A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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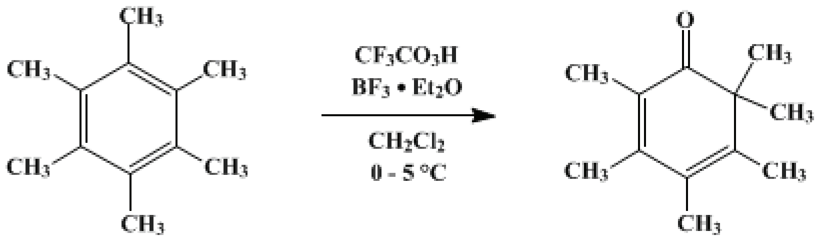
2,3,4,5,6,6-HEXAMETHYL-2,4-CYCLOHEXADIEN-1-ONE

[2,4-Cyclohexadien-1-one, 2,3,4,5,6,6-hexamethyl-]



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1. Procedure

Caution! The preparation and handling of peroxytrifluoroacetic acid should be carried out behind a safety screen. Precautions to be observed with 90% hydrogen peroxide are described in (Note 3) and should be followed carefully.

To a 300-ml. three-necked flask equipped with a glass Trubore stirrer and two loose-fitting ground-glass stoppers are added 46.2 g. (0.22 mole) of trifluoroacetic anhydride and 50 ml. of methylene chloride (Note 1). The stirred solution is cooled in an ice bath, and 5.40 ml. (0.20 mole) of 90% hydrogen peroxide is added from a 10-ml. graduated cylinder in *ca.* 1-ml. portions over a period of 10 minutes (Note 2),(Note 3), and (Note 4). When the mixture has become homogeneous, it is allowed to warm to room temperature for a few minutes and is then cooled once more in an ice bath to 0°.

A solution of 24.2 g. (0.15 mole) of hexamethylbenzene in 300 ml. of distilled methylene chloride is prepared in a 1-l. three-necked flask equipped with two ice-jacketed addition funnels (Note 5) and a thermometer. The solution is cooled to 5° in an ice-ethanol bath and is agitated by a magnetic stirrer. The cold peroxytrifluoroacetic acid solution is added at a constant rate to the hexamethylbenzene solution from one of the ice-jacketed addition funnels at the same time that 63.3 ml. of technical (48%) boron trifluoride etherate is added from the second addition funnel. The additions require *ca.* 45 minutes, and as far as possible they should be completed at the same time. During this period the temperature of the reaction mixture is maintained between 0° and 5° (Note 6) and (Note 7).

The mixture is stirred at 0–5° for 1 hour after addition is complete and then is hydrolyzed with 100 ml. of water, which is added quickly. The reaction mixture is extracted consecutively with two 100-ml. portions of water, three 100-ml. portions of saturated aqueous sodium bicarbonate, one 75-ml. portion of aqueous 5% sodium hydroxide, and two 75-ml. portions of water. The organic phase is dried over anhydrous magnesium sulfate, and the solvent is removed on a rotary evaporator. The residue, a mobile yellow oil, is distilled through a 6-in. Vigreux column under reduced pressure to give pure (Note 8) 2,3,4,5,6,6-hexamethyl-2,4-cyclohexadien-1-one, b.p. 85–87° (1.0 mm.). The yield is 22–24 g. (82–90%) (Note 9) and (Note 10).

2. Notes

1. Excess anhydride is used to remove water introduced during the addition of 90% hydrogen peroxide.
2. Available from FMC Corp., Inorganic Chemicals Division, 808 Gwynne Building, Cincinnati 2, Ohio.
3. The precautions to be observed with 90% hydrogen peroxide have been described in detail.[2] In essence it is important to prevent contact of this reagent with any easily oxidizable substrates, such as wood, alcohols, and sugars and with heavy-metal salts, since the latter catalyze its decomposition.

Storage of hydrogen peroxide in the laboratory should be arranged in such a way that, even if the bottle containing the reagent breaks, the hydrogen peroxide does not come into contact with any materials of this kind. Small samples of 90% hydrogen peroxide are regularly shipped in vented glass bottles provided with a protective outside metal container, and it is desirable to use this container while storing the reagent in the laboratory. If spillage of the reagent occurs, dilution with at least several volumes of water is recommended. In weighing out 90% hydrogen peroxide it is good practice never to return excess reagent to the stock bottle; rather it should be diluted with water and discarded to avoid any possibility that the stock bottle will be contaminated.

4. The hydrogen peroxide may be added in one portion, but then an appreciable exotherm is noted.

5. A simple procedure for the construction of a jacketed addition funnel has been described.[3]

6. Boron trifluoride gas may be used in place of the etherate. In this case a fritted-glass gas-dispersion tube that extends below the liquid surface replaces the second addition funnel. Boron trifluoride gas (0.20 mole, 4.48 l.) is passed through the solution as the peroxytrifluoroacetic acid is added. The boron trifluoride may be metered into the mixture through a calibrated flowmeter containing carbon tetrachloride as the indicator liquid. Alternatively, a premeasured quantity of boron trifluoride may be displaced by carbon tetrachloride from a gas bulb. The yield is approximately the same regardless of the source of boron trifluoride.

7. If boron trifluoride is omitted as a reactant, the yield falls to about 67%.

8. This material should be at least 98% pure by vapor-phase chromatography (SE-30 column at 180–200°). It usually crystallizes if stored in a refrigerator. Unreacted hexamethylbenzene, present if insufficient oxidant is used, can best be removed by column chromatography on alumina with pentane as eluant.

9. The reaction can be used to prepare hexaethyl-2,4-cyclohexadienone, m.p. 44–45°, in 82% yield from hexaethylbenzene and 3,4,6,6-tetramethyl-2,4-cyclohexadienone from durene in over 80% yield.

10. One can use a solution of 90% hydrogen peroxide (*Caution!* see (Note 3) in acetic-sulfuric acid as the oxidant in place of peroxytrifluoroacetic acid-boron trifluoride. The reaction is less exothermic, therefore easier to control. The generality of the procedure for other polyalkylbenzenes has not been tested. A typical procedure is as follows: To a well-stirred slurry of 100 g. (0.618 mole) of hexamethylbenzene in 200 ml. of methylene chloride, 400 ml. of glacial acetic acid, and 300 ml. of concentrated sulfuric acid maintained at 0–10° there is added, during 30 minutes, a solution of 28 ml. (0.75 mole) of 90% hydrogen peroxide in 45 ml. of glacial acetic acid and 30 ml. of concentrated sulfuric acid. After addition, the mixture is stirred at 0° for 4 hours before workup, which is essentially as described in the original procedure. The yield of hexamethyl-2,4-cyclohexadienone is 95 g. (88%). The procedure is derived from that of Hart, Collins, and Warning[4] (private communication from H. Hart).

3. Discussion

The method described is that of Waring and Hart.[5] Dienones of this type have not been available by any previously described synthetic route.

4. Merits of the Preparation

Dienones of this class are useful starting materials for the preparation of bicyclic compounds via Diels-Alder reactions[5] and for the synthesis of small ring compounds.[6] The 2,4-dienone can be converted quantitatively to the 2,5-isomer by treatment with fuming sulfuric acid and subsequent hydrolysis.[7] The oxidation procedure is also applicable to the conversion of mesitylene to mesitol or of isodurene to isodurenol,[8] and can be used to convert tetramethylethylene quantitatively and directly to pinacolone.[9] A review which includes references to many applications of the procedure described here is available.[10]

References and Notes

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

acetic-sulfuric acid

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

sodium hydroxide (1310-73-2)

sodium bicarbonate (144-55-8)

carbon tetrachloride (56-23-5)

Pinacolone (75-97-8)

hydrogen peroxide (7722-84-1)

Mesitylene (108-67-8)

Pentane (109-66-0)

methylene chloride (75-09-2)

tetramethylethylene (563-79-1)

magnesium sulfate (7487-88-9)

Durene (95-93-2)

Hexamethylbenzene (87-85-4)

Isodurene (527-53-7)

boron trifluoride (7637-07-2)

mesitol (527-60-6)

boron trifluoride etherate (109-63-7)

peroxytrifluoroacetic acid

trifluoroacetic anhydride (407-25-0)

2,3,4,5,6,6-Hexamethyl-2,4-cyclohexadien-1-one,
2,4-Cyclohexadien-1-one, 2,3,4,5,6,6-hexamethyl-,
hexamethyl-2,4-cyclohexadienone (3854-96-4)

hexaethyl-2,4-cyclohexadienone

hexaethylbenzene (604-88-6)

3,4,6,6-tetramethyl-2,4-cyclohexadienone

peroxytrifluoroacetic acid-boron trifluoride

isodurenol