



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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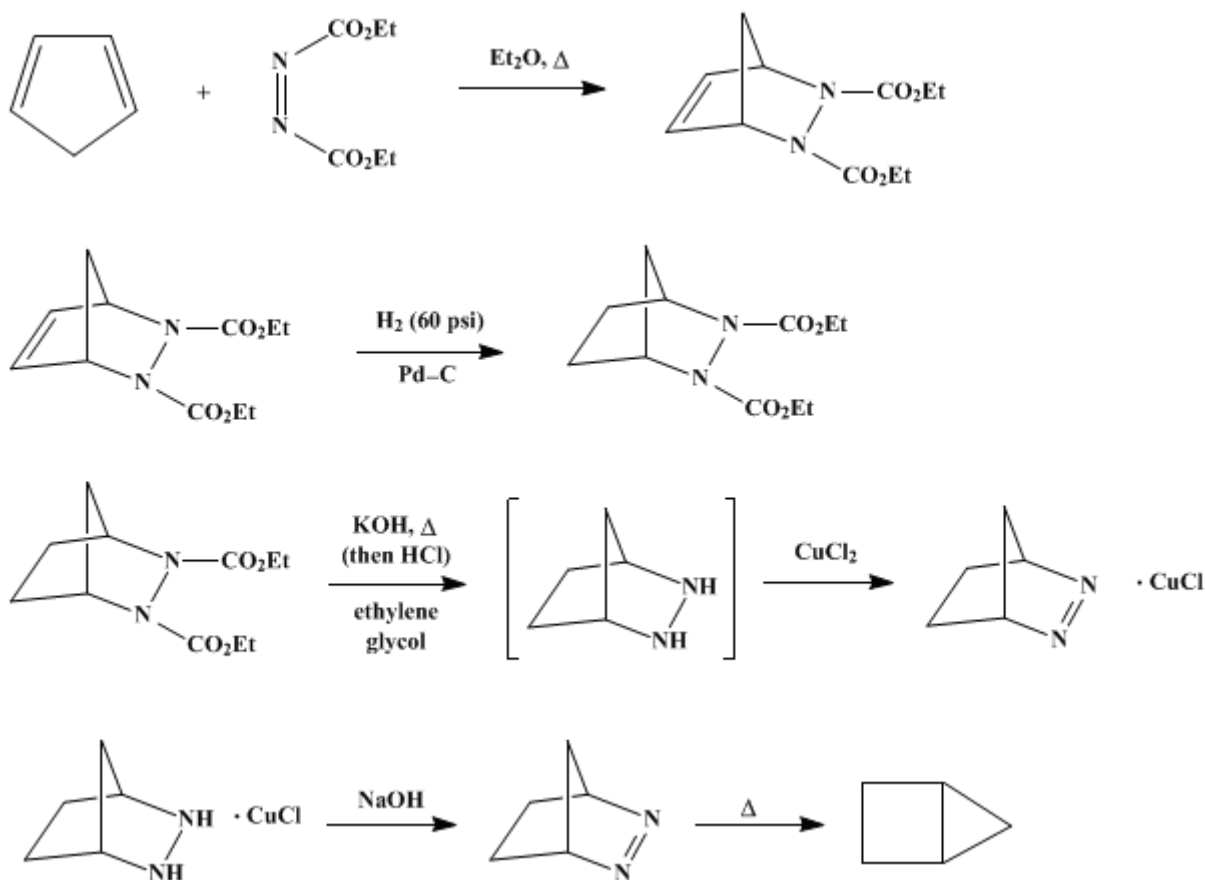
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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BICYCLO[2.1.0]PENTANE



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1. Procedure

A. *Diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate*. In a 1-l., three-necked, round-bottomed flask equipped with a constant-pressure dropping funnel, a mechanical stirrer, and a reflux condenser is placed 174 g. (1.0 mole) of *ethyl azodicarboxylate*² in 150 ml. of *ether*. Freshly prepared *cyclopentadiene*³ (70 g., 1.06 moles) is added dropwise over a 1-hour period to the stirred ethereal solution of *diethyl azodicarboxylate*. During the addition a gentle reflux is maintained by external cooling with an ice-water bath as needed. When the addition is complete, the reaction mixture is allowed to stand for 4 hours, or less if the yellow color of the azodicarboxylic acid ester disappears. The dropping funnel and condenser are replaced by a glass stopper and a short distillation head, respectively. The ether and unreacted diene are distilled off on a steam bath and the residue is transferred to a 500-ml. round-bottomed boiling flask equipped with a 30-cm. Vigreux column. After a small forerun the *diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate* distills to give 218–228 g. (91–95%) of a colorless or very pale yellow, viscous liquid, b.p. 119–120° (0.4 mm.).

B. *Diethyl 2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate*. A mixture of 112 g. (0.47 mole) of *diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate* and 125 ml. of absolute *ethanol* is placed in a standard Paar bottle along with 0.2 g. of 5% *palladium* on *carbon* catalyst (Note 1). The bottle is attached to the Paar hydrogenation apparatus, and shaking is begun using an initial pressure of 60 p.s.i. After 2 hours, *hydrogen* uptake ceases. The mixture is gravity-filtered twice and the *ethanol* is removed using a rotary evaporator. The entire procedure is repeated on a second batch and the crude product

from the combined runs is placed in a 500-ml. round-bottomed boiling flask fitted with a 15-cm. Vigreux column. Fractional distillation gives 218–223 g. (95–97%) of diethyl 2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate, b.p. 107–108° (0.05 mm.), $n^{22D} = 1.4730$.

C. *2,3-Diazabicyclo[2.2.1]hept-2-ene*. A slow stream of nitrogen is bubbled through 1.2 l. of ethylene glycol (Note 2) for 20 minutes in a mechanically stirred 2-l. three-necked flask with mild heating (Note 3). The gas inlet tube is replaced with a condenser and a thermometer which reaches below the level of the ethylene glycol, and 275 g. (4.2 moles) of reagent grade potassium hydroxide pellets (85% pure) is added in four portions. A constant-pressure dropping funnel containing 223 g. (0.92 moles) of diethyl 2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate is connected and the reaction vessel is flushed with nitrogen. The ethylene glycol solution is heated to 125° and the diethyl 2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate is added as rapidly as is permitted by its viscous nature. The heating source is removed whenever the reaction temperature approaches 130°. After the addition is complete, the reaction mixture is stirred at 125° for 1 hour. The reaction mixture is allowed to cool and then poured slowly into a 4-l. beaker which contains 1 kg. each of ice and water and 450 ml. of concentrated hydrochloric acid (*Caution. Vigorous foaming occurs*) (Note 4). When the acidification is complete, the reaction mixture is warmed to about 40° and neutralized with 5N ammonium hydroxide. Half of this neutral solution is transferred to a second 4-l. beaker and subsequent operations are carried out on both batches.

The solution is stirred slowly and *ca.* 25 ml. of 2N cupric chloride solution is added slowly. The blue-green color of the cupric chloride is rapidly discharged and a brick red coloration occurs, followed by the precipitation of voluminous bright red crystals of the cuprous chelate of 2,3-diazabicyclo[2.2.1]hept-2-ene. The pH is adjusted to 5–6 by the addition of 5N ammonium hydroxide. Addition of 25 ml. of the cupric chloride solution followed by neutralization of the generated hydrochloric acid with 5N ammonium hydroxide is repeated five times. The precipitate is collected by filtration and the filtrate is again treated with 25-ml. portions of cupric chloride solution and 5N ammonium hydroxide. The procedure is repeated until the filtrate is clear red at pH 3–4 and returns to a cloudy green at pH 6 with no further formation of precipitate (Note 5).

The combined precipitate from the two batches is carefully washed with 500 ml. of 20% ammonium chloride solution, two 400-ml. portions of 95% ethanol, and two 300-ml. portions of cold water. The product is sucked as dry as possible in the suction funnel.

The damp product is broken up and transferred to a 1-l. flask containing a magnetic stirring bar and 400 ml. of water. A cold solution of 60 g. of sodium hydroxide in 100 ml. of water is added slowly with magnetic stirring. The stirred yellow-orange suspension is then continuously extracted with 700 ml. of pentane for 48 hours.

The pentane extract is dried over 10 g. of anhydrous potassium carbonate. After removal of the drying agent by filtration, the pentane is slowly removed from the product by distillation through a 20-cm. Hempel column packed with glass helices (Note 6). When the pentane is removed, a white crystalline residue remains which weighs 78–83 g. (88–94% yield based on the hydrogenated Diels-Alder adduct). This 2,3-diazabicyclo[2.2.1]hept-2-ene melts at 98.0–99.5° (Note 7).

D. *Bicyclo[2.1.0]pentane*. Finely powdered 2,3-diazabicyclo[2.2.1]hept-2-ene (83 g., crude product from above) is placed in a 500-ml., one-necked, round-bottomed flask. The flask is heated at 130–140° in an oil bath to completely remove any traces of pentane. A 25-cm. unpacked Hempel column is installed and connected directly to a 100-ml. receiver flask having a side arm to which is attached a drying tube packed with silica gel. The receiver is cooled in a dry ice-acetone bath. The azobicyclic is pyrolyzed by heating the oil bath to 180–195°. At the preferred rate of pyrolysis, the starting material condenses about one fourth of the way up the column. Occasional flaming of the column may be necessary to prevent plugging of the column by the solidifying starting material. At the end of the pyrolysis (8 hours) only a small, black, nonvolatile residue remains: The condensed bicyclo[2.1.0]pentane is allowed to warm to room temperature, dried over anhydrous magnesium sulfate, and the drying agent removed by filtration through glass wool into a 100-ml. distillation flask. (*Caution! Bicyclo[2.1.0]pentane is a very volatile hydrocarbon and requires appropriate handling for high yields.*) Distillation leaves a residue of about 1 g. of the starting azobicyclic and affords 53.5–55.5 g.

(90.0–93.5%) of bicyclo[2.1.0]pentane, b.p. 45.5°, n_D^{20} 1.4220 (Note 8).

2. Notes

1. The submitters effected the hydrogenation using a medium-capacity, rocker-type, high-pressure hydrogenator with an initial hydrogen pressure of 700 p.s.i. By employing these conditions, the reaction time is reduced to 20–30 minutes. The yield is unchanged.
2. Technical grade ethylene glycol such as that sold by Union Carbide Corp. is suitable for this purpose.
3. A large oil bath supported by a laboratory jack is used for this and subsequent operations when rapid removal of the heat source might be necessary.
4. Foaming may easily be controlled even with rapid addition of the basic solution by vigorous stirring employing the mechanical stirrer used during the reaction.
5. The precipitation of copper oxides in slightly alkaline solution should not be confused with the formation of the bright red crystals of the organocuprous complex. Recrystallization of the crude copper complex from boiling 20% ammonium chloride (pH 4) affords lustrous brick red needles. Analytically pure material is obtained on a second recrystallization from 0.001*N* hydrochloric acid followed by drying over phosphorus pentoxide.
6. If the supersaturated pentane solution tends to foam toward the end of the distillation, the pot should be allowed to cool. This causes the product to crystallize. Once the crystals start to form, foaming is no longer a problem.
7. This material may be further purified (m.p. 99.5–100.0°) by recrystallization from pentane or methanol, or by sublimation at 85° (60 mm.). Owing to the unusually high vapor pressure of this product, large losses may be encountered on recrystallization or sublimation unless due care is exercised.
8. If all the pentane is removed before pyrolysis, the bicyclo [2.1.0]pentane shows no impurities on vapor phase chromatography with a 20% Dow 710 on 50/60 U Anaprep column. Analysis by n.m.r. also revealed the absence of any traces of cyclopentene in the spectrum consisting of three complex multiplets at 0.3–0.8, 1.1–1.7, and 1.9–2.4 p.p.m. (downfield from internal tetramethylsilane reference).

3. Discussion

The procedure described is a modification of that developed by Diels⁴ and Criegee.⁵ Bicyclo[2.1.0]pentane has been prepared by the pyrolysis of 2,3-diazabicyclo[2.2.1]hept-2-ene,^{5,6} the photolysis of 2,3-diazabicyclo[2.2.1]hept-2-ene,⁷ the pyrolysis of *N*-phenyl-2-oxo-3-azabicyclo[2.2.1]heptane,⁸ and the addition of methylene to cyclobutene.⁹

The procedure described is suitable for the preparation of bicyclo [2.1.0]pentane on a large scale. The product is obtained free of impurities and the general method is relatively safe. The starting materials are readily available. The hydrolysis of the diester is very reproducible, a feature that was not true of the literature procedure.⁴ The pyrolysis step is much simpler and cleaner than the published description.⁵ In addition, the procedure described gives a general method of hydrazo oxidation and for the pyrolysis of azo compounds. Oxidations of the type described in this procedure have been used to prepare a wide variety of cyclic azo compounds. Highly unstable azo compounds have been isolated as the stable crystalline cupric chloride complexes.^{10,11,12} The thermolysis (and/or photolysis) of appropriately substituted cyclic azo compounds has become a highly useful method for the preparation of strained ring systems.^{13,14,15,16,17,18}

References and Notes

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

cuprous chelate of 2,3-diazabicyclo[2.2.1]hept-2-ene

ethanol (64-17-5)

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether (60-29-7)

ammonium chloride (12125-02-9)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

nitrogen (7727-37-9)

carbon (7782-42-5)

potassium hydroxide (1310-58-3)

palladium (7440-05-3)

ethylene glycol (107-21-1)

cupric chloride (7758-89-6)

ammonium hydroxide (1336-21-6)

methylene (2465-56-7)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

Cyclopentene (142-29-0)

Ethyl azodicarboxylate

diethyl azodicarboxylate (1972-28-7)

CYCLOPENTADIENE (542-92-7)

Bicyclo[2.1.0]pentane,
bicyclo [2.1.0]pentane (185-94-4)

Diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate,
diethyl 2,3-diazabicyclo[2.2.1] hept-5-ene-2,3-dicarboxylate (14011-60-0)

Diethyl 2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (18860-71-4)

2,3-Diazabicyclo[2.2.1]hept-2-ene,
2,3-diazabicyclo [2.2.1]hept-2-ene

tetramethylsilane (75-76-3)

N-phenyl-2-oxo-3-azabicyclo[2.2.1]heptane

cyclobutene (822-35-5)

phosphorus pentoxide (1314-56-3)