Facile Optical Resolution of *tert*-Butanethiosulfinate by Molecular Complexation with (*R*)-BINOL and Study of Chiral Discrimination of the Diastereomeric Complexes

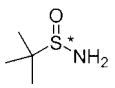
Jian Liao, Xiaoxia Sun, Xin Cui, Kaibei Yu, Jin Zhu, and Jingen Deng*[a]

Abstract: An important synthon, *tert*-butanethiosulfinate (**2**), has been effectively resolved by forming molecular complexes with (*R*)-2,2′-dihydroxy-1,1′-binaphthyl (BINOL, **3**) in high enantioselectivity (>99% *ee*). The present procedure represents the first example of the resolution of thiosulfinate. The mechanism of chiral discrimination is discussed in terms of molecular recognition based on IR and X-ray analyses of the diastereomeric complexes during the resolution. In the less-soluble complex, (*R*)-**3** and (*R*)-**2** self-assembled as a linear supramolecule; however, in the more-soluble complex, (*R*)-**3** and (*S*)-**2** formed a simple bimolecular complex by one stronger hydrogen bond. Hydrogen bonding is the major driving force for effective resolution.

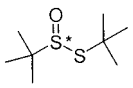
Keywords: (*R*)-BINOL · *tert*-butanethiosulfinate · molecular complex · molecular recognition · self-assembly

Introduction

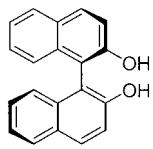
Chiral sulfoxides are useful synthons for the asymmetric synthesis of biologically active compounds,[1] while sulfinamides are increasingly utilized as versatile chiral nitrogen intermediates for the preparation of a range of chiral amines.[2] However, practical methods for the preparation of enantiopure sulfinamides are very few. During the past few years, the versatility of *tert*-butanesulfinamide (**1**) for the asymmetric synthesis of amines has been well documented,[3] so it is very important to develop a highly efficient method to prepare enantiopure **1**. In 1997, Ellman and co-workers developed an elegant method for the preparation of enantiopure (*R*)-**1** by means of catalytic asymmetric oxidation of di-*tert*-butyldisulfide followed by amidation of (*R*)-*tert*-butanethiosulfinate (**2**).[4] (*R*)-**1** has recently been synthesized by Senanayake and co-workers by the chemoselective ring-opening of enantiopure *N*-sulfonyl-1,2,3-oxathiazolidine-2-oxide agents.[5] In addition, Ellman's group also tried to obtain enantiopure **1** by resolving *rac*-**1**, unfortunately, no satisfactory results were given.[6] But this concept provides us with an alternative route to get enantiopure **1**, which might be obtained by resolution of its precursor *rac*-**2**. Over the past few years, our group[7] has also been engaged in the resolution of chiral sulfoxide synthons, alkyl pyridyl sulfoxides, and the chiral drugs, omeprazole and lansoprazole (proton-pump inhibitors), through molecular complexation with chiral host compounds.[8, 9] Herein, we would like to report the preparation of both enantiopure isomers of **2** by inclusion complexation with one enantiomer of the chiral host compound, (*R*)-2,2′-dihydroxy-1,1′-binaphthyl (BINOL, **3**) for the first time.



1



2



(*R*)-**3**

As is well known, the molecular recognition between host and guest molecules is directed by specific intermolecular forces (e.g., hydrogen bonding and second-order interactions), as well as by steric complementarity. It is important to elucidate the resolution mechanism in terms of molecular recognition between host and two enantiomers of guest in the solid state, especially by X-ray crystallographic analyses.

[a] Prof. Dr. J. Deng, Dr. J. Liao, X. Sun, X. Cui, Prof. K. Yu, Prof. J. Zhu
Union Laboratory of Asymmetric Synthesis
Chengdu Institute of Organic Chemistry
Chinese Academy of Sciences, Chengdu 610041 (China)
Fax: (+86) 28-8522-3978
E-mail: jgdeng@cioc.ac.cn

Supporting information for this article is available on the WWW under http://www.chemeurj.org or from the author: NMR and IR spectra of all compounds plus DSC analyses of the complexes.

 DOI: 10.1002/chem.200204653

To the best of our knowledge, relatively few reports have probed both crystal structures of the less- and more-soluble diastereomers of host–guest complexes to gain insight into the mechanism of chiral discrimination,[10] and furthermore, no example concerns the less- and more-soluble diastereomeric complexes of sulfoxides.[9] Herein, we will study the molecular recognition during resolution by X-ray crystallographic analysis, as well as IR spectroscopic analysis of the less-soluble molecular complex, which consists of (*R*)-**3** and (*R*)-**2**, and the more-soluble molecular complex, which consists of (*R*)-**3** and (*S*)-**2**.

Results and Discussion

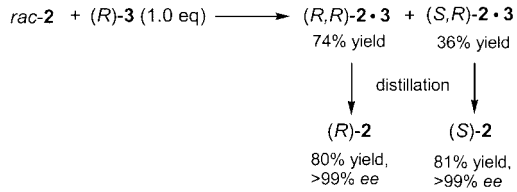
Inclusion crystallization has been used since the early 1980s to selectively and reversibly include chiral guest molecules into host lattices of chiral molecules.[8] To the best of our knowledge, successful resolution has been limited to the preparation of enantiopure aryl- or alkylsulfoxides to date.[8, 9] The only two other examples for chiral sulfur-containing compounds are the resolution of sulfoximines[8] and alkyl phenylsulfinates.[9e] Thus, we initially utilized chiral host (*S*,*S*)-(+)-*trans*-4,5-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxolane (TADDOL),[11] to resolve *rac*-**2**, which gave low resolving efficiency (<28% *ee*). Fortunately, while the readily available (*R*)-**3**[12] was used as chiral host,[13] successful resolution of *rac*-**2** was achieved. In order to improve the efficiency of the resolution, several kinds of solvents and their mixtures were examined, and ethanol was found to be an excellent solvent (Table 1, entry 7).

A typical resolution process is described as follows. (*R*)-**3** (17.34 g, 60.6 mmol) and *rac*-**2** (11.76 g, 60.6 mmol) were dissolved in ethanol (60 mL), and the mixture was kept at room temperature for 12 h. An inclusion complex, (*R*,*R*)-**2·3** in a 1:1 ratio was obtained as colorless crystals by filtration. After recrystallization from ethanol, the complex, (*R*,*R*)-**2·3** was heated in vacuo to give (*R*)-**2** by distillation (72 °C/40 Pa) with >99% *ee*. The filtrate was concentrated, and the 1:1 complex of (*S*,*R*)-**2·3** was obtained as colorless crystals. After twice being recrystallized from ethanol, the inclusion complex of (*S*,*R*)-**2·3** was also heated in vacuo to give (*S*)-**2** by distillation (64 °C/30 Pa) with >99% *ee* (Scheme 1). The host

Table 1. Resolution of *rac*-**2** with (*R*)-**3** in different solvents.[a]

	Solvent (*v*/*v*)	*ee* [%][b,c]	Yield [%][c,d]
1	toluene	86.1(73.9)	98.3(72.3)
2	acetone	91.7(41.3)	43.7(134.4)
3	acetone/hexane (1:2)	95.0(63.3)	58.3(132.6)
4	acetone/hexane (1:3)	76.3(70.5)	80.0(105.0)
5	butanone	92.1(55.7)	54.6(137.8)
6	butanone/hexane (1:3)	92.0(77.1)	77.3(109.2)
7	ethanol	91.7(85.3)	91.7(105.0)
8	ethanol/hexane (1:1)	88.2(76.8)	93.6(100.0)
9	*i*PrOH	78.0(88.4)	120.0(67.2)
10	*i*PrOH/hexane (2.5:1)	82.3(76.9)	113.1(63.9)

[a] Resolution with a 1:1 molar ratio of host (*R*)-**3** and guest *rac*-**2** on a scale of 2.5 mmol. [b] Enantiomeric excess of **2** was determined by chiral HPLC analysis (Chiral Pak AS column). [c] The value of the (*S*,*R*)-**2·3** complex is in parenthesis. [d] Yield based on half of the starting *rac*-**2**.



Scheme 1. The resolution of *rac*-**2** by inclusion crystallization. The yields are calculated on the basis of half of the starting *rac*-**2**.

(*R*)-**3** left after separation of **2** by distillation can be used again.

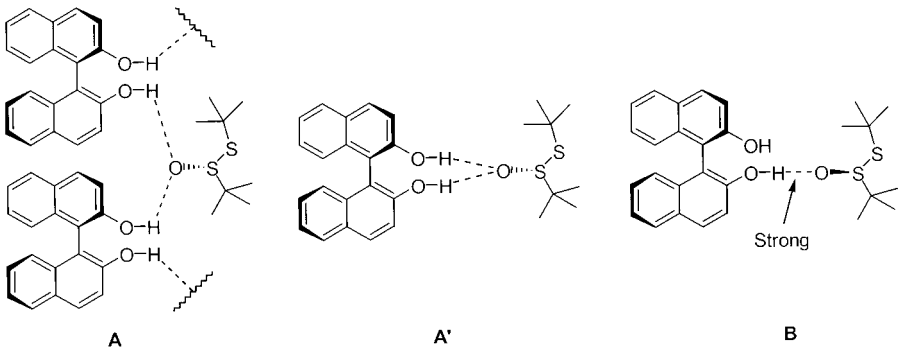
In our previous works,[7] we found that IR spectroscopic analysis is an effective approach to elucidate the interactions between host and guest molecules, because of the characteristic peaks between the hydrogen-bonded and free sulfoxides. In this work, we systematically studied the interactions between (*R*)-**3** and two enantiomers of **2** by IR spectroscopic analysis (Table 2).

Table 2. IR spectroscopic data of host and guest compounds and inclusion complexes.[a]

	Compound	$\tilde{\nu}_{OH}$ [cm^{-1}]	$\tilde{\nu}_{OH}$ [cm^{-1}]	$\tilde{\nu}_{S=O}$ [cm^{-1}]
1	(*R*)-**3**	3509(*s*)	3435(*s*)	
2	*rac*-**2**			1075
3	(*R*)-**2**			1075
4	(*S*)-**2**			1075
5	(*R*,*R*)-**2·3**		3324 (br s)	995
6	(S,R)-**2·3**	3534 (s)	3254 (br s)	1039

[a] Samples in nujol for entries 1, 5, and 6, and neat for entries 2, 3, and 4.

The IR spectrum of host (*R*)-**3** exhibits two sharp and strong hydroxyl absorption bands at 3509 cm^{-1} and 3435 cm^{-1} (Table 2, entry 1), and guest compound **2**, racemate and enantiomers, exhibits a strong sulfinyl absorption band at 1075 cm^{-1} (Table 2, entries 2, 3 and 4). Meanwhile, in the less-soluble complex (*R*,*R*)-**2·3**, the two original hydroxyl absorption bands of (*R*)-**3** disappear and a new absorption band appears at 3324 cm^{-1}. The sulfinyl absorption band of **2** appears at 995 cm^{-1}, a shift to lower wavenumber of 80 cm^{-1}. In the more-soluble complex, (*S*,*R*)-**2·3**, both original hydroxyl absorption bands of (*R*)-**3** also disappear and two new bands appear at 3534 cm^{-1} and 3254 cm^{-1}. The sulfinyl absorption band of **2** appears at 1039 cm^{-1}; a smaller shift to lower wavenumber, of 36 cm^{-1}, than for (*R*,*R*)-**2·3**. Moreover, in the more-soluble complex, (*S*,*R*)-**2·3**, one hydroxyl group of (*R*)-**3** shifts further towards lower wavenumbers (181 cm^{-1}) than that in (*R*,*R*)-**2·3** (111 cm^{-1}). These results showed that in the less-soluble complex, (*R*,*R*)-**2·3**, two (*R*)-**3** hydroxyl groups formed hydrogen bonds and the sulfinyl group formed two hydrogen bonds; but in the more-soluble complex, (*S*,*R*)-**2·3**, only one stronger hydrogen bond exists between (*S*)-**2** and (*R*)-**3** (Scheme 2). Thus, two possible hydrogen-bonding models between (*R*)-**2** and (*R*)-**3** were proposed for (*R*,*R*)-**2·3** (Scheme 2A and A′). Interestingly (*S*,*R*)-**2·3** consists of locally hydrogen-bonded 1:1 host–guest entities (Scheme 2B), which are usually observed in the less-soluble complexes of TADDOLs.[7a, 14]



Scheme 2. Proposed hydrogen bond relationship for inclusion complexes, (*R*,*R*)-**2**·**3** (A and A′) and (*S*,*R*)-**2**·**3** (B).

In order to clarify the interactions between (*R*)-**3** and (*R*)-**2**, we prepared a single crystal of the less-soluble complex, (*R*,*R*)-**2**·**3** and studied the structure by X-ray crystallographic analysis (Figure 1).[15]

Figure 1A illustrates the intermolecular hydrogen-bonding scheme found in the crystal structure of (*R*,*R*)-**2**·**3**. It consists of continuous hydrogen-bonded chains that are aligned along the *a* axis of the crystal. This confirmed that the correct hydrogen interaction proposed by IR is model A (Scheme 2). The sulfoxide moiety acts as a proton acceptor from, and thus bridges between, two different binaphthol molecules, which are related to each other by the two-fold screw symmetry (Figure 1A); the hydrogen bonding distances are 2.747 Å and 2.907 Å. This result showed that the molecular recognition is on the basis of an enantiodifferentiating self-assembly of host (*R*)-**3** and guest (*R*)-**2**[16, 17] that is different from Ogura's[9b,d,f] and Fantin's[9c] results in the inclusion phenomena. In the later cases, the guest molecules were included in the void constructed by the supramolecules, which formed by the self-assembly of the host molecules only.[9b, 18] It is noticeable that a large dihedral angle (107.3°) between the two naphthyl units of (*R*)-**3**[9i] is due to the steric complementarity of the bulky *tert*-butyl groups of (*R*)-**2**.[12a,b]

Gratifyingly, we also obtained a single crystal of the more-soluble complex, (*S*,*R*)-**2**·**3**, and studied the crystal structure (Figure 1B)[15] in order to reveal the chiral discrimination of the diastereomeric complexes.[13b,c] (*R*)-**3** and (*S*)-**2** formed a molecular complex through a hydrogen bond with a shorter distance of 2.658 Å than that proposed above by IR analysis (Scheme 2B).[19] Again, the large dihedral angle (107.4°) between the two naphthyl units of (*R*)-**3** is due to the steric complementarity of the bulky *tert*-butyl groups of (*S*)-**2**,[13c] and it is noteworthy that this steric complementarity is also related to the different conformations of (*R*)- and (*S*)-**2** in the diastereomeric complexes. The C1-S1-S2-C5 torsion angles of **2** in both complexes are obviously different, −135.27° for (*R*,*R*)-**2**·**3** and 175.67° for (*S*,*R*)-**2**·**3**, in which two bulky *tert*-butyl groups from (*S*)-**2** exhibit a strained *anti* arrangement. No second-order interactions, such as a C-H···π interaction between the methyl groups of **2** and the naphthalene rings of (*R*)-**3** were found in the crystal structures of the less- and more-soluble complexes. Crystal packing is stabilized by weaker van der-Waals forces among the linear supramolecules in (*R*,*R*)-**2**·**3**, as well as the bimolecular complexes in (*S*,*R*)-**2**·**3** (Figure 1). The preferential crystallization of (*R*,*R*)-**2**·**3** is due to the dual hydrogen bonds of (*R*)-**2**, which contribute to the thermodynamic stability of the complex. Differential scanning calorimetric (DSC) analysis[20] demonstrated that the heats of fusion are large differences between the more- and less-soluble complexes (38.9 kJ mol^{-1} and 58.9 kJ mol^{-1}, respectively) and a higher melting point was observed in the less-soluble complex (see the Experimental Section). The different hydrogen-bonding relationships in the diastereomeric complexes are the key factor for the successful resolution of *rac*-**2** with host compound (*R*)-**3**.

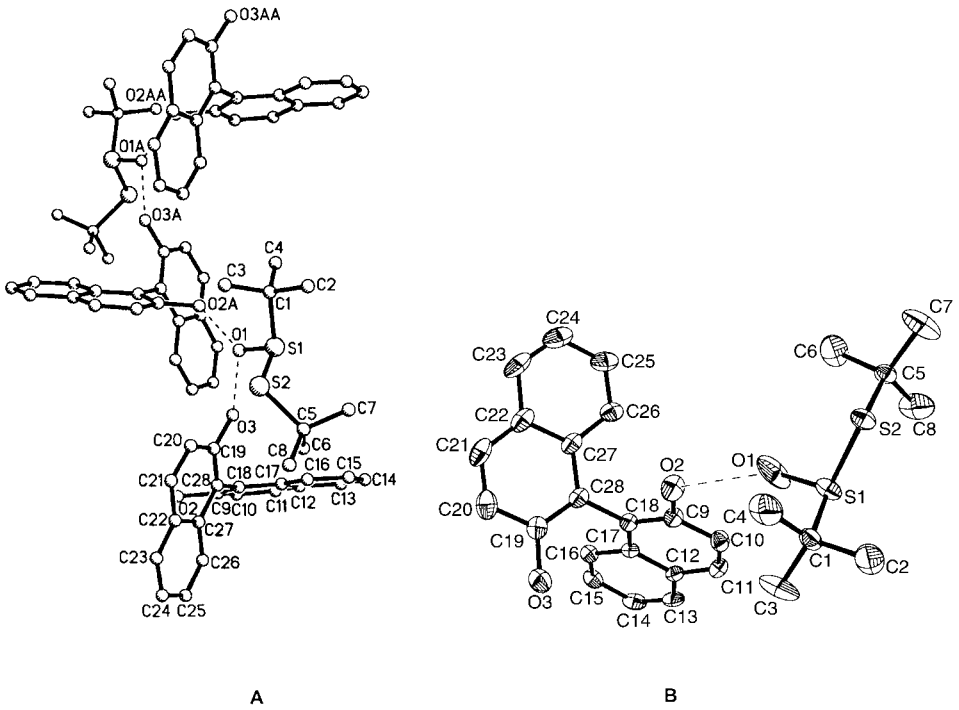


Figure 1. Stereoview of the hydrogen bond relationship of molecular complexes (*R*,*R*)-**2**·**3** (A) and (*S*,*R*)-**2**·**3** (B).

Conclusion

In summary, we have demonstrated a highly efficient and practical optical resolution of the important synthon, *tert*-butanethiosulfinate (**2**), by inclusion crystallization with (*R*)-2,2′-dihydroxy-1,1′-binaphthyl (BINOL, **3**), which is the first example of the optical resolution of the thiosulfinate. Both enantiomers of **2** were prepared in high enantiomeric purity (>99% *ee*) with one enantiomer of the chiral host, (*R*)-**3**. IR spectroscopic analysis was found to be an effective tool for studying the molecular recognition of sulfoxides. The structures of the diastereomeric complexes, (*R*,*R*)-**2·3** and (*S*,*R*)-**2·3**, was studied by IR spectroscopic and X-ray crystallographic analyses for the chiral discrimination. In the less-soluble complex, host (*R*)-**3** and guest (*R*)-**2** self-assembled as a linear supramolecule along the *a* axis of the crystal by dual hydrogen bonds; however, the more-soluble (*R*)-**3** and (*S*)-**2** formed a bimolecular complex that consists of locally hydrogen-bonded 1:1 host–guest entities. Different hydrogen bonding contributes to the chiral discrimination of the diastereomeric complexes and the successful resolution of racemic **2** with host (*R*)-**3**. It is noteworthy that the large dihedral angle (107.3°and 107.4° for (*R*,*R*)-**2·3** and (*S*,*R*)-**2·3**, respectively) between two naphthalene units of (*R*)-**3** is due to the flexibility of the BINOL molecule, which might contribute to the effective resolution of a variety of chiral compounds with BINOLs by steric complementarity.[8, 12, 13] This will provide a guiding concept for us to design novel hosts and improve the resolving efficiency of *tert*-butanethiosulfinate in the future.[7, 17]

Experimental Section

General: ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ on a Bruker 300 (300 MHz) spectrometer and are reported in ppm (δ) relative to $CDCl_3$ as internal references, unless otherwise noted. Infrared spectra were recorded on a NICOLET 200SXV FTIR spectrometer. Melting points were determined on a digital melting-point apparatus and uncorrected. Optical rotations were measured on a Perkin–Elmer 341 polarimeter. Liquid-chromatographic analyses were conducted on a Beckman 110 instrument equipped with a model 168 detector as ultraviolet light source (254 nm). Differential scanning calorimetry (DSC) was performed with a Perkin–Elmer DSC7 system. Racemic *tert*-butanethiosulfinate (**2**) was prepared according to the reported procedure.[21] (*R*)-BINOL (**3**) is a commercially available product.

Optical resolution of *tert*-butanethiosulfinate (2): A mixture of (*R*)-BINOL (**3**) (17.34 g, 60.6 mmol) and racemic *tert*-butanethiosulfinate (**2**) (11.76 g, 60.6 mmol) in anhydrous ethanol (60 mL) was heated under reflux until the solid was dissolved, then allowed to cool to room temperature, and kept for 12 h. The colorless crystals were collected by filtration and after recrystallization from ethanol (1×), the enantiopure complex, (*R*,*R*)-**2·3** was obtained. Yield: 10.81 g (74.3%);[22] m.p. 151.0–153.0 °C; $[\alpha]_D^{20} = +80$ (c = 0.4 in acetone); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.40$ (s, 9H; *tert*-butyl CH_3), 1.55 (s, 9H; *tert*-butyl CH_3), 7.14–7.19 (m, 12H; ArH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 24.1$, 32.2, 48.6, 59.4, 111.2, 117.8, 123.8, 124.2, 127.2, 128.2, 129.3, 131.1, 133.4, 152.6; IR (Nujol): $\tilde{\nu} = 3324$, 2925, 995 cm^{-1}; elemental analysis calcd (%) for $C_{28}H_{32}S_2O_3$: C 69.96, H 6.71, S 13.34; found: C 70.15, H 6.66, S 13.46.

(*R*)-**2** was obtained (3.50 g, 80.1%,[22] 99.5% *ee*) by distillation (72 °C/40 Pa). $[\alpha]_D^{24} = +159$ (c = 0.58 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.39 (s, 9H; *tert*-butyl CH_3), 1.57 (s, 9H; *tert*-butyl CH_3); IR (Neat): $\tilde{\nu} =$ 2962, 1075 cm^{-1}; elemental analysis calcd (%) for $C_8H_{18}S_2O$: C 49.44, H 9.33, S 33.00; found: C 49.24, H 9.23, S 33.14. Enantiomeric purity was determined by HPLC on a Chiral Pak AS column with propan-2-ol/hexanes (5:95 *v*/*v*) as eluent, 1.0 mL min^{-1}, $t_S = 5.6$ min, $t_R = 7.2$ min.

The mother liquid was condensed to about 30 mL and kept at room temperature for 12 h. The colorless crystalline solid was collected by filtration and after recrystallization from ethanol (2×), the enantiopure complex (*S*,*R*)-**2·3** was obtained. Yield: 5.20 g (35.7%);[22] m.p. 136.0–138.0 °C, $[\alpha]_D^{20} = -43$ (c = 0.4 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.40$ (s, 9H; *tert*-butyl CH_3), 1.58 (s, 9H; *tert*-butyl CH_3), 7.16–8.01 (m, 12H; ArH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 24.1$, 32.2, 48.7, 59.4, 111.4, 117.8, 123.7, 124.3, 127.1, 128.2, 129.2, 131.0, 133.5, 152.7; IR (Nujol): $\tilde{\nu} =$ 3324, 2925, 995 cm^{-1}; elemental analysis calcd (%) for $C_{28}H_{32}S_2O_3$: C 69.96, H 6.71, S 13.34; found: C 70.02, H 6.71, S 13.38.

(*S*)-**2** was obtained (1.69 g, 80.5%,[22] 99.2% *ee*) by distillation (64 °C/30 Pa). $[\alpha]_D^{24} = -159$ (c = 0.57 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.39 (s, 9H; *tert*-butyl CH_3), 1.57 (s, 9H; *tert*-butyl CH_3); IR (Neat): $\tilde{\nu} =$ 2962, 1075 cm^{-1}; elemental analysis calcd (%) for $C_8H_{18}S_2O$: C 49.44, H 9.33, S 33.00; found: C 49.32, H 9.23, S 33.08.

Crystal data for (*R*,*R*)-2·3: $M_w = 480.66$, crystal size 0.52 × 0.50 × 0.50 mm, orthorhombic, space group $P2_12_12_1$, $a = 12.979(2)$, $b = 13.133(2)$, $c =$ 14.953(2) Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90°$, $V = 2548.8(6)$ Å^3, $Z = 4$, $D_{calcd} =$ 1.253 Mg m^{-3}, $F(000) = 1024$, $T = 296(2)$ K. Final R indices [$I > 2\sigma(I)$]: $R1 = 0.0357$, $wR2 = 0.0739$. All non-hydrogen atoms were anisotropically generated, whereas the hydrogen atoms were generated geometrically. The Flack parameter,[23] $x = 0.02(6)$, confirms the absolute configuration.

Crystal data for (*S*,*R*)-2·3: $M_w = 480.66$, crystal size 0.52 × 0.46 × 0.46 mm, triclinic, space group $P1$, $a = 8.661(2)$, $b = 8.827(2)$, $c = 9.346(2)$ Å, $\alpha =$ 67.22(2), $\beta = 86.86(1)$, $\gamma = 79.52(2)°$, $V = 647.7(3)$ Å^3, $Z = 1$, $D_{calcd} =$ 1.232 Mg m^{-3}, $F(000) = 256$, $T = 289(2)$ K. Final R indices [$I > 2\sigma(I)$]: $R1 = 0.0409$, $wR2 = 0.1084$. All non-hydrogen atoms were anisotropically generated, whereas the hydrogen atoms were generated geometrically. The Flack parameter,[23] $x = 0.01(8)$, confirms the absolute configuration.

Crystal structure determinations: Both single crystals of (*R*,*R*)-**2·3** and (*S*,*R*)-**2·3** were grown from an ethanol/hexane mixture. All X-ray diffraction data were collected on a Siemens P4 automatic four-circle diffractometer by using graphite monochromatic $Mo_{K\alpha}$ radiation ($\lambda =$ 0.71073 Å) at room temperature. The structure was solved by direct method by using SHELXS-97[24] and refined by full-matrix least-square calculation on F^2 with SHELXL-97.[25] Calculations were performed on a PII-350 computer with the Siemens SHELXTL program package.[26] Further data have been deposited with the Cambridge Crystallographic Data Centre.[15]

Acknowledgement

This work was supported by the National Natural Science Foundation of China (Grants No. 29790125, 29972039, 20025205).

[1] For a comprehensive review, see: M. C. Carreno, *Chem. Rev.* **1995**, *95*, 1717–1760.

[2] For comprehensive reviews, see: a) P. Zhou, B.-C. Chen, F. A. Davis in *Advances in Sulfur Chemistry*, *Vol. 2* (Eds.: C. M. Raynor), JAI Press, Stamford, CT, **2000**, pp. 249–282; b) F. A. Davis, P. Zhou, B.-C. Chen, *Chem. Soc. Rev.* **1998**, *27*, 13–18; c) F. A. Davis, R. E. Reddy, *Phosphorus*, *Sulfur*, *Silicon Relat. Elem.* **1997**, *120/121*, 291–303.

[3] For a review, see: a) J. A. Ellman, T. D. Owens, T. P. Tang, *Acc. Chem. Res.* **2002**, *35*, 984–995; for more recent papers, see: b) T. D. Owens, A. J. Souers, J. A. Ellman, *J. Org. Chem.* **2003**, *68*, 3–10; c) T. P. Tang, J. A. Ellman, *J. Org. Chem.* **2002**, *67*, 7819–7832; d) D. D. Staas, K. L. Savage, C. F. Homnick, N. N. Tsou, R. G. Ball, *J. Org. Chem.* **2002**, *67*, 8276–8279; e) G. K. S. Prakash, M. Mandal, *J. Am. Chem. Soc.* **2002**, *124*, 6538–6539.

[4] a) G. Liu, D. A. Cogan, J. A. Ellman, *J. Am. Chem. Soc.* **1997**, *119*, 9913–9914; b) S. A. Blum, R. G. Bergman, J. A. Ellman, *J. Org. Chem.* **2003**, *68*, 150–155.

[5] a) Z. Han, D. Krishnamurthy, P. Grover, Q. K. Fang, C. H. Senanayake, *J. Am. Chem. Soc.* **2002**, *124*, 7880–7881; b) Z. Han, D. Krishnamurthy, P. Grover, Q. K. Fang, C. H. Senanayake, *Org. Lett.* **2002**, *4*, 4025–4028.

[6] D. A. Cogan, G. Liu, K. Kim, B. Backes, J. A. Ellman, *J. Am. Chem. Soc.* **1998**, *120*, 8011–8019.

[7] a) J. Zhu, Y. Qin, Z. He, F. Fu, Z. Zhou, J. Deng, Y. Jiang, T. Chau, *Tetrahedron: Asymmetry* **1997**, *8*, 2505–2508; b) J. Deng, Y. Chi, F. Fu, X. Cui, K. Yu, J. Zhu, Y. Jiang, *Tetrahedron: Asymmetry* **2000**, *11*, 1729–1732; c) J. Zhu, X. Peng, X. Cui, K. Yu, J. Deng, unpublished results.

[8] For comprehensive reviews, see: a) G. Kaupp, *Angew. Chem.* **1994**, *106*, 768–770; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 728–729; b) F. Toda, *Top. Curr. Chem.* **1987**, *140*, 43–69; c) F. Toda in *Advances in Supramolecular Chemistry*, *Vol. 2* (Eds.: G. W. Gokel), JAI Press Ltd., **1992**, pp. 141–191.

[9] For the resolution of sulfoxides for other groups, see: a) H. Miyamoto, S. Yasaka, R. Takaoka, K. Tanaka, F. Toda, *Enantiomer* **2001**, *6*, 51–55; b) M. Akazome, Y. Ueno, H. Ooiso, K. Ogura, *J. Org. Chem.* **2000**, *65*, 68–76; c) O. Bortolini, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *Chem. Commun.* **2000**, 365–366; d) M. Akazome, M. Noguchi, O. Tanaka, A. Sumikawa, T. Uchida, K. Ogura, *Tetrahedron* **1997**, *53*, 8315–8322; e) F. Toda, K. Tanaka, T. Okada, *J. Chem. Soc. Chem. Commun.* **1995**, 639–640; f) K. Ogura, T. Uchida, M. Noguchi, M. Minoguchi, A. Murata, M. Fujita, K. Ogata, *Tetrahedron Lett.* **1990**, *31*, 3331–3334; g) F. Toda, K. Mori, *J. Chem. Soc. Chem. Commun.* **1986**,1059–1060; h) F. Toda, K. Tanaka, S. Nagamatsu, *Tetrahedron Lett.* **1984**, *25*, 4929–4932; i) F. Toda, K. Tanaka, T. C. W. Mak, *Chem. Lett.* **1984**, 2085–2088.

[10] For selected examples of the crystallographic studies on both the diastereomeric complexes, see: S. Hanessian, R. Saladino, R. Margarita, M. Simard, *Chem. Eur. J.* **1999**, *5*, 2169–2183 and references cited therein.

[11] For a comprehensive review, see: D. Seebach, A. K. Beck, A. Heckel, *Angew. Chem.* **2001**, *113*, 96–142; *Angew. Chem. Int. Ed.* **2001**, *40*, 92–138.

[12] a) Y. Wang, J. Sun, K. Ding, *Tetrahedron* **2000**, 56, 4447–4451; b) F. Toda, K. Tanaka, Z. Stein, I. Goldberg, *J. Org. Chem.* **1994**, *59*, 5748–5751; c) D. Cai, D. L. Hughes, T. R. Verhoeven, P. J. Reider, *Tetrahedron Lett.* **1995**, *36*, 7991–7994; d) Q.-S. Hu, D. Vitharana, L. Pu, *Tetrahedron: Asymmetry* **1995**, *6*, 2123–2126.

[13] For other chiral compounds resolved by BINOLs, see: a) K. Mori, F. Toda, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2127–2128; b) F. Toda, K. Mori, Z. Stein, I. Goldberg, *Tetrahedron Lett.* **1989**, *30*, 1841–1844; c) F. Toda, K. Mori, Z. Stein, I. Goldberg, *J. Org. Chem.* **1988**, *53*, 308–312; d) F. Toda, K. Mori, *J. Chem. Soc. Chem. Commun.* **1986**, 1357–1359.

[14] For the molecular structures of the less-soluble complexes of TADDOLs,[11] see: a) T. Olszewska, M. J. Milewska, M. Gdaniec, T. Polonski, *J. Chem. Soc. Chem. Commun.* **1999**, 1385–1386; b) Y. Takemoto, S. Kuraoka, N. Hamaue, K. Aoe, H. Hiramatsu, C. Iwata, *Tetrahedron* **1996**, *52*, 14177–14188; c) F. Toda, K. Tanaka, M. Watanabe, T. Abe, N. Harada, *Tetrahedron: Asymmetry* **1995**, *6*, 1495–1498; d) F. Toda, K. Tanaka, L. Infantes, C. Foces-Foces, R. M. Claramunt, J. Elguero, *J. Chem. Soc. Chem. Commun.* **1995**, 1453–1454; e) F. Toda, K. Tanaka, C. W. Leung, A. Meetsma, B. L. Feringa, *J. Chem. Soc. Chem. Commun.* **1994**, 2371–2372.

[15] CCDC-195000 [(*R*,*R*)-**2**·**3**] and 195001 [(*S*,*R*)-**2**·**3**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336033; or deposit@ccdc.cam.uk).

[16] The formation of supramolecular layers in the homochiral inclusion complex of lansoprazole, BINOL, and benzene in a ratio of 1:2:1 was recently observed by X-ray analysis.[7c]

[17] A supramolecular nanotube with a right-handed helical structure was observed in the complex of *N*-benzyl cinchonidiniumchloride and (*S*)-1,1′-spirobiindane-7,7′-diol, See: J. H. Zhang, J. Liao, X. Cui, K. B. Yu, J. Zhu, J. G. Deng, L. X. Wang, Q. L. Zhou, W. Chung, T. Ye, *Tetrahedron: Asymmetry* **2002**, *13*, 1363–1366.

[18] a) V. Bertolasi, O. Bortolini, M. Fogagnolo, G. Fantin, P. Pedrini, *Tetrahedron Lett.* **2001**, *12*, 1479–1483; b) M. Gdaniec, M. J. Milewska, T. Polonski, *Angew. Chem.* **1999**, *111*, 405–408; *Angew. Chem. Int. Ed.* **1999**, *38*, 392–395.

[19] A locally hydrogen bonded 1:1 host–guest complex was found in the less-soluble inclusion complexes, for BINOL see: M. Periasamy, L. Venkatraman, K. R. J. Thomas, *J. Org. Chem.* **1997**, *62*, 4302–4306; for 10,10′-dihydroxy-9,9′-biphenanthryl, also see: ref. [12b].

[20] The details of the DSC analyses are shown in the Supporting Information.

[21] J. L. Kice, T. W. S. Lee, *J. Am. Chem. Soc.* **1978**, *100*, 5094–5102.

[22] The yield is calculated on the basis of half of the starting *rac*-**2**.

[23] H. D. Flack, *Acta Crystallogr. Sect. A* **1983**, *39*, 876–881.

[24] G. M. Sheldrick, *SHELXS 97, Program for Crystal Structure Determination*, University of Göttingen, **1997**.

[25] G. M. Sheldrick, *SHELXS 97, Program for Crystal Structure Refinement*, University of Göttingen, **1997**.

[26] a) *XSCANS*, *Version 2.1*, Siemens Analytical X-ray Instruments, Madison, WI, **1994**; b) *SHELEXTL*, *Version 5.1*, Siemens Industrial Automation, Analytical Instruments, Madison, WI, **1995**.

Received: December 9, 2002 [F4653]

