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Copper(I)-Catalyzed Regio- and Stereoselective Intramolecular Alkylboration of Propargyl Ethers and Amines

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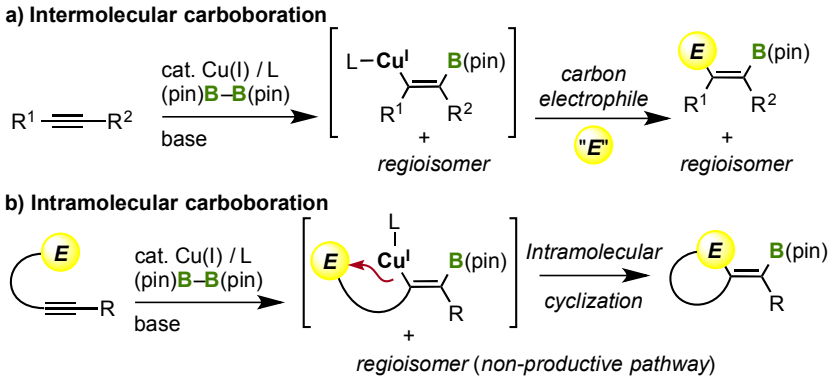
KEYWORDS: Alkenylboronates, Heterocyclic compounds, Carboboration, Copper(I) catalyst, Diboron

ABSTRACT: The copper(I)-catalyzed regio- and stereoselective intramolecular alkylation of propargyl ethers and amines bearing an alkyl electrophilic moiety has been developed. The reaction showed high functional group tolerance and gave highly functionalized alkenylboronates bearing heterocyclic rings, which are versatile synthetic intermediates in organic chemistry. The borylation products can be transformed into multi-substituted alkenes through stereospecific transformations. Mechanistic studies showed that the chemo- and stereoselectivity of copper(I)-catalyzed borylation depends on the type of leaving group. Density functional theory calculations suggested that the regioselectivity of borylcupration of the alkyne is controlled by the electronic effect of the oxygen atom of the propargyl ether in combination with the steric congestion between the boryl group and the substituent at the propargylic position.

Introduction

Multi-substituted alkenes are important structures in various functional and natural organic compounds.[1] Alkenylboronates are versatile intermediates for the synthesis of multi-substituted alkenes because they can be derivatized through stereospecific transformations.[2,3] Considerable research has therefore been devoted to the development of transition-metal-catalyzed stereoselective synthesis of alkenylboron compounds.[4] Copper(I)-catalyzed carboboration of alkynes with carbon electrophiles is a useful method for the synthesis of multi-substituted alkenylboronates.[5] In most cases, the carboboration regioselectivity depends on the nature of the alkyne substituent. Aryl and silyl groups, and propargyl ethers are strong directing groups for the regioselective carboboration of C≡C bonds to provide multi-substituted alkenylboronates.[6] However, controlling the regioselectivity of the carboboration is often difficult when asymmetric internal alkynes or aliphatic terminal alkynes are used as the substrates (Scheme 1a).[7]

Scheme 1. Copper(I)-Catalyzed Carboboration of Alkynes.

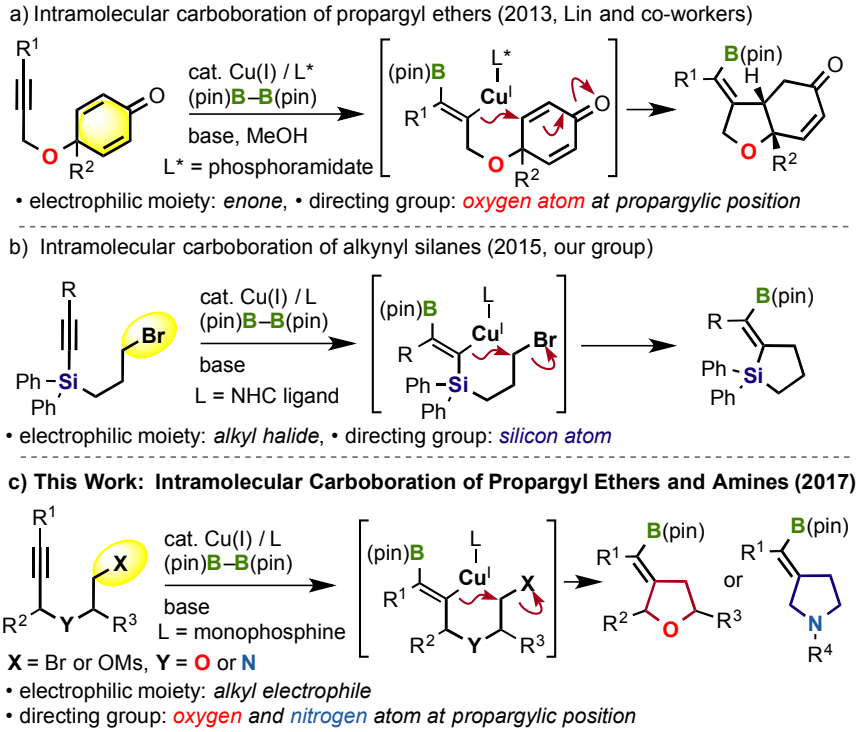


A few examples of copper(I)-catalyzed intramolecular carboborations of alkynes have been reported. These reactions offer concise methods for the synthesis of cyclic compounds with boryl-substituted *exo*-methylene structures. In the design of these reactions, it is necessary to achieve high regioselectivity in the borylcupration step and to install an appropriate functional

group that reacts selectively with the alkenylcopper(I) intermediate (Scheme 1b). In 2013, Lin and co-workers reported the intramolecular carboboration of propargyl ethers bearing an enone moiety to afford alkenylboronates bearing a hydrobenzofuran framework (Scheme 2a).[8] This reaction is useful for the construction of fused-ring structures, but it requires the introduction of a highly reactive enone moiety to trap the alkenylcopper(I) intermediate. They suggested that coordination of the oxygen atom in the propargyl ether to copper(I) contributes to the regioselectivity of the borylcupration step, but no detailed studies of the regioselectivity were conducted. Recently, our group reported a stereoselective copper(I)-catalyzed borylative cyclization of alkynylsilanes bearing an unactivated and simple alkyl bromide moiety to give alkenylboronates containing a silolane structure, based on silyl-group-directed regiocontrol (Scheme 2b).[9] Furthermore, during the course of our study, the transition-metal catalyzed borylative cyclization reactions of the enyne substrate have been reported.[10] Although this intramolecular carboboration strategy is a promising approach for synthesizing cyclic compounds with multi-substituted alkenylboron moieties, a few examples described above have been reported.

In this work, we developed a copper(I)-catalyzed stereo- and regioselective intramolecular carboboration of alkynes bearing an alkyl halide or alkyl mesylate moiety. This reaction was applicable to substrates with propargyl ethers or amines (Scheme 2c). The reaction using a monophosphine ligand afforded the corresponding multi-substituted alkenylboronates containing a tetrahydrofuran or pyrrolidine framework. Density functional theory (DFT) calculations suggested that both the electronic and steric effects of propargyl ethers contribute to the regioselectivity of borylcupration of the propargyl ether.[11]

Scheme 2. Copper(I)-Catalyzed Stereoselective Intramolecular Carboboration of Alkynes.

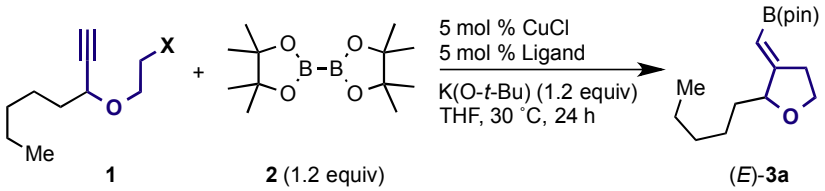


Results and discussion

First, we investigated the reaction conditions for the intramolecular alkylboration of propargyl ether **1a** (Table 1). The reaction with an *N*-heterocyclic carbene ligand (IMes·HCl) resulted in moderate conversion of the starting material to give the desired product (*E*)-**3a** as a single isomer (entry 1: 43%, *E*/*Z* = >95:5). The bisphosphine ligand Xantphos showed low reactivity, but dppp showed moderate reactivity and gave the corresponding cyclization product in good yield with excellent stereoselectivity (entry 2: 7% and entry 3: 57%, *E*/*Z* = >95:5). The reaction using the monophosphine ligand PCy_3 afforded the product in moderate yield (entry 4: 48%), whereas PPh_3 showed high reactivity and gave the product in good yield (entry 5: 75%). The use of triarylphosphine ligands bearing an electron-donating or -withdrawing substituent on the phenyl ring did not improve the yield (entry 6: 71% and entry 7: 75%). The yield of (*E*)-**3a** improved

slightly when (o-MeO-C_6H_4)$_3$P was used (entry 8: 77%). The reaction with (o-tol)$_3$P showed high reactivity and gave the corresponding borylative cyclization product in high yield with high stereoselectivity (entry 9: 88%, E/Z = >95:5). We then identified the optimum leaving group from the substrate. The reactivity of the substrate bearing iodide **1b** was higher reactivity than that of the substrate with bromide **1a**, but the yield was moderate (entry 10: 58%). In contrast, the borylative cyclization of **1c** gave the product in good yield (entry 11: 61%).

Table 1. Catalyst Optimization for Copper(I)-Catalyzed Intramolecular Alkylboration of 1.[a]



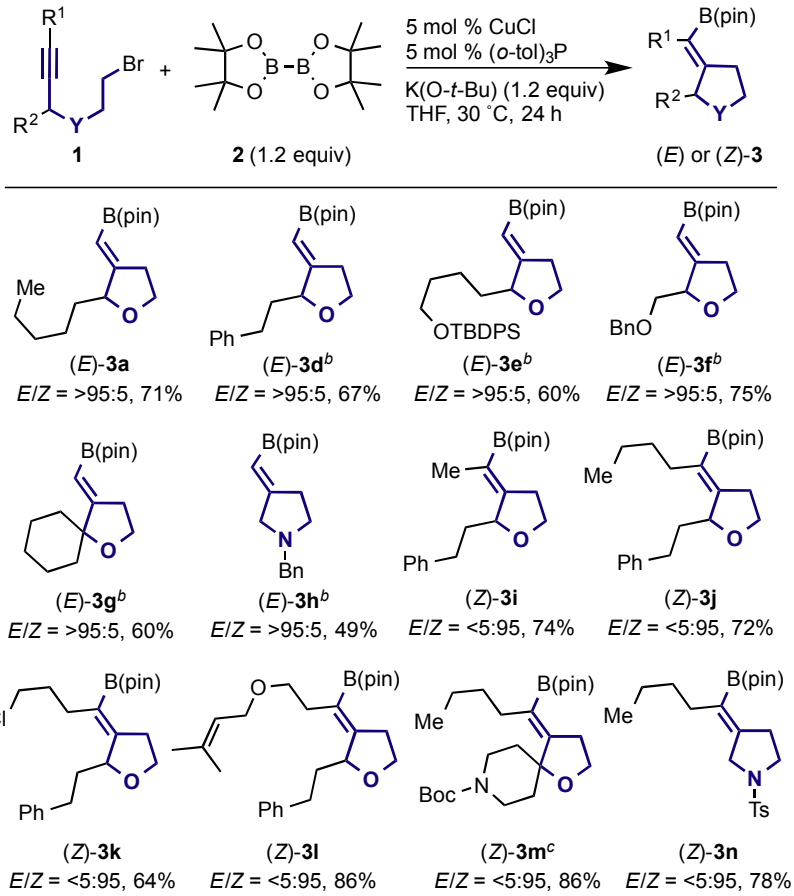
1 **2** (1.2 equiv) (*E*)-**3a**

Entry	Ligand	X	Yield of **3a** (%)[b]	*E*/*Z*[c]
1	IMes•HCl	Br (**1a**)	43	>95:5
2	Xantphos	Br (**1a**)	7	>95:5
3	dppp	Br (**1a**)	57	>95:5
4	PCy_3	Br (**1a**)	48	>95:5
5	PPh_3	Br (**1a**)	75	>95:5
6	(p-MeO-C_6H_4)$_3$P	Br (**1a**)	71	>95:5
7	(p-F-C_6H_4)$_3$P	Br (**1a**)	75	>95:5
8	(o-MeO-C_6H_4)$_3$P	Br (**1a**)	77	>95:5
9	(o-tol)$_3$P	Br (**1a**)	88 (71)	>95:5
10[d]	(o-tol)$_3$P	I (**1b**)	58	>95:5
11[e]	(o-tol)$_3$P	OMs (**1c**)	61	>95:5

[a]Conditions: **1** (0.5 mmol), CuCl (0.025 mmol), ligand (0.025 mmol), **2** (0.6 mmol), base (0.6 mmol) in THF (1.0 mL). [b]NMR yield was determined by ^{1}H NMR analysis of crude material using an internal standard. Isolated yield is shown in parentheses. [c]Determined by ^{1}H NMR analysis of crude material. [d]Reaction time was 3 h. [e]OMs: mesylate (OSO_2Me).

With the optimized conditions in hand, we conducted substrate screening (Table 2). The reactions of alkyl- substituted terminal propargyl ethers gave the corresponding cyclization products (*E*)-**3a** and (*E*)-**3d** in good yields [(*E*)-**3a**: 71%, (*E*)-**3d**: 67%]. Products bearing silyl ether (*E*)-**3e** or benzyl ether (*E*)-**3f** were obtained in good yields [(*E*)-**3e**: 60%, (*E*)-**3f**: 75%]. The substrate prepared from tertiary propargyl alcohol reacted under the borylative cyclization reaction conditions to afford a product containing a spiro-cyclic moiety, (*E*)-**3g**, in moderate yield (60%). The reaction of a benzyl-protected propargylamine substrate gave a product containing a pyrrolidine moiety, (*E*)-**3h**, in moderate yield (49%). We then tested internal propargyl ether and amine substrates. The reactions of internal propargyl ethers bearing a methyl group or alkyl chain gave the corresponding products (*Z*)-**3i** and (*Z*)-**3j** in good yields with excellent stereoselectivities [(*Z*)-**3i**: 74%, (*Z*)-**3j**: 72%]. The catalytic system gave excellent chemoselectivity. The reaction of the internal propargyl ether containing an alkyl chloride moiety gave the corresponding cyclization product (*Z*)-**3k** in good yield (64%).[12] The propargyl ether bearing a prenyl ether moiety was smoothly converted to the desired product (*Z*)-**3l** in high yield (86%). A spiro-cyclic product consisting of piperidine and furan rings, (*Z*)-**3m**, was obtained in excellent yield with perfect stereoselectivity (86%). The alkyl-substituted internal propargylamine participated in this borylative cyclization to give the desired tetrasubstituted alkenylboronate bearing a pyrrolidine moiety (*Z*)-**3n** (78%).[13]

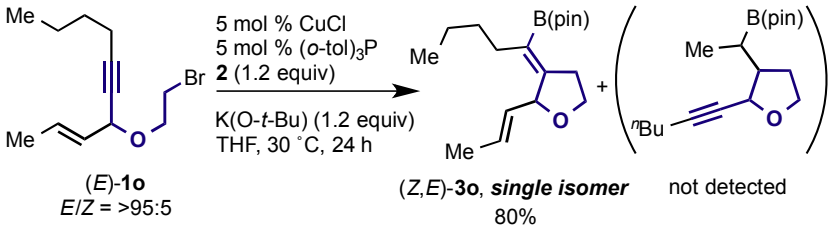
Table 2. Substrate Scope of Intramolecular Alkylboration of Propargyl Ethers and Amines.[a]



[a]Conditions: **1** (0.5 mmol), CuCl (0.025 mmol), ligand (0.025 mmol), **2** (0.6 mmol), base (0.6 mmol) in THF (1.0 mL) at 30 °C. [b]Reaction temperature was 50 °C. [c]PPh_3 was used as a ligand instead of $(o\text{-tol})_3P$.

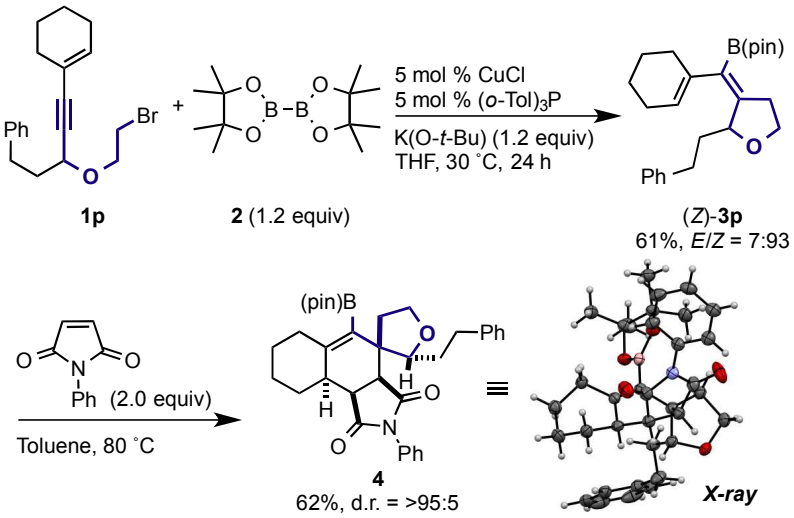
To investigate the chemoselectivity of this intramolecular alkylboration, we performed the reaction using a propargyl allyl ether substrate (*E*)-**1o** (Scheme 3). This catalytic system showed perfect chemoselectivity and gave the alkenylboronate (*Z*,*E*)-**3o** as a single isomer; this is formed in high yield and with perfect chemo- and stereo-selectivity by reaction with the alkyne moiety, rather than the alkene group. The alkylboronate, which is formed by reaction with the alkene moiety, was not detected.[14]

Scheme 3. Chemoselective Intramolecular Alkylboration of Propargyl Allyl Ether (*E*)-1o.



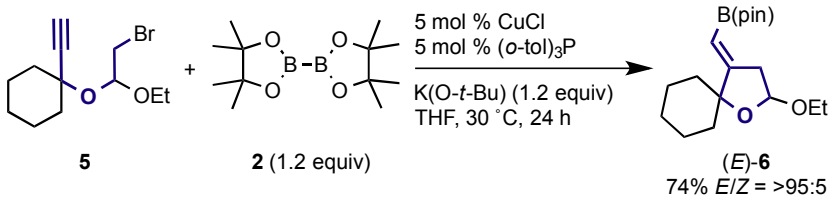
We then tested the substrate bearing an enyne moiety **1p** (Scheme 4). The reaction of **1p** gave successful conversion to the desired borylation product containing a diene structure, (*Z*)-**3p**, with good stereoselectivity. The Diels–Alder reaction of (*Z*)-**3p** with a dienophile proceeded with excellent diastereoselectivity to give the corresponding alkenylboronate **4** containing a highly fused ring system as a single isomer in good yield. The configuration of **4** was confirmed by single-crystal X-ray structural analysis and the nOe technique. The stereoselectivity of this reaction was completely controlled by the stereocenter at the allylic position of (*Z*)-**3p**.

Scheme 4. Regio- and Stereoselective Intramolecular Alkylboration of Enyne Substrate 1p and Stereoselective Diels–Alder Reaction of Borylation Product (*Z*)-3p.



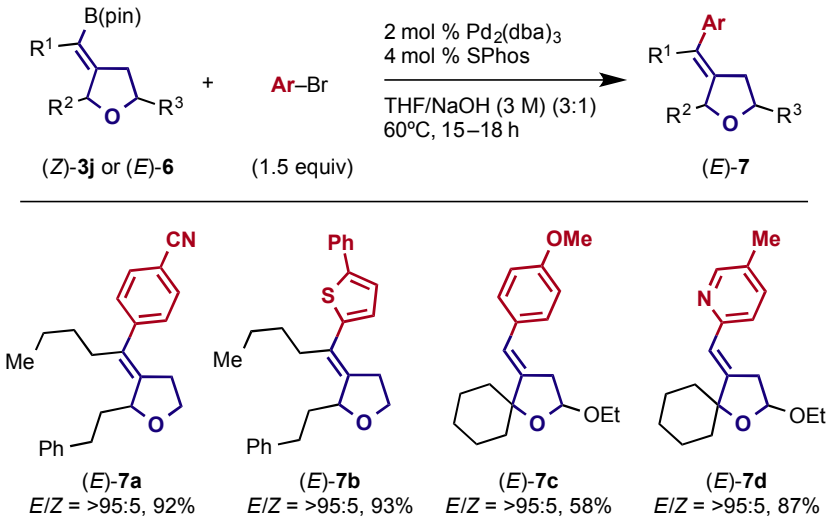
Next, we applied this intramolecular alkylboration to a Ueno–Stork-type haloacetal substrate, which is often used under radical cyclization conditions (Scheme 5).[15,16] Our borylative cyclization method was successfully used with haloacetal substrate **5**. The corresponding trisubstituted alkenylboronate containing an acetal moiety, (*E*)-**6**, was obtained in high yield with excellent stereoselectivity.

Scheme 5. Stereoselective Intramolecular Alkylboration of Alkyne Bearing a Haloacetal Moiety.



To demonstrate the utility of these alkenylboronates synthesized via our borylative cyclization reaction, we conducted Suzuki–Miyaura cross-couplings of alkenylboronates **3** and **6** (Table 3).[17] The reactions of the tetra-substituted alkenylboronate (*Z*)-**3j** with aryl or heteroaromatic bromides gave the corresponding tetra-substituted alkenes (*E*)-**7a** and (*E*)-**7b** stereospecifically and in excellent yields [(*E*)-**7a**: 92%, (*E*)-**7b**: 93%]. The alkenylboronate (*E*)-**6** containing an acetal moiety was used in the cross-coupling reaction. The corresponding trisubstituted alkenes bearing methoxybenzene and pyridine substituents, (*E*)-**7c** and (*E*)-**7d**, were obtained in high yields [(*E*)-**7c**: 58%, (*E*)-**7d**: 87%].

Table 3. Suzuki–Miyaura Cross-Coupling of Borylation Products.[a]

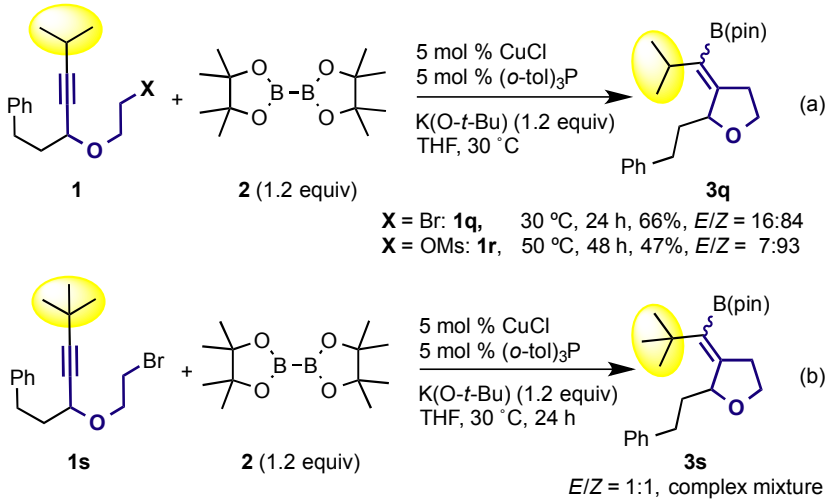


[a]Conditions: (*Z*)-**3j** or (*E*)-**6** (0.2 mmol), Pd_2dba_3 (0.004 mmol), SPhos (0.006 mmol), ArBr (0.3 mmol) in THF (1.8 mL), and NaOH aq (3 M) (0.6 mL) at 60 °C.

The reactions of bulky substrates showed different selectivities. The cyclizations of internal alkyne substrates bearing bulky substituents such as secondary or tertiary alkyl groups were conducted (Scheme 6). The bromide substrate **1q** gave the corresponding product **3q** in good yield, but the stereoselectivity was moderate (Scheme 6a, 66%, *E*/*Z* = 16:84). The reaction of the substrate containing a tertiary-butyl group, **1s**, afforded a mixture of stereoisomers of **3s** (Scheme 6b, *E*/*Z* = 1:1). The stereoselectivity improved when substrate **1r**, bearing a mesylate moiety as the leaving group, was used (Scheme 6a, 47%, *E*/*Z* = 7:93). This result shows that the stereoselectivity depends on the leaving group for an alkyne substrate with a bulky substituent, although the stereoselectivities of less bulky substrates do not depend on the leaving group (Table 1, entries 10 and 11). Recently, our group reported a copper(I)-catalyzed borylative radical cyclization of alkenes bearing alkyl halide moieties.[14] As discussed later, we postulate that this low stereoselectivity with a bulky substrate is attributable to the radical reactivity of the copper(I) salt/diboron catalytic system with an alkyl halide.[12,18] The alkenyl radical intermediate

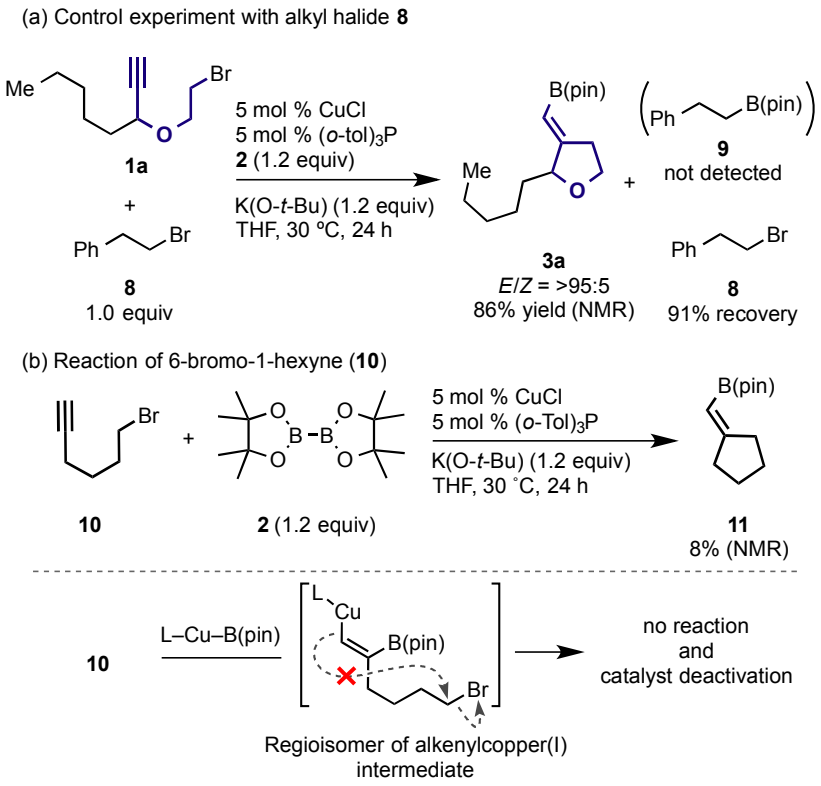
species isomerizes easily.[19] However, a sulfonate leaving group such as mesylate improves the stereoselectivity because mesylate is less reactive in the radical pathway under the conditions of a copper(I)-catalyzed borylation reaction.[12b]

Scheme 6. Intramolecular Alkylboration of Propargyl Ethers Bearing Bulky Substituents and Leaving Group Effect.



To investigate the reaction mechanism, we conducted a competitive experiment using a mixture of **1a** and alkyl halide **8** (Scheme 7a). The reaction gave only the borylative cyclization product (*E*)-**3a** in high yield, and alkyl halide **8** recovery was satisfactory (91%). This result suggests that our catalytic system first reacts selectively with the alkyne moiety of **1a** rather than the alkyl halide. This initial step in the reaction pathway first gives the alkenyl copper(I) intermediate and then intramolecular substitution of the bromide moiety occurs rapidly to produce the cyclization product **3a** (Scheme 2). We then conducted the borylation reaction of 6-bromo-1-hexyne (**10**) (Scheme 7b). The reaction showed low reactivity and the corresponding intramolecular alkylboration product **11** was obtained in low yield (8%). This indicates that the propargyl ether or amine moiety is important for this borylative cyclization and generation of the regioisomer of alkenylcopper(I) intermediate would lead to deactivation of the catalyst.

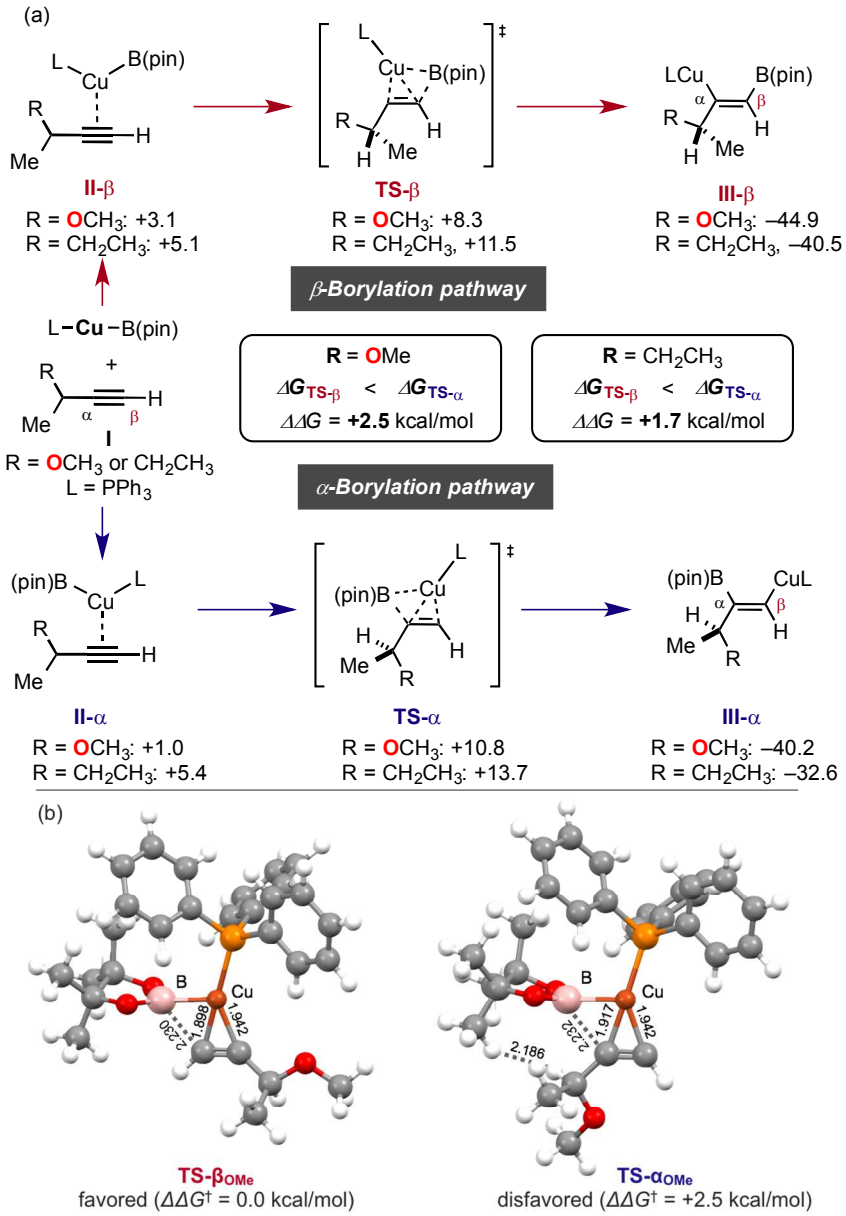
Scheme 7. Mechanistic Study.



Next, DFT calculations were performed, using the borylcupration of propargyl ether as a model compound, to investigate the regioselectivity of this borylation reaction. Partly conflicting discussions appear in the literature on the regioselectivity of the borylcupration of propargylic substrates. Carretero and co-workers previously reported DFT calculation results for the regioselective protoboration of a "*primary*" propargyl ether. They concluded that "*the electronic effect*" of the oxygen atom of propargyl ether predominantly controls the regioselectivity of the borylcupration step.[11a] In contrast, Lin and co-workers suggested that "*the coordination of the oxygen atom*" at the propargylic position to the copper(I) center controls the regioselectivity, based on their experimental results.[8] To clarify the main factors in the regioselectivity of our system, we performed DFT calculations on borylcupration using terminal "*secondary*" propargyl ethers and 3-methyl-1-pentyne lacking an oxygen atom at the propargylic position (Scheme

8a).[20] Both of the transition states (TS-β) in borylcupration that introduce the boryl group at the β-position of the alkyne were observed. The difference between the activation energies of borylcupration of the propargyl ether via TS-β and TS-α (+2.5 kcal/mol) was larger than that for 3-methyl-1-pentyne (+1.7 kcal/mol). These calculation results suggest that the electronic effect of the oxygen atom of the propargyl ether contributes to the high regioselectivity.[11a] In addition, the results for 3-methyl-1-pentyne, which lacks an oxygen atom, also suggest that the steric interaction between the B(pin) group and the substituent on the propargylic position would also enhance the regioselectivity (Scheme 8b).[21] The transition state in which the oxygen atom coordinates to the copper was not observed in our calculations. We suggest that a combination of electronic and steric effects decides the regioselectivity of the borylcupration step in our system.

Scheme 8. DFT Calculation for Borylcupration Step [ω B97XD/6-311G(d,p), SDD for Cu in THF (IEF-PCM)].[a]

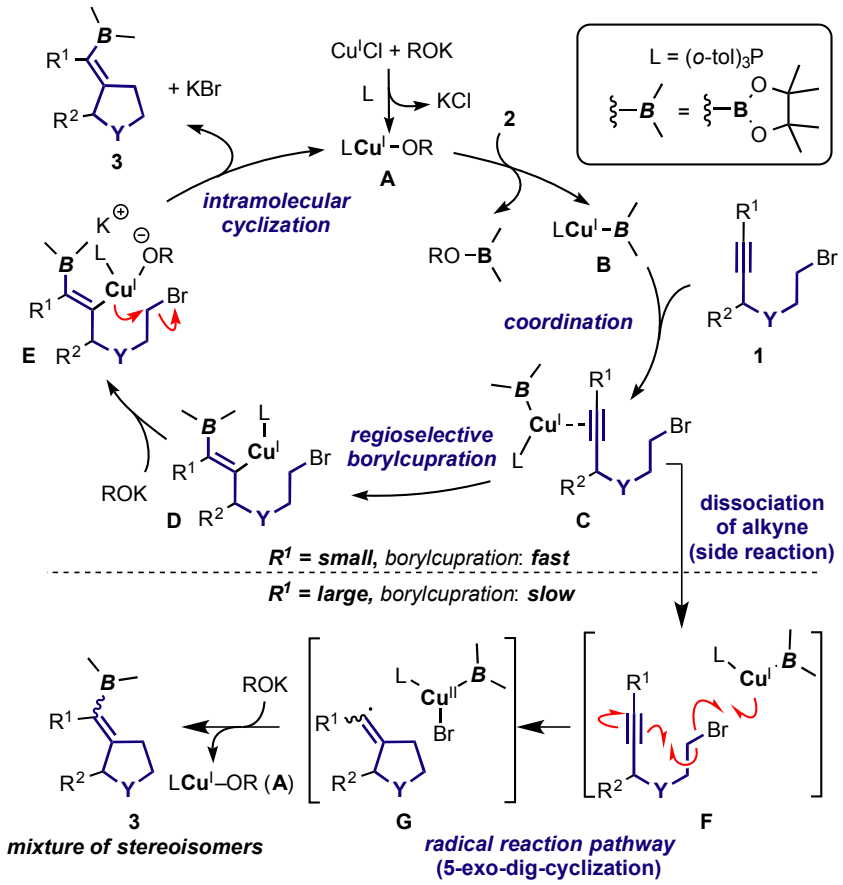


[a]Relative *G* value (kcal/mol) at 298 K in THF.

A plausible catalytic cycle for the intramolecular alkylboration of propargyl ethers and propargylamines, based on the above experimental and theoretical results, is shown in Scheme 9. The copper(I) alkoxide **A** is formed from copper(I) chloride and potassium alkoxide. The

reaction between **A** and diboron reagent **2** produces the borylcopper(I) intermediate **B**. The alkyne substrate **1** strongly coordinates to intermediate **B** to give the π-complex **C**. The alkenylcopper(I) intermediate **D** is formed through borylcupration of the alkene, with *syn* selectivity. The regioselectivity of this borylcupration is controlled by the electronic effect of the ether or amine moiety, and the steric congestion between the B(pin) moiety and the substituents at the propargylic position. This process is faster than the reaction with the C–Br moiety, based on the experiments shown in Scheme 7a. Strong coordination of the alkyne moiety leads to chemoselectivity over the alkene and alkyl halide moieties. Coordination of the alkoxide base to the copper(I) center **D** gives cuprate **E**. The intramolecular cyclization of **E** provides the intramolecular alkylboration product **3** and regenerates the copper(I) alkoxide **A**.[9,22] The bulkiness of the substrate results in slow borylcupration and dissociation of borylcopper moiety **B** from **C,** followed by a radical reaction between borylcopper moiety **B** and the free substrate **1**. The resulting alkenyl radical intermediate **G** gives the stereoisomer of **3**.[12] However, the sulfonate leaving group suppresses this radical reaction pathway, which improves the stereoselectivity for (*Z*)-**3q** (Scheme 6).

Scheme 9. Plausible Reaction Mechanism.



Conclusions

In summary, we developed a chemo-, regio-, and stereoselective copper(I)-catalyzed intramolecular alkylboration of propargyl ethers and amines to provide alkenylboronates containing heterocyclic moieties. Derivatization of the products gave highly functionalized multi-substituted alkenes. Mechanistic studies showed that the borylcopper(I) intermediate selectively reacts with an alkyne moiety of the substrate rather than an alkyl halide moiety. DFT calculations suggested that the electronic effect of the oxygen atom of the propargyl ether and steric congestion between the B(pin) group and the substituents on the propargylic position contributed to the controlling regioselectivity of the borylcupration step.

Experimental Section

General. Materials were obtained from commercial suppliers and purified by standard procedures unless otherwise noted. Solvents were also purchased from commercial suppliers, degassed via three freeze-pump-thaw cycles, and further dried over molecular sieves (MS 4A). NMR spectra were recorded on JEOL JNM-ECX400P and JNM-ECS400 spectrometers (^{1}H: 400 MHz and ^{13}C: 100 MHz). Tetramethylsilane (^{1}H) and $CDCl_3$ (^{13}C) were employed as the external standards, respectively. CuCl (ReagentPlus® grade, 224332-25G, ≥99%) and K(O-*t*-Bu)/THF (1.0 M, 328650-50ML) were purchased from Sigma-Aldrich Co. and used as received. GC analyses were conducted with a Shimadzu GC-2014 or GC-2025 equipped with a ULBON HR-1 glass capillary column (Shinwa Chemical Industries) and a FID detector. High-resolution mass spectra were recorded by Thermo Fisher Scientific Q Exactive Hybrid Quadrupole-Orbitrap Mass Spectrometer for ESI-Orbitrap analysis and JEOL JMS-T100GCV High Performance Gas Chromatograph – Time-of-Flight Mass Spectrometer for EI-TOF analysis at the Global Facility Center, Hokkaido University.

Preparation of Starting Materials.

Preparation of 3-(2-Bromoethoxy)oct-1-yne (1a) (Method A). In a vacuum dried 200 mL two-neck round-bottomed flask, 2-bromoethan-1-ol (7.50 g, 60.0 mmol) and pyridinium *p*-toluenesulfonate (PPTS, 1.51 g, 6.00 mmol) were dissolved in dry CH_2Cl_2 (60 mL), and the mixture was cooled to 0 ºC under a nitrogen atmosphere. 3,4-dihydro-2H-pyran (DHP, 7.57 g, 90.0 mmol) was added to the mixture, and the mixture was warmed to room temperature. After the mixture was stirred for 18 h, the reaction mixture was quenched by H_2O and extracted with CH_2Cl_2 three times. The combined organic layer was then dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The crude product was purified by flash column

chromatography to obtain the corresponding THP-protected product (11.4 g, 54.5 mmol, 90%) as a colorless oil.

In a vacuum dried 200 mL two-neck round-bottomed flask, oct-1-yn-3-ol (3.79 g, 30.0 mmol) was added dropwise to a suspension of NaH (60% in mineral oil, washed with hexane three times under a nitrogen atmosphere, 1.58 g, 39.0 mmol) in DMF (60 mL) at 0 ºC under a nitrogen atmosphere. Then, it was warmed to room temperature and stirred for 1 h. After the mixture was cooled to 0 ºC, THP-protected bromoethanol (9.41 g, 45.0 mmol) was added dropwise. Then, the mixture was warmed to room temperature and stirred for 6 h. The reaction mixture was quenched by H_2O and extracted with EtOAc/Hexane (1:4) three times. The combined organic layer was washed with brine and dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain the corresponding ether (6.40 g, 25.2 mmol, 84%) as a colorless oil.

In an open 100 mL round-bottomed flask, the ether (6.40 g, 25.2 mmol) and *p*-toluenesulfonic acid monohydrate (0.24 g, 1.30 mmol) were dissolved in dry MeOH (50 mL) at room temperature under air. After the mixture was stirred for 2 h, the reaction mixture was quenched by saturated $NaHCO_3$ aq. and extracted with Et_2O three times. The combined organic layer was then dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain the corresponding alcohol (2.00 g, 11.8 mmol, 47%) as a colorless oil.

In a vacuum dried 100 mL two-neck round-bottomed flask, 2-(oct-1-yn-3-yloxy)ethan-1-ol (2.00 g, 11.8 mmol) and carbon tetrabromide (4.30 g, 13.0 mmol) were dissolved in dry THF (24 mL), and the mixture was cooled to 0 ºC under a nitrogen atmosphere. Triphenylphosphine (3.41 g, 13.0 mmol) was added to the mixture, and the mixture was warmed to room temperature.

After the mixture was stirred for 4 h, the solvents were removed by evaporation. The crude product was purified by flash column chromatography and bulb-to-bulb distillation to obtain the corresponding bromide **1a** (1.34 g, 5.74 mmol, 49%) as a colorless oil. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.90 (t, *J* = 6.9 Hz, 3H), 1.26–1.38 (m, 4H), 1.43–1.50 (m, 2H), 1.66–1.81 (m, 2H), 2.45 (d, *J* = 2.0 Hz, 1H), 3.44–3.53 (m, 2H), 3.73 (dt, *J* = 6.4, 10.8 Hz, 1H), 4.04 (dt, *J* = 6.1, 10.6 Hz, 1H), 4.10 (td, *J* = 2.0, 6.7 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.9 (*C*H_3), 22.4 (*C*H_2), 24.7 (*C*H_2), 30.1 (*C*H_2), 31.3 (*C*H_2), 35.4 (*C*H_2), 68.5 (*C*H_2), 69.6 (*C*H), 73.9 (*C*), 82.4 (*C*H). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{10}H_{17}BrONa$, 255.0355; found, 255.0361.

Preparation of [3-(2-Bromoethoxy)pent-4-yn-1-yl]benzene (1d) (Method B). In a vacuum dried 200 mL two-neck round-bottomed flask, 3-phenylpropionaldehyde (2.68 g, 20.0 mmol) was dissolved in dry Et_2O (56 mL), and the mixture was cooled to 0 ºC under a nitrogen atmosphere. Ethynylmagnesium bromide solution in THF (0.5 M, 48.0 mL, 24.0 mmol) was added dropwise to the mixture, and the mixture was warmed to room temperature. After the mixture was stirred for 12 h, the reaction mixture was quenched by saturated NH_4Cl aq. and extracted with Et_2O three times. The combined organic layer was then dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain the corresponding propargyl alcohol (1.95 g, 12.2 mmol, 61%) as a colorless oil.

In a vacuum dried 50 mL two-neck round-bottomed flask, the propargyl alcohol (1.95 g, 12.2 mmol) was added dropwise to a suspension of NaH (60% in mineral oil, washed with hexane three times under a nitrogen atmosphere, 0.54 g, 13.4 mmol) in THF (7.4 mL) at 0 ºC under a nitrogen atmosphere. Then, the mixture was warmed to room temperature and stirred for 1 h.

After the mixture was cooled to 0 ºC, ethyl bromoacetate (2.45 g, 14.6 mmol) was added dropwise to the mixture. Then, the mixture was warmed to room temperature and stirred for 16 h. The reaction mixture was quenched by saturated NH_4Cl aq. and extracted with Et_2O three times. The combined organic layer was then dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The corresponding crude ether was used to the next reaction without further purification.

In a vacuum dried 300 mL two-neck round-bottomed flask, the solution of the crude product in THF (30 mL) was added dropwise to a suspension of $LiAlH_4$ (0.51 g, 13.4 mmol) in THF (60 mL) at –30 ºC under a nitrogen atmosphere. After the mixture was stirred for 16 h, the reaction mixture was quenched by MeOH (1.4 mL), then NaOH aq. (1 M, 0.5 mL) and H_2O (1.5 mL). After filtration, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain the corresponding reduction product (2.22 g, 10.9 mmol, 89%) as a colorless oil.

In a vacuum dried 100 mL two-neck round-bottomed flask, the reduction product (2.22 g, 10.9 mmol) and carbon tetrabromide (3.62 g, 10.9 mmol) were dissolved in dry THF (22 mL), and the mixture was cooled to 0 ºC under a nitrogen atmosphere. Triphenylphosphine (2.85 g, 10.9 mmol) was added to the mixture, and the mixture was warmed to room temperature. After the mixture was stirred for 10 h, the solvents were removed by evaporation. The crude product was purified by flash column chromatography and bulb-to-bulb distillation to obtain the corresponding bromide **1d** (2.33 g, 8.73 mmol, 80%) as a colorless oil. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.98–2.16 (m, 2H), 2.48 (d, J = 2.4 Hz, 1H), 2.81 (t, J = 7.6 Hz, 2H), 3.45–3.54 (m, 2H), 3.71 (dt, J = 6.5, 10.8 Hz, 1H), 4.02–4.08 (m, 2H), 7.18–7.22 (m, 3H), 7.27–7.31 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 30.2 (CH_2), 31.1 (CH_2), 36.9 (CH_2), 68.45 (CH_2), 68.51 (CH),

74.4 (*C*), 82.1 (*C*H), 125.9 (*C*H), 128.3 (*C*H), 128.4 (*C*H), 140.9 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{13}H_{15}BrONa$, 289.0199; found, 289.0199.

*{[5-(2-Bromoethoxy)hept-6-yn-1-yl]oxy}(tert-butyl)diphenylsilane (**1e**).* **1e** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.05 (s, 9H), 1.52–1.63 (m, 4H), 1.66–1.81 (m, 2H), 2.44 (d, *J* = 2.2 Hz, 1H), 3.43–3.52 (m, 2H), 3.65–3.74 (m, 3H), 4.00–4.10 (m, 2H), 7.36–7.45 (m, 6H), 7.65–7.68 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 19.1(*C*), 21.4 (*C*H_2), 26.8 (*C*H_3), 30.1 (*C*H_2), 32.0 (*C*H_2), 35.2 (*C*H_2), 63.5 (*C*H_2), 68.5 (*C*H_2), 69.6 (*C*H), 74.1 (*C*), 82.4 (*C*), 127.5 (*C*H), 129.5 (*C*H), 133.9 (*C*), 135.5 (*C*H). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{25}H_{33}BrO_2SiNa$, 495.1325; found, 495.1330.

*({[2-(2-Bromoethoxy)but-3-yn-1-yl]oxy}methyl)benzene (**1f**).* **1f** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 2.50 (d, *J* = 2.0 Hz, 1H), 3.50 (t, *J* = 6.5 Hz, 2H), 3.67 (s, 1H), 3.69 (d, *J* = 0.8 Hz, 1H), 3.81 (dt, *J* = 6.6, 10.7 Hz, 1H), 4.06 (dt, *J* = 6.4, 10.8 Hz, 1H), 4.36 (ddd, *J* = 2.2, 5.1, 5.9 Hz, 1H), 4.64 (dd, *J* = 12.2, 22.3 Hz, 2H), 7.27–7.38 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 29.8 (*C*H_2), 68.7 (*C*H_2), 69.3 (*C*H), 71.8 (*C*H_2), 73.2 (*C*H_2), 75.2 (*C*), 79.5 (*C*H), 127.5 (*C*H), 128.1 (*C*H), 137.6 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{13}H_{15}BrO_2$, 282.0255; found, 282.0252.

*1-(2-Bromoethoxy)-1-ethynylcyclohexane (**1g**).* **1g** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.26–1.35 (m, 1H), 1.48–1.72 (m, 7H), 1.86–1.90 (m, 2H), 2.48 (s, 1H), 3.48 (t, *J* = 6.5 Hz, 2H), 3.88 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 22.3 (*C*H_2), 25.1 (*C*H_2), 30.8 (*C*H_2), 36.8

(CH_2), 63.4 (CH_2), 73.5 (C), 73.9 (C), 84.6 (CH). HRMS (EI-TOF) (m/z): [M]+ calcd for $C_{10}H_{15}BrO$, 230.0306; found, 230.0311.

*[3-(2-Bromoethoxy)hex-4-yn-1-yl]benzene (**1i**).* **1i** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^1H NMR (392 MHz, $CDCl_3$, δ): 1.87 (d, J = 2.4 Hz, 3H), 1.93–2.10 (m, 2H), 2.79 (t, J = 7.4 Hz, 2H), 3.45–3.53 (m, 2H), 3.68 (dt, J = 6.5, 11.1 Hz, 1H), 3.98–4.05 (m, 2H), 7.16–7.22 (m, 3H), 7.26–7.30 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 3.5 (CH_3), 30.4 (CH_2), 31.3 (CH_2), 37.3 (CH_2), 68.3 (CH_2), 69.1 (CH), 77.6 (C), 82.4 (C), 125.8 (CH), 128.3 (CH), 128.4 (CH), 141.3 (C). HRMS (ESI-Orbitrap) (m/z): [M+Na]+ calcd for $C_{14}H_{17}BrONa$, 303.0355; found, 303.0357.

*[3-(2-Bromoethoxy)non-4-yn-1-yl]benzene (**1j**).* **1j** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^1H NMR (392 MHz, $CDCl_3$, δ): 0.92 (t, J = 7.1 Hz, 3H), 1.37–1.54 (m, 4H), 1.93–2.11 (m, 2H), 2.23 (td, J = 2.0, 7.0 Hz, 2H), 2.79 (t, J = 7.6 Hz, 2H), 3.45–3.54 (m, 2H), 3.70 (dt, J = 6.6, 10.7 Hz, 1H), 3.98–4.08 (m, 2H), 7.17–7.22 (m, 3H), 7.27–7.30 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.5 (CH_3), 18.2 (CH_2), 21.8 (CH_2), 30.3 (CH_2), 30.6 (CH_2), 31.3 (CH_2), 37.4 (CH_2), 68.2 (CH_2), 69.0 (CH), 78.4 (C), 86.9 (C), 125.7 (CH), 128.2 (CH), 128.4 (CH), 141.3 (C). HRMS (ESI-Orbitrap) (m/z): [M+Na]+ calcd for $C_{17}H_{23}BrONa$, 345.0825; found, 345.0828.

*[3-(2-Bromoethoxy)-8-chlorooct-4-yn-1-yl]benzene (**1k**).* **1k** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^1H NMR (392 MHz, $CDCl_3$, δ): 1.93–2.12 (m, 4H), 2.44 (td, J = 1.8, 6.7 Hz, 2H), 2.79 (t, J = 7.9 Hz, 2H), 3.45–3.54 (m, 2H), 3.64–3.72 (m, 3H), 3.98–4.07 (m, 2H), 7.17–7.22 (m, 3H), 7.27–7.31 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 16.0 (CH_2), 30.4 (CH_2), 31.2 (CH_2), 31.3 (CH_2), 37.3 (CH_2), 43.5 (CH_2),

68.3 (*C*H_2), 69.0 (*C*H), 79.5 (*C*), 84.8 (*C*), 125.8 (*C*H), 128.3 (*C*H), 128.4 (*C*H), 141.2 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{16}H_{20}BrClONa$, 365.0278; found, 369.0280.

*{3-[2-Bromoethoxy]-7-[(3-methylbut-2-en-1-yl)oxy]hept-4-yn-1-yl}benzene (**1l**).* **1l** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.68 (s, 3H), 1.74 (s, 3H), 1.93–2.11 (m, 2H), 2.52 (td, *J* = 1.8, 7.2 Hz, 2H), 2.79 (t, *J* = 7.4 Hz, 2H), 3.47–3.56 (m, 4H), 3.69 (dt, *J* = 6.6, 10.8 Hz, 1H), 3.98–4.07 (m, 4H), 5.33–5.37 (m, 1H), 7.17–7.21 (m, 3H), 7.27–7.30 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 17.8 (*C*H_3), 20.0 (*C*H_2), 25.6 (*C*H_3), 30.3 (*C*H_2), 31.2 (*C*H_2), 37.2 (*C*H_2), 67.1 (*C*H_2), 68.0 (*C*H_2), 68.2 (*C*H_2), 68.9 (*C*H), 79.3 (*C*), 83.7 (*C*), 120.7 (*C*H), 125.7 (*C*H), 128.2 (*C*H), 128.3 (*C*H), 136.9 (*C*), 141.2 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{20}H_{27}BrO_2Na$, 401.1087; found, 401.1089.

*tert-Butyl 4-(2-bromoethoxy)-4-(hex-1-yn-1-yl)piperidine-1-carboxylate (**1m**).* **1m** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.92 (t, *J* = 7.2 Hz, 3H), 1.36–1.54 (m, 4H), 1.46 (s, 9H), 1.66–1.72 (m, 2H), 1.81–1.84 (br, 2H), 2.23 (t, *J* = 7.0 Hz, 2H), 3.27 (ddd, *J* = 3.8, 9.2, 13.3 Hz, 2H), 3.47 (t, *J* = 6.3 Hz, 2H), 3.70–3.73 (br, 2H), 3.87 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.6 (*C*H_3), 18.3 (*C*H_2), 21.9 (*C*H_2), 28.4 (*C*H_3), 30.7 (*C*H_2), 31.0 (*C*H_2), 36.7 (*C*H_2), 40.0 (*C*H_2), 40.9 (*C*H_2), 63.6 (*C*H_2), 72.4 (*C*), 79.3 (*C*), 79.5 (*C*), 88.0 (*C*), 154.6 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{18}H_{30}O_3NBrNa$, 410.1301; found, 410.1299.

*(E)-4-(2-Bromoethoxy)dec-2-en-5-yne [(E)-**1o**]*. **1o** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.92 (t, *J* = 7.2 Hz, 3H), 1.37–1.56 (m, 4H), 1.75 (d, *J* = 6.7 Hz, 3H), 2.26 (dt, *J* = 1.9, 7.1 Hz, 2H), 3.48 (dt, *J* = 1.1, 6.7 Hz, 2H), 3.75 (dt, *J* = 6.6, 10.7 Hz, 1H), 3.90 (dt, *J* = 6.5, 10.4 Hz, 1H),

4.62 (d, *J* = 8.1 Hz, 1H), 5.52–5.59 (m, 1H), 5.87–5.96 (m, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.5 (*C*H_3), 17.4 (*C*H_3), 18.3 (*C*H_2), 21.9 (*C*H_2), 30.2 (*C*H_2), 30.6 (*C*H_2), 67.2 (*C*H_2), 70.3 (*C*H), 76.8 (*C*), 88.1 (*C*), 128.3 (*C*H), 129.9 (*C*H). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{12}H_{19}OBr$, 258.0619; found, 258.0619.

*[3-(2-Bromoethoxy)-5-(cyclohex-1-en-1-yl)pent-4-yn-1-yl]benzene (**1p**).* **1p** was prepared as a colorless oil from the corresponding propargyl alcohol according to Method B. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.57‑1.70 (m, 4H), 1.97‑2.14 (m, 6H), 2.81 (t, *J* = 7.7 Hz, 2H), 3.45–3.57 (m, 2H), 3.68–3.74 (m, 1H), 4.03 (dt, *J* = 6.1, 10.8 Hz, 1H), 4.18 (t, *J* = 6.6 Hz, 1H), 6.12 (quint, *J* = 2.0 Hz, 1H), 7.17–7.23 (m, 3H), 7.27–7.31 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.3 (*C*H_2), 22.1 (*C*H_2), 25.5 (*C*H_2), 29.1 (*C*H_2), 30.4 (*C*H_2), 31.3 (*C*H_2), 37.3 (*C*H_2), 68.3 (*C*H_2), 69.2 (*C*H), 84.6 (*C*), 88.1 (*C*), 119.9 (*C*), 125.8 (*C*H), 128.2 (*C*H), 128.4 (*C*H), 135.2 (*C*H), 141.2 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{19}H_{23}BrONa$, 369.0825; found, 369.0822.

Preparation of *N*-Benzyl-*N*-(2-bromoethyl)prop-2-yn-1-amine (1h). 2-[Benzyl(prop-2-yn-1-yl)amino]ethan-1-ol was synthesized through the reaction of the corresponding ethanolamine derivative according to the literature procedure.[23] In a vacuum dried 100 mL two-neck round-bottomed flask, 2-[benzyl(prop-2-yn-1-yl)amino]ethan-1-ol (2.89 g, 15.3 mmol) and carbon tetrabromide (5.06 g, 15.3 mmol) were dissolved in dry THF (22 mL), and the mixture was cooled to 0 ºC under a nitrogen atmosphere. Triphenylphosphine (4.00 g, 15.9 mmol) was added to the mixture, and the mixture was warmed to room temperature. After the mixture was stirred for 10 h, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain *N*-benzyl-*N*-(2-bromoethyl)prop-2-yn-1-amine (**1h**) (2.94 g, 11.7 mmol, 76%) as a colorless oil. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 2.26 (t, *J* = 2.2 Hz, 1H), 3.00 (t, *J* = 7.0 Hz, 2H), 3.36 (d, *J* = 2.2 Hz, 2H), 3.44 (t, *J* = 7.2 Hz, 2H), 3.70 (s, 2H), 7.25–

7.38 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 30.0 (*C*H_2), 41.6 (*C*H_2), 54.9 (*C*H_2), 57.6 (*C*H_2), 73.5 (*C*), 78.1 (*C*H), 127.3 (*C*H), 128.3 (*C*H), 128.9 (*C*H), 138.0 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+H]+ calcd for $C_{12}H_{15}BrN$, 252.0382; found, 252.0384.

Preparation of *N*-(2-Bromoethyl)-4-methyl-*N*-(oct-2-yn-1-yl)benzenesulfonamide (1n). In a vacuum dried 100 mL two-neck round-bottomed flask, 1-chlorooct-2-yne (2.17 g, 15.0 mmol), 4-methylbenzenesulfonamide (10.3 g, 60.0 mmol) and potassium carbonate (2.08 g, 15.0 mmol) were dissolved in dry acetonitrile (40 mL), and then the mixture was warmed to 80 ºC. After the mixture was stirred for 16 h, the solid was filtered off and the filtrate was concentrated *in vacuo*. The crude product was purified by flash column chromatography to obtain 4-methyl-*N*-(oct-2-yn-1-yl)benzenesulfonamide (2.00 g, 7.14 mmol, 48%) as a white solid (m.p. = 36–37 ℃).

In a vacuum dried 50 mL round-bottomed flask, 4-methyl-*N*-(oct-2-yn-1-yl)benzenesulfonamide (0.83 g, 3.00 mmol), 1,2-dibromoethane (5.63 g, 30.0 mmol) and cesium carbonate (1.47 g, 4.50 mmol) were dissolved in dry acetonitrile (12 mL), and then warmed to 80 ºC. After the mixture was stirred for 15 h, the solid was filtered off and the filtrate was concentrated *in vacuo*. The crude product was purified by flash column chromatography to obtain *N*-(2-bromoethyl)-4-methyl-*N*-(oct-2-yn-1-yl)benzenesulfonamide (**1n**) (0.93 g, 2.40 mmol, 80%) as a colorless oil. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 7.0 Hz, 3H), 1.16–1.33 (m, 6H), 1.96 (tt, *J* = 2.2, 7.0 Hz, 2H), 2.43 (s, 3H), 3.52 (s, 4H), 4.13 (t, *J* = 2.2 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 2H), 7.72–7.75 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.8 (*C*H_3), 18.3 (*C*H_2), 21.4 (*C*H_3), 22.0 (*C*H_2), 27.8 (*C*H_2), 29.0 (*C*H_2), 30.8 (*C*H_2), 38.3 (*C*H_2), 48.1 (*C*H_2), 72.3 (*C*), 86.7 (*C*), 127.5 (*C*H), 129.4 (*C*), 135.6 (*C*), 143.5 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{17}H_{24}BrO_2NSNa$, 408.0603; found, 408.0605.

Preparation of 1-(2-Bromo-1-ethoxyethoxy)-1-ethynylcyclohexane (5). In a vacuum dried 100 mL two-neck round-bottomed flask, 1-ethynylcyclohexan-1-ol (1.26 g, 10.0 mmol) and ethoxyethene (2.28 mL, 24.0 mmol) were dissolved in dry CH_2Cl_2 (34 mL), and the mixture was cooled to 0 ºC under a nitrogen atmosphere. *N*-Bromosuccinimide (1.78 g, 10.0 mmol) was added portionwise to the mixture, and the mixture was warmed to room temperature. After the mixture was stirred for 3 h, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain 1-(2-bromo-1-ethoxyethoxy)-1-ethynylcyclohexane (**5**) (1.27 g, 4.60 mmol, 46%) as a colorless oil. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.19–1.29 (m, 4H), 1.51–1.64 (m, 5H), 1.67–1.74 (m, 2H), 1.87–1.92 (m, 1H), 2.00–2.14 (m, 1H), 2.59 (s, 1H), 3.37–3.44 (m, 2H), 3.61 (dq, J = 7.1, 9.1 Hz, 1H), 3.75 (dq, J = 7.2, 9.2 Hz, 1H), 5.17 (dd, J = 4.5, 6.3 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 15.0 (*C*H_3), 22.8 (*C*H_2), 25.0 (*C*H_2), 33.3 (*C*H_2), 38.2 (*C*H_2), 38.5 (*C*H_2), 61.7 (*C*H_2), 74.5 (*C*), 75.4 (*C*), 84.3 (*C*), 97.5 (*C*H). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{12}H_{19}BrO_2Na$, 297.0461; found, 297.0460.

Preparation of 3-(2-Iodoethoxy)oct-1-yne (1b). In a vacuum dried 200 mL two-neck round-bottomed flask, triphenylphosphine (3.94 g, 15.0 mmol), imidazole (1.27 g, 18.6 mmol) and iodine (4.15 g, 16.4 mmol) were dissolved in dry CH_2Cl_2 (100 mL) under a nitrogen atmosphere. 2-(oct-1-yn-3-yloxy)ethan-1-ol (1.66 g, 10.0 mmol) synthesized through Method A was added dropwise to the mixture. After the mixture was stirred for 1 h, 100 mL of EtOAc was added to the reaction mixture. The organic layer was washed with 50 mL of saturated aqueous $Na_2S_2O_3$ solution, 150 mL of saturated aqueous $NaHCO_3$ solution and then 150 mL of brine. The organic layer was then dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain 3-(2-iodoethoxy)oct-1-yne (**1b**) (2.56 g, 9.14 mmol, 94%) as a colorless oil. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.90 (t, J

= 6.7 Hz, 3H), 1.26–1.38 (m, 4H), 1.41–1.53 (m, 2H), 1.65–1.81 (m, 2H), 2.44 (d, *J* = 1.8 Hz, 1H), 3.23–3.32 (m, 2H), 3.68 (dt, *J* = 7.1, 10.6 Hz, 1H), 3.98 (ddd, *J* = 6.2, 7.3, 10.7 Hz 1H), 4.09 (dt, *J* = 2.1 6.6 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 2.8 (*C*H_2), 14.0 (*C*H_3), 22.5 (*C*H_2), 24.8 (*C*H_2), 31.3 (*C*H_2), 35.5 (*C*H_2), 69.3 (*C*H_2), 69.4 (*C*H), 73.9 (*C*), 82.6 (*C*H). HRMS (EI-TOF) (*m*/*z*): [M–pentyl]+ calcd for C_5H_6IO, 208.9463; found, 208.9463.

Preparation of 2-(Oct-1-yn-3-yloxy)ethyl methanesulfonate (1c). In a vacuum dried 50 mL two-neck round-bottomed flask, 2-(oct-1-yn-3-yloxy)ethan-1-ol (1.69 g, 10.0 mmol) synthesized through Method A and triethylamine (1.53 mL, 11.0 mmol) were dissolved in dry CH_2Cl_2 (15 mL), and the mixture was cooled to 0 ºC under a nitrogen atmosphere. Methanesulfonyl chloride (1.26 g, 11.0 mmol) was added dropwise to the mixture. After the mixture was stirred for 5 h, the reaction mixture was quenched by H_2O and extracted with Et_2O three times. The combined organic layer was then dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The crude product was purified by flash column chromatography to obtain 2-(oct-1-yn-3-yloxy)ethyl methanesulfonate (**1c**) (2.23 g, 8.97 mmol, 90%) as a colorless oil. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.90 (t, *J* = 6.7 Hz, 3H), 1.25–1.38 (m, 4H), 1.45 (quint, *J* = 7.5 Hz, 2H), 1.65–1.80 (m, 2H), 2.46 (d, *J* = 1.8 Hz, 1H), 3.06 (s, 3H), 3.68 (ddd, *J* = 3.5, 5.9, 11.3 Hz, 1H), 4.00 (ddd, *J* = 3.4, 5.4, 11.5 Hz, 1H), 4.09 (td, *J* = 1.8, 6.7 Hz, 1H), 4.36–4.45 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.8 (*C*H_3), 22.3 (*C*H_2), 24.6 (*C*H_2), 31.2 (*C*H_2), 35.2 (*C*H_2), 37.5 (*C*H_3), 66.2 (*C*H_2), 69.2 (*C*H_2), 69.8 (*C*H), 74.3 (*C*), 82.0 (*C*H). HRMS (ESI-Orbitrap) (*m*/*z*): [M+H]+ calcd for $C_{11}H_{21}O_4SNa$, 249.1155; found, 249.1154.

*2-[(6-Methyl-1-phenylhept-4-yn-3-yl)oxy]ethyl methanesulfonate (**1r**).* **1r** was prepared as a colorless oil from the corresponding primary alcohol according to the procedure described above. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.18 (d, *J* = 7.2 Hz, 6H), 1.90–2.08 (m, 2H), 2.55–2.66

(m, 1H), 2.77 (t, J = 7.9 Hz, 2H), 3.06 (s, 3H), 3.60–3.67 (m, 1H), 3.97 (ddd, J = 3.6, 5.2, 11.5 Hz, 1H), 4.05 (dt, J = 1.8, 6.5 Hz, 1H), 4.36–4.45 (m, 2H), 7.18–7.21 (m, 3H), 7.26–7.31 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.3 (*C*H), 22.8 (*C*H_3), 31.2 (*C*H_2), 37.2 (*C*H_2), 37.4 (*C*H_3), 65.9 (*C*H_2), 69.20 (*C*H), 69.24 (*C*H_2), 77.0 (*C*), 92.8 (*C*), 125.7 (*C*H), 128.2 (*C*H), 128.3 (*C*H), 141.1 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{17}H_{24}O_4SNa$, 347.1288; found, 347.1287.

General Procedure for the Copper(I)-Catalyzed Intramolecular Alkylboration of 1a. Copper chloride (2.5 mg, 0.025 mmol) and bis(pinacolato)diboron (**2**) (152.4 mg, 0.60 mmol), tri(*o*-tolyl)phosphine (7.6 mg, 0.025 mmol) were placed in an oven-dried reaction vial. After the vial was sealed with a screw cap containing a teflon-coated rubber septum, the vial was connected to a vacuum/nitrogen manifold through a needle. It was evacuated and then backfilled with nitrogen. This cycle was repeated three times. Dry THF (0.4 mL) and K(O-*t*-Bu)/THF (1.0 M, 0.6 mL, 0.6 mmol) were added in the vial through the rubber septum using a syringe. After stirring for 30 min, **1a** (117.0 mg, 0.50 mmol) was added to the mixture at 30°C. After the reaction was complete, the reaction mixture was passed through a short silica gel (*Φ*: 10 mm, height of the silica-gel column: ca. 30 mm) eluting with Et_2O. The crude material was purified by flash column chromatography (SiO_2, Et_2O /hexane, typically 0:100–14:86) to give the corresponding borylation product (*E*)-**3a** as a colorless oil.

*(E)-4,4,5,5-Tetramethyl-2-{[2-pentyldihydrofuran-3(2H)-ylidene]methyl}-1,3,2-dioxaborolane [(E)-**3a**]*. The reaction was conducted with 117.0 mg (0.50 mmol) of **1a**. The product (*E*)-**3a** was obtained as a colorless oil in 71% yield (100.3 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.88 (t, J = 6.9 Hz, 3H), 1.22–1.34 (m, 16H), 1.37–1.55 (m, 3H), 1.60–1.69 (m, 1H), 2.67–2.77 (m, 1H), 2.87–2.94 (m, 1H), 3.75 (td, J = 6.8, 8.4 Hz, 1H), 4.03 (td, J = 3.9, 8.3 Hz,

1H), 4.20–4.22 (m, 1H), 5.19 (q, J = 2.1 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (CH_3), 22.5 (CH_2), 24.78 (CH_3), 24.80 (CH_3), 25.2 (CH_2), 31.8 (CH_2), 33.6 (CH_2), 34.6 (CH_2), 66.8 (CH_2), 82.3 (CH), 82.8 (C), 106.6 (br, B–CH), 168.2 (C). HRMS (EI-TOF) (m/z): [M]+ calcd for $C_{16}H_{29}{}^{11}BO_3$, 280.2210; found, 280.2223.

*(E)-4,4,5,5-Tetramethyl-2-{[2-phenethyldihydrofuran-3(2H)-ylidene]methyl}-1,3,2-dioxaborolane [(E)-**3d**]*. The reaction was conducted with 132.7 mg (0.50 mmol) of **1d**. The product (E)-**3d** was obtained as a white solid (m.p. = 49–51 ℃) in 67% yield (105.1 mg) with E/Z = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.27 (s, 12H), 1.79–1.88 (m, 1H), 1.93–2.02 (m, 1H), 2.67–2.83 (m, 3H), 2.88–2.96 (m, 1H), 3.79 (td, J = 7.1, 8.6 Hz, 1H), 4.07 (td, J = 4.3, 8.3 Hz, 1H), 4.24–4.26 (m, 1H), 5.21 (q, J = 2.2 Hz, 1H), 7.15–7.21 (m, 3H), 7.25–7.29 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 24.79 (CH_3), 24.82 (CH_3), 31.6 (CH_2), 33.7 (CH_2), 36.2 (CH_2), 66.9 (CH_2), 81.4 (CH), 82.8 (C), 106.9 (br, B–CH), 125.6 (CH), 128.2 (CH), 128.4 (CH), 142.0 (C), 167.8 (C). HRMS (EI-TOF) (m/z): [M]+ calcd for $C_{19}H_{27}{}^{11}BO_3$, 314.2053; found, 314.2057.

*(E)-tert-Butyldiphenyl{4-{3-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene]-tetrahydrofuran-2-yl}butoxy}silane [(E)-**3e**]*. The reaction was conducted with 229.6 mg (0.50 mmol) of **1e**. The product (*E*)-**3e** was obtained as a colorless oil in 60% yield (151.8 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.04 (s, 9H), 1.27 (s, 12H), 1.43–1.66 (m, 6H), 2.65–2.75 (m, 1H), 2.86–2.94 (m, 1H), 3.65 (t, J = 6.3 Hz, 2H), 3.74 (td, J = 6.7, 8.8 Hz, 1H), 4.01 (td, J = 4.0, 8.3 Hz, 1H), 4.19–4.20 (m, 1H), 5.17 (q, J = 2.1 Hz, 1H), 7.35–7.44 (m, 6H), 7.65–7.67 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 19.1 (CH_2), 21.7 (C), 24.82 (CH_3), 24.85 (CH_3), 26.8 (CH_3), 32.5 (CH_2), 33.7 (CH_2), 34.3 (CH_2), 63.8 (CH_2) 66.9 (CH_2), 82.2 (CH), 82.8 (C), 106.8 (br, B–CH), 127.5 (CH), 129.4 (CH), 134.0 (C), 135.5 (CH), 168.1 (C). HRMS (ESI-Orbitrap) (m/z): [M+Na]+ calcd for $C_{31}H_{45}{}^{11}BO_4SiNa$, 543.3072; found, 543.3078.

*(E)-2-{{2-[(Benzyloxy)methyl]dihydrofuran-3(2H)-ylidene}methyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(E)-**3f**]*. The reaction was conducted with 140.1 mg (0.50 mmol) of **1f**. The product (*E*)-**3f** was obtained as a colorless oil in 75% yield (122.3 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.26 (s, 12H), 2.72–2.81 (m, 1H), 2.85–2.93 (m, 1H), 3.51 (dd, *J* = 7.1, 10.6 Hz, 1H), 3.59 (dd, *J* = 3.1, 10.2 Hz, 1H), 3.85 (q, *J* = 7.8 Hz, 1H), 4.07 (td, *J* = 4.8, 8.3 Hz, 1H), 4.48–4.51 (m, 1H), 4.59 (q, *J* = 12.3 Hz, 2H), 5.23 (q, *J* = 2.2 Hz, 1H), 7.26–7.38 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 24.8 (*C*H_3), 33.5 (*C*H_2), 67.5 (*C*H_2), 72.4 (*C*H_2), 73.2 (*C*H_2), 81.4 (*C*H), 82.9 (*C*), 108.3 (br, B–*C*H), 127.4 (*C*H), 127.6 (*C*H), 128.2 (*C*H), 138.0 (*C*), 164.5 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{19}H_{27}{}^{11}BO_4$, 330.2002; found, 330.2014.

*(E)-2-[(1-Oxaspiro[4.5]decan-4-ylidene)methyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(E)-**3g**]*. The reaction was conducted with 116.3 mg (0.50 mmol) of **1g**. The product (*E*)-**3g** was obtained as a colorless oil in 60% yield (83.5 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.18–1.35 (m, 14H), 1.54–1.70 (m, 8H), 2.85 (td, *J* = 2.2, 6.9 Hz, 2H), 3.84 (t, *J* = 6.9 Hz, 2H), 5.11 (t, *J* = 2.2 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 22.3 (*C*H_2), 24.8 (*C*H_3), 25.4 (*C*H_2), 33.4 (*C*H_2), 35.2 (*C*H_2), 64.3 (*C*H_2), 82.8 (*C*), 83.8 (*C*), 105.6 (br, B–*C*H), 172.6 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{16}H_{27}{}^{11}BO_3$, 278.2053; found, 278.2057.

*(E)-1-Benzyl-3-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene]pyrrolidine [(E)-**3h**]*. The reaction was conducted with 126.9 mg (0.50 mmol) of **1h**. The product (*E*)-**3h** was obtained as a colorless oil in 49% yield (73.9 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.24 (s, 12H), 2.67–2.74 (m, 4H), 3.20 (s, 2H), 3.62 (s, 2H), 5.23 (t, *J* = 1.8 Hz, 1H), 7.23–7.27 (m, 2H), 7.29–7.35 (m, 3H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 24.8 (*C*H_3), 32.4 (*C*H_2), 54.5 (*C*H_2), 60.6 (*C*H_2), 61.9 (*C*H_2), 82.6 (*C*), 108.0 (br, B–*C*H), 126.9 (*C*H), 128.2 (*C*H), 128.7 (*C*H), 138.8

(*C*), 165.9 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+H]+ calcd for $C_{18}H_{27}{}^{11}BNO_2$, 300.2129; found, 300.2129.

*(Z)-4,4,5,5-Tetramethyl-2-{1-[2-phenethyldihydrofuran-3(2H)-ylidene]ethyl}-1,3,2-dioxaborolane [(Z)-**3i**]*. The reaction was conducted with 138.8 mg (0.50 mmol) of **1i**. The product (*Z*)-**3i** was obtained as a colorless oil in 74% yield (119.1 mg) with *E*/*Z* = <5:95. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.26 (s, 12H), 1.65 (s, 3H), 1.74–1.84 (m, 1H), 1.86–1.94 (m, 1H), 2.64–2.73 (m, 2H), 2.76–2.84 (m, 1H), 2.89–2.96 (m, 1H), 3.81 (q, *J* = 7.7 Hz, 1H), 4.02 (td, *J* = 5.0, 8.3 Hz, 1H), 4.56 (d, *J* = 9.0 Hz, 1H), 7.15–7.22 (m, 3H), 7.25–7.29 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 16.8 (*C*H_3), 24.7 (*C*H_3), 24.9 (*C*H_3), 31.9 (*C*H_2), 33.3 (*C*H_2), 34.5 (*C*H_2), 66.8 (*C*H_2), 79.2 (*C*H), 82.9 (*C*), 116.5 (br, B–*C*), 125.6 (*C*H), 128.2 (*C*H), 128.4 (*C*H), 142.1 (*C*), 158.3 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{20}H_{29}{}^{11}BO_3$, 328.2210; found, 328.2209.

*(Z)-4,4,5,5-Tetramethyl-2-{1-[2-phenethyldihydrofuran-3(2H)-ylidene]pentyl}-1,3,2-dioxaborolane [(Z)-**3j**]*. The reaction was conducted with 161.3 mg (0.50 mmol) of **1j**. The product (*Z*)-**3j** was obtained as a colorless oil in 72% yield (133.5 mg) with *E*/*Z* = <5:95. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.86 (t, *J* = 7.1 Hz, 3H), 1.19–1.35(m, 16H), 1.79–1.86 (m, 2H), 1.97–2.01 (m, 2H), 2.64–2.74 (m, 2H), 2.76–2.91 (m, 2H), 3.81 (q, *J* = 7.7 Hz, 1H), 4.00 (td, *J* = 5.2, 8.3 Hz, 1H), 4.55–4.57 (m, 1H), 7.15–7.21 (m, 3H), 7.25–7.29 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (*C*H_3), 22.8 (*C*H_2), 24.6 (*C*H_3), 24.8 (*C*H_3), 31.5 (*C*H_2), 31.9 (*C*H_2), 32.3 (*C*H_2), 33.1 (*C*H_2), 35.8 (*C*H_2), 66.6 (*C*H_2), 78.7 (*C*H), 82.8 (*C*), 123.0 (br, B–*C*), 125.6 (*C*H), 128.2 (*C*H), 128.4 (*C*H), 142.1 (*C*), 156.3 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{23}H_{35}{}^{11}BO_3$, 370.2679; found, 370.2681.

*(Z)-2-{4-Chloro-1-[2-phenethyldihydrofuran-3(2H)-ylidene]butyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(Z)-**3k**]*. The reaction was conducted with 171.4 mg (0.50 mmol) of **1k**. The

product (*Z*)-**3k** was obtained as a colorless oil in 64% yield (124.4 mg) with *E*/*Z* = <5:95. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.25 (s, 12H), 1.73–1.88 (m, 4H), 2.08–2.16 (m, 2H), 2.66–2.75 (m, 2H), 2.78–2.94 (m, 2H), 3.40–3.53 (m, 2H), 3.84 (q, *J* = 7.8 Hz, 1H), 4.00 (td, *J* = 5.4, 8.3 Hz, 1H), 4.58–4.61 (m, 1H), 7.16–7.30 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 24.7 (*C*H_3), 24.8 (*C*H_3), 29.1 (*C*H_2), 31.9 (*C*H_2), 32.8 (*C*H_2), 33.1 (*C*H_2), 35.6 (*C*H_2), 45.0 (*C*H_2), 66.5 (*C*H_2), 78.7 (*C*H), 83.0 (*C*), 120.7 (br, B–*C*), 125.6 (*C*H), 128.2 (*C*H), 128.5 (*C*H), 141.9 (*C*), 158.7 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{22}H_{32}{}^{11}BClO_3$, 390.2133; found, 390.2137.

*(Z)-4,4,5,5-Tetramethyl-2-{3-[(3-methylbut-2-en-1-yl)oxy]-1-[2-phenethyldihydrofuran-3(2H)-ylidene]propyl}-1,3,2-dioxaborolane [(Z)-**3l**]*. The reaction was conducted with 189.5 mg (0.50 mmol) of **1l**. The product (*Z*)-**3l** was obtained as a colorless oil in 86% yield (183.2 mg) with *E*/*Z* = <5:95. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.25 (s, 12H), 1.65 (s 3H), 1.72 (s, 3H), 1.75–1.94 (m, 2H), 2.28–2.44 (m, 2H), 2.65–2.74 (m, 2H), 2.77–2.84 (m, 1H), 2.87–2.95 (m, 1H), 3.36–3.42 (m, 2H), 3.83 (q, *J* = 7.8 Hz, 1H), 3.91 (d, *J* = 6.7 Hz, 2H), 4.01 (td, *J* = 5.4, 8.3Hz, 1H), 4.62 (d, *J* = 9.0 Hz, 1H), 5.30–5.35 (m, 1H), 7.14–7.22 (m, 3H), 7.24–7.28 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 17.8 (*C*H_3), 24.5 (*C*H_3), 24.7 (*C*H_3), 25.6 (*C*H_3), 31.8 (*C*H_2), 32.3 (*C*H_2), 33.2 (*C*H_2), 35.7 (*C*H_2), 66.4 (*C*H_2), 67.0 (*C*H_2), 69.6 (*C*H_2), 78.9 (*C*H), 82.8 (*C*), 118.2 (br, B–*C*), 121.3 (*C*H), 125.5 (*C*H), 128.1 (*C*H), 128.2 (*C*H), 136.1 (*C*), 142.0 (*C*), 159.1 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{26}H_{39}{}^{11}BO_4$, 426.2941; found, 426.2941.

*tert-Butyl (Z)-4-[1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentylidene]-1-oxa-8-azaspiro-[4.5]decane-8-carboxylate [(Z)-**3m**]*. The reaction was conducted with 194.1 mg (0.50 mmol) of **1m**. The product (*Z*)-**3m** was obtained as a white solid (m.p. = 101–103 ºC) in 86% yield (186.8 mg) with *E*/*Z* = <5:95. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.90 (t, *J* = 6.7 Hz, 3H), 1.19–1.35 (m, 16H), 1.47 (s, 9H), 1.56–1.59 (m, 2H), 1.93 (br-s, 2H), 2.16 (br-s, 2H), 2.78 (t, *J* = 6.7 Hz, 2H),

3.04 (br-s, 2H), 3.78 (t, *J* = 6.7 Hz, 2H), 3.92 (br-s, 1H), 4.02 (br-s, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (*C*H_3), 22.7 (*C*H_2), 24.7 (*C*H_3), 28.4 (*C*H_3), 30.1 (*C*H_2), 32.9 (*C*H_2), 33.1 (*C*H_2), 33.5 (*C*H_2), 35.2 (*C*H_2), 40.2 (*C*H_2), 41.2 (*C*H_2), 64.4 (*C*H_2), 79.1 (*C*), 81.2 (*C*), 83.0 (*C*), 154.9 (*C*), 155.6 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{24}H_{42}{}^{11}BNO_5$, 435.3160; found, 435.3150.

*(Z)-3-(1-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)hexylidene)-1-tosylpyrrolidine [(Z)-**3n**]*. The reaction was conducted with 192.6 mg (0.50 mmol) of **1n**. The product (*Z*)-**3n** was obtained as a white solid (m.p. = 112–114 ºC) in 78% yield (169.4 mg) with *E*/*Z* = <5:95. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 7.0 Hz, 3H), 1.18–1.30 (m, 18H), 1.95 (t, *J* = 7.0 Hz, 2H), 2.43 (s, 3H), 2.74 (t, *J* = 7.0 Hz, 2H), 3.23 (t, *J* = 7.0 Hz, 2H), 3.81 (s, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.70–7.73 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.8 (*C*H_3), 21.3 (*C*H_3), 22.4 (*C*H_2), 24.6 (*C*H_3), 28.9 (*C*H_2), 31.6 (*C*H_2), 31.8 (*C*H_2), 32.0 (*C*H_2), 48.0 (*C*H_2), 50.9 (*C*H_2), 82.9 (*C*), 125.2 (br, B–*C*), 127.8 (*C*H), 129.5 (*C*H), 132.0 (*C*), 143.5 (*C*), 149.9 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{23}H_{36}{}^{11}BNO_4S$, 433.2458; found, 433.2461.

*4,4,5,5-Tetramethyl-2-{(Z)-1-{2-[(E)-prop-1-en-1-yl]dihydrofuran-3(2H)-ylidene}pentyl}-1,3,2-dioxaborolane [(Z,E)-**3o**]*. The reaction was conducted with 129.6 mg (0.50 mmol) of (*E*)-**1o**. The product (*Z*,*E*)-**3o** was obtained as a colorless oil in 80% yield (121.9 mg) with *E*/*Z* = <5:95. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 7.0 Hz, 3H), 1.21–1.36 (m, 4H), 1.27 (s, 12H), 1.69 (dd, *J* = 1.3, 6.3 Hz, 3H), 2.04–2.08 (m, 2H), 2.66–2.74 (m, 1H), 2.87 (dt, *J* = 6.0, 16.5 Hz,, 1H), 3.77 (dt, *J* = 7.8, 15.3 Hz, 1H), 3.97 (dt, *J* = 4.9, 8.1 Hz, 1H), 4.90 (d, *J* = 7.8 Hz, 1H), 5.40–5.46 (m, 1H), 5.72 (dq, J = 6.5, 15.3 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.1 (*C*H_3), 17.7 (*C*H_2), 22.9 (*C*H_2), 24.7 (*C*H_3), 24.9 (*C*H_3), 31.2 (*C*H_2), 32.0 (*C*H_2), 33.4 (*C*H_2), 66.9 (*C*H_2), 80.4

(*C*H), 82.9 (*C*), 128.2 (*C*H), 130.0 (*C*H), 154.8 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{18}H_{31}{}^{11}BO_3$, 306.2370; found, 306.2363.

*(Z)-2-{Cyclohex-1-en-1-yl[2-phenethyldihydrofuran-3(2H)-ylidene]methyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(Z)-**3p**]*. The reaction was conducted with 173.7 mg (0.50 mmol) of **1p**. The product (*Z*)-**3p** was obtained as a white solid (m.p. = 74–77 ºC) in 61% yield (120.2 mg) with *E*/*Z* = 7:93. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.25 (d, *J* = 5.8 Hz, 12H), 1.49–1.64 (m, 4H), 1.70–1.84 (m, 2H), 1.85–1.92 (m, 2H), 1.93–2.03 (m, 1H), 2.06–2.13 (m, 1H), 2.61–2.80 (m, 4H), 3.81 (q, *J* = 7.8 Hz, 1H), 3.99 (dt, *J* = 6.6, 8.2 Hz, 1H), 4.66 (d, *J* = 9.0 Hz, 1H), 5.28 (quint, *J* = 1.8 Hz, 1H), 7.14–7.28 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 22.0 (CH_2), 22.8 (CH_2), 24.3 (CH_3), 25.0 (CH_2, CH_3), 29.3 (CH_2), 31.9 (CH_2), 33.7 (CH_2), 34.3 (CH_2), 66.4 (CH_2), 78.7 (*C*H), 82.9 (*C*), 122.3 (*C*H), 125.5 (*C*H), 128.1 (*C*H), 128.5 (*C*H), 138.6 (*C*), 142.1 (*C*), 157.0 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{25}H_{35}{}^{11}BO_3$, 394.2679; found, 394.2687.

*(Z)-4,4,5,5-Tetramethyl-2-{2-methyl-1-[2-phenethyldihydrofuran-3(2H)-ylidene]propyl}-1,3,2-dioxaborolane [(Z)-**3q**]*. The reaction was conducted with 162.2 mg (0.50 mmol) of the corresponding sulfonate **1r**. The product (*Z*)-**3q** was obtained as a colorless oil in 47% yield (83.4 mg) with *E*/*Z* = 7:93. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.02 (d, *J* = 6.7 Hz, 3H), 1.06 (d, *J* = 6.7 Hz, 3H), 1.27 (s, 12H), 1.80–1.86 (m, 2H), 2.39 (septet, *J* = 6.7 Hz, 1H), 2.61–2.73 (m, 2H), 2.74–2.85 (m, 2H), 3.82 (dt, *J* = 7.8, 16.0 Hz, 1H), 3.98 (dt, *J* = 5.2, 8.2 Hz, 1H), 4.59 (t, *J* = 5.4 Hz, 1H), 7.15–7.22 (m, 3H), 7.24–7.29 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 22.1 (CH_3), 24.7 (CH_3), 24.9 (CH_3), 31.7 (*C*H), 32.0 (CH_2), 32.9 (CH_2), 36.1 (CH_2), 66.5 (CH_2), 78.7 (*C*H), 82.7 (*C*), 125.6 (*C*H), 128.2 (*C*H), 128.4 (*C*H), 142.2 (*C*), 152.7 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{22}H_{33}{}^{11}BO_3$, 356.2527; found, 356.2518.

Experimental Procedure of Diels–Alder Reaction. (*Z*)-**3p** (31.6 mg, 0.080 mmol) and *N*-phenylmaleimide (27.7 mg, 0.16 mmol) were placed in a reaction vial. Dry toluene (0.4 mL) was added to the vial. Then, the reaction mixture was stirred at 100 ºC for five days. After the reaction was complete, the reaction mixture was cooled to room temperature and the solvent was removed in vacuo. The crude mixture was purified by flash column chromatography (SiO_2, AcOEt/hexane, 0:100–28:72) to give the corresponding cycloaddition product **4** (28.1 mg, 0.050 mmol, 62%) as a white solid (m.p. = 73–74 ºC). ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.26–1.40 (14H), 1.51–1.72 (m, 3H), 1.74–1.94 (m, 3H), 2.14–2.25 (m, 3H), 2.34 (quint, *J* = 6.9 Hz, 1H), 2.63 (dt, *J* = 8.3, 13.7 Hz, 1H), 2.80–2.91 (m, 2H), 3.07 (d, *J* = 8.6 Hz, 1H), 3.22 (t, *J* = 8.2 Hz, 1H), 3.88–3.95 (m, 2H), 4.10 (td, *J* = 2.8, 8.8 Hz, 1H), 7.16–7.30 (m, 7H), 7.34–7.38 (m, 1H), 7.41–7.46 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 23.4 (*C*H_2), 23.9 (*C*H_2), 24.8 (*C*H_3), 25.2 (*C*H_3), 26.4 (*C*H_2), 31.7 (*C*H_2), 31.8 (*C*H_2) 32.6 (*C*H_2), 33.9 (*C*H_2), 37.6 (*C*H), 43.4 (*C*H), 44.7 (*C*H), 50.7 (*C*), 65.8 (*C*H_2), 83.4 (*C*), 83.5 (*C*H), 125.7 (*C*H), 126.7 (*C*H), 128.3 (*C*H), 128.5 (*C*H), 128.6 (*C*H), 129.0 (*C*H), 131.9 (*C*), 142.1 (*C*), 149.4 (*C*), 176.7 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{35}H_{42}{}^{11}BNO_5Na$, 590.3048; found, 590.3043.

General Procedure for the Palladium-Catalyzed Suzuki–Miyaura Coupling of Borylation Products. The palladium catalyzed cross-coupling reaction with aryl halide was performed according to the literature procedure.[15] 4-Bromobenzonitrile (135.3 mg, 0.75 mmol), $Pd_2(dba)_3$ (9.3 mg, 0.010 mmol) and SPhos (8.2 mg, 0.020 mmol) was placed in an oven-dried reaction vial under a nitrogen atmosphere. A solution of (*Z*)-**3j** (185.8 mg, 0.50 mmol, *E*/*Z* = <5:95) in dry THF (1 mL) was added to the vial followed by addition of dry THF (3.5 mL) and 3 M NaOH aq (1.5 mL). Then, the mixture was warmed to 60 ºC and stirred for 18 h. After the reaction mixture was cooled to room temperature, the reaction mixture was quenched by H_2O and extracted with

Et_2O three times. The combined organic layer was then dried over $MgSO_4$. After filtration, the solvents were removed by evaporation. The crude mixture was purified by flash column chromatography (SiO_2, AcOEt/hexane, 0:100–14:86) to give the corresponding coupling product (*E*)-**7a** (159.9 mg, 0.463 mmol, 92%, *E*/*Z* = >95:5) as a colorless oil.

*(E)-4-{1-[2-Phenethyldihydrofuran-3(2H)-ylidene]pentyl}benzonitrile [(E)-**7a**]*. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.80 (t, *J* = 7.0 Hz, 3H), 1.10–1.28 (m, 4H), 1.90–1.96 (m, 2H), 2.21–2.30 (m, 3H), 2.49 (quint, *J* = 7.9 Hz, 1H), 2.73–2.89 (m, 2H), 3.71 (td, *J* = 8.3, 6.7 Hz, 1H), 4.00 (td, *J* = 8.3, 4.0 Hz, 1H), 4.65 (t, *J* = 5.4 Hz, 1H), 7.19–7.33 (m, 7H), 7.61–7.63 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.7 (*C*H_3), 22.4 (*C*H_2), 30.2 (*C*H_2), 31.5 (*C*H_2), 31.9 (*C*H_2), 33.4 (*C*H_2), 36.4 (*C*H_2), 66.6 (*C*H_2), 78.2 (*C*H), 110.0 (*C*), 118.7 (*C*), 125.6 (*C*H), 128.2 (*C*H), 128.3 (*C*H), 128.6 (*C*H), 131.5 (*C*), 131.8 (*C*H), 140.3(*C*), 141.7 (*C*), 147.3 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{24}H_{27}NO$, 345.2093; found, 345.2091.

*(E)-2-Phenethyl-3-[1-(5-phenylthiophen-2-yl)pentylidene]tetrahydrofuran [(E)-**7b**]*. The reaction was conducted with 74.1 mg (0.2 mmol) of (*Z*)-**3j**. The product (*E*)-**7b** was obtained as an orange solid (m.p. = 41–42 ºC) in 93% yield (75.0 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 7.0 Hz, 3H), 1.26–1.52 (m, 4H), 1.89–1.95 (m, 2H), 2.30 (t, *J* = 7.9 Hz, 2H), 2.71–2.88 (m, 4H), 3,86 (dt, *J* = 7.8, 15.7 Hz, 1H), 4.09 (dt, *J* = 5.1, 8.0 Hz, 1H), 4.69 (t, *J* = 5.6 Hz, 1H), 6.90 (d, *J* = 4.0 Hz, 1H), 7.18–7.38 (m, 9H), 7.59 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (*C*H_3), 23.1 (*C*H_2), 31.3 (*C*H_2), 32.0 (*C*H_2), 33.2 (*C*H_2), 34.4 (*C*H_2), 36.3 (*C*H_2), 67.0 (*C*H_2), 79.3 (*C*H), 122.9 (*C*H), 125.7 (*C*H), 125.9 (*C*H), 126.0 (*C*), 126.3 (*C*H), 127.4 (*C*H), 128.5 (*C*H), 128.7 (*C*H), 129.0 (*C*H), 134.5 (*C*), 140.0 (*C*), 142.1 (*C*), 142.7 (*C*), 144.3 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{27}H_{30}OS$, 402.2017; found, 402.2016.

*(E)-2-Ethoxy-4-(4-methoxybenzylidene)-1-oxaspiro[4.5]decane [(E)-**7c**]*. The reaction was conducted with 64.5 mg (0.2 mmol) of (*E*)-**6**. The product (*E*)-**7c** was obtained as a colorless oil in 58% yield (34.9 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.15–1.33 (m, 5H), 1.42–1.74 (m, 2H), 1.90–1.94 (m, 1H), 2.92 (d, *J* = 17.1 Hz, 1H), 3.05 (ddd, *J* = 3.1, 5.4, 16.6 Hz, 1H), 3.43–3.51 (m, 1H), 3.78–3.86 (m, 4H), 5.26 (d, *J* = 5.4 Hz, 1H), 6.15 (t, *J* = 2.5 Hz, 1H), 6.86 (dt, *J* = 2.5, 9.3 Hz, 2H), 7.22 (dt, *J* = 2.7, 9.0 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 15.1 (*C*H_3), 22.7 (*C*H_2), 23.0 (*C*H_2), 25.5 (*C*H_2), 38.4 (*C*H_2), 38.8 (*C*H_2), 55.2 (*C*H_3), 62.2 (*C*H_2), 85.4 (*C*), 101.9 (*C*H), 113.6 (*C*H), 119.5 (*C*H), 129.3 (*C*H), 130.6 (*C*), 144.9 (*C*), 158.0 (*C*). HRMS (EI-TOF) (*m*/*z*): [M]+ calcd for $C_{19}H_{26}O_3$, 302.1882; found, 302.1888.

*(E)-2-[(2-Ethoxy-1-oxaspiro[4.5]decan-4-ylidene)methyl]-5-methylpyridine [(E)-**7d**]*. The reaction was conducted with 108.4 mg (0.34 mmol) of (*E*)-**6**. The product (*E*)-**7d** was obtained as a colorless oil in 87% yield (84.2 mg) with *E*/*Z* = >95:5. ^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.17 (t, *J* = 7.1 Hz, 3H), 1.23–1.33 (m, 1H), 1.43–1.59 (m, 2H), 1.63–1.75 (m, 6H), 1.93–1.97 (m, 1H), 2.30 (s, 3H), 3.16 (ddd, *J* = 3.2, 5.3, 17.9 Hz, 1H), 3.26 (ddd, *J* = 1.0, 2.0, 17.9 Hz, 1H), 3.44–3.52 (m, 1H), 3.82 (dq, *J* = 7.2, 9.5 Hz, 1H), 5.28 (d, *J* = 5.0 Hz, 1H), 6.29 (t, *J* = 2.6 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.42 (ddd, *J* = 0.6, 2.3, 8.0 Hz, 1H), 8.40 (d, *J* = 2.2 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 15.0 (*C*H_3), 18.1 (*C*H_3), 22.6 (*C*H_2), 22.8 (*C*H_2), 25.4 (*C*H_2), 38.3 (*C*H_2), 38.6 (*C*H_2), 39.1 (*C*H_2), 62.1 (*C*H_2), 85.4 (*C*), 102.0 (*C*H), 119.7 (*C*H), 122.6 (*C*H), 130.0 (*C*), 136.3 (*C*H), 149.5 (*C*H), 151.2 (*C*), 153.9 (*C*). HRMS (ESI-Orbitrap) (*m*/*z*): [M+Na]+ calcd for $C_{18}H_{25}NO_2Na$, 310.1778; found, 310.1776.

ASSOCIATED CONTENT

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Detailed results and discussions of substrate scope and DFT study and NMR spectra for all compounds

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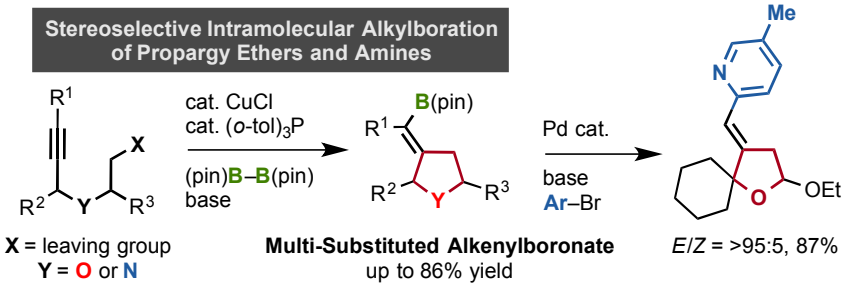

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