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.

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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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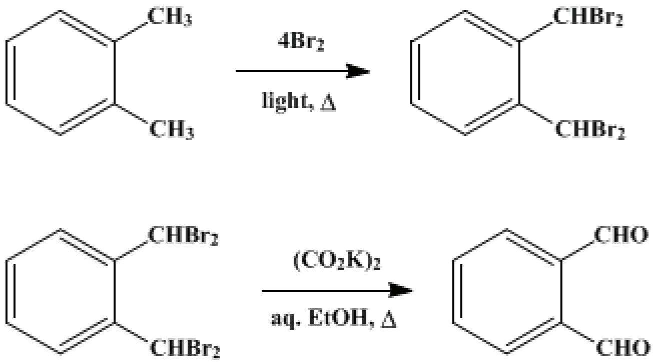
o-PHTHALALDEHYDE

[Phthalaldehyde]



Submitted by J. C. Bill and D. S. Tarbell[1].
Checked by Arthur C. Cope and Harris E. Petree.

1. Procedure

This preparation should be conducted in a hood, and rubber gloves should be worn, to avoid exposure to bromine as well as the by-product o-xylylene dibromide which is a lachrymator and skin irritant.

A. α,α,α',α'-*Tetrabromo-o-xylene*. In a 2-l. three-necked flask equipped with an oil-lubricated Trubore stirrer, a dropping funnel, a thermometer extending nearly to the bottom of the flask, and a reflux condenser (Note 1) attached to a gas absorption trap[2] is placed 117 g. (1.1 moles) of dry *o*-xylene (Note 2). An ultraviolet lamp such as a General Electric R.S. Reflector Type 275-watt sun lamp is placed about 1 cm. from the flask so as to admit the maximum amount of light. The stirrer is started, and the *o*-xylene is heated to 120° with an electric heating mantle. A total of 700 g. (4.4 moles) of bromine (N.F. grade) is added in portions from the dropping funnel to the reaction flask at such a rate that the bromine color is removed as fast as it is added. After approximately one-half of the bromine has been added, the temperature is slowly increased to 175° for the remainder of the addition; the mixture becomes very dark toward the end of the reaction. The bromine can be added rapidly at first, but toward the end it must not be added at a rate exceeding 4–5 drops per minute in order to avoid loss of a visible amount of bromine with the evolved hydrogen bromide. After all the bromine has been added (10–14 hours), the mixture is illuminated and stirred at 170° for 1 hour. After removal of the stirrer, etc., the mixture is cooled and allowed to stand overnight to crystallize in the reaction flask exposed to the air.

The dark, solid tetrabromide is dissolved in 2 l. of hot chloroform (Note 3) and treated with 100 g. of 325-mesh Norit. The mixture is filtered with slight suction, the Norit is washed with hot chloroform, and the Norit treatment is repeated. The tancolored filtrate from the second Norit treatment is concentrated to 250–300 ml. by distillation under reduced pressure and chilled to 0°. The solid product is collected on a cold Büchner funnel and washed with a small amount of cold chloroform. The filtrate is concentrated further and cooled to obtain a second crop of crystals, which is purified by recrystallization from chloroform. The yield of the tetrabromide obtained from the first crop (white) and second crop after recrystallization (light tan) is 344–370 g. (74–80%), m.p. 115–116°.

B. *o-Phthalaldehyde.* The α,α,α',α'-tetrabromo-*o*-xylene (344–370 g.) obtained as described above, part A, is placed in a 5-l. round-bottomed flask with 4 l. of 50% (by volume) ethanol and 275 g. of potassium oxalate. The mixture is heated under reflux for 50 hours (a clear yellow solution is formed after 25–30 hours). About 1750 ml. of the ethanol is then removed by distillation (which is stopped before the product begins to steam-distil), and 700 g. of disodium monohydrogen phosphate dodecahydrate ($Na_2HPO_4 \cdot 12H_2O$) is added to the aqueous residue. The mixture is steam-distilled rapidly (Note 4), using an efficient condenser, until 10–12 l. of distillate is collected and the distillate no longer gives a black color test for *o*-phthalaldehyde[3] when a portion is treated with concentrated ammonium hydroxide followed by glacial acetic acid. The distillate is then saturated with sodium sulfate at room temperature and divided into portions of approximately 4 l.; each portion is extracted first with 200 ml. and then with six 100-ml. portions of ethyl acetate. The combined ethyl acetate extracts are dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue is crystallized from 90–100° ligroin, and a second crop is obtained by concentration of the mother liquor. The total yield of *o*-phthalaldehyde, m.p. 55.5–56°, is 87–94 g. (74–80% based on the tetrabromide, or 59–64% based on *o*-xylene).

2. Notes

1. Best results are obtained if an all-glass apparatus with ground-glass connections is used, as noted by Wawzonek and Karll.[4]

2. Pure commercial *o*-xylene (99% or higher purity) is dried by distillation until the distillate shows no further turbidity, and the residue is used.

3. The chloroform is allowed to stand over anhydrous calcium chloride overnight to remove water and ethanol.

4. The submitters state that the steam distillation is much more efficient if superheated (175–180°) steam is used, in which case special care must be taken to condense all the distillate.

3. Discussion

o-Phthalaldehyde has been made by the action of potassium hydroxide on *o*-(dichloromethyl) benzaldehyde,[5] by the hydrolysis of α,α,α',α'-tetrachloro-*o*-xylene,[6] by the hydrolysis of the α,α,α',α'-tetraacetate of *o*-phthalaldehyde,[3] by the oxidation of α,α'-dihydroxy-*o*-xylene with selenium dioxide[7] or N-chlorosuccinimide,[8] and by the reduction of phthalic acid N-methylanilide with diisobutylaluminum hydride.[9] The present method is essentially that of Thiele and Günther.[10,11] Hydrolysis of the tetrabromide may also be carried out by treatment with fuming sulfuric acid followed by water.[12] For small-scale preparations of *o*-phthalaldehyde the reduction of N,N,N',N'-tetramethylphthalamide with lithium aluminum hydride is the method of preference.[13]

References and Notes

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11. Cope and Fenton, *J. Am. Chem. Soc.*, **73**, 1672 (1951).
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Appendix

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

ligroin

o-phthalaldehyde

α,α,α',α'-tetraacetate of o-phthalaldehyde

ethanol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ethyl acetate (141-78-6)

chloroform (67-66-3)

hydrogen bromide (10035-10-6)

bromine (7726-95-6)

sodium sulfate (7757-82-6)

Norit (7782-42-5)

selenium dioxide (7446-08-4)

potassium hydroxide (1310-58-3)

ammonium hydroxide (1336-21-6)

N-chlorosuccinimide (128-09-6)

lithium aluminum hydride (16853-85-3)

PHTHALALDEHYDE (643-79-8)

diisobutylaluminum hydride (1191-15-7)

o-Xylylene dibromide (91-13-4)

Tetrabromo-o-xylene

potassium oxalate

disodium monohydrogen phosphate dodecahydrate (10039-32-4) phthalic acid N-methylanilide

α,α'-dihydroxy-o-xylene (612-14-6)

o-Xylene (95-47-6)

o-(dichloromethyl)benzaldehyde

α,α,α',α'-tetrabromo-o-xylene (13209-15-9)

α,α,α',α'-tetrachloro-o-xylene

N,N,N',N'-tetramethylphthalamide