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Enantioselective Reaction of α-Lithiated Dithioacetals Using Chiral Bis(oxazoline)s: New Chiral Formyl Anion Equivalents

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Received October 21, 2003

The enantioselective reaction of various α-lithiated dithioacetals with aldehydes or a ketone in the presence of bis(oxazoline)s was examined. Among them, unsymmetrical dithioacetals were found to be the best choice for attaining high enantioselectivity. The reaction of lithiated *tert*-butylthio(2-pyridylthio)methane with aldehydes proceeded with good diastereoselectivity as well as with good enantioselectivity. The enantioselective reaction was shown to proceed through dynamic thermodynamic resolution. Mercury(II) chloride effected hydrolysis of the dithioacetal moiety of the products to 2-hydroxyaldehydes, which were directly reduced to give the optically active 1,2-diols.

Introduction

The study of chiral formyl anion equivalents is of vital interest. Intensive studies have so far been focused mainly on diastereoselective reactions employing dithioacetals,[1] hemithioacetals,[2] 1,3-dioxolanes,[3] 1,3-oxazolidines,[4] oxazolidinones,[5] and formaldehyde hydrazones[6] as chiral auxiliaries. The enantioselective version should be a very desirable yet challenging subject of study for developing formyl anion equivalents as an efficient tool for asymmetric synthesis. Enantioselective reactions of *N*,*O*-acetals[7] and 1,3-dithiane have been previously described.[8] These reactions show good enantioselectivity only when benzaldehyde is used as an electrophile, inasmuch as much poorer enantioselectivity results with other aldehydes.[8] We focused on a detailed study of the enantioselective reaction using lithiated dithioacetals, because there was no systematic study of this kind of asymmetric syntheses. We have previously reported highly enantioselective lithiation−substitution reactions of benzyl sulfides in the presence of bis(oxazoline)s.[9,10] Herein we report an enantioselective reaction of a variety of lithiated dithioacetals with various aldehydes.

Reactions of Lithiated Dithioacetals. Initially, we examined the reaction of lithiated symmetrical dithioacetals **1**−**6**. Dithioacetals **1**−**6** were lithiated with *n*-BuLi in the presence of bis(oxazoline)s **7** and subsequently reacted with benzaldehyde. The results are shown in Table 1. Treatment of bis(phenylthio)methane **1** with 1.2 equiv of *n*-BuLi and 1.25 equiv of bis(oxazoline)-^{i}Pr **7a** in cumene for 30 min at −78 °C, followed by the addition of benzaldehyde (1.3 equiv) gave the product **8** in high yield but with low enantioselectivity (entry 1). Bis(oxazoline)-^{t}Bu **7b** slightly improved the enantioselectivity (entry 2). Dithioacetals such as 1,3-dithiane **2**, bis(*tert*-butylthio)methane **3**, and bis(2,4,6-trimethylphenylthio)methane **4** are not acidic enough to give the product in high yield (entries 4−6), whereas bis(2-pyridylthio)methane **5** and bis(2-quinolylthio)methane **6** gave the products **12** and **13** in high yields, respectively, but again with low enantioselectivities (entries 7 and 8).[11] We concluded from these results that symmetrical dithioacetals were not the proper choice for the enantioselective

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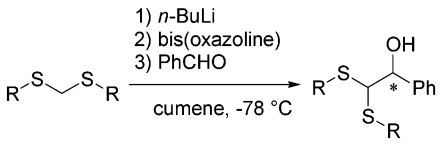
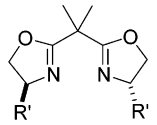
(11) Intramolecular coordination of the pyridyl or quinolyl nitrogen atom to the lithium ion promotes deprotonation.

10.1021/jo035558e CCC: $27.50
Published on Web 02/06/2004

TABLE 1. Enantioselective Reaction of Symmetrical Dithioacetals with Benzaldehyde



1-6 **8-13**



bis(oxazoline) **7a**, R' = ^{i}Pr
7b, R' = ^{t}Bu
7c, R' = Ph

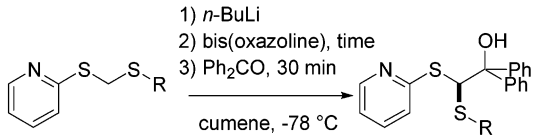
entry	dithioacetal R		bis(oxazoline) 7	product	yield (%)	ee[a] (%)
1	Ph	**1**	**7a**	**8**	73	24
2	Ph	**1**	**7b**	**8**	99	33
3	Ph	**1**	**7c**	**8**	55	6
4	$-(CH_2)_3-$	**2**	**7a**	**9**	0	
5	^{t}Bu	**3**	**7a**	**10**	14	5
6	Mes	**4**	**7a**	**11**	8	9
7	2-Py	**5**	**7a**	**12**	95	5[b]
8	2-Quinolyl	**6**	**7a**	**13**	87	4

[a] Determined by HPLC analysis using Chiralpak AD-H unless otherwise noted. [b] Determined by HPLC analysis using Chiralcel OD-H.

reaction with aldehydes and next examined the reaction using unsymmetrical dithioacetals.

We chose a pyridyl group as one of the substituents in unsymmetrical dithioacetals, because we have previously succeeded in a highly enantioselective reaction of the α-(2-pyridylthio) carbanion involving intramolecular coordination of the pyridyl nitrogen to the lithium ion.[9,12] To optimize the reaction conditions, the reaction of alkyl- or arylthio(2-pyridylthio)methanes **14**−**19** with benzophenone was examined under various conditions (Table 2). The reaction of lithiated *tert*-butylthio(2-pyridylthio)-methane Li-**14** with benzophenone in the presence of bis-(oxazoline)s **7** as chiral ligands gave the product **20** with good enantioselectivities (entries 1−4). Interestingly, the enantioselectivity of **20** using **7c** depends on the time for lithiation, shorter lithiating times giving higher enantioselectivity (entries 3 vs 4).[13] This is probably because bis(oxazoline)-Ph **7c** is partially isomerized to the *meso*-isomer during lithiation.[14] Isopropylthio(2-pyridylthio)-methane **15** afforded **21** with good enantioselectivity (entry 5). Introduction of a methylthio group as a less hindered substituent lowered the enantioselectivity (entries 6 and 7). Phenylthio(2-pyridylthio)methane **17** showed low enantioselectivity (entries 8 and 9), whereas 2,4,6-trimethylphenylthio(2-pyridylthio)methane **18** gave

TABLE 2. Enantioselective Reaction of Various Unsymmetrical Dithioacetals with Benzophenone in the Presence of Bis(oxazoline)s 7



14-19 **20-25**

entry	dithioacetal R		bis(oxazoline) 7	time (min)	product	yield (%)	ee[a] (%)
1	^{t}Bu	**14**	**7a**	60	**20**	73	61
2	^{t}Bu	**14**	**7b**	60	**20**	53	68
3	^{t}Bu	**14**	**7c**	60	**20**	86	61
4	^{t}Bu	**14**	**7c**	15	**20**	80	68
5	^{i}Pr	**15**	**7c**	15	**21**	92	68
6	Me	**16**	**7a**	60	**22**	73	40
7	Me	**16**	**7c**	15	**22**	80	42
8	Ph	**17**	**7a**	60	**23**	79	3[b]
9	Ph	**17**	**7c**	15	**23**	75	18[b]
10	Mes	**18**	**7a**	60	**24**	99	60[b]
11	Mes	**18**	**7c**	15	**24**	47	57[b]
12	Tip	**19**	**7a**	60	**25**	76	29[b]
13	Tip	**19**	**7c**	15	**25**	81	71[b]

[a] Determined by HPLC analysis using Chiralpak AD-H unless otherwise noted. [b] Determined by HPLC analysis using Chiralcel OD-H.

24 with good enantioselectivity (entries 10 and 11). The reaction of dithioacetal **19** having a bulkier 2,4,6-triisopropylphenylthio group in the presence of **7c** afforded **25** with high enantioselectivity (entry 13).

The reaction of dithioacetals **14**−**16** and **19** with various aldehydes in the presence of **7c** was examined, and the results are shown in Table 3. Treatment of unsymmetrical dithioacetals **14** with 1.2 equiv of *n*-BuLi and 1.25 equiv of **7c** in cumene for 30 min at −78 °C, followed by the addition of benzaldehyde (1.3 equiv), gave the product **26** in 91% yield in an anti/syn ratio of 83:17 (entry 1). Diastereomers of **26** could be easily separated by column chromatography, and the optical purities of *anti*- and *syn*-**26** were found to be 85 and 76% ee, respectively, by HPLC analysis using Chiralpak AD-H.[15] Methylthio- and isopropylthio(2-pyridylthio)methanes **15** and **16** showed low diastereoselectivity but high enantioselectivity (entries 2 and 3). Expecting a highly enantioselective result as in the case of Table 2, entry 13, we examined the reaction of the dithioacetal **19** having a bulky substituent, 2,4,6-triisopropylphenyl group; unfortunately, the anti and syn isomers could not be separated (entry 4).[16] A mixture of **14**, *n*-BuLi, and **7c** was stirred for 15 min at −78 °C and then cooled to −95 °C. Benzaldehyde was added at this temperature to give the product **26** with substantially the same enantioselectivity as that obtained in the reaction performed at −78 °C but with slightly higher diastereoselectivity (entries 1 vs 5). Thus, the reaction of **14** with various aromatic aldehydes such as 2,4,6-trimethylbenzaldehyde, 2-naphthaldehyde,

(12) Methylthio(phenylthio)methane and *tert*-butylthio(phenylthio)-methane afforded products with low ee (20−30% ee). *tert*-Butylthio-(2-imidazolylthio)methane showed good enantioselectivity, but the product could not be converted to the aldehyde in good yield.

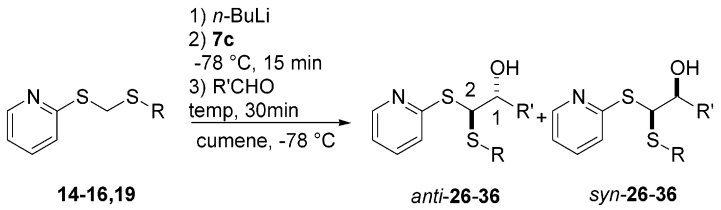
(13) Enantioselectivity of the reaction with other bis(oxazoline)s was not affected by the lithiating time.

(14) Formation of a small amount of the *meso*-isomer of **7c** was detected in the reaction of *n*-BuLi and **7c** in cumene for 30 min at −78 °C.

(15) Enantioselective reaction in the presence of (−)-sparteine afforded the product in 70% yield in a diastereomer ratio of 75:25 but with 7% ee for the major isomer.

(16) We observed that diastereomers formed in the reaction of alkylthio(2-pyridylthio)methanes could be separated by column chromatography more easily than those from arylthio(2-pyridylthio)-methanes.

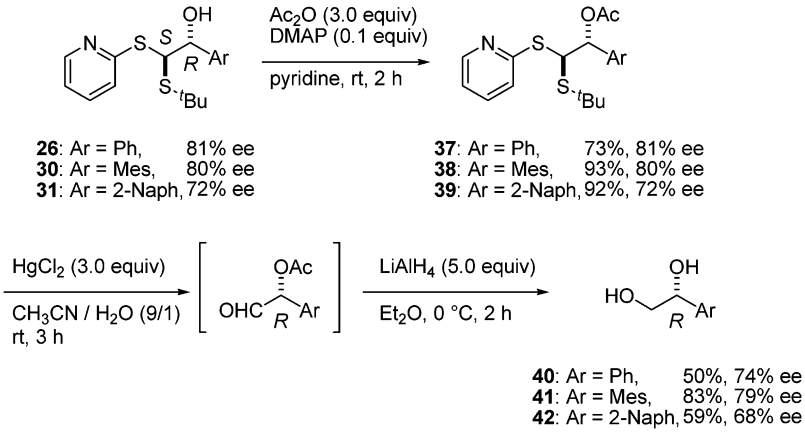
TABLE 3. Enantioselective Reaction of Unsymmetrical Dithioacetals 14−16 and 19 with Various Aldehydes in the Presence of 7c



entry	dithioacetal R		R′CHO	temp	product	yield (%)	diastereomer ratio[a] anti:syn	ee (%)[b] anti	ee (%)[b] syn
1	^{t}Bu	**14**	PhCHO	−78	**26**	91	83:17	85	76
2	^{i}Pr	**15**	PhCHO	−78	**27**	85	65:35	84	c
3	Me	**16**	PhCHO	−78	**28**	99	60:40	72	60
4	Tip	**19**	PhCHO	−78	**29**	69	67:33	c	c
5	^{t}Bu	**14**	PhCHO	−95	**26**	93	86:14	85	73
6	^{t}Bu	**14**	MesCHO	−95	**30**	83	90:10	85	69
7	^{t}Bu	**14**	2-NaphCHO	−95	**31**	92	80:20	83	69
8	^{t}Bu	**14**	*p*-MeOC$_6$H$_4$CHO	−95	**32**	65	81:19	75	55
9	^{t}Bu	**14**	*p*-ClC$_6$H$_4$CHO	−95	**33**	91	85:15	88	71
10	^{t}Bu	**14**	^{i}PrCHO	−95	**34**	57	63:37	80	65
11	^{t}Bu	**14**	*c*-HexCHO	−95	**35**	63	68:32	81	64
12	^{t}Bu	**14**	^{t}BuCHO	−95	**36**	71	55:45	84	70

[a] Determined by the ^{1}H NMR analysis. [b] Determined by the HPLC analysis using Chiralpak AD-H. [c] Enantiomers were not separable by the HPLC analysis using chiral columns.

SCHEME 1



4-methoxybenzaldehyde, and 4-chlorobenzaldehyde was carried out at −95 °C, giving products **30**−**33** with high diastereoselectivities and high enantioselectivities (entries 6−9). The reaction with 2-methylpropanal, cyclohexanecarbaldehyde, or 2,2-dimethylpropanal also afforded products **34**−**36** with high enantioselectivities (entries10−12).[17] It should be noted that high enantioselectivity was achieved in the reaction with such aliphatic aldehydes, since only poor or no results have so far been reported in enantioselective reactions of formyl anion equivalents.[7,8] Thus, the present reaction provides a generally acceptable method for the highly enantioselective reaction with aromatic as well as aliphatic aldehydes.

The relative stereochemistry of *anti*-**26** was confirmed by X-ray analysis (see Supporting Information), and the absolute configuration of **26** was determined after transformation to the known diol as shown in the next section. From the above results, the relative stereochemistry of major isomers **30**−**36** was tentatively assigned as anti.

Preparation of Chiral Diols. Major diastereomers **26**, **30**, and **31** were reacted with acetic anhydride in pyridine in the presence of 4-*N*,*N*-(dimethylamino)pyridine at room temperature to give **37**, **38**, and **39**, respectively, which were then treated with $HgCl_2$ in CH_3CN/H_2O at room temperature (Scheme 1).[18] The formed acetoxyaldehydes were treated, without purification, with $LiAlH_4$ in Et_2O at 0 °C to give known chiral diols **40**−**42**.[19,20] Optical purities of **40** and **41** were determined by comparison with the values of specific rotation with those

(17) Enantiomeric products obtained in the reaction with 1-pentanal were not separable by HPLC analysis using various chiral columns.

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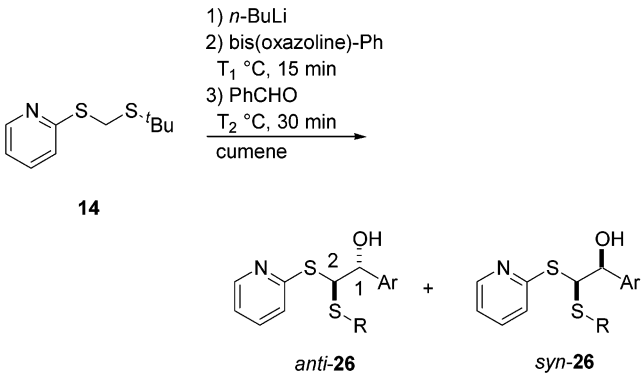
TABLE 4. Temperature Dependence of Enantioselective Reaction of 14 with Benzaldehyde



entry	T_1 (°C)	T_2 (°C)	yield (%)	diastereomer ratio anti:syn	ee (%) anti	ee (%) syn
1	−30	−30	87	78:22	75	65
2	−50	−50	80	79:21	78	65
3	−78	−78	91	83:17	85	76
4	−78	−95	93	86:14	85	73
5	−95	−95	88	84:16	19	8
6	−78	−78[a]	47	76:24	76	55

[a] PhCHO (0.2 equiv) was used.

reported.[21−23] The optical purity of the product **42** was determined by the HPLC analysis using Chiralcel OD-H. Their stereochemistry was determined to be *R* by the sign of specific rotation. From these results, the absolute stereochemistry of the major diastereomers of dithioacetals **26**, **30**, and **31** was determined to be (1*R*,2*S*).

Reaction Mechanism. To define the enantio-determining step in the reaction of α-lithiated dithioacetals, we studied the temperature dependence of the stereochemical outcome in the reaction of α-lithiated *tert*-butylthio-(2-pyridylthio)methane **14** with benzaldehyde (Table 4). Reaction with benzaldehyde performed at −30 and −50 °C slightly lowered the enantioselectivity in comparison with the result performed at −78 °C (entries 1 and 2 vs entry 3). The enantioselectivity was lowered when deprotonation was carried out at −95 °C (entry 5), whereas deprotonation at −78 °C followed by the reaction with benzaldehyde at −95 °C showed substantially the same enantioselectivity as that obtained in the reaction performed at −78 °C at both reaction steps (entries 3 vs 4). These results indicate that the diastereomeric complexes derived from lithiated **14** and the bis(oxazoline) **7c** are configurationally stable at temperatures lower than −78 °C at least on the time scale of the reaction with an aldehyde.[24] Thus, the enantioselective reaction of lithiated **14** would proceed through a dynamic thermodynamic resolution pathway at −78 °C, where the enantiomeric excess of the product reflects the ratio of the two diastereomeric Li-**14**-bis(oxazoline)-Ph complexes.[25,26] Furthermore, the reaction with an insufficient amount of benzaldehyde resulted in slightly lower enantioselectivity in comparison with that obtained in the reaction using a stoichiometric amount of benzaldehyde (entry 6), and thus the minor diastereomeric complex, which gives the minor enantiomer, would have slightly lower activation energy in the reaction with an electrophile.

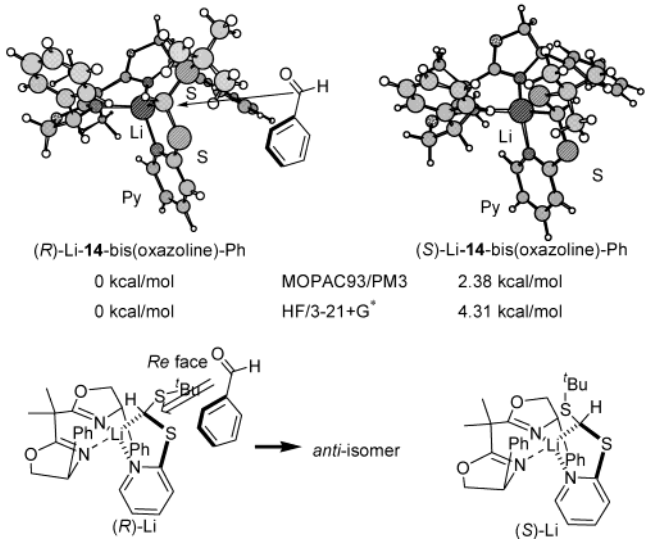


FIGURE 1. Optimized structures and energies of diastereomeric complexes of (*R*)- and (*S*)-Li−**14** with bis(oxazoline)-Ph **7c**.

The diastereomeric complexes of lithiated **14** with **7c** were estimated by the MO calculation using MOPAC 93/PM3[27] and Gaussian 98 HF/3-21+G* methods.[28] The relative energies of the optimized structures obtained by the calculation are depicted in Figure 1. Both calculations showed that the (*R*)-Li-**14**-bis(oxazoline)-Ph complex was more stable than the (*S*)-Li-**14**-bis(oxazoline)-Ph complex, where the lithium ion was coordinated with a pyridyl nitrogen as well as two nitrogens of the bis(oxazoline), giving the fully coordinated lithium complex. In the most stable (*R*)-Li-**14**-bis(oxazoline)-Ph **7c** complex, the S−$C_{t\mathrm{Bu}}$ bond is arranged anti to the C−Li bond by the stabilizing

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(24) Another reaction pathway in which the reaction at −95 °C proceeds through an incompletely coordinated intermediate is ruled out, since the lithiation of **14** without **7c** hardly proceeds at this temperature.

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effect of the $n - \sigma^*$ negative hyperconjugation,[5c,29,30] which was estimated to be 13.0 kcal/mol by the NBO calculations.[31,32] The anti conformation of the Li−C−S−$C_{t\mathrm{Bu}}$ bond would play an important role in controlling the face of approach of the aldehyde to the C−Li bond. The aldehyde approaches the carbanionic center avoiding steric interaction with the *tert*-butyl group to give the anti isomer predominantly. In the (*R*)-Li-**14** complex, an electrophile such as benzophenone or benzaldehyde approaches the reaction site from the side opposite the C−Li bond to form the product with inversion of configuration.[33] This stereochemical course is in accord with that in the reaction of lithiated benzyl 2-pyridyl sulfide and lithiated benzyl 2-quinolyl sulfide[9] as well as that in the reaction of chiral α-thiobenzyllithium derived from chiral thiocarbamates.[34]

Summary

We have demonstrated a highly enantioselective reaction of lithiated unsymmetrical dithioacetals, especially those having a 2-pyridyl group, not only with aromatic aldehydes but also with aliphatic aldehydes. The reaction was shown to proceed through a dynamic thermodynamic resolution pathway with inversion of configuration of the carbanion. The present enantioselective reaction together with deprotection and reduction provides an efficient method for the preparation of chiral diols.

Experimental Section

Typical Procedure for the Preparation of Symmetrical Dithioacetals: Bis(2,4,6-trimethylphenylthio)methane (4). A solution of 2,4,6-trimethylbenzenethiol (3.8 g, 24.9 mmol) and DBU (4.1 mL, 27.4 mmol) in dibromomethane (3.9 mL) was stirred at room temperature for 4 h. Aqueous NH_4Cl was added to the reaction mixture, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (silica gel 70 g, hexane) to give **4** (1.74 g, 44%): mp 57−58 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.25, (s, 6H), 2.40 (s, 12H), 3.77 (s, 2H), 6.89 (s, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.7, 22.5, 42.5, 129.3, 130.3, 138.8, 143.2; IR (KBr) 2948, 2915, 1602, 1461, 1199, 850, 730 cm^{-1}, EIMS *m*/*z* 316 (M^+), 165, 119, 91; Anal. Calcd for $C_{19}H_{24}S_2$: C, 72.10; H, 7.64. Found: C, 72.06; H, 7.74.

Bis(2-quinolylthio)methane (6): mp 133−134 °C; ^{1}H NMR δ 5.39 (s, 2H), 7.17−8.02 (m, 12H); ^{13}C NMR δ 30.3, 120.6, 125.1, 125.8, 127.3, 127.9, 129.4, 135.2, 147.8, 157.6; IR (KBr) 3051, 2984, 2922, 1592, 1419, 1292, 1137, 1088, 818, 745 cm^{-1}; EIMS *m*/*z* 334 (M^+) 174, 128, 101; Anal. Calcd for $C_{19}H_{14}N_2S_2$: C, 68.23; H, 4.22; N, 8.38. Found: C, 68.23; H, 4.26; N, 8.38.

Typical Procedure for Reaction of Symmetrical Dithioacetals with Benzaldehyde in the Presence of Chiral Ligands: 2,2-Bis(phenylthio)-1-phenylethanol (8). *n*-BuLi (0.095 mL, 1.53 mol/L solution in hexane, 0.148 mmol) was added to a solution of bis(phenylthio)methane **1** (29 mg, 0.12 mmol) in cumene (0.5 mL) at −78 °C, and the solution was stirred for 10 min. A solution of bis(oxazoline)-Ph **7c** (51 mg, 0.154 mmol) in cumene (0.2 mL) was then added. After stirring for 15 min, benzaldehyde (0.02 mL, 0.160 mmol) was added and the reaction mixture was stirred for 30 min. Saturated aqueous NH_4Cl was then added to the reaction mixture, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (silica gel 20 g, hexane/ethyl acetate = 97:3) to give **8** (23 mg, 55%). The enantiomeric excess was determined by the HPLC analysis using Chiralpak AD-H: ^{1}H NMR δ 3.24 (d, J = 2.1 Hz, 1H), 3.98 (d, J = 2.1 Hz, 1H), 4.72 (s, 1H), 7.20−7.40 (m, 15H); ^{13}C NMR δ 68.3, 74.3, 126.5, 127.7, 127.8, 128.6, 128.8, 132.6, 133.5, 139.3; IR (neat) 3447, 3058, 1581, 1452, 1187, 848, 726 cm^{-1}; EIMS *m*/*z* 338 (M^+), 231, 153, 122, 91; Anal. Calcd for $C_{20}H_{18}OS_2$: C, 70.97; H, 5.36. Found: C, 71.08; H, 5.52. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 95/5, 0.5 mL/min) t_R 13.2 and 19.2 min (6% ee).

2,2-Bis(*tert*-butylthio)-1-phenylethanol (10): mp 67−68 °C; ^{1}H NMR δ 1.17 (s, 9H), 1.43 (s, 9H), 3.26 (d, J = 3.6 Hz, 1H), 4.11 (d, J = 3.6 Hz, 1H), 5.02 (s, 1H), 7.25−7.46 (m, 5H); ^{13}C NMR δ 31.2, 31.8, 75.7, 116.5, 126.7, 127.2, 127.4, 139.9; IR (KBr) 3390, 2960, 1460, 1364, 1157, 1055, 851, 730 cm^{-1}; EIMS *m*/*z* 298 (M^+), 209, 191, 135, 107. Anal. Calcd for $C_{16}H_{26}OS_2$: C, 64.38; H, 8.78. Found: C, 64.14; H, 8.66. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 98/2, 0.5 mL/min) t_R 28.3 and 43.8 min (5% ee).

1-Phenyl-2,2-bis(2,4,6-trimethylphenylthio)ethanol (11): mp 48−49 °C; ^{1}H NMR δ 2.16 (s, 6H), 2.22 (s, 6H), 2.24, (s, 3H), 2.25 (s, 3H), 3.24 (d, J = 2.1 Hz, 1H), 3.98 (d, J = 2.1 Hz, 1H), 4.72 (s, 1H), 6.85 (s, 2H), 6.89 (s, 2H), 7.20−7.40 (m, 5H); ^{13}C NMR δ 21.0, 21.2, 21.6, 21.6, 67.9, 74.4, 126.3, 127.1, 127.5, 127.8, 128.9, 129.3, 138.6, 138.8, 139.9, 142.8, 143.5; IR (KBr) 3526, 2919, 1453, 1186, 851, 729 cm^{-1}; EIMS *m*/*z* 405 (M^+ − OH), 315, 271, 151, 119, 91. Anal. Calcd for $C_{26}H_{30}OS_2$: C, 73.89; H, 7.15. Found: C, 73.75; H, 7.22. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 95/5, 0.5 mL/min) t_R 14.5 and 21.0 min (9% ee).

1-Phenyl-2,2-bis(2-pyridylthio)ethanol (12). ^{1}H NMR δ 2.05 (s, 1H), 5.48 (d, J = 3.6 Hz, 1H), 6.15 (d, J = 3.6 Hz, 1H), 7.00−7.80 (m, 11H), 8.40−8.55 (m, 2H); ^{13}C NMR δ 56.8, 76.3, 120.0, 122.8, 126.4, 127.2, 127.6, 136.2, 136.2, 141.9, 148.5, 148.7, 156.1, 156.9; IR (KBr) 3396, 3061, 2850, 1730, 1577, 1281, 1121, 854, 757 cm^{-1}; EIMS *m*/*z* 340 (M^+), 233, 211, 122, 76. Anal. Calcd for $C_{18}H_{16}N_2OS_2$: C, 63.50; H, 4.74; N, 8.23. Found: C, 63.57; H, 4.83; N, 8.10. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 80/20, 0.5 mL/min) t_R 31.0 and 37.2 min (5% ee).

1-Phenyl-2,2-bis(2-quinolylthio)ethanol (13): mp 61−62 °C; ^{1}H NMR δ 1.40−1.80 (br, 1H), 5.64 (d, J = 3.2 Hz, 1H),

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6.62 (d, J = 3.2 Hz, 1H), 7.14−8.03 (m, 17H); ^{13}C NMR δ 56.4, 120.7, 120.8, 125.6, 125.8, 125.9, 126.4, 127.2, 127.4, 127.7, 129.8, 135.8, 142.1, 147.3, 157.8; IR (KBr) 3410, 3059, 2920, 1591, 1496, 1137, 1088, 816, 749 cm^{-1}; EIMS m/z 440 (M^+), 307, 196, 168,124, 77. Anal. Calcd for $C_{26}H_{20}N_2OS_2$: C, 70.88; H, 4.58; N, 6.36. Found: C, 70.86; H, 4.81; N, 6.14. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 98/2, 0.9 mL/min) t_R 52.5 and 57.8 min (1% ee).

Typical Procedure for Preparation of Unsymmetrical Dithioacetals: *tert*-Butylthio(2-pyridylthio)methane (14). To a solution of 2-pyridinethiol (365 mg, 3.28 mmol) and DBU (0.52 mL, 3.61 mmol) in acetonitrile (5 mL) was added bromochloromethane (4.5 mL, 32.8 mL) at room temperature. The resulting solution was stirred at room temperature for 2 h. The reaction mixture was concentrated under reduced pressure to afford the crude product containing mainly chloromethyl 2-pyridyl sulfide. To a solution of the crude product in acetonitrile (10 mL) was added 1,1-dimethylethanethiol (0.44 mL, 4.92 mmol) and DBU (0.76 mL, 5.24 mmol) at room temperature, and the reaction mixture was stirred for 3 h. Aqueous NH_4Cl was added to the reaction mixture, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (silica gel 30 g, hexane/ethyl acetate = 98:2) to give **14** (497 mg, 71%): ^{1}H NMR δ 1.41 (s, 9H), 4.40 (s, 2H), 6.98−8.47 (m, 4H); ^{13}C NMR δ 29.8, 30.9, 119.7, 122.2, 136.0, 149.5; IR (neat) 3044, 2960, 2862, 1577, 1454, 1414, 1281, 1122, 1042, 757 cm^{-1}; EIMS m/z 213 (M^+), 156, 112, 57. Anal. Calcd for $C_{10}H_{15}NS_2$: C, 56.30; H, 7.09; N, 6.56. Found: C, 56.46; H, 7.07; N, 6.42.

Isopropylthio(2-pyridylthio)methane (15).[36] ^{1}H NMR δ 1.31 (d, J = 3.3 Hz, 6H), 3.17 (sep, J = 3.3 Hz, 1H), 4.39 (s, 2H), 6.95−8.42 (m, 4H): ^{13}C NMR δ 23.2, 32.0, 35.2, 119.5, 122.1, 135.7, 149.1, 157.6; IR (neat) 2958, 2923, 1577, 1453, 1415, 1122, 758 cm^{-1}; EIMS m/z 199 (M^+), 156, 123, 112, 77. Anal. Calcd for $C_9H_{13}NS_2$: C, 54.23; H, 6.57; N, 7.02. Found: C, 54.16; H, 6.75; N, 7.05.

Methylthio(2-pyridylthio)methane (16).[37] ^{1}H NMR δ 2.24 (s, 3H), 4.36 (s, 2H), 6.98−8.47 (m, 4H); IR (neat) 3044, 2980, 2913, 1576, 1414, 1207, 1122, 985, 756 cm^{-1}; EIMS m/z 171 (M^+), 156, 123, 112, 77, 61.

Phenylthio(2-pyridylthio)methane (17): mp 35−36 °C; ^{1}H NMR δ 4.72 (s, 2H), 6.95−8.45 (m, 9H); ^{13}C NMR δ 35.6, 119.6, 122.3, 126.6, 128.6, 130.4, 135.1, 135.8, 149.1, 156.0; IR (KBr) 3037, 2987, 1577, 1453, 1411, 1208, 1122, 800, 730 cm^{-1}; EIMS m/z 233 (M^+), 124, 77. Anal. Calcd for $C_{12}H_{11}NS_2$: C, 61.76; H, 4.75; N, 6.00. Found: C, 61.86; H, 4.77; N, 6.01.

2-Pyridylthio(2,4,6-trimethylphenylthio)methane (18): mp 34−35 °C; ^{1}H NMR δ 2.25 (s, 3H), 2.52 (s, 6H), 4.45 (s, 2H), 6.91 (s, 2H), 6.95−8.46 (m, 4H); ^{13}C NMR δ 21.1, 22.2, 36.6, 77.6, 119.5, 122.2, 128.6, 135.6, 138.3, 143.0, 149.0, 157.2, 167.6; IR (KBr) 2994, 2914, 1577, 1452, 1160, 1124, 849, 726 cm^{-1}; EIMS m/z 275 (M^+), 228, 195, 164, 123, 76, 50. Anal. Calcd for $C_{15}H_{17}NS_2$: C, 65.41; H, 6.22; N, 5.09. Found: C, 65.50; H, 6.26; N, 5.27.

2-Pyridylthio(2,4,6-triisopropylphenylthio)methane (19): mp 65−66 °C; ^{1}H NMR δ 1.23 (d, J = 6.8 Hz, 12H), 1.24 (d, J = 7.0 Hz, 6H), 2.86 (sep, J = 7.0 Hz, 1H), 3.97 (sep, J = 6.8 Hz, 2H), 4.42 (s, 2H), 7.01 (s, 2H), 6.95−8.43 (m, 4H); ^{13}C NMR δ 23.7, 24.3, 31.1, 34.1, 37.7, 119.2, 121.2, 121.9, 127.3, 135.4, 148.2, 149.3, 152.6, 156.8; IR (KBr) 2961, 2865, 1577, 1453, 1148, 878, 725 cm^{-1}; EIMS m/z 359, 233, 191, 149, 124, 77. Anal. Calcd for $C_{21}H_{29}NS_2$: C, 70.14; H, 8.13; N, 3.90. Found: C, 70.18; H, 8.24; N, 3.91.

Typical Procedure for the Reaction of Unsymmetrical Dithioacetals with Electrophiles. 2-(*tert*-Butylthio)-1,1-diphenyl-2-(2-pyridylthio)ethanol (20). *n*-BuLi (0.055 mL, 1.49 mol/L solution in hexane, 0.078 mmol) was added at −78 °C to a solution of **14** (14 mg, 0.065 mmol) in cumene (0.5 mL), and the solution was stirred for 10 min. A solution of **7c** (27 mg, 0.081 mmol) in cumene (0.2 mL) was then added. After the reaction mixtre was stirred for 15 min, a solution of benzophenone (15 mg, 0.084 mL) in cumene (0.1 mL) was added and the reaction mixture was stirred for an additional 30 min. Saturated aqueous NH_4Cl was then added to the reaction mixture, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product which was purified by column chromatography (silica gel 15 g, hexane/ethyl acetate = 98:2) to give 20 (18 mg, 70%). The enantiomeric excess was determined by HPLC analysis using Chiralpak AD-H: mp 128−129 °C; $[\alpha]^{20}_D$ −9.76 (c 0.444, $CHCl_3$, 61% ee); ^{1}H NMR δ 1.21 (s, 9H), 5.60 (s, 1H), 6.73 (s, 1H), 7.00−8.45 (m, 14H); ^{13}C NMR δ 30.6, 45.4, 59.8, 82.8, 120.1, 123.3, 126.7, 127.2, 127.5, 127.8, 136.5, 136.7, 146.3, 148.5, 157.7; IR (KBr) 3456, 2965, 1573, 1454, 1363, 1119, 1049, 802, 750, 701 cm^{-1}; EIMS m/z 378 (M^+ − OH), 319, 212, 182, 155, 111, 56. Anal. Calcd for $C_{23}H_{25}NOS_2$: C, 69.83; H, 6.37; N, 3.54. Found: C, 69.62; H, 6.59; N, 3.53. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL/min) t_R 8.4 (*S*) and 16.5 (*R*) min (61% ee).

2-Isopropylthio-1,1-diphenyl-2-(2-pyridylthio)ethanol (21): mp 101 °C; $[\alpha]^{20}_D$ 26.2 (c 0.202, $CHCl_3$, 68% ee); ^{1}H NMR δ 1.15 (d, J = 6.6 Hz, 3H), 1.25 (d, J = 6.6 Hz, 3H), 2.91 (sep, J = 6.6 Hz, 1H), 5.75 (s, 1H), 6.58 (s, 1H), 6.99−8.45 (m, 14H); ^{13}C NMR δ 22.8, 23.3, 36.7, 61.9, 120.1, 123.5, 126.4, 126.7, 127.3, 127.4, 136.2, 144.0, 145.9, 148.2, 155.4; IR (KBr) 3456, 2965, 1573, 1454, 1363, 1119, 1049, 802, 750, 701 cm^{-1}; EIMS m/z 364 (M^+ − OH), 320, 241, 199, 156, 124, 77. Anal. Calcd for $C_{22}H_{23}NOS_2$: C, 69.26; H, 6.08; N, 3.67. Found: C, 69.08; H, 6.19; N, 3.67. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 97/3, 0.5 mL/min) t_R 14.1 (*S*) and 17.9 (*R*) min (68% ee).

2-Methylthio-1,1-diphenyl-2-(2-pyridylthio)ethanol (22): mp 96−97 °C; $[\alpha]^{20}_D$ −38.1 (c 0.340, $CHCl_3$, 42% ee); ^{1}H NMR δ 2.12 (s, 3H), 5.63 (s, 1H), 6.75 (s, 1H), 7.00−8.49 (m, 14H); ^{13}C NMR δ 16.8, 65.4, 81.1, 120.4, 123.9, 126.3, 126.6, 127.7, 128.4, 136.7, 144.7, 146.5, 148.6, 156.9; IR (KBr) 3440, 3031, 2817, 1589, 1468, 1134, 1074, 740, 700 cm^{-1}; EIMS m/z 353 (M^+), 288, 213, 171, 124, 77; Anal. Calcd for $C_{20}H_{19}NOS_2$: C, 67.96; H, 5.42; N, 3.96. Found: C, 67.92; H, 5.56; N, 4.15. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 95/5, 0.5 mL/min) t_R 22.6 (*R*) and 30.4 (*S*) min (42% ee).

1,1-Diphenyl-2-phenylthio-2-(2-pyridylthio)ethanol (23). $[\alpha]^{20}_D$ 33.1 (c 0.226, $CHCl_3$, 18% ee); ^{1}H NMR δ 5.30 (s, 1H), 5.95 (s, 1H), 7.04−8.28 (m, 19H); ^{13}C NMR δ 67.5, 81.5, 120.6, 124.4, 126.2, 126.4, 126.9, 128.7, 132.7, 135.0, 136.8, 144.9, 146.7, 148.6, 156.4; IR (KBr) 3056, 2824, 1583, 1456, 1413, 804, 729 cm^{-1}; EIMS m/z 398 (M^+ − OH), 288, 233, 167, 124, 77. Anal. Calcd for $C_{25}H_{21}NOS_2$: C, 72.26; H, 5.09; N, 3.37. Found: C, 72.16; H, 5.27; N, 3.28. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 14.2 (*S*) and 17.8 (*R*) min (18% ee).

1,1-Diphenyl-2-(2-pyridylthio)-2-(2,4,6-trimethylphenylthio)ethanol (24): mp 129−130 °C; $[\alpha]^{20}_D$ 17.8 (c 0.188, $CHCl_3$, 57% ee); ^{1}H NMR δ 2.11 (s, 3H), 2.23 (s, 6H), 5.27 (s, 1H), 6.26 (s, 1H), 6.64 (s, 2H), 6.88−8.29 (m, 14H); ^{13}C NMR δ 22.1, 65.8, 81.2, 119.6, 123.0, 126.0, 126.1, 126.6, 126.8, 127.4, 127.6, 127.9, 128.2, 135.5, 138.1, 143.6, 147.7; IR (KBr) 3064, 1582, 1456, 1123, 852, 699 cm^{-1}; EIMS m/z 440 (M^+ − OH), 306, 275, 195, 167, 124, 91. Anal. Calcd for $C_{28}H_{27}NOS_2$: C, 73.49; H, 5.95; N, 3.06. Found: C, 73.53; H, 6.10; N, 2.99. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 44.9 (*S*) and 50.7 (*R*) min (57% ee).

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1,1-Diphenyl-2-(2-pyridylthio)-2-(2,4,6-triisopropylphenylthio)ethanol (25): $[\alpha]^{20}_D$ 95.8 (*c* 0.352, $CHCl_3$, 71% ee); ^1H NMR δ 0.97 (d, $J = 7.0$ Hz, 6H), 1.03 (d, $J = 7.0$ Hz, 6H), 1.14 (d, $J = 7.0$ Hz, 6H), 2.74 (sep, $J = 7.0$ Hz, 1H), 3.32 (br, 2H), 5.71 (s, 1H), 6.88 (s, 2H), 7.00 (s, 1H), 6.88−8.31 (m, 14H); ^{13}C NMR δ 23.9, 24.5, 31.2, 34.2, 53.4, 69.1, 81.7, 119.7, 121.4, 123.0, 126.5, 127.8, 136.0, 144.9, 146.2, 148.1, 149.9, 153.9, 157.3; IR (KBr) 3480, 2960, 1581, 1450, 1121, 876, 702 cm^{-1}; EIMS *m*/*z* 524 (M^+ − OH), 358, 325, 195, 167, 124, 91. Anal. Calcd for $C_{34}H_{39}NOS_2$: C, 75.37; H, 7.26; N, 2.59. Found: C, 75.16; H, 7.52; N, 2.53. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 95/5, 0.5 mL/min) t_R 9.7 (*R*) and 16.4 (*S*) min (71% ee).

2-(*tert*-Butylthio)-1-phenyl-2-(2-pyridylthio)ethanol (26). *anti*-26: mp 75−76 °C; $[\alpha]^{20}_D$ −57.3 (*c* 0.272, $CHCl_3$, 85% ee); ^1H NMR δ 1.21 (s, 9H), 4.28 (d, $J = 3.0$ Hz, 1H), 5.28 (d, $J = 3.0$ Hz, 1H), 5.73 (s, 1H), 7.20−8.50 (m, 9H); ^{13}C NMR δ 30.8, 44.5, 56.2, 77.6, 120.1, 123.0, 127.1, 127.3, 127.5, 127.6, 136.6, 140.8, 148.9; IR (KBr) 3398, 3047, 2954, 1579, 1556, 1455, 1364, 1154, 1220, 848 cm^{-1}; EIMS *m*/*z* 319 (M^+), 243, 211, 155, 111. Anal. Calcd for $C_{17}H_{21}NOS_2$: C, 63.91; H, 6.63; N, 4.38. Found: C, 63.84; H, 6.73; N, 4.38. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 5.9 (1*R*,2*S*) and 8.1 (1*S*,2*R*) min (85% ee). ***syn*-26:** $[\alpha]^{20}_D$ 16.0 (*c* 0.332, $CHCl_3$, 71% ee); ^1H NMR δ 1.26 (s, 9H), 4.85 (d, $J = 6.5$ Hz, 1H), 4.90−5.00 (br, 1H), 6.30−6.40 (br, 1H), 7.20−8.55 (m, 9H); ^{13}C NMR δ 30.7, 45.0, 56.5, 78.0, 120.3, 123.5, 127.2, 127.5, 127.8, 136.7, 142.6, 148.8; IR (neat) 3430, 3061, 2959, 1578, 1454, 1415, 1120, 759 cm^{-1}; EIMS *m*/*z* 319 (M^+), 243, 211, 155, 111. Anal. Calcd for $C_{17}H_{21}NOS_2$: C, 63.91; H, 6.63; N, 4.38. Found: C, 63.89; H, 6.82; N, 4.26. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 98/2, 0.5 mL/min) t_R 19.2 (1*S*,2*S*) and 21.4 (1*R*,2*R*) min (71% ee).

2-Isopropylthio-1-phenyl-2-(2-pyridylthio)ethanol (27). *anti*-27: $[\alpha]^{20}_D$ −75.8 (*c* 0.350, $CHCl_3$, 85% ee); ^1H NMR δ 1.18 (d, $J = 6.6$ Hz, 6H), 3.05 (sep, $J = 6.6$ Hz, 1H), 5.06 (d, $J = 3.2$ Hz, 1H), 5.19 (d, $J = 3.2$ Hz, 1H), 6.20 (s, 1H), 7.00−8.44 (m, 9H); ^{13}C NMR δ 23.1, 23.8, 36.1, 58.4, 77.9, 120.3, 123.2, 127.2, 127.6, 127.7, 136.7, 140.7, 148.7, 158.5; IR (neat) 3411, 3061, 2959, 2924, 1721, 1579, 1453, 1415, 1121, 1054, 851, 700 cm^{-1}; EIMS *m*/*z* 288 (M^+ − OH), 243, 199, 155, 111. Anal. Calcd for $C_{16}H_{19}NOS_2$: C, 62.92; H, 6.27; N, 4.59. Found: C, 62.70; H, 6.43; N, 4.64. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 97/3, 0.5 mL/min) t_R 26.3 (1*S*,2*R*) and 31.8 (1*R*,2*S*) min (85% ee). ***syn*-27:** $[\alpha]^{20}_D$ 62.2 (*c* 0.154, $CHCl_3$); ^1H NMR δ 1.20 (d, $J = 6.4$ Hz, 6H), 3.08 (sep, $J = 6.4$ Hz, 1H), 4.89 (d, $J = 6.4$ Hz, 1H), 4.97 (d, $J = 6.4$ Hz, 1H), 6.36 (s, 1H), 7.04−8.45 (m, 9H); ^{13}C NMR δ 22.8, 23.6, 35.9, 58.1, 76.6, 120.2, 123.0, 126.9, 127.3, 136.4, 140.4, 148.5, 158.2; IR (neat) 3391, 3061, 2959, 2923, 1578, 1453, 1415, 1121, 1050, 854, 760 cm^{-1}; EIMS *m*/*z* 305 (M^+), 286, 243, 199, 155, 111. Anal. Calcd for $C_{16}H_{19}NOS_2$: C, 62.92; H, 6.27; N, 4.59. Found: C, 62.71; H, 6.45; N, 4.60.

2-Methylthio-1-phenyl-2-(2-pyridylthio)ethanol (28). *anti*-28: $[\alpha]^{20}_D$ −122 (*c* 0.340, $CHCl_3$, 69% ee); ^1H NMR δ 2.15 (s, 3H), 4.93 (d, $J = 3.3$ Hz, 1H), 5.34 (d, $J = 3.3$ Hz, 1H), 6.19 (s, 1H), 7.03−8.42 (m, 9H); ^{13}C NMR δ 15.7, 61.8, 77.5, 120.2, 123.3, 126.8, 127.5, 127.6, 136.5, 140.3, 148.5, 157.8; IR (neat) 3412, 3061, 2915, 2851, 1579, 1453, 1415, 849, 759, 456 cm^{-1}; EIMS *m*/*z* 260 (M^+-OH), 243, 169, 122, 90. Anal. Calcd for $C_{14}H_{15}NOS_2$: C, 60.62; H, 5.45; N, 5.05. Found: C, 60.65; H, 5.47; N, 4.98. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL/min) t_R 17.7 (1*R*,2*S*) and 19.7 (1*S*,2*R*) min (69% ee). ***syn*-28:** $[\alpha]^{20}_D$ 69.0 (*c* 0.350, $CHCl_3$, 57% ee); ^1H NMR δ 2.20 (s, 3H), 4.73 (d, $J = 6.8$ Hz, 1H), 5.00 (d, $J = 6.8$ Hz, 1H), 6.59 (d, $J = 6.8$ Hz, 1H), 7.26−8.42 (m, 9H); ^{13}C NMR δ 16.1, 61.8, 77.1, 120.4, 123.9, 126.4, 127.5, 127.8, 136.7, 143.3, 148.3, 160.5; IR (neat) 3368, 3060, 2916, 2853, 1453, 1415, 853, 761 cm^{-1}; EIMS *m*/*z* 277 (M^+), 243, 169, 122, 90. Anal. Calcd for $C_{14}H_{15}NOS_2$: C, 60.61; H, 5.45; N, 5.05. Found: C, 60.60; H, 5.66; N, 5.20. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL/min) t_R 22.0 (1*S*,2*S*) and 27.0 (1*R*,2*R*) min (57% ee).

1-Phenyl-2-(2-pyridylthio)-2-(2,4,6-triisopropylphenylthio)ethanol (29). An inseparable diastereomeric mixture of **29**: mp 124−125 °C; ^1H NMR δ 0.92−1.23 (m, 18H), 1.62 (s, 1H), 2.79 (sep, $J = 6.6$ Hz, 1H (major)), 3.10−3.30 (m, 2H (major), 1H (minor)), 3.67 (sep, $J = 6.4$ Hz, 2H (minor)), 4.58 (d, $J = 5.8$ Hz, 1H (minor)), 4.62 (d, $J = 1.8$ Hz, 1H (major)), 5.15 (br, 1H (major)), 5.54 (br, 1H (major)), 6.88 (s, 2H (major)), 6.96 (s, 2H (minor)), 7.02−7.67 (m, 8H), 8.41 (m, 1H); ^{13}C NMR δ 14.1, 14.6, 22.7, 23.9, 24.1, 24.6, 28.1, 31.1, 31.5, 34.2, 38.9, 66.7, 74.6, 78.0, 119.8, 120.1, 121.5, 121.6, 123.0, 125.6, 126.0, 126.2, 126.6, 127.2, 127.4, 127.5, 127.7, 128.1, 136.2, 141.1, 142.0, 148.1, 148.2, 149.6, 153.1, 153.3, 157.1, 158.0; IR (KBr) 3398, 2620, 1582, 1456, 1414, 1060, 877, 761, 707 cm^{-1}; EIMS *m*/*z* 465 (M^+), 358, 243, 211, 122. Anal. Calcd for $C_{28}H_{35}NOS_2$: C, 72.21; H, 7.57; N, 3.01. Found: C, 72.06; H, 7.71; N, 3.01.

2-*tert*-Butylthio-2-(2-pyridylthio)-1-(2,4,6-trimethylphenyl)ethanol (30). *anti*-30: $[\alpha]^{20}_D$ −26.3 (*c* 0.108, $CHCl_3$, 85% ee); ^1H NMR δ 1.52 (s, 9H), 2.05 (s, 3H), 2.45 (s, 6H), 3.52 (s, 1H), 5.13 (d, $J = 10.0$ Hz, 1H), 5.63 (d, $J = 10.0$ Hz, 1H), 6.47 (s, 2H), 6.65−8.29 (m, 4H); ^{13}C NMR δ 20.7, 21.6, 31.4, 45.9, 54.1, 73.2, 73.2, 119.7, 122.5, 129.2, 131.2, 135.1, 136.1, 137.0, 148.2, 156.8; IR (neat) 3486, 2961, 1725, 1576, 1453, 1425, 1120, 1042, 849, 733 cm^{-1}; EIMS *m*/*z* 361 (M^+), 285, 212, 155, 111. Anal. Calcd for $C_{20}H_{27}NOS_2$: C, 66.44; H, 7.53; N, 3.87. Found: C, 66.57; H, 7.82; N, 3.84. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 95/5, 0.7 mL/min) t_R 10.4 (1*S*,2*R*) and 12.6 (1*R*,2*S*) min (85% ee). ***syn*-30:** $[\alpha]^{20}_D$ 11.2 (*c* 0.84, $CHCl_3$, 77% ee): ^1H NMR δ 1.17 (s, 9H), 2.24 (s, 3H), 2.53 (s, 6H), 2.89 (s, 1H), 5.21 (d, $J = 10.4$ Hz, 1H), 5.28 (d, $J = 10.4$ Hz, 1H), 6.78 (s, 2H), 7.03−8.42 (m, 4H); ^{13}C NMR δ 20.9, 21.5, 30.8, 45.2, 120.2, 123.1, 129.6, 134.2, 136.1, 136.5, 148.3, 158.8; IR (neat) 3400, 2959, 1578, 145, 1415, 1120, 851, 759 cm^{-1}; EIMS *m*/*z* 287 (M^+ − OH, $-C_4H_9$), 285, 212, 155, 111. Anal. Calcd for $C_{20}H_{27}NOS_2$: C, 66.44; H, 7.53; N, 3.87. Found: C, 66.15; H, 7.50; N, 4.18. HPLC (Daicel Chiralpak OJ-H, hexane/*i*PrOH 98/2, 0.5 mL/min) t_R 25.9 (1*S*,2*S*) and 29.3 (1*R*,2*R*) min (77% ee).

2-*tert*-Butylthio-1-(2-naphthyl)-2-(2-pyridylthio)ethanol (31). *anti*-31: mp 92−93 °C; $[\alpha]^{20}_D$ −47.7 (*c* 0.166, $CHCl_3$, 83% ee); ^1H NMR δ 1.18 (s, 9H), 5.07 (d, $J = 2.8$ Hz, 1H), 5.45 (d, $J = 2.8$ Hz, 1H), 5.95−6.09 (br, 1H), 7.06−8.49 (m, 11H); ^{13}C NMR δ 30.8, 44.6, 56.2, 77.7, 119.9, 122.9, 125.1, 125.3, 126.1, 126.8, 127.2, 127.9, 132.6, 132.7, 136.3, 138.0, 145.9, 148.5, 158.2; IR (KBr) 3438, 3053, 2958, 1454, 1414, 1120, 858, 802, 759 cm^{-1}; EIMS *m*/*z* 311 ($M^+ - C_4H_9$), 293, 257, 212, 155, 111. Anal. Calcd for $C_{21}H_{23}NOS_2$: C, 68.26; H, 6.27; N, 3.79. Found: C, 68.35; H, 6.26; N, 3.78. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL/min) t_R 24.5 (1*R*,2*S*) and 43.0 (1*S*,2*R*) min (83% ee). ***syn*-31:** $[\alpha]^{20}_D$ 51.3 (*c* 0.306, $CHCl_3$, 69% ee); ^1H NMR δ 1.27 (s, 9H), 5.05 (d, $J = 6.4$ Hz, 1H), 5.16 (d, $J = 6.4$ Hz, 1H), 6.58−6.65 (br, 1H), 7.09−8.50 (m, 11H); ^{13}C NMR δ 30.1, 45.0, 56.5, 78.2, 116.5, 120.1, 123.3, 124.7, 125.4, 125.5, 126.0, 127.2, 127.3, 127.8, 132.6, 135.4, 139.8, 148.4, 157.5; IR (neat) 3404, 3053, 2959, 145, 1415, 1121, 857, 803, 748 cm^{-1}; EIMS *m*/*z* 311 ($M^+ - C_4H_9$), 293, 257, 212, 155, 111. Anal. Calcd for $C_{21}H_{23}NOS_2$: C, 68.26; H, 6.27; N, 3.79. Found: C, 68.46; H, 6.21; N, 3.90. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 98/2, 1.0 mL/min) t_R 38.1 (1*R*,2*R*) and 48.3 (1*S*,2*S*) min (69% ee).

2-*tert*-Butylthio-1-(4-methoxyphenyl)-2-(2-pyridylthio)-ethanol (32). *anti*-32: mp 88−89 °C; $[\alpha]^{20}_D$ 15.5 (*c* 0.092, $CHCl_3$, 75% ee); ^1H NMR δ 1.23 (s, 9H), 3.79 (s, 3H), 5.08 (br, 1H), 5.24 (d, $J = 3.0$ Hz, 1H), 5.82 (s, 1H), 6.81−8.45 (m, 8H); ^{13}C NMR δ 30.9, 45.0, 55.2, 56.5, 77.4, 112.9, 120.0, 123.2, 128.0, 134.5, 136.4, 148.4, 158.5; IR (KBr) 3350, 3046, 2954, 1582, 1514, 1456, 1416, 1252, 1120, 830, 762 cm^{-1}; EIMS *m*/*z* 349 (M^+), 331, 212, 155, 111. Anal. Calcd for $C_{18}H_{23}NO_2S_2$: C, 61.86; H, 6.63; N, 4.01. Found: C, 62.10; H, 6.79; N, 4.14. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL/min) t_R 26.3 (1*R*,2*S*) and 43.4 (1*S*,2*R*) min (75% ee). ***syn*-32:** $[\alpha]^{20}_D$ 31.3 (*c* 0.474, $CHCl_3$, 55% ee); ^1H NMR δ 1.26 (s, 9H), 3.89 (s, 3H), 4.95 (d, $J = 6.4$ Hz, 1H), 5.05 (br, 1H), 6.09−6.21

(br, 1H), 6.85−8.53 (m, 8H); ^{13}C NMR δ 30.9, 44.9, 55.2, 56.5, 77.4, 112.9, 120.0, 123.2, 127.9, 134.5, 136.3, 148.4, 157.8, 158.5; IR (neat) 3435, 3046, 2958, 1578, 1511, 1455, 1415, 1247, 1120, 831, 760 cm^{-1}; EIMS *m*/*z* 349 (M^+), 273, 212, 155, 111, 56. Anal. Calcd for $C_{18}H_{23}NO_2S_2$: C, 61.86; H, 6.63; N, 4.01. Found: C, 61.87; H, 6.86; N, 3.77. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 95/5, 0.5 mL/min) t_R 25.6 (1*R*,2*R*) and 30.0(1*S*,2*S*) min (55% ee).

1-(4-Chlorophenyl)-2-*tert*-butylthio-2-(2-pyridylthio)-ethanol (33). *anti*-33: mp 115−116 °C; $[\alpha]^{20}_D$ −44.6 (*c* 0.298, $CHCl_3$, 88% ee); ^{1}H NMR δ 1.22 (s, 9H), 4.92 (d, *J* = 3.0 Hz, 1H), 5.26 (d, *J* = 3.0 Hz, 1H), 6.04 (s, 1H), 7.08−8.45 (m, 8H); ^{13}C NMR δ 30.9, 44.7, 55.8, 77.5, 120.0, 122.8, 127.3, 128.5, 133.0, 136.5, 138.9, 148.5, 158.0; IR (KBr) 3293, 2957, 1582, 1557, 1490, 1456, 1416, 1216, 1159, 1121, 813, 765 cm^{-1}; EIMS *m*/*z* 295 ($M^+ - C_4H_9$), 277, 212, 155, 111. Anal. Calcd for $C_{17}H_{20}ClNOS_2$: C, 57.69; H, 5.70; N, 3.96. Found: C, 57.78; H, 5.82; N, 3.91. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL/min) t_R 13.7 (1*R*,2*S*) and 22.9 (1*S*,2*R*) min (88% ee). ***syn*-33:** $[\alpha]^{20}_D$ 30.6 (*c* 0.158, $CHCl_3$, 71% ee); ^{1}H NMR δ 1.25 (s, 9H), 4.76 (d, *J* = 6.6 Hz, 1H), 4.92 (d, *J* = 6.4 Hz, 1H), 6.42 (s, 1H), 6.85−8.53 (m, 8H); ^{13}C NMR δ 30.8, 45.1, 56.2, 77.3, 120.2, 123.3, 127.5, 128.3, 132.8, 136.5, 140.9, 148.4, 157.5; IR (neat) 3450, 2959, 1721, 1579, 1454, 1119, 811, 760 cm^{-1}; EIMS *m*/*z* 296 ($M^+ - C_4H_9$), 277, 212, 155, 111, 56. Anal. Calcd for $C_{17}H_{20}ClNOS_2$: C, 57.69; H, 5.70; N, 3.96. Found: C, 57.53; H, 5.95; N, 3.86. HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 98/2, 0.5 mL/min) t_R 29.8 (1*R*,2*R*) and 43.7 (1*S*,2*S*) min (72% ee).

1-(*tert*-Butylthio)-3-methyl-1-(2-pyridylthio)butan-2-ol (34). An inseparable diastereomeric mixture of **34**; ^{1}H NMR δ 0.89−1.06 (m, 6H), 1.38 (s, 9H (major)), 1.39 (s, 9H (minor)), 1.77 (s, 1H), 2.04 (sep, *J* = 7.4 Hz, 1H (minor)), 2.08 (sep, *J* = 6.8 Hz, 1H (major)), 3.46−3,56 (br, 1H (minor)), 3.63 (dd, *J* = 2.8, 7.8 Hz, 1H (major)), 4.65 (s, 1H (major)), 4.97 (d, *J* = 5.8 Hz, 1H (minor)), 5.05 (d, *J* = 2.8 Hz, 1H (major)), 6.95−7.56 (m, 3H), 8.34−8.40 (m, 1H); ^{13}C NMR δ 17.4, 19.0, 19.8, 20.0, 31.2, 31.3, 44.2, 45.0, 53.6, 53.7, 80.7, 81.4, 119.7, 119.8, 122.7, 123.7, 136.1, 136.3, 148.4, 148.6, 155.6, 157.7; IR (neat) 3435, 2959, 1578, 1556, 1454, 1120, 1046, 759 cm^{-1}; EIMS *m*/*z* 285 (M^+), 243, 199, 155, 111, 77. Anal. Calcd for $C_{14}H_{23}NOS_2$: C, 58.90; H, 8.12; N, 4.91. Found: C, 59.01; H, 8.21; N, 4.70. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 16.6 (1*S*,2*S*), 18.9 (1*R*,2*S*), 30.6 (1*R*,2*R*), and 38.1 (1*S*,2*R*) min.

2-(*tert*-Butylthio)-1-cyclohexyl-2-(2-pyridylthio)ethanol (35). *anti*-35: $[\alpha]^{20}_D$ −94.5 (*c* 0.400, $CHCl_3$, 81% ee); ^{1}H NMR δ 1.00−1.36 (m, 4H), 1.39 (s, 9H), 1.57−2.18 (m, 7H), 3.68 (dd, *J* = 2.4, 7.4 Hz, 1H), 4.58 (s, 1H), 5.05 (d, *J* = 2.4 Hz, 1H), 6.99−7.56 (m, 3H), 8.35−8.39 (m, 1H); ^{13}C NMR δ 25.9, 26.1, 26.4, 28.9, 29.8, 31.2, 40.5, 44.2, 53.4, 80.1, 119.6, 122.6, 136.0, 148.5, 157.8; IR (neat) 3466, 2922, 1579, 1452, 1414, 1162, 1121, 759 cm^{-1}; EIMS *m*/*z* 325 (M^+), 307, 250, 156, 111, 82; Anal. Calcd for $C_{14}H_{23}NOS_2$: C, 62.72; H, 8.36; N, 4.30. Found: C, 62.50; H, 8.22; N, 4.28. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 23.6 (1*R*,2*S*) and 50.6 (1*S*,2*R*) min. ***syn*-35:** $[\alpha]^{20}_D$ −46.3 (*c* 0.160, $CHCl_3$, 64% ee); ^{1}H NMR δ 1.01−1.38 (br, 4H), 1.37 (s, 9H), 1.60−2.18 (m, 7H), 3.54 (dd, *J* = 2.8, 7.8 Hz, 1H), 4.82 (br, 1H), 5.01 (d, *J* = 5.4 Hz, 1H), 6.99−7.59 (m, 3H), 8.34−8.40 (m, 1H); ^{13}C NMR δ 25.9, 26.0, 26.48, 28.1, 30.0, 31.28, 41.5, 45.0, 53.1, 80.0, 119.8, 123.3, 136.1, 148.4, 157.3; IR (neat) 3435, 2922, 1578, 1453, 1159, 1121, 758 cm^{-1}; EIMS *m*/*z* 325 (M^+), 307, 250, 156, 111, 82. Anal. Calcd for $C_{14}H_{23}NOS_2$: C, 62.72; H, 8.36; N, 4.30. Found: C, 62.51; H, 8.36; N, 4.04. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 95/5, 0.5 mL/min) t_R 59.9 (1*S*,2*S*) and 64.9 (1*R*,2*R*) min.

1-*tert*-Butyl-2-(*tert*-butylthio)-2-(2-pyridylthio)ethanol (36). *anti*-36: mp 72−73 °C; $[\alpha]^{20}_D$ −238.5 (*c* 0.152, $CHCl_3$, 88% ee); ^{1}H NMR δ 1.08 (s, 9H), 1.39 (s, 9H), 3.87 (br, 1H), 5.01 (d, *J* = 1.4 Hz, 1H), 5.16 (s, 1H), 6.98−8.43 (m, 4H); ^{13}C NMR δ 27.3, 31.5, 36.2, 44.1, 53.0, 85.0, 119.7, 123.1, 136.2, 148.6, 157.7; IR (KBr) 3400, 2954, 1646, 1455, 1417, 1154, 1122, 1071, 753 cm^{-1}; EIMS *m*/*z* 299 (M^+), 242, 223, 155, 111, 56. Anal. Calcd for $C_{15}H_{25}NOS_2$: C, 60.16; H, 8.41; N, 4.68. Found: C, 60.06; H, 8.48; N, 4.52. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 20.7 (1*R*,2*S*) and 37.7 (1*S*,2*R*) min (88% ee). ***syn*-36:** mp 55−56 °C; $[\alpha]^{20}_D$ −179.7 (*c* 0.182, $CHCl_3$, 70% ee); ^{1}H NMR δ 1.05 (s, 9H), 1.36 (s, 9H), 3.74 (br, 1H), 4.97 (d, *J* = 2.8 Hz, 1H), 5.60 (s, 1H), 7.01−8.44 (m, 4H); ^{13}C NMR δ 26.8, 31.0, 36.8, 45.1, 52.3, 83.6, 119.9, 123.7, 136.2, 148.3, 156.2; IR (KBr) 3389, 2957, 1577, 1453, 1413, 1280, 1125, 1075, 755 cm^{-1}; EIMS *m*/*z* 299(M^+), 242, 223, 155, 111, 56. Anal. Calcd for $C_{15}H_{25}NOS_2$: C, 60.16; H, 8.41; N, 4.68. Found: C, 60.26; H, 8.49; N, 4.66. HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 98/2, 0.5 mL/min) t_R 13.6 (1*S*,2*S*) and 15.4 (1*R*,2*R*) min (88% ee).

Acetylation of Ethanols 26, 30, and 31: 1-Acetoxy-2-(*tert*-butylthio)-1-phenyl-2-(2-pyridylthio)ethane (37). To a solution of *anti*-**26** (132 mg, 0.413 mmol) in pyridine (1.0 mL) were added DMAP (5.1 mg, 0.04 mmol) and acetic anhydride (0.08 mL, 0.826 mmol) at room temperature, and the mixture was stirred for 3 h. Saturated aqueous NH_4Cl was then added to the reaction mixture, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (silica gel 25 g, hexane/ethyl acetate = 96:4) to give **37** (110 mg, 73%). The enantiomeric excess was determined by HPLC analysis using Chiralpak AD-H: ^{1}H NMR δ 1.34 (s, 9H), 1.94 (s, 3H), 5.75 (d, *J* = 5.6 Hz, 1H), 6.06 (d, *J* = 5.6 Hz, 1H), 7.00−8.41 (m, 9H); IR (KBr) 3055, 2969, 2953, 1738, 1578, 1234, 758 cm^{-1}; HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 10.9 (1*R*,2*S*) and 15.6 (1*S*,2*R*) min (81% ee).

1-Acetoxy-2-(*tert*-butylthio)-2-(2-pyridylthio)-1-(2,4,6-trimethylphenyl)ethane (38): ^{1}H NMR δ 1.47 (s, 9H), 2.05 (s, 3H), 2.08 (s, 3H), 2.47 (s, 6H), 5.71 (d, *J* = 10.4 Hz, 1H), 6.34 (d, *J* = 10.4 Hz, 1H), 6.64 (s, 2H), 7.16−8.30 (m, 4H); HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 98/2, 0.3 mL/min) t_R 21.2 (1*R*,2*S*) and 24.0 (1*S*,2*R*) min (85% ee).

1-Acetoxy-2-(*tert*-butylthio)-1-(2-nathtyl)-2-(2-pyridylthio)ethane (39): ^{1}H NMR δ 1.09 (s, 9H), 2.15 (s, 3H), 5.43 (br, 1H), 6.42 (br, 1H), 7.04−8.58 (m, 11H); HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90/10, 0.5 mL/min) t_R 14.2 (1*R*,2*S*) and 25.4 (1*S*,2*R*) min (72% ee).

Deprotection of Dithioacetals 37−39 Subsequent Reduction: (*R*)-1-Phenyl-1,2-ethanediol (40). To a solution of **37** (41 mg, 0.11 mmol) in aqueous acetonitrile (2.0 mL, acetonitrile/H_2O = 9:1) was added $HgCl_2$ (80.3 mg, 0.34 mmol) at room temperature, and the mixture was stirred for 3 h. The reaction mixture was filtered, and the mother liquid was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude acetoxyaldehyde, an ethereal solution of which was then added to a solution of $LiAlH_4$ (21 mg, 0.56 mmol) in Et_2O (1.0 mL) at 0 °C. After 3 h, saturated aqueous NH_4Cl was added and the mixture was extracted with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (silica gel 25 g, hexane/ethyl acetate = 65:35) to give **40** (12 mg, 77%): $[\alpha]^{20}_D$ −57.5 (*c* 0.238, $CHCl_3$, 83% ee) (lit.[19] $[\alpha]^{20}_D$ −69 (*c* 1, $CHCl_3$)); ^{1}H NMR δ 1.95 (br, 2H), 3.61 (m, 2H), 4.83 (m, 1H), 7.35 (br, 5H).

(*R*)-1-(2,4,6-Trimethylphenyl)-1,2-ethanediol (41). $[\alpha]^{20}_D$ −43.0 (*c* 0.334, $CHCl_3$, 79% ee) (lit.[23] $[\alpha]^{20}_D$ −53.0 (*c* 1.01, $CHCl_3$)); ^{1}H NMR δ 1.60−2.05 (br, 2H), 2.24 (s, 3H), 2.40 (s, 6H), 3.67 (dd, *J* = 3.8, 10.8 Hz, 1H), 3.96 (t, *J* = 10.8 Hz, 1H), 5.25 (dd, *J* = 3.8, 10.8 Hz, 1H), 6.82 (s, 2H).

(*R*)-1-(2-naphthyl)-1,2-ethanediol (42). $[\alpha]^{20}_D$ −30.0 (*c* 0.035, MeOH, 68% ee) (lit.[23] $[\alpha]^{20}_D$ −43.9 (*c* 1.00, MeOH)); ^{1}H NMR δ 2.03 (br, 1s), 2.60 (br, 1s), 3.71−3.90 (m, 2H), 4.99−

5.05 (m, 1H), 7.45−7.86 (m, 7H); HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 70/30, 0.5 mL/min) t_R 13.7 (*R*) and 15.9 (*S*) min (68% ee).

Acknowledgment. We thank Dr. Shinya Kusuda, Ono Pharmaceutical Co., Ltd., for X-ray crystallographic analysis. This work was supported by a Grant-in-Aid for Scientific Research (No. 11650890) from the Ministry of Education, Science, Sports and Culture of Japan.

Supporting Information Available: X-ray structure of *anti*-**26**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO035558E