New Methods of Resolution and Enrichment of Enantiomeric Excesses of 1,1′-Bi-2-naphthol

Mariappan Periasamy,*,† Lakshmanan Venkatraman,† and K. R. Justin Thomas‡

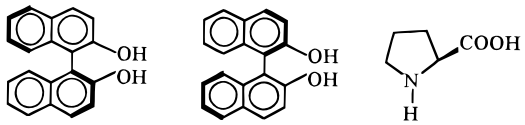
School of Chemistry, University of Hyderabad, Central University P.O., Hyderabad 500 046, India, and RSIC, Indian Institute of Technology, Madras 600 036, India

Received October 16, 1996 (Revised Manuscript Received April 1, 1997[⊗] *)*

Partial resolution of racemic 1,1′-bi-2-naphthol (**1**) was readily achieved to obtain enriched (scalemic) **1** using (*S*)-proline (**2**). The structure of the complex **3** formed between **1** (2 equiv) and (*S*)-proline (1 equiv) was characterized by an X-ray diffraction method. Enantiomeric excesses of the incompletely resolved **1** were enriched to obtain essentially pure (*R*)- and (*S*)-**1** following a simple procedure using $B(OH)_3$ and TMEDA.

Introduction

The C_2-symmetric chiral 1,1′-bi-2-naphthol (**1**) is useful in getting higher levels of asymmetric induction in asymmetric synthesis.[1] Many chiral auxiliaries developed from this compound are highly efficient in stoichiometric and catalytic processes like asymmetric reductions,[2] Diels−Alder reactions,[3] glyoxylate−ene reactions,[4] Mukaiyama aldol−ene reactions,[5] aza Diels-Alder reactions,[6] Michael reactions,[7] enantioselective protonations,[8] and nitroaldol reactions.[9]



(S) - **1** (R) - **1** **2**

The enantiodifferentiating property of **1** has been found to be outstanding. However, applications of chiral auxiliaries incorporating this material are hindered because of the expense of the chiral **1** and the difficulties involved in getting it in enantiomerically pure forms. Several methods such as optical resolutions through formation of diastereomers,[10] enzymatic resolution,[11] resolution through inclusion complexes[12] and asymmetric synthesis from 2-naphthol[13] are available to obtain **1** in enantiopure form. The most widely used method of synthesis of chiral **1** involves optical resolution through formation of diastereomeric complexes using a chiral source. The procedures developed in this way often require expensive chiral sources, and the experimental parts are highly complicated. This inspired us to look for a simple way of resolving racemic **1** using readily available and inexpensive amino acids. We describe here results of this study.

Results and Discussion

Partial Resolution of 1,1′-Bi-2-naphthol Using (*S*)-Proline. Initially, it was discovered in this laboratory that racemic **1** upon refluxing with (*S*)-proline (**2**) in benzene leads to precipitate and filtrate fractions that after dilute HCl treatment give partially resolved **1**.[14] Repetition of the experiment successively three times resulted in essentially complete resolution. Since benzene is not an acceptable solvent, we were looking for an alternative solvent.

Comparable results were obtained using solvents such as methanol, dichloromethane, and methanol−dichloromethane mixtures (Scheme 1, Table 1). It appears that the complex formation is essentially complete in 0.5 h in methanol (Table 1, entry 2). Filtering the reaction mixture under hot conditions gave the (*S*)-(−)-isomer with 59% ee but only in 7% yield. The results of reaction for 3 and 12 h are similar in dichloromethane. Also, refluxing the mixture for 36 h in dichloromethane resulted in slight improvement in the ee of the (*S*)-(−)-isomer.

The effect of concentration of the chiral source used was studied to find out the optimum amounts of resolving agent required for the resolution. The use of **1** and **2** in a 1:1 ratio gives better results (Table 2, entries 1−4).

Since amino acids exist in the form of zwitterion (i.e., **2a**), it was obviously of interest to study the effect of deprotonated (**2b**) and protonated (**2c**) forms toward complexation with **1**. To examine this, experiments were

[⊗] Abstract published in *Advance ACS Abstracts*, May 15, 1997.
† University of Hyderabad.
‡ Indian Institute of Technology.

(1) Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503.
(2) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishigava, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709.
(3) (a) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007. (b) Bao, J.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1993**, *114*, 3814. (c) Kobayashi, M.; Araki, M.; Hachiya, I. *J. Org. Chem.* **1994**, *59*, 3758. (d) Ishihama, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 1561. (e) Kaufmann, D.; Boese, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 545.
(4) Van der Meer, F. T.; Feringa, F. L. *Tetrahedron Lett.* **1992**, *33*, 6695.
(5) Mikami, K.; Matsukawa, S. *J. Am. Chem. Soc.* **1993**, *115*, 7309.
(6) Hattori, K.; Yamamoto, H. *J. Org. Chem.* **1992**, *57*, 3264.
(7) Kobayashi, S.; Suda, S.; Yamada, M.; Mukaiyama, T. *Chem. Lett.* **1994**, *97*, 1.
(8) Ishihara, K.; Kaneeda, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 11179.
(9) Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418.
(10) (a) Jacques, J.; Fouquey, C.; Viterbo, R. *Tetrahedron Lett.* **1971**, 4617. (b) Jacques, J.; Fouquey, C. *Org. Synth.* **1988**, *67*, 13. (c) Gong, B.; Chen, W.; Hu, B. *J. Org. Chem.* **1991**, *56*, 423. (d) Brunel, J. M.; Buono, G. *J. Org. Chem.* **1993**, *58*, 7313.
(11) Kazlauskas, R. J. *J. Am. Chem. Soc.* **1989**, *111*, 4953.
(12) (a) Kawashima, M.; Hirayama, A. *Chem. Lett.* **1990**, 2299. (b) Tanaka, K.; Okada, T.; Toda, F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1147. (c) Toda, F.; Tanaka, K.; Stein, Z.; Goldberg, I. *J. Org. Chem.* **1994**, *59*, 5748. (d) Hu, Q. S.; Vitharna, D.; Pu, L. *Tetrahedron: Asymmetry* **1995**, *6*, 2123.
(13) (a) Brussee, J.; Jansen, A. C. A. *Tetrahedron Lett.* **1983**, *24*, 3261. (b) Smrcina, M.; Lorenc, M.; Hanus, V.; Sedmera, P.; Kocovsky, P. *J. Org. Chem.* **1992**, *51*, 1917.
(14) Periasamy, M.; Prasad, A. S. B.; Kanth, J. V. B.; Reddy, Ch. K. *Tetrahedron: Asymmetry* **1995**, *6*, 341.

S0022-3263(96)01937-8 CCC: $14.00

Scheme 1

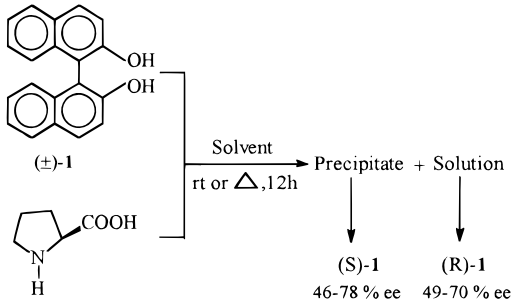


Table 1. Partial Resolution of Racemic 1,1′-Bi-2-naphthol (1) Using (*S*)-Proline in Various Solvents[a]

			1,1′-bi-2-naphthol from			
			precipitate		filtrate	
S. no.	reaction time (h)	solvent	% ee	% yield	% ee	% yield
1[b]	12	CH_3OH	*S*, 46	49	*R*, 54	43
2[b]	0.5	CH_3OH	*S*, 50	55	*R*, 66	38
3[c]	12	CH_2Cl_2	*S*, 52	49	*R*, 70	40
4[c]	3	CH_2Cl_2	*S*, 46	56	*R*, 73	35
5[c]	36	CH_2Cl_2	*S*, 66	52	*R*, 63	38
6[d]	12	CH_3CN	*S*, 52	43	*R*, 52	40
7[e]	12	$CHCl_3$	*S*, 49	48	*R*, 58	39
8[f]	12	$CH_3OH + CH_2Cl_2$	*S*, 78	32	*R*, 49	52

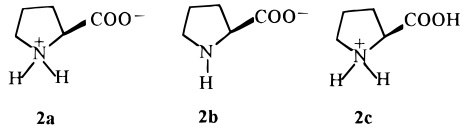
[a] All experiments were performed using racemic 1,1′-bi-2-naphthol (5 mmol) and (*S*)-proline (5 mmol). [b] The substrate was taken in methanol (15 mL), and the contents were heated at 60 °C for 10 min and left at 25 °C. [c] The substrate was taken in dichloromethane (20 mL), and the contents were refluxed. [d] The substrate was taken in acetonitrile (15 mL), and the contents were heated at 60 °C for 10 min and left at 25 °C. [e] The substrate was taken in chloroform (30 mL), and the contents were heated at 60 °C for 10 min and left at 25 °C. [f] Dichloromethane (10 mL) and methanol (1 mL) were added, and the contents were refluxed.

Table 2. Partial Resolution of Racemic 1,1′-Bi-2-naphthol: Effect of Concentration of (*S*)-Proline and the Additives KOH and PTSA[a]

		1,1′-bi-2-naphthol from			
		precipitate		filtrate	
S. no.	(*S*)-proline (mmol)	% ee	% yield	% ee	% yield
1	2.5	*S*, 46	49	*R*, 54	43
2	5.0	*S*, 52	49	*R*, 70	40
3	7.5	*S*, 52	43	*R*, 52	40
4	10	*S*, 49	48	*R*, 58	39
5[b]	5	*S*, 60	25	*R*, 21	69
6[c]	5			*R,S*, 00	100

[a] All the experiments were carried out using racemic 1,1′-bi-2-naphthol (1) (5 mmol) in methanol. In entries 1 and 2, methanol (15 mL) and in other entries 25 mL of methanol was used. The components were heated at 60 °C for 10 min and left at 25 °C for 12 h. [b] KOH (1.5 mmol) was added to the reaction mixture. [c] *p*-Toluenesulfonic acid (5 mmol) was added to the reaction mixture.

carried out in the presence of KOH and *p*-toluenesulfonic acid (PTSA) in methanol (Table 2, entries 5 and 6). Addition of KOH, which is expected to favor the formation of **2b**, gave results without improvement. Interestingly, in the presence of PTSA, no precipitation occurred, indicating that the carboxylate form may be necessary for the resolution (Table 2, entries 5 and 6).



2a **2b** **2c**

Scheme 2

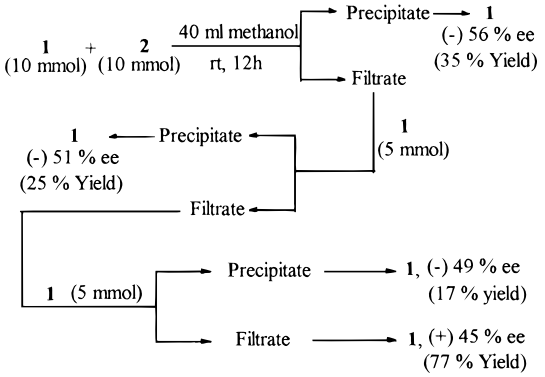


Table 3. Enrichment of Enantiomeric Excesses of Partially Resolved (Scalemic) (1) Using (*S*)-Proline[a]

		1,1′-bi-2-naphthol (**1**) from			
	1,1′-bi-2-naphthol	precipitate		filtrate	
S. no.	(**1**) (% ee)	% ee	% yield	% ee	% yield
1[b]	*S*, 47	*S*, 70	62	*R*, 03	27
2[c]	*S*, 57	*S*, 83	69	*R*, 40	14
3[c]	*R*, 47	*S*, 43	12	*R*, 71	73
4[d]	*R*, 73		00	*R*, 73	100
5[e]	*S*, 69	*S*, 85	70	*S*, 18	17
6[f]	*S*, 66	*S*, 81	62	*S*, 09	21

[a] In all experiments, 1,1′-bi-2-naphthol (5 mmol) and (*S*)-proline (5 mmol) were used. [b] The components were dissolved in methanol (15 mL), heated at 60 °C for 10 min, and left at 25 °C for 12 h. [c] Refluxed in dichloromethane (25 mL) for 12 h (in entry 3, 20 mL of dichloromethane was used). [d] Refluxed in dichloromethane (20 mL) for 12 h. [e] Refluxed in acetonitrile (20 mL) for 12 h. [f] Refluxed in methanol (1 mL) and dichloromethane (10 mL) mixture for 12 h.

An interesting observation was made when (*S*)-proline (10 mmol) was taken in methanol and portions of **1** were added successively to obtain the complex as precipitate that on ether/dilute HCl treatment gave partially resolved **1** (Scheme 2). In this way, mixtures of **1** enriched in the *S* isomer were obtained in 49−56% ee (43% yield), and the **1** enriched in the *R* isomer (45% ee) was obtained in 77% yield.

Enrichment of Enantiomeric Excesses of Partially Resolved (Scalemic) 1 Using (*S*)-Proline. After recrystallization of the complex obtained between racemic **1** and (*S*)-proline in methanol followed by dilute HCl treatment, the (*S*)-(−)-isomer was obtained in 81% ee (12% yield). The (*S*)-(−)-isomer with 37% ee (24% yield) was recovered from the solution. Since this crystallization method was not satisfactory, we decided to repeat the experiments starting from the partially resolved **1** using an equivalent amount of (*S*)-proline again. The results are summarized in Table 3. The ee of the *S* isomer could be further enhanced in this way (Table 3, entries 1 and 2, 5 and 6).

Structural Characterization of the Inclusion Complex. The crystals obtained in the reaction of racemic **1** and (*S*)-proline in methanol were not suitable for X-ray crystal structure analysis. Fortunately, the crystals obtained from (*S*)-(95% ee)-**1** and (*S*)-proline could be analyzed using the X-ray diffraction method.

Final atomic coordinates of the complex **3** prepared by the reaction of (*S*)-(−)-**1** and (*S*)-proline in methanol, along with lists of anisotropic thermal parameters, hydrogen coordinates, bond lengths, and bond angles, have been deposited with the Cambridge Crystallographic Data Centre. They can be obtained, on request,

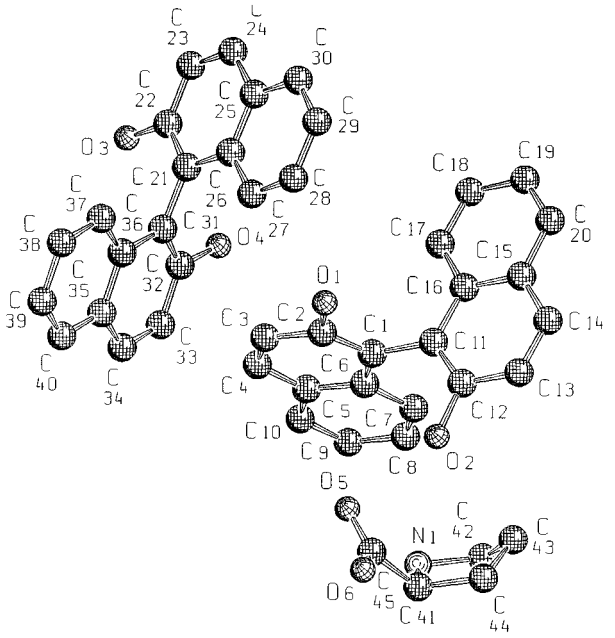


Figure 1. Perspective view of the complex **3**.

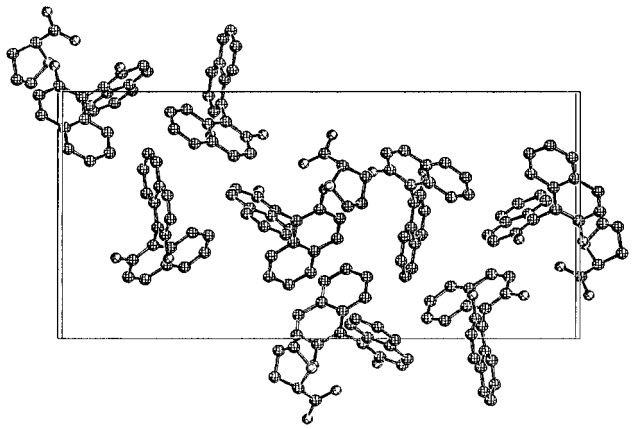


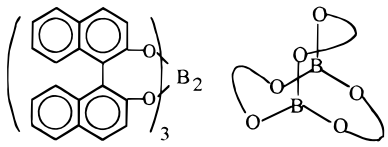
Figure 2. Packing diagram of the crystal structure of the complex **3**.

from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. The intermolecular organization and association in the inclusion complex are depicted in Figures 1 and 2. The structural parameters exhibited for the various moieties in the inclusion complex are in good agreement with that of the standard values. Minor deviations can be attributed to the packing of these molecules in the unit cell.

The carboxylate and quaternary ammonium groups of the proline molecule make T-shaped hydrogen bonds with the hydroxyl group of the one binaphthol with the OH···N and O···HO distances of 2.088 and 2.109 Å, respectively, leading to the locally hydrogen-bonded 1:1 host-to-guest complex. The host−guest interaction between one binaphthol and proline is complemented by a $\pi-\pi$ stacking interaction between the binaphthols C21C22C23C24-C26C27C28C29C30 and C11C12C13C14C15C16C17-C18C19C20. Within the binaphthol that exhibits hydrogen-bonding interactions with the proline molecule the two naphthyl moieties are nearly perpendicular to each other with the dihedral angle between the mean planes 94.0°. However, in the other binaphthol the dihedral angle between the mean planes of the naphthyl rings is 73.5°. Here, the larger binaphthyl groups probably prevent a simultaneous close approach of the two binaphthols near the proline molecule. There is also an another hydrogen-bonding interaction between the two binaphthols where one CH group of the naphthyl ring acts as a proton donor and the oxygen site of the hydroxyl group acts as a proton acceptor at a CH···O distance of 2.715 Å.

Enhancement of Enantiomeric Excesses of Scalemic 1,1′-Bi-2-naphthol Using $B(OH)_3$ and TMEDA. Although the (*S*)-proline used in the resolution and enrichment procedures can be recovered easily, it would be better if the partially resolved **1** could be enriched further without using another chiral source. Some time ago, Horeau reported that chemical duplication of a nonracemic(scalemic) substrate, for example, through formation of two diastereomeric carbonate diesters from a scalemic alcohol, separation of the homochiral (*RR*, *SS*), chiral dimer and the achiral (*RS*) meso dimer, and regeneration of the alcohol from the homochiral dimer, provided the scalemic alcohol with amplified enantiomeric excess.[15a] This idea was recently applied by Fleming to enrich the enantiomeric excess of a scalemic alcohol using oxalyl chloride from 92.6% to 99.6%.[15c] Fleming has also shown that if there is no stereoselection, the derivative ML_2 will be formed following the algebraic expression, $X^2:Y^2:2XY$. If the starting enantiomeric excess is 80%, (i.e., X:Y = 90:10, X,Y are the concentrations of *R* and *S*, respectively) and since ($X^2 + Y^2$) and 2XY are diastereomers, separation of the *RR* and *SS* diastereomers ($X^2 + Y^2$) from the above mixture and regeneration of *R* and *S* enantiomers should give *R*:*S* in the ratio ($X^2:Y^2$) 8100:100 = 98.8:1.2, corresponding to an ee of 97.6%.

We were interested in adopting a similar idea for the enrichment of the enantiomeric excess of scalemic **1**. Since **1** is a bifuntional molecule it can form a complex of the type B_2L_3 (L = 1,1′-bi-2-naphthyloxy) (**4a**).



4a **4b**

Four isomers derived from *RRR*, *SSS*, *RRS*, and *RSS* combinations of binaphthol would be expected in the ratio of $X^3:Y^3:3X^2Y:3XY^2$. An initial ratio of *R*:*S* (i.e., X:Y) 90:10 (i.e., 80% ee), would lead to the *R*:*S* ratio of $X^3:Y^3$ (i.e., 99.86:0.14, 99.72% ee) after separation of *RRR* and *SSS* ($X^3 + Y^3$) isomers and regeneration of *R* and *S*. However, it should be pointed out that this product distribution can be expected only if there is no stereoselectivity in the formation of *RRR*, *SSS* or *RRS*, *SSR*.

We have carried out a series of experiments to examine these possibilities. Initially, we have attempted to prepare the B_2L_3 complex from $B(OH)_3$ and **1** in benzene using a Dean−Stark apparatus. Unfortunately, the enriched enantiomer was obtained only in low yields (Table 4, entry 1).[16] Fortunately, better results were obtained when **1** and $B(OH)_3$ were taken in a 3:2 ratio in

(15) (a) Vigneron, J. P.; Dhaenens, M.; Horeau, A. *Tetrahedron* **1973**, *29*, 1055. (b) Rautenstrauch, V.; Megard, P.; Bourdin, B.; Furrer, A. *J. Am. Chem. Soc.* **1992**, *114*, 1418. (c) Fleming, I.; Ghosh, S. K. *J. Chem. Soc., Chem. Commun.* **1994**, 99.

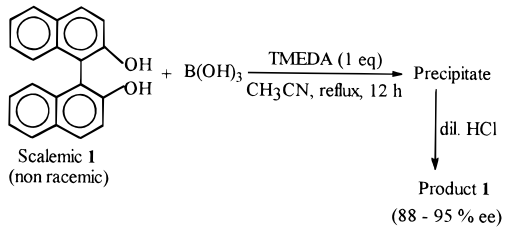
(16) Venkatraman, L.; Periasamy, M. *Tetrahedron: Asymmetry* **1996**, *7*, 2471.

Table 4. Enhancement of Enantiomeric Excesses of 1,1′-Bi-2-naphthol (1) Using $B(OH)_3$ and TMEDA[a]

			product (**1**) obtained from			
			precipitate		filtrate	
entry no.	(**1**) (% ee)	$B(OH)_3$ (mmol)	% ee	yield[d] (%)	% ee	yield (%)
1	*S*, 47	2.0	*S*, 91	20	*S*, 38	69
2[b]	*R*, 62	2.0	*R*, 73	78	*R*, 40	06
3	*R*, 34	2.0	*R*, 51	47	*S*, 03	33
4[b]	*R*, 16	2.0	*R*, 41	28	*R*, 01	56
5[b]	*S*, 28	2.0	*S*, 58	38	*R*, 03	52
6	*S*, 18	2.0	*S*, 31	57	*S*, 05	30
7	*R*, 34	2.0	*R*, 88	38	*R*, 12	48
8	*R*, 17	0.57	*R*, 88	11	*R*, 03	76
9	*R*, 34	1.14	*R*, 92	31	*S*, 05	55
10	*R*, 52	1.80	*R*, 95[c]	30	*R*, 20	53
11	*R*, 68	2.30	*R*, 94	41	*R*, 52	45
12	*R*, 75	2.50	*R*, 93	48	*R*, 63	39
13	*S*, 18	0.60	*S*, 89	13	*S*, 05	75
14	*S*, 34	1.10	*S*, 95	28	*S*, 01	54
15	*S*, 52	1.80	*S*, 95	38	*S*, 16	47
16	*S*, 69	2.30	*S*, 93	52	*S*, 34	36
17	*S*, 85	2.90	*S*, 93[c]	53	*S*, 73	33
18	*R*, 79	2.67	*R*, 93	77	*S*, 06	10
19	*S*, 75	2.50	*S*, 95	77	*R,S*, 00	10

[a] All experiments were carried out using 5 mmol of (**1**) in acetonitrile (20 mL). In entries 1−3, 3 mmol of (**1**) was used. In entries 1−17, 1 mmol of TMEDA and in entries 18 and 19 5 mmol of TMEDA was used. [b] In these experiments, benzene (40 mL) was used as solvent, and the contents were refluxed for 12 h. [c] HPLC analysis on a chiralpak OP using methanol as eluent did not detect the presence of the other enantiomer. [d] Yields are based on the amount of scalemic (**1**) used.

Scheme 3



acetonitrile and TMEDA was used to precipitate the complex (Table 4, entries 2 and 3). However, the results were still poor. Better results were obtained when the scalemic **1** and $B(OH)_3$ were taken in 5:2 ratio (Table 4, entries 4−7; Scheme 3). It was clear from the results that the precipitate fraction contains the enriched isomer, leaving behind the mixture with low ee in solution. So, it was decided to use $B(OH)_3$ equivalent to the enantiomer present in excess over the racemic to form the B_2L_3 complex. This led to very good results (Table 4, entries 8−17). In the experiments using mixtures with high ee, the yields of enriched material were somewhat low and more amounts were left in solution (Table 4, entries 11 and 12, 16 and 17). This problem was rectified by using an excess of TMEDA (5 equiv) to precipitate the B_2L_3 complex (Table 4, entries 18 and 19).

The results are in accordance with the selective formation of *RRR* or *SSS* complexes derived from the enantiomer present in excess over the racemic mixture. The poor results obtained when scalemic **1** and $B(OH)_3$ were used in a 3:2 ratio further illustrates the point that the *RRS* and *RSS* isomers might not have formed in these experiments. Kaufmann has previously noted that the reaction of racemic **1** with $BrBH_2{\cdot}SMe_2$ results in the formation of enantiomers of the C_3-symmetric propeller compound (**4b**).[3e] It appears that the 1,1′-bi-2-naphthol tends to form the symmetric *RRR* and *SSS* compounds rather than the unsymmetrical *SRR* and *RSS* isomers. Unfortunately, the nature of the TMEDA complex of the borate obtained under the present conditions is not clearly understood. The complex is not crystalline enough for X-ray crystal structure analysis, and we could not arrive at a molecular formula on the basis of elemental analysis and H^1 NMR spectral data. However, we have observed that the reaction of racemic **1** (3 equiv) and boric acid (2 equiv) in refluxing benzene (Dean−Stark setup) resulted in the formation of Kaufmann's C_3 symmetric *RRR* and *SSS* propeller **4b**.[17]

Experimental Section

Racemic 1,1′-bi-2-naphthol was prepared by coupling β-naphthol using $FeCl_3$ in water followed by recrystallization from benzene or toluene.[18] Commercial (*S*)-proline supplied by Aldrich was used. Enantiomeric excesses were calculated from α^{25}_D values measured on a Autopol-II automatic polarimeter. It was also confirmed for a few samples of 1,1′-bi-2-naphthol by HPLC analysis using chiralpak OP column with methanol as solvent. Elemental analyses were performed on a Perkin-Elmer elemental analyzer model 240C.

Resolution of Racemic 1,1′-Bi-2-naphthol Using (*S*)-Proline. Typical Procedure. 1,1′-Bi-2-naphthol (5 mmol, 1.43 g) and (*S*)-proline (5 mmol, 0.58g) were taken in methanol (20 mL). The contents were heated at 60 °C for 12 h. Then the reaction mixture was brought to 25 °C and filtered. Methanol was evaporated to obtain a residue. The precipitate and the residue were treated with diethyl ether (100 mL) and dilute HCl (3 N, 20 mL) in separate runs. The organic layer was separated, washed successively with water (2 × 10 mL) and brine (10 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated to obtain 1,1′-bi-2-naphthol. The ee values are based on $\alpha^{25}_D = 34.5$ (C1, THF) for the compound with 100% ee.[19]

Since the complex formed between **1** and **2** in methanol was not soluble in most of the solvents, NMR spectra of the complex could not be recorded. However, elemental analysis of the complex had revealed that **1** and **2** are present in the ratio of 2:1 in the complex (Anal. Calcd for $C_{45}NO_6H_{37}$: C, 78.58; H, 5.42; N, 2.46. Found: C, 78.36; H, 5.50, N, 2.04). This was also confirmed by X-ray diffraction analysis.

Enrichment of Enantiomeric Excesses of Partially Resolved 1,1′-Bi-2-naphthol Using (*S*)-Proline. Partially enriched **1** (5 mmol, 1.43 g) and (*S*)-proline (5 mmol, 0.58 g) were taken in dichloromethane (20 mL), and the contents were refluxed for 12 h. The reaction mixture was brought to 25 °C and filtered. The solvent was evaporated to obtain a residue. The precipitate and the residue were stirred in diethyl ether (100 mL) and dilute HCl (3 N, 20 mL) in separate runs. The organic layer was separated, washed successively with water (2 × 10 mL) and brine (10 mL), and dried over anhydrous $MgSO_4$. The solvent was evaporated to isolate **1**.

Enhancement of Enantiomeric Excesses of Partially Resolved (Scalemic) 1,1′-Bi-2-naphthol. Scalemic **1** (5 mmol), $B(OH)_3$, and TMEDA (1 mmol) were taken in acetonitrile (20 mL). The resulting suspension was refluxed for 12 h. The reaction mixture was cooled to 25 °C and filtered. The filtrate was concentrated to obtain a residue. In separate runs, the precipitate and the residue were treated with diethyl ether (100 mL) and dilute HCl (3 N, 20 mL) for 10 min, washed successively with water (2 × 10 mL) and brine (10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed to obtain **1.**

(17) The ^1H NMR (400 MHz) spectral data were identical to the reported data (ref 3e).

(18) Vogel, A. I. *Text Book of Practical Organic Chemistry*; Longman: Birmingham, AL, 1978.

(19) Various authors report the values of α^{25}_D from 33.2 (ref 12b) to 35.2 (ref 12d) (C1, THF) for 1,1′-bi-2-naphthol of 100% ee. The Fluka catalog (1995−96) reports the α^{25}_D value of 34.5 ± 1 for a sample of purity >99% ee (HPLC). We have calculated the ee values on the basis of the value of $\alpha^{25}_D = 34.5$ (C1, THF) for 100% ee.

X-ray Crystal Structure Analysis. Suitable crystals of 1,1′-bi-2-naphthol−(*S*)-proline complex were obtained as follows. (*S*)-(−)-**1** (5 mmol) was dissolved in methanol (20 mL). To the solution, was added **2** (5 mmol). The contents were heated at 60 °C gently for 10 min and left at 25 °C for 12 h. The precipitated complex was redissolved in hot methanol (20 mL) and left at room temperature for 12 h to obtain the crystals of the complex.

A colorless prismatic crystal of dimensions 0.35 × 0.25 × 0.52 mm suitable for X-ray diffraction was mounted on a glass capillary using glue and transferred to an automated Enraf-Nonius CAD4 diffractometer equipped with a graphite monochromator. Cell dimensions were obtained by the least-squares refinement of well centered 25 reflections in the θ range 2.5−60.0°. Intensity data were collected using Cu Kα (λ = 1.541 84 Å) radiation by the $\omega - 2\theta$ scan mode with a constant scan speed of 4 deg/min. Decay of the crystal during the measurement was monitored by measuring the intensity of two standard reflections at regular intervals, and no appreciable deterioration of the crystal was noticed. 2933 unique data were collected out of which 2839 reflections had $I > 2\sigma(I)$ and were flagged observed for subsequent calculations. The data were corrected for Lorentz and polarization effects.

The structure was solved by direct methods (SIR92) and refined on F^2 using a full-matrix least-squares technique (SHELXL92). All of the hydrogens were located directly in different Fourier maps and refined isotropically. Convergence was achieved at $R = 0.0280$ and w$R = 0.0756$ for 2839 observed reflections. The final difference map revealed no chemically significant information, and the residual density had a maximum peak 0.314e Å^3 and minimum trough at −0.245eÅ^3.

Crystal data for **3** ($C_{45}NO_6H_{37}$): θ range 3.22−59.93°; formula weight 687.76, orthorhombic, space group *P*21 21 21, a = 9.0610(10) Å, b = 13.943(2) Å, c = 27.480(4) Å, V = 3471.8(8) Å^3, Z = 4, D_{calc} = 1.316 g cm^{-3}, μ_{calc} = 6.99 cm^{-1}, $F(000)$ = 1448, index ranges $0 \le h \le 10$, $0 \le k \le 15$, $0 \le l \le 30$, S = 1.144.

Conclusion

Simple and efficient procedures for resolving racemic 1,1′-bi-2-naphthol (**1**) and enrichment of enantiomeric excesses of scalemic mixtures of **1** were developed. The 2:1 complex obtained by the interaction of (*S*)-(−)-**1** and (*S*)-proline was characterized by X-ray diffraction analysis. Besides being useful for the synthesis of chiral 1,1′-bi-2-naphthol, the methods described here should also stimulate further work in this area.

Acknowledgment. We are thankful to the UGC, New Delhi, for support under a Special Assistance Program. We thank Prof. P. T. Manoharan, RSIC, IIT, Madras, for extending us the use of the X-ray diffraction facilities.

JO961937E