

## The Combination of Potassium Fluoride and Calcium Fluoride: A Useful Heterogeneous Fluorinating Reagent

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The combination of potassium fluoride and calcium fluoride was found to be an effective and practical solid reagent for the fluorination of various organic chlorides and bromides under mild conditions.

Among the methods available for the introduction of fluorine into organic compounds, the substitution of organic halides and sulphonates by the fluoride anion has widely been used. However use of alkali metal fluorides generally requires high temperatures and/or long reaction times because of both the low solubility and the low nucleophilicity of fluoride salts in polar aprotic solvents. There have been a number of reports of methods of improving the reaction.<sup>1-6</sup> Heterogeneous nucleophilic substitution of alkyl halide with alkali metal acetate or cyanide in organic solvents is promoted by use of alumina, silica gel, or molecular sieve.<sup>7</sup> We have previously reported that alkali metal fluorides supported on alumina are versatile solid reagents for alkylation, elimination, addition, and condensation reactions.<sup>8</sup> In these cases, however, impregnated fluoride reagents did not promote heterogeneous nucleophilic substitution, but enhanced the potential basicity of the potassium fluoride. Taking into account this behaviour of the fluoride anion, we have investigated effective solid reagents for fluorination. In this communication we report that a calcined mixture of potassium fluoride and calcium fluoride is a useful solid fluorinating reagent.

The heterogeneous fluorination of benzyl bromide was carried out as follows. Commercially available potassium

fluoride was mixed with calcium fluoride (Wako's guaranteed reagent)<sup>†</sup> at a 1:2 or 1:4 weight ratio. After grinding, the mixture was dried at 150 °C under vacuum for several hours.

**Table 1.** The substitution of benzyl bromide with fluoride ion.<sup>a</sup>

Fluoride reagent	G.l.c. yield of PhCH <sub>2</sub> F/%	
	70 °C, 24 h	reflux, 10 h
KF	1.5	0.6
CaF <sub>2</sub>	0.1	0.3
KF-CaF <sub>2</sub>	38	89
Spray-dried KF <sup>b</sup>		68
KF-18-crown-6 <sup>c</sup>		50

<sup>a</sup> The reaction of benzyl bromide (5 mmol) with fluoride ion (10 mmol) was carried out in acetonitrile. <sup>b</sup> Data from ref. 4. <sup>c</sup> Data from ref. 1.

<sup>†</sup> Finely powdered fluorite was not effective. Surface areas were measured by the Brunauer-Emmett-Teller method using argon gas on a Micromeritics High Speed Surface Area Analyzer 2205. Interestingly, the effective calcium fluoride showed much greater specific surface area (ca. 14 m<sup>2</sup>/g) than that of natural fluorite (unmeasurable value) or potassium fluoride (0.1 m<sup>2</sup>/g).<sup>4</sup>

**Table 2.** Heterogeneous fluorination using the KF-CaF<sub>2</sub> reagent.<sup>a</sup>

Substrate	Solvent	Temp/°C	Time/h	Product	Yield/%	
					G.l.c.	Isolated
PhCOCl	<sup>b</sup>	Room temp.	3	PhCOF		81
MeSO <sub>2</sub> Cl	<sup>b</sup>	Room temp.	3	MeSO <sub>2</sub> F		78
PhSO <sub>2</sub> Cl	<sup>b</sup>	Room temp.	5	PhSO <sub>2</sub> F	100	87
<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> Cl	MeCN	Room temp.	4	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> F	100	82
<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> Cl	MeCN	Room temp.	3	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> F		68
EtOCOCl	MeCN	Room temp.	24	EtOCOF	95	
Me <sub>2</sub> NCOCl	MeCN	50	24	Me <sub>2</sub> NCOF	100	
$\overline{\text{CH}_2\text{OCH}_2\text{CH}_2\text{Cl}}$	<sup>b</sup>	110	60	$\overline{\text{CH}_2\text{OCH}_2\text{CH}_2\text{F}}$	46	
ClCH <sub>2</sub> CO <sub>2</sub> Et	<sup>b</sup>	110	48	FCH <sub>2</sub> CO <sub>2</sub> Et	75	
PhCH <sub>2</sub> Cl	MeCN	Reflux	48	PhCH <sub>2</sub> F	77	
PhCH <sub>2</sub> Br	MeCN	Reflux	15	PhCH <sub>2</sub> F	95	81
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	MeCN	Reflux	45	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> F	99	73
1-C <sub>8</sub> H <sub>17</sub> Br	Tetraglyme	100	48	1-C <sub>8</sub> H <sub>17</sub> F	40 <sup>c</sup>	

<sup>a</sup> The molar ratio of substrate to KF in the KF-CaF<sub>2</sub> reagent was 1:2. <sup>b</sup> Without solvent. <sup>c</sup> 2% Oct-1-ene was formed.

This heterogeneous mixture of KF-CaF<sub>2</sub> (2.5 g, containing 8 mmol of KF) and benzyl bromide (0.69 g, 4 mmol) was heated to reflux with stirring in acetonitrile (3.5 cm<sup>3</sup>). The reaction proceeded smoothly to afford the corresponding fluoride in 69, 89, and 95% yield after 6, 10, and 15 h, respectively, as determined by g.l.c. analysis. After 15 h, the solid materials were filtered off and washed with diethyl ether, and solvent was then evaporated. Benzyl fluoride was isolated in 81% yield by molecular distillation.

Under the same conditions nucleophilic substitution hardly occurred when either KF powder or CaF<sub>2</sub> powder were used separately. Thus, it is the combination of KF and CaF<sub>2</sub> that accelerates the heterogeneous fluorination. As shown in Table 1, the reactivity of this KF-CaF<sub>2</sub> reagent is higher than that of agents such as 'spray-dried' KF and the KF-18-crown-6 complex.

The KF-CaF<sub>2</sub> reagent was used successfully in the preparation of various organo fluorine compounds. Typical examples are summarised in Table 2. Moderately reactive and moisture sensitive chlorides or bromides were fluorinated by use of the KF-CaF<sub>2</sub> reagent in good yields. The fluorination of carboxylic and sulphonic acid chlorides proceeded very slowly with KF powder alone in acetonitrile at room temperature, but the reaction was completed within a few hours when the KF-CaF<sub>2</sub> reagent was used. In these experiments the reaction could be carried out with or without solvent.

Other combinations of alkali metal fluorides and alkaline earth metal fluorides were found to produce higher nucleophilicity than either of the individual fluorides. For example, a CsF-BaF<sub>2</sub> reagent was more efficient than CsF, and a NaF-CaF<sub>2</sub> reagent was able to promote fluorination of aryl and sulphonyl chlorides on gentle heating.

From powder X-ray diffraction analysis of the KF-CaF<sub>2</sub> reagent no chemical interaction was observed between the two fluorides. Analysis of the inorganic materials recovered after use in the fluorination of benzyl bromide showed the presence of KBr together with KF and CaF<sub>2</sub>, but no CaBr<sub>2</sub>. Thus,

calcium fluoride may act as a simple support to disperse potassium fluoride on its surface and enhance the nucleophilicity of the KF, possibly by physical interaction.

The results from the fluorination of chloroarenes bearing electron attracting groups such as NO<sub>2</sub> or CN will be published elsewhere.

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