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THE REACTIONS OF NUCLEOPHILES WITH ACYLOXYSILANES

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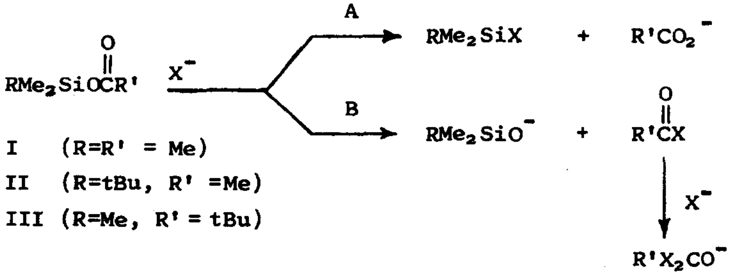
Nucleophiles can react with acyloxysilanes[2] in two distinct ways: by displacement at silicon (path A below) or by reaction at the carbonyl group (path B). As part of a program designed to utilize organosilicon compounds in organic synthesis, we have been interested in the possibility of directing the site of nucleophilic attack to either silicon or carbonyl by suitable modifications of the substrate, the nucleophile, or the experimental conditions. We have found that alkoxide nucleophiles are particularly effective in displacements at the silicon atom (path A)[3] of trialkylacyloxysilanes (e.g. I), while alkyllithium reagents, in accord with a previous example,[8,9] show a preference for carbonyl (path B). In addition, we find that the introduction of a bulky t-butyl group on the substrate and the use of different cations and solvents can have a marked effect on the course of the former reaction.[10] These observations are of potential applicability in organic syntheses employing trialkylsilyl groups.[11,12]



I (R=R' = Me)
II (R=tBu, R' =Me)
III (R=Me, R' = tBu)

We have found that the reaction of acetoxytrimethylsilane[13,14] (I) with sodium n-butoxide (dimethoxyethane, 25°) gives n-butoxytrimethylsilane[15] (via path A) as the only product. In contrast, the reaction of acetoxy-t-butyldimethylsilane[16] (II) with sodium n-butoxide under the same conditions gives a mixture of products, with butyl acetate (from path B) predominating. The influence of solvent and cation on this reaction is shown in the following table. With lithium butoxide in ether the butyl acetate is formed in nearly quantitative yields, whereas with sodium or potassium butoxides in more polar solvents, the reaction occurs mainly at silicon.

TABLE

Reactions of $tBuMe_2SiOAc$[16] (II) with Butoxide

Reactants, Solvent[a]		Mole Ratio A/B[b]	Yields[c] A/B
BuOLi,	Et_2O	0.4 / 99.6	0.4 / 99
BuOLi,	Glyme[d]	3.5 / 96.5	3.5 / 95
BuONa,	Et_2O	6 / 94	4 / 60
BuONa,	Glyme	26 / 74	15 / 42
BuONa,	BuOH[e]	80 / 20	82 / 20
BuONa,	Glyme-HMP (4:1)	98.6/ 1.4	85 / 1.2
BuOK,	Glyme	64 / 36	28 / 16

(a) All reactions were done under nitrogen at room temperature. Samples were removed at intervals for analysis by VPC (Carbowax 20 M) and the reaction worked up after 1-2 hours.

(b) The products were identified by comparison with authentic samples of $BuOSiMe_2tBu$[16] (A) and BuOAc (B) on two different VPC columns (10% SE-30 and 20% Carbowax 20 M). After aqueous workup, the VPC showed an additional peak due to $tBuMe_2SiOH$[17] (aqueous workup did not significantly change the ratio of A to B). The analyses shown are those obtained after 5-10 minutes unless otherwise indicated. With longer reaction times, particularly with the sodium and potassium butoxide reactions, the BuOAc peak gradually decreased, presumably due to Claisen-type condensations.

(c) Yields (based on II) were determined by VPC, using ethylbenzene or p-xylene as an internal standard.

(d) 1,2-dimethoxyethane.

(e) Analysis after aqueous workup after 85 min.

In a preliminary examination of the effect of a t-butyl group on the opposite (carbonyl) end of the molecule,[18] we have found that the reaction of either trimethylsilyl acetate (I) or trimethylsilyl pivalate[13] (III) with butyllithium results in the formation of the corresponding tertiary alcohol (from path B) as the predominant product, with only traces of butyltrimethylsilane[15,19] (from path A) being detectable.

The large directive effect observed in placing a t-butyl group on the silicon atom is reasonable in view of the fact that the hydrolysis of phenoxy-t-butyl-dimethylsilane was found to be slower than that of phenoxytrimethylsilane by a factor of more than 10^4 in both acid and base,[20] and that the hydrolysis of enol silyl ethers was similarly retarded.[21] The influence of the cation and the solvent can be rationalized if one assumes that in poorly ionized systems (e.g. Li), coordination of the metal ion with the carbonyl oxygen is important, resulting in increased preference for nucleophilic attack at the carbonyl carbon (path B).

In view of the hydrolytic stability of the t-butyldimethylsilyl group, one might expect that nucleophilic displacements at the silicon atom of this group would require rather vigorous conditions. We were therefore very pleased to find that the reaction of acetoxy-t-butyldimethylsilane (II) with butoxide proceeded quickly under mild conditions, and that the effect of cation and solvent was sufficiently dramatic to result in almost complete attack at silicon or at carbonyl, depending on the choice of experimental conditions. In view of the recent use of nucleophilic displacements at silicon to generate synthetic intermediates,[12] we believe that these results may find use in a variety of systems.

We plan to investigate the reactions of acyloxysilanes with other nucleophiles, and apply these findings to other systems containing carbonyl and trialkylsilyl groups. Synthetic applications for nucleophilic reaction at both carbonyl and silicon are envisioned.[22,23]

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15. Authentic specimens of BuOSiMe$_3$[14] and BuSiMe$_3$[14] were prepared from the reactions of trimethylchlorosilane with sodium butoxide and butyllithium, respectively.

16. tBuMe$_2$SiOAc (II) was prepared from tBuMe$_2$SiCl[17] by the procedure of reference 13; the compound has b.p. 72-74° (40 mm), IR (film) 1724, 1366, 1250, 1151 cm^{-1}; the NMR and mass spectra were in accord with the structure. The reaction of tBuMe$_2$SiCl[17] with sodium butoxide gave a sample of BuOSiMe$_2$tBu, which was purified by short-path distillation at 70° (11 mm); IR, NMR, and mass spectra were consistent with the assigned structure.

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