C_2-Symmetric Bis-sulfoxide: A Novel Chiral Auxiliary for Asymmetric Desymmetrization of Cyclic *meso*-1,2-Diols

Naoyoshi Maezaki,[†] Atsunobu Sakamoto,[†] Noboru Nagahashi,[†] Motohiro Soejima,[†] Ying-Xia Li,[†] Tsuneaki Imamura,[†] Naoto Kojima,[†] Hirofumi Ohishi,[‡] Ken-ichi Sakaguchi,[§] Chuzo Iwata,[†] and Tetsuaki Tanaka*[,†]

Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan, Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahara, Takatsuki, Osaka 569-1094, Japan, and Research Center for Protein Engineering, Institute for Protein Research, Osaka University, 3-2 Yamadaoka, Suita, Osaka 565-0871, Japan

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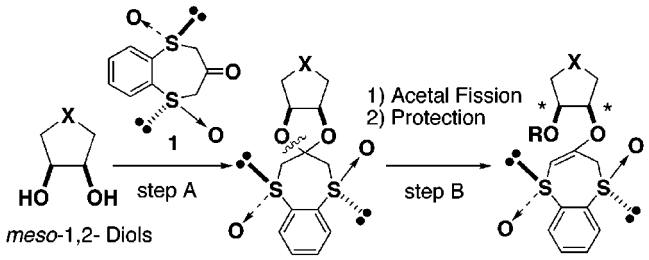
A new heterocyclic compound, C_2-symmetric bis-sulfoxide **1**, has been found to be an efficient chiral auxiliary for asymmetric desymmetrization of cyclic *meso*-1,2-diols via diastereoselective acetal fission. Both (*R*,*R*)- and (*S*,*S*)-**1** are readily synthesized with high optical purity via asymmetric oxidation of 1,5-benzodithiepan-3-one (**2**). After acetalization of *meso*-1,2-diols **6a**−**e** and a mono-TMS ether **6f** with this chiral auxiliary **1**, the resulting acetals **7a**−**f** were subjected to base-promoted acetal fission upon treatment with potassium hexamethyldisilazide (KHMDS) followed by acetylation or benzylation to give the desymmetrized diol derivatives **8a**−**f** with high diastereoselectivity. The chiral auxiliary **1** is readily removed by acid-promoted hydrolysis and can be recovered without a loss in enantiomeric excess.

Introduction

Asymmetric desymmetrization of compounds with a σ-symmetric plane is an important transformation for synthesizing versatile chiral building blocks for various natural products. This area of chemistry has been extensively investigated in an effort to develop efficient methods.[1] Recently, we reported a novel asymmetric desymmetrization of σ-symmetric diols based on the base-promoted diastereoselective acetal fission of α-sulfinyl acetals using a new chiral auxiliary, **1**, with C_2-symmetry as shown in Scheme 1.[2] This methodology was successfully applied to a synthesis of (−)-allosamizoline[3] and (−)-*gala*-quercitol.[4] One of the advantages of this chiral auxiliary is that acetalization of *meso*-diols gives only one product (step A), whereas production of more than one product is an inevitable problem with chiral auxiliaries lacking symmetry. In addition, no regio- and geometric isomers of the enol ether are formed in the acetal cleavage reaction (step B), thereby making the whole process simple. To the best of our knowledge, this is the first use of a C_2-symmetric chiral auxiliary for the asymmetrization of σ-symmetric diols.[5] In addition, this methodology constitutes a conceptually novel application of an α-sulfinyl carbanion for asymmetric reaction.[6]

In this paper, we report the full details of the synthesis of the C_2-symmetric bis-sulfoxide **1** and its application to asymmetric desymmetrization of cyclic *meso*-1,2-diols.

Scheme 1



Results and Discussion

Synthesis of C_2-Symmetric Bis-sulfoxide and Structural Determination. As shown in Schemes 2 and 3, the standard samples of optically pure (*R*,*R*)- and (*S*,*S*)-**1** were synthesized via optical resolution using diethyl tartrate as a chiral auxiliary. 1,2-Benzenedithiol[7] was condensed with 1,3-dichloroacetone in the presence of DMAP to give **2** in 76% yield. After the ketone **2** was acetalized with the bis-trimethylsilyl ether of (+)-diethyl tartrate by Noyori's method,[8] one of the sulfide moieties

[†] Graduate School of Pharmaceutical Sciences, Osaka University.
[‡] Osaka University of Pharmaceutical Sciences.
[§] Institute for Protein Research, Osaka University.

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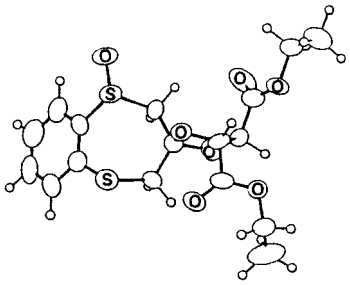
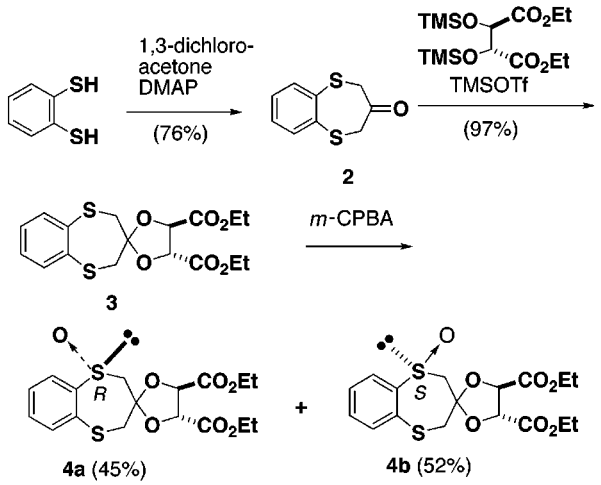
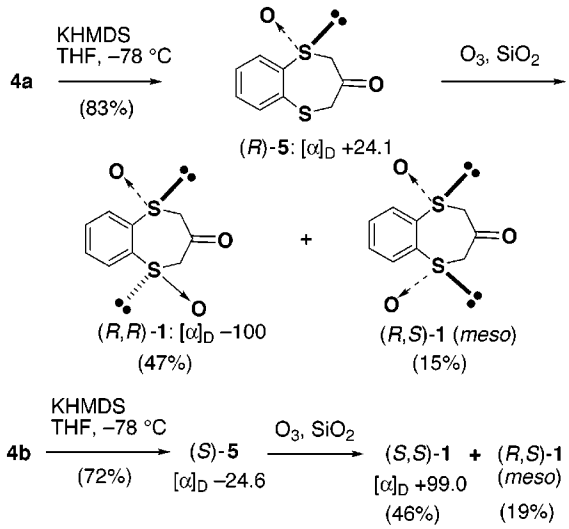


Figure 1. ORTEP drawing of **4a**.

Scheme 2



Scheme 3



in **3** was oxidized to sulfoxide with 1 equiv of *m*-CPBA to give the separable diastereomeric isomers **4a** and **4b**. The absolute configuration of **4a** was unambiguously determined as the *R* configuration by single-crystal X-ray analysis (Figure 1).[9] Thus, the absolute configuration at the sulfoxide was established as *R* in **4a**.

Acid-promoted hydrolysis of the acetal **4a** (*p*-TsOH·H_2O or H_2SO_4 in THF−water) was not successful in that it gave many unidentified products, whereas base-promoted deacetalization of **4a** with KHMDS proceeded smoothly to give the ketosulfoxide (*R*)-**5** in 83% yield. Although

(9) Friedel pair reflections and anomalous scatterings were used to determine the absolute configuration.

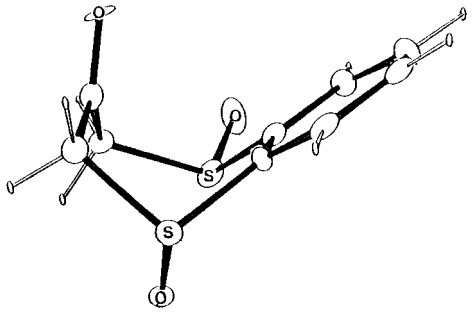


Figure 2. ORTEP drawing of (*R*,*R*)-**1**.

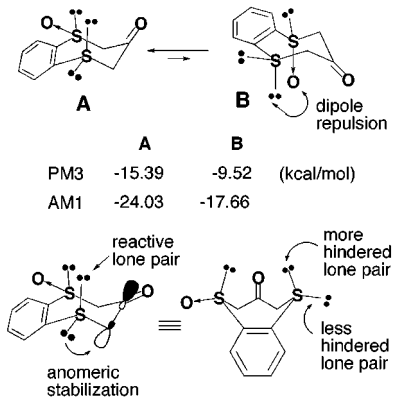


Figure 3. Conformational energies of mono-sulfoxide **5** and plausible mechanism of diastereoselective oxidation.

various oxidation conditions of racemic **5** were examined, the undesirable *meso*-**1** was a major product, e.g., *m*-CPBA [(±)-**1**:*meso* = 1:2], dimethyldioxirane (1:2),[10] H_2O_2/SeO_2 (*meso* only).[11] Only ozone oxidation (dry ozonation)[12] provided mainly (±)-**1** (3:1); thus bis-sulfoxides (*R*,*R*)- and (*S*,*S*)-**1** were obtained as the main products from (*R*)- and (*S*)-**5**, respectively.[13] The X-ray single-crystal structural analysis of (*R*,*R*)-**1** revealed its absolute configuration and boat conformation of the seven-membered ring (Figure 2).[9] The bis-sulfoxide **1** is a stable crystal and can be stored for at least 1 month at room temperature without loss of its chemical and optical purities (Scheme 3).

The reversed selectivity observed in ozone oxidation of the mono-sulfoxide **5** is rationalized as follows. The conformational equilibrium between the two conformers **A** and **B** would lie preferentially to conformer **A**, since the axial lone pair of the sulfide moiety in conformer **B** suffers from unfavorable dipole−dipole interaction with the axial sulfoxide, as shown in Figure 3. Conformational analysis using the MOPAC program (AM1[14] and PM3[15] methods) supported this speculation. The heat of formation of **A** is about 6 kcal/mol more stable than that of **B**. In the conformer **A**, the sulfide's nucleophilic attack on the bulky oxidants would proceed at the equatorial lone

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Table 1. Asymmetric Oxidation of 1,5-Benzodithiepane-3-one (2)

entry	conditions (equiv)	time (days)	yield[a] (%)	ee[b] (%)	confign
1	Davis' reagent (1.0)	3	87	27	*S*
2	TBHP (1.1), Ti(O-*i*-Pr)$_4$ (1.0), (+)-DET (2.0), H_2O (1.0)	7	20	0	
3	TBHP (1.0), Ti(O-*i*-Pr)$_4$ (1.0), (+)-DET (2.0)	7	56	84	*R*
4	TBHP (2.0), Ti(O-*i*-Pr)$_4$ (1.0), (+)-DET (4.0)	2	82	86	*R*
5	CHP (1.1), Ti(O-*i*-Pr)$_4$ (1.0), (+)-DET (2.0)	7	44	73	*R*
6	CHP (2.0), Ti(O-*i*-Pr)$_4$ (1.0), (+)-DET (4.0)	2	56	97	*R*

[a] Isolated yield. [b] Determined by the specific rotation; Davis' reagent = (+)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine; TBHP = *tert*-butyl hydroperoxide; DET = diethyl tartrate; CHP = cumene hydroperoxide.

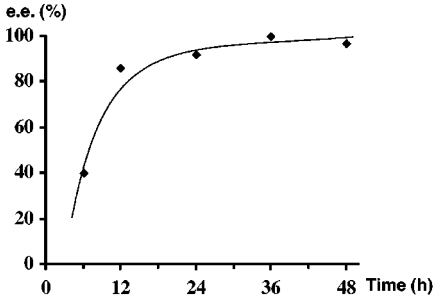


Figure 4. Time course of ee (%) of (*R*)-**5**.

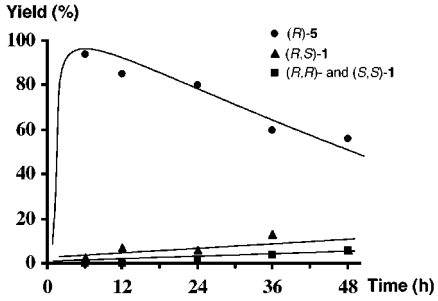


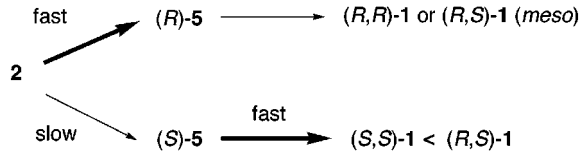
Figure 5. Time course of yields of products in asymmetric oxidation of **2**.

pair rather than at the axial one, since the equatorially oriented lone pair is relatively unhindered. Consequently, stereochemical outcomes of bulky oxidants such as *m*-CPBA, dimethyldioxirane, and HOSe(O)OH are controlled by the reagent approach to give mainly the *meso*-isomer.[13] On the other hand, ozone is a small and highly electrophilic oxidant and reacts more with a nucleophilic lone pair rather than with a less hindered one.[13] Since the equatorial lone pair on the sulfide would be stabilized by the anomeric effect resulting from an $n_s \rightarrow \sigma^*_{C-C(O)}$ interaction,[16] the oxidation of the sulfide with ozone proceeds at the reactive axial lone pair to give mainly the desired *trans*-isomer.

Synthesis of Chiral Auxiliary via Asymmetric Oxidation. We attempted to establish a more efficient synthetic route to the mono-sulfoxide **5** via asymmetric oxidation of 1,5-benzodithiepan-3-one (**2**). We examined the representative methodologies developed by Davis,[17] Kagan,[18] and Modena.[19] The results are summarized in Table 1. Davis' reagent and Kagan's procedure were not efficient for this substrate (entries 1 and 2), while Modena's procedure afforded better selectivities (entries 3 and 4). When 2 equiv of cumene hydroperoxide (CHP) was used as an oxidant,[20] the ee was increased up to 97% (entry 6).

To determine the optimum conditions, we examined the time course of the ee of (*R*)-**5** and the product yields (Figures 4 and 5). Although the ee of mono-sulfoxide (*R*)-**5** was initially low (6 h, 40% ee), the ee increased and reached a maximum value (36 h, >98% ee). During this period, the yield of (*R*)-**5** decreased. Alternatively, (*R*,*S*)-**1** (*meso*) and (*R*,*R*)-**1** (36 h, 70% ee) gradually increased. Thus, optically pure (*R*)-**5** was efficiently prepared from **2** in 60% yield in one step. Since both enantiomers of diethyl tartrate are available, this methodology can be applied to the synthesis of (*S*)-**5**. In fact, (*S*)-**5** was synthesized in the same yield with high optical purity.

Scheme 4



The enhancement of ee can be explained as follows (Scheme 4). In this reaction, the rate of oxidation of the main mono-sulfoxide (*R*)-**5** is slower than that of bis-sulfide **2**. This indicates that the chiral oxidant and the mono-sulfoxide (*R*)-**5** are mismatched, while the matched enantiomer (*S*)-**5** would be promptly oxidized to bis-sulfoxides (*R*,*S*)-**1** (*meso*-form) rather than (*S*,*S*)-**1**. Thus, the optical purity of the initially formed (*R*)-**5** would be enhanced by rapid consumption of the minor enantiomer (*S*)-**5**.[21] It is obvious that a kinetic resolution took place in this reaction.

Base-Promoted Diastereoselective Acetal Fission. With the chiral auxiliary in hand, we examined the acetalization and asymmetric desymmetrization of *meso*-1,2-diols (Scheme 5). We found that Terashima's procedure[22] was suitable for acetalization of *meso*-diols using the C_2-symmetric bis-sulfoxide.[23] Thus, the *meso*-1,2-diols **6a**−**e** were acetalized with (*R*,*R*)- or (*S*,*S*)-bis-sulfoxide **1** in the presence of TMSOTf and 2,6-lutidine at 0 °C in good yields to give the acetals **7a**−**e** (Table 2). Only the reaction of the nitrogen-containing *meso*-diol (the free alcohol of **6f**) was sluggish, resulting in a poor yield (4 °C, 82 h, 38%). This problem was overcome by employing

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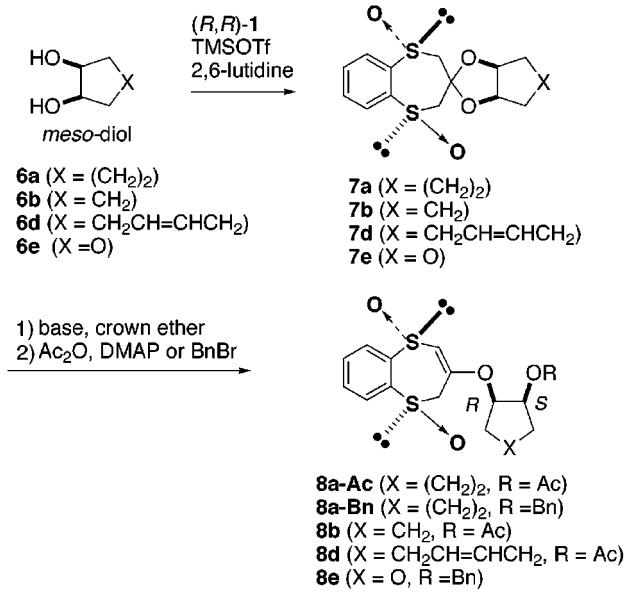
(23) The reaction should be carried out below 5 °C to avoid partial racemization of **1**.

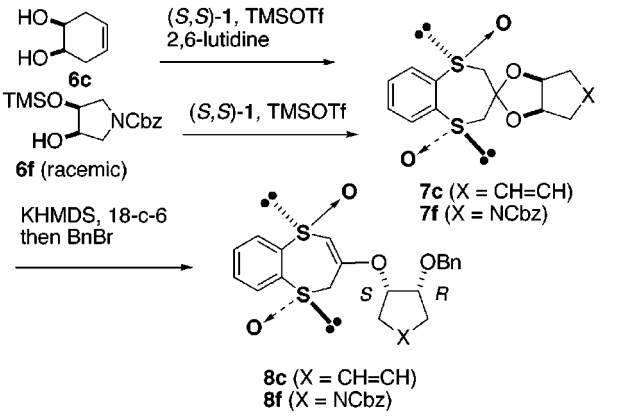
Table 2. Acetalization of 6a−f

acetalization diol	X	acetal	yield (%)[a]
6a	$(CH_2)_2$	**7a**	86
6b	CH_2	**7b**	83
6c	CH=CH	**7c**[b]	89
6d	$CH_2CH{=}CHCH_2$	**7d**	90
6e	O	**7e**	80
6f[c]	NCbz	**7f**[b]	89

[a] Isolated yield. [b] Acetalized with (*S*,*S*)-bis-sulfoxide. [c] Mono-TMS ether was employed.

Scheme 5





mono-TMS ether **6f** in the presence of TMSOTf in $CHCl_3$ to give a good yield of **7f** (4 °C, 6 h, 89%).

Base-promoted acetal fission of **7a** with LDA or LHMDS and 12-crown-4[24] followed by acetylation of the resulting alkoxide to prevent recyclization afforded **8a-Ac** in good yield, but with poor diastereoselectivity (Table 3, entries 1 and 2).[25] Interestingly, the countercation in the base had a remarkable effect. Selectivity was dramatically increased in the order Li ≪ Na < K (entries 1−4). The best results were obtained using 3 equiv of KHMDS and 18-crown-6 in THF, which led to the formation of acetate **8a-Ac** in 91% chemical yield and >96% ee (entry 4). No solvent effect on the selectivity was observed (entries 4−6).

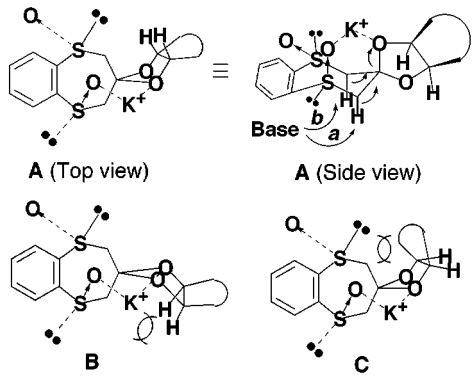


Figure 6. Possible chelation intermediates of base-promoted acetal fission.

Table 3. Base-Promoted Acetal Fission of 7a

entry	conditions (equiv)[a]	yield[b] (%)	de[c] (%)
1	LDA (3), 12-c-4 (3), THF	79	14
2	LHMDS (3), 12-c-4 (3), THF	79	8
3	NaHMDS (3), 15-c-5 (3), THF	83	90
4	KHMDS (3), 18-c-6 (3), THF	91	>96
5	KHMDS (3), 18-c-6 (3), DME	75	>96
6	KHMDS (3), 18-c-6 (3), toluene	80	>96

[a] The reaction was carried out at −78 °C, and the resulting alcohol was acetylated with acetic anhydride. [b] Isolated yield after acetylation. [c] Determined by 500 MHz ^{1}H NMR spectroscopy.

Taking account of the remarkable effect of the metal cation on diastereoselectivity, we assumed a chelation-controlled mechanism as shown in Figure 6. The potassium cation would coordinate between polar sulfinyl oxygen and the axially oriented acetal oxygen to form the six-membered ring chelation intermediates. Since the intermediates **B** and **C** giving minor products have congested structures, the reaction would proceed via intermediate **A** which has the least steric demand. Thus, the major products would be formed via stereoelectronically favorable *anti*-elimination through path a or b. This speculation regarding the favorable conformation was supported by the X-ray structure of racemic acetal (±)-**7c** (Figure 7), which was almost consistent with that of chelation intermediate **A**. The coordination of the sodium or potassium cation would stabilize the preferred conformation, thereby giving high diastereoselectivity. On the other hand, the lower selectivity observed in LHMDS could be attributed to the short atomic radius of the lithium cation, which could not stabilize the preferred conformation by the chelation.

Various *meso*-diols were desymmetrized with very high and predictable diastereoselectivities via base-promoted acetal fission of **7a**−**f** to give **8a**−**f**, respectively, after trapping the resulting alkoxides as the acetates or benzyl ethers (Table 4). When (*R*,*R*)-**1** is used as a chiral auxiliary, the stereochemistry of the resulting alkoxides have an *S*-configuration.[26] On the other hand, acetalization of the acyclic *meso*-1,2-diols, *meso*-erythrytol 1,4-dibenzyl ether, was sluggish and caused decomposition of the bis-sulfoxide, although the diastereoselectivity of acetal fission was very high (>96% de).

(24) In the absence of crown ether, the acetate **8a-Ac** was formed in a poor yield (56%) and a considerable amount of acetal **7a** was recovered (28%).

(25) After the addition of the base, the reaction was quenched with acetic anhydride at −78 °C, and the mixture was transferred into a saturated NH_4Cl aqueous solution. This workup was essential to prevent undesirable recyclization of the product. The partially acetylated product was filtrated through a short pad of silica gel and then completely acetylated with acetic anhydride and DMAP.

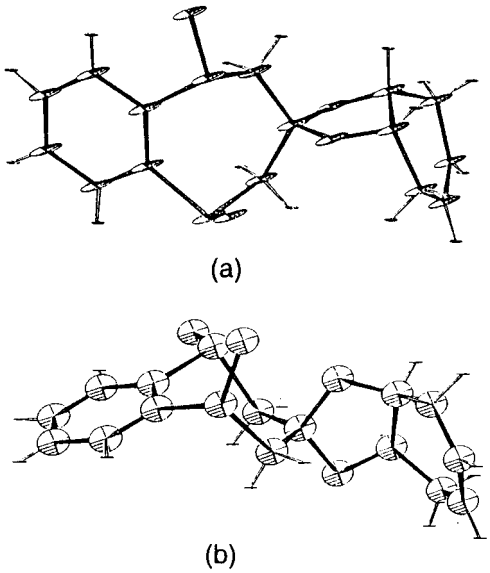


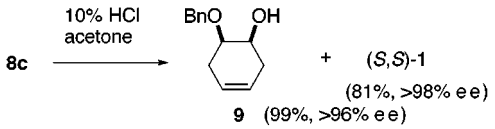
Figure 7. ORTEP drawing of *ent*-**7c**. (a) Top view. (b) Side view.

Table 4. Diastereoselective Acetal Fission of Acetals 7a−f

acetal	X	method[a]	product	R	yield (%)[b]	de (%)[c]	config[d]
7a	$(CH_2)_2$	A	**8a-Ac**	Ac	91	>96	(1*R*,2*S*)
		B	**8a-Bn**	Bn	92	>96	(1*R*,2*S*)
7b	CH_2	A	**8b**	Ac	78	>96	(1*R*,2*S*)
7c	CH=CH	B	**8c**	Bn	85	>96	(1*S*,2*R*)[e]
7d	CH_2CH=$CHCH_2$	A	**8d**	Ac	89	91	(1*R*,2*S*)
7e	O	B	**8e**	Bn	71	>96	(1*R*,2*S*)
7f	NCbz	B	**8f**	Bn	84	>96	(1*S*,2*R*)[e]

[a] Method A, (i) KHMDS (3), 18-c-6 (3), THF, −78 °C, then Ac_2O; (ii) DMAP, Ac_2O, CH_2Cl_2, 0 °C → rt; Method B, KHMDS (3), 18-c-6 (3), THF, −78 °C, then BnBr. [b] Isolated yield. [c] Determined by 500 MHz ^{1}H NMR spectroscopy. [d] See ref 26. [e] (*S*,*S*)-**1** was used as a chiral auxiliary.

Scheme 6



The chiral auxiliary could be removed by acid hydrolysis with 10% HCl in acetone in good yield, as shown in Scheme 6. The chiral auxiliary (*S*,*S*)-**1** was recovered in 81% chemical yield without decreasing the enantiomeric excess (>98% ee) and was reusable.

Conclusion

We developed a novel C_2-symmetric bis-sulfoxide, **1**, which was found to be an efficient chiral auxiliary for the asymmetric desymmetrization of cyclic *meso*-1,2-diols via acetalization followed by highly diastereoselective acetal fission. This unique heterocyclic compound **1** can be readily synthesized with high optical purity from commercially available 1,2-benzenedithiol in three steps via asymmetric oxidation. Because of its C_2 symmetry, the formation of diastereomeric isomers at the acetalization step can be avoided. In addition, its ability to differentiate was high enough to be used as a complement to the enzymatic method. Our method affords a powerful tool for the synthesis of natural products.

Experimental Section

All melting points are uncorrected. NMR spectra were recorded in a $CDCl_3$ solution at 500 MHz (^{1}H) and 75 MHz (^{13}C). IR absorption spectra (FT: diffuse reflectance spectroscopy) were recorded with KBr powder, and only noteworthy absorptions (cm^{-1}) are listed. Column chromatography was carried out using Merck silica gel 60 (70−230 mesh). All air- or moisture-sensitive reactions were carried out in flame-dried glassware under an atmosphere of Ar or N_2. All solvents were dried and distilled according to standard procedures. All organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated with a rotary evaporator under reduced pressure.

1,5-Benzodithiepan-3-one (2). A solution of 1,3-dichloroacetone (10.3 g, 81.4 mmol) in CH_2Cl_2 (100 mL) was added to a solution of 1,2-benzenedithiol (10.5 g, 74.0 mmol) and DMAP (19.9 g, 162 mmol) in CH_2Cl_2 (750 mL) with stirring at −30 °C under N_2. After 5 min at −30 °C, the reaction was quenched with 1 N HCl and the organic layer was washed with water and brine prior to drying and solvent evaporation. The residue was chromatographed on silica gel with hexane−AcOEt (1:1) to give **2** (11.1 g, 76%) as a colorless powder. Mp: 76.0−77.0 °C (hexane−AcOEt). ^{1}H NMR δ: 3.60 (s, 4H), 7.28 (dd, 2H, J = 6.0, 3.4 Hz), 7.68 (dd, 2H, J = 6.0, 3.4 Hz). ^{13}C NMR δ: 41.9 (2C), 128.7 (2C), 133.5 (2C), 138.6 (2C), 202.9. IR 1713, 1680. MS *m*/*z* (%): 196 (M^+, 65.7), 153 (100). Anal. Calcd for $C_9H_8OS_2$: C, 55.07; H, 4.11; S, 32.67. Found: C, 55.05; H, 4.11; S, 32.62.

(4′*R*,5′*R*)-Spiro[1,5-benzodithiepane-3,2′-[4,5]diethoxycarbonyl[1,3]dioxolane] (3). Trimethylsilyl trifluoromethanesulfonate (4.92 mL, 25.5 mmol) was added slowly to a solution of **2** (10.0 g, 50.9 mmol) and (+)-diethyl tartrate bis-trimethylsilyl ether (18.8 g, 53.5 mmol) in CH_2Cl_2 (500 mL) with stirring at rt under N_2. The whole was refluxed for 1 h. After cooling, the mixture was partitioned between CH_2Cl_2 and saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water and brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with hexane−AcOEt (5:1) to give **3** (19.0 g, 97%) as a colorless powder. Mp: 74.5−75.0 °C (hexane−AcOEt). $[\alpha]^{25}_D$ −21.6 (*c* 1.01, $CHCl_3$). ^{1}H NMR δ: 1.34 (t, 6H, J = 7.3 Hz), 3.15 (br s, 4H), 4.27−4.33 (m, 4H), 4.91 (s, 2H), 7.18−7.20 (m, 2H), 7.59 (br s, 2H). ^{13}C NMR δ: 14.0 (2C), 40.5 (2C), 62.1 (2C), 78.0 (2C), 114.1, 128.0 (2C), 133.3 (2C), 139.7 (2C), 169.3 (2C). IR 1755, 1739. MS *m*/*z* (%): 384 (M^+, 8.7), 154 (100). Anal. Calcd for $C_{17}H_{20}O_6S_2$: C, 53.11; H, 5.24; S, 16.68. Found: C, 52.88; H, 5.17; S, 16.61.

(1*R*,4′*R*,5′*R*)- and (1*S*,4′*R*,5′*R*)-Spiro[1,5-benzodithiepane-3,2′-[4,5]diethoxycarbonyl-[1,3]dioxolane] 1-Oxide (4a and 4b). *m*-CPBA (8.11 g, 37.6 mmol) was added to a solution of **3** (14.5 g, 37.6 mmol) in CH_2Cl_2 (350 mL) with stirring at rt, and the whole was stirred at rt for 2 h. The mixture was washed with saturated $NaHCO_3$, water, and brine prior to drying and solvent evaporation. The residue was chromatographed on silica gel with hexane−AcOEt (1:1) to give **4a** (6.76 g, 45%) and **4b** (7.79 g, 52%) each as a colorless powder. **4a** (less polar): mp 113.5−114.0 °C (hexane−AcOEt). $[\alpha]^{28}_D$ +82.6 (*c* 1.11, $CHCl_3$). ^{1}H NMR δ: 1.34 (t, 3H, J = 7.3 Hz), 1.36 (t, 3H, J = 7.3 Hz), 2.58 (d, 1H, J = 15.4 Hz), 3.16 (dd, 1H, J = 15.4, 2.6 Hz), 3.33 (d, 1H, J = 12.8 Hz), 3.56 (dd, 1H, J = 12.8, 2.6 Hz), 4.27−4.35 (m, 4H), 4.90 (d, 1H, J = 3.4 Hz), 5.08 (d, 1H, J = 3.4 Hz), 7.44−7.47 (m, 1H), 7.63−7.66 (m, 2H), 7.90 (d, 1H, J = 7.7 Hz). ^{13}C NMR δ: 14.1 (2C), 42.3, 62.4 (2C), 64.8, 78.2, 78.5, 111.8, 124.8, 130.2, 130.3, 130.6,

(26) The absolute configurations of the benzyl ethers **8a-Bn**, **8c**, and **8e**−**f** were established by Mosher's method after removal of the chiral auxiliary with 10% HCl followed by conversion into the MTPA esters. Those of the acetates **8a-Ac** and **8b** were determined by Mosher's method after converting the alkoxides from **7a** and **7b** into the corresponding MTPA esters. The stereochemistry of **8d** was assumed by analogy with others: Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543−2549; *J. Am. Chem. Soc.* **1973**, *95*, 512−519.

134.9, 151.4, 168.7, 169.2. IR 1757, 1740, 1059. MS *m*/*z* (%): 400 (M^+, 3.9), 243 (100). Anal. Calcd for $C_{17}H_{20}O_7S_2$: C, 50.99; H, 5.03; S, 16.01. Found: C, 50.98; H, 4.96; S, 15.85. **4b** (more polar): mp 106.0−107.0 °C (hexane−AcOEt). $[\alpha]^{27}_D$ −161.3 (*c* 1.01, $CHCl_3$). ^{1}H NMR δ 1.33 (t, 3H, J = 7.1 Hz), 1.44 (t, 3H, J = 7.1 Hz), 2.67 (d, 1H, J = 15.0 Hz), 3.22 (dd, 1H, J = 15.0, 2.6 Hz), 3.27 (d, 1H, J = 12.8 Hz), 3.48 (dd, 1H, J = 12.8, 2.6 Hz), 4.29 (q, 2H, J = 7.1 Hz), 4.39−4.43 (m, 2H), 4.97 (d, 1H, J = 4.3 Hz), 4.99 (d, 1H, J = 4.3 Hz), 7.44−7.48 (m, 1H), 7.64−7.67 (m, 2H), 7.90 (d, 1H, J = 6.9 Hz). ^{13}C NMR δ: 14.1 (2C), 42.5, 62.4, 62.9, 64.4, 78.0, 78.7, 111.6, 124.7, 130.0, 130.3, 130.7, 135.1, 151.7, 168.9, 169.2. IR 1753, 1736, 1061. MS *m*/*z* (%): 400 (M^+, 4.7), 243 (100). Anal. Calcd for $C_{17}H_{20}O_7S_2$: C, 50.99; H, 5.03; S, 16.01. Found: C, 50.96; H, 4.97; S, 15.96.

The colorless needle crystals of racemic **4a** were grown from a hexane−AcOEt solution. The crystals were suitable for X-ray crystallographic analysis, and their dimensions were 0.2 × 0.2 × 0.3 mm^3. Crystallographic data of **4a** are as follows: $C_{17}H_{20}O_7S_2$, MW = 400.46, monoclinic, space group $P2_1$ with the cell dimensions a = 5.427(2) Å, b = 15.858(1) Å, c = 11.021(1) Å, β = 95.82°(2), V = 944(1) A^3, Z = 2, density(calcd) = 1.41 g cm^{-3}, F(000) = 420, λ = 1.5418 Å, T = 293 K, μ(Cu Kα) = 2.829 cm^{-1}. Intensity data were collected on a Rigaku AFC5R diffractometer using monochromated Cu Kα radiation. The data were obtained up to 0.89 Å resolution. The 2θ value was 120°; 1643 unique reflections were observed. The 1507 reflections with $I > 3.00\sigma(I)$ were used in refinement: the final R value was 7.06%.

(*R*)-1,5-Benzodithiepan-3-one 1-Oxide [(*R*)-5]. KHMDS (0.5 M toluene solution, 0.310 mL, 0.155 mmol) was added dropwise to a solution of **4a** (41.4 mg, 0.103 mmol) in THF (4.0 mL) with stirring at −78 °C under N_2. After 15 min, the reaction was quenched with saturated NH_4Cl and the resulting mixture was extracted with AcOEt. The extracts were washed with water and brine prior to drying and solvent evaporation. The residue was chromatographed on silica gel with hexane−AcOEt (3:2) to give (*R*)-**5** (18.3 mg, 83%) as a colorless powder. Mp: 135.0−136.0 °C (hexane−AcOEt). $[\alpha]^{27}_D$ +24.1 (*c* 0.94, $CHCl_3$). ^{1}H NMR δ: 3.29 (d, 1H, J = 13.7 H), 3.45 (dd, 1H, J = 13.7, 1.7 Hz), 3.76 (d, 1H, J = 11.1 Hz), 4.38 (dd, 1H, J = 11.1, 1.7 Hz), 7.54 (dt, 1H, J = 7.7, 1.7 Hz), 7.67 (d, 1H, J = 7.7 Hz), 7.72 (dt, 1H, J = 7.7, 1.7 Hz), 7.96 (dd, 1H, J = 7.7, 1.7 Hz). ^{13}C NMR δ: 45.7, 68.3, 126.3, 129.3, 131.2, 131.6, 135.5, 150.3, 191.3. IR 1701, 1605. MS *m*/*z* (%): 212 (M^+, 14.3), 153 (36.9), 140 (100). HRMS calcd for $C_9H_8O_2S_2$: 211.9966. Found: 211.9974.

(*S*)-1,5-Benzodithiepan-3-one 1-Oxide [(*S*)-5]. Using the procedure for (*R*)-**5** from **4a**, **4b** (5.86 g, 14.6 mmol) was converted into (*S*)-**5** (2.76 g, 89%). Mp: 138.5−139.0 °C (hexane−AcOEt). $[\alpha]^{30}_D$ −24.6 (*c* 1.00, $CHCl_3$). Anal. Calcd for $C_9H_8O_2S_2$: C, 50.92; H, 3.80; S, 30.21. Found: C, 50.82; H, 3.73; S, 30.06.

(1*R*,5*R*)-1,5-Benzodithiepane-3-one 1,5-Dioxide [(*R*,*R*)-1]. Ozone was passed through (*R*)-**5** (950 mg, 4.16 mmol) absorbed on silica gel (20 g) at −78 °C for 15 min. Then, the whole was allowed to stand at −20 °C for 45 min. After the protocol was repeated five times, the excess ozone was removed by blowing an N_2 stream through the solution. The mixture was packed on a chromatography column and eluted with hexane−AcOEt (2:1) to give (*R*,*R*)-**1** (475 mg, 47%) and (*R*,*S*)-**1** (154 mg, 15%), each as a colorless powder. (*R*,*R*)-**1**: mp 195.0−196.0 °C (dec) (hexane−AcOEt). $[\alpha]^{25}_D$ −100.3 (*c* 0.29, $CHCl_3$). ^{1}H NMR δ: 4.03 (d, 2H, J = 12.0 Hz), 4.31 (d, 2H, J = 12.0 Hz), 7.74−7.78 (m, 2H), 7.98−8.02 (m, 2H). ^{13}C NMR δ: 68.2 (2C), 126.7 (2C), 132.4 (2C), 143.2 (2C), 189.3. IR 1697, 1064. MS *m*/*z* (%): 228 (M^+, 12.1), 121 (100). Anal. Calcd for $C_9H_8O_3S_2$: C, 47.35; H, 3.53; S, 28.09. Found: C, 47.06; H, 3.56; S, 27.87. (*R*,*S*)-**1**: colorless powder; mp 221.5−222.5 °C (AcOEt−MeOH). ^{1}H NMR δ: 3.76 (d, 2H, J = 11.5 Hz), 4.48 (d, 2H, J = 11.5 Hz), 7.84−7.86 (m, 2H), 8.12−8.14 (m, 2H). ^{13}C NMR δ: 69.6 (2C), 123.6 (2C), 132.5 (2C), 139.7 (2C), 187.0. IR 1701, 1076. MS *m*/*z* (%): 228 (M^+, 28.4), 108 (100). HRMS calcd for $C_9H_8O_3S_2$: 227.9915. Found: 227.9915.

The colorless prism crystals of racemic (*R*,*R*)-**1** were grown from a hexane−AcOEt solution. The crystals were suitable for X-ray crystallographic analysis, and their dimensions were 0.5 × 0.5 × 1.0 mm^3. Crystallographic data of (*R*,*R*)-**1** are as follows: $C_9H_8O_3S_2$, MW = 228.28, orthorhombic, space group $P2_12_12_1$ with the cell dimensions a = 8.16(1) Å, b = 16.448(6) Å, c = 7.130(5) Å, V = 957(1) A^3, Z = 4, density(calcd) = 1.58 g cm^{-3}, F(000) = 472, λ = 1.5418 Å, T = 293 K, μ(Cu Kα) = 4.804 cm^{-1}. Intensity data were collected on a Rigaku AFC7R diffractometer using monochromated Cu Kα radiation. The data were obtained up to 0.86 Å resolution. The 2θ value was 125°; 976 unique reflections were observed. The 960 reflections with $I > 3.00\sigma(I)$ were used in refinement: the final R value was 8.32%.

(1*S*,5*S*)-1,5-Benzodithiepane-3-one 1,5-Dioxide [(*S*,*S*)-1]. Using the procedure for (*R*,*R*)-**1** from (*R*)-**5**, (*S*)-**5** (1.31 g, 6.18 mmol) was converted into (*S*,*S*)-**1** (641 mg, 46%) as a colorless powder along with (*R*,*S*)-**1** (*meso*) (263 mg, 19%) and (*S*)-**5** (86 mg, 7%). Mp: 194.0−195.0 °C (dec) (hexane−AcOEt). $[\alpha]^{30}_D$ +98.5 (*c* 0.34, $CHCl_3$). Anal. Calcd for $C_9H_8O_3S_2$: C, 47.35; H, 3.53; S, 28.09. Found: C, 47.23; H, 3.53; S, 27.89.

Asymmetric Oxidation of 1,2-Benzodithiepan-3-one (2) (Table 1). Using Davis' Reagent (Entry 1). A solution of [(8,8-dichlorocamphoryl)sulfonyl]oxaziridine (77.9 mg, 0.261 mmol) in CH_2Cl_2 (3.0 mL) was added to a solution of **3** (51.3 mg, 0.261 mmol) in CH_2Cl_2 (5.0 mL) with stirring at −20 °C under N_2. The stirring was continued at rt for 3 d. Saturated $NaHCO_3$ was added to the mixture. After 1 h, the mixture was extracted with $CHCl_3$ and the extract was washed with brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with hexane−AcOEt (1:1) to give (*S*)-**5** [48 mg, 87%, $[\alpha]^{25}_D$ −6.7 (*c* 0.93, $CHCl_3$), 27% ee] as a colorless powder.

Using a Modified Sharpless Epoxidation Reagent (General Procedure) (Entry 6). A solution of **2** (101.2 mg, 0.516 mmol) in CH_2Cl_2 (2.0 mL) was added to a mixture of Ti(O-*i*-Pr)$_4$ (1 M in CH_2Cl_2) (0.516 mL, 0.516 mmol) and (+)-diethyl tartrate (0.353 mL, 2.06 mmol) in CH_2Cl_2 (5.0 mL) with stirring at rt. Cumene hydroperoxide (0.190 mL, 1.03 mmol) was slowly added to the mixture, and stirring was continued at −20 °C for 2 d. The reaction was quenched with a 5% aqueous Na_2SO_3 solution, and the whole was stirred for 30 min at rt. The mixture was extracted with $CHCl_3$. After the addition of 10% hydrochloric acid, the mixture was washed with 5% Na_2SO_3 and saturated $NaHCO_3$ prior to drying and solvent evaporation. The crude was chromatographed on silica gel using hexane−AcOEt (1:1) to give (*R*)-**5** [61.4 mg, 56%, $[\alpha]^{28}_D$ +23.4 (*c* 1.04, $CHCl_3$), 97% ee] as a colorless powder.

General Procedure for Acetalization. 2,6-Lutidine (32 μL, 0.27 mmol) was added to a solution of (1*R*,5*R*)-**1** (20.7 mg, 0.0907 mmol) and *cis*-cyclohexane-1,2-diol (31.6 mg, 0.272 mmol) in CH_2Cl_2 (3.5 mL) with stirring at 0 °C under N_2. After 5 min, trimethylsilyl trifluoromethanesulfonate (70 μL, 0.36 mmol) was added dropwise. Stirring was continued at 0 °C for 4 h. The reaction was quenched with saturated $NaHCO_3$, and the mixture was extracted with CH_2Cl_2. The extracts were washed with brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with AcOEt to give **8a** (25.4 mg, 86%) as a colorless powder.

(1*R*,5*R*)-Spiro[1,5-benzodithiepane-3,8′-[7,9]dioxabicyclo[4.3.0]nonane] 1,5-Dioxide (7a). Yield: 86% (colorless powder). Mp: 196.0−198.0 °C (acetone). $[\alpha]^{20}_D$ +164.7 (*c* 0.45, MeOH). ^{1}H NMR δ: 1.25−1.30 (m, 2H), 1.45−1.54 (m, 2H), 1.66−1.78 (m, 4H), 3.88 (d, 1H, J = 2.6 Hz), 3.40 (d, 1H, J = 2.6 Hz), 3.55 (d, 1H, J = 13.7 Hz), 3.61 (d, 1H, J = 13.7 Hz), 4.19−4.20 (m, 2H), 7.64 (dt, 1H, J = 7.7, 1.7 Hz), 7.68 (dt, 1H, J = 7.7, 1.7 Hz), 7.87 (dd, 1H, J = 7.7, 1.7 Hz), 7.96 (d, 1H, J = 7.7 Hz). ^{13}C NMR δ: 20.5, 20.5, 27.9, 28.2, 61.2, 63.1, 74.5, 74.6, 104.4, 126.2, 126.5, 131.2, 131.8, 142.2, 143.9. IR 1059. MS *m*/*z* (%): 326 (M^+, 2.0), 180 (27.6), 153 (28.6), 140 (49.6), 81 (100). Anal. Calcd for $C_{15}H_{18}O_4S_2$: C, 55.19; H, 5.56; S, 19.65. Found: C, 54.89; H, 5.45; S, 19.34.

(1*R*,5*R*)-Spiro[1,5-benzodithiepane-3,3′-[2,4]dioxabicyclo[3.3.0]octane] 1,5-Dioxide (7b). Yield: 83% (colorless powder). Mp: 207.0−208.5 °C (acetone−MeOH). $[\alpha]^{25}_D$ +198.9 (*c* 0.38, MeOH). ^{1}H NMR δ: 1.39−1.49 (m, 2H), 1.57−1.64 (m, 2H), 1.77−1.81 (m, 1H), 1.92−1.96 (m, 1H), 3.16 (d, 1H, J =

15.0 Hz), 3.29 (d, 1H, J = 13.7 Hz), 3.56 (d, 1H, J = 15.0 Hz), 3.64 (d, 1H, J = 13.7 Hz), 4.69 (t, 1H, J = 5.6 Hz), 4.77 (t, 1H, J = 5.6 Hz), 7.62 (t, 1H, J = 7.7 Hz), 7.71 (dt, 1H, J = 7.7, 1.7 Hz), 7.80 (d, 1H, J = 7.7 Hz), 8.03 (d, 1H, J = 7.7 Hz). ^{13}C NMR δ: 22.2, 33.0, 33.1, 59.9, 60.3, 81.7, 82.0, 105.6, 126.3, 126.4, 130.9, 132.2, 140.9, 144.9. IR 1067. MS m/z (%): 312 (M^+, 2.0), 126 (60), 67 (100). Anal. Calcd for $C_{14}H_{16}O_4S_2$: C, 53.83; H, 5.16; S, 20.53. Found: C, 53.66; H, 5.09; S, 20.45.

(1*S*,5*S*)-Spiro[1,5-benzodithiepane-3,8′-[7,9]dioxabicyclo[4.3.0]non-3-ene] 1,5-Dioxide (7c). Yield: 89% (colorless powder). Mp: 210.5−212.0 °C (hexane−AcOEt). $[\alpha]^{26}_D$ −226.5 (*c* 0.50, $CHCl_3$). ^{1}H NMR δ: 2.12−2.22 (m, 3H), 2.30−2.35 (m, 1H), 3.19 (d, 1H, J = 14.0 Hz), 3.33 (d, 1H, J = 13.4 Hz), 3.54 (d, 1H, J = 14.0 Hz), 3.61 (d, 1H, J = 13.4 Hz), 4.48−4.57 (m, 2H), 5.74−5.79 (m, 2H), 7.62 (t, 1H, J = 7.3 Hz), 7.70 (t, 1H, J = 7.3 Hz), 7.81 (d, 1H, J = 7.9 Hz), 8.01 (d, 1H, J = 7.3 Hz). ^{13}C NMR δ: 27.6, 27.8, 60.9, 61.2, 74.2, 74.3, 104.5, 125.4, 125.5, 126.3, 126.3, 131.0, 131.9, 141.5, 144.5. IR 1059. MS m/z (%): 324 (M^+, 87), 79 (100). Anal. Calcd for $C_{15}H_{16}O_4S_2$: C, 55.53; H, 4.97; S, 19.77. Found: C, 55.34; H, 4.97; S, 19.49.

The colorless needle crystals of racemic **7c** were grown from a hexane−AcOEt solution. The crystals were suitable for X-ray crystallographic analysis, and their dimensions were 0.6 × 0.4 × 0.3 mm^3. Crystallographic data of **7c** are as follows: $C_{15}H_{16}O_4S_2$, MW = 324.40, triclinic, space group P-1 with cell dimensions a = 11.979(2) Å, b = 12.001(1) Å, c = 5.250(4) Å, α = 99.45°(2), β = 94.78°(1), γ = 102.60(1), V = 720.9(5) A^3, Z = 2, density(calcd) = 1.49 g cm^{-3}, $F(000)$ = 340, λ = 1.5418 Å, T = 293 K, μ(Cu Kα) = 4.804 cm^{-1}. Intensity data were collected on a Rigaku AFC5R diffractometer using monochromated Cu Kα radiation. The data were obtained up to 0.86 Å resolution. The 2θ value was 125°; 2312 unique reflections were observed. The 2035 reflections with $I > 2.00\sigma(I)$ were used in refinement: the final R value was 10.57%.

(1*R*,5*R*)-Spiro[1,5-benzodithiepane-3,10′-[9,11]dioxabicyclo[6.3.0]undeca-4-ene] 1,5-Dioxide (7d). Yield: 90% (colorless powder). Mp: 280.5−282.0 °C (MeOH). $[\alpha]^{26}_D$ +205.4 (*c* 0.52, $CHCl_3$). ^{1}H NMR δ: 1.79−1.85 (m, 1H), 1.89−1.94 (m, 1H), 1.98−2.06 (m, 4H), 2.43−2.48 (m, 2H), 3.31 (d, 1H, J = 13.9 Hz), 3.32 (d, 1H, J = 13.9 Hz), 3.52 (d, 1H, J = 13.9 Hz), 3.60 (d, 1H, J = 13.9 Hz), 4.29−4.32 (m, 2H), 5.56 (s, 2H), 7.62 (t, 1H, J = 6.8 Hz), 7.68 (d, 1H, J = 7.7 Hz), 7.83 (d, 1H, J = 6.8 Hz), 7.97 (d, 1H, J = 7.7 Hz). ^{13}C NMR δ: 23.3 (2C), 28.0, 28.1, 61.2, 62.8, 79.2 (2C), 102.9, 126.2, 126.4, 128.9 (2C), 131.0, 131.8, 141.8, 144.0. IR 1063. MS m/z (%): 352 (M^+, 28), 107 (82), 79 (100). HRMS calcd for $C_{17}H_{20}O_4S_2$: 352.0803. Found: 352.0791.

(1*R*,5*R*)-Spiro[1,5-benzodithiepane-3,3′-[2,4,8]trioxabicyclo[3.3.0]octane] 1,5-Dioxide (7e). $CHCl_3$ was used was a solvent. Yield: 80% (colorless powder). Mp: 233.0−233.5 °C (hexane−AcOEt). $[\alpha]^{26}_D$ +159.7 (*c* 0.28, $CHCl_3$).^{1}H NMR δ: 3.31 (d, 1H, J = 13.4 Hz), 3.35−3.38 (m, 2H), 3.41 (dd, 1H, J = 11.0, 3.7 Hz), 3.64 (d, 1H, J = 13.4 Hz), 3.70 (d, 1H, J = 14.0 Hz), 3.94 (d, 1H, J = 11.0 Hz), 4.10 (d, 1H, J = 11.0 Hz), 4.86 (dd, 1H, J = 6.1, 3.7 Hz), 4.93 (dd, 1H, J = 5.5, 4.0 Hz), 7.63 (t, 1H, J = 7.6 Hz), 7.71 (t, 1H, J = 7.6 Hz), 7.81 (d, 1H, J = 7.3 Hz), 8.03 (d, 1H, J = 7.3 Hz). ^{13}C NMR δ: 59.9, 61.9, 73.4, 73.6, 81.7, 81.8, 108.2, 126.2, 126.3, 131.1, 132.0, 141.4, 144.2. IR 1643, 1063. MS (FAB) m/z: 315 $(M+H)^+$. HRMS (FAB) calcd for $C_{13}H_{14}O_5S_2 + H^+$: 315.0361. Found: 315.0368.

(1*S*,5*S*)-Spiro[1,5-benzodithiepane-3,7′-[3′-(benzyloxycarbonyl)-[3]aza-[6,8]dioxabicyclo[3.3.0]octane]] 1,5-Dioxide (7f). Trimethylsilyl trifluoromethanesulfonate (74 μL, 0.38 mmol) was added to a solution of (1*S*,5*S*)-**1** (87.0 mg, 0.38 mmol) and *cis*-1-(benzyloxycarbonyl)pyrrolidine-3,4-diol monotrimethylsilyl ether (300 mg, 1.15 mmol) in $CHCl_3$ (1.74 mL) with stirring at 0 °C under N_2. Stirring was continued at 4 °C for 6 h. The reaction was quenched with saturated $NaHCO_3$, and the mixture was extracted with $CHCl_3$. The extracts were washed with brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with AcOEt to give **7f** (152 mg, 89%, 1:1 mixture of amide bond rotamers) as a colorless oil. $[\alpha]^{32}_D$ −135.6 (*c* 0.89, $CHCl_3$). ^{1}H NMR δ: 3.04 (d, 1H, J = 14.0 Hz), 3.22−3.25 (m, 2H), 3.33 (dd, 1H, J = 12.8, 4.3 Hz), 3.51−3.53 (m, 1H), 3.73 (d, 1H, J = 12.2 Hz), 3.83 (br s, 1H), 3.91 (d, 1H, J = 13.4 Hz), 4.78 (br s, 1H), 4.86 (t, 1H, J = 5.2 Hz), 5.13 (s, 2H), 7.32−7.39 (m, 5H), 7.60 (t, 1H, J = 7.6 Hz), 7.71−7.74 (m, 2H), 8.06 (br s, 1H). ^{13}C NMR δ: 51.6, 51.9, 59.4 (1/2C), 60.4 (1/2C), 61.0 (1/2C), 62.2 (1/2C), 67.3, 79.6, 80.2, 107.9, 126.3 (2C), 128.1 (2C), 128.2, 128.5 (2C), 130.9, 132.4, 136.3, 139.6 (1/2C), 140.8 (1/2C), 144.6 (1/2C), 145.5 (1/2C), 155.0. IR 1703, 1063. MS m/z (%): 447 (M^+, 0.9), 149 (100). HRMS calcd for $C_{21}H_{21}NO_6S_2$: 447.0810. Found: 447.0816.

General Procedure of Acetal Fission. Method A: (1*R*,5*R*)-3-[[(1*R*,2*S*)-2-(Acetoxy)cyclohexyl]oxy]-4*H*-1,5-benzodithiepine 1,5-Dioxide (8a-Ac). KHMDS (0.5 M toluene solution) (0.24 mL, 0.119 mmol) was added to a solution of acetal **7a** (13.0 mg, 0.039 mmol) and 18-crown-6 (31.6 mg, 0.119 mmol) in THF (4 mL) with stirring at −78 °C under N_2. After 15 min, acetic anhydride (23.0 μL, 0.120 mmol) was added and the mixture was poured onto saturated NH_4Cl. The aqueous layer was extracted with AcOEt, and the extracts were washed with saturated $NaHCO_3$, water, and brine prior to drying and solvent evaporation. Acetic anhydride (11 μL, 0.12 mmol) was added dropwise to the mixture of the crude and DMAP (13.5 mg, 0.119 mmol) in CH_2Cl_2 (1 mL) with stirring at rt, and the whole was stirred at rt for 10 min. After the addition of water, the mixture was extracted with CH_2Cl_2. The extracts were washed with brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with AcOEt to give **8a-Ac** (13.4 mg, 91%) as a colorless oil. $[\alpha]^{27}_D$ −94.1 (*c* 0.75, $CHCl_3$). ^{1}H NMR δ: 1.37−1.43 (m, 2H), 1.53−1.68 (m, 4H), 1.82−1.85 (m, 1H), 1.90−1.92 (m, 1H), 1.95 (s, 3H), 4.09 (d, 1H, J = 15.8 Hz), 4.29−4.31 (m, 1H), 4.36 (d, 1H, J = 15.8 Hz), 4.91−4.94 (m, 1H), 5.87 (s, 1H), 7.63 (t, 1H, J = 7.7 Hz), 7.69 (t, 1H, J = 7.7 Hz), 7.86 (d, 1H, J = 7.7 Hz), 8.00 (dd, 1H, J = 7.7, 1.7 Hz). ^{13}C NMR δ: 20.9, 21.0, 21.8, 26.7, 27.1, 56.5, 70.8, 75.9, 109.6, 125.2, 129.1, 131.5, 131.9, 141.7, 144.7, 152.7, 170.3. IR 1736, 1059. MS m/z (%): 368 (M^+, 1.5), 99 (100), 81 (82). HRMS calcd for $C_{17}H_{20}O_5S_2$: 368.0750. Found: 368.0739.

Method B: (1*R*,5*R*)-3-[[(1*R*,2*S*)-2-(Benzyloxy)cyclohexyl]oxy]-4*H*-1,5-benzodithiepine 1,5-Dioxide (8a-Bn). KHMDS (0.5 M toluene solution) (0.206 mL, 0.103 mmol) was added to a solution of acetal **7a** (11.2 mg, 0.0343 mmol) and 18-crown-6 (27.2 mg, 0.103 mmol) in THF (3.5 mL) with stirring at −78 °C under N_2. After 5 min, benzyl bromide (4.1 μL, 0.034 mmol) was added to the mixture, and the whole was stirred for 15 min at −78 °C. The reaction was quenched with saturated NH_4Cl, and the mixture was extracted with AcOEt. The extracts were washed with water and brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with AcOEt to give **8a-Bn** (13.2 mg, 92%) as a colorless oil. $[\alpha]^{29}_D$ −44.0 (*c* 1.11, $CHCl_3$). ^{1}H NMR δ: 1.23−1.34 (m, 2H), 1.45−1.56 (m, 3H), 1.65−1.71 (m, 1H), 1.82−1.89 (m, 1H), 1.90−1.96 (m, 1H), 3.60 (dt, 1H, J = 7.9, 3.1 Hz), 4.12 (d, 1H, J = 15.6 Hz), 4.18−4.20 (m, 1H), 4.25 (d, 1H, J = 15.6 Hz), 4.45 (d, 1H, J = 12.5 Hz), 4.56 (d, 1H, J = 12.5 Hz), 5.81 (s, 1H), 7.24−7.32 (m, 5H), 7.63 (dt, 1H, J = 7.6, 1.2 Hz), 7.68 (dt, 1H, J = 7.6, 1.2 Hz), 7.87 (dd, 1H, J = 7.3, 1.2 Hz), 7.97 (dd, 1H, J = 7.3, 1.2 Hz). ^{13}C NMR δ: 21.4, 21.8, 26.4, 27.5, 56.6, 70.9, 75.2, 77.7, 110.1, 125.1, 127.5 (2C), 127.6, 128.4 (2C), 129.3, 131.5, 131.7, 138.4, 141.7, 145.0, 152.5. IR 1606, 1059. MS (FAB) m/z: 417 $(M + H)^+$. HRMS (FAB) calcd for $C_{22}H_{24}O_4S_2 + H^+$: 417.1195. Found: 417.1197.

(1*R*,5*R*)-3-[[(1*R*,2*S*)-2-(Acetoxy)cyclopentyl]oxy]-4*H*-1,5-benzodithiepine 1,5-Dioxide (8b). Yield: 78% (colorlss oil). $[\alpha]^{30}_D$ −104.6 (*c* 0.50, $CHCl_3$). ^{1}H NMR δ: 1.56−1.61 (m, 1H), 1.78−1.88 (m, 3H), 1.91 (s, 3H), 1.94−2.00 (m, 2H), 3.94 (d, 1H, J = 15.9 Hz), 4.41 (d, 1H, J = 15.9 Hz), 4.48−4.50 (m, 1H), 5.00−5.04 (m, 1H), 5.88 (s, 1H), 7.62 (t, 1H, J = 7.6 Hz), 7.70 (t, 1H, J = 7.6 Hz), 7.82 (d, 1H, J = 7.3 Hz), 8.03 (d, 1H, J = 7.3 Hz). ^{13}C NMR δ: 19.1, 20.8, 28.1, 28.5, 56.5, 73.9, 78.4, 108.6, 125.4, 128.6, 131.4, 132.0, 142.0, 144.4, 153.5, 170.5. IR 1732, 1597, 1061. MS m/z (%): 354 (M^+, 2.0), 156 (34), 85 (100). HRMS calcd for $C_{16}H_{18}O_5S_2$: 354.0596. Found: 354.0597.

(1*S*,5*S*)-3-[[(1*S*,6*R*)-6-(Benzyloxy)-3-cyclohexen-1-yl]oxy]-4*H*-1,5-benzodithiepine 1,5-Dioxide (8c). Yield: 85% (color-

less oil). $[\alpha]^{25}_D$ +74.3 (*c* 0.88, $CHCl_3$). ^1H NMR δ: 2.25−2.46 (m, 4H), 3.77−3.79 (m, 1H), 4.06 (d, 1H, J = 15.9 Hz), 4.23 (d, 1H, J = 15.9 Hz), 4.37−4.39 (m, 1H), 4.51 (d, 1H, J = 12.2 Hz), 4.60 (d, 1H, J = 12.7 Hz), 5.49−5.51 (m, 1H), 5.59−5.61 (m, 1H), 5.84 (s, 1H), 7.23−7.32 (m, 5H), 7.62−7.70 (m, 2H), 7.86 (d, 1H, J = 7.3 Hz), 7.97 (d, 1H, J = 7.9 Hz). ^{13}C NMR δ: 28.0, 28.7, 56.6, 71.3, 73.3, 75.5, 110.0, 122.9, 124.4, 125.3, 127.7 (2C), 127.9, 128.5 (2C), 129.1, 131.7, 131.9, 138.3, 141.8, 145.0, 152.8. IR 1597, 1059. MS (FAB) *m*/*z*: 415 $(M + H)^+$. HRMS (FAB) calcd for $C_{22}H_{22}O_4S_2 + H^+$: 415.1036. Found: 415.1044.

(1*R*,5*R*)-3-[[(1*R*,2*S*)-2-(Acetoxy)-5-cycloocten-1-yl]oxy]-4*H*-1,5-benzodithiepine 1,5-Dioxide (8d). Yield: 90% (colorless oil). $[\alpha]^{23}_D$ −9.8 (*c* 0.65, $CHCl_3$). ^1H NMR δ: 1.64−1.69 (m, 1H), 1.72−1.78 (m, 1H), 1.90−1.98 (m, 4H), 2.05 (s, 3H), 2.50−2.51 (m, 2H), 4.16 (d, 1H, J = 15.3 Hz), 4.28 (d, 1H, J = 15.3 Hz), 4.39 (dd, 1H, J = 7.0, 4.0 Hz), 5.16 (dd, 1H, J = 8.5, 3.7 Hz), 5.70−5.72 (m, 2H), 5.83 (s, 1H), 7.65 (dt, 1H, J = 7.3, 1.4 Hz), 7.69 (dt, 1H, J = 7.3, 1.4 Hz), 7.91 (dd, 1H, J = 7.3, 1.2 Hz), 7.97 (dd, 1H, J = 7.3, 1.2 Hz). ^{13}C NMR δ: 21.5, 23.1, 23.6, 28.3, 29.5, 56.1, 74.8, 77.2, 110.7, 125.2, 129.3, 129.8, 130.2, 131.6, 131.8, 141.4, 145.1, 152.0, 170.0. IR 1736, 1606, 1059. MS *m*/*z* (%): 394 (M^+, 2.8), 378 (3.5), 107 (100), 79 (97). HRMS calcd for $C_{19}H_{22}O_5S_2$: 394.0908. Found: 394.0885.

(1*R*,5*R*)-3-[[(3*R*,4*S*)-4-(Benzyloxy)tetrahydropyran-3-yl]oxy]-4*H*-1,5-benzodithiepine 1,5-Dioxide (8e). Yield: 71% (yellow oil). $[\alpha]^{30}_D$ −21.2 (*c* 0.44, $CHCl_3$). ^1H NMR δ: 3.76 (dd, 1H, J = 9.2, 6.19 Hz), 3.81 (dd, 1H, J = 10.4, 3.7 Hz), 3.93 (dd, 1H, J = 9.2, 6.1 Hz), 3.99 (dd, 1H, J = 9.8, 5.2 Hz), 4.09 (d, 1H, J = 16.5 Hz), 4.12−4.17 (m, 1H), 4.24 (d, 1H, J = 16.5 Hz), 4.46−4.52 (m, 3H), 5.72 (s, 1H), 7.24−7.33 (m, 5H), 7.65−7.69 (m, 2H), 7.92−7.94 (m, 2H). ^{13}C NMR δ: 55.1, 70.0, 70.2, 72.8, 76.2, 76.7, 110.8, 125.0, 127.8 (2C), 128.1, 128.5 (2C), 128.7, 131.7, 131.9, 137.0, 140.8, 145.5, 151.8. IR 1599, 1059. MS (FAB) *m*/*z*: 405 $(M + H)^+$. HRMS (FAB) calcd for $C_{20}H_{20}O_5S_2 + H^+$: 405.0830. Found: 405.0828.

(1*S*,5*S*)-3-[[(3*S*,4*R*)-4-(Benzyloxy)-1-(Benzyloxycarbonyl)pyrrolidine-3-yl]oxy]-4*H*-1,5-benzodithiepine 1,5-Dioxide (8f). Yield: 84% (colorless oil, 1:1 mixture of amide bond rotamers). $[\alpha]^{29}_D$ +12.2 (*c* 1.2, $CHCl_3$). ^1H NMR δ: 3.40−3.67 (m, 4H), 4.05 (d, 1H, J = 16.5 Hz), 4.08−4.11 (m, 1H), 4.19 (d, 1H, J = 16.5 Hz), 4.44−4.48 (m, 2H), 4.55 (t, 1H, J = 11.3 Hz), 5.06 (d, 1H, J = 12.2 Hz), 5.11 (d, 1H, J = 12.2 Hz), 5.72 (s, 1H), 7.24−7.35 (m, 10H), 7.65−7.69 (m, 2H), 7.89−7.94 (m, 2H). ^{13}C NMR δ: 47.7 (1/2C), 48.0 (1/2C), 48.1 (1/2C), 48.5 (1/2C), 54.9 (1/2C), 55.1 (1/2C), 67.2, 72.4 (1/2C), 72.5 (1/2C), 75.2 (1/2C), 76.02 (1/2C), 77.2, 111.0 (1/2C), 111.7 (1/2C), 125.0 (1/2C), 125.1 (1/2C), 127.8, 128.0, 128.1, 128.2, 128.5 (3C), 128.6 (3C), 129.0, 131.66 (1/2C), 131.74 (1/2C), 131.8 (1/2C), 132.0 (1/2C), 136.3 (1/2C), 136.9 (1/2C), 140.4, 145.4 (1/2C), 145.9 (1/2C), 150.7 (1/2C), 151.4 (1/2C), 154.5 (1/2C), 154.6 (1/2C), 178.6. IR 1705, 1603, 1061. MS (FAB) *m*/*z*: 538 $(M + H)^+$. HRMS (FAB) calcd for $C_{28}H_{27}O_6S_2 + H^+$: 538.1358. Found: 538.1380.

(1*S*,6*R*)-6-(Benzyloxy)-3-cyclohexen-1-ol (9). A drop of 10% HCl was added to a solution of **8d** (493 mg, 1.19 mmol) in acetone (12.0 mL) with stirring at rt. The stirring was continued for 20 min. The reaction was quenched with saturated $NaHCO_3$, and the mixture was extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine prior to drying and solvent evaporation. The crude was chromatographed on silica gel with hexane−AcOEt (1:3) to give **9** (240 mg, 99%) as a colorless oil along with (*S*,*S*)-**1** (220 mg, 81%) as a colorless powder. $[\alpha]^{27}_D$ −24.1 (*c* 1.13, $CHCl_3$). ^1H NMR δ: 2.16 (d, 1H, J = 4.9 Hz), 2.32−2.34 (m, 4H), 3.67−3.70 (m, 1H), 4.09−4.12 (m, 1H), 4.58 (d, 3H, J = 12.2 Hz), 4.65 (d, 3H, J = 12.2 Hz), 5.56−5.61 (m, 2H), 7.29−7.38 (m, 5H). ^{13}C NMR δ: 27.2, 31.6, 66.7, 70.3, 75.9, 123.6, 123.8, 127.6, 127.7, 128.4, 138.4. IR 3450. MS *m*/*z* (%): 204 (M^+, 16.5), 91 (100). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.26; H, 7.90.

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Supporting Information Available: The data (^1H, ^{13}C, IR, and MS) for **4a**, **4b**, (*S*)-**5**, (*S*,*S*)-**1**, **7c**, and **8c** and structural determination summaries and tables of X-ray structural data for **4a**, (*R*,*R*)-**1**, and (±)-**7c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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