



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.

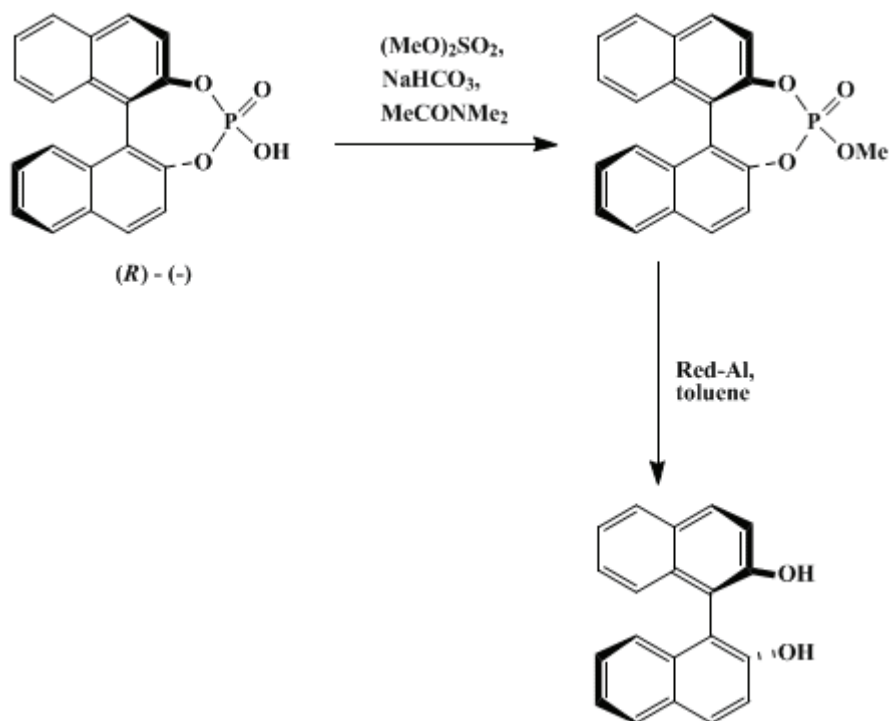
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries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

These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 8, p.46 (1993); Vol. 67, p.13 (1989).

(*R*)-(+)-1,1'-BINAPHTHALENE-2,2'-DIOL

[1,1'-Binaphthalene]-2,2'-diol,(*R*)-]



Submitted by Larry K. Truesdale¹

Checked by Georg W. Schröder and K. Barry Sharpless.

1. Procedure

A. (*R*)-(-)-Methyl 1,1'-binaphthyl-2,2'-diylphosphate. A 200-mL, three-necked flask equipped with a magnetic stirrer and a gas bubbler is charged with 20.0 g (57.4 mmol) of (*R*)-(-)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate (Note 1), 40 mL of *N,N*-dimethylacetamide, and 10.0 mL (105.7 mmol) of dimethyl sulfate (Note 2). The resulting pale-yellow oil is then treated cautiously in small portions with 10.4 g (123.8 mmol) of sodium bicarbonate. The addition causes gas evolution and foaming. Foaming subsides after ca. 20 min, and the resulting turbid yellow solution is stirred overnight at room temperature (Note 3).

The reaction mixture is poured into a mixture of 300 mL of toluene and 100 mL of ethyl acetate. The resulting milky solution is washed twice with 100-mL portions of deionized water and twice with 100-mL portions of brine and then dried over anhydrous sodium sulfate. The drying agent is removed by filtration and the filtrate is concentrated on a rotary evaporator under reduced pressure in a 50°C bath. The semisolid residue is slurried in 55 mL of ether and then collected by filtration on a sintered-glass funnel. After the solid is washed 4 times with 10 mL of ether, it is set aside and the filtrate is evaporated to dryness. The residue is slurried in 10 mL of ether. The solid is collected on a glass frit and washed twice with 10 mL of ether. Both solids are combined and dried under reduced pressure to give 16.4 g (45.2 mmol) (79%) of phosphate as an off-white powder, mp 215–217°C; [α]_D²⁵ -526.8° (THF, c 1.16) (Note 4).

B. Crude (*R*)-(+)-1,1'-binaphthalene-2,2'-diol.

[Caution! Gases evolved in this step create a stench and are toxic. The use of an efficient fume hood is imperative (Note 5).]

A 2-L, three-necked flask equipped with Y-tube, magnetic stirrer, dropping funnel topped with gas bubbler, thermometer, and drying tube is charged with 14.7 g (40.6 mmol) of crude (*R*)-(-)-methyl 1,1'-binaphthyl-2,2'-diyl phosphate and 350 mL of dry **toluene**. The mixture is stirred under **nitrogen** and heated with a steam bath until dissolution occurs (44°C). The solution is then cooled in an ice-water bath to 10°C. The cooling bath is removed and a solution of 27.0 mL (91.8 mmol) of Red-Al (**Note 6**) in 35 mL of **toluene** is added from the dropping funnel over a 90-min period. The mixture turns yellow, evolves a gas, and heats up to 26°C. Gas evolution ceases 20 min after the addition is completed. TLC analysis (silica gel plate developed with **ethyl acetate**) indicates that the reaction is complete.

The entire reaction mixture is poured into 430 mL of 10% **hydrochloric acid** (mild exothermic reaction). The organic layer is separated and washed with another 430-mL portion of 10% **hydrochloric acid**. After further washes with 150 mL of brine and 160 mL of deionized water, all aqueous layers are combined and back-extracted with a 550-mL portion of 3 : 2 **toluene** : **methanol** and two 300-mL portions of **toluene**. The combined organic layers are dried over anhydrous **sodium sulfate**, and filtered. The solvent is removed on a rotary evaporator under reduced pressure in a 45°C bath to give 11.4 g (98%) of crude product as a bright-yellow microcrystalline solid, mp 203–205°C.

C. *Recrystallization of (R)-(+)-1,1'-binaphthalene-2,2'-diol*. A 200-mL flask with a reflux condenser is charged with 11.4 g of crude (*R*)-(+)-1,1'-binaphthalene-2,2'-diol and 1.5 g of **Norit A**, and refluxed for 5 min. The hot solution is filtered through a pad of 5 g of Celite on a glass frit. The Celite and **Norit A** from the frit are slurried together with 1.5 g of **Norit A** in 70 mL of **toluene**, refluxed for 5 min, and filtered hot through a pad of 5 g of Celite on a glass frit. The Celite is washed with 70 mL of hot **toluene**. The combined filtrates are warmed to 50°C to dissolve the precipitated crystals and filtered once again while warm through a pad of 5 g of Celite on a glass frit, which is then washed with 40 mL of hot **toluene**. The filtrate is freed from solvent on a rotary evaporator and the residue is recrystallized from 75 mL of **toluene** with stirring. The mixture is stirred overnight at ambient temperature. The resulting suspension is filtered and the filter cake is washed with two 10-mL portions of **toluene**. The recrystallized product is then dried under reduced pressure (high vacuum) to give 9.62 g of white, microcrystalline material in the first crop. This material melts at 207–209°C, $[\alpha]_D^{25} +33.6^\circ$ (THF, c 1.11) (**Note 7**) and (**Note 8**).

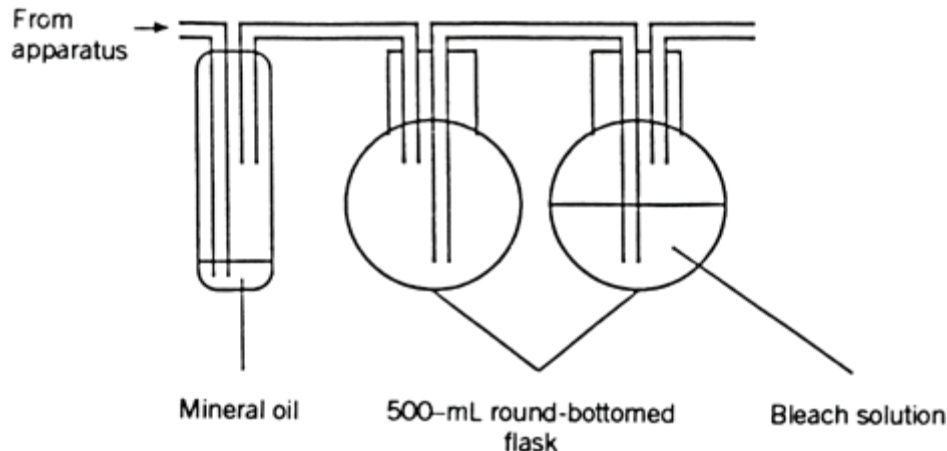
Concentration of the filtrate and **toluene** washings under reduced pressure to ca. 11 mL affords, after cooling, collecting, washing 3 times with 3 mL of **toluene**, and drying the solid material, a second crop of product that weighs 1.04 g. This crop is an off-white microcrystalline powder, mp 204–206°C and $[\alpha]_D^{25} +33.6^\circ$ (THF, c 1.12) (**Note 9**).

The two crops (10.66 g) represent 94% recovery on recrystallization. The yield of recrystallized product is 92% in the reductive cleavage of the phosphate ester and 73% overall.

2. Notes

1. The starting material was prepared by the method described in the companion procedure of Fouquey and Jacques (*Org. Synth., Coll. Vol. VIII, 1993, 50*) and had $[\alpha]_D^{25} -704.7$ (MeOH, c 1.0).
2. **Dimethyl sulfate** was obtained from Aldrich Chemical Company, Inc. It is highly toxic and carcinogenic, and it should be handled only in a well-ventilated hood.
3. The reaction was complete by TLC (silica gel plate) analysis. The consumption of starting material and the formation of product can be monitored using a 5 : 2 (v : v) mixture of **ethyl acetate** : **hexane** as the solvent.
4. The enantiomeric excess of this product was determined to be >99.5% using a chiral stationary phase HPLC (preparative Regis Pirkle Type 1-A, 10 × 250 mm id., 7.5 mL/min flow rate, 100-psi pressure, 10% **2-propanol** in **hexane**, detector at 284 nm). The *R*-(-)-enantiomer is eluted first and the peaks are well separated.² Another batch of phosphate ($[\alpha]_D^{25} -507.7^\circ$, THF, c 1.17) was shown to have 96.5% ee using the same conditions. The same reaction was also checked on a slightly smaller scale, using 18.8 g (54.0 mmol) of (*R*)-(-)-1,1'-binaphthyl-2,2'-diyl phosphate. The yield was 81%. The submitters report a yield of 80% for the reaction run on a 1.6-mol scale.
5. The **phosphorus hydride** that evolves is highly toxic and creates a stench. Therefore, the checkers recommend that this reaction as well as the workup be performed in an efficient fume hood. The checkers found it advantageous to scrub the **phosphorus hydride** that formed in a trap (shown below) by

bubbling the evolving gases through a solution of 250 mL of bleach (5% sodium hypochlorite in water). During the reaction a constant flow of nitrogen was applied to avoid contamination of the reaction flask with wet gases from the traps.



6. Red-Al is the Aldrich Chemical Company, Inc., brand of sodium bis(2-methoxyethoxy)aluminum hydride in 3.4 M toluene solution.

7. The enantiomeric excess of this product was determined to be >99.5% using the same conditions as mentioned in (Note 4). The peaks are well separated and the *R*(+)-enantiomer is eluted second.² Another batch obtained from reduction of phosphate having 96.5% ee had mp 207–209°C and $[\alpha]_{\text{D}}^{25} +33.5^\circ$ (THF, c 1.12). This material had an enantiomeric excess of >99.5%, determined under the same conditions as described in (Note 4). The submitters report $[\alpha]_{\text{D}}^{25} +24.7^\circ$ (THF, c 1.035) for material with mp 207–209°C [lit.³ mp 206.5–207.5°C, $[\alpha]_{\text{D}}^{25} +34.3^\circ$ (THF, c 1.1)].

8. The product has the following spectral properties: ¹H NMR (1 : 1 CDCl₃ : *d*₆-DMSO) δ: 7.04 (d, 2H, *J* = 8.8), 7.20–7.35 (m, 4 H), 7.40 (d, 2H, *J* = 8.8), 7.92 (d, 2 H, *J* = 8.8), 9.21 (s, 2 H).

9. The enantiomeric excess of this product was determined to be >99.5% using the same conditions as mentioned in (Note 4). The second crop obtained from the reduction of phosphate having 96.5% ee had mp 200–204°C and $[\alpha]_{\text{D}}^{25} +20.7^\circ$ (THF, c 1.13). This (second crop) material had an enantiomeric excess of 86.5%, determined under the same conditions as described in (Note 4). The submitters report $[\alpha]_{\text{D}}^{25} +33.5^\circ$ (THF, c 0.775) for material with mp 204–206°C.

3. Discussion

Enantiomerically pure 1,1'-binaphthalene-2,2'-diols are used in various types of asymmetric syntheses, for example, as chiral auxiliaries in a method for the asymmetric reduction of ketones.⁴

The previously published method^{5,3} for the liberation of the diol from the resolved 1,1'-binaphthyl-2,2'-diyl hydrogen phosphate entailed esterification with diazomethane and reductive cleavage with lithium aluminum hydride. The procedure presented here is felt to be safer in that it circumvents the hazards associated with using diazomethane and lithium aluminum hydride on a large scale.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 8, 50
- Org. Syn. Coll. Vol. 9, 77
- Org. Syn. Coll. Vol. 10, 93

References and Notes

1. Chemistry Research Department, Hoffmann-La Roche Inc., Nutley, NJ 07110.
2. Pirkle, W. H.; Schreiner, J. L. *J. Org. Chem.* **1981**, *46*, 4988.

3. 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.
 4. Fieser, M.; Danheiser, R. L.; Roush, W. in "Fieser and Fieser's Reagents for Organic Synthesis," Wiley-Interscience: New York, 1981, Vol. 9, pp. 169–170.
 5. Jacques, J.; Fouquey, C.; Viterbo, R. *Tetrahedron Lett.* **1971**, 4617.
-

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

silica gel

brine

(R)-(+)-1,1'-BINAPHTHALENE-2,2'-DIOL

(R)-(-)-Methyl 1,1'-binaphthyl-2,2'-diylphosphate

(R)-(-)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate

Crude (R)-(+)-1,1'-binaphthalene-2,2'-diol

(R)-(-)-methyl 1,1'-binaphthyl-2,2'-diyl phosphate

Red-Al

(R)-(-)-1,1'-binaphthyl-2,2'-diyl phosphate

1,1'-Binaphthalene]-2,2'-diol,(R)-

[hydrochloric acid \(7647-01-0\)](#)

[ethyl acetate \(141-78-6\)](#)

[methanol \(67-56-1\)](#)

[ether \(60-29-7\)](#)

[sodium bicarbonate \(144-55-8\)](#)

[sodium sulfate \(7757-82-6\)](#)

[nitrogen \(7727-37-9\)](#)

[dimethyl sulfate \(77-78-1\)](#)

[Norit A \(7782-42-5\)](#)

[toluene,](#)

M toluene (108-88-3)

2-propanol (67-63-0)

sodium hypochlorite (7681-52-9)

Diazomethane (334-88-3)

lithium aluminum hydride (16853-85-3)

hexane (110-54-3)

phosphate

N,N-dimethylacetamide (127-19-5)

sodium bis(2-methoxyethoxy)aluminum hydride

phosphorus hydride (7723-14-0)

1,1'-binaphthyl-2,2'-diyl hydrogen phosphate (39648-67-4)