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Enantioselective Conjugate Addition of Thiols to Cyclic Enones and Enals Catalyzed by Chiral *N*,*N*′-Dioxide–Cadmium Iodide Complex

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Abstract—Chiral *N*,*N*′-dioxide–cadmium iodide complex has been shown to catalyze enantioselective conjugate additions of thiols to cyclic enones and enals. The sulfides are generated in high yields and in good enantioselectivities up to 78% ee using 1 mol% of the chiral catalyst. The present reaction provides the first example of utilizing a cadmium complex as a catalyst in enantioselective reaction.

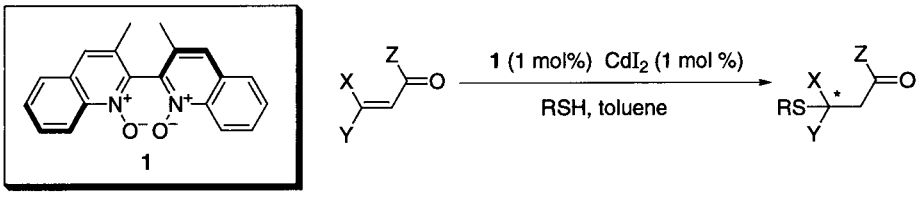
Introduction

The design of chiral ligands plays a key role in the development of enantioselective reactions. Many recent studies have therefore focused on the development of novel chiral ligands for metal-catalyzed reactions. Although *N*-oxide is now known to be a unique functional group, possessing a notable electron-donating property, which allows it to form complexes with a variety of metals,[1] there have been few attempts to employ *N*-oxides as chiral ligands.[2] We have recently reported an enantioselective allylation of aldehydes with allyltrichlorosilanes utilizing chiral *N*,*N*′-dioxide **1** as a catalyst, in which the electron-donating property of *N*-oxide played a pivotal role.[3c] As part of our program directed at the development of *N*-oxide-mediated reaction,[3] herein we describe a detail of an enantioselective conjugate addition of thiols to enones and enals catalyzed by chiral *N*,*N*′-dioxide–cadmium iodide complex (Eq. (1)).[4]

Results and Discussion

Since the first enantioselective conjugate addition of thiols catalyzed by cinchona alkaloid was reported,[5a] several chiral amine-catalyzed reactions have been discussed.[5] The recent discovery of a lithium thiolate complex of amino bisether,[6] heterobimetallic complex,[7] or nickel oxazoline complex[8] as the catalysts for the enantioselective conjugate addition has received considerable attention, due to their high efficacy.

Recently, we described the optical resolution of **1** through the formation of a hydrogen-bonding complex between **1** and optically active binaphthol.[3a] This prompted our hypothesis that thiophenol forms a hydrogen-bonding complex with **1**, which is expected to control the nucleophilicity and steric accessibility of thiophenol in its enantioselective conjugate addition to electron-deficient olefin. To test this hypothesis, we initially employed 10 mol% of **1** as a



(1)

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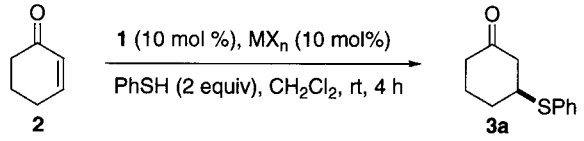
Table 1. Enantioselective conjugate addition of thiophenol to **2** with **1** and various metal salts



2 **3a**

Entry	MX_n	Conversion, %[a]	ee, %[b]
1	CuCl	>95	16
2	$ZnCl_2$	>95	7
3	$PdCl_2$	>95	9
4	AgCl	80	19
5	$SnCl_2$	>95	7
6	HgCl	>95	13
7	$BiCl_3$	>95	8
8	$CdCl_2$	>95	30
9	$CdBr_2$	>95	46
10	CdI_2	>95	57

[a] Determined by NMR measurement.
[b] Determined by HPLC analysis employing Daicel Chiralpak AD.

Table 2. Stoichiometric study in enantioselective conjugate addition of thiophenol to **2** (**2** (1 mmol) CdI_2 (10 μmol) PhSH (2 mmol), toluene, rt)

Entry	Mol% of **1**	Time, h	Yield, %[a]	ee, %[b]
1	2	6	96	78
2	1	6	96	78
3	0.5	4	97	34
4	0	1	96	–

[a] Isolated yield.
[b] Determined by HPLC analysis employing Daicel Chiralpak AD.

catalyst in the conjugate addition of thiophenol to 2-cyclohexen-1-one (**2**) in dichloromethane. The reaction produced a significant yield of the corresponding sulfide **3a**, although the observed enantioselectivity was quite low (rt, 24 h, 35%, 12% ee).

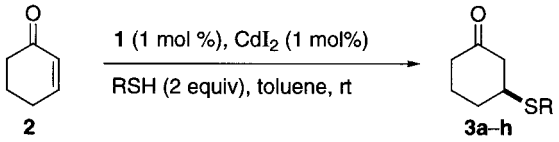
To enhance the reactivity and enantioselectivity, we used 10 mol% metal salt as an additive expected to coordinate with carbonyl oxygen. Table 1 shows some representative results using various metal salts which gave the sulfide **3a** in high yield with observable enantioselectivity. Among various metal chlorides surveyed, addition of cadmium chloride yielded the corresponding sulfide quantitatively with 30% ee (entry 8). Further investigation revealed that cadmium iodide was the optimal additive, affording the sulfide in 57% ee (entry 10). Enantioselectivity increased up to 78% when the reaction was performed in toluene, whereas polar solvents decreased enantioselectivity (tetrahydrofuran: 99%, 0% ee; acetonitrile: 97%, 33% ee). Stoichiometric studies using 1 mol% of cadmium iodide revealed that equimolar amounts of **1** and cadmium iodide are sufficient for optimum enantioselectivity (Table 2, entry 2). The reaction was promoted by cadmium iodide in the absence of *N*-oxide to produce the sulfide in 96% yield (entry 4). These results suggest that a 1:1 complex of **1** and cadmium iodide[9] functions as a catalyst in this enantioselective addition. This is the first example of an enantioselective reaction utilizing a cadmium compound,[10] exhibiting a distinctive binding to *N*-oxide.

Table 3 summarizes the conjugate addition of various thiols to **2** under optimized conditions. Introduction of one or two methyl groups into *ortho*-position of thiophenol decreased both chemical yield and enantioselectivity, probably due to the steric hindrance (entries 2, 3). It is surprising that the reaction of 4-substituted thiophenols (entries 4–7), except for 4-methoxybenzenethiol (entry 7) gave low selectivity as compared to that of thiophenol (entry 1), though the steric environment around the reaction center seems quite similar. Benzyl mercaptan (entry 8) also gave lower reactivity and selectivity.

The scope of the acceptor in the conjugate addition was then investigated (Table 4). Slight modifications of the substrate strongly influenced enantioselectivity. 2-Cyclohepten-1-one **4** (entry 2) gave an enantioselectivity comparable to that of **2** (entry 1), while 2-cyclopenten-1-one **5** (entry 3) demonstrated low selectivity. Introduction of substituent into 3- or 4-position of cyclohexenone resulted in decline in both chemical yield and enantioselectivity, probably for the steric reason (entries 4, 5).

While attempts to employ acyclic conjugate ketones as the substrate such as chalcone were unsuccessful (30%, 10%

Table 3. Enantioselective conjugate addition of thiols to **2** catalyzed by **1**–CdI_2 complex

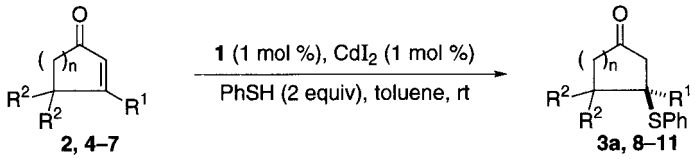


2 **3a–h**

Entry	R	Time, h	Product	Yield, %[a]	ee, %[b]	Confign[c]	$[\alpha]_D$[d]
1	Ph	6	**3a**	96	78	*S*	−68.7
2	2-MeC_6H_4	24	**3b**	28	29	–	−25.5
3	2,6-$Me_2C_6H_3$	48	**3c**	8	33	–	−26.0
4	4-MeC_6H_4	12	**3d**	74	29	*S*	−23.7
5	4-$^tBuC_6H_4$	12	**3e**	78	40	*S*	−30.8
6	4-ClC_6H_4	3	**3f**	98	24	*S*	−19.8
7	4-$MeOC_6H_4$	6	**3g**	91	58	*S*	−43.2
8	$PhCH_2$	12	**3h**	48	40	*S*	−43.1

[a] Isolated yield.
[b] Determined by HPLC analysis employing Daicel Chiralpak AD.
[c] Configuration assignment by comparison to literature[5b] values of optical rotations.
[d] *c* 1, $CHCl_3$.

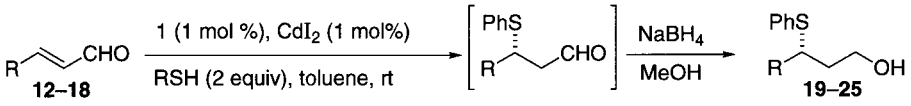
Table 4. Enantioselective conjugate addition of thiols to enones catalyzed by **1**–CdI_2 complex



Entry	Enone	*n*	R^1	R^2	Time, h	Product	Yield, %[a]	ee, %[b]	$[\alpha]_D$[c]
1	**2**	2	H	H	6	**3a**	96	78	−68.7
2	**4**	3	H	H	24	**8**	68	61	−27.2
3	**5**	1	H	H	4	**9**	94	21	+1.8
4	**6**	2	Me	H	48	**10**	43	10	−4.2
5	**7**	2	H	Me	48	**11**	79	26	−29.0

[a] Isolated yield.
[b] Determined by HPLC analysis employing Daicel Chiralpak AD or AS.
[c] *c* 1, $CHCl_3$.

Table 5. Enantioselective conjugate addition of thiophenol to enals catalyzed by **1**–CdI_2 complex



Entry	Enal	R	Time, h[a]	Product	Yield, %[b]	ee, %[c]	$[\alpha]_D$[d]
1	**12**	Me	12	**19**	89	69[e]	+24.9
2	**13**	Et	12	**20**	91	70	+14.0
3	**14**	Pr	24	**21**	66	65	+16.4
4	**15**	^{i}Pr	24	**22**	80	63	+24.8
5	**16**	$PhCH_2$	24	**23**	76	52	+5.2
6	**17**	^{t}Bu	48	**24**	67	39	+8.3
7	**18**	Ph	48	**25**	34	9	−19.9

[a] Reaction time of conjugate addition.
[b] Isolated yield of alcohol.
[c] Determined by HPLC analysis employing Daicel Chiralcel OD.
[d] *c* 1, $CHCl_3$.
[e] Absolute configuration was determined to be *S* by comparison to the values of optical rotation of **19** prepared from methyl 3-phenylthiobutanoate.[6a]

ee), the reaction of acyclic conjugate aldehydes afforded the corresponding sulfides in high chemical yields and with enantioselectivities up to 70% ee after conversion to the corresponding alcohol (Table 5). Aliphatic enals (entries 1–6) except for **17** having bulky *tert*-butyl group (entry 6) gave almost the same degree of enantioselectivities, while conjugate enal **18** (entry 7) gave unsuccessful result. The mildness of the reaction conditions allows the enantioselective conjugate addition of thiols to enals, a reaction never previously reported due to the lability of aldehydes.

To gain an insight into the reaction mechanism, we examined the influence of enantioselectivity by the stereochemistry of the carbon–carbon double bond in enal. Surprisingly, addition of thiophenol to a 1:1 mixture of (*E*)- and (*Z*)-2-pentenal exhibited the same sense and degree of enantioselectivity (86%, 68% ee) as (*E*)-2-pentenal **13** (Table 5, entry 2) without observable isomerization of the starting olefin. We next investigated several additives to the reaction of **2** and thiophenol in toluene. Addition of cyclohexanone (1.0 equiv.) influenced neither chemical yield nor enantioselectivity (92%, 74% ee) of the reaction. The addition of cyclohexene (1.0 equiv.), however, dramatically reduced enantioselectivity (92%, 45% ee). These results suggest the importance of the coordination of cadmium complex to carbon–carbon double bond. To examine the influence of ligand purity on the enantioselectivity, we carried out a series of conjugate addition of thiophenol to **2** with mixtures of the (*R*)- and (*S*)-**1**. When the enantioselectivity of the product was plotted against the optical purity of **1**, a slight nonlinear effect[11] was observed as can be seen in Fig. 1. These results imply the possibility of the aggregation of the *N*,*N*′-dioxide–cadmium iodide complex, though the detail is not clear.

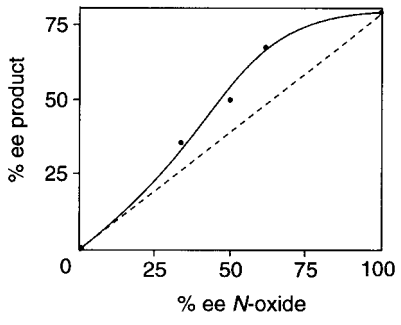


Figure 1. Nonlinear effect in the conjugate addition of thiophenol to **2** catalyzed by **1**–CdI_2 complex

Conclusions

We have demonstrated the effectiveness of a chiral *N*,*N*′-dioxide–cadmium iodide complex as a catalyst for enantioselective conjugate addition of thiols. Cyclic enones and enals can be employed as acceptors, utilizing 1 mol% catalyst loadings, to afford the sulfides in high yields and with good enantioselectivities of up to 78% ee. The present reaction provides the first example of utilizing cadmium complex in enantioselective reaction.

Experimental

General

Melting points were measured using a Büchi 535 melting point apparatus and were not corrected. Optical rotations were obtained on a JASCO P-1030 digital polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL EX-270 (^{1}H, 270 MHz; ^{13}C, 68 MHz) spectrometer in deuteriochloroform. Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Coupling constants (*J*) are reported in Hertz (Hz). Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, br, broad. Infrared spectra (IR) were recorded on a JASCO FT/IR-5300 spectrometer. Mass spectra were obtained on a JEOL JMS-FABmate spectrometer by electron impact (EI) with ionization voltage of 70 eV.

Enantioselective conjugate addition of thiols to enones

Thiol (2.0 mmol) in toluene (1 mL) was added to a stirred solution of enone (1.0 mmol), *N*-oxide **1** (3.2 mg, 10 mmol) and cadmium iodide (3.6 mg, 10 mmol) in toluene (7 mL) and stirred at rt. The reaction mixture was diluted in toluene and successively washed with aq. NaOH and brine. The solvent was evaporated and the residue was chromatographed on silica gel column (eluent, toluene/AcOEt) to afford the corresponding sulfide. *N*-Oxide **1** was recovered by elution with 10% ethanol in dichloromethane without a loss of optical purity. The enantiomeric excess of the product was determined by chiral HPLC.

(*S*)-3-(Phenylthio)-cyclohexanone (3a).[5b] $[\alpha]_D^{23}=-68.7$ (*c* 1.1, $CHCl_3$), $[\alpha]_{577}^{24}=-72.7$ (*c* 1.1, CCl_4) for 78% ee (lit. 5b; $[\alpha]_{578}^{21}=+53$ (*c* 1, CCl_4) for (*R*)-**3a** 54% ee). HPLC: t_R (*S*), 8.5 min, (*R*), 10.0 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=9:1). ^{1}H NMR: δ 1.59–1.82 (m, 2H), 2.07–2.22 (m, 2H), 2.24–2.43 (m, 3H), 2.64–2.77 (m, 1H), 3.39–3.45 (m, 1H), 7.26–7.36 (m, 3H), 7.39–7.45 (m, 2H).

(−)-3-[(2-Methylphenyl)thio]-cyclohexanone (3b).[5j] $[\alpha]_D^{24}=-25.5$ (*c* 0.9, $CHCl_3$) for 29% ee. HPLC: t_R (+), 14.0 min, (−), 16.0 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=99:1). ^{1}H NMR: δ 1.61–1.84 (m, 2H), 2.08–2.22 (m, 2H), 2.29–2.46 (m, 3H), 2.43 (s, 3H), 2.65–2.72 (m, 1H), 3.36–3.49 (m, 1H), 7.11–7.25 (m, 3H), 7.36–7.41 (m, 1H).

(−)-3-[(2,6-Dimethylphenyl)thio]-cyclohexanone (3c).[5j] Mp 91.0–92.0°C. $[\alpha]_D^{24}=-26.0$ (*c* 0.9, $CHCl_3$) for 33% ee. HPLC: t_R (+), 9.0 min, (−), 10.0 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=99:1). ^{1}H NMR: δ 1.58–1.86 (m, 2H), 2.01–2.20 (m, 2H), 2.25–2.48 (m, 3H), 2.52 (s. 6H), 2.53–2.64 (m, 1H), 3.12–3.24 (m, 1H). 3.34–3.46 (m, 1H), 7.08–7.13 (m, 3H).

(*S*)-3-[(4-Methylphenyl)thio]-cyclohexanone (3d).[5h] $[\alpha]_D^{24}=-23.7$ (*c* 1.2, $CHCl_3$), $[\alpha]_{577}^{25}=-17.2$ (*c* 1.9, benzene) for 29% ee (lit. 5h; $[\alpha]_{578}^{20}=-33.2$ (*c* 2.1, benzene) for (*S*)-**3d** 47% ee). HPLC: t_R (*S*), 8.0 min, (*R*), 9.5 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=9:1). ^{1}H NMR: δ 1.64–1.80 (m, 2H), 2.05–2.21 (m, 2H), 2.23–2.41 (m, 3H), 2.34 (s, 3H), 2.62–2.72 (m, 1H), 3.28–3.41 (m, 1H), 7.13 (d, 2H, *J*=8.3 Hz), 7.33 (d, 2H, *J*=8.3 Hz).

(*S*)-3-[(4-*tert*-butylphenyl)thio]-cyclohexanone (3e).[5b] $[\alpha]_D^{24}=-30.8$ (*c* 1.4, $CHCl_3$), $[\alpha]_{577}^{24}=-34.6$ (*c* 1.6, CCl_4) for 40% ee (lit. 5b; $[\alpha]_{578}^{21}=+47$ (*c* 1, CCl_4) for (*R*)-**3e** 62% ee). HPLC: t_R (*S*), 6.0 min, (*R*), 7.0 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=9:1). ^{1}H NMR: δ 1.31 (s, 9H), 1.61–1.82 (m, 2H), 2.07–2.22 (m, 2H), 2.24–2.43 (m, 3H), 2.64–2.72 (m, 1H), 3.32–3.41 (m, 1H), 7.30–7.40 (m, 4H).

(*S*)-3-[(4-Chlorophenyl)thio]-cyclohexanone (3f).[5b] Mp 56.0–57.0°C. $[\alpha]_D^{25}=-19.8$ (*c* 1.2, $CHCl_3$), $[\alpha]_{577}^{25}=-21.8$ (*c* 1.6, CCl_4) for 24% ee (lit. 5b; $[\alpha]_{578}^{21}=+31$ (*c* 1, CCl_4) for (*R*)-**3f** 35% ee). HPLC: t_R (*S*), 13.0 min, (*R*), 14.5 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=19:1). ^{1}H NMR: δ 1.61–1.82 (m, 2H), 2.08–2.22 (m, 2H), 2.26–2.45 (m, 3H), 2.63–2.74 (m, 1H), 3.34–3.46 (m, 1H), 7.29 (d, 2H, *J*=8.6 Hz), 7.36 (d, 2H, *J*=8.6 Hz).

(*S*)-3-[(4-Methoxyphenyl)thio]-cyclohexanone (3g).[5b] $[\alpha]_D^{25}=-43.2$ (*c* 1.2, $CHCl_3$), $[\alpha]_{577}^{25}=-50.8$ (*c* 1.1, CCl_4) for 58% ee (lit. 5b; $[\alpha]_{578}^{21}=+43$ (*c* 1, CCl_4) for (*R*)-**3g** 50% ee). HPLC: t_R (*S*), 11.5 min, (*R*), 15.0 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=9:1). ^{1}H NMR: δ 1.61–1.78 (m, 2H), 2.05–2.20 (m, 2H), 2.25–2.39 (m, 3H), 2.59–2.68 (m, 1H), 3.18–3.41 (m, 1H), 3.81 (s, 3H), 6.87 (d, 2H, *J*=8.6 Hz), 7.40 (d, 2H, *J*=8.6 Hz).

(*S*)-3-[(Phenylmethyl)thio]-cyclohexanone (3h).[7b] $[\alpha]_D^{24}=-43.1$ (*c* 1.3, $CHCl_3$) for 40% ee (lit. 7b; $[\alpha]_D^{27}=+49.0$ (*c* 0.93, $CHCl_3$) for (*R*)-**3h** 52% ee). HPLC: t_R (*R*), 8.5 min, (*S*), 10.0 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=9:1). ^{1}H NMR: δ 1.61–1.78 (m, 2H), 2.04–2.18 (m, 2H), 2.31–2.43 (m, 3H), 2.64–2.71 (m, 1H), 2.88–3.01 (m, 1H), 3.75 (d, 1H, *J*=13.8 Hz), 3.77 (d, 1H, *J*=13.8 Hz), 7.18–7.32 (m, 5H).

(−)-3-(Phenylthio)-cycloheptanone (8). $[\alpha]_D^{24}=-27.2$ (*c* 1.1, $CHCl_3$) for 61% ee. HPLC: t_R (+), 15.0 min, (−), 23.0 min (Daicel Chiralpak AS, 1.0 mL/min, hex/IPA=9:1). IR: (neat) 1701 cm^{-1}. ^{1}H NMR: δ 1.48–1.64 (m, 1H), 1.65–1.79 (m, 2H), 1.80–2.04 (m, 2H), 2.10–2.21 (m, 1H), 2.42–2.64 (m, 2H), 2.72 (dd, 1H, *J*=9.6, 14.9 Hz), 2.79 (ddd, 1H, *J*=1.3, 3.6, 14.9 Hz), 3.41 (ddt, 1H, *J*=2.6, 3.0, 9.6 Hz), 7.24–7.35 (m, 3H), 7.38–7.43 (m, 2H). ^{13}C NMR: δ 23.9, 28.1, 36.9, 44.0, 44.2, 49.5, 127.5, 129.1, 132.5, 134.1, 221.4. MS: *m*/*z* 220(M^+), 111, 110(bp). Anal. Calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32. Found: C, 70.89; H, 7.28.

(+)-3-(Phenylthio)-cyclopentanone (9).[7a] $[\alpha]_D^{23}=+1.8$ (*c* 1.3, $CHCl_3$) for 21% ee. HPLC: t_R (+), 12.5 min, (−), 14.0 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=19:1). ^1H NMR: δ 1.96–2.09 (m, 1H), 2.16–2.55 (m, 4H), 2.61 (dd, 1H, *J*=7.3, 18.5 Hz), 3.84–3.93 (m, 1H), 7.20–7.37 (m, 3H), 7.39–7.45 (m, 2H).

(−)-3-Methyl-3-(phenylthio)-cyclohexanone (10). $[\alpha]_D^{22}=-4.2$ (*c* 1.1, $CHCl_3$) for 10% ee. HPLC: t_R (−), 8.5 min, (+), 9.5 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=19:1). IR: (neat) 1711 cm^{-1}. ^1H NMR: δ 1.29 (s, 3H), 1.80–1.99 (m, 3H), 2.12–2.39 (m, 3H), 2.33 (d, 1H, *J*=13.9 Hz), 2.51 (d, 1H, *J*=13.9 Hz), 7.31–7.43 (m, 3H), 7.50–7.54 (m, 2H). ^{13}C NMR: δ 22.1, 28.5, 36.8, 40.4, 51.8, 53.2, 128.7, 129.2, 130.3, 137.8, 209.0. MS: *m/z* 220(M^+), 111(bp). Anal. Calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32. Found C, 70.91; H, 7.35.

(−)-4,4-Dimethyl-3-(phenylthio)-cyclohexanone (11). Mp 61.5°C. $[\alpha]_D^{25}=-29.0$ (*c* 1.1, $CHCl_3$) for 26% ee. HPLC: t_R (+), 8.5 min, (−), 9.5 min (Daicel Chiralpak AD, 1.0 mL/min, hex/IPA=40:1). IR: (neat) 1705 cm^{-1}. ^1H NMR: δ 1.22 (s, 3H), 1.28 (s, 3H), 1.64 (ddd, 1H, *J*=5.3, 12.5, 13.9 Hz), 1.90 (ddd, 1H, *J*=4.6, 6.3, 13.9 Hz), 2.30 (dddd, 1H, *J*=1.3, 4.6, 5.3, 15.2 Hz), 2.45 (ddd, 1H, *J*=6.3, 12.5, 15.2 Hz), 2.54 (dd, 1H, *J*=10.6, 15.2 Hz), 2.63 (ddd, 1H, *J*=1.3, 5.3, 15.2 Hz), 3.17 (dd, 1H, *J*=5.3, 10.6 Hz), 7.20–7.33 (m, 3H), 7.38–7.43 (m, 2H). ^{13}C NMR: δ 21.0, 29.0, 34.6, 37.8, 38.6, 45.4, 57.6, 127.4, 129.0, 132.7, 134.6, 208.9. MS: *m/z* 234(M^+), 125, 110(bp). Anal. Calcd for $C_{14}H_{18}OS$: C, 71.75; H, 7.74. Found C, 71.77; H, 7.74.

Enantioselective conjugate addition of thiophenol to enal

Thiol (2.0 mmol) in toluene (1 mL) was added to a stirred solution of enal (1.0 mmol), **1** (3.2 mg, 10 μmol) and cadmium iodide (3.6 mg, 10 μmol) in toluene (7 mL) and stirred at rt. The reaction mixture was diluted with toluene and successively washed with 15% NaOH aq, satd NH_4Cl aq and brine. The solvent was evaporated and the residue was dissolved in MeOH (4 mL). Sodium borohydride (30 mg) was added to the solution and the mixture was stirred for 10 min. The reaction was quenched with brine and the mixture was extracted with AcOEt. The organic layer was washed with brine and evaporated. The residue was purified by silica gel column chromatography (eluent, hexane/AcOEt) to give the corresponding alcohol. *N*-Oxide **1** was quantitatively recovered by further elution with 10% EtOH in $CHCl_3$ without any loss of optical purity.

(*S*)-3-(Phenylthio)-1-butanol (19). $[\alpha]_D^{23}=+24.9$ (*c* 1.2, $CHCl_3$) for 69% ee. HPLC: t_R (*R*), 7.5 min, (*S*), 9.0 min (Daicel Chiralcel OD, 1.0 mL/min, hex/IPA=9:1). IR (neat) 3355 cm^{-1}. ^1H NMR: δ 1.33 (d, 3H, *J*=6.6 Hz), 1.57 (br, 1H), 1.73–1.93 (m, 2H), 3.31–3.48 (m, 1H), 3.73–3.91 (m, 2H), 7.21–7.33 (m, 3H), 7.41–7.44 (m, 2H). ^{13}C NMR: δ 21.0, 39.2, 40.4, 60.6, 127.0, 128.8, 132.2, 134.7. MS: *m/z* 182(M^+), 137, 110(bp). Anal. Calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74. Found C, 65.63; H, 7.80.

(+)-3-(Phenylthio)-1-pentanol (20). $[\alpha]_D^{22}=+14.0$ (*c* 1.1, $CHCl_3$) for 70% ee. HPLC: t_R (−), 7.5 min, (+), 10.0 min (Daicel Chiralcel OD, 1.0 mL/min, hex/IPA=9:1). IR: (neat) 3347 cm^{-1}. ^1H NMR: δ 1.04 (t, 3H, *J*=7.3 Hz), 1.57 (br, 1H), 1.59–1.97 (m, 4H), 3.15–3.25 (m, 1H), 3.76–3.93 (m, 2H), 7.20–7.33 (m, 3H), 7.41–7.44 (m, 2H). ^{13}C NMR: δ 11.2, 27.9, 36.8, 47.9, 60.7, 126.8, 128.9, 132.1, 135.1. MS: *m/z* 196(M^+), 110(bp). Anal. Calcd for $C_{11}H_{16}OS$: C, 67.30; H, 8.22. Found C, 67.05; H, 8.27.

(+)-3-(Phenylthio)-1-hexanol (21). $[\alpha]_D^{23}=+16.4$ (*c* 1.1, $CHCl_3$) for 65% ee. HPLC: t_R (−), 7.0 min, (+), 8.0 min (Daicel Chiralcel OD, 1.0 mL/min, hex/IPA=9:1). IR: (neat) 3358 cm^{-1}. ^1H NMR: δ 0.94 (t, 3H, *J*=7.1 Hz), 1.45–1.62 (m, 5H), 1.72–1.91 (m, 2H), 3.21–3.28 (m, 1H), 3.76–3.91 (m, 2H), 7.18–7.33 (m, 3H), 7.40–7.45 (m, 2H). ^{13}C NMR: δ 13.9, 20.0, 37.3, 37.4, 46.1, 60.7, 126.8, 128.8, 132.1, 135.1. MS: *m/z* 210(M^+), 110(bp). Anal. Calcd for $C_{12}H_{18}OS$: C, 68.52; H, 8.63. Found C, 68.31; H, 8.64.

(+)-4-Methyl-3-(phenylthio)-1-pentanol (22). $[\alpha]_D^{23}=+24.8$ (*c* 1.1, $CHCl_3$) for 63% ee. HPLC: t_R (−), 6.0 min, (+), 8.0 min (Daicel Chiralcel OD, 1.0 mL/min, hex/IPA=9:1). IR: (neat) 3354 cm^{-1}. ^1H NMR: δ 0.99 (d, 3H, *J*=6.6 Hz), 1.02 (d, 3H, *J*=6.6 Hz), 1.58 (br, 1H), 1.63–1.79 (m, 1H), 1.87–2.04 (m, 2H), 3.21 (dt, 1H, *J*=4.0, 10.6 Hz), 3.78–3.93 (m, 2H), 7.16–7.31 (m, 3H), 7.40–7.44 (m, 2H). ^{13}C NMR: δ 19.1, 19.2, 32.3, 34.5, 53.6, 61.2, 126.5, 128.9, 131.2, 136.7. MS: *m/z* 210(M^+), 167, 137, 123, 110(bp). Anal. Calcd for $C_{12}H_{18}OS$: C, 68.52; H, 8.63. Found C, 68.48; H, 8.62.

(+)-4-Phenyl-3-(phenylthio)-1-butanol (23). $[\alpha]_D^{22}=+5.2$ (*c* 1.3, benzene) for 52% ee. HPLC: t_R (−), 10.0 min, (+), 11.5 min (Daicel Chiralcel OD, 1.0 mL/min, hex/IPA=9:1). IR: (neat) 3356 cm^{-1}. ^1H NMR: δ 1.55 (br, 1H), 1.67–1.77 (m, 1H), 1.87–1.94 (m, 1H), 2.80 (dd, 1H, *J*=8.2, 13.9 Hz), 3.03 (dd, 1H, *J*=5.9, 13.9 Hz), 3.46–3.52 (m, 1H), 3.77–3.85 (m, 1H), 7.15–7.34 (m, 8H), 7.37–7.44 (m, 2H). ^{13}C NMR: δ 36.3, 42.1, 47.7, 60.7, 126.5, 127.1, 128.4, 129.0, 129.3, 132.3, 134.8, 139.0. MS: *m/z* 258(M^+), 167, 137, 123, 91(bp). Anal. Calcd for $C_{16}H_{18}OS$: C, 74.38; H, 7.02. Found C, 74.36; H, 7.18.

(+)-4,4-Dimethyl-3-(phenylthio)-1-pentanol (24). $[\alpha]_D^{22}=+8.3$ (*c* 1.1, $CHCl_3$) for 39% ee. HPLC: t_R (−), 6.0 min, (+), 7.5 min (Daicel Chiralcel OD, 1.0 mL/min, hex/IPA=9:1). IR: (neat) 3360 cm^{-1}. ^1H NMR: δ 1.04 (s, 9H), 1.53 (br, 1H), 1.57–1.72 (m, 1H), 2.08–2.21 (m, 1H), 3.07 (dd, 1H, *J*=2.6, 11.9 Hz), 3.88–3.93 (m, 2H), 7.14–7.19 (m, 1H), 7.24–7.32 (m, 2H), 7.42–7.47 (m, 2H). ^{13}C NMR: δ 27.8, 34.5, 36.2, 59.7, 61.5, 126.0, 128.9, 130.4, 138.7. MS: *m/z* 224(M^+), 167, 137(bp), 123, 110, 97. Anal. Calcd for $C_{13}H_{20}OS$: C, 69.59; H, 8.98. Found C, 69.80; H, 9.02.

(−)-3-Phenyl-3-(phenylthio)-1-propanol (25). Mp 54.0–55.0°C. $[\alpha]_D^{22}=-19.9$ (*c* 1.2, $CHCl_3$) for 9% ee. HPLC: t_R (−), 13.0 min, (+), 14.0 min (Daicel Chiralcel OD, 1.0 mL/min, hex/IPA=9:1). IR: (nujol) 3358 cm^{-1}. ^1H NMR: δ 1.53 (br, 1H), 2.07–2.31 (m, 2H), 3.60 (ddt, 1H, *J*=2.0, 5.7, 11.2 Hz), 3.76 (ddt, 1H, *J*=1.3, 5.9, 11.2 Hz), 4.36 (dd, 1H, *J*=7.3, 7.9 Hz), 7.18–7.39 (m, 10H). ^{13}C

NMR: δ 38.8, 50.2, 60.5, 127.21, 127.24, 127.8, 128.5, 128.7, 132.5, 134.6, 141.7. MS: *m/z* 244(M^+), 135, 105(bp), 91. Anal. Calcd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60. Found C, 73.61; H, 6.43.

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