RĪGAS TEHNISKĀ UNIVERSITĀTE

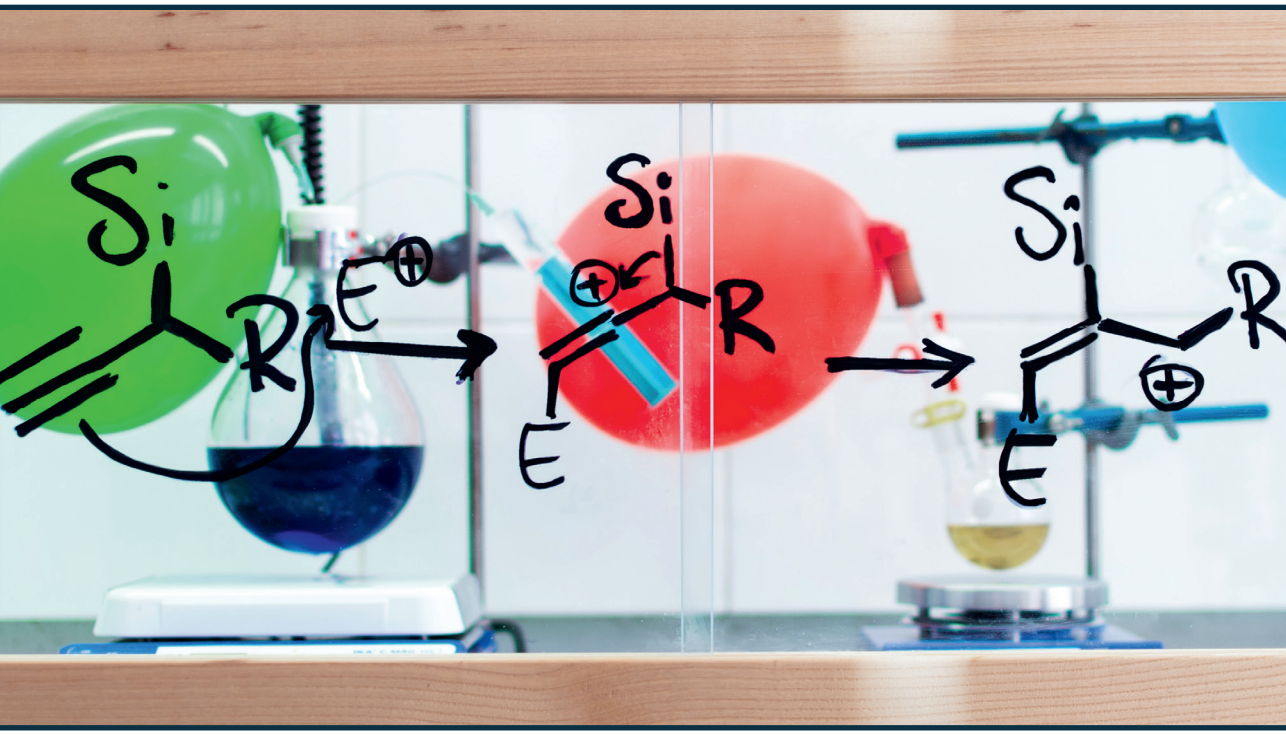
Rūdolfs Beļaunieks

SILILGRUPAS 1,2-NOBĪDES PIELIETOJUMS FUNKCIONALIZĒTU ALKĒNU SINTĒZĒ NO PROPARGILSILĀNIEM

Promocijas darbs

HARNESSING THE 1,2-SILYL SHIFT FOR THE SYNTHESIS OF FUNCTIONALIZED ALKENES FROM PROPARGYL SILANES

Doctoral Thesis



RTU Izdevniecība
RTU Press
Rīga 2023

RĪGAS TEHNISKĀ UNIVERSITĀTE
Materiālzinātnes un lietišķās ķīmijas fakultāte
Organiskās ķīmijas tehnoloģijas institūts
Bioloģiski aktīvo savienojumu ķīmijas tehnoloģijas katedra

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Doctoral Thesis

Zinātniskais vadītājs / Supervisor
profesors *Dr. chem.* MĀRIS TURKS

Rīga / Riga
RTU Izdevniecība / RTU Press
2023

Beļaunieks, R. Sililgrupas 1,2-nobīdes pielietojums funkcionalizētu alkēnu sintēzē no propargilsilāniem. Promocijas darbs. – Rīga: RTU Izdevniecība, 2023. – 75 lpp.

Beļaunieks, R. Harnessing the 1,2-Silyl Shift for the Synthesis of Functionalized Alkenes From Propargyl Silanes. Summary of the Doctoral Thesis. Riga: RTU Press, 2023. 75 p.

Iespiests saskaņā ar RTU promocijas padomes "RTU P-01" 2023. gada 12. septembra lēmumu, protokols Nr. 04030-9.1/56.

Published in accordance with the decision of the RTU Promotion Council "P-01" of September 12, 2023, Minutes No. 04030-9.1/43.

PATEICĪBAS

Milzīgs paldies manam draugam Mikum Puriņam un "Propargilsilānu" komandai – Rasmai Kroņkalnei, Rebekai Annai Līpiņai un Artjomam Ubaidullajevam par ieguldījumu šī darba tapšanā un paveikto kopīgu mērķu sasniegšanai!

Liels paldies manai ģimenei – mammai Emeritai, tētim Valdim, brālim Krišjānim un pārējiem par ieguldījumu, uzmundrinājumu un centību šad un tad saprast, ar ko es vispār nodarbojos!

Paldies arī maniem draugiem – Dacei, Kristeram, Agnijai, Nikam, Gintam, Elīzai, Reinim, Viktoram – par atbalstu, idejām, uzmundrinājumu un tām reizēm, kurās es nedomāju par šī darba izstrādi!

Visdziļākā pateicība manam darba vadītājam profesoram Mārim Turkam par zinātniskajām idejām, izaicinājumiem un sniegtajām zināšanām, kā arī par pasaules garšu izzināšanu formālās un neformālās sarunās!

Vissirsnīgākais paldies manai neoficiālajai darba vadītājai – sievai Santai par atbalstu, motivāciju un iedrošināšanu visu šo gadu laikā!

Promocijas darba pētījumi izstrādāti, pateicoties Eiropas Sociālā fonda finansējumam projektā Nr. 8.2.2.0/20/I/008 "Rīgas Tehniskās universitātes un Banku augstskolas doktorantu un akadēmiskā personāla stiprināšana stratēģiskās specializācijas jomās", kā arī Rīgas Tehniskās universitātes doktorantūras grantam.

ACKNOWLEDGEMENTS

My deepest gratitude to my dear friend Mikus Puriņš and "Team Propargyl Silanes" – Rasma Kroņkalne, Rebeka Anna Līpiņa, and Artjoms Ubaidullajevs for their contribution to the development of the Thesis!

I am grateful to my mom Emerita, dad Valdis, brother Krišjānis, and the rest of my family for their investment, encouragement, and for occasionally trying to understand what I was doing!

I am thankful to my friends – Dace, Kristers, Agnija, Niks, Gints, Elīza, Reinis, and Viktors – for their support, ideas, encouragement and for the special occasions where I was not thinking about this work!

My profound appreciation to my supervisor Professor Maris Turks, for the scientific ideas, challenges, and knowledge that I have gained, as well for the opportunity to discover diverse tastes of the world through our formal and informal conversations!

I sincerely appreciate my unofficial supervisor, my wife Santa, for all the conversations, support, and motivation during these years!

The Thesis research was supported by the European Social Fund within project No. 8.2.2.0/20/I/008 "Strengthening of Ph. D. students and academic personnel of Riga Technical University and BA School of Business and Finance in the strategic fields of specialization" and by Riga Technical University doctoral grant.

PROMOCIJAS DARBS IZVIRZĪTS ZINĀTNES DOKTORA GRĀDA IEGŪŠANAI RĪGAS TEHNISKAJĀ UNIVERSITĀTĒ

Promocijas darbs zinātnes doktora (*Ph. D.*) grāda iegūšanai ķīmijas nozares organiskās ķīmijas apakšnozarē tiek publiski aizstāvēts 2023. gada 13. oktobrī plkst. 14:00 Rīgas Tehniskās universitātes Materiālzinātnes un lietišķās ķīmijas fakultātē, Rīgā, Paula Valdena ielā 3, 272. auditorijā.

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APSTIPRINĀJUMS

Apstiprinu, ka esmu izstrādājis 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.

Rūdolfs Beļaunieks ……..….
(*paraksts*)

Datums …...……...….

Promocijas darbs sagatavots kā tematiski vienotu zinātnisko publikāciju kopa ar kopsavilkumu latviešu un angļu valodā. Tajā ietverti četri zinātniskie oriģinālraksti. Publikācijas zinātniskajos žurnālos uzrakstītas angļu valodā, to kopējais apjoms, ieskaitot pielikumus, ir 204 lpp.

SATURS

Pielikums V: Līpiņa, R.A., Beļaunieks, R., Turks, M. Enantioselektīvas metodes izstrāde elektrofīlu ierosinātām termināli funkcionalizētu propargilsilānu heterociklizācijas reakcijām. *Nepublicēti rezultāti.*

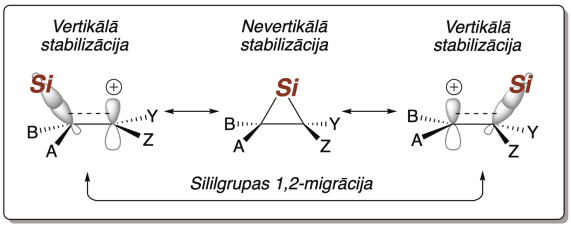
Pielikums VI: Beļaunieks, R., Turks, M. Propargilsilānu arilēšanas reakcijas ar hipervalentā joda reaģentiem vara katalizētos apstākļos. *Nepublicēti rezultāti.*

PROMOCIJAS DARBA VISPĀRĒJS RAKSTUROJUMS

Tēmas aktualitāte

Organiskās ķīmijas kontekstā silīcijs bieži vien tiek uzskatīts kā analogs ogleklim. Abi ir 14. grupas elementi, līdz ar to tiem ir raksturīga tetravalentā konfigurācija. Tie abi galvenokārt veido kovalentās saites, kas ar elektronegatīviem atomiem ir īpaši stipras,[1] un to ķīmiskās reaģētspējas īpatnības, piemēram, nukleofīlās aizvietošanas reakcijas ar stereocentra konfigurācijas inversiju uz centrālā atoma,[2] vairumā gadījumu sakrīt. Atšķirības starp abiem elementiem ievieš silīcija atrašanās trešajā periodā, kas saskaņā ar vispārējām likumsakarībām palielina atoma izmēru,[3] samazina tā elektronegativitāti[4] un padara enerģētiski pieejamākas vakantās *d*-orbitāles.[5] Visu šo efektu kopsumma nodrošina silīcijam papildu īpašības, kas ir pamatā tā plašajam lietojumam organiskajā sintēzē: 1) efektīvas aizsarggrupas spirtiem un termināliem alkīniem;[6] 2) spēja veidot hipervalentās saites,[7] padarot to par spēcīgu Luisa skābi; 3) C-Si saites polarizējamība Tamao-Fleminga oksidēšanas[8] un Hijamas-Denmarka šķērssametināšanas reakcijās.[9]

Papildus tam silīcijam raksturīga un organiskajā ķīmijā plaši lietota īpašība ir tam piemītošā β-pozīcijā esošu karbkatjonu stabilizācija, kas plašāk zināma kā β-silīcija efekts.[10] Šis efekts var izpausties divos galvenajos ceļos – vertikālā stabilizācija (C-Si saites hiperkonjugācija ar nepiesātināto π-sistēmu) vai nevertikālā stabilizācija (trīs atomu, četru elektronu cikliska silonija jona veidošanās; 1. shēma). Abi šie stabilizācijas veidi atrodas nepārtrauktā līdzsvarā, tāpēc, veidojoties jaunajai C-Si saitei cikliskajā stabilizācijas formā un pēc tam šķeļoties vecajai C-Si saitei, molekulā ir iespējams novērot izmaiņas tās skeleta struktūrā – 1,2-siligrupas migrāciju, iegūstot jau citu β-stabilizētu katjonu.[10]



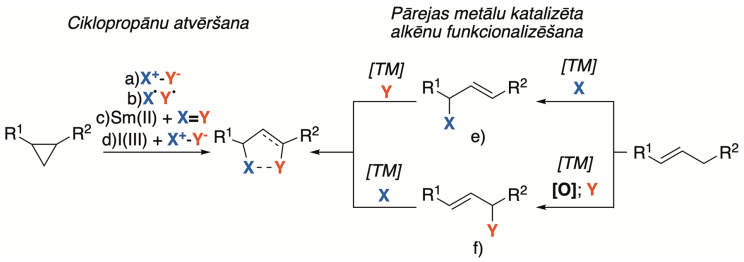
1. shēma. β-Silīcija efekts – vertikālā un nevertikālā stabilizācija karbēnija jonos un iespējamā sililgrupas 1,2-migrācija.

Sililgrupas pārnese galvenokārt ir raksturīga sistēmām, kas vai nu saskaņotā migrācijas rezultātā izraisa stabilāka produkta veidošanos, vai arī vairāku efektu rezultātā veido enerģētiski izdevīgāku reakcijas starpstāvokli. Tipiski šādas pārgrupēšanās ir novērotas un līdz ar to pētītas dažādās elektrofīlu reakcijās ar nepiesātinātām sistēmām.

Visbiežāk vienkāršākās nepiesātinātās sistēmas, piemēram, alkēni, allēni un alkīni, kā arī to konjugētie analogi, ir plaši pētītas 1,2- un 1,4-difunkcionalizēšanas kontekstā. Savukārt alil-, allenil- un propargilsilāni elektrofīlu reakcijās ar nepiesātināto sistēmu var ierosināt sililgrupas

1,2-migrāciju, formāli veidojot 1,3-dipolu. Tas, reaģējot ar reakcijas vidē esošajiem nukleofīliem, noslēdz šādu nepiesātināto sistēmu 1,3-difunkcionalizēšanu.[10]

Vispārīgi literatūrā 1,3-difunkcionalizēšana ir pētīta salīdzinoši mazāk nekā analogās 1,2- un 1,4-difunkcionalizēšanas reakcijas. Kā galvenos piemērus var minēt (2. shēma): a) donoro un akceptoro grupu saturošo ciklopropānu atvēršanas reakcijas ar elektrofīla/nukleofīla pāriem;[11] b) ciklu atvēršanu ar reaģentiem, kas veido radikāļu vai katjonradikāļu starpsavienojumus;[12] c) ciklu atvēršana reducējošos apstākļos, izmantojot SmI_2 kā reducētāju;[13] d) hipervalentā joda katalizēta cikla atvēršana;[14] e) pārejas metālu katalizētas 1,2-pievienošanās-nepiesātinātās sistēmas izomerizēšanās-reducējošā eliminēšana;[15] f) alkēnu alilpozīcijas oksidēšana ar sekojošu nepiesātinātās sistēmas funkcionalizēšanu.[16] Diemžēl neviena no šīm piedāvātajām metodēm neļauj veikt vienkāršu un secīgu izvēlētās triādes funkcionalizēšanu.



2. shēma. Ciklopropānu atvēršanas un pārejas metālu katalizētas alkēnu reakcijas 1,3-difunkcionalizētu produktu iegūšanai.

Promocijas darbā izstrādātas jaunas metodes, kas ļauj veikt propargilsilānu 1,3-difunkcionalizēšanu ar dažādiem elektrofīla/nukleofīla pāriem. Turklāt atkarībā no konkrētās metodes iegūtie produkti var saturēt līdz pat trīs reakcijas centriem C1, C2 un C3 pozīcijā. Tas paver iespēju šo būvbloku tālākai izmantošanai farmācijā vai materiālzinātnē noderīgu savienojumu selektīvā sintēzē.

Pētījuma mērķis un uzdevumi

Promocijas darba mērķis ir teorētiskā koncepta attīstīšana un jaunu sintēzes metožu izstrāde, ģenerējot alilkatjonus no propargilsilāniem un pārvēršot tos par funkcionalizētiem produktiem.

Darba mērķa īstenošanai definēti vairāki uzdevumi.

1. Izpētīt šķidrā SO_2 kā Luisa skāba šķīdinātāja izmantošanu silildiēnu iegūšanai, kas reakcijas vidē tūlītēji piedalītos heletropajā reakcijā ar SO_2, dodot sililsulfolēnus viena reaktora sintēzē no propargilsilāniem.
2. Izstrādāt metodes alilfunkcionalizētu vinilsilānu iegūšanai elektrofīlu ierosinātās propargilsilānu reakcijās ar šķīdinātājiem kā ārējiem nukleofīliem.
3. Piedalīties kopprojektā par terminālo alkīnu un iekšējo nukleofīlu saturošu propargilsilānu elektrofīlu ierosinātas heterociklizācijas metodikas izstrādi un iegūto

produktu tālākas funkcionalizēšanas iespējamību. Pārbaudīt asimetriskās indukcijas koncepta iespējamību šo reakciju kontekstā.

4. Pārbaudīt propargilsilānu arilēšanas iespējas ar hipervalentajiem joda savienojumiem vara katalizētos apstākļos.

Zinātniskā novitāte un galvenie rezultāti

Veikto pētījumu rezultātā izstrādātas jaunas organiskās sintēzes metodes, kas nostiprina propargilsilānu kā formālu 1,3-dipolu lietojumu. Tas ir iespējams, pateicoties β-silīcija efektam un no tā izrietošajai sililgrupas 1,2-migrācijai. Jauniegūtie savienojumi tika demonstrēti kā vērtīgas izejvielas tālākās funkcionalizēšanas reakcijās.

Promocijas darbā izstrādāta metode, kurā silildiēnus ir iespējams sintezēt no propargilsilāniem šķidrā SO_2 kā Luisa skābā vidē. Tas ļauj samazināt procesa aktivācijas barjeru un izmantot daudz vājākas Brensteda skābes, piemēram, TsOH un pat H_2O (salīdzinot ar iepriekš lietotajām TfOH un $HNTf_2$). Iegūtie silildiēni šajos pašos reakcijas apstākļos stājās heletropajās reakcijās ar SO_2, ļaujot iegūt sililsulfolēnus viena reaktora sintēzē.

Promocijas darbā radīta jauna sintēzes metode (*E*)-selektīvai alilfunkcionalizētu trīsaizvietotu vinilsilānu iegūšanai elektrofīlu ierosinātās propargilsilānu reakcijās ar nukleofīliem šķīdinātājiem. Šis koncepts izmantots arī (*E*)-selektīvai iekšējo nukleofīlu saturošu propargilsilānu heterociklizācijai, iegūstot heterociklus ar funkcionalizētu vinilsilānu sānu ķēdi. Tika veiksmīgi demonstrēta jauniegūto savienojumu, kas satur divus vai trīs reakcijspējīgus centrus, tālāka funkcionalizēšana pārejas metālu katalizētā šķērssametināšanas, silīcija elektrofīlās aizvietošanas un joniskās iekšmolekulārās ciklizācijas reakcijās. Pierādīta asimetriskās katalīzes koncepta iespējamība propargilsilānu heterociklizācijas reakcijās hirālu Brensteda skābju klātienē.

Promocijas darbā piemeklēti eksperimentālie apstākļi propargilsilānu arilēšanas reakcijām ar hipervalentā joda reaģentiem vara katalizētos apstākļos, kas nākotnē tiks izstrādāta kā jauna sintēzes metode.

Darba struktūra un apjoms

Promocijas darbs sagatavots kā tematiski vienotu zinātnisko publikāciju kopa, kas veltīta pētījumiem par propargilsilānu izmantošanu augsti funkcionalizētu alkēnu sintēzē ar sililgrupas 1,2-migrāciju. Tas ietver trīs oriģinālpublikācijas *SCI* žurnālos un vienu apskatrakstu.

Darba aprobācija un publikācijas

Promocijas darba galvenie rezultāti publicēti trīs zinātniskajos oriģinālrakstos. Promocijas darba izstrādes laikā sagatavots viens apskatraksts. Pētījumu rezultāti prezentēti 10 zinātniskajās konferencēs.

Zinātniskās publikācijas

1. Kroņkalne, R., **Beļaunieks, R.**, Ubaidullajevs, A., Mishnev, A., Turks, M. 1,2-Silyl Shift-Induced Heterocyclization of Propargyl Silanes: Synthesis of Five-Membered Heterocycles Containing Functionalized Olefin Side Chain. *J. Org. Chem.* **2023**, DOI: 10.1021/acs.joc.3c01481.
2. **Beļaunieks, 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*, 4627.
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Pētījumu rezultāti prezentēti 10 zinātniskajās konferencēs.

1. **Beļaunieks, R.**, Puriņš, M., Līpiņa, R. A., Turks, M. Synthesis of Allyl Functionalized Vinyl Silanes from Propargyl Silanes via 1,2-Silyl Migration. In: *International Symposium on Synthesis and Catalysis, Book of Abstracts*, Portugal, Evora, September 5–8, **2023**, p. 126.
2. **Beļaunieks, R.**, Puriņš, M., Līpiņa, R. A., Turks, M. Use of Propargylsilanes for the Preparation of Highly Functionalized Alkenes via 1,2-Silyl Migration. In: *81st International Scientific Conference of the University of Latvia, Chemistry section, Book of Abstracts*, Latvia, Riga, March 17, 2023. Riga: University of Latvia, 2023, p. 15.
3. Kroņkalne, R., **Beļaunieks, 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, Chemistry section, Book of Abstracts* Latvia, Riga, March 17, 2023. Riga: University of Latvia, 2023, 14.
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6. **Beļaunieks, R.**, Puriņš, M., Kroņkalne, R., Līpiņa, R. A., Ubaidullajevs, A., Turks, M. Synthesis of Highly Functionalized Alkenes from Propargyl Silanes via 1,2-Silyl Migration. In: *Stereoselective Alkene Functionalizations: Beilstein Organic Chemistry Symposium 2022*, Germany, Rüdesheim am Rhein, April 26-28, **2022**. Beilstein Institut, 2022, p. 32.

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10. **Beļaunieks, R.**, Puriņš, M. Synthesis of Silyl Sulfolenes in Tandem Transformation from Propargyl Silanes in Liquid SO2. In: *78st International Scientific Conference of the University of Latvia, Chemistry section, Book of Abstracts*, Latvia, Rīga, March 6, 2020. Riga: University of Latvia, 2020, p. 46.

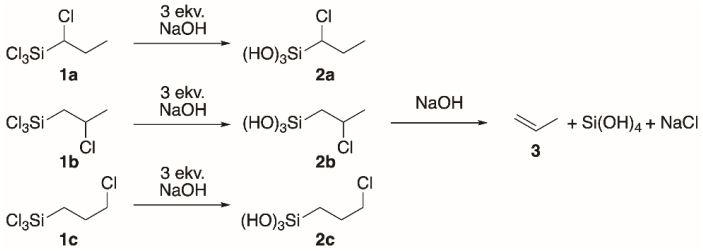
PROMOCIJAS DARBA GALVENIE REZULTĀTI

Silīcija atvasinājumus organiskajā sintēzē lieto kā efektīvas aizsarggrupas gan spirtiem, gan terminālajiem alkīniem.[6] To lietojums ir arī salīdzinoši plaši aptverts tādās reakcijās kā Pītersona olefinēšana,[17] Tamao-Fleminga oksidēšana,[8] kā arī Hijamas-Denmarka[9] šķērssametināšanas reakcija. Turpretim β-silīcija efekts ir labi izpētīta, bet mazāk izmantota silīcijam raksturīga īpašība organisko pārvērtību veikšanai. Kā galveno piemēru, kurā β-silīcija efektam ir liela nozīme, var minēt alilsilānu pāvērtības Hosomi-Sakurai tipa reakcijās.[18] Tajās elektrofīls inducē katjona veidošanos nepiesātinātās sistēmās, ko stabilizē β-pozīcijā esošā sililgrupa. Šāda tipa reakcijās spēj piedalīties arī propargilsilāni. Literatūrā ir zināmi piemēri propargilsilānu elektrofīlai aktivācijai ar sekojošu sililgrupas eliminēšanos, bet promocijas darba autoram sintētiski interesantāka likās pēc aktivācijas sekojoša sililgrupas 1,2-migrācija, kas paver iespēju propargilsilānus izmantot kā formālus 1,3-dipolus.

Promocijas darbā izstrādātas jaunas sintētiskās metodes ar mērķi paplašināt propargilsilānu lietojumu kā formālu 1,3-dipolu un iegūt organiskajā sintēzē plaši lietojamas, augsti funkcionalizētas atomu triādes.

1. β-Silīcija efekts un tā lietojums 1,2-sililgrupas migrēšanai propargilsilānos

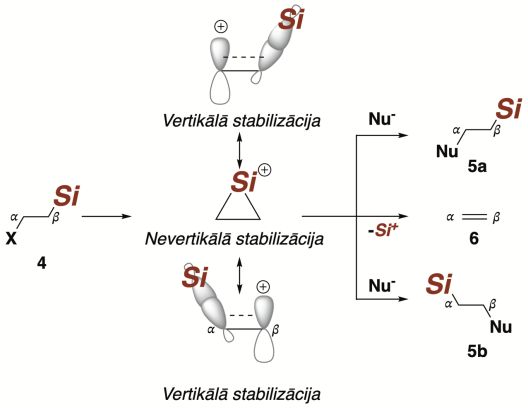
Pirmie ziņojumi par reaģētspējas izmaiņām, ko veicina β-silīcija aizvietotājs, tika publicēti 1946. gadā no Sommera (*Sommer*) un Vitmora (*Whitmore*) laboratorijas.[19,20] Titrējot dažādus 1-trihlorsililpropāna monohlorētos reģioizomērus **1a-c** ar 3 ekvivalentiem auksta 0.5 M NaOH šķīduma, visos gadījumos tika novēroti Si-Cl saites hidrolīzes produkti **2a-c** (3. shēma). Pārsteidzoši, ka, turpinot bāzes šķīduma pievienošanu, tikai β-aizvietotais 2-hlor-1-trihlorsililpropāns **1b** turpināja reaģēt ar papildu 1 ekvivalentu NaOH, dodot eliminēšanās produktu propēnu (**3**).



3. shēma. Pirmie demonstrējumi β-silīcija efektam – monohlorētu 1-trihlorsililpropāna reaģētspēja ar 0.5 M NaOH šķīdumu.

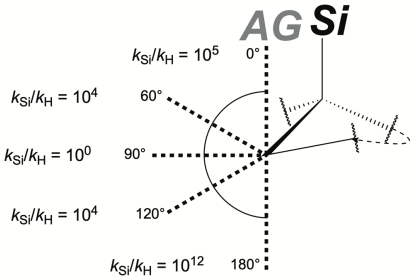
Papildu eksperimenti eliminēšanās produkta veidošanās mehānisma izpratnei liecināja par to, ka šāda tipa solvolīzes reakcijas noris caur E1 tipa mehānismu, kur pirmais un lēnākais solis ir aizejošās grupas saites šķelšana, veidojoties β-silīcija stabilizētam karbēnija jonam. Šo parādību postulēja kā β-silīcija efektu[10] – stabilu reakcijas starpstāvokli, kuram tika piedāvāti divi izšķirami strukturāli modeļi pozitīvā lādiņa stabilizācijai: vertikālās stabilizācijas

starpstāvoklis, kur hiperkonjugācijas rezultātā C-Si σ-saites elektroni tiek donēti vakantajā *p*-orbitālē vai nevertikālais stabilizācijas starpstāvoklis, kur veidojas četru elektronu, trīs atomu cikliskais silonija jons, kur pozitīvais lādiņš ir delokalizēts uz silīcija atoma (4. shēma).



4. shēma. Iespējamie starpstāvokļi β-silīcija stabilizētos karbēnija jonos.

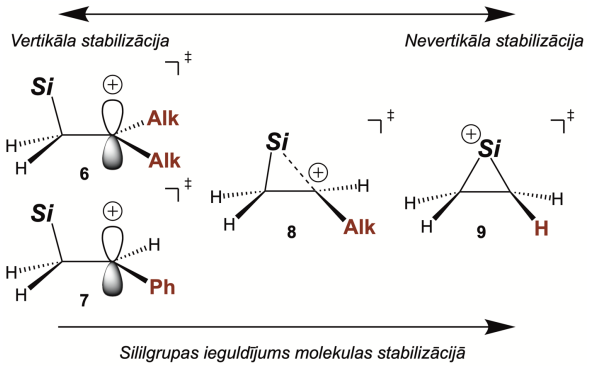
β-Silīcija aizvietotāju ietekme uz aizejošās grupas jonizācijas ātrumu var sasniegt līdz pat 12 kārtu paātrinājumu, tāpēc vairākas zinātnieku grupas ķērās klāt šī fenomena izpratnei. Lai noteiktu konformacionālos ierobežojumus, lielu ieguldījumu ir sniedzis Lamberts (*Lambert*) ar darba grupu (5. shēma).[21–25] Sintezējot dažādus konformacionāli ierobežotus sililatvasinājumus, kur silīcija un aizejošās grupas (AG) torsijas leņķis ir fiksēts, iegūtie savienojumi tika salīdzināti solvolīzes reakcijās ar to nesililētiem analogiem. Tika noskaidrots, ka lielākais reakcijas ātruma pieaugums ir novērojams *anti*-periplanārā novietojumā – 10^{12} reižu. *Sin*-periplanārā novietojumā tika novērots mazāks reakcijas ātruma pieaugums, ko, iespējams, kavēja aizejošās grupas mijiedarbība ar stabilizējošo sililaizvietotāju – 10^5 reizes.



5. shēma. Solvolīzes ātruma izmaiņas atkarībā no Si-C-C-AG torsijas leņķa.

Reakcijas ātruma pieaugums tika novērots arī *gauche* un *anti*-klinālajā konformācijā (10^4 reizes). Tas netieši liecina, ka β-silīcija efekts var izpausties arī ar daļēju orbitāļu pārklāšanos. Savukārt ortogonālajā konfigurācijā netika novērots nekāds reakcijas ātruma pieaugums, kas liecina, ka β-silīcija efekta izpausme ir iespējama, pateicoties vertikālajai un nevertikālajai stabilizācijai, bet ne indukcijas efektam no elektronus donējošā sililaizvietotāja.[21–25]

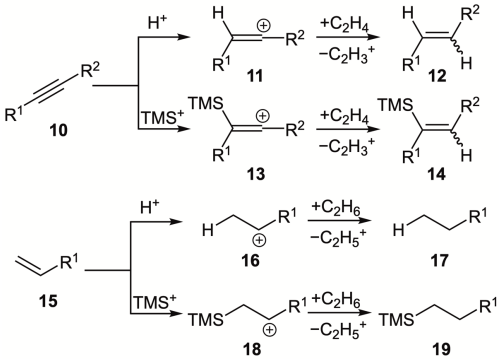
Konformacionāli ierobežotie silāni gan nesniedz atbildi, vai un kāda nozīme β-silīcija efekta izpausmē ir nevertikāli stabilizētajam starpstāvoklim, jo iepriekšējos rezultātus var viegli pamatot ar hiperkonjugācijas esamību. Jorgensena (*Jorgensen*) grupas kvantu aprēķini[26, 27] un Fudžio (*Fujio*) grupas (6. shēma) veiktie eksperimenti[28–31], kas tika interpretēti ar Jukavas-Cuno (*Yukawa-Tsuno*) vienādojuma palīdzību, deva ieskatu šajā jautājumā.



6. shēma. MP3/6-31G* līmeņa stabilizācijas enerģijas aprēķini dažādām β-silīcija karbkatjonu sistēmām un vertikālās un nevertikālās stabilizācijas nozīme atkarībā no aizvietotājiem pie katjonā centra.

No rezultātiem tika secināts, ka sistēmās bez stabilizējošām grupām pie katjona centra, kā tas ir savienojumā **9**, dominē nevertikālais stabilizācijas modelis un sililgrupas ieguldījums tās stabilizācijā ir salīdzinoši lielāks. Savukārt dialkilaizvietotos katjonos **6** un benzilkatjonos **7** dominē vertikālais stabilizācijas modelis, kā arī sililaizvietotāja ieguldījums kopējā molekulas stabilizācijā ir salīdzinoši zemāks nekā savienojumā **9**. Monoalkilaizvietotos β-silīcija stabilizētos karbkatjonos **8** rezultāti liecina par nenoteiktu stāvokli starp vertikālo un nevertikālo stabilizāciju.[26–31]

β-Silīcija stabilizācijas spējas ir pētītas arī vinilkatjonos. Stouns (*Stone*)[32] un viņa līdzstrādnieki analizēja termodinamiskos datus elektrofīlu (TMS^+ un H^+) pievienošanai dažādi aizvietotiem alkīniem un alkēniem (7. shēma). No izmērītajām rašanās ΔH vērtībām var secināt, ka β-silīcija efekta pienesums, kas tika noteikts kā starpība starp sililētu karbkatjonu **11** un nesililētu karbkatjonu **13** rašanās vērtībām, $\Delta\Delta H$ ir 8.8–11.6 kkal/mol. Līdzīgi tika noteikta arī β-silīcija efekta ieguldījums karbkatjonu **16** un **18** stabilizēšanā. Alkilaizvietotu karbkatjonu gadījumā sililgrupas pienesums $\Delta\Delta H$ bija pat 26,2 kkal/mol, savukārt ar arilaizvietotāju – vien 16.7 kkal/mol, kas apstiprina iepriekš aprakstītos rezultātus.

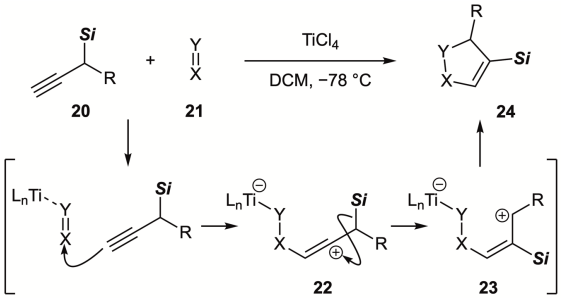


R^1	R^2	ΔH_{Stab} **11**, kkal/mol	ΔH_{Stab} **13**, kkal/mol	$\Delta\Delta H$, kkal/mol
H	*n*-C_4H_9	44.2	54.9	10.7
CH_3	*n*-C_3H_7	46.2	57.8	11.6
H	C_6H_5	49.6	58.4	8.8

R^1	ΔH_{Stab} **16**, kkal/mol	ΔH_{Stab} **18**, kkal/mol	$\Delta\Delta H$, kkal/mol
n-C_4H_9	34.1	60.3	26.2
C_6H_5	43.6	60.3	16.7

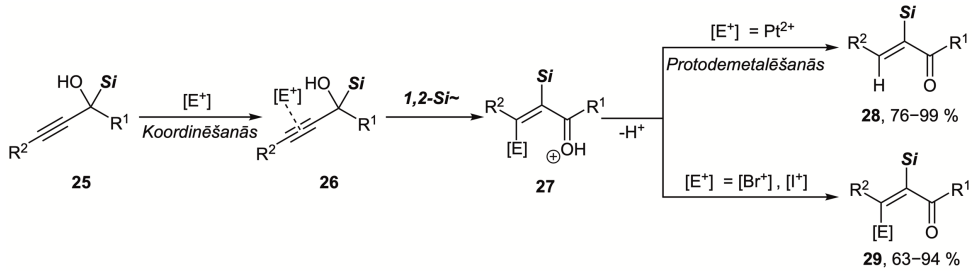
7. shēma. Sililvinil- un sililkarbkatjonu un to ģenerēšana hiperkonjugācijas efektu pētīšanai.

β-Sililgrupu saturošs karbkatjons var veidot nevertikāli stabilizēto silonija jonu, kurā var notikt sililgrupas 1,2-migrācija, ja tas saskaņotā procesā izraisa stabilāka produkta rašanos vai vairāku apstākļu rezultātā rodas enerģētiski izdevīgāks starpprodukts. Pirmo reizi sililgrupas 1,2-migrāciju propargilsilānos novēroja 1985. gadā Miginjaka (*Miginiac*) grupā kā blakusreakciju starp propargilsilāniem un acetāliem.[33] Tālākus plašus pētījumus šajā virzienā veica Danheizers (*Danheiser*) ar līdzstrādniekiem [2 + 3] annulēšanas ķīmijā. Pēc vispārējās shēmas 1,2-dipola **21** elektrofīlā daļa reaģē ar propargilsilānu **20**, un pēc sililgrupas 1,2-migrācijas veidojas starpsavienojums **23**, kas tālāk saslēdz ciklu, alilkatjonam reaģējot ar iekšmolekulāro nukleofīlo centru. Tādējādi rodas [2 + 3] ciklizēšanās produktu **24** – ciklopentēni, 1,2,5,7a-tetrahidro-*3H*-pirolizīn-3-oni, izoksazoli un azulēni (8. shēma).[34]



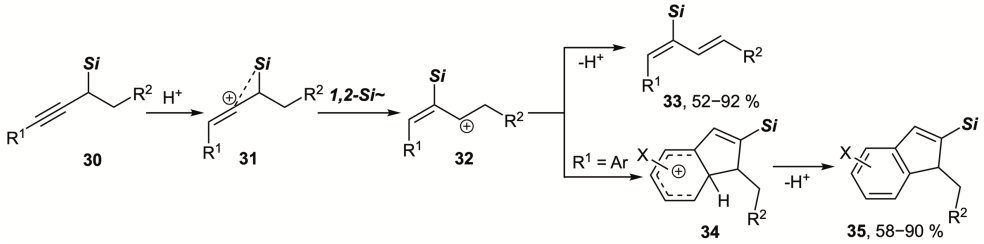
8. shēma. Vispārīgā shēma annulēšanas reakcijām no 1,2-dipoliem un propargilsilāniem.

Līdz šim visās apskatītajās reakcijas ar propargilsilāniem pamatā bija divu stuktūrfragmentu saistīšana, veidojot sarežģītākas molekulārās struktūras no vienkāršām izejvielām. Nozīmīgu ieguldījumu propargilsilānu funkcionalizēšanā ir veikusi Fereiras (*Ferreira*) grupa. Viņi pirmo reizi demonstrēja, ka α-hidroksipropargilsilānus **25** ir iespējams aktivēt un ierosināt semisililpinakola tipa sililgrupas 1,2-migrāciju ar pārejas metālu un halogēnu elektrofīlajiem reaģentiem (9. shēma). Tiek ģenerēts oksokarbēnija jons **27**, kas pēc sekojošas deprotonēšanas dod α,β-nepiesātinātus ketonus **28** un **29** ar augstu stereokontroli un tālākām funkcionalizēšanas iespējām.[35, 36]



9. shēma. α-Hidroksipropargilsilānu **25** aktivēšanas reakcijas ar pārejas metālu un halogēnu elektrofīliem.

Savukārt promocijas darba autora zinātniskajā grupā tika atklāts, ka ar Brensteda superskābēm (TfOH, Tf_2NH, Tf_3CH) ir iespējams aktivēt un inducēt sililgrupas 1,2-migrāciju propargilsilānos **30**, ģenerējot alilkatjonu **32**. Atkarībā no reakcijas apstākļiem un molekulas struktūras tas var veikt vai nu β-protona eliminēšanu, veidojot silildiēnus **33**, vai iekšmolekulāru ciklizācijas reakciju un dot sililindēnus **35**, ja molekula satur piemērotu π-nukleofīlu (10. shēma).[37]



10. shēma. Propargilsilānu **30** aktivēšanas reakcijas ar Brensteda superskābēm.

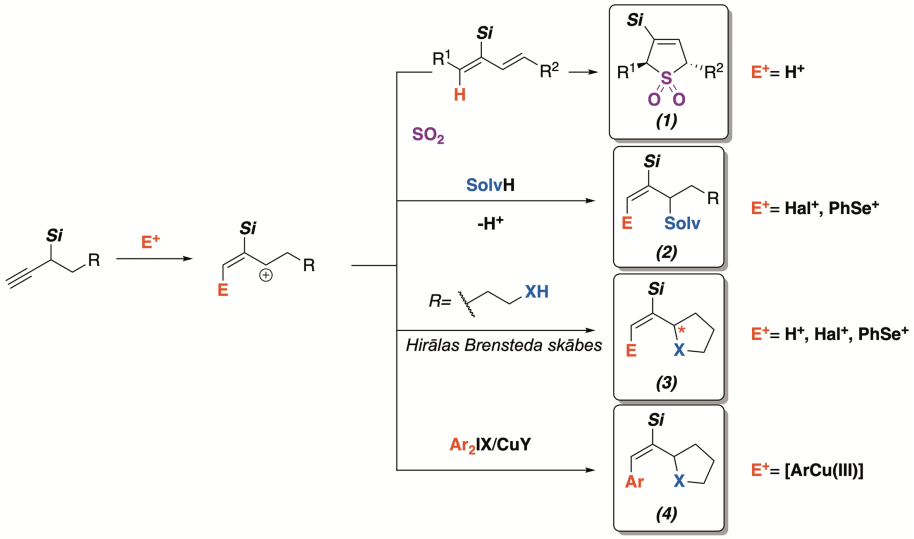
Balstoties iepriekš ziņotajos panākumos propargilsilānu 1,3-difunckionalizēšanas reakcijās, promocijas darbā veiktie pētījumi tika veltīti jaunu sintēzes metožu izstrādei, kas paplašina šo pētījumu virzienu. Promocijas darbs tika iedalīts četros virzienos (11. shēma):

(1) šķidrā SO_2 kā Luisa skābas reakcijas vides izmantošana sililgrupas 1,2-migrācijas ierosināšanai propargilsilānos, dodot silildiēnus, kas uzreiz tiktu saistīti heletropās ciklopievienošanās reakcijā ar SO_2, dodot sililsulfolēnus viena reaktora sintēzē;

(2) propargilsilānu izmantošana elektrofīlu ierosinātās sililgrupas 1,2-migrācijas reakcijās ar šķīdinātājiem kā nukleofīliem (*E*)-selektīvai alilfunkcionalizētu vinilsilānu iegūšanai;

(3) terminālo alkīnu un iekšējo nukleofīlu saturošu propargilsilānu izmantošana elektrofīlu ierosinātās heterociklizācijas reakcijās un tās asimetriskās versijas koncepta izstrāde;

(4) jaunu "C-elektrofīlu" sintonu meklējumi propargilsilānu aktivēšanai ar sekojošu sililgrupas 1,2-nobīdi, kas noslēdzas ar alilkatjona dzēšanu nukleofīla pievienošanās rezultātā.

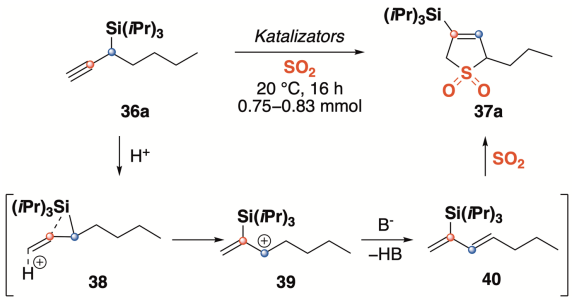


11. shēma. Promocijas darba pētījumu virzieni.

1.1. Sililsulfolēnu sintēze no propargilsilāniem šķidrā sēra dioksīdā

Iepriekš promocijas darba autora pētniecības grupā šķidrais sēra dioksīds ir demonstrēts kā lieliska alternatīva klasiskajiem šķīdinātājiem. Normālos apstākļos SO_2 ir bezkrāsaina gāze ar asu smaržu, bet tā relatīvi augstā viršanas temperatūra (–10°C) un zemais tvaika spiediens (3 bar, 20 °C; 20 bar 100 °C) ļauj to viegli sašķidrināt un izmantot plašā temperatūru diapazonā, kā arī pēc tam viegli aizvākt no reakcijas vides, mainot temperatūras un spiediena parametrus. Šķidrs SO_2 ir uzskatāms par vidēji polāru (dipola moments – 1.75, dielektriskā konstante – 20.6), aprotonu šķīdinātāju. To pārāku par citiem šķīdinātājiem padara tā izteiktās Luisa skābes īpašības[38], kas ļauj tam veicināt reakcijas, kas noris ar katjona centra veidošanos. Tādas, piemēram, ir alkīnu[39] un metilēnciklopropānu[40] hidrofunkcionalizēšanas reakcijas un glikozilēšanas reakcijas.[41]

Promocijas darba autora grupā iepriekš izstrādātajai skābes katalizētajai propargilsilānu **36** izomerizēšanas reakcijai par 2-silil-1,3-diēniem **40** bija nepieciešami tādi šķīdinātāji kā CH_2Cl_2 un $CHCl_3$ un Brensteda superskābes kā TfOH, Tf_2NH un Tf_3CH.[37] Tika izvirzīta hipotēze, ka, pateicoties šķidrā SO_2 Luisa skābes īpašībām, šo transformāciju būtu iespējams veikt ar ievērojami vājākām Brensteda skābēm (12. shēma). Šoreiz iegūtie silildiēni **40** būtu tikai starpprodukti, kas uzreiz iesaistītos heletropajā ciklopievienošanās reakcijā ar SO_2, ģenerējot 3-silil-3-sulfolēnus **37**. Tas paver iespējas produktus **37** izmantot kā formālu ekvivalentu attiecīgajiem silildiēniem **40** šo savienojumu atvieglotai attīrīšanai un 1,4-funkcionalizēšanai.[42]



12. shēma. Tandēmā sililgrupas 1,2-migrācijas – heletropā pievienošanās sekvence viena reaktora sintēzē sililsulfolēna **37a** iegūšanai un tās piedāvātais reakcijas mehānisms.

Pētījumi tika sākti ar piemērotākā katalizatora noskaidrošanu (1. tab.). Veicot reakcijas komerciāli pieejamajā SO_2, kas satur līdz 50 ppm ūdens, tādas skābes kā $TsOH \cdot H_2O$, PhCOOH, $(NH_4)_2SO_4$ bija pietiekami spēcīgas, lai ierosinātu šo pārvērtību. Par pārsteigumu reakcijas ierosināšanai pietika pat tikai ar SO_2 esošajām ūdens zīmēm. Tādi spirti kā *t*BuOH un tādi fenoli kā BHT molekulāro sietu klātbūtnē gan nespēja ierosināt šo pārvērtību. 1.–4. eksperiments (1. tab.) liecina, ka ūdens zīmes netraucē reakcijas norisei, lietojot Brensteda skābes šķidrā SO_2 vidē pK_A diapazonā no ūdens līdz TsOH.

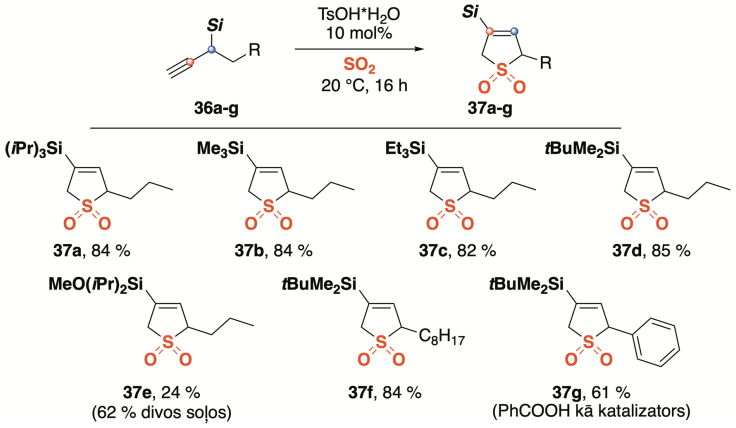
1. tabula

Piemērotākā katalizatora pārbaude tandēmā sililgrupas 1,2-migrācija – heletropā pievienošanās reakcijai saskaņā ar 12. shēmu

Nr. p. k.	Katalizators (mol %)	KMR iznākums produktam **37a**,[a] %
1.	$TsOH \cdot H_2O$ (10)	84
2.	PhCOOH (10)	72
3.	$(NH_4)_2SO_4$ (10)	75
4.	H_2O (100)	67
5.	H_2O[b]	75
6.	3 Å MS	< 5
7.	*t*BuOH (10) + 3 Å MS	< 5
8.	BHT (10) + 3 Å MS	< 5

[a] Difenilmetāns kā iekšējais standarts, vidējais rezultāts no diviem eksperimentiem.
[b] Ūdens (līdz 50 ppm) komerciāli pieejamajā SO_2.

Labāko iznākumu uzrādīja $TsOH \cdot H_2O$, tāpēc tas tika izvēlēts tālākiem substrātu klāsta pētījumiem (13. shēma).

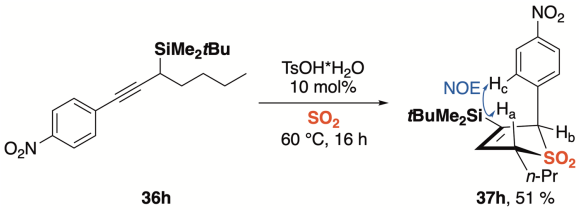


13. shēma. Produktu klāsts tandēmā sililgrupas 1,2-migrācijas – heletropā pievienošanās sekvencē viena reaktora sintēzē.

Tika noskaidrots, ka vienkāršākās trialkilsililgrupas reakcijas iznākumu pārāk neietekmē, ļaujot iegūt sililsulfolēnus **37a-d** ar ļoti labiem iznākumiem (82–85 %). Augstu 84 % iznākumu izdevās sasniegt arī produktam **37f** ar *n*-oktilaizvietotāju. Propargilsilāns **36e**, kas satur elektronus atvelkošo metoksiaizvietotāju uz silīcija grupas, produktu **37e** deva ar zemu iznākumu – 24 %. Nedz katalizatora maiņa, nedz temperatūras pazemināšana (–20 °C) neļāva uzlabot reakcijas iznākumu. Papildu eksperimenti pazeminātās temperatūrās liecināja par to, ka izejvielas degradācija notiek zemākās temperatūrās nekā vēlamā skābes katalizētā izomerizācijas reakcija par silildiēnu. Reakcijas iznākumu izdevās uzlabot, veicot šo procedūru divos soļos: 1) TfOH katalizēta izomerizācija dihlormetānā; 2) heletropā reakcija šķidrā SO_2, iegūstot sililsulfolēnu **37e** ar 62 % iznākumu divās stadijās. Fenilgrupas ievadīšana

propargilsilānā **36g** arī paātrināja blakus reakciju norisi, ko izdevās novērst, nomainot katalizatoru uz maigāku skābi – PhCOOH. Tas ļāva iegūt vēlamo sililsulfolēnu **37g** ar 61 % iznākumu.

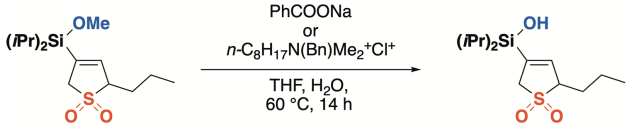
Arī 4-nitrofenilaizvietotais propargilsilāns **36h** uzrādīja reaģētspēju konkrētajos reakcijas apstākļos (14. shēma). Sililsulfolēns **37h** tika iegūts ar 51 % iznākumu kā *trans* diastereomērs. To izdevās apstiprināt ar kodolu Overhauzera efektu, kas vēlreiz pierāda promocijas darba autora grupas iepriekšējos novērojumus par selektīvu *E*,*Z*-diēnu ieguvi.[37]



36h **37h**, 51 %

14. shēma. 2,5-*Trans*-diaizvietota sulfolēna **37h** sintēze.

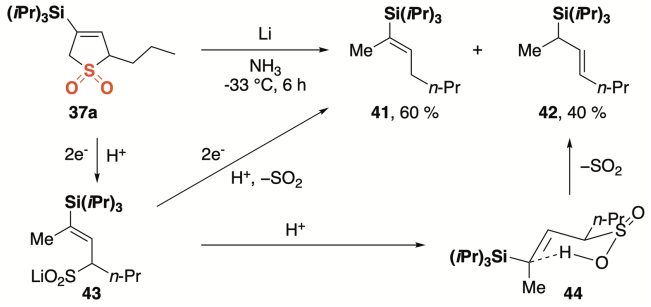
Tika veikti arī tālāki pētījumi par sulfolēnu ķīmiskajām īpašībām. Tika pārbaudīta sililsulfolēna **37e** hidrolīzes iespējas par savienojumu **37i** – substrātu, kas būtu piemērots Hijamas-Denmarka šķērssametināšanas reakcijām (15. shēma). Tika noskaidrots, ka vidēji stipras nukleofīlās grupas kā benzoāts un hlorīds spēj hidrolizēt sililētera grupu par silanolu **37i** ar gandrīz kvantitatīvu iznākumu.



37e **37i**, 93 %

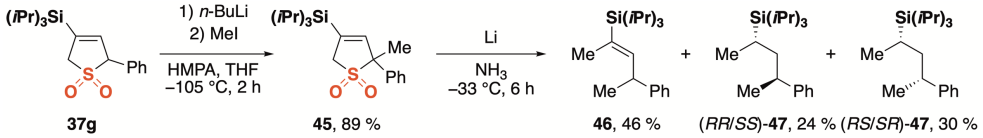
15. shēma. Sililētera **37e** hidrolīze.

Tika veikti arī eksperimenti, lai pārbaudītu sililsulfolēnu desulfitēšanas iespējas reducējošos apstākļos (16. shēma). Izmantojot metālisko litiju kā reducētāju šķidrā NH_3,[43] tika novērota pilna izejvielas sililsulfolēna **37a** konversija, iegūstot vinilsilānu **41** ar 60 % iznākumu. Reakcijas gaitā kā galvenais blakusprodukts radās alilsilāns **42**, ko skaidrojams kā retro-*ēna* eliminēšanās produkts no intermediāta **44**. Produktu rašanās attiecība 60 : 40 palika nemainīga arī citos reakcijas apstākļos, lietojot papildu šķīdinātāju, citu protonu avotu, papildu bāzi vai arī nomainot reducējošo reaģentu.



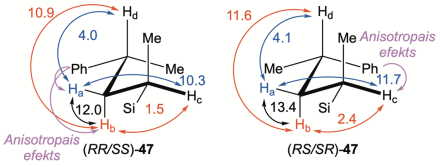
16. shēma. Sililsulfolēna **37e** desulfatēšana.

Pārbaudot sulfolēnu **37g** dotajos apstākļos, tika novērota izejvielas degradācija. Savukārt, pakļaujot reducēšanas reakcijai selektīvi metilēto savienojuma **45**, tika iegūts trīs produktu maisījums – sagaidāmais vinilsilāns **46** un pārreducēšanas produkts **47**. Interesanti, ka, izmantojot pat lielu Li pārākumu, fenilgrupas reducēšana netika novērota. Lai iespējami novirzītu reducēšanu kāda konkrēta produkta rašanās virzienā, šajos apstākļos tika pārbaudīts, kā aizvietotājs sulfolēnā pie C2 varētu ietekmēt produktu veidošanās attiecību (17. shēma).



17. shēma. Sulfolēna **45** iegūšana un desulfitēšana.

Abi savienojuma **47** diastereomēri tika raksturoti ar 1D un 2D KMR (*COSY*, *HSQC*, *HMBC*) analīzes metodēm (1. att.). Sadarbības konstanšu analīze liecina par to, ka molekulas cenšas ieņemt konformāciju, kurā tiek mazināta *sin*-pentāna mijiedarbība – H_d un viena no metilgrupām novietojas pseidoaksiālā pozīcijā. Līdz ar to savienojumā (*RS*/*SR*)-**47** H_c protonam būtu jānovēro anizotropais efekts no fenilgrupas *sin*-periplanārajā novietojumā. Tik tiešām, salīdzinot H_c KMR signāla nobīdes silāniem (*RS*/*SR*)-**47** ar (*RR*/*SS*)-**47**, savienojumam (*RS*/*SR*)-**47** ir novērojama spēcīga H_c signāla nobīde stiprākos laukos (0.50 ppm un 0.97 ppm). Līdzīgi, tikai apgriezti, šo efektu var novērot arī H_b KMR signālam (1.67 ppm savienojumam (*RR*/*SS*)-**47** un 1.81 ppm savienojumam (*RS*/*SR*)-**47**). Šos pašus rezultātus arī papildina un apstiprina šo signālu izmaiņa pazeminātās temperatūrās (pazeminot temperatūru ekranētajiem protoniem, tiek novērota izteiktāka nobīde stiprākos laukos).



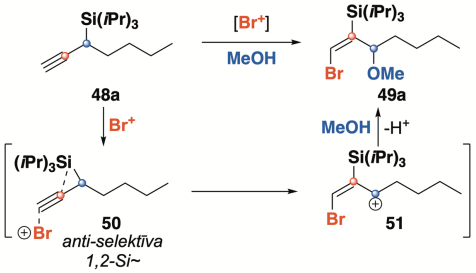
1. att. Diastereomēru **47** KMR analīze (sadarbības konstantes norādītas Hz).

1.2. Elektrofīlu ierosināta alilfunkcionalizētu vinilsilānu sintēze no propargilsilāniem

Tādi propargilsilāni kā 1,3-dipoli galvenokārt ir izmantoti [2 + 3] annulēšanas reakcijās, savukārt promocijas darba autora grupu ieintriģēja ar elektrofīlu reaģentu ierosinātas sililgrupas 1,2-nobīdes rezultātā izveidotā alilkatjona iespēja pievienot ārēju nukleofīlu, kas nav saistīts nedz ar elektrofīlo reaģentu, nedz ar propargilsilāna struktūru. Līdz šim veiktajos pētījumos ģenerētā katjona dzēšana notika ar tālākām strukturālām izmaiņām – nepiesātinātās sistēmas veidošanos pašā substrātā. Tika izvirzīta hipotēzi, ka šo ģenerēto alilkatjonu būtu iespējams "notvert" ar kādu citu, ārēju nukleofīlu. Kā pirmie šādas pārvērtības veikšanai tika izvēlēti polāri, nukleofīli šķīdinātāji, jo tie nodrošinātu gan stabilizētu vidi ģenerētajām lādētajām daļiņām, gan, pateicoties augstajai koncentrācijai, ātru reakcijas norisi.

2. tabula

Propargilsilāna **48a** brommetoksilēšanas reakcijas apstākļu optimizācija un iespējamais reakcijas mehānisms



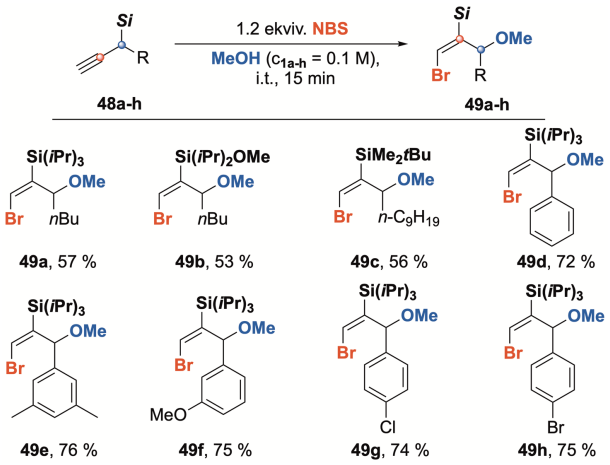
Nr. p. k.	Reakcijas apstākļi[a]	KMR iznākums **49a**,[b] %
1.	NBS (1.2 ekviv.), i. t.	60 (57)[c]
2.	NBS (1.2 ekviv.), temperatūru diapazonā = –78 °C, 0 °C, 50 °C	52–58
3.	NBS (1.2 ekviv.), i. t. c_{1a} diapazonā 0.05–0.2 M	55–56
4.	NBS (2.0 ekviv.), i. t.	49–52
5.	NBS (1.2 ekviv.), i. t. 10 % MeOH šķīdums $(CF_3)_2CHOH$	46
6.	Br_2 (1.0 ekviv.), i. t.	49
7.	$TsNBr_2$ (1.2 ekviv.), i. t.	56
8.	MeC(O)NHBr (1.2 ekviv.), i. t.	53
9.	1,3-Dibrom-5,5-dimetilhidantoīns (0.6 ekviv.), i. t.	57
10.	Dibromizocianūrskābe (0.6 ekviv.), i. t.	51

[a] Standarta apstākļi: c_{1a} = 0.1 M, reakcijas laiks 15 min.
[b] Difenilmetāns kā iekšējais standarts.
[c] Izdalītais iznākums.

Pirmais eksperiments, ko promocijas darba autora grupa izvēlējās veikt, bija propargilsilāna **48a** reakcija ar *N*-bromsukcinimīdu (NBS) (1.2 ekviv) metanolā (0.1 M) istabas temperatūrā (2. tab., 1. rinda). Jau pēc 15 minūtēm tika novērota pilna izejvielas konversija, un metilēteris

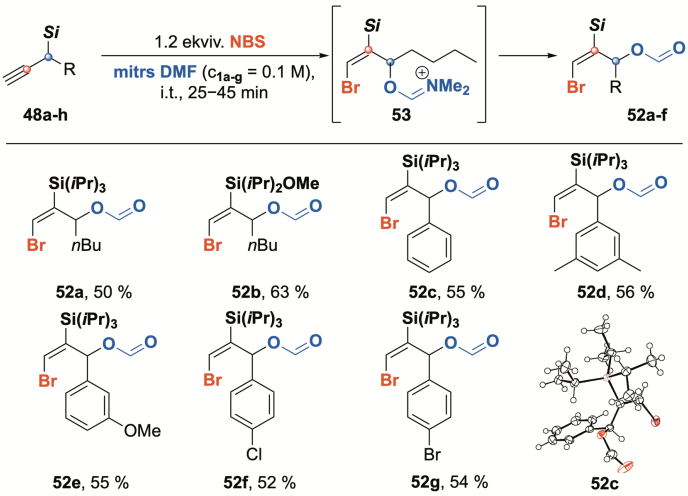
49a tika izdalīts ar 57 % iznākumu. Tālāk tika izvērtēta temperatūras, koncentrācijas, NBS daudzuma un papildu šķīdinātāja, kā arī citu elektrofīlo broma reaģentu avotu ietekme uz reakcijas iznākumu, bet nekāds būtisks uzlabojums vai pasliktināšanās reakcijas gaitā novērota netika. Līdz ar to tālākos pētījumos par substrātu klāstu tika izvēlēti tehniski vieglākie pirmie pārbaudītie apstākļi.

Reaģētspēja tika pārbaudīta arī citiem 3-alkilpropargilsilāniem **48b,c** (18. shēma). Nedz alkilgrupas ķēdes garums, nedz izmaiņas silīcija aizvietotājā reakcijas iznākumu un gaitu pārāk neietekmēja, ļaujot izdalīt metilēterus **49b** un **49c** ar 53 % un 56 % iznākumiem. Būtisku uzlabojumu reakcijas iznākumā deva arilaizvietotāja ievadīšana propargilpozīcijā. Visi pārbaudītie 3-arilpropargilsilāni **48d-h** ļāva iegūt metilēterus **49d-h** ar iznākumiem no 72 % līdz 76 % un ar tik pat labiem reakcijas laikiem kā iepriekš – 5–15 min. Tas ļauj spriest, ka arilaizvietotājs spēj nodrošināt gan papildu stabilizāciju reaģētspējīgajam starpstāvoklim, gan samazināt dažādu degradācijas procesu norisi neatkarīgi no elektroniskajiem efektiem, ko ievieš aizvietotāji uz konkrētās arilgrupas.



18. shēma. Propargilsilānu **48a-h** brommetoksilēšanas produkti **49a-h**.

Kā nākamais šķīdinātājs tika izvēlēts DMF, kas šajās reakcijās piedalās kā formiātgrupas ekvivalents (19. shēma). Veicot reakcijas mitrā DMF, līdzīgi kā iepriekš, vienkāršākie alkilaizvietotie propargilsilāni **48a,b** deva formiātus **52a** un **52b** ar vidējiem iznākumiem – 50 % un 63 %.

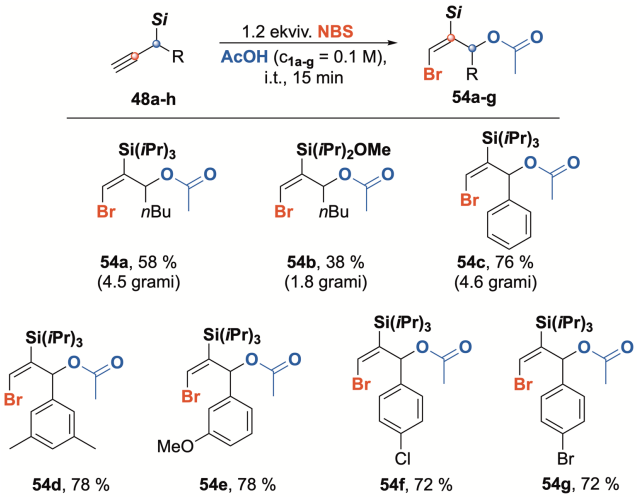


19. shēma. Propargilsilānu **48a-h** bromformiloksilēšanas produkti **52a-f**, iespējamais reakcijas mehānisms un savienojuma **52c** *ORTEP* attēlojums.

Interesanti, ka arilaizvietotie propargilsilāni uzrādīja ļoti līdzvērtīgus, viduvējus rezultātus, ļaujot iegūt formiātus **52c-d** robežās no 52 % līdz 56 % 25–45 min Zemāki iznākumi un lēnāka reakcijas gaita nekā produktu **49a-h** sintēzē liecina, ka DMF ir salīdzinoši vājāks nukleofīls nekā metanols un izraisa nevēlamas blakus reakciju norises, ko var novērot ar GH-MS analīzes palīdzību.

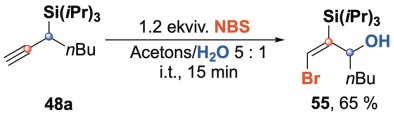
Savienojuma **52c** gadījumā izdevās iegūt monokristālus, kas bija piemēroti rentgenstruktūranalīzei un kas neapšaubāmi pierādīja gan iegūto savienojuma **52c** struktūru, gan (*E*)-ģeometrijas selektivitāti pārgrupēšanās reakcijām.

Trešais šķīdinātājs, kas tika pārbaudīts kā potenciālais nukleofīls, bija etiķskābe (20. shēma). Ņemot vērā to, ka iepriekš promocijas darba autora grupā izstrādātā metode propargilsilānu aktivēšanai balstījās Brensteda skābju katalīzē, māca šaubas par substrātu stabilitāti skābā vidē. Šīs bažas apstiprinājās tikai daļēji, jo vienīgais substrāts, kas uzrādīja pazeminātu iznākumu, bija di-*izo*-propilmetoksisililgrupu saturošais propargilsilāns **48b**. Pārējie propargilsilāni uzrādīja līdzīgu reaģētspēju iepriekš apskatītajām reakcijām metanolā. Arī etiķskābē arilaizvietotie propargilsilāni izrādījās pārāki pār alkilaizvietotajiem, dodot arilaizvietotos acetātus **54c-g** ar iznākumiem robežās no 72 % līdz 78 % un alkilaizvieto acetātu **54a** ar 58 % iznākumu. Tika demonstrēts arī šo reakciju lietojums vairāku gramu apjomā, iegūstot, piemēram, produktu **54c** (4.6 g) ar 76 % iznākumu.



20. shēma. Propargilsilānu **43a-h** bromacetoksilēšanas produkti **54a-g**.

Tika veikti arī pētījumi ar citu elektrofīlu/nukleofīlu pāru pievienošanu. Sekmīgi izdevās veikt bromhidroksilēšanas reakciju acetons/ūdens (5 : 1) sistēmā, iegūstot spirtu **55** ar 65 % iznākumu (21. shēma). Promocijas darba autora grupu pārsteidza 3-arilpropargilsilānu inertums šajos reakcijas apstākļos, ko varētu skaidrot ar ūdens kā pārāk vāja nukleofīla reaģētspēju un alilbenzilkatjona kā potenciālā starpstāvokļa pārāk augsto stabilitāti.

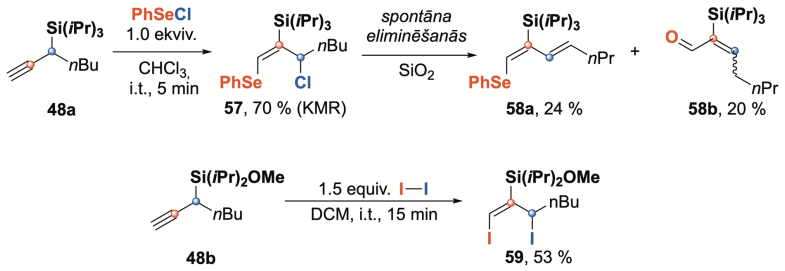


21. shēma. Propargilsilāna **48a** bromhidroksilēšanas reakcija.

N-Jodsukcinimīds (NIS) metanolā uzrādīja salīdzinoši līdzīgu reaģētspēju NBS, un atbilstošais jodmetoksilēšanas produkts **56** tika iegūts ar vidēju iznākumu – 42 % (22. shēma).

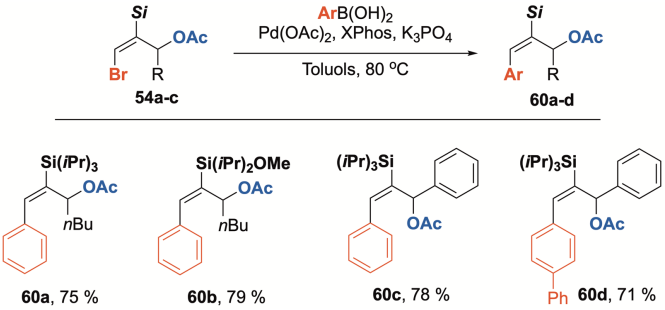
22. shēma. Propargilsilāna **48a** jodmetoksilēšanas reakcija.

Izdevās arī demonstrēt 1,3-difunkcionalizēšanu ar tādiem elektrofīla/nukleofīla pāriem kā fenilselenilhlorīds un elementārais jods (23. shēma). Propargilsilāns **48a** reaģēja ar PhSeCl 5 min. dodot vinilselenīdu **57** ar 70 % KMR iznākumu. Šo savienojumu gan neizdevās izdalīt un veikt tā pilnu raksturošanu, jo, veicot attīrīšanu gan uz tiešās, gan uz apgrieztās fāzes silikagēla, tika novērota savienojuma degradācija. Tika izdalīts Cl^- eliminēšanās produkts diēns **58a** ar 24 % iznākumu un hidrolīzes produkts aldehīds **58b** ar 20 % iznākumu. Savukārt 1,3-dijodēšanas produktu **59** izdevās izdalīt ar 53 % iznākumu.



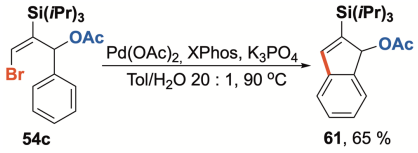
23. shēma. Propargilsilānu funkcionalizēšana ar elektrofīla/nukleofīla pāriem.

Jauniegūtie savienojumi pēc reakcijas satur trīs reakcijas centrus, un tos ir iespējams izmantot kā efektīvus būvblokus selektīvai alkēnu sintēzei. Lai to demonstrētu, vispirms vinilbromīdus **54a-c** tika izmantotas Suzuki-Mijauras šķērssametināšanas reakcijas (24. shēma). Izmantojot modificētus Bakvalda (*Buchwald*) izstrādātos reakcijas apstākļus,[44] šķērssametināšanas produktus **60a-d** izdevās iegūt ar labiem 71–79 % iznākumiem.



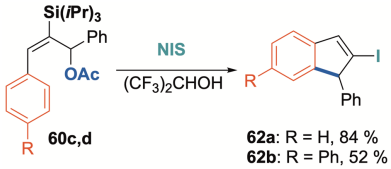
24. shēma. Vinilbromīdu **54a-c** šķērssametināšanas reakcijas.

Reakcijas vidē nepievienojot arilborskābi, izdevās iegūt iekšmolekukāras ciklizācijas C-H aktivēšanas produktu **61** ar 65 % iznākumu (25. shēma).



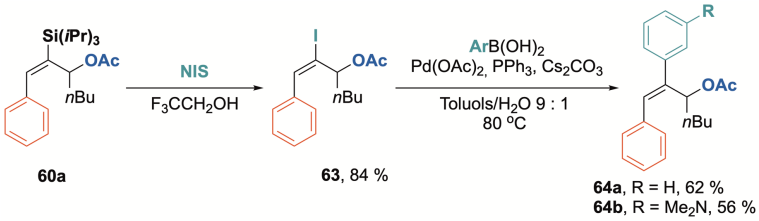
25. shēma. Vinilbromīda **54c** iekšmolekulāras ciklizācijas C-H aktivācijas reakcija.

Tālākā darba gaitā promocijas darba autora grupa pievērsās sililgrupas selektīvai funkcionalizēšanai. Lai to paveiktu, tika nolemts izmantot sililgrupas elektrofīlās apmaiņas reakciju ar NIS. Tika novērots, ka savienojumi, kas satur arilaizvietotāju alilpozīcijā, visos pārbaudītajos apstākļos veic iekšmolekulāru ciklizēšanos. Attiecīgos jodindēnus **62a,b** izdevās iegūt ar līdz pat 84 % iznākumu 1,1,1,3,3,3-heksafluorizopropanolā (HFIP) (26. shēma).



26. shēma. Vinilsilānu **60c,d** tandēmā ciklizēšanās – elektrofīlā apmaiņas reakcija.

Ciklizēšanos bija iespējams novērst, kā substrātu izmantojot alkilaizvietoto vinilsilānu **60a**. Samazinot alilpozīcijas jonizēšanās potenciālu un nomainot šķīdinātāju uz 2,2,2-trifluoretanolu, attiecīgais viniljodīds **63** tika iegūts ar 84 % iznākumu (27. shēma). Pēc tam, atkal izmantojot Suzuki-Mijauras šķērssametināšanas reakciju, viniljodīds **63** tika pārvērsts attiecīgajos stilbēnos **64a** un **64b** ar attiecīgu 62 % un 56 % iznākumu. Iegūtie stilbēni **64a,b** ir saglabājuši orģinālo dubultsaites ģeometriju (pierādīts ar ^{1}H-^{1}H-NOESY KMR) cauri visai reakciju sekvencei, sākot no savienojuma **54a**.

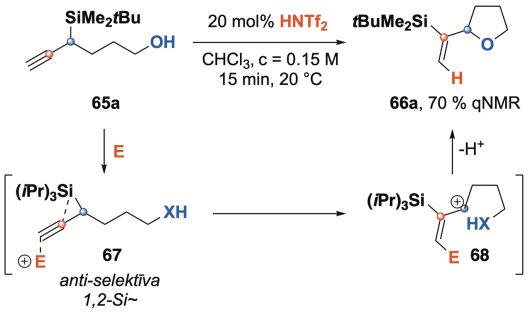


27. shēma. Vinilsilāna **60a** sililgrupas funkcionalizēšana.

1.3. Elektrofīlu ierosināta heterociklisku savienojumu ar vinilsilānu sānu ķēdi sintēze no termināli funkcionalizētiem propargilsilāniem

Starp visiem mazmolekulārajiem zāļu savienojumiem, kas ir apstiprināti ASV Pārtikas un zāļu pārvaldē (*Food and Drug Administration*), 59 % saturēja kādu no slāpekļa (2014. gada dati)[45] un 27 % kādu no skābekļa heterocikliem (2018. gada dati).[46] Lai paplašinātu pieejamo sintētisko metožu klāstu heterociklisko savienojumu iegūšanai, kopā ar Rasmu Kroņkalni un Artjomu Ubaidullajevu tika izvirzīta hipotēze, ka, lietojot dažādus nukleofīlus saturošus propargilsilānus, būtu iespējams ģenerēt alilkatjonu, kas iekšmolekulāras ciklizācijas rezultātā dotu dažādus heterocikliskus atvasinājumus.

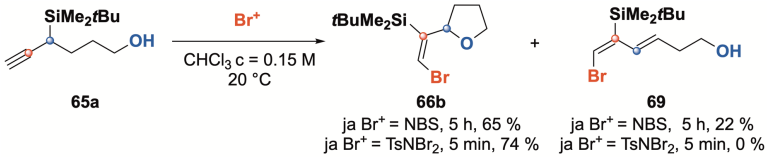
Pētījumus tika nolemts sākt, pārbaudot savienojuma **65a** heterociklizāciju skābes katalizētos apstākļos ar kvantitatīvās KMR spektroskopijas palīdzību. Pirmie eksperimenti tiešām uzrādīja vēlamā tetrahidrofurāna **66a** veidošanos, un pēc apstākļu optimizācijas kā piemērotākie tika izvēlēti $HNTf_2$ katalizators hloroforma šķīdumā istabas temperatūrā ar reakcijas laiku 15 min. (28. shēma).



28. shēma. Piemērotākie apstākļi tetrahidrofurāna **66a** iegūšanai un iespējamais reakcijas mehānisms.

Līdzīgus rezultātus ir iespējams sasniegt, izmantojot arī tādas superskābes kā TfOH vai veicot reakciju šķīdinātājos, kas nenivelē doto katalizatoru. Samazinot temperatūru un katalizatora daudzumu, tika novērota tikai reakcijas ātruma samazināšanās.

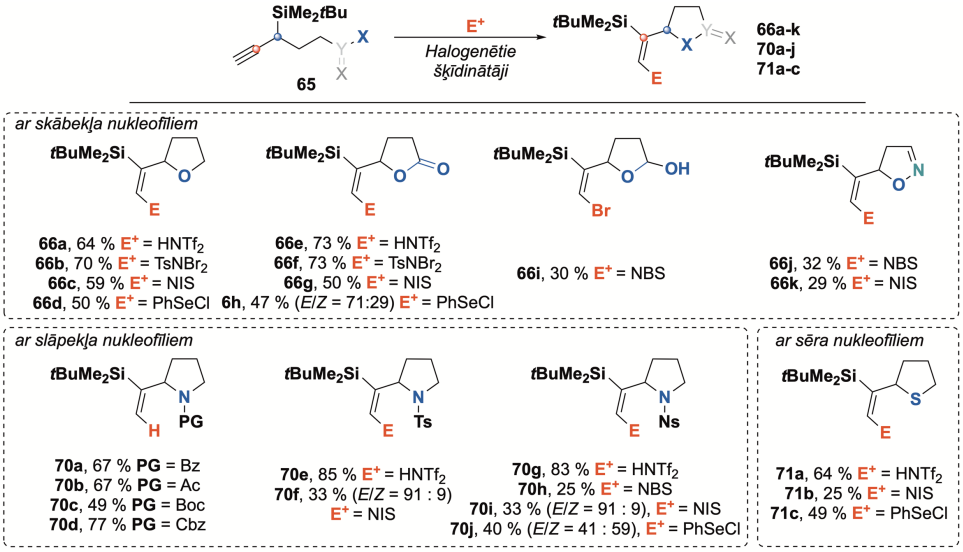
Pēc tam tika nolemts pārbaudīt propargilsilānu **65a** heterociklizāciju elektrofīlā reaģenta NBS klātienē (29. shēma). Tika pārbaudīta gan šķīdinātāja, gan temperatūras ietekme, tomēr visos gadījumos ar NBS tika novērota arī diēna **69** veidošanās, ko vismazāk varēja novērot, veicot reakciju hloroformā. Arī reakcijas ilgums šajā gadījumā bija daudz garāks, salīdzinot ar skābes katalizētajām reakcijām. Pilnu izejvielas konversiju hloroformā bija iespējams sasniegt vien pēc 5 h, ko var skaidrot ar NBS zemo šķīdību halogenētos šķīdinātājos.



29. shēma. Piemērotākie apstākļi tetrahidrofurāna **66b** iegūšanai.

Līdz ar to tika nolemts papildus apskatīt arī citus elektrofīlā broma avotus. Jau pirmajā eksperimentā ļoti labu reaģētspēju uzrādīja *N*,*N*-dibrom-4-metilbenzolsulfonamīds ($TsNBr_2$), kam ir augsta šķīdība halogenētajos šķīdinātājos. Pilna izejvielas konversija tika sasniegta mazāk kā pēc 5 min. (laikā no parauga pievienošanas KMR stobriņā līdz spektra uzņemšanai jau bija sasniegta pilna konversija). Reakcijas maisījumā tika novērota tikai vēlamā tetrahidrofurāna **66b** veidošanās, iespējams, mazāk bāziskā sulfonilamīda anjona dēļ.

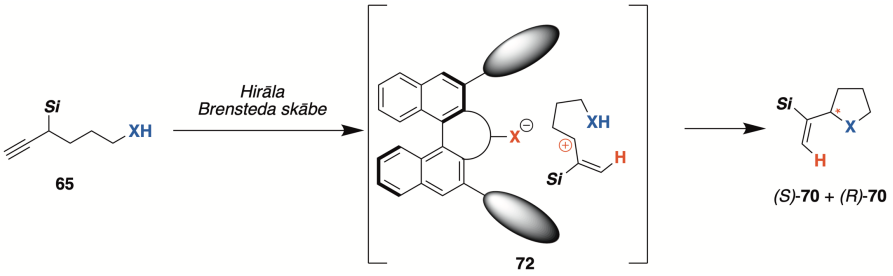
Pēc vēlamo apstākļu noskaidrošanas, Rasma Kroņkalne kopā ar Artjomu Ubaidullajevu veica substrāta tvēruma izpēti. Tika pārbaudītas dažādas heterociklizācijas reakcijas ar iekšmolekulāriem skābekļa (spirti, aldehīdi, karbonskābes un oksīmi), slāpekļa (amīdi, karbamāti un sulfonamīdi) un sēra (tioacetāts) nukleofīliem kombinācijā ar elektrofīlajiem reaģentiem (Brensteda superskābes, NBS, $TsNBr_2$ NIS, PhSeCl) (30. shēma).



30. shēma. Produktu tvērums iekšējo nukleofīlu saturošu propargilsilānu **65** iekšmolekulārās ciklizācijas reakcijās (sadarbībā ar R. Kroņkalni un A. Ubaidullajevu).

Reakciju rezultātā ar iznākumiem no 25 % līdz 85 % tika iegūti tetrahidrofurāna **66a-d**, γ-butirolaktona **66e-h**, tetrahidrofurān-ola **66i**, 2-izoksazola **66j-k**, pirolidīna **70a-j** un tiolāna **70a-c** atvasinājumi ar funkcionalizētu alkēna sānu ķēdi.

Izstrādātā metode iekšmolekulārai ciklizācijai balstās uz alilkatjona kā reakcijas starpstāvokļa veidošanos, tāpēc tika izvirzīta hipotēze, ka, pamatojoties uz asimetrisko pretjona virzīto katalīzi (*ACDC*),[47] nukleofīlās grupas uzbrukumu reakcijas centram būtu iespējams panākt ar enantiodiskrimināciju (eksperimentālie dati – 5. pielikumā). Lai to paveiktu, kā hirālās informācijas avots tika izvēlētas BINOL atvasinātās Brensteda skābes (31. shēma).



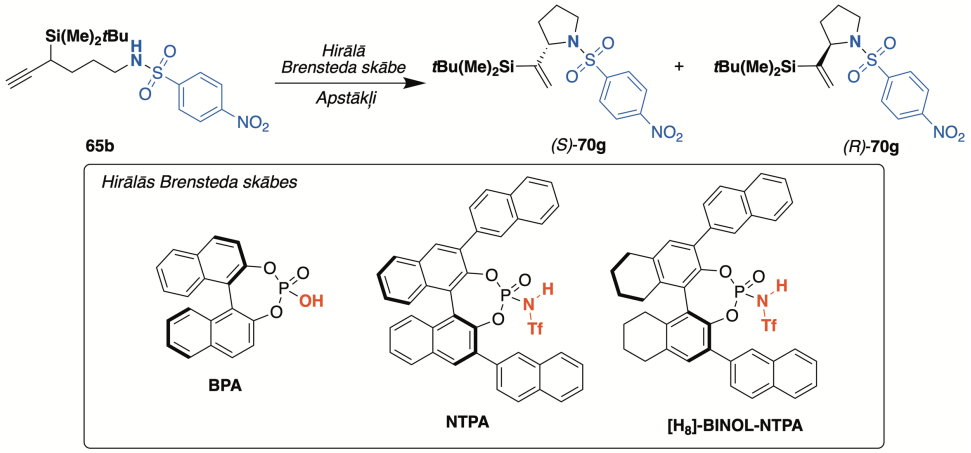
31. shēma. Hirālas Brensteda skābes katalizēta iekšmolekulāra ciklizēšanās reakcija.

Eksperimenti tika sākti ar substrāta un hromatogrāfiskās analīzes metodes identificēšanu. Kā piemērotākie substrāti tika izvēlēti savienojumi ar nitrobenzolsulfonilamīdu tā hromoforo īpašību dēļ, kas ļautu viegli kvantificēt iegūto enantiomēru attiecību ar AEŠH sistēmām, kas sajūgtas ar UV detektoru. Labāko enantiomēru sadalījumu izdevās iegūt, izmantojot (*R*,*R*)-Whelk-O 1 hirālo stacionāro fāzi un 5 % *i*PrOH/Hex (v/v) kā mobilo fāzi.

Enantiomērā pārākuma iegūšanai tika izmēģinātas pieejamās hirālās Brensteda skābes. Mēģinot atkārtot racēmiskā produkta **70 g** sintēzes apstākļus un aizstājot $HNTf_2$ ar fosforskābes-BINOL esteri, izejviela nereaģēja (3. tab., 1. rinda). Aizstājot DCM ar hloroformu un vārot, pēc 72 stundām tika izdalīti 13 % vēlamā produkta, diemžēl enantiomērā pārākuma veidošanās netika novērota.

3. tabula

Hirālu Brensteda skābju katalizētas propargilsilāna **65b** ciklizēšanas apstākļi

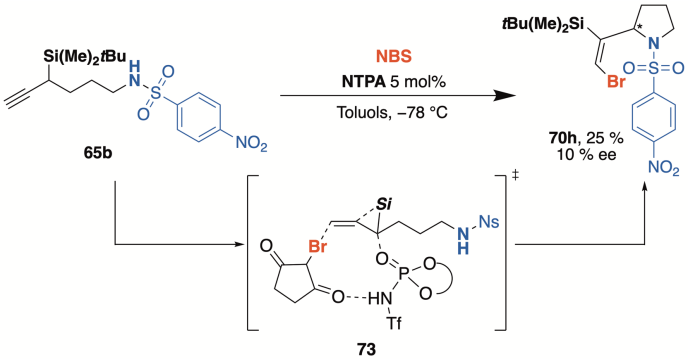


Nr. p. k.	Katalizators	Šķīdinātājs	T, °C	t, h	Iznākums, %	ee, %
1.	**BPA**	DCM	20	24	–	–
2.		$CHCl_3$	63	72	13	0
3.	**NTPA** 5 mol%	Toluols	60	19	56	6
4.		Cikloheksāns	60	18	62	11
5.	**NTPA** 10 mol%	Cikloheksāns	i.t.	19	52	11
6.	**[H_8]-BINOL-NTPA** 5 mol%	Cikloheksāns	60	21	45	12

Nākamie eksperimenti tika veikti ar komerciāli pieejamajiem *N*-trifluormetānsulfonilfosfoimidātiem **NTPA** un **[H_8]-BINOL-NTPA**, kuru skābums, salīdzinot ar BINOL-atvasinātajām fosforskābēm **BPA**, ir daudz augstāks, kā arī tie 2,2'-pozīcijās satur stēriski lielus aizvietotājus hiralitātes efektīvākai pārnešanai. Pirmo reakciju promocijas darba autora grupa izvēlējās veikt toluolā 60 °C temperatūrā ar **NTPA** (3. tab., 3. rinda). Vēlamais produkts pēc 19 stundām tika izdalīts ar 56 % iznākumu un 6 % enantiomēro pārākumu. Lai to uzlabotu, tika nolemts veikt eksperimentu cikloheksānā, kas varētu nodrošināt ciešāku jonu pāra veidošanos. Veicot eksperimentu istabas temperatūrā gan ar **NTPA** (3. tabu., 5 rinda), gan ar **[H_8]-BINOL-NTPA** (3. tab., 6 rinda), tika novērota gan pieņemama reaģētspēja, gan enantiomērā pārākuma veidošanās līdz 12 %.

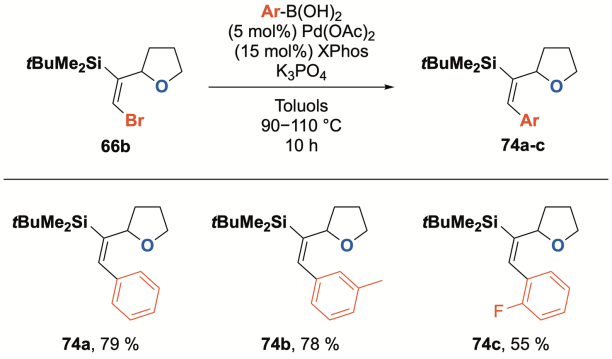
Ņemot vērā to, ka ir zināmi arī piemēri, kad hirālas Brensteda skābes spēj aktivēt ahirālus elektrofīlos halogēnu reaģentus un nodrošināt enantiomērā pārākuma veidošanos, tika

izmēģināta reakcija ar NBS **NTPA** klātbūtnē (32. shēma). Pirolidīns **70h** tika iegūts ar 25 % iznākumu un 10 % enantiomēro pārākumu. 3. tabulā un 31. shēmā apkopotie pirmējie eksperimentālie rezultāti parāda asimetriskās katalīzes koncepta iespējamību promocijas darba autora grupas izstrādātajai heterociklizācijas reakcijai ar sililgrupas 1,2-nobīdi. Pētījumi šajā virzienā tiek turpināti.



32. shēma. Hirālas Brensteda skābes ierosināta propargilsilāna **65b** bromciklizācija.

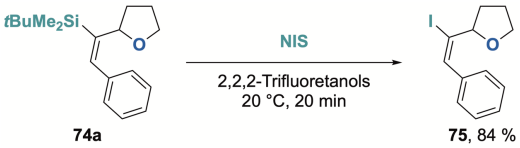
Ņemot vērā iegūtās zināšanas par vinilaizvietotāja reaģētspējas īpatnībām iepriekš apskatītajos savienojumos **54**, arī jauniegūtajiem heterocikliskajiem savienojumiem tika demonstrētas to tālākas funkcionalizēšanas iespējas. Kā modeļsubstrāts tika izvēlēts visvieglāk un ātrāk iegūstamais vinilbromīds **66b**, kam tika veikta Suzuki-Mijauras šķērssametināšanas reakcija (33. shēma). Izmantojot modificētos Bakvalda apstākļus ar dažādām arilborskābēm, tika iegūti sililstiroli **74a-c** ar vidējiem līdz labiem rezultātiem – 55–79 %.



33. shēma. Vinilbromīda **66b** funkcionalizēšana Suzuki-Mijauras šķērssametināšanas reakcijās.

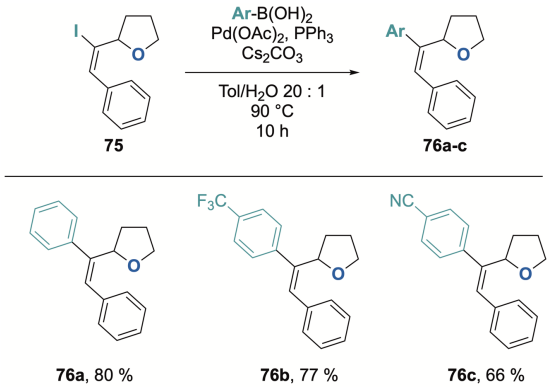
Pēc tam savienojums **74a** tika izmantots silīcija elektrofīlajai apmaiņai, lai iegūtu viniljodīdu **75** (34. shēma). Veicot reakciju HFIP, tika novērota strauja reakcijas gaita, dodot vēlamo produktu mazāk kā 15 minūšu laikā. Diemžēl šajā gadījumā tika novērota dubultsaites izomerizācija, dodot *E*/*Z* maisījumu attiecībā 4 : 1. Šo problēmu veiksmīgi izdevās novērst,

nomainot reakcijas šķīdinātāju no HFIP uz 2,2,2-trifluoretanolu. Vēlamais viniljodīds **75** tika iegūts ar 84 % iznākumu, pilnībā saglabājot dubultsaites konfigurāciju.



34. shēma. Vinilsilāna **74** elektrofīlās apmaiņas reakcija.

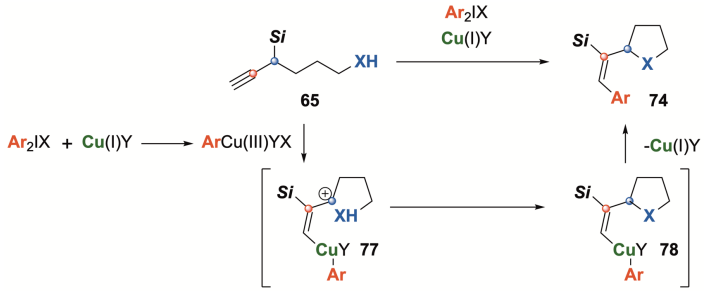
Iegūtais viniljodīds **75** tika veiksmīgi izmantots Suzuki-Mijauras šķērssametināšanas reakcijas apstākļos, lai iegūtu tetrahidrofurānus ar trīsaizvietotu alkēna sānu ķēdi **76a-c** ar labiem iznākumiem – 66–80 % (35. shēma), saglabājot oriģinālo dubultsaites konfigurāciju, kas tika iegūta savienojuma **66b** sintēzes rezultātā.



35. shēma. Jodstirola **75** funkcionalizēšana Suzuki-Mijauras šķērssametināšanas reakcijās.

1.4. Propargilsilānu arilēšana ar joda(III) reaģentiem vara katalizētos apstākļos

Parādot iegūto ciklizēto produktu kā lietderīgu būvbloku lietojumu, uzmanību piesaistīja nepiesātināto sistēmu arilēšana ar hipervalentajiem joda reaģentiem vara katalizētos apstākļos.[48] Ja šo konceptu pielāgotu iekšējo nukleofīlu saturošiem propargilsilāniem **65**, tad vienā sintēzes solī būtu iespējams veikt gan sililgrupas 1,2-migrāciju, gan iekšmolekulāro ciklizāciju, gan arī alkēna arilfunckionalizēšanu, iegūstot savienojumus **74** (36. shēma; eksperimentālie dati – 6. pielikumā).

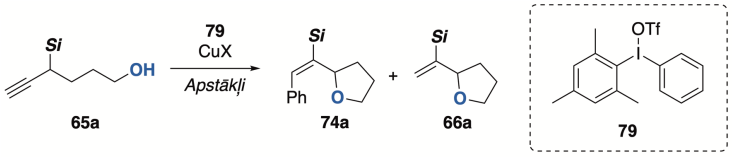


36. shēma. Iespējamā propargilsilānu **65** arilēšana ar joda(III) reaģentiem vara katalizētos apstākļos.

Pirmais eksperiments, ko promocijas darba autora grupa nolēma veikt, bija spirta **65a** reakcija ar ariljodānu **79** CuCl klātbūtnē (4. tab., 1 rinda). Šajā gadījumā tika novērota skābes ciklizētā produkta **66a** veidošanās, ko var skaidrot ar iespējamo TfOH zīmju klātbūtni no ariljodāna **79**. Savukārt, ja reakcijas maisījumam pievieno 2,6-di-*t*-butilpiridīnu un paaugstina procesa temperatūru (4. tab., 3 rinda), vēlamais produkts **74a** tiek iegūts pat ar 76 % iznākumu (82 % KMR). Līdzīgu reakcijspēju uzrādīja arī CuOTf·PhH kā vara avots. Tālāka apstākļu optimizācija uzlabotus rezultātus pagaidām nedeva.

4. tabula

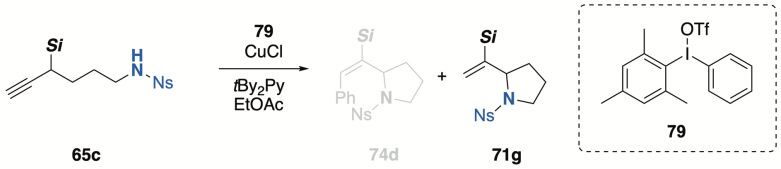
Propargilsilānu **65a** arilēšanas ar jods(III) reaģentiem vara katalizētos apstākļos optimizācijas tabula



Nr. p. k.	CuX	Šķīdinātājs	T, °C	Piedeva	**74a**, % (KMR)	**66a**, % (KMR)
1.	CuCl	EtOAc	20	–	0	69
2.		EtOAc	20	*t*Bu$_2$Py	0	0
3.		EtOAc	60		82 (76 izdalīts)	0
4.		THF	60		56	0
5.		$CHCl_3$	60		59	0
6.		Toluols	60		17	0
7.		MEK	60		0	0
8.		MeCN	60		0	0
9.		EtOAc	60	Lutidīns	0	0
10.		EtOAc	60	Et_3N	0	0
11.	CuI	EtOAc	60	*t*Bu$_2$Py	0	0
12.	CuOTf·PhH	EtOAc	60		84	0

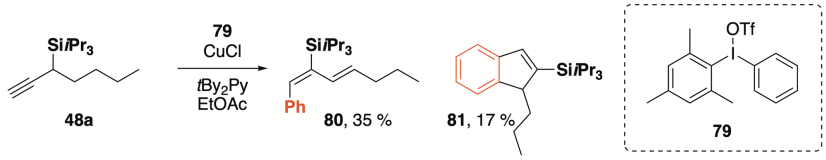
Tika izmēģināta arī sulfonilamīda **65b** ciklizācija optimizētajos apstākļos (37. shēma). Diemžēl vēlamā produkta veidošanās netika novērota, tika iegūts tikai pirolidīnu **71g**. To var skaidrot ar sulfonilamīda palielināto skābumu un stērisko mijiedarbību starp iespējamo vara

intermediātu un ienākošo nukleofīlo grupu (35. shēma, starpsavienojums **78**), kas, visticamāk, izraisa protodemetalēšanos, nevis vēlamās reducējošās eliminēšanos.



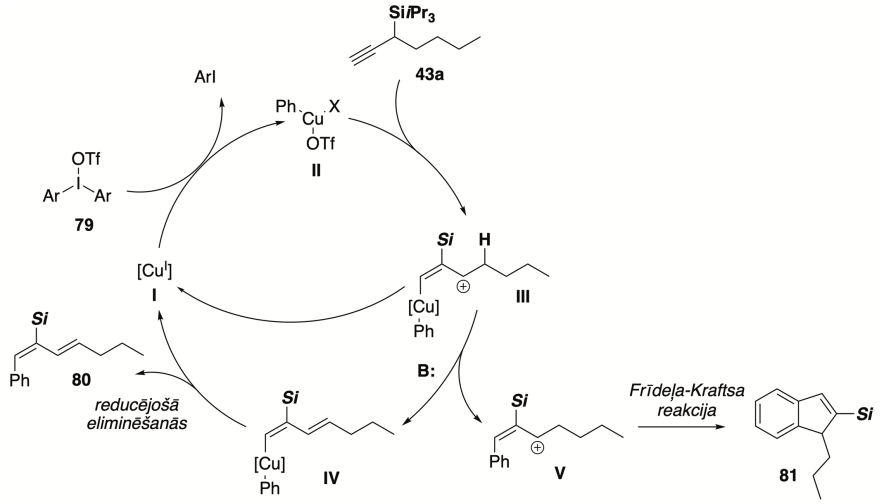
37. shēma. Propargilsilāna **65b** arilēšanas mēģinājums.

Arilēšanas reakcijā tika pārbaudīts arī propargilsilāns **48a**, kas nesatur iekšmolekulāro nukleofīlo grupu (38. shēma). Veicot reakciju optimizētajos apstākļos, tika iegūts divu vielu maisījumus, kas satur arildiēnu **80** un indēnu **81** attiecībā ~ 2 : 1 ar kopējo iznākumu 52 %.



38. shēma. Propargilsilāna **48a** arilēšanas reakcija ar joda(III) reaģentiem vara katalizētos apstākļos.

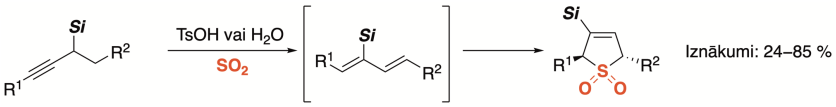
Abu produktu veidošanās mehānisms piedāvāts 39. shēmā. Reakcijas sākumā no vara(I) avota **I** oksidējošās pievienošanās rezultātā rodas vara(III) savienojums **II**, kas elektrofīlā reakcijā inducē sililgrupas 1,2-migrāciju, veidojot intermediātu **III**. Šajā brīdi intermediāts **III** var reaģēt ar bāzi, veidojot intermediātu **IV**, kas pēc reducējošās eliminēšanas dod arildiēnu **80**. Intermediāts **III** var veikt arī reducējošo eliminēšanu, veidojot intermediātu **V**, kas tūlīt pat veic iekšmolekulāru ciklizācijas reakciju, dodot indēnu **81**. Līdzšinējie optimizācijas eksperimenti vēl nav devuši iespēju selektīvi iegūt vai nu silildiēnu **80**, vai indēnu **81**, bet eksperimentālais darbs tiek turpināts.



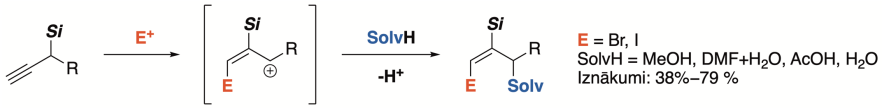
39. shēma. Propargilsilāna **48a** arilēšanas reakcija ar joda(III) reaģentu vara katalizētos apstākļos.

SECINĀJUMI

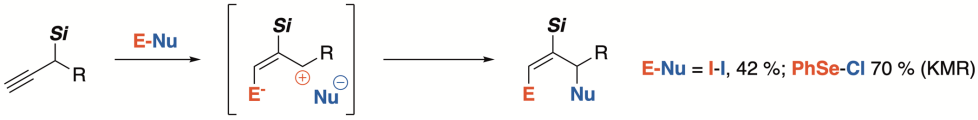
1. Šķidrs sēra dioksīds ir piemērota reakcijas vide sililsulfolēnu sintēzei no propargilsilāniem, kas ietver vāju skābju katalizētu propargilsilānu izomerizēšanu un heletropo ciklopievienošanu.



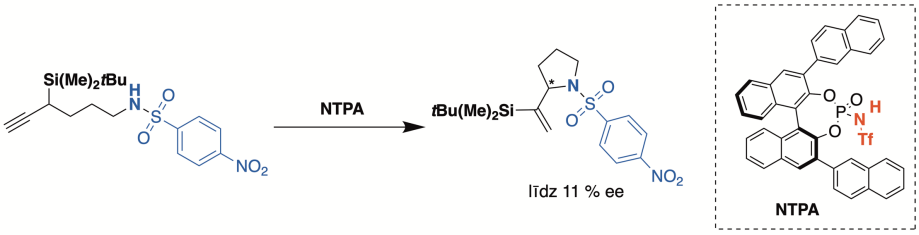
2. Elektrofīlu halogēnu saturoši reaģenti spēj ierosināt 1,3-difunkcionalizēšanas reakcijas propargilsilānos, kurās kā skābekļa nukleofīlu var izmantot šķīdinātāju (MeOH, DMF, AcOH, H_2O). Šķīdinātājs vienlaikus nodrošina gan polāru reakcijas vidi, gan augstu nukleofīlā reaģenta koncentrāciju. Izstrādātā metodoloģija dod funkcionalizētas atomu triādes ar fiksētu (*E*)-dubultsaites konfigurāciju.



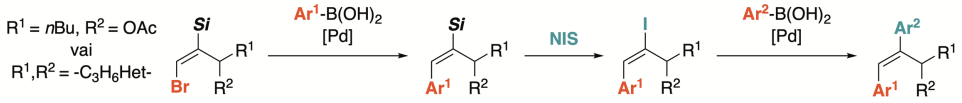
3. Propargilsilāniem ir iespējams veikt 1,3-difunkcionalizēšanu ar elektrofīla/nukleofīla pāriem nenukleofīlos šķīdinātājos (halogēnalkānos).



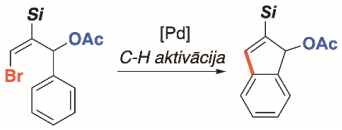
4. Hirālas Brensteda skābes ir spējīgas inducēt enantiomēro pārākumu propargilsilānos, kas alkilķēdē ir saistīti ar iekšmolekulāro nukleofīlo grupu. Izmantojot *N*-trifluormetānsulfonilfosfoimidātu **NTAP**, tika sasniegts 11 % enantiomērais pārākums. Tas pierāda hiralitātes pārneses koncepta iespējamību pētītajās reakciju sistēmās.



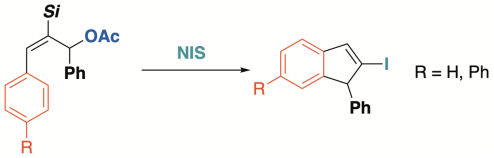
5. Iegūtie bromvinilsilāni, kas satur alkil- vai heterociklisku sānu ķēdi, ir lietojami kā vērtīgas izejvielas telpiski definētu trīsaizvietotu alkēnu sintēzei, veicot selektīvas Suzuki-Mijauras šķērssametināšanas un elektrofīlās apmaiņas reakcijas. Reakciju sekvence nodrošina dubultsaites sākotnējās konfigurācijas saglabāšanu.



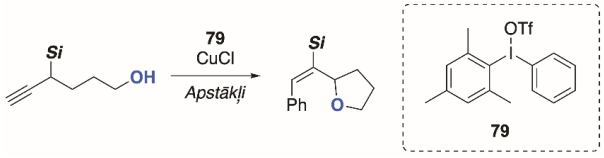
6. Bromvinilsilāni, kas alilpozīcijā satur acetoksi- un fenilaizvietotājus, palādija katalizētos apstākļos veic iekšmolekulāru C-H aktivācijas reakciju, dodot attiecīgo acetoksiindēnu.



7. Veicot silīcija-joda apmaiņu ar NIS sililstirolos, kas alilpozīcijā satur acetoksi- un fenilaizvietotājus, papildus silīcija nomaiņai tiek novērota acetāta grupas jonizēšanās. Iegūtais karbkatjons piedalās joniskā ciklizēšanās reakcijā, dodot attiecīgos jodindēnus.



8. Terminālo alkīnu un iekšmolekulāro O-nukleofīlu saturošiem propargilsilāniem ir iespējams veikt C-C arilēšanu ar sekojošu sililgrupas 1,2-migrāciju un ciklizēšanos, lietojot ariljodānus vara katalizētos apstākļos.



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

To be granted the scientific degree of Doctor of Science (*Ph. D.*), the present Doctoral Thesis has been submitted for the defense at the open meeting of the RTU Promotion Council on 11 October 2023 at the Faculty of Materials Science and Applied Chemistry of Riga Technical University, 3 Paula Valdena Street, Room 272.

OFFICIAL REVIEWERS

Associate Professor Dr. chem. Kaspars Traskovskis
Riga Technical University

Senior Lecturer Dr. Mark McLaughlin
Queen's University Belfast, United Kingdom

Associate Professor Dr. Grzegor Hreczycho
Adam Mickiewicz University in Poznań, Poland

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 (Ph. D.) is my own. I confirm that this Doctoral Thesis has not been submitted to any other university for promotion to a scientific degree.

Rūdolfs Beļaunieks ……..….
(*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 four scientific publications. The scientific publications have been written in English, with a total volume of 204 pages, including supplementary data.

CONTENTS

Appendix V: Līpiņa, R.A., Beļaunieks, R., Turks, M. Development of enantioselective electrophile-induced heterocyclization of terminally functionalized propargyl silanes. *Unpublished results.*

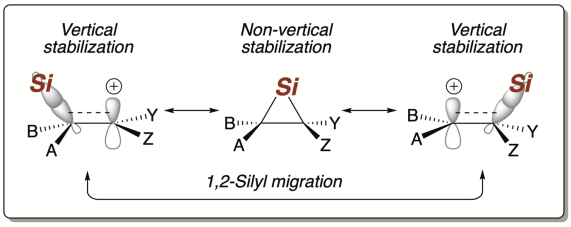
Appendix VI: Beļaunieks, R., Turks, M. Copper-catalyzed propargyl silane arylation with hypervalent iodine reagents. *Unpublished results.*

GENERAL OVERVIEW OF THE THESIS

Introduction

In organic chemistry, silicon has usually been directly compared to carbon. Both of them are group 14 elements; both have their typical tetravalent configuration; in almost all cases, they form covalent bonds, which are especially strong with elements possessing high electronegativity;[1] their chemical reactivity, like nucleophilic substitution with the inversion of the central atom configuration,[2] in most cases match. The difference between the two elements starts to appear because of the silicon's place in 3rd period. As a rule, that means a larger atomic radius,[3] lower electronegativity,[4] and more accessible vacant *d*-orbitals.[5] The contribution of these properties is what makes silicon useful as a protecting group for alcohols and terminal alkynes.[6] Its capability to form hypervalent intermediates[7] makes it a strong Lewis acid. Additionally, the polarizability of the C-Si bond makes Tamao–Fleming oxidation[8] and Hiyama–Denmark cross-coupling reactions possible.[9]

Another characteristic property of silicon that has gained a fair share of attention in the context of organic chemistry is its intrinsic ability to stabilize carbocations in the β-position, more commonly known as the β-silicon effect.[10] It can be explained by two structural proposals: vertical stabilization (hyperconjugation between the C-Si bond and unsaturated system) and non-vertical stabilization (formation of 3 atom, 4 electron cyclic silonium ion) (Scheme 1). It is believed that both modes of stabilization are in rapid equilibrium; therefore, while the new C-Si bond is formed in the non-vertical stabilization mode followed by the dissociation of the old bond, changes in the skeletal scaffold can be observed, that is, 1,2-silyl migration has taken place – a new cation is formed that is again stabilized by the β-silicon effect.[10]



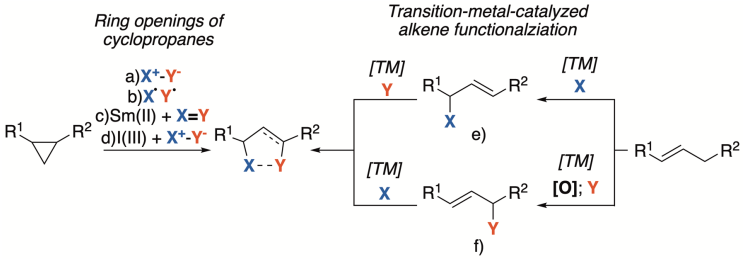
Scheme 1. β-Silicon effect – vertical and non-vertical stabilization in carbenium ions and plausible 1,2-silyl migration.

The silyl group migration is typically observed in systems that might either yield the product concertedly or form a more stable reaction intermediate owing to the combination of multiple stabilizing effects. This is commonly observed and studied in reactions between electrophiles and unsaturated systems.

Unsaturated systems like alkenes, allenes, and alkynes, as well as their conjugated analogs, have been broadly discussed in the context of 1,2- and 1,4-difunctionalization. On the contrary, allyl, allenyl, and propargyl silanes, upon their activation with an electrophile, undergo 1,2-silyl migration, creating a formal 1,3-dipole. The reaction of the latter with an appropriate

nucleophile presented in the reaction medium accomplishes the 1,3-difunctionalization of the unsaturated system.[10]

Compared to 1,2- and 1,4-difunctionalization, synthetic methods to obtain 1,3-difunctionalized products are far less studied. Some prominent examples include (Scheme 2): a) ring-opening reactions of donor-acceptor cyclopropanes with nucleophile/electrophile pairs;[11] b) ring-opening reactions with radical initiators;[12] c) ring-opening under reductive conditions;[13] d) hypervalent iodine-catalyzed ring-openings of cyclopropanes;[14] e) transition-metal-catalyzed 1,2-addition – isomerization of unsaturated system – reductive elimination;[15] f) alkene allylic oxidation – unsaturated system functionalization.[16] Unfortunately, none of these proposed methods provides simple and sequential functionalization of the obtained triad, including its C2 atom.



Scheme 2. 1,3-Difunctionalization examples – ring-opening reactions of cyclopropanes and transition-metal-catalyzed alkene functionalization.

The Doctoral Thesis has been devoted to developing novel synthetic strategies for propargyl silane 1,3-difunctionalization using various electrophile/nucleophile pairs. Moreover, depending on the procedure, obtained products may contain up to three reaction centers in the C1, C2, and C3 positions that open further functionalization possibilities for selective and direct synthesis of relevant compounds for the pharmaceutical and materials science industries.

Aims and objectives

The aim of the Thesis was to develop novel synthetic strategies for the synthesis of functionalized products based on the theoretical concept of allylic cation generation from propargyl silanes.

The following tasks were defined.

1. To investigate the use of liquid SO_2 as a Lewis acidic reaction media to obtain silyl dienes that in the given reaction medium will participate in the cheletropic reaction with SO_2 to yield silyl sulfolenes from propargyl silanes in a one-pot reaction.
2. To develop a method for the electrophile-induced synthesis of allyl-functionalized vinyl silanes from propargyl silanes in the reaction with solvent as an external nucleophile.
3. To participate in a co-project about the electrophile-induced heterocyclization of propargyl silanes that contain terminal alkyne and internal nucleophile moieties and to investigate further functionalization possibilities of the obtained products. Furthermore, the concept of asymmetric catalysis should be tested in this reaction series.

4. To test the copper-catalyzed arylation reactions of propargyl silanes using hypervalent iodine reagents.

Scientific novelty and main results

As a result of this Doctoral Thesis, novel synthetic methodologies have been developed that broaden the use of propargyl silanes as formal 1,3-dipoles and harness the 1,2-silyl migration arising from the β-silicon effect. Furthermore, obtained compounds are useful synthetic building blocks for further reactions that build up molecular complexity.

A method was developed in which liquid SO_2 was used as a Lewis acidic solvent to promote the synthesis of silyl sulfolenes from propargyl silanes. This permits the use of significantly weaker Brønsted acids like TsOH and H_2O (compared to previously used TfOH and $HNTf_2$). Obtained silyl dienes immediately participate in the cheletropic reaction with SO_2 to yield silyl sulfolenes in a one-pot procedure.

A novel methodology was developed for (*E*)-selective synthesis of allyl functionalised trisubstituted vinyl silanes in the electrophile-induced addition of nucleophilic solvents to propargyl silane. This concept was also employed for (*E*)-selective intramolecular heterocyclization of propargyl silanes containing internal nucleophiles, to yield heterocycles with functionalized vinyl silane side chain. The newly obtained compounds have up to three continuous reactive centers, and their application was demonstrated in transition-metal-catalyzed cross-coupling, electrophilic silicon exchange, and intramolecular ionic reactions. The possibility of asymmetric catalysis was demonstrated in propargyl silane heterocyclisation reactions in the presence of chiral Brønsted acids.

Experimental conditions were also investigated for copper-catalyzed arylation reactions of propargyl silanes with hypervalent iodine reagents. This will be further developed as a new synthetic method in the future.

Structure and volume of the Thesis

This Doctoral Thesis was prepared as a collection of thematically related scientific publications by the author, dedicated to applying 1,2-silyl migration for the functionalization of propargyl silanes. The Thesis unites three original publications in SCI journals and a review article.

Publications and approbation of the Thesis

The results of the Thesis are reported in three original experimental publications. A review article has been published. The main results were presented at nine conferences.

Scientific publications

1. Kroņkalne, R., **Beļaunieks, R.**, Ubaidullajevs, A., Mishnev, A., Turks, M. Synthesis of Five-Membered Heterocycles Containing Olefin Side Chain by 1,3-Difunctionalization of Propargyl Silanes with a Concomitant 1,2-Silyl Shift. *J. Org. Chem.* **2023**, DOI: 10.1021/acs.joc.3c01481
2. **Beļaunieks, 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**, in press.
3. **Beļaunieks, R.**, Puriņš, M., Kumpiņš, V., Turks, M. Synthesis of 3-Sylilated 3-Sulfolenes from Propargylsilanes and their Reductive Desulfitation. *Chem. Heterocycl. Compd.* **2021**, *3*, 18065.
4. **Beļaunieks, R.**, Puriņš, M., Turks, M. Manifestation of the β-Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift. *Synhtesis* **2020**, *52*(15), 2147–2161.

The results of the Thesis were presented at the following conferences.

1. **Beļaunieks, R.**, Puriņš, M., Līpiņa, R.A., Turks, M. Synthesis of Allyl Functionalized Vinyl Silanes from Propargyl Silanes via 1,2-Silyl Migration. In: *International Symposium on Synthesis and Catalysis, Book of Abstracts*, Portugal, Evora, September 5–8, **2023**, p. 126.
2. **Beļaunieks, R.**, Puriņš, M., Līpiņa, R.A., Turks, M. Use of Propargylsilanes for the Preparation of Highly Functionalized Alkenes via 1,2-Silyl Migration. In: *81st International Scientific Conference of the University of Latvia, Chemistry section, Book of Abstracts*, Latvija, Riga, March 17, 2023. Riga: University of Latvia, 2023, p. 15.
3. Kroņkalne, R., **Beļaunieks, 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, Chemistry section, Book of Abstracts* Latvia, Riga, March 17, 2023. Riga: University of Latvia, 2023, 14.
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5. **Beļaunieks, R.**, Līpiņa, R.A., Puriņš, M., Turks, M. Synthesis of Trisubstituted Vinyl Silanes from Propargyl Silanes via 1,2-Silyl Migration. In: *Balticum Organicum Syntheticum 2022: Program and Abstract Book*, Lithuania, Vilnius, July 3–6, **2022**. Vilnius: UAB Kalanis, 2022, p. 52.
6. **Beļaunieks, R.**, Puriņš, M., Kroņkalne, R., Līpiņa, R., Ubaidullajevs, A., Turks, M. Synthesis of Highly Functionalized Alkenes from Propargyl Silanes via 1,2-Silyl Migration. In: *Stereoselective Alkene Functionalizations: Beilstein Organic Chemistry Symposium 2022*, Germany, Rüdesheim am Rhein, April 26–28, **2022**. Beilstein Institut, 2022, p. 32.
7. **Beļaunieks, R.**, Puriņš, M. Electrophile-Induced Transformations of Propargyl Silanes. In: *Riga Technical University 62nd International Scientific Conference "Materials Science*

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9. **Beļaunieks, R.** Use of Propargylsilanes in Tandem Transformation for the Synthesis of Silyl Sulfolenes. In: *Materials Science and Applied Chemistry 2020*, Latvia, Riga, October 23, 2020. Riga: Riga Technical University 2020, p. 13.
10. **Beļaunieks, R.**, Puriņš, M. Synthesis of Silyl Sulfolenes in Tandem Transormation from Propargyl Silanes in Liquid SO2. In: *78th International Scientific Conference of the University of Latvia, Chemistry section, Book of Abstracts*, Latvia, Riga, March 6, 2020. Riga: University of Latvia, 2020, p. 46.

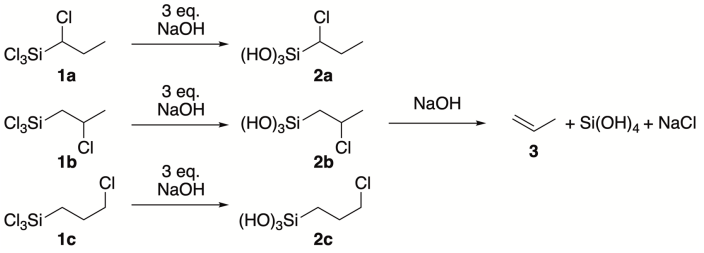
MAIN RESULTS OF THE THESIS

In organic synthesis, organosilicon compounds have been used as protecting groups for alcohols and terminal alkenes.[6] Their application is also broadly covered in reactions like Peterson olefination,[17] Tamao–Fleming oxidation,[8] and Hiyama–Denmark cross-coupling.[9] In contrast, the β-silicon effect is a well-studied but less-used concept. A prominent example where the β-silicon effect contributes to the synthetic transformation is Hosomi-Sakurai-type reactions,[18] where electrophiles induce cation generation in unsaturated systems that are stabilized by a β-silyl substituent. Propargyl silanes can also participate in this type of reaction. Literature reports multiple examples of electrophile-induced elimination of the silyl group; however, activation followed by 1,2-silyl migration seemed synthetically more intriguing, as it opens up the possibility of using propargyl silanes as formal 1,3-dipoles.

The synthetic methods developed during the Doctoral Thesis aim to expand the application of propargyl silanes as formal 1,3-dipoles and obtain highly functionalized atom triads widely applicable in organic synthesis.

1. β-Silicon effect and its contribution to 1,2-silyl migration in propargyl silanes

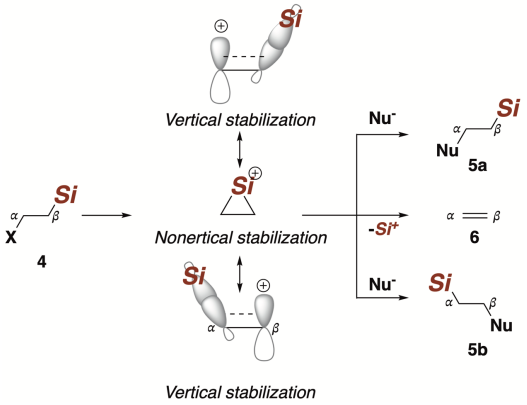
The first reports on changes in substrate reactivity attributed to the β-silyl substituent were reported in 1946 by Sommer and Whitmore.[19, 20] By titrating different regioisomers of 1-trichlorosilylpropane monochlorides **1a-c** with 3 equivalents of cold 0.5M NaOH solution, hydrolysis products of the Si-Cl bond were observed in all cases (Scheme 3). Surprisingly, upon further addition of the base solution, only the β-substituted 2-chloro-1-trichlorosilyl propane (**1b**) continued to react with an additional equivalent of NaOH, yielding the elimination product propene (**3**).



Scheme 3. First demonstration of the β-silicon effect – reactivity of monochlorinated 1-trichlorosilylpropanes with 0.5 M NaOH solution.

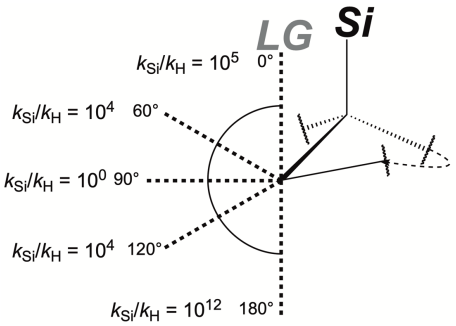
In addition, further experiments aimed at elucidating the mechanism of elimination product formation concluded that solvolysis reactions proceed via the E1 type mechanism, where the first and rate-determining step is the cleavage of the leaving group bond, which forms a β-silyl substituted and stabilized carbocation. This phenomenon was postulated as the β-silicon effect[10] – a stable reaction intermediate, to which two structurally defined stabilization models were

proposed (Scheme 4): the vertical stabilization, where, due to the hyperconjugation, C-Si σ-bond electrons are donated into the vacant *p*-orbital or the non-vertical stabilization, where 4-electron, 3-atom cyclic silonium ion is formed, and the positive charge is delocalized onto silicon itself.



Scheme 4. Possible intermediates in β-silicon-stabilized carbocations.

As the reaction rate due to the β-silicon substituent can experience an increase of up to 12 orders of magnitude, several groups of scientists embarked on the investigation of the phenomenon. To determine conformational constraints, significant contributions have been made by Lambert *et al.* (Scheme 5).[21–25] By synthesizing conformationally restricted silyl derivatives, where the torsional angle between the silyl substituent and the leaving group (LG) was fixed, the obtained compounds were compared in solvolysis reactions with their non-silylated analogs. The highest reaction rate increase, $k_{Si}/k_H = 10^{12}$, was observed in the *anti*-periplanar conformation. In addition, a significant but lower increase was observed for *sin*-planar confirmation – 10^5 times. The decrease in the reactivity could be explained by the interactions between the leaving group and the stabilizing silyl substituent.

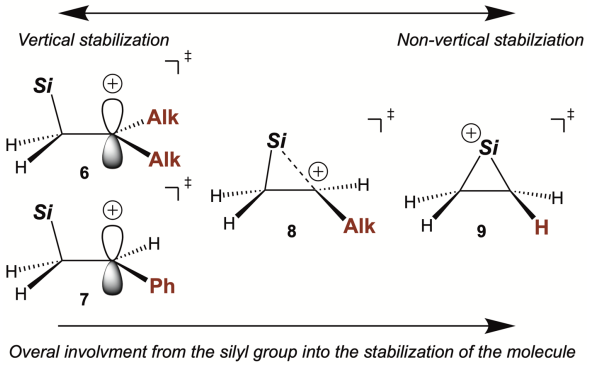


Scheme 5. Changes in the solvolysis rates depending on the torsional angle of Si-C-C-LG.

An increase in reaction rates was also observed in *gauche* and *anti*-clinal conformations (10^4 times), suggesting that the β-silicon effect can play a role in the sub-optimal overlap of the

orbitals involved. In contrast, no increase in the reaction rate was observed in the orthogonal confirmation, indicating that the β-silicon effect is most probably caused by vertical or non-vertical stabilization rather than the positive induction effect of the silyl group. [21–25]

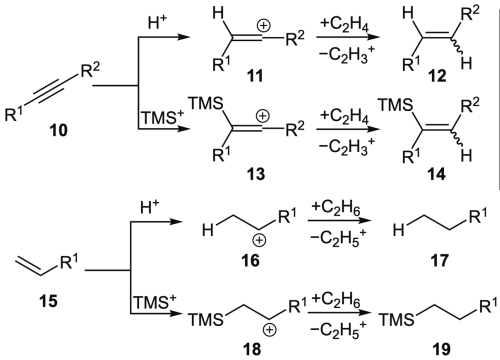
However, these structurally defined silanes do not provide a definitive answer to the question of non-vertical stabilization involvement in the β-silicon effect, as all previous results can be explained only by hyperconjugation. Hence, quantum calculations from the Jorgensen group [26, 27] and experiments interpreted by the Yukawa–Tsuno equation performed by the Fujio group [28–31] provided insight into this question (Scheme 6).



Scheme 6. MP3/6-31G* level calculations on stabilization energy for various β-silyl carbocation systems and investigating the significance of vertical and non-vertical stabilization in relation to the substituents at the cationic reaction center.

The obtained results indicate that in systems lacking stabilizing groups at the cationic center, such as compound **9**, the non-vertical stabilization model dominates, and the contribution of the latter in its overall stability is relatively significant. In contrast, in dialkyl substituted cations **6** and benzyl cations **7**, the vertical stabilization model dominates, and the involvement of the silyl substituent in stabilizing the carbocation is far less pronounced compared to cation **9**. Monosubstituted cation **8** indicates an indeterminate state between vertical and non-vertical stabilization.[26–31]

The β-silicon effect has also been studied in vinyl cations by Stone and co-workers.[32] They analyzed thermodynamic data for the addition of electrophiles (TMS^+ and H^+) to various substituted alkynes and alkenes (Scheme 7). From the measured ΔH values for the formation of carbocations **11** and **13**, the contribution of the β-silicon effect $\Delta\Delta H$ can be measured in-between 8.8-11.6 kcal/mol compared to their non-silylated analogs. Similar experiments were performed for carbocations **16** and **18**. In the case of alkyl-substituted carbocation formation, involvement from the β-silicon effect was measured much higher up to kcal/mol; however, aryl-substituted systems showed only 16.7 kcal/mol involvement from the silyl substituent, which is in a good agreement with the previously obtained results.

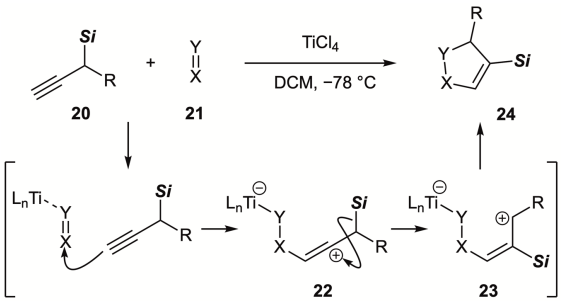


R^1	R^2	ΔH_{Stab} **11,** kcal/mol	ΔH_{Stab} **13,** kcal/mol	$\Delta\Delta H$, kcal/mol
H	*n*-C_4H_9	44.2	54.9	10.7
CH_3	*n*-C_3H_7	46.2	57.8	11.6
H	C_6H_5	49.6	58.4	8.8

R^1	ΔH_{Stab} **16,** kcal/mol	ΔH_{Stab} **18,** kcal/mol	$\Delta\Delta H$, kcal/mol
n-C_4H_9	34.1	60.3	26.2
C_6H_5	43.6	60.3	16.7

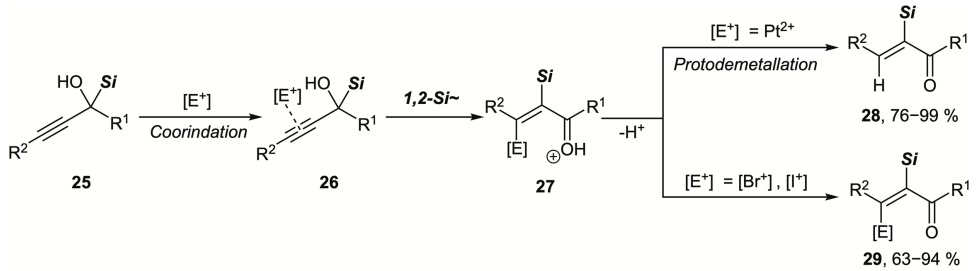
Scheme 7. Silyl vinyl and silyl alkyl carbocation generation to determine the stabilization effects arising from hyperconjugation.

A β-silyl-substituted carbocation can easily form cyclic silonium ions via a non-vertical stabilization model and eventually undergo 1,2-silyl migration through a concerted fashion to result in an energetically more favored product or, due to the multiple stabilizing contributions, form a more stable reaction intermediate. The 1,2-silyl shift in propargyl silanes was first reported in 1985 by the Miginiac group as a side reaction between the latter and acetals. [33] Further substantial contribution to the field of the [2 + 3] annulation chemistry was done by Danheiser *et al.* (Scheme 8). This transformation is initiated by the electrophilic activation of propargyl silane **20** by 1,2-dipole **21** to form intermediate **22,** which undergoes a 1,2-silyl shift to form allylic cation **23**. The latter reacts with the intramolecular nucleophilic center to form the annulation products **24** – cyclopentenes, 1,2,5,7a-tetrahydro-*3H*-pyrrolizine-3-ones, isoxazoles, and azulenes.[34]



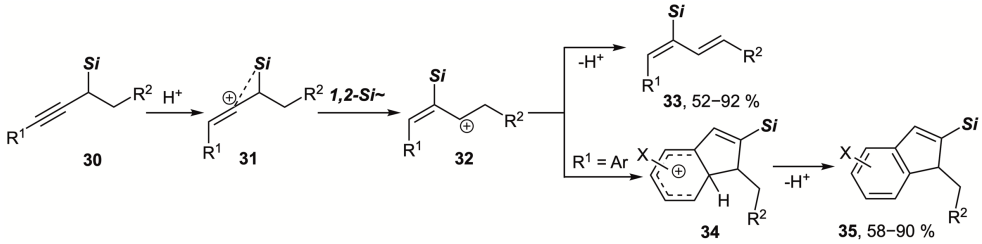
Scheme 8. General scheme for the annulation reactions of 1,2-dipoles and propargyl silanes.

So far, to achieve chemical complexity, 1,3-difunctionalization reactions of propargyl silanes are based on combining two structural scaffolds. Ferreira *et al*. made significant contributions to the functionalization of propargyl silanes. For the first time, they demonstrated that α-hydroxy propargyl silanes **25** could be activated by either transition metals or electrophilic halogen sources to induce semi-silylpinacol-type 1,2-silyl migration to form oxocarbenium ions **27** (Scheme 9). After deprotonation, the latter yields α,β-unsaturated ketones **28** and **29** with high stereoselectivity and further functionalization potential.[35, 36]



Scheme 9. Use of α-hydroxy propargyl silanes **25** in electrophilic halogen and transition metal-induced reactions.

Our research group has previously reported that by treating propargyl silanes **30** with Brønsted superacids (TfOH, Tf_2NH, Tf_3CH), 1,2-silyl migration can be induced to form an allylic cation **31**. Depending on the reaction conditions and substrate's structure, it can undergo either β-proton elimination to form silyl dienes **33** or, if the molecule holds an appropriate nucleophile like aromatic system, participate in intramolecular cyclization to yield silyl indenes **35** (Scheme 10).[37]



Scheme 10. Activation of propargyl silane **30** with Brønsted superacids.

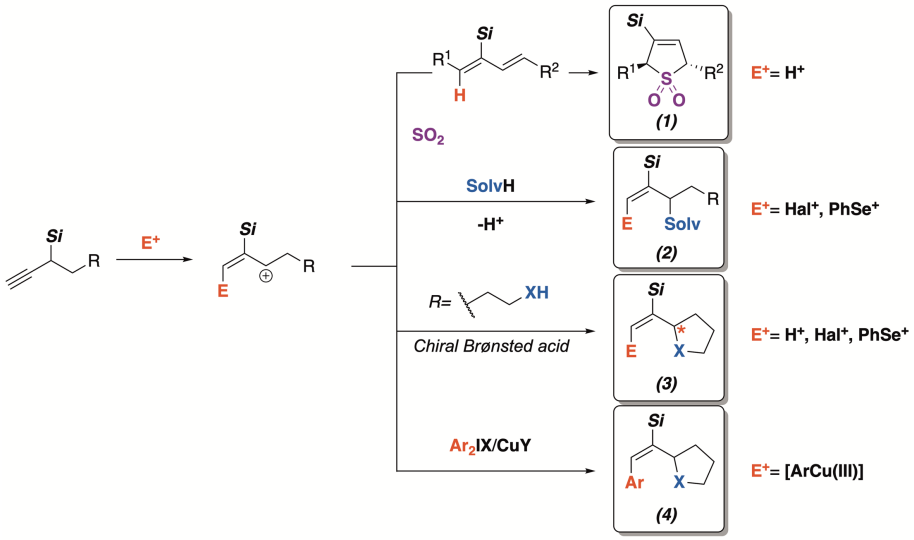
Based on previous achievements in reactions of propargyl silanes for 1,3-difunctionalization, the research conducted in this Doctoral Thesis was dedicated to the development of new synthetic methods that broaden this field. The Doctoral research was divided into four parts (Scheme 11):

(1) The use of liquid SO_2 as a Lewis acidic reaction medium for Brønsted acid-induced 1,2-silyl migration in propargyl silanes, resulting in silyl dienes that would undergo cheletropic cyclization reaction with SO_2, leading to the synthesis of silyl sulfolenes in one-pot reaction.

(2) Employing propargyl silanes in electrophile-induced 1,2-silyl migration reactions with solvents as nucleophiles to obtain allyl-functionalized vinyl silanes with (*E*)-selectivity.

(3) Utilizing propargyl silanes containing terminal alkyne and internal nucleophile moieties in electrophile-induced heterocyclization reactions and developing the concept of its asymmetric version.

(4) Exploring new "C-eletrophilic" synthons for activating propargyl silanes, followed by 1,2-silyl migration, which concludes with the quenching of allylic cation by nucleophilic addition.

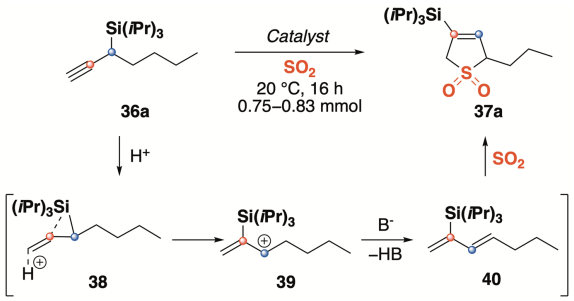


Scheme 11. Research directions for the Doctoral Thesis.

1.1. Synthesis of silyl sulfolenes from propargyl silanes in liquid sulfur dioxide

In our research group, liquid sulfur dioxide has been demonstrated to be an outstanding alternative to conventional solvents. Under normal conditions, SO_2 is a colorless gas with a pungent odor. However, its relatively high boiling point (–10 °C) and low vapor pressure (3 bar, 20 °C; 20 bar, 100 °C) allow easy liquefaction and utilization in a wide temperature range. Furthermore, it can be easily removed from the reaction environment by adjusting temperature and pressure parameters. Although liquid SO_2 is considered a moderately polar (dipole moment 1.75, dielectric constant 20.6) and aprotic solvent, the substantial advantage of SO_2 over other solvents arises from its high Lewis acidity.[38] This can facilitate reactions that proceed via the formation of cationic intermediates, such as alkyne[39] and methylene cyclopropane[40] hydrofunctionalization or glycosylation reactions.[41]

In our group, the previously developed acid-catalyzed isomerization of propargyl silanes **36** into 2-silyl-1,3-dienes **40** required the use of Brønsted superacids like TfOH, Tf_2NH, and Tf_3CH in chlorinated solvents such as CH_2Cl_2 and $CHCl_3$.[37] We hypothesized that due to the Lewis acidic properties of SO_2, this transformation could be achieved with significantly weaker Brønsted acids. Furthermore, the resulting silyl dienes would immediately participate in a cheletropic reaction with SO_2 to yield 3-silyl-3-sulfolenes **37**. The latter can be viewed as formal equivalents of the corresponding silyl dienes **40,** facilitating their purification and enabling further 1,4-functionalization.[42]



Scheme 12. Tandem 1,2-silyl migration – cheletropic addition sequence for the synthesis of silyl sulfolene **37a** and the proposed reaction mechanism.

This research was initiated by identifying the most suitable catalyst (Table 1). As expected, when running reactions in commercially available SO_2 that contains up to 50 ppm residual water, acids such as $TsOH \cdot H_2O$, PhCOOH, and $(NH_4)_2SO_4$ were sufficiently strong to initiate this transformation. Surprisingly, even the residual water was enough to carry out the reaction. However, alcohols such as *t*BuOH and phenols such as BHT, in the presence of molecular sieves, could not initiate this reaction. Experiments 1–4 (Table 1) demonstrate that water traces from SO_2 do not interfere with the reaction when using Brønsted acids within the pK_a range from water to TsOH.

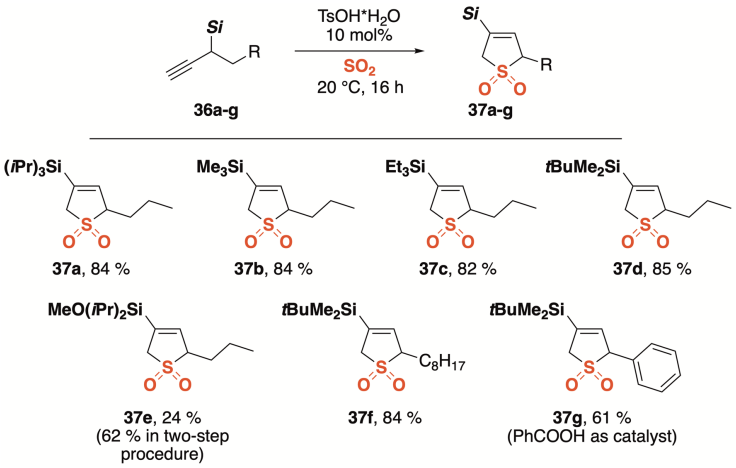
Table 1

Catalyst screening for the tandem 1,2-silyl migration – cheletropic addition sequence displayed in Scheme 12.

No.	Catalyst (mol %)	NMR yield for product **37a**,[a] **%**
1	$TsOH{\cdot}H_2O$ (10)	84
2	PhCOOH (10)	72
3	$(NH_4)_2SO_4$ (10)	75
4	H_2O (100)	67
5	H_2O[a]	75
6	3 Å MS	<5
7	*t*BuOH (10) + 3 Å MS	<5
8	BHT (10) + 3 Å MS	<5

[a] Diphenyl methane as internal standard, an average of two runs
[b] Water (up to 50 ppm) in the commercially available SO_2

Next, $TsOH{\cdot}H_2O$ was tested as the catalyst of choice for the substrate scope (Scheme 13).

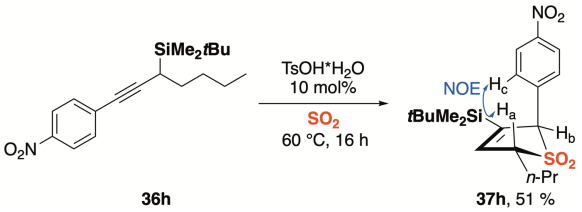


Scheme 13. Substrate scope for the tandem reaction of 1,2-silyl migration and cheletropic addition.

It was found that simple trialkyl silyl groups did not significantly affect the outcome of the reaction, as silyl sulfolenes **37a-d** were obtained in good yields (82–85 %). A high yield was also obtained for product **37f** with a longer *n*-octyl substituent (84 %). Propargyl silanes with electron-withdrawing methoxy substituent on the silicon group afforded product **37e** in a low yield of 24 %. Neither change of the catalyst nor lowering the temperature (–20 °C) did improve the reaction yield. Additional experiments at reduced temperatures indicated that the degradation of starting material occurred at lower temperatures than the desired acid-catalyzed isomerization can be observed. The reaction yield can be improved by performing a two-step procedure: 1) TfOH-catalyzed isomerization in DCM and 2) cheletropic addition of SO_2. This yielded silyl sulfolene **37e** in 62 % yield over two steps. Also, phenyl-substituted propargyl

silane **36e** was prone to side reactions. However, changing the catalyst to less acidic PhCOOH suppressed the formation of byproducts and improved the product **37g** yield to 61 %.

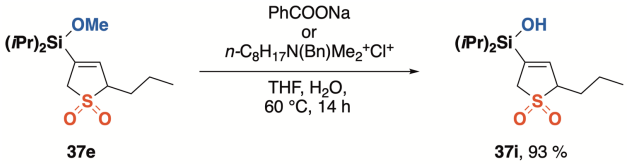
Similarly, 4-nitrophenyl substituted propargyl silane **36h** showed decent reactivity under the given conditions (Scheme 14). Silyl sulfolene **37h** was obtained in 51 % yield as a *trans* diastereomer, which was confirmed by the nuclear Overhauser effect and confirmed our previous findings on selective *E*,*Z*-diene synthesis.[37]



36h **37h**, 51 %

Scheme 14. Synthesis of 2,5-*trans*-disubstituted silyl sulfolene **37h**.

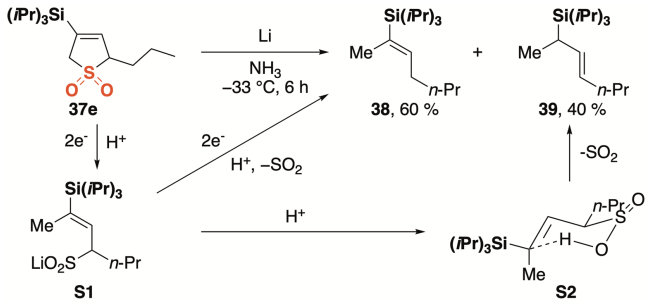
Next, the chemical properties of the obtained sulfolenes were investigated. We tested the possibility of silyl sulfolene **37e** hydrolysis to obtain compound **37i**, a substrate that would be suitable for Hiyama–Denmark cross-coupling reactions (Scheme 15). This was achieved by employing mild nucleophilic groups as mediators to obtain silanol **37i** with a nearly quantitative yield of 93 %.



37e **37i**, 93 %

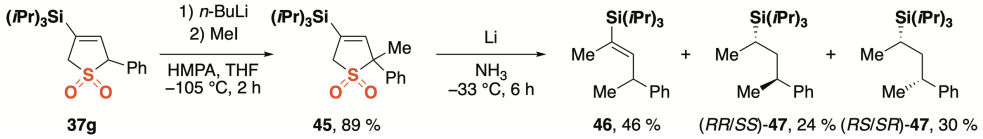
Scheme 15. Hydrolysis of silyl ether **37e**.

We also conducted experiments to test the possibility of sulfolene desulfitation under reducing conditions (Scheme 16). Using lithium as a reductant in liquid NH_3,[43] full conversion of the starting material was obtained, yielding vinyl silane **38** in 60 % yield. However, we also observed the formation of allyl silane **39** in 40 % yield, which could be explained by the retro-*ene* reaction of intermediate **S2**. The product ratio of 60 : 40 remained intact in all of the tested reaction conditions: addition of co-solvent, different proton source, additional base, or the change of the reducing reagent.



Scheme 16. Desulfitation of silyl sulfolene **37e**.

To potentially direct the reduction to either vinyl or allyl silane, we tested how substitution at C2 might affect the product ratio (Scheme 17). When sulfolene **37g** was tested under the given conditions, only degradation of the starting material was observed. However, selective methylation at the C2 position of compound **37g** to obtain compound **45**, followed by reduction, resulted in the formation of three products: the expected vinyl silane **46** and over-reduction products **47**. Interestingly, even with a large excess of lithium, reduction of the phenyl group was not observed.



Scheme 17. The desulfitation of silyl sulfolene **45**.

Both diastereomers of compound **47** were fully characterized by 1D and 2D NMR (COSY, HSQC, HMBC) analysis methods (Fig. 1). Analysis of coupling constants indicates that both diastereomers tend to adopt the conformation in which the *sin*-pentane interactions are minimized – H_d and one of the methyl groups are positioned in a pseudo-axial position. This, in fact, should lead to an observable upfield shift of the H_c proton in compound (*RS*/*SR*)-**47** owing to the anisotropic effect arising from the aryl group. Indeed, comparing (*RS*/*SR*)-**47** with (*RR*/*SS*)-**47**, a significant H_c shift is observed (0.50 ppm compared to 0.97 ppm). Similarly, only reversed effects can be observed for the H_b proton, which resonates at 1.67 ppm for compound (*RR*/*SS*)-**47** and at 1.81 ppm for compound (*RS*/*SR*)-**47**. These results are further supported by the changes in these signals at reduced temperatures; shielded protons experience increased upfield shift as the temperature decreases.

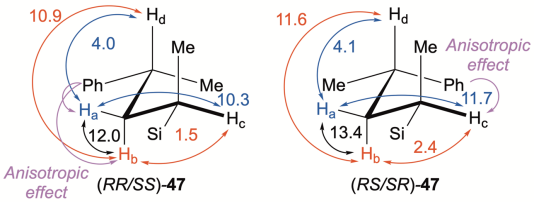


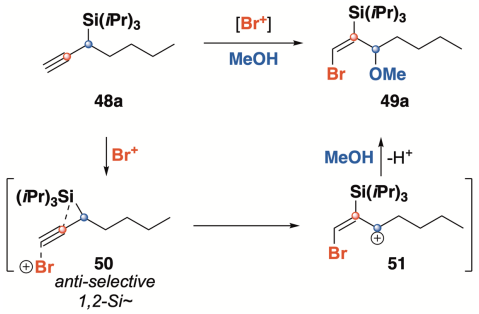
Figure 1. NMR analysis of diastereomers **47**.

1.2. Electrophile-induced synthesis of allyl-functionalized vinyl silanes from propargyl silanes

Propargyl silanes have typically been used as 1,3-dipoles in [2 + 3] annulation reactions. However, we were intrigued by propargyl silane activation using various electrophilic reagents that initiate 1,2-silyl migration to generate the corresponding allylic cation, which could then readily combine with nucleophiles present in the reaction environment. In previous studies, the quenching of this cation was achieved through structural changes such as the formation of an unsaturated system within the substrate itself. We hypothesized that the generated allylic cation could be trapped by an external nucleophile. As the first choice for performing such transformations, we selected polar nucleophilic solvents, as they would provide both a stabilized environment for the generated charged species and facilitate the last step due to the high nucleophile concentration.

Table 2

Optimization of propargyl silane **48a** bromo methoxylation



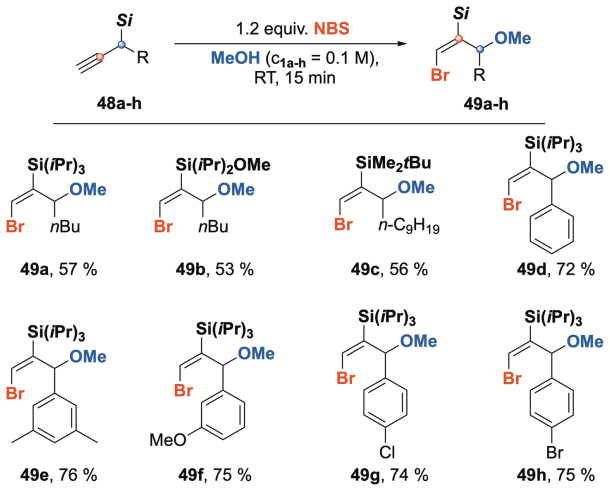
No.	Reaction conditions	NMR yield **49a**, %
1	NBS (1.2 equiv.), RT	60 (57)[c]
2	NBS (1.2 equiv.), Range of temperature = –78, 0, 50 °C	52–58
3	NBS (1.2 equiv.), RT c_{1a} 0.05 M – 0.2 M	55–56
4	NBS (0.6–2.0 equiv.), RT	49–52
5	NBS (1.2 equiv.), RT 10 % MeOH solution $(CF_3)_2CHOH$	46
6	Br_2 (1.0 equiv.), RT	49
7	$TsNBr_2$ (1.2 equiv.), RT	56
8	MeC(O)NHBr (1.2 equiv.), RT	57
9	1,3-Dibromo-5,5-dimethylhidantoine (0.6 equiv.), RT	57
10	Dibromoisocyanuric acid (0.6 equiv.), RT	51

[a] Standard conditions: c_{1a} = 0.1 M, reaction time 15 min
[b] Diphenyl methane as internal standard
[c] Isolated yield

In the first experiment, we decided to perform the reaction of propargyl silane **48a** with *N*-bromosuccinimide (NBS) (1.2 equiv.) in methanol (0.1M) at room temperature (Table 2, Entry

1). After just 15 min, complete conversion of the starting material was observed, and methyl ester **49a** was isolated in 57 % yield. Next, we evaluated the effects of temperature, concentration, amount of NBS, the addition of a co-solvent, and other sources of electrophilic bromine species. Nevertheless, no significant improvement or deterioration was observed; hence, operationally simple initial conditions were chosen to investigate the range of substrates.

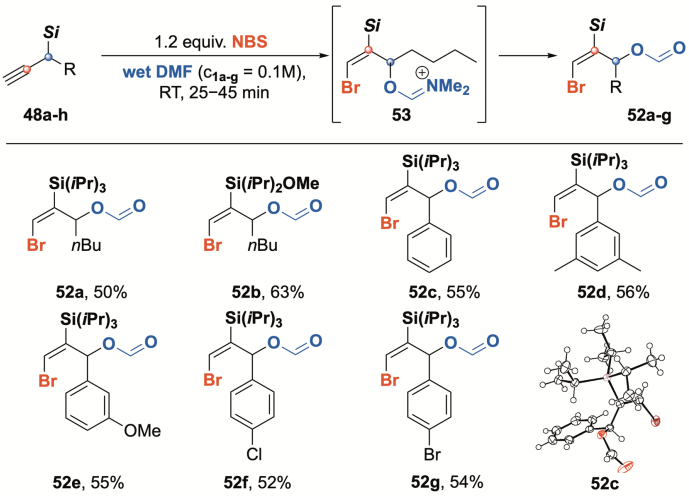
The reactivity was also examined with other 3-alkyl propargyl silanes **48a,b** (Scheme 18). Neither the length of the alkyl chain nor the modification of the silyl substituent significantly affected the reaction outcome and progress, affording methyl esters **49b** and **49c** in 53 % and 56 % yields, respectively. The introduction of an aryl substituent at the propargylic position resulted in a significant improvement in the reaction yield. All tested 3-aryl propargyl silanes **48a-h** yielded methyl esters **49d-h** with yields ranging from 72 % to 76 % with reaction times similar to the previous cases. This suggests that the aryl substituent can provide additional stabilization to the reactive intermediate and reduce the occurrence of various degradation processes regardless of the electronic effects introduced by the substituents on the specific aryl group.



Scheme 18. Bromomethoxylation products **49a-h** of propargyl silane **48a-h**.

As the next nucleophilic solvent to investigate, we chose DMF, which participated as a formate group equivalent (Scheme 19). Conducting the reactions in wet DMF, alkyl-substituted propargyl silanes **48a,b** yielded formates **52a**,**b** in moderate 50 % and 63 % yields, respectively.

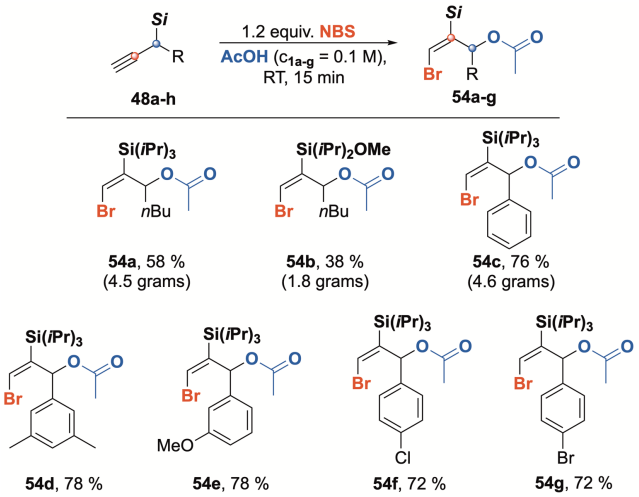
Interestingly, the aryl-substituted propargyl silanes exhibited very comparable moderate results, giving formates **52c-g** in the range of 52–56 % within 25–45 minutes. Lower reaction yields and longer reaction times indicate that DMF is a relatively weaker nucleophile compared to methanol, leading to undesired side reactions, which can be observed in the GC-MS analysis.



Scheme 19. Bromoformyloxylation products **52a-g** of propargyl silanes **48a-h** and ORTEP representation of compound **52c**.

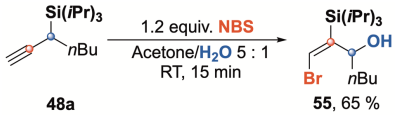
Single crystals of compound **52c** were obtained that were suitable for X-ray analysis, which unambiguously confirmed the structure of compound **52c** and (*E*)-double bond selectivity for the 1,2-silyl migration event.

The third tested solvent was acetic acid (Scheme 20). Considering that the previously developed method by our group for activating propargyl silanes relied on Brønsted acid-catalysis, we had concerns about substrate stability in an acidic environment. Yet, these concerns turned out to be only partially met, as the only substrate that showed decreased yield was propargyl silane **48b**. The other propargyl silanes showed reactivity comparable to previous results in methanol, as aryl-substituted propargyl silanes gave superior yields compared to alkyl silanes, yielding aryl-substituted acetates in 72–78 % yield and alkyl-substituted acetate **46a** in 58 % yield. In addition, we demonstrated the scalability of this reaction on a multi-gram scale, obtaining product **54c** (4.6 g) in a yield of 76 %.



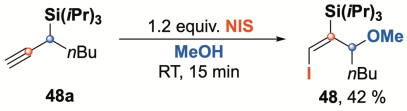
Scheme 20. Bromoacetoxylation products **54a-g** of propargyl silanes **48a-h**.

The addition of other electrophile/nucleophile pairs was also examined. We successfully performed the bromohydroxylation in an acetone/water (5 : 1) system. Alcohol **55** was obtained in a 65 % yield (Scheme 21). We were surprised by the inertness of 3-aryl propargyl silanes under the given reaction conditions, which could be attributed to the weak nucleophilicity of water and the potentially high stability of the formed allyl benzylic cation.



Scheme 21. Bromohydroxylation product of propargyl silane **48a**.

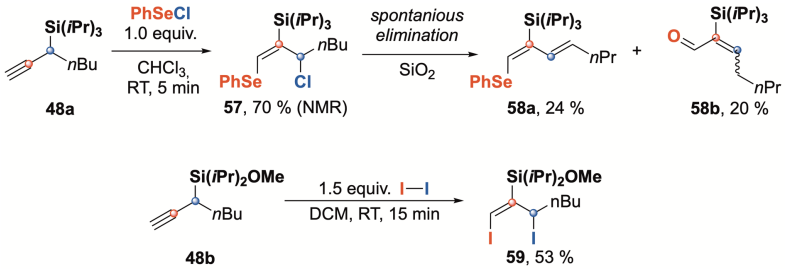
N-Iodosuccinimide (NIS) in methanol exhibits a relatively similar reactivity to NBS. The corresponding iodo methoxylation product **56** was obtained in a 42 % yield (Scheme 22).



Scheme 22. Iodo methoxylation product of propargyl silane **48a**.

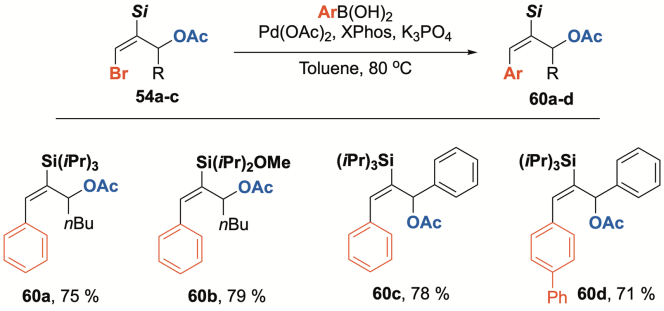
1,3-Difunctionalization was also feasible with electrophile/nucleophile pairs, such as phenylselenyl chloride and elemental iodine, in halogenated solvents (Scheme 23). The reaction between propargyl silane **48a** and PhSeCl was finished in 5 min, yielding vinyl selenide **57** with a 70 % NMR yield. Unfortunately, we were unable to isolate the product for full characterization. Upon purification on direct and reverse phase silica, compound **57** spontaneously decomposed, and we isolated the elimination product diene **58a** with a 24 %

yield and the hydrolysis product aldehyde **58b** with a 20 % yield. On the other hand, 1,3-diiodination product **59** was successfully isolated with a 53 % yield.



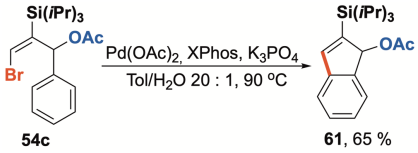
Scheme 23. Difunctionalization of propargyl silanes with electrophile/nucleophile pairs.

The newly obtained compounds contain three reaction centers and can be potentially used as effective building blocks for site-selective alkene synthesis. To demonstrate the latter, we utilized vinyl bromides **54a-c** in a Suzuki–Miyaura cross-coupling reaction. By employing modified Buchwald conditions,[44] cross-coupling products **60a-d** were obtained with good yields ranging from 71 % to 79 % (Scheme 24).



Scheme 24. Cross-coupling reactions of vinyl bromides **60a-c**.

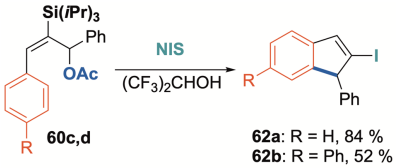
Furthermore, by excluding the aryl boronic acid from the reaction medium, we successfully obtained the intramolecular C-H-activation-cyclization product **61** with a 65 % yield (Scheme 25).



Scheme 25. Intramolecular cyclization reaction of vinyl bromide **54c** via C-H activation.

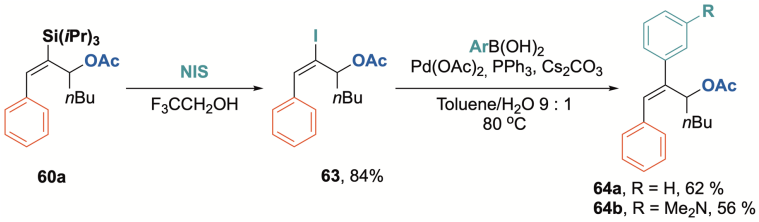
The next step was focused on the selective functionalization of the silicon group. To achieve this, we employed electrophilic silyl group exchange with NIS. Interestingly, we observed that compounds bearing the aryl group in the allylic position underwent intramolecular cyclization

under all tested conditions. The corresponding iodo indenes **62a** and **b** were obtained in up to 84% yield in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) (Scheme 26).



Scheme 26. Tandem cyclization – electrophilic exchange reaction of vinyl silanes **60c,d**.

Cyclization was prevented by using an alkyl-substituted vinyl silane **60a**. By reducing the ionization potential and changing the solvent from HFIP to 2,2,2-trifluoroethanol, vinyl iodide **63** was obtained with 84% yield (Scheme 27). Subsequently, by repeating the Suzuki-Miyaura cross-coupling reaction, the latter was transformed into the corresponding stilbenes **64a,b** in 62% and 56% yields, respectively. Stilbenes **64a,b** retained the original double-bond configuration (as evidenced by ^{1}H-^{1}H-NOESY NMR) throughout the entire reaction sequence, starting from compound **54a**.

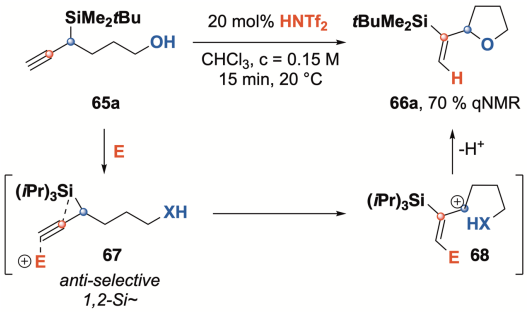


Scheme 27. Functionalization of silicon moiety in vinyl silane **60a**.

1.3. Electrophile-induced synthesis of heterocycles with vinyl silane side chain from terminally functionalized propargyl silanes

Among all small-molecule drug compounds approved by the U.S. Food and Drug Administration (FDA), 59% contained nitrogen (data from 2014), [45] and 27% contained oxygen heterocycles (data from 2018).[46] In order to expand the available synthetic methods for obtaining heterocyclic compounds, together with Rasma Kroņkalne and Artjoms Ubaidullajevs, a hypothesis was proposed that using propargyl silanes linked to various nucleophilic groups could generate allylic cations, which could then undergo intramolecular cyclization to form diverse heterocyclic derivatives.

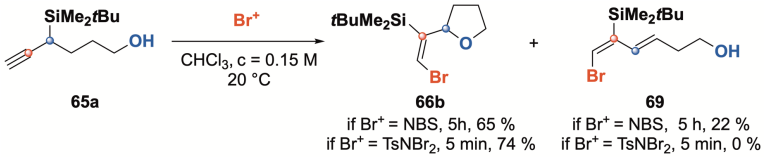
We decided to initiate the research by examining the heterocyclization of compound **65a** under acid-catalyzed conditions using quantitative NMR analysis. The initial experiments indeed showed the desired formation of tetrahydrofuran **66a**. After optimizing the reaction conditions, the most suitable conditions were determined to be using $HNTf_2$ in chloroform at room temperature with a reaction time of 15 min (Scheme 28).



Scheme 28. Optimized conditions for the synthesis of tetrahydrofuran **66a**.

Similar results can be achieved by using similar Brønsted superacids such as TfOH or by conducting the reaction in a solvent that does not level the acidity of the catalyst. Lowering the temperature or the catalyst loading only led to a decrease in the reaction rate.

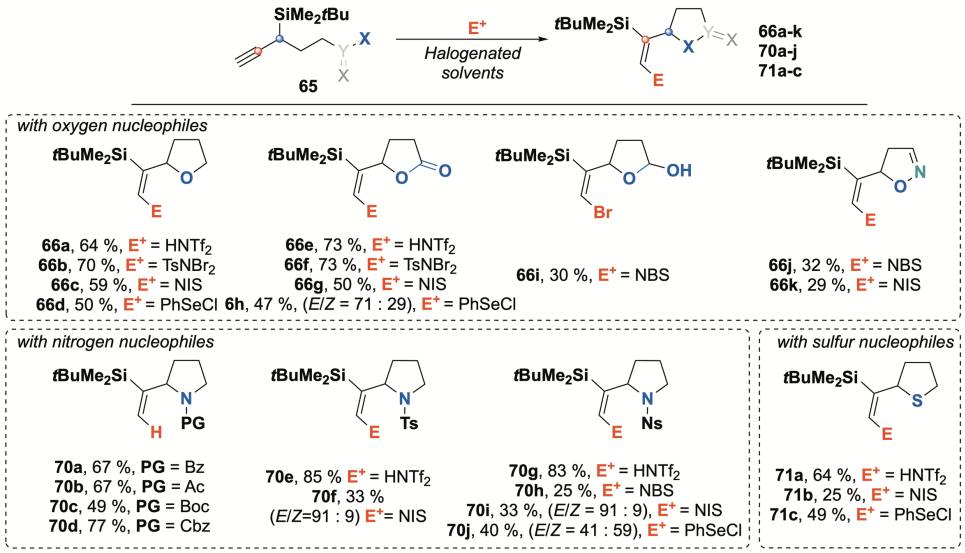
Next, propargyl silane **65a** was tested for electrophilic halogen activation using NBS (Scheme 29). The influence of solvent and reaction temperature was examined; however, under all the tested conditions, the formation of diene **69** was observed alongside the desired product **66b.** The formation of the latter was least pronounced by carrying the reaction in $CDCl_3$. In addition, the reaction times were significantly prolonged compared to the acid-catalyzed reactions; full conversion in $CDCl_3$ was achieved only after 5 h, which can be attributed to the low solubility of NBS in halogenated solvents.



Scheme 29. Optimized conditions for the synthesis of tetrahydrofuran **66b**.

Therefore, we decided to explore other electrophilic bromine sources. Fortunately, in the first experiment, *N*,*N*-dibromo-4-methylbenzene sulfonamide showed high reactivity, benefiting from its solubility in halogenated solvents. Full conversion of the starting material was achieved in less than 5 min (the time required to add the reagent and acquire the NMR spectra). In these conditions, only the formation of desired tetrahydrofuran **66b** was observed, probably due to the lower basicity of the corresponding sulfonamide anion.

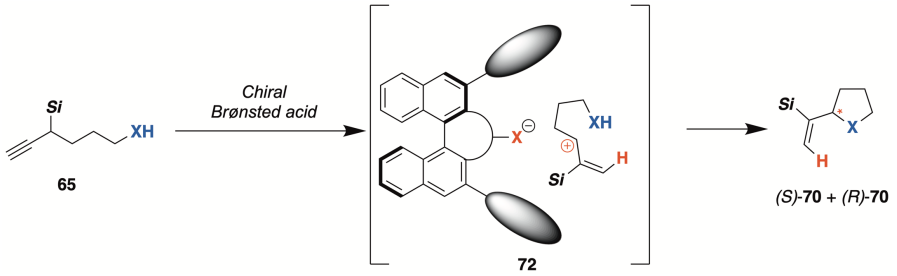
After identifying the optimal conditions, the substrate scope was investigated by Rasma Kroņkalne and Artjoms Ubaidullajevs (Scheme 30). Various heterocyclization reactions were tested using intramolecular oxygen (alcohols, aldehydes, carboxylic acids, and oximes), nitrogen (amides, carbamates, and sulfonamides) and sulfur (thioacetate) nucleophiles in combination with electrophilic reagents (Brønsted superacids, NBS, $TsNBr_2$, NIS, PhSeCl).



Scheme 30. Substrate scope for intramolecular heterocyclization reactions from propargyl silanes **65** (in collaboration with R. Kroņkalne and A. Ubaidullajevs).

The reactions resulted in the formation of heterocyclic derivatives with yields ranging from 25 % to 85 %. The method allowed obtaining tetrahydrofuran **66a-d**, γ-butyrolactone **66e-h**, tetrahydrofuran-2-ol **66i**, 2-isoxazole **66j-k**, pyrrolidine **70a-j** and thiolane **70a-c** derivatives with olefine sidechain.

Since our developed method for intramolecular cyclization is based on the putative formation of stable allylic cation intermediate, we hypothesized that asymmetric counteranion-directed catalysis (*ACDC*) [47] could enable nucleophilic attack by introducing enantiodiscrimination. To achieve this, BINOL-derived Brønsted acids were selected as a source of chiral information (Scheme 31; for experimental procedures, see Appendix V).



Scheme 31. Use of chiral Brønsted acid-catalysis for intramolecular cyclization reaction.

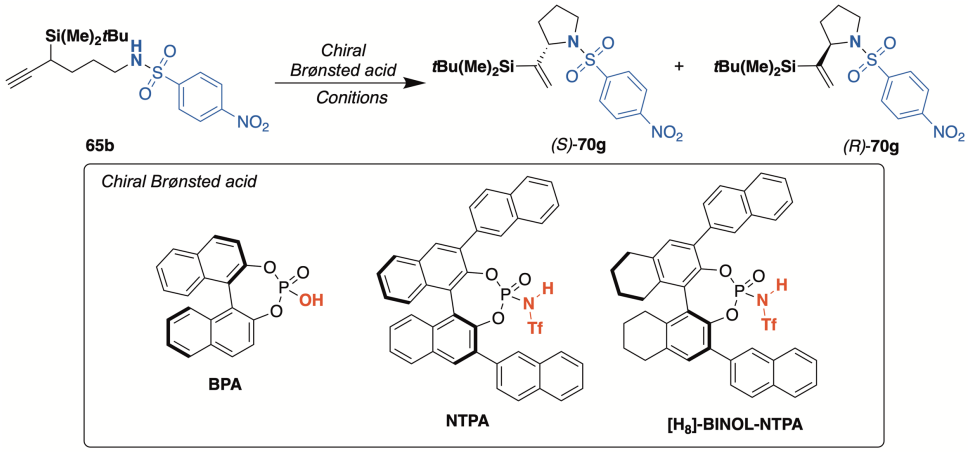
The initial experiments involved selecting the appropriate substrate and establishing a chromatographic analysis method. Propargyl silane **65b**, containing a nitrobenzene sulfonyl amide group, was chosen due to its chromophoric properties, enabling convenient quantification of the obtained enantiomeric ratio using HPLC systems coupled with a UV

detector. The optimal enantiomeric separation was achieved using (R,R)-Whelk-O 1 as a chiral stationary phase and 5 % *i*PrOH/Hex (v/v) as a mobile phase.

In order to obtain enantiomeric excess, we tested the available chiral Brønsted acids. When $HNTf_2$ was replaced with BINOL-derived phosphoric acid, the starting material **65b** was not reactive (Table 3, Entry 1). Substituting DCM with chloroform and refluxing for 72 hours resulted in the isolation of 13 % of the desired product; however, asymmetric induction formation was not observed.

Table 3

Chiral Brønsted acid-catalyzed cyclization conditions of propargylsilane **65b**.

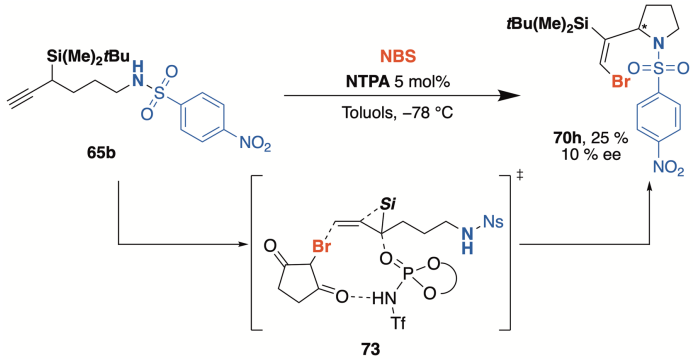


No.	Catalyst	Solvent	T, °C	t, h	Yield, %	ee, %
1	**BPA**	DCM	20	24	-	-
2		$CHCl_3$	63	72	13	0
3	**NTPA** 5 mol%	PhMe	60	19	56	6
4		Cyclohexane	60	18	62	11
5	**NTPA** 10 mol%	Cyclohexane	i.t.	19	52	11
6	**[H_8]-BINOL-NTPA** 5 mol%	Cyclohexane	60	21	45	12

The next set of experiments was conducted using commercially available *N*-trifluoromethane sulfonyl phosphoimidates **NTPA** and **[H_8]-BINOL-NTPA**, which are more acidic compared to phosphoric acid (**BPA**) and also contain bulky substituents at the 2,2'-positions to enhance chirality transfer. The first reaction was performed in toluene at 60 °C with **NTPA** (Table 3, Entry 3). The desired product was obtained after 19 hours with a 56 % yield and 6 % enantiomeric excess. To improve the latter, we performed experiments in cyclohexane, which could promote tighter ion pair formation. Conducting the experiments at room temperature with **NTPA** (Table 3, Entry 5) and **[H_8]-BINOL-NTPA** (Table 3, Entry 6) resulted in acceptable reactivity and enantiomeric excess up to 12 %.

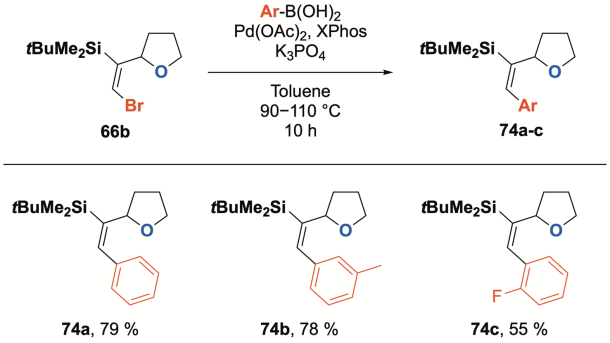
Since there are known examples of chiral Brønsted acids activating achiral electrophilic halogenating reagents and enabling enantioselective transformations, we explored the reaction with NBS in the presence of **NTPA** (Scheme 31). Pyrrolidine **70h** was obtained with a 25 % yield and 10 % enantiomeric excess. Results in Scheme 32 and Table 3 demonstrate the proof

of concept and open the possibility of developing enantioselective synthesis of various heterocycles from propargyl silanes.



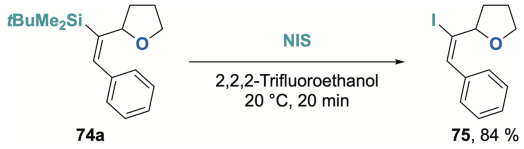
Scheme 32. Chiral Brønsted acid-catalyzed cyclization of **65b**.

Next, we translated the previously developed functionalization approach of compounds **54** to heterocyclization product **66b**. As a model substrate, we chose the easily accessible vinyl bromide **66b** and performed Suzuki–Miyaura cross-coupling reactions (Scheme 33). By employing modified Buchwald conditions with various aryl boronic acids, we obtained silyl styrenes **74a-c** in moderate to very good yields of 55–79 %.



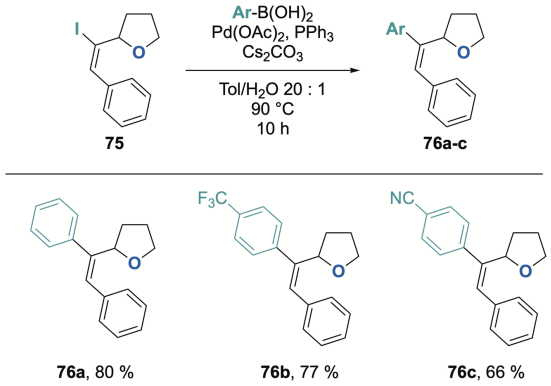
Scheme 33. Suzuki–Miyaura cross-coupling reactions of vinyl bromide **66b**.

Compound **74a** was used for electrophilic exchange of silicon to obtain vinyl iodide **75** (Scheme 34). When the reaction was performed in HFIP, a rapid reaction rate was observed that yielded the desired product **75** in less than 15 min. However, under these conditions, we observed double bond isomerization, yielding an *E*/*Z* ratio of 4 : 1. Fortunately, we resolved this issue by changing the reaction solvent from HFIP to 2,2,2-trifluoroethanol. Vinyl iodide **75** was obtained with an 84 % yield while preserving the double-bond configuration.



Scheme 34. Electrophilic exchange reaction of vinyl silane **74a**.

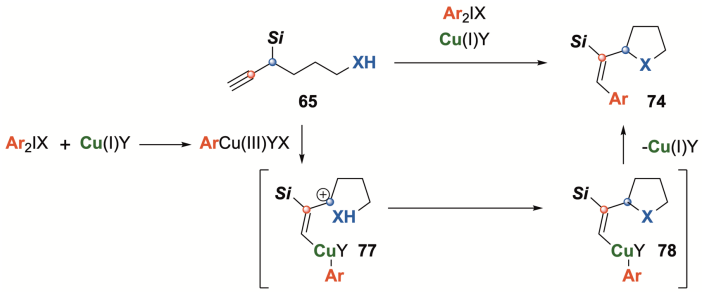
The obtained vinyl iodide **75** was successfully utilized in Suzuki–Miyaura cross-coupling reactions, yielding tetrahydrofurans **76a-c** with trisubstituted alkene sidechain with a 66–80 % yield (Scheme 35) while preserving the original double bond geometry, which was obtained from the synthesis of compound **66b**.



Scheme 35. Suzuki–Miyaura cross-coupling reactions of iodo styrene **75**.

1.4. Copper-catalyzed propargyl silane arylation with hypervalent iodine reagents

While demonstrating the utility of the obtained cyclic products as useful building blocks, our attention was drawn to synthetic methods of unsaturated system arylation with hypervalent iodine reagents under copper catalysis.[48] If this concept could be adapted to propargyl silanes **65**, it would enable to accomplish 1,2-silyl migration, intramolecular cyclization, and aryl functionalization of the alkene in a single synthetic step, resulting in the formation of compounds **74** (Scheme 36, for experimental procedures, see Appendix VI).



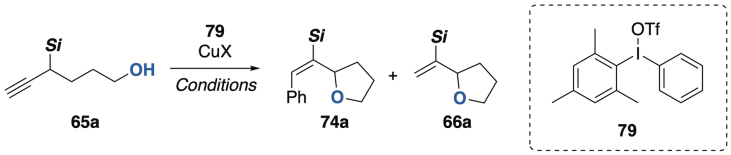
Scheme 36. Proposed copper-catalyzed arylation of propargyl silane **65** with hypervalent iodine reagents.

For the first experiment, we chose to react alcohol **65a** with aryl iodide **79** in the presence of CuCl (Table 4, Entry 1). In this case, the formation of the acid-cyclized product **66a** was observed, which could be explained by the possible generation of TfOH *in situ* from aryl iodide **79**. However, when 2,6-di-*tert*-butylpyridine was added and the reaction temperature increased (Table 4, Entry 1), the desired product **74a** was obtained with a yield of 76 % (82 % NMR).

Similar reactivity was observed when CuOTf·PhH was used as a copper source. Further optimization of the reaction conditions did not lead to improved results.

Table 4

Copper-catalyzed arylation of propargyl silanes **65a** with aryl iodane **79**

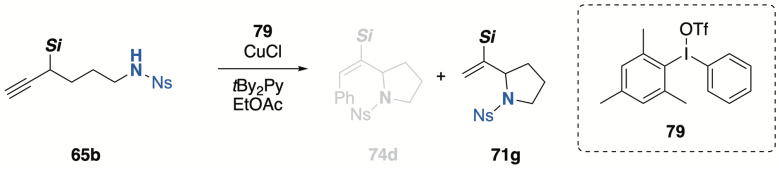


65a 74a 66a 79

No	CuX	Solvent	T, °C	Additive	**74a**, % (NMR)	**66a**, % (NMR)
1	CuCl	EtOAc	20	-	0	69
2		EtOAc	20	*t*Bu$_2$Py	0	0
3		EtOAc	60		82 (76)[a]	0
4		THF	60		56	0
5		$CHCl_3$	60		59	0
6		PhMe	60		17	0
7		MEK	60		0	0
8		MeCN	60		0	0
9		EtOAc	60	Lutidine	0	0
10		EtOAc	60	Et_3N	0	0
11	CuI	EtOAc	60	*t*Bu$_2$Py	0	0
12	CuOTf·PhH	EtOAc	60		84	0

[a] Isolated yield

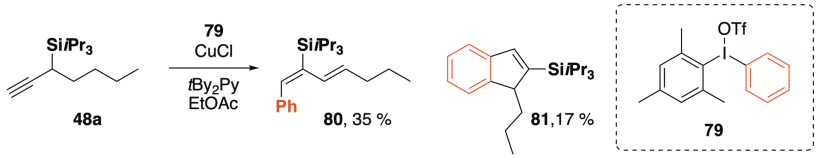
An attempted cyclization of sulfonamide **65b** under the optimized conditions did not result in the formation of the desired product, and instead, pyrrolidine **71g** was obtained (Scheme 37). This can be attributed to the acidity of the sulfonamide and the steric interaction between the forming copper intermediate and the incoming nucleophilic group (Scheme 36, intermediate **78**), which likely leads to protodemetalation rather than the desired reductive elimination.



65b 74d 71g 79

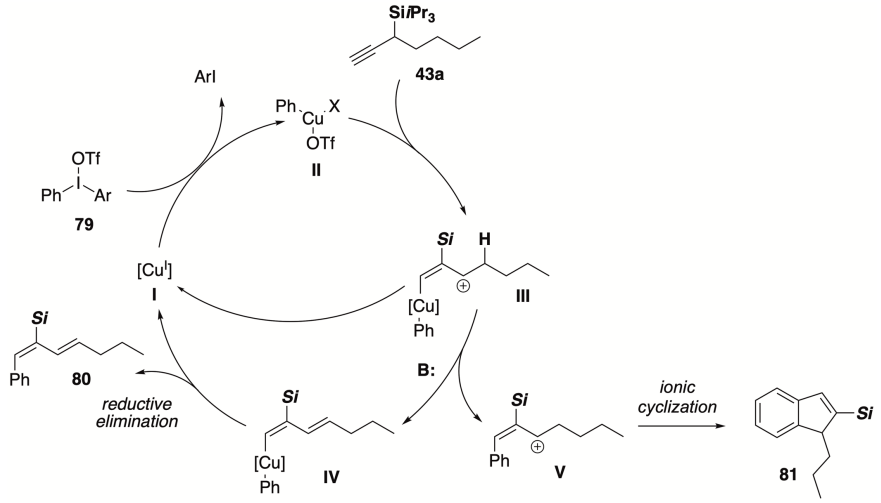
Scheme 37. The attempt of propargyl silane **65b** arylation.

In the arylation reaction, propargyl silane **48a**, which does not contain an intramolecular nucleophilic group, was also tested (Scheme 38). When the reaction was performed under optimized conditions, a mixture of two compounds, aryl diene **80** in 35 % and indene **81** in 17 % yield, was obtained.



Scheme 38. Copper-catalyzed propargyl silane **48a** arylation with hypervalent iodine reagents.

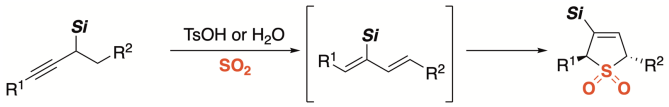
We suggest the mechanism of formation for both products in Scheme 39. Initially, the copper(I) source **I,** upon the oxidative addition, forms the copper (III) complex **II**, which in an electrophilic reaction induces the 1,2-silyl migration, forming the intermediate **III**. At this point, intermediate **III** can react with the base to form intermediate **IV**, which, after a reductive elimination, yields aryl diene **80**. Otherwise, intermediate **III** can directly undergo reductive elimination to form intermediate **V**, which immediately undergoes an intramolecular cyclization reaction, resulting in the formation of indene **81**. So far, the ongoing optimization experiments have not allowed for the selective formation of either the aryl diene **80** or the indene **81**, but the experimental work is still in progress.



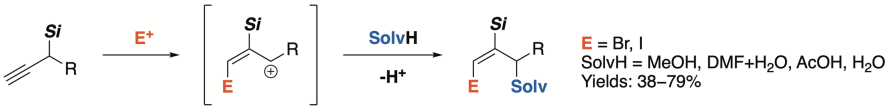
Scheme 39. Proposed reaction mechanism for copper-catalyzed propargyl silane **48a** arylation with hypervalent iodine reagents.

CONCLUSIONS

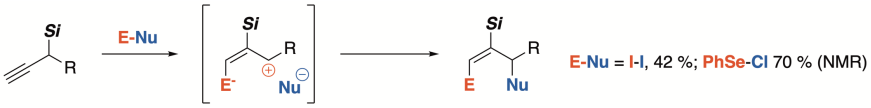
1. Liquid sulfur dioxide is a suitable reaction medium for the synthesis of silyl sulfolenes from propargyl silanes through a weak acid-catalyzed propargyl silane isomerization – cheletropic cycloaddition sequence in a one-pot procedure.



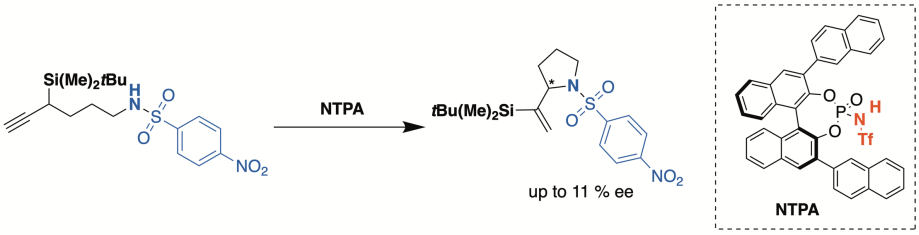
2. Electrophilic halogen reagents are capable of inducing 1,3-difunctionalization reactions in propargyl silanes, which are terminated by the addition of O-nucleophilic solvents (MeOH, DMF, AcOH, H_2O). The solvent simultaneously ensures a polar reaction environment and a high concentration of nucleophilic reagent. The developed methodology yields functionalized triads with a fixed (*E*)-double bond configuration.



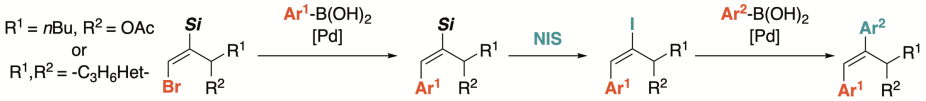
3. Propargyl silanes can be used in 1,3-difunctionalization reactions with electrophile/nucleophile pairs in non-nucleophilic solvents (haloalkanes).



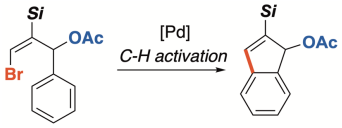
4. Chiral Brønsted acids can provide asymmetric induction in propargyl silane heterocyclization reactions. Using *N*-trifluoromethane sulfonylphosphoimidates (**NTAP**), an enantiomeric excess of 11 % was achieved. This demonstrates the possibility of chirality transfer in the investigated chemical transformations.



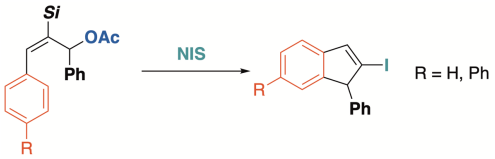
5. Obtained bromovinyl silanes containing alkyl or heterocyclic side chains are valuable starting materials for synthesizing configurationally defined trisubstituted alkenes. This can be achieved through selective Suzuki–Miyaura cross-coupling and electrophilic exchange reactions. The reaction sequence ensures the preservation of the initial double bond configuration.



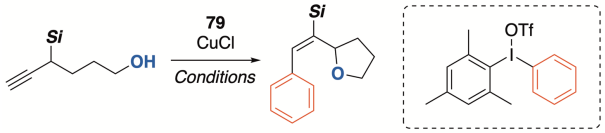
6. Bromovinyl silanes containing acetoxy and phenyl substituents in the allylic position undergo intramolecular C-H activation reaction under palladium-catalyzed conditions, resulting in the corresponding acetoxyindenes.



7. Electrophilic exchange reactions with NIS on the silyl styrenes containing acetoxy and phenyl substituents in the allylic position led to the ionization of the acetate group alongside silicon exchange. This induces an intramolecular cyclization reaction, yielding corresponding iodo indenes.



8. Propargyl silanes containing terminal alkyne and intramolecular *O*-nucleophile moiety can undergo C-C arylation with subsequent 1,2-silyl migration and cyclization by using aryl iodanes under copper-catalyzed conditions.



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PIELIKUMI / APPENDICES

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Appendix 1

Manifestation of the β-Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift

Rūdolfs Beļaunieks, Mikus Puriņš, Māris Turks

Synthesis. **2020**, *52*(15), 2147–2161

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Rüdigerstraße 14
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ISSN 0039-7881

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Synthesis R. Beļaunieks et al. Short Review

Manifestation of the β-Silicon Effect in the Reactions of Unsaturated Systems Involving a 1,2-Silyl Shift

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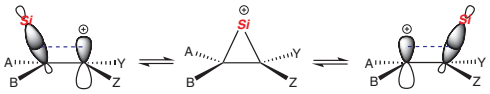

Received: 31.01.2020
Accepted after revision: 30.03.2020
Published online: 20.04.2020
DOI: 10.1055/s-0039-1690898; Art ID: ss-2020-m0063-sr

Abstract Many chemical transformations of organosilicon compounds proceed due to the capability of silyl substituents to stabilize a positive charge in its β-position. This short review provides an overview of the present understanding of the β-silicon effect and focusses on the synthetic applications of 1,2-silyl shifts resulting from non-vertical stabilization of alkylcarbenium ions and vinyl cations. The reactions of silicon containing unsaturated starting materials, alkenes, allenes, and alkynes, involving β-silyl group stabilized cationic intermediates, transition metal carbenes, or vinylidene complexes will be discussed.

Key words β-silicon effect, 1,2-silyl migration, carbocations, allenylsilanes, propargylsilanes, allylsilanes, silylvinylidenes

Rūdolfs Beļaunieks (left) obtained his B.Sc. and M.Sc. from Riga Technical University (RTU) in 2017 and 2019, respectively. Currently he is pursuing his doctoral degree under the supervision of Prof. M. Turks. His research is focused on novel synthetic methodologies involving 1,2-silyl shift.
Mikus Puriņš (middle) obtained his B.Sc. and M.Sc. from RTU under the supervision of Prof. M. Turks in 2017 and 2019, respectively. Currently he is pursuing his doctoral degree under the supervision of Professor Jérôme Waser at Swiss Federal Institute of Technology, Lausanne (EPFL), Switzerland. His research interests include tethered strategies for selective functionalization of small molecules.
Professor **Māris Turks** (right) obtained his B.Sc. in chemistry from the University of Latvia in 1998 and his M.Sc. from Riga Technical University in 2000. In 2005 he earned his Dr. ès. sc. degree in synthetic organic chemistry from EPFL, Switzerland under the direction of Professor Pierre Vogel. Then he spent one year as SNSF Postdoctoral Fellow at Stanford University in the group of Professor Barry M. Trost. In 2007, he accepted an academic position at the Faculty of Materials Science and Applied Chemistry, RTU, where he is currently Dean of Faculty and Director of the Institute of Technology of Organic Chemistry. Prof. Turks' current research interests are in organosilicon chemistry, application of sulfur dioxide in organic synthesis, and purine and triterpenoid chemistry.

1 Introduction

In the family of group IV elements, carbon plays a central role as the main building block of organic chemistry. Silicon, albeit related, offers some curious differences. Although, silicon and carbon share the archetypal tetravalency, silicon's position in the 3rd period of Mendeleev's periodic table unlocks many pathways impossible for its neighbor, carbon. The clear differences are its increased size,[2] higher energy p-orbitals,[3] accessible vacant d-orbitals,[4] and diminished electronegativity.[5] This amounts to remarkable differences in the bonding properties of silicon. The C–Si bond (1.85 Å) is considerably longer than the C–C bond (1.54 Å),[6] although of comparable strength. Silicon also forms high strength bonds with electronegative elements, which is a driving force for many organosilicon-based reactions.[7] The unique affinity of silicon towards fluorine offers

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orthogonal deprotection conditions, which cements the silyl group's position as one of the most useful protecting groups for oxygen-containing compounds.[8] Silicon even holds a near monopoly for the protection of sp hybridized carbons.[8] Moreover, the activation via 'ate' complexes has realized the possibility of harnessing the intrinsic polarity of the C–Si bond, exemplified by the Tamao–Fleming oxidation or the Hiyama–Denmark cross-coupling reactions.[9,10]

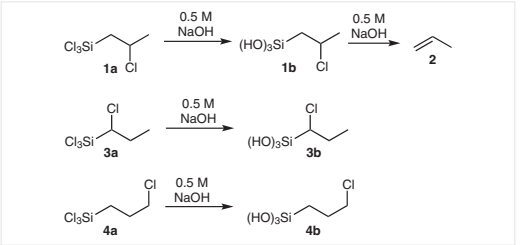
The most intriguing property of silicon is that of the stabilization of electron-deficient carbon atoms in β-silicon carbenium ions, widely recognized as the β-silicon effect. In fact, this effect is responsible for most of the observed reactivity of unsaturated organosilicon compounds.[11] However, historically the explanation of the β-silicon effect has not been a trivial task. Various experimental observations of products where silicon had changed its position on the carbon backbone led to different interpretations of the structure of the β-silicon carbenium ion (*vide infra*). This question was parallel to the famous debate of Winstein and Brown on the non-classical carbocations, albeit not as vocal and publicized.[12] Just as for the question on the structure of the 2-norbornyl cation, the resulting experimental and theoretical studies have increased the understanding of β-silicon carbenium ions.

Synthetic methods involving 1,2-silyl migration have been developed since the 1980s and have been previously reviewed by Aye and co-workers for the reactions of allenyl, propargyl, and vinylsilanes;[13] Knölker and co-workers[14,15] and Landais and co-workers[16] have reviewed allylsilane annulation reactions. This review aims to introduce the origins of the β-silicon effect and its manifestation in some synthetic methodologies of the last decade that involve a 1,2-silyl shift, yet discussing them in the context of previous research.

2 Origins of the β-Silicon Effect

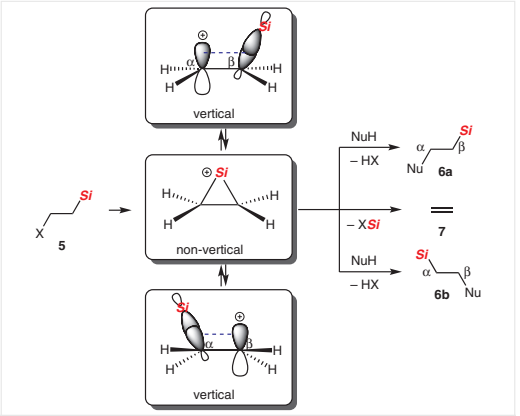
The first observation of enhanced reactivity or a change in chemoselectivity caused by a β-silyl substituent was reported by Sommer and Whitmore.[17,18] They observed that when treating β-silicon alkyl chloride **1a** with sodium hydroxide only the elimination product, propylene (**2**), was obtained (Scheme 1). Under the same reaction conditions, the regioisomeric silylalkyl chlorides **3a** and **4a** afforded only the hydrolysis products of the Si–Cl bond. Further investigations concluded that similar elimination reactions proceed via the E1 reaction mechanism, where the rate determining step is the dissociation of C–X bond.[19]

The twelve-fold increase of the solvolysis rate can be explained by the formation of a carbenium ion that is stabilized by the β-silyl group. This intermediate is described by two possible structural proposals: (1) a vertically stabilized carbenium ion (i.e., hyperconjugation by the neighboring



Scheme 1 Hydrolysis of silylalkyl chlorides

C–Si bond) where no notable changes in lengths of bonds are observed; (2) a non-vertically stabilized silonium ion, where the lengths of the bonds alter significantly (Scheme 2).[20] The question between vertical and non-vertical stabilization is that of whether the non-vertically stabilized form can be regarded as a feasible transition state for two different structures in rapid equilibrium, or as a true intermediate (energy minimum).



Scheme 2 Vertical and non-vertical stabilization of carbenium ions by β-silicon substituent. Here and further in text substituent '***Si***' is used as generic description of the R_3Si group (R = alkyl and/or aryl).

The geometry required for the manifestation of the β-silicon effect was convincingly demonstrated with cyclic and conformationally restricted model substrates possessing a distinct dihedral angle between the leaving group and the β-silyl substituent (Figure 1).[21–24] Compared to non-silylated analogues a greater increase of the solvolysis rate was observed in *anti*-periplanar conformation **12**, up to 10^{12} times. The *syn*-periplanar conformation **8** showed a significant increase as well (10^5 times), though not as notable as the *anti*-periplanar conformation. The elimination from compound **8** indicates the existence of vertical stabilization in the intermediate β-silyl carbenium ion. On the

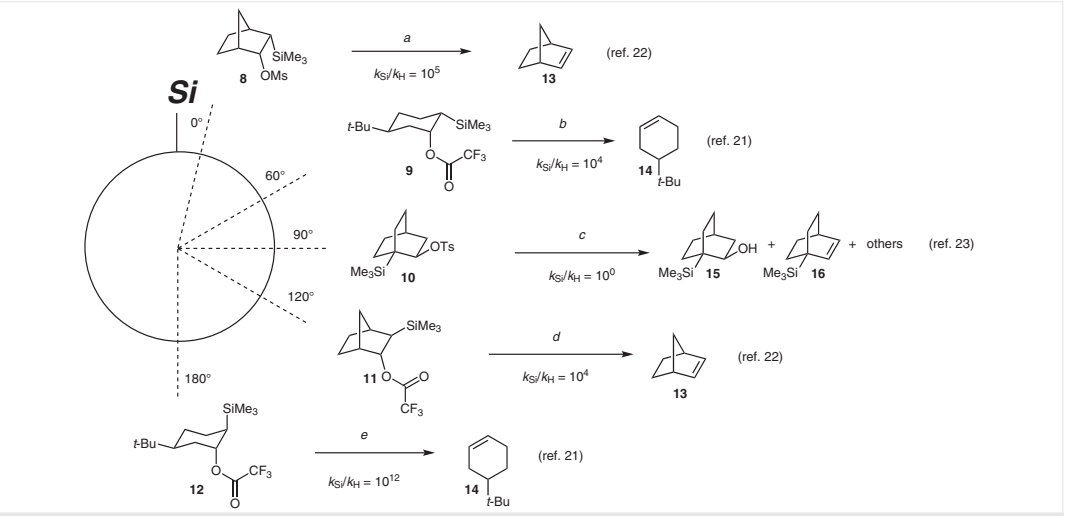


Figure 1 Comparison of solvolysis rate constants in CF_3CH_2OH at 25 °C (*a*, *d*, and *e* are extrapolated from experiments at other temperatures)

contrary, the non-vertical stabilization of the intermediate during the reaction **8** → **13** is disturbed by the *syn*-periplanar placement of the silyl group and the mesylate leaving group. However, the observations do not exclude non-vertical stabilization effects in *anti* conformation **12**. The increase of the rates in gauche (**9**) and anticlinal (**11**) conformations by a factor of 10^4 clearly states that the partial overlap can increase the reaction rates as well. As predicted, in orthogonal conformation **10**, where neither hyperconjugation, nor formation of silonium ion can take place, no increase in the reaction rate was observed. In conclusion, the experimental evidence indicates that formation of carbenium ion in the above-mentioned and other conformationally unrestricted β-silyl systems is mainly due to both vertical and non-vertical stabilization (Scheme 2), but not from the induction effects of the electron-donating silyl group.

These suggestions are in the same vein as computer-aided modeling (Figure 2). MP3/6-31G* level calculations of simple systems showed a 38.0 kcal/mol increase in the stabilization energy for the vertical (open) transition state **19b** in comparison to the unsubstituted ethyl cation (**17**). The primary carbenium ion **19a**, in which the C–Si bond is orthogonal to the empty orbital, is stabilized by 8.9 kcal/mol, suggesting the existence of induction and polarization effects arising from the C–Si bond. However, the cyclic silonium ion **19c** was found to be even more stable by 2.4 kcal/mol than the open structure **19b**. In spite of the latter, further calculations showed that for tertiary carbenium ions (e.g., intermediate **20**) the added donating substituents compete for their role in the overall stabilization of the system. Therefore, the necessity for silonium ion formation is

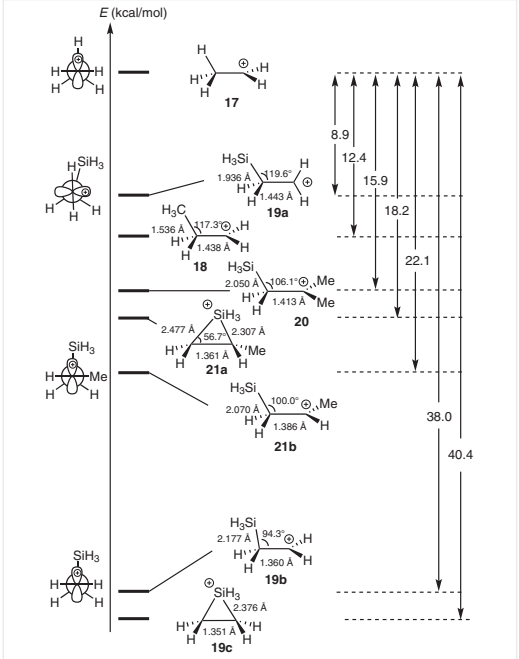


Figure 2 Calculation of stabilization energy for different β-silylcarbenium systems

diminished. Finally, the non-vertically and vertically stabilized secondary carbenium ions **21a** and **21b** differ by 3.9 kcal/mol with the latter being more stable.[25,26]

To determine transition state structures, the solvolysis kinetics of β-silyl systems **22** were measured for variously substituted β-aryldimethylsilyl systems (Figure 3).[27–30] The obtained data were interpreted with the Yukawa–Tsuno equation, a modification of the Hammett equation that accounts for the resonance effects on a reactive center (Equation 1). The parameter ρ describes the sensitivity of the transition state towards the electronic effects of its substituents. It shows the relative amount of charge on the silicon center: a strongly negative ρ-value indicates an enhanced positive charge on the silicon (i.e., greater importance of the non-vertical stabilization).

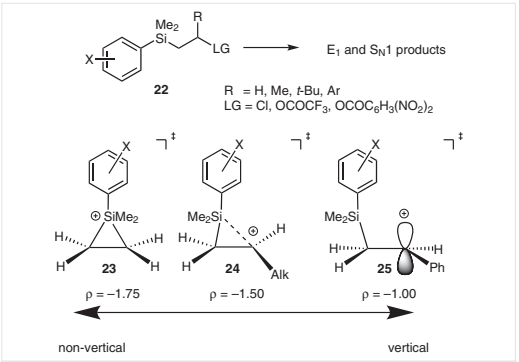


Figure 3 Kinetic studies of transition states of β-silylcarbenium systems

$$\lg\left(\frac{k_x}{k_h}\right) = \rho\left(\sigma^\circ + r^+ \Delta\bar{\sigma}_R^+\right)$$

Equation 1 Yukawa–Tsuno equation: k_x = reaction rate constant for X-substituted arylsilane; k_h = reaction rate constant for unsubstituted phenylsilane, ρ = reaction constant, σ° = Hammett substituent constant; r^+ = enhanced resonance parameter, $\Delta\sigma^+_R$ = Hammett resonance substituent constant.

It was concluded that for α-unsubstituted systems **23** ρ = –1.75, alkyl-substituted systems **24** ρ = –1.50, and aryl-substituted systems **25** ρ = –1.10 to –0.80. Combined quantum chemical calculations and kinetic data showed that the less stabilized, unsubstituted systems prefer non-vertical stabilization, but for the benzyl carbenium ion vertical stabilization is the dominant one. The alkyl-substituted system behaved as a non-discrete structure between vertical and non-vertical stabilization. These findings correlate with previously described solvolysis and DFT calculation results.

The stabilization of vinyl cations by the β-silyl group initially was studied by DFT calculations. Compared to the unsubstituted vinyl cation **26** its counterpart, the vinylsilane **29**, is by 28.6 kcal/mol more stable (Figure 4).[25]

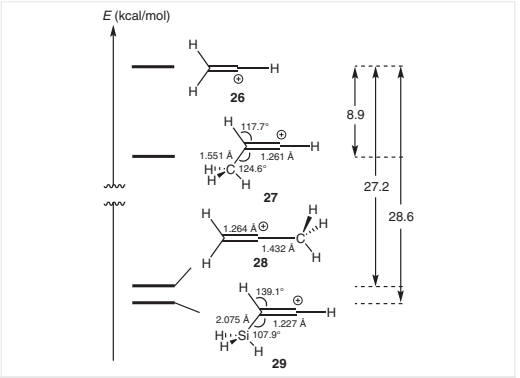
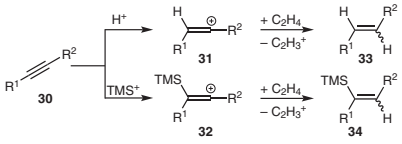
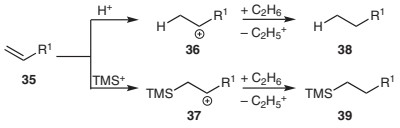


Figure 4 Stabilization of vinyl cation by β-silicon effect

To assess the stabilization effects of the β-silyl carbocation, Stone and co-workers analyzed thermodynamic data of electrophile [TMS$^+$ (TMS = trimethylsilyl) or H$^+$] addition to differently substituted alkynes and alkenes (Scheme 3). From the measured ΔH_f of cations **31** and **32** and alkenes **33** and **34** the corresponding stabilization energies: ΔH_{stab} were calculated. The β-silyl effect stabilizes vinyl carbocation **32** by 8.8–11.6 kcal/mol in comparison to its non-silylated counterpart **31**. In a similar way $\Delta\Delta H$ were determined between sp^2-carbenium ions **36** and **37**. In this case,



R^1	R^2	$\Delta H_{Stab\ 31}$, kcal/mol	$\Delta H_{Stab\ 32}$, kcal/mol	$\Delta\Delta H$, kcal/mol
H	*n*-Bu	44.2	54.9	10.7
Me	*n*-Pr	46.2	57.8	11.6
H	Ph	49.6	58.4	8.8

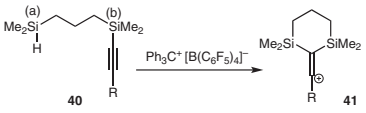


R^1	$\Delta H_{Stab\ 36}$, kcal/mol	$\Delta H_{Stab\ 37}$, kcal/mol	$\Delta\Delta H$, kcal/mol
n-Bu	34.1	60.3	26.2
Ph	43.6	60.3	16.7

Scheme 3 Formation of silylvinyl cations for studying effects of hyperconjugation

the stabilization resulting from the presence of the silyl group was doubled and the intermediate **37** was by 26.2 kcal/mol more stable than **36**. Finally, if a substituent at α-position is more stabilizing, e.g. aryl groups, the participation of the silicon in the stabilization is lower when compared to α-alkyl substituents (Scheme 3).[31]

It was discovered that β,β-silyl disubstituted vinyl cations **41** are surprisingly stable in solution and as anhydrous salts with tetrakis(pentafluorophenyl)borate as counterion. Their NMR,[32] X-ray diffraction,[33] and IR spectroscopy[34] studies revealed further correlation between cation stabilization from an α-aryl substituent and hyperconjugation from the β-silyl group (Scheme 4). In ^{29}Si NMR the presence of a single signal indicates the formation of symmetrical species. A significant low-field shift difference of Δδ ^{29}Si ~ 29–42 ppm can also be observed between compounds **40** and **41**. The such significant deshielding was attributed to the localization of the positive charge on the silicon due to hyperconjugation effects. In addition, the correlation between deshielding and donating/withdrawing effects can be observed as the most deshielded silicon was with R = fluorophenyl and the least deshielded, with R = ferrocenyl. The same goes with the $^{1}J_{C\text{-}Si}$ coupling constants showing lower values for more electron-deficient systems indicating reduced degree of bonding between Si–C$^{\beta}$.[32] Similar conclusions can be drawn when studying these substances with IR spectroscopy. By decreasing the electron-donating effects, the C=C^{+} bond order increases indicating a growing importance of hyperconjugation by silicon.[34]

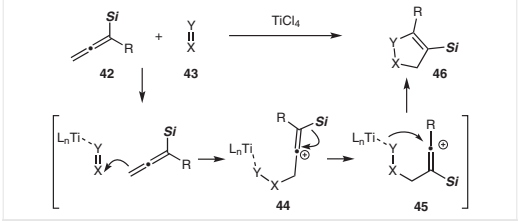


Scheme 4 Formation of β,β-silyl disubstituted vinyl cations

In summary, the β-silicon effect is an established phenomenon that has resulted in useful synthetic transformations of vinyl, allyl, propargyl, allenyl, and other silanes via a β-silyl carbenium ion intermediates. On several occasions, the lower energy of the intermediate β-silyl carbenium ion is due to non-vertical stabilization. This, in turn, can lead to 1,2-silyl shift that produces a more stable ionic species than the initial one.

3 Reactions of Allenylsilanes

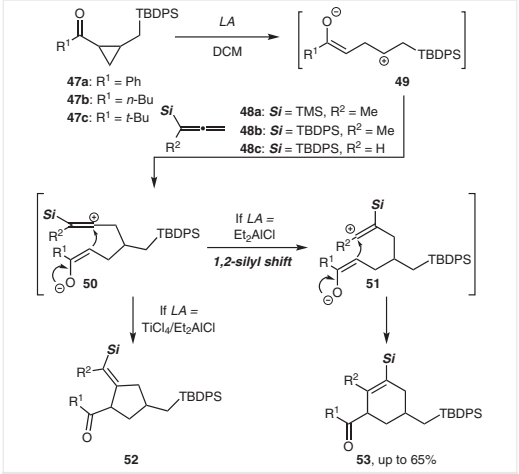
The first reports of 1,2-silyl migration come from the Danheiser group back in 1981.[35] Treating the α,β-unsaturated ketone **43** with allenylsilanes **42** forms the cationic intermediate **44** which undergoes silyl migration to form the novel vinyl carbocation ion **45** that ultimately affords the favorable cyclopentane **46** (Scheme 5). This formal use of allenylsilanes **42** as a 1,3-dipole in reactions with 1,2-unsaturated systems **43** was established further. Following the reaction pattern of [3+2] addition, Danheiser developed methods for the formation of other 5-membered rings **46** like azulene,[36] pyrrole,[37] furan,[37,38] and isoxazole derivatives.[39]



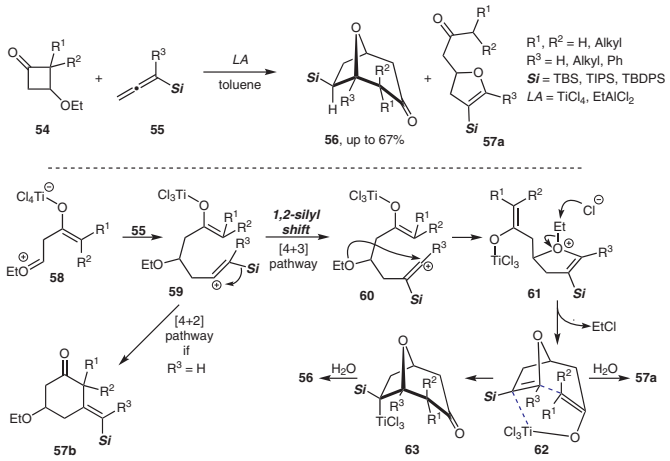
Scheme 5 Cyclopentene annulation reaction; the Danheiser annulation

In 2018, a novel method using the Danheiser annulation was developed to synthesize *cis*-hydrindan-2,4-diones that could further be used for the synthesis of lycopodium alkaloids.[40]

The use of allenylsilanes as 1,3-dipoles was extended to other cycloadditions. Under Lewis acidic conditions cyclopropanes **47** can serve as 1,3-dipolar synthons and participate in cycloaddition reactions with allenylsilanes **48** (Scheme 6).[41]



Scheme 6 Reaction and plausible mechanism of [3+3] and [3+2] addition of cyclopropanes and allenylsilanes



Scheme 7 Reaction and mechanism of cyclobutanone and allenylsilanes

The cyclopropane **47a** underwent ring-opening and annulation at –78 °C with (trimethylsilyl)allene **48a** using $TiCl_4$ as a catalyst; these catalytic conditions induced protodesilylation. To overcome this problem, a mixture of $TiCl_4$ and Et_2AlCl was used and product **52** was obtained. This selectivity of [3+2] addition was switched by increasing the reaction temperature to 25 °C and using Et_2AlCl as the only Lewis acid. This change promoted intermediate **50** to undergo complete migration of the silyl group to the intermediate **51** that, after cyclization, resulted in [3+3] addition product **53**.

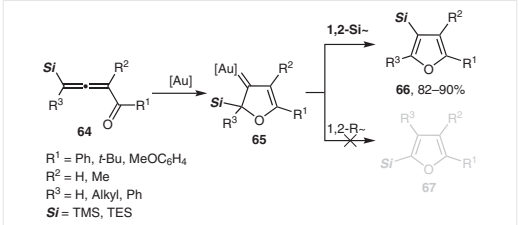
The reaction was also studied with unsubstituted allenylsilane **48c**. This reaction afforded only the [3+2] addition products **52**, as the transition state **51** for this compound is hypothesized to be much higher in energy than transition state **50**. The reaction scope could be extended to spirocyclic cyclopropanes to construct the corresponding spiro[4.4], -[4.5], and -[5.5] compounds from the corresponding cyclopropanones.

1,4-Dipoles can be obtained in a similar fashion from cyclobutanones as previously described with cyclopropanes. The Matsuo group worked on various [4+3] annulation reactions in order to uniquely obtain 8-oxabicyclo-[3.2.1]octan-3-ones via Lewis acid mediated reactions involving 1,2-silyl migration (Scheme 7).[42]

The reaction mechanism proceeds with an initial Lewis acid promoted ring-opening of the butanone cycle. This results in the addition of the allene **55** to the oxocarbenium ion **58**. Further 1,2-silyl migration promotes an intramolecular transetherification along with EtCl formation. The resulting cyclization and hydrolysis afford the desired product **56** (Scheme 7). The most successful results (product **56** yields up to 67% and product **57a** as low as 3%) were achieved by using $TiCl_4$. A series of other Lewis acids yielded no product with the only exception being $EtAlCl_2$ which in combination with $TiCl_4$ gave product **56** in 52% yield.

The highest yields of product **56** were obtained with the *tert*-butyldiphenylsilyl (TBDPS) group. The relatively smaller triisopropylsilyl (TIPS) and *tert*-butyldimethylsilyl (TBS) groups showed a decrease in overall reactivity and greater formation of product **57a**, even after prolonged heating. Larger substituents at the α-position of the silicon decreased yields of the bicyclic product **56**, whereas the unsubstituted allenylsilane **55** (***Si*** = TBDPS, $R^1 = R^2 = Me$, R^3 = H) gave only the [4+2] addition product **57b** without 1,2-silyl migration.

Allenylsilanes can also be used in cycloisomerization reactions. Gevorgyan and co-workers used DFT calculations to develop a method that employs a 1,2-silyl migration (Scheme 8).[43]



Scheme 8 Gold-catalyzed furan synthesis with 1,2-silyl migration

Calculations in gas phase and solution both revealed that a 1,2-silyl migration is also possible for the late transition metal stabilized carbenes and they are strongly favored over 1,2-shifts of Me, Ph, and even H (Table 1). The results

Table 1 Predicted Relative Activation Energies of Silicon vs Substituent R^3 for 1,2-Migrations in Intermediate **65** (R^1 = R^2 = H, R^3 = H, Me, Ph)

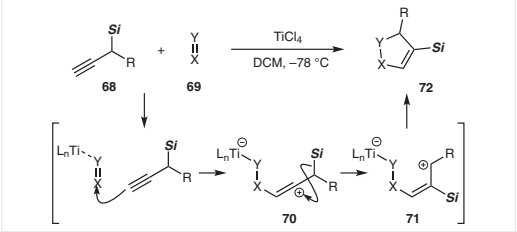
1,2-Migrating group	ΔΔG‡ (kcal/mol)		Gold catalyst
	Gas phase	Solution	
Me	22.7	–	[Au] = $AuCl_3$
Ph	18.1	–	
H	11.1	12.8	
TMS	0.0	0.0	
H	–	12.2	[Au] = H_3PAu^+
TMS	–	0.0	

showed that α-alkyl, α-aryl, and even unsubstituted allenylsilanes **64** proceeded smoothly to afford the corresponding 3-silylfurans **66** in good yields (Scheme 8).

4 Reactions of Alkynes

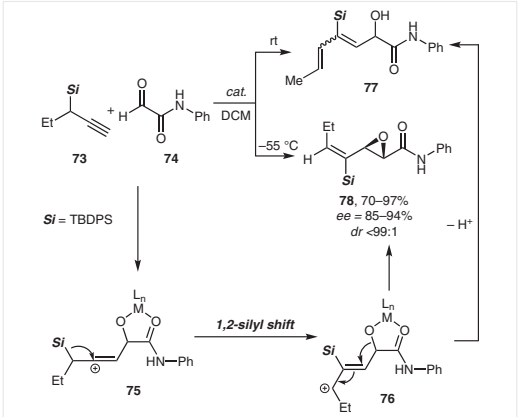
4.1 Propargylsilanes

Rearrangement reactions with 1,2-silyl migration in propargylsilanes **68** were first observed in 1985 by Miginiac and co-workers as a side reaction between propargylsilanes and acetals.[44] Further investigations on reactions of propargylsilanes were performed by Danheiser and co-workers, continuing their success in annulation chemistry. This annulation reaction, with a similar mechanism to that of allenylsilanes, affords a variety of 5-membered rings **72**, cyclopentenes, 1,2,5,7a-tetrahydro-3*H*-pyrrolizin-3-ones, isoxazoles, and azulenes (Scheme 9).[45]



Scheme 9 Synthesis of 5-membered rings from propargylsilanes

Evans and Aye developed a catalytic, enantio- and diastereoselective method for synthesis of highly functionalized vinylepoxides from propargylsilanes and *N*-phenylglyoxamide (Scheme 10).[46] The propargylsilane **73** and the glyoxamide **74** gave the Hosomi–Sakurai product **77** under $Sc(OTf)_3$ catalysis at ambient temperature. However, when lowering the temperature to –55 °C the reaction afforded only the vinylepoxide **78**. The reaction starts with the π-nucleophile addition to the activated carbonyl group. The intermediate **75** undergoes 1,2-silyl shift to the more stable allyl cation **76**, whereas, at –55 °C **76** is trapped kinetically. When the reaction is carried out at ambient temperature deprotonation of **76** takes place and thermodynamic product **77** is obtained.



Scheme 10 Epoxide synthesis from propargylsilanes

To make this reaction enantioselective, it was concluded that highest stereoselectivity was achieved using the TBDPS moiety. Although Sc(III) showed the highest reaction chemoselectivity and yield, Al(III)–sal-BINAM (Figure 5) in combination with AgOTf was used for the enantioselective catalytic system, as it resulted in much higher enantiomeric excess.

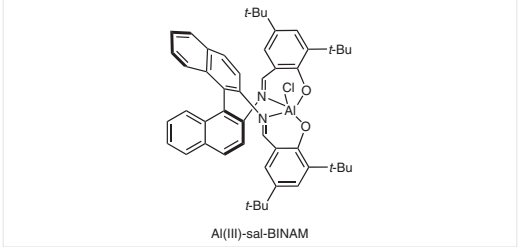
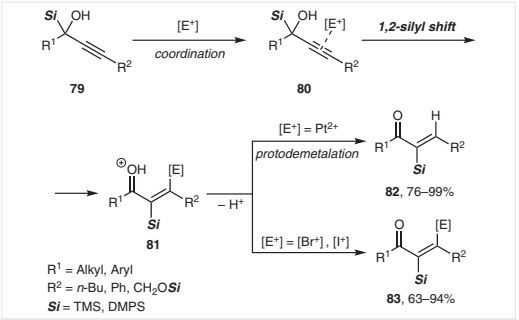


Figure 5 Structure of Al(III)–sal-BINAM

Ferreira and co-workers developed a synthesis of highly functionalized alkenes from α-hydroxypropargylsilanes in electrophilic activation reactions (Scheme 11).[47] Initially, the isomerization of α-hydroxypropargylsilanes **79** to the corresponding α,β-unsaturated ketones **82** was promoted by transition metals. The highest yields of products **82** were obtained with $PtCl_2$. The reactions proceeded smoothly

with high stereoselectivity [up to 19:1 favoring (Z)-isomer] even with highly functionalized alkynes and tolerated a wide variety of functional groups.

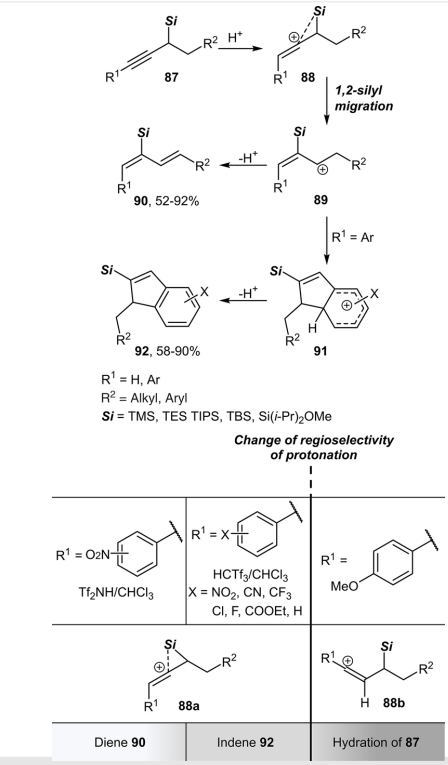


Scheme 11 Synthesis of highly functionalized alkenes from propargylsilanes (DMPS = $SiMe_2Ph$)

In addition to Pt(II) salts, the alkyne moiety was also activated with other electrophiles. Halogenating electrophiles such as *N*-bromosuccinimide (at ambient temperature), *N*-iodosuccinimide (at –10 to 0 °C) were successful for this transformation affording the products **83** with high stereoselectivity [>19:1 favoring (*E*)-isomer]. The reactions proceeded smoothly with a wide variety of substituents at alkynyl and propargylic positions.[48] The obtained alkenes could easily undergo cross-coupling reactions to achieve high complexity of either tri- or tetrasubstituted alkenes.

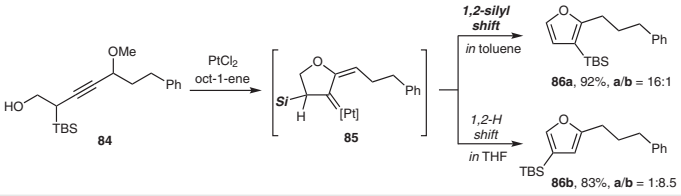
Ferreira and co-workers also developed a cyclomerization reaction for generating α,β-unsaturated platinum carbenes **85** that would afford the corresponding furans **86**. Depending on the solvent, it was possible to migrate either a hydrogen atom or the TBS group (Scheme 12).[49] It was found that the highest selectivity for silyl group migration could be obtained using $PtCl_2$ with oct-1-ene in toluene. On the other hand, the highest H-migration was observed using same system in THF.

A method for generating an allyl cation as a useful intermediate from propargylsilanes using a Brønsted acid catalyst was developed by Turks and co-workers (Scheme 13).[50] Protonation of propargylsilanes **87** with a strong Brønsted acid formed vinyl cation **88** which underwent 1,2-silyl migration to afford more stable allyl cation **89**. Deprotonation of the latter provided diene **90**, when terminal alkynes (R^1 = H) were used.



Scheme 13 Synthesis of dienes and indenes from propargylsilanes

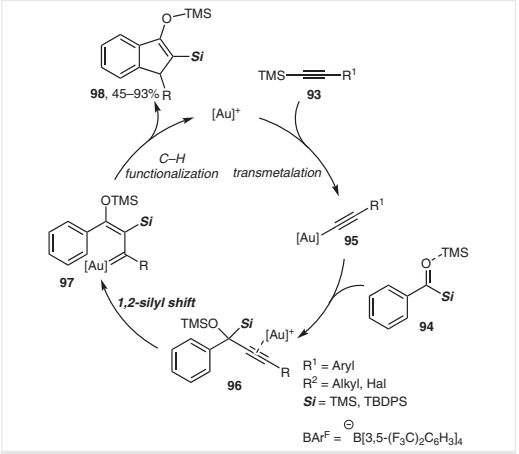
The reactivity of aryl-substituted systems **87** (R^1 = Ar) was altered either by changing the proton source or the electronic character of the aryl substituent. The use of $HNTf_2$ on the nitrophenyl-substituted propargylsilane **87** in $CHCl_3$ gave the corresponding dienes **90** in up to 92% yield with (*E*,*E*)/(*E*,*Z*) 10:1. The use of any other less electron-withdrawing substituent on the phenyl ring resulted in exclusive formation of the indene **92**. When changing the



Scheme 12 Synthesis of furans from propargylsilanes

TBS group to the more sterically hindered TIPS group in combination with $HCTf_3$ as the proton source gave silylindenes **92** in up to 90% yield with a wide variety of electron-withdrawing substituents on the aryl group. A change in the protonation regioselectivity was observed with electron-donating substituents, as the 4-methoxyphenyl derivative leads to the vinyl cation at the benzylic position followed by hydrolysis.

Synthesis of indanones **98** from in situ generated propargylsilanes was developed by Ballesteros and co-workers. In the presence of a gold catalyst, the cyclization reaction between alkynylsilanes **93** and acylsilanes **94** takes place. It is operational with a wide variety of either electron-withdrawing or -donating aryl substituents on the alkynylsilane and with different alkyl and halogen substituents on the acylsilane. The reaction proceeds with good to excellent yields (45–93%). The transformation can also be performed with fused acylsilanes and with a silyl(2-thienyl)methanone (Scheme 14).[51]



Scheme 14 Synthesis of indenes from in situ generated propargylsilanes

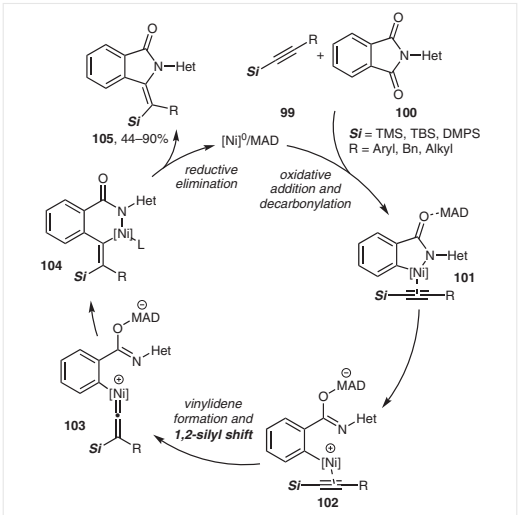
The catalytic cycle is initiated by a silicon–gold transmetalation of the alkynylsilane to form the gold acetylide **95**. The latter attacks the activated carbonyl group of the acylsilane **94** and forms the intermediate **96** that is further complexed by the gold catalyst to initiate the silyl migration. The following C–H functionalization affords the final indene **98** (Scheme 14).

The proof of concept was established by verifying the separate reaction steps. The reaction proceeds with 5 mol% isolated gold acetylide **95**, as a catalyst, in the presence of $TMSNTf_2$. Without $TMSNTf_2$ the reaction did not proceed. The migration of the silyl group was confirmed by using the corresponding TBS acylsilane **94**. The results showed complete migration of TBS group in the final product. Additionally, $(D_3C)_3Si$ alkynylsilane **93** was used with TMS acylsilane **94** and showed no scrambling of the silyl groups.

4.2 Alkynylsilanes

The combination of alkynes with transition-metal catalysis can lead to highly reactive intermediates, such as, metal–vinylidene complexes. In the context of this review their formation is determined by the phenomenon of metal complex back-donation in combination with the 1,2-migration of silyl substituents.

Matsubara and co-workers reported isoindole synthesis from alkynylsilanes **99** and phthalimides **100** via decarbonylative alkylation.[52] The developed catalytic system consists of $Ni(cod)_2/PMe_3$ in combination with methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) as a sterically bulky and monomeric homogeneous Lewis acid. Products **105** were obtained with high *E*/*Z* selectivity in 44–90% yield (Scheme 15).



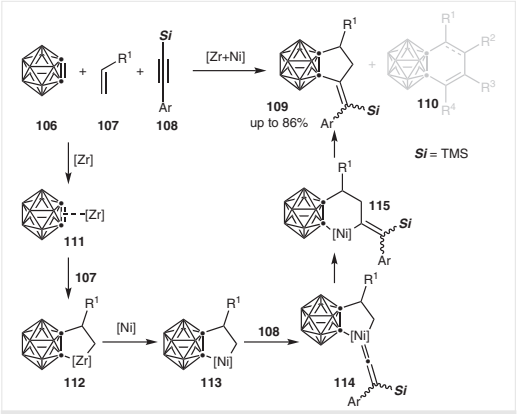
Scheme 15 Synthesis of isoindoles from alkynylsilanes

The proposed reaction mechanism starts with the oxidative addition of nickel to the C(O)–N bond followed by decarbonylation. Then, the complexation of the alkyne affords the nickel complex **101**. The complexation with MAD as a Lewis acid endorses the formation of the acyclic cationic nickel intermediate **102** and the 1,2-silyl shift promotes the formation of vinylidene complex **103**. Further insertion of the vinylidene in the neighboring C–Ni bond affords the six-membered nickelacycle **104** that undergoes reductive elimination to form the desired product **105**.

The double bond geometry is established when the vinylidene inserts into the C–Ni bond. It is understood to be controlled by the steric interactions between the silyl group and the phosphine ligand of the nickel intermediate.

The reaction tolerates a wide variety of substituents on the alkynyl substrate, including a multitude of functional groups.

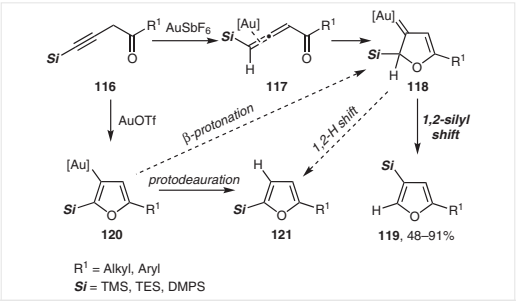
In a similar fashion, Xie and co-workers developed a method where TMS alkynylsilanes can be used in [2+2+1] cycloaddition reactions with unactivated alkenes and carboryne.[53] Alongside the desired [2+2+1] addition product **109**, they observed also formation of the [2+2+2] product **110**. They suggest that a Zr-catalyzed cycloisomerization provides intermediate **112**. The latter undergoes transmetalation with the nickel source affording the cyclic nickel species **113**. The alkyne coordinates to intermediate **113** and undergoes 1,2-silyl migration to form the corresponding vinylidene **114**. The latter inserts into the Ni–C bond to form the cyclic intermediate **115**, which after reductive elimination provides the [2+2+1] addition product **109** (Scheme 16).



Scheme 16 Annulation reaction of carboryne, unactivated alkenes, and alkynylsilanes

In the presence of PPh_3, the nickelacycle **113** can also enter [2+2+2] cyclotrimerization and provide product **110**. This can be altered by choosing right phosphine ligand. In this case, the use of PMe_3 leads to the formation of product **109**.

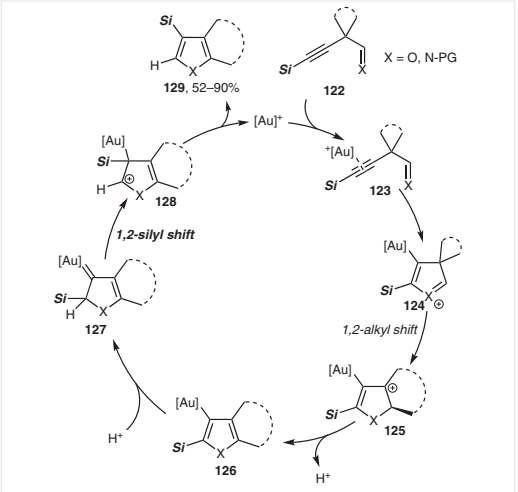
Alkynylsilanes **116** similarly to allenylsilanes can be used to obtain furans **119** in a gold-catalyzed transformation (Scheme 17). Based on DFT calculations, Gevorgyan and co-workers developed counterion and solvent dependent reactions towards silylated furans **119** and **121**. Thus, the use of SbF_6^- directs the mechanism via a possible formation of allene **117** that cyclizes afterwards. On the other hand, TfO^- in a non-polar solvent favors a direct cyclization to Au–furan **120** which, after protodeauration, leads to the formal 1,2-H migration product **121**. However, the use of polar solvents leads to Au–carbene **118**, from which the triflate ligand dissociates, thus facilitating 1,2-silyl migration.[43]



Scheme 17 Synthesis of furans from alkynylsilanes

Indeed, the experimental results agreed with the calculations. The use of $Ph_3PAuSbF_6$ smoothly afforded the desired furans **119** with a wide variety of substituents in good to high yields (65–91%).

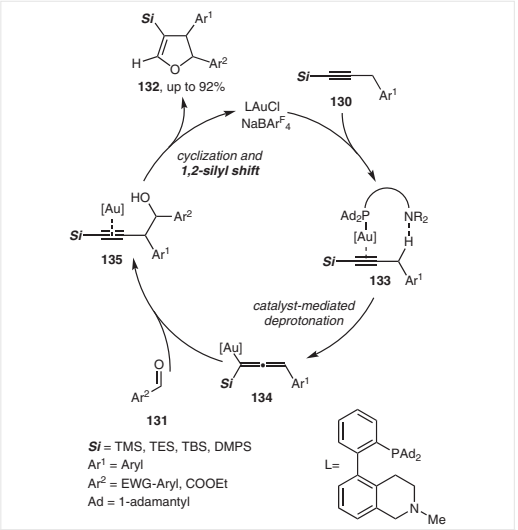
Further expansion of this concept to homopropargylic ketones or imines led to reactions involving double rearrangements.[54] When studying gold-catalyzed $[(C_6F_5)_3PAuSbF_6]$ reactions with substrates of type **122** possessing a cyclic substituent at propargylic position, the formation of the fused ring **129** was observed (Scheme 18).[54] It was suggested that this reaction proceeds via an initial activation of the triple bond followed by cyclization to obtain



Scheme 18 Double migration in the synthesis of furans and pyrroles

intermediate **124**. The latter undergoes alkyl group migration and proton elimination affords intermediate **126**. Further protonation of the silylated carbon initiates 1,2-silyl migration and deauration yields product **129**.

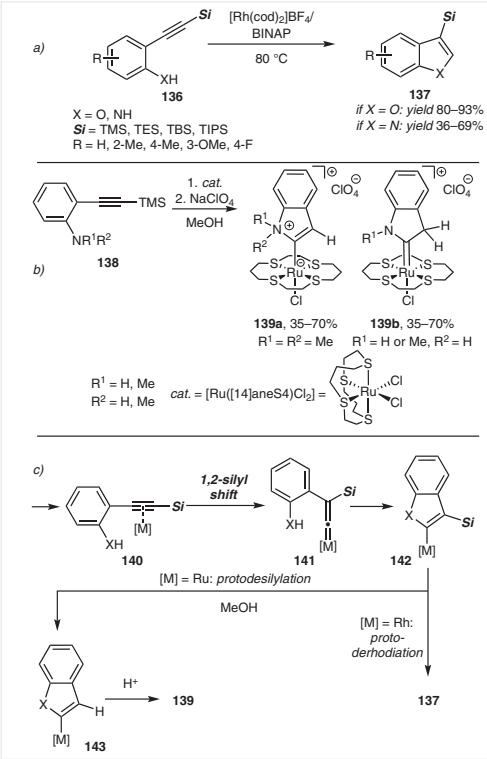
Similarly, dihydrofurans **132** can be obtained by combining alkynylsilanes **130** and the corresponding aldehydes **131** (Scheme 19).[55] The reaction tolerates a variety of Ar^1 substituents, phenyl and heterocyclic motifs with both electron-withdrawing and -donating effects, affording the desired product in good to excellent yields. However, larger Ar^1 groups can affect the reactivity with bulkier silyl groups, like a TBS group. Ar^2 groups are required to induce significant electrophilicity on the carbonyl group as benzaldehyde and aliphatic aldehydes did not participate in this reaction.



Scheme 19 Synthesis of dihydrofurans from alkynylsilanes

It was proposed that the reaction mechanism is initiated by the formation of gold complex **133**. Intramolecular deprotonation yields Au–allene **134** that further reacts with the aldehyde **131** to afford alkyne **135**. The latter undergoes a gold-catalyzed dihydrofuran formation resulting from the 1,2-silyl shift in a similar fashion to Scheme 18.

Tanaka and co-workers developed a synthetic procedure similar to the previously described methods for benzofuran and indole synthesis using a rhodium catalyst (Scheme 20a).[56] Various transition metal complexes could be obtained using a similar reaction, as reported by Wong and co-workers. The first ever isolable Ru(II)–indole zwitterion **139a** complex was obtained from aniline-tethered alkynes (Scheme 20b).[57]

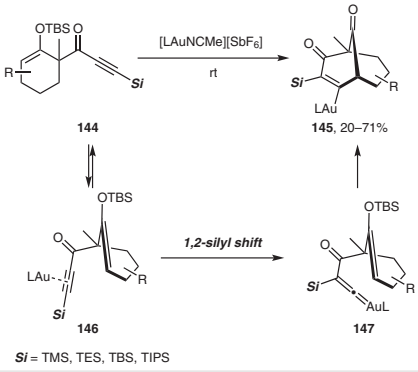


Scheme 20 (a) Synthesis of benzofurans and indoles from alkynylsilanes. (b) Synthesis of ruthenium complex from alkynylsilanes. (c) Reaction mechanism for rhodium- and ruthenium-catalyzed reactions for synthesis of **137** and **139**.

Both reactions follow a similar pattern (Scheme 20c). First, the transition metal coordinates to the alkyne moiety inducing 1,2-silyl migration and vinylidene **141** formation. Cyclization of the latter affords the desired benzofuran or indole scaffold **142**. Depending on the transition metal, the heterocycle undergoes protodemetalation or protodesilylation.

The rhodium-catalyzed reaction **136** → **137** is highly applicable, it tolerates a wide selection of aryl substituents with a broad variety of silyl groups. For the ruthenium-catalyzed reaction, DFT calculations revealed that activation energy for the TMS migration was 7.0 kcal/mol lower than of that of hydrogen for a terminal alkyne. This was also proved synthetically, as *N*,*N*-disubstituted indole zwitterion **139a** was obtained in 90% yield compared to 35–70% for its counterparts arising from terminal alkynes. Unfortunately, all Ru-catalyzed reactions underwent protodesilylation.

During the total synthesis of acylphloroglucinol, Barriault, Korobkov, and co-workers observed and isolated a vinyl–gold complex that was obtained from 1,2-silyl migration.[58] Treating the starting material **144** with a gold source effectively resulted in the coordination of the triple bond to the gold species. However, further migration to afford intermediate **147** in such a sterically demanding environment was only possible with small to moderate silyl groups. Thus, the TBS group showed a decrease in the reaction yields of the cyclization products **145**. Furthermore, the TIPS-containing substrate gave only 35% yield (Scheme 21).



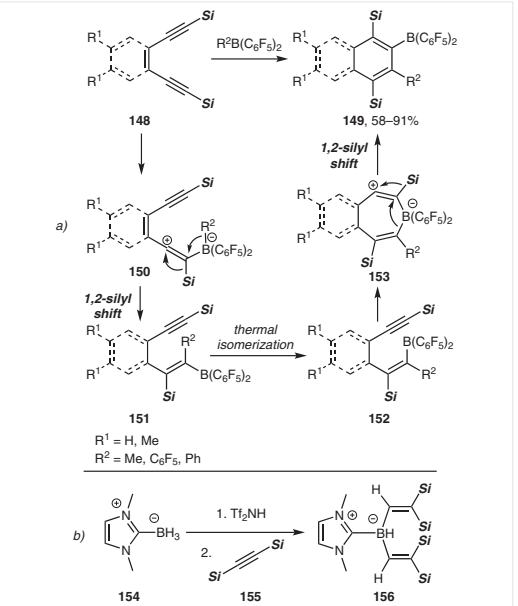
Scheme 21 Synthesis of stable gold complex from propargylsilanes

To confirm the intramolecular silyl group migration, an experiment was performed with a mixture of starting materials **144** with two different silyl groups. The crossover products were not observed thus confirming an intramolecular process.

In addition, boron-based Lewis acids can activate alkynylsilanes similarly to transition metals in a Wrackmeyer reaction modification. Erker and co-workers developed a method where, from 1,2-bis(alkynyl)benzenes **148**, the corresponding naphthalenes **149** are synthesized via consecutive 1,1-carboboration and silyl migration reactions. The entire process proceeds easily with high yields (Scheme 22a).[59] The reaction scope can be further enhanced using heterocyclic bis-silylacetylenes resulting in the corresponding carbazoles, benzothiophenes, and quinolones.[60]

Curran and co-workers developed a method for bis-silylacetylene hydroboration reactions with *N*-heterocyclic carbene-borane that involves a 1,2-silyl migration (Scheme 22b).[61]

Similarly to the borenium-catalyzed hydroboration of allylsilanes, it was expected that the alkynylsilanes would undergo hydroboration in the typical 1,2-fashion, but only the 1,1-hydroboration product was observed. Using the diprotected TMS,TIPS-acetylene, only a single hydroboration occurred and formed solely the (*E*)-stereoisomer, as confirmed by ^{1}H-NOESY NMR.

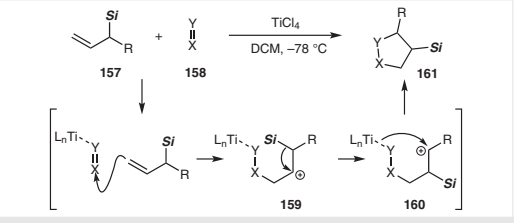


Scheme 22 (a) Naphthalene synthesis from alkynylsilanes. (b) Bis-silylacetylene hydroboration reactions.

5 Reactions of Alkenes

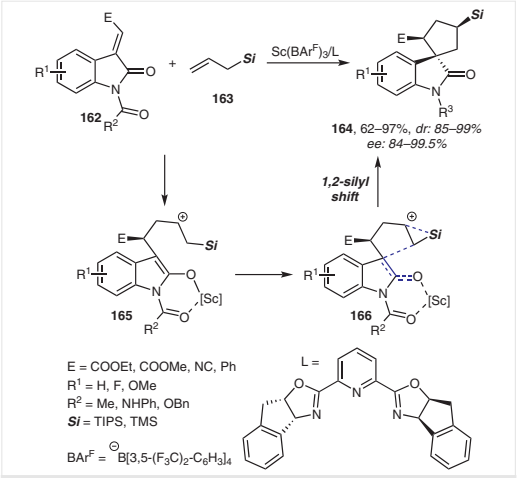
5.1 Allylsilanes

The initial reports for rearrangements using allylsilanes **157** came from Knölker and co-workers. The main byproduct of the Hosomi–Sakurai reaction on α,β-unsaturated ketones resulting in the [3+2] annulation product was observed.[62] Further major contributions to this field were done by Knölker,[63–67] Danheiser,[68] Monti,[69] and Meyers[70] (Scheme 23).



Scheme 23 [3+2] Annulation reactions of allylsilanes

The catalytic enantioselective annulation between oxindoles **162** and allylsilanes **163** was developed by Franz and co-workers.[71] Scandium(III)/pybox complexes with $NaBAr^F$ allowed significant reactivity and selectivity for the formation of [3+2] annulation products **164** (Scheme 24). These products were obtained in high yields (up to 97%), high diastereoselectivity (up to 99:1) and enantioselectivity (up to 99.5:0.5). The reaction tolerates a wide variety of oxindole substrates bearing ester and nitrile groups.[71]



Scheme 24 Catalytic and enantioselective annulation reaction of allylsilanes

Another catalytic stereoselective reaction of allylsilanes was developed by Ohe and co-workers.[72] Five-membered [3+2] annulation products **169** were obtained from unsaturated β-silyl ketones **167** and allylsilanes **168** using $Sc(OTf)_3$ (Scheme 25).

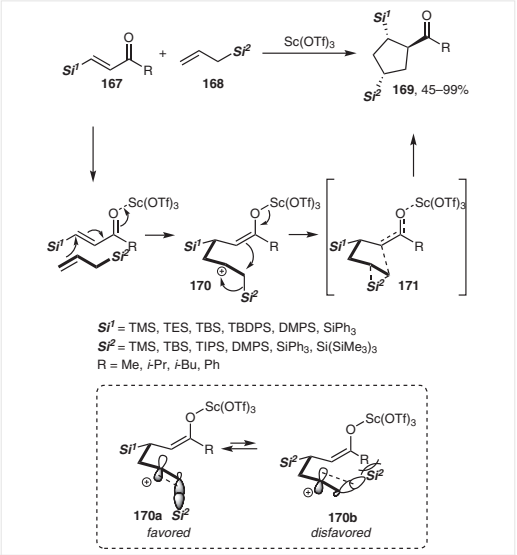
The reaction proceeded with full conversion yielding the desired annulation product as the main product. The Hosomi–Sakurai pathway resulted in minor product formation. The transformation occurred with a wide variety of β-silyl ketones and allylsilanes bearing different silyl groups and different substituents on the ketone. The reaction with allylsilane **168** bearing the super silyl group [$Si(SiMe_3)_3$] afforded the annulation product in 99% yield.[72]

The reaction mechanism starts with the enone activation by the Lewis acid followed by nucleophilic 1,4-addition of allylsilane. Then, in a typical manner, 1,2-silyl migration takes place to allow further cyclization to the corresponding cycle **169**.

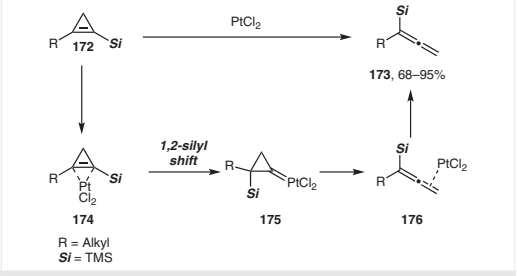
5.2 Vinylsilanes

Lee and co-workers developed a method for the synthesis of allenes **173** from silylcyclopropenes **172**. This method employs $PtCl_2$ to perform the ring-opening with a variety of substituted cyclopropenes bearing aliphatic substitution and tolerating unsaturation and remote aryl substitutions. The only limitation to this reaction is substrates bearing unhindered alkene functions or a phenyl ring at close proximity to the Pt complexation site on the cyclopropane ring, possibly explained by interference with the formation of the productive Pt complex (Scheme 26).[73]

Two possible pathways were originally proposed as confirmed by ^{13}C labeling, this was reduced to one by DFT calculations. The reaction is initiated by platinum coordination to the double bond affording intermediate **174**. Then, the reaction goes directly through 1,2-silyl shift to give intermediate **175** that, after rearrangement and Pt elimination, yields the desired product **173**.[74]

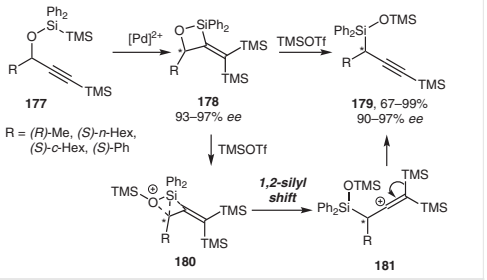


Scheme 25 Enantioselective cyclopropenyl ketone synthesis from allylsilanes



Scheme 26 Allenylsilane synthesis from cyclopropenylsilanes

An interesting reaction was developed by Ito and coworkers. Their strategy involves an intramolecular disilylation of propargyl silyl ethers **177** followed by ether cleavage under Brønsted or Lewis acidic conditions to ultimately initiate a 1,2-silyl migration yielding propargylsilanes **179** (Scheme 27).[75]



Scheme 27 Propargylsilane synthesis from vinylsilanes

The rearrangement is initiated by the activation of the oxygen with TMSOTf. This is followed by the cleavage of the C–O bond which is facilitated by the β-silicon effect and results in 1,2-silyl migration. The reaction has high stereoretention and, hence, it is hypothesized that the rearrangement takes place in a concerted manner as the *syn*-periplanar stabilization should be responsible for the *syn*-migration. The 1,2-silyl migration is also enhanced by the two sterically repulsive geminal TMS groups and by stabilizing the resulting cation by the β-effect. Finally, nucleophile-induced mono-desilylation provides the product **179**.

6 Conclusions

This short review highlights the importance of the β-silicon effect in reactions involving 1,2-silyl migration. The interactions of the high energy β-C–Si σ-bond with the empty p orbital of a electron deficient carbon have been extensively studied. In conclusion for symmetrical systems the non-vertical stabilization (closed – silonium ion) is dominant. For non-symmetrical systems, both non-vertical and vertical (open – hyperconjugation) stabilization are possible. The more electron deficient the α-carbon and less electron deficient the β-carbon, the more dominant the non-vertical structure is and vice versa. In more complex systems, hyperconjugation can still play a crucial role in the stabilization of carbenium ions. In the reviewed examples the combination of multiple effects can explain why many reactions tend to undergo 1,2-silyl shift via a pseudo-non-vertically stabilized transition state.

Strategies involving 1,2-silyl shift can result in the formation of complex cyclic or unsaturated structures conveniently equipped with a handle for further functionalization. Currently, research of high interest revolves around the synthesis of metal–vinylidene complexes, where the 1,2-silyl migration plays a crucial role. Several experimental and theoretical studies show the importance of silicon migration for improved reactivities due to the reduction of their activation energies. For these reasons, further development in this area of organosilicon chemistry is expected in the future.

Funding Information

This work was supported by a grant from Latvian Council of Science (grant No. LZP-2018/1-0315) and doctoral student grant from Riga Technical University (grant No. DOK.MLKF/19).

Acknowledgement

The authors thank Ms. Stephanie G. E. Amos for helpful discussions.

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Appendix 2

Synthesis of 3-silylated 3-sulfolenes from propargylsilanes and their reductive desulfitation

Rūdolfs Beļaunieks, Mikus Puriņš, Vikotrs Kumpiņš, Māris Turks

Chem. Heterocycl. Comp. **2021**, *57*(1), 20–25

DOI 10.1007/s10593-021-02862-1

Chemistry of Heterocyclic Compounds **2021**, *57*(1), 20–25

Synthesis of 3-silylated 3-sulfolenes from propargylsilanes and their reductive desulfitation

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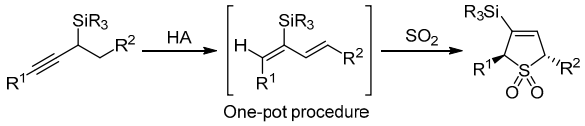
Published in Khimiya Geterotsiklicheskikh Soedinenii, 2021, *57*(1), 20–25

Submitted October 6, 2020
Accepted October 30, 2020



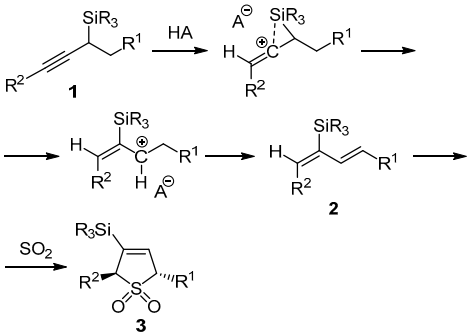
Protonation of propargylsilanes induces 1,2-silyl group shift and provides 2-silylated dienes. If this reaction is performed in liquid SO_2, the diene formation is followed by instant cheletropic SO_2 addition, and 3-silylated 3-sulfolenes are obtained. Liquid SO_2 as polar and Lewis acidic reaction medium makes it possible to use relatively weak Brønsted acid catalysts such as H_2O and benzoic acid. Depending on the starting material, reductive desulfitation of 3-silylated 3-sulfolenes provides vinyl, allyl, or aliphatic silanes.

Keywords: propargylsilanes, silyl sulfolenes, cheletropic addition, desulfitation, 1,2-silyl migration.

Sulfone moiety is abundant in many pharmaceuticals, agrochemicals, and materials.[1] A special class of sulfones is constituted by the cyclic five-membered 3-sulfolenes.[2] The latter can be obtained by metathesis,[3] other transition metal catalyzed reactions,[4] as well as oxidation of 2,5-dihydrothiophenes.[5] However, the most direct approach to 3-sulfolenes is the cheletropic addition of SO_2 to 1,3-dienes – a reaction known since 1914.[6] Recently, a tandem 1,3-diene synthesis followed by SO_2 addition has been reported.[2,7] This approach can solve the practical problems associated with preparation of volatile and unstable 1,3-dienes.

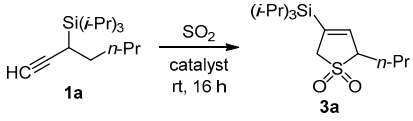
We have recently reported a proton-catalyzed isomerization of propargylsilanes to 2-silyl-1,3-dienes.[8] This transformation is driven by a 1,2-silyl group shift to generate a more stable allylic carbocation from a vinyl cation.[9] The rearrangement of propargylsilanes in traditional solvents like CH_2Cl_2 required Brønsted superacids (TfOH, Tf_2NH, Tf_3CH). We have also recently shown that the Lewis acidic properties of liquid SO_2 makes it an excellent choice for transformations involving cationic intermediates.[10] Therefore, we hypothesized that liquid SO_2 could be used as a polar solvent for the rearrangement of propargylsilanes in combination with a weaker protic acid catalysts. The formed dienes would then react with the liquid SO_2 to give silyl-substituted sulfolenes. The additional alkenylsilane functionality can be potentially used in cross-coupling reactions as well as in C–O bond forming reactions. Moreover, a 3-silyl substituent changes the alkylation regioselectivity due to the stabilization of α-silicon carbanions.[11–13] Herein, we report the formation of 3-silylated 3-sulfolenes **3** *via* a tandem propargylsilane **1** isomerization to diene **2** and cheletropic addition of SO_2 (Scheme 1).

Scheme 1. General scheme of tandem propargylsilane **1** isomerization – 3-sulfolene **3** formation in liquid SO_2



We began our studies with the catalyst screening (Table 1) on TIPS-substituted alkyne **1a** as the substrate. As expected, comparably weaker Brønsted acids (e.g., $TsOH \cdot H_2O$, PhCOOH, $(NH_4)_2SO_4$) in liquid SO_2 were able to catalyze this transformation. It was even possible to use just the residual H_2O (50 ppm) from the commercially available SO_2 (Table 1, entry 5). The reaction stops when

Table 1. Catalyst screening for tandem 1,2-silyl shift – cheletropic addition*



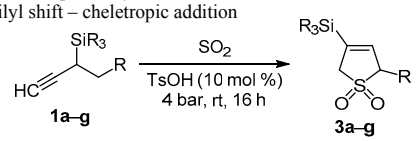
Entry	Catalyst (mol %)	NMR yield of product **3a**,** %
1	$TsOH·H_2O$ (10)	84
2	PhCOOH (10)	72
3	$(NH_4)_2SO_4$ (10)	75
4	H_2O (100)	67
5	H_2O***	75
6	3 Å MS	<5

* Compound **1a** (190–210 mg, 0.75–0.83 mmol), SO_2 (~15 g, 23 mmol).
** Determined using Ph_2CH_2 as internal standard, average of 2 runs.
*** Trace H_2O (50 ppm) in commercial SO_2 (10 g of liquid SO_2 contains 0.5 mg H_2O).

molecular sieves were added to the reaction mixture (entry 6). Alcohols (*t*-BuOH) or phenols (BHT) in the presence of molecular sieves were not able to catalyze the transformation.

$TsOH·H_2O$ appeared to be the most active catalyst, and it was further used with other substrates bearing various silyl groups (Table 2). It was found that propargyltrialkylsilanes **1a–d**,**f**,**g** gave the expected products **3a–d**,**f**,**g** with good to excellent yields. The use of methoxy-substituted silicon (compound **1e**) in a tandem process gave low yield of product **3e** (24%). Weaker acids such as PhCOOH or H_2O and lowering the reaction temperature (–20°C) did not provide any improvements. Fortunately, it was found that sulfolene **3e** can be obtained in a two-step procedure with a reasonably high 62% yield: 1) **1e** + TfOH → **2e**; 2) **2e** + SO_2 → **3e**. On the other hand, introduction of phenyl substituent in compound **3g** made the substrate more reactive in the first isomerization step. Therefore, the use of milder catalyst – PhCOOH instead of TsOH gave a better isolated yield (61%).

Table 2. Scope of silyl substituents in tandem 1,2-silyl shift – cheletropic addition

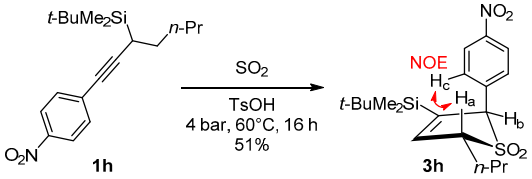


Starting material	R_3Si	R	Product	Yield, %
1a	(*i*-Pr)$_3$Si	*n*-Pr	**3a**	84
1b	Me_3Si	*n*-Pr	**3b**	52
1c	Et_3Si	*n*-Pr	**3c**	82
1d	*t*-BuMe_2Si	*n*-Pr	**3d**	85
1e	(*i*-Pr)$_2$(MeO)Si	*n*-Pr	**3e**	24 (62)*
1f	*t*-BuMe_2Si	*n*-C_8H_{17}	**3f**	84
1g	*t*-BuMe_2Si	Ph	**3g**	61**

* Two-step procedure (see text).
** PhCOOH was used as a catalyst instead of TsOH at 11 bar, 60°C, 16 h.

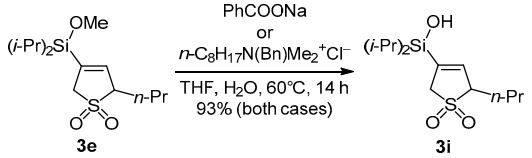
The reaction was performed also with 4-nitrophenyl-substituted propargylsilane **1h**, and sulfolene **3h** was isolated in 51% yield as a single diastereomer after column chromatography. Its *trans* substitution pattern was confirmed by the nuclear Overhauser effect (Scheme 2). This agrees with the previous observations that propargylsilanes of type **1h** provide *E*,*Z*-dienes.[11] This, in turn, after the cheletropic addition of SO_2 results in *trans*-sulfolene **3h**.

Scheme 2. Synthesis of 2,5-*trans*-disubstituted sulfolene **3h**



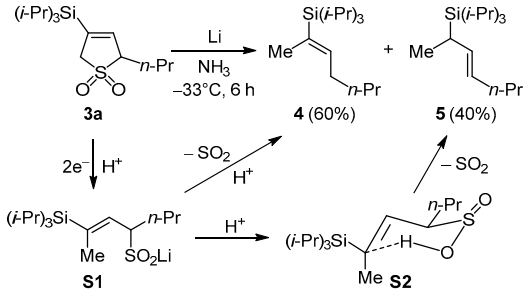
With sulfolenes **3a–h** in hand, we briefly explored their chemical properties. Thus, diisopropylmethoxysilyl group present in compound **3e** is reported to be suitable for Hiyama–Denmark coupling,[8,14] and its hydrolysis product, the silanol moiety, is reported to be the active intermediate in the transmetalation step. We have found that mild nucleophiles like chloride or benzoate each provided nearly quantitative hydrolysis of methoxy group into silanol **3i** (Scheme 3). This sets a stage for further cross-coupling reactions employing product **3i**, which is beyond the scope of this communication.

Scheme 3. Further functionalization of compound **3e**



We have also explored reductive desulfitation of silyl sulfolenes, which provides silylated olefins. Using Li as the reductant in liquid NH_3, we were able to cleave C–S bonds in sulfolene **3a** with a full conversion of the starting material (Scheme 4).[15] Vinylsilane **4** was obtained in 60% yield along with its double bond isomer – allylsilane **5** (in 40% yield). Product **4** results from direct SO_2 elimination

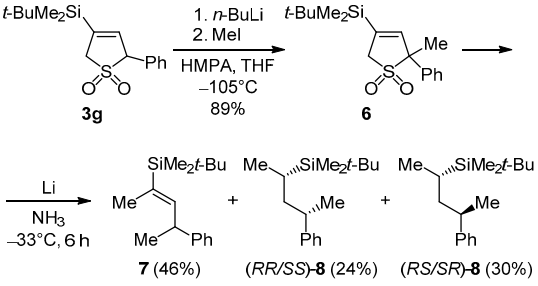
Scheme 4. Reductive desulfitation of sulfolene **3a**



from intermediate **S1**, but formation of product **5** can be explained by a retro-*ene* elimination of SO_2 from the intermediate **S2**. Change of the reaction conditions (temperature, addition of THF as cosolvent, additional base, another proton source or change of reducing agent) showed no deviation from the initially obtained product ratio **4**/**5** = 60:40.

We hypothesized, that the change of substituents at the C-2 atom of sulfolene ring could affect the ratio between compounds of type **4** and **5**. However, 2-phenyl sulfolene **3g**, which was thought to provide double bond isomerization under the Li/NH_3 conditions, gave only degradation products (Scheme 5). Interestingly, the introduction of a quaternary center in sulfolene **6** made it more stable, and its metal reduction gave a mixture of three compounds – the expected vinylsilane **7** (46%) and over-reduction products **8**. No reduction of phenyl group was observed under the given conditions even in the presence of the excess of Li.

Scheme 5. Reductive desulfitation of sulfolene **6**



Both diastereoisomers of compound **8** were assigned by careful analysis of 1D and 2D NMR (^{1}H–^{13}C COSY, HSQC, HMBC) spectra (Fig. 1). Coupling constant analysis shows that both molecules prefer conformation that avoids *syn*-pentane interactions, positioning H_d and one of the methyl groups in pseudoaxial position.[16] Following this pattern, it becomes evident, that H_c for compound (*RS*/*SR*)-**8** should experience a significant upfield shift by the anisotropic effect of phenyl group (0.50 ppm compared to 0.97 ppm) and a minor upfield shift of H_b for compound (*RR*/*SS*)-**8** (1.67 ppm compared to 1.81 ppm).

In summary, we have developed a simple synthetic procedure to obtain 3-silyl-3-sulfolenes from propargylsilanes in one-pot procedure. This tandem process can be performed on terminal alkynes and 1-aryl-substituted 3-silyl-1-butynes in good to excellent yields. 5-Alkyl-2-aryl-substituted 3-silyl-3-sulfolene was obtained with excellent *trans* selectivity. The method avoids isolation of dienes that are prone to polymerization. Additionally, the partially hydrolyzed silanol has synthetic potential for further transition metal catalyzed cross coupling studies. 3-Silyl-3-sulfolenes proved to be reactive in Li/NH_3 reduction, and the distribution of the corresponding vinylsilanes, allylsilanes, and alkylsilanes as products was found to be substrate-selective.

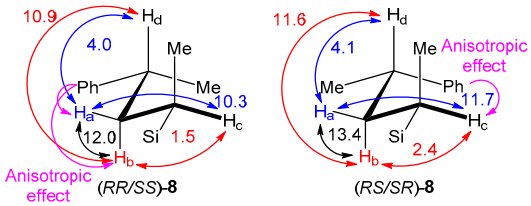


Figure 1. Structure assignment of diastereomers **8** (*J* constants are given in Hz).

Experimental

Fourier transform infrared spectra were recorded in the attenuated total reflectance mode on a Varian 800 FT-IR Scimitar Series spectrometer equipped with a Pike Technologies GladiATR™ single reflection accessory with the internal range 400–4000 cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Ascend 500 spectrometer at 500 and 126 MHz, respectively, in $CDCl_3$. For quantitative ^{1}H NMR, relaxation time was increased (d_1 10 s). GCMS analyses were performed using an Agilent Technologies 6890 gas chromatograph with mass-selective detector (EI), equipped with an Agilent Technologies DB-1MS capillary column (30 m × 0.32 mm × 0.25 μm); injection temperature 250°C; injection volume 1 μl (splitless mode); carrier gas He; flow rate 2.0 ml/min; detector temperature 230°C. High-resolution ESI mass spectra were recorded on an Agilent 1290 Infinity series ultra-high pressure liquid chromatograph connected to an Agilent 6230 time-of-flight mass spectrometer. Reaction mixtures and chromatographic purification were monitored by TLC on E. Merck Kieselgel 60 F_{254} plates with detection by UV light (254 nm) or I_2 as a visualizing agent. Column chromatography was performed on ROCC silica gel (60 Å, 40–60 μm).

Commercially available reagents were used as received. Starting materials **1a**–**h** were obtained by a reported method.[8]

Synthesis of 2-substituted 4-silylsulfol-3-enes 3a–h (General method). Acid catalyst (0.1 equiv) and propargylsilane (170–230 mg, 1.0 equiv) was added to 135-ml stainless steel reactor, equipped with a glass tube and magnetic stirring bar. SO_2 (15–20 g) was transferred into the reactor at –78°C by distillation. The reactor was sealed and left to warm to room temperature and stirred for 16 h under 4 bar pressure. The reactor was then connected to either the storage cylinder of SO_2 for the solvent recycling or a trap containing aqueous $NaHCO_3$ solution for SO_2 removal. Then CH_2Cl_2 (10 ml) and aqueous $NaHCO_3$ (10 ml) were added. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2×5 ml). The organic layers were combined and washed with distilled H_2O (10 ml) and brine (10 ml), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by column chromatography (hexane–EtOAc, 100:0→95:5).

2-Propyl-4-(triisopropylsilyl)-2,5-dihydrothiophene 1,1-dioxide (3a) was synthesized from 3-(triisopropylsilyl)-hept-1-yne (**1a**) (208 mg, 0.79 mmol, 1.0 equiv) with TsOH·H_2O (15 mg, 79 μmol, 0.1 equiv) as a catalyst. Yield 210 mg (84%), yellowish oil. ^{1}H NMR spectrum, δ, ppm

(*J*, Hz): 0.99 (3H, t, *J* = 7.1, CH_3); 1.03–1.10 (18H, m, $3(C\underline{H}_3)_2CH$); 1.11–1.21 (3H, m, $3(CH_3)_2C\underline{H}$); 1.47–1.70 (3H, m) and 1.87–1.99 (1H, m, $(CH_2)_2$); 3.62–3.78 (3H, m, $CH_2S(O_2)CH$); 6.19 (1H, q, *J* = 2.3, =CH). ^{13}C NMR spectrum, δ, ppm: 10.9; 14.0; 18.6; 20.5; 30.9; 59.5; 64.6; 135.0; 140.1. Found, *m/z*: 317.1992. $C_{16}H_{33}O_2SSi$. Calculated, *m/z*: 317.1965.

2-Propyl-4-(trimethylsilyl)-2,5-dihydrothiophene 1,1-dioxide (3b) was synthesized from 3-(trimethylsilyl)-hept-1-yne (**1b**) (203 mg, 1.20 mmol, 1.0 equiv) with $TsOH\cdot H_2O$ (23 mg, 120 μmol, 0.1 equiv) as a catalyst. Yield 145 mg (52%), yellowish oil. IR spectrum, ν, cm^{-1}: 1306, 1251. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.12 (9H, s, $Si(CH_3)_3$); 0.97 (3H, t, *J* = 7.0, CH_3); 1.46–1.64 (3H, m) and 1.85–1.96 (1H, m, $(CH_2)_2$); 3.58–3.77 (3H, m, $CH_2S(O_2)CH$); 6.10 (1H, q, *J* = 2.3, =CH). ^{13}C NMR spectrum, δ, ppm: –2.3; 14.0; 20.5; 30.7; 58.4; 65.4; 137.2; 139.0. Found, *m/z*: 233.1048 $[M+H]^+$. $C_{10}H_{21}O_2SSi$. Calculated, *m/z*: 233.1026.

2-Propyl-4-(triethylsilyl)-2,5-dihydrothiophene 1,1-dioxide (3c) was synthesized from 3-(triethylsilyl)hept-1-yne (**1c**) (176 mg, 0.83 mmol, 1.0 equiv) with $TsOH\cdot H_2O$ (16 mg, 83 μmol, 0.1 equiv) as a catalyst. Yield 187 mg (82%), yellowish oil. IR spectrum, ν, cm^{-1}: 1306, 1229. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.64 (6H, q, *J* = 7.9, $3C\underline{H}_2CH_3$); 0.94 (9H, t, *J* = 8.1, $3CH_2C\underline{H}_3$); 0.99 (3H, t, *J* = 7.1, CH_3); 1.47–1.68 (3H, m) and 1.87–1.98 (1H, m, $(CH_2)_2$); 3.62–3.76 (3H, m, $CH_2S(O_2)CH$); 6.13 (1H, q, *J* = 2.2, =CH). ^{13}C NMR spectrum, δ, ppm: 2.5; 7.3; 14.0; 20.5; 30.8; 58.8; 65.0; 136.5; 138.7. Found, *m/z*: 275.1497 $[M+H]^+$. $C_{13}H_{27}O_2SSi$. Calculated, *m/z*: 275.1496.

4-(*tert*-Butyldimethylsilyl)-2-propyl-2,5-dihydrothiophene 1,1-dioxide (3d) was synthesized from 3-(*tert*-butyldimethylsilyl)hept-1-yne (**1d**) (176 mg, 0.83 mmol, 1.0 equiv) with $TsOH\cdot H_2O$ (17 mg, 91 μmol, 0.1 equiv) as a catalyst. Yield 211 mg (85%), yellowish oil. IR spectrum, ν, cm^{-1}: 1361, 1251. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.11 (6H, s, $Si(CH_3)_2$); 0.89 (9H, s, $C(CH_3)_3$); 0.99 (3H, t, *J* = 6.9, CH_3); 1.48–1.68 (3H, m) and 1.87–1.98 (1H, m, $(CH_2)_2$); 3.64–3.80 (3H, m, $CH_2S(O_2)CH$); 6.15 (1H, q, *J* = 2.2, =CH). ^{13}C NMR spectrum, δ, ppm: –6.7; –6.6; 14.0; 20.5; 26.6; 30.8; 59.4; 65.0; 137.1; 139.1. Found, *m/z*: 275.1518 $[M+H]^+$. $C_{13}H_{27}O_2SSi$. Calculated, *m/z*: 275.1496.

4-[Diisopropyl(methoxy)silyl]-2-propyl-2,5-dihydrothiophene 1,1-dioxide (3e) was synthesized from 3-(diisopropylmethoxysilyl)hept-1-yne (**1e**) (200 mg, 0.83 mmol, 1.0 equiv) with $TsOH\cdot H_2O$ (15 mg, 79 μmol, 0.1 equiv) as a catalyst. Yield 61 mg (24%), yellowish oil. IR spectrum, ν, cm^{-1}: 1305, 1124. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 (3H, t, *J* = 7.1, CH_3); 1.02 (6H, d, *J* = 7.2, $2CH_3$); 1.05 (6H, d, *J* = 6.9, $2CH_3$); 1.07–1.16 (2H, m, 2CH); 1.47–1.68 (3H, m) and 1.88–1.99 (1H, m, $(CH_2)_2$); 3.54 (3H, s, OCH_3); 3.67 (1H, tm, *J* = 7.3, $S(O_2)CH$); 3.69 (1H, td, *J* = 16.7, *J* = 1.7) and 3.75 (1H, ddd, *J* = 16.7, *J* = 2.2, *J* = 1.2, $CH_2S(O_2)$); 6.28 (1H, q, *J* = 2.2, =CH). ^{13}C NMR spectrum, δ, ppm: 11.9 (2C); 14.0; 17.3 (3C); 20.4; 30.7; 52.0; 58.9; 64.7; 134.3; 140.6. Found, *m/z*: 322.1877 $[M+NH_4]^+$. $C_{14}H_{32}O_3SSi$. Calculated, *m/z*: 322.1867.

Synthesis of compound 3e by two-step procedure. A solution of TfOH (62.4 mg, 0.416 mmol, 0.05 equiv) in CH_2Cl_2 (1 ml) was added to a solution of 3-(diisopropylmethoxysilyl)hept-1-yne (**1e**) (2.0 g, 8.32 mmol, 1.0 equiv) in CH_2Cl_2 (20 ml), and the resulting mixture was stirred for 15 min at 22°C. The reaction mixture was filtered through K_2CO_3 followed by filtration through silica and evaporated. The residue was transferred to a 135-ml stainless steel reactor, equipped with a glass tube and magnetic stirring bar. SO_2 (35 g) was transferred into the reactor at –78°C by distillation. The further procedure and workup followed general method. Yield 1.56 g (62%).

4-(*tert*-Butyldimethylsilyl)-2-octyl-2,5-dihydrothiophene 1,1-dioxide (3f) was synthesized from 3-(*tert*-butyldimethylsilyl)dodec-1-yne (**1f**) (176 mg, 675 μmol, 1.0 equiv) with $TsOH\cdot H_2O$ (13 mg, 68 μmol, 0.1 equiv) as a catalyst. Yield 195 mg (84%), yellowish oil. IR spectrum, ν, cm^{-1}: 1359, 1252. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.10 (6H, s, $Si(CH_3)_2$); 0.87 (3H, t, *J* = 7.2, CH_3); 0.88 (9H, s, $C(CH_3)_3$); 1.20–1.40 (10H, m), 1.41–1.68 (3H, m), and 1.93 (1H, dddd, *J* = 12.7, *J* = 10.2, *J* = 7.1, *J* = 5.1, $7CH_2$); 3.64 (1H, tm, *J* = 7.1, $S(O_2)CH$); 3.69 (1H, dt, *J* = 16.6, *J* = 1.6) and 3.76 (1H, ddd, *J* = 16.6, *J* = 2.2, *J* = 1.2, $CH_2S(O_2)$); 6.15 (1H, q, *J* = 2.2, =CH). ^{13}C NMR spectrum, δ, ppm: –6.7; –6.6; 14.2; 22.8; 26.6; 27.1; 28.8; 29.3; 29.4; 29.5; 32.0; 59.4; 65.3; 137.1; 139.2. Found, *m/z*: 345.2242 $[M+H]^+$. $C_{18}H_{37}O_2SSi$. Calculated, *m/z*: 345.2278.

4-(*tert*-Butyldimethylsilyl)-2-phenyl-2,5-dihydrothiophene 1,1-dioxide (3g) was synthesized from 3-(diisopropylmethoxysilyl)hept-1-yne (**1g**) (234 mg, 0.96 mmol, 1.0 equiv) using PhCOOH (11.7 mg, 96 μmol, 0.1 equiv) as a catalyst (after the addition of SO_2, the reaction was carried out at 60°C under pressure of 11 bar for 16 h). Yield 180 mg (61%), viscous wax. IR spectrum, ν, cm^{-1}: 2850, 1353, 1250. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.19 (6H, s, $Si(CH_3)_2$); 0.98 (9H, s, $C(CH_3)_3$); 3.86 (1H, d, *J* = 16.9) and 3.90 (1H, d, *J* = 16.9, $CH_2S(O_2)$); 4.97 (1H, s, $S(O_2)CH$); 6.36 (1H, q, *J* = 2.2, =CH); 7.27–7.32 (2H, m, H Ph); 7.40–7.47 (3H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: –6.6; –6.5; 17.7; 26.6; 58.8; 70.7; 129.1; 129.3 (2C); 130.4; 138.3; 139.2. Found, *m/z*: 309.1341$[M+H]^+$. $C_{16}H_{25}O_2SSi$. Calculated, *m/z*: 309.1339.

***trans*-4-(*tert*-Butyldimethylsilyl)-2-(4-nitrophenyl)-5-(*n*-propyl)-2,5-dihydrothiophene 1,1-dioxide (3h)** was synthesized from 3-(*tert*-butyldimethylsilyl)-1-(4-nitrophenyl)-hept-1-yne (**1h**) (176 mg, 0.675 mmol, 1.0 equiv) with $TsOH\cdot H_2O$ (12 mg, 60 μmol, 0.1 equiv) as a catalyst. Yield 136 mg (51%), yellowish oil. IR spectrum, ν, cm^{-1}: 1470, 1385, 1350, 1248. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): –0.31 (3H, s, $SiCH_3$); 0.13 (3H, s, $SiCH_3$); 0.89 (9H, s, $C(CH_3)_3$); 1.01 (3H, t, *J* = 7.3, CH_3); 1.49–1.69 (2H, m), 1.71–1.81 (1H, m) and 1.97–2.08 (1H, m, $(CH_2)_2$); 3.75 (1H, br. t, *J* = 7.4, $S(O_2)C\underline{H}CH_2$); 4.93 (1H, s, $CHS(O_2)$); 6.44 (1H, s, =CH); 7.40 (2H, d, *J* = 8.6, H Ar); 8.26 (2H, d, *J* = 8.6, H Ar). ^{1}H NMR spectrum, δ, ppm: –6.1; –5.8; 14.0; 17.4; 20.7; 26.6; 29.1; 63.0; 74.9; 124.4; 130.0 139.7; 141.3; 141.6; 148.4. Found, *m/z*: 396.1676 $[M+H]^+$. $C_{19}H_{30}NO_3SSi$. Calculated, *m/z*: 396.1659.

4-(Hydroxydiisopropylsilyl)-2-propyl-2,5-dihydrothiophene 1,1-dioxide (3i). Compound **3e** (352 mg, 1.15 mmol, 1.0 equiv) and PhCOONa (331 mg, 2.30 mmol, 2.0 equiv) were placed into a flask equipped with magnetic stirrer. THF (5 ml) and H_2O (0.05 ml) were added, and the solution was stirred for 14 h at 60°C. The reaction mixture was filtered and evaporated to dryness. The residue was purified by column chromatography (eluent hexane–EtOAc, 100:0→93:7) Yield 310 mg (93%), yellowish oil. IR spectrum, ν, cm^{-1}: 3320, 1350, 1248. ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.95–1.10 (17H, m, CH_3, $2(CH_3)_2CH$); 1.48–1.68 (3H, m) and 1.86–1.98 (1H, m, $(CH_2)_2$); 2.10 (1H, br. s, OH); 3.67 (1H, tm, *J* = 7.2, $S(O_2)CH$); 3.70 (1H, d *J* = 16.5) and 3.76 (1H, d, *J* = 16.5, $CH_2S(O_2)$); 6.31 (1H, s, =CH). ^{13}C NMR spectrum, δ, ppm: 12.3; 12.4; 14.0; 16.9 (2C); 17.1 20.4; 30.7; 58.7; 64.8; 135.2; 140.1. Found, *m*/*z*: 291.1471 $[M+H]^+$. $C_{13}H_{27}O_3SSi$. Calculated, *m*/*z*: 291.1445.

4-(*tert*-Butyldimethylsilyl)-2-methyl-2-phenyl-2,5-dihydrothiophene 1,1-dioxide (6). 2.45 M *n*-BuLi (91.8 μl, 227 μmol, 1 equiv) was added to a solution of sulfolene **3g** (70 mg, 227 μmol, 1 equiv) in THF (2 ml) and HMPA (0.5 ml) at –105°C and stirred for 15 min. MeI (48 mg, 21 μl, 341 μmol, 1.5 equiv) was added, and the reaction mixture was left to heat up to 22°C. CH_2Cl_2 (2 ml) and aqueous NH_4Cl (2 ml) were added. Layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 ml). The organic layers were combined and washed with aqueous NH_4Cl (2×2 ml), distilled H_2O (2 ml), aqueous NaCl (2 ml), dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was dissolved in CH_2Cl_2 and filtered through silica. Yield 65 mg (89%), viscous wax. IR spectrum, ν, cm^{-1}: 2845, 1365, 1250. ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.19 (3H, s, $SiCH_3$); 0.20 (3H, s, $SiCH_3$); 0.96 (9H, s, $C(CH_3)_3$); 1.87 (3H, s, CH_3); 3.82 (2H, d, *J* = 1.9, $S(O_2)CH_2$); 6.45 (1H, t, *J* = 1.9, =CH); 7.34–7.44 (5H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: –6.6; –6.5; 17.3; 22.0; 26.7; 57.3; 69.4; 127.8; 128.8; 128.9; 134.9; 136.1; 145.6. Found, *m*/*z*: 323.1501 $[M+H]^+$. $C_{17}H_{27}O_2SSi$. Calculated, *m*/*z*: 323.1496.

Synthesis of alkenes 4, 5, 7, 8 from sulfolenes by reduction with Li (General method). Metallic Li was added portionwise to a solution of sulfolene **3a** or **6** (100–200 mg, 1 equiv) in liquid NH_3 (3 ml) at –78°C. The resulting blue reaction mixture was left to warm up to –33°C and refluxed at this temperature for 6 h. The reaction mixture was cooled to –78°C, and aqueous saturated NH_4Cl solution (5 ml) was added. The flask was connected to a trap containing aqueous HCl (1 M) and was left to evaporate NH_3 gas. CH_2Cl_2 (5 ml) was added, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2×3 ml). The organic layers were combined and washed with aqueous NH_4Cl (2×5 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure.

Mixture of (*E*)-hept-2-en-2-yltriisopropylsilane (4) and (*E*)-hept-3-en-2-yltriisopropylsilane (5) was obtained from compound **3a** (100 mg, 316 μmol, 1 equiv) using metallic Li (44 mg, 6.32 mmol, 20 equiv). Yield of products **4** and **5** was 92 mg (quant.). Ratio **4**/**5** = 60:40.

(*E*)-Hept-2-en-2-yltriisopropylsilane (4). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.87–0.93 (3H, m, CH_3); 1.04 (18H, d, *J* = 7.3, $3(C\underline{H}_3)_2CH$); 1.10–1.21 (3H, m, $3(CH_3)_2C\underline{H}$); 1.26–1.42 (4H, m, $(CH_2)_2$); 1.67 (3H, d, *J* = 1.6, CH_3); 2.14 (2H, q, *J* = 6.9, $C\underline{H}_2CH$=); 5.72 (1H, tq, *J* = 6.9, *J* = 1.6, CH=). ^{13}C NMR spectrum, δ, ppm: 11.0; 14.2; 16.4; 18.9; 22.6; 28.3; 31.8; 130.4; 143.0. Mass spectrum, *m*/*z* (I_{rel}, %): 254 $[M]^+$ (2), 211 (12), 158 (15), 157 (100), 115 (87), 101 (14), 87 (47), 73 (53), 59 (64), 45 (11).

(*E*)-Hept-3-en-2-yltriisopropylsilane (5). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.87–0.93 (3H, m, CH_3); 1.05–1.14 (21H, m, $3(CH_3)_2CH$); 1.16 (3H, d, *J* = 7.6, $C\underline{H}_3CHCH$=); 1.32–1.41 (2H, m, CH_2); 1.92 (1H, q, *J* = 7.6, $C\underline{H}CH$=); 1.97 (2H, qd, *J* = 6.8, *J* = 1.2, $C\underline{H}_2CH$=); 5.26 (1H, dtd, *J* = 15.2, *J* = 6.8, *J* = 1.2, $CH_2C\underline{H}$=); 5.60 (1H, ddt, *J* = 15.2, *J* = 7.6, *J* = 1.2, $CHC\underline{H}$=). ^{13}C NMR spectrum, δ, ppm: 11.5; 13.9; 15.6; 19.2; 19.3; 22.8; 23.2; 35.4; 126.2; 134.3. Mass spectrum, *m*/*z* (I_{rel}, %): 254 $[M]^+$ (1), 211 (100), 169 (69), 141 (13), 113 (17), 99 (20); 85 (14), 73 (21), 59 (34).

Mixture of (*E*)-*tert*-butyldimethyl(4-phenylpent-2-en-2-yl)silane (7), (*RR*/*SS*)-*tert*-butyldimethyl(4-phenylpentan-2-yl)silane ((*RR*/*SS*)-8), and (*RS*/*SR*)-*tert*-butyldimethyl-(4-phenylpentan-2-yl)silane ((*RS*/*SR*)-8) was obtained from compound **6** (50 mg, 155 μmol, 1 equiv), using metallic Li (11 mg, 1.58 mmol, 10 equiv). Total quantitative yield of products **7** was 40 mg with ratio **7**/(*RR*/*SS*)-**8**/(*RS*/*SR*)-**8** = = 46:24:30.

(*E*)-*tert*-Butyldimethyl(4-phenylpent-2-en-2-yl)silane (7). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.04 (6H, s, $Si(CH_3)_2$); 0.86 (9H, s, $C(CH_3)_3$); 1.33 (3H, d, *J* = 7.0, $CHC\underline{H}_3$); 1.75 (3H, d, *J* = 1.5, CH_3C=); 3.88 (1H, dq, *J* = 8.9, *J* = 7.0, PhCH); 5.84 (1H, dq, *J* = 8.9, *J* = 1.5, =CH); 7.15–7.32 (5H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: –6.2 (2C); 16.3; 17.5; 22.1; 27.0; 38.1; 125.8; 127.1; 132.8; 146.3; 146.8. Mass spectrum, *m*/*z* (I_{rel}, %): 260 $[M]^+$ (4), 203 (100), 143 (16), 135 (64), 105 (76), 73 (69), 59 (23).

(*RR*/*SS*)-*tert*-Butyldimethyl(4-phenylpentan-2-yl)silane ((*RR*/*SS*)-8). ^1H NMR spectrum, δ, ppm (*J*, Hz): –0.08 (3H, s, $SiCH_3$); –0.07 (3H, s, $SiCH_3$); 0.92 (9H, s, $C(CH_3)_3$); 0.92–0.99 (4H, m, CH_3CHSi); 1.20 (3H, d, *J* = 7.3, $CHC\underline{H}_3$); 1.39 (1H, ddd, *J* = 12.0, *J* = 9.3, *J* = 4.0) and 1.67 (1H, ddd, *J* = 12.0, *J* = 10.9, *J* = 1.5, CH_2); 2.84 (1H, dqd, *J* = 10.9, *J* = 7.0, *J* = 4.0, PhCH); 7.15–7.32 (5H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: –7.2 (2C); 15.0; 17.7; 19.9; 27.7; 37.2; 41.9; 127.0; 127.5; 128.5; 146.9. Mass spectrum, *m*/*z* (I_{rel}, %): 260 $[M]^+$ (4), 203 (100), 143 (16), 135 (64), 105 (76), 73 (69), 59 (23).

(*RS*/*SR*)-*tert*-Butyldimethyl(4-phenylpentan-2-yl)silane ((*RS*/*SR*)-8). ^1H NMR spectrum, δ, ppm (*J*, Hz): –0.15 (3H, s, $SiCH_3$); –0.13 (3H, s, $SiCH_3$); 0.50 (1H, dqd, *J* = 11.7, *J* = 7.3, *J* = 2.4, $CH_3C\underline{H}Si$); 0.81 (9H, s, $C(CH_3)_3$); 0.95 (3H, d, *J* = 7.3, $C\underline{H}_3CHSi$); 1.23 (3H, d, *J* = 7.3, $CHC\underline{H}_3$); 1.38 (1H, ddd, *J* = 13.4, *J* = 11.7, *J* = 4.1) and 1.81 (1H, ddd, *J* = 13.4, *J* = 11.6, *J* = 2.4, CH_2); 2.89 (1H, dqd, *J* = 11.6, *J* = 7.3, *J* = 4.1, PhCH); 7.15–7.32 (5H, m, H Ph). ^{13}C NMR, δ, ppm: –7.3; –7.1; 14.8; 17.6; 19.9; 24.2; 27.5 37.7; 41.0; 125.9; 127.0; 128.5; 146.5. Mass spectrum, *m*/*z* (I_{rel}, %): 260 $[M]^+$ (4), 203 (100), 143 (16), 135 (64), 105 (76), 73 (69), 59 (23).

Supplementary information file containing ^{1}H and ^{13}C NMR spectra, lithium reduction conditions for C–S bond cleavage, and temperature-dependent NMR spectral analysis for reduction product structure elucidation is available at the journal website at http://link.springer.com/journal/10593.

The authors thank the Latvian Council of Science (grant LZP-2018/1-0315).

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Appendix 3

1,3-Difunctionalization of Propargyl Silanes with Concomitant 1,2-Silyl Shift: Synthesis of Allyl Functionalized Vinyl Silanes

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Org. Lett. **2023**, *25*, 4627–4631

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1,3-Difunctionalization of Propargyl Silanes with Concomitant 1,2-Silyl Shift: Synthesis of Allyl Functionalized Vinyl Silanes

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Cite This: *Org. Lett.* 2023, 25, 4627−4631 Read Online

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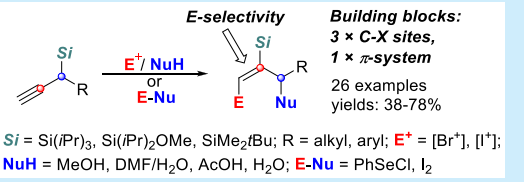
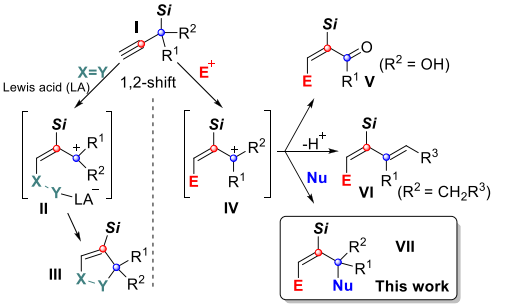
ABSTRACT: Terminal alkynes with a silyl group at the propargylic position upon activation with electrophiles such as *N*-bromosuccinimide undergo (*E*)-selective 1,2-silyl group migration. Subsequently, an allyl cation is formed that is intercepted by an external nucleophile. This approach provides allyl ethers and esters with stereochemically defined vinyl halide and silane handles for further functionalization. The scope of propargyl silanes and electrophile−nucleophile pairs are investigated, and various trisubstituted olefins are prepared in up to 78% yield. The obtained products have been demonstrated to serve as building blocks for transition-metal-catalyzed cross-couplings of vinyl halides, silicon-halogen exchange, and allyl acetate functionalization reactions.



Contrary to the 1,2- and 1,4-additions that are broadly described in organic chemistry textbooks, 1,3-additions are far less common in organic synthesis.[1] Among others, examples of 1,3-difunctionalization include the well-reviewed ring opening of donor−acceptor cyclopropanes[2] and recently emerging cycle opening approaches involving radical[3] or radical cation intermediates,[4] reductive methods,[5] or catalysis by iodine(III) reagents.[6] On the other hand, transition metal-catalyzed 1,2-additions can lead to 1,3-difunctionalized products, if the initial adduct undergoes metal hydride isomerization prior to reductive elimination.[7] Alternatively, 1,3-difunctionalization of olefins can be achieved via transition-metal-catalyzed allylic oxidation accompanied by functionalization of the olefin π-system.[8] Nevertheless, the latter does not include a straightforward functionalization of the internal C2-position, for which specific procedures have been developed.[9]

Allyl, allenyl, and propargyl silanes stand out with their potential to serve as 1,3-dipoles. Upon activation by an appropriate electrophile, the silyl group can undergo a 1,2-silyl shift to an adjacent position,[10] uncovering an electrophilic carbon center that can be trapped by a nucleophile. This type of annulation approach, using propargyl silanes and Lewis acid activated aldehydes or similar X = Y systems, has been reported by the research groups of Danheiser,[11] Knölker,[12] and others,[13] and has been reviewed (**I** → **II** → **III**, Scheme 1).[14] However, simple electrophiles lacking a tethered nucleophile will form intermediate **IV**, which must be quenched via an alternative process. The latter approach is far less known, and the few reported examples include a loss of proton giving products of type **V**[15] and **VI**,[13,16] or intramolecular cyclization arising from the nucleophilic moiety present in R^1/R^2 groups.[17]

Scheme 1. Reactivity of Propargyl Silanes I toward Electrophiles with Concomitant 1,2-Silyl Shift



We were intrigued to generalize the use of propargyl silanes as valuable starting materials for 1,3-difuntionalization, and to do so by adding a nonconnected electrophile−nucleophile pair across the propargyl system with concomitant 1,2-silyl shift (Scheme 1, product **VII**). To the best of our knowledge, only a topologically related, albeit mechanistically different, approach has been reported for radical 1,3-difunctionalization of allylboronic esters with a concomitant 1,2-boron shift.[18] Our

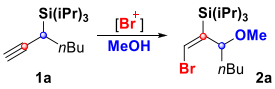
Received: April 16, 2023
Published: June 15, 2023

https://doi.org/10.1021/acs.orglett.3c01245
Org. Lett. 2023, 25, 4627−4631

described methodology offers an (*E*)-selective, simple, and transition-metal-free synthesis of versatile (*E*)-3-bromo-2-(trialkylsilyl)allyl ethers and esters possessing a trisubstituted olefin moiety and functionalized allylic position.

In our initial screening, we decided to use a polar nucleophilic solvent that could facilitate the formation of ionic intermediates and react with the allyl cation. Thus, the reaction of the known propargyl silane **1a**[17a] with electrophilic bromine species in methanol (c_{1a} = 0.1 M) was chosen as the model reaction. In the first experiment, in which propargyl silane **1a** was treated with 1.2 equiv of *N*-bromosuccinimide (NBS) at ambient temperature, the formation of allyl methyl ether **2a** was achieved, and the product was isolated in 57% yield (Table 1, entry 1). The effects of temperature, the concentration of **1a** in the reaction mixture, and the molar ratio of NBS were probed, but they had little effect on the product yield (Table 1, entries 2–5; for the full data set, see Supporting Information Table S1). Similarly, other electrophilic bromine sources (Table 1, entries 6–10) also provided the same range of yields of product **1a**. Therefore, the operationally simple initial conditions with NBS as the electrophile source were also applied to other substrates.

Table 1. Optimization of Bromo Methoxylation Conditions of Propargyl Silane 1a

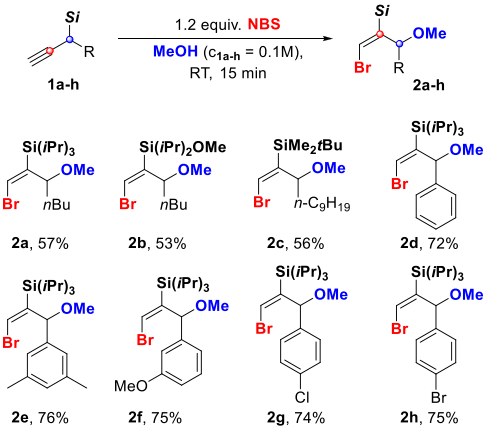


Entry	Reaction conditions[a]	NMR yield of product **2a**,[b] %
1	NBS (1.2 equiv.), RT	60 (57)[c]
2	NBS (1.2 equiv.), at temperatures = -78, 0, 50 °C	52 - 58
3	NBS (1.2 equiv.), RT c_{1a} range 0.05 M - 0.2 M	55 - 56
4	NBS (2.0 equiv.), RT	49
5	NBS (1.2 equiv.), RT, 10% MeOH in $(CF_3)_2CHOH$	46
6	Br_2 (1.0 equiv.), RT	49
7	$TsNBr_2$ (1.2 equiv.), RT	56
8	MeC(O)NHBr (1.2 equiv.), RT	53
9	 (0.6 equiv.), RT	57
10	 (0.6 equiv.), RT	51

[a]Standard conditions: c_{1a} = 0.1 M, reaction time 15 min, if not indicated otherwise. [b]NMR yield with diphenylmethane as internal standard. [c]Isolated yield.

Other 3-alkyl propargyl silanes **1b,c** performed similarly in the bromo methoxylation reaction, and methyl ethers **2b,c** were isolated in 53% and 56% yields, respectively (Scheme 2). The main observed side reactions were: (1) proton loss[13,17] from the intermediate allyl cation, which provides 1-bromobuta-1,3-dien-2-yl-silanes; and (2) nucleophile (methanol) addition to the terminal position of the allyl cation, which

Scheme 2. Bromo Methoxylation of Propargyl Silanes 1a–h



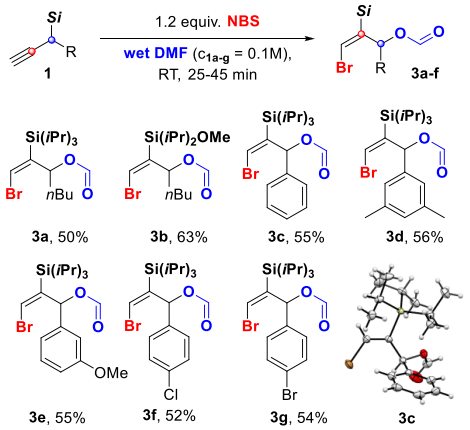
after hydrolysis gives the corresponding unsaturated aldehyde (see Supporting Information Scheme S1). As expected, aryl-substituted propargyl silanes **1d–h**, which can generate resonance-stabilized allylbenzyl cations, gave cleaner and better yielding reactions providing products **2d–h** in the range of 72–76% (Scheme 2). The typical reaction time for all substrates **1a–h** was 5–15 min. It is reasonable to assume that additional stabilization of the intermediary allyl cation by the aryl group facilitates the 1,2-silyl shift and suppresses other degradation processes prior to the nucleophilic attack. The corresponding starting materials **1d–h** were obtained by silylation of the lithiated benzylic position of trimethyl(3-arylprop-1-yn-1-yl)silanes, followed by the chemoselective removal of trimethylsilyl group from the terminal alkyne position (see Supporting Information Scheme S4).

Next, we turned our attention to other polar nucleophilic solvents, such as DMF. Interestingly, DMF acted as a formate group equivalent in this reaction. In the reaction of propargyl silane **1a** with NBS, allyl formate **3a** was isolated in a 50% yield (Scheme 3). To facilitate the final hydrolysis, moist DMF with 0.4% water content was used as determined by Karl Fischer titration (~2 equiv to propargyl silane). Strikingly, for this choice of nucleophile, the product **3a–f** yields (50–63%) were similar for both alkyl- and aryl-substituted propargyl silanes **1a,b** and **1c–g**. We suspect that longer reaction times (25–45 min) indicate weaker nucleophilicity of the carbonyl group leading to unwanted side reactions observed by GC-MS. For product **3c**, single crystals suitable for X-ray analysis were obtained,[19] which unambiguously confirmed both the structure and (*E*)-geometry of the double bond.

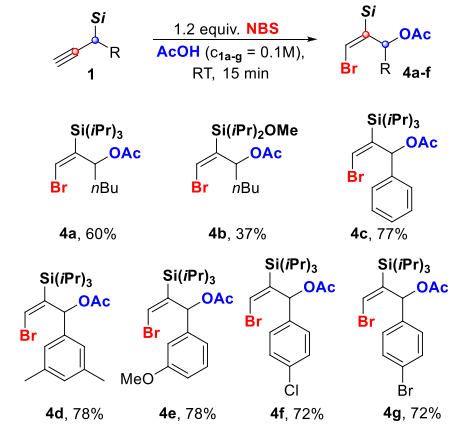
Acetic acid was also tested as the nucleophilic solvent. Initial concerns that the substrates would be too unstable in acidic media turned out to be partially true only for the substrate with a more labile methoxy silyl substituent (Scheme 4), decreasing the yield of product **4b** to 38%. However, all other tested substrates performed similarly to the reactions in other solvents (*vide supra*), yielding allyl acetate **4a** with an alkyl substituent in 60% yield and products **4c–g** bearing stabilizing aryl substituents in 72–78% yield. It should also be mentioned that conducting these reactions on a gram scale provided the

https://doi.org/10.1021/acs.orglett.3c01245
Org. Lett. 2023, 25, 4627–4631

Scheme 3. Bromo Formyloxylation of Propargyl Silanes 1a–g and ORTEP Representation of Compound 3c

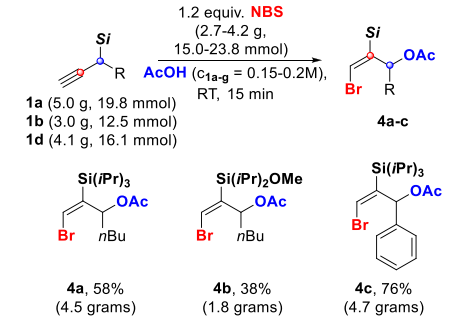


Scheme 4. Bromo Acetoxylation of Propargyl Silanes 1a–g



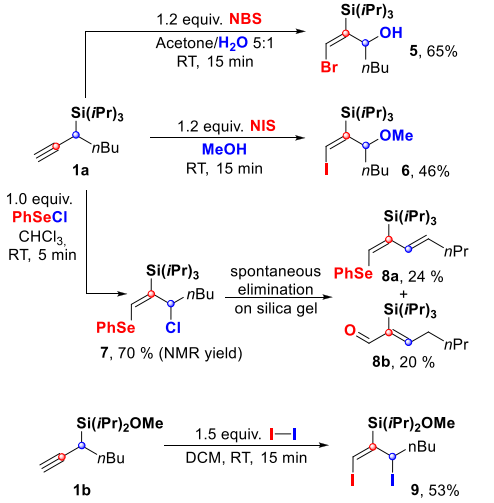
same level of isolated yields, reaching 76% for product **4c**, which was obtained at 4.7 g in one run (Scheme 5).

Scheme 5. Gram-Scale Reactions of Propargyl Silanes 1a–c



Next, other electrophile–nucleophile pairs were briefly explored (Scheme 6). Thus, the bromo hydroxylation of propargyl silane **1a** was achieved in a mixed solvent system of acetone/H_2O 5:1 to give allyl alcohol **5** in 65% yield. Surprisingly, 3-aryl propargyl silanes were unreactive in this system. More nucleophilic systems with larger water contents are not technically feasible because of the low solubility of the starting materials in aqueous media. It has been previously shown that water in acetone or acetonitrile solutions is a weaker nucleophile than methanol and ethanol.[20] Additionally, transformations involving carbocation intermediates can occur with the accumulation of the latter, and the nucleophilic attack of water can be slowed if the intermediate carbocation is intrinsically stabilized.[21] It should be mentioned that compounds of type **5** are useful starting materials in a concise approach to polysubstituted furans.[22] Also the combination of other sources of electrophilic halonium ions like *N*-iodosuccinimide (NIS) with methanol provides a similar reactivity, giving product **6** in 46% yield. In contrast, the use of chlorinated solvents permitted 1,3-chloroselenation (**1a** → **7**) and 1,3-diiodination (**1b** → **9**) with a concomitant 1,2-silyl shift (Scheme 6). It is worth mentioning that compound **7** appeared to be rather unstable; therefore, full characterization was provided for its congeners **8a,b** after HCl elimination or hydrolysis.

Scheme 6. 1,3-Addition of Various Electrophile/Nucleophile Pairs to Propargyl Silanes 1a,b



Finally, we demonstrate the synthetic application of the obtained 1,3-addition products containing a triad of functionalized carbon atoms. We performed a series of Suzuki–Miyaura cross-coupling reactions under modified Buchwald conditions[23] (Scheme 7), yielding the desired products **10a–d** in good yields (71–79%), indicating the stability of both residual functionalities—allyl acetate and vinyl silane. Furthermore, removal of boronic acid from the reaction mixture allowed us to obtain C–H activation product **11** in 65% yield.

https://doi.org/10.1021/acs.orglett.3c01245
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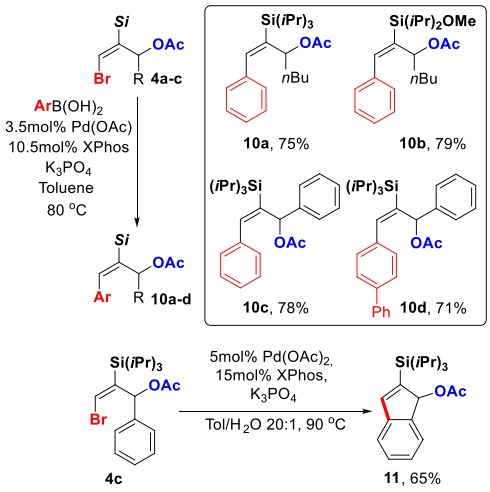
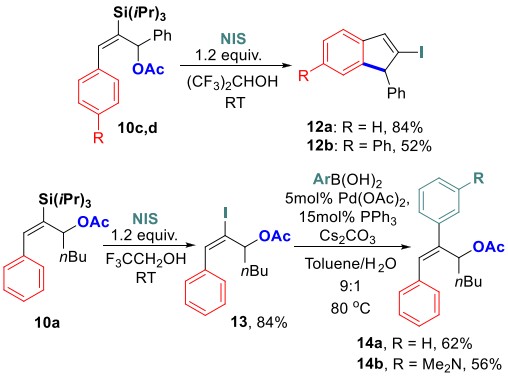
Scheme 7. Suzuki−Miyaura Coupling and C−H Activation Reactions of (*E*)-3-Bromo-2-Silylated Allyl Acetates



In the next attempt to functionalize the silyl moiety, vinyl silanes **10a,c,d** were subjected to electrophilic substitution reactions of the silyl moiety with NIS (Scheme 8). We

Scheme 8. Further Functionalization of Vinyl Silane and Allylic Acetate Moieties of the Obtained Compounds



observed that substrates bearing an aryl group in the allyl position underwent simultaneous intramolecular ionic cyclization under all tested conditions, showing the highest yields of indenes **12a,b** in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) in 84% and 52% yields, respectively. To our delight, the cyclization was suppressed by employing substrate **10a**. Reducing the ionization potential of the allyl position and changing the previously used HFIP to 2,2,2-trifluoroethanol afforded vinyl iodide **13** in 84% yield (Scheme 8). The latter was employed further in the Suzuki−Miyaura reaction to yield stilbenes **14a,b** in 62% and 56% yields, respectively, while simultaneously preserving the original double bond geometry throughout the sequence **4a** → **10a** → **13** → **14a,b**. It is worth noting that synthesis of geometrically defined tri- and tetra-substituted olefins[24] including those with vinylsilane moiety[25] or with allylic functionality[26] is still a challenging task. In this context, the newly obtained building blocks **2**−**4** have been demonstrated to be versatile triads for further derivatization, maintaining the double bond geometry, which originates from (*E*)-selective 1,2-silyl group migration.

In summary, we showed that propargyl silanes with a terminal alkyne moiety readily undergo 1,3-difunctionalization with concomitant 1,2-silyl shift in the presence of electrophile−nucleophile pairs. To the best of our knowledge, this straightforward synthetic protocol is the first report on the external nucleophile trapping of an intermediate allylic cation, which is formed as a result of the 1,2-silyl shift. This approach provides a functionalized atom triad with (*E*)-selectivity, and the isolated yields of the products reach up to 78%. We have also demonstrated the synthetic utility of the obtained triads by transforming them into geometrically defined trisubstituted olefins via cross-coupling reactions. Other tested transformations included C−H activation and ionic cyclization. Further studies are ongoing in our laboratory to advance this methodology using the rich chemistry of allyl cations, which, among others, implies the synthesis of various heterocycles and carbocycles in both intramolecular and multicomponent cyclization reactions, including asymmetric versions. In addition, we are looking to extend this approach for the synthesis of tetra-substituted olefins containing a functionalized allylic position.

■ 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.orglett.3c01245.

Experimental procedures and characterization data (PDF)

Accession Codes

CCDC 2241598 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.

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https://doi.org/10.1021/acs.orglett.3c01245
Org. Lett. 2023, 25, 4627−4631

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

R.B. is thankful for financial support from the European Social Fund within the Project No. 8.2.2.0/20/I/008 and from Riga Technical University for a doctoral student grant.

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Appendix 4

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

Rasma Kroņkalne, Rūdolfs Beļaunieks, Artjoms Ubaidullajevs, Anatoly Mishnev, Māris Turks

J. Org. Chem.. **2023**, DOI: 10.1021/acs.joc.3c01481

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

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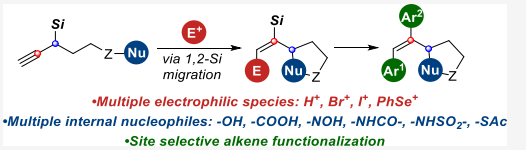
ABSTRACT: Propargyl silanes with a terminal alkyne moiety undergo a 1,2-silyl shift when activated with electrophiles such as H^+, Br^+, I^+, and $PhSe^+$. A method was developed to trap 1,3-transposed electrophilic centers with various internal O-, N-, and S-nucleophiles in a 5-exo manner. This synthetic 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.



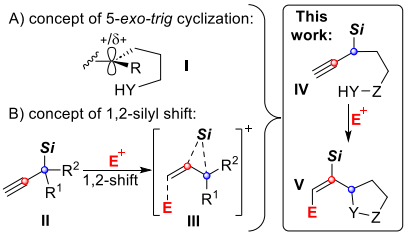
INTRODUCTION

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 terrestrial[4] and marine organisms,[5] and as such, it has raised the attention of communities of synthetic[6] 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 oxygen[9] and nitrogen nucleophile[10] in hetero-Michael reactions or intramolecular S_N1, S_N2, and S_N2' processes, hydro- and haloetherification, as described in several review articles. Similar approaches are used also for the synthesis of thiolane cycles.[8]

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

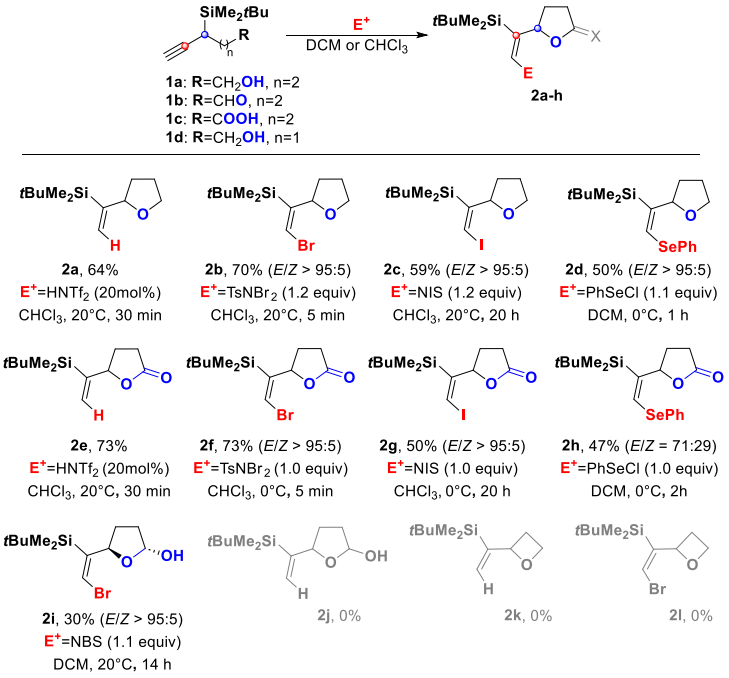


The required vacant π-orbital for the cyclization event can be that of a carbocation, and the use of propargyl silanes as 1,3-dipoles for their 1,3-difuntionalization in this context is an underexplored synthetic route. Indeed, electrophilic activation of propargyl silanes under certain circumstances 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-difuntionalization event.[11] Yet, most of the

Received: July 3, 2023

https://doi.org/10.1021/acs.joc.3c01481
J. Org. Chem. XXXX, XXX, XXX−XXX

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)sulfonimide (Tf_2NH) 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 Tf_2NH, 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

https://doi.org/10.1021/acs.joc.3c01481
J. Org. Chem. XXXX, XXX, XXX−XXX

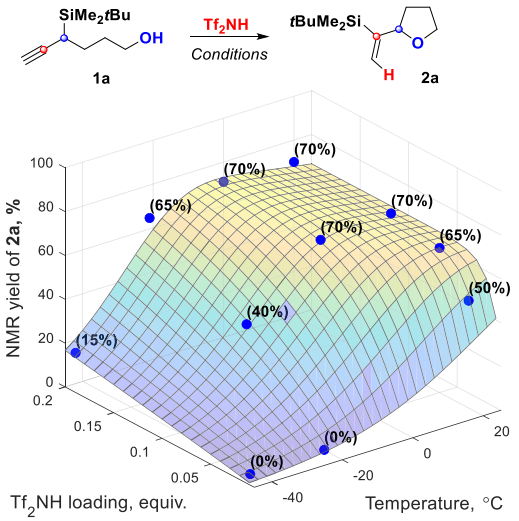
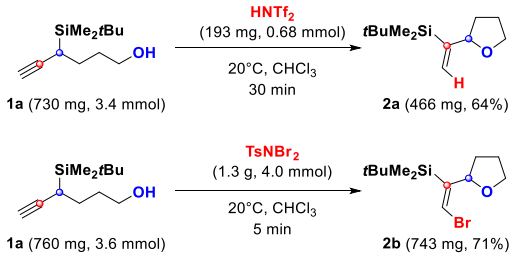


Figure 1. Optimization of Tf_2NH-catalyzed tetrahydrofuran **2a** Synthesis in $CDCl_3$. [a]Diphenylmethane internal standard; c_{1a} = ~0.15 M, $CDCl_3$, 1 h; conversion less than 5% is considered below the limit of detection; the results are rounded by 5% increments.

the easier dosage of solid Tf_2NH, we decided to develop a cyclization methodology with the latter. Finally, the optimal cyclization conditions (0.15−0.20 equiv of Tf_2NH, in DCM or chloroform, 0−20 °C, 1h) 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 Tf_2NH 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 $(CH_2)_2$-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-

https://doi.org/10.1021/acs.joc.3c01481
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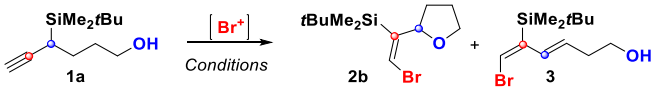
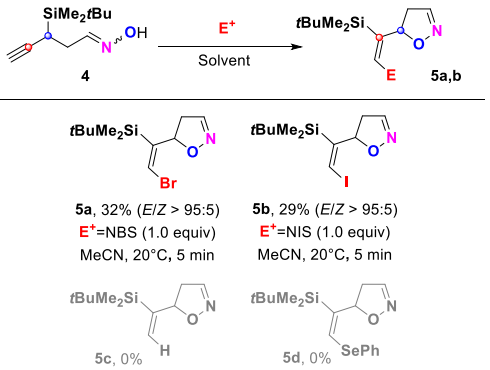
Table 1. Study of Tetrahydrofuran 2b Synthesis in the Bromoetherification Reaction



					compound distribution (qNMR)[b,c]		
entry	Br^+ (equiv)	T, (°C)	solvent[a]	reaction time	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_6D_6	24 h	20	10	30
4		20	THF-d_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

[a] c_{1a} = ∼0.15 M. [b] Diphenylmethane internal standard. [c] NMR 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 $HNTf_2$ (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 $HNTf_2$.

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}−$\pi_{C=C}$ → $\sigma^*_{C\text{-heteroatom}}$ 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

https://doi.org/10.1021/acs.joc.3c01481
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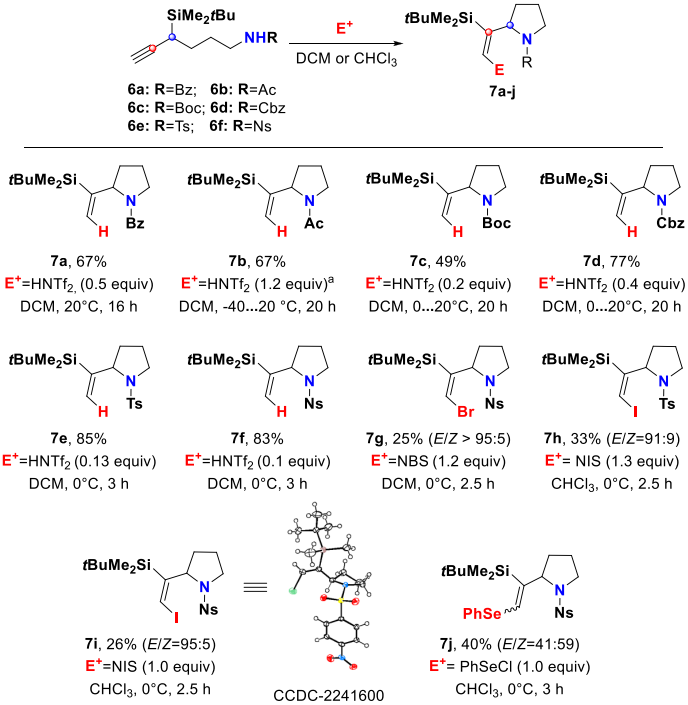
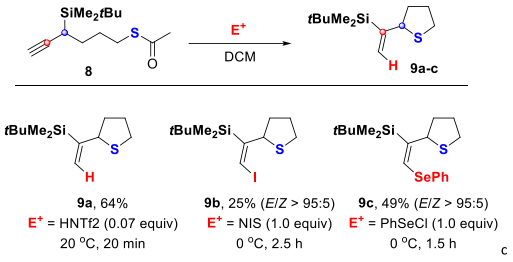
Scheme 5. Product Scope for the Synthesis of Pyrrolidine Derivatives 7a−j



conditions (Scheme 6). After brief optimization of the reaction conditions (7 mol % of $HNTf_2$, 20 °C), thiolane **9a** was 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.

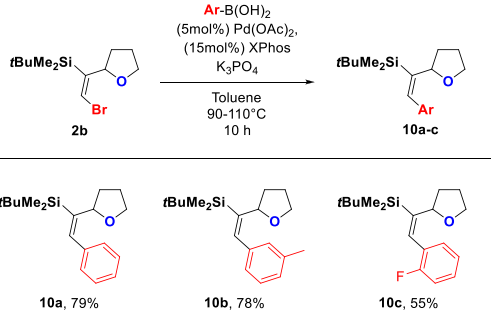
Scheme 6. Synthesis of Thiolanes 9a−c



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



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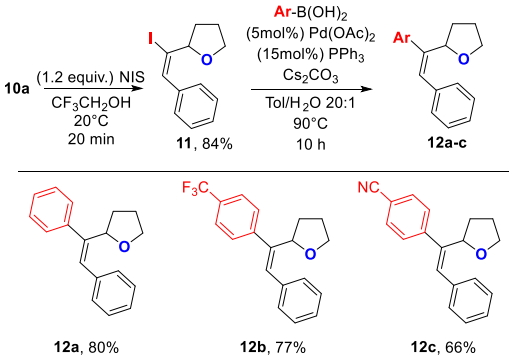
J. Org. Chem. XXXX, XXX, XXX−XXX

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 devolved 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 Kieselgel 60 F254, with detection by UV Full Paper light or developed using generic $KMnO_4$ or I_2 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). ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded using Bruker AVANCE Neo 500 and AVANCE 300 MHz spectrometers in $CDCl_3$, DMSO-d_6, and MeOH-d_4. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are reported in Hz. Residual solvent (^{1}H) or solvent (^{13}C) peaks were used as an internal reference ($CDCl_3$: δ = 7.26 ppm for ^{1}H NMR; $CDCl_3$: δ = 77.16 ppm for ^{13}C{^{1}H} NMR; DMSO-d_6: δ = 2.50 ppm for ^{1}H NMR; DMSO-d_6: δ = 39.52 ppm for ^{13}C{^{1}H} NMR; MeOH-d_4: δ = 3.31 ppm for ^{1}H NMR; and MeOH-d_4 δ = 49.00 ppm for ^{13}C{^{1}H} 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-ol[15] (**1d**; 1.50 g, 7.6 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 (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. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{11}H_{21}OSi^+$ [M + H]$^+$, 197.1356; found, 197.1337.

(6-Azidohex-1-yn-3-yl)(*tert*-butyl)dimethylsilane (Int2). A solution of 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-yl 4-methylbenzenesulfonate[22] (2.8 g, 7.6 mmol, 1.0 equiv) in anh. DMF (5 mL) under an argon atmosphere was added dropwise to a suspension of NaN_3 (1.0 g, 15.4 mmol, 2.0 equiv) in anh. 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 reaction[22]). Toluene (50 mL) and H_2O (100 mL) were added to the reaction mixture. The organic layer was separated, washed with H_2O (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. ^{1}H NMR (500 MHz, $CDCl_3$): 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

https://doi.org/10.1021/acs.joc.3c01481
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(dddd, 1H, J = 13.3, 11.7, 9.8, 4.5), 0.98 (s, 9H), 0.10 (s, 3H), 0.03 (s, 3H). $^{13}C\{^1H\}$ 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 $C_{12}H_{24}N_3Si^+$ $[M + H]^+$, 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-ol[15] (**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 → 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). $^{13}C\{^1H\}$ 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 $C_{12}H_{23}OSi^+$ $[M + H]^+$, 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 × 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 → 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). $^{13}C\{^1H\}$ 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 $C_{11}H_{19}O_2Si^+$ $[M - CH_3]^+$, 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 ultrasonification. 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_{Ph2Me} of diphenylmethane was set to 1000. The yield for the compound was determined by the formula

$$\eta_{1a} = \frac{\left(\frac{I_{1a}}{2}\right)\cdot\left(\frac{m_{Ph_2Me}}{M_{Ph_2Me}}\right)}{\left(\frac{I_{Ph_2Me}}{6}\right)}\cdot\frac{1}{n_{1a}}$$

$$\eta_{2a} = \frac{\left(\frac{I_{2a}}{1}\right)\cdot\left(\frac{m_{Ph_2Me}}{M_{Ph_2Me}}\right)}{\left(\frac{I_{Ph_2Me}}{6}\right)}\cdot\frac{1}{n_{1a}}$$

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) was 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 ultrasonification. 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 = 10.0s. 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_{Ph2Me} of diphenylmethane was set to 1000. The yield for the compound was determined by the formula

$$\eta_{1a} = \frac{\left(\frac{I_{1a}}{2}\right)\cdot\left(\frac{m_{Ph_2Me}}{M_{Ph_2Me}}\right)}{\left(\frac{I_{Ph_2Me}}{2}\right)}\cdot\frac{1}{n_{1a}}$$

$$\eta_{2b} = \frac{\left(\frac{I_{2b}}{1}\right)\cdot\left(\frac{m_{Ph_2Me}}{M_{Ph_2Me}}\right)}{\left(\frac{I_{Ph_2Me}}{2}\right)}\cdot\frac{1}{n_{1a}}$$

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 $HNTf_2$ (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 → 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 $HNTf_2$ (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 × 15 mL). The combined organic layer was washed with saturated aqueous NaCl (2 × 20 mL). Column chromatography (eluent: DCM/Hex 20 → 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). $^{13}C\{^1H\}$ 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 $C_{12}H_{25}OSi^+$ $[M + H]^+$, 213.1669; found, 213.1661.

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

https://doi.org/10.1021/acs.joc.3c01481
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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. ^{1}H 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}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 148.7, 112.9, 82.8, 67.9, 31.3, 27.4, 25.6, 17.3[1], −3.5, −4.2. HRMS (ESI): m/z calcd for $C_{12}H_{24}BrOSi^+$ [M + H]$^+$, 291.0774; found, 291.0771.

Mixture of (*E*)-(2-Bromo-1-(tetrahydrofuran-2-yl)vinyl)(*tert*-butyl)dimethylsilane (2b) and (3*E*,5*E*)-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 5h. 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**: ^{1}H NMR (500 MHz, $CDCl_3$): 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}C{^{1}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. ^{1}H 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}C{^{1}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 $C_{12}H_{24}IOSi^+$ [M + H]$^+$, 339.0636; found, 339.0662.

(*E*)-*tert*-Butyldimethyl(2-(phenylselanyl)-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), phenylselenyl 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. ^{1}H 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}C{^{1}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 $C_{18}H_{29}OSeSi^+$ [M + H]$^+$, 369.1148; found, 369.1164.

5-(1-(*tert*-butyldimethylsilyl)vinyl)dihydrofuran-2(3*H*)-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), $HNTf_2$ (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. ^{1}H 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}C{^{1}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 $C_{12}H_{23}O_2Si^+$ [M + H]$^+$, 227.1462; found, 227.1458.

(*E*)-5-(2-Bromo-1-(*tert*-butyldimethylsilyl)vinyl)-dihydrofuran-2(3*H*)-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*-dibromomethylbenzenesulfonylamide (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. ^{1}H 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}C{^{1}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 $C_{12}H_{22}BrO_2Si^+$ [M + H]$^+$, 305.0567; found, 305.0561.

(*E*)-5-(1-(*tert*-Butyldimethylsilyl)-2-iodovinyl)dihydrofuran-2(3*H*)-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. ^{1}H 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}C{^{1}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 $C_{12}H_{22}IO_2Si^+$ [M + H]$^+$, 353.0428; found, 353.0423.

Mixture of (*E*)- and (*Z*)-Isomers of 5-(1-(*tert*-butyldimethylsilyl)-2-(phenylselanyl)vinyl)dihydrofuran-2(3*H*)-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), phenylselenyl 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**: ^{1}H 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}C{^{1}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 $C_{18}H_{27}O_2SeSi$ [M + H]$^+$, 383.0940; found, 383.0935. Characterization of compound (*Z*)-**2h**: ^{1}H 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}C{^{1}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 $C_{18}H_{27}O_2SeSi^+$ [M + 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-al (**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 furanol **2i** (130 mg, 30%) as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$): 6.32 (d, 1H, ^4J = 1.7), 5.49 (dd, 1H, ^3J = 5.5, 2.2), 4.91 (dt, 1H, ^3J = 7.9, ^4J = 1.7), 2.52 (dtd, 1H, ^2J = 12.5, ^3J = 7.9, 4.7), 2.09 (dddd, 1H, ^2J = 13.2, ^3J = 8.2, 7.9, 4.7), 1.87 (dddd, 1H, ^2J = 13.2, ^3J = 7.9, 4.7, 2.2), 1.46 (dq, 1H, ^2J = 12.5, ^3J = 7.9), 0.90 (s,

https://doi.org/10.1021/acs.joc.3c01481
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9H), 0.09 (s, 6H). $^{13}C\{^1H\}$ 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 $C_{12}H_{22}BrOSi^+$ $[M - OH]^+$, 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, $NH_2OH{\cdot}HCl$ (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 × 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 → 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). $^{13}C\{^1H\}$ 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). $^{13}C\{^1H\}$ 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 $C_{11}H_{22}NOSi^+$ $[M + H]^+$, 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 °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). $^{13}C\{^1H\}$ 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 $C_{11}H_{21}BrNOSi^+$ $[M + H]^+$, 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 °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). $^{13}C\{^1H\}$ 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 $C_{11}H_{21}INOSi^+$ $[M + H]^+$, 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 °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 °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 °C, reaction time 22 h. The reaction mixture was quenched with aqueous NH_4Cl (30 mL) and extracted with toluene (3 × 30 mL). Column chromatography (eluent: DCM/Hex: 40 → 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). $^{13}C\{^1H\}$ 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 $C_{19}H_{30}NOSi^+$ $[M + H]^+$, 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 °C), reaction temperature 20 °C, reaction time 16 h. The reaction mixture was quenched with aqueous 0.01 M HCl (20 mL) at 0 °C and extracted with EtOAc (3 × 30 mL). Column chromatography (eluent: acetone/DCM: 1 → 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). $^{13}C\{^1H\}$ 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 $C_{14}H_{28}NOSi^+$ $[M + H]^+$, 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 °C for 1 h. Then, it was cooled to 0 °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 °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 × 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). $^{13}C\{^1H\}$ 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 $C_{17}H_{34}NO_2Si^+$ $[M + H]^+$, 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 °C, reaction temperature 20 °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

https://doi.org/10.1021/acs.joc.3c01481
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isolated by EtOAc extraction (3 × 20 mL). Column chromatography (eluent: DCM/Hex: 50 → 60%) afforded benzylcarbamate **6d** (510 mg, 71%) as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{20}H_{32}NO_2Si^+$ [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-azidohex-1-yn-3-yl)(*tert*-butyl)dimethylsilane (**Int2**, 184 mg, 0.77 mmol, 1.0 equiv) and Ph_3P (203 mg, 0.77 mmol, 1.0 equiv) in THF (5 mL) and H_2O (0.05 mL). Step 2: DCM (10 mL), Et_3N (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 NH_4Cl (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. ^{1}H NMR (500 MHz, $CDCl_3$ + D_2O): 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, H_3C), 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{19}H_{32}NO_2SSi^+$ [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-azidohex-1-yn-3-yl)(*tert*-butyl)dimethylsilane (**Int2**, 1.40 g, 5.8 mmol, 1.0 equiv) and Ph_3P (1.80 g, 6.9 mmol, 1.2 equiv) in THF (60 mL) and H_2O (1 mL). Step 2: DCM (50 mL), Et_3N (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 NH_4Cl (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. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{18}H_{29}N_2O_4SSi^+$ [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*-butyldimethylsilyl)hex-5-yn-1-yl)benzamide (**6a**; 28 mg, 0.089 mmol, 1.0 equiv) and $HNTf_2$ (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. ^{1}H 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, $^2J_{H-H}$ = 1.6, $^4J_{H-H}$ = 1.4, $H_aC(6)$), 5.43 (d, 1H, $^2J_{H-H}$ = 1.6, $H_bC(6)$), 4.93 (dd, 1H, $^3J_{H-H}$ = 7.8, 4.6, HC(4)), 3.59 (ddd, 1H, $^2J_{H-H}$ = 10.6, $^3J_{H-H}$ = 7.2, 6.1, $H_2C(1)$), 3.49−3.37 (m, 1H, $H_2C(1)$), 2.22 (dq, 1H, $^2J_{H-H}$ = 12.4, $^3J_{H-H}$ = 7.8, $H_2C(3)$), 2.02−1.86 (m, 1H, $H_2C(2)$), 1.85−1.72 (m, 1H, $H_2C(2)$), 1.71−1.63 (m, 1H, $H_2C(3)$), 1.01 (s, 9H, $H_3C(1')$), 0.19 (s, 3H, $H_3C(2')$), 0.17 (s, 3H, $H_3C(2')$); ^{1}H 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, ^2J = 1.5, ^4J = 1.5, $H_aC(6)$), 5.53 (t, 1H, ^2J = 1.5, ^4J = 1.5, $H_bC(6)$), 4.69−4.62 (m, 1H, HC(4)), 3.69 (dd, 2H, $^3J_{H-H}$ = 9.4, 5.1, $H_2C(1)$), 2.18−2.04 (m, 1H, $H_2C(3)$), 2.02−1.86 (m, 2H, $H_2C(2)$), 1.85−1.72 (m, 1H, $H_2C(3)$), 0.67 (s, 9H, $H_3C(1')$), −0.07 (s, 3H, $H_3C(2')$), −0.08 (s, 3H, $H_3C(2')$). ^{13}C{^{1}H} 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; ^{13}C{^{1}H} 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 $C_{19}H_{30}NOSi^+$ [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*-butyldimethylsilyl)hex-5-yn-1-yl)acetamide (**6b**; 47 mg, 0.19 mmol, 1.0 equiv) in DCM (4 mL), solution of $HNTf_2$ (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 ^{1}H NMR spectrum, the peaks will be assigned by proton groups. ^{13}C NMR spectrum will be provided as a collection of peaks of all rotamers. ^{1}H NMR (500 MHz, $CDCl_3$): 6.25−5.26 (2H, $H_2C(6)$), 5.12−4.44 (1H, HC(4)), 3.62−3.22 (2H, $H_2C(1)$), 2.41−1.56 (7H, $H_2C(2)$, $H_2C(3)$, $H_3C(1')$), 1.02−0.77 (9H, 3 × $H_3C(1')$), 0.19 to −0.03 (6H, 2 × $H_3C(2')$). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{14}H_{28}NOSi^+$ [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*-butyldimethylsilyl)hex-5-yn-1-yl)-carbamate (**6c**; 205 mg, 0.66 mmol, 1.0 equiv) in DCM (3 mL), solution of $HNTf_2$ (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 $CDCl_3$, it is comprised of isomers α and β in a ratio of 3:7. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.54 (s, 1H, $H_aC(6)$), 5.36 (s, 1H, $H_bC(6)$), 3.50−3.29 (m, 2H, $H_2C(1)$), 2.06−1.86 (m, 1H, $H_2C(3)$), 1.83−1.70 (m, 2H, $H_2C(2)$), 1.69−1.56 (m, 1H, $H_2C(3)$), 0.93 (s, 9H, $H_3C(1')$), 0.10 (s, 3H, $H_3C(2')$), 0.09 (s, 3H, $H_3C(2')$). Peaks corresponding to α conformer: 4.56, (br, 1H, HC(4)), 1.44 (s, 9H, $H_3C(1'')$); peaks corresponding to β conformer: 4.49 (br.d., 1H, $^3J_{H-H}$ = 7.7 Hz, HC(4)), 1.40 (s, 9H, $H_3C(1'')$). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{17}H_{34}NO_2Si^+$ [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*-butyldimethylsilyl)hex-5-yn-1-yl)-carbamate (**6d**) (31 mg, 0.085 mmol, 1.0 equiv) in DCM (2 mL), $HNTf_2$ (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. ^{1}H NMR (500 MHz, DMSO-d_6, 100 °C): δ 7.41−7.26 (m, 5H, H−C(3″, 4″, 5″)), 4.54 (d, 1H, $^3J_{H-H}$ = 8.2, HC(4)), 3.45 (t, 2H, $^3J_{H-H}$ = 7.9, $H_2C(1)$), 2.13−2.02 (m, 1H, $H_2C(3)$), 1.85−1.73 (m, 2H, $H_2C(2)$), 1.61−1.52 (m, 1H, $H_2C(3)$), 0.89 (s, 9H, $H_3C(1')$), 0.08 (s, 6H, $H_3C(2')$). Peaks corresponding to α conformer: 5.55 (d, 1H, $^2J_{H-H}$ = 1.4, $H_aC(6)$), 5.34 (s, 1H, $H_bC(6)$); peaks corresponding to β conformer: 5.27 (d, 1H, $^2J_{H-H}$ = 2.4 Hz, $H_aC(6)$), 5.17 (d, 1H, $^2J_{H-H}$ = 2.4 Hz, $H_bC(6)$). ^{13}C{^{1}H} 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 $C_{20}H_{32}NO_2Si^+$ [M + H]$^+$, 346.2197; found, 346.2219.

https://doi.org/10.1021/acs.joc.3c01481
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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 $HNTf_2$ (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. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{19}H_{32}NO_2SSi^+$ [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 $HNTf_2$ (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. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{18}H_{29}N_2O_4SSi^+$ [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 $CHCl_3$ (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. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{18}H_{28}BrN_2O_4SSi^+$ [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 $CHCl_3$ (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**: ^{1}H NMR (500 MHz, $CDCl_3$): 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 (dtd, 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{19}H_{31}INO_2SSi^+$ [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 $CHCl_3$ (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). ^{1}H NMR (500 MHz, $CDCl_3$): 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 (ddtd, 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{18}H_{27}N_2O_4SSi^+$ [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 C_{18}-silica gel (eluent: NH_4HCO_3 solution in H_2O (pH 7.9)/MeCN = 20:80) afforded silyl pyrrolidine (*Z*-**7j**) and silyl pyrrolidine (*E*-**7j**) as amorphous solids.

Characterization of Compound *E*-7j. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{24}H_{33}N_2O_4SSeSi^+$ [M + H]$^+$, 553.1090; found, 553.1073.

Characterization of Compound *Z*-7j. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{24}H_{33}N_2O_4SSeSi+$ [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-methylbenzenesulfonamide[19] (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 $NaHCO_3$ (15 mL) and brine (2 × 10 mL), dried over anhydrous Na_2SO_4, 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. ^{1}H NMR (500 MHz, $CDCl_3$): 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). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): 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 $C_{14}H_{27}OSSi^+$ [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), $HNTf_2$ (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. ^{1}H NMR (500 MHz, $CDCl_3$): 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

https://doi.org/10.1021/acs.joc.3c01481
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(m, 1H), 1.72−1.64 (m, 1H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H). $^{13}C\{^1H\}$ 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 $C_{12}H_{25}SSi^+$ $[M + H]^+$, 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*-butyldimethylsilyl)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). $^{13}C\{^1H\}$ 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 $C_{12}H_{24}ISSi^+$ $[M + H]^+$, 355.0407; found, 355.0435.

(*E*)-*tert*-Butyldimethyl(2-(phenylselanyl)-1-(tetrahydrothiophen-2-yl)vinyl)silane (9c). The reaction was performed following general procedure A: 4-(*tert*-butyldimethylsilyl)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). $^{13}C\{^1H\}$ 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 $C_{18}H_{29}SSeSi^+$ $[M + H]^+$, 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), $ArB(OH)_2$ (0.51−0.68 mmol, 3.0−4.0 equiv), $Pd(OAc)_2$ (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*-Butyldimethyl(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), $PhB(OH)_2$ (835 mg, 6.8 mmol, 4.0 equiv), $Pd(OAc)_2$ (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). $^{13}C\{^1H\}$ 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 $C_{18}H_{29}OSi^+$ $[M + H]^+$, 289.1982; found, 289.1979.

(*E*)-*tert*-Butyldimethyl(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), $Pd(OAc)_2$ (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). $^{13}C\{^1H\}$ 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 $C_{19}H_{31}OSi^+$ $[M + H]^+$, 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), $Pd(OAc)_2$ (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). $^{13}C\{^1H\}$ 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 $C_{18}H_{28}FOSi^+$ $[M + H]^+$, 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*-butyldimethyl(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% $Na_2S_2O_3$ solution (30 mL) were added. The organic layer was separated and washed with brine (2 × 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). $^{13}C\{^1H\}$ 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 $C_{12}H_{14}IO^+$ $[M + H]^+$, 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), $PhB(OH)_2$ (48 mg, 0.40 mmol, 3.0 equiv), $Pd(OAc)_2$ (1.5 mg, 6.6 μmol, 5 mol %), PPh_3 (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). $^{13}C\{^1H\}$ 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 $C_{18}H_{19}O$ $[M + H]^+$, 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

https://doi.org/10.1021/acs.joc.3c01481
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acid (95 mg, 0.50 mmol, 3.0 equiv), $Pd(OAc)_2$ (1.9 mg, 8.3 μmol, 5 mol %), PPh_3 (6.5 mg, 25.0 μmol, 0.15 equiv), Cs_2CO_3 (163 mg, 0.50 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 **12b** (40 mg, 77%) as a white amorphous solid. ^1H NMR (500 MHz, $CDCl_3$): 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). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): 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 = 272), 76.9, 68.5, 30.8, 26.7. HRMS (ESI): m/z calcd for $C_{19}H_{18}F_3O^+$ $[M + H]^+$, 319.1304; found, 319.1299.

(*Z*)-4-(2-Phenyl-1-(tetrahydrofuran-2-yl)vinyl)benzonitrile (12c). 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-cyanophenyl boronic acid (74 mg, 0.50 mmol, 3.0 equiv), $Pd(OAc)_2$ (1.9 mg, 8.3 μmol, 5 mol %), PPh_3 (6.5 mg, 25.0 μmol, 0.15 equiv), Cs_2CO_3 (163 mg, 0.50 mmol, 3.0 equiv), toluene (2 mL), and H_2O (0.1 mL). For workup, EtOAc (5 mL) was added, and the mixture was filtered through a Na_2SO_4 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, $CDCl_3$): 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). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): 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 $C_{19}H_{18}NO^+$ $[M + H]^+$, 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.

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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/I/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.

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(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.

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https://doi.org/10.1021/acs.joc.3c01481
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5. pielikums
Appendix 5

Enantioselektīvas metodes izstrāde elektrofīlu ierosinātām termināli funkcionalizētu propargilsilānu heterociklizācijas reakcijām

Development of enantioselective electrophile-induced heterocyclization of terminally functionalized propargyl silanes

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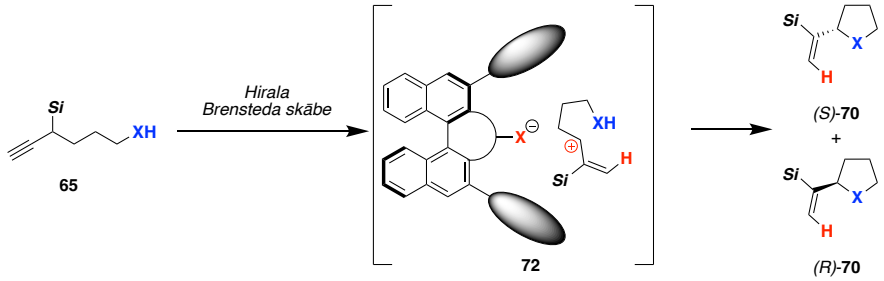
Nepublicētie rezultāti / Unpublished results

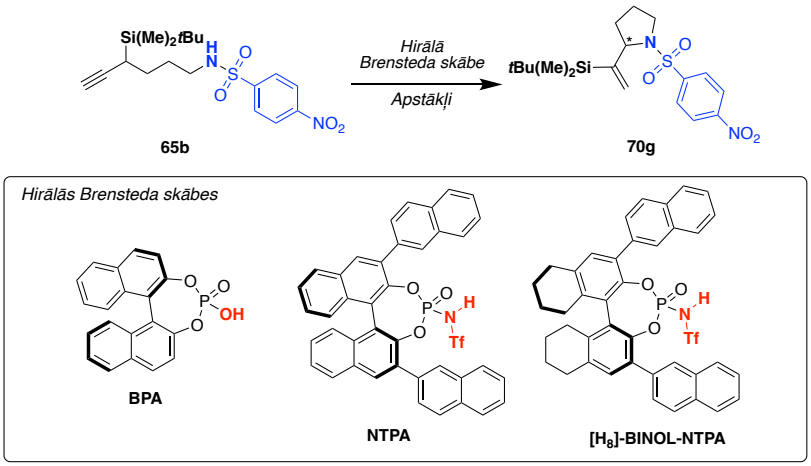
Enantioselektīvas metodes izstrāde elektrofīlu ierosinātām termināli funkcionalizētu propargilsilānu heterociklizācijas reakcijām

Pētījumi par enantioselektīvas metodes izstrādi propargilsilānu heterociklizācijas reakcijām tika balstīti uz asimetriskās pretjona virzītās katalīzes (*ACDC*) konceptu. Kā hirālās informācijas avoti tika izvēlētas BINOL atvasinātās fosforskābes un *N*-trifluormetānsulfonlilfosfoimidāti, kas ar propargilsilāniem **65** pēc protonēšanas un sililgrupas 1,2-migrācijas veidos ciešu jonu pāri **72** hirālās informācijas pārnešanai, lai panāktu enantiodiskrimināciju heterociklā **70** (R1. shēma).



R1. shēma. Hirālas Brensteda skābes katalizēta iekšmolekulāra ciklizēšanās reakcija.

Koncepta pierādīšanai kā modeļreakcija tika izvēlēta propargilsilāna **65b** skābes katalizēta ciklizēšanās reakcija ar komerciāli pieejamajām skābēm **BPA**, **NTPA** un **[H$_8$]-BINOL-NTPA** (R2. shēma).



R2. shēma. Modeļreakcija enantioselektīvas metodes izstrādei propargilsilānu ciklizēšanas reakcijām.

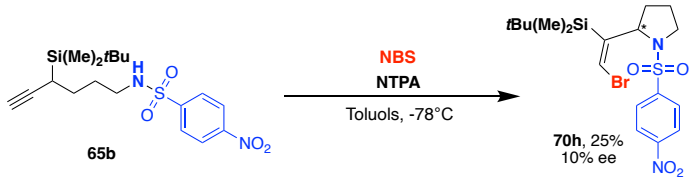
Veiktie eksperimenti apkopoti R1. tabulā un eksperimentu rezultāti analizēti ar AEŠH (R7. lpp), kas sajūgts ar UV detektoru kā stacionāro fāzi izmantojot (R,R)-Whelk-O 1 hirālo kolonnu un mobīlo fāzi 5% *i*PrOH/heksāna (v/v) maisījumu.

R1. tabula

Hirālu Brensteda skābju katalizētas propargilsilāna **65b** ciklizēšanas apstākļi

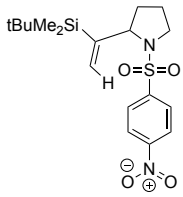
Nr.	Katalizators	Šķīdinātājs	T, °C	t, h	Iznākums	ee, %
1	**BPA**	DCM	20	24	-	-
2		$CHCl_3$	63	72	13	0
3	**NTPA** 5 mol%	Toluols	60	19	56	6
4		Cikloheksāns	60	18	62	11
5	**NTPA** 10 mol%	Cikloheksāns	20	19	52	11
6	**[H_8]-BINOL-NTPA** 5 mol%	Cikloheksāns	60	21	45	12

Koncepta iespējamība tika pārbaudīta arī *halo*-ciklizēšanas reakcijās, kurās ahirālais elektrofīlais halogēna avots tiek aktivēts ar hirālu Brensteda skābi. Kā modeļreakcija tika izvēlēta propargilsilāna **65b** reakcija ar *N*-bromsukcinimīdu kā katalizatoru izmantojot **NTPA** (R3. shēma) (R10. lpp).



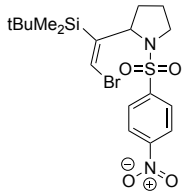
R3. shēma. Modeļreakcija enantioselektīvas metodes izstrādei propargilsilānu *halo*-ciklizēšanas reakcijām.

Eksperimentālās procedūras



2-(1-(*terc*-Butildimetilsilil)vinil)-1-((4-nitrofenil)sufonil)pirolidīns (**70**): Racemāts tika sintezēts pēc metodes, kas publicēta 4. pielikumā.

Metode ar hirālu Brensteda skābi: apaļkolbu ar magnētisko maisītāju, kas izkarsēti žāvskapī, izpūš ar argonu un zem slāpekļa plūsmas pievieno hirālu Brensteda skābi (6.3-12.6 μmol, 5-10 mol%). Kolbu degazē ar argonu pie Šlenka līnijas. Pievieno šķīdinātāju un *N*-(4-(*terc*-butildimetilsilil)heks-5-īn-1-il)-4-nitrobenzsulfonamīda **65b** (0.126 mmol, 1.0 ekv.) šķīdumu un maisa 18h R1. tabulā uzrādītajos apstākļos. Reakcijas maisījumu neitralizē ar pies. $NaHCO_3$ ūdens šķīdumu (5 mL). Ūdens slāni ekstrahē ar DCM (2 x 5 mL). Organiskās fāzes apvieno un mazgā ar pies. NaCl ūdens šķīdumu (5 mL), zāvē virs bezūdens Na_2SO_4, filtrē un iekoncentrē pazeminātā spiedienā. Maisījumu attīra hromatogrāfiski uz silikagela (DCM/Hex 40%→60%). Produktu **70** iegūst kā baltu amorfu vielu. Enantiomēro attiecību nosaka ar AEŠH uz hirālās stacionārās fāzes: (R,R) Whelk-O 1 4.6 x 250 mm; 5% *i*PrOH/heksāns, 0.8 mL/min, 254 nm (R7. lpp).



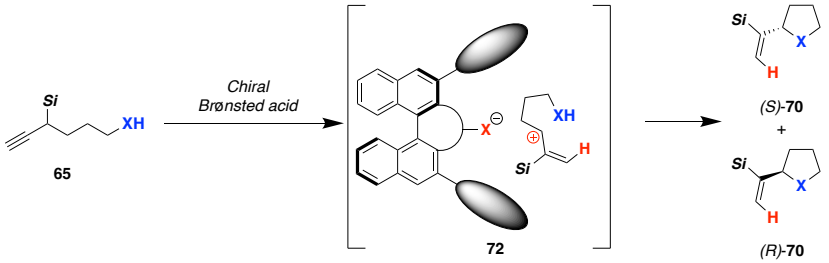
(*E*)-2-(2-Brom-1-(*terc*-butildimetilsilil)vinil)-1-((4-nitrofenil)sulfonil)-pirolidīns (**70h**):

Racemāts tika sintezēts pēc metodes, kas publicēta 4. pielikumā.

Metode ar hirālu Brensteda skābi: apaļkolbu ar magnētisko maisītāju, kas izkarsēti žāvskapī, izpūš ar argonu un zem slāpekļa plūsmas pievieno *N*-bromsukcinimīdu (23 mg, 0.13 mmol, 1.0 ekv.) un **NTPA** (5 mg, 7.0 μmol, 5 mol%). Kolbu degazē ar argonu pie Šlenka līnijas, atdzesē līdz -78°C, pievieno *N*-(4-(*terc*-butildimetilsilil)heks-5-īn-1-il)-4-nitrobenzsulfonamīda **65b** (50 mg, 0.13 mmol, 1.0 ekv.) šķīdumu abs. toluolā (1 mL). Iegūto reakcijas masu maisa 6h -78°C, un tad ļauj uzsilt līdz +5°C 17h laikā. Reakcijas maisījumu neitralizē ar pies. $NaHCO_3$ ūdens šķīdumu (5 mL). Ūdens slāni ekstrahē ar DCM (3 x 5mL). Organiskās fāzes apvieno un mazgā ar pies. NaCl ūdens šķīdumu (5 mL), zāvē virs bezūdens Na_2SO_4, filtrē un iekoncentrē pazeminātā spiedienā. Maisījumu attīra hromatogrāfiski uz silikagela (DCM/Hex 0%→60%). Produktu **70** iegūst kā baltu amorfu vielu (15 mg, η = 25%, ee 10%). Enantiomēro attiecību nosaka ar AEŠH uz hirālas stacionārās fāzes: (R,R) Whelk-O 1 4.6 x 250 mm; 5% *i*PrOH/heksāns, 0.8 mL/min, 254 nm (R10. lpp).

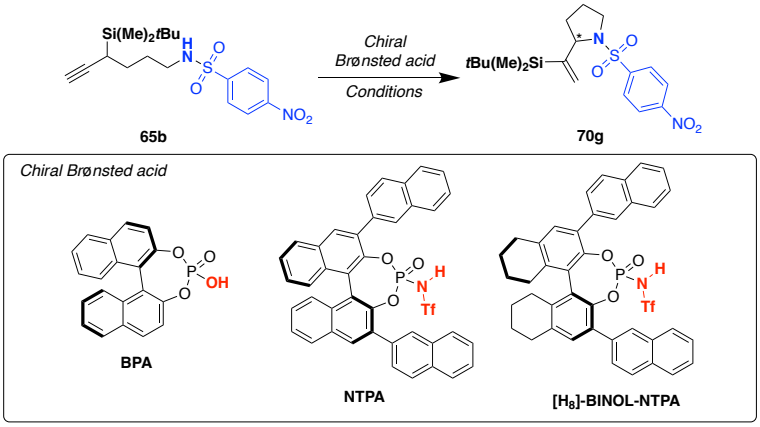
Development of enantioselective electrophile-induced heterocyclization of terminally functionalized propargyl silanes

The enantioselective heterocyclization of propargyl silanes was based on asymmetric counteranion-directed catalysis (*ACDC*). BINOL-derived phosphoric and *N*-trifluoromethane sulfonylphosphoimidates were chosen as a source of chirality. In the reaction with propargyl silanes **65** they would form an ion pair for chirality transfer, inducing enantiodiscrimination for heterocycle **70** (Scheme R1).



Scheme R1. Chiral Brønsted acid-catalyzed intramolecular cyclization of propargyl silane **65**.

The model reaction of the acid-catalyzed intramolecular cyclization of propargyl silane **65b** with commercially available acids **BPA**, **NTPA**, and **[H$_8$]-BINOL-NTPA** was chosen as a proof of concept (Scheme R2).



Scheme R2. Model reaction for the enantioselective cyclization of propargyl silanes **65b**.

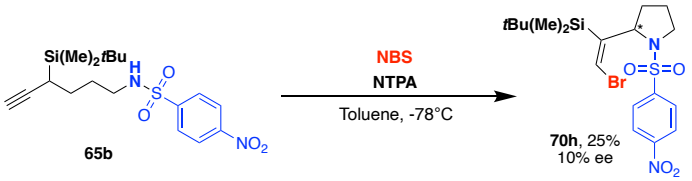
The experimental results are summarized in Table R1. The enantiomeric ratio was determined using HPLC equipped with a UV detector, (R,R)-Whelk-O 1 chiral column as the stationary phase, and a 5% *i*PrOH/hexane (v/v) mixture as the mobile phase (p. R7).

Table R1.

Conditions for chiral Brønsted acid-catalyzed cyclization of propargyl silane **65b**.

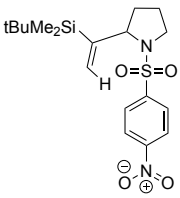
Nr.	Catalyst	Solvent	T, °C	t, h	Yield, %	ee, %
1	**BPA**	DCM	20	24	-	-
2		$CHCl_3$	63	72	13	0
3	**NTPA** 5 mol%	Toluene	60	19	56	6
4		Cyclohexane	60	18	62	11
5	**NTPA** 10 mol%	Cyclohexane	20	19	52	11
6	**[H_8]-BINOL-NTPA** 5 mol%	Cyclohexane	60	21	45	12

The proof of concept was also performed for *halo*-cyclization reactions, in which an achiral electrophilic halogen source can be activated by a chiral Brønsted acid. As a model reaction, **the NTPA**-catalyzed heterocyclization of propargyl silane **65b** with NBS was selected. (Scheme R3) (p. R10).



Scheme R3. Model reaction for the enantioselective *halo*-cyclization of propargyl silanes **65b**.

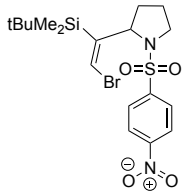
Experimental procedure



2-(1-(*tert*-Butyldimethylsilyl)vinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (**70g**):

Racemate was synthesized according to a previously described procedure in App. 4.

Procedure using a chiral Brønsted acid: An oven-dried round-bottom flask equipped with a magnetic stirrer was charged with argon. A chiral Brønsted acid (6.3-12.6 μmol, 5-10 mol%) was added under nitrogen flow. Flask was evacuated and charged with argon using Schlenk line. The solvent and *N*-(4-(*tert*-butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzenesulfonamide **65b** (0.126 mmol, 1.0 eq.) was added, and the mixture was stirred for 18 h as indicated in Table R1. The reaction was quenched with saturated $NaHCO_3$ aqueous solution (5 mL). The aqueous layer was extracted using DCM (2 x 5 mL). The organic layers were combined and washed with saturated NaCl aqueous solution (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography on silica gel (DCM/Hex 40%→60%). Product **70g** was obtained as a white amorphous solid. The enantiomeric ratio was determined by chiral HPCL: Whelk-O 1 4.6 x 250 mm; 5% *i*PrOH/hexane, 0.8 mL/min, 254 nm (p. R7).

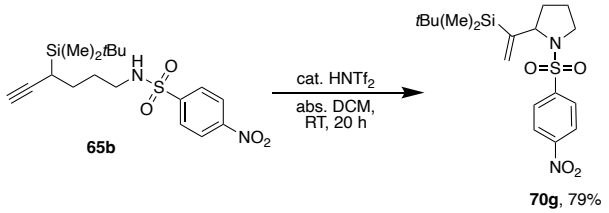


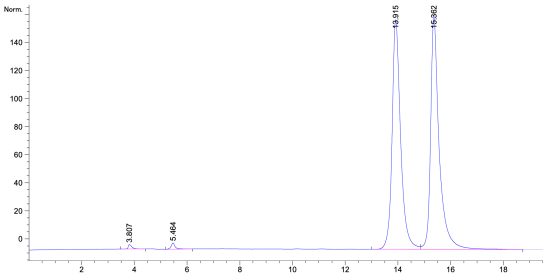
(*E*)-2-(2-Bromo-1-(*tert*-butyldimethylsilyl)vinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (**70h**):

The racemate was synthesized according to the procedure described in Appendix 4.

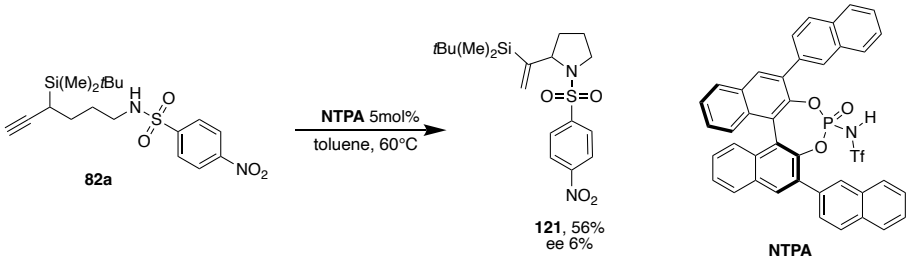
Procedure using a chiral Brønsted acid: An oven-dried round-bottom flask equipped with a magnetic stirrer was charged with argon. *N-bromosuccinimide* (23 mg, 0.13 mmol, 1.0 eq.) and **NTPA** (5 mg, 7.0 μmol, 5 mol%) were added under a flow of nitrogen. Flask was evacuated and charged with argon using Schlenk line, cooled to -78°C, of solution of *N*-(4-(*terc*-butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzene sulfonamide **65b** (50 mg, 0.13 mmol, 1.0 eq.) abs. toluene (1 mL) was added. The resulting reaction was stirred at -78°C for 6h and then was allowed to reach +5°C in 17h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (5 mL). The aqueous layer was extracted using DCM (3 x 5 mL). The organic layers were combined and washed with saturated NaCl aqueous solution (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography on silica gel (DCM/Hex 0%→60%). Product **70h** was obtained as a white amorphous solid (15 mg, η = 25%, ee 10%). The enantiomeric ratio was determined by chiral HPCL: (R,R) Whelk-O 1 4.6 x 250 mm; 5% *i*PrOH/hexane, 0.8 mL/min, 254 nm (p. R10).

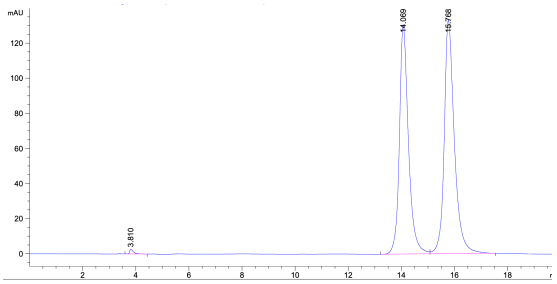
AEŠH analīzes uz hirālas stacionārās fāzes / Chiral HPLC analysis



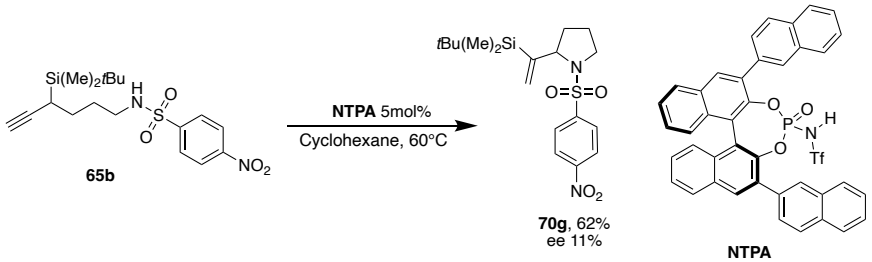


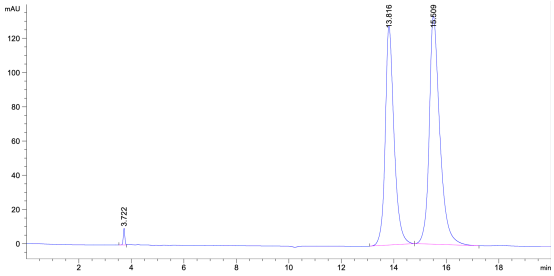
RT (min)	Area (mAU*s)	Area (%)
13.915	3320.04395	49.9494
15.362	3391.15015	49.9977



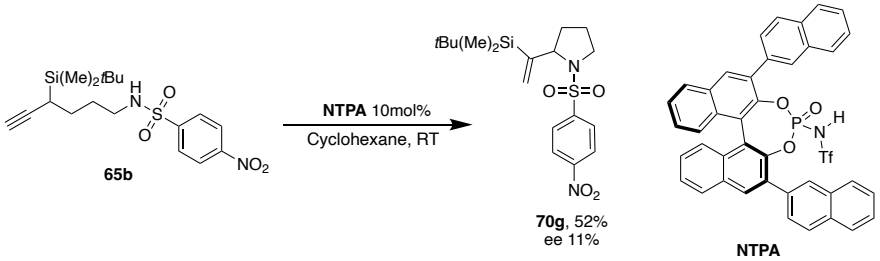


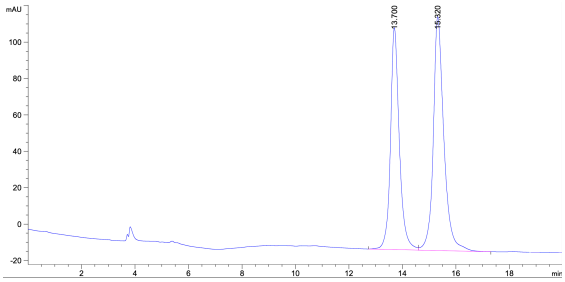
RT (min)	Area (mAU*s)	Area (%)
14.069	3102.62329	46.6543
15.768	3521.86597	52.9585



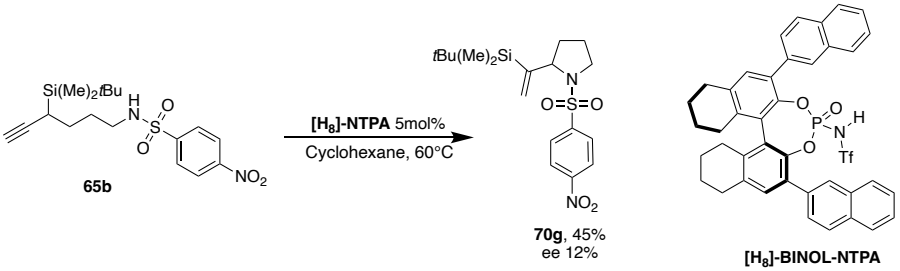


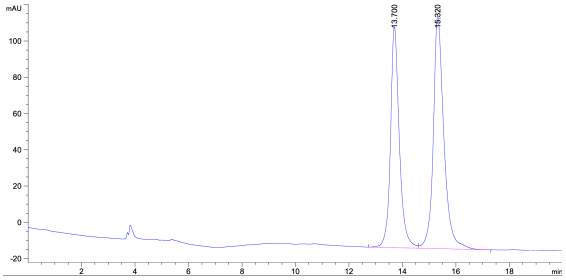
RT (min)	Area (mAU*s)	Area (%)
13.816	2988.41553	44.1951
15.509	3733.89331	52.2198



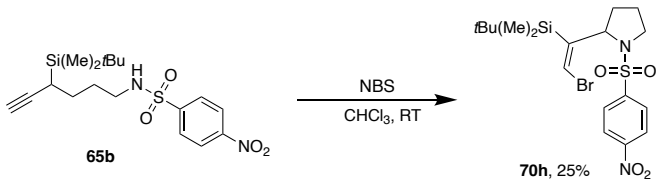


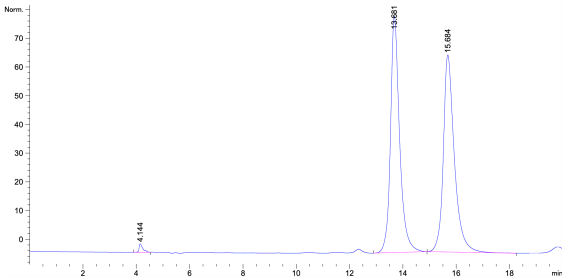
RT (min)	Area (mAU*s)	Area (%)
13.700	2804.99634	44.2895
15.320	3528.32983	55.7105



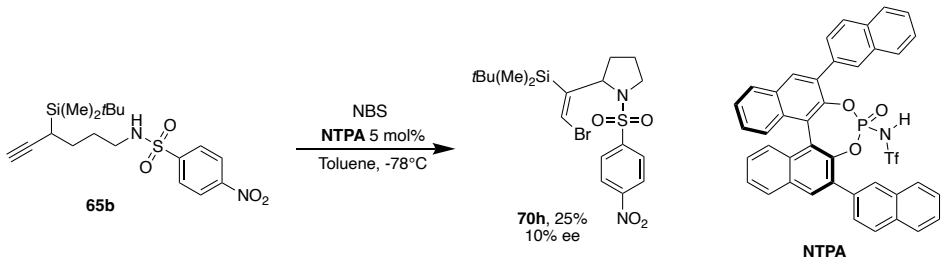


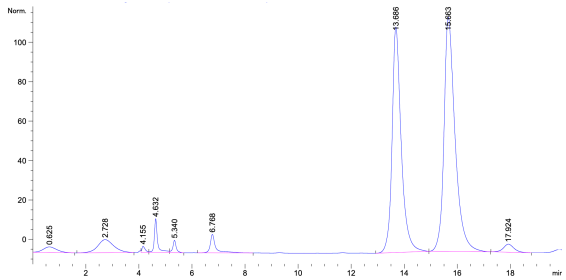
RT (min)	Area (mAU*s)	Area (%)
13.818	3881.08154	44.0720
15.438	4925.15088	55.9280





RT (min)	Area (mAU*s)	Area (%)
13.681	1767.35962	49.4570
15.684	1780.61707	49.8280





RT (min)	Area (mAU*s)	Area (%)
13.686	2467.43872	38.8549
15.663	3105.84692	48.9080

6. pielikums
Appendix 6

Propargilsilānu arilēšanas reakcijas ar hipervalentā joda reaģentiem vara katalizētos apstākļos

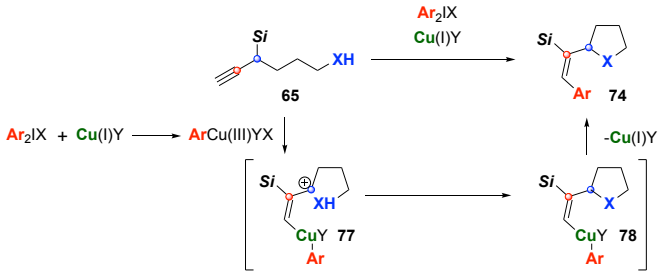
Copper-catalyzed propargyl silane arylation with hypervalent iodine reagents

Rūdolfs Beļaunieks, Māris Turks

Nepublicētie rezultāti / Unpublished results

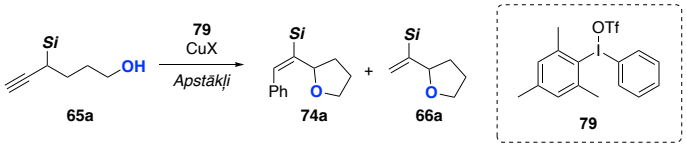
Propargilsilānu arilēšanas reakcijas ar hipervalentā joda reaģentiem vara katalizētos apstākļos

Propargilsilānu C-C arilēšanas reakcijām tika izvēlētas vara katalizētas reakcijas ar ariljodāniem (S1. shēma). Reakcijas maisījumā vara sāls ar ariljodānu ģenerē arilvara(III) savienojumus, kas ir spēcīgi elektrofīlie reaģenti. Tie, reaģējot ar propargilsilānu **65**, ierosina sililgrupas 1,2-migrāciju, atklājot alilkatjonu **77** reakcijai ar iekšmolekulāro nukleofīlo grupu, kas pēc iekšmolekulārās heterociklizācijas ģenerē starpsavienojumu **78**. Sekojoša reducējošās eliminēšanas reakcija noved pie produkta **74** veidošanās.



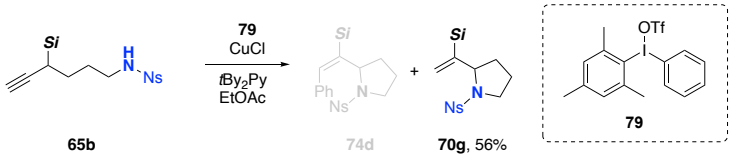
S1. shēma. Koncepts propargilsilānu C-C arilēšanas reakcijām ar ariljodāniem vara katalizētos apskākļos.

Koncepeta pierādīšanai kā modeļreakcija tika izvēlēta propargilsilānu **65a** reakcija ar jodānu **79** vara katalizētos apstākļos (S2. shēma). Optimizācijas rezultāti apkopoti S1. tabulā/Table S1 (S7. lpp).



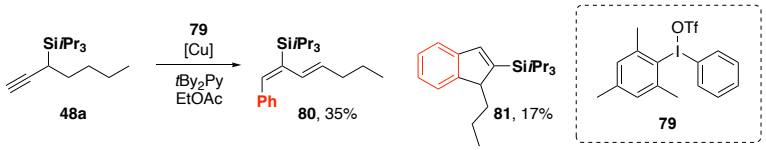
S2. shēma. Propargilsilāna **65a** C-C arilēšanas reakcija.

Optimizētajos apstākļos tika veikta arī propargilsilānu **65b** reakcija ar ariljodānu **79** (S3. shēma). Veiktajā reakcijā novēroja produkta **70g** veidošanos nevis vēlamo arilēšanas produktu **74d**.



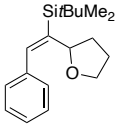
S3. shēma. Propargilsilāna **65b** C-C arilēšanas reakcijas mēģinājums.

Arilēšanas reakcijā tika pārbaudīts arī propargilsilāns **48a**, kas nesatur iekšmolekulāro nukleofīlo grupu. Veicot reakciju ar jodānu **79**, tika iegūts divu produktu maisījums, kas satur arildiēnu **80** un indēnu **81** attiecībā 2:1 (S4. shēma). Optimizācijas rezultāti apkopoti S2. tabulā/Table S2 (S8 lpp).

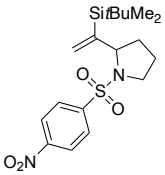


S4. shēma. Propargilsilāna **48a** C-C arilēšanas reakcija.

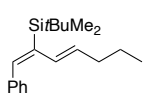
Eksperimentālās procedūras

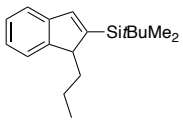


(*E*)-*terc*-Butildimetil(2-fenil-1-(tetrahidrofuran-2-il)vinil)silāns (**74a**): Apaļkolbu ar magnētisko maisītāju, kas izkarsēta žāvskapī, izpūš ar argonu. Kolbā iesver MesPhIOTf **79** (2.1 g, 4.41 mmol, 1.2 ekv.), CuCl (0.22 g, 0.21 mmol, 0.05 ekv.), 4-(*terc*-butildimetilsilil)heks-5-īn-1-olu (**65a**) (0.89 g, 4.20 mmol, 1.0 ekv.). Kolbas saturu degazē ar argonu pie Šlenka līnijas. Pievieno etilacetātu (50 mL) un 2,6-di-*terc*-butilpiridīnu (0.96 g, 5.03 mmol, 1.2 ekv.) un iegūto maisījumu silda 60°C 3h. Reakcijas maisījumu atdzesē un pievieno piesātinātu Na_2CO_3 ūdens šķidumu (30 mL) un DCM (30 mL). Ūdens slāni ekstrahē ar DCM (2x15 mL). Organiskās fāzes apvieno un mazgā ar piesātinātu Na_2CO_3 ūdens šķīdumu (2x30 mL), piesātinātu NaCl ūdens šķīdumu (30 mL), žāvē virs Na_2SO_4, filtrē un ietvaicē pazeminātā spiedienā. Maisījumu attīra hromatogrāfiski uz silikagela (DCM/Hex 10%→20%). Produktu **74a** iegūst kā baltu amorfu vielu (920 mg, η = 76%). ^{1}H KMR (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). Savienojuma dati sakrīt ar literatūrā norādītajiem.



2-(1-(*terc*-Butildimetilsilil)vinil)-1-((4-nitrofenil)sulfonil)pirolidīns (**70g**): Apaļkolbu ar magnētisko maisītāju, kas izkarsēta žāvskapī, izpūš ar argonu. Kolbā iesver MesPhIOTf **79** (90 mg, 0.15 mmol, 1.2 ekv.), CuCl (1 mg, 6.3 μmol, 0.05 ekv.), *N*-(4-(*terc*-butildimetilsilil)heks-5-īn-1-il)-4-nitrobenzsulfonamīda **65b** (50 mg, 0.13 mmol, 1.0 ekv.). Kolbas saturu degazē ar argonu pie Šlenka līnijas. Pievieno etilacetātu (5 mL) un 2,6-di-*terc*-butilpiridīnu (29 mg, 1.5 mmol, 1.2 ekv.) un iegūto maisījumu silda 60°C 3h. Reakcijas maisījumu atdzesē un pievieno piesātinātu Na_2CO_3 ūdens šķīdumu (10 mL) un DCM (5 mL). Ūdens slāni ekstrahē ar DCM (2x5 mL). Organiskās fāzes apvieno un mazgā ar piesātinātu Na_2CO_3 ūdens šķidumu (2x10 mL), piesātinātu NaCl ūdens šķīdumu (10 mL), žāvē virs Na_2SO_4, filtrē un ietvaicē pazeminātā spiedienā. Maisījumu attīra hromatogrāfiski uz silikagela (DCM/Hex 40%→50%). Produktu **70g** iegūst kā baltu amorfu vielu (51 mg, η = 56%). ^{1}H KMR (500 MHz, $CDCl_3$): δ 8.40 (d, 2H, *J* = 8.9), 8.12 (d, 2H, *J* = 8.9), 6.65 (d, 1H, *J* = 0.8), 4.26 (dd, 1H, *J* = 9.5, 7.4), 3.57 (dt, 2H, *J* = 11.3, 6.7), 3.50 (ddd, 1H, *J* = 11.3, 8.0, 2.3), 2.02 (ddtd, 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), 1.62 (dddd, 1H, *J* = 12.7, 11.3, 9.3, 6.6), 1.36 – 1.26 (m, 1H), 0.94 (s, 9H), 0.31 (s, 3H), 0.28 (s, 3H). Savienojuma dati sakrīt ar literatūrā norādītajiem.



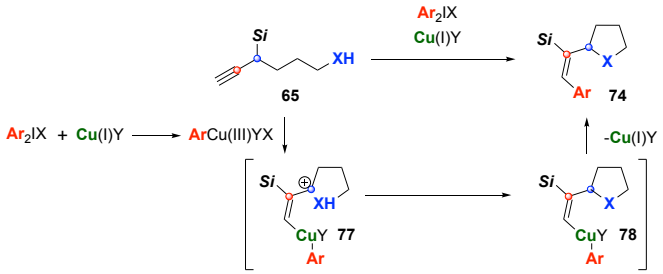


terc-Butildimetil-((1*E*,3*E*)-1-fenilhepta-1,3-diēn-2-il)silāna (**80**) un *terc*-Butildimetil-(1-propil-1*H*-inden-2-il)silāna (**81**) maisījums.

Apaļkolbu ar magnētisko maisītāju, kas izkarsēta žāvskapī, izpūš ar argonu. Kolbā iesver MesPhIOTf **79** (690 mg, 1.41 mmol, 3.0 ekv.), CuCl (2 mg, 12.6 μmol, 0.05 ekv.), hept-1-īn-3-il-*terc*-Butildimetilsilānu **48b** (100 mg, 0.47 mmol, 1.0 ekv.). Kolbas saturu degazē ar argonu pie Šlenka līnijas. Pievieno etilacetātu (5 mL) un 2,6-di-*terc*-butilpiridīnu (108 mg, 0.56 mmol, 1.2 ekv.) un iegūto maisījumu silda 60°C 3h. Reakcijas maisījumu atdzesē un pievieno piesātinātu Na_2CO_3 ūdens šķidumu (15 mL) un DCM (5 mL). Ūdens slāni ekstrahē ar DCM (2x5 mL). Organiskās fāzes apvieno un mazgā ar piesātinātu Na_2CO_3 ūdens šķīdumu (2x15 mL), piesātinātu NaCl ūdens šķīdumu (15 mL), žāvē virs Na_2SO_4, filtrē un ietvaicē pazeminātā spiedienā. Maisījumu attīra hromatogrāfiski uz silikagela (Hex) Produktu 80 (35%) un **81** (17%) maisījumu attiecībā 2:1 iegūst kā iedzeltenu eļļu (76 mg) Savienojuma **80** ^{1}K NMR (500 MHz, $CDCl_3$): 7.46 – 7.14 (m, 5H), 6.68 (s, 1H), 6.42 (d, 1H, J = 16.0), 5.68 (dt, 1H, J = 16.0, 6.3), 2.14 – 2.10 (m, 2H), 1.46 – 1.36 (m, 2H), 0.94 (s, 9H), 0.91 (t, 3H, J = 7.4), 0.21 (s, 6H). Savienojuma **80** ^{1}H KMR (500 MHz, $CDCl_3$): δ 7.42 (d, 1H, J = 7.2), 7.35 (d, 1H, J = 7.2), 7.25–7.14 (m, 2H), 7.10 (s, 1H), 3.70 (br s, 1H), 2.24–1.96 (m, 1H), 1.92 – 1.66 (m, 1H), 1.32–1.10 (m, 2H), 0.94 (br s, 10H), 0.88 – 0.72 (m, 4H), 0.24 (s, 3H), 0.19 (s, 3H). Savienojuma dati sakrīt ar literatūrā norādītajiem.

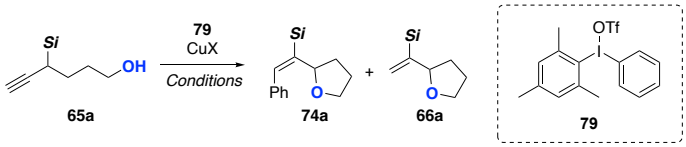
Copper-catalyzed propargyl silane arylation with hypervalent iodine reagents

Copper catalysis was chosen for the propargyl silane C-C arylation reaction with aryl iodane reagent. In the reaction mixture, the copper salt and aryl iodane generate aryl copper (III) species, which are strong electrophilic reagents. The latter reaction with propargyl silane **65** induces 1,2-silyl migration, generating allylic cation **77**, which heterocyclizes into intermediate **7**.. Product **74** was then obtained by reductive elimination (Scheme S1).



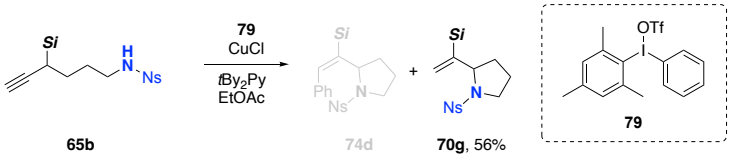
Scheme S1. Proposed reaction concept of copper-catalyzed propargyl silane C-C arylation with aryl iodane reagents

The reaction of propargyl silane **65a** with iodane (**79**) using a copper catalyst was chosen as a model reaction for the proof of concept (Scheme S2). The optimized reaction conditions were compiled in a Table S1 (p. S7).



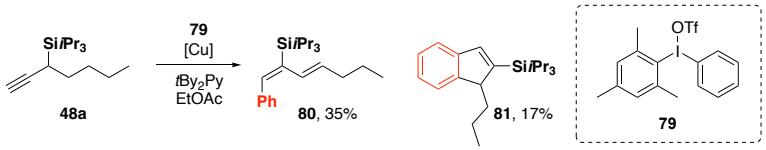
Scheme S2. C-C arylation of propargyl silane **65a**.

Propargyl silane **65b** was used in the reaction with aryl iodane **79** under optimized conditions (Scheme S3). The reaction yielded product **70g** instead of the desired arylation product, **74h**.



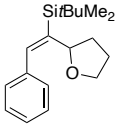
Scheme S3. C-C arylation attempt of propargyl silane **65b**.

For the arylation reaction, propargyl silane **48b**, which has no internal nucleophile, was subjected to optimized arylation conditions. In the reaction with iodane **79**, a mixture of arylidene **80** and indene **81** was obtained in 2:1 ratio (Scheme 4). Optimization of the reaction conditions are compiled in Table S2 (p. S8).

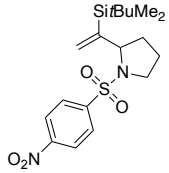


Scheme 4. C-C arylation reaction of propargyl silane **48b**

Experimental procedures

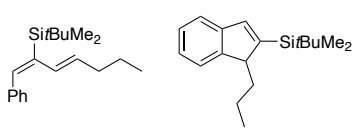


(*E*)-*tert*-Butyldimethyl(2-phenyl-1-(tetrahydrofuran-2-yl)vinyl)silane (**74a**):
An oven-dried round-bottom flask equipped with a magnetic stirrer was charged with Ar. MesPhIOTf **79** (2.1 g, 4.41 mmol, 1.2 eq.), CuCl (0.22 g, 0.21 mmol, 0.05 eq.), 4-(*tert*-butyldimethylsilyl)hex-5-yn-1-ol (**65a**) (0.89 g, 4.20 mmol, 1.0 ekv.) was added. The flask was then evacuated and charged with argon using a Schlenk line. Ethyl acetate (50 mL) and 2,6-di-*tert*-butylpyridine (0.96 g, 5.03 mmol, 1.2 eq.) were added, and the reaction mixture was heated at 60°C for 3h. The reaction mixture was cooled to room temperature and saturated Na_2CO_3 aqueous solution (30 mL) and DCM (30 mL) were added. The aqueous layer was extracted with DCM (2 × 15 mL). The organic layers were combined and washed with saturated Na_2CO_3 aqueous solution (2 × 30 mL) and saturated NaCl aqueous solution (30 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography on silica gel (DCM/Hex 10%→20%). Product **74a** was obtained as a white amorphous solid (920 mg, η = 76%). ^{1}H 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). Spectral data matches those in the literature



2-(1-(*tert*-Butyldimethylsilyl)vinyl)-1-((4-nitrophenyl)sulfonyl)pyrrolidine (**70g**):
An oven-dried round-bottom flask equipped with a magnetic stirrer was charged with Ar. MesPhIOTf **79** (90 mg, 0.15 mmol, 1.2 q.), CuCl (1 mg, 6.3 µmol, 0.05 q.), *N*-(4-(*tert*-butyldimethylsilyl)hex-5-yn-1-yl)-4-nitrobenzene sulfonamide **65b** (50 mg, 0.13 mmol, 1.0 eq.) was added. The flask was then evacuated and charged with argon using a Schlenk line. Ethyl acetate (5 mL) and 2,6-di-*tert*-butylpyridine (29 mg, 1.5 mmol, 1.2 eq.) were added, and the reaction mixture was heated at 60°C for 3h. The reaction mixture was cooled to room temperature and saturated Na_2CO_3 aqueous solution (10 mL) and DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The organic layers were combined and washed with saturated Na_2CO_3 aqueous solution (2 × 10 mL) and saturated NaCl aqueous solution (10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography on silica gel (DCM/Hex 40%→50%). Product **70g** was obtained as a white amorphous solid (51 mg, η = 56%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (d, 2H, *J* = 8.9), 8.12 (d, 2H, *J* = 8.9), 6.65 (d, 1H, *J* = 0.8), 4.26 (dd, 1H, *J* = 9.5, 7.4), 3.57 (dt, 2H, *J* = 11.3, 6.7), 3.50 (ddd, 1H, *J* = 11.3, 8.0, 2.3), 2.02 (ddtd, 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), 1.62 (dddd, 1H,

J = 12.7, 11.3, 9.3, 6.6), 1.36 – 1.26 (m, 1H), 0.94 (s, 9H), 0.31 (s, 3H), 0.28 (s, 3H). Spectral data matches those in the literature



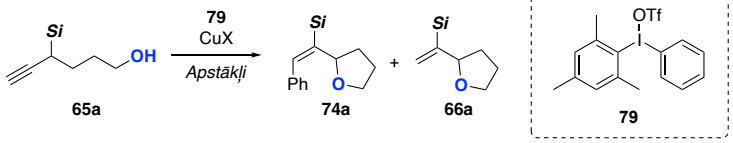
A mixture of *tert*-butyldimethyl-((1*E*,3*E*)-1-phenylhepta-1,3-dien-2-yl)silane (**80**) and *tert*-butyldimethyl-(1-propyl-1*H*-inden-2-yl)silane (**81**).

An oven-dried round-bottom flask equipped with a magnetic stirrer was charged with Ar. MesPhIOTf **79** (690 mg, 1.41 mmol, 3.0 eq.), CuCl (2 mg, 12.6 μmol, 0.05 eq.), hept-1-yn-3-yl-*tert*-butyldimethylsilane **43b** (100 mg, 0.47 mmol, 1.0 ekv.) was added. The flask was then evacuated and charged with argon using a Schlenk line. Ethyl acetate (5 mL) and 2,6-di-*tert*-butylpyridine (108 mg, 0.56 mmol, 1.2 ekv.) were added, and the reaction mixture was heated at 60°C for 3h. The reaction mixture was cooled to room temperature and saturated Na_2CO_3 aqueous solution (15 mL) and DCM (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL). The organic layers were combined and washed with saturated Na_2CO_3 aqueous solution (2 × 15 mL) and saturated NaCl aqueous solution (15 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography on silica gel (Hex) Mixture of products **80** un **81** in the ratio of 2:1 was obtained as a yellowish oil (76 mg, η = 52%). Compound **80** ^{1}H NMR (500 MHz, $CDCl_3$): 7.46 – 7.14 (m, 5H), 6.68 (s, 1H), 6.42 (d, 1H, *J* = 16.0), 5.68 (dt, 1H, *J* = 16.0, 6.3), 2.14 – 2.10 (m, 2H), 1.46 – 1.36 (m, 2H), 0.94 (s, 9H), 0.91 (t, 3H, *J* = 7.4), 0.21 (s, 6H). Compound **80** ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, 1H, *J* = 7.2), 7.35 (d, 1H, *J* = 7.2), 7.25–7.14 (m, 2H), 7.10 (s, 1H), 3.70 (br s, 1H), 2.24–1.96 (m, 1H), 1.92 – 1.66 (m, 1H), 1.32–1.10 (m, 2H), 0.94 (br s, 10H), 0.88 – 0.72 (m, 4H), 0.24 (s, 3H), 0.19 (s, 3H). Spectral data matches those in the literature.

S1. tabula
Table S1.

Vara katalizētas propargilsilāna **65a** arilēšanas izpēte ar ariljodānu **79**

Copper-catalyzed arylation of propargyl silane **65a** with aryl iodane **79**



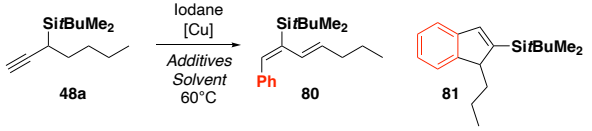
65a **74a** **66a** **79**

Nr.	CuX	Solvent	T, °C	Additive	**74a**, % (NMR)	**66a**, % (NMR)
1	CuCl	EtOAc	20	-	0	69
2		EtOAc	20	*t*Bu$_2$Py	0	0
3		EtOAc	60		82 (76 isolated)	0
4		THF	60		56	0
5		$CHCl_3$	60		59	0
6		PhMe	60		17	0
7		MEK	60		0	0
8		MeCN	60		0	0
9		EtOAc	60	Lutidine	0	0
10		EtOAc	60	Et_3N	0	0
11	CuI	EtOAc	60	*t*Bu$_2$Py	0	0
12	CuOTf·PhH	EtOAc	60		84	0

S2. tabula
Table S2.

Vara katalizētas propargilsilāna **48a** arilēšanas izpēte ar ariljodāniem

Copper-catalyzed arylation of propargyl silane **65a** with aryl iodane**s**



	Solvent	T, °C	Iodane (3 eq)	[Cu]	Base	Additive	SM **48a**, %	Diene **80**, %	Indene **81**, %
1	EtOAc	60	MesPhIOTf	CuCl (0.2 ekv)	2,6-*t*Bu$_2$Py	-	0	**60**	**40**
2	DCE			CuCl (0.2 ekv)		-	90	**0**	**5**
3	$MeNO_2$					-	69	**0**	**0**
4	Tol					-	78	**17**	**5**
5	DMF					-	54	**0**	**0**
6	MeCN					-	91	**0**	**0**
7	Dioxane					-	76	**10**	**4**
8	MEK					-	100	**0**	**0**
9	PhCl					-	0	**15**	**10**
10	Py					-	0	**20**	**13**
11	EtOAc					Cs_2CO_3	94	**0**	**0**
12						NaOAc	44	**56**	**35**
13						PPh_3	91	**0**	**2**
14					1,6-Lutidine	-	95	**0**	**0**

S2. Tabulas turpinājums
Table S2, continued

	Solvent	T, °C	Iodane (3 eq)	[Cu]	Base	Additive	SM **48a**, %	Diene **80**, %	Indene **81**, %
15	EtOAc	60	MesPhIOTf		TMEDA	-	69	**3**	**0**
16					Et_3N	-	61	**2**	**0**
17					Proton sponge	-	61	**2**	**0**
18					DBU	-	98	**0**	**0**
19		90			2,6-*t*Bu_2Py	PPh_3	0	**40**	**26**
20						XPhos	0	**43**	**22**
21		60		$Cu(OTf)_2$		-	63	**12**	**8**
22				CuOTf*PhH		-	42	**32**	**15**
23				CuI		-	82	**0**	**0**
24				CuCN		-	71	**0**	**0**
25				Cu thiophene-2-carboxylate		-	100	**0**	**0**
26				Cu, $Cu(OTf)_2$		-	0	**13**	**6**
27				$CuBF_4(MeCN)_4$		-	0	**60**	**35**
28			Ph_2IBF_4	CuCl (0.2 ekv)		-	98	**0**	**0**
29			MesPhIOTs			-	97	**0**	**0**

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