Asymmetric Addition of Alkyllithium to Chiral Imines: α-Naphthylethyl Group as a Chiral Auxiliary

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The diastereoselective nucleophilic addition of alkyllithium to *N*-alkylidene-α-naphthylethylamine was carried out. In the presence of Lewis acids or Lewis bases, organolithiums reacted smoothly with imines to give the corresponding amines in high stereoselectivity (up to 100% de). Furthermore, the resulting optically active amines were found to be useful for asymmetric reactions as chiral ligands.

Introduction

Chiral amines are often critical components of biologically active compounds and pharmaceutical agents. The nucleophilic addition of organometallic reagents to imines is one of the key methods for preparing various amines. A variety of asymmetric alkylations of imines have been explored to date.[1] The diastereoselective addition of organometallic reagents to the C═N bond of chiral compounds such as imines,[2] hydrazones,[3] oxime ethers,[4] sulfinimines,[5] and chiral acyliminium ions[6] with organometallic reagents is an appealing route to obtain enantiomerically pure amines after removing chiral auxiliaries. Also, the enantioselective alkylation of achiral imines has been investigated using various external chiral ligands.[7]

As part of a project aimed at developing a method for the synthesis of enantiomerically pure amines, we previously reported the asymmetric reduction of imines using newly developed chiral boranes,[8] and more recently we reported the first enantioselective asymmetric Pictet−Spengler reaction of nitrones (**1a)**,[9] which is considered an intramolecular addition of an indole ring to imines (Scheme 1). We also found that the diastereoselective Pictet−Spengler reaction of **1b** proceeded with moderate stereoselectivity (up to 72% de) using an α-phenylethyl group as a chiral auxiliary,[10] whereas the bulkier α-naph-

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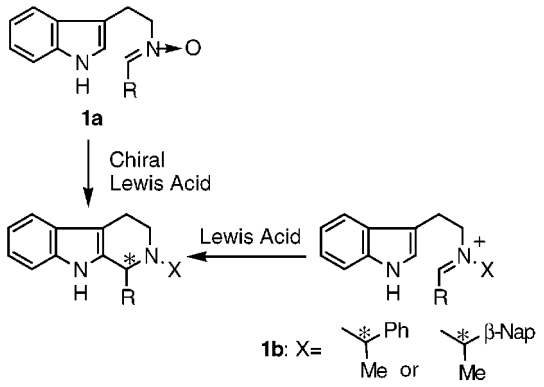
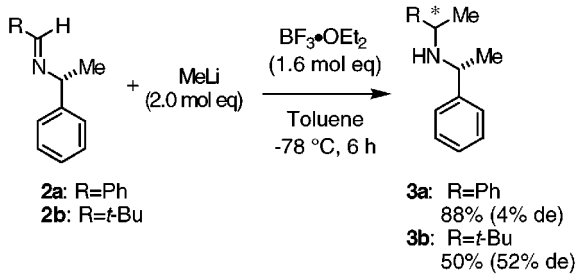
Scheme 1



Scheme 2



thylethyl group[11] gave higher diastereoselectivity (up to 86% de). On the other hand, in the diastereoselective nucleophilic addition of imines using an α-phenylethyl group, Yamamoto and co-workers[2e] reported that Cram selectivity is remarkably enhanced in the reaction of imines with allyl-9-BBN. In addition, Savoia and co-worker[2h] found that methylcopper−boron trifluoride reacted with imines derived from chiral amines in high stereoselectivity.

These results prompted us to investigate the intermolecular asymmetric addition to imines. In this paper, we report the details of the highly diastereoselective addition of organolithium reagents to imines, in which a chiral α-naphthylethyl group is used as a chiral auxiliary.[12]

Results and Discussion

In preliminary reactions, we carried out the reaction of methyllithium with a chiral imine, which was prepared from (*R*)-α-phenylethylamine with benzaldehyde and pivalaldehyde, respectively (Scheme 2). However, the results were not satisfactory. Therefore, we chose a bulkier α-naphthylethylamine to improve the asymmetric induction. The requisite chiral *N*-alkylidenenaphthylethylamines **4**−**11** were simply prepared from (*R*)-α-naphthylethylamine and the corresponding aldehydes (Scheme 3). We first focused our attention on the addition of *n*-butyllithium to a typical imine substrate **4**. The results are presented in Table 1. The addition of *n*-butyllithium (2.0 equiv) to a toluene solution of (*R*)-**4** at −78 °C gave a mixture of alkylated amines (*R*,*R*)-**12** and

Scheme 3

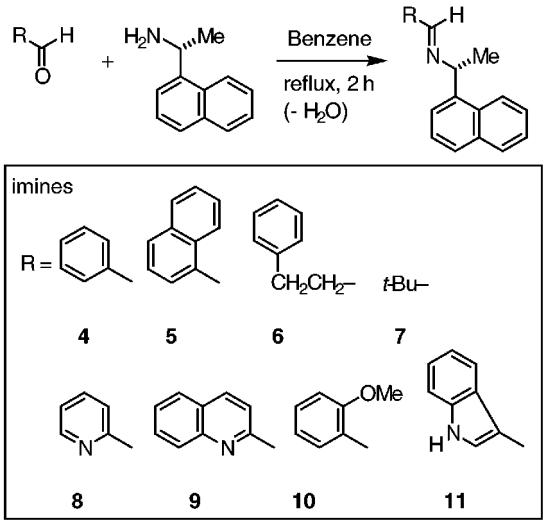
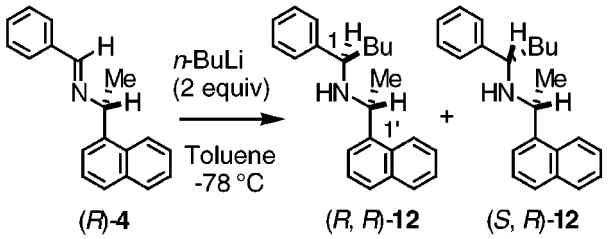


Table 1. Diastereoselective Alkylation of Imine 4



run	additive	time (h)	yield (%)	(*R*,*R*):(*S*,*R*)	% de
1	none	3	32	79:21	58
2	BF_3·OEt_2[a]	1	76	93:7	86
3	BF_3·OEt_2[b]	0.7	92	92:8	84
4	BF_3·OEt_2[a,d]	1	84	87:13	74
5	BF_3·OEt_2[a,e]	2	80	79:21	58
6	TMEDA[c]	1	99	90:10	80
7	*l*-sparteine[c]	1.2	66	98:2	96
8	*l*-sparteine[c,f]	4.5	41	71:29 [(*S*,*S*):(*R*,*S*)]	42

[a] 1.6 equiv. [b] 3 equiv. [c] 2 equiv. [d] −45 °C. [e] −20 °C. [f] (*S*)-**4** was used.

(*S*,*R*)-**12** in 32% yield (run 1). The diastereomeric excess was determined to be 58% de by ^{1}H NMR analysis of the amines before and/or after purification. The proton at the new stereocenter appeared as two clearly separated signals (*R*,*R*: 3.35 ppm; *S*,*R*: 3.76 ppm) for the two diastereoisomers, and there were two well-separated methine protons at the 1′ position (*R*,*R*: 4.36 ppm; *S*,*R*: 4.48 ppm). The absolute configuration of the newly formed chiral center in the adducts was confirmed as described below. Tomioka and co-workers reported the asymmetric addition of methyllithium to imine in the presence of chiral ligands,[7a] in which a coordinated Li cation activated the imines as a Lewis acid. In our reaction, however, the use of excess *n*-butyllithium (5.0 equiv) did not improve the yield or selectivity.

Therefore, we investigated the effect of Lewis acids on the addition of alkyllithium. Although the addition of $MgBr_2$·OEt_2 (no reaction) or $Mg(OEt)_2$ (21% yield, 52% de) was not effective, the addition of BF_3·OEt_2 to the reaction of (*R*)-**4** with *n*-butyllithium increased the chemical yield with a high diastereomeric excess. Thus, the reaction of (*R*)-**4** with *n*-butyllithium in the presence of BF_3·OEt_2 (1.6 equiv) proceeded smoothly to give **12** within 1 h in 76% yield with 86% de (run 2), whereas

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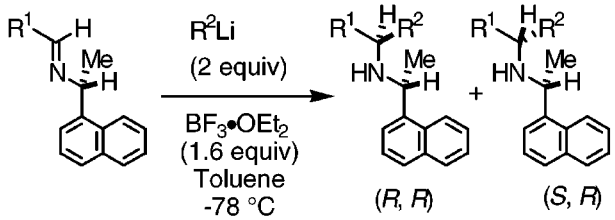
Table 2. Diastereoselective Alkylation of Various Imines



run	imine	R^2Li	time (h)	amine	yield (%)	(*R*,*R*):(*S*,*R*)	% de
1	**4**	*n*-Bu	1	**12**	76	93:7	86
2		Me	2	**13**	88	92:8	84
3		*t*-Bu	6	**14**	5	41:59	18
4		*t*-Bu[a]	1	**14**	99	63:37	26
5	**5**	Me	1	**15**	98	95:5	90
6	**6**	Me	4	**16**	56	>99:1	∼100
7		*n*-Bu	25	**17**	26	>99:1	∼100
8	**7**	Me	1.5	**18**	76	>99:1	∼100
9		*n*-Bu	1.5	**19**	93	85:15	70

[a] THF was used.

when 3.0 equiv of BF_3·OEt_2 was used, the yield increased dramatically up to 92% (run 3). Thus, it appears that BF_3·OEt_2 activated not only the C=N double bonds but also controlled the conformation of the α-naphthylethyl group.

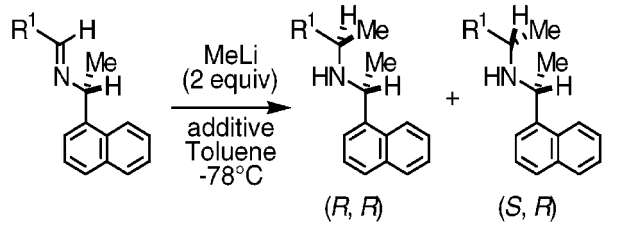
In the presence of BF_3·OEt_2, the diastereoselectivity decreased with an increase in the reaction temperature (runs 4 and 5). Changing solvents from toluene to THF, Et_2O, and CH_2Cl_2 had only a small effect on the chemical yields and diastereoselectivities.

The addition of a Lewis base such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) enhanced the reaction of *n*-butyllithium with imine (*R*)-**4** to give a nearly quantitative yield with high diastereomeric excess (80% de, run 6). Furthermore, the addition of *l*-sparteine as a chiral Lewis base gave the best results, with a diastereomeric excess of 96% de (run 7), whereas a similar reaction with (*S*)-**4** gave **12** in 41% yield with poor diastereoselectivity (42% de, run 8), indicating a mismatched pair. These results suggest that the addition of Lewis acids or Lewis bases improves the yield and diastereoselectivity.

A range of commercially available alkyllithium compounds was also added to a wide range of imines under BF_3·OEt_2-assisted conditions, and the results were studied in detail (Table 2). Reaction of (*R*)-**4** with methyllithium gave **13** in 88% yield in a diastereomeric ratio of 92:8 (run 2). A significantly lower yield and selectivity were observed for the reaction of (*R*)-**4** with *tert*-butyllithium in toluene. In THF, however, *tert*-butyllithium reacted with (*R*)-**4** quantitatively (run 4). The reaction of (*R*)-**5**, derived from 1-naphthaldehyde, with methyllithium gave (*R*,*R*)-**15** in 90% de. Reaction of the imine (*R*)-**6**, which has α-hydrogens, with either methyllithium or *n*-butyllithium resulted in the corresponding amines in low chemical yield but gave excellent diastereoselectivity. Reaction of imine (*R*)-**7**, which has a branched alkyl group, with methyllithium gave the best result, with a diastereomeric excess of ∼100% de (run 8).

This reaction was extended to other imines bearing an alkoxyphenyl group or a pyridine or quinoline ring, which may chelate to alkyllithiums or additives and enhance the stereoselectivity of organometallic addition to a carbonyl group (Table 3). When methyllithium was added to imines with a pyridine or quinoline ring, such as (*R*)-**8** or (*R*)-**9,** in BF_3·OEt_2-mediated conditions, low yields and modest diastereoselectivities were observed (runs 3 and 7), suggesting that boron trifluoride coordinated to a ring nitrogen atom. Therefore, we carried out the reaction of (*R*)-**8** with methyllithium without using BF_3·OEt_2 and found that the yield increased up to 63% (run 4). Interestingly, in contrast to the BF_3·OEt_2-mediated reaction of **8**, the opposite diastereomer (*S*,*R*)-**20** was the major product in 70% de. Furthermore, the addition of TMEDA increased the yield and diastereoselectivity (93%, 76% de, run 5). The addition of *l*-sparteine showed similar results and gave the (*S*,*R*) isomer as the major product. The same procedures were applied to quinoline derivative (*R*)-**9**, which also furnished the (*S*,*R*) isomer as the major product, provided TMEDA or *l*-sparteine was used. The reaction of methyllithium with imine (*R*)-**10**, derived from 2-methoxybenzaldehyde, also showed a similar trend. In contrast, methyllithium did not react with the imine **11**, which has an indole ring. The above results indicated that the reaction of (*R*)-**8**−(*R*)-**10** in the presence of BF_3·OEt_2 gave (*R*,*R*)-amines predominantly, whereas when a Lewis base was used, (*S*,*R*)-amines were the major diastereomers.

Table 3. Effect of Additives on the Diastereoselective Alkylation of Various Imines



run	imine	additive (equiv)	time (h)	amine	yield (%)	(*R*,*R*):(*S*,*R*)	% de
1	**4**	none[a]	3	**12**	32	79:21	58
2		BF_3·OEt_2 (1.6)	2	**13**	88	92:8	84
3	**8**	BF_3·OEt_2 (1.6)	3	**20**	46	84:16	68
4		none	3		63	15:85	70
5		TMEDA (2)	3		93	12:88	76
6		*l*-sparteine (2)	1		83	24:76	52
7	**9**	BF_3·OEt_2 (3.2)	4	**21**	52	72:28	44
8		TMEDA (2)	3		96	19:81	62
9		*l*-sparteine[b] (2)	6		56	24:76	52
10	**10**	BF_3·OEt_2 (1.6)	3	**22**	76	88:12	76
11		TMEDA (2)	6		32	35:65	30
12	**11**	BF_3·OEt_2[b] (3.2)	4	**23**	NR		

[a] *n*-BuLi (2 equiv) was used. [b] MeLi (4 equiv) was used.

The absolute configuration of the newly formed chiral center was determined as follows. The chiral auxiliary was removed from **18** by hydrogenolysis [H_2, $Pd(OH)_2$/C], and the resulting chiral amine was converted to known *N*-tosyl-3,3-dimethyl-2-butylamine **24**[13] (Scheme 4). Comparison of the specific rotation of **24** ($[\alpha]^{15}_D$ +39.3 (*c* 1.05, EtOH)) with the reported value[13] ($[\alpha]_D$ −12.85 (EtOH) for 59.6% ee (*S*)) showed that the absolute configuration of **24** was (*R*), and hence the absolute configuration of **18** was (1*R*,1′*R*). The configuration of **24** was confirmed by X-ray analysis.[14] Similarly, hydrogenolysis of **16** followed by tosylation gave sulfonamide **25**[2a] ($[\alpha]^{25}_D$ +22.1 (*c* 0.88, EtOH)). The newly formed

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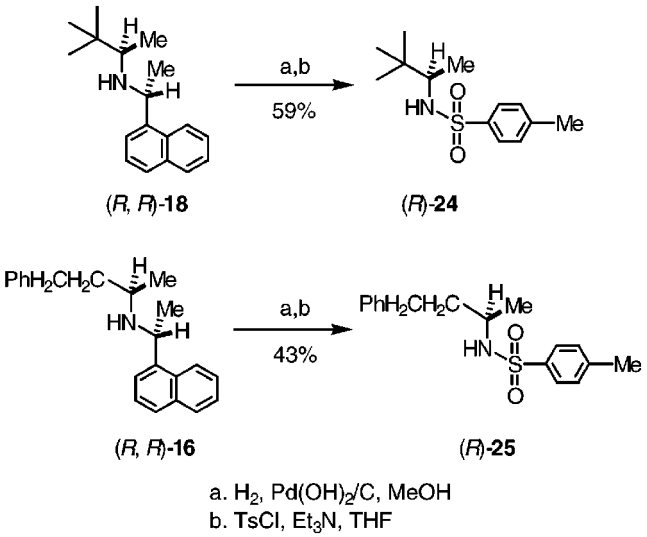
(14) The experimental details of X-ray analysis are provided as Supporting Information.

Scheme 4



chiral center was assigned to be (*R*) on the basis of the reported specific rotation ($[\alpha]^{23}_D$ +28 (*c* 1.7, EtOH) for (*R*)-**25**). The stereochemistry of **15** was determined to be (1*R*,1′*R*) on the basis of a comparison of its ^{1}H NMR spectrum with published data.[15] The crystallographic structure of (*R*,*R*)-**13** also confirmed that the absolute configuration of the new stereogenic center was (*R*).[14] In the ^{1}H NMR spectra of these diastereomeric mixtures, the two methine protons of the (*R*,*R*) diastereomers gave signals at fields higher than those of the (*S*,*R*) diastereomers.

Although the detail course of stereoselective reaction pathway is yet unclear, we have tried a semiempirical molecular orbital calculation of BF_3-complexed (*R*)-**4**[16] and the lowest-energy conformation of BF_3-complexed (*R*)-**4** is shown in Figure 1 (transition state A). In this conformation, the naphthyl group is almost perpendicular to the π-plane, which consists of C=N double bonds and the phenyl group, and shields the bottom face of the π-plane. Therefore, the alkyllithium reagent should attack from the top of the π-plane and give the observed diastereomer predominantly. This model may be supported by the poor asymmetric induction obtained by the reaction using an α-phenylethyl group as a chiral auxiliary (4% de, Scheme 2).

In the case of imine (*R*)-**8**, which has a pyridine ring, alkylation proceeded smoothly without BF_3·OEt_2 to give the (*S*,*R*) diastereomer predominantly. It seemed that methyllithium coordinated to two nitrogen atoms to form a rigid five-membered ring to stabilize the transition state. When alkylation occurs with methyllithium, with coordination of the lithium atom in the five-membered ring, the reagent will attack from the *si* face to avoid unfavorable interaction with the α-methyl group (transition states B and C). A similar approach can be used to explain why alkylation of imines (*R*)-**8** or (*R*)-**9** gave an opposite stereoselectivity using BF_3·OEt_2 or TMEDA.

Recently, the asymmetric deprotonation of prochiral ketones using chiral lithium amides has been widely studied.[17] The resulting chiral amines (*R*,*R*)-**13**, (*R*,*R*)-**15**, and (*R*,*R*)-**22** were converted into chiral lithium amides and tested in the asymmetric deprotonation of *tert*-butylcyclohexanone **26** under the conditions developed by Simpkins[17a] (Table 4). When (*R*,*R*)-**13** or (*R*,*R*)-**15** was used, silylenolether (*S*)-**27** was obtained predominantly (runs 2 and 3). Interestingly, the introduction of a 2-methoxy group to the phenyl ring of (*R*,*R*)-**22** gave the opposite stereoselectivity. While the mechanism of the asymmetric induction is not yet clear, these finding may be useful for designing new chiral amines for asymmetric deprotonation.

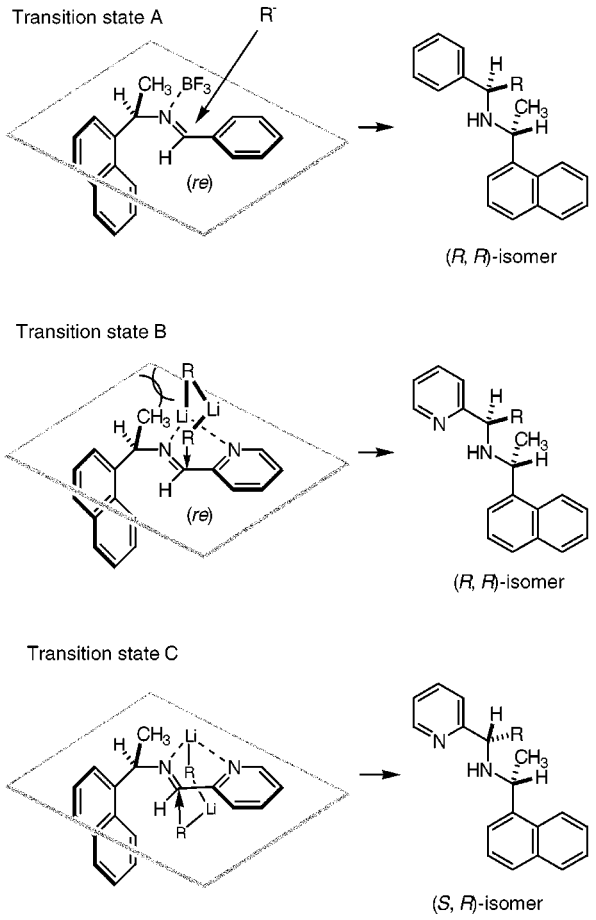


Figure 1. Transition state models for the diastereoselective alkylation of imines.

In summary, high diastereoselectivity was observed in the reaction of organolithiums and chiral imines that contain an α-naphthylethyl group as a chiral auxiliary. Transition state models to explain this diastereoselectivity were presented. The application of the resulting chiral amines to other asymmetric reactions is in progress.

Experimental Section

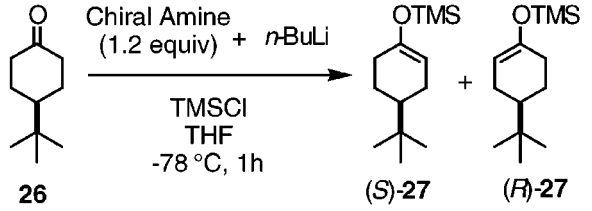
Synthesis of (*R*)-*N*-Benzylidene-1-phenylethylamine (2a). Typical Procedure. A mixture of benzaldehyde (3.1 mL, 30.4 mmol) and (*R*)-α-phenylethylamine (3.8 mL, 29.4 mmol) in benzene (50 mL) was heated for 2 h at reflux temperature using a Dean−Stark apparatus. The mixture was concentrated under reduced pressure to give the imine **2a** (5.90 g, 96%) as

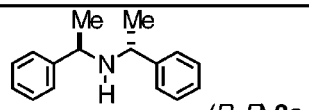
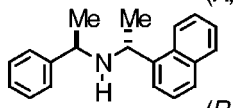
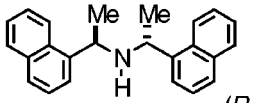
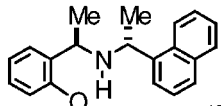
(15) Majewski, M.; MacKinnon, J. *Can. J. Chem.* **1994**, *72*, 1699−1704.

(16) The calculation (MOPAC, AM1) was carried out using CAChe system Version 3.8, CAChe Scientific Inc., 1995.

(17) (a) Cousins, R. P. C.; Simpkins, N. S. *Tetrahedron Lett.* **1989**, *30*, 7241−7244. (b) Cox, P. J.; Simpkins, N. S. *Tetrahedron: Asymmetry* **1991**, *2*, 1−26. (c) Koga, K. *J. Synth. Org. Chem., Jpn.* **1990**, *48*, 463−475. (d) Koga, K.; Shindo, M. *J. Synth. Org. Chem., Jpn.* **1995**, *53*, 1021−1032.

Table 4. Asymmetric Deprotonation of 4-*tert*-butylcyclohexanone using Chiral Lithium Amide



run	Chiral amine	Yield (%)	% ee
1	 (*R*, *R*)-**3a**	73	69 (*S*) [a]
2	 (*R*, *R*)-**13**	48	69 (*S*)
3	 (*R*, *R*)-**15**	18	57 (*S*)
4	 (*R*, *R*)-**22**	32	45 (*R*)

[a] Reference 17a.

a yellow oil; **2a** was used for the next reaction without further purification: $[\alpha]^{27}_D$ −64.7 (*c* 1.0, $CHCl_3$); IR (neat) 3060, 1645, 1600, 1580, 1490 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59 (3H, d, J = 6.8 Hz), 4.55 (1H, q, J = 6.6 Hz), 7.22−7.44 (8H, m), 7.78 (2H, m), 8.37 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.83, 69.65, 126.57, 126.76, 128.20, 128.35, 128.45, 130.98, 136.36, 145.15, 159.35; LRFABMS *m*/*z* 210 (M^+ + H); HRFABMS calcd for $C_{15}H_{16}N$ (M^+ + H) 210.1283, found 210.1298.

(*R*)-*N*-(2,2-Dimethylpropylidene)-1-phenylethylamine (2b). 98% yield (reflux, 2 h); colorless oil; $[\alpha]^{27}_D$ +60.2 (*c* 1.0, $CHCl_3$); IR (neat) 3060, 1665, 1600, 1490 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (9H, s), 1.45 (3H, d, J = 6.8 Hz), 4.27 (1H, q, J = 6.7 Hz), 7.21 (1H, m), 7.29−7.36 (4H, m), 7.61 (1H, d, J = 0.7 Hz); ^{13}C NMR ($CDCl_3$) δ 24.96, 26.95, 35.97, 68.99, 126.38, 126.45, 128.20, 145.59, 170.18; LRFABMS *m*/*z* 190 (M^+ + H); HRFABMS calcd for $C_{13}H_{20}N$ (M^+ + H) 190.1596, found 190.1578.

Synthesis of (1*R*,1′*R*)-Bis(1-phenylethyl)amine [(*R*,*R*)-3a] and (1*S*,1′*R*)-Bis(1-phenylethyl)amine [(*S*,*R*)-3a]. Typical Procedure. Methyllithium (2.64 mL of a 1.14 M solution of Et_2O, 3.0 mmol) was added dropwise to a stirred solution of the imine **2a** (314.4 mg, 1.5 mmol) and $BF_3{\cdot}OEt_2$ (0.30 mL, 2.4 mmol) in dry toluene (35 mL) at −78 °C under an argon atmosphere for 2 min. After being stirred at −78 °C for 6 h, the reaction was quenched with saturated $NaHCO_3$ (20 mL). The reaction mixture was diluted with AcOEt (20 mL), and the organic layer was separated, washed with brine (20 mL), and dried over Na_2SO_4. After removal of the solvent, the yellow oil was subjected to column chromatography on silica gel with AcOEt/*n*-hexane (1/40) to give a diastereomeric mixture of (*R*,*R*)-**3a** and (*S*,*R*)-**3a** (298.0 mg, 88%) as a pale yellow oil. ^1H NMR analysis of the product indicated a 52:48 ratio of diastereomers, which were inseparable by column chromatography: IR (neat) 3080, 1600, 1495, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) **(*R*,*R*)-3a**[18] (major isomer) δ 1.27 (6H, d, J = 6.6 Hz), 1.57 (1H, brs), 3.50 (2H, q, J = 6.6 Hz), 7.20−7.36 (10H, m); **(*S*,*R*)-3a** (minor isomer) δ 1.35 (6H, d, J = 6.6 Hz), 1.57 (1H, brs), 3.76 (2H, q, J = 6.6 Hz), 7.20−7.36 (10H, m); LRFABMS *m*/*z* 226 (M^+ + H).

(2*R*,1′*R*)-*N*-(1′-Phenylethyl)-3,3-dimethyl-2-butylamine [(*R*,*R*)-3b] and (2*S*,1′*R*)-*N*-(1′-Phenylethyl)-3,3-dimethyl-2-butylamine [(*S*,*R*)-3b]. 50% yield (76:24, −78 °C, 6 h); colorless oil. **(*R*,*R*)-3b** (major isomer): colorless oil; $[\alpha]^{26}_D$ −5.5 (*c* 1.2, $CHCl_3$); IR (neat) 3080, 1600, 1495, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (3H, d, J = 6.6 Hz), 0.89 (9H, s), 1.18 (1H, brs), 1.28 (3H, d, J = 6.6 Hz), 2.30 (1H, q, J = 6.5 Hz), 3.77 (1H, q, J = 6.6 Hz), 7.16 (1H, m), 7.28−7.36 (4H, m); ^{13}C NMR ($CDCl_3$) δ 15.95, 23.61, 26.53, 34.74, 57.07, 59.62, 126.67, 126.70, 128.25, 147.49; LRFABMS *m*/*z* 206 (M^+ + H); HRFABMS calcd for $C_{14}H_{24}N$ (M^+ + H) 206.1909, found 206.1906. **(*S*,*R*)-3b** (minor isomer): colorless oil; $[\alpha]^{26}_D$ +98.3 (*c* 1.5, $CHCl_3$); IR (neat) 3060, 1600, 1490, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (9H, s), 0.95 (3H, d, J = 6.3 Hz), 1.16 (1H, brs), 1.32 (3H, d, J = 6.6 Hz), 2.00 (1H, q, J = 6.3 Hz), 3.86 (1H, q, J = 6.6 Hz), 7.20−7.32 (5H, m); ^{13}C NMR ($CDCl_3$) δ 14.20, 25.59, 26.47, 34.11, 55.36, 58.04, 126.58, 126.99, 128.09, 146.16; LRFABMS *m*/*z* 206 (M^+ + H); HRFABMS calcd for $C_{14}H_{24}N$ (M^+ + H) 206.1909, found 206.1905.

Synthesis of (*R*)-*N*-Benzylidene-1-(1-naphthyl)ethylamine (4). Typical Procedure. A mixture of benzaldehyde (3.10 mL, 30.5 mmol) and (*R*)-1-(1-naphthyl)ethylamine (5.14 g, 30.0 mmol) in benzene (50 mL) was heated for 2 h at reflux temperature using a Dean−Stark apparatus. The mixture was concentrated under reduced pressure, and the residue was recrystallized from *n*-hexane to give the imine **4** (7.42 g, 95%) as orange prisms: mp 89.5−90.5 °C (*n*-hexane); $[\alpha]^{15}_D$ −250.3 (*c* 1.04, $CHCl_3$); $[\alpha]^{17}_D$ +250.4 (*c* 1.0, $CHCl_3$) for (*S*)-**4**; IR (KBr) 3040, 1640, 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72 (3H, d, J = 6.6 Hz), 5.33 (1H, q, J = 6.6 Hz), 7.36−7.52 (6H, m), 7.72−7.85 (5H, m), 8.24 (1H, d, J = 8.0 Hz), 8.39 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.53, 65.56, 123.59, 124.00, 125.28, 125.66, 125.75, 127.29, 128.24, 128.49, 128.90, 130.53, 130.64, 133.97, 136.49, 141.16, 159.56; LRFABMS *m*/*z* 260 (M^+ + H). Anal. calcd for $C_{19}H_{17}N$: C, 87.99; H, 6.61; N, 5.40. Found: C, 88.30; H, 6.69; N, 5.51.

(*R*)-*N*-[(1-Naphthyl)methylene]-1-(1-naphthyl)ethylamine (5). 98% yield (reflux, 3 h); brown oil; $[\alpha]^{22}_D$ −231.6 (*c* 0.98, $CHCl_3$); IR (neat) 3050, 1640, 1620, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.82 (3H, d, J = 6.6 Hz), 5.42 (1H, q, J = 6.6 Hz), 7.45−7.61 (6H, m), 7.75 (1H, d, J = 8.0 Hz), 7.83−7.91 (5H, m), 8.32 (1H, d, J = 8.6 Hz), 9.00 (1H, d, J = 8.5 Hz), 9.04 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.89, 67.00, 123.63, 124.10, 124.55, 125.15, 125.31, 125.71, 125.78, 125.94, 127.05, 127.33, 128.53, 128.94, 129.17, 130.62, 130.92, 131.29, 131.78, 133.79, 134.01, 141.24, 159.50; LRFABMS *m*/*z* 310 (M^+ + H); HRFABMS calcd for $C_{23}H_{20}N$ (M^+ + H) 310.1596, found 310.1604.

Synthesis of (*R*)-*N*-(3-Phenylpropylidene)-1-(1-naphthyl)ethylamine (6). A solution of 3-phenylpropionaldehyde (1.0 mL, 8.0 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise to a stirred solution of the amine (1.3 mL, 8.0 mmol) in the presence of anhydrous $MgSO_4$ (4.0 g) in dry CH_2Cl_2 (90 mL) at 0 °C over a period of 20 min. After being stirred at 0 °C for 2 h, the mixture was filtered through a Celite pad. The filtrate was concentrated under reduced pressure to give the imine **6** (2.27 g, 99%) as a yellow oil: IR (neat) 3060, 1665, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68 (3H, d, J = 6.8 Hz), 2.62 (2H, dt, J = 4.7, 7.8 Hz), 2.87 (2H, t, J = 7.7 Hz), 5.11 (1H, q, J = 6.7 Hz), 7.22−7.26 (5H, m), 7.42−7.51 (3H, m), 7.65 (1H, d, J = 6.8 Hz), 7.73 (1H, d, J = 8.1 Hz), 7.82−7.86 (2H, m), 8.10 (1H, d, J = 6.8 Hz); LRFABMS *m*/*z* 288 (M^+ + H). This compound was not stable enough to give a satisfactory HRFABMS and was used for the next reaction.

(*R*)-*N*-(2,2-Dimethylpropylidene)-1-(1-naphthyl)ethylamine (7). 96% yield (reflux, 2 h); orange oil; $[\alpha]^{18}_D$ −36.9 (*c* 0.99, $CHCl_3$); IR (neat) 3040, 1670, 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (9H, s), 1.58 (3H, d, J = 6.9 Hz), 5.06 (1H, q, J = 6.6 Hz), 7.35 (1H, d, J = 0.7 Hz), 7.43−7.54 (3H, m), 7.72 (2H,

(18) Eleveld, M. B.; Hogeveen, H.; Schudde, E. P. *J. Org. Chem.* **1986**, *51*, 3635−3642.

m), 7.84 (1H, m), 8.15 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 24.63, 26.87, 36.03, 65.07, 123.56, 123.66, 125.10, 125.49, 125.59, 126.96, 128.77, 130.53, 133.83, 141.47, 170.07; LRFABMS m/z 240 (M^+ + H); HRFABMS calcd for $C_{17}H_{22}N$ (M^+ + H) 240.1752, found 240.1733.

(*R*)-*N*-[(2-Pyridyl)methylene]-1-(1-naphthyl)ethylamine (8). 96% yield (reflux, 3 h); brown oil; $[\alpha]^{26}_D$ −196.1 (c 1.1, $CHCl_3$); IR (neat) 3050, 1650, 1585 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.77 (3H, d, J = 6.6 Hz), 5.47 (1H, q, J = 6.6 Hz), 7.30 (1H, ddd, J = 1.2, 4.9, 7.6 Hz), 7.46−7.55 (3H, m), 7.72−7.81 (3H, m), 7.87 (1H, dd, J = 1.5, 8.1 Hz), 8.15 (1H, dt, J = 1.0, 7.8 Hz), 8.25 (1H, d, J = 8.6 Hz), 8.51 (1H, s), 8.63 (1H, ddd, J = 1.0, 1.7, 4.9 Hz); ^{13}C NMR ($CDCl_3$) δ 24.07, 65.10, 121.32, 123.44, 123.95, 124.58, 125.28, 125.52, 125.82, 127.45, 128.85, 130.62, 133.93, 136.36, 140.30, 149.22, 154.74, 160.60; LRFABMS m/z 261 (M^+ + H); HRFABMS calcd for $C_{18}H_{17}N_2$ (M^+ + H) 261.1392, found 261.1394.

(*R*)-*N*-[(2-Quinolyl)methylene]-1-(1-naphthyl)ethylamine (9). 99% yield (reflux, 3 h); brown oil; $[\alpha]^{27}_D$ −130.6 (c 0.83, $CHCl_3$); IR (neat) 3040, 1645, 1595 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.80 (3H, d, J = 6.5 Hz), 5.54 (1H, q, J = 6.6 Hz), 7.47−7.67 (4H, m), 7.73 (1H, ddd, J = 1.4, 7.0, 8.4 Hz), 7.78 (1H, d, J = 8.1 Hz), 7.83−7.89 (3H, m), 8.10 (1H, d, J = 8.3 Hz), 8.19 (1H, d, J = 8.3 Hz), 8.28 (1H, d, J = 8.5 Hz), 8.32 (1H, d, J = 8.6 Hz), 8.69 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.07, 65.19, 118.49, 123.49, 124.03, 125.32, 125.55, 125.86, 127.25, 127.53, 127.59, 128.66, 128.87, 129.42, 129.64, 130.67, 133.97, 136.33, 140.23, 147.63, 155.00, 161.10; LRFABMS m/z 311 (M^+ + H); HRFABMS calcd for $C_{22}H_{19}N_2$ (M^+ + H) 311.1548, found 311.1527.

(*R*)-*N*-(2-Methoxybenzylidene)-1-(1-naphthyl)ethylamine (10). 95% yield (reflux, 2 h); brown oil; $[\alpha]^{27}_D$ −157.5 (c 1.0, $CHCl_3$); IR (neat) 3040, 1635, 1600, 1285, 1245, 1180 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.73 (3H, d, J = 6.6 Hz), 3.85 (3H, s), 5.35 (1H, q, J = 6.6 Hz), 6.90 (1H, d, J = 8.0 Hz), 7.00 (1H, t, J = 7.5 Hz), 7.37 (1H, ddd, J = 1.7, 7.3, 8.3 Hz), 7.45−7.55 (3H, m), 7.66 (1H, d, J = 7.4 Hz), 7.83−7.87 (2H, m), 8.12 (1H, dd, J = 1.9, 7.8 Hz), 8.28 (1H, d, J = 8.8 Hz), 8.91 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.78, 55.44, 66.09, 110.92, 120.76, 123.63, 123.93, 124.96, 125.19, 125.66, 125.69, 127.11, 127.56, 128.86, 130.62, 131.74, 133.96, 141.67, 155.66, 158.75; LRFABMS m/z 290 (M^+ + H); HRFABMS calcd for $C_{20}H_{20}NO$ (M^+ + H) 290.1545, found 290.1575.

(*R*)-*N*-[(3-Indolyl)methylene]-1-(1-naphthyl)ethylamine (11). 96% yield (reflux, 3 h); brown amorphous solid; $[\alpha]^{27}_D$ −330.9 (c 0.80, $CHCl_3$); IR (KBr) 3400, 3045, 1630, 1620, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.76 (3H, d, J = 6.8 Hz), 5.27 (1H, q, J = 6.6 Hz), 7.28−7.36 (3H, m), 7.42 (1H, s), 7.45−7.56 (3H, m), 7.74 (1H, d, J = 8.0 Hz), 7.87 (1H, d, J = 8.0 Hz), 7.92 (1H, d, J = 6.8 Hz), 8.32−8.35 (2H, m), 8.56 (1H, m), 8.62 (1H, s); ^{13}C NMR ($CDCl_3$) δ 25.01, 66.16, 111.23, 115.56, 121.25, 121.86, 123.14, 123.80, 124.07, 125.24, 125.42, 125.67, 125.75, 127.10, 128.65, 128.87, 130.70, 133.95, 136.65, 141.93, 154.07; LRFABMS m/z 299 (M^+ + H); HRFABMS calcd for $C_{21}H_{19}N_2$(M^+ + H) 299.1548, found 299.1539.

Diastereoselective Alkylation of Imines. Synthesis of (1*R*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-1-phenyl-1-pentylamine [(*R*,*R*)-12] and (1*S*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-1-phenyl-1-pentylamine [(*S*,*R*)-12)]. Typical Procedure (Table 1, run 2). *n*-Butyllithium (0.63 mL of a 1.6 M solution of *n*-hexane, 1.0 mmol) was added dropwise to a stirred solution of the imine **4** (129.5 mg, 0.5 mmol) and BF_3·OEt_2 (0.10 mL, 0.8 mmol) in dry toluene (10 mL) at −78 °C under an argon atmosphere for 2 min. After being stirred at −78 °C for 1 h, the reaction was quenched with saturated $NaHCO_3$ (10 mL). The reaction mixture was diluted with AcOEt (10 mL), and the organic layer was separated, washed with brine (10 mL), and dried over Na_2SO_4. After removal of the solvent, the yellow oil was subjected to column chromatography on silica gel with AcOEt/*n*-hexane (1/30−1/10) to give a diastereomeric mixture of (*R*,*R*)-**12** and (*S*,*R*)-**12** (120.1 mg, 76%) as a pale yellow oil. ^{1}H NMR analysis of the product indicated a 93:7 ratio of diastereomers, which were inseparable by column chromatography. IR (neat) 3060, 1600, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) **(*R*,*R*)-12** (major isomer) δ 0.79 (3H, t, J = 7.2 Hz), 1.08−1.28 (4H, m), 1.35 (3H, d, J = 6.6 Hz), 1.53−2.74 (3H, m), 3.35 (1H, t, J = 7.1 Hz), 4.36 (1H, q, J = 6.7 Hz), 7.09−7.11 (2H, m), 7.21−7.60 (6H, m), 7.69−7.76 (2H, m), 7.81−7.89 (2H, m); **(*S*,*R*)-12** (minor isomer) δ 0.82 (3H, t, J = 7.1 Hz), 1.08−1.28 (4H, m), 1.49 (3H, d, J = 6.3 Hz), 1.53−2.74 (3H, m), 3.76 (1H, dd, J = 5.8, 8.0 Hz), 4.48 (1H, q, J = 6.4 Hz), 7.09−7.11 (2H, m), 7.21−7.60 (6H, m), 7.69−7.76 (2H, m), 7.81−7.89 (2H, m); LRFABMS m/z 318 (M^+ + H); HRFABMS calcd for $C_{23}H_{28}N$ (M^+ + H) 318.2222, found 318.2218.

(1*R*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-1-phenylethylamine [(*R*,*R*)-13] and (1*S*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-1-phenylethylamine [(*S*,*R*)-13] (Table 2, run 2). 88% yield (92:8, −78 °C, 2 h); colorless solid. **(*R*,*R*)-13** (major isomer): colorless prisms; mp 95.5−96.0 °C (AcOEt/*n*-hexane); $[\alpha]^{17}_D$ +89.3 (c 0.98, $CHCl_3$); IR (KBr) 3320, 3040, 1595, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, d, J = 6.9 Hz), 1.38 (3H, d, J = 6.6 Hz), 1.57 (1H, brs), 3.58 (1H, q, J = 6.7 Hz), 4.39 (1H, q, J = 6.8 Hz), 7.15−7.53 (8H, m), 7.68 (1H, d, J = 6.6 Hz), 7.76 (1H, d, J = 8.0 Hz), 7.86−7.90 (2H, m); ^{13}C NMR (DMSO-d_6) δ 24.38, 24.81, 50.34, 54.83, 122.56, 122.74, 125.12, 125.47, 125.68, 126.39, 126.57, 128.09, 128.61, 130.91, 133.48, 141.61, 146.25; LRFABMS m/z 276 (M^+ + H). Anal. calcd for $C_{20}H_{21}N$: C, 87.22; H, 7.69; N, 5.09. Found: C, 87.29; H, 7.57; N, 5.01. **(*S*,*R*)-13** (minor isomer): ^{1}H NMR ($CDCl_3$) δ 1.39 (3H, d, J = 6.9 Hz), 1.49 (3H, d, J = 6.3 Hz), 1.57 (1H, brs), 3.89 (1H, q, J = 6.8 Hz), 4.58 (1H, q, J = 6.4 Hz), 7.15−7.53 (8H, m), 7.68 (1H, d, J = 6.6 Hz), 7.76 (1H, d, J = 8.0 Hz), 7.86−7.90 (2H, m).

(1*R*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-2,2-dimethyl-1-phenyl-1-propylamine [(*R*,*R*)-14] and (1*S*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-2,2-dimethyl-1-phenyl-1-propylamine [(*S*, *R*)-14] (Table 2, run 4). 99% yield (63:37, THF, −78 °C, 1 h); brown oil. The diastereomers were partially separated by flash column chromatography. **(*R*,*R*)-14** (major isomer): yellow oil; $[\alpha]^{25}_D$ +96.9 (c 0.56, $CHCl_3$); IR (neat) 3060, 1595, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (9H, s), 1.37 (3H, d, J = 6.8 Hz), 1.85 (1H, brs), 3.07 (1H, s), 4.25 (1H, q, J = 6.6 Hz), 7.10 (2H, brs), 7.22−7.32 (4H, m), 7.40 (1H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.46 (1H, t, J = 7.6 Hz), 7.65 (1H, d, J = 6.1 Hz), 7.72 (1H, d, J = 8.2 Hz), 7.82 (1H, d, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 24.83, 27.23, 34.66, 51.04, 69.37, 123.34, 123.66, 125.10, 125.21, 125.59, 126.54, 126.90, 127.46, 128.64, 128.91, 131.64, 133.84, 141.82, 142.18; LRFABMS m/z 318 (M^+ + H); HRFABMS calcd for $C_{23}H_{28}N$ (M^+ + H) 318.2222, found 318.2229. **(*S*,*R*)-14** (minor isomer): yellow oil; $[\alpha]^{25}_D$ −21.0 (c 0.90, $CHCl_3$); IR (neat) 3060, 1595, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (9H, s), 1.41 (3H, d, J = 6.3 Hz), 1.71 (1H, brs), 3.61 (1H, s), 4.28 (1H, q, J = 6.3 Hz), 7.20−7.43 (8H, m), 7.62 (1H, d, J = 6.8 Hz), 7.71 (1H, d, J = 8.3 Hz), 7.81 (1H, d, J = 8.0 Hz), 7.92 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 21.25, 27.32, 35.01, 50.62, 69.33, 123.43, 123.78, 125.19, 125.40, 125.57, 126.60, 127.09, 127.51, 128.67, 128.91, 130.91, 133.86, 141.71, 142.90; LRFABMS m/z 318 (M^+ + H); HRFABMS calcd for $C_{23}H_{28}N$ (M^+ + H) 318.2222, found 318.2226.

(1*R*,1′*R*)-Bis[1-(1-naphthyl)ethyl]amine [(*R*,*R*)-15] and (1*S*,1′*R*)-Bis[1-(1-naphthyl)ethyl]amine [(*S*,*R*)-15] (Table 2, run 5). 98% yield (95:5, −78 °C, 1 h); yellow oil. The diastereomers were separated by column chromatography. **(*R*,*R*)-15** (major isomer): yellow oil; $[\alpha]^{30}_D$ −31.5 (c 0.79, $CHCl_3$); $[\alpha]^{25}_D$ −81.2 (c 3.9, MeOH) ($[\alpha]^{22}_D$ −53.59 (c 3.9, MeOH)[14]); IR (neat) 3340, 3050, 1595, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.44 (6H, d, J = 6.8 Hz), 1.85 (1H, brs), 4.50 (2H, q, J = 6.6 Hz), 7.19 (2H, ddd, J = 1.4, 6.9, 8.3 Hz), 7.35 (2H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.49 (2H, t, J = 7.7 Hz), 7.70−7.76 (6H, m), 7.81 (2H, m); ^{13}C NMR ($CDCl_3$) δ 24.45, 51.26, 122.67, 123.07, 125.16, 125.39, 125.63, 127.08, 128.65, 131.45, 133.89, 141.94; LRFABMS m/z 326 (M^+ + H); HRFABMS calcd for $C_{24}H_{24}N$ (M^+ + H) 326.1909, found 326.1905. **(*S*,*R*)-15** (minor isomer): yellow oil; IR (neat) 3320, 3050, 1595, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25 (1H, brs), 1.53 (6H, d, J = 6.6 Hz), 4.75 (2H, q, J = 6.6 Hz), 7.40−7.48 (6H, m), 7.63 (2H, d, J = 7.1 Hz), 7.76 (2H, d, J = 8.3 Hz), 7.87 (2H, d, J = 7.5 Hz), 8.01 (2H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 23.34, 50.16, 123.01, 123.10, 125.34, 125.67, 125.74, 127.24, 128.90, 131.16, 133.96, 141.72; LRFABMS m/z 326 (M^+ + H); HRFABMS calcd for $C_{24}H_{24}N$ (M^+ + H) 326.1909, found 326.1933.

(2*R*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-4-phenyl-2-butylamine [(*R*,*R*)-16] and (2*S*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-4-phenyl-2-butylamine [(*S*,*R*)-16] (Table 2, run 6). 56% yield (>99:1, −78 °C, 4 h); yellow oil, inseparable mixture. **(*R*,*R*)-16** (major isomer): yellow oil; $[\alpha]^{26}_D$ +46.8 (*c* 0.96, $CHCl_3$); IR (neat) 3060, 1600, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (3H, d, J = 6.6 Hz), 1.42−1.44 (4H, m), 1.64 (1H, m), 1.83 (1H, m), 2.50−2.72 (3H, m), 4.75 (1H, q, J = 6.6 Hz), 7.11−7.23 (5H, m), 7.42−7.50 (3H, m), 7.62 (1H, d, J = 6.3 Hz), 7.71 (1H, d, J = 8.1 Hz), 7.85 (1H, m), 8.19 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 21.13, 23.89, 32.14, 38.44, 50.06, 50.29, 122.83, 122.91, 125.23, 125.58, 125.61, 125.70, 127.01, 128.24, 128.35, 128.92, 131.19, 133.93, 142.04, 142.52; LRFABMS *m*/*z* 304 (M^+ + H); HRFABMS calcd for $C_{22}H_{26}N$ (M^+ + H) 304.2065, found 304.2049.

(*R*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-1-phenyl-3-heptylamine [(*R*,*R*)-17] and (3*S*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-1-phenyl-3-heptylamine [(*S*,*R*)-17] (Table 2, run 7). 26% yield (>99:1, −78 °C, 25 h); yellow oil, inseparable mixture. **(*R*,*R*)-17** (major isomer): yellow oil; $[\alpha]^{27}_D$ +54.8 (*c* 1.06, $CHCl_3$); IR (neat) 3060, 1600, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (3H, t, J = 7.2 Hz), 1.17−1.47 (10H, m), 1.74 (2H, m), 2.49−2.69 (3H, m), 4.75 (1H, q, J = 6.6 Hz), 7.13−7.16 (3H, m), 7.21−7.25 (2H, m), 7.44−7.50 (3H, m), 7.64 (1H, d, J = 6.4 Hz), 7.72 (1H, d, J = 8.3 Hz), 7.85 (1H, m), 8.22 (1H, d, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 14.04, 22.86, 24.26, 27.96, 31.65, 34.36, 35.54, 50.27, 53.98, 122.99, 123.18, 125.18, 125.56, 125.60, 126.98, 128.25, 128.90, 131.30, 133.92, 141.99, 142.78; LRFABMS *m*/*z* 346 (M^+ + H); HRFABMS calcd for $C_{25}H_{32}N$ (M^+ + H) 346.2535, found 346.2538.

(2*R*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-3,3-dimethyl-2-butylamine [(*R*,*R*)-18] and (2*S*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-3,3-dimethyl-2-butylamine [(*S*,*R*)-18] (Table 2, run 8). 76% yield (>99:1, −78 °C, 1.5 h); yellow oil, inseparable mixture. **(*R*,*R*)-18** (major isomer): yellow oil; $[\alpha]^{15}_D$ −17.4 (*c* 1.06, $CHCl_3$); IR (neat) 3030, 1595, 1510 $cm^{-1;}$ ^1H NMR ($CDCl_3$) δ 0.93−0.96 (12H, m), 1.02 (1H, brs), 1.42 (3H, dd, J = 1.0, 6.6 Hz), 2.44 (1H, q, J = 6.5 Hz), 4.63 (1H, q, J = 6.5 Hz), 7.43−7.51 (3H, m), 7.71−7.72 (2H, m), 7.85 (1H, dd, J = 1.2, 6.8 Hz), 8.28 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 15.65, 23.02, 26.62, 34.71, 52.15, 59.76, 123.41, 125.19, 125.54, 125.63, 126.96, 128.86, 131.02, 133.92, 143.52; LRFABMS *m*/*z* 256 (M^+ + H); HRFABMS calcd for $C_{18}H_{26}N$ (M^+ + H) 256.2065, found 256.2063. **(*S*,*R*)-18** (minor isomer): ^1H NMR ($CDCl_3$) δ 0.68 (9H, s), 1.02 (1H, brs), 1.37 (3H, d, J = 6.8 Hz), 1.71 (3H, d, J = 7.0 Hz), 3.83 (1H, q, J = 6.5 Hz), 5.22 (1H, q, J = 7.1 Hz), 7.43−8.28 (7H, m).

(3*R*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-2,2-dimethyl-3-heptylamine [(*R*,*R*)-19] and (3*S*,1′*R*)-*N*-[1′-(1-Naphthyl)ethyl]-2,2-dimethyl-3-heptylamine [(*S*,*R*)-19] (Table 2, run 9). 93% yield (85:15, −78 °C, 1.5 h); colorless oil; inseparable mixture. IR (neat) 3040, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) **(*R*,*R*)-19** (major isomer) δ 0.66 (9H, s), 0.97 (3H, t, J = 7.2 Hz), 1.05−1.85 (10H, m), 3.17 (1H, d, J = 10.7 Hz), 5.05 (1H, q, J = 7.1 Hz), 7.40−7.51 (3H, m), 7.58−7.61 (1H, m), 7.69−7.73 (1H, m), 7.83−7.86 (1H, m), 7.89−8.03 (1H, m); **(*S*,*R*)-19** (minor isomer) δ 0.67 (9H, s), 1.00 (3H, t, J = 7.2 Hz), 1.05−1.85 (10H, m), 3.64 (1H, dd, J = 1.6, 10.6 Hz), 5.14 (1H, q, J = 6.4 Hz), 7.40−8.03 (7H, m); LRFABMS *m*/*z* 298 (M^+ + H); HRFABMS calcd for $C_{12}H_{32}N$ (M^+ + H) 298.2535, found 298.2523.

(1*R*,1′*R*)-*N*-[1′-(1-Naphthy)ethyl]-1-(2-pyridyl)ethylamine [(*R*,*R*)-20] and (1*S*,1′*R*)-*N*-[1′-(1-Naphthy)ethyl]-1-(2-pyridyl)ethylamine [(*S*,*R*)-20] (Table 3, run 3). 46% yield (84:16, −78 °C, 3 h); yellow oil. The diastereomers were separated by preparative TLC. **(*R*,*R*)-20** (major isomer): yellow oil; $[\alpha]^{27}_D$ +114.7 (*c* 0.46, $CHCl_3$); IR (neat) 3320, 3050, 1590, 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (3H, d, J = 6.8 Hz), 1.40 (3H, d, J = 6.6 Hz), 2.11 (1H, brs), 3.68 (1H, q, J = 6.8 Hz), 4.32 (1H, q, J = 6.6 Hz), 6.93 (1H, d, J = 7.6 Hz), 7.14 (1H, m), 7.37 (1H, ddd, J = 1.5, 6.9, 8.4 Hz), 7.42 (1H, m), 7.48−7.54 (2H, m), 7.73−7.79 (2H, m), 7.85 (1H, d, J = 8.0 Hz), 7.93 (1H, d, J = 8.5 Hz), 8.61 (1H, m); ^{13}C NMR ($CDCl_3$) δ 23.33, 24.49, 51.36, 56.42, 121.74, 122.06, 122.94, 123.19, 125.09, 125.36, 125.72, 127.01, 128.78, 131.38, 133.92, 136.08, 141.17, 149.54, 164.78; LRFABMS *m*/*z* 277 (M^+ + H); HRFABMS calcd for $C_{19}H_{21}N_2$ (M^+ + H) 277.1705, found 277.1711. **(*S*,*R*)-20** (minor isomer): yellow oil; $[\alpha]^{26}_D$ −37.0 (*c* 0.37, $CHCl_3$); IR (neat) 3320, 3050, 1590, 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (3H, d, J = 6.6 Hz), 1.54 (3H, d, J = 6.6 Hz), 1.96 (1H, brs), 4.00 (1H, q, J = 6.6 Hz), 4.64 (1H, q, J = 6.6 Hz), 7.14 (1H, dd, J = 4.8, 7.3 Hz), 7.20 (1H, d, J = 7.8 Hz), 7.41−7.45 (3H, m), 7.58 (1H, dt, J = 5.8, 7.5 Hz), 7.66 (1H, d, J = 7.3 Hz), 7.71 (1H, d, J = 8.1 Hz), 7.84 (1H, m), 8.01 (1H, m), 8.56 (1H, d, J = 4.9 Hz); ^{13}C NMR ($CDCl_3$) δ 22.15, 23.01, 50.19, 56.14, 121.28, 121.81, 123.00, 123.17, 125.21, 125.66, 127.12, 128.85, 131.10, 133.90, 136.34, 141.34, 149.24, 164.40; LRFABMS *m*/*z* 277 (M^+ + H); HRFABMS calcd for $C_{19}H_{21}N_2$ (M^+ + H) 277.1705, found 277.1711.

(1*R*,1′*R*)-*N*-[1′-(1-Naphthy)ethyl]-1-(2-quinolyl)ethylamine [(*R*,*R*)-21] and (1*S*,1′*R*)-*N*-[1′-(1-Naphthy)ethyl]-1-(2-quinolyl)ethylamine [(*S*,*R*)-21] (Table 3, run 7). 52% yield (72:28, −78 °C, 4 h); brown oil. The diastereomers were partially separated by flash chromatography. **(*R*,*R*)-21** (major isomer): brown oil; $[\alpha]^{27}_D$ +201.0 (*c* 0.51, $CHCl_3$); IR (neat) 3320, 3060, 1620, 1600, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (6H, d, J = 6.6 Hz), 2.43 (1H, brs), 3.91 (1H, q, J = 6.8 Hz), 4.45 (1H, q, J = 6.6 Hz), 7.23 (1H, d, J = 8.3 Hz), 7.32 (1H, ddd, J = 1.5, 6.9, 8.4 Hz), 7.41 (1H, m), 7.48−7.52 (2H, m), 7.70 (1H, ddd, J = 1.5, 6.9, 8.4 Hz), 7.74 (1H, d, J = 8.1 Hz), 7.78−7.85 (3H, m), 7.90 (1H, d, J = 8.8 Hz), 8.03 (1H, d, J = 8.6 Hz), 8.08 (1H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 23.61, 24.45, 51.81, 57.43, 120.14, 123.05, 123.10, 125.13, 125.41, 125.74, 125.82, 127.06, 127.37, 127.49, 128.77, 129.17, 129.22, 131.44, 133.94, 136.19, 141.43, 147.89, 165.58; LRFABMS *m*/*z* 327 (M^+ + H); HRFABMS calcd for $C_{23}H_{23}N_2$ (M^+ + H) 327.1861, found 327.1848. **(*S*,*R*)-21** (minor isomer): brown oil, $[\alpha]^{30}_D$ −55.2 (*c* 0.88, $CHCl_3$); IR (neat) 3320, 3050, 1620, 1600, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.49 (3H, d, J = 6.9 Hz), 1.58 (3H, d, J = 6.6 Hz), 2.23 (1H, brs), 4.24 (1H, q, J = 6.6 Hz), 4.69 (1H, q, J = 6.6 Hz), 7.35−7.44 (4H, m), 7.50 (1H, m), 7.65 (1H, d, J = 7.1 Hz), 7.68−7.72 (2H, m), 7.78 (1H, d, J = 8.0 Hz), 7.82 (1H, m), 8.04−8.10 (3H, m); ^{13}C NMR ($CDCl_3$) δ 22.52, 22.64, 50.29, 56.90, 119.57, 123.15, 123.18, 125.21, 125.63, 125.92, 127.14, 127.31, 127.47, 128.77, 129.18, 129.27, 131.13, 133.87, 136.35, 141.47, 147.66, 164.81; LRFABMS *m*/*z* 327 (M^+ + H); HRFABMS calcd for $C_{23}H_{23}N_2$ (M^+ + H) 327.1861, found 327.1848.

(1*R*,1′*R*)-*N*-[1′-(1-Naphthy)ethyl]-1-(2-methoxyphenyl)-ethylamine [(*R*,*R*)-22] and (1*S*,1′*R*)-*N*-[1′-(1-Naphthy)-ethyl]-1-(2-methoxyphenyl)ethylamine [(*S*,*R*)-22] (Table 3, run 10). 76% yield (88:12, −78 °C, 3 h); yellow oil. The distereomers were separated by preparative TLC. **(*R*,*R*)-22** (major isomer): yellow oil; $[\alpha]^{25}_D$ +27.7 (*c* 0.83, $CHCl_3$); IR (neat) 3360, 3060, 1595, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (3H, d, J = 6.8 Hz), 1.38 (3H, d, J = 6.5 Hz), 1.98 (1H, brs), 3.53 (3H, s), 3.87 (1H, q, J = 6.8 Hz), 4.40 (1H, q, J = 6.6 Hz), 6.80 (1H, dd, J = 1.0, 8.1 Hz), 6.90 (1H, dt, J = 1.0, 7.4 Hz), 7.14 (1H, dd, J = 1.7, 7.5 Hz), 7.20 (1H, ddd, J = 1.7, 7.3, 8.0 Hz), 7.34 (1H, ddd, J = 1.7, 6.8, 8.5 Hz), 7.41 (1H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.50 (1H, dd, J = 7.4, 8.1 Hz), 7.73 (1H, d, J = 8.1 Hz), 7.76 (1H, d, J = 7.0 Hz), 7.84 (1H, m), 7.89 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 22.71, 24.62, 50.82, 51.05, 54.82, 110.53, 120.53, 122.96, 123.11, 124.97, 125.19, 125,74, 126.79, 127.47, 127.70, 128.67, 131.53, 133.50, 133.87, 141.80, 157.36; LRFABMS *m*/*z* 306 (M^+ + H); HRFABMS calcd for $C_{21}H_{24}NO$ (M^+ + H) 306.1858, found 306.1870. **(*S*,*R*)-22** (minor isomer): yellow oil; $[\alpha]^{26}_D$ −37.6 (*c* 1.0, $CHCl_3$); IR (neat) 3330, 3050, 1595, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (3H, d, J = 6.6 Hz), 1.50 (3H, d, J = 6.6 Hz), 1.73 (1H, brs), 3.73 (3H, s), 4.28 (1H, q, J = 6.6 Hz), 4.53 (1H, q, J = 6.6 Hz), 6.88 (1H, d, J = 8.2 Hz), 6.95 (1H, dt, J = 1.2, 7.5 Hz), 7.22−7.29 (2H, m), 7.39 (1H, ddd, J = 1.5, 6.9, 8.4 Hz), 7.42 (1H, dd, J = 1.6, 7.9 Hz), 7.45 (1H, t, J = 7.7 Hz), 7.67 (1H, d, J = 7.1 Hz), 7.72 (1H, d, J = 8.3 Hz), 7.84 (1H, m), 7.87 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 21.89, 22.26, 49.77, 50.40, 55.07, 110.58, 120.67, 123.03, 123.27, 125.14, 125.52, 125.65, 127.05, 127.64, 127.70, 128.78, 131.04, 133.22, 133.85, 141.83; LRFABMS *m*/*z* 306 (M^+ + H); HRFABMS calcd for $C_{21}H_{24}NO$ (M^+ + H) 306.1858, found 306.1864.

Synthesis of (*R*)-*N*-(*p*-Toluenesulfonyl)-3,3-dimethyl-2-butylamine (24). A mixture of the amine **18** (1.9 g, 7.4 mmol) and 20% $Pd(OH)_2$ on carbon (0.75 g) in methanol (35 mL) was stirred under a hydrogen atmosphere at room temperature for 6 h. The catalyst was filtered through a Celite pad, and the filtrate was concentrated under atmospheric pressure to give the amine as a colorless oil, which was used for the next reaction without further purification. A solution of *p*-toluenesulfonyl chloride (1.7 g, 8.9 mmol) in dry THF (15 mL) was added dropwise to a stirred solution of the amine and Et_3N (1.24 mL, 8.9 mmol) in dry THF (35 mL) for 7 min at 0 °C under an argon atmosphere. The reaction mixture was stirred for at 0 °C 30 min and then at room temperature for 40 h. A solution of 3 N hydrochloric acid was added dropwise to the mixture (∼pH 3) at 0 °C, and then the organic layer was separated, washed with H_2O (10 mL) and brine (10 mL), and dried over Na_2SO_4. After removal of the solvent, the yellow solid was subjected to column chromatography on silica gel with AcOEt/*n*-hexane (1/8−1/2). The first eluted material was 1-ethylnaphthalene (1.0 g, 87%, from **18**), and the second was the sulfonamide **24** (1.1 g, 59%, from **18**) as a colorless solid. Recrystallization from AcOEt/*n*-hexane gave the sulfonamide **24** as colorless prisms: mp 130.0−131.0 °C (AcOEt/*n*-hexane); $[\alpha]^{15}_D$ +39.3 (*c* 1.05, EtOH) ($[\alpha]_D$ −12.85 (EtOH) for 59.6% ee (*S*)-**24**);[13] ^{1}H NMR ($CDCl_3$) δ 0.83 (9H, s), 0.88 (3H, d, J = 6.6 Hz), 2.42 (3H, s), 3.05 (1H, dq, J = 6.6, 8.5 Hz), 4.49 (1H, d, J = 8.5 Hz), 7.29 (2H, d, J = 7.8 Hz), 7.77 (2H, dt, J = 2.0, 8.7 Hz); ^{13}C NMR (DMSO-d_6) δ 15.21, 20.90, 26.18, 34.23, 57.53, 126.51, 129.37, 139.24, 142.12; IR (KBr) 3300, 3240, 3060, 1600, 1320, 1170 cm^{-1}; LRFABMS *m*/*z* 256 (M^+ + H). Anal. calcd for $C_{13}H_{21}NO_2S$: C, 61.14; H, 8.29; N, 5.48. Found: C, 61.17; H, 8.38; N, 5.42.

(*R*)-*N*-(*p*-Toluenesulfonyl)-4-phenyl-2-butylamine (25). 43% yield (2 steps); (hydrogenolysis, rt, 8 h; tosylation, 0 °C, 1 h, then rt, 23 h); pale yellow oil; $[\alpha]^{25}_D$ +22.1 (*c* 0.88, EtOH) ($[\alpha]^{23}_D$ +28 (*c* 1.7, EtOH) for (*R*)-**25**);[2a] IR (neat) 3280, 3060, 1600, 1320, 1160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (3H, d, J = 6.5 Hz), 1.67 (2H, m), 2.41 (3H, s), 2.55 (2H, m), 3.34 (1H, m), 4.84 (1H, d, J = 7.8 Hz), 7.03 (2H, m), 7.13−7.28 (5H, m), 7.76 (2H, m); ^{13}C NMR ($CDCl_3$) δ 21.43, 21.57, 31.75, 39.02, 49.60, 125.80, 127.00, 128.25, 128.29, 129.60, 138.17, 141.30, 143.14; LRFABMS *m*/*z* 304 (M^+ + H); HRFABMS calcd for $C_{17}H_{22}NO_2S$ (M^+ + H) 304.1371, found 304.1353.

Asymmetric Deprotonation of 4-*tert*-Butylcyclohexanone (26). *n*-Butyllithium (1.5 mL of a 1.6 M solution in *n*-hexane, 2.4 mmol) was added dropwise to a stirred solution of the amine (*R*,*R*)-**13** (716.0 mg, 2.6 mmol) in dry THF (40 mL) at −78 °C under an argon atmosphere. After being stirred at −78 °C for 5 min, the reaction mixture was warmed to room temperature for 20 min and stirred for 40 min. After the mixture was cooled to −78 °C again, TMSCl (1.3 mL, 10.1 mmol) was added. A solution of 4-*tert*-butylcyclohexanone **26** (308.0 mg, 2.0 mmol) in dry THF (10 mL) was added dropwise to the mixture over a period of 8 min. After the mixture stirred at −78 °C for 1 h, Et_3N (4 mL) and saturated $NaHCO_3$ (10 mL) were added. The organic layer was separated and extracted with petroleum ether (15 mL × 2). The combined organic extracts were washed with saturated NH_4Cl (20 mL × 2) and saturated $NaHCO_3$ (20 mL × 2) and dried over Na_2SO_4. Evaporation of the solvent gave the colorless oil, which was subjected to column chromatography on silica gel with *n*-hexane, AcOEt/*n*-hexane (1/10), and AcOEt to give the silylenolether **27** (286.3 mg, 63%) as a colorless oil. For further purification, the silylenolether **27** was distilled under a reduced pressure (Kugelrohr, 130 °C/2 mmHg) to give **27** (217.1 mg, 48%) as a colorless oil. The enantiomeric excess of this compound was determined by measuring the optical rotation, which indicated 69% ee (*S*).

4-*tert*-Butyl-1-(trimethylsilyloxy)cyclohexene 27. Colorless oil; bp 130 °C/2 mmHg (Kugelrohr) (66−67 °C/0.44 mmHg (Kugelrohr));[16a] $[\alpha]^{26}_D$ −54.7 (*c* 1.5, $CHCl_3$) for 69% ee for (*S*)-isomer ($[\alpha]^{22}_D$ −69.2 (*c* 1.5, $CHCl_3$) for 88% ee (*S*)-**27**);[16a] ^{1}H NMR ($CDCl_3$) δ 0.18 (9H, s), 0.87 (9H, s), 1.19−1.30 (2H, m), 1.75−1.84 (2H, m), 1.95−2.12 (3H, m), 4.84 (1H, m).

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Supporting Information Available: ^{1}H NMR and X-ray analysis data. This material is available free of charge via the Internet at http://pubs.acs.org.

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