



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.

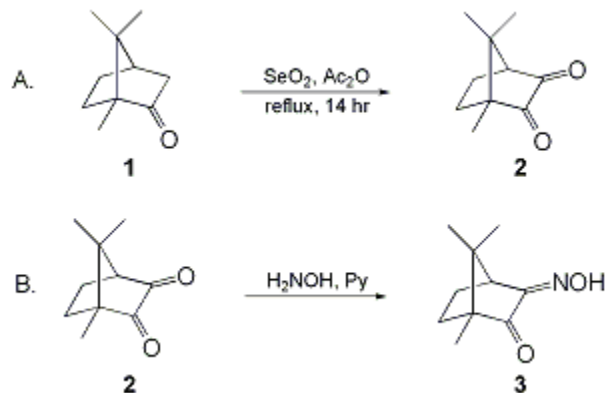
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions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

Organic Syntheses, Coll. Vol. 10, p.204 (2004); Vol. 79, p.125 (2002).

CAMPHORQUINONE AND CAMPHORQUINONE MONOXIME

[**Bicyclo[2.2.1]heptane-2,3-dione, 1,7,7-trimethyl-, (1R)-** and **Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-3-oxime, (1R)-**]



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1. Procedure

Caution! Parts A and B should be carried out in a well ventilated hood since toxic selenium dioxide is used.

A. (1R,4S)-(-)-Camphorquinone (Note 1). A 125-mL, three-necked, round-bottomed flask, equipped for mechanical stirring and outfitted with a reflux condenser, is charged with 20.0 g (0.13 mol) of (+)-camphor (**1**) (Note 2), 8.0 g (0.07 mol) of selenium dioxide (*Caution! Selenium dioxide is toxic*) (Note 3), and 14.0 mL of reagent grade acetic anhydride (Note 4). The green mixture is stirred at reflux for 1 hr, cooled to ambient temperature, and an additional 8.0 g (0.07 mol) of selenium dioxide is added. The mixture is again heated to reflux, and two further batches of 8.0 g (0.07 mol) of selenium dioxide are added at 2.5-hr and 6-hr intervals. After the reaction is heated at reflux for an additional 8 hr, during which time precipitation of selenium metal is observed, it is cooled to ambient temperature and transferred to a 125-mL beaker with the aid of 50 mL of ethyl acetate. The black precipitate is removed by filtration, and the filtrate is diluted with 100 mL of toluene (Note 5). Concentration of the filtrate by rotary evaporation gives crude **2** as an orange solid. This is dissolved in 200 mL of ethyl acetate, and the solution is filtered by vacuum filtration through Celite. The filtrate is transferred to a 1-L separatory funnel and is washed successively with 200 mL of 10% aqueous sodium hydroxide solution and 100 mL of saturated aqueous sodium chloride solution. The organic solution is dried over magnesium sulfate, filtered, and concentrated by rotary evaporation to afford 20.89 g of crude (1R,4S)-(-)-camphorquinone (**2**) as yellow crystals, mp 198-199°C (Notes 6 and 7). This material is suitable for the next reaction without purification.

B. (1R,4S)-(-)-Camphorquinone monoxime. A 500-mL, single-necked, round-bottomed flask equipped with a magnetic stirring bar is charged with 10.0 g (0.060 mol) of crude (1R)-(-)-camphorquinone (**2**), 240 mL of ethanol, 40 mL of pyridine (Note 8) and 5.44 g (0.078 mol) of hydroxylamine hydrochloride (NH₂OH·HCl) (Note 9). The solution is stirred for 20 min, and the ethanol is removed by rotary evaporation at 40°C. The resulting oil is diluted with 100 mL of hexane and 100 mL of ethyl acetate, and the solution is transferred to a 1-L separatory funnel. The organic phase is separated and washed successively with 125 mL of 5% hydrochloric acid solution, 300 mL of water, and 300 mL of saturated aqueous sodium chloride solution. The organic solution is dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The residue is taken up in 65 mL

of [heptane](#) and heated to reflux. After reflux is maintained for 2 min, the mixture is allowed to cool to room temperature. The solid is collected by vacuum filtration, and the filter cake is dried under high vacuum to provide 8.63 g (79%) of (1R)-(-)-camphorquinone oxime (**3**) as an off-white solid ([Note 10](#)). This is a mixture of syn- and anti-oxime isomers, mp 148-151°C [α]_D²² +184° (CH₂Cl₂, c 3.5) ([Note 11](#)).

2. Notes

1. [Camphorquinone](#) is available in racemic and both enantiomeric forms from Aldrich Chemical Company, Inc.
2. (+)-[Camphor](#) was purchased from Aldrich Chemical Company, Inc. and was used without purification.
3. [Selenium dioxide](#) was purchased from Aldrich Chemical Company, Inc.
4. Reagent grade [acetic anhydride](#) was purchased from Fischer Scientific .
5. Addition of [toluene](#) at this stage aids the removal of traces of [acetic acid](#) .
6. The crude product (**2**) is of sufficient purity for the next step even if trace amounts of [acetic acid](#) and [selenium dioxide](#) remain. The material can be purified by crystallization from a mixture of [hexane](#) and [2-propanol](#) to provide a product with mp 198-199°C (lit. mp 199°C)² and [α]_D²² -103° ([toluene](#), c 2.0).
7. The spectral properties of (1R,4S)-(-)-camphorquinone (**2**) are as follows: ¹H NMR (300 MHz, CDCl₃) δ : 0.92 (s, 3 H), 1.03 (s, 3 H), 1.08 (s, 3 H), 1.52-1.68 (m, 2 H), 1.79-1.94 (m, 1 H), 2.06-2.22 (m, 1 H), 2.62 (d, 1 H, J = 5.4) ; ¹³C NMR (75 MHz, CDCl₃) δ : 8.9, 17.6, 21.3, 22.4, 30.1, 42.8, 58.1, 58.8, 203.0, 205.0 ; IR (film) cm⁻¹: 1767, 1746, 994
8. Reagent grade [pyridine](#) was purchased from Fischer Scientific Company .
9. Analytical reagent grade [hydroxylamine hydrochloride](#) was purchased from Mallinckrodt Inc.
10. The [camphorquinone monoxime 3](#) is not completely soluble in 65 mL of boiling [heptane](#) , but it is nevertheless obtained in pure form after this step.
11. The spectral properties of syn- and anti-(1R,4S)-(-)-camphorquinone monoxime (**3**) are as follows: ¹H NMR (300 MHz, CDCl₃) δ : 0.84 (s, 2.6 H), 0.88 (s, 0.4 H), 0.96 (s, 3 H), 0.97 (s, 0.4 H), 0.98 (s, 2.6 H), 1.47-2.12 (comp, 5 H), 2.68 (d, 0.1 H, J = 4.1), 3.23 (d, 0.9 H, J = 4.6) ; ¹³C NMR (75 MHz, CDCl₃) δ (major isomer): 8.9, 17.6, 20.6, 23.7, 30.6, 44.8, 46.6, 58.5, 159.6, 204.3 ; IR (CHCl₃) cm⁻¹: 3262, 2963, 2878, 1748, 1654 ; mass spectrum (CI) m/z 182.1179 [C₁₀H₁₅NO₂ (M+1) requires 182.1181], 182 (base), 136 .

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

(-)-Camphorquinone (**2**) is most conveniently prepared from (1R,4R)-(+)-[camphor](#) (**1**) by the method of Rupe,³ and is converted to a mixture of syn and anti monoximes **3** by the method of Cherry, et al.² The oxime **3** has also been obtained by nitrosation of [camphor](#) .⁴

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 10, 305](#)

References and Notes

1. Department of Chemistry, Oregon State University, Corvallis, OR 97331-4003.
2. Cherry, P. C.; Cottrell, W. R. T.; Meakins, G. D.; Richards, E. E *J. Chem. Soc. (C)* **1968**, 459.
3. Rupe, H.; Tommasi di Vignano, A. *Helv. Chim. Acta* **1937**, *20*, 1078.
4. Forster, M. O.; Rao, K. S. N. *J. Chem. Soc.* **1926**, 2670.

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

(1R,4S)-(-)-Camphorquinone:
Bicyclo[2.2.1]heptane-2,3-dione, 1,7,7-trimethyl-, (1R)-; (10334-26-6)

(1R,4S)-(-)-Camphorquinone monoxime:
2,3-Bornanedione, 3-oxime (9);
Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-, 3-oxime, (1R)- (12); (663-17-2)

(+)-Camphor:
Camphor, (1R,4R)-(+)- (8);
Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-, (1R)-; (464-49-3)

Selenium dioxide:
Selenium oxide (8,9); (7446-08-4)

Acetic anhydride (8);
Acetic acid, anhydride (9); (108-24-7)

Hydroxylamine hydrochloride (8);
Hydroxylamine, hydrochloride (9); (5470-11-1)