# Enantioselective conversion of *meso*-cyclic disulfides to chiral cyclic sulfides *via* desulfurization with chiral aminophosphines

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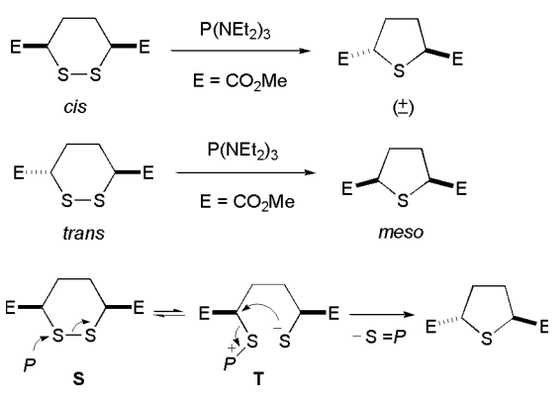
Enantioselective desymmetrization of *meso*-cyclic disulfides has been investigated on the basis of the desulfurization with chiral phosphines. Chiral *tert*-aminophosphines enable the desulfurization of a six-membered disulfide, *cis*-3,6-bis(alkoxycarbonyl)-1,2-dithiane **2**, to give an enantiomerically enriched five-membered sulfide, *trans*-2,5-bis(alkoxycarbonyl)thiolane **5**, with up to 36% ee. The desulfurization of a seven-membered disulfide, *cis*-3,7-bis(alkoxycarbonyl)-1,2-dithiepane **3**, with chiral aminophosphines also gives a six-membered sulfide, *trans*-2,6-bis(alkoxycarbonyl)thiane **6**, with up to 30% ee.

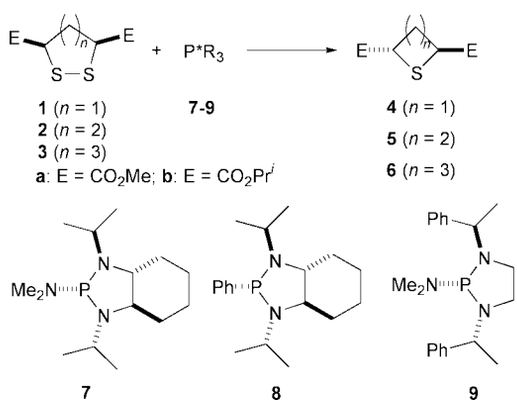
## Introduction

Enantioselective desymmetrization of σ-symmetric *meso*-compounds is an attractive and challenging subject in asymmetric synthesis.[1] A number of enantiodifferentiation methodologies have been developed so far. *meso*-Compounds, such as *meso*-1,*n*-diols ($n = 2$–4), *meso*-1,2-diesters, and *meso*-epoxides, have been mainly examined using enzymic[2] and chemical[1,3] methods to demonstrate the validity of this concept and its application in targeted syntheses of chiral molecules. We report herein the enantioselective desymmetrization of *meso*-cyclic disulfides which have not so far been dealt with in the enantioselective desymmetrization of *meso*-compounds. Harpp *et al*. reported the stereospecific desulfurization of *cis*- and *trans*-3,6-bis(methoxycarbonyl)-1,2-dithiane with a tris(dialkylamino)phosphine to produce *trans*- and *cis*-2,5-bis(methoxycarbonyl)thiolane, respectively (Scheme 1).[4] The




**Scheme 1**

desulfurization has been proposed to proceed in an $S_N2$ fashion involving the heterolytic cleavage of an S–S bond of disulfide **S** with the aminophosphine followed by an intramolecular nucleophilic substitution in the phosphonium intermediate **T**. This work stimulated us to investigate the enantioselective desulfurization of *meso*-cyclic disulfides. Thus, in σ-symmetric cyclic disulfides (**1**–**3**) the effective discrimination of two sulfurs to be eliminated with a chiral phosphorus reagent such as **7**, **8** or **9** might be expected to give chiral cyclic sulfides (Scheme 2). This transformation can also provide a viable route to chiral sulfides with $C_2$-symmetry. Recently, $C_2$-symmetric thiolanes have attracted a great deal of interest in asymmetric syntheses,

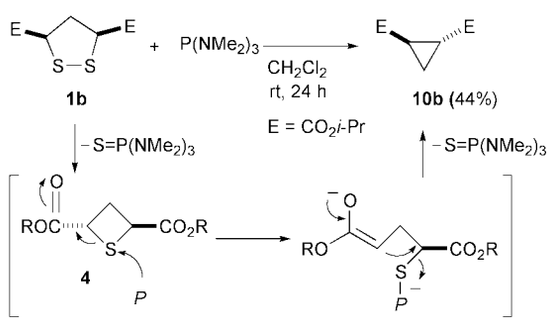



**Scheme 2**

since they have so far been prepared by the transformation of chiral precursors or, otherwise, by resolution of racemic substrates.[5]

## Results and discussion

First, the desulfurization of five-membered *cis*-3,5-bis(alkoxycarbonyl)-1,2-dithiolanes **1** with aminophosphines was attempted. Prior to asymmetric application the reaction with achiral hexamethylphosphorus triamide (HMPT) was carried out. Reaction of *cis*-3,5-bis(isopropoxycarbonyl)-1,2-dithiolane **1b** (0.2 mmol) with HMPT (0.2 mmol) in $CH_2Cl_2$ (2 ml) at room temperature for 24 h afforded *trans*-1,2-bis(isopropoxycarbonyl)cyclopropane **10b** in 44% yield in place of the expected *trans*-2,4-bis(isopropoxycarbonyl)thietane **4b** [equation (1)]. This result indicated that **1b** is prone to eliminate two sulfur atoms *via* two desulfurization steps as shown in equation (1). On the other hand, when HMPT was slowly




(1)

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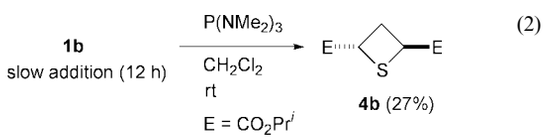
**Table 1** Asymmetric desulfurization of *cis*-3,6-bis(alkoxycarbonyl)-1,2-dithianes **2**[a] and *cis*-3,7-bis(alkoxycarbonyl)-1,2-dithiepanes **3**[b]

| | | | | | Product | |
|---|---|---|---|---|---|---|
| Entry | Disulfide | Phosphine | Solvent | *t*/h | Yield (%)[c] | Ee (%)[d] |
| 1 | **2a** | **7** | $CH_2Cl_2$ | 6 | **5a** 95 | 2 |
| 2 | | **7** | THF | 24 | 88 | 12 |
| 3 | | **7** | $C_6H_{12}$ | 96 | 26 | 36 |
| 4[e] | | **7** | $C_6H_{12}$ | 48 | 52 | 2 |
| 5[f] | | **7** | $C_6H_{12}$ | 96 | 78 | 19 |
| 6 | | **8** | $C_6H_{12}$ | 96 | 37 | 11 |
| 7 | | **9** | $C_6H_{12}$ | 96 | 37 | 15 |
| 8 | **2b** | **7** | $C_6H_{12}$ | 96 | **5b** 8 | 15 |
| 9 | **3a** | **7** | $CH_2Cl_2$ | 48 | **6a** 38 | 21 |
| 10[g] | | **7** | $CH_2Cl_2$ | 60 | 58 | 13 |
| 11 | | **7** | DMA | 85 | 52 | 15 |
| 12 | | **7** | $Pr^iOH$ | 25 | 53 | 3 |
| 13[f] | | **7** | $C_6H_{12}$ | 96 | 25 | 30 |
| 14 | | **8** | $CH_2Cl_2$ | 48 | 39 | 14 |
| 15 | | **9** | $CH_2Cl_2$ | 48 | 38 | 7 |
| 16 | **3b** | **7** | $CH_2Cl_2$ | 48 | **6b** 42 | 15 |

[a] Conditions: **2** (0.2 mmol), phosphine (0.2 mmol), solvent (2 ml), and at room temperature unless otherwise noted. [b] Conditions: **3** (0.2 mmol), phosphine (0.2 mmol), solvent (0.2 ml), and at room temperature unless otherwise noted. [c] Isolated yields. [d] Enantiomeric excess determined by HPLC equipped with chiral columns. [e] At reflux temperature. [f] MS4A was used. [g] At 0 °C.

added to the solution of **1b** over 12 h using a syringe pump, the expected thietane **4b** was mainly produced in 27% yield [equation (2)]. Attempted enantioselective reaction of **1b** with a



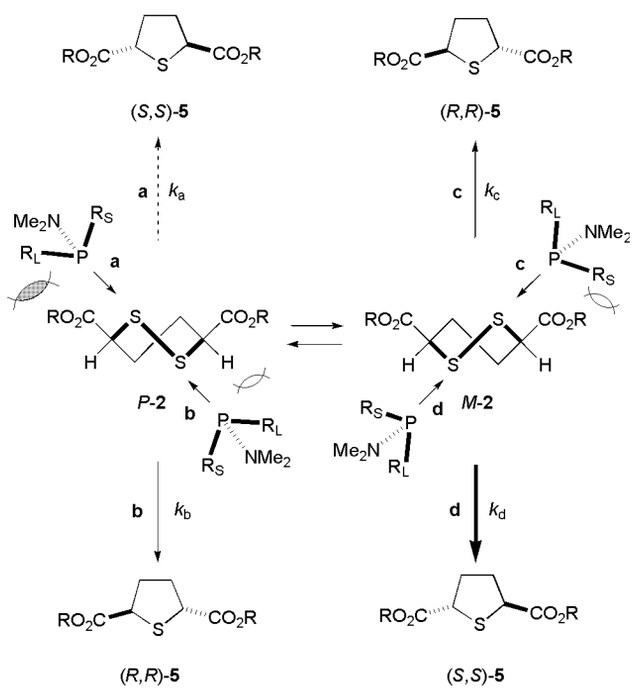
(2)

chiral aminophosphine **7**[6] was, however, in vain under such slow-addition conditions, giving only a trace amount of **4b**.

Next, we examined the enantioselective desulfurization of six- and seven-membered disulfides **2** and **3** to obtain enantiomerically enriched thiolane **5** and thiane **6**. Results under different conditions are summarized in Table 1. The reaction of *cis*-3,6-bis(alkoxycarbonyl)dithianes **2** with chiral aminophosphines was expected to give the $C_2$-symmetric *trans*-2,5-bis(alkoxycarbonyl)thiolane **5**. The reaction of **2a** (0.2 mmol) with **7** (0.2 mmol) in $CH_2Cl_2$ (2 ml) at room temperature for 6 h produced thiolane **5a** quantitatively, but no asymmetric induction occurred (entry 1). The same reaction in THF gave **5a** in 88% yield with 12% ee (entry 2). The highest enantiomeric excess (36% ee) was observed when the reaction was carried out in cyclohexane at room temperature (entry 3). Reflux conditions were not effective for asymmetric induction (2% ee) (entry 4). The addition of MS4A (molecular sieves, 4 Å) accelerated the reaction of **2a** in cyclohexane to give a higher chemical yield of **5a**, but it did not improve the enantioselectivity (19% ee) (entry 5). Other chiral aminophosphines **8** and **9** did not show much influence on the enantioselectivity of the desulfurization of **2a** (entries 6 and 7). The reaction of **2b** having the sterically demanding isopropoxy group afforded **5b** in lower chemical yield with 15% ee (entry 8).

Next, we attempted the enantioselective desulfurization of the seven-membered disulfides **3**. Compared with the six-membered disulfides **2**, the desulfurization of the seven-membered disulfides **3** required higher concentrations of both substrate and phosphine. The reaction of **3a** (0.2 mmol) using chiral phosphine **7** (0.2 mmol) in $CH_2Cl_2$ (0.2 ml) at rt for 48 h afforded thiane **6a** in 38% yield with 21% ee (entry 9). Lower reaction temperature at 0 °C did not improve the enantioselectivity (entry 10). *N*,*N*-Dimethylacetamide (DMA) as a solvent in place of $CH_2Cl_2$ was also effective for the desulfurization of **3a**, providing **6a** in 52% with 15% ee (entry 11). However, $Pr^iOH$ was not effective as a solvent for this enantioselective desulfurization of **3a**, although the reaction was accelerated (entry 12).[7] No reaction took place in a less polar solvent such as cyclohexane. Interestingly, the addition of MS4A promoted the desulfurization of **3a** in cyclohexane to give **6a** with higher enantioselectivity (30% ee) (entry 13). The use of other aminophosphines **8** and **9** in $CH_2Cl_2$ did not improve the enantioselectivity (entries 14 and 15). Higher enantioselectivity in the desulfurization of **3b** having a bulky alkoxy group was expected, but the enantiomeric excess of **6b** was at most 15% ee (entry 16).

The level of enantioselectivity of **5** and **6** was moderate (up to 36% ee), but the enantioselective desulfurization of six- and seven-membered disulfides was found to be a viable process. In the case of the seven-membered disulfides **3** the enantioselective discrimination of sulfur atoms occurred to give the enantiomerically enriched product **6**. In the six-membered disulfide **2**, the enantiotopic discrimination is more complicated.[8] The principle of the enantiotopic discrimination of **2** can be explained by assuming the transition-state structures shown in Scheme 3. Dodson and Nelson claimed that the equilibration between two mirror-image twist structures, *P*-**2** and *M*-**2**, having



**Scheme 3**

helicity denoted by *P* and *M* is established in solution.[9] In the transition state of this desulfurization, four approaching directions (**a**–**d**) of a chiral aminophosphine to the S–S bond of **2** are postulated. The desulfurization of *P*-**2** and *M*-**2** can give rise to both stereoisomers, (2*R*,2*R*)- and (2*S*,2*S*)-thiolane **5**. Approach **a** to *P*-**2** leading to (2*S*,2*S*)-**5** might be most unfavorable due to the steric interaction between the largest group ($R_L$) of an aminophosphine and an alkoxycarbonyl group of **2**. Approach **d** leading to (2*S*,2*S*)-**5** might be the most favorable course. In fact, the *S*,*S*-configuration for the major enantiomer of **5a** was determined by the plus sign of its reported optical rotation.[10,11] This result supports the discrimination process for the six-membered disulfide **2** as shown in Scheme 3.[12]

In conclusion, we have demonstrated the asymmetric desulfurization of *meso*-cyclic disulfides with chiral phosphines. Although a high level of ee has not yet been attained, this reaction represents a unique *meso*-trick involving the configurational inversion of a stereogenic center of the substrate.

## Experimental

### General

All reactions were performed in oven-dried or flame-dried glassware under an atmosphere of dry Ar or $N_2$ unless otherwise noted. Solvents and chemicals were obtained commercially and purified by standard procedures. $^1$H NMR spectra were recorded on a 270 or 400 MHz FT-NMR spectrometer, and $^{13}$C NMR spectra were recorded on a 67.5 or 100 MHz FT-NMR spectrometer. Chemical shifts are reported in ppm relative to TMS in the solvents specified. $^1$H NMR data are reported as follows: chemical shift in ppm ($\delta_H$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, c = complex), coupling constant (Hz), relative intensity, and interpretation. $^{13}$C NMR data are reported as follows: chemical shift in ppm ($\delta_C$) and interpretation. High-resolution mass spectra (HRMS) were obtained with a JEOL JMS-SX102A spectrometer. Mps were measured on a Yanaco MP-J3 micro-melting-point apparatus and are uncorrected. Analytical TLC was performed with silica gel 60 Merck F-254 plates. Column chromatography on $SiO_2$ was performed with Merck silica gel 60. HPLC analyses were performed on a Hitachi L-7000 instrument using Daicel Chiralcel OD and AD columns at 30 °C or 40 °C. Elemental analyses were performed at the Microanalytical Center of Kyoto University. *meso*-Cyclic disulfides **2a**[4] and chiral diazaphospholidines **7**–**9**[6] were prepared by the reported methods.

### Preparation of *cis*-3,5-bis(methoxycarbonyl)-1,2-dithiolane 1a

*meso*-α,α′-Dibromoglutaric acid was prepared by the reported method.[13] To a green solution of $Na_2S$ (0.234 g, 3.0 mmol) and sulfur powder (0.096 g, 3.0 mmol) in DMF (10 ml) was added a solution of dimethyl α,α′-dibromoglutarate (0.645 g, 2 mmol) in DMF (1 ml) at 0 °C. After the exothermic reaction had subsided, the reaction mixture was stirred for 4 h at room temperature. The mixture was poured into saturated aq. $NH_4Cl$ and extracted with $Et_2O$ (3 × 30 ml). The ether layer was dried over $MgSO_4$ and concentrated under vacuum. The yellow oil was subjected to column chromatography on $SiO_2$ with hexane–EtOAc (5:1) as eluent to give a mixture of *trans*- and *cis*-3,5-bis(methoxycarbonyl)-1,2-dithiolane (0.206 g, 46%). *cis*-3,5-Bis(methoxycarbonyl)-1,2-dithiolane **1a** was isolated in pure form by HPLC with $CHCl_3$ eluent as a yellow oil; $\nu_{max}$(neat)/cm$^{-1}$ 1732 (CO); $\delta_H$(400 MHz; $CDCl_3$) 2.77 (t, *J* 5.4 Hz, 2H), 3.77 (s, 6H), 4.40 (t, *J* 5.4 Hz, 2H); $\delta_C$(100 MHz; $CDCl_3$) 38.0 ($CH_2$), 52.9 ($CH_3$), 54.3 (SCH), 171.1 (CO); *m*/*z* EIMS 222 ($M^+$) [HRMS (EI): Calc. for $C_7H_{10}O_4S_2$: 222.0020. Found: *m*/*z*, 222.0027] (Calc. for $C_7H_{10}O_4S_2$: C, 37.83; H, 4.53; S, 28.85. Found: C, 38.35; H, 4.58; S, 28.48%).

### Preparation of *cis*-3,7-bis(methoxycarbonyl)-1,2-dithiepane 3a

*meso*-α,α′-Dimercaptopimelic acid was prepared by the reported method.[13] Dry HCl gas (dried in a conc. $H_2SO_4$ tower) was passed through a suspension of *meso*-α,α′-dimercaptopimelic acid (7.34 g, 33 mmol) in methanol (550 ml) with stirring at 0 °C for 2.5 h. The methanol was removed under vacuum, $Et_2O$ (100 ml) was added, and the solution was dried over $MgSO_4$. The solvent was evaporated to give dimethyl *meso*-α,α′-dimercaptopimelate (5.67 g, 22 mmol, 66% yield) as a yellow oil. A saturated solution of iodine in chloroform was added dropwise to a solution of dimethyl *meso*-α,α′-dimercaptopimelate (5.67 g, 22 mmol) and triethylamine (5.7 ml, 41 mmol) in chloroform (150 ml) until a slight excess of $I_2$ was evidenced by its color. The solution was washed successively with saturated aq. $Na_2S_2O_3$ and dil. HCl, and then dried over $MgSO_4$. The solvent was evaporated under reduced pressure to give a brown oil, which was subjected to column chromatography on $SiO_2$ with hexane–diethyl ether (1:1) as eluent to give *cis*-3,7-bis(methoxycarbonyl)-1,2-dithiepane **3a** (2.95 g, 55% yield) as a colorless oil; $\nu_{max}$(neat)/cm$^{-1}$ 1731 (CO); $\delta_H$(270 MHz; $CDCl_3$) 1.89–2.35 (m, 6H), 3.51–3.56 (m, 2H), 3.73 (s, 6H); $\delta_C$(67.5 MHz; $CDCl_3$) 14.1 ($CH_2CH_2CH_2$), 23.9 ($CH_2$), 52.5 ($CH_3$), 54.4 (SCH), 171.7 (CO) (Calc. for $C_9H_{14}O_4S_2$: C, 43.18; H, 5.64; S, 25.61. Found: C, 43.10; H, 5.63; S, 25.65%).

### Preparation of *cis*-bis(isopropoxycarbonyl)-1,2-dithiacycloalkanes 1b–3b[14]

To a solution of a methyl ester **1a**–**3a** (1.3 mmol) and propan-2-ol (7.1 ml) was added tetraisopropyl titanate (40 µl, 0.13 mmol) under nitrogen. The mixture was stirred at reflux temperature for 5 h. After the removal of the produced methanol *in vacuo*, the oily residue was dissolved in propan-2-ol (7.1 ml) and the mixture was refluxed for 5 h. The solvent was removed and the resultant yellow oil was dissolved in diethyl ether (5 ml). Water (5 ml) was added to the mixture, which was stirred for 10 min. The resulting mixture was extracted with diethyl ether (3 × 30 ml) and the extract was dried over $MgSO_4$. The solvent was removed under reduced pressure to give a pale yellow oil. Purification by silica gel column chromatography with hexane–EtOAc (5:1) as eluent gave the corresponding isopropyl ester.

***cis*-3,5-Bis(isopropoxycarbonyl)-1,2-dithiolane 1b.** A yellow oil (42%); $\nu_{max}$(neat)/cm$^{-1}$ 1735 (CO); $\delta_H$(270 MHz; $CDCl_3$) 1.27 (d, *J* 6.3 Hz, 12H), 2.73 (t, *J* 5.8 Hz, 2H), 4.35 (t, *J* 5.8 Hz, 2H), 5.04 (sept, *J* 6.3 Hz, 2H); $\delta_C$(67.5 MHz; $CDCl_3$) 21.5 ($CH_3$), 21.7 ($CH_3$), 37.8 ($CH_2$), 54.9 (SCH), 69.5 (OCH), 170.1 (CO) (Calc. for $C_{11}H_{18}O_4S_2$: C, 47.46; H, 6.52; S, 23.03. Found: C, 47.86; H, 6.73; S, 23.03%).

***cis*-3,6-Bis(isopropoxycarbonyl)-1,2-dithiane 2b.** A white solid (83%); mp 59–61 °C; $\nu_{max}$(KBr)/cm$^{-1}$ 1711 (CO); $\delta_H$(270 MHz; $CDCl_3$) 1.20 (d, *J* 6.31 Hz, 6H), 1.21 (d, *J* 6.31 Hz, 6H), 2.09–2.13 (m, 2H), 2.38–2.45 (m, 2H), 3.52–3.54 (m, 2H), 5.00 (tt, *J* 6.31, 6.31 Hz, 2H); $\delta_C$(67.5 MHz; $CDCl_3$) 21.5 ($CH_3$), 21.6 ($CH_3$), 27.5 ($CH_2$), 45.7 (SCH), 69.1 (OCH), 169.5 (CO) (Calc. for $C_{12}H_{20}O_4S_2$: C, 49.29; H, 6.89; S, 21.93. Found: C, 49.13; H, 6.84; S, 21.85%).

***cis*-3,7-Bis(isopropoxycarbonyl)-1,2-dithiepane 3b.** A colorless oil (65%); $\nu_{max}$(neat)/cm$^{-1}$ 1731 (CO); $\delta_H$(270 MHz; $CDCl_3$) 1.24 (d, *J* 6.3 Hz, 6H), 1.25 (d, *J* 6.3 Hz, 6H), 2.29–2.50 (m, 6H), 3.43–3.49 (m, 2H), 5.01 (tt, *J* 6.3, 6.3 Hz, 2H); $\delta_C$(67.5 MHz; $CDCl_3$) 21.4 ($CH_3$), 21.5 ($CH_3$), 23.8 ($CH_2CHS$), 32.0 ($CH_2CH_2CH_2$), 55.1 (SCH), 68.7 (OCH), 170.6 (CO) (Calc. for $C_{13}H_{22}O_4S_2$: C, 50.95; H, 7.24; S, 20.92. Found: C, 50.94; H, 7.30; S, 20.67%).

### Desulfurization of 1b with HMPT

To a solution of **1b** (55.7 mg, 0.20 mmol) in $CH_2Cl_2$ (2 ml) was added HMPT (40.0 μl, 0.22 mmol) at room temperature and the mixture was stirred for 24 h. The solvent was removed under vacuum. Purification by silica gel column chromatography with hexane–EtOAc (20 : 1) as eluent gave *trans*-1,2-bis(isopropoxycarbonyl)cyclopropane **10b** (18.9 mg, 44%) as a colorless oil; $\delta_H$(270 MHz; $CDCl_3$) 1.24 (d, *J* 6.3 Hz, 12H), 1.36–1.41 (c, 2H), 2.08–2.13 (c, 2H), 4.99 (sept, *J* 6.3 Hz, 2H); $\delta_C$(100 MHz; $CDCl_3$) 15.3 (*C*HCH$_2$), 21.8 (CH$_3$), 22.5 (CH$_2$), 68.5 (O*C*H), 171.3 (CO); *m*/*z* EIMS 215 (M + H) [HRMS (EI): Calc. for $C_{11}H_{19}O_4$: 215.1283. Found: *m*/*z*, 215.1291].

### Desulfurization of 1b with HMPT using a syringe pump

To a stirred solution of **1b** (55.7 mg, 0.20 mmol) in $CH_2Cl_2$ (2 ml) was added HMPT (40.0 μl, 0.22 mmol) at room temperature over a period of 12 h using a syringe pump. The solvent was evaporated under vacuum to give a yellow liquid. Purification by silica gel column chromatography with hexane–EtOAc (40 : 1) as eluent gave *trans*-2,4-bis(isopropoxycarbonyl)-thietane **4b** (13.3 mg, 27%) as a yellow oil; $\delta_H$(270 MHz; $CDCl_3$) 1.256 (d, *J* 6.4 Hz, 6H), 1.262 (d, *J* 6.4 Hz, 6H), 3.25 (t, *J* 7.3 Hz, 2H), 4.05 (d, *J* 7.3 Hz, 2H), 5.06 (sept, *J* 6.4 Hz, 2H); $\delta_C$(100 MHz; $CDCl_3$) 21.6 (CH*C*H$_3$), 21.7 (CH*C*H$_3$), 30.2 (CH$_2$), 35.3 (SCH), 69.1 (OCH), 172.5 (CO); *m*/*z* FABMS 247 (M + H) [HRMS (FAB): Calc. for $C_{11}H_{18}O_4S$: 247.1004. Found: *m*/*z*, 247.1004].

### General procedure for asymmetric desulfurization of *meso*-cyclic disulfides

A solution of chiral phosphorus compound (0.2 mmol) and the *meso*-cyclic disulfide (0.2 mmol) in a solvent (0.2–2 ml) was stirred under nitrogen at room temperature. After the reaction was complete, evaporation of the solvent left a pale yellow oil. Purification by silica gel chromatography gave the corresponding cyclic monosulfide in pure form. Enantiomeric excesses were determined by HPLC using a suitable chiral column.

***trans*-2,5-Bis(methoxycarbonyl)thiolane 5a.**[4,10] A colorless oil; $\nu_{max}$(neat)/cm$^{-1}$ 1736 (CO); $\delta_H$(270 MHz; $CDCl_3$) 2.26–2.42 (m, 4H), 3.72 (s, 6H), 4.05–4.09 (m, 2H); ee was determined by Daicel Chiralcel OD; 40 °C; 1.0 ml min$^{-1}$, hexane–propan-2-ol (80 : 20); (*R*,*R*) $t_1$ = 4.70 min, (*S*,*S*) $t_2$ = 5.36 min.

***trans*-2,5-Bis(isopropoxycarbonyl)thiolane 5b.** A white solid; mp 51–52 °C; ee was determined by Daicel Chiralpak AD; 30 °C; 0.2 ml min$^{-1}$, hexane–methanol (200 : 1); $t_1$ = 34.23 min, $t_2$ = 45.06 min; $\nu_{max}$(KBr)/cm$^{-1}$ 1727 (CO); $\delta_H$(270 MHz; $CDCl_3$) 1.24 (d, *J* 6.32 Hz, 12H), 2.25–2.40 (m, 4H), 3.97–3.99 (m, 2H), 5.00 (sept, *J* 6.32 Hz, 2H); $\delta_C$(67.5 MHz; $CDCl_3$) 21.5 (CH$_3$), 21.7 (CH$_3$), 32.8 (CH$_2$), 48.8 (SCH), 68.7 (OCH), 172.4 (CO) (Calc. for $C_{12}H_{20}O_4S$: C, 55.36; H, 7.74; S, 12.31. Found: C, 55.09; H, 7.78; S, 12.32%).

***trans*-2,6-Bis(methoxycarbonyl)thiane 6a.** Ee was determined by Daicel Chiralcel OD; 40 °C; 0.5 ml min$^{-1}$, hexane–propan-2-ol (91 : 9); $t_1$ = 11.80 min, $t_2$ = 14.26 min; $\nu_{max}$(neat)/cm$^{-1}$ 1732 (CO); $\delta_H$(270 MHz; $CDCl_3$) 1.82–2.69 (m, 6H), 3.74 (s, 6H), 3.81 (dd, *J* 3.98, 7.01 Hz, 2H); $\delta_C$(67.5 MHz; $CDCl_3$) 21.2 (CH$_2$*C*H$_2$CH$_2$), 28.7 (*C*H$_2$CH), 41.5 (SCH), 52.2 (CH$_3$), 172.3 (CO) (Calc. for $C_9H_{14}O_4S$: C, 49.53; H, 6.46; S, 14.69. Found: C, 49.17; H, 6.42; S, 15.30%).

***trans*-2,6-Bis(isopropoxycarbonyl)thiane 6b.** Ee was determined by Daicel Chiralcel OD; 30 °C; 0.1 ml min$^{-1}$, hexane–*tert*-butyl methyl ether (92 : 8); $t_1$ = 104.46 min, $t_2$ = 112.98 min; $\nu_{max}$(neat)/cm$^{-1}$ 1727 (CO); $\delta_H$(270 MHz; $CDCl_3$) 1.25 (d, *J* 6.23 Hz, 6H), 1.26 (d, *J* 6.23 Hz, 6H), 1.80–2.08 (m, 6H), 3.76 (dd, *J* 3.98, 7.28 Hz, 2H), 5.03 (tt, *J* 6.23, 6.23 Hz, 2H); $\delta_C$(67.5 MHz; $CDCl_3$) 21.3 (CH$_2$*C*H$_2$CH$_2$), 21.67 (CH$_3$), 21.72 (CH$_3$), 28.9 (*C*H$_2$CH), 41.9 (SCH), 68.8 (OCH), 171.6 (CO) (Calc. for $C_{13}H_{22}O_4S$: C, 56.91; H, 8.08; S, 11.68. Found: C, 56.84; H, 7.86; S, 11.84%).

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11 The desymmetrization of **2b** and the seven-membered disulfides, **3a** and **3b**, is assumed to be in the same sense by analogy.
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