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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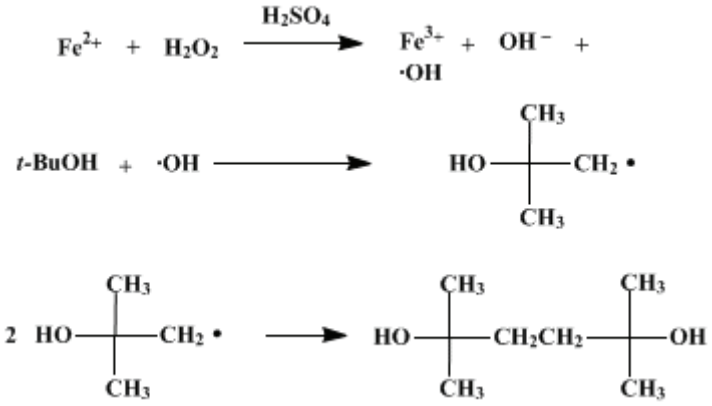
α,α,α',α'-TETRAMETHYLTETRAMETHYLENE GLYCOL

[2,5-Hexanediol, 2,5-dimethyl-]



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1. Procedure

Tertiary butyl alcohol (900 ml., 702 g., 9.47 moles) is dissolved in a solution prepared by mixing 28 ml. (0.50 mole) of concentrated sulfuric acid with 1.5 l. of water in a 5-l. round-bottomed flask (Note 1) equipped with a thermometer, stirrer, gas inlet tube, and two addition burets. One buret is charged with 86 ml. (1 mole) of 11.6*M* hydrogen peroxide (Note 2), and the other with a solution of 278 g. (1 mole) of ferrous sulfate pentahydrate and 55.5 ml. (1 mole) of concentrated sulfuric acid in 570 ml. of water (Note 3). The reaction flask is swept out with nitrogen and cooled to 10° by means of an ice bath. Stirring is commenced and the two solutions are added simultaneously and equivalently over a period of 20 minutes. The temperature is held below 20°.

When the addition is completed, 50 ml. (1 mole) of 52% sodium hydroxide is added with stirring and cooling, and then 450 g. of anhydrous sodium sulfate (not all of the salt dissolves). The cold solution is transferred to a separatory funnel and the phases are separated. The organic layer is neutralized with 52% sodium hydroxide; approximately 20 ml. is required to bring the pH to 7. The aqueous layer, including the precipitated ferric hydroxide, is added to the aqueous portion of the reaction mixture and the whole is extracted with 400 ml. of *t*-butyl alcohol. This extract is similarly treated with 52% sodium hydroxide (about 5 ml. is required). The resulting aqueous layer is combined with the main aqueous fraction, which is again extracted with 400 ml. of *t*-butyl alcohol. This whole process is again repeated so that the organic phases comprise the three extracts and the phase which separated initially from the reaction mixture.

The four organic fractions are combined and distilled under reduced pressure. The distillation is continued until the temperature of the flask is about 70°/5 mm. in order to remove most of the *t*-butyl alcohol. The still residue is then extracted with 2 l. of ether and the extract is treated with decolorizing carbon and diatomaceous earth. Distillation of the ether at slightly reduced pressure from a water bath yields α,α,α',α'-tetramethyltetramethylene glycol as a pale yellow crystalline residue weighing 30–45 g. (41–62% yield based on hydrogen peroxide employed). The crude product is digested at room temperature in a mixture of 30 ml. of ether and 70 ml. of cyclohexane. The resulting slurry is filtered to yield 29–34 g. (40–46%; (Note 4)) of the glycol as a white crystalline solid, m.p. 87–88°. The product, which is pure enough for most purposes, can be further purified by recrystallization from ethyl acetate (1 g. in 4 ml.), cyclohexane (1 g. in 20 ml.), or water (1 g. in 2 ml.).

2. Notes

1. The flask should have creased sides and a conical indentation in the bottom and should be equipped with a high-speed, propeller-type stirrer rotated to force the liquid downwards. The stirrer should be constructed of glass because metals may interfere with the generation and utilization of the hydroxyl free radicals.
2. Commercial 35% hydrogen peroxide was employed. Any concentration from 5% to 50% may be used.
3. It is convenient to calibrate the burets so that the liquid is divided into 20 equal portions. Then, in the addition of the reagents, these calibrations aid in synchronizing the rates.
4. The submitter reports yields of 48–55%, which are slightly higher than those given here.

3. Discussion

α,α,α',α'-Tetramethyltetramethylene glycol has been prepared by the action of methylmagnesium bromide on acetonylacetone,[2,3,4] on ethyl levulinate,[5] and on ethyl succinate.[6,7] It has also been made by the hydrogenation of 2,5-dimethyl-3-hexyne-2,5-diol over nickel[8,9] and over platinum[10,11] and by the hydrogenation of 2,5-dihydroperoxy-2,5-dimethyl-3-hexyne.[12] Other methods of preparation include the autoxidation of 2,5-dimethylhexane[13] and the alkaline hydrolysis of 2,5-dibromo-2,5-dimethylhexane.[6] The present method, the hydroxyl- radical coupling of *t*-butyl alcohol,[14] is a one-step synthesis using readily available starting materials. A similar technique may be used to synthesize α,α,α',α'-tetramethyladipic acid from pivalic acid, α,α,α',α'-tetramethyltetramethylenediamine from *t*-butylamine, and α,α,α',α'-tetramethyladiponitrile from pivalonitrile.[14]

References and Notes

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

sulfuric acid (7664-93-9)

ethyl acetate (141-78-6)

ether (60-29-7)

sodium hydroxide (1310-73-2)

ethyl succinate

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

platinum (7440-06-4)

cyclohexane (110-82-7)

nickel (7440-02-0)

decolorizing carbon (7782-42-5)

hydrogen peroxide (7722-84-1)

Acetonylacetone (110-13-4)

Pivalic acid (75-98-9)

methylmagnesium bromide (75-16-1)

Tertiary butyl alcohol,
t-butyl alcohol (75-65-0)

2,5-dimethyl-3-hexyne-2,5-diol (142-30-3)

2,5-Hexanediol, 2,5-dimethyl-,
α,α,α',α'-Tetramethyltetramethylene glycol (110-03-2)

ferrous sulfate pentahydrate

ferric hydroxide (1309-33-7)

ethyl levulinate (539-88-8)

2,5-dihydroperoxy-2,5-dimethyl-3-hexyne (3491-36-9)

2,5-dimethylhexane (592-13-2)

2,5-dibromo-2,5-dimethylhexane

pivalonitrile (630-18-2)

t-butylamine (75-64-9)

α,α,α',α'-tetramethyladipic acid

α,α,α',α'-tetramethyltetramethylenediamine

α,α,α',α'-tetramethyladiponitrile