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Highly efficient substitution of allylic picolinates with copper reagents derived from aryl-, alkenyl-, furyl-, and thienyl-lithiums

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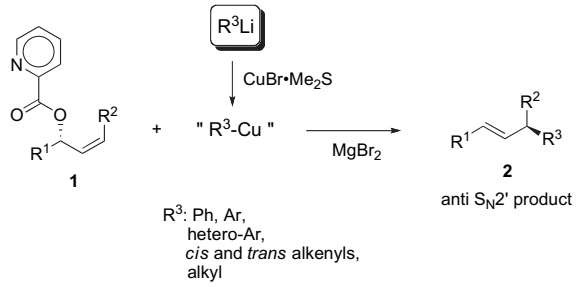
ABSTRACT

Substitution of optically active allylic picolinate, *cis* R^1-CH(OC(O)(2-Py))CH=CHR^2 (R^1=$(CH_2)_2$Ph, R^2=CH_2OTBS), with phenylcopper reagents derived from salt free PhLi (2 equiv) and CuBr·Me_2S (2 and 1 equiv, respectively) was highly promoted by $MgBr_2$ (3 equiv), producing *anti* S_N2' product regio- and stereoselectively. This reagent system was proven to be general with several picolinates (R^1, R^2: $Ph(CH_2)_2$, $PMBO(CH_2)_3$, Me, $TBSOCH_2$, $PMBOCH_2$, *c*-Hex). Furthermore, aryl copper reagents prepared from ArLi, which was in turn prepared by Li–halogen exchange, was proven to be compatible with the substitution in the presence of larger quantity of $MgBr_2$ than that of LiX coproduced by the exchange. Substitution was not interfered with the steric hindrance on aryl coppers (Ar: 2-$MeOC_6H_4$, 2,6-$(MOMO)_2$-4-MeC_6H_2, 2,6-$Me_2C_6H_3$, etc.). Similarly, stereodefined *cis* and *trans* alkenyl, furyl, and thienyl reagents gave the corresponding *anti* S_N2' products efficiently.

1. Introduction

Allylic substitution of secondary allylic alcohol derivatives with organocopper reagents is a potentially useful tool to create chiral carbon center by C–C bond formation.[1] Although copper reagents prefer *anti* S_N2' pathway,[2] regio- and stereoselectivities are generally dependent on the potency of a leaving group, nucleophilicity of copper reagent, and electronic/steric factors of reagents and the allylic moiety. To attain high selectivity, several excellent leaving groups such as *o*-$(Ph_2P)C_6H_4CO_2$,[3] *o*-$(Ph_2P{=}O)C_6H_4CO_2$,[4] $C_6F_5CO_2$,[5] $(RO)_2P(O)O$[6] have been developed. Unfortunately, the potency of these groups was insufficient for aryl and alkenyl copper reagents that are less nucleophilic than alkyl reagents. Recently, we have introduced the picolinoxy leaving group, which showed high reactivity toward aryl and alkenyl copper reagents derived from Grignard reagents.[7] We then turned our attention to organolithium-based copper reagents with expectation of that the scope of copper reagents for the allylic substitution would be expanded with the various preparations of RLi such as halogen–lithium exchange, *ortho* lithiation, and direct lithiation. Preliminary study along this line was published as a communication.[8] Herein, we report a full account of the study, focusing on synthetic advantage of the lithium strategy (Scheme 1).



Scheme 1. Allylic substitution of picolinates.
Although the (*S*) chirality is drawn for **1**, a (*R*) isomer is used in some cases.

2. Results and discussion

Salt free PhLi[9] (2 equiv per picolinate) was mixed with different quantities of CuBr·Me_2S (2, 1, and 0.5 equiv) at 0 °C for 20–30 min to prepare three phenylcopper reagents formulated as PhCu, Ph_2CuLi, and Ph_2CuLi+2 PhLi, which are defined herein as Ph/Cu (2:2, 2:1, and 2:0.5) reagents, respectively. However, the major course of reaction with *rac*-**1a** (R^1=$(CH_2)_2$Ph, R^2=CH_2OTBS) in THF at 0 °C for 1 h was attack to the carbonyl carbon to produce alcohol *rac*-**4a** in considerable yields (Table 1, entries 1, 3, and 7).

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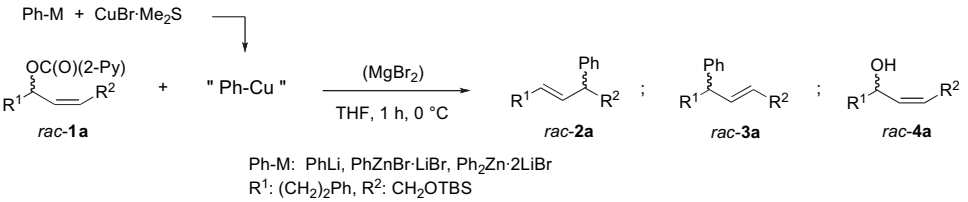
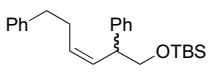
Table 1
Preliminary study using *rac*-**1a**[a]



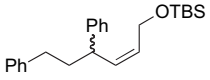
Entry	Ph-M[b] (equiv)	CuBr·Me_2S (equiv)	$MgBr_2$ (equiv)	Ratio[c] of *rac*-**2a**:-**3a**:-**4a**:-**1a**	Yield[d,e] (%)
1	PhLi (2)	2	0	9:0:69:22	nd
2[f]	PhLi (2)	2	3	100:0:0:0	97
3	PhLi (2)	1	0	11:0:47:42	nd
4	PhLi (2)	1	2	84:0:15:1	nd
5[f]	PhLi (2)	1	3	100:0:0:0	94
6	PhLi (2)	1	4	98:0:2:0	92
7	PhLi (2)	0.5	0	48:0:44:8	nd
8[f]	PhLi (2)	0.5	3	98:2:0:0	95
9	PhZnBr·LiBr[g] (2)	0.5	0	17:0:47:36	nd
10	PhZnBr·LiBr[g] (2)	0.5	3	94:0:6:0	nd
11[h]	Ph_2Zn·2LiBr[i] (3)	1.5	0	31:0:46:23	nd
12	Ph_2Zn·2LiBr[i] (3)	1.5	6	100:0:0:0	89

[a] Reactions were carried out at 0 °C unless otherwise noted.
[b] Salt free PhLi was used.
[c] Determined by ^1H NMR spectroscopy of the crude products.
[d] Isolated combined yields of *rac*-**2a** and -**3a**.
[e] nd: not determined.
[f] Reaction at −60 to −50 °C afforded essentially the same result.
[g] Prepared from PhLi (2 equiv per *rac*-**1a**) and $ZnBr_2$ (3 equiv).
[h] Cited from Ref. 7.
[i] Prepared from PhLi (6 equiv per *rac*-**1a**) and $ZnBr_2$ (3 equiv).

Fortunately, $MgBr_2$ (3 equiv) added to the reaction mixture was found to promote the allylic substitution to be completed within 1 h, furnishing *rac*-**2a** (*trans* olefin, $J_{CH=CH}$=15 Hz) with almost complete regioselectivity in high yields (entries 2, 5, and 8).[10] Regioisomer *rac*-**3a**, prepared independently (see Table 3, entry 1), was produced in a trace yields (0–2%). Reactions at −60 to −50 °C with these reagents gave comparable results to those at 0 °C (footnote f in entries 2, 5, and 8). In these entries formation of *cis* isomers **5** and **6** was not detected by ^1H NMR spectroscopy.[11] To optimize quantity of $MgBr_2$, less or more than 3 equiv of $MgBr_2$ were added to a solution of the Ph/Cu (2:1) reagent. With 2 equiv of $MgBr_2$, production of *rac*-**2a** was appreciably improved, but was in an insufficient level (entry 4 vs entry 3), whereas 4 equiv of $MgBr_2$ promoted almost complete production of *rac*-**2a** (entry 6). These results led us to state that the larger equivalent of $MgBr_2$ than Li^+ is necessary to attain high reactivity and regioselectivity (*requirement 1*).[12] It is likely that the picolinoxy group is activated by $MgBr_2$ through coordination to the carbonyl oxygen and the pyridyl nitrogen.

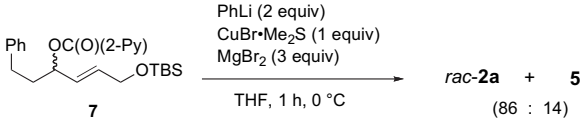


5



6

The above conditions were applied to *trans* picolinate **7** to examine the importance of the cis geometry of the picolinate (Scheme 2). The reaction completed within 1 h at 0 °C with excellent regioselectivity (>95%). However, a mixture of *rac*-**2a** and the *cis* isomer **5** was obtained in a 86:14 ratio, indicating importance of the *cis* geometry for the high selectivity. Interestingly, this selectivity is different from that obtained with PhMgBr/CuBr·Me_2S in a 2:1 ratio, which produced regioisomers *rac*-**2a** and *rac*-**3a** (*trans* isomer of **5**) in a 60:40 ratio.[7]



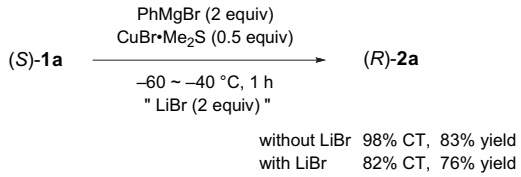
Scheme 2. Substitution of *trans* picolinate **7**.

Zinc reagents derived from PhLi and $ZnBr_2$ were examined next as sources of the Ph/Cu reagent. Two (2) equiv of PhZnBr·LiBr was mixed with CuBr·Me_2S (0.5 equiv) at 0 °C for 30 min to prepare the Ph/Cu (2:0.5) reagent, which was subjected to reaction with *rac*-**1a** at 0 °C for 1 h in the absence and presence of $MgBr_2$ (3 equiv). As expected, high efficiency was provided with $MgBr_2$ (entry 10 vs entry 9). A similar result was observed with a copper reagent derived from Ph_2Zn·2LiBr and CuBr·Me_2S (entry 12 vs entry 11). These results would be useful in a case that zinc reagent is available easily.[13]

The three copper reagent systems used in entries 2, 5, and 8 of Table 1 were applied to (*S*)-**1a**[13] (95–98% ee), which afforded (*R*)-**2a** in high yields. The *R* configuration was determined by comparison of the retention time on a chiral HPLC with an authentic sample of the known configuration,[7] thus confirming the *anti* S_N2' pathway of the reaction. Excellent CT (98%), defined as percentage (%) of enantiomeric excess (ee) of product over picolinate, was attained with the Ph/Cu (2:2 and 2:1) reagents and little dependent on reaction temperatures (entries 1–4). On the other hand, Ph/Cu (2:0.5) gave somewhat low CT of 71% (entry 5), which was not fully improved at −60 °C (entry 6). Thus, 2–1 equiv of CuBr·Me_2S toward RLi (2 equiv) was established to realize high CT (*requirement 2*). Additionally, the use of 2–1 equiv of CuBr·Me_2S is operational advantage in that precise measurement of CuBr·Me_2S for preparation of copper reagent and control of temperatures in a narrow range are not necessary.

To obtain more information about the low CT observed in entries 5 and 6, LiBr (2 equiv) was added to the Ph copper reagent derived from PhMgBr (2 equiv) and CuBr·Me_2S (0.5 equiv). Indeed, LiBr lowered the original CT (98%) to 82% (Scheme 3), thus proving the

negative effect of LiBr co-generated in the preparation of the Ph/Cu reagent from PhLi and CuBr·Me_2S.



Scheme 3. Influence of LiBr on CT.

The requirements 1 ($MgBr_2$>LiBr) and 2 (Ph/Cu=1–2:1) established above for the copper reagents derived from salt free PhLi should be applicable to organolithiums prepared by the methods such as direct lithiation and *ortho* lithiation. Successful examples of this statement are presented in the latter paragraphs.

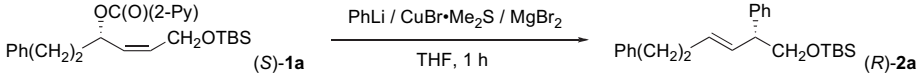
Next, PhLi prepared in situ by Li–halogen exchange was investigated. First, 4 equiv of *t*-BuLi were added to 2 equiv of PhBr at 0 °C in Et_2O. After 30 min, PhLi (2 equiv) coproduced with LiBr (2 equiv), $Me_2C{=}CH_2$ (2 equiv), and *t*-BuH (2 equiv) was mixed with CuBr·Me_2S (1 equiv) to produce the Ph/Cu (2:1) reagent and LiBr (totally 4 equiv). According to *requirement 1* substitution of (*S*)-**1a** with this Ph/Cu reagent was carried out with 5 equiv of $MgBr_2$ to furnish (*R*)-**2a** with excellent product selectivity and reactivity (Table 2, entry 8). The Ph/Cu prepared from PhI and *t*-BuLi gave a similar result (entry 10). In contrast, use of *n*-BuLi (2 equiv) for lithiation of PhX (X=Br, I; 2 equiv) afforded unidentified products (entries 7 and 9).

effective (entry 3). Substitution of (*S*)-**1d** at the established temperature (0 °C) gave **2d** with a slightly low ee of 94% ee (entry 4), which was improved to 97% by conducting the reaction at −60 °C (see result in a parenthesis). These results coupled with that obtained with (*S*)-**1a** (Table 2) imply that the substitution is marginally interfered with the sizes of a methylene and an alkoxymethyl substituents on the allylic moiety. A larger *c*-hexyl group attached to the olefin carbon did not interfere with the efficiency as well (entry 5).

Bulky copper reagents were examined next. First, a lithium reagent prepared from anisole by *ortho* lithiation[16] with *n*-BuLi was converted to the corresponding copper reagent of the 2:1 type according to *requirement 2*. This reagent underwent substitution smoothly with (*S*)-**1a** to produce **2f** in 85% yield with comparable CT to that obtained with the Ph/Cu reagent (entry 6). In a similar manner, the lithium anion produced by *ortho* lithiation of 1,3-$(MOMO)_2$-5-MeC_6H_3 was converted to copper reagent, which furnished **2g** in 97% yield without any loss in CT (entry 7). Next, 2,6-dimethylphenylcopper reagent was prepared by Li–Br exchange of 1-Br-2,6-$Me_2C_6H_3$ with *t*-BuLi followed by reaction with CuBr·Me_2S. Substitution of (*S*)-**1a** with this copper reagent proceeded well in the presence of 5 equiv of $MgBr_2$ according to *requirement 1*, delivering **2h** with 97% CT in 88% yield (entry 8). Another bulky reagent that possesses a latent CO_2R group also furnished product **2i** highly efficiently (entry 9). We think these examples are surely enough to demonstrate the high potency of the picolinate strategy.

The *p*-F-C_6H_4 copper reagent bearing the electron-withdrawing group afforded compound **2j** with a slightly low CT of 95% in 92%

Table 2
Allylic substitution of (*S*)-**1a**[a] with Ph copper reagents derived from PhLi



Entry	Source of PhLi (equiv)	CuBr·Me_2S (equiv)	$MgBr_2$ (equiv)	Temp (°C)	Product (*R*)-**2a**[b]	
					CT[c,d] (%)	Yield (%)
1	Salt free PhLi[e] (2)	2	3	0	98	97
2	Salt free PhLi[e] (2)	2	3	−60 to −50	98	92
3	Salt free PhLi[e] (2)	1	3	0	98	92
4	Salt free PhLi[e] (2)	1	3	−60 to −50	98	92
5	Salt free PhLi[e] (2)	0.5	3	0	71	92
6	Salt free PhLi[e] (2)	0.5	3	−60 to −50	84	90
7	PhBr (2)+*n*-BuLi (2)	1	3	0	—	0[f]
8	PhBr (2)+*t*-BuLi (4)	1	5	0	98	93
9	PhI (2)+*n*-BuLi (2)	1	3	0	—	0[f]
10	PhI (2)+*t*-BuLi (4)	1	5	0	98	90

[a] 95–98% ee.
[b] The absolute configuration was determined by chiral HPLC analysis.
[c] Chirality transfer (CT) defined by (% ee of (*R*)-**2a**/% ee of (*S*)-**1a**)×100.
[d] Determined by chiral HPLC analysis.
[e] Obtained from a company.
[f] Unidentified compounds were produced.

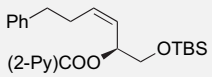
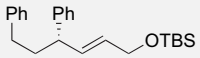
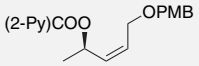
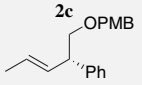
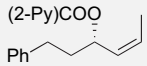
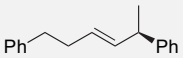
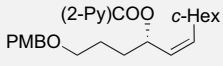
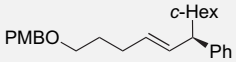
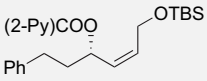
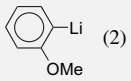
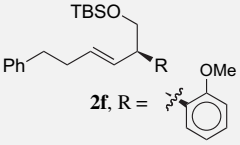
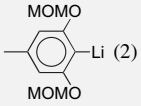
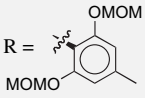
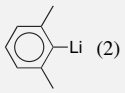
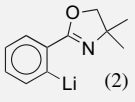
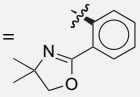
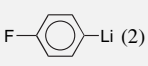
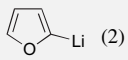
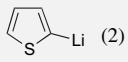
To examine the potency of the present allylic substitution, the Ph/Cu (2:1 and 1:1) reagents were applied to several picolinates bearing different substituents. These picolinates were prepared according to the recent papers,[7,14] in which asymmetric hydrogen transfer reaction of acetylenic ketones with (*S*,*S*)-chiral Ru catalyst[15] was used to synthesize 94–99% ee of (*S*)-**1a**, -**d**, and -**1e**.

Substitution of (*S*)-**1b**, the regioisomer of (*S*)-**1a**, with the Ph/Cu (2:1) reagent at 0 °C for 1 h in the presence of $MgBr_2$ (3 equiv) produced the regioisomer of **2a** (i.e., **2b**) with excellent efficiency, which is similar to that of **2a** (Table 3, entry 1; cf. Table 2, entry 3). Picolinate (*R*)-**1c** showed similar reactivity toward the Ph/Cu (2:1) reagent (entry 2). The other Ph/Cu (1:1) reagent was also yield (entry 10). However, the CT was improved easily by conducting the reaction at −20 °C (see the result in a parenthesis).

Copper reagents derived from furan and thiophene by direct lithiation are marginally reactive toward conjugate addition to enones.[17,18] Due to the low reactivity, the latter is used as a dummy ligand in the Lipshutz reagent (Fig. 1).[18] In contrast, these copper reagents showed sufficient reactivity in the present substitution to furnish **2k** and **2l** in good yields with high CT (entries 11 and 12).

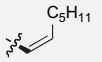
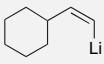
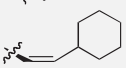
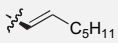
Usually, direct insertion of Mg to *cis* *R*-CH=CH-Br suffers from isomerization of the double bond to such extend that depends on the size of a substituent (*R*) on the olefinic carbon.[19] In cases of R=*n*-C_6H_{13} and Me, for example, 15% and 3% isomerizations have

Table 3
Allylic substitution of optically active picolinates with copper reagents[a]

Entry	Allylic picolinate (% ee)	RLi (equiv)	Method giving RLi	CuBr/Me_2S (equiv)	$MgBr_2$ (equiv)	*anti* S_N2' product [b,c]		
						Structure	CT (%)	Yield (%)
1	 (*S*)-**1b** (99% ee)	PhLi (2)	—	1	3	 **2b**	99	87
2	 (*R*)-**1c** (99% ee)	PhLi (2)	—	1	3		98	84
3	(*R*)-**1c** (99% ee)	PhLi (2)	—	2	3	**2c**	98	87
4	 (*S*)-**1d** (94% ee)	PhLi (2)	—	1	3	 **2d**	94 (97)	82 (92)[d]
5	 (*S*)-**1e** (99% ee)	PhLi (2)	—	1	3	 **2e**	98	94
6	 (*S*)-**1a** (95% ee)	 (2)	*ortho* Lithiation using *n*-BuLi	1	3	 **2f**, R =	99	85
7	(*S*)-**1a** (98% ee)	 (2)	*ortho* Lithiation using *n*-BuLi	1	3	 **2g**, R =	>99	97
8	(*S*)-**1a** (97% ee)	 (2)	Li–Br exchange[e]	1	5	 **2h**, R =	97	88
9	(*S*)-**1a** (97% ee)	 (2)	*ortho* Lithiation using *n*-BuLi	1	3	 **2i**, R =	>99	98
10	(*S*)-**1a** (98% ee)	 (2)	Li–Br exchange[e]	1	5	 **2j**, R =	95 (97)	92 (92)[d]
11	(*S*)-**1a** (95% ee)	 (2)	Direct lithiation using *n*-BuLi	1	3	 **2k**, R =	99	86
12	(*S*)-**1a** (97% ee)	 (2)	Direct lithiation using *n*-BuLi	1	3	 **2l**, R =	99	83

(*continued on next page*)

Table 3 (*continued*)

Entry	Allylic picolinate (% ee)	RLi (equiv)	Method giving RLi	$CuBr/Me_2S$ (equiv)	$MgBr_2$ (equiv)	*anti* S_N2' product [b,c]		
						Structure	CT (%)	Yield (%)
13	(*S*)-**1a** (98% ee)	C_5H_{11}–Li (3)	Li–I exchange[e]	1.5	7	**2m**, R = 	98	75
14	(*S*)-**1a** (95% ee)	 (3)	Li–I exchange[e]	1.5	7	**2n**, R = 	99	82
15	(*S*)-**1a** (95% ee)	C_5H_{11}–Li (2)	Li–I exchange[e]	1	5	**2o**, R = 	98	93

[a] Reactions were carried out at 0 °C for 1 h unless otherwise noted.
[b] Regioselectivities for all of the reactions were >97% by ^1H NMR spectroscopy.
[c] The absolute configurations of **2b** and **2d** were determined by comparison of the retention times on a chiral HPLC with authentic samples of the known configuration. Those of other products were determined by analogy of **2a**, **2b**, and **2d**.
[d] At −60 °C (entry 4); −20 °C (entry 10).
[e] Corresponding halide (3 or 2 equiv) and *t*-BuLi (6 or 4 equiv).

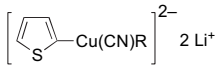
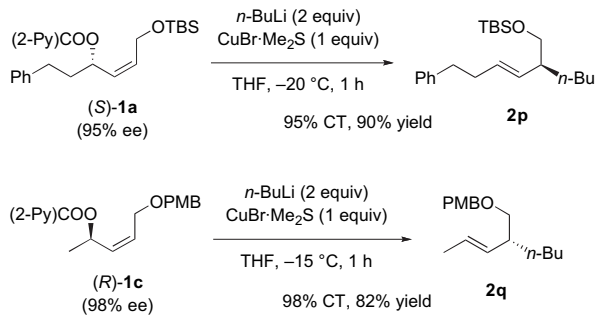


Figure 1. Lipshutz reagent for conjugate addition to enones.

been observed, respectively.[19b,c] In contrast, Li–halogen exchange of *cis* R-CH=CH-X (X=Br, I) with *t*-BuLi proceeds with retention of the cis geometry. This method was coupled with the present substitution to deliver *n*-C_5H_{11}- and *c*-C_6H_{11}-substituted cis olefin moieties to the allylic position of (*S*)-**1a** in good yields and with high CT (entries 13 and 14). Substitution with *trans* 1-heptenyl copper reagent afforded **2o** efficiently (entry 15).

We then applied the present protocol to alkyllithium. As shown in Scheme 4, *n*-$Bu_2CuLi{\cdot}LiBr$ underwent substitution even in the absence of $MgBr_2$, furnishing the *anti* S_N2' products **2p** and **2q** from (*S*)-**1a** and (*R*)-**1c**, respectively. High reactivity of the Bu reagent is probably attributable to the nucleophilicity of the Bu anion, that is, stronger than that of aryl and alkenyl anions.



Scheme 4. Reaction with the *n*-BuLi/$CuBr{\cdot}Me_2S$ reagent.

3. Conclusions

Substitution of allylic picolinates with aryl, alkenyl, and heteroaryl coppers derived from the organolithiums and $CuBr{\cdot}Me_2S$ was studied. We found that addition of $MgBr_2$ substantially enhanced the substitution, giving *anti* S_N2' products highly selectively in good yields. Furthermore, we elucidated the following requirements for high efficiency: (1) quantity of $MgBr_2$ should be more than that of Li^+ (*requirement 1*); (2) 1–2 equiv of $CuBr{\cdot}Me_2S$ should be used toward 2 equiv of RLi (*requirement 2*). With these requirements, not only sterically bulky reagents but also electronically less nucleophilic reagents furnished *anti* S_N2' products efficiently as summarized in Tables 2 and 3. In addition, *cis* alkenyl copper reagents underwent substitution with retention of the *cis* geometry.

4. Experimental

4.1. General

Infrared (IR) spectra are reported in wave numbers (cm^{-1}). The ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured in $CDCl_3$ using $SiMe_4$ (δ=0 ppm) and the center line of $CDCl_3$ triplet (δ=77.1 ppm) as internal standards, respectively. Signal patterns are indicated as br s, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in hertz (Hz). In some cases chemical shifts of carbons accompany plus (for C and CH_2) and minus (for CH and CH_3) signs of APT experiments (Attached Proton Test). After the reactions, organic extracts were concentrated by using a rotary evaporator and residues were purified by chromatography on silica gel (Merck, silica gel 60; Kanto, spherical silica gel 60 N).

4.2. Allylic substitution

The reactions of (*S*)-**1a** with Ph coppers prepared by various ways are described below (Section 4.2.1) as the general methods.

*4.2.1. (R,E)-1-[(tert-Butyldimethylsilyl)oxy]-2,6-diphenyl-3-hexene ((R)-**2a**).* Table 2, entry 1: to an ice-cold suspension of $CuBr{\cdot}Me_2S$ (39.5 mg, 0.192 mmol) in THF (1.6 mL) were added PhLi (0.180 mL, 1.08 M in cyclohexane/Et_2O, 0.194 mmol) and $MgBr_2$ (1.40 mL, 0.20 M in THF, 0.280 mmol). After 30 min at 0 °C, a solution of (*S*)-**1a** (39.5 mg, 0.0960 mmol, 98% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h, and diluted with hexane and saturated NH_4Cl with vigorous stirring. The layers were separated and the aqueous layer was extracted with hexane twice. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford (*R*)-**2a** (34.0 mg, 97%, 96% ee, 98% CT). The ^1H NMR spectrum and retention time of (*R*)-**2a** on chiral HPLC were identical with those reported.[7]

Table 2, entry 3: to an ice-cold suspension of $CuBr{\cdot}Me_2S$ (22.0 mg, 0.107 mmol) in THF (1.4 mL) were added PhLi (0.200 mL, 1.08 M in cyclohexane/Et_2O, 0.216 mmol) and $MgBr_2$ (1.60 mL, 0.20 M in THF, 0.320 mmol). After 30 min at 0 °C, a solution of (*S*)-**1a** (44.1 mg, 0.107 mmol, 98% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford (*R*)-**2a** (36.2 mg, 92%, 96% ee, 98% CT by chiral HPLC analysis).

Table 2, entry 8: to an ice-cold solution of PhBr (0.022 mL, 0.209 mmol) in Et_2O (1 mL) was added *t*-BuLi (0.250 mL, 1.57 M in pentane, 0.393 mmol) slowly. After 30 min at 0 °C, a solution of

$MgBr_2$ (2.40 mL, 0.20 M in THF, 0.480 mmol) and CuBr·Me_2S (19.9 mg, 0.0968 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (39.8 mg, 0.0967 mmol, 95% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h, to afford (*R*)-**2a** (33.0 mg, 93%, 93% ee, 98% CT by chiral HPLC analysis).

Table 2, entry 10: to an ice-cold solution of PhI (0.024 mL, 0.214 mmol) in Et_2O (1 mL) was added *t*-BuLi (0.250 mL, 1.57 M in pentane, 0.393 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (2.40 mL, 0.20 M in THF, 0.480 mmol) and CuBr·Me_2S (19.7 mg, 0.0958 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (39.5 mg, 0.0960 mmol, 95% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford (*R*)-**2a** (31.8 mg, 90%, 93% ee, 98% CT by chiral HPLC analysis).

*4.2.2. (S,E)-1-[(tert-Butyldimethylsilyl)oxy]-4,6-diphenylhex-2-ene (**2b**).* Table 3, entry 1: to an ice-cold suspension of CuBr·Me_2S (19.5 mg, 0.0949 mmol) in THF (1.6 mL) were added PhLi (0.180 mL, 1.08 M in cyclohexane/Et_2O, 0.194 mmol) and $MgBr_2$ (1.40 mL, 0.20 M in THF, 0.280 mmol). After 30 min at 0 °C, a solution of (*S*)-**1b** (39.0 mg, 0.0947 mmol, 99% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2b** (30.1 mg, 87%, 98% ee, 99% CT). The ^{1}H NMR spectrum and retention time of **2b** were identical with those reported.[7]

*4.2.3. (S,E)-5-((4-Methoxybenzyl)oxy)-4-phenylhex-2-ene (**2c**).* Table 3, entry 2: to an ice-cold suspension of CuBr·Me_2S (23.6 mg, 0.115 mmol) in THF (1.3 mL) were added PhLi (0.210 mL, 1.08 M in cyclohexane/Et_2O, 0.227 mmol) and $MgBr_2$ (1.70 mL, 0.20 M in THF, 0.340 mmol). After 30 min at 0 °C, a solution of (*R*)-**1c** (37.4 mg, 0.115 mmol, 99% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2c** (27.1 mg, 84%, 97% ee, 98% CT). The ^{1}H NMR spectrum of **2c** was identical with that reported.[7]

*4.2.4. (R,E)-1,5-Diphenylhex-3-ene (**2d**).* Table 3, entry 4: to an ice-cold suspension of CuBr·Me_2S (16.8 mg, 0.0817 mmol) in THF (1.6 mL) were added PhLi (0.15 mL, 1.08 M in cyclohexane/Et_2O, 0.162 mmol) and $MgBr_2$ (1.30 mL, 0.20 M in THF, 0.260 mmol). After 30 min at 0 °C, a solution of (*S*)-**1d** (23.0 mg, 0.0817 mmol, 94% ee) in THF (1 mL) was added to it dropwise at −60 °C. The resulting mixture was stirred at −60 °C for 1 h to afford **2d** (17.8 mg, 92%, 91% ee, 97% CT). The ^{1}H and ^{13}C NMR spectra of **2d** and its retention time were identical with that reported.[7]

*4.2.5. (R,E)-1-Cyclohexyl-6-((4-methoxybenzyl)oxy)-1-phenylhex-2-ene (**2e**).* Table 3, entry 5: to an ice-cold suspension of CuBr·Me_2S (18.3 mg, 0.0890 mmol) in THF (1.5 mL) were added PhLi (0.170 mL, 1.08 M in cyclohexane/Et_2O, 0.184 mmol) and $MgBr_2$ (1.40 mL, 0.20 M in THF, 0.280 mmol). After 30 min at 0 °C, a solution of (*S*)-**1e** (37.8 mg, 0.0892 mmol, 99% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2e** (31.9 mg, 94%): IR (neat) 1612, 1513, 1248 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.70–0.96 (m, 2H), 1.04–1.28 (m, 3H), 1.32–1.90 (m, 8H), 2.07 (dt, *J*=7, 7 Hz, 2H), 2.86 (dd, *J*=9, 9 Hz, 1H), 3.40 (t, *J*=7 Hz, 2H), 3.80 (s, 3H), 4.39 (s, 2H), 5.38 (dt, *J*=15, 7 Hz, 1H), 5.57 (dd, *J*=15, 9 Hz, 1H), 6.87 (d, *J*=9 Hz, 2H), 7.06–7.30 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.47 (+), 26.49 (+), 26.6 (+), 29.2 (+), 29.6 (+), 31.4 (+), 31.5 (+), 42.6 (−), 55.3 (−), 56.4 (−), 69.5 (+), 72.6 (+), 113.8 (−), 125.8 (−), 127.9 (−), 128.3 (−), 129.3 (−), 130.2 (−), 130.8 (+), 133.3 (−), 145.0 (+), 159.2 (+); HRMS (FAB) calcd for $C_{26}H_{34}O_2Na$ [(M+Na)$^+$] 401.2457, found 401.2447. The enantiomeric information (97% ee, 98% CT) was determined by chiral HPLC analysis: Chiralcel OD-H; hexane/*i*-PrOH=98/2, 0.2 mL/min, rt; t_R (min)=41.9 (*R*), 47.9 (*S*).

*4.2.6. (R,E)-1-[(tert-Butyldimethylsilyl)oxy]-2-(2-methoxyphenyl)-6-phenylhex-3-ene (**2f**).* Table 3, entry 6: to an ice-cold solution of anisole (0.025 mL, 0.23 mmol) in THF (1.4 mL) was added *n*-BuLi (0.13 mL, 1.60 M in hexane, 0.208 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (1.60 mL, 0.20 M in THF, 0.32 mmol) and CuBr·Me_2S (21.2 mg, 0.103 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (42.4 mg, 0.103 mmol, 95% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2f** (34.6 mg, 85%, 94% ee, 99% CT). The ^{1}H NMR spectrum of **2f** was identical with that reported.[7]

*4.2.7. (R,E)-2-[(2,6-Bis(methoxymethoxy)-4-methyl)phenyl]-1-[(tert-butyldimethylsilyl)oxy]-6-phenylhex-3-ene (**2g**).* Table 3, entry 7: to an ice-cold solution of 1,3-bis(methoxymethoxy)-5-methylbenzene (43.9 mg, 0.207 mmol) in THF (1.6 mL) was added *n*-BuLi (0.120 mL, 1.60 M in hexane, 0.192 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (1.40 mL, 0.20 M in THF, 0.280 mmol) and CuBr·Me_2S (19.3 mg, 0.0939 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (38.7 mg, 0.0940 mmol, 98% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford a mixture of **2g** and (2,6-$(MOMO)_2$-4-MeC_6H_2)$_2$ in a 84:16 ratio by ^{1}H NMR analysis (54.1 mg in total, 97% yield of **2g**): ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.08 (s, 3H), −0.07 (s, 3H), 0.78 (s, 9H), 2.21 (s, 3H), 2.15–2.28 (m, 2H), 2.57 (t, *J*=8 Hz, 1H), 3.39 (s, 6H), 3.72 (dd, *J*=10, 6 Hz, 1H), 3.96 (dd, *J*=10, 9 Hz, 1H), 4.08 (ddd, *J*=9, 7, 6 Hz, 1H), 5.06 (s, 4H), 5.46 (dt, *J*=15, 7 Hz, 1H), 5.86 (dd, *J*=15, 8 Hz, 1H), 6.52 (s, 2H), 7.03–7.12 (m, 3H), 7.13–7.22 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.1, 18.5, 21.8, 26.0, 34.8, 36.1, 42.5, 56.2, 65.3, 94.6, 109.2, 117.2, 125.7, 128.3, 128.5, 130.6, 130.7, 137.7, 142.4, 156.0.

Transformation of **2g** to alcohol for determination of the structure: to a solution of the above mixture of **2g** and (2,6-$(MOMO)_2$-4-MeC_6H_2)$_2$ in THF (1 mL) was added Bu_4NF (0.14 mL, 1.0 M in THF, 0.14 mmol). The reaction was carried out at rt overnight to furnish the corresponding alcohol (34.1 mg, 94% from (*S*)-**1a**): IR (neat) 3430, 1610, 1583, 1046 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (br s, 1H), 2.29 (s, 3H), 2.32 (ddd, *J*=8, 7, 7 Hz, 2H), 2.63 (dt, *J*=14, 8 Hz, 1H), 2.71 (dt, *J*=14, 7 Hz, 1H), 3.46 (s, 6H), 3.70–3.81 (m, 1H), 3.85–3.95 (m, 1H), 4.18 (dt, *J*=8, 8 Hz, 1H), 5.14 (s, 4H), 5.62 (dt, *J*=15, 7 Hz, 1H), 5.87 (dd, *J*=15, 8 Hz, 1H), 6.61 (s, 2H), 7.11–7.20 (m, 3H), 7.22–7.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8 (−), 34.6 (+), 35.9 (+), 42.8 (−), 56.2 (−), 64.5 (+), 94.5 (+), 109.3 (−), 116.1 (+), 125.9 (−), 128.3 (−), 128.5 (−), 129.9 (−), 132.2 (−), 138.3 (+), 142.0 (+), 155.9 (+); HRMS (FAB) calcd for $C_{23}H_{30}O_5Na$ [(M+Na)$^+$] 409.1991, found 409.1988. The enantiomeric information (98% ee, >99% CT) was determined by chiral HPLC analysis: Chiralcel AD-H; hexane/*i*-PrOH=98/2, 0.3 mL/min, rt; t_R (min)=108.2 (*S*), 112.5 (*R*).

*4.2.8. (R,E)-1-[(tert-Butyldimethylsilyl)oxy]-2-(2,6-dimethylphenyl)-6-phenylhex-3-ene (**2h**).* Table 3, entry 8: to an ice-cold solution of 2-bromo-1,3-dimethylbenzene (0.026 mL, 0.195 mmol) in Et_2O (1 mL) was added *t*-BuLi (0.280 mL, 1.57 M in pentane, 0.361 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (2.30 mL, 0.20 M in THF, 0.460 mmol) and CuBr·Me_2S (18.8 mg, 0.0914 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (37.6 mg, 0.0913 mmol, 97% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2h** (31.7 mg, 88%): IR (neat) 1255, 1099, 836 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.06 (s, 3H), −0.02

(s, 3H), 0.84 (s, 9H), 2.25–2.38 (m, 8H), 2.65 (t, *J*=8 Hz, 2H), 3.72–3.84 (m, 1H), 3.96–4.07 (m, 2H), 5.39 (dt, *J*=16, 7 Hz, 1H), 5.81 (dm, *J*=16 Hz, 1H), 6.93–7.04 (m, 3H), 7.11–7.19 (m, 3H), 7.21–7.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.3 (−), 18.3 (+), 21.8 (−), 26.0 (−), 34.9 (+), 36.0 (+), 46.4 (−), 65.2 (+), 125.8 (−), 126.2 (−), 128.3 (−), 128.5 (−), 130.0 (−), 130.3 (−), 138.8 (+), 142.2 (+); HRMS (FAB) calcd for $C_{26}H_{38}OSiNa$ [(M+Na)$^+$] 417.2590, found 417.2592. The enantiomeric information (94% ee, 97% CT) was determined by chiral HPLC analysis of the corresponding alcohol: Chiralcel OD-H; hexane/*i*-PrOH=98/2, 0.4 mL/min, rt; t_R (min)=50.1 (*S*), 71.9 (*R*).

*4.2.9. (R,E)-1-[(tert-Butyldimethylsilyl)oxy]-2-[2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)phenyl]-6-phenylhex-3-ene (**2i**).* Table 3, entry 9: to an ice-cold solution of 4,4-dimethyl-2-phenyl-2-oxazoline (0.035 mL, 0.205 mmol) in THF (1.6 mL) was added *n*-BuLi (0.12 mL, 1.60 M in hexane, 0.192 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (1.40 mL, 0.20 M in THF, 0.280 mmol) and $CuBr\cdot Me_2S$ (19.1 mg, 0.0929 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (38.3 mg, 0.0930 mmol, 97% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford a mixture of **2i** and Ar_2 in a 82:18 ratio by ^{1}H NMR analysis (48.8 mg in total, 98% yield of **2i**): IR (neat) 1645, 1102, 1038, 837 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.06 (s, 3H), −0.04 (s, 3H), 0.84 (s, 9H), 1.38 (s, 6H), 2.39 (ddd, *J*=8, 7, 7 Hz, 2H), 2.67 (dd, *J*=8, 7 Hz, 2H), 3.75 (dd, *J*=10, 7 Hz, 1H), 3.81 (dd, *J*=10, 6 Hz, 1H), 4.06 (s, 3H), 4.40 (ddd, *J*=7, 7, 6 Hz, 1H), 5.56 (dt, *J*=16, 7 Hz, 1H), 5.70 (dd, *J*=16, 7 Hz, 1H), 7.13–7.29 (m, 7H), 7.34 (ddd, *J*=8, 8, 1 Hz, 1H), 7.66 (dd, *J*=8, 1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.3 (−), 18.3 (+), 26.0 (−), 28.4 (−), 34.8 (+), 36.0 (+), 46.3 (−), 67.1 (+), 67.9 (+), 78.9 (+), 125.7 (−), 125.9 (−), 128.2 (+), 128.3 (−), 128.6 (−), 128.7 (−), 130.0 (−), 130.2 (−), 131.1 (−), 131.4 (−), 142.2 (+), 142.4 (+), 162.9 (+); HRMS (FAB) calcd for $C_{29}H_{41}NO_2SiNa$ [(M+Na)$^+$] 486.2804, found 486.2799.

Transformation of **2i** to alcohol for determination of the structure: to a solution of the above mixture of **2i** and Ar_2 in THF (1 mL) was added Bu_4NF (0.14 mL, 1.0 M in THF, 0.14 mmol). The reaction was carried out at rt overnight to furnish the corresponding alcohol (30.6 mg, 94% from (*S*)-**1a**): IR (neat) 3292, 1739, 1642, 1046 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 3H), 1.41 (s, 3H), 2.31–2.44 (m, 2H), 2.67 (dt, *J*=14, 8 Hz, 1H), 2.72 (dt, *J*=14, 8 Hz, 1H), 3.61 (dd, *J*=10, 10 Hz, 1H), 4.07 (dd, *J*=10, 5 Hz, 1H), 4.10 (d, *J*=8 Hz, 1H), 4.14 (d, *J*=8 Hz, 1H), 4.48 (ddd, *J*=10, 10, 5 Hz, 1H), 5.43 (br s, 1H), 5.48–5.62 (m, 2H), 7.14–7.32 (m, 7H), 7.40 (ddd, *J*=8, 8, 1 Hz, 1H), 7.67 (dm, *J*=8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.2 (−), 28.8 (−), 34.7 (+), 35.8 (+), 45.1 (−), 68.1 (+), 68.5 (+), 79.2 (+), 125.9 (−), 126.1 (−), 127.6 (+), 128.2 (−), 128.4 (−), 128.6 (−), 129.1 (−), 130.9 (−), 131.1 (−), 131.2 (−), 141.8 (+), 143.8 (+), 163.0 (+); HRMS (EI) calcd for $C_{23}H_{27}NO_2$ [M$^+$] 349.2042, found 349.2046. The enantiomeric information (97% ee, >99% CT) was determined by chiral HPLC analysis: Chiralcel OD-H; hexane/*i*-PrOH=97/3, 0.5 mL/min, rt; t_R (min)=33.7 (*R*), 41.3 (*S*).

*4.2.10. (R,E)-1-[(tert-Butyldimethylsilyl)oxy]-2-(4-fluorophenyl)-6-phenylhex-3-ene (**2j**).* Table 3, entry 10: to an ice-cold solution of 1-bromo-4-fluorobenzene (0.020 mL, 0.182 mmol) in Et_2O (1 mL) was added *t*-BuLi (0.220 mL, 1.57 M in pentane, 0.345 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (2.20 mL, 0.20 M in THF, 0.440 mmol) and $CuBr\cdot Me_2S$ (17.8 mg, 0.0866 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, cooled to −20 °C. A solution of (*S*)-**1a** (39.8 mg, 0.0967 mmol, 97% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at −20 °C for 1 h to afford **2j** (30.6 mg, 92%): IR (neat) 1509, 1099, 836 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.07 (s, 3H), −0.06 (s, 3H), 0.83 (s, 9H), 2.34 (ddd, *J*=8, 6, 6 Hz, 2H), 2.68 (dd, *J*=8, 6 Hz, 2H), 3.40 (ddd, *J*=7, 7, 7 Hz, 1H), 3.68 (dd, *J*=10, 7 Hz, 1H), 3.74 (dd, *J*=10, 7 Hz, 1H), 5.51 (dt, *J*=16, 6 Hz, 1H), 5.61 (dd, *J*=16, 7 Hz, 1H), 6.95 (ddt, *J*=9, 9, 2 Hz, 2H), 7.07–7.21 (m, 5H), 7.22–7.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.4 (−), 18.3 (+), 25.9 (−), 34.7 (+), 35.9 (+), 50.5 (−), 67.5 (+), 114.9 (d, *J*=21 Hz) (−), 125.8 (−), 128.3 (−), 128.6 (−), 129.7 (d, *J*=7 Hz) (−), 131.0 (−), 131.3 (−), 138.3 (d, *J*=3 Hz) (+), 142.0 (+), 161.6 (d, *J*=242 Hz) (+); HRMS (FAB$^+$) calcd for $C_{24}H_{33}FOSiNa$ [(M+Na)]$^+$ 407.2194, found 407.2182. The enantiomeric information (94% ee, 97% CT) was determined by chiral HPLC analysis of the corresponding alcohol: Chiralcel OD-H; hexane/*i*-PrOH=98/2, 0.5 mL/min, rt; t_R (min)=64.3 (*R*), 75.2 (*S*).

*4.2.11. (S,E)-1-[(tert-Butyldimethylsilyl)oxy]-2-(furan-2-yl)-6-phenylhex-3-ene (**2k**).* Table 3, entry 11: to an ice-cold solution of furan (0.015 mL, 0.206 mmol) in THF (1.6 mL) was added *n*-BuLi (0.120 mL, 1.60 M in hexane, 0.192 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (1.40 mL, 0.20 M in THF, 0.280 mmol) and $CuBr\cdot Me_2S$ (19.2 mg, 0.0934 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (38.4 mg, 0.0933 mmol, 95% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2k** (28.5 mg, 86%): IR (neat) 1471, 1255, 1105, 837 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.01 (s, 6H), 0.88 (s, 9H), 2.32–2.44 (m, 2H), 2.70 (t, *J*=8 Hz, 2H), 3.44 (ddd, *J*=7, 7, 7 Hz, 1H), 3.75 (dd, *J*=10, 7 Hz, 1H), 3.86 (dd, *J*=10, 7 Hz, 1H), 5.53–5.68 (m, 2H), 6.03 (dd, *J*=3, 1 Hz, 1H), 6.31 (dd, *J*=3, 2 Hz, 1H), 7.17–7.23 (m, 3H), 7.26–7.33 (m, 2H), 7.34 (dd, *J*=2, 1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.39 (−), −5.36 (−), 18.4 (+), 25.9 (−), 34.6 (+), 35.8 (+), 45.5 (−), 65.5 (+), 105.8 (−), 110.1 (−), 125.8 (−), 128.3 (−), 128.4 (−), 128.5 (−), 132.3 (−), 141.1 (−), 142.0 (+), 155.7 (+); HRMS (FAB) calcd for $C_{22}H_{32}O_2SiNa$ [(M+Na)$^+$] 379.2069, found 379.2071. The enantiomeric information (94% ee, 99% CT) was determined by chiral HPLC analysis of the corresponding alcohol: Chiralcel OB-H; hexane/*i*-PrOH=98/2, 0.2 mL/min, 40 °C; t_R (min)=93.5 (*S*), 110.0 (*R*).

*4.2.12. (S,E)-1-[(tert-Butyldimethylsilyl)oxy]-6-phenyl-2-(thiophen-2-yl)hex-3-ene (**2l**).* Table 3, entry 12: to an ice-cold solution of thiophene (0.016 mL, 0.200 mmol) in THF (1.6 mL) was added *n*-BuLi (0.12 mL, 1.60 M in hexane, 0.192 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (1.40 mL, 0.20 M in THF, 0.280 mmol) and $CuBr\cdot Me_2S$ (18.9 mg, 0.0919 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (37.8 mg, 0.0918 mmol, 97% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2l** (28.5 mg, 83%): IR (neat) 1255, 1107, 837 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.93 (s, 9H), 2.37–2.48 (m, 2H), 2.75 (dd, *J*=9, 7 Hz, 2H), 3.70–3.86 (m, 3H), 5.60–5.74 (m, 2H), 6.85 (dt, *J*=4, 1 Hz, 1H), 6.99 (dd, *J*=5, 4 Hz, 1H), 7.21 (dd, *J*=5, 1 Hz, 1H), 7.22–7.27 (m, 3H), 7.29–7.37 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.3 (−), 18.4 (+), 26.0 (−), 34.5 (+), 35.9 (+), 46.8 (−), 67.8 (+), 123.5 (−), 124.1 (−), 125.9 (−), 126.4 (−), 128.4 (−), 128.6 (−), 130.8 (−), 131.9 (−), 142.0 (+), 145.7 (+); HRMS (FAB) calcd for $C_{22}H_{32}OSSiNa$ [(M+Na)$^+$] 395.1841, found 395.1842. The enantiomeric information (96% ee, 99% CT) was determined by chiral HPLC analysis of the corresponding alcohol: Chiralcel OB-H; hexane/*i*-PrOH=97/3, 0.3 mL/min, rt; t_R (min)=62.1 (*R*), 64.9 (*S*).

*4.2.13. (S,1′E,3Z)-1-[(tert-Butyldimethylsilyl)oxy]-2-(4′-phenyl-1′-butenyl)non-3-ene (**2m**).* Table 3, entry 13: to an ice-cold solution of (*Z*)-1-iodo-1-heptene (58.1 mg, 0.259 mmol) in Et_2O (1 mL) was added *t*-BuLi (0.320 mL, 1.57 M in pentane, 0.502 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (2.90 mL, 0.20 M in THF, 0.580 mmol) and $CuBr\cdot Me_2S$ (25.8 mg, 0.125 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (34.4 mg, 0.0836 mmol, 98%

ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2m** (24.1 mg, 75%): IR (neat) 1255, 1103, 836 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 6H), 0.85–0.94 (m, 3H), 0.89 (s, 9H), 1.23–1.38 (m, 6H), 2.03 (dt, *J*=8, 6 Hz, 2H), 2.31 (dt, *J*=7, 8 Hz, 2H), 2.66 (t, *J*=8 Hz, 2H), 3.16 (ddt, *J*=9, 7, 7 Hz, 1H), 3.47 (d, *J*=7 Hz, 2H), 5.20 (dd, *J*=11, 9 Hz, 1H), 5.39 (dd, *J*=16, 7 Hz, 1H), 5.39–5.57 (m, 2H), 7.14–7.23 (m, 3H), 7.24–7.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.2 (−), 14.2 (−), 18.5 (+), 22.7 (+), 26.0 (−), 27.7 (+), 29.5 (+), 31.7 (+), 34.8 (+), 36.1 (+), 43.7 (−), 67.0 (+), 125.8 (−), 128.3 (−), 128.5 (−), 129.3 (−), 130.2 (−), 130.9 (−), 131.4 (−), 142.2 (+); HRMS (FAB) calcd for $C_{25}H_{42}OSiNa$ [(M+Na)$^+$] 409.2903, found 409.2899. The enantiomeric information (96% ee, 98% CT) was determined by chiral HPLC analysis of the corresponding alcohol: Chiralcel AD-H; hexane/*i*-PrOH=99/1, 0.2 mL/min, 40 °C; t_R (min)=69.2 (*R*), 76.2 (*S*).

*4.2.14. (R,1Z,4E)-3-[(tert-Butyldimethylsilyl)oxymethyl]-1-cyclohexyl-7-phenylhepta-1,4-diene (**2n**).* Table 3, entry 14: to an ice-cold solution of (*Z*)-(2-iodovinyl)cyclohexane (61.7 mg, 0.261 mmol) in Et_2O (1 mL) was added *t*-BuLi (0.32 mL, 1.57 M in pentane, 0.502 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (3.00 mL, 0.20 M in THF, 0.600 mmol) and $CuBr\cdot Me_2S$ (26.0 mg, 0.126 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (34.7 mg, 0.0843 mmol, 95% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2n** (27.5 mg, 82%): IR (neat) 1255, 1105, 837, 775, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.89 (s, 9H), 0.96–1.35 (m, 6H), 1.53–1.76 (m, 4H), 2.18–2.36 (m, 3H), 2.66 (dd, *J*=8, 6 Hz, 2H), 3.18 (ddt, *J*=10, 6, 7 Hz, 1H), 3.47 (d, *J*=7 Hz, 2H), 5.09 (dd, *J*=11, 10 Hz, 1H), 5.30 (dd, *J*=11, 10 Hz, 1H), 5.40 (dd, *J*=16, 6 Hz, 1H), 5.52 (dd, *J*=16, 7 Hz, 1H), 7.13–7.21 (m, 3H), 7.23–7.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.2 (−), −5.1 (−), 18.5 (+), 25.99 (+), 26.04 (+), 26.07 (−), 26.13 (+), 33.3 (+), 33.6 (+), 34.8 (+), 36.1 (+), 36.8 (−), 43.9 (−), 67.2 (+), 125.8 (−), 127.5 (−), 128.3 (−), 128.5 (−), 130.1 (−), 131.2 (−), 137.3 (−), 142.2 (+); HRMS (FAB) calcd for $C_{26}H_{42}OSiNa$ [(M+Na)$^+$] 421.2903, found 421.2902. The enantiomeric information (94% ee, 99% CT) was determined by chiral HPLC analysis of the corresponding alcohol: Chiralcel OD-H; hexane/*i*-PrOH=98/2, 0.2 mL/min, 40 °C; t_R (min)=52.5 (*R*), 55.5 (*S*).

*4.2.15. (S,1′E,3E)-1-[(tert-Butyldimethylsilyl)oxy]-2-(4′-phenyl-1′-butenyl)non-3-ene (**2o**).* Table 3, entry 15: to an ice-cold solution of (*E*)-1-iodo-1-heptene (49.8 mg, 0.222 mmol) in Et_2O (1 mL) was added *t*-BuLi (0.260 mL, 1.57 M in pentane, 0.404 mmol) slowly. After 30 min at 0 °C, a solution of $MgBr_2$ (2.50 mL, 0.20 M in THF, 0.500 mmol) and $CuBr\cdot Me_2S$ (20.8 mg, 0.101 mmol) were added to the solution. The resulting mixture was stirred at 0 °C for 30 min, and a solution of (*S*)-**1a** (41.6 mg, 0.101 mmol, 95% ee) in THF (1 mL) was added to it dropwise. The resulting mixture was stirred at 0 °C for 1 h to afford **2o** (36.4 mg, 93%): IR (neat) 1255, 1104, 836 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 6H), 0.85–0.94 (m, 3H), 0.89 (s, 9H), 1.23–1.41 (m, 6H), 1.99 (dt, *J*=7, 7 Hz, 2H), 2.32 (dt, *J*=8, 6 Hz, 2H), 2.68 (t, *J*=8 Hz, 2H), 2.81 (ddt, *J*=7, 7, 7 Hz, 1H), 3.49 (d, *J*=7 Hz, 2H), 5.32 (dd, *J*=16, 7 Hz, 1H), 5.32–5.43 (m, 1H), 5.43 (dd, *J*=16, 7 Hz, 1H), 5.51 (dt, *J*=16, 6 Hz, 1H), 7.14–7.22 (m, 3H), 7.24–7.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.2 (−), 14.2 (−), 18.5 (+), 22.6 (+), 26.0 (−), 29.2 (+), 31.5 (+), 32.8 (+), 34.8 (+), 36.1 (+), 48.5 (−), 67.0 (+), 125.8 (−), 128.3 (−), 128.6 (−), 130.0 (−), 130.6 (−), 131.1 (−), 131.9 (−), 142.2 (+); HRMS (FAB) calcd for $C_{25}H_{42}OSiNa$ [(M+Na)$^+$] 409.2903, found 409.2897. The enantiomeric information (93% ee, 98% CT) was determined by chiral HPLC analysis of the corresponding alcohol: Chiralcel OD-H; hexane/*i*-PrOH=98/2, 0.2 mL/min, 40 °C; t_R (min)=51.2 (*R*), 57.8 (*S*).

*4.2.16. (S,E)-1-[(tert-Butyldimethylsilyl)oxy]-2-butyl-6-phenylhex-2-ene (**2p**).* To a suspension of $CuBr\cdot Me_2S$ (18.8 mg, 0.116 mmol) in THF (2 mL) was added *n*-BuLi (0.12 mL, 1.55 M in hexane, 0.186 mmol) slowly at −20 °C. The resulting mixture was stirred at −20 °C for 30 min, and a solution of (*S*)-**1a** (37.6 mg, 0.0913 mmol, 95% ee) in THF (1 mL) was added to it dropwise. The mixture was allowed to warm to −20 °C for 1 h to afford **2p** (28.6 mg, 90%, 90% ee, 95% CT). The ^1H NMR spectrum of **2p** was identical with that reported.[7]

*4.2.17. (R,E)-1-[(2-Butylpent-3-enyloxy)methyl]-4-methoxybenzene (**2q**).* To a suspension of $CuBr\cdot Me_2S$ (22.4 mg, 0.109 mmol) in THF (2 mL) was added *n*-BuLi (0.13 mL, 1.66 M in hexane, 0.216 mmol) slowly at −15 °C. The resulting mixture was stirred at −15 °C for 30 min, and a solution of (*R*)-**1c** (35.4 mg, 0.109 mmol, 98% ee) in THF (1 mL) was added to it dropwise. The mixture was allowed to warm to 0 °C for 1 h to afford **2q** (23.5 mg, 82%): IR (neat) 1612, 1513, 1248, 1092, 1038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J*=7 Hz, 3H), 1.11–1.36 (m, 5H), 1.40–1.52 (m, 1H), 1.67 (dd, *J*=6, 1 Hz, 3H), 2.20–2.32 (m, 1H), 3.30 (d, *J*=9 Hz, 2H), 3.80 (s, 3H), 4.43 (s, 2H), 5.23 (ddq, *J*=16, 8, 1 Hz, 1H), 5.47 (dq, *J*=16, 6 Hz, 1H), 6.87 (d, *J*=8 Hz, 2H), 7.25 (d, *J*=8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (−), 18.2 (−), 22.9 (+), 29.3 (+), 31.5 (+), 43.0 (−), 55.3 (−), 72.6 (+), 74.1 (+), 113.8 (−), 125.9 (−), 129.2 (−), 130.9 (+), 133.1 (−), 159.1 (+); HRMS (FAB) calcd for $C_{17}H_{26}O_2$ [M$^+$] 262.1933, found 262.1939. The enantiomeric information (96% ee, 98% CT) was determined by chiral HPLC: Chiralcel OB-H; hexane/*i*-PrOH=98/2, 0.2 mL/min, 40 °C; t_R (min)=61.8 (*R*), 72.9 (*S*).

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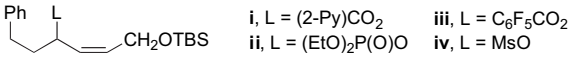
10. Attempted reaction with PhLi (2 equiv) and $MgBr_2$ (3 equiv) produced a mixture of *rac*-**4a** and -**1a** in a 21:79 ratio.
11. The *cis* isomers were synthesized by the method of Ref. 7.
12. We also examined reaction of several allylic esters **i**–**iii** with the Ph reagent derived from PhLi (2 equiv), $CuBr{\cdot}Me_2S$ (1 equiv), and $MgBr_2$ (3 equiv) under the optimized conditions mentioned in entry 5 of Table 1. No reaction took place with the isonicotinate **i**, which possesses the nitrogen atom at the 4 position, while pentafluorobenzoate **iii** gave 4% of *rac*-**2a**. In contrast, phosphate **ii** showed slightly lower reactivity than picolinate *rac*-**1a**, affording a mixture of *rac*-**2a** and **ii** in a 90:10 ratio by ^1H NMR spectroscopy. Preparation of mesylate **iv** was unsuccessful due to decomposition during the purification.



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