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Article

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Copper/Bisphosphine Catalysts in Internally Borylative Aminoboration of Unactivated Terminal Alkenes with Bis(pinacolato)diboron

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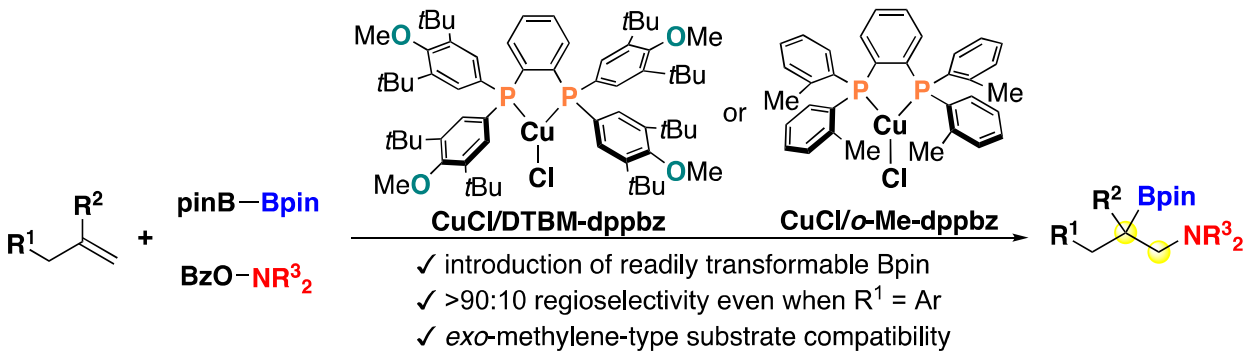


Abstract: Cu(I)/modified dppbz catalyst systems for the regioselective aminoboration of unactivated terminal alkenes have been developed. The bisphosphine-based Cu catalysis enables the introduction of readily transformable Bpin group at the more congested internal position and shows better regioselectivity for broader terminal alkenes involving sterically demanding allylbenzenes, which are

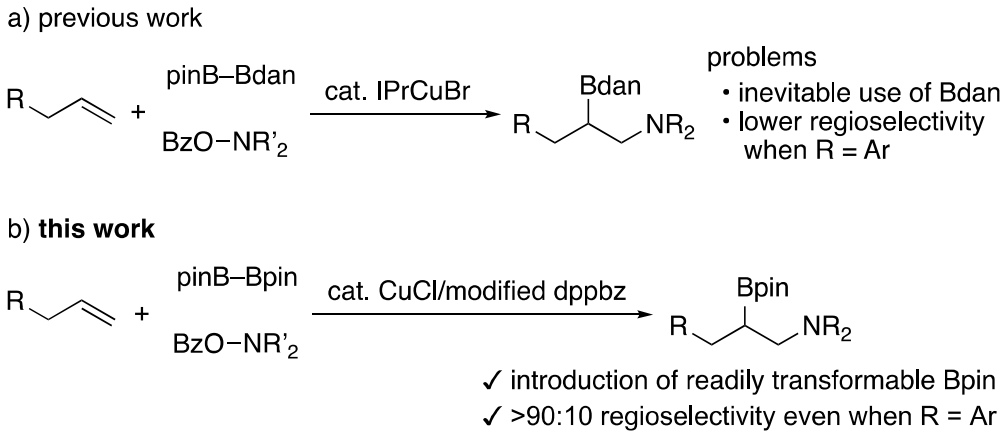
relatively challenging substrates in the previous IPrCuBr catalysis. Additionally, the second generation catalyst systems accommodate the *exo*-methylene-type disubstituted alkenes to deliver the corresponding aminoborated products in good yield with high regioselectivity.

Introduction

The catalytic difunctionalization of simple and abundant terminal alkenes is highly attractive from the synthetic point of view because both positions of the π bond are simultaneously functionalized in a single synthetic operation. Particularly, the aminative difunctionalization can readily transform the olefinic feedstock materials into the functionalized alkylamines of great interest in both bulk and fine chemical syntheses.[1] In this context, we reported the Cu-catalyzed aminoboration of unactivated terminal alkenes with hydroxylamines and diboron reagents as the amino electrophiles[2] and boryl nucleophiles,[3] respectively. Additionally, the ligand-controlled regiodivergency was achieved: the CuCl(xantphos) complex guided the boron and amino groups to the terminal and internal positions, respectively, whereas the opposite regioisomers were selectively obtained under the IPrCuBr (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) catalysis.[4] However, the latter has two drawbacks (Scheme 1a). One is the use of pinB-Bdan (pin = pinacolato, dan = 1,8-diamiononaphthyl) as the boryl source, in which the Bdan group is selectively introduced to the product. The Bdan is more stable and easy-to-handle boron masking group but sometimes needs tedious deprotection steps for the latent boron functionalization. Another is lower regioselectivity for relatively sterically hindered terminal alkenes such as allylbenzene and vinylcyclohexene.

On the other hand, the research groups of Ito,[5a] Xiao and Fu,[5b] and Montgomery,[5c] independently, recently developed Cu-catalyzed highly regioselective hydroboration and alkylboration of unactivated terminal alkenes, in which the readily transformable Bpin group was selectively incorporated at the internal carbon with pinB–Bpin as the boryl source. Inspired by these works, we reinvestigated the catalytic system, particularly, ancillary ligand to overcome the above limitations of the IPrCuBr-based first generation catalyst system. Here, we report Cu/modified dppbz (dppbz = 1,2-bis(diphenylphosphino)benzene) catalysis for highly regioselective aminoboration of terminal alkenes (Scheme 1b). The second generation catalysts enable the use of pinB-Bpin and give better regioselectivity for broader terminal alkenes.

Scheme 1. Copper-Catalyzed Internally Borylative Aminoboration of Unactivated Terminal Alkenes with Bis(pinacolato)diboron

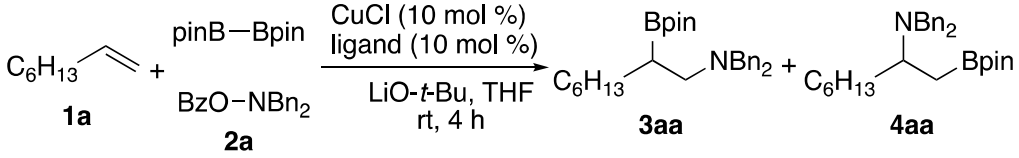


Results and Discussion

Table 1 summarizes ligand optimization studies, in conjunction with a CuCl catalyst and a LiO-*t*-Bu base, using 1-octene (**1a**), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (**2a**), and pinB–Bpin as model substrates. Entries 1 and 2 show our previous results in THF solvent: the use of IPr ligand gave high regioselectivity of **3aa**:**4aa** = 96:4 albeit with low yield (24% judged by ^{1}H NMR), whereas dppbz showed moderate regioselectivity (**3aa**:**4aa** = 69:31) and reaction efficiency (31% ^{1}H NMR yield).[4a] According to the works by Montgomery[5c] and Xiao and Fu,[5b] we initially tested IPr in CH_3CN solvent[6] and Cy-Xantphos in DMAc or THF solvent, but the satisfactory yield was not obtained (entries 3–5). On the other hand, the *o*-Me-dppbz ligand originally developed by Ito[5a] increased the yield to 55% with maintenance of good **3aa**:**4aa** selectivity (92:8; entry 6). Thus, we extensively investigated modified dppbz ligands.[7] While the introduction of electron-withdrawing F or CF_3 group resulted in lower regioselectivity and/or yield (entries 7–9), electron-donating groups generally improved the ratio of **3aa**:**4aa** (entries 10–12). Particularly, the substituents at the meta position dramatically increased the regioselectivity (entries 13–15), finally with electron-rich and bulky DTBM-dppbz proving to be optimal in view of both regioselectivtiy and yield (entry 16). The reaction under the previous optimal

conditions using the pre-formed IPrCuBr was unsuccessful, thus confirming the advantage of newly developed Cu(I)/DTBM-dppbz system (entry 17).

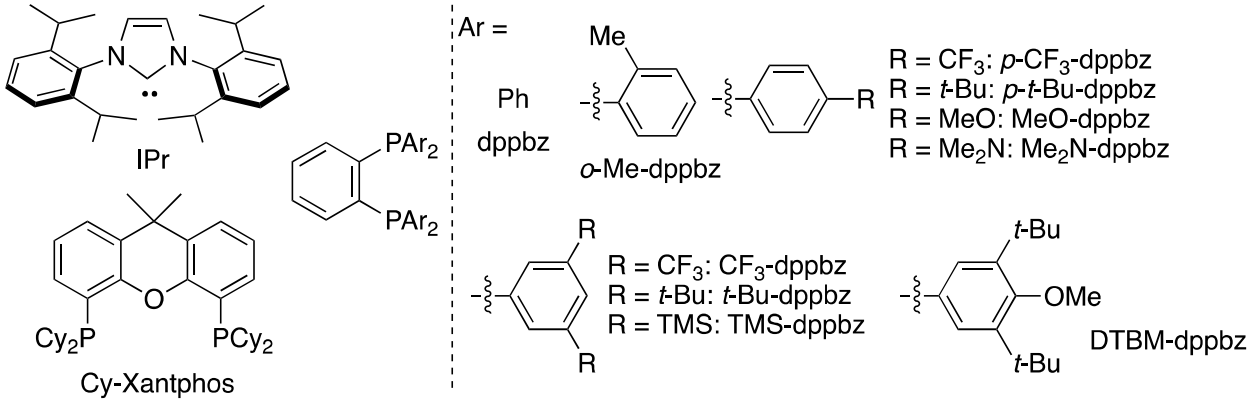
Table 1. Optimization for Copper-Catalyzed Internally Borylative Aminoboration of 1-Octene (1a) with *O*-Benzoyl-*N,N*-dibenzylhydroxylamine (2a) and Bis(pinacolato)diboron[a]



entry	ligand	solvent	yield (%)[b]	**3aa**:**4aa**[c]
1	IPr	THF	24	96:4
2	dppbz	THF	31	69:31
3	IPr	CH_3CN	12	64:37
4	Cy-Xantphos	DMAc	18	84:16
5	Cy-Xantphos	THF	7	82:18
6[d]	*o*-Me-dppbz	THF	55	92:8
7	*p*-CF_3-dppbz	THF	54	66:34
8	F_3-dppbz	THF	20	78:22
9	CF_3-dppbz	THF	30	50:50
10	*p*-*t*-Bu-dppbz	THF	64	73:27
11	MeO-dppbz	THF	52	77:23
12	Me_2N-dppbz	THF	37	81:19
13	TMS-dppbz	THF	62	87:13
14	*t*-Bu-dppbz	THF	30	91:9

15	DTBM-dppbz	THF	52	93:7
16[d]	DTBM-dppbz	THF	76 (60)	91:9 (92:8)
17[e]	IPrCuBr	THF	4	ca. 90:10

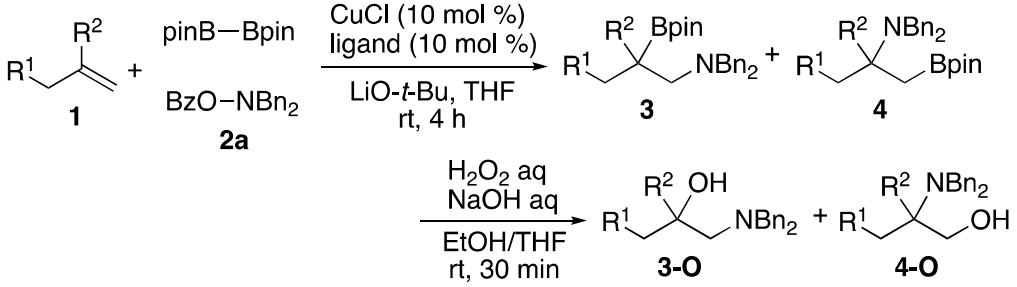
[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.38 mmol), pinB–Bpin (0.38 mmol), CuCl (0.025 mmol), ligand (0.025 mmol), LiO-*t*-Bu (0.75 mmol), solvent (1.5 mL), 4 h, rt, N_2. [b] ^{1}H NMR yield. Isolated yield is in parentheses. [c] Determined by ^{1}H NMR of the crude mixture. The ratio of isolated product in parentheses. [d] With **2a** (0.75 mmol), pinB–Bpin (0.75 mmol), and LiO-*t*-Bu (1.0 mmol). [e] With the pre-formed IPrCuBr instead of CuCl and ligand.

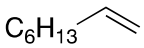
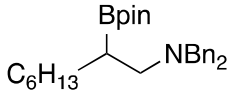
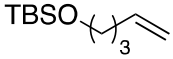
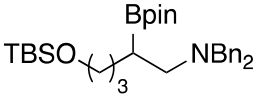


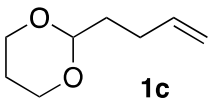
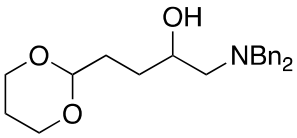
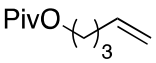
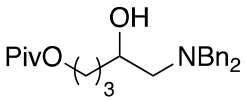
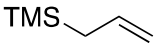
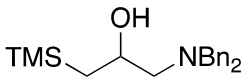
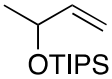
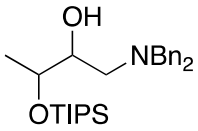
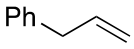
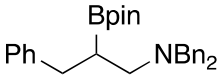
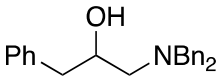
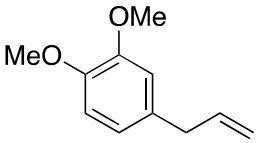
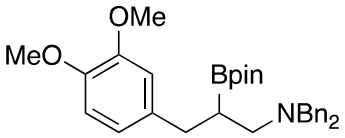
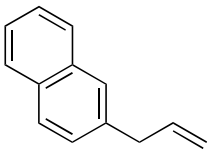
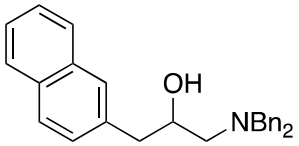
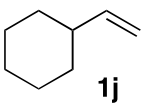
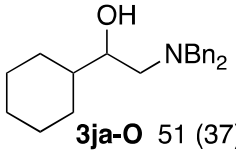
We next examined the scope of unactivated terminal alkenes with the hydroxylamine **2a** (Table 2). The CuCl/DTBM-dppbz catalysis could be applied to not only the simple terminal alkene **1a** (entry 1) but also functionalized alkenes including silyl ether **1b**, acetal **1c**, and pivaloyl ester **1d**, and the desired internally borylated products **3ba**–**3da** were formed with >90:10 regioselectivity (entries 2–4). In the cases of **1c** and **1d**, the aminoborated products **3ca** and **3da** were somewhat unstable for chromatographic purification and thus isolated as the corresponding aminoalcohols after oxidation with H_2O_2/NaOH aq. The reaction of **1a** could also be conducted on a 1.0 mmol scale with acceptable yield and regioselectivity, thus indicating the good reproducibility of this process (entry 1). Allylsilane **1e** and allylic alcohol derivative (**1f**) also provided high regioselectivity (>99:1) albeit with lower yields

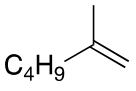
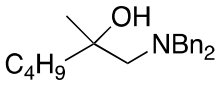
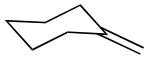
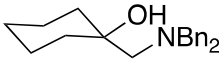
(entries 5 and 6). On the other hand, the relatively sterically demanding allylbenzene (**1g**) decreased the **3ga**:**4ga** ratio to 71:29 (entry 7). However, to our delight, the use of *o*-Me-dppbz improved the regioselectivity to 92:8 (entry 8). The *o*-Me-dppbz ligand also accommodated 3,4-dimethoxyallylbenzene (**1h**) and 2-allylnaphthalene (**1i**) (entries 9 and 10). Additionally, much bulkier vinylcyclohexene (**1j**) also underwent the aminoboration with 91:9 regioselectivity (entry 11). The observed high regioselectivity toward allylbenzenes and vinylcyclohexene deserves significant attention because the previous IPrCuBr catalysis only showed 83:17–87:13 regioselectivity.[4a] Particularly notable is the successful regioselective aminoboration of 1,1-disubstituted alkenes **1k** and **1l** by using the DTBM-dppbz ligand (entries 12 and 13): such *exo*-methylene-type substrates did not provide any aminoborated products at all under the first generation IPrCuBr catalysis.[4a]

Table 2. Copper-Catalyzed Internally Borylative Aminoboration of Various Unactivated Terminal Alkenes 1 with *O*-Benzoyl-*N,N*-dibenzylhydroxylamine (2a) and Bis(pinacolato)diboron[a]



entry	**1**	ligand	**3** or **3-O**, yield (%)[b], **3**:**4**[c]
1	 **1a**	DTBM-dppbz	 **3aa** 76 (60), 91:9 68 (56), 90:10[d]
2	 **1b**	DTBM-dppbz	 **3ba** 94 (70), 90:10

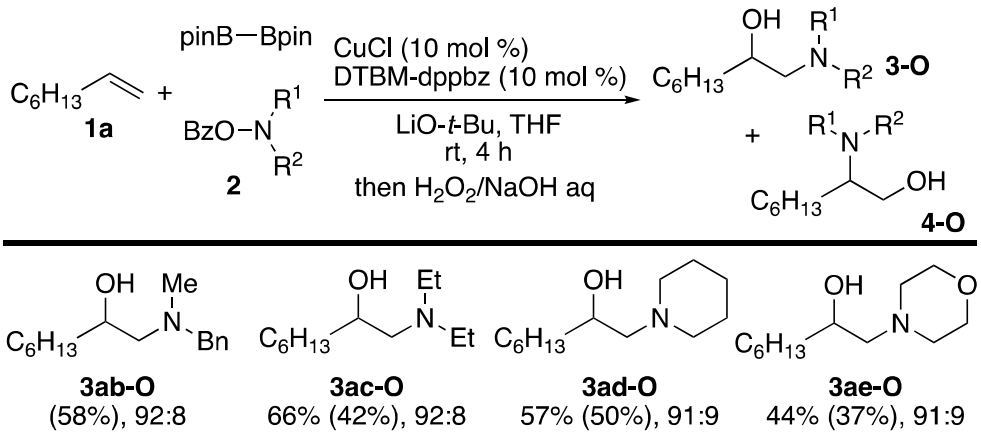
3	 **1c**	DTBM-dppbz	 **3ca-O** 86 (61), 90:10
4	 **1d**	DTBM-dppbz	 **3da-O** (51), 90:10
5	 **1e**	DTBM-dppbz	 **3ea-O** (31), >99:1
6	 **1f**	DTBM-dppbz	 **3fa-O** (22), >99:1[e]
7	 **1g**	DTBM-dppbz	 **3ga** 77, 71:29
8	**1g**	*o*-Me-dppbz	 **3ga-O** 56 (39), 92:8
9	 **1h**	*o*-Me-dppbz	 **3ha** (52), 93:7
10	 **1i**	*o*-Me-dppbz	 **3ia-O** 56 (34), 90:10
11	 **1j**	*o*-Me-dppbz	 **3ja-O** 51 (37), 91:9

12	 **1k**	DTBM-dppbz	 **3ka-O** 82 (60), 94:6
13	 **1l**	DTBM-dppbz	 **3la-O** (54), >99:1

[a] Reaction conditions: **1** (0.25 mmol), **2a** (0.75 mmol), pinB–Bpin (0.75 mmol), CuCl (0.025 mmol), ligand (0.025 mmol), LiO-*t*-Bu (1.0 mmol), THF (1.5 mL), 4 h, rt, N_2. [b] ^{1}H NMR yield of **3** (Bpin form). Isolated yields (**3** or **3-O**) are in parentheses. [c] The regioisomeric ratio of **3**:**4** was determined by ^{1}H NMR of the crude mixture. [d] 1.0 mmol scale. [e] 92:8 diastereomeric ratio. The relative stereochemistry was not determined.

The generality of hydroxylamines **2** was also briefly investigated with 1-octene (**1a**) (Scheme 2). The CuCl/DTBM-dppbz catalysis was compatible with other acyclic amines such as *N*-benzyl-*N*-methylamine (**3ab-O**) and *N,N*-diethylamine (**3ac-O**). The cyclic piperizine and morpholine were also viable substrates, and the desired aminoalcohol derivatives **3ad-O** and **3ae-O** were obtained in synthetically acceptable yield. Also in these cases, the regioselectivity was substantially high (**3**:**4** >91:9).

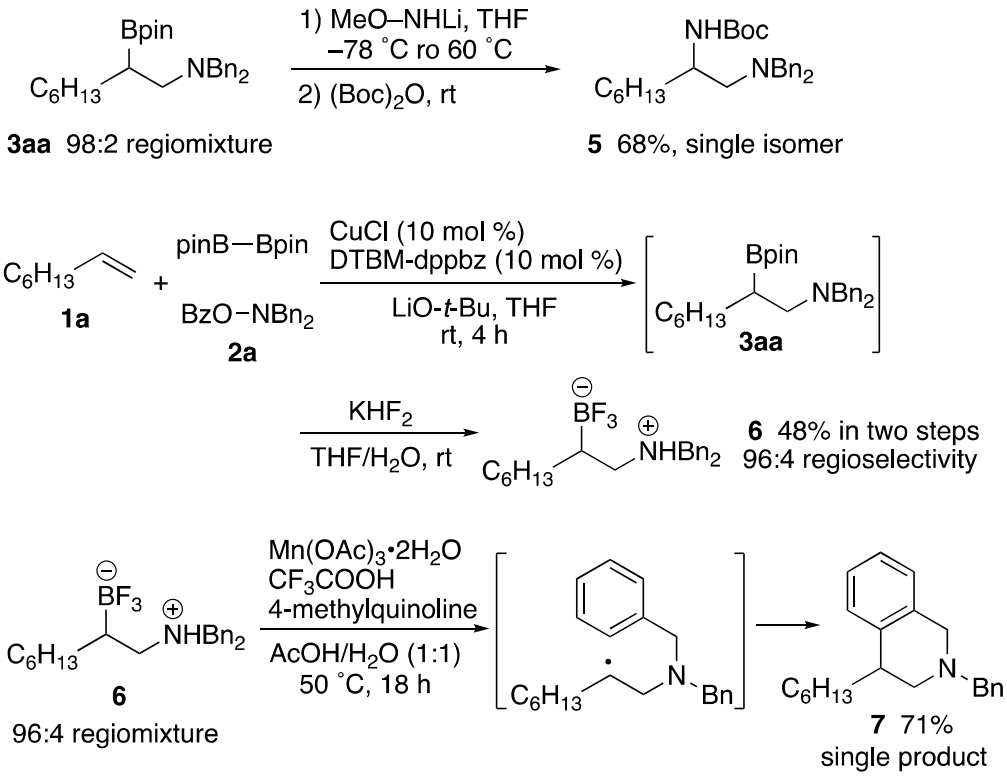
Scheme 2. Cu/DTBM-dppbz-Catalyzed Internally Borylative Aminoboration of 1-Octene (1a) with Several Hydroxylamines 2 and Bis(pinacolato)diboron[a]



[a] Reaction conditions: see footnote of Table 2. ^{1}H NMR yields of **3** (Bpin form) are given. Isolated yields of **3-O** are in parentheses. The regioisomeric ratio of **3**:**4** was determined by ^{1}H NMR.

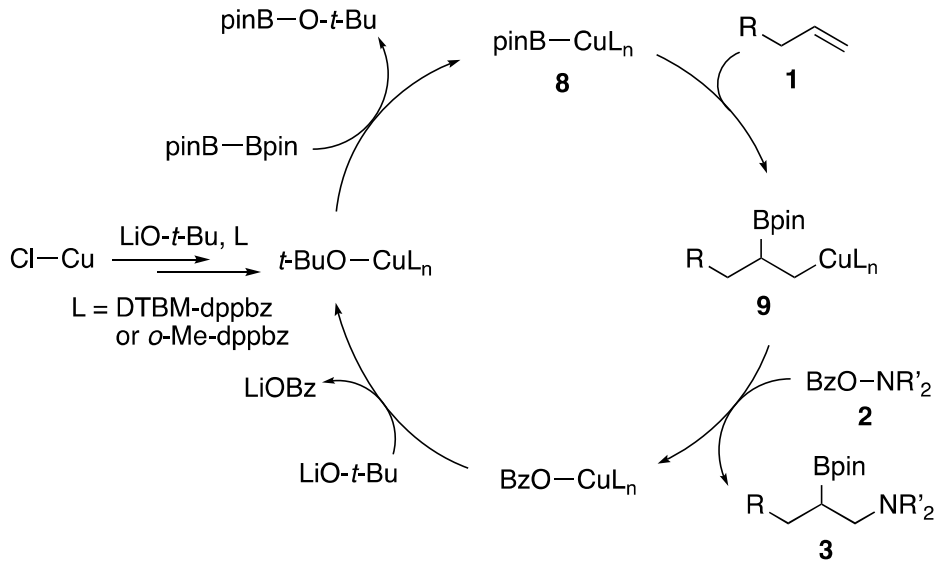
The Bpin moiety of **3aa** can be a useful synthetic handle (Scheme 3). Upon treatment with MeO-NHLi followed by $(Boc)_2O$,[8] **3aa** could be directly converted into the corresponding 1,2-diamine **5** without any additional deprotection of the boryl group. Additionally, the reaction of crude **3aa** with KHF_2 afforded the more stable internal ammonium borate salt **6** in 48% overall yield from 1-octene (**1a**).[9] This protocol is beneficial from the technical point of view because the borate **6** was readily purified by simple filtration without column chromatography. Furthermore, the Mn(III)-mediated oxidative radical cyclization of **6** proceeded to afford the tetrahydroisoquinoline framework **7** in 71% yield.[10]

Scheme 3. Transformation of Bpin moiety of 3aa



Although the mechanistic detail is unclear at present, the overall regioselectivity of aminoboration reaction can be determined in the insertion step of alkene **1** into the pinB–CuL_n intermediate **8**,[11] in which the more congested copper center is located at the terminal carbon (**9**; Scheme 4).[5,12] Subsequent C–N forming process[13] with the hydroxylamine **2** occurs to form the observed internally borylative aminoborated product **3**. The formed $Cu(OBz)L_n$ is again converted to **8** via $Cu(O\text{-}t\text{-}Bu)L_n$. The above assumption is consistent with the trend observed in Table 1: the ratio of **3**:**4** increased with increasing the size of ligand substituent. However, it cannot completely explain the decreased regioselectivity when the bulky *meta*-CF_3-substituted ligand (CF_3-dppbz) is employed (Table 1, entry 9). Thus, electronic effects[11b] are not negligible. Further studies are essential for the clarification of the mechanism.

Scheme 4. Plausible Mechanism



Conclusion

We have developed two Cu(I)/modified dppbz catalyst systems for regioselective aminoboration of unactivated terminal alkenes with bis(pinacolato)diboron. The bisphosphine-based catalysis allows the introduction of readily transformable Bpin group and shows better internally borylation regioselectivity for broader terminal alkenes. Moreover, the second generation catalyst is compatible with 1,1-disubstituted alkenes, which are inaccessible substrates under the IPrCuBr-based first generation catalysis. Further development of related electrophilic amination as well as alkene difunctionalization reactions is ongoing in our laboratory and will be reported in due course.

Experimental Section

Instrumentation and Chemicals ^{1}H, $^{13}C\{^{1}H\}$, ^{11}B, and $^{19}F\{^{1}H\}$ NMR spectra were recorded at 400 MHz, 100 MHz, 128 MHz, and 376 MHz, respectively, for $CDCl_3$ solutions. HRMS data were obtained by APCI or ESI using TOF. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Wako NH_2 Silica gel $60F_{254}$ or Merck silica gel $60F_{254}$. Silica gel (Wakogel $50NH_2$ or Wakosil C-200) was used for column chromatography. Gel permeation chromatography (GPC) was performed by by LC-20AR (pump, SHIMADZU, 7.5 mL/min EtOAc) and SPD-20A (UV

detector, SHIMADZU, 254 nm) with two in-line YMC-GPC T2000 (20 x 600 mm, particle size: 10 μm) (preparative columns, YMC, EtOAc eluent). Unless otherwise noted, materials obtained from commercial suppliers were used as received. Anhydrous THF was purchased and used out of the bottle without further purification. CuCl was washed sequentially with 1 M HCl aq., EtOH, and Et_2O three times at each step and dried under high vacuum for 6 h before use. Modified dppbz ligands were synthesized according to the literature.[7a,b,14] *O*-Benzoyl-*N,N*-diethylhydroxylamine **2c** was prepared by the condensation of diethylhydroxylamine and benzoyl chloride. Others were readily accessible through the nucleophilic substitution of the corresponding secondary amines with benzoyl peroxide.[15a,b] All reactions were carried out under nitrogen atmosphere unless otherwise noted.

The regiochemistry of **3aa** was determined by derivatization into the known diamine **5**.[4a] The isomers **4aa**, **4ba**, and **4ha** were already prepared and reported in our previous work.[4a] The regiochemistry of other aminoborated products was assigned by analogy.

Typical Procedure for Cu/DTBM-dppbz-Catalyzed Regioselective Aminoboration of Unactivated Terminal Alkenes with Bis(pinacolato)diboron. The synthesis of **3aa** is representative (Table 2, entry 1). CuCl (2.5 mg, 0.025 mmol), 1,2-bis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino)benzene (DTBM-dppbz, 25 mg, 0.025 mmol), and LiO*t*Bu (80 mg, 1.0 mmol) were placed in a 20 mL two-necked reaction flask, which was filled with nitrogen by using the Schlenk technique. THF (0.75 mL) was then added to the flask, and the suspension was stirred for 15 min at ambient temperature. A solution of 1-octene (**1a**, 28 mg, 0.25 mmol), bis(pinacolato)diboron (0.19 g, 0.75 mmol), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**, 0.24 g, 0.75 mmol) in THF (0.75 mL) were added dropwise. The solution was stirred at ambient temperature for additional 4 h. The resulting mixture was filtered through a short pad of sodium sulfate and neutral alumina. After evaporation of the volatile materials, the residue was purified by gel permeation chromatography (GPC) with ethyl acetate to yield a 91:9 mixture of *N*,*N*-dibenzyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-1-amine (**3aa**) and

N,*N*-dibenzyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-amine (**4aa**) in 60% combined yield (65 mg, 0.15 mmol).

A 91:9 Regiomixture of *N*,*N*-Dibenzyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-1-amine (3aa) and ***N*,*N*-Dibenzyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-amine** (**4aa**): oil; 65 mg, 60%; ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 0.76-0.81 (m, 0.09 x 1H for **4aa**), 0.87 (t, *J* = 6.8 Hz, 0.91 x 3H for **3aa**), 0.84-0.89 (m, 0.09 x 3H for **4aa**), 1.24 (s, 0.91 x 6H for **3aa**), 1.26 (s, 0.91 x 6H for **3aa**), 1.23-1.30 (m, 0.91 x 8H for **3aa**), 1.23-1.30 (m, 0.09 x 21H for **4aa**), 1.35-1.49 (m, 0.91 x 3H for **3aa**), 1.54-1.68 (m, 0.09 x 2H for **4aa**), 2.39 (dd, *J* = 7.0, 12.1 Hz, 0.91 x 1H for **3aa**), 2.58 (dd, *J* = 8.2, 12.1 Hz, 0.91 x 1H for **3aa**), 2.83-2.90 (m, 0.09 x 1H for **4aa**), 3.38 (d, *J* = 13.8 Hz, 0.09 x 2H for **4aa**), 3.45 (d, *J* = 13.7 Hz, 0.91 x 2H for **3aa**), 3.56 (d, *J* = 13.7 Hz, 0.91 x 2H for **3aa**), 3.64 (d, *J* = 13.8 Hz, 0.09 x 2H for **4aa**), 7.18-7.22 (m, 0.09 x 2H for **4aa**), 7.20 (d, *J* = 7.1 Hz, 0.91 x 2H for **3aa**), 7.25-7.30 (m, 0.09 x 4H for **4aa**), 7.28 (t, *J* = 7.1 Hz, 0.91 x 4H for **3aa**), 7.34 (d, *J* = 7.1 Hz, 0.91 x 4H for **3aa**), 7.32-7.38 (m, 0.09 x 4H for **4aa**); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) for mixture δ 15.7, 22.8, 24.7, 24.85, 24.89, 25.1, 29.1, 29.3, 29.4, 29.7, 29.8, 33.4, 56.1, 58.2, 82.9, 83.0, 126.6, 126.7, 128.1, 129.1, 129.2, 139.8 (All observed signals were shown because of the complexity associated with the regioisomer. The carbon signal bound to boron was not observed due to quadrupolar relaxation.); ^{11}B NMR (128 MHz, $CDCl_3$) for mixture δ 33.99; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{28}H_{43}BNO_2$, 436.3386. Found 436.3379.

A 90:10 Regiomixture of *N*,*N*-Dibenzyl-5-((*tert*-butyldimethylsilyl)oxy)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-1-amine (3ba) and *N*,*N*-Dibenzyl-5-((*tert*-butyldimethylsilyl)oxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-amine (4ba): oil; 91 mg, 70%; ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 0.01 (s, 0.10 x 6H for

4ba), 0.08 (s, 0.90 x 6H for **3ba**), 0.77-0.82 (m, 0.10 x 1H for **4ba**), 0.87 (s, 0.10 x 9H for **4ba**), 0.89 (s, 0.90 x 9H for **3ba**), 1.21-1.23 (m, 0.10 x 1H for **4ba**)1.23 (s, 0.10 x 6H for **4ba**), 1.24 (s, 0.90 x 6H for **3ba**), 1.25 (s, 0.90 x 6H for **3ba**), 1.26 (s, 0.10 x 6H for **4ba**), 1.33-1.51 (m, 0.90 x 5H for **3ba**), 1.33-1.51 (m, 0.10 x 3H for **4ba**), 1.69-1.79 (m, 0.10 x 1H for **4ba**), 2.40 (dd, *J* = 7.4, 12.2 Hz, 0.90 x 1H for **3ba**), 2.58 (dd, *J* = 8.2, 12.2 Hz, 0.90 x 1H for **3ba**), 2.82-2.89 (m, 0.10 x 1H for **4ba**), 3.38 (d, *J* = 13.7 Hz, 0.10 x 2H for **4ba**), 3.47 (d, *J* = 13.8 Hz, 0.90 x 2H for **3ba**), 3.55-3.58 (m, 0.10 x 2H for **4ba**), 3.55 (d, *J* = 13.8 Hz, 0.90 x 2H for **3ba**), 3.56 (t, *J* = 6.2 Hz, 0.90 x 2H for **3ba**), 3.65 (d, *J* = 13.7 Hz, 0.10 x 2H for **4ba**), 7.16-7.24 (m, 0.10 x 2H for **4ba**), 7.21 (d, *J* = 7.0 Hz, 0.90 x 2H for **3ba**), 7.23-7.30 (m, 0.10 x 4H for **4ba**), 7.27 (d, *J* = 7.0 Hz, 0.90 x 4H for **3ba**), 7.32-7.37 (m, 0.10 x 4H for **4ba**), 7.33 (d, *J* = 7.0 Hz, 0.90 x 4H for **3ba**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) for mixture δ -5.09, -5.08, 14.3, 18.5, 21.2, 24.7, 24.9, 25.05, 25.08, 25.6, 25.7, 26.2, 32.1, 32.6, 56.1, 58.2, 60.5, 63.7, 83.1, 126.65, 126.74, 128.1, 129.16, 129.20, 139.8 (All observed signals were shown because of the complexity associated with the regioisomer. The carbon signal bound to boron was not observed due to quadrupolar relaxation.); ^{11}B NMR (128 MHz, $CDCl_3$) for mixture δ 34.99; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{31}H_{51}BNO_3Si$, 524.3731. Found 524.3738.

Typical Procedure for Cu/*o*-Me-dppbz-Catalyzed Regioselective Aminoboration of Unactivated Terminal Alkenes with Bis(pinacolato)diboron. The synthesis of **3ha** is representative (Table 2, entry 7). CuCl (2.5 mg, 0.025 mmol), 1,2-bis(di-*o*-tolylphosphino)benzene (*o*-Me-dppbz, 13 mg, 0.025 mmol), and LiO*t*Bu (80 mg, 1.0 mmol) were placed in a 20 mL two-necked reaction flask, which was filled with nitrogen by using the Schlenk technique. THF (0.75 mL) was then added to the flask, and the suspension was stirred for 15 min at ambient temperature. A solution of 4-allyl-1,2-dimethoxybenzene (**1h**, 45 mg, 0.25 mmol), bis(pinacolato)diboron (0.19 g, 0.75 mmol), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**, 0.24 g, 0.75 mmol) in THF (0.75 mL) were added dropwise. The solution was stirred at ambient temperature for additional 4 h. The resulting mixture

was filtered through a short pad of sodium sulfate and neutral alumina. After evaporation of the volatile materials, the residue was purified by gel permeation chromatography (GPC) with ethyl acetate to yield a 93:7 mixture of *N,N*-dibenzyl-3-(3,4-dimethoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-amine (**3ha**) and *N,N*-dibenzyl-1-(3,4-dimethoxyphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-amine (**4ha**) in 52% combined yield (65 mg, 0.13 mmol).

A 93:7 Regiomixture of *N,N*-Dibenzyl-3-(3,4-dimethoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-amine (3ha) and *N,N*-Dibenzyl-1-(3,4-dimethoxyphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-amine (4ha): oil; 65 mg, 52%; ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 0.88-0.92 (m, 0.07 x 1H for **4ha**), 1.11 (s, 0.93 x 6H for **3ha**), 1.17 (s, 0.93 x 6H for **3ha**), 1.22 (s, 0.07 x 6H for **4ha**), 1.23 (s, 0.07 x 6H for **4ha**), 1.20-1.25 (m, 0.07 x 1H for **4ha**), 1.78-1.86 (m, 0.93 x 1H for **3ha**), 2.45 (dd, *J* = 7.5, 12.2 Hz, 0.93 x 1H for **3ha**), 2.50-2.60 (m, 0.07 x 1H for **4ha**), 2.52 (dd, *J* = 9.9, 13.7 Hz, 0.93 x 1H for **3ha**), 2.65 (dd, *J* = 8.8, 12.2 Hz, 0.93 x 1H for **3ha**), 2.79 (dd, *J* = 6.2, 13.7 Hz, 0.93 x 1H for **3ha**), 2.83-3.20 (m, 0.07 x 2H for **4ha**), 3.47 (d, *J* = 13.7 Hz, 0.93 x 2H for **3ha**), 3.52 (d, *J* = 14.2 Hz, 0.07 x 2H for **4ha**), 3.61 (d, *J* = 13.7 Hz, 0.93 x 2H for **3ha**), 3.66 (d, *J* = 14.2 Hz, 0.07 x 2H for **4ha**), 3.72 (s, 0.07 x 3H for **4ha**), 3.82 (s, 0.93 x 3H for **3ha**), 3.83 (s, 0.93 x 3H for **3ha**), 3.88 (s, 0.07 x 3H for **4ha**), 6.69-6.75 (m, 0.93 x 3H for **3ha**), 6.51-6.75 (m, 0.07 x 3H for **4ha**), 7.20 (d, *J* = 7.0 Hz, 0.93 x 2H for **3ha**), 7.18-7.23 (m, 0.07 x 6H for **4ha**), 7.28 (t, *J* = 7.0 Hz, 0.93 x 4H for **3ha**), 7.34 (d, *J* = 7.0 Hz, 0.93 x 4H for **3ha**), 7.24-7.30 (m, 0.07 x 4H for **4ha**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) for mixture δ 25.0, 25.1, 53.5, 55.8, 56.1, 58.3, 77.4, 83.2, 111.1, 112.2, 120.8, 126.8, 128.1, 129.2, 134.9, 139.6, 147.1, 148.6 (All observed signals were shown because of the complexity associated with the regioisomer. The carbon signal bound to boron was not observed due to quadrupolar relaxation.); ^{11}B NMR (128 MHz,

$CDCl_3$) for mixture δ 34.81; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{31}H_{41}BNO_4$, 502.3129. Found 502.3122.

Typical Procedure for Cu/Bisphosphine-Catalyzed Regioselective Aminoboration of Unactivated Terminal Alkenes with Bis(pinacolato)diboron followed by Oxidation with H_2O_2. The synthesis of **3ad-O** is representative (Scheme 2). CuCl (2.5 mg, 0.025 mmol), 1,2-bis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino)benzene (DTBM-dppbz, 25 mg, 0.025 mmol), and Li*O*tBu (80 mg, 1.0 mmol) were placed in a 20 mL two-necked reaction flask, which was filled with nitrogen by using the Schlenk technique. THF (0.75 mL) was then added to the flask, and the suspension was stirred for 15 min at ambient temperature. A solution of 1-octene (**1a**, 28 mg, 0.25 mmol), bis(pinacolato)diboron (0.19 g, 0.75 mmol), and piperidin-1-yl benzoate (**2d**, 0.15 g, 0.75 mmol) in THF (0.75 mL) were added dropwise. The solution was stirred at ambient temperature for additional 4 h. The resulting mixture was quenched with water and then extracted with ethyl acetate three times. The combined organic layer was dried over sodium sulfate and concentrated in vacuo. The residual materials were dissolved in THF/EtOH (1.0 mL/0.5 mL), and NaOH aq. (3.0 M, 0.50 mL) and H_2O_2 aq. (30%, 0.50 mL) were added in one portion. The resulting mixture was stirred for 30 min under air. The reaction was quenched with sat. $Na_2S_2O_3$ aq. The mixture was extracted with Et_2O three times. The combined organic layer was dried over sodium sulfate and concentrated in vacuo. The residue was purified by NH_2 silica gel column chromatography with hexane/ethyl acetate (5:1, v/v) as an eluent to give a 91:9 mixture of 1-(piperidin-1-yl)octan-2-ol (**3ad-O**) and 2-(piperidin-1-yl)octan-1-ol (**4ad-O**) in 50% overall yield (31 mg, 0.13 mmol).

A 91:9 Regiomixture of 1-(Piperidin-1-yl)octan-2-ol (3ad-O) and 2-(Piperidin-1-yl)octan-1-ol (4ad-O): oil; 27 mg, 50%; ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 0.88 (t, J = 6.9 Hz, 0.91 x 3H for **3ad-O**), 0.86-0.90 (m, 0.09 x 3H for **4ad-O**), 1.26-1.36 (m, 0.91 x 10H for **3ad-O**), 1.26-1.36 (m, 0.09 x 10H for **4ad-O**), 1.39-1.48 (m, 0.91 x 4H for **3ad-O**), 1.39-1.48 (m, 0.09 x 4H for **4ad-O**), 1.51-1.64

(m, 0.91 x 4H for **3ad-O**), 1.51-1.64 (m, 0.09 x 4H for **4ad-O**), 2.17 (dd, *J* = 10.6, 12.2 Hz, 0.91 x 1H for **3ad-O**), 2.27 (dd, *J* = 3.1, 12.2 Hz, 0.91 x 1H for **3ad-O**), 2.27-2.36 (m, 0.09 x 2H for **4ad-O**), 2.53-2.66 (m, 0.91 x 2H for **3ad-O**), 2.53-2.66 (m, 0.09 x 1H for **4ad-O**), 3.19 (dd, *J* = 10.2, 10.7 Hz, 0.09 x 1H for **4ad-O**), 3.48 (dd, *J* = 5.3, 10.2 Hz, 0.09 x 1H for **4ad-O**), 3.64 (m, 0.91 x 1H for **3ad-O**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) for mixture δ 14.2, 22.8, 24.5, 25.8, 26.3, 29.6, 32.0, 35.2, 54.8, 65.0, 66.2 (All observed signals were shown because of the complexity associated with the regioisomer.); HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{13}H_{28}NO$, 214.2165. Found 214.2165.

A 90:10 Regiomixture of 1-(Dibenzylamino)-4-(1,3-dioxan-2-yl)butan-2-ol (3ca-O) and 2-(Dibenzylamino)-4-(1,3-dioxan-2-yl)butan-1-ol (4ca-O): oil; 54 mg, 61%; ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 1.28-1.34 (m, 0.90 x 1H for **3ca-O**), 1.28-1.34 (m, 0.10 x 1H for **4ca-O**), 1.34-1.51 (m, 0.90 x 2H for **3ca-O**), 1.34-1.51 (m, 0.10 x 2H for **4ca-O**), 1.55-1.67 (m, 0.90 x 1H for **3ca-O**), 1.55-1.67 (m, 0.10 x 1H for **4ca-O**), 1.69-1.78 (m, 0.90 x 1H for **3ca-O**), 1.69-1.78 (m, 0.10 x 1H for **4ca-O**), 1.83-1.94 (m, 0.10 x 1H for **4ca-O**), 1.98-2.16 (m, 0.90 x 1H for **3ca-O**), 2.43 (dd, *J* = 5.6, 8.8 Hz, 0.90 x 2H for **3ca-O**), 2.79-2.82 (m, 0.10 x 1H for **4ca-O**), 3.39 (d, *J* = 13.4 Hz, 0.90 x 2H for **3ca-O**), 3.41-3.54 (m, 0.10 x 4H for **4ca-O**), 3.66-3.77 (m, 0.90 x 3H for **3ca-O**), 3.66 -3.77 (m, 0.10 x 3H for **4ca-O**), 3.82 (d, *J* = 13.4 Hz, 0.90 x 2H for **3ca-O**), 3.79-3.86 (m, 0.10 x 2H for **4ca-O**), 4.08 (dd, *J* = 1.0, 5.0 Hz, 0.90 x 2H for **3ca-O**), 4.04-4.15 (m, 0.10 x 2H for **4ca-O**), 4.49 (t, *J* = 5.0 Hz, 0.90 x 1H for **3ca-O**), 7.23-7.36 (m, 0.90 x 10H for **3ca-O**), 7.23-.7.36 (m, 0.10 x 10H for **4ca-O**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) for mixture δ 19.4, 25.9, 29.1, 31.3, 31.4, 32.6, 53.2, 58.5, 59.7, 60.9, 61.2, 66.8, 67.0, 101.9, 102.2, 127.4, 128.5, 128.6, 129.2, 138.5, 139.4 (All observed signals were shown because of the complexity associated with the regioisomer.); HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{22}H_{30}NO_3$, 356.2220. Found 356.2213.

5-(Dibenzylamino)-4-hydroxypentyl pivalate (3da-O): oil; 49 mg, 51%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 9H), 1.29–1.41 (m, 2H), 1.59–1.68 (m, 1H), 1.68–1.82 (m, 1H), 2.43 (dd, *J* = 3.8, 7.1

Hz, 2H), 3.34 (bs, 1H), 3.34 (d, *J* = 13.4 Hz, 2H), 3.67-3.73 (m, 1H), 3.84 (d, *J* = 13.4 Hz, 2H), 3.98-4.08 (m, 2H), 7.24-7.35 (m, 10H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 25.0, 27.3, 31.1, 38.8, 58.5, 59.8, 64.4, 66.6, 127.4, 128.6, 129.1, 138.5, 178.7; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{24}H_{34}NO_3$, 384.2533. Found 384.2527.

1-(Dibenzylamino)-3-(trimethylsilyl)propan-2-ol (3ea-O): oil; 25 mg, 31%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 9H), 0.57 (dd, *J* = 6.1, 14.5 Hz, 1H), 0.74 (dd, *J* = 7.6, 14.5 Hz, 1H), 2.41 (d, *J* = 5.8 Hz, 2H), 3.40 (d, *J* = 13.5 Hz, 2H), 3.77-3.83 (m, 1H), 3.83 (d, *J* = 13.5 Hz, 2H), 7.24-7.35 (m, 10H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ -0.5, 23.0, 58.7, 63.0, 65.2, 127.4, 128.6, 129.2, 138.7; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{29}H_{30}NOSi$, 328.2091. Found 328.2086.

1-(Dibenzylamino)-3-((triisopropylsilyl)oxy)butan-2-ol (3fa-O): An amount of minor diastereomer was quite small, and thus we could not assign all ^{1}H NMR signals because of low intensity; oil; 25 mg, 31%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 9H), 0.57 (dd, *J* = 6.1, 14.5 Hz, 1H), 0.74 (dd, *J* = 7.6, 14.5 Hz, 1H), 2.41 (d, *J* = 5.8 Hz, 2H), 3.40 (d, *J* = 13.5 Hz, 2H), 3.77-3.83 (m, 1H), 3.83 (d, *J* = 13.5 Hz, 2H), 7.24-7.35 (m, 10H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ -0.5, 23.0, 58.7, 63.0, 65.2, 127.4, 128.6, 129.2, 138.7; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{29}H_{30}NOSi$, 328.2091. Found 328.2086.

1-(Dibenzylamino)-3-phenylpropan-2-ol (3ga-O): oil; 32 mg, 39%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (dd, *J* = 4.4, 12.6 Hz, 1H), 2.50 (dd, *J* = 8.8, 12.6 Hz, 1H), 2.58 (dd, *J* = 5.7, 13.6 Hz, 1H), 2.73 (dd, *J* = 7.2, 13.6 Hz, 1H), 3.31 (bs, 1H), 3.37 (d, *J* = 13.4 Hz, 2H), 3.80 (d, *J* = 13.4 Hz, 2H), 3.90-3.97 (m, 1H), 7.16-7.34 (m, 15H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 41.4, 58.5, 59.3, 68.4, 126.4, 127.4, 128.5, 128.6, 129.1, 129.2, 129.4, 138.6; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{23}H_{26}NO$, 332.2009. Found 332.1998.

1-(Dibenzylamino)-3-(naphthalen-2-yl)propan-2-ol (3ia-O): oil; 32 mg, 37%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47-2.57 (m, 2H), 2.75 (dd, *J* = 7.0, 13.7 Hz, 1H), 2.89 (dd, *J* = 7.0, 13.7 Hz, 1H), 3.39 (d, *J* = 13.4 Hz, 2H), 3.80 (d, *J* = 13.4 Hz, 2H), 3.99-4.06 (m, 1H), 7.24-7.32 (m, 12H), 7.41-7.45 (m, 2H), 7.47 (s, 1H), 7.60-7.81 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 41.5, 58.3, 59.2, 68.1, 125.4, 126.0, 127.4, 127.66, 127.71, 127.9, 128.0, 128.6, 128.8, 129.2, 132.3, 133.6, 136.1, 138.5.; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{27}H_{28}NO$, 382.2165. Found 382.2160.

1-Cyclohexyl-2-(dibenzylamino)ethan-1-ol (3ja-O): oil; 30 mg, 37%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88-1.02 (m, 2H), 1.07-1.27 (m, 4H), 1.55 (d, *J* = 12.9 Hz, 1H), 1.06-1.64 (m, 1H), 1.67-1.73 (m, 2H), 1.83 (d, *J* = 12.9 Hz, 1H), 2.47 (m, 2H), 3.35 (d, *J* = 13.4 Hz, 2H), 3.46 (ddd, *J* = 2.1, 6.6, 11.7 Hz, 1H), 3.53 (bs, 1H), 3.87 (d, *J* = 13.4 Hz, 2H), 7.24-7.35 (m, 10H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 26.1, 26.2, 26.7, 28.7, 29.0, 42.3, 57.3, 58.3, 70.7, 127.4, 128.6, 129.2, 138.5; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{22}H_{30}NO$, 324.2322. Found 324.2325.

1-(Dibenzylamino)-2-methylhexan-2-ol (3ka-O): oil; 47 mg, 60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, *J* = 7.3 Hz, 3H), 1.06 (s, 3H), 1.10-1.25 (m, 4H), 1.33-1.38 (m, 2H), 2.51 (d, *J* = 13.8 Hz, 1H), 2.51 (bs, 1H), 2.60 (d, *J* = 13.8 Hz, 1H), 3.66 (d, *J* = 13.6 Hz, 2H), 3.70 (d, *J* = 13.6 Hz, 2H), 7.23-7.28 (m, 2H), 7.30-7.34 (m, 8H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 14.2, 23.5, 26.0, 26.1, 41.0, 60.6, 63.0, 72.2, 127.3, 128.5, 129.2, 139.5; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{21}H_{30}NO$, 312.2322. Found 312.2323.

1-((Dibenzylamino)methyl)cyclohexan-1-ol (3la-O): oil; 42 mg, 54%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28–1.29 (m, 3H), 1.33–1.39 (m, 2H), 1.46–1.61 (m, 5H), 2.55 (s, 2H), 2.66 (bs, 1H), 3.68 (s, 4H), 7.23-7.28 (m, 2H), 7.30-7.34 (m, 8H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 22.3, 26.0, 37.1, 60.7, 63.6, 70.7, 127.3, 128.5, 129.2, 139.4; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{21}H_{28}NO$, 310.2165. Found 310.2159.

A 92:8 Regiomixture of 1-(Benzyl(methyl)amino)octan-2-ol (3ab-O) and 2-(Denzyl(methyl)amino)octan-1-ol (4ab-O): oil; 36 mg, 58%; ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 0. 87 (t, *J* = 7.0 Hz, 0.92 x 3H for **3ab-O**), 0.86-0.90 (m, 0.08 x 3H for **4ab-O**), 1.28-1.40 (m, 0.92 x 8H for **3ab-O**), 1.28-1.40 (m, 0.08 x 8H for **4ab-O**), 1.42-1.47 (m, 0.92 x 2H for **3ab-O**), 1.42-1.47 (m, 0.08 x 2H for **4ab-O**), 2.18 (s, 0.08 x 3H for **4ab-O**), 2.24 (s, 0.92 x 3H for **3ab-O**), 2.34 (dd, *J* = 3.3, 12.3 Hz, 0.92 x 1H for **3ab-O**), 2.41 (dd, *J* = 10.2, 12.3 Hz, 0.92 x 1H for **3ab-O**), 2.77-2.83 (m, 0.08 x 1H for **4ab-O**), 3.31-3.37 (m, 0.08 x 2H for **4ab-O**), 3.46 (d, *J* = 13.1 Hz, 0.92 x 1H for **3ab-O**), 3.57 (dd, *J* = 4.9, 10.6 Hz, 0.08 x 1H for **4ab-O**), 3.70 (d, *J* = 13.1 Hz, 0.92 x 1H for **3ab-O**), 3.67-3.74 (m, 0.92 x 1H for **3ab-O**), 3.67-3.74 (m, 0.08 x 2H for **4ab-O**), 7.25-7.35 (m, 0.92 x 5H for **3ab-O**), 7.25-7.35 (m, 0.08 x 5H for **4ab-O**); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) for mixture δ 11.1, 14.2, 22.7, 23.9, 25.8, 28.5, 29.6, 31.9, 33.4, 35.0, 38.9, 42.1, 51.0, 62.6, 63.6, 66.9, 127.2, 127.3, 127.7, 128.3, 128.5, 129.0, 129.1, 129.8 (All observed signals were shown because of the complexity associated with the regioisomer.); HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{16}H_{28}NO$, 250.2165. Found 250.2162.

A 92:8 Regiomixture of 1-(Diethylamino)octan-2-ol (3ac-O) and 2-(Diethylamino)octan-1-ol (4ac-O): oil; 21 mg, 42%; ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 0.88 (t, *J* = 7.0 Hz, 0.92 x 3H for **3ac-O**), 1.02-1.04 (m, 0.08 x 3H for **4ac-O**), 1.02 (t, *J* = 7.1 Hz, 0.92 x 6H for **3ac-O**), 1.04 (t, *J* = 7.0 Hz, 0.08 x 6H for **4ac-O**), 1.25-1.37 (m, 0.92 x 8H for **3ac-O**), 1.25-1.37 (m, 0.08 x 8H for **4ac-O**), 1.39-1.55 (m, 0.92 x 2H for **3ac-O**), 1.39-1.55 (m, 0.08 x 2H for **4ac-O**), 2.20 (dd, *J* = 10.6, 12.5 Hz, 0.92 x 1H for **3ac-O**), 2.40 (dd, *J* = 3.1, 12.5 Hz, 0.92 x 1H for **3ac-O**), 2.39-2.42 (m, 0.08 x 2H for **4ac-O**), 2.42-2.51 (m, 0.92 x 2H for **3ac-O**), 2.57-2.68 (m, 0.08 x 2H for **4ac-O**), 2.57-2.68 (m, 0.92 x 2H for **3ac-O**), 2.73-2.80 (m, 0.08 x 1H for **4ac-O**), 3.15 (dd, *J* = 10.1, 10.6 Hz, 0.08 x 1H for **4ac-O**), 3.49 (dd, *J* = 5.2, 10.1 Hz, 0.08 x 1H for **4ac-O**), 3.53-3.59 (m, 0.92 x 1H for **3ac-O**), 3.82 (bs, 0.92 x 1H for **3ac-O**); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) for mixture δ 12.2, 14.2, 14.9, 22.8, 25.9, 29.7, 29.8,

32.0, 35.2, 43.2, 47.1, 59.7, 66.9 (All observed signals were shown because of the complexity associated with the regioisomer.); HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{12}H_{28}NO$, 202.2165. Found 202.2167.

A 91:9 Regiomixture of 1-Morpholinooctan-2-ol (3ae-O) and 2-Morpholinooctan-1-ol (4ae-O): oil; 20 mg, 37%; ^1H NMR (400 MHz, $CDCl_3$) for mixture δ 0.88 (t, *J* = 6.8 Hz, 0.91 x 3H for **3ae-O**), 0.86-0.91 (m, 0.09 x 3H for **4ae-O**), 1.26-1.40 (m, 0.91 x 8H for **3ae-O**), 1.26-1.40 (m, 0.09 x 8H for **4ae-O**), 1.41-1.51 (m, 0.09 x 2H for **4ae-O**), 1.41-1.51 (m, 0.91 x 2H for **3ae-O**), 2.25 (dd, *J* = 10.5, 12.3 Hz, 0.91 x 1H for **3ae-O**), 2.22-2.78 (m, 0.09 x 1H for **4ae-O**), 2.34 (dd, *J* = 3.0, 12.3 Hz, 0.91 x 1H for **3ae-O**), 2.30-2.35 (m, 0.09 x 1H for **4ae-O**), 2.36-2.42 (m, 0.09 x 2H for **4ae-O**), 2.38 (d, *J* = 6.6 Hz, 0.91 x 2H for **3ae-O**), 2.65 (d, *J* = 6.6 Hz, 0.91 x 2H for **3ae-O**), 2.63-2.76 (m, 0.09 x 2H for **4ae-O**), 2.74-2.77 (m, 0.09 x 1H for **4ae-O**), 3.39 (bs, 0.91 x 1H for **3ae-O**), 3.66-3.76 (m, 0.91 x 5H for **3ae-O**), 3.66-3.76 (m, 0.09 x 4H for **4ae-O**); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) for mixture δ 14.21, 14.24, 22.7, 22.8, 24.5, 25.7, 29.6, 31.7, 31.9, 35.0, 53.8, 64.9, 66.1, 67.2 (All observed signals were shown because of the complexity associated with the regioisomer.); HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{12}H_{26}NO_2$, 216.1958. Found 216.1956.

Procedure for Amination of 3aa (Scheme 3). *O*-Methylhydroxylamine (1.2 M THF solution, 0.5 mL, 0.6 mmol) in THF (1.3 mL) was placed in a 20 mL two-necked reaction flask, which was flushed with nitrogen. BuLi (1.6 M hexane solution, 0.4 mL, 0.6 mmol) was added to the flask at –78 °C, and the suspension was stirred for 30 min at the same temperature. A THF (0.8 mL) solution of a 98:2 regiomixture of *N*,*N*-dibenzyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-1-amine (**3aa**) and *N*,*N*-dibenzyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-amine (**4aa**) (44 mg, 0.1 mmol) was then added dropwise to the solution, and the solution was then stirred at 60 °C for 24 h. The resulting mixture was allowed to cool to room temperature, and Boc_2O (0.13 g, 0.6 mmol) was then added dropwise via a syringe. After being stirred at room temperature for additional 2 h, the resulting mixture was quenched with water. The mixture was extracted with ethyl acetate, and the combined

organic layer was dried over sodium sulfate. Concentration in vacuo and purification by silica gel column chromatography with hexane/ethyl acetate (10:1, v/v) gave *tert*-butyl (1-(dibenzylamino)octan-2-yl)carbamate (**5**, 29 mg, 0.07 mmol) in 68% yield.

***tert*-Butyl (1-(dibenzylamino)octan-2-yl)carbamate (5):** oil; 29 mg, 68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 6.7 Hz, 3H), 1.22-1.27 (m, 10H), 1.48 (s, 9H), 2.30-2.39 (m, 2H), 3.47 (d, J = 13.4 Hz, 2H), 3.63 (d, J = 13.4 Hz, 2H), 3.76-3.79 (m, 1H), 4.25 (bs, 1H), 7.21-7.35 (m, 10H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 14.2, 22.7, 25.6, 28.6, 29.4, 31.9, 33.8, 48.7, 57.9, 58.7, 78.9, 127.1, 128.3, 129.2, 139.6, 156.1; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{27}H_{41}N_2O_2$, 425.3163. Found 425.3165.

Procedure for Synthesis of Internal Ammonium Borate Salt 6 (Scheme 3). The catalytic aminoboration was conducted with 1-octene (**1a**, 28 mg, 0.25 mmol) and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**, 0.24 g, 0.75 mmol) under the above standard conditions. The crude aminoborated product was dissolved in THF/H_2O (1.3/0.3 mL), and KHF_2 (156 mg, 2.0 mmol) was added. After the resulting mixture was stirred at ambient temperature for 2 h, the mixture was concentrated in vacuo. The dried solids were triturated with acetone and filtered to remove inorganic salts. The resulting filtrate was concentrated, and the residual solids was collected and rinsed with Et_2O to give a 96:4 mixture of (1-(dibenzylammonio)octyl)trifluoroborate (**6**) and (2-(dibenzylammonio)octyl)trifluoroborate (**6'**) in 48% overall yield (45 mg, 0.12 mmol).

A 96:4 Regiomixture of (1-(Dibenzylammonio)octan-2-yl)trifluoroborate (6) and (2-(Dibenzylammonio)octyl)trifluoroborate (6'): light yellow solid; 126-129 ^{o}C; 45 mg, 48% overall yield; ^{1}H NMR (400 MHz, $CDCl_3$) for major isomer **6** δ 0.86 (t, J = 7.0 Hz, 3H), 0.89-0.96 (m, 1H), 1.02-1.11 (m, 1H), 1.19-1.31 (m, 8H), 1.55-1.63 (m, 1H), 3.01-3.06 (m, 1H), 3.20 (dd, J = 11.5, 13.0 Hz, 1H), 3.96 (d, J = 13.3 Hz, 1H), 3.99 (d, J = 13.3 Hz, 1H), 4.22 (d, J = 13.2 Hz, 1H), 4.57 (d, J = 13.2 Hz, 1H), 7.29-7.34 (m, 2H), 7.44-7.47 (m, 3H), 7.47-7.51 (m, 5H), 8.19 (bs, 1H) (An amount of

minor regioisomer **6'** was quite small, and thus we could not assign all ^{1}H NMR signals because of low intensity); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) for mixture δ 14.3, 22.9, 28.9, 29.9, 32.0, 56.7, 58.6, 60.0, 129.0, 129.8, 129.9, 130.0, 130.47, 130.52, 130.6 (All observed signals were shown because of the complexity associated with the regioisomer. The carbon signal bound to boron was not observed due to quadrupolar relaxation.); ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.92.; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -141.58, -135.77; HRMS (ESI) m/z ($[M-F]^+$) calcd for $C_{22}H_{31}BF_2N$, 358.2516. found 358.2512.

Procedure for Mn(III)-Mediated Oxidative Radical Cyclization of 6 to 7 (Scheme 3). A 96:4 mixture of (1-(dibenzylammonio)octyl)trifluoroborate (**6**) and (2-(dibenzylammonio)octyl)trifluoroborate (**6'**) (38 mg, 0.1 mmol) was placed in a 20 mL two-necked reaction flask, which was filled with nitrogen by using the Schlenk technique. AcOH (1.0 ml), water (1.0 mL), 4-methylquinoline (14 mg, 0.1 mmol), and trifluoroacetic acid (0.1 mmol, 7.7 μL) were then added to the flask, and the resulting mixture was stirred at room temperature until complete dissolution then manganese(III) acetate (0.3 mmol, 58 mg) was added in one portion. The mixture was stirred at 50 °C for 18 h. After cooling to room temperature, the mixture was slowly added to a saturated Na_2CO_3 aq. (20 mL). The aqueous layer was then extracted with EtOAc three times. The organic layers were washed with water then dried (Na_2SO_4), filtered, and concentrated in vacuo, and purification by NH_2 silica gel column chromatography with hexane/ethyl acetate (20:1, v/v) gave 2-benzyl-4-hexyl-1,2,3,4-tetrahydroisoquinoline (**7**, 22 mg, 0.07 mmol) in 71% yield.

2-Benzyl-4-hexyl-1,2,3,4-tetrahydroisoquinoline (7): oil; 22 mg, 71%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.1 Hz, 3H), 1.20-1.32 (m, 8H), 1.63-1.68 (m, 1H), 1.72-1.82 (m, 1H), 2.57 (dd, *J* = 4.1, 11.6 Hz, 1H), 2.68 (dd, *J* = 4.1, 11.6 Hz, 1H), 2.73-2.79 (m, 1H), 3.48 (d, *J* = 14.7 Hz, 1H), 3.55 (d, *J* = 12.8 Hz, 1H), 3.73 (d, *J* = 12.8 Hz, 1H), 3.74 (d, *J* = 14.7 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 7.07-7.12 (m, 1H), 7.14-7.18 (m, 2H), 7.26 (d, *J* = 7.0 Hz, 1H), 7.33 (t, *J* = 7.0 Hz, 2H), 7.39 (d, *J* = 7.0 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 14.3, 22.8, 27.6, 29.7, 32.0, 36.2, 38.9, 54.4, 57.0, 63.0, 125.6,

126.2, 126.5, 127.1, 128.35, 128.41, 129.1, 135.0, 138.9, 139.7; HRMS (APCI) *m/z* $(M+H)^+$ Calcd for $C_{22}H_{30}N$, 308.2373. Found 308.2375.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publication website at DOI: 10.1021/acs.joc.xxxx.

^1H, $^{13}C\{^1H\}$, ^{11}B, and $^{19}F\{^1H\}$ NMR spectra for products and kinetic profiles (PDF)

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Notes

The authors declare no competing financial interest.

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