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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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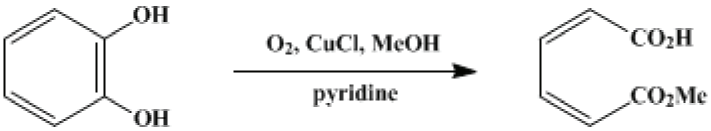
OXIDATIVE CLEAVAGE OF AN AROMATIC RING: *cis,cis*-MONOMETHYL MUCONATE FROM 1,2-DIHYDROXYBENZENE

[2,4-Hexadienedioic acid, monomethyl ester, (*Z,Z*)-]



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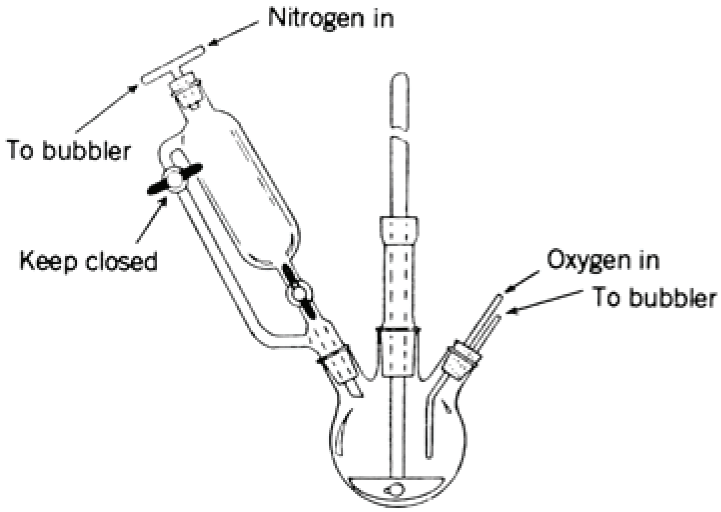
Checked by Won Hun Ham and Leo A. Paquette.

1. Procedure

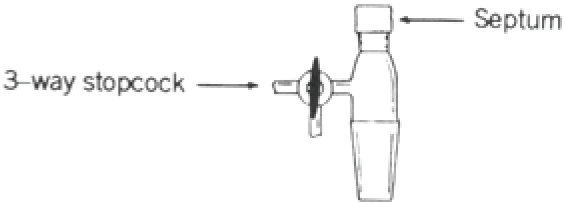
A. *cis,cis-Monomethyl muconate.* A 1000-mL, three-necked, round-bottomed flask is equipped with a mechanical stirrer and an addition funnel ((Note 1), Fig. 1). The flask is charged with 400 mL of pyridine, 5 mL (0.12 mol) of methanol and 9.9 g (0.10 mol) of cuprous chloride under an atmosphere of nitrogen (Note 2). The resultant yellow solution is stirred vigorously at room temperature until the cuprous chloride dissolves (Note 3). The nitrogen is removed and oxygen is bubbled into the flask below the surface of the liquid for approximately 30 min (Note 4). A solution, composed of 1000 mL of pyridine, 5.5 g (0.05 mol) of 1,2-dihydroxybenzene (catechol), and 5 mL (0.12 mol) of methanol, is degassed and slowly added to the flask over a 2-hr period with efficient stirring (Note 5). The reaction mixture is stirred for an additional 30 min before the pyridine is removed at reduced pressure. The dark green residue is dissolved in 300 mL of ethyl ether (Note 6) and 300 mL of 6 *N* hydrochloric acid; this solution is stirred for 10 min and filtered over Celite, and the organic layer is isolated. The ether is removed at reduced pressure and the resultant brown residue is boiled sequentially with six 50-mL portions of hexane (Note 7). The hot liquid is carefully decanted, leaving behind most of the dark residue. The yellow-to-colorless solid is crystallized from hot hexane (or methanol) to yield 5.6–6.2 g (71–80%) of colorless needles, mp 80–81°C (Note 8).

Figure 1



2. Notes

1. The checkers employed an alternate device of the following type and introduced the methanolic catechol solution subsequently via syringe.



2. Pyridine (Mallinckrodt Inc., reagent grade) was distilled over potassium hydroxide, bp 114–116°C. Cuprous chloride was prepared fresh,[2] washed with anhydrous methanol (distilled from magnesium metal), and dried under reduced pressure. Methanol (Fisher Scientific Company, purified grade) was dried over molecular sieves. The concentration of the methanol should be within the range of 3–8 mol/mol of catechol[3,4] and anhydrous conditions are necessary[4].

3. Dissolution requires 1.5–2 hr. If the solution is not properly degassed, it will turn green prematurely. The green color indicates that oxygen absorption by the cuprous chloride–pyridine complex has occurred, but it also means that any undissolved cuprous chloride has been oxidized. Therefore, nitrogen should be bubbled into the flask at a brisk rate and stirring should not commence until addition of the cuprous chloride is complete.

4. As oxygen is introduced into the flask the solution becomes dark green and slightly viscous.

5. Catechol was purchased from Fisher Scientific Company (resublimed). The addition funnel should be charged with a nitrogen atmosphere throughout addition to obviate oxidation of the catechol.

6. Ethyl ether was purchased from Mallinckrodt, Inc. (analytical grade); methylene chloride may be substituted, but the monomethyl ester is more soluble in ether. At least two other extractions will be necessary to optimize the yield when methylene chloride is used.

7. Hexane was purchased from Fisher Scientific Company (technical grade).

8. The spectral properties are as follows: ^{1}H NMR (300 MHz, CCl_4) δ: 3.74 (s, 3 H); 5.88–6.09 (m, 2 H); 7.75–8.26 (m, 2 H); 11.29 (s, 1 H).

3. Discussion

Phenol also undergoes oxidative cleavage in the presence of O_2/CuCl/pyridine and methanol to give *cis,cis*-monomethyl muconate, but the yield is not high.[4,5] It has also been observed that catechol, under anaerobic conditions, reacts with cupric methoxy chloride in pyridine containing water and methanol to give *cis,cis*-monomethyl muconate in high yield.[6] Catechol and phenol may also be converted to *cis,cis*-muconic acid by a metal-catalyzed peracetic acid oxidation;[7] subsequently, treatment with diazomethane gives the monomethyl or dimethyl ester.

References and Notes

1. Laboratory of J. C. Barborak, Department of Chemistry, University of North Carolina at Greensboro, Greensboro, NC 27412. Present address: Burroughs Wellcome, Organic Chemistry Department, 3030 Cornwallis, Research Triangle Park, NC 27709.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

cupric methoxy chloride

CuCl

O_2

hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether,
ethyl ether (60-29-7)

magnesium (7439-95-4)

phenol (108-95-2)

oxygen (7782-44-7)

nitrogen (7727-37-9)

pyridine (110-86-1)

potassium hydroxide (1310-58-3)

Catechol,
1,2-DIHYDROXYBENZENE (120-80-9)

cuprous chloride (7758-89-6)

methylene chloride (75-09-2)

Diazomethane (334-88-3)

peracetic acid (79-21-0)

hexane (110-54-3)

cis,cis-Monomethyl muconate,
2,4-Hexadienedioic acid, monomethyl ester, (Z,Z)- (61186-96-7)

cis,cis-muconic acid (505-70-4)