FLUORIDE-CATALYZED CONVERSION OF ACYLSILANES TO ALDEHYDES AND KETONES

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SUMMARY: Acylsilanes undergo efficient protodesilylation upon treatment with fluoride ion in moist DMSO, HMPT, or THF. The reaction is also catalyzed by methoxide ion in methanol or DMSO, but not by chloride ion or bromide ion. Fluoride-catalyzed desilylation in the presence of alkyl halides, aldehydes, or ketones results in modest yields of the corresponding alkylated products.

It has been known since 1957 that acylsilanes are cleaved by dilute alkaline solutions to give aldehydes and other more complex rearrangement products.[1,2] A recent report by groups in England and Italy concerning the fluoride-catalyzed de-silylation of acylsilanes[3] has prompted us to submit a preliminary report of our own investigations along these lines.

Treatment of benzoyltrimethylsilane (1)[4] with KF and two equivalents of H_2O in DMSO at room temperature for 1 hr gives benzaldehyde in 75% isolated yield. Protodesilylation may also be accomplished with KF in wet hexamethylphosphoric triamide (HMPT) or with tetra-n-butylammonium fluoride (TBAF) in wet THF. Use of KF and D_2O in DMSO-d_6 provides deuteriated benzaldehyde. Similar results are obtained with p-anisoyltrimethylsilane (2), which is converted into p-anisaldehyde.


1: R=H
2: R=MeO
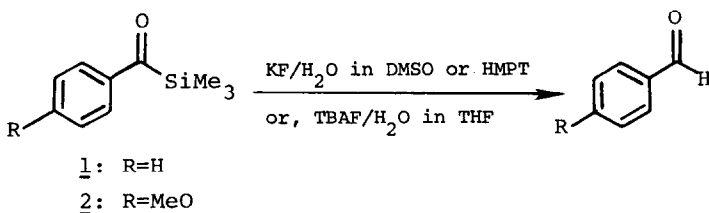
Desilylation is not brought about by chloride or bromide ion (KCl or KBr in DMSO, tetraethylammonium chloride or bromide in THF). However, as has been shown by Brook,[1] smooth desilylation of 1 is accomplished by sodium methoxide in methanol at room temperature.

When the fluoride-catalyzed desilylation is carried out in the presence of electrophiles other than water, corresponding alkylated products are obtained.

Thus, reaction of acylsilane $\underline{1}$ with KF and methyl iodide in DMSO or HMPT affords acetophenone ($\underline{3}$) in 55% yield. Use of KF and n-butyl iodide in HMPT gives valerophenone ($\underline{4}$) in 35% yield.


$$\underline{1} \xrightarrow{\text{KF/RI in DMSO or HMPT}}$$

$\underline{3}$: R=Me
$\underline{4}$: R=n-Bu
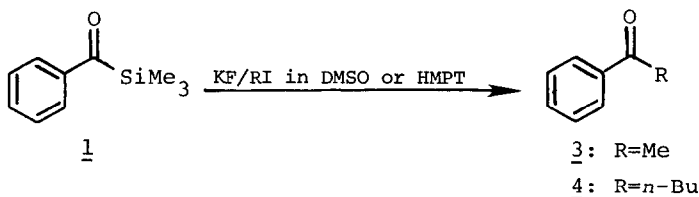
Reaction of compound $\underline{1}$ with TBAF in THF solutions containing benzaldehyde, acetone, or cyclohexanone gives benzoin ($\underline{5}$, 50%), hydroxy ketone $\underline{6}$ (35%), and hydroxy ketone $\underline{7}$ (35%), respectively. Benzoin is also produced when desilylation of $\underline{1}$ is carried out with KF in anhydrous HMPT or with NaOMe in dry DMSO.

$\underline{5}$ $\underline{6}$ $\underline{7}$
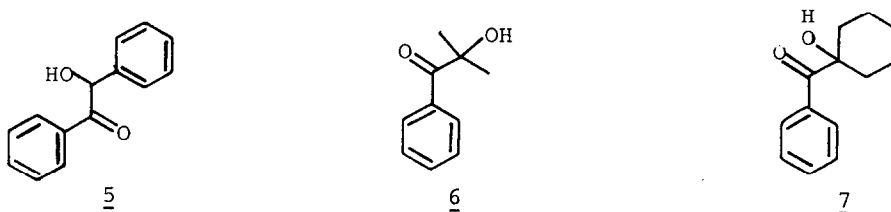
Three mechanisms come to mind in connection with these reactions. The first, proposed by Brook and Schwartz in 1962,[5] involves initial attack of the nucleophile on the carbonyl carbon, carbon-to-oxygen migration of the silyl group, protonation or alkylation of the resulting benzyl anion, and collapse of the resulting geminal fluoro ether:
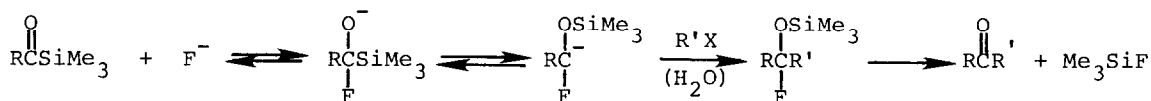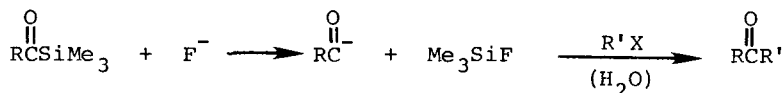

The second mechanism would involve initial attack of the nucleophile at silicon, leading to a pentacoordinated silicon anion. The weakened carbon-silicon bond would then be cleaved by an appropriate electrophile:
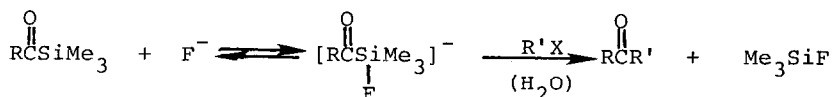
The third mechanism which one might consider, also suggested by Brook and Schwartz[4],

is *direct displacement* of an acyl anion. Alternatively, the initially formed pentacoordinated silicon anion might collapse to the acyl anion. Capture of the acyl anion by an electrophile would lead to the observed cleavage products:

$$RC\overset{\overset{O}{\|}}{}SiMe_3 + F^- \longrightarrow RC\overset{\overset{O}{\|}}{}^- + Me_3SiF \xrightarrow[(H_2O)]{R'X} RC\overset{\overset{O}{\|}}{}R'$$

The Si-F, Si-O, Si-Cl, and Si-Br bond dissociation energies are 142, 106, 97, and 76 kcal mole^{-1}, respectively.[6] Since fluoride and methoxide ions bring about the desilylation reactions and chloride and bromide do not, a mechanism involving obligatory attack of the nucleophile on silicon is attractive.

In order to gain further insight into the possible mechanism of the reaction, we carried out competitive protodesilylations of acylsilanes 1 and 2. In the KF/H$_2$O/DMSO system, compound 1 reacts 5.1±0.5 times faster than 2. In the MeO$^-$/MeOH system, compound 1 is 3.9±0.8 times more reactive than 2.[7] These effects of the *p*-methoxy group correspond to Hammett ρ-values of +2.6 and +2.2, respectively. Such a ρ suggests considerable accumulation of negative charge in the transition state. Alkaline hydrolysis of ethyl benzoates gives rise to ρ-values in the range +2 to +2.5.[8] However, the equilibrium ρ-values for ionization of phenols and arylthiols are similar, falling in the range +2 to +3.[9] Thus, the substituent effect does not provide a distinction between mechanisms involving addition of a nucleophile to the carbonyl and direct formation of an anion in which the negative charge is conjugated with the aromatic ring. However, it seems likely that a mechanism involving rate-determining formation of a pentacoordinated silicon anion intermediate would probably not give rise to such a large value of ρ, since the length of the carbon-silicon bond would cause the charge accumulation to be rather far from the ring. It should be noted that hydrolysis of aryl triethylsilyl ethers by hydroxide ion in aqueous ethanol, a reaction which *must* involve nucleophilic attack at silicon, gives a ρ of +1.99.[9]

The foregoing preliminary data lead us to speculate that the actual mechanism of the desilylation reaction, at least in the case of the fluoride-catalyzed process, involves direct displacement of the benzoyl or *p*-anisoyl anion. As has recently been pointed out by Schleyer and coworkers,[10] acyl anions should not be inaccessible reaction intermediates. In fact, benzoyl anion ought to be somewhat

more stable than the α-styryl anion, due to the inductive effect of the carbonyl

oxygen. If we assume that this inductive effect would be worth about 2 pK units,

then one might expect the pK of the acyl hydrogen to be about 39 in DMSO. Further

indication that the benzoyl anion might be a thermodynamically accessible species

comes from flowing afterglow experiments which suggest that benzaldehyde is de-

protonated in the gas phase both from the ring and from the acyl position.[11] A

definitive answer to these mechanistic questions must await further experiments.[12]

REFERENCES AND NOTES:

1. A.G. Brook, *J. Am. Chem. Soc.*, $\underline{79}$, 4373 (1957).

2. A.G. Brook, *Acc. Chem. Res.*, $\underline{7}$, 77 (1974).

3. A. Degl'Innocenti, S. Pike, D.R.M. Walton, G. Seconi, A. Ricci, and M. Fiorenza, *J.C.S. Chem. Comm.*, 1201 (1980).

4. A.G. Brook, J.M. Duff, P.F. Jones, and N.R. Davis, *J. Am. Chem. Soc.*, $\underline{89}$, 431 (1967).

5. A.G. Brook and N.V. Schwartz, *J. Org. Chem.*, $\underline{27}$, 2311 (1962).

6. E.A.V. Ebsworth, in "Organometallic Compounds of the Group IV Elements", Ed. A.G. MacDiarmid, Marcel Dekker, New York, 1968, Vol. 1, Part 1.

7. Relative rate constants for protodesilylation were determined using initially equimolar sol-utions of the two silanes at room temperature. Aliquots were withdrawn at 5, 10, 15, 20, 25, and 30 minutes and analyzed by analytical hplc using an ultraviolet detector. Assuming that the two acylsilanes react by the same mechanism in each system, relative rate constants were determined using the relationship:

$$\frac{k_a}{k_b} = \frac{\ln\left(\frac{A}{C} + 1\right)}{\ln\left(\frac{B}{D} + 1\right)}$$

where A, B, C, and D are the relative concentrations of acylsilanes $\underline{1}$, $\underline{2}$, benzaldehyde, and *p*-anisaldehyde, respectively. The time period utilized corresponds to about 30 to 94% reaction for acylsilane $\underline{1}$ and 13 to 43% reaction for acylsilane $\underline{2}$.

8. H.H. Jaffé, *Chem. Rev.*, $\underline{53}$, 191 (1953).

9. P.R. Wells, *ibid.*, $\underline{63}$, 171 (1963).

10. J. Chandrasekhar, J.G. Andrade, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, in press.

11. C.H. Depuy and R. Squires, private communication.

12. NOTE ADDED IN PROOF (3-2-81): We have now found that fluoride-catalyzed protodesilylation may be carried out on *aliphatic* acylsilanes:

$$n\text{-}C_5H_{11}\overset{\underset{|}{OH}}{C}H\overset{\underset{|}{CH_3}}{C}H\overset{O}{C}SiR_3 + F^-/H_2O/MeCN \longrightarrow n\text{-}C_5H_{11}\overset{\underset{|}{OH}}{C}H\overset{\underset{|}{CH_3}}{C}HCHO + n\text{-}C_5H_{11}CH=CHCHO$$