



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 10, p.93 (2004); Vol. 76, p.1 (1999).

RESOLUTION OF 1,1'-BI-2-NAPHTHOL

[1,1'-Binaphthalene]-2,2'-diol]



Submitted by Dongwei Cai, David L. Hughes, Thomas R. Verhoeven, and Paul J. Reider¹.
 Checked by Rachel van Rijn and Amos B. Smith, III.
 Discussion Addendum *Org. Synth.* **2014**, *91*, 1

1. Procedure

A 500-mL flask, equipped with a magnetic stirring bar and a reflux condenser, is charged with 1,1'-bi-2-naphthol (23.0 g, 80 mmol) and N-benzylcinchonidinium chloride (18.6 g, 44 mmol) (Note 1). Acetonitrile (300 mL) is added, and the resulting suspension is refluxed for 4 hr, cooled and stirred at room temperature overnight. The mixture is then cooled to 0–5°C, kept at that temperature for 2 hr, and filtered (Note 2). The filtrate is concentrated to dryness, redissolved in ethyl acetate (300 mL), and washed with 1 N hydrochloric acid (HCl, 2 × 100 mL) (Note 3) and brine (100 mL). The organic layer is dried over sodium sulfate (Na₂SO₄), filtered, and concentrated to a light brown solid [10.28–10.65 g, mp 205–206°C, 89–93% recovery, 99.0% ee S-enantiomer [α]_D²¹ –27.6–29.4° (THF, c 1)] (Note 4), (Note 5), (Note 6).

The solid complex is washed with acetonitrile (50 mL). This acetonitrile solution is discarded because of the low ee (~80% ee of the S-enantiomer is contained). The resulting solid complex (96% ee, R-enantiomer) is transferred to a 250-mL flask. Methanol (100 mL) is added, and the resulting suspension is refluxed for 24 hr to upgrade the enantiomeric excess to >99% ee. After the mixture is cooled to room temperature, it is filtered and the solid washed with methanol (20 mL). The solid complex is suspended in a mixture of ethyl acetate (300 mL) and 1 N HCl (150 mL) and stirred until complete dissolution occurs (0.5 hr). The solution is transferred to a separatory funnel, and the organic layer is separated and then washed with 1 N HCl (150 mL) and brine (150 mL). The organic layer is dried over Na₂SO₄, filtered, and concentrated to an off-white crystalline solid [9.83–10.16 g, 85–88% recovery, mp 206–207°C, >99.8% ee of the R-enantiomer [α]_D²¹ 26.2–30.9° (THF, c 1)] (Note 4), (Note 5), (Note 6).

2. Notes

1. Racemic 1,1'-bi-2-naphthol and N-benzylcinchonidinium chloride were purchased from Aldrich Chemical Company, Inc., acetonitrile (LC grade) was obtained from Fisher Scientific.
2. The enantiomeric excess of 1,1'-bi-2-naphthol in the filtrate at room temperature is 98.6% and at 0–5°C 99.0%.
3. These acid washes are to remove residual N-benzylcinchonidinium chloride in the filtrate.
4. Numerous chiral HPLC columns have been used for determination of chiral purity of 1,1'-bi-2-naphthol.^{2,3} The submitters used Diacel Chiralpak OP(+) column (4.6 mm × 250 mm) at room temperature for their chiral assay. Typical retention times of 1,1'-bi-2-naphthol are 14 min (R-enantiomer) and 20 min (S-enantiomer) using methanol as an eluting solvent at 0.5 mL/min. The submitters' detection limit of minor enantiomers is about 0.1%. The checkers used a Pirkle covalent D-phenylglycine column using isopropyl alcohol:hexane (5:95) as the eluting solvent at 1.0 mL/min with UV at 312 nm.
5. Enrichment to >99.8% ee is possible by recrystallization from a tert-butyl methyl ether

(MTBE)/hexane mixture: 1.0 g of (S)-1,1'-bi-2-naphthol is dissolved in MTBE (10 mL), then hexane is added (20 mL). The resulting solid is stirred at room temperature for 2 hr, then filtered to provide a white crystalline solid (0.65 g, >99.8% ee, >99 wt% purity).

6. Other physical properties of the products are as follows: IR cm^{-1} : 3550 (s), 3050 (m), 1610 (m), 1590 (m), 1390 (m), 1180 (s), 1140 (s); ^1H NMR (250 MHz, CDCl_3) δ : 5.0 (s, 2 H, OH), 7.16 (d, 2 H, J = 8.3), 7.30 (m, 2 H), 7.38 (m, 4 H), 7.90 (d, 2 H, J = 8.1), 7.99 (d, 2 H, J = 8.9); ^{13}C NMR (62.9 MHz, CDCl_3) δ : 110.8, 117.8, 124.0, 124.2, 127.5, 128.4, 129.5, 131.4, 133.4, 152.8; HRMS (FAB, m-nitrobenzyl alcohol): R enantiomer, m/z 304.1335 [(M+ NH_4^+); calcd for $\text{C}_{20}\text{H}_{14}\text{O}_2+\text{NH}_4^+$: 304.1337]; S-enantiomer, m/z 304.1331 [(M+ NH_4^+); calcd for $\text{C}_{20}\text{H}_{14}\text{O}_2+\text{NH}_4^+$: 304.1337].

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

Both enantiomers of 1,1'-bi-2-naphthol are widely used for various applications: 1) chiral inducing agents for catalytic, asymmetric reactions such as the Diels-Alder reaction,⁴ ene reaction,^{5 6} or as Lewis acids;^{7 8} 2) enantioselective reduction of ketones;^{9 10} 3) synthesis of chiral macrocycles^{11 12} and other interesting compounds.¹³ Previously reported resolutions include: 1) making a cyclic phosphate of binaphthol, then resolution and subsequent reduction to release the pure binaphthol,^{14 2 15 16 17 18} 2) using enzymatic hydrolysis of the diester of binaphthol;^{19 3} and 3) forming inclusion complexes with suitable compounds.^{20 21 22} The use of N-benzylcinchonidinium chloride to make inclusion complexes was reported by Tanaka and co-workers for obtaining one enantiomer of binaphthol.^{23 24} Using acetonitrile as solvent, in which the inclusion complex has very low solubility, allows for the isolation of both enantiomers with high enantiomeric excess. This simple and efficient procedure represents a much better resolution for 1,1'-bi-2-naphthol.²⁵

References and Notes

1. Merck Research Labs, P.O. Box 2000, Rahway, NJ 07065.
2. Jacques, J.; Fouquey, C. *Org. Synth., Coll. Vol. VIII* **1993**, 50;
3. Kazlauskas, R. J. *Org. Synth., Coll. Vol. IX* **1998**, 77.
4. Bao, J.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1993**, *115*, 3814.
5. Terada, M.; Motoyama, Y.; Mikami, K. *Tetrahedron Lett.* **1994**, *35*, 6693;
6. Mikami, K.; Matsukawa, S. *Tetrahedron Lett.* **1994**, *35*, 3133.
7. Sakane, S.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1985**, *26*, 5535;
8. Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310.
9. Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709;
10. Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717.
11. Sogah, G. D. Y.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3035;
12. Lehn, J.-M.; Simon, J.; Moradpour, A. *Helv. Chim. Acta* **1978**, *61*, 2407.
13. Miyano, S.; Tobita, M.; Nawa, M.; Sato, S.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1980**, 1233.
14. Fabbri, D.; Delogu, G.; De Lucchi, O. *J. Org. Chem.* **1993**, *58*, 1748;
15. Truesdale, L. K. *Org. Synth., Coll. Vol. VIII* **1993**, 46;
16. Kyba, E. P.; Gokel, G. W.; de Jong, F.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173;
17. Gong, B.-q.; Chen, W.-y.; Hu, B.-f. *J. Org. Chem.* **1991**, *56*, 423;
18. Brunel, J.-M.; Buono, G. *J. Org. Chem.* **1993**, *58*, 7313.
19. Kazlauskas, R. J. *J. Am. Chem. Soc.* **1989**, *111*, 4953;
20. Toda, F.; Tanaka, K. *J. Org. Chem.* **1988**, *53*, 3607;
21. Kawashima, M.; Hirata, R. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2002;
22. Periasamy, M.; Bhanu Prasad, A. S.; Bhaskar Kanth, J. V.; Reddy, C. K. *Tetrahedron*:

- Asymmetry* **1995**, *6*, 341.
23. Tanaka, K.; Okada, T.; Toda, F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1147;
24. Toda, F.; Tanaka, K.; Stein, Z.; Goldberg, I. *J. Org. Chem.* **1994**, *59*, 5748.
25. Cai, D.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett.* **1995**, *36*, 7991.
-

Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

1,1'-Bi-2-naphthol:
[1,1'-Binaphthalene]-2,2'-diol (8,9); (602-09-5)

N-Benzylcinchonidinium chloride:
Cinchonanium, 9-hydroxy-1-(phenylmethyl)-, chloride, (9S)- (10); (69221-14-3)

Acetonitrile: TOXIC (8,9); (75-05-8)

(S)-(-)-1,1'-Bi-2-naphthol:
[1,1'-Binaphthalene]-2,2'-diol, (S)-(-)- (8);
[1,1'-Binaphthalene]-2,2'-diol, (S)- (9); (1853-99-2)

(R)-(+)-1,1'-Bi-2-naphthol:
[1,1'-Binaphthalene]-2,2'-diol, (R)-(+)- (8);
[1,1'-Binaphthalene]-2,2'-diol, (R)- (9); (18531-94-7)