Unusual O-Alkylation with Iodomethyltrimethylsilane

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Iodomethyltrimethylsilane alkylates alkoxide ions giving rise to O-methyl and O-trimethylsilyl ethers which are formed by cleavage of the silicon–carbon bond.
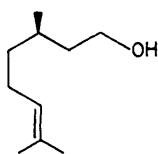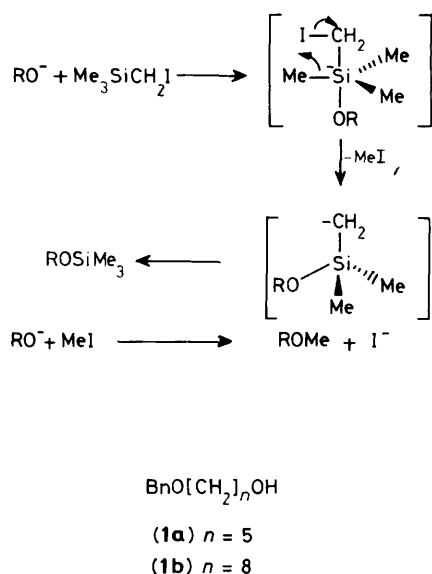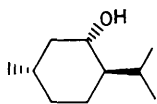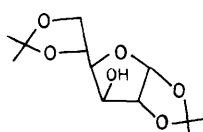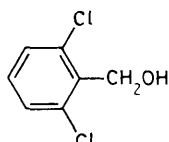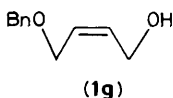
Synthetic uses of organosilicon compounds under nucleophilic catalysis conditions have gained increasing importance in recent years.[1] During an attempt to study fluoride ion induced nucleophilic addition reactions of trimethylsilylmethyl ethers, we decided first to develop a general method for the synthesis of these ethers. However treatment of alkoxide ions with halogenomethyltrimethylsilane produced only the cleavage product, *viz.* methyl (2) and trimethylsilyl (3) ethers with no trace of the expected trimethylsilylmethyl ether. This unex-

pected result prompted us to investigate further this unusual O-alkylation process and to suggest a plausible mechanism. The results of our study are summarised in Table 1. In the case of primary alcohols (1a—c) (entries I—III) when treated with equimolar amounts of iodomethyltrimethylsilane, the reac-

$$RO^- \xrightarrow{\;ICH_2SiMe_3\;} ROMe \;+\; ROSiMe_3$$

$$\quad(1)\qquad\qquad\qquad(2)\qquad\;(3)$$
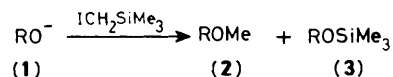
tions were instantaneous and the trimethylsilyl ether was formed as the major product. When reactions were carried out with 0.6 mol. equiv. of iodomethyltrimethylsilane (entry Ib) the trimethylsilyl and methyl ethers were formed in equal amounts, leaving no unchanged starting material. Under similar conditions secondary alcohols (**1d,e**) (entries IV, V) reacted slowly with an equimolar amount of iodomethyltrimethylsilane to give (**2**) and (**3**) in almost 1:1 ratio. With allylic and benzylic alcohols (**1f,g**) (entries VI, VII) the reactions were faster with a *ca.* 1:1 ratio of (**2**) and (**3**). All reactions were carried out in the presence of a catalytic amount of tetra-n-butylammonium iodide (TBAI, 0.1 mol. equiv.). In its absence, reactions followed the same course but were slower, particularly the secondary alcohols. For example, substrate (**1a**) reacted completely in three hours without TBAI, though the product ratio remained the same. Chloromethyltrimethylsilane gave the same products, but reactions were extremely slow and never went to completion.[2]

Silicon with a Pauling electronegativity of 1.9, and carbon with a value of 2.55,[3] give polarized silicon–carbon bonds as $Si^{\delta+}-C^{\delta-}$ which are, therefore, susceptible to nucleophilic attack at the silicon. This results in cleavage of the bond, especially when the carbon fragment which is being expelled is a good leaving group.[4] Our results can only be explained by Si–C bond heterolysis, resulting from the nucleophilic attack on silicon giving rise to methyl iodide as a side product, which subsequently alkylates the remaining alkoxide ions. This generates a carbanion α to silicon which is highly stabilized because of the $p\pi$–$d\pi$ back–bonding.[4] Halogenomethyltrimethylsilanes exhibit the stabilization order I > Br > Cl contrasting with alkyl halides where the stability order is Cl > Br > I.[5] The bonds in iodomethyltrimethylsilane are polarized as $C^{\delta-}-Si^{\delta+}-C^{\delta-}-I^{\delta+}$, making iodine electropositive relative to carbon. This rules out attack by the alkoxide ion on the terminal electronegative carbon, which would have generated the silene intermediate,[6] an alternate pathway which was envisaged earlier.[2c,d,7] This also explains the easy elimination of suitably positioned electron deficient iodine and electronegative terminal methyl groups in the form of methyl iodide. Whether this takes place *via* a concerted mechanism or through a penta-co-ordinated silicon intermediate[8] is not yet understood. For primary alcohols with an equimolar amount of silyl reagent very little alkoxide ion remained free to react with the methyl iodide generated as a by-product in the first step which involved the formation of the trimethylsilyl ether. This also explains why with 0.6 mol. equiv. of the reagent the methyl ether and trimethylsilyl ether are formed in *ca.* 1:1 ratio.†

BnO[CH₂]ₙOH

(**1a**) *n* = 5

(**1b**) *n* = 8

(**1c**)

(**1d**)

(**1e**)

(**1f**)

(**1g**)

Bn = PhCH₂

Table 1.[a]

Entry	Alcohol	Molar equiv. of halo comp.[b]	Reaction time/min	Reaction temp./°C[c]	Ratio (2):(3)	Yield /%[d]
Ia	(**1a**)	1.2	30	0—5	1:3.3	90
Ib	(**1a**)	0.6	30	0—5	1:1.1	89
II	(**1b**)	1.2	30	0—5	1:1.7	87
III	(**1c**)	1.2	30	0—5	1:3.5	91
IV	(**1d**)	1.5	60	0—25	1.1:1	72[e]
V	(**1e**)	1.5	30	0—25	1.3:1	75[e]
VI	(**1f**)	1.2	120	0—25	1.2:1	82
VII	(**1g**)	1.2	30	0—25	1:1.4	85

[a] Alkoxides were generated with 1 mol. equiv. of sodium hydride in tetrahydrofuran(THF)–dimethylformamide (DMF) (1:1; 0.1 M).‡ In all cases catalytic amounts of tetra-n-butylammonium iodide (TBAI, 0.1 mol. equiv.) were added to the reaction mixture prior to the addition of iodomethyltrimethylsilane. All products were characterized by standard spectroscopic methods (n.m.r., i.r., m.s.) and compared with authentic products.§ [b] Halo compound = iodomethyltrimethylsilane[ICH₂SiMe₃]. [c] Iodomethyltrimethylsilane was always added at 0 °C. [d] Yields refer to isolated yields. [e] Yields based on recovered starting material.

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† A referee suggested an alternative mechanism involving iodide mediated formation of trimethylsilyl iodide *via* $^-CH_2SiMe_2I$ and methyl iodide from iodomethyltrimethylsilane, but this may be ruled out since reactions without tetra-n-butylammonium iodide also gave the same products in the same ratios.

$$Me_3SiCH_2I \xrightarrow{I^-} Me_3SiI + MeI$$
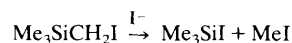
‡ Reactions were very slow in THF alone, though the product ratio remained the same.

§ Authentic products were made by methylation of alkoxides with methyliodide and silylation of alcohols with trimethylsilyl chloride/imidazole in DMF.

Thus, the reverse order of polarization of bonds in iodomethyltrimethylsilane explains this O-alkylation which possibly involves the heterolysis of the silicon–carbon bond where the carbon is expelled, even though at first glance it does not appear to be a good leaving group.

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