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A FACILE LARGE SCALE PREPARATION OF RACEMIC 2.2′-DIHYDROXY-1,1′-BINAPHTHYL

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A FACILE LARGE SCALE PREPARATION OF RACEMIC 2,2'-DIHYDROXY-1,1'-BINAPHTHYL

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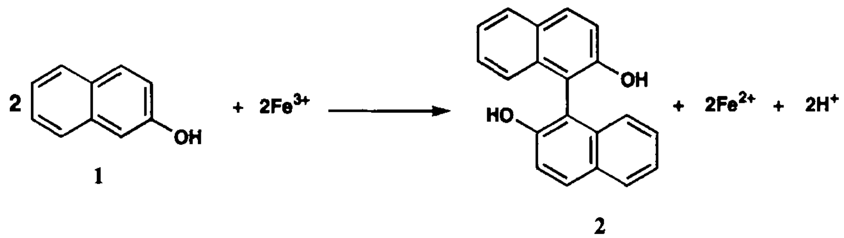
Optically pure 2,2'-dihydroxy-1,1'-binaphthyl (BN) (**2**) has been widely utilized in a variety of syntheses as a chiral auxiliary in enantioselective reactions,[1] as chiral shift reagent,[2] and as a moiety incorporated in chiral crown ethers for complexation of amino acids.[3] Due to the importance of chiral BN and its derivatives in organic synthesis as chirality inducers, much attention has been paid to its synthesis. Several analytical and preparative methods for the preparation of enantiomerically pure BN have been reported. They include chromatography using a chiral stationary phase,[4] oxidative dimerization of β-naphthols with chiral copper (II) amine complexes as oxidants,[5] and the resolution of the dimethyl ether of BN without chiral auxiliaries by entrainment.[6] The most conventional preparation of optically pure BN has so far been the fractional crystallization of the cinchonine salt of 1,1'-binaphthyl-2,2'-diyl hydrogen phosphate described by Jaques and Fouquey,[7] followed by the reductive removal of the phosphoric acid moiety with Red-Al[8] after esterfication. However, all these methods become less useful when the preparation of large amounts of optically pure BN (**2**) is desired.



The resolution by hydrolysis of BN diesters catalyzed by cholesterol esterase was reported by Kazlauskas[9] in 1989. This process allows the preparation of optically pure BN (**2**) on a 0.5 mol scale. Furthermore it involves fewer manipulations and is simpler and faster than the cinchonine method. It appears as the method of choice for the preparation of larger amounts of optically pure BN. There is, however, no large scale preparation for the starting material, racemic BN (**2**) actually in the literature. The common method for the synthesis of racemic BN is the oxidative coupling of β-naphthol (**1**). This usually is performed in water using iron(III) chloride as the oxidizing reagent[10] and gives racemic BN (**2**) in 52-77% yield. The method is limited to the synthesis of small amounts of BN (**2**) because of the low solubility of β-naphthol in water. The solubility problem might be circumvented by solid state coupling.[11] However, this method has not yet been shown to be suitable for large scale preparations, although the reported yields of small scale preparations were high. A disadvantage of this method is the necessity of using of finely powdered ferric chloride.

In the search for a suitable solvent where both ferric chloride and β-naphthol (**1**) show excellent solubility, the coupling reaction was performed in THF. This allows the facile synthesis of large amounts of BN using the least volume of solvent of all procedures reported in the literature[12] and gave a total yield of 60%. We thus describe a rapid, large scale synthesis of racemic BN (**2**) by using β-naphthol (**1**) and a large excess of ferric chloride hexahydrate in THF (all of inexpensive technical grades). This allows the preparation of racemic BN on a 2.5 mol laboratory scale using only 1.3 L of solvent. The relatively final low yield is offset by the easy work up, where products such as quinones and unreacted ß-naphthol (**1**) are readily removed by washing with water followed by a single crystallization from toluene, thus in our opinion, making this method superior to other routes.

EXPERIMENTAL SECTION

The ^{1}H-NMR spectrum was recorded in $CDCl_3$ on a Varian Unity 400. The chemical shifts are reported in δ (ppm) relative to TMS as internal standard. The mass spectrum was recorded on a VG Masslab12-250 spectrometer. Elemental analyses were performed at the Microanalysis Laboratory at the University of Copenhagen. The mps were measured on a Büchi apparatus and are uncorrected. All solvents and reagents were of technical grade, obtained from commercial sources and used without further purification. Silica was purchased from Merck: Kieselgel 60, 0.063-0.200 mm, 70-230 mesh ASTM.

(R,S)-2,2'-Dihydroxy-1,1'-binaphthyl (2).- A 5 L round bottom flask equipped with a mechanical stirrer (or magnetic stir bar) and a reflux condenser was charged with $FeCl_3$•$6H_2O$ (2162.4g, 8.0 mol) and 1.3 L of THF. The $FeCl_3$•$6H_2O$ usually dissolved completely after standing at room temperature overnight. β-Naphthol (**1**) (720.85 g, 5.0 mol) was added to the stirred solution, and the mixture was refluxed for 3 hrs. After cooling to room temperature the dark brown reaction mixture was transferred into approx. 10 L of ice cold dilute hydrochloric acid (ca. 3 %) with stirring (three 5 L Erlenmeyer flasks) and stirred magnetically for about 1 hr after complete addition. The greasy brown and grey solid precipitates were then collected using a glass frit, washed with dilute hydrochloric acid (ca. 3%), and stirred overnight as a suspension in approximately 10 liters of dilute hydrochloric acid (ca. 3%). The usually grey powder formed was collected using a glass frit and washed thoroughly with 3% hydrochloric acid and water. The wet product was transferred into a 5 L round-bottomed flask equipped with a Dean-Stark trap and a magnetic stirr bar. Toluene (2.5 L) was added and the water was removed by azeotropic distillation to dissolve the product completely. Upon slow cooling overnight to room temperature, white crystals formed and were collected (glass frit) and thoroughly washed with light petroleum ether and dried in air to give BN (**2**) (386.5 g, 54 % yield) as white crystals, mp. 216-218°, lit.[10c] mp. 213.5-216°. A second crop may be obtained from the mother liquor: filteration through a pad of silica (4 cm), and concentration gave an additional amount of BN (**2**) (42.9

g, 6% yield), mp. 214-217°. ^{1}H NMR: δ 7.97 (d, J = 9 Hz, 2H), 7.89 (d, J = 8 Hz, 2H), 7.38 (d, J = 9 Hz, 2H), 7.37 (ddd, J = 7/8/1.5 Hz, 2H), 7.30 (ddd, J = 7/8/1.5 Hz, 2H), 7.15 (d, J = 8 Hz, 2H), 4.99-5.08 (broad, -OH, 2H). MS (EI): m/e = 286.

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.90; H, 4.93. Found: C, 84.02; H, 4.92

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