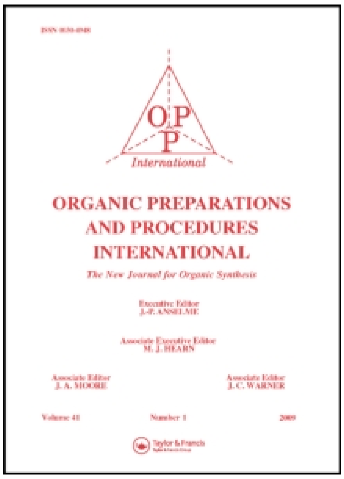

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

THE SYNTHESIS OF TRIMETHYLSILYLMETHOXYMETHYL CHLORIDE

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To cite this Article Schultz, Arthur G. and Wang, Yongwen(1995) 'THE SYNTHESIS OF TRIMETHYLSILYLMETHOXYMETHYL CHLORIDE', Organic Preparations and Procedures International, 27: 5, 572 — 574

To link to this Article: DOI: 10.1080/00304949509458506

URL: http://dx.doi.org/10.1080/00304949509458506

^{1}H NMR: δ 7.51 (d, J = 8.7 Hz, 1), 7.25 (d, J = 3.7 Hz, 1), 6.95 (dd, J_1 = 8.7 Hz, J_2 =3 .7 Hz, 1), 4.05 (t, J = 7.0 Hz, 2), 3.43 (d, J = 14.0 Hz, 2), 2.94 (m, 2), 2.83 (dd, J_1 = 12.9 Hz, J_2 = 10.7 Hz, 2), 1.88 (d, J = 13.5 Hz, 2), 1.75-1.60 (m, 5), 1.1.49-1.60 (m, 2), 1.35-1.25 (m, 4), 0.89 (t, 6.7 Hz, 3). EI MS: m/z = 343 (5%, molecular ion), m/z = 286 (base peak).

Anal. Calcd for $C_{18}H_{28}Cl_3NO$: C, 56.77; H, 7.41; N, 3.68. Found: C, 56.80; H, 7.63; N, 3.64

REFERENCES

1. C. D. Benham *et al.*, *Neuropharmacology*, **32**, 1249 (1993).

2. T. H. Brown and D. G. Cooper, World Patent WO 92/02502; *Chem. Abs.*, **116**, 235459 (1992).

3. Cesium carbonate proved to be a much more efficient base than potassium carbonate. With the latter, only a 3% yield of **1** was obtained after 15 hrs at 195°. The crude product from this reaction was of much lower purity and required chromatographic purification.

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THE SYNTHESIS OF TRIMETHYLSILYLMETHOXYMETHYL CHLORIDE

Submitted by (02/13/95)

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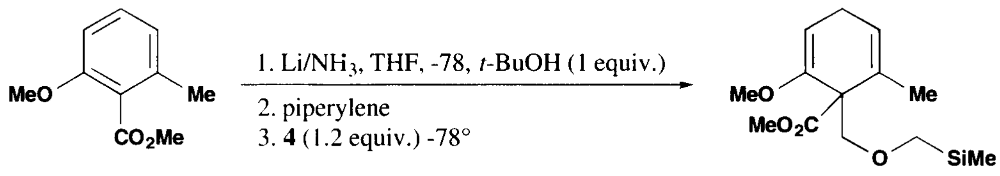
The direct oxidation of aliphatic ethers is difficult because of their high oxidation potential ($\geq$ 2.5 V vs. Ag/AgCl).[1] Substitution of a silyl group for a hydrogen atom at the α-position of ethers results in a significant decrease in oxidation potentials (1.6 to 1.7 V).[2] In connection with a study of photoinduced single electron transfer (SET) reactions in the 2,5-cyclohexadien-1-one series, we desired a practical synthesis of 1,4-cyclohexadiene **2** from methyl 2-methoxy-6-methylbenzoate (**1**).



1 **2**

Alkylation of the corresponding primary alcohol with halomethyltrimethylsilanes was expected to be problematic;[3] consequently, we developed a direct synthesis of **2** by Birch reduction of **1**, followed by alkylation of the resulting ester enolate with trimethylsilylmethoxymethyl chloride (**4**).

In this note, we describe the synthesis of **4** by chloromethylation of trimethylsilylmethanol (**3**).[4] Trimethylsilylmethanol is commercially available[5] or can be prepared from trimethylsilyl chloride.[6] Trimethylsilylmethoxymethyl chloride (**4**) is obtained in 84% yield as a colorless liquid by distillation at reduced pressure. Cyclohexadiene **2** is prepared in good yield by a standard reductive alkylation[7] of **1** at -78° with 1.2 equiv. of **4**.[8]

$$\underset{\mathbf{3}}{Me_3SiCH_2OH} \xrightarrow[\text{HCl, }0^\circ]{\text{paraformaldehyde}} \underset{\mathbf{4}\,(84\%)}{Me_3SiCH_2OCH_2Cl}$$

EXPERIMENTAL SECTION

^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-200 (200 MHz) spectrometer. Infrared spectra were obtained on a Perkin-Elmer 298 spectrometer. Elemental analysis was determined by Quantitative Technologies, Inc., Whitehouse, NJ. Solvents were removed under reduced pressure with a Buchi Rotevapor rotary evaporator while immersing the trap in an ice bath.

Trimethylsilylmethoxymethyl Chloride (4).- A steady stream of dry HCl gas was passed into a mixture of trimethylsilylmethanol (**3**, 4.01 g, 38.5 mmol) and paraformaldehyde (1.27 g, 42.3 mmol) at 0° until a clear solution resulted. Pentane was added and the solution was dried over $MgSO_4$, filtered and evaporated *in vacuo* to give a colorless oil. Distillation under reduced pressure provided **4** (4.9 g, 84%). ^{1}H NMR ($CDCl_3$): δ 0.05 (s, 9H), 3.36 (s, 2H), 5.48 (s, 2H); ^{13}C NMR ($CDCl_3$): δ -3.32, 64.27, 87.23; IR (film) 2950, 2880, 2820, 1430, 1310, 1250, 1120 cm^{-1}.
Anal. Calcd for $C_5H_{13}ClOSi$: C, 39.33; H, 8.58. Found: C, 39.44; H, 8.58

Acknowledgements.- This work was supported by the National Institutes of Health (GM 26568).

REFERENCES

1. T. Shono in *The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and Their Sulfur Analogues.*, S. Patai, Ed., Wiley & Sons, New York, NY, 1980; CH 8.

2. J.-I. Yoshida, T. Maekawa, T. Murata, S.-I. Matsunaga and S. Isoe, *J. Am. Chem. Soc.*, **112**, 1962 (1990).

3. For the unusual *O*-alkylation of alkoxides with iodomethyltrimethylsilane to give *O*-methyl and *O*-trimethylsilyl ethers, see: T. K. Chakraborty and G.V. Reddy, *Chem. Commun.*, 251 (**1989**).

4. For the preparation of β-(trimethylsilyl)ethoxymethyl chloride by a chloromethylation procedure, see: B. H. Lipshutz and J. J. Pegram, *Tetrahedron Lett.*, 21, 3343 (1980).

5. Trimethylsilylmethanol is available from Aldrich Chemical Co. (30,529-4).

6. S. Ambasht, S. K. Chiu, P. E. Peterson and J. Queen, *Synth. Commun.*, 318 (**1980**).

7. A. G. Schultz, F. P. Lavieri, M. Macielag and M. Plummer, *J. Am. Chem. Soc.*, **109**, 3991 (1987).

8. For a study of photoinduced SET reactions of 2,5-cyclohexadienones derived from **1**, see A. G. Schultz, J. E. Reilly and Y. Wang, *Tetrahedron Lett.*, In press.

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A CONVENIENT LARGE-SCALE PREPARATION OF *endo*-2-METHYLBICYCLO[2.2.1]HEPT-5-ENE-*exo*-2-CARBOXYLIC ACID

Submitted by
(01/26/95)

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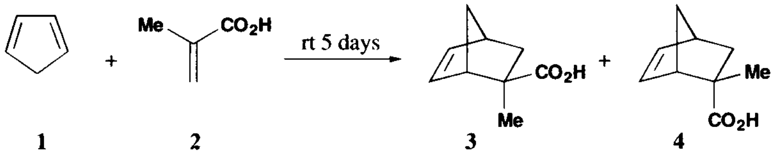
The Diels-Alder condensation of cyclopentadiene (**1**) with methacrylic acid (**2**) has been reported on several occasions.[1-3] In each case, the reaction gave mixtures of the *exo* (**3**) and *endo* isomers (**4**) which were separated either by repeated fractional recrystallization[3] or *via* a multistep lactonization method.[1] However, there are substantial discrepancies in the *exo/endo* isomer ratios reported by these groups. For example, Meek and Trapp[1] have reported that heating methacrylic acid and cyclopentadiene in toluene at 150° (sealed tube) gave a mixture of *exo* and *endo* isomers in a ratio of 65 to 35, while Moriarty *et al.*[3] obtained a ratio of 90 to 10 when methacrylic acid and cyclopentadiene were heated at reflux for 4 hrs. In connection with other work, we needed to prepare the pure *exo* isomer in quantity. Accordingly, this reaction has been reinvestigated and optimized.



1 **2** **3** **4**