

Trimethylene Oxide



[503-30-0] C_3H_6O (MW 58.09)

InChI = 1/C3H6O/c1-2-4-3-1/h1-3H2

InChIKey = AHHWIHXENZJRFQ-UHFFFAOYAE

(three-carbon homologation)

Alternate Name: oxetane.

Physical Data: bp 50 °C; d 0.893 g cm⁻³.

Solubility: sol H₂O and most common organic solvents.

Form Supplied in: commercially available in 97% purity.

Preparative Methods: from 3-chloropropyl acetate and **Potassium Hydroxide**;¹ from **1,3-Propanediol** and **Diethyl Azodicarboxylate/Triphenylphosphine**.²

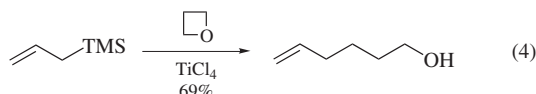
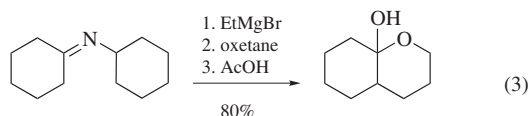
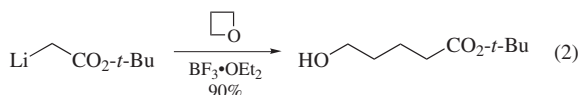
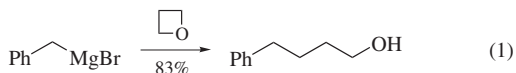
Purification: by distillation.

Original Commentary

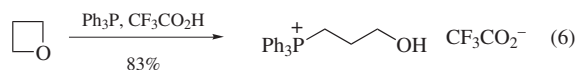
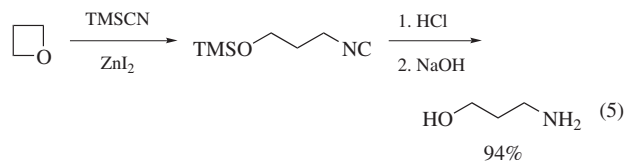
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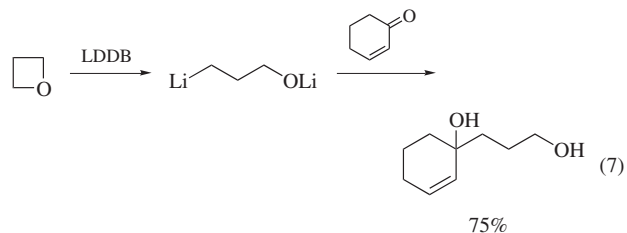
Reaction with Carbon Nucleophiles. Trimethylene oxide readily undergoes ring opening with a variety of carbon nucleophiles to give the three-carbon homologated alcohol. Substituted oxetanes undergo analogous reactions. Grignard reagents and alkyllithiums react cleanly, although reduced yields are obtained with secondary Grignard reagents (eq 1).³ Alkyl cuprates,⁴ alkenyllithium,⁵ alkenylaluminum,⁶ alkynyllithium,⁷ and allyllithium⁸ reagents have been used to open oxetane. Reaction with ester and amide enolates provides access to 5-hydroxy esters and amides (eq 2)⁹ and ketone imine salts react with oxetane (eq 3) as well.¹⁰ **Boron Trifluoride Etherate** is frequently used to assist the ring opening. Oxetane reacts with allylsilanes and **Titanium(IV) Chloride** to give the ring-opened products (eq 4).¹¹



Reaction with Heteroatom Nucleophiles. Trimethylene oxide undergoes ring opening with a wide variety of heteroatom nucleophiles. Reaction with **Cyanotrimethylsilane** gives, after hydrolysis of the isocyanide, 3-aminopropanol (eq 5).^{12,13} 3-Hydroxydimethylsulfonium salts are obtained on reaction with **Trifluoromethanesulfonic Acid** and **Dimethyl Sulfide**.¹⁴ Phosphonium salts are obtained on reaction with **Triphenylphosphine** and **Trifluoroacetic Acid** or triflic acid (eq 6).¹⁵ Reaction with phosphine anions gives the 3-hydroxypropylphosphines.¹⁶ Trimethylene oxide is readily opened by selenium nucleophiles, such as phenylselenide anion, which gives 3-hydroxypropyl phenyl selenide.¹⁷



Reductive Opening of Oxetane. Reduction with **Lithium 4,4'-Di-tert-butylbiphenylide** (LDDB) gives the 3-lithioalkoxide, which reacts with a wide variety of electrophiles (eq 7).¹⁸ A similar opening occurs with the **Potassium/18-Crown-6** complex.¹⁹



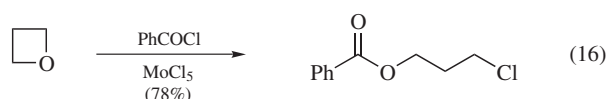
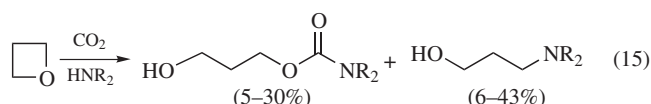
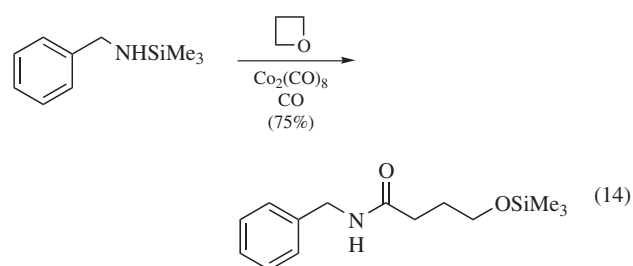
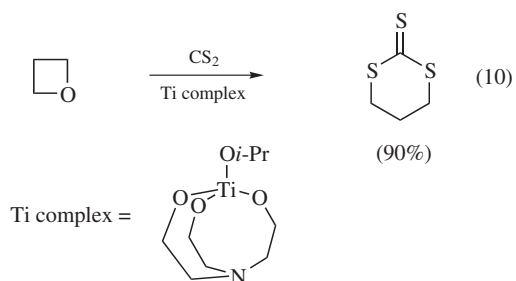
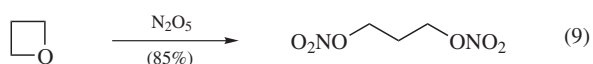
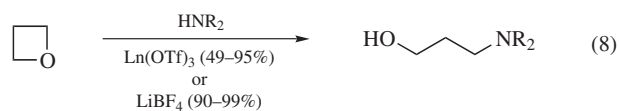
First Update

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More Recent Uses of Trimethylene Oxide.

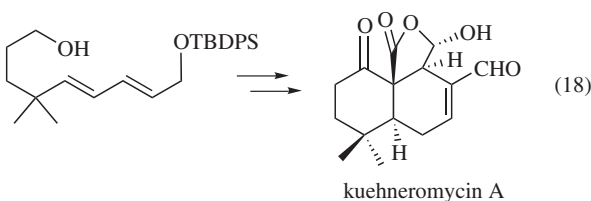
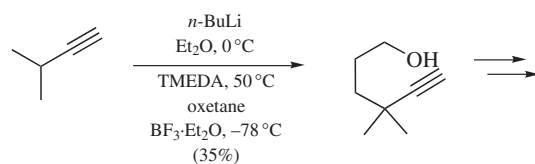
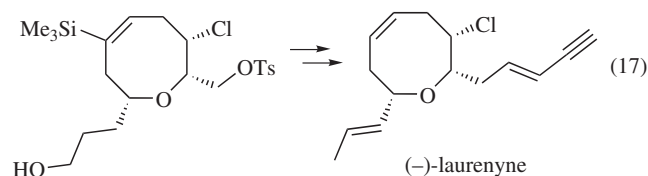
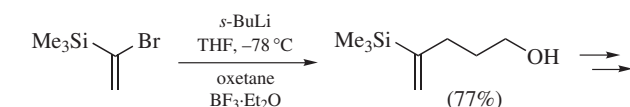
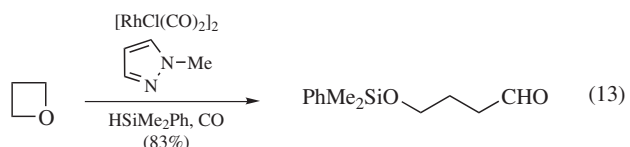
Further Reactions with Heteroatom Nucleophiles. Recent advances in the ring opening of trimethylene oxide with heteroatom nucleophiles have centered on nitrogen and sulfur containing reagents. Direct formation of aminols from the reaction of amines with trimethylene oxide eliminates the traditional need for formation of the isocyanide and subsequent hydrolysis (eq 5). The aminolysis of trimethylene oxide has been promoted by either Lewis acids²⁰ or lanthanide(III) salts (eq 8).^{21,22} Dinitrogen pentoxide reacts with trimethylene oxide to afford the ring-opened dinitrate (eq 9).²³ Catalyzed by a highly Lewis acidic titanotriane, trimethylene oxide reacts with 2 equiv of carbon disulfide to afford cyclic trithiocarbonates (eq 10).²⁴



Further Reactions with Carbon Nucleophiles. Cyanotrimethylsilane has previously been shown to open trimethylene oxide to the isonitrile; utilization of a solid base, MgO, results in formation of the nitrile (eq 11).²⁵ Ring opening with α -halogenalkyllithiums leads to the chain extended halo-substituted butanol (eq 12).²⁶



Ring-opening Carbonylation of Oxetane. Silylformylation of trimethylene oxide with dimethylphenylsilane and carbon monoxide is catalyzed by rhodium in the presence of an amine base to suppress side reactions (eq 13).²⁷ Dicobalt octacarbonyl catalyzes ring opening with *N*-silylamines and CO to afford amides (eq 14).²⁸ Carbamate formation is possible without the presence of a catalyst. The reaction of an amine and carbon dioxide (40 atm) yields the carbamate anion, which acts as a nucleophile to give the desired product. However, in this scheme formation of the aminol by direct reaction of amine with trimethylene oxide could not be suppressed (eq 15).²⁹ Acylative cleavage of trimethylene oxide is possible with standard Lewis acids, e.g., AlCl₃, however, group five and group six metal halides are more reactive and afford higher yields with shorter reaction times (eq 16).³⁰



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