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INTERACTION OF CHLOROAROMATIC COMPOUNDS WITH ALKALI METAL FLUORIDES IN THE PRESENCE OF CROWN-ETHERS

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SUMMARY

The influence of various crown-ethers on the reactions of polychloroaromatic compounds with alkali metal fluorides (KF, RbF, CsF) has been studied. It is shown that the catalytic effect of the crown-ether is almost independent of the nature of the polychloroaromatic substrate and that it is most effective only in a definite range of reaction rates.

INTRODUCTION

Substitution of chlorine in the aromatic ring by fluorine from alkali metal fluorides is one of the most efficient methods of synthesis of fluoroaromatic compounds [1-5]. Lithium and sodium fluorides proved to be inactive in these reactions and the activity of other fluorides increases with the size of the metal cation in the order: KF <RbF <CsF [3-5]. Since the most active, rubidium and caesium fluorides, are expensive reagents not readily available, only potassium fluoride is of practical value for the synthesis of fluoroaromatic compounds. However, the reactions of substitution of chlorine by fluorine in aromatic rings require rigid conditions. For example, the reaction of such an activated compound as 2,4-dinitrochlorobenzene with caesium fluoride in the absence of a solvent proceeds only at high temperatures (up to 200°C) after 10 hours. Due to this, further studies were aimed at finding efficient catalytic systems for the

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reactions of aromatic nucleophilic substitution, to improve yields of products, lower reaction temperatures and reduce reaction times.

These studies have resulted in various advances. Thus the use of dipolar aprotic solvents has led to sharp increases in the rates of aromatic nucleophilic substitution reactions [6]. Further, new catalysts have appeared which have expanded the range of compounds involved in such reactions and allowed the processes to proceed under milder conditions. These catalysts are quaternary ammonium salts [7,14,15] , metal carbonyls [8] , crown-ethers [9,12,14,15] and cryptates [13-15].

RESULTS AND DISSCUSSION

Crown-ethers are very efficient catalysts to increase the activity of alkali metal fluorides in aromatic nucleophilic substitution reactions [9-13]. Such an increase in reaction rates may be explained by two reasons: first, by the increased solubility of the alkali metal fluorides and thence the increased concentration of fluorine-ion, and second, by the increased nucleophilicity of fluorine-ion as a consequence of complexing of the alkali metal cations by crown-ethers. Therefore it seemed reasonable to study quantitatively the catalytic activity of crown-ethers in substitutions of aromatically bound chlorine by fluorine using efficient fluorinating agents, such as potassium, rubidium and caesium fluorides. For these quantitative studies we used the model reactions of 2,4-dinitrochlorobenzene (2,4-DNCB) with these fluorides, which proceed smoothly and do not form by-products (Table 1). As a solvent we used the aprotic bipolar solvent acetonitrile, which has high solvating ability and dielectric permeability ($\mathcal{E}$ =37.4).

As expected, 2,4-DNCB reacted most slowly with potassium fluoride. To obtain a 50% yield of 2,4-dinitrofluorobenzene (2,4-DNFB), the reaction had to be maintained for 14-15 hours. The use of rubidium fluoride accelerated the reaction, at the initial stage by a factor of around 8, then by a factor of 3, and preparation of 50% of 2,4-DNFB required less than 30 minutes.

It should be noted that the accelerating effect of macrocyclic ethers - crown-ethers(CE) on the reaction of substitution of chlorine by fluorine in 2,4-DNCB has been shown earlier [1,3], though there were insufficient quantitative data for this reaction. The present work deals with quantitative characteristics of the reactions of 2,4-DNCB with various alkali metal fluorides in the presence of some CE. The results of these studies are presented in Tables 1-5 and Fig. 1-4.

As seen from these data, even small amounts of CE markedly promote substitution of chlorine by fluorine in 2,4-DNCB. It should be noted that the yield of 2,4-DNFB linearly depends on concentration of CE only at the initial stage of reaction (3 and 7 min), and this dependence holds for all the fluorides investigated (Fig.1). The catalytic effect of CE is highest also at the initial stage of the reaction and, depending on the type of CE and its concentration, may reach 2 orders (Table 5). The greatest difference between the rates of catalysed and non-catalysed reactions is observed for the least active fluoride under investigation - potassium fluoride (Table 5), and the smallest difference for the most active caesium fluoride (Table 2).

The catalytic activity of CE under study in this reaction increases in the order: dibenzo-24-crown-8 < dicyclohexyl-18-crown-6 < 18-crown-6 (Figs. 2-4), and this order holds for all the fluorides (Tables 2-4).

Cations of rubidium (2.96 Å) and caesium (3.38 Å) better fit dibenzo-24-crown-8(DB-24-C-8) with the hole size 4.5 Å, than 18-crown-6(18-C-6) with the hole 2.6-3.2 Å, therefore the first CE would be expected to show the higher catalytic activity in the reactions of rubidium and caesium fluorides with 2,4-DNCB. However, in the reaction under study, DB-24-C-8 had a lower catalytic activity than 18-C-6 and dicyclohexyl-18-crown-6(DCH-18-6). This may be explained by the fact that under the influence of the cation force field, 18-C-6 exists predominantly as a conformational isomer, the complexing ability of which is higher than of DB-24-C-8. A slightly smaller efficiency of DCH-18-C-6 as compared to 18-C-6 might result from the fact that DCH-18-C-6 was used as various stereoisomers, which differ greatly in catalytic activity [16].

It was also of interest to study the influence of the nature of the aromatic substrate on the rate of substitution of chlorine in various chloroaromatic compounds by fluorine of alkali metal fluorides. We studied chloroaromatic compounds of very different reactivities. As a fluorinating agent, caesium fluoride was taken, which is the most active in these reactions. Since it is difficult to determine absolute constants because of the heterogeneity of the processes, and the precision of such determinations will be low, we calculated relative constants, which were given as the ratio of the slowest, or non-catalytic process, to the time of the catalytic process, during which the same extent of conversion, for example 30%, is achieved (Table 6). As seen from Table 6, 18-C-6 promotes substitution of chlorine by fluorine by a factor of 5-18 for chloroaromatic substrates of varied reactivity, and raising the amount of CE in the reaction mixture does not reveal any considerably dependence of the catalytic effect on the nature of a substrate.

These data suggest that the highest catalytic effect is observed only in a definite range of reaction rates. Thus 18-C-6 promotes the reaction of 2,4-DNCB or pentachloropyridine with caesium fluoride by factors of 6.2 and 5.2, respectively. At the same time, the reaction of 2,4-DNCB with potassium fluoride is promoted by the same amount of 18-C-6 relative to the non-catalytic process by a factor of more than 30 (Table 5).

Thus the dependence of the catalytic effect of CE on the nature of a substrate is low (maximal acceleration is 1-2 orders depending on the quantity of CE).

However the catalytic effect of CE strongly depends on the nature of the nucleophilic reagent - alkaline metal fluoride. This effect is highest for the least reactive potassium fluoride, and only at the initial stage of the reaction.

TABLE 1

Interaction of 2,4-DNCB with alkali metal fluorides*

N	MF	Yield of 2,4-DNFB (in % , by GLC)									
		Time, min									
		15	$\frac{\tau\,KF}{\tau\,MF}$	30	$\frac{\tau\,KF}{\tau\,MF}$	60	$\frac{\tau\,KF}{\tau\,MF}$	120	$\frac{\tau\,KF}{\tau\,MF}$	240	$\frac{\tau\,KF}{\tau\,MF}$
1	KF	1	1	2	1	5	1	10	1	18	1
2	RbF	8	8	16	8	30	6	44	4.4	62	3.4
3	CsF	28	28	56	28	80	16	92	9.2	95	5.3

*Mole ratio 2,4-DNCB:MF = 1:1; CH_3CN, 80°C.
LiF and NaF do not react in these condition.

TABLE 2

Interaction of 2,4-DNCB with caesium fluoride in the presence of crown-ethers*

N	Crown-ether	Yield of 2,4-DNFB (in % , by GLC)							
		Time, min							
		3	$\frac{\tau\,No\ CE}{\tau\,CE}$	7	$\frac{\tau\,No\ CE}{\tau\,CE}$	15	$\frac{\tau\,No\ CE}{\tau\,CE}$	30	$\frac{\tau\,No\ CE}{\tau\,CE}$
1	No CE	6	1	13	1	28	1	56	1
2	DB-24-C-8	20	3.3	52	4	77	2.8	91	1.6
3	DCH-18-C-6	38	6.3	56	4.3	79	2.8	93	1.7
4	18-C-6	43	7.2	70	5.4	90	3.2	96	1.7

*Mole ratio 2,4-DNCB:CsF:CE = 1:1:0.18; CH_3CN, 80°C

TABLE 3

Interaction of 2,4-DNCB with rubidium fluoride in the presence of crown-ethers*

N	Crown-ether	Yield of 2,4-DNFB (in % , by GLC)							
		Time, min							
		3	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	7	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	15	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	30	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$
1	No CE	2	1	5	1	10	1	16	1
2	DB-24-C-8	8	4	16	3.2	33	3.3	53	3.3
3	DCH-18-C-6	18	9	34	6.8	64	6.4	78	4.9
4	18-C-6	22	11	41	8.2	71	7.1	83	5.2

*Mole ratio 2,4-DNCB:RbF:CE = 1:1:0.18; CH_3CN, 80°C

TABLE 4

Interaction of 2,4-DNCB with potassium fluoride in the presence of crown-ethers*

N	Crown-ether	Yield of 2,4-DNFB (in % , by GLC)							
		Time, min							
		15	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	30	$\frac{\tau \text{ NO CE}}{\tau \text{ CE}}$	60	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	90	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$
1	No CE	1	1	3	1	5	1	8	1
2	DB-24-C-8	7	7	13	4.3	27	5.4	38	4.8
3	DCH-18-C-6	13	13	26	8.7	47	9.4	64	8
4	18-C-6	45	45	67	22	84	16.8	89	11

*Mole ratio 2,4-DNCB:KF:CE = 1:1:0.18; CH_3CN, 80°C

TABLE 5

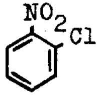
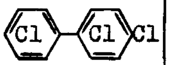
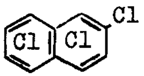
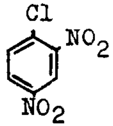
Interaction of 2,4-DNCB with potassium fluoride in the presence of 18-C-6*

N	Mole ratio	Time, min										
	2,4-DNCB : CE	3	7	15	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	22	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	30	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$	60	$\frac{\tau \text{ No CE}}{\tau \text{ CE}}$
		Yield of 2,4-DNFB (in %, by GLC)									
1	No CE	-	-	1	1.0	2	1.0	3	1.0	5	1.0
2	1 : 0.033	2	4	12	12.0	23	12.5	32	10.7	60	12.0
3	1 : 0.077	4	6	26	26.0	40	21.0	52	17.3	74	14.8
4	1 : 0.182	6	12	45	45.0	58	29.0	67	22.3	84	16.8
5	1 : 0.357	9	18	58	58.0	72	36.0	77	25.0	86	17.2
6	1 : 0.556	16	30	64	64.0	73	37.5	83	27.7	90	18.0
7	1 : 0.714	20	39	66	66.0	75	37.5	85	28.3	92	18.4
8	1 : 1.428	30	48	72	72.0	80	40.0	86	28.7	92	18.4
9	1 : 2.941	56	71	83	83.0	88	44.0	91	30.3	95	19.0

*Ratio 2,4-DNCB : KF = 1:1; CH_3CN, 80°C.

TABLE 6

Interaction of polychloroaromatic compounds ($ArCl_n$) with caesium fluoride in the presence of 18-C-6$^+$

														
Mole ratio $ArCl_n$:18-C-6	Time required to obtain 30% of monofluoroaromatic compound $ArCl_{n-1}F$, min													
	τ	τ no CE / τ CE	τ	τ no CE / τ CE	τ	τ no CE / τ CE	τ	τ no CE / τ CE	τ	τ no CE / τ CE	τ	τ no CE / τ CE	τ	τ no CE / τ CE
1:0.182	2020	11	1940	11	1530	11	1350	9	50	18	2.6	6.2	2.3	5.2
1:0.714	610	37	580	38	400	44	320	37	12	75	1	10	0.5	24
1:1.148	230	99	220	100	180	97	130	90	10	90	-	-	-	-
No CE	22700	1	22060	1	17300	1	12000	1	900	1	16	1	12	1
		1*		1.03		1.3		1.9		25		1420		1900
		1**		1.04		1.3		1.5		40		780		880

$^+$Mole ratio $ArCl_n$:CsF = 1:1; CH_3CN, 80° C.

* τ o-$NO_2C_6H_4Cl$/ τ ArCl in the absence of CE

** τ o-$NO_2C_6H_4Cl$/ τ ArCl in the presence of 0.182 mol of 18-C-6

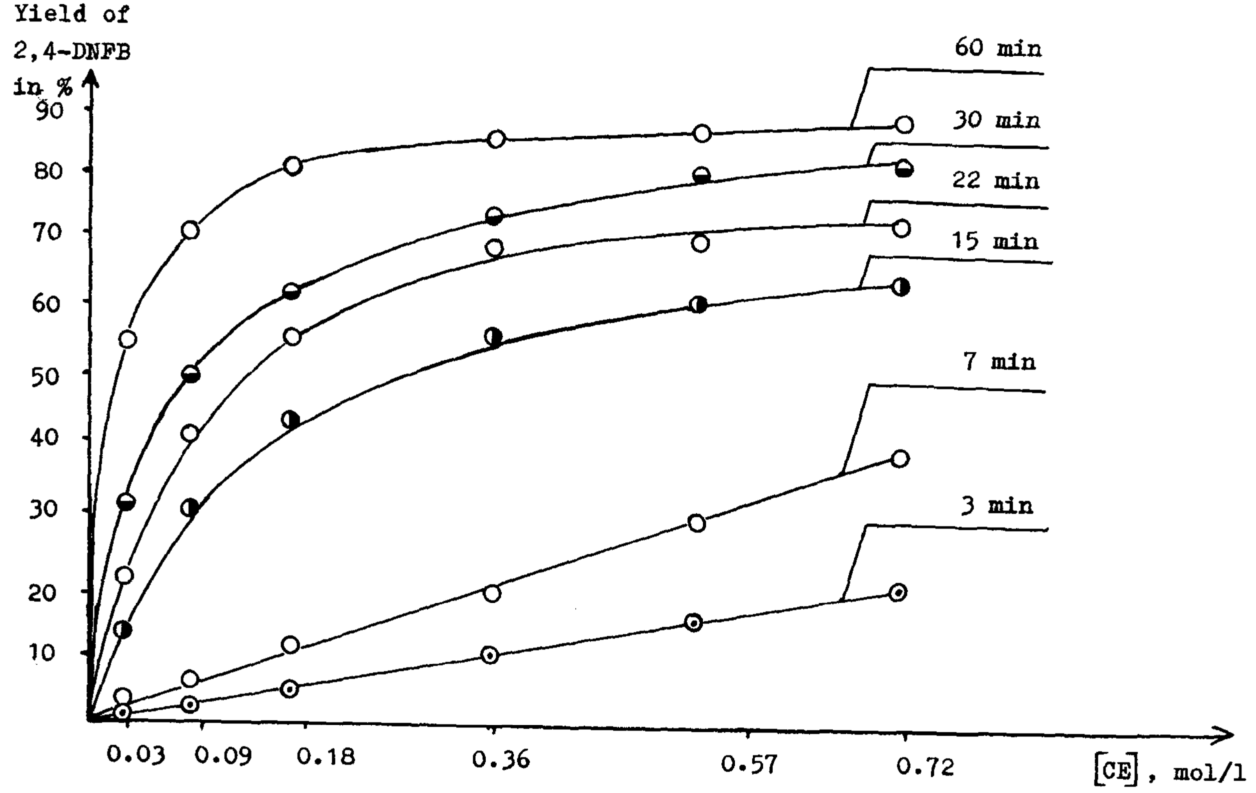


Fig. 1. Influence of 18-C-6 concentration on the yield of 2,4-DNFB in the reaction of equimolar quantities of 2,4-DNCB and potassium fluoride (CH_3CN, 80°C).

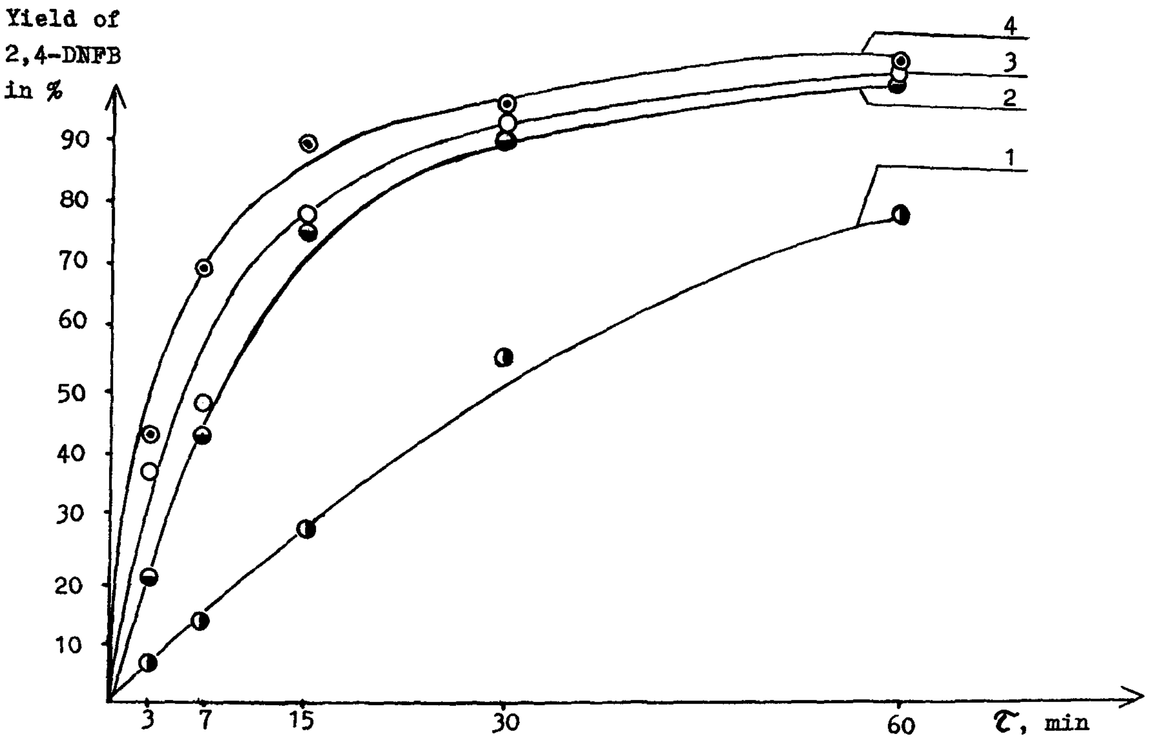


Fig. 2. Influence of CE type on the yield of 2,4-DNFB in the reaction of 2,4-DNCB with caesium fluoride (Mole ratio 2,4-DNCB:CsF:CE=1:1:0.18; CH_3CN, 80°C). 1 Non-catalysed process; 2 In the presence of DB-24-C-8; 3 In the presence of DCH-18-C-6; 4 In the presence of 18-C-6

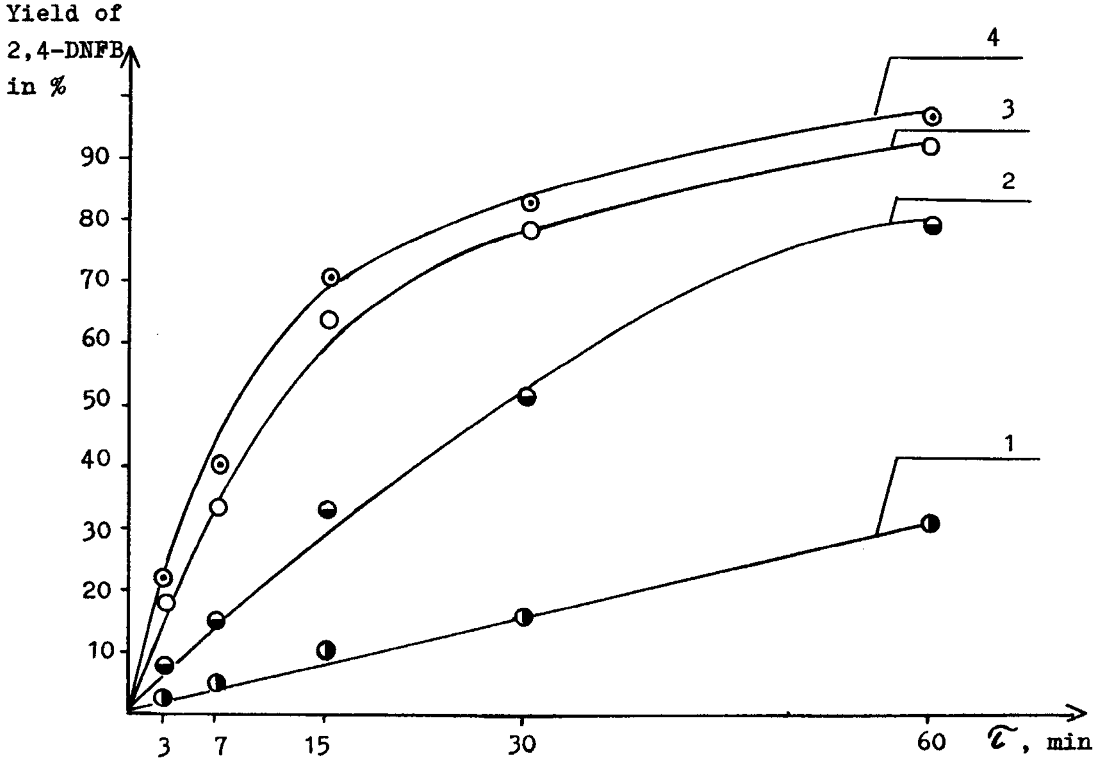


Fig. 3. Influence of CE type on the yield of 2,4-DNFB in the reaction of 2,4-DNCB with rubidium fluoride (Mole ratio 2,4-DNCB:RbF:CE=1:1:0.18; CH_3CN, 80°C). 1 Non-catalysed process; 2 In the presence of DB-24-C-8; 3 In the presence of DCH-18-C-6; 4 In the presence of 18-C-6.

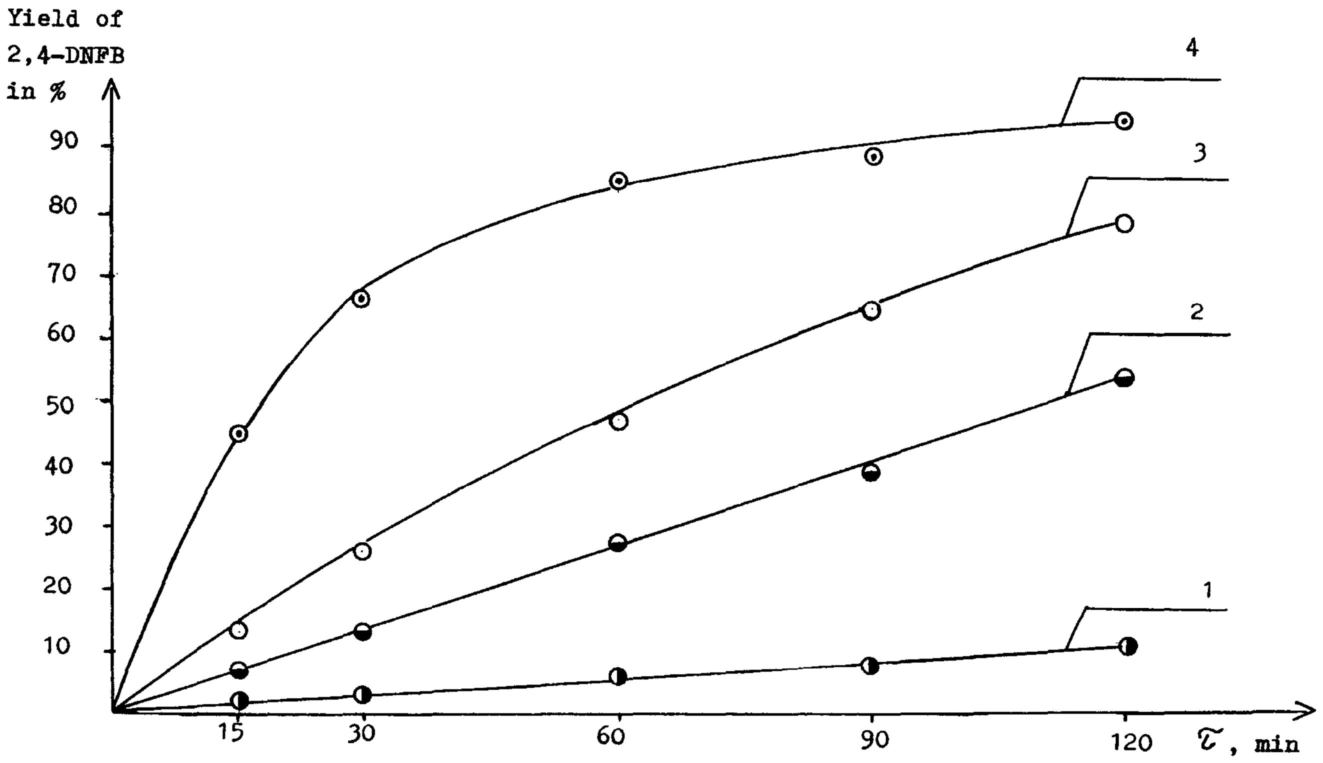


Fig. 4. Influence of CE type on the yield of 2,4-DNFB in the reaction of 2,4-DNCB with potassium fluoride (Mole ratio 2,4-DNCB:KF:CE=1:1:0.18; CH_3CN, 80°C). 1 Non-catalysed process; 2 In the presence of DB-24-C-8; 3 In the presence of DCH-18-C-6; 4 In the presence of 18-C-6.

EXPERIMENTAL

^{19}F and ^{1}H NMR spectra were recorded on a Varian A56-60A spectrometer at 56.4 and 60 MHz respectively, for 25% solutions in CCl_4.

Starting compounds: 2,4-dinitrochlorobenzene, o-nitro- and p-nitrochlorobenzene of pure grade were used without additional purification. Hexachlorobenzene, pentachloropyridine, octachloronaphthalene and decachlorodiphenyl produced at the Institute of Organic Chemistry, were used after additional purification by sublimation. Potassium, rubidium and caesium fluorides of the chemically pure grade were calcinated before reaction for 4 h at 400 °C. Acetonitrile was purified and dried by three distillations over phosphorus pentaoxide, whereupon it was stored over freshly calcinated 5 Å sieves. 18-Crown-6-ether was used as an acetonitrile complex. Dicyclohexyl-18-crown-6-ether was used without additional purification. Dibenzo-24-crown-8-ether was purified by recrystallization from toluene.

The reaction products: 2,4-DNFB, o-nitro- and p-nitrofluorobenzene, 4-fluorotetrachloropyridine, fluoropentachlorobenzene, 2-fluoroheptachloronaphthalene and 4-fluorononachlorodiphenyl were obtained by known literature procedures.

Reactions of aryl chlorides with alkali melal fluorides

A typical experiment (ArCl ; MF = 1:1, CH_3CN, 80 °C)

An alkali metal fluoride in 10 ml solvent was placed in a flask provided with a stirrer and a reflux condenser and flushed previously with an inert gas. The required quantity of crown-ether was then added and the mixture was stirred for 10 min, whereupon an aryl chloride in 10 ml of the solvent was added. The amount of crown-ether was varied from 1/30 to 3.0 mol of CE per 1 mol of the aryl chloride. After the reaction mixture had been kept for some time, it was cooled to 20 °C, diluted with 50 ml of distilled water, and the organic layer was separated and the aqueous one extracted with ether (3x15 ml). The ether extracts were combined with the organic layer, dried over $CaCl_2$ and the solvent was distilled off. The residue was analysed by GLC, ^{19}F and ^{1}H NMR.

Analysis of reaction mixtures

The quantitative GLC analysis was carried out by internal normalisation. The reaction products and the starting compounds were identified by adding authentic compounds to the mixture being analysed. The GLC analysis was carried out on an LHM-7A chromatograph with programming of temperature from 100 to 270 °C at the rate of 10 deg per min, detector - catharometer, column 400x4 cm, gas-carrier helium 60 ml/min. The stationary phase 15% SKTFT-50 or SE-80 of the weight of carrier of chromosorb-W-DMCS.

Parallel control of the course of the reaction was carried out by determing the decrease of fluorine-ion concentration, by direct potentiometry with a fluorine-selective electrode, and also by determing accumulation of the chlorine-ion by mercurometry.

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