Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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.

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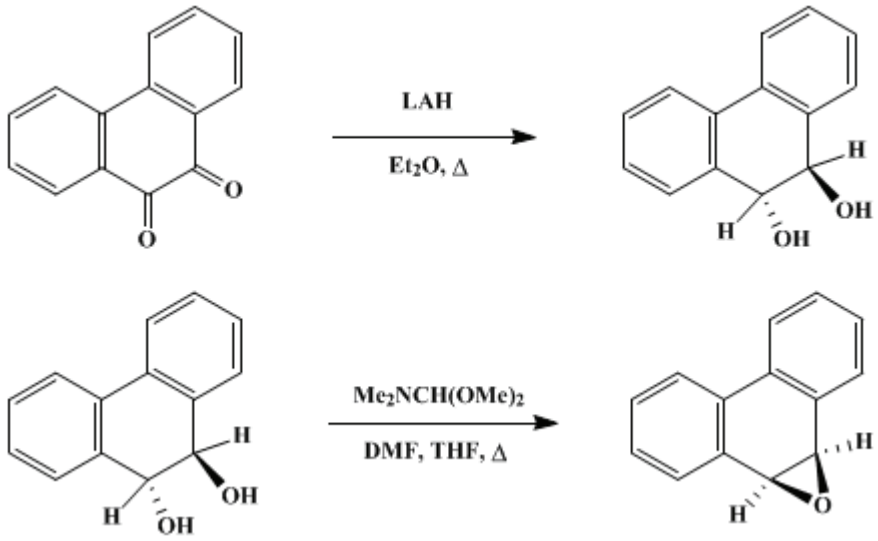
ARENE OXIDE SYNTHESIS: PHENANTHRENE-9,10-OXIDE

[Phenanthro[9,10-*b*]oxirene, 1*a*,9*b*-dihydro-]



Submitted by Cecilia Cortez and Ronald G. Harvey[1].
Checked by James Jackson and Orville L. Chapman.

1. Procedure

Caution! Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A. trans-9,10-*Dihydro*-9,10-*phenanthrenediol* (**1**). Phenanthrenequinone (6 g., 0.03 mole) (Note 1) is placed in a fritted-glass (coarse porosity) extraction thimble of a Soxhlet apparatus over a 1-l. flask containing a suspension of 3 g. of lithium aluminum hydride in 500 ml. of anhydrous diethyl ether (Note 2). Extraction of the quinone over a period of 16 hours affords a green solution (Note 3). The reaction is quenched by the cautious addition of water (Note 4) and neutralized with glacial acetic acid. The ether layer is separated, and the aqueous layer is extracted with two 200-ml. portions of ether. The combined ether extracts are washed consecutively with aqueous sodium hydrogen carbonate and water, then dried over magnesium sulfate. Evaporation of the solvent under reduced pressure gives the crude product (Note 5), which is recrystallized from benzene, giving 3.8–4.1 g. (62–68%) of pure diol **1** as fluffy, white needles, m.p. 185–190°, (Note 6).

B. *Phenanthrene*-9,10-*oxide* (**2**). A solution of 10.6 g. (0.0500 mole) of **1** and 13 g. of *N,N*-dimethylformamide dimethyl acetal (Note 7) in 40 ml. of *N,N*-dimethylformamide (Note 8) and 100 ml. of dry tetrahydrofuran (Note 9) is heated at reflux for 16 hours. The solution is then allowed to cool to room temperature, and 200 ml. of water and 100 ml. of ether are added. The organic layer is separated, the aqueous layer is washed with two 200-ml. portions of ether, and the combined ether phases are dried over magnesium sulfate. Evaporation of the solvent under reduced pressure gives 9.6 g. of a yellow solid. Trituration with 25 ml. of hexane removes colored impurities, and recrystallization from benzene–cyclohexane (Note 10) gives 5.6–6.2 g. (58–64%) of oxide **2** as off-white plates, m.p. 125° (dec.) (Note 11). A second crop of 1.0 g can be obtained, for an overall yield of 68–74% (Note 12).

2. Notes

1. Phenanthrenequinone, free of anthraquinone, is available from Aldrich Chemical Company, Inc., or from J. T. Baker Chemical Company and should be recrystallized from benzene before use.
2. Use of more efficient solvents (tetrahydrofuran, isopropyl ether, dimethoxyethane) or more soluble metal hydride reagents (sodium borohydride, lithium tributoxy aluminum hydride, sodium bis(2-methoxyethyl) aluminum hydride) favors the alternative reduction pathway to the hydroquinone.
3. The checkers noted that use of a paper thimble resulted in increased time for extraction. The submitters recommend use of a glass thimble, since prolonged heating can lead to lower yields. It is easier to determine when extraction is complete with a transparent thimble. Other quinones may require longer extraction periods.
4. Care must be taken to add water cautiously and slowly, since the reaction between water and lithium aluminum hydride is vigorous. The reaction is quenched when the solution stops refluxing.
5. The crude product may darken on drying because of the presence of minor amounts of the air-sensitive hydroquinone by-product.
6. Large-scale reactions usually result in lower yields. The checkers obtained product, m.p. 189–191°, in runs with slightly lower yields.
7. *N,N*-Dimethylformamide dimethyl acetal, obtained from Aldrich Chemical Company, Inc., was redistilled before use.
8. *N,N*-Dimethylformamide was distilled under reduced pressure and stored over molecular sieves, type 4Å.
9. Tetrahydrofuran was distilled from lithium aluminum hydride. For a warning concerning potential hazards of this procedure, see *Org. Synth.*, **Coll. Vol. 5**, 976 (1973).
10. Excessive heating during recrystallization should be avoided because it can lead to thermal decomposition of the product.
11. Because of the relative facility of thermal rearrangement to phenols, melting points of arene oxides are not an entirely reliable index of purity. The checkers found variation from 119 to 135° (dec.). Purification by chromatography on activity IV alumina is also possible, but residence time on the column should be held to a minimum.
12. The ^{1}H NMR spectrum ($CDCl_3$) of pure **2** showed a characteristic oxiranyl singlet peak at δ 4.67 (s, 2H) and an aromatic signal at 7.2–7.8 (m, 8H).

3. Discussion

The method employed here is essentially that reported earlier,[2] modified by subsequent experience.[3] In the second step, *N,N*-dimethylformamide dimethyl acetal acts as a dehydrating agent, giving the epoxide, and is converted to *N,N*-dimethylformamide and methanol. Phenanthrene-9,10-oxide has also been prepared by cyclization of 2,2'-biphenyldicarboxaldehyde with hexamethylphosphorus triamide[4] and by dehydrohalogenation of 10-chloro-9,10-dihydro-9-phenanthrenyl acetate, obtained through reaction of the corresponding 2-alkoxy-1,3-dioxolane with trimethylsilyl chloride.[5] The present procedure is simpler, requiring fewer steps from readily available starting materials; both alternative procedures start with phenanthrene. The product is relatively easy to purify, since the only by-products are *N,N*-dimethylformamide and methanol (an important consideration with molecules sensitive to decomposition), and appears to be more stable on storage than the compound obtained *via* the dialdehyde route.

The cyclization method utilized in this synthesis appears quite general in its applicability, having been applied successfully in our laboratory[3] to the preparation of the K-region arene oxides[6] of benz[*a*]anthracene, chrysene, dibenz[*a,h*]anthracene, benzo[*c*]phenanthrene, pyrene, 1-methylphenanthrene, benzo[*a*]pyrene, and 7,12-dimethylbenz[*a*]anthracene, among others. The latter two are potent carcinogens; the K-region oxides of these have been shown to be formed metabolically and exhibit significant biological activity.[7]

The K-region quinones required as starting materials in this synthesis are in certain cases (*e.g.*, phenanthrene, chrysene, benzo[*c*]phenanthrene) available from direct oxidation of the parent hydrocarbons with chromic acid. When oxidation occurs preferentially elsewhere in the molecule, the K-region dihydroaromatic derivatives can often be converted to the corresponding quinone through oxidation with dichromate in acetic acid–acetic anhydride;[8] yields, however, are only in the 20–30% range. Alternatively, the K-region quinones may be obtained from the hydrocarbons through oxidation

with osmium tetroxide to the corresponding *cis*-diols, followed by a second oxidation with pyridine–sulfur trioxide and dimethyl sulfoxide,[2,3] generally the most useful procedure. A significant advantage is that all possible K-region oxidized derivatives (*cis*-diols, quinones, *trans*-diols, phenols,[3] and hydroquinones[9]) with intact ring systems can be obtained directly or by appropriate modification of the general sequence. The disadvantages of this method, and of any alternative procedure[4,5] involving the *cis*-diol, is the hazardous and expensive osmium tetroxide employed.

References and Notes

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4. M. S. Newman and S. Blum, *J. Am. Chem. Soc.*, **86**, 5598 (1964).
5. P. Dansette and D. M. Jerina, *J. Am. Chem. Soc.*, **96**, 1224 (1974).
6. The K-region of a polycyclic aromatic hydrocarbon is typified by the 9,10-bond of phenanthrene. According to the Schmidt–Pullman electronic theory, an unsubstituted K-region is a requirement for carcinogenic activity; see A. Pullman, and B. Pullman, "La Cancerisation par les Substances Chimiques et la Structure Moleculaire," Masson, Paris, 1955.
7. For leading references see K. W. Jennette, A. M. Jeffrey, S. H. Blobstein, F. A. Beland, R. G. Harvey, and I. B. Weinstein, *Biochemistry*, **16**, 932 (1977).
8. H. Cho and R. G. Harvey, *Tetrahedron Lett.*, 1491 (1974).
9. H. Cho and R. G. Harvey, *J. Chem. Soc., Perkin Trans. I*, 836 (1976).

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

alumina

acetic acid (64-19-7)

Benzene (71-43-2)

methanol (67-56-1)

ether,
diethyl ether (60-29-7)

acetic anhydride (108-24-7)

sulfur trioxide (7446-11-9)

hydroquinone (123-31-9)

sodium hydrogen carbonate (144-55-8)

Anthraquinone (84-65-1)

cyclohexane (110-82-7)

pyridine (110-86-1)

chromic acid (7738-94-5)

phenanthrenequinone (84-11-7)

magnesium sulfate (7487-88-9)

phenanthrene (85-01-8)

Tetrahydrofuran (109-99-9)

isopropyl ether (108-20-3)

lithium aluminum hydride (16853-85-3)

Benz[a]anthracene (56-55-3)

pyrene (129-00-0)

N,N-dimethylformamide (68-12-2)

osmium tetroxide (20816-12-0)

hexane (110-54-3)

dimethyl sulfoxide (67-68-5)

dimethoxyethane (534-15-6)

sodium borohydride (16940-66-2)

hexamethylphosphorus triamide (680-31-9)

chrysene (218-01-9)

trimethylsilyl chloride (75-77-4)

Phenanthrene-9,10-oxide

sodium bis(2-methoxyethyl) aluminum hydride

10-chloro-9,10-dihydro-9-phenanthrenyl acetate

N,N-dimethylformamide dimethyl acetal (4637-24-5)

2,2'-biphenyldicarboxaldehyde (1210-05-5)

benzo[c]phenanthrene (195-19-7)

trans-9,10-Dihydro-9,10-phenanthrenediol (25061-61-4)

Phenanthro[9,10-b]oxirene, 1a,9b-dihydro- (585-08-0)

lithium tributoxy aluminum hydride

dibenz[a,h]anthracene (53-70-3)

1-methylphenanthrene (832-69-9)

benzo[a]pyrene (50-32-8)

7,12-dimethylbenz[a]anthracene (57-97-6)