THE INTERACTION OF ELECTROPHILIC SILANES (Me$_3$SiX, X = ClO$_4$, I, CF$_3$SO$_3$, Br, Cl)

WITH NUCLEOPHILES.   THE NATURE OF SILYLATION MIXTURES IN SOLUTION.

Alan R Bassindale* and Tim Stout

Chemistry Department, The Open University, Walton Hall, Milton Keynes, MK7 6AA, U.K.

Summary. Silanes, Me$_3$SiX, and Nucleophiles, Nu, form 1:1 salts, Me$_3$Si$\overset{+}{N}$uX$^-$ in solution. The effect of both nucleophile and silane on salt formation has been studied, and the implications for the design of more efficient silylation mixtures are discussed.

Mixtures of electrophilic trimethylsilyl compounds and nucleophiles, such as amines and amides, are common silylation agents[1-3], and salts 1 have frequently been invoked as the active silylation species[4-7]

$$Me_3SiX + Nu \rightleftharpoons Me_3Si\overset{+}{N}uX^- \qquad\qquad -1$$

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There is evidence for such salt formation in solution in some cases[8,9], and the x-ray crystal structure of a salt 1(X = I, Nu = pyridine) has recently been obtained[10].

As a first stage in a programme investigating the mechanism of silylations using highly electrophilic silanes (X = ClO$_4$, I, CF$_3$SO$_3$) we have studied, by ^{29}Si, ^{13}C and ^{1}H n.m.r. spectroscopy and conductivity measurements, the structures in solution, of silane-nucleophile mixtures. We report that for a wide range of nucleophiles, Nu, and Me$_3$SiX, the equilibrium shown in equation 1 lies substantially to the right, with 1, being the almost exclusive species in CD$_2$Cl$_2$, CDCl$_3$ or CD$_3$CN solution.   A wide variety of nucleophiles forming salts, 1, with Me$_3$SiOSO$_2$CF$_3$ is given in the Table, together with the ^{29}Si n.m.r. chemical shifts of 1, and other data discussed below.

An interesting anomaly was the reaction between Me$_3$SiOSO$_2$CF$_3$ and trimethylamine (a common nucleophile used in silylations) which gives a solid salt[4,11], but in solution at ambient temperature consists almost exclusively of unchanged reactants. However at 190 K 1(X = I or CF$_3$SO$_3$, Nu = TEA) was the major species in CD$_2$Cl$_2$ solution (δ ^{29}Si 1, 46.0 p.p.m.).

As one of the aims of our work is to develop more efficient silylation agents it was necessary to determine the relative effectiveness of different Me$_3$SiX and Nu in forming salts. To determine the relative abilities of Me$_3$SiX(X = ClO$_4$, CF$_3$SO$_3$, I, Br, Cl, OOCCH$_3$) to form the four-coordinate silicon salts 1, we chose the common silylation mixtures of Me$_3$SiX with N-trimethylsilylimidazole (NTMSIm). In these experiments mixtures of two Me$_3$SiX compounds (2 mmole in each) were added to NTMSIm (2 mmole) in CD$_2$Cl$_2$ (2 cm^3) and the n.m.r.

spectra used to determine which of the silanes reacted with NTMSIm. For example, in the case of trimethylsilylperchlorate (TMSP), TMSI and NTMSIm, the ^{29}Si n.m.r. spectrum showed only peaks assignable to the bistrimethylsilylimidazolium ion ($\delta 26.6$ ppm) and TMSI ($\delta 10.2$ ppm). No peak at $\delta 46$ ppm (TMSP) was observed. Therefore TMSP preferentially coordinates to NTMSIm to form $\underline{1}$ (Nu=NTMSIm; X=ClO$_4$). A complete series of competition reactions led to the order X=ClO$_4$>I>CF$_3$SO$_3$>Br>>Cl>OAc for effectiveness in salt formation. We also note that with the nucleophiles in the Table salt formation is essentially complete for X= ClO$_4$, CF$_3$SO$_3$ and I, whereas for X=Br equilibrium is incomplete, to varying extents, and for X=Cl and OAc, immeasurably small, at ambient temperature. For X=Cl and Nu=NTMSIm, salt formation is almost complete at 180 K, but for X=OAc no salt formation has been observed to date.

Similar experiments were carried out to determine the effectiveness of the nucleophiles. Competition reactions between nucleophiles, Nu and Nu' allowed the equilibrium constants for reaction 2 to be determined.

$$\text{Nu} + \overset{+}{\text{Nu}}\text{'SiMe}_3 \rightleftharpoons \overset{+}{\text{NuSiMe}}_3 + \text{Nu'} \qquad\qquad 2$$

The ^{29}Si n.m.r. spectra of equimolar mixtures of Nu, Nu' and TMST (or TMSI) always consisted of a single resonance at ν_3, intermediate between ν_1 ($\underline{1}$,Nu) and ν_2 ($\underline{1}$,Nu'). The equilibrium shown in equation 2 is therefore fast on the n.m.r. time scale, and the equilibrium constant, K, can be determined simply from ν_1, ν_2 and ν_3. These competition reactions showed that the ability to form salts with Me$_3$SiX decreases in the order, Nu=NMI>DMAP>HMPA>DMI>NMPO>PNO> TPPO>DMPU>2,>4DMP>NMP>DMF>3,5DMP>DMEV>PY(>TEA). The Table also gives K_{rel} for reaction 2 relative to NMP. (For nucleophiles with K_{rel}>>1 the value was determined from several experiments by substitution).

No detailed analysis of these results is attempted here, but it is worth noting that there is a fair correlation between $\ln K_{rel}$ and the Taft β-constant[12] which is usually taken as a measure of nucleophilicity (high β-values indicate high nucleophilicity). Similarly, and not unreasonably,[13] there is good correlation between the ^{29}Si n.m.r. shift of $\underline{1}$ and $\ln K_{rel}$, with the most readily formed complexes having the highest frequency chemical shifts.

The results in the Table can be used to aid efficient silylation procedures. Chojnowski[8], Frye[7], Choudhary and Hernandez[6] and ourselves[9] have all recently suggested that the first step in many silylations, is a pre-equilibrium quaternisation of a nucleophile (equation 1). Frye[7] showed that powerful nucleophiles such as DMAP, produced large rate increases in the alcoholysis of Ph$_2$SiCl$_2$. A number of different nucleophiles were studied and where the nucleophiles in Frye's work and this study were the same there is a remarkably good correlation between our $\ln K_{rel}$ and $\ln k$, for silylation. Choudhary and Hernandez[6] found that DMAP promoted certain silylations whereas triethylamine and pyridine did not. These results are consistent with our findings and suggest that the best silylation mixtures are those containing a reasonable concentration of salts, $\underline{1}$. Our results also help to explain the superiority of trimethylsilyltriflate and iodide - nucleophile combinations.

Corey[14] routinely uses DMF as a solvent in combination with ^{t}BuMe$_2$SiCl and imidazole. The role of the DMF, as solvent, could be to aid pre-equilibrium salt formation, either with DMF itself, or imidazole.

Table: ^{29}Si n.m.r. chemical shifts and Relative Equilibrium Constants for salts, 1, from the reaction of Nucleophiles with Me$_3$SiOSO$_2$CF$_3$ in CD$_2$Cl$_2$ [a]

	Nucleophile	Abbreviation	δ^{29}Si[b]	K_{rel}[c]	$\ln K_{rel}$	β[d]
1.	Pyridine	PY	42.3	0.10	-2.3	0.64
2.	Dimethyethylene urea	DMEU	40.1	0.11	-2.2	0.75
3.	3,5-Dimethylpyridine	3,5DMP	41.2	0.55	-0.6	0.70
4.	Dimethylformamide	DMF	44.0	0.81	-0.2	0.69
5.	N-methylpyridone	NMP	39.4	1.0	0.0	0.78
6.	2,4-Dimethylpyridine	2,4DMP	40.8	1.2	0.2	0.74
7.	Dimethylpropylene urea	DMPU	36.6	9.0	2.2	0.79
8.	Triphenylphosphine oxide	TPPO	37.5	11.0	2.4	0.94
9.	Pyridine N-oxide	PNO	49.4	66	4.2	0.85
10.	N-methyl-2-pyridone	NMPO	35.8	182	5.2	0.78
11.	1,2-Dimethylimidazole	DMI	25.1	5430	8.6	-
12.	Hexamethylphosphoramide	HMPA	28.8	9900	9.2	1.05
13.	4-N,N dimethylaminopyridine	DMAP	31.7	32800	10.4	0.87
14.	N-methylimidazole	NMI	26.8	32800	10.4	0.82
15.	N,N,N',N'-tetramethylurea	TMU	36.5	-	-	-
16.	N-trimethylsilylimidazole	NTMSIm	26.6	-	-	-

a. Typically the procedure was as follows. NMI (2 mmole) was added to Me$_3$SiOSO$_2$CF$_3$ (2 mmole) in CD$_2$Cl$_2$ (2 cm^3). The Me$_3$SiOSO$_2$CF$_3$ ^{29}Si n.m.r. resonance at δ46 ppm disappeared immediately and was replaced by a single resonance at δ26.8 ppm. In the ^{1}H n.m.r. spectrum the H-2, H-3 and H-4 resonances of NMI were deshielded relative to NMI alone (e.g. H-2; NMI δ7.41 ppm; NMI/TMST δ8.39 ppm). The ^{29}Si n.m.r. spectrum of a similar mixture of Me$_3$SiI and NMI (TMSI: δ^{29}Si 10.2 ppm) was identical to that of the NMI/TMST spectrum, confirming that the reaction shown in equation 1 is essentially complete. Similar experiments were carried out for the other nucleophiles. The conductivity of the salt solution was high whereas the individual components were almost non-conducting. In many cases solid adducts, 1, were isolated and had satisfactory microanalytical data.

b. at 17.76 MHz and relative to internal TMS.

c. Equilibrium constant for reaction 2, Nu^1=NMP

d. Taft β-constant from ref 12.

From our results, and those of others, it appears that an ideal silylation mixture should consist of: a polar solvent to stabilise salts, $\underline{1}$,; a highly electrophilic silane, such as $Me_3SiOSO_2CF_3$, $Me_3SiOClO_3$ or Me_3SiI, a strong nucleophile, such as NMI, DMAP or HMPA; and, particularly in the presence of HMPA, a proton acceptor, such as triethylamine. We find that NMI is both an excellent nucleophile and proton acceptor and in combination with trimethylsilyltriflate in dichloromethane gives excellent results in silylations.

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