



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.

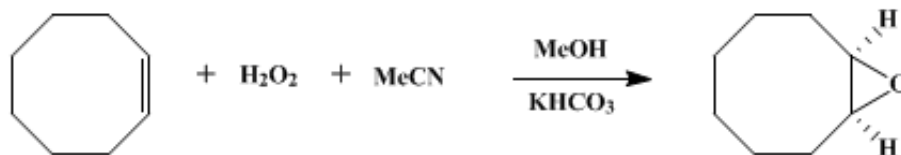
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

EPOXIDATION OF OLEFINS BY HYDROGEN PEROXIDE- ACETONITRILE: *cis*-CYCLOOCTENE OXIDE

[*cis*-9-Oxabicyclo [6.1.0] nonane]



Submitted by R. D. Bach and J. W. Knight¹.

Checked by K. W. Fowler and G. Büchi.

1. Procedure

*Caution! Reactions and subsequent operations involving peracids and peroxy compounds should be run behind a safety shield. Peroxy compounds should be added to the organic material, never the reverse. For relatively fast reactions, the rate of addition of the peroxy compound should be slow enough so that it reacts rapidly and no significant unreacted excess is allowed to build up. The reaction mixture should be stirred efficiently while the peroxy compound is being added, and cooling should generally be provided since many reactions of peroxy compounds are exothermic. New or unfamiliar reactions, particularly those run at elevated temperatures, should be run first on a small scale. Reaction products should never be recovered from the final reaction mixture by distillation until all residual active oxygen compounds (including unreacted peroxy compounds) have been destroyed. Decomposition of active oxygen compounds may be accomplished by the procedure described in Korach, M.; Nielsen, D. R.; Rideout, W. H. *Org. Synth.* 1962, 42, 50 (*Org. Synth.* 1973, Coll. Vol. 5, 414). [Note added January 2011].*

In a 5-L, three-necked, round-bottomed flask fitted with a mechanical overhead stirrer, addition funnel, and thermometer are placed 484 g (4.4 mol) of *cis*-cyclooctene, 3 L of reagent methanol (Note 1), 330 g (8.04 mol) of acetonitrile, and 77 g (0.77 mol) of potassium bicarbonate (Note 2). To the resulting heterogeneous mixture is added dropwise 522 g (4.6 mol) of 30% hydrogen peroxide with cooling at a rate that maintains the temperature of the reaction at 25–35°C (Note 3). Following the addition of hydrogen peroxide, the ice bath is removed and the reaction mixture is allowed to stir at room temperature overnight. The reaction mixture is divided in half, and each portion is diluted with 500 mL of a saturated sodium chloride solution. Each portion is then extracted with four 500-mL portions of methylene chloride (Note 4). The organic phases are combined, dried over magnesium sulfate, and concentrated at reduced pressure by rotary evaporation. Short-path distillation of the crude product (Note 5) under reduced pressure gives 333–337 g (60–61%) of *cis*-cyclooctene oxide, bp 85–87°C (20 mm), as a white solid, mp 53–56°C (Note 6).

2. Notes

- Omission of the methanol resulted in substantially reduced yields.
- The reaction does not proceed well when sodium bicarbonate is used as the base.
- The reaction is exothermic and caution should be exercised to keep the reaction temperature from rising. The time required for complete addition of the hydrogen peroxide is ca. 2–3 hr. The temperature is maintained at 25–35°C by employing an ice-water bath. When the hydrogen peroxide was added too rapidly, the reaction temperature rose until the solvents refluxed.
- To check for organic-soluble peroxides, add several milliliters of the methylene chloride solution to a solution containing ca. 1 mg of sodium dichromate, 1 mL of water, and 1 drop of dilute sulfuric acid. A

blue color in the organic layer is a positive test for perchromate ion. The checkers found that the combined organic phases exhibited a positive test and therefore stirred them overnight with a solution of 100 g of sodium metabisulfite in 500 mL of water prior to drying.

5. Heat from an IR lamp or heat gun must be applied to the condenser to keep the product from solidifying. The distillation pot should not be taken to dryness because of the possibility of the presence of organic peroxides.

6. The crude product may be used in many cases without further purification. Sublimation of the distilled oxirane affords the product as white needles, mp 56–57°C. The checkers obtained a broader melting point of the distillate, but the product was pure by analytical VPC.

3. Discussion

cis-Cyclooctene oxide has been prepared from *cis*-cyclooctene by the action of perbenzoic acid,² hydrogen peroxide,³ molybdenum hexacarbonyl and *tert*-butyl hydroperoxide,⁴ peracetic acid,⁵ chromic acid,⁶ and polymer-supported peracids.⁷

Oxiranes are typically formed by the action of a peracid such as *m*-chloroperbenzoic acid⁸ on an alkene.⁹ The present method has the advantage of being useful for both large- and small-scale reactions. The actual epoxidizing agent is generated in situ from the addition of hydrogen peroxide to a nitrile, forming a peroxyimidic acid.¹⁰ This procedure is an adaptation of the method of Payne that utilized an intermediate peroxyimidic acid derived from the reaction of hydrogen peroxide with acetonitrile¹¹ and benzonitrile.¹² The alkaline hydrogen peroxide-benzonitrile system has more recently been used with steroids,¹³ and in the total synthesis of prostaglandin F_{2α}.¹⁴ The present method does not require the separation of benzamide from the product. In addition, the reagents are inexpensive and the method is convenient and safe since it does not require large-scale preparation and handling of an organic peracid. Recently, it has been shown that substitution of trichloroacetonitrile for acetonitrile produces an even more reactive reagent.¹⁵

This epoxide has been found to be particularly useful in the laboratory in the large-scale preparation of *trans*-cyclooctene using the procedure of Whitham.¹⁶ *trans*-Cyclooctane-1,2-diol is obtained from *cis*-cyclooctene oxide on treatment with sodium acetate in acetic acid and alkaline hydrolysis of the intermediate *trans*-2-acetoxycyclooctanol. The *trans* diol is converted to its benzaldehyde acetal, which on treatment with butyllithium affords *trans*-cyclooctene in a stereospecific manner.

References and Notes

1. Department of Chemistry, Wayne State University, Detroit, MI 48202.
2. Godchot, M.; Cauquil, G. *C. R.* **1931**, *192*, 962.
3. Treibs, W. *Chem. Ber.* **1939**, *72*, 7–10.
4. Sheng, M. N. *Synthesis*, **1972**, 194–195.
5. Cope, A. C.; Fenton, S. W.; Spencer, C. F. *J. Am. Chem. Soc.* **1952**, *74*, 5884–5888.
6. Cope, A. C.; Kinter, M. R.; Keller, R. T. *J. Am. Chem. Soc.* **1952**, *76*, 2757–2760.
7. Harrison, C. R.; Hodge, P. J. *Chem. Soc. Chem. Commun.* **1974**, 1009–1010; Harrison, C. R.; Hodge, P. J. *Chem. Soc., Perkin Trans. 1* **1976**, 605–609.
8. Fieser, M.; Fieser, L. F. "Reagents for Organic Synthesis"; Wiley-Interscience: New York, 1967; Vol. 1, p. 135.
9. Swern, D. *Org. React.* **1953**, *7*, 378–433; Harrison, I. T.; Harrison, S. "Compendium of Organic Synthetic Methods"; Wiley-Interscience: New York, 1971; Vol. 1, pp 325–326; Harrison, I. T.; Harrison, S. "Compendium of Organic Synthetic Methods"; Wiley-Interscience: New York, 1974; Vol. 2, pp 134–135.
10. Wiberg, K. B. *J. Am. Chem. Soc.* **1953**, *75*, 3961–3964.
11. Payne, G. B.; Deming, P. H.; Williams, P. H. *J. Org. Chem.* **1961**, *26*, 659–663;
12. Payne, G. B. *Tetrahedron* **1962**, *18*, 763–765.

13. Ballantine, J. D.; Sykes, P. J. *J. Chem. Soc. C* **1970**, 731–735.
14. Woodward, R. B.; Gosteli, J.; Ernest, I.; Friary, R. J.; Nestler, G.; Raman, H.; Sitrin, R.; Suter, Ch.; Whitesell, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 6853–6858.
15. Arias, L. A.; Adkins, S.; Nacel, C. S.; Bach, R. D. *J. Org. Chem.* **1983**, *48*, 888.
16. Hines, J. N.; Peagram, M. J.; Thomas, E. J.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2332–2337.
-

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

sodium metabisulfite

Oxiranes

peroxyimidic acid

[sulfuric acid](#) (7664-93-9)

[acetic acid](#) (64-19-7)

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

[sodium acetate](#) (127-09-3)

[acetonitrile](#) (75-05-8)

[benzonitrile](#) (100-47-0)

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

[sodium chloride](#) (7647-14-5)

[benzamide](#) (55-21-0)

[chromic acid](#) (7738-94-5)

[oxirane](#) (75-21-8)

[sodium dichromate](#) (7789-12-0)

[hydrogen peroxide](#) (7722-84-1)

[methylene chloride](#) (75-09-2)

[trichloroacetonitrile](#) (545-06-2)

[magnesium sulfate](#) (7487-88-9)

[butyllithium](#) (109-72-8)

[peracetic acid](#) (79-21-0)

[potassium bicarbonate](#) (298-14-6)

[Perbenzoic acid](#) (93-59-4)

tert-butyl hydroperoxide (75-91-2)

HYDROGEN PEROXIDE-ACETONITRILE

cis-Cyclooctene oxide (286-62-4)

molybdenum hexacarbonyl (13939-06-5)

benzaldehyde acetal

m-Chloroperbenzoic acid (937-14-4)

cis-cyclooctene (931-87-3)

trans-Cyclooctene (931-89-5)

trans-Cyclooctane-1,2-diol

trans-2-acetoxycyclooctanol

cis-9-Oxabicyclo [6.1.0] nonane (4925-71-7)