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Copper-catalyzed enantioselective allylic cross-coupling with alkylboranes

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ABSTRACT

We have presented full details of our work on alkylboranes, which we have introduced as new reagents for copper-catalyzed S_N2'-type enantioselective allylic substitutions. The copper catalysis delivered enantioenriched chiral products containing tertiary or quaternary carbon stereogenic centers branched with functionalized sp^3-alkyl groups. The wide availability of alkylboranes via the established alkene hydroboration reaction is an attractive feature of these transformations. Various functional groups are tolerated in the substrates. A reaction pathway involving addition–elimination of a neutral alkylcopper(I) species with the allyl chloride substrate is proposed.

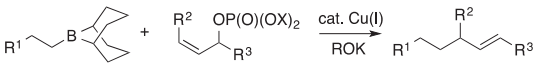
1. Introduction

Enantioselective allylic substitutions of organometallic reagents under the influence of chiral transition metal catalysts are efficient and versatile methods for asymmetric carbon–carbon bond formation.[1] In recent decades, reactions using organoboron compounds as organometallic reagents for allylic substitutions have achieved remarkable advances, given their broad substrate scopes and functional group compatibilities.[2–6] Unfortunately, however, usable organoboron reagents have generally been limited to aryl-, alkenyl-, allyl-, and allenylboron compounds, and the reactions of alkylboron derivatives have been rare and underdeveloped until very recently.[7a] In 2012, we reported the first catalytic enantioselective allylic substitution reaction with alkylboron compounds under catalysis of a chiral Cu(I) complex system. Later, the system was extended to catalytic enantioselective construction of all-carbon quaternary stereogenic centers.[7b] Herein, we present full details of our studies on the use of alkylboranes for copper-catalyzed S_N2'-type enantioselective allylic substitutions.[8,9]

2. Results/discussion

2.1. Construction of tertiary carbon stereogenic centers using γ-monosubstituted primary allylic substrates

2.1.1. Optimization. Previously, we reported that the allyl–alkyl coupling between enantioenriched chiral secondary (*Z*)-allylic phosphates and alkyl-9-BBN reagents proceeded with excellent γ-selectivity and stereospecificity under the influence of a catalytic amount of a copper(I) salt and a stoichiometric potassium alkoxide base (Scheme 1).[8a–c] On the basis of this knowledge, we initiated a program to develop an unprecedented catalytic enantioselective allylic alkylation with alkylboranes. Initial screening of ligands was conducted for the reaction of alkylborane **2a** (0.25 mmol), which was prepared from dimethoxyallylbenzene (**1a**), and γ-monosubstituted primary allyl chloride (*Z*)-**3a** (0.2 mmol) in the presence of CuCl (5 mol %) and MeOK in 1,4-dioxane at 35 °C (Table 1).[10] The ring-unsaturated C_2-symmetric *N*-heterocyclic carbene ligand



Scheme 1. Copper-catalyzed cross-coupling between alkylboranes and secondary (*Z*)-allylic phosphates.

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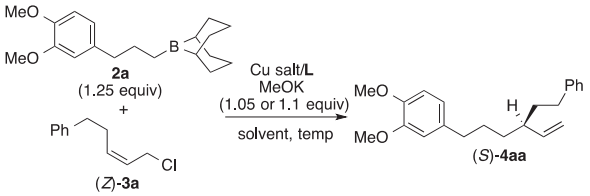
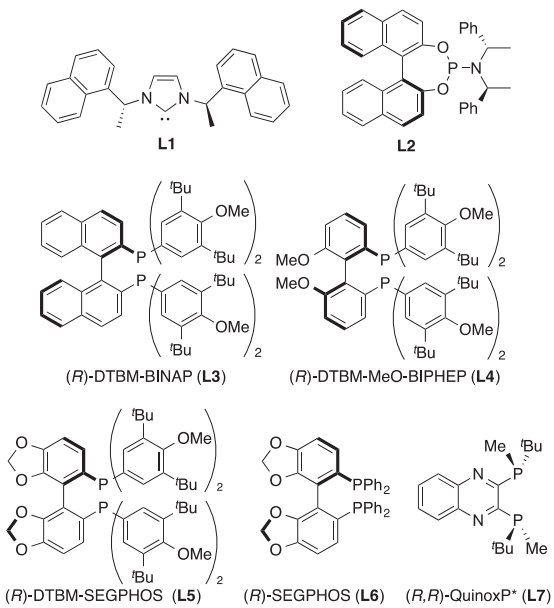
0040-4020/

Table 1
Copper-catalyzed enantioselective allylic substitutions between alkylborane **2a** and (*Z*)-**3a** under various conditions[a]



Entry	Cu/L (mol %)	Cu salt	L	Solvent	Temp (°C)	Yield[b,c] (%)	ee[d] (%)
1	5	CuCl	**L1**	Dioxane	35	3	0
2	5	CuCl	**L2**	Dioxane	35	0	—
3	5	CuCl	**L3**	Dioxane	35	5	37
4	5	CuCl	**L4**	Dioxane	35	25	47
5	5	CuCl	**L5**	Dioxane	35	48	61
6	5	CuCl	**L6**	Dioxane	35	0	—
7	5	CuCl	**L7**	Dioxane	35	99	7
8	5	CuCl	**L5**	THF	35	11	40
9	5	CuCl	**L5**	Toluene	35	7	41
10	5	CuCl	**L5**	DCM	35	Trace	—
11	10	CuCl	**L5**	Dioxane	10	23	74
12	10	CuCl	**L5**	Dioxane/DCM	10	81	77
13	10	CuOTf·(toluene)$_{0.5}$	**L5**	Dioxane/DCM	10	83	77
14	10	CuOTf·(toluene)$_{0.5}$	**L5**	Dioxane/DCM	5	55	80

[a] The reaction was carried out with (*Z*)-**3a** (0.2 mmol), **2a** (0.25 mmol), Cu salt, ligand (**L**), and MeOK (0.21 mmol, entries 1–10; 0.22 mmol, entries 11–14) in solvent (0.8 mL) for 12 h (entries 1–10) or 48 h (entries 11–14). Alkylborane **2** was prepared in advance by hydroboration of **1** with the 9-BBN dimer at 60 °C (1 h) and used without purification.
[b] The yield was determined by ^{1}H NMR.
[c] Constitutional isomer ratio γ/α>20:1 (determined by ^{1}H NMR analysis of the crude product).
[d] The enantiomeric excess was determined by HPLC analysis.



(**L1**)[11] having 1-(1-naphthyl)ethyl groups at both nitrogen atoms gave racemic **4aa** (entry 1). The chiral phosphoramidite ligand (**L2**) did not form an active catalyst (entry 2). Further screening of various chiral ligands revealed that introducing 3,5-di-*tert*-butyl-4-methoxyphenyl (DTBM) substituents on the phosphorus atoms of chiral bisphosphines was essential not only for enantiocontrol, but also for catalytic activity with bisphosphine-based chiral copper catalysts. (*R*)-DTBM-BINAP (**L3**) induced low catalytic activity and enantioselectivity (entry 3). The use of DTBM-MeO-BIPHEP (**L4**) gave better product yield and enantioselectivity (entry 4). The use of (*R*)-DTBM-SEGPHOS[12] (**L5**) led to an improvement in the product yield and enantioselectivity (entry 5), giving the branched γ-substitution product (*S*)-**4aa** (γ/α>20:1). In contrast, non-DTBM-substituted chiral bisphosphines, (*R*)-SEGPHOS (**L6**) or (*R*,*R*)-Quinox P* (**L7**),[13] resulted in complete inhibition of the reaction or loss of enantiocontrol, respectively (entries 6 and 7). The introduction of the DTBM substituents may have induced the deaggregation of alkylcopper(I) species to form a catalytically active monomeric copper complex.[14]

Next, the effect of solvent was examined in the reaction between **2a** and (*Z*)-**3a** with the CuCl–**L5** catalyst system (Table 1, entries 8–12). The use of THF or toluene as a solvent instead of 1,4-dioxane resulted in poor yields (11% and 7%) and lower enantioselectivities (40% and 41% ees) (entries 8 and 9). Dichloromethane (DCM) as solvent inhibited the reaction almost completely (entry 10). The enantioselection was improved to 74%

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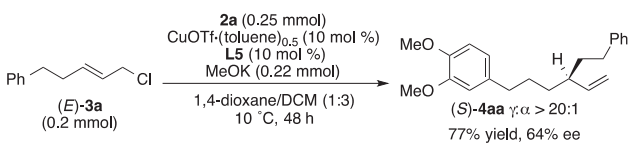
ee by carrying out the reaction at 10 °C with 10 mol % catalyst loading in 1,4-dioxane, but with a serious reduction of the yield (23%, entry 11). Finally, we found that the reaction proceeded much more efficiently in a mixed solvent system, 1,4-dioxane/DCM (1:3). The reaction with 10 mol % catalyst loading at 10 °C afforded (*S*)-**4aa** with 77% ee in 81% yield (entry 12). A slightly higher yield (83%) was obtained by changing CuCl to CuOTf·(toluene)$_{0.5}$ with the enantioselectivity unchanged (entry 13). The enantioselection could be improved to 80% ee by reducing the reaction temperature to 5 °C at the expense of the yield (55%) (entry 14).

2.1.2. Effects of leaving groups and bases. Effects of leaving groups and bases were examined in the reaction of **2a** and (Z)-**3a** under the conditions for Table 1, entry 5 [CuCl/**L5**, 1,4-dioxane, 35 °C] (Table 2).[10] Replacing the leaving group with a bromide or phosphate caused drastic reductions of the product yield and enantioselectivity (entries 1–3).

2.1.3. Effect of alkene geometry. The reaction of allyl chloride **3a** with *E*-configuration under the optimized conditions (the conditions for Table 1, entry 13) provided the product with the same absolute configuration with 64% ee (Scheme 2, see Section 2.5 for discussion on the effect of alkene geometries).[10,15]

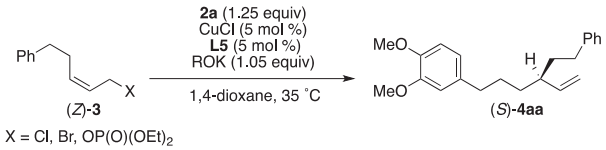


Scheme 2. Copper-catalyzed allylic substitutions of alkylborane and (*E*)-allyl chloride.

2.1.4. Substrate scopes. Various terminal alkenes (**1**) and *Z*-allyl chlorides (**3**) were subjected to 9-BBN-hydroboration and were used for the enantioselective allylic substitution with the CuOTf·(toluene)$_{0.5}$/(*R*)-DTBM-SEGPHOS (**L5**) catalyst system (Table 3).[10] The reactions proceeded with excellent γ-selectivities (γ/α>20:1) and high enantioselectivities (76–90% ee). Terminal alkenes having functional groups such as acetal, silyl ether, ester, and phthalimide moieties at the terminal of the aliphatic chain were compatible with the protocol (entries 1–8). Functional groups such as chloro and silyl ether moieties in the allylic substrates were also tolerated (entries 2, 7 and 8).

The tolerance of this reaction toward smaller or sterically more demanding γ-substituents is demonstrated in the successful conversion of the γ-methyl or γ-cyclohexyl-substituted allyl chlorides (**3d**, **e**), although reductions in yield and enantioselection were observed (**4dd**, 70%, 81% ee; **4de**, 53%, 76% ee, Table 3, entries 4 and 5). Unfortunately, the attempt to use the alkylborane (**2g**) derived from styrene (**1g**) failed (entry 9).

Table 2
Effect of leaving groups and bases[a]



Entry	Leaving group	ROK	Yield[b,c] (%)	ee[d] (%)
1	Cl (Table 1, entry 5)	MeOK	48	61
2	Br	MeOK	18	34
3	OP(O) $(OEt)_2$	MeOK	5	13
4	Cl	*t*-BuOK	39	57
5	Cl	PhOK	0	—
6	Cl	MeOLi	Trace	—
7	Cl	MeONa	0	—

[a] The reaction was carried out with **3** (0.2 mmol), **2a** (0.25 mmol), Cu salt (5 mol %), **L5** (5 mol %), and base (0.21 mmol) in 1,4-dioxane (0.8 mL) for 12 h. Alkylborane **2** was prepared in advance by hydroboration of **1** with the 9-BBN dimer at 60 °C (1 h) and used without purification.
[b] The yield was determined by ^{1}H NMR.
[c] Constitutional isomer ratio γ/α>20:1 (determined by ^{1}H NMR analysis of the crude product).
[d] The enantiomeric excess was determined by HPLC analysis.

Changing the alkoxide base from MeOK to the bulkier *t*-BuOK decreased the yield (39%) and enantioselectivity (57% ee) (Table 2, entry 4). No reaction occurred with the weaker base PhOK (entry 5). The use of Li or Na methoxides also resulted in virtually no reaction (entries 6 and 7).

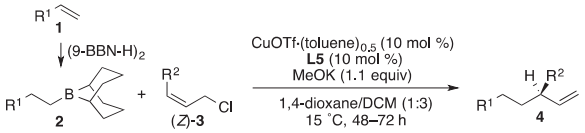
The inefficiency of the Li or Na methoxides may reflect higher solubilities of Li or Na salts, which may cause inhibitory effects in the hydrophobic solution phase of the reaction mixture. This assumption also explains the increase in the reaction efficiency when DCM was used as a co-solvent with 1,4-dioxane (Table 1, entry 12).

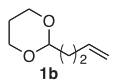
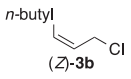
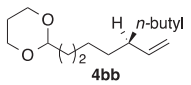
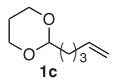
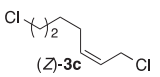
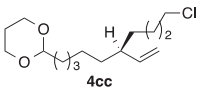
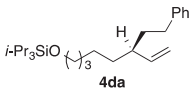
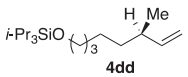
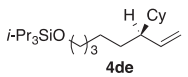
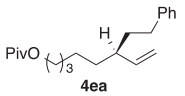
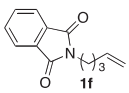
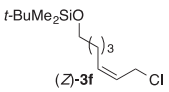
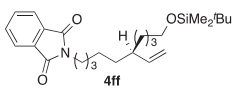
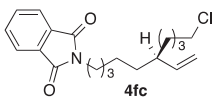
2.1.5. Synthesis of chiral allylsilanes. The reaction between a γ-silylated allyl chloride (**3g**) and alkylboranes afforded enantioenriched α-stereogenic chiral allylsilanes (Table 4).[10,16–18] For instance, the reaction between alkylborane **2h**, which was derived from terminal alkene **1h**, and **3g** under the conditions optimized for the reaction of (*Z*)-**3a** proceeded with complete γ-selectivity, and afforded chiral allylsilane **4hg** with 91% ee in 77% yield (entry 1). The terminal alkenes (**1c**,**e**,**f**,**i**) bearing acetal, ester, phthalimide or chloro moieties were also compatible with the protocol with comparable enantioselectivities (entries 2–5).

2.2. Construction of quaternary carbon stereogenic centers using γ,γ-disubstituted primary allylic substrates

2.2.1. Background on construction of quaternary carbon stereogenic centers. Catalytic enantioselective construction of all-carbon quaternary stereogenic centers in acyclic systems is one of the biggest challenges in organic synthesis.[19] One of the obstacles is low reactivity due to the steric repulsion that occurs in the carbon–carbon bond formation step. It is also difficult to discriminate the enantiotopic faces due to steric congestion and the diminished steric difference between the non-hydrogen substituents. To this end, transition-metal-catalyzed

Table 3
Scope of enantioselective allylic substitution with alkylboranes[a]



Entry	Alkene	Allyl chloride	Product	Yield[b,c] (%)	ee[d] (%)
1[e]	 **1b**	 (*Z*)-**3b**	 **4bb**	93	88
2	 **1c**	 (*Z*)-**3c**	 **4cc**	71	83
3	 **1d**	(*Z*)-**3a**	 **4da**	71	88
4[f]	**1d**	 (*Z*)-**3d**	 **4dd**	70	81
5	**1d**	 (*Z*)-**3e**	 **4de**	53	76
6	 **1e**	(*Z*)-**3a**	 **4ea**	73	88
7	 **1f**	 (*Z*)-**3f**	 **4ff**	73	88
8	**1f**	(*Z*)-**3c**	 **4fc**	72	90
9	 **1g**	(*Z*)-**3a**	—	0	—

[a] The reaction was carried out with (*Z*)-**3** (0.2 mmol), **2** (0.25 mmol), CuOTf·(toluene)$_{0.5}$ (10 mol %), **L5** (10 mol %), and MeOK (0.22 mmol) in 1,4-dioxane/DCM (1:3, 0.8 mL) at 10 °C (entry 3) or 15 °C (entries 1, 2, and 4–9) for 48 h (entries 2, 3, 7, and 9) or 72 h (entries 1, 4–6, and 8). Alkylborane **2** was prepared in advance by hydroboration of **1** with the 9-BBN dimer at 60 °C (1 h) and used without purification.
[b] The yield of the isolated product.
[c] Constitutional isomer ratio γ/α>20:1 (determined by ^{1}H NMR analysis of the crude product).
[d] The enantiomeric excess was determined by HPLC analysis.
[e] Reaction on 1.0 mmol scale.
[f] Compound **2** (0.34 mmol) and MeOK (0.3 mmol) were used.

enantioselective allylic substitutions with organometallic nucleophiles such as organolithium, Grignard, diorganozinc or triorganoaluminum reagents have proven to be effective strategies.[1] Organoboron compounds have also been used for enantioselective construction of all-carbon quaternary stereogenic centers through allylic substitution.[4,5b] However, the methodology has not yet been generalized to allow the reaction of sp^3-alkylboron nucleophiles.

The aforementioned enantioselective copper-catalyzed reaction was not applicable to the construction of quaternary stereogenic centers (Section 2.1). However, only a slight modification to the catalyst system enabled the construction of a quaternary stereogenic carbon center through copper-catalyzed enantioselective allylic substitution of alkylboranes and γ,γ-disubstituted allyl chlorides.

2.2.2. Optimization. As shown in Table 5, we examined copper complexes prepared from CuOTf·(toluene)$_{0.5}$ (10 mol %) and various DTBM-substituted chiral bisphosphine ligands for catalytic activity, γ-regioselectivity, and enantioselectivity in the reaction of γ,γ-disubstituted allyl chloride (*E*)-**5a** with alkylborane **2a** in the presence of EtOK in 1,4-dioxane/DCM (1:3) at 25 °C over 20 h (**5a**/**2a**/EtOK 1:1.25:1.1) (Table 5, entries 1–4).[20] Specifically, the catalyst prepared from the DTBM-substituted TunePHOS-type chiral bisphosphine (**L8**) did not promote the reaction at all (entry 1).[21] (*R*)-DTBM-BINAP (**L3**) induced only low catalytic activity, γ-selectivity, and enantioselectivity (entry 2). (*R*)-DTBM-SEGPHOS (**L5**), which exhibited high performance in the reaction with γ-monosubstituted primary allyl chlorides (Section 2.1), imparted moderate γ-selectivity (γ/α 6:1) and enantioselectivity (47% ee), but the product yield was lower than that with **L3** (entry 3). To our delight,

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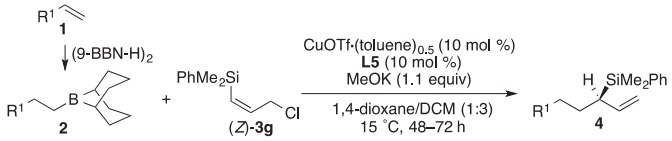
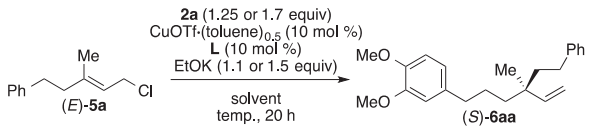
Table 4
Synthesis of chiral allylsilanes[a]



Entry	Alkene	Product	Yield[b,c] (%)	ee[d] (%)
1	*n*-hexyl, **1h**	*n*-hexyl, H, $SiMe_2Ph$, **4hg**	77	91
2	**1c**	O, O, 3, H, $SiMe_2Ph$, **4cg**	66	91
3	**1e**	PivO, 3, H, $SiMe_2Ph$, **4eg**	52	87
4	**1f**	O, N, O, 3, H, $SiMe_2Ph$, **4fg**	85	90
5[e]	Cl, 4, **1i**	Cl, 4, H, $SiMe_2Ph$, **4ig**	88	91

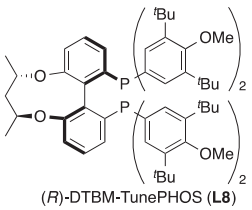
[a] The reaction was carried out with (*Z*)-**3g** (0.2 mmol), **2** (0.25 mmol), CuOTf·(toluene)$_{0.5}$ (10 mol %), **L5** (10 mol %), and MeOK (0.22 mmol) in 1,4-dioxane/DCM (1:3, 0.8 mL) at 15 °C for 48 h (entries 1, 2, 4, and 5) or 72 h (entry 3). Alkylborane **2** was prepared in advance by hydroboration of **1** with the 9-BBN dimer at 60 °C (1 h) and used without purification.
[b] The yield of the isolated product.
[c] Linear isomer was not detected: γ/α>99:1 (^{1}H NMR).
[d] The enantiomeric excess was determined by HPLC analysis.
[e] Reaction on 1.0 mmol scale.

Table 5
Copper-catalyzed enantioselective allylic substitutions between **2a** and (*E*)-**5a** under various conditions[a]



Entry	Ligand (L)	Solvent	Temp (°C)	Yield[b] (%)	γ/α[c]	ee[d] (%)
1	**L8**	Dioxane/DCM	25	0	—	—
2	**L3**	Dioxane/DCM	25	38	3.5:1	21
3	**L5**	Dioxane/DCM	25	15	6:1	47
4	**L4**	Dioxane/DCM	25	26	>20:1	83
5	**L4**	THF/DCM	25	56	>20:1	81
6[e]	**L4**	THF/DCM	15	65	>20:1	81

[a] The reaction was carried out with (*E*)-**5a** (0.2 mmol), **2a** (0.25 mmol), CuOTf·(toluene)$_{0.5}$ (10 mol %), ligand (**L**) (10 mol %), and EtOK (0.22 mmol) in solvent (0.8 mL) for 20 h. Alkylborane **2** was prepared in advance through hydroboration of **1** with the 9-BBN dimer at 60 °C (1 h) and used without purification.
[b] Yield of the isolated product.
[c] Determined by ^{1}H NMR analysis of the crude product.
[d] The enantiomeric excess was determined by HPLC analysis.
[e] Reaction on 0.3 mmol scale. Compound **2a** (0.52 mmol) and EtOK (0.45 mmol) were used.



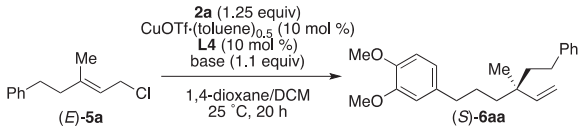
(*R*)-DTBM-TunePHOS (**L8**)

the use of (*R*)-DTBM-MeO-BIPHEP (**L4**) led to a significant improvement in the regioselectivity and enantioselectivity (entry 4). The alkylation occurred at the disubstituted γ-carbon atom of **5a** (γ/α>20:1), constructing the all-carbon quaternary stereogenic center with 83% ee in favor of the formation of (*S*)-**6aa** (*si*-face attack), albeit still with a low product yield.

The product yield with the Cu–(*R*)-DTBM-MeO-BIPHEP (**L4**) system could be increased to 56% by changing the solvent to THF/DCM (1:3) with the enantioselectivity almost unchanged (81% ee) (Table 5, entry 5).[20] The yield was further improved to 65% by conducting the reaction at 15 °C with an increased amount of the **2a**/EtOK reagent (**5a**/**2a**/EtOK 1:1.7:1.5) (entry 6).

2.2.3. Effect of bases. The effect of bases is summarized in Table 6. The use of MeOK instead of EtOK under the conditions for Table 5, entry 4 [CuOTf·(toluene)$_{0.5}$, **L4**, dioxane/DCM, 25 °C] decreased the product yield (14% yield) with the regioselectivity and enantioselectivity unchanged (entry 2). The use of *t*-BuOK resulted in no reaction (entry 3).

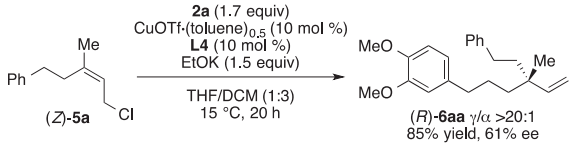
Table 6
Effect of bases[a]



Entry	Base	Yield[b] (%)	γ/α[c]	ee[d] (%)
1 (Table 5, entry 4)	EtOK	26	20:1	83
2	MeOK	14	20:1	83
3	*t*-BuOK	0	—	—

[a] The reaction was carried out with (*E*)-**5a** (0.2 mmol), **2a** (0.25 mmol), CuOTf·(toluene)$_{0.5}$ (10 mol %), **L4** (10 mol %), and EtOK (0.22 mmol) in solvent (0.8 mL) for 20 h. Alkylborane **2** was prepared in advance through hydroboration of **1** with the 9-BBN dimer at 60 °C (1 h) and used without purification.
[b] Yield of the isolated product.
[c] Determined by ^{1}H NMR analysis of the crude product.
[d] The enantiomeric excess was determined by HPLC analysis.

2.2.4. Effect of alkene geometry. The reaction of (*Z*)-**5a** under the optimized conditions (the conditions for Table 5, entry 6) provided (*R*)-**6aa**, the antipode of the product derived from (*E*)-**5a**, with 61% ee in 85% yield (Scheme 3).[20] This enantioselectivity is lower than that for the reaction of (*E*)-**5a** (see Section 2.5 for discussion on enantioselection models).



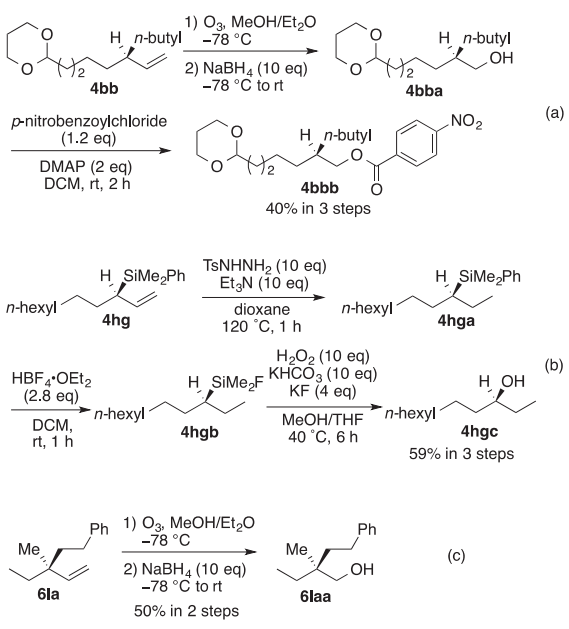
Scheme 3. Copper-catalyzed allylic substitution of γ,γ-disubstituted (Z)-allyl chloride.

2.2.5. Substrate scopes. Various terminal alkenes having different functional groups such as acetal, silyl ether, ester, chloro or benzyl ether in the aliphatic chain were compatible with this protocol as demonstrated by their reactions with (*E*)-**5a** (Table 7, entries 1–6).[20] Ethylene also served as a suitable substrate (entry 7).[20] This reaction delivered an ethyl group to the fully substituted γ-carbon atom of **5a** with enantioselectivity at a useful level.

The scope of γ,γ-disubstituted allyl chlorides (**5**) successfully employed is also shown in Table 7 (entries 8–10).[20] An additional trisubstituted alkene moiety in the allylic substrate **5b** was tolerated during the formation of diene **6ab** (entry 8). The copper catalyst system enabled the enantioselective coupling of allyl chlorides having two alkyl substituents of almost equal steric demands at the γ-position (entries 9 and 10). For example, allyl chloride **5c** having ethyl and phenylethyl groups at the γ-position reacted with high enantioselectivity (81% ee) (entry 9). Replacing the ethyl group at the γ-position of **5c** with a propyl group caused only a slight reduction in the enantioselectivity (entry 10).

2.3. Determination of absolute configurations of allylic coupling products

Transformation of the coupling product **4bb** to the *p*-nitrobenzoate derivative **4bbb**[8c] through ozonolysis and reduction with $NaBH_4$ followed by benzoylation confirmed the (*R*) absolute configuration of **4bb** (Scheme 4a). The absolute configuration of allylsilane **4hg** was determined to be *R* by the optical rotation of (*S*)-undecan-3-ol (**4hgc**)[22] by alkene reduction followed by Fleming–Tamao oxidation[23] with retention of configuration (Scheme 4b). The absolute configuration of the coupling product **6la** with a quaternary stereogenic center was confirmed by optical rotation of (*S*)-2-ethyl-2-methyl-4-phenyl-1-butanol (**6laa**) obtained by ozonolysis followed by reduction with $NaBH_4$ (Scheme 4c).[24] Absolute configurations of the other coupling products were assigned by consideration of the stereochemical pathway.

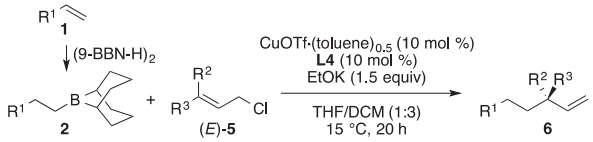


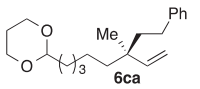
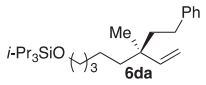
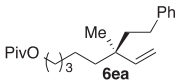
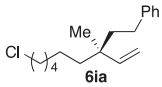
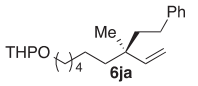
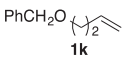
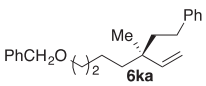
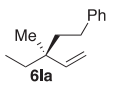
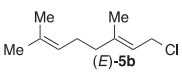
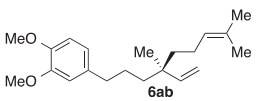
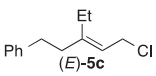
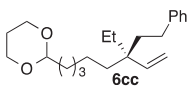
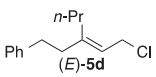
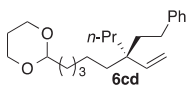
Scheme 4. Determination of absolute configuration.

2.4. Proposed reaction pathway for the copper-catalyzed allylic alkylations

As proposed for the Cu-catalyzed allyl–alkyl coupling between secondary allylic phosphates and alkylboranes,[8a–c] an active organocopper species is likely in the form of a neutral organocopper(I) species (**C**) rather than a monoorganoheterocuprate, since an alkoxide base is consumed for the formation of borate **B**, and the copper center bearing the alkyl ligand and the bisphosphine ligand

Table 7
Scope of enantioselective allylic substitutions with alkylboranes[a]



Entry	Alkene	Allyl chloride	Product	Yield[b,c] (%)	ee[d] (%)
1	**1c**	(*E*)-**5a**	 **6ca**	79	90
2	**1d**	(*E*)-**5a**	 **6da**	85	83
3	**1e**	(*E*)-**5a**	 **6ea**	66	81
4[e]	**1i**	(*E*)-**5a**	 **6ia**	80	86
5[f]	 **1j**	(*E*)-**5a**	 **6ja**	70	86
6	 **1k**	(*E*)-**5a**	 **6ka**	68	81
7	 **1l**	(*E*)-**5a**	 **6la**	63	71
8	**1a**	 (*E*)-**5b**	 **6ab**	54	73
9[e]	**1c**	 (*E*)-**5c**	 **6cc**	75	81
10[e]	**1c**	 (*E*)-**5d**	 **6cd**	67	71

[a] The reaction was carried out with (*E*)-**5** (0.2 mmol), **2** (0.34 mmol), CuOTf·(toluene)$_{0.5}$ (5 mol %), (*R*)-DTBM-MeO-BIPHEP (**L4**) (10 mol %), and EtOK (0.3 mmol) in THF/DCM (1:3, 0.8 mL) at 15 °C for 20 h. Alkylborane **2** was prepared in advance through hydroboration of **1** with the 9-BBN dimer at 60 °C (1 h) and used without purification.
[b] Yield of the isolated product.
[c] Constitutional isomer ratio γ/α>20:1 (determined by ^{1}H NMR analysis of the crude product).
[d] The enantiomeric excess was determined by HPLC analysis.
[e] Constitutional isomer ratio γ/α>10:1.
[f] Diastereomeric ratio (1:1).

is coordinatively saturated upon alkene coordination. Therefore, the addition of alkylcopper(I) species **C** would occur with *anti* stereochemistry with respect to the leaving group, being followed by *anti*-β-elimination (Fig. 1).

Earlier, we proposed that the alkoxyborane, which is derived from the transmetalation between CuX–bisphosphine [**A**, X=OMe, OEt or Cl] and a trialkyl(alkoxo)borate **B**, might activate the chloride leaving group through its Lewis-acidic character during the organocopper addition–elimination pathway [**D**/**E**→**F-TS**/**G-TS**→**H**/**I**→**4** or **6**] (Fig. 1).[7] However, our ongoing theoretical calculations indicate that the alkoxyborane is not able to coordinate to the chloride leaving group.[25]

The formation of the α-coupling product in the reaction of γ,γ-disubstituted primary allylic substrates with (*R*)-DTBM-BINAP (**L3**) or (*R*)-DTBM-SEGPHOS (**L5**) might be due to the formation of an alkyl(ethoxo)cuprate species upon dissociation of one or two P atoms of the chiral ligands (Table 5, entries 2 and 3). Such cuprate species would undergo oxidative addition with **5** to form an isomeric mixture of ([σ+π]-allyl)copper(III) species with a C–Cu σ bond either at the α or γ carbon atoms. Reductive elimination of

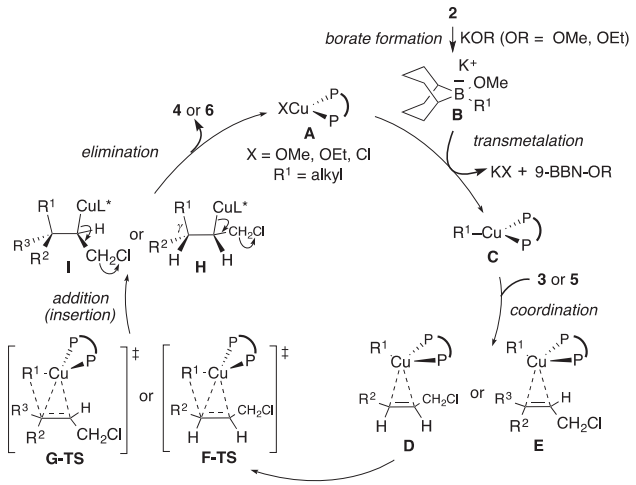


Fig. 1. Possible catalytic cycle.

these allylcopper(III) intermediates may form a mixture of the α- and γ-coupling products as minor products.[26,27]

2.5. Proposed models for enantiodiscrimination

The enantioselection likely occurs at transition states of the R^1—Cu addition across the C—C double bond. Enantioselection models for the reaction of γ-monosubstituted primary allylic phosphates (*Z*)-**3** are given in Fig. 2 (**F-TS-1** and **F-TS-2**). In this model, the copper adopts tetrahedral coordination geometry, in which the axis of the C—C double bond is coplanar with the Cu—R^1 bond, Ar^1 and Ar^3 are equatorial, and Ar^2 and Ar^4 are axial. Importantly, Ar^1 points toward the allyl chloride substrate more significantly than the other equatorial aryl group (Ar^3). The axial aryl groups (Ar^2 and Ar^4) are much more distal to the substrate. According to these assumptions, **F-TS-1** has less steric strain than **F-TS-2**, because Ar^1 is close to both the R^2 and $ClCH_2$ substituents in **F-TS-2**, while **F-TS-1** encounters the corresponding steric repulsions only between Ar^3 and the R^2 substituent, which should be relatively small due to the distal location of Ar^3.

In the case of the reaction with (*E*)-**3**, Ar^1 causes steric repulsions toward either the $ClCH_2$ (**F-TS-3**) or R^2 substituents (**F-TS-4**) (Fig. 2). Consequently, the energy difference between **F-TS-3** and **F-TS-4** is smaller than that between **F-TS-1** and **F-TS-2**. These considerations explain the more efficient enantioselection in the reaction with the allylic substrate with *Z*-configuration (Table 1, entry 13 vs Scheme 2). The observed stereoconvergency from the *Z* and *E* allylic substrates affording the product with the identical absolute configuration suggests Ar^1 has greater steric interaction with the R^2 substituent (**F-TS-4**) than with the $ClCH_2$ substituent (**F-TS-3**).

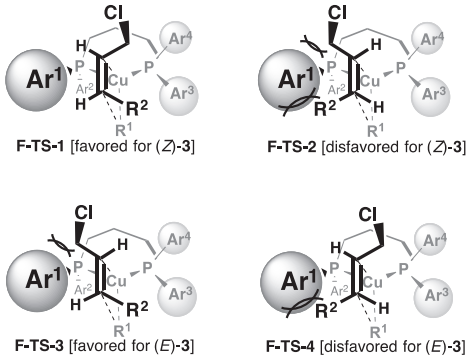


Fig. 2. Models for enantiodiscrimination. Ar^1—Ar^4 are the P-substituents of **L5**. The biaryl scaffold of **L5** is simplified with a polygonal line.

Enantioselection models for the reaction of γ,γ-disubstituted primary allylic phosphates are depicted in Fig. 3 based on the fact that the reactions of *E*- and *Z*-isomers of **5a** gave the antipodes of **6**, respectively, the former showing higher enantioselectivity (Table 5, entry 6 vs Scheme 3). In the π-complex **E** (see Fig. 1), the allyl chloride substrate (**5**) bound to the tetrahedral copper center is in proximity to the two P-substituents Ar^1 and Ar^3, which are axial and equatorial substituents, respectively, of the bisphosphine—Cu chelate ring. The axial substituent Ar^1 points toward the substrate more than the equatorial Ar^3. R_l and R_s indicate the larger and smaller γ-substituents of **5**, respectively. **E-1**, which leads to the major enantiomer of **6** in the reaction of (*E*)-**5**, has steric repulsion only between R_s and Ar^3, while the corresponding π-complex (**E-2**) leading to the minor enantiomer has larger steric repulsions between the $ClCH_2$ group and Ar^1 and between Ar^3 and R_l. A similar discussion should be applicable for the transition state (**G-TS**).

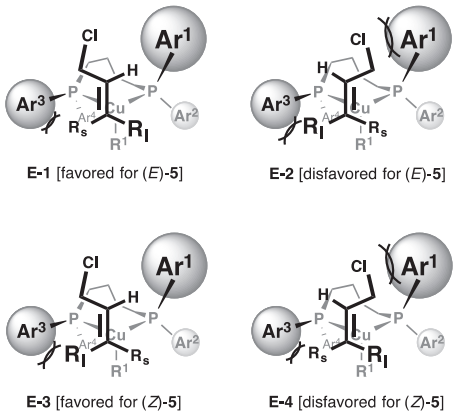


Fig. 3. Proposed models for enantiodiscrimination. R_l and R_s are the larger and smaller γ-substituents of **5**, respectively. Ar^1—Ar^4 are the P-substituents of **L4**. The biaryl scaffold of **L4** is simplified with a polygonal line.

In the case of the reaction of (*Z*)-**5**, the π-complex (**E-3**) leading to the major enantiomer, the antipode of the product from **E-1**, has a steric repulsion between Ar^3 and R_l, which should be larger than the steric repulsion that occurs in **E-1** (R_l vs R_s) (Fig. 3). On the other hand, the steric repulsion between Ar^3 and R_s in **E-4** should be smaller than that between Ar^3 and R_l in **E-2**. These considerations also match the observed trend that the enantioselectivity gradually decreased with the increase of the size of the R_s substituent of (*E*)-**5** (Table 7, entries 1, 9, and 10). This can be explained by the increasing steric repulsion between Ar^3 and R_s in **E-1**.

3. Conclusion

Here we have presented full details of our work on alkylboranes, which we have introduced as new reagents for copper-catalyzed S_N2'-type enantioselective allylic substitutions. The copper catalysis delivered enantioenriched chiral products containing tertiary or quaternary carbon stereogenic centers branched with functionalized sp^3-alkyl groups. The wide availability of alkylboranes via the established alkene hydroboration reaction is an attractive feature of these transformations. Various functional groups are tolerated in the substrates. The introduction of DTBM substituents on the phosphorus atoms of chiral bisphosphines was important for promotion of the reaction. The catalytic activity, γ-selectivity, and enantioselectivity of the reaction were very sensitive to the

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dihedral angle of the axially chiral biaryl scaffolds in the Cu(I)–bisphosphine complexes. A reaction pathway involving addition–elimination of a neutral alkylcopper(I) species with the allyl chloride substrate is proposed.

4. Experimental section

4.1. General

NMR spectra were recorded on a Varian Gemini 2000 spectrometer, operating at 300 MHz for ^{1}H NMR and 75.4 MHz for ^{13}C NMR, and a JEOL ECX-400, operating at 100.5 MHz for ^{13}C NMR. Chemical shift values for ^{1}H and ^{13}C are referenced to Me_4Si and the residual solvent resonances, respectively. Chemical shifts are reported in δ ppm. Mass spectra were obtained with Thermo Fisher Scientific Exactive, JEOL JMS-T100LP or JEOL JMS-700TZ at the Instrumental Analysis Division, Equipment Management Center, Creative Research Institution, Hokkaido University. Elemental analysis was performed at the Instrumental Analysis Division, Equipment Management Center, Creative Research Institution, Hokkaido University. HPLC analyses were conducted on a HITACHI ELITE LaChrom system with a HITACHI L-2455 diode array detector. IR spectra were recorded on a Perkin–Elmer Spectrum One. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F_{254}. Silica gel (Kanto Chemical Co., Silica gel 60 N, spherical, neutral) was used for column chromatography. Melting points were measured on a Yanaco MP-500D apparatus. Gel permeation chromatography (GPC) was performed by LC-908 (Japan Analytical Industry Ltd., two in-line JAIGEL-2H, $CHCl_3$, 3.5 mL/min, UV and RI detectors).

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. 9-Borabicyclo[3,3,1]nonane dimer (9-BBN-H)$_2$, CuOTf·(toluene)$_{0.5}$, MeOK, EtOK, (*R*)-DTBM-MeO-BIPHEP (**L4**), and (*R*)-DTBM-BINAP (**L3**) were purchased from Aldrich Chemical Co., stored under nitrogen, and used as it is. (*R*)-DTBM-SEGPHOS (**L5**) was purchased from Strem Chemicals Inc., stored under nitrogen, and used as it is. (*R*)-DTBM-TunePHOS (**L8**) was prepared according to the literature procedure.[21] Dichloromethane (DCM) was purchased from Kanto Chemical Co., stored over 4 Å molecular sieves under nitrogen. 1,4-Dioxane was purchased from Kanto Chemical Co., distilled from sodium/benzophenone and stored over 4 Å molecular sieves under nitrogen. Alkenes **1a**–**l** are well known compounds. Allyl chrolides **3d**, (*E*)-**5a**,**b** are found in the literature.[28]

4.2. Preparation of allyl chlorides

*4.2.1. Preparation of (Z)-allyl chlorides **3a**–**c**, **e**, and **f**.* Addition of the lithium acetylides to formaldehyde gave the corresponding propargylic alcohols. Next, Lindlar reduction followed by chlorination (NCS, PPh_3, DCM, rt) afforded the allylic chlorides **3a**–**c**, **e**, and **f**.

*4.2.2. Preparation of (Z)-1-dimethylphenysilyl-3-chloro-1-pentene (**3g**).* THP-protection of 2-propyn-1-ol followed by silylation gave γ-silylated propargylic alcohol derivative. Next, DIBAL-H reduction followed by deprotection (*p*-TsOH, MeOH) afforded γ-silylated allylic alcohol. Finally, **3g** was prepared by chlorination (NCS, PPh_3, DCM, rt) of the γ-silylated allylic alcohol.

*4.2.3. Preparation of γ,γ-disubstituted (E)-allyl chlorides **5a**, **c**, and **d**.* The preparation of **5a** is representative. To a solution of CuI (1.8 g, 9.6 mmol) and TMEDA (3.6 mL, 24 mmol) in THF (1.0 mL) was added 2-phenylethylmagnesium bromide (0.7 M in THF, 13.7 mL, 9.6 mmol) at −40 °C, and the resulting mixture was stirred at −40 °C for 30 min. To the mixture was added ethyl 2-butynoate (0.9 g, 8 mmol) at −78 °C, and the mixture was stirred at −78 °C for 2 h. Saturated NH_4Cl aq was added and the mixture was allowed to warm to rt. The resulting slurry was diluted with EtOAc (50 mL) and washed with H_2O and brine. The organic layer was separated and dried over $MgSO_4$. Then, the drying agent was removed by filtration, and the resulting solution was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (0–10% EtOAc/hexane) provided ethyl (*E*)-3-methyl-5-phenyl-2-pentenoate (1.7 g, 7.6 mmol) in 95% yield.

To a stirred solution of ethyl (*E*)-3-methyl-5-phenyl-2-pentenoate (1.7 g, 7.6 mmol) in DCM was dropped DIBAL-H (16.4 mL in 1.02 M hexane solution, 16.7 mmol) at −78 °C and the reaction was continued for 30 min at the same temperature. Satd NH_4Cl was added and the mixture was vigorously stirred for 10 min. Solid was filtered through Celite pad and the filtrate was extracted with ether. The crude product was purified by flash chromatography on silica gel (10–20% EtOAc/hexane) to give (*E*)-3-methyl-5-phenyl-2-penten-1-ol (1.2 g, 6.6 mmol) in 87% yield.

To a solution of (*E*)-3-methyl-5-phenyl-2-penten-1-ol (1.2 g, 6.6 mmol) in DCM (13.2 mL), NCS (1.0 g, 7.3 mmol) and PPh_3 (2.0 g, 7.9 mmol) were sequentially added at 0 °C. After being stirred at rt for 2 h, the solvent was removed under reduced pressure, and then residue was filtered through a pad of Celite with EtOAc as an eluant. The filtrate was evaporated under reduced pressure. The residue was purified through flash chromatography on silica gel (hexane) followed by Kugelrohr disitillation provided **5a** (1.1 g, 5.6 mmol) in 80% yield.

*4.2.4. Preparation of γ,γ-Disubstituted (E)-Allyl chloride **5b**.* To a solution of geraniol (1.5 g, 10 mmol) in DCM (20 mL), NCS (1.5 g, 11 mmol) and PPh_3 (3.1 g, 12 mmol) were sequentially added at 0 °C. After being stirred at rt for 2 h, the solvent was removed under reduced pressure, and then residue was filtered through a pad of Celite with hexane as an eluant. The filtrate was evaporated under reduced pressure. The residue was purified by Kugelrohr disitillation to provide **5b** (1.4 g, 8 mmol) in 80% yield.

4.3. Procedures for copper-catalyzed enantioselective allylic substitution with alkylboranes

4.3.1. Typical procedure for copper-catalyzed allylic substitutions with γ-monosubstituted primary allyl chlorides (Table 3, entry 1). 2-(3-Buten-1-yl)-1,3-dioxane (**1b**) (196.6 μL, 1.3 mmol) and (9-BBN-H)$_2$ (151.2 mg, 0.625 mmol) were placed in a vial containing a magnetic stirring bar. The vial was sealed with a Teflon®-coated silicon rubber septum and the vial was evacuated and filled with argon. 1,4-Dioxane (1.0 mL) was added to the vial, and then the mixture was stirred at 60 °C for 1 h to prepare an alkylborane. On the other hand, CuOTf·(toluene)$_{0.5}$ (26 mg, 0.1 mmol), (*R*)-DTBM-SEGPHOS (**L5**) (118 mg, 0.1 mmol), and MeOK (77 mg, 1.1 mmol) were placed in another vial. The vial was sealed with a Teflon®-coated silicon rubber septum and the vial was evacuated and filled with argon. After DCM (3.0 mL) was added to the vial, the mixture was stirred at 25 °C for 1 h. Next, the alkylborane solution was transferred to the vial containing a Cu(I)–**L5** complex. Then, allyl chloride **3b** (132.6 mg, 1.0 mmol) was added. After 72 h stirring at 15 °C, diethyl ether was added to the mixture. The mixture was filtered through a short plug of silica gel, which was then washed with diethyl ether. After the solvent was removed under reduced

pressure, flash chromatography on silica gel (0–5% EtOAc/hexane) provided **4bb** (223.6 mg, 0.93 mmol) in 93% yield.

4.3.2. Typical procedure for synthesis of chiral allylsilanes (Table 4, entry 5). 6-Chloro-1-hexene (**1i**) (172 μL, 1.3 mmol) and $(9\text{-BBN-H})_2$ (151.2 mg, 0.625 mmol) were placed in a vial containing a magnetic stirring bar. The vial was sealed with a Teflon®-coated silicon rubber septum and the vial was evacuated and filled with argon. 1,4-Dioxane (1.0 mL) was added to the vial, and then the mixture was stirred at 60 °C for 1 h to prepare an alkylborane. On the other hand, $CuOTf\cdot(toluene)_{0.5}$ (26 mg, 0.1 mmol), (*R*)-DTBM-SEGPHOS (**L5**) (118 mg, 0.1 mmol), and MeOK (77 mg, 1.1 mmol) were placed in another vial. The vial was sealed with a Teflon®-coated silicon rubber septum and the vial was evacuated and filled with argon. After DCM (3.0 mL) was added to the vial, the mixture was stirred at 25 °C for 1 h. Next, the alkylborane solution was transferred to the vial containing a Cu(I)–**L5** complex. Then, allyl chloride **3g** (211 mg, 1.0 mmol) was added. After 48 h stirring at 15 °C, diethyl ether was added to the mixture. The mixture was filtered through a short plug of silica gel, which was then washed with diethyl ether. After the solvent was removed under reduced pressure, flash chromatography on silica gel (hexane) provided **4ig** (259.5 mg, 0.88 mmol) in 88% yield.

4.3.3. Typical procedure for construction of quaternary carbon stereogenic centers using γ,γ-disubstituted primary allyl chlorides (Table 5, entry 6). 3,4-Dimethoxy-1-allylbenzene (**1a**) (93.4 μL, 0.54 mmol) and $(9\text{-BBN-H})_2$ (64.2 mg, 0.26 mmol) were placed in a vial containing a magnetic stirring bar. The vial was sealed with a Teflon®-coated silicon rubber septum and the vial was evacuated and filled with argon. THF (0.3 mL) was added to the vial, and then the mixture was stirred at 60 °C for 1 h to prepare an alkylborane. Meanwhile, $CuOTf\cdot(toluene)_{0.5}$ (7.8 mg, 0.03 mmol), (*R*)-DTBM-MeO-BIPHEP (**L4**) (35.5 mg, 0.03 mmol), and EtOK (39.9 mg, 0.45 mmol) were placed in another vial. This vial was sealed with a Teflon®-coated silicon rubber septum and then evacuated and filled with argon. After DCM (0.9 mL) was added to the vial, the mixture was stirred at 25 °C for 1 h. Next, the alkylborane solution was transferred to the vial containing the Cu(I)–**L4** complex. Next, allyl chloride (*E*)-**5a** (58.5 mg, 0.3 mmol) was added. After 20 h stirring at 15 °C, diethyl ether was added to the mixture. The mixture was filtered through a short plug of silica gel, which was then washed with diethyl ether. After the solvent was removed under reduced pressure, flash chromatography on silica gel (0–3% EtOAc/hexane) provided **6aa** (66.0 mg, 0.20 mmol) at 81% ee in 65% yield.

4.4. Characterization data

*4.4.1. (Z)-(5-Chloro-3-penten-1-yl)benzene (**3a**).* Colorless oil. IR (neat) 697, 742, 1250, 1453, 1496, 1652, 2931, 3027 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.41–2.47 (m, 2H), 2.71 (t, *J*=7.2 Hz, 2H), 3.94–4.01 (m, 2H), 5.60–5.71 (m, 2H), 7.17–7.25 (m, 3H), 7.27–7.32 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 28.9, 35.3, 39.2, 126.0, 126.1, 128.5, 128.5, 134.1, 141.3. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{11}H_{13}Cl$, 180.07058; found, 180.07060.

*4.4.2. (Z)-1-Chloro-2-heptene (**3b**).* Colorless oil. IR (neat) 756, 1250, 1458, 1652, 2930 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J*=7.2 Hz, 3H), 1.27–1.39 (m, 4H), 2.09–2.18 (m, 2H), 4.10 (d, *J*=4.5 Hz, 2H), 5.58–5.69 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.8, 22.2, 26.7, 31.3, 39.5, 125.1, 135.6. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_7H_{13}Cl$, 132.07058; found, 132.07047.

*4.4.3. (Z)-1,7-Dichloro-2-heptene (**3c**).* Colorless oil. IR (neat) 756, 1251, 1454, 1652, 2941 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.51–1.61 (m, 2H), 1.75–1.85 (m, 2H), 2.13–2.20 (m, 2H), 3.55 (t, *J*=6.6 Hz, 2H), 4.09 (d, *J*=7.2 Hz, 2H), 5.58–5.72 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 26.2, 26.3, 31.9, 39.2, 44.7, 125.9, 134.7. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_7H_{12}Cl_2$, 166.03161; found, 166.03168.

*4.4.4. (Z)-(3-Chloro-1-propen-1-yl)cyclohexane (**3e**).* Colorless oil. IR (neat) 766, 890, 1249, 1448, 1651, 2850, 2924 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.03–1.36 (m, 5H), 1.55–1.75 (m, 5H), 2.31–2.34 (m, 1H), 4.11 (d, *J*=7.2 Hz, 2H), 5.43–5.57 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.6, 25.7, 32.9, 36.2, 39.8, 123.3, 141.4. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_9H_{15}Cl$, 158.08623; found, 158.08626.

*4.4.5. (Z)-tert-Butyl[(7-chloro-5-hepten-1-yl)oxy]dimethylsilane (**3f**).* Colorless oil. IR (neat) 773, 833, 1097, 1252, 1472, 2858, 2930 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.41–1.56 (m, 4H), 2.11–2.18 (m, 2H), 3.62 (t, *J*=6.0 Hz, 2H), 4.10 (d, *J*=6.6 Hz, 2H), 5.62–5.66 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.5, 18.2, 25.5, 25.9, 26.7, 32.2, 39.4, 62.8, 125.4, 135.4. HRMS-EI (*m*/*z*): $[M-Cl]^+$ calcd for $C_{13}H_{27}OSi$, 227.1831; found, 227.1832.

*4.4.6. (Z)-1-Dimethylphenysilyl-3-chloro-1-pentene (**3g**).* Colorless oil. IR (neat) 698, 782, 818, 1111, 1250, 1427, 1604, 2958 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.42 (s, 6H), 3.95 (d, *J*=7.8 Hz, 2H), 5.92 (d, *J*=14.1 Hz, 1H), 6.51 (dt, *J*=14.1, 7.8 Hz, 1H), 7.36–7.38 (m, 3H), 7.53–7.56 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −1.2, 43.8, 128.1, 129.4, 132.7, 133.7, 138.3, 144.0. HRMS-EI (*m*/*z*): $[M-CH_3]^+$ calcd for $C_{10}H_{12}ClSi$, 195.0397; found, 195.0399.

*4.4.7. (S)-1,2-Dimethoxy-4-(4-phenethyl-5-hexen-1-yl)benzene (**4aa**).* The product **4aa** was purified by flash chromatography on silica gel (0–10% EtOAc/hexane) followed by GPC ($CHCl_3$) [59% isolated yield from (*Z*)-**3a**]. Colorless oil. IR (neat) 699, 749, 1030, 1140, 1235, 1515, 1591, 2932 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.29–1.74 (m, 6H), 1.98–2.06 (m, 1H), 2.45–2.60 (m, 2H), 2.62–2.69 (m, 2H), 3.85 (s, 3H), 3.86 (s, 3H), 4.97–5.07 (m, 2H), 5.57 (dt, *J*=17.1, 9.6 Hz, 1H), 6.69 (d, *J*=6.6 Hz, 2H), 6.78 (d, *J*=8.7 Hz, 1H), 7.15–7.19 (m, 3H), 7.25–7.30 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 29.1, 33.4, 34.5, 35.5, 36.7, 43.6, 55.7, 55.8, 111.1, 111.7, 115.0, 120.2, 125.7, 128.3, 128.5, 135.4, 142.9, 142.9, 147.1, 148.8. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{22}H_{28}O_2$, 324.20893; found, 324.20883. $[\alpha]_D^{25}$ −0.75 (*c* 1.03, $CHCl_3$) (77% ee). HPLC analysis [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=97:3, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=19.5 min for *R* isomer and 20.9 min for *S* isomer] revealed that the enantiomeric excess of **4aa** was 77%. The absolute configuration of **4aa** was assigned by consideration of the stereochemical pathway.

*4.4.8. (R)-2-(5-Vinylnonyl)-1,3-dioxane (**4bb**).* The product **4bb** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (93% isolated yield). Colorless oil. IR (neat) 908, 995, 1144, 1640, 2851, 2925 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J*=7.2 Hz, 3H), 1.17–1.36 (m, 13H), 1.54–1.60 (m, 2H), 1.85–2.00 (m, 1H), 2.01–2.16 (m, 1H), 3.76 (td, *J*=12.0, 2.1 Hz, 2H), 4.10 (dd, *J*=10.5, 4.8 Hz, 2H), 4.50 (t, *J*=5.1 Hz, 1H), 4.89–4.96 (m, 2H), 5.51 (ddd, *J*=16.8, 10.5, 8.7 Hz, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.0, 22.7, 24.0, 25.7, 26.9, 29.3, 34.6, 34.8, 35.1, 43.9, 66.9, 102.5, 113.9, 143.7. HRMS-EI (*m*/*z*): $[M-H]^+$ calcd for $C_{15}H_{27}O_2$, 239.20110; found, 239.20061. $[\alpha]_D^{25}$ +0.33 (*c* 1.20, $CHCl_3$). The ee value (88% ee) was determined by chiral HPLC analysis of the *p*-nitrobenzoate derivative obtained by the ozonolysis, reduction with $NaBH_4$ followed by benzoylation (*p*-nitrobenzoylchloride, DMAP, DCM, rt) from **4bb** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=99:1, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=42.3 min for *R* isomer and 44.2 min for *S* isomer]. The literature data of the *p*-nitrobenzoate

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derivative **4bbb** confirmed the (*R*) absolute configuration of **4bb** (Scheme 4a).[8c]

*4.4.9. (S)-2-(10-Chloro-6-vinyldecyl)-1,3-dioxane (**4cc**).* The product **4cc** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) followed by GPC ($CHCl_3$) (71% isolated yield). Colorless oil. IR (neat) 910, 995, 1144, 1640, 2851, 2925 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.21–1.47 (m, 13H), 1.56–1.69 (m, 2H), 1.71–1.80 (m, 2H), 1.91–1.93 (m, 1H), 2.00–2.14 (m, 1H), 3.52 (t, *J*=6.6 Hz, 2H), 3.76 (td, *J*=12.3, 2.4 Hz, 2H), 4.08–4.12 (m, 2H), 4.50 (t, *J*=5.2 Hz, 1H), 4.93 (dd, *J*=16.5, 2.1 Hz, 1H), 4.96 (dd, *J*=10.2, 2.1 Hz, 1H), 5.49 (ddd, *J*=16.5, 10.2, 8.7 Hz, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 23.8, 24.4, 25.7, 26.9, 29.4, 32.6, 34.1, 34.8, 35.1, 43.9, 45.0, 66.9, 102.5, 114.4, 143.1. HRMS-EI (*m*/*z*): $[M-H]^+$ calcd for $C_{16}H_{28}ClO_2$, 287.17778; found, 287.17776. $[\alpha]_D^{25}$ +4.80 (*c* 1.10, $CHCl_3$). The ee value (83% ee) was determined by chiral HPLC analysis of the *p*-nitrobenzoate derivative obtained by the ozonolysis, reduction with $NaBH_4$ followed by benzoylation (*p*-nitrobenzoylchloride, DMAP, DCM, rt) from **4cc** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=97:3, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=35.4 min for *R* isomer and 39.1 min for *S* isomer]. The absolute configuration of **4cc** was assigned by consideration of the stereochemical pathway.

*4.4.10. (S)-Triisopropyl[(6-phenethyl-7-octen-1-yl)oxy]silane (**4da**).* The product **4da** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (71% isolated yield). Colorless oil. IR (neat) 679, 882, 1103, 1462, 2864, 2931 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.01–1.14 (m, 21H), 1.28–1.50 (m, 6H), 1.52–1.63 (m, 3H), 1.65–1.75 (m, 1H), 1.93–2.05 (m, 1H), 2.51 (ddd, *J*=13.8, 10.2, 6.6 Hz, 1H), 2.65 (ddd, *J*=13.8, 10.2, 5.2 Hz, 1H), 3.65 (t, *J*=6.6 Hz, 2H), 4.96–5.05 (m, 2H), 5.57 (ddd, *J*=17.1, 10.4, 8.7 Hz, 1H), 7.15–7.18 (m, 3H), 7.24–7.30 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.3, 18.3, 26.2, 27.3, 33.3, 33.9, 35.4, 37.2, 44.1, 63.8, 115.1, 126.1, 128.8, 128.9, 143.3, 143.6. HRMS-EI (*m*/*z*): $[M-C_3H_7]^+$ calcd for $C_{22}H_{37}OSi$, 345.26137; found, 345.26098. $[\alpha]_D^{25}$ −3.07 (*c* 1.01, $CHCl_3$). The ee value (88% ee) was determined by chiral HPLC analysis of the alcohol derivative obtained by hydroboration with 9-BBN-H from **4da** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=98:2, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=27.2 min for *R* isomer and 31.4 min for *S* isomer]. The absolute configuration of **4da** was assigned by consideration of the stereochemical pathway.

*4.4.11. (R)-Triisopropyl[(6-methyl-7-octen-1-yl)oxy]silane (**4dd**).* The product **4dd** was purified by flash chromatography on silica gel (hexane) (70% isolated yield). Colorless oil. IR (neat) 881, 909, 994, 1103, 1462, 2865, 2930 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.97 (d, *J*=6.9 Hz, 3H), 1.01–1.10 (m, 21H), 1.10–1.40 (m, 6H), 1.44–1.61 (m. 2H), 2.10 (m, 1H), 3.66 (t, *J*=12.3 Hz, 3H), 4.88–4.97 (m, 2H), 5.69 (ddd, *J*=17.7 10.5, 7.8 Hz, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 11.9, 17.9, 20.1, 25.8, 27.0, 32.9, 36.6, 37.7, 63.4, 112.3, 145.1. HRMS-EI (*m*/*z*): $[M-C_3H_7]^+$ calcd for $C_{15}H_{31}OSi$, 255.21442; found, 255.21457. $[\alpha]_D^{26}$ −4.88 (*c* 0.64, $CHCl_3$). The ee value (81% ee) was determined by chiral HPLC analysis of the *p*-nitrobenzoate derivative obtained by the ozonolysis, reduction with $NaBH_4$, benzoylation (*p*-nitrobenzoylchloride, DMAP, DCM, rt) followed by desilylation from **4dd** [CHIRALCEL® OJ-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=95:5, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=40.3 min for *R* isomer and 42.4 min for *S* isomer]. The absolute configuration of **4dd** was assigned by consideration of the stereochemical pathway.

*4.4.12. (R)-[(6-Cyclohexyl-7-octen-1-yl)oxy]triisopropylsilane (**4de**).* The product **4de** was purified by flash chromatography on silica gel (hexane) followed by GPC ($CHCl_3$) (53% isolated yield). Colorless oil. IR (neat) 679, 882, 909, 997, 1103, 1449, 1639, 2864, 2924 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.83–1.80 (m, 32H), 1.06 (s, 9H), 3.66 (t, *J*=12.3 Hz, 2H), 4.89 (dd, *J*=17.1, 2.1 Hz, 1H), 4.97 (dd, *J*=9.9, 2.1 Hz, 1H), 5.54 (dt, *J*=17.1, 9.1 Hz, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 11.9, 17.9, 25.8, 26.6, 26.6, 26.7, 27.3, 29.6, 31.1, 31.6, 32.9, 41.7, 50.0, 63.5, 114.8, 141.9. HRMS-EI (*m*/*z*): $[M-C_3H_7]^+$ calcd for $C_{20}H_{39}OSi$, 323.27702; found, 323.27741. $[\alpha]_D^{25}$ −4.08 (*c* 1.12, $CHCl_3$). The ee value (76% ee) was determined by chiral HPLC analysis of the *p*-nitrobenzoate derivative obtained by the ozonolysis, reduction with $NaBH_4$ followed by benzoylation (*p*-nitrobenzoylchloride, DMAP, DCM, rt) from **4de** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane, 0.25 mL/min, 40 °C, 254 nm UV detector, retention time=61.0 min for *R* isomer and 67.2 min for *S* isomer]. The absolute configuration of **4de** was a assigned by consideration of the stereochemical pathway.

*4.4.13. (S)-6-Phenethyl-7-octen-1-yl pivalate (**4ea**).* The product **4ea** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (73% isolated yield). Colorless oil. IR (neat) 698, 910, 1151, 1284, 1455, 1480, 1727, 2931 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.24–1.42 (m, 6H), 1.47–1.74 (m, 4H), 1.93–2.04 (m, 1H), 2.51 (ddd, *J*=13.8, 10.2, 6.6 Hz, 1H), 2.65 (ddd, *J*=13.8, 10.2, 5.4 Hz, 1H), 4.03 (t, *J*=6.6 Hz, 2H), 4.96–5.06 (m, 2H), 5.57 (ddd, *J*=17.1, 10.2, 8.7 Hz, 1H), 7.15–7.18, (m, 3H), 7.24–7.30 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 25.9, 26.7, 27.1, 28.4, 33.4, 34.8, 36.8, 38.6, 43.7, 64.4, 114.9, 125.7, 128.3, 128.5, 142.9, 143.0, 178.8. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{21}H_{32}O_2$, 316.24023; found, 316.24035. $[\alpha]_D^{25}$ −4.30 (*c* 1.25, $CHCl_3$). The ee value (88% ee) was determined by chiral HPLC analysis of the *p*-nitrobenzoate derivative obtained by the ozonolysis, reduction with $NaBH_4$ followed by benzoylation (*p*-nitrobenzoylchloride, DMAP, DCM, rt) from **4ea** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=95:5, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=20.5 min for *S* isomer and 22.5 min for *R* isomer]. The absolute configuration of **4ea** was assigned by consideration of the stereochemical pathway.

*4.4.14. (S)-2-{10-[(tert-Butyldimethylsilyl)oxy]-6-vinyldecyl}isoindoline-1,3-dione (**4ff**).* The product **4ff** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) followed by GPC ($CHCl_3$) (73% isolated yield). Colorless oil. IR (neat) 718, 774, 834, 1096, 1254, 1395, 1712, 2857, 2929 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.89 (s, 9H), 1.16–1.35 (m, 10H), 1.42–1.53 (m, 2H), 1.61–1.71 (m, 2H), 1.86–1.95 (m, 1H), 3.58 (t, *J*=6.6 Hz, 2H), 3.67 (t, *J*=7.5 Hz, 2H), 4.91 (dd, *J*=16.8, 2.1 Hz, 1H), 4.94 (dd, *J*=10.5, 2.1 Hz, 1H), 5.48 (ddd, *J*=16.8, 10.5, 8.7 Hz, 1H), 7.70–7.73 (m, 2H), 7.83–7.86 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.4, 18.2, 23.2, 25.9, 26.6, 26.9, 28.5, 32.8, 34.7, 34.7, 38.0, 44.0, 63.2, 114.2, 123.2, 132.3, 133.9, 143.3, 168.6. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{26}H_{41}O_3NNaSi$, 466.27479; found, 466.27496. $[\alpha]_D^{25}$ −0.41 (*c* 1.05, $CHCl_3$). The ee value (88% ee) was determined by chiral HPLC analysis of the *p*-nitrobenzoate derivative obtained by the ozonolysis, reduction with $NaBH_4$ followed by benzoylation (*p*-nitrobenzoylchloride, DMAP, DCM, rt) from **4ff** [CHIRALCEL® AD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=97:3, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=32.2 min for *R* isomer and 35.1 min for *S* isomer]. The absolute configuration of **4ff** was assigned by consideration of the stereochemical pathway.

*4.4.15. (S)-2-(10-Chloro-6-vinyldecyl)isoindoline-1,3-dione (**4fc**).* The product **4fc** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (72% isolated yield). Colorless oil. IR (neat) 717, 911, 1394, 1708, 1773, 2932 cm^{-1}. ^1H NMR (300 MHz,

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$CDCl_3$) δ 1.18–1.47 (m, 10H), 1.62–1.77 (m, 4H), 1.86–1.97 (m, 1H), 3.52 (t, *J*=6.6 Hz, 2H), 3.67 (t, *J*=7.2 Hz, 2H), 4.93 (dd, *J*=16.8, 1.8 Hz, 1H), 4.95 (dd, *J*=10.2, 1.8 Hz, 1H) 5.48 (ddd, *J*=16.8, 10.2, 9.0 Hz, 1H), 7.69–7.74 (m, 2H), 7.82–7.87 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.4, 26.6, 26.8, 28.4, 32.6, 34.1, 34.7, 37.9, 43.8, 45.0, 114.6, 123.2, 132.2, 133.9, 143.0, 168.6. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{26}O_2NClNa$, 370.15443; found, 370.15468. $[\alpha]_D^{25}$ +0.53 (*c* 1.07, $CHCl_3$). The ee value (90% ee) was determined by chiral HPLC analysis of the *p*-nitrobenzoate derivative obtained by the ozonolysis, reduction with $NaBH_4$ followed by benzoylation (*p*-nitrobenzoylchloride, DMAP, DCM, rt) from **4fc** [CHIRALCEL® AD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=97:3, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=166.9 min for *R* isomer and 179.2 min for *S* isomer]. The absolute configuration of **4fc** was assigned by consideration of the stereochemical pathway.

*4.4.16. (R)-Dimethylphenyl(1-undecen-3-yl)silane (**4hg**).* The product **4hg** was purified by flash chromatography on silica gel (hexane) (77% isolated yield). Colorless oil. IR (neat) 698, 811, 1113, 1248, 1428, 1626, 2924 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 3H), 0.26 (s, 3H), 0.86 (t, *J*=6.6 Hz, 3H), 1.13–1.37 (m, 14H), 1.62–1.76 (m, 1H), 4.77–4.83 (m, 1H), 4.88 (dd, *J*=10.2, 2.1 Hz, 1H), 5.58 (dt, *J*=17.1, 10.2 Hz, 1H), 7.32–7.36 (m, 3H), 7.48–7.51 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.8, −5.0, 13.6, 22.2, 27.9, 28.7, 28.8, 28.9, 29.0, 31.4, 33.9, 112.0, 127.2, 128.5, 133.7, 137.7, 139.6. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{19}H_{32}Si$, 288.22733; found, 288.22732. $[\alpha]_D^{27}$ −7.05 (*c* 1.23, $CHCl_3$). HPLC analysis [CHIRALCEL® OJ-3 column, 4.6 mm×250 mm/OJ-3 column, 4.6 mm×250 mm/OJ-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane, 0.25 mL/min, 40 °C, 254 nm UV detector, retention time=55.0 min for *S* isomer and 56.4 min for *R* isomer] revealed that the enantiomeric excess of **4hg** was 91%.

Derivatization of **4hg** (Scheme 4b). *p*-Toluenesulfonyl hydrazide (186.2 mg, 1.0 mmol) was placed in a screw-top test tube. Allylsilane **4hg** (28.9 mg, 0.1 mmol), 1,4-dioxane (1 mL), and triethylamine (0.14 mL, 1.0 mmol) were sequentially added to the test tube at 25 °C. The resulting mixture was stirred at reflux for 24 h (monitored by TLC). After the mixture was cooled to 25 °C, water was added. The aqueous layer was extracted with hexane (three times). The combined organic layer was washed with water and brine, and then was dried and concentrated. The crude product was used in the next step without further purification. A vial containing the crude material of **4hga** (29.1 mg, 0.1 mmol) was filled with argon. CH_2Cl_2 (1.0 mL) and $HBF_4{\cdot}OEt_2$ (0.23 mL, 0.28 mmol) were sequentially added at 25 °C. After 1.5 h stirring at 25 °C, the mixture was quenched with water. The aqueous layer was extracted with hexane (three times). The combined organic layer was washed with water and brine, and then was dried and concentrated. The crude product was used in the next step without further purification. The fluorinated compound **4hgb** (23.2 mg, 0.1 mmol) was placed in a screw-top test tube. THF (0.4 mL), MeOH (0.4 mL), KF (23.2 mg, 0.4 mmol), $KHCO_3$ (100.2 mg, 1 mmol), 30% H_2O_2 aq (113.4 mg, 1 mmol) were sequentially added at 25 °C. After being stirred at 40 °C for 24 h, the mixture was quenched with $Na_2S_2O_3$ aq. The aqueous layer was extracted with ethyl acetate (three times). The combined organic layer was washed with water and brine, and then was dried and concentrated. The crude product was purified by flash column chromatography (5–20% EtOAc/hexane) to yield (*S*)-undecan-3-ol (**4hgc**) as a colorless oil (10.2 mg, 0.06 mmol, 59% in 3 steps) $[\alpha]_D^{25}$ +4.38 (*c* 0.51, $CHCl_3$). {lit.[22] (*S*) isomer, 84% ee, $[\alpha]_D^{20}$ +5.2 (*c* 1, $CHCl_3$)}.

*4.4.17. (R)-[8-(1,3-Dioxan-2-yl)-1-octen-3-yl]dimethylphenylsilane (**4cg**).* The product **4cg** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) followed by GPC ($CHCl_3$) (66% isolated yield). Colorless oil. IR (neat) 699, 996, 1144, 1246, 1625, 2850, 2953 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 3H), 0.26 (s, 3H), 1.13–1.41 (m, 9H), 1.50–1.57 (m, 2H), 1.62–1.75 (m, 1H), 2.00–2.13 (m, 1H), 3.74 (dt, *J*=12.0, 2.4 Hz, 2H), 4.06–4.11 (m, 2H), 4.47 (t, *J*=5.1 Hz, 1H), 4.75–4.82 (m, 1H), 4.87 (dd, *J*=10.2, 1.8 Hz, 1H), 5.56 (dt, *J*=17.1, 10.2 Hz, 1H), 7.32–7.37 (m, 3H), 7.46–7.50 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.4, −4.6, 23.8, 25.7, 28.2, 29.0, 29.1, 34.3, 35.1, 66.9, 102.4, 112.5, 127.7, 128.9, 134.1, 138.0, 139.9. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{32}O_2NaSi$, 355.20638; found, 355.20672. $[\alpha]_D^{26}$ −5.64 (*c* 1.17, $CHCl_3$). HPLC analysis [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=99.9:0.1, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=17.4 min for *S* isomer and 18.1 min for *R* isomer] revealed that the enantiomeric excess of **4cg** was 91%. The absolute configuration of **4cg** was assigned by consideration of the stereochemical pathway.

*4.4.18. (R)-6-(Dimethylphenylsilyl)-7-octen-1-yl pivalate (**4eg**).* The product **4eg** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (52% isolated yield). Colorless oil. IR (neat) 600, 812, 1152, 1284, 1626, 1727, 2932 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 3H), 0.26 (s, 3H), 1.18 (s, 9H), 1.10–1.50 (m, 6H), 1.52–1.60 (m, 2H), 1.69–1.76 (m, 1H), 4.00 (t, *J*=6.6 Hz, 2H), 4.78–4.83 (m, 1H), 4.88 (dd, *J*=10.2, 1.8 Hz, 1H), 5.57 (dt, *J*=17.1, 10.2 Hz, 1H), 7.34–7.36 (m, 3H), 7.47–7.51 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.4, −4.6, 25.5, 27.1, 28.2, 28.4, 28.7, 34.2, 38.6, 64.4, 112.6, 127.7, 129.0, 134.1, 137.9, 139.8, 178.8. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{21}H_{34}O_2NaSi$, 369.22203; found, 369.22208. $[\alpha]_D^{25}$ −8.09 (*c* 1.27, $CHCl_3$). HPLC analysis [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane, 0.25 mL/min, 40 °C, 254 nm UV detector, retention time=41.1 min for *S* isomer and 43.0 min for *R* isomer] revealed that the enantiomeric excess of **4eg** was 87%. The absolute configuration of **4eg** was assigned by consideration of the stereochemical pathway.

*4.4.19. (R)-2-[6-(Dimethylphenylsilyl)-7-octen-1-yl]isoindoline-1,3-dione (**4fg**).* The product **4fg** was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (85% isolated yield). Colorless oil. IR (neat) 717, 1394, 1624, 1708, 1773, 2931 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.24 (s, 3H), 0.25 (s, 3H), 1.16–1.43 (m, 6H), 1.54–1.74 (m, 3H), 3.63 (t, *J*=7.2 Hz, 2H), 4.75–4.81 (m, 1H), 4.86 (dd, *J*=10.2, 1.8 Hz, 1H), 5.55 (dt, *J*=17.1, 10.2 Hz, 1H), 7.31–7.34 (m, 3H), 7.46–7.49 (m, 2H), 7.69–7.73 (m, 2H), 7.81–7.85 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.4, −4.6, 26.5, 28.1, 28.4, 28.8, 34.2, 38.0, 112.6, 123.2, 127.7, 129.0, 132.3, 133.9, 134.1, 137.9, 139.8, 168.6. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{29}O_2NNaSi$, 414.18598; found, 414.18631. $[\alpha]_D^{27}$ +4.99 (*c* 0.75, $CHCl_3$). HPLC analysis [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=99.5:0.5, 0.5 mL/min, 40 °C, 254 nm UV detector, retention time=31.6 min for *S* isomer and 33.4 min for *R* isomer] revealed that the enantiomeric excess of **4fg** was 90%. The absolute configuration of **4fg** was assigned by consideration of the stereochemical pathway.

*4.4.20. (R)-(9-Chloro-1-nonen-3-yl)dimethylphenylsilane (**4ig**).* The product **4ig** was purified by flash chromatography on silica gel (hexane) (88% isolated yield). Colorless oil. IR (neat) 699, 894, 1122, 1248, 1427, 1625, 2855, 2928 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 3H), 0.26 (s, 3H), 1.13–1.41 (m, 8H), 1.66–1.76 (m, 3H), 3.49 (t, *J*=6.9 Hz, 2H), 4.78–4.84 (m, 1H), 4.89 (dd, *J*=9.9, 1.8 Hz, 1H), 5.58 (dt, *J*=17.1, 9.9 Hz, 1H), 7.33–7.36 (m, 3H), 7.46–7.51 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ −5.4, −4.6, 26.6, 28.2, 28.4, 28.9, 32.5, 34.2, 45.1, 112.6, 127.7, 129.0, 134.1, 138.0, 139.9. HRMS-FI (*m*/*z*): $[M]^+$ calcd for $C_{17}H_{27}ClSi$, 294.15705; found, 294.15724. $[\alpha]_D^{25}$ −10.36 (*c* 1.30, $CHCl_3$). HPLC analysis [CHIRALCEL® OJ-3 column,

4.6 mm×250 mm/OJ-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane, 0.25 mL/min, 40 °C, 254 nm UV detector, retention time=36.9 min for *S* isomer and 38.1 min for *R* isomer] revealed that the enantiomeric excess of **4ig** was 91%. The absolute configuration of **4ig** was assigned by consideration of the stereochemical pathway.

*4.4.21. (S)-1,2-Dimethoxy-4-(4-methyl-4-phenethyl-5-hexen-1-yl) benzene (**6aa**).* The product (*S*)-**6aa** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) followed by GPC ($CHCl_3$) (65% isolated yield). Colorless oil. IR (neat) 698, 1030, 1236, 1260, 1515, 2935 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (s, 3H), 1.35–1.40 (m, 2H), 1.55–1.65 (m, 4H), 2.45–2.55 (m, 4H), 3.85 (s, 3H), 3.87 (s, 3H), 4.94 (d, *J*=17.4 Hz, 1H), 5.04 (d, *J*=10.8 Hz, 1H), 5.74 (dd, *J*=17.4, 10.8 Hz, 1H), 6.70–6.72 (m, 2H), 6.79 (m, 1H), 7.13–7.18 (m, 3H), 7.24–7.29 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 22.5, 26.2, 30.7, 36.2, 39.6, 40.5, 43.0, 55.8, 55.9, 111.1, 111.6, 112.0, 120.1, 125.5, 128.3 (2C), 135.3, 143.3, 146.9, 147.0, 148.7. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{23}H_{30}O_2$, 338.22458; found, 338.22391. $[\alpha]_D^{23}$ +5.81 (*c* 1.10, $CHCl_3$). HPLC analysis [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=99.5:0.5, 0.5 mL/min, 40 °C, 220 nm UV detector, retention time=106.7 min for *R* isomer and 112.5 min for *S* isomer] revealed that the enantiomeric excess of **6aa** was 81% ee. The absolute configuration of **6aa** was assigned by consideration of the stereochemical pathway.

*4.4.22. (S)-2-(6-Methyl-6-phenethyl-7-octen-1-yl)-1,3-dioxane (**6ca**).* The product **6ca** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (79% isolated yield). Colorless oil. IR (neat) 698, 909, 996, 1143, 2849, 2929 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (s, 3H), 1.26–1.43 (m, 8H), 1.54–1.64 (m, 5H), 2.08 (m, 1H), 2.46–2.52 (m, 2H), 3.76 (dt, J=12.0, 2.4 Hz, 2H), 4.08–4.13 (m, 2H), 4.50 (t, *J*=5.1 Hz, 1H), 4.93 (dd, *J*=17.4, 1.5 Hz, 1H), 5.02 (dd, *J*=10.8, 1.5 Hz, 1H), 5.74 (dd, *J*=17.4, 10.8 Hz, 1H), 7.15–7.19 (m, 3H), 7.25–7.30 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 22.6, 23.9, 24.0, 25.8, 30.3, 30.7, 35.2, 39.6, 40.7, 43.0, 66.9, 102.4, 111.8, 125.5, 128.3 (2C), 143.4, 147.1. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{21}H_{32}O_2$, 316.24023; found, 316.24002. $[\alpha]_D^{26}$ +2.06 (*c* 1.08, $CHCl_3$). The ee value (90% ee) was determined by chiral HPLC analysis of the aldehyde derivative obtained by the ozonolysis followed by reduction with Me_2S from **6ca** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=96:4, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time=54.1 min for *R* isomer and 55.7 min for *S* isomer]. The absolute configuration of **6ca** was assigned by consideration of the stereochemical pathway.

*4.4.23. (S)-Triisopropyl[(6-methyl-6-phenethyl-7-octen-1-yl)oxy]silane (**6da**).* The product **6da** was purified by flash chromatography on silica gel (0–1% EtOAc/hexane) (85% isolated yield). Colorless oil. IR (neat) 679, 910, 1106, 1463, 2864, 2938 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.05–1.12 (m, 24H), 1.21–1.32 (m, 6H), 1.50–1.64 (m, 4H), 2.47–2.53 (m, 2H), 3.66 (t, *J*=6.6 Hz, 2H), 4.94 (dd, *J*=17.4, 1.5 Hz, 1H), 5.04 (dd, *J*=11.1, 1.5 Hz, 1H), 5.75 (dd, *J*=17.4, 11.1 Hz, 1H), 7.15–7.17 (m, 3H), 7.24–7.29 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 12.0, 18.0, 22.6, 23.9, 26.6, 30.7, 33.0, 39.6, 40.9, 43.0, 63.4, 111.8, 125.5, 128.3 (2C), 143.4, 147.1. HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{26}H_{47}OSi$, 403.33907; found, 403.33838. $[\alpha]_D^{27}$ +6.31 (*c* 0.92, $CHCl_3$). The ee value (83% ee) was determined by chiral HPLC analysis of the aldehyde derivative obtained by the ozonolysis, reduction with Me_2S from **6da** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=98:2, 0.3 mL/min, 40 °C, 220 nm UV detector, retention time=17.9 min for *R* isomer and 18.6 min for *S* isomer]. The absolute configuration of **6da** was assigned by consideration of the stereochemical pathway.

*4.4.24. (S)-6-Methyl-6-phenethyl-7-octen-1-yl pivalate (**6ea**).* The product **6ea** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (66% isolated yield). Colorless oil. IR (neat) 698, 1284, 1151, 1727, 2862, 2935 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (s, 3H), 1.19 (s, 9H), 1.29–1.32 (m, 6H), 1.52–1.64 (m, 4H), 2.47–2.53 (m, 2H), 4.04 (t, *J*=6.6 Hz, 2H), 4.95 (d, *J*=17.4 Hz, 1H), 5.04 (d, *J*=11.1 Hz, 1H), 5.75 (dd, *J*=17.4, 11.1 Hz, 1H), 7.15–7.19 (m, 3H), 7.25–7.30 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 22.5, 23.7, 26.8, 27.2, 28.6, 30.7, 38.7, 39.6, 40.9, 43.0, 64.4, 112.0, 125.6, 128.3 (2C), 143.3, 146.9, 178.7. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{22}H_{34}O_2$, 330.25588; found, 330.25630. $[\alpha]_D^{25}$ +7.36 (*c* 0.58, $CHCl_3$). The ee value (81% ee) was determined by chiral HPLC analysis of the aldehyde derivative obtained by the ozonolysis followed by reduction with Me_2S from **6ea** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=96:4, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time=29.7 min for *R* isomer and 30.6 min for *S* isomer]. The absolute configuration of **6ea** was assigned by consideration of the stereochemical pathway.

*4.4.25. (S)-(9-Chloro-3-methyl-3-vinylnonyl)benzene (**6ia**).* The product **6ia** was purified by flash chromatography on silica gel (hexane) followed by GPC ($CHCl_3$) (80% isolated yield). Colorless oil. IR (neat) 696, 909, 1453, 1495, 2858, 2930 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (s, 3H), 1.26–1.48 (m, 6H), 1.52–1.61 (m, 4H), 1.72–1.79 (m, 2H), 2.47–2.53 (m, 2H), 3.53 (t, *J*=6.6 Hz, 2H), 4.95 (dd, *J*=17.4, 1.5 Hz, 1H), 5.04 (dd, *J*=11.1, 1.5 Hz, 1H), 5.75 (dd, *J*=17.4, 11.1 Hz, 1H), 7.15–7.20 (m, 3H), 7.25–7.30 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 22.5, 23.9, 26.9, 29.7, 30.7, 32.6, 39.6, 40.8, 43.0, 45.2, 111.9, 125.5, 128.3 (2C), 143.3, 147.0. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{18}H_{27}Cl$, 278.1803; found, 278.18100. $[\alpha]_D^{26}$ +6.49 (*c* 0.30, $CHCl_3$). The ee value (86% ee) was determined by chiral HPLC analysis of the aldehyde derivative obtained by the ozonolysis followed by reduction with Me_2S from **6ia** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=96:4, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time=39.6 min for *R* isomer and 41.3 min for *S* isomer]. The absolute configuration of **6ia** was assigned by consideration of the stereochemical pathway.

*4.4.26. 2-[{(S)-7-Methyl-7-phenethyl-8-nonen-1-yl}oxy]tetrahydro-2H-pyran (**6ja**).* Diastereomeric ratio 1:1. The product **6ja** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (70% isolated yield). Colorless oil. IR (neat) 1022, 1032, 1119, 2859, 2931 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.02 (s, 3H), 1.23–1.36 (m, 6H), 1.54–1.87 (m, 12H), 2.47–2.53 (m, 2H), 3.38 (m, 1H), 3.51 (m, 1H), 3.73 (m, 1H), 3.87 (m, 1H), 4.58 (m, 1H), 4.94 (d, *J*=17.4 Hz, 1H), 5.03 (d, *J*=11.1 Hz, 1H), 5.75 (dd, *J*=17.4, 11.1 Hz, 1H), 7.15–7.18 (m, 3H), 7.25–7.30 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 19.7, 22.6, 24.0, 25.5, 26.3, 29.8, 30.3, 30.7, 30.8, 39.6, 40.9, 43.0, 62.4, 67.7, 98.8, 111.8, 125.5, 128.3 (2C), 143.4, 147.1. HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{23}H_{36}O_2$, 344.27153; found, 344.27045. $[\alpha]_D^{28}$ +5.94 (*c* 0.87, $CHCl_3$). The ee value (86% ee) was determined by chiral HPLC analysis of 7-(dimethoxymethyl)-7-methyl-9-phenyl-1-nonanol obtained by the ozonolysis, reduction with Me_2S followed by acetalization (MeOH, *p*-TsOH, rt) from **6ja** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=96:4, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time=39.6 min for *R* isomer and 41.2 min for *S*

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isomer]. The absolute configuration of **6ja** was assigned by consideration of the stereochemical pathway.

*4.4.27. (S)-[7-(Benzyloxy)-3-methyl-3-vinylheptyl]benzene (**6ka**).* The product **6ka** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (68% isolated yield). Colorless oil. IR (neat) 696, 733, 1102, 1454, 2862, 2936 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (s, 3H), 1.23–1.37 (m, 4H), 1.52–1.64 (m, 4H), 2.47–2.52 (m, 2H), 3.46 (t, J=6.6 Hz, 2H), 4.50 (s, 2H), 4.94 (d, J=17.4 Hz, 1H), 5.04 (d, J=10.8 Hz, 1H), 5.75 (dd, J=17.4, 10.8 Hz, 1H), 7.14–7.18 (m, 3H), 7.24–7.34 (m, 7H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 20.7, 22.5, 30.5, 30.7, 39.6, 40.7, 42.9, 70.3, 72.9, 111.9, 125.5, 127.5, 127.7 (2C), 128.3 (2C), 138.6, 143.3, 147.0. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{23}H_{30}ONa$, 345.21889; found, 345.21869. $[\alpha]_D^{22}$ +8.32 (c 0.43, $CHCl_3$). HPLC analysis [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=95:5, 0.5 mL/min, 40 °C, 220 nm UV detector, retention time=49.1 min for *R* isomer and 51.7 min for *S* isomer] revealed that the enantiomeric excess of **6ka** was 81% ee. The absolute configuration of **6ka** was assigned by consideration of the stereochemical pathway.

*4.4.28. (S)-(3-Ethyl-3-methyl-4-penten-1-yl)benzene (**6la**).* The product **6la** was purified by flash chromatography on silica gel (hexane) followed by GPC ($CHCl_3$) (63% isolated yield). Colorless oil. IR (neat) 696, 752, 910, 1454, 2933, 2965 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.82 (t, J=7.5 Hz, 3H), 1.01 (s, 3H), 1.39 (q, J=7.5 Hz, 2H), 1.51–1.61 (m, 2H), 2.47–2.53 (m, 2H), 4.95 (dd, J=17.4, 1.5 Hz, 1H), 5.05 (dd, J=10.8, 1.5 Hz, 1H), 5.74 (dd, J=17.4, 10.8 Hz, 1H), 7.15–7.21 (m, 3H), 7.25–7.29 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 8.4, 22.0, 30.7, 33.1, 39.8, 42.6, 112.0, 125.5, 128.3 (2C), 143.4, 146.8. HRMS-EI (m/z): $[M]^+$ calcd for $C_{14}H_{20}$, 188.15650; found, 188.15651. $[\alpha]_D^{22}$ +16.69 (c 0.63, $CHCl_3$). The ee value (71% ee) was determined by chiral HPLC analysis of 2-ethyl-2-methyl-4-phenyl-1-butanol obtained by the ozonolysis followed by reduction with $NaBH_4$ from **6la** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=96:4, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time=39.6 min for *R* isomer and 44.5 min for *S* isomer].

Derivatization of **6la** (Scheme 4c). Ozone was bubbled into a solution of **6la** (7.4 mg, 0.04 mmol) in MeOH/diethyl ether (1:10, 5.0 mL) at −78 °C. After the starting material was completely disappeared (monitored by TLC), $NaBH_4$ (15.1 mg, 0.4 mmol) was added and the mixture was allowed to warm to rt and it was further stirred at the rt for 1 h. The mixture was quenched with water. The aqueous layer was extracted with EtOAc (three times). The combined organic layer was washed with water and brine, and then was dried and concentrated. Purification by column chromatography (silica gel, 5–15% EtOAc/hexane) yielded (*S*)-2-ethyl-2-methyl-4-phenyl-1-butanol (**6laa**) (3.8 mg, 0.02 mmol). {lit.[24] (*S*) isomer, 96% ee, $[\alpha]_D^{20}$ −12.48 (c 0.125, CH_2Cl_2)}.

*4.4.29. (S)-4-(4,8-Dimethyl-4-vinyl-7-nonen-1-yl)-1,2-dimethoxybenzene (**6ab**).* The product **6ab** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) followed by GPC ($CHCl_3$) (54% isolated yield). Colorless oil. IR (neat) 1031, 1235, 1260, 1515, 2854, 2933 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 3H), 1.25–1.35 (m, 4H), 1.46–1.61 (m, 5H), 1.67 (s, 3H), 1.80–1.89 (m, 2H), 2.51 (t, J=7.5 Hz, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 4.87 (dd, J=17.4, 1.5 Hz, 1H), 4.97 (dd, J=10.8, 1.5 Hz, 1H), 5.08 (m, 1H), 5.68 (dd, J=17.4, 10.8 Hz, 1H), 6.69–6.72 (m, 2H), 6.79 (m, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 17.6, 22.5, 22.8, 25.7, 26.3, 36.3, 39.4, 40.4, 40.7, 55.8, 55.9, 111.1, 111.5, 111.7, 120.1, 125.0, 131.0, 135.4, 147.0, 147.2, 148.7. HRMS-EI (m/z): $[M]^+$ calcd for $C_{21}H_{32}O_2$, 316.24023; found, 316.24053. $[\alpha]_D^{23}$ +8.40 (c 0.50, $CHCl_3$). The ee value (73% ee) was determined by chiral HPLC analysis of 2-[3-(3,4-dimethoxyphenyl)propyl]-2-methyl-6-oxabicyclo[3.1.0]hexane obtained by the ring closing metathesis (Grubbs second catalyst, DCM, 40 °C) followed by epoxidation (*m*-CPBA, $NaHCO_3$, DCM, 0 °C) from **6ab** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=99:1, 0.5 mL/min, 40 °C, 220 nm UV detector, retention time=46.0 min and 65.7 min for *R* isomer and 48.2 min and 85.3 min for *S* isomer]. The absolute configuration of **6ab** was assigned by consideration of the stereochemical pathway.

*4.4.30. (S)-2-(6-Ethyl-6-phenethyl-7-octen-1-yl)-1,3-dioxane (**6cc**).* The product **6cc** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) followed by GPC ($CHCl_3$) (75% isolated yield). Colorless oil. IR (neat) 698, 909, 998, 1143, 2851, 2929 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.79 (t, J=7.2 Hz, 3H), 1.20–1.45 (m, 10H), 1.53–1.63 (m, 5H), 2.08 (m, 1H), 2.41–2.47 (m, 2H), 3.76 (td, J=12.0, 2.4 Hz, 2H), 4.08–4.13 (m, 2H), 4.51 (t, J=5.1 Hz, 1H), 4.91 (dd, J=17.4, 1.5 Hz, 1H), 5.08 (dd, J=11.1, 1.5 Hz, 1H), 5.64 (dd, J=17.4, 11.1 Hz, 1H), 7.15–7.19 (m, 3H), 7.25–7.30 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 7.8, 23.3, 24.0, 25.9, 28.4, 30.1, 30.4, 35.3, 35.6, 38.3, 42.1, 66.9, 102.4, 112.7, 125.5, 128.3 (2C), 143.5, 146.6. HRMS-EI (m/z): $[M]^+$ calcd for $C_{22}H_{34}O_2$, 330.25588; found, 330.25466. $[\alpha]_D^{26}$ −5.63 (c 0.48, $CHCl_3$). The ee value (81% ee) was determined by chiral HPLC analysis of the aldehyde derivative obtained by the ozonolysis followed by reduction with Me_2S from **6cc** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=96:4, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time=37.4 min for *S* isomer and 42.5 min for *R* isomer]. The absolute configuration of **6cc** was assigned by consideration of the stereochemical pathway.

*4.4.31. (S)-2-(6-Phenethyl-6-vinylnonyl)-1,3-dioxane (**6cd**).* The product **6cd** was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) followed by GPC ($CHCl_3$) (67% isolated yield). Colorless oil. IR (neat) 698, 908, 998, 1144, 2850, 2929 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J=6.9 Hz, 3H), 1.19–1.47 (m, 12H), 1.53–1.62 (m, 5H), 2.04 (m, 1H), 2.41–2.47 (m, 2H), 3.76 (t, J=12.0 Hz, 2H), 4.08–4.13 (m, 2H), 4.51 (t, J=5.1 Hz, 1H), 4.90 (d, J=17.4 Hz, 1H), 5.06 (d, J=11.1 Hz, 1H), 5.65 (dd, J=17.4, 11.1 Hz, 1H), 7.14–7.18 (m, 3H), 7.24–7.29 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 14.9, 16.6, 23.3, 24.0, 25.9, 30.1, 30.4, 35.3, 36.2, 38.7, 38.8, 42.1, 66.9, 102.4, 112.4, 125.5, 128.3 (2C), 143.4, 146.9. HRMS-EI (m/z): $[M]^+$ calcd for $C_{23}H_{36}O_2$, 344.27153; found, 344.27039. $[\alpha]_D^{22}$ −3.06 (c 0.23, $CHCl_3$). The ee value (71% ee) was determined by chiral HPLC analysis of the aldehyde derivative obtained by the ozonolysis followed by reduction with Me_2S from **6cd** [CHIRALCEL® OD-3 column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm/CHIRALCEL® OD-H column, 4.6 mm×250 mm, Daicel Chemical Industries, hexane/2-propanol=96:4, 0.7 mL/min, 40 °C, 220 nm UV detector, retention time=29.9 min for *S* isomer and 32.6 min for *R* isomer]. The absolute configuration of **6cd** was assigned by consideration of the stereochemical pathway.

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