Convenient Source of 'Naked' Fluoride: Tetra-n-butylammonium Chloride and Potassium Fluoride Dihydrate

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Summary A mixture of tetra-n-butylammonium chloride and potassium fluoride dihydrate in acetonitrile can be used as a convenient source of active fluoride ion in place of tetra-alkylammonium fluoride or potassium fluoride–crown ether combinations.

Recently, much use has been made in a variety of synthetic reactions of 'naked' fluoride[1] as a moderately strong base[1,2] or potent nucleophile.[1b] Two sources of active fluoride have commonly been used: (a) anhydrous tetra-alkylammonium fluorides (especially tetra-n-butyl)[1a,2] or (b) potassium fluoride in the presence of a crown ether.[1b,3] The former are generally obtained by hydrofluoric acid neutralization of aqueous solutions of the corresponding hydroxides and are very hygroscopic and difficult to obtain in an anhydrous state.[4] Crown ethers are relatively expensive and sometimes difficult to remove from desired products.

We now report an extremely simple yet broadly applicable method of generating *in situ* a fluoride reagent which shows reactivity comparable to those previously used. It is only necessary to stir together in an appropriate solvent (*e.g.* acetonitrile) a mixture of commercial tetra-n-butylammonium chloride and potassium fluoride dihydrate and the substrates of interest.[5] Examples of the reagent's use include the de-blocking of the β-(trimethylsilyl)ethyloxycarbonyl (TEOC) amino-protecting group,[6] the de-blocking of t-butyldimethylsilyl ethers,[1a] catalysis of Michael additions,[7] and the *C*-alkylation of β-diketones.[8] Results are summarised in the Table. Previous studies[6] have

Table. Reactions effected by $R_4NCl–KF{\cdot}2H_2O$[a]

	Reactants (mmol)	Solvent/ml (MeCN)	Temp./°C	Time/h	Products(%)[b]	
1	$PhCH{=}CHCOPh$ (1·25), $MeNO_2$ (25), Bu^n_4NCl (0·05), $KF{\cdot}2H_2O$ (0·25)	10	25	0·5	$PhCH(CH_2NO_2)CH_2COPh$	(94)
2	$PhCH{=}CHCOPh$ (1·25), $MeNO_2$ (25), $KF{\cdot}2H_2O$ (0·25)	10	25	2	,,	(10)
3	$PhCH{=}CHCOPh$ (5), $MeNO_2$ (100), KF (1·0)	65	81	48	,,	(70)
4[c–f]	$PhCH_2OSiMe_2Bu^t$ (1·35), Bu^nNCl (4·31), $KF{\cdot}2H_2O$ (4·1)	5	25	4	$PhCH_2OH$	(95)
5	TEOC-NHC_6H_4Cl-*p* (2·0), Bu^n_4NCl (6·0), $KF{\cdot}2H_2O$ (8·0)	10	50	8	*p*-$H_2NC_6H_4Cl$	(93)
6	TEOC-NHC_6H_4Cl-*p* (1·0), Bu^n_4NCl (3·0), $KF{\cdot}2H_2O$ (4·2)	10	28	70	*p*-$H_2NC_6H_4Cl$	(90)
7	$(PhCO)_2CH_2$ (2·5), MeI (10), Bu^n_4NCl (2·5), $KF{\cdot}2H_2O$ (10)	15	25	9	$(PhCO)_2CHMe$	(93)
8	$PhCOCH_2COMe$ (5·0), MeI (10), Bu^n_4NCl (5·0), $KF{\cdot}2H_2O$ (10)	15	25	9	$PhCOCH(Me)COMe$	(94)

[a] All reactions were carried out by stirring a mixture of the reactants in acetonitrile under the conditions given. The potassium fluoride dihydrate was finely powdered and on very humid days the mixture of $KF{\cdot}2H_2O$ and Bu^n_4NCl dried at 25 °C for 30 min *in vacuo* at 0·1 mmHg prior to initiating the reaction. [b] Yields given are of isolated products except in the case of reaction 2, which was estimated by t.l.c. [c] If Bu^n_4NBr was substituted for the chloride no reaction took place. [d] When anhydrous KF was substituted for the dihydrate no reaction took place at 25 °C. If 1–2 equiv. of water were added complete reaction occurred after 5 h. [e] If Et_4NCl was substituted for Bu^n_4NCl reaction was complete in 12 h at 25 °C. [f] If tetrahydrofuran was substituted for MeCN reaction was complete in 12 h at 66 °C.

shown that the presence of sufficient water completely suppresses de-blocking of the TEOC group and so we first employed a mixture of tetra-alkylammonium chloride and *anhydrous* potassium fluoride. To our surprise, this combination, although effective with the TEOC group, did not cause cleavage of t-butyldimethylsilyl ethers although the addition of 1—2 equiv. of water caused reaction to take place. Added water appeared to be captured by the anhydrous potassium fluoride and indeed subsequent studies demonstrated potassium fluoride dihydrate to be the reagent of choice. It is assumed that the necessary exchange between R_4NCl and KF to give a small equilibrium concentration of soluble R_4NF takes place on the surface of the crystalline dihydrate and is accelerated by the presence of water in the crystal lattice.

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[3] For a recent review on the general utility of crown ethers, see G. W. Gokel and H. D. Durst, *Synthesis*, 1976, 168.

[4] Binding of tetra-alkylammonium fluorides to silica gel has recently been proposed as a solution to problems associated with the hygroscopic nature of these salts (J. H. Clark, *J.C.S. Chem. Comm.*, 1978, 789).

[5] This is an example of the relatively rarely-used liquid–solid phase transfer catalysis (For general reviews of phase transfer catalysis see E. V. Dehmlow, *Angew. Chem.*, 1974, **86**, 187; 1977, **89**, 521; J. Dockx, *Synthesis*, 1973, 441). For previous non-crown examples see: H. D. Durst and L. Liebeskind, *J. Org. Chem.*, 1974, **39**, 3271; J. E. Baldwin, A. Au, M. Christie, S. B. Haber, and D. Hesson, *J. Amer. Chem. Soc.*, 1975, **97**, 5957; E. V. Dehmlow, *Tetrahedron Letters*, 1976, 91; E. V. Dehmlow and T. Remmler, *J. Chem. Research*, 1977, (*S*) 72; (*M*) 0766.

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