

An improved approach to (*R*)-(+)-1,1'-bi-2-naphthol of 100% enantiomeric excess via a cyclic borate ester

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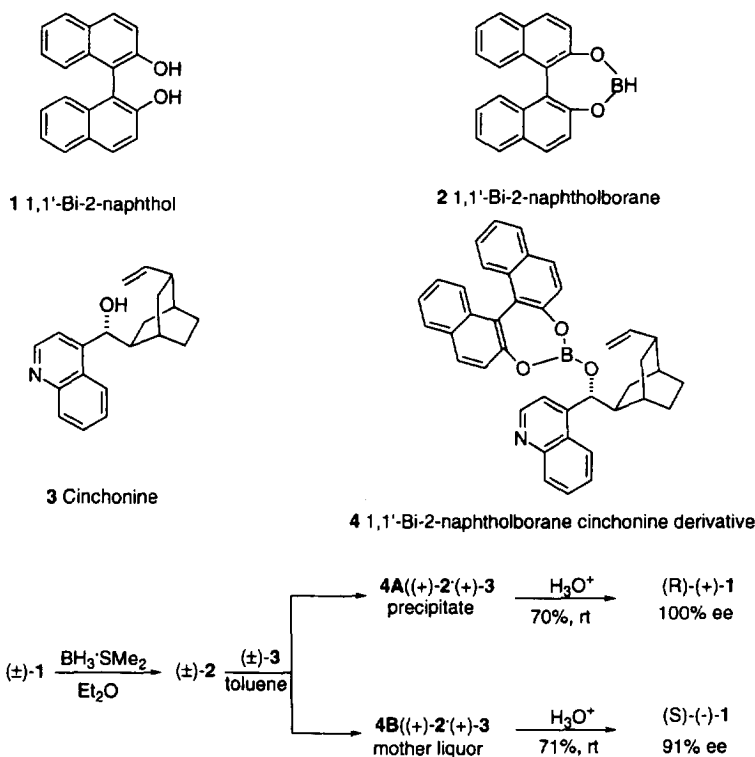
Abstract: The preparation for (*R*)-(+)-1,1'-bi-2-naphthol of 100% ee using cinchonine as a resolving agent via a cyclic borate ester is described. © 1997 Elsevier Science Ltd

C₂ chiral 1,1'-bi-2-naphthols occupy a position of prime importance in a wide range of enantioselective reactions.¹ Numerous synthetic approaches to these two compounds, namely (*R*)-(+)- and (*S*)-(–)-1,1'-bi-2-naphthols have been developed. We recently reported the preparation of enantiomerically pure 1,1'-bi-2-naphthols via a cyclic borate ester formed from the reaction of racemic 1,1'-bi-2-naphtholborane **2** with quinine in tetrahydrofuran.² Under the experimental conditions, one diastereomer is soluble, and the other precipitates. This precipitated diastereomer, after being simply treated, offered (*S*)-(–)-1,1'-bi-2-naphthol of 100% ee. However, the separation and the purification of the other diastereomer dissolved in tetrahydrofuran is quite troublesome, though it could give (*R*)-(+)-1,1'-bi-2-naphthol with high enantiomeric excess. In order to search for a convenient preparation of (*R*)-(+)-1,1'-bi-2-naphthol of high enantiomeric purity, we examined the reaction of 1,1'-bi-2-naphtholborane **2** with cinchonine **3**. Here we wish to report our primary research results. We found that both diastereomers of 1,1'-bi-2-naphtholborane cinchonine derivative **4** can not be separated efficiently in tetrahydrofuran. Fortunately, in toluene one diastereomer of 1,1'-bi-2-naphtholborane cinchonine derivative **4A** can produce nearly quantitatively a white precipitate, which, treated with 2N hydrochloric acid and the product liberated recrystallized from Et₂O, provides (*R*)-(+)-1,1'-bi-2-naphthol with 100% ee in 70% yield. The other diastereomer **4B** dissolved in toluene is obtained as a solid residue after the solvent is removed under reduced pressure. This residue is worked up as in the above procedure to furnish (*S*)-(–)-1,1'-bi-2-naphthol with 91% ee in 71% yield. It appears that the present approach and the method we had previously found to obtain 100% ee (*S*)-(–)-1,1'-bi-2-naphthol² are complementary to each other. Now we are in position to obtain both enantiomers of 1,1'-bi-2-naphthol with 100% ee in high yield by relatively simple procedures. The preparation of enantiomerically pure 1,1'-bi-2-naphthols using cinchonine as a resolving agent via cyclic borate ester is shown in Scheme 1.

Experimental

A sufficiently dry 100 ml round-bottom two-neck flask fitted with a magnetic stirring bar, a rubber septum and an oil bubbler with a stopcock was charged with 2.0 g (7 mmol) of racemic 1,1'-bi-2-naphthol. 50 ml of anhydrous Et₂O was introduced under a positive pressure of argon and stirred, the solid 1,1'-bi-2-naphthol gradually dissolved to give a clear solution. 1 mL 9.0 M of H₃B•S(CH₃)₂³ was added dropwise by a syringe with constant stirring and maintained the reaction temperature below 20°C. After the evolution of hydrogen stopped, the solvent and the volatile substances were removed under reduced pressure. To the solid residue was added 40 mL anhydrous toluene, stirred until the solid dissolved completely, then 2.10 g (7.14 mmol) of cinchonine was added with stirring. The reaction mixture was refluxed for 3 h, then cooled to room temperature, filtered, the white solid

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Scheme 1.

separated was washed with toluene (10 ml \times 2) and anhydrous Et₂O (10 ml \times 2) successively, dried under reduced pressure, 2.0 g of powdery white solid (4A) was obtained, m.p. 238–240°C, yield 97%. IR (cm⁻¹): 1640w (ν_{CH=CH2}); 1330s, 1074s (ν_{B-O}); 1246s, 1045s (ν_{C-O}); MS:M⁺, 588 (calcd. for BC₃₉H₃₃N₂O₃, 588). The solid was transferred into 100 ml flask, added 20 ml methylene chloride, 15 ml 2N HCl and stirred at room temperature for 2 h, the organic layer was separated, the water phase was extracted with methylene chloride (8 ml \times 2), the organic phase was combined and dried over anhydrous Na₂SO₄, filtered, the filtrate was evaporated to dryness under reduced pressure to provide 0.86 g of crude (R)-(+)-1,1'-bi-2-naphthol, which was recrystallized from Et₂O to give 0.70 g of transparent crystal, the yield is 70% (based on racemate 1). m.p. 206–207°C. [α]_D²⁰=+35.3 (C=1, THF), 100% ee. ¹H NMR analysis showed the absence of impurity.

The toluene mother liquor removed from the white precipitate was concentrated to dryness, 1.95 g solid residue was obtained, yield 95%. m.p. 238–240°C, IR (cm⁻¹): 1640 w (ν_{CH=CH2}); 1337s, 1117vs (ν_{B-O}); 1253s, 1070s (ν_{C-O}). MS: M⁺ 588. (calcd. for BC₃₉H₃₃N₂O₃, 588). The solid was treated as above procedure to offer 0.71 g crystals, yield 71%. m.p. 206–207°C [α]_D²⁰=-32.2 (C=1, THF). 91% ee.

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