Pergamon

Tetrahedron 55 (1999) 3893–3896

TETRAHEDRON

Resolution of Racemic 1,1′-Bi-2-naphthol Using (*S*)-Proline via a Cyclic Borate Ester

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Received 23 November 1998; revised 5 January 1999; accepted 21 January 1999

ABSTRACT: 1,1′-Bi-2-naphtholborane generated from racemic 1,1′-bi-2-naphthol and borane dimethyl sulfide complex reacted with (*S*)-proline in tetrahydrofuran to form a spirocyclic 1,1′-bi-2-naphtholboric proline anhydride. Its two diastereoisomers could be separated efficiently under the experimental conditions, from which enantiomerically pure (*R*)-(+)- and (*S*)-(-)-1,1′-bi-2-naphthol were obtained in ca. 80% overall yield, respectively.

KEYWORDS: resolution, 1,1′-bi-2-naphthol, (*S*)-proline, cyclic borate ester.

1. INTRODUCTION

An important role of 1,1′-bi-2-naphthols with very high enantiomeric purity in asymmetric syntheses has been widely recognized.[1] In order to obtain optically active 1,1′-bi-2-naphthols, a number of preparations have been developed.[2-5] In the course of looking for a convenient preparation of (*S*)-(-)- and (*R*)-(+)-1,1′-bi-2-naphthol, we found that it is a better approach to prepare enantiomerically pure 1,1′-bi-2-naphthols via a cyclic borate ester formed from racemic 1,1′-bi-2-naphthol (**1**), boron compounds and some chiral auxiliaries.[6] There are a number of advantages for the cyclic borate ester method. This method is easy to carry out, it has a short period for the preparation, it can offer both enantiomers of 100% ee in high yield, and it is without using lithium aluminium hydride for liberating enantiomers from the diastereoisomers as compared with the cyclic phosphate ester method.[2] Recently, we described a resolution method for racemic 1,1′-bi-2-naphthol using an alkaloid as the resolving agent via a cyclic borate ester.[7] Although the selected alkaloids can be conveniently obtained from the chiral pool, the price of them is high from a preparative point of view. In order to reduce the cost for preparing enantiomerically pure 1,1′-bi-2-naphthols, we attempted to displace the alkaloids by a naturally occurring amino acid. Fortunately, we met with success through the reaction of racemic 1,1′-bi-2-naphtholborane (**2**) with (*S*)-proline (**3**). We report herein the new procedure for preparing enantiomerically pure 1,1′-bi-2-naphthols using (*S*)-proline as the resolving agent (Scheme 1).

2. RESULTS AND DISSCUSSIONS

Racemic 1,1′-bi-2-naphthol (**1**) reacted with borane dimethyl sulfide complex in diethyl ether at room temperature to give a homogeneous solution with the evolution of hydrogen. The solvent and the volatile

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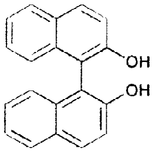
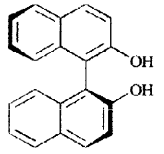
PII: S0040-4020(99)00085-X

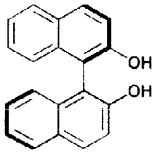
substances were removed under reduced pressure, the residual solid was dissolved in fresh dry tetrahydrofuran and dry (*S*)-proline powder (**3**) (the molar number of proline added is the same as that of 1,1'-bi-2-naphthol) was added. The mixture was refluxed with constant stirring for 3 hours to produce a large amount of white precipitate (a THF solvolyte of **4A**), cooled to room temperature, filtered and a solid was collected. It did not melt below 300℃. After the recrystallization from acetonitrile, the elemental analysis, ^{1}H NMR spectrum and Mass Spectrum of the sample obtained demonstrated that it was a 1,1'-bi-2-naphtholborane proline derivative **4A** ($C_{25}H_{20}BNO_4$). The compound **4A** was different from 1,1'-bi-2-naphtholborane quinine or cinchonine derivatives[7] which were sensitive to moisture; **4A** was stable in air, and it did not decompose in an acid solution under constant stirring for 24 hours at room temperature. It is difficult for 4A to dissolve in petroleum, benzene, toluene, chloroform, diethyl ether, tetrahydrofuran, acetone, ethanol and water. However, it is soluble in acetonitrile, DMF and DMSO. The stability of compound **4A** to hydrolysis might be in close relationship with its structure. There is a strong absorption at ca. 1230 cm^{-1} in the IR spectrum of **4A**. This fact implied that the compound might possess a N→B coordinated bond. That is, **4A** might be a chelate compound (see Scheme 1).



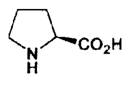
rac-**1**
Rac-1,1'-bi-2-naphthol



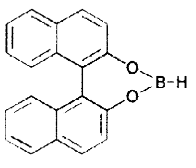
(*S*)-(-)-**1**
(*S*)-1,1'-bi-2-naphthol



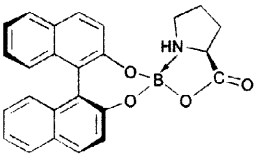
(*R*)-(+)-**1**
(*R*)-1,1'-bi-2-naphthol

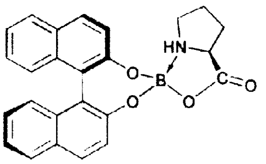


(*S*)-**3**
(*S*)-proline

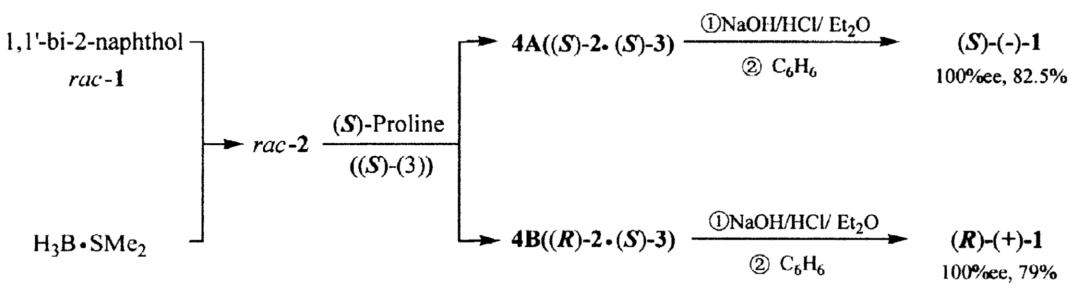


rac-**2**
1,1'-bi-2-naphtholborane





4A((*S*)-**2**·(*S*)-**3**) **4B**((*R*)-**2**·(*S*)-**3**)
1,1'-bi-2-naphtholboric proline anhydride



Scheme 1

The tetrahydrofuran mother liquor removed from the solid was evaporated under reduced pressure to give another solid with IR and MS similar to those of **4A**. It was clear that it was the other diastereomer **4B** of 1,1'-bi-2-naphtholborane (*S*)-proline derivative. The remarkable difference in the solubility in tetrahydrofuran between **4A** and **4B** is just a basis of separating two diastereomers of 1,1'-bi-2-

naphtholborane proline derivative. Both solids thus obtained ware treated separately with a dilute NaOH and HCl with stirring and extracted with diethyl ether. The extracts were dried over Na_2SO_4, filtered and the solvent removed to give (*S*)-(-)-1,1′-bi-2-naphthol of ca. 95% ee and (*R*)-(+)-1,1′-bi-2-naphthol of ca. 90% ee. In order to obtain both enantiomers of 100% ee, the products enriched in (*S*)-(-)- or (*R*)-(+)- isomer were purified further by "kinetic" crystallization.[5a] They were dissolved in an appropriate amount of boiling benzene and cooled slowly to ambient temperature to give the desired massy crystalline products in about 80 % overall yield (cacld. from racemic 1,1′-bi-2-naphthol), respectively.

Resolution of racemic 1,1′-bi-2-naphthol utilizing (*S*)-proline was previously reported. Periasamy[8] et al. made racemic 1,1′-bi-2-naphthol (**1**) react with (*S*)-proline (**2**) in a 1 : 1 molar ratio in benzene under refluxing condition for 24 hours to provide 65% ee (*S*)-(-)-1,1′-bi-2-naphthol and 44% ee (*R*)-(+)-1,1′-bi-2-naphthol, and, in order to obtain both enantiomers of 1,1′-bi-2-naphthol with very high optical purity, they did either by three successive repetitions of the above procedure or by enriching the excess enantiomer in boric acid-N,N,N′,N′-tetramethylethylenediamine system. This is quite troublesome. Even so, the overall yields of (*S*)-(-)- and (*R*)-(+)-isomer are merely 43% and 31.8%, respectively. As compared with their method, our resolution method is not only different in preparative principle, but also possesses some outstanding advantages. Perhaps it is one of the most efficient methods for preparing rapidly enantiomerically pure 1,1′-bi-2-naphthols in high yield at the present time.

3. EXPERIMENTAL

2.86 g (10mmol) of racemic 1,1′-bi-2-naphthol **1** and 60 mL of dry diethyl ether were added to a dry 100 mL round-bottomed two-neck flask (fitted with a magnetic stirring bar, a 25 ml pressure-equalized additive funnel covered with a rubber septum and an oil bubbler with a stopcock), under argon atmosphere. To the flask, a solution of 1.5 mL of 8.86 M borane dimethyl sulfide in 15 mL of diethyl ether was added dropwise with stirring. Hydrogen gas evolved in the course of the addition and the reaction temperature was maintained below 20℃. After the ethereal solution was completely added, stirring was continued for an additional 3 hours. The solvent and the volatile substances were removed under reduced pressure. To the residue, 50 mL of newly dried tetrahydrofuran was added and stirred to give a clear solution, which was followed by adding 1.15 g (10mmol) of dry (*S*)-proline powder **3** with constant stirring. The mixture was refluxed for 3 hours to produce a large amount of white precipitate, cooled to room temperature and filtered. The solid was washed with fresh tetrahydrofuran, dried under reduced pressure to give 2.3g of product (a solvolyte formed **4A** with THF). It did not melt below 300℃. ν_{max}(KBr disk, cm^{-1}): 1750s (ν^{as}_{COOB}); 1335ms ($\nu^{as}_{B\text{-}O}$); 1250vs ($\nu^{as}_{binaph\text{-}O}$)†; 1230s,sh ($\nu^{as}_{N\rightarrow B}$); 1080vs ($\nu^{s}_{B\text{-}O}$); 1020vvs ($\nu^{s}_{C\text{-}O}$). After the recrystallization from acetonitrile, pure **4A** was obtained. Found: C, 73.21; H, 4.81; N, 3.24; B, 2.61. $C_{25}H_{20}BNO_4$ requires C, 73.37; H, 4.93; N, 3.42; B,2.64. δ_H (89.55MHz DMSO-d_6+CD_3CN): 1.65-2.33 (4H, m, CH_2CH_2)‡; 2.70-3.40 [3H, m, NCH_2+NH(3.26, 1H, S)]; 4.53 (1H, t, NCHCOO); 6.97-7.55 (8H, m, 5,6,7,3,5′,6′,7′,3′-binaph-H); 7.77-8.03 (4H, dd, 4,4′,8,8′-binaph-H). MS (EI, 70ev): m/z, 409 (44, M^+), 312 (13), 268 (15), 239 (14), 70 (100%). The THF solvolyte of **4A** was treated with 20 mL of 2N sodium hydroxide for 0.5 hours under stirring, followed by adding 20 mL of 2N hydrochloric acid and 40 mL diethyl ether and stirred for an additional 0.5 hours to give a clear two phase solution. The organic phase was separated, dried over anhydrous sodium sulfate and filtered. The organic phase was collected and evaporated to give 1.3g of solid residue. To the residue 15 mL of benzene were added and heated to dissolve completely. The solution was cooled slowly to room temperature to isolate a massy transparent crystal, filtered, 1.18g of the crystals of (*S*)-(-)-1,1′-bi-2-naphthol were obtained, m.p. 207-208℃, $[\alpha]_D^{25}$ −35.4 (*c* 1, THF), 100 % ee [Lit.,[2a] $[\alpha]_D^{25}$ −34 (*c* 1, THF)], the overall yield was 82.5%.

The tetrahydrofuran mother liquor removed from the solvolyte of **4A** was evaporated under reduced pressure to give 2.35g of yellowish solid, which was essentially a THF solvolyte of **4B**. The solid did not melt below 300℃. It did not need to be purified and treated directly through the alkalification, the acidification and "kinetic" crystallization in a similar procedure as above to give 1.13g of massy transparent crystals of (*R*)-(+)-1,1'-bi-2-naphthol, m.p. 207-208℃, $[\alpha]_D^{25}$ +35.3 (*c* 1, THF), 100 % ee, the overall yield was 79%.

† "binaph" is an abbreviation for binaphthyl moiety.

‡ There is an impure peak of undeuterated acetonitrile at ca. 2ppm.

4. ACKNOWLEDGMENT

Financial support by the National Natural Science Foundation of China and the Natural Science Foundation of Hubei Province is gratefully acknowledged.

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