Organic Syntheses

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.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 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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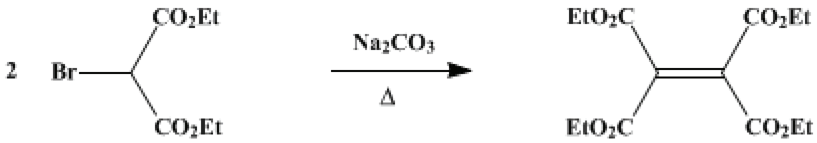
ETHYL ETHYLENETETRACARBOXYLATE

[Ethylenetetracarboxylic acid, tetraethyl ester]



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1. Procedure

A mixture of 200 g. (1.9 moles) of anhydrous sodium carbonate (Note 1) and 300 g. (1.25 moles) of ethyl bromomalonate (Org. Syn. Coll. Vol. I, **1941**, 245) is heated for three hours in a 1-l. flask (Note 2) immersed in an oil bath at 150–160° (Note 3). After the heating period, 300 cc. of xylene (Note 4) is added while the contents of the flask are still hot (Note 5). The solid is broken up carefully with a rod, and the mixture is transferred to a 2-l. beaker. The reaction flask is then rinsed with a mixture of 100 cc. of xylene and 100 cc. of water. This washing is poured into the 2-l. beaker, and an additional 600 cc. of water is added. The solid readily dissolves upon stirring. The liquid mixture is transferred to a separatory funnel, shaken well, and allowed to settle (Note 6). The lower aqueous layer is discarded (Note 7). The xylene layer is transferred to a 1-l. distilling flask and distilled until the temperature of the liquid itself is 170°. The liquid residue is then transferred to a 500-cc. Claisen flask and distilled under reduced pressure. The fore-run up to 170°/15 mm. is discarded. The product, which is collected at 170–230°/15 mm. (Note 8) and (Note 9), solidifies within about fifteen minutes. The yield is 150–160 g. (75–80 per cent of the theoretical amount).

The crude product is dissolved in 75 cc. of 95 per cent alcohol at a temperature of 40°, which is sufficient to ensure complete solution. The alcoholic solution is cooled to 12° (Note 10) and (Note 11) and filtered. The yield of air-dried, colorless product melting at 52.5–53.5° is 95–110 g. (47–55 per cent of the theoretical amount). By evaporation of the alcohol, distillation of the residue under reduced pressure, and recrystallization of the solidified distillate, the yield may be increased to 110–115 g. (55–57 per cent of the theoretical amount).

2. Notes

1. The sodium carbonate should be fine enough to pass through a 100-mesh sieve.
2. The mixture is heated in an open flask. Owing to the high boiling points of ethyl bromomalonate and ethyl ethylenetetracarboxylate, there is but little loss by volatilization. The yield is lowered by the use of a condenser, presumably because the water formed by the reaction is kept in the reaction mixture with resultant hydrolysis of one or both of the esters.
3. The flask is placed in the cold bath. The three hours are counted from the time the temperature of the bath reaches 150°.
4. Toluene or benzene can be substituted for xylene, but xylene is preferable because of its higher boiling point.
5. If the mixture is allowed to cool, it solidifies and is difficult to remove.
6. A good separation is obtained in ten minutes.
7. Experiment has shown that the amount of product in the aqueous layer is negligible.
8. Ethyl ethylenetetracarboxylate boils at 197°/8 mm.; 203°/13 mm.; 210°/22 mm.; 221°/33 mm.; 234°/48 mm.
9. There is very little residue left in the flask. Distillation should be stopped as soon as dark yellow drops of distillate begin to come over.
10. The crystallization mixture is a thick slush with low heat conductivity, hence a rather long cooling period is necessary to lower the temperature to 12°. A thermometer should be used because it is

important that the mixture be cooled to 12°, since the solubility curve begins to rise above 12°. There is no advantage in cooling below 12°.

11. The solubility of ethyl ethylenetetracarboxylate in 100 cc. of 95 per cent ethyl alcohol is as follows:

2.0 g. at 0°	16.0 g. at 30°
2.5 g. at 11°	19.0 g. at 31°
4.0 g. at 16°	28.0 g. at 33°
8.0 g. at 23°	35.0 g. at 34°
9.7 g. at 26°	61.0 g. at 36.5°

3. Discussion

Ethyl ethylenetetracarboxylate has been prepared from monochloro-and monobromomalonic ester through removal of halogen acid with sodium,[1] sodium ethoxide,[2] potassium acetate,[3] potassium carbonate,[4] sodium urethane,[5] sodium formanilide and sodium acetanilide.[6] It has also been prepared by treating the disodium derivative of ethyl ethane-1,1,2,2-tetracarboxylate with bromine,[7] or iodine;[8] by treating dibromomalonic ester with sodium,[9] or sodium ethoxide,[10] or sodium malonic ester followed by potash;[11] and by treating the disodium derivative of malonic ester with iodine.[12] It is reported that the use of moist benzene as the medium in the reaction between bromomalonic ester and potassium carbonate increases the yield of ethylenetetracarboxylic ester to 80 per cent.[13]

References and Notes

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

sodium malonic ester

potash

monochloro-and monobromomalonic ester

sodium urethane

disodium derivative of ethyl ethane-1,1,2,2-tetracarboxylate dibromomalonic ester

disodium derivative of malonic ester

ethylenetetracarboxylic ester

ethyl alcohol,
alcohol (64-17-5)

potassium carbonate (584-08-7)

Benzene (71-43-2)

sodium carbonate (497-19-8)

bromine (7726-95-6)

iodine (7553-56-2)

toluene (108-88-3)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

xylene (106-42-3)

Ethyl bromomalonate

potassium acetate (127-08-2)

Ethyl ethylenetetracarboxylate

Ethylenetetracarboxylic acid, tetraethyl ester

sodium formanilide

sodium acetanilide