Preparation of Trimethylsilylmethyl Derivatives Using Phase Transfer Methods

Saket AMBASHT, Sai Keung CHIU, Paul E. PETERSON*, Jeffrey QUEEN

Department of Chemistry, University of South Carolina, Columbia, South Carolina 29208, U.S.A.

In this paper we describe several procedures for the preparation of some trimethylsilyl compounds which are either commercially unavailable or expensive. Trimethylsilylmethyl acetate (**2**), trimethylsilylmethyl iodide (**5**), and trimethylsilylmethyl bromide (**6**) were prepared by phase transfer catalytic methods, and trimethylsilylmethyl trifluoromethanesulfonate (**4**) was prepared by a non-catalytic phase transfer method. We also report an improved yield in the preparation of trimethylsilylmethanol (**3**) by the reduction of **2** with lithium aluminium hydride.

We shall first mention the previously used preparations and our new ones for the related compounds **2**, **3**, and **4**. The most used preparation for the acetate **2** has been the inconvenient reaction of trimethylsilylmethyl chloride (**1**) and potassium acetate in acetic acid under high pressure and temperature[1,2,3]. Two rarely used methods are the reaction of silver acetate and **5**[4] and the reaction of **1** and potassium acetate in dimethylformamide in the presence of a catalytic amount of hydroquinone[5]. Acetate **2** is a significant precursor of alcohol **3**, an antiseptic[6]. The best known route to **3** has been the lengthy acid methanolysis[1] of **2** which requires, in our hands, several stages with distillative removal of methyl acetate and methanol in each stage. Other methods such as the air oxidation of trimethylsilylmethylmagnesium chloride[4,7]; the alcoholysis of trimethylsilyl methyl peroxide[8]; the hydrolysis of the trimethylsilyl methyl ether[9]; and the oxidation of tris[trimethylsilylmethyl]borane[10] are seldom used due to low yields or impractical starting materials. Reduction of acetate **2** by lithium aluminium hydride has been reported[6] once to give only 33% of alcohol **3**.

We have obtained the acetate **2** in 82% yield by a phase transfer reaction of chloride **1** with solid fused sodium acetate. Tetrabutylammonium chloride, the more effective catalyst, or tetrabutylammonium iodide, the less costly catalyst, and tetrachloromethane solvent were used. The previously employed[6] reduction of **2** by lithium aluminium hydride in ether gave, in our work, 80% of trimethylsilylmethanol **3**.

Generally, alkyl trifluoromethanesulfonates or triflates, which are known for their ease of displacement, are obtained by the addition of trifluoromethanesulfonic anhydride to a mixture of alcohol and base such as pyridine[11]. Triflate **4** has been prepared by this method from alcohol **3**[12]. The triflate **4** has recently proved to be the key to the preparation of silicon-containing sulfonium and other ylids[13]. The reaction of **3** and trifluoromethanesulfonic anhydride in tetrachloromethane does not go to completion.

$$(H_3C)_3Si-CH_2-Cl \xrightarrow{(n\text{-}C_4H_9)_4N^{\oplus}X^{\ominus}/CCl_4/NaOAc}$$

1

$$(H_3C)_3Si-CH_2-OAc \xrightarrow{LiAlH_4} (H_3C)_3Si-CH_2-OH$$

2 **3**

$$\xrightarrow{(F_3C-SO_2)_2O/H_2O/CCl_4} (H_3C)_3Si-CH_2-OSO_2-CF_3$$

4

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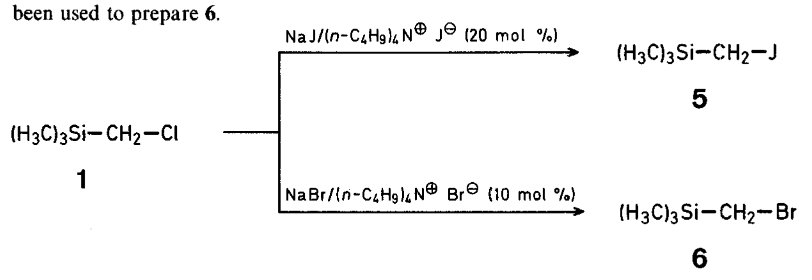
The ^{1}H-N.M.R. spectrum of the reaction mixture shows peaks which are attributable to the protonated form of alcohol **3** and to triflate **4**. The addition of water which acts as a base, converted the remaining **3** to **4**. The use of pyridine and its separation by extraction is avoided by this noncatalytic phase transfer method. (This previously unpublished method was first employed by Peterson and Boron to prepare 3-halo-1-butyl triflates.)[14] The yield of **4** was improved from the reported 68%[12] to 79%. In our judgment, our routes to **2**, **3**, and **4** should become the methods of choice by a wide margin compared to previously used methods.

We now consider the preparation of the halides **5** and **6**. These are potentially better alkylating agents for ylids and other species[15] than the more readily available chloride. These halides are of potential interest as carbanion precursors, although present work has involved deprotonation of the chloride **1** and the methyl ether of alcohol **3**[16]. The expensive iodide **5** has been synthesized either by the reaction of chlorodimethylsilylmethyl chloride and methylmagnesium iodide in low yield[17] or by the heating of a mixture of **1** and potassium/sodium iodide in acetone in a yield of 70%[18,19]. Bromide **6** has been formed by the chlorine and light-catalyzed bromination of tetramethylsilane at reflux[20]. The reaction of chlorodimethylsilylmethyl bromide and methylmagnesium bromide[21] has been used to prepare **6**.



The reaction of chloride **1**, without an added solvent, and sodium iodide with about 20 mol percent of tetrabutylammonium iodide as a phase transfer catalyst gave iodide **6** in 2.5 h. The reaction of **1** and sodium bromide in the presence of about ten mol percent of tetrabutylammonium bromide yielded bromide **6** in eleven days.

We judged that the better previously used methods for the preparation of **5** and **6** are reasonably satisfactory. Our preparation of **6** has the possible disadvantage of a relatively long reaction time, used to minimize the amount of catalyst needed and achieve a high degree of completion. Otherwise our phase transfer methods for the preparation of **5** and **6** offer operational simplicity and the potential for large scale work of reactions which are carried out without the use of an organic solvent (except in workup).

^{1}H-N.M.R. spectra were recorded on a Perkin-Elmer R-32 instrument at 90 MHz.

Trimethylsilylmethyl Acetate (2):

Method A: A mixture of trimethylsilylmethyl chloride[22] (**1**; 10.0 g, 81.5 mmol), sodium acetate (7.5 g, 91.5 mmol), tetrabutylammonium chloride (1.1 g, 4.1 mmol), and tetrachloromethane (140 ml) is heated at reflux for 4 days. After the reaction mixture has cooled to room temperature, the reaction is found to be 98% complete by ^{1}H-N.M.R. Distillation gives **2**; yield: 9.8 g (82%); b.p. 63–65 °C/55 torr; Lit.[1] b.p. 136.8 °C/748 torr.

^{1}H-N.M.R. (CCl_4): $\delta = 0.07$ (s, 9H); 2.02 (s, 3H); 3.75 ppm (s, 2H).

Method B: After a mixture of trimethylsilylmethyl chloride (10.0 g, 81.5 mmol), sodium acetate (7.5 g, 91.5 mmol), tetrabutylammonium iodide (3.0 g, 8.15 mmol), and tetrachloromethane (140 ml) has been heated at reflux for 6 days, it is cooled to room temperature. The ^{1}H-N.M.R. spectra then shows that the reaction is 96% complete. Distillation gives product **2** free of tetrachloromethane (G.L.C.); yield: 9.6 g (81%).

Trimethylsilylmethanol (3):

A suspension of lithium aluminium hydride (2.6 g, 68.5 mmol) in anhydrous ether (250 ml) is heated at reflux for 1 h. After the suspension has been cooled to room temperature a solution of trimethylsilylmethyl acetate (**2**; 10.0 g, 68.5 mmol) in ether (50 ml) is added dropwise. The mixture is then heated at reflux for 24 h. After the mixture has cooled to room temperature, ice/water (100 ml) is added cautiously to decompose excess lithium aluminium hydride. The ether layer is further washed with 5% sulfuric acid (2 × 50 ml) and water (2 × 50 ml). It is then dried with magnesium sulfate, filtered, and distilled to give product **3**; yield: 5.7 g (80%); b.p. 120–122 °C; Lit.[1] b.p. 121.6 °C.

^{1}H-N.M.R. (CCl_4): $\delta = -0.03$ (s, 9H); 3.21 (s, 2H); 4.34 ppm (s, 1H).

Trimethylsilylmethyl Trifluoromethanesulfonate (4):

To a solution of **3** (3.3 g, 31.7 mmol) in tetrachloromethane (15 ml) is added dropwise at 0 °C a solution of trifluoromethanesulfonic anhydride (10.0 g, 35.5 mmol) in tetrachloromethane (20 ml). After the mixture has been stirred to room temperature for 2 h, a ^{1}H-N.M.R. spectrum is recorded. Besides the signals of **3** and **4**, the acid proton appears as a singlet at $\delta = 12.45$ ppm. Water (20 ml) is then added dropwise at room temperature. The mixture is stirred for 1 h, and the tetrachloromethane layer is separated and washed with water (2 × 25 ml). The combined water layer is extracted with tetrachloromethane (2 × 25 ml) which is washed again with water (25 ml). The combined tetrachloromethane layer is dried with magnesium sulfate, filtered, and distilled to give **4**; yield: 5.9 g (79%), b.p. 50–51 °C/9 torr; Lit.[12] b.p. 49–51 °C/9 torr.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 0.19$ (s, 9H), 4.20 ppm (s, 2H).

Trimethylsilylmethyl Iodide (5):

A mixture of **1** (13.2 g, 107.5 mmol), sodium iodide (32.2 g, 215.0 mmol), tetrabutylammonium iodide (7.9 g, 21.5 mmol), and water (18 ml) is heated under reflux for 2.5 h. The reaction is then found to be 98% complete by ^{1}H-N.M.R. spectrometry. After cooling to room temperature, the liquid layers are decanted into a separatory funnel. The solid residue in the reaction flask is washed with water and pentane (3 × 3 ml). The separated pentane layer (plus 2 × 3 ml of pentane washings) contain **5** in 86% yield based on gas chromatographic analysis in which a standard solution of **5** is used for comparison. Distillation gives the pure product; yield: 18.5 g (80%); b.p. 59 °C/48 torr; Lit.[19] b.p. 139.5 °C/747 torr.

^{1}H-N.M.R. (neat): $\delta = 0.18$ (s, 9H); 1.95 ppm (s, 2H); no signals for pentane detected.

Trimethylsilylmethyl Bromide (6):

A mixture of **1** (5.0 g, 40.8 mmol), sodium bromide (12.6 g, 122.3 mmol), tetrabutylammonium bromide (1.312 g, 4.1 mmol), and water (30 ml) is heated at reflux for 11 days. The ^{1}H-N.M.R. spectrum of the organic layer then shows that the reaction is 98% complete. The water layer is separated and extracted with ether (3 × 25 ml). The combined organic layers are dried with magnesium sulfate, filtered, and distilled to give **6**; yield: 5.6 g (82%); b.p. 55–57 °C/60 torr; Lit.[21] b.p. 115.5 °C/742 torr.

^{1}H-N.M.R. (neat): $\delta = 0.13$ (s, 9H); 2.40 ppm (s, 2H); no signals for ether detected.

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* Correspondence address.

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[22] Trimethylsilylmethyl chloride (**1**) was obtained from Petrarch Systems Inc., P. O. Box 141, Levittown, PA, 19059. It gave one peak upon gas chromatography and showed no impurity by ^{1}H-N.M.R. analysis.

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