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ALKALINE METAL FLUORIDES IN GRAPHITE - NEW CATALYSTS IN ORGANIC SYNTHESIS. I. REACTIONS OF POLYFLUOROAROMATIC COMPOUNDS WITH O- AND N-NUCLEOPHILIC AGENTS

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SUMMARY

The paper reports the use of new catalysts - alkaline metal fluorides in graphite of the general formula C_8MF, where M=Li, Na, K, Rb or Cs, in the reactions of polyfluoroaromatic compounds with aromatic OH-acids and piperidine. These compounds are shown to have a high activity in the above processes, exceeding that of similar free fluorides of alkaline metals.

INTRODUCTION

In recent years there has been growing interest in the catalysts applied to insoluble supports [1,2]. Such catalytic systems have some advantages over the unsupported catalysts when used in organic processes · the possibility to be recycled, ease of their separation from the reaction mixture and regeneration, performing synthesis in flow systems, and higher ecological "purity".

As supported catalysts, alkali metal fluorides on inorganic supports are widely used now [3-5]. The use of supported ionic fluorides in base-catalysed processes (elimination, alkylation, arylation, condensations, etc.) allows to carry them out in relatively mild conditions, with high selectivity and good yields. Supported alkali metal fluorides may have considerably changed properties and catalytic activity. Thus tetrabutylammonium fluoride supported on alumina proved to be less hygroscopic than the free fluoride. At the same time, this supported catalyst is less active in some alkylation reactions [5], whereas potassium fluoride supported on alumina is more active in these reactions than the free fluoride. This demonstrates the possibility of significant modification of the activity of supported catalysts.

The compounds generally used as supports (matrices) are zeolites, silica gel , and alumina [3, 6]. A prospective and accessible support for various catalysts is graphite. It has layered structure, with linkages between carbon layers being very weak, which allows to intercalate there various compounds. There are graphite intercalates of acidic (HNO_3 , H_2SO_4, HSO_3F, SbF_5, AsF_5, etc.) and basic compounds (alkaline metals) [7, 8].

RESULTS AND DISCUSSION

We have first obtained graphite intercalation compounds of alkaline metal fluorides. These compounds are obtained by the reactions of perfluoroorganic compounds with pre-formed alkaline metal graphite intercalates in the inert atmosphere [9].

Alkaline metal fluorides in graphite are the free- flowing and slightly caking (upon storage) compounds of the general formula C_nMF (n=8,10,12,24,36,48,60, M=Li,Na,K,Rb,Cs), whose composition has been confirmed by the elemental (Table 1) and radiometric (Table 2) analyses data [9]. Alkaline metal fluoride graphite intercalates appeared to be far less hygroscopic than the free fluorides (Table 3, Fig.1). This allows to use them as catalysts of organic reactions without preliminary dehydration and grinding before the reaction, and without inert atmosphere.

We have shown alkaline metal fluorides in graphite to be effective catalysts of some aromatic nucleophilic substitution reactions. Thus, in the presence of these compounds, pentafluoropyridine reacts in mild conditions with pentafluorophenol (Table 4) to form the previously described compounds I - V [10]

TABLE 1

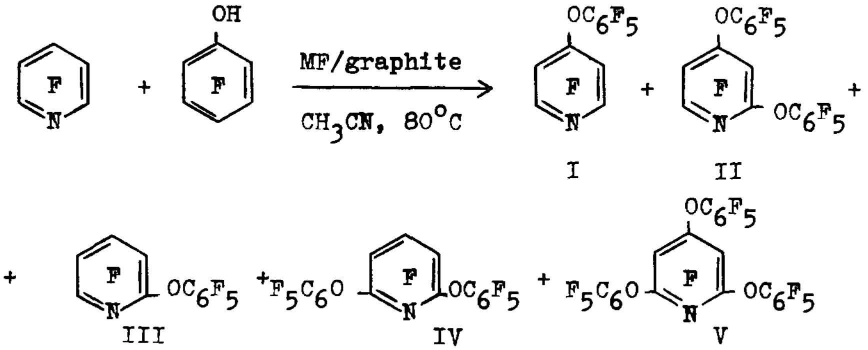
Elemental analysis of alkaline metal fluorides in graphite

MF / Graphite	Found (%)			Calculated (%)			Formula
	C	F	Ash	C	F	M	
LiF / graphite	76.6	14.9	8.3	78.7	15.6	5.7	C_8LiF
NaF / graphite	68.0	14.5	17.4	69.6	13.8	16.7	C_8NaF
KF / graphite	60.9	11.8	27.2	62.3	12.3	25.4	C_8KF
CsF /graphite	38.2	6.8	54.9	38.8	7.7	53.6	C_8CsF
RbF /graphite	47.5	8.6	43.8	49.9	9.5	42.6	C_8RbF

TABLE 2

Concentration of alkaline metals in MF/graphite determined by the X-ray radiometric method

MF / graphite	Found of metal (%)	Calculated of metal (%)
C_8KF	25.28	25.36
C_8RbF	42.56	42.62
C_8CsF	53.50	53.59



It is interesting to note that lithium and sodium fluorides in graphite show marked activity in this reaction (Table 4, Nos. 1-5, 6-8, 11-15), whereas the respective free fluorides only slightly initiate this reaction (cf. [10]). As expected, more active catalysts for the reaction of pentafluoropyridine with pentafluorophenol are potassium, rubidium, and caesium fluorides in graphite (Table 4, Nos. 19-24, 29-32, 35-38).

TABLE 3

Variation in the mass of alkaline metal fluoride and alkaline metal fluoride/graphite samples in air (mass 1.0000 g , t 23°C, air moisture 28–30%)

Fluoride	Exposition time , h				
	10	25	50	75	100
	Increase of mass in % to the initial				
LiF	0.00	0.00	0.02	0.03	0.06
NaF	0.00	0.00	0.01	0.04	0.06
KF	0.36	1.44	2.93	4.48	5.98
RbF	5.54	11.19	20.26	29.13	35.44
CsF	5.01	9.48	17.79	28.91	35.06
LiF/graphite	0.00	0.00	0.00	0.00	0.03
NaF/graphite	0.00	0.00	0.00	0.02	0.04
KF /graphite	0.00	0.01	0.08	0.61	1.13
RbF/graphite	0.88	1.84	3.46	5.82	8.04
CsF/graphite	0.66	1.56	3.08	4.98	7.23

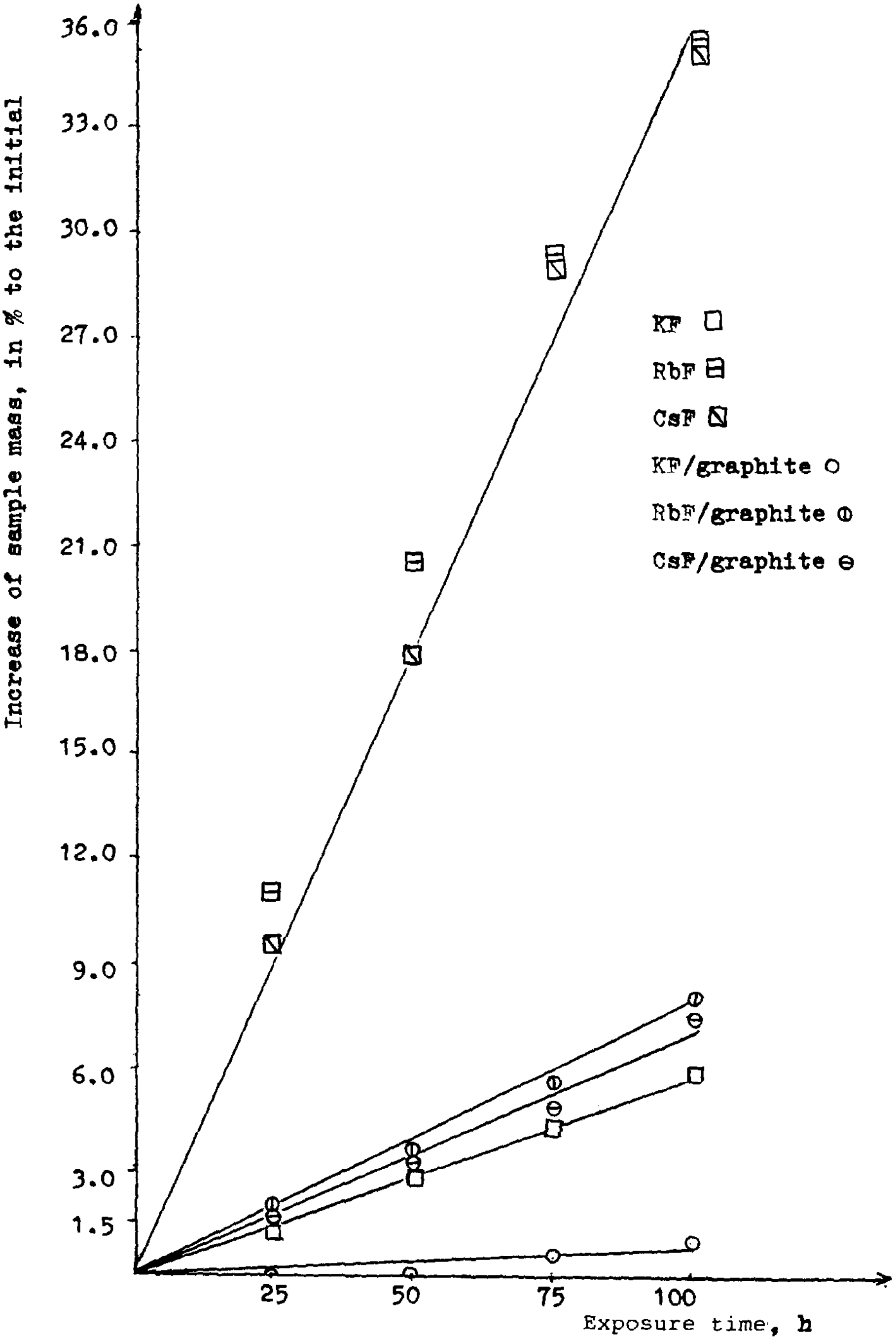


Fig. 1. Variation of the mass of alkaline metal fluoride and graphite samples in air (mass 1.0000 g, T=23°C, moisture 28-30%)

TABLE 4

Interaction of pentafluorophenol with pentafluoropyridine in the presence of alkaline metal fluoride/graphite (80°C , 2 h)

No	Alkaline metal fluoride/graphite		Ratio of C_5F_5N C_8MF(mol) considering pure fluoride	Solvent	Yield of reaction product by GLC(%)				
	type	reuse			I	II	III	IV	V
I	2	3	4	5	6	7	8	9	10
1	LiF/graphite	first	1·0.5	CH_3CN	4				
2	"	"	1·1	"	10				
3	"	"	1·2	"	16				
4	"	second	1 1	"	8				
5	"	third	1 1	"	7				
6	"	first	1 0.5	DMF	9				
7	"	"	1 1	"	19	1			
8	"	"	1·2	"	26	2			
9	"	second	1 1	"	15				
10	"	third	1 1	"	12				
11	NaF/graphite	first	1:0.5	CH_3CN	9				
12	"	"	1 1	"	19	2			

(Continued overleaf)

TABLE 4 (<u>cont</u>)

1	2	3	4	5	6	7	8	9	10
13	"	"	1.2	"	25	2			
14	"	"	1 0.5	DMF	16	1			
15	"	"	1 1	"	27	3			
16	"	"	1·2	"	32	4			
17	"	second	1·1	"	21	2			
18	"	third	1·1	"	17	1			
19	KF/graphite	first	1 0.5	CH_3CN	31	2			
20	"	"	1.1	"	48	3	1		
21	"	"	1.2	"	62	5	2		
22	"	"	1 0.5	DMF	47	3	1		
23	"	"	1 1	"	76	7	2	2	
24	"	"	1 2	"	52	11	3	2	2
25	"	second	1 1	"	61	3			
26	"	third	1:1	"	52	1			
27	KF	first	1:0.5	CH_3CN	13				
28	"	"	1 1	"	29	2			
29	RbF/graphite	first	1 0.25	"	55	2	1		
30	"	"	1·0.5	"	64	6	2	1	
31	"	"	1·1	"	69	9	3	2	
32	"	"	1·2	"	48	13	6	3	
33	"	second	1:1	"	51	3	1		

34	"	third	1·1	"	37	2			
35	CsF/graphite	first	1·0.5	"	63	4	2	1	
36	"	"	1·0.25	DMF	54	2	1		
37	"	"	1·0.5	"	66	9	4	3	
38	"	"	1 1	"	40	15	9	4	2
39	"	second	1.0.5	"	50	3	1		
40	"	third	1 0.5	"	33	1			
41	CsF	first	1.0.25	"	19				
42	"	"	1:0.5	"	43	3	2	1	
43	"	"	1 1	"	52	10	4	1	1
44	Graphite	"	1:2	"	-	-	-	-	-
45	KF/Al_2O_3	first	1:1	CH_3CN	46	2	1		
46	"	"	1·1	DMF	51	2	1		
47	"	second	1 1	"	31				
48	"	third	1 1	"	14				
49	CsF/Al_2O_3	first	1·0.5	"	72	2	2	1	
50	"	"	1.1	"	52	11	4	2	
51	"	second	1·1	"	28	4			
52	"	third	1·1	"	11				
53	Al_2O_3	first	1 2	"	-	-	-	-	-

TABLE 5

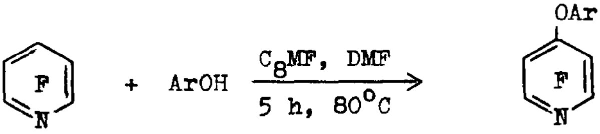
Interaction of pentafluoropyridine with 4-nitrophenol in the presence of alkaline metal fluoride/graphite (80°C , 5 h)

No	MF/Graphite		Ratio of (mol)		Solvent	Yield of compound VI (%), for the compound isolated
	type	reuse	C_5F_5N	C_8MF		
1	LiF/graphite	first	1	0.5	CH_3CN	17
2	"	"	1	1	"	28
3	"	"	1	2	"	34
4	"	"	1	0.5	DMF	26
5	"	"	1	1	"	35
6	"	"	1	2	"	44
7	"	second	1	1	"	30
8	"	third	1	1	"	25
9	NaF/graphite	first	1	0.5	CH_3CN	21
10	"	"	1	1	"	33
11	"	"	1	2	"	40
12	"	"	1	0.5	DMF	38
13	"	"	1	1	"	52
14	"	"	1	2	"	57
15	"	second	1	1	"	47
16	"	third	1	1	"	41

17	KF/graphite	first	1 0.5	CH_3CN	70
18	"	"	1.1	"	86
19	"	"	1.2	"	94
20	"	"	1·0.5	DMF	75
21	"	"	1·1	"	91
22	"	"	1 2	"	96
23	"	second	1 1	"	61
24	"	third	1·1	"	52
25	RbF/graphite	first	1·0.5	"	81
26	"	"	1 1	"	96
27	"	"	1 2	"	95
28	"	second	1·1	"	61
29	"	third	1 1	"	47
30	CsF/graphite	first	1 0.5	"	84
31	"	"	1 1	"	97
32	"	second	1 1	"	60
33	"	third	1 1	"	44

Interaction of 4-nitrophenol with pentafluoropyridine in the presence of fluoride graphite intercalates leads to the formation of 4-(4'-nitrophenoxy)-2,3,5,6-tetrafluoropyridine (VI) in a high yield (Table 5). In this reaction the catalytic activity of fluorides in graphite also exceeds that of the free fluorides (cf. [11]), the most active initiators being the fluorides of higher metals (K,Rb,Cs) in graphite. It should be noted that the above reactions require the smaller (1.5-2 times as small) amount of intercalated fluoride (considering pure fluoride) per 1 mole of the aromatic substrate.

Potassium and caesium fluorides in graphite also effectively catalyse the reactions of other phenols and naphthols with pentafluoropyridine.



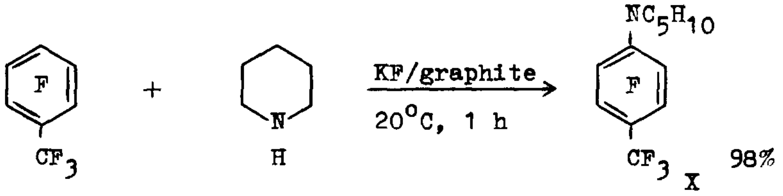
VII - IX

M=K, Ar(yield of VII-IX,%)= $I\text{-}C_{10}F_7$(71), $2\text{-}C_{10}F_7$ (63), $4\text{-}CH_3C_6F_4$ (78).

M= Cs, Ar (yield of VII-IX,%) = $I\text{-}C_{10}F_7$ (79), $2\text{-}C_{10}F_7$ (70), $4\text{-}CH_3C_6F_4$ (87).

Hence the catalytic activity of alkaline fluoride metals in graphite in the reactions of aromatic OH-acids with pentafluoropyridine increases in the series. $C_8LiF \simeq C_8NaF < C_8KF < C_8RbF \simeq C_8CsF$, which is similar to the activity sequence of free fluorides used as basic catalysts [12]. The solvent also has some effect on the activity of fluorides in graphite. Thus in acetonitrile, the product yields in the reaction of pentafluoropyridine both with pentafluorophenol (Table 4) and 4-nitrophenol (Table5) are much smaller than in DMF. This must be due to the higher solubility of alkaline metal fluorides in the latter solvent [13].

Potassium fluoride in graphite also catalyses other aromatic nucleophilic substitution reactions. Thus in its presence, octafluorotoluene reacts in mild conditions with an equimolar amount of piperidine, giving 1-trifluoromethyl-4-N-piperidino-2,3,5,6-tetrafluorobenzene (X) in a high yield



One of the important advantages of alkaline metal fluorides in graphite as catalysts is the possibility of their reuse as bases in organic reactions. In the reactions of pentafluoropyridine with phenols they may be used at least three times without additional regeneration (Table 4, Nos.4, 5,9,10,17,18,25,26,33,34,39,40, Table 5, Nos. 7,8,15,16,23, 24,28,29,32,33). Thus, with KF /graphite used for the third time, the reaction of pentafluoropyridine with phenols proceeds for more than 50%(Table 4, No. 26, Table 5, No.24). It should be noted that the activity of higher alkaline metal (K,Rb,Cs) fluorides in graphite reused in the reaction decreases to a greater extent than that of lithium or sodium fluorides in graphite (Table 4, Nos.25,26,33,34,39,40, cf. Nos.7,8,15,16). This may result from the higher hygroscopicity of the former group of reagents as compared with the latter one.

It was interesting to compare the activity of alkaline metal fluorides in graphite with that of the respective fluorides applied to other supports. For comparison we prepared potassium and caesium fluorides on alumina, which are effective catalysts for many organic reactions [3,4] .

Potassium and caesium fluorides on alumina also proved to be effective catalysts for the reaction of pentafluoropyridine with pentafluorophenol, but in activity they are still second to the respective graphite intercalates(Table 4, Nos.

20,23, cf. Nos. 45,46, Nos. 37,38 cf. Nos. 49,50). It is interesting to note that the catalytic activity of fluorides on alumina upon their reuse decreases to a much greater extent than that of the respective fluorides in graphite(Table 4, Nos. 25,26 cf. Nos. 47,48, Nos. 33,34 cf. Nos. 51,52). Such a difference between the activities of alkaline metal fluorides in graphite and on alumina may be explained by the character of fluoride incorporation into support. In the case of alumina, fluorides occupy exclusively the surface of the support, whereas in graphite the guest species also penetrate between the carbon layers. Evidently, the fluoride located on the surface is desorbed quicker in the reaction than that intercalated between the layers, which gradually diffuses onto the surface of support. On the other hand, the surface-located fluorides undergo more side-reactions, leading to general deactivation of a catalyst. It was shown that pure graphite and alumina do not initiate the above reactions (Table 4, Nos. 44,53).

Thus, the alkaline fluoride metals in graphite are the new effective prolonged-activity catalytic systems for the reactions of polyfluoroaromatic compounds with the O- and N-nucleophilic agents. These compounds have some advantages over the free alkaline metal fluorides and known supported catalysts, which allows to hope for their extended use in fine organic synthesis.

EXPERIMENTAL

Starting compounds - pentafluoropyridine (b.p. 83-84°C), 1-$C_{10}F_7OH$ (m.p. 103-104°C), 2-$C_{10}F_7OH$ (m.p. 124-126°C), and C_6F_5OH (b.p. 144-145°C), produced at a pilot plant of the Novosibirsk Institute of Organic Chemistry.

4-Nitrophenol is a commercial product recrystallised from ethanol (m.p. 112-113°C).

4-$CH_3C_6F_4OH$ was prepared acc. to [14] (m.p. 50-51°C).

CH_3CN is a commercial product purified by distillation over P_2O_5 , stored over the freshly calcinated 4Å molecular sieves.

DMF was purified by distillation and stored over the freshly calcinated 4Å molecular sieves.

The alkaline metal fluorides on Al_2O_3 were prepared acc. to [3].

The GLC analysis was carried out on the LKhM-7A instrument with thermal detector and linear programming of temperature in the 50 - 270°C range at the rate of 10°/min., 4x4000 mm column, stationary phase - 15% of silicone SE-54, SKTFT-803 or SE-30 on the W-DMCS chromosorb or N chromatone. Carrier gas - He (60 ml/min), the quantitative analysis of mixtures was carried out by the internal standard method. Mixture components were identified by adding authentic samples.

X-Ray radiometric determination of alkaline metal concentration in alkaline metal fluoride/graphite intercalates

Metal concentrations were determined by comparing the analytic line intensity of the sample with that of a reference.

For potassium concentration determination, the $K\alpha_1$ and $K\alpha_2$ lines were used, with the energy of 3.313 and 3.310 keV respectively. For excitation of the characteristic $K\alpha$ radiation of potassium, the Fe^{55} radioisotope was taken with the excitation energy of 5.9 keV. For excitation of the $K\alpha_1$ and $K\alpha_2$ lines of rubidium with the energies of 13.353 and 13.333 keV respectively, the Cd^{109} source was used with the energy of 22.54 keV. The analysis for caesium was carried out according to the $K\alpha_1$ and $K\alpha_2$ lines with the energies of 30.968 and 30.620 keV respectively. For excitation of the characteristic radiation of caesium, the 59.536 keV line of Am^{241} isotope was used. As a radiation detector, the silicon-lithium semiconductor detector BRDK-1-50 was used, having a 350 eV resolution on the 5.9 keV line. The radiation source was placed into a cylindric collimator to produce a narrow beam and defend the detector from the direct light. The secondary radiation was recorded by the LP-4900 analyzer.

The calibration diagram was plotted for references with preset concentrations by the least-squares method, using five points.

Measurements have been carried out at the Laboratory of Physical Methods of Investigation, Novosibirsk Institute of Geology and Geophysics.

Reaction of Polyfluoroaromatic compounds with nucleophilic agents in the presence of alkaline metal fluorides applied on insoluble support (Al_2O_3, or intercalated into graphite) (a typical experiment).

A sample of catalyst and 8-10 ml of solvent were placed into a flask, and stirred for 8-10 min. at room temperature, whereupon 0.01 mol of the reagent (phenol, napthol, or piperidine) was added. The mixture was stirred for further 5-10 min., then 0.01 mol of polyfluoroaromatic substrate in 10 ml of a solvent was added. The mixture was kept at 80°C for some time (see Tables 4 and 5), whereupon it was washed with 5% HCl and filtered. The precipitate on the filter was washed with two 5-7 ml portions of the solvent and two 10 ml portions of sulphuric ether. The catalyst was dried for 2 h at 100-120°C to be recycled. The reaction mixture was neutralised with 5% HCl solution (80-100 ml), extracted with sulphuric ether (3x10 ml), and dried over $MgSO_4$. Then the solvent was distilled off, and the residue analysed by GLC.

Conditions and results of the experiments are listed in Tables 4 and 5.

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