Journal of Organometallic Chemistry, 358 (1988) 57–66
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

On the nucleophilic activation of silyl enol ethers and esters; a survey and mechanistic interpretation

Claude Chuit, Robert J.P. Corriu * and Catherine Reyé

Institut de Chimie Fine, Université des Sciences et Techniques du Languedoc, Unité Associée CNRS U.A., No. 1097, Place Eugène Bataillon 34060 Montpellier Cedex (France)

(Received May 6th, 1988)

Abstract

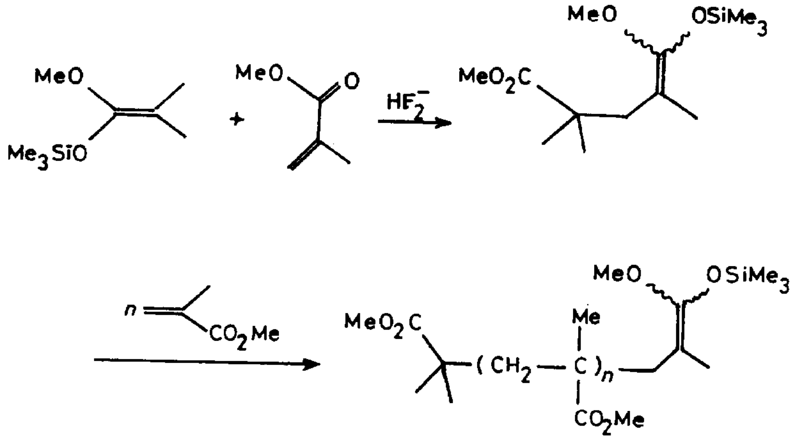
Two distinct mechanisms of nucleophilic activation of silyl enol ethers and esters which have been put forward in the literature are described. The first involves the formation of a "naked" enolate anion and the second involves hypervalent silicon intermediates. A unified approach accounting for the various experimental results is proposed. The first step is common to both, and involves the formation of a pentacoordinate species whatever the catalyst. Subsequently two competing processes can take place, depending on the fluoride anion source, both involving nucleophilic attack on the pentacoordinate silicon species: with "naked" fluoride anion a free enolate is formed, whereas with the less reactive fluoride anion the silicon is further coordinated by the substrate (carbonyl compound) to give a hexacoordinate silicon intermediate.

Silyl enol ethers and silyl ketene acetals have been used in synthesis with great success in the past two decades [1,2]. They are versatile intermediates in organic synthesis, and they make possible a great variety of synthetic transformations. Reactions of silyl enol ethers or esters with electrophiles are catalyzed by Lewis acids such as $TiCl_4$ [3–6] or by nucleophiles such as fluoride anion [7–19].

The aim of this essay is to outline the mechanisms of nucleophilic activation of silyl enol ethers and esters that have been proposed in the literature and provide a unified approach which accounts for all the experimental results.

Nucleophilic activation of silyl enol ethers and esters, especially by fluoride ion, has led to new aldol condensations [7,11,13,14,19], monoalkylation of ketones [10,12,14], Michael reactions [8,9,18], and a new form of polymerization through a living polymer. This latter process, termed "group transfer polymerization" (GTP), involves an anion-catalyzed Michael addition of silyl ketene acetals to α,β-unsaturated esters (Scheme 1).

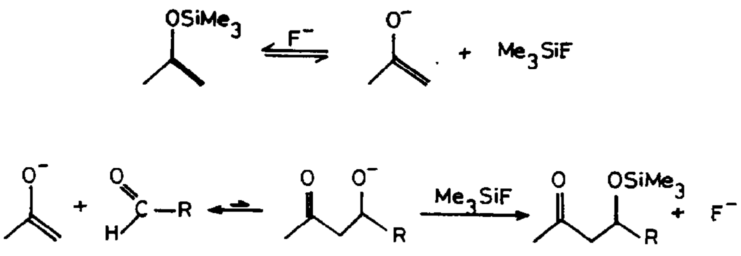
0022-328X/88/$03.50



Scheme 1

Two very different mechanisms have been proposed to explain these fluoride catalyzed reactions.

The first mechanism, advanced mainly by organic chemists [13,14], involves the formation of a "naked" enolate anion by nucleophilic attack of F^- at silicon (Scheme 2). The naked enolate anion undergoes (reversible) addition to an aldehyde to give the aldol anion. This, in turn, is trapped by the Me_3SiF produced in the first step.



Scheme 2

The second, less popular, mechanism [16,20], involves hypervalent silicon intermediates. In the first step a pentacoordinate silicon is formed by coordination of the fluoride anion to the silicon atom. In the rate-determining step this intermediate undergoes a synchronous process involving nucleophilic attack at silicon and electrophilic attack at the carbon of the attacking reagent within a hexacoordinate silicon intermediate (Scheme 3).

An analysis of the various reports on nucleophilic activation of silyl enol ethers and esters leads to the following conclusions:

The first mechanism (Scheme 2) is based on the suggestion of Noyori and Kuwajima [13,14], who used quaternary ammonium fluoride (R_4NF) or tris(diethylamino)sulfonium difluorotrimethylsiliconate ($TAS^+ \; Me_3SiF_2^-$) as catalyst. Because of the large counter-cation the fluoride anion of these salts is very reactive, and under these conditions silyl enol ethers are able to react with organic halides to give regiospecific *C*-alkylation products [10,12,14]. Furthermore the reactions with aldehydes give crossed aldol products [11,13,14,19] with a high stereoselectivity; in most cases the major products have *erythro* stereochemistry regardless of the enolate configuration.

This first mechanism (Scheme 2), involving the formation of naked enolates, is consistent with accepted concepts in organic chemistry. It is interesting to recall that silyl enol ethers were originally introduced as precursors for enolates. The structures and reactivities of enolates are known to be highly dependent on the nature of the counter-cations [21]. With the large counterions TAS^+ or R_4N^+, free enolates can be generated.

The second mechanism (Scheme 3) was proposed by us to account for the anionic activation of Si–O bonds by fluoride anion (CsF, KF) under heterogeneous conditions (aldol condensation, Michael reactions [20]). Recently, studies performed on GTP of α,β-unsaturated esters catalysed by KHF_2 led to similar conclusions [15,16]. This mechanism is questioned by most organic chemists because it requires the involvement of hypervalent silicon entities.

The basic features of this second mechanism include:

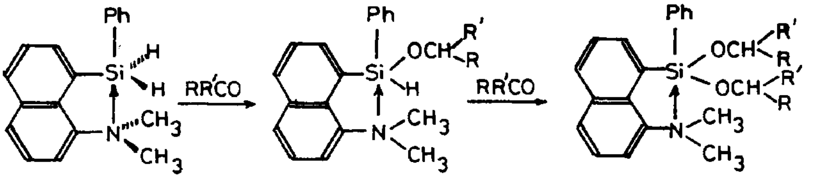
(1) Coordination of a nucleophilic catalyst at silicon to generate a pentacoordinate species.

(2) Higher reactivity of the pentacoordinate species than of its tetravalent precursor.

(3) Formation of hexacoordinate silicon species in the rate-determining step.

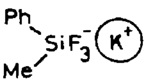
The surprising aspect of this proposal is the assumption that a hypervalent pentacoordinate silicon species can still be electrophilic and susceptible to nucleophilic attack, and furthermore be more reactive than the four-coordinate silicon species. However, this mechanism is supported by several recent studies performed on hypervalent silicon species.

(1) The reactivities of the Si–H bonds [22] in pentacoordinated silicon dihydrides towards nucleophiles was found to be markedly greater than that of the corresponding tetracoordinate species. For example, the pentacoordinate silicon dihydride **1** reacts with carbonyl compounds in the absence of any activating agent.

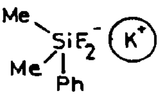


1

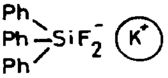
(2) The reactivity of 18-crown-6 potassium salts of the trifluoromethylphenyl (**2**), difluorodimethylphenyl (**3**), difluorotriphenyl (**4**) and dimethoxytriphenylsiliconates (**5**) toward strong nucleophiles (RLi, RMgX, H^-, RO^-) has been studied [23] and compared with that of the corresponding four-coordinate neutral species. The results clearly show the enhanced reactivity of the pentavalent species in such nucleophilic reactions: in some cases the enhancement of reactivity involves a factor of > 150.



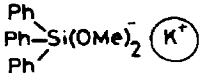
2



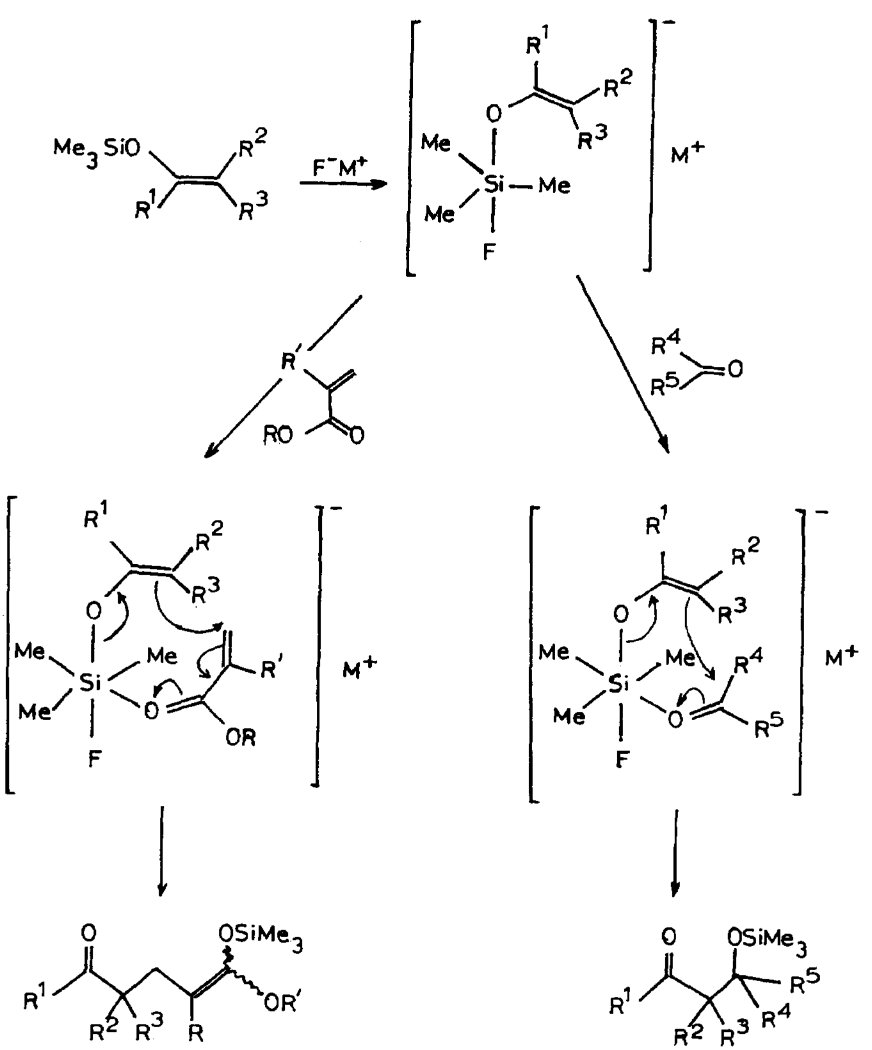
3



4

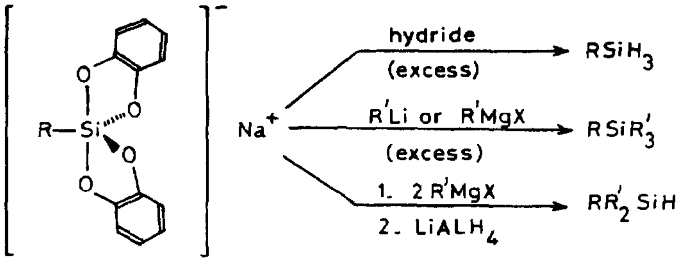


5

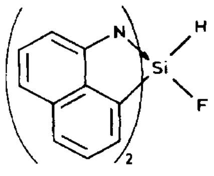


Scheme 3

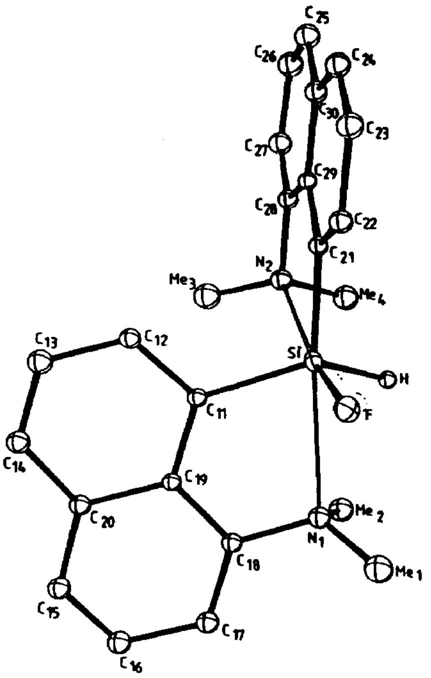
(3) Studies [24] on anionic pentacoordinated siliconates of catechol **6** reveal that pentacoordinated anionic silicon species can undergo nucleophilic attack at silicon by strong nucleophiles such as hydrides, R′MgX and R′Li to give organosilanes (Scheme 4).



Scheme 4



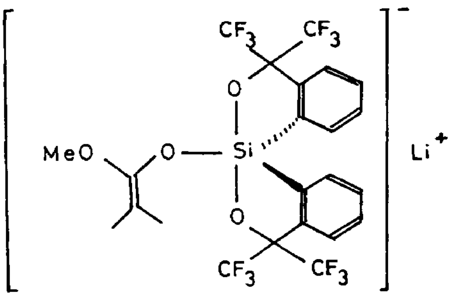
(7)



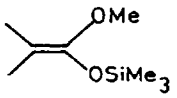
(4) Recently the reactivity of pentacoordinate allylsilicates has been studied [25–27], and found to be completely different from that of four-coordinate allyltrimethoxysilane.

(5) The existence of hexacoordinate silicon compounds has been established recently both in the solid state and in solution [28]. Derivatives such as 7 have been prepared, and the X-ray structures determined. The structures observed correspond to a tetrahedrally distorded silicon center with two additional dative Si ← N bonds which, following the concepts developed by Dunitz [29], mimic the attack of two nucleophiles at silicon. The ^1H NMR spectral data show that the hexacoordination persists in solution. The same geometry is preserved, with a barrier for isomerisation > 15 kcal/mole.

Furthermore, the elegant mechanistic studies [15,16] performed on GTP reactions demonstrate unambiguously the role of hypervalent silicon species (penta- and hexa-coordinate) during the course of the reaction.



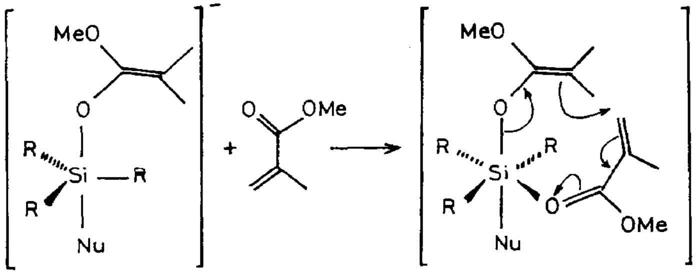
8



9

(1) It was shown [16] that with the stable pentacoordinate silyl enolate **8** as substrate no catalyst was required for the polymerization, whereas a nucleophilic catalyst was necessary for reaction of the silyl ketene acetal **9**. This was considered as corroborative evidence for the involvement of pentacoordinate silicon species in GTP. This also represent another case in which a pentacoordinate siliconate **8** is more reactive than the corresponding four-coordinate species **9**.

(2) This pentacoordinate silicon intermediate then reacts with methyl methacrylate (MMA) to form new C–C and Si–O bonds with cleavage of the old Si–O bond via a hexacoordinate transition/state (Scheme 5) [16].

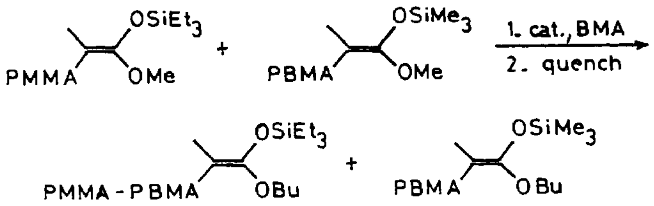


Scheme 5

The "hexacoordinate intermediate" hypothesis was put forward when silyl exchange among growing chains was ruled out [16]. This was demonstrated by several experiments; particularly important was the observation that polymerization of MMA with the phenyldimethylsilyl initiator **10**, in the presence of an equimolar quantity of tolyldimethylsilyl fluoride with $TASHF_2$ catalyst, provided an oligomer which contained no detectable tolyldimethylsilyl end group. Had a dissociative mechanism been operating, oligomers with a mixture of phenyldimethylsilyl and tolyldimethylsilyl end groups would have been obtained.

10

To shed further light on this question, double labelling studies were performed [16]. A mixture of living polymethylmethacrylate (PMMA) and poly(n-butyl methacrylate) (PBMA) was used to initiate the GTP of n-butyl methacrylate (BMA) in the presence of bifluoride ion (Scheme 6) and the reaction was quenched when about 70% of the added BMA was consumed. The PMMA-PBMA block copolymer which separated out from dry hexane contained only the triethylsilyl ketene acetal end group. The hexane-soluble PBMA contained only the trimethylsilyl ketene acetal functional group. Both polymers had molecular weights expected from the relative amounts of oligomers used and BMA consumed. No cross-over products were detected. These results support an "intramolecular" silyl transfer mechanism, in which the silyl group migrates from the oxygen of the initiator to the carbonyl oxygen of the incoming monomer via a hypervalent silicon intermediate (Scheme 5), and are incompatible with the naked enolate mechanism (Scheme 2).



Scheme 6

Taking account of the arguments and experimental results outlined, we propose the existence of two competing mechanisms, both of which involve the pentacoordinate silicon intermediate **A** (Scheme 7). In the first step the nucleophilic catalyst coordinates to the silicon atom to provide a pentacoordinate species **A** whatever the catalyst (R_4NF, $TASMe_3SiF_2$, CsF, KF, F_2HK). At this stage two competing processes may take place depending on the fluoride anion source; both involve nucleophilic attack on the pentacoordinate silicon species.

(1) In the case of the catalysts $[(C_2H_5)_2N]_3S^+(CH_3)_3SiF_2^-$ [14,18] or R_4NF [10–13,17,19] the fluoride anion is associated with a large counter-cation and is very reactive. A "naked fluoride anion" [14b] could attack the pentacoordinate silicon atom to displace free enolate and form $Me_3SiF_2^-$ via the hexacoordinate intermediate **B**. The "free enolate" could then react with organic halides to provide monoalkylation of ketones [10,12,14], or with aldehydes to give cross aldol reactions with the expected diastereoselection [11,13,14,19].

(2) In contrast, with the less reactive catalysts such as CsF and KF used under heterogeneous conditions [7–9,20] or KHF_2 used in the GTP process [15,16], the initial attack at the silicon center to give the pentacoordinate silicon intermediate **A** is possible, but the reactivity of F^- under these conditions is insufficient to displace the enolate ion via an intermediate **B**. A reaction can only take place with compounds having two reactive centres (for example a nucleophilic oxygen and an electrophilic carbon) leading to intermediate **C** or **D** (Scheme 7). There is good evidence that the KHF_2-catalyzed GTP process takes place via intermediate **D**. It can reasonably be assumed that the heterogeneous CsF (or KF) catalysed reaction of enol ethers with carbonyl compounds or α,β-unsaturated ketones takes place via intermediates **C** and **D**. Under these conditions enol ethers do not react with organic halides.

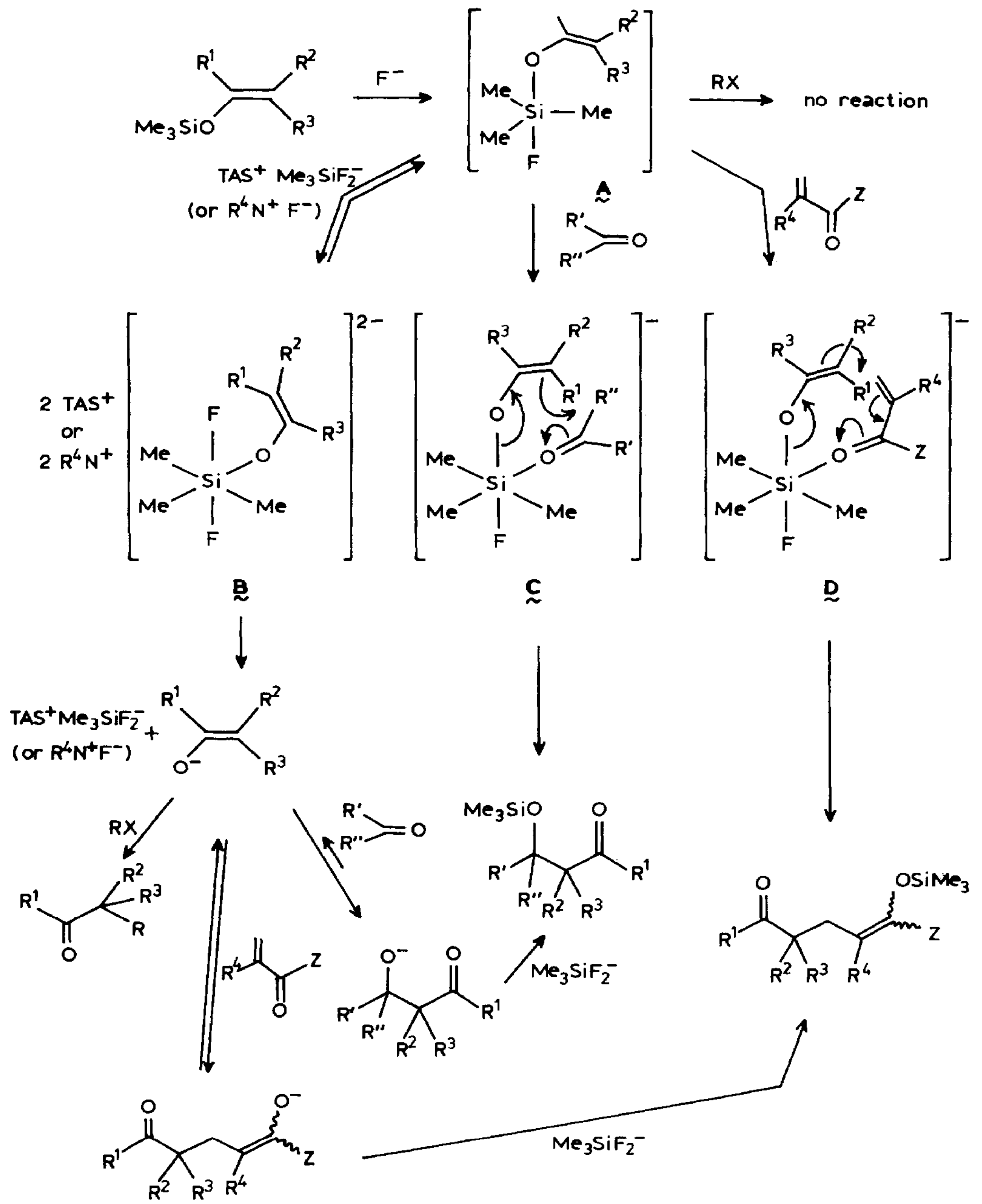
The outcome of the competition between the two modes of reaction of the intermediate **A** depends essentially on the reactivity of the fluoride anion.

The mechanism which we propose involves two molecules of catalyst for the formation of free enolate. In silicon chemistry, involvement of two molecules of nucleophilic catalyst is a well-substantiated process. For instance, the racemization [30] of various chloro- and bromo-silanes is induced by nucleophiles (HMPT, DMSO, DMF), and there is a second order dependance on the nucleophile:

$$V_{\mathrm{rac}}^{\mathrm{Si}} = k_{\mathrm{rac}}^{\mathrm{Si}}[\mathrm{Nu}]^2[\mathrm{R_3SiCl}]$$

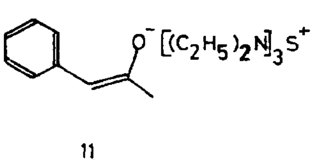
(Nu = HMPT, DMSO or DMF)

It was also reported [31] that base-catalysed hydrolysis of aryloxytriphenylsilanes in 60% acetonitrile/40% water is second order in hydroxide ion at low base concentrations though this has been questioned [32].

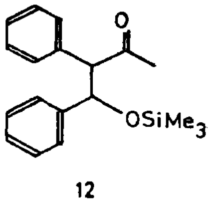


Scheme 7

Another important point in our proposed mechanism is that $Me_3SiF_2^-$ is the silylating agent and not Me_3SiF. Observations by Noyori corroborate this hypothesis [14]. The isolated TAS enolate **11** and benzaldehyde failed to give the corresponding aldol product after aqueous work up. However when 5 equiv. of fluorotrimethylsilane were added to the reaction system, the aldol reaction proceeded smoothly to give the corresponding β-trimethylsiloxy ketone **12** in 65% yield. The need for an excess of Me_3SiF to trap the anion is surprising in terms of the mechanism proposed by Noyori which involves the silylation of the aldol anion by an equimolecular amount of Me_3SiF. This supports our suggestion that the silylating reagent is not Me_3SiF but $Me_3SiF_2^-$ (Scheme 7).



11



12

Finally studies performed in GTP reveal clearly the competition between the two mechanisms (Scheme 7): when the polymerization is performed with $TAS^+ Me_3SiF_2^-$ as catalyst, partial exchange of silyl groups takes place because of the intervention of a naked enolate anion. For instance, at −70 °C the exchange is almost complete within 0.5 h. However, use of low temperatures (−90 °C) and shorter reaction times (5 min) greatly reduces the extent of silyl group exchange; the reaction then takes place via the hexacoordinate intermediate C, which is the most effective under these conditions. The existence of this competition is consistent with the mechanism described in Scheme 7, but is incompatible with the direct formation of the enolate (Scheme 2), since in this case all the reactions would proceed via a naked enolate when $TAS^+ Me_3SiF_2^-$ is used as catalyst.

In conclusion, the operation of the two competiting processes shown in Scheme 7 account for all the observations on the reactions of silyl enol ethers and esters activated by nucleophiles. The outcome of the competition between the two pathways depends on the reactivity of the anionic catalyst, which is a function of the nature of the anion and cation, the solvent, the temperature, and whether heterogeneous or homogeneous conditions are used. Two limiting cases can be recognised: catalysis by KF, CsF or KHF_2, and catalysis by fluoride anion associated with very large counter-action (TAS^+ or R_4N^+).

In the first case, the reaction takes place via a hexacoordinate intermediate, as was clearly demonstrated in the GTP studies. The alkylation of ketones by organic halides is not possible and the diastereoselection observed agrees with coordination of the carbonyl compound at the silicon atom.

In the second case the process involves free enolates. Alkylation of ketones is then possible, and the diastereoselection is controlled by the repulsion between the electronegative oxygen atoms.

References

1 P. Brownbridge, Synthesis, (1983) 1.
2 P. Brownbridge, Synthesis, (1983) 85.
3 T. Mukaiyama, K. Narasaka, K. Banno, Chem. Lett., (1973) 1011.
4 T. Mukaiyama, T. Izawa, K. Saigo, Chem. Lett., (1974) 323.
5 T. Mukaiyama, K. Banno, K. Narasaka, J. Am. Chem. Soc., 96 (1974) 7503.
6 M.T. Reetz, W.F. Maier, Angew. Chem. Int. Ed. Engl., 17 (1978) 48.
7 J. Boyer, R.J.P. Corriu, R. Perz, C. Reyé, J. Organomet. Chem., 184 (1980) 157; C. Chuit, R.J.P. Corriu, C. Reyé, Synthesis, (1983) 294.
8 C. Chuit, R.J.P. Corriu, C. Reyé, Tetrahedron Lett., 23 (1982) 5531.

9 C. Chuit, R.J.P. Corriu, R. Perz, C. Reyé, Tetrahedron, 42 (1986) 2293.
10 I. Kuwajima, E. Nakamura, J. Am. Chem. Soc., 97 (1975) 3257.
11 R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura, M. Shimizu, J. Am. Chem. Soc., 99 (1977) 1265.
12 I. Kuwajima, E. Nakamura, M. Shimizu, J. Am. Chem. Soc., 104 (1982) 1025.
13 E. Nakamura, M. Shimizu, I. Kuwajima, J. Sakata, K. Yokoyama, R. Noyori, J. Org. Chem., 48 (1983) 932.
14 (a) R. Noyori, I. Nishida, J. Sakata, M. Nishizawa, J. Am. Chem. Soc., 102 (1980), 1223; (b) R. Noyori, I. Nishida, J. Sakata, ibid., 105 (1983) 1598.
15 O.W. Webster, W.R. Hertler, D.Y. Sogah, W.B. Farnham, T.V. Rajanbabu, J. Am. Chem. Soc., 105 (1983) 5706.
16 D.Y. Sogah, W.B. Farnham, in H. Sakurai (Ed.), Organosilicon and Bioorganosilicon Chemistry, Ellis Horwood Lt., 1985, p. 219.
17 R.A. Olofson, J. Cuomo, Tetrahedron Lett., 21 (1980) 819.
18 T.V. Rajanbabu, G.S. Reddy, T. Fukunaga, J. Am. Chem. Soc., 107 (1985) 5473.
19 C.W. Jefford, D. Jaggi, J. Boukouvalas, Tetrahedron Lett., 28 (1987) 4037.
20 R.J.P. Corriu, R. Perz, C. Reyé, Tetrahedron, 39 (1983) 999.
21 S.A. Shevelev, Russ. Chem. Rev. (Engl. Transl.), 39 (1970) 844; L.M. Jackman, B.C. Lange, Tetrehedron, 33 (1977) 2737.
22 J. Boyer, C. Brelière, R.J.P. Corriu, A. Kpoton, M. Poirier, G. Royo, J. Organometal. Chem., 311 (1986) C39.
23 R.J.P. Corriu, C. Guerin, B.J.L. Henner, W.W.C. Wong Chi Man, Organometallics, 7 (1988) 237.
24 A. Boudin, G. Cerveau, C. Chuit, R.J.P. Corriu, C. Reyé, Angew. Chem. Int. Ed. Engl., 25 (1986) 473; A. Boudin, G. Cerveau, C. Chuit, R.J.P. Corriu, C. Reyé, Bull. Chem. Soc. Jpn., 61 (1988) 101.
25 G. Cerveau, C. Chuit, R.J.P. Corriu, C. Reyé, J. Organomet. Chem., 328 (1987) C17.
26 M. Kira, M. Kobayashi, H. Sakurai, Tetrahedron Lett., 28 (1987) 4081.
27 A. Hosomi, S. Kohra, Y. Tominaga, J. Chem. Soc. Chem. Commun., (1987) 1517.
28 C. Brelière, F. Carré, R.J.P. Corriu, G. Royo, J. Zwecker, to be published.
29 H.B. Bürgi, J.D. Dunitz, Acc. Chem. Res., 16 (1983) 153.
30 R.J.P. Corriu, M. Henner, J. Organomet. Chem., 74 (1974) 1; R.J.P. Corriu, G. Dabosi, M. Martineau, ibid., 150 (1978) 27; R.J.P. Corriu, G. Dabosi, M. Martineau, ibid., 186 (1980) 25.
31 C.G. Swain, K.R. Pörschke, W. Ahmed, R.L. Schowen, J. Am. Chem. Soc., 96 (1974) 4700.
32 C. Eaborn, R. Eidenschink, D.R.M. Walton, J. Chem. Soc, Chem. Commun., (1975) 388.