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ENHANCED CATALYTIC EFFECT OF FREEZE-DRIED POTASSIUM FLUORIDE FOR ALKYLATION OF PROTIC COMPOUNDS

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Freeze-dried potassium fluoride was found to be much more effective as a hydrogen-bond forming catalytic reagent for alkylation of protic compounds than usual calcine-dried potassium fluoride. Phenol, thiophenol, aniline, and acetylacetone were easily alkylated with methyl or ethyl iodide in the presence of the reagent. Freeze-dried potassium fluoride, however, had no effect for the fluorination of activated chlorine compounds.

An importance of fluoride ion as a catalyst to promote various types of base-catalyzed reactions in organic synthesis has been recognized in recent years.1) The work of Clark and Miller,2) in particular, revealed that fluoride ion has an effect on condensation reactions by its high capability of a hydrogen-bond formation.2) As reagents generating fluoride ion in these reactions, potassium, cesium, and tetraalkylammonium fluorides are generally used so far. However, it is not easy to handle these hygroscopic reagents and the reproducibility of the reactions is invariably poor. Recently, low hygroscopic reagents generating a fluoride ion were designed by allowing potassium fluoride to be adsorbed on a celite or alumina carrier.3) Although these reagents with a carrier are effective in some reactions, reproducibility of the preparation of the reagents is not so good and reactions result in different yields in our experiments.

We now wish to report a new-type potassium fluoride which is very effective and useful in hydrogen-bond assisted organic reactions. Fine-powdered potassium fluoride obtained by freeze-drying was found to be much less hygroscopic than usual calcine-dried potassium fluoride and to have a greatly enhanced catalytic effect in synthetic reactions.

For example, alkylation of protic compounds such as phenol, thiophenol, aniline, and acetylacetone, with alkyl iodide in acetonitrile proceeded smoothly in the presence of freeze-dried potassium fluoride even at room temperature (Table 1). Calcine-dried potassium fluoride, in contrast, gave only a trace of alkylated product under the same conditions.

The difference between freeze- and calcine-dried potassium fluoride in hygroscopicity and in the effect for such a hydrogen-bond assisted reaction is very interesting. When freeze- and calcine-dried potassium fluorides were allowed to be exposed to an atomosphere at the same time, the latter was found to have absorbed as much humidity as 23% of its weight in one hour, while the former have done only 8%. Further, when fresh freeze-dried potassium fluoride in a suspension in dried acetonitrile was tested for water content by the Karl-Fischer's method, it was revealed that only 0.08 - 0.13% of water was occluded in the crystals.

Curiously enough, freeze-dried potassium fluoride was much less effective than calcine-dried potassium fluoride for the fluorination of active chlorine compounds. For example, by the 3 h's reaction of benzoyl chloride in acetonitrile at room temperature in the presence of polyethyleneglycol,[4)] calcine-dried potassium fluoride afforded benzoyl fluoride in a quantitative yield, whereas freeze-dried potassium fluoride gave only a trace of the fluoride.

These striking contrasts between freeze- and calcine-dried potassium fluorides in their chemical behavior are supposed to be ascribed to the difference in structure of their crystals. Extending studies on the surface properties and the chemical reactivities of these potassium fluorides are in progress.

Table 1. Alkylation catalyzed by freeze-dried KF

Substrate		Product	Temp. (^oC)	Time (h)	Yield[b)] (%)
PhOH	MeI	PhOMe	r.t.	8	88
"	CH_2=$CHCH_2Br$	$PhOCH_2CH$=CH_2	r.t.	24	24
"	"	"	refl.	10	77
PhSH	MeI	PhSMe	r.t.	1	86
"	EtI	PhSEt	r.t.	5	77
$PhNH_2$	MeI	PhNHMe & $PHNMe_2$	r.t.	10	83[c)]
$(CH_3CO)_2CH_2$	"	$(CH_3CO)_2CHMe$[a)]	r.t.	5	84
"	EtI	$(CH_3CO)_2CHEt$[a)]	r.t.	5	57

a) Only C-alkylated product was obtained. b) Isolated yield. The product was identified by various spectral data. c) A mixture of mono- and dimethylanilines (1 : 0.24 by ^1H nmr) was formed.

Experimental

Freeze-dried potassium fluoride: Commercially available crystals of potassium fluoride (150 g) were dissolved in distilled water (220 ml) and the solution was freezed at -75 ~ -70 ^oC for 20 min using a dry ice-acetone bath. The frozen solid was freeze-dried in a vacuum for six days at room temperature, affording fine powder of potassium fluoride.

Alkylation: A mixture of a protic compound (10 ml), alkyl iodide (10 mmol), freeze-dried potassium fluoride (30 mmol), and dried acetonitrile (20 ml) was stirred for prescribed hours. Potassium fluoride was removed by filtration and the filtrate was poured into water. Oily material separated was extracted with diethyl ether and after removing the solvent it was subjected to distillation.

References

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