DOI: 10.1002/ejoc.201300792

Installation of a Chiral Side Chain to a 2-Alkylidene-1-cycloalkan-1-ol Unit by Using Allylic Substitution

Chao Feng[a] and Yuichi Kobayashi*[a]

Keywords: Synthetic methods / Allylic compounds / Nucleophilic substitution / Copper / Magnesium / Regioselectivity

The allylic substitution of optically active exocyclic allylic esters of cyclopentane and cyclohexane with ArMgBr-based copper reagents (Ar = aryl) was examined. ArMgBr/$Cu(acac)_2$ in a 2:1 ratio was an adequate reagent to produce the *anti*-S_N2' products efficiently in terms of regioselectivity (95–99 %), chirality transfer (91–99 %), and yield (71–91 %). The Ar groups that were successfully installed include Ph and *p*-tolyl, those with electron-donating (i.e., *p*-$MeOC_6H_4$) and electron-withdrawing groups (i.e., *p*-FC_6H_4), and those with sterically demanding groups (i.e., *o*-tolyl, *o*-$MeOC_6H_4$). In an examination of an alkyl reagent, BuMgBr/CuBr·Me_2S in a 2:1 ratio in the presence of ZnI_2 afforded the product with high regioselectivity (99 %) and in good yield (91 %).

Introduction

The allylic substitution of secondary allylic esters with organocopper reagents that are prepared in situ or generated under catalytic conditions has recently been actively investigated with highly activated leaving groups[1] such as *o*-$(PPh_2)C_6H_4CO_2$, *o*-$[P(O)Ph_2]C_6H_4CO_2$, $C_6F_5CO_2$, $(RO)_2PO_2$, and 2-$PyCO_2$ (Py = pyridine). By employing these leaving groups, alkyl copper reagents as well as less reactive aryl, alkenyl, heteroaryl, and alkynyl reagents can take part in substitution reactions that furnish γ products with high regio- and stereoselectivity.[2,3] The 2-$PyCO_2$ leaving group that we introduced was activated by Mg^{2+} and/or Zn^{2+} to allow for the participation of the above classes of reagents.[3] Furthermore, ArMgBr-based copper reagents could be used for the efficient construction of a quaternary carbon.[4]

During the investigation, we learned that acyclic and cyclic allylic esters of types **I** and **II** as shown in Figure 1 have been used as test substrates and that exocyclic allylic esters **III** that are part cyclic and acyclic have been studied in a few cases. In brief, the methylation of 2-butylidene-1-cyclopentyl alcohol derivatives **III** [(*Z*) olefin, *n* = 1, R = Pr, L = OCO-*t*Bu, OCONHPh] afforded the desired γ product regioselectively.[5] However, the scope of the reagents that includes aromatic compounds is unclear.[6] In contrast, the CuCl-catalyzed substitution of 2-benzylidene-1-cycloalkyl acetates **III** [(*E*) olefin, *n* = 1, 2, R = Ph, L = OAc) with alkyl- and arylMgBr gave α products with 65–100% regioselectivity, which depended on the ring size of the substrates and the reagents.[7] With these publications in mind, we selected picolinates **1** with *n* = 1, 2 as in **III** and studied their allylic substitution with aryl copper reagents as depicted in Scheme 1 as well as with an alkyl copper reagent. The structure of the γ product **2** evokes several biologically

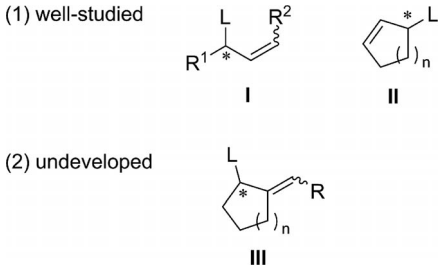
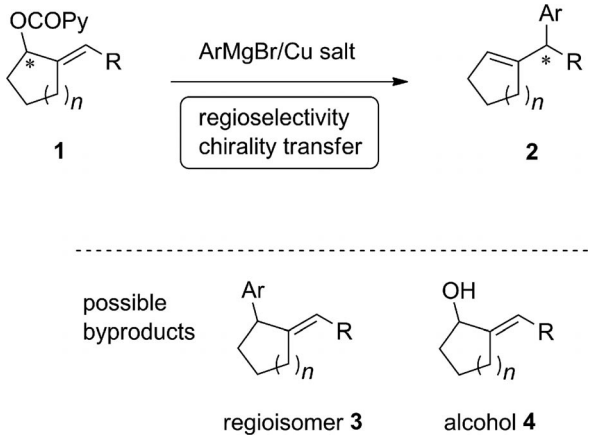


Figure 1. Substrate types for the allylic substitution (L = leaving group).



Scheme 1. Goal of the present allylic substitution reaction.

[a] Department of Bioengineering, Tokyo Institute of Technology, Box B52, Nagatsuta-cho 4259, Midori-ku, Yokohama 226-8501, Japan
E-mail: ykobayas@bio.titech.ac.jp
Homepage: http://www.kobayashi.bio.titech.ac.jp

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201300792.

active compounds such as classical steroids, vitamin D compounds, the OSW-1 series of compounds, ophiobolins, biyouyanagin A, zingiberene, and the heliannuols (see Figure 2), which are characterized by chiral side chains. Herein, we present the results of this investigation, which focuses on regioselectivity (**2** over **3**) and chirality transfer (C.T.).[8,9]

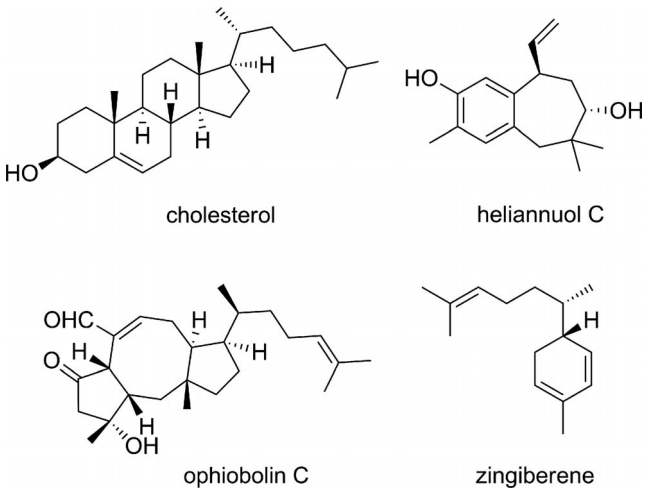


Figure 2. Natural products that possess a chiral carbon on a side chain.

Results and Discussion

The allylic substrates shown in Figure 3 were synthesized by methods delineated in Scheme 2. In brief, the aldol reaction of cyclopentanone and 3-phenylpropionaldehyde followed by elimination of the hydroxy group with MsCl and Et_3N produced (*E*)-olefin **5a** in a 40% unoptimized yield. The examination of the ^1H NMR spectrum of crude **5a** indicated the absence of the (*Z*) isomer [olefinic H of **5a**, multiplet, 6.50–6.63 ppm; olefinic H of (*Z*) isomer, probably 5.6–6.0 ppm[10]]. A Corey–Bakshi–Shibata (CBS) reduction[11] using (*S*)-3,3-diphenyl-1-methylpyrrolidino[1,2-*c*]-1,3,2-oxazaborole [(*S*)-MeCBS] was applied to the enone, and the resulting alcohol (*R*)-**4a** was converted into picolinate (*R*)-**1a** in 72% yield by employing a DCC-mediated (DCC = *N*,*N*′-dicyclohexylcarbodiimide) condensation with

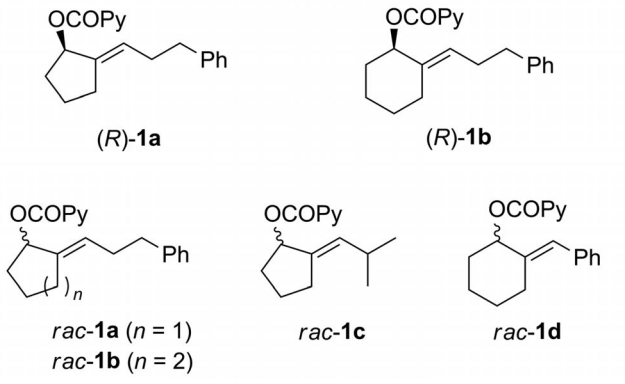
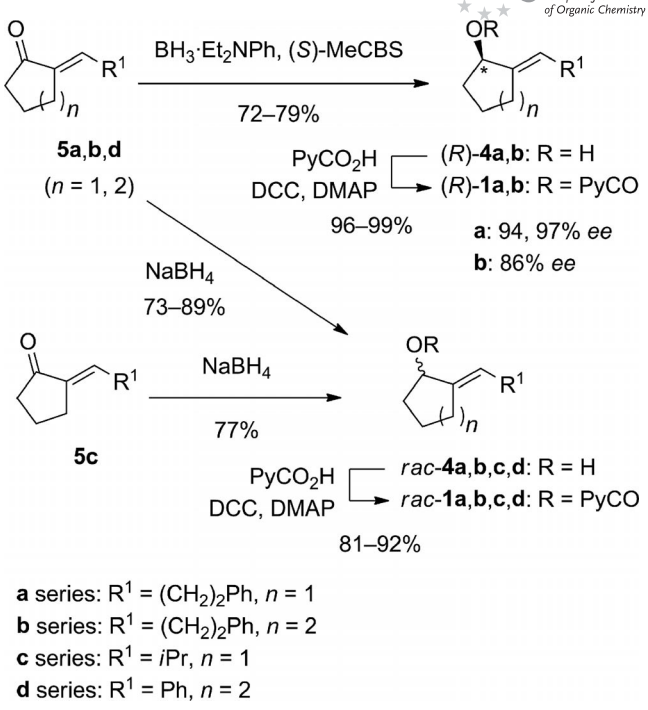
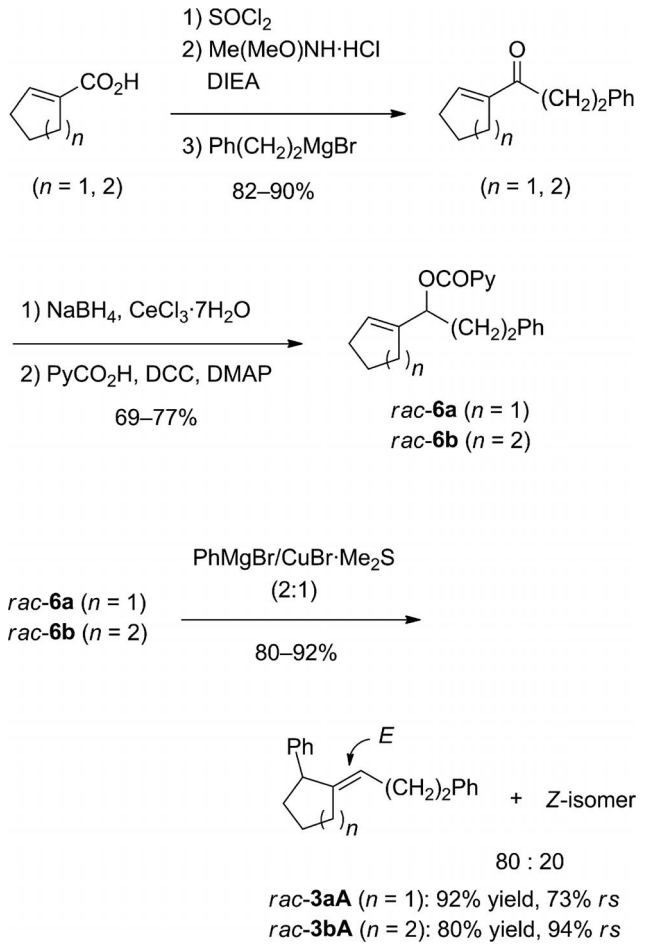


Figure 3. Substrates for the present study.



Scheme 2. Synthesis of the substrates [DMAP = 4-(dimethylamino)pyridine].

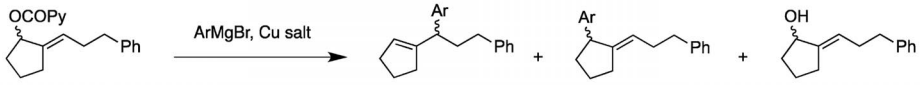
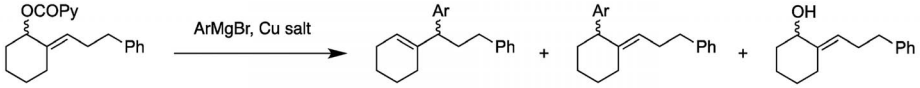
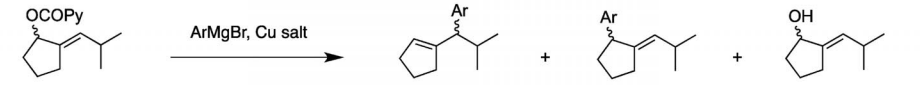
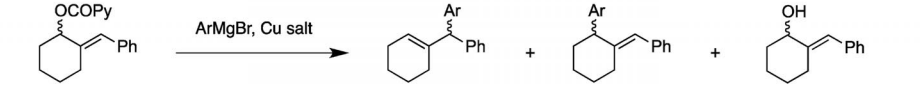


Scheme 3. Synthesis of regioisomers (DIEA = *N*,*N*-diisopropylethylamine, *rs* = regioselectivity).

$PyCO_2H$. The enantiomeric purity of (*R*)-**1a**, which was prepared twice, was 94 and 97%*ee* as determined by chiral HPLC analysis. Likewise, picolinate (*R*)-**1b** with 86%*ee* was synthesized from cyclohexanone through enone **5b**.[12] For a preliminary investigation, racemic picolinates *rac*-**1a** and -**1b** were synthesized in yields of 73–80% from enones **5a** and **5b** by reduction with $NaBH_4$ followed by a DCC-assisted esterification with $PyCO_2H$. Similarly, enone **5c** was prepared through an aldol condensation of cyclopentanone with isobutyraldehyde followed by conversion into racemic picolinate *rac*-**1c**, which was used to examine the steric influence of the bulky side chain on the allylic substitution reaction. To examine influence of an aryl substituent on the regioselectivity of the reaction, *rac*-**1d** was prepared.

The allylic substitution of *rac*-**1a** was first investigated by using phenyl reagents that were derived from PhMgBr and $CuBr{\cdot}Me_2S$ in ratios of 1:1 and 2:1 in tetrahydrofuran (THF) at an initial temperature of –40 or –30 °C that was gradually increased to –10 or 0 °C over 2 h to afford *rac*-**2aA** as the major product. To calculate the regioselectivity of *rac*-**2aA** over *rac*-**3aA** by ^1H NMR spectroscopy, the allylation of regioisomeric substrate *rac*-**6a** with a 2:1 ratio of $PhMgBr/CuBr{\cdot}Me_2S$ was carried out to produce *rac*-**3aA** as a 4:1 mixture with its (*Z*) isomer (see Scheme 3).[13] The reaction proceeded regioselectively (>95:5) with a 1:1 ratio of $PhMgBr/CuBr{\cdot}Me_2S$ (1.5 equiv.), but 7% of *rac*-**1a** was recovered (data not shown). On the other hand, 3 equiv. of the reagent completely consumed the substrate to afford *rac*-**2aA** with 96% regioselectivity (see Table 1, Entry 1). The substitution of *rac*-**1a** with 1 equiv. of the 2:1 $PhMgBr/CuBr{\cdot}Me_2S$ reagent afforded *rac*-**2aA** with a similar regioselectivity (see Table 1, Entry 2). The completion of the reaction within 2 h, even with 1 equiv. of the reagent, suggests the participation of the 1:1 $PhMgBr/CuBr{\cdot}Me_2S$ reagent,

Table 1. Optimization of conditions.

Entry	Substrate	ArMgBr [equiv.]	Cu salt [equiv.]	Ar/Cu	ZnI_2 [equiv.]	Temp. [°C][a]	**2**/**3**/**4**/**1**[b]	Yield of **2** + **3**[c,d]
								
	rac-**1a**		Ar = Ph *rac*-**2aA** *p*-Tol *rac*-**2aB**			*rac*-**3aA** *rac*-**3aB**	*rac*-**4a**	
1	*rac*-**1a**	PhMgBr (3.0)	$CuBr{\cdot}Me_2S$ (3.0)	1:1	–	–30	96:4:0:0	n.d.
2	*rac*-**1a**	PhMgBr (2.2)	$CuBr{\cdot}Me_2S$ (1.0)	2:1	–	–40	95:5:0:0	85
3	*rac*-**1a**	PhMgBr (3.0)	$CuBr{\cdot}Me_2S$ (1.5)	2:1	1.5	–40	90:10:0:0	n.d.
4	*rac*-**1a**	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	96:4:0:0	n.d.
5	*rac*-**1a**	*p*-TolMgBr (3.0)	$CuBr{\cdot}Me_2S$ (3.0)	1:1	–	–40	80:20:0:0	n.d.
6	*rac*-**1a**	*p*-TolMgBr (2.2)	$CuBr{\cdot}Me_2S$ (1.0)	2:1	–	–40	60:40:<5:0	80
7	*rac*-**1a**	*p*-TolMgBr (3.0)	$CuBr{\cdot}Me_2S$ (1.5)	2:1	1.5	–40	86:14:<5:0	>95
8	*rac*-**1a**	*p*-TolMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	98:2:0:0	88
								
	rac-**1b**		Ar = Ph *rac*-**2bA** *p*-Tol *rac*-**2bB**			*rac*-**3bA** *rac*-**3bB**	*rac*-**4b**	
9	*rac*-**1b**	PhMgBr (3.0)	$CuBr{\cdot}Me_2S$ (3.0)	1:1	–	–40	94:5:1:0	93
10	*rac*-**1b**	PhMgBr (2.2)	$CuBr{\cdot}Me_2S$ (1.0)	2:1	–	–40	94:0:0:6	n.d.
11	*rac*-**1b**	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	99:1:0:0	n.d.
12	*rac*-**1b**	*p*-TolMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	96:4:0:0	82
								
	rac-**1c**		Ar = Ph *rac*-**2cA** *p*-Tol *rac*-**2cB**			*rac*-**3cA** *rac*-**3cB**	*rac*-**4c**	
13	*rac*-**1c**	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	99:1:0:0	96
14	*rac*-**1c**	*p*-TolMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	95:5:0:0	87
								
	rac-**1d**		Ar = Ph *rac*-**2dA** *p*-Tol *rac*-**2dB**			*rac*-**3dA** *rac*-**3dB**	*rac*-**4d**	
15	*rac*-**1d**	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	>99:<1:0:0	89
16	*rac*-**1d**	*p*-TolMgBr (3.0)	$Cu(acac)_2$ (1.5)	2:1	–	–40	>99:<1:0:0	82

[a] Reaction temperature was gradually raised to –10 or 0 °C over 2 h for Entries 1–14 and over 3 h for Entries 15 and 16. [b] Determined by ^1H NMR spectroscopic analysis. [c] Isolated yield. [d] n.d.: not determined.

which is produced in situ through a reaction with the 2:1 reagent. In fact, the 1:1 reagent produced *rac*-**2aA** regioselectively (see Table 1, Entry 1). The 2:1 reagent in the presence of ZnI_2 resulted in somewhat lower regioselectivity (see Table 1, Entry 3). The reagent that was derived from a 2:1 ratio of PhMgBr and $Cu(acac)_2$ (acac = acetylacetonate) furnished *rac*-**2aA** with 96% regioselectivity (see Table 1, Entry 4).

The *rac*-**1a** substrate from Table 1, Entries 1–4 was then treated with *p*-TolMgBr. The $Cu(acac)_2$-based reagent showed high regioselectivity (98%)[14] to produce *rac*-**2aB** [**B** refers to *p*-tolyl (*p*-Tol) as the Ar group, see Table 1, Entry 8], whereas low regioselectivity was observed with the CuBr·Me_2S-based reagents (see Table 1, Entries 5–7).

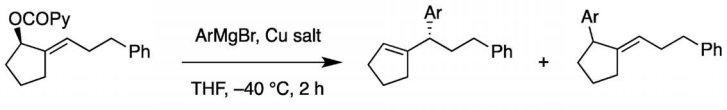
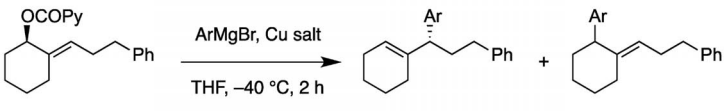
With the above results in hand, the six-membered ring substrate *rac*-**1b** was submitted to the substitution reactions with the Ph and *p*-Tol copper reagents. Regioisomer *rac*-**3bA** with the Ph substituent was independently synthesized through the reaction shown in Scheme 3 to determine the diagnostic absorbance in its ^{1}H NMR spectrum to estimate the regioselectivity of the reaction. As summarized in Table 1, Entries 11 and 12, the $Cu(acac)_2$-derived Ph and *p*-Tol reagents afforded *rac*-**2bA** and -**2bB**, respectively, with high regioselectivity (99% and 96%).[14] Similar regioselectivity results were obtained in the phenylation reactions that used 1:1 and 2:1 ratios of PhMgBr/CuBr·Me_2S (see Table 1, Entries 9 and 10).

Next, the influence of steric factors on the regioselectivity was examined by employing the *i*Pr-substituted substrate *rac*-**1c**, which was treated with the $Cu(acac)_2$-derived Ph and *p*-Tol reagents. The reactions proceeded without delay to afford *rac*-**2cA** and -**2cB** regioselectively[14] (see Table 1, Entries 13 and 14).

The influence of an aryl group attached to the allylic moiety on the regioselectivity was examined by using *rac*-**1d**, which upon reaction with the 2:1 PhMgBr/$Cu(acac)_2$ reagent afforded *rac*-**2dA** with a regioselectivity of >99% (see Table 1, Entry 15; the ^{1}H NMR of regioisomer *rac*-**3dA** is published[7] and was used to calculate the regioselectivity). Such a high regioselectivity was also attained with the 2:1 *p*-TolMgBr/$Cu(acac)_2$ reagent (see Table 1, Entry 16).

Throughout the above examination, the 2:1 ArMgBr/$Cu(acac)_2$ reagents (Ar = Ph, *p*-Tol) provided high regioselectivity in all of the reactions. As for the 2:1 ArMgBr/CuBr·Me_2S reagents, the Ph reagent was highly regioselective, but that with *p*-Tol was not. With these results in hand, the allylic substitution of (*R*)-**1a** (94 and 97%*ee*) and (*R*)-**1b** (86%*ee*) was studied to evaluate the chirality transfer (C.T.)[8] and determine the stereochemical course of the reaction. The 2:1 PhMgBr/$Cu(acac)_2$ reagent was first subjected to reaction with the five-membered substrate (*R*)-**1a** to produce (*R*)-**2aA** (Ar = Ph) with a C.T. of >99% and a regioselectivity of >99% in 80% isolated yield (see Table 2, Entry 1). The 2:1 PhMgBr/CuBr·Me_2S reagent produced (*R*)-**2aA** with a C.T. of 98% as well (see Table 2, Entry 2). Similarly, the *p*-Tol, *p*-$MeOC_6H_4$, and *p*-FC_6H_4 reagents participated in the substitution reaction to afford (*R*)-**2aB**, -**2aD**, and -**2aF** efficiently (see Table 2, Entries 3, 5, and 7). The steric congestion from the Me and MeO groups in the *o*-Tol and *o*-$MeOC_6H_4$ reagents, respectively, resulted in a slight decrease to the C.T. and regioselectivity, but the selectivity was still at an acceptable level (see Table 2, Entries 4

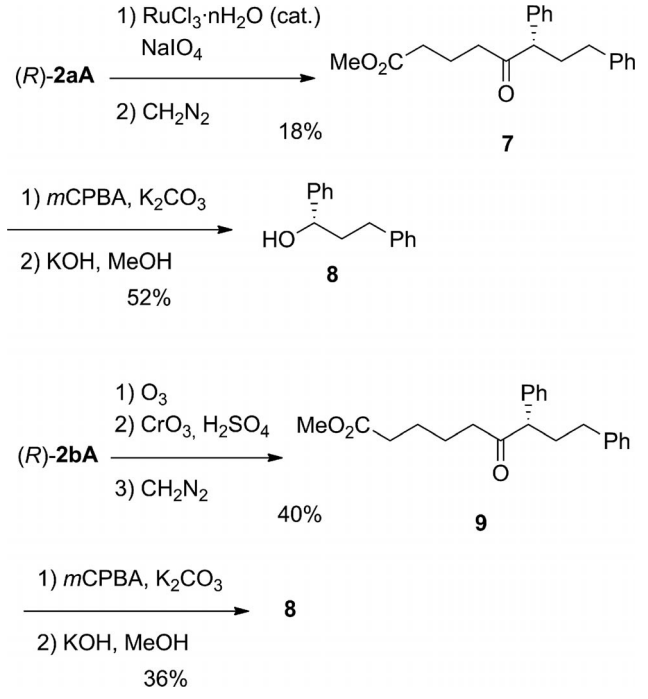
Table 2. Allylic substitution with optically active picolinates (*R*)-**1a** and -**1b**.

Entry	Substrate[a]	ArMgBr [equiv.]	Copper source [equiv.]	Product	2/3	C.T.[b]	Yield [%][c]
							
	(*R*)-**1a**			(*R*)-**2aA~F**	**3aA~F**		
1	(*R*)-**1a**	PhMgBr (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2aA**,[d] Ar = Ph	>99:1	>99%	80
2	(*R*)-**1a**	PhMgBr (2.2)	CuBr·Me_2S (1.0)	(*R*)-**2aA**, Ar = Ph	98:2	98%	89
3	(*R*)-**1a**	*p*-TolMgBr (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2aB**, Ar = *p*-Tol	>99:1	>99%	80
4	(*R*)-**1a**	*o*-TolMgBr (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2aC**, Ar = *o*-Tol	98:2	96%	87
5	(*R*)-**1a**	*p*-$MeOC_6H_4MgBr$ (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2aD**, Ar = *p*-$MeOC_6H_4$	>99:1	97%	91
6	(*R*)-**1a**	*o*-$MeOC_6H_4MgBr$ (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2aE**, Ar = *o*-$MeOC_6H_4$	95:5	91%	82
7	(*R*)-**1a**	*p*-FC_6H_4MgBr (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2aF**, Ar = *p*-FC_6H_4	>99:1	96%	86
							
	(*R*)-**1b**			(*R*)-**2bA**,-**2bD**,-**2bE**	**3bA**,**D**,**E**		
8	(*R*)-**1b**	PhMgBr (2.2)	CuBr·Me_2S (1.0)	(*R*)-**2bA**,[d] Ar = Ph	>99:1	>99%	89
9	(*R*)-**1b**	*p*-$MeOC_6H_4MgBr$ (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2bD**, Ar = *p*-$MeOC_6H_4$	>99:1	93%	87
10	(*R*)-**1b**	*o*-$MeOC_6H_4MgBr$ (3.0)	$Cu(acac)_2$ (1.5)	(*R*)-**2bE**, Ar = *o*-$MeOC_6H_4$	97:3	96%	71

[a] (*R*)-**1a** (94 or 97%*ee*), (*R*)-**1b** (86%*ee*). [b] Enantiomeric excess value for calculation of C.T. was determined by chiral HPLC analysis. [c] Isolated combined yield of **2** and **3**. [d] Absolute configuration was determined as described in the text.

and 6). Comparable results were also observed with the six-membered substrate (*R*)-**1b** (see Table 2, Entries 8–10).

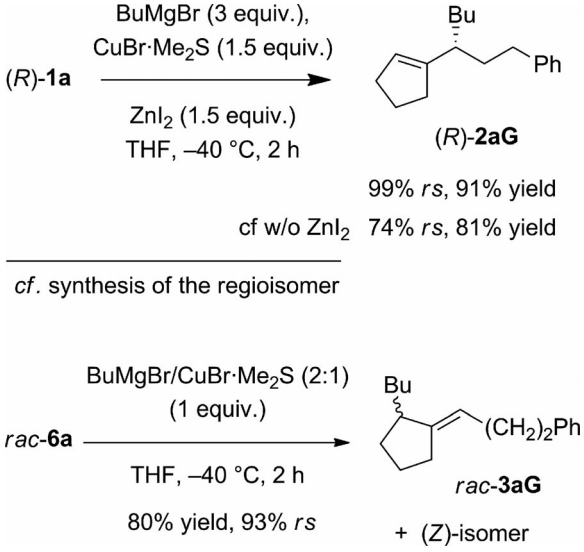
Scheme 4 shows the transformation[15] of (*R*)-**2aA** and -**2bA** into known alcohol **8**, and the specific rotations of **8** were compared with the literature value[16] to establish not only the *R* configuration of **2aA** and **2bA** but also the *anti*-S_N2' pathway of the allylic substitution. The configurations of the other products were determined by analogy.



Scheme 4. Transformation of (*R*)-**2aA** and -**2bA** into the known alcohol (*S*)-**8**.

Next, we turned our attention to a butyl copper reagent as a typical example of alkyl copper reagents. Surprisingly, the 2:1 BuMgBr/CuBr·Me_2S reagent was less regioselective (rs of 74%, see Scheme 5). As observed in the previous experiment, the regioselectivity of (*R*)-**2aG** was greatly improved at 99% by the addition of ZnI_2. The activation of the 2-$PyCO_2$ group through chelation was stronger to Zn^{2+} than to Mg^{2+}, which might be a reason for the high regioselectivity. In contrast, the 2:1 BuMgBr/Cu(acac)$_2$ reagent was regioselective to produce (*R*)-**2aG**, but the product was contaminated with unidentified compound(s).[17]

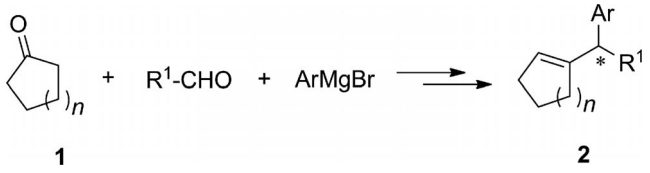
A possible pathway based on a recent mechanism for allylic substitution[2b,2c,18] is illustrated in Scheme 6. The reaction of ArMgBr and Cu(acac)$_2$ in a 2:1 ratio produces the $[ArCu(acac)]^-$ species and $(MgBr)^+$. This Ar–Cu species coordinates to the double bond as the latter cation activates the $PyCO_2$ leaving group through chelation to facilitate the subsequent elimination of the $PyCO_2$ group and produce the *anti*-S_N2' product with high γ selectivity.



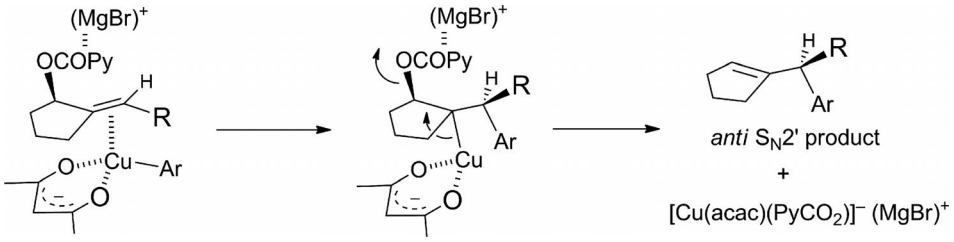
Scheme 5. Allylation of (*R*)-**1a** with butyl copper reagent (*rs* = regioselectivity; the ^1H NMR spectrum of *rac*-**3aG** was used as a reference to calculate the regioselectivity of (*R*)-**2aG**).

Conclusions

We have developed a method to construct a cycloalkenyl-substituted carbon unit through an allylic substitution that employs 2:1 ArMgBr/Cu(acac)$_2$ reagents and proceeds with excellent regioselectivity and C.T.[19] Reagents with sterically demanding groups as well as those with electron-donating and electron-withdrawing groups were successfully used in the reaction. Overall, the present results provide the transformation as depicted in Scheme 7. The total synthesis of biologically active compounds by employing this transformation will be reported in the near future.



Scheme 7. Overall transformation.



Scheme 6. Plausible mechanism.

Experimental Section

General Methods: The ^1H (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) spectroscopic data were recorded in $CDCl_3$ using $SiMe_4$ (δ = 0 ppm) and the centerline of the triplet (δ = 77.1 ppm), respectively, as internal standards. Signal patterns are indicated as br. s (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants (J) are given in Hertz (Hz). Chemical shifts of carbons are accompanied by minus (for C and CH_2) and plus (for CH and CH_3) signs of the attached proton test (APT) experiments. The solvents that were distilled prior to use are THF (from Na/benzophenone), Et_2O (from Na/benzophenone), and CH_2Cl_2 (from CaH_2). After the reactions were completed, the organic extracts were concentrated by using an evaporator, and then the residues were purified by chromatography on silica gel (Kanto, spherical silica gel 60N). $Cu(acac)_2$ was purchased from TCI, Japan and used without purification, whereas $CuBr{\cdot}Me_2S$ was prepared as described previously.[3e]

Synthesis of Picolinates (*R*)-1a and *rac*-1a

(*E*)-2-(3-Phenylpropylidene)cyclopentanone (5a): To an ice-cold solution of diisopropylamine (0.80 mL, 5.69 mmol) in THF (8 mL) was added *n*BuLi (1.65 M in hexane, 3.0 mL, 4.95 mmol) dropwise. The solution was stirred for 15 min at 0 °C and then cooled to –70 °C. Cyclopentanone (0.30 mL, 3.47 mmol) was added to the solution. After 30 min of stirring at –70 to –50 °C, 3-phenylpropionaldehyde (0.30 mL, 2.28 mmol) was added dropwise at –70 °C. After 30 min of stirring at –70 °C, the solution was poured into a mixture of EtOAc and saturated NH_4Cl with vigorous stirring. The layers were separated, and the aqueous layer was extracted with EtOAc (2×). The combined extracts were washed with brine, dried with $MgSO_4$, and concentrated to give a residue that was passed through a short column of silica gel (hexane/EtOAc) to afford the aldol, which was used for the next reaction without further purification. To an ice-cold solution of the alcohol, Et_3N (0.45 mL, 3.26 mmol), and DMAP (29.0 mg, 0.237 mmol) in CH_2Cl_2 (10 mL) was added MsCl (0.17 mL, 2.18 mmol) dropwise. The solution was warmed to room temp. over 2 h and then diluted with saturated $NaHCO_3$ with vigorous stirring. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×). The extracts were washed with brine, dried with $MgSO_4$, and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish **5a** (182 mg, 40% over two steps). IR (neat): $\tilde{\nu}$ = 1723, 1651, 1454, 747, 699 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.87 (quintet, J = 8 Hz, 2 H), 2.30 (t, J = 8 Hz, 2 H), 2.40–2.53 (m, 4 H), 2.77 (t, J = 8 Hz, 2 H), 6.50–6.63 (m, 1 H), 7.16–7.38 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.8 (–), 26.8 (–), 31.7 (–), 34.6 (–) 38.7 (–), 126.2 (+), 128.47 (+), 128.50 (+), 134.7 (+), 138.0 (–), 141.2 (–), 207.2 (–) ppm. HRMS (EI): calcd. for $C_{14}H_{16}O$ $[M]^+$ 200.1201; found 200.1202.

(*R*,*E*)-2-(3-Phenylpropylidene)cyclopentanol [(*R*)-4a]: To a solution of (*S*)-methyl oxazaborolidine (1.0 M in toluene, 0.11 mL, 0.11 mmol) and *N*,*N*-diethylaniline–borane (0.11 mL, 0.619 mmol) at –20 °C in THF (3 mL) was added a solution of enone **5a** (110.4 mg, 0.551 mmol) in THF (3 mL) over 60 min. After stirring at –20 °C for 1 h, the reaction was quenched carefully by the addition of cold MeOH (3 mL, –20 °C). After additional stirring for 1 h at room temp., the solution was concentrated to afford a residue, which was passed through a pad of silica gel (hexane/EtOAc) to furnish alcohol (*R*)-**4a** (80.1 mg, 72%). IR (neat): $\tilde{\nu}$ = 3348, 1496, 1453, 1080, 748, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.45 (br. s, 1 H), 1.53–1.66 (m, 2 H), 1.74–1.90 (m, 2 H), 2.04–2.16 (m, 1 H), 2.22–2.38 (m, 3 H), 2.69 (t, J = 7.5 Hz, 2 H), 4.34 (br. s, 1 H), 5.53–5.62 (m, 1 H), 7.15–7.22 (m, 3 H), 7.25–7.32 (m, H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0 (–), 27.0 (–), 31.3 (–), 35.6 (–), 35.7 (–), 75.7 (+), 123.3 (+), 125.9 (+), 128.4 (+), 128.5 (+), 142.1 (–), 146.8 (–) ppm. HRMS (EI): calcd. for $C_{14}H_{18}O$ $[M]^+$ 202.1358; found 202.1356.

(*R*,*E*)-2-(3-Phenylpropylidene)cyclopentyl Picolinate [(*R*)-1a]: To an ice-cold solution of (*R*)-**4a** (80.1 mg, 0.396 mmol) in CH_2Cl_2 (5 mL) were added DCC (109 mg, 0.528 mmol), DMAP (49.0 mg, 0.401 mmol), and picolinic acid (59.0 mg, 0.479 mmol). The mixture was stirred at room temp. for 2 h and then diluted with Et_2O. The resulting mixture was 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 (*R*)-**1a** (120 mg, 99%). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.66–1.77 (m, 1 H), 1.84–2.07 (m, 3 H), 2.10–2.22 (m, 1 H), 2.29–2.42 (m, 3 H), 2.61–2.76 (m, 2 H), 5.74–5.82 (m, 2 H), 7.13–7.20 (m, 3 H), 7.20–7.27 (m, 2 H), 7.46 (ddd, J = 8, 5, 1 Hz, 1 H), 7.83 (dt, J = 2, 8 Hz, 1 H), 8.08 (dt, J = 8, 1 Hz, 1 H), 8.78 (dm, J = 5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.8 (–), 27.3 (–), 31.7 (–), 33.1 (–), 35.4 (–), 79.1 (+), 125.1 (+), 125.8 (+), 126.7 (+), 127.1 (+), 128.3 (+), 128.6 (+), 136.9 (+), 141.3 (–), 142.0 (–), 148.7 (–), 150.1 (+), 165.1 (–) ppm. HRMS (EI): calcd. for $C_{20}H_{21}NO_2$ $[M]^+$ 307.1572; found 307.1578. The enantiomeric purity (97%*ee*) was determined by chiral HPLC analysis (Chiralcel OD-H; hexane/*i*PrOH, 98:2; 0.5 mL/min; 25 °C): t_R = 40.8 (*R* isomer) and 46.0 min (*S* isomer). The reaction was repeated to obtain (*R*)-**1a** with 94%*ee*.

(*E*)-2-(3-Phenylpropylidene)cyclopentyl Picolinate (*rac*-1a): To an ice-cold solution of **5a** (70.4 mg, 0.352 mmol) and $CeCl_3{\cdot}7H_2O$ (135 mg, 0.362 mmol) in MeOH (4 mL) was added $NaBH_4$ (13.0 mg, 0.344 mmol). After stirring at room temp. for 1 h, the solution was diluted with HCl (1 N solution) and Et_2O with vigorous stirring. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3×). The combined extracts were dried with $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish alcohol *rac*-**4a** (55.4 mg, 80%). The ^1H NMR spectrum was identical with that of (*R*)-**4a**. According to the procedure for synthesis of (*R*)-**1a**, *rac*-**4a** (55.0 mg, 0.272 mmol) was subjected to esterification with picolinic acid (42.0 mg, 0.341 mmol), DCC (74.0 mg, 0.359 mmol), and DMAP (34.0 mg, 0.278 mmol) in CH_2Cl_2 (2 mL) at room temp. for 2 h to furnish *rac*-**1a** (73.1 mg, 87%). The ^1H and ^{13}C NMR spectra were identical with those of (*R*)-**1a**.

Synthesis of Picolinates (*R*)-1b and *rac*-1b

(*E*)-2-(3-Phenylpropylidene)cyclohexanone (5b): According to the procedure for the synthesis of **5a**, cyclohexanone (2.30 mL, 22.3 mmol) was converted into the aldol as a mixture of diastereomers through the reaction with 3-phenylpropionaldehyde (2.00 mL, 15.2 mmol), diisopropylamine (6.30 mL, 44.8 mmol), and *n*BuLi (1.62 M in hexane, 23.0 mL, 37.3 mmol) in THF (50 mL). The aldol was subjected to a reaction with MsCl (1.90 mL, 24.5 mmol), Et_3N (5.10 mL, 36.6 mmol), and DMAP (1.50 g, 12.3 mmol) in CH_2Cl_2 (40 mL) at 0 °C to room temp. for 2 h to furnish **5b** (1.73 g, 53% over two steps). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.59–1.72 (m, 2 H), 1.75–1.87 (m, 2 H), 2.30–2.48 (m, 6 H), 2.70–2.79 (m, 2 H), 6.63 (tt, J = 8, 2 Hz, 1 H), 7.12–7.32 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4 (–), 23.6 (–), 26.7 (–), 29.8 (–), 34.7 (–), 40.3 (–), 126.2 (+), 128.5 (+), 137.0 (–), 138.0 (+), 141.3 (–), 201.3 (–) ppm. HRMS (EI): calcd. for $C_{15}H_{18}O$ $[M]^+$ 214.1358; found 214.1363. The ^1H and ^{13}C NMR spectra were consistent with those reported.[12]

(*R*,*E*)-2-(3-Phenylpropylidene)cyclohexanol [(*R*)-4b]: According to the procedure for the synthesis of (*R*)-**4a**, a solution of enone **5b** (202 mg, 0.942 mmol) in THF (9 mL) was added over 50 min to a solution of (*S*)-methyl oxazaborolidine (1.0 M in toluene, 0.20 mL, 0.200 mmol) and *N*,*N*-diethylaniline–borane (0.18 mL, 1.01 mmol) in THF (5 mL) at –20 °C. The solution was stirred at –20 °C for 30 min to afford alcohol (*R*)-**4b** (162 mg, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23–1.62 (m, 5 H), 1.68–1.96 (m, 3 H), 2.26–2.40 (m, 3 H), 2.66 (t, *J* = 8 Hz, 2 H), 4.00–4.08 (m, 1 H), 5.39 (dt, *J* = 1, 7 Hz, 1 H), 7.12–7.20 (m, 3 H), 7.22–7.29 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.0 (–), 26.1 (–), 27.2 (–), 28.9 (–), 36.2 (–), 36.3 (–), 73.8 (+), 120.1 (+), 125.8 (+), 128.2 (+), 128.5 (+), 141.7 (–), 142.0 (–) ppm. HRMS (EI): calcd. for $C_{15}H_{20}O$ $[M]^+$ 216.1514; found 216.1518.

(*R*,*E*)-2-(3-Phenylpropylidene)cyclohexyl Picolinate [(*R*)-1b]: According to the procedure for the synthesis of (*R*)-**1a**, a solution of (*R*)-**4b** (162 mg, 0.749 mmol), picolinic acid (115.6 mg, 0.939 mmol), DCC (214 mg, 1.04 mmol), and DMAP (91.7 mg, 0.751 mmol) in CH_2Cl_2 (8 mL) was stirred at room temp. for 2 h to furnish (*R*)-**1b** (231 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28–1.42 (m, 1 H), 1.44–1.64 (m, 2 H), 1.76–1.98 (m, 3 H), 2.09–2.19 (m, 1 H), 2.22–2.40 (m, 3 H), 2.65 (t, *J* = 8 Hz, 2 H), 5.49–5.56 (m, 2 H), 7.10–7.18 (m, 3 H), 7.18–7.26 (m, 2 H), 7.46 (ddd, *J* = 8, 5, 1 Hz, 1 H), 7.82 (dt, *J* = 1, 8 Hz, 1 H), 8.09 (d, *J* = 8 Hz, 1 H), 8.79 (dm, *J* = 5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6 (–), 26.0 (–), 26.7 (–), 28.9 (–), 33.0 (–), 35.9 (–), 77.3 (+), 123.6 (+), 125.0 (+), 125.7 (+), 126.6 (+), 128.2 (+), 128.6 (+), 136.67 (–), 136.86 (+), 141.8 (–), 148.7 (–), 150.0 (+), 164.1 (–) ppm. HRMS (EI): calcd. for $C_{21}H_{23}NO_2$ $[M]^+$ 321.1729; found 321.1729. The enantiomeric purity (86%*ee*) was determined by chiral HPLC analysis (Chiralcel OD-H; hexane/*i*PrOH, 98:2; 0.8 mL/min; 25 °C): t_R = 29.0 (*R* isomer) and 32.7 min (*S* isomer).

(*E*)-2-(3-Phenylpropylidene)cyclohexanol (*rac*-4b): According to the procedure for the synthesis of *rac*-**4a**, the reduction of **5b** (183 mg, 0.855 mmol) with $NaBH_4$ (32.4 mg, 0.856 mmol) was carried out in the presence of $CeCl_3{\cdot}7H_2O$ (330 mg, 0.885 mmol) in MeOH (9 mL) at room temp. for 1 h to furnish racemic alcohol *rac*-**4b** (135 mg, 73%). The ^{1}H and ^{13}C NMR spectra were identical with those of (*R*)-**4b**.

(*E*)-2-(3-Phenylpropylidene)cyclohexyl Picolinate (*rac*-1b): According to the procedure for the synthesis of *rac*-**1a**, the condensation of *rac*-**4b** (135 mg, 0.624 mmol) with picolinic acid (99.5 mg, 0.808 mmol) was carried out with DCC (175 mg, 0.848 mmol) and DMAP (73.5 mg, 0.602 mmol) in CH_2Cl_2 (7 mL) at room temp. for 2 h to furnish *rac*-**1b** (163 mg, 81%). The ^{1}H and ^{13}C NMR spectra were identical with those of (*R*)-**1b**.

Synthesis of Picolinate *rac*-1c

(*E*)-2-(2-Methylpropylidene)cyclopentanone (5c): According to the procedure for the synthesis of **5a**, cyclopentanone (1.48 mL, 16.7 mmol) was converted into the aldol as a mixture of diastereomers through the reaction with isobutyraldehyde (1.02 mL, 11.1 mmol), diisopropylamine (4.66 mL, 33.2 mmol), and *n*BuLi (1.60 M in hexane, 17.2 mL, 27.5 mmol) in THF (36 mL). To an ice-cold solution of the aldol and Et_3N (4.64 mL, 33.3 mmol) in CH_2Cl_2 (30 mL) was added MsCl (1.72 mL, 22.2 mmol) dropwise. The solution was stirred between 0 °C and room temp. for 2 h and then poured into saturated $NaHCO_3$ with vigorous stirring. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×). The combined extracts were washed with brine, dried with $MgSO_4$, and concentrated to afford the corresponding mesylate. To an ice-cold solution of the mesylate in THF (40 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 3.31 mL, 22.2 mmol). The mixture was stirred at room temp. for 1 h and then diluted with HCl (aqueous 1 N solution) and Et_2O with vigorous stirring. The organic layer was separated, and the aqueous layer was extracted with Et_2O (2×). The combined extracts were dried with $MgSO_4$ and concentrated to afford an oil, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish **5c** (715 mg, 47% over three steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (d, *J* = 6 Hz, 6 H), 1.94 (tt, *J* = 8, 8 Hz, 2 H), 2.33 (t, *J* = 8 Hz, 2 H), 2.41–2.55 (m, 1 H), 2.60 (dt, *J* = 2.5, 7 Hz, 2 H), 6.38 (dt, *J* = 10, 2.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.9 (–), 21.8 (+), 26.6 (–), 29.2 (+), 38.6 (–), 135.0 (–), 142.6 (+), 207.9 (–) ppm.

(*E*)-2-(2-Methylpropylidene)cyclopentanol (*rac*-4c): According to the procedure for the synthesis of *rac*-**4a**, the reduction of enone **5c** (89.6 mg, 0.648 mmol) with $NaBH_4$ (25.0 mg, 0.661 mmol) and $CeCl_3{\cdot}7H_2O$ (250 mg, 0.671 mmol) in MeOH (7 mL) gave alcohol *rac*-**4c** (70.2 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.966 (d, *J* = 7 Hz, 3 H), 0.971 (d, *J* = 7 Hz, 3 H), 1.54–1.73 (m, 2 H), 1.75–1.91 (m, 2 H), 2.14–2.26 (m, 1 H), 2.30–2.46 (m, 2 H), 4.33–4.41 (m, 1 H), 5.36 (dm, *J* = 9 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.2 (–), 22.6 (+), 22.8 (+), 26.7 (–), 28.9 (+), 35.6 (–), 75.8 (+), 131.8 (+), 143.6 (–) ppm.

(*E*)-2-(2-Methylpropylidene)cyclopentyl Picolinate (*rac*-1c): According to the procedure for the synthesis of *rac*-**1a**, the condensation of *rac*-**4c** (180 mg, 1.28 mmol) with picolinic acid (198.6 mg, 1.61 mmol) in CH_2Cl_2 (12 mL) was carried out with DCC (348.4 mg, 1.69 mmol) and DMAP (155.5 mg, 1.27 mmol) at room temp. for 1 h to furnish picolinate *rac*-**1c** (291 mg, 92%). IR (neat): $\tilde{\nu}$ = 1714, 1304, 1245, 1127 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 7 Hz, 3 H), 0.96 (d, *J* = 7 Hz, 3 H), 1.69–1.85 (m, 1 H), 1.85–2.11 (m, 3 H), 2.21–2.54 (m, 3 H), 5.54 (dm, *J* = 9.5 Hz, 1 H), 5.76 (tm, *J* = 4 Hz, 1 H), 7.43 (ddd, *J* = 8, 5, 1 Hz, 1 H), 7.80 (dt, *J* = 2, 8 Hz, 1 H), 8.07 (dm, *J* = 8 Hz, 1 H), 8.75 (dm, *J* = 5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5 (+), 22.6 (+), 22.9 (–), 27.1 (–), 29.2 (+), 33.1 (–), 79.3 (+), 125.1 (+), 126.6 (+), 135.4 (+), 136.9 (+), 138.1 (–), 148.8 (–), 150.0 (+), 165.0 (–) ppm. HRMS (EI): calcd. for $C_{15}H_{19}NO_2$ $[M]^+$ 245.1416; found 245.1420.

Synthesis of Picolinate *rac*-1d

(*E*)-2-Benzylidenecyclohexanol (*rac*-4d): According to the procedure for the synthesis of *rac*-**4a**, the reduction of commercially available enone **5d** (160.5 mg, 0.862 mmol) with $NaBH_4$ (33.1 mg, 0.875 mmol) and $CeCl_3{\cdot}7H_2O$ (323 mg, 0.876 mmol) in MeOH (9 mL) gave alcohol *rac*-**4d** (144.1 mg, 89%). IR (neat): $\tilde{\nu}$ = 3347, 1445, 1076, 738, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36–1.68 (m, 4 H), 1.76–1.91 (m, 1 H), 1.92–2.03 (m, 1 H), 2.03–2.14 (m, 1 H), 2.24 (br. s, 1 H), 2.71 (dt, *J* = 13.5, 5 Hz), 4.17–4.24 (m, 1 H), 6.51 (s, 1 H), 7.14–7.23 (m, 3 H), 7.25–7.33 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2 (–), 27.0 (–), 27.4 (–), 36.6 (–), 73.7 (+), 120.8 (+), 126.2 (+), 128.1 (+), 128.9 (+), 137.7 (–), 144.4 (–) ppm. The ^{1}H and ^{13}C NMR spectra were identical with those reported.[20]

(*E*)-2-Benzylidenecyclohexyl Picolinate (*rac*-1d): According to the procedure for the synthesis of *rac*-**1a**, the condensation of *rac*-**4d** (144.1 mg, 0.765 mmol) with picolinic acid (122.6 mg, 0.996 mmol) in CH_2Cl_2 (4 mL) was carried out with DCC (205.7 mg, 0.997 mmol) and DMAP (94.0 mg, 0.769 mmol) at room temp. for 2 h to furnish picolinate *rac*-**1d** (202.3 mg, 90%). IR (neat): $\tilde{\nu}$ = 1738, 1715, 1583, 1301, 1243, 1133 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54–1.75 (m, 3 H), 1.85–2.12 (m, 3 H), 2.40 (dt, *J* = 14, 6 Hz, 1 H), 2.67 (dt, *J* = 14, 6 Hz, 1 H), 5.71 (t, *J* = 5.5 Hz, 1 H), 6.60 (s, 1 H), 7.46 (ddd, *J* = 7.5, 4.5, 1 Hz, 1 H), 7.84 (dt, *J* =

2, 7.5 Hz, 1 H), 8.16 (d, J = 7.5 Hz, 1 H), 8.79 (d, J = 4.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.0 (–), 27.1 (–), 27.2 (–), 33.4 (–), 77.0 (+), 123.7 (+), 125.1 (+), 126.5 (+), 126.7 (+), 128.1 (+), 129.0 (+), 136.9 (+), 137.2 (–), 139.1 (–), 148.7 (–), 150.1 (+), 164.1 (–) ppm. HRMS (EI): calcd. for $C_{19}H_{19}NO_2$ $[M]^+$ 293.1416; found 293.1423.

General Procedure for Allylation To Afford (*R*)-[1-(Cyclopent-1-en-1-yl)propane-1,3-diyl]dibenzene [(*R*)-2aA]

Allylation with Cu(acac)$_2$: (see Table 2, Entry 1). To an ice-cold suspension of $Cu(acac)_2$ (281.3 mg, 1.07 mmol) in THF (7 mL) was added PhMgBr (1.05 M in THF, 2.00 mL, 2.10 mmol) slowly. The mixture was stirred at 0 °C for 60 min and then cooled to –40 °C. A solution of picolinate (*R*)-**1a** (220.0 mg, 0.716 mmol, 94%*ee*) in THF (3 mL) was added. The resulting mixture was warmed to –5 °C over 2 h to afford (*R*)-**2aA** (149.5 mg, 80%). The enantiomeric purity (95%*ee*) was determined by chiral HPLC analysis.

Allylation with CuBr·Me$_2$S: (see Table 2, Entry 2). To an ice-cold suspension of CuBr·Me_2S (20.4 mg, 0.0992 mmol) in THF (1 mL) was added PhMgBr (0.91 M in THF, 0.23 mL, 0.21 mmol) slowly. The mixture was stirred at 0 °C for 30 min and then cooled to –40 °C. A solution of picolinate (*R*)-**1a** (30.3 mg, 0.0986 mmol, 97%*ee*) in THF (1 mL) was added. The resulting mixture was warmed to –10 °C over 1 h to give (*R*)-**2aA** (23.0 mg, 89%). $[\alpha]_D^{21}$ = +27 (c = 0.12, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3025, 1602, 1494, 1452, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.76–1.84 (m, 2 H), 2.00–2.25 (m, 4 H), 2.27–2.39 (m, 2 H), 2.43–2.62 (m, 2 H), 3.32 (t, J = 7 Hz, 1 H), 5.52 (s, 1 H), 7.10–7.23 (m, 6 H), 7.23–7.35 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3 (–), 32.4 (–), 33.7 (–), 34.1 (–), 35.8 (–), 47.2 (+), 123.9 (+), 125.8 (+), 126.2 (+), 128.0 (+), 128.4 (+), 128.5 (+), 142.6 (–), 143.9 (–), 147.3 (–) ppm. HRMS (EI): calcd. for $C_{20}H_{22}$ $[M]^+$ 262.1722; found 262.1725. The enantiomeric purity (94%*ee*) was determined by chiral HPLC analysis (Chiralcel OJ-H; hexane/*i*PrOH, 99.6:0.4; 0.3 mL/min; 25 °C): t_R = 34.4 (*S* isomer) and 39.4 min (*R* isomer).

Allylation Products

(*R*)-1-[1-(Cyclopent-1-en-1-yl)-3-phenylpropyl]-4-methylbenzene [(*R*)-2aB]: (see Table 2, Entry 3). Colorless oil (80% yield). IR (neat): $\tilde{\nu}$ = 1604, 1512, 1496, 1454, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.72–1.84 (m, 2 H), 1.97–2.23 (m, 4 H), 2.33 (s, 3 H), 2.27–2.35 (m, 2 H), 2.51 (t, J = 8 Hz, 2 H), 3.29 (t, J = 8 Hz, 1 H), 5.50 (s, 1 H), 7.05–7.20 (m, 6 H), 7.23–7.29 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (+), 23.3 (–), 32.4 (–), 33.7 (–), 34.1 (–), 35.8 (–), 46.8 (+), 123.7 (+), 125.7 (+), 127.9 (+), 128.3 (+), 128.5 (+), 129.0 (+), 135.6 (–), 140.9 (–), 142.7 (–), 147.5 (–) ppm. HRMS (EI): calcd. for $C_{21}H_{24}$ $[M]^+$ 276.1878; found 276.1882. The enantiomeric purity (97%*ee*) was determined by chiral HPLC analysis (Chiralcel OJ-H; hexane/*i*PrOH, 99.6:0.4; 0.3 mL/min; 25 °C): t_R = 25.1 (*S* isomer) and 31.7 min (*R*-isomer).

(*R*)-1-[1-(Cyclopent-1-en-1-yl)-3-phenylpropyl]-2-methylbenzene [(*R*)-2aC]: (see Table 2, Entry 4). Colorless oil (87% yield). $[\alpha]_D^{21}$ = –4 (c = 0.47, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1603, 1454, 754, 729, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.72–1.86 (m, 2 H), 1.98–2.07 (m, 1 H), 2.07–2.14 (m, 2 H), 2.23 (s, 3 H), 2.15–2.26 (m, 1 H), 2.28–2.35 (m, 2 H), 2.48–2.63 (m, 2 H), 3.60 (t, J = 7 Hz, 1 H), 5.47 (s, 1 H), 7.06–7.21 (m, 6 H), 7.23–7.29 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.6 (+), 23.2 (–), 32.3 (–), 33.6 (–), 34.0 (–), 35.6 (–), 42.1 (+), 124.1 (+), 125.66 (+), 125.71 (+), 126.0 (+), 126.5 (+), 128.3 (+), 128.4 (+), 130.2 (+), 136.2 (–), 141.8 (–), 142.5 (–), 146.5 (–) ppm. HRMS (EI): calcd. for $C_{21}H_{24}$ $[M]^+$ 276.1878; found 276.1871. The enantiomeric purity (90%*ee*) was determined by chiral HPLC analysis (Chiralcel OJ-H; hexane/*i*PrOH; 92:8; 0.3 mL/min; 25 °C): t_R = 16.5 (*R* isomer) and 17.8 min (*S* isomer).

(*R*)-1-[1-(Cyclopent-1-en-1-yl)-3-phenylpropyl]-4-methoxybenzene [(*R*)-2aD]: (see Table 2, Entry 5). Colorless oil (91% yield). $[\alpha]_D^{27}$ = +27 (c = 0.47, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1609, 1507, 1246, 1176, 1039 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.85 (m, 2 H), 1.93–2.23 (m, 4 H), 2.24–2.38 (m, 2 H), 2.50 (t, J = 8 Hz, 2 H), 3.26 (t, J = 7 Hz, 1 H), 3.79 (s, 3 H), 5.47 (s, 1 H), 6.82 (d, J = 8 Hz, 2 H), 7.03–7.19 (m, 5 H), 7.20–7.26 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2 (–), 32.3 (–), 33.6 (–), 34.0 (–), 35.8 (–), 46.2 (+), 55.2 (+), 113.6 (+), 123.5 (+), 125.6 (+), 128.2 (+), 128.4 (+), 128.8 (+), 135.9 (–), 142.6 (–), 147.6 (–), 157.9 (–) ppm. HRMS (EI): calcd. for $C_{21}H_{24}O$ $[M]^+$ 292.1827; found 292.1825. The enantiomeric purity (91%*ee*) was determined by chiral HPLC analysis (Chiralcel OD-H; hexane/*i*PrOH, 99.8:0.2; 0.4 mL/min; 25 °C): t_R = 24.7 (*S* isomer) and 26.6 min (*R* isomer).

(*R*)-1-[1-(Cyclopent-1-en-1-yl)-3-phenylpropyl]-2-methoxybenzene [(*R*)-2aE]: (see Table 2, Entry 6). Colorless oil (82% yield). $[\alpha]_D^{20}$ = +12 (c = 0.26, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1599, 1492, 1241, 1031, 751, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.71–1.87 (m, 2 H), 1.94–2.05 (m, 1 H), 2.09–2.20 (m, 3 H), 2.32 (tt, J = 7, 2.5 Hz, 2 H), 2.49 (ddd, J = 14, 10, 6 Hz, 1 H), 2.58 (ddd, J = 14, 10, 6 Hz, 1 H), 3.80 (s, 3 H), 3.92 (t, J = 7 Hz, 1 H), 5.50 (s, 1 H), 6.87 (d, J = 8 Hz, 1 H), 6.92 (dt, J = 1, 8 Hz, 1 H), 7.12–7.20 (m, 5 H), 7.22–7.28 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3 (–), 32.5 (–), 34.20 (–), 34.22 (–), 35.9 (–), 38.6 (+), 55.6 (+), 110.7 (+), 120.6 (+), 123.8 (+), 125.6 (+), 126.9 (+), 127.8 (+), 128.2 (+), 128.4 (+), 132.4 (–), 143.0 (–), 147.0 (–), 157.4 (–) ppm. HRMS (EI): calcd. for $C_{21}H_{24}O$ $[M]^+$ 292.1827; found 292.1828. The enantiomeric purity (85%*ee*) was determined by chiral HPLC analysis (Chiralcel OD-H; hexane/*i*PrOH, 99.9:0.1; 1.0 mL/min; 25 °C): t_R = 9.5 (*S* isomer) and 10.3 min (*R* isomer).

(*R*)-1-[1-(cyclopent-1-en-1-yl)-3-phenylpropyl]-4-fluorobenzene [(*R*)-2aF]: (see Table 2, Entry 7). Colorless oil (86% yield). $[\alpha]_D^{21}$ = +22 (c = 0.36, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1602, 1508, 1498, 1223, 1156 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.73–1.87 (m, 2 H), 1.96–2.25 (m, 4 H), 2.27–2.36 (m, 2 H), 2.50 (t, J = 8 Hz, 2 H), 3.30 (t, J = 8 Hz, 1 H), 5.50 (s, 1 H), 6.98 (tt, J = 8, 2.5 Hz, 2 H), 7.09–7.21 (m, 5 H), 7.23–7.30 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3 (–), 32.4 (–), 33.7 (–), 34.0 (–), 35.9 (–), 46.4 (+), 115.1 (d, J = 21 Hz, +), 124.1 (+), 125.8 (+), 128.4 (+), 128.5 (+), 129.3 (d, J = 8 Hz, +), 139.5 (d, J = 3 Hz, –), 142.4 (–), 147.2 (–), 161.4 (d, J = 242 Hz, –) ppm. HRMS (EI): calcd. for $C_{20}H_{21}F$ $[M]^+$ 280.1627; found 280.1621. The enantiomeric purity (90%*ee*) was determined by chiral HPLC analysis (Chiralcel OJ-H; hexane/*i*PrOH, 99.6:0.4; 1.0 mL/min; 25 °C): t_R = 8.7 (*S* isomer) and 10.8 min (*R* isomer).

(*R*)-[1-(Cyclohex-1-en-1-yl)propane-1,3-diyl]dibenzene [(*R*)-2bA]: (see Table 2, Entry 8). Colorless oil (89% yield). $[\alpha]_D^{21}$ = –3 (c = 0.26, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3025, 1602, 1494, 1451, 699 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44–1.62 (m, 4 H), 1.65–1.90 (m, 2 H), 1.92–2.22 (m, 4 H), 2.42–2.62 (m, 2 H), 3.13 (t, J = 7 Hz, 1 H), 5.62 (s, 1 H), 7.08–7.32 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.8 (–), 23.2 (–), 25.6 (–), 26.7 (–), 34.3 (–), 34.6 (–), 52.6 (+), 121.6 (+), 125.6 (+), 126.0 (+), 127.9 (+), 128.1 (+), 128.2 (+), 128.4 (+), 139.8 (–), 142.6 (–), 144.2 (–) ppm. HRMS (EI): calcd. for $C_{21}H_{24}$ $[M]^+$ 276.1878; found 276.1875. The enantiomeric purity (86%*ee*) was determined by chiral HPLC analysis (Chiralcel OD-H; hexane/*i*PrOH, 100:0; 0.8 mL/min; 20 °C): t_R = 13.2 (*S* isomer) and 14.1 min (*R* isomer).

1-[1-(Cyclohex-1-en-1-yl)-3-phenylpropyl]-4-methylbenzene (*rac*-2bB): (see Table 1, Entry 12). Colorless oil (82% yield). IR (neat): $\tilde{\nu}$ = 1511, 1496, 1453, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48–1.56 (m, 4 H), 1.67–1.87 (m, 2 H), 1.94–2.17 (m, 4 H), 2.32 (s, 3 H), 2.46–2.62 (m, 2 H), 3.10 (t, J = 7.0 Hz, 1 H), 5.62 (s, 1 H), 7.06–7.30 (m, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (+), 22.8 (–), 23.1 (–), 25.5 (–), 26.6 (–), 34.2 (–), 34.6 (–), 52.1 (+), 121.5 (+), 125.7 (+), 127.9 (+), 128.3 (+), 128.5 (+), 128.9 (+), 135.5 (–), 140.1 (–), 141.3 (–), 142.8 (–) ppm. HRMS (EI): calcd. for $C_{22}H_{26}$ $[M]^+$ 290.2035; found 290.2035.

(*R*)-1-[1-(Cyclohex-1-en-1-yl)-3-phenylpropyl]-4-methoxybenzene [(*R*)-2bD]: (see Table 2, Entry 9). Colorless oil (87% yield). $[\alpha]_D^{21}$ = –2 (c = 0.498, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1608, 1509, 1246, 1177, 1039 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.46–1.60 (m, 4 H), 1.66–1.86 (m, 2 H), 1.92–2.16 (m, 4 H), 2.44–2.59 (m, 2 H), 3.08 (t, J = 8 Hz, 1 H), 3.80 (s, 3 H), 5.61 (s, 1 H), 6.83 (dm, J = 9 Hz, 2 H), 7.09–7.20 (m, 4 H), 7.23–7.29 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7 (–), 23.1 (–), 25.4 (–), 26.6 (–), 34.2 (–), 34.7 (–), 51.6 (+), 55.3 (+), 113.5 (+), 121.4 (+), 125.7 (+), 128.3 (+), 128.5 (+), 128.8 (+), 136.4 (–), 140.2 (–), 142.8 (–), 157.9 (–) ppm. HRMS (EI): calcd. for $C_{22}H_{26}O$ $[M]^+$ 306.1984; found 306.1981. The enantiomeric purity (80%*ee*) was determined by chiral HPLC analysis (Chiralcel OD-H; hexane/*i*PrOH, 99.9:0.1; 1.0 mL/min; 20 °C): t_R = 16.7 (*S* isomer) and 22.5 min (*R* isomer).

(*R*)-1-[1-(Cyclohex-1-en-1-yl)-3-phenylpropyl]-2-methoxybenzene [(*R*)-2bE]: (see Table 2, Entry 10). Colorless oil (71% yield). $[\alpha]_D^{20}$ = +6 (c = 0.36, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1598, 1490, 1460, 1241 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.44–1.64 (m, 4 H), 1.76–1.87 (m, 2 H), 1.87–1.99 (m, 1 H), 2.00–2.14 (m, 3 H), 2.47 (ddd, J = 14, 10, 6 Hz, 1 H), 2.59 (ddd, J = 14, 10, 6 Hz, 1 H), 3.71 (t, J = 8 Hz, 1 H), 3.79 (s, 3 H), 5.61 (s, 1 H), 6.82–6.88 (m, 1 H), 6.91 (t, J = 7 Hz, 1 H), 7.11–7.21 (m, 5 H), 7.22–7.28 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.8 (–), 23.2 (–), 25.5 (–), 27.7 (–), 34.3 (–), 35.1 (–), 43.6 (+), 55.6 (+), 110.7 (+), 120.5 (+), 121.3 (+), 125.6 (+), 126.8 (+), 127.6 (+), 128.2 (+), 128.5 (+), 133.0 (+), 139.5 (+), 143.2 (+), 157.7 (+) ppm. HRMS (EI): calcd. for $C_{22}H_{26}O$ $[M]^+$ 306.1984; found 306.1986. The enantiomeric purity (83%*ee*) was determined by chiral HPLC analysis (Chiralcel OD-H; hexane/*i*PrOH, 99.9:0.1; 1.0 mL/min; 20 °C): t_R = 9.9 (*S* isomer) and 11.3 min (*R* isomer).

[1-(Cyclopent-1-en-1-yl)-2-methylpropyl]benzene (*rac*-2cA): (see Table 1, Entry 13). Colorless oil (96% yield). IR (neat): $\tilde{\nu}$ = 1493, 1451, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.71 (d, J = 6 Hz, 3 H), 0.96 (d, J = 6 Hz, 3 H), 1.77 (tt, J = 8, 8 Hz, 2 H), 2.06–2.23 (m, 3 H), 2.23–2.35 (m, 2 H), 3.00 (d, J = 10 Hz, 1 H), 5.52 (s, 1 H), 7.13–7.21 (m, 3 H), 7.22–7.29 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (+), 22.0 (+), 23.3 (–), 30.1 (+), 32.2 (–), 32.9 (–), 56.7 (+), 124.5 (+), 125.9 (+), 128.1 (+), 128.4 (+), 143.7 (–), 146.8 (–) ppm. HRMS (EI): calcd. for $C_{15}H_{20}$ $[M]^+$ 200.1565; found 200.1559.

1-[1-(Cyclopent-1-en-1-yl)-2-methylpropyl]-4-methylbenzene (*rac*-2cB): (see Table 1, Entry 14). Colorless oil (87% yield). IR (neat): $\tilde{\nu}$ = 1512, 1465, 1384, 815 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.71 (d, J = 6.5 Hz, 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 1.72–1.83 (m, 2 H), 2.07–2.36 (m, 5 H), 2.31 (s, 3 H), 2.97 (d, J = 10 Hz, 1 H), 5.50 (s, 1 H), 7.03–7.12 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (+), 21.3 (+), 22.0 (+), 23.3 (–), 30.1 (+), 32.2 (–), 32.9 (–), 56.3 (+), 124.2 (+), 128.3 (+), 128.8 (+), 135.2 (–), 140.6 (–), 147.0 (–) ppm. HRMS (EI): calcd. for $C_{16}H_{22}$ $[M]^+$ 214.1722; found 214.1722.

(Cyclohex-1-en-1-ylmethylene)dibenzene (*rac*-2dA): (see Table 1, Entry 15). Colorless oil (89% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.49–1.68 (m, 4 H), 1.89–1.98 (m, 2 H), 1.99–2.08 (m, 2 H), 4.62 (s, 1 H), 5.16–5.24 (m, 1 H), 7.11–7.22 (m, 6 H), 7.23–7.30 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6 (–), 23.3 (–), 25.6 (–), 29.1 (–), 59.0 (+), 125.54 (+), 125.58 (+), 126.1 (+), 128.2 (+), 129.4 (+), 140.0 (–), 143.1 (–) ppm. The ^1H NMR spectrum was identical with that reported.[21]

1-[Cyclohex-1-en-1-yl(phenyl)methyl]-4-methylbenzene (*rac*-2dB): (see Table 1, Entry 16). Colorless oil (82% yield). IR (neat): $\tilde{\nu}$ = 1511, 1448, 800, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.51–1.66 (m, 4 H), 1.88–1.98 (m, 2 H), 1.98–2.08 (m, 2 H), 2.31 (s, 3 H), 4.58 (s, 1 H), 5.17–5.22 (m, 1 H), 7.00–7.11 (m, 4 H), 7.11–7.20 (m, 3 H), 7.23–7.29 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (+), 22.6 (–), 23.3 (–), 25.6 (–), 29.1 (–), 58.6 (+), 125.31 (+), 125.35 (+), 126.1 (+), 128.2 (+), 128.9 (+), 129.3 (+), 129.4 (+), 135.6 (–), 140.05 (–), 140.11 (–), 143.3 (–) ppm. HRMS (EI): calcd. for $C_{20}H_{22}$ $[M]^+$ 262.1722; found 262.1723.

(*R*)-[3-(Cyclopent-1-en-1-yl)heptyl]benzene [(*R*)-2aG]: (see Scheme 5). Colorless oil (91% yield). IR (neat): $\tilde{\nu}$ = 1500, 1455, 1260, 1032, 804, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 7 Hz, 3 H), 1.15–1.40 (m, 6 H), 1.58–1.72 (m, 2 H), 1.85 (quintet, J = 7 Hz, 2 H), 2.12–2.27 (m, 3 H), 2.27–2.36 (m, 2 H), 2.40–2.60 (m, 2 H), 5.36–5.41 (m, 1 H), 7.13–7.19 (m, 3 H), 7.23–7.30 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (+), 22.9 (–), 23.5 (–), 29.8 (–), 31.0 (–), 32.1 (–), 33.5 (–), 34.0 (–), 35.6 (–), 41.0 (+), 125.1 (+), 125.6 (+), 128.3 (+), 128.5 (+), 143.2 (–), 147.1 (–) ppm.

Determination of Configuration of (*R*)-2aA

(*S*)-Methyl 5-Oxo-6,8-diphenyloctanoate (7): To an ice-cold solution of (*R*)-**2aA** (43.9 mg, 0.167 mmol) in CCl_4 (2 mL), MeCN (2 mL), and H_2O (3 mL) were added $NaIO_4$ (150 mg, 0.701 mmol) and $RuCl_3{\cdot}nH_2O$ (ca. 16 mg). The mixture was stirred at room temp. for 7 h and then diluted with CH_2Cl_2 (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×). The combined organic layers were dried by $MgSO_4$ and concentrated to afford a residue, which was passed through a pad of Celite with Et_2O to remove the remaining Ru species. The filtrate was concentrated to afford a crude oil, which was passed through a short column and then used for the next reaction without further purification. To an ice-cold solution of the oil in Et_2O (2 mL) was added a solution of CH_2N_2 in Et_2O (2 mL). After 5 min at 0 °C, the solution was concentrated to afforded a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish **7** [9.7 mg, 18% from (*R*)-**2aA**]. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.68–1.86 (m, 2 H), 1.94–2.07 (m, 1 H), 2.08–2.26 (m, 2 H), 2.26–2.45 (m, 3 H), 2.49 (tm, J = 7 Hz, 2 H), 3.53–3.61 (m, 1 H), 3.57 (s, 3 H), 7.08–7.13 (m, 2 H), 7.15–7.19 (m, 3 H), 7.22–7.28 (m, 3 H), 7.28–7.34 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.9 (–), 32.9 (–), 33.4 (–), 40.6 (–), 51.6 (+), 58.2 (+), 126.0 (+), 127.4 (+), 128.44 (+), 128.48 (+), 128.53 (+), 129.1 (+), 138.7 (–), 141.6 (–), 173.6 (–), 209.4 (–) ppm.

(*S*)-1,3-Diphenylpropan-1-ol (8): To a solution of **7** (15.3 mg, 0.0472 mmol) in CH_2Cl_2 (5 mL) were added K_2CO_3 (72.2 mg, 0.522 mmol) and *meta*-chloroperoxybenzoic acid (*m*CPBA, 77% purity, 92.3 mg, 0.412 mmol). The reaction was carried out at room temp. for 40 h and then quenched by the addition of aqueous $Na_2S_2O_3$ and CH_2Cl_2. The organic layer was separated, and the aqueous phase was extracted with EtOAc (2×). The combined extracts were dried with $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to afford a residue, which was used for the following reaction without further purification. A mixture of the product and aqueous KOH (1.8 N, 0.10 mL) in MeOH (1 mL) was stirred at room temp. over-

night and then diluted with H_2O and Et_2O. The organic layer was separated, and the aqueous phase was extracted with Et_2O (3×). The combined extracts were dried with $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to furnish **8** (5.2 mg, 52% over two steps). $[a]_D^{23}$ = –13 (*c* = 0.17, $CHCl_3$); {cf. $[a]_D^{20}$ = –27.1 (*c* = 0.52, $CHCl_3$) for the *S* enantiomer with >99%*ee*}.[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84 (br. s, 1 H), 1.97–2.20 (m, 2 H), 2.62–2.81 (m, 2 H), 4.70 (dd, *J* = 8, 5.5 Hz, 1 H), 7.15–7.22 (m, 3 H), 7.25–7.32 (m, 3 H), 7.33–7.37 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.2 (–), 40.6 (–), 74.0 (+), 125.95 (+), 126.01 (+), 127.7 (+), 128.48 (+), 128.52 (+), 128.62 (+), 141.8 (–), 144.6 (–) ppm. The ^{1}H and ^{13}C NMR spectra were consistent with those reported.[17]

Determination of the Configuration of (*R*)-2bA

(*S*)-Methyl 6-Oxo-7,9-diphenylnonanoate (9): A stream of ozone in oxygen was slowly bubbled into a solution of (*R*)-**2bA** (43.1 mg, 0.156 mmol) in CH_2Cl_2 (8 mL) at –78 °C until the solution turned to pale blue (5 min). The excess amount of ozone that remained in the solution was removed by bubbling argon at –78 °C for 5 min, and PPh_3 (52.0 mg, 0.198 mmol) was added. The solution was gradually warmed to room temp., stirred overnight, and concentrated to afford a residue that was passed through a short column of silica gel (hexane/EtOAc) to furnish a crude aldehyde, which was used for the next reaction without further purification. To a solution of the crude aldehyde in acetone (5 mL) was added Jones reagent (4 M solution, 9 drops) at 0 °C. After 30 min at 0 °C, *i*PrOH was added to quench the excess amount of reagent. After concentration, the residue was passed through a short column, and the filtrate was concentrated to afford a residue, which was used directly for the next reaction without further purification. To an ice-cold solution of the residue in Et_2O (2 mL) was added a solution of CH_2N_2 in Et_2O (2 mL). After 5 min, the solution was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish ester **9** [21.3 mg, 40% from (*R*)-**2bA**]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38–1.66 (m, 4 H), 1.94–2.10 (m, 1 H), 2.15–2.25 (m, 2 H), 2.28–2.44 (m, 3 H), 2.45–2.56 (m, 2 H), 3.54–3.65 (m, 1 H), 3.62 (s, 3 H), 7.06–7.21 (m, 5 H), 7.21–7.36 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2 (–), 24.3 (–), 33.42 (–), 33.45 (–), 33.8 (–), 41.3 (–), 51.6 (+), 58.2 (+), 126.0 (+), 127.4 (+), 128.44 (+), 128.45 (+), 128.52 (+), 129.0 (+), 138.8 (–), 141.6 (–), 173.9 (–), 209.8 (–) ppm.

(*S*)-1,3-Diphenylpropan-1-ol (8): According to the above procedure, a mixture of **9** (21.3 mg, 0.0629 mmol), K_2CO_3 (105 mg, 0.760 mmol), and *m*CPBA (77% purity, 128.3 mg, 0.0.572 mmol) in CH_2Cl_2 (6 mL) was stirred at room temp. for 48 h to afford the ester product, which was subjected to hydrolysis with aqueous KOH (1.8 N, 0.15 mL) in MeOH (2 mL) at room temp. overnight to furnish **8** (4.8 mg, 36% from **9**). $[a]_D^{23}$ = –23 (*c* = 0.25, $CHCl_3$); {cf. $[a]_D^{20}$ = –27.1 (*c* = 0.52, $CHCl_3$) for the *S* enantiomer with >99%*ee*}.[17]

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of the intermediates, the picolinate substrates, allylation products, and compounds **7**–**9**.

Acknowledgments

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan.

[1] For reviews, see: a) J. F. Teichert, B. L. Feringa, *Angew. Chem.* **2010**, *122*, 2538; *Angew. Chem. Int. Ed.* **2010**, *49*, 2486–2528; b) B. Breit, Y. Schmidt, *Chem. Rev.* **2008**, *108*, 2928–2951; c) S. R. Harutyunyan, T. den Hartog, K. Geurts, A. J. Minnaard, B. L. Feringa, *Chem. Rev.* **2008**, *108*, 2824–2852; d) A. Alexakis, J. E. Bäckvall, N. Krause, O. Pàmies, M. Diéguez, *Chem. Rev.* **2008**, *108*, 2796–2823; e) C. A. Falciola, A. Alexakis, *Eur. J. Org. Chem.* **2008**, 3765–3780; f) H. Yorimitsu, K. Oshima, *Angew. Chem.* **2005**, *117*, 4509; *Angew. Chem. Int. Ed.* **2005**, *44*, 4435–4439.

[2] For recent publications, see: a) R. Shintani, K. Takatsu, M. Takeda, T. Hayashi, *Angew. Chem.* **2011**, *123*, 8815; *Angew. Chem. Int. Ed.* **2011**, *50*, 8656–8659; b) H. Ohmiya, U. Yokobori, Y. Makida, M. Sawamura, *J. Am. Chem. Soc.* **2010**, *132*, 2895–2897; c) H. Ohmiya, N. Yokokawa, M. Sawamura, *Org. Lett.* **2010**, *12*, 2438–2440; d) H. Ohmiya, Y. Makida, T. Tanaka, M. Sawamura, *J. Am. Chem. Soc.* **2008**, *130*, 17276–17277; e) D. Soorukram, P. Knochel, *Angew. Chem.* **2006**, *118*, 3768; *Angew. Chem. Int. Ed.* **2006**, *45*, 3686–3689; f) P. Demel, M. Keller, B. Breit, *Chem. Eur. J.* **2006**, *12*, 6669–6683; g) B. Breit, P. Demel, D. Grauer, C. Studte, *Chem. Asian J.* **2006**, *1*, 586–597; h) B. Breit, P. Demel, C. Studte, *Angew. Chem.* **2004**, *116*, 3874; *Angew. Chem. Int. Ed.* **2004**, *43*, 3786–3789.

[3] a) Q. Wang, Y. Kobayashi, *Org. Lett.* **2011**, *13*, 6252–6255; b) Y. Kiyotsuka, Y. Kobayashi, *Tetrahedron* **2010**, *66*, 676–684; c) Y. Kiyotsuka, Y. Kobayashi, *J. Org. Chem.* **2009**, *74*, 7489–7495; d) Y. Kiyotsuka, Y. Katayama, H. P. Acharya, T. Hyodo, Y. Kobayashi, *J. Org. Chem.* **2009**, *74*, 1939–1951; e) Y. Kiyotsuka, H. P. Acharya, Y. Katayama, T. Hyodo, Y. Kobayashi, *Org. Lett.* **2008**, *10*, 1719–1722.

[4] a) C. Feng, Y. Kobayashi, *J. Org. Chem.* **2013**, *78*, 3755–3766; b) Y. Kaneko, Y. Kiyotsuka, H. P. Acharya, Y. Kobayashi, *Chem. Commun.* **2010**, *46*, 5482–5484.

[5] T. B. RajanBabu, W. A. Nugent, D. F. Taber, P. J. Fagan, *J. Am. Chem. Soc.* **1988**, *110*, 7128–7135.

[6] C. C. Tseng, S. D. Paisley, H. L. Goering, *J. Org. Chem.* **1986**, *51*, 2884–2891.

[7] M. C. Warner, A. Nagendiran, K. Bogár, J.-E. Bäckvall, *Org. Lett.* **2012**, *14*, 5094–5097.

[8] Defined as (% *ee* of **2**) × 100/(% *ee* of **1**).

[9] For previous preparations of compounds that correspond to the γ products, see: a) C. S. Yi, D. W. Lee, *Organometallics* **2010**, *29*, 1883–1885; b) J. Almena, F. Foubelo, M. Yus, *Tetrahedron* **1997**, *53*, 5563–5572.

[10] a) J. K. Crandall, J. P. Arrington, J. Hen, *J. Am. Chem. Soc.* **1967**, *89*, 6208–6213; b) S. Nakamura, T. Hayakawa, T. Nishi, Y. Watanabe, T. Toru, *Tetrahedron* **2001**, *57*, 6703–6711; c) K. Shimoda, N. Kubota, H. Hamada, M. Kaji, T. Hirata, *Tetrahedron: Asymmetry* **2004**, *15*, 1677–1679.

[11] E. J. Corey, C. J. Helal, *Angew. Chem.* **1998**, *110*, 2092; *Angew. Chem. Int. Ed.* **1998**, *37*, 1986–2012.

[12] a) J. R. Falck, A. He, L. M. Reddy, A. Kundu, D. K. Barma, A. Bandyopadhyay, S. Kamila, R. Akella, R. Bejot, C. Mioskowski, *Org. Lett.* **2006**, *8*, 4645–4647; b) A. Yanagisawa, R. Goudu, T. Arai, *Org. Lett.* **2004**, *6*, 4281–4283.

[13] The diagnostic olefin protons in the ^{1}H NMR spectrum for *rac*-**3aA** and its *Z* isomer (4:1) are at δ = 4.93 (tt, *J* = 7, 2.5 Hz, 0.8 H) and 5.47 (tm, *J* = 7 Hz, 0.2 H) ppm. The diagnostic olefin protons in the ^{1}H NMR spectrum for *rac*-**3bA** and its *Z* isomer (4:1) are at δ = 4.66 (t, *J* = 7 Hz, 0.8 H) and 5.43 (t, *J* = 7 Hz, 0.2 H) ppm. The major absorbance at δ = 4.93 and 4.66 ppm was coincident with the minor signals seen in the spectra of *rac*-**2aA** and -**2bA**, respectively. On the other hand, the signals of the olefin protons of *rac*-**3aG** and its *Z* isomer were overlapped at δ = 5.12–5.32 (m, 1 H) ppm.

[14] The olefin and/or allylic signals of *rac*-**3aB**, -**3bB**, -**3cA**, and -**3cB** in the ^{1}H NMR spectra were assigned by analogy to *rac*-**3aA** and -**3bA**.

[15] Although the $RuCl_3$-catalyzed oxidation of (*R*)-**2aA** with $NaIO_4$ followed by esterification with CH_2N_2 suffered from a low yield of ketone **7** as a result of the difficult separation from the side product(s), the Baeyer–Villiger oxidation of **7** and sub-

sequent hydrolysis gave a sufficient quantity of **8** to determine the specific rotation. To avoid this problem, an ozonolysis reaction followed by a Jones oxidation was applied to (*R*)-**2bA** to produce ketone **9** in moderate yield. A further transformation furnished **8** as well.

[16] Z. Cao, Z. Liu, Y. Liu, H. Du, *J. Org. Chem.* **2011**, *76*, 6401–6406.

[17] The stereochemistry of the product was speculated. The *ee* value and, thus, the C. T. could not be determined by HPLC analysis, even with six attempted chiral columns.

[18] a) N. Yoshikai, E. Nakamura, *Chem. Rev.* **2012**, *112*, 2339–2372; b) N. Yoshikai, S.-L. Zhang, E. Nakamura, *J. Am. Chem. Soc.* **2008**, *130*, 12862–12863.

[19] To compare leaving groups, the substitution of the allylic mesylate and acetate with the PhMgBr/Cu(acac)$_2$ reagent was attempted. However, the mesylation of alcohol *rac*-**4a** gave a mixture of products, most likely because of the instability of the allylic mesylate. On the other hand, the acetate, which was prepared from *rac*-**4a**, showed no reactivity toward the 2:1 PhMgBr/Cu(acac)$_2$ reagent under the conditions presented in Table 1, Entry 4.

[20] A. Martinez-Grau, D. P. Curran, *Tetrahedron* **1997**, *53*, 5679–5698.

[21] E. Wenkert, T. W. Ferreira, *Organometallics* **1982**, *1*, 1670–1673.

Received: May 28, 2013
Published Online: August 27, 2013

