Pergamon

Tetrahedron, Vol. 52, No. 23, pp. 7817-7832, 1996
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0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00370-5

Asymmetric Ring Opening Reactions of Symmetrical *N*-Acylaziridines with Thiols Catalyzed by Chiral Dialkyl Tartrate–Diethylzinc Complexes

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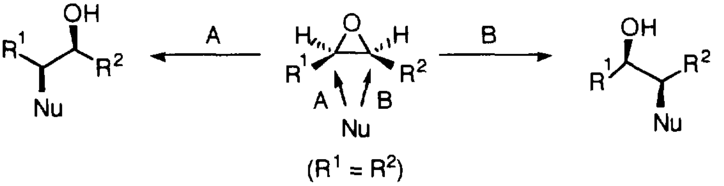
Abstracts: The asymmetric ring opening reaction of 1,2-(*N*-acylimino)cyclohexanes (*N*-acylaziridines) with some thiols proceeded in the presence of chiral zinc complexes prepared from diethylzinc and dialkyl L-(+)-tartrate to afford *trans* 2-(*N*-acylamino)-1-arylthiocyclohexane in up to 93% ee. The enantioselectivity is highly influenced by the molar ratio of the reactants and the nature of chiral dialkyl tartrate. The chemical structure of dialkyl L-(+)-tartrate–zinc complex is discussed on their ^{1}H NMR spectra and molecular weight.

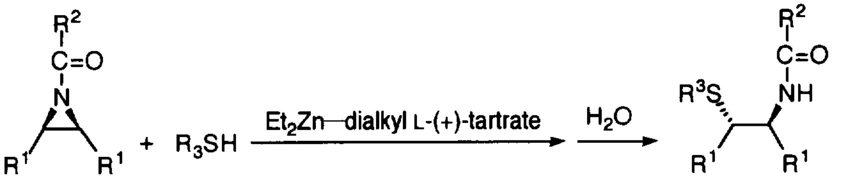
Introduction

The asymmetric synthesis of optically active organic compounds from symmetrical precursors has attracted much attention these days, and various biological[1] and chemical[2] methods have been reported in this field. Among those, in particular, the enantioselective ring opening of symmetrical epoxides with some nucleophiles in the presence of chiral catalysts has become attractive synthetic methods, because this method offers the opportunity to generate two chiral centers with a single operation (eq. 1). Mukaiyama first reported the asymmetric ring opening reaction of cyclohexene oxide with some thiols by the use of a heterogeneous chiral catalyst.[3] After that report, several asymmetric ring opening reactions of symmetrical epoxides with some heteroatom nucleophiles have been reported.[4]



(eq. 1)

On the other hand, the asymmetric ring cleavage of symmetrical *N*-substituted aziridines with nucleophiles has not been reported so far.[5] This paper deals with the first report on the highly enantioselective ring opening reaction of the symmetrical *N*-acylaziridines with arenethiols catalyzed by dialkyl L-(+)-tartrate–diethylzinc complexes and the study on the structure of zinc compounds in solution (eq. 2).[6]


(eq. 2)

Results and Discussion

Asymmetric Ring Opening Reaction of 1,2-[*N*-(*p*-Nitrobenzoyl)imino]cyclohexane (1a) with *p-tert*-Butylbenzenethiol. First, we investigated the reactions of **1a** with *p-tert*-butylbenzenethiol in the presence of an equimolar amount of chiral zinc complexes prepared from diisopropyl L-(+)-tartrate (DIPT) and diethylzinc in dichloromethane (eq. 3). During the screening of a variety of reaction conditions, we found that the enantioselectivity was much influenced by the molar ratio of the reactants. As shown in Table 1, the highest enantioselectivity was achieved when the reaction was carried out by using 1:3:1:4.8 molar ratio of **1a**:diethylzinc:L-(+)-DIPT:thiol. Under these conditions, the ring opening product, 1-(*p-tert*-butylphenylthio)-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (**2a**) was obtained in 88% ee and 98% yield (entry 8).

Table 1. Effect of Molar Ratio on Enantioselectivity in the Reaction of **1a** with *p-tert*-Butylbenzenethiol Promoted by L-(+)-DIPT–Et_2Zn Complex[a]

	molar ratio			product	
entry	Et_2Zn	L-(+)-DIPT	thiol	% yield[b]	% ee[c,d]
1	1	1	1	83	22
2	1	1	2	95	66
3	2	1	2	96	12
4	2	1	3	96	70
5	2	1	3.6	97	82
6	2	1	4	97	67
7	3	1	3	90	29
8	3	1	4.8	98	88
9	3	1	5	98	85
10	3	1	5.2	98	85
11	3	1	6	94	69

[a] All reactions were carried out in dichloromethane at 0 °C for 14–96 h. [b] Isolated yield after column chromatography. [c] HPLC analysis (SUMIPAX OA-4000). [d] Absolute configuration of the product was (1*S*, 2*S*).

For the purpose to achieve higher enantioselectivity, we have investigated the effects of the nature of solvents and of the alkyl groups in dialkyl tartrate on the enantioselectivity of the reaction. The results obtained in solvent other than dichloromethane were as follows: toluene (98% yield, 85% ee), chloroform (98% yield, 80% ee), 1,2-dichloroethane (98% yield, 63% ee), and THF (75% yield, 33% ee). Among the various alkyl esters of L-(+)-tartaric acid, such as diethyl tartrate (DET), dicyclohexyl tartrate (DCHT), and di-*tert*-butyl tartrate (DTBT) the highest enantioselectivity (93% ee) was attained when the reaction was undertaken in toluene using L-(+)-DCHT (entry 4 in Table 2). The reaction using 1,2-(*N*-benzoylimino)cyclohexane (**1b**) instead of **1a** as a substrate gave the ring opening product in 81% ee under the same condition using L-(+)-DCHT.

Table 2. Effect of the Nature of Dialkyl L-(+)-Tartrate on Enantioselectivity in Toluene[a]

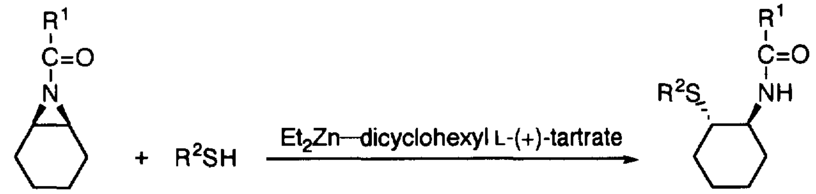
		product	
entry	dialkyl L-(+)-tartrate[b]	% yield[c]	% ee[d]
1	L-(+)-DET	98	90
2	L-(+)-DIPT	98	85
3	L-(+)-DIBT	98	89
4	L-(+)-DCHT	98	93
5	L-(+)-DTBT	98	65

[a] All reactions were carried out in toluene at 0 °C for 14 h. [b] DET = diethyl tartrate. DIPT = diisopropyl tartrate. DIBT = diisobutyl tartrate. DCHT = dicyclohexyl tartrate. DTBT = di-*tert*-butyl tartrate. [c] Isolated yield. [d] HPLC analysis.

The ee of the ring opening product **2a** was determined by HPLC analysis on chiral stationary phase (SUMIPAX OA-4000). The absolute configuration of **2a** was determined as (1*S*, 2*S*), which was confirmed by the correlation of the optical rotation value after derivatizing to *trans*-2-(*p*-*tert*-butylphenylthio)cyclohexanol whose absolute configuration was known.[3]

Reaction of 1a with a Variety of Thiols. Then we examined the reactions of **1a** with a variety of thiols using the catalyst system composed of diethylzinc and L-(+)-DCHT in toluene. The results are summarized in Table 3. Generally, the arenethiols react with **1a** smoothly to give the ring opening products in moderate to high optical yield. Among the arenethiols we examined, *p*-*tert*-butylbenzenethiol gave the highest enantioselectivity (93% ee), whereas the reaction of **1a** with benzenethiol afforded the product **3** in low level of enantioselectivity (45% ee). When benzenethiol derivatives possessing methyl or methoxy group at 3 or 4 position were employed, the ring opening products were obtained in high optical yield (79–89% ee). In all cases, the ee of the products was determined by HPLC analysis using chiral stationary phase (SUMIPAX OA-4000 or CHIRALCED OD). The absolute configurations of the products were also determined by the correlation of the optical rotation value and retention time of HPLC analysis after derivatizing to *trans*-2-

thiocyclohexanols. It should be noted that the reactions of **1a** with the alkanethiols, such as *n*-butanethiol and benzyl mercaptan proceeded in a non-enantioselective manner (entries 7 and 8).



(eq. 3)

1a; $R^1 = p\text{-}NO_2C_6H_4$
(**1b**; $R^1 = C_6H_5$)

2; $R^2 = p\text{-}(CH_3)_3CC_6H_4$
3; $R^2 = C_6H_5$
4; $R^2 = m\text{-}CH_3C_6H_4$
5; $R^2 = p\text{-}CH_3C_6H_4$
6; $R^2 = p\text{-}CH_3OC_6H_4$
7; R^2 = β-naphthyl
8; $R^2 = C_6H_5CH_2$
9; $R^2 = n\text{-}C_4H_9$

Table 3. Asymmetric Ring Opening Reactions of **1a** with a Variety of Thiols[a]

entry	thiol	time/h	product		
			% yield[b]	% ee[c]	$[\alpha]_D^{24}$[d]
1	p-$(CH_3)_3CC_6H_4SH$	14	98	93	+48.69
2	C_6H_5SH	24	99	45	+26.38
3	m-$CH_3C_6H_4SH$	24	92	79	+39.07
4	p-$CH_3C_6H_4SH$	24	91	89	+70.19
5	p-$CH_3OC_6H_4SH$	23	81	80	+96.23
6	β-naphtharenethiol	24	88	76[e]	+50.82
7	$C_6H_5CH_2SH$	96	53	2	—
8	n-C_4H_9SH	96	68	1	—

[a] All reactions were carried out in toluene using 1:3:1:4.8 molar ratio of **1a**:Et_2Zn:L-(+)-DCHT:thiol. [b] Isolated yield. [c] HPLC analysis (Sumipax OA 4000) unless otherwise noted. [d] Measured in $CHCl_3$ (c 1.0). [e] CHIRALCEL OD was used.

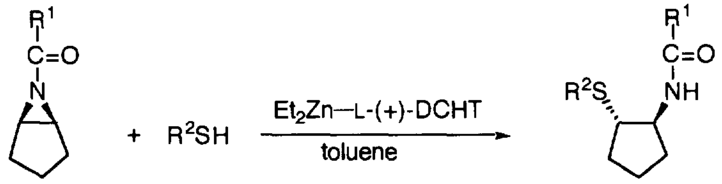
Catalytic Reactions. The reaction with a small amount of the catalyst induced the decrease of enantioselectivity in comparison with that of the equimolar reaction, although the yield of the reaction was highly independent of the amount of catalyst (Table 4). The products of 78 and 17% ee were obtained by the use of 50 and 20 mol% of catalyst, respectively.

Table 4. Catalytic Reaction of **1a** with *p*-*tert*-Butylbenzenethiol[a]

entry	catalyst/mol%	time/h	product	
			% yield[b]	% ee[c]
1[d]	100	14	98	93
2[e]	50	16	95	78
3[f]	20	96	93	17

[a] All reactions were carried out in toluene at 0 °C. [b] Isolated yield after column chromatography. [c] HPLC analysis (SUMIPAX OA-4000). [d] **1a**:L-(+)-DCHT:Et_2Zn:thiol = 1:1:3:4.8. [e] **1a**:L-(+)-DCHT:Et_2Zn:thiol = 1:0.5:1:3. [f] **1a**:L-(+)-DCHT:Et_2Zn:thiol = 1:0.2:0.4:3.

Reaction of Other *N*-Acylaziridines. The reactions of *N*-acylaziridines other than 1,2-[*N*-(*p*-nitrobenzoyl)imino]cyclohexane with thiols were examined. The reaction of 1,2-[*N*-(*p*-nitrobenzoyl)imino]cyclopentane (**1c**) with *p*-*tert*-butylbenzenethiol gave the ring opening product in 85% ee in 89% yield.



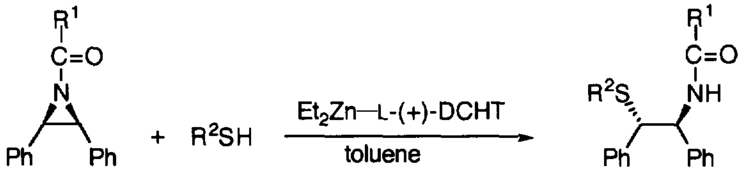
(eq. 4)

1c; $R^1 = p\text{-}NO_2C_6H_4$

89% yield
85% ee

10; $R^2 = p\text{-}(CH_3)_3CC_6H_4$

The reaction of *p*-nitrobenzoyl-*cis*-2,3-diphenylaziridine (**1d**) with *p*-*tert*-butylbenzenethiol gave also the ring opening product in 84% ee and in 94% yield. However, when *p*-methylbenzenethiol or *p*-methoxybenzenethiol was reacted, the ring opening products were obtained in low level of enantioselectivity (eq. 5 and Table 5). These observations were common features as the reaction of **1c**.



(eq. 5)

1d; $R^1 = p\text{-}NO_2C_6H_4$

11; $R^2 = p\text{-}(CH_3)_3CC_6H_4$
12; $R^2 = p\text{-}CH_3C_6H_4$
13; $R^2 = p\text{-}CH_3OC_6H_4$

Table 5. Asymmetric Ring Opening Reactions of **1d** with Thiols[a]

entry	thiol	time/h	product % yield[b]	product % ee[c]
1	4-$(CH_3)_3CC_6H_4SH$	14	94	84
2	4-$CH_3C_6H_4SH$	24	83	22
3	4-$CH_3OC_6H_4SH$	24	82	30[d]

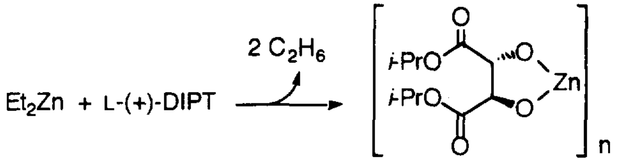
[a] All reactions were carried out in toluene using 1:3:1:4.8 molar ratio of **1d**:Et_2Zn:L-(+)-DCHT:thiol. [b] Isolated yield. [c] HPLC analysis (Sumichiral OA 4600) unless otherwise noted. [d] CHIRALCEL OD was used.

Structure of the catalyst. In order to obtain the information on the solution structure of the dialkyl L-(+)-tartrate–diethylzinc complexes, we measured the ^1H NMR spectrum of the reaction product of diethylzinc and L-(+)-DIPT (molar ratio of 1:1) in chloroform-d.[7] As shown in Figure 1, the proton peaks assigned to ethyl group of diethylzinc and hydroxy group of L-(+)-DIPT disappeared. This would indicate the formation of zinc alkoxide complex **A** with the evolution of ethane according to eq. 6. The complexity of the peaks in the region of methyl (1.0–1.5 ppm) and methine (4–5.4 ppm) suggests that the complex **A** exists in a oligomeric form in solution. Indeed, the molecular weight measurement of 1:1 mixture of diethylzinc and L-(+)-DIPT indicated that the complex **A** exists as aggregates in solution. The degree of association proved to be dependent on the concentration of the reactants (Table 6).

Table 6. Molecular Weight Determination of the Reaction Product of Et_2Zn and L-(+)-DIPT (1:1 Molar Ratio) by Cryoscopic Method in Benzene[a]

entry	ω[b]	ΔT[c]	K_f[d]	MW[e]	AN.[f]
1	8.6	0.04	6.2	1437	4.8
2	10.8	0.07	6.2	1008	3.4
3	11.7	0.07	6.2	1034	3.5
4	15.0	0.03	6.2	3315	11.2
5	19.0	0.04	6.2	3188	10.8
6	37.1	0.07	6.2	3434	11.6
7	41.0	0.08	6.2	3099	10.4

[a] The procedure for molecular weight determination is described in experimental section. [b] Weight (g) of solute in 1000 g of benzene. [c] Depression (°C). [d] Molar depression of the solvent (benzene). [e] Molecular weight. [f] AN = association number, MW = 297 (n = 1 for complex **A**).



complex **A**

(eq. 6)

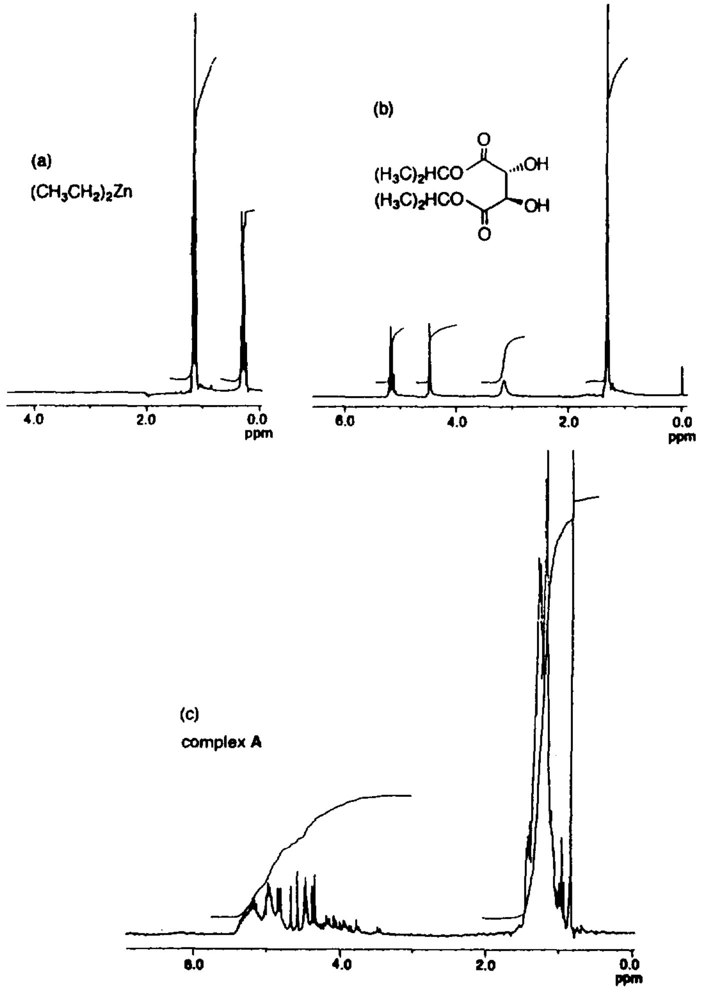


Figure 1. ^{1}H NMR of (a) Et$_2$Zn; (b) L-(+)-DIPT; (c) complex **A**

However, it was found that the addition of *p-tert*-butylbenzenethiol into a chloroform-d solution of complex **A** dramatically brought about the change of the ^{1}H NMR spectrum due to the ligand exchange of zinc complexes. The change of structure began by the addition of 0.5 equiv. (per zinc atom) of *p-tert*-butylbenzenethiol as shown in Figure 2(a), and the ligand exchange was accomplished completely by the addition of 2 equiv. of thiol (Figure 2(c)). In this process, the peaks assignable to free L-(+)-DIPT, *tert*-butyl (0.9–1.3 ppm) and aromatic protons (6.4–7.6 ppm) were observed, in which only the peaks based on L-(+)-

DIPT appeared as sharp signals. Furthermore, the addition of 3 equiv. of thiol increased the peak intensity of free *p-tert*-butylbenzenethiol (Figure 2(d)). These results would indicate that two thiolate groups could combine on one zinc atom.

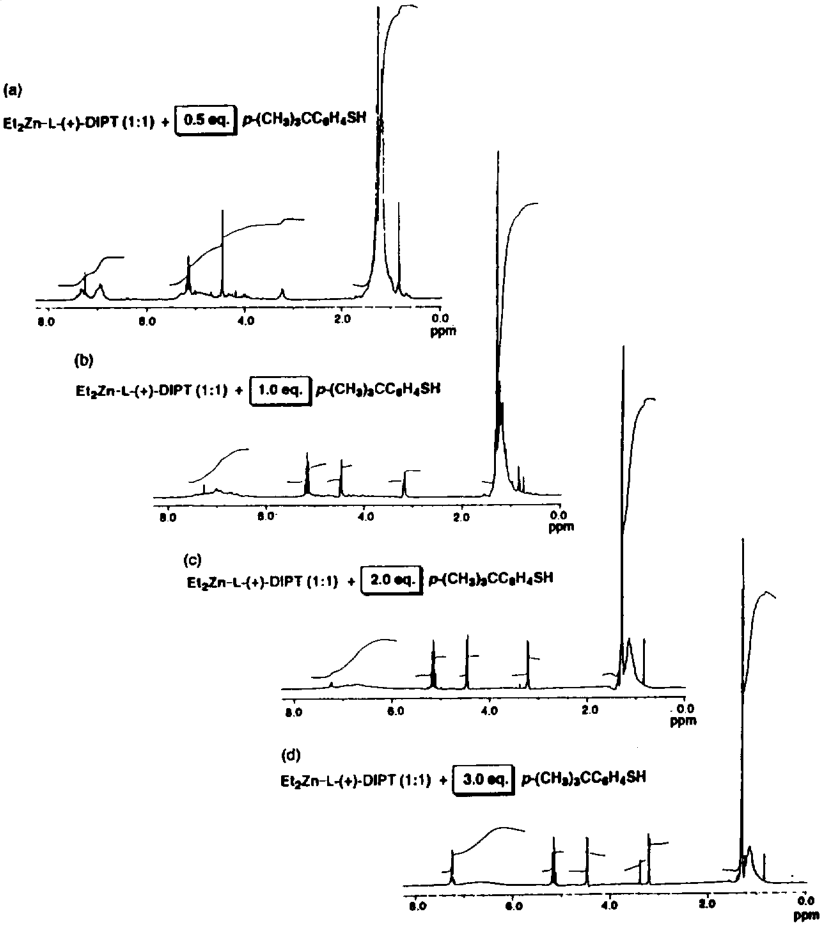
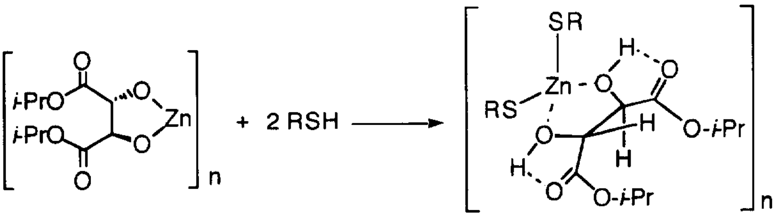


Figure 2. ^1H NMR of Et_2Zn–L-(+)-DIPT (1:1) + n p-$(CH_3)_3CC_6H_4SH$ (n = 0.5, 1, 2, 3)

Based on these observations, the structure of chiral zinc-thiolate complex formed by the reaction of complex **A** with 2 equiv. of *p-tert*-butylbenzenethiol will be estimated as the four coordinated zinc complex **B** (eq. 7).

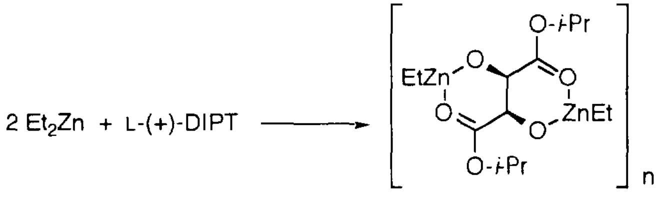


(eq. 7)

complex **A** complex **B**

The clear signal of doublet resonanced at 3.2 and 4.5 ppm (the proton peak of hydroxy and methine group of L-(+)-DIPT, respectively) in Figure 2(c) would be reasonably assignable to the intramolecular hydrogen bonding between the carbonyl oxygen of esters and the proton of hydroxy group. It should be noted that the order of the addition of the reagents had no effect on the formation of complex **B**. That is, the addition of diethylzinc into a mixture of *p-tert*-butylbenzenethiol and L-(+)-DIPT (2:1 ratio) also would lead to the formation of complex **B**, which was confirmed by ^{1}H NMR spectra. These phenomena would be due to the strong affinity of zinc to sulfur atom.

The ^{1}H NMR spectra of 2:1 mixture of diethylzinc and L-(+)-DIPT were also measured (eq. 8 and Figure 3). In this case, the presence of ethyl group attached to zinc atom was observed (complex **C**). Interestingly, the spectrum obtained by the addition of 4 equiv. of *p-tert*-butylbenzenethiol to the solution of complex **C** was quite similar to the one observed in the formation of complex **B** (Figure 4). This result means the same zinc thiolate complexes were formed by the reaction of 2 equiv. of thiol with 1:1 complex of diethylzinc–L-(+)-DIPT and 4 equiv. of thiol with 2:1 complex of diethylzinc–L-(+)-DIPT. In the latter case, one equivalent of $Zn(SR)_2$ (R = p-$NO_2C_6H_4$) complex also produced in addition to complex **B** (eq. 9). On the basis of the above spectroscopic results, we assume the complex **B** to be the main active species in solution regardless of



complex **C**

(eq. 8)

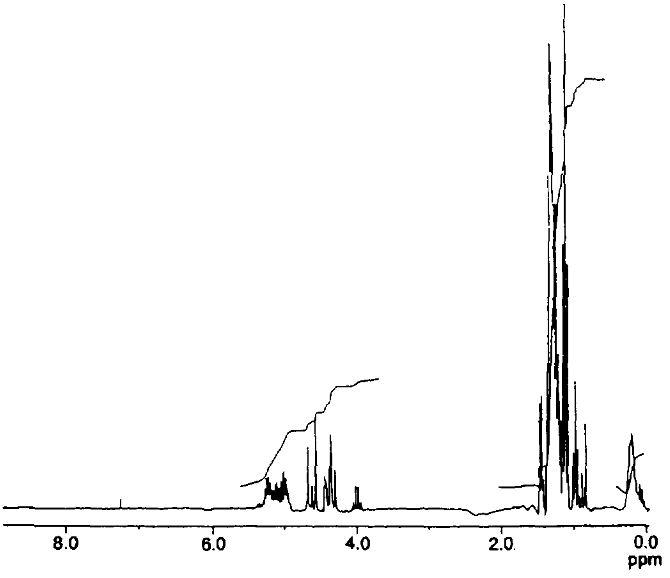
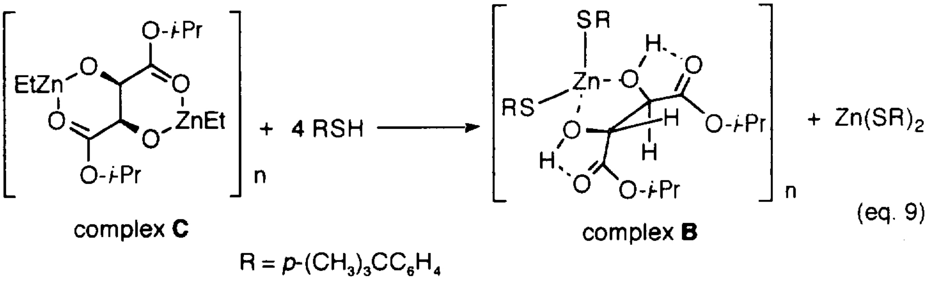


Figure 3. ^{1}H NMR of Et_2Zn–L-(+)-DIPT (2:1)

the molar ratio of the reactants. The reaction would proceed via several types of competitive reaction paths, and be very complicated.



(eq. 9)

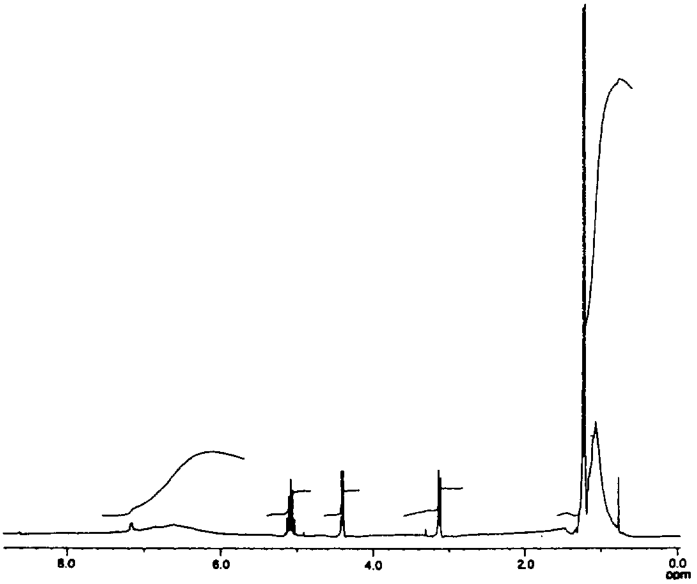


Figure 4. ^{1}H NMR of Et_2Zn–L-(+)-DIPT (2:1) + 4 *p*-$(CH_3)_3CC_6H_4SH$

Conclusion

Highly enantioselective ring opening reaction of symmetrical *N*-acylaziridines with some arenethiols has been realized by the promotion of chiral zinc complexes composed of dialkyl L-(+)-tartrate–diethylzinc complexes to give *trans* 2-(*N*-acylamino)-1-arylthioalkanes in high chemical and optical yield.

Experimental Section

General. All melting points were measured by using a Yanaco MP-500D apparatus and were uncorrected. ^{1}H NMR spectra (250 MHz) were measured on Hitachi R-250 Fourier Transfer NMR spectrometer using chloroform-d as a solvent and recorded in ppm relative to internal tetramethylsilane standard.

J Values are given in Hz. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; m, multiplet; br, broad peak. High resolution mass spectra (HRMS) were measured on a Hitachi M-2500 (EI, 4 kV). IR spectra were obtained with a Hitachi 270-50. Elemental analyses were performed at UBE Scientific Analysis Laboratory Inc. Optical rotations were measured on a JASCO DIP-4 digital polarimeter for solutions in a 5 dm cell. Preparative silica-gel column chromatography was carried out on a Wacogel-200 column. HPLC analyses were carried out on a JASCO PU-980 liquid chromatography with a JASCO UV-970 detector. Dichloromethane was distilled from P_4O_{10}. Toluene, diethyl ether and benzene were distilled from sodium benzophenone ketyl under argon. All experiments were carried out under an argon atmosphere.

1,2-[*N*-(*p*-Nitrobenzoyl)imino]cyclohexane (1a): To a mixture of 1,2-iminocyclohexane (20.1 g, 0.207 mmol) and triethylamine (28.9 mL, 0.207 mol) in diethyl ether (200 mL) was added *p*-nitrobenzoyl chloride (35.5 g, 0.207 mol) in diethyl ether (200 mL) at room temperature, and the whole was stirred for 1 h at this temperature. After filtration, the solid was recrystallized from ethanol to give **1a** (30.7 g, 60%) as pale yellow crystals. m.p. 118–122 °C. IR (KBr) ν_{max}: 2936, 1670, 1606, 1522, 1356, 1344, 1292, 722 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.3–1.4 (m, 2H), 1.4–1.6 (m, 2H), 1.9–2.1 (m, 4H), 2.8 (t, *J* = 1.2 Hz, 2H), 8.13 (d, *J* = 8.5 Hz, 2H), 8.30 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{13}H_{14}N_2O_3$; C, 63.40; H, 5.73; N, 11.38: Found; C, 63.40; H, 5.62; N, 11.35.

1,2-(*N*-Benzoylimino)cyclohexane (1b): To a mixture of 1,2-iminocyclohexane (5 g, 0.05 mol) and diethyl ether (50 mL) was added 20% aqueous NaOH solution (125 mL) at 0 °C, and the mixture was stirred for 30 min at this temperature. Benzoyl chloride (7 g, 0.05 mol) in diethyl ether was added to the above mixture. After being stirred for 1 h, the mixture was filtered. The obtained solid was silicagel column chromatographed (eluent, hexane:ethyl acetate 12:1) to give **1b** (7.35 g, 71%) as a colorless crystal. m.p. 79–80 °C (lit.[8] 70–72 °C). IR (KBr) ν_{max}: 2932, 1670, 1452, 1412, 1314, 1294, 736 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.3–1.5 (m, 2H), 1.5–1.6 (m, 2H), 1.8–2.0 (m, 2H), 2.0–2.2 (m, 2H), 2.76 (d, *J* = 1.8 Hz, 2H), 7.4–7.6 (m, 3H), 8.0 (d, *J* = 6.7 Hz, 2H). Anal. Calcd for $C_{13}H_{15}NO$; C, 77.58; H, 7.51; N, 6.96: Found; C, 77.57; H,7.57; N, 7.06.

1,2-[*N*-(*p*-Nitrobenzoyl)imino]cyclopentane (1c): To a mixture of 1,2-iminocyclopentane[5] (6.9 g, 83 mmol) and triethylamine (11.6 mL, 83 mmol) in diethyl ether (150 mL) was added *p*-nitrobenzoyl chloride (15.4 g, 83 mmol) in diethyl ether (50 mL) at 0 °C, and the whole was stirred for 1 h at room temperature. After filtration, the solid was recrystallized from ethanol to give **1c** (3.18 g, 17%) as pale yellow crystals. m.p. 112–114 °C. IR (KBr) ν_{max}: 2960, 1660, 1652, 1602, 1384, 1334, 1316, 1284 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.3–1.8 (m, 4H), 2.1–2.2 (m, 2H), 3.25 (s, 2H), 8.12 (d, *J* =9.2 Hz, 2H), 8.29 (d, *J* = 9.2 Hz, 2H). Anal. Calcd for $C_{12}H_{12}N_2O_3$; C, 62.06; H, 5.21; N, 12.06: Found; C, 62.32; H, 5.18; N, 12.05.

***p*-Nitrobenzoyl-*cis*-2,3-diphenylaziridine (1d):** To a mixture of *cis*-2,3-diphenylaziridine (4.0 g, 21 mmol), triethylamine (2.1 g, 21 mmol), and diethyl ether (50 mL) was added *p*-nitrobenzoyl chloride (3.8 g, 21 mmol) at 0 °C. The mixture was stirred for 15 h at room temperature. After this, the brine (50 mL) was added, then extracted with ethyl acetate (50 mL x 3). The organic layer was concentrated, and the obtained residue was recrystallized from ethanol to give **1d** (3.88 g, 55%) as a colorless crystal. m.p. 156–158 °C. IR (KBr) ν_{max}: 1688, 1524, 1320, 1308, 1288, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ 4.12 (s, 2H), 7.2 (m, 10H), 8.2–8.3 (m 4H). Anal. Calcd for $C_{21}H_{16}N_2O_3$; C, 73.24; H, 4.68; N, 8.13: Found; C, 73.51; H, 4.63; N, 8.18.

General Procedure for the Asymmetric Ring Opening Reaction of 1,2-[*N*-(*p*-Nitrobenzoyl)imino]cyclohexane (1a) with Thiols. In a Schlenk tube were placed dialkyl L-(+)-tartrate (2.0 mmol) and dry toluene (30 mL). The mixture was cooled to 0 °C and diethylzinc (0.62 mL, 6.0 mmol) was added slowly. After being stirred for 1 h at room temperature, thiol (9.6 mmol) and then **1a** (2.0 mmol) in toluene (10 mL) were added at 0 °C, and the above mixture was stirred for 14 h at this temperature. The brine (100 mL) was added to the mixture, and stirred vigorously for 30 min at room temperature. The mixture was filtered through a pad of Celite, then extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4. After evaporation, the obtained residue was chromatographed on silica-gel (eluent, $CHCl_3$) to afford *trans* 2-(*N*-acylamino)-1-arylthiocyclohexane.

(1*S*,2*S*)-1-(*p*-*tert*-Butylphenylthio)-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (2a). 820 mg (98%). m.p. 66–68 °C. $[\alpha]_D^{25}$ +48.91 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3316, 2932, 1642, 1528, 1344 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.28 (s, 9H), 1.3–1.5 (m, 4H), 1.7–1.8 (m, 2H), 2.2–2.3 (m, 1H), 2.3–2.4 (m, 1H), 3.0–3.1 (m, 1H), 3.9–4.0 (m, 1H), 6.4 (m, 1H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 9.2 Hz, 2H), 7.83 (d, *J* = 9.2 Hz, 2H), 8.22 (d, *J* = 9.2 Hz, 2H). Anal. Calcd for $C_{23}H_{28}N_2O_3S$; C, 66.96; H, 6.85; N, 6.79: Found: C, 67.04; H, 7.01; N, 6.68. The ee of the reaction product was determined as 93% ee by HPLC analysis. t_R of (1*R*,2*R*)-isomer: 13 min; t_R of (1*S*,2*S*)-isomer: 14 min [column; SUMIPAX OA-4000, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

(1*S*,2*S*)-2-(*N*-Benzoylamino)1-(*p*-*tert*-butylphenylthio)cyclohexane (2b). 760 mg (98%). m.p. 160–165 °C. $[\alpha]_D^{25}$ +48.69 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3308, 2960, 2936, 1636, 1546, 1492 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.29 (s, 9H), 1.2–1.4 (m, 4H), 1.7–1.8 (m, 2H), 2.1–2.2 (m, 1H), 2.3–2.4 (m, 1H), 2.9–3.0 (m, 1H), 3.9 (m, 1H), 6.2–6.3 (m, 1H), 7.3–7.5 (m, 7H), 7.7 (m, 2H). Anal. Calcd for $C_{23}H_{29}NOS$; C, 75.16; H, 7.95; N, 3.81: Found: C, 75.28; H, 8.07; N, 3.80. The ee of the reaction product was determined as 81% ee by HPLC analysis. t_R of (1*R*,2*R*)-isomer: 9 min; t_R of (1*S*,2*S*)-isomer: 15 min [column; CHIRALCEL OD, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

(1*S*,2*S*)-1-Phenylthio-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (3). 720 mg (99%). m.p. 133–136 °C. $[\alpha]_D^{25}$ +26.38 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3320, 2936, 1652, 1604, 1556, 1354, 1316 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.3–1.5 (m, 4H), 1.7–1.8 (m, 2H), 2.1–2.2 (m, 1H), 2.3–2.4 (m, 1H), 3.0–3.1 (m, 1H), 3.9–4.0 (m, 1H), 6.2–6.3 (m, 1H), 7.2–7.3 (m, 3H), 7.4–7.5 (m, 2H), 7.76 (d, *J* = 9.2 Hz, 2H), 8.23 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{19}H_{20}N_2O_3S$; C, 64.02; H, 5.66; N, 7.86: Found: C, 64.00; H, 5.68; N, 7.87. The ee of the reaction product was determined as 45% ee by HPLC analysis. t_R of (1*R*,2*R*)-isomer: 19 min; t_R of (1*S*,2*S*)-isomer: 22 min [column; SUMIPAX OA 4000, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

(1*S*,2*S*)-1-(*m*-Methylphenylthio)-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (4). 700 mg (92%). m.p. 141–143 °C. $[\alpha]_D^{25}$ +39.07 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3308, 2940, 1640, 1602, 1548, 1522, 1346 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.2–1.6 (m, 4H), 1.7–1.9 (m, 2H), 2.2–2.4 (m, 2H), 2.25 (s, 3H), 3.0–3.2 (m, 1H), 3.9–4.0 (m, 1H), 6.2–6.3 (m, 1H), 7.0–7.1 (m, 1H), 7.1–7.3 (m, 3H), 7.73 (d, *J* = 8.5 Hz, 2H), 8.20 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{20}H_{22}N_2O_3S$; C, 64.84; H, 5.99; N, 7.56: Found: C, 64.59; H, 5.94; N, 7.56. The ee of the reaction product was determined as 79% e.e. by HPLC analysis. t_R of (1*R*,2*R*)-isomer: 16 min; t_R of (1*S*,2*S*)-isomer: 18 min [column; SUMIPAX OA 4000, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

(1*S*,2*S*)-1-(*p*-Methylphenylthio)-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (5). 680 mg (91%). m.p. 181–183 °C. $[\alpha]_D^{25}$ +70.19 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3336, 2940, 1640, 1538, 1520, 1494, 1352, 1328 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.2–1.5 (m, 4H), 1.7–1.8 (m, 2H), 2.1–2.2 (m, 1H), 2.31 (s, 3H), 2.3–2.4 (m, 1H), 2.9–3.0 (m, 1H), 3.8–3.9 (m, 1H), 6.2–6.3 (m, 1H), 7.07 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.80 (d, *J* = 8.5 Hz, 2H), 8.23 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{20}H_{22}N_2O_3S$; C, 64.84; H, 5.99; N, 7.56: Found: C, 64.87; H, 6.07; N, 7.23. The ee of the reaction product was determined as 89% ee by HPLC analysis. t_R of (1*R*,2*R*)-isomer: 16 min; t_R of (1*S*,2*S*)-isomer: 19 min [column; SUMIPAX OA 4000, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

(1*S*,2*S*)-1-(*p*-Methoxylphenylthio)-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (6). 620 mg (81%). m.p. 179–182 °C. $[\alpha]_D^{25}$ +96.23 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3308, 2940, 1640, 1602, 1594, 1548, 1522, 1496, 1346 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.3–1.5 (m, 4H), 1.7–1.8 (m, 2H), 2.1–2.2 (m, 1H), 2.3–2.4 (m, 1H), 2.8–2.9 (m, 1H), 3.77 (s, 3H), 3.8–3.9 (m, 1H), 6.1–6.2 (m, 1H), 6.80 (d, *J* = 9.2 Hz, 2H), 7.36 (d, *J* = 9.2 Hz, 2H), 7.88 (d, *J* = 8.5 Hz, 2H), 8.28 (d, *J* = 9.2 Hz, 2H). HRMS (EI) *m/z* Calcd for $C_{20}H_{22}N_2O_4S$ (M^+): 386.1317. Found: 386.1303. The ee of the reaction product was determined as 80% ee by HPLC analysis. t_R of (1*R*,2*R*)-isomer: 28 min; t_R of (1*S*,2*S*)-isomer: 31 min [column; SUMIPAX OA 4000, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

(1*S*,2*S*)-1-(β-Naphthylthio)-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (7). 720 mg (88%). m.p. 160–161 °C. $[\alpha]_D^{25}$ +50.82 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3308, 2928, 1640, 1600, 1548, 1524, 1344, 1328, 852 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.3–1.6 (m, 4H), 1.7–1.8 (m, 2H), 2.2–2.4 (m, 2H), 3.2–3.3 (m, 1H), 4.0–4.1 (m, 1H), 6.0–6.1 (m, 1H), 7.4–7.6 (m, 6H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.85 (s, 1H), 7.96 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{23}H_{22}N_2O_3S$; C, 67.95; H, 5.46; N, 6.89: Found: C, 68.09; H, 5.47; N, 6.93. The ee of the reaction product was determined as 76% ee by HPLC analysis. t_R of (1*R*,2*R*)-isomer: 20 min; t_R of (1*S*,2*S*)-isomer: 26 min [column; CHIRALCEL OD, eluent; hexane–ethanol (95:5), 1.0 mL/min, 254 nm].

***trans* 2-[*N*-(*p*-Nitrobenzoyl)amino]-1-(α-toluenethio)cyclohexane (8).** 400 mg (53%). m.p. 150–151 °C. IR (KBr) ν_{max}: 3304, 2928, 1638, 1600, 1550, 1526, 1344, 1334, 704 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.2–1.6 (m, 4H), 1.6–1.8 (m, 2H), 2.2–2.3 (m, 1H), 2.3–2.4 (m, 1H), 2.4–2.6 (m, 1H), 3.7–3.9 (m, 3H), 6.0–6.1 (m, 1H), 7.2–7.4 (m, 5H), 7.81 (d, *J* = 8.5 Hz, 2H), 8.26 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{20}H_{22}N_2O_3S$; C, 64.84; H, 5.99; N, 7.56: Found: C, 64.80; H, 5.98; N, 7.55. The ee of the reaction product was determined as 2% ee by HPLC analysis. t_R 34 min, 38 min [column; SUMIPAX OA 4000, eluent; hexane–ethanol (97:3), 0.5 mL/min, 254 nm].

***trans* 1-*n*-Butylthio-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane (9).** 460 mg (68%). m.p. 157–159 °C. IR (KBr) ν_{max}: 3288, 2928, 1640, 1602, 1554, 1522, 1352 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.3 Hz, 3H), 1.3–1.7 (m, 8H), 1.8–1.9 (m, 2H), 2.1–2.2 (m, 1H), 2.4–2.5 (m, 1H), 2.54 (t, *J* = 7.3 Hz, 2H), 2.6–2.7 (m, 1H), 3.8–3.9 (m, 1H), 6.3–6.4 (m, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 8.30 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{17}H_{24}N_2O_3S$; C, 60.69; H, 7.19; N, 8.33: Found: C, 60.59; H, 7.21; N, 8.33. The ee of the reaction product was determined as 1% ee by HPLC analysis. t_R 25 min, 28 min [column; SUMIPAX OA 4000, eluent; hexane–ethanol (97:3), 0.5 mL/min, 254 nm].

***trans* 1-(*p*-*tert*-Butylphenylthio)-2-[*N*-(*p*-nitrobenzoyl)amino]cyclopentane (10).** 720 mg (88%). m.p. 43–46 °C. $[\alpha]_D^{25}$ +50.28 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3288, 2960, 1640, 1602, 1530, 1348 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.26 (s, 9H), 1.5–1.6 (m, 1H), 1.7–1.8 (m, 3H), 2.2–2.3

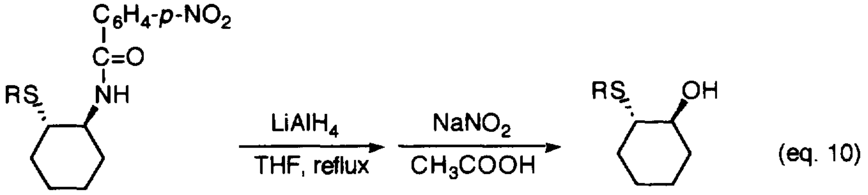
(m, 1H), 2.3–2.4 (m, 1H), 3.3–3.4 (m, 1H), 4.1–4.2 (m, 1H), 6.0–6.1 (m, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.77 (d, *J* = 8.5 Hz, 2H), 8.24 (d, *J* = 8.5 Hz, 2H). Anal. Calcd for $C_{22}H_{26}N_2O_3S$; C, 66.31; H, 6.58; N, 7.03: Found: C, 66.48; H, 6.71; N, 7.01. The ee of the reaction product was determined as 85% ee by HPLC analysis. t_R of minor-isomer: 17 min; t_R of major-isomer: 19 min [column; SUMIPAX OA-4000, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

trans **2-(*p*-*tert*-Butylphenylthio)-3-[*N*-(*p*-nitrobenzoyl)amino]-2,3-diphenylethane (11).** 980 mg (94%). m.p. 155–157 °C. $[\alpha]_D^{25}$ +33.43 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3296, 2960, 1644, 1602, 1530, 1490, 1348 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (s, 9H), 4.68 (d, *J* = 7.9 Hz, 1H), 5.62 (dd, *J* = 7.9 Hz, *J* = 7.9 Hz, 1H), 7.02 (d, *J* = 7.9 Hz, 1H), 7.1–7.2 (m, 14 H), 7.87 (d, *J* = 9.2 Hz, 2H), 8.25 (d, *J* = 9.2 Hz, 2H). HRMS (EI) *m/z* Anal. Calcd for $C_{21}H_{17}N_2O_3$ (M^+-$SC_6H_4C_4H_9$): 345.1239. Found: 345.1212. The ee of the reaction product was determined as 84% ee by HPLC analysis. t_R of major-isomer: 20 min; t_R of minor-isomer: 22 min [column; SUMICHIRAL OA-4600, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

trans **2-(*p*-Methylphenylthio)-3-[*N*-(*p*-nitrobenzoyl)amino]-2,3-diphenylethane (12).** 800 mg (83%). m.p. 86–89 °C. $[\alpha]_D^{25}$ +13.31 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 3264, 1640, 1602, 1526, 1492, 1350 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.26 (s, 3H), 4.66 (d, *J* = 8.5 Hz, 1H), 5.59 (dd, *J* = 7.9 Hz, 8.5 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 7.0–7.2 (m, 14 H), 7.86 (d, *J* = 8.5 Hz, 2H), 8.22 (d, *J* = 8.5 Hz, 2H). HRMS (EI) *m/z* Anal. Calcd for $C_{21}H_{17}N_2O_3$ (M^+-$SC_6H_4CH_3$): 345.1239. Found: 345.1210. The ee of the reaction product was determined as 22% ee by HPLC analysis. t_R of major-isomer: 24 min; t_R of minor-isomer: 27 min [column; CHIRALCEL-OD, eluent; hexane–ethanol (97:3), 1.0 mL/min, 254 nm].

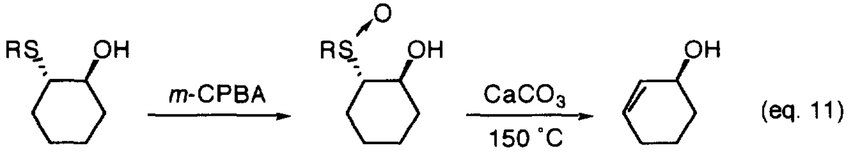
trans **2-(*p*-Methoxylphenylthio)-3-[*N*-(*p*-nitrobenzoyl)amino]-2,3-diphenylethane (13).** 800 mg (82%). m.p. 60–63 °C. $[\alpha]_D^{25}$ +14.82 (*c* 1.0, $CHCl_3$). IR (KBr) ν_{max}: 2928, 2856, 1640, 1600, 1532, 1496, 1350, 1288, 1248 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.74 (s, 3H), 4.54 (d, *J* = 8.5 Hz, 1H), 5.58 (dd, *J* = 7.9 Hz, 8.5 Hz, 1H), 6.71 (d, *J* =7.9 Hz, 1H), 7.0–7.2 (m, 14 H), 7.93 (d, *J* = 9.2 Hz, 2H), 8.30 (d, *J* = 9.2 Hz, 2H). HRMS (EI) *m/z* Anal. Calcd for $C_{21}H_{17}N_2O_3$ (M^+-$SC_6H_4OCH_3$): 345.1239. Found: 345.1227. The ee of the reaction product was determined as 30% ee by HPLC analysis. t_R of minor-isomer: 35 min; t_R of major-isomer: 40 min [column; CHIRALCEL-OD, eluent; hexane–ethanol (95:5), 1.0 mL/min, 254 nm].

Determination of Absolute Configurations. The absolute configuration of the ring opening product **2a** and **5** was determined as (1*S*, 2*S*), which was confirmed by the correlation of the optical rotation value after derivatizing to *trans*-2-(*p*-*tert*-butylphenylthio)cyclohexanol whose absolute configuration was known (eq. 10).[3] The procedure is as follows: In a three-necked flask were placed *trans* 1-thio-2-[*N*-(*p*-nitrobenzoyl)amino]cyclohexane and THF. To this mixture was added $LiAlH_4$ in THF. The mixture was refluxed for 18 h. Usual aqueous workup afforded *trans* 2-amino-1-(*p*-*tert*-butylphenylthio)cyclohexane. This aminothiol was converted to *trans* 1-hydroxy-2-(*p*-*tert*-butylbenzenethio)cyclohexane by the treatment with $NaNO_2$ in acetic acid. For other products (**3**, **4**, **6**, and **7**), the absolute configurations of the corresponding 1-hydroxy-2-thiocyclohexane were unknown. Therefore, further derivatization to (*S*)-(-)-2-cyclohexene-1-ol



2a: R = *p*-$(CH_3)_3CC_6H_4$
5: R = *p*-$CH_3C_6H_4$

by oxidation of 1-hydroxy-2-thiocyclohexane with *m*-chloroperbenzoic acid (*m*-CPBA) and successive thermal decomposition of the resulting *S*-oxides (*S*)-(-)-2-cyclohexene-1-ol proved to be the absolute configurations of



3, **5**, **6**, and **7** were (1*S*, 2*S*) (eq. 11). The absolute configurations of **10**, **11**, **12**, and **13** were assumed as (1*S*,2*S*) by comparison with the sign of optical rotation values and the retention time in HPLC analysis.

Acknowledgments. The present work was supported by a Grant-in-Aid from the Ministry of Education, Science and Culture of Japan. We also thank Tosoh Akzo Corporation for a generous gift of diethylzinc and UBE Scientific Analysis Laboratory Inc. for measurement of elememtal analyses and HRMS. M. H. also appreciate Sumitomo Foundation and Watanabe Memorial Foundation for financial support.

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5. Recently Scheffold reported the isomerization of achiral *N*-acylaziridines to optically active *N*-acyl-allylic amines catalyzed by cob(I)alamin: Zhang, Z.; Scheffold, R. *Helv. Chim. Acta* **1993**, *76*, 2602.
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7. Fairly good result could be obtained when the reaction of **1a** with *p-tert*-butylbenzenethiol was carried out in chloroform using L-(+)-DCHT–Et$_2$Zn system, that is, the ring opening product **2a** was produced in 96% yield and in 84% ee. The investigation of the catalyst structure was done mainly in CDCl$_3$, because the solubility of zinc-thiolate-tartrate complex in toluene was not high. The ^{1}H NMR spectra of zinc-thiolate-tartrate complex in toluene-d_8 were similar to those of in CDCl$_3$.
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(*Received in Japan* 2 *October* 1995; *accepted* 8 *April* 1996)