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## Calcium Fluoride-supported Alkali Metal Fluorides. New Reagents for Nucleophilic Fluorine Transfer Reactions

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The reactivity of the alkali metal fluorides KF and CsF as sources of nucleophilic fluorine is appreciably enhanced by the presence of calcium fluoride and in particular by the use of the supported reagents KF–CaF<sub>2</sub> and CsF–CaF<sub>2</sub>.

Ionic fluorides are widely used as sources of nucleophilic fluorine in the preparation of organofluorine compounds.<sup>1,2</sup> Potassium fluoride is the most popular of these reagents in that it represents a thermally stable and relatively inexpensive source of fluorine. The major drawback with the use of KF is its very low solubility in all but a few protic solvents (which

cannot normally be used in nucleophilic fluorine transfer reactions owing to strong  $F^-$  solvent hydrogen bonding<sup>3</sup>) and very many attempts have been made to alleviate this problem, usually by phase transfer catalysis. One of the more soluble (but also more expensive) sources of  $F^-$  is CsF which can be used as a more reactive source of  $F^-$  or as a 'catalyst' to

Table 1. Fluorination using KF-CaF<sub>2</sub> and CsF-CaF<sub>2</sub>.

Substrate	Reagent	Solvent	Temp./°C	Time/h	Product	Yielda
PhCH <sub>2</sub> Br	KF-CaF <sub>2</sub> <sup>b</sup>	Sulpholane	120	2	PhCH <sub>2</sub> F	92
PhCH <sub>2</sub> Br	KF-CaF <sub>2</sub> <sup>c</sup>	Sulpholane	120	2	$PhCH_{2}F$	74
PhCH <sub>2</sub> Br	KFCaF <sub>2</sub> <sup>b</sup>	Acetonitrile	80	16	PhCH <sub>2</sub> F	68
PhCH <sub>2</sub> Br	KF-CaF <sub>2</sub> <sup>c</sup>	Acetonitrile	80	24	PhCH <sub>2</sub> F	67
PhCH <sub>2</sub> Br	CsF-CaF <sub>2</sub> <sup>b</sup>	Sulpholane	80	0.25	PhCH <sub>2</sub> F	95
PhCH <sub>2</sub> Br	$CsF-CaF_2^{c}$	Sulpholane	80	2	PhCH <sub>2</sub> F	97
$1 - C_{12} \overline{H}_{25} Br$	KF-CaF <sub>2</sub> <sup>c</sup>	Sulpholane	200	1	$1 - C_{12}H_{25}F$	74ª
$1 - C_{12}H_{25}Br$	KF-CaF <sub>2</sub> <sup>c</sup>	Sulpholane	160	5	$1 - C_{12}H_{25}F$	84 <sup>d</sup>
PhCOCI	KF-CaF <sub>2</sub> <sup>b</sup>	Sulpholane	19	0.2	PhCOF	71
MeCOCl	KF–CaF <sub>2</sub> <sup>b</sup>	Sulpholane	30	0.2	MeCOF	74

<sup>&</sup>lt;sup>a</sup> G.l.c. conversion. <sup>b</sup> Supported reagent (dried at 80 °C under reduced pressure for 1 h). <sup>c</sup> Added CaF<sub>2</sub>. <sup>d</sup> Complete conversion of the substrate occurred; the remaining product was dodec-1-ene.



**Figure 1.** Rate of production of PhCH<sub>2</sub>F from PhCH<sub>2</sub>Br in MeCN at 80 °C using (a) CsF-CaF<sub>2</sub> (dried at 80 °C for 1 h under reduced pressure); (b) CsF (dried at 80 °C for 1 h under reduced pressure); (c) CsF with added CaF<sub>2</sub> (untreated laboratory reagents); and (d) CsF (untreated laboratory reagent).

accelerate KF reactions. An interesting alternative to the use of phase transfer catalysis to improve the reactivity of inorganic reagents in general is the use of supported reagents<sup>4</sup> which owe much of their improved reactivity to increased reagent surface area. KF-alumina is one example of a supported reagent which we and others have successfully applied in many organic reactions<sup>5—7</sup> but the reactivity of this reagent as a source of nucleophilic fluorine is very low, presumably owing to surface OH-F<sup>-</sup> hydrogen bonding.<sup>7,8</sup> We have therefore turned our attention to the possibility of using non-surface hydroxylated high surface area inert support materials for enhancing alkali metal fluoride reactivity in organofluorinations. We report here our preliminary results from an investigation into the use of  $CaF_2$ , a 'surface-inert' material of typical surface area *ca*. 10 m<sup>2</sup>/g<sup>+</sup> as a support in some typical aliphatic fluorinations using KF and CsF as the source of nucleophilic fluorine.

We have found that addition of pure CaF<sub>2</sub>‡ results in an appreciable rate acceleration in the reaction of KF with benzyl bromide in sulpholane as bulk solvent. At 80 °C for example, KF alone gives <10% conversion to benzyl fluoride after 10 h whereas the same reaction carried out in the presence of CaF<sub>2</sub> (5 mol equiv. with respect to KF) gives 30% conversion after the same period of time under the same conditions. At 120 °C the same reaction gives 74% fluorination using KF with added CaF<sub>2</sub> after 2 h compared to 36% fluorination after 2 h using KF alone.

A supported reagent, KF–CaF<sub>2</sub>, can be prepared by slowly evaporating to dryness a slurry of pure CaF<sub>2</sub> in a solution of KF in methanol (we routinely used a KF–CaF<sub>2</sub> mole ratio of 1:5) for *ca*. 1 h at 80 °C under reduced pressure. This reagent appears to have a higher reactivity than the combination of KF with added CaF<sub>2</sub>. Thus for example at 120 °C in sulpholane, the conversion of benzyl bromide to fluoride after 2 h is 92% using the supported reagent KF–CaF<sub>2</sub>. Similar effects can be obtained using acetonitrile as bulk solvent.

In an attempt to learn more about the reactivity of the supported reagent we have compared its reactivity after drying under different conditions. We have found that the best reactivity is achieved with moderate drying conditions. Thus the reactivity of the KF–CaF<sub>2</sub> supported reagent dried only briefly at 80 °C under vacuum is less than that of a reagent dried for 1 h under these conditions. More forcing conditions (*i.e.* 280 °C for 16 h) also result in a loss in reagent reactivity.

We have also observed rate enhancements due to the presence of  $CaF_2$  in the fluorination of other substrates (Table 1).

‡ BDH extra purity grade.

<sup>&</sup>lt;sup>†</sup> This is much less than the surface area of more conventional supports such as alumina (100–200 m<sup>2</sup>/g) but much greater than the surface area of normal KF (0.1 m<sup>2</sup>/g) or even spray dried KF (1.3 m<sup>2</sup>/g).<sup>7.9</sup>

The reactivity of CsF as a source of nucleophilic fluorine is also enhanced by the presence of  $CaF_2$  and especially by the use of the supported reagent CsF-CaF<sub>2</sub> (Figure 1).

In conclusion, it is clear that the presence of pure  $CaF_2$ enhances the reactivity of KF and CsF in aliphatic fluorination reactions. We believe that the improvement in reactivity is due to the CaF<sub>2</sub> acting as an inert high surface area support material so that the pre-supported materials are especially effective.§ Our observations concerning the effects of reagent drying lead us to believe that the presence of a small amount of water (or methanol) is important in achieving optimum reactivity for our reagents. This may well be due to the water (or methanol) helping to bind the alkali metal fluoride to the CaF<sub>2</sub> support.

No chemical interaction between the alkali metal fluoride and the  $CaF_2$  support is apparent. Thus KF or CsF is easily removed from the reagent by aqueous washing. High resolution solid state n.m.r. spectroscopy shows no change in the <sup>19</sup>F chemical shifts of KF and CsF on supporting the reagents on  $CaF_2$ .<sup>10</sup>

§ The increase in reactivity on increasing surface area would seem to be consistent with the improvement observed on going from ordinary KF to the higher surface area 'spray dried' KF.<sup>9</sup> The results from the effects of  $CaF_2$  on the fluorination of aryl halides will be published elsewhere.

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