

Optical Resolution of Methyl Phenyl and Benzyl Methyl Sulfoxides and Alkyl Phenylsulfonates by Complexation with Chiral Host Compounds Derived from Tartaric Acid

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The title sulfoxides and sulfonates are resolved by complexation with chiral host compounds derived from tartaric acid.

Optically active sulfoxides are important synthons of various chiral compounds.¹ However, the difficulty of preparation of the chiral sulfoxides causes problems. For example, optical resolution of menthyl phenylsulfinate followed by reaction with Me₂CuLi gave (–)-**1a** of 96% e.e. in only 16% yield.² By a similar method, (–)-**1d** has been prepared in low yield.³

Previously, we reported a convenient preparative method of optically active methyl *m*-tolyl sulfoxide **1c** through resolution by complexation with optically active 2,2'-dihydroxy-1,1'-binaphthyl **2**.^{4,5} This method is not, however, effective for the resolution of methyl phenyl sulfoxide **1a**, and the *ortho* **1b** and *para* (**1d**) isomers of **1c**.^{4,5} Optically active **1a** is the most useful chiral synthon, because methyl phenyl sulfide is commercially

available and its oxidation gives **1a** easily. Therefore, chemists are eager to develop a simple method for the resolution of *rac*-**1a**. We found that the chiral host compounds **3a–c**, derived from tartaric acid, are very useful for the resolution of not only **1a** and **1d** but also benzyl methyl sulfoxide **4** and alkyl phenylsulfonates **6**.

Optically pure (*R*)-(+)-**1a** and (*S*)-(–)-**1a** of 95% e.e. were obtained by complexation with chiral *trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[5.4]decane **3c**.^{6,7} For example, when a solution of (*R,R*)-(–)-**3c** (7.42 g, 14.6 mmol) and *rac*-**1a** (4.11 g, 29.3 mmol) in toluene (30 ml) was kept at room temperature for 12 h, a 1 : 1 inclusion complex of (*R,R*)-(–)-**3c** and (*R*)-(+)-**1a** was obtained as colourless crystals (8.28 g, 87% yield). Four recrystallisations of the crystals from toluene gave pure inclusion crystals (5.8 g, 61% yield, mp 160–161 °C), which upon heating *in vacuo* gave (*R*)-(+)-**1a** of 100% e.e. {1.2 g, 56% yield, [α]_D+145 (c 0.56, MeOH)} by distillation. From the filtrate left after separation of the crude inclusion complex of (*R,R*)-(–)-**3c** and (*R*)-(+)-**1a**, crude (*S*)-(–)-**1a** (1.36 g) was obtained by column chromatography on silica gel. A solution of the crude (*S*)-(–)-**1a** (1.36 g, 9.9 mmol) and (*S,S*)-(+)-**3c** (4.94 g, 9.75 mmol) in toluene (30 ml) was kept at room temperature for 12 h. The crude inclusion complex of (*S,S*)-(+)-**3c** and (*S*)-(–)-**1a** formed was recrystallized three times from toluene to give pure crystals which upon heating *in vacuo* gave (*S*)-(–)-**1a** of 95% e.e. {0.87 g, 42% yield, [α]_D–138 (c 0.55, MeOH)} by distillation (Table 1). The host compound left after separation of the resolved **1a** by distillation can be used again. The optical purity of (*R*)-(+)- and (*S*)-(–)-**1a** was determined by HPLC using Chiralcel OB† as the chiral solid phase.

By the same method, **1c** and **1d** were also resolved [Table 1; only those enantiomers obtained by complexation with (*R,R*)-(–)-**3c** are shown]. Compound **1b** does not form an inclusion complex with any of the compounds **3a–c**, so that resolution of **1b** was unsuccessful. Inclusion complexes of compounds **1** with compounds **3** are produced by the formation of hydrogen bonds between the two components, as has been shown by X-ray analysis of the inclusion complexes of **3** with various guest compounds^{8,9} and that of **2** with **1c**.⁵ In the case of **1b**, however, hydrogen bond formation between the hydroxy group of **3** and the sulfoxide oxygen of **1b** would be disfavoured owing to the steric restriction of the *ortho* methyl group of **1b**.

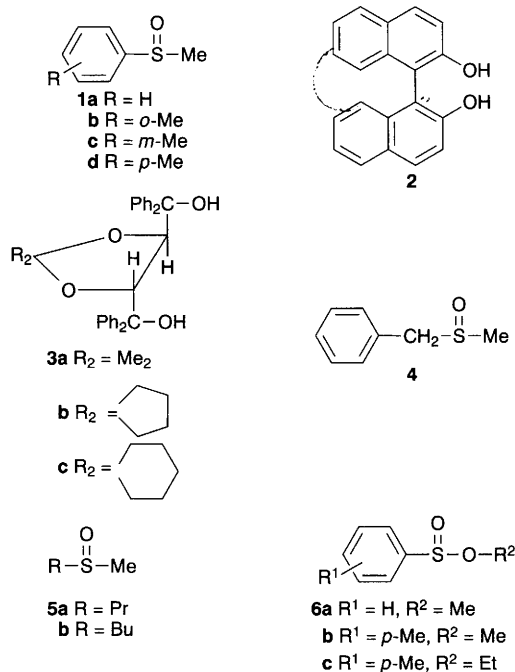


Table 1 Optical resolution of **1** and **4** by complexation with **3**

Racemic sulfoxide	Chiral host compound	Mp of inclusion complex/°C	No. of recrystallisations ^a	Product ^b	Yield (%)	Optical purity (% e.e.) ^c
1a	(<i>R,R</i>)-(–)- 3c	160–161	3	(<i>R</i>)-(+)- 1a	56	100
1b	—	—	—	—	—	—
1c	(<i>R,R</i>)-(–)- 3c	105–113	3	(+)- 1c	32	96
1d	(<i>R,R</i>)-(–)- 3c	Not clear	3	(<i>R</i>)-(+)- 1d	14	94
4	(<i>R,R</i>)-(–)- 3a	106–111	1	(–)- 4	15	100

^a Inclusion complex was purified by repeating the recrystallization from toluene. ^b Only the absolute configurations of **1a** and **1d** have been clarified.²

^c Optical purity was determined by HPLC containing Chiralcel OB† as the chiral solid phase.

Benzyl methyl sulfoxide **4** was resolved very efficiently by complexation with (*R,R*)-(-)-**3a**, and (-)-**4** of 100% e.e. was obtained in 15% yield (Table 1).

The optical resolution of dialkyl sulfoxide by complexation with **3** was less efficient than that with **2**.^{4,10} For example, although optically pure enantiomers of methyl propyl (**5a**) and methyl butyl sulfoxide (**5b**) were easily obtained by complexation with optically active **2**,^{4,10} resolution with **3c** gave unsatisfactory results. Complexation of *rac*-**5b** with (*R,R*)-(-)-**3c** in toluene followed by five recrystallisations of the resulting inclusion complex from toluene gave a 1:1 inclusion complex of (-)-**5b** with the chiral host, which upon heating *in vacuo* gave (-)-**5b** of 65% e.e. in 31% yield.

It was also found that **3** is also useful for the resolution of alkyl phenylsulfonates **6**. When a solution of (*R,R*)-(-)-**3c** (0.38 g, 0.75 mmol) and *rac*-methyl sulfinate **6a** (0.26 g, 1.5 mmol) in diethyl ether-hexane (5:1, v/v) was kept at room temperature for 12 h, a 1:1 inclusion complex of (+)-**6a** and the host **3** was obtained as colourless needles (m.p. 130–134 °C), which upon column chromatography on silica gel gave (+)-**6a** of 69% e.e. (0.02 g, 18% yield, $[\alpha]_D^{+173}$ (c 0.15, MeOH)). The optical purity was determined by HPLC containing Chiralcel OD[†] as the chiral solid phase. By a similar method, **6b** and **6c** were resolved by **3b** and **3c**, respectively, and gave (+)-**6b** of 77% e.e. (20% yield) and (-)-**6c** of 56% e.e. (27% yield), respectively. In all cases, the host compound **3** was recovered unchanged and can be reused.

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[†] Chiralcel OB and OD are available from Daicel Chemical Co. Ltd, Himeji, Japan.

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