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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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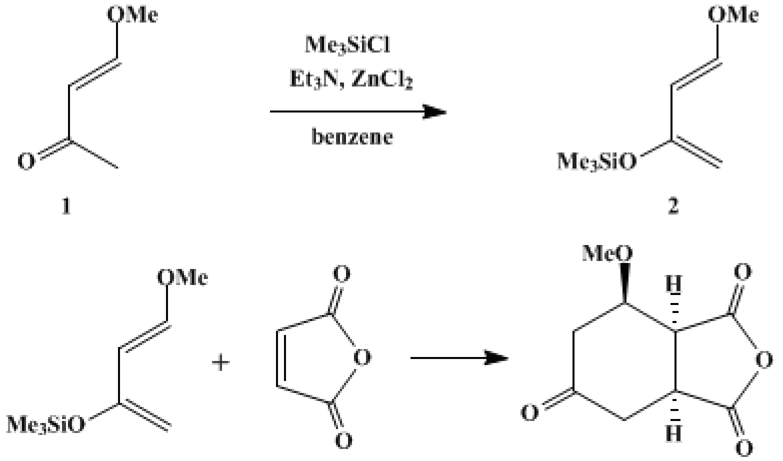
PREPARATION AND DIELS–ALDER REACTION OF A HIGHLY NUCLEOPHILIC DIENE: *trans*-1-METHOXY-3-TRIMETHYLSILOXY-1,3-BUTADIENE AND 5β-METHOXYCYCLOHEXAN-1-ONE-3β,4β-DICARBOXYLIC ACID ANHYDRIDE

[Silane, [(3-methoxy-1-methylene-2-propenyl)oxy]trimethyl-]



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Checked by Dennis Golob, John Dynak, and Robert V. Stevens.

1. Procedure

Caution! Benzene (see Section B) has been identified as a carcinogen; ***OSHA*** *has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.*

A. *Preparation of the zinc chloride*. Reagent-grade zinc chloride (50 g) is placed in an evaporating dish and heated in a fume hood with a Fisher burner until no more water vapor is driven off. The hot dish is rapidly transferred to a glove bag that has been maintained under nitrogen. After the zinc chloride has cooled to a transparent glassy solid, it is ground to a fine powder with a mortar and pestle. The solid is transferred to a tightly stoppered bottle and stored in a desiccator over Drierite.

B. *Preparation of 1-methoxy-3-trimethylsiloxy-1,3-butadiene*. Triethylamine (575 g, 5.7 mol) is stirred mechanically in a three-necked flask (Note 1). To this is added 10.0 g (0.07 mol) of zinc chloride prepared as described above. The mixture is stirred at room temperature under nitrogen for 1 hr. A solution of 250 g (2.50 mol) of 4-methoxy-3-buten-2-one (from Aldrich Chemical Company, Inc.) in 750 mL of benzene is added all at once. Mechanical stirring is continued for 5 min. Chlorotrimethylsilane (542 g, 5.0 mol) is added rapidly. The reaction mixture first turns pink, then red, and finally brown. Heat is evolved and the reaction is kept below 45°C by cooling in an ice bath. After 30 min, the mechanically stirred solution is heated by a heating mantle to 43°C (Note 2). This temperature is maintained for 12 hr. The reaction mixture becomes very thick during this time. After the mixture cools to ambient temperature, it is poured, with mixing, into 5 L of ether. The solid material is filtered through Celite. The Celite and solid material are removed and stirred with 4 L more of ether and refiltered through Celite. The combined ether washings are evaporated under reduced pressure (rotary evaporator) to a brown, sweet-smelling oil. The oil is transferred to a 1-L, single-necked flask equipped with an 18-in. Vigreux column (Note 3). Careful fractional distillation under water vacuum affords a forerun of approximately 16 g that boils at 70–78°C (22 mm). This fraction consists of impure diene that contains 4-methoxy-3-buten-2-one. The main fraction boils at 78–81°C (23 mm) and consists of 245 g of diene (Note 4) with approximately 5–10% of 4-methoxy-3-buten-2-one (Note 5). This material is suitable for most purposes. If higher purity is desired, the second fraction may be redistilled under reduced pressure through an 18-in. Vigreux column to afford 200 g (46%) of *trans*-1-methoxy-3-trimethylsiloxy-1,3-butadiene (Note 6).

C. *5β-Methoxycyclohexan-1-one-3β,4β-dicarboxylic acid anhydride*. To 3.00 g (0.174 mol) of 1-methoxy-3-trimethylsiloxy-1,3-butadiene at 0°C (ice bath) is added a total of 980 mg (0.01 mol) of freshly sublimed maleic anhydride in portions of 70–80 mg each over a period of 25 min. When the addition is complete, the ice bath is removed and the clear solution is stirred for 15 min at room temperature (Note 7). Three 5-mL portions of a solution of tetrahydrofuran (35 mL) and 0.1 *N* hydrochloric acid (15 mL) are added and the solution is stirred for 1 min. The remaining acid solution (35 mL) is added all at once and the resulting solution is poured into 100 mL of chloroform and treated with 25 mL of water. The organic layer is separated and the aqueous layer is extracted four times with 100-mL portions of chloroform. The extracts are combined and dried over anhydrous magnesium sulfate. The solvent is then removed under reduced pressure (Note 8) to provide 2.0 g of an oil which solidifies. Pentane (10 mL) is added to the oily solid and small portions of ether (total of 6 mL) are added; trituration is continued until the crystals become free flowing. The crystals are isolated by filtration and washed with 10 mL of 2 : 1 pentane/ether to afford 1.75 g (90%) of the anhydride, mp 87–89°C. Further recrystallization affords an analytically pure sample, mp 97–98°C.

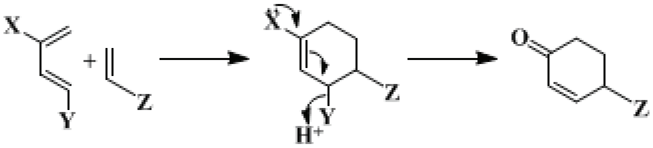
2. Notes

1. The checkers dried all reagents by allowing them to stand over molecular sieves (Type 4A), with the exception of triethylamine, which was dried over potassium hydroxide pellets. The reaction flask was flame-dried. Because of evolution of triethylamine hydrochloride that was encountered during addition of the chlorotrimethylsilane and in the workup, the reaction should be carried out in a hood.
2. The checkers did not cool the reaction, which allowed the temperature to rise to 55°C. After 30 min, the solution was heated overnight with a heating mantle. After 12 hr, the reaction temperature was 67°C.
3. A 16-in. Widmer column packed with 3-mm glass helices may also be used for the distillation.
4. *Caution! When the temperature begins to drop, heating must be stopped. Otherwise, on occasion, a violent reaction may occur with formation of a gas and rapid expansion of the residual tars.*
5. The checkers performed this distillation at a lower pressure (1–10 mm) through a similar Vigreux column to yield 225 g of clear liquid containing fluffy white material (triethylamine hydrochloride) that could not be removed by filtration. The purity of this distillate, determined by NMR, was 90 : 10 (diene : ketone). No forerun was obtained which contained more than 15% ketone.
6. The checkers carefully redistilled the impure distillate through the same previously mentioned distillation apparatus under water vacuum. Six fractions of various amounts were collected and combined to yield (1) a forerun of 64 g, bp 70–78°C (23–25 mm), purity 77 : 23 (diene : ketone); and (2) 145 g of pure diene, bp 78–81°C (23–25 mm). This second distillation seemed to remove the triethylamine hydrochloride from the product.
7. The reaction mixture is initially yellow, but turns colorless when the solution is warmed to room temperature.
8. When the chloroform extract is concentrated, care must be exercised to avoid overheating. The temperature should be no greater than 40°C.

3. Discussion

The procedure described here is a scale-up of the published method[2] for the preparation of 1-methoxy-3-trimethylsiloxy-1,3-butadiene (**2**) from readily available reagents. The preparation of this diene has recently been complemented by a report of the preparation of 1,3-bis(trimethysiloxy)-1,3-butadiene,[3] and earlier by a reported synthesis of a 1,3-dialkoxy-1,3-butadiene.[4]

The electron-donating nature of this diene confers high reactivity and orientational specificity in its reaction with unsymmetrical dienophiles.[5] This fact, coupled with the readily available conversion to the α,β-unsaturated ketone from the imparted functionality, makes 1-methoxy-3-trimethylsiloxy-1,3-butadiene (**2**) a potentially very valuable reagent in organic synthesis. The general reaction scheme is illustrated below:



The high reactivity of the diene is shown by reaction with notoriously unreactive dienophiles such as 1-carbomethoxycyclohexene, 2,5-dihydrobenzoic acid methyl ester,[6] and 2-methylcyclohex-2-en-1-one to give, after mild work-up, the corresponding α,β-unsaturated ketones in quite respectable yields.[5]

The Diels–Alder reaction with maleic anhydride is illustrative of the high reactivity and potential utility of this diene.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 8, 38
- Org. Syn. Coll. Vol. 10, 301

References and Notes

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

1,3-bis(trimethysiloxy)-1,3-butadiene

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

chloroform (67-66-3)

nitrogen (7727-37-9)

potassium hydroxide (1310-58-3)

zinc chloride (7646-85-7)

Triethylamine hydrochloride (554-68-7)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

maleic anhydride (108-31-6)

2-methylcyclohex-2-en-1-one (1121-18-2)

triethylamine (121-44-8)

4-methoxy-3-buten-2-one

CHLOROTRIMETHYLSILANE (75-77-4)

Silane, [(3-methoxy-1-methylene-2-propenyl)oxy]trimethyl-,
1-Methoxy-3-trimethylsiloxy-1,3-butadiene

1-carbomethoxycyclohexene

trans-1-METHOXY-3-TRIMETHYLSILOXY-1,3-BUTADIENE (59414-23-2)

5β-Methoxycyclohexan-1-one-3β,4β-dicarboxylic acid anhydride (87334-37-0)