



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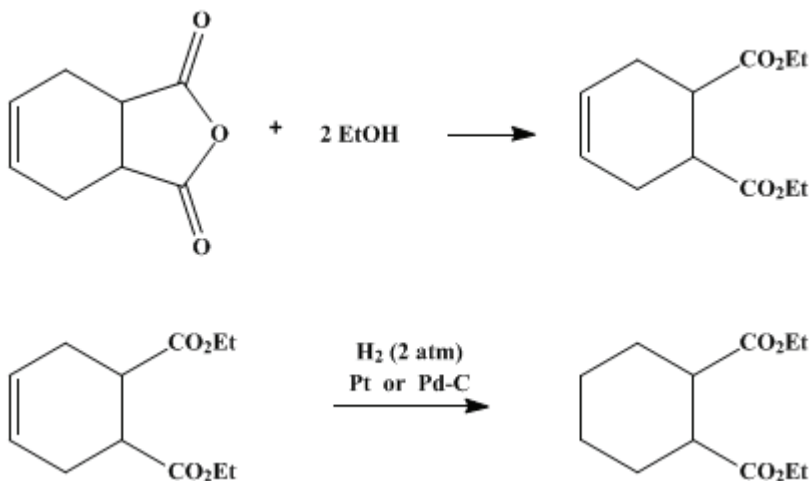
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.304 (1963); Vol. 30, p.29 (1950).

DIETHYL *cis*- Δ^4 -TETRAHYDROPHTHALATE AND DIETHYL *cis*-HEXAHYDROPHTHALATE

[4-Cyclohexene-1,2-dicarboxylic acid, diethyl ester, *cis*-, and 1,2-Cyclohexanedicarboxylic acid, diethyl ester, *cis*-]



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1. Procedure

A. *Diethyl cis- Δ^4 -tetrahydrophthalate*. In a 2-l. round-bottomed flask are placed 228 g. (1.5 moles) of *cis*- Δ^4 -tetrahydrophthalic anhydride (p. 890), 525 ml. (9 moles) of commercial absolute ethanol, and 2.5 g. of *p*-toluenesulfonic acid monohydrate. The flask is connected to a reflux condenser and heated in an oil bath maintained at 95–105° for 12–16 hours.

At this time 270 ml. of toluene is added to the mixture and the condenser is changed for distillation. An azeotropic mixture of ethanol, toluene, and water is distilled at 75–78° with the bath at 105–110°. When the temperature begins to drop (Note 1), 525 ml. of commercial absolute ethanol is added and the mixture is again heated under reflux for 12–16 hours (Note 2). Again 270 ml. of toluene is added, and the azeotropic mixture is distilled until the vapor temperature falls to 68°. After the residue is cooled, the system is evacuated to 25–35 mm. and the remaining ethanol and toluene are distilled.

The residual liquid is diluted with 200 ml. of ether. The ether solution is washed twice with 100-ml. portions of 3% sodium carbonate solution (Note 3). The combined carbonate solutions are extracted three times with 100-ml. portions of ether, and the ether solutions are combined and washed with 100 ml. of distilled water. The ether solution is dried over magnesium sulfate, filtered, and concentrated, and the residue is distilled under reduced pressure. The yield of product boiling at 129–131°/5 mm., n_D^{25} 1.4605–1.4610, is 280–292 g. (83–86%) (Note 4).

B. *Diethyl cis-hexahydrophthalate*. The reaction is carried out in a low-pressure catalytic hydrogenation apparatus.² In a 500-ml. Pyrex centrifuge bottle are placed 0.5 g. of Adams platinum oxide catalyst (Note 5) and 20 ml. of commercial absolute ethanol (Note 6). The bottle is connected to a calibrated low-pressure hydrogen tank and alternately evacuated and filled with hydrogen twice. Hydrogen is then admitted to the system until the pressure is 1–2 atmospheres (15–30 lb.), and the bottle is shaken for 20–30 minutes to reduce the platinum oxide. The shaker is stopped, the bottle is evacuated, and air is admitted. Two hundred and twenty-six grams (1 mole) of diethyl *cis*- Δ^4 -tetrahydrophthalate is placed in the bottle. The container in which the ester was weighed is rinsed with 10 ml. of absolute ethanol, which is added to the ester. The bottle is alternately evacuated and filled with hydrogen twice.

Hydrogen is admitted to the system until the pressure is 25–30 lb. (approximately 2 atmospheres), and the bottle is shaken until the pressure drop indicates that the theoretical amount (1 mole) of hydrogen has been taken up and the absorption ceases (3–5 hours). The bottle is evacuated and then air is admitted. The catalyst is removed by filtration through a small Hirsch funnel. The bottle is washed with 15 ml. of alcohol, which is poured through the funnel. Most of the solvent is distilled at 25–35 mm. Distillation of the residue under reduced pressure yields 215–219 g. (94–96%) of diethyl *cis*-hexahydrophthalate, b.p. 130–132°/9 mm., n_D^{25} 1.4508–1.4510 (Note 7).

2. Notes

1. A period of 5–8 hours is required for this distillation and for the similar subsequent distillation.
2. If the second period of reflux and azeotropic distillation is omitted the yield is decreased to 66%.
3. The product should be washed with sodium carbonate solution until the aqueous solution remains basic.
4. Dimethyl *cis*- Δ^4 -tetrahydrophthalate can be prepared by a similar procedure. *cis*- Δ^4 -Tetrahydrophthalic anhydride (228 g., 1.5 moles) is heated under reflux with 364 ml. (9 moles) of commercial anhydrous methanol and 2.5 g. of *p*-toluenesulfonic acid monohydrate for 12–16 hours. At this time 270 ml. of toluene is added and the mixture is distilled. When the distillation temperature drops from 68–70° to 45°, after about 4–6 hours, 364 ml. of absolute methanol is added and the mixture again is heated under reflux for 12–16 hours. An additional 270 ml. of toluene is added, and distillation is continued for 4–6 hours. The residual liquid is purified by a procedure similar to the one described for the ethyl ester. The yield of dimethyl *cis*- Δ^4 -tetrahydrophthalate, boiling at 120–122°/5 mm., n_D^{25} 1.4700, is 239 g. (80%).
5. The platinum oxide catalyst was obtained from Baker and Company, Newark, New Jersey. Platinum oxide may also be obtained from the American Platinum Works, Newark, New Jersey.
6. The reduction also may be carried out using 1 g. of palladium on carbon,³ in which case no solvent is required and prereduction of the catalyst is unnecessary.
7. Dimethyl *cis*-hexahydrophthalate also may be prepared by a similar reduction of dimethyl *cis*- Δ^4 -tetrahydrophthalate. With 0.5 g. of prereduced Adams platinum oxide catalyst, 198 g. (1 mole) of dimethyl *cis*- Δ^4 -tetrahydrophthalate was reduced to give 196 g. (98%) of dimethyl *cis*-hexahydrophthalate, b.p. 110–112°/5 mm., n_D^{25} 1.4570.

3. Discussion

Diethyl *cis*-hexahydrophthalate has been prepared from *cis*-hexahydrophthalic acid, absolute ethanol, and sulfuric acid,^{4,5} and from *cis*-hexahydrophthalic anhydride, absolute ethanol, and sulfuric acid.⁶ Diethyl *cis*- Δ^4 -tetrahydrophthalate has been prepared from *cis*- Δ^4 -tetrahydrophthalic acid or its anhydride, ethanol, and sulfuric acid.⁷ Dimethyl *cis*- Δ^4 -tetrahydrophthalate and dimethyl *cis*-hexahydrophthalate have been synthesized by the procedures of this preparation.⁸

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 890
- Org. Syn. Coll. Vol. 6, 454

References and Notes

1. Massachusetts Institute of Technology, Cambridge, Massachusetts.
2. Suitable apparatus is described in *Org. Syntheses Coll. Vol. 1*, 61 (1941).
3. *Org. Syntheses Coll. Vol. 3*, 385 (1955).
4. von Auwers and Ottens, *Ber.*, **57**, 437 (1924).
5. Hückel and Goth, *Ber.*, **58**, 447 (1925).
6. Price and Schwarcz, *J. Am. Chem. Soc.*, **62**, 2891 (1940).
7. Brooks and Cardarelli, U. S. pat. 1,824,069 [*C. A.*, **26**, 152 (1932)].
8. Cope and Herrick, *J. Am. Chem. Soc.*, **72**, 983 (1950).

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

Diethyl cis- Δ^4 -tetrahydrophthalate

cis- Δ^4 -Tetrahydrophthalic anhydride

Dimethyl cis- Δ^4 -tetrahydrophthalate

cis- Δ^4 -tetrahydrophthalic acid or its anhydride

ethanol (64-17-5)

sulfuric acid (7664-93-9)

methanol (67-56-1)

ether (60-29-7)

hydrogen (1333-74-0)

sodium carbonate (497-19-8)

platinum oxide

carbon (7782-42-5)

toluene (108-88-3)

palladium (7440-05-3)

magnesium sulfate (7487-88-9)

p-toluenesulfonic acid monohydrate (6192-52-5)

Diethyl cis-hexahydrophthalate,
1,2-Cyclohexanedicarboxylic acid, diethyl ester, cis- (10138-59-7)

4-Cyclohexene-1,2-dicarboxylic acid, diethyl ester, cis- (4841-85-4)

Dimethyl cis-hexahydrophthalate (1687-29-2)

cis-hexahydrophthalic acid (610-09-3)

cis-hexahydrophthalic anhydride