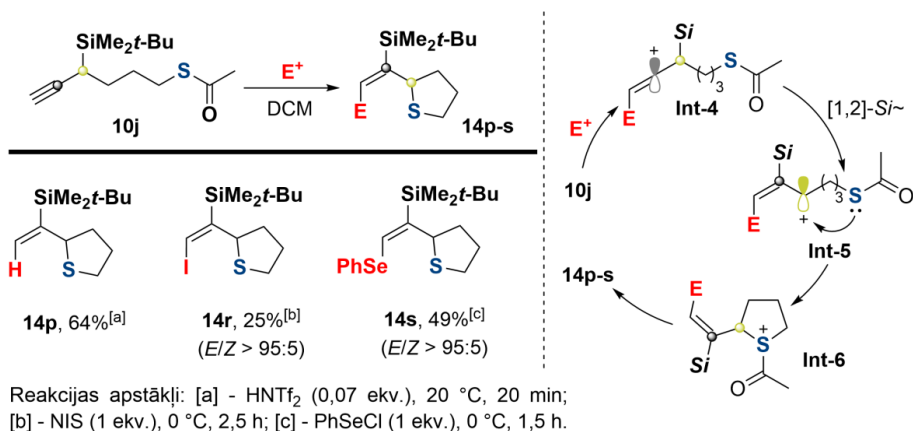
[a] – THF/H₂O (1:1) šķīdinātāju sistēma un 1 h maisīšana reducēšanas solim.

Spēcīgu elektrofilu (H⁺, Hal⁺, RSe⁺) klātbūtnē *N*-nukleofilu saturošie propargilsilāni **10i** ciklizējas par pirolidīna atvasinājumiem **14l-o** (8. shēma). Brensteda skābes HNTf₂ katalizētās heterociklizēšanas reakcijās sulfonamīdi (R = Ts, Ns) deva augstākos pirolidīnu **14l** iznākumus (83–85 %). Karbamātu (R = Boc, Cbz) un amīdu (R = Ac, Bz) gadījumā pirolidīnu **14l** iznākumi variēja 49–77 % robežās. Izmantojot elektrofilos halogenēšanas reaģentus (NIS, NBS) propargilsistēmas aktivēšanai, iznākumi bija zemāki (**14m-n**, 25–33 %), taču iegūtie produkti saturēja augsti funkcionalizētu C=C saiti, kur (*E/Z*)-selektivitāte bija robežās no 91:9 līdz 95:5. Trīsaizvietoto C=C saišu (*E*)-ģeometriju apstiprināja gan KMR 2D kodolu Overhauzera efekta spektroskopija (NOESY, korelācija starp C=C-H un *t*-BuMe₂Si-), gan arī monokristālu rentgenstaru difrakcijas (SCXRD) analīze pirolidīnam **14m-Ns**. Savukārt, izmantojot PhSeCl kā elektrofilu avotu, tika iegūts pirolidīns **14o** (40 % izdalīts) kā (*E/Z*)-izomēru maisījums (41:59). Iespējams, ka selenilgrupas gadījumā izveidotais alilkatjons ir papildus stabilizēts ar α-selēna efektu, kas var dot tam laiku izomerizēties pirms nukleofila uzbrukuma.



8. shēma. Slāpekļa heterociklu **14l-o** sintēze.

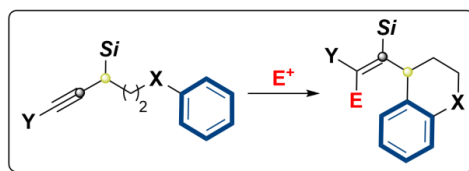
Tālāk tika apskatīta sēra heterociklu ieguve (9. shēma). Tiolānu **14p-s** sintēzei par izejvielu tika izmantots tioacetāts **10j**, ko iegūst, maisot tozilātu **10g**^[32] ar KSAc (1,4 equiv) acetonitrilā (20°C , 16 h, 87 % iznākums **10j**). Vislabāk ciklizēšanās noritēja HNTf₂ katalizētos apstākļos (**14p**, 64 %). Ar zemāku iznākumu bija iespējams iegūt arī trīsaizvietotu alkēnu sānu ķēdi saturošus tiolānus **14r-s** (25–49 %), izmantojot NIS (I⁺) un PhSeCl (PhSe⁺) propargilsistēmas aktivēšanai. Ciklizēšanās tioacetāta **10j** gadījumā, visticamāk, notiek ar sulfonija jonu **Int-6**, kas sabrūk par tiolānu **14p-s**.



9. shēma. Tiolānu sintēze no tioacetāta **10j**.

Iegūtie rezultāti liecina, ka β -silīcija stabilizētus alilkatjonus var iekšmolekulāri dzēst ar dažādiem *O*-, *N*- un *S*-nukleofiliem, lai iegūtu pieclocēkļu heterociklus, kas satur gemināli divaizvietotas vai stereodefinētas trīsaizvietotas alkēnu sānu virknes. Izmantojot elektrofilos halogenēšanas reaģentus (NBS, NIS) propargilsilānu aktivēšanai, tika iegūtas alkēnu sānu virknes ar (*E/Z*)-selektivitāti līdz pat 95:5. Pilns pētījuma rezultātu izklāsts ir pieejams publikācijā Kroņkalne, R.; Beļainieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.*, **2023**, 88 (19), 13857-13870. (1. pielikums).^[29]

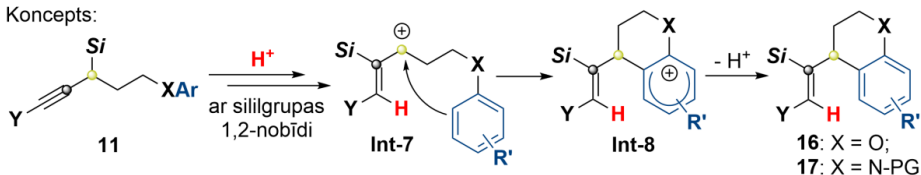
1.2. Propargilsilānu heterociklizācija arēniem kā iekšējiem C-nukleofiliem, reaģējot ar β -silīcija stabilizētu alilkatjonu



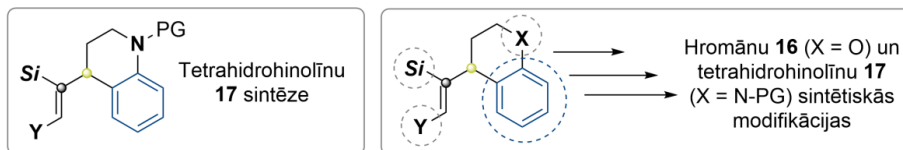
Iepriekšējā nodaļā demonstrēts, kā sililgrupas 1,2-migrācijas rezultātā ģenerētu alilkatjonu var dzēst iekšmolekulāri, veidojot jaunas C-O, C-N un C-S saites. Šī nodaļa veltīta analogiskai pārvērtībai, kurā heterociklizācija norit ar iekšmolekulāru C-C saites veidošanu Frīdela-Kraftsa tipa reakcijā (10. shēma). Alilkatjona **Int-7** iekšmolekulāra dzēšana ar elektroniem bagātu arilsistēmu paver iespējas biciklisku savienojumu sintēzei. Kopā ar Artjomu Ubaidullajevu tika izstrādāta metode biciklisku heterociklu – hromānu **16** (X = O) un tetrahidrohinolīnu **17** (X = N-

PG) sintēzei.^[33] Šajā promocijas darbā apskatīta tetrahidrohinolīnu **17** (X = N-PG) iegūšana no propargilsilāniem, kā arī demonstrēts hromānu **16** (X = O) un tetrahidrohinolīnu **17** (X = N-PG) lietojums tālākās sintētiskās modifikācijās.

Koncepts:



Šajā darbā:



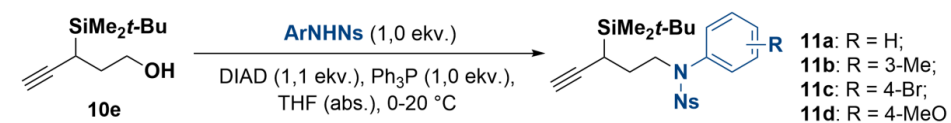
10. shēma. Koncepts propargilsilānu **11** ciklizēšanai Frīdela-Kraftsa tipa reakcijā un produktu **16-17** tālākās modifikēšanas iespējas.

1.2.1. Tetrahidrohinolīnu sintēze no propargilsilāniem

Par stratēģiskajām izejvielām tetrahidrohinolīnu sintēzei tika izvēlēti anilīna funkcionālo grupu saturoši propargilsilāni **11a-f**. Viena no stratēģijām to iegūšanai bija Micunobu (*Mitsunobu*) reakcija starp nozilgrupu saturošiem anilīniem (ArNHNS) un spirta funkcionālo grupu saturošo silānu **10e**, kas deva stratēģiskās izejvielas **11a-d** ar 66–75 % iznākumu (2. tabula).

2. tabula

N-Nozilēta anilīna funkcionalitāti saturošu propargilsilānu sintēze Micunobu reakcijas apstākļos

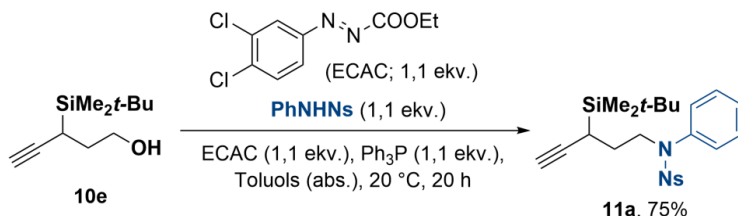


Nr. p. k. ^[a]	Ar	Laiks (h)	Produkts (%) ^[b]
1.	Ph	21,0	11a , 66
2.	<i>m</i> -MeC ₆ H ₄	15,0	11b , 67
3.	<i>p</i> -BrC ₆ H ₄	15,5	11c , 75
4.	<i>p</i> -MeOC ₆ H ₄	17,0	11d , 74

[a] Visas reakcijas tika veiktas 2,5 mmol mērogā. [b] Izdalītais iznākums.

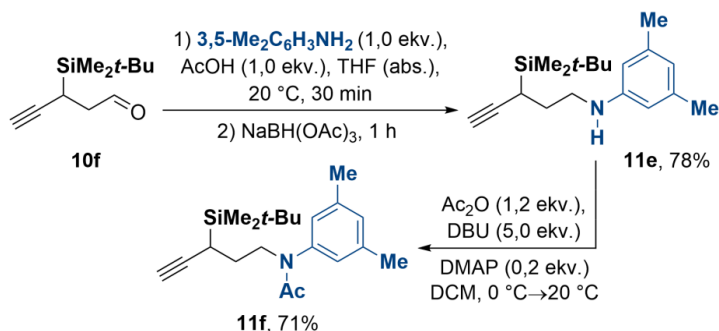
DIAD vietā izmantojot ECAC, kas ir otrās paaudzes Micunobu reaģents, trešējā amīda iznākumi palielinājās (11. shēma). Piemēram, savienojuma **11a** gadījumā iznākums pieauga no

66 % (ar DIAD) līdz 75 % (ar ECAC). Identiskus apstākļus A. Ubaidullajevs izmantoja skābekļa tilpiņu saturošu izejvielu **11** (Y = H, X = O) iegūšanai.^[33]



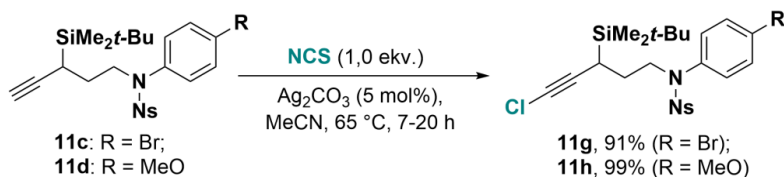
11. shēma. *N*-Nozilēta anilīna funkcionalitāti saturoša propargilsilāna **11a** pagatavošana, izmantojot ECAC reāģentu.

Micunobu stratēģija bija piemērojama tikai ar sulfonilgrupu aizsargātu anilīnu gadījumā. Lai iegūtu ar acetamīda grupu funkcionalizētus propargilsilānus **11f**, tika izmantota aldehīdu reducējošās aminēšanas stratēģija (12. shēma). Aldehīdam **10f** etiķskābes klātbūtnē pievienojot 3,5-dimetilanilīnu, kā starpprodukts izveidojās imīns, kuru reducējot ar NaBH(OAc)3, tika iegūts produkts **11e**. Sekojoša acetilgrupas uzlikšana ļāva iegūt *N*-acetilētu produktu **11f**.



12. shēma. Ar acetamīda grupu funkcionalizēta propargilsilāna **11f** sintēze, izmantojot reducējošās aminēšanas paņēmieni.

Termināli halogenētu izejvielu **11g-h** iegūšanai propargilsilāni **11c-d** tika apstrādāti ar NCS sudraba katalizatora (Ag2CO3, 5 mol%) klātbūtnē. Tas deva vēlamos produktus **11g-h** ar 91–99 % iznākumu (13. shēma).

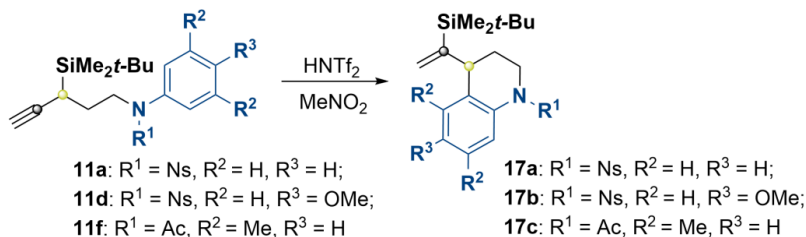


13. shēma. Termināli halogenētu propargilsilānu **11g-h** iegūšana.

Tālāk tika veikti ciklizēšanas eksperimenti ar funkcionalizētiem propargilsilāniem **11**, tos pārvēršot par tetrahidrohinolīna atvasinājumiem **17** (3. tabula). Reakcijas tika veiktas nitrometānā (MeNO₂), izmantojot bistriflimīdu (HNTf₂) kā Brensteda skābi. Reakcijas optimizācija parādīja, ka HNTf₂ ir vēlams pievienot ekvimolārā daudzumā vai nelielā pārkumā – tas saīsināja reakcijas laiku un palielināja produkta **17a** iznākumu. To pašu novēroja A. Ubaidullajevs hromānu sintēzes optimizācijā, kur reakcijas iznākums palielinājās līdz ar pievienotā HNTf₂ daudzumu.^[33]

3. tabula

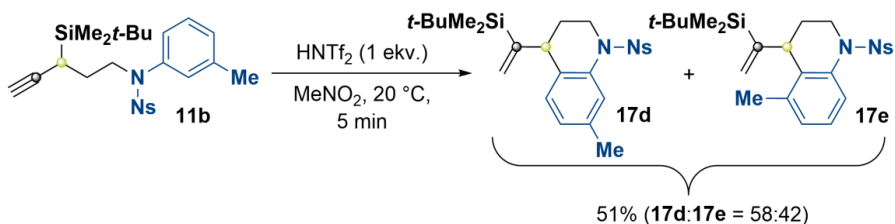
Tetrahidrohinolīnu **17a-c** sintēze no propargilsilāniem **11a**, **11d** un **11f**



Nr. p. k.	Silāns	HNTf ₂ (ekv.)	T (°C)	Laiks (min)	11 (%) ^[a]	Produkts (%)
1.	11a	0,2	50	10	53	17a , 15 ^[a]
2.	11a	0,2	0→20	70	55	17a , 15 ^[a]
3.	11a	0,2	0→20	1020	11	17a , 12 ^[a]
4.	11a	1,0	0	60	0	17a , 41 ^[a] (40 ^[b])
5.	11d	1,0	20	5	0	17b , 47 ^[a] (43 ^[b])
6.	11f	1,0	20	5	40	17c , 10 ^[a]
7.	11f	3,0	20	30	0	17c , 47 ^[a] (45 ^[b])

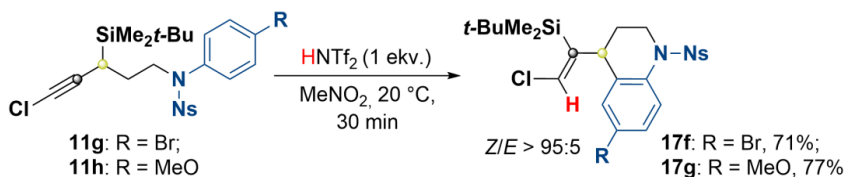
[a] KMR iznākums. [b] Izdalītais iznākums.

Nesimetriski aizvietota anilīna **11b** gadījumā ciklizācija ar HNTf₂ deva reģioizomēru **17d/17e** maisījumu attiecībā 58:42 (14. shēma).



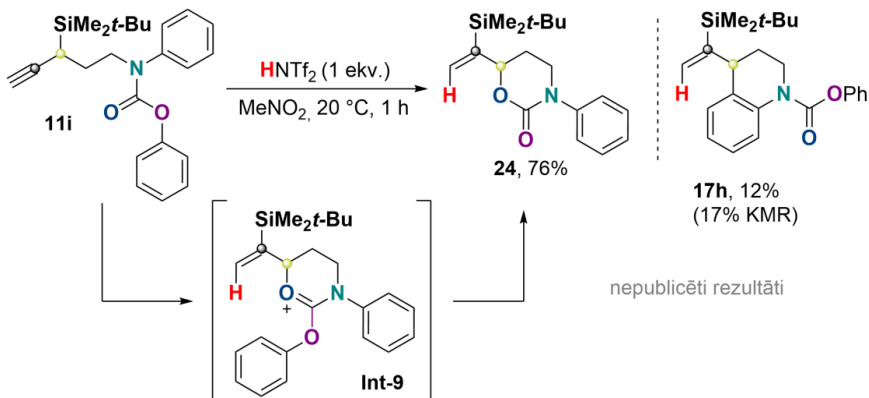
14. shēma. Tetrahydrohinolīnu sintēze no propargilsilāna **11b**, kas satur nesimetriski aizvietotu anilīna fragmentu.

Termināli halogenētu propargilsilānu **11g-h** ciklizēšanas reakcija noritēja ar izcilu *Z/E* selektivitāti, ļaujot iegūt tetrahydrohinolīnus **17f-g** ar 71–77 % iznākumu (15. shēma).



15. shēma. Tetrahydrohinolīnu **17f-g** sintēze no termināli halogenētiem propargilsilāniem.

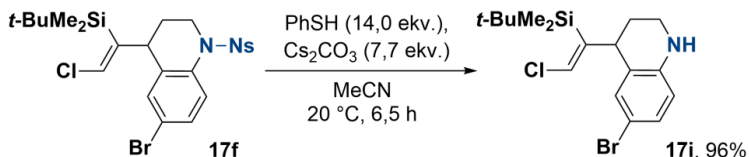
Cita tipa reakcija tika novērota, mēģinot ciklizēt ar karbamāta grupu aizsargātu anilīnu **11i**, kas kā galveno produktu deva 1,3-oksazinān-2-onu **24** ar 76 % iznākumu (16. shēma). Reakcija, visticamāk, notiek ar starpstāvoli **Int-9**. Tetrahydrohinolīns **17h** tika novērots kā minora produkts ar 17 % KMR iznākumu.



16. shēma. 1,3-Oksazinān-2-ona **24** sintēze.

1.2.2. Iegūto tetrahidrohinolīnu un hromānu modificēšanas iespējas

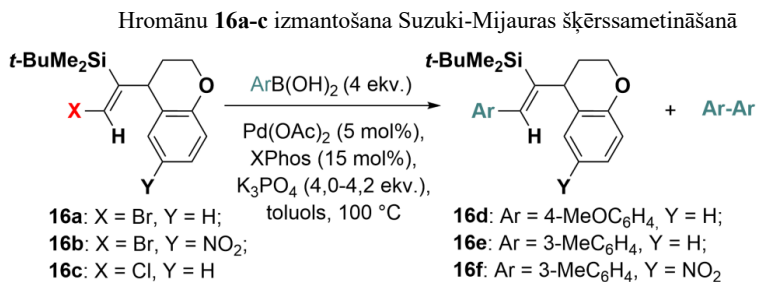
Kā pirmā iespējamā modifikācija tika parādīta *N*-aizsarggrupas noņemšanas iespēja tetrahidrohinolīnos. Klasiskos apstākļos, izmantojot tiofenolu (PhSH) bāzes (Cs_2CO_3) klātbūtnē, ar 96 % iznākumu tika iegūts tetrahidrohinolīns **17i**, kam ir iespējama tālāka *N*-funkcionalizēšana (17. shēma).



17. shēma. Nozilgrupas nošķelšana tetrahidrohinolīna **17i** iegūšanai.

Tālāk ar Suzuki-Mijauras šķērssametināšanas reakciju tika modificēti hromāna atvasinājumi **16a-c** (4. tabula). Vinilbromīda **16a** reakcijā ar 4-metoksifenilborskābi iegūto stirola atvasinājumu **16d** bija grūti atdalīt no pašsametināšanās blakusprodukta (Ar-Ar) abu līdzīgās polaritātes dēļ, līdz ar to hromatogrāfiski izdalītais iznākums bija zems (**16d**, 6 %). Turpretim 3-metilfenilborskābe ar vinilbromīdiem **16a-b** deva vieglāk izdalāmus produktus, un stirolī **16e-f** tika iegūti ar 92–97 % iznākumu. Kā sagaidāms, reakcijas iznākums vinilhlorīda **16c** gadījumā bija būtiski zemāks (**16e**, 27 %) nekā to bromu saturošajiem analogiem **16a-b**.

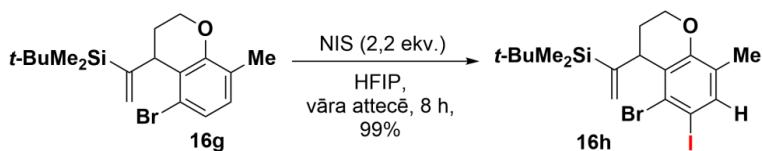
4. tabula



Nr. p. k.	X	Y	Ar	t (h)	Produkts (%)
1. ^[c, d]	Br	H	4-MeOC ₆ H ₄	14	16d , 45 ^[a] , 6 ^[b]
2.	Br	H	3-MeC ₆ H ₄	44	16e , 97 ^[b]
3.	Br	NO ₂	3-MeC ₆ H ₄	22	16f , 92 ^[b]
4.	Cl	H	3-MeC ₆ H ₄	26	16e , 27 ^[b]

[a] KMR iznākums (%). [b] Izdalītais iznākums (%). [c] Šķērssametināšanas produkts **16d** veidoja nesadalāmu maisījumu ar pašsametināšanās blakusproduktu (Ar-Ar). [d] Modificēti reakcijas apstākļi: 3 ekv. $\text{ArB}(\text{OH})_2$, 7 mol% $\text{Pd}(\text{OAc})_2$, 21 mol% XPhos, 4,9 ekv. K_3PO_4 .

Līdzīgi, kā tas aprakstīts promocijas darba autores un kolēģu grupas iepriekšējos darbos,^[19, 29] tika veikta sililgrupas-halogēna apmaiņa hromānam **16g**, izmantojot NIS heksafluorizopropanolā (HFIP). Pārsteidzošā kārtā, pat izmantojot NIS pārākumu (2,2 ekv.) un reakciju vārot, *Si*→*I* apmaiņa nenotika. Tā vietā tika iegūts arilgredzenā monojodētais produkts **16h** ar kvantitatīvu iznākumu (18. shēma).

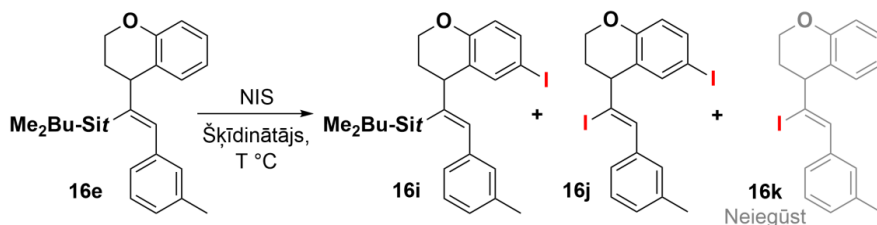


18. shēma. Arilsistēmā monojodētā produkta **16h** iegūšana.

Si→*Hal* apmaiņa notiek caur silīcija-virzītu elektrofila (Hal^+) pievienošanās vinilsilānam $\text{R}_2\text{C}=\text{C}(\text{Si})-\text{R}'$, veidojot β -silīcija stabilizētu karbēnija jona starpsavienojumu $\text{R}_2\text{C}^+-\text{C}(\text{Si})(\text{Hal})-\text{R}'$.^[34] Terminālu vinilsilānu gadījumā veidotos destabilizēts pirmējais karbēnija jons, kas padara reakciju nevēlamu. Savukārt stirola atvasinājuma **16e** gadījumā reakcija var noritēt, veidojoties iespējamam benzilkatjona starpsavienojumam. Jodēšanas eksperimenti stirola atvasinājumam **16e** apstiprināja šo hipotēzi, kur tika novērota gan arilsistēmas jodēšanās, gan *Si*→*I* apmaiņa (5. tabula).

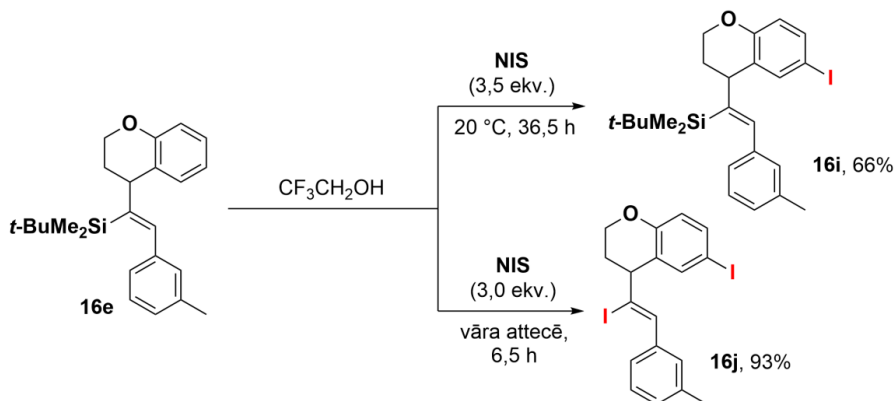
5. tabula

Jodēšanas eksperimenti stirola atvasinājumam **16e**



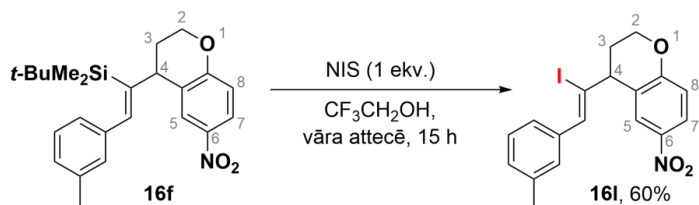
Nr. p. k.	NIS (ekv.)	Šķīdinātājs	T °C	Laiks (h)	Izejvielas 16e / produktu 16i-j molārā attiecība KMR		
					16e	16i	16j
1.	1,0	HFIP	20	0,5	31	49	20
2.	2,5			1,5	0	0	100
3.	1,0	TFE		18,0	33	67	0
4.	2,0			17,5	20	80	0
5.	3,5			36,5	13	87	0
6.	10,8			1,5	5	35	60
7.	1,0		75–80	6,5	38	62	0
8	3,0	71,0		28	72	0	
		6,5	0	0	100		

Jodējot stirola atvasinājumu **16e** ar ekvimolāru daudzumu NIS, izmantojot HFIP kā šķīdinātāju, tika iegūts maisījums ar monojodēto produktu **16i** un diiodēto produktu **16j** (49:20), bet NIS pārākumā (2,5 ekv.) tika iegūts vienīgi diiodētais produkts **16j**. Izmantojot TFE kā šķīdinātāju, reakcija notika ievērojami lēnāk, kas ļāva vieglāk kontrolēt produktu veidošanos atkarībā no reakcijas laika. Apstādinot reakciju pēc 36,5 h, tika iegūts monojodētais produkts **16i** ar 66 % iznākumu (71 % KMR). Augsts diiodētā produkta **16j** iznākums (93 % izdalīts) tika iegūts, hromānam **16e** pievienojot NIS pārākumu (3 ekv.) un karsējot 75–80 °C (spiediena mēģenē) 6,5 h (19. shēma).



19. shēma. Hromāna **16e** mono- un diiodēšanas eksperimenti optimizētos apstākļos.

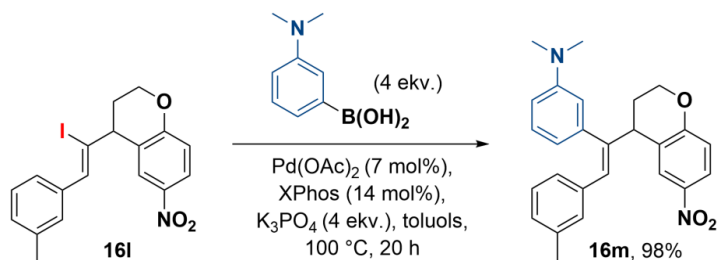
Ievadot hromāna 6. pozīcijā elektronatvelkošo nitrogrupu, aromātiskā gredzena jodēšanās iepriekš minētajos apstākļos vairs netika novērota. Hromānam **16f** paaugstinātā temperatūrā reaģējot ar NIS (1 ekv.) trifluoetanolā, selektīvi notika silīcija – joda apmaiņa, kas ļāva iegūt viniljodīdu **16l** ar 60 % iznākumu (20. shēma).



20. shēma. Si→I apmaiņas reakcija hromānā **16f**.

Noslēdzot hromānu tālāko modifikāciju tēmu, tika demonstrēts iegūtā viniljodīda **16l** lietojums šķērssametīnāšanā Suzuki-Mijauras apstākļos (21. shēma). Izmantojot (3-

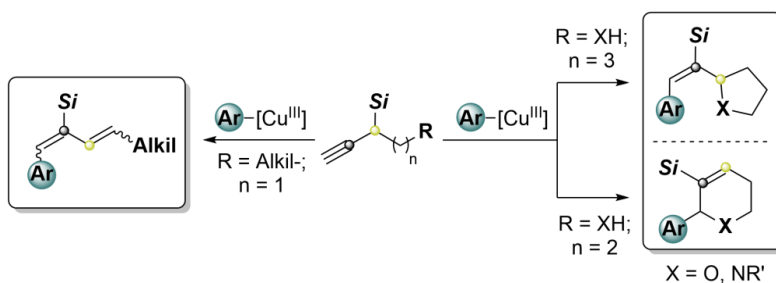
(dimetilamino)fenil)borskābi kā reaģentu, pallādija katalīzes apstākļos tika iegūts šķērssametināšanas produkts **16m** ar iznākumu tuvu kvantitatīvam (98 % izdalīts).



21. shēma. Viniljodīda **16l** lietojums Suzuki-Mijauras šķērssametināšanā.

Šajā nodaļā parādīts, ka Brensteda skābes katalīzes apstākļos propargilsilāni, kas caur slāpekļa tiltiņu ir funkcionalizēti ar arilgrupu, Frīdela-Kraftsa tipa reakcijā ciklizējas par tetrahidrohinolīna **17** atvasinājumiem. Termināli hlorētu propargilsilānu **11g-h** gadījumā ciklizēšanās reakcija ir augsti stereoselektīva, un tiek iegūti produkti **17f-g** ar (*Z*)-ģeometriju alkēnu sānu virknē. Rezultējošās vinilhalīdu sānu virknes var modificēt Suzuki-Mijauras šķērssametināšanas reakcijās, savukārt sililgrupu var aizstāt ar jodu elektrofilās apmaiņas reakcijā sintētiski noderīgu viniljodīda fragmentu iegūšanai. Pilns pētījuma rezultātu izklāsts pieejams publikācijā Ubaidullajevs, A.; Kronkalne, R.; Mishnev, A.; Turks, M. Synthesis of Substituted Chromanes and Tetrahydroquinolines *via* Tandem 1,2-Silyl Shift – Friedel–Crafts cyclization. *J. Org. Chem.*, **2026**, *91* (17), 5785–5810 (2. pielikums).^[33]

1.3. Arilētu heterociklu un diēnu sintēze reakcijā ar diaril- λ^3 -jodāniem vara katalīzes apstākļos

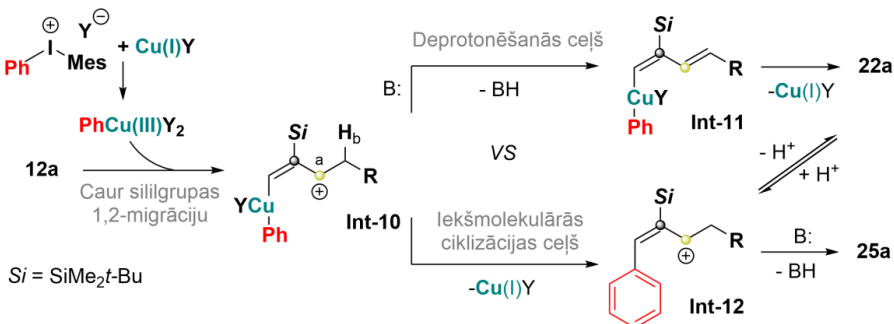
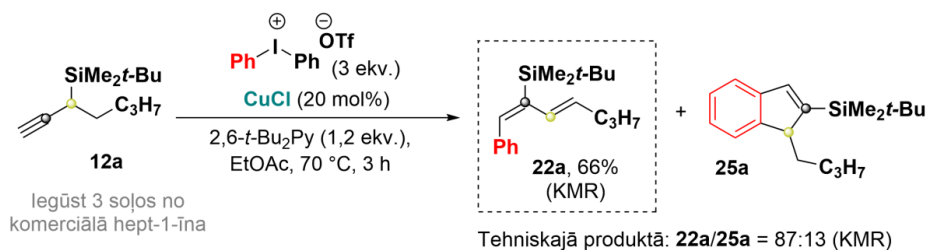


Iepriekš tika apskatīta propargilsilānu aktivēšana heterociklu sintēzei, izmantojot Brensteda skābes vai elektrofilos halogenēšanas reaģentus. Oglekļa elektrofilu izmantošana analogiskas

pārvērtības īstenošanai ir atsevišķs pētījumu virziens, kas tika izstrādāts kopā ar Rūdolfu Beļunieku un Armandu Sebrī.^[35]

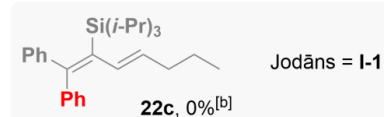
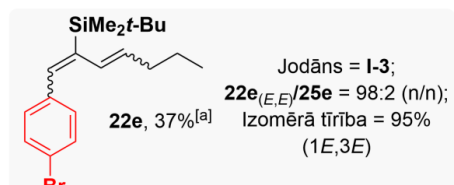
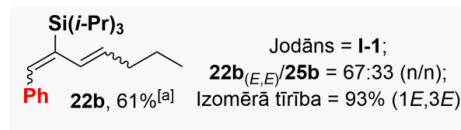
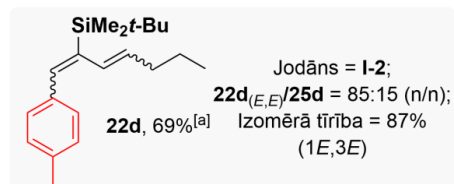
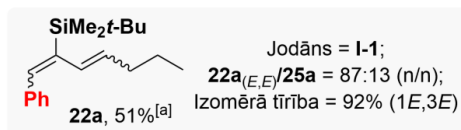
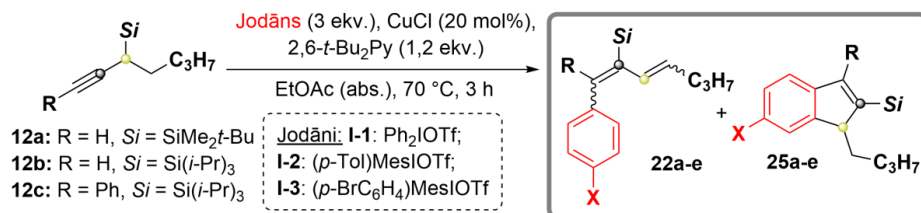
Diaryl- λ^3 -jodānus izmanto arilgrupas ievadīšanai π -sistēmās, kur arilgrupa nodrošina formālo Ar^+ sintonu, tostarp alkīnu 1,2-difunkcionalizēšanas reakcijās.^[36] Šādos gadījumos hipervalentā joda(III) reaģentus aktivē ar vara vai pallādija katalizatoriem.^[37, 38] Tā kā propargilsilāni elektrofilās aktivācijas apstākļos spēj dod formālus 1,3-dipolus, ko nodrošina sililgrupas 1,2-nobīde, var panākt 1,3-difunkcionalizēšanu, kas ir daudz retāk sastopama par 1,2-difunkcionalizēšanu. Šajā darbā tika izstrādāta vara katalizēta metode diaryl- λ^3 -jodānu izmantošanai propargilsilānu 1,3-difunkcionalizēšanas reakcijās dažādu sānu virknē arilētu heterociklu un silildiēnu iegūšanai.

Meklējot piemērotus reakcijas apstākļus propargilsilānu arilēšanai, tika nolemts iesākt ar vienkāršākajiem substrātiem – alkilvirtni saturošiem silāniem **12a**.^[18] Tika novērots, ka reakcijas gaitā veidojās arilēta silildiēna **22a** un sililindēna **25a** maisījums (22. shēma). Šo produktu veidošanos var skaidrot ar divu konkurējošu reakciju norisi, kur vienā no gadījumiem eliminējas alilkatjona **Int-10** β -pozīcijas protons, veidojot diēnu **22a**. Otrā gadījumā notiek starpsavienojuma **Int-12** iekšmolekulāra ciklizēšanās, kas rezultējas sililindēnos **25a**. Optimizētos apstākļos (3 ekv. Ph_2IOTf , 20 mol% $CuCl$, 1,2 ekv. 2,6-*t*-Bu₂Py, EtOAc, 70 °C) silildiēna **22a**/indēna **25a** attiecība reakcijas maisījumā bija 87:13, diēna **22a** iznākums – 66 % pēc KMR. Izmantojot $PhMesIOTf$, tika iegūts līdzīgs diēna **22a** iznākums (59 % pēc KMR), bet diēna **22a** veidošanās selektivitāte bija zemāka ($PhMesIOTf$: **22a**/**25a** = 71:22).



22. shēma. Arilēta silildiēna **22a** sintēze – reakcijas koncepti un konkurējošās reakcijas.

Izmantojot apstākļus, kuros var iegūt augstākos diēna **22a** iznākumus, tika turpināts apskatīt substrātu klāstu (23. shēma). Arilēšanas reakcijā ar elektroniem bagātu arilsistēmu (*p*-Tol) saturošo jodānu **I-2** tika iegūti augstākie iznākumi (**22d**, 69 %). Visaugstākā selektivitāte attiecībā pret diēna veidošanos (**22e/25e** = 98:2) tika iegūta reakcijā ar *p*-bromaizvietoto jodānu **I-3**. No substrātiem **12b**, kas saturēja stēriski apjomīgo triizopropilsililgrupu (TIPS), tika iegūts maisījums ar palielinātu indēna proporciju (**22b/25b** = 67:33). Visos gadījumos (1*E*,3*E*)-diēni **22a-e** tika iegūti kā mažorie izomēri, kur (1*E*,3*E*)-izomēra saturs maisījumā bija 87–95 %. Nelielos daudzumos varēja detektēt arī pārējos izomērus ((1*Z*,3*E*)-, (1*E*,3*Z*)- un (1*Z*,3*Z*)-**22**) pēc to raksturīgajiem signāliem ¹H-KMR spektros. Iekšējais alkīns **12c** (R = Ph, Si = TIPS) nereaģēja ne standarta reakcijas apstākļos (EtOAc, 70 °C), ne arī paaugstinātā temperatūrā (*n*-BuOAc, 110 °C). Abos gadījumos tika atgūta izejviela bez degradācijas pazīmēm. Tas liecināja, ka šī metode ir izmantojama tikai propargilsilāniem, kas satur terminālas alkīna grupas.



[a] - Iznākums **22** + **25** maisījumam.
[b] - Reakcija nenotiek arī 110 °C BuOAc (17 h).

23. shēma. Substrātu klāsts arilētiem silildiēniem.

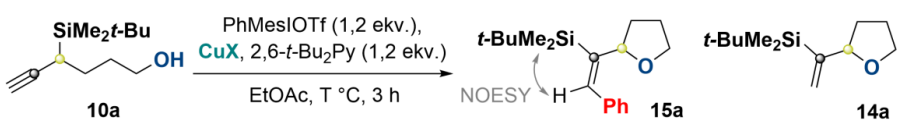
Iepriekš tika demonstrēts, ka iekšējus nukleofilus saturoši substrāti paver iespējas heterociklizācijai. Piemēram, terminālo spirta grupu saturošais propargilsilāns **10a** tika izmantots tetrahidrofurānu sintēzei.^[29] Sānu virknē arilētu tetrahidrofurānu sintēzei tika testēti dažādi Cu(I) katalizatori (6. tabula), kur CuCl un CuOTf benzola komplekss deva līdzīgi labus iznākumus

(**15a**, 82–84 % KMR), CuBF₄ acetonitrila komplekss bija nākamā labākā izvēle (**15a**, 77 %), savukārt heterogēnās katalīzes apstākļos ar Cu₂O tika iegūts maisījums ar arilēto produktu **15a** un protodemetalēšanas blakusproduktu **14a**, kur abiem bija zems iznākums. Nepievienojot reakcijas maisījumam nenukleofilu bāzi (2,6-di-*tert*-butilpiridīnu = 2,6-*t*-Bu₂Py), iespējams selektīvi iegūt protodemetalēšanas produktu **14a** (69 % KMR iznākums). Strukturāli līdzīgais, bet mazāk stēriski traucētais lutidīns, kā arī Et₃N, arilēšanas-heterociklizēšanas reakcijā nedeva vēlamu produktu **15a**.

Iegūtās C=C saites ģeometrija produktā **15a** tika pierādīta ar 2D-KMR NOESY spektroskopiju. Arilēšanas-ciklizēšanas kaskādes reakcija uzrādīja augstu stereoselektivitāti – vienīgais ar spektroskopiskām metodēm detektējais C=C saites izomērs bija (*E*)-**15a**.

6. tabula

Propargilsilāna **10a** arilēšanas-heterociklizēšanas reakcijas optimizācija, variējot Cu(I) katalizatorus un temperatūru

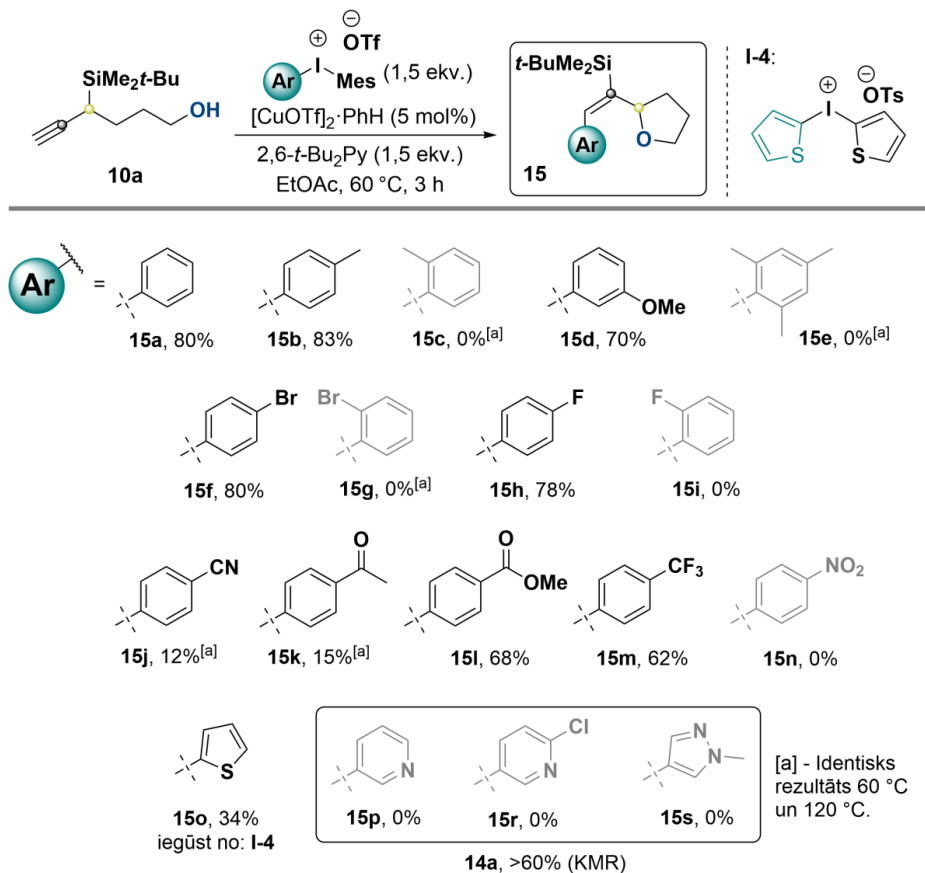


Nr. p. k.	CuX (mol%)	T (°C)	15a, % (KMR)	14a, % (KMR)
1. ^[a]	CuCl (2,5)	20	0	69
2.	CuCl (2,5)	20	0	0
3.	CuCl (5)	60	82, 76^[c]	0
4.	CuI (5)	60	0	0
5. ^[b]	[CuOTf] ₂ ·PhH (5)	60	84	0
6.	Cu(MeCN) ₄ BF ₄ (5)	70	77	0
7.	Cu ₂ O (5)	70	6	2
8.	[CuOTf] ₂ ·PhH (2,5)	70	70	0
9. ^[d]	[CuOTf] ₂ ·PhH (2,5)	70	43	0
10.	[CuOTf] ₂ ·PhH (11)	70	47	0

[a] Bez 2,6-*t*-Bu₂Py. [b] Reakcijas laiks – 2 h (pilna konversija). [c] Izdalītais iznākums (%). [d] 15 mol% of H₂O kā piedeva.

Optimizētajos apstākļos ar dažādiem diaril-λ³-jodāniem tika panākta arī citu arilgrupu ievadišana molekulā (24. shēma). Jodāni, kas saturēja elektroniem bagātas arilgrupas (*p*-Tol, *m*-MeOC₆H₄, Ph) vai halogēnus (Br, F), deva labus arilēto tetrahidrofurānu **15** iznākumus (70–83 %). Turpretim elektronatvelkošas grupas saturoši jodāni, īpaši tie, kas satur nukleofilus

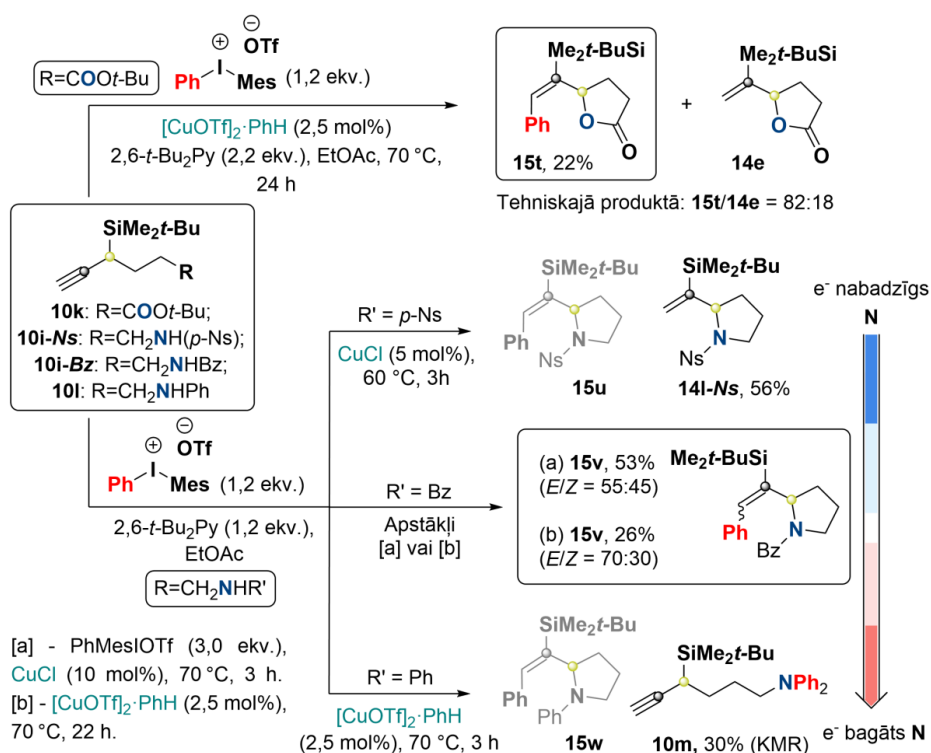
heteroatomus ($CN \approx COR \gg NO_2$), reaģēja vāji. Savukārt jodāni, kas saturēja citas elektronatvelkošas grupas (CF_3 , CO_2Me), deva vidējus iznākumus (62–68 %). *Orto*-aizvietoti jodāni neatkarīgi no to elektroniskajām īpašībām nereaģēja vispār. Jodāni, kas saturēja *N*-heterociklus, kā piridīnu vai pirazolu, deva nearilēto tetrahidrofurānu **14a** kā galveno reakcijas produktu, kas, visticamāk, radās pēc protodekuprēšanas mehānisma. Tiofēnilgrupu gan varēja veiksmīgi izmantot propargilsilānu hetarilēšanai, par reaģentu lietojot simetrisko ditiofēn-2-iljodonija *p*-tozilātu (**I-4**). Ir vērts pieminēt, ka visi arilētie tetrahidrofurāni tika iegūti ar ekskluzīvu (*E*)-selektivitāti alkēnu sānu ķēdē.



24. shēma. Substrātu klāsts stīrilaizvietotu tetrahidrofurānu sintēzei.

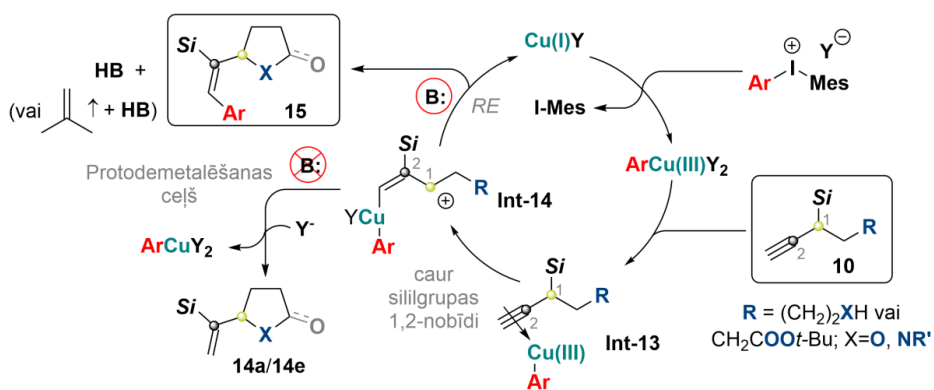
Interesanti, ka iepriekš aprakstītajos arilēšanas apstākļos tikai iekšēji *O*-nukleofīli reakcijā deva 1,3-difunkcionalizētus produktus. Arēju *O*-nukleofīlu R-OX (5 ekv.) klātbūtnē alifātisko sānu ķēdi saturošā propargilsilāna **12b** arilēšanas mēģinājums rezultējās *O*-nukleofīla arilēšanā. Tas tika novērots spirtiem, karbonskābēm, to nātrija sāļiem un sililētām karbonskābēm.

Tālāk autore un kolēģi vēlējās noskaidrot, kādi citi iekšējie nukleofili ir savietojami ar arilēšanas-heterociklizācijas reakcijas apstākļiem (25. shēma). Karbonskābi saturošais silāns **10b** nedeļa vēlamo laktona **15t** produktu karbonskābes *O*-arilēšanās dēļ. Savukārt *tert*-butilesteris **10t** deva gaidīto arilēšanas produktu **15t** kopā ar protodekuprēšanas produktu **14e**, kas tika iegūts pārākumā standarta arilēšanas apstākļos (1,2 ekv. ArMesIOTf, 5 mol% [CuOTf]₂·PhH, 1,2 ekv. 2,6-*t*-Bu₂Py, EtOAc, 60 °C, 3h). Lielāks pievienotās bāzes daudzums (kopā 2,2 ekv. 2,6-*t*-Bu₂Py) palīdzēja iegūt arilēto laktonu **15t** kā galveno reakcijas produktu. *N*-Nozilētā izejviela **10i-Ns** standarta arilēšanas reakcijas apstākļos deva fenilgrupu nesaturošo pirolidīnu **14i-Ns** ar 56 % iznākumu. Šajā gadījumā sulfonamīda N-H bija pārāk skābs, un tas veicināja protodekuprēšanos. Turpretī benzamīds **10i-Bz** arilējošos apstākļos deva arilēto pirolidīna atvasinājumu **15v** kā C=C saites izomēru maisījumu (*E/Z* = 55:45). Anilīna **10l** (R = CH₂NHPh) gadījumā notika N-H arilēšanās, nevis heterociklizācija, kas liecina par pārāk augstu *N*-nukleofilītāti. No šiem rezultātiem var secināt, ka acilamīdiem piemīt optimāls pK_a un nukleofilītāte, lai reaģētu atbilstoši vēlamo arilēšanas-heterociklizācijas mehānismam.



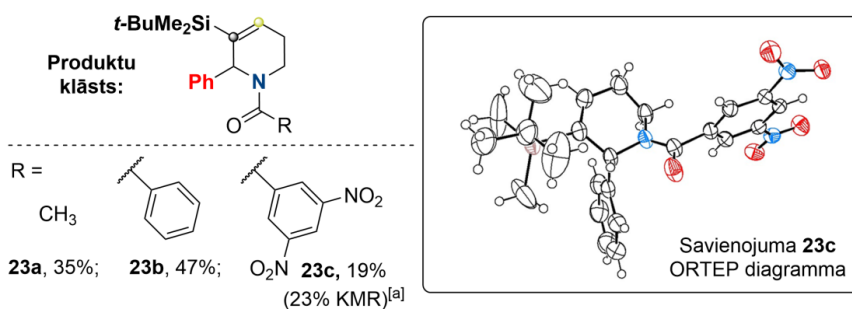
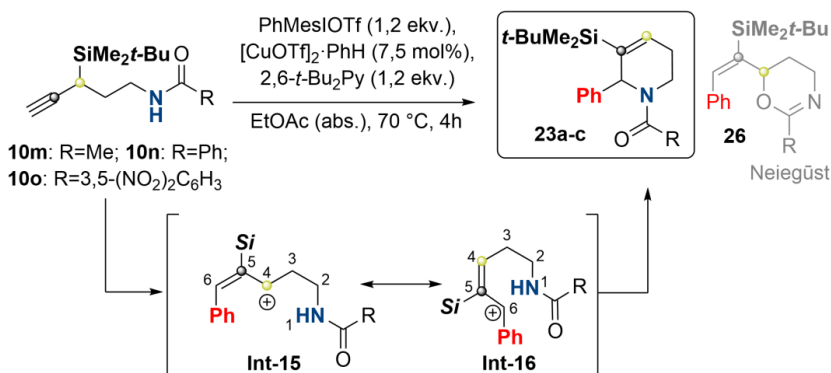
25. shēma. Arilēšanas-heterociklizēšanas reakciju pārbaude propargilsilāniem, kas satur iekšēju *N*-nukleofilu vai karbonskābes estera grupu.

Pētot arilētu silildiēnu **22a** sintēzi (3. pielikums), tika noskaidrots, ka šī tipa reakcijā Cu(I) sāļi ir reaģētspējīgāki nekā Cu(II) sāļi. Tas netieši liecina par to, ka, visticamāk, reakcija notiek ar Cu(I/III) katalītisko ciklu. Balstoties eksperimentālajos novērojumos, kā arī literatūrā iztirtajos mehānismos π -sistēmu arilēšanai vara katalīzes apstākļos,^[37] tika piedāvāts arilēšanas-heterociklizēšanas reakcijas mehānisms (26. shēma). Vispirms vara(I) sāls reaģē ar diaril- λ^3 -jodānu (ArMesIY), lai ģenerētu arilvaru(III), kas kā spēcīgs elektrofilis aktivē propargilsistēmu, inducējot sililgrupas 1,2-nobīdi. Tas rezultējas β -silīcija efekta stabilizētā alilkatjona starpstāvoklī **Int-14**. Sekojošs iekšējā nukleofila (O-, N-) uzbrukums un reducējošā eliminācija dod arilētus heterociklus **15** ar vienlaicīgu Cu(I) katalizatora reģenerāciju. Pievienotā bāze (B = 2,6-*t*-Bu₂Py) neitralizē katalītiskajā ciklā ģenerēto H⁺. *Terc*-butilestera **10k** gadījumā papildus tiek ģenerēts viens ekvivalents izobutilēna gāzes. Ja reakcijā netiek pievienota bāze, protodekuprēšanas mehānisms ir dominējošais un galvenokārt veidojas arilgrupu nesaturoši heterocikli **14a/14e**.



26. shēma. Piedāvātais mehānisms propargilsilānu arilēšanas-heterociklizēšanas reakciju kaskādei.

Mainot oglekļa atomu virknes izmēru, ir iespējamas reakcijas mehānisma variācijas, kā tas tika novērots, veicot reakcijas ar acilamīdiem **10m-o**. Sākotnēji tika sagaidīta imidāta **26** veidošanās,^[39] taču tika iegūti tetrahidropiridīni **23a-c**, kas veidojās caur nukleofila uzbrukumu alilkatjona rezonanses formai **Int-16**, kurai piemīt papildu arilgrupas stabilizācija (27. shēma). Iegūtā tetrahidropiridīna **23c** struktūra viennozīmīgi tika pierādīta ar rentgenstruktūranalīzes palīdzību.

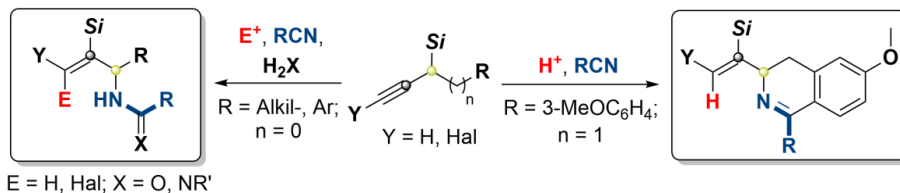


[a] - Modificēti apstākļi: **Ph₂IOTf** (3,0 ekv.), 20 h.

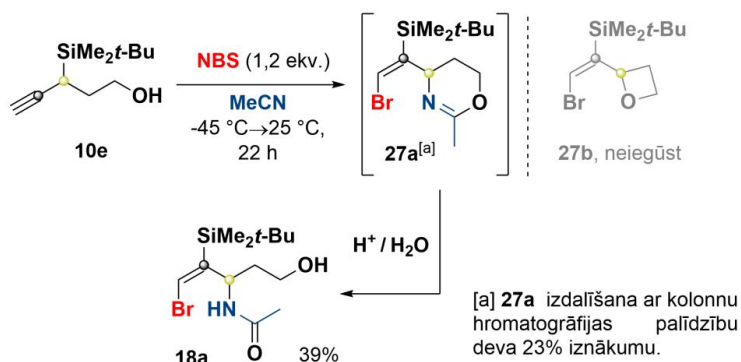
27. shēma. Tetrahidropiridīnu **23** sintēze no propargilsilāniem.

No iegūtajiem rezultātiem var secināt, ka alilkatjonu, kurus iegūst no iekšēju nukleofilu saturošiem propargilsilāniem **10**, iekšmolekulāras dzēšanas reģioselektivitāti nosaka izejvielas oglekļa atomu virknes izmērs. Substrātiem, kur ir iespējama pieclocēkļu cikla veidošanās, tiek novērota 1,3-difunkcionalizēšana, kur rodas tetrahidrofurāni **15** (X = O) vai pirolidīni **15** (X = N-PG), kas sānu ķēdē funkcionalizēti ar stirilgrupu. Substrātiem **10m-o**, kas satur īsākas sānu virknes, tika novērota 1,1-difunkcionalizēšana, kur veidojās tetrahidropiridīni **23**. Demonstrētā pieeja izrādījās efektīvāka stirilgrupu saturošu heterociklu **15** sintēzei, salīdzinot ar iepriekš zināmajām stratēģijām.^[29] Pilns pētījuma rezultātu izklāsts ir pieejams publikācijā Kronkalne, R.; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. *Beilstein J. Org. Chem.*, **2025**, *21*, 1984–1994 (3. pielikums).^[35]

1.4. Ritera tipa reakcija ar β -silīcija stabilizētu alilkatjonu

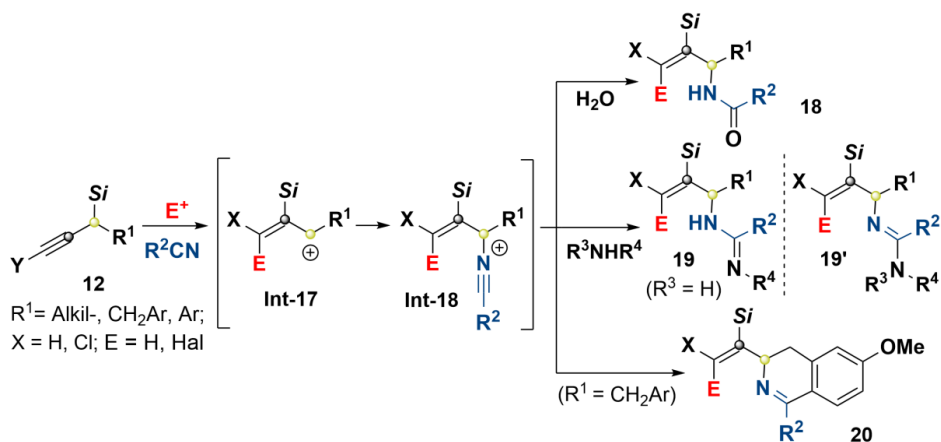


Mēģinot heterociklizēt spirtu **10e** NBS klātbūtnē analogiski 1.1. nodaļā aprakstītajām pārvērtībām, taču izmantojot acetonitrilu (MeCN) kā šķīdinātāju, tika novērota Ritera tipa reakcija, kur tika iegūts oksazīna atvasinājums **27a**, nevis gaidītais oksetāna atvasinājums **27b** (28. shēma). Cikliskais produkts **27a** viegli hidrolizējās par acetamīdu **18a** – klasisko Ritera reakcijas produktu.



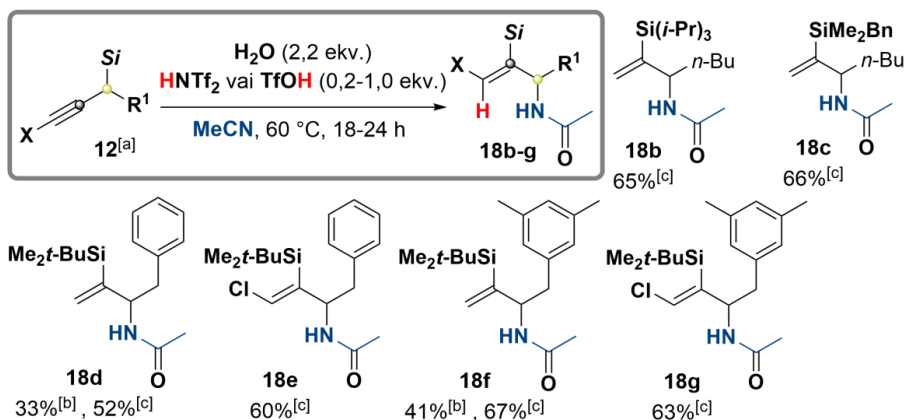
28. shēma. Spirta **10e** heterociklizēšana Ritera tipa reakcijas apstākļos.

Lietojot nitrilus, tie kā primārais nukleofils pievienojas alilkatjonam **Int-17**, veidojot nitrilija jonu **Int-18**, kas tiek dzēsts ar sekundāro nukleofīlu (H_2O , R^1R^2NH , Ar). Tas dod iespēju sintezēt gan cikliskus, gan acikliskus produktus, ko vieno funkcionālizētas alkēnu sānu virknes klātbūtne (29. shēma). Apskatītā daudzkomponentu reakcija ir izaicinoša no entropijas skatupunkta, jo ir jāpanāk secīga četru kovalento saišu veidošanās, reakcijas komponentēm reaģējot vēlamajā secībā. Neskatoties uz sistēmas sarežģītību, kopā ar Sandru Turku,^[40] Raimonu Rogaļevu^[41] un Miku Puriņu^[42] tika izstrādāta metodoloģija propargilsilānu izmantošanai funkcionālizētu alilamīdu **18**, amidīnu **19** un dihidroizohinolīnu **20** sintēzei Ritera tipa reakcijas apstākļos.



29. shēma. Propargilsilānu lietojums Ritera tipa reakcijā.

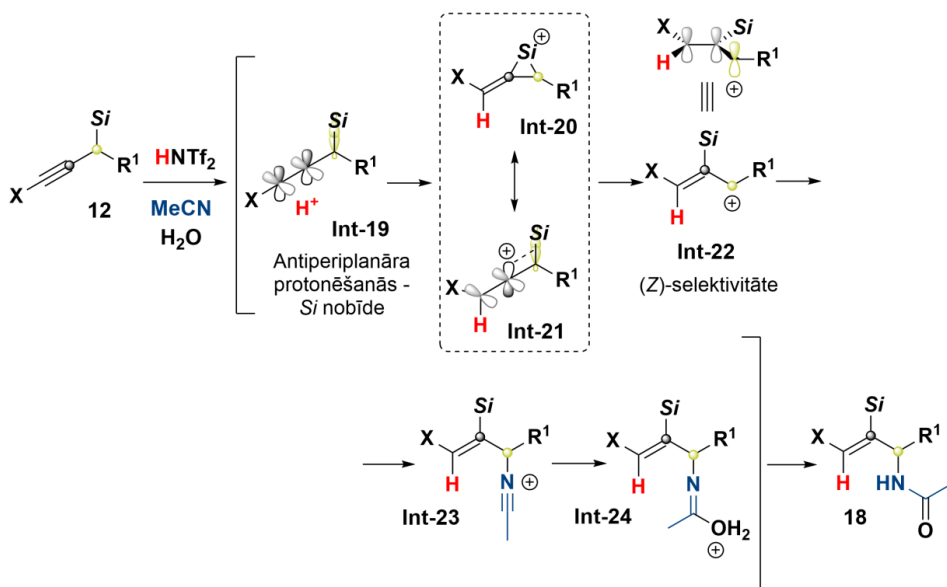
Vispirms tika apskatītas sistēmas, kur reakcijas apstākļi ir visvairāk pietuvināti klasiskajiem Ritera reakcijas apstākļiem, kas apvieno Brensteda skābi (TfOH vai HNTf₂) karbkatjona ģenerēšanai, MeCN kā primāro nukleofilu un šķīdinātāju, kā arī ūdeni kā sekundāro nukleofilu. Šādos apstākļos tika iegūti alilamīda funkcionalitāti saturoši produkti **18b-g** (30. shēma). Tika novērots, ka, izmantojot ekvimolāru daudzumu skābes (1 ekv. HNTf₂: **18f**, 67 %), produktu iznākumi bija augstāki nekā ar katalītisku skābes daudzumu (0,2 ekv. TfOH: **18f**, 41 %). Termināli halogenētu propargilsilānu **12** (X = Cl) gadījumā tika iegūti trīsaizvietotu C=C saiti saturoši produkti **18e** un **18g**, kas reakcijas maisījuma ¹H-KMR spektrā tika novēroti kā (Z/E)-isomēru maisījums (9:1). Mažorais (Z)-izomērs tika izdalīts ar kolonnu hromatogrāfijas palīdzību.



[a] Silāni: **12b** ($\text{X} = \text{H}$, $\text{R}^1 = n\text{-Bu}$, $\text{Si} = (i\text{-Pr})_3\text{Si}$), **12d** ($\text{X} = \text{H}$, $\text{R}^1 = n\text{-Bu}$, $\text{Si} = \text{BnMe}_2\text{Si}$), **12e** ($\text{X} = \text{H}$, $\text{R}^1 = \text{Bn}$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **12f** ($\text{X} = \text{Cl}$, $\text{R}^1 = \text{Bn}$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **12g** ($\text{X} = \text{H}$, $\text{R}^1 = \text{CH}_2(3,5\text{-Me}_2\text{C}_6\text{H}_3)$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **12h** ($\text{X} = \text{Cl}$, $\text{R}^1 = \text{CH}_2(3,5\text{-Me}_2\text{C}_6\text{H}_3)$, $\text{Si} = t\text{-BuMe}_2\text{Si}$). [b] 0.2 ekv. TfOH kā H^+ avots. [c] 1 ekv. HNTf_2 kā H^+ avots.

30. shēma. Alilamīdu sintēze no propargilsilāniem.

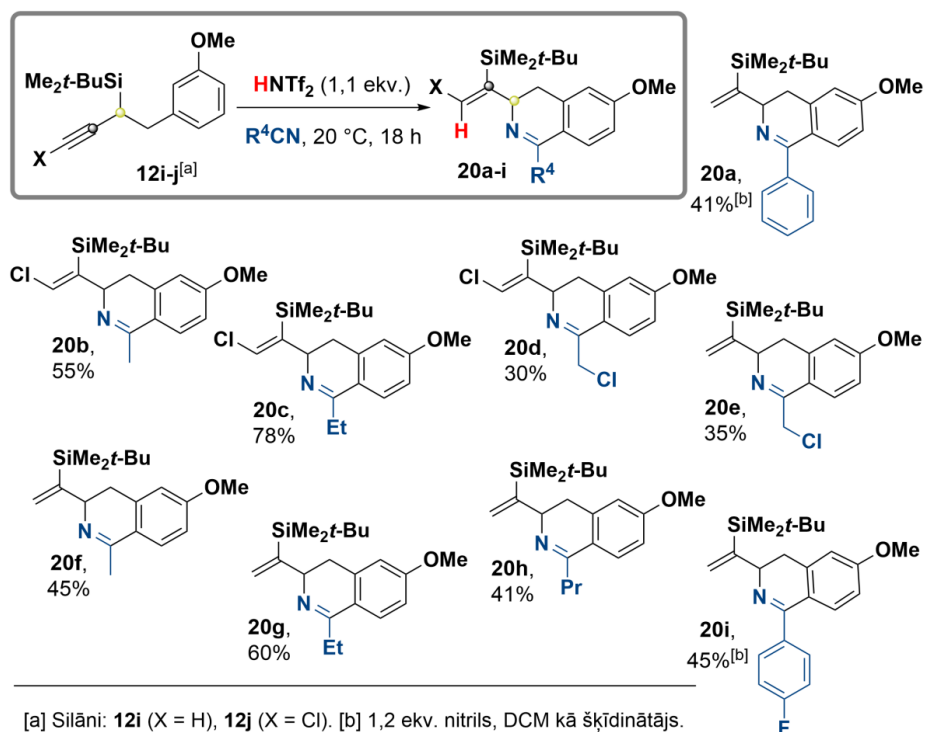
(Z)-Dubultsaites veidošanos alilamīdu **18e/18g** gadījumā var skaidrot ar alkīna protonēšanos antiperiplanārā pozīcijā attiecībā pret migrējošo sililgrupu (31. shēma).



31. shēma. Produktu (Z)-ģeometrijas racionalizācija propargilsilānu Ritera reakcijā.

Elektroniem bagātu arilsistēmu **12i-j** gadījumā tika novērota Bišlera–Napirālska (*Bischler–Napieralski*) tipa reakcija, kur arilsistēma reaģēja kā sekundārais nukleofils nitrīlija jona dzēšanai,

kā rezultātā tika iegūti dihidroizohinolīna atvasinājumi **20a-i** (32. shēma). Analogiski iepriekš novērotajai sakarībai alilamīdu sintēzē, no termināli halogenētā silāna **12j** tika iegūti produkti **20b-d** ar (*Z*)-ģeometriju alkēnu sānu ķēdē. Halogenētais silāns **12j** deva augstākus produkta **20** iznākumus (līdz 78 %) nekā tā nehalogenētais analogs **12i** (līdz 60 %). Atšķirībā no alilamīdu **18** sintēzes (kurai bija nepieciešama karsēšana līdz 60 °C), dihidroizohinolīnu **20** sintēze efektīvi noritēja istabas temperatūrā (20 °C). Lietojot alifātiskos (MeCN, EtCN, PrCN) un halogenētos nitrilus (ClCH₂CN) kā šķīdinātājus, tika iegūti dihidroizohinolīni **20b-h** ar 30–78 % iznākumu. Aromātiskos nitrilus Ritera-tipa reakcijās kā šķīdinātājus izmanto reti^[43] – tie visbiežāk ir augsti virstoši šķidrums vai cietvielas.^[44, 45] Šādos gadījumos kā šķīdinātājs tika izmantots DCM, pievienojot augsti virstošos nitrilus (PhCN, 4-FC₆H₄CN) nelielā pārākumā (1,2 ekv.). Tas ļāva iegūt dihidroizohinolīnus **20a/20i** ar iznākumiem 41–45 % robežās.



32. shēma. Dihidroizohinolīnu sintēze no propargilsilāniem Bišlera–Napiraļska tipa reakcijā.

Tālāk tika apskatītas komplicētākas sistēmas – Ritera tipa reakcija, kur nitrīlija jona dzēšanai tiek pievienots ārējais slāpekļa nukleofils. Brensteda skābes aktivācijas apstākļos amidīna **19** tipa produkti netika iegūti. Silānam **12b** reaģējot ar 1,2 ekv. TfOH un 2,0 ekv. TsNH₂ acetonitrilā (T = –45 °C), vienīgais identificētais produkts bija (*E*)-hepta-1,3-diēn-2-iltriizopropilsilāns^[18] (30 % KMR iznākums). Savukārt ar HNTf₂ reakcija nenotika, un tika

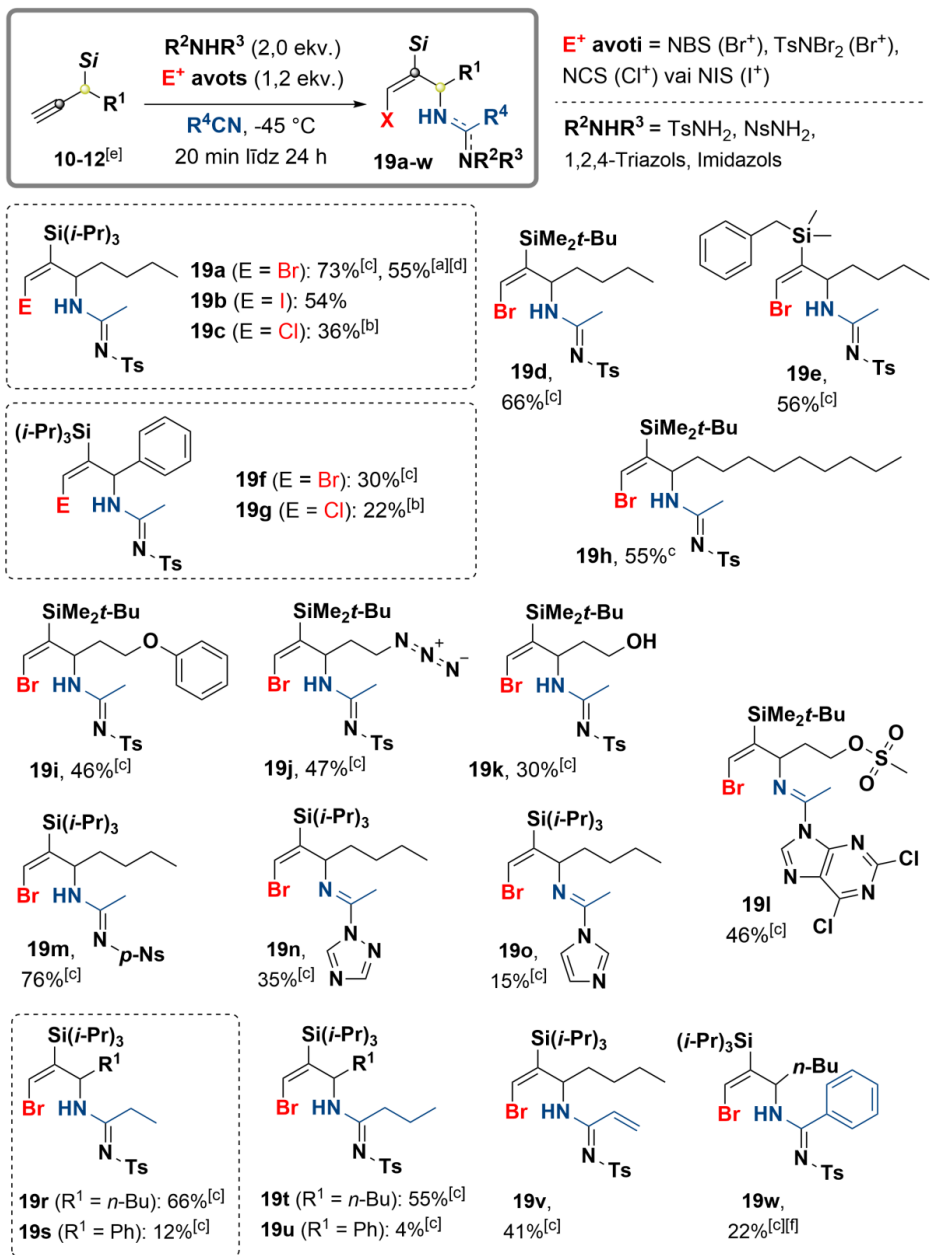
atgūtas izejvielas. Toties, aktivējot propargilsistēmu ar NBS, kā galvenais reakcijas produkts tika iegūts amidīns **19a** ar 56 % KMR iznākumu (apstākļi: 1,2 ekv. NBS, 1,1 ekv. TsNH₂, MeCN, 20 °C). Veicot tālāku reakcijas optimizāciju, tika noskaidrots, ka augstākos amidīna **19a** iznākumus (75 % KMR) var iegūt šādos apstākļos: T = -45 °C, MeCN kā šķīdinātājs, 2 ekv. TsNH₂ un 1,2 ekv. NBS.

Optimizētajos reakcijas apstākļos tika turpināta substrātu klāsta izpēte (33. shēma). Halogēna aizvietotāju dažādība pie produktu **19a-c** C=C saites tika panākta, izmantojot dažādus elektrofilās halogenēšanas reaģentus: NBS, NCS un NIS. Augstākie amidīnu **19** iznākumi (līdz 76 %) tika iegūti ar propargilsilāniem **12a,b,d**, kas satur vienkāršas alifātiskās virknes. Arilgrupu saturošais propargilsilāns **12k**^[18] Ritera tipa reakcijas apstākļos deva zemus amidīnu iznākumus (22–30 %). Iespējams, ka papildu stabilizācija alilkatjonam, ko dod blakus esošā arilgrupa (R¹ = Ar), palēnina nitrila pievienošanos, ko netieši apstiprina papildus nepieciešamais reakcijas laiks. Piemēram, alkilsilāns **12b** bija pilnībā izreaģējis jau pēc 45 minūtēm, savukārt arilsilānam **12k** bija nepieciešama 1,5 stunda.

Substrāti, kas saturēja terminālu arilētera grupu **11i**, azīdu **10p**, mezilātu **10r** un pat brīvu spirta grupu **10e**, Ritera tipa reakcijā deva amidīna produktus **19** ar iznākumiem 30–47 % robežās.

Starp alternatīviem sekundārajiem nukleofiliem amidīnu **19** sintēzei, sulfonamīdi (NsNH₂, TsNH₂) deva augstākos produktu **19** iznākumus (73–76 %). Daži slāpekļa heterocikli, lai arī ar zemāku iznākumu (15–46 %), arī bija izmantojami šīm mērķim, piemēram, 2,6-dihlorpurīns, 1,2,4-triazols un imidazols. Spēcīgāki nukleofili, kā cikloheksanols, cikloheksiltiols un cikloheksilamīns, standarta reakcijas apstākļos (silāns **12b**, 1,2 ekv. NBS, -45 °C, MeCN kā šķīdinātājs) nedeva gaidītos imidāta/tioimidāta/amidīna produktus.

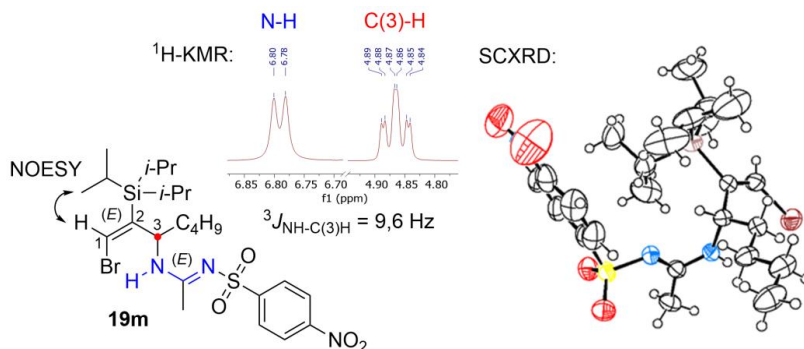
Garākas alkilvirknes (C₃-C₄) saturoši nitrili, kā arī akrilnitrils reakcijā ar alifātisko silānu **12b** deva salīdzinoši zemākus amidīnu **19** iznākumus (41–66 %), nekā iepriekš tika iegūti ar acetonitrilu. Benzonitrila gadījumā bija nepieciešams izvairīties no tā kristalizēšanās reakcijas apstākļos (-45 °C), tādēļ tika izmantota jaukta šķīdinātāju sistēma: PhCN/DCM (4:3 v/v). Benzonitrils šajos apstākļos nebija pietiekami reaģētspējīgs (amidīns **19w** tika iegūts tikai ar 22 % iznākumu), un galvenokārt notika deprotonēšanās, veidojot diēnu.^[18]



[a] KMR iznākums. [b] T = -45→20 °C. [c] NBS kā Br^+ avots. [d] $TsNBr_2$ kā Br^+ avots. [e] Silani: **12a** ($R^1 = n-Bu$, $Si = t-BuMe_2Si$), **12k** ($R^1 = Ph$, $Si = (i-Pr)_3Si$), **12l** ($R^1 = C_9H_{19}$, $Si = t-BuMe_2Si$), **11i** ($R^1 = CH_2CH_2OPh$, $Si = t-BuMe_2Si$), **10p** ($R^1 = CH_2CH_2N_3$, $Si = t-BuMe_2Si$), **10e** ($R^1 = CH_2CH_2OH$, $Si = t-BuMe_2Si$), **10r** ($R^1 = CH_2CH_2OMs$, $Si = t-BuMe_2Si$). [f] Tika izmantota modificēta šķīdinātāju sistēma: PhCN/DCM (4:3 v/v).

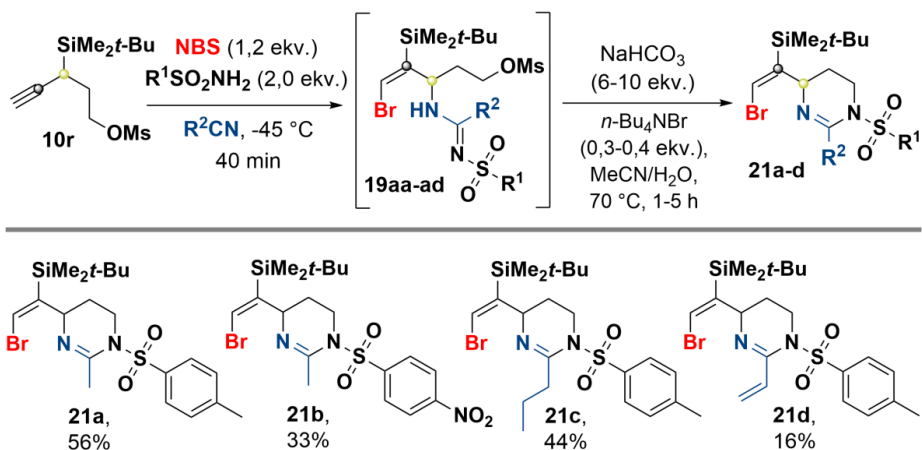
33. shēma. Amidiņu sintēze Ritera tipa reakcijā no propargilsilāniem.

Amidīniem šķīdumā ir iespējams novērot gan konfigurācijas izomērus (C=N saitei ir iespējama (*E*)- vai (*Z*)-konfigurācija), gan rotācijas izomērus (sin/anti), kas veidojas, rotējot ap C-N saiti. Tautomērija arī ir būtisks faktors, kas apgrūtina šo savienojumu analīzi.^[46] Analizējot amidīnus **19a-w** ar KMR spektroskopijas palīdzību, CDCl₃ visbiežāk tika novēroti divi signālu komplekti, savukārt DMSO-*d*₆ bija redzams tikai viens izomērs. Amidīna **19m** gadījumā mažorā/minorā izomēra attiecība CDCl₃ bija 96:4 (integrāļu attiecība ¹H KMR). N-H signāls ¹H-KMR deva dubletu ar ³*J* = 9,6 Hz sadarbības konstanti ar C(3)-H, kas liecina par N-H vicinālo pozīciju attiecībā pret C(3)-H (1. attēls). Tas pats tika novērots visiem pārējiem amidīniem, kas saturēja brīvu N-H grupu. Kamēr atbilstošo amidīna tautomēru varēja noteikt ar spektroskopiskām metodēm, C=N saites ģeometrijas noteikšana bija sarežģītāka. Produkta **19m** gadījumā C=N saites (*E*)-izomērs tika pierādīts ar rentgenstruktūranalīzi. (*E*)-ģeometrija tika apstiprināta arī C=C dubultsaitei, un tas saskan ar iepriekšējiem novērojumiem propargilsilānu elektrofilās halogenēšanas reakcijās.^[19]



1. attēls. Amidīna **19m** struktūras pierādīšana.

Noslēgumā darba autore un kolēģi apskatīja aciklisko Ritera tipa produktu lietojumu heterociklu sintēzē. Standarta Ritera tipa reakcijas apstākļos (1,2 ekv. NBS, 2,0 ekv. R¹SO₂NH₂, R²CN kā šķīdinātājs, T = -45 °C) no mezilāta **10r** tika iegūti amidīni **19aa-ad**, kas bāzes klātbūtnē (NaHCO₃) ciklizējās iekšmolekulārā S_N2 tipa reakcijā par tetrahidropirimidīna atvasinājumiem **21a-d** (34. shēma).

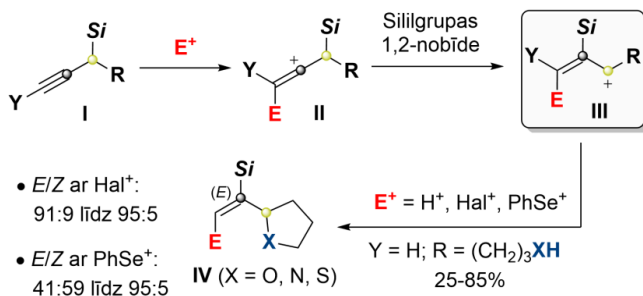


34. shēma. Ritera tipa reakcija tetrahidropirimidīnu **21** sintēzei.

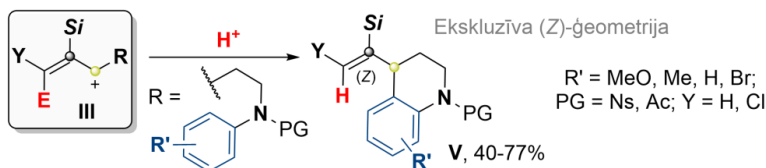
Šajā nodaļā tika demonstrēts, ka propargilsilānu pārvērtības Ritera tipa apstākļos var sniegt plašu produktu klāstu, sākot no acikliskām struktūrām – alilamīdiem **18** un amidīniem **19** –, līdz pat heterocikliem **20-21**. Apvienojot ārēju elektrofilu pievienošanās propargilsilāna trīskāršajai saitei ar vinil-alilkatjonu pārgrupēšanos sililgrupas 1,2-migrācijas rezultātā un divu secīgu nukleofilu uzbrukumu, tika iegūtas komplicētas, alilamīna struktūrfragmentu saturošas struktūras no vienkāršām izejvielām. Pilns pētījuma rezultātu izklāsts pieejams 6. pielikumā: Turka S.; Kroņkalne R.; Rogaļevs R.; Puriņš M.; Mishnev A.; Turks M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives (nepublicēts manuskripts).

SECINĀJUMI

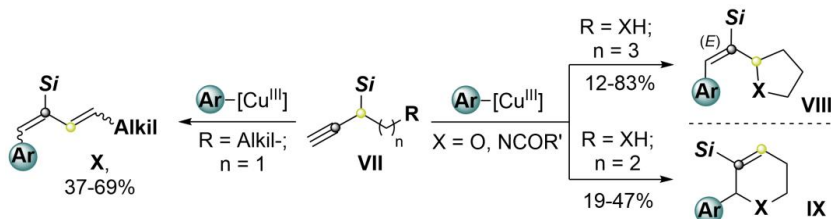
1. Elektrofīli propargilsilānos **I** ierosina sililgrupas 1,2-nobīdi, veidojot reaģētspējīgus alilkatjonus **III**. Tos dzēšot ar iekšējiem *O*-, *N*- un *S*-nukleofiliem, tiek iegūti piesātināti pieclocēkļu heterocikli **IV** – tetrahidrofurāni ($X = O$), pirolidīni ($X = N\text{-PG}$) un tiolāni ($X = S$) –, kas funkcionalizēti ar gemināli divaizvietotu ($E = H$) vai stereodefinētu trīsaizvietotu ($E = \text{Hal}, \text{PhSe}$) alkēnu sānu ķēdi.



2. Iekšmolekulāri dzēšot β -silīcija stabilizēto alilkatjonu **III** ar elektroniem bagātām arilsistēmām Brensteda skābes ierosinātā Frīdela-Kraftsa tipa reakcijā, tiek iegūti bicikliski, daļēji piesātināti heterocikli **V**, kas satur stereodefinētu (*Z*)-ģeometrijas alkēnu sānu ķēdi.

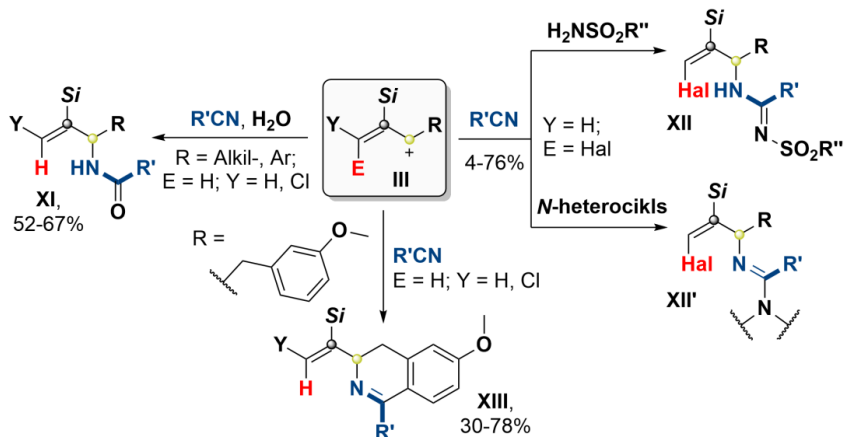


3. Kombinējot diaril- λ^3 -jodānus ar Cu(I) katalizatoru, var ģenerēt elektrofilus Ar-Cu(III) reaģentus, kas kā formāli Ar^+ sintoni pievienojas propargilsilānu trīskāršajai saitei un ierosina arilēšanas – sililgrupas 1,2-nobīdes – heterociklizēšanas sekvenču **VII**→**VIII** un **VII**→**IX** atkarībā no sānu virknes izmēra. Savukārt, ja propargilsilāns nesatur reaģētspējīgus iekšējos nukleofilus, tiek iegūti arilēti silīdiēni **X**.

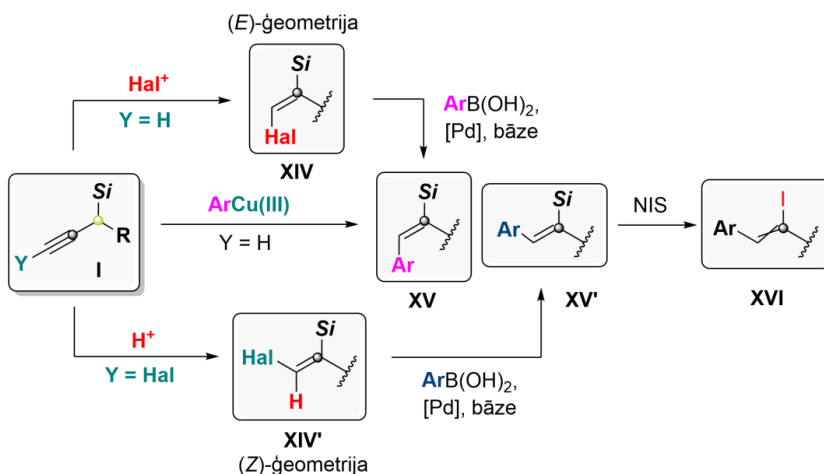


4. Ritera tipa reakcijas apstākļos propargilsilānus var kombinēt ar divu secīgu nukleofīlu uzbrukumu, iegūstot alilamīdus **XI** ($X = O$) un amidīnus **XII** ($X = N\text{-PG}$), kas satur augsti funkcionalizētu olefīnu struktūrfragmentu. Propargilsilānus ar elektroniem bagātām

arilsistēmām sānu virknē var pakļaut Bišlera–Napiraļska tipa reakcijai, kurā ir iegūstami dihidroizohinolīnu atvasinājumi **XIII**.



5. Dubultsaišu ģeometriju var kontrolēt, kombinējot: (a) nehalogenētus propargilsilānus **I** ($Y = H$) ar elektrofilās halogenēšanas reagentiem ($E^+ = Hal^+$) (**E**)-ģeometrijas iegūšanai vai (b) halogenētus propargilsilānus **I** ($Y = Hal$) ar Brensteda skābes aktivāciju ($E^+ = H^+$) (**Z**)-ģeometrijas iegūšanai. Olefīnu sānu ķēdi var tālāk modificēt šķērssametināšanas reakcijās, kā arī veicot $Si \rightarrow I$ apmaiņu, saglabājot alkēna konfigurāciju. Propargilsilānu **I** aktivējot ar $Ar-Cu(III)$, stirola atvasinājumus **XV** var iegūt vienā stadijā, izlaižot Pd -katalizēto vinilhalīdu šķērssametināšanas soli.



LITERATŪRAS SARAKSTS

- [1] Lecourt, C.; Dhambri, S.; Allievi, L.; Sanogo, Y.; Zeghib, N.; Othman, R. Ben; Lannou, M.-I.; Sorin, G.; Ardisson, J. Natural Product Reports Natural Products and Ring-Closing Metathesis: Synthesis of Sterically Congested Olefins. *Nat. Prod. Rep.* **2018**, *35*, 105–124. <https://doi.org/10.1039/C7NP00048K>.
- [2] Singh, M.; Ravichandiran, V.; Bharitkar, Y. P.; Hazra, A. Natural Products Containing Olefinic Bond: Important Substrates for Semi-Synthetic Modification Towards Value Addition. *Curr. Org. Chem.* **2020**, *24*, 709–745. <https://doi.org/10.2174/1385272824666200312125734>.
- [3] Dragutan, V.; Dragutan, I.; Demonceau, A.; Delaude, L. Combining Enyne Metathesis with Long-Established Organic Transformations: A Powerful Strategy for the Sustainable Synthesis of Bioactive Molecules. *Beilstein J. Org. Chem.* **2020**, *16*, 738–755. <https://doi.org/10.3762/bjoc.16.68>.
- [4] Pederson, R. L.; Fellows, I. M.; Ung, T. A.; Ishihara, H.; Hajela, S. P. Applications of Olefin Cross Metathesis to Commercial Products. *Adv. Synth. Catal.* **2002**, *344*, 728–735. [https://doi.org/https://doi.org/10.1002/1615-4169\(200208\)344:6/7<728::AID-ADSC728>3.0.CO;2-4](https://doi.org/https://doi.org/10.1002/1615-4169(200208)344:6/7<728::AID-ADSC728>3.0.CO;2-4).
- [5] Grubbs, R. H. Olefin-Metathesis Catalysts for the Preparation of Molecules and Materials (Nobel Lecture). *Angew. Chem. Int. Ed.* **2006**, *45*, 3760–3765. <https://doi.org/10.1002/anie.200600680>.
- [6] Kutateladze, D. A.; Mai, B. K.; Dong, Y.; Zhang, Y.; Liu, P.; Buchwald, S. L. Stereoselective Synthesis of Trisubstituted Alkenes *via* Copper Hydride-Catalyzed Alkyne Hydroalkylation. *J. Am. Chem. Soc.* **2023**, *145* (32), 17557–17563. <https://doi.org/https://doi.org/10.1021/jacs.3c06479>.
- [7] Flynn, A. B.; Ogilvie, W. W. Stereocontrolled Synthesis of Tetrasubstituted Olefins. *Chem. Rev.* **2007**, *107*, 4698–4745. <https://doi.org/10.1021/cr050051k>.
- [8] Zhao, Y.; Liu, C.-F.; Lin, L. Q. H.; Chan, A. S. C.; Koh, M. J. Stereoselective Synthesis of Trisubstituted Alkenes by Nickel-Catalyzed Benzylolation and Alkene Isomerization. *Angew. Chem. Int. Ed.* **2022**, *61*, e202202674. <https://doi.org/10.1002/anie.202202674>.
- [9] Hoveyda, A. H.; Qin, C.; Sui, X. Z.; Liu, Q.; Li, X.; Nikbakht, A. Taking Olefin Metathesis to the Limit: Stereocontrolled Synthesis of Trisubstituted Alkenes. *Acc. Chem. Res.* **2023**, *56* (18), 2426–2446. <https://doi.org/https://doi.org/10.1021/acs.accounts.3c00341>.

- [10] Koengeter, T.; Qin, C.; Mai, B. K.; Liu, Q.; Mu, Y.; Liu, P.; Hoveyda, A. H. Catalytic Cross-Metathesis Reactions That Afford *E*- and *Z*-Trisubstituted Alkenyl Bromides: Scope, Applications, and Mechanistic Insights. *J. Am. Chem. Soc.* **2023**, *145* (6), 3774–3785. <https://doi.org/10.1021/jacs.2c13289>.
- [11] Nguyen, T. T.; Koh, M. J.; Mann, T. J.; Schrock, R. R.; Hoveyda, A. H. Article Synthesis of *E*- and *Z*-Trisubstituted Alkenes by Catalytic Cross-Metathesis. *Nat. Publ. Gr.* **2017**, *552* (7685), 347–354. <https://doi.org/10.1038/nature25002>.
- [12] Mukherjee, N.; Planer, S.; Grela, K. Formation of Tetrasubstituted C-C Double Bonds *via* Olefin Metathesis: Challenges, Catalysts, and Applications in Natural Product Synthesis. *Org. Chem. Front.* **2018**, *5*, 494–516. <https://doi.org/10.1039/C7QO00800G>.
- [13] Negishi, E.; Wang, G.; Rao, H.; Xu, Z. Alkyne Elementometalation – Pd-Catalyzed Cross-Coupling. Toward Synthesis of All Conceivable Types of Acyclic Alkenes in High Yields, Efficiently, Selectively, Economically, and Safely: “Green” Way. *J. Org. Chem.* **2010**, *75*, 3151–3182. <https://doi.org/10.1021/jo1003218>.
- [14] Edwards, J. T.; Merchant, R. R.; McClymont, K. S.; Knouse, K. W.; Qin, T.; Malins, L. R.; Vokits, B.; Shaw, S. A.; Bao, D.-H.; Wei, F.-L.; Zhou, T.; Eastgate, M. D.; Baran, P. S. Decarboxylative Alkenylation. *Nature* **2017**, *545*, 213–218. <https://doi.org/10.1038/nature22307>.
- [15] Buttard, F.; Sharma, J.; Champagne, P. A. Recent Advances in the Stereoselective Synthesis of Acyclic All-Carbon Tetrasubstituted Alkenes. *Chem. Commun.* **2021**, *57*, 4071–4088. <https://doi.org/10.1039/d1cc00596k>.
- [16] Ghosh, S.; Chakraborty, R.; Ganesh, V. Dual Functionalization of Alkynes Utilizing the Redox Characteristics of Transition Metal Catalysts. *ChemCatChem* **2021**, *13*, 4262–4298. <https://doi.org/10.1002/cctc.202100838>.
- [17] Eissen, M.; Lenoir, D. Mass Efficiency of Alkene Syntheses with Tri- and Tetrasubstituted Double Bonds. *ACS Sustain. Chem. Eng.* **2017**, *5*, 10459–10473. <https://doi.org/10.1021/acssuschemeng.7b02479>.
- [18] Puriņš, M.; Mishnev, A.; Turks, M. Brønsted Acid Catalyzed 1,2-Silyl Shift in Propargyl Silanes: Synthesis of Silyl Dienes and Silyl Indenes. *J. Org. Chem.* **2019**, *84* (6), 3595–3611. <https://doi.org/10.1021/acs.joc.8b02735>.
- [19] Beļāunieks, R.; Puriņš, M.; Līpiņa, R. A.; Mishnev, A.; Turks, M. 1,3-Difunctionalization of Propargyl Silanes with Concomitant 1,2-Silyl Shift: Synthesis of Allyl Functionalized Vinyl Silanes. *Org. Lett.* **2023**, *25* (25), 4627–4631.

<https://doi.org/10.1021/acs.orglett.3c01245>.

- [20] Roberts, D. D.; McLaughlin, M. G. Strategic Applications of the β -Silicon Effect. *Adv. Synth. Catal.* **2022**, *364*, 2307–2332. <https://doi.org/10.1002/adsc.202200237>.
- [21] Beļāunieks, R.; Puriņš, M.; Turks, M. Manifestation of the β -Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift. *Synthesis (Stuttg)*. **2020**, *52* (15), 2147–2161. <https://doi.org/10.1055/s-0039-1690898>.
- [22] Lamberth, C.; Dinges, J. The Significance of Heterocycles for Pharmaceuticals and Agrochemicals. In *Bioactive Heterocyclic Compound Classes*; Lamberth, C., Dinges, J., Eds.; 2012. <https://doi.org/10.1002/9783527664412.ch1>.
- [23] Reymond, J. The Chemical Space Project. *Acc. Chem. Res.* **2015**, *48*, 722–730. <https://doi.org/10.1021/ar500432k>.
- [24] Reiser, O. Heterocyclic Chemistry – A Mature Area in Its Infancy! *Eur. J. Org. Chem.* **2019**, 4973–4975. <https://doi.org/10.1002/ejoc.201901162>.
- [25] Zhang, Y.; Li, Q.; Hu, Z.; Leng, Z.; Zhang, W.; Das, S. Innovative Approaches to the Synthesis of Five-Membered Heteroaromatics with Emerging Synthetic Methodologies. *Chem. Soc. Rev.* **2027**. <https://doi.org/10.1039/d5cs01300c>.
- [26] Cabrele, C.; Reiser, O. The Modern Face of Synthetic Heterocyclic Chemistry. *J. Org. Chem.* **2016**, *81*, 10109–10125. <https://doi.org/10.1021/acs.joc.6b02034>.
- [27] Beļāunieks, R.; Puriņš, M.; Kumpiņš, V.; Turks, M. Synthesis of 3-Silylated 3-Sulfolenes from Propargylsilanes and Their Reductive Desulfitation. *Chem. Heterocycl. Compd.* **2021**, *57* (1), 20–25. <https://doi.org/10.1007/s10593-021-02862-1>.
- [28] Roberts, D. D.; McLaughlin, M. G. Strategic Applications of the β -Silicon Effect. *Adv. Synth. Catal.* **2022**, *364* (14), 2307–2332. <https://doi.org/10.1002/adsc.202200237>.
- [29] Kronkalne, R.; Beļāunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.* **2023**, *88* (19), 13857–13870. <https://doi.org/10.1021/acs.joc.3c01481>.
- [30] Beļāunieks, R. Harnessing the 1,2-Silyl Shift for the Synthesis of Functionalized Alkenes from Propargyl Silanes. Doctoral Thesis, Riga Technical University, 2023. <https://doi.org/10.7250/9789934229640>.
- [31] Wang, X.; Gao, Q.; Buevich, A. V.; Yasuda, N.; Zhang, Y.; Yang, R.; Zhang, L.-K.; Martin, G. E.; Williamson, R. T. Unexpected Propargylic Retro-Brook Rearrangements in

- Alkynes. *J. Org. Chem.* **2019**, *84* (16), 10024–10031. <https://doi.org/10.1021/acs.joc.9b01190>.
- [32] Kronkalne, R.; Beļāunieks, R.; Turks, M. Synthesis of 4-(*Tert*-Butyldimethylsilyl)-4,5,6,7-Tetrahydro-[1,2,3]Triazolo[1,5-*a*]Pyridine. *Molbank* **2022**, *2022* (3), M1427. <https://doi.org/10.3390/M1427>.
- [33] Ubaidullajevs, A.; Kronkalne, R.; Mishnev, A.; Turks, M. Synthesis of Substituted Chromanes and Tetrahydroquinolines *via* Tandem 1,2-Silyl Shift – Friedel–Crafts Cyclization. *J. Org. Chem.* **2026**. <https://doi.org/10.1021/acs.joc.5c03136>.
- [34] Chan, T. H.; Fleming, I. Electrophilic Substitution of Organosilicon Compounds-Applications to Organic Synthesis. *Synthesis (Stuttg)*. **1979**, *10*, 761–786. <https://doi.org/10.1055/s-1979-28829>.
- [35] Kronkalne, R.; Beļāunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. *Beilstein J. Org. Chem.* **2025**, *21*, 1984–1994. <https://doi.org/10.3762/bjoc.21.154>.
- [36] Wang, D.; Li, Q.; Li, M.; Du, Z.; Fu, Y. Recent Progress in Arylation Reactions with Diaryliodonium Salts. *Curr. Org. Chem.* **2021**, *25* (11), 1298–1320. <https://doi.org/10.2174/1385272825666210512015410>.
- [37] Fañanás-Mastral M. Copper-Catalyzed Arylation with Diaryliodonium Salts. *Synthesis (Stuttg)*. **2017**, *49* (09), 1905–1930. <https://doi.org/10.1055/s-0036-1589483>.
- [38] Deprez, N. R.; Sanford, M. S. Reactions of Hypervalent Iodine Reagents with Palladium: Mechanisms and Applications in Organic Synthesis. *Inorg. Chem.* **2007**, *46* (6), 1924–1935. <https://doi.org/10.1021/ic0620337>.
- [39] Sinai, Á.; Mészáros, Á.; Gáti, T.; Kudar, V.; Palló, A.; Novák, Z. Copper-Catalyzed Oxidative Ring Closure and Carboarylation of 2-Ethynylanilides. *Org. Lett.* **2013**, *15* (22), 5654–5657. <https://doi.org/10.1021/ol402600r>.
- [40] Turka, S. Tandēmas sililgrupas 1,2-nobīdes – Ritera – tipa reakcijas pielietojums funkcionālizētu olefīnu sintēzē. Bakalaura darbs, Rīgas Tehniskā universitāte, 2025.
- [41] Rogaļevs, R. Sililgrupas 1,2-nobīdes – Ritera reakcijas kaskāde alilamīdu un dihidroizohinolīnu sintēzē. Bakalaura darbs, Rīgas Tehniskā universitāte, 2024.
- [42] Puriņš, M. Elektrofīlu Inducētas Pārgrupēšanās Reakcijas Propargilsilānos. Maģistra darbs, Rīgas Tehniskā universitāte, 2019.

- [43] Chen, M.-E.; Chen, X.-W.; Hu, Y.-H.; Ye, R.; Lv, J.-W.; Li, B.; Zhang, F.-M. Recent Advances of Ritter Reaction and Its Synthetic Applications. *Org. Chem. Front.* **2021**, 8 (16), 4623–4664. <https://doi.org/10.1039/d1qo00496d>.
- [44] Kahlenberg, L. On an Improved Method of Determining Latent Heat of Evaporation, and on the Latent Heat of Evaporation of Pyridine, Acetonitrile, and Benzonitrile. *J. Phys. Chem.* **1901**, 5 (4), 215–232. <https://doi.org/10.1021/j150031a001>.
- [45] Takao Maki, K. T. Benzoic Acid and Derivatives. *Ullmann's Encyclopedia of Industrial Chemistry*; 2012. <https://doi.org/10.1002/14356007.a03>.
- [46] Kalz, K. F.; Hausmann, A.; Dechert, S.; Meyer, S.; John, M. Solution Chemistry of *N, N'*-Disubstituted Amidines: Identification of Isomers and Evidence for Linear Dimer Formation. *Chem. Eur. J.* **2016**, 22 (50), 18190–18196. <https://doi.org/10.1002/chem.201603850>.

PATEICĪBAS

Šī darba tapšana nebūtu iespējama bez RTU Ķīmijas un ķīmijas tehnoloģijas institūta “propargilsilānu komandas”. Paldies Artjomam Ubaidullajevam, Rūdolfam Beļauņiem, Sandrai Turkai un Mikum Puriņam, kas sniedza būtisku ieguldījumu šī darba tapšanā! Vēlos pateikties arī darba vadītājam profesoram Mārim Turkam par idejām, motivēšanu un palīdzību sarežģītu sintētisko problēmu risināšanā! Paldies Anatolijam Mišņevam par monokristālu rentgenstaru difrakcijas analīzi!

Šis pētījums tika izstrādāts ar Latvijas Zinātnes padomes granta LZP-2023/1-0576 un Eiropas Savienības Atveseļošanas un noturības mehānisma finansētā projekta Nr. 5.2.1.1.i.0/2/24/1/CFLA/003 “Konsolidācijas un pārvaldības izmaiņu ieviešana Rīgas Tehniskajā universitātē, Liepājas Universitātē, Rēzeknes Tehnoloģiju akadēmijā un Latvijas Jūras akadēmijā un Liepājas Jūrmieciņas koledža virzībai uz izcilību augstākajā izglītībā, zinātnē un inovācijās” akadēmiskās karjeras doktorantūras granta (ID 1134) atbalstu.

DOCTORAL THESIS PROPOSED TO RIGA TECHNICAL UNIVERSITY FOR PROMOTION TO THE SCIENTIFIC DEGREE OF DOCTOR OF SCIENCE

To be granted the scientific degree of Doctor of Science (PhD), the present Doctoral Thesis has been submitted for defense at the open meeting of the RTU Promotion Council on 23 September 2026 at the Faculty of Natural Sciences and Technology of Riga Technical University, Paula Valdena iela 3/7, Room 272.

OFFICIAL REVIEWERS

Associate Professor Dr. chem. Eduards Baķis
University of Latvia, Latvia

Professor PhD Maria Asuncion Barbero Perez
University of Valladolid, Spain

Professor Dr. sc. Dean Marković
University of Rijeka, Croatia

DECLARATION OF ACADEMIC INTEGRITY

I hereby declare that the Doctoral Thesis submitted for review to Riga Technical University for promotion to the scientific degree of Doctor of Science (PhD) is my own. I confirm that this Doctoral Thesis has not been submitted to any other university for promotion to a scientific degree.

Rasma Kronkalne

(signature)

Date

The Doctoral Thesis has been prepared as a collection of thematically related scientific publications complemented by summaries in Latvian and English. The Doctoral Thesis unites three original research articles in SCI journals, one review, one manuscript in preparation and unpublished results. The scientific publications have been written in English.

CONTENTS

ABBREVIATIONS	56
GENERAL OVERVIEW OF THE THESIS.....	57
Relevance of the Topic	57
Aims and objectives.....	59
Scientific novelty and main results.....	60
Structure and volume of the Thesis	61
Publications and approbation of the Thesis	61
MAIN RESULTS OF THE THESIS	66
1.1. Propargyl silane heterocyclization by intramolecular O-/N-/S-nucleophile attack on β -silicon-stabilized allyl cation.....	67
1.2. Propargyl silane heterocyclization by reacting β -silicon stabilized allyl cations with arenes as internal C-nucleophiles	72
1.3. Synthesis of arylated heterocycles and dienes using diaryl- λ^3 -iodanes under copper-catalyzed conditions.....	80
1.4. Ritter-type reaction with β -silicon stabilized allyl cations.....	87
CONCLUSIONS	95
REFERENCES	97
ACKNOWLEDGEMENTS.....	102
PIELIKUMI / APPENDICES.....	103

Appendix I:	Kronkalne, R.; Beļunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. <i>J. Org. Chem.</i> , 2023 , 88 (19), 13857-13870. https://doi.org/10.1021/acs.joc.3c01481
Appendix II:	Ubaidullajevs, A.; Kronkalne, R.; Mishnev, A.; Turks, M. Synthesis of Substituted Chromanes and Tetrahydroquinolines via Tandem 1,2-Silyl Shift – Friedel–Crafts cyclization. <i>J. Org. Chem.</i> , 2026 , 91 (17), 5785–5810. https://doi.org/10.1021/acs.joc.5c03136
Appendix III:	Kronkalne, R.; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. <i>Beilstein J. Org. Chem.</i> , 2025 , 21, 1984-1994. https://doi.org/10.3762/bjoc.21.154
Appendix IV:	Kronkalne, R.; Turks, M. Recent Advances in Intramolecular C-N Bond Formation for Pyrrolidine Synthesis. <i>ChemistryOpen</i> , 2026 , 15 (6), e70182.

<https://doi.org/10.1002/open.70182>

- Appendix V: Kronkalne, R.; Turks, M. Experimental procedures for the synthesis of 1,3-oxazinan-2-one derivative and that of its starting materials. (*Unpublished results*)
- Appendix VI: Turka, S.; Kronkalne, R.; Rogaļevs, R.; Puriņš, M.; Mishnev, A.; Turks, M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives. (*Manuscript in preparation*)
- Appendix VII: Kronkalne, R.; Turks, M. Synthesis procedures and characterization data for iodinated chromane derivatives. (*Unpublished results*)

ABBREVIATIONS

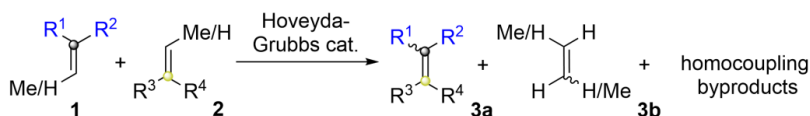
Ac	acetyl
Ar	aryl
B:	base
Boc	<i>t</i> -butyloxycarbonyl
Bu	butyl
Bz	benzoyl
Cbz	benzyloxycarbonyl
DBU	2,3,4,6,7,8,9,10-octahydropyrimido[1,2- <i>a</i>]azepine
DCE	1,2-dichloroethane
DCM	dichloromethane
DIAD	diisopropyl azodicarboxylate
DMAP	<i>N,N</i> -dimethylpyridin-4-amine
DMF	<i>N,N</i> -dimethylformamide
ECAC	ethyl 2-(3,4-dichlorophenyl)diazene-1-carboxylate
Et	ethyl
Hal	halogen
HFIP	1,1,1,3,3,3-hexafluoropropan-2-ol
NMR	nuclear magnetic resonance
Me	methyl
Mes	mesityl
Ms	methanesulfonyl
NBS	<i>N</i> -bromosuccinimide
NCS	<i>N</i> -chlorosuccinimide
NIS	<i>N</i> -iodosuccinimide
PCC	pyridinium chlorochromate
Ph	phenyl
Pr	propyl
Py	pyridine
Ns	<i>p</i> -nitrobenzenesulfonyl, nosyl
Su	succinimide
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
TFE	2,2,2-trifluoroethan-1-ol
Tf	trifluoromethanesulfonyl
THF	oxolane
Ts	<i>p</i> -toluenesulfonyl
XPhos	dicyclohexyl[2',4',6'-tris(propan-2-yl)[1,1'-biphenyl]-2-yl]phosphane

GENERAL OVERVIEW OF THE THESIS

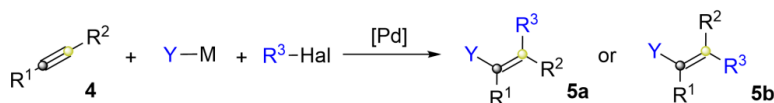
Relevance of the Topic

Olefins are a class of widespread carbofunctional compounds – they are ubiquitous motifs in both natural products and synthetic compounds.^[1–3] Olefins serve as precursors for countless organic transformations, enabling access to a broad spectrum of valuable products.^[4,5] The geometry of olefins and their substituents directly influences the properties of the resulting products, which is an important factor in bioactive compounds, polymers, and substrates for asymmetric catalysis.^[6] Despite this, the stereoselective synthesis of tri- and tetrasubstituted olefins remains challenging even in the 21st century.^[7] (*E/Z*)-selectivity is often determined by the relative size of substituents.^[8] The (*E*)-isomer is typically obtained as the thermodynamic product, whereas the synthesis of the energetically less favorable (*Z*)-alkenes is more problematic. Furthermore, many classical olefin synthesis methods, such as the Wittig reaction or the Julia-Kocienski olefination, exhibit limited applicability in the stereoselective synthesis of tri- and tetrasubstituted olefins.^[6,9] This motivates the development of alternative strategies for olefin synthesis, such as olefin metathesis (Scheme 1).^[10–12] For the synthesis of highly functionalized double bonds, reaction sequences that combine alkyne hydrometallation, carbometallation, or haloboration with cross-coupling reactions,^[13–16] as well as transition-metal-catalyzed alkyne hydroalkylation are also employed.^[6] Unfortunately, these methods are often not sufficiently stereoselective.^[6] Increasing mass efficiency in the synthesis of tri- and tetrasubstituted olefins also remains an important objective.^[17]

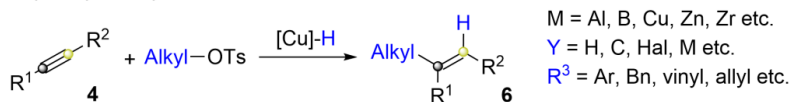
A) Olefin metathesis



B) Alkyne 1,2-difunctionalization

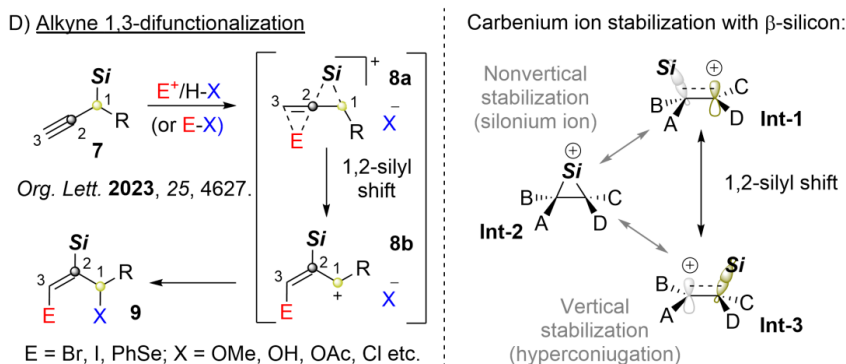


C) Alkyne hydroalkylation



Scheme 1. Contemporary strategies for stereoselective highly functionalized olefin synthesis.

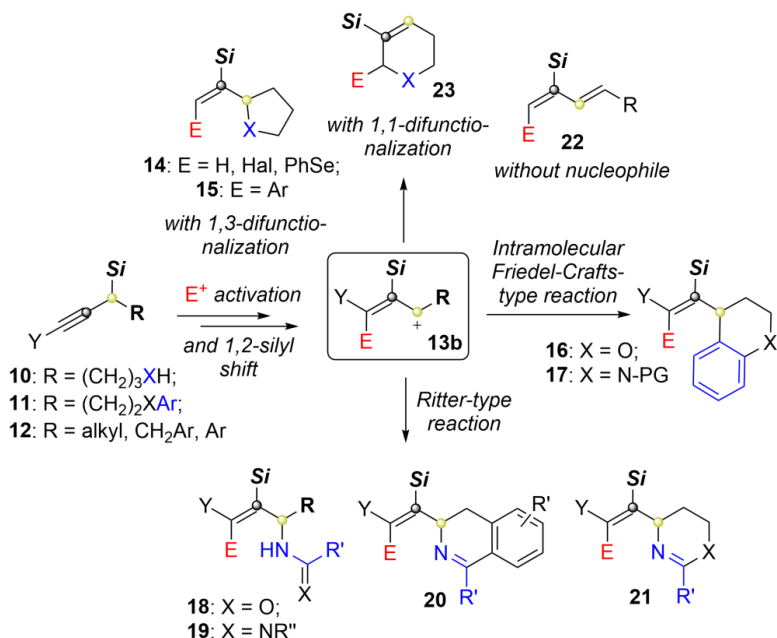
A new approach for the stereoselective synthesis of trisubstituted olefins **9** by 1,3-difunctionalization of propargyl silanes **7** was recently demonstrated by our group (Scheme 2).^[18, 19] In this approach, the propargylic system is activated with external electrophiles (Hal⁺, RSe⁺) to induce the 1,2-silyl shift.^[19] In many cases, formation of a β -silyl carbocation as the possible intermediate is facilitated by non-vertical stabilization (**Int-2**), which promotes migration of the silyl group toward formation of a more stabilized allyl cation.^[20, 21] These β -silicon-stabilized carbocation intermediates **8b** subsequently serve as building blocks for the incorporation of trisubstituted olefin fragments with high stereoselectivity.^[19]



Scheme 2. Alkyne difunctionalization by 1,2-silyl shift.

Although synthetic methods involving the 1,2-silyl shift have been known since the 1980s, examples of their application in the synthesis of stereodefined olefins containing three or more substituents remain limited. The concept of silicon rearrangement in the synthesis of heterocyclic structures has also been relatively underexplored.^[20, 21] The importance of heterocycles in organic chemistry is undeniable. Statistical data show that the majority of modern pharmaceuticals and agrochemicals contain at least one heterocyclic structural fragment.^[22] For example, in 2019, at least half of the drugs approved by the U.S. Food and Drug Administration (FDA) were heterocycle derivatives.^[23, 24] This drives continued interest in the development of new and efficient synthetic strategies for the preparation of functionalized heterocyclic structures, thereby expanding the diversity of accessible synthetic derivatives.^[25, 26]

Taking into account that silicon rearrangement in propargyl silanes remains a relatively underexplored topic in organic chemistry,^[20, 21] as well as the need for new methods for the synthesis of stereodefined, highly functionalized olefins and small-molecule heterocycles, the author set out to further develop the concept of 1,3-difunctionalization of propargyl silanes for the synthesis of heterocyclic structures containing a stereodefined olefin side chain (Scheme 3).



Scheme 3. General concept for the synthesis of highly functionalized olefin side chain-containing heterocycles from propargyl silanes **10-12**.

Aims and objectives

This Doctoral Thesis aims to develop a new methodology in organic synthesis for obtaining saturated and partially saturated heterocycles that contain a stereochemically defined, highly functionalized double bond in the side chain. This will be achieved by activating propargyl silanes with electrophiles to induce the 1,2-silyl shift, thus generating an allyl cation intermediate or its equivalent. Ring-closure will be achieved by subsequent attack of internal *O*-, *N*-, *S*-, or *C*-centered nucleophiles. In addition, the application of propargyl silanes under Ritter-type reaction conditions will be investigated, where a nitrile acts as the primary nucleophile toward a β -silicon-stabilized carbocation. The resulting nitrilium ion intermediate will be quenched by internal or external nucleophiles to afford products containing stereochemically defined allylamine fragments.

To achieve the aim of the study, several tasks were defined.

- 1) To investigate literature-reported methods for the synthesis of saturated heterocycles *via* intramolecular cyclization, identifying the advantages and limitations of existing methodologies, and to compile these findings in the form of a review article.

- 2) To participate in a collaborative project, directed towards the development of a synthetic methodology, which incorporates the 1,2-silyl shift and subsequent C-Het bond formation *via* internal *O*-, *N*-, or *S*-nucleophile attack on reactive β -silicon-stabilized allyl cation intermediates **13b**, to transform propargyl silanes **10** into five-membered heterocycles **14** – tetrahydrofurans (X = O), pyrrolidines (X = N-PG), and thiolanes (X = S).
- 3) To participate in a collaborative project aimed at adapting the propargyl silane heterocyclization methodology to a Friedel-Crafts-type reaction, in which the β -silicon-stabilized allyl cation **13b** reacts intramolecularly with aryl systems (C-nucleophiles) to form bicyclic partially saturated heterocycles **17**. To perform further modifications of the obtained tetrahydroquinolines **17** (X = N-PG) and their oxygen analogs **16** (X = O) to demonstrate their potential for further synthetic applications.
- 4) To participate in a collaborative project investigating the use of diaryl- λ^3 -iodanes as formal C-electrophiles for activation of propargyl silanes **10** and **12** under copper-catalyzed conditions, enabling the synthesis of arylated heterocyclic products **15** and **23**, as well as arylated silyl dienes **22**.
- 5) To study the induction of 1,2-silyl shift in propargyl silanes **10-12** under Ritter-type reaction conditions for the synthesis of various acyclic products **18-19** (X = O, N-PG) and cyclic products **20-21** containing highly functionalized C=C bonds.

Scientific novelty and main results

As a result of the conducted research, a synthetic methodology has been developed for the preparation of saturated and partially saturated heterocycles from propargyl silanes, incorporating a highly functionalized olefin side chain into the molecular framework. The key transformation underlying this methodology is the generation of β -silicon-stabilized allyl cations *via* 1,2-silyl shift, which occurs upon activation of the propargyl silane triple bond by strong electrophiles. The resulting reactive allyl cation intermediates are subsequently quenched by intramolecular nucleophiles, leading to the formation of a series of heterocyclic structures – tetrahydrofurans, pyrrolidines, thiolanes, tetrahydroquinolines, etc.

For the synthesis of tetrahydrofurans, pyrrolidines, and thiolanes, propargyl silanes containing internal *O*-, *N*-, and *S*-nucleophiles were synthesized starting from commercially available hex-5-yn-1-ol. These substrates were then activated in the presence of strong electrophiles (H^+ , Hal^+ , RSe^+), inducing a 1,2-silyl migration-heterocyclization sequence. Ring closure by formation of a C-Het bond occurs *via* intramolecular nucleophilic attack on the β -silicon-stabilized allyl cation. The obtained products contain heterocyclic motifs, such as

tetrahydrofuran, pyrrolidine and thiolane derivatives, which are prevalent in pharmaceuticals, and highly functionalized C=C bonds with excellent (*E*)-selectivity.

For the synthesis of bicyclic, partially saturated heterocycles – namely tetrahydroquinolines – the propargyl silane heterocyclization concept was adapted to an intramolecular Friedel-Crafts-type reaction. In this transformation, the allyl cation generated *via* 1,2-silyl migration is intramolecularly quenched by an electron-rich aryl system acting as a *C*-nucleophile. To enable this transformation, an aryl unit was introduced into the propargyl silane structure *via* a nitrogen linker. Functionalized aryl amide derivatives were synthesized from commercially available pent-4-yn-1-ol. The resulting bicyclic heterocycles contained highly functionalized olefin side chains with defined (*Z*)-geometry.

The use of diaryl- λ^3 -iodanes as formal *C*-electrophile sources under copper-catalyzed conditions was developed for arylation-heterocyclization sequences of propargyl silanes. This approach enabled the synthesis of tetrahydrofuran, pyrrolidine, and tetrahydropyridine derivatives bearing arylated side chains. This method provides an efficient route to heterocycles containing a functionalized styryl side chain, while reducing the total number of required synthetic steps compared to previously known strategies.

Activation of propargyl silanes with electrophiles under Ritter-type reaction conditions enabled the synthesis of dihydroisoquinoline and tetrahydropyrimidine derivatives, as well as acyclic products – amidines and allylamides – featuring highly functionalized C=C bonds. From an entropic standpoint, these transformations are particularly complex: in a multicomponent reaction, the sequential formation of four new covalent bonds was achieved in a single step, resulting in the formation of complex molecular structures from simple starting materials.

Structure and volume of the Thesis

The Doctoral Thesis is structured as a collection of thematically unified scientific publications dedicated to the use of propargyl silanes in the synthesis of small-molecule heterocycles containing highly functionalized olefin side chains, utilizing 1,2-silicon shift to generate β -silicon-stabilized allyl cation intermediates. The Thesis comprises one review article and three original research publications in SCI-indexed journals, one publication manuscript in preparation and related unpublished results.

Publications and approbation of the Thesis

The main results of the Doctoral Thesis have been published in three original scientific research articles. During the course of the doctoral study, one review article was also prepared. The research findings have been presented at 20 scientific conferences.

Scientific publications

1. **Kronkalne, R.**; Beļunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.*, **2023**, *88* (19), 13857–13870. Available from: <https://doi.org/10.1021/acs.joc.3c01481>
2. **Kronkalne, R.**; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. *Beilstein J. Org. Chem.*, **2025**, *21*, 1984–1994. Available from: <https://doi.org/10.3762/bjoc.21.154>
3. Ubaidullajevs, A.; **Kronkalne, R.**; Mishnev, A.; Turks, M. Synthesis of Substituted Chromanes and Tetrahydroquinolines *via* Tandem 1,2-Silyl Shift – Friedel–Crafts Cyclization. *J. Org. Chem.* **2026**, *91* (17), 5785–5810. Available from: <https://doi.org/10.1021/acs.joc.5c03136>
4. **Kronkalne, R.**; Turks, M. Recent Advances in Intramolecular C-N Bond Formation for Pyrrolidine Synthesis. *ChemistryOpen*, **2026**, *15* (6), e70182. Available from: <https://doi.org/10.1002/open.70182>
5. Turka, S.; **Kronkalne, R.**; Rogaļevs, R.; Puriņš, M.; Mishnev, A.; Turks, M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives. (*Manuscript in preparation*)

The results of the Thesis were presented at 20 conferences

1. **Kronkalne, R.**; Ubaidullajevs, A.; Turks, M. Synthesis of Fused Heterocycles by a Novel Cascade 1,2-Silyl Shift – Friedel–Crafts Cyclization. In: *Balticum Organicum Syntheticum 2026: Program and Abstract Book*, Estonia, Tallinn, June 28 – July 1, **2026**. Tallinn: 2026.
2. **Kronkalne, R.**; Beļunieks, R.; Sebris, A.; Turks, M. Copper-Catalyzed Arylation and Subsequent Cyclization of Terminally Functionalized Propargyl Silanes. In: *83rd International Scientific Conference of the University of Latvia 2025, Chemistry Section and Section of Institute of Chemical Physics: Book of Abstracts*, Latvia, Riga, February 14, **2025**. Riga: University of Latvia, 2025, p. 40. ISBN 978-9934-36-369-6. Available from: <https://doi.org/10.22364/iscul.83.cs.ba>
3. **Kronkalne, R.**; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Copper-Catalyzed Arylation of Propargyl Silanes with Iodanes Featuring 1,2-Silyl Shift and Cascade Cyclization. In: *ISySyCat: International Symposium on Synthesis and Catalysis 2025*:

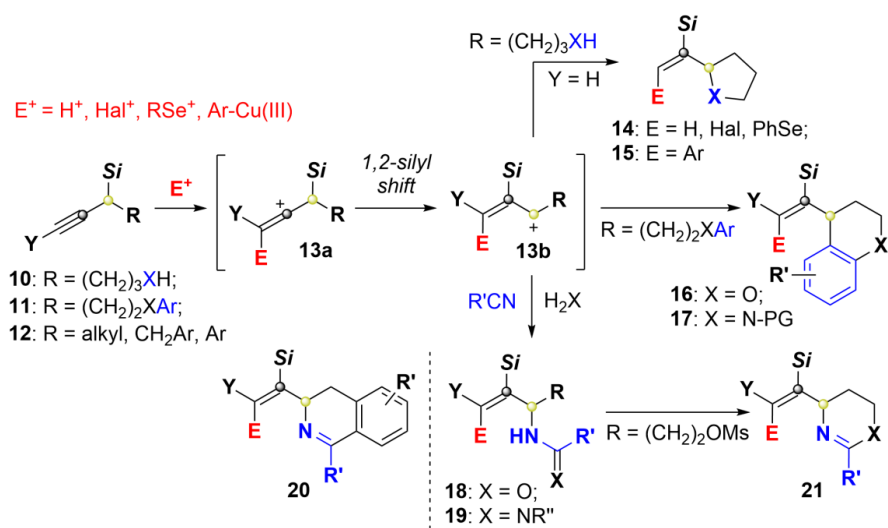
- Book of Abstracts*, Portugal, Coimbra, September 2–5, **2025**. Coimbra: 2025, p. 206. ISBN 978-989-95050-9-4
4. **Kronkalne, R.**; Turks, M. Copper-Catalyzed Arylation of Propargyl Silanes with Iodanes Featuring the 1,2-Silyl Shift. In: *Paul Walden 14th Symposium on Organic Chemistry: Program and Abstract Book*, Latvia, Riga, September 25–26, **2025**. Riga: 2025, p. 63.
 5. Rogaļevs, R.; Turka, S.; **Kronkalne, R.**; Ubaidullajevs, A.; Puriņš, M.; Turks, M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives. In: *International Symposium on Synthesis and Catalysis (ISySyCat 2025): Book of Abstracts*, Portugal, Coimbra, September 2–5, **2025**. Coimbra: 2025, p. 200.
 6. Ubaidullajevs, A.; **Kronkalne, R.**; Turks, M. Synthesis of Substituted Chromanes via Tandem 1,2-silyl shift – Friedel–Crafts Cyclization. In: *82nd International Scientific Conference of the University of Latvia: Organic Chemistry Session*, Latvia, Riga, March 15, **2024**. Riga: 2024, p. 8.
 7. Ubaidullajevs, A.; **Kronkalne, R.**; Turks, M. Synthesis of Vinyl Chromanes from Propargyl Silanes via Tandem Electrophilic Activation – 1,2-Silyl Shift – Friedel–Crafts Cyclization. In: *24th Tetrahedron Symposium*, France, Montpellier, June 18–21, **2024**. Montpellier: 2024.
 8. Ubaidullajevs, A.; **Kronkalne, R.**; Gercāns, K.; Mishnev, A.; Turks, M. Synthesis of Fused Heterocycles by a Novel 1,2-Silyl Shift – Friedel–Crafts Domino Process. In: *29th International Society of Heterocyclic Chemistry Congress: Program*, Portugal, Aveiro, July 21–26, **2024**. Aveiro: 2024, p. 5.
 9. Ubaidullajevs, A.; **Kronkalne, R.**; Gercāns, K.; Turks, M. Synthesis of Fused Heterocycles via Cascade 1,2-Silyl Shift – Friedel–Crafts Cyclization. In: *Balticum Organicum Syntheticum 2024: Program and Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 157.
 10. **Kronkalne, R.**; Ubaidullajevs, A.; Beļuniekš, R.; Turks, M. Expanding the Possibilities for Heterocycle Synthesis by Propargyl Silane Cyclization via the 1,2-Silyl Shift. In: *Balticum Organicum Syntheticum 2024: Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 79.
 11. **Kronkalne, R.**; Ubaidullajevs, A.; Beļuniekš, R.; Turks, M. Inducing 1,2-Silyl Migration in Propargyl Silanes for the Synthesis of 5- and 6-Membered Heterocycles. In: *24th Tetrahedron Symposium*, France, Montpellier, June 18–21, **2024**. Montpellier: 2024.

12. Sebris, A.; Beļauņieks, R.; **Kronkalne, R.**; Turks, M. Copper-Catalyzed Arylation of Propargyl Silanes with Consequent Internal Cyclization. In: *Balticum Organicum Syntheticum 2024: Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 139.
13. Turks, M.; **Kronkalne, R.**; Ubaidullajevs, A.; Beļauņieks, R.; Sebris, A.; Puriņš, M.; Rogaļevs, R. One, Two, Three, Go: Novel Applications of 1,2-Silyl Shift for 1,3-Difunctionalization of Propargyl Silanes. In: *Balticum Organicum Syntheticum 2024: Abstract Book*, Latvia, Riga, July 7–10, **2024**. Riga: 2024, p. 156.
14. Turks, M.; Beļauņieks, R.; **Kronkalne, R.**; Ubaidullajevs, A.; Līpiņa, R. Synthesis of Allylic Systems and Heterocycles with Highly Functionalized Olefin Side Chain from Propargyl Silanes via 1,2-Silyl Shift. In: *International Symposium on Synthesis and Catalysis 2023: Program and Abstract Book*, Portugal, Evora, September 5–8, **2023**. Evora: 2023, p. 16.
15. **Kronkalne, R.**; Beļauņieks, R.; Turks, M. Electrophile-Induced 1,2-Silyl Migration in Propargyl Silanes: a Pathway towards Saturated Heterocycles. In: *13th Paul Walden Symposium on Organic Chemistry: Program and Abstract Book*, Latvia, Riga, September 14–15, **2023**. Riga: 2023, p. 45.
16. **Kronkalne, R.**; Ubaidullajevs, A.; Beļauņieks, R.; Turks, M. Electrophile-Induced 1,2-Silyl Shift in Terminally Functionalized Propargyl Silanes for the Synthesis of Small Heterocycles. In: *International Symposium on Synthesis and Catalysis 2023: Book of Abstracts*, Portugal, Evora, September 5–8, **2023**. Evora: 2023, p. 244.
17. **Kronkalne, R.**; Beļauņieks, R.; Ubaidullajevs, A.; Turks, M. Use of Terminally Functionalized Propargyl Silanes for the Synthesis of Various 5-Membered Heterocycles via 1,2-Silyl Migration. In: *81st International Scientific Conference of the University of Latvia: Organic Chemistry Session*, Latvia, Riga, March 17, **2023**. Riga: 2023, p. 14.
18. Turks, M.; Beļauņieks, R.; **Kronkalne, R.**; Puriņš, M.; Līpiņa, R.; Ubaidullajevs, A.; Rogaļevs, R. Synthesis of Allylic Systems or Heterocycles with Highly Functionalized Olefin Side Chain from Propargyl Silanes via 1,2-Silyl Migration. In: *ACS Fall 2023 – Sessions*, United States of America, San Francisco, August 13–17, **2023**. San Francisco: 2023, p. 3915259.
19. Ubaidullajevs, A.; **Kronkalne, R.**; Turks, M. Tandem 1,2-silyl shift – Friedel–Crafts Synthetic Approach to Substituted Vinyl Chromanes. In: *13th Paul Walden Symposium: Program and Abstracts*, Latvia, Riga, September 14–15, **2023**. Riga: 2023, p. 35.
20. **Kronkalne, R.**; Beļauņieks, R.; Turks, M. Heterocyclization of Terminally Functionalized C6-Chain Containing Propargyl Silanes via 1,2-Silyl Shift.

In: *Materials Science and Applied Chemistry 2022: Programme and Abstract Book*,
Latvia, Riga, October 21, **2022**. Riga: 2022, p. 4.

MAIN RESULTS OF THE THESIS

The concept of propargyl silane heterocyclization is based on the generation of β -silicon-stabilized carbocations through the addition of a strong electrophile (E^+) to the triple bond. The initially formed vinyl cation **13a** undergoes rearrangement *via* 1,2-silyl shift to form the more stable allyl cation **13b**. Subsequent quenching by intramolecular nucleophiles (heteroatoms or $C(sp^2)$) leads to cyclic structures bearing a functionalized olefin side chain (Scheme 4).

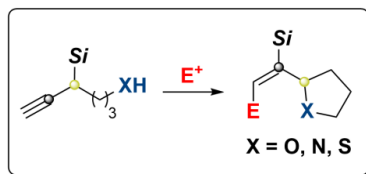


Scheme 4. Main research directions for heterocycle synthesis from propargyl silanes **10-12**.

Within the scope of this Thesis, the following transformations are investigated:

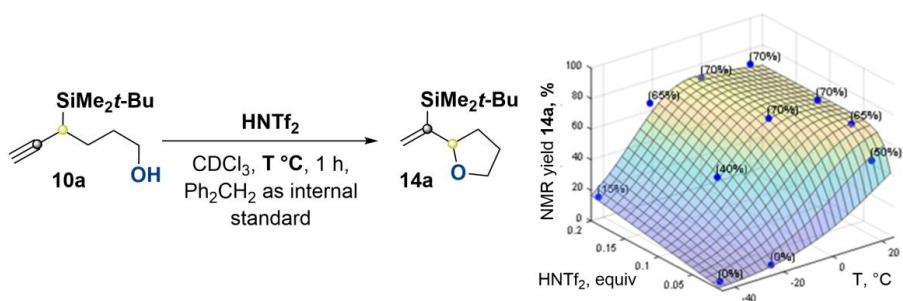
- electrophile-induced 1,2-silyl shift-heterocyclization of propargyl silanes containing internal *O*-, *N*-, or *S*-nucleophiles for the synthesis of five-membered heterocycles **14** – tetrahydrofurans ($X = O$), pyrrolidines ($X = N-PG$), and thiolanes ($X = S$);
- intramolecular Friedel-Crafts-type reactions for the synthesis of tetrahydroquinolines **17** ($X = N-PG$), and further synthetic modifications of the obtained products **17** and their oxygen analogs **16**;
- copper-catalyzed arylation-heterocyclization reactions using diaryl- λ^3 -iodanes as formal Ar^+ synthons ($E^+ = Ar-Cu(III)$);
- Ritter-type reactions for the synthesis of functionalized allylamines **18** ($X = O$), amidines **19** ($X = NR''$), dihydroisquinolines **20**, and tetrahydropyrimidines **21** ($X = N-PG$).

1.1. Propargyl silane heterocyclization by intramolecular O-/N-/S-nucleophile attack on β -silicon-stabilized allyl cation



In previous studies, it was demonstrated that under electrophilic activation conditions (Brønsted acids or Hal^+), propargyl silanes can generate reactive allyl cation synthons. These intermediates can be further utilized in the synthesis of silyl dienes or indenenes,^[18] 1,3-difunctionalized olefins,^[19] sulfolenes,^[27] and other valuable products.^[28] Within the scope of this study, the author sought to expand the application of propargyl silanes by adapting this concept to the synthesis of small-molecule heterocycles. For this purpose, in collaboration with Rūdolfs Beļāuniņš and Artjoms Ubaidullajevs, a heterocyclization strategy was developed in which an allyl cation is generated *via* electrophile-induced 1,2-silyl migration and then intramolecularly trapped by a heteroatom nucleophile (*O*, *N*, *S*). This enables the synthesis of various five-membered heterocycles.^[29] The findings of this study were partially discussed within the framework of R. Beļāuniņš' Thesis, but the core process of synthetic methodology was developed within this Thesis.^[30]

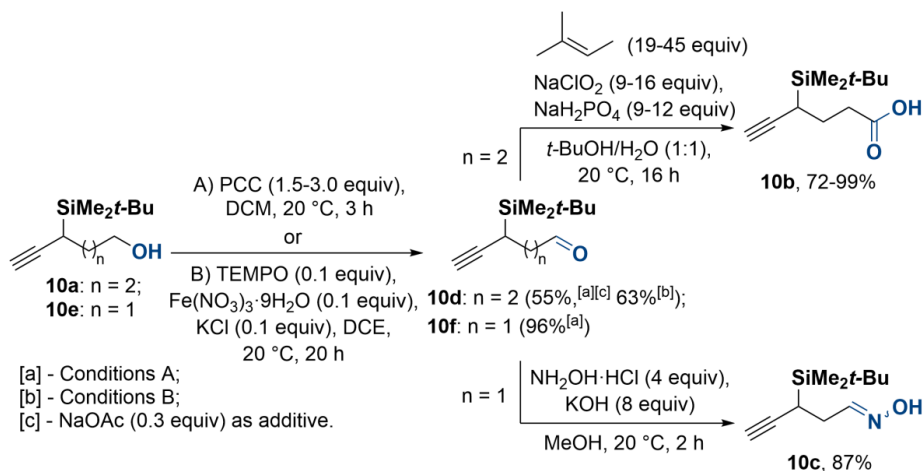
The key starting material for tetrahydrofuran synthesis was 4-(tert-butyldimethylsilyl)hex-5-yn-1-ol (**10a**), which was obtained from *O*-silylated commercially available hex-5-yn-1-ol using the retro-Brook rearrangement procedure described by Wang and Gao.^[31] Subsequent activation of propargyl silane **10a** with Brønsted acids (HNTf_2 or TfOH) afforded the heterocyclization product **14a**.



Scheme 5. Optimization of reaction conditions for Brønsted acid-catalyzed propargyl silane **10a** heterocyclization.

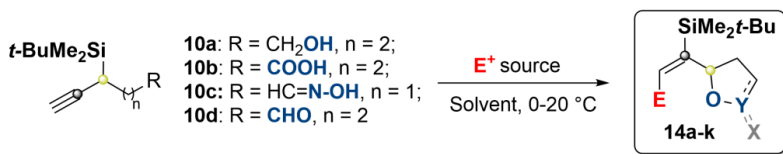
The main conclusions from the Brønsted acid-catalyzed reaction optimization were as follows: 1) the optimal temperature for tetrahydrofuran synthesis was 0–20 °C; 2) the optimal catalyst loading was 10–20 mol%; 3) the solvent choice was influenced by their leveling effects, where aprotic solvents CDCl₃ and CD₂Cl₂ afforded the highest yields (**14a**, 70 % NMR), but in benzene-d₆ and CD₃NO₂ the yields were lower (65 % and 50 % of **14a**, respectively); 4) under optimal reaction conditions (0.2 equiv H⁺, CDCl₃, 0 °C, 1 h) HNTf₂ and TfOH afforded similar yields (70 % by NMR), whereas conc. H₂SO₄ was unreactive. A detailed correlation between acid catalyst loading (Tf₂NH, equiv) and reaction temperature with tetrahydrofuran **14a** NMR yield is graphically depicted in Scheme 5.

Other oxygen nucleophile-containing propargyl silanes **10b–f** were synthesized by modifying alcohol **10a** and its C5-chain analogue **10e**, as it is depicted in Scheme 6. Alcohol **10e** itself was prepared according to the method described by Wang and Gao using commercial pent-4-yn-1-ol.^[31]

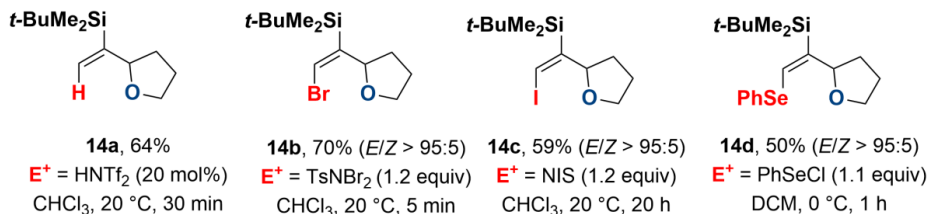


Scheme 6. Synthesis of oxygen nucleophile-containing propargyl silanes **10b–f**.

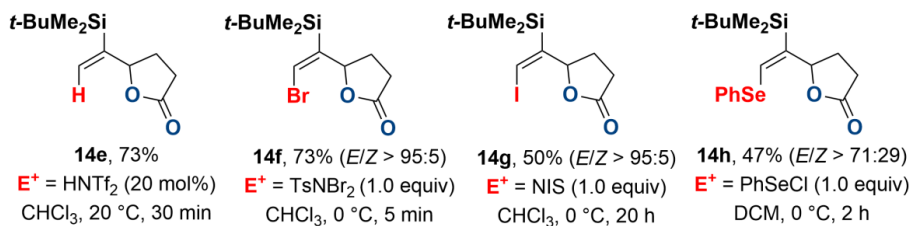
Under optimized conditions, cyclization of propargyl silanes **10a–d** containing internal oxygen nucleophiles was performed (Scheme 7). Using electrophilic halogenating reagents to induce 1,2-silyl migration, such as TsNBr₂, *N*-bromosuccinimide (NBS), *N*-iodosuccinimide (NIS) or PhSeCl, heterocycles bearing functionalized vinyl halide or vinyl selenide side chains were obtained. Alcohol **10a** afforded tetrahydrofuran derivatives **14a–d** in yields of 50–70 %, carboxylic acid **10b** cyclized to lactone derivatives **14e–h** (47–73 % yields), whereas oxime **10c** gave 4,5-dihydroisoxazole derivatives **14i–j** (29–32 % yields). Aldehyde **10d**, upon cyclization with NBS in the presence of water, produced hemiacetal **14k** (30 % yield).



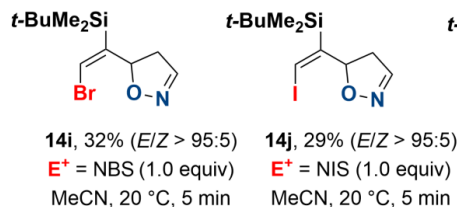
From alcohol **10a** (R = CH_2OH , n = 2):



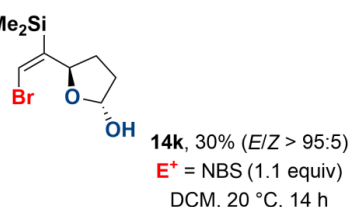
From carboxylic acid **10b** (R = COOH , n = 2):



From oxime **10c** (R = HC=N-OH , n = 1):



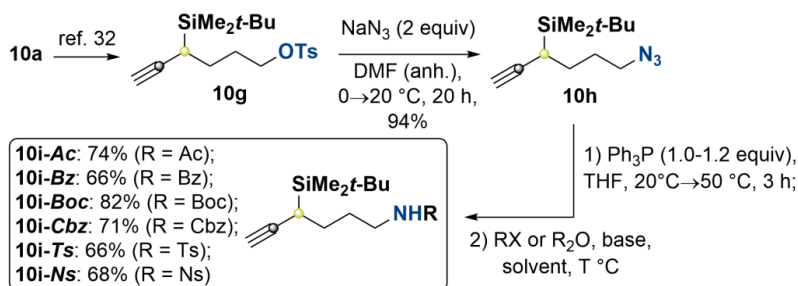
From aldehyde **10d** (R = CHO , n = 2):



Scheme 7. Heterocyclization of oxygen nucleophile-containing propargyl silanes **10a-d**.

The alcohol-containing propargyl silane **10a** was further modified to obtain substrates bearing nitrogen nucleophiles **10i** (Table 1). Tosylate **10g** was prepared according to a literature procedure.^[32] Subsequent azidation followed by reduction of azide **10h** under Staudinger conditions, and installation of an *N*-protecting group, yielded amides **10i-Ac** and **10i-Bz**, carbamates **10i-Boc** and **10i-Cbz**, as well as sulfonamides **10i-Ts** and **10i-Ns**.

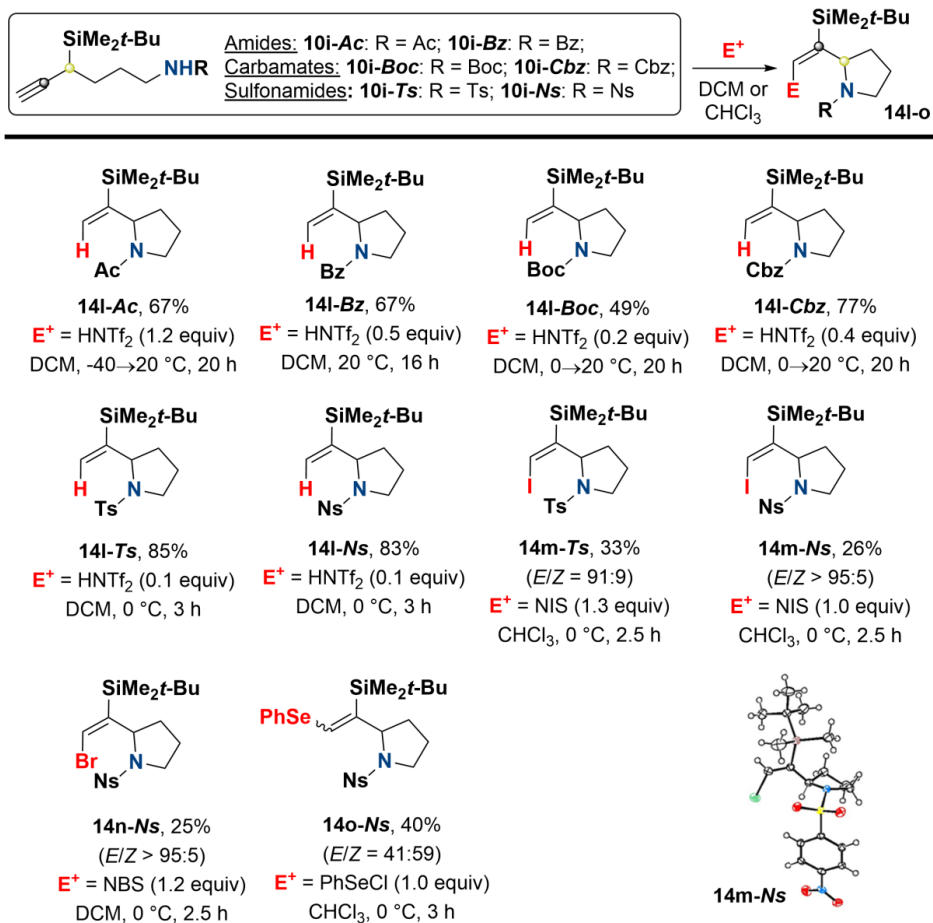
Table 1

Synthesis of propargyl silanes **10i** bearing internal nitrogen nucleophiles

Entry	RX/R ₂ O (equiv)	Base/additive (equiv)	Solvent	T (°C)	t (h)	Product yield
1	Ac ₂ O (2.0)	DMAP (0.5)	Py	0–20	16	10i-Ac , 74 %
2	Bz ₂ O (2.0)	DMAP (1.0)	DMF	60	22	10i-Bz , 66 %
3	Boc ₂ O (1.2)	NaHCO ₃ (3.0)	THF/H ₂ O (1:1)	0–20	14	10i-Boc , 82 % ^[a]
4	Cbz-OSu (1.2)	NaHCO ₃ (2.7)	MeCN/H ₂ O (1:1)	0–20	16	10i-Cbz , 71 %
5	TsCl (2.0)	Et ₃ N (5.0)	DCM	0–20	6	10i-Ts , 66 %
6	NsCl (2.0)	Et ₃ N (5.0)	DCM	0–20	6	10i-Ns , 68 %

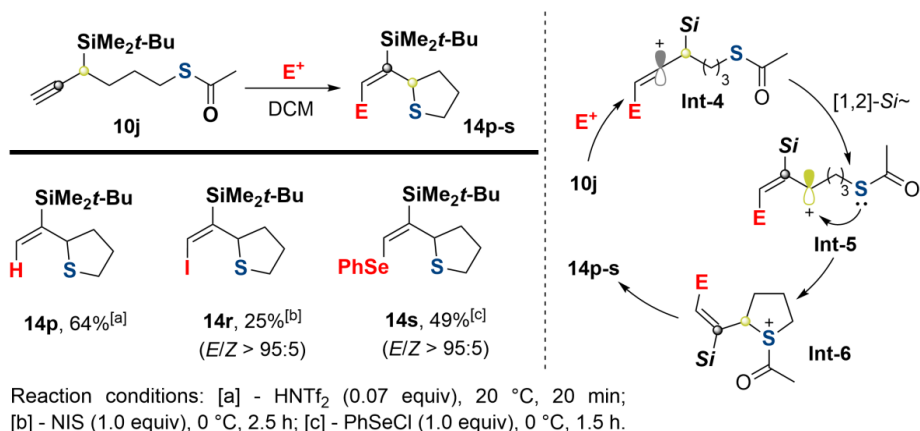
^[a] THF/H₂O (1:1) solvent system and 1 h stirring time for the reduction step.

In the presence of strong electrophiles (H⁺, Hal⁺, RSe⁺), *N*-nucleophile-containing propargyl silanes **10i** cyclized to give pyrrolidine derivatives **14l-o** (Scheme 8). Under HNTf₂-catalyzed conditions, sulfonamides **10i** (R = Ts, Ns) gave the highest yields of pyrrolidine **14l** (83–85 %). Carbamates **10i** (R = Boc, Cbz) and amides **10i** (R = Ac, Bz) gave yields in the range of 49–77 %. By using electrophilic halogenating reagents (NIS, NBS) to activate the propargylic system, the obtained yields were lower (25–33 %), but the products **14m-n** contained highly functionalized olefin side chains with (*E/Z*)-selectivity of 91:9 to 95:5. The absolute geometry of the trisubstituted double bonds in products **14m-n** was confirmed using 2D NOESY nuclear Overhauser effect spectroscopy (NOESY), where a correlation signal between C=C-H and *t*-BuMe₂Si-group was observed for the (*E*)-isomer. Single-crystal X-ray diffraction (SCXRD) analysis of compound **14m-Ns** confirmed the previous findings. When PhSeCl was used as the electrophile source, pyrrolidine **14o** was obtained as an (*E/Z*) mixture (41:59). This can be explained by the additional stabilization provided by the α-selenium effect to the intermediate allyl cation, which affords more time for isomerization before the allyl cation is quenched by an internal nucleophile.



Scheme 8. Synthesis of nitrogen heterocycles **14l-o**.

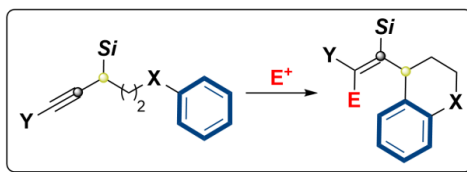
For the synthesis of sulfur-containing heterocycles, thioacetate **10j** was used as the starting material (Scheme 9). It was obtained by reacting tosylate **10g** with potassium thioacetate (KSAC) in acetonitrile (20°C , 16 h, 87 % yield). Cyclization proceeded most efficiently under HNTf₂-catalyzed conditions, yielding thiolane **14p** (64 %). Lower yields of thiolanes **14r-s** (25–49 %) were obtained when electrophilic reagents (NIS, PhSeCl) were used to generate products **14r-s** containing trisubstituted olefin side chains. The cyclization likely proceeds *via* a sulfonium ion intermediate **Int-6**, which releases the thiolane product **14p-s**.



Scheme 9. Synthesis of thiolanes from thioacetate **10j**.

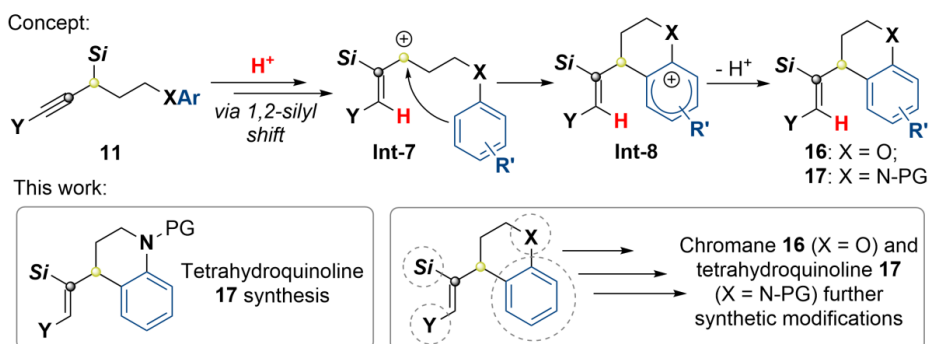
The author can conclude from these results that β -silicon-stabilized allyl cations may be quenched intramolecularly by *O*-, *N*- and *S*-nucleophiles to obtain five-membered heterocycles, which contain geminally disubstituted or stereodefined trisubstituted olefin side chains. By activating propargyl silanes with electrophilic halogenating reagents (NBS, NIS), olefins with high (*E/Z*)-selectivity (up to 95:5) are obtained. Full details of this research are described in the publication Kropkalne, R.; Beļunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.*, **2023**, 88 (19), 13857–13870 (Appendix 1).^[29]

1.2. Propargyl silane heterocyclization by reacting β -silicon stabilized allyl cations with arenes as internal C-nucleophiles



In the previous section, it was demonstrated that allyl cations generated *via* 1,2-silyl migration can be intramolecularly quenched to form new C-O, C-N, and C-S bonds. This section is devoted to an analogous transformation in which heterocyclization proceeds *via* intramolecular C-C bond formation in a Friedel-Crafts-type reaction (Scheme 10). Intramolecular trapping of the

allyl cation intermediate **Int-7** by an electron-rich aryl system enables the synthesis of bicyclic structures. In collaboration with A. Ubaidullajevs, a method was developed for the synthesis of bicyclic heterocycles, namely chromanes **16** (X = O) and tetrahydroquinolines **17** (X = N-PG).^[33] Within this Thesis, the focus is on the synthesis of tetrahydroquinolines **17** from propargyl silanes, as well as the demonstration of further synthetic transformations of both chromanes **16** (X = O) and tetrahydroquinolines **17** (X = N-PG).



Scheme 10. The concept for propargyl silane **11** cyclization in a Friedel-Crafts-type reaction and further modification possibilities of products **16** and **17**.

1.2.1. Synthesis of tetrahydroquinolines from propargyl silanes

Propargyl silanes **11a-f** bearing an aniline functionality were identified as the key starting materials for tetrahydroquinoline synthesis. One approach to their preparation involved the Mitsunobu reaction between nosyl group-bearing anilines (ArNHNs) and the alcohol functionality-bearing silane **10e**. This allowed the preparation of key intermediates **11a-d** in yields of 66–75 % (Table 2).

Table 2

Synthesis of propargyl silanes bearing the *N*-nosylaniline functionality under Mitsunobu reaction conditions

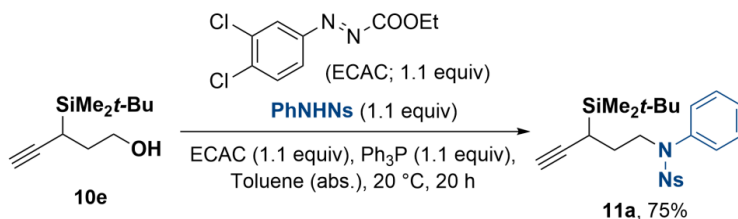
10e $\xrightarrow[\text{DIAD (1.1 equiv), Ph}_3\text{P (1.0 equiv), THF (abs.), 0-20}^\circ\text{C}]{\text{ArNHNs (1.0 equiv)}}$ 11a-d

11a: R = H;
11b: R = 3-Me;
11c: R = 4-Br;
11d: R = 4-MeO

Entry ^[a]	Ar	Time (h)	Product (%) ^[b]
1	Ph	21.0	11a , 66
2	<i>m</i> -MeC ₆ H ₄	15.0	11b , 67
3	<i>p</i> -BrC ₆ H ₄	15.5	11c , 75
4	<i>p</i> -MeOC ₆ H ₄	17.0	11d , 74

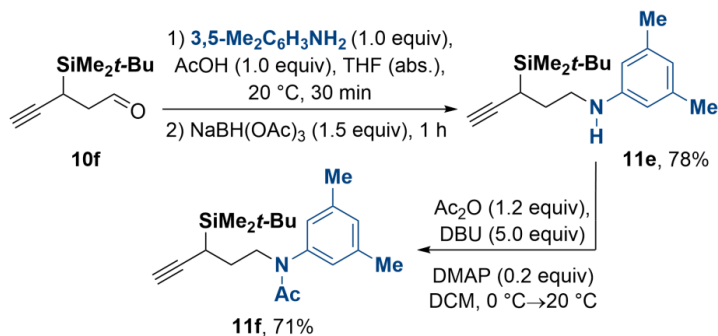
^[a] All reactions were performed on a 2.5 mmol scale. ^[b] Isolated yield.

It was later found that replacing DIAD with ECAC, which is a second-generation Mitsunobu reagent, improved the yields of tertiary amines (Scheme 11). For example, in the case of compound **11a**, the yield increased from 66 % (with DIAD) to 75 % (with ECAC). The same conditions were used by A. Ubaidullajevs for the preparation of oxygen-bridged analogues **11** (Y = H, X = O).^[33]



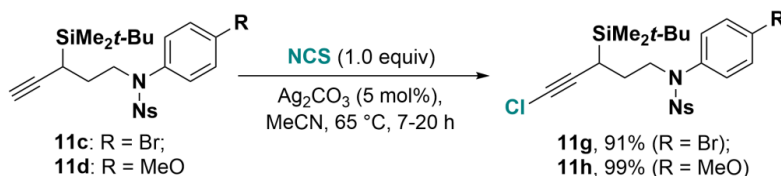
Scheme 11. Synthesis of propargyl silane **11a** bearing the *N*-nosylaniline functionality using the ECAC reagent.

The Mitsunobu strategy was applicable only to anilines bearing strongly electron-withdrawing sulfonyl protecting groups. When less electron-withdrawing groups (e.g., Ac) were used, the reaction did not proceed. To obtain propargyl silanes **11f** functionalized with acetamide groups, a reductive amination strategy was employed (Scheme 12). Aldehyde **10f** was reacted with 3,5-dimethylaniline in the presence of acetic acid to form an imine intermediate. The imine was reduced using NaBH(OAc)₃ to give product **11e**. Subsequent acetylation afforded the *N*-acetylated product **11f**.



Scheme 12. Synthesis of propargyl silanes **11f** bearing the acetamide functionality by employing the reductive amination strategy.

To obtain terminally halogenated substrates **11g-h**, propargyl silanes **11c-d** were treated with an equimolar amount of NCS in the presence of a silver catalyst (Ag_2CO_3 , 5 mol%). The chlorinated propargyl silanes **11g-h** were obtained in excellent yields (91–99 %) (Scheme 13).

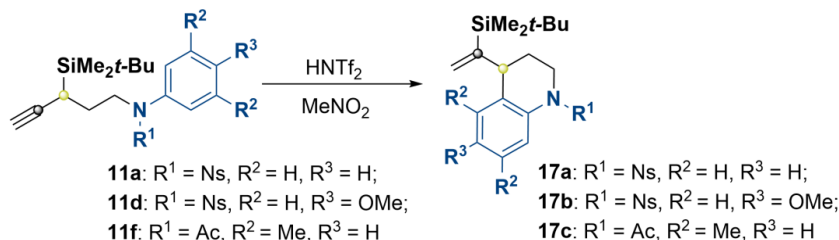


Scheme 13. Synthesis of terminally halogenated propargyl silanes **11g-h**.

Next, the author explored the cyclization reactions of aniline-functionalized propargyl silanes **11** to transform them into tetrahydroquinoline **17** derivatives (Table 3). The reactions were performed in nitromethane (MeNO_2), using HNTf_2 for activation of the propargylic moiety. Reaction optimization revealed that HNTf_2 is most effective when used in equimolar amounts or even in slight excess. Similar trends were observed in chromane **16** synthesis by A. Ubaidullajevs, where the reaction yields improved by increasing the HNTf_2 loading.^[33]

Table 3

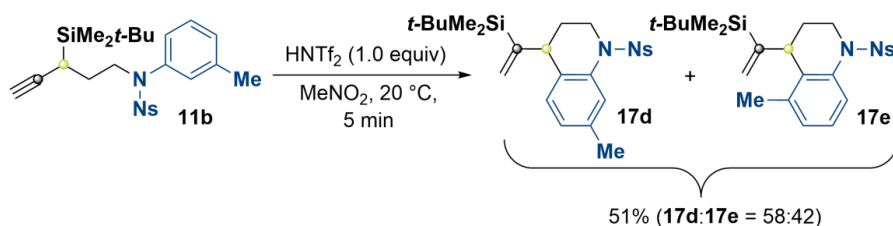
Synthesis of tetrahydroquinolines **17a-c** from propargyl silanes **11a**, **11d** and **11f**



Entry ^[c]	Silane	HNTf_2 (equiv)	T (°C)	t (min)	11 (%) ^[a]	Product (%)
1	11a	0.2	50	10	53	17a , 15 ^[a]
2	11a	0.2	0→20	70	55	17a , 15 ^[a]
3	11a	0.2	0→20	1020	11	17a , 12 ^[a]
4	11a	1.0	0	60	0	17a , 41 ^[a] (40 ^[b])
5	11d	1.0	20	5	0	17b , 47 ^[a] (43 ^[b])
6	11f	1.0	20	5	40	17c , 10 ^[a]
7	11f	3.0	20	30	0	17c , 47 ^[a] (45 ^[b])

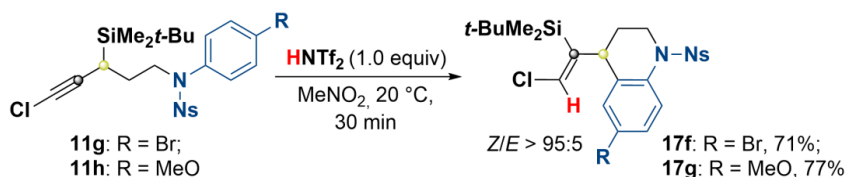
^[a] NMR yield. ^[b] Isolated yield. ^[c] All reactions were performed on a 0.1–0.4 mmol scale.

In the case of unsymmetrically substituted aniline **11b**, cyclization with HNTf_2 produced a mixture of regioisomers **17d/17e** in a ratio of 58:42 (Scheme 14).



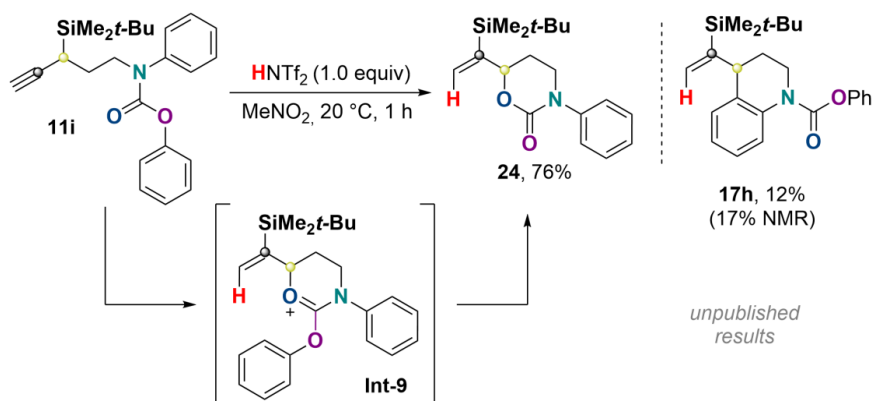
Scheme 14. Synthesis of isomeric tetrahydroquinolines from unsymmetrically substituted aniline **11b**.

Cyclization of terminally halogenated substrates **11g-h** proceeded with excellent *Z/E* selectivity, yielding tetrahydroquinolines **17f-g** in 71–77 % yields (Scheme 15).



Scheme 15. Synthesis of tetrahydroquinolines **17f-g** from terminally halogenated propargyl silanes.

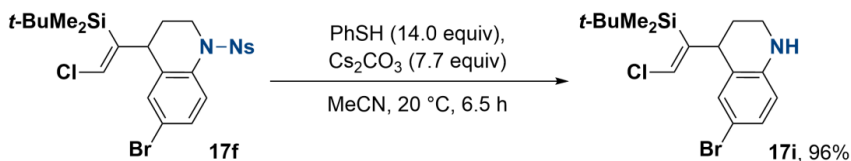
Unexpected reactivity was observed during the attempts to cyclize the carbamate-protected aniline **11i**. The major reaction product was 1,3-oxazinan-2-one derivative **24**, which was isolated in 76 % yield, whereas only small quantities of tetrahydroquinoline **17h** were obtained (17 % by NMR). This suggests that under these conditions, an alternative cyclization pathway becomes favorable, likely involving intermediate **Int-9**, which decomposes to product **24** (Scheme 16).



Scheme 16. Synthesis of 1,3-oxazinan-2-one derivative **24**.

1.2.2. Further modifications of the obtained tetrahydroquinoline and chromane derivatives

Firstly, the author aimed to access tetrahydroquinoline products containing a free N-H group from the previously synthesized tetrahydroquinoline **17f**. Under typical nosyl group deprotection conditions, combining thiophenol (PhSH) and a base (Cs₂CO₃), tetrahydroquinoline **17i** was obtained in 96 % yield, which possesses potential for further *N*-functionalization (Scheme 17).

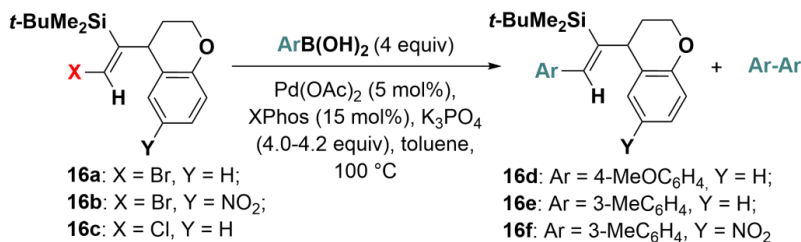


Scheme 17. Synthesis of tetrahydroquinoline **17i** by nosyl group deprotection.

For the modification of chromanes **16a-c**, Suzuki-Miyaura cross-coupling reactions were performed (Table 4). Cross-coupling of vinyl bromide **16a** with 4-methoxyphenylboronic acid afforded styrene derivative **16d**. The latter was difficult to separate from the homocoupling by-product (4,4'-dimethoxy-1,1'-biphenyl) due to similar polarity, resulting in a low isolated yield (**16d**, 6 %). In contrast, 3-methylphenylboronic acid reacted with vinyl bromides **16a-b** to give more easily separable products, and styrenes **16e-f** were isolated in high yields (92–97 %). As expected, vinyl chloride **16c** afforded significantly lower cross-coupling product yields (**16e**, 27 %) than its brominated analogues **16a-b**.

Table 4

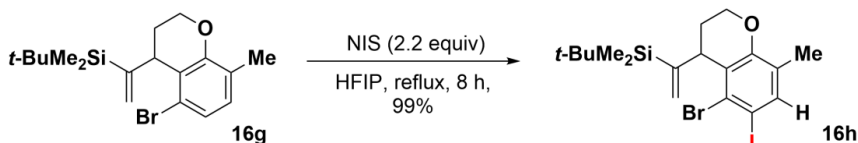
The application of chromanes **16a-c** in Suzuki-Miyaura cross-coupling reactions



Entry	X	Y	Ar	Time (h)	Product (%)
1 ^{[c][d]}	Br	H	4-MeOC ₆ H ₄	14	16d , 45 ^[a] , 6 ^[b]
2	Br	H	3-MeC ₆ H ₄	44	16e , 97 ^[b]
3	Br	NO ₂	3-MeC ₆ H ₄	22	16f , 92 ^[b]
4	Cl	H	3-MeC ₆ H ₄	26	16e , 27 ^[b]

^[a] NMR yield (%). ^[b] Isolated yield (%). ^[c] The cross-coupling product **16d** formed an inseparable mixture with the homocoupling product (Ar-Ar). ^[d] Modified reaction conditions were used: 3 equiv ArB(OH)₂, 7 mol% Pd(OAc)₂, 21 mol% XPhos, 4.9 equiv K₃PO₄.

Similarly to previous studies,^{[19], [29]} the author attempted a silicon-halogen exchange in chromane **16g** using NIS in hexafluoroisopropanol (HFIP). Unexpectedly, even with an excess of NIS (2.2 equiv) and under reflux conditions, *Si*→*I* exchange did not occur. Instead, monoiodination of the aromatic ring afforded product **16h** in quantitative yield (Scheme 18).

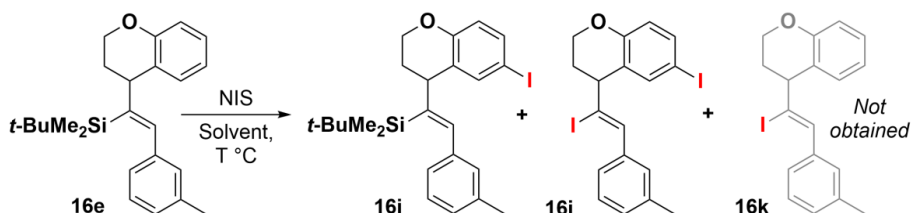


Scheme 18. Synthesis of monoiodinated product **16h**.

The electrophilic *Si*→*Hal* exchange is achieved through silicon-directed addition of an electrophilic species (Hal^+) to the vinyl silane $\text{R}_2\text{C}=\text{C}(\text{Si})\text{-R}'$, forming a β -silicon-stabilized carbenium ion intermediate $\text{R}_2\text{C}^+-\text{C}(\text{Si})(\text{Hal})\text{-R}'$.^[34] In the case of terminal $\text{C}=\text{C}$ bonds, a destabilized primary carbenium ion would be formed, making the reaction unfavorable. For styrene derivatives, however, the reaction becomes feasible due to a plausible benzylic cation intermediate. Iodination experiments performed on styrene derivative **16e** support this hypothesis (Table 5).

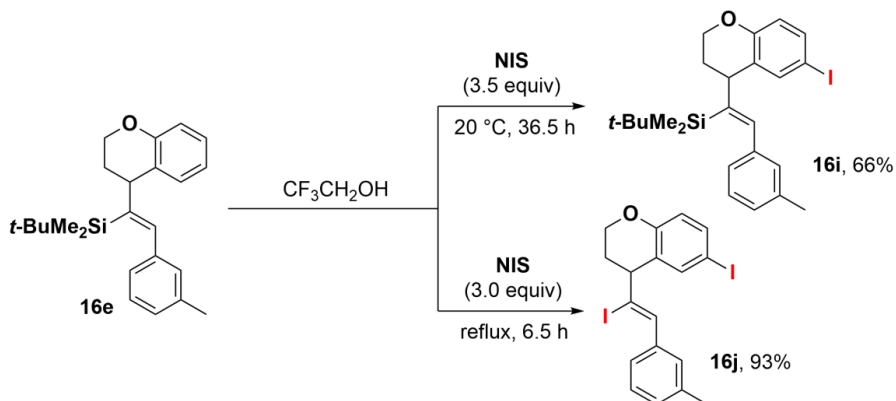
Table 5

Iodination experiments on styrene derivative **16e**



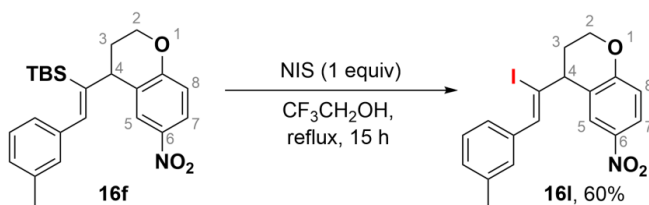
Entry	NIS (equiv)	Solvent	T °C	Time (h)	Starting material 16e/product 16i-j molar ratio by NMR		
					16e	16i	16j
1	1.0	HFIP	20	0.5	31	49	20
2	2.5			1.5	0	0	100
3	1.0	TFE		18.0	33	67	0
4	2.0			17.5	20	80	0
5	3.5			36.5	13	87	0
6	10.8			1.5	5	35	60
7	1.0		75–80	6.5	38	62	0
				71.0	28	72	0
8	3.0	6.5		0	0	100	

Using equimolar NIS in HFIP, a mixture of mono-iodinated product **16i** and diiodinated product **16j** (49:20) was obtained. With excess NIS (2.5 equiv), only the diiodinated product **16j** was formed. Using TFE as solvent, the reaction proceeded more slowly, allowing better control over product formation. By stopping the reaction after 36.5 h, mono-iodinated product **16i** was isolated in 66 % yield (71 % by NMR). High yields of diiodinated product **16j** (93 % isolated) were obtained using excess NIS (3 equiv) at elevated temperatures (75–80 °C, pressure flask, 6.5 h). Optimized conditions for selective mono- or diiodination are depicted in Scheme 19.



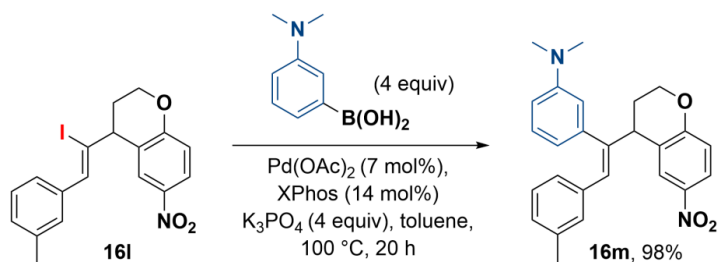
Scheme 19. Chromane **16e** mono- and diiodination experiments under optimized conditions.

Introduction of an electron-withdrawing nitro group at the chromane 6-position suppressed aromatic iodination, as observed by reacting nitro chromane **16f** with NIS (1 equiv) in trifluoroethanol at reflux temperature. In this case, selective *Si*→*I* exchange was achieved, yielding vinyl iodide **16l** in 60 % yield (Scheme 20).



Scheme 20. *Si*→*I* exchange reaction using chromane **16f**.

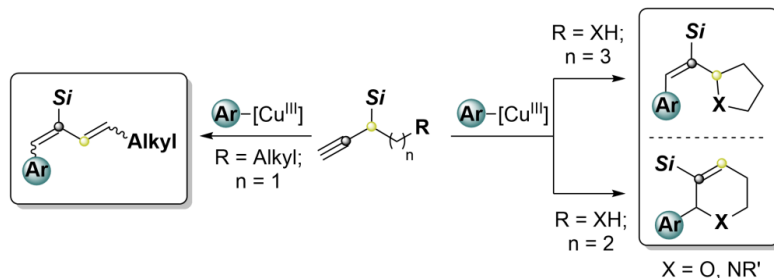
Finally, the synthetic utility of vinyl iodide **16l** was demonstrated in Suzuki-Miyaura cross-coupling reactions (Scheme 21). Using (3-(dimethylamino)phenyl)boronic acid as coupling partner under palladium catalysis, product **16m** was obtained in nearly quantitative yield (98 % isolated).



Scheme 21. Vinyl iodide **16l** application in Suzuki-Miyaura cross-coupling.

In this chapter, the author demonstrated propargyl silane heterocyclization *via* a Friedel-Crafts type reaction, where the propargylic system was activated by a Brønsted-acid. For terminally chlorinated propargyl silanes **11g-h**, cyclization occurred stereoselectively, affording tetrahydroquinolines **17** with exclusive (*Z*)-geometry for the resulting olefin side chain. The formed vinyl halide fragments were further modified by Suzuki-Miyaura cross-coupling and electrophilic silicon-iodine exchange to obtain synthetically useful vinyl iodides. Full details of this research are described in publication Ubaidullajevs, A.; Kroņkalne, R.; Mishnev, A.; Turks, M. Synthesis of Substituted Chromanes and Tetrahydroquinolines *via* Tandem 1,2-Silyl Shift – Friedel-Crafts cyclization. *J. Org. Chem.*, **2026**, 91 (17), 5785–5810 (Appendix 2).^[33]

1.3. Synthesis of arylated heterocycles and dienes using diaryl- λ^3 -iodanes under copper-catalyzed conditions

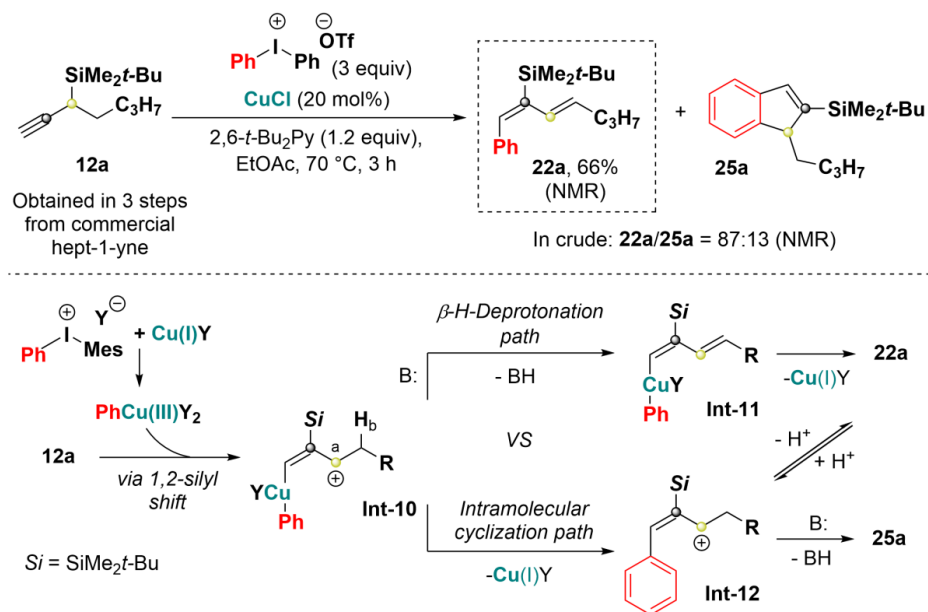


Previously, the author described activation of propargyl silanes for heterocycle synthesis using Brønsted acids or electrophilic halogenating reagents. The use of carbon electrophiles for analogous transformations represents a separate research direction developed in collaboration with Rūdolfs Beļunieks and Armands Sebris.^[35]

Diaryl- λ^3 -iodanes are commonly used to introduce aryl groups into π -systems, particularly in transformations requiring a formal Ar^+ species. This approach has been applied for 1,2-difunctionalization of alkynes.^[36] In the latter context, hypervalent iodine(III) reagents are

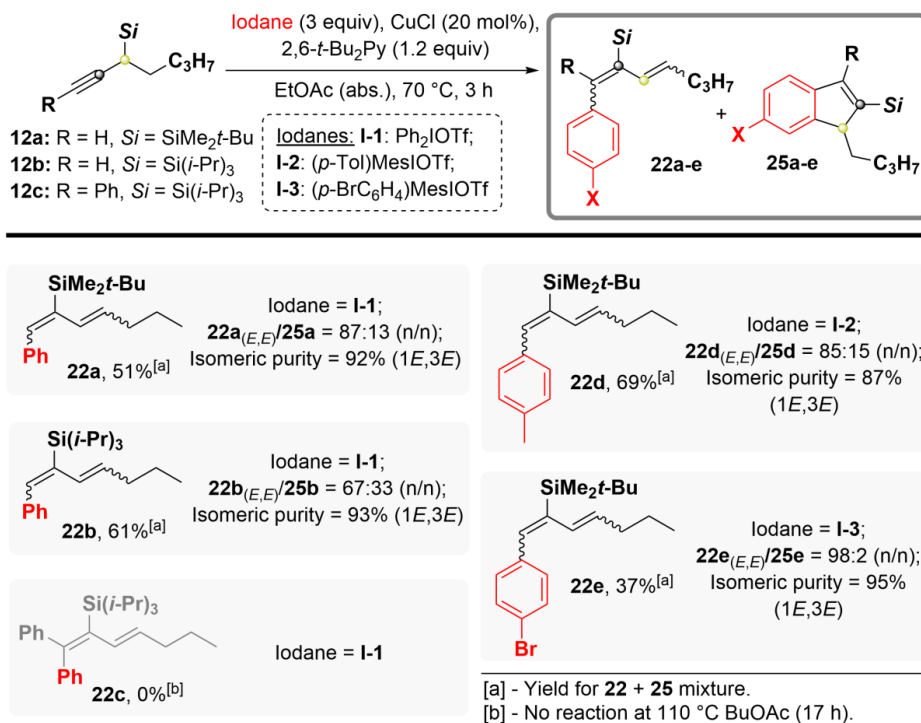
typically activated by copper or palladium catalysts.^{[37], [38]} Since propargyl silanes under electrophilic activation conditions can act as formal 1,3-dipoles due to 1,2-silyl migration, it is possible to achieve 1,3-difunctionalization, which is significantly less common than its 1,2-counterpart. In this study, the author developed a copper-catalyzed method for the 1,3-difunctionalization of propargyl silanes using diaryl- λ^3 -iodanes to obtain arylated heterocyclic structures and silyl dienes.

While searching for suitable reaction conditions for the arylation of propargyl silanes, the author began with simple silanes **12a**^[18] bearing an alkyl side chain. Its reaction gave a mixture of arylated silyl diene **22a** and silylindene **25a** (Scheme 22). The formation of these products can be explained by two competing reaction pathways: (a) elimination of a β -proton from allyl cation intermediate **Int-10** leads to formation of diene **22a**; (b) intramolecular cyclization of intermediate **Int-12** occurs, resulting in silylindene **25a**. Under optimized conditions (3.0 equiv Ph_2IOTf , 20 mol% CuCl , 1.2 equiv 2,6-*t*-Bu₂Py, EtOAc, 70 °C), the diene **22a**/indene **25a** ratio in the crude reaction mixture was 87:13, with a 66 % NMR yield of diene **22a**. Use of PhMesIOTf gave similar yields of diene **22a** (59 % by NMR), but lower selectivity toward diene formation (**22a**/**25a** = 71:22).



Scheme 22. Synthesis of arylated silyl diene **22a**: reaction concept and competing reaction pathways.

Using the conditions that provided the highest diene **22a** yield, the substrate scope was further investigated (Scheme 23). Arylation of silane **12a** with iodane **I-2**, which contains an electron-rich aryl system (*p*-tolyl), afforded the highest diene yields (**22d**, 69 %). The highest selectivity toward diene formation (**22e/25e** = 98:2) was observed with a *p*-bromo-substituted iodane **I-3**. Substrate **12b** bearing a bulky triisopropylsilyl (TIPS) group gave a mixture with a higher proportion of indene (**22b/25b** = 67:33). In all cases, (*1E,3E*)-dienes **22a-e** were obtained as the major isomers, with 87–95 % content. Minor amounts of other isomers ((*1Z,3E*)-, (*1E,3Z*)-, and (*1Z,3Z*)-**22**) were detected by their characteristic signals in ¹H NMR spectra. Internal alkyne **12c** (R = Ph, Si = TIPS) did not react under standard (EtOAc, 70 °C) or elevated temperature conditions (*n*-BuOAc, 110 °C), and the starting material was recovered unchanged. This indicates that the method is limited to propargyl silanes containing terminal alkyne groups.



Scheme 23. Substrate scope for arylated silyl dienes.

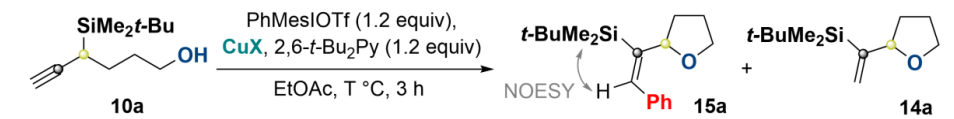
It was previously demonstrated that substrates containing internal nucleophiles enable heterocyclization. For example, propargyl silane **10a** bearing a terminal alcohol group was used for tetrahydrofuran synthesis.^[29] To achieve an arylation-heterocyclization cascade reaction, various alternative Cu(I) catalysts were tested (Table 6). CuCl and the CuOTf benzene complex

gave similarly high yields (**15a**, 82–84 % by NMR), while Cu(MeCN)₄BF₄ gave a slightly lower yield (**15a**, 77 %). Heterogeneous catalysis using Cu₂O afforded a mixture of arylated product **15a** and protodemetalation by-product **14a**, both in low yields. In the absence of a non-nucleophilic base (2,6-di-*tert*-butylpyridine = 2,6-*t*-Bu₂Py), selective formation of the protodemetalation product **14a** (69 % by NMR) was observed. Other, less sterically hindered bases (lutidine, Et₃N) did not afford the desired product.

The geometry of the olefin side chain in **15a** was confirmed using 2D NOESY NMR spectroscopy. The reaction exhibited high stereoselectivity, with only the (*E*)-isomer detected.

Table 6

Copper(I)-catalyst and temperature screening for the arylation-heterocyclization reaction of propargyl silane **10a**

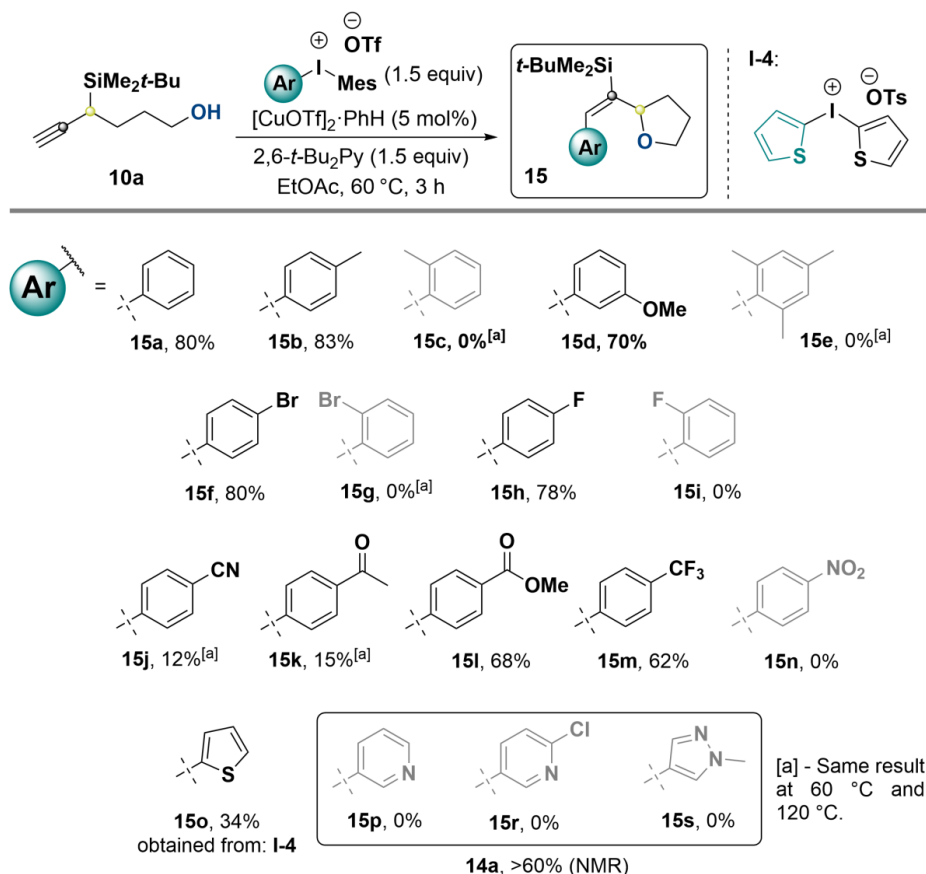


N°	CuX (mol%)	T (°C)	15a, % (NMR)	14a, % (NMR)
1 ^[a]	CuCl (2.5)	20	0	69
2	CuCl (2.5)	20	0	0
3	CuCl (5)	60	82, 76^[c]	0
4	CuI (5)	60	0	0
5 ^[b]	[CuOTf] ₂ ·PhH (5)	60	84	0
6	Cu(MeCN) ₄ BF ₄ (5)	70	77	0
7	Cu ₂ O (5)	70	6	2
8	[CuOTf] ₂ ·PhH (2.5)	70	70	0
9 ^[d]	[CuOTf] ₂ ·PhH (2.5)	70	43	0
10	[CuOTf] ₂ ·PhH (11)	70	47	0

^[a] Without 2,6-*t*-Bu₂Py. ^[b] Reaction time – 2 h (full conv.). ^[c] Isolated yield (%). ^[d] 15 mol% of H₂O as additive.

Under optimized conditions, the scope of arylated tetrahydrofurans **15** was examined (Scheme 24). Iodonium salts with electron-rich aryl groups (Ar = *p*-tolyl, *m*-methoxyphenyl, phenyl) and those containing halogens (Br, F) gave the highest yields (**15**, 70–83 %). In contrast, iodonium salts bearing electron-poor aryl groups, especially those containing nucleophilic heteroatoms (CN ≈ COR >> NO₂), reacted poorly. Aryl iodanes, bearing other electron-

withdrawing groups (CF₃, CO₂Me) gave moderate yields (62–68 %). Ortho-substituted iodonium salts were unreactive. Iodonium salts containing *N*-heterocycles (e.g., pyridine, pyrazole) gave predominantly non-arylated product **14a** via protodecupration. The only heterocycle-containing iodane, which led to heteroarylated tetrahydrofuran derivatives **15o**, was the thiophenyl group-containing symmetrical iodane **I-4**. It should be noted that all arylated tetrahydrofurans **15a-o** were obtained with exclusive (*E*)-selectivity for the olefin side chain.

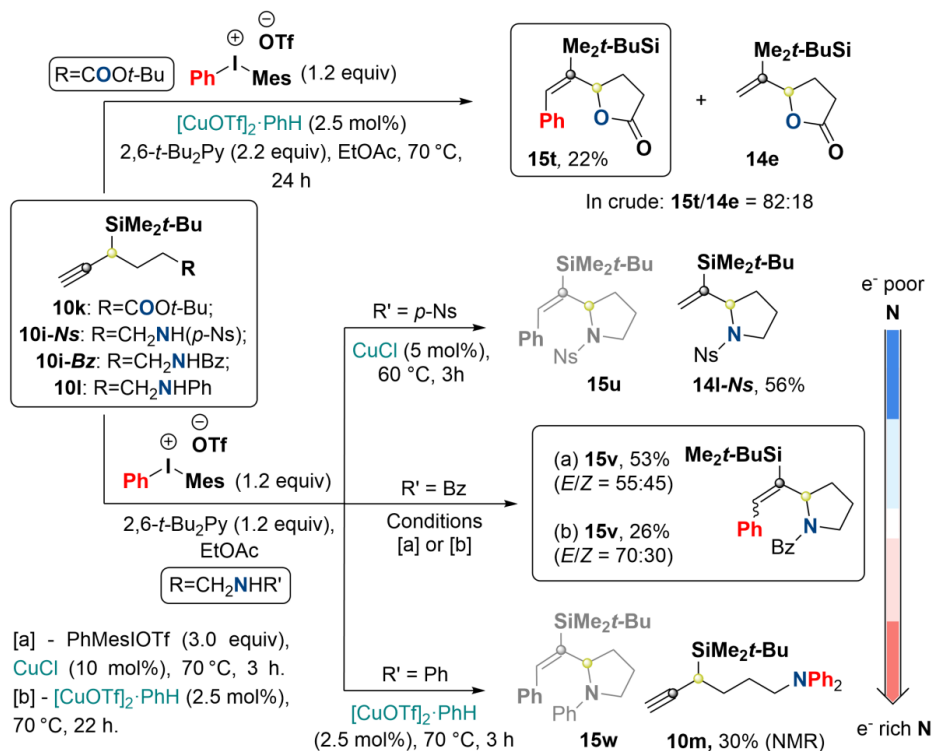


Scheme 24. Substrate scope for arylated tetrahydrofurans.

It was found that under the described arylation conditions, only internal *O*-nucleophiles reacted to afford 1,3-carbofunctionalized products. Attempts to perform arylation of propargyl silane **12b** in the presence of external *O*-nucleophiles (alcohols, carboxylic acids or their salts, silylated acids) resulted in arylation of the nucleophile itself, rather than formation of the desired product.

The author proceeded to explore other propargyl silanes as starting materials, bearing internal nucleophiles (Scheme 25). Carboxylic acid-containing substrate **10b** did not yield the

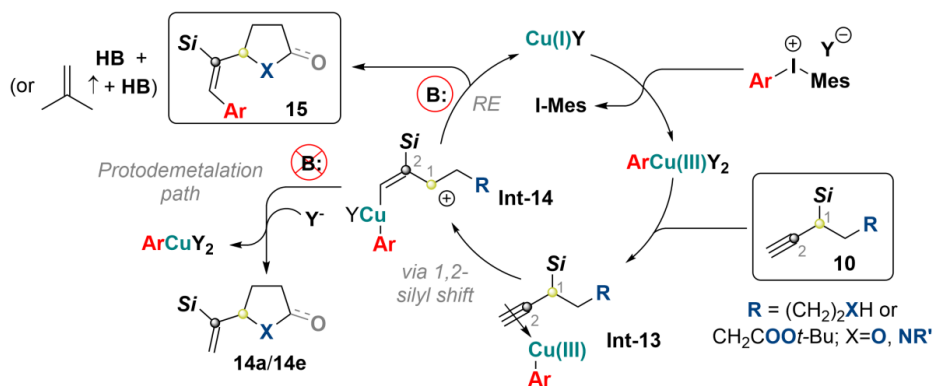
desired lactone **15t**, due to competing *O*-arylation forming phenyl alkyl esters. Its *tert*-butyl ester analogue **10t**, however, yielded the desired product **15t**, although the protodecupration product **14e** was also formed. Increasing the base loading reduced formation of **14e** and improved selectivity toward **15t**. *N*-Nosyl substrate **10i-Ns** yielded the non-arylated pyrrolidine **14i-Ns** (56 %) due to excessive acidity promoting protodecupration, whereas benzamide **10i-Bz** gave the arylated pyrrolidine **15v** as an *E/Z* mixture (55:45). Highly nucleophilic amine **10l** ($R = \text{CH}_2\text{NHPh}$) underwent *N*-arylation instead of forming heterocycles. These results indicate that acylamides possess optimal pKa and nucleophilicity for the desired arylation-heterocyclization reaction pathway.



Scheme 25. Arylation of amides **10i**, **10l** and carboxylic acid ester **10k**.

From previous optimization studies (see Appendix 3), it was established that Cu(I) salts are more reactive than Cu(II) salts, suggesting a Cu(I/III) catalytic cycle. Therefore, for the arylation-heterocyclization sequence, a Cu(I/III) catalytic cycle is proposed, which we based on experimental observations and mechanistic rationalizations for copper-catalyzed arylations in other π -systems.^[37] In the proposed mechanism, Cu(I) reacts with the diaryl- λ^3 -iodane to generate a highly electrophilic Ar-Cu(III) species, which activates the propargyl system (Scheme 26).

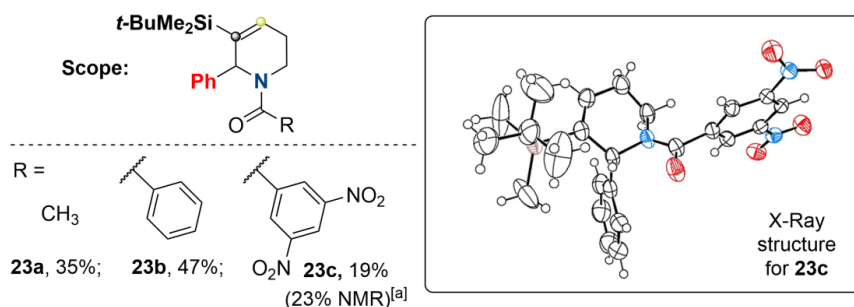
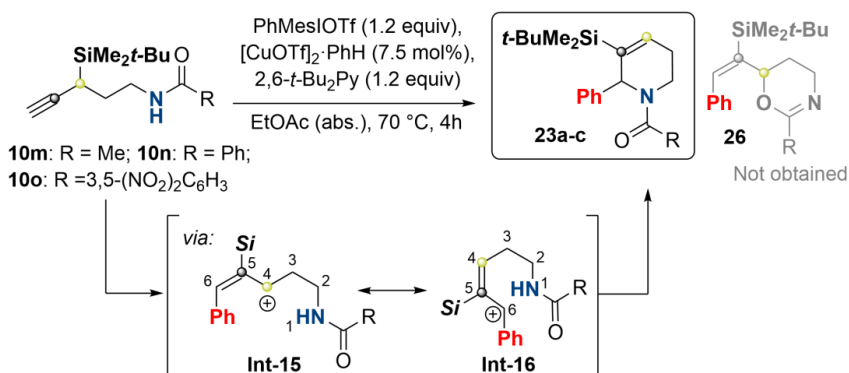
Silicon 1,2-migration affords a β -silicon-stabilized allyl cation intermediate **Int-14**. Next events include cyclization with the internal nucleophile and reductive elimination leading to arylated heterocycle **15** and regenerating Cu(I). In the case of *tert*-butyl ester **10k** ($R = \text{CH}_2\text{COO}t\text{-Bu}$), 1 equiv of isobutylene gas is also generated. The external base ($B = 2,6\text{-}t\text{-Bu}_2\text{Py}$) neutralizes the acid generated in the catalytic cycle and suppresses the formation of undesired protodecupration side-products **14a/14e**.



Scheme 26. Proposed mechanism for propargyl silane arylation-heterocyclization.

For substrates with shorter carbon chains **10m-o**, an alternative mechanism was observed (Scheme 27). Instead of the initially expected imidates **26**,^[39] tetrahydropyridines **23a-c** were formed *via* nucleophilic attack on the allyl cation resonance form **Int-16**, which was additionally stabilized by the aryl group. The structure of product **23c** was unambiguously confirmed by X-ray structure analysis.

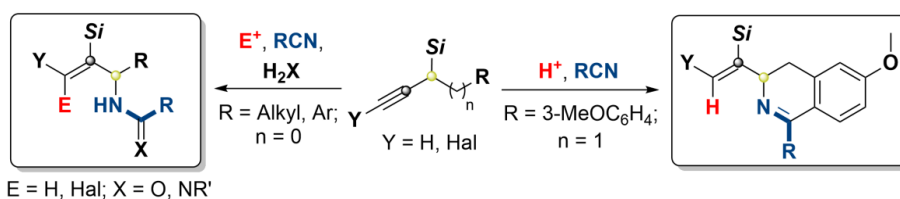
From this, the author concludes that the regioselectivity of propargyl silane **10** arylation-heterocyclization depends on the substrate carbon chain size. In systems where five-membered cycle formation is possible, 1,3-difunctionalization is observed, resulting in tetrahydrofurans **15** ($X = \text{O}$) and pyrrolidines **15** ($X = \text{N-PG}$). Substrates **10m-o** bearing shorter carbon chains undergo 1,1-difunctionalization, forming tetrahydropyridines **23**. The author's demonstrated approach offers a more efficient route towards heterocycles bearing a styryl side chain compared to previously explored strategies.^[29] Full details of this research are described in the publication Kronkalne, R.; Beļāunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. *Beilstein J. Org. Chem.*, **2025**, *21*, 1984–1994 (Appendix 3).^[35]



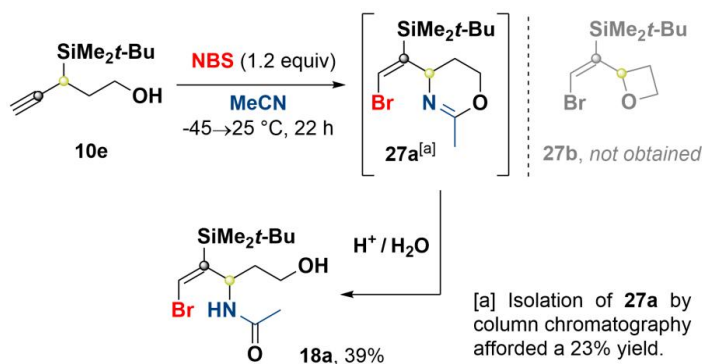
[a] - Modified conditions: **Ph₂IOTf** (3.0 equiv), 20 h.

Scheme 27. Tetrahydropyridine **23** synthesis from propargyl silanes.

1.4. Ritter-type reaction with β -silicon stabilized allyl cations

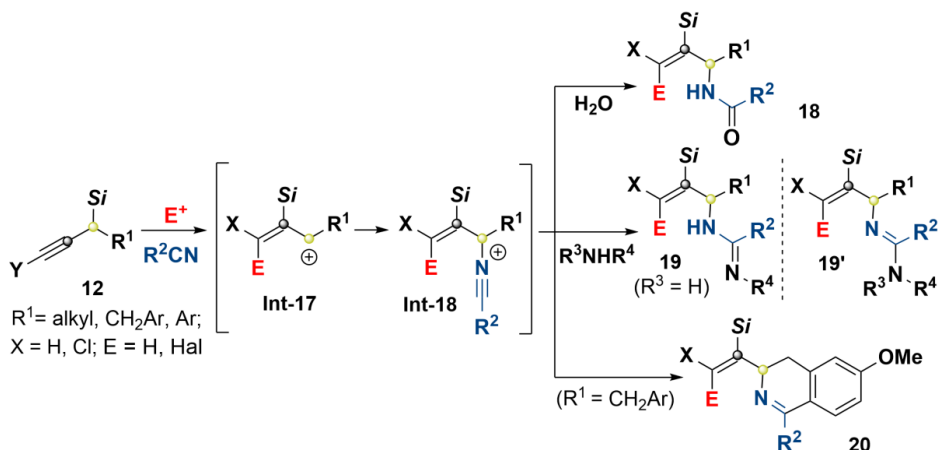


Attempts to perform heterocyclization of alcohol **10e** using NBS, analogously to the transformations described earlier in Section 1.1, but with acetonitrile (MeCN) as solvent, resulted in the formation of oxazine derivative **27a** rather than the expected oxetane derivative **27b** (Scheme 28). The cyclic product **27a** readily underwent hydrolysis to give acetamide **18a** – a classical Ritter reaction product. This observation encouraged further investigations into the application of 1,2-silyl shift in Ritter-type reactions.



Scheme 28. Heterocyclization of alcohol **10e** under Ritter reaction conditions.

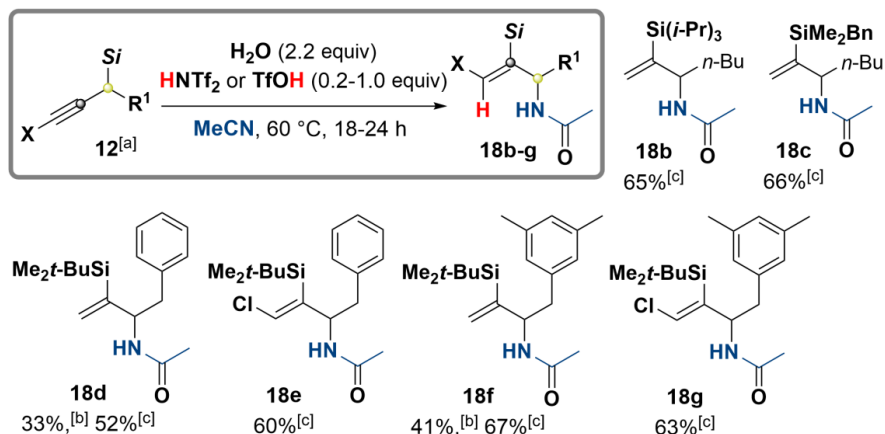
In this transformation, the nitrile acts as the primary nucleophile, attacking the allyl cation intermediate **Int-17** to form a nitrilium ion **Int-18** (Scheme 29). This intermediate is subsequently quenched by a secondary nucleophile (H_2O , ROH, $\text{R}_1\text{R}_2\text{NH}$, Ar), leading to the formation of cyclic or acyclic products that share a common feature – a functionalized olefin side chain. From an entropic perspective, this multicomponent reaction is particularly complex, as it involves the sequential formation of four covalent bonds in a single step. Despite this complexity, a methodology was developed for the use of propargyl silanes **12** in the synthesis of functionalized allylamides **18**, amidines **19**, and dihydroisoquinolines **20** under Ritter-type conditions. This study was conducted in collaboration with Sandra Turka,^[40] Raimonds Rogaļevs^[41] and Mikus Purīņš,^[42] and the results are yet to be published.



Scheme 29. The application of propargyl silanes in Ritter-type reaction.

Initially, systems most closely resembling classical Ritter reaction conditions were investigated. These conditions combined a Brønsted acid (TfOH or HNTf₂) for carbocation

generation, MeCN as both solvent and primary nucleophile, and water as a secondary nucleophile. Under these conditions, products **18b-g** bearing the allylamide functionality were obtained (Scheme 30).

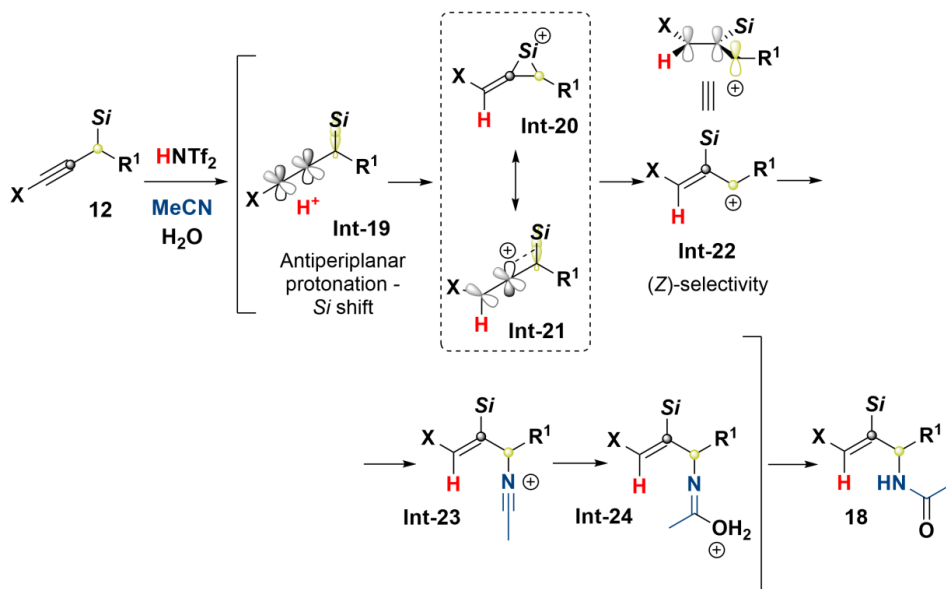


[a] Silanes: **12b** (X = H, R¹ = *n*-Bu, Si = (*i*-Pr)₃Si), **12d** (X = H, R¹ = *n*-Bu, Si = BnMe₂Si), **12e** (X = H, R¹ = Bn, Si = *t*-BuMe₂Si), **12f** (X = Cl, R¹ = Bn, Si = *t*-BuMe₂Si), **12g** (X = H, R¹ = CH₂(3,5-Me₂C₆H₃), Si = *t*-BuMe₂Si), **12h** (X = Cl, R¹ = CH₂(3,5-Me₂C₆H₃), Si = *t*-BuMe₂Si). [b] 0.2 equiv TfOH as H⁺ source. [c] 1.0 equiv HNTf₂ as H⁺ source.

Scheme 30. Synthesis of allylamides from propargyl silanes.

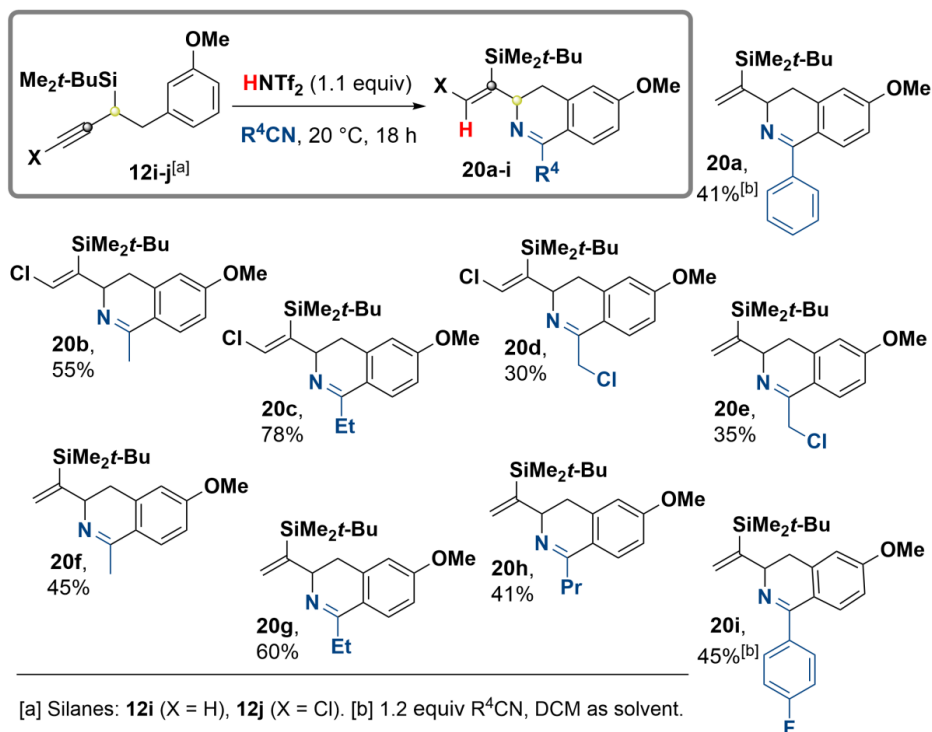
It was observed that using stoichiometric amounts of acid (1.0 equiv HNTf₂: **18f**, 67 % yield) resulted in higher yields compared to catalytic amounts (0.2 equiv TfOH: **18f**, 41 % yield). In the case of terminally halogenated propargyl silanes **12** (X = Cl), products **18e** and **18g** were obtained with trisubstituted olefin side chains, showing a (*Z/E*)-isomer ratio of 9:1 prior to purification. The major (*Z*)-isomer could be isolated by column chromatography.

The formation of the (*Z*)-configured double bond in allylamides **18e/18g** can be explained by protonation of the alkyne in an antiperiplanar orientation relative to the migrating silyl group (Scheme 31).



Scheme 31. Mechanistic rationalization for the formation of olefin (Z)-geometry.

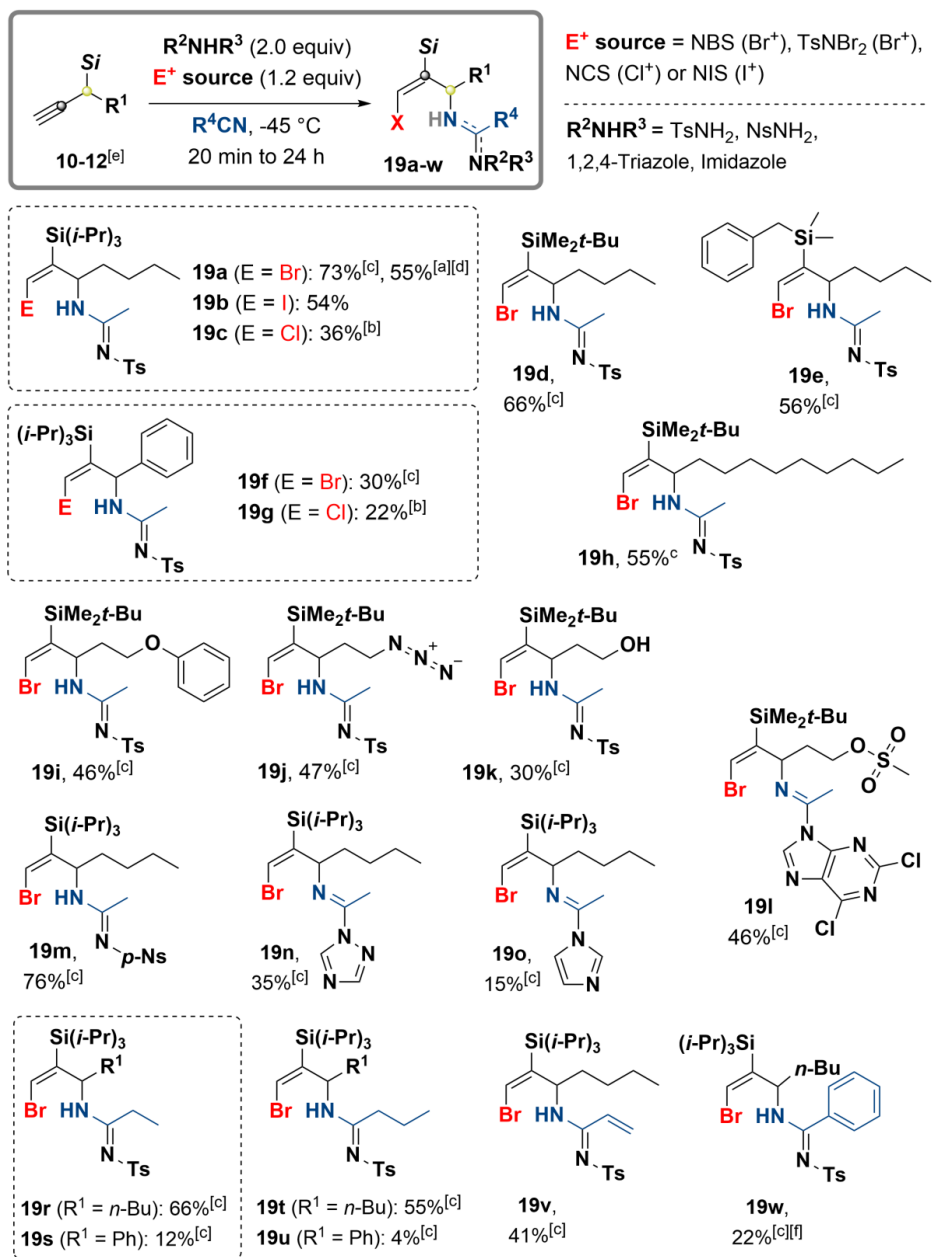
For substrates **12i-j** bearing electron-rich aromatic systems, a Bischler-Napieralski-type transformation was observed (Scheme 32). In this case, the aromatic ring acts as the secondary nucleophile, quenching the nitrilium ion and forming dihydroisoquinoline derivatives **20a-i**. Consistent with earlier observations, terminally halogenated substrate **12j** yielded products **20b-d** with (Z)-configured olefin side chains. The halogenated substrate **12j** also gave higher product **20** yields (up to 78 %) compared to the non-halogenated analogue **12i** (up to 60 %). Unlike the synthesis of allylamide **18** (which required heating to 60 °C), the synthesis of dihydroisoquinolines **20** proceeded efficiently at room temperature (20 °C). Using various aliphatic (MeCN, EtCN, PrCN) and halogenated (ClCH₂CN) nitriles, products **20b-h** were obtained in 30–78 % yields. Aromatic nitriles are less commonly used as solvents in Ritter-type reactions due to their high boiling points or solid state.^{[43], [44], [45]} To overcome this issue, dichloromethane (DCM) was used as solvent, with aromatic nitriles (PhCN, 4-FC₆H₄CN) added in quantities near stoichiometric ones (1.2 equiv). Under these conditions, products **20a** and **20i** were obtained in 41–45 % yields.



Scheme 32. Synthesis of dihydroisoquinolines from propargyl silanes in a Bischler-Napieralski-type reaction.

Next, more complex systems were investigated, where an external nitrogen nucleophile participates in nitrilium ion quenching. Under Brønsted acid activation conditions, the reaction either produced only diene by-products or did not proceed. For example, (*E*)-hepta-1,3-dien-2-yltriisopropylsilane^[18] was formed with 30 % NMR yield when silane **12b** (1.0 equiv) was reacted with TfOH (1.2 equiv) and TsNH_2 (2.0 equiv) in MeCN ($T = -45\text{ }^\circ\text{C}$), whereas with HNTf_2 (1.2 equiv) under identical conditions the reaction did not proceed. However, activation using the electrophilic brominating reagent NBS led to formation of amidine **19a** with 56 % yield by NMR (conditions: 1.2 equiv NBS, 1.1 equiv TsNH_2 , MeCN, $20\text{ }^\circ\text{C}$). Further optimization demonstrated that the highest amidine **19a** yields (75 % by NMR) were obtained under the following conditions: $T = -45\text{ }^\circ\text{C}$, MeCN as solvent, 2 equiv TsNH_2 and 1.2 equiv NBS.

Using the optimized reaction conditions ($T = -45\text{ }^\circ\text{C}$, RCN as solvent, 2 equiv TsNH_2), the author proceeded with the investigation of the substrate scope (Scheme 33).



[a] NMR yield. [b] T = $-45 \rightarrow 20\text{ }^\circ\text{C}$. [c] NBS as Br^+ source. [d] TsNBr_2 as Br^+ source. [e] Silanes: **12a** ($\text{R}^1 = n\text{-Bu}$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **12k** ($\text{R}^1 = \text{Ph}$, $\text{Si} = (i\text{-Pr})_3\text{Si}$), **12l** ($\text{R}^1 = \text{C}_9\text{H}_{19}$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **11i** ($\text{R}^1 = \text{CH}_2\text{CH}_2\text{OPh}$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **10p** ($\text{R}^1 = \text{CH}_2\text{CH}_2\text{N}_3$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **10e** ($\text{R}^1 = \text{CH}_2\text{CH}_2\text{OH}$, $\text{Si} = t\text{-BuMe}_2\text{Si}$), **10r** ($\text{R}^1 = \text{CH}_2\text{CH}_2\text{OMs}$, $\text{Si} = t\text{-BuMe}_2\text{Si}$). [f] A modified solvent system was used: PhCN/DCM (4:3 v/v).

Scheme 33. Synthesis of amidines in a Ritter-type reaction.

Variation of substituents at the product C=C bond was achieved by employing different electrophilic halogenating reagents (NBS, NCS, NIS), enabling the synthesis of vinyl halide-containing products **19a-c** (Hal = Br, Cl, I). The highest yields of amidines **19** (up to 76 %) were obtained from substrates containing simple aliphatic chains **12a,b,d**. In contrast, aryl-substituted propargyl silane **12k**^[18] afforded lower amidine yields (22–30 %) under Ritter-type conditions. Additional stabilization of the carbocation intermediate by a neighboring aryl group (R¹ = Ar) likely slows down nitrile addition, as indirectly evidenced by increased reaction time. For example, alkylsilane **12b** reached full conversion after 45 minutes, whereas arylsilane **12k** required 1.5 hours.

Compatibility with various functional groups was also examined. Substrates containing a terminal aryl ether **11i**, azide **10p**, mesylate **10r**, and even a free alcohol group **10e**, underwent Ritter-type reactions to give amidine products **19** in moderate yields (30–47 %).

Among alternative secondary nucleophiles for amidine synthesis, sulfonamides (NsNH₂, TsNH₂) gave the highest amidine **19** yields (73–76 %). Nitrogen heterocycles (e.g., 2,6-dichloropurine, 1,2,4-triazole, imidazole) were also compatible, although the yields were lower (15–46 %). Stronger nucleophiles such as cyclohexanol, cyclohexanethiol, and cyclohexylamine did not afford the expected imidate/thioimidate/amidine products under standard conditions.

Nitriles with longer alkyl chains (C₃–C₄) and acrylonitrile gave lower amidine **19** yields (41–66 %) compared to acetonitrile. In the case of benzonitrile, a mixed solvent system (PhCN/DCM, 4:3 v/v) was used to avoid freezing at –45 °C. However, benzonitrile exhibited low selectivity towards Ritter-type product formation, yielding amidine **19w** in only 22 %. Instead, the reaction predominantly followed a β-H elimination pathway, forming the respective diene.^[18]

In solution, amidines can exhibit configurational isomerism ((*E*)/(*Z*) around the C=N bond), rotational isomerism (syn/anti around the C–N bond), and tautomerism, all of which complicate structural analysis.^[46] NMR studies of amidines **19a-w** showed the following: in CDCl₃, two sets of signals were typically observed, whereas in DMSO-*d*₆, only one isomer was detected. For amidine **19m**, the major/minor isomer ratio in CDCl₃ was 96:4. The N–H signal appeared as a doublet with a coupling constant of ³*J* = 9.6 Hz relative to the C(3)–H proton, indicating a vicinal relationship. Additionally, the geometry of amidine **19m** was determined using X-ray structure analysis, which established the (*E*)-configuration for both the C=N and C=C bonds (Fig. 1). This was further confirmed by 2D NOESY NMR correlations between the C(1)–H proton and the (*i*-Pr)₃Si group. These findings are consistent with previous observations in electrophilic halogenation of propargyl silanes, which preferentially yielded (*E*)-configured trisubstituted olefins.^[19]

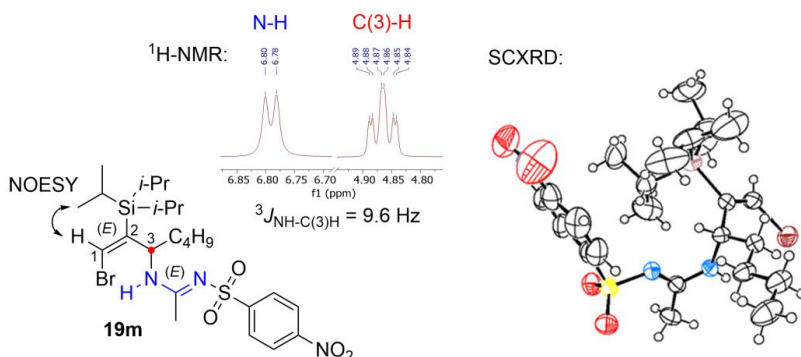
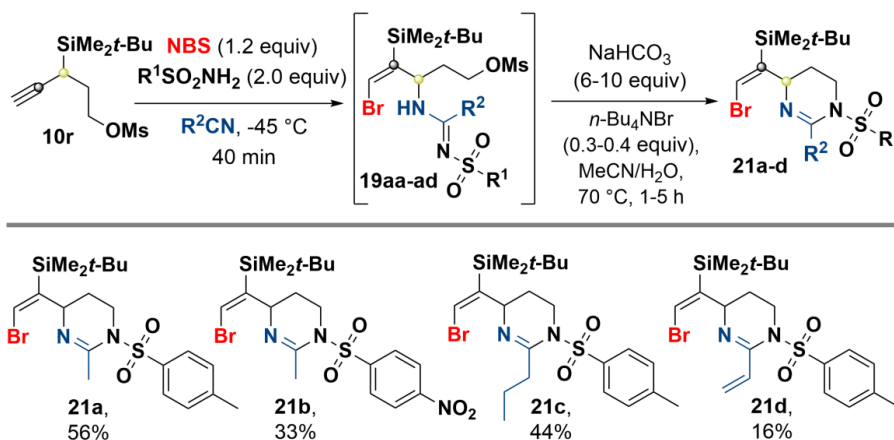


Fig. 1. Elucidation of amidine **19m** structure.

Finally, the synthetic utility of acyclic Ritter-type products was demonstrated in heterocycle synthesis (Scheme 34). Under standard Ritter-type conditions (1.2 equiv NBS, 2.0 equiv TsNH₂, nitrile solvent, T = -45 °C), mesylate **10r** afforded amidines **19aa-ad** that underwent intramolecular S_N2 cyclization in the presence of a base (NaHCO₃) to yield tetrahydropyrimidine derivatives **21a-d**.

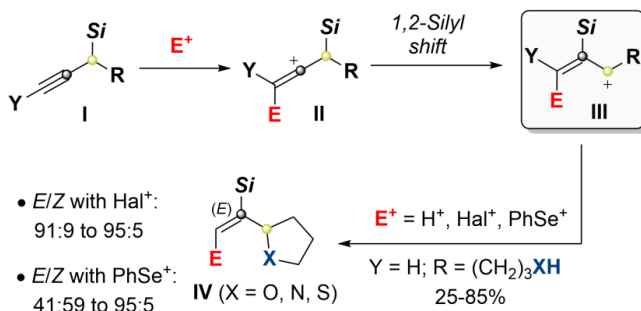


Scheme 34. Ritter-type reaction for the synthesis of tetrahydropyrimidine derivatives **21**.

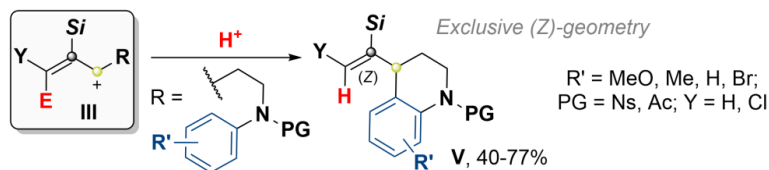
In conclusion, propargyl silane transformations under Ritter-type conditions afforded a broad spectrum of products, starting from acyclic structures – allylamides **18** and amidines **19** – to heterocycles **20-21**. By combining external electrophile attack on the propargyl silane triple bond with vinyl-allyl cation rearrangement *via* the 1,2-silyl shift, and two subsequent nucleophile attacks, the author obtained structurally complex motifs from simple starting materials. Full details of this research are described in Appendix 6: Turka, S.; Kronkalne, R.; Rogaļevs, R.; Puriņš, M.; Mishnev, A.; Turks, M. 1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives (*Manuscript in preparation*).

CONCLUSIONS

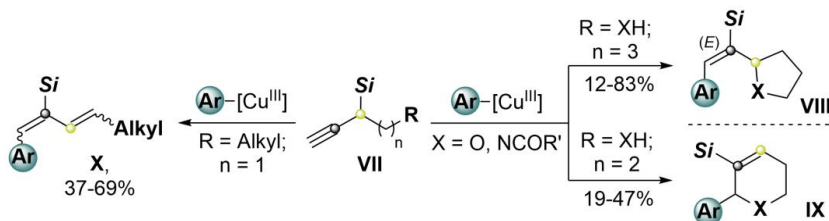
1. Electrophile-induced 1,2-silyl shift in propargyl silanes affords reactive allyl cation intermediates **III** that can be quenched by internal *O*-, *N*- and *S*-nucleophiles to form five-membered heterocycles **IV**: tetrahydrofurans ($X = O$), pyrrolidines ($X = N\text{-PG}$), and thiolanes ($X = S$), bearing geminally disubstituted ($E = H$) or stereodefined trisubstituted ($E = \text{Hal}$, PhSe) olefin side chains.



2. Quenching the β -silicon-stabilized allyl cation intermediates **III** with internal electron-rich aryl systems affords bicyclic heterocycles **V** with (*Z*)-configured olefin side chains *via* Brønsted acid-promoted Friedel-Crafts-type cyclization.

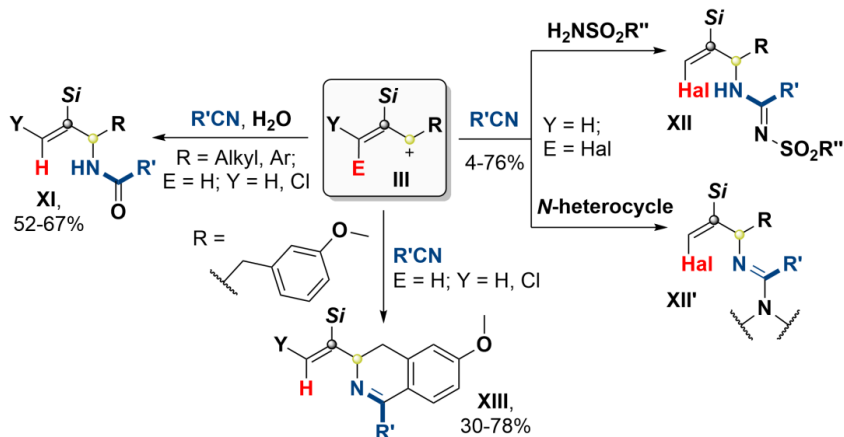


3. Combination of diaryl- λ^3 -iodanes with a Cu(I) catalyst enables in situ generation of electrophilic Ar-Cu(III) reagents, which, as formal Ar^+ synthons, add to the propargyl silane triple bond to induce arylation – 1,2-silyl shift – heterocyclization sequences **VII**→**VIII** and **VII**→**IX** depending on the side chain length. In the absence of reactive internal nucleophiles, arylated silyl dienes **X** are obtained instead.

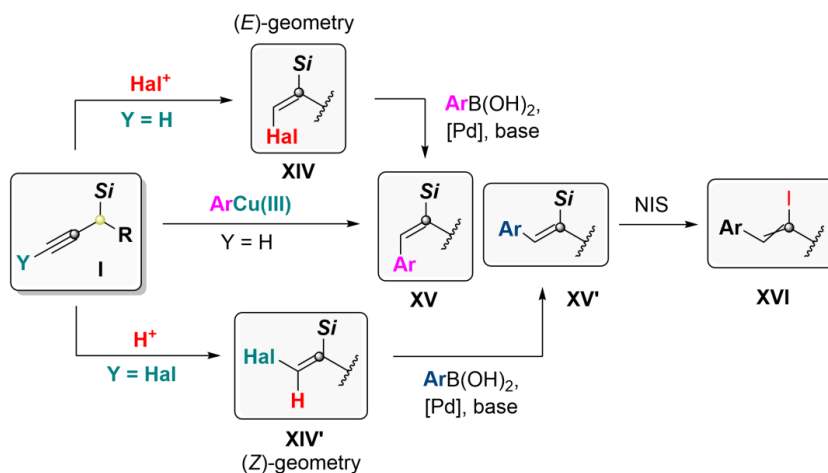


4. Under Ritter-type conditions, propargyl silanes can be combined with two incoming nucleophiles to afford allylamides **XI** ($X = O$) and amidines **XII** ($X = N\text{-PG}$) with highly

functionalized olefin fragments. Propargyl silanes bearing electron-rich aryl systems can be subjected to a Bischler-Napieralski-type reaction to yield dihydroisoquinolines **XIII**.



5. Olefin geometry can be controlled by combining: (a) non-halogenated silanes **I** ($Y = H$) with electrophilic halogenation ($E^+ = Hal^+$) reagents to achieve (*E*)-**geometry**; or (b) halogenated silanes **I** ($Y = Hal$) with Brønsted acid activation ($E^+ = H^+$) to achieve (*Z*)-**geometry**. The olefin side chain can be further modified by cross-coupling reactions or electrophilic $Si \rightarrow I$ exchange with retention of the alkene configuration. By activating propargyl silane **I** with $Ar-Cu(III)$, styrene derivatives **XV** are obtained directly, omitting the Pd-catalyzed vinyl halide cross-coupling step.



REFERENCES

- [1] Lecourt, C.; Dhambri, S.; Allievi, L.; Sanogo, Y.; Zeghib, N.; Othman, R. Ben; Lannou, M.-I.; Sorin, G.; Ardisson, J. Natural Product Reports Natural Products and Ring-Closing Metathesis: Synthesis of Sterically Congested Olefins. *Nat. Prod. Rep.* **2018**, *35*, 105–124. <https://doi.org/10.1039/C7NP00048K>.
- [2] Singh, M.; Ravichandiran, V.; Bharitkar, Y. P.; Hazra, A. Natural Products Containing Olefinic Bond: Important Substrates for Semi-Synthetic Modification Towards Value Addition. *Curr. Org. Chem.* **2020**, *24*, 709–745. <https://doi.org/10.2174/1385272824666200312125734>.
- [3] Dragutan, V.; Dragutan, I.; Demonceau, A.; Delaude, L. Combining Enyne Metathesis with Long-Established Organic Transformations: A Powerful Strategy for the Sustainable Synthesis of Bioactive Molecules. *Beilstein J. Org. Chem.* **2020**, *16*, 738–755. <https://doi.org/10.3762/bjoc.16.68>.
- [4] Pederson, R. L.; Fellows, I. M.; Ung, T. A.; Ishihara, H.; Hajela, S. P. Applications of Olefin Cross Metathesis to Commercial Products. *Adv. Synth. Catal.* **2002**, *344*, 728–735. [https://doi.org/https://doi.org/10.1002/1615-4169\(200208\)344:6/7<728::AID-ADSC728>3.0.CO;2-4](https://doi.org/https://doi.org/10.1002/1615-4169(200208)344:6/7<728::AID-ADSC728>3.0.CO;2-4).
- [5] Grubbs, R. H. Olefin-Metathesis Catalysts for the Preparation of Molecules and Materials (Nobel Lecture). *Angew. Chem. Int. Ed.* **2006**, *45*, 3760–3765. <https://doi.org/10.1002/anie.200600680>.
- [6] Kutateladze, D. A.; Mai, B. K.; Dong, Y.; Zhang, Y.; Liu, P.; Buchwald, S. L. Stereoselective Synthesis of Trisubstituted Alkenes *via* Copper Hydride-Catalyzed Alkyne Hydroalkylation. *J. Am. Chem. Soc.* **2023**, *145* (32), 17557–17563. <https://doi.org/https://doi.org/10.1021/jacs.3c06479>.
- [7] Flynn, A. B.; Ogilvie, W. W. Stereocontrolled Synthesis of Tetrasubstituted Olefins. *Chem. Rev.* **2007**, *107*, 4698–4745. <https://doi.org/10.1021/cr050051k>.
- [8] Zhao, Y.; Liu, C.-F.; Lin, L. Q. H.; Chan, A. S. C.; Koh, M. J. Stereoselective Synthesis of Trisubstituted Alkenes by Nickel-Catalyzed Benzylation and Alkene Isomerization. *Angew. Chem. Int. Ed.* **2022**, *61*, e202202674. <https://doi.org/10.1002/anie.202202674>.
- [9] Hoveyda, A. H.; Qin, C.; Sui, X. Z.; Liu, Q.; Li, X.; Nikbakht, A. Taking Olefin Metathesis to the Limit: Stereocontrolled Synthesis of Trisubstituted Alkenes. *Acc. Chem. Res.* **2023**, *56* (18), 2426–2446. <https://doi.org/https://doi.org/10.1021/acs.accounts.3c00341>.

- [10] Koengeter, T.; Qin, C.; Mai, B. K.; Liu, Q.; Mu, Y.; Liu, P.; Hoveyda, A. H. Catalytic Cross-Metathesis Reactions That Afford *E*- and *Z*-Trisubstituted Alkenyl Bromides: Scope, Applications, and Mechanistic Insights. *J. Am. Chem. Soc.* **2023**, *145* (6), 3774–3785. <https://doi.org/10.1021/jacs.2c13289>.
- [11] Nguyen, T. T.; Koh, M. J.; Mann, T. J.; Schrock, R. R.; Hoveyda, A. H. Article Synthesis of *E*- and *Z*-Trisubstituted Alkenes by Catalytic Cross-Metathesis. *Nat. Publ. Gr.* **2017**, *552* (7685), 347–354. <https://doi.org/10.1038/nature25002>.
- [12] Mukherjee, N.; Planer, S.; Grela, K. Formation of Tetrasubstituted C-C Double Bonds *via* Olefin Metathesis: Challenges, Catalysts, and Applications in Natural Product Synthesis. *Org. Chem. Front.* **2018**, *5*, 494–516. <https://doi.org/10.1039/C7QO00800G>.
- [13] Negishi, E.; Wang, G.; Rao, H.; Xu, Z. Alkyne Elementometalation – Pd-Catalyzed Cross-Coupling. Toward Synthesis of All Conceivable Types of Acyclic Alkenes in High Yields, Efficiently, Selectively, Economically, and Safely: “Green” Way. *J. Org. Chem.* **2010**, *75*, 3151–3182. <https://doi.org/10.1021/jo1003218>.
- [14] Edwards, J. T.; Merchant, R. R.; McClymont, K. S.; Knouse, K. W.; Qin, T.; Malins, L. R.; Vokits, B.; Shaw, S. A.; Bao, D.-H.; Wei, F.-L.; Zhou, T.; Eastgate, M. D.; Baran, P. S. Decarboxylative Alkenylation. *Nature* **2017**, *545*, 213–218. <https://doi.org/10.1038/nature22307>.
- [15] Buttard, F.; Sharma, J.; Champagne, P. A. Recent Advances in the Stereoselective Synthesis of Acyclic All-Carbon Tetrasubstituted Alkenes. *Chem. Commun.* **2021**, *57*, 4071–4088. <https://doi.org/10.1039/d1cc00596k>.
- [16] Ghosh, S.; Chakraborty, R.; Ganesh, V. Dual Functionalization of Alkynes Utilizing the Redox Characteristics of Transition Metal Catalysts. *ChemCatChem* **2021**, *13*, 4262–4298. <https://doi.org/10.1002/cctc.202100838>.
- [17] Eissen, M.; Lenoir, D. Mass Efficiency of Alkene Syntheses with Tri- and Tetrasubstituted Double Bonds. *ACS Sustain. Chem. Eng.* **2017**, *5*, 10459–10473. <https://doi.org/10.1021/acssuschemeng.7b02479>.
- [18] Puriņš, M.; Mishnev, A.; Turks, M. Brønsted Acid Catalyzed 1,2-Silyl Shift in Propargyl Silanes: Synthesis of Silyl Dienes and Silyl Indenes. *J. Org. Chem.* **2019**, *84* (6), 3595–3611. <https://doi.org/10.1021/acs.joc.8b02735>.
- [19] Beļāunieks, R.; Puriņš, M.; Līpiņa, R. A.; Mishnev, A.; Turks, M. 1,3-Difunctionalization of Propargyl Silanes with Concomitant 1,2-Silyl Shift: Synthesis of Allyl Functionalized Vinyl Silanes. *Org. Lett.* **2023**, *25* (25), 4627–4631.

<https://doi.org/10.1021/acs.orglett.3c01245>.

- [20] Roberts, D. D.; McLaughlin, M. G. Strategic Applications of the β -Silicon Effect. *Adv. Synth. Catal.* **2022**, *364*, 2307–2332. <https://doi.org/10.1002/adsc.202200237>.
- [21] Beļāunieks, R.; Puriņš, M.; Turks, M. Manifestation of the β -Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift. *Synthesis (Stuttg.)*. **2020**, *52* (15), 2147–2161. <https://doi.org/10.1055/s-0039-1690898>.
- [22] Lamberth, C.; Dinges, J. The Significance of Heterocycles for Pharmaceuticals and Agrochemicals. In *Bioactive Heterocyclic Compound Classes*; Lamberth, C., Dinges, J., Eds.; 2012. <https://doi.org/10.1002/9783527664412.ch1>.
- [23] Reymond, J. The Chemical Space Project. *Acc. Chem. Res.* **2015**, *48*, 722–730. <https://doi.org/10.1021/ar500432k>.
- [24] Reiser, O. Heterocyclic Chemistry – A Mature Area in Its Infancy! *Eur. J. Org. Chem.* **2019**, 4973–4975. <https://doi.org/10.1002/ejoc.201901162>.
- [25] Zhang, Y.; Li, Q.; Hu, Z.; Leng, Z.; Zhang, W.; Das, S. Innovative Approaches to the Synthesis of Five-Membered Heteroaromatics with Emerging Synthetic Methodologies. *Chem. Soc. Rev.* **2027**. <https://doi.org/10.1039/d5cs01300c>.
- [26] Cabrele, C.; Reiser, O. The Modern Face of Synthetic Heterocyclic Chemistry. *J. Org. Chem.* **2016**, *81*, 10109–10125. <https://doi.org/10.1021/acs.joc.6b02034>.
- [27] Beļāunieks, R.; Puriņš, M.; Kumpiņš, V.; Turks, M. Synthesis of 3-Silylated 3-Sulfolenes from Propargylsilanes and Their Reductive Desulfitation. *Chem. Heterocycl. Compd.* **2021**, *57* (1), 20–25. <https://doi.org/10.1007/s10593-021-02862-1>.
- [28] Roberts, D. D.; McLaughlin, M. G. Strategic Applications of the β -Silicon Effect. *Adv. Synth. Catal.* **2022**, *364* (14), 2307–2332. <https://doi.org/10.1002/adsc.202200237>.
- [29] Kronkalne, R.; Beļāunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.* **2023**, *88* (19), 13857–13870. <https://doi.org/10.1021/acs.joc.3c01481>.
- [30] Beļāunieks, R. Harnessing the 1,2-Silyl Shift for the Synthesis of Functionalized Alkenes from Propargyl Silanes. Doctoral Thesis, Riga Technical University, 2023. <https://doi.org/10.7250/9789934229640>.
- [31] Wang, X.; Gao, Q.; Buevich, A. V.; Yasuda, N.; Zhang, Y.; Yang, R.; Zhang, L.-K.; Martin, G. E.; Williamson, R. T. Unexpected Propargylic Retro-Brook Rearrangements in

- Alkynes. *J. Org. Chem.* **2019**, *84* (16), 10024–10031. <https://doi.org/10.1021/acs.joc.9b01190>.
- [32] Kronkalne, R.; Beļāunieks, R.; Turks, M. Synthesis of 4-(*Tert*-Butyldimethylsilyl)-4,5,6,7-Tetrahydro-[1,2,3]Triazolo[1,5-*a*]Pyridine. *Molbank* **2022**, *2022* (3), M1427. <https://doi.org/10.3390/M1427>.
- [33] Ubaidullajevs, A.; Kronkalne, R.; Mishnev, A.; Turks, M. Synthesis of Substituted Chromanes and Tetrahydroquinolines *via* Tandem 1,2-Silyl Shift – Friedel–Crafts Cyclization. *J. Org. Chem.* **2026**. <https://doi.org/10.1021/acs.joc.5c03136>.
- [34] Chan, T. H.; Fleming, I. Electrophilic Substitution of Organosilicon Compounds-Applications to Organic Synthesis. *Synthesis (Stuttg)*. **1979**, *10*, 761–786. <https://doi.org/10.1055/s-1979-28829>.
- [35] Kronkalne, R.; Beļāunieks, R.; Sebris, A.; Mishnev, A.; Turks, M. Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis. *Beilstein J. Org. Chem.* **2025**, *21*, 1984–1994. <https://doi.org/10.3762/bjoc.21.154>.
- [36] Wang, D.; Li, Q.; Li, M.; Du, Z.; Fu, Y. Recent Progress in Arylation Reactions with Diaryliodonium Salts. *Curr. Org. Chem.* **2021**, *25* (11), 1298–1320. <https://doi.org/10.2174/1385272825666210512015410>.
- [37] Fañanás-Mastral M. Copper-Catalyzed Arylation with Diaryliodonium Salts. *Synthesis (Stuttg)*. **2017**, *49* (09), 1905–1930. <https://doi.org/10.1055/s-0036-1589483>.
- [38] Deprez, N. R.; Sanford, M. S. Reactions of Hypervalent Iodine Reagents with Palladium: Mechanisms and Applications in Organic Synthesis. *Inorg. Chem.* **2007**, *46* (6), 1924–1935. <https://doi.org/10.1021/ic0620337>.
- [39] Sinai, Á.; Mészáros, Á.; Gáti, T.; Kudar, V.; Palló, A.; Novák, Z. Copper-Catalyzed Oxidative Ring Closure and Carboarylation of 2-Ethynylanilides. *Org. Lett.* **2013**, *15* (22), 5654–5657. <https://doi.org/10.1021/ol402600r>.
- [40] Turka, S. Tandēmas sililgrupas 1,2-nobīdes – Ritera – tipa reakcijas pielietojums funkcionālizētu olefīnu sintēzē. Bakalaura darbs, Rīgas Tehniskā universitāte, 2025.
- [41] Rogaļevs, R. Sililgrupas 1,2-nobīdes – Ritera reakcijas kaskāde alilamīdu un dihidroizohinolīnu sintēzē. Bakalaura darbs, Rīgas Tehniskā universitāte, 2024.
- [42] Puriņš, M. Elektrofīlu Inducētas Pārgrupēšanās Reakcijas Propargilsilānos. Maģistra darbs, Rīgas Tehniskā universitāte, 2019.

- [43] Chen, M.-E.; Chen, X.-W.; Hu, Y.-H.; Ye, R.; Lv, J.-W.; Li, B.; Zhang, F.-M. Recent Advances of Ritter Reaction and Its Synthetic Applications. *Org. Chem. Front.* **2021**, 8 (16), 4623–4664. <https://doi.org/10.1039/d1qo00496d>.
- [44] Kahlenberg, L. On an Improved Method of Determining Latent Heat of Evaporation, and on the Latent Heat of Evaporation of Pyridine, Acetonitrile, and Benzonitrile. *J. Phys. Chem.* **1901**, 5 (4), 215–232. <https://doi.org/10.1021/j150031a001>.
- [45] Takao Maki, K. T. Benzoic Acid and Derivatives. *Ullmann's Encyclopedia of Industrial Chemistry*; 2012. <https://doi.org/10.1002/14356007.a03>.
- [46] Kalz, K. F.; Hausmann, A.; Dechert, S.; Meyer, S.; John, M. Solution Chemistry of *N*, *N'*-Disubstituted Amidines: Identification of Isomers and Evidence for Linear Dimer Formation. *Chem. Eur. J.* **2016**, 22 (50), 18190–18196. <https://doi.org/10.1002/chem.201603850>.

ACKNOWLEDGEMENTS

This research would not be possible without the joint efforts of the RTU Institute of Chemistry and Chemical Technology “Propargyl silane team”. Many thanks to Artjoms Ubaidullajevs, Rūdols Beļāunieks, Sandra Turka, Raimonds Rogaļevs and Mikus Puriņš, who have contributed to this work! I also thank my supervisor, Professor Māris Turks for invaluable insights, motivation and assistance in complex problem solving! Anatoly Mishnev is also kindly acknowledged for X-Ray analysis.

The Thesis research was supported by the Latvian Council of Science Grant LZP-2023/1-0576 and the European Union Recovery and Resilience Facility within project No. 5.2.1.1.i.0/2/24/1/CFLA/003 "Consolidation and implementation of management changes at Riga Technical University, Liepāja University, Rezekne Academy of Technologies, Latvian Maritime Academy and Liepāja Maritime College for the advancement of excellence in higher education, science and innovation" academic career doctoral grant (ID 1134).

PIELIKUMI / APPENDICES

1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain

Kronkalne, R.; Beļunieks, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M.

J. Org. Chem., **2023**, 88 (19), 13857-13870

Pārpublicēts ar *ACS Publications* atļauju

Copyright © 2023 American Chemical Society

Republished with permission from *ACS Publications*

Copyright © 2023 American Chemical Society

1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain

Rasma Kropkalne, Rūdolfs Beļauņieks, Artjoms Ubaidullajevs, Anatoly Mishnev, and Māris Turks*

Cite This: *J. Org. Chem.* 2023, 88, 13857–13870

Read Online

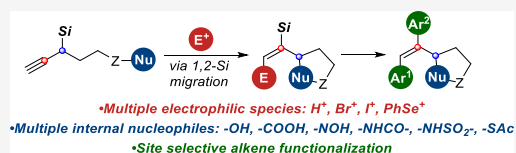
ACCESS |

Metrics & More

Article Recommendations

Supporting Information

ABSTRACT: Propargyl silanes with a terminal alkyne moiety undergo a 1,2-silyl shift when activated with electrophiles such as H^+ , Br^+ , I^+ , and $PhSe^+$. A method was developed to trap 1,3-transposed electrophilic centers with various internal O-, N-, and S-nucleophiles in a 5-exo manner. This synthetic procedure provided five-membered heterocycles containing a trisubstituted olefin side chain. The scope of the method includes access to tetrahydrofuran, γ -butyrolactone, 2-isooxazoline, pyrrolidine, and thiolane derivatives in yields ranging from 25 to 85% (23 examples in total). Reactions with $TsNBr_2$ ensured complete (*E*)-selectivity of the newly formed olefins. Further functionalization of the obtained 1-trialkylsilyl-2-bromovinyl side chain was demonstrated by double-bond geometry-preserving electrophilic substitution and cross-coupling reactions that provided heterocycles with a trisubstituted vinyl moiety.



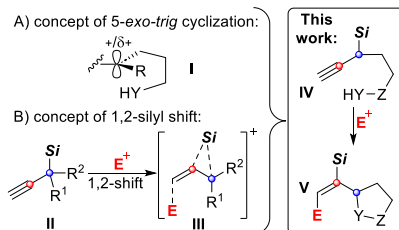
INTRODUCTION

Natural compounds and small-molecule drugs bearing heterocyclic motifs have demonstrated an exceptional variety of biological activities and pharmaceutical applications. The 2014 review of all the U.S. FDA-approved pharmaceuticals has shown that approximately 59% of all small drugs contain nitrogen-bearing heterocycles, with pyrrolidine being the most prominent five-membered and fifth overall nitrogen-containing heterocycle.¹ Nitrogen heterocycles continue to dominate U.S. FDA-approved drugs in the period 2015–2020,² and among them, pyrrolidine derivatives play a prominent role.³

On the other hand, the tetrahydrofuran moiety is broadly present in biologically active natural products of both terrestrial⁴ and marine organisms,⁵ and as such, it has raised the attention of communities of synthetic⁶ and medicinal chemists.⁷ Also, thiolane cycle-containing natural products, and their synthetic analogs have found therapeutic applications, been studied as antibiotics, antiviral, and anticancer agents or have been used in traditional Ayurvedic medicine to treat the metabolic syndrome.⁸

There are multiple ways to synthesize heterocycles, including a variety of condensation reactions, transition-metal-catalyzed cyclizations, and pericyclic reactions. However, a well-established strategy for preparing small, partially, and fully saturated heterocycles involves an internal nucleophilic attack on an accessible σ^* or vacant π system, leading to intramolecular cyclization (intermediate I, Scheme 1). This involves the reaction of oxygen⁹ and nitrogen nucleophile¹⁰ in hetero-Michael reactions or intramolecular S_N1 , S_N2 , and S_N2' processes, hydro- and haloetherification, as described in several

Scheme 1. Heterocyclization of Electrophile-Activated Propargyl Silanes with Concomitant 1,2-Silyl shift



review articles. Similar approaches are used also for the synthesis of thiolane cycles.⁸

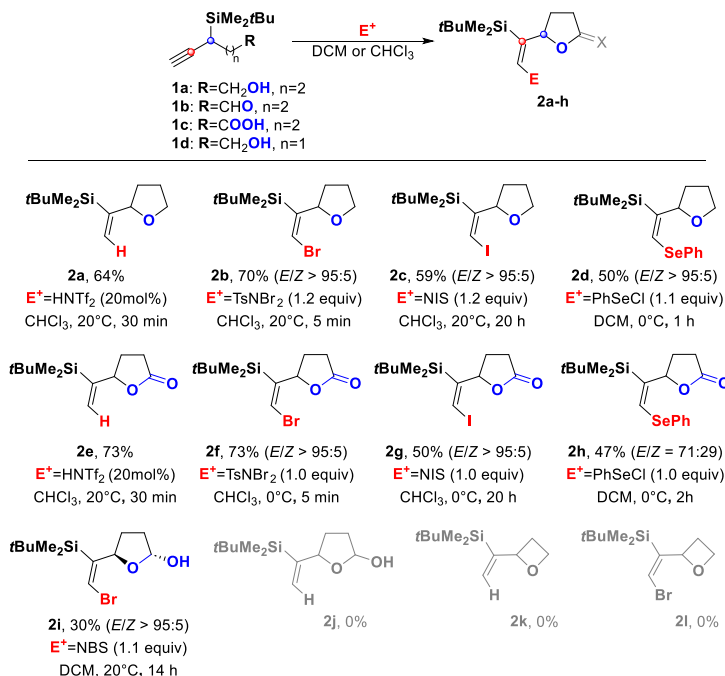
The required vacant π -orbital for the cyclization event can be that of a carbocation, and the use of propargyl silanes as 1,3-dipoles for their 1,3-difunctionalization in this context is an underexplored synthetic route. Indeed, electrophilic activation of propargyl silanes under certain circumstances is known to induce a 1,2-silyl shift by setting the molecule for the addition of a nucleophile at the newly formed allylic position, thus completing the 1,3-difunctionalization event.¹¹ Yet, most of the

Received: July 3, 2023

Published: September 22, 2023



Scheme 2. Synthesis of Tetrahydrofuran Derivatives 2a–i Containing Vinyl Silane Side Chain (Sub-millimolar Scale, Isolated Yields Provided)



previously reported methods have been developed for annulations with intrinsically bounded electrophile–nucleophile pairs (for example, Lewis acid-activated aldehyde or α,β -unsaturated carbonyl compound), which add across the propargyl silane 1,3-dipole forming [3 + 2] cycloadduct. Among the scarce examples of 1,2-silyl shift in propargyl silanes leading to intramolecular heterocyclizations, surprisingly there are no examples that would resemble an extended version of halo- or selenoetherification or esterification (electrophilic activation of π -system—1,2-silyl shift—intramolecular quench of the resulting carbocation with a nucleophile in 5-*exo-trig* fashion).¹²

Herein, we report a successful combination of allyl cation formation via a 1,2-silyl shift in electrophile-activated propargyl silanes and their reactions with internal N-, O-, and S-nucleophiles, which are not part of the electrophilic initiators. We have previously reported such allyl cation formation, which after deprotonation provided 2-silyl-1,4-dienes (proton loss from R^1/R^2 groups in intermediate III, Scheme 1).¹³ Alternatively, if propargyl silane activation with electrophile occurs in a nucleophilic solvent, (*E*)-selective 1,3-difunctionalization of the starting material takes place by the addition of the solvent, and (*E*)-3-bromo-2-(trialkylsilyl)allyl esters and ethers are obtained.¹⁴ Now, the design of propargyl silanes of type IV and the use of a non-nucleophilic solvent allowed us to obtain five-membered heterocycles V (pyrrolidines, tetrahydrofurans, butyrolactones, thiolanes, and isoxazolines) with geometrically defined olefin side chains (Scheme 1).

RESULTS AND DISCUSSION

We began our research by developing the synthesis of tetrahydrofuran derivatives 2a–h (Scheme 2). Reaction conditions were optimized on propargyl silane 1a, which was obtained by *retro*-Brook rearrangement of *O*-silyl-protected hex-5-yn-1-ol, as described previously by the Wang group.¹⁵ Reaction optimization was performed by running reactions in NMR tubes and observing the conversion in the presence of a diphenylmethane internal standard (Figure 1). For the full data set, see Supporting Information Table S1). First, strong Brønsted acids were tested for the sequence of protonation/1,2-silyl migration/cyclization. Indeed, superacids such as trifluoromethanesulfonic acid (TfOH) and bis-(trifluoromethane)sulfonylimide (Tf₂NH) both gave comparably good NMR yields (70%) of planned product 2a in $CDCl_3$ solution after 1 h at 0 °C. This indicates that the counterion effects of these superacids (i.e., basicity, which might lead to diene formation) play a negligible role if the starting material contains an appropriate intramolecular nucleophile that can rapidly react with the formed reaction center. However, experiments with H_2SO_4 indicated that this acid, under the given reaction conditions, was too weak to initiate the expected reaction sequence. The choice of solvent was determined by its catalyst's acidity-leveling effects. Thus, $CDCl_3$ and CD_2Cl_2 provided practically identical 70% NMR yields of product 2a (0.2 equiv of Tf₂NH, 0 °C, 1 h), whereas in C_6D_6 the NMR yield was somewhat lower (65%), but CD_3NO_2 gave only 50% of 2a. On the other hand, the use of Lewis basic THF-*d*₈ and CD_3CN leveled Brønsted acidity and provided compound 2a in 10% NMR yield only. Because of the practical reasons for

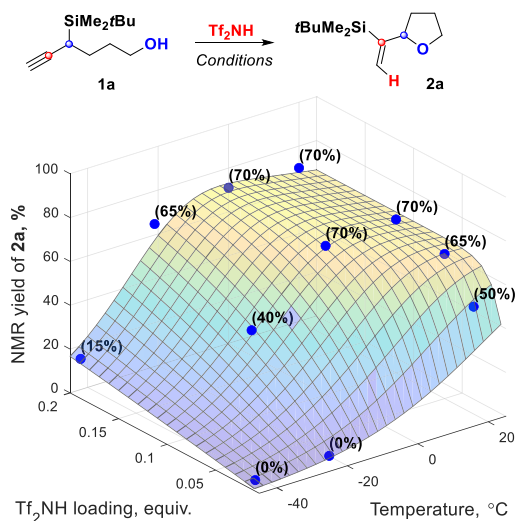
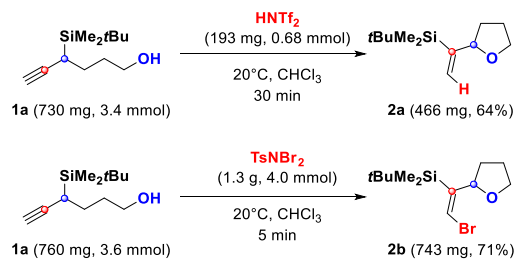


Figure 1. Optimization of $\text{ Tf}_2\text{NH}$ -catalyzed tetrahydrofuran **2a** synthesis in CDCl_3 . ^3D iphenylmethane internal standard; $c_{1a} \sim 0.15 \text{ M}$, CDCl_3 , 1 h; conversion less than 5% is considered below the limit of detection; the results are rounded by 5% increments.

the easier dosage of solid $\text{ Tf}_2\text{NH}$, we decided to develop a cyclization methodology with the latter. Finally, the optimal cyclization conditions (0.15–0.20 equiv of $\text{ Tf}_2\text{NH}$, in DCM or chloroform, 0–20 °C, 1 h) were found by exploring several catalyst loadings, reaction temperatures, and times (Figure 1). On a preparative scale, the transformation **1a** → **2a** was performed with the same 64% isolated yield of product **2a** at both submillimolar and millimolar scales (Schemes 2 and 3). It was also found that for the reaction, upscale $\text{ Tf}_2\text{NH}$ loadings of 20 mol % were more beneficial in terms of reproducible yields and fewer side products.

Scheme 3. Synthesis of Tetrahydrofuran Derivatives **2a** and **2b** in the Millimolar Scale



Next, we investigated the use of electrophilic halogen sources. The initial experiments with *N*-bromosuccinimide (NBS) in CDCl_3 gave the expected product **2b** and ambient temperature provided the optimal reaction time (Table 1, entries 1 and 2). However, the formation of diene **3b** was observed in substantial amounts (25%). We also observed that reactions with NBS required a much longer time than those with HNTf_2 to reach completion. This may be partially explained by the poor solubility of NBS in chlorinated solvents.

In other solvents (Table 1, entries 3 and 4), the conversion of starting material **1a** occurred with an increased amount of the diene **3b** side product and reaction time. To our surprise, bromine appeared to be less reactive than NBS (Table 1, entry 5). Fortunately, the use of *N,N*-dibromo tosylamide (TsNBr_2) significantly shortened the reaction time and suppressed the formation of diene **3b** (Table 1, entries 6–8). The optimal conditions for bromoetherification (1.2 equiv of TsNBr_2 in CDCl_3 , 20 °C, 5 min) gave 75% conversion to tetrahydrofuran **2b** (Table 1, entry 6). On a preparative scale, the transformation **1a** → **2b** was performed with practically the same 70 and 71% isolated yield of product **2b** at both submillimolar and millimolar scales (Schemes 2 and 3).

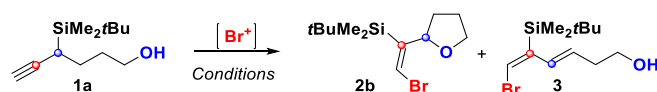
Next, we tested the iodoetherification of **1a** with a concomitant 1,2-silyl shift in the presence of *N*-iodosuccinimide (NIS) and vinyl iodide **2c** and obtained with 59% yield (Scheme 2). Interestingly, in this case, we did not observe the formation of the corresponding diene, as was the case with NBS. In addition, selenoetherification in the presence of PhSeCl was successful, and product **2d** was isolated in 50% yield as a pure (*E*)-isomer.

To expand the scope of the tetrahydrofuran derivatives, we tested the cyclization of carboxylic acid **1c** with various electrophiles. The required starting material **1c** was obtained by the oxidation of alcohol **1a**. Thus, the protic conditions applied to acid **1c** provided γ -butyrolactone derivative **2e** in 73% yield. Carboxylic acid **1c** also underwent a 1,2-silyl shift/halolactonization with TsNBr_2 and NIS, yielding lactones **2f** and **2g** in 73% and 50% yields, respectively. Next, selenolactonization was attempted with PhSeCl , and product **2h** was obtained in 47% (60% NMR) yield as a mixture of *E/Z* isomers in a ratio of 71:29. We hypothesize that phenylselenide can provide additional stability to the intermediate allyl cation, which, in combination with the carboxylate moiety as a good leaving group, can lead to isomerization.

We also achieved bromolactolization with a concomitant 1,2-silyl shift when aldehyde **1b** was mixed with NBS in wet DCM (for the synthesis of the starting material, see the Experimental Section). Only the cyclic form was observed, and the corresponding hemiacetal **2i** was isolated in 30% yield as a more stable α -anomer, apparently due to the anomeric effect. However, the lactolization of aldehyde **1b** under acidic conditions with HNTf_2 was not successful, providing a complex, unidentifiable product mixture. Similarly, alcohol **1d** with a shorter $(\text{CH}_2)_2$ -linker degraded in the presence of HNTf_2 or NBS and did not yield oxetane derivatives **2k** and **2l**. Alcohol **1a** was also used on the millimolar scale to synthesize both vinyl silane **2a** and bromo vinyl silane **2b** in 64 and 71% yields, respectively, showing the potential for direct scalability of these reactions.

Aldehyde **1b** can be easily transformed to oxime **4**, which can serve as an additional starting material bearing an internal *O*-nucleophile (see the Experimental Section). With starting material **4** in hand, we tested its cyclization options (Scheme 4). It appears that oxime **4** is inactive toward cyclization under acidic conditions, which can be explained by the leveling of the acidity due to *N*-protonation. It remained inactive under buffered conditions (phosphate salt/ HNTf_2 catalyst) in a variety of solvents (DCM, MeCN, and THF). In addition, selenocyclization of oxime **4** with PhSeCl did not yield any product. On the other hand, 1,2-silyl shift/ring closure was possible in the presence of NBS (for optimization table, see Supporting Information Table S2) and NIS, providing 4,5-

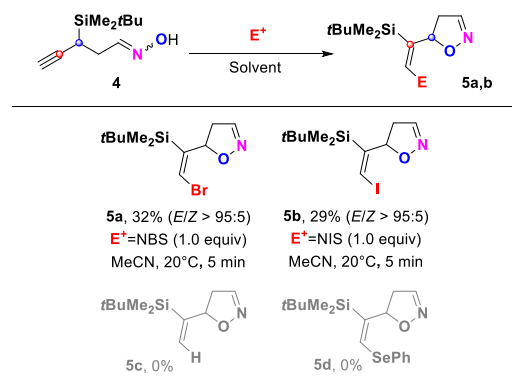
Table 1. Study of Tetrahydrofuran 2b Synthesis in the Bromoetherification Reaction



entry	Br ⁺ (equiv)	T _r (°C)	solvent ^a	reaction time	compound distribution (qNMR) ^{b,c}		
					starting material 1a, (%)	product 2b, (%)	side product 3, (%)
1	NBS (1.2)	−20	CDCl ₃	8 h	45	40	10
2		20	CDCl ₃	5 h	0	65	25
3		20	C ₆ D ₆	24 h	20	10	30
4		20	THF- <i>d</i> ₈	48 h	30	40	15
5	Br ₂ (1.2)	50	CDCl ₃	30 h	35	13	0
6	TsNBr ₂ (1.2)	20	CDCl ₃	5 min	0	75	0
7	TsNBr ₂ (1.0)	20	CDCl ₃	5 min	0	65	5
8	TsNBr ₂ (0.55)	20	CDCl ₃	5 min	0	55	10

^ac_{1a} = ~0.15 M. ^bDiphenylmethane internal standard. ^cNMR yields less than 5% are considered below the limit of detection; the results are rounded by 5% increments.

Scheme 4. Synthesis of 4,5-Dihydroisoxazole Derivatives 5a,b



dihydroisoxazoles **5a** and **5b** bearing vinyl halide/silane side chains in 32 and 29% yields, respectively.

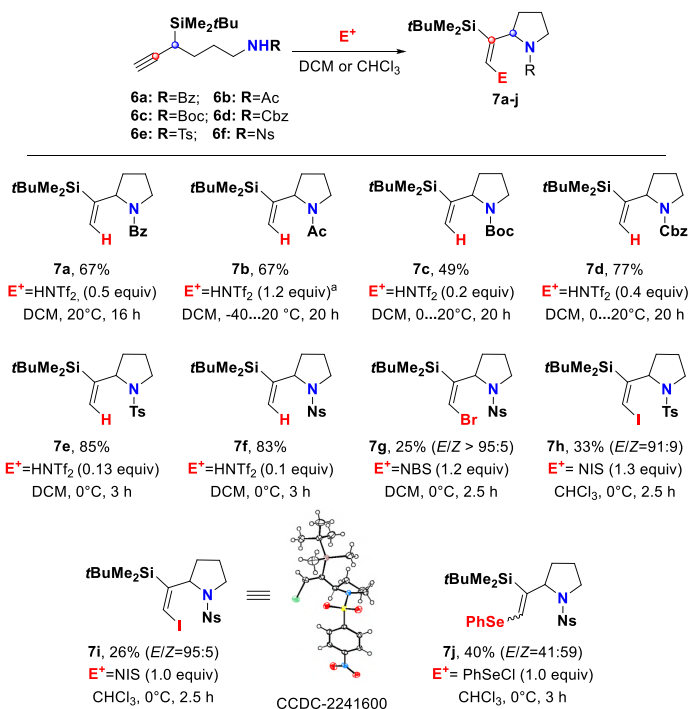
Next, we turned our attention to reactions with nitrogen nucleophiles (Scheme 5), and starting materials of type **6** were prepared from alcohol **1a** by nucleophilic substitution with azide, followed by reduction and *N*-functionalization (see the Experimental Section). We focused on amides, sulfonamides, and carbamates as more appropriate nucleophiles. As a test reaction, we attempted the cyclization of benzoyl amide **6a**. We observed that amides showed lower reactivity than oxygen nucleophiles; therefore, with an increase in the catalyst loading of HNTf₂ (0.5 equiv), we were able to obtain pyrrolidine **7a** 67% yield (84% crude). However, acetamide **6b** showed unexpectedly poor reactivity under catalytic conditions, eventually inhibiting the catalyst and stopping the reaction. However, we were still able to obtain 67% yield of pyrrolidine **7b** using an equimolar amount (1.2 equiv) and the gradual addition of HNTf₂.

As expected, the carbamates also underwent cyclization, providing pyrrolidines **7c** and **7d** in 49 and 77% yields, respectively. The yield of the *N*-Boc-protected product was somewhat lower than that of the *N*-Cbz group, yet with a lower catalyst loading, it still partially resisted acidic reaction conditions. The best yields in this series were obtained with

sulfonamide starting materials **6e,f**, which gave products **7e** and **7f** in 85 and 83% yields, respectively. Sulfonamides **6e,f** were also tested for bromoamination (NBS), iodoamination (NIS), and selenoamination (PhSeCl) with concomitant 1,2-silyl shift. Reactions with NBS and NIS afforded products **7g–i** with a vinyl halide side chain in low yields (33 and 26%). In the case of vinyl iodides, double-bond isomers were also observed; however, the (*E*)-selectivity was maintained at >90%. Cyclization with PhSeCl gave a somewhat better yield (product **7j**: 40%), but with no selectivity for olefin geometry. Thus, it can be concluded that reactions with sterically larger electrophiles (I⁺, PhSe⁺) deviate from complete (*E*)-selectivity. In the case of vinyl iodides, only minor erosion was observed, and (*Z*)-isomers were observed at <10% for products **7h,i**. However, for phenyl selenide **7j**, there was even a flip in the selectivity, providing the (*Z*)-isomer as the major component: *Z/E* ~ 3:2. We can speculate that the newly formed vinylsilane moiety can be protonated (no base additive during cyclization), and in such a case, the intermediate carbenium ion is stabilized by both the β-silicon effect and α-heteroatom effect. Protonated intermediates of type PhSe(H)C⁺-C(Si)(H)-R is better stabilized than Hal(H)C⁺-C(Si)(H)-R due to the intrinsic properties of the selenyl substituent; therefore, compounds containing the PhSe moiety are more prone to isomerization. On the other hand, 1,3-allylic strain can preorganize the product conformation so that the vinylogous anomeric effect (*n*_{Se}–π_{C=C} → σ^{*}_{C-heteroatom} interaction)¹⁶ can play a role in weakening the C-heteroatom bond in the allylic position and lead to the *E/Z*-isomerization. A single crystal suitable for X-ray analysis was obtained for product **7i**, confirming both the double bond geometry and the structure in addition to the 2D-NOESY spectroscopic studies.¹⁷ It is worth noting that acylamides **7a,b** and carbamates **7c,d** typically show complex NMR spectra due to rotational and conformational constraints. Typically, the most suitable solvent and temperature had to be found to decrease the number of conformers and identify the obtained products.¹⁸

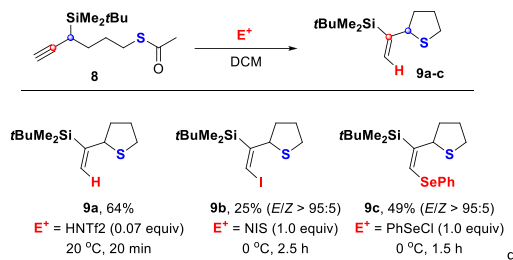
Finally, we also tested thiolane cyclization, for which the corresponding sulfur-containing starting materials can be obtained by the straightforward nucleophilic substitution of alcohol **1a** (see the Experimental Section). Our initial attempts with unprotected thiol or disulfide were unsuccessful; therefore, we turned our attention to thioesters. To our delight, thioacetate **8** gave cyclization product **9a** under acidic

Scheme 5. Product Scope for the Synthesis of Pyrrolidine Derivatives 7a–j



conditions (Scheme 6). After brief optimization of the reaction conditions (7 mol % of HNTf₂, 20 °C), thiolane 9a was

Scheme 6. Synthesis of Thiolanes 9a–c



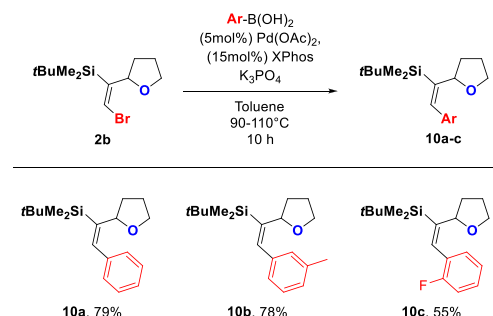
isolated in 64% yield. Next, we turned to halocyclization, and even if the sulfur center reacted with NIS to give the degradation products, we succeeded in isolating vinyl iodide 9b in 25% yield. To our delight, PhSeCl exhibited reasonable reactivity and selectivity, and thiolane 9c with a vinyl selenide side chain was obtained in 49% yield. For all cyclization cases covered in Schemes 2–6 we were able to identify, isolate, and prove structures only for the five-membered cycles. This indicates that the 1,2-silyl shift in these molecular systems occurs faster than the following cyclization and that the six-membered cycle closure is slower than the 1,2-silyl shift. On the other hand, the six-membered cycle formation would

provide enol (thio)ethers and enamine derivatives that might be unstable in the presence of the used electrophiles.

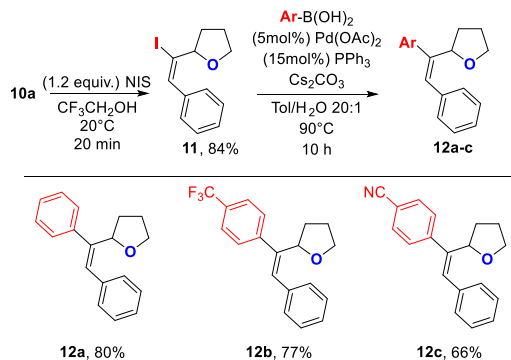
To demonstrate the synthetic utility of the obtained products, we performed a series of Suzuki–Miyaura cross-coupling reactions on vinyl bromide 2b under modified Buchwald conditions (Scheme 7).¹⁹ Vinyl bromide participated in the coupling reactions with various aryl boronic acids to yield silyl styrenes 10a–c in the yield range of 55–79%.

Next, we exchanged the vinyl silane moiety in compound 10a for vinyl iodide 11 (Scheme 8).²⁰ If performed in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), this transformation

Scheme 7. Suzuki–Miyaura Cross-coupling Reactions of Vinyl Bromide 2b



Scheme 8. Synthesis of Tetrahydrofurans with Trisubstituted Olefin Side Chain 12a–c by Electrophilic Substitution of the Silyl Group and Suzuki–Miyaura Cross-coupling Reactions



resulted in rapid electrophilic exchange in less than 15 min, providing an *E/Z*-mixture of compound **11**. Enhanced acidity, hydrogen bond donating ability, and cation stabilization by HFIP are likely responsible for such an outcome.²¹ Fortunately, switching to somewhat less polar 2,2,2-trifluoroethanol allowed us to obtain the desired vinyl iodide **11** in 84% yield with a completely conserved double bond geometry.

Compound **11** was successfully used again in Suzuki–Miyaura cross-coupling reactions with another set of boronic acids to yield tetrahydrofurans with trisubstituted olefin side chains **12a–c** in the yield range of 66–80%.

CONCLUSIONS

In summary, we have shown that propargyl silanes containing a terminal alkyne moiety from one side and tethered nucleophilic groups from another side readily undergo electrophile-induced intramolecular cyclization with a concomitant 1,2-silyl shift. This approach can be viewed as an extended version of halo- and selenoheterocyclization, which makes use of propargyl silanes as 1,3-dipoles. The developed method is suitable for the synthesis of five-membered heterocycles with a highly functionalized trisubstituted alkene side chain. Typically, a 1,2-silyl shift provides excellent (*E*)-double-bond selectivity, with the exception when a sterically demanding electrophile is combined with a big incoming nucleophile. The resulting heterocycles were obtained in up to 85% yields. The synthetic utility of the alkene side chain was demonstrated by transforming the latter into geometrically defined trisubstituted olefins by a sequence of Suzuki–Miyaura cross-coupling–electrophilic silicon exchange—Suzuki–Miyaura cross-coupling reactions. The developed methodology will be useful for the synthesis of natural products, their analogs, and pharmaceutically or agrochemically important heterocycles. The development of the enantioselective version of this methodology by the use of asymmetric counteranion-directed catalysis by Brønsted acids is underway in our laboratory and will be reported elsewhere.

EXPERIMENTAL SECTION

The solvents used in the reactions were dried using standard drying agents and freshly distilled prior to use. Commercially available reagents were used as received. Compounds **1a** and **1d** were prepared

according to the procedures described in the literature.¹⁵ All reactions were followed by TLC on E. Merck Kiesegel 60 F254, with detection by UV Full Paper light or developed using generic KMnO₄ or I₂ stain, GC analysis, and NMR analysis. Direct-phase column chromatography was performed using silica gel (60 Å, 40–63 μm, ROCC). Reverse-phase column chromatography was performed on C18 silica gel (25–40 μm, LiChroprep RP-18). Preparative HPLC was performed using an Agilent Technologies 1200 Series system equipped with an Eclipse XDB-C18 column, 9.4 × 250 mm, particle size 5 μm). ¹H and ¹³C{¹H} NMR spectra were recorded using Bruker AVANCE Neo 500 and AVANCE 300 MHz spectrometers in CDCl₃, DMSO-*d*₆, and MeOH-*d*₄. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are reported in Hz. Residual solvent (¹H) or solvent (¹³C) peaks were used as an internal reference (CDCl₃: δ = 7.26 ppm for ¹H NMR; CDCl₃: δ = 77.16 ppm for ¹³C{¹H} NMR; DMSO-*d*₆: δ = 2.50 ppm for ¹H NMR; DMSO-*d*₆: δ = 39.52 ppm for ¹³C{¹H} NMR; MeOH-*d*₄: δ = 3.31 ppm for ¹H NMR; and MeOH-*d*₄: δ = 49.00 ppm for ¹³C{¹H} NMR). The multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), hept (heptet), m (multiplet), and b (broad). The structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. Crystallographic diffraction data were collected with a NoniusKappa CCD diffractometer (Mo Kα, λ = 0.71073 Å) equipped with a low-temperature Oxford Cryosystems Cryostream Plus device. GC analyses were performed using a Hewlett-Packard Agilent Technologies 6890 gas chromatograph with a mass-selective detector equipped with a capillary column Agilent Technologies DB-1MS (30 m × 0.32 mm × 0.25 μm). Injection temperature: 250 °C; splitless and injection volume 1 μL or split 1:300 and injection volume 0.2 μL; gas type: helium; flow rate: 1.2 mL/min; detector temperature: 230 °C; MS-detector (EI, 70 eV). High-resolution mass spectra (ESI) were recorded with an Agilent 1290 Infinity series UPLC connected to an Agilent 6230 TOF mass spectrometer (calibration at *m/z* = 121.050873 and *m/z* = 922.009798) or (ESI) Thermo Fisher Scientific Orbitrap Exploris 120 mass spectrometer operating in the Full Scan mode at the 120000 resolutions.

3-(tert-Butyldimethylsilyl)pent-4-ynal (Int1). 3-(tert-Butyldimethylsilyl)pent-4-yn-1-ol¹⁵ (**1d**; 1.50 g, 7.6 mmol, 1.0 equiv) and anhydrous Na₂SO₄ (3.2 g) were suspended in DCM (150 mL) in a disposable polypropylene cup. Pyridinium chlorochromate (4.9 g, 22.7 mmol, 3.0 equiv) was slowly added, and the reaction mixture was stirred at ambient conditions for 3 h (TLC control). The reaction mixture was filtered through a silica plug (DCM/Hex: 50 → 100%) and concentrated in vacuo to afford aldehyde **Int1** (1.37 g, 96%) as a clear oil. ¹H NMR (500 MHz, CDCl₃): δ 9.83 (dd, 1H, *J* = 2.2, 1.3), 2.55 (ddd, 1H, *J* = 16.6, 11.2, 2.2), 2.45 (ddd, 1H, *J* = 16.6, 3.8, 1.3), 2.29 (ddd, 1H, *J* = 11.2, 3.8, 2.8), 2.04 (d, 1H, *J* = 2.8), 0.98 (s, 9H), 0.13 (s, 3H), 0.04 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 201.9, 85.3, 70.3, 43.8, 27.2, 17.8, 10.8, −6.9, −7.4. HRMS (ESI): *m/z* calcd for C₁₁H₂₁OSi⁺ [*M* + H]⁺, 197.1356; found, 197.1337.

(6-Azidohex-1-yn-3-yl)(tert-butyl)dimethylsilane (Int2). A solution of 4-(tert-butyl)dimethylsilyl)hex-5-yn-1-yl 4-methylbenzenesulfonate²² (2.8 g, 7.6 mmol, 1.0 equiv) in anhyd. DMF (5 mL) under an argon atmosphere was added dropwise to a suspension of NaN₃ (1.0 g, 15.4 mmol, 2.0 equiv) in anhyd. DMF (15 mL) at 0 °C. The resulting reaction mixture was stirred at ambient temperature for 20 h (elevated temperature leads to spontaneous intramolecular 1,3-dipolar cycloaddition reaction²³). Toluene (50 mL) and H₂O (100 mL) were added to the reaction mixture. The organic layer was separated, washed with H₂O (2 × 100 mL), and concentrated in vacuo, keeping the bath temperature <30 °C. The obtained residue was suspended in hexanes (30 mL), the resulting suspension was filtered through a silica plug (DCM/Hex: 20%), and the filtrate was concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: EtOAc/Hex 0–5%) to afford azide **Int2** (1.7 g, 94%) as a yellow oil. ¹H NMR (500 MHz, CDCl₃): δ 3.38–3.27 (m, 2H), 2.07–1.94 (m, 1H), 2.00 (d, 1H, *J* = 2.7), 1.76 (dt, 1H, *J* = 11.8, 3.4), 1.73–1.65 (m, 1H), 1.59 (dddd, 1H, *J* = 13.3, 9.8, 6.4, 3.6), 1.47

(dddd, 1H, $J = 13.3, 11.7, 9.8, 4.5$), 0.98 (s, 9H), 0.10 (s, 3H), 0.03 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 86.6, 69.9, 51.2, 28.7, 27.3, 27.0, 17.7, 16.6, -7.1, -7.2. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{24}\text{N}_3\text{Si}^+ [\text{M} + \text{H}]^+$, 238.1734; found, 238.1727.

4-(*tert*-Butyldimethylsilyl)hex-5-ynal (1b). Pyridinium chlorochromate (3.7 g, 17.2 mmol, 1.5 equiv) and NaOAc (0.3 g, 3.5 mmol, 0.3 equiv) were suspended in DCM (40 mL) in a disposable polypropylene cup. 4-(*tert*-Butyldimethylsilyl)hex-5-yn-1-ol¹⁵ (1a; 2.4 g, 11.3 mmol, 1.0 equiv) was slowly added, and the resulting reaction mixture was stirred at ambient conditions for 3 h (TLC control). The reaction mixture was filtered through a silica plug (DCM/Hex: 50 $\rightarrow$ 100%) and concentrated in vacuo to afford aldehyde 1b (1.3 g, 55%) as a yellow oil. ^1H NMR (500 MHz, CDCl_3): δ 9.83 (s, 1H), 2.80 (ddd, $J = 17.8, 7.7, 5.7$, 1H), 2.65 (dt, $J = 17.8, 7.6$, 1H), 2.02 (d, $J = 2.7$, 1H), 1.92–1.85 (m, 1H), 1.77 (dt, $J = 12.2, 2.7$, 1H), 1.71–1.60 (m, 1H), 0.96 (s, 9H), 0.10 (s, 3H), 0.04 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 178.8, 86.1, 70.4, 33.4, 27.3, 25.1, 17.7, 16.6, -7.2, -7.3. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{23}\text{OSi}^+ [\text{M} + \text{H}]^+$, 211.1513; found, 211.1530.

4-(*tert*-Butyldimethylsilyl)hex-5-ynoic Acid (1c). In a 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer, 4-(*tert*-butyldimethylsilyl)hex-5-ynal (1b; 87 mg, 0.42 mmol, 1.0 equiv) and 2-methylbut-2-ene (2 mL) were dissolved in *t*-BuOH (10 mL). NaClO_2 (425 mg, 80%, 3.8 mmol, 9.0 equiv) and NaH_2PO_4 (456 mg, 3.8 mmol, 9.0 equiv) solution in H_2O (10 mL) was added dropwise, and the resulting reaction mixture was stirred for 16 h at ambient temperature. The reaction mixture was concentrated in vacuo and then suspended in H_2O (10 mL). The resulting mixture was extracted with DCM (3 $\times$ 15 mL). The combined organic phase was washed with saturated aqueous NaCl (10 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (eluent: Hex/DCM: 70 $\rightarrow$ 100%) to afford carboxylic acid 1c (68 mg, 72%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 2.74 (ddd, $J = 16.6, 8.6, 4.9$, 1H), 2.53 (dt, $J = 16.6, 8.3$, 1H), 2.02 (d, $J = 2.7$, 1H), 1.93–1.83 (m, 1H), 1.82 (dt, $J = 12.4, 2.7, 2.6$, 1H), 1.67 (tdd, $J = 12.4, 8.3, 4.9$, 1H), 0.96 (s, 9H), 0.10 (s, 3H), 0.04 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 179.6, 86.0, 70.4, 33.6, 27.2, 25.1, 17.7, 16.6, -7.2, -7.3. HRMS (ESI): m/z calcd for $\text{C}_{11}\text{H}_{19}\text{O}_2\text{Si}^+ [\text{M} - \text{CH}_3]^+$, 211.1149; found, 211.1152.

Experimental Procedure for Tf_2NH -catalyzed Tetrahydrofuran 2a Synthesis Optimization Using qNMR. In an NMR tube, precisely weighted propargylsilane 1a (20 mg, 0.094 mmol) and precisely weighted diphenylmethane (12 mg, 99% purity, 0.071 mmol) were dissolved in deuterated solvent (0.65 mL). The NMR tube was adjusted to the indicated temperature, and Brønsted acid catalyst was added, as indicated in Figure 1. The resulting reaction mixture was allowed to react for the indicated amount of time (Figure 1). If required, the homogenization of the sample was achieved by ultrasonication. The reaction mixture was quenched by the addition of 2,6-di-*tert*-butylpyridine in excess (19 mg, 0.100 mmol, 1.06 equiv). The NMR tube was subjected to an NMR analysis. The NMR spectrum was registered in the inverse gated C^{13} decoupled proton NMR (“PROTON_C13DC_IG”) mode and setting NS = 16, DS = 2, and D1 = 10.0 s. Corresponding peaks for the analysis were chosen (CDCl_3): for propargyl silane 1a: δ 3.54 (t, 2H, $J = 6.5$); for tetrahydrofuran 2a: δ 5.40 (dd, 1H, $J = 2.8, 0.9$); and for diphenylmethane, δ 7.18–7.11 (m, 6H). The integral value $I_{\text{Ph}_2\text{Me}}$ of diphenylmethane was set to 1000. The yield for the compound was determined by the formula

$$\eta_{1a} = \frac{\left(\frac{I_{1a}}{2}\right) \cdot \left(\frac{m_{\text{Ph}_2\text{Me}}}{M_{\text{Ph}_2\text{Me}}}\right)}{\left(\frac{I_{\text{Ph}_2\text{Me}}}{6}\right)} \cdot \frac{1}{n_{1a}}$$

$$\eta_{2a} = \frac{\left(\frac{I_{2a}}{1}\right) \cdot \left(\frac{m_{\text{Ph}_2\text{Me}}}{M_{\text{Ph}_2\text{Me}}}\right)}{\left(\frac{I_{\text{Ph}_2\text{Me}}}{6}\right)} \cdot \frac{1}{n_{1a}}$$

Experimental Procedure the Study of Tetrahydrofuran 2b Synthesis in the Bromoetherification Reaction. In an NMR tube precisely weighted propargylsilane 1a (20 mg, 0.094 mmol) and precisely weighted diphenylmethane (12 mg, 0.071 mmol) were dissolved in deuterated solvent (0.65 mL). The NMR tube was adjusted to the indicated temperature, and an electrophilic halogen source was added (see Table 1). If required, the homogenization of the sample was achieved by ultrasonication. The resulting reaction mixture was allowed to react for the indicated time (Table 1). The NMR tube was subjected to NMR analysis. NMR spectrum was registered in the inverse gated C^{13} decoupled proton NMR (“PROTON_C13DC_IG”) mode and setting NS = 16, DS = 2, and D1 = 10.0 s. Corresponding peaks for the analysis were chosen (CDCl_3): for propargyl silane 1a: δ 3.54 (t, 2H, $J = 6.5$); for tetrahydrofuran 2b: 4.69–4.64 (m, 1H); and for diphenylmethane δ 3.92 (s, 2H). The integral value $I_{\text{Ph}_2\text{Me}}$ of diphenylmethane was set to 1000. The yield for the compound was determined by the formula

$$\eta_{1a} = \frac{\left(\frac{I_{1a}}{2}\right) \cdot \left(\frac{m_{\text{Ph}_2\text{Me}}}{M_{\text{Ph}_2\text{Me}}}\right)}{\left(\frac{I_{\text{Ph}_2\text{Me}}}{2}\right)} \cdot \frac{1}{n_{1a}}$$

$$\eta_{2b} = \frac{\left(\frac{I_{2b}}{1}\right) \cdot \left(\frac{m_{\text{Ph}_2\text{Me}}}{M_{\text{Ph}_2\text{Me}}}\right)}{\left(\frac{I_{\text{Ph}_2\text{Me}}}{2}\right)} \cdot \frac{1}{n_{1a}}$$

General Procedure A for Electrophile-induced Intramolecular Cyclization Reactions with Concomitant 1,2-Silyl Shift. In a round-bottom flask equipped with a Teflon-coated magnetic stirrer, propargylsilane (1.0 equiv) was dissolved in solvent (0.1 mmol in 1.0–3.0 mL) under an argon atmosphere. The reaction mixture was cooled to the indicated temperature, and Brønsted acid catalyst/electrophilic reagent (0.05–1.2 equiv) was added. The resulting reaction mixture was stirred at the indicated temperature and for the indicated reaction time (TLC control). The reaction mixture was quenched by addition of saturated aqueous NaHCO_3 solution, the layers were separated, and the aqueous layer was extracted with DCM (2 times). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The crude reaction mixture was purified by column chromatography on silica gel.

tert-Butyldimethyl(1-(tetrahydrofuran-2-yl)vinyl)silane (2a).

The reaction was performed following general procedure A. For submillimolar-scale synthesis: 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (1a; 50 mg, 0.24 mmol, 1.0 equiv) in CHCl_3 (3 mL), solution of HNTf₂ (13 mg, 0.05 mmol, 0.2 equiv) in CHCl_3 (0.5 mL) was added dropwise at 20 °C, reaction time 30 min at 20 °C. Column chromatography (eluent: DCM/Hex 20 $\rightarrow$ 30%) on silica gel afforded silyl furan 2a (32 mg, 64%) as a clear oil.

For millimolar-scale synthesis: 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (1a; 730 mg, 3.4 mmol, 1.0 equiv) in CHCl_3 (50 mL), 0.2 M HNTf₂ (193 mg, 0.69 mmol, 0.2 equiv) solution in CHCl_3 was added dropwise at 20 °C, reaction time 30 min at 20 °C. Reaction mixture was quenched with saturated aqueous NaHCO_3 (50 mL) at 0 °C. The layers were separated, and the aqueous layer was extracted with CHCl_3 (2 $\times$ 15 mL). The combined organic layer was washed with saturated aqueous NaCl (2 $\times$ 20 mL). Column chromatography (eluent: DCM/Hex 20 $\rightarrow$ 30%) on silica gel afforded silyl furan 2a (464 mg, 64%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 5.96 (dd, 1H, $J = 2.8, 1.6$), 5.40 (dd, 1H, $J = 2.8, 0.9$), 4.45 (brt, 1H, $J = 7.2$), 3.95 (dd, 1H, $J = 14.4, 7.4$), 3.78 (dd, 1H, $J = 14.4, 7.6$), 2.07 (dt, 1H, $J = 12.0, 6.9$), 1.98–1.82 (m, 2H), 1.54 (dq, 1H, $J = 12.0, 7.9$), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 151.1, 124.5, 82.1, 68.1, 33.4, 27.1, 25.9, 17.1, -4.8, -5.2. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{25}\text{OSi}^+ [\text{M} + \text{H}]^+$, 213.1669; found, 213.1661.

(E)-(2-Bromo-1-(tetrahydrofuran-2-yl)vinyl)(*tert*-butyldimethylsilane (2b). The reaction was performed following general procedure A. For submillimolar-scale synthesis: 4-(*tert*-

butyldimethylsilyl)hex-5-yn-1-ol (**1a**; 100 mg, 0.47 mmol, 1.0 equiv) in CHCl_3 (5 mL) and N,N -dibromo-4-methylbenzenesulfonamide (185 mg, 0.56 mmol, 1.2 equiv), reaction temperature 20 °C, reaction time 5 min. Column chromatography (eluent: DCM/Hex 20 → 30%) on silica gel afforded silyl furan **2b** (96 mg, 70%) as a clear oil.

For millimolar-scale synthesis: 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (**1a**; 760 mg, 3.60 mmol, 1.0 equiv) in CHCl_3 (50 mL), N,N -dibromo-4-methylbenzenesulfonamide (1.3 g, 3.96 mmol, 1.1 equiv), reaction temperature 20 °C, reaction time 5 min. Reaction mixture was quenched with saturated aqueous NaHCO_3 (50 mL) at 0 °C. The layers were separated, and the aqueous layer was extracted with CHCl_3 (2 × 15 mL). The combined organic layer was washed with saturated aqueous NaCl (2 × 20 mL). Column chromatography (eluent: DCM/Hex 20 → 25%) afforded silyl furan **2b** (743 mg, 71%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 6.31 (d, 1H, J = 1.2), 4.69–4.64 (m, 1H), 3.95 (dd, 1H, J = 15.2, 7.1), 3.71 (dd, 1H, J = 15.2, 7.1), 2.39 (td, 1H, J = 12.4, 6.4), 1.95–1.87 (m, 2H), 1.44 (dq, 1H, J = 12.4, 9.2, 9.1), 0.91 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 148.7, 112.9, 82.8, 67.9, 31.3, 27.4, 25.6, 17.3¹, –3.5, –4.2. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{24}\text{BrO}_2\text{Si}^+ [\text{M} + \text{H}]^+$, 291.0774; found, 291.0771.

Mixture of (E)-(2-Bromo-1-(tetrahydrofuran-2-yl)vinyl)(*tert*-butyldimethylsilyl)ane (**2b**) and (3E,5E)-6-Bromo-5-(*tert*-butyldimethylsilyl)hexa-3,5-dien-1-ol (**3**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (**1a**; 900 mg, 4.2 mmol, 1.0 equiv) in DCM (20 mL), and NBS (754 mg, 4.2 mmol, 1.0 equiv) was added at –20 °C. The resulting reaction mixture was warmed to 20 °C and stirred for 5 h. Column chromatography (eluent: EtOAc/Hex 5 → 10%) afforded silyl furan **2b** (550 mg, 47%) as a clear oil. Continuing column chromatography (eluent: EtOAc/Hex 10 → 20%) afforded silyl diene **3** (184 mg, 15%) as a clear oil. NMR data for compound **3**: ^1H NMR (500 MHz, CDCl_3): δ 6.38 (d, 1H, J = 16.0), 6.38 (s, 1H), 5.80 (dt, 1H, J = 16.2, 7.1), 3.71 (t, 2H, J = 6.3), 2.41 (dt, 2H, J = 7.1, 6.3), 0.90 (s, 9H), 0.17 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 141.9, 133.1, 132.3, 115.6, 61.9, 37.0, 27.1, 17.5, –4.4. Compound **3** appeared to be too unstable for HRMS and elemental analysis.

(E)-*tert*-Butyl(2-iodo-1-(tetrahydrofuran-2-yl)vinyl)-dimethylsilane (**2c**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (**1a**; 50 mg, 0.24 mmol, 1.0 equiv) in CHCl_3 (3 mL), NIS (75 mg, 0.34 mmol, 1.2 equiv), reaction temperature 20 °C, reaction time 20 h. Column chromatography (eluent: DCM/Hex 10 → 20%) afforded silyl furan **2c** (47 mg, 59%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 6.50 (d, 1H, J = 1.7), 4.44 (ddd, 1H, J = 9.8, 6.6, J = 1.7), 3.98 (ddd, 1H, J = 14.8, 6.7, 0.7), 3.74 (ddd, 1H, J = 14.8, 7.5, 1.0), 2.47–2.34 (m, 1H), 1.96–1.88 (m, 2H), 1.40 (dq, 1H, J = 12.5, 9.2), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 155.9, 89.0, 88.0, 68.1, 31.0, 27.4, 25.5, 17.3, –3.3, –4.3. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{24}\text{IO}_2\text{Si}^+ [\text{M} + \text{H}]^+$, 339.0636; found, 339.0662.

(E)-*tert*-Butyldimethyl(2-(phenylselenanyl)-1-(tetrahydrofuran-2-yl)vinyl)silane (**2d**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (**1a**; 40 mg, 0.19 mmol, 1.0 equiv) in DCM (14 mL), phenylselenenyl chloride (40 mg, 0.21 mmol, 1.1 equiv), reaction temperature 0 °C, reaction time 1 h. Column chromatography (eluent: DCM/Hex 10 → 20%) afforded silyl furan **2d** (35 mg, 50%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 7.53–7.49 (m, 2H), 7.33–7.24 (m, 3H), 6.93 (s, 1H), 4.39 (dd, 1H, J = 10.7, 6.2), 3.20 (td, 1H, J = 10.7, 5.6), 2.95 (dd, 1H, J = 10.7, 8.1), 2.35 (dt, 1H, J = 12.4, 5.4), 2.23 (qd, 1H, J = 12.4, 5.4), 2.17–2.09 (m, 1H), 1.85 (tp, 1H, J = 12.4, 5.4), 0.91 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 141.7, 134.7, 134.4, 132.5, 129.3, 127.2, 51.8, 35.2, 33.2, 32.4, 27.1, 17.9, –5.2, –5.3. HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{29}\text{OSeSi}^+ [\text{M} + \text{H}]^+$, 369.1148; found, 369.1164.

5-(1-(*tert*-butyldimethylsilyl)vinyl)dihydrofuran-2(3H)-one (**2e**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-ynoic acid (**1c**; 26 mg, 0.12 mmol, 1.0 equiv) in CHCl_3 (2 mL), HNTf₂ (8 mg, 0.030 mmol, 0.2 equiv) was

added dropwise (0.2 M solution in CHCl_3), reaction temperature 20 °C, reaction time 30 min. Column chromatography (eluent: DCM/Hex 50 → 60%) afforded silyl furanone **2e** (19 mg, 73%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 5.96 (s, 1H), 5.51 (s, 1H), 5.10 (brt, 1H, J = 7.1), 2.58–2.50 (m, 2H), 2.42 (dq, 1H, J = 12.9, 7.1), 1.94 (dq, 1H, J = 12.9, 9.0, 7.1), 0.91 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 177.2, 147.8, 126.3, 83.1, 29.9, 28.8, 26.9, 17.1, –5.0, –5.3. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{23}\text{O}_2\text{Si}^+ [\text{M} + \text{H}]^+$, 227.1462; found, 227.1458.

(E)-5-(2-Bromo-1-(*tert*-butyldimethylsilyl)vinyl)-dihydrofuran-2(3H)-one (**2f**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-ynoic acid (**1c**; 50 mg, 0.22 mmol, 1.0 equiv) in CHCl_3 (2 mL), N,N -dibromomethylbenzenesulfonamide (73 mg, 0.22 mmol, 1.0 equiv), reaction temperature 0 °C, reaction time 5 min. Column chromatography (eluent: DCM/Hex 30 → 40%) afforded silyl furanone **2f** (49 mg, 73%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 6.44 (d, 1H, J = 1.6), 5.40 (ddd, 1H, J = 9.7, 7.0, 1.6), 2.80–2.73 (m, 1H), 2.64–2.49 (m, 2H), 1.88 (ddt, 1H, J = 11.5, 11.2, 9.7), 0.93 (s, 9H), 0.16 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 176.7, 146.0, 114.6, 83.5, 28.7, 28.0, 27.2, 17.4, –3.6, –4.4. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{22}\text{BrO}_2\text{Si}^+ [\text{M} + \text{H}]^+$, 305.0567; found, 305.0561.

(E)-5-(1-(*tert*-Butyldimethylsilyl)-2-iodovinyl)dihydrofuran-2(3H)-one (**2g**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-ynoic acid (**1c**; 50 mg, 0.22 mmol, 1.0 equiv) in CHCl_3 (2 mL), NIS (50 mg, 0.22 mmol, 1.0 equiv), reaction temperature 0 °C, reaction time 20 h. Column chromatography (eluent: DCM/Hex 30 → 50%) afforded silyl furanone **2g** (39 mg, 50%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 6.65 (d, 1H, J = 1.4), 5.19 (ddd, 1H, J = 9.6, 7.0, 1.3), 2.80–2.72 (m, 1H), 2.64–2.49 (m, 2H), 1.82c (ddt, 1H, J = 13.1, 11.4, 9.9), 0.92 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 176.8, 153.3, 90.4, 88.5, 28.6, 27.7, 27.2, 17.4, –3.4, –4.4. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{22}\text{IO}_2\text{Si}^+ [\text{M} + \text{H}]^+$, 353.0428; found, 353.0423.

Mixture of (E)- and (Z)-Isomers of 5-(1-(*tert*-butyldimethylsilyl)-2-(phenylselenanyl)vinyl)dihydrofuran-2(3H)-one (**2h**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-ynoic acid (**1c**; 49 mg, 0.22 mmol, 1.0 equiv) in DCM (15 mL), phenylselenenyl chloride (42 mg, 0.22 mmol, 1.0 equiv), reaction temperature 0 °C, reaction time 2 h. Column chromatography (eluent: DCM/Hex 20 → 30%) afforded silyl furanone **2h** (39 mg, 47%, E/Z = 71:29) as a clear oil. Characterization of compound (E)-**2h**: ^1H NMR (500 MHz, CDCl_3): δ 7.51–7.46 (m, 2H), 7.36–7.29 (m, 3H), 6.95 (s, 1H), 5.32 (dd, 1H, J = 9.4, 7.0), 2.64–2.57 (m, 2H), 2.54–2.46 (m, 1H), 2.08 (dq, 1H, J = 12.7, 10.4), 0.93 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 176.8, 142.1, 134.0, 132.6, 131.5, 129.6, 127.8, 83.0, 29.3, 28.6, 27.2, 17.6, –4.1, –4.8. HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{27}\text{O}_2\text{SeSi}^+ [\text{M} + \text{H}]^+$, 383.0940; found, 383.0935. Characterization of compound (Z)-**2h**: ^1H NMR (500 MHz, CDCl_3): δ 7.51 (s, 1H), 7.50–7.46 (m, 2H), 7.36–7.29 (m, 3H), 5.05 (t, 1H, J = 7.6), 2.58–2.52 (m, 2H), 2.41 (dq, 1H, J = 12.8, 6.3), 1.95 (dq, 1H, J = 12.8, 9.3), 1.01 (s, 9H), 0.34 (s, 3H), 0.24 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 177.0, 138.6, 137.5, 132.7, 129.6, 127.8, 84.1, 31.0, 29.2, 27.5, 19.3, –3.3, –3.9. HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{27}\text{O}_2\text{SeSi}^+ [\text{M} + \text{H}]^+$, 383.0940; found, 383.0931.

trans-(E)-5-(2-Bromo-1-(*tert*-butyldimethylsilyl)vinyl)-tetrahydrofuran-2-ol (**2i**). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (**1b**; 300 mg, 1.4 mmol, 1.0 equiv) in wet CHCl_3 (20 mL), NBS (278 mg, 1.6 mmol, 1.1 equiv), reaction temperature 20 °C, reaction time 14 h. Washed with saturated aqueous NaHCO_3 (20 mL) and saturated aqueous NaCl (10 mL). Column chromatography (eluent: DCM/Hex 10 → 30%) afforded silyl furanone **2i** (130 mg, 30%) as a clear oil. ^1H NMR (500 MHz, CDCl_3): δ 6.32 (d, 1H, J = 1.7), 5.49 (dd, 1H, J = 5.5, 2.2), 4.91 (dt, 1H, J = 7.9, J = 1.7), 2.52 (dtd, 1H, J = 12.5, J = 7.9, 4.7), 2.09 (dddd, 1H, J = 13.2, J = 8.2, 7.9, 4.7), 1.87 (dddd, 1H, J = 13.2, J = 7.9, 4.7, 2.2), 1.46 (dq, 1H, J = 12.5, J = 7.9), 0.90 (s,

9H), 0.09 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 148.5, 113.0, 99.5, 81.2, 31.9, 30.2, 27.5, 17.4, -3.5, -4.3. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{22}\text{BrOSi}^+ [\text{M} - \text{OH}]^+$, 289.0618; found, 289.0613.

Mixture of (E)- and (Z)-Isomers of 3-(tert-Butyldimethylsilyl)pent-4-ynal Oxime (4). In a 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer, $\text{NH}_2\text{OH}\cdot\text{HCl}$ (2.3 g, 33.2 mmol, 4.0 equiv) was dissolved in MeOH (80 mL) by ultrasonication. KOH (4.4 g, 66.4 mmol, 8 equiv) in MeOH (80 mL) was added, and the resulting reaction mixture was stirred until a white precipitate formed. 3-(tert-Butyldimethylsilyl)pent-4-ynal (**Int1**; 1.6 g, 8.3 mmol, 1.0 equiv) was added, and the resulting mixture was stirred for 2 h at ambient temperature (TLC control). The reaction mixture was concentrated in vacuo to approximately 30 mL volume and filtered through a Celite pad. DCM (150 mL) was added to the filtrate, and the organic phase was successively washed with H_2O (3 $\times$ 25 mL) and saturated aqueous NaCl (40 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: Hex/DCM: 10 $\rightarrow$ 100%) to afford oxime **4** (1.5 g, 87%) as a clear oil. NMR data for *E*-isomer: ^1H NMR (500 MHz, CDCl_3): δ 8.94 (br s, 1H), 7.61 (dd, J = 6.6, J = 5.7, 1H), 2.40 (ddd, 1H, J = 14.6, 6.6, 3.9), 2.30 (ddd, 1H, J = 14.6, 11.2, 5.7), 2.05 (d, 1H, J = 2.8), 1.94 (ddd, 1H, J = 11.2, 3.9, 2.8), 0.97 (s, 9H), 0.12 (s, 3H), 0.05 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) of the *E*-isomer: δ 152.1, 85.4, 70.3, 27.2, 25.6, 17.7, 14.1, -7.0, -7.4. NMR data for *Z*-isomer: ^1H NMR (500 MHz, CDCl_3): δ 9.45 (br s, 1H), 6.99 (dd, 1H, J = 5.3, 4.8), 2.67 (ddd, 1H, J = 16.4, 5.3, 4.0), 2.39 (ddd, 1H, J = 16.4, 11.6, 4.8), 2.04 (d, 1H, J = 2.8), 1.96 (ddd, 1H, J = 11.6, 4.0, 2.8), 0.96 (s, 9H), 0.10 (s, 3H), 0.04 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) of the *Z*-isomer: δ 151.7, 85.9, 70.7, 30.1, 27.2, 17.7, 15.2, -7.1, -7.4. HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{22}\text{NOSi}^+ [\text{M} + \text{H}]^+$, 212.1465; found, 212.1468.

(E)-5-(2-Bromo-1-(tert-butyldimethylsilyl)vinyl)-4,5-dihydroisoxazole (5a). The reaction was performed following general procedure A: oxime **4** (200 mg, 1.0 mmol, 1.0 equiv) in MeCN (5 mL), NBS (170 mg, 1.0 mmol, 1.0 equiv), reaction temperature 20 $^\circ\text{C}$, reaction time 5 min. Prior to the extractive workup, ethyl acetate (20 mL) was added. Column chromatography (eluent: toluene) afforded silyl dihydroisoxazole **5a** (88 mg, 32%) as a yellow oil. ^1H NMR (500 MHz, CDCl_3): δ 7.18 (s, 1H), 6.46 (s, 1H), 5.34 (dd, 1H, J = 11.4, 11.2), 3.50 (dd, 1H, J = 17.8, 11.4), 2.63 (dd, 1H, J = 17.8, 11.2), 0.93 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 147.8, 146.4, 115.11, 82.2, 42.3, 27.3, 17.3, -3.7, -4.8. HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{21}\text{BrNOSi}^+ [\text{M} + \text{H}]^+$, 290.0570; found, 290.0566.

(E)-5-(1-(tert-Butyldimethylsilyl)-2-iodovinyl)-4,5-dihydroisoxazole (5b). The reaction was performed following general procedure A: oxime **4** (250 mg, 1.2 mmol, 1.0 equiv) in MeCN (5 mL), NIS (277 mg, 1.2 mmol, 1.0 equiv), reaction temperature 20 $^\circ\text{C}$, reaction time 5 min. Prior to the extractive workup, ethyl acetate (20 mL) was added. Column chromatography (eluent: toluene) afforded silyl dihydroisoxazole **5b** (116 mg, 29%) as a yellow oil. ^1H NMR (500 MHz, CDCl_3): δ 7.18 (t, 1H, J = 2.1), 6.69 (d, 1H, J = 1.8), 5.15 (dd, 1H, J = 11.6, 11.1 Hz), 3.51 (ddd, 1H, J = 17.8, 11.6, 1.8), 2.57 (ddd, 1H, J = 17.8, 11.1 Hz, 1.8), 0.93 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 155.2, 146.3, 91.7, 87.3, 42.0, 27.3, 17.4, -3.5, -4.9. HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{21}\text{INOSi}^+ [\text{M} + \text{H}]^+$, 338.0432; found, 338.0427.

General Procedure B for the Two-step Synthesis of Acetamides, Carbamates, and Sulfonamides 6a–f from Azide Int2. Step 1: Ph_3P (1.0 mmol, 1.0–1.2 equiv) was added to a solution of azide **Int2** (1.0 mmol, 1.0 equiv) in wet THF (5–20 mL/1 mmol) at ambient temperature. The resulting reaction mixture was stirred and heated in an oil bath at 50 $^\circ\text{C}$ for 3 h and concentrated in vacuo. Step 2: the crude reaction mixture containing the intermediate amine and triphenylphosphine oxide was redissolved in reaction solvent (5–20 mL/1.0 mol), and the corresponding acylating/carboxylating/sulfonating reagent (1.0–3.0 mmol, 1.0–3.0 equiv) and base (3.0–5.0 mmol, 3.0–5.0 equiv) were added. The resulting reaction mixture was stirred at the respective temperature (at

elevated temperatures, heating was done by using an oil bath) until completion (TLC control). Saturated aqueous NH_4Cl and an extraction solvent (DCM, EtOAc, or toluene) were added to the mixture at 20 $^\circ\text{C}$. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel.

N-(4-(tert-Butyldimethylsilyl)hex-5-yn-1-yl)benzamide (6a). The reaction was performed following general procedure B. Step 1: (6-azidohex-1-yn-3-yl)(tert-butyl)dimethylsilane (**Int2**, 502 mg, 2.1 mmol, 1.0 equiv) and Ph_3P (670 mg, 2.5 mmol, 1.2 equiv) in THF (20 mL)/ H_2O (0.05 mL). Second step: anh. DMF (8 mL), DMAP (258 mg, 2.1 mmol, 1.0 equiv), solution of Bz_2O (962 mg, 4.3 mmol, 2.0 equiv) in anh. DMF (4 mL), reaction temperature 60 $^\circ\text{C}$, reaction time 22 h. The reaction mixture was quenched with aqueous NH_4Cl (30 mL) and extracted with toluene (3 $\times$ 30 mL). Column chromatography (eluent: DCM/Hex: 40 $\rightarrow$ 100%) afforded benzoylamide **6a** (414 mg, 66%) as a yellow oil. ^1H NMR (500 MHz, CDCl_3): δ 7.75 (d, 2H, J = 7.5), 7.49 (t, 1H, J = 7.5), 7.43 (t, 2H, J = 7.5), 6.20 (br, 1H), 3.50 (q, 2H, J = 6.6), 2.03 (d, 1H, J = 2.6), 2.01–1.92 (m, 1H), 1.83–1.72 (m, 2H), 1.64–1.56 (m, 1H), 1.56–1.46 (m, 1H), 0.95 (s, 9H), 0.09 (s, 3H), 0.02 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 167.7, 135.0, 131.5, 128.7, 127.0, 87.2, 69.9, 39.7, 29.4, 27.3, 27.3, 17.8, 16.7, -7.0, -7.3. HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{29}\text{NOSi}^+ [\text{M} + \text{H}]^+$, 316.2091; found, 316.2096.

N-(4-(tert-Butyldimethylsilyl)hex-5-yn-1-yl)acetamide (6b). The reaction was performed following general procedure B. Step 1: (6-azidohex-1-yn-3-yl)(tert-butyl)dimethylsilane (**Int2**, 748 mg, 3.1 mmol, 1.0 equiv) and Ph_3P (909 mg, 3.5 mmol, 1.1 equiv) in THF (10 mL) and H_2O (0.05 mL). Step 2: anh. pyridine (10 mL), DMAP (192 mg, 1.6 mmol, 0.5 equiv), Ac_2O (0.59 mL, 6.3 mmol, 2.0 equiv; added at 0 $^\circ\text{C}$), reaction temperature 20 $^\circ\text{C}$, reaction time 16 h. The reaction mixture was quenched with aqueous 0.01 M HCl (20 mL) at 0 $^\circ\text{C}$ and extracted with EtOAc (3 $\times$ 30 mL). Column chromatography (eluent: acetone/DCM: 1 $\rightarrow$ 2%) afforded acetamide **6b** (582 mg, 74%) as yellow oil. ^1H NMR (300 MHz, CDCl_3): δ 5.48 (br, 1H), 3.27 (q, 2H, J = 6.7), 2.00 (d, 1H, J = 3.0), 1.97 (s, 3H), 1.92–1.79 (m, 1H), 1.75 (dt, 1H, J = 11.4, 3.0), 1.69–1.57 (m, 1H), 1.57–1.34 (m, 2H), 0.95 (s, 9H), 0.08 (s, 3H), 0.01 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 170.1, 87.1, 69.8, 39.3, 29.4, 27.3, 27.2, 23.5, 17.7, 16.7, -7.0, -7.3. HRMS (ESI): m/z calcd for $\text{C}_{14}\text{H}_{28}\text{NOSi}^+ [\text{M} + \text{H}]^+$, 254.1935; found, 254.1936.

tert-Butyl (4-(tert-Butyldimethylsilyl)hex-5-yn-1-yl)carbamate (6c). Ph_3P (88 mg, 0.34 mmol, 1.0 equiv) was added to a solution of (6-azidohex-1-yn-3-yl)(tert-butyl)dimethylsilane (**Int2**, 80 mg, 0.34 mmol, 1.0 equiv) in THF (7 mL) and H_2O (7 mL). The resulting reaction mixture was stirred at 50 $^\circ\text{C}$ for 1 h. Then, it was cooled to 0 $^\circ\text{C}$ and NaHCO_3 (85 mg, 1.0 mmol, 3 equiv) was added, followed by Boc_2O (90 mg, 0.41 mmol, 1.2 equiv). The resulting reaction mixture was stirred at 20 $^\circ\text{C}$ for 14 h and then concentrated in vacuo. The residue was dissolved in DCM (30 mL), and the mixture was washed with brine (2 $\times$ 10 mL). The crude reaction mixture was purified by column chromatography on silica (eluent: DCM/Hex: 50%) to afford carbamate **6c** (83 mg, 82%) as a colorless oil. ^1H NMR (500 MHz, CDCl_3): δ 4.51 (br s, 1H), 3.21–3.04 (m, 2H), 1.98 (s, 1H), 1.90–1.79 (m, 1H), 1.79–1.69 (m, 1H), 1.62–1.36 (m, 12H), 0.95 (s, 9H), 0.08 (s, 3H), 0.01 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 156.1, 87.1, 69.6, 40.1, 30.0, 28.6, 27.3, 27.1, 17.7, 16.7, -7.0, -7.2. HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{34}\text{NO}_2\text{Si}^+ [\text{M} + \text{H}]^+$, 312.2353; found, 312.2349.

Benzyl (4-(tert-Butyldimethylsilyl)hex-5-yn-1-yl)carbamate (6d). The reaction was performed following general procedure B. Step 1: (6-azidohex-1-yn-3-yl)(tert-butyl)dimethylsilane (**Int2**, 495 mg, 2.1 mmol, 1.0 equiv) and Ph_3P (663 mg, 2.5 mmol, 1.2 equiv) in THF (50 mL) and H_2O (0.05 mL). Step 2: MeCN (20 mL), H_2O (20 mL), NaHCO_3 (465 mg, 5.5 mmol, 2.7 equiv), addition of benzyl *N*-succinimidylcarbonate (631 mg, 2.5 mmol, 1.2 equiv) at 0 $^\circ\text{C}$, reaction temperature 20 $^\circ\text{C}$, reaction time 16h. The reaction mixture was quenched with aqueous saturated NH_4Cl (20 mL), the excess of MeCN was evaporated under reduced pressure, and the product was

isolated by EtOAc extraction (3 × 20 mL). Column chromatography (eluent: DCM/Hex: 50 → 60%) afforded benzylcarbamate **6d** (510 mg, 71%) as a clear oil. ¹H NMR (500 MHz, CDCl₃): δ 7.38–7.34 (m, 4H), 7.32 (t, 1H, *J* = 4.2), 5.10 (s, 2H), 4.77 (br, 1H), 3.24 (m, 2H), 1.99 (d, 1H, *J* = 2.7), 1.92–1.82 (m, 1H), 1.73 (dt, 1H, *J* = 11.3, 2.7), 1.67–1.58 (m, 1H), 1.55–1.47 (m, 1H), 1.47–1.37 (m, 1H), 0.95 (s, 9H), 0.08 (s, 3H), 0.01 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 156.5, 136.8, 128.7, 128.3, 128.3, 87.0, 69.8, 66.8, 40.8, 29.8, 27.3, 27.0, 17.7, 16.7, –7.0, –7.3. HRMS (ESI): *m/z* calcd for C₂₀H₃₂NO₂Si⁺ [*M* + *H*]⁺, 346.2197; found, 346.2188.

N-(4-(tert-Butyldimethylsilyl)hex-5-yn-1-yl)-4-methylbenzenesulfonamide (6e). The reaction was performed following general procedure B. Step 1: (6-azidohept-1-yn-3-yl)(tert-butyl)dimethylsilane (**Int2**, 184 mg, 0.77 mmol, 1.0 equiv) and Ph₃P (203 mg, 0.77 mmol, 1.0 equiv) in THF (5 mL) and H₂O (0.05 mL). Step 2: DCM (10 mL), Et₃N (0.54 mL, 3.87 mmol, 5.0 equiv), addition of 4-toluenesulfonyl chloride (295 mg, 1.55 mmol, 2.0 equiv) at 0 °C, reaction temperature 20 °C, reaction time 5.5 h. The reaction mixture was quenched with aqueous saturated NH₄Cl (30 mL) and extracted with DCM (3 × 15 mL). Column chromatography (eluent: DCM/Hex: 30 → 50%) afforded sulfonamide **6e** (187 mg, 66%) as a clear oil. ¹H NMR (500 MHz, CDCl₃ + D₂O): δ 7.75 (d, 2H, *J* = 8.1), 7.30 (d, 2H, *J* = 8.1), 2.98 (t, 2H, *J* = 6.9), 2.42 (s, 3H, H₃C), 1.95 (d, 1H, *J* = 2.9), 1.87–1.73 (m, 1H), 1.65 (dt, 1H, *J* = 11.1, 2.9), 1.62–1.52 (m, 1H), 1.52–1.43 (m, 1H), 1.40–1.30 (m, 1H), 0.93 (s, 9H), 0.04 (s, 3H), –0.03 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 143.5, 137.1, 129.9, 127.3, 86.8, 69.9, 42.9, 29.4, 27.3, 26.8, 21.7, 17.7, 16.5, –7.1, –7.3. HRMS (ESI): *m/z* calcd for C₁₉H₃₂NO₂Si⁺ [*M* + *H*]⁺, 366.1918; found, 366.1931.

N-(4-(tert-Butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzenesulfonamide (6f). The reaction was performed following general procedure B. Step 1: (6-azidohept-1-yn-3-yl)(tert-butyl)dimethylsilane (**Int2**, 1.40 g, 5.8 mmol, 1.0 equiv) and Ph₃P (1.80 g, 5.9 mmol, 1.2 equiv) in THF (60 mL) and H₂O (1 mL). Step 2: DCM (50 mL), Et₃N (4.00 mL, 28.7 mmol, 5.0 equiv), addition of 4-nitrobenzenesulfonyl chloride (1.30 g, 5.8 mmol, 2.0 equiv) at 0 °C, reaction temperature 20 °C, reaction time 6 h. The reaction mixture was quenched with aqueous saturated NH₄Cl (50 mL) and extracted with DCM (3 × 30 mL). Column chromatography (eluent: DCM/Hex: 50 → 70%) afforded sulfonamide **6f** (1.60 g, 68%) as an amorphous solid. ¹H NMR (500 MHz, CDCl₃): δ 8.37 (d, 2H, *J* = 8.9), 8.06 (d, 2H, *J* = 8.9), 4.58 (t, 1H, *J* = 6.5), 3.08 (q, 2H, *J* = 6.5), 1.97 (d, 1H, *J* = 3.0), 1.89–1.77 (m, 1H), 1.67 (dt, 1H, *J* = 11.8, 3.0), 1.65–1.57 (m, 1H), 1.53–1.44 (m, 1H), 1.37 (dddd, 1H, *J* = 13.5 Hz, 11.8, 9.2, 4.9), 0.93 (s, 9H), 0.05 (s, 3H), –0.02 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 150.2, 146.2, 128.4, 124.6, 86.7, 70.1, 43.1, 29.5, 27.2, 26.7, 17.7, 16.5, –7.1, –7.3. HRMS (ESI): *m/z* calcd for C₁₈H₂₉N₂O₄Si⁺ [*M* + *H*]⁺, 397.1612; found, 397.1604.

(2-(1-(tert-Butyldimethylsilyl)vinyl)pyrrolidin-1-yl)(phenyl)methanone (7a). The reaction was performed following general procedure A: (N-(4-(tert-butylidimethylsilyl)hex-5-yn-1-yl)benzamide (**6a**; 28 mg, 0.089 mmol, 1.0 equiv) and HNTf₂ (15 mg, 0.050 mmol, 0.5 equiv) in DCM (6 mL) solution, reaction temperature 20 °C, reaction time 16 h. Column chromatography (eluent: EtOAc/Hex: 5 → 10%) afforded silyl pyrrolidine **7a** (17 mg, 67%) as a yellow oil. In solutions product **7a** was observed (NMR) as a mixture of several rotamers. In MeOH-*d*₄ it is comprised of rotamers *α* and *β* in a ratio of 1:1. ¹H NMR (500 MHz, MeOH-*d*₄) of *α* conformer: δ 7.54–7.49 (m, 2H, H–C(2'')), 7.48–7.43 (m, 3H, H–C(3', 4'')), 5.80 (dd, 1H, ²*J*_{H–H} = 1.6, ³*J*_{H–H} = 1.4, H₂C(6')), 5.43 (d, 1H, ²*J*_{H–H} = 1.6, H₂C(6')), 4.93 (dd, 1H, ²*J*_{H–H} = 7.8, 4.6, HC(4')), 3.59 (ddd, 1H, ²*J*_{H–H} = 10.6, ³*J*_{H–H} = 7.2, 6.1, H₂C(1')), 3.49–3.37 (m, 1H, H₂C(1')), 2.22 (dq, 1H, ²*J*_{H–H} = 1.24, ³*J*_{H–H} = 7.8, H₂C(3')), 2.02–1.86 (m, 1H, H₂C(2')), 1.85–1.72 (m, 1H, H₂C(2')), 1.71–1.63 (m, 1H, H₂C(3')), 1.01 (s, 9H, H₃C(1')), 0.19 (s, 3H, H₃C(2')), 0.17 (s, 3H, H₃C(2')). ¹H NMR (500 MHz, MeOH-*d*₄) of *β* conformer: δ 7.42–7.35 (m, 5H, H–C(2'', 3', 4'')), 5.66 (t, 1H, ²*J* = 1.5, ³*J* = 1.5, H₂C(6')), 5.53 (t, 1H, ²*J* = 1.5, ³*J* = 1.5, H₂C(6')), 4.69–4.62 (m, 1H, HC(4')), 3.69 (dd, 2H, ²*J*_{H–H} = 9.4, 5.1, H₂C(1')), 2.18–2.04 (m, 1H, H₂C(3')), 2.02–1.86 (m, 2H, H₂C(2')), 1.85–1.72 (m, 1H, H₂C(3')), 0.67 (s, 9H,

H₃C(1')), –0.07 (s, 3H, H₃C(2')), –0.08 (s, 3H, H₃C(2')). ¹³C{¹H} NMR (126 MHz, MeOH-*d*₄) of *α* conformer: δ 171.6, 151.4, 138.6, 131.1, 129.6, 127.9, 123.1, 62.9, 51.8, 33.6, 27.3, 24.9, 18.0, –4.8, –5.2; ¹³C{¹H} NMR (126 MHz, MeOH-*d*₄) of *β* conformer: δ 173.0, 151.9, 138.7, 130.8, 129.5, 127.6, 126.4, 65.5, 47.9, 32.6, 27.2, 21.6, 17.6, –4.3, –5.2. HRMS (ESI): *m/z* calcd for C₁₉H₃₀NOSi⁺ [*M* + *H*]⁺, 316.2091; found, 316.2090.

1-(2-(1-(tert-Butyldimethylsilyl)vinyl)pyrrolidin-1-yl)ethan-1-one (7b). The reaction was performed following general procedure A: (N-(4-(tert-butylidimethylsilyl)hex-5-yn-1-yl)acetamide (**6b**; 47 mg, 0.19 mmol, 1.0 equiv) in DCM (4 mL), solution of HNTf₂ (64 mg, 0.23 mmol, 1.2 equiv) in DCM (1 mL) was added at –40 °C. Then, the reaction mixture was warmed to 20 °C, stirred for 20 h. Column chromatography (eluent: acetone/DCM 10 → 20%) afforded silyl pyrrolidine (**7b**) (30 mg, 67%) as a clear oil. In solutions, silyl pyrrolidine **7b** was observed (NMR) as a mixture of several rotamers. Conditions in DMSO-*d*₆ at 80 °C ensured only the interconversion of rotamers and signal broadening. Hence, in the ¹H NMR spectrum, the peaks will be assigned by proton groups. ¹³C NMR spectrum will be provided as a collection of peaks of all rotamers. ¹H NMR (500 MHz, CDCl₃): δ 6.25–5.26 (2H, H₂C(6')), 5.12–4.44 (1H, HC(4')), 3.62–3.22 (2H, H₂C(1')), 2.41–1.56 (7H, H₂C(2), H₂C(3), H₃C(1')), 1.02–0.77 (9H, 3 × H₃C(1')), 0.19 to –0.03 (6H, 2 × H₃C(2')). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 170.0, 149.7, 137.8, 128.0, 127.5, 125.5, 122.6, 63.1, 61.1, 48.5, 46.7, 39.2, 33.2, 32.6, 31.2, 27.1 (2C), 26.8, 22.8 (2C), 21.1, 17.3, –4.4, –4.8, –5.0, –5.1, –5.3. HRMS (ESI): *m/z* calcd for C₁₄H₂₈NOSi⁺ [*M* + *H*]⁺, 254.1935; found, 254.1930.

tert-Butyl 2-(1-(tert-Butyldimethylsilyl)vinyl)pyrrolidine-1-carboxylate (7c). The reaction was performed following general procedure A: (tert-butyl (4-(tert-butylidimethylsilyl)hex-5-yn-1-yl)carbamate (**6c**; 205 mg, 0.66 mmol, 1.0 equiv) in DCM (3 mL), solution of HNTf₂ (37 mg, 0.13 mmol, 0.2 equiv) in DCM (1 mL) was added at 0 °C, reaction temperature 20 °C, reaction time 20 h. Column chromatography (eluent: DCM/Hex: 40 → 50%) afforded silyl pyrrolidine **7c** (198 mg, 49%) as a clear oil. Product **7c** was observed (NMR) as a mixture of conformational isomers in solutions. In CDCl₃, it is comprised of isomers *α* and *β* in a ratio of 3:7. ¹H NMR (500 MHz, CDCl₃): δ 5.54 (s, 1H, H₂C(6')), 5.36 (s, 1H, H₂C(6')), 3.50–3.29 (m, 2H, H₂C(1')), 2.06–1.86 (m, 1H, H₂C(3')), 1.83–1.70 (m, 2H, H₂C(2')), 1.69–1.56 (m, 1H, H₂C(3')), 0.93 (s, 9H, H₃C(1')), 0.10 (s, 3H, H₃C(2')), 0.09 (s, 3H, H₃C(2')). Peaks corresponding to *α* conformer: 4.56 (br, 1H, HC(4')), 1.44 (s, 9H, H₃C(1')); peaks corresponding to *β* conformer: 4.49 (br, 1H, ³*J*_{H–H} = 7.7 Hz, HC(4')), 1.40 (s, 9H, H₃C(1')). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 154.8, 149.8, 123.6, 123.2, 79.4, 61.5, 47.2, 46.9, 32.2, 31.5, 28.8, 28.6, 27.1, 22.5, 21.6, 17.2, –4.2, –5.0. HRMS (ESI): *m/z* calcd for C₁₇H₃₄NO₂Si⁺ [*M* + *H*]⁺, 312.2353; found, 312.2348.

Benzyl 2-(1-(tert-Butyldimethylsilyl)vinyl)pyrrolidine-1-carboxylate (7d). The reaction was performed following general procedure A: benzyl (4-(tert-butylidimethylsilyl)hex-5-yn-1-yl)carbamate (**6d**) (31 mg, 0.085 mmol, 1.0 equiv) in DCM (2 mL), HNTf₂ (9 mg, 0.030 mmol, 0.4 equiv) added at 0 °C, reaction temperature 20 °C, reaction time 20 h. Column chromatography (eluent: DCM/Hex: 90 → 100%) afforded silyl pyrrolidine **7d** (24 mg, 77%) as a clear oil. Compound **7d** was observed (NMR) as a mixture of conformational isomers in solutions. In DMSO-*d*₆, it is comprised of isomers *α* and *β* in a ratio of 3:1. ¹H NMR (500 MHz, DMSO-*d*₆, 100 °C): δ 7.41–7.26 (m, 5H, H–C(3', 4'', 5'')), 4.54 (d, 1H, ³*J*_{H–H} = 8.2, HC(4')), 3.45 (t, 2H, ²*J*_{H–H} = 7.9, H₂C(1')), 2.13–2.02 (m, 1H, H₂C(3')), 1.85–1.73 (m, 2H, H₂C(2')), 1.61–1.52 (m, 1H, H₂C(3')), 0.89 (s, 9H, H₃C(1')), 0.08 (s, 6H, H₃C(2')). Peaks corresponding to *α* conformer: 5.55 (d, 1H, ²*J*_{H–H} = 1.4, H₂C(6')), 5.34 (s, 1H, H₂C(6')), peaks corresponding to *β* conformer: 5.27 (d, 1H, ²*J*_{H–H} = 2.4 Hz, H₂C(6')), 5.17 (d, 1H, ²*J*_{H–H} = 2.4 Hz, H₂C(6')). ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆, 100 °C): δ 153.4, 150.2, 136.8, 127.8, 127.1, 126.1, 122.3, 65.3, 60.7, 46.8, 31.5, 26.2, 21.3, 16.3, –5.6, –5.9. HRMS (ESI): *m/z* calcd for C₂₀H₃₃NO₂Si⁺ [*M* + *H*]⁺, 346.2197; found, 346.2219.

2-(1-(tert-Butyldimethylsilyl)vinyl)-1-tosylpyrrolidine (7e).

The reaction was performed following general procedure A: *N*-(4-(tert-butyldimethylsilyl)hex-5-yn-1-yl)-4-methylbenzenesulfonamide (**6e**; 110 mg, 0.30 mmol, 1.0 equiv) in DCM (5 mL), solution of HNTf₂ (11 mg, 0.040 mmol, 0.13 equiv) in DCM (1 mL) was added at 0 °C, reaction temperature 0 °C, reaction time 3 h. Column chromatography (eluent: DCM/Hex: 40 → 50%) afforded silyl pyrrolidine **7e** (93 mg, 85%) as an amorphous solid. ¹H NMR (500 MHz, CDCl₃): δ 7.69 (d, 2H, *J* = 8.2), 7.30 (d, 2H, *J* = 8.2), 5.93 (dd, 1H, *J* = 2.4, 2.0), 5.46 (d, 1H, *J* = 2.4, 0.6), 4.45 (pl.d., 1H, *J* = 7.2), 3.46 (ddd, 1H, *J* = 9.7, 7.5, 2.8), 3.23 (td, 1H, *J* = 9.7, 6.6), 2.42 (s, 3H), 1.85–1.72 (m, 1H), 1.69–1.54 (m, 2H), 1.54–1.46 (m, 1H), 0.95 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 149.7, 143.2, 135.6, 129.7, 127.5, 126.2, 64.2, 49.1, 33.0, 26.9, 23.1, 21.7, 17.3, –4.9, –5.1. HRMS (ESI): *m/z* calcd for C₁₉H₃₂N₂O₄SSi⁺ [M + H]⁺, 366.1918; found, 366.1916.

2-(1-(tert-Butyldimethylsilyl)vinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (7f). The reaction was performed following general procedure A: *N*-(4-(tert-butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzenesulfonamide (**6f**; 23 mg, 0.057 mmol, 1.0 equiv) in DCM (2 mL), solution of HNTf₂ (9 mg, 5.7 μmol, 0.1 equiv) in DCM (0.5 mL) was added at 0 °C, reaction temperature 0 °C, reaction time 3 h. Column chromatography (eluent: DCM/Hex: 50 → 60%) afforded silyl pyrrolidine **7f** (19 mg, 83%) as an amorphous solid. ¹H NMR (500 MHz, CDCl₃): δ 8.36 (d, 2H, *J* = 8.8), 7.98 (d, 2H, *J* = 8.8), 5.73 (s, 1H), 5.43 (d, 1H, *J* = 1.2), 4.54 (br.d., 1H, *J* = 7.3), 3.51 (ddd, 1H, *J* = 9.5, 7.0, 2.7), 3.30 (dt, 1H, *J* = 9.5, 6.4), 1.92–1.80 (m, 1H), 1.78–1.68 (m, 2H), 1.59 (dt, 1H, *J* = 9.6, 2.9), 0.96 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 150.1, 149.4, 144.7, 128.6, 126.1, 124.4, 64.6, 49.2, 33.1, 26.8, 23.0, 17.3, –5.0, –5.2. HRMS (ESI): *m/z* calcd for C₁₈H₂₉N₂O₄SSi⁺ [M + H]⁺, 397.1612; found, 397.1594.

(E)-2-(2-Bromo-1-(tert-butyldimethylsilyl)vinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (7g). The reaction was performed following general procedure A: *N*-(4-(tert-butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzenesulfonamide (**6f**; 50 mg, 0.13 mmol, 1.0 equiv) in CHCl₃ (3 mL), NBS (26 mg, 0.16 mmol, 1.2 equiv) was added at 0 °C, reaction temperature 0 °C, reaction time 2.5 h. Column chromatography (eluent: DCM/Hex: 30 → 50%) afforded silyl pyrrolidine **7g** (15 mg, 25%) as an amorphous solid. ¹H NMR (500 MHz, CDCl₃): δ 8.39 (d, 2H, *J* = 8.5), 8.08 (d, 2H, *J* = 8.5), 6.48 (s, 1H), 4.58–4.50 (m, 1H), 3.59–3.48 (m, 2H), 2.04 (dt, 1H, *J* = 12.6, 6.7), 1.91–1.82 (m, 1H), 1.82–1.71 (m, 1H), 1.39–1.28 (m, 1H), 0.95 (s, 9H), 0.31 (s, 3H), 0.28 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 150.3, 145.2, 142.8, 129.3, 124.4, 115.4, 64.7, 50.3, 32.3, 27.3, 24.8, 17.8, –3.5, –3.9. HRMS (ESI): *m/z* calcd for C₁₈H₂₈BrN₂O₄SSi⁺ [M + H]⁺, 475.0717; found, 475.0710.

(E)-2-(1-(tert-Butyldimethylsilyl)-2-iodovinyl)-1-tosylpyrrolidine (7h). The reaction was performed following general procedure A: *N*-(4-(tert-butyldimethylsilyl)hex-5-yn-1-yl)-4-methylbenzenesulfonamide (**6e**; 20 mg, 0.06 mmol, 1.0 equiv) in CHCl₃ (3 mL), NIS (18 mg, 0.082 mmol, 1.3 equiv) was added at 0 °C, reaction temperature 0 °C, reaction time 2.5 h. Column chromatography (eluent: DCM/Hex: 30 → 50%) afforded silyl pyrrolidine **7h** (9 mg, 33%, *E/Z* = 91:9) as an amorphous solid. NMR data are provided for (*E*)-**7h**: ¹H NMR (500 MHz, CDCl₃): δ 7.83 (d, 2H, *J* = 8.2), 7.34 (d, 2H, *J* = 8.2), 6.61 (s, 1H), 4.25 (dd, 1H, *J* = 9.3, 7.6), 3.47 (dd, 2H, *J* = 9.1, 4.3), 2.44 (s, 3H), 1.99 (ddd, 1H, *J* = 12.7, 7.6, 2.5), 1.79–1.69 (m, 1H), 1.62 (dddd, 1H, *J* = 12.7, 11.3, 9.3, 6.6), 1.24–1.14 (m, 1H), 0.95 (s, 9H), 0.31 (s, 3H), 0.27 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.4, 143.7, 133.7, 129.8, 128.5, 91.4, 71.1, 50.5, 31.9, 27.4, 24.5, 21.7, 17.9, –3.2, –3.6. HRMS (ESI): *m/z* calcd for C₁₉H₃₁INO₂SSi⁺ [M + H]⁺, 492.0884; found, 492.0860.

(E)-2-(1-(tert-Butyldimethylsilyl)-2-iodovinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (7i). The reaction was performed following general procedure A: *N*-(4-(tert-butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzenesulfonamide (**6f**; 50 mg, 0.13 mmol, 1.0 equiv) in CHCl₃ (3 mL), NIS (28 mg, 0.13 mmol, 1.0 equiv) was added at 0 °C, reaction temperature 0 °C, reaction time 2.5 h. Column chromatography (eluent: DCM/Hex: 30 → 40%) afforded

silyl pyrrolidine **7i** (17 mg, 26%) as an amorphous solid. Compound **7i** (2 mg) was suspended in DCM (0.6 mL) and EtOH (0.3 mL), heated in an oil bath at 70 °C until dissolution and left to recrystallize to afford monocrystals suitable for X-ray crystallography analysis.¹⁶ mp 160–161 °C (decomposes >165 °C). ¹H NMR (500 MHz, CDCl₃): δ 8.40 (d, 2H, *J* = 8.9), 8.12 (d, 2H, *J* = 8.9), 6.65 (d, 1H, *J* = 0.8), 4.25 (dd, 1H, *J* = 9.5, 7.4), 3.56 (dt, 1H, *J* = 11.3, 6.7), 3.50 (ddd, 1H, *J* = 11.3, 8.0, 2.3), 2.02 (dddd, 1H, *J* = 14.1, 13.1, 6.7, 2.2), 1.85 (ddq, 1H, *J* = 13.1, 6.8, 2.3), 1.80–1.65 (m, 1H), 1.36–1.26 (m, 1H), 0.94 (s, 9H), 0.31 (s, 3H), 0.28 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 152.6, 150.4, 142.5, 129.6, 124.5, 117.6, 92.2, 50.6, 31.9, 27.4, 24.6, 17.9, –3.3, –3.8. HRMS (ESI): *m/z* calcd for C₁₈H₂₇N₂O₄SSi⁺ [M – I]⁺, 395.1455; found, 395.1451.

Mixture of (Z)- and (E)-Isomers of 2-(1-(tert-Butyldimethylsilyl)-2-(phenylselanyl)vinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (7j). The reaction was performed following general procedure A: *N*-(4-(tert-butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzenesulfonamide (**6f**; 20 mg, 0.050 mmol, 1.0 equiv) in DCM (6 mL), PhSeCl (10 mg, 0.050 mmol, 1.0 equiv) was added at 0 °C, reaction temperature 0 °C, reaction time 3 h. Column chromatography (eluent: DCM/Hex: 30 → 50%) afforded silyl pyrrolidine **7j** (11 mg, 40%, *E/Z* = 41:59) as an amorphous solid. Preparative HPLC on C₁₈-silica gel (eluent: NH₄HCO₃ solution in H₂O (pH 7.9)/MeCN = 20:80) afforded silyl pyrrolidine (*Z*-**7j**) and silyl pyrrolidine (*E*-**7j**) as amorphous solids.

Characterization of Compound E-7j. ¹H NMR (500 MHz, CDCl₃): δ 8.15 (d, 2H, *J* = 8.8), 7.87 (d, 2H, *J* = 8.8), 7.33–7.27 (m, 2H), 7.26–7.21 (m, 3H), 6.98 (s, 1H), 4.68 (dd, 1H, *J* = 5.8, 1.5), 3.43–3.38 (m, 1H), 1.95–1.81 (m, 3H), 1.68–1.60 (m, 1H), 1.07 (s, 9H), 0.34 (s, 3H), 0.18 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 149.8, 144.9, 140.9, 135.3, 132.3, 131.7, 129.5, 128.2, 127.4, 124.3, 66.6, 49.4, 34.2, 27.5, 23.1, 19.5, –3.2, –3.9. HRMS (ESI): *m/z* calcd for C₂₄H₃₃N₂O₄SSeSi⁺ [M + H]⁺, 553.1090; found, 553.1073.

Characterization of Compound Z-7j. ¹H NMR (500 MHz, CDCl₃): δ 8.36 (d, 2H, *J* = 8.8), 8.08 (d, 2H, *J* = 8.8), 7.49–7.45 (m, 2H), 7.34–7.28 (m, 3H), 6.89 (s, 1H), 4.46 (t, 1H, *J* = 7.7), 3.70 (ddd, 1H, *J* = 10.8, 8.5, 6.0), 3.47 (ddd, 1H, *J* = 10.8, 7.4, 4.0), 2.01–1.83 (m, 3H), 1.51–1.42 (m, 1H), 0.96 (s, 9H), 0.20 (s, 3H), 0.18 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 150.3, 143.1, 142.4, 133.1, 132.4, 129.5, 129.3, 127.5, 124.3, 64.1, 50.0, 33.6, 27.2, 25.3, 18.0, –4.4, –4.5. HRMS (ESI): *m/z* calcd for C₂₄H₃₃N₂O₄SSeSi⁺ [M + H]⁺, 553.1090; found, 553.1084.

4-(tert-Butyldimethylsilyl)hex-5-yn-1-yl Thioacetate (8). *N*-(4-(tert-butyldimethylsilyl)hex-5-yn-1-yl)-4-methylbenzenesulfonamide¹⁹ (926 mg, 2.5 mmol, 1.0 equiv) was added to a suspension of potassium thioacetate (415 mg, 3.6 mmol, 1.4 equiv) in MeCN (50 mL) at ambient temperature. The resulting reaction mixture was stirred at ambient temperature for 16 h (TLC control) and concentrated in vacuo. DCM (50 mL) was added, and the resulting mixture was washed with saturated aqueous NaHCO₃ (15 mL) and brine (2 × 10 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The crude reaction mixture was purified by column chromatography on silica (eluent: hexanes) to afford thioacetate **8** (592 mg, 87%) as a yellow oil. ¹H NMR (500 MHz, CDCl₃): δ 2.97–2.83 (m, 2H), 2.32 (s, 3H), 2.01–1.89 (m, 1H), 1.98 (s, 1H), 1.79–1.63 (m, 2H), 1.62–1.40 (m, 2H), 0.95 (s, 9H), 0.07 (s, 3H), 0.01 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 196.1, 86.8, 69.7, 30.8, 29.2, 28.9, 28.7, 27.3, 17.7, 16.5, –7.1, –7.2. HRMS (ESI): *m/z* calcd for C₁₄H₂₇OSSi⁺ [M + H]⁺, 271.1546; found, 271.1536.

tert-Butyldimethyl(1-(tetrahydrothiophen-2-yl)vinyl)silane (9a). The reaction was performed following general procedure A: 4-(tert-butyldimethylsilyl)hex-5-yn-1-yl thioacetate (**8**; 101 mg, 0.37 mmol, 1.0 equiv) in DCM (10 mL), HNTf₂ (7.3 mg, 0.026 mmol, 0.07 equiv) solution in DCM (5 mL), reaction temperature 20 °C, reaction time 20 min. Column chromatography (eluent: Hex/DCM: 1 → 10%) afforded silyl thiolane **9a** (55 mg, 64%) as a clear oil. ¹H NMR (500 MHz, CDCl₃): δ 6.20 (dd, 1H, *J* = 2.2, 1.2), 5.51 (d, 1H, *J* = 2.2), 4.15 (ddd, 1H, *J* = 7.5, 5.8, 1.2), 3.00 (ddd, 1H, *J* = 10.1, 8.0, 6.2), 2.88 (ddd, 1H, *J* = 10.1, 6.9, 4.9), 2.19–2.03 (m, 2H), 1.96–1.82

(m, 1H), 1.72–1.64 (m, 1H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 150.5, 127.7, 53.1, 38.9, 32.9, 30.4, 27.0, 17.2, –5.2, –5.2. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{25}\text{SSi}^+$ [$\text{M} + \text{H}^+$], 229.1441; found, 229.1445.

(E)-tert-Butyl(2-iodo-1-(tetrahydrothiophen-2-yl)vinyl)-dimethylsilane (9b). The reaction was performed following general procedure A: 4-(tert-butylidimethylsilyl)hex-5-yn-1-yl thioacetate (**8**; 30 mg, 0.11 mmol, 1.0 equiv) in DCM (2 mL), NIS (25 mg, 0.11 mmol, 1.0 equiv) was added at 0 °C, reaction temperature 0 °C, reaction time 2.5 h. Column chromatography (eluent: DCM/Hex: 1 → 10%) afforded silyl thiolane **9b** (10 mg, 25%) as a yellow oil. ^1H NMR (500 MHz, CDCl_3): δ 6.62 (s, 1H), 4.47 (dd, 1H, J = 11.0, 6.3), 2.98 (dd, 2H, J = 9.2, 3.7), 2.38–2.30 (m, 1H), 2.24–2.16 (m, 1H), 1.95–1.75 (m, 2H), 0.92 (s, 9H), 0.22 (s, 3H), 0.21 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 152.2, 93.6, 58.6, 35.8, 33.9, 31.9, 27.3, 17.7, –3.2, –3.3. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{24}\text{ISSi}^+$ [$\text{M} + \text{H}^+$], 355.0407; found, 355.0435.

(E)-tert-Butylidimethyl(2-(phenylselanyl)-1-(tetrahydrothiophen-2-yl)vinyl)silane (9c). The reaction was performed following general procedure A: 4-(tert-butylidimethylsilyl)hex-5-yn-1-yl thioacetate (**8**; 30 mg, 0.11 mmol, 1.0 equiv) in DCM (15 mL), PhSeCl (21 mg, 0.11 mmol, 1.0 equiv) was added at 0 °C, reaction temperature 0 °C, reaction time 1.5 h. Column chromatography (eluent: DCM/Hex: 10 → 20%) afforded silyl thiolane **9c** (21 mg, 49%) as a yellow oil. ^1H NMR (500 MHz, CDCl_3): δ 7.50 (dd, 2H, J = 8.1, 1.8), 7.33–7.25 (m, 3H), 6.93 (s, 1H), 4.39 (dd, 1H, J = 10.7, 6.1), 3.20 (dt, 1H, J = 10.6, 5.7), 2.98–2.92 (m, 1H), 2.35 (dt, 1H, J = 12.3, 5.3), 2.28–2.18 (m, 1H), 2.17–2.10 (m, 1H), 1.91–1.79 (m, 1H), 0.91 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 141.7, 134.7, 134.4, 132.5, 129.3, 127.2, 51.8, 35.2, 33.2, 32.4, 27.1, 17.9, –5.2, –5.3. HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{29}\text{SSeSi}^+$ [$\text{M} + \text{H}^+$], 385.0919; found, 385.0914.

General Procedure C for Suzuki–Miyaura Coupling Reactions. An oven-dried three-neck round-bottom flask equipped with a reflux condenser, Teflon-coated magnetic stirrer, and three-way valve adapter was evacuated and backfilled with nitrogen. Then vinyl halide (0.17 mmol, 1.0 equiv), $\text{ArB}(\text{OH})_2$ (0.51–0.68 mmol, 3.0–4.0 equiv), $\text{Pd}(\text{OAc})_2$ (8.6 μmol , 5 mol %), phosphine ligand (25.5 μmol , 15 mol %), base (0.68 mmol, 4.0 equiv), and solvent were added. For the resulting mixture, three freeze–thaw cycles (liquid nitrogen/ 10^{-2} mbar vacuum) were applied. Then the resulting mixture was stirred under reflux in an oil bath for 10 h (GC–MS analysis). The reaction mixture was cooled to ambient temperature, EtOAc was added, and the resulting mixture was filtered through a celite or silica pad and concentrated in vacuo. The crude material was purified by column chromatography on a silica gel.

(E)-tert-Butylidimethyl(2-phenyl-1-(tetrahydrofuran-2-yl)vinyl)silane (10a). The reaction was performed following general procedure C: (E)-(2-bromo-1-(tetrahydrofuran-2-yl)vinyl)(tert-butyl)dimethylsilane (**2b**; 500 mg, 1.71 mmol, 1.0 equiv), $\text{PhB}(\text{OH})_2$ (835 mg, 6.8 mmol, 4.0 equiv), $\text{Pd}(\text{OAc})_2$ (20 mg, 0.085 mmol, 5 mol %), XPhos (120 mg, 0.26 mmol, 0.15 equiv), K_3PO_4 (1.46 g, 6.8 mmol, 4.0 equiv), and toluene (50 mL). For workup, DCM (50 mL) was added, and the mixture was filtered through a silica pad. Column chromatography (eluent: DCM/Hex 0 → 30%) afforded vinyl silane **10a** (401 mg, 79%) as a white amorphous solid. ^1H NMR (500 MHz, CDCl_3): δ 7.33 (t, 2H, J = 7.4), 7.22 (t, 1H, J = 7.4), 7.18 (d, 2H, J = 7.4), 6.86 (s, 1H), 4.69 (dd, 1H, J = 9.8, 6.9), 3.92 (dt, 1H, J = 14.4, 7.1), 3.62 (dt, 1H, J = 14.4, 7.2), 2.06–1.97 (m, 1H), 1.97–1.85 (m, 2H), 1.67 (m, 1H), 0.96 (s, 9H), 0.18 (s, 3H), 0.17 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 144.8, 140.9, 138.7, 128.6, 128.1, 126.9, 79.4, 33.4, 27.7, 26.1, 17.6, –3.1, –3.7. HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{29}\text{OSi}^+$ [$\text{M} + \text{H}^+$], 289.1982; found, 289.1979.

(E)-tert-Butylidimethyl(1-(tetrahydrofuran-2-yl)-2-(*m*-tolyl)-vinyl)silane (10b). The reaction was performed following general procedure C: (E)-(2-bromo-1-(tetrahydrofuran-2-yl)vinyl)(tert-butyl)dimethylsilane (**2b**; 50 mg, 0.17 mmol, 1.0 equiv), 3-methylphenylboronic acid (93 mg, 0.68 mmol, 4.0 equiv), $\text{Pd}(\text{OAc})_2$ (2 mg, 8.6 μmol , 5 mol %), XPhos (12 mg, 25.5 μmol , 0.15 equiv), K_3PO_4 (146 mg, 0.68 mmol, 4.0 equiv), and toluene (10 mL). For

workup, DCM (5 mL) was added, and the mixture was filtered through a silica pad. Column chromatography (eluent: DCM/Hex 0 → 30%) afforded vinyl silane **10b** (40 mg, 78%) as a white amorphous solid. ^1H NMR (500 MHz, CDCl_3): δ 7.20 (t, 2H, J = 7.5), 7.04 (t, 1H, J = 7.5), 6.99 (s, 1H), 6.98 (d, 1H, J = 7.5), 6.83 (s, 1H), 4.69 (ddd, 1H, J = 9.9, 6.7, 1.3), 3.92 (td, 1H, J = 14.1, 8.0), 3.61 (dd, 1H, J = 14.1, 6.7), 2.34 (s, 3H), 2.05–1.97 (m, 1H), 1.96–1.80 (m, 2H), 1.66 (dtd, 1H, J = 12.0, 9.7, 7.8), 0.96 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 144.5, 141.1, 138.7, 137.7, 129.4, 128.0, 127.6, 125.6, 79.5, 67.6, 33.4, 27.7, 26.1, 21.6, 17.6, –3.1, –3.7. HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{29}\text{OSi}^+$ [$\text{M} + \text{H}^+$], 303.2139; found, 303.2134.

(E)-tert-Butyl(2-(2-fluorophenyl)-1-(tetrahydrofuran-2-yl)vinyl)dimethylsilane (10c). The reaction was performed following general procedure C: (E)-(2-bromo-1-(tetrahydrofuran-2-yl)vinyl)(tert-butyl)dimethylsilane (**2b**; 50 mg, 0.17 mmol, 1.0 equiv), 2-fluorophenylboronic acid (95 mg, 0.68 mmol, 4.0 equiv), $\text{Pd}(\text{OAc})_2$ (2 mg, 8.6 μmol , 5 mol %), XPhos (12 mg, 25.5 μmol , 0.15 equiv), K_3PO_4 (146 mg, 0.68 mmol, 4.0 equiv), and toluene (10 mL). For workup, DCM (5 mL) was added, and the mixture was filtered through a silica pad. Column chromatography (eluent: DCM/Hex 0 → 40%) afforded vinyl silane **10c** (29 mg, 55%) as a white amorphous solid. ^1H NMR (500 MHz, CDCl_3): δ 7.24–7.19 (m, 1H), 7.18–7.13 (m, 1H), 7.07 (t, 1H, J = 7.5), 7.02 (t, 1H, J = 8.9), 6.78 (s, 1H), 4.56 (dd, 1H, J = 9.2, 6.5), 3.89 (td, 1H, J = 14.4, 7.6), 3.61 (td, 1H, J = 14.4, 8.1), 1.99–1.77 (m, 3H), 1.69–1.59 (m, 1H), 0.97 (s, 9H), 0.18 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 159.8 (d, J = 246), 147.5, 133.5 (d, J = 2), 130.5 (d, J = 4), 128.8 (d, J = 8), 126.4 (d, J = 16), 123.6 (d, J = 4), 115.4 (d, J = 22), 79.9, 67.7, 33.1, 27.6, 26.0, 17.4, –3.3, –3.8. HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{22}\text{FOSi}^+$ [$\text{M} + \text{H}^+$], 307.1888; found, 307.1880.

(E)-2-(1-iodo-2-phenylvinyl)tetrahydrofuran (11). In a 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer, (E)-tert-butylidimethyl(2-phenyl-1-(tetrahydrofuran-2-yl)vinyl)silane (**10a**) (250 mg, 0.86 mmol, 1.0 equiv) was dissolved in 2,2,2-trifluoroethanol (6 mL). NIS (230 mg, 1.0 mmol, 1.2 equiv) was added, and the resulting reaction mixture was stirred for 20 min at ambient temperature. DCM (30 mL), and an aqueous 10% $\text{Na}_2\text{S}_2\text{O}_3$ solution (30 mL) were added. The organic layer was separated and washed with brine (2 $\times$ 10 mL), dried over anhydrous Na_2SO_4 , filtered through a silica pad, and concentrated in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (eluent: DCM/Hex 0 → 30%) to afford vinyl iodide **11** (220 mg, 84%) as a yellow oil. ^1H NMR (500 MHz, CDCl_3): δ 7.46 (s, 1H), 7.36–7.31 (m, 2H), 7.31–7.27 (m, 1H), 7.20–7.17 (m, 2H), 4.20 (t, 1H, J = 7.2), 4.17 (td, 1H, J = 13.8, 7.3), 4.07 (td, 1H, J = 13.8, 7.9), 2.18–2.03 (m, 2H), 2.02–1.83 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 142.7, 137.6, 128.5, 128.4, 127.8, 114.0, 77.5, 69.3, 33.7, 26.7. HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{14}\text{IO}^+$ [$\text{M} + \text{H}^+$], 301.0084; found, 301.0080.

(Z)-2-(1,2-Diphenylvinyl)tetrahydrofuran (12a). The reaction was performed following general procedure C: (E)-2-(1-iodo-2-phenylvinyl)tetrahydrofuran (**11**; 40 mg, 0.13 mmol, 1.0 equiv), $\text{PhB}(\text{OH})_2$ (48 mg, 0.40 mmol, 3.0 equiv), $\text{Pd}(\text{OAc})_2$ (1.5 mg, 6.6 μmol , 5 mol %), PPh₃ (5.6 mg, 20.0 μmol , 0.15 equiv), Cs_2CO_3 (130 mg, 0.40 mmol, 3.0 equiv), toluene (2 mL), and H_2O (0.1 mL). For workup, DCM (5 mL) was added, and the mixture was filtered through a Na_2SO_4 and silica pad. Column chromatography (eluent: DCM/Hex 0 → 40%) afforded vinyl silane **12a** (28 mg, 80%) as a white amorphous solid. ^1H NMR (500 MHz, CDCl_3): δ 7.51 (m, 2H), 7.40–7.27 (m, 8H), 6.75 (s, 1H), 4.98 (dd, 1H, J = 8.3, 7.0), 3.90 (td, 1H, J = 13.8, 7.9), 3.78 (td, 1H, J = 13.8, 7.6), 1.96–1.88 (m, 1H), 1.88–1.73 (m, 2H), 1.68 (dq, 1H, J = 11.2, 8.2). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 142.5, 141.5, 137.1, 133.2, 129.2, 128.9, 128.3, 128.0, 127.2, 127.1, 77.1, 68.5, 30.8, 26.8. HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{19}\text{O}^+$ [$\text{M} + \text{H}^+$], 251.1430; found, 251.1427.

(Z)-2-(2-Phenyl-1-(4-(trifluoromethyl)phenyl)vinyl)-tetrahydrofuran (12b). The reaction was performed following general procedure C: (E)-2-(1-iodo-2-phenylvinyl)tetrahydrofuran (**11**; 50 mg, 0.17 mmol, 1.0 equiv), 4-trifluoromethylphenyl boronic

acid (95 mg, 0.50 mmol, 3.0 equiv), Pd(OAc)₂ (1.9 mg, 8.3 μmol, 5 mol %), PPh₃ (6.5 mg, 25.0 μmol, 0.15 equiv), Cs₂CO₃ (163 mg, 0.50 mmol, 3.0 equiv), toluene (2 mL), and H₂O (0.1 mL). For workup, DCM (5 mL) was added, and the mixture was filtered through a Na₂SO₄ and silica pad. Column chromatography (eluent: DCM/Hex 0 → 40%) afforded vinyl silane **12b** (40 mg, 77%) as a white amorphous solid. ¹H NMR (500 MHz, CDCl₃): δ 7.64 (d, 2H, *J* = 8.3), 7.60 (d, 2H, *J* = 8.3), 7.41–7.36 (m, 4H), 7.33–7.28 (m, 1H), 6.76 (s, 1H), 4.99 (dd, 1H, *J* = 8.5, 6.9), 3.89 (td, 1H, *J* = 13.7, 6.7), 3.78 (td, 1H, *J* = 13.7, 7.7), 1.95 (tdd, 1H, *J* = 11.9, 8.5, 4.8), 1.90–1.83 (m, 1H), 1.83–1.73 (m, 1H), 1.61 (qd, 1H, *J* = 12.0, 8.5). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 145.1, 141.5, 136.5, 134.2, 129.4 (q, *J* = 32), 129.3, 129.2, 128.4, 127.5, 124.9 (q, *J* = 4), 124.5 (q, *J* = 27.2), 76.9, 68.5, 30.8, 26.7. HRMS (ESI): *m/z* calcd for C₁₉H₁₈F₃O⁺ [M + H]⁺, 319.1304; found, 319.1299.

(Z)-4-(2-Phenyl-1-(tetrahydrofuran-2-yl)vinyl)benzonitrile (12c). The reaction was following general procedure C: (E)-2-(1-iodo-2-phenylvinyl)tetrahydrofuran (**11**; 50 mg, 0.17 mmol, 1.0 equiv), 4-cyanophenyl boronic acid (74 mg, 0.50 mmol, 3.0 equiv), Pd(OAc)₂ (1.9 mg, 8.3 μmol, 5 mol %), PPh₃ (6.5 mg, 25.0 μmol, 0.15 equiv), Cs₂CO₃ (163 mg, 0.50 mmol, 3.0 equiv), toluene (2 mL), and H₂O (0.1 mL). For workup, EtOAc (5 mL) was added, and the mixture was filtered through a Na₂SO₄ and silica pad. Column chromatography on silica (eluent: DCM/Hex 80–100%) afforded vinyl silane **12c** (30 mg, 66%) as a white, amorphous solid. ¹H NMR (500 MHz, CDCl₃): δ 7.66 (m, 4H), 7.41–7.34 (m, 4H), 7.31–7.28 (m, 1H), 6.77 (s, 1H), 4.98 (dd, 1H, *J* = 8.6, 6.7), 3.89 (td, 1H, *J* = 13.8, 7.9), 3.78 (td, 1H, *J* = 13.8, 7.7), 1.99–1.91 (m, 1H), 1.91–1.83 (m, 1H), 1.82–1.73 (m, 1H), 1.58 (qd, 1H, *J* = 11.8, 8.1). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 146.3, 141.1, 136.2, 134.8, 131.9, 129.6, 129.1, 128.5, 127.7, 119.2, 111.0, 76.8, 68.5, 30.9, 26.7. HRMS (ESI): *m/z* calcd for C₁₉H₁₈NO⁺ [M + H]⁺, 276.1383; found, 276.1377.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

■ Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.3c01481>.

Experimental procedures and characterization data (PDF)

Accession Codes

CCDC 2241600 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Māris Turks – Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga LV-1048, Latvia; orcid.org/0000-0001-5227-0369; Email: Maris.Turks@rtu.lv

Authors

Rasma Krokāle – Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga LV-1048, Latvia
Rūdolfs Beļauņieks – Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga LV-1048, Latvia

Artjoms Ubaidullajevs – Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, Riga LV-1048, Latvia
Anatolij Mishnev – Latvian Institute of Organic Synthesis, Riga LV-1006, Latvia

Complete contact information is available at: <https://pubs.acs.org/doi/10.1021/acs.joc.3c01481>

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

R.K. and R.B. thank the European Social Fund for financial support within project Nr. 8.2.2.0/20/1/008 and Riga Technical University doctoral student grants. The Latvian Council of Science Grant LZP-2023/1-0576 is kindly acknowledged. The authors thank Rebeka Anna Līpiņa for technical support.

■ REFERENCES

- (1) Vitaku, E.; Smith, D. T.; Njardarson, J. T. Analysis of the Structural Diversity, Substitution Patterns, and Frequency of Nitrogen Heterocycles among U.S. FDA Approved Pharmaceuticals: Mini-perspective. *J. Med. Chem.* **2014**, *57* (24), 10257–10274.
- (2) (a) Bhutani, P.; Joshi, G.; Raja, N.; Bachhav, N.; Rajanna, P. K.; Bhutani, H.; Paul, A. T.; Kumar, R. U.S. FDA Approved Drugs from 2015–June 2020: A Perspective. *J. Med. Chem.* **2021**, *64* (5), 2339–2381. (b) Heravi, M. M.; Zadsirjan, V. Prescribed drugs containing nitrogen heterocycles: an overview. *RSC Adv.* **2020**, *10*, 44247–44311.
- (3) (a) Jeelan Basha, N.; Basavarajaiah, S. M.; Shyamsunder, K. Therapeutic potential of pyrrole and pyrrolidine analogs: an update. *Mol. Diversity* **2022**, *26*, 2915–2937. (b) Li Petri, G.; Raimondi, M. V.; Spanò, V.; Holl, R.; Barraja, P.; Montalbano, A. Pyrrolidine in Drug Discovery: A Versatile Scaffold for Novel Biologically Active Compounds. *Top. Curr. Chem.* **2021**, *379*, 34. (c) Bhat, A. A.; Tandon, N.; Tandon, R. Pyrrolidine Derivatives as Anti-diabetic Agents: Current Status and Future Prospects. *ChemistrySelect* **2022**, *7*, No. e202103757. (d) Bhat, A. A.; Singh, I.; Tandon, N.; Tandon, R. Structure activity relationship (SAR) and anticancer activity of pyrrolidine derivatives: Recent developments and future prospects (A review). *Eur. J. Med. Chem.* **2023**, *246*, 114954.
- (4) Yao, S.-C.; Xiao, J.; Nan, G. M.; Peng, Y. Progress on total synthesis and their divergent transformations of aryltetrahydrofuran-type lignans. *Tetrahedron Lett.* **2023**, *115*, 154309.
- (5) (a) González-Andrés, P.; Fernández-Peña, L.; Díez-Poza, C.; Barbero, A. The Tetrahydrofuran Motif in Marine Lipids and Terpenes. *Mar. Drugs* **2022**, *20*, 642. (b) Fernández-Peña, L.; Díez-Poza, C.; González-Andrés, P.; Barbero, A. The Tetrahydrofuran Motif in Polyketide Marine Drugs. *Mar. Drugs* **2022**, *20*, 120.
- (6) Fernandes, R. A.; Gorve, D. A.; Pathare, R. S. Emergence of 2,3,5-trisubstituted tetrahydrofuran natural products and their synthesis. *Org. Biomol. Chem.* **2020**, *18*, 7002–7025.
- (7) Ghosh, A. K.; Anderson, D. D. Tetrahydrofuran, tetrahydropyran, triazoles and related heterocyclic derivatives as HIV protease inhibitors. *Future Med. Chem.* **2011**, *3* (9), 1181–1197.
- (8) (a) Rodrigues, L.; Tilve, S. G.; Majik, M. S. Synthetic access to thiolane-based therapeutics and biological activity studies. *Eur. J. Med. Chem.* **2021**, *224*, 113659. (b) Benetti, S.; De Risi, C.; Pollini, G. P.; Zanirato, V. Synthetic routes to chiral non-racemic and racemic dihydro- and tetrahydrothiophenes. *Chem. Rev.* **2012**, *112*, 2129–2163. (c) Wang, N.; Saidharedy, P.; Xuefeng, J. Construction of sulfur-containing moieties in the total synthesis of natural products. *Nat. Prod. Rep.* **2020**, *2*, 246.
- (9) (a) Ahmad, T.; Ullah, N. The oxo-Michael reaction in the synthesis of 5- and 6-membered oxygen-containing heterocycles. *Org.*

Chem. Front. **2021**, *8*, 1329–1344. (b) Wolfe, J. P.; Hay, M. B. Recent advances in the stereoselective synthesis of tetrahydrofurans. *Tetrahedron* **2007**, *63*, 261–290. (c) De la Torre, A.; Cuyamendous, C.; Bultel-Poncé, V.; Durand, T.; Galano, J.-M.; Oger, C. Recent advances in the synthesis of tetrahydrofurans and applications in total synthesis. *Tetrahedron* **2016**, *72*, S003–S025.

(10) (a) Lazib, Y.; Naves, J. G.; Labande, A.; Dauban, P.; Saget, T. Asymmetric Syntheses of Enantioenriched 2,5-Disubstituted Pyrrolidines. *ACS Org. Inorg. Au* **2023**, *3*, 120–129. (b) Byatt, B. J.; Pyne, S. G. The Chemical Synthesis of the 1-C-Alkyl Substituted Pyrrolidine and Piperidine Iminosugar Natural Products and their Analogues. *Curr. Org. Chem.* **2023**, *26*, 2071–2097. (c) Stocker, B. L.; Dangerfield, E. M.; Win-Mason, A. L.; Haslett, G. W.; Timmer, M. S. M. Recent Developments in the Synthesis of Pyrrolidine-Containing Iminosugars. *Eur. J. Org. Chem.* **2010**, *2010*, 1615–1637. (d) Sharma, P.; Gupta, R.; Bansal, R. K. Recent advances in organocatalytic asymmetric aza-Michael reactions of amines and amides. *Beilstein J. Org. Chem.* **2021**, *17*, 2585–2610.

(11) (a) Turks, M.; Bejaunies, R.; Puriş, M. Manifestation of the β -Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift. *Synthesis* **2020**, *52* (15), 2147–2161. (b) Roberts, D. D.; McLaughlin, M. G. Strategic Applications of the β -Silicon Effect. *Adv. Synth. Catal.* **2022**, *364*, 2307–2332. (c) Knölker, H.-J.; Schmidt, A. Cycloadditions of Allylsilanes - Part 22. [1] Stereoselective Synthesis of Cyclopentanes and Cyclobutanes by Lewis Acid Promoted [3 + 2] and [2 + 2] Cycloadditions of Allylsilanes. *Synlett* **2010**, *15*, 2207–2239. (d) Curtis-Long, M. J.; Aye, Y. Vinyl-Propargyl- and Allenylsilicon Reagents in Asymmetric Synthesis: A Relatively Untapped Resource of Environmentally Benign Reagents. *Chem.—Eur. J.* **2009**, *15*, 5402–5416. (e) Chabaud, L.; James, P.; Landais, Y. Allylsilanes in Organic Synthesis – Recent Developments. *Eur. J. Org. Chem.* **2004**, *2004*, 3173–3199. (f) Knölker, H.-J. Cycloadditions of allylsilanes. Part 10. Stereoselective Construction of Ring Systems by Cycloaddition Reactions of allyltriisopropylsilane. *J. Prakt. Chem.* **1997**, *339*, 304–314.

(12) (a) Barczak, N. T.; Rooke, D. A.; Menard, Z. A.; Ferreira, E. M. Stereoselective Synthesis of Tetrasubstituted Olefins through a Halogen-Induced 1,2-Silyl Migration. *Angew. Chem., Int. Ed.* **2013**, *52*, 7579–7582. (b) Wang, Y.; Ready, J. M. Cyclocondensation of Amino-Propargyl Silanes. *Org. Lett.* **2012**, *14*, 2308–2311. (c) Rooke, D. A.; Ferreira, E. M. Stereoselective Syntheses of Trisubstituted Olefins via Platinum Catalysis: α -Silylenones with Geometrical Complementarity. *J. Am. Chem. Soc.* **2010**, *132*, 11926–11928. (d) Buckle, M. J. C.; Fleming, I.; Gil, S.; Pang, K. L. C. Accurate determinations of the extent to which the S_E2' reactions of allyl-allyl- and propargylsilanes are stereospecifically anti. *Org. Biomol. Chem.* **2004**, *2*, 749–769. (e) Evans, D. A.; Aye, Y. Aluminum-Catalyzed Enantio- and Diastereoselective Carbonyl Addition of Propargylsilanes. A New Approach to Enantioenriched Vinyl Epoxides. *J. Am. Chem. Soc.* **2007**, *129*, 9606–9607. (f) Danheiser, R. L.; Dixon, B. R.; Gleason, R. W. Five-membered ring annulation via propargyl- and allylsilanes. *J. Org. Chem.* **1992**, *57*, 6094–6097. (g) Mergardt, B.; Weber, K.; Adiwidjaja, G.; Schaumann, E. Tandem Silyl Migrations Leading to α,β -Bis-silylated Enals and Enones. *Angew. Chem., Int. Ed.* **1991**, *30*, 1687–1688. (h) Pornet, J.; Damour, D.; Miginiac, L. Synthèse régiospécifique d'allènes terminaux à partir de propargyltriméthylsilanes simples ou fonctionnels. *J. Organomet. Chem.* **1987**, *319*, 333–343. (i) Pornet, J.; Miginiac, L.; Jaworski, K.; Randrianoelina, B. Regiospecific allenylation of acetals with propargyltrimethylsilanes catalyzed by a Lewis acid: synthesis of α -allyl-allyl ethers and 3-silylated 3,4-dihydrofurans. *Organometallics* **1985**, *4*, 333–338. (j) Danheiser, R. L.; Kwasigroch, C. A.; Tsai, Y. M. Application of Allenylsilanes in [3 + 2] Annulation Approaches to Oxygen and Nitrogen Heterocycles. *J. Am. Chem. Soc.* **1985**, *107*, 7233–7235. (k) Danheiser, R. L.; Carini, D. J.; Basak, A. (Trimethylsilyl)cyclopentene annulation: a regiocontrolled approach to the synthesis of five-membered rings. *J. Am. Chem. Soc.* **1981**, *103*, 1604–1606.

(13) (a) Puriş, M.; Mishnev, A.; Turks, M. Brønsted Acid Catalyzed 1,2-Silyl Shift in Propargyl Silanes: Synthesis of Silyl Dienes and Silyl Indenes. *J. Org. Chem.* **2019**, *84* (6), 3595–3611. (b) Bejaunies, R.; Puriş, M.; Kumpinş, V.; Turks, M. Synthesis of 3-Silylated 3-Sulfolenes from Propargylsilanes and their Reductive Desulfitation. *Chem. Heterocycl. Compd.* **2021**, *57*, 20–25.

(14) Bejaunies, R.; Puriş, M.; Lipiņa, R. A.; Mishnev, A.; Turks, M. 1,3-Difunctionalization of Propargyl Silanes with Concomitant 1,2-Silyl Shift: Synthesis of Allyl Functionalized Vinyl Silanes. *Org. Lett.* **2023**, *25*, 4627–4631.

(15) Wang, X.; Gao, Q.; Buevich, A. V.; Yasuda, N.; Zhang, Y.; Yang, R.-S.; Zhang, L.-K.; Martin, G. E.; Williamson, R. T. Unexpected Propargylic Retro-Brook Rearrangements in Alkynes. *J. Org. Chem.* **2019**, *84* (16), 10024–10031.

(16) (a) Denmark, S. E.; Dappen, M. S.; Sear, N. L.; Jacobs, R. T. The vinylogous anomeric effect in 3-alkyl-2-chlorocyclohexanone oximes and oxime ethers. *J. Am. Chem. Soc.* **1990**, *112*, 3466–3474. (b) Katritzky, A. R.; Steel, P. J.; Denisenko, S. N. X-Ray crystallographic evidence for a vinylogous anomeric effect in benzotriazole-substituted heterocycles. *Tetrahedron* **2001**, *57*, 3309–3314. (c) Torabi, M.; Zolfigol, M. A.; Yarie, M.; Notash, B.; Azizian, S.; Azandaryani, M. M. Synthesis of triarylpyridines with sulfonate and sulfonamide moieties via a cooperative vinylogous anomeric-based oxidation. *Sci. Rep.* **2021**, *11*, 16846.

(17) Crystallographic data for compound **7h** has been deposited with the Cambridge Crystallographic Data Center as a supplementary publication no. CCDC-2241600.

(18) The issue with rotamers did not allow us to make straightforward conclusions on the electrophilic activation of acyl amides **6a,b** with NBS or NIS. During screening of experimental conditions, the signals of the expected cyclization products were registered by GC–MS chromatograms, but their convoluted NMR spectra did not allow us to prove the correct identities of the obtained products.

(19) Altman, R. A.; Buchwald, S. L. Pd-catalyzed Suzuki–Miyaura reactions of aryl halides using bulky biarylmonophosphine ligands. *Nat. Protoc.* **2007**, *2* (12), 3115–3121.

(20) (a) Miller, R. B.; Reichenbach, T. The stereospecific synthesis of vinyl halides using a vinylsilane as the synthetic precursor. *Tetrahedron Lett.* **1974**, *15* (6), 543–546. (b) Huynh, C.; Linstrumelle, G. A new synthesis of substituted vinylsilanes and vinyl iodides. *Tetrahedron Lett.* **1979**, *20* (12), 1073–1076.

(21) (a) Colomer, I.; Chamberlain, A. E. R.; Haughey, M. B.; Donohoe, T. J. Hexafluoroisopropanol as a highly versatile solvent. *Nat. Rev. Chem.* **2017**, *1*, 0088. (b) Pozhydaiev, V.; Power, M.; Gandon, V.; Moran, J.; Lebœuf, D. Exploiting hexafluoroisopropanol (HFIP) in Lewis and Brønsted acid-catalyzed reactions. *Chem. Commun.* **2020**, *56*, 11548–11564. (c) An, X.-D.; Xiao, J. Fluorinated Alcohols: Magic Reaction Medium and Promoters for Organic Synthesis. *Chem. Rec.* **2020**, *20*, 142–161.

(22) Kropkalne, R.; Bejaunies, R.; Turks, M. Synthesis of 4-(tert-Butyldimethylsilyl)-4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-a]pyridine. *Molbank* **2022**, *2022*, M1427.

**Synthesis of Substituted Chromanes and Tetrahydroquinolines via
Tandem 1,2-Silyl Shift – Friedel–Crafts cyclization**

Ubaidullajevs, A.; Kronkalne, R.; Mishnev, A.; Turks, M.

J. Org. Chem., **2026**, *91* (17), 5785–5810

Pārpublicēts ar *ACS Publications* atļauju

Copyright © 2026 American Chemical Society

Republished with permission from *ACS Publications*

Copyright © 2026 American Chemical Society

Synthesis of Substituted Chromanes and Tetrahydroquinolines via Tandem 1,2-Silyl Shift–Friedel–Crafts Cyclization

Arjoms Ubaidullajevs, Rasma Kronkalne, Anatoly Mishnev, and Māris Turks*

Cite This: <https://doi.org/10.1021/acs.joc.5c03136>

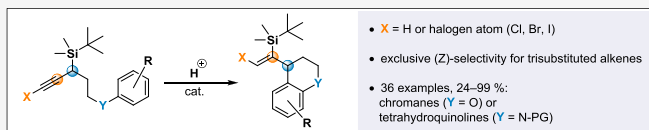
Read Online

ACCESS |

Metrics & More

Article Recommendations

Supporting Information



ABSTRACT: Propargyl silanes bearing an aryl ether or aniline moiety undergo acid-promoted 1,2-silyl shift to generate an allyl cation, which subsequently alkylates the adjacent aryl group in a Friedel–Crafts fashion. The developed methodology furnishes chromanes in 24–99% yields and 1,2,3,4-tetrahydroquinolines in 21–77% yields, depending on the substitution pattern. The distinctive feature of the developed methodology is the synthesis of (trialkylsilyl)vinyl- and (Z)-2-halo-1-(trialkylsilyl)vinyl-substituted heterocycles. Propargyl silanes bearing chloro- and bromoalkyne motifs afford cyclization products in higher yields than their terminally unsubstituted alkyne counterparts, providing access to trisubstituted (Z)-alkenes with high stereoselectivity. The paper also reports an improved protocol for silver-catalyzed haloalkyne synthesis, which is enabled by the use of Ag_2CO_3 or AgOAc catalysts.

INTRODUCTION

Chromane and 1,2,3,4-tetrahydroquinoline (THQ) structural motifs appear in various natural products with a wide range of structural modifications and biological roles (Figure 1).

Chromane core is widespread among flavonoids and polyphenolic compounds with antioxidant properties.^{1–3} On the other hand, the tetrahydroquinoline motif is found in many

alkaloids that exhibit high pathogen toxicity and anticancer potential.^{4–6} Natural products containing the chromane heterocycle include vitamin E family, the psychoactive compound trans- Δ^9 -tetrahydrocannabinol⁷ and the platelet activation inhibitor glabridin.⁸ Whereas the THQ scaffold is found in diverse alkaloids such as antibacterial agent helmintholone,⁹ benzastatin D (a free radical scavenger),¹⁰ aspernigerin (anticancer and fungicidal properties),^{11,12} and some alkaloids isolated from *Lyngbya majuscula*.¹³ Both chromane and THQ structural motifs are regarded as privileged structures in medicinal chemistry, with successful applications as lead compounds in drug discovery and as marketed therapeutics. Notable examples of the latter include the β -blocker nebivolol,¹⁴ the nonsteroidal oral contraceptive ormeloxifene,^{15,16} and the antischistosomiasis drug oxamniquine,¹⁷ to name but a few (Figure 1).

The significance of the aforementioned applications has driven the development of synthetic methodologies for the preparation of chromanes and THQs, and this has been the subject of recent reviews.^{18–23} If the $\text{C}_4\text{--C}_{4a}$ bond formation (Scheme 1) is regarded as the key step in the synthesis of the title compounds, it can be achieved through a well-established Heck

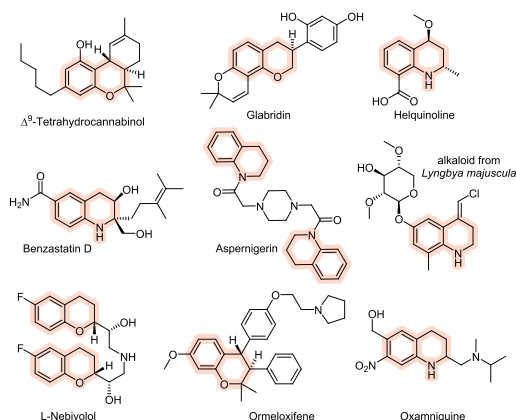


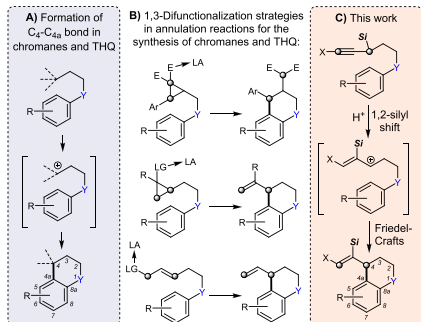
Figure 1. Natural products and marketed drugs containing chromane and 1,2,3,4-tetrahydroquinoline cores.

Received: December 14, 2025

Revised: March 7, 2026

Accepted: March 20, 2026

Scheme 1. Annulation Strategies for C₄–C_{4a} Bond Formation in Chromanes and Tetrahydroquinolines via 1,3-Difunctionalization of Linkers and Harnessing the 1,3-Dipole Nature of Propargyl Silanes; THQ = 1,2,3,4-Tetrahydroquinoline, Y = O, NR; E = Ester, Ar = Aryl; LG = Leaving Group, LA = Lewis Acid, X = H, Cl, Br, I



type process.^{24–27} However, this approach requires the presence of an appropriate halide substituent on the aromatic cycle, except in certain advanced cases.²⁸ Alternatively, an electrophilic reaction center can be created at the C₄ atom, which will then enter into Friedel–Crafts-type cyclization (Scheme 1A).^{29–38} This approach can be combined with the 1,3-difunctionalization^{39,40} of the attached linker, if the latter consists of systems as exemplified by donor–acceptor cyclopropane,⁴¹ cyclopropyl cation precursor,⁴² allylic system bearing leaving group,⁴³ or Michael acceptor (Scheme 1B).^{43,44} From the described methods, only few provide 4-vinyl-substituted chromanes and THQs,^{42,43,45} but the latter are considered as important building blocks in the synthesis of structurally diverse natural product analogs^{46,47} and prospective anticancer agents.^{48,49}

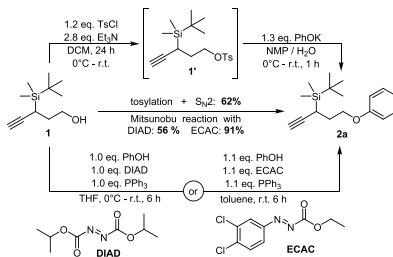
Hence, we propose harnessing the intrinsic 1,3-dipole character of propargyl silanes, which is enabled by the possibility of a 1,2-silyl shift once this molecular fragment is activated by an electrophile (Scheme 1C).^{50–52} If the silyl group is placed internally, the initially formed vinyl cation, upon 1,2-migration of the silyl group, will rearrange to a more stable allyl cation, which in turn can be quenched by a nucleophilic component. Applying this concept, we have recently reported the synthesis of silyl dienes,^{53,54} allyl-functionalized vinyl silanes,⁵⁵ and five-membered heterocycles.⁵⁶ Herein, we demonstrate that the intramolecularly offered aryl moiety, acting as a π -nucleophile, triggers an intramolecular Friedel–Crafts reaction, affording chromanes or THQs bearing a 4-vinyl group. This also includes important variations of products with geometrically controlled (Z)-2-halo-1-(trialkylsilyl)vinyl moiety. To the best of our knowledge, allyl and propargyl silane chemistry remains largely unexplored in the synthesis of chromanes and THQs, and the few reported methods do not involve the application of a 1,2-silyl shift.^{57–59}

RESULTS AND DISCUSSION

We envisaged the use of 3-silyl pent-4-yn-1-ol (**1**) as strategic starting material, which can be readily obtained from commercially available pent-4-yn-1-ol in 84% yield via successive silylation and retro-Brook rearrangement⁶⁰ under Schlosser conditions.⁶¹ Synthesis of aryl ether **2** from alcohol **1** was investigated and optimized. We have explored both classical

nucleophilic substitutions using the tosylate leaving group and the Mitsunobu reaction (Scheme 2). We observed degradation

Scheme 2. Synthesis of Phenyl Ether **2a by Various Approaches**

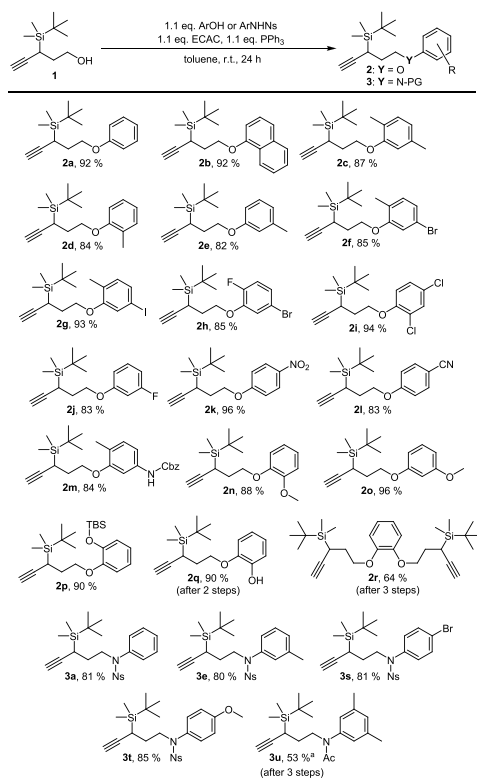


of tosylate **1'** during its purification on silica gel and also during storage, even at 5 °C. Moreover, the use of rather basic phenolates in the S_N2 step resulted in partial allenization of the propargyl silane moiety.

On the other hand, standard Mitsunobu conditions employing diisopropyl azodicarboxylate (DIAD) with phenol as a weak acid provided similarly mediocre (56%) yield of product **2a**. To our delight, the use of second-generation Mitsunobu reagents such as ethyl 2-(3,4-dichlorophenyl)azocarboxylate (ECAC)⁶² proved to be effective, and the desired product **2a** was isolated in 91% yield (for the synthesis and regeneration^{63–65} of ECAC, see the experimental part). The Mitsunobu conditions employing ECAC were therefore applied to various phenols, affording aryl ethers **2a–r** in yields up to 96% (Scheme 3). ECAC was also more efficient than DIAD in the reactions with aniline nucleophiles, providing products **3a,e,s,t** in 80–85% yields. For comparison, product **3a** was obtained in only 66% yield using DIAD.

With the starting materials in hand, we investigated the acid-promoted cyclization of functionalized propargyl silanes **2** and **3**. Optimization of the cyclization reaction was carried out on the simplest substrate, phenyl ether **2a**, by testing different solvents and Brønsted acids (Table 1). Good yields of product **4a** were obtained with HNTf₂ in halogenated solvents, but the best yield was observed in nitromethane, which was therefore chosen as the solvent for the methodology described herein (Table 1, entry 7). This observation is consistent with the commonly preferred solvents for Friedel–Crafts reactions, owing to their stability toward superacids. Next, catalyst loading and the reaction temperature were checked (Table 2). We found that chromane formation proceeds more efficiently with larger amounts of acid. However, at ambient temperature (20 °C), the reaction yield reaches an upper limit of around 75%, with no significant improvement above 20 mol % loading of the acid promoter (Table 2, entries 6–8). Additionally, we observed a slight improvement in product purity and yield in more concentrated reaction mixtures. For instance, in the transformation **2a** → **4a** with 10 mol % Tf₂NH loading, the difference in product **4a** yield between 0.2 and 0.05 M substrate solutions were 68 and 64%, respectively (Table 2, entries 2 and 3). A similar pattern was observed in the case of 15 mol % Tf₂NH loading: 68% for 0.05 M substrate concentration and 72% for 0.2 M substrate concentration. (Table 2, entries 4 and 5). This counterintuitive observation for an intramolecular reaction can be explained by HNTf₂ degradation during the diffusion process,

Scheme 3. Synthesis of Propargyl Silanes 2 and 3



^aProduct 3u was synthesized by a different approach: alcohol 2a was oxidized to aldehyde followed by reductive amination with 3,5-dimethylaniline and acetylation.

which may also account for the degradation of the substrate or product. An alternative explanation involves stabilization of the transition state by the bistriflimide counterion. Even more intriguing, the acid-promoted chromane-forming reaction performed best at 60 °C, and besides occurring faster, afforded purer product 4a than at lower temperatures (Table 2, entry 9).

According to the found optimized conditions, propargyl silanes 2 and 3 were cyclized to the corresponding chromanes 4a–r (yields up to 87%) and THQs 5a,e,t,u (yields up to 45%) (Scheme 4). The variations with solvent (MeNO₂ versus dichloroethane/MeNO₂) were determined by substrate solubility. Chromane 4a–r synthesis was found to be more successful, and their yields correlate with the electronic density of the benzene ring. Aryl groups with electron-withdrawing substituents (F, Cl, Br, I, CN, NO₂) exhibited reduced reactivity compared to those bearing electron-donating substituents (Me, OMe, OH). Somewhat unexpectedly, lower yields were obtained for the compounds 4m and 4o. Both compounds contain heteroatoms in *ortho*-position near the cyclization site, which may interact unfavorably with the intermediate allyl cation. It should be noted that *meta*-substituted propargyl silanes (2e,j and 3e) did not provide reasonable regioselectivity, and products 4e,j and 5e were obtained as a mixture of isomers. Nevertheless, starting material 2o gave only one product 4o.

Table 1. Optimization of Solvent and Acid Promoter

entry	acid	solvent	yield, % ^a
1	HNTf ₂	MeCN	17
2	HNTf ₂	C ₆ H ₆	19
3	HNTf ₂	CHCl ₃	63
4	HNTf ₂	ClCH ₂ CH ₂ Cl	74
5	HNTf ₂	CH ₂ Cl ₂	73
6	HNTf ₂	dioxane	20
7	HNTf ₂	MeNO ₂	76
8	HNTf ₂	THF	15
9	HNTf ₂	toluene	14
10	HNTf ₂	CF ₃ COOH	11
11	HNTf ₂	trifluorotoluene	63
12	HOTf	CHCl ₃	51
13	HOTf	CH ₂ Cl ₂	56
14	HN(SO ₂ CF ₃) ₂ CF ₃	CHCl ₃	n.r. ^b
15	HN(SO ₂ CF ₃) ₂ CF ₃	CH ₂ Cl ₂	n.r. ^b

^aNMR yield using 1,4-dinitrobenzene as an internal standard. ^bNo reaction after 2 h.

Table 2. Optimization of Solvent and Acid Catalyst

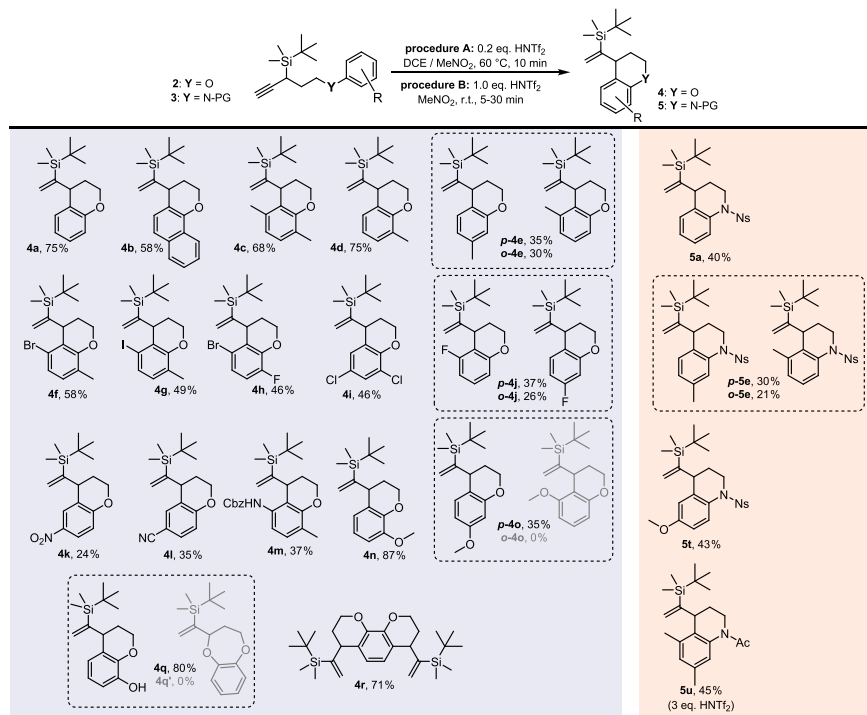
entry	HNTf ₂ equiv	temperature, °C	yield, % ^a
1	0.05	20	65
2	0.10	20	68
3 ^b	0.10	20	64
4	0.15	20	72
5 ^b	0.15	20	68
6	0.20	20	75
7	0.40	20	76
8	1.00	20	76
9	0.20	60	85

^aNMR yield using 1,4-dinitrobenzene as an internal standard. ^b0.05 M phenyl ether 2a.

Interestingly, substrate 2q bearing a phenolic OH group reacted exclusively as π -nucleophile, and product 4q was isolated with 80% yield. Last but not least, with substrate 2r, we have demonstrated double cyclization to product 4r, which was obtained in 71% yield. It should be pointed out that the substituted anilines 3 exhibited lower reactivity than the corresponding aryl ethers. A stoichiometric amount of acid was required to achieve cyclization to THQs 5a,e,t,u. The reduced reactivity of substrate 3 can be explained by the protonation of the *N*-protecting group, leading to deactivation of the π -nucleophile.

While the isolation and purification of products 4 and 5 generally proceeded smoothly, allene byproducts arising from desilylation were occasionally observed. For the nonpolar chromanes 4a–4f, this presented a practical challenge during chromatography, as the byproducts exhibited retention factors close to those of the main products across various eluent systems. We resolved this issue by employing AgNO₃-

Scheme 4. Synthesis of Chromanes and Tetrahydroquinolines via Tandem 1,2-Silyl Shift–Friedel–Crafts Cyclization

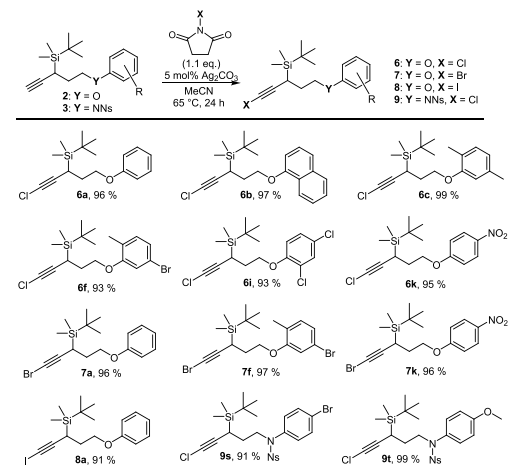


impregnated silica gel. Silver-assisted chromatography enabled excellent separation through selective interactions with different types of π -bond systems.⁶⁶

In our previous studies, halogen electrophiles were used stoichiometrically to obtain vinyl halides via tandem electrophile addition—1,2-silyl shift—nucleophile addition, where heteroatom-based electrophiles and nucleophiles were used.^{55,56} This approach was not productive in the present reaction manifold involving a π -nucleophile for Friedel–Crafts cyclization. However, this limitation can be overcome by introducing a halide at the terminal position of the alkyne moiety and employing the previously described acid-catalyzed cyclization.

Haloalkynes are nontrivial but easy-to-prepare and relatively stable reagents, excluding fluoroalkynes.⁶⁷ The preparation of bromoalkynes and iodoalkynes requires a silver catalyst (AgNO₃) in combination with the appropriate *N*-halosuccinimide, and typically proceeds well in acetone or acetonitrile under ambient conditions.⁶⁸ It appeared that this approach cannot be universally extrapolated to the chloroalkynes. In our hands, the tested substrates remained unreactive toward *N*-chlorosuccinimide under the previously described reaction conditions.^{69,70} To our delight, we found that more basic conditions involving Ag₂CO₃ catalysis in acetonitrile are a more general method for the synthesis of chloro-, bromo-, and iodoalkynes (Scheme 5). This protocol affords excellent yields and enables nearly complete regeneration of the catalyst due to its low solubility. Less basic catalysts like silver succinimide or AgOAc are also effective for haloalkyne synthesis. Basic silver salt catalysts seem to be more effective also in the case of bromo-

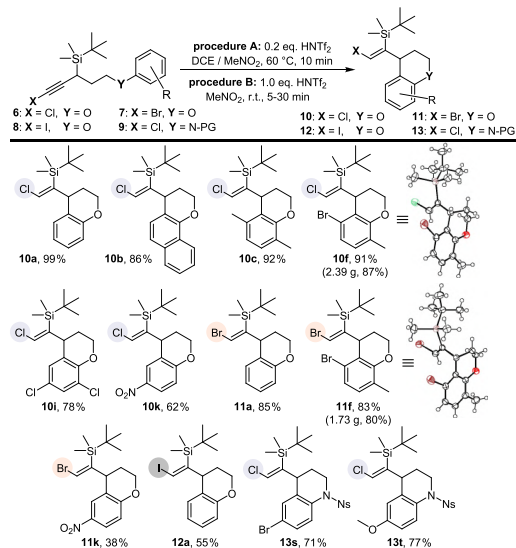
Scheme 5. Synthesis of of Haloalkynes 6–9



and iodoalkynes because they accelerate the alkyne deprotonation step, which is presumed to be rate-limiting.^{71,72}

Haloalkynes 6–9 smoothly underwent acid-catalyzed tandem 1,2-silyl shift–Friedel–Crafts cyclization and afforded the expected chromanes 10–12 and THQs 13 (Scheme 6). Iodoalkyne 8a gave chromane 12a in an average yield of 55%, whereas chloro- and bromoalkynes appeared to be more reactive

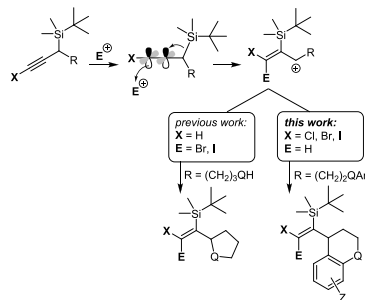
Scheme 6. Synthesis of Chromanes and Tetrahydroquinolines 10–13 Containing (Z)-2-Halo-1-(trialkylsilyl)vinyl Moiety



in cyclization reactions than their nonhalogenated counterparts. Thus, 5-chlorochromane **10f** containing (Z)-2-chloro-1-(*tert*-butyldimethylsilyl)vinyl moiety was obtained in 91% yield (Scheme 6) versus its nonchlorinated congener **4f** (58%) (Scheme 4). A similar pattern favoring chloroalkyne reactivity was observed in the product pairs **4i** (46%) versus **10i** (78%) and **4k** (24%) versus **10k** (62%), the latter containing an electron-poor nitroaryl moiety. The geometry of the vinyl substituent in products 10–13 was established by 2D-NOESY spectra, and in the case of products **10f** and **11f**, it was unambiguously proved by single-crystal X-ray diffraction analysis.⁷³ Also, the synthesis of THQs **13s,t** bearing (Z)-2-chloro-1-(*tert*-butyldimethylsilyl)vinyl moiety proceeded more cleanly and in higher yields than for those employing nonhalogenated propargyl silanes.

The (Z)-selective double bond formation during propargyl silane–vinyl silane rearrangement can be explained by the antiperiplanarity requirement during protonation of the π -system, which is followed by its overlapping with the adjacent C–Si bond, as depicted in Scheme 7. In our previous work, 1,2-silyl shift in propargyl silanes followed a similar selectivity pattern: a combination of terminally unsubstituted alkyne systems with halogen electrophiles afforded predominantly (E)-isomers.^{55,56} In the present case of chromane and THQ formation, proton delivery to the alkyne can be implemented both intermolecularly by superacid or intramolecularly by the protonated electron-rich aromatic cycle or heteroatom from the linker. This is in agreement with literature reports describing proton transfer between protonated π -systems or protonated heteroatom and double bond.^{74–77} The protonation–1,2-silyl shift process is apparently followed by a fast intramolecular Friedel–Crafts cyclization that favors the newly formed (Z)-double bond due to minimized steric interaction with the incoming aromatic cycle.

Scheme 7. Mechanism Proposal for (Z)-Selective Double Bond Formation during 1,2-Silyl Shift and Tandem Cyclization



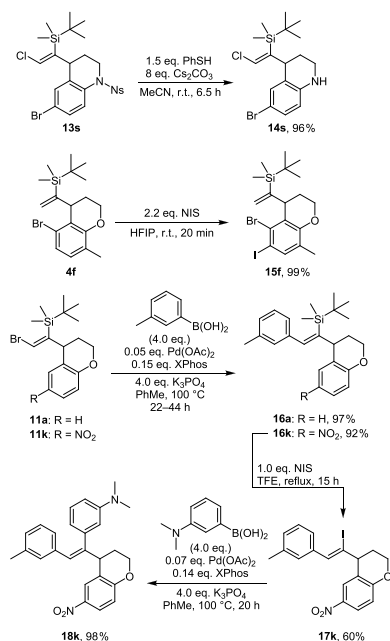
The observed halogen effect can be rationalized as possible by stabilization of the intermediate allyl cation (Scheme 7) through electron donation from chloride and bromide substituents. While the orbital overlap between the carbenium ion and chloride substituent is the best among the tested halogens, this stabilizing resonance effect is significantly weaker for the iodo substituent due to poorer orbital overlap. In the latter case, the resulting negative inductive effect is expected to destabilize the allyl cation. As discussed above, the corresponding fluoroalkynes could not be obtained, and their reactivity therefore could not be tested. The instability of fluoroalkynes has been reported in the literature and is most often attributed to their spontaneous dimerization.⁷⁸ All attempts to access fluorinated alkynes via a deprotonation–electrophilic fluorination quench sequence resulted in degradation of the corresponding propargyl silanes.

With the whole chromane and tetrahydroquinoline library in hand, we briefly explored their synthetic potential. Thus, the nosyl group in compound **13s** was efficiently cleaved by a literature-known procedure⁷⁹ in almost quantitative yield (Scheme 8). In another experiment, chromane **4f** reacted quantitatively and selectively with NIS at its 6-position (*para* to oxygen substituent), affording product **15f**. Under these experimental conditions, silicon–iodine exchange was not observed. Next, application of the Suzuki–Miyaura cross-coupling protocol⁵⁵ to compounds **11a** and **11k** demonstrated the geometrically controlled transformation of the vinyl bromide, despite the steric hindrance from the adjacent silyl group. Electrophilic silicon–iodine exchange on styrene **16k** in TFE and at elevated temperature provided iodide **17k** in 60% yield. The latter was further employed in the construction of trisubstituted alkene **18k**, which maintains the double bond geometry initially constructed during the tandem protonation–1,2-silyl shift process.

CONCLUSIONS

We have developed a novel synthetic pathway to substituted chromanes and 1,2,3,4-tetrahydroquinolines. The method employs a tandem acid-induced 1,2-silyl shift and Friedel–Crafts cyclization of propargyl silanes bearing an aryl ether or aniline fragment. The cyclization yields for simple propargyl silanes follow the general trends of Friedel–Crafts alkylations depending on the electron density of the employed aromatic rings. Notably, we have found that the cyclization outcomes can be significantly improved by using propargyl silanes containing chloro- and bromoalkyne moieties. The latter substitution

Scheme 8. Postfunctionalization of Cyclization Products



pattern presumably stabilizes the intermediate allyl cation, with the effect being most pronounced in the case of chloroalkynes. The developed tandem haloalkyne cyclization proceeds with high stereoselectivity, affording fused heterocycles with a trisubstituted (Z)-alkene side chain. The obtained (Z)-2-bromo-1-(trialkylsilyl)vinyl heterocycles can be further modified by cross-coupling chemistry despite the steric hindrance from the neighboring silyl group. During the course of our investigations, we have also improved the synthetic protocol for terminal haloalkynes by uncovering silver catalysis with more basic silver sources such as Ag_2CO_3 or AgOAc . The developed access to vinyl-substituted chromanes and 1,2,3,4-tetrahydroquinolines efficiently provides compound libraries useful for further applications in medicinal and materials chemistry.

EXPERIMENTAL SECTION

The solvents used in the reactions were dried using standard drying agents and freshly distilled prior to use. Commercially available reagents were used as received. Solvents were absolutized as follows: acetonitrile (MeCN), benzene (PhH), dichloroethane (DCE), dichloromethane (DCM), dimethylformamide (DMF), pyridine (Py), *N*-methyl-2-pyrrolidinone (NMP), and toluene (PhMe) were distilled from calcium hydride, tetrahydrofuran (THF) was distilled from metallic sodium, chloroform (CHCl_3) and hexanes (Hex) were dried over molecular sieves (4 Å). Acetone (Me_2CO), ethanol (EtOH), 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), and nitromethane (MeNO_2) purchased from *Fluorochem* or *Alfa Aesar* were used without additional purification.

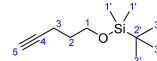
Direct-phase column chromatography was performed using *Upasil* silica gel (60 Å, 40–62 μm) and silver-impregnated silica gel (10 wt % AgNO_3). Thin-layer chromatography aluminum plates, precoated with *Merck* silica gel (60 Å, fluorescent indicator F_{254}) were used. For silver impregnation, TLC plates were immersed for 5 min in AgNO_3 acetonitrile solution (5 wt %) and dried. TLC plates were visualized

by UV light (254 nm) or developed using basic KMnO_4 solution (3 g KMnO_4 , 0.25 g NaOH, and 20 g K_2CO_3 dissolved in 300 mL of water).

NMR spectra were recorded using a *Bruker* AVANCE Neo 500 MHz spectrometer in chloroform- d . ^1H NMR spectra were taken at 500 MHz, and data are reported relative to CHCl_3 (7.26 ppm). ^{13}C $\{^1\text{H}\}$ NMR spectra (CPD and APT) were taken at 126 MHz, and data are reported relative to CHCl_3 (77.16 ppm). Additional optimization experiments were performed in acetonitrile- d_3 , benzene- d_6 , dichloromethane- d_2 , dioxane- d_6 , tetrahydrofuran- d_8 , toluene- d_8 , and trifluoroacetic acid- d . Chemical shifts (δ) are measured in ppm, coupling constants (J) are measured in Hz. The multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad signal). The structural assignments were made with additional information from 2D-spectra: ^1H – ^1H COSY, ^1H – ^{13}C HSQC, ^1H – ^{13}C HMBC, and ^1H – ^1H NOESY. Purity of compounds was determined via quantitative NMR using 1,4-dinitrobenzene as an internal standard.

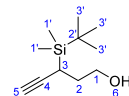
Crystallographic diffraction data were collected with a *Rigaku* Corporation XtaLAB Synergy-S diffractometer (Cu K α , $\lambda = 1.54184$ Å) equipped with a HyPix-6000HE detector at 170 K temperature. Data collection, cell refinement, and data reduction were performed with *CrysAlis PRO* 1.171.42.93a (*Rigaku* OD, 2023). *SHELXT* 2014/4 (*Sheldrick*, 2014) and *SHELXL*2018/3 (*Sheldrick*, 2018) programs were used for structure solving. High-resolution mass spectra (ESI) were recorded with a *Thermo Fisher Scientific* Orbitrap Exploris 120 mass spectrometer operating in the full scan mode at 120,000 resolution.

tert-Butyldimethyl(pent-4-yn-1-yloxy)silane



In a previously dried 2 L flask, imidazole (242.8 g, 1.545 mol, 3 equiv), *tert*-butyldimethylsilyl chloride (210.2 g, 2.171 mol, 1.15 equiv), and dichloromethane (1.2 L) were added and stirred for 10 min, and then pent-4-yn-1-ol (100.1 g, 1.189 mol, 1 equiv) was slowly added. The mixture was stirred at room temperature for 24 h, then quenched with water, and the aqueous phase was once extracted with DCM (200 mL). The organic layer was washed with saturated NaCl solution, then dried over anhydrous Na_2SO_4 , filtered through a short silica gel plug, and concentrated in vacuo to give a crude oil, which was purified by vacuum distillation to give silyl ether *tert*-butyldimethyl(pent-4-yn-1-yloxy)silane as a colorless oil (230.2 g, 98%). ^1H NMR (500 MHz, CDCl_3): δ 3.70 (t, $^3J_{\text{H-H}} = 6.0$ Hz, 2H, H_2C^1), 2.27 (td, $^3J_{\text{H-H}} = 7.1$, $^4J_{\text{H-H}} = 2.6$ Hz, 2H, H_2C^2), 1.92 (t, $^4J_{\text{H-H}} = 2.6$ Hz, 1H, HC^3), 1.72 (tt, $^3J_{\text{H-H}} = 7.1$, 6.0 Hz, 2H, H_2C^3), 0.89 (s, 9H, H_3C^4), 0.05 (s, 6H, H_3C^5). ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 84.3 (C^1), 68.2 (C^2), 61.4 (C^3), 31.5 (C^4), 25.9 (C^5), 18.32 (C^6), 14.8 (C^7), -5.4 (C^8). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{23}\text{OSi}$ 199.1513; Found 199.1515. Spectral data for the compound is consistent with the reported in literature.⁸⁰

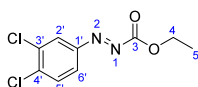
3-(*tert*-Butyldimethylsilyl)pent-4-yn-1-ol (1)



In a previously dried 1 L flask with an argon atmosphere, *tert*-butyldimethyl(pent-4-yn-1-yloxy)silane (20.0 g, 0.101 mol, 1 equiv) and hexane (320 mL) were added, and then the reaction mixture was cooled with a dry ice and ethanol mixture down to -78 °C for 20 min. Then, *n*-butyllithium solution in hexane (2.4 M, 126 mL, 0.303 mol, 3 equiv) and potassium *tert*-butoxide solution in dry THF (1.6 M, 190 mL, 0.303 mol, 3 equiv) were slowly and consequently added. After 15 min, the reaction was quenched with saturated NH_4Cl solution, and the aqueous phase was extracted with hexanes (4×100 mL). The organic layer was washed with saturated NaCl solution, then dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo to give a crude oil, which was purified by vacuum distillation to afford propargyl silyl alcohol 3 as a colorless oil (16.8 g, 86%). ^1H NMR (500 MHz, CDCl_3):

δ 3.90–3.80 (m, 2H, H₂C¹), 2.01 (d, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC⁵), 1.93 (ddd, $^4J_{\text{H-H}} = 2.8$ Hz, $^3J_{\text{H-H}} = 12.1$, 3.6 Hz, 1H, HC³), 1.75 (br, 1H, HO⁶), 1.74 (dddd, $^2J_{\text{H-H}} = 13.6$ Hz, $^3J_{\text{H-H}} = 8.1$, 6.4, 3.6 Hz, 1H, H₂C²), 1.64 (dddd, $^2J_{\text{H-H}} = 13.6$ Hz, $^3J_{\text{H-H}} = 12.1$, 5.4, 4.8 Hz, 1H, H₂C²), 0.97 (s, 9H, H₃C^{3'}), 0.10 (s, 3H, H₃C^{1'}), 0.03 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 86.7 (C⁴), 69.9 (C⁵), 62.6 (C¹), 32.4 (C²), 27.3 (C³), 17.8 (C^{2'}), 13.4 (C³), –7.0 (C^{1'}), –7.3 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₁H₂₃OSi 199.1513; Found 199.1515. Spectral data for the compound is consistent with the reported in the literature.⁶⁰

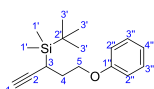
(E)-Ethyl 2-(3,4-dichlorophenyl)azocarboxylate (ECAC)



A 250 mL round-bottom flask was charged with 3,4-dichlorophenylhydrazine hydrochloride (13.07 g, 60.0 mmol, 1.0 equiv), and then, consequently, MeCN (120 mL) and pyridine (10.00 g, 126.0 mmol, 2.1 equiv) were added through a septum. The obtained solution was cooled down to 0 °C, ethyl chloroformate (7.16 g, 66 mmol, 1.1 equiv) was added dropwise, and then the reaction mixture was allowed to warm to room temperature and stir for 1 h. Then, water (120 mL) was added, and the reaction mixture was acidified with concentrated aqueous HCl (~4 mL) until pH = 3–4. The product was extracted with DCM (5 × 50 mL). The organic layer was washed with saturated NaHCO₃ solution (60 mL) and saturated NaCl solution (60 mL) and dried over anhydrous Na₂SO₄. Filtration and concentration in vacuo provided ethyl 2-(3,4-dichlorophenyl)hydrazine-1-carboxylate intermediate as a pale brown crystalline solid, which was used in further synthesis without additional purification. Crude material was dissolved in 80 wt % aqueous AcOH (280 mL) in a 1 L beaker. The reaction mixture was cooled in a NaCl/ice bath down to 0 °C, and then NaNO₂ (8.25 g, 119.7 mmol, 2.00 equiv) solution in water (280 mL) was added dropwise while the temperature did not exceed 5 °C, accompanied by vigorous stirring by a mechanical stirrer. After all the nitrite solution was added, the reaction mixture was allowed to stir for 1 h at room temperature. Then, the reaction mixture was extracted with DCM (3 × 100 mL), the organic layer was washed with saturated NaHCO₃ solution (100 mL), saturated NaCl solution (60 mL), and dried over anhydrous Na₂SO₄. Filtration and concentration in vacuo afforded ECAC as a red solid (14.33 g, 95% after 2 steps). ¹H NMR (500 MHz, CDCl₃): δ 8.02 (s, 1H, H–C^{2'}), 7.81 (d, $^3J_{\text{H-H}} = 8.5$ Hz, 1H, H–C^{6'}), 7.63 (d, $^3J_{\text{H-H}} = 8.5$ Hz, 1H, H–C^{5'}), 4.53 (q, $^3J_{\text{H-H}} = 7.2$ Hz, 2H, H₂C⁴), 1.47 (t, $^3J_{\text{H-H}} = 7.2$ Hz, 3H, H₃C⁵). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 161.8 (C²), 150.4 (C^{1'}), 138.3 (C⁴), 134.1 (C³), 131.4 (C⁵), 124.7 (C^{2'}), 123.7 (C^{6'}), 65.0 (C¹), 14.3 (C⁵). Spectral data for the compound is consistent with the reported in the literature.⁶⁴

General Procedure A: Synthesis of Aryl Ethers 2. A 25 mL vial was charged with propargyl silyl alcohol **1** (500 mg, 2.52 mmol, 1.0 equiv), corresponding phenol (2.77 mmol, 1.1 equiv), triphenylphosphine (726 mg, 2.77 mmol, 1.1 equiv), and toluene (5 mL). Then, ethyl 2-(3,4-dichlorophenyl)azocarboxylate (684 mg, 2.77 mmol, 1.1 equiv) was added, and the reaction mixture was allowed to stir at room temperature for 24 h. Then, it was concentrated in vacuo and purified on silica gel column (eluent system: toluene in hexanes, gradient change 0 → 20%; for aryl ethers **2k–2q** 100% toluene was used as eluent). For the synthesis of aryl ethers, O-TBS-protected phenol **2q** was first deprotected.

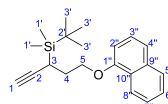
tert-Butyldimethyl(5-phenoxy)pent-1-yn-3-yl)silane (2a)



The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and phenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2a** as a colorless oil (635 mg,

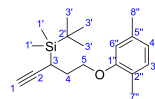
92%). ¹H NMR (500 MHz, CDCl₃): δ 7.31–7.26 (m, 2H, H–C^{3''}), 6.97–6.91 (m, 3H, H–C^{2''}, H–C^{4''}), 4.22 (ddd, $J = 9.5, 7.2, 3.9$ Hz, 1H, H–C⁵), 4.13 (td, $J = 8.5, 6.4$ Hz, 1H, H–C⁵), 2.06–1.99 (m, 3H, H–C¹, H–C³, H–C⁴), 1.84 (dddd, $J = 13.2, 12.0, 6.2, 3.6$ Hz, 1H, H–C⁴), 1.00 (s, 9H, H₃C^{3'}), 0.13 (s, 3H, H₃C^{1'}), 0.08 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 159.1 (C^{1''}), 129.6 (C^{3''}), 120.7 (C^{4''}), 114.7 (C^{2''}), 86.4 (C²), 69.8 (C¹), 66.9 (C⁵), 29.7 (C⁴), 27.3 (C^{3'}), 17.8 (C^{2'}), 13.4 (C³), –7.1 (C^{1'}), –7.2 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₇H₂₇OSi 275.1826; Found 275.1827.

tert-Butyldimethyl(5-(naphthalen-1-yloxy)pent-1-yn-3-yl)silane (2b)

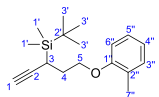


The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 1-naphthol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2b** as a yellowish solid (751 mg, 92%). ¹H NMR (500 MHz, CDCl₃): δ 8.27 (dd, $^3J_{\text{H-H}} = 7.1$ Hz, $^4J_{\text{H-H}} = 2.3$ Hz, 1H, H–C^{8'}), 7.81 (dd, $^3J_{\text{H-H}} = 7.1$ Hz, $^4J_{\text{H-H}} = 2.3$ Hz, 1H, H–C^{8'}), 7.49 (td, $^3J_{\text{H-H}} = 6.9$ Hz, $^4J_{\text{H-H}} = 1.6$ Hz, 1H, H–C^{6''}), 7.47 (td, $^3J_{\text{H-H}} = 6.9$ Hz, $^4J_{\text{H-H}} = 1.6$ Hz, 1H, H–C^{7''}), 7.43 (d, $^3J_{\text{H-H}} = 8.0$ Hz, 1H, H–C^{4'}), 7.38 (t, $^3J_{\text{H-H}} = 7.9$ Hz, 1H, H–C^{3'}), 6.88 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H, H–C^{2'}), 4.38 (ddd, $^2J_{\text{H-H}} = 8.9$, $^3J_{\text{H-H}} = 6.6, 3.9$ Hz, 1H, H₂C⁵), 4.34 (ddd, $^2J_{\text{H-H}} = 8.9$, $^3J_{\text{H-H}} = 8.8, 6.0$ Hz, 1H, H₂C⁵), 2.24–2.13 (m, 2H, HC³, H₂C⁴), 2.02 (d, $^4J_{\text{H-H}} = 2.7$ Hz, 1H, HC¹), 2.01–1.93 (m, 1H, H₂C⁴), 1.03 (s, 9H, H₃C^{3'}), 0.17 (s, 3H, H₃C^{1'}), 0.13 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 154.9 (C^{1''}), 134.7 (C^{9''}), 127.6 (C^{5''}), 126.4 (C^{6'}), 126.1 (C^{3'}), 125.9 (C^{10''}), 125.2 (C^{7''}), 122.1 (C^{8'}), 120.2 (C^{3''}), 104.9 (C^{2''}), 86.4 (C²), 69.7 (C¹), 67.2 (C⁵), 29.9 (C⁴), 27.3 (C^{3'}), 17.8 (C^{2'}), 13.6 (C³), –7.1 (C^{1'}), –7.2 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for C₂₁H₂₉OSi 325.1982; Found 325.1984.

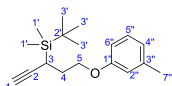
tert-Butyl(5-(2,5-dimethylphenoxy)pent-1-yn-3-yl)-dimethylsilane (2c)



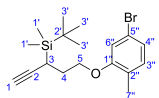
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 2,5-dimethylphenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2c** as a colorless oil (661 mg, 87%). ¹H NMR (500 MHz, CDCl₃): δ 7.01 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H, H–C^{3''}), 6.68 (s, 1H, H–C^{6''}), 6.67 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H), 4.17 (ddd, $^2J_{\text{H-H}} = 9.0$ Hz, $^3J_{\text{H-H}} = 6.5, 3.7$ Hz, 1H, H₂C⁵), 4.12 (ddd, $^2J_{\text{H-H}} = 9.0$ Hz, $^3J_{\text{H-H}} = 8.8, 5.4$ Hz, 1H, H₂C⁵), 2.32 (s, 3H, H₃C^{8''}), 2.18 (s, 3H, H₃C^{8''}), 2.10 (dt, $^3J_{\text{H-H}} = 12.1, 2.7$ Hz, $^4J_{\text{H-H}} = 2.7$ Hz, 1H, HC³), 2.05 (dddd, $^2J_{\text{H-H}} = 13.7$ Hz, $^3J_{\text{H-H}} = 8.8, 6.5, 2.7$ Hz, 1H, H₂C⁴), 1.99 (d, $^4J_{\text{H-H}} = 2.7$ Hz, 1H, HC¹), 1.84 (dddd, $^2J_{\text{H-H}} = 13.7$ Hz, $^3J_{\text{H-H}} = 12.1, 5.4, 3.7$ Hz, 1H, H₂C⁴), 1.00 (s, 9H, H₃C^{3'}), 0.14 (s, 3H, H₃C^{1'}), 0.08 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.1 (C^{1''}), 136.7 (C^{5''}), 130.4 (C^{3''}), 123.7 (C^{2''}), 120.8 (C^{4''}), 112.3 (C^{6''}), 86.6 (C²), 69.4 (C¹), 66.8 (C⁵), 30.2 (C⁴), 27.3 (C^{3'}), 21.6 (C^{8''}), 17.8 (C^{2'}), 16.0 (C^{7''}), 13.4 (C³), –7.1 (C^{1'}), –7.1 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₉H₃₁OSi 303.2139; Found 303.2140.

tert-Butyldimethyl(5-(2-methylphenoxy)pent-1-yn-3-yl)-silane (2d)

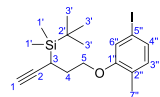
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 2-methylphenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2d** as a colorless oil (609 mg, 84%). ¹H NMR (500 MHz, CDCl₃): δ 7.15 (t, ³J_{H-H} = 7.7 Hz, 1H, H-C⁵ⁿ), 7.14 (d, ³J_{H-H} = 7.7 Hz, 1H, H-C³ⁿ), 6.87 (d, ³J_{H-H} = 7.7 Hz, 1H, H-C⁶ⁿ), 6.85 (t, ³J_{H-H} = 7.7 Hz, 1H, H-C⁴ⁿ), 4.19 (ddd, ²J_{H-H} = 9.0 Hz, ³J_{H-H} = 6.6, 3.6 Hz, 1H, H₂C⁵), 4.14 (ddd, ²J_{H-H} = 9.0 Hz, ³J_{H-H} = 8.8, 5.5 Hz, 1H, H₂C⁵), 2.23 (s, 3H, H₃C⁷ⁿ), 2.10 (dt, ³J_{H-H} = 12.1, 2.8, ⁴J_{H-H} = 2.7 Hz, 1H, HC³), 2.06 (dddd, ²J_{H-H} = 13.8, ³J_{H-H} = 8.8, 6.6, 2.8 Hz, 1H, H₂C⁴), 1.99 (d, ⁴J_{H-H} = 2.7 Hz, 1H, HC¹), 1.84 (dddd, ²J_{H-H} = 13.8, ³J_{H-H} = 12.1, 5.5, 3.7 Hz, 1H, H₂C⁴), 1.00 (s, 9H, H₃C³ⁿ), 0.14 (s, 3H, H₃C¹ⁿ), 0.08 (s, 3H, H₃C¹ⁿ). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.3 (C¹ⁿ), 130.7 (C³ⁿ), 126.9 (C²ⁿ, C⁵ⁿ), 120.3 (C⁴ⁿ), 111.2 (C⁶ⁿ), 86.6 (C²), 69.5 (C¹), 66.8 (C⁵), 30.1 (C⁴), 27.3 (C³), 17.8 (C²), 16.40 (C⁷ⁿ), 13.4 (C³), -7.1 (C¹), -7.2 (C¹). HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₈H₂₉OSi [M + H]⁺ 289.1982; Found 289.1983.

tert-Butyldimethyl(5-(3-methylphenoxy)pent-1-yn-3-yl)-silane (2e)

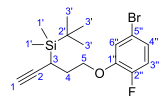
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 3-methylphenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2e** as a colorless oil (595 mg, 82%). ¹H NMR (500 MHz, CDCl₃): δ 7.16 (t, ³J_{H-H} = 8.0 Hz, 1H, H-C⁵ⁿ), 6.78–6.72 (m, 3H, H-C²ⁿ, H-C⁴ⁿ, H-C⁶ⁿ), 4.33 (ddd, ²J_{H-H} = 9.1 Hz, ³J_{H-H} = 7.1, 3.8 Hz, 1H, H₂C⁵), 4.13 (ddd, ²J_{H-H} = 9.1 Hz, ³J_{H-H} = 8.3, 6.3 Hz, 1H, H₂C⁵), 2.33 (s, 3H, H₃C⁷ⁿ), 2.05–1.96 (m, 3H, HC³, HC³, H₂C⁴), 1.82 (dddd, ²J_{H-H} = 13.7, ³J_{H-H} = 12.5, 6.3, 3.8 Hz, 1H, H₂C⁴), 0.99 (s, 9H, H₃C³ⁿ), 0.12 (s, 3H, H₃C¹ⁿ), 0.07 (s, 3H, H₃C¹ⁿ). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 159.1 (C¹ⁿ), 139.6 (C⁷ⁿ), 129.3 (C⁵ⁿ), 121.6 (C⁴ⁿ), 115.6 (C²ⁿ), 111.6 (C⁶ⁿ), 86.4 (C²), 69.7 (C¹), 66.9 (C⁵), 29.7 (C⁴), 27.3 (C³), 21.7 (C⁷ⁿ), 17.8 (C²), 13.3 (C³), -7.1 (C¹), -7.2 (C¹). HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₈H₂₉OSi 289.1982; Found 289.1982.

(5-(5-Bromo-2-methylphenoxy)pent-1-yn-3-yl)(tert-butyl)-dimethylsilane (2f)

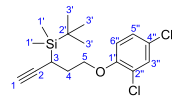
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 5-bromo-2-methylphenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2f** as a pale yellow solid (785 mg, 85%). ¹H NMR (500 MHz, CDCl₃): δ 6.97 (s, 3H, H-C³ⁿ, H-C⁴ⁿ, H-C⁶ⁿ), 4.16–4.07 (m, 2H, H₂C⁵), 2.15 (s, 3H, H₃C⁷ⁿ), 2.09–1.97 (m, 3H, HC³, HC³, H₂C⁴), 1.87–1.77 (m, 1H, H₂C⁴), 0.99 (s, 9H, H₃C³ⁿ), 0.13 (s, 3H, H₃C¹ⁿ), 0.07 (s, 3H, H₃C¹ⁿ). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.9 (C¹ⁿ), 131.7 (C³ⁿ), 125.9 (C²ⁿ), 123.2 (C⁴ⁿ), 119.6 (C⁵ⁿ), 114.6 (C⁶ⁿ), 86.3 (C²), 69.7 (C¹), 67.1 (C⁵), 30.0 (C⁴), 27.3 (C³), 17.8 (C²), 16.0 (C⁷ⁿ), 13.3 (C³), -7.2 (C¹). HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₈H₂₈BrOSi 367.1087; Found 367.1088.

tert-Butyl(5-(5-iodo-2-methylphenoxy)pent-1-yn-3-yl)-dimethylsilane (2g)

The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 5-iodo-2-methylphenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2g** as a pale yellow solid (976 mg, 93%). ¹H NMR (500 MHz, CDCl₃): δ 7.17 (d, ³J_{H-H} = 7.8 Hz, 1H, H-C⁴ⁿ), 7.14 (s, 1H, H-C⁶ⁿ), 6.84 (d, ³J_{H-H} = 7.8 Hz, 1H, H-C³ⁿ), 4.15–4.06 (m, 2H, H₂C⁵), 2.15 (s, 3H, H₃C⁷ⁿ), 2.09–2.01 (m, 2H, H₂C⁴, H₂C⁴), 2.00 (d, ⁴J_{H-H} = 2.7 Hz, 1H, HC³), 1.86–1.77 (m, 1H, H₂C⁴), 0.98 (s, 9H, H₃C³ⁿ), 0.13 (s, 3H, H₃C¹ⁿ), 0.07 (s, 3H, H₃C¹ⁿ). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.9 (C¹ⁿ), 132.1 (C³ⁿ), 129.4 (C⁵ⁿ), 126.7 (C²ⁿ), 120.4 (C⁶ⁿ), 90.6 (C⁵ⁿ), 86.3 (C²), 69.7 (C¹), 67.1 (C⁵), 30.0 (C⁴), 27.3 (C³ⁿ), 17.8 (C²), 16.1 (C⁷ⁿ), 13.3 (C³), -7.2 (C¹). C₁₈H₂₈IOSi [M + H]⁺ 415.0949; Found 415.0950. HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₈H₂₈IOSi 415.0949; Found 415.0948.

(5-(5-Bromo-2-fluorophenoxy)pent-1-yn-3-yl)(tert-butyl)-dimethylsilane (2h)

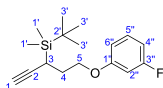
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 5-bromo-2-fluorophenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2h** as a pale yellow solid (792 mg, 85%). ¹H NMR (500 MHz, CDCl₃): δ 7.14 (dd, ⁴J_{H-F} = 7.5 Hz, ⁴J_{H-H} = 2.3 Hz, 1H, H-C⁶ⁿ), 7.00 (ddd, ⁴J_{H-F} = 4.0 Hz, ³J_{H-H} = 8.6 Hz, ⁴J_{H-H} = 2.3 Hz, 1H, H-C⁴ⁿ), 6.94 (dd, ³J_{H-F} = 10.8 Hz, ³J_{H-H} = 8.6 Hz, 1H, H-C³ⁿ), 4.24 (ddd, ²J_{H-F} = 9.0 Hz, ³J_{H-H} = 7.0, 4.4 Hz, 1H, H₂C⁵), 4.16 (ddd, ²J_{H-H} = 9.0 Hz, ³J_{H-H} = 8.4, 6.4 Hz, 1H, H₂C⁵), 2.09–1.99 (m, 3H, HC³, HC³, H₂C⁴), 1.85 (ddd, ²J_{H-F} = 13.2 Hz, ³J_{H-H} = 10.9, 8.4, 4.4 Hz, 1H, H₂C⁴), 0.99 (s, 9H, H₃C³ⁿ), 0.13 (s, 3H, H₃C¹ⁿ), 0.07 (s, 3H, H₃C¹ⁿ). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 151.9 (d, ¹J_{C-F} = 246.3 Hz, C²ⁿ), 147.9 (d, ¹J_{C-F} = 11.5 Hz, C¹ⁿ), 123.6 (d, ⁴J_{C-F} = 6.6 Hz, C⁴ⁿ), 118.1 (d, ⁴J_{C-F} = 2.1 Hz, C⁶ⁿ), 117.3 (d, ²J_{C-F} = 19.7 Hz, C³ⁿ), 116.3 (d, ²J_{C-F} = 3.7 Hz, C⁵ⁿ), 85.9 (C²), 69.9 (C¹), 68.5 (C⁵), 29.4 (C⁴), 27.1 (C³ⁿ), 17.6 (C²), 13.1 (C³), -7.2 (C¹), -7.4 (C¹). HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₇H₂₅BrFOSi 371.0837; Found 371.0830.

tert-Butyl(5-(2,4-dichlorophenoxy)pent-1-yn-3-yl)-dimethylsilane (2i)

The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 2,4-dichlorophenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2i** as a colorless oil (812 mg, 94%). ¹H NMR (500 MHz, CDCl₃): δ 7.35 (d, ⁴J_{H-H} = 2.6 Hz, 1H, H-C³ⁿ), 7.17 (dd, ³J_{H-H} = 8.8 Hz, ⁴J_{H-H} = 2.6 Hz, 1H, H-C⁵ⁿ), 6.89 (d, ³J_{H-H} = 8.8 Hz, 1H, H-C⁶ⁿ), 4.23 (ddd, ²J_{H-H} = 9.3, ³J_{H-H} = 6.5, 3.6 Hz, 1H, H₂C⁵), 4.15 (ddd, ²J_{H-H} = 9.3, ³J_{H-H} = 8.5, 5.7 Hz, 1H, H₂C⁵), 2.10 (ddd, ³J_{H-H} = 12.7, 2.8 Hz, ⁴J_{H-H} = 2.7 Hz, 1H, HC³), 2.07 (dddd, ²J_{H-H} = 13.4 Hz, ³J_{H-H} = 8.5, 6.5, 2.8 Hz, 1H, H₂C⁴), 1.98 (d, ⁴J_{H-H} = 2.8 Hz, 1H, HC¹), 1.84 (dddd, ²J_{H-H} = 13.6 Hz, ³J_{H-H} = 12.8, 5.7, 3.6 Hz, 1H, H₂C⁴), 0.99 (s, 9H, H₃C³ⁿ), 0.13 (s, 3H, H₃C¹ⁿ), 0.07 (s, 3H, H₃C¹ⁿ). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.6 (C¹ⁿ),

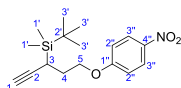
130.0 (C³ⁿ), 127.7 (C⁵ⁿ), 125.7 (C⁴ⁿ), 123.9 (C²ⁿ), 114.3 (C⁶ⁿ), 86.3 (C²), 69.8 (C¹), 68.4 (C⁵), 29.7 (C⁴), 23.3 (C³), 17.8 (C²), 13.2 (C³), -7.1 (C^{1'}), -7.2 (C^{1''}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₅Cl₂OSi 343.1046; Found 343.1047.

tert-Butyl(5-(3-fluorophenoxy)pent-1-yn-3-yl)-dimethylsilane (2j)



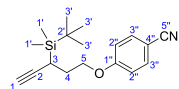
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 3-fluorophenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 → 20%), provided compound **2j** as a colorless oil (611 mg, 83%). ¹H NMR (500 MHz, CDCl₃): δ 7.21 (ddd, ³J_{H-F} = 6.9 Hz, ³J_{H-H} = 8.9, 8.3 Hz, 1H, H-C⁵ⁿ), 6.71 (dd, ³J_{H-F} = 2.3 Hz, ³J_{H-H} = 8.3 Hz, 1H, H-C⁶ⁿ), 6.67–6.62 (m, 2H, H-C²ⁿ, H-C⁴ⁿ), 4.18 (ddd, ²J_{H-H} = 9.1 Hz, ³J_{H-H} = 7.1, 3.8 Hz, 1H, H₂C⁵), 4.11 (ddd, ²J_{H-H} = 9.1 Hz, ³J_{H-H} = 8.3, 6.4 Hz, 1H, H₂C⁵), 2.04–1.97 (m, 3H, H₃C¹, H₃C², H₃C³), 1.82 (tdd, ²J_{H-H} = 13.7, ³J_{H-H} = 13.7, 6.4, 3.8 Hz, 1H, H₂C⁴), 0.99 (s, 9H, H₃C³ⁿ), 0.13 (s, 3H, H₃C^{1'}), 0.07 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 163.7 (d, ¹J_{C-F} = 244.9 Hz, C³ⁿ), 160.4 (d, ³J_{C-F} = 10.9 Hz, C¹ⁿ), 130.1 (d, ³J_{C-F} = 10.1 Hz, C⁵ⁿ), 110.4 (d, ⁴J_{C-F} = 2.8 Hz, C⁶ⁿ), 107.4 (d, ²J_{C-F} = 21.3 Hz, C²ⁿ), 102.1 (d, ²J_{C-F} = 24.8 Hz, C²ⁿ), 86.0 (C²), 69.8 (C¹), 67.1 (C⁵), 29.4 (C⁴), 27.2 (C³), 17.7 (C²), 13.1 (C³), -7.1 (C^{1'}), -7.4 (C^{1''}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₆FOSi 293.1731; Found 293.1731.

tert-Butyldimethyl(5-(4-nitrophenoxy)pent-1-yn-3-yl)-silane (2k)



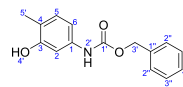
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 4-nitrophenol to yield crude product, which, after column chromatography (eluent: toluene), provided compound **2k** as a pale yellow solid (771 mg, 96%). ¹H NMR (500 MHz, CDCl₃): δ 7.58 (d, ³J_{H-H} = 9.3 Hz, 2H, H-C⁵ⁿ), 6.97 (d, ³J_{H-H} = 9.3 Hz, 2H, H-C⁶ⁿ), 4.26–4.15 (m, 2H, H₂C⁵), 2.06–1.97 (m, 3H, H₃C¹, H₃C², H₃C³), 1.88–1.79 (m, 1H, H₂C⁴), 0.98 (s, 9H, H₃C³ⁿ), 0.12 (s, 3H, H₃C^{1'}), 0.07 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 162.5 (C¹ⁿ), 134.1 (C³ⁿ), 119.5 (C⁵ⁿ), 115.4 (C²ⁿ), 104.0 (C⁴ⁿ), 85.9 (C²), 70.1 (C¹), 67.4 (C⁵), 29.4 (C⁴), 27.3 (C³), 17.8 (C²), 13.3 (C³), -7.1 (C^{1'}), -7.3 (C^{1''}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₆NO₃Si 320.1676; Found 320.1678.

4-((3-(tert-Butyldimethylsilyl)pent-4-yn-1-yl)oxy)-benzonitrile (2l)



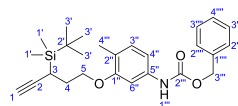
The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 4-hydroxybenzonitrile to yield crude product, which, after column chromatography (eluent: toluene), provided compound **2l** as a pale yellow solid (625 mg, 83%). ¹H NMR (500 MHz, CDCl₃): δ 7.58 (d, ³J_{H-H} = 9.3 Hz, 2H, H-C⁵ⁿ), 6.97 (d, ³J_{H-H} = 9.3 Hz, 2H, H-C⁶ⁿ), 4.26–4.15 (m, 2H, H₂C⁵), 2.06–1.97 (m, 3H, H₃C¹, H₃C², H₃C³), 1.88–1.79 (m, 1H, H₂C⁴), 0.98 (s, 9H, H₃C³ⁿ), 0.12 (s, 3H, H₃C^{1'}), 0.07 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 162.5 (C¹ⁿ), 134.1 (C³ⁿ), 119.5 (C⁵ⁿ), 115.4 (C²ⁿ), 104.0 (C⁴ⁿ), 85.9 (C²), 70.1 (C¹), 67.4 (C⁵), 29.4 (C⁴), 27.3 (C³), 17.8 (C²), 13.3 (C³), -7.1 (C^{1'}), -7.3 (C^{1''}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₆NO₂Si 300.1778; Found 300.1779.

Benzyl (3-Hydroxy-4-methylphenyl)carbamate



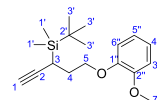
A 100 mL round-bottom flask with a Teflon-coated magnetic stirrer and septum was charged with 5-amino-2-methylphenol (1.23 g, 10 mmol, 1.0 equiv). THF (50 mL) was added, and the reaction mixture was stirred until the dissolution of the starting material. Then, *N*-(Benzyloxycarbonyloxy)succinimide (3.38 g, 15 mmol, 1.5 equiv) was added, and the reaction mixture was allowed to stir at room temperature. After 24 h, the reaction mixture was concentrated and purified on a silica gel column (eluent system: EtOAc in hexanes, gradient change 10 → 25%), yielding benzyl (3-hydroxy-4-methylphenyl)carbamate as a white solid (1.80 g, 70%). ¹H NMR (500 MHz, CDCl₃): δ 7.44–7.31 (m, 5H, H-C²ⁿ, H-C³ⁿ, H-C⁴ⁿ), 7.19 (br, 1H, H-C²), 7.00 (d, ³J_{H-H} = 8.0 Hz, 1H, H-C⁵), 6.64 (br, 1H, HN^{2'}), 6.61 (dd, ³J_{H-H} = 8.0 Hz, ⁴J_{H-H} = 2.3 Hz, 1H, H-C⁶), 5.55 (br, 1H, HO⁴), 5.19 (s, 2H, H₂C³), 2.18 (s, 3H, H₃C⁵). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 154.6 (C³), 153.6 (C^{1'}), 136.7 (C¹), 136.1 (C¹ⁿ), 131.2 (C³), 128.8 (C^{2n/3n/4n}), 128.6 (C^{2n/3n/4n}), 128.5 (C^{2n/3n/4n}), 119.4 (C⁴), 110.7 (C⁶), 105.9 (C²), 67.3 (C³), 15.4 (C⁵). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₅H₁₆NO₃ 258.1125; Found 258.1124.

Benzyl (3-((3-(tert-Butyldimethylsilyl)pent-4-yn-1-yl)-oxy)-4-methylphenyl)carbamate (2m)



The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and benzyl (3-hydroxy-4-methylphenyl)carbamate to yield crude product, which, after column chromatography (eluent: toluene), provided compound **2m** as a viscous yellow oil (926 mg, 84%). ¹H NMR (500 MHz, CDCl₃): δ 7.39–7.30 (m, 5H, H-C²ⁿ, H-C³ⁿ, H-C⁴ⁿ), 7.12 (br, 1H, H-C²), 7.02 (d, ³J_{H-H} = 8.1 Hz, 1H, H-C⁵), 6.72 (d, ³J_{H-H} = 8.1 Hz, 1H, H-C⁶), 6.61 (br, 1H, HN^{2'}), 5.19 (s, 2H, H₂C³), 4.16–4.10 (m, 2H, H₂C⁵), 2.16 (s, 3H, H₃C⁵ⁿ), 2.09 (ddd, ³J_{H-H} = 12.2, 2.8, 2.7 Hz, 1H, H₂C⁴), 2.04 (ddd, ²J_{H-H} = 13.5 Hz, ³J_{H-H} = 9.2, 6.6, 2.8 Hz, 1H, H₂C⁴), 1.97 (d, ⁴J_{H-H} = 2.7, 1H, H₂C⁴), 1.81 (ddt, ³J_{H-H} = 13.5 Hz, ³J_{H-H} = 12.2, 5.2, 3.9 Hz, 1H, H₂C⁴), 0.99 (s, 9H, H₃C³ⁿ), 0.13 (s, 3H, H₃C^{1'}), 0.07 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.6 (C¹ⁿ), 153.5 (C²ⁿ), 136.7 (C⁵ⁿ), 136.3 (C¹ⁿ), 130.6 (C³ⁿ), 128.8 (C^{2n/3n/4n}), 128.5 (C^{2n/3n/4n}), 128.4 (C³ⁿ), 122.0 (C²ⁿ), 110.3 (C⁴ⁿ), 102.7 (C⁶ⁿ), 86.5 (C²), 69.6 (C¹), 67.1 (C³ⁿ), 66.8 (C³), 30.1 (C⁴), 27.3 (C³), 17.8 (C⁵), 15.8 (C⁴ⁿ), 13.3 (C³), -7.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₆H₃₆NO₃Si 438.2459; Found 438.2453.

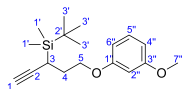
tert-Butyl(5-(2-methoxyphenoxy)pent-1-yn-3-yl)-dimethylsilane (2n)



The reaction was performed according to general procedure A from propargyl silyl alcohol **1** and 2-methoxyphenol to yield crude product, which, after column chromatography (eluent: toluene), provided compound **2n** as a colorless solid (675 mg, 88%). ¹H NMR (500 MHz, CDCl₃): δ 6.99–6.94 (m, 1H, H-C⁶ⁿ), 6.94–6.87 (m, 3H, H-C³ⁿ, H-C⁴ⁿ, H-C⁵ⁿ), 4.33 (td, ²J_{H-H} = 9.0 Hz, ³J_{H-H} = 9.0, 4.0 Hz, 1H, H₂C⁵), 4.33 (dt, ²J_{H-H} = 9.0 Hz, ³J_{H-H} = 7.5 Hz, 1H, H₂C⁵), 3.86 (s, 3H, H₃C⁷ⁿ), 2.11–2.03 (m, 1H, H₂C⁴), 2.01–1.96 (m, 2H, H₂C⁴, H₃C³), 1.91 (ddd, ²J_{H-H} = 11.8, ³J_{H-H} = 7.5, 4.0 Hz, 1H, H₂C⁴), 0.98 (s, 9H,

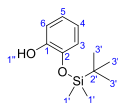
$\text{H}_3\text{C}^{3'}$), 0.12 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.06 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 149.6 ($\text{C}^{2''}$), 148.7 ($\text{C}^{1''}$), 121.1 ($\text{C}^{4''}$, $\text{C}^{5''}$), 113.6 ($\text{C}^{6''}$), 112.0 ($\text{C}^{3''}$), 86.4 (C^2), 69.8 (C^1), 68.5 (C^5), 56.1 ($\text{C}^{7''}$), 29.5 (C^4), 27.3 ($\text{C}^{3'}$), 17.8 ($\text{C}^{2'}$), 13.3 (C^3), -7.0 ($\text{C}^{1'}$), -7.3 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{29}\text{O}_2\text{Si}$ 305.1931; Found 305.1928.

tert-Butyl(5-(3-methoxyphenoxy)pent-1-yn-3-yl)-dimethylsilane (2o)



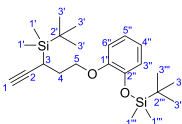
The reaction was performed according to general procedure A from propargyl silyl alcohol 1 and 3-methoxyphenol to yield crude product, which, after column chromatography (eluent: toluene), provided compound **2o** as a yellowish oil (735 mg, 96%). ^1H NMR (500 MHz, CDCl_3): δ 7.18 (t, $^3J_{\text{H-H}} = 8.1$ Hz, 1H, $\text{H}-\text{C}^{5''}$), 6.55–6.48 (m, 3H, $\text{H}-\text{C}^{2''}$, $\text{H}-\text{C}^{4''}$, $\text{H}-\text{C}^{6''}$), 4.19 (ddd, $^2J_{\text{H-H}} = 9.3$ Hz, $^3J_{\text{H-H}} = 7.0$, 4.1 Hz, 1H, H_2C^5), 4.11 (ddd, $^2J_{\text{H-H}} = 9.3$ Hz, $^3J_{\text{H-H}} = 7.9$, 6.5 Hz, 1H, H_2C^5), 3.79 (s, 3H, $\text{H}_3\text{C}^{7''}$), 2.04–1.97 (m, 3H, HC^3 , HC^3 , H_2C^4), 1.82 (dddd, $^2J_{\text{H-H}} = 12.5$ Hz, $^3J_{\text{H-H}} = 13.7$, 6.5, 4.1 Hz, 1H, H_2C^4), 0.99 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.12 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.07 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 161.0 ($\text{C}^{3''}$), 160.4 ($\text{C}^{1''}$), 130.0 ($\text{C}^{5''}$), 106.9 ($\text{C}^{4''/6''}$), 106.4 ($\text{C}^{4''/6''}$), 101.1 ($\text{C}^{2''}$), 86.3 (C^2), 69.8 (C^1), 67.0 (C^5), 29.6 (C^4), 27.3 ($\text{C}^{3'}$), 17.8 ($\text{C}^{2'}$), 13.3 (C^3), -7.0 ($\text{C}^{1'}$), -7.3 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{28}\text{O}_2\text{Si}$ 305.1931; Found 305.1933.

2-((tert-Butyldimethylsilyl)oxy)phenol



A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer and septum was charged with catechol (4.35 g, 40 mmol, 1.0 equiv), and DMF (25 mL) was added. The reaction mixture was cooled with NaCl/ice bath down to 0 °C. Imidazole (5.64 g, 83 mmol, 2.1 equiv) and tert-butyldimethylsilyl chloride (5.95 g, 40 mmol, 1.0 equiv) were added, and the reaction mixture was allowed to stir for 3 h at room temperature. Then, water was added, and the product was extracted with Et_2O (3 $\times$ 25 mL). The organic layer was washed with brine (30 mL), dried over anhydrous Na_2SO_4 , and concentrated in vacuo to afford a pale yellow liquid. Purification on silica gel column (eluent system: EtOAc in hexanes, gradient change: 20 $\rightarrow$ 60%) provided 2-((tert-butyldimethylsilyl)oxy)phenol as a colorless oil (5.76 g, 65%). ^1H NMR (500 MHz, CDCl_3): δ 6.93 (d, $^3J_{\text{H-H}} = 8.0$ Hz, 1H, $\text{H}-\text{C}^6$), 6.87 (dd, $^3J_{\text{H-H}} = 7.8$, 7.5 Hz, 1H, $\text{H}-\text{C}^5$), 6.82 (d, $^3J_{\text{H-H}} = 8.0$ Hz, 1H, $\text{H}-\text{C}^3$), 6.75 (dd, $^3J_{\text{H-H}} = 7.8$, 7.5 Hz, 1H, $\text{H}-\text{C}^4$), 5.47 (s, 1H, $\text{HO}^{1''}$), 1.02 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.28 (s, 6H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 147.4 (C^1), 142.5 (C^2), 122.3 (C^5), 120.2 (C^4), 118.0 (C^3), 115.0 (C^6), 25.9 ($\text{C}^{3'}$), 18.4 ($\text{C}^{2'}$), -4.2 ($\text{C}^{1'}$). Spectral data for the compound is consistent with that reported in the literature.⁸¹

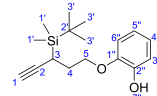
tert-Butyl(5-(2-((tert-butyldimethylsilyl)oxy)phenoxy)pent-1-yn-3-yl)dimethylsilane (2p)



The reaction was performed according to general procedure A from propargyl silyl alcohol 1 and 2-((tert-butyldimethylsilyl)oxy)phenol to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 $\rightarrow$ 20%), provided compound **2p** as a colorless oil (922 mg, 90%). ^1H NMR (500 MHz, CDCl_3): δ 6.93–6.87 (m, 2H, $\text{H}-\text{C}^{5''}$, $\text{H}-\text{C}^{6''}$), 6.86–6.78 (m, 2H, $\text{H}-\text{C}^{3''}$, $\text{H}-\text{C}^{4''}$), 4.20–4.12 (m, 2H, H_2C^5), 2.08–2.00 (m, 2H, HC^3 , H_2C^4), 1.99 (d, $^4J_{\text{H-H}} = 2.6$ Hz, 1H, HC^3), 1.88–1.78 (m, 1H, H_2C^4), 1.01 (s, 9H, $\text{H}_3\text{C}^{3''}$), 0.99 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.17 (s, 6H, $\text{H}_3\text{C}^{1''}$), 0.12 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.06 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 150.7 ($\text{C}^{1''}$), 145.2 ($\text{C}^{2''}$), 121.9 ($\text{C}^{5''}$), 121.2 ($\text{C}^{3''}$), 120.9 ($\text{C}^{4''}$), 113.6 ($\text{C}^{6''}$), 86.2 (C^2), 69.9 (C^1), 67.5 (C^5), 29.7 (C^4), 27.3 ($\text{C}^{3'}$), 25.9 ($\text{C}^{3''}$), 18.5 ($\text{C}^{2''}$), 17.8 ($\text{C}^{2'}$), 13.3 (C^3), -4.4 ($\text{C}^{1''}$), -7.0 ($\text{C}^{1'}$), -7.4 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{41}\text{O}_2\text{Si}_2$ 405.2640; Found 405.2639.

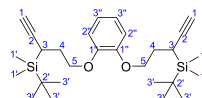
$\text{H}-\text{C}^{3''}$, $\text{H}-\text{C}^{4''}$), 4.20–4.12 (m, 2H, H_2C^5), 2.08–2.00 (m, 2H, HC^3 , H_2C^4), 1.99 (d, $^4J_{\text{H-H}} = 2.6$ Hz, 1H, HC^3), 1.88–1.78 (m, 1H, H_2C^4), 1.01 (s, 9H, $\text{H}_3\text{C}^{3''}$), 0.99 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.17 (s, 6H, $\text{H}_3\text{C}^{1''}$), 0.12 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.06 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 150.7 ($\text{C}^{1''}$), 145.2 ($\text{C}^{2''}$), 121.9 ($\text{C}^{5''}$), 121.2 ($\text{C}^{3''}$), 120.9 ($\text{C}^{4''}$), 113.6 ($\text{C}^{6''}$), 86.2 (C^2), 69.9 (C^1), 67.5 (C^5), 29.7 (C^4), 27.3 ($\text{C}^{3'}$), 25.9 ($\text{C}^{3''}$), 18.5 ($\text{C}^{2''}$), 17.8 ($\text{C}^{2'}$), 13.3 (C^3), -4.4 ($\text{C}^{1''}$), -7.0 ($\text{C}^{1'}$), -7.4 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{41}\text{O}_2\text{Si}_2$ 405.2640; Found 405.2639.

2-((3-(tert-Butyldimethylsilyl)pent-4-yn-1-yl)oxy)phenol (2q)



A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with TBS-protected alkylated catechol **2p** (727 mg, 2.50 mmol, 1.0 equiv). Catechol **2p** was suspended in a wet MeCN mixture (5 mL, 5% H_2O by volume). DBU (380 mg, 0.37 mL, 2.50 mmol, 1.0 equiv) was slowly added, and the reaction mixture was allowed to stir for 3 h under ambient conditions. Then, the reaction mixture was concentrated in vacuo, dissolved in a small amount of hexane/EtOAc mixture (1:3), and filtered through a short silica gel plug. The filtrate was concentrated in vacuo to yield crude product, which, after column chromatography (eluent: toluene), provided compound **2q** as a white solid (723 mg, 99%). ^1H NMR (500 MHz, CDCl_3): δ 6.95–6.81 (m, 4H, $\text{H}-\text{C}^{5''}$, $\text{H}-\text{C}^{6''}$, $\text{H}-\text{C}^{3''}$, $\text{H}-\text{C}^{4''}$), 5.77 (s, 1H, $\text{HO}^{1''}$), 4.29–4.20 (m, 2H, H_2C^5), 2.08–1.94 (m, 3H, HC^3 , H_2C^4), 1.94–1.85 (m, 1H, H_2C^4), 0.99 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.13 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.07 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 146.2 ($\text{C}^{2''}$), 146.0 ($\text{C}^{1''}$), 121.8 ($\text{C}^{5''}$), 120.2 ($\text{C}^{4''}$), 114.7 ($\text{C}^{3''}$), 112.3 ($\text{C}^{6''}$), 86.6 (C^2), 70.0 (C^1), 68.7 (C^5), 29.7 (C^4), 27.3 ($\text{C}^{3'}$), 17.8 ($\text{C}^{2'}$), 13.9 (C^3), -7.0 ($\text{C}^{1'}$), -7.2 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{27}\text{O}_2\text{Si}$ 291.1775; Found 291.1773.

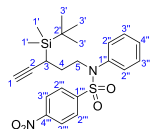
1,2-Bis((3-(tert-butyldimethylsilyl)pent-4-yn-1-yl)oxy)benzene (2r)



The reaction was performed according to general procedure A from propargyl silyl alcohol 1 and monoprotected catechol **2q** to yield crude product, which, after column chromatography (eluent system: toluene in hexanes, gradient change 0 $\rightarrow$ 20%), provided compound **2r** as a colorless solid (1187 mg, 71%). ^1H NMR (500 MHz, CDCl_3): δ 6.95 (dd, $^3J_{\text{H-H}} = 6.0$ Hz, $^4J_{\text{H-H}} = 3.7$ Hz, 2H, $\text{H}-\text{C}^{2''}$), 6.90 (dd, $^3J_{\text{H-H}} = 6.0$ Hz, $^4J_{\text{H-H}} = 3.7$ Hz, 2H, $\text{H}-\text{C}^{3''}$), 4.31–4.24 (m, 2H, H_2C^5), 4.15–4.08 (m, 2H, H_2C^5), 2.10–1.97 (m, 6H, HC^3 , HC^3 , H_2C^4), 1.91–1.81 (m, 2H, H_2C^4), 0.98 (s, 18H, $\text{H}_3\text{C}^{3'}$), 0.12 (s, 6H, $\text{H}_3\text{C}^{1'}$), 0.06 (s, 6H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 149.1 ($\text{C}^{1''}$), 121.3 ($\text{C}^{3''}$), 114.1 ($\text{C}^{2''}$), 86.4 (C^2), 69.7 (C^1), 68.4 (C^5), 68.3 (C^5), 29.7 (C^4), 27.1 ($\text{C}^{3'}$), 17.8 ($\text{C}^{2'}$), 13.4 (C^3), 13.3 (C^3), -7.0 ($\text{C}^{1'}$), -7.2 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{47}\text{O}_2\text{Si}_2$ 471.3109; Found 471.3112.

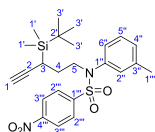
General Procedure B: Synthesis of Nosylamides 3. A 25 mL vial was charged with propargyl silyl alcohol 1 (198 mg, 1.00 mmol, 1.0 equiv), corresponding *N*-sulfonamide (1.10 mmol, 1.1 equiv), triphenylphosphine (289 mg, 1.10 mmol, 1.1 equiv), and toluene (3 mL). Then, ethyl 2-(3,4-dichlorophenyl)azocarboxylate (272 mg, 1.10 mmol, 1.1 equiv) was added, and the reaction mixture was allowed to stir at room temperature for 24 h. The reaction mixture was concentrated under reduced pressure. The residue was suspended in 30–60% DCM/Hex (20–30 mL) and filtered through a short silica gel pad. Recrystallization from MeOH afforded pure tertiary amide **3**.

***N*-(3-(*tert*-Butyldimethylsilyl)-pent-4-yn-1-yl)-4-nitro-*N*-phenylbenzenesulfonamide (3a)**



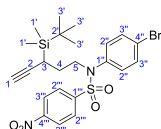
The reaction was performed according to general procedure B from alcohol **1** and 4-nitro-*N*-phenylbenzenesulfonamide to yield compound **3a** as a colorless solid (371 mg, 81%). ^1H NMR (500 MHz, CDCl_3): δ 8.30 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{3''}$), 7.78 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{2''}$), 7.36–7.32 (m, 3H, H-C $^{3''}$), 7.03 (dd, $^3J_{\text{H-H}} = 6.6$ Hz, $^4J_{\text{H-H}} = 3.0$ Hz, 2H, H-C $^{2''}$), 3.86 (dt, $^2J_{\text{H-H}} = 13.0$ Hz, $^3J_{\text{H-H}} = 8.0$ Hz, 1H, H-C 4), 3.72 (ddd, $^2J_{\text{H-H}} = 13.0$ Hz, $^3J_{\text{H-H}} = 8.0$, 4.2 Hz, 1H, H-C 5), 1.98 (d, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 1), 1.77 (ddd, $^3J_{\text{H-H}} = 12.6$, 3.0 Hz, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 3), 1.65 (dtd, $^2J_{\text{H-H}} = 13.0$ Hz, $^3J_{\text{H-H}} = 8.0$, 3.0 Hz, 1H, H-C 4), 1.56 (dddd, $^2J_{\text{H-H}} = 13.0$ Hz, $^3J_{\text{H-H}} = 12.6$, 8.0, 4.2 Hz, 1H, H-C 4), 0.87 (s, 9H, H-C 3), 0.01 (s, 3H, H-C 1), -0.11 (s, 3H, H-C 1). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 150.2 (C $^{4''}$), 144.1 (C $^{1''}$), 138.4 (C $^{1''}$), 129.5 (C $^{3''}$), 129.0 (C $^{2''}$), 128.6 (C $^{2''}$), 128.6 (C $^{4''}$), 124.2 (C $^{3''}$), 85.6 (C 2), 70.2 (C 1), 50.7 (C 5), 29.0 (C 4), 27.1 (C 3), 17.6 (C 2), 14.1 (C 3), -7.2 (C 1), -7.4 (C 1). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{31}\text{N}_2\text{O}_4\text{SSi}$ 459.1774; Found 459.1756.

***N*-(3-(*tert*-Butyldimethylsilyl)-pent-4-yn-1-yl)-4-nitro-*N*-(3-methylphenyl)-benzenesulfonamide (3e)**



The reaction was performed according to general procedure B from alcohol **1** and 4-nitro-*N*-(3-methylphenyl)benzenesulfonamide to yield compound **3e** as a colorless solid (379 mg, 80%). ^1H NMR (500 MHz, CDCl_3): δ 8.30 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{3''}$), 7.80 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{2''}$), 7.19 (t, $^3J_{\text{H-H}} = 7.7$ Hz, 1H, H-C $^{5''}$), 7.14 (d, $^3J_{\text{H-H}} = 7.7$ Hz, 1H, H-C $^{6''}$), 6.92 (s, 1H, H-C $^{2''}$), 6.73 (d, $^3J_{\text{H-H}} = 7.7$ Hz, 1H, H-C $^{4''}$), 3.85 (dt, $^2J_{\text{H-H}} = 12.9$ Hz, $^3J_{\text{H-H}} = 7.9$ Hz, 1H, H-C 4), 3.68 (ddd, $^2J_{\text{H-H}} = 12.9$ Hz, $^3J_{\text{H-H}} = 7.9$, 4.0 Hz, 1H, H-C 5), 2.32 (s, 3H, H-C $^{1''}$), 1.99 (d, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 1), 1.77 (dd, $^3J_{\text{H-H}} = 12.1$, 2.8 Hz, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 3), 1.68–1.49 (m, 2H, H-C 4), 0.87 (s, 9H, H-C 3), 0.01 (s, 3H, H-C 1), -0.11 (s, 3H, H-C 1). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 150.1 (C $^{4''}$), 144.2 (C $^{1''}$), 139.6 (C $^{3''}$), 138.3 (C $^{1''}$), 129.8 (C $^{2''}$), 129.4 (C $^{6''}$), 129.2 (C $^{5''}$), 129.0 (C $^{2''}$), 125.1 (C $^{4''}$), 124.1 (C $^{3''}$), 85.7 (C 2), 70.1 (C 1), 50.7 (C 5), 28.9 (C 4), 27.1 (C 3), 21.4 (C $^{1''}$), 17.6 (C 2), 14.0 (C 3), -7.2 (C 1), -7.4 (C 1). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{24}\text{H}_{33}\text{N}_2\text{O}_4\text{SSi}$ 473.1930; Found 473.1911.

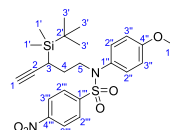
***N*-(4-Bromophenyl)-*N*-(3-(*tert*-butyldimethylsilyl)-pent-4-yn-1-yl)-4-nitrobenzenesulfonamide (3s)**



The reaction was performed according to general procedure B from propargyl silyl alcohol **1** and 4-nitro-*N*-(4-bromophenyl)benzenesulfonamide to yield compound **3s** as a colorless solid (435 mg, 81%). ^1H NMR (500 MHz, CDCl_3): δ 8.32 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{3''}$), 7.78 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{2''}$), 7.47 (d, $^3J_{\text{H-H}} = 8.7$ Hz, 2H, H-C $^{3''}$), 6.93 (d, $^3J_{\text{H-H}} = 8.7$ Hz, 2H, H-C $^{2''}$), 3.81 (dt, $^2J_{\text{H-H}} = 13.1$ Hz, $^3J_{\text{H-H}} = 8.1$ Hz, 1H, H-C 4), 3.69 (ddd, $^2J_{\text{H-H}} = 13.1$ Hz,

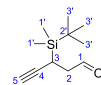
$^3J_{\text{H-H}} = 8.1$, 4.2 Hz, 1H, H-C 5), 1.98 (d, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 1), 1.74 (ddd, $^3J_{\text{H-H}} = 12.2$, 3.0 Hz, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 3), 1.66 (dtd, $^2J_{\text{H-H}} = 16.2$ Hz, $^3J_{\text{H-H}} = 8.1$, 3.0 Hz, 1H, H-C 4), 1.60–1.50 (m, 1H, H-C 5), 0.89 (s, 9H, H-C 3), 0.02 (s, 3H, H-C 1), -0.08 (s, 3H, H-C 1). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 150.3 (C $^{4''}$), 143.7 (C $^{1''}$), 137.6 (C $^{1''}$), 132.8 (C $^{3''}$), 130.1 (C $^{2''}$), 129.0 (C $^{2''}$), 124.3 (C $^{3''}$), 122.6 (C $^{4''}$), 85.5 (C 2), 70.4 (C 1), 50.8 (C 5), 29.0 (C 4), 27.1 (C 3), 17.6 (C 2), 14.1 (C 3), -7.1 (C 1), -7.4 (C 1). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{30}\text{BrN}_2\text{O}_4\text{SSi}$ 537.0873; Found 537.0860.

***N*-(3-(*tert*-Butyldimethylsilyl)-pent-4-yn-1-yl)-4-nitro-*N*-(4-methoxyphenyl)-benzenesulfonamide (3t)**



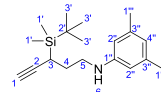
The reaction was performed according to general procedure B from alcohol **1** and 4-nitro-*N*-(4-methoxyphenyl)benzenesulfonamide to yield compound **3t** as a colorless solid (414 mg, 85%). ^1H NMR (500 MHz, CDCl_3): δ 8.32 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{3''}$), 7.78 (d, $^3J_{\text{H-H}} = 8.8$ Hz, 2H, H-C $^{2''}$), 7.47 (d, $^3J_{\text{H-H}} = 8.7$ Hz, 2H, H-C $^{3''}$), 6.93 (d, $^3J_{\text{H-H}} = 8.7$ Hz, 2H, H-C $^{2''}$), 3.81 (s, 3H, H-C $^{1''}$), 3.85–3.77 (m, 1H, H-C 4), 3.69 (ddd, $^2J_{\text{H-H}} = 13.1$ Hz, $^3J_{\text{H-H}} = 8.1$, 4.2 Hz, 1H, H-C 5), 1.98 (d, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 1), 1.74 (ddd, $^3J_{\text{H-H}} = 12.2$, 3.0 Hz, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 3), 1.66 (dtd, $^2J_{\text{H-H}} = 16.2$ Hz, $^3J_{\text{H-H}} = 8.1$, 3.0 Hz, 1H, H-C 4), 1.60–1.50 (m, 1H, H-C 5), 0.89 (s, 9H, H-C 3), 0.02 (s, 3H, H-C 1), -0.08 (s, 3H, H-C 1). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 159.5 (C $^{4''}$), 150.1 (C $^{1''}$), 144.2 (C $^{1''}$), 130.8 (C $^{1''}$), 129.9 (C $^{2''}$), 129.0 (C $^{2''}$), 124.2 (C $^{3''}$), 114.7 (C $^{3''}$), 85.7 (C 2), 70.2 (C 1), 55.6 (C $^{1''}$), 51.0 (C 2), 29.0 (C 4), 27.2 (C 3), 17.7 (C 2), 14.1 (C 3), -7.1 (C 1), -7.4 (C 1). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{24}\text{H}_{33}\text{N}_2\text{O}_5\text{SSi}$ 489.1879; Found 489.1864.

3-(*tert*-Butyldimethylsilyl)pent-4-ynal



Propargyl silyl alcohol **1** (1.50 g, 7.60 mmol, 1.0 equiv) and anhydrous Na_2SO_4 (3.2 g) were suspended in DCM (150 mL) in a disposable polypropylene cup. Pyridinium chlorochromate (4.9 g, 22.7 mmol, 3.0 equiv) was slowly added, and the reaction mixture was stirred at ambient conditions for 3 h. The reaction mixture was filtered through a silica gel plug (eluent system: DCM in hexanes, gradient change: 50 $\rightarrow$ 100%) and concentrated in vacuo to afford **3-(*tert*-butyldimethylsilyl)pent-4-ynal** as a pale yellow oil (1.37 g, 96%). ^1H NMR (500 MHz, CDCl_3): δ 9.83 (dd, $^3J_{\text{H-H}} = 2.2$, 1.3 Hz, 1H, HC 1), 2.55 (ddd, $^3J_{\text{H-H}} = 16.6$, 11.2, 2.2 Hz, 1H, H-C 2), 2.45 (ddd, $^3J_{\text{H-H}} = 16.6$, 3.8, 1.3 Hz, 1H, H-C 2), 2.29 (ddd, $^3J_{\text{H-H}} = 11.2$, 3.8 Hz, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 3), 2.04 (d, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC 3), 0.98 (s, 9H, H-C 3), 0.13 (s, 3H, H-C 1), 0.04 (s, 3H, H-C 1). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 201.9 (C 1), 85.3 (C 4), 70.3 (C 5), 43.8 (C 2), 27.2 (C 3), 17.8 (C 2), 10.8 (C 3), -6.9 (C 1), -7.4 (C 1). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{21}\text{OSi}$ 197.1356; Found, 197.1337. Spectral data for the compound is consistent with the reported in the literature.⁵⁶

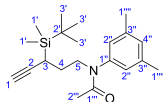
***N*-(3-(*tert*-Butyldimethylsilyl)-pent-4-yn-1-yl)-3,5-dimethylaniline**



A 25 mL two-neck round-bottom flask equipped with a Teflon-coated magnetic stirrer and a reflux condenser was charged with NaBH_4 (29 mg, 0.8 mmol, 1.5 equiv), evacuated, and backfilled with argon. Dry

THF (6 mL) was added. Then, AcOH (0.13 mL, 2.3 mmol, 4.5 equiv) was added to the suspension, and the reaction mixture was refluxed for 15–20 min, providing $\text{NaBH}(\text{OAc})_3$ solution, which was left to cool to room temperature before further use. Another 25 mL flask, equipped with a Teflon-coated magnetic stirrer was charged with 3-(*tert*-butyldimethylsilyl)pent-4-ynal (100 mg, 0.5 mmol, 1.0 equiv) and THF (4 mL) under an inert atmosphere. 3,5-Dimethylaniline (0.06 mL, 0.5 mmol, 1.0 equiv) and AcOH (0.03 mL, 0.5 mmol, 1.0 equiv) were added to the solution at room temperature. After stirring the solution for 30 min, the previously prepared $\text{NaBH}(\text{OAc})_3$ solution was added dropwise via syringe. The reaction was stirred for 1 h and quenched with saturated NaHCO_3 solution (10 mL). The product was extracted with DCM (3×10 mL), the organic layer was dried over anhydrous Na_2SO_4 , filtered, and concentrated under vacuo. Crude product was purified on silica gel column (eluent: toluene) to yield *N*-(3-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)-3,5-dimethylaniline as a yellow oil (119 mg, 78%). ^1H NMR (500 MHz, $\text{CDCl}_3 + \text{D}_2\text{O}$): δ 6.36 (s, 1H, H-C⁴ⁿ), 6.28 (s, 2H, H-C²ⁿ), 3.43 (ddd, $^3J_{\text{H-H}} = 12.6$ Hz, $^3J_{\text{H-H}} = 8.0$, 4.6 Hz, 1H, H₃C⁵), 3.24 (dt, $^2J_{\text{H-H}} = 12.6$ Hz, $^3J_{\text{H-H}} = 7.7$ Hz, 1H, H₃C⁵), 2.23 (s, 6H, H₃C¹ⁿ), 2.04 (d, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, HC¹), 1.86 (ddd, $^3J_{\text{H-H}} = 12.3$, 3.0 Hz, $^3J_{\text{H-H}} = 2.8$ Hz, 1H, HC¹), 1.79 (dddd, $^3J_{\text{H-H}} = 13.2$ Hz, $^3J_{\text{H-H}} = 8.0$, 7.7, 3.0 Hz, 1H, H₃C⁴), 1.66 (dddd, $^3J_{\text{H-H}} = 13.2$ Hz, $^3J_{\text{H-H}} = 12.3$, 7.7, 4.6 Hz, 1H, H₃C⁴), 0.95 (s, 9H, H₃C³ⁿ), 0.09 (s, 3H, H₃C^{1'}), 0.02 (s, 3H, H₃C^{1'}). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 148.5 (C¹ⁿ), 139.0 (C³ⁿ), 119.4 (C⁴ⁿ), 110.9 (C²ⁿ), 86.7 (C²), 69.9 (C¹), 43.8 (C⁵), 29.6 (C⁴), 27.2 (C³), 21.6 (C¹ⁿ), 17.8 (C³), 14.7 (C¹ⁿ), -7.0 (C^{1'}), -7.3 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for $\text{C}_{19}\text{H}_{32}\text{NSi}$ 302.2304; Found 302.2283.

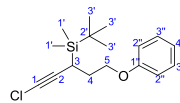
N-(3-(*tert*-Butyldimethylsilyl)pent-4-yn-1-yl)-*N*-(3,5-dimethylphenyl)acetamide (3u)



A 25 mL round-bottom flask was charged with *N*-(3-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)-3,5-dimethylaniline (294 mg, 0.97 mmol, 1.0 equiv), DMAP (24 mg, 0.20 mmol, 0.2 equiv), and DCM (10 mL). Ac_2O (0.11 mL, 1.2 mmol, 1.2 equiv) and DBU (0.73 mL, 4.9 mmol, 5.0 equiv) were added while stirring the solution at 0 °C. The reaction mixture was warmed to room temperature and stirred for an additional 3 h. The reaction was quenched by the addition of 0.1 M HCl solution (10 mL). The organic layer was separated and dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. Crude material was purified on silica gel column (eluent system: acetone in DCM, gradient change: 0 → 3%) to yield the product **3u** as a yellow oil (237 mg, 71%). ^1H NMR (500 MHz, CDCl_3): δ 6.96 (s, 1H, H-C⁴ⁿ), 6.76 (s, 2H, H-C²ⁿ), 3.91–3.76 (m, 2H, H₃C⁵), 2.32 (s, 6H, H₃C¹ⁿ), 1.94 (d, $^4J_{\text{H-H}} = 2.3$ Hz, 1H, HC¹), 1.83 (s, 3H, H₃C²ⁿ), 1.80–1.71 (m, 2H, HC³, H₃C⁴), 1.67–1.53 (m, 1H, H₃C⁴), 0.92 (s, 9H, H₃C³ⁿ), 0.05 (s, 3H, H₃C^{1'}), -0.01 (s, 3H, H₃C^{1'}). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 170.6 (C¹ⁿ), 143.3 (C¹ⁿ), 139.5 (C³ⁿ), 129.5 (C⁴ⁿ), 125.7 (C²ⁿ), 86.3 (C²), 69.8 (C¹), 49.5 (C⁵), 27.8 (C⁴), 27.2 (C³), 23.0 (C²ⁿ), 21.3 (C¹ⁿ), 17.7 (C²), 14.6 (C³), -7.0 (C^{1'}), -7.3 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for $\text{C}_{21}\text{H}_{34}\text{NOSi}$ 344.2410; Found 344.2387.

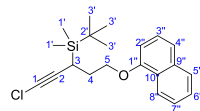
General Procedure C: Synthesis of Chloroalkynes 6 and 9. A 20 mL vial equipped with a Teflon-coated magnetic stirrer was charged with silver carbonate (13.8 mg, 0.05 mmol, 5 mol %) and corresponding terminal alkyne **2** or **3** (1.00 mmol, 1.0 equiv). Then, MeCN (16 mL) was added, and the flask was coated with aluminum foil. The reaction mixture was heated in an oil bath up to 60–65 °C, and *N*-chlorosuccinimide (151 mg, 0.55 mmol, 1.10 equiv) was added portionwise. After 24 h, the reaction mixture was cooled down to ~40 °C and concentrated in vacuo. The product was purified by filtration via a short silica gel pad by washing with 25% DCM solution in hexane. The filtrate was concentrated to afford pure haloalkynes **6** and **9**.

tert-Butyl(1-chloro-5-phenoxy)pent-1-yn-3-yl)-dimethylsilane (6a)



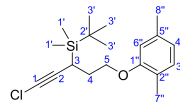
The reaction was performed according to the general procedure C from aryl ether **2a** to yield chloroalkyne **6a** as a colorless oil (297 mg, 96%). ^1H NMR (500 MHz, CDCl_3): δ 7.31–7.26 (m, 2H, H-C³ⁿ), 6.97–6.92 (m, 1H, H-C⁴ⁿ), 6.92 (d, $^3J_{\text{H-H}} = 8.6$ Hz, 2H, H-C²ⁿ), 4.22 (ddd, $^2J_{\text{H-H}} = 9.2$ Hz, $^3J_{\text{H-H}} = 6.8$, 3.8 Hz, 1H, H₃C⁵), 4.13 (ddd, $^2J_{\text{H-H}} = 9.2$ Hz, $^3J_{\text{H-H}} = 8.3$, 6.0 Hz, 1H, H₃C⁵), 2.01 (dd, $^3J_{\text{H-H}} = 13.0$, 3.1 Hz, 1H, HC³), 1.99 (dddd, $^2J_{\text{H-H}} = 11.2$ Hz, $^3J_{\text{H-H}} = 8.3$, 6.8, 3.1 Hz, 1H, H-C⁴), 1.84 (dddd, $^2J_{\text{H-H}} = 11.2$ Hz, $^3J_{\text{H-H}} = 13.0$, 6.0, 3.8 Hz, 1H, H-C⁴), 1.00 (s, 9H, H₃C³ⁿ), 0.13 (s, 3H, H₃C^{1'}), 0.08 (s, 3H, H₃C^{1'}). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 159.1 (C¹ⁿ), 129.6 (C³ⁿ), 120.8 (C⁴ⁿ), 114.7 (C²ⁿ), 71.5 (C²), 67.0 (C⁵), 57.9 (C¹), 29.7 (C⁴), 27.2 (C³), 17.6 (C^{2'}), 13.7 (C³), -6.9 (C^{1'}), -7.2 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for $\text{C}_{17}\text{H}_{26}\text{ClOSi}$ 309.1436; Found 309.1435.

tert-Butyl(1-chloro-5-(naphthalen-1-yloxy)pent-1-yn-3-yl)-dimethylsilane (6b)



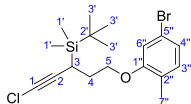
The reaction was performed according to the general procedure C from aryl ether **2b** to yield chloroalkyne **6b** as a colorless solid (348 mg, 97%). ^1H NMR (500 MHz, CDCl_3): δ 8.25 (d, $^3J_{\text{H-H}} = 7.8$ Hz, 1H, H-C⁸ⁿ), 7.80 (d, $^3J_{\text{H-H}} = 7.8$ Hz, 1H, H-C⁶ⁿ), 7.49 (dd, $^3J_{\text{H-H}} = 7.8$, 6.9 Hz, 1H, H-C⁶ⁿ), 7.47 (dd, $^3J_{\text{H-H}} = 7.8$, 6.9 Hz, 1H, H-C⁷ⁿ), 7.43 (d, $^3J_{\text{H-H}} = 8.2$ Hz, 1H, H-C⁴ⁿ), 7.39 (dd, $^3J_{\text{H-H}} = 8.2$, 7.5 Hz, 1H, H-C³ⁿ), 6.86 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H, H-C²ⁿ), 4.36–4.24 (m, 2H, H₃C⁵), 2.22–2.11 (m, 2H, HC³, H₃C⁴), 2.01–1.89 (m, 1H, H₃C⁴), 1.01 (s, 9H, H₃C³ⁿ), 0.14 (s, 3H, H₃C^{1'}), 0.10 (s, 3H, H₃C^{1'}). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 154.8 (C¹ⁿ), 134.6 (C⁹ⁿ), 127.6 (C⁵ⁿ), 126.5 (C⁶ⁿ), 126.1 (C³ⁿ), 125.8 (C¹⁰ⁿ), 125.2 (C⁷ⁿ), 122.1 (C⁸ⁿ), 120.3 (C³ⁿ), 104.9 (C²ⁿ), 71.4 (C²), 67.2 (C⁵), 57.9 (C¹), 29.9 (C⁴), 27.2 (C³), 17.7 (C^{2'}), 14.0 (C³), -6.9 (C^{1'}), -7.1 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for $\text{C}_{21}\text{H}_{26}\text{ClOSi}$ 359.1592; Found 359.1593.

tert-Butyl(1-chloro-5-(2,5-dimethylphenoxy)pent-1-yn-3-yl)-dimethylsilane (6c)



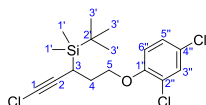
The reaction was performed according to the general procedure C from aryl ether **2c** to yield chloroalkyne **6c** as a colorless solid (332 mg, 99%). ^1H NMR (500 MHz, CDCl_3): δ 7.01 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H, H-C³ⁿ), 6.69 (s, 1H, H-C⁶ⁿ), 6.67 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H), 4.16–4.10 (m, 1H, H₃C⁵), 4.10–4.03 (m, 1H, H₃C⁵), 2.33 (s, 3H, H₃C⁸ⁿ), 2.17 (s, 3H, H₃C⁷ⁿ), 2.08 (dd, $^3J_{\text{H-H}} = 12.4$, 2.6 Hz, 1H, HC³), 2.07–1.97 (m, 1H, H₃C⁴), 1.86–1.76 (m, 1H, H₃C⁴), 0.99 (s, 9H, H₃C³ⁿ), 0.12 (s, 3H, H₃C^{1'}), 0.07 (s, 3H, H₃C^{1'}). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 157.0 (C¹ⁿ), 136.7 (C⁵ⁿ), 130.4 (C³ⁿ), 123.7 (C²ⁿ), 120.9 (C⁴ⁿ), 112.3 (C⁶ⁿ), 71.7 (C²), 66.9 (C⁵), 57.6 (C¹), 30.1 (C⁴), 27.2 (C³), 21.6 (C⁸ⁿ), 17.6 (C^{2'}), 16.0 (C⁷ⁿ), 13.7 (C³), -7.0 (C^{1'}), -7.1 (C^{1'}). HRMS (ESI) m/z : [M + H]⁺ Calcd for $\text{C}_{19}\text{H}_{30}\text{ClOSi}$ 337.1749; Found 337.1750.

(5-(5-Bromo-2-methylphenoxy)-1-chloropent-1-yn-3-yl)-(tert-butyl)dimethylsilane (6f)



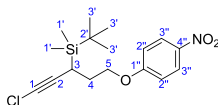
The reaction was performed according to the general procedure C from aryl ether **2f** to yield chloroalkyne **6f** as a colorless solid (373 mg, 93%). ¹H NMR (500 MHz, CDCl₃): δ 7.00–6.96 (m, 3H, H–C^{3''}, H–C^{4''}, H–C^{6''}), 4.13–4.02 (m, 2H, H₂C⁵), 2.15 (s, 3H, H₃C^{7''}), 2.05 (dd, ³J_{H–H} = 12.3, 2.6 Hz, 1H, HC³), 2.05–1.98 (m, 1H, H–C⁴), 1.84 (dddd, ²J_{H–H} = 9.1 Hz, ³J_{H–H} = 12.3, 9.2, 5.1 Hz, 1H, H–C⁴), 0.98 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.06 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.8 (C^{1''}), 131.7 (C^{3''}), 125.9 (C^{2''}), 123.3 (C^{4''}), 119.6 (C^{5''}), 114.6 (C^{6''}), 71.4 (C²), 67.2 (C⁵), 57.9 (C¹), 29.9 (C⁴), 27.2 (C³), 17.6 (C^{2'}), 16.0 (C^{7''}), 13.7 (C³), –7.0 (C^{1'}), –7.1 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₇BrClOSi 401.0698; Found 401.0695.

tert-Butyl(1-chloro-5-(2,4-dichlorophenoxy)-pent-1-yn-3-yl)dimethylsilane (6i)



The reaction was performed according to the general procedure C from aryl ether **2i** to yield chloroalkyne **6i** as a colorless oil (351 mg, 93%). ¹H NMR (500 MHz, CDCl₃): δ 7.36 (d, ³J_{H–H} = 2.6 Hz, 1H, H–C^{3''}), 7.18 (dd, ³J_{H–H} = 8.8 Hz, ⁴J_{H–H} = 2.6 Hz, 1H, H–C^{5''}), 6.88 (d, ³J_{H–H} = 8.8 Hz, 1H, H–C^{6''}), 4.19 (ddd, ²J_{H–H} = 9.0 Hz, ³J_{H–H} = 6.7, 3.7 Hz, 1H, H₂C⁵), 4.11 (ddd, ²J_{H–H} = 9.0 Hz, ³J_{H–H} = 8.9, 5.8 Hz, 1H, H₂C⁵), 2.09 (dd, ³J_{H–H} = 12.1, 3.0 Hz, 1H, HC³), 2.04 (dddd, ²J_{H–H} = 13.7 Hz, ³J_{H–H} = 8.9, 6.7, 3.0 Hz, 1H, H₂C⁴), 1.84 (dddd, ²J_{H–H} = 13.7 Hz, ³J_{H–H} = 12.1, 5.8, 3.7 Hz, 1H, H₂C⁴), 0.97 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.06 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.5 (C^{1''}), 130.1 (C^{3''}), 127.7 (C^{5''}), 125.7 (C^{4''}), 123.8 (C^{2''}), 114.3 (C^{6''}), 71.4 (C²), 68.5 (C⁵), 58.0 (C¹), 29.7 (C⁴), 27.2 (C³), 17.6 (C^{2'}), 13.6 (C³), –7.0 (C^{1'}), –7.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₄Cl₃OSi 377.0657; Found 377.0639.

tert-Butyl(1-chloro-5-(4-nitrophenoxy)pent-1-yn-3-yl)dimethylsilane (6k)



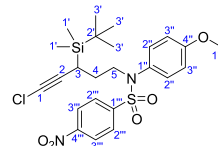
The reaction was performed according to the general procedure C from aryl ether **2k** to yield chloroalkyne **6k** as a pale yellow solid (167 mg, 95%). ¹H NMR (500 MHz, CDCl₃): δ 8.21 (d, ³J_{H–H} = 9.1 Hz, 2H, H–C^{3''}), 6.97 (d, ³J_{H–H} = 9.1 Hz, 2H, H–C^{2''}), 4.27–4.15 (m, 2H, H₂C⁵), 2.06–1.97 (m, 2H, HC³, H₂C⁴), 1.89–1.80 (m, 1H, H₂C⁴), 0.98 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.06 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 164.2 (C^{1''}), 141.6 (C^{4''}), 126.1 (C^{3''}), 114.6 (C^{2''}), 71.0 (C²), 67.9 (C⁵), 58.4 (C¹), 29.4 (C⁴), 27.2 (C³), 17.6 (C^{2'}), 13.7 (C³), –6.9 (C^{1'}), –7.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₅ClNO₃Si 354.1287; Found 354.1285.

N-(4-Bromophenyl)-N-(3-(tert-butylidimethylsilyl)-5-chloropent-4-yn-1-yl)-4-nitrobenzenesulfonamide (9r)



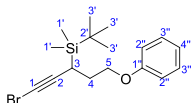
The reaction was performed in a 25 mL round-bottom flask coated with aluminum foil according to the general procedure C with minor deviations from the original amounts and stoichiometry. Nosylamide **3r** (507 mg, 0.94 mmol, 1.0 equiv), NCS (126 mg, 0.94 mmol, 1.0 equiv), Ag₂CO₃ (13 mg, 0.05 mmol, 5 mol %), and MeCN (16 mL) were used to yield chloroalkyne **9r** as a colorless solid (493 mg, 91%). ¹H NMR (500 MHz, CDCl₃): δ 8.33 (d, ³J_{H–H} = 8.6 Hz, 2H, H–C^{3''}), 7.78 (d, ³J_{H–H} = 8.6 Hz, 2H, H–C^{2''}), 7.48 (d, ³J_{H–H} = 8.4 Hz, 2H, H–C^{3''}), 6.93 (d, ³J_{H–H} = 8.4 Hz, 2H, H–C^{2''}), 3.76 (dt, ²J_{H–H} = 13.0 Hz, ³J_{H–H} = 7.9 Hz, 1H, H₂C⁵), 3.64 (ddd, ²J_{H–H} = 13.0 Hz, ³J_{H–H} = 8.0, 4.1 Hz, 1H, H₂C⁵), 1.73 (dd, ³J_{H–H} = 12.4, 4.1 Hz, 1H, HC³), 1.70–1.59 (m, 1H, H₂C⁴), 1.53 (tdd, ²J_{H–H} = 12.4 Hz, ³J_{H–H} = 12.4, 7.9, 4.1 Hz, 1H, H₂C⁴), 0.88 (s, 9H, H₃C^{3'}), 0.01 (s, 3H, H₃C^{1'}), –0.09 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 150.3 (C^{4''}), 143.7 (C^{1''}), 137.6 (C^{1''}), 132.8 (C^{3''}), 130.1 (C^{2''}), 129.0 (C^{2''}), 124.4 (C^{3''}), 122.6 (C^{4''}), 70.7 (C²), 58.6 (C¹), 50.9 (C⁵), 29.0 (C⁴), 27.0 (C³), 17.5 (C^{2'}), 14.5 (C³), –7.0 (C^{1'}), –7.3 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₃H₂₉BrClN₂O₄SSi 571.0489; Found 571.0474.

N-(3-(tert-Butylidimethylsilyl)-5-chloropent-4-yn-1-yl)-N-(4-methoxyphenyl)-4-nitrobenzenesulfonamide (9s)

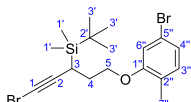


The reaction was performed in a 25 mL round-bottom flask coated with aluminum foil according to the general procedure C with minor deviations from the original amounts and stoichiometry. Nosylamide **3s** (317 mg, 0.65 mmol, 1.0 equiv), NCS (94 mg, 0.68 mmol, 1.0 equiv), Ag₂CO₃ (8 mg, 0.03 mmol, 5 mol %) and MeCN (10 mL) were used to yield chloroalkyne **9s** as a yellow solid (340 mg, 99%). ¹H NMR (500 MHz, CDCl₃): δ 8.31 (d, ³J_{H–H} = 8.7 Hz, 2H, H–C^{3''}), 7.79 (d, ³J_{H–H} = 8.7 Hz, 2H, H–C^{2''}), 6.93 (d, ³J_{H–H} = 8.8 Hz, 2H, H–C^{3''}), 6.84 (d, ³J_{H–H} = 8.8 Hz, 2H, H–C^{2''}), 3.81 (s, 3H, H₃C^{1''}), 3.84–3.71 (m, 1H, H₂C⁵), 3.69–3.55 (m, 1H, H₂C⁵), 1.76 (ddd, ³J_{H–H} = 12.1, 2.8 Hz, 1H, HC³), 1.68–1.58 (m, 1H, H₂C⁴), 1.60–1.50 (m, 1H, H₂C⁴), 0.88 (s, 9H, H₃C^{3'}), 0.01 (s, 3H, H₃C^{1'}), –0.10 (s, 3H, H₃C^{2'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 159.6 (C^{4''}), 150.1 (C^{1''}), 144.2 (C^{1''}), 130.8 (C^{1''}), 129.9 (C^{2''}), 129.0 (C^{2''}), 124.2 (C^{3''}), 114.7 (C^{3''}), 70.9 (C²), 58.4 (C¹), 55.6 (C^{1''}), 51.1 (C⁵), 28.9 (C⁴), 27.1 (C³), 17.5 (C^{2'}), 14.4 (C³), –7.0 (C^{1'}), –7.3 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₄H₃₂ClN₂O₅SSi 523.1490; Found 523.1472.

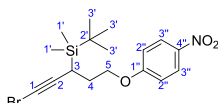
General Procedure D: Synthesis of Bromoalkynes 7 and Iodoalkyne 8a. A 10 mL vial equipped with a Teflon-coated magnetic stirrer was charged with silver nitrate (17.0 mg, 0.10 mmol, 10 mol %) and corresponding terminal alkyne **2** (1.00 mmol, 1.0 equiv). Then, MeCN (16 mL) was added, and the flask was covered with aluminum foil. N-Bromosuccinimide (197 mg, 1.10 mmol, 1.10 equiv) or N-iodosuccinimide (248 mg, 1.10 mmol, 1.10 equiv) was added portionwise. The reaction mixture was stirred under ambient conditions for 3 h and then concentrated in vacuo. The product was purified by filtration via a short silica gel pad by washing with 25% DCM solution in hexane. The filtrate was concentrated to afford pure haloalkynes **7** and **8**.

(1-Bromo-5-phenoxy)pent-1-yn-3-yl)(tert-butyl)-dimethylsilane (7a)

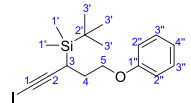
The reaction was performed according to the general procedure D from aryl ether **2a** to yield bromoalkyne **7a** as a colorless solid (337 mg, 96%). ^1H NMR (500 MHz, CDCl_3): δ 7.31–7.27 (m, 2H, $\text{H}-\text{C}^{3n}$), 6.97–6.90 (m, 3H, $\text{H}-\text{C}^{2n}$, $\text{H}-\text{C}^{4n}$), 4.17 (ddd, $^3J_{\text{H}-\text{H}} = 9.2$ Hz, $^3J_{\text{H}-\text{H}} = 7.1$, 4.0 Hz, 1H, H_2C^5), 4.08 (ddd, $^3J_{\text{H}-\text{H}} = 9.2$ Hz, $^3J_{\text{H}-\text{H}} = 8.4$, 6.4 Hz, 1H, H_2C^3), 2.01 (dd, $^3J_{\text{H}-\text{H}} = 12.3$, 3.1 Hz, 1H, HC^4), 1.99 (dddd, $^3J_{\text{H}-\text{H}} = 13.5$ Hz, $^3J_{\text{H}-\text{H}} = 8.4$, 7.1, 3.1 Hz, 1H, $\text{H}-\text{C}^4$), 1.84 (dddd, $^3J_{\text{H}-\text{H}} = 13.5$ Hz, $^3J_{\text{H}-\text{H}} = 12.3$, 6.4, 4.0 Hz, 1H, $\text{H}-\text{C}^4$), 0.98 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.11 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.06 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 159.1 ($\text{C}^{1'}$), 129.6 (C^{3n}), 120.8 (C^{2n}), 114.8 (C^{2n}), 96.2 (C^2), 67.1 (C^5), 29.8 (C^4), 27.3 ($\text{C}^{3'}$), 17.7 ($\text{C}^{2'}$), 13.4 (C^3), –6.9 ($\text{C}^{1'}$), –7.2 ($\text{C}^{1'}$), –7.5 (C^1). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{26}\text{BrOSi}$ 353.0931; Found 353.0931.

(1-Bromo-5-(5-bromo-2-methylphenoxy)pent-1-yn-3-yl)-(tert-butyl)dimethylsilane (7f)

The reaction was performed according to the general procedure D from aryl ether **2f** to yield bromoalkyne **7f** as a colorless solid (431 mg, 97%). ^1H NMR (500 MHz, CDCl_3): δ 7.05–6.94 (m, 3H, $\text{H}-\text{C}^{3n}$, $\text{H}-\text{C}^{4n}$, $\text{H}-\text{C}^{6n}$), 4.14–4.02 (m, 2H, H_2C^5), 2.15 (s, 3H, H_3C^{7n}), 2.09 (dd, $^3J_{\text{H}-\text{H}} = 12.3$, 2.8 Hz, 1H, HC^4), 2.06–1.97 (m, 1H, $\text{H}-\text{C}^4$), 1.89–1.77 (m, 1H, $\text{H}-\text{C}^4$), 0.98 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.12 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.07 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 157.8 ($\text{C}^{1'}$), 131.7 (C^{3n}), 125.9 (C^{2n}), 123.3 (C^{4n}), 119.6 (C^{5n}), 114.6 (C^{6n}), 82.0 (C^2), 67.2 (C^5), 38.1 (C^1), 29.8 (C^4), 27.2 ($\text{C}^{3'}$), 17.6 ($\text{C}^{2'}$), 16.0 (C^{7n}), 14.8 (C^3), –7.0 ($\text{C}^{1'}$), –7.1 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{27}\text{Br}_2\text{OSi}$ 445.0192; Found 445.0192.

(1-Bromo-5-(4-nitrophenoxy)pent-1-yn-3-yl)-(tert-butyl)-dimethylsilane (7k)

The reaction was performed according to the general procedure D from aryl ether **2k** to yield bromoalkyne **7k** as a colorless solid (367 mg, 92%). ^1H NMR (500 MHz, CDCl_3): δ 8.21 (abd, $^3J_{\text{H}-\text{H}} = 9.2$ Hz, $^4J_{\text{H}-\text{H}} = 2.7$ Hz, 2H, $\text{H}-\text{C}^{3n}$), 6.98 (abd, $^3J_{\text{H}-\text{H}} = 9.2$ Hz, $^4J_{\text{H}-\text{H}} = 2.7$ Hz, 2H, $\text{H}-\text{C}^{2n}$), 4.27–4.22 (m, 1H, H_2C^5), 4.22–4.16 (m, 1H, H_2C^5), 2.06–1.98 (m, 2H, HC^4 , H_2C^3), 1.91–1.82 (m, 1H, H_2C^3), 0.98 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.11 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.07 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 164.2 ($\text{C}^{1'}$), 141.6 (C^{3n}), 126.1 (C^{2n}), 114.6 (C^{2n}), 81.5 (C^2), 67.9 (C^5), 38.7 (C^4), 29.3 (C^4), 27.2 ($\text{C}^{3'}$), 17.6 ($\text{C}^{2'}$), 14.8 (C^3), –6.9 ($\text{C}^{1'}$), –7.2 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{25}\text{BrNO}_2\text{Si}$ 398.0782; Found 398.0783.

tert-Butyl(1-iodo-5-phenoxy)pent-1-yn-3-yl)dimethylsilane (8a)

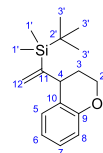
The reaction was performed according to the general procedure D from aryl ether **2a** to yield iodoalkyne **8a** as a colorless solid (364 mg, 91%).

^1H NMR (500 MHz, CDCl_3): δ 7.31–7.26 (t, $^3J_{\text{H}-\text{H}} = 7.7$ Hz, 2H, $\text{H}-\text{C}^{3n}$), 6.94 (t, $^3J_{\text{H}-\text{H}} = 7.4$ Hz, 1H, $\text{H}-\text{C}^{4n}$), 6.92 (d, $^3J_{\text{H}-\text{H}} = 7.9$ Hz, 2H, $\text{H}-\text{C}^{2n}$), 4.22 (ddd, $^3J_{\text{H}-\text{H}} = 8.5$ Hz, $^3J_{\text{H}-\text{H}} = 6.3$, 4.0 Hz, 1H, H_2C^5), 4.13 (td, $^3J_{\text{H}-\text{H}} = 8.5$ Hz, $^3J_{\text{H}-\text{H}} = 8.5$, 6.5 Hz, 1H, H_2C^5), 2.23 (dd, $^3J_{\text{H}-\text{H}} = 13.0$, 3.3 Hz, 1H, HC^4), 1.98 (dd, $^3J_{\text{H}-\text{H}} = 11.8$ Hz, $^3J_{\text{H}-\text{H}} = 8.5$, 8.3, 3.3 Hz, 1H, $\text{H}-\text{C}^4$), 1.85 (dddd, $^3J_{\text{H}-\text{H}} = 11.8$ Hz, $^3J_{\text{H}-\text{H}} = 13.0$, 6.5, 4.0 Hz, 1H, $\text{H}-\text{C}^4$), 0.98 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.10 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.06 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 159.1 ($\text{C}^{1'}$), 129.6 (C^{3n}), 120.8 (C^{2n}), 114.8 (C^{2n}), 96.2 (C^2), 67.1 (C^5), 29.8 (C^4), 27.3 ($\text{C}^{3'}$), 17.7 ($\text{C}^{2'}$), 13.4 (C^3), –6.9 ($\text{C}^{1'}$), –7.2 ($\text{C}^{1'}$), –7.5 (C^1). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{26}\text{IOSi}$ 401.0792; Found 401.0792.

General Procedure E: Synthesis of Chromanes 4, 10, 11, 12. A

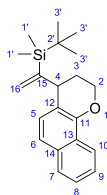
10 mL vial equipped with a Teflon-coated magnetic stirrer was charged with the corresponding aryl ether **2**, **6**, **7**, or **8** (0.80 mmol, 1.0 equiv), then 1,2-dichloroethane (3 mL) was added, and the reaction mixture was heated up to 60 °C on the hot plate. Bistriflimide ($\text{HN}(\text{TF}_2)_2$) solution in nitromethane (0.16 M, 1 mL, 0.16 mmol, 0.2 equiv) was added, coloring the solution dark red. The reaction mixture was allowed to stir for an additional 10 min, then it was cooled down to room temperature, and two drops of triethyl amine were added, causing the color to turn yellow. Crude mixture was filtered through a short silica gel plug, the filtrate was concentrated in vacuo and additionally filtered through a short silica gel plug, washing with a 25% DCM solution in hexanes. The filtrate was concentrated and purified by column chromatography on silica gel or AgNO_3 -impregnated silica gel (eluent system: toluene solution in hexanes, gradient 12 $\rightarrow$ 100%) to afford chromanes **4**, **10**, **11**, or **12**.

AgNO₃-Impregnated Silica Gel Preparation. Silver nitrate (20 g) was totally dissolved in MeCN (600 mL), and silica gel (200 g) was added to the solution upon vigorous stirring. The suspension was left to stir for an additional 2 h at ambient conditions in the dark, and then it was filtered on a fritted glass filter protected from light with aluminum foil. Silica gel was collected, heated for 2 h at 100 °C, and then stored in a closed container protected from light.

tert-Butyl(1-(chroman-4-yl)vinyl)dimethylsilane (4a)

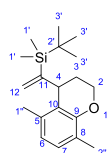
The reaction was performed according to the general procedure E from aryl ether **2a** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 25%), provided chromane **4a** as a colorless oil (165 mg, 75%). ^1H NMR (500 MHz, CDCl_3): δ 7.09 (ddd, $^3J_{\text{H}-\text{H}} = 8.2$, 7.2 Hz, $^4J_{\text{H}-\text{H}} = 1.7$ Hz, 1H, $\text{H}-\text{C}^7$), 6.96 (dd, $^3J_{\text{H}-\text{H}} = 7.7$ Hz, $^4J_{\text{H}-\text{H}} = 1.7$ Hz, 1H, $\text{H}-\text{C}^5$), 6.81 (dd, $^3J_{\text{H}-\text{H}} = 7.7$, 7.2 Hz, $^4J_{\text{H}-\text{H}} = 1.2$ Hz, 1H, $\text{H}-\text{C}^6$), 6.80 (dd, $^3J_{\text{H}-\text{H}} = 8.2$ Hz, $^4J_{\text{H}-\text{H}} = 1.2$ Hz, 1H, $\text{H}-\text{C}^8$), 5.64 (d, $^2J_{\text{H}-\text{H}} = 2.3$ Hz, 1H, H_2C^{12}), 5.39 (dd, $^3J_{\text{H}-\text{H}} = 2.3$ Hz, $^4J_{\text{H}-\text{H}} = 1.2$ Hz, 1H, H_2C^{12}), 4.15 (ddd, $^2J_{\text{H}-\text{H}} = 14.3$ Hz, $^3J_{\text{H}-\text{H}} = 8.4$, 3.0 Hz, 1H, H_2C^2), 4.13 (ddd, $^2J_{\text{H}-\text{H}} = 14.3$ Hz, $^3J_{\text{H}-\text{H}} = 10.7$, 4.0 Hz, 1H, H_2C^2), 3.78 (dd, $^3J_{\text{H}-\text{H}} = 6.1$, 5.3 Hz, 1H, HC^4), 2.11 (dddd, $^3J_{\text{H}-\text{H}} = 13.9$ Hz, $^3J_{\text{H}-\text{H}} = 8.4$, 6.1, 4.0 Hz, 1H, H_2C^3), 1.77 (dddd, $^3J_{\text{H}-\text{H}} = 13.9$ Hz, $^3J_{\text{H}-\text{H}} = 10.7$, 5.3, 3.0 Hz, 1H, H_2C^3), 0.97 (s, 9H, $\text{H}_3\text{C}^{3'}$), 0.11 (s, 3H, $\text{H}_3\text{C}^{1'}$), 0.09 (s, 3H, $\text{H}_3\text{C}^{1'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): δ 155.6 (C^9), 155.0 (C^{11}), 130.9 (C^{12}), 130.7 (C^5), 127.7 (C^7), 125.0 (C^{10}), 120.3 (C^6), 116.7 (C^8), 62.8 (C^2), 40.9 (C^4), 28.7 (C^3), 27.3 ($\text{C}^{3'}$), 17.7 ($\text{C}^{2'}$), –4.8 ($\text{C}^{1'}$), –5.1 ($\text{C}^{1'}$). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{22}\text{OSi}$ 275.1826; Found 275.1828.

1-(Benzo[*h*]chroman-4-yl)vinyl)(*tert*-butyl)dimethylsilane (4b)



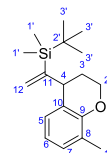
The reaction was performed according to the general procedure E from aryl ether **2b** to yield crude product, which, after column chromatography on AgNO₃-impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 → 35%), provided chromane **4b** as a colorless oil (151 mg, 58%). ¹H NMR (500 MHz, CDCl₃): δ 8.20–8.14 (m, 1H, H-C⁷), 7.77–7.70 (m, 1H, H-C¹⁰), 7.45 (ddd, ³J_{H-H} = 8.7, 6.8 Hz, ⁴J_{H-H} = 1.9 Hz, 1H, H-C⁸), 7.43 (ddd, ³J_{H-H} = 8.7, 6.8 Hz, ⁴J_{H-H} = 2.1 Hz, 1H, H-C⁹), 7.30 (d, ³J_{H-H} = 8.5 Hz, 1H, H-C⁶), 7.03 (d, ³J_{H-H} = 8.5 Hz, 1H, H-C⁵), 5.67 (d, ²J_{H-H} = 2.3 Hz, 1H, H₂C¹⁶), 5.34 (dd, ²J_{H-H} = 2.3 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C¹⁶), 4.35 (ddd, ²J_{H-H} = 10.7 Hz, ³J_{H-H} = 4.7, 3.5 Hz, 1H, H₂C²), 4.26 (ddd, ²J_{H-H} = 10.7 Hz, ³J_{H-H} = 10.3, 2.5 Hz, 1H, H₂C²), 3.89 (ddd, ³J_{H-H} = 6.3, 3.8 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.24 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 10.3, 6.3, 3.5 Hz, 1H, H₂C³), 1.83 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 4.7, 3.8, 2.5 Hz, 1H, H₂C³), 1.01 (s, 9H, H₃C^{3'}), 0.16 (s, 3H, H₃C^{1'}), 0.15 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.9 (C¹⁵), 150.6 (C¹¹), 133.4 (C¹⁴), 131.2 (C¹⁶), 128.6 (C⁷), 127.5 (C¹⁰), 125.9 (C⁹), 125.3 (C⁸), 125.2 (C¹³), 121.7 (C⁷), 119.5 (C⁶), 118.0 (C¹²), 62.4 (C²), 40.5 (C⁴), 28.3 (C³), 27.2 (C^{3'}), 17.6 (C^{2'}), -4.9 (C^{1'}), -5.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₁H₂₉OSi 325.1982; Found 325.2005.

***tert*-Butyl(1-(5,8-dimethylchroman-4-yl)vinyl)-dimethylsilane (4c)**



The reaction was performed according to the general procedure E from aryl ether **2c** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 25%), provided chromane **4c** as a colorless oil (165 mg, 68%). ¹H NMR (500 MHz, CDCl₃): δ 6.90 (d, ³J_{H-H} = 7.4 Hz, 1H, H-C⁵), 6.61 (d, ³J_{H-H} = 7.4 Hz, 1H, H-C⁶), 5.63 (d, ²J_{H-H} = 2.3 Hz, 1H, H₂C¹²), 5.14 (dd, ²J_{H-H} = 2.3 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C¹²), 4.20 (ddd, ²J_{H-H} = 10.7 Hz, ³J_{H-H} = 3.8, 2.5 Hz, ⁴J_{H-H} = 1.2 Hz, 1H, H₂C²), 4.01 (ddd, ²J_{H-H} = 10.7 Hz, ³J_{H-H} = 12.9, 2.0 Hz, 1H, H₂C²), 3.78 (dddd, ³J_{H-H} = 5.9, 1.7 Hz, ⁴J_{H-H} = 1.2, 1.1 Hz, 1H, HC⁴), 2.16 (s, 3H, H₃C^{2'}), 2.08 (s, 3H, H₃C^{1'}), 2.06 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 12.9, 5.9, 3.8 Hz, 1H, H₂C³), 1.79 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 2.5, 1.7, 2.0 Hz, 1H, H₂C³), 0.97 (s, 9H, H₃C^{3'}), 0.18 (s, 3H, H₃C^{1'}), 0.18 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.5 (C⁹), 152.1 (C¹¹), 134.9 (C⁵), 130.7 (C¹²), 128.4 (C⁷), 123.1 (C⁸), 121.9 (C¹⁰), 121.2 (C⁶), 60.5 (C²), 37.9 (C⁴), 27.4 (C^{3'}), 26.3 (C³), 19.2 (C^{1'}), 17.5 (C^{2'}), 16.3 (C^{2''}), -3.6 (C^{1'}), -4.8 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₃₁OSi 303.2139; Found 303.2141.

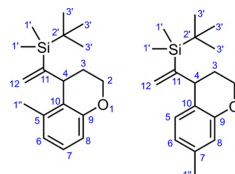
***tert*-Butyldimethyl(1-(8-methylchroman-4-yl)vinyl)silane (4d)**



The reaction was performed according to the general procedure E from aryl ether **2d** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 25%), provided chromane **4d** as a colorless oil (173 mg, 75%). ¹H NMR (500 MHz, CDCl₃): δ 6.96 (dd, ³J_{H-H} = 7.2 Hz, ⁴J_{H-H} = 1.8 Hz, 1H, H-C⁷), 6.81 (dd, ³J_{H-H} = 7.8 Hz, ⁴J_{H-H} = 1.8 Hz, 1H, H-C⁸), 6.72 (dd, ³J_{H-H} = 7.8, 7.2 Hz, 1H, H-C⁶), 5.64 (d, ²J_{H-H} = 2.3 Hz, 1H, H₂C¹²), 5.39 (dd, ²J_{H-H} = 2.3 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C¹²), 4.19–4.14 (m, 2H, H₂C²), 3.78 (ddd, ³J_{H-H} = 6.2, 4.9 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.19 (s, 3H, H₃C^{1'}), 2.10 (dq, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 6.2 Hz, 1H, H₂C³), 1.76 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 4.9, 3.8 Hz, 1H, H₂C³), 0.97 (s, 9H, H₃C^{3'}), 0.12 (s, 3H, H₃C^{1'}), 0.10 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 154.1 (C¹¹), 153.7 (C⁹), 130.7 (C¹²), 128.6 (C⁷), 128.2 (C⁵), 125.6 (C⁸), 124.2 (C¹⁰), 119.5 (C⁶), 62.6 (C²), 40.9 (C⁴), 28.6 (C³), 27.2 (C^{3'}), 17.6 (C^{2'}), 16.4 (C^{1''}), -4.9 (C^{1'}), -5.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₉OSi 289.1982; Found 289.1982.

***tert*-Butyldimethyl(1-(5-methylchroman-4-yl)vinyl)silane (o-4e) and**

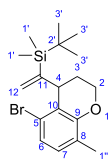
***tert*-butyldimethyl(1-(7-methylchroman-4-yl)vinyl)silane (p-4e)**



The reaction was performed according to the general procedure E from aryl ether **2e** to yield crude product mixture, which, after column chromatography on AgNO₃-impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 → 35%), provided a colorless oil (150 mg, 65%) consisting of two isomers **o-4e** and **p-4e** with corresponding ratio 46:54. Compound **o-4e** data: ¹H NMR (500 MHz, CDCl₃): δ 7.04 (dd, ³J_{H-H} = 8.2, 7.4 Hz, 1H, H-C⁷), 6.71 (d, ³J_{H-H} = 7.4 Hz, 1H, H-C⁸), 6.69 (d, ³J_{H-H} = 8.2 Hz, 1H, H-C⁶), 5.64 (d, ²J_{H-H} = 2.2 Hz, 1H, H₂C¹²), 5.15 (dd, ²J_{H-H} = 2.2 Hz, ⁴J_{H-H} = 1.5 Hz, 1H, H₂C¹²), 4.19–4.12 (m, 1H, H₂C²), 4.01 (ddd, ²J_{H-H} = 12.8 Hz, ³J_{H-H} = 10.7, 2.1 Hz, 1H, H₂C²), 3.72 (dd, ³J_{H-H} = 5.9 Hz, ⁴J_{H-H} = 1.5 Hz, 1H, HC⁴), 2.12 (s, 3H, H₃C^{1'}), 2.13–2.05 (m, 1H, H₂C³), 1.79 (dddd, ²J_{H-H} = 14.1 Hz, ³J_{H-H} = 3.1, 2.1 Hz, ⁴J_{H-H} = 1.5 Hz, 1H, H₂C³), 0.98 (s, 9H, H₃C^{3'}), 0.19 (s, 3H, H₃C^{1'}), 0.18 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 155.4 (C¹¹), 151.9 (C⁹), 137.6 (C⁵), 130.7 (C¹²), 127.3 (C⁷), 122.5 (C¹⁰), 122.1 (C⁹), 114.4 (C⁸), 60.5 (C²), 37.6 (C⁴), 27.4 (C^{3'}), 26.3 (C³), 19.4 (C^{1''}), 17.5 (C^{2'}), -3.6 (C^{1'}), -4.8 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₉OSi 289.1982; Found 289.1982 (for mixture). Compound **p-4e** data: ¹H NMR (500 MHz, CDCl₃): δ 6.84 (d, ³J_{H-H} = 7.7 Hz, 1H, H-C⁷), 6.65 (d, ³J_{H-H} = 7.7 Hz, 1H, H-C⁸), 6.63 (s, 1H, H-C⁶), 5.63 (d, ²J_{H-H} = 2.3 Hz, 1H, H₂C¹²), 5.39 (dd, ²J_{H-H} = 2.3 Hz, ⁴J_{H-H} = 0.9 Hz, 1H, H₂C¹²), 4.15–4.07 (m, 2H, H₂C²), 3.75 (dd, ³J_{H-H} = 5.8, 5.4 Hz, ⁴J_{H-H} = 0.9 Hz, 1H, HC⁴), 2.28 (s, 3H, H₃C^{1'}), 2.14–2.05 (m, 1H, H₂C³), 1.75 (ddd, ²J_{H-H} = 13.7 Hz, ³J_{H-H} = 5.4, 2.9 Hz, 1H, H₂C³), 0.97 (s, 9H, H₃C^{3'}), 0.12 (s, 3H, H₃C^{1'}), 0.09 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 155.3 (C¹¹), 153.9 (C⁹), 137.5 (C⁷), 130.6 (C⁵), 130.3 (C¹²), 121.8 (C¹⁰), 121.3 (C⁶), 116.9 (C⁸), 62.6 (C²), 40.5 (C⁴), 28.7 (C³), 27.2 (C^{3'}), 21.2 (C^{1''}), 17.6 (C^{2'}), -4.9 (C^{1'}), -5.3 (C^{1'}). HRMS (ESI) *m/z*:

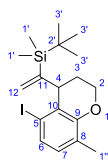
z: $[M + H]^+$ Calcd for $C_{18}H_{29}OSi$ 289.1982; Found 289.1982 (for mixture).

(1-(5-Bromo-8-methylchroman-4-yl)vinyl)(tert-butyl)-dimethylsilane (4f)



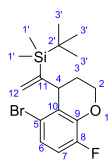
The reaction was performed according to the general procedure E from aryl ether **2f** to yield crude product, which, after column chromatography on $AgNO_3$ -impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 35%), provided chromane **4f** as a colorless solid (170 mg, 58%). 1H NMR (500 MHz, $CDCl_3$): δ 7.00 (d, $^3J_{H-H} = 7.9$ Hz, 1H, H-C⁶), 6.86 (d, $^3J_{H-H} = 7.9$ Hz, 1H, H-C⁷), 5.64 (d, $^2J_{H-H} = 2.1$ Hz, 1H, H₂C¹²), 5.04 (dd, $^3J_{H-H} = 2.1$ Hz, $^4J_{H-H} = 1.3$ Hz, 1H, H₂C¹²), 4.23 (dddd, $^2J_{H-H} = 10.7$ Hz, $^3J_{H-H} = 3.8$, 2.4 Hz, $^4J_{H-H} = 1.3$ Hz, 1H, H₂C²), 4.04 (dddd, $^2J_{H-H} = 10.7$ Hz, $^3J_{H-H} = 12.9$, 2.1 Hz, 1H, H₂C²), 3.90 (ddt, $^3J_{H-H} = 5.7$, 1.7 Hz, $^4J_{H-H} = 1.3$ Hz, 1H, HC⁴), 2.14 (s, 3H, H₃C¹⁰), 2.03 (dddd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 12.9$, 5.7, 3.8 Hz, 1H, H₂C³), 1.80 (dddd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 2.4$, 2.1, 1.7 Hz, 1H, H₂C³), 0.97 (s, 9H, H₃C^{3'}), 0.21 (s, 3H, H₃C^{1'}), 0.20 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 154.6 (C⁹), 151.7 (C¹¹), 130.6 (C¹²), 129.6 (C⁷), 125.0 (C⁸), 123.7 (C⁶), 123.1 (C¹⁰), 122.7 (C⁵), 61.1 (C²), 40.7 (C⁴), 27.5 (C^{3'}), 25.8 (C³), 17.5 (C^{2'}), 16.3 (C^{10'}), -3.5 (C^{1'}), -5.0 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{18}H_{28}BrOSi$ 367.1087; Found 367.1089.

tert-Butyl(1-(5-iodo-8-methylchroman-4-yl)vinyl)-dimethylsilane (4g)



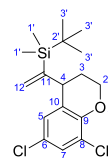
The reaction was performed according to the general procedure E from aryl ether **2g** to yield crude product, which, after column chromatography on $AgNO_3$ -impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 35%), provided chromane **4g** as a pale yellow solid (144 mg, 49%). 1H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, $^3J_{H-H} = 7.9$ Hz, 1H, H-C⁶), 6.71 (d, $^3J_{H-H} = 7.9$ Hz, 1H, H-C⁷), 5.67 (d, $^2J_{H-H} = 2.0$ Hz, 1H, H₂C¹²), 5.02 (dd, $^3J_{H-H} = 2.0$ Hz, $^4J_{H-H} = 1.6$ Hz, 1H, H₂C¹²), 4.20 (dddd, $^2J_{H-H} = 10.7$ Hz, $^3J_{H-H} = 4.0$, 3.3 Hz, $^4J_{H-H} = 1.6$ Hz, 1H, H₂C²), 4.03 (ddd, $^2J_{H-H} = 10.7$ Hz, $^3J_{H-H} = 12.9$, 2.1 Hz, 1H, H₂C²), 3.75 (ddt, $^3J_{H-H} = 5.5$, 0.9 Hz, $^4J_{H-H} = 1.6$ Hz, 1H, HC⁴), 2.14 (s, 3H, H₃C¹⁰), 2.04 (dddd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 12.9$, 5.5, 4.0 Hz, 1H, H₂C³), 1.81 (dddd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 3.3$, 2.1, 0.9 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.25 (s, 3H, H₃C^{1'}), 0.23 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 154.4 (C⁹), 151.5 (C¹¹), 131.4 (C¹²), 130.6 (C⁶), 130.4 (C⁷), 126.1 (C⁸), 125.9 (C¹⁰), 99.8 (C⁵), 61.6 (C²), 45.3 (C⁴), 27.6 (C^{3'}), 26.0 (C³), 17.5 (C^{2'}), 16.3 (C^{10'}), -3.2 (C^{1'}), -5.3 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{18}H_{28}IOSi$ 415.0949; Found 415.0948.

(1-(5-Bromo-8-fluorochroman-4-yl)vinyl)(tert-butyl)-dimethylsilane (4h)



The reaction was performed according to the general procedure E from aryl ether **2h** to yield crude product, which, after column chromatography on $AgNO_3$ -impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 35%), provided chromane **4h** as a colorless solid (137 mg, 46%). 1H NMR (500 MHz, $CDCl_3$): δ 7.02 (d, $^3J_{H-H} = 4.6$ Hz, $^3J_{H-H} = 8.7$ Hz, 1H, H-C⁶), 6.86 (d, $^3J_{H-H} = 10.5$ Hz, $^3J_{H-H} = 8.7$ Hz, 1H, H-C⁷), 5.66 (d, $^2J_{H-H} = 1.7$ Hz, 1H, H₂C¹²), 5.04 (dd, $^2J_{H-H} = 1.7$ Hz, $^4J_{H-H} = 1.4$ Hz, 1H, H₂C¹²), 4.31 (dddd, $^2J_{H-H} = 10.8$ Hz, $^3J_{H-H} = 3.9$, 2.2 Hz, $^4J_{H-H} = 1.3$ Hz, 1H, H₂C²), 4.06 (ddd, $^2J_{H-H} = 10.8$ Hz, $^3J_{H-H} = 13.0$, 2.2 Hz, 1H, H₂C²), 3.89 (ddt, $^3J_{H-H} = 5.6$, 1.9 Hz, $^4J_{H-H} = 1.4$, 1.3 Hz, 1H, HC⁴), 2.07 (dddd, $^2J_{H-H} = 14.2$ Hz, $^3J_{H-H} = 13.0$, 5.6, 3.9 Hz, 1H, H₂C³), 1.85 (dddd, $^2J_{H-H} = 14.2$ Hz, $^3J_{H-H} = 2.2$, 1.9 Hz, 1H, H₂C³), 0.97 (s, 9H, H₃C^{3'}), 0.21 (s, 3H, H₃C^{1'}), 0.20 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 151.1 (C¹¹), 151.1 (d, $^1J_{C-F} = 245.0$ Hz, C⁸), 145.0 (d, $^2J_{C-F} = 11.4$ Hz, C⁹), 130.8 (C¹²), 126.4 (C⁷), 123.2 (d, $^3J_{C-F} = 6.8$ Hz, C⁶), 119.2 (d, $^3J_{C-F} = 3.3$ Hz, C¹⁰), 115.1 (d, $^2J_{C-F} = 19.3$ Hz, C⁷), 61.4 (C²), 40.7 (d, $^4J_{C-F} = 2.0$ Hz, C⁴), 27.4 (C^{3'}), 25.5 (C³), 17.4 (C^{2'}), -3.5 (C^{1'}), -5.0 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{17}H_{25}BrFOSi$ 371.0837; Found 371.0836.

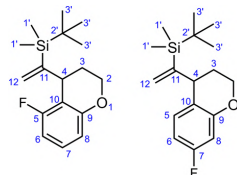
tert-Butyl(1-(6,8-dichlorochroman-4-yl)vinyl)-dimethylsilane (4i)



The reaction was performed according to the general procedure E from aryl ether **2i** to yield crude product, which, after column chromatography on $AgNO_3$ -impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 35%), provided chromane **4i** as a colorless solid (126 mg, 46%). 1H NMR (500 MHz, $CDCl_3$): δ 7.20 (d, $^3J_{H-H} = 2.5$ Hz, 1H, H-C⁷), 6.83 (d, $^3J_{H-H} = 2.5$ Hz, 1H, H-C⁶), 5.68 (s, 1H, H₂C¹²), 5.35 (s, 1H, H₂C¹²), 4.29–4.18 (m, 2H, H₂C²), 3.74 (dd, $^3J_{H-H} = 6.0$, 5.0 Hz, 1H, HC⁴), 2.09 (dddd, $^2J_{H-H} = 14.1$ Hz, $^3J_{H-H} = 8.8$, 6.0, 4.0 Hz, 1H, H₂C³), 1.80 (dddd, $^2J_{H-H} = 14.1$ Hz, $^3J_{H-H} = 5.4$, 5.0, 2.7 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.12 (s, 3H, H₃C^{1'}), 0.09 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 153.0 (C¹¹), 149.9 (C⁹), 131.6 (C¹²), 128.6 (C⁵), 128.0 (C⁷), 127.7 (C¹⁰), 124.5 (C⁶), 122.2 (C⁸), 63.5 (C²), 41.0 (C⁴), 27.7 (C³), 27.2 (C^{3'}), 17.6 (C^{2'}), -4.9 (C^{1'}), -5.1 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{17}H_{25}Cl_2OSi$ 343.1046; Found 343.1046.

tert-Butyl(1-(5-fluorochroman-4-yl)vinyl)dimethylsilane (o-4j) and

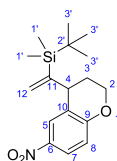
tert-Butyl(1-(7-fluorochroman-4-yl)vinyl)dimethylsilane (p-4j)



The reaction was performed according to the general procedure E from aryl ether **2j** to afford crude product mixture, which, after column chromatography on $AgNO_3$ -impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 35%), provided colorless oil (148 mg, 63%) consisting of two isomers **o-4j** and **p-4j** with ratio 41:59. Compound **o-4j** data: 1H NMR (500 MHz, $CDCl_3$): δ 7.06 (dt, $^4J_{H-F} = 6.6$ Hz, $^3J_{H-H} = 8.3$ Hz, 1H, H-C⁷), 6.63 (d, $^3J_{H-H} = 8.3$ Hz, 1H, H-C⁶), 6.55 (dd, $^3J_{H-F} = 8.4$ Hz, $^3J_{H-H} = 8.3$ Hz, 1H, H-C⁶), 5.59 (d, $^2J_{H-H} = 2.1$ Hz, 1H, H₂C¹²), 5.22 (dd, $^2J_{H-H} = 2.1$ Hz, $^4J_{H-H} = 1.1$ Hz,

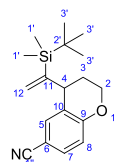
1H, H₂C¹²), 4.16 (dddd, ²J_{H-H} = 10.8 Hz, ³J_{H-H} = 3.6, 2.3 Hz, ⁴J_{H-H} = 1.0 Hz, 1H, H₂C²), 4.06 (ddd, ²J_{H-H} = 10.8 Hz, ³J_{H-H} = 12.6, 2.1 Hz, 1H, H₂C²), 3.89 (ddd, ³J_{H-H} = 5.9, 2.3 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.07 (dddd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 12.6, 5.9, 3.6 Hz, 1H, H₂C³), 1.85 (dddd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 2.3, 2.3, 2.1 Hz, 1H, H₂C³), 0.97 (s, 9H, H₃C^{3'}), 0.19 (s, 3H, H₃C^{1'}), 0.14 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 160.7 (d, ¹J_{C-F} = 245.5 Hz, C⁵), 156.6 (d, ¹J_{C-F} = 8.5 Hz, C⁹), 152.4 (C¹¹), 129.4 (C¹²), 127.8 (d, ³J_{C-F} = 10.6 Hz, C⁷), 112.6 (d, ²J_{C-F} = 21.3 Hz, C¹⁰), 112.1 (d, ⁴J_{C-F} = 3.1 Hz, C⁸), 106.6 (d, ²J_{C-F} = 22.1 Hz, C⁶), 60.9 (C²), 34.2 (d, ³J_{C-F} = 2.7 Hz, C⁴), 26.9 (C³), 26.3 (C³), 17.3 (C^{2'}), -4.8 (C^{1'}), -4.9 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₆FOSi 293.1731; Found 293.1732 (for mixture). Compound **p-4j** data: ¹H NMR (500 MHz, CDCl₃): δ 6.58 (dd, ⁴J_{H-F} = 6.6 Hz, ³J_{H-H} = 8.4 Hz, 1H, H-C⁷), 6.53 (dd, ³J_{H-F} = 9.4 Hz, ²J_{H-H} = 8.4 Hz, ⁴J_{H-H} = 2.6 Hz, 1H, H-C⁶), 6.50 (dd, ³J_{H-F} = 10.3 Hz, ²J_{H-H} = 2.6 Hz, 1H, H-C⁸), 5.62 (d, ²J_{H-H} = 2.2 Hz, 1H, H₂C¹²), 5.37 (dd, ²J_{H-H} = 2.2 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C²), 4.14–4.09 (m, 2H, H₂C²), 3.73 (ddd, ³J_{H-H} = 6.3, 5.0 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.08 (dddd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 6.3, 5.0, 2.0 Hz, 1H, H₂C³), 1.75 (dtd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 5.0, 3.4 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.08 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 162.0 (d, ¹J_{C-F} = 243.2 Hz, C⁷), 156.2 (d, ¹J_{C-F} = 11.9 Hz, C⁹), 153.7 (C¹¹), 131.3 (d, ³J_{C-F} = 9.76 Hz, C⁵), 130.8 (C¹²), 120.5 (d, ⁴J_{C-F} = 3.2 Hz, C¹⁰), 107.5 (d, ⁴J_{C-F} = 21.6 Hz, C⁶), 103.5 (d, ²J_{C-F} = 24.0 Hz, C⁸), 62.8 (C²), 40.4 (C⁴), 28.3 (C³), 27.2 (C^{3'}), 17.5 (C^{2'}), -4.9 (C^{1'}), -5.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₆FOSi 293.1731; Found 293.1732 (for mixture).

tert-Butyldimethyl(1-(6-nitrochroman-4-yl)vinyl)silane (**4k**)



The reaction was performed according to the general procedure E from aryl ether **2k** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 100%), provided chromane **4k** as a pale yellow solid (61 mg, 24%). ¹H NMR (500 MHz, CDCl₃): δ 7.37 (dd, ³J_{H-H} = 8.5 Hz, ⁴J_{H-H} = 2.0 Hz, 1H, H-C⁷), 7.26 (dd, ⁴J_{H-H} = 2.0 Hz, 1H, H-C⁵), 6.84 (dd, ³J_{H-H} = 8.5 Hz, 1H, H-C⁸), 5.68 (d, ²J_{H-H} = 1.9 Hz, 1H, H₂C¹²), 5.30 (dd, ²J_{H-H} = 1.9 Hz, ⁴J_{H-H} = 1.2 Hz, 1H, H₂C²), 4.20 (ddd, ²J_{H-H} = 11.2 Hz, ³J_{H-H} = 6.0, 4.5 Hz, 1H, H₂C²), 4.18 (ddd, ²J_{H-H} = 11.2 Hz, ³J_{H-H} = 8.2, 3.2 Hz, 1H, H₂C²), 3.75 (ddd, ³J_{H-H} = 6.0, 4.8 Hz, ⁴J_{H-H} = 1.2 Hz, 1H, HC⁴), 2.10 (dddd, ²J_{H-H} = 14.3 Hz, ³J_{H-H} = 8.2, 6.0, 4.5 Hz, 1H, H₂C³), 1.80 (dddd, ²J_{H-H} = 14.3 Hz, ³J_{H-H} = 5.2, 4.8, 3.2 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.12 (s, 3H, H₃C^{1'}), 0.10 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 159.1 (C⁹), 153.0 (C¹¹), 135.0 (C⁵), 131.6 (C⁷), 125.3 (C¹²), 126.1 (C¹⁰), 119.7 (C^{1'}), 117.8 (C⁸), 103.4 (C⁶), 63.2 (C²), 40.4 (C⁴), 27.7 (C³), 27.1 (C^{3'}), 17.6 (C^{2'}), -4.9 (C^{1'}), -5.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₆NO₃Si 320.1676; Found 320.1676.

4-(1-(*tert*-Butyldimethylsilyl)vinyl)chromane-6-carbonitrile (**4l**)

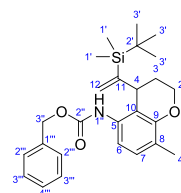


The reaction was performed according to the general procedure E from aryl ether **2l** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 100%), provided chromane **4l** as a pale yellow

solid (85 mg, 35%). ¹H NMR (500 MHz, CDCl₃): δ 8.00 (dd, ³J_{H-H} = 9.0 Hz, ⁴J_{H-H} = 2.8 Hz, 1H, H-C⁷), 7.91 (dd, ³J_{H-H} = 2.8 Hz, ⁴J_{H-H} = 0.9 Hz, 1H, H-C⁵), 6.86 (dd, ³J_{H-H} = 9.0 Hz, ⁴J_{H-H} = 0.9 Hz, 1H, H-C⁸), 5.71 (d, ²J_{H-H} = 1.8 Hz, 1H, H₂C¹²), 5.34 (dd, ²J_{H-H} = 1.8 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C²), 4.25 (ddd, ²J_{H-H} = 11.2 Hz, ³J_{H-H} = 4.8, 4.6 Hz, 1H, H₂C²), 4.22 (ddd, ²J_{H-H} = 11.2 Hz, ³J_{H-H} = 7.8, 3.4 Hz, 1H, H₂C²), 3.81 (ddd, ³J_{H-H} = 5.9, 5.3 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.12 (dddd, ²J_{H-H} = 14.1 Hz, ³J_{H-H} = 7.5, 5.9, 4.7 Hz, 1H, H₂C³), 1.86 (dddd, ²J_{H-H} = 14.1 Hz, ³J_{H-H} = 5.3, 4.8, 3.4 Hz, 1H, H₂C³), 0.98 (s, 9H, H₃C^{3'}), 0.14 (s, 3H, H₃C^{1'}), 0.10 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 160.9 (C⁹), 152.8 (C¹¹), 141.2 (C⁶), 131.7 (C¹²), 126.7 (C⁵), 125.4 (C¹⁰), 123.8 (C⁷), 117.3 (C⁸), 63.7 (C²), 40.9 (C⁴), 27.6 (C³), 27.2 (C^{3'}), 17.5 (C^{2'}), -4.9 (C^{1'}), -5.0 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₆NOSi 300.1778; Found 300.1777.

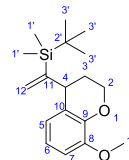
Benzyl

4-(1-(*tert*-butyldimethylsilyl)-vinyl)-8-methylchroman-5-yl)carbamate (**4m**)



The reaction was performed according to the general procedure E from aryl ether **2m** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 100%), provided chromane **4m** as a pale yellow solid (131 mg, 37%). ¹H NMR (500 MHz, CDCl₃): δ 7.39–7.30 (m, 5H, H-C^{2''}, H-C^{3''}, H-C^{4''}), 7.26–7.13 (m, 1H, H-C⁶), 7.01 (d, ³J_{H-H} = 8.1 Hz, 1H, H-C⁷), 6.24 (s, 1H, H₂C¹²), 5.73 (d, ⁴J_{H-H} = 1.8 Hz, 1H, H₂C¹²), 5.34 (br, 1H, HN^{1''}), 5.19 (d, ²J_{H-H} = 12.3 Hz, 1H, H₂C^{3''}), 5.14 (d, ²J_{H-H} = 12.3 Hz, 1H, H₂C^{3''}), 4.25 (dddd, ²J_{H-H} = 10.8 Hz, ³J_{H-H} = 3.5, 2.9, 1.1 Hz, 1H, H₂C²), 4.18 (ddd, ²J_{H-H} = 10.8 Hz, ³J_{H-H} = 12.6, 1.8 Hz, 1H, H₂C²), 3.63 (ddd, ²J_{H-H} = 6.4, 1.8 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.16 (s, 3H, H₃C^{4''}), 2.06 (dddd, ²J_{H-H} = 13.9 Hz, ³J_{H-H} = 12.6, 6.4, 3.5 Hz, 1H, H₂C³), 1.80 (dtd, ²J_{H-H} = 13.9 Hz, ³J_{H-H} = 2.9, 1.8 Hz, 1H, H₂C³), 0.95 (s, 9H, H₃C^{3'}), 0.17 (s, 3H, H₃C^{1'}), 0.16 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 154.0 (C^{2''}), 153.7 (C⁹), 152.0 (C¹¹), 136.4 (C^{1''}), 133.4 (C⁵), 131.8 (C¹²), 128.9 (C⁷), 128.6 (C⁶), 128.4 (C^{2''}), 128.4 (C^{4''}), 128.3 (C^{3''}), 122.1 (C⁸), 114.7 (C¹⁰), 113.8 (C⁶), 67.0 (C^{3''}), 60.4 (C²), 37.1 (C⁴), 27.3 (C^{3'}), 26.5 (C³), 17.3 (C^{2'}), 16.1 (C^{4''}), -3.7 (C^{1'}), -4.8 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₆H₃₆NO₃Si 438.2459; Found 438.2454.

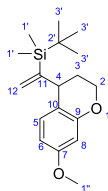
tert-Butyl(1-(8-methoxychroman-4-yl)vinyl)dimethylsilane (**4n**)



The reaction was performed according to the general procedure E from aryl ether **2n** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 100%), provided chromane **4n** as a colorless solid (212 mg, 87%). ¹H NMR (500 MHz, CDCl₃): δ 6.77 (dd, ³J_{H-H} = 8.1, 7.8 Hz, ⁴J_{H-H} = 1.8 Hz, 1H, H-C⁶), 6.71 (dd, ³J_{H-H} = 8.1 Hz, ⁴J_{H-H} = 1.6 Hz, 1H, H-C⁵), 6.58 (ddd, ³J_{H-H} = 7.8 Hz, ⁴J_{H-H} = 1.8, 0.7 Hz, 1H, H-C⁷), 5.64 (d, ²J_{H-H} = 2.3 Hz, 1H, H₂C¹²), 5.38 (dd, ²J_{H-H} = 2.3 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C²), 4.25 (ddd, ²J_{H-H} = 10.9 Hz, ³J_{H-H} = 5.1, 3.7

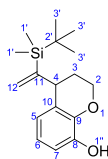
H₂, 1H, H₂C²), 4.20 (ddd, ²J_{H-H} = 10.9 Hz, ³J_{H-H} = 9.2, 2.7 Hz, 1H, H₂C³), 3.88 (s, 3H, H₃C¹⁰), 3.79 (td, ³J_{H-H} = 6.1, 4.8 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.13 (dddd, ²J_{H-H} = 13.9 Hz, ³J_{H-H} = 9.2, 6.1, 3.7 Hz, 1H, H₂C³), 1.76 (dddd, ²J_{H-H} = 13.9 Hz, ³J_{H-H} = 5.1, 4.8, 2.7 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.10 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.7 (C¹¹), 148.3 (C⁸), 145.0 (C⁹), 130.9 (C¹²), 125.4 (C¹⁰), 122.4 (C⁷), 119.5 (C⁶), 108.9 (C⁵), 62.8 (C²), 55.9 (C^{1'}), 40.5 (C⁴), 28.2 (C³), 27.2 (C^{3'}), 17.6 (C^{2'}), -4.9 (C^{1'}), -5.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₉O₂Si 305.1931; Found 305.1932.

tert-Butyl(1-(7-methoxychroman-4-yl)vinyl)dimethylsilane (4o)



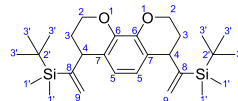
The reaction was performed according to the general procedure E from aryl ether **2o** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 100%), provided chromane **4o** as a colorless solid (85 mg, 35%). ¹H NMR (500 MHz, CDCl₃): δ 6.96 (dd, ³J_{H-H} = 8.4 Hz, ⁵J_{H-H} = 0.8 Hz, 1H, H-C⁵), 6.44 (dd, ³J_{H-H} = 8.4 Hz, ⁴J_{H-H} = 2.6 Hz, 1H, H-C⁶), 6.72 (dd, ⁴J_{H-H} = 2.6 Hz, ³J_{H-H} = 0.8 Hz, 1H, H-C⁸), 5.64 (d, ²J_{H-H} = 2.4 Hz, 1H, H₂C¹²), 5.39 (dd, ³J_{H-H} = 2.4 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C¹²), 4.25 (ddd, ³J_{H-H} = 10.9 Hz, ²J_{H-H} = 8.3, 3.0 Hz, 1H, H₂C²), 4.20 (ddd, ³J_{H-H} = 10.9 Hz, ²J_{H-H} = 5.3, 4.0 Hz, 1H, H₂C²), 3.76 (s, 3H, H₃C¹⁰), 3.72 (ddd, ³J_{H-H} = 6.2, 5.3 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.10 (dddd, ²J_{H-H} = 13.9 Hz, ³J_{H-H} = 8.3, 6.2, 4.0 Hz, 1H, H₂C³), 1.76 (ddd, ²J_{H-H} = 13.9 Hz, ³J_{H-H} = 5.3, 3.0 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.09 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 159.2 (C⁷), 156.2 (C⁹), 154.0 (C¹¹), 131.0 (C⁵), 130.5 (C¹²), 117.0 (C¹⁰), 107.5 (C⁶), 101.0 (C⁸), 62.8 (C²), 55.4 (C^{1'}), 40.3 (C⁴), 28.7 (C³), 27.2 (C^{3'}), 17.6 (C^{2'}), -4.9 (C^{1'}), -5.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₉O₂Si 305.1931; Found 305.1933.

4-(1-(*tert*-Butyldimethylsilyl)vinyl)chroman-8-ol (4q)



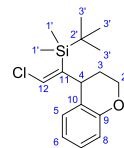
The reaction was performed according to the general procedure E from aryl ether **2q** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 100%), provided chromane **4q** as a colorless solid (186 mg, 80%). ¹H NMR (500 MHz, CDCl₃): δ 6.75 (dd, ³J_{H-H} = 7.8 Hz, ⁴J_{H-H} = 1.8 Hz, 1H, H-C⁵), 6.72 (dd, ³J_{H-H} = 7.8, 7.6 Hz, 1H, H-C⁶), 6.51 (ddd, ³J_{H-H} = 7.6 Hz, ⁴J_{H-H} = 1.8, 0.8 Hz, 1H, H-C⁷), 5.63 (d, ²J_{H-H} = 2.2 Hz, 1H, H₂C¹²), 5.49 (s, 1H, HO^{1'}), 5.40 (dd, ³J_{H-H} = 2.2 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C¹²), 4.24–4.17 (m, 2H, H₂C²), 3.78 (td, ³J_{H-H} = 5.1 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.13 (dddd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 7.5, 6.0, 5.1 Hz, 1H, H₂C³), 1.79 (dddd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 5.2, 5.1, 3.4 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.09 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.5 (C¹¹), 144.7 (C⁹), 142.6 (C⁷), 130.8 (C¹²), 125.1 (C¹⁰), 121.3 (C⁷), 120.1 (C⁶), 112.2 (C⁵), 63.2 (C²), 41.3 (C⁴), 28.7 (C³), 27.2 (C^{3'}), 17.6 (C^{2'}), -4.9 (C^{1'}), -5.3 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₇O₂Si [M + H]⁺ 291.1775; Found 291.1770.

4,7-Bis(1-(*tert*-butyldimethylsilyl)-vinyl)-2,3,4,7,8,9-hexahydopyrano[3,2-*h*]chromene (4r)



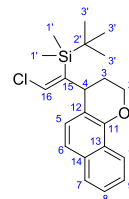
The reaction was performed according to the general procedure E from aryl ether **2r** to yield crude product, which, after column chromatography on AgNO₃-impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 → 67%), provided chromane **4r** as a colorless solid (266 mg, 71%). ¹H NMR (500 MHz, CDCl₃): δ 6.43 (s, 2H, H-C⁵), 5.62 (d, ²J_{H-H} = 2.3 Hz, 2H, H₂C⁹), 5.40 (dd, ³J_{H-H} = 2.3 Hz, ⁴J_{H-H} = 1.1 Hz, 2H, H₂C⁹), 4.25 (ddd, ³J_{H-H} = 10.9 Hz, ²J_{H-H} = 5.1, 3.5 Hz, 2H, H₂C²), 4.18 (ddd, ³J_{H-H} = 10.9 Hz, ²J_{H-H} = 9.8, 2.5 Hz, 2H, H₂C²), 3.76 (ddd, ³J_{H-H} = 6.2, 4.2 Hz, ⁴J_{H-H} = 1.1 Hz, 2H, HC⁴), 2.14 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 9.8, 6.2, 3.5 Hz, 2H, H₂C³), 1.72 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 5.1, 3.8, 2.5 Hz, 2H, H₂C³), 0.96 (s, 18H, H₃C^{3'}), 0.10 (s, 12H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.8 (C⁸), 144.1 (C⁶), 130.7 (C⁹), 122.9 (C⁷), 121.1 (C⁵), 62.4 (C²), 40.5 (C⁴), 28.2 (C³), 27.2 (C^{3'}), 17.6 (C^{2'}), -5.0 (C^{1'}), -5.3 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₈H₄₇O₂Si₂ 471.3109; Found 471.3101.

(*Z*)-*tert*-Butyl(2-chloro-1-(chroman-4-yl)vinyl)-dimethylsilane (10a)



The reaction was performed according to the general procedure E from chloroalkyne **6a** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 30%), provided chromane **10a** as a colorless solid (246 mg, 99%). ¹H NMR (500 MHz, CDCl₃): δ 7.10 (ddd, ³J_{H-H} = 7.9, 7.1 Hz, ⁴J_{H-H} = 1.7 Hz, 1H, H-C⁷), 6.99 (dd, ³J_{H-H} = 7.9 Hz, ⁴J_{H-H} = 1.7 Hz, ⁵J_{H-H} = 0.3 Hz, 1H, H-C⁸), 6.84 (ddd, ³J_{H-H} = 7.9, 7.1 Hz, ⁴J_{H-H} = 1.3 Hz, 1H, H-C⁸), 6.80 (dd, ³J_{H-H} = 7.9 Hz, ⁴J_{H-H} = 1.3 Hz, ⁵J_{H-H} = 0.3 Hz, 1H, H-C⁸), 6.44 (d, ⁴J_{H-H} = 0.9 Hz, 1H, HC¹²), 4.21–4.11 (m, 2H, H₂C²), 3.79 (ddd, ³J_{H-H} = 6.0, 4.8 Hz, ⁴J_{H-H} = 0.9 Hz, 1H, HC⁴), 2.11 (dddd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 7.9, 6.0, 5.1 Hz, 1H, H₂C³), 1.78 (ddd, ²J_{H-H} = 14.0 Hz, ³J_{H-H} = 4.8, 3.3 Hz, 1H, H₂C³), 1.05 (s, 9H, H₃C^{3'}), 0.34 (s, 3H, H₃C^{1'}), 0.18 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 155.3 (C⁹), 145.4 (C¹¹), 133.4 (C¹²), 130.4 (C⁵), 128.0 (C⁷), 124.1 (C¹⁰), 120.7 (C⁶), 117.0 (C⁸), 62.3 (C²), 40.4 (C⁴), 28.9 (C³), 27.9 (C^{3'}), 19.4 (C^{2'}), -3.0 (C^{1'}), -4.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₆ClO₂Si 309.1436; Found 309.1434.

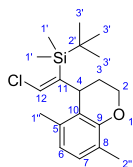
(*Z*)-*tert*-Butyl(1-(benzo[*h*]chroman-4-yl)-2-chlorovinyl)-dimethylsilane (10b)



The reaction was performed according to the general procedure E from chloroalkyne **6b** to yield crude product, which, after column chromatography on AgNO₃-impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 → 30%), provided chromane **10b** as a colorless solid (246 mg, 86%). ¹H NMR (500 MHz, CDCl₃): δ

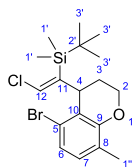
8.19–8.15 (m, 1H, H-C⁷), 7.77–7.71 (m, 1H, H-C¹⁰), 7.49–7.44 (m, 2H, H-C⁸, H-C⁹), 7.32 (d, ³J_{H-H} = 8.5 Hz, 1H, H-C⁶), 7.06 (d, ³J_{H-H} = 8.5 Hz, 1H, H-C⁵), 6.19 (s, 1H, HC¹⁶), 4.39 (ddd, ²J_{H-H} = 11.1 Hz, ³J_{H-H} = 4.7, 3.5 Hz, 1H, H₂C²), 4.26 (ddd, ²J_{H-H} = 11.1 Hz, ³J_{H-H} = 10.9, 2.4 Hz, 1H, H₂C²), 3.90 (ddd, ³J_{H-H} = 6.3, 3.4 Hz, 1H, HC⁴), 2.26 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 10.9, 6.3, 3.5 Hz, 1H, H₂C³), 1.83 (dddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 4.7, 3.4, 2.4 Hz, 1H, H₂C³), 1.09 (s, 9H, H₃C^{3'}), 0.35 (s, 3H, H₃C^{1'}), 0.25 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 150.5 (C¹¹), 145.5 (C¹⁵), 134.0 (C¹⁶), 133.5 (C¹⁴), 128.2 (C⁵), 127.5 (C¹⁰), 126.3 (C^{8/9}), 125.5 (C^{8/9}), 125.2 (C¹³), 121.8 (C⁷), 120.1 (C⁶), 117.0 (C¹²), 62.1 (C²), 40.2 (C⁴), 28.6 (C³), 27.9 (C^{3'}), 19.4 (C^{2'}), -3.0 (C^{1'}), -4.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₁H₂₈ClOSi 359.1592; Found 359.1593.

(Z)-tert-Butyl(2-chloro-1-(5,8-dimethylchroman-4-yl)vinyl)-dimethylsilane (10c)



The reaction was performed according to the general procedure E from chloroalkyne **6c** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 20%), provided chromane **10c** as a colorless solid (249 mg, 92%). ¹H NMR (500 MHz, CDCl₃): δ 6.91 (d, ³J_{H-H} = 7.5 Hz, 1H, H-C⁵), 6.62 (d, ³J_{H-H} = 7.5 Hz, 1H, H-C⁶), 5.96–5.94 (m, 1H, HC¹²), 4.25 (dddd, ²J_{H-H} = 11.0 Hz, ³J_{H-H} = 3.7, 2.5 Hz, ⁴J_{H-H} = 1.4 Hz, 1H, H₂C²), 4.03 (ddd, ²J_{H-H} = 11.0 Hz, ³J_{H-H} = 12.7, 2.0 Hz, 1H, H₂C²), 3.70 (dd, ³J_{H-H} = 5.7, 1.7 Hz, 1H, HC⁴), 2.16 (s, 3H, H₃C^{2'}), 2.10 (s, 3H, H₃C^{1'}), 2.07 (dddd, ²J_{H-H} = 13.5 Hz, ³J_{H-H} = 12.7, 5.7, 3.7 Hz, 1H, H₂C³), 1.82 (dddd, ²J_{H-H} = 13.5 Hz, ³J_{H-H} = 2.5, 1.7, 2.0 Hz, 1H, H₂C³), 1.04 (s, 9H, H₃C^{3'}), 0.35 (s, 3H, H₃C^{1'}), 0.29 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.1 (C⁹), 144.3 (C¹¹), 134.5 (C⁵), 132.5 (C¹²), 128.8 (C⁷), 123.5 (C⁸), 121.62 (C¹⁰), 121.2 (C⁶), 60.3 (C²), 37.6 (C⁴), 28.8 (C^{3'}), 26.6 (C³), 19.2 (C^{1'}), 18.6 (C^{2'}), 16.3 (C^{2'}), -3.5 (C^{1'}), -3.5 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₃₀ClOSi 337.1749; Found 337.1749.

(Z)-1-(5-Bromo-8-methylchroman-4-yl)-2-chlorovinyl)-tert-butyl)-dimethylsilane (10f)

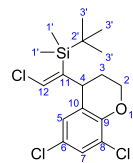


The reaction was performed according to the general procedure E from chloroalkyne **6f** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 20%), provided chromane **10f** as a colorless solid (292 mg, 91%). ¹H NMR (500 MHz, CDCl₃): δ 7.01 (d, ³J_{H-H} = 8.0 Hz, 1H, H-C⁶), 6.87 (d, ³J_{H-H} = 8.0 Hz, 1H, H-C⁵), 5.85 (d, ⁴J_{H-H} = 1.3 Hz, 1H, HC¹²), 4.28 (dddd, ²J_{H-H} = 11.0 Hz, ³J_{H-H} = 3.8, 2.4 Hz, ⁴J_{H-H} = 1.3 Hz, 1H, H₂C²), 4.05 (ddd, ²J_{H-H} = 11.0 Hz, ³J_{H-H} = 12.9, 2.1 Hz, 1H, H₂C²), 3.89 (dt, ³J_{H-H} = 5.7, 1.3 Hz, ⁴J_{H-H} = 1.3 Hz, 1H, HC⁴), 2.14 (s, 3H, H₃C^{1'}), 2.04 (dddd, ²J_{H-H} = 14.1 Hz, ³J_{H-H} = 12.9, 5.7, 3.8 Hz, 1H, H₂C³), 1.86 (dddd, ²J_{H-H} = 14.1 Hz, ³J_{H-H} = 2.4, 2.1, 1.7 Hz, 1H, H₂C³), 1.03 (s, 9H, H₃C^{3'}), 0.38 (s, 3H, H₃C^{1'}), 0.31 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 154.3 (C⁹), 144.1 (C¹¹), 132.3 (C¹²), 130.0 (C⁷), 125.4 (C⁸), 124.0 (C⁵), 122.5 (C^{5/10}), 122.4 (C^{5/10}), 61.0 (C²), 40.4 (C⁴), 28.9 (C^{3'}), 26.2 (C³), 18.5 (C^{2'}), 16.3 (C^{1'}), -3.5 (C^{1'}), -3.6 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₇BrClOSi 401.0698; Found 401.0695.

Gram-Scale Synthesis of Chromane 10f

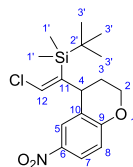
A 50 mL round-bottom flask, equipped with a Teflon-coated magnetic stirrer, was charged with aryl ether **6f** (2.75 g, 7.50 mmol, 1.0 equiv), then 1,2-dichloroethane (24 mL) was added, and the reaction mixture was heated up to 60 °C in the oil bath. Bistriflimide (HNTf₂) solution in 1,2-dichloroethane (0.25 M, 6 mL, 1.50 mmol, 0.2 equiv) was added, coloring the solution dark red and then dark violet within 1 min. Then, the reaction mixture was quenched by dropwise addition of triethylamine until decoloration (mixture becomes light yellow). The crude mixture was filtered through a short silica gel plug. The filtrate was concentrated in vacuo and filtered through a short silica gel plug, followed by washing with a 25% DCM solution in hexanes. The filtrate was concentrated and purified by column chromatography on silica gel (eluent system: DCM solution in hexanes, gradient 0 → 12%) to afford chromane **10f**, as a colorless solid (2.40 g, 87%).

(Z)-tert-Butyl(2-chloro-1-(6,8-dichlorochroman-4-yl)vinyl)-dimethylsilane (10i)



The reaction was performed according to the general procedure E from chloroalkyne **6i** to yield crude product, which, after column chromatography on AgNO₃-impregnated silica gel (eluent system: toluene in hexanes, gradient change 12 → 35%), provided chromane **10i** as a colorless solid (234 mg, 78%). ¹H NMR (500 MHz, CDCl₃): δ 7.22 (d, ⁴J_{H-H} = 2.5 Hz, 1H, H-C⁷), 6.87 (d, ⁴J_{H-H} = 2.5 Hz, 1H, H-C⁵), 6.21 (s, 1H, H₂C¹²), 4.15 (ddd, ²J_{H-H} = 11.4 Hz, ³J_{H-H} = 5.2, 3.5 Hz, 1H, H₂C²), 4.13 (ddd, ²J_{H-H} = 11.4 Hz, ³J_{H-H} = 9.7, 2.7 Hz, 1H, H₂C²), 3.78 (dd, ³J_{H-H} = 6.0, 4.6 Hz, 1H, HC⁴), 2.11 (dddd, ²J_{H-H} = 14.2 Hz, ³J_{H-H} = 9.7, 6.0, 3.5 Hz, 1H, H₂C³), 1.77 (dddd, ²J_{H-H} = 14.2 Hz, ³J_{H-H} = 5.2, 4.6, 2.7 Hz, 1H, H₂C³), 1.04 (s, 9H, H₃C^{3'}), 0.34 (s, 3H, H₃C^{1'}), 0.18 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 149.7 (C⁹), 144.7 (C¹¹), 133.9 (C¹²), 128.5 (C⁷), 128.3 (C⁵), 126.9 (C¹⁰), 124.9 (C⁶), 122.7 (C⁸), 63.2 (C²), 40.6 (C⁴), 28.1 (C³), 27.9 (C^{3'}), 19.3 (C^{2'}), -3.1 (C^{1'}), -4.1 (C^{1'}). HRMS (ESI) *m/z*: [M - Bu]⁺ Calcd for C₁₃H₁₄Cl₂OSi 318.9874; Found 318.9871.

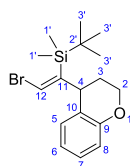
(Z)-tert-Butyl(2-chloro-1-(6-nitrochroman-4-yl)vinyl)-dimethylsilane (10k)



The reaction was performed according to the general procedure E from chloroalkyne **6k** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 → 100%), provided chromane **10k** as a colorless solid (87 mg, 62%). ¹H NMR (500 MHz, CDCl₃): δ 8.01 (dd, ³J_{H-H} = 9.1 Hz, ⁴J_{H-H} = 2.8 Hz, 1H, H-C⁷), 7.95 (d, ⁴J_{H-H} = 2.8 Hz, 1H, H-C⁵), 6.88 (d, ³J_{H-H} = 9.1 Hz, 1H, H-C⁸), 6.20 (s, 1H, H₂C¹²), 4.29 (ddd, ²J_{H-H} = 11.4 Hz, ³J_{H-H} = 5.6, 3.9 Hz, 1H, H₂C²), 4.24 (ddd, ²J_{H-H} = 11.4 Hz, ³J_{H-H} = 9.2, 2.9 Hz, 1H, H₂C²), 3.81 (dd, ³J_{H-H} = 5.8, 5.0 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, HC⁴), 2.12 (dddd, ²J_{H-H} = 14.1 Hz, ³J_{H-H} = 9.2, 5.8, 3.9 Hz, 1H, H₂C³), 1.87 (dddd, ²J_{H-H} = 14.1 Hz, ³J_{H-H} = 5.6, 5.0, 2.9 Hz, 1H, H₂C³), 1.06 (s, 9H, H₃C^{3'}), 0.35 (s, 3H, H₃C^{1'}), 0.20 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 160.5 (C⁹), 144.7 (C¹¹), 141.4 (C⁶), 133.9 (C¹²), 126.5 (C⁵), 124.7 (C¹⁰), 124.2 (C⁷), 117.7 (C⁸), 63.4 (C²), 40.5 (C⁴), 27.9 (C³), 27.9 (C^{3'}), 19.3 (C^{2'}), -3.1 (C^{1'}), -4.0 (C^{1'}). HRMS

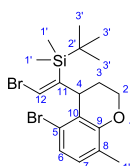
(ESI) m/z : $[M + H]^+$ Calcd for $C_{17}H_{25}ClNO_3Si$ 354.1287; Found 354.1286.

(Z)-(2-Bromo-1-(chroman-4-yl)vinyl)(tert-butyl)-dimethylsilane (11a)



The reaction was performed according to the general procedure E from bromoalkyne **7a** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 20%), provided chromane **11a** as a colorless solid (241 mg, 85%). 1H NMR (500 MHz, $CDCl_3$): δ 7.10 (ddd, $^3J_{H-H} = 8.2$, 7.1 Hz, $^4J_{H-H} = 1.7$ Hz, 1H, H-C⁷), 6.99 (dd, $^3J_{H-H} = 7.8$ Hz, $^4J_{H-H} = 1.7$ Hz, 1H, H-C⁵), 6.84 (ddd, $^3J_{H-H} = 7.8$, 7.1 Hz, $^4J_{H-H} = 1.3$ Hz, 1H, H-C⁶), 6.80 (dd, $^3J_{H-H} = 8.2$ Hz, $^4J_{H-H} = 1.3$ Hz, 1H, H-C⁸), 6.44 (d, $^4J_{H-H} = 0.9$ Hz, 1H, HC¹²), 4.18–4.06 (m, 2H, H₂C²), 3.83 (ddd, $^3J_{H-H} = 6.1$, 4.8 Hz, $^4J_{H-H} = 0.9$ Hz, 1H, HC⁴), 2.13 (dddd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 8.8$, 6.1, 4.3 Hz, 1H, H₂C³), 1.76 (dtd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 4.8$, 2.9 Hz, 1H, H₂C³), 1.07 (s, 9H, H₃C^{3'}), 0.39 (s, 3H, H₃C^{1'}), 0.23 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 155.4 (C⁹), 149.0 (C¹¹), 130.4 (C⁵), 128.1 (C⁷), 123.9 (C¹⁰), 122.4 (C¹²), 120.7 (C⁶), 117.0 (C⁸), 62.2 (C²), 42.2 (C⁴), 28.8 (C³), 28.0 (C^{3'}), 19.5 (C^{2'}), –2.5 (C^{1'}), –3.9 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{17}H_{26}BrOSi$ 353.0931; Found 353.0929.

(Z)-(2-Bromo-1-(5-bromo-8-methylchroman-4-yl)vinyl)-(tert-butyl)dimethylsilane (11f)



The reaction was performed according to the general procedure E from bromoalkyne **7f** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 20%), provided chromane **11f** as a colorless solid (297 mg, 83%). 1H NMR (500 MHz, $CDCl_3$): δ 7.01 (d, $^3J_{H-H} = 8.0$ Hz, 1H, H-C⁶), 6.88 (d, $^3J_{H-H} = 8.0$ Hz, 1H, H-C⁷), 6.08 (d, $^4J_{H-H} = 1.3$ Hz, 1H, HC¹²), 4.23 (dddd, $^2J_{H-H} = 11.1$ Hz, $^3J_{H-H} = 3.8$, 2.4 Hz, $^4J_{H-H} = 1.3$ Hz, 1H, H₂C²), 4.04 (ddd, $^2J_{H-H} = 11.1$ Hz, $^3J_{H-H} = 12.8$, 2.1 Hz, 1H, H₂C²), 3.91 (ddt, $^3J_{H-H} = 5.7$, 1.7 Hz, $^4J_{H-H} = 1.3$ Hz, 1H, HC⁴), 2.14 (s, 3H, H₃C^{1'}), 2.01 (dddd, $^2J_{H-H} = 14.1$ Hz, $^3J_{H-H} = 12.9$, 5.7, 3.8 Hz, 1H, H₂C³), 1.87 (dddd, $^2J_{H-H} = 14.1$ Hz, $^3J_{H-H} = 2.4$, 2.1, 1.7 Hz, 1H, H₂C³), 1.06 (s, 9H, H₃C^{3'}), 0.42 (s, 3H, H₃C^{1'}), 0.34 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 154.4 (C⁹), 147.7 (C¹¹), 130.1 (C⁷), 125.4 (C⁸), 124.1 (C⁶), 122.5 (C⁵), 122.3 (C¹⁰), 121.2 (C¹²), 70.0 (C²), 42.4 (C⁴), 29.2 (C³), 26.0 (C³), 18.5 (C^{2'}), 16.2 (C^{1'}), –3.1 (C^{1'}), –5.1 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{18}H_{27}Br_2OSi$ 445.0192; Found 445.0191.

Gram-Scale Synthesis of Chromane 11f

A 50 mL round-bottom flask, equipped with a Teflon-coated magnetic stirrer, was charged with aryl ether **7f** (2.16 g, 4.84 mmol, 1.0 equiv), then 1,2-dichloroethane (18 mL) was added, and the reaction mixture was heated up to 60 °C in the oil bath. Bistriflimide (HNTrf) solution in 1,2-dichloroethane (0.16 M, 6 mL, 0.96 mmol, 0.2 equiv) was added, coloring the solution dark red and then dark violet within 1 min. Then, the reaction mixture was quenched by dropwise addition of triethylamine until decoloration (mixture becomes light yellow). The crude mixture was filtered through a short silica gel plug. The filtrate was concentrated in vacuo and filtered through a short silica gel plug,

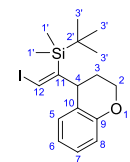
followed by washing with a 25% DCM solution in hexanes. The filtrate was concentrated and purified by column chromatography on silica gel (eluent system: DCM solution in hexanes, gradient 0 $\rightarrow$ 12%) to afford chromane **11f**, as a colorless solid (1.72 g, 80%).

(Z)-(2-Bromo-1-(6-nitrochroman-4-yl)vinyl)(tert-butyl)-dimethylsilane (11k)



The reaction was performed according to the general procedure E from bromoalkyne **7k** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 100%), provided chromane **11k** as a colorless solid (121 mg, 38%). 1H NMR (500 MHz, $CDCl_3$): δ 8.01 (dd, $^3J_{H-H} = 9.1$ Hz, $^4J_{H-H} = 2.8$ Hz, 1H, H-C⁷), 7.94 (dd, $^4J_{H-H} = 2.8$ Hz, $^5J_{H-H} = 0.9$ Hz, 1H, H-C⁵), 6.88 (dd, $^3J_{H-H} = 9.1$ Hz, $^5J_{H-H} = 0.9$ Hz, 1H, H-C⁸), 6.40 (s, 1H, H₂C¹²), 4.29 (ddd, $^2J_{H-H} = 11.4$ Hz, $^3J_{H-H} = 5.1$, 3.7 Hz, 1H, H₂C²), 4.22 (ddd, $^2J_{H-H} = 11.4$ Hz, $^3J_{H-H} = 9.7$, 2.8 Hz, 1H, H₂C²), 3.86 (dd, $^3J_{H-H} = 5.8$, 4.6 Hz, 1H, HC⁴), 2.13 (dddd, $^2J_{H-H} = 14.1$ Hz, $^3J_{H-H} = 9.7$, 5.8, 3.7 Hz, 1H, H₂C³), 1.85 (dddd, $^2J_{H-H} = 14.1$ Hz, $^3J_{H-H} = 5.1$, 4.6, 2.8 Hz, 1H, H₂C³), 1.08 (s, 9H, H₃C^{3'}), 0.40 (s, 3H, H₃C^{1'}), 0.25 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 160.6 (C⁹), 148.3 (C¹¹), 141.4 (C⁶), 126.5 (C⁵), 124.4 (C¹⁰), 124.2 (C⁷), 122.7 (C¹²), 117.7 (C⁸), 63.2 (C²), 42.1 (C⁴), 28.0 (C³), 27.7 (C³), 19.5 (C^{2'}), –2.6 (C^{1'}), –3.7 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{17}H_{23}BrNO_3Si$ 398.0782; Found 398.0780.

(Z)-tert-Butyl(1-(chroman-4-yl)-2-iodovinyl)dimethylsilane (12a)

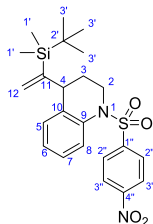


The reaction was performed according to the general procedure E from iodoalkyne **8a** to yield crude product, which, after column chromatography on silica gel (eluent system: toluene in hexanes, gradient change 12 $\rightarrow$ 20%), provided chromane **12a** as a colorless solid (175 mg, 55%). 1H NMR (500 MHz, $CDCl_3$): δ 7.11 (ddd, $^3J_{H-H} = 8.2$, 7.1 Hz, $^4J_{H-H} = 1.7$ Hz, 1H, H-C⁷), 6.98 (ddd, $^3J_{H-H} = 7.7$ Hz, $^4J_{H-H} = 1.7$ Hz, $^5J_{H-H} = 0.8$ Hz, 1H, H-C⁵), 6.84 (ddd, $^3J_{H-H} = 7.7$, 7.1 Hz, $^4J_{H-H} = 1.3$ Hz, 1H, H-C⁶), 6.80 (ddd, $^3J_{H-H} = 8.2$ Hz, $^4J_{H-H} = 1.3$ Hz, $^5J_{H-H} = 0.8$ Hz, 1H, H-C⁸), 6.64 (d, $^4J_{H-H} = 0.9$ Hz, 1H, HC¹²), 4.15 (ddd, $^2J_{H-H} = 11.2$ Hz, $^3J_{H-H} = 5.2$, 3.6 Hz, 1H, H₂C²), 4.13 (ddd, $^2J_{H-H} = 11.2$ Hz, $^3J_{H-H} = 9.4$, 2.7 Hz, 1H, H₂C²), 3.78 (dd, $^3J_{H-H} = 6.1$, 4.4 Hz, $^4J_{H-H} = 0.9$ Hz, 1H, HC⁴), 2.11 (dddd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 9.4$, 6.1, 3.6 Hz, 1H, H₂C³), 1.77 (dddd, $^2J_{H-H} = 14.0$ Hz, $^3J_{H-H} = 5.2$, 4.4, 2.7 Hz, 1H, H₂C³), 1.09 (s, 9H, H₃C^{3'}), 0.45 (s, 3H, H₃C^{1'}), 0.28 (s, 3H, H₃C^{1'}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 156.0 (C⁹), 155.5 (C¹¹), 130.4 (C⁵), 128.1 (C⁷), 123.8 (C¹⁰), 120.7 (C⁶), 117.0 (C⁸), 94.5 (C¹²), 62.2 (C²), 44.4 (C⁴), 28.9 (C³), 28.1 (C³), 19.8 (C^{2'}), –2.0 (C^{1'}), –3.7 (C^{1'}). HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{17}H_{26}IOSi$ 401.0792; Found 401.0793.

General Procedure F: Synthesis of Tetrahydroquinolines 5 and 13. A 10 mL vial, equipped with a Teflon-coated magnetic stirrer, was charged with the corresponding tertiary amide **3** or **9** (1.0 equiv), and nitromethane $MeNO_2$ was added to get a 0.2 M solution. While stirring, bistriflimide (HNTrf) solution in nitromethane (0.6 M, 1.0 equiv) was added in one portion to the solution, and the reaction mixture was allowed to stir for 30 min. Then, the reaction was quenched by the addition of a few drops of triethylamine and concentrated in

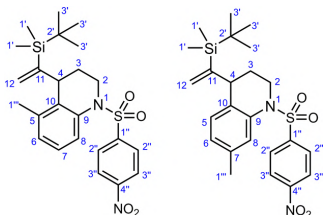
vacuo. The crude product was purified by column chromatography on silica gel (eluent system: 30 → 50% DCM solution in hexanes) to afford pure tetrahydroquinolines **5** or **13**.

4-(1-(*tert*-Butyldimethylsilyl)vinyl)-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (**5a**)



The reaction was performed according to the general procedure with minor deviations from the original amounts and stoichiometry. Nossylamide **3a** (50 mg, 0.11 mmol, 1.0 equiv), HNTf₂ (0.1 M solution in MeNO₂, 1.3 mL, 0.11 mmol, 1.0 equiv), and MeNO₂ (2 mL) were used for the reaction proceeding at 0 °C for 1 h, and 0.03 mL Et₃N was used for workup. The reaction mixture was concentrated in vacuo and purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change 50 → 60%) to yield tetrahydroquinoline **5a** as a yellow solid (20 mg, 40%). ¹H NMR (500 MHz, CDCl₃): δ 8.24 (d, ³J_{H-H} = 8.8 Hz, 2H, H-C^{3a}), 7.86 (dd, ³J_{H-H} = 8.3 Hz, ⁴J_{H-H} = 1.6 Hz, 1H, H-C⁸), 7.80 (d, ³J_{H-H} = 8.8 Hz, 2H, H-C^{2a}), 7.23 (ddd, ³J_{H-H} = 8.3, 7.3 Hz, ⁴J_{H-H} = 1.6 Hz, 1H, H-C⁷), 7.09 (ddd, ³J_{H-H} = 7.7, 7.3 Hz, ⁴J_{H-H} = 1.2 Hz, 1H, H-C⁶), 6.96 (dd, ³J_{H-H} = 7.7 Hz, ⁴J_{H-H} = 1.6 Hz, 1H, H-C⁵), 5.40 (d, ²J_{H-H} = 1.8 Hz, 1H, H₂C¹²), 4.91 (s, 1H, H₂C¹²), 3.93–3.77 (m, 2H, H₂C³), 3.35 (t, ³J_{H-H} = 6.2 Hz, 1H, HC⁴), 1.83–1.72 (m, 1H, H₂C³), 1.55–1.46 (m, 1H, H₂C³), 0.85 (s, 9H, H₃C^{3'}), 0.01 (s, 3H, H₃C^{1'}), –0.05 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.2 (C¹¹), 150.2 (C^{4a}), 145.1 (C^{1a}), 136.5 (C⁹), 133.4, 130.3 (C⁸), 130.1 (C¹²), 128.5 (C^{2a}), 127.2 (C⁷), 125.5 (C⁶), 124.3 (C^{3a}), 123.9 (C⁸), 44.5 (C²), 42.2 (C⁴), 28.5 (C³), 27.0 (C^{3'}), 17.4 (C^{2'}), –5.3 (C^{1'}), –5.5 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₃H₃₁N₂O₄Si 459.1774; Found 459.1756.

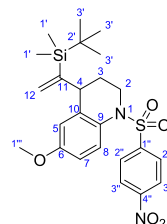
4-(1-(*tert*-Butyldimethylsilyl)vinyl)-5-methyl-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (**o**-**5e**) and 4-(1-(*tert*-butyldimethylsilyl)vinyl)-7-methyl-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (**p**-**5e**)



The reaction was performed according to the general procedure with minor deviations from the original amounts and stoichiometry. Nossylamide **3e** (150 mg, 0.32 mmol, 1.0 equiv), HNTf₂ (0.1 M solution in MeNO₂, 3.2 mL, 0.32 mmol, 1.0 equiv), and MeNO₂ (6 mL) were used for the reaction, and 0.08 mL of Et₃N was used for workup. The reaction mixture was concentrated in vacuo and purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change 40 → 50%) to afford yellow solid (76 mg, 51%) consisting of two isomers **o**-**5e** and **p**-**5e** with the ratio 42:58. Compound **o**-**5e** data: ¹H NMR (500 MHz, CDCl₃): δ 8.22 (d, ³J_{H-H} = 8.7 Hz, 2H, H-C^{3a}), 7.85 (d, ³J_{H-H} = 8.6 Hz, 1H, H-C⁸), 7.82 (d, ³J_{H-H} = 8.7 Hz, 2H, H-C^{2a}), 7.13 (dd, ³J_{H-H} = 8.6, 7.4 Hz, 1H, H-C⁷), 6.94 (d, ³J_{H-H} = 7.4 Hz, 1H, H-C⁶), 5.12 (dd, ²J_{H-H} = 1.7 Hz, 1H,

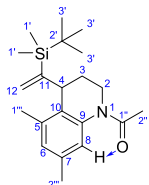
H₂C¹²), 4.37 (t, ^{2,4}J_{H-H} = 1.7 Hz, 1H, H₂C¹²), 4.10 (dt, ²J_{H-H} = 12.9 Hz, ³J_{H-H} = 3.9 Hz, 1H, H₂C³), 3.62 (d, ³J_{H-H} = 5.5 Hz, 1H, HC⁴), 3.45 (td, ²J_{H-H} = 12.9 Hz, ³J_{H-H} = 12.9, 3.2 Hz, 1H, H₂C²), 2.05 (s, 3H, H₃C^{1a}), 1.84–1.62 (m, 2H, H₂C³), 0.90 (s, 9H, H₃C^{3'}), 0.10 (s, 3H, H₃C^{1'}), 0.09 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 151.1 (C¹¹), 150.3 (C^{4a}), 144.8 (C^{1a}), 137.5 (C⁹), 137.0 (C⁹), 129.9 (C¹⁰), 129.5 (C¹²), 128.7 (C^{2a}), 127.3 (C⁶), 126.9 (C⁷), 124.2 (C^{3a}), 120.4 (C⁸), 42.6 (C²), 39.9 (C⁴), 27.3 (C^{3'}), 25.5 (C³), 20.0 (C^{1a}), 17.4 (C^{2'}), –3.5 (C^{1'}), –5.0 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₄H₃₃N₂O₄Si 473.1930; Found 473.1912 (for mixture). Compound **p**-**5e** data: ¹H NMR (500 MHz, CDCl₃): δ 8.24 (d, ³J_{H-H} = 8.8 Hz, 2H, H-C^{3a}), 7.80 (d, ³J_{H-H} = 8.8 Hz, 2H, H-C^{2a}), 7.68 (s, 1H, H-C⁸), 6.91 (d, ³J_{H-H} = 7.9 Hz, 1H, H-C⁶), 6.83 (d, ³J_{H-H} = 7.9 Hz, 1H, H-C⁵), 5.39 (d, ²J_{H-H} = 2.1 Hz, 1H, H₂C¹²), 4.92 (dd, ²J_{H-H} = 2.1 Hz, ⁴J_{H-H} = 1.1 Hz, 1H, H₂C¹²), 3.90–3.73 (m, 2H, H₂C³), 3.30 (t, ³J_{H-H} = 6.4 Hz, 1H, HC⁴), 2.36 (s, 3H, H₃C^{1a}), 1.84–1.62 (m, 1H, H₂C³), 1.52–1.38 (m, 1H, H₂C³), 0.84 (s, 9H, H₃C^{3'}), 0.00 (s, 3H, H₃C^{1'}), –0.05 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 153.4 (C¹¹), 150.2 (C^{4a}), 145.2 (C^{1a}), 136.7 (C⁹), 136.3 (C⁷), 130.4 (C¹⁰), 130.0 (C⁵), 129.8 (C¹²), 128.5 (C^{2a}), 126.6 (C⁶), 124.5 (C⁸), 124.3 (C^{3a}), 44.6 (C²), 41.8 (C⁴), 28.9 (C³), 27.0 (C^{3'}), 21.5 (C^{1a}), 17.4 (C^{2'}), –5.4 (C^{1'}), –5.5 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₄H₃₃N₂O₄Si 473.1930; Found 473.1912 (for mixture).

4-(1-(*tert*-Butyldimethylsilyl)vinyl)-6-methoxy-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (**5t**)



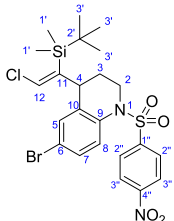
The reaction was performed following general procedure F: nossylamide **3t** (150 mg, 0.31 mmol, 1.0 equiv), HNTf₂ (0.1 M solution in MeNO₂, 3.6 mL, 0.31 mmol, 1.0 equiv), and MeNO₂ (6 mL). For workup, 0.08 mL of Et₃N was added. The reaction mixture was concentrated in vacuo and purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change 40 → 50%) to yield tetrahydroquinoline **5t** as a colorless solid (64 mg, 43%). ¹H NMR (500 MHz, CDCl₃): δ 8.24 (d, ³J_{H-H} = 8.9 Hz, 2H, H-C^{3a}), 7.79 (d, ³J_{H-H} = 9.0 Hz, 1H, H-C⁸), 7.75 (d, ³J_{H-H} = 8.9 Hz, 2H, H-C^{2a}), 6.80 (dd, ³J_{H-H} = 9.0 Hz, ⁴J_{H-H} = 3.0 Hz, 1H, H-C⁷), 6.48 (d, ⁴J_{H-H} = 3.0 Hz, 1H, H-C⁵), 5.41 (d, ²J_{H-H} = 2.0 Hz, 1H, H₂C¹²), 4.99 (dd, ²J_{H-H} = 2.0 Hz, ⁴J_{H-H} = 1.0 Hz, 1H, H₂C¹²), 3.89–3.76 (m, 2H, H₂C³), 3.75 (s, 3H, H₃C^{1a}), 3.20 (td, ³J_{H-H} = 6.7 Hz, ⁴J_{H-H} = 1.0 Hz, 1H, HC⁴), 1.78–1.66 (m, 1H, H₂C³), 1.47–1.34 (m, 1H, H₂C³), 0.83 (s, 9H, H₃C^{3'}), –0.01 (s, 3H, H₃C^{1'}), –0.07 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.2 (C⁶), 152.9 (C¹¹), 150.2 (C^{4a}), 145.1 (C^{1a}), 135.7 (C⁹), 130.1 (C¹²), 129.4 (C¹⁰), 128.6 (C^{2a}), 126.1 (C⁸), 124.3 (C^{3a}), 114.7 (C⁵), 112.8 (C⁷), 55.4 (C^{1a}), 44.9 (C²), 42.2 (C⁴), 28.9 (C³), 27.0 (C^{3'}), 17.4 (C^{2'}), –5.5 (C^{1'}), –5.6 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₄H₃₃N₂O₅Si 489.1879; Found 489.1850.

N-Acetyl-4-(1-(*tert*-butyldimethylsilyl)-vinyl)-5,7-dimethyl-1,2,3,4-tetrahydroquinoline (5u)



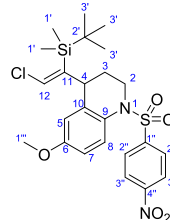
The reaction was performed following a slightly modified general procedure F: aryl acetamide **3u** (62 mg, 0.18 mmol, 1.0 equiv), HNTf₂ (0.7 M solution in MeNO₂, 0.77 mL, 0.54 mmol, 3.0 eq.) and MeNO₂ (2 mL). For workup, 0.04 mL of Et₃N was added. The reaction mixture was concentrated in vacuo and purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change 80 → 90%) to yield tetrahydroquinoline **5u** as a colorless oil (28 mg, 45%). ¹H NMR (500 MHz, CDCl₃): δ 6.85 (br, 1H, H-C⁸), 6.82 (s, 1H, H-C⁶), 5.36 (s, 1H, H₂C¹²), 5.09 (s, 1H, H₂C¹²), 3.87–3.80 (m, 1H, HC⁴), 3.80–3.64 (m, 1H, H₂C²), 3.64–3.49 (m, 1H, H₂C²), 2.31 (s, 3H, H₃C^{2''}), 2.20 (s, 3H, H₃C^{2''}), 2.16 (s, 3H, H₃C^{1''}), 2.13–2.05 (m, 1H, H₂C³), 1.91–1.80 (m, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.18 (s, 3H, H₃C^{1'}), 0.15 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): 170.5 (C^{1''}), 149.1 (C¹¹), 139.3 (C⁹), 136.1 (C⁵), 135.7 (C⁷), 130.8 (C¹⁰), 127.8 (C⁶), 127.8 (C¹²), 123.2 (C⁸), 41.6 (C²), 40.7 (C⁴), 28.8 (C^{3'}), 27.3 (C³), 23.5 (C^{2''}), 21.4 (C^{2''}), 19.7 (C^{1''}), 17.4 (C^{2'}), –3.7 (C^{1'}), –4.7 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₁H₃₄NOSi 344.2410; Found 344.2386.

(Z)-6-Bromo-4-(1-(*tert*-butyldimethylsilyl)-2-chlorovinyl)-1-(4-nitrophenyl)sulfonyl-1,2,3,4-tetrahydroquinoline (13r)



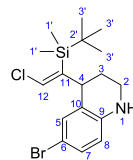
The reaction was performed according to the general procedure F. Chloroalkyne **9r** (100 mg, 0.17 mmol, 1.0 equiv), HNTf₂ (0.6 M solution in MeNO₂, 0.29 mL, 0.17 mmol, 1.0 equiv), and MeNO₂ (4 mL) were used for the reaction, and 0.06 mL Et₃N was used for workup. The reaction mixture was concentrated in vacuo and purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change 30 → 50%) to yield tetrahydroquinoline **13r** as a light-yellow solid (71 mg, 71%). ¹H NMR (500 MHz, CDCl₃): δ 8.30 (d, ³J_{H-H} = 8.6 Hz, 2H, H-C^{3''}), 7.83 (d, ³J_{H-H} = 8.6 Hz, 2H, H-C^{2''}), 7.81 (d, ³J_{H-H} = 8.9 Hz, 1H, H-C⁸), 7.36 (dd, ³J_{H-H} = 8.9 Hz, ⁴J_{H-H} = 2.4 Hz, 1H, H-C⁷), 7.08 (d, ⁴J_{H-H} = 2.4 Hz, 1H, H-C⁵), 5.59 (s, 1H, HC¹²), 3.89–3.75 (m, 2H, H₂C²), 3.36 (t, ³J_{H-H} = 6.3 Hz, 1H, HC⁴), 1.89–1.79 (m, 1H, H₂C³), 1.61–1.51 (m, 1H, H₂C³), 0.92 (s, 9H, H₃C^{3'}), 0.12 (s, 3H, H₃C^{1'}), 0.10 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 150.5 (C^{4''}), 144.4 (C¹¹), 144.3 (C^{1''}), 135.5 (C¹⁰), 134.8 (C⁹), 133.1 (C¹²), 132.8 (C⁵), 130.8 (C⁷), 128.5 (C^{2''}), 125.5 (C⁸), 124.6 (C^{3''}), 119.1 (C⁶), 44.4 (C²), 42.3 (C⁴), 28.5 (C³), 27.7 (C^{3'}), 19.1 (C^{2'}), –3.6 (C^{1'}), –4.0 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₃H₂₉BrClN₂O₄SSi 571.0484; Found 571.0479.

(Z)-4-(1-(*tert*-Butyldimethylsilyl)-2-chlorovinyl)-6-methoxy-1-(4-nitrophenyl)sulfonyl-1,2,3,4-tetrahydroquinoline (13t)



The reaction was performed according to the general procedure F. Chloroalkyne **9t** (100 mg, 0.19 mmol, 1.0 equiv), HNTf₂ (0.6 M solution in MeNO₂, 0.32 mL, 0.19 mmol, 1.0 equiv), and MeNO₂ (4 mL) were used for the reaction, and 0.04 mL Et₃N was used for workup. The reaction mixture was concentrated in vacuo and purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change 30 → 50%) to yield tetrahydroquinoline **13t** as a light-yellow solid (77 mg, 77%). ¹H NMR (500 MHz, CDCl₃): δ 8.26 (d, ³J_{H-H} = 8.7 Hz, 2H, H-C^{3''}), 7.81 (d, ³J_{H-H} = 9.1 Hz, 1H, H-C⁸), 7.77 (d, ³J_{H-H} = 8.7 Hz, 2H, H-C^{2''}), 6.81 (dd, ³J_{H-H} = 9.1 Hz, ⁴J_{H-H} = 2.9 Hz, 1H, H-C⁷), 6.48 (d, ⁴J_{H-H} = 2.9 Hz, 1H, H-C⁵), 5.63 (s, 1H, HC¹²), 3.89 (ddd, ²J_{H-H} = 13.3 Hz, ³J_{H-H} = 6.7 Hz, 4.2 Hz, 1H, H₂C²), 3.76 (s, 3H, H₃C^{1''}), 3.80–3.71 (m, 1H, H₂C²), 3.29 (t, ³J_{H-H} = 6.9 Hz, 1H, HC⁴), 1.85–1.77 (m, 1H, H₂C³), 1.47–1.38 (m, 1H, H₂C³), 0.91 (s, 9H, H₃C^{3'}), 0.11 (s, 3H, H₃C^{1'}), 0.08 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 157.4 (C⁹), 150.3 (C^{4''}), 144.8 (C¹¹), 144.8 (C^{1''}), 135.0 (C¹⁰), 132.8 (C¹²), 129.2 (C⁹), 128.6 (C^{2''}), 126.3 (C⁸), 124.4 (C^{3''}), 114.7 (C⁵), 113.2 (C⁷), 55.5 (C^{1''}), 45.0 (C²), 42.3 (C⁴), 29.4 (C³), 27.5 (C^{3'}), 19.1 (C^{2'}), –3.6 (C^{1'}), –4.1 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₄H₃₂ClN₂O₅SSi 523.1490; Found 523.1463.

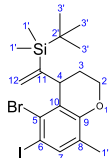
(Z)-6-Bromo-4-(1-(*tert*-butyldimethylsilyl)-2-chlorovinyl)-1,2,3,4-tetrahydroquinoline (14s)



The procedure was done according to the literature.⁷⁹ A 10 mL round-bottom flask, equipped with a Teflon-coated magnetic stirrer and septum, was charged with protected tetrahydroquinoline **13s** (20 mg, 0.035 mmol, 1.0 equiv) and Cs₂CO₃ (88 mg, 0.270 mmol, 7.7 equiv). The flask was evacuated and backfilled with argon. Then, MeCN (3 mL) was added, and the reaction mixture was stirred for 15 min at room temperature. To the resulting mixture, PhSH (0.05 mL, 0.49 mmol, 14.0 equiv) was added portionwise by syringe (0.01 mL at the start of the reaction, 0.02 mL after 1 h of stirring, and the last 0.02 mL of PhSH after 2 h of stirring). After an additional 4.5 h, the reaction was quenched by the addition of saturated NaHCO₃ (10 mL) solution, and the product was extracted with DCM (3 × 5 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. Crude product was purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change: 10 → 20%) to yield tetrahydroquinoline **14s** (13 mg, 96%) as a yellow oil. ¹H NMR (500 MHz, CDCl₃): δ 7.05 (d, ³J_{H-H} = 8.5 Hz, 1H, H-C⁷), 6.98 (s, 1H, H-C⁵), 6.36 (d, ³J_{H-H} = 8.5 Hz, 1H, H-C⁸), 6.15 (s, 1H, HC¹²), 3.95 (br, 1H, NH), 3.69 (t, ³J_{H-H} = 4.8 Hz, 1H, HC⁴), 3.30–3.15 (m, 2H, H₂C²), 1.92 (ddt, ³J_{H-H} = 13.8, 9.5, 4.8 Hz, 1H, H₂C³), 1.81–1.68 (m, 1H, H₂C³), 1.03 (s, 9H, H₃C^{3'}), 0.32 (s, 3H, H₃C^{1'}), 0.19 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 145.2 (C¹¹), 143.8 (C⁹), 133.2 (C¹²), 132.4 (C⁵), 130.3 (C⁷), 124.9 (C¹⁰), 115.7 (C⁸), 108.5 (C⁶),

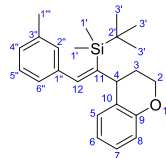
42.2 (C⁴), 37.5 (C²), 28.0 (C^{3'}), 27.4 (C³), 19.3 (C^{2'}), −3.1 (C^{1'}), −4.0 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₆BrClNSi 386.0706; Found 386.0686.

(1-(5-Bromo-6-iodo-8-methylchroman-4-yl)vinyl)-(tert-butyl)dimethylsilane (15f)



A 10 mL round-bottom flask, equipped with a Teflon-coated magnetic stirrer and a reflux condenser and shielded from light with aluminum foil coating, was charged with chromane **4f** (40 mg, 0.11 mmol, 1.0 equiv), and HFIP (3 mL) was added. An excess of NIS (54 mg, 0.24 mmol, 2.2 equiv) was added to the suspension upon stirring, and the temperature was raised to reflux. After 8 h, the reaction mixture was quenched by the addition of aqueous 10% Na₂S₂O₃ solution (4 mL), and the product was extracted with DCM (3 × 5 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. Crude product was purified by column chromatography on silica gel (eluent: hexanes) to yield aryl iodide **15f** as a colorless oil (53 mg, 99%). ¹H NMR (500 MHz, CDCl₃): δ 7.52 (s, 1H, H-C⁷), 5.63 (s, 1H, H₂C¹²), 5.03 (s, 1H, H₂C¹²), 4.22 (brd, ³J_{H-H} = 10.7 Hz, 1H, H₂C²), 4.06–3.93 (m, 2H, H₂C², HC⁴), 2.09 (s, 3H, H₃C^{1'}), 2.00 (tt, ²J_{H-H} = 13.6 Hz, ³J_{H-H} = 13.6, 4.8 Hz, 1H, H₂C³), 1.78 (brd, ³J_{H-H} = 13.6 Hz, 1H, H₂C³), 0.96 (s, 9H, H₃C^{3'}), 0.20 (s, 3H, H₃C^{1'}), 0.19 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 154.4 (C⁹), 151.3 (C¹¹), 139.2 (C⁷), 130.7 (C¹²), 129.2 (C³), 127.4 (C⁸), 125.3 (C¹⁰), 90.1 (C⁶), 60.9 (C²), 43.1 (C⁴), 27.5 (C^{3'}), 25.9 (C³), 17.5 (C^{2'}), 16.0 (C^{1''}), −3.5 (C^{1'}), −5.0 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₇BrIOsi 493.0054; Found 493.0080.

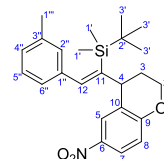
(Z)-tert-Butyl(1-(chroman-4-yl)-2-(*m*-tolyl)vinyl)-dimethylsilane (16a)



The procedure was done according to the literature.⁵⁵ An oven-dried three-neck round-bottom flask, equipped with a reflux condenser, magnetic stirrer, and a three-way valve adapter, was evacuated and backfilled with argon. The vinyl bromide **11a** (201 mg, 0.57 mmol, 1.0 equiv), 3-tolylboronic acid (310 mg, 2.28 mmol, 4.0 equiv), Pd(OAc)₂ (6 mg, 0.03 mmol, 5 mol %), XPhos (41 mg, 0.09 mmol, 15 mol %), K₃PO₄ (511 mg, 2.50 mmol, 4.2 equiv) and dry toluene (20 mL) were added. The resulting mixture was evacuated using 3 freeze–thaw cycles (liquid N₂/0.01 mbar) and backfilled with argon. The reaction was stirred for 44 h at 100 °C, then cooled to room temperature, diluted with EtOAc (40 mL), filtered through a Celite pad, and concentrated in vacuo. Crude product was purified by column chromatography on silica gel (eluent system: DCM in hexanes, gradient change: 10 → 20%) to yield cross-coupling product **16a** as a white solid (200 mg, 97%). ¹H NMR (500 MHz, CDCl₃): δ 7.14 (d, ³J_{H-H} = 7.8 Hz, 1H, H-C⁵), 7.11 (t, ³J_{H-H} = 7.7 Hz, 1H, H-C^{5''}), 7.09 (dd, ³J_{H-H} = 8.7, 8.1 Hz, 1H, H-C⁷), 7.03 (s, 1H, HC¹²), 7.00 (d, ³J_{H-H} = 7.7 Hz, 1H, H-C^{4''}), 6.91 (s, 1H, H-C^{2''}), 6.89 (d, ³J_{H-H} = 7.7 Hz, 1H, H-C^{6''}), 6.86 (dd, ³J_{H-H} = 8.7, 7.8 Hz, 1H, H-C⁶), 6.80 (d, ³J_{H-H} = 8.1 Hz, 1H, H-C⁸), 4.32 (ddd, ²J_{H-H} = 10.8 Hz, ³J_{H-H} = 8.2, 2.7 Hz, 1H, H₂C²), 4.18 (ddd, ²J_{H-H} = 10.8 Hz, ³J_{H-H} = 7.0, 2.8 Hz, 1H, H₂C²), 3.92 (t, ³J_{H-H} = 5.6 Hz, 1H, HC⁴), 2.30 (s, 3H, H₃C^{1''}), 2.27–2.17 (m, 1H, H₂C³), 1.94–1.83 (m, 1H, H₂C³), 0.98 (s, 9H, H₃C^{3'}), 0.00 (s, 3H, H₃C^{1'}), −0.21 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 155.8 (C⁹), 148.0 (C¹²),

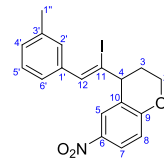
146.4 (C¹¹), 140.4 (C^{1''}), 137.0 (C^{3''}), 130.6 (C⁵), 129.3 (C^{2''}), 127.5 (C⁷), 127.5 (C^{5''}), 127.5 (C^{4''}), 126.3 (C¹⁰), 125.6 (C^{6''}), 120.4 (C⁶), 116.7 (C⁸), 63.4 (C²), 40.3 (C⁴), 30.6 (C³), 28.0 (C^{3'}), 21.4 (C^{1''}), 18.7 (C²), −2.6 (C^{1'}), −3.2 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₄H₃₃Osi 365.2295; Found 365.2310.

(Z)-tert-Butyl(1-(6-nitrochroman-4-yl)-2-(*m*-tolyl)-vinyl)silane (16k)



The procedure was done according to the literature.⁵⁵ A round-bottom flask (50 mL), equipped with a Teflon-coated magnetic stirrer, was charged with vinyl bromide **11k** (300 mg, 0.75 mmol, 1.0 equiv), 3-tolylboronic acid (410 mg, 3.01 mmol, 4.0 equiv), XPhos (54 mg, 0.11 mmol, 0.15 equiv), Pd(OAc)₂ (8 mg, 0.04 mmol, 0.05 equiv) and K₃PO₄ (639 mg, 3.01 mmol, 4.0 equiv). The reaction flask was closed with a septum and then evacuated and backfilled with argon 3 times using a Schlenk line. In a separate vessel, toluene (dried over 4 Å MS) was degassed by repeated sonication under vacuum (2 cycles, 7 min each) and replenished with argon. The degassed toluene (30 mL) was then added to the reaction mixture. The reaction was heated in an oil bath (100 °C) for 22 h. After cooling the mixture to room temperature, it was filtered through a Celite patch, and the filtrate was concentrated in vacuo. Purification by column chromatography (eluent system: DCM in hexanes, gradient change: 10 → 30%) afforded the cross-coupling product **16k** as a yellow, viscous oil (281 mg, 92%). ¹H NMR (500 MHz, CDCl₃): δ 8.12 (d, ³J_{H-H} = 2.8 Hz, 1H, H-C⁵), 8.00 (dd, ³J_{H-H} = 9.0 Hz, ⁴J_{H-H} = 2.8 Hz, 1H, H-C⁷), 7.14 (t, ³J_{H-H} = 7.6 Hz, 1H, H-C^{5''}), 7.03 (d, ³J_{H-H} = 7.6 Hz, 1H, H-C^{6''}), 6.97 (s, 1H, HC¹²), 6.92 (s, 1H, H-C^{3''}), 6.89 (d, ³J_{H-H} = 7.6 Hz, 1H, H-C^{4''}), 6.87 (d, ³J_{H-H} = 9.0 Hz, 1H, H-C⁸), 4.42 (ddd, ²J_{H-H} = 11.0 Hz, ³J_{H-H} = 7.7, 3.1 Hz, 1H, H₂C²), 4.30 (ddd, ²J_{H-H} = 11.0 Hz, ³J_{H-H} = 7.2, 3.2 Hz, 1H, H₂C²), 3.94 (t, ³J_{H-H} = 5.8 Hz, 1H, HC⁴), 2.31 (s, 3H, H₃C^{1''}), 2.24 (ddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 7.7, 5.8, 3.2 Hz, 1H, H₂C³), 1.96 (ddd, ²J_{H-H} = 13.8 Hz, ³J_{H-H} = 7.2, 5.8, 3.1 Hz, 1H, H₂C³), 0.99 (s, 9H, H₃C^{3'}), 0.00 (s, 3H, H₃C^{1'}), −0.17 (s, 3H, H₃C^{1'}). ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 161.1 (C⁹), 148.5 (C¹²), 145.6 (C¹¹), 141.2 (C⁷), 139.7 (C^{1''}), 129.2 (C^{3''}), 127.9 (C^{5''}), 127.7 (C^{5''}), 127.0 (C¹⁰), 126.7 (C³), 125.5 (C^{4''}), 123.7 (C⁷), 117.3 (C⁸), 64.5 (C²), 40.2 (C⁴), 29.7 (C³), 28.0 (C^{3'}), 21.4 (C^{1''}), 18.6 (C²), −2.8 (C^{1'}), −3.3 (C^{1'}). HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₄H₃₂NO₃Si 410.2146; Found 410.2170.

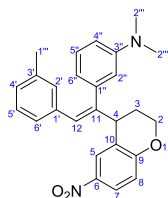
(Z)-4-(1-Iodo-2-(*m*-tolyl)vinyl)-6-nitrochromane (17k)



A two-neck round-bottom flask (10 mL), equipped with a Teflon-coated magnetic stirrer and a reflux condenser, was charged with vinyl silane **16k** (100 mg, 0.24 mg, 1.0 equiv), trifluoroethanol (6 mL), and *N*-iodosuccinimide (55 mg, 0.24 mg, 1.0 equiv). The resulting suspension was refluxed while heating in an oil bath for 15 h. The reaction mixture was cooled to room temperature, quenched by the addition of a 10% Na₂S₂O₃ aqueous solution (10 mL), extracted with DCM (3 × 15 mL), the organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. Column chromatography (eluent system: DCM in hexanes, gradient change: 20 → 30%) afforded the vinyl iodide **17k** as a white, amorphous solid (62 mg, 60%). ¹H NMR (500 MHz, CDCl₃): δ 8.12 (d, ³J_{H-H} = 2.6 Hz, 1H, H-C⁵), 8.09 (dd,

$^3J_{\text{H-H}} = 9.0$ Hz, $^4J_{\text{H-H}} = 2.6$ Hz, 1H, H-C⁷), 7.32–7.23 (m, 3H, H-C^{2i,5i,6i}), 7.14 (d, $^3J_{\text{H-H}} = 7.3$ Hz, 1H, H-C⁴ⁱ), 6.94 (d, $^3J_{\text{H-H}} = 9.0$ Hz, 1H, H-C⁸), 6.74 (s, 1H, HC¹²), 4.41 (ddd, $^2J_{\text{H-H}} = 11.0$ Hz, $^3J_{\text{H-H}} = 7.2$, 3.4 Hz, 1H, H₂C³), 4.34 (ddd, $^2J_{\text{H-H}} = 11.0$ Hz, $^3J_{\text{H-H}} = 7.6$, 3.0 Hz, 1H, H₂C²), 3.91 (t, $^3J_{\text{H-H}} = 6.0$ Hz, 1H, HC⁴), 2.45 (dddd, $^2J_{\text{H-H}} = 14.6$ Hz, $^3J_{\text{H-H}} = 7.6$, 6.0, 3.4 Hz, 1H, H₂C³), 2.38 (s, 3H, H₃C¹⁹), 2.14 (dddd, $^2J_{\text{H-H}} = 14.6$ Hz, $^3J_{\text{H-H}} = 7.2$, 6.0, 3.0 Hz, 1H, H₂C³). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl₃): δ 160.6 (C⁹), 141.5 (C⁶), 139.2 (C¹²), 138.0 (C³), 137.6 (C¹), 129.5 (C^{2'}), 129.2 (C^{4'}), 128.2 (C^{5'}), 126.7 (C⁵), 125.8 (C^{6'}), 124.7 (C⁷), 123.4 (C¹⁰), 117.9 (C⁸), 110.7 (C¹¹), 64.4 (C²), 49.1 (C⁴), 28.4 (C³), 21.5 (C¹⁹). HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₈H₁₇INO₃ 422.0248; Found 422.0260.

(Z)-N,N-Dimethyl-3-(1-(6-nitrochroman-4-yl)-2-(*m*-tolyl)-vinyl)aniline (18k)



The procedure was done according to the literature.⁵⁵ A round-bottom flask (10 mL), equipped with a Teflon-coated magnetic stirrer, was charged with iodide 17k (25 mg, 0.059 mmol, 1.0 equiv), 3-dimethylaminophenylboronic acid (38 mg, 0.230 mmol, 3.9 equiv), XPhos (4 mg, 0.008 mmol, 0.14 equiv), Pd(OAc)₂ (1 mg, 0.004 mmol, 0.07 equiv), and K₃PO₄ (49 mg, 0.231 mmol, 3.9 equiv). The reaction flask was closed with a septum and then evacuated and backfilled with argon 3 times using a Schlenk line. In a separate vessel, toluene (dried over 4 Å MS) was degassed by repeated sonication under vacuum (2 cycles, 7 min each) and replenished with argon. The degassed toluene (8 mL) was then added to the reaction mixture. The reaction was heated in an oil bath (100 °C) for 20 h. After cooling the mixture to room temperature, it was filtered through a Celite patch, and the filtrate was concentrated in vacuo. Purification by column chromatography (eluent system: DCM in hexanes, gradient change: 15 → 70%) afforded the cross-coupling product 18k as a yellow, viscous oil (24 mg, 98%). ^1H NMR (500 MHz, CDCl₃): δ 8.26 (d, $^3J_{\text{H-H}} = 2.8$ Hz, 1H, H-C⁵), 8.08 (dd, $^3J_{\text{H-H}} = 9.1$ Hz, $^4J_{\text{H-H}} = 2.8$ Hz, 1H, H-C⁷), 7.19 (t, $^3J_{\text{H-H}} = 8.1$ Hz, 1H, H-C^{5'}), 6.98–6.91 (m, 2H, H-C^{8,5'}), 6.88 (d, $^3J_{\text{H-H}} = 7.6$ Hz, 1H, H-C^{4'}), 6.74 (s, 1H, H-C^{2'}), 6.71–6.66 (m, 2H, H-C^{6',4'}), 6.50–6.46 (m, 2H, H-C^{2,6''}), 5.96 (s, 1H, HC¹²), 4.31–4.25 (m, 2H, H₂C³), 4.02 (t, $^3J_{\text{H-H}} = 5.0$ Hz, 1H, HC⁴), 2.87 (s, 6H, H₃C^{2''}), 2.16 (s, 3H, H₃C¹⁹), 2.08–1.94 (m, 2H, H₂C³). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl₃): δ 160.9 (C⁹), 151.1 (C^{3''}), 145.1 (C¹¹), 141.2 (C⁶), 140.4 (C^{1''}), 137.4 (C³), 136.5 (C^{1'}), 131.5 (C¹²), 130.3 (C²), 129.6 (C^{5''}), 127.8 (C⁵), 127.6 (C^{4'}), 127.5 (C⁵), 126.0 (C⁶), 124.2 (C⁷), 124.1 (C¹⁰), 117.7 (C⁸), 117.4 (C^{2''/6''}), 113.1 (C^{2''/6''}), 111.9 (C^{4''}), 64.1 (C²), 43.8 (C⁴), 40.7 (C^{2''}), 25.4 (C³), 21.4 (C^{1''}). HRMS (ESI) m/z : [M + H]⁺ Calcd for C₂₆H₂₇N₂O₃ 415.2016; Found 415.2040.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.5c03136>.

Optimization tables, characterization, and crystallographic data (PDF)

Accession Codes

Deposition Numbers 2350768, 2350770, and 2350772 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via the joint Cambridge Crystallographic Data Centre (CCDC) and Fachinformationszentrum Karlsruhe [Access Structures service](#).

■ AUTHOR INFORMATION

Corresponding Author

Māris Turks – Faculty of Natural Sciences and Technology, Riga Technical University, Riga LV-1048, Latvia;
 orcid.org/0000-0001-5227-0369; Email: maris.turks@rtu.lv

Authors

Artjoms Ubaidullajevs – Faculty of Natural Sciences and Technology, Riga Technical University, Riga LV-1048, Latvia
 Rasma Kronkalne – Faculty of Natural Sciences and Technology, Riga Technical University, Riga LV-1048, Latvia
 Anatoly Mishnev – Latvian Institute of Organic Synthesis, Riga LV-1006, Latvia

Complete contact information is available at:
<https://pubs.acs.org/10.1021/acs.joc.5c03136>

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work is financed by the Latvian Council of Science Grant No. LZP-2023/1-0576. A.U. expresses his deepest gratitude to the Riga Technical University Master Grant No. ZM-2024/6. R. K. thanks the EU RRF within project No 5.2.1.1.i.0/2/24/J/CFLA/003 academic career doctoral grant, ID 1134. Edvards Merzvinšis, Matīss Gercāns, and Ieva Jaunzeme are kindly acknowledged for technical support.

■ REFERENCES

- (1) Pietta, P. G. Flavonoids as Antioxidants. *J. Nat. Prod.* **2000**, 63 (7), 1035–1042.
- (2) Hussain, N.; Ishak, I.; Coorey, R.; Abd Ghani, M.; Ping, T. C. Tocopherols. *Centum of Valuable Plant Bioactives*; Mushtaq, M., Anwar, F., Eds.; Academic Press, 2021; pp 707–731.
- (3) Pecio, L.; Pecio, S.; Mroczek, T.; Oleszek, W. Spiro-Flavonoids in Nature: A Critical Review of Structural Diversity and Bioactivity. *Molecules* **2023**, 28 (14), 5420.
- (4) Khadem, S.; Marles, R. J. Tetrahydroquinoline-containing natural products discovered within the last decade: occurrence and bioactivity. *Nat. Prod. Res.* **2025**, 39 (1), 182–194.
- (5) O'Neill, E. J.; Termini, D.; Albano, A.; Tsiani, E. Anti-Cancer Properties of Theaflavins. *Molecules* **2021**, 26 (4), 987.
- (6) Yadav, P.; Kumar, A.; Althagafi, I.; Nemaysh, V.; Rai, R.; Pratap, R. Recent development of tetrahydro-quinoline/isoquinoline based compounds as anticancer agents. *Curr. Top. Med. Chem.* **2021**, 21 (17), 1587–1622.
- (7) Nain, S.; Singh, N.; Schlag, A. K.; Barnes, M. The impact of cannabis use on ageing and longevity: a systematic review of research insights. *J. Cannabis Res.* **2025**, 7 (1), S2.
- (8) Chung, C. L.; Chen, J. H.; Huang, W. C.; Sheu, J. R.; Hsia, C. W.; Jayakumar, T.; Hsia, C. H.; Chiou, K. R.; Hou, S. M. Glabridin, a Bioactive Flavonoid from Licorice, Effectively Inhibits Platelet Activation in Humans and Mice. *Int. J. Mol. Sci.* **2022**, 23 (19), 11372.
- (9) Asolkar, R. N.; Schröder, D.; Heckmann, R.; Lang, S.; Wagner-Döbler, I.; Laatsch, H. Helquinoline, a new tetrahydroquinoline

antibiotic from *Janibacter limosus* Hel 1. *J. Antibiot.* **2004**, *57* (1), 17–23.

(10) Kim, W. G.; Kim, J. P.; Kim, C. J.; Lee, K. H.; Yoo, I. D. Benzastatins A, B, C, and D: new free radical scavengers from *Streptomyces nitrosporeus* 30643. I. Taxonomy, fermentation, isolation, physico-chemical properties and biological activities. *J. Antibiot.* **1996**, *49* (1), 20–25.

(11) Shen, L.; Ye, Y.; Wang, X.; Zhu, H.; Xu, C.; Song, Y.; Li, H.; Tan, R. Structure and Total Synthesis of Aspernigerin: A Novel Cytotoxic Endophyte Metabolite. *Chem. - Eur. J.* **2006**, *12* (16), 4393–4396.

(12) Lei, P.; Zhang, X.; Xu, Y.; Xu, G.; Liu, X.; Yang, X.; Zhang, X.; Ling, Y. Synthesis and fungicidal activity of pyrazole derivatives containing 1,2,3,4-tetrahydroquinoline. *Chem. Centr. J.* **2016**, *10*, 40.

(13) Nogle, L. M.; Gerwick, W. H. Diverse Secondary Metabolites from a Puerto Rican Collection of *Lyngbya majuscula*. *J. Nat. Prod.* **2003**, *66* (2), 217–220.

(14) Ignarro, L. J. Different Pharmacological Properties of Two Enantiomers in a Unique β -Blocker. *Nebivolol*. *Cardiovasc. Ther.* **2008**, *26* (2), 115–134.

(15) Lal, J. Clinical pharmacokinetics and interaction of centchroman - A mini review. *Contraception* **2010**, *81* (4), 275–280.

(16) Shelly, W.; Draper, M. W.; Krishnan, V.; Wong, M.; Jaffe, R. B. Selective Estrogen Receptor Modulators: An Update on Recent Clinical Findings. *Obstet. Gynecol. Surv.* **2008**, *63* (3), 163–181.

(17) Villamizar-Monsalve, M. A.; López-Abán, J.; Vicente, B.; Peláez, R.; Muro, A. Current drug strategies for the treatment and control of schistosomiasis. *Expert Opin. Pharmacother.* **2024**, *25* (4), 409–420.

(18) Muthukrishnan, I.; Sridharan, V.; Menéndez, J. C. Progress in the Chemistry of Tetrahydroquinolines. *Chem. Rev.* **2019**, *119* (8), 5057–5191.

(19) Vidal-Albalat, A.; Matos Paz, B. Organocatalytic Enantioselective Syntheses of Flavonoids and Cannabinoids. *Adv. Synth. Catal.* **2024**, *366*, 1032.

(20) Das, T.; Mohapatra, S.; Pradhan, A. K.; Nayak, S. Recent Advances of Michael/hetero-Michael Addition Reaction in the Synthesis of 3-Nitro-2H-chromene Derivatives. *ChemistrySelect* **2023**, *8* (14), No. e202300477.

(21) Masesane, I. B.; Desta, Z. Y. Reactions of salicylaldehyde and enolates or their equivalents: versatile synthetic routes to chromane derivatives. *Beilstein J. Org. Chem.* **2012**, *8*, 2166–2175.

(22) Dalpozzo, R.; Mancuso, R. Recent Advances in Organocatalyzed Asymmetric Synthesis of Benzopyran and Benzodihydropyran (Chromane) Nuclei. *Symmetry* **2019**, *11* (12), 1510.

(23) Nammalwar, B.; Bunce, R. A. Recent Syntheses of 1,2,3,4-Tetrahydroquinolines, 2,3-Dihydro-4(1H)-quinolones and 4(1H)-Quinolones using Domino Reactions. *Molecules* **2014**, *19* (1), 204–232.

(24) Tietze, L. F.; Diefert, A. Multiple Pd-catalyzed reactions in the synthesis of natural products, drugs, and materials. *Pure Appl. Chem.* **2010**, *82* (7), 1375–1392.

(25) Doggett, A.; Hay, M.; McKenna, S.; Saurer, E. M.; Steinhardt, S.; Tan, Y.; Wilbert, C. R.; Wisniewski, S. R. Development of a Chromane-Forming Heck Reaction: Bisphosphine Mono-Oxide Mediated Regioselectivity Perturbed by Solvent-Based Peroxide Formation. *Org. Process Res. Dev.* **2023**, *27* (6), 1129–1135.

(26) Reznikov, A. N.; Ashatkina, M. A.; Klimochkin, Y. N. Recent developments in asymmetric Heck type cyclization reactions for Constructions of complex molecules. *Org. Biomol. Chem.* **2021**, *19* (26), 5673–5701.

(27) Martínez-Estibalez, U.; García-Calvo, O.; Ortiz-de-Elguea, V.; Sotomayor, N.; Lete, E. Intramolecular Mizoroki–Heck Reaction in the Regioselective Synthesis of 4-Alkylidene-tetrahydroquinolines. *Eur. J. Org. Chem.* **2013**, *2013* (15), 3013–3022.

(28) Tan, X.; Jing, Y.; Wu, J.; Li, J.; Yang, Z.; Wu, W.; Ke, Z.; Jiang, H. Palladium catalyzed *ortho*-C(sp²)-H activation/cyclization of aryl amines assisted by imine and vinylacetic acid. *Nat. Commun.* **2024**, *15*, 9877.

(29) Shukla, P. M.; Bhattacharya, A.; Pratap, A.; Pradhan, A.; Sinha, P.; Soni, T.; Maji, B. HFIP-promoted halo-carbocyclizations of N- and O-

tethered arene–alkene substrates to access all halo (X = Br, I, Cl)-functionalized tetrahydroquinoline and chroman cores. *Org. Biomol. Chem.* **2022**, *20* (41), 8136.

(30) Luo, J.; Zhang, Y.; Zhong, F.; Zhao, X. Catalytic Enantioselective Construction of Chiral Benzo-Fused N-Heterocycles through Friedel–Crafts-Type Electrophilic Chlorination. *CCS Chem.* **2022**, *4*, 1486–1498.

(31) Sarie, J. C.; Thiehoff, C.; Neufeld, J.; Daniliuc, C. G.; Gilmour, R. Enantioselective Synthesis of 3-Fluorochromanes via Iodine(I)/Iodine(III) Catalysis. *Angew. Chem., Int. Ed.* **2020**, *59* (35), 15069–15075.

(32) Minić, A.; Stevanović, D.; Vukićević, M.; Bogdanović, G. A.; d'Hooghe, M.; Radulović, N. S.; Vukićević, R. D. Synthesis of novel 4-ferrocenyl-1,2,3,4-tetrahydroquinolines and 4-ferrocenylquinolines via α -ferrocenyl carbenium ions as key intermediates. *Tetrahedron* **2017**, *73* (44), 6268–6274.

(33) Compain, G.; Bonneau, C.; Martin-Mingot, A.; Thibaudau, S. Selective anti-Markovnikov cyclization and hydrofluorination reaction in superacid HF/SbF₅: A tool in the design of nitrogen-containing (fluorinated) polycyclic systems. *J. Org. Chem.* **2013**, *78* (9), 4463–4472.

(34) Nammalwar, B.; Bunce, R. A. Friedel–Crafts cyclization of tertiary alcohols using bismuth(III) triflate. *Tetrahedron Lett.* **2013**, *54* (32), 4330–4332.

(35) Bunce, R. A.; Cain, N. R.; Cooper, J. G. Tetrahydroquinolines by Lewis Acid-promoted Friedel–Crafts Cyclizations. *Org. Prep. Proced. Int.* **2013**, *45* (1), 28–43.

(36) Zhang, Y.; Ding, S.; Meng, L.; Tao, C.; Wang, H.; Xu, S. Catalytic Enantioselective Friedel–Crafts Reactions of Arenes Enabled by Iridium/Iridium-Ion-Triggered Electrophilic Functionalization. *Synlett* **2025**, *36* (12), 1642–1658.

(37) Barluenga, J.; Trincado, M.; Rubio, E.; González, J. M. Intramolecular Arylation Reactions of Alkenes: A Flexible Approach to Chromans and Tetrahydroquinoline Derivatives. *J. Am. Chem. Soc.* **2004**, *126* (11), 3416–3417.

(38) Maji, B. Stereoselective Haliranium, Thiiranium and Seleniranium Ion-Triggered Friedel–Crafts-Type Alkylations for Polyene Cyclizations. *Adv. Synth. Catal.* **2019**, *361* (15), 3453–3489.

(39) Wang, D.-K.; Li, L.; Xu, Q.; Zhang, J.; Zheng, H.; Wei, W.-T. 1,3-Difunctionalization of alkenes: state-of-the-art and future challenges. *Org. Chem. Front.* **2021**, *8* (24), 7037–7049.

(40) Pirenne, V.; Muriel, B.; Waser, J. Catalytic Enantioselective Ring-Opening Reactions of Cyclopropanes. *Chem. Rev.* **2021**, *121*, 227.

(41) Devaraj, T.; Srinivasan, K. Ytterbium Triflate-Catalyzed Intramolecular Arylative Ring Opening of Arylaminomethyl-Substituted Donor–Acceptor Cyclopropanes: Access to Tetrahydroquinolines. *J. Org. Chem.* **2024**, *89* (19), 13886–13893.

(42) Novikau, I.; Leushukou, A.; Tsiuryan, M.; Hurski, A. Construction of tetralin and chromane cores by the Lewis acid promoted ring-opening cyclization of cyclopropyl methanesulfonates. *Tetrahedron Lett.* **2022**, *104*, No. 154025.

(43) Giera, D. S.; Schneider, C. InCl₃-Catalyzed Allylic Friedel–Crafts Reactions toward the Stereocontrolled Synthesis of 1,2,3,4-Tetrahydroquinolines. *Org. Lett.* **2010**, *12* (21), 4884–4887.

(44) Bryant, L. A.; Shankland, K.; Straker, H. E.; Johnston, C. D.; Lees, N. R.; Cobb, A. J. A. Enantioselective Organocatalytic Synthesis of Bicyclic Resorcinols via an Intramolecular Friedel–Crafts-Type 1,4-Addition: Access to Cannabidiol Analogues. *Adv. Synth. Catal.* **2021**, *363* (16), 4067–4074.

(45) Kariya, T.; Hirokane, T.; Yoshida, M. Synthesis of tetrahydroquinolines by gold-catalyzed cascade ring-opening–intramolecular hydroarylation of 2-alkynylazetidines. *Tetrahedron* **2024**, *150*, No. 133777.

(46) Brion, A.; Martini, V.; Lombard, M.; Retaillieu, P.; Della Ca', N.; Neuville, L.; Masson, G. Phenolic Dienes as Highly Selective Dienophiles in the Asymmetric Organocatalyzed Three-Component Vinylogous Povarov Reaction. *J. Org. Chem.* **2024**, *89* (17), 12298–12306.

- (47) Mei, G.-J.; Li, D.; Zhou, G.-X.; Shi, Q.; Cao, Z.; Shi, F. A catalytic asymmetric construction of a tetrahydroquinoline-based spirooxindole framework via a diastereo- and enantioselective decarboxylative [4 + 2] cycloaddition. *Chem. Commun.* **2017**, 53 (72), 10030.
- (48) Wei, Q.; Tu, L.; Li, S.; Zheng, Y.; Liu, J. Palladium-Catalyzed [4 + 2] Cycloaddition of Vinyl Benzoxazinones with 1,3-Indanedione: Approach to Spiro-Tetrahydroquinoline Scaffolds. *Eur. J. Org. Chem.* **2023**, 2023 (39), No. e202300499.
- (49) Goebel, G. L.; Hohnen, L.; Borgelt, L.; Hommen, P.; Qiu, X.; Lightfoot, H.; Wu, P. Small molecules with tetrahydroquinoline-containing Povarov scaffolds as inhibitors disrupting the Protein–RNA interaction of LIN28–let-7. *Eur. J. Med. Chem.* **2022**, 228, No. 114014.
- (50) Bejaunies, R.; Puriņš, M.; Turks, M. Manifestation of the β -Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift. *Synthesis* **2020**, 52 (15), 2147–2161.
- (51) Roberts, D. D.; McLaughlin, M. G. Strategic Applications of the β -Silicon Effect. *Adv. Synth. Catal.* **2022**, 364 (14), 2307–2332.
- (52) Curtis-Long, M. J.; Aye, Y. Vinyl-, Propargyl-, and Allenylsilicon Reagents in Asymmetric Synthesis: A Relatively Untapped Resource of Environmentally Benign Reagents. *Chem. - Eur. J.* **2009**, 15 (22), 5402–5416.
- (53) Puriņš, M.; Mishnev, A.; Turks, M. Brønsted Acid Catalyzed 1,2-Silyl Shift in Propargyl Silanes: Synthesis of Silyl Dienes and Silyl Indenes. *J. Org. Chem.* **2019**, 84 (6), 3595–3611.
- (54) Bejaunies, R.; Puriņš, M.; Kumpiņš, V.; Turks, M. Synthesis of 3-Silylated 3-Sulfolenes from Propargylsilanes and their Reductive Desulfuration. *Chem. Heterocycl. Compd.* **2021**, 57 (1), 20–25.
- (55) Bejaunies, R.; Puriņš, M.; Līpiņa, R. A.; Mishnev, A.; Turks, M. 1,3-Difunctionalization of Propargyl Silanes with Concomitant 1,2-Silyl Shift: Synthesis of Allyl Functionalized Vinyl Silanes. *Org. Lett.* **2023**, 25 (25), 4627–4631.
- (56) Kronkalne, R.; Bejaunies, R.; Ubaidullajevs, A.; Mishnev, A.; Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain. *J. Org. Chem.* **2023**, 88 (19), 13857–13870.
- (57) Wang, Y.; Ready, J. M. Cyclocondensation of Amino-propargyl Silanes. *Org. Lett.* **2012**, 14 (9), 2308–2311.
- (58) Akiyama, T.; Suzuki, M.; Kagoshima, H. Lewis Acid Promoted [4 + 2] Annulation of Allylsilane and Allylgermane with Aldimine; Preparation of Tetrahydroquinolines. *Heterocycles* **2000**, 52 (2), 529.
- (59) Katritzky, A. R.; Cui, X.; Long, Q. Reactions of N-aryl-1H-benzotriazolyl-1-methanamines with allyl trimethylsilanes. A facile route to trialkylsilane tetrahydroquinolines. *J. Heterocycl. Chem.* **1999**, 36, 371.
- (60) Wang, X.; Gao, Q.; Buevich, A. V.; Yasuda, N.; Zhang, Y.; Yang, R. S.; Zhang, L. K.; Martin, G. E.; Williamson, R. T. Unexpected Propargylic Retro-Brook Rearrangements in Alkynes. *J. Org. Chem.* **2019**, 84 (16), 10024–10031.
- (61) Schlosser, M. Superbases for Organic Synthesis. *Pure Appl. Chem.* **1988**, 60 (11), 1627–1634.
- (62) Hirose, D.; Gazvoda, M.; Košmrlj, J.; Taniguchi, T. Systematic Evaluation of 2-Arylazocarboxylates and 2-Arylazocarboxamides as Mitsunobu Reagents. *J. Org. Chem.* **2018**, 83, 4712.
- (63) Hashimoto, T.; Hirose, D.; Taniguchi, T. Recyclable Mitsunobu Reagents: Catalytic Mitsunobu Reactions with an Iron Catalyst and Atmospheric Oxygen. *Adv. Synth. Catal.* **2015**, 357 (8), 3346–4729.
- (64) Hirose, D.; Taniguchi, T.; Ishibashi, H. Recyclable Mitsunobu Reagents: Catalytic Mitsunobu Reactions with an Iron Catalyst and Atmospheric Oxygen. *Angew. Chem., Int. Ed.* **2013**, 52 (17), 4613–4617.
- (65) Urankar, D.; Steinbücher, M.; Kosjek, J.; Košmrlj, J. N-(Propargyl)diazene-carboxamides for 'click' conjugation and their 1,3-dipolar cycloadditions with azidoalkylamines in the presence of Cu(II). *Tetrahedron* **2010**, 66 (14), 2602–2613.
- (66) Morita, M.; Mihashi, S.; Itokawa, H.; Hara, S. Silver nitrate impregnation of preparative silica gel columns for liquid chromatography. *Anal. Chem.* **1983**, 55 (2), 412–414.
- (67) Hall, L. M.; Tew, D. P.; Pridmore, N. E.; Whitwood, A. C.; Lynam, J. M.; Slattery, J. M. A Structurally Characterized Fluoroalkyne. *Angew. Chem., Int. Ed.* **2017**, 56 (26), 7551–7556.
- (68) Nishikawa, T.; Shibuya, S.; Hosokawa, S.; Isobe, M. One pot synthesis of haloacetylenes from trimethylsilylacetylenes. *Synlett* **1994**, 1994 (7), 485–486.
- (69) Shi, D.; Liu, Z.; Zhang, Z.; Shi, W.; Chen, H. Silver-Catalyzed Synthesis of 1-Chloroalkynes Directly from Terminal Alkynes. *ChemCatChem* **2015**, 7 (9), 1424–1426.
- (70) Nicolai, S.; Sedigh-Zadeh, R.; Waser, J. Pd(0)-Catalyzed Alkene Oxy- and Aminoalkynylation with Aliphatic Bromoacetylenes. *J. Org. Chem.* **2013**, 78 (8), 3783–3801.
- (71) Leyva-Pérez, A.; Rubio-Marqués, P.; Al-Deyab, S. S.; Al-Resayes, S. I.; Corma, A. Cationic Gold Catalyzes ω -Bromination of Terminal Alkynes and Subsequent Hydroaddition Reactions. *ACS Catal.* **2011**, 1 (6), 601–606.
- (72) Yamamoto, Y. Silver-Catalyzed $C_{sp}-H$ and $C_{sp}-Si$ Bond Transformations and Related Processes. *Chem. Rev.* **2008**, 108 (8), 3199–3222.
- (73) Deposition numbers CCDC-2350770 (for **10f**) and CCDC-2350772 (for **11f**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.
- (74) Surendra, K.; Corey, E. J. Rapid and Enantioselective Synthetic Approaches to Germanicol and Other Pentacyclic Triterpenes. *J. Am. Chem. Soc.* **2008**, 130 (27), 8865–8869.
- (75) Kuck, D.; Baether, W.; Gruetzmacher, H. F. Intramolecular ring-to-ring proton transfer in gaseous (ω -phenylalkyl)benzenium ions. *J. Am. Chem. Soc.* **1979**, 101 (24), 7154–7157.
- (76) Miura, K.; Okajima, S.; Hondo, T.; Nakagawa, T.; Takahashi, T.; Hosomi, A. Acid-Catalyzed Cyclization of Vinylsilanes Bearing a Hydroxy Group: A New Method for Stereoselective Synthesis of Disubstituted Tetrahydrofurans. *J. Am. Chem. Soc.* **2000**, 122 (46), 11348–11357.
- (77) Miura, K.; Hondo, T.; Nakagawa, T.; Takahashi, T.; Hosomi, A. Acid-Catalyzed Cyclization of Vinylsilanes Bearing an Amino Group. Stereoselective Synthesis of Pyrrolidine. *Org. Lett.* **2000**, 2 (3), 385–388.
- (78) Fabig, S.; Haberhauer, G.; Gleiter, R. Dimerization of Two Alkyne Units: Model Studies, Intermediate Trapping Experiments, and Kinetic Studies. *J. Am. Chem. Soc.* **2015**, 137 (5), 1833–1843.
- (79) Kress, S.; Weckesser, J.; Schulz, S. R.; Blechert, S. Concise Total Syntheses of Dipiperidine Alkaloids Virgividarine and Virgiboidine through Ru-Mediated Ene-Ene-Yne Ring Rearrangement Metathesis (RRM). *Eur. J. Org. Chem.* **2013**, 2013 (7), 1346–1355.
- (80) Parsons, S. R.; Hooper, J. F.; Willis, M. C. O-Substituted Alkyl Aldehydes for Rhodium-Catalyzed Intermolecular Alkyne Hydroacylation: The Utility of Methylthiomethyl Ethers. *Org. Lett.* **2011**, 13 (5), 998–1000.
- (81) Bastos, E. L.; Ciscato, L. F. M. L.; Baader, W. J. Microwave-Assisted Protection of Phenols as *tert*-Butyldimethylsilyl (TBDMS) Ethers Under Solvent-Free Conditions. *Synth. Commun.* **2005**, 35 (11), 1501–1509.

**Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization
of Propargylsilanes under Copper Catalysis**

Kroņkalne, R.; Beļunieks, R.; Sebris, A.; Mishnev, A.; Turks, M.

Beilstein J. Org. Chem., **2025**, *21*, 1984-1994

Pārpublicēts no brīvpiekļuves publikācijas saskaņā ar *Creative Commons Attribution* licenci (CC BY 4.0).

Copyright © 2025 Kroņkalne et al.; licensee Beilstein-Institut.

Reproduced from an Open Access publication under the *Creative Commons Attribution* License (CC BY 4.0).

Copyright © 2025 Kroņkalne et al.; licensee Beilstein-Institut.



Aryl iodane-induced cascade arylation–1,2-silyl shift–heterocyclization of propargylsilanes under copper catalysis

Rasma Kronkalne¹, Rūdolfs Beļunieks¹, Armands Sebris¹, Anatoly Mishnev² and Māris Turks^{*1}

Full Research Paper

Open Access

Address:

¹Institute of Chemistry and Chemical Technology, Faculty of Natural Sciences and Technology, Riga Technical University, P. Valdena str. 3, LV-1048, Riga, Latvia and ²Latvian Institute of Organic Synthesis, Aizkraukles str. 21, LV-1006, Riga, Latvia

Email:

Māris Turks^{*} - Maris.Turks@rtu.lv

^{*} Corresponding author

Keywords:

arylation reactions; copper-catalysis; iodanes; propargylsilanes; 1,2-silyl shift

Beilstein J. Org. Chem. **2025**, *21*, 1984–1994.

<https://doi.org/10.3762/bjoc.21.154>

Received: 19 June 2025

Accepted: 15 September 2025

Published: 26 September 2025

Associate Editor: J. G. Hernández



© 2025 Kronkalne et al.; licensee Beilstein-Institut.
License and terms: see end of document.

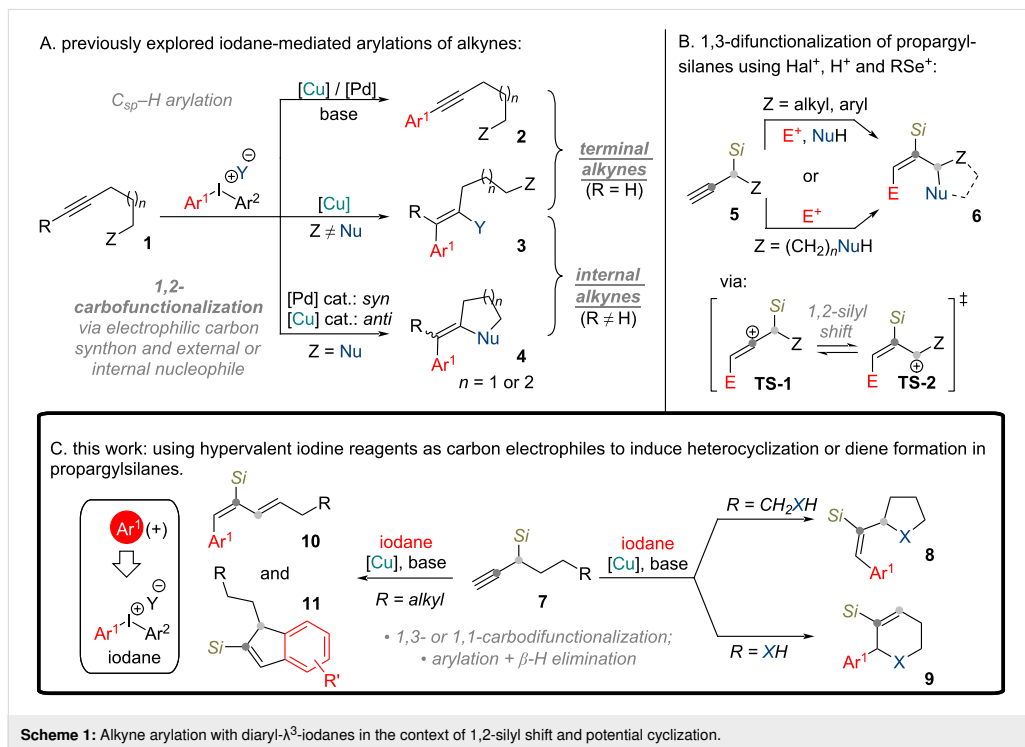
Abstract

A novel copper-catalyzed arylation strategy for propargylsilanes utilizing diaryl- λ^3 -iodanes has been developed, enabling a cascade sequence involving 1,2-silyl migration and heterocyclization. The β -silicon effect facilitates the formation of stabilized allyl cation intermediates that undergo regioselective trapping by internal *O*- and *N*-nucleophiles furnishing functionalized heterocycles. This method provides access to tetrahydrofuran or pyrrolidine frameworks, each bearing a trifunctionalized (*E*)-configured vinyl side chain. The use of a shorter linker provides entry to 1,2,3,6-tetrahydropyridines. Additionally, in the absence of internal nucleophiles, this methodology yields aryl-substituted 1,3-dienes. This work introduces a palladium-free, single-step alternative to multi-step heterocycle construction from propargylsilanes and highlights the synthetic potential of iodane-mediated carbofunctionalization under copper catalysis.

Introduction

Highly electrophilic hypervalent iodine(III) reagents are considered as arene electrophilic synthons, making them the reagents of choice for arylation reactions, where an umpolung of reactivity is required [1]. Arylations employing diaryl- λ^3 -iodanes can be performed under metal-free [2] or metal-catalyzed conditions. For alkyne arylations [Cu] [3] or [Pd] catalysis [4–6] is typically employed. Internal alkynes undergo 1,2-carbofunctionalization, where the highly electrophilic Ar–M species adds

to the alkyne, generating a vinyl cation intermediate [7], which typically reacts with an internal nucleophile to form five- [8,9] or six-membered rings [7,9,10] (Scheme 1A). Thus far the internal nucleophilic species are limited to aryl- [7,8,10] or heteroaryl groups [7,8]. In one example methyl ethers were used [9]. Under [Pd]-catalyzed conditions a *syn*-type addition is observed [8,11], while [Cu] catalysts promote *anti*-addition [7,10]. In substrates prone to cationic rearrangements (or



hydride shifts), more interesting reaction patterns can be observed. For example, branched aliphatic chain-containing alkynes are arylated and carbocyclized into cyclopentene derivatives [12,13].

The triflate moiety of the diaryl- λ^3 -iodane may act as an external nucleophile, resulting in 1,2-carbotriflation products [14]. Interestingly, this also works for terminal alkynes, which are typically known to undergo direct $\text{C}(\text{sp})\text{--H}$ arylation instead [15,16]. In the context of 1,2-carbofunctionalization, terminal alkynes are more scarcely studied. Among those few examples is a trifluoromethylative thiocyclization reaction [17] and a [4 + 2] annulation reaction between *o*-carboxylic ester-containing diaryl- λ^3 -iodanes and some terminal alkynes [18].

Looking to expand the possibilities for terminal alkyne carbofunctionalization, we turned our attention to propargylsilanes, which are prone to undergo cationic rearrangements via the 1,2-silyl shift, enabled by the β -cation-stabilizing properties of silyl groups [19,20]. This phenomenon has been successfully employed in 1,3-difunctionalization events in both intermolecular [21] and intramolecular fashion [22] (Scheme 1B). Thus far such propargylsilane rearrangements have been induced by ad-

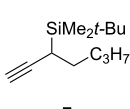
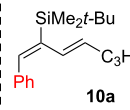
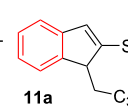
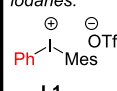
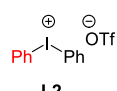
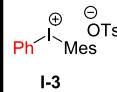
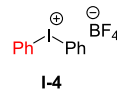
dition of external halogen or selenium electrophiles and Brønsted acids. This encouraged us to develop a methodology involving a copper-catalyzed terminal alkyne arylation of propargylsilanes by diaryl- λ^3 -iodanes, followed by 1,2-silyl shift and terminated by nucleophile addition on intermediate allyl cation (Scheme 1C). The obtained tetrahydrofuran and pyrrolidine derivatives with highly substituted vinyl side-chains are regarded as privileged structures in medical chemistry [23,24]. Moreover, the resulting styryl functionality (Ph-C=C-) is often found in drug molecules as it improves lipophilicity, oral absorption and biological activity [25].

Results and Discussion

Arylation of aliphatic chain-containing propargylsilanes

We started our investigation with the arylation of aliphatic chain-containing propargylsilanes. The starting material – *tert*-butyl(hept-1-yn-3-yl)dimethylsilane (**7a**) – and analogous aliphatic chain-containing propargylsilanes **7b,c** were obtained from the commercial hept-1-yne [26]. While searching for appropriate arylation conditions (Table 1, entry 1) we observed the formation of both the arylated diene **10a**

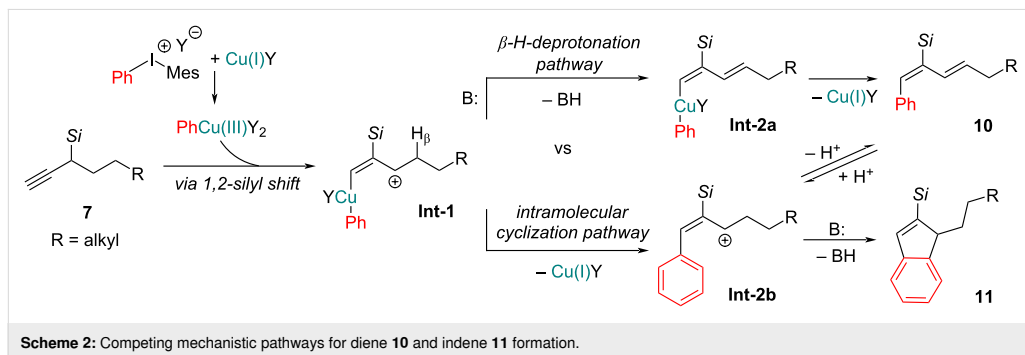
Table 1: Reaction conditions optimization for the arylation of aliphatic chain-containing propargylsilane **7a**.

 7a obtained in 3 steps from commercial hept- 1-yne. [Cu], iodane base (B1–3) solvent, T °C 3 h can be separated only by prep. HPLC  10a  11a B1 = 2,6-(<i>t</i>-Bu)₂Py; B2 = 2,6-lutidine; B3 = Et₃N								
 I-1  I-2  I-3  I-4								
Entry	Iodane (equiv)	[Cu] (mol %)	Base (equiv)	Solvent (abs.) ^a	T (°C)	Recovered 7a (%) ^b	(1 <i>E</i> ,3 <i>E</i>)- 10a / 11a (ratio) ^c	(1 <i>E</i> ,3 <i>E</i>)- 10a , (%) ^b
1 ^d	I-1 (1)	CuCl (20)	B1 (1.3)	EtOAc	60	52	75:25	35
2 ^d	I-1 (1)	[CuOTf] ₂ ·PhH (15)	B1 (1.3)	EtOAc	60	42	68:32	32
3 ^d	I-1 (1)	Cu(OTf) ₂ (23)	B1 (1.3)	EtOAc	60	63	60:40	12
4 ^d	I-1 (1)	CuCl (20)	B1 (1.3)	Tol	60	78	77:33	17
5 ^d	I-1 (1)	CuCl (20)	B1 (1.3)	DCE	60	53	72:28	34
6 ^d	I-1 (1)	CuCl (20)	B1 (1.3)	MeNO ₂	60	69	–	0
7 ^d	I-1 (1)	CuCl (20)	B2 (1.2)	EtOAc	60	95	–	0
8 ^d	I-1 (1)	CuCl (20)	B3 (1.2)	EtOAc	60	61	–	2
9 ^d	I-1 (3)	CuCl (20)	B1 (3.0)	EtOAc	60	0	60:40	60
10 ^d	I-1 (3)	CuCl (5)	B1 (3.0)	EtOAc	60	0	67:33	35
11 ^e	I-2 (3)	CuCl (20)	B1 (1.2)	EtOAc	60	0	84:16	38
12 ^d	I-3 (3)	CuCl (20)	B1 (1.3)	EtOAc	60	97	–	0
13 ^d	I-4 (4)	CuCl (20)	B1 (1.3)	EtOAc	60	98	–	0
14 ^d	I-1 (3)	Cu(MeCN) ₄ BF ₄ (8)	B1 (1.3)	EtOAc	60	0	63:37	60
15 ^e	I-1 (3)	CuCl (20)	B1 (1.2)	EtOAc	70	0	71:29	59
16 ^e	I-2 (3)	CuCl (20)	B1 (1.2)	EtOAc	70	0	85:15	63
17 ^f	I-2 (3)	CuCl (20)	B1 (1.2)	EtOAc	70	0	87:13	66
18 ^e	I-2 (3)	CuCl (20)	B1 (1.2)	EtOAc c _{7a} = 0.05 mmol/mL	70	0	98:2	35

^aStarting material **7a** concentration in solvent was 0.1 mmol/mL unless stated otherwise. ^bNMR yield. ^cMolar ratio of products in the crude mixture, determined by ¹H NMR in CDCl₃. ^dReaction scale: 0.24 mmol of **7a**. ^eReaction scale: 0.48 mmol of **7a**. ^fReaction scale: 1.90 mmol of **7a**.

and silylindene **11a** (≈75:25). Both products are likely formed via the allylic cation intermediate **Int-1** (Scheme 2), from where on two competing mechanistic pathways are possible. Depro-

tonation of the β-H and reductive elimination affords diene **10**. Alternatively, an intramolecular cyclization leads to silylindenes **11**.



We were interested to see whether the reaction selectivity can be directed towards the formation of arylated dienes **10**, which would directly contribute to our previous work [26]. Therefore, we performed optimization of the arylation conditions (Table 1) to improve the reaction selectivity towards the aryl diene **10a** formation, indicated by the diene/indene **10a/11a** molar ratio (determined by NMR).

Among the tested diaryl- λ^3 -iodanes, only those containing a triflate anion showed reactivity. PhMesIOTf (**I-1**) and Ph₂IOTf (**I-2**) showed comparable results in terms of diene yield, however, the symmetrical iodane **I-2** displayed better chemoselectivity towards diene formation (Table 1, entries 15 and 16).

In accordance with the proposed reaction mechanism (Scheme 2), an equimolar amount of protons is generated in the reaction, which would likely induce the formation of additional side-products either by protodecupration [27] or the acid-catalyzed propargylsilane activation pathway [26]. Therefore, the presence of a base was imperative. The only applicable base was found to be the non-nucleophilic 2,6-di-*tert*-butylpyridine (**B1**, Table 1, entries 1–6, 9–18). We also considered the structurally similar, but less sterically hindered 2,6-lutidine (**B2**, Table 1, entry 7) and Et₃N (**B3**, Table 1, entry 8), both of which effectively halted the reaction. The same was observed when using *N,N,N',N'*-tetramethylnaphthalene-1,8-diamine (“Proton sponge”) or TMEDA (see Supporting Information File 1 for details). In the case of Et₃N (**B3**) and TMEDA, partial degradation of the starting material **7a** was also observed.

Among the tested solvents, EtOAc gave the best results (Table 1, entries 1–3, 7–18). As for reaction catalysts, Cu(I) salts demonstrated far better reactivity than Cu(II) salts, likely because the reaction proceeds via the Cu(I/III) catalytic cycle [28]. However, in the case of Cu(OTf)₂, the active catalytic species must be generated in situ. The highest diene **10a** NMR yields (63–66%) were achieved by using 20 mol % of CuCl,

3.0 equiv of Ph₂IOTf (**I-2**) and 1.2 equiv of 2,6-di-*tert*-butylpyridine (**B1**) in EtOAc at 70 °C (Table 1, entries 16 and 17). The obtained diene **10a** contained 13–15% of silylindene **11a** as impurity. Products **10a** and **11a** are separable by preparative HPLC. Lowering the starting material concentration in the reaction mixture to 0.05 mmol/mL significantly decreased the diene **10a** yield due to the formation of other unidentified impurities. However, it turned out to be the key to achieving the best diene/indene ratio **10a/11a** = 98:2. With the optimized conditions for aryl diene synthesis (Table 1, entries 16 and 17) we proceeded to explore the substrate scope (Table 2).

Arylations employing aryl groups with electron-donating substituents demonstrated higher yields (*p*-Tol > *p*-BrC₆H₄) (Table 2, entries 3 and 4). The *p*-bromo-substituted iodane **I-6**, albeit in a more modest yield, gave the diene **10d** with 98:2 selectivity. Switching to the more sterically challenged triisopropylsilyl (TIPS) group (Table 2, entry 2) resulted in higher indene proportion in the resulting mixture (**10b/11b** = 67:33). In all cases the (1*E*,3*E*)-dienes **10a–e** were obtained as the major isomer (87–95% isomeric purity). In small quantities the other isomers (1*Z*,3*E*) and (1*E*,3*Z*) or (1*Z*,3*Z*) were also detected by their characteristic signals in the ¹H NMR spectra.

Interestingly, the internal alkyne **7c** (R = Ph, Si = TIPS) was completely unreactive under both standard arylation conditions (70 °C in EtOAc) and higher reaction temperatures (110 °C in BuOAc). In these cases, the starting material was recovered with no signs of degradation. This indicates that the provided method is limited to propargylsilanes containing a terminal alkyne group.

Arylation of internal nucleophile-containing propargylsilanes

Internal nucleophile-containing substrates are interesting, because they offer the possibility of heterocyclization, as described in our previous work [22]. The internal *O*-nucleophile-

Table 2: Aryldiene scope.

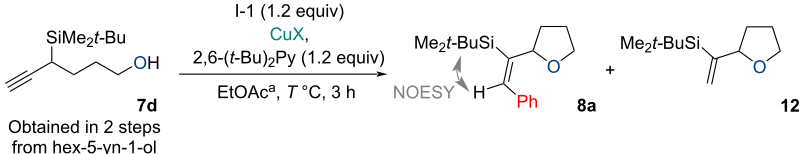
7a: R = H, Si = SiMe₂t-Bu 7b: R = H, Si = Si(iPr)₃ 7c: R = Ph, Si = Si(iPr)₃						
Entry	Product	Iodane	10/11 ^a (mol/mol)	Yield 10 + 11 (%)	Isomeric ratio for diene 10 (mol/mol) ^b	
					(1E,3E)	Σ(1E,3Z) + (1Z,3E) + (1Z,3Z)
1		I-2	87:13	51 ^c	92	8
2		I-2	67:33	61 ^d	93	7
3		I-5	85:15	69 ^d	87	13
4		I-6	98:2	37 ^d	95	5
5		I-2	—	0 ^e	—	—

^aRatio after column chromatography. ^bDetermined after C18 silica gel column chromatography by ¹H NMR in CDCl₃. ^cReaction scale: 1.90 mmol of 7. ^dReaction scale: 0.48 mmol of 7. ^eNo reaction at 70 °C in EtOAc (3 h) or 110 °C in BuOAc (17 h).

containing starting material, 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (**7d**), was obtained from the commercial hex-5-yn-1-ol by a *O*-silylation and subsequent retro-Brook reaction sequence [29]. Arylation of silane **7d** with 1.2 equiv PhMesIOTf (**I-1**), 5 mol % CuCl and 1.2 equiv 2,6-(*t*-Bu)₂Py in EtOAc gave the styryl side chain-containing tetrahydrofuran **8a** with 82% NMR yield after 3 h at 60 °C (Table 3, entry 2). The formed double-bond geometry in product **8a** was proved by the 2D-NOESY

spectrum. The corresponding (*Z*)-isomer was not detected by NMR spectroscopy techniques, indicating that the observed arylation–cyclization cascade reaction is highly stereospecific. With this result in hand, we performed copper catalyst screening (Table 3).

We observed that CuCl and the CuOTf benzene complex gave similarly good yields (82–84% by NMR, Table 3, entries 2 and

Table 3: Conditions screening for copper-catalyzed arylation–cyclization of propargylsilane **7d**.


Entry	CuX (mol %)	T (°C)	8a , % (NMR)	12 , % (NMR)
1 ^b	CuCl (2.5)	20	0	0
2 ^c	CuCl (5)	60	82, 76^d	0
3 ^b	CuI (5)	60	0	0
4 ^{e,f}	[CuOTf]₂·PhH (5)	60	84	0
5 ^e	Cu(MeCN) ₄ BF ₄ (5)	70	77	0
6 ^e	Cu ₂ O (5)	70	6	2
7 ^e	[CuOTf] ₂ ·PhH (2.5)	70	70	0
8 ^{e,g}	[CuOTf] ₂ ·PhH (2.5)	70	43	0
9 ^b	[CuOTf] ₂ ·PhH (11)	70	47	0

^a*c*_{7d} = 0.10 mmol/mL, ^bReaction scale: 0.24 mmol of **7d**, ^cReaction scale: 4.2 mmol of **7d**, ^dIsolated yield (%), ^eReaction scale: 0.47 mmol of **7d**.^fReaction time: 2 h (full conv.), ^g15 mol % of H₂O as additive.

4), while the CuBF₄ acetonitrile complex was the next best choice (77% by NMR, Table 3, entry 5). Heterogenous catalysis using Cu₂O gave a mixture of the arylated product **8a** and protodecupration side-product **12**, both in poor yields (Table 3, entry 6). Increased catalyst loading (11 mol % of [CuOTf]₂·PhH) resulted in the formation of more side products (Table 3, entry 9), and we therefore decided to proceed with 5 mol % of the catalyst for the substrate scope.

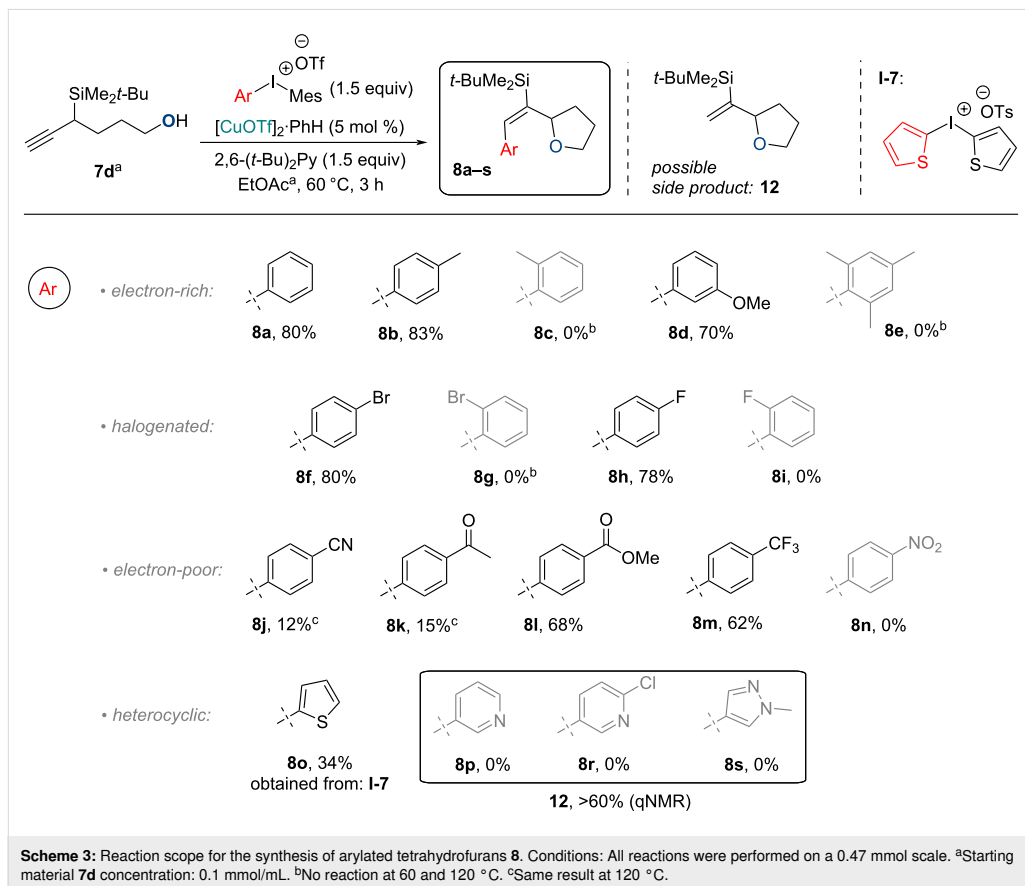
We also observed that, in the absence of base, even at room temperature, only the protodecupration product **12** was obtained (with up to 69% NMR yield). A reaction temperature of 60 °C was found to be optimal and lower temperatures resulted in incomplete conversion.

Under the optimized conditions we explored the reaction scope (Scheme 3). Unlike the previously explored dienes **10**, the obtained tetrahydrofuran products **8** were easy to purify by standard column chromatography techniques (30–50% DCM). Iodanes, containing electron-rich aryl groups (*p*-Tol, *m*-MeO-C₆H₄, Ph) or halogens (Br, F) gave the highest tetrahydrofuran **8** yields (70–83%). In contrast, electron-withdrawing group-containing iodanes, especially those holding nucleophilic heteroatoms (CN ≈ COR >> NO₂) reacted poorly. Iodanes, containing electron-withdrawing groups with low nucleophilicity (CF₃), however, gave fair yields. We also found that *ortho*-substituted iodanes did not provide arylation products, which can be attributed to the unfavorable steric hindrance [30].

Iodanes containing *N*-heterocycles, such as pyridine and pyrazole, provided the non-arylated tetrahydrofuran **12** as the main reaction product (Scheme 3), which is likely formed via the protodecupration pathway. However, to our delight the thiophenyl group was successfully added to the propargylsilane with 34% yield by using the symmetrical dithiophen-2-ylidonium *p*-tosylate (**1-7**). It should be noted that all products **8** were obtained with exclusive (*E*)-selectivity.

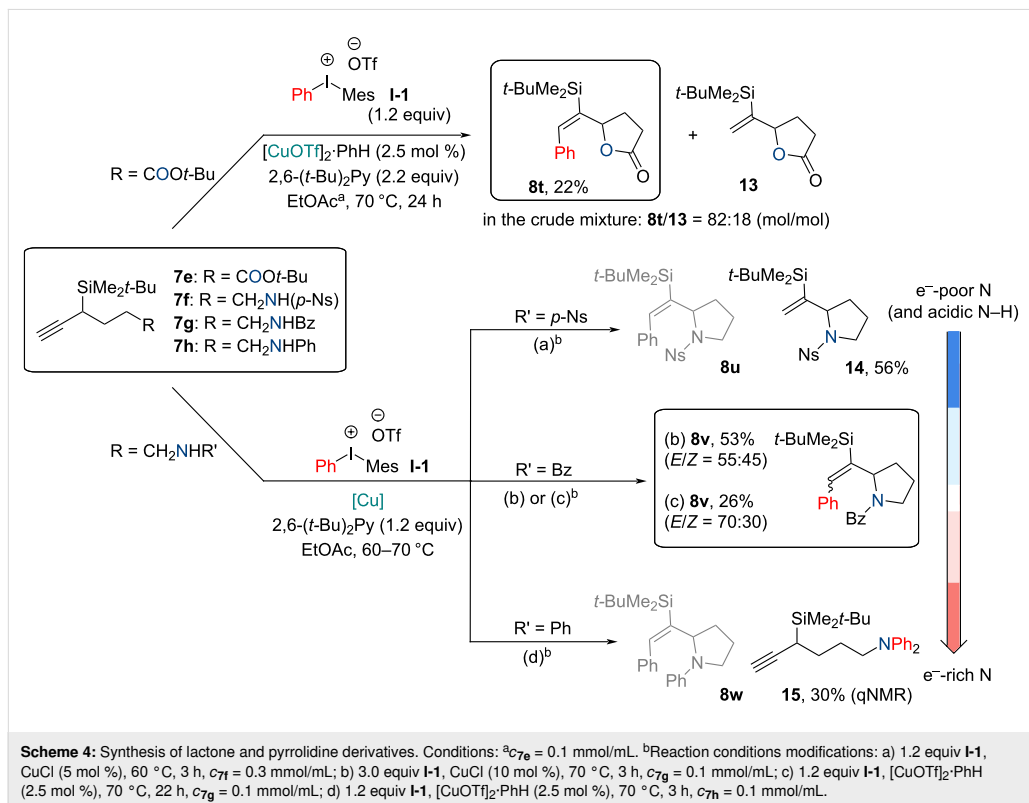
Tetrahydrofuran **8a** and some analogous compounds could be synthesized previously from alcohol **7d**, but in two steps, employing a halogen electrophile-induced propargylsilane **7d** halogenation–cyclization cascade and Suzuki–Miyaura cross-coupling in the second step [22]. Thus, we have developed a faster and palladium-free route towards tetrahydrofurans **8**. The latter can still be modified further through silicon–halide exchange followed by cross-coupling chemistry as described by us recently, among other possible transformations [21,22].

Interestingly, the addition of *O*-nucleophiles to form 1,3-carbofunctionalization products, can only be achieved in an intramolecular fashion. In the presence of an excess (5 equiv) of external an *O*-nucleophile R–OX (alcohol, carboxylic acid, its sodium salt or the silylated carboxylic acid), the arylation reaction of aliphatic chain-containing propargylsilane **7b** (standard conditions; see Scheme 3) only resulted in the arylation of the oxygen nucleophile itself.



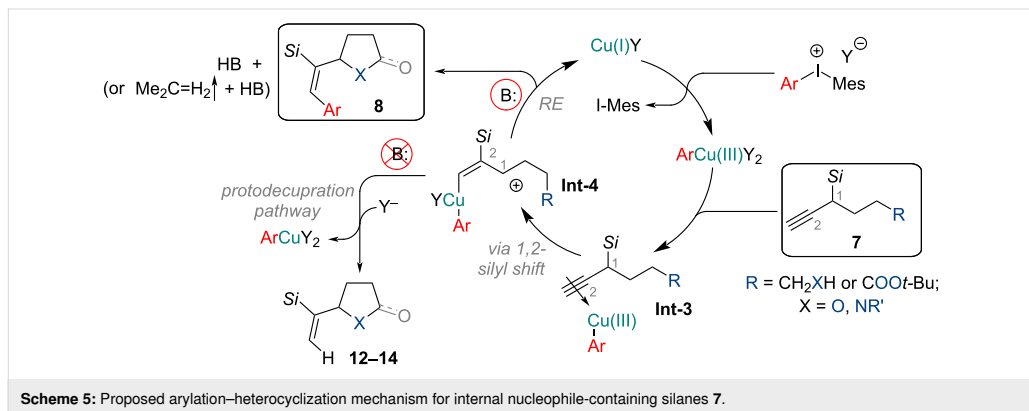
Next, we proceeded to expand the substrate scope by exploring other internal nucleophiles (Scheme 4), that could be used instead of the alcohol. The carboxylic acid-containing silane **7** ($\text{R} = \text{COOH}$), which was obtained by stepwise oxidation of the alcohol **7d**, failed to give the desired lactone **8t** product due to *O*-arylation of the carboxylic acid, leading to phenyl alkyl ester formation. Its silylated version (**7**, where $\text{R} = \text{COOSi}(\text{Me})_3$) only resulted in starting material degradation. Interestingly, *tert*-butyl ester **7e** ($\text{R} = \text{COO-}t\text{-Bu}$) provided the desired arylated lactone **8t**, along with the protodecupration product **13**, which was formed in excess under the standard arylation conditions (Scheme 4). An additional equivalent of base (2.2 equiv of 2,6-(*t*-Bu) $_2$ Py) helped to suppress the formation of the non-arylated product **13**, making the arylated lactone **8t** the main reaction product. By adding a larger excess of base, conversion rates were significantly reduced. For detailed reaction optimization see Supporting Information File 1.

Next, we switched to internal *N*-nucleophiles. *N*-Nosylated starting material **7f** under standard arylation conditions gave the 2-(1-(*tert*-butyldimethylsilyl)vinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (**14**) with a 56% yield. Most likely in this case sulfonamide *N*-H is too acidic and this may lead to protodecupration. The arylation–cyclization of benzamide **7g** afforded the pyrrolidine derivative **8v** as a mixture of (*E/Z*)-isomers. By treating the isomeric mixture (*E/Z* = 55:45) with HNTf $_2$ (0.9 equiv) in DCM (0.03 mmol/mL) and stirring at 0 °C to rt for 3 h, (*Z*)-**8v** selectively degraded and the pure product (*E*)-**8v** could be isolated with 47% yield. On the other hand, if the amine group was too nucleophilic, as in the case of *N*-(4-(*tert*-butyldimethylsilyl)hex-5-yn-1-yl)aniline (**7h**), the amine *N*-H was arylated instead of the alkyne, resulting in the formation of *N*-(4-(*tert*-butyldimethylsilyl)hex-5-yn-1-yl)-*N*-phenylaniline (**15**). Thus, acylamides were found to have optimal $\text{p}K_a$ and nucleophilicity to react according to our desired pathway (Scheme 4).



For the heterocyclization mechanism under arylating conditions, we propose a Cu(I/III) catalyzed pathway (Scheme 5). Firstly, the copper(I) salt reacts with the diaryl- λ^3 -iodane (ArMesIY) to generate the strongly electrophilic arylcopper(III) species. The latter activates the propargylic system to induce the

1,2-silyl shift, producing the allylic cation intermediate **Int-4**, which is stabilized by the β -silicon effect. A following attack of an internal nucleophile (*O*-, *N*-) and reductive elimination affords the arylated product **8** and regenerates the Cu(I) catalyst. The added base (B:) traps the H⁺, generated in this catalytic



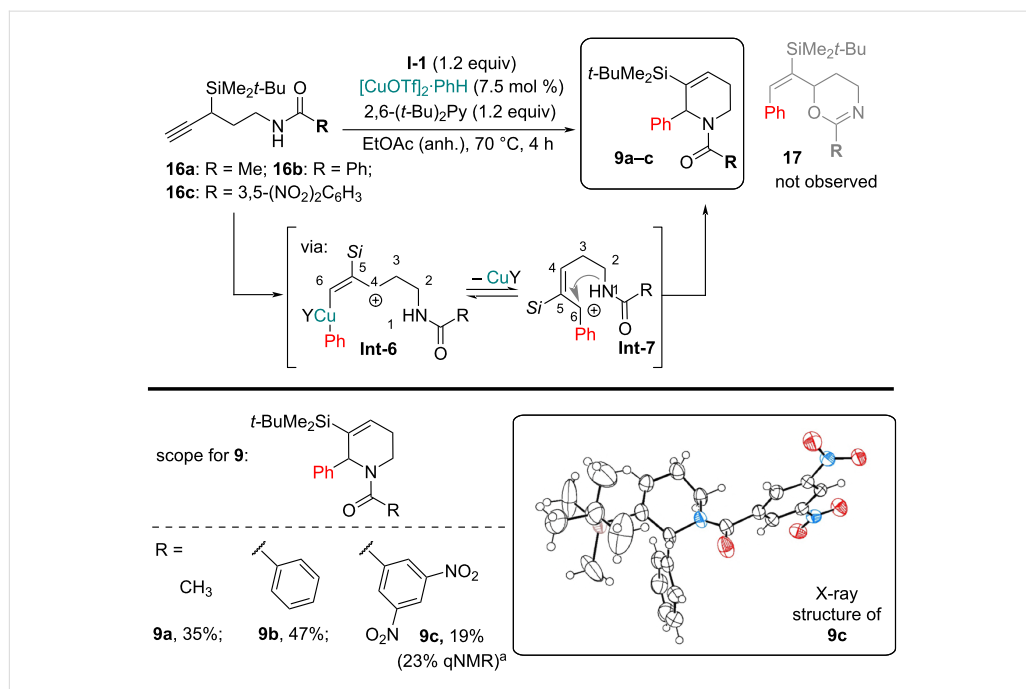
cycle. In the case of *tert*-butyl esters (**7**: R = COO*t*-Bu) an equivalent of isobutylene gas is released as a side-product. In the absence of a base, the protodecupration pathway is predominant, affording non-arylated heterocycles **12–14** instead.

When considering shorter carbon chain-containing acylamides **16a–c** as starting materials, we expected a similar cyclization pattern, involving imidate formation [10]. Instead aminopentynes **16a–c** underwent allylic rearrangement, affording tetrahydropyridines **9** (Scheme 6). The tetrahydropyridine core was confirmed unambiguously by X-ray structure analysis of dinitrobenzamide **9c**. More electron-rich acylamides reacted faster and gave less side-products, compared to more electron-poor analogs, that needed longer reaction times to reach full conversion (4 h for R = Ph, Me; 20 h for R = 3,5-(NO₂)₂C₆H₃).

Conclusion

In this work we have reported copper-catalyzed arylation reactions of propargylsilanes, using iodonanes as the electrophilic aryl synthon equivalents. For internal nucleophile-containing propargylsilanes subsequent heterocyclization was observed, and, depending on the chain length, giving either 1,3- or 1,1-carbofunctionalization products: tetrahydrofuran **8a–o** and

pyrrolidine **8v** derivatives, containing a functionalized styryl group in the side chain, and 1,2,3,6-tetrahydropyridine derivatives **9a–c**. We observed a distinct preference for (*E*)-geometry formation in the resulting C=C bond. Internal alcohol, ester, and acylamide functional groups were found to be compatible with the reaction conditions, whereas for external nucleophiles *N*- or *O*-arylation precedes that of the alkyne. In the absence of reactive nucleophiles, aryl-substituted 1,3-dienes were obtained. The presented conditions were best applicable for arylations introducing aryl fragments with medium to high electron density, although some less electron-rich iodonanes could be used, albeit in more modest yields. In contrast to previously studied alkyne 1,2-carbofunctionalization reactions [7–10], which were mostly limited to internal alkynes, only terminal alkyne-containing propargylsilanes were found to be reactive under these conditions. In summary, we have demonstrated that under copper-catalyzed conditions aryl iodonanes can arylate propargylsilanes and induce a 1,2-silyl shift to generate β-Si-stabilized allyl cations. Compared to the previously employed two-step halocyclization–cross-coupling sequence [22], this approach offers a shorter, [Pd]-free synthetic sequence to the modified styryl-containing tetrahydrofuran **8a** and its previously unknown analogs. Efforts to broaden the scope of propargylsi-



Scheme 6: Arylation of C5-chain containing acylamides **16a–c**. ^aThe reaction was performed under modified conditions: I-2 (3.0 equiv), 20 h because under standard reaction conditions incomplete conversion was observed (with 48% recovered **16c**).

lanes by modifying their backbones, which connect the propargylic position with the internal nucleophile, are currently underway in our laboratory and will be reported elsewhere.

Supporting Information

Supporting Information File 1

Experimental data, synthesis procedures, ^1H and ^{13}C NMR spectra, and X-ray data.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-154-S1.pdf>]

Funding

This work was supported by the Latvian Council of Science Grant LZP-2023/1-0576 and the EU RRF within project No 5.2.1.1.i.0/2/4/I/CFLA/003 academic career doctoral grant, ID 1134.

Author Contributions

Rasma Kronkalne: funding acquisition; investigation; writing – original draft. Rūdolfs Bejaunieks: investigation; methodology. Armands Sebris: investigation. Anatoly Mishnev: investigation. Māris Turks: conceptualization; funding acquisition; methodology; supervision; writing – review & editing.

ORCID® iDs

Rasma Kronkalne - <https://orcid.org/0009-0003-8194-2445>

Anatoly Mishnev - <https://orcid.org/0009-0005-6835-2103>

Māris Turks - <https://orcid.org/0000-0001-5227-0369>

Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

References

- Rani, N.; Soni, R.; Sihag, M.; Kinger, M.; Aneja, D. K. *Adv. Synth. Catal.* **2022**, *364*, 1798–1848. doi:10.1002/adsc.202200088
- Mamgain, R.; Sakthivel, K.; Singh, F. V. *Beilstein J. Org. Chem.* **2024**, *20*, 2891–2920. doi:10.3762/bjoc.20.243
- Fañanás-Mastral, M. *Synthesis* **2017**, *49*, 1905–1930. doi:10.1055/s-0036-1589483
- Kang, S.-K.; Kim, J.-S.; Choi, S.-C.; Lim, K.-H. *Synthesis* **1998**, 1249–1251. doi:10.1055/s-1998-6086
- Deprez, N. R.; Sanford, M. S. *Inorg. Chem.* **2007**, *46*, 1924–1935. doi:10.1021/ic0620337
- Wang, D.; Li, Q.; Li, M.; Du, Z.; Fu, Y. *Curr. Org. Chem.* **2021**, *25*, 1298–1320. doi:10.2174/1385272825666210512015410
- Walkinshaw, A. J.; Xu, W.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 12532–12535. doi:10.1021/ja405972h
- Tang, S.; Peng, P.; Zhong, P.; Li, J.-H. *J. Org. Chem.* **2008**, *73*, 5476–5480. doi:10.1021/jo8008808
- Chen, J.; Chen, C.; Chen, J.; Wang, G.; Qu, H. *Chem. Commun.* **2015**, *51*, 1356–1359. doi:10.1039/c4cc08363f
- Sinai, Á.; Mészáros, Á.; Gáti, T.; Kudar, V.; Palló, A.; Novák, Z. *Org. Lett.* **2013**, *15*, 5654–5657. doi:10.1021/ol402600r
- Suarez, L. L.; Greaney, M. F. *Chem. Commun.* **2011**, *47*, 7992. doi:10.1039/c1cc13094c
- Peng, J.; Chen, C.; Chen, J.; Su, X.; Xi, C.; Chen, H. *Org. Lett.* **2014**, *16*, 3776–3779. doi:10.1021/ol501655g
- Villo, P.; Olofsson, B. Arylations Promoted by Hypervalent Iodine Reagents. *Patai's Chemistry of Functional Groups*; John Wiley & Sons: Hoboken, NJ, USA, 2018; pp 1–61. doi:10.1002/9780470682531.pat0950
- Suero, M. G.; Bayle, E. D.; Collins, B. S. L.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 5332–5335. doi:10.1021/ja401840j
- Kang, S.-K.; Yoon, S.-K.; Kim, Y.-M. *Org. Lett.* **2001**, *3*, 2697–2699. doi:10.1021/ol0162825
- Radhakrishnan, U.; Stang, P. J. *Org. Lett.* **2001**, *3*, 859–860. doi:10.1021/ol015555t
- Kwak, Y.; Choi, Y. R.; Yu, J.; Choi, S.; Hong, K. B. *Asian J. Org. Chem.* **2023**, *12*, e202300235. doi:10.1002/ajoc.202300235
- Wang, W.; Zhou, J.; Wang, C.; Zhang, C.; Zhang, X.-Q.; Wang, Y. *Commun. Chem.* **2022**, *5*, 145. doi:10.1038/s42004-022-00768-3
- Bejaunieks, R.; Puriņš, M.; Turks, M. *Synthesis* **2020**, *52*, 2147–2161. doi:10.1055/s-0039-1690898
- Roberts, D. D.; McLaughlin, M. G. *Adv. Synth. Catal.* **2022**, *364*, 2307–2332. doi:10.1002/adsc.202200237
- Bejaunieks, R.; Puriņš, M.; Līpiņa, R. A.; Mishnev, A.; Turks, M. *Org. Lett.* **2023**, *25*, 4627–4631. doi:10.1021/acs.orglett.3c01245
- Kronkalne, R.; Bejaunieks, R.; Ubaidullajeva, A.; Mishnev, A.; Turks, M. *J. Org. Chem.* **2023**, *88*, 13857–13870. doi:10.1021/acs.joc.3c01481
- Delost, M. D.; Smith, D. T.; Anderson, B. J.; Njardarson, J. T. *J. Med. Chem.* **2018**, *61*, 10996–11020. doi:10.1021/acs.jmedchem.8b00876
- Vitaku, E.; Smith, D. T.; Njardarson, J. T. *J. Med. Chem.* **2014**, *57*, 10257–10274. doi:10.1021/jm501100b
- Bhurta, D.; Bharate, S. B. *ChemMedChem* **2022**, *17*, e202100706. doi:10.1002/cmde.202100706
- Puriņš, M.; Mishnev, A.; Turks, M. *J. Org. Chem.* **2019**, *84*, 3595–3611. doi:10.1021/acs.joc.8b02735
- Yamamoto, Y. *J. Org. Chem.* **2018**, *83*, 12775–12783. doi:10.1021/acs.joc.8b02215
- Chen, B.; Hou, X.-L.; Li, Y.-X.; Wu, Y.-D. *J. Am. Chem. Soc.* **2011**, *133*, 7668–7671. doi:10.1021/ja201425e
- Wang, X.; Gao, Q.; Buevich, A. V.; Yasuda, N.; Zhang, Y.; Yang, R.-S.; Zhang, L.-K.; Martin, G. E.; Williamson, R. T. *J. Org. Chem.* **2019**, *84*, 10024–10031. doi:10.1021/acs.joc.9b01190
- Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172–8174. doi:10.1021/ja801767s

License and Terms

This is an open access article licensed under the terms of the Beilstein-Institut Open Access License Agreement (<https://www.beilstein-journals.org/bjoc/terms>), which is identical to the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0>). The reuse of material under this license requires that the author(s), source and license are credited. Third-party material in this article could be subject to other licenses (typically indicated in the credit line), and in this case, users are required to obtain permission from the license holder to reuse the material.

The definitive version of this article is the electronic one which can be found at:
<https://doi.org/10.3762/bjoc.21.154>

Recent Advances in Intramolecular C-N Bond Formation for Pyrrolidine Synthesis

Kroņkalne, R.; Turks, M.

ChemistryOpen, **2026**, 15 (6), e70182

Pārpublicēts no brīvpiekļuves publikācijas saskaņā ar *Creative Commons Attribution* licenci (CC BY 4.0).

Copyright © 2026 Kroņkalne et al.; licensee Wiley-VCH GmbH.

Reproduced from an Open Access publication under the *Creative Commons Attribution* License (CC BY 4.0).

Copyright © 2026 Kroņkalne et al.; licensee Wiley-VCH GmbH.

REVIEW OPEN ACCESS

Recent Advances in Intramolecular C–N Bond Formation for Pyrrolidine Synthesis

Rasma Kropķalne | Māris Turks 

Institute of Chemistry and Chemical Technology, Faculty of Natural Sciences and Technology, Riga Technical University, Riga, Latvia

Correspondence: Māris Turks (maris.turks@rtu.lv)

Received: 1 February 2026 | Revised: 24 February 2026 | Accepted: 27 February 2026

Keywords: C–H activation | C–N bond formation | heterocyclization | intramolecular amination | pyrrolidines

ABSTRACT

Pyrrolidines constitute a privileged class of nitrogen heterocycles that are ubiquitous in pharmaceuticals, bioactive molecules, and functional materials, thereby continuing to stimulate the development of efficient and versatile synthetic strategies. Among these, intramolecular C–N bond formation represents one of the most fundamental and broadly applicable approaches for the construction of pyrrolidine frameworks. Despite its central importance, a systematic overview focusing specifically on this ring-closing paradigm has been lacking. This review summarizes key advances reported between 2013 and 2025 in the synthesis of pyrrolidines via intramolecular C–N bond formation, focusing specifically on examples featuring a polar ring-closure step $N: \rightarrow C(+/\delta^+)$. The discussion is organized according to the ring-formation mechanism, encompassing transition-metal-catalyzed and metal-free cyclization of alkenyl and alkynyl amines, tandem annulation processes, intramolecular nucleophilic additions to carbonyl compounds, nucleophilic substitution reactions, and regioselective $C(sp^3)\text{--}H$ activation of aliphatic amines, including Hofmann–Löffler–Freitag-type transformations. By highlighting mechanistic features, substrate scope, and synthetic utility, this review aims to provide a comprehensive and practical reference for the design of new pyrrolidine syntheses based on intramolecular C–N bond formation.

1 | Introduction

The pyrrolidine scaffold is a privileged structural motif in medicinal chemistry and ranks among the most frequently encountered frameworks in small-molecule drugs [1, 2] and bioactive compounds [3–5]. Over the past decade, pyrrolidines have remained prominent targets in synthetic chemistry, motivating the development of a wide array of methodologies for the preparation of structurally diverse derivatives. Several recent target-oriented reviews have highlighted the synthesis of pyrrolidine-based organocatalysts [6], pharmaceutical agents and their precursors [7], spiro-pyrrolidines [8, 9], and other pyrrolidine scaffolds bearing specific substitution patterns [10–15]. Complementary methodology-focused reviews have summarized advances in photochemical approaches [16, 17], Lewis-acid-catalyzed cyclizations of propargyl and homopropargyl amines [18], enantioselective silver-catalyzed reactions [19], copper-catalyzed alkyne aminations [20], glycine-

based [3 + 2] cycloadditions for the synthesis of polycyclic architectures [21], multicomponent reactions [22], palladium-catalyzed annulations [23], and oxidative addition of sulfonamides to allylic substrates [24].

In this review, we aim to showcase the diversity of modern synthetic strategies for constructing the pyrrolidine framework via intramolecular C–N bond formation. This transformation, typically proceeding through a cationic mechanism, occurs in polar systems that combine a nucleophilic nitrogen center with an electrophilic carbon species. Representative substrates include alkenyl and alkynyl amines, γ -amino carbonyl compounds, amino alcohols, and sulfinimines bearing suitable leaving groups. Furthermore, through C–H activation pathways, even aliphatic amines can be induced to cyclize via intramolecular C–N bond formation. Despite the fundamental importance of this ring-closing strategy in contemporary pyrrolidine synthesis, a

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2026 The Author(s). *ChemistryOpen* published by Wiley-VCH GmbH.

comprehensive review focusing specifically on intramolecular C–N bond formation as the defining step in pyrrolidine construction was lacking.

Herein, we summarize key developments reported between 2013 and 2025 in the field of intramolecular C–N bond formation leading to pyrrolidine frameworks. The review is organized into five thematic sections: (a) transition-metal-catalyzed and metal-free activation of electrophilic carbon centers (C^+ / C^{6+}) in alkenyl and alkynyl amines; (b) tandem annulation reactions featuring C–N bond formation as the pivotal step; (c) intramolecular nucleophilic additions to carbonyl compounds; (d) intramolecular nucleophilic substitution reactions; and (e) regioselective $C(sp^3)$ -H activation of aliphatic amines, including Hofmann–Löffler–Freitag-type transformations (Scheme 1).

2 | Intramolecular Amination of Double/Triple Bonds

Intramolecular amination of unsaturated C–C bonds might be the most extensively studied heterocyclization approach in the past decade, leading to pyrrolidines bearing diverse substitution patterns. For simplicity, we categorized the relevant examples by their cyclization mechanism according to Baldwin's rules [25]. In this section, we discuss both transition-metal (TM)-catalyzed and metal-free activation conditions to enable intramolecular amination, including examples for asymmetric synthesis.

2.1 | 5-Exo-Trig-Cyclization

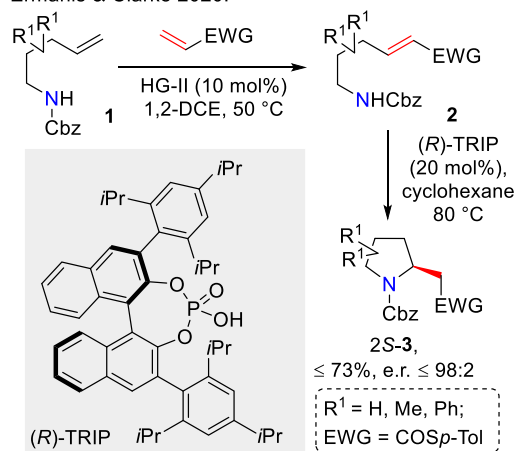
Olefin $C=C$ bond polarization by the introduction of an electron-withdrawing substituent (EWG) enables intramolecular amination in *aza*-Michael fashion. While such transformations are common in their racemic version, the number of asymmetric examples is still limited [26]. Asymmetric *aza*-Michael cyclizations have found applicability in the synthesis of natural products and biologically active heterocycles [27–30]. One of such asymmetric examples, incorporating cyclization via the 5-*exo-trig*-mechanistic pathway, was demonstrated by Ermanis and Clarke, where cross-metathesis

between amine-containing alkenes **1** and thioacrylate using the Hoveyda-Grubbs second-generation catalyst (HG-II) provided EWG-activated alkenes **2**, and the latter underwent intramolecular *aza*-Michael cyclization to give pyrrolidine derivatives **3** (Scheme 2). The cyclization step was catalyzed by (*R*)-TRIP, a chiral phosphoric acid, to obtain 2*S*-pyrrolidines [26]. The opposite stereoselectivity was achieved with (*R*)-TIPSY as the chiral acid catalyst, yielding 2*R*-substituted pyrrolidines **3** [31].

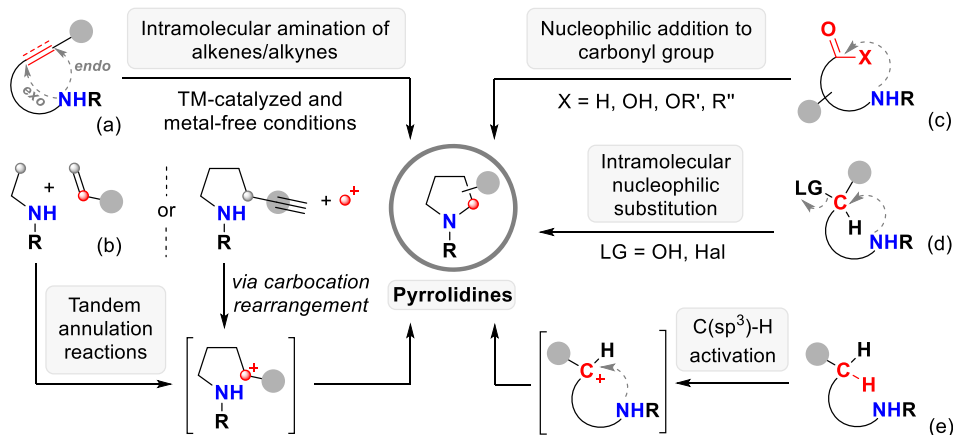
The Huang group used a reversible *aza*-Henry reaction, followed by dynamic kinetic resolution (DKR)-driven *aza*-Michael cyclization to obtain pyrrolidines **6** with up to three stereogenic centers (Scheme 3). Ee's up to 97% could be achieved by using Cinchona alkaloid-derived amine/amide organocatalyst **7** [32].

More recently, Fuwa and coworkers reported a tandem synthesis of 2-carbonylmethyl pyrrolidines **11a** from propargyl alcohols **8** in a three-step, one-pot process (Scheme 4). First, the propargyl alcohol

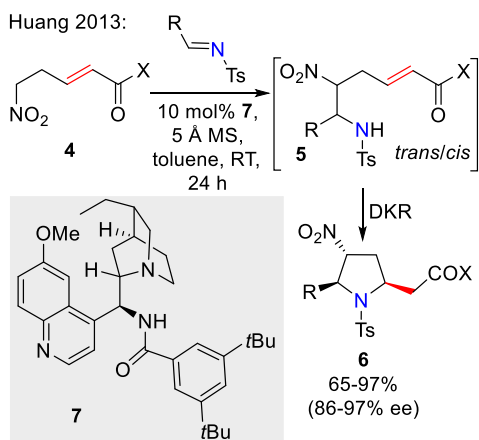
Ermanis & Clarke 2020:



SCHEME 2 | Asymmetric synthesis of pyrrolidines by chiral phosphoric acid-catalyzed *aza*-Michael reaction.



SCHEME 1 | Overview on intramolecular C–N bond formation reactions for pyrrolidine synthesis.



SCHEME 3 | A DKR-driven approach towards asymmetric synthesis of pyrrolidines.

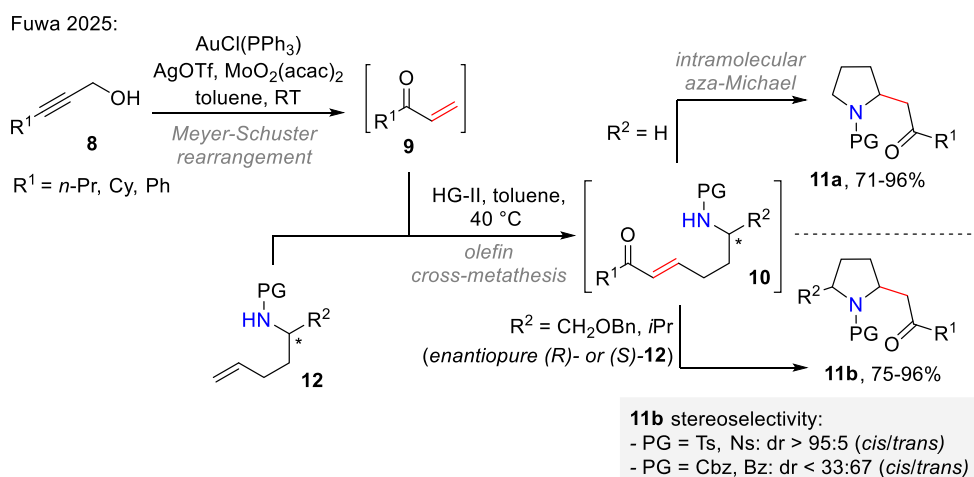
8 was converted to vinyl ketone **9** by a Au/Mo-catalyzed Meyer-Schuster reaction. Next, cross metathesis with amino olefin **12** using **HG-II** catalyst afforded an α,β -unsaturated ketone, which further participated in an intramolecular *aza*-Michael addition to afford pyrrolidine **11a**. In some cases, where the *N*-protected amino group was less nucleophilic (PG = Ns, Bz; $R^2 \neq \text{H}$), catalytic amounts of $\text{Bi}(\text{OTf})_3$ were added to promote the cyclization step. In the absence of an additional Lewis acid, the cationic $(\text{Ph}_3\text{P})\text{Au}^+$ catalyst promoted the *aza*-Michael addition step. α,β -Unsaturated ketones, derived from enantiopure amino olefins (*R*)- or (*S*)-**12** ($R^2 \neq \text{H}$), cyclized to afford 2,5-disubstituted pyrrolidines **11b**, where *cis/trans* selectivity was dependent on the amine protecting group. Cbz- or Bz-protected amines gave a *cis/trans* isomer mixture with slight preference for the *trans*-pyrrolidine **11b** (dr < 33:67 *cis/trans*).

trans). Sulfonamides (PG = Ts, Ns), on the other hand, displayed excellent selectivity for *cis*-product **11b** formation (dr > 95:5 *cis/trans*) [33].

As demonstrated by previous examples [26, 31–33], the *aza*-Michael cyclization approach requires multistep synthesis of the α,β -unsaturated ester/thioester/ketone intermediate, bearing an intrinsic amine moiety. The nucleophilic attack, however, occurs under relatively mild conditions, which is attributed to activation by electron withdrawing olefin substituents. Intramolecular amination of electron-rich (unactivated) alkenes, however, is more challenging and often requires activation by transition metal catalysts [34]. Another possibility for electron-rich olefin hydroamination is to employ photoredox catalysis, as demonstrated by Knowles group. They used aminium radical cation intermediates for the C–N bond construction [35].

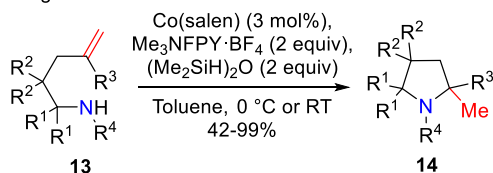
The application of photoredox techniques for C–N bond formation in related systems was highlighted in recently published reviews [36–38]. Our focus being the C–N bond formation strategies proceeding via a cationic mechanism, we wanted to explore in more depth some of the transition metal-catalyzed approaches. In one such example, Shigehisa et al. transformed unactivated alkenylamines **13** into 2-methylpyrrolidines **14** by using the Co(salen) catalyst in combination with *N*-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate and disiloxane (Scheme 5). Exceptional functional group tolerance was observed under these conditions, allowing diverse *N*-functionalization possibilities [39].

In the proposed reaction mechanism (Scheme 6), the *N*-fluoro-2,4,6-trimethylpyridinium salt fluorinated the Co(II) catalyst to form the F-Co(III) intermediate, which was hydrosilylated to afford the active catalytic H-Co(III) species. Cobalt(III) hydride was then added to the olefin **13** according to Markovnikov's rule. Homolytic cleavage of the C-Co(III) bond afforded the radical intermediate **16**, which was oxidized to the carbocation **17** by the present Co(III) species. Lastly, the C–N bond was formed by nucleophilic attack of the tethered amide, affording the 2-methylpyrrolidine product **14** [39].



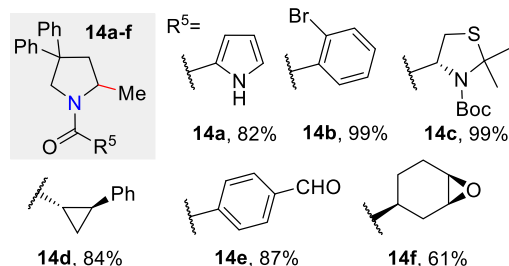
SCHEME 4 | Tandem synthesis of 2-carbonylmethyl pyrrolidines **11a** and their 2,5-substituted analogs **11b**.

Shigehisa 2014:



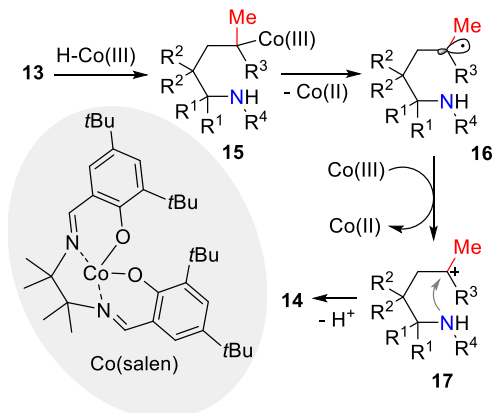
$R^1 = \text{H, Me}; R^2 = \text{H, Ph}; R^3 = \text{H, Me, Ph};$
 $R^4 = \text{COR}^5, \text{COOR}^5, \text{SO}_2\text{R}^5$

Selected examples:



SCHEME 5 | Pyrrolidine synthesis by Co-catalyzed amination of alkene 13.

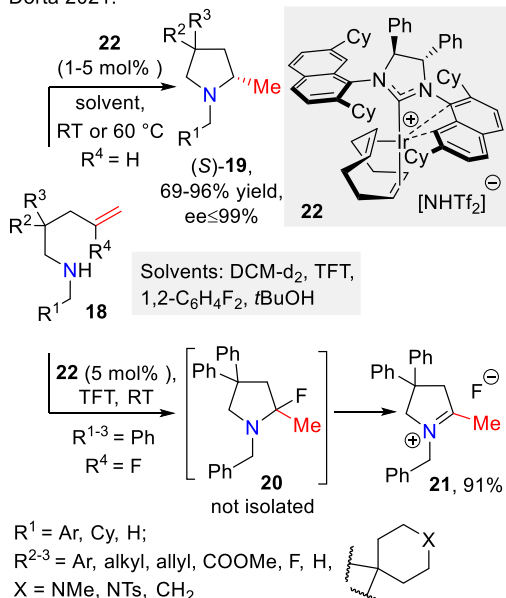
Proposed mechanism: (Shigehisa 2014)



SCHEME 6 | Proposed mechanism for Co-catalyzed amination of alkene 13.

Asymmetric hydroamination of unactivated aminoalkenes **18** was achieved by Dorta and coworkers using a cationic iridium system **22** with the general formula $[(\text{NHC}^*)\text{Ir}(\text{COD})][\text{X}]$ (Scheme 7). Noteworthy features of this method include high enantioselectivity, ensured by incorporation of a chiral monodentate NHC steering ligand, and high functional group tolerance, where excellent results could be achieved with both electron-rich and poor benzylic substituents. *N*-Alkyl substituents gave equally good results, although a slight decrease in enantioselectivity was observed with the *N*-methyl substituted substrate **18** ($R^1 = \text{H}$, $R^{2,3} = \text{Ph}$), indicating that a more sterically

Dorta 2021:



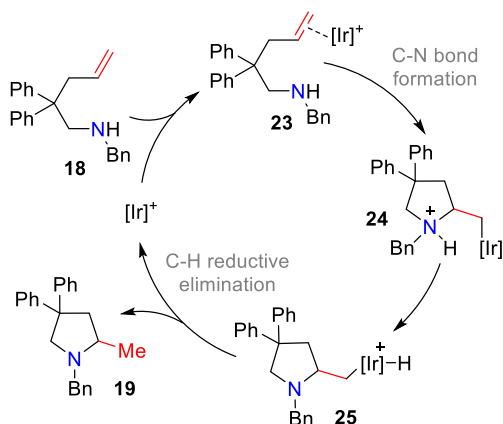
SCHEME 7 | Asymmetric hydroamination of unactivated aminoalkenes 18.

obstructing *N*-substituent is favorable. Interestingly, switching to the similarly sized, but electronically distinct *N*-phenyl substituent decreased reactivity and the resulting 2-methylpyrrolidine **19** was no longer obtained in optically enriched form ($R^{2,3} = \text{Ph}$, 92% yield, 9% ee), limiting this method to the *N*- RCH_2 -moiety containing substrates **18**. Fluorinated olefin **18** ($R^{1-3} = \text{Ph}$, $R^4 = \text{F}$), when subjected to the reaction conditions (5 mol% of catalyst **22**, (trifluoromethyl)benzene (TFT) as solvent), gave the unstable 2-fluoropyrrolidine intermediate **20**, which decomposed in the reaction mixture to the iminium fluoride **21** [40].

As mechanistic studies suggested, the above mentioned reaction proceeded by coordination of the olefin functionality in substrate **18** to the catalytically active 14-electron iridium species via the following steps: 1) C–N bond formation during the amine attack; 2) hydrogen transfer from the ammonium species to the iridium, forming Ir(III)-hydride intermediates; and lastly, 3) reductive elimination, affording 2-methyl pyrrolidines **19** (Scheme 8) [40].

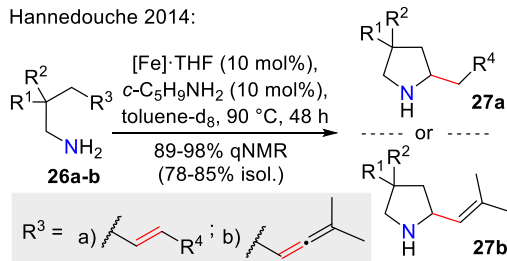
Hydroamination of unprotected primary alkenylamines **26a** is more challenging, especially if we wish to avoid using noble metal catalysis due to their limited availability, price, and toxicity. One of the few available strategies for sustainable hydroamination of unprotected alkenylamines was reported by Hannedouche et al., who used iron(II) complexes as low-cost, nontoxic, and abundant metal catalysts for this transformation (Scheme 9). Interestingly, allenes **26b** also participated in this reaction, forming 2-vinyl substituted pyrrolidines **27b** [41].

Although pyrrolidines **27a-b** were obtained as major products, the formation of side products **31** and **32** in smaller quantities was also observed. Experimental observations suggested that the reaction selectivity was influenced by the concentration of

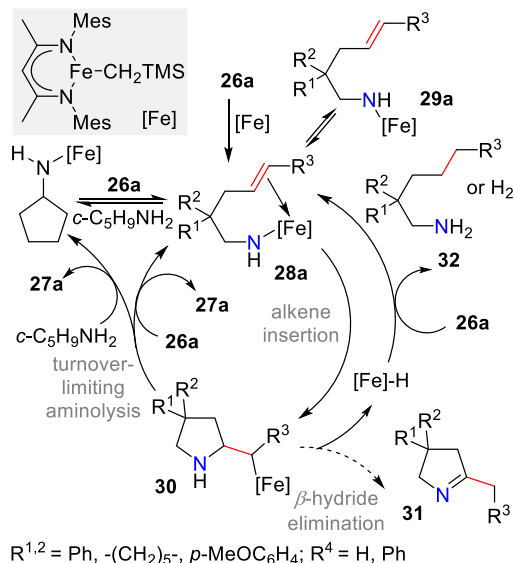


SCHEME 8 | Proposed mechanism for hydroamination of unactivated aminoalkenes **18**.

Hannedouche 2014:



Proposed mechanism:



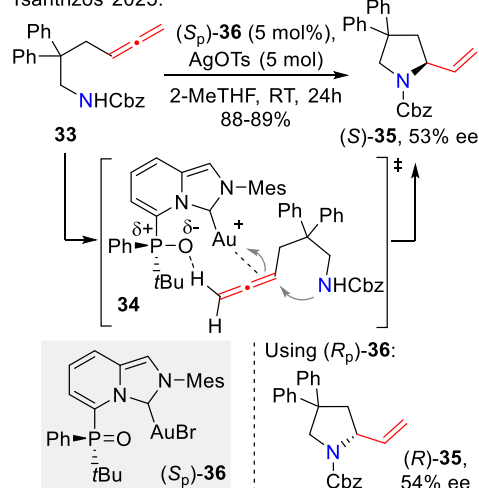
SCHEME 9 | Hydroamination of unprotected primary alkenylamines **26a-b** employing Fe catalysis.

primary amine present in the mixture. By adding a noncyclizable primary amine—cyclopentylamine (cPentNH₂)—to the reaction mixture, the reaction selectivity was greatly improved, reducing the side product formation to trace amounts. Mechanistic studies, however, stated that the alkene migratory insertion into the Fe—NHR bond happens without the assistance of the additional amine (cPentNH₂). Aminolysis was determined as the turnover-limiting step of the proposed catalytic cycle (Scheme 9) [41].

Enantioenriched 2-vinyl pyrrolidines **35** were obtained by the Tsantrizos group, using *P*-chiral phosphine oxide *N*-heterocyclic carbene-Au(I) catalysts (*S_p*)- and (*R_p*)-**36** for stereoselective intramolecular hydroamination of allenes **33**. (*S_p*)-PO-NHC-Au(I) catalyst (*S_p*)-**36** afforded the (*S*)-pyrrolidine **35** in excess (53% ee), whereas (*R_p*)-PO-NHC-Au(I) catalyst (*R_p*)-**36** favored formation of the opposite enantiomer (*R*)-**35** (55% ee). The observed reaction rates were higher compared with the corresponding NHC-Au(I) catalysts. The reaction rate acceleration was attributed to the formation of a hydrogen bond between the terminal allene proton and catalyst P=O, which provided additional stability to the Au(I)-allene π -bond complex in transition state **34** (Scheme 10) [42].

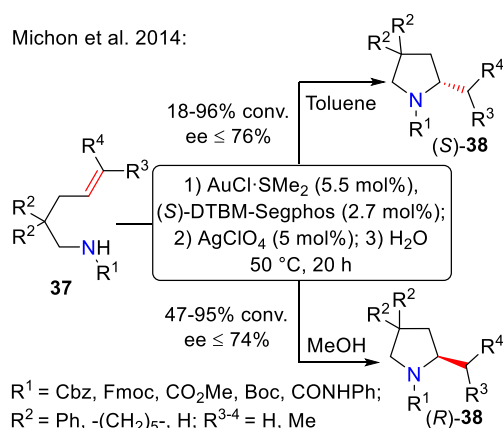
Higher ee (up to 76%) for intramolecular hydroamination of alkenes **37** was achieved using a selected diphosphine binuclear gold(I) chloride complex in a combination with silver salt under mild conditions (Scheme 11). While the control experiments showed that AgClO₄ by itself cannot facilitate this reaction, it played a key role in generating reactive gold cationic species by abstraction of halides from the neutral gold complex, thus greatly improving reactivity. In several cases, conversions up to 96% could be achieved. The reactivity was influenced by alkene **37** *R*^{3,4} substituents in the following manner: H (most reactive) >> Me (least reactive). The substituents in C2 position (*R*²) also had a critical effect on conversion: Ph (highest conversion) > -(CH₂)₅ >> H (lowest conversion). Thorpe–Ingold effects, created by bulky *R*² substituents, also contributed to the stereochemical outcome: -(CH₂)₅ (highest ee) > Ph >> H (lowest ee) [34].

Tsantrizos 2025:



SCHEME 10 | Synthesis of enantioenriched 2-vinyl pyrrolidine **35** from allene **33** using chiral Au-catalysts.

Michon et al. 2014:

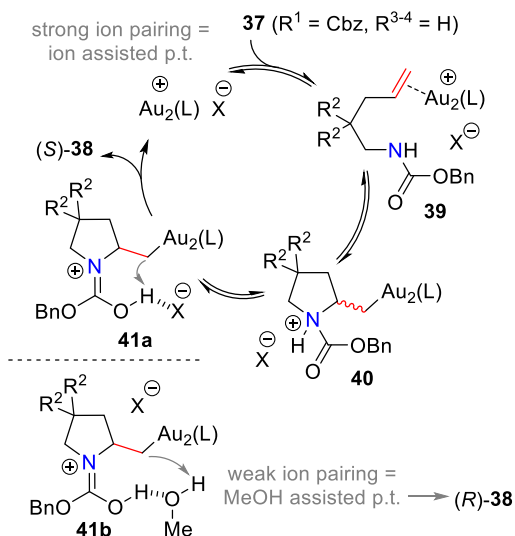


SCHEME 11 | Au-catalyzed asymmetric alkene **37** hydroamination.

Interestingly, by controlling the molecular ion pairs through the solvent polarity, both enantiomers of the product **38** could be obtained. Stronger ion pairing, as observed in toluene, favored the formation of (2*S*)-stereoisomers (Scheme 12). Methanol as a solvent likely assisted in proton transfer, weakening the ion pairing; thus, the opposite stereoselectivity was obtained [34].

The introduction of fluorine-containing functionalities in the pyrrolidine side chain has gained much interest due to the abundance of fluorinated drugs [43–45]. Several new cyclization methods, following the 5-*exo-trig*-pathway, have been developed for the synthesis of fluorinated pyrrolidines **43a–e** as summarized in Scheme 13 [46–50]. Liu and coworkers used palladium-catalyzed intramolecular oxidative amination of alkenes for

Proposed mechanism: (Michon et al. 2014)



SCHEME 12 | Solvent-dependent proton transfer mechanism in Au-catalyzed alkene **37** hydroamination.

the synthesis of CF₃O-group-containing pyrrolidines **43a** (Schemes 13 and 14). In this case, AgOCF₃ was used as the trifluoromethoxide source and SelectFluor as an oxidant. Regarding the substrate design, the amine protecting group had a significant influence on selectivity between the competing 5-*exo-trig*- and 6-*endo-trig* cyclization pathways. Following amine protecting groups promoted the 5-*exo-trig* pathway, leading to pyrrolidines **43a**: Bz (lowest yield) < *N*-Me₂NCO < Boc (highest yield). Sulfonamide protecting groups (SO₂NMe₂) promoted the competing 6-*endo-trig*-pathway instead, affording 3-CF₃O-piperidines as major products [46].

Mechanistic studies confirmed that the above-mentioned reaction proceeded via the palladacycle intermediate **45** (Scheme 14). The insertion of the CF₃O group in the pyrrolidine side chain was likely the result of reductive elimination from the Pd(IV)-intermediate **46** [46].

In a mechanistically analogous process, the Liu group achieved aminofluorination of similar substrates **42b** by using Pd(OAc)₂ as a catalyst and the AgF/PhI(OPiv)₂ system as a fluorinating agent, affording in the side chain monofluorinated pyrrolidines **43b** (Scheme 13) [47].

For the incorporation of the CHF₂ functionality into the pyrrolidine side chain, the Dolbier group used the Cu(dap)₂Cl photoredox catalyst instead (Scheme 13). In the proposed mechanism (Scheme 15), the photoexcited Cu(I)-catalyst generated the HCF₂ radical by single electron reduction of HCF₂SO₂Cl. The HCF₂ radical reacted with the alkene **42c**, forming radical intermediate **47**. Following oxidation afforded the carbenium ion intermediate **48**, which was then quenched by the internal amide nucleophile, forming the pyrrolidine ring **43c** with a CHF₂ functionality in the side chain. Addition of Ag₂CO₃ to the reaction mixture ensured chemoselectivity by suppressing the formation of chlorinated side products **48a** [48].

In another copper-catalyzed process, Tan and Liu obtained CF₃-containing pyrrolidines **43d**, wherein Togni II reagent served as CF₃ radical source to furnish an intramolecular aminotrifluoromethylation sequence in unactivated alkenes **42d** (Scheme 13). Two mechanistic pathways were proposed for the aminotrifluoromethylation reaction (Scheme 16). In pathway A, Cu(I)-catalyzed aminocupration of the alkene **42d**, followed by homolytic cleavage of the C–Cu bond, afforded the primary radical **49**, which recombined with the CF₃ radical, forming the fluorinated pyrrolidine derivative **43d**. In pathway B, the CF₃ radical reacted with the alkene **42d** to form the radical intermediate **50**, which was further oxidized to the carbenium ion **51** via a single electron transfer (SET) process. Following C–N bond formation via amide nucleophilic attack provided the cyclic product **43d** [49].

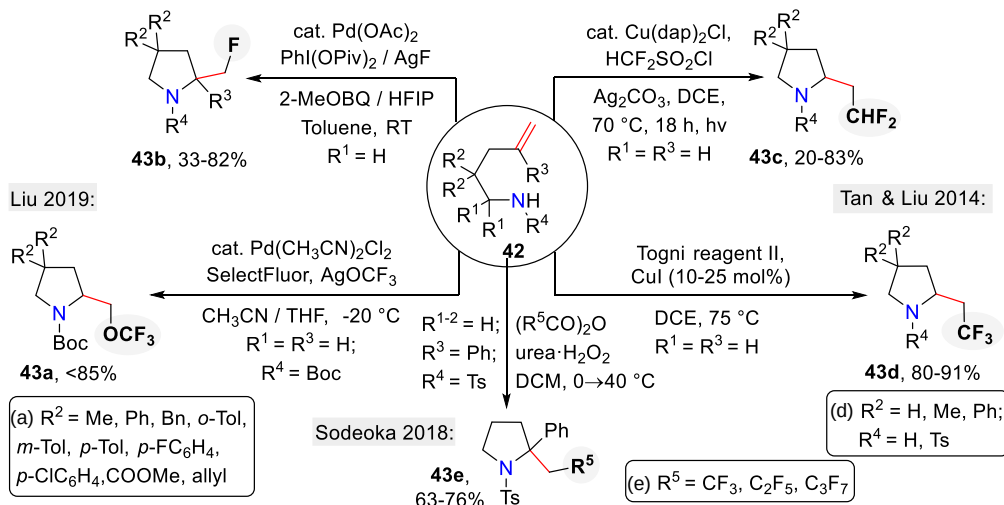
As an alternative to the transition metal-catalyzed approaches, Sodeoka demonstrated a unique reactivity pattern between styrenes **42e** and bis(perfluoroacyl) peroxides, generated in situ from perfluoro acid anhydrides (Schemes 13 and 17). Through a radical-carbenium ion cascade reaction, perfluoroalkylated pyrrolidines **43e** were obtained [50].

Other halides (I, Br) were introduced into the pyrrolidine side chain via an electrochemical halo-amination approach by Wu and Yin, employing anodic oxidation to generate molecular I₂ and Br₂ species in situ from the corresponding lithium salts (Scheme 18). The alkene **55** was activated by formation of the iodonium/bromonium intermediate **57**, followed by intramolecular nucleophilic

Liu 2013:

(b) $R^2 = \text{Ph, Me, H; } R^3 = \text{H, Me; } R^4 = \text{CONMe}_2, \text{CONPr}_2, \text{CONBn}_2, \text{CONHMe, CONHPh}$

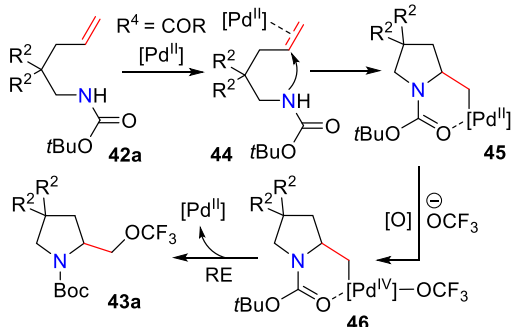
Dolbier 2015:

(c) $R^2 = \text{Me, H, } i\text{-Pr, } p\text{-ClC}_6\text{H}_4, \text{Ph, COOEt, COOMe; } R^4 = \text{Ts, SO}_2\text{C}_6\text{H}_4\text{OMe}$ 

SCHEME 13 | Synthesis of fluorinated pyrrolidines 43.

Proposed mechanism:

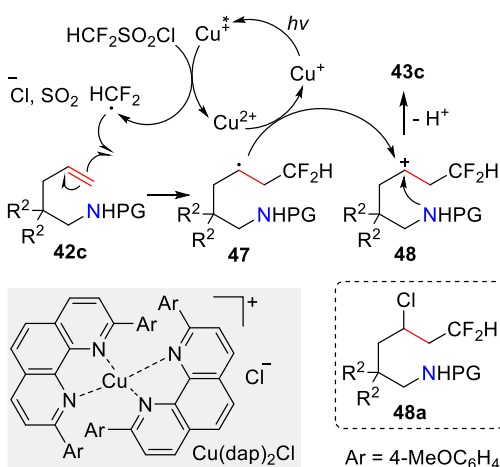
(Liu 2019)

SCHEME 14 | Proposed mechanism for the synthesis of CF_3O -group-containing pyrrolidines 43a.

substitution via amide attack to afford the pyrrolidine **56**, bearing a halogen atom in the side chain. In contrast to the previously discussed intramolecular amination methods, the electrochemical approach was mild and did not rely on external oxidants or transition metal catalysis. Furthermore, the synthetic utility of electrochemical halo-amination was demonstrated by the late-stage functionalization of drug molecules *celecoxib* and *valdecoxib* [51]. Introduction of an additional amine functionality into the pyrrolidine side chain was enabled by Liu and coworkers, who developed a ligand-controlled system for Pd-catalyzed diamination of unactivated olefins **58** (Scheme 19). The choice of palladium ligand was crucial in determining the cyclization regioselectivity—the

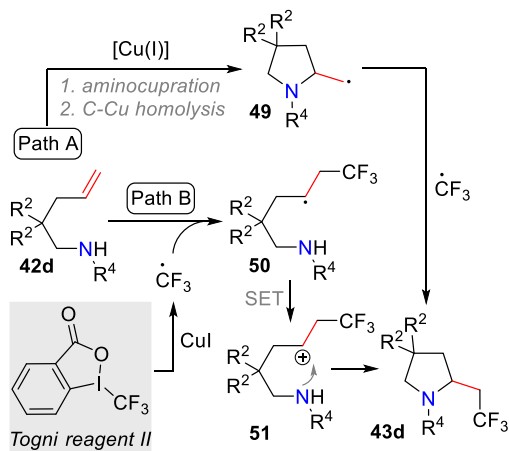
Proposed mechanism:

(Dolbier 2015)

SCHEME 15 | Proposed mechanism for the synthesis of CHF_2 functionality bearing pyrrolidines 43c.

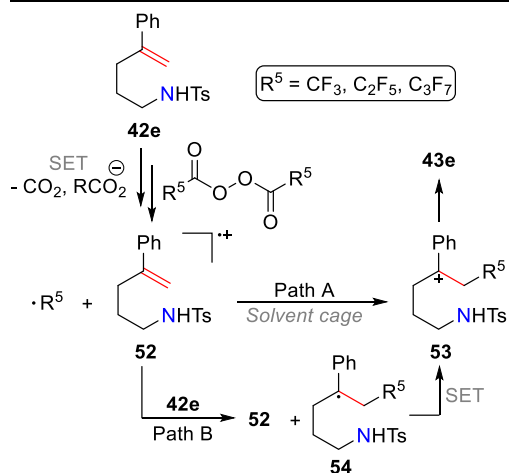
bulky pyox ligand (**L1**) favored the 5-*exo*-cyclization pathway to give pyrrolidines **59**. The less hindered quinox ligand (**L2**), however, promoted the 6-*endo*-cyclization pathway, leading to piperidine rings. The reaction presumably proceeded through a reversible aminopalladation step, following oxidative addition of $\text{R}_2\text{N-F}$ (rate-limiting step) and C–N bond formation via a reductive elimination pathway [52].

Proposed mechanism: (Tan & Liu 2014)



SCHEME 16 | Proposed mechanism for the synthesis of CF_3 -group-containing pyrrolidines **43d**.

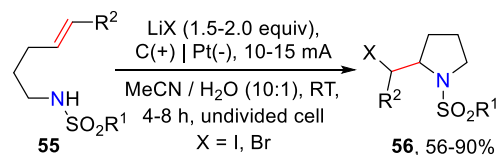
Proposed mechanism: (Sodeoka 2018)



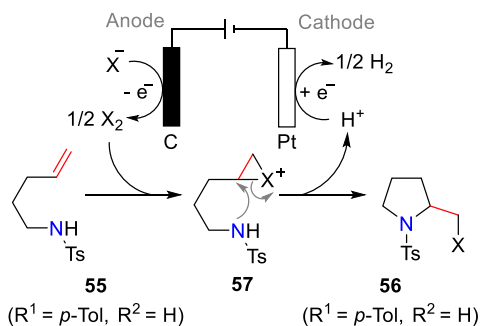
SCHEME 17 | Proposed mechanism for transition-metal-free synthesis of perfluoroalkylated pyrrolidines **43e**.

Under aerobic conditions, palladium-catalyzed alkene **60** difunctionalization led to side chain acetoxylation, as demonstrated by Grubbs and Stoltz (Scheme 20). Oxidation of the alkylpalladium(II) intermediate **63** with O_2 as the only oxidant was kinetically challenging; therefore, facile β -hydride elimination was an issue. To access the high-valent palladium(IV) intermediate **64** more easily, catalytic NO_x species were added to serve as electron transfer mediators. While $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ afforded the highest pyrrolidine **61** yields (up to 83%), nitrites, such as AgNO_2 or $i\text{BuONO}$, were also applicable. After Pd oxidation (II $\rightarrow$ IV), C–O bond forming reductive elimination and acetolysis of the formed cationic intermediate **65**, afforded the aminoacetoxylation product **61** [53].

Wu & Yin 2021:

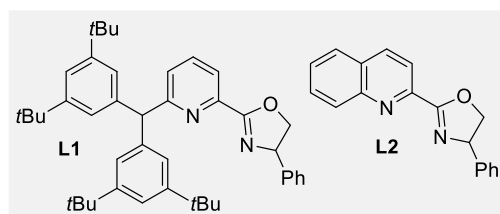
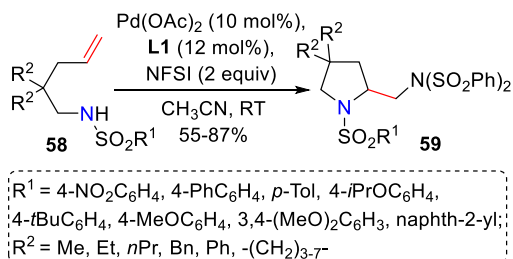


Proposed mechanism:



SCHEME 18 | Electrochemical synthesis of halogenated pyrrolidines **56**.

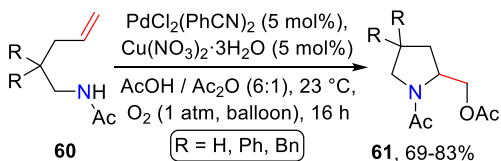
Liu et al. 2020:



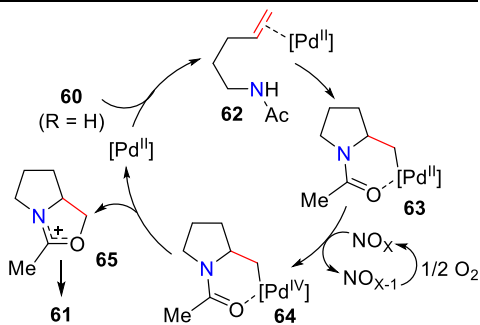
SCHEME 19 | Pd-catalyzed diamination of unactivated olefins.

Copper(I) catalysis under aerobic conditions, on the other hand, led to the synthesis of 2-formyl and 2-ketopyrrolidines **67**, as demonstrated in the aminoxyoxygenation approach by the Chemler group (Scheme 21). Depending on the substitution pattern, moderate to high diastereoselectivity for the formed pyrrolidines **67**

Grubbs & Stoltz 2016:

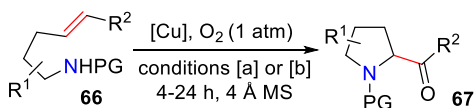


Proposed mechanism:



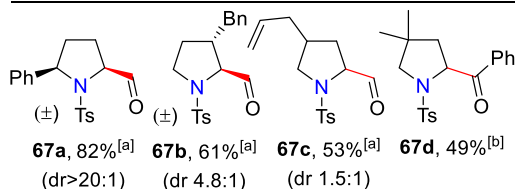
SCHEME 20 | Pd-catalyzed aminoacetoxylation of olefins **60**.

Chemler 2017:



[a] CuCl (20 mol%), PhCH₃, 105–120 °C.
[b] CuCl (15 mol%), **L3** (17 mol%), PhCF₃, 120 °C.

Selected examples:



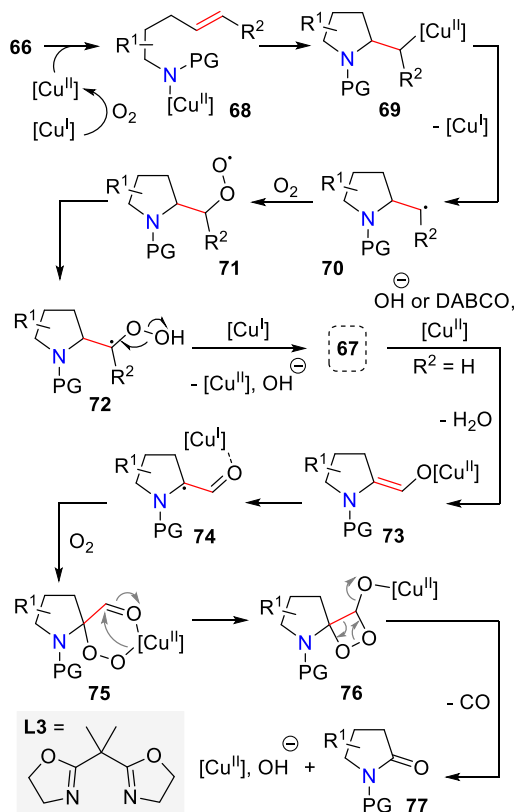
SCHEME 21 | Copper-catalyzed aminooxygenation for the synthesis of 2-formyl and 2-ketopyrrolidines.

was observed, for example, 2,5-disubstituted pyrrolidines were obtained with excellent *cis*-selectivity (*dr* > 20:1). Interestingly, 2-formylpyrrolidines ($R^2 = H$) could be oxidized further to pyrrolid-2-ones **77** by slightly adjusting the reaction conditions, that is, adding the bis(oxazoline) ligand **L3** and an external base (DABCO). For 2-ketopyrrolidines ($R^2 = Ph$), the reaction stopped at product **67**, even in the presence of ligand **L3** [54].

In the hypothesized aminooxygenation mechanism (Scheme 22), the copper(I) catalyst was oxidized to copper(II) in an O₂ atmosphere. Next, alkene **66** *cis*-aminocupration occurred, forming the unstable intermediate **69**, which underwent C–Cu homolysis, liberating the secondary radical species **70**. Molecular O₂ reacted

Proposed mechanism:

(Chemler 2017)

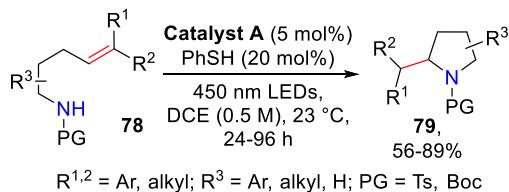


SCHEME 22 | Proposed mechanism for copper-catalyzed aminooxygenation of alkene **66**.

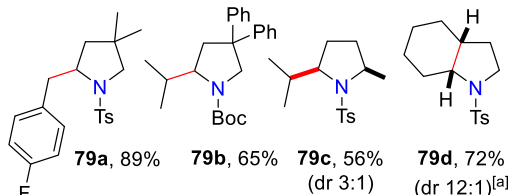
with the formed radical to form the 2-formyl / ketopyrrolidine structure **67**. Unless isolated, formylpyrrolidines ($R^2 = H$) could react further with an in situ-formed hydroxide or external base (DABCO) to form an enolate intermediate **73**. Further reaction with molecular oxygen afforded peroxy intermediates **75** and then **76**. Subsequent oxidative C–C bond cleavage resulted in pyrrolid-2-one **77** formation [54].

A metal-free approach was demonstrated by the Nicewicz group, who performed direct anti-Markovnikov hydroamination of unsaturated amines **78** (Scheme 23). It required visible-light irradiation and catalytic quantities of 9-mesityl-10-methylacridinium tetrafluoroborate (photocatalyst **A**; 5 mol%). Thiophenol (20 mol) was added as a hydrogen atom donor. In substrates where the 5-*exo-trig* cyclization pathway was not feasible due to carbon chain length, 5-*endo-trig* cyclization occurred, as demonstrated by example **79d**, where the bicyclic pyrrolidine structure was obtained with excellent diastereoselectivity. (*dr* 12:1). For 2,5-disubstituted pyrrolidines, the *cis*-selectivity was less pronounced (e.g., **79c**, *dr* 3:1). Electron-rich substrates (PG = Bn, H) afforded poor yields (5%–15%) due to being prone to oxidation. Ts- or Boc-protected amines **78**, however, afforded pyrrolidines **79** with 56%–89% yields [55].

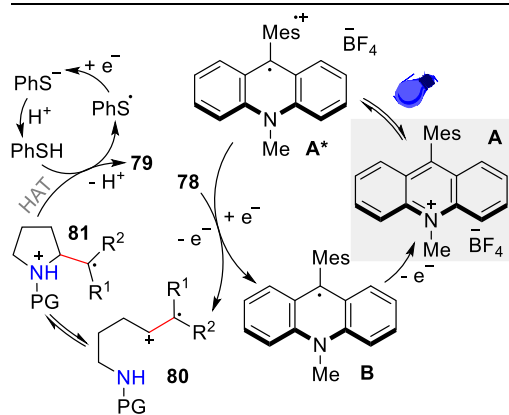
Nicewicz 2013:



Selected examples:



Proposed mechanism:



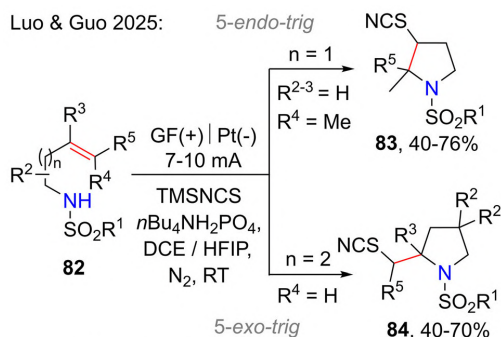
[a] Obtained by 5-endo-trig cyclization.

SCHEME 23 | Organic photoredox system-catalyzed hydroamination of alkenes **78**.

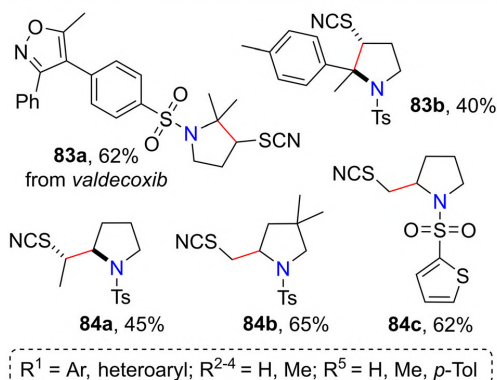
For the mechanistic rationale (Scheme 23), a catalytic cycle was proposed, where the photoexcited catalyst **A*** oxidized the olefin **78** to a radical cation **80**. Subsequent anti-Markovnikov addition of the amine gave intermediate **81**. The catalytic cycle was finalized by H-atom transfer from PhSH to obtain pyrrolidine **79** after proton loss. The liberated thiyl radical (PhS·) was proposed to assist in reoxidation of the acridine radical **B**, thus facilitating the regeneration of the photocatalyst **A** [55].

To conclude with 5-*exo-trig* cyclizations, an electrochemical aminothiocyation method was developed for sulfonamide-containing unactivated olefins **82**. Depending on the carbon chain length, cyclization occurred either via the 5-*endo-trig* or 5-*exo-trig* pathway to afford the thiocyanate functionality-bearing pyrrolidines **83** or **84**, respectively (Scheme 24). Electrochemical aminothiocyation offered the advantage of mild reaction conditions, as well as good regioselectivity. Some examples for late-stage functionalization of bioactive molecules were also

Luo & Guo 2025:



Selected examples:



SCHEME 24 | Electrochemical aminothiocyation of olefins **82** for the synthesis of functionalized products **83** and **84**.

demonstrated, such as *valdecoxib* and *celecoxib*. This reaction was compatible with various functional groups in the aryl and heteroaryl (R^1) sulfonamide ring: OMe, OCF₃, CF₃, Me, *t*Bu, F, Cl, and Br. In substrates, where the formation of two stereogenic centers was possible, aminothiocyation proceeded diastereoselectively to afford the *anti*-products—**83b** and **84a** [56].

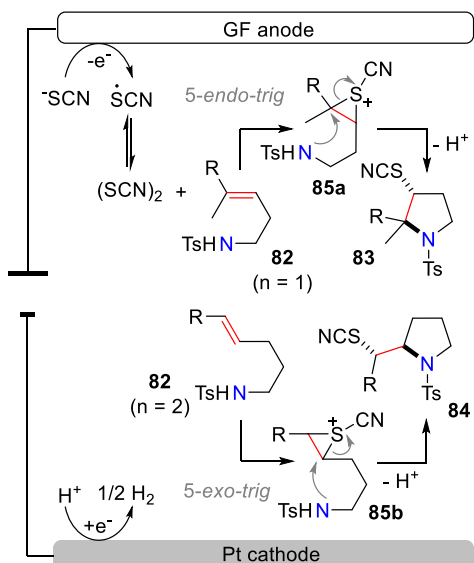
Mechanistic investigations for the electrochemical aminothiocyation approach suggested that the cyclization step might proceed via a sulfonium ion **85a-b** (Scheme 25). Ring opening by nucleophilic attack via the 5-*endo-trig* or 5-*exo-trig* pathway resulted in thiocyanation of the pyrrolidine C3-position or the side chain, respectively [56].

2.2 | 5-Endo-Trig-Cyclization

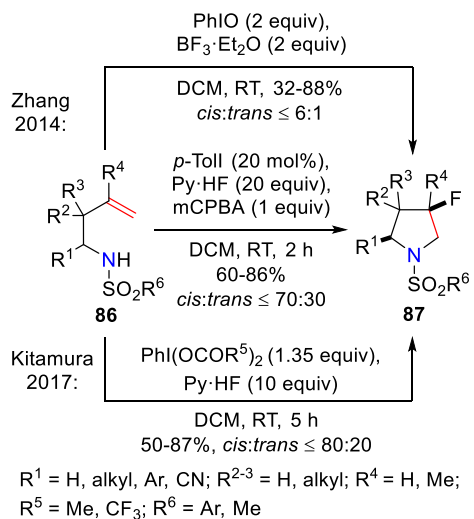
Zhang and coworkers combined PhIO-facilitated cyclization of homoallylic amines **86** with BF₃·Et₂O as a fluoride source to furnish a new pathway towards 3-fluoropyrrolidines **87** (Scheme 26). In the case of 2-alkyl or aryl substituted homoallylic amines ($R^1 = \text{Et, } t\text{Bu, Ph, 4-}t\text{BuC}_6\text{H}_4, 3\text{-CF}_3\text{C}_6\text{H}_4$; $R^{2-4} = \text{H}$), the fluorinated products **87** were obtained with moderate diastereoselectivity, varying from dr 4.3:1 to 6.0:1 (*cis/trans*) [57].

Similarly, 3-fluoropyrrolidines **87** were synthesized by Kitamura and coworkers using a reagent system of PhI(OAc)₂ and Py·HF

Proposed mechanism: (Luo & Guo 2025)



SCHEME 25 | Mechanistic proposal for electrochemical aminothio-cyanation of olefins **82**.

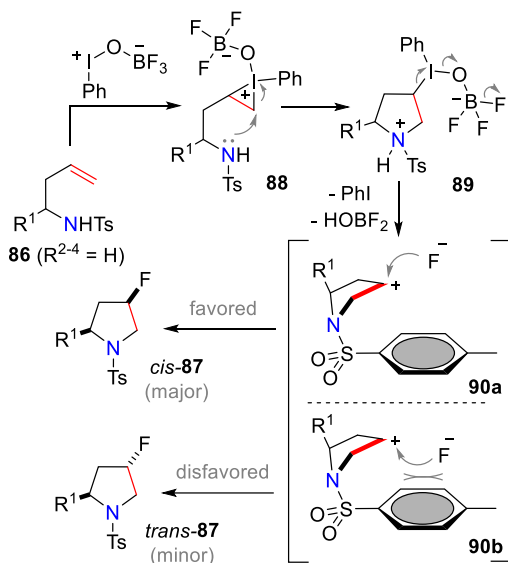


SCHEME 26 | 3-Fluoropyrrolidine **87** synthesis.

(Scheme 26) [58]. Other hypervalent iodine reagents, such as $\text{PhI}(\text{OCOCF}_3)_2$, were also applicable in this reaction. In the catalytic version, also explored by Kitamura, 20 mol% of *p*-iodotoluene was combined with $\text{Py} \cdot \text{HF}$ as a fluoride source and *m*CPBA as an oxidant to afford 3-fluoropyrrolidines **87** with yields up to 86% [58].

Based on experimental evidence, a mechanism involving a carbenium ion intermediate was proposed for the iodosobenzene-

Proposed mechanism: (Zhang 2014)

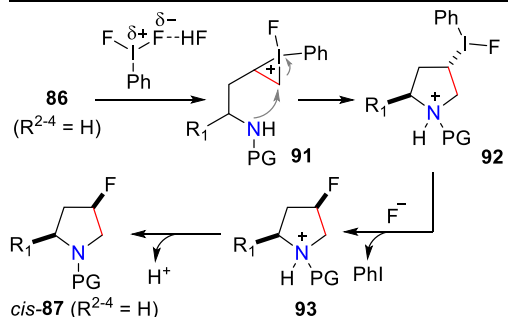


SCHEME 27 | Mechanistic proposal for the $\text{PhIO}/\text{BF}_3 \cdot \text{Et}_2\text{O}$ facilitated aminofluorination of olefins **86**.

mediated transformation **86**→**87** (Scheme 27). First, iodine(III) intermediate was formed by activation of PhIO with $\text{BF}_3 \cdot \text{Et}_2\text{O}$. The iodine(III) reagent then reacted with the alkene **86** ($R^{2-4} = \text{H}$) to give an iodonium intermediate **88**. Subsequent nucleophilic attack of the amino group closed the pyrrolidine ring **89**. The hypervalent iodine(III) intermediate then underwent reductive elimination to afford the cyclic carbocation **90a-b**, which was quenched by the fluoride anion to afford the fluorinated product **87** ($R^{2-4} = \text{H}$). The preference for *cis*-selectivity could be explained by the steric hindrance from the sulfonyl group, where one side of the pyrrolidine ring is blocked against the nucleophilic attack of the fluoride ion [57].

A slightly different interpretation of the mechanism was later offered by Kitamura and coworkers (Scheme 28), where the

Proposed mechanism: (Kitamura 2017)



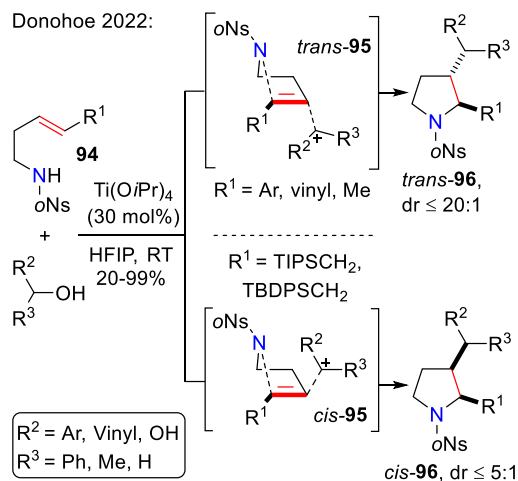
SCHEME 28 | Mechanistic rationale for aminofluorination of olefins **86**, involving an $\text{S}_{\text{N}}2$ -type step for C–F bond formation.

C–F bond was formed by S_N2 -type substitution during the fluoride ion attack on intermediate **92**. The preferential formation of the *cis*-**87** isomer was explained by the formation of the sterically favored intermediate *trans*-**92**. Mechanistic studies suggested that the reaction proceeded via the iodonium intermediate **91** [58].

Other than hypervalent iodine(III)-mediated cyclizations, some new Lewis acid-catalyzed methods were explored as well. One of them was a highly diastereoselective $Ti(OiPr)_4$ -catalyzed approach towards 2,3-substituted pyrrolidines **96**, which was offered by the Donohoe group (Scheme 29). The reaction was triggered by the generation of a cationic intermediate from allylic or benzylic alcohols, followed by simultaneous C–C and C–N bond formation with the alkenylamide **94**. The size of substituent R^1 was crucial in determining 2,3-*cis*- or *trans*-product formation. Bulky TIPSCH₂- or TBDPSCCH₂-groups promoted *cis*-product formation, possibly due to creating a steric clash with the incoming allyl/benzylic cation in the transition state **95**. Interestingly, when allylic alcohols bearing two different terminal substituents were used, partial regiocontrol could be achieved. It was presumably due to a preferential attack at the least hindered end of an unsymmetrical allyl cation intermediate [59].

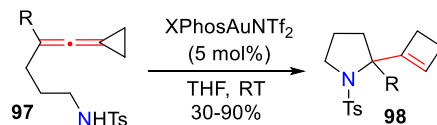
Wei and Shi reported a gold(I)-catalyzed cascade cyclization of *N*-nucleophile tethered vinylidenecyclopropanes **97**, resulting in pyrrolidine scaffolds **98**, bearing a cyclobutene moiety in the side chain (Scheme 30). This transformation occurred via ring expansion of the cyclopropane unit, followed by gold carbene-induced vinylogous nucleophilic addition in 5-*endo-trig* fashion. Regarding the applicable substrates for the gold-catalyzed cyclization, apart from alkyl and benzyl substituted (R = alkyl, Bn) allenenes **97**, some more complex substrates **97**, functionalized with a terminal olefin or 1,3-dioxolan-2-yl group in the side chain (R = but-3-en-1-yl or 2-(1,3-dioxolan-2-yl)ethyl) also afforded the desired product **98**, whereas substrates bearing aromatic groups (R = 4-ClC₆H₄) did not. Lower yields were obtained for sterically hindered alkyl substituents (R = *i*Pr, Cy) [60].

Donohoe 2022:

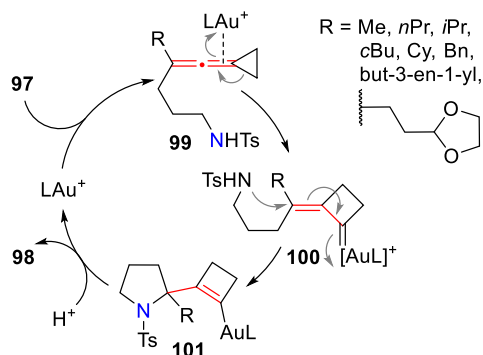


SCHEME 29 | Titanium-catalyzed diastereoselective synthesis of 2,3-disubstituted pyrrolidines **96**.

Wei & Shi 2023:



Proposed mechanism:



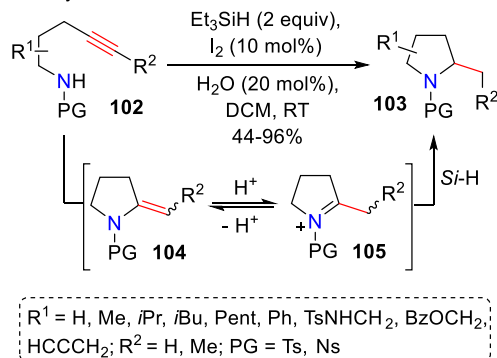
SCHEME 30 | Gold-catalyzed cascade cyclization of vinylidenecyclopropanes **97**.

2.3 | 5-Exo-Dig-Cyclization

While there are several transition-metal-free methods for intramolecular amination of unactivated alkenes, the same for unactivated alkynes has rarely been reported. The inherent instability of a vinyl cation intermediate was one of the obstacles, preventing further development of transition-metal-free procedures. Shibuya and coworkers addressed this problem by using a silane-iodine system for the intramolecular hydroamination/reduction of unactivated alkynes **102** (Scheme 31) [61].

The above-mentioned reaction likely proceeded through an exocyclic enamine intermediate **104**, which rearranged to provide an iminium intermediate **105**. Further reduction by Et₃SiH produced pyrrolidines **103**. High diastereoselectivity was achieved

Shibuya 2017:



SCHEME 31 | Pyrrolidine **103** synthesis from alkynes **102** by a hydroamination/reduction sequence.

under these conditions—dr 10:1 (*cis/trans*) for 2,4-disubstituted pyrrolidines **103** and dr 23:1 (*cis/trans*) for 2,5-disubstituted products **103** [61].

2.4 | 5-Endo-Dig-Cyclization

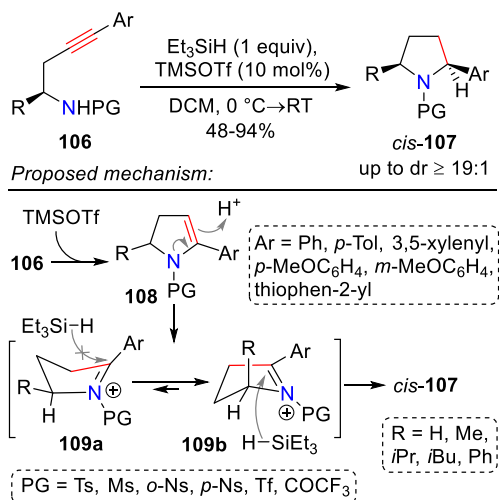
Pyrrolidine synthesis via the 5-*endo-dig*-cyclization pathway has been studied more extensively in recent years than its *exo*-counterpart. The Gharpure group reported a TMSOTf-mediated reductive hydroamination of chiral homopropargylic amines **106** for the diastereoselective synthesis of 2,5-disubstituted pyrrolidines **107** (Scheme 32). Reduction of the intermediate iminium ion with triethylsilane from the least hindered face (transition state **109b**) favored the formation of *cis*-2,5-disubstituted pyrrolidines **107** (up to dr $\geq$ 19:1) [62].

The same Et₃SiH / TMSOTf system, when used for reductive hydroamination of alkenynes **110**, bearing a pendant sulfonamide, afforded pyrrolidines **111**, bearing longer hydrophobic chains in the C2-site (Scheme 33). The alkenyne substrate **110** was conveniently prepared in one step via *Sonogashira* coupling between the corresponding monosubstituted terminal alkyne and vinyl halide. This cyclization approach was employed in the synthesis of various pyrrolidine alkaloids, namely ($\pm$)-*cis*-225H, ($\pm$)-*epi*-197B, ($\pm$)-*epi*-225C, and ($\pm$)-*bgugaine* [63].

Gold catalysis also enabled intramolecular hydroamination of chiral homopropargyl sulfonamides **116**, as demonstrated by Ye and coworkers (Scheme 34). The reaction proceeded via the 2,3-dihydropyrrole intermediate **120**, which could undergo further azidation or allylation to yield the corresponding enantioenriched 2,5-disubstituted pyrrolidines **117** and **118** [64].

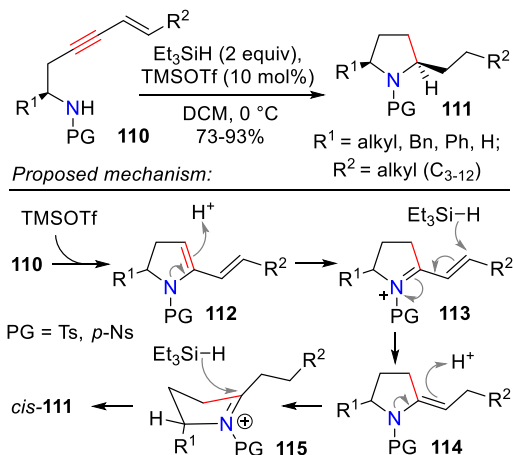
Similarly, homopropargylic sulfonamides **124** could be activated using a silver catalyst (20 mol% AgOAc), inducing the 5-*endo*-

Gharpure 2019:

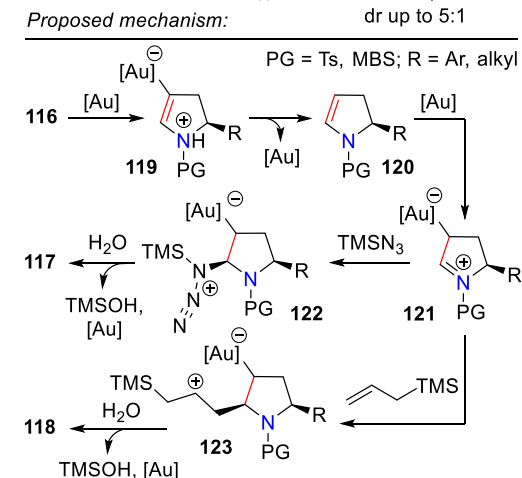
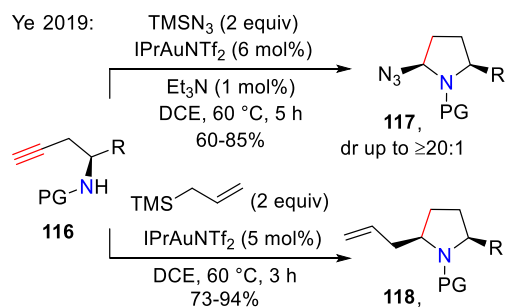


SCHEME 32 | Diastereoselective synthesis of *cis*-2,5-disubstituted pyrrolidines **107** from chiral alkynes **106**.

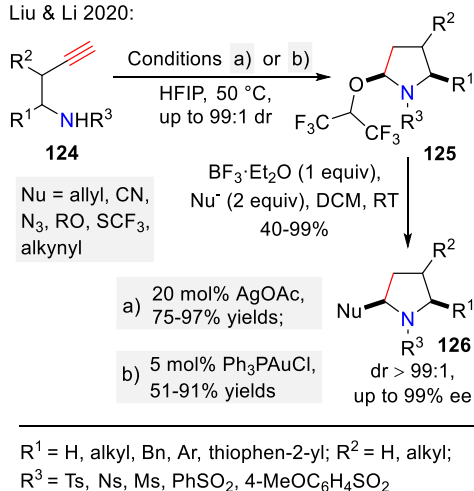
Gharpure 2023:



SCHEME 33 | Synthesis of 2,5-disubstituted pyrrolidines **111**, bearing long hydrophobic side chains.



SCHEME 34 | Gold-catalyzed hydroamination of chiral homopropargyl sulfonamides **116**.



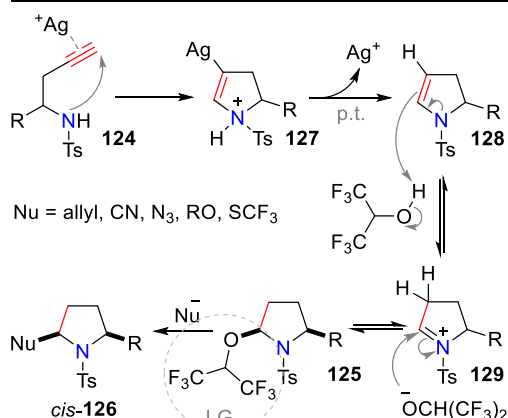
SCHEME 35 | Cyclization of homopropargylic sulfonamides **124** with further side chain derivatization.

dig-type cyclization (Scheme 35). Gold catalysis also facilitated this transformation and with lower catalyst loading (5 mol% Ph₃PAuCl). Using the weakly nucleophilic HFIP as solvent, isolatable *N*, *O*-acetals **125** as intermediates were obtained. Notably, nearly all the 2-hexafluoroisopropoxyppyrridine products **125** were obtained in the *cis*-configuration. The only exception were *N*-4-nitrobenzenesulfonyl-substituted products (R¹ = Ph, R² = H, R³ = Ns), where the *trans*-isomer **125** was obtained as the main product (dr = 1:6.6 *cis/trans*), possibly due to the electronic effects on the sulfonyl aromatic ring. Additionally, complete chirality retention was observed in reactions with enantiopure homopropargylic sulfonamides **124**, which afforded *cis*-2,5-disubstituted pyrrolidines **125** with high diastereoselectivity (up to 99:1 dr). Further reactions of the obtained *N*, *O*-acetals were investigated by the addition of external nucleophiles. The (CF₃)₂CHO- substituent acted as a good leaving group, and 2,5-bifunctionalized pyrrolidines **126** were obtained. In this manner, several new C–C and C–Het (Het = N, O, S) bonds were constructed. Moreover, applications of this approach were tested for the synthesis of the pharmaceutical intermediate of *trandolapril* **126** (R^{1,2} = -(CH₂)₄, R³ = Ts, Nu = CN) from the corresponding homoallylic sulfonamide **124** (R^{1,2} = -(CH₂)₄, R³ = Ts) in 75% yield over 2 steps. Also, successful late-stage functionalization of *β*-estradiol was achieved using this approach [65].

Mechanistic studies suggested a reaction pathway involving dihydropyrrole intermediate **128** (Scheme 36). Control experiments demonstrated that the hydroalkoxylation step with HFIP proceeded with no requisition of the Ag(I) catalyst, but at a slower rate, for example, 3.5 h in the presence of AgOAc and 48 h without the catalyst [65].

3 | Tandem Annulation Strategies Incorporating Intramolecular C–N Bond Formation as a Key Step

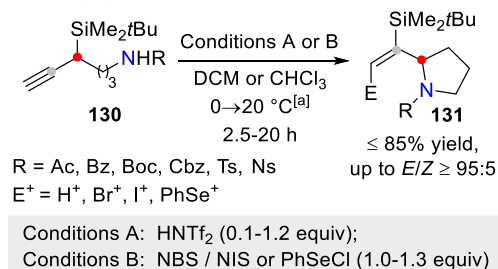
Instead of direct intramolecular amination, propargylic silicon-containing alkynes can undergo cationic rearrangement to form stabilized allylic cations before participating in the key C–N bond



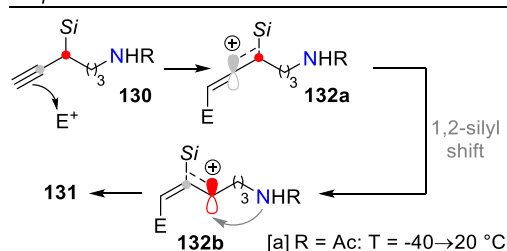
SCHEME 36 | Mechanistic proposal for silver-catalyzed cyclization of homopropargylic sulfonamides **124**.

formation step. This was demonstrated in a recent example by the Turks group, where propargyl silanes **130**, containing a tethered amide nucleophile, were heterocyclized to afford functionalized olefin side chain containing pyrrolidines **131** (Scheme 37). Upon electrophilic activation of the propargyl silane moiety, the formed vinyl cation **132a** rearranged to the more stabilized allyl cation **132b** via the 1,2-silyl shift. The allylic cation **132b** was then quenched by the internal amine, forming the pyrrolidine ring **131** [66]. This transformation was possible due to the *β*-carbocation-stabilizing properties of silicon [67]. In addition to pyrrolidine ring formation, a highly stereodefined olefin side chain was introduced in the

Turks 2023:



Proposed mechanism:



SCHEME 37 | Pyrrolidine **131** synthesis from propargyl silanes **130** via the 1,2-silyl shift.

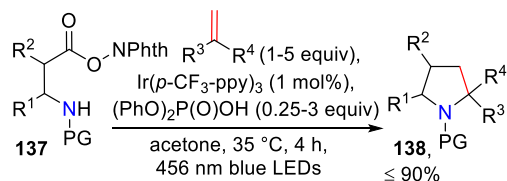
pyrrolidine C(2)-position. Further utility of the vinyl halide-containing reaction products was demonstrated by participation in Suzuki-Miyaura coupling reactions. As for the possibilities to displace the silyl group, electrophilic substitution using NIS in 2,2,2-trifluoroethanol was successfully performed, while preserving the double-bond geometry [66].

Similarly, a copper-catalyzed arylation-ring closure strategy was developed for direct synthesis of pyrrolidines **134**, bearing a functionalized styrene side chain, utilizing diaryl- λ^3 -iodanes and propargyl silanes **133** as starting materials (Scheme 38). Although this method was primarily designed for terminal alcohol group-containing silanes (C–O bond formation), benzamide **133** also underwent a similar arylation-cyclization sequence, affording pyrrolidine **134** [68].

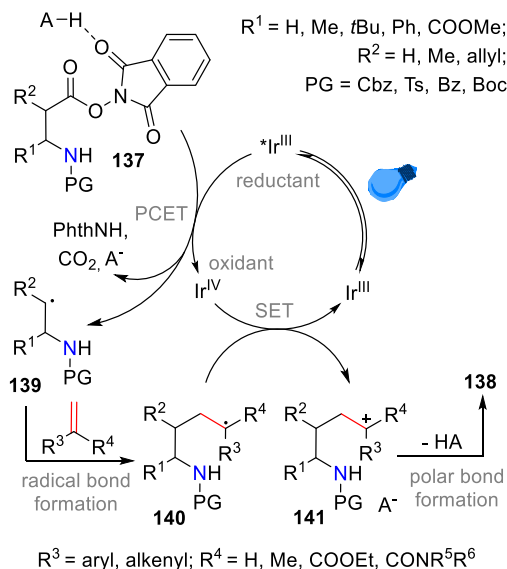
For the above-mentioned transformation, a Cu(I/III) catalytic cycle was proposed (Scheme 38), where Cu(I) reacted with the diaryl- λ^3 -iodane to generate the strongly electrophilic Ar–Cu(III) species, which activated the propargylic system to induce 1,2-silyl migration. The afforded allylic cation intermediate **136** was trapped by the internal amide group to form the pyrrolidine ring **134**. Lastly, reductive elimination regenerated the Cu(I) catalyst [68].

Multistep synthesis of starting materials, bearing both the amide and alkene/alkyne functionalities, is the general drawback in the so far discussed intramolecular C–N bond strategies. Tandem processes, such as recent radical redox annulation strategies, aim to streamline the synthesis of pyrrolidine **138** by offering a direct route from alkenes and *N*-hydroxyphthalimide esters **137**. In one example by Doyle and Knowles, an iridium(III)-catalyzed photocatalytic approach was employed for annulation of alkenes with bifunctional reagents **137**, containing *N*-hydroxyphthalimide ester (NHPI) and tethered 2° amide functionalities (Scheme 39). Visible light irradiation (456 nm) activated the iridium(III) photocatalyst. This initiated single-electron reduction of the NHPI ester **137**, leading to fragmentation into radical species **139**. The latter reacted

Doyle & Knowles 2022:

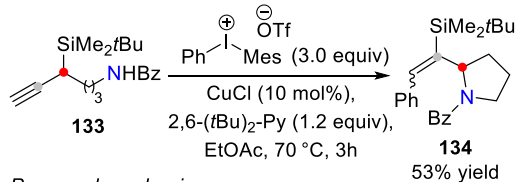


Proposed mechanism:

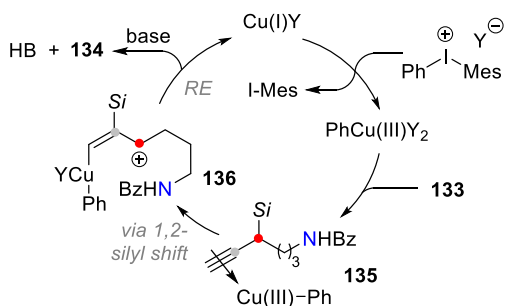


SCHEME 39 | Iridium-catalyzed annulation strategy, involving a polar C–N bond formation step.

Turks 2025:



Proposed mechanism:



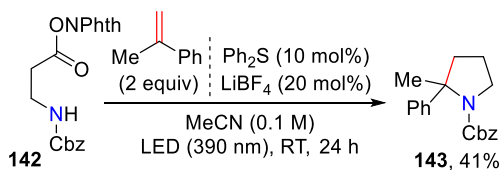
SCHEME 38 | Copper-catalyzed arylation-cyclization sequence for propargyl silanes **133**.

with an external alkene in anti-Markovnikov fashion, forming intermediate **140**, containing both the radical and tethered amide functionalities. Single-electron oxidation provided the strategic intermediate **141**, which participated in the polar C–N bond formation step, affording pyrrolidine **138**. Although the substrate scope was limited to aryl alkenes and dienes (cyclic and acyclic), this reaction found some interesting applications in the late-stage derivatization of pharmaceutical compounds, such as *ezetimibe*, *febuxostat*, and *amoxepine* [69].

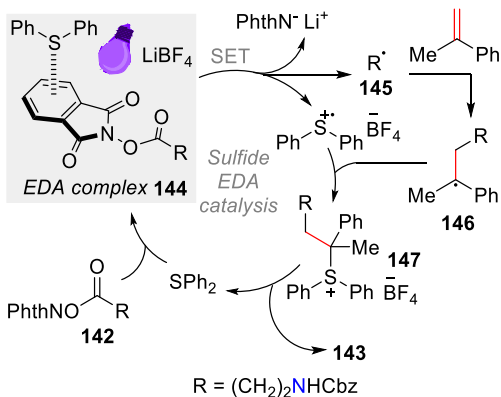
Similarly, under visible-light-driven conditions, an electron donor–acceptor (EDA) system, consisting of the *N*-hydroxyphthalimide ester **142** and diphenyl sulfide (electron donor), was used to induce phthalimide ester fragmentation via a SET process to afford reactive radical species **145** (Scheme 40). Radical **145** was captured by an olefin, followed by the addition of diphenyl sulfide cation radical to form the sulfonium species **147**. Intramolecular cyclization by *N*-nucleophile attack afforded the pyrrolidine **143** scaffold. Lewis acidic lithium ions were added to enhance the interactions within the EDA complex. This visible-light-driven method was compatible with water and air, signifying the overall robustness of this method [70].

In a mechanistically similar approach, the carbenium ion intermediate **154** was generated under catalyst-free conditions from

Tayu & Saito 2025:



Proposed mechanism:

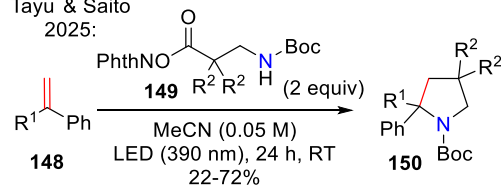


SCHEME 40 | Visible-light-driven synthesis of pyrrolidines **143**, utilizing a phthalimide ester/sulfide EDA system.

styrenes **148** and *N*-hydroxyphthalimide esters **149**, bearing a tethered carbamate (Scheme 41). It was suggested that in this reaction, styrene formed an EDA complex **151** with the phthalimide ester. LED irradiation caused a SET process, followed by fragmentation to a radical cation **152** and an alkyl radical **153**. Their recombination to cationic intermediate **154**, followed by intramolecular cyclization, afforded the pyrrolidine **150** scaffold. Pyrrolidine **150** yields were generally higher, with aromatic or heteroaromatic R^1 substituents (up to 72%), whereas aliphatic R^1 substituents (Me, H) gave poor yields (22%–24%). While the catalyst-free visible-light induced method, which proceeded via an electron donor–acceptor complex, was more sustainable, much higher yields were obtained with iridium catalysis. For comparison, the synthesis of *tert*-butyl 4,4-dimethyl-2,2-diphenylpyrrolidine-1-carboxylate **150** (R^1 = Ph, R^2 = Me) in accordance with the conditions presented in Scheme 41, afforded the product in 42% yield. Alternatively, performing the reaction using [Ir(dF(CF₃)ppy)₂bpy]PF₆ (1 mol%), *i*Pr₂S (10 mol%) in MeCN (0.05 M) under LED (390 nm) at room temperature for 24 h afforded the same product **150** (R^1 = Ph, R^2 = Me) in quantitative yield [71].

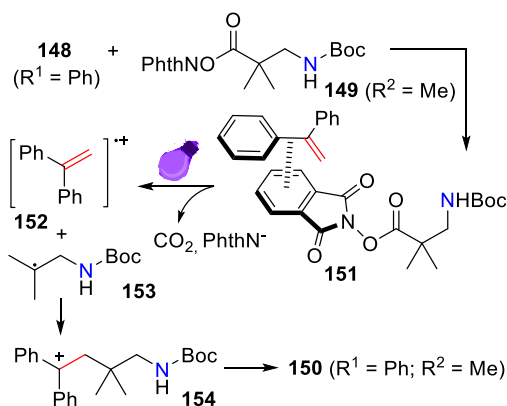
In a non-photocatalytic approach, featuring Cu(II)-catalyzed coupling of potassium β -aminoethyl trifluoroborates **155** with styrenes and dienes, 2-aryl- and 2-vinylpyrrolidines **156** were obtained (Scheme 42). Both 1,2-disubstituted and 1,1-disubstituted vinyl arenes participated in this reaction. It was also shown that alkenynes could participate in this reaction, producing 2-alkynyl-substituted pyrrolidines **156**. This intermolecular coupling reaction occurred via a copper-catalyzed/MnO₂ mediated stepwise oxidative coupling sequence, where Cu(II)-catalyzed oxidation of the alkylborane **155**

Tayu & Saito 2025:



R^1 = 4-MeOC₆H₄, 4-ClC₆H₄, Ph, 1-naphthyl, 2-furyl, 2-(benzo[d][1,3]dioxol-5-yl), Me, H;
 R^2 = Me, H, -(CH₂)₅-

Proposed mechanism:



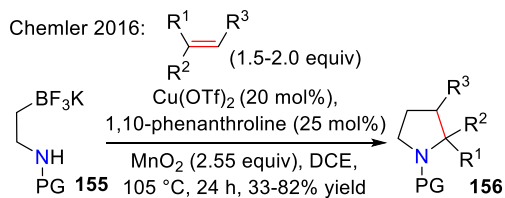
SCHEME 41 | Visible-light-induced aminoalkylation of alkenes **148**.

liberated the alkyl radical **157**, which added to styrene to produce the stabilized benzylic radical **158**. Next, recombination with Cu(II) afforded the alkylcopper(III) intermediate **159**, which underwent further reductive elimination (path I). Alternatively, the stabilized radical **158** could undergo oxidation by MnO₂ to the carbenium ion **160**, which is prone to undergo nucleophilic attack by the pendant amide, resulting in pyrrolidine **156** formation (path II) [72].

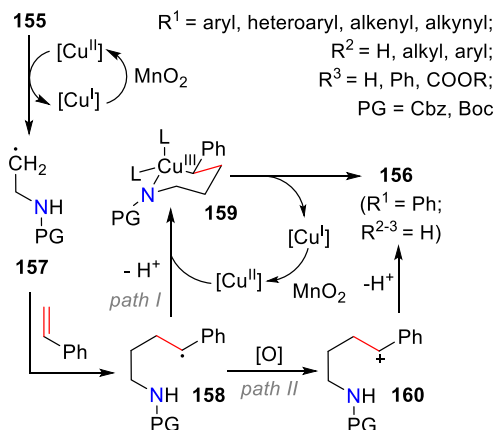
Later, a Rh(III)-catalyzed approach was developed, involving a possible rhodium nitrene **165** formation step from 4-methyl-*N*-(pivaloyloxy)benzenesulfonamide (**163**) and subsequent aziridination of olefin **161** (Scheme 43; path A). An alternative pathway for aziridine intermediate **167** formation was also plausible, featuring a migratory insertion step between alkene **161** and intermediate **164**, with a subsequent C–N bond formation step in concerted fashion and N–O bond cleavage (path B). Aziridine **167** ring expansion was succeeded by a combination of sequential hydride shifts and elimination/protonation pathways until the carbenium ion was quenched at the C4 position, forming the pyrrolidine product **162** [73].

4 | Nucleophilic Addition to the Carbonyl Group

Intramolecular amination of carbonyl compounds is a well-established C–N bond formation strategy. The majority of recent studies has focused on its practical applications in natural product synthesis or reductive amination strategies, aiming to simplify the



Proposed mechanism:



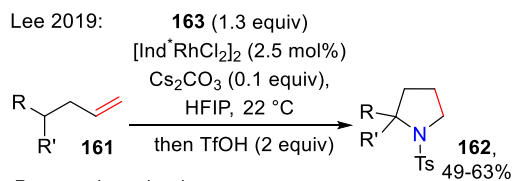
SCHEME 42 | Copper-catalyzed annulation of β -aminoethyl trifluoroborates **155** with styrenes/dienes for the synthesis of pyrrolidines **156**.

substrate design, as scaffolds, bearing both the carbonyl moiety and an internal *N*-nucleophile, require multistep synthesis to attain.

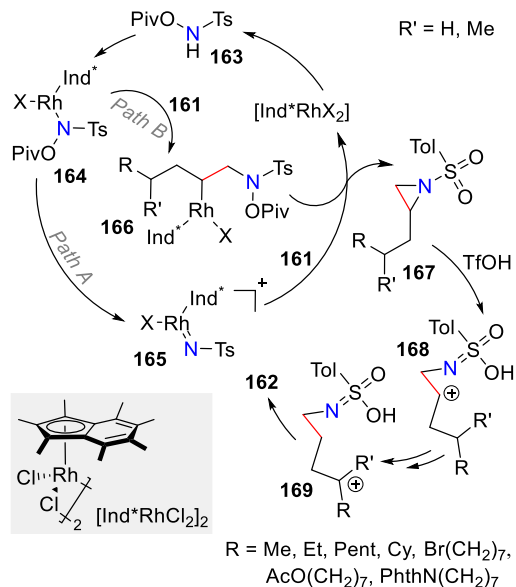
Ramesh and coworkers applied intramolecular amination of aldehyde **172** as the pyrrolidine ring-formation step in the total synthesis of 1,4-dideoxy-1,4-imino-*L*-xylitol (**175**)—a potential glucosidase inhibitor (Scheme 44). Before the C–N bond formation step, the aldehyde **172** was obtained by oxidative cleavage of vicinal diol **171**. Aldehyde **172** heterocyclization afforded the hemiaminal **173**, which was further deoxygenated to pyrrolidine **174** with Et_3SiH in the presence of $\text{BF}_3 \cdot \text{OEt}_2$. Deprotection under Birch conditions afforded 1,4-dideoxy-1,4-imino-*L*-xylitol (**175**) [74].

Budynina and Trushkov included a chiral γ -azidoester **176** amination step into the synthetic route toward (–)-nicotine (**181**) – a pyrrolidine ring containing alkaloid (Scheme 45). The γ -azidoester **176** was obtained by ring-opening of cyclopropanes with the azide ion in an $\text{S}_{\text{N}}2$ -like reaction. Reduction of the azido group in starting material **176** under Staudinger conditions, followed by cyclization, afforded the lactam scaffold **179**. The latter was reduced with LiAlH_4 and methylated to produce (–)-nicotine (**181**) [75].

Darcel and coworkers employed silane RSiH_3 as a mild reducing agent for the reductive amination of levulinic acid **182** ($\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$) and its esters (Scheme 46). The reaction was catalyzed by an NHC–iron complex: $\text{Fe}(\text{CO})_4(\text{IMes})$ (**[Fe]-1**). In the proposed reaction mechanism, oxocarboxylic acid **182** ($\text{R}^2 = \text{H}$) condensed with aniline R^3NH_2 , forming the imine intermediate **185**, and silyl derivatization of the carboxylic acid incorporated the O–Si moiety. Next, iron-catalyzed hydrosilylation led to the silyl amine **186** and subsequent ring closure by transamidation afforded the



Proposed mechanism:



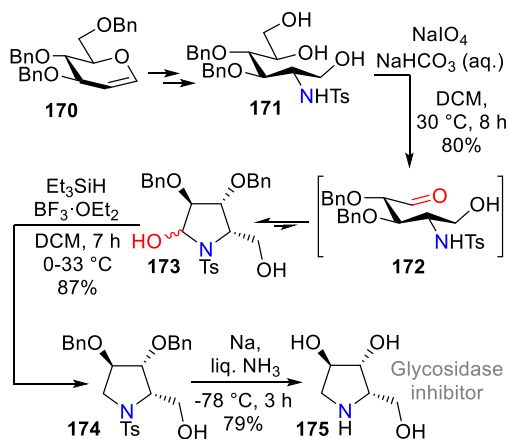
SCHEME 43 | Rhodium-catalyzed olefin **161** aziridination/cyclization sequence for the synthesis of pyrrolidines **162**.

pyrrolid-2-one intermediate **184**. The latter was reduced to the pyrrolidine **183** in another hydrosilylation event. A few additional details should be pointed out: 1) visible light was crucial for generation of the active 16 electron $[\text{Fe}^0]$ -species, required to promote the silane oxidative addition step; 2) depending on the employed iron catalyst, the reaction proceeded as described before or stalled at the pyrrolid-2-one intermediate **184**, even when an excess of PhSiH_3 (4 equiv) was used [76]. Also, the polarity of starting materials could be easily reversed, for example, amino acids reacted with aldehydes under similar conditions to form pyrrolidines [77].

Similarly, the reductive amination of biomass-derived keto acids **187a** with amines in a $\text{Ca}(\text{NTf}_2)_2$ catalyzed process was used to directly access polyhalogenated pyrrolidine-2-ones **188a** (Scheme 47). Alternatively, pyrrolidine-2-ones **188b** were synthesized by reacting amino acids **187b** with carbonyl derivatives under the same conditions. Both approaches displayed chemospecificity and good substrate tolerance, offering a broad range of applications, which was demonstrated by late-stage functionalization of drug molecules, such as *amlodipine*, *lenalidomide*, and *nabumetone* [78].

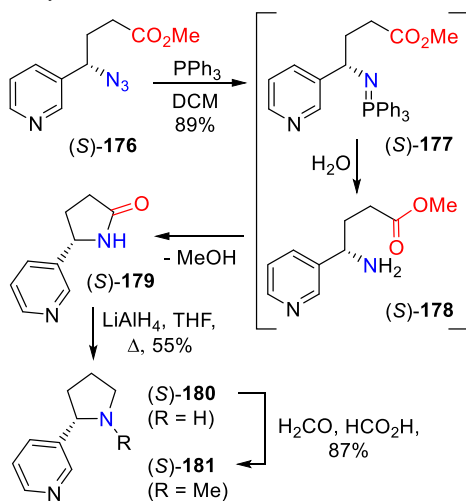
Pyrrolidin-2,5-diones **190** were accessed by isomerization and carbonylative functionalization of alkenes **189**, enabled by low-valent tungsten redox catalysis (Scheme 48). In the presence

Ramesh 2020:



SCHEME 44 | Synthetic route toward 1,4-dideoxy-1,4-imino-*L*-xylitol (175).

Budynina & Trushkov 2015:

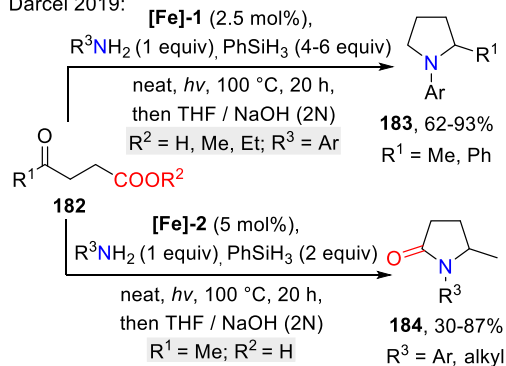


SCHEME 45 | Synthetic route toward (-)-nicotine (181).

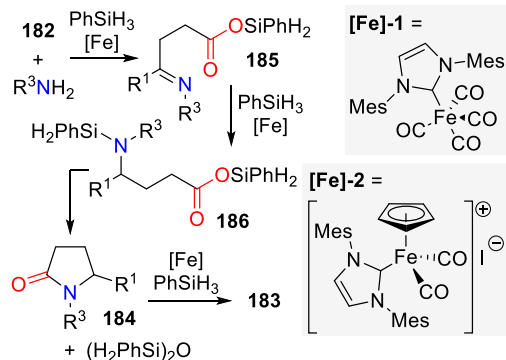
of a W(CO)₆ catalyst, the aminoalkene **189** C=C bond was isomerized to unactivated internal positions, resulting in regioselective formation of pyrrolidine rings **190**, regardless of the substrate **189** C-chain length ($n = 0–5$). The hydrocarbonylation step was performed under a CO atmosphere. The key mechanistic factors were six- to seven-coordinate geometry changes, characteristic of the W(0)/W(II) redox cycle, and the conformationally flexible pyridin-2-ylmethyl directing group effect (Scheme 49) [79].

Huang and coworkers devised a one-pot strategy for the enantioselective synthesis of α -alkyl pyrrolidines **200** from amides **198a** and alkynes (Scheme 50). This method was employed for the total synthesis of chiral alkaloids, such as (-)- and (+)-*bugaine* ((*R*)- and (*S*)-**200**). Depending on the chirality of the *N*-PINAP catalyst,

Darcel 2019:



Proposed mechanism:



SCHEME 46 | Reductive amination of levulinic acid **182** and its esters.

the key intermediate **199a** could be obtained as either (*R*)- or (*S*)-enantiomer, with enantioselectivity up to 94% ee. Then, reductive amination of an acetal group-containing alkyne **199a** (R³ = HC(OEt)₂) provided either of the *bugaine* isomers **200** [80].

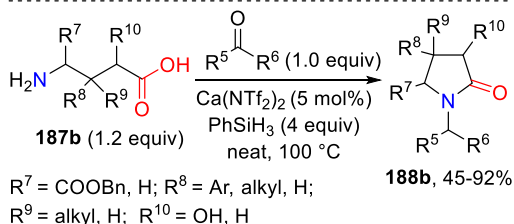
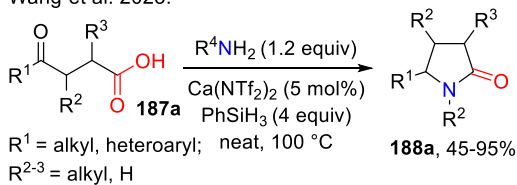
The aliphatic amide **198a** enantioselective alkynylation step likely proceeded via the mechanism proposed by Huang and Wang, involving an Ir/Cu/chiral ligand (L*)-catalyzed sequence (Scheme 50) [81]. Following tandem benzylic deprotection-reductive cyclization step, using Pd(OH)₂/C and H₂, afforded pyrrolidine ring formation [80]. A mechanistically similar strategy was employed for the asymmetric synthesis of *anticaprant*—a κ -opioid receptor antagonist—where *N*-Boc-*L*-proline induced chirality instead of *N*-PINAP catalysts [82].

In the case of aliphatic chain-containing alkynes (R³ = alkyl), a γ -carbonyl group present in the amide **198b** served as an electrophilic center for the internal nucleophile attack (Scheme 51). In this case, 2,5-disubstituted pyrrolidine **204** was formed instead, as illustrated by the synthesis of the alkaloid (-)-*cis*-225C (**204**) hydrochloride form [80].

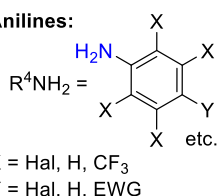
5 | Intramolecular Nucleophilic Substitution

Amino alcohols are common precursors for synthesizing the pyrrolidine scaffold via the 5-*exo-tet* ring closing pathway.

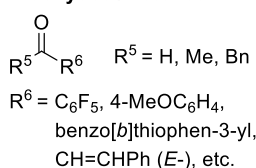
Wang et al. 2023:



Anilines:

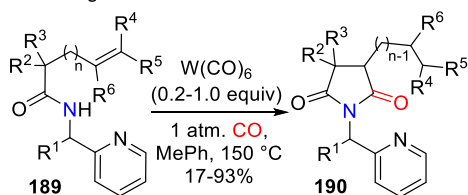


Aldehydes / ketones:



SCHEME 47 | Synthesis of pyrrolidin-2-ones **188a-b** by reductive amination.

Liu & Engle 2022:



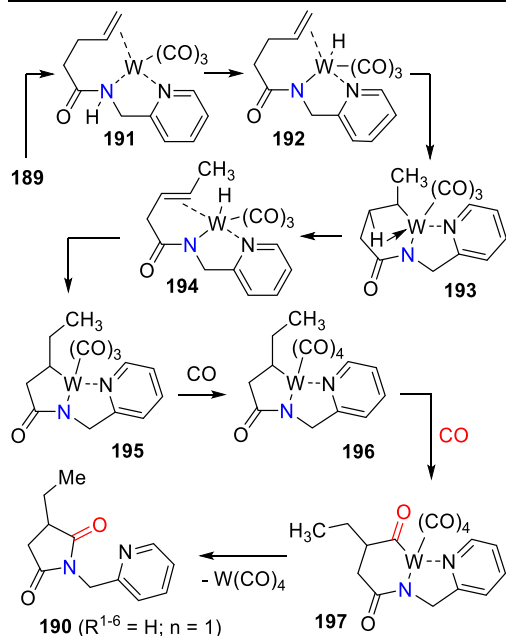
SCHEME 48 | Tungsten redox catalysis for pyrrolidin-2,5-dione **190** synthesis via carbonylative functionalization.

Conventionally, the alcohol is first converted into a good leaving group, such as a halide or sulfonate ester, whereas direct ring closure of amino alcohols is a less studied subject. Many substrates fail to tolerate the harsh conditions required (strong acids, heating) to displace the alcohol moiety with an incoming amine nucleophile [83], thus encouraging the development of milder activation methods.

Direct alcohol displacement in amino alcohols **205** was achieved by combining trimethyl orthobenzoate (TMOB) with Lewis acidic $\text{BF}_3\cdot\text{OEt}_2$ (Scheme 52). Under these conditions, the hydroxyl group was transformed into a leaving group, which

Proposed mechanism:

(Liu & Engle 2022)

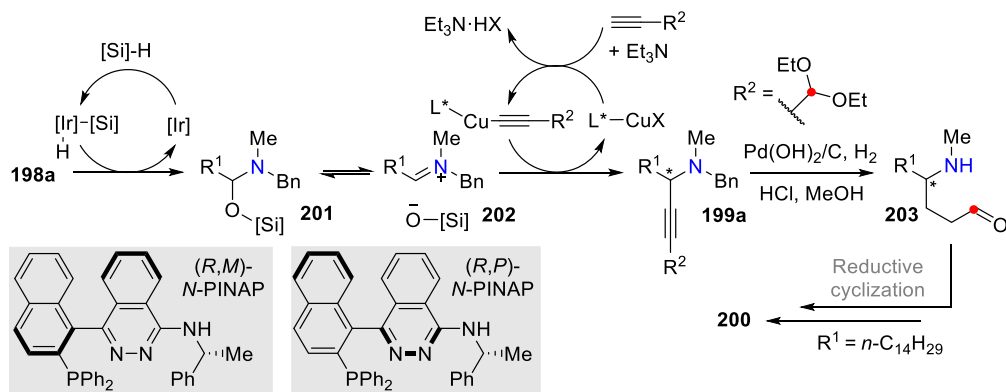
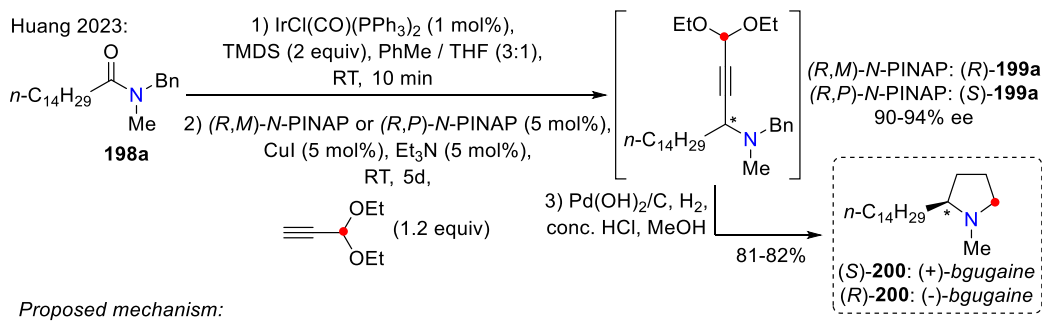
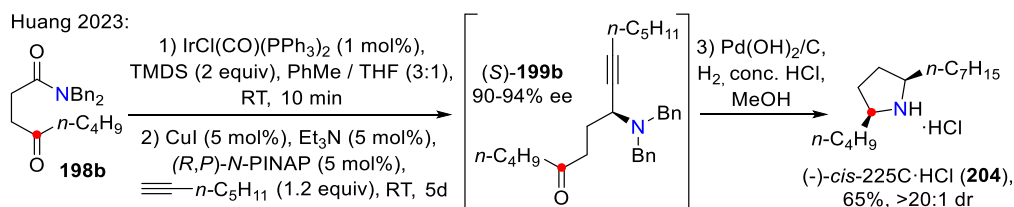


SCHEME 49 | Mechanistic proposal for pyrrolidin-2,5-dione **190** synthesis via tungsten redox catalysis.

was then displaced by an internal amide group to afford pyrrolidines **207** (Scheme 53). The reaction scope was extended from monoalcohols to vicinal diols **206** ($\text{R}^1 = \text{HOCH}_2$) as starting materials. Enantiomerically pure substrates (> 99% ee) afforded prolinol benzoates **208** ($\text{R}^3 = \text{BzOCH}_2$) with complete inversion of configuration at the chiral center, suggesting a $\text{S}_\text{N}2$ -like mechanism. The incorporation of the benzoate group into the product suggested a cyclic oxocarbenium intermediate **211**, formed on the diol moiety (Scheme 54) [84].

The same amino alcohol transformation (**205** $\rightarrow$ **207**) was achieved with *N,N*-dimethylacetamide dimethyl acetal (DMADA) and SnCl_4 (10 mol%) as the Lewis acid catalyst (Schemes 52 and 53). With comparable yields, HCl (1 equiv.) could also promote this reaction instead of the SnCl_4 catalyst. A practical application for direct activation of alcohols using the DMADA / H^+ system was demonstrated in the synthesis of natural product *crispine A* [83].

Alternatively, secondary alcohols **212** could be transformed in situ into leaving groups using iron(III) -catalysis under non-solvolytic conditions (Scheme 55). The iron-catalyzed approach for C–N bond formation was advantageous because the only stoichiometric byproduct was water. $\text{Fe}(\text{SbF}_6)_3$ was proposed to be the active catalytic species since the best yields were observed when using three equivalents of AgSbF_6 relative to Fe^{3+} . It was also confirmed by DFT calculations that the energy barrier for C–N bond formation with iron catalysts decreased in the following order: FeCl_3 (highest) > $\text{Fe}(\text{SbF}_6)_2\text{Cl}_2$ > $\text{Fe}(\text{SbF}_6)_2\text{Cl}$ > $\text{Fe}(\text{SbF}_6)_3$ (lowest). The intramolecular displacement of chiral $\text{ROH}\text{-[Fe]}$ species with tethered sulfonamide nucleophiles in transition state **214** occurred with inversion of stereochemistry. This was ensured by applying the

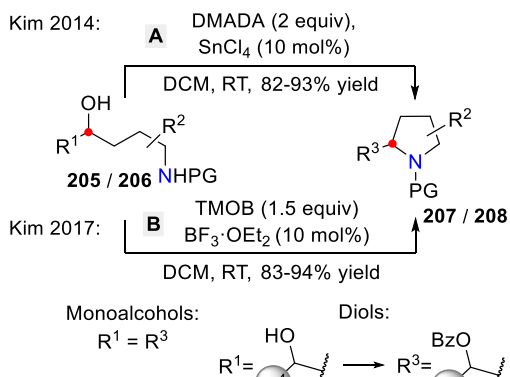
SCHEME 50 | Enantioselective synthesis of α -alkyl pyrrolidines **200**.SCHEME 51 | Enantioselective synthesis of α,α' -dialkyl pyrrolidines **204**.

tight ion pairing concept, where the departing iron hydroxide blocked one face of the carbocation, favoring rapid attack of the sulfonamide from the opposite face, thus ensuring facial selectivity. This remained true for simple alkyl chains ($R = \text{Me}$, $n\text{Pr}$, $t\text{Bu}$); however, benzylic alcohols $R = p\text{-MeOC}_6\text{H}_4$ gave racemic pyrrolidines **213c** instead, likely due to the formation of a stabilized benzylic carbocation intermediate [85].

As demonstrated by previous examples, C–N bond formation via intramolecular nucleophilic substitution offers the possibility of chiral pyrrolidine synthesis by inversion of stereochemistry. This requires chirality to be present at the reactive site of the starting material (**206/212**), which is not always easy to introduce. A convenient alternative for the stereoselective synthesis of 2-substituted pyrrolidines involves the use of chiral sulfinimines **216** as starting materials [86–89].

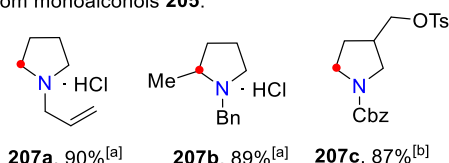
In one example by the Prasad group, deprotonated diphenylmethyl ethers were added to the chiral imine **216**, bearing an intrinsic leaving group (Scheme 56). The sulfinamide intermediate **219** further cyclized to afford pyrrolidine **217a**. Further treatment with HCl in MeOH afforded the enantiopure pyrrolidine organo-catalyst **218** in a quantitative yield. Interestingly, the same conditions could also be used to construct heterocycles of smaller ring size, such as aziridines and azetidines. Piperidine ring formation was also possible, but under modified conditions (NaH in THF and heating for the cyclization step) [86].

Quintavalla and Lombardo switched to the carbenoid (chlorodiphenylmethyl)lithium species to diastereoselectively obtain in the side chain chlorinated pyrrolidine **217b** (Scheme 56). In this case, the reactive organolithium species was generated via

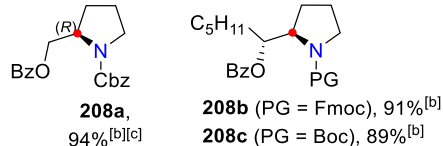


Selected examples:

• From monoalcohols **205**:



• From diols **206**:

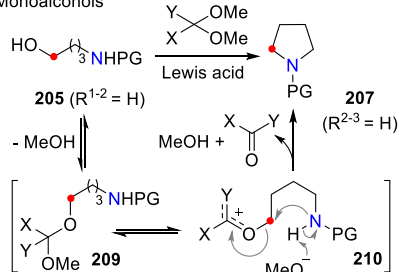


[a] Reaction conditions **A**; [b] Reaction conditions **B**;
 [c] From benzyl (S)-(4,5-dihydroxypentyl)carbamate.

SCHEME 52 | C–N bond formation in amino alcohols **205/206** by directly displacing the hydroxyl group.

Proposed mechanism: (Kim 2014)

• Monoalcohols



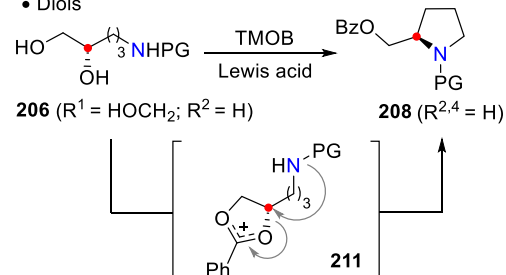
TMOB: X = Ph, Y = OMe; DMADA: X = Me, Y = NMe₂

SCHEME 53 | C–N bond formation in aminoalcohols.

chlorine-lithium exchange. The obtained chlorinated pyrrolidines **217b** were further converted to ether-type products **217a** by S_N1 reaction with a variety of alcohols [87].

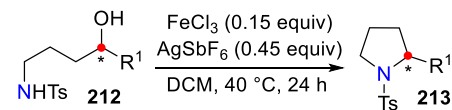
Proposed mechanism: (Kim 2017)

• Diols

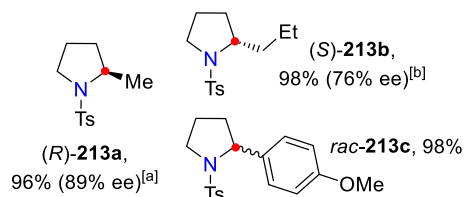


SCHEME 54 | C–N bond formation in aminodiols **206**.

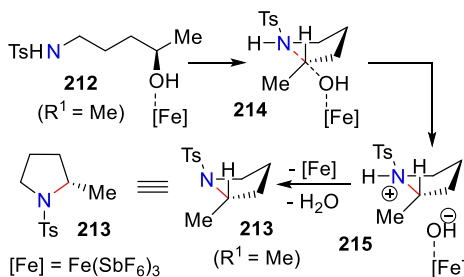
Baik & Cook 2019:



Selected examples:



Proposed mechanism:



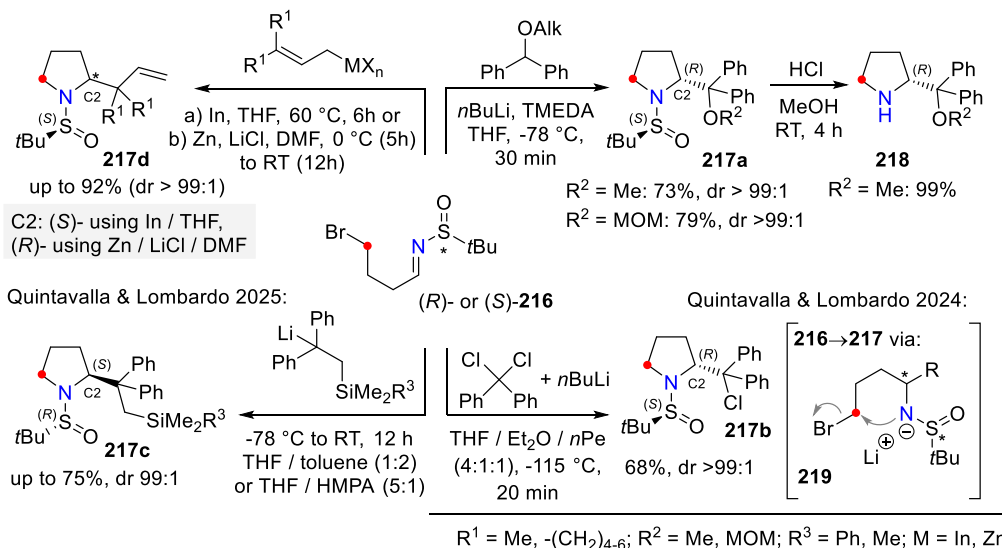
[a] From (S)-**212**; [b] From (R)-**212**

SCHEME 55 | Iron-catalyzed amino alcohol **212** heterocyclization into pyrrolidines **213**.

A similar approach was used for the synthesis of silyl-substituted pyrrolidines **217c** (Scheme 56). Enantiopure (R)-sulfinimine **216** reacted with the silyl-substituted diphenylethyllithium reagent and underwent cyclization to afford (2S)-stereocenter-containing pyrrolidine **217c**. Before addition, the organolithium reagent was prepared in situ by silyllithium reagent R³Me₂SiLi addition to 1,1-diphenylethylene. The (S)-specific stereochemistry for the newly formed stereocenter (C2) was attributed to an open anti-periplanar transition state for the nucleophilic addition to the

Quintavalla & Lombardo 2023:

Prasad 2018:

SCHEME 56 | Diastereoselective synthesis of pyrrolidines **217a-d**, containing chiral sulfinyl N-auxiliaries.

imine step. This method was applied for the synthesis of Hayashi–Jørgensen organocatalyst methylene isosteres [88].

Diastereoselective allylation of chiral sulfinyl imines **216**, followed by intramolecular cyclization, afforded the synthetic precursors for α -disubstituted β -homoprolines **217d** (Scheme 56). The absolute configuration of the newly formed stereocenter at the C2 position was modified depending on the allylation protocol: (a) In(0) in THF; or b) Zn(0), LiCl in DMF. Alternatively, the C2 position stereochemistry could also be modulated by using a *tert*-butanesulfinide chiral auxiliary with reverse configuration [89].

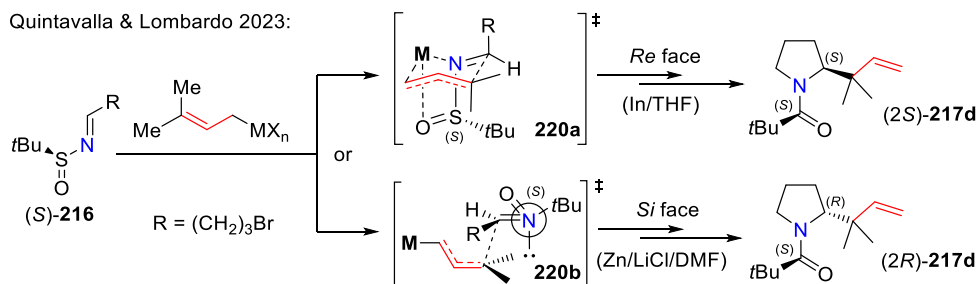
The stereochemistry for the C2 position in pyrrolidine **217d** could be explained by two distinct transition states (Scheme 57). The in situ generated allyl indium reagent reacted with the chiral imine **216** via a closed six-membered transition state **220a**, whereas the allyl zinc reagent in strongly coordinating solvents (DMF) and in the presence of LiCl favored an open antiperiplanar transition state **220b** [89].

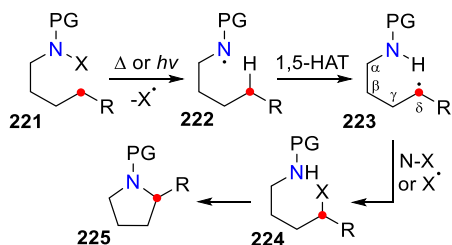
6 | C(sp³)-H Activation in Alkylamines

The concept of remote C₆(sp³)-H activation at otherwise unfunctionalized positions in *N*-haloamines **221**, resulting in heterocyclic five-membered ring **225** formation, namely, the Hofmann–Löffler–Freitag (HLF) reaction, is known for over a century (Scheme 58) [90, 91]. The original harsh conditions proposed by Löffler and Freitag [92, 93] limited wider application; therefore, several modifications to this reaction have been studied since.

Noteworthy examples include the in situ formation of *N*-iodinated sulfonamides, by combining iodine(III) reagents with catalytic amounts of I₂ under visible light irradiation [94]. However, using molecular iodine often led to undesired decomposition; therefore, the Nagib group suggested generating I₂ in situ by oxidation of I[−] salts [95]. Copper catalysts could be used instead of halide sources, as was demonstrated by Yang and coworkers [96]. These and some other examples, involving iodine(III) reagents, were discussed in detail in the recently published review by Wang et al. [97].

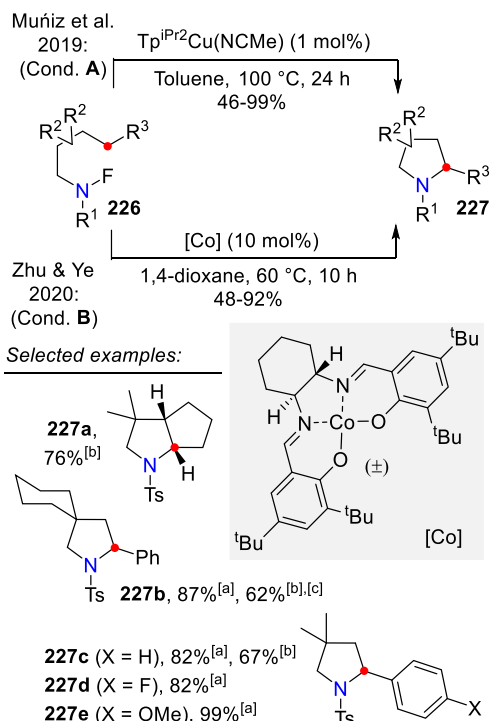
Quintavalla & Lombardo 2023:

SCHEME 57 | Transition states for allyl indium and allyl zinc addition to chiral sulfinimine **216**.



SCHEME 58 | General concept for the HLF reaction.

Surprisingly, *N*-fluorinated sulfonamides have not found much application in the field of HLF-type $C_6(sp^3)$ -H functionalizations. In contrast to its heavier halogen analogs, *N*-F bonds have a lower tendency for homolytic cleavage, required for the HLF-type reaction pathway. Using copper(I) catalysts, which are known to promote single-electron transfer (SET), Muñiz et al. achieved *N*-F bond cleavage and subsequent intramolecular amination, resulting in pyrrolidines **227** (Scheme 59; conditions A) [98]. Cobalt(II) catalysts also facilitated this transformation, as it was demonstrated by Zhu and Ye (conditions B) [99].



[a] Reaction conditions A; [b] Reaction conditions B; [c] Reaction in DCM

SCHEME 59 | HLF-type $C_6(sp^3)$ -H functionalization in *N*-fluorinated sulfonamides **226**.

Further mechanistic studies elucidated that the heterocyclization step proceeded through intermediate **230**, which was further oxidized to a cationic species **232** via a SET mechanism, followed by ring closure and HF formation (Scheme 60). It was also demonstrated that the fluoroalkane **234** was not an intermediate in the catalytic formation of pyrrolidines from the *N*-F reactants [100].

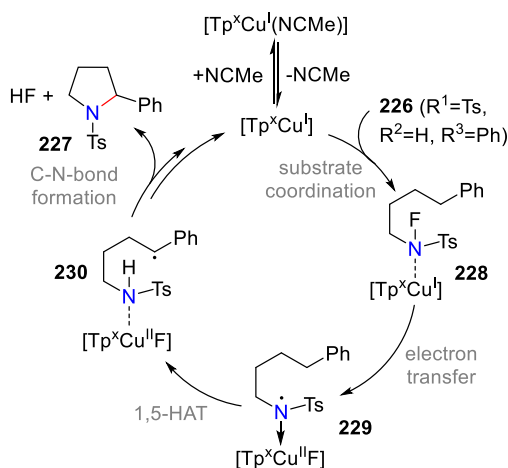
Furthermore, using *N*-fluorinated substrates **226** was preferential to analogical *N*-chlorinated substrates due to more favorable reaction pathways, which was reflected in product **227** yields. For instance, *N*-Cl-sulfonamide ($R^1 = Ts$, $R^2 = Me$, $R^3 = Ph$), when subjected to identical reaction conditions (1 mol% $Tp^{iPr_2}Cu(NCMe)$, toluene, 100 °C, 24 h, afforded pyrrolidine **227** in 83% yield (NMR); meanwhile, its *N*-F fluorinated analog **226** afforded pyrrolidine **227** with 99% yield by NMR [100].

A modified catalytic system for the HLF-type reaction was proposed by Yang and coworkers, who reacted *N*-fluorinated aliphatic amines **235** with phenyl disulfide in the presence of $Cu(acac)_2$, 1,10-phenanthroline, Na_2HPO_4 and indium powder under blue LED light (Scheme 61). This transformation afforded 2-phenylthio-substituted pyrrolidines **236** via site-selective $C(sp^3)$ -S bond formation. For the reaction to yield cyclization products **236**, the substrate needed to contain the OTBDS or OBn group at the C(4) position; otherwise, acyclic sulfides were obtained instead. Control experiments demonstrated that the reaction could proceed in the absence of light, but with a significant decrease in yield [101].

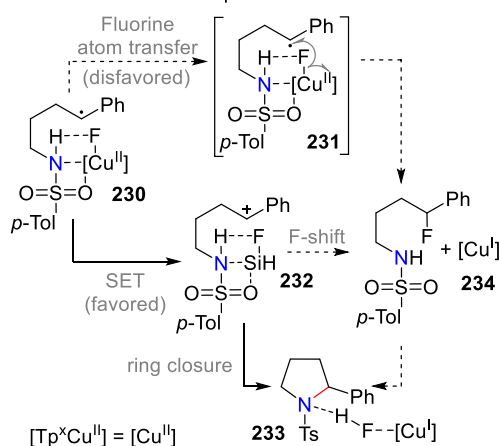
While the *N*-fluorinated amide starting materials could be sufficiently easily prepared from the respective sulfonamides by deprotonation with NaH (6 equiv) and subsequent treatment with NFSI (3 equiv) [100], it is much more convenient to generate the *N*-halogenated amides in situ. Such was the case in the photochemical approach devised by the Shi group, where phthaloyl peroxide (PPO) was combined with iodide salts as a halogenating system to perform the HLF-type reaction on amides **241** (Scheme 62). Both electron-rich and electron-poor benzylic systems ($R^1 = Ar$) were applicable for this reaction, with one example of allylic C-H functionalization ($R^1 = vinyl$) [102].

Li and Wang proposed a halogen-free approach toward direct $C_6(sp^3)$ -H amination in arylamines **247**, containing either a benzylic or an allylic site (Scheme 63). $Cu(OAc)_2$ was used to generate an *N*-centered radical **249**, which subsequently rearranged to the stabilized benzylic/allylic radical **250** via a 1,5-HAT process. The in situ-generated radical **250** was then oxidized to carbenium ion **251**, which then underwent intramolecular amination. In addition to five-membered ring formation, as commonly observed in HLF reaction pathways, the ring size could be altered to obtain four- and six-membered azacycles during the 1,*n*-HAT process [91].

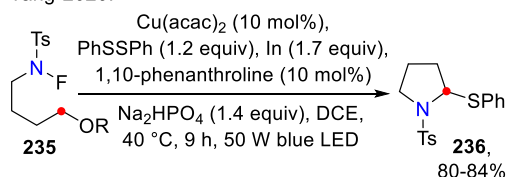
An asymmetric version of the copper-catalyzed Hofmann-Löffler-Freytag-type reaction was reported by Liu and coworkers (Scheme 64). By using a redox $Cu(I)$ / chiral phosphoric acid catalytic system in combination with 4-Methoxy-NHPI (NHPI = *N*-hydroxyphthalimide) as HAT mediator precursor, enantioselective intramolecular $C(sp^3)$ -H amination of allylic and benzylic positions was achieved, yielding 2*S*-pyrrolidines **253**. In the proposed reaction mechanism, the $Cu(I)$ catalyst reacted with the Zn-complex-activated peroxide to generate the alkoxy radical ($tBuO\cdot$) and the chiral $Cu(II)$ phosphate complex. The formed alkoxy radical reacted further with 4-MeO-NHPI to provide the 4-methoxy-PINO (PINO = phthalimide *N*-oxyl) radical. In



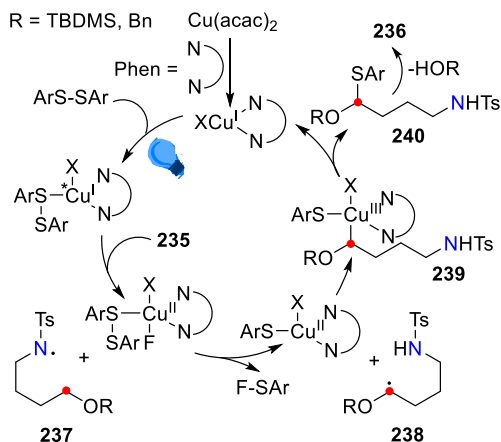
C-N bond formation step:

SCHEME 60 | Catalytic cycle and C-N bond formation step for the HLF-type reaction in *N*-fluorinated sulfonamides **226**.

Yang 2020:

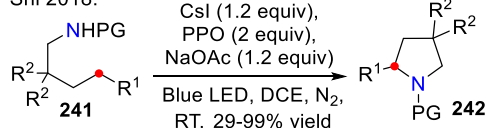


Proposed mechanism:

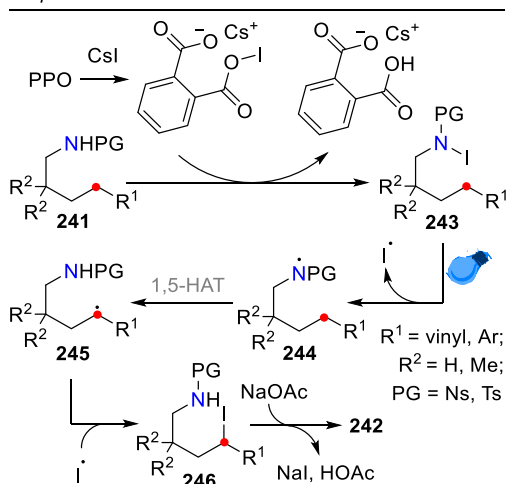
SCHEME 61 | Synthesis of 2-PhS-substituted pyrrolidines **236**.

the presence of the chiral $\text{Cu}(\text{II})$ and $\text{Zn}(\text{II})$ phosphate complexes, 4-MeO-PINO selectively abstracted the hydrogen atom from allylic/benzylic position of the substrate **252** to produce the stabilized radical **255**. The latter underwent oxidation by $\text{Cu}(\text{II})$, followed by ring closure to afford chiral pyrrolidine **253** [103].

Shi 2018:

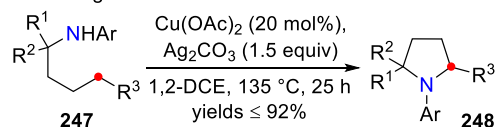


Proposed mechanism:

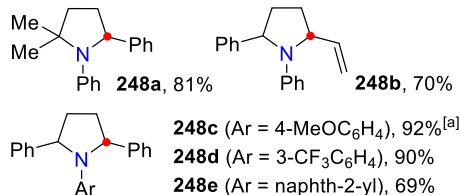
SCHEME 62 | HLF-type reaction, including in situ generation of *N*-iodinated amide **243**.

Some electrochemical approaches have been demonstrated as well, obviating the need for metal catalysts, halogenated reagents, and stoichiometric additional oxidants. Lei and coworkers employed a $\text{C}(+)|\text{Pt}(-)$ system under constant-current electrolysis conditions (15 mA) for oxidative intramolecular $\text{C}(\text{sp}^3)\text{-H}$ bond amination of

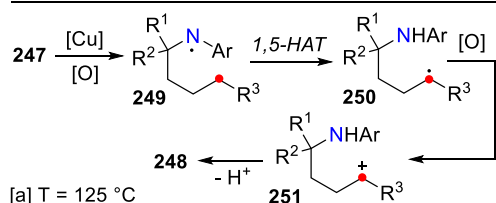
Li & Wang 2021:



Selected examples:



Proposed mechanism:



SCHEME 63 | Copper-catalyzed halogen-free approach towards pyrrolidine **248** synthesis via C–H activation.

sulfonamides **256**, resulting in pyrrolidines **257** (Scheme 65; conditions A) [104]. A similar system for electrochemical synthesis of pyrrolidines **257** was devised by Muñiz and coworkers, where Bu₄NBF₄ was used as the supporting electrolyte. Gratifyingly, they managed to decrease the electric current rate to I = 2.5 mA (2.2 F), with only a slight increase in reaction time (4.7 h) [105].

The Rueping group demonstrated that the electrochemical dehydrogenative C(sp³)-H amination (**256**→**257**) could be performed

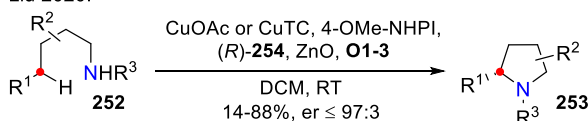
under both bromide-mediated and halogen-free conditions (Scheme 65; conditions B). This approach was applicable for batch and continuous flow processes. Good functional group tolerance and regioselectivity were observed for this method, allowing the synthesis of pyrrolidines **257**, containing more exotic functional groups, for example, 2-ferrocenylpyrrolidine **257d**. Large-scale synthesis was also possible—the anodic transformation of Ts-iso-Leu-OMe was performed on a 50 g scale, obtaining N-tosyl-3-methyl-prolinecarboxylate **257e** with 73% yield [106].

Some key differences could be observed in the mechanism for pyrrolidine **257** formation via the bromine-mediated and halogen-free electrochemical processes (Scheme 65). In the bromine-mediated reaction, the intermediate N-radical **260** was obtained by homolysis of the N-Br species **259**, generated in situ by reacting the amide anion **258** with methyl hypobromite (ROBr), where the latter was also electrochemically generated in the reaction mixture. After the 1,5-HAT event, the C-centered radical **261** was quenched by the MeOBr or N-Br species **259** (although a simple anodic oxidation to the carbocation was also plausible), and a nucleophilic substitution event afforded the pyrrolidine scaffold **257**. In the halogen-free approach, the N-radical **260** generation occurred by anodic oxidation of the amide anion **258**. In the same manner, the C-centered radical **261** was oxidized to carbocation **263**. Subsequent ring closure by nucleophilic attack of the internal amide afforded pyrrolidine **257** [106].

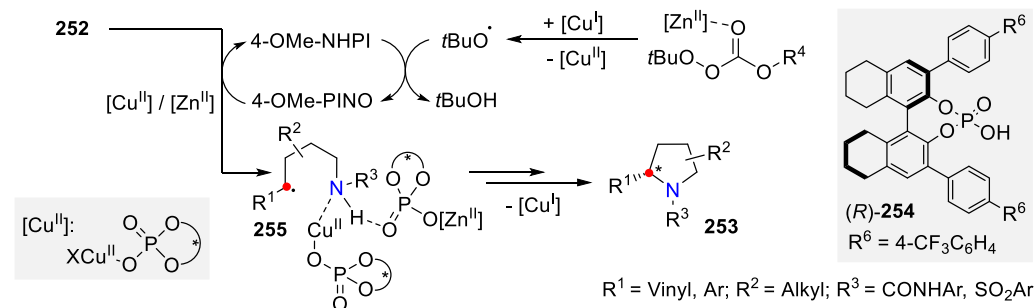
Combining electricity and light in a synergistic catalysis approach is an emerging paradigm in heterocycle synthesis [107]. This approach obviates the need for chemical oxidants and, in some cases, enhances reaction selectivity [108].

In an illustrative example by the Stahl research group, a photo/electrochemical iodide-mediated strategy was developed for the synthesis of pyrrolidines **265** (Scheme 66). The reaction was performed under constant potential (CP) conditions using KPF₆ (0.1 M) as the supporting electrolyte. Tetra-*n*-butylammonium iodide (TBAI, 10 mol%) as an electrochemical mediator allowed the electrochemical process to proceed at low electrode potentials, ensuring reaction selectivity for substrates **264** bearing

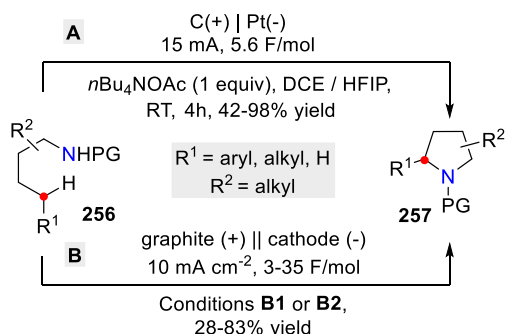
Liu 2020:



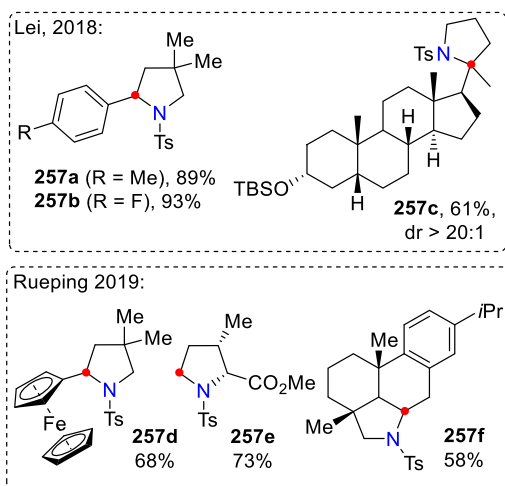
Proposed mechanism:



SCHEME 64 | Asymmetric pyrrolidine **253** synthesis by C(sp³)-H activation.



Selected examples:



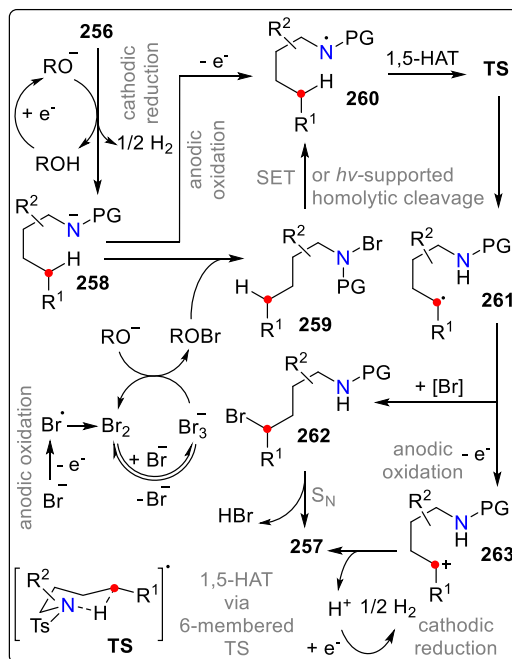
SCHEME 65 | Electrochemical C₈(sp³)-H amination for the synthesis of pyrrolidines **257**.

electron-rich substituents, which were otherwise prone to unwanted side reactions. This was highlighted by the synthesis of pyrrolidine **265a**, bearing the electron-rich methoxynaphthyl substituent (72% yield). For comparison, only negligible C(sp³)-H activation was observed (**265a**, <10%) [109] when using the earlier discussed HLF-reaction conditions provided by Muñiz [105] and Lei [104].

The electrochemical part of the reaction mechanism is based on anodic generation of I₂ from an iodide (I⁻). Hydrogen evolution occurred on the cathode with additional generation of a Brønsted base (CF₃CH₂O⁻), which is required to promote substrate **264** N-H iodination. In bulk solution, photolytic homolysis of the N–I bond enabled a C(sp³)-H functionalization sequence, involving sequential *N*-centered radical **267** formation, a 1,5-HAT event to generate an alkyl radical **268** and alkyl iodide **269** generation. The sequence was finalized by a Brønsted base-promoted cyclization to form the pyrrolidine scaffold **265** [109].

One of the main limitations for the intramolecular C–N bond formation strategy remains complex starting material synthesis, requiring the incorporation of an electrophilic center and the nucleophilic amine functionality for the heterocyclization to occur. Li and coworkers addressed this problem by devising a strategy for

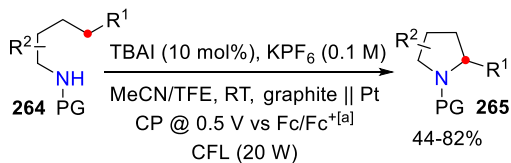
Proposed mechanism:



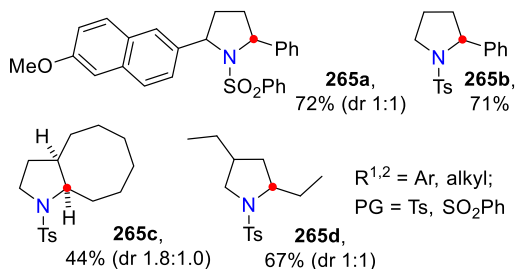
two consecutive C(sp³)-H aminations in simple hydrocarbons **270**, which are easily accessible starting materials (Scheme 67). This was achieved through a halogen bonding charge-transfer complex, which initiated visible light absorption, inducing *N*-radical formation in sulfonamides and a subsequent HAT process. Two consecutive C(sp³)-H aminations took place, forming pyrrolidines **272**. The reaction intermediates—*N*-benzyl sulfonamides **271**—could be isolated with yields up to 98% if the reaction was quenched after 16 h and the used *N*-succinimide (NIS) amount did not exceed 3 equiv. This approach was used to derivatize the sulfonamide moiety-containing anti-inflammatory drug *Celebrex*, introducing a pyrrolidine ring in its molecule [110].

Lastly, Dauban and coworkers demonstrated a diastereoselective strategy for pyrrolidine **277** synthesis by two sequential C(sp³)-H functionalizations of simple hydrocarbons **275** (Scheme 68). A regio- and stereoselective nitrene C–H insertion (**275**→**276**) was performed using a chiral rhodium catalyst and iodine(III) reagent. To achieve regioselective amination of the benzylic site in non-symmetrical hydrocarbons **275**, the aromatic groups had to be differentiated by the introduction of electron-donating or withdrawing substituents, for example, the first benzylic amination occurred preferentially next to the more electron-rich aryl group. While

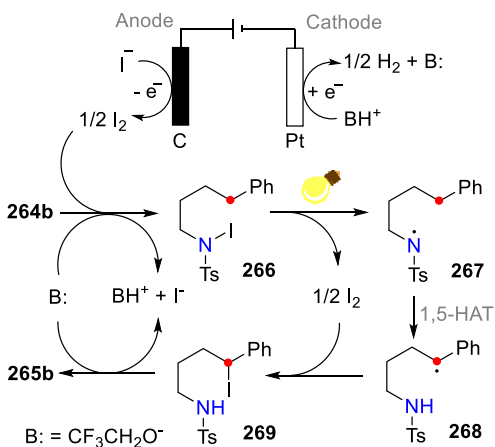
Stahl 2019:



Selected examples:



Proposed mechanism:



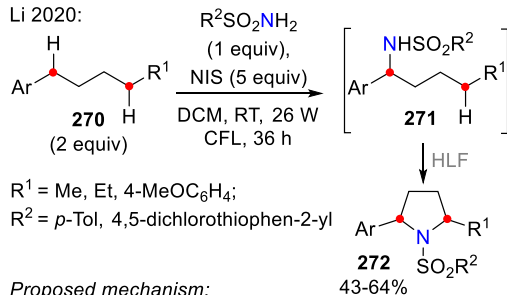
[a] Ferrocene/ferrocenium (Fc/Fc⁺) redox system as internal reference.

SCHEME 66 | Electrochemical amination of C(sp³)-H bonds incorporating visible light.

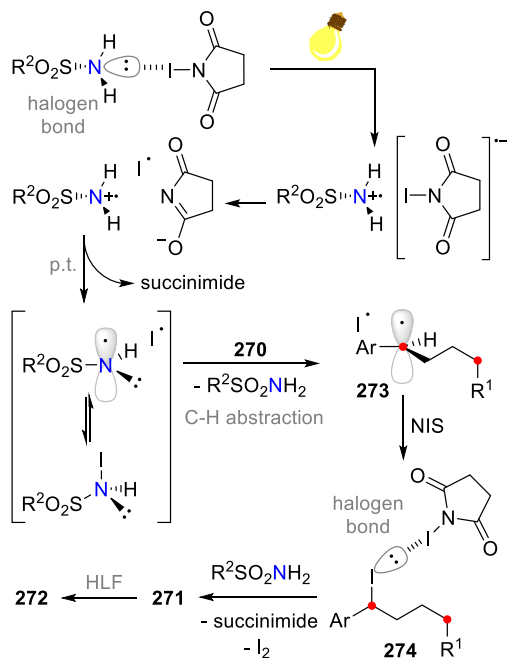
dibenzyl substrates ($R^{1,2}$ = aryl) provided higher pyrrolidine **277** yields (up to 70%), aliphatic substrates also underwent this transformation, as demonstrated by example **277b** [111].

The mechanism for stereoselective nitrene C–H insertion involved three main mechanistic steps: 1) iminoiodane $S^*N = IPh$ generation from $PhI(OPiv)_2$ and chiral auxiliary-containing amide S^*NH_2 ; 2) rhodium(II) complex oxidation by the iminoiodane; and C–H insertion into the formed rhodium-nitrene intermediate $S^*N = [Rh]$ (Scheme 69). Two distinct transition states were proposed for the latter transformation, featuring 1) asynchronous concerted C–H insertion of the metallocarbene ($[TS1]^{\ddagger}$);

Li 2020:



Proposed mechanism:

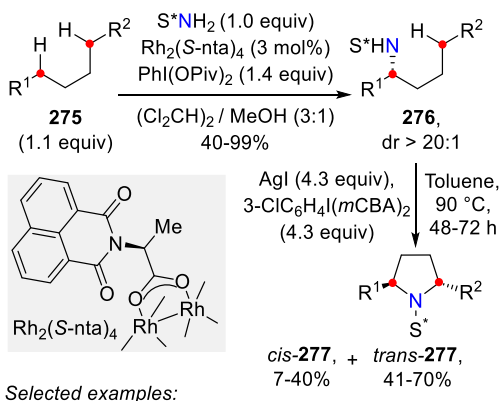


SCHEME 67 | Pyrrolidine **272** synthesis from hydrocarbons **264** by two sequential C(sp³)-H aminations.

or 2) H-abstraction/radical rebound mechanism ($[TS2]^{\ddagger}$) [112]. Control experiments on the *N*-iodoamide **278** *N*-chlorinated analog suggested a synergistic effect between AgI and the iodine(III) reagent in advancing the reaction onward. Subsequent HLF-type cyclization, involving 1,5-hydrogen atom transfer (HAT) from the *N*-centered radical **279**, led to the diastereoselective formation of pyrrolidines **277**. The involvement of a cationic intermediate **281b** for the cyclization step was indicated by the obtained diastereomeric ratios ($dr \leq 8:1$ *trans/cis*). The alternative S_N2 -type cyclization route via intermediate **281a** was excluded, as radical trapping far from the stereogenic center would occur with poor stereocontrol [111].

Afterwards, the sulfonimidamide *N*-protecting group, which served as a chiral auxiliary for the heterocyclization step (**276**→**277**), could be conveniently removed using $Mg/MeOH$ under sonification, affording *trans*-2,5-disubstituted pyrrolidines with further N–H functionalization possibilities [111].

Dauban et al. 2021:



SCHEME 68 | Diastereoselective strategy for pyrrolidine **271** synthesis by two sequential C(sp³)-H functionalizations.

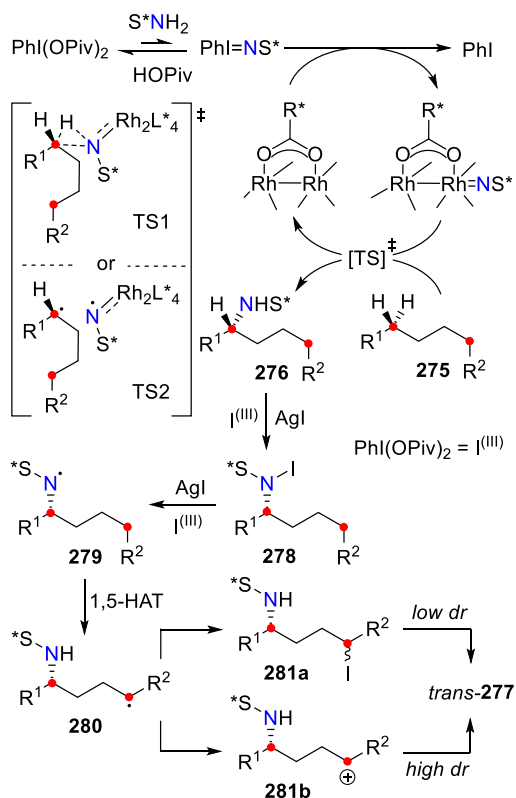
7 | Summary and Outlook

In this review, we summarize methodologies for intramolecular C–N bond formation in systems that combine a nucleophilic nitrogen center with an electrophilic carbon species, leading to the synthesis of pyrrolidine derivatives. The survey covers literature published between 2013 and 2025, including examples for 1) intramolecular amination of double and triple bonds; 2) tandem annulation strategies, featuring intramolecular C–N bond formation as key step; 3) *N*-nucleophile additions to C=O groups; 4) intramolecular nucleophilic substitution and 5) C(sp³)-H activation strategies, leading to pyrrolidines.

During the covered timeframe, significant progress has been made toward addressing key challenges associated with intramolecular C–N bond formation, including the structural complexity of starting materials, the need for side chain functionalization, as well as regio- and stereoselectivity control. Considerable effort has been directed toward incorporating principles of sustainable synthesis—catalytic reaction design, reduced reagent toxicity, and streamlined synthetic sequences to minimize the overall number of required synthetic steps, with electrochemical approaches providing particularly notable examples.

Of special interest is the emerging potential of regio- and stereoselective C(sp³)-H bond functionalization, which enables access to pyrrolidines from more readily available substrates, including alkylamines and hydrocarbons. Rare but important contributions

Proposed mechanism: (Dauban et al. 2008 & 2021)



SCHEME 69 | Mechanistic proposal for diastereoselective pyrrolidine **277** synthesis by two sequential C(sp³)-H functionalizations.

to asymmetric pyrrolidine synthesis via C(sp³)-H amination are also highlighted.

Acknowledgments

This work was supported by the Latvian Council of Science Grant LZP-2023/1-0576 and the EU RRF within project No 5.2.1.1.i.0/2/24/1/CFLA/003 academic career doctoral grant, ID 1134.

Funding

This study was supported by Latvijas Zinātnes Padome (LZP-2023/1-0576); Central Finance and Contracting Agency of Republic of Latvia (5.2.1.1.i.0/2/24/1/CFLA/003, ID 1134).

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. E. Vitaku, D. T. Smith, and J. T. Njardarson, "Analysis of the Structural Diversity, Substitution Patterns, and Frequency of Nitrogen Heterocycles

- among U.S. FDA Approved Pharmaceuticals," *Journal of Medicinal Chemistry* 57, no. 24 (2014): 10257–10274, <https://doi.org/10.1021/jm501100b>.
2. S. Poyraz, H. A. Dönda, N. Yaktubay, and J. M. Sansano, "Recent Insights about Pyrrolidine Core Skeletons in Pharmacology," *Frontiers in Pharmacology* 14 (2023): 1239658, <https://doi.org/10.3389/fphar.2023.1239658>.
 3. A. Ahmad, N. Tandon, I. Singh, and R. Tandon, "Structure-Activity Relationship (SAR) and Antibacterial Activity of Pyrrolidine Based Hybrids: A Review," *Journal of Molecular Structure* 1283 (2023): 135175, <https://doi.org/10.1016/j.molstruc.2023.135175>.
 4. S. Kumar, R. Kohal, D. Mondal, et al., "Unveiling the Research Directions for Pyrrolidine-Based Small Molecules as Versatile Antidiabetic and Anticancer Agents," *Future Medicinal Chemistry* 17, no. 9 (2025): 1039–1053, <https://doi.org/10.1080/17568919.2025.2501923>.
 5. G. Li Petri, M. V. Raimondi, V. Spanò, R. Holl, P. Baraja, and A. Montalbano, "Pyrrolidine in Drug Discovery: A Versatile Scaffold for Novel Biologically Active Compounds," *Topics in Current Chemistry* 379, no. 5 (2021): 34, <https://doi.org/10.1007/s41061-021-00347-5>.
 6. A. Quintavalla, D. Carboni, and M. Lombardo, "Recent Advances in Asymmetric Synthesis of Pyrrolidine-Based Organocatalysts and Their Application: A 15-Year Update," *Molecules* 28, no. 5 (2023): 2234, <https://doi.org/10.3390/molecules28052234>.
 7. A. Smolobochkin, A. Gazizov, N. Appazov, O. Sinyashin, and A. Burilov, "Progress in the Stereoselective Synthesis Methods of Pyrrolidine-Containing Drugs and Their Precursors," *International Journal of Molecular Sciences* 25, no. 20 (2024): 11158, <https://doi.org/10.3390/ijms252011158>.
 8. M. B. Alshammari, A. A. Aly, A. Ahmad, A. B. Brown, and A. H. Mohamed, "Recent Synthetic Strategies of Spiro-Azetidin-2-One, -Pyrrolidine, -Indol(One) and -Pyran Derivatives-a Review," *RSC Advances* 13 (2023): 32786–32823, <https://doi.org/10.1039/d3ra06054c>.
 9. I. A. Andreev and N. K. Ratmanova, "Synthesis of 3-Spiro-Annulated Pyrrolidine-2-Thiones (Microreview)," *Chemistry of Heterocyclic Compounds* 59 (2023): 540–542, <https://doi.org/10.1007/s10593-023-03230-x>.
 10. E. M. Afsah and S. M. Abdelmageed, "Pyrrolidine-2,3-diones: Synthesis, Reactions and Biological Activity," *Journal of Heterocyclic Chemistry* 57, no. 11 (2020): 3763–3783, <https://doi.org/10.1002/jhet.4098>.
 11. S. S. Bondarenko and D. A. Lega, "Recent Advances in the Chemistry of Pyrrolidine-2,3-Diones (Microreview)," *Chemistry of Heterocyclic Compounds* 60 (2024): 118–120, <https://doi.org/10.1007/s10593-024-03303-5>.
 12. P. Dauban, T. Saget, Y. Lazib, and J. G. Naves, "Asymmetric Syntheses of Enantioenriched 2,5-Disubstituted Pyrrolidines," *ACS Organic & Inorganic Au* 3, no. 3 (2023): 120–129, <https://doi.org/10.1021/acscorginorgau.2c00061>.
 13. A. S. Gazizov, A. V. Smolobochkin, A. R. Burilov, and M. A. Pudovik, "3-Ylidene-1-Pyrrolines: Synthesis Reactions and Perspectives," *Tetrahedron Letters* 61, no. 39 (2020): 152371, <https://doi.org/10.1016/j.tetlet.2020.152371>.
 14. A. V. Smolobochkin and A. S. Gazizov, "Synthesis of 3-Arylidene-pyrrolidines (Microreview)," *Chemistry of Heterocyclic Compounds* 55, no. 9 (2019): 815–817, <https://doi.org/10.1007/s10593-019-02541-2>.
 15. A. V. Smolobochkin, T. S. Rizbayeva, A. S. Melyashova, et al., "Acid-Catalyzed Cascade Reaction of 4-Aminobutanal Derivatives with (Hetero)Aromatic Nucleophiles: A Versatile One-Pot Access to 2-(Hetero)Arylpyrrolidines," *ChemistrySelect* 4, no. 32 (2019): 9322–9330, <https://doi.org/10.1002/slct.201902011>.
 16. A. Das, S. Gouthamana, and K. R. J. Thomas, "Photocatalysis as a Green Alternative Toolkit for the Construction of Nitrogen-Enriched Heterocycles via the Direct and Indirect Activation of Alkynes/Alkenes," *Green Chemistry* 26 (2024): 1223–1280, <https://doi.org/10.1039/d3gc03971d>.
 17. Y. B. Sharma, S. Saha, and M. Mohan, "Photochemical Synthesis of Chiral Heterocycles via Asymmetric Carbon-Heteroatom Bond Formation," *Advanced Synthesis & Catalysis* 366, no. 11 (2024): 2432–2449, <https://doi.org/10.1002/adsc.202400307>.
 18. B. K. Behera, P. Ghosh, and A. K. Saikia, "Recent Advances in the Synthesis of N-Heterocycles via Lewis Acid-Catalyzed/Mediated Cyclization of Propargyl- and Homopropargyl-Amines and Their Derivatives," *Tetrahedron* 162 (2024): 134123, <https://doi.org/10.1016/j.tet.2024.134123>.
 19. H. Pellissier, "Synthesis of Chiral Heterocycles Through Enantioselective Silver-Catalyzed Transformations," *European Journal of Organic Chemistry* 28, no. 8 (2025): e202401284, <https://doi.org/10.1002/ejoc.202401284>.
 20. M. Kalimullah, D. Chaudhary, and R. K. Saunthwal, "Harnessing the Reactivity of Alkyne by Cu-Catalyst: Assembly of Highly Functionalized Five-Membered N-Heterocycles," *Advanced Synthesis & Catalysis* 367 (2025): e70170, <https://doi.org/10.1002/adsc.70170>.
 21. T. Zhou, X. Zhang, D. Zhan, W. Zhang, "Glycine-Based [3+2] Cycloaddition for the Synthesis of Pyrrolidine-Containing Polycyclic Compounds," *Molecules* 29, no. 23 (2024): 5726.
 22. H. N. Fatima, M. Ahmad, M. S. N. S. Akram, and S. Aslam, "Recent Synthetic Methodologies for Pyrrolidine Derivatives through Multicomponent Reactions," *Synthetic Communications* 55, no. 16 (2025): 1201–1227, <https://doi.org/10.1080/00397911.2025.2503341>.
 23. K. Wang, Q. Wang, M. Xu, and L. Er-qing, "Recent Advances in Palladium-Catalyzed Annulations for the Synthesis of Pyrrolidines," *Journal of Molecular Structure* 1325 (2025): 141010, <https://doi.org/10.1016/j.molstruc.2024.141010>.
 24. A. S. Ganin, M. M. Sobyana, and M. Y. Moskalik, "Synthesis of N-Heterocycles and Linear Adducts from Allyl-Containing Substrates and Sulfonamides," *Current Organic Chemistry* 29, no. 15 (2025): 1145–1158, <https://doi.org/10.2174/0113852728348072250113115434>.
 25. K. Gilmore, R. K. Mohamed, and I. V. Alabugin, "The Baldwin Rules: Revised and Extended," *WIREs Computational Molecular Science* 6, no. 5 (2016): 487–514, <https://doi.org/10.1002/wcms.1261>.
 26. C. J. Maddocks, K. Ermanis, and P. A. Clarke, "Asymmetric "Clip-Cycle" Synthesis of Pyrrolidines and Spiropyrrolidines," *Organic Letters* 22, no. 20 (2020): 8116–8121, <https://doi.org/10.1021/acs.orglett.0c03090>.
 27. M. Sánchez-rostelló, M. Escolano, and D. Gaviña, "Two Decades of Progress in the Asymmetric Intramolecular Aza-Michael Reaction," *The Chemical Record* 22 (2022): e202100161, <https://doi.org/10.1002/ctr.202100161>.
 28. M. Sánchez-Roselló, J. L. Aceña, A. Simón-Fuentes, and C. del Pozo, "A General Overview of the Organocatalytic Intramolecular Aza-Michael Reaction," *Chemical Society Reviews* 43, no. 21 (2014): 7430–7453, <https://doi.org/10.1039/C4CS00156G>.
 29. M. G. Vinogradov, O. V. Turova, and S. G. Zlotin, "Recent Advances in the Asymmetric Synthesis of Pharmacology-Relevant Nitrogen Heterocycles via Stereoselective Aza-Michael Reactions," *Organic & Biomolecular Chemistry* 17, no. 15 (2019): 3670–3708, <https://doi.org/10.1039/C8OB03034K>.
 30. Z. Amara, J. Caron, and D. Joseph, "Recent Contributions from the Asymmetric Aza-Michael Reaction to Alkaloids Total Synthesis," *Natural Product Reports* 30 (2013): 1211–1225, <https://doi.org/10.1039/c3np20121j>.
 31. H. Liu, C. Zeng, J. Guo, M. Zhang, and S. Yu, "Enantioselective Synthesis of 2-Substituted Pyrrolidines via Domino Cross Metathesis/Intramolecular Aza-Michael Addition," *RSC Advances* 3, no. 6 (2013): 1666–1668, <https://doi.org/10.1039/C2RA22374K>.

32. T. Cheng, S. Meng, and Y. Huang, "A Highly Diastereoselective and Enantioselective Synthesis of Polysubstituted Pyrrolidines via an Organocatalytic Dynamic Kinetic Resolution Cascade," *Organic Letters* 15, no. 8 (2013): 1958–1961, <https://doi.org/10.1021/ol4006129>.
33. T. Ishii, E. Nezu, and H. Fuwa, "Tandem Synthesis of Pyrrolidine and Piperidine Derivatives from Propargylic Alcohols Under Multimetallic Catalysis," *European Journal of Organic Chemistry* 28, no. 23 (2025): e202500226, <https://doi.org/10.1002/ejoc.202500226>.
34. M.-A. Abadie, X. Trivelli, F. Medina, et al., "Asymmetric Intramolecular Hydroamination of Alkenes in Mild and Wet Conditions-Structure and Reactivity of Cationic Binuclear Gold(I) Catalysts," *ChemCatChem* 6, no. 8 (2014): 2235–2239, <https://doi.org/10.1002/cctc.201402350>.
35. A. J. Musacchio, L. Q. Nguyen, G. H. Beard, and R. R. Knowles, "Photoredox Method for Direct C–N Bond Formation," *Journal of the American Chemical Society* 136, no. 35 (2014): 12217–12220, <https://doi.org/10.1021/ja5056774>.
36. Y. Zhao and W. Xia, "Recent Advances in Radical-Based C–N Bond Formation via Photo-/Electrochemistry," *Chemical Society Reviews* 47 (2018): 2591–2608, <https://doi.org/10.1039/C7CS00572E>.
37. X. Yu, Q. Zhao, J. Chen, W. Xiao, and J. Chen, "When Light Meets Nitrogen-Centered Radicals: From Reagents to Catalysts," *Accounts of Chemical Research* 53, no. 5 (2020): 1066–1083, <https://doi.org/10.1021/acs.accounts.0c00090>.
38. J.-L. Tu, Y. Zhu, P. Li, and B. Huang, "Visible-Light Induced Direct C(Sp³)–H Functionalization: Recent Advances and Future Prospects," *Organic Chemistry Frontiers* 11 (2024): 5278–5305, <https://doi.org/10.1039/D4OQ001179A>.
39. H. Shigehisa, N. Koseki, N. Shimizu, M. Fujisawa, M. Niitsu, and K. Hiroya, "Catalytic Hydroamination of Unactivated Olefins Using a Co Catalyst for Complex Molecule Synthesis," *Journal of the American Chemical Society* 136, no. 39 (2014): 13534–13537, <https://doi.org/10.1021/ja507295u>.
40. D. Foster, P. Gao, Z. Zhang, et al., "Design, Scope and Mechanism of Highly Active and Selective Chiral NHC-Iridium Catalysts for the Intramolecular Hydroamination of a Variety of Unactivated Aminoalkenes," *Chemical Science* 12, no. 10 (2021): 3751–3767, <https://doi.org/10.1039/d0sc05884j>.
41. E. Bernoud, P. Oulié, R. Guillot, M. Mellah, and J. Hannedouche, "Well-Defined Four-Coordinate Iron(II) Complexes For Intramolecular Hydroamination of Primary Aliphatic Alkenylamines," *Angewandte Chemie International Edition* 53, no. 19 (2014): 4930–4934, <https://doi.org/10.1002/anie.201402089>.
42. I. Kazi, I. I. Mbaezue, S.-G. Li, et al., "Synthesis and Application of a P-Chiral Phosphine Oxide N-Heterocyclic Carbene-Au(I) Catalyst," *Organometallics* 44, no. 19 (2025): 2146–2150, <https://doi.org/10.1021/acs.organomet.5c00280>.
43. N. A. Meanwell, "Fluorine and Fluorinated Motifs in the Design and Application of Bioisosteres for Drug Design," *Journal of Medicinal Chemistry* 61, no. 14 (2018): 5822–5880, <https://doi.org/10.1021/acs.jmedchem.7b01788>.
44. H. Mei, A. M. Remete, Y. Zou, et al., "Fluorine-Containing Drugs Approved by the FDA in 2019," *Chinese Chemical Letters* 31, no. 9 (2020): 2401–2413, <https://doi.org/10.1016/j.ccllet.2020.03.050>.
45. G. Shabir, A. Saeed, W. Zahid, et al., "Chemistry and Pharmacology of Fluorinated Drugs Approved by the FDA (2016–2022)," *Pharmaceuticals* 16, no. 8 (2023): 1162, <https://doi.org/10.3390/ph16081162>.
46. C. Chen, C. Hou, P. Chen, and G. Liu, "Palladium(II)-Catalyzed Aminotrifluoromethoxylation of Alkenes: Mechanistic Insight into the Effect of N-Protecting Groups," *Chinese Journal of Chemistry* 38, no. 4 (2020): 346–350, <https://doi.org/10.1002/cjoc.201900516>.
47. T. Wu, J. Cheng, P. Chen, and G. Liu, "Regioselective Palladium-Catalyzed Intramolecular Oxidative Aminofluorination of Unactivated Alkenes," *Chemical Communications* 49, no. 77 (2013): 8707, <https://doi.org/10.1039/c3cc44711a>.
48. Z. Zhang, X. Tang, C. S. Thomason, and W. R. Dolbier, "Photoredox-Catalyzed Intramolecular Aminodifluoromethylation of Unactivated Alkenes," *Organic Letters* 17, no. 14 (2015): 3528–3531, <https://doi.org/10.1021/acs.orglett.5b01616>.
49. J. Lin, Y. Xiong, C. Ma, L. Zhao, B. Tan, and X. Liu, "Efficient Copper-Catalyzed Direct Intramolecular Aminotrifluoromethylation of Unactivated Alkenes with Diverse Nitrogen-Based Nucleophiles," *Chemistry – A European Journal* 20, no. 5 (2014): 1332–1340, <https://doi.org/10.1002/chem.201303387>.
50. E. Valverde, S. Kawamura, D. Sekine, and M. Sodeoka, "Metal-Free Alkene Oxy- and Amino-Perfluoroalkylations via Carbocation Formation by Using Perfluoro Acid Anhydrides: Unique Reactivity between Styrenes and Perfluoro Diacyl Peroxides," *Chemical Science* 9, no. 35 (2018): 7115–7121, <https://doi.org/10.1039/C8SC02547A>.
51. Y. He, X. Qin, X. He, X. Wu, and Z. Yin, "Practical Synthesis of Halogenated N-Heterocycles via Electrochemical Anodic Oxidation of Unactivated Alkenes," *European Journal of Organic Chemistry* 2021, no. 42 (2021): 5831–5834, <https://doi.org/10.1002/ejoc.202101189>.
52. X. Liu, C. Hou, Y. Peng, P. Chen, and G. Liu, "Ligand-Controlled Regioselective Pd-Catalyzed Diamination of Alkenes," *Organic Letters* 22, no. 23 (2020): 9371–9375, <https://doi.org/10.1021/acs.orglett.0c03634>.
53. J. Li, R. H. Grubbs, and B. M. Stoltz, "Palladium-Catalyzed Aerobic Intramolecular Aminoacetoxylation of Alkenes Enabled by Catalytic Nitrate," *Organic Letters* 18, no. 21 (2016): 5449–5451, <https://doi.org/10.1021/acs.orglett.6b02722>.
54. T. Wdowik and S. R. Chemler, "Direct Synthesis of 2-Formylpyrrolidines, 2-Pyrrolidinones and 2-Dihydrofuranones via Aerobic Copper-Catalyzed Aminoacetoxylation and Dioxygenation of 4-Pentenylsulfonamides and 4-Pentenylalcohols," *Journal of the American Chemical Society* 139, no. 28 (2017): 9515–9518, <https://doi.org/10.1021/jacs.7b05680>.
55. T. M. Nguyen and D. A. Nicewicz, "Anti-Markovnikov Hydroamination of Alkenes Catalyzed by an Organic Photoredox System," *Journal of the American Chemical Society* 135, no. 26 (2013): 9588–9591.
56. R. Shi, L. Wang, L. Luo, J. Zhang, X. Gao, and W. Guo, "Electrochemically Promoted Aminothiocyanylation of Unactivated Alkenes for the Synthesis of Thiocyanated Pyrrolidines," *European Journal of Organic Chemistry* 28 (2025): e202500895, <https://doi.org/10.1002/ejoc.202500895>.
57. J. Cui, Q. Jia, R. Feng, S. Liu, T. He, and C. Zhang, "Boron Trifluoride Etherate Functioning as a Fluorine Source in an Iodosobenzene-Mediated Intramolecular Aminofluorination of Homoallylic Amines," *Organic Letters* 16, no. 5 (2014): 1442–1445, <https://doi.org/10.1021/ol500238k>.
58. T. Kitamura, A. Miyake, K. Muta, and J. Oyama, "Hypervalent Iodine/HF Reagents for the Synthesis of 3-Fluoropyrrolidines," *The Journal of Organic Chemistry* 82, no. 22 (2017): 11721–11726, <https://doi.org/10.1021/acs.joc.7b01266>.
59. L. Cox, Y. Zhu, P. J. Smith, K. E. Christensen, M. Sidera Portela, and T. J. Donohoe, "Alcohols as Alkylating Agents in the Cation-Induced Formation of Nitrogen Heterocycles," *Angewandte Chemie International Edition* 61, no. 34 (2022): e202206800, <https://doi.org/10.1002/anie.202206800>.
60. J. Wei, Z. Xu, Y. Wei, and M. Shi, "Gold (I)-Catalyzed Cascade Cyclization of Nitrogen or Oxygen Containing Nucleophile Tethered-Vinylidenecyclopropanes to Pyrrole, Furan, Pyrrolidine and Piperidine Skeletons," *Advanced Synthesis & Catalysis* 365 (2023): 1864–1870, <https://doi.org/10.1002/adsc.202300261>.
61. S. Fujita, M. Shibuya, and Y. Yamamoto, "Intramolecular Hydroalkoxylation/Reduction and Hydroamination/Reduction of

- Unactivated Alkynes Using a Silane–Iodine Catalytic System,” *Synthesis* 49, no. 18 (2017): 4199–4204, <https://doi.org/10.1055/s-0036-1588436>.
62. S. J. Gharpure, D. S. Vishwakarma, and R. K. Patel, “TMSOTf Mediated 5/6- *endo-dig* Reductive Hydroamination for the Stereoselective Synthesis of Pyrrolidine and Piperidine Derivatives,” *Chemical Communications* 55, no. 48 (2019): 6858–6861, <https://doi.org/10.1039/C9CC03127H>.
63. S. J. Gharpure, R. K. Patel, and K. S. Gupta, “Total Synthesis of Pyrrolidine and Piperidine Natural Products via TMSOTf-Mediated “5/6- *endo-dig*” Reductive Hydroamination of Enynyl Amines,” *Organic Letters* 25, no. 31 (2023): 5850–5855, <https://doi.org/10.1021/acs.orglett.3c02115>.
64. T.-D. Tan, Y.-B. Chen, M.-Y. Yang, et al., “Stereoselective Synthesis of 2,5-Disubstituted Pyrrolidines via Gold-Catalysed Anti-Markovnikov Hydroamination-Initiated Tandem Reactions,” *Chemical Communications* 55, no. 67 (2019): 9923–9926, <https://doi.org/10.1039/C9CC05295J>.
65. W. Wang, X. Cao, X. Cao, et al., “Stereospecific Synthesis of *cis*-2,5-Disubstituted Pyrrolidines via *N*, *O*-Acetals Formed by Hydroamination Cyclization–Hydroalkoxylation of Homopropargylic Sulfonamides in HFIP,” *The Journal of Organic Chemistry* 85, no. 11 (2020): 7045–7059, <https://doi.org/10.1021/acs.joc.0c00403>.
66. R. Kropka, R. Bejauniek, A. Ubaidullajevs, A. Mishnev, and M. Turks, “1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain,” *The Journal of Organic Chemistry* 88, no. 19 (2023): 13857–13870, <https://doi.org/10.1021/acs.joc.3c01481>.
67. R. Bejauniek, M. Puriq, and M. Turks, “Manifestation of the β -Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift,” *Synthesis* 52, no. 15 (2020): 2147–2161, <https://doi.org/10.1055/s-0039-1690898>.
68. R. Kropka, R. Bejauniek, A. Sebris, A. Mishnev, and M. Turks, “Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift-Heterocyclization of Propargylsilanes under Copper Catalysis,” *Beilstein Journal of Organic Chemistry* 21 (2025): 1984–1994, <https://doi.org/10.3762/bjoc.21.154>.
69. P. R. D. Murray, I. N.-M. Leibler, S. M. Hell, E. Villalona, A. G. Doyle, and R. R. Knowles, “Radical Redox Annulations: A General Light-Driven Method for the Synthesis of Saturated Heterocycles,” *ACS Catalysis* 12, no. 21 (2022): 13732–13740, <https://doi.org/10.1021/acscatal.2c04316>.
70. K. Matsukuma, M. Tayu, M. Noji, S. Hayashi, S. Ohnui, and N. Saito, “A General Catalytic Sulfide-Based Electron Donor-Acceptor Complex Platform for Decarboxylative Transformations of *N*-Hydroxyphthalimide Esters,” *Advanced Synthesis & Catalysis* 367, no. 10 (2025): e202500196, <https://doi.org/10.1002/adsc.202500196>.
71. M. Tayu, K. Matsukuma, T. Ogino, S. Ohnui, and N. Saito, “Aminoalkylation of Alkenes for Modular Pyrrolidine Synthesis via Electron Donor – Acceptor Complexes Generated from Alkenes and Amine-Tethered *N*-Hydroxyphthalimide Esters,” *Chemical and Pharmaceutical Bulletin* 73, no. 8 (2025): 738–744.
72. C. Um and S. R. Chemler, “Synthesis of 2-Aryl- and 2-Vinylpyrrolidines via Copper-Catalyzed Coupling of Styrenes and Dienes with Potassium β -Aminoethyl Trifluoroborates,” *Organic Letters* 18, no. 10 (2016): 2515–2518, <https://doi.org/10.1021/acs.orglett.6b01259>.
73. S. Lee, H. Lei, and T. Rovis, “A Rh(III)-Catalyzed Formal [4+1] Approach to Pyrrolidines from Unactivated Terminal Alkenes and Nitrone Sources,” *Journal of the American Chemical Society* 141, no. 32 (2019): 12536–12540, <https://doi.org/10.1021/jacs.9b07012>.
74. V. K. Harit and N. G. Ramesh, “A Common Strategy towards the Synthesis of 1,4-Dideoxy-1,4-Imino-1-Xylitol, Deacetyl (+)-Anisomycin and Amino-Substituted Piperidine Iminosugars,” *Carbohydrate Research* 492 (2020): 107988, <https://doi.org/10.1016/j.carres.2020.107988>.
75. K. L. Ivanov, E. V. Villemson, E. M. Budynina, O. A. Ivanova, I. V. Trushkov, and M. Y. Melnikov, “Ring Opening of Donor-Acceptor Cyclopropanes with the Azide Ion: A Tool for Construction of *N*-Heterocycles,” *Chemistry – A European Journal* 21, no. 13 (2015): 4975–4987, <https://doi.org/10.1002/chem.201405551>.
76. D. Wei, C. Netkaew, and C. Darcel, “Iron-Catalysed Switchable Synthesis of Pyrrolidines Vs Pyrrolidinones by Reductive Amination of Levulinic Acid Derivatives via Hydrosilylation,” *Advanced Synthesis & Catalysis* 361, no. 8 (2019): 1781–1786, <https://doi.org/10.1002/adsc.201801656>.
77. D. Wei, C. Netkaew, V. Carré, and C. Darcel, “Iron-Catalysed Reductive Amination of Carbonyl Derivatives with Ω -Amino Fatty Acids to Access Cyclic Amines,” *ChemSusChem* 12, no. 13 (2019): 3008–3012, <https://doi.org/10.1002/cssc.201900519>.
78. H. Li, F. Huang, H. Gao, et al., “Calcium(II)-Catalyzed Reductive Amination of Biomass-Derived Keto Acids to Functionalized Lactams under Solvent-Free Conditions,” *Organic Letters* 25, no. 14 (2023): 2504–2508, <https://doi.org/10.1021/acs.orglett.3c00676>.
79. T. C. Jankins, W. C. Bell, Y. Zhang, et al., “Low-Valent Tungsten Redox Catalysis Enables Controlled Isomerization and Carbonylative Functionalization of Alkenes,” *Nature Chemistry* 14, no. 6 (2022): 632–639, <https://doi.org/10.1038/s41557-022-00951-y>.
80. F.-F. Xu, J.-Q. Chen, D.-Y. Shao, and P.-Q. Huang, “Catalytic Enantioselective Reductive Alkynylation of Amides Enables One-Pot Syntheses of Pyrrolidine, Piperidine and Indolizidine Alkaloids,” *Nature Communications* 14 (2023): 6251, <https://doi.org/10.1038/s41467-023-41846-x>.
81. Z. Li, F. Zhao, W. Ou, P. Huang, and X. Wang, “Asymmetric Reactions Asymmetric Deoxygenative Alkynylation of Tertiary Amides Enabled by Iridium / Copper Bimetallic Relay Catalysis,” *Angewandte Chemie International Edition* 60 (2021): 26604–26609, <https://doi.org/10.1002/anie.202111029>.
82. H. Chen, Z. Wu, D. Shao, and P. Huang, “Multicatalysis Protocol Enables Direct and Versatile Enantioselective Reductive Transformations of Secondary Amides,” *Science Advances* 8, no. 47 (2022): eade3431.
83. S. Hwang, H. Park, Y. Kwon, and S. Kim, “Acid Promoted Cyclodehydration of Amino Alcohols with Amide Acetal,” *RSC Advances* 4, no. 104 (2014): 60017–60024, <https://doi.org/10.1039/C4RA10625C>.
84. H. Park, Y. Kwon, J. Shin, et al., “Orthoester in Cyclodehydration of Carbamate-Protected Amino Alcohols under Acidic Conditions,” *Synthesis* 49, no. 12 (2017): 2761–2767, <https://doi.org/10.1055/s-0036-1588750>.
85. P. T. Marcy, L. R. Jefferies, D. I. AbuSalim, M. Pink, M. Baik, and S. P. Cook, “Stereoconversion of Unactivated Alcohols by Tethered Sulfonamides,” *Angewandte Chemie International Edition* 58, no. 6 (2019): 1727–1731, <https://doi.org/10.1002/anie.201812894>.
86. A. A. Reddy and K. R. Prasad, “Addition of the Lithium Anion of Diphenylmethanol Methyl/Methoxymethyl Ether to Nonracemic Sulfinimines: Two-Step Asymmetric Synthesis of Diphenylprolinol Methyl Ether and Chiral (Diphenylmethoxymethyl)Amines,” *The Journal of Organic Chemistry* 83 (2018): 10776–10785, <https://doi.org/10.1021/acs.joc.8b01381>.
87. D. Carboni, D. Remigio, A. Quintavalla, and M. Lombardo, “Diastereoselective Synthesis and Functionalization of *tert* -Butylsulfenyl-2-(Chlorodiphenylmethyl)Pyrrolidine,” *European Journal of Organic Chemistry* 27, no. 24 (2024): e202400208, <https://doi.org/10.1002/ejoc.202400208>.
88. D. Carboni, G. Casagrande, S. Di Remigio, A. Mirone, A. Quintavalla, and M. Lombardo, “Diastereoselective Synthesis of Silyl-Substituted Pyrrolidines,” *The Journal of Organic Chemistry* 90, no. 26 (2025): 9160–9169, <https://doi.org/10.1021/acs.joc.5c01023>.

89. A. Quintavalla, D. Carboni, M. Simeone, and M. Lombardo, "Stereoselective Synthesis of A-Disubstituted B-Homoprolines," *Organic Letters* 25 (2023): 7067–7071, <https://doi.org/10.1021/acs.orglett.3c02891>.
90. S. Shkunnikova, H. Zipse, and D. Šakić, "Role of Substituents in the Hofmann–Löffler–Freitag Reaction. A Quantum-Chemical Case Study on Nicotine Synthesis," *Organic & Biomolecular Chemistry* 19, no. 4 (2021): 854–865, <https://doi.org/10.1039/D0OB02187C>.
91. R.-X. Jin, J.-C. Dai, Y. Li, and X.-S. Wang, "Copper-Catalyzed Intramolecular Amination of C(sp³)–H Bond of Secondary Amines to Access Azacycles," *Organic Letters* 23, no. 2 (2021): 421–426, <https://doi.org/10.1021/acs.orglett.0c03934>.
92. K. Löffler and C. Freytag, "Über Eine Neue Bildungsweise von N-alkylierten Pyrrolidinen," *Berichte der Deutschen Chemischen Gesellschaft* 42, no. 3 (1909): 3427–3431, <https://doi.org/https://doi.org/10.1002/cber.19090420377>.
93. K. Löffler and S. Kober, "Über die Bildung des i-Nicotins aus N-Methyl- p-pyridyl-butylamin (Dihydropyridine)," *Berichte der Deutschen Chemischen Gesellschaft* 42, no. 3 (1909): 3431–3438, <https://doi.org/10.1002/cber.19090420378>.
94. C. Martínez and K. Muñoz, "An Iodine-Catalyzed Hofmann–Löffler Reaction," *Angewandte Chemie International Edition* 54, no. 28 (2015): 8287–8291, <https://doi.org/10.1002/anie.201501122>.
95. E. A. Wappes, S. C. Fosú, T. C. Chopko, and D. A. Nagib, "Triiodide-Mediated δ -Amination of Secondary C–H Bonds," *Angewandte Chemie International Edition* 55, no. 34 (2016): 9974–9978, <https://doi.org/10.1002/anie.201604704>.
96. D. Meng, Y. Tang, J. Wei, X. Shi, and M. Yang, "Copper-Catalyzed Remote (δ) C(sp³)–H Bond Amination: A Practical Strategy to Construct Pyrrolidine Derivatives," *Chemical Communications* 53, no. 42 (2017): 5744–5747, <https://doi.org/10.1039/c7cc02624b>.
97. X. Teng, T. Yu, J. Shi, et al., "Recent Advances in the Functionalization of Remote C–H Bonds by Hofmann–Löffler–Freitag-Type Reactions," *Advanced Synthesis & Catalysis* 365 (2023): 3211–3226, <https://doi.org/10.1002/adsc.202300718>.
98. D. Bafaluy, J. M. Muñoz-Molina, I. Funes-Ardoiz, et al., "Copper-Catalyzed N–F Bond Activation for Uniform Intramolecular C–H Amination Yielding Pyrrolidines and Piperidines," *Angewandte Chemie International Edition* 58 (2019): 8912–8916, <https://doi.org/10.1002/anie.201902716>.
99. P. Guo, Y. Li, X.-G. Zhang, et al., "Redox Neutral Radical-Relay Cobalt Catalysis toward C–H Fluorination and Amination," *Organic Letters* 22, no. 9 (2020): 3601–3606, <https://doi.org/10.1021/acs.orglett.0c01072>.
100. J. M. Muñoz-Molina, D. Bafaluy, I. Funes-Ardoiz, et al., "Mechanistic Studies on the Synthesis of Pyrrolidines and Piperidines via Copper-Catalyzed Intramolecular C–H Amination," *Organometallics* 41, no. 9 (2022): 1099–1105, <https://doi.org/10.1021/acs.organomet.2c00095>.
101. Y. Qin, Y. Han, Y. Tang, J. Wei, and M. Yang, "A General Method for Site-Selective Csp³–S Bond Formation via Cooperative Catalysis," *Chemical Science* 11, no. 5 (2020): 1276–1282, <https://doi.org/10.1039/C9SC04169A>.
102. D. Chang, R. Zhao, C. Wei, Y. Yao, Y. Liu, and L. Shi, "Sulfonamide-Directed Chemo- and Site-Selective Oxidative Halogenation/Amination Using Halogenating Reagents Generated In Situ from Cyclic Diacyl Peroxides," *The Journal of Organic Chemistry* 83, no. 6 (2018): 3305–3315, <https://doi.org/10.1021/acs.joc.8b00243>.
103. L. Ye, Y. Tian, X. Meng, Q. Gu, and X. Liu, "Enantioselective Copper(I)/Chiral Phosphoric Acid Catalyzed Intramolecular Amination of Allylic and Benzylic C–H Bonds," *Angewandte Chemie International Edition* 59, no. 3 (2020): 1129–1133, <https://doi.org/10.1002/anie.201911742>.
104. X. Hu, G. Zhang, F. Bu, L. Nie, and A. Lei, "Electrochemical-Oxidation-Induced Site-Selective Intramolecular C(sp³)–H Amination," *ACS Catalysis* 8, no. 10 (2018): 9370–9375, <https://doi.org/10.1021/acscatal.8b02847>.
105. S. Herold, D. Bafaluy, and K. Muñoz, "Anodic Benzylic C(sp³)–H Amination: Unified Access to Pyrrolidines and Piperidines," *Green Chemistry* 20, no. 14 (2018): 3191–3196, <https://doi.org/10.1039/C8GC01411F>.
106. P. Nikolaienko, M. Jentsch, A. P. Kale, Y. Cai, and M. Rueping, "Electrochemical and Scalable Dehydrogenative C(sp³)–H Amination via Remote Hydrogen Atom Transfer in Batch and Continuous Flow," *Chemistry – A European Journal* 25, no. 29 (2019): 7177–7184, <https://doi.org/10.1002/chem.201806092>.
107. Y. Chen and B. Huang, "Harnessing the Synergistic Power of Light and Electricity: An Emerging Frontier in Catalytic Heterocycle Synthesis," *Organic Chemistry Frontiers* 12 (2025): 6614–6630, <https://doi.org/10.1039/D5QO01097G>.
108. Z. Shen, J.-L. Tu, and B. Huang, "Unleashing the Potentiality of Metals: Synergistic Catalysis with Light and Electricity," *Organic Chemistry Frontiers* 11 (2024): 4024–4040, <https://doi.org/10.1039/D4QO00797B>.
109. F. Wang and S. S. Stahl, "Synthetic Methods Very Important Paper Merging Photochemistry with Electrochemistry: Functional-Group Tolerant Electrochemical Amination of C(sp³) Å H Bonds," *Angewandte Chemie International Edition* 58, no. 19 (2019): 6385–6390, <https://doi.org/10.1002/anie.201813960>.
110. F. Wu, J. P. Ariyaratna, N. Kaur, et al., "Halogen-Bond-Induced Consecutive C_{sp}³–H Aminations via Hydrogen Atom Transfer Relay Strategy," *Organic Letters* 22, no. 6 (2020): 2135–2140, <https://doi.org/10.1021/acs.orglett.0c00081>.
111. Y. Lazib, P. Retailleau, T. Saget, B. Darses, and P. Dauban, "Asymmetric Synthesis of Enantiopure Pyrrolidines by C(sp³)–H Amination of Hydrocarbons," *Angewandte Chemie* 133, no. 40 (2021): 21876–21880, <https://doi.org/10.1002/ange.202107898>.
112. C. Liang, F. Collet, F. Robert-Peillard, P. Müller, R. H. Dodd, and P. Dauban, "Toward a Synthetically Useful Stereoselective C–H Amination of Hydrocarbons," *Journal of the American Chemical Society* 130 (2008): 343–350, <https://doi.org/10.1021/ja076519d>.

Biographies



Rasma Kronkalne obtained her MSc in chemical engineering in 2022 from the Riga Technical University (RTU). She is currently working toward her PhD under supervision of Prof. Māris Turks at RTU. Her research focuses on reactions of silanes and their application in heterocycle synthesis.



In 2007, **Māris Turks** began his independent academic career at Riga Technical University, where he has been a Full Professor of Organic Chemistry since 2012. He currently serves as Dean of the Faculty of Natural Sciences and Technology. Prof. Turks' research interests include the chemistry of organometalloids, natural triterpenoids, the application of sulfur dioxide in organic synthesis, and the chemistry of functionalized heterocycles, including their energetic applications.

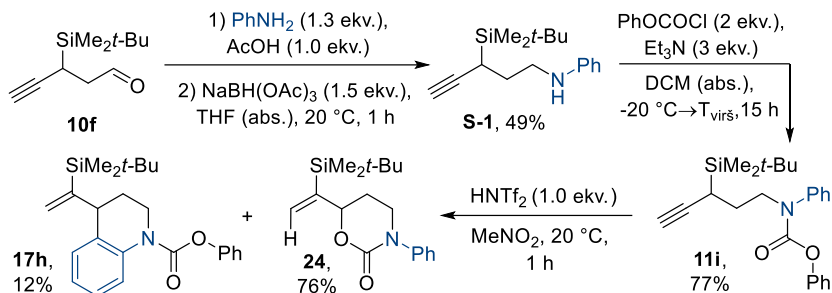
**Eksperimentālās procedūras 1,3-oksazinān-2-ona atvasinājuma un tā
izejvielu sintēzei**

**Experimental procedures for the synthesis of 1,3-oxazinan-2-one
derivative and that of its starting materials**

Kronkalne, R.; Turks, M.

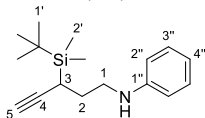
Nepublicētie rezultāti / Unpublished results

Eksperimentālās procedūras un raksturojumi izejvielām – S-1 un 11i



E1 shēma. Sintētiskais ceļš 1,3-oksazinān-2-ona **24** un hinolīna **17h** iegūšanai.

N-(3-(*tert*-Butildimetilsilil)pent-4-īn-1-il)anilīns (**S-1**)



Sintēzes procedūra:

Reakcija tika veikta sausus apstākļos zem argona. **NaBH(OAc)₃ pagatavošana:** Sausā 25 ml divkaklu apaļkolbā, kas aprīkota ar Teflona-pārklātu magnētisko maisītāju un atteces dzesinātāju, NaBH₄ (87 mg, 2.29 mmol, 1.5 ekv.) suspendē abs. THF (6 ml). Suspensijai istabas temperatūrā pievieno AcOH (0.39 ml, 6.88 mmol, 4.5 ekv.) un vāra attiecē 60 minūtes. *In situ* ģenerēto NaBH(OAc)₃ suspensiju THF atdzesē līdz istabas temperatūrai pirms izmantošanas tālākajā sintēzē. **Reducējošā aminēšana:** Sausā 25 ml divkaklu apaļkolbā, kas aprīkota ar Teflona pārklātu magnētisko maisītāju, 3-(*tert*-butildimetilsilil)pent-4-īnālu (**10f**) (300 mg, 1.53 mmol, 1.0 ekv.) šķīdina abs. THF (10 ml). Šķīdumam istabas temperatūrā (20 °C) pievieno PhNH₂ (0.18 ml, 1.99 mmol, 1.3 ekv.), AcOH (0.09 ml, 1.53 mmol, 1.0 ekv.) un maisa 60 min. Pēc tam pakāpeniski pievieno svaigi pagatavoto NaBH(OAc)₃ (1.5 ekv.) suspensiju abs. THF. Pēc 2.5 h maisīšanas istabas temperatūrā reakciju dzēš ar piesātinātu NaHCO₃ šķīdumu (10 ml). Ekstrakcija ar DCM (3 x 10 ml), kurai seko žāvēšana virs bezūdens Na₂SO₄, filtrēšana un ietvaicēšana pie pazemināta spiediena deva tehnisko produktu. Maisījumu attīra hromatogrāfiski uz silikagēla (20→30% DCM/Hex). Anilīnu **S-1** iegūst kā dzeltenu eļļu (274 mg, 74% tīrība, γ = 49%).

Savienojuma S-1 raksturojums:

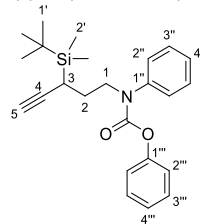
¹H KMR (500 MHz, CDCl₃): δ 7.17 (t, ³J_{H-H} = 7.7 Hz, 1H, H-C(3'')), 6.69 (t, ³J_{H-H} = 7.7 Hz, 1H, H-C(4'')), 6.64 (d, ³J_{H-H} = 7.7 Hz, 1H, H-C(2'')), 3.46

(ddd, ²J_{H-H} = 12.7 Hz, ³J_{H-H} = 7.9, 4.6 Hz, 1H, H_aC(1)), 3.27 (dt, ²J_{H-H} = 12.7 Hz, ³J_{H-H} = 7.6 Hz, 1H, H_bC(1)), 2.05 (d, ⁴J_{H-H} = 2.9 Hz, 1H, HC(5)), 1.87 (dt, ³J_{H-H} = 12.1 Hz, ^{3,4}J_{H-H} = 2.9 Hz, 1H, HC(3)), 1.84 – 1.76 (m, 1H, H_aC(2)), 1.74 – 1.62 (m, 1H, H_bC(2)), 0.95 (s, 9H, 3 x H₃C(1')), 0.09 (s, 3H, H₃C(2')), 0.02 (s, 3H, H₃C(2')).

¹³C KMR (126 MHz, CDCl₃): δ 148.4, 129.4, 117.4, 113.0, 86.7, 70.0, 43.7, 29.4, 27.3, 17.8, 14.6, -7.0, -7.3.

AIMS: C₁₇H₂₈NSi⁺ [M + H]⁺ aprēķināts 274.1986, atrasts 274.1977.

Fenil(3-(*tert*-butildimetilsilil)pent-4-īn-1-il)(fenil)karbamāts (**11i**)



Sintēzes procedūra:

Reakcija tika veikta sausus apstākļos zem argona. Sausā 25 ml divkaklu apaļkolbā, kas aprīkota ar Teflona pārklātu magnētisko maisītāju un atteces dzesinātāju, pievieno N-(3-(*tert*-butildimetilsilil)pent-4-īn-1-il)anilīnu (**S-1**) (115 mg, 0.42 mmol, 1.0 ekv.), abs. DCM (10 ml), Et₃N (0.18 ml, 1.26 mmol, 3.0 ekv.) un atdzesē līdz -20 °C temperatūrai NaCl / ledus (1:3) vannā. Tālāk atdzesētajam šķīdumam pievieno fenilhlorformātu (0.11 ml, 0.84 mmol, 2.0 ekv.) un maisa 15 minūtes. Pēc tam reakcijas maisījumu uzsilda eļļas vannā līdz viršanas temperatūrai un turpina vārīt 15 h. Reakcijas uzstrādei maisījumu atdzesē līdz istabas temperatūrai (20 °C), organisko daļu mazgā ar piesātinātu NH₄Cl šķīdumu, piesātinātu NaCl

šķīdumu, žāvē virs bezūdens Na₂SO₄, filtrē un iekoncentrē pie pazemināta spiediena. Maisījumu attīra hromatogrāfiski uz silikagēla (50→60% DCM/Hex). Karbamātu **11i** iegūst kā dzeltenu eļļu (174 mg, 73% tīrība, η = 77%).

Savienojuma **11i** raksturojums:

¹H KMR (500 MHz, CDCl₃): δ 7.40 (t, ³J_{H-H} = 7.7 Hz, 2H, H-C(3'')), 7.34 (d, ³J_{H-H} = 7.7 Hz, 2H, H-C(2'')), 7.34 – 7.27 (m, 3H, H-C(4''), 2'''/3'''), 7.17 (t, ³J_{H-H} = 7.1 Hz, 1H, H-C(4''')), 7.10 (br s, 2H, H-C(2'''/3''')), 4.19 – 3.78 (m, 2H, H₂C(1)), 1.97 (d, ⁴J_{H-H} = 2.5 Hz, 1H, HC(5)), 1.93 – 1.84 (m, 1H, H_aC(2)), 1.82 – 1.68 (m, 2H, HC(3), H_bC(2)), 0.93 (s, 9H, 3 × H₃C(1')), 0.07 (s, 3H, H₃C(2')), -0.01 (s, 3H, H₃C(2')).

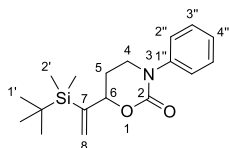
¹³C KMR (126 MHz, CDCl₃): δ 154.0, 151.5, 141.8, 129.3, 129.3, 127.3, 127.0, 125.4, 121.8, 86.1, 70.0, 51.1, 28.4, 27.2, 17.7, 14.5, -7.0, -7.3.

AIMS: C₂₄H₃₂NO₂Si⁺ [M + H]⁺ aprēķināts 394.2197, atrasts 394.2181.

Sintētiskā procedūra 6-(1-(*terc*-butildimetilsilil)vinil)-3-fenil-1,3-oksazinān-2-ona (**24**) un fenil-4-(1-(*terc*-butildimetilsilil)vinil)-3,4-dihidrohinalīn-1(2H)-karboksilāta (**17h**) iegūšanai

10 ml pudelītē, kas aprīkota ar Teflona pārklātu magnētisko maisītāju, istabas temperatūrā (20 °C) pievieno fenil(3-(*terc*-butildimetilsilil)pent-4-īn-1-il)(fenil)karbamātu (**11i**) (61 mg, 0.15 mmol, 1.0 equiv), MeNO₂ (2 ml), HNTf₂ šķīdumu MeNO₂ (0.07 ml, 0.43 M, 0.03 mmol, 20 mol%) un maisa 1 h. Reakciju dzēš, pievienojot Et₃N (3 pil.), un iekoncentrē pie pazemināta spiediena. Maisījumu attīra hromatogrāfiski uz silikagēla. Hinalīnu **17h** (eluents: 40→50% DCM/Hex) iegūst kā bezkrāsainu eļļu (7 mg, η = 12%), un 1,3-oksazinān-2-onu **24** (eluents: 0→5% EtOAc/DCM) iegūst kā baltu, cietu vielu (36 mg, η = 76%).

6-(1-(*terc*-Butildimetilsilil)vinil)-3-fenil-1,3-oksazinān-2-ons (**24**)



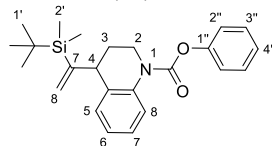
Savienojuma **24** raksturojums:

¹H KMR (500 MHz, CDCl₃): δ 7.39 (t, ³J_{H-H} = 7.8 Hz, 2H, H-C(3'')), 7.33 (d, ³J_{H-H} = 7.8 Hz, 2H, H-C(2'')), 7.26 (t, ³J_{H-H} = 7.8 Hz, 1H, H-C(4'')), 6.14 (s, 1H, H_aC(8)), 5.66 (s, 1H, H_bC(8)), 5.04 (br d, ³J_{H-H} = 9.3 Hz, 1H, HC(6)), 3.72 (td, ^{2,3}J_{H-H} = 11.3 Hz, ³J_{H-H} = 5.0 Hz, 1H, H_aC(4)), 3.64 (dt, ²J_{H-H} = 11.3 Hz, ³J_{H-H} = 5.0 Hz, 1H, H_bC(4)), 2.31 – 2.19 (m, 1H, H_aC(5)), 2.00 (dtd, ²J_{H-H} = 14.5 Hz, ³J_{H-H} = 9.3, 5.0 Hz, 1H, H_bC(5)), 0.93 (s, 9H, 3 × H₃C(1')), 0.16 (s, 3H, H₃C(2')), 0.14 (s, 3H, H₃C(2')).

¹³C KMR (126 MHz, CDCl₃): δ 153.1, 146.9, 143.1, 129.3, 128.4, 126.9, 126.0, 79.8, 47.7, 29.1, 26.9, 17.3, -4.9, -5.3.

AIMS: C₁₈H₂₈NO₂Si⁺ [M + H]⁺ aprēķināts 318.1884, atrasts 318.1875.

Fenil-4-(1-(*terc*-butildimetilsilil)vinil)-3,4-dihidrohinalīn-1(2H)-karboksilāts (**17h**)



Savienojuma **17h** raksturojums:

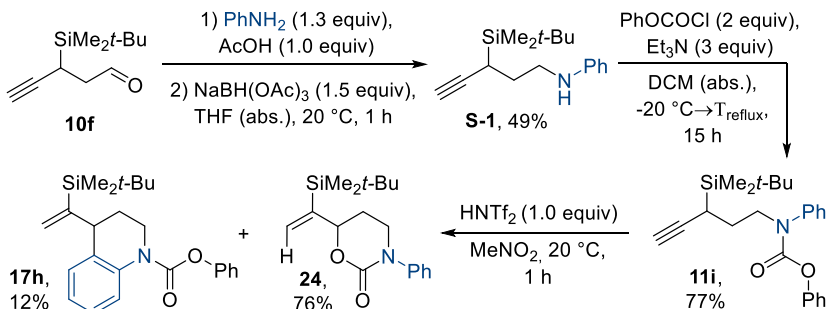
¹H KMR (500 MHz, CDCl₃): δ 7.87 – 7.72 (m, 1H, H-C(8)), 7.38 (t, ³J_{H-H} = 7.8 Hz, 2H, H-C(3'')), 7.25 – 7.13 (m, 4H, H-C(2'', 4'', 6)), 7.08 (d, ³J_{H-H} = 7.1 Hz, 1H, H-C(5)), 7.04 (t, ³J_{H-H} = 7.4 Hz, 1H, H-C(7)), 5.63 (d, ²J_{H-H} = 2.2 Hz, 1H, H_aC(8)), 5.47 (s, 1H, H_bC(8)), 3.98 – 3.82 (m, 2H, H₂C(2)), 3.78 (t, ³J_{H-H} = 6.3 Hz, 1H, HC(4)), 2.13 (tt, ^{2,3}J_{H-H} = 13.5 Hz, ³J_{H-H} = 6.3 Hz, 1H, H_aC(3)), 1.92 (dtd, ²J_{H-H} = 13.5 Hz, ³J_{H-H} = 6.3, 4.5 Hz, 1H, H_bC(3)), 0.97 (s, 9H, 3 × H₃C(1')), 0.12 (s, 3H, H₃C(2')), 0.11 (s, 3H, H₃C(2')).

¹³C KMR (126 MHz, CDCl₃): δ 153.4, 152.5, 151.3, 138.2, 133.0,¹ 129.9, 129.5, 129.3, 126.5, 125.6, 124.2, 123.9, 121.9, 43.8, 43.1, 29.9, 27.2, 17.6, -4.9, -5.1.

AIMS: C₂₄H₃₂NO₂Si⁺ [M + H]⁺ aprēķināts 394.2197, atrasts 394.2185.

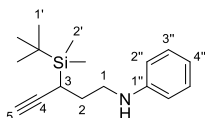
¹ Noteikts pēc HMBC spektra.

Synthesis procedures and characterization data for starting materials S-1 and 11i



Scheme E1. Synthetic route towards 1,3-oxazinan-2-one **24** and quinoline **17h**.

N-(3-(*tert*-Butyldimethylsilyl)pent-4-yn-1-yl)aniline (**S-1**)



Synthesis procedure:

The reaction was performed in dry conditions and under argon. **Preparation $\text{NaBH}(\text{OAc})_3$:** In a dry 25 ml two-neck round bottom flask, equipped with a Teflon-coated magnetic stirrer and a reflux condenser, NaBH_4 (87 mg, 2.29 mmol, 1.5 equiv) was suspended in abs. THF (6 ml). AcOH (0.39 ml, 6.88 mmol, 4.5 equiv) was added to the suspension at ambient temperature and refluxed for 60 minutes. The *in situ* generated $\text{NaBH}(\text{OAc})_3$ suspension in THF was left to cool to room temperature before further use. **Reductive amination:** In a dry 25 ml flask, equipped with a Teflon-coated magnetic stirrer, 3-(*tert*-butyldimethylsilyl)pent-4-ynal (**10f**) (300 mg, 1.53 mmol, 1.0 equiv) was dissolved in abs. THF (10 ml). PhNH_2 (0.18 ml, 1.99 mmol, 1.3 equiv) and AcOH (0.09 ml, 1.53 mmol, 1.0 equiv) were added to the solution at ambient temperature (20°C). After stirring the solution for 60 minutes, the freshly prepared $\text{NaBH}(\text{OAc})_3$ (1.5 equiv) in abs. THF was added dropwise via syringe. The reaction was stirred for 2.5 hours, before quenching with aq. NaHCO_3 (10 ml). Extraction with DCM (3 x 10 ml), drying over anhydrous Na_2SO_4 , filtering and concentrating under reduced pressure afforded the crude product. Purification by column chromatography (40 g silica gel, 20 $\rightarrow$ 30% DCM/Hex) afforded the aniline **S-1** (274 mg, 74% purity, $\gamma = 49\%$) as a yellow oil.

Characterization data for S-1:

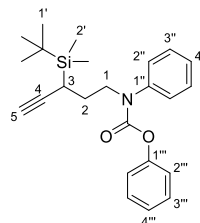
^1H NMR (500 MHz, CDCl_3): δ 7.17 (t, $^3J_{\text{H-H}} = 7.7$ Hz, 1H, H-C(3'')), 6.69 (t, $^3J_{\text{H-H}} = 7.7$ Hz, 1H, H-

C(4'')), 6.64 (d, $^3J_{\text{H-H}} = 7.7$ Hz, 1H, H-C(2'')), 3.46 (ddd, $^2J_{\text{H-H}} = 12.7$ Hz, $^3J_{\text{H-H}} = 7.9$, 4.6 Hz, 1H, $\text{H}_\text{a}\text{C}(1)$), 3.27 (dt, $^2J_{\text{H-H}} = 12.7$ Hz, $^3J_{\text{H-H}} = 7.6$ Hz, 1H, $\text{H}_\text{b}\text{C}(1)$), 2.05 (d, $^4J_{\text{H-H}} = 2.9$ Hz, 1H, HC(5)), 1.87 (dt, $^3J_{\text{H-H}} = 12.1$ Hz, $^3,^4J_{\text{H-H}} = 2.9$ Hz, 1H, HC(3)), 1.84 – 1.76 (m, 1H, $\text{H}_\text{a}\text{C}(2)$), 1.74 – 1.62 (m, 1H, $\text{H}_\text{b}\text{C}(2)$), 0.95 (s, 9H, $3 \times \text{H}_3\text{C}(1')$), 0.09 (s, 3H, $\text{H}_3\text{C}(2')$), 0.02 (s, 3H, $\text{H}_3\text{C}(2'')$).

^{13}C NMR (126 MHz, CDCl_3): δ 148.4, 129.4, 117.4, 113.0, 86.7, 70.0, 43.7, 29.4, 27.3, 17.8, 14.6, -7.0, -7.3.

HRMS: $\text{C}_{17}\text{H}_{28}\text{NSi}^+ [\text{M} + \text{H}]^+$ calc. 274.1986, found 274.1977.

Phenyl (3-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)(phenyl)carbamate (**11i**)



Synthesis procedure:

The reaction was performed in dry conditions and under argon. A 25 ml two-neck round bottom flask, equipped with a Teflon-coated magnetic stirrer and a reflux condenser, was charged with *N*-(3-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)aniline (**S-1**) (115 mg, 0.42 mmol, 1.0 equiv), abs. DCM (10 ml), Et_3N (0.18 ml, 1.26 mmol, 3.0 equiv) and cooled to -20°C in a NaCl / ice (1:3) bath. Next, phenyl chloroformate (0.11 ml, 0.84 mmol, 2.0 equiv) was added to the cooled solution. After stirring for 15 minutes, the solution was heated to reflux temperature in an oil bath and boiled for 15 h. For work-up, the reaction was cooled to ambient temperature (20°C), the organic layer was washed with saturated aqueous NH_4Cl

and saturated aqueous NaCl, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by column chromatography (50→60% DCM/Hex) afforded the carbamate **11i** (174 mg, 73% purity, η = 77%) as a yellow oil.

Characterization data for **11i**:

¹H NMR (500 MHz, CDCl₃): δ 7.40 (t, ³*J*_{H-H} = 7.7 Hz, 2H, H-C(3'')), 7.34 (d, ³*J*_{H-H} = 7.7 Hz, 2H, H-C(2'')), 7.34 – 7.27 (m, 3H, H-C(4''), 2'''/3'''), 7.17 (t, ³*J*_{H-H} = 7.1 Hz, 1H, H-C(4''')), 7.10 (br s, 2H, H-C(2'''/3''')), 4.19 – 3.78 (m, 2H, H₂C(1)), 1.97 (d, ⁴*J*_{H-H} = 2.5 Hz, 1H, HC(5)), 1.93 – 1.84 (m, 1H, H₂C(2)), 1.82 – 1.68 (m, 2H, HC(3), H₂C(2)), 0.93 (s, 9H, 3 × H₃C(1')), 0.07 (s, 3H, H₃C(2')), -0.01 (s, 3H, H₃C(2')).

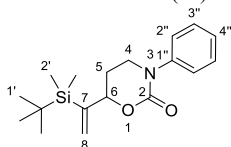
¹³C NMR (126 MHz, CDCl₃): δ 154.0, 151.5, 141.8, 129.3, 129.3, 127.3, 127.0, 125.4, 121.8, 86.1, 70.0, 51.1, 28.4, 27.2, 17.7, 14.5, -7.0, -7.3.

HRMS: C₂₄H₃₂NO₂Si⁺ [M + H]⁺ calc. 394.2197, found 394.2181.

Synthesis procedure for 6-(1-(*tert*-butyldimethylsilyl)vinyl)-3-phenyl-1,3-oxazinan-2-one (**24**) and phenyl 4-(1-(*tert*-butyldimethylsilyl)vinyl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (**17h**)

A 10 ml vial, equipped with a Teflon-coated magnetic stirrer, was charged with phenyl (3-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)(phenyl)carbamate (**11i**) (61 mg, 0.15 mmol, 1.0 equiv) and MeNO₂ (2 ml). A solution of HNTf₂ in MeNO₂ (0.07 ml, 0.43 M, 0.03 mmol, 20 mol%) was added to the carbamate **11i** solution at ambient temperature (20 °C). After stirring for 1 hour, the reaction was quenched by addition of Et₃N (3 drops). The resulting solution was concentrated under reduced pressure and purified by column chromatography to afford quinoline **17h** (eluent: 40→50% DCM/Hex) as a colorless oil (7 mg, η = 12%) and 1,3-oxazinan-2-one **24** (eluent: 0→5% EtOAc/DCM) as a white solid (36 mg, η = 76%).

6-(1-(*tert*-Butyldimethylsilyl)vinyl)-3-phenyl-1,3-oxazinan-2-one (**24**)



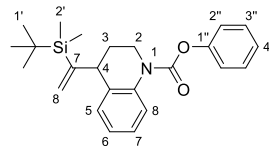
Characterization data for **24**:

¹H NMR (500 MHz, CDCl₃): δ 7.39 (t, ³*J*_{H-H} = 7.8 Hz, 2H, H-C(3'')), 7.33 (d, ³*J*_{H-H} = 7.8 Hz, 2H, H-C(2'')), 7.26 (t, ³*J*_{H-H} = 7.8 Hz, 1H, H-C(4'')), 6.14 (s, 1H, H₂C(8)), 5.66 (s, 1H, H₂C(8)), 5.04 (br d, ³*J*_{H-H} = 9.3 Hz, 1H, HC(6)), 3.72 (td, ^{2,3}*J*_{H-H} = 11.3 Hz, ³*J*_{H-H} = 5.0 Hz, 1H, H₂C(4)), 3.64 (dt, ²*J*_{H-H} = 11.3 Hz, ³*J*_{H-H} = 5.0 Hz, 1H, H₂C(4)), 2.31 – 2.19 (m, 1H, H₂C(5)), 2.00 (dtd, ²*J*_{H-H} = 14.5 Hz, ³*J*_{H-H} = 9.3, 5.0 Hz, 1H, H₂C(5)), 0.93 (s, 9H, 3 × H₃C(1')), 0.16 (s, 3H, H₃C(2')), 0.14 (s, 3H, H₃C(2')).

¹³C NMR (126 MHz, CDCl₃): δ 153.1, 146.9, 143.1, 129.3, 128.4, 126.9, 126.0, 79.8, 47.7, 29.1, 26.9, 17.3, -4.9, -5.3.

HRMS: C₁₈H₂₈NO₂Si⁺ [M + H]⁺ calc. 318.1884, found 318.1875.

Phenyl 4-(1-(*tert*-butyldimethylsilyl)vinyl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (**17h**)



Characterization data for **17h**:

¹H NMR (500 MHz, CDCl₃): δ 7.87 – 7.72 (m, 1H, H-C(8)), 7.38 (t, ³*J*_{H-H} = 7.8 Hz, 2H, H-C(3'')), 7.25 – 7.13 (m, 4H, H-C(2'', 4'', 6)), 7.08 (d, ³*J*_{H-H} = 7.1 Hz, 1H, H-C(5)), 7.04 (t, ³*J*_{H-H} = 7.4 Hz, 1H, H-C(7)), 5.63 (d, ²*J*_{H-H} = 2.2 Hz, 1H, H₂C(8)), 5.47 (s, 1H, H₂C(8)), 3.98 – 3.82 (m, 2H, H₂C(2)), 3.78 (t, ³*J*_{H-H} = 6.3 Hz, 1H, HC(4)), 2.13 (tt, ^{2,3}*J*_{H-H} = 13.5 Hz, ³*J*_{H-H} = 6.3 Hz, 1H, H₂C(3)), 1.92 (dtd, ²*J*_{H-H} = 13.5 Hz, ³*J*_{H-H} = 6.3, 4.5 Hz, 1H, H₂C(3)), 0.97 (s, 9H, 3 × H₃C(1')), 0.12 (s, 3H, H₃C(2')), 0.11 (s, 3H, H₃C(2')).

¹³C NMR (126 MHz, CDCl₃): δ 153.4, 152.5, 151.3, 138.2, 133.0, 129.9, 129.5, 129.3, 126.5, 125.6, 124.2, 123.9, 121.9, 43.8, 43.1, 29.9, 27.2, 17.6, -4.9, -5.1.

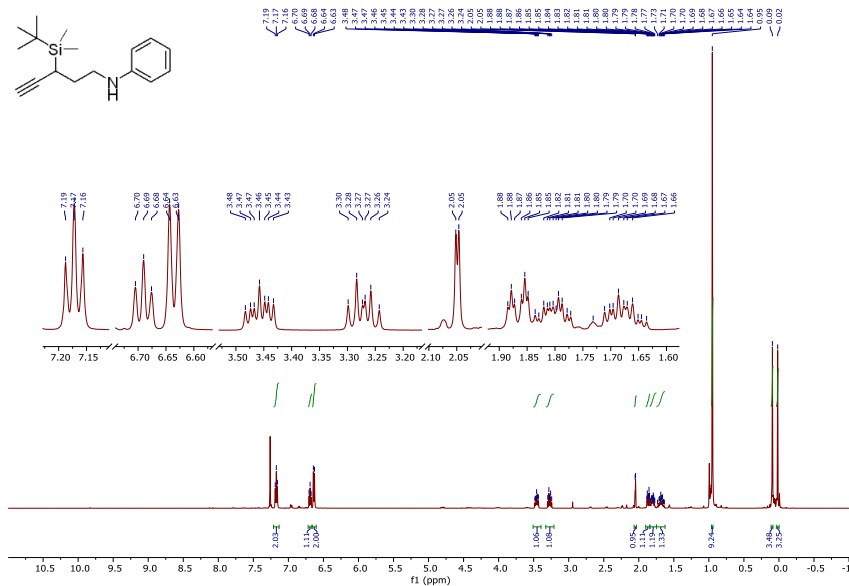
HRMS: C₂₄H₃₂NO₂Si⁺ [M + H]⁺ calc. 394.2197, found 394.2185.

² Determined by HMBC spectra.

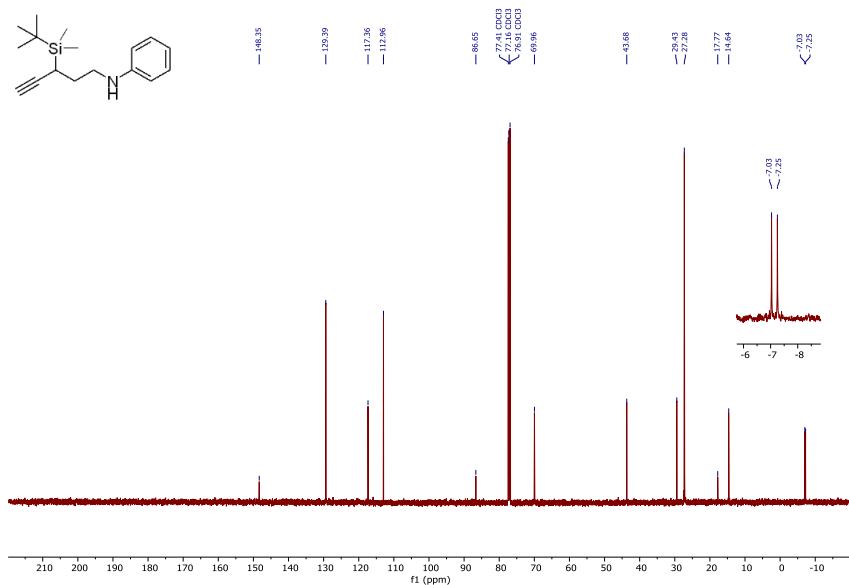
¹H un ¹³C KMR spektri / ¹H and ¹³C NMR spectra

N-(3-(*tert*-Butyldimetilsilil)pent-4-yn-1-yl)anilīns / *N*-(3-(*tert*-Butyldimetilsilil)pent-4-yn-1-yl)aniline (**S-1**)

¹H-KMR (500 MHz, CDCl₃) / ¹H-NMR (500 MHz, CDCl₃)

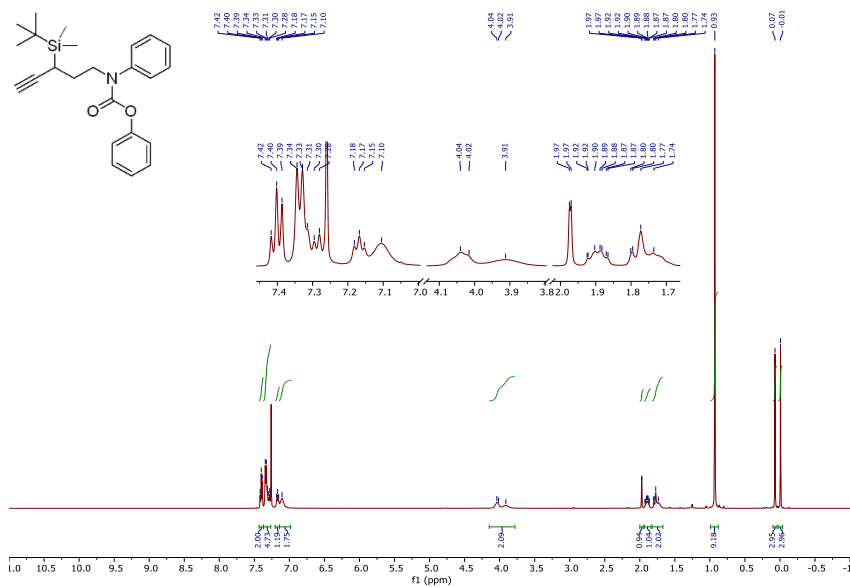


¹³C {¹H} KMR (126 MHz, CDCl₃) / ¹³C {¹H} NMR (126 MHz, CDCl₃)

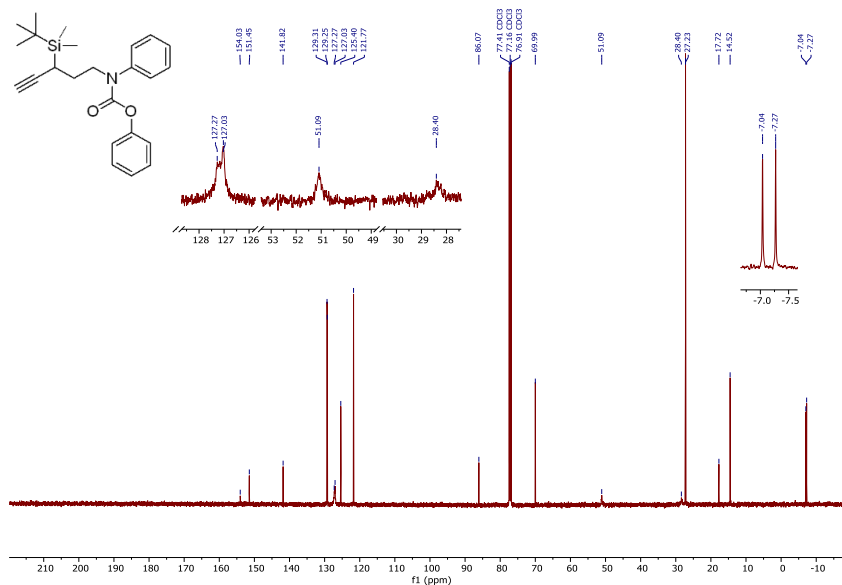


Fenil(3-(*tert*-butildimetilsilil)pent-4-īn-1-il)(fenil)karbamāts / Phenyl (3-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)(phenyl)carbamate (**11i**)

^1H -KMR (500 MHz, CDCl_3) / ^1H -NMR (500 MHz, CDCl_3)

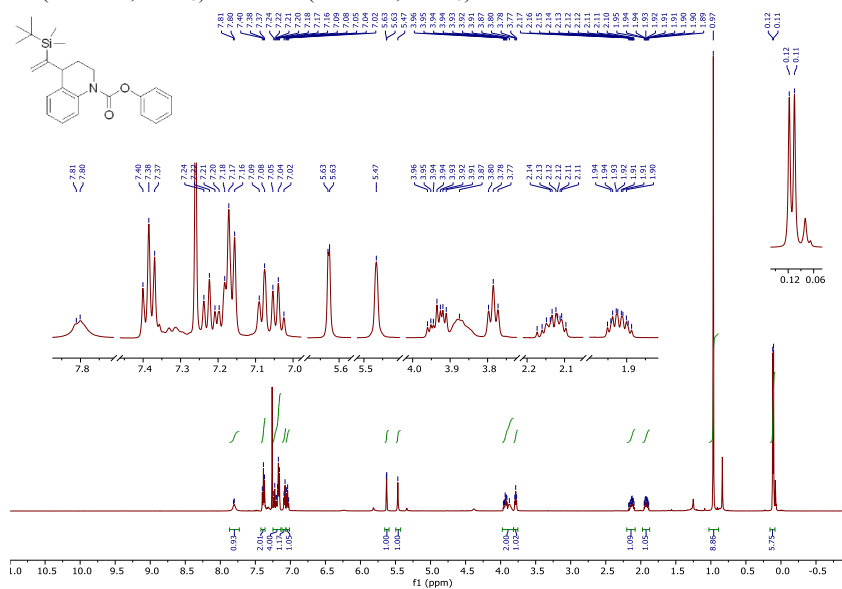


^{13}C $\{^1\text{H}\}$ KMR (126 MHz, CDCl_3) / ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

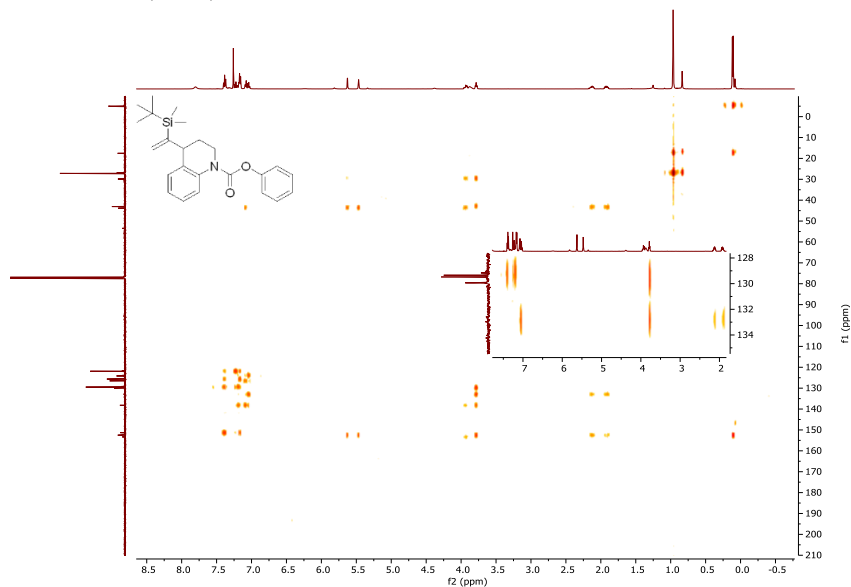


Phenyl 4-(1-(*tert*-butyldimethylsilyl)vinyl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (**17h**)

^1H -KMR (500 MHz, CDCl_3) / ^1H -NMR (500 MHz, CDCl_3)

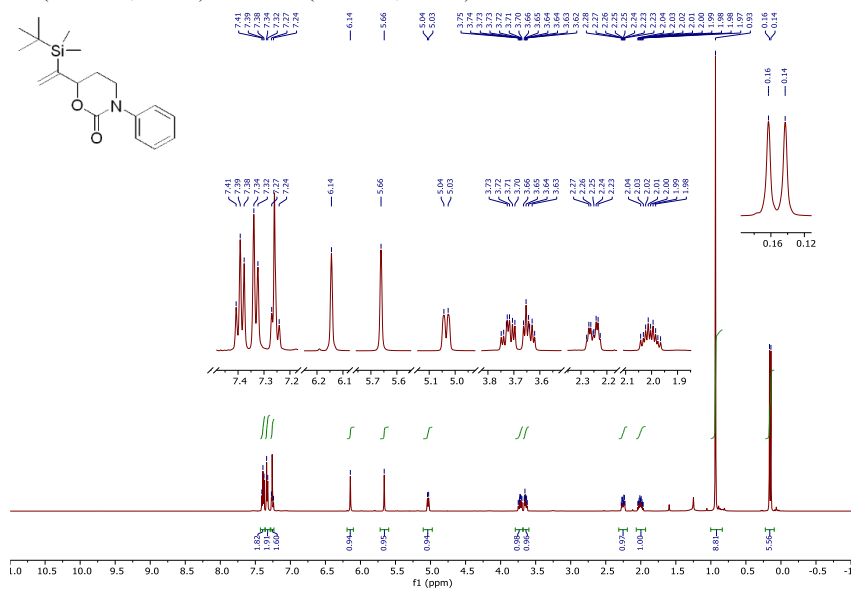


^1H - ^{13}C -HMBC NMR (CDCl_3)

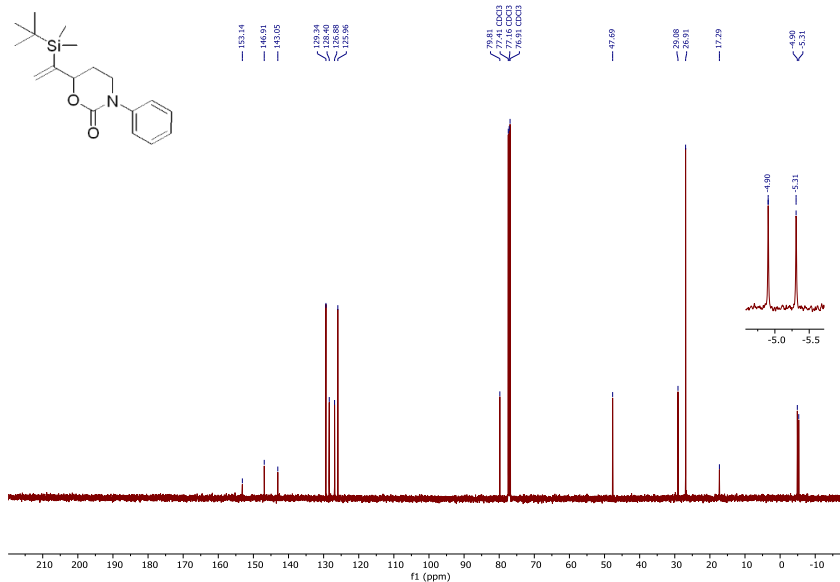


6-(1-(*tert*-Butyldimethylsilyl)vinyl)-3-fenil-1,3-oksazinān-2-ons / 6-(1-(*tert*-Butyldimethylsilyl)vinyl)-3-phenyl-1,3-oxazinan-2-one (**24**)

^1H -KMR (500 MHz, CDCl_3) / ^1H -NMR (500 MHz, CDCl_3)

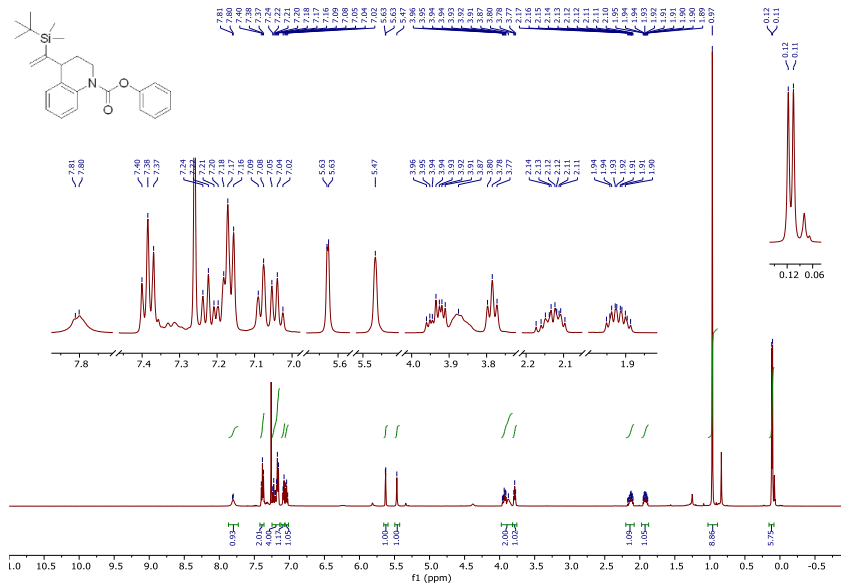


$^{13}\text{C} \{^1\text{H}\}$ KMR (126 MHz, CDCl_3) / $^{13}\text{C} \{^1\text{H}\}$ NMR (126 MHz, CDCl_3)

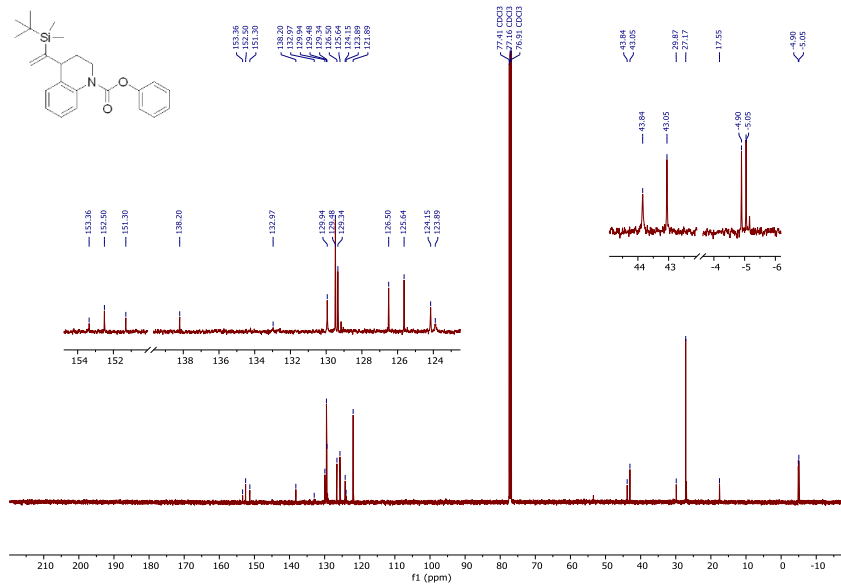


Phenyl 4-(1-(*tert*-butyldimethylsilyl)vinyl)-3,4-dihydroquinoline-1(2*H*)-carboxylate (17h)

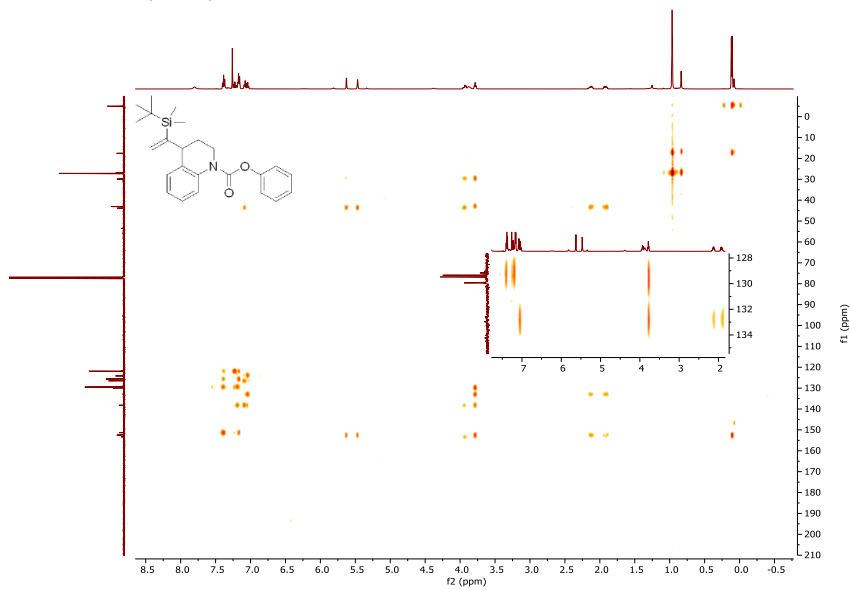
^1H -KMR (500 MHz, CDCl_3) / ^1H -NMR (500 MHz, CDCl_3)



$^{13}\text{C} \{^1\text{H}\}$ KMR (126 MHz, CDCl_3) / $^{13}\text{C} \{^1\text{H}\}$ NMR (126 MHz, CDCl_3)



^1H - ^{13}C -HMBC NMR (CDCl_3)



**1,2-Sililnobīdes-Ritera reakcijas kaskāde dihidroizohinolīnu un alilamīna
atvasinājumu sintēzei**

**1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of
Dihydroisoquinolines and Allylamine Derivatives**

Turka, S.; Kroņkalne, R.; Roģaļevs, R.; Puriņš, M.; Mishnev, A.; Turks, M.

Nepublicētais manuskripts / Unpublished manuscript

1,2-Silyl Shift – Ritter Reaction Cascade for the Synthesis of Dihydroisoquinolines and Allylamine Derivatives

Sandra Turka^[a], Rasma Kronkalne^[a], Raimonds Rogaļevs^[a], Mikus Puriņš^[a], Anatoly Mishnev^[b] and Māris Turks^{*[a]}

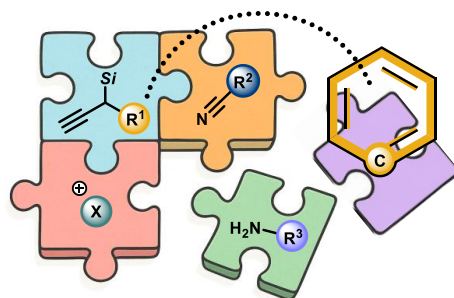
[a] S. Turka, R. Kronkalne, R. Rogaļevs, M. Puriņš, M. Turks
Institute of Chemistry and Chemical Technology
Riga Technical University
P. Valdena str. 3, LV-1048, Riga, Latvia
E-mail: maris.turks@rtu.lv

[b] A. Mishnev
Latvian Institute of Organic Synthesis
Aizkraukles str. 21, LV-1006, Riga, Latvia

Supporting information for this article is given via a link at the end of the document.

Abstract: Herein, we report an unprecedented cascade Ritter-type reaction featuring a 1,3-difunctionalization strategy for the synthesis of allylamine-containing products. This approach employs propargylsilanes as stereodefined allyl cation precursors, enabling access to difunctionalized Ritter-type products with fixed (*E*)- or (*Z*)-geometry of the newly formed C=C bond. Trapping of the key nitrilium intermediate with a range of external nucleophiles (H₂O or R¹R²NH) affords allyl amide and amidine derivatives through a one-step, four-bond-forming process. Electron-rich aryl substituents on the silanes promote intramolecular nucleophilic capture, leading to the formation of dihydroisoquinoline scaffolds. Overall, this study highlights the versatility of propargylsilanes in Ritter-type chemistry and provides efficient access to

structurally diverse acyclic and heterocyclic frameworks.



Introduction

The Ritter reaction is a classic synthetic route towards amides, which has found application for the synthesis of numerous amide functionality bearing bioactive compounds^[1–7] and functional materials.^[8–9] Modifications of this reaction, substituting alkenes and alcohols as primary carbocation sources with other functionalities, are referred to as the Ritter-type reaction.^[1]

The key mechanistic steps of the Ritter-type reaction involve carbocation (R₃C⁺) generation, followed by interception with a nitrile (R'¹CN) to form a nitrilium ion intermediate (R₃C-N⁺≡C-R'). This intermediate is subsequently trapped by an external or internal nucleophile to afford an array of products, including amides,^[10–12] amidines,^[13–14] imidates^[15–16]

thioimides,^[16–17] imides,^[18] ketimines^{[14],[19]} or heterocyclic structures.^[20–22]

More complex molecular architectures are accessible via tandem Ritter-type reactions, among which difunctionalization of unsaturated systems remains comparatively underexplored.^[1] Most reported examples of olefin difunctionalization rely on radical-mediated pathways.^[23–29] In contrast, difunctionalizations proceeding exclusively through cationic mechanisms are much less common. In these reactions, the key intermediate is typically a halonium^[30–31] or sulfonium ion.^[32] To date, olefin difunctionalization via halonium-ion intermediates in Ritter-type reaction context has been demonstrated only for a limited scope of substrates, including allyl ethers,^[33] allyl amides,^[31] and vinyl silanes.^[34–35] Unactivated alkyne difunctionalizations in Ritter-type reaction context are particularly rare.^[36]

RESEARCH ARTICLE

Due to the scarcity of examples discussing cationic Ritter-type difunctionalizations, especially those involving alkynes,^[36] we wanted to look further into acyclic π -systems, which could act as possible nucleophilic partners for such transformations. Allylsilanes have been reported even less frequently than vinyl silanes in the context of Ritter-type reactions. In one notable example, they were employed as nucleophilic partners in a Prins–Ritter-type cyclization cascade.^[37] To the best of our knowledge, there are no reports on the use of allenyl- or propargylsilanes in Ritter-type difunctionalization reactions.

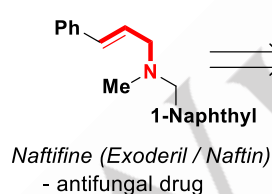
Propargylsilanes, however, are well established as effective precursors to β -silicon-stabilized allyl cations.^[38] Upon electrophile-induced 1,2-silyl migration, propargylsilanes are transformed into allyl cations, thereby generating highly reactive formal 1,3-dipoles. Subsequent nucleophilic trapping furnishes 1,3-difunctionalized products,^[39–41] a transformation that is considerably less common in organic synthesis than its 1,2-counterpart, which predominates in alkene- and alkyne-based tandem Ritter-type difunctionalizations.^[1] This process is enabled by the ability of silicon to stabilize positive charge at the β -position, either through hyperconjugation with the C–Si σ -bond (vertical stabilization) and / or via formation of a silylium ion intermediate (non-vertical stabilization), collectively referred to as the β -silicon effect.^[42]

Existing literature precedents for carbocation rearrangement in tandem Ritter-type reaction context

predominantly consist of Wagner–Meerwein rearrangements (1,2-shift of an adjacent skeletal C–C bond)^[43–47] and the Prins–Ritter reaction.^[48] In rare examples, a combination of the two latter is observed (i.e. the Prins–Wagner–Ritter reaction),^[49] as well as allylic rearrangements^[50] and other.^[1] We envisioned that by combining the unique 1,3-dipolar reactivity characteristic to propargyl silanes with conditions suitable for a Ritter-type reaction, we could achieve a so far unprecedented cascade Ritter-type reaction, featuring 1,3-difunctionalization for the synthesis of allyl amide functionality containing products.

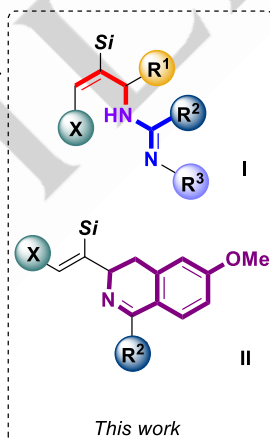
The cascade 1,2-silyl shift – Ritter reaction strategy enables the synthesis of compounds featuring the allylamine functionality – a commonly found motif in antifungal compounds (Scheme 1).^[51–52] Likewise, another pharmacologically significant structure – the amidine group – can be accessed by introducing external *N*-nucleophiles to capture the intermediate nitrilium ion species.^[53] We were also interested in exploring the Bischler–Napieralski-type modifications that feature ring closure by an internal C-nucleophile attack as observed with electron-rich arenes.^[54–55] This enables the synthesis of dihydroisoquinoline scaffolds, which mimic a series of natural alkaloids^[56–57] and bioactive molecules.^[58–61] Dihydroisoquinolines also serve as synthetic precursors to chiral bioactive tetrahydroisoquinolines (THIQs),^[62–64] further illustrating their significance in pharmacology.

Allylamine functionality

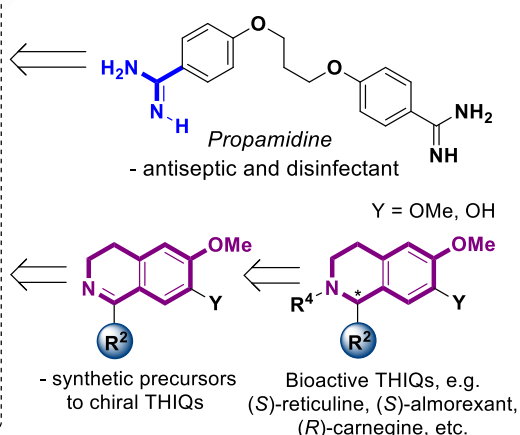


Dihydroisoquinoline functionality

- pharmacologically relevant scaffolds



Amidine functionality



Scheme 1. Introduction to allylamine, amidine and dihydroisoquinoline prevalence in biologically active products.

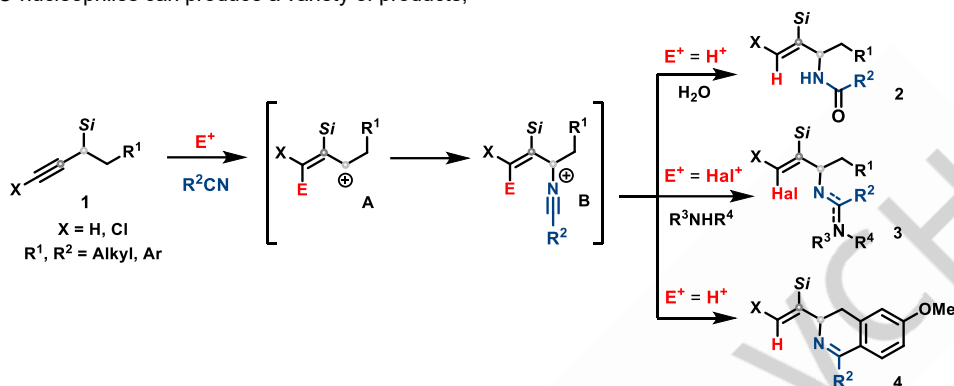
For the cascade 1,2-silyl shift – Ritter reaction strategy we propose a reaction pathway in which the propargyl silane becomes activated through attack by

an electrophile, such as a Brønsted acid or a halogen source. This leads to the formation of a vinyl cation intermediate, which then rearranges into a more stable

RESEARCH ARTICLE

allyl cation species **A**, as commonly seen in related systems.^{[39-42],[65]} The nitrile then serves as the primary nucleophile, attacking to generate the nitrilium ion intermediate **B**. Finally, quenching with secondary *N*-, O- or C-nucleophiles can produce a variety of products,

including amides **2**, amidines **3** and dihydroisoquinolines **4** (Scheme 2).



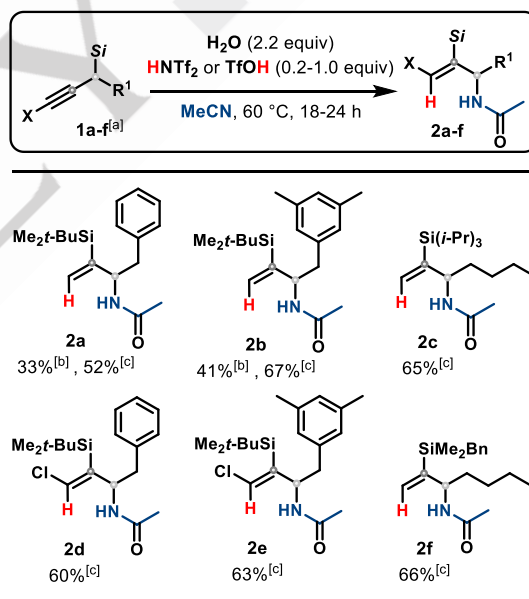
Scheme 2. Propargyl silane application in the Ritter-type reaction as allyl-cation source.

Results and Discussion

Allylamides

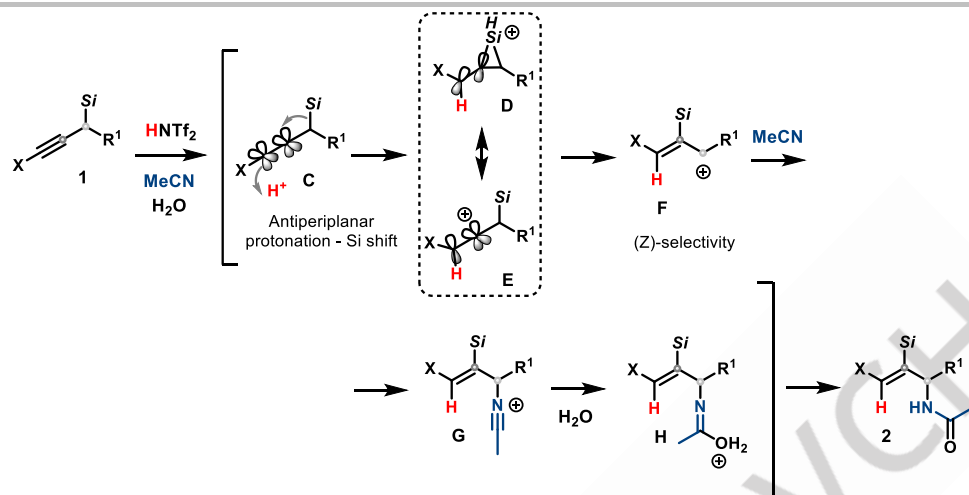
Before proceeding to the synthesis of more complicated scaffolds, namely amidines **3** and dihydroisoquinolines **4**, we tested the reactivity of propargylsilanes **1** under the classical Ritter reaction conditions, leading to amides (Scheme 3). We compared two sets of conditions for the Brønsted acid-promoted amide **2a-f** synthesis: 1) TsOH (20 mol%), H₂O (2.2 equiv), MeCN, 60 °C; and 2) HNTf₂ (1.0 equiv), H₂O (2.2 equiv), MeCN, 60 °C. The latter conditions gave significantly higher amide **2a-f** yields (52-67%). Heating at 60 °C was also preferential to performing the reaction at room temperature, as the reaction proceeded rather slowly (18 - 24 h). Interestingly, no allylamide **2** products were observed when using NBS as electrophile source (conditions: silane **1a**, **1b** or **1g**, 1.2 equiv NBS, 2.2 equiv H₂O, MeCN, 60 °C, 3h).

Aryl silanes **1a** and **1b**, when subjected to the Brønsted acid-catalyzed Ritter reaction, afforded allylamides **2a** and **2b**, respectively. In these cases, no intramolecular cyclization occurred (see "Dihydroisoquinoline synthesis"), even under anhydrous conditions. Aliphatic chain-containing silanes reacted similarly well to afford Ritter amides **2c** (65%) and **2f** (66%). Terminally halogenated silanes **1d** and **1e** gave a mixture of C=C bond isomers (*Z/E* = 9:1 in the crude mixture), which were separated by column chromatography to afford the pure (*Z*)-isomers **2d** and **2e**.



[a] List of silanes **1**: **1a** (X = H, R¹ = Bn, Si = *t*-BuMe₂Si), **1b** (X = H, R¹ = CH₂(3,5-(CH₃)₂-C₆H₃), Si = *t*-BuMe₂Si), **1c** (R¹ = C₄H₉, Si = *i*-Pr₃Si), **1d** (X = Cl, R¹ = Bn, Si = *t*-BuMe₂Si), **1e** (X = Cl, R¹ = CH₂(3,5-(CH₃)₂-C₆H₃), Si = *t*-BuMe₂Si), **1f** (R¹ = C₄H₉, Si = BnMe₂Si). [b] 0.2 equiv TfOH as H⁺ source. [c] 1.0 equiv HNTf₂ as H⁺ source.

Scheme 3. Reaction scope for allylamides **2a-f**.

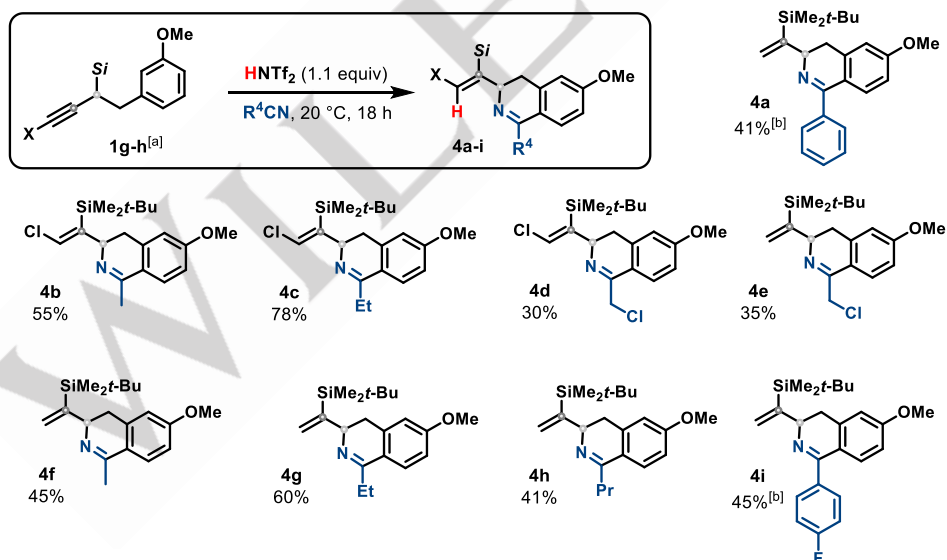


Scheme 4. Mechanistic rationale for the formation of (Z)-olefin geometry in allylamides **2**.

Allylamide **2d-e** (Z)-isomer formation can be explained by alkyne **1** protonation in an antiperiplanar position to the silyl group, and simultaneous silyl migration in a concerted process without a pronounced vinyl cation intermediate **E** to afford the most stable allyl cation **F** (Scheme 4).

Dihydroisoquinolines

In the case of methoxysubstituted arylsilane **1g**, the aromatic system was nucleophilic enough to trap the intermediate nitrilium ion **B** in intramolecular fashion, resulting in dihydroisoquinolines **4** (Scheme 5).



[a] List of silanes **1**: **1g** ($\text{X} = \text{H}$), **1h** ($\text{X} = \text{Cl}$). [b] 1.2 equiv of nitrile, DCM as solvent.

Scheme 5. Reaction scope for dihydroisoquinolines **4**.

RESEARCH ARTICLE

The reaction towards dihydroisoquinolines **4a-i** proceeded well at room temperature (20 °C) (scheme 5). Generally higher yields were obtained by using terminally halogenated substrates **1h** (up to 78%). Exclusive (*Z*)-geometry formation for the resulting C=C bond in dihydroisoquinolines **4b-d** was observed.

Nitriles containing alkyl chains of various lengths (C₁-C₃) were applicable for dihydroisoquinoline **4** synthesis. Terminally chlorinated nitriles also gave the desired dihydroisoquinolines **4d-e**, albeit in more modest yields (30-35%). The use of benzonitrile derivatives as reaction solvents was problematic, as they are either high-boiling liquids^[66] or solids.^[67] The application of solid nitriles in the Ritter reaction is generally rare, as most literature methods rely on the use of nitrile as solvent.^[1] To overcome this challenge, we performed the Ritter-type reaction under slightly modified conditions: DCM as solvent and nitrile (1.2 equiv) as reactant. This allowed us to obtain dihydroisoquinolines **4a** and **4i** from benzonitrile and 4-fluorobenzonitrile, respectively, affording yields up to 45%.

Amidine synthesis

Having confirmed the utility of propargyl silanes as allyl cation precursors under the classical Ritter (amidation) and Bischler-Napieralski-type reaction (dihydroisoquinoline synthesis) conditions, we proceeded to more complex synthetic targets – amidines **3**. For this we subjected silane **1c** to Brønsted acid-promoted conditions, such as TfOH (H⁺ source) to induce the transformation to amidines **3** (conditions: 1.2 equiv TfOH, 2.0 equiv TsNH₂, MeCN, -45 °C), but the only obtained product was (*E*)-hepta-1,3-dien-2-yltriisopropylsilane^[65] (30% by NMR). No reaction was observed with HNTf₂ (conditions: silane **1c**, 1.2 equiv HNTf₂, 2.0 equiv TsNH₂, MeCN, -45 °C). To our delight, when NBS (1.2 equiv) was used as an electrophilic Br⁺ source, TsNH₂ as a secondary nucleophile and MeCN as both reactant and a solvent, the desired amidine product **3a** was formed at room temperature with 56% NMR yield (Table 1, entry 1).

Further optimization of the reaction conditions demonstrated that sub-zero temperatures were more favourable. The highest yields for amidine **3a** were obtained when performing the reaction in a liquid N₂ / acetonitrile cooling bath (-45 °C). This allowed us to increase the product **3a** yield to 75% by NMR (Table 1, entry 12). The optimal starting material **1c** concentration in the reaction mixture was found to be 0.10 mmol/ml. Using TsNH₂ in slight excess (2 equiv) also benefited the reaction (Table 1, entry 2-3). Acetonitrile could be

used either as solvent or in reactant quantities (2.0 equiv), while other solvents served as reaction media (DCM, hexanes, toluene). The product **3a** yield in these cases was considerably reduced, e.g. DCM as solvent with the addition of 2 equiv of MeCN afforded amidine **3a** in 40% NMR yield (Table 1, entry 8). Using the nitrile in reactant quantities can be useful in cases where the nitrile is a solid or possesses a high boiling point, making it difficult to remove from the reaction mixture by standard laboratory techniques, as this was demonstrated in dihydroisoquinoline **4a** / **4i** synthesis. Although various other solvent systems could be used to attain amidine **3a**, such as MeCN / HFIP (Table 1, entry 6) or MeCN saturated with SO₂ (Table 1, entry 7), we found that pure acetonitrile gave the highest product **3a** yields.

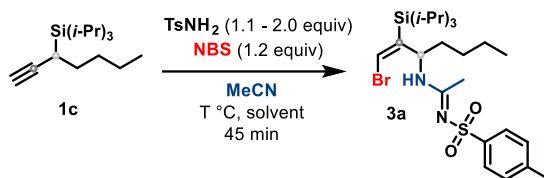
With our optimized conditions (T = -45 °C, RCN as solvent, c = 0.1 M, 2 equiv TsNH₂) we proceeded to explore the reaction scope (Scheme 6). First, we considered alternative electrophile sources to achieve amidine formation. A series of *N*-halogenated succinimides (NBS, NCS, NIS,) promoted the proposed transformation, introducing various halides (Br, Cl, I) to the resulting double bond. In the case of NCS (Cl⁺ source) longer reaction times were required as chlorine is more electronegative and thus less reactive in electrophilic addition reactions. The iodinated product **3b**, obtained in the reaction with NIS (I⁺ source), displayed poor stability at room temperature, as indicated by the formation of I₂. As an alternative to succinimide-based halogen electrophile sources we also tested TsNBr₂, which afforded the desired amidine product **3a**, but in a slightly reduced yield (55% by NMR) than previously with NBS (73% isolated). Overall, bromination afforded the highest results, therefore we continued exploring the rest of the scope with NBS as Br⁺ electrophile source.

We compared aliphatic chain-containing propargyl silanes **1c** (Si = (*i*-Pr)₃Si) / **1f** (Si = BnMe₂Si) / **1i** (Si = *t*-BuMe₂Si) in terms of reactivity depending on the installed silyl group. Among the explored silyl groups, (*i*-Pr)₃Si provided the highest amidine **3** yields (Scheme 6). The BnMe₂Si group, however, is more synthetically useful – it is directly employable in cross coupling reactions.^[68] Aliphatic chain-containing silanes **1c**, **1f**, **1i** and **1k** performed significantly better than silanes derived from arenes **1j** (short alkyl chain > long alkyl chain > aromatic). We hypothesized that additional stabilization of the intermediate carbocation by an adjacent aryl group could slow down addition of the nitrile, which is indirectly confirmed by prolonged reaction times (e.g. for alkyl silane **1c**, the reaction time was 45 minutes, but for aryl silane **1j** – 1.5 hours). We also explored functional group tolerance for this reaction. Substrates which were terminally functionalized with an aryl ether **1l**, azide **1m**, mesylate **1o** and even a free

RESEARCH ARTICLE

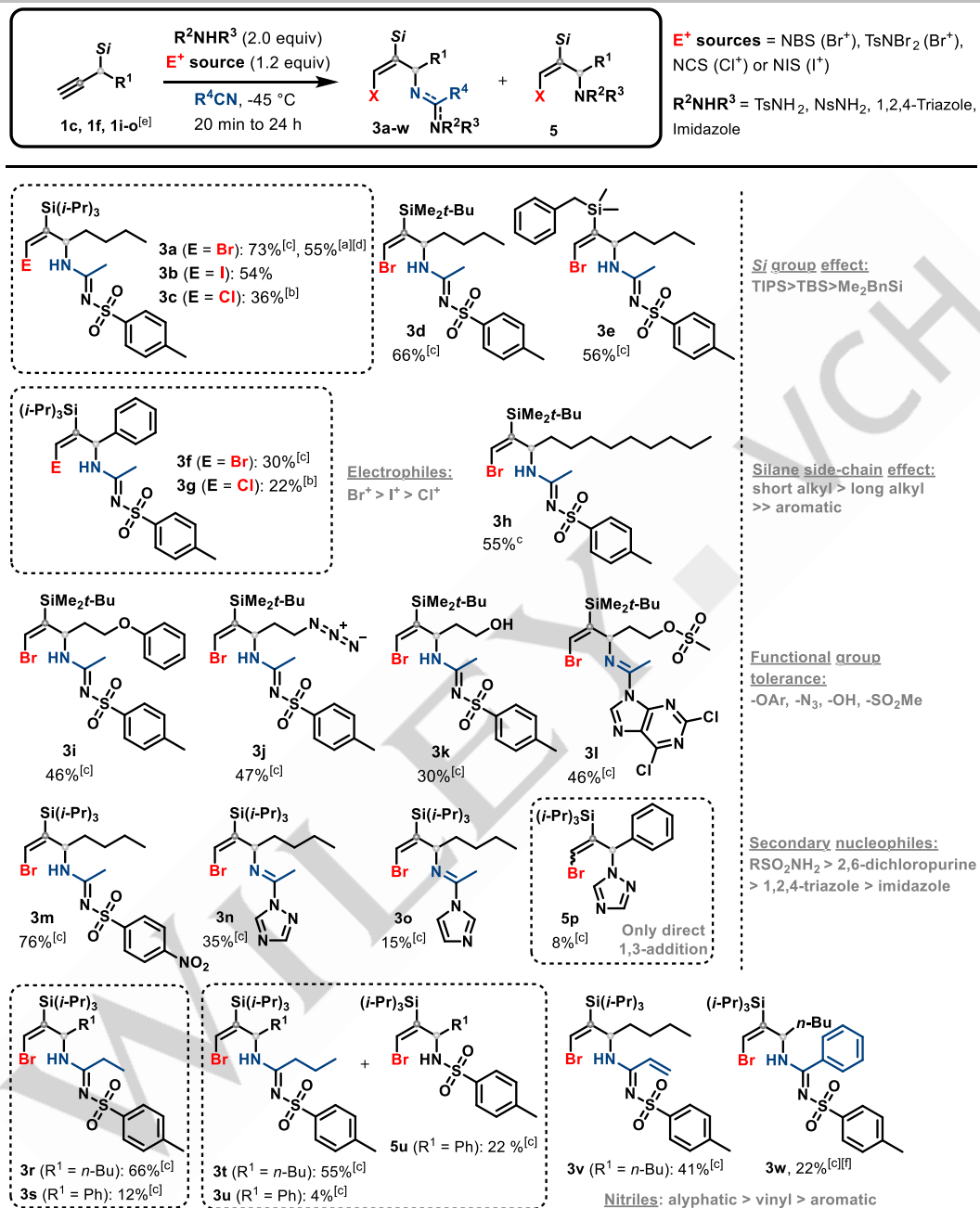
alcohol group **1n** afforded the desired amidine product **3** with 30-47% yields.

Table 1. Optimization of reaction parameters for the synthesis of amidine **3a**.



entry	T (°C)	Solvent	Additives	TsNH_2 (equiv)	Starting material 1c concentration (mmol / ml)	NMR yield for 3a (%) ^[a]
1	20	MeCN	-	1.1	0.10	56
2	0	MeCN	-	1.1	0.10	61
3	0	MeCN	-	2.0	0.10	66 (62 ^[c])
4	0	MeCN (4 Å MS)	-	2.0	0.10	64
5	0	MeCN (4 Å MS)	-	2.0	0.10	55 ^[b]
6	0	MeCN / HFIP (5:1)	-	2.0	0.10	54
7	0	MeCN (saturated with SO_2)	-	2.0	0.10	45
8	0	DCM	MeCN (2.0 equiv) ^[d]	2.0	0.10	40
9	0	Hexanes	MeCN (2.0 equiv) ^[d]	2.0	0.10	32
10	0	Toluene	MeCN (2.0 equiv) ^[d]	2.0	0.10	36
11	-10	MeCN	-	2.0	0.10	65
12	-45	MeCN ^[d]	-	2.0	0.10	75 (73 ^[c])
13	-45	MeCN ^[d]	-	2.0	0.20	73
14	-45	MeCN ^[d]	-	2.0	0.04	64
15	-70	DCM / MeCN ^[d] (1:1)	-	2.0	0.10	60

[a] Internal standard – Ph_2CH_2 . [b] The reaction was performed under inert atmosphere (Ar). [c] Isolated yield. [d] MeCN was dried over 4 Å molecular sieves prior to use.



[a] NMR yield. [b] T = -45 °C → 20 °C. [c] NBS as Br^+ source. [d] TsNBr₂ as Br^+ source. [e] List of silanes: **1i** (R^1 = C₄H₉, Si = *t*-BuMe₂Si), **1j** (R^1 = Ph, Si = (*i*-Pr)₃Si), **1k** (R^1 = C₉H₁₉, Si = *t*-BuMe₂Si), **1l** (R^1 = CH₂CH₂OPh, Si = *t*-BuMe₂Si), **1m** (R^1 = CH₂CH₂N₃, Si = *t*-BuMe₂Si), **1n** (R^1 = CH₂CH₂OH, Si = *t*-BuMe₂Si), **1o** (R^1 = CH₂CH₂OMs, Si = *t*-BuMe₂Si). [f] A modified solvent system of PhCN / DCM (4:3 v/v) was used.

Scheme 6. Substrate scope for amidines **3**.

RESEARCH ARTICLE

Regarding alternative secondary nucleophiles for amidine **3** synthesis, sulfonamides (NsNH_2 , TsNH_2) reacted to afford the highest product **3** yields (73–76%). Some nitrogen heterocycles were also applicable, such as 2,6-dichloropurine, 1,2,4-triazole and imidazole, albeit providing more modest amidine **3** yields (15–46%). In more sterically challenging cases, such as when using aromatic silane **1j** as starting material, only direct 1,3-addition products **5p** were obtained. Interestingly, for compound **5p** C=C bond isomerization occurred, providing an (*E/Z*)-isomer mixture (88:12). Strongly nucleophilic species, such as cyclohexanol, cyclohexylthiol and cyclohexylamine as secondary nucleophiles under standard reaction conditions (silane **1c**, 1.2 equiv NBS, -45°C , MeCN as solvent) failed to provide the imide / thioimide / amidine product.

Lastly, we explored the scope of nitriles applicable in this reaction (Scheme 6). We tested aliphatic nitriles with varying C-chain length. Longer C-chain signified a slight decrease in the amidine **3** yield (73→55%). When using butyronitrile in combination with aryl silane **1j**, the direct 1,3-addition product **5u** was also obtained. Acrylonitrile also reacted to give the amidine product **3v** in 41% yield. We slightly adjusted the reaction conditions for benzonitrile to avoid freezing of the solvent at -45°C (benzonitrile m.p. = -13.8°C ^[69]). A solvent mixture of PhCN / DCM (4:3 v/v) was used to afford amidine **3w** with 22% yield. The main byproduct observed in the reaction with benzonitrile was ((1*E*,3*E*)-1-bromohepta-1,3-dien-2-yl)triisopropylsilane (detected by the characteristic signals on NMR), indicating that benzonitrile was not reactive enough, and the substrate reacted predominantly according to the β -H elimination pathway.^[65]

In solution, both the configurational isomerism of the amidine C=N bond (*E/Z*), as well as rotational isomerism (*syn/anti*) with respect to the C-N bond, are possible. Tautomerism is also a factor to consider.^[70] When performing NMR spectral analysis of amidines **3a-w** in CDCl_3 , typically two sets of signals were observed, whereas only one isomer was seen in $\text{DMSO}-d_6$. In the case of amidine **3m**, the major / minor isomer ratio in CDCl_3 was 96:4 (integral ratio). The N-H signal in ^1H NMR appeared as a doublet, with a 3J coupling constant of 9.6 Hz between N-H and C(3)-H, suggesting that the N-H is tautomerized into the vicinal position in regard to C(3) (Figure 1). The same was observed for all other amidines **3** bearing a free N-H group. While the respective amidine tautomer could be determined using spectroscopic methods, the correct C=N bond configuration was more challenging to assign. To gain further insights into the structural properties of amidines **3**, we performed single crystal X-ray diffraction (SCXRD) analysis of compound **3m** (Figure 1).^[71] (*E*)-Geometry for the allylic C=C bond was confirmed by the absolute structure obtained from SCXRD (represented by thermal ellipsoids with 50% probability) and spatial

interactions between C(1)-H and the (*i*-Pr)₃Si- fragment in 2D-NOESY NMR spectra. This observation complements to our previous findings regarding electrophilic halogenation of propargyl silanes, resulting in olefins.^[39] In the ellipsoid structure of **3m**, the sulfonyl group is oriented in *trans*-position with respect to the RNH-fragment, i.e., the (*E*)-amidine isomer was obtained.

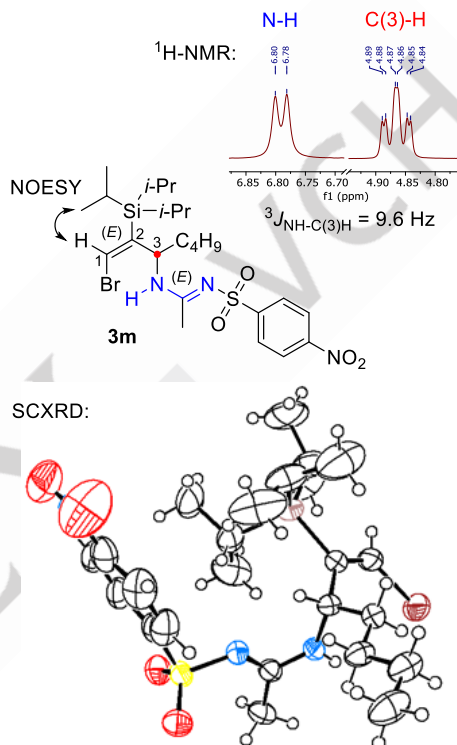
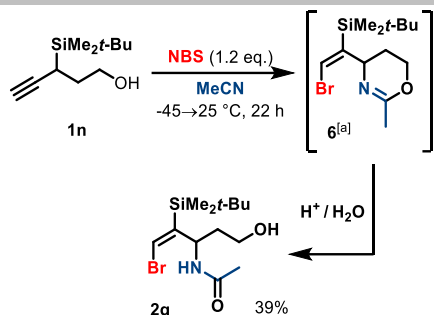


Figure 1. Structural elucidation of amidine **3m** using NMR and SCXRD techniques.

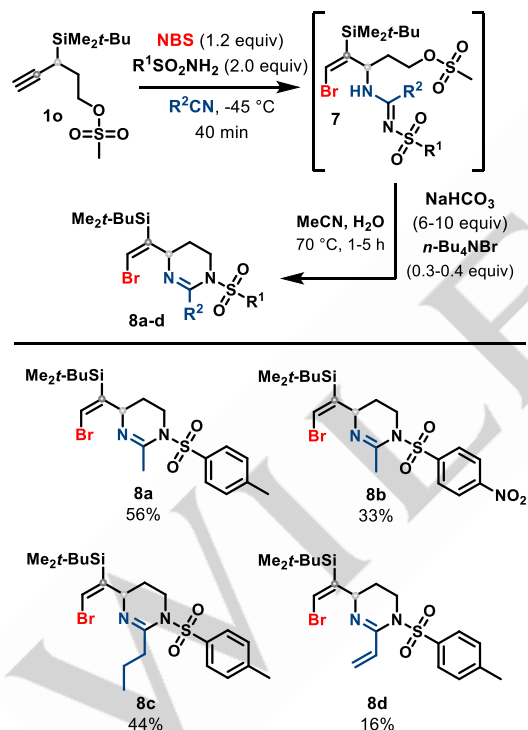
Oxazine synthesis

Under standard amidine synthesis conditions, the alcohol-group containing silane **1n** reacted according to our desired pathway to form amidine **3k** (Scheme 7). We were interested to see whether in the absence of an external nitrogen nucleophile, the nitrilium ion would be trapped intramolecularly to form an oxazine ring instead (Scheme 6). We found that small quantities (up to 23% yield) of the desired oxazine product **6** can be isolated, but due to stability issues in acidic media (silica gel) it readily hydrolyzes to afford amide **2g** (39% without isolation of the oxazine intermediate).



[a] Isolation of **6** gave 23% yield after column chromatography.

Scheme 7. Ritter-type reaction for alcohol **1n** in the absence of an external nucleophile.



Scheme 8. Ritter-type reaction for mesylate **1o**, followed by intramolecular cyclization.

Tetrahydropyrimidines

Lastly, we wanted to explore the application of acyclic Ritter-type reaction products for the synthesis of heterocyclic structures. We were inspired by the work of

Shaiyuan and coworkers, who synthesized imidazoles from vinyl silanes in a Ritter-type reaction – cyclization sequence.^[35] For tetrahydropyrimidine synthesis we subjected mesylate **1o** to the Ritter amidine synthesis conditions (1.2 equiv NBS, 2.0 equiv $TsNH_2$, R^4CN as solvent, $T = -45$ °C). The obtained amidine intermediate **7** was then heated in the presence of a mild base ($NaHCO_3$) to achieve an intramolecular S_N2 type reaction, forming the tetrahydropyrimidine ring **8** (Scheme 8). By using acetonitrile as solvent and $TsNH_2$ as secondary nucleophile the tetrahydropyrimidine product **8a** was obtained with 56% yield over two steps. An analogous structure **8b** obtained from using $NsNH_2$ displayed lower stability, therefore the isolated yield was only 33%. Other nitriles, such as butyronitrile or acrylonitrile, were also applicable in this reaction.

Conclusion

In conclusion, we have developed a new approach for carbocation generation under Ritter-type reaction conditions. Propargyl silanes, serving as highly stereoselective and functionalized allyl cation precursors, enabled the synthesis of allylamine functionality-containing products with a fixed (*E*)- or (*Z*)-configuration of the resulting C=C bond. Terminally halogenated propargyl silanes **1**, when activated by Brønsted acids, predominantly afforded Ritter-type reaction products (amides **2d-e** and dihydroisoquinolines **4b-d**) with a (*Z*)-configured olefin side chain. In contrast, when non-halogenated propargyl silanes **1** were activated by electrophilic halogenation reagents (NBS, NIS, etc.), the Ritter-type reaction products (amidines **3a-w**) were obtained with reversed stereoselectivity for the resulting olefin side chain.

In combination with sulfonamides or *N*-heterocycles as secondary nucleophiles for quenching the intermediate nitrilium ion, a variety of amidine derivatives **3a-w** were obtained. This transformation proceeds through the formation of four new bonds in a single step – a process that is notably challenging from an entropic standpoint. In the presence of an internal leaving group, such as a mesylate, the amidines undergo further intramolecular cyclization to furnish tetrahydropyrimidines **8a-d**. Furthermore, we demonstrated that intramolecular trapping of the nitrilium ion by an aromatic moiety to form dihydroisoquinolines **4** is feasible under these conditions; however, this requires an electron-rich aromatic system—otherwise, amides **2** are formed instead.

Overall, these results highlight the versatility of propargyl silanes as reaction partners in the Ritter-type

RESEARCH ARTICLE

reaction, giving access to a broad range of acyclic and heterocyclic products, including allylamides **2a–g**, amidines **3a–w**, dihydroisoquinolines **4a–i**, oxazine derivatives **6** and tetrahydropyrimidines **8a–d**.

Experimental

General procedure for the synthesis of allylamides 2a–f. A round-bottom flask, equipped with a Teflon-coated magnetic stirrer, was charged with silane **1a–f** (0.20 – 2.15 mmol, 1.0 equiv), dest. H₂O (2.2 equiv), a pre-made solution of HNTf₂ / MeCN (c = 0.3 M, 1.0 equiv), and heated to 60 °C in an oil bath. The resulting mixture was stirred for 18 to 24 hours, then cooled to ambient temperature (20 °C), neutralized with Et₃N (0.3 ml, ~5 equiv), filtered through a silica plug using EtOAc, and concentrated *in vacuo*. Column chromatography (0→100% DCM / Hex) afforded amide **2a–f**.

General procedure for the synthesis of amidines 3a–w. A round-bottom flask, equipped with a Teflon-coated magnetic stirrer, was charged with silane **1c** / **1f** / **1i–o** (0.18 – 3.96 mmol, 1.0 equiv), NBS / NCS / NIS (1.2 equiv), R²NHR³ (2.0 equiv), and cooled to –45 °C in an acetonitrile / liquid N₂ bath. Cold R⁴CN (2–39 ml) was added to the reaction, and the resulting mixture was stirred at –45 °C for 20 min to 24 hours, then warmed to ambient temperature (20 °C) and concentrated *in vacuo*. Column chromatography (0→40% EtOAc / Hex) afforded amidine **3a–w**.

General procedure for the synthesis of dihydroisoquinolines 4a–i. The reaction was performed in 10 ml flask (dried at 120 °C), equipped with a Teflon-coated magnetic stirrer, under inert atmosphere (argon). A pre-made solution of HNTf₂ / RCN (c = 0.3 M, 1.1 equiv) was added to the silane **1g–h** (0.18 – 0.36 mmol, 1.0 equiv) at ambient temperature (20 °C). The resulting mixture was stirred for 18 hours, then cooled to ambient temperature (20 °C), neutralized with Et₃N (~5 equiv), filtered through a silica plug using EtOAc, and concentrated *in vacuo*. Column chromatography (0→5% EtOAc / DCM or 50→100% DCM/Hex) afforded dihydroisoquinoline **4a–i**.

General procedure for the synthesis of tetrahydropyrimidines 8a–d. A round-bottom flask, equipped with a Teflon-coated magnetic stirrer, was charged with mesylate **1o** (0.17 – 1.00 mmol, 1.0 equiv), R²CN (2 – 10 ml) and R¹SO₂NH₂ (2.0 equiv). The resulting mixture was cooled to –45 °C in an acetonitrile / liquid N₂ bath. NBS (1.2 equiv) was added to the cooled mixture. After continuously stirring for 40 min, the reaction mixture was warmed to ambient temperature (20 °C). The reaction mixture was diluted

with MeCN (6 – 8 ml). Dest. H₂O (10 ml), NaHCO₃ (6–10 equiv) and *n*-Bu₄NBr (0.3 – 0.4 equiv) were added, and the resulting mixture was heated at 70 °C in an oil bath for 1 – 5 hours. For work-up, the reaction mixture was diluted with EtOAc (30 ml), the water layer was separated, and the organic layer was washed with a saturated aqueous NaHCO₃ solution (2 x 20 ml), saturated aqueous NaCl solution (20 ml), dried over anhydrous Na₂SO₄, filtered and concentrated *in vacuo*. Column chromatography (30→50% DCM / Hex or 5→10% EtOAc / Hex) afforded tetrahydropyrimidine **8a–d**.

Associated content

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The authors have cited additional references within the Supporting Information.^{[72][73][74][75]}

Acknowledgements

This work was supported by the Latvian Council of Science Grant LZP-2023/1-0576 and the EU RRF within project No 5.2.1.1.i.0/2/24//CFLA/003 academic career doctoral grant, ID 1134.

Keywords: Ritter-type reaction • propargylsilanes • amidines • dihydroisoquinolines • heterocyclization

References

- [1] M.-E. Chen, X.-W. Chen, Y.-H. Hu, R. Ye, J.-W. Lv, B. Li, F.-M. Zhang, "Recent Advances of Ritter Reaction and Its Synthetic Applications" *Org. Chem. Front.* **2021**, *8*, 4623. <https://doi.org/10.1039/d1qo00496d>.
- [2] L. Tian, J. Li, K. Wu, "Synthesis of 3-Hydroxy Desloratadine, the Hydroxyl Metabolite of Loratadine" *J. Chem. Pharm. Res.* **2014**, *6*, 982.
- [3] D. B. Vu, T. Van Nguyen, S. T. Le, C. Di. Phan, "An Improved Synthesis of Amantadine Hydrochloride" *Org. Process Res. Dev.* **2017**, *21*, 1758. <https://doi.org/10.1021/acs.oprd.7b00242>.
- [4] M. Biermann, G. Zheng, M. Hojamat, N. V. Moskalev, P. A. Crooks, "Asymmetric Synthesis of (S)- and (R)-Norketamine via Sharpless Asymmetric Dihydroxylation/Ritter Amination Sequence" *Tetrahedron Lett.* **2015**, *56*, 2608. <https://doi.org/10.1016/j.tetlet.2015.04.050>.
- [5] C. Feng, B. Yan, W. Yao, J. Chen, M. Ji, "Zn(ClO₄)₂·6H₂O-Catalyzed One-Pot Synthesis of Amides via

RESEARCH ARTICLE

- Ritter Reaction with Alcohols, Acetic Anhydride and Nitriles" *ChemistrySelect* **2018**, *3*, 11775. <https://doi.org/10.1002/slct.201802386>.
- [6] T. Nakaya, A. Matsuda, S. Ichikawa, "Design, Synthesis and Biological Evaluation of 5'-C-Piperidinyl-5'-O-Aminoribosyluridines as Potential Antibacterial Agents" *Org. Biomol. Chem.* **2015**, *13*, 7720. <https://doi.org/10.1039/c5ob01037c>.
- [7] Z.-Y. Gan, Y.-H. Hu, Z.-J. He, L.-H. Zhang, X.-M. Zhang, F.-M. Zhang, "Total Synthesis of Natural Alkaloids via Ritter Reaction" *Asian J. Org. Chem.* **2025**, 202500094. <https://doi.org/10.1002/ajoc.202500094>.
- [8] S. Narasimhan, S. Maheshwaran, I. A. Abu-Yousef, A. F. Majdalawieh, J. Rethavathi, P. E. Das, P. Poltronieri, "Anti-Bacterial and Anti-Fungal Activity of Xanthenes Obtained via Semi-Synthetic Modification of α -Mangostin from *Garcinia Mangostana*" *Molecules* **2017**, *22*, 275. <https://doi.org/10.3390/molecules22020275>.
- [9] A. C. De Leon, L. Alonso, J. D. Mangadlao, R. C. Advincula, E. Pentzer, "Simultaneous Reduction and Functionalization of Graphene Oxide via Ritter Reaction" *ACS Appl. Mater. Interfaces* **2017**, *9*, 14265. <https://doi.org/10.1021/acsami.7b01890>.
- [10] J. J. Ritter, P. P. Minieri, "A New Reaction of Nitriles. I. Amides from Alkenes and Mononitriles" *J. Am. Chem. Soc.* **1948**, *70*, 4045. <https://doi.org/10.1021/ja01192a022>.
- [11] J. J. Ritter, J. Kalish, "A New Reaction of Nitriles. II. Synthesis of *t*-Carbinamines" *J. Am. Chem. Soc.* **1948**, *70*, 4048. <https://doi.org/10.1021/ja01192a023>.
- [12] H. Plaut, J. J. Ritter, "A New Reaction of Nitriles. VI. Unsaturated Amides" *J. Am. Chem. Soc.* **1951**, *73*, 4076. <https://doi.org/10.1021/ja01153a005>.
- [13] Z. Xiang, S. Zhang, Z. Zhang, H. Liu, J. Wang, W. Chen, Y. Wang, X. Wan, "Vicinal Difunctionalization of Nitriles: Modular Construction of *N*-Alkyl Amidines and Late-Stage Modification" *New J. Chem.* **2024**, *48*, 11834. <https://doi.org/10.1039/D4NJ02051K>.
- [14] Y. Zhang, Z. Chen, "Three Component Reaction of Aryl Diazonium Salt with Sulfonamide & Acetonitrile to Synthesize *N*-Sulfonyl Amidine" *Tetrahedron Lett.* **2018**, *59*, 4183. <https://doi.org/10.1016/j.tetlet.2018.10.027>.
- [15] E. V. Bogdanova, Y. Stogniy, L. A. Chekulaeva, A. A. Anisimov, Y. Suponitsky, I. B. Sivaev, M. A. Grin, A. F. Mironov, V. I. Bregadze, "Synthesis and Reactivity of Propionitrilium Derivatives of Cobalt and Iron Bis(Dicarbollides)" *New J. Chem.* **2020**, *44*, 15836. <https://doi.org/10.1039/d0nj03017a>.
- [16] R. Z. Zhang, W. Huang, R. X. Zhang, C. Xu, M. Wang, "Synthesis of *N*-CF₃ Amidines/Imidates/Thioimidates via *N*-CF₃ Nitrilium Ions" *Org. Lett.* **2022**, *24*, 2393. <https://doi.org/10.1021/acs.orglett.2c00647>.
- [17] S.-Z. Tang, K. Xiang, R. Ye, M.-E. Chen, J.-C. Yu, Z.-J. He, F.-M. Zhang, "Preparation of Thioamides from Alkyl Bromides, Nitriles, and Hydrogen Sulfide through a Thio-Ritter-Type Reaction" *Chem. Commun.* **2022**, *58*, 11430. <https://doi.org/10.1039/D2CC04210J>.
- [18] R. Ma, Y. Ren, Z. Deng, K.-H. Wang, J. Wang, D. Huang, X. Lv, Y. Hu, "Visible-Light-Induced Four-Component Ritter-Type Reaction: Access to β -Trifluoromethyl Imides" *Org. Lett.* **2023**, *25*, 4080. <https://doi.org/10.1021/acs.orglett.3c01291>.
- [19] M. Ramanathan, Y. Wang, Y. Liu, S. Peng, Y. Cheng, S. Liu, "Preparation of Ketimines from Aryldiazonium Salts, Arenes, and Nitriles via Intermolecular Arylation of *N*-Arylnitrilium Ions" *J. Org. Chem.* **2018**, *83*, 6133. <https://doi.org/10.1021/acs.joc.8b01000>.
- [20] M. Ramanathan, S. Liu, "Cascade Annulations of Aryldiazonium Salts, Nitriles and Haloalkynes Leading to 3-Haloquinolines" *Tetrahedron* **2017**, *73*, 4317. <https://doi.org/10.1016/j.tet.2017.05.085>.
- [21] Y. V. Shklyayev, Y. S. Rozhkova, A. N. Perevoshchikova, A. A. Gorbunov, "Regioselective Synthesis of 1-Substituted 6-Methoxy-3,3,4,4-Tetramethyl-3,4-Dihydroisoquinolines via Ritter Reaction" *Russ. Chem. Bull.* **2014**, *63*, 2087. <https://doi.org/10.1007/s11172-014-0706-4>.
- [22] J. Bolsakova, A. Jirgensons, "The Ritter Reaction for the Synthesis of Heterocycles" *Heterocycl. Comp.* **2017**, *53*, 1167. <https://doi.org/10.1007/s10593-018-2189-y>.
- [23] M. Lepori, C. Pratley, I. Dey, V. Butera, V. Roider, J. P. Barham, "Photocatalysis Enables Chemodivergent Radical Polar Crossover: Ritter-Type Amidation vs Heck-Type Olefin Carbofunctionalizations" *Chem. Eur. J.* **2025**, e202500666. <https://doi.org/10.1002/chem.202500666>.
- [24] Y. Guan, X. Min, G.-C. He, D.-W. Ji, S.-Y. Guo, Y.-C. Hu, Q.-A. Chen, "The Serendipitous Effect of KF in Ritter Reaction: Photo-Induced Amino-Alkylation of Alkenes" *iScience* **2021**, *24*, 102969. <https://doi.org/10.1016/j.isci.2021.102969>.
- [25] R. Ma, Y. Ren, Z. Deng, K.-H. Wang, J. Wang, D. Huang, X. Lv, Y. Hu, "Visible-Light-Induced Four-Component Ritter-Type Reaction: Access to β -Trifluoromethyl Imides" *Org. Lett.* **2023**, *25*, 4080. <https://doi.org/10.1021/acs.orglett.3c01291>.
- [26] R. Liu, Y. Tian, J. Wang, Z. Wang, X. Li, C. Zhao, R. Yao, S. Li, L. Yuan, J. Yang, D. Shi, "Visible Light-Initiated Radical 1,3-Difunctionalization of β,γ -Unsaturated Ketones" *Sci. Adv.* **2022**, *8*, eabq8596. <https://doi.org/10.1126/sciadv.abq8596>.
- [27] M. Lepori, I. Dey, C. Pratley, J. P. Barham, "Merging New and Old Concepts: Tandem Oxidative Radical-Polar Crossover Ritter Amidation via Multicomponent Photo- and Electrochemical Processes" *Eur. J. Org. Chem.* **2024**, *27*, e202400840. <https://doi.org/10.1002/ejoc.202400840>.
- [28] W. Xu, N. Zhang, C. Li, H. Ma, B. Wang, Z. Chen, Y. Xia, S. Wu, W. Jin, P. Yan, C. Liu, Y. Zhang, "Electrochemical Vicinal Amidoselenation of Unactivated Olefins via a Tandem

RESEARCH ARTICLE

- Ritter Reaction" *Green Chem.* **2025**, *27*, 7114. <https://doi.org/10.1039/d5gc01259g>.
- [29] S. Schmid, S. Wu, I. Dey, M. Domański, X. Tian, J. P. Barham, "Photoelectrochemical Heterodifunctionalization of Olefins: Carboamidation Using Unactivated Hydrocarbons" *ACS Catal.* **2024**, *14*, 9648. <https://doi.org/10.1021/acscatal.4c02320>.
- [30] S. W. Park, S. Kim, J. Song, G. Y. Park, D. Kim, T. Nam, K. B. Hong, "Hypervalent Iodine-Mediated Ritter-Type Amidation of Terminal Alkenes: The Synthesis of Isoxazoline and Pyrazoline Cores" *Beilstein J. Org. Chem.* **2018**, *14*, 1028. <https://doi.org/10.3762/bjoc.14.89>.
- [31] D. C. Steigerwald, B. Soltanzadeh, A. Sarkar, C. C. Morgenstern, R. J. Staples, B. Borhan, "Ritter-Enabled Catalytic Asymmetric Chloroamidation of Olefins" *Chem. Sci.* **2021**, *12*, 1834. <https://doi.org/10.1039/d0sc05224h>.
- [32] J. Luo, Z. Zhu, Y. Liu, X. Zhao, "Diaryl Selenide Catalyzed Vicinal Trifluoromethylthioamination of Alkenes" *Org. Lett.* **2015**, *17*, 3620. <https://doi.org/10.1021/acs.orglett.5b01727>.
- [33] A. S. Ganin, M. Y. Moskalik, V. V. Astakhova, I. V. Sterkhova, B. A. Shainyan, "Heterocyclization and Solvent Interception upon Oxidative Triflamidation of Allyl Ethers, Amines and Silanes" *Tetrahedron* **2020**, *76*, 131374. <https://doi.org/10.1016/j.tet.2020.131374>.
- [34] M. Y. Moskalik, V. V. Astakhova, B. A. Shainyan, "Divergent Reactivity of Divinylsilanes toward Sulfonamides in Different Oxidative Systems" *RSC Adv.* **2020**, *10*, 40514. <https://doi.org/10.1039/d0ra07469a>.
- [35] V. V. Astakhova, M. Y. Moskalik, B. A. Shainyan, "Solvent Interception, Heterocyclization and Desilylation upon NBS-Induced Sulfamidation of Trimethyl(Vinyl)Silane" *Org. Biomol. Chem.* **2019**, *17*, 7927. <https://doi.org/10.1039/C9OB01689A>.
- [36] J. Chai, W. Ding, C. Wang, S. Ito, J. Wu, N. Yoshikai, "Ritter-Type Iodo(III)Amidation of Unactivated Alkynes for the Stereoselective Synthesis of Multisubstituted Enamides" *Chem. Sci.* **2021**, *12*, 15128. <https://doi.org/10.1039/d1sc05240c>.
- [37] B. V. S. Reddy, S. Ghanty, "O-Benzenedisulfonimide as a Recyclable Homogeneous Organocatalyst for an Efficient and Facile Synthesis of 4-Amidotetrahydropyran Derivatives Through Prins–Ritter Reaction" *Synth. Commun.* **2014**, *44*, 2545. <https://doi.org/10.1080/00397911.2014.909488>.
- [38] D. D. Roberts, M. G. McLaughlin, "Strategic Applications of the β -Silicon Effect" *Adv. Synth. Catal.* **2022**, *364*, 2307. <https://doi.org/10.1002/adsc.202200237>.
- [39] R. Bejaunieks, M. Puriņš, R. A. Līpiņa, A. Mishnev, M. Turks, "1,3-Difunctionalization of Propargyl Silanes with Concomitant 1,2-Silyl Shift: Synthesis of Allyl Functionalized Vinyl Silanes" *Org. Lett.* **2023**, *25*, 4627. <https://doi.org/10.1021/acs.orglett.3c01245>.
- [40] R. Kronkalne, R. Bejaunieks, A. Ubaidullaievs, A. Mishnev, M. Turks, "1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing a Functionalized Olefin Side Chain" *J. Org. Chem.* **2023**, *88*, 13857. <https://doi.org/10.1021/acs.joc.3c01481>.
- [41] R. Kronkalne, R. Bejaunieks, A. Sebris, A. Mishnev, M. Turks, "Aryl Iodane-Induced Cascade Arylation–1,2-Silyl Shift–Heterocyclization of Propargylsilanes under Copper Catalysis" *Beilstein J. Org. Chem.* **2025**, *21*, 1984. <https://doi.org/10.3762/bjoc.21.154>.
- [42] R. Bejaunieks, M. Puriņš, M. Turks, "Manifestation of the β -Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift" *Synthesis (Stuttg.)* **2020**, *52*, 2147. <https://doi.org/10.1055/s-0039-1690898>.
- [43] D. Djaidi, I. S. H. Leung, R. Bishop, D. C. Craig, M. L. Scudder, "Ritter Reactions. Part 14. Rearrangement of 3,3,7,7-Tetramethyl-6-Methylenecyclo[3.3.1]Nonan-2-One" *J. Chem. Soc. Perkin Trans. 1* **2000**, 2037. <https://doi.org/10.1039/b002544p>.
- [44] Z. Sun, C. Song, Y. Meng, Y. Dou, "Synthesis of 2,3-Benzobicyclo[3.3.1]Non-2-Enes via a Cascade of Domino Carbocation Migration/Interrupted Ritter Reaction and Dienone-Phenol Rearrangement" *J. Org. Chem.* **2024**, *89*, 14520. <https://doi.org/10.1021/acs.joc.4c01516>.
- [45] S. S. Koval, N. G. Kozlov, V. Kulcitki, A. Aricu, N. Ungur, "Transformation of Sclareol under Ritter Reaction Conditions" *Russ. J. Org. Chem.* **2013**, *49*, 303. <https://doi.org/10.1134/S1070428013020218>.
- [46] V. R. Kartashov, A. V. Arkhipova, K. V. Malkova, T. N. Sokolova, "Synthesis of *N*-Substituted Amides by the Ritter Reaction with Heteropoly Acids as Catalysts" *Russ. Chem. Bull.* **2006**, *55*, 387.
- [47] E. Torres, R. Fernández, S. Miquet, M. Font-Bardia, E. Vanderlinden, L. Naesens, S. Vázquez, "Synthesis and Anti-Influenza A Virus Activity of 2,2-Dialkylamantadines and Related Compounds" *ACS Med. Chem. Lett.* **2012**, *3*, 1065. <https://doi.org/10.1021/ml300279b>.
- [48] K. Indukuri, R. Unnava, M. J. Deka, A. K. Saikia, "Stereoselective Synthesis of Amido and Phenyl Azabicyclic Derivatives via a Tandem Aza Prins–Ritter/Friedel–Crafts Type Reaction of Endocyclic *N*-Acyliminium Ions" *J. Org. Chem.* **2013**, *78*, 10629. <https://doi.org/10.1021/jo401450j>.
- [49] B. V. S. Reddy, K. Muralikrishna, J. S. Yadav, N. J. Babu, K. Sirisha, A. V. S. Sarma, "Tandem Prins/Wagner/Ritter Process for the Stereoselective Synthesis of (3-Oxabicyclo[4.2.0]-Octanyl)Amide and (1-(5-Aryltetrahydrofuran-3-yl)-Cyclobutyl)Amide Derivatives" *Org. Biomol. Chem.* **2015**, *13*, 5532. <https://doi.org/10.1039/c5ob00031a>.
- [50] M. M. Sá, M. Ferreira, G. F. Caramori, L. Zaramello, A. J. Bortoluzzi, D. Faggion, J. B. Domingos, "Investigating the Ritter Type Reaction of α -Methylene- β -hydroxy Esters in

RESEARCH ARTICLE

- Acidic Medium: Evidence for the Intermediacy of an Allylic Cation" *European J. Org. Chem.* **2013**, 2013, 5180. <https://doi.org/10.1002/ejoc.201300035>.
- [51] J. E. Birnbaum, E. Hanover, "Pharmacology of the Allylamines" *J. Am. Acad. Dermatol.* **1990**, 23, 782. [https://doi.org/10.1016/0190-9622\(90\)70288-S](https://doi.org/10.1016/0190-9622(90)70288-S).
- [52] A. K. Gupta, R. R. Mays, K. A. Foley. Topical Antifungal Agents. In *Comprehensive Dermatologic Drug Therapy*, (Ed.: S. E. Wolverson), Elsevier, **2021**, pp 480–492. <https://doi.org/10.1016/B978-0-323-61211-1.00042-5>.
- [53] A. Zainal Abidin, M. N. F. Norraahim, N. N. S. Mohamed Shakrin, B. Ibrahim, N. Abdullah, J. I. Abdul Rashid, N. A. Mohd Kasim, N. A. Ahmad Shah, "Amidine Containing Compounds: Antimicrobial Activity and Its Potential in Combating Antimicrobial Resistance" *Heliyon* **2024**, 10, e32010. <https://doi.org/10.1016/j.heliyon.2024.e32010>.
- [54] M. M. Heravi, N. Nazari, "Bischler-Napieralski Reaction in Total Synthesis of Isoquinoline-Based Natural Products. An Old Reaction, a New Application" *J. Curr. Org. Chem.* **2015**, 19, 2358. <https://doi.org/10.2174/1385272819666150730214506>.
- [55] L. Min, W. Yang, Y. Weng, W. Zheng, X. Wang, Y. Hu, "A Method for Bischler-Napieralski-Type Synthesis of 3,4-Dihydroisoquinolines" *Org. Lett.* **2019**, 21, 2574. <https://doi.org/10.1021/acs.orglett.9b00534>.
- [56] D. Wang, L. Qin, C. Jing, G. Wang, H. Zhou, P. Deng, S. Zhang, Y. Wang, Y. Ding, Z. Zhang, Z. Wu, Y. Liu, "Biologically Active Isoquinoline Alkaloids Covering 2019–2022" *Bioorg. Chem.* **2024**, 145, 107252. <https://doi.org/10.1016/j.bioorg.2024.107252>.
- [57] L. Y. Wang, B. L. Qiu, H. Xia, G. Y. Xia, B. B. Xiao, J. F. Zhang, W. C. Zhong, S. Lin, "Yanhusanines A-F, Isoquinoline-Derived Alkaloid Enantiomers from *Corydalis Yanhusuo* and Their Biological Activity" *J. Nat. Prod.* **2020**, 83, 489. <https://doi.org/10.1021/acs.jnatprod.9b01155>.
- [58] O. V. Surikova, A. G. Mikhailovskii, B. Y. Syropyatov, M. I. Vakhnin, "Synthesis, Anthelmintic, and Insecticidal Activity of 2-(3-Methyl-6-Methoxy-7-Ethoxy-3,4-Dihydroisoquinolyl-1)Ethanoic Acid Amides" *Pharm. Chem. J.* **2015**, 48, 665. <https://doi.org/10.1007/s11094-015-1166-3>.
- [59] A. G. Mikhailovskii, O. V. Gashkova, I. P. Rudakova, S. V. Chashchina, A. S. Yusov, "Synthesis and Biological Activity of 1-Chloromethyl- and 1-Dichloromethyl-3,3-Dialkyl-3,4-Dihydroisoquinolinium Chlorides" *Pharm. Chem. J.* **2018**, 52, 400. <https://doi.org/10.1007/s11094-018-1829-y>.
- [60] O. V. Gashkova, A. G. Mikhailovskii, I. P. Rudakova, A. V. Starkova, A. S. Yusov, "Synthesis and Antiarrhythmic and Hemostatic Activity of [3,3-Dialkyl-3, 4-Dihydroisoquinolin-1(2H)-Ylidene]-N-Alkylacetamides" *Pharm. Chem. J.* **2019**, 53, 507. <https://doi.org/10.1007/s11094-019-02028-6>.
- [61] O. V. Surikova, A. S. Yusov, R. R. Makhmudov, A. G. Mikhailovskii, "Synthesis and Analgesic Activity of 1-Substituted 3-Methyl-6-Methoxy-7(*n*-Butoxy)-3,4-Dihydroisoquinolines" *Pharm. Chem. J.* **2017**, 51, 18. <https://doi.org/10.1007/s11094-017-1549-8>.
- [62] M. A. Asif, S. R. Lisa, N. Qais, "Introduction of Chirality at C1 Position of 1-Substituted-3,4-Dihydroisoquinoline by Its Enantioselective Reduction: Synthesis of Chiral 1-Substituted-1,2,3,4-Tetrahydroisoquinoline – a Review" *RSC Adv.* **2023**, 13, 11010. <https://doi.org/10.1039/d3ra01413d>.
- [63] M. Cárdenas-fernández, R. Roddan, E. M. Carter, H. C. Hailes, J. M. Ward, "The Discovery of Imine Reductases and Their Utilisation for the Synthesis of Tetrahydroisoquinolines" *ChemCatChem* **2023**, 15, e202201126. <https://doi.org/10.1002/cctc.202201126>.
- [64] Y. Ji, Q. Gao, W. Han, "Recent Advances in the Synthesis of Chiral Tetrahydroisoquinolines via Asymmetric Reduction" *Catalysts* **2024**, 14, 884. <https://doi.org/https://doi.org/10.3390/catal14120884>.
- [65] M. Puriš, A. Mishnev, M. Turks, "Brønsted Acid Catalyzed 1,2-Silyl Shift in Propargyl Silanes: Synthesis of Silyl Dienes and Silyl Indenes" *J. Org. Chem.* **2019**, 84, 3595. <https://doi.org/10.1021/acs.joc.8b02735>.
- [66] L. Kahlenberg, "On an Improved Method of Determining Latent Heat of Evaporation, and on the Latent Heat of Evaporation of Pyridine, Acetonitrile, and Benzonitrile" *J. Phys. Chem.* **1901**, 5, 215. <https://doi.org/10.1021/j150031a001>.
- [67] V. Vasylyeva, K. Merz, "Fluorobenzonitriles: Influence of the Substitution Pattern on Melting and Crystallization Properties" *Cryst. Growth Des.* **2010**, 10, 4250. <https://doi.org/10.1021/cg100794s>.
- [68] B. M. Trost, M. R. Machacek, Z. T. Ball, S. U. V, "Ruthenium-Catalyzed Vinylsilane Synthesis and Cross-Coupling as a Selective Approach to Alkenes: Benzyldimethylsilyl as a Robust Vinylmetal Functionality" *Org. Lett.* **2003**, 4, 1073. <https://doi.org/10.1021/ol034463w>.
- [69] K. T. Takao Maki, Benzoic Acid and Derivatives. In *Ullmann's Encyclopedia of Industrial Chemistry*, **2012**. <https://doi.org/10.1002/14356007.a03>.
- [70] K. F. Kalz, A. Hausmann, S. Dechert, S. Meyer, M. John, "Solution Chemistry of *N*, *N'*-Disubstituted Amidines: Identification of Isomers and Evidence for Linear Dimer Formation" *Chem. Eur. J.* **2016**, 22, 18190. <https://doi.org/10.1002/chem.201603850>.
- [71] Deposition number CCDC 2514696 (for **3m**) contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe [Access Structures](https://www.rsc.org/openaccess/doi/10.1039/C9CC00000A) service.
- [72] L. F. Tietze, T. Neumann, M. Kajino, M. Pretor, "Efficient Synthesis of Branched Propargyl- and Allylsilanes" *Synthesis (Stuttg.)*. **1995**, 1995, 1003. <https://doi.org/10.1055/s-1995-4034>.

RESEARCH ARTICLE

[73] P. C. Bulman Page, S. Rosenthal, "Simple Preparation of α -Bromo Acyl Silanes α -Ketoacyl Silanes and α -Ketoesters from Silyl Acetylenes" *Tetrahedron* **1990**, *46*, 2573. [https://doi.org/10.1016/S0040-4020\(01\)82037-8](https://doi.org/10.1016/S0040-4020(01)82037-8).

[74] X. Wang, Q. Gao, A. V Buevich, N. Yasuda, Y. Zhang, R. Yang, L.-K. Zhang, G. E. Martin, R. T. Williamson, "Unexpected Propargylic Retro-Brook Rearrangements in Alkynes" *J. Org. Chem.* **2019**, *84*, 10024. <https://doi.org/10.1021/acs.joc.9b01190>.

[75] A. Ubaidullajevs, R. Kronkalne, A. Mishnev, M. Turks, "Synthesis and of Substituted Chromanes and Tetrahydroquinolines via Tandem 1,2-Silyl Shift – Friedel–Crafts Cyclization" *J. Org. Chem.* **2026**, *91* (17), 5785. <https://doi.org/10.1021/acs.joc.5c03136>.

Sintēzes procedūras un raksturojumi jodētiem hromānu atvasinājumiem

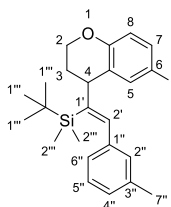
Synthesis procedures and characterization data for iodinated chromane derivatives

Kroņkalne, R.; Turks, M.

Nepublicētie rezultāti / Unpublished results

Sintēzes procedūras un raksturojumi jodētiem hromānu atvasinājumiem

(*Z*)-*tert*-Butil(1-(6-jodhromān-4-il)-2-(*m*-tolil)vinil)dimetilsilāns (**16i**)



Sintēzes procedūra:

Reakciju veic tumsā. 10 ml apaļkolbā, kas aprīkota ar magnētisko maisītāju, pievieno (*Z*)-*tert*-butil(1-(hromān-4-il)-2-(*m*-tolil)vinil)dimetilsilānu (**16e**) (50 mg, 0.14 mmol, 1.0 ekv.) un CF₃CH₂OH (5 ml). Iegūtajai suspensijai pievieno NIS (62 mg, 0.28 mmol, 2.0 ekv.). Reakciju maisa 17.5 h istabas temperatūrā (20 °C), tad pievieno papildus NIS (46 mg, 0.21 mmol, 1.5 ekv.) un turpina maisīt 19 h. Reakciju dzēš ar 10% Na₂S₂O₃ ūdens šķīdumu (5 ml), un produktu ekstrahē ar DCM (3 × 8 ml). Organisko slāni žāvē virs bezūdens Na₂SO₄, filtrē, un iekoncentrē *in vacuo*. Pēc kolonnu hromatogrāfijas (5-10% DCM/Hex) iegūst ariljodīdu **16i** (44 mg, γ = 66%) kā bezkrāsainu eļļu.

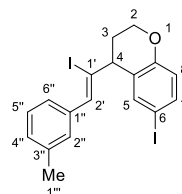
Savienojuma 16i raksturojums:

¹H KMR (500 MHz, CDCl₃): δ 7.40 (dd, ³*J*_{H-H} = 2.2 Hz, ⁴*J*_{H-H} = 0.9 Hz, 1H), 7.35 (dd, ³*J*_{H-H} = 8.6, 2.2 Hz, 1H, H-C(7)), 7.13 (t, ³*J*_{H-H} = 7.5 Hz, 1H, H-C(5'')), 7.02 (d, ³*J*_{H-H} = 7.5 Hz, 1H, H-C(4'')), 6.99 (s, 1H, HC(2'')), 6.92 (s, 1H, H-C(2'')), 6.90 (d, ³*J*_{H-H} = 7.5 Hz, 1H, H-C(6'')), 6.57 (d, ³*J*_{H-H} = 8.6 Hz, 1H, H-C(8)), 4.29 (ddd, ²*J*_{H-H} = 11.0 Hz, ³*J*_{H-H} = 8.6, 2.9 Hz, 1H, H_aC(2)), 4.17 (ddd, ²*J*_{H-H} = 11.0 Hz, ³*J*_{H-H} = 6.1, 3.2 Hz, 1H, H_bC(2)), 3.86 (t, ³*J*_{H-H} = 6.1 Hz, 1H, HC(4)), 2.31 (s, 3H, H₃C(7'')), 2.17 (dddd, ²*J*_{H-H} = 14.0 Hz, ³*J*_{H-H} = 8.6, 6.1, 3.2 Hz, 1H, H_aC(3)), 1.86 (dtd, ²*J*_{H-H} = 14.0 Hz, ³*J*_{H-H} = 6.1, 2.9 Hz, 1H, H_bC(3)), 0.96 (s, 9H, H₃C(1''')), -0.02 (s, 3H, H₃C(2'')), -0.19 (s, 3H, H₃C(2''')).

¹³C KMR (126 MHz, CDCl₃): δ 155.6, 148.3, 146.0, 140.1, 139.1, 137.2, 136.3, 129.3, 129.1, 127.7, 127.6, 125.6, 119.1, 82.4, 63.3, 40.1, 29.96, 28.0, 21.4, 18.6, -2.6, -3.1.

AIMS: C₂₄H₃₂IOSi⁺ [M + H]⁺ aprēķināts 491.1262, atrasts 491.1266.

(*Z*)-6-Jod-4-(1-jod-2-(*m*-tolil)vinil)hromāns (**16j**)



Sintēzes procedūra:

Reakciju veic tumsā. 10 ml apaļkolbā, kas aprīkota ar magnētisko maisītāju, pievieno (*Z*)-*tert*-butil(1-(hromān-4-il)-2-(*m*-tolil)vinil)dimetilsilānu (**16e**) (45 mg, 0.12 mmol, 1.0 ekv.) un CF₃CH₂OH (4 ml). Iegūtajai suspensijai istabas temperatūrā (20 °C) pievieno NIS (84 mg, 3.0 ekv.), un reakcijas maisījumu vāra attecē 6.5 h. Reakciju dzēš ar 10% Na₂S₂O₃ ūdens šķīdumu (4 ml) un produktu ekstrahē ar DCM (3 × 5 ml). Organisko slāni žāvē virs bezūdens Na₂SO₄, filtrē, un iekoncentrē *in vacuo*. Pēc apgriezās fāzes kolonnu hromatogrāfijas (90-95% MeOH/H₂O) iegūst dijodēto produktu **16j** (58 mg, γ = 93%) kā bezkrāsainu eļļu.

Savienojuma 16j raksturojums:

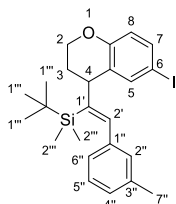
¹H KMR (500 MHz, CD₂Cl₂): δ 7.45 (s, 1H, H-C(5)), 7.46 – 7.43 (dd, ³*J*_{H-H} = 8.4, 2.2 Hz, 1H, H-C(7)), 7.31 – 7.22 (m, 3H, H-C(2''), 5'', 6''), 7.14 (d, ³*J*_{H-H} = 7.4 Hz, 1H, H-C(4'')), 6.74 (s, 1H, HC(2'')), 6.62 (d, ³*J*_{H-H} = 8.4 Hz, 1H, H-C(8)), 4.28 (ddd, ²*J*_{H-H} = 10.8 Hz, ³*J*_{H-H} = 7.1, 3.3 Hz, 1H, H_aC(2)), 4.20 (ddd, ²*J*_{H-H} = 10.8 Hz, ³*J*_{H-H} = 7.9, 2.8 Hz, 1H, H_bC(2)), 3.83 (t, ³*J*_{H-H} = 6.1 Hz, 1H, HC(4)), 2.37 (s, 3H, H₃C(1''')), 2.37 – 2.30 (m, 1H, H_aC(3)), 2.07 (dddd, ²*J*_{H-H} = 14.0 Hz, ³*J*_{H-H} = 7.1, 6.1, 2.8 Hz, 1H, H_bC(3)).

¹³C KMR (126 MHz, CD₂Cl₂): δ 155.6, 139.1, 138.7, 138.4, 138.3, 137.6, 129.7, 129.1, 128.3, 126.1, 126.1, 119.7, 112.6, 82.5, 63.9, 49.29, 29.0, 21.5.

AIMS: C₁₈H₁₇I₂O⁺ [M + H]⁺ aprēķināts 502.9363 atrasts 502.9326.

Synthesis procedures and characterization data for iodinated chromane derivatives

(*Z*)-*tert*-Butyl(1-(6-iodochroman-4-yl)-2-(*m*-tolyl)vinyl)dimethylsilane (**16i**)



Synthesis procedure:

In a 10 ml round-bottom flask, equipped with a magnetic stirrer and shielded from light with aluminum foil coating, (*Z*)-*tert*-butyl(1-(chroman-4-yl)-2-(*m*-tolyl)vinyl)dimethylsilane (**16e**) (50 mg, 0.14 mmol, 1.0 equiv) was suspended in $\text{CF}_3\text{CH}_2\text{OH}$ (5 ml). NIS (62 mg, 0.28 mmol, 2.0 equiv) was added to the reaction mixture. After stirring for 17.5 hours at ambient temperature (20 °C), additional NIS (46 mg, 0.21 mmol, 1.5 equiv) was added to the mixture and stirred for another 19 hours. The reaction was quenched by addition of 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution (5 ml), extracted with DCM (3 × 8 ml), the organic layer was dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. Column chromatography (5-10% DCM/Hex) afforded the aryl iodide **16i** (44 mg, γ = 66%) as a colorless oil.

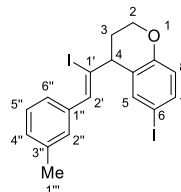
Characterization data for **16i**:

^1H NMR (500 MHz, CDCl_3): δ 7.40 (dd, $^3J_{\text{H-H}} = 2.2$ Hz, $^4J_{\text{H-H}} = 0.9$ Hz, 1H), 7.35 (dd, $^3J_{\text{H-H}} = 8.6$, 2.2 Hz, 1H, H-C(7)), 7.13 (t, $^3J_{\text{H-H}} = 7.5$ Hz, 1H, H-C(5'')), 7.02 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H, H-C(4'')), 6.99 (s, 1H, HC(2')), 6.92 (s, 1H, H-C(2'')), 6.90 (d, $^3J_{\text{H-H}} = 7.5$ Hz, 1H, H-C(6'')), 6.57 (d, $^3J_{\text{H-H}} = 8.6$ Hz, 1H, H-C(8)), 4.29 (ddd, $^2J_{\text{H-H}} = 11.0$ Hz, $^3J_{\text{H-H}} = 8.6$, 2.9 Hz, 1H, $\text{H}_\text{a}\text{C}(2)$), 4.17 (ddd, $^2J_{\text{H-H}} = 11.0$ Hz, $^3J_{\text{H-H}} = 6.1$, 3.2 Hz, 1H, $\text{H}_\text{b}\text{C}(2)$), 3.86 (t, $^3J_{\text{H-H}} = 6.1$ Hz, 1H, HC(4)), 2.31 (s, 3H, $\text{H}_3\text{C}(7'')$), 2.17 (dddd, $^2J_{\text{H-H}} = 14.0$ Hz, $^3J_{\text{H-H}} = 8.6$, 6.1, 3.2 Hz, 1H, $\text{H}_\text{a}\text{C}(3)$), 1.86 (dtd, $^2J_{\text{H-H}} = 14.0$ Hz, $^3J_{\text{H-H}} = 6.1$, 2.9 Hz, 1H, $\text{H}_\text{b}\text{C}(3)$), 0.96 (s, 9H, $\text{H}_3\text{C}(1''')$), -0.02 (s, 3H, $\text{H}_3\text{C}(2''')$), -0.19 (s, 3H, $\text{H}_3\text{C}(2''')$).

^{13}C NMR (126 MHz, CDCl_3): δ 155.6, 148.3, 146.0, 140.1, 139.1, 137.2, 136.3, 129.3, 129.1, 127.7, 127.6, 125.6, 119.1, 82.4, 63.3, 40.1, 29.96, 28.0, 21.4, 18.6, -2.6, -3.1.

HRMS: $\text{C}_{24}\text{H}_{32}\text{IOSi}^+$ [$\text{M} + \text{H}$] $^+$ calc. 491.1262, found 491.1266.

(*Z*)-6-Iodo-4-(1-iodo-2-(*m*-tolyl)vinyl)chromane (**16j**)



Synthesis procedure:

In a 20 ml pressure flask, equipped with a magnetic stirrer and shielded from light with aluminum foil coating, (*Z*)-*tert*-butyl(1-(chroman-4-yl)-2-(*m*-tolyl)vinyl)dimethylsilane (**16e**) (45 mg, 0.12 mmol, 1.0 equiv) was suspended in $\text{CF}_3\text{CH}_2\text{OH}$ (4 ml). NIS (84 mg, 3.0 equiv) was added to the suspension (at room temperature), and the reaction mixture was refluxed for 6.5 hours. The reaction was quenched by addition of aqueous 10% $\text{Na}_2\text{S}_2\text{O}_3$ solution (4 ml), extracted with DCM (3 × 5 ml). The organic layer was dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure to afford the crude product. Reversed-phase column chromatography (90-95% MeOH/ H_2O) afforded the diiodinated product **16j** (58 mg, γ = 93%) as a colorless oil.

Characterization data for **16j**:

^1H NMR (500 MHz, CD_2Cl_2): δ 7.45 (s, 1H, H-C(5)), 7.46 – 7.43 (dd, $^3J_{\text{H-H}} = 8.4$, 2.2 Hz, 1H, H-C(7)), 7.31 – 7.22 (m, 3H, H-C(2''), 5'', 6''), 7.14 (d, $^3J_{\text{H-H}} = 7.4$ Hz, 1H, H-C(4'')), 6.74 (s, 1H, HC(2')), 6.62 (d, $^3J_{\text{H-H}} = 8.4$ Hz, 1H, H-C(8)), 4.28 (ddd, $^2J_{\text{H-H}} = 10.8$ Hz, $^3J_{\text{H-H}} = 7.1$, 3.3 Hz, 1H, $\text{H}_\text{a}\text{C}(2)$), 4.20 (ddd, $^2J_{\text{H-H}} = 10.8$ Hz, $^3J_{\text{H-H}} = 7.9$, 2.8 Hz, 1H, $\text{H}_\text{b}\text{C}(2)$), 3.83 (t, $^3J_{\text{H-H}} = 6.1$ Hz, 1H, HC(4)), 2.37 (s, 3H, $\text{H}_3\text{C}(1''')$), 2.37 – 2.30 (m, 1H, $\text{H}_\text{a}\text{C}(3)$), 2.07 (dddd, $^2J_{\text{H-H}} = 14.0$ Hz, $^3J_{\text{H-H}} = 7.1$, 6.1, 2.8 Hz, 1H, $\text{H}_\text{b}\text{C}(3)$).

^{13}C NMR (126 MHz, CD_2Cl_2): δ 155.6, 139.1, 138.7, 138.4, 138.3, 137.6, 129.7, 129.1, 128.3, 126.1, 126.1, 119.7, 112.6, 82.5, 63.9, 49.29, 29.0, 21.5.

HRMS: $\text{C}_{18}\text{H}_{17}\text{I}_2\text{O}^+$ [$\text{M} + \text{H}$] $^+$ calc. 502.9363, found 502.9326.

Cc1ccc(cc1)/C=C/C2C(=C(C=C2)OC)C(=C)C3=CC=CC=C3

Chemical structure of compound 10: Cc1ccc(cc1)/C=C/C2COC(=C2)c3ccc(I)cc3

¹H NMR spectrum (CDCl₃) of compound 10. The spectrum shows peaks in the aromatic region (6.5–7.5 ppm), a methine proton (2.4 ppm), a methoxy singlet (3.8 ppm), and aliphatic protons (2.2–2.6 ppm). Integration values are provided below the peaks.

Chemical Shift (ppm)	Integration
7.44	1.00
7.43	3.11
7.38	1.00
7.25	3.11
7.13	0.99
7.11	0.99
6.63	0.99
6.61	0.99
4.30	1.00
4.29	1.00
4.28	1.00
4.27	1.00
4.26	1.00
4.23	1.00
4.22	1.00
4.21	1.00
4.20	1.00
4.19	1.00
4.18	1.00
3.84	1.00
3.83	1.00
3.82	1.00
2.57	4.21
2.56	1.10
2.55	1.10
2.54	1.10
2.53	1.10
2.52	1.10
2.51	1.10
2.50	1.10
2.49	1.10
2.48	1.10
2.47	1.10
2.46	1.10
2.45	1.10
2.44	1.10
2.43	1.10
2.42	1.10
2.41	1.10
2.40	1.10
2.39	1.10
2.38	1.10
2.37	1.10
2.36	1.10
2.35	1.10
2.34	1.10
2.33	1.10
2.32	1.10
2.31	1.10
2.30	1.10
2.29	1.10
2.28	1.10
2.27	1.10
2.26	1.10
2.25	1.10
2.24	1.10
2.23	1.10
2.22	1.10
2.21	1.10
2.20	1.10
2.19	1.10
2.18	1.10
2.17	1.10
2.16	1.10
2.15	1.10
2.14	1.10
2.13	1.10
2.12	1.10
2.11	1.10
2.10	1.10
2.09	1.10
2.08	1.10
2.07	1.10
2.06	1.10
2.05	1.10
2.04	1.10
2.03	1.10
2.02	1.10
2.01	1.10
2.00	1.10
1.99	1.10
1.98	1.10
1.97	1.10
1.96	1.10
1.95	1.10
1.94	1.10
1.93	1.10
1.92	1.10
1.91	1.10
1.90	1.10
1.89	1.10
1.88	1.10
1.87	1.10
1.86	1.10
1.85	1.10
1.84	1.10
1.83	1.10
1.82	1.10
1.81	1.10
1.80	1.10
1.79	1.10
1.78	1.10
1.77	1.10
1.76	1.10
1.75	1.10
1.74	1.10
1.73	1.10
1.72	1.10
1.71	1.10
1.70	1.10
1.69	1.10
1.68	1.10
1.67	1.10
1.66	1.10
1.65	1.10
1.64	1.10
1.63	1.10
1.62	1.10
1.61	1.10
1.60	1.10
1.59	1.10
1.58	1.10
1.57	1.10
1.56	1.10
1.55	1.10
1.54	1.10
1.53	1.10
1.52	1.10
1.51	1.10
1.50	1.10
1.49	1.10
1.48	1.10
1.47	1.10
1.46	1.10
1.45	1.10
1.44	1.10
1.43	1.10
1.42	1.10
1.41	1.10
1.40	

Chemical structure of compound 10: Cc1c(Cc2ccc(I)cc2)oc3ccc(I)cc31

¹³C NMR spectrum (CDCl₃) of compound 10. The spectrum shows peaks at the following chemical shifts (ppm): 159.59, 139.07, 138.94, 138.95, 138.95, 137.61, 137.61, 129.68, 129.61, 129.61, 126.06, 125.72, 112.57, 55.51, 53.91, 53.29, 28.95, and 21.45.



Rasma Kroņkalne dzimusi 1997. gadā Rīgā. Rīgas Tehniskajā universitātē (RTU) ieguvusi bakalaura (2020) un maģistra (2022) grādu ķīmijas tehnoloģijā. Kopš 2020. gada ir RTU Organiskās ķīmijas tehnoloģijas institūta (tagad – Ķīmijas un ķīmijas tehnoloģijas institūts) zinātniskā asistente, kopš 2022. gada – pētniece. Zinātniskās intereses saistītas ar silīcijorganisko savienojumu reakcijām un to lietojumu heterociklu sintēzē.

Rasma Kroņkalne was born in 1997 in Riga. She obtained a Bachelor's degree (2020) and a Master's degree (2022) in Chemical Engineering from Riga Technical University (RTU). Since 2020, she has been a research assistant, and since 2022, a researcher at the RTU Institute of Technology of Organic Chemistry (now the Institute of Chemistry and Chemical Technology). Her research focuses on the reactions of silanes and their application in heterocycle synthesis.