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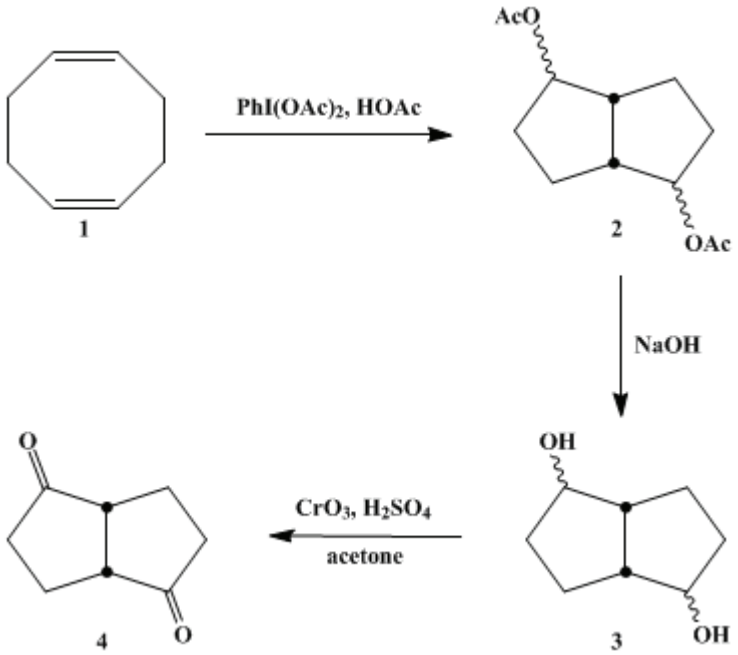
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.068.0175

Organic Syntheses, Coll. Vol. 8, p.43 (1993); Vol. 68, p.175 (1990).

INTRAMOLECULAR CYCLIZATION OF *cis,cis*-1,5-CYCLOOCTADIENE USING HYPERVALENT IODINE: BICYCLO [3.3.0]OCTANE-2,6-DIONE

[1,4-Pentalenedione, hexahydro-]



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Checked by Deng Bing and Ekkehard Winterfeldt.

1. Procedure

A. *2,6-Diacetoxybicyclo[3.3.0]octane.* (Compound **2**; (Note 1) and (Note 2).) An ovendried. 1-L round-bottomed flask, equipped with a magnetic stirring bar, a reflux condenser, and a drying tube (Drierite), is charged with iodosobenzene diacetate (IBD) (100 g. 0.31 mol) and 300 mL of glacial acetic acid. To this stirred mixture, 25 g (0.23 mol) of *cis,cis*-1,5-cyclooctadiene (COD) is added. The resulting mixture is then heated to reflux for 16 hr (Note 3), at which time the colorless solution has become brown-orange. At the end of this time the acetic acid is evaporated using a rotary evaporator (15 mm). Reduced-pressure distillation (74–84°C at 0.060 mm) yields 29.1–30.5 g (56–58%) of 2.6-diacetoxybicyclo[3.3.0]octane, as a pale-yellow liquid (lit.[3] bp 84–88°C at 0.2 mm) (Note 4).

B. *Bicyclo[3.3.0]octane-2,6-diol.* (Compound **3**; (Note 5).) An ice-cooled aqueous 10% solution of sodium hydroxide (100 mL) is placed in a 250-mL, round-bottomed flask equipped with a magnetic stirring bar and a stopper. To this ice-cooled solution 27.8 g of diacetate 2 (0.123 mol) is added dropwise over a few minutes. The cooled solution is slowly allowed to warm to room temperature (1 hr) and stirring is continued for 15 hr. at which time the colorless solution has become yellow-orange (Note 6).

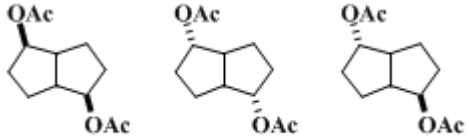
The reaction mixture is then extracted continuously with ether for a 3 days. After extraction the ether is removed by rotary evaporation. The crude viscous liquid that results after evaporation (Note 7) is distilled (Note 8) under reduced pressure (106–111°C at 0.06 mm) (lit.[3] bp 90–96°C at 0.3 mm) to yield 14.5–16.2 g (83–93%) of **3**, pure bicyclo[3.3.0]octane-2,6-diol, as a yellow viscous liquid (Note 9).

C. *Bicyclo[3.3.0]octane-2,6-dione.* (Compound **4**; (Note 10).) Diol 3, 12.6 g (0.089 mol), is placed in a 250-ml, three-necked, round-bottomed flask equipped with a mechanical stirrer and a reflux condenser. Acetone (125 mL) is added and the mixture is cooled to 0°C. A 2.7 *M* solution of Jones reagent (Note 11) (70 mL) is slowly added dropwise over 10 min at 0°C. The solution is allowed to warm slowly to room temperature (1 hr) and stirring is continued for an additional 15 hr.

After 15 hr the acetone is removed on a rotary evaporator and water (125 mL) is added. The dark-green aqueous mixture is extracted continuously with ether for 3 days. The ether is removed by rotary evaporation, which results in a yellow oil. The oil is then distilled under reduced pressure (74–79°C at 0.06 mm) to yield analytically pure bicyclo[3.3.0]octane-2,6-dione, **4** (6.4–7.1 g, 52–58%) as a white crystalline solid, mp 45–46°C (lit.[4] mp 45.1–46.3°C) (Note 12) and (Note 13).

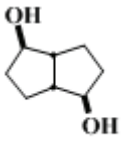
2. Notes

1. *cis,cis*-1,5-Cyclooctadiene (COD) and iodosobenzene diacetate (IBD) are purchased from Aldrich Chemical Company, Inc.
2. The diacetate **(2)** is a mixture of three difficultly separable stereoisomers [the di-*exo*-diacetate **(2a)**, di-*endo*-diacetate **(2b)**, and the *exo–endo*-diacetate **(2c)**]. The major isomer is the di-*exo*-diacetate **(2a)** based on ^{13}C-NMR of the known di-*exo*-diol (Note 9).



2a **2b** **2c**

3. This solution of iodosobenzene, acetic acid, and *cis,cis*-1,5-cyclooctadiene should continue to be stirred and should not be allowed to react for more than 20 hr (at refluxing temperature) to prevent decomposition of the product diacetate.
4. The ^{1}H NMR spectrum ($CDCl_3$) is as follows δ: 1.60 (m, 8 H, CH_2), 1.97 (s, 6 H, OAc), 2.55 (br, s, 2 H, CH), 4.90 (br, s, 2 H, CHOAc). The IR spectrum (neat) shows a carbonyl peak at 1738 cm^{-1}.
5. This procedure for the preparation of the diol is an adapted version of that by Cantrell and Strasser.[3] It is a procedure superior to that of Crandall and Mayer.[5]
6. The checkers monitored the reaction by TLC using ethyl acetate as the developing solvent.
7. This viscous liquid **(3)** is easily transferred to a distilling flask by using acetone.
8. The use of a heat gun aids the distillation because the product is extremely viscous.
9. The ^{1}H NMR spectrum ($CDCl_3$) is as follows δ: 1.70 (m, 8 H, CH_2), 2.61 (m, 2 H, CH), 3.05 (s, 2 H, OH), 3.90 (m, 2 H, CHOH). The IR spectrum shows a broad peak at 3500 cm^{-1}. The major peaks in the ^{13}C NMR spectrum ($CDCl_3$) are δ: 27.41 (C-4), 33.81 (C-3), 50.64 (C-1), 79.54 (C-2). The ^{13}C NMR indicates that the major stereoisomer is **3a**, the *exo,exo*-2,6-dihydroxy-*cis*-bicyclo[3.3.0]octane [lit.[6] ^{13}C NMR δ: 27.8 (C-4), 34.2 (C-3), 51.0 (C-1), 79.9 (C-2)].



3a

10. Other oxidation procedures were used, including pyridinium chlorochromate (Corey's reagent),[7] and dipyridine Cr(VI) oxide (Collins' reagent),[8] but did not produce yields comparable to the Jones method.
11. Jones reagent was prepared by the method in Fieser and Fieser:[9] Dissolve 13.36 g of chromium trioxide in 11.5 mL of concd sulfuric acid, and carefully dilute this cooled solution (0°C) with water to 50 mL.
12. The ^{1}H NMR spectrum ($CDCl_3$) is as follows δ: 2.23 (m, 8 H, CH_2), 3.00 (m, 2 H, CH). The IR spectrum (Nujol) shows a carbonyl peak at 1745 cm^{-1}.
13. GLC analysis shows that the product is contaminated by small amounts of diol. If desired, purer material could be obtained by sublimation at 35–40°C at 0.01 mm onto a cold finger kept at 0°C.[4]

3. Discussion

The preparation of bicyclo[3.3.0]octane-2,6-dione has been accomplished by intermolecular reactions,[4,10] intramolecular reactions,[3,11] and degradation reactions.[5,12]

Bicyclo[3.3.0]octane-2,6-dione has been known since 1934,[10] but extant procedures for large-scale multigram synthesis of this versatile intermediate are cumbersome, except for the recently published results of Hagedorn and Farnum.[4] Whitesell and Matthews[6] have shown that bicyclo[3.3.0]octanes are valuable intermediates for the total synthesis of natural products.

We now report a simple, three-step synthesis of the dione, which uses simple procedures and inexpensive starting materials, to procure multigram amounts of bicyclo[3.3.0]octane-2,6-dione in reasonable yields.

References and Notes

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

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ethyl acetate (141-78-6)

ether (60-29-7)

sodium hydroxide (1310-73-2)

iodine (7553-56-2)

acetone (67-64-1)

chromium trioxide (1333-82-0)

Iodosobenzene diacetate (3240-34-4)

pyridinium chlorochromate (26299-14-9)

Bicyclo[3.3.0]octane-2,6-dione,
1,4-Pentalenedione, hexahydro- (77483-80-8)

2.6-diacetoxybicyclo[3.3.0]octane,
2,6-Diacetoxybicyclo[3.3.0]octane (17572-85-9)

Bicyclo[3.3.0]octane-2,6-diol (17572-86-0)

iodosobenzene, acetic acid

cis,cis-1,5-cyclooctadiene

exo,exo-2,6-dihydroxy-cis-bicyclo[3.3.0]octane