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Synthesis of Some (Trimethylsilyl)methyl Compounds

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The reaction of methoxymethyllithium with chlorotrimethylsilane was used to prepare (trimethylsilyl)methyl methyl ether (1). The reaction of 1 with chlorotrimethylsilane and sodium iodide in acetonitrile gave (trimethylsilyl)methyl iodide, 1 with chlorotrimethylsilane and lithium bromide in acetonitrile gave (trimethylsilyl)methyl bromide, and 1 with methyl trifluoromethanesulfonate (neat) gave (trimethylsilyl)methyl trifluoromethanesulfonate.

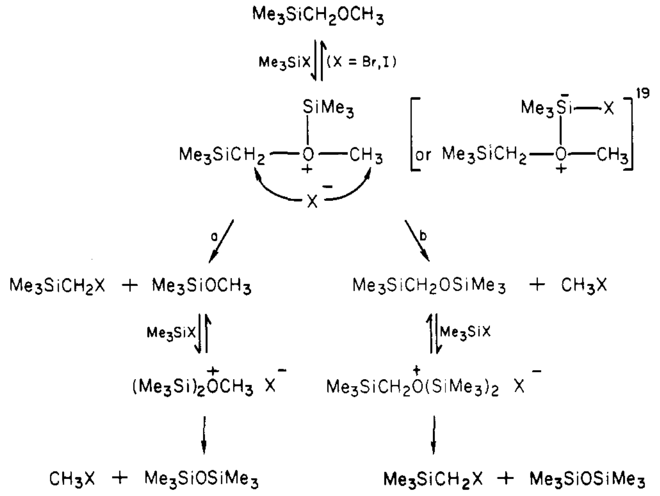
A number of (trimethylsilyl)methyl compounds have found recent utility in synthesis. Among these are (trimethylsilyl)methyl methyl ether (1),[1] (trimethylsilyl)methyl iodide (2)[2] and bromide (3),[3] and (trimethylsilyl)methyl trifluoromethanesulfonate (4).[4] Peterson has recently summarized the available routes to the last three compounds and has reported improved procedures for the formation of these species.[5] All of these approaches are based on the substitution chemistry of (trimethylsilyl)methyl chloride. We here present an alternative entry into the (trimethylsilyl)methyl system based on a new preparation and chemistry of 1 which appears to be competitive in utility with existing procedures.

Results and Discussion

In the present approach, C-functionality is introduced at silicon by chlorotrimethylsilane derivatization of methoxymethyllithium[6,7] to form ether 1 (eq 1). This is

$$CH_3OCH_2Cl \xrightarrow[DMM]{Li} CH_3OCH_2Li \xrightarrow{Me_3SiCl} \underset{1}{CH_3OCH_2SiMe_3} \quad (1)$$

Scheme I



a high yield, one-pot reaction sequence which affords high purity samples of 1 in synthetically useful quantities. To our knowledge, this preparation of 1 represents the only alternative to the synthesis of Speier[10] which employs (trimethylsilyl)methyl chloride and sodium methoxide.

Conversion of 1 into the iodide 2 was effected by the method of Olah.[11] Thus, treatment of 1 with sodium

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(1) Magnus, P. D.; Roy, G. *J. Chem. Soc., Chem. Commun.* **1979**, 822.

(2) (a) Seyferth, D.; Wursthorn, K. R.; Mammarella, R. E. *J. Org. Chem.* **1977**, *42*, 3104. (b) Fleming, I.; Paterson, I. *Synthesis* **1979**, 446. (c) Fleming, I.; Goldhill, J. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1493. (d) Schmid, R.; Huesmann, P. L.; Johnson, W. S. *J. Am. Chem. Soc.* **1980**, *102*, 5122.

(3) Abel, E. W.; Farrow, G. W. *J. Chem. Res., Synop.* **1979**, 278.

(4) (a) Vedejs, E.; Martinez, G. R. *J. Am. Chem. Soc.* **1979**, *101*, 6452. (b) Chiu, S. K.; Peterson, P. E. *Tetrahedron Lett.* **1980**, *21*, 4047. (c) Despo, A. D.; Chiu, S. K.; Flood, T.; Peterson, P. E. *J. Am. Chem. Soc.* **1980**, *102*, 5120.

(5) Ambasht, S.; Chiu, S. K.; Peterson, P. E.; Queen, J. *Synthesis* **1980**, 318.

(6) Schöllkopf, U.; Küppers, H. *Tetrahedron Lett.* **1964**, 1503.

(7) Although existing reports[8] would suggest that methoxymethylmagnesium chloride[9] might generally couple with chlorosilanes, we obtained no significant amounts of 1 using this approach.

(8) (a) Lefort, M. French Patent No. 1 303 195, 1962; *Chem. Abstr.* **1963**, *58*, 7975b. (b) Kumada, M.; Ishikawa, M.; Tamao, K. *J. Organomet. Chem.* **1966**, *5*, 226.

(9) Nützel, K.; In "Methoden der Organischen Chemie"; Muller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1973; Vol. 13/2a, pp 114–115.

(10) Speier, J. L. *J. Am. Chem. Soc.* **1948**, *70*, 4142.

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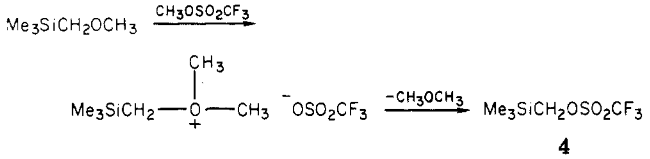
Scheme II



iodide and chlorotrimethylsilane in acetonitrile at 25 °C for 4 h gave **2** in 87% yield (eq 2). In contrast to the

$$1 + \mathrm{NaI} \xrightarrow[\mathrm{CH_3CN,\ 25\ ^\circ C}]{\mathrm{Me_3SiCl}} \underset{\mathbf{2}}{\mathrm{Me_3SiCH_2I}} \qquad (2)$$

behavior[12] of asilyl[13] ethers, this approach was extendable to the preparation of the bromide **3** as well. Refluxing a mixture of **1**, lithium bromide, and chlorotrimethylsilane in acetonitrile afforded a 73% yield of **3** (eq 3). Although

$$1 + \mathrm{LiBr} \xrightarrow[\mathrm{CH_3CN,\ 82\ ^\circ C}]{\mathrm{Me_3SiCl}} \underset{\mathbf{3}}{\mathrm{Me_3SiCH_2Br}} \qquad (3)$$

hexamethyldisiloxane was a coproduct in these preparations of **2** and **3**, it could be easily removed prior to final distillation by a concentrated sulfuric acid wash.

The success of this latter transformation is believed due to the facility of nucleophilic substitution reactions under aprotic conditions at the carbon α to silicon.[14] The conundrum of trace HI or HBr intervention aside, Scheme I indicates that at least two pathways, identical in stoichiometry and final products, may be written for ether cleavage under the present conditions. Major or exclusive reaction by path a assumes operation of the "α effect". Negative experimental support for this pathway comes from our observation that in a cleavage run in which **1**, chlorotrimethylsilane, and sodium iodide were taken in *equimolar* ratios (instead of 1:2:2; see Experimental Section), no $\mathrm{Me_3SiCH_2OSiMe_3}$ was observed by GLPC analysis either during reaction or after a fixed product ratio was attained (**1**, hexamethyldisiloxane, and **2** were then present).[15] The possibility still exists that path b is to some extent operative but that $\mathrm{Me_3SiCH_2OSiMe_3}$ is converted to products much faster than it is formed, but this point has not been investigated.

The preparation of (trimethylsilyl)methyl trifluoromethanesulfonate (**4**) has to date necessitated the intermediacy of (trimethylsilyl)methanol, the formation of which is a two-step sequence away from (trimethylsilyl)methyl chloride.[16] Drawing on the ability of methyl trifluoromethanesulfonate (**5**) to alkylate ethers,[17] we allowed a mixture of **1** and **5** to react at 42 °C for 19 h, after which time simple distillation afforded 93% of **4**. Scheme II suggests that the transformation involves trifluoromethanesulfonate ion attack at the α-silyl carbon with displacement of dimethyl ether. It is noted that the latter is a better leaving group (from its oxonium salts) than is the trifluoromethanesulfonate ion in nucleophilic substitution reactions.[18]

Experimental Section

General Data. Acetonitrile and trifluoromethanesulfonic anhydride were purified by distillation from P_2O_5. Chlorotrimethylsilane and chloromethyl methyl ether were distilled from calcium hydride. Dimethoxymethane (DMM) was stirred with CaH_2 and the solvent refluxed with sodium and distilled. Sodium iodide and lithium bromide were stored over P_2O_5 and flame-dried in situ before use. Lithium dispersion (1% Na, 30% in mineral oil) was obtained from Lithium Corp. of America, Bessemer City, NC. All glassware was flame-dried under nitrogen unless otherwise indicated. Distillations employed a 6-in. Vigreux column unless noted otherwise. All final products were obtained in greater than 95% purity as judged by GLPC (10 ft × 0.25 in. 20% SE-30 stainless-steel column used for all analyses).

(Trimethylsilyl)methyl Methyl Ether (1). Lithium dispersion (48.6 g) was freed of mineral oil by DMM washing under helium so as to afford 14.6 g (2.1 mol) of lithium sand. This and 250 mL of DMM was charged to a flask equipped with mechanical stirrer, addition funnel, and helium inlet, and the flask was cooled to −40 to −50 °C. Chloromethyl methyl ether (67.6 g, 0.84 mol) in DMM (210 mL) was then added dropwise over 7 h, after which the mixture was maintained at temperature for an additional 30 min. After the mixture was further cooled to −75 °C, chlorotrimethylsilane (68.4 g, 0.63 mol) was added dropwise during 90 min, and the mixture was then allowed to attain room temperature overnight. Salts and excess lithium metal were removed through a filter tube (sintered glass) under helium, the solids were washed with pentane, and the filtrate was then extracted with water. The organic phase was isolated, dried (Na_2SO_4), and distilled. A forerun containing some DMM (21.6 g) was followed by pure **1** (51.3 g), bp 83 °C (760 mm) [lit.[10] bp 83 °C (740 mm)]. Refractionation of the forerun afforded an additional 9.1 g of **1** for a total yield of 60.4 g (81%).

(Trimethylsilyl)methyl Iodide (2). A flask bearing a side arm with septum closure was charged with sodium iodide (15 g, 100 mmol), acetonitrile (100 mL), and **1** (5.9 g, 50 mmol). The mixture was magnetically stirred for 10 min before chlorotrimethylsilane (10.9 g, 100 mmol) was added dropwise over 15 min. After 4 h at 25 °C, GLPC analysis indicated complete consumption of **1**. Water (100 mL) was added, ether extraction (3 × 50 mL) was carried out, and the ether extracts were washed successively with 5% sodium thiosulfate solution, brine, and water. After the solution was dried (Na_2SO_4), ether was removed by distillation, and the residue was dissolved in pentane (25 mL) and stirred with 5 mL of concentrated sulfuric acid for 15 min. After phase separation and a second such treatment, all hexamethyldisiloxane had been removed. Pentane was removed by distillation and the residue was distilled (short path) to give 9.3 g (87%) of **2**, bp 69–70 °C (71 mm).

(Trimethylsilyl)methyl Bromide (3). A flask with side arm (septum closure) and condenser was charged with lithium bromide (8.7 g, 100 mmol), acetonitrile (100 mL), chlorotrimethylsilane (13.5 g, 124 mmol), and **1** (5.9 g, 50 mmol). After 42 h at 82 °C, GLPC indicated complete consumption of **1**. Pentane was added (150 mL), and the mixture was washed successively with water, sodium bicarbonate solution, and brine. After the pentane solution was dried (Na_2SO_4), 10 mL of concentrated sulfuric acid was added and the mixture stirred 15 min. Phase separation was followed by a second such treatment, after which hexamethyldisiloxane was shown to be absent by GLPC. Pentane was removed by distillation, and the residue was distilled (short path) to give 6.1 g (73%) of (trimethylsilyl)methyl bromide, bp 48–50 °C (70 mm).

(Trimethylsilyl)methyl Trifluoromethanesulfonate (4). A flask was charged with methyl trifluoromethanesulfonate (14.3 g, 87.0 mmol) and **1** (10.1 g, 85.5 mmol). After 19 h at 42 °C, GLPC (50–110 °C) indicated that **1** was completely consumed. Distil-

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[11] Olah, G. A.; Narang, S. C.; Gupta, B.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247.

[12] Olah, G. A., private communication.

[13] Following an established pattern which includes terms such as "achiral" and "acyclic", the use of this term is suggested as an equivalency to "nonsilicon containing".

[14] (a) Eaborn, C.; Jeffrey, J. C. *J. Chem. Soc.* **1954**, 4266. (b) Huang, C.-T.; Wang, P.-J. *Hua Hsueh Hsueh Pao* **1959**, *25*, 330; *Chem. Abstr.* **1960**, *54*, 16375d. (c) For examples of preferred α-opening of epoxysilanes, see: Hudrlik, P. F.; Hudrlik, A. M.; Misra, R. N.; Peterson, D.; Withers, G. P.; Kulkarni, A. K. *J. Org. Chem.* **1980**, *45*, 4444 and references therein.

[15] No check was made for the presence of lower boiling products.

[16] (a) Baum, K.; Lerdal, D. A.; Horn, J. C. *J. Org. Chem.* **1978**, *43*, 203. (b) Reference 4. (c) Reference 5.

[17] Gramstad, T.; Haszeldine, R. N. *J. Chem. Soc.* **1957**, 4069.

[18] Kevill, D. N.; Lin, G. M. L. *Tetrahedron Lett.* **1978**, 949.

[19] Intramolecular transfer of halide within a betaine intermediate could give results identical with those obtained from the ion pair structures shown.

lation afforded 18.8 g (93%) of **4**, bp 48–50 °C (10 mm). A run carried out at 25 °C was complete in 50 h and afforded a 97% yield of **4**.

Methyl Trifluoromethanesulfonate (5).[17] A flask provided with magnetic stirrer, reflux condenser, and addition funnel was flame-dried and charged with trifluoromethanesulfonic anhydride (100 g, 355 mmol). Dry methanol was then added dropwise at 25 °C (exothermic) until GLPC (50 °C) indicated complete consumption of the anhydride. This point was reached after 45 min, at which time 13.0 g (407 mmol) of methanol had been added. A Vigreux distillation head was attached, and volatiles were condensed in a −78 °C receiver at 25 °C (10 mm) (59.7 g). Redistillation from P_2O_5 afforded 56.8 g (98%) of **5**, bp 27 °C (33 mm). (*Caution: powerful alkylating agent; inhalation may cause pulmonary edema.*)

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Registry No. 1, 14704-14-4; **2**, 4206-67-1; **3**, 18243-41-9; **4**, 64035-64-9; **5**, 333-27-7; chloromethyl methyl ether, 107-30-2; chlorotrimethylsilane, 75-77-4; trifluoromethanesulfonic anhydride, 358-23-6.

Effect of Transition-Metal Complexation on the Stereodynamics of 1,2-Dineopentyl-3,4,5,6-tetramethylbenzene

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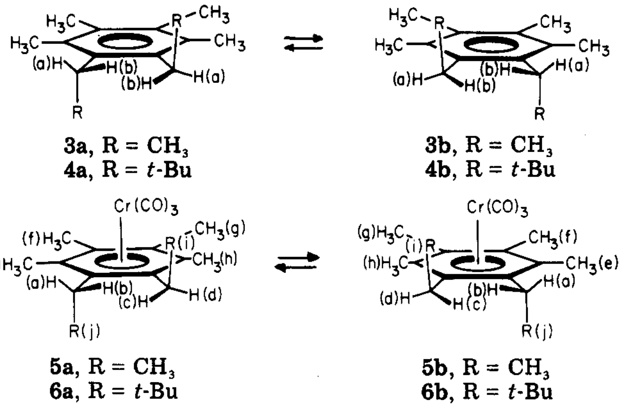
Variable-temperature ^1H NMR measurements have yielded $\Delta G^{\ddagger}$ values of 16.2 and 12.0 kcal mol^{-1} for the barriers to enantiomerization, by aryl–alkyl bond rotation, of 1,2-dineopentyl-3,4,5,6-tetramethylbenzene (**4**) and tricarbonyl(1,2-dineopentyl-3,4,5,6-tetramethylbenzene)chromium(0) (**6**), respectively. Empirical force field calculations on **4** have provided mechanistic details of this process. Starting from the C_2 ground state, in which the *tert*-butyl groups are on opposite sides of the benzene ring, the rearrangement proceeds in stepwise fashion through an achiral intermediate in which both *tert*-butyl groups are located on the same side of the ring and which is 6.4 kcal mol^{-1} less stable than the ground state. The calculated barrier height for the enantiomerization is 14.7 kcal mol^{-1}. The substantially lower barrier for **6** is assumed to be due to an increase in ground-state energy resulting from nonbonded interactions between the tricarbonylchromium fragment and the proximal *tert*-butyl group.

A recent dynamic NMR (DNMR) study[1] of tricarbonyl(hexaethylbenzene)chromium(0) and -molybdenum(0) yielded values of 11.5 ± 0.6 and 11.6 ± 0.2 kcal mol^{-1} for the barriers ($\Delta G^{\ddagger}_{300}$) to ethyl group rotation about the aryl–alkyl bonds. In the observed topomerization process, the methyl groups which project toward the complexed (proximal) side of the ring undergo site exchange with those pointing toward the uncomplexed (distal) side. Although observation of similar site-exchange phenomena in the uncomplexed arene is precluded by the symmetry (D_{3d}) of the molecule, simulation of ethyl group rotation in hexaethylbenzene by the empirical force field (EFF) method yielded a value of 11.8 kcal mol^{-1} for the topomerization barrier,[1] in excellent agreement with the experimentally determined barriers for the π complexes.

The present work was undertaken in order to provide data for an experimental comparison between aryl–alkyl rotation barriers in an uncomplexed alkyl-substituted arene and in the corresponding η^6-arene transition-metal complex. To the best of our knowledge, no such comparison has previously been described in the literature. The closest example is found in the work of van Meurs et al.,[2a] who reported a barrier ($\Delta G^{\ddagger}$) of 16.9 kcal mol^{-1} for rotation about the aryl–alkyl single bond in tricarbonyl(2,2,4,4-tetramethyl-3-phenylpentane)chromium(0) (**1**), as compared to 22.2 kcal mol^{-1} for the corresponding barrier in 2-nitro-4-(2,2,4,4-tetramethyl-3-pentyl)acetanilide (**2**).[2b]

Scheme I

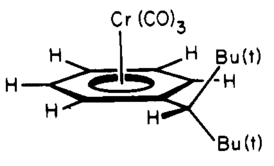


3a, R = CH_3
4a, R = *t*-Bu

3b, R = CH_3
4b, R = *t*-Bu

5a, R = CH_3
6a, R = *t*-Bu

5b, R = CH_3
6b, R = *t*-Bu



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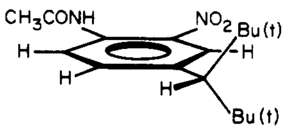

2

Experimental Design. To remain faithful to our objective, a system had to be chosen with the same arene in

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[1] Iverson, D. J.; Hunter, G.; Blount, J. F.; Damewood, J. R., Jr.; Mislow, K. *J. Am. Chem. Soc.* **1981**, *103*, 6073.

[2] (a) van Meurs, F.; Baas, J. M. A.; van der Toorn, J. M.; van Bekkum, H. *J. Organomet. Chem.* **1976**, *118*, 305. (b) Baas, J. M. A. *Recl. Trav. Chim. Pays-Bas* **1972**, *91*, 1287.