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Allylic Substitution for Construction of a Chiral Quaternary Carbon Possessing an Aryl Group

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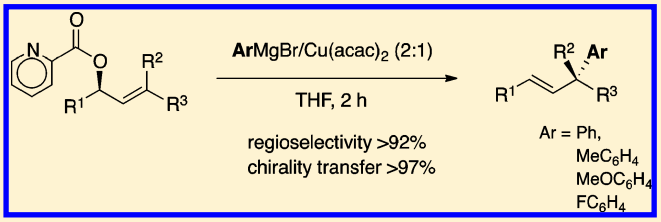
Supporting Information

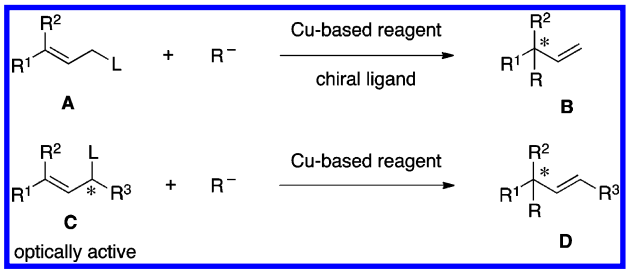
ABSTRACT: Phenylcopper reagents derived from 2:1 PhMgBr/Cu(acac)$_2$ and 3:1:1 PhMgBr/Cu(acac)$_2$/ZnI$_2$ were found to be highly reactive and regioselective in the allylic substitution of γ,γ-disubstituted secondary allylic picolinates designed for construction of a quaternary carbon, whereas the previous 2:1 ArMgBr/CuBr·Me$_2$S reagent and that with ZnX$_2$ were unsuccessful. The generality of the ArMgBr/Cu(acac)$_2$ reagent was examined with enantiomerically enriched allylic picolinates, which furnished quaternary carbons with high efficiency in >92% regioselectivity and >97% chirality transfer. Two cyclohexanes with a quaternary carbon were synthesized by using these reagents.



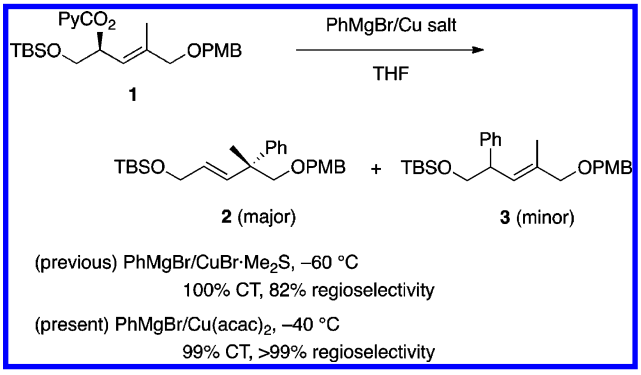
INTRODUCTION

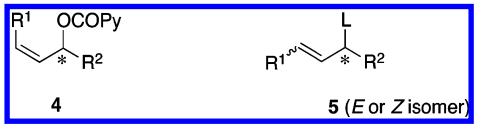
Exploration of a method for construction of a quaternary carbon in an enantiomerically enriched form has been an active area of investigation in connection with synthesis of biologically important molecules.[1] In the past decade, the two types of allylic substitution shown in Scheme 1 have been studied actively for this purpose.[2] Until now, the former substitution using *primary* allylic substrates of type **A** has proceeded with alkyl as well as alkenyl-, allenyl-, and alkynylcopper reagents, producing olefin **B** with high efficiency in terms of enantio- and regioselectivity.[3] Substitution with arylcopper reagents was also reported in one case.[3h] On the other hand, a group of copper reagents that react with *secondary* allylic esters of type **C** to produce **D** is limited to the alkyl group.[4] As for aryl reagents, the substitution shown in Scheme 2 resulted in 82% regioselectivity using the picolinoxy leaving group.[5] However, the regioselectivity is somewhat lower than that observed in the substitution of the allylic picolinates of type **4**.[6,7] Similarly, application of other highly potent leaving groups such as *o*-(PPh$_2$)C$_6$H$_4$CO$_2$ and *o*-(P(O)Ph$_2$)C$_6$H$_4$CO$_2$ originally developed for allylic substitution of type **5** suffers from low regioselectivity.[4b,d] Low nucleophilicity of aryl reagents and increased congestion around secondary substrates and aryl reagents as such are likely reasons for the low efficiency. Recently, Pd/Ag-catalyzed substitution of allylic acetates with PhB(OH)$_2$ was applied to allylic acetates of type **C** (L = OAc),[8] but stereochemical outcome and any reason for the moderate yields were uncertain.[9] Because of the importance of this subject in organic synthesis,[2,10] substitution of allylic picolinates was reinvestigated to find highly efficient reagents derived from ArMgBr and Cu(acac)$_2$ as presented in this publication.

Scheme 1. Two Types of Allylic Substitution for Construction of a Quaternary Carbon



Scheme 2. Previous and Present Results





RESULTS AND DISCUSSION

Preparation. Allylic picolinates shown in Figure 1 were used for the present investigation (see Tables 1–4 and Scheme 4).

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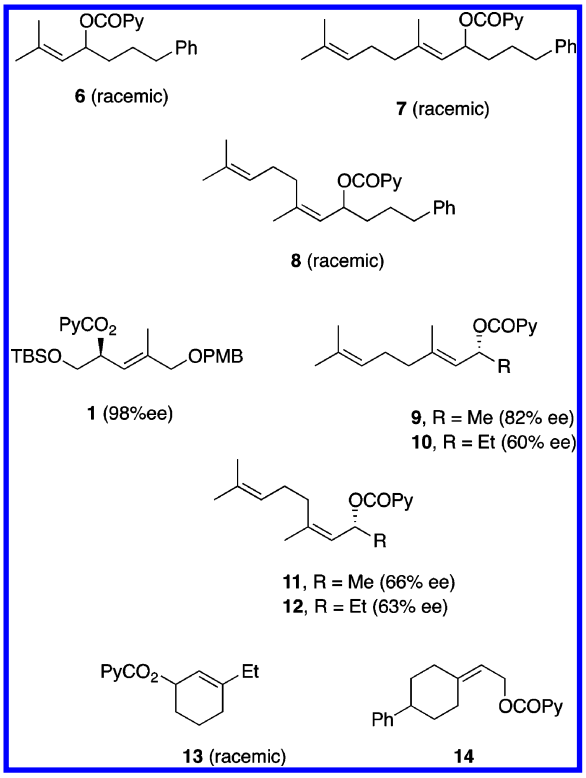


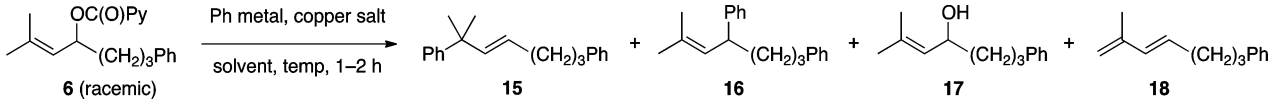
Figure 1. Substrates examined (Py = 2-pyridyl).

The picolinates **1** and **14** were prepared by the methods published previously,[5,7] while other picolinates **6**–**8** and **9**–**13** were synthesized by methods delineated in Scheme 3. Briefly, Grignard addition to aldehyde **19** produced racemic alcohol **17**, which upon DCC-mediated condensation with $PyCO_2H$ afforded picolinate **6** in 74% yield. Similarly, aldehydes **20** and **22**, prepared from geraniol and nerol by oxidation, were converted to **7** and **8**, respectively. For preparation of optically active picolinates **9**–**12**, Corey–Bakshi–Shibata reduction (CBS reduction) of the corresponding ketones with (*S*)-MeCBS[11] was used for our convenience to afford alcohols **24**–**27**, which exhibited enantioenrichment (i.e., 60–82% ee) as measured by chiral HPLC analysis, though preparation of similar alcohols with high ee has been published.[4c,e,12] The alcohols were then converted to picolinates **9**–**12**. The absolute configuration of alcohol **24** was determined by comparison of the $[\alpha]_D$ value with that reported[13] and was consistent with the sense of the CBS reduction. The same configuration was assigned to the other alcohols **25**–**27** by analogy.

Phenylation of Allylic Picolinate 6. Substitution of picolinate **6** with Ph copper reagents was studied using 30–50 mg of **6** at various temperatures in THF or in other solvents for 2 h (in most cases) and the product ratios are presented in Table 1 and Table S1 (Supporting Information). The procedure developed by us[5] for picolinates **4** was examined first with the reagent derived from PhMgBr and $CuBr{\cdot}Me_2S$ in a 2:1 ratio in THF to afford a mixture of the expected product **15**, regioisomer **16**, alcohol **17**, and the starting picolinate **6** (entry 1).[14] The calculated regioselectivity of **15** over **16** was 76%, which is similar to that obtained for picolinate **1** (82%). No cis isomer was detected by ^1H NMR spectroscopy of the crude product. In entry 2, 50% more reagent was used at a higher temperature (−18 °C) to complete the reaction, but with low product selectivity. The ZnI_2-promoted reaction, developed for allylation of cyclic substrates such as **14**,[7] raised the selectivity up to 78% (entry 3). Other ZnX_2 (X = Br, Cl, TsO, $PhCO_2$) resulted in slightly or substantially lower selectivity (Table S1, Supporting Information) than that in entry 3. In Et_2O, a mixture of **15**–**17** and diene **18** was produced, whereas reaction with ZnI_2 in CH_2Cl_2-THF, the mixed solvent for the allylic substitution with alkynyl copper reagents,[15] showed a moderate product selectivity (62% in Table S1, Supporting Information). The PhLi-based reagent in the presence or absence of ZnI_2 produced **18** as the major product (entries 4 and 5).

Recently, $Cu(acac)_2$-based alkynyl reagents were found to be highly regioselective in the substitution of cyclic allylic picolinates.[16] By intuition, we envisaged high efficiency with reagents derived from PhMgBr and $Cu(acac)_2$. In fact, a Ph reagent derived from PhMgBr and $Cu(acac)_2$ in a 2:1 ratio at

Table 1. Preliminary Investigation of Allylic Substitution of Racemic 6 with Ph Copper Reagents



entry	Ph metal (equiv)	copper salt (equiv)	Ph/Cu	additive (equiv)	solvent	temp (°C)	product ratio[a] (%) **15**:**16**:**17**:**18**:**6**
1	PhMgBr (2.0)	$CuBr{\cdot}Me_2S$ (1.0)	2:1		THF	−60	53:17:16:0:14
2	PhMgBr (3.0)	$CuBr{\cdot}Me_2S$ (1.5)	2:1		THF	−18	54:45:1:0:0
3	PhMgBr (3.2)	$CuBr{\cdot}Me_2S$ (1.5)	2.1:1	ZnI_2 (1.5)	THF	−18	78:13:3:6:0
4	PhLi (3.2), $MgBr_2$ (4.0)	$CuBr{\cdot}Me_2S$ (1.5)	2.1:1		THF	−60	0:20:16:64:0
5	PhLi (3.2), $MgBr_2$ (4.0)	$CuBr{\cdot}Me_2S$ (1.5)	2.1:1	ZnI_2 (1.5)	THF	−60	0:14:27:58:0
6	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1		THF	−40	>99:0:0:0:0[b]
7	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	ZnI_2 (1.5)	THF	−40	no reaction
8	PhMgBr (4.7)	$Cu(acac)_2$ (1.5)	3.1:1		THF	−40	44:41:15:0:0
9	PhMgBr (4.7)	$Cu(acac)_2$ (1.5)	3.1:1	ZnI_2 (1.5)	THF	−40	98:2:0:0:0[b]
10	PhMgBr (4.7)	$Cu(acac)_2$ (1.5)	3.1:1	$ZnBr_2$ (1.5)	THF	−40	97:3:0:0:0[b]
11	PhMgBr (4.7)	$Cu(acac)_2$ (1.5)	3.1:1	$ZnCl_2$ (1.5)	THF	−40	95:5:1:0:0
12	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1		THF	−30	99:1:0:0:0
13	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1		THF	−20	95:3:2:0:0
14	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1		THF	0	85:13:2:0:0

[a]Determined by ^1H NMR integration ratios of the protons at δ 5.44 (dt, 1 H) and 5.64 (d, 1 H) for **15**, 5.26 (d, 1 H) for **16**, (5.15 (dm, 1 H) for **17**, 6.15 (d, 1 H) and 4.87 (s, 2 H) for **18**, and 5.80–5.89 (m, 1 H) for **6**. [b]Isolated yields of **15**: 100% (entry 6), 87% (entry 9), and 90% (entry 10).

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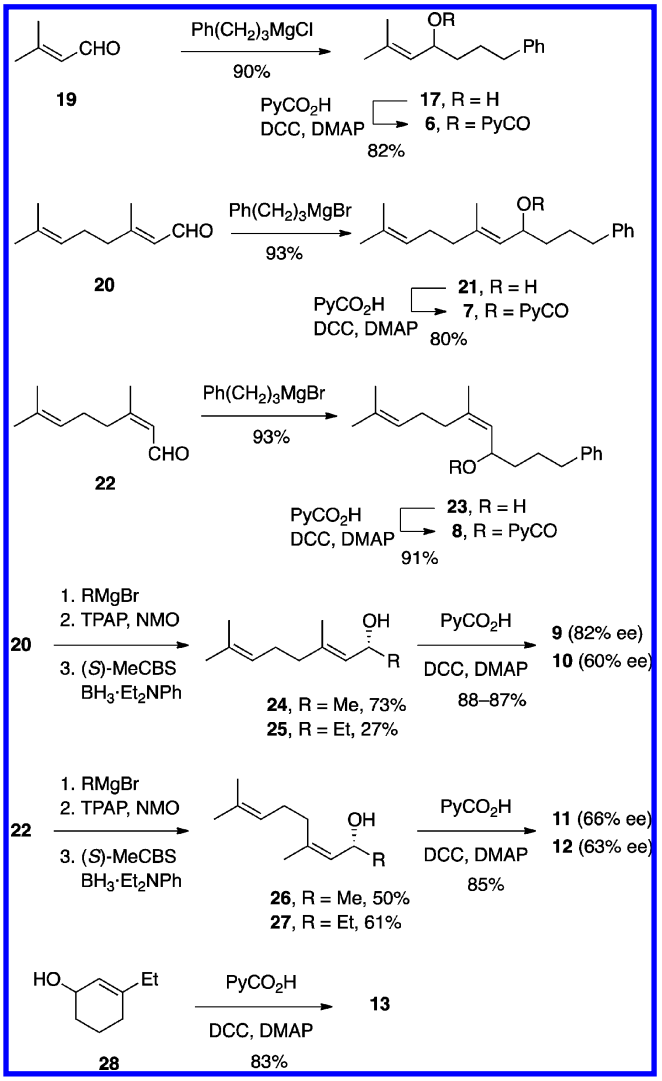
Scheme 3. Synthesis of Picolinates 6−8 and 9−13[a]



[a]Reagents: TPAP, Pr_4NRuO_4; (*S*)-MeCBS, (*S*)-3,3-diphenyl-1-methylpyrrolidino[1,2-*c*]-1,3,2-oxazaborole.

−40 °C for 2 h produced **15** exclusively in quantitative yield (entry 6). This reagent was highly product selective (and thus regioselective) even at −30 and −20 °C (entries 12 and 13) but moderately selective at 0 °C (entry 14). In contrast, addition of ZnI_2 prevented the reaction at all (entry 7). Different from the 2:1 PhMgBr/$Cu(acac)_2$ reagent, a reagent derived from PhMgBr and $Cu(acac)_2$ in a 3:1 ratio showed almost no regioselectivity (entry 8), whereas the selectivity was drastically improved by addition of ZnX_2 (X = I, Br, Cl), among which ZnI_2 provided the best selectivity (entries 9−11). In addition, ZnI_2 is less hygroscopic than the other ZnX_2 and thus more practical. An attempted reaction with a 1:1 PhMgBr/$Cu(acac)_2$ reagent even at 0 °C resulted in recovery of picolinate **6** (data not shown). We also examined reagents derived from $Cu(OAc)_2$ and $Cu(OMe)_2$. As shown in Table S1 (Supporting Information), a reagent derived from PhMgBr and $Cu(OAc)_2$ in a 2:1 ratio produced diene **18** as the major product, while that prepared from $Cu(OMe)_2$ afforded **15** with somewhat low selectivity of 88%.[17] The attempted reaction with 10 mol % of $Cu(acac)_2$ afforded a mixture of **15**/**16**/**17** in a 20:56:24 ratio.

In summary of the preliminary investigation (Table 1 and Table S1, Supporting Information), product selectivity of the phenylcopper reagents producing **15** in the reaction of picolinate **6** was highly dependent on the copper source, composition with PhMgBr, and addition of ZnX_2. The results obtained with the $Cu(acac)_2$-based reagents are summarized in Table 2. First, $Cu(acac)_2$ was found to be a better source of the copper reagent than CuBr·Me_2S (result 1). Second, ZnI_2 was found to raise the selectivity of the 3:1 PhMgBr/$Cu(acac)_2$ reagent (result 4 vs result 3), whereas the reaction with the 2:1 reagent was totally prevented by ZnI_2 (result 2). From a practical point of view we recommend the 2:1 PhMgBr/$Cu(acac)_2$ reagent on the basis of the quantity of PhMgBr. The procedure using the 2:1 PhMgBr/$Cu(acac)_2$ reagent could be scaled up to 3.1 g of **6** (10 mmol), which afforded **15** with 99% regioselectivity and 92% yield after purification by chromatography.

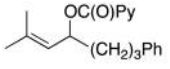
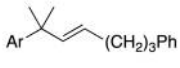
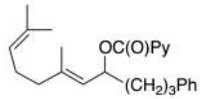
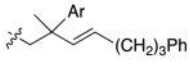
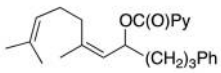
Table 2. Potential of the Reagents

result	entry of Table 1	Ph/Cu[a]	ZnI_2	remaining **6** (%)	product selectivity of **15**[b] (%)
1	**6**	**2:1**		**0**	**>99**
2	7	2:1	added[c]	100	
3	8	3:1		0	44
4	**9**	**3:1**	**added**[c]	**0**	**98**

[a]Quantity of $Cu(acac)_2$ was 1.5 equiv per picolinate **6**, and that of PhMgBr was 3−3.1 and 4.5−4.7 equiv per **6** for the 2:1 and 3:1 Ph/Cu ratios. [b]Based on the products **15**−**18** and **6**. [c]1.5 equiv per **6**.

Allylic Substitution with Arylcopper Reagents. The reagent system used in entry 6 of Table 1 was applied to allylic substitution summarized in Table 3. The reactions in all entries completed within 2 h. However, regioselectivity and yields varied slightly. Thus, the Me substituent at the para and ortho positions furnished similar regioselectivity and yield (entries 1 and 2), whereas the MeO group at the ortho position slightly lowered the selectivity and yield (entry 4 vs entries 1−3).

Table 3. Allylic Substitution of Racemic 6−8 with ArMgBr/$Cu(acac)_2$[a]

entry	picolinate	product	regioselectivity[b] (%)	isolated yield (%)
				
1	**6**	**29**, Ar = *p*-MeC_6H_4	>99	93
2	**6**	**30**, Ar = *o*-MeC_6H_4	96	96
3	**6**	**31**, Ar = *p*-$MeOC_6H_4$	98	82
4	**6**	**32**, Ar = *o*-$MeOC_6H_4$	90	65
5	**6**	**33**, Ar = *p*-FC_6H_4	98	84
				
6	**7**	**34**, Ar = Ph	>99	95
				
7	**8**	**34**, Ar = Ph	99	88
8	**7** + **8** (3:2)	**35**, Ar = *p*-FC_6H_4	99	80

[a]ArMgBr (3 equiv), $Cu(acac)_2$ (1.5 equiv), THF, from −40 to −20 or −10 °C, 2 h. [b]Determined by ^1H NMR integration ratios for the olefinic protons.

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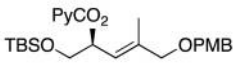
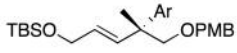
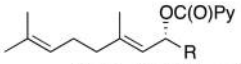
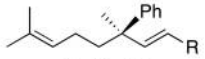
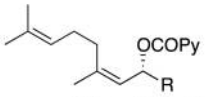
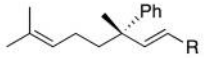
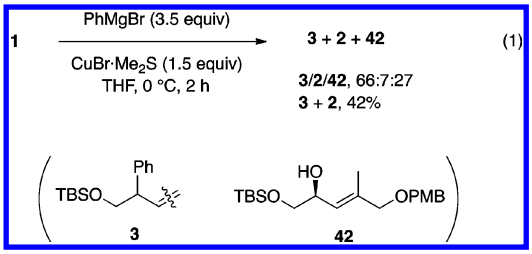
Table 4. Substitution of Chiral Picolinates with Arylcopper Reagents[a]

entry	substrate[b]	source of reagents (equiv)	product	regioselectivity[c] (%)	isolated yield (%)	CT[b,d] (%)
						
1	**1** (98% ee)	PhMgBr (3), $Cu(acac)_2$ (1.5)	**2**, Ar = Ph	96	49[e]	98
2	**1**	PhMgBr (6), $Cu(acac)_2$ (3)	**2**	>99	86	99
3	**1**	*p*-MeC_6H_4MgBr (6), $Cu(acac)_2$ (3)	**36**, Ar = *p*-MeC_6H_4	92	93	99
4	**1**	*o*-MeC_6H_4MgBr (6), $Cu(acac)_2$ (3)	**37**, Ar = *o*-MeC_6H_4	96	95	>99
5	**1**	*p*-$MeOC_6H_4MgBr$ (6), $Cu(acac)_2$ (3)	**38**, Ar = *p*-$MeOC_6H_4$	93	94	99
6	**1**	*p*-FC_6H_4MgBr (6), $Cu(acac)_2$ (3)	**39**, Ar = *p*-FC_6H_4	>99	>99	>99
						
7	**9**, R = Me (82% ee)	PhMgBr (3), $Cu(acac)_2$ (1.5)	**40**, R = Me	98	85	99
8	**10**, R = Et (60% ee)	PhMgBr (3), $Cu(acac)_2$ (1.5)	**41**, R = Et	>99	90	97
						
9	**11**, R = Me (66% ee)	PhMgBr (3), $Cu(acac)_2$ (1.5)	*ent*-**40**, R = Me	98	88	>99
10	**12**, R = Et (63% ee)	PhMgBr (3), $Cu(acac)_2$ (1.5)	*ent*-**41**, R = Et	99	82	98

[a]Reactions in entry 1 and entries 2–10 were carried out for 3 and 2 h, respectively, at −40 to −10 or to 0 °C. [b]Enantiomeric excess (ee) was determined by HPLC analysis using DAICEL chiral columns. [c]Determined by ^1H NMR integration ratios for the olefinic protons. [d]CT (chirality transfer) was calculated by (% ee of product) × 100/(% ee of substrate). [e]Remaining **1** was detected by ^1H NMR and TLC analysis.

The reaction with the *p*-FC_6H_4 reagent proceeded efficiently as well (entry 5). Substitution of picolinates **7** and **8** was not affected by the bulkiness of the alkyl groups on the reacting carbon (γ position), and S_N2' product **34** was obtained selectively (entries 6 and 7). A similar selectivity was observed in entry 8 to produce **35**.

Arylation of Enatiomerically Enriched Allylic Picolinates. The above reagent system consisting of 2:1 ArMgBr/$Cu(acac)_2$ was applied to enantiomerically enriched picolinates **1**[18] and **9**–**12** to determine chirality transfer (CT) of the allylic substitution (Table 4). Substitution of **1** (98% ee) with the Ph copper reagent for 3 h, however, afforded a mixture of **2** and the starting picolinate **1** (entry 1 and footnote e), suggesting lower reactivity of **1** than the substrates examined above. Fortunately, full conversion was attained by doubling the quantity of the reagent to produce **2** with 99% CT and >99% regioselectivity in 86% yield (entry 2). The absolute configuration of **2** was determined by the specific rotation [[α]$^{25}_D$ +2.5 (*c* 0.16, $CHCl_3$) [lit.[5] [α]$^{30}_D$ +1.5 (*c* 0.40, $CHCl_3$)]] and retention time on chiral HPLC (Supporting Information), establishing anti S_N2' pathway. On the other hand, the authentic regioisomer **3** was synthesized with 91% regioselectivity along with alcohol **42** (**3**/**2**/**42** = 67:7:26) using the $CuBr{\cdot}Me_2S$-based copper reagent (eq 1), which afforded a 45:55 mixture of **16** and **15** from substrate **6** (Table 1, entry 2). The different regioselectivity between **1** and **6** implies that the γ position of **1** is more congested than **6**, rendering the position less accessible. Similarly, substituted aryl reagents shown in entries 3–6 afforded **36**–**39** with high CT in high yields. These results demonstrate high potency of the ArMgBr/$Cu(acac)_2$ reagents, which would not be influenced by steric and electronic biases. Next, allylic substitution of picolinates **9**–**12** was examined (entries 7–10). The reactions proceeded with the standard quantity of the Ph reagent and afforded the anti S_N2' products with high CT



and regioselectivity in good yields.[19] These results indicate that these picolinates are more susceptible to the reaction than **1**.

Construction of a Quaternary Carbon on the Cyclohexane Ring. The above protocol was applied to picolinates to create a quaternary carbon on the cyclohexane ring (Scheme 4). Reaction of **13** with the 2:1 PhMgBr/$Cu(acac)_2$ and 3:1:1 PhMgBr/$Cu(acac)_2$/ZnI_2 reagents gave **43** with 82–87% regioselectivity over the regioisomer **44** in good yields. The next substrate was **14**, in which the α carbon is less congested than that of the other substrates examined in Tables 1, 3, and 4, thus rendering the γ position less accessible than α. Nevertheless, both of the reagents afforded the desired product **45** with >81% regioselectivity over the regioisomer **46**. Furthermore, the ^1H NMR spectrum of **45** indicates >99% stereoselectivity, and the trans 1,4-diphenyl stereochemistry is assigned on the basis of the previous results with alkylcopper reagents.[7]

Mechanism. As mentioned in the phenylation of allylic picolinate **6**, no reaction took place with the 1:1 PhMgBr/$Cu(acac)_2$ reagent. This result is consistent with stoichiometric consumption of PhMgBr for reduction of $Cu(acac)_2$ to a Cu^+ species,[20] and thus, 2 and 3 equiv of PhMgBr per $Cu(acac)_2$ should afford species of the formal "Ph–Cu" and "Ph_2Cu^-" types, respectively. The former species is sufficiently reactive

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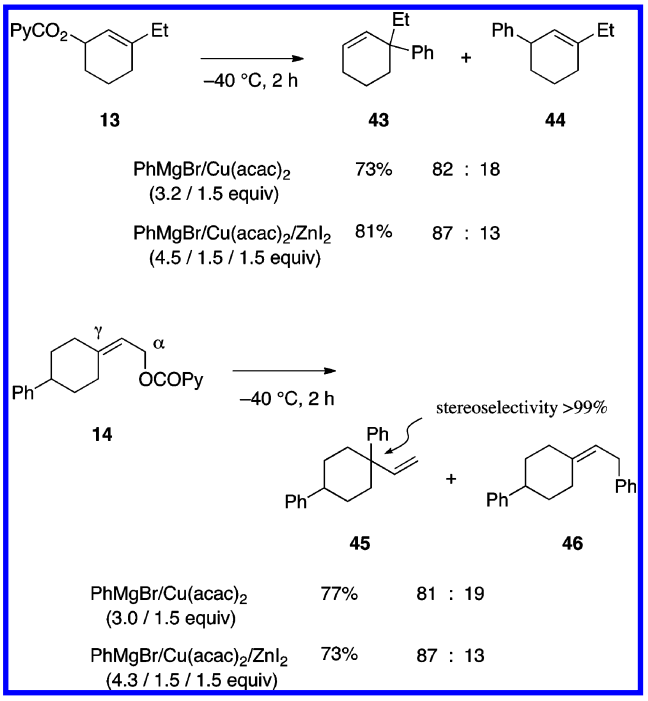
Scheme 4. Construction of a Quaternary Carbon on the Cyclohexane Ring



toward picolinate **6** to produce **15** highly regioselectively (>99%) (cf. the 1:1 PhMgBr/CuBr·Me_2S reagent, however, generated a 88:12 mixture of **15** and **16**, data not shown). The latter is also reactive but suffers from low regioselectivity. The selectivity is highly improved by addition of ZnI_2 without substantial reduction of yield. On the other hand, allylic substitution of the previous picolinates **4** with "Ar–Cu" and "Ar_2Cu^-" species derived from CuBr·Me_2S and ArMgBr in 1:1 or 1:2 ratios proceeds efficiently as published previously.[5] To explain these results, a likely mechanism along the lines of recent publications[8,21] is proposed in Scheme 5, in which the previous and present picolinates are depicted as **47a** (R^1 = H) and **47b** (R^1 = alkyl), respectively. Electron withdrawal by the pyridyl group and chelation of the picolinoxy group to M^{2+} (Mg^{2+} generated in situ) cooperatively facilitate complexation of $[ArCuX]^-$ to **47a** to furnish the π-complex **48a**, in which the Ar group occupies the space opposite the leaving group ($PyCO_2$), eventually producing the anti S_N2' product **50a** through (enyl)Cu species **49a**. In contrast, R^1 in **47b** interferes the complexation to form **48b** and/or the subsequent step to afford **49b**, thus resulting in not only a decrease in reactivity but also competition to form **51b**, which in turn gives regioisomer **53b**. In practice, however, $[ArCu(acac)]^-$ with the acac ligand are highly reactive to produce **50b**, regioselectively, whereas $[ArCuX]^-$ (X = Ar, Br) are less potent, resulting in low regioselectivity. The recovery of the regioselectivity by the addition of ZnX_2 probably reflects stronger chelation of the leaving group to ZnX_2 to form **48b** (M^{2+} = Zn^{2+}) than that to $MgBr_2$. However, the remaining issues to be clarified are (1) a mechanism for $[ArCu(acac)]^-$ to show high reactivity to form **48b**/**49b** and (2) different levels of the ZnI_2-assisted recovery of the regioselectivity between $[Ar_2Cu]^-$ derived from CuBr·Me_2S and that from $Cu(acac)_2$.

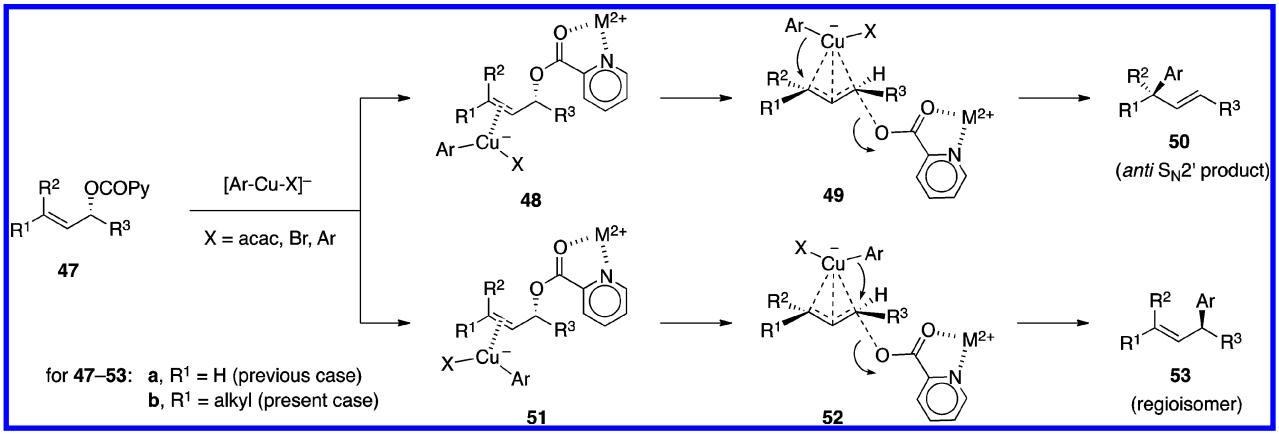
CONCLUSION

In conclusion, we have developed the 2:1 ArMgBr/$Cu(acac)_2$ and 3:1:1 ArMgBr/$Cu(acac)_2$/ZnI_2 reagents for construction of a quaternary carbon by allylic substitution, which proceeds with high stereo-, regio-, and product-selectivity. We found furthermore that the olefin geometry in allylic picolinate does not affect CT and regioselectivity but dictates chirality of the product. This fact would be synthetically convenient for designing biologically important compounds, which consist of a chiral quaternary carbon possessing an aryl group.[10b,e,f,22]

EXPERIMENTAL SECTION

General Remarks. The ^1H NMR (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) spectra were measured in $CDCl_3$ using $SiMe_4$ (δ = 0 ppm) and the centerline of the triplet (δ = 77.1 ppm) as internal standards, respectively. Signal patterns are indicated as follows: br s, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (J) are given in hertz (Hz). Chemical shifts in the ^{13}C NMR spectra accompany minus (for C and CH_2) and plus (for CH and CH_3) signs of APT experiments. High-resolution mass spectroscopy (HRMS) experiments were performed with a double-focusing mass spectrometer with an ionization mode of positive FAB or EI as indicated for each compound. The following solvents were distilled beforehand: THF (from Na/benzophenone), Et_2O (from Na/benzophenone), and CH_2Cl_2 (from CaH_2). After the reactions were finished, the organic extracts were concentrated by using evaporators, and the residues were purified by chromatography on silica gel (spherical silica gel 60 N). $Cu(acac)_2$ was purchased from a commercial supplier and used without purification, whereas CuBr·Me_2S was prepared as described previously.[6b] Picolinates **1** (98% ee) and **14**

Scheme 5. Plausible Mechanism



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were prepared according to the literature procedures published from our laboratory.[5,7]

Synthesis of Racemic Picolinates 6–8 and 13. *2-Methyl-7-phenylhept-2-en-4-yl Picolinate (6).* To an ice-cold solution of 3-methyl-2-butenal (**19**) (1.14 g, 13.6 mmol) in THF (60 mL) was added $Ph(CH_2)_3MgCl$ (26.5 mL, 0.77 M in THF, 20.4 mmol). The solution was stirred at rt for 2 h, and saturated NH_4Cl and EtOAc were added with vigorous stirring. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined extracts were dried over $MgSO_4$, washed with brine, and concentrated to afford a residue, which was purified by chromatography on silica gel with hexane/EtOAc to furnish alcohol **17** (2.49 g, 90%) as a colorless oil: IR (neat) 3361, 1453, 748, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28–1.34 (m, 1 H), 1.42–1.54 (m, 1 H), 1.55–1.74 (m, 2 H), 1.67 (d, J = 1 Hz, 3 H), 1.72 (d, J = 1 Hz, 3 H), 2.63 (t, J = 7 Hz, 2 H), 4.35 (dt, J = 8, 6 Hz, 1 H), 5.15 (dm, J = 9 Hz, 1 H), 7.14–7.21 (m, 3 H), 7.25–7.31 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3 (+), 25.9 (+), 27.4 (−), 36.0 (−), 37.4 (−), 68.6 (+), 125.8 (+), 128.2 (+), 128.4 (+), 128.5 (+), 135.4 (−), 142.5 (−); HRMS (EI) calcd for $C_{14}H_{20}O$ (M^+) 204.1514, found 204.1516.

To an ice-cold suspension of picolinic acid (1.67 g, 13.6 mmol) in CH_2Cl_2 (30 mL) were added DMAP (746 mg, 6.11 mmol) and DCC (3.29 g, 15.9 mmol). The mixture was stirred at 0 °C for 30 min, and a solution of alcohol **17** (2.49 g, 12.2 mmol) in CH_2Cl_2 (20 mL) was added. The resulting mixture was stirred at 0 °C for 2 h, diluted with Et_2O, and filtered through a pad of Celite. The filtrate was concentrated to give a residue, which was purified by chromatography on silica gel with hexane/EtOAc to afford picolinate **6** (3.09 g, 82%) as a colorless oil: IR (neat) 1737, 1713, 1245, 1133, 747, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.63–1.78 (m, 3 H), 1.73 (d, J = 1 Hz, 3 H), 1.80 (d, J = 1 Hz, 3 H), 1.87–1.98 (m, 1 H), 2.65 (t, J = 7 Hz, 2 H), 5.29 (dm, J = 10 Hz, 1 H), 5.80–5.89 (m, 1 H), 7.14–7.20 (m, 3 H), 7.23–7.30 (m, 2 H), 7.44 (ddd, J = 8, 5, 1 Hz, 1 H), 7.81 (dt, J = 8, 2 Hz, 1 H), 8.10 (dt, J = 8, 1 Hz, 1 H), 8.77 (ddd, J = 5, 2, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.7 (+), 25.9 (+), 27.2 (−), 34.6 (−), 35.7 (−), 73.3 (+), 123.4 (+), 125.2 (+), 125.8 (+), 126.7 (+), 128.4 (+), 128.5 (+), 136.9 (+), 138.2 (−), 142.2 (−), 148.7 (−), 150.0 (+), 164.7 (−); HRMS (EI) calcd for $C_{20}H_{23}NO_2$ (M^+) 309.1729, found 309.1730.

(E)-6,10-Dimethyl-1-phenylundeca-5,9-dien-4-ol (21). To a suspension of molecular sieves 4A (1.65 g), TPAP (116.0 mg, 0.330 mmol), and NMO (590.0 mg, 5.04 mmol) in CH_2Cl_2 (20 mL) was added a solution of geraniol (501.6 mg, 3.25 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at rt for 1 h and filtered through a pad of Celite. The filtrate was concentrated to afford a residual oil, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish **20** (433.9 mg, 88%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 1.61 (s, 3 H), 1.69 (s, 3 H), 2.15–2.28 (m, 4 H), 2.17 (s, 3 H), 5.04–5.12 (m, 1 H), 5.88 (d, J = 8 Hz, 1 H), 10.00 (d, J = 8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7 (+), 17.8 (+), 25.7 (+), 25.8 (−), 40.7 (−), 122.7 (+), 127.5 (+), 133.0 (−), 163.9 (−), 191.4 (+). The ^1H and ^{13}C NMR spectra were consistent with those reported.[23]

According to the Grignard addition to aldehyde **19**, aldehyde **20** (433.9 mg, 2.85 mmol) in THF (25 mL) was subjected to reaction with $Ph(CH_2)_3MgBr$ (5.00 mL, 0.80 M in THF, 4.00 mmol) at rt for 1 h to produce alcohol **21** (723.7 mg, 93%) as a colorless oil: IR (neat) 3377, 1453, 748, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (br s, 1 H), 1.42–1.54 (m, 1 H), 1.57–1.74 (m, 3 H), 1.59 (s, 3 H), 1.67 (s, 6 H), 2.01 (t, J = 7.5 Hz, 2 H), 2.05–2.14 (m, 2 H), 2.63 (t, J = 7 Hz, 2 H), 4.37 (dt, J = 9, 6 Hz, 1 H), 5.07 (t, J = 7 Hz, 1 H), 5.16 (d, J = 9 Hz, 1 H), 7.14–7.20 (m, 3 H), 7.23–7.30 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.7 (+), 17.8 (+), 25.7 (+), 26.4 (−), 27.3 (−), 36.0 (−), 37.3 (−), 39.6 (−), 68.5 (+), 124.0 (+), 125.8 (+), 128.0 (+), 128.3 (+), 128.5 (+), 131.8 (−), 138.7 (−), 142.5 (−); HRMS (FAB) calcd for $C_{19}H_{28}ONa$ [$(M + Na)^+$] 295.2038, found 295.2036.

(E)-6,10-Dimethyl-1-phenylundeca-5,9-dien-4-yl Picolinate (7). According to the preparation of picolinate **6**, alcohol **21** (155.8 mg, 0.572 mmol) was subjected to condensation with picolinic acid (95.9 mg, 0.779 mmol), DMAP (69.6 mg, 0.570 mmol), and DCC (156.0 mg, 0.756 mmol) in CH_2Cl_2 (3 + 2 mL) at rt for 2 h to afford picolinate **7** (172.1 mg, 80%) as a colorless oil: IR (neat) 1738, 1713, 1245, 1132, 746, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.54–1.82 (m, 3 H), 1.57 (s, 3 H), 1.63 (s, 3 H), 1.79 (d, J = 2 Hz, 3 H), 1.86–1.98 (m, 1 H), 1.98–2.14 (m, 4 H), 2.66 (t, J = 7 Hz, 2 H), 5.05 (tm, J = 7 Hz, 1 H), 5.28 (dd, J = 9, 1 Hz, 1 H), 5.86 (dt, J = 9, 6 Hz, 1 H), 7.13–7.20 (m, 3 H), 7.22–7.30 (m, 2 H), 7.44 (ddd, J = 7.5, 5, 1 Hz, 1 H), 7.81 (dt, J = 2, 7.5 Hz, 1 H), 8.10 (dt, J = 7.5, 1 Hz, 1 H), 8.76 (dm, J = 5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.0 (+), 17.8 (+), 25.7 (+), 26.3 (−), 27.1 (−), 34.6 (−), 35.7 (−), 39.6 (−), 73.2 (+), 123.2 (+), 123.9 (+), 125.2 (+), 125.8 (+), 126.6 (+), 128.4 (+), 128.5 (+), 131.8 (−), 136.9 (+), 141.4 (−), 142.2 (−), 148.8 (−), 150.0 (+), 164.7 (−); HRMS (FAB) calcd for $C_{25}H_{31}NO_2Na$ [$(M + Na)^+$] 400.2252, found 400.2253.

(Z)-6,10-Dimethyl-1-phenylundeca-5,9-dien-4-ol (23). According to the oxidation of geraniol, a mixture of nerol (501.6 mg, 3.25 mmol), TPAP (114.0 mg, 0.324 mmol), NMO (570.0 mg, 4.87 mmol), and molecular sieves 4A (1.63 g) in CH_2Cl_2 (20 + 10 mL) was stirred at rt for 1 h to furnish **22** (445.5 mg, 90%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 1.59 (s, 3 H), 1.68 (d, J = 1 Hz, 3 H), 1.98 (d, J = 1 Hz, 3 H), 2.24 (dt, J = 7, 7.5 Hz, 2 H), 2.59 (t, J = 7.5 Hz, 2 H), 5.10 (tm, J = 7 Hz, 1 H), 5.88 (d, J = 8 Hz, 1 H), 9.90 (d, J = 8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8 (+), 25.1 (+), 25.7 (+), 27.1 (−), 32.7 (−), 122.4 (+), 128.8 (+), 133.8 (−), 163.9 (−), 190.9 (+). The ^1H and ^{13}C NMR spectra were consistent with those reported.[24]

According to the Grignard addition to aldehyde **19**, aldehyde **22** (445.5 mg, 2.93 mmol) in THF (25 mL) was subjected to reaction with $Ph(CH_2)_3MgBr$ (5.10 mL, 0.80 M in THF, 4.08 mmol) at rt for 1 h to furnish alcohol **23** (737.7 mg, 93%) as a colorless oil: IR (neat) 3364, 1452, 748, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (br s, 1 H), 1.41–1.53 (m, 1 H), 1.55–1.77 (m, 3 H), 1.59 (s, 3 H), 1.68 (s, 3 H), 1.72 (d, J = 1 Hz, 3 H), 2.00–2.17 (m, 4 H), 2.63 (t, J = 7 Hz, 2 H), 4.33 (dt, J = 9, 6 Hz, 1 H), 5.06–5.14 (m, 1 H), 5.18 (d, J = 9 Hz, 1 H), 7.13–7.20 (m, 3 H), 7.23–7.30 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7 (+), 23.37 (+), 23.39 (+), 25.7 (+), 26.6 (−), 27.5 (−), 32.4 (−), 36.0 (−), 37.2 (−), 68.0 (+), 124.0 (+), 125.8 (+), 128.3 (+), 128.5 (+), 129.1 (+), 132.5 (−), 138.9 (−), 142.5 (−); HRMS (FAB) calcd for $C_{19}H_{28}ONa$ [$(M + Na)^+$] 295.2038, found 295.2066.

(Z)-6,10-Dimethyl-1-phenylundeca-5,9-dien-4-yl Picolinate (8). According to the preparation of picolinate **6**, alcohol **23** (294.1 mg, 1.08 mmol) was subjected to condensation with picolinic acid (167.9 mg, 1.36 mmol), DMAP (101.1 mg, 0.828 mmol), and DCC (297.5 mg, 1.44 mmol) in CH_2Cl_2 (8 + 2 mL) at rt for 2 h to produce picolinate **8** (369.3 mg, 91%) as a colorless oil: IR (neat) 1738, 1713, 1245, 1132, 747, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.58 (s, 3 H), 1.62 (s, 3 H), 1.74 (d, J = 1.5 Hz, 3 H), 1.64–1.80 (m, 3 H), 1.86–1.98 (m, 1 H), 2.00–2.20 (m, 3 H), 2.28–2.38 (m, 1 H), 2.65 (t, J = 7 Hz, 2 H), 5.11 (tm, J = 7 Hz, 1 H), 5.31 (dd, J = 10, 1 Hz, 1 H), 5.89 (dt, J = 10, 7 Hz, 1 H), 7.12–7.20 (m, 3 H), 7.22–7.29 (m, 2 H), 7.43 (ddd, J = 8, 5, 1 Hz, 1 H), 7.80 (dt, J = 2, 8 Hz, 1 H), 8.10 (dt, J = 8, 1 Hz, 1 H), 8.76 (ddd, J = 5, 2, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7 (+), 23.4 (+), 25.7 (+), 26.7 (−), 27.3 (−), 32.7 (−), 34.8 (−), 35.8 (−), 72.8 (+), 123.9 (+), 124.0 (+), 125.2 (+), 125.8 (+), 126.6 (+), 128.4 (+), 128.5 (+), 132.0 (−), 136.9 (+), 141.7 (−), 142.1 (−), 148.8 (−), 149.9 (+), 164.6 (−); HRMS (FAB) calcd for $C_{25}H_{32}NO_2$ [$(M + H)^+$] 378.2433, found 378.2441.

3-Ethylcyclohex-2-enyl Picolinate (13). According to the preparation of picolinate **6**, alcohol **28**[25] (208.1 mg, 1.65 mmol) was subjected to condensation with picolinic acid (245.0 mg, 1.99 mmol), DMAP (202.1 mg, 1.65 mmol), and DCC (450.0 mg, 2.18 mmol) in CH_2Cl_2 (14 + 2 mL) to give picolinate **13** (318.4 mg, 83%) as a colorless oil: IR (neat) 1736, 1713, 1245, 1133, 911, 748, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.03 (t, J = 7.5 Hz, 3 H), 1.65–1.76 (m, 1 H), 1.81–2.11 (m, 7 H), 5.57–5.66 (m, 2 H), 7.45 (dm, J = 7.5 Hz, 1 H), 7.83 (dt, J = 1.5, 7.5 Hz, 1 H), 8.13 (d, J = 7.5 Hz, 1 H), 8.78 (dm, J = 5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9 (+), 19.5 (−), 28.4 (−), 28.5 (−), 30.4 (−), 70.9 (+), 118.1 (+), 125.2 (+), 126.7 (+), 136.9 (+), 146.7 (−), 148.9 (−), 150.0 (+), 165.1 (−); HRMS (FAB) calcd for $C_{14}H_{18}NO_2$ (M)$^+$ 232.1338, found 232.1343.

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Synthesis of Optically Active Picolinates 9−12. *(E)-4,8-Dimethylnona-3,7-dien-2-one.* According to the Grignard addition to aldehyde **19**, aldehyde **20** (466.5 mg, 3.06 mmol) in THF (30 mL) was subjected to reaction with MeMgBr (4.60 mL, 0.99 M in THF, 4.55 mmol) at rt for 1 h to furnish racemic alcohol *rac*-**24** (467.1 mg, 91%) as a colorless oil.

According to the oxidation of geraniol, a mixture of *rac*-**24** (228.2 mg, 1.36 mmol), TPAP (47.2 mg, 0.134 mmol), NMO (318.0 mg, 2.71 mmol), and molecular sieves 4A (677.0 mg) in CH_2Cl_2 (12 + 2 mL) was stirred at rt for 2 h to furnish the title ketone (188.1 mg, 83%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61 (s, 3 H), 1.69 (s, 3 H), 2.10−2.20 (m, 4 H), 2.13 (d, J = 1 Hz, 3 H), 2.17 (s, 3 H), 5.02−5.12 (m, 1 H), 6.06 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7 (+), 19.3 (+), 25.7 (+), 26.2 (−), 31.8 (+), 41.2 (−), 123.1 (+), 123.7 (+), 132.6 (−), 158.3 (−), 198.9 (−). The ^{1}H and ^{13}C NMR spectra were identical with those reported.[26]

(R,E)-4,8-Dimethylnona-3,7-dien-2-ol (***24***). To a solution of (*S*)-methyl oxazaborolidine (0.030 mL, 1.0 M in toluene, 0.030 mmol) and *N*,*N*-diethylaniline borane (0.036 mL, 0.202 mmol) in THF (1 mL) at −20 °C was added a solution of the above ketone (30.2 mg, 0.182 mmol) in THF (2 mL) over 5 h. After the addition, the solution was stirred at −20 °C for further 3 h. Cold MeOH (3 mL) was added slowly to the solution at −20 °C, and the cooling bath was removed. The solution was stirred at rt for 1 h and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish **24** (29.7 mg, 97%) as a colorless oil: $[\alpha]^{24}_D$ +23 (*c* 0.60, $CHCl_3$) (cf. $[\alpha]^{20}_D$ +21.6 (*c* 0.3, $CHCl_3$) for the *R* enantiomer of 98% ee);[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (d, J = 6 Hz, 3 H), 1.43 (br s, 1 H), 1.60 (s, 3 H), 1.679 (s, 3 H), 1.682, (s, 3 H), 1.99 (t, J = 7 Hz, 2 H), 2.05−2.14 (m, 2 H), 4.57 (dq, J = 8, 6 Hz, 1 H), 5.08 (tm, J = 7 Hz, 1 H), 5.21 (dm, J = 8, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5 (+), 17.7 (+), 23.7 (+), 25.7 (+), 26.5 (−), 39.5 (−), 64.8 (+), 124.0 (+), 129.2 (+), 131.7 (−), 137.6 (−); HRMS (EI) calcd for $C_{11}H_{20}O$ (M^+) 168.1514, found 168.1514. The ^{1}H and ^{13}C NMR spectra were identical with those reported.[26] The enantiomeric purity of 82% ee was determined by chiral HPLC analysis: Chiralcel OD-H, hexane/*i*-PrOH = 99.5/0.5, 0.700 mL/min, 30 °C, t_R/min =19.7 (*R*-isomer), 20.7 (*S*-isomer).

(R,E)-4,8-Dimethylnona-3,7-dien-2-yl Picolinate (***9***). According to the preparation of picolinate **6**, alcohol **24** (29.7 mg, 0.176 mmol) was subjected to condensation with picolinic acid (31.2 mg, 0.253 mmol), DMAP (21.7 mg, 0.178 mmol), and DCC (47.7 mg, 0.231 mmol) in CH_2Cl_2 (1 + 1 mL) at rt for 2 h to afford **9** (42.4 mg, 88%) as a colorless oil: $[\alpha]^{23}_D$ −17 (*c* 0.26, $CHCl_3$); IR (neat) 1738, 1715, 1132, 747, 708 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (d, J = 6 Hz, 3 H), 1.59 (s, 3 H), 1.65 (s, 3 H), 1.78 (d, J = 1 Hz, 3 H), 1.99−2.05 (m, 2 H), 2.06−2.15 (m, 2 H), 5.07 (tm, J = 7 Hz, 1 H), 5.37 (dq, J = 9, 1 Hz, 1 H), 5.95 (dq, J = 9, 6 Hz, 1 H), 7.44 (ddd, J = 8, 4.5, 1 Hz, 1 H), 7.82 (dt, J = 2, 8 Hz, 1 H), 8.12 (dt, J = 8, 1 Hz, 1 H), 8.77 (ddd, J = 5, 2, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.8 (+), 17.7 (+), 21.0 (+), 25.7 (+), 26.3 (−), 39.5 (−), 70.0 (+), 123.9 (+), 124.4 (+), 125.1 (+), 126.6 (+), 131.7 (−), 136.9 (+), 140.2 (−), 148.8 (−), 149.9 (+), 164.7 (−); HRMS (EI) calcd for $C_{17}H_{23}NO_2$ (M^+) 273.1729, found 273.1733.

(E)-5,9-Dimethyldeca-4,8-dien-3-one. According to the Grignard addition to aldehyde **19**, aldehyde **20** (410.9 mg, 2.70 mmol) in THF (25 mL) was subjected to reaction with EtMgBr (4.80 mL, 0.80 M in THF, 3.84 mmol) at rt for 1 h to furnish racemic alcohol *rac*-**25** (463.0 mg, 94%) as a colorless oil.

According to the oxidation of geraniol, a mixture of alcohol *rac*-**25** (212.1 mg, 1.16 mmol), TPAP (41.0 mg, 0.117 mmol), NMO (260.0 mg, 2.22 mmol), and molecular sieves 4A (598.4 mg) in CH_2Cl_2 (10 + 2 mL) was stirred at rt for 2 h to produce the title ketone (176.8 mg, 84%) as a colorless oil: IR (neat) 1688, 1621, 1122 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, J = 7 Hz, 3 H), 1.61 (s, 3 H), 1.69 (s, 3 H), 2.10−2.22 (m, 4 H), 2.14 (s, 3 H), 2.44 (q, J = 7 Hz, 2 H), 5.02−5.12 (m, 1 H), 6.05 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.2 (+), 17.7 (+), 19.4 (+), 25.7 (+), 26.2 (−), 37.5 (−), 41.3 (−), 123.0 (+), 123.1 (+), 132.5 (−), 157.9 (−), 201.8 (−); HRMS (EI) calcd for $C_{12}H_{20}O$ (M^+) 180.1514, found 180.1510.

(R,E)-5,9-Dimethyldeca-4,8-dien-3-ol (***25***). According to the CBS reduction to afford alcohol **24**, a solution of the above ketone (77.6 mg, 0.426 mmol) in THF (2 mL) was added to a solution of (*S*)-methyloxazaborolidine (0.090 mL, 1.0 M in toluene, 0.090 mmol) and *N*,*N*-diethylaniline borane (0.080 mL, 0.450 mmol) in THF (4 mL) at −40 °C over 60 min, and the solution was allowed to warm to −20 °C over 3 h. Cold MeOH (3 mL) was added at −20 °C, and the solution was stirred at rt for 1 h to furnish alcohol **25** (26.8 mg, 34%) as a colorless oil: IR (neat) 3369, 1454, 1378 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 8 Hz, 3 H), 1.38−1.54 (m, 2 H), 1.60 (s, 3 H), 1.680 (s, 3 H), 1.683, (s, 3 H), 2.02 (t, J = 8 Hz, 2 H), 2.06−2.16 (m, 2 H), 4.28 (dt, J = 8.5, 7 Hz, 1 H), 5.09 (tm, J = 7 Hz, 1 H), 5.16 (dd, J = 8.5, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.8 (+), 16.7 (+), 17.7 (+), 25.7 (+), 26.5 (−), 30.6 (−), 39.7 (−), 70.1 (+), 124.0 (+), 127.9 (+), 131.7 (−), 138.7 (−); HRMS (EI) calcd for $C_{12}H_{22}O$ (M^+) 182.1671, found 182.1671. The ^{1}H and ^{13}C NMR spectra were identical with those reported.[27] The enantiomeric purity of 60% ee was determined by chiral HPLC analysis: Chiralcel OD-H, hexane/*i*-PrOH = 99.8/0.2, 0.700 mL/min, 30 °C, t_R/min =18.8 (*R*-isomer), 19.6 (*S*-isomer).

(R,E)-5,9-Dimethyldeca-4,8-dien-3-yl Picolinate (***10***). According to the preparation of picolinate **6**, alcohol **25** (26.8 mg, 0.147 mmol) was subjected to condensation with picolinic acid (24.2 mg, 0.197 mmol), DCC (40.0 mg, 0.194 mmol), and DMAP (17.8 mg, 0.146 mmol) in CH_2Cl_2 (1 + 1 mL) at rt for 2 h to give picolinate **10** (36.6 mg, 87%) as a colorless oil: $[\alpha]^{26}_D$ −11 (*c* 0.31, $CHCl_3$): IR (neat) 1714, 1438, 1245, 1134, 747, 708 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, J = 7 Hz, 3 H), 1.58 (s, 3 H), 1.65 (s, 3 H), 1.66−1.78 (m, 1 H), 1.80 (d, J = 1 Hz, 3 H), 1.84−1.96 (m, 1 H), 2.00−2.16 (m, 4 H), 5.07 (tm, J = 7 Hz, 1 H), 5.29 (dm, J = 7 Hz, 1 H), 5.76 (dt, J = 9, 7 Hz, 1 H), 7.44 (ddd, J = 7.5, 5, 1 Hz, 1 H), 7.82 (dt, J = 2, 7.5 Hz, 1 H), 8.12 (dt, J = 7.5, 1 Hz, 1 H), 8.77 (ddd, J = 5, 2, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.6 (+), 17.0 (+), 17.7 (+), 25.6 (+), 26.3 (−), 28.0 (−), 39.6 (−), 74.6 (+), 123.1 (+), 123.9 (+), 125.1 (+), 126.5 (+), 131.7 (−), 136.8 (+), 141.3 (−), 148.8 (−), 149.9 (+), 164.7 (−); HRMS (EI) calcd for $C_{18}H_{25}NO_2$ (M^+) 287.1885, found 287.1887.

(Z)-4,8-Dimethylnona-3,7-dien-2-one. According to the Grignard addition to aldehyde **19**, aldehyde **22** (520.0 mg, 3.42 mmol) in THF (25 mL) was subjected to reaction with MeMgBr (5.18 mL, 0.99 M in THF, 5.13 mmol) at rt for 2 h to produce racemic alcohol *rac*-**26** (492.0 mg, 86%) as a colorless oil.

According to the oxidation of geraniol, a mixture of *rac*-**26** (267.5 mg, 1.59 mmol), TPAP (53.4 mg, 0.152 mmol), NMO (381.0 mg, 3.25 mmol), and molecular sieves 4A (800.1 mg) in CH_2Cl_2 (12 + 3 mL) was stirred at rt for 3 h to produce the title ketone (204.8 mg, 77%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 3 H), 1.68 (s, 3 H), 1.87 (d, J = 1 Hz, 3 H), 2.09−2.19 (m, 2 H), 2.15 (s, 3 H), 2.58 (t, J = 7.5 Hz, 2 H), 5.14 (tm, J = 7.5 Hz, 1 H), 6.06 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6 (+), 25.6 (+), 25.7 (+), 26.8 (−), 31.7 (+), 33.8 (−), 123.8 (+), 124.3 (+), 132.2 (−), 158.9 (−), 198.2 (−). The ^{1}H and ^{13}C NMR spectra were identical with those reported.[26]

(R,Z)-4,8-Dimethylnona-3,7-dien-2-ol (***26***). According to the CBS reduction to afford alcohol **24**, a solution of the above ketone (109.2 mg, 0.657 mmol) in THF (4 mL) was mixed with a solution of (*S*)-methyl oxazaborolidine (0.13 mL, 1.0 M in toluene, 0.13 mmol) and *N*,*N*-diethylaniline borane (0.13 mL, 0.731 mmol) in THF (5 mL) at −20 °C over 4 h, and the solution was stirred at −20 °C for 3 h. Cold MeOH (3 mL) was added dropwise at −20 °C, and the solution was stirred at rt for 1 h to furnish alcohol **26** (82.5 mg, 75%) as a colorless oil: $[\alpha]^{20}_D$ +14 (*c* 0.80, $CHCl_3$); IR (neat) 3340 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (d, J = 6 Hz, 3 H), 1.46 (br s, 1 H), 1.61 (s, 3 H), 1.70 (s, 3 H), 1.72 (d, J = 1 Hz, 3 H), 2.02−2.16 (m, 4 H), 4.53 (dq, J = 9, 6 Hz, 1 H), 5.07−5.15 (m, 1 H), 5.23 (dd, J = 9, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7 (+), 23.3 (+), 23.6 (+), 25.7 (+), 26.5 (−), 32.3 (−), 64.3 (+), 124.0 (+), 130.3 (+), 132.5 (−), 137.7 (−). The ^{1}H and ^{13}C NMR spectra were identical with those reported.[26] The enantiomeric purity of 66% ee was determined by chiral HPLC analysis of the corresponding picolinate as described below.

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*(R,Z)-4,8-Dimethylnona-3,7-dien-2-yl Picolinate (**11**).* According to the preparation of picolinate **6**, alcohol **26** (82.5 mg, 0.490 mmol) was subjected to condensation with picolinic acid (82.5 mg, 0.670 mmol), DCC (131.6 mg, 0.638 mmol), and DMAP (56.2 mg, 0.460 mmol) in CH_2Cl_2 (2 + 1 mL) at rt for 2 h to afford **11** (114.5 mg, 85%) as a colorless oil: $[\alpha]^{22}_D$ −76 (*c* 0.53, $CHCl_3$); IR (neat) 1713, 1245, 1127, 747, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (d, *J* = 6 Hz, 3 H), 1.60 (s, 3 H), 1.65 (s, 3 H), 1.75 (d, *J* = 1 Hz, 3 H), 2.00−2.22 (m, 3 H), 2.28−2.39 (m, 1 H), 5.06−5.16 (m, 1 H), 5.39 (d, *J* = 9.5 Hz, 1 H), 5.95 (dq, *J* = 9.5, 6 Hz, 1 H), 7.44 (ddd, *J* = 8, 5, 1 Hz, 1 H), 7.82 (dt, *J* = 2, 8 Hz, 1 H), 8.12 (dt, *J* = 8, 1 Hz, 1 H), 8.76 (ddd, *J* = 5, 2, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6 (+), 21.2 (+), 23.3 (+), 25.7 (+), 26.6 (−), 32.5 (−), 69.6 (+), 123.8 (+), 125.1 (+), 125.2 (+), 126.6 (+), 132.0 (−), 136.8 (+), 140.5 (−), 148.8 (−), 149.9 (+), 164.6 (−); HRMS (EI) calcd for $C_{17}H_{23}NO_2$ (M^+) 273.1729, found 273.1722. The enantiomeric purity of 66% ee was determined by chiral HPLC analysis: Chiralcel OD-H, hexane/*i*-PrOH = 99/1, 0.300 mL/min, 30 °C, t_R/min = 46.4 (*R*-isomer), 53.7 (*S*-isomer).

(Z)-5,9-Dimethyldeca-4,8-dien-3-one. According to the Grignard addition to aldehyde **19**, aldehyde **22** (440.3 mg, 2.89 mmol) in THF (25 mL) was subjected to an addition reaction with EtMgBr (5.10 mL, 0.80 M in THF, 4.08 mmol) at rt for 1 h to furnish racemic alcohol *rac*-**27** (459.8 mg, 87%) as a colorless oil.

According to the oxidation of geraniol, a mixture of *rac*-**27** (206.3 mg, 1.13 mmol), TPAP (36.5 mg, 0.104 mmol), NMO (267.8 mg, 2.29 mmol), and molecular sieves 4A (570.2 mg) in CH_2Cl_2 (9 + 2 mL) was stirred at rt for 3 h to give the title ketone (162.6 mg, 80%) as a colorless oil: IR (neat) 1688, 1621, 1125 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (t, *J* = 7 Hz, 3 H), 1.62 (s, 3 H), 1.67 (d, *J* = 1 Hz, 3 H), 1.87 (d, *J* = 1 Hz, 3 H), 2.07−2.20 (m, 2 H), 2.42 (q, *J* = 7 Hz, 2 H), 2.59 (t, *J* = 7.5 Hz, 2 H), 5.13 (tm, *J* = 7.5 Hz, 1 H), 6.03 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.2 (+), 17.7 (+), 25.6 (+), 25.7 (+), 26.9 (−), 33.9 (−), 37.4 (−), 123.7 (+), 123.9 (+), 132.1 (−), 158.5 (−), 201.2 (−); HRMS (EI) calcd for $C_{12}H_{20}O$ (M^+) 180.1514, found 180.1519.

*(R,Z)-5,9-Dimethyldeca-4,8-dien-3-ol (**27**).* According to the CBS reduction to afford alcohol **24**, a solution of the above ketone (96.3 mg, 0.534 mmol) in THF (3 mL) was added to a solution of (*S*)-methyloxazaborolidine (0.11 mL, 1.0 M in toluene, 0.11 mmol) and *N*,*N*-diethylaniline borane (0.11 mL, 0.619 mmol) in THF (5 mL) at −20 °C over 2 h, and the solution was stirred at −20 °C for 6 h. Cold MeOH (3 mL) was added at −20 °C, and the solution was stirred at rt for 1 h to furnish alcohol **27** (83.9 mg, 88%) as a colorless oil: $[\alpha]^{22}_D$ +3 (*c* 0.68, $CHCl_3$); IR (neat) 3357, 1448, 1002, 959 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, *J* = 8 Hz, 3 H), 1.34−1.66 (m, 3 H), 1.61 (s, 3 H), 1.69 (s, 3 H), 1.73 (d, *J* = 1.5 Hz, 3 H), 2.00−2.20 (m, 4 H), 4.23 (dt, *J* = 9, 7 Hz, 1 H), 5.06−5.14 (m, 1 H), 5.17 (d, *J* = 9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9 (+), 17.7 (+), 23.3 (+), 25.7 (+), 26.6 (−), 30.4 (−), 32.4 (−), 69.5 (+), 124.0 (+), 128.9 (+), 132.4 (−), 138.9 (−); HRMS (EI) calcd for $C_{12}H_{22}O$ (M^+) 182.1671, found 182.1672. The enantiomeric purity of 63% ee was determined by chiral HPLC analysis of the corresponding picolinate as described below.

*(R,Z)-5,9-Dimethyldeca-4,8-dien-3-yl Picolinate (**12**).* According to the preparation of picolinate **6**, alcohol **27** (83.9 mg, 0.460 mmol) was subjected to condensation with picolinic acid (78.8 mg, 0.640 mmol), DCC (139.1 mg, 0.674 mmol), and DMAP (64.8 mg, 0.530 mmol) in CH_2Cl_2 (4 + 1 mL) at rt for 2 h to afford picolinate **12** (112.0 mg, 85%) as a colorless oil: $[\alpha]^{23}_D$ −64 (*c* 0.60, $CHCl_3$); IR (neat) 1714, 1245, 1137, 747, 707 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, *J* = 7 Hz, 3 H), 1.61 (s, 3 H), 1.62−1.78 (m, 1 H), 1.65 (s, 3 H), 1.76 (d, *J* = 1.5 Hz, 3 H), 1.82−1.96 (m, 1 H), 2.00−2.20 (m, 3 H), 2.32−2.42 (m, 1 H), 5.10−5.18 (m, 1 H), 5.32 (d, *J* = 10 Hz, 1 H), 5.79 (dt, *J* = 10, 7 Hz, 1 H), 7.44 (ddd, *J* = 8, 5, 1 Hz, 1 H), 7.81 (dt, *J* = 2, 8 Hz, 1 H), 8.12 (dt, *J* = 8, 1 Hz, 1 H), 8.76 (ddd, *J* = 5, 2, 1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9 (+), 17.6 (+), 23.4 (+), 25.6 (+), 26.6 (−), 28.1 (−), 32.6 (−), 74.2 (+), 123.8 (+), 123.9 (+), 125.1 (+), 126.5 (+), 131.9 (−), 136.8 (+), 141.7 (−), 148.8 (−), 149.9 (+), 164.6 (−). HRMS (EI) calcd for $C_{18}H_{25}NO_2$ (M^+) 287.1885, found 287.1887. The enantiomeric purity of 63% ee was determined by chiral HPLC analysis: Chiralcel OD-H, hexane/*i*-PrOH = 99/1, 0.500 mL/min, 30 °C, t_R/min =28.1 (*R*-isomer), 30.5 (*S*-isomer).

Substitution of Allylic Picolinates. *General Procedure for the Allylation: Synthesis of (E)-(6-Methylhept-4-ene-1,6-diyl)dibenzene (**15**).* (Table 1, entry 6): To an ice-cold suspension of $Cu(acac)_2$ (38.1 mg, 0.146 mmol) in THF (1 mL) was added a solution of PhMgBr (0.36 mL, 0.81 M in THF, 0.292 mmol) slowly. The mixture was stirred at 0 °C for 60 min and cooled to −40 °C before addition of a solution of picolinate **6** (30.0 mg, 0.0970 mmol) in THF (1 mL). The resulting mixture was allowed to warm to −20 °C over 2 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 **15** (25.9 mg, 100%).

(Table 1, entry 7): To an ice-cold suspension of $Cu(acac)_2$ (38.3 mg, 0.146 mmol) and ZnI_2 (46.8 mg, 0.147 mmol) in THF (1 mL) was added PhMgBr (0.56 mL, 0.81 M in THF, 0.454 mmol). After being stirred at 0 °C for 1 h, the mixture was cooled to −40 °C and a solution of picolinate **6** (29.7 mg, 0.0960 mmol) in THF (1 mL) was added. The mixture was allowed to warm to −10 °C over 2 h to afford **15** (22.4 mg, 87%) after purification by chromatography.

(Large-scale reaction): A solution of picolinate **6** (3.10 g, 10.02 mmol) in THF (15 mL) was added to a mixture of $Cu(acac)_2$ (3.93 g, 15.01 mmol) in THF (15 mL) and PhMgBr (32.0 mL, 0.95 M in THF, 30.02 mmol), which had been stirred at 0 °C for 60 min and cooled to −40 °C before the addition. The mixture was allowed to warm to −10 °C over 2 h to afford **15** (2.44 g, 92%) after purification by chromatography on silica gel.

Product **15**: colorless oil; IR (neat) 1495, 1454, 975, 763, 746, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 6 H), 1.72 (quint, *J* = 7 Hz, 2 H), 2.09 (dt, *J* = 7, 7 Hz, 2 H), 2.62 (t, *J* = 8 Hz, 2 H), 5.44 (dt, *J* = 16, 7 Hz, 1 H), 5.64 (d, *J* = 16 Hz, 1 H), 7.13−7.21 (m, 4 H), 7.22−7.32 (m, 4 H), 7.32−7.38 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.0 (+), 31.5 (−), 32.2 (−), 35.5 (−), 40.4 (−), 125.70 (+), 125.73 (+), 126.1 (+), 126.2 (+), 128.1 (+), 128.3 (+), 128.5 (+), 140.6 (+), 142.7 (−), 149.4 (−); HRMS (EI) calcd for $C_{20}H_{24}$ (M^+) 264.1878, found 264.1881.

*(E)-1-Methyl-4-(2-methyl-7-phenylhept-3-en-2-yl)benzene (**29**).* (Table 3, entry 1): According to the general procedure, a solution of **6** (30.0 mg, 0.0970 mmol) in THF (1 mL) was added to a mixture of *p*-MeC_6H_4MgBr (0.34 mL, 0.86 M in THF, 0.292 mmol) and $Cu(acac)_2$ (38.0 mg, 0.146 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −20 °C over 2 h to afford **29** (25.1 mg, 93%) as a colorless oil: IR (neat) 1512, 1454, 975, 817, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 6 H), 1.66−1.76 (m, 2 H), 2.04−2.12 (m, 2 H), 2.31 (s, 3 H), 2.62 (t, *J* = 8 Hz, 2 H), 5.43 (dt, *J* = 16, 7 Hz, 1 H), 5.62 (d, *J* = 16 Hz, 1 H), 7.06−7.13 (m, 2 H), 7.14−7.20 (m, 3 H), 7.21−7.30 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0 (+), 29.1 (+), 31.5 (−), 32.3 (−), 35.5 (−), 40.0 (−), 125.7 (+), 125.9 (+), 126.1 (+), 128.3 (+), 128.6 (+), 128.8 (+), 135.2 (−), 140.8 (+), 142.7 (−), 146.5 (−); HRMS (EI) calcd for $C_{21}H_{26}$ (M^+) 278.2035, found 278.2036.

*(E)-1-Methyl-2-(2-methyl-7-phenylhept-3-en-2-yl)benzene (**30**).* (Table 3, entry 2): According to the general procedure, a solution of **6** (30.1 mg, 0.0973 mmol) in THF (1 mL) was added to a mixture of *o*-MeC_6H_4MgBr (0.33 mL, 0.87 M in THF, 0.287 mmol) and $Cu(acac)_2$ (38.1 mg, 0.146 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −20 °C over 2 h to afford **30** (26.0 mg, 96%) as a colorless oil: IR (neat) 1495, 1454, 975, 760, 728, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 6 H), 1.63−1.73 (m, 2 H), 2.02−2.10 (m, 2 H), 2.39 (s, 3 H), 2.60 (t, *J* = 8 Hz, 2 H), 5.32 (dt, *J* = 16, 7 Hz, 1 H), 5.66 (d, *J* = 16 Hz, 1 H), 7.10−7.20 (m, 5 H), 7.24−7.30 (m, 3 H), 7.35−7.39 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7 (+), 29.4 (+), 31.4 (−), 32.3 (−), 35.6 (−), 41.1 (−), 125.67 (+), 125.73 (+), 126.1 (+), 126.2 (+), 126.3 (+), 128.3 (+), 128.5 (+), 132.4 (+), 137.1 (−), 140.5 (+), 142.7 (−), 146.4 (−); HRMS (EI) calcd for $C_{21}H_{26}$ (M^+) 278.2035, found 278.2037.

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*(E)-1-Methoxy-4-(2-methyl-7-phenylhept-3-en-2-yl)benzene (**31**).* (Table 3, entry 3): According to the general procedure, a solution of **6** (29.5 mg, 0.0953 mmol) in THF (1 mL) was added to a mixture of *p*-$MeOC_6H_4MgBr$ (0.32 mL, 0.93 M in THF, 0.298 mmol) and $Cu(acac)_2$ (37.8 mg, 0.144 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **31** (23.1 mg, 82%) as a colorless oil: IR (neat) 1511, 1250, 1181, 1037, 829, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 6 H), 1.66−1.76 (m, 2 H), 2.04−2.12 (m, 2 H), 2.62 (t, J = 8 Hz, 2 H), 3.78 (s, 3 H), 5.41 (dt, J = 16, 7 Hz, 1 H), 5.62 (d, J = 16 Hz, 1 H), 6.83 (dm, J = 9 Hz, 2 H), 7.14−7.20 (m, 3 H), 7.22−7.30 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.2 (+), 31.5 (−), 32.2 (−), 35.5 (−), 39.8 (−), 55.3 (+), 113.4 (+), 125.7 (+), 125.9 (+), 127.2 (+), 128.3 (+), 128.5 (+), 140.9 (+), 141.6 (−), 142.7 (−), 157.6 (−); HRMS (EI) calcd for $C_{21}H_{26}O$ (M^+) 294.1984, found 294.1986.

*(E)-1-Methoxy-2-(2-methyl-7-phenylhept-3-en-2-yl)benzene (**32**).* (Table 3, entry 4): According to the general procedure, a solution of **6** (30.4 mg, 0.0983 mmol) in THF (1 mL) was added to a mixture of *o*-$MeOC_6H_4MgBr$ (0.33 mL, 0.89 M in THF, 0.294 mmol) and $Cu(acac)_2$ (38.0 mg, 0.145 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −20 °C over 2 h to afford **32** (18.8 mg, 65%) as a colorless oil: IR (neat) 1490, 1455, 1241, 1031, 750, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 6 H), 1.63−1.74 (m, 2 H), 2.02−2.11 (m, 2 H), 2.61 (t, J = 8 Hz, 2 H), 3.78 (s, 3 H), 5.32 (dt, J = 15.5, 7 Hz, 1 H), 5.78 (dt, J = 15.5, 2 Hz, 1 H), 6.83−6.92 (m, 2 H), 7.12−7.22 (m, 4 H), 7.22−7.30 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9 (+), 31.6 (−), 32.3 (−), 35.4 (−), 39.9 (−), 55.1 (+), 111.8 (+), 120.3 (+), 125.2 (+), 125.7 (+), 127.2 (+), 127.3 (+), 128.3 (+), 128.6 (+), 137.2 (−), 140.4 (+), 142.9 (−), 158.3 (−); HRMS (EI) calcd for $C_{21}H_{26}O$ (M^+) 294.1984, found 294.1983.

*(E)-1-Fluoro-4-(2-methyl-7-phenylhept-3-en-2-yl)benzene (**33**).* (Table 3, entry 5): According to the general procedure, a solution of **6** (29.8 mg, 0.0963 mmol) in THF (1 mL) was added to a mixture of *p*-FC_6H_4MgBr (0.32 mL, 0.92 M in THF, 0.294 mmol) and $Cu(acac)_2$ (38.4 mg, 0.147 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **33** (22.8 mg, 84%) as a colorless oil: IR (neat) 1508, 1230, 1163, 976, 834, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 6 H), 1.66−1.77 (m, 2 H), 2.03−2.13 (m, 2 H), 2.62 (t, J = 8 Hz, 2 H), 5.42 (dt, J = 16, 7 Hz, 1 H), 5.60 (dt, J = 16, 1 Hz, 1 H), 6.91−7.00 (m, 2 H), 7.14−7.21 (m, 3 H), 7.23−7.32 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.2 (+), 31.5 (−), 32.2 (−), 35.5 (−), 40.0 (−), 114.7 (d, J = 21 Hz) (+), 125.8 (+), 126.4 (+), 127.7 (d, J = 8 Hz) (+), 128.4 (+), 128.5 (+), 140.4 (+), 142.6 (−), 145.1 (d, J = 3 Hz) (−), 161.1 (d, J = 242 Hz) (−); HRMS (EI) calcd for $C_{20}H_{23}F$ (M^+) 282.1784, found 282.1792.

*(E)-(6,10-Dimethylundeca-4,9-diene-1,6-diyl)dibenzene (**34**).* (Table 3, entry 6): According to the general procedure, a solution of **7** (38.4 mg, 0.102 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.31 mL, 1.02 M in THF, 0.316 mmol) and $Cu(acac)_2$ (39.6 mg, 0.151 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **34** (32.1 mg, 95%).

(Table 3, entry 7): According to the general procedure, a solution of **8** (37.1 mg, 0.0983 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.29 mL, 1.02 M in THF, 0.296 mmol) and $Cu(acac)_2$ (38.9 mg, 0.149 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **34** (28.9 mg, 88%).

Product **34**: a colorless oil; IR (neat) 1495, 1453, 1445, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 3 H), 1.50 (s, 3 H), 1.65 (s, 3 H), 1.60−1.90 (m, 6 H), 2.10 (dt, J = 8, 8 Hz, 2 H), 2.62 (t, J = 8 Hz, 2 H), 5.02−5.12 (m, 1 H), 5.42 (dt, J = 16, 7 Hz, 1 H), 5.63 (dt, J = 16, 1 Hz, 1 H), 7.10−7.20 (m, 4 H), 7.20−7.33 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.8 (+), 23.6 (−), 25.8 (+), 25.9 (+), 31.6 (−), 32.5 (−), 35.6 (−), 41.8 (−), 43.6 (−), 124.8 (+), 125.56 (+), 125.64 (+), 126.6 (+), 127.1 (+), 128.0 (+), 128.2 (+), 128.4 (+), 131.2 (−), 139.3 (+), 142.5 (−), 148.2 (−); HRMS (FAB) calcd for $C_{25}H_{32}Na$ [$(M + Na)^+$] 355.2402, found 355.2393.

*(E)-1-(2,6-Dimethyl-11-phenylundeca-2,7-dien-6-yl)-4-fluorobenzene (**35**).* (Table 3, entry 8): According to the general procedure, a solution of **7** and **8** (3:2) (37.8 mg, 0.100 mmol) in THF (1 mL) was added to a mixture of *p*-FC_6H_4MgBr (0.33 mL, 0.92 M in THF, 0.304 mmol) and $Cu(acac)_2$ (39.4 mg, 0.151 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **35** (28.2 mg, 80%) as a colorless oil: IR (neat) 1603, 1508, 1232, 834, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 3 H), 1.50 (s, 3 H), 1.65 (s, 3 H), 1.60−1.90 (m, 6 H), 2.10 (dt, J = 8, 8 Hz, 2 H), 2.62 (t, J = 8 Hz, 2 H), 5.03−5.10 (m, 1 H), 5.42 (dt, J = 16, 7 Hz, 1 H), 5.61 (dt, J = 16, 1 Hz, 1 H), 6.91−7.00 (m, 2 H), 7.14−7.21 (m, 3 H), 7.22−7.31 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6 (+), 23.4 (−), 25.8 (+), 25.9 (+), 31.5 (−), 32.4 (−), 35.5 (−), 41.9 (−), 43.2 (−), 114.7 (d, J = 21 Hz) (+), 124.7 (+), 125.8 (+), 127.4 (+), 128.2 (d, J = 8 Hz) (+), 128.4 (+), 128.5 (+), 131.4 (−), 139.3 (+), 142.6 (−), 144.0 (d, J = 3 Hz) (−), 161.1 (d, J = 242 Hz) (−); HRMS (FAB) calcd for $C_{25}H_{31}F$ [$(M)^+$] 350.2410, found 350.2410.

*(R,E)-tert-Butyl((5-((4-methoxybenzyl)oxy)-4-methyl-4-phenylpent-2-en-1-yl)oxy)dimethylsilane (**2**).* (Table 4, entry 2): According to the general procedure, a solution of **1** (98% ee, 30.5 mg, 0.0647 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.38 mL, 1.00 M in THF, 0.38 mmol) and $Cu(acac)_2$ (50.1 mg, 0.191 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to 0 °C over 2 h to afford **2** (23.6 mg, 86%) as a colorless oil: $[\alpha]^{25}_D$ +2.5 (c 0.16, $CHCl_3$) (cf. $[\alpha]^{30}_D$ +1.5 (c 0.40, $CHCl_3$) for the *R* enantiomer of 98% ee);[5] ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6 H), 0.90 (s, 9 H), 1.43 (s, 3 H), 3.55 (d, J = 9 Hz, 1 H), 3.60 (d, J = 9 Hz, 1 H), 3.80 (s, 3 H), 4.20 (dd, J = 5, 1.5 Hz, 2 H), 4.42 (s, 2 H), 5.55 (dt, J = 16, 5 Hz, 1 H), 5.91 (dt, J = 16, 1.5 Hz, 1 H), 6.84 (d, J = 8 Hz, 2 H), 7.14−7.21 (m, 2 H), 7.24−7.35 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0 (+), 18.5 (−), 23.8 (+), 26.1 (+), 44.9 (−), 55.3 (+), 64.3 (−), 73.0 (−), 77.6 (−), 113.7 (+), 126.1 (+), 127.1 (+), 128.07 (+), 128.12 (+), 129.1 (+), 130.7 (−), 136.7 (+), 145.8 (−), 159.1 (−). The ^1H NMR and ^{13}C NMR spectra were consistent with data reported in the literature.[5] The enantiomeric purity of 97% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99/1, 0.300 mL/min, 30 °C, t_R/min = 24.9 (*S*-isomer), 33.6 (*R*-isomer).

*(E)-tert-Butyl((5-((4-methoxybenzyl)oxy)-4-methyl-2-phenylpent-3-en-1-yl)oxy)dimethylsilane (Regioisomer **3**).* To an ice-cold suspension of CuBr·Me_2S (19.8 mg, 0.0963 mmol) in THF (1 mL) was added a solution of PhMgBr (0.25 mL, 0.90 M in THF, 0.225 mmol) slowly. The mixture was stirred at 0 °C for 30 min, and a solution of picolinate **1** (30.1 mg, 0.0638 mmol) in THF (1 mL) was added. The mixture was stirred at 0 °C for 2 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 the regioisomer **3** and **2** in a 91:9 ratio (11.3 mg, 42%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ −0.07 (s, 3 H), −0.06 (s, 3 H), 0.82 (s, 9 H), 1.69 (s, 3 H), 3.70−3.82 (m, 3 H), 3.80 (s, 3 H), 3.91 (s, 2 H), 4.37 (s, 2 H), 5.69 (d, J = 7 Hz, 1 H), 6.86 (d, J = 8.5 Hz, 2 H), 7.14−7.35 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.4 (+), 14.5 (+), 18.4 (−), 25.9 (+), 47.1 (+), 55.3 (+), 67.9 (−), 71.0 (−), 75.8 (−), 113.8 (+), 126.3 (+), 128.1 (+), 128.3 (+), 128.5 (+), 129.4 (+), 130.7 (−), 134.1 (−), 142.7 (−), 159.2 (−).

*(R,E)-tert-Butyl((5-((4-methoxybenzyl)oxy)-4-methyl-4-(4-methylphenyl)pent-2-en-1- yl)oxy)dimethylsilane (**36**).* (Table 4, entry 3): According to the general procedure, a solution of **1** (98% ee, 34.9 mg, 0.0740 mmol) in THF (1 mL) was added to a mixture of *p*-MeC_6H_4MgBr (0.48 mL, 0.93 M in THF, 0.446 mmol) and $Cu(acac)_2$ (58.4 mg, 0.223 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to 0 °C over 2 h to afford **36** (30.2 mg, 93%) as a colorless oil: $[\alpha]^{22}_D$ +1.9 (c 0.16, $CHCl_3$); IR (neat) 1513, 1249, 1098, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6 H), 0.90 (s, 9 H), 1.41 (s, 3 H), 2.31 (s, 3 H), 3.52 (d, J = 9 Hz, 1 H), 3.58 (d, J = 9 Hz, 1 H), 3.80 (s, 3 H), 4.19 (dd, J = 5, 1 Hz, 2 H), 4.42 (s, 2 H), 5.54 (dt, J = 16, 5 Hz, 1 H), 5.90 (d, J = 16 Hz, 1 H), 6.84 (d, J = 8 Hz, 2 H), 7.06−7.12 (m, 2 H), 7.15−7.27 (m, 4 H); ^{13}C NMR

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(100 MHz, $CDCl_3$) δ −5.0 (+), 18.5 (−), 21.0 (+), 23.8 (+), 26.1 (+), 44.6 (−), 55.3 (+), 64.4 (−), 73.0 (−), 77.7 (−), 113.7 (+), 126.9 (+), 128.0 (+), 128.8 (+), 129.1 (+), 130.8 (−), 135.6 (−), 136.9 (+), 142.8 (−), 159.1 (−); HRMS (FAB) calcd for $C_{27}H_{39}O_3Si$ [$(M - H)^+$] 439.2668, found 439.2669. The enantiomeric purity of 97% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99.8/0.8, 0.300 mL/min, 30 °C, t_R/min = 30.5 (*S*-isomer), 40.1 (*R*-isomer).

*(R,E)-tert-Butyl((5-((4-methoxybenzyl)oxy)-4-methyl-4-(2-methylphenyl)pent-2-en-1-yl)oxy)dimethylsilane (**37**).* (Table 4, entry 4): According to the general procedure, a solution of **1** (98% ee, 34.8 mg, 0.0738 mmol) in THF (1 mL) was added to a mixture of *o*-MeC_6H_4MgBr (0.52 mL, 0.85 M in THF, 0.442 mmol) and $Cu(acac)_2$ (58.2 mg, 0.222 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **37** (30.9 mg, 95%) as a colorless oil: $[\alpha]^{22}_D$ −7 (*c* 0.52, $CHCl_3$); IR (neat) 1613, 1513, 1463, 1250, 1097, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 6 H), 0.90 (s, 9 H), 1.49 (s, 3 H), 2.31 (s, 3 H), 3.59 (d, *J* = 9 Hz, 1 H), 3.63 (d, *J* = 9 Hz, 1 H), 3.80 (s, 3 H), 4.14 (dd, *J* = 5, 1.5 Hz, 2 H), 4.45 (s, 2 H), 5.38 (dt, *J* = 16, 6 Hz, 1 H), 5.94 (dt, *J* = 16, 1.5 Hz, 1 H), 6.85 (dm, *J* = 9 Hz, 2 H), 7.06−7.16 (m, 3 H), 7.20 (dm, *J* = 9 Hz, 2 H), 7.34−7.40 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0 (+), 18.5 (−), 22.9 (+), 24.5 (+), 26.0 (+), 45.7 (−), 55.3 (+), 64.2 (−), 73.0 (−), 77.2 (−), 113.7 (+), 125.6 (+), 126.4 (+), 127.6 (+), 128.0 (+), 129.2 (+), 130.7 (−), 132.4 (+), 136.9 (+), 137.1 (−), 143.3 (−), 159.1 (−); HRMS (FAB) calcd for $C_{27}H_{39}O_3Si$ [$(M - H)^+$] 439.2668, found 439.2669. The enantiomeric purity of 98% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99.5/0.5, 0.300 mL/min, 30 °C, t_R/min = 35.4 (*S*-isomer), 40.0 (*R*-isomer).

*(R,E)-tert-Butyl((5-((4-methoxybenzyl)oxy)-4-(4-methoxyphenyl)-4-methylpent-2-en-1-yl)oxy)dimethylsilane (**38**).* (Table 4, entry 5): According to the general procedure, a solution of **1** (98% ee, 47.2 mg, 0.100 mmol) in THF (1 mL) was added to a mixture of *p*-$MeOC_6H_4MgBr$ (0.64 mL, 0.93 M in THF, 0.595 mmol) and $Cu(acac)_2$ (78.2 mg, 0.299 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **38** (43.1 mg, 94%) as a colorless oil: $[\alpha]^{21}_D$ −1 (*c* 0.79, $CHCl_3$); IR (neat) 1513, 1249, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6 H), 0.90 (s, 9 H), 1.41 (s, 3 H), 3.51 (d, *J* = 9 Hz, 1 H), 3.56 (d, *J* = 9 Hz, 1 H), 3.79 (s, 3 H), 3.80 (s, 3 H), 4.19 (dd, *J* = 5, 2 Hz, 2 H), 4.42 (s, 2 H), 5.53 (dt, *J* = 16, 5 Hz, 1 H), 5.88 (dt, *J* = 16, 2 Hz, 1 H), 6.80−6.87 (m, 4 H), 7.15−7.21 (m, 2 H), 7.21−7.27 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0 (+), 18.5 (−), 23.9 (+), 26.1 (+), 44.3 (−), 55.3 (+), 64.3 (−), 73.0 (−), 77.7 (−), 113.4 (+), 113.7 (+), 127.9 (+), 128.1 (+), 129.1 (+), 130.8 (−), 137.0 (+), 137.9 (−), 157.9 (−), 159.1 (−); HRMS (FAB) calcd for $C_{27}H_{40}O_4SiNa$ [$(M + Na)^+$] 479.2594, found 479.2613. The enantiomeric purity of 97% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99/1, 0.500 mL/min, 30 °C, t_R/min = 35.6 (*S*-isomer), 46.3 (*R*-isomer).

*(R,E)-tert-Butyl((4-(4-fluorophenyl)-5-((4-methoxybenzyl)oxy)-4-methylpent-2-en-1-yl)oxy)dimethylsilane (**39**).* (Table 4, entry 6): According to the general procedure, a solution of **1** (98% ee, 48.4 mg, 0.103 mmol) in THF (1 mL) was added to a mixture of *p*-FC_6H_4MgBr (0.65 mL, 0.92 M in THF, 0.598 mmol) and $Cu(acac)_2$ (77.9 mg, 0.298 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to 0 °C over 2 h to afford **39** (45.6 mg, >99%) as a colorless oil: $[\alpha]^{21}_D$ −2.7 (*c* 0.33, $CHCl_3$); IR (neat) 1510, 1249, 1097, 835, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 6 H), 0.90 (s, 9 H), 1.41 (s, 3 H), 3.52 (d, *J* = 9 Hz, 1 H), 3.55 (d, *J* = 9 Hz, 1 H), 3.80 (s, 3 H), 4.19 (dd, *J* = 5, 2 Hz, 2 H), 4.42 (s, 2 H), 5.53 (dt, *J* = 16, 5 Hz, 1 H), 5.88 (dt, *J* = 16, 2 Hz, 1 H), 6.84 (d, *J* = 8.5 Hz, 2 H), 6.91−7.00 (m, 2 H), 7.16 (d, *J* = 8.5 Hz, 2 H), 7.24−7.31 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0 (+), 18.5 (−), 24.0 (+), 26.1 (+), 44.5 (−), 55.3 (+), 64.2 (−), 73.0 (−), 77.5 (−), 113.7 (+), 114.7 (d, *J* = 21 Hz), 128.3 (+), 128.7 (d, *J* = 8 Hz), 129.1 (+), 130.5 (−), 136.4 (+), 141.4 (d, *J* = 3 Hz), 159.1 (−), 161.3 (d, *J* = 243 Hz); HRMS (FAB) calcd for $C_{26}H_{36}FO_3Si$ [$(M - H)^+$] 443.2418, found 443.2406. The enantiomeric purity of >97% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99/1, 0.300 mL/min, 30 °C, t_R/min = 26.7 (*S*-isomer), 33.6 (*R*-isomer).

*(R,E)-(4,8-Dimethylnona-2,7-dien-4-yl)benzene (**40**).* (Table 4, entry 7): According to the general procedure, a solution of **9** (82% ee, 31.5 mg, 0.115 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.34 mL, 1.01 M in THF, 0.343 mmol) and $Cu(acac)_2$ (45.0 mg, 0.172 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **40** (22.3 mg, 85%) as a colorless oil: $[\alpha]^{24}_D$ +3 (*c* 0.75, $CHCl_3$); IR (neat) 1445, 973, 762, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 3 H), 1.51 (s, 3 H), 1.62−1.90 (m, 4 H), 1.65 (s, 3 H), 1.72 (dd, *J* = 6, 1.5 Hz, 3 H), 5.04−5.12 (m, 1 H), 5.43 (dq, *J* = 16, 6 Hz, 1 H), 5.65 (dq, *J* = 16, 1.5 Hz, 1 H), 7.13−7.19 (m, 1 H), 7.24−7.34 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6 (+), 18.3 (+), 23.5 (−), 25.6 (+), 25.8 (+), 41.9 (−), 43.6 (−), 122.1 (+), 125.0 (+), 125.6 (+), 126.7 (+), 128.0 (+), 131.3 (−), 140.1 (+), 148.5 (−); HRMS (EI) calcd for $C_{17}H_{24}$ (M^+) 228.1878, found 228.1873. The enantiomeric purity of 81% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99.8/0.2, 0.300 mL/min, 30 °C, t_R/min =17.8 (*S*-isomer), 18.9 (*R*-isomer).

*(R,E)-(5,9-Dimethyldeca-3,8-dien-5-yl)benzene (**41**).* (Table 4, entry 8) According to the general procedure, a solution of **10** (60% ee, 23.3 mg, 0.0811 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.24 mL, 1.01 M in THF, 0.242 mmol) and $Cu(acac)_2$ (31.6 mg, 0.121 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford **41** (17.7 mg, 90%) as a colorless oil: $[\alpha]^{24}_D$ +4 (*c* 0.22, $CHCl_3$); IR (neat) 1445, 977, 763, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, *J* = 7.5 Hz, 3 H), 1.35 (s, 3 H), 1.51 (s, 3 H), 1.62−1.92 (m, 4 H), 1.65 (s, 3 H), 2.02−2.14 (m, 2 H), 5.02−5.12 (m, 1 H), 5.45 (dt, *J* = 16, 6 Hz, 1 H), 5.60 (dt, *J* = 16, 1 Hz, 1 H), 7.10−7.18 (m, 1 H), 7.22−7.34 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2 (+), 17.6 (+), 23.5 (−), 25.7 (+), 25.8 (+), 26.0 (−), 41.9 (−), 43.4 (−), 125.0 (+), 125.6 (+), 126.7 (+), 128.0 (+), 129.3 (+), 131.2 (−), 137.8 (+), 148.6 (−); HRMS (EI) calcd for $C_{18}H_{26}$ (M^+) 242.2035, found 242.2033. The enantiomeric purity of 59% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99.8/0.2, 0.300 mL/min, 30 °C, t_R/min = 21.3 (*S*-isomer), 22.6 (*R*-isomer).

*(S,E)-(4,8-Dimethylnona-2,7-dien-4-yl)benzene (ent-**40**).* (Table 4, entry 9): According to the general procedure, a solution of **11** (66% ee, 29.5 mg, 0.108 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.33 mL, 1.01 M in THF, 0.333 mmol) and $Cu(acac)_2$ (42.7 mg, 0.163 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford *ent*-**40** (21.6 mg, 88%) as a colorless oil: $[\alpha]^{23}_D$ −2 (*c* 0.76, $CHCl_3$). The ^1H and ^{13}C NMR spectra were identical with those for **40**. The enantiomeric purity of 66% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99.8/0.2, 0.300 mL/min, 30 °C, t_R/min = 19.3 (*S*-isomer), 20.8 (*R*-isomer).

*(S,E)-(5,9-Dimethyldeca-3,8-dien-5-yl)benzene (ent-**41**).* (Table 4, entry 10): According to the general procedure, a solution of **12** (63% ee, 29.9 mg, 0.104 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.31 mL, 1.01 M in THF, 0.313 mmol) and $Cu(acac)_2$ (41.2 mg, 0.157 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford *ent*-**41** (20.7 mg, 82%) as a colorless oil: $[\alpha]^{23}_D$ −3 (*c* 0.27, $CHCl_3$). The ^1H and ^{13}C NMR spectra were identical with those for **41**. The enantiomeric purity of 62% ee was determined by chiral HPLC analysis: Chiralcel OJ-H, hexane/*i*-PrOH = 99.8/0.2, 0.300 mL/min, 30 °C, t_R/min = 29.4 (*S*-isomer), 31.2 (*R*-isomer).

*1-Ethyl-1-phenyl-2-cyclohexene (**43**).* Phenylation with 2:1 PhMgBr/$Cu(acac)_2$: A solution of **13** (24.6 mg, 0.106 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.35 mL, 0.98 M in THF, 0.343 mmol) and $Cu(acac)_2$ (42.3 mg, 0.162 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford a mixture of **43** and **44** in a 82:18 ratio (14.4 mg, 73%).

Phenylation with 3:1:1 PhMgBr/$Cu(acac)_2$/ZnI_2: To an ice-cold suspension of $Cu(acac)_2$ (42.5 mg, 0.162 mmol) and ZnI_2 (51.0 mg, 0.160 mmol) in THF (1 mL) was added PhMgBr (0.63 mL, 0.77 M in

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THF, 0.485 mmol). After being stirred at 0 °C for 1 h, the mixture was cooled to −40 °C, and a solution of picolinate **13** (25.3 mg, 0.109 mmol) in THF (1 mL) was added. The mixture was allowed to warm to −10 °C over 2 h to afford a mixture of **43** and **44** in a 87:13 ratio (16.5 mg, 81%).

Product **43**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73 (t, J = 7.5 Hz, 3 H), 1.45−2.08 (m, 8 H), 5.85 (dm, J = 10 Hz, 1 H), 5.90 (dt, J = 10, 3 Hz, 1 H), 7.13−7.23 (m, 2 H), 7.24−7.34 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.7 (+), 19.0 (−), 25.6 (−), 35.1 (−), 36.7 (−), 43.1 (−), 125.4 (+), 127.3 (+), 127.93 (+), 127.95 (+), 132.9 (+), 148.3 (−). The ^{1}H NMR spectrum was consistent with data reported in the literature.[4b]

*1,4-Diphenyl-1-vinylcyclohexane (**45**).* Phenylation with 2:1 PhMgBr/$Cu(acac)_2$: A solution of **14**[7] (29.6 mg, 0.0963 mmol) in THF (1 mL) was added to a mixture of PhMgBr (0.26 mL, 1.14 M in THF, 0.296 mmol) and $Cu(acac)_2$ (39.0 mg, 0.149 mmol) in THF (1 mL) at −40 °C, and the mixture was allowed to warm to −10 °C over 2 h to afford a mixture of **45** and **46** in a 81:19 ratio (19.4 mg, 77%).

Phenylation with 3:1:1 PhMgBr/$Cu(acac)_2$/ZnI_2: To an ice-cold suspension of $Cu(acac)_2$ (38.0 mg, 0.145 mmol) and ZnI_2 (46.4 mg, 0.145 mmol) in THF (1 mL) was added PhMgBr (0.49 mL, 0.85 M in THF, 0.417 mmol). After being stirred at 0 °C for 1 h, the mixture was cooled to −40 °C and a solution of picolinate **14** (29.5 mg, 0.0960 mmol) in THF (1 mL) was added. The mixture was allowed to warm to −10 °C over 2 h to afford a mixture of **45** and **46** in a 87:13 ratio (18.4 mg, 73%).

Product **45**: amorphous solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80−1.96 (m, 6 H), 2.28 (dm, J = 10 Hz, 2 H), 2.50−2.64 (m, 1 H), 5.16 (dd, J = 18, 1 Hz, 1 H), 5.33 (dd, J = 11, 1 Hz, 1 H), 5.88 (dd, J = 18, 11 Hz, 1 H), 7.16−7.26 (m, 4 H), 7.27−7.35 (m, 4 H) 7.39−7.44 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5 (−), 36.4 (−), 44.0 (−), 44.3 (+), 115.1 (−), 125.9 (+), 126.0 (+), 126.2 (+), 127.0 (+), 128.2 (+), 128.4 (+), 144.6 (+), 147.5 (−), 149.3 (−); HRMS (FAB) calcd for $C_{20}H_{22}$ (M^+) 262.1722, found 262.1720.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of all compounds prepared. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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