

## A New, Convenient Method of Resolution of Racemic 1,1'-Bi-2-naphthol Using Boric Acid and (*R*)-(+)- $\alpha$ -Methylbenzylamine

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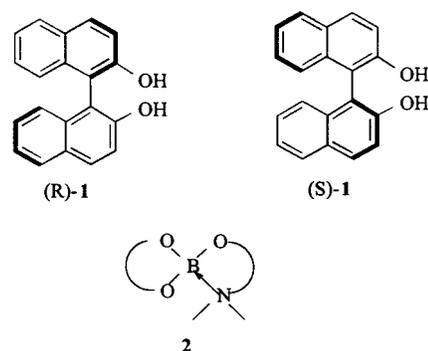
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### Introduction

The  $C_2$ -chiral 1,1'-bi-2-naphthol **1** is one of the widely used chiral auxiliaries in stoichiometric and catalytic asymmetric synthesis, such as enantioselective reduction of ketones,<sup>2</sup> in various catalytic asymmetric Diels–Alder reactions,<sup>3</sup> ene reactions,<sup>4</sup> asymmetric Michael additions,<sup>5</sup> hydroformylations,<sup>6</sup> alkylations,<sup>7</sup> oxidations,<sup>8</sup> epoxidations,<sup>9</sup> and nitroaldol reactions.<sup>10</sup> It has been also used as a chiral host for optical resolution and chiral shift reagent for the determination of the optical purity and absolute configurations of a wide range of chiral compounds.<sup>11</sup> In this regard, preparation of enantiomerically pure **1** is of current interest. There are numerous methods for the preparation of enantiomerically pure **1** such as enzymatic resolution,<sup>12</sup> separation of diastereomers using cinchonidinium derivatives,<sup>13</sup> a tartaric acid amide,<sup>14</sup> binaphthyl phosphoric acid,<sup>15</sup> and boric acid derivatives.<sup>16,17</sup>

During our efforts on the preparation of diastereomeric borate complexes such as **2** using boric acid, racemic



diols, and amino acid derivatives, it was discovered that **1** forms a 2:1 complex with (*S*)-proline **3** in methanol.<sup>16</sup>

Decomposition of the complex gives partially resolved **1** (Scheme 1). The enantiomeric purity of the sample was further enriched through preparation of a borate complex using  $B(OH)_3$  and TMEDA in  $CH_3CN$ .<sup>16c,d</sup> Although this two-step procedure of resolution of **1** involves inexpensive reagents, recovery of the water-soluble (*S*)-proline is somewhat difficult. Therefore, we have undertaken studies to explore the development of a convenient resolution procedure using  $B(OH)_3$  and a chiral amine. We wish to report that the readily accessible chiral  $\alpha$ -methylbenzylamine is useful in obtaining both *S* and *R* isomers of **1** in >99% ee (52–70% of theoretical yields).

### Results and Discussion

We have observed that the (*R*)-(+)- $\alpha$ -methylbenzylamine,  $B(OH)_3$ , and racemic **1** give a precipitate on heating at reflux in  $CH_3CN$ . Decomposition of the precipitate with dilute HCl gives the (*S*)-(–)-**1** in >99% ee (29% yield, 58% of theoretical). The filtrate upon evaporation followed by dilute HCl treatment of the residue gives the (*R*)-(+)-**1** in 56% ee (53% yield). The use of (*S*)-(–)- $\alpha$ -methylbenzylamine gave the (*R*)-(+)-**1** in >99% ee and (*S*)-(–)-**1** in 52% ee in similar yields.

We have used **1** and boric acid in a 3:2 ratio in these experiments, since heating of a mixture of these substrates in benzene leads to the formation of a  $C_3$ -symmetric propeller **5**,<sup>16d</sup> previously reported in the reaction of  $BrBH_2 \cdot SMe_2$  with binaphthol.<sup>3e</sup>

Unfortunately, recrystallization of the precipitate obtained in Scheme 2 using ( $\pm$ )-**1**, boric acid, and  $\alpha$ -methylbenzylamine did not yield crystals suitable for X-ray crystal structure analysis. However, the filtrate on standing yielded crystals suitable for X-ray analysis

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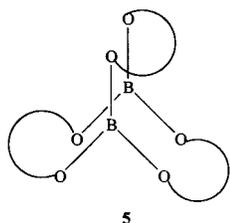
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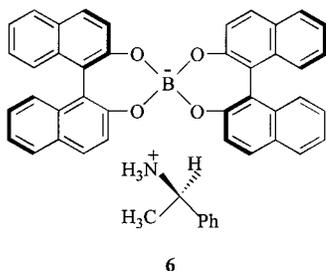
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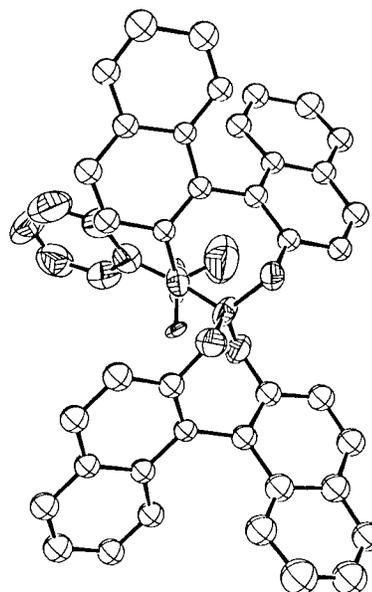
(Scheme 2). The data revealed that the crystal obtained in this way is a Bronsted acid–amine complex **6**.<sup>19</sup>



Clearly, the 1,1'-bi-2-naphthol and boric acid tend to form a complex of the type **6** in the presence of  $\alpha$ -methylbenzylamine. Therefore, we have carried out the resolution experiments using racemic **1** and boric acid in a 2:1 ratio with different amounts of (*R*)-(+)- $\alpha$ -methylbenzylamine in CH<sub>3</sub>CN. The results are summarized in Table 1.

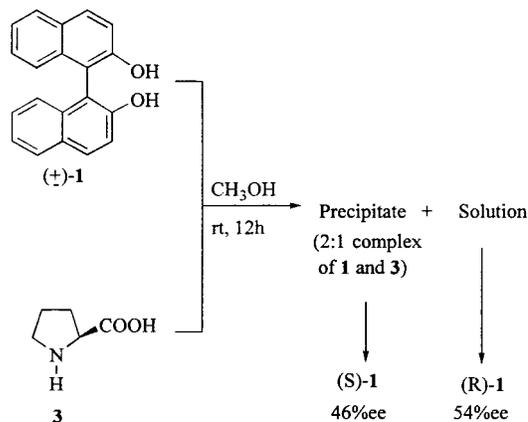
The partially enriched **1** gives better results (Table 1, entry 3). Moreover, it was observed that when THF was used as a solvent, the opposite enantiomer was isolated from the precipitate in 95% ee (Table 1, entry 4). Again, the results are better when partially enriched **1** was used (Table 1, entries 5 and 6). Obviously, one of the diastereomers is insoluble in CH<sub>3</sub>CN and the other is insoluble in THF.

We have exploited this difference in solubility in CH<sub>3</sub>CN and THF of the diastereomeric complexes to develop a convenient, practical method of resolution as illustrated



**Figure 1.** Perspective view of the complex **6**.

### Scheme 1



**Table 1.** Resolution of 1,1'-Bi-2-naphthol Using B(OH)<sub>3</sub> and (*R*)-(+)- $\alpha$ -Methylbenzylamine<sup>a</sup>

S no.	<b>1</b> % ee	( <i>R</i> )-(+)- <b>4</b> (mmol)	solvent	optically active <b>1</b> from			
				precipitate		filtrate	
				% ee	yield (%)	% ee	yield (%)
1	0	15	CH <sub>3</sub> CN	<i>S</i> , 91	40	<i>R</i> , 61	50
2	0	10	CH <sub>3</sub> CN	<i>S</i> , 81	45	<i>R</i> , 40	50
3	<i>S</i> , 30	10	CH <sub>3</sub> CN	<i>S</i> , 97	55	<i>R</i> , 55	38
4	0	5	THF	<i>R</i> , 95	24	<i>S</i> , 20	70
5	<i>R</i> , 20	5	THF	<i>R</i> , 97	25	<i>S</i> , 20	68
6	<i>R</i> , 34	5	THF	<i>R</i> , > 99	28	<i>S</i> , 25	65

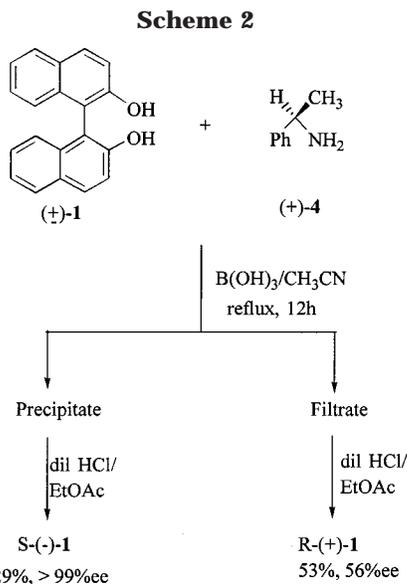
<sup>a</sup> All experiments were performed using 1,1'-bi-2-naphthol (10 mmol), B(OH)<sub>3</sub> (5 mmol), and (*R*)-(+)- $\alpha$ -methylbenzylamine as mentioned. The substrates were taken in the solvent (20 mL), and the contents were refluxed for 12 h (see the Experimental Section for workup).

in Scheme 3. In this way, (*S*)-(–)-**1** was obtained in >99% ee (35% yield, i.e., 70% of theoretical) and (*R*)-(+)-**1** was obtained in >99% ee (26% yield, i.e., 52% of theoretical).

The recovered (*S*)-(–)-**1** (62% ee, 2% yield) and (*R*)-(+)-**1** (10% ee, 35% yield) have been recycled to obtain **1** with >99% ee (Table 1 and Scheme 3). The experiment was also carried out using 50 mmol of racemic **1** and proportional amounts of other reagents to obtain chiral **1** in >99% ee without significant change in yields. The

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(19) **Crystal Structure Analysis.** The X-ray diffraction measurements were carried out at 293 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite-monochromated Mo K $\alpha$  ( $\lambda = 0.71073$  Å) radiation. Intensity data were collected by the  $\omega$ -scan mode. The data were reduced using the XTAL program. No absorption correction was applied.  $\theta$  range for data collection is 1.63–21.98°. Crystal structure data for **6**: empirical formula C<sub>152</sub>H<sub>119</sub>B<sub>3</sub>N<sub>4</sub>O<sub>12</sub>; colorless rectangular prism (0.4 × 0.4 × 0.6 mm); crystal system is triclinic; space group P1; unit cell dimensions,  $a = 17.979(8)$  Å,  $b = 19.72(7)$  Å,  $c = 20.96(2)$  Å;  $\alpha = 114.16^\circ$ ,  $\beta = 93.52^\circ$ ,  $\gamma = 96.35^\circ$ ; volume 6691(24) Å<sup>3</sup>,  $Z = 2$ ,  $D_{\text{calc}} = 1.105$  Mg/m<sup>3</sup>, absorption coefficient is 0.069 mm<sup>-1</sup>,  $F(000) = 2340$ , index ranges  $0 \leq h \leq 18$ ,  $-20 \leq k \leq 20$ ,  $-22 \leq l \leq 21$ , total reflections collected were 16524 out of which 16350 were independent reflections with  $R(\text{int}) = 0.0000$  and  $R(\sigma) = 0.1137$ . The structure was solved by direct methods and refined by a full-matrix least-squares procedure using the SHELX 86 and SHELX 97 program packages, respectively. The refinement was carried out using 16350 observed [ $F > 4\sigma(F)$ ] reflections and converged to a final  $R_1 = 0.1743$ ,  $wR_2 = 0.4390$  and goodness of fit of 1.516 with a largest difference peak and hole of 1.538 and  $-0.560$  e Å<sup>-3</sup>, respectively. The structure of the complex was confirmed from the bond angles and bond lengths. The bond angles O<sub>1</sub>–B<sub>1</sub>–O<sub>2</sub> = 112.578°, O<sub>1</sub>–B<sub>1</sub>–O<sub>3</sub> = 118.054°, O<sub>1</sub>–B<sub>1</sub>–O<sub>4</sub> = 100.790°, O<sub>2</sub>–B<sub>1</sub>–O<sub>3</sub> = 103.660°, O<sub>2</sub>–B<sub>1</sub>–O<sub>4</sub> = 112.190°, and O<sub>3</sub>–B<sub>1</sub>–O<sub>4</sub> = 109.831° showed the existence of boron in tetracoordinate form. The bond distances between boron B1 and four oxygens, B<sub>1</sub>–O<sub>1</sub> = 1.4849 Å, B<sub>1</sub>–O<sub>2</sub> = 1.4425 Å, B<sub>1</sub>–O<sub>3</sub> = 1.4588 Å, and B<sub>1</sub>–O<sub>4</sub> = 1.5016 Å, supports the “ate” complex nature of boron.



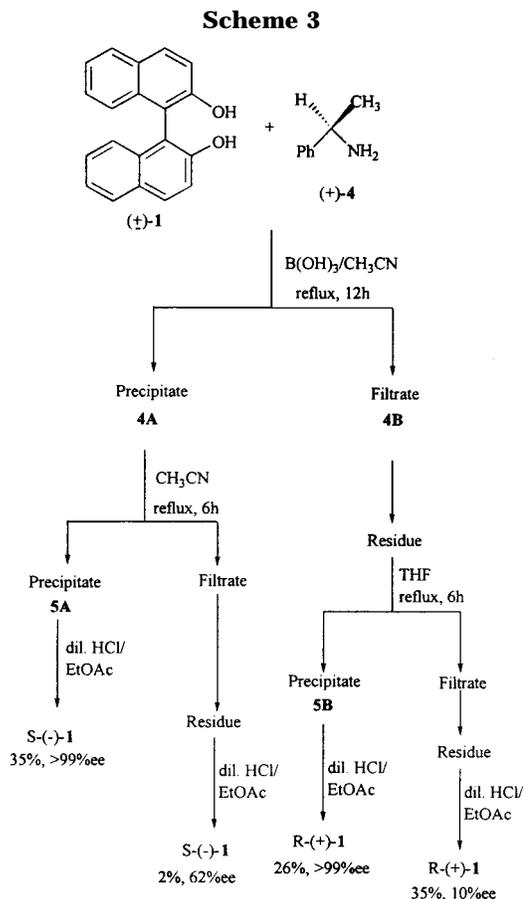
chiral amine and all the solvents can be readily recovered for use again. Therefore, the procedure described here for the resolution of 1,1'-bi-2-naphthol using inexpensive reagents should be highly economical.

### Experimental Section

The racemic 1,1'-bi-2-naphthol was prepared in high yield by oxidative coupling of  $\beta$ -naphthol using  $\text{CuCl}(\text{OH})\text{-TMEDA}$  catalyst and air in MeOH followed by recrystallization from chlorobenzene.<sup>18a-c</sup> It was also prepared using  $\text{FeCl}_3$  in water by recrystallization from toluene.<sup>18d</sup> Chiral resolving agent (*R*)-(+)- $\alpha$ -methylbenzylamine with 98%-99% ee was used. Enantiomeric excesses were calculated from values measured on an Autopol-II automatic polarimeter. It was also confirmed for samples of 1,1'-bi-2-naphthol with >99% ee by HPLC analysis using a CHIRALPAK OP column with MeOH as solvent.

**Resolution of Racemic 1,1'-Bi-2-naphthol Using  $\text{B(OH)}_3$  and (*R*)-(+)- $\alpha$ -Methylbenzylamine (Scheme 3).** Racemic 1,1'-bi-2-naphthol **1** (10 mmol, 2.86 g),  $\text{B(OH)}_3$  (5 mmol, 0.31 g), and (*R*)-(+)- $\alpha$ -methylbenzylamine (15 mmol, 1.995 mL) were refluxed in  $\text{CH}_3\text{CN}$  (20 mL) for 12 h. The reaction mixture was cooled to rt and filtered. To the precipitate **4A** was added  $\text{CH}_3\text{CN}$  (10 mL) and the mixture refluxed for 6 h. The contents were brought to rt and filtered. The precipitate **5A** was suspended in a mixture of EtOAc (25 mL) and dilute HCl (1 N, 20 mL) and stirred until complete dissolution occurred. The organic layer was collected, and the aqueous layer was extracted with EtOAc (10 mL  $\times$  2). The organic extracts were combined and washed with saturated brine, dried over magnesium sulfate, and evaporated to dryness to obtain (*S*)-(-)-**1**, 0.96 g, >99% ee (35% yield, 70% of theoretical), mp 208–210 °C (lit.<sup>15d</sup> mp 209–210 °C). The ee values are based on  $[\alpha]_D^{25} = 34.5$  (*c* 1, THF).<sup>16d</sup>

The filtrate **4B** was concentrated. The residue was refluxed for 6 h in THF (20 mL). The reaction mixture was brought to rt and filtered. The precipitate **5B** was digested in a mixture of EtOAc (25 mL) and dilute HCl (1 N, 20 mL) followed by workup as outlined above to obtain the (*R*)-(+)-**1**, 0.75 g, >99% ee (26%



yield, 52% of theoretical), mp 208–210 °C (lit.<sup>15d</sup> mp 209–210 °C). The ee values are based on  $[\alpha]_D^{25} = 34.5$  (*c* 1, THF).<sup>16d</sup> The chiral resolving agent (*R*)-(+)- $\alpha$ -methylbenzylamine, **4**, was recovered by NaOH treatment of the combined dilute HCl fractions followed by extraction with diethyl ether (25 mL  $\times$  2). After evaporation of the combined ether layers, the residue was distilled under reduced pressure to isolate **4** in 90% yield (99% ee).

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