Aldol Condensations Promoted by a Tetraalkoxysilane in the Presence of Fluoride Ions

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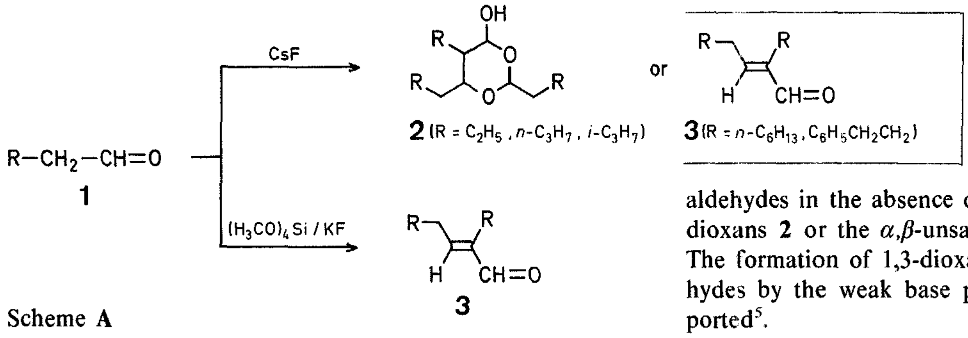
We have recently shown that potassium fluoride or caesium fluoride is able to promote, under heterogeneous conditions, reactions such as selective reduction of carbonyl compounds by hydrosilanes[1], aldol-type condensations of silyl enol ethers with carbonyl compounds[2], and Michael-type additions of silyl enol ethers with α,β-unsaturated carbonyl compounds[2]. The fluoride ion provides activation of the Si—O or Si—H bonds.

We have also reported that the system caesium fluoride/tetraalkoxysilane is able to promote the Michael addition of carbonyl compounds with α,β-unsaturated ketones, esters, and nitriles[3]. We now report that the same system can be used for cross aldol-type condensations of carbonyl derivatives, thus avoiding the additional step of silyl enol ether preparation. When the heterogeneous system aldehyde **1**/tetraalkoxysilane/potassium fluoride is stirred in the absence of a solvent, the α,β-unsaturated aldehyde **3** is obtained in good yield (Scheme A). Ketones are less reactive and require the use of the caesium fluoride/tetraalkoxysilane system. Reactions of α,β-unsaturated aldehydes under the above conditions gave complex product mixtures whereas α,β-unsaturated ketones and esters gave products of a self-Michael condensation. In the absence of the silane, caesium fluoride (but not potassium fluoride) is a sufficiently strong base[4] to induce aldolisation of aldehydes in the absence of a solvent to give either the 1,3-dioxans **2** or the α,β-unsaturated aldehydes **3** (Scheme A). The formation of 1,3-dioxans from the aldolisation of aldehydes by the weak base potassium carbonate has been reported[5].



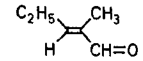
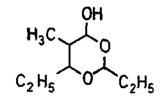
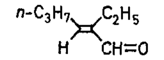
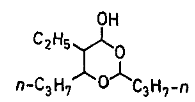
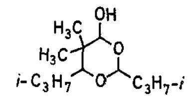
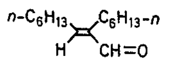
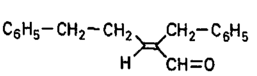
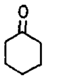
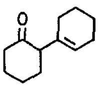
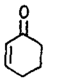
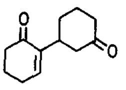
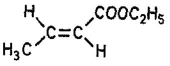
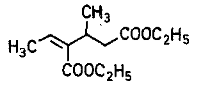
2 (R = C_2H_5, n-C_3H_7, i-C_3H_7)

3 (R = n-C_6H_{13}, $C_6H_5CH_2CH_2$)

3

Scheme A

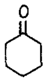
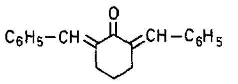
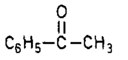
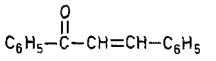
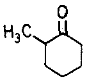
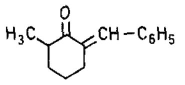
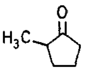
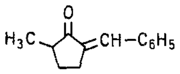
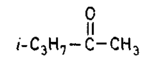
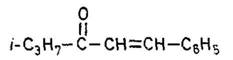
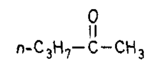
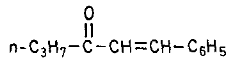
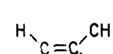
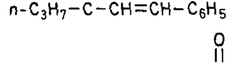
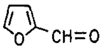
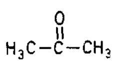
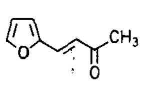
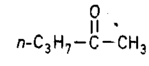
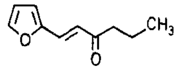
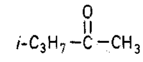
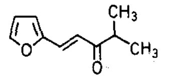
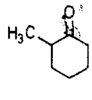
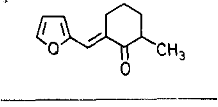
Table 1. Self-Condensation of Carbonyl Compounds or Ethyl 2-Butenoate Promoted by Tetraalkoxysilane/Alkali Metal Fluoride and/or Caesium Fluoride in the Absence of Solvent (Scheme A)

Carbonyl Compound **1**	Product **2** or **3**	Reaction Conditions			Yield [%]	Purity [%][a]	b.p. [°C]/torr	
		Base	Temperature	Time			found	reported
$H_3C-CH_2-CH=O$		$(H_3CO)_4Si$/KF	20 °C	2.5 h	32	98	59-61°/40	38-39°/18[8]
		CsF	0 °C	1 h	83	95[b]	60-65°/0.1	89-90°/1.2[5]
n-$C_3H_7-CH=O$		$(H_3CO)_4Si$/KF	55 °C	1 h	69	98	78-79°/30	65-66°/14[9]
		CsF	0 °C	2 h	62	95[b]	85-95°/0.05	89-91°/0.1[5]
i-$C_3H_7-CH=O$		CsF	20 °C	1.5 h	80	~100[b]	73-75°/0.1	110-111°/8[10]
n-$C_6H_{13}-CH=O$		$(H_3CO)_4Si$/KF CsF	55 °C 55 °C	4 h 3 h	70 60	~100 99	102-105°/0.3 90-93°/0.1	146°/16[11]
$C_6H_5-CH_2-CH_2-CH=O$		$(H_3CO)_4Si$/KF CsF	60 °C 60 °C	5.5 h 2 h	72 74	~100[b] ~100[b]	145-152°/0.05 150-155°/0.1	—[c]
		$(H_3CO)_4Si$/CsF	60 °C	15 h	65	98	142°/13	142°/13[12]
		$(H_3CO)_4Si$/KF	60 °C	3 h	63	98	138-140°/0.5	148-154°/1.8[13]
		$(C_2H_5O)_4Si$/CsF	60 °C	12 h	85	99	95°/0.5	84-85°/0.3[14]

[a] Purity by G.L.C. (10% polyethylene glycol 20 M) unless otherwise stated.
[b] Purity by ^{1}H-N.M.R. spectrometry.

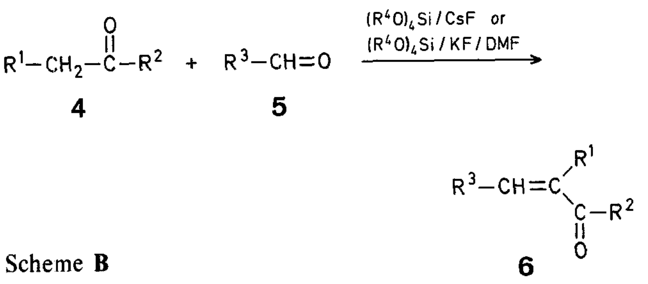
[c] $C_{18}H_{18}O$ (250.3)	calc.	C 86.35	H 7.25
	found	86.51	7.02

Table 2. Condensations of Ketones **4** with Non-Enolizable Aldehydes **5** Promoted by Tetraalkoxysilane/Alkali Metal Fluoride in the Presence or Absence of Dimethylformamide (Scheme **B**)

Aldehyde **5**	Ketone **4**	Product **6**	Reaction Conditions		Yield [%]	Purity [%][a]	m.p. [°C] or b.p. [°C]/torr	
			Base/Solvent	Temp., Time			found	reported
$C_6H_5-CH=O$			$(C_2H_5O)_4Si$/CsF/—	25 °C, 15 h	95	99	115°	117°[15]
	 $C_6H_5-\overset{\overset{O}{\|}}{C}-CH_3$	 $C_6H_5-\overset{\overset{O}{\|}}{C}-CH=CH-C_6H_5$	$(C_2H_5O)_4Si$/CsF/—	25 °C, 0.35 h	95	99	125°/1	208°/25[8]
			$(H_3CO)_4Si$/KF/DMF	70 °C, 5 h	52	99	105°/0.05	153-154°/4[1]
			$(H_3CO)_4Si$/KF/DMF	80 °C, 2 h	57	98	140-145°/0.1	181-181.5°/19[17]
	 $i-C_3H_7-\overset{\overset{O}{\|}}{C}-CH_3$	 $i-C_3H_7-\overset{\overset{O}{\|}}{C}-CH=CH-C_6H_5$	$(H_3CO)_4Si$/KF/DMF	60 °C, 16 h	72	98	160°/20	147°/11[18]
			$(H_3CO)_4Si$/CsF/—	25 °C, 0.5 h	85	99	90°/0.5	
	 $n-C_3H_7-\overset{\overset{O}{\|}}{C}-CH_3$	 $n-C_3H_7-\overset{\overset{O}{\|}}{C}-CH=CH-C_6H_5$	$(H_3CO)_4Si$/KF/DMF	55 °C, 15 h	81	98	143°/18	88°/0.8[19]
	$C_6H_5-CH=O$	 $C_6H_5-CH=CH-CH=CH-\overset{\overset{O}{\|}}{C}-C_6H_5$	$(C_2H_5O)_4Si$/CsF/—	25 °C, 1 h	75	98	98°	100°[2]
	 $H_3C-\overset{\overset{O}{\|}}{C}-CH_3$		$(H_3CO)_4Si$/KF/DMF	55 °C, 1.3 h	20	95	87-88°/6	112-115°/10[18]
	 $n-C_3H_7-\overset{\overset{O}{\|}}{C}-CH_3$		$(H_3CO)_4Si$/KF/DMF	50 °C, 5 h	43	97	95°/0.5	121°/8[7]
	 $i-C_3H_7-\overset{\overset{O}{\|}}{C}-CH_3$		$(H_3CO)_4Si$/KF/DMF	50 °C, 15 h	78	99	72°/0.6	101-102°/5[20]
			$(H_3CO)_4Si$/KF/DMF	55 °C, 15 h	85	99	46-51°	51°[21]

[a] Purity by G.L.C. (10% polyethylene glycol 20 M).

As a result of the self-condensation of aldehydes, crossed aldolisation between aldehydes **5** and ketones **4** can only occur with non-enolisable aldehydes (Scheme **B** and Table 2).



Scheme **B**

The reaction is promoted by the systems tetraalkoxysilane/caesium fluoride in the absence of a solvent or tetraalkoxysilane/potassium fluoride/dimethylformamide. With symmetrical ketones such as cyclohexanone, double aldolisation occurs whereas, with unsymmetrical ketones, only the less-hindered site reacts, as is usually observed with base-catalysed aldolisation[6]. With the present catalyst system, both benzaldehyde and furfural gave clean reactions instead of the product mixtures previously reported[7]. However, under our conditions, formaldehyde and α,β-unsaturated aldehydes gave complex product mixtures.

All reactions are carried out under a nitrogen atmosphere. The salts are dried by heating at 100 °C/1 torr for 1 h before use. The reactions are monitored by G.L.C. or I.R. spectroscopy.

Tetraalkoxysilane/Fluoride Ion-Promoted Aldol Condensation; General Procedure:

The carbonyl compound(s) (20 mmol for self-condensation or 10 mmol each for cross-aldolisation) and the catalyst system [caesium fluoride (10 mmol) or tetraalkoxysilane (5 mmol)/potassium (or caesium) fluoride (10 mmol) in the presence (or absence) of dimethylformamide (5 ml)] are heated with stirring at the temperature given in the Tables. Usually the mixture solidifies when the reaction is completed and, at this point, water (20 ml) is added (when caesium fluoride is used) or 10% hydrochloric acid (20 ml) is added (when a silane system is used). The product is extracted with ether (3 × 20 ml), washed with water (3 × 10 ml) to remove dimethylformamide, and dried with magnesium sulphate. The solvent is evaporated and the product distilled (Tables).

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J. Boyer, R. J. P. Corriu, R. Perz, M. Poirier, C. Reyé, *Synthesis* **1981**, 558.

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