

## Unusual Lability of Pentafluorophenoxy Group in Reactions of Potassium Aroxides with Pentafluoropyridine

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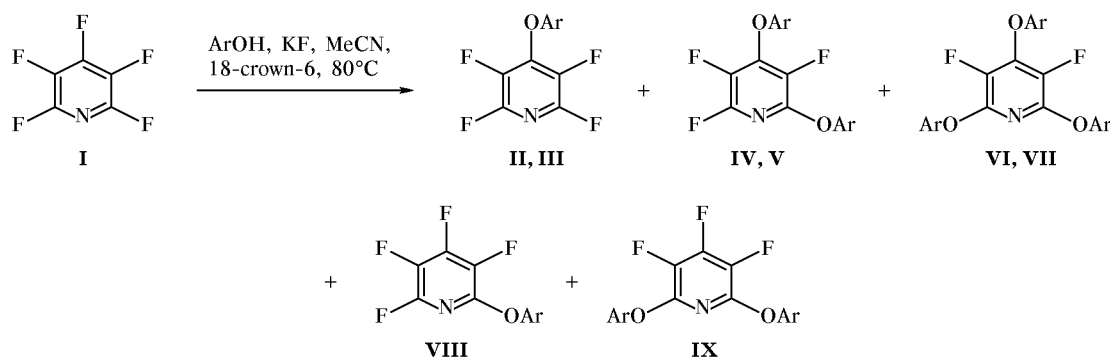
**Abstract**—The kinetics of the reactions of pentafluoropyridine with potassium aroxides, leading to formation of polyfluorinated aryl pyridyl ethers, conform to the Brønsted equation. The data obtained for potassium pentafluorophenoxide deviate from the general correlation because of readily occurring reverse reaction, replacement of the pentafluorophenoxy group by released fluoride ion. PM3 calculations of the electronic structure of the reagents, intermediate  $\sigma$ -complexes, and products showed that the replacement of fluorine in pentafluoropyridine is a charge-controlled process, whereas unusually easy replacement of the pentafluorophenoxy group in the corresponding aryl pyridyl ether by fluorine is explained by structural features of its lowest unoccupied molecular orbital.

We previously showed [1] that the reactions of pentafluorophenol and 4-nitrophenol with pentafluoropyridine in the presence of potassium fluoride and 18-crown-6 (18C6) give product mixtures with considerably different compositions (Scheme 1). The reaction with 4-nitrophenol yields only products **III**, **V**, and **VII** formed by replacement of one, two, and three fluorine atoms in positions 4, 2,4, and 2,4,6, respectively. Pentafluorophenol reacts with pentafluoropyridine to give also the corresponding 2-mono- and 2,6-disubstituted derivatives **VIII** and **IX**. The formation of the latter is explained by replacement of the pentafluorophenoxy group in 3,5,6-trifluoro-2,4-

bis(pentafluorophenoxy)pyridine (**IV**) and 3,5-difluoro-2,4,6-tris(pentafluorophenoxy)pyridine (**VI**) by the action of fluoride ion [1]. Taking into account a relatively small difference in the basicity of pentafluorophenoxide and 4-nitrophenoxide ions in acetonitrile (cf.  $pK_a$  values in Table 1), we thought it reasonable to extend the range of basicity of aroxide ions with the goal of elucidating factors determining unusual lability of the pentafluorophenoxy group in the above process.

Table 1 contains published data on the acidity of phenols and naphthols **X–XVI** in acetonitrile and in the gas phase. The two sets of values give rise to

Scheme 1.



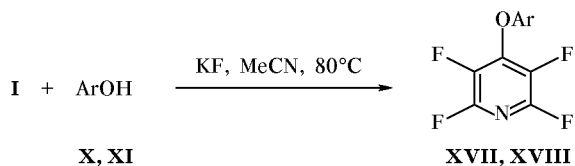
**II, IV, VI, VIII, IX**, Ar = C<sub>6</sub>F<sub>5</sub>; **III, V, VII**, Ar = 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>.

**Table 1.** Gas-phase ( $\Delta G_g^0$ ) and liquid-phase acidity in MeCN ( $pK_a$ ) of naphthols **X** and **XI** and phenols **XII–XVI**

Comp. no.	Ar in ArOH	$pK_a$ [2]	$\Delta G_g^0$ [4], kcal/mol
<b>X</b>	2-C <sub>10</sub> F <sub>7</sub>	17.8	312.4
<b>XI</b>	1-C <sub>10</sub> F <sub>7</sub>	19.4	314.0
<b>XII</b>	C <sub>6</sub> F <sub>5</sub>	19.5	320.8
<b>XIII</b>	3-Cl-4-NO <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	19.9 [3]	–
<b>XIV</b>	4-CH <sub>3</sub> C <sub>6</sub> F <sub>4</sub>	20.3	–
<b>XV</b>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	20.9 [3]	320.9
<b>XVI</b>	Ph	27.4	342.3

a satisfactory correlation:  $pK_a = 0.31 \Delta G_g^0 - 77.9$  ( $r = 0.981$ ,  $s = 0.85$ ,  $n = 5$ ). Obviously, the existence of such correlation indicates the absence of strong specific solvation of the C<sub>6</sub>F<sub>5</sub> group and allows us to focus on its electronic and steric properties in comparison to other aryl groups in ArOH compounds. For this purpose, we examined reactions of heptafluoronaphthols **X** and **XI** and phenols **XIII**, **XIV**, and **XV** with pentafluoropyridine under the conditions specified in Scheme 1.

Heptafluoro-2-naphthol (**X**) and heptafluoro-1-naphthol (**XI**), which are characterized by the lowest  $pK_a$  values in the examined series (Table 1), react with pentafluoropyridine (**I**) in the presence of potassium fluoride to give the corresponding monosubstituted products, 2,3,5,6-tetrafluoro-4-(heptafluoro-2-naphthoxy)pyridine (**XVII**) and 2,3,5,6-tetrafluoro-4-(heptafluoro-1-naphthoxy)pyridine (**XVIII**) (Table 2, runs nos. 1–4 and 7–10; Scheme 2).

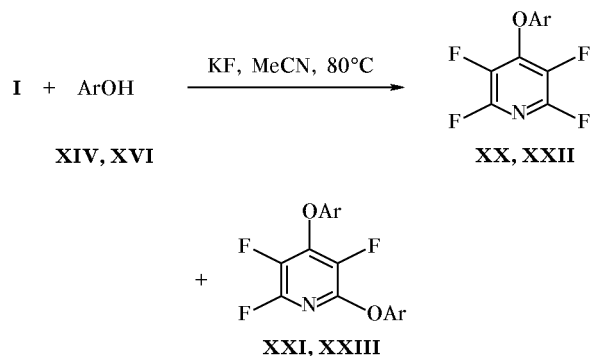
**Scheme 2.**

**X, XVII**, Ar = 2-C<sub>10</sub>F<sub>7</sub>; **XI, XVIII**, Ar = 1-C<sub>10</sub>F<sub>7</sub>.

An appreciable activating effect of 18-crown-6 in reactions of **I** with naphthols **X** and **XI** should be noted: the yield of products **XVII** and **XVIII** rises more than twofold, as compared with reactions in the absence of 18C6 (Table 2; runs nos. 3, 4, 7, and 8). Compounds **XVII** and **XVIII** are resistant to potassium fluoride even in the presence of 18C6, and no appreciable replacement of perfluoronaphthoxy groups

by fluorine occurs (Table 2; runs nos. 5, 6, 11, 12). The reaction of equimolar amounts of compound **I** with 3-chloro-4-nitrophenol (**XIII**) under analogous conditions gave 4-(3-chloro-4-nitrophenoxy)-2,3,5,6-tetrafluoropyridine (**XIX**) as the major product (Table 2, runs nos. 13–16). Addition of a catalytic amount of 18-crown-6 considerably increases the yield of **XIX** (Table 2, runs nos. 14 and 16). Compound **XIX** is also resistant to potassium fluoride in the presence of 18C6 (Table 2, runs nos. 17 and 18).

Disubstituted derivatives of **I** were detected in the reactions of equimolar amounts of 2,3,5,6-tetrafluoro-4-methylphenol (**XIV**) and phenol (**XVI**) with pentafluoropyridine (**I**) (Table 2, runs nos. 19, 20, and 24–26; Scheme 3).

**Scheme 3.**

**XIV, XX, XXI**, Ar = 4-CH<sub>3</sub>C<sub>6</sub>F<sub>4</sub>; **XVI, XXII, XXIII**, Ar = Ph.

Likewise, compounds **XX** and **XXII** did not react with potassium fluoride (Table 2, runs nos. 21, 22, 27, and 28).

On the basis of our present results and previous data [1] (Scheme 1) we can propose two schemes for reactions of compound **I** with phenols and naphthols in the presence of a source of fluoride ion. The first of these (more general) is shown in Scheme 4. It is typical of most of the examined naphthols (**X**, **XI**) and phenols (**XIII–XVI**). The second scheme (Scheme 5) describes the reaction of pentafluoropyridine (**I**) with pentafluorophenol (**XII**), which leads to formation of products **II**, **IV**, **VI**, **VIII**, and **IX**. Thus the reaction of **I** with pentafluorophenol (**XII**) in the presence of potassium fluoride and 18-crown-6 takes an essentially different pathway, as compared to analogous reactions with the other naphthols and phenols. This difference originates from the ability of the C<sub>6</sub>F<sub>5</sub>O group in compounds **II**, **IV**, and **VI** to readily be replaced by fluoride ion [1]. The same follows from the quantitative data obtained by studying the kinetics

**Table 2.** Reactions of pentafluoropyridine (**I**) with naphthols and phenols ArOH (**X**, **XI**, **XIII**, **XIV**, **XVI**) in the presence of potassium fluoride and 18-crown-6 and of diaryl ethers ArOAr' with KF in the presence of 18C6; acetonitrile, 80°C, **I**: ArOH(or ArOAr'):KF:18C6 = 1:1:2:0.1

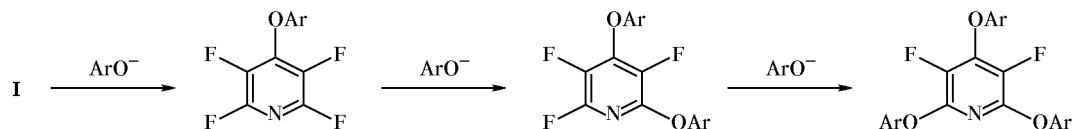
Run no.	ArOH or ArOAr'	Time, h	Product (yield, %)	Run no.	ArOH or ArOAr'	Time, h	Product (yield, %)
1 <sup>a</sup>	<b>X</b>	1	<b>XVII</b> (5)	15 <sup>a</sup>	<b>XIII</b>	5	<b>XIX</b> (48)
2	<b>X</b>	1	<b>XVII</b> (12)	16	<b>XIII</b>	5	<b>XIX</b> (78)
3 <sup>a</sup>	<b>X</b>	5	<b>XVII</b> (31)	17 <sup>a</sup>	–	1	<b>XIX</b> (92)
4	<b>X</b>	5	<b>XVII</b> (64)	18	–	1	<b>XIX</b> (89)
5 <sup>a</sup>	–	1	<b>XVII</b> (94)	19 <sup>a</sup>	<b>XIV</b>	5	<b>XX</b> (89), <b>XXI</b> (1)
6	–	1	<b>XVII</b> (90)	20	<b>XIV</b>	5	<b>XX</b> (70), <b>XXI</b> (14)
7 <sup>a</sup>	<b>XI</b>	5	<b>XVIII</b> (33)	21 <sup>a</sup>	–	1	<b>XX</b> (94)
8	<b>XI</b>	5	<b>XVIII</b> (68)	22	–	1	<b>XX</b> (89)
9 <sup>a</sup>	<b>XI</b>	1	<b>XVIII</b> (7)	23 <sup>a</sup>	<b>XVI</b>	5	<b>XXII</b> (68)
10	<b>XI</b>	1	<b>XVIII</b> (14)	24	<b>XVI</b>	5	<b>XXII</b> (86), <b>XXIII</b> (2)
11 <sup>a</sup>	–	5	<b>XVIII</b> (96)	25 <sup>a,b</sup>	<b>XVI</b>	5	<b>XXII</b> (60), <b>XXIII</b> (6)
12	–	5	<b>XVIII</b> (88)	26 <sup>b,c</sup>	<b>XVI</b>	5	<b>XXII</b> (71), <b>XXIII</b> (9)
13 <sup>a</sup>	<b>XIII</b>	1	<b>XIX</b> (14)	27 <sup>a,b</sup>	–	1	<b>XXII</b> (92)
14	<b>XIII</b>	1	<b>XIX</b> (29)	28 <sup>a,b</sup>	–	1	<b>XXII</b> (88)

<sup>a</sup> In the absence of 18-crown-6.

<sup>b</sup> Cesium fluoride (2 mol) was taken instead of potassium fluoride (2 mol).

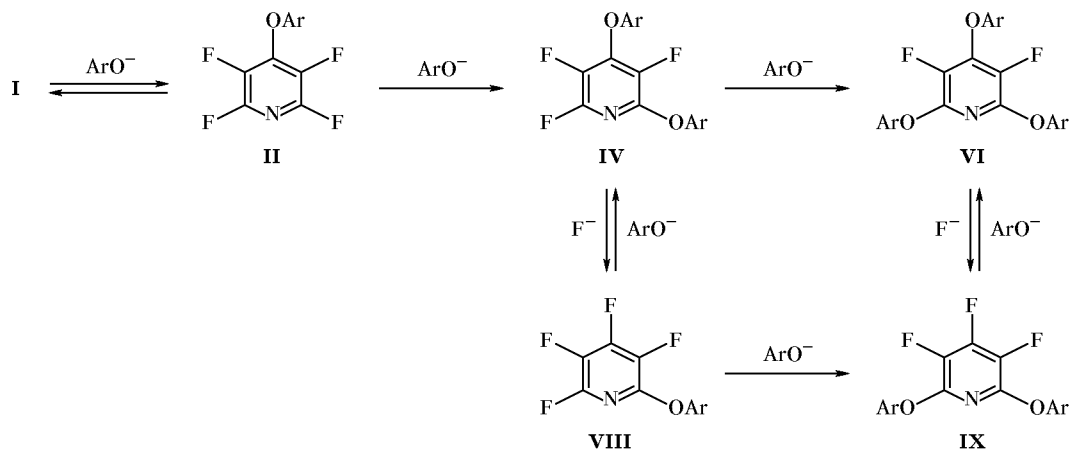
<sup>c</sup> Dibenzo-24-crown-8 (0.1 mol) was taken instead of dibenzo-18-crown-6 (0.1 mol).

**Scheme 4.**



Ar = 1-C<sub>10</sub>F<sub>7</sub>, 2-C<sub>10</sub>F<sub>7</sub>, 4-MeC<sub>6</sub>F<sub>4</sub>, 3-Cl-4-NO<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>, Ph.

**Scheme 5.**



Ar = C<sub>6</sub>F<sub>5</sub>.

**Table 3.** Rate constants and activation parameters of the reactions of pentafluoropyridine (**I**) in acetonitrile with potassium aroxides derived from phenols and naphthols **X–XV**

Comp. no.	<i>T</i> , °C	<i>k</i> <sub>2</sub> , l mol <sup>-1</sup> s <sup>-1</sup>	<i>k</i> <sub>rel</sub> at 20°C (50°C)	<i>E</i> , kJ/mol	log <i>A</i>
<b>X</b>	20	0.0011	1	56	6.66
	30	0.0018 <sup>a</sup>			
	50	0.0047			
	80	0.037			
	100	0.15			
<b>XI</b>	20	0.018	16	59	8.72
	30	0.038 <sup>b</sup>			
	50	0.144			
	80	1.15			
<b>XII</b>	20	0.006	26	49 <sup>c</sup>	7.18 <sup>c</sup>
		0.0288 <sup>d,e</sup>			
	30	0.0105			
		0.054 <sup>d,f</sup>			
	40	0.014			
	50	0.033			
<b>XIII</b>	20	0.10	91	49	7.74
	30	0.19			
	40	0.31			
	50	0.68			
	80	1.85 <sup>d,g</sup>			
<b>XIV</b>	20	0.14	127	51	8.20
	30	0.26			
	50	0.96			
<b>XV</b>	20	0.38	346	51	8.66
	30	0.72			
	50	2.6			

<sup>a</sup> Calculated by the equation  $\log k_2 = 6.84 - 2902.3/T$  ( $r = 0.989$ ,  $s = 0.18$ ,  $n = 4$ ).

<sup>b</sup> Calculated by the equation  $\log k_2 = 8.78 - 3089.4/T$  ( $r = 0.999$ ,  $s = 0.064$ ,  $n = 3$ ).

<sup>c</sup> Calculated for the fluorine replacement reaction.

<sup>d</sup> Rate constant for fluorine replacement, calculated by the Brønsted equation.

<sup>e</sup> Calculated by the equation  $\log k_2(20^\circ\text{C}) = 0.84\text{p}K_a - 17.92$  ( $r = 0.993$ ,  $s = 0.14$ ,  $n = 5$ ).

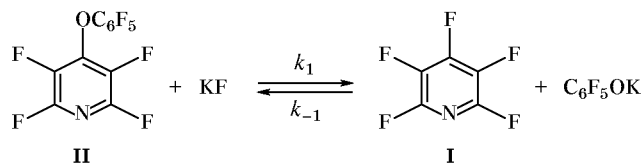
<sup>f</sup> Calculated by the equation  $\log k_2(30^\circ\text{C}) = 0.86\text{p}K_a - 18.0$  ( $r = 0.994$ ,  $s = 0.13$ ,  $n = 5$ ).

<sup>g</sup> Calculated by the equation  $\log k_2(50^\circ\text{C}) = 0.91\text{p}K_a - 18.4$  ( $r = 0.994$ ,  $s = 0.14$ ,  $n = 5$ ).

of the reactions of pentafluoropyridine (**I**) with potassium aroxides derived from compounds **X–XV**. Table 3 contains the second-order rate constants at 20–100°C and activation parameters of these reactions. The latter are typical of S<sub>N</sub>Ar reactions of

charged nucleophiles with pentafluorobenzenes having electron-acceptor substituents [5].

The reaction rate is related to the nucleophile basicity by the Brønsted equation:  $\log k_2(20^\circ\text{C}) = 0.84\text{p}K_a - 17.92$  ( $r = 0.993$ ,  $s = 0.14$ ,  $n = 5$ ) (Fig. 1). The point corresponding to pentafluorophenoxide ion (**XII**) deviates from the straight line because of the reverse reaction of 2,3,5,6-tetrafluoro-4-pentafluorophenoxypyridine (**II**) with fluoride ion (Scheme 6).

**Scheme 6.**

The rate constant  $k_{-1}(20^\circ\text{C})$  for fluorine replacement in pentafluoropyridine (**I**) by the action of potassium pentafluorophenoxide (**II**) in acetonitrile at 20°C, calculated by the Brønsted equation, is equal to 0.0288 l mol<sup>-1</sup> s<sup>-1</sup>. As follows from the apparent rate constant  $k_2$  and the calculated rate constant  $k_{-1}$  (Table 3), the rate constants for replacement of the pentafluorophenoxy group by fluoride ion at 20, 30, and 50°C are 4.80, 5.14, and 5.61 l mol<sup>-1</sup> s<sup>-1</sup>, respectively. Then, the ratio  $k_1/k_{-1}$  is 167 for the reaction shown in Scheme 6 at 20°C. The high rate of replacement of the C<sub>6</sub>F<sub>5</sub>O group in **II** by fluoride ion is responsible for reduction of the apparent rate constant  $k_2$  for the reaction of pentafluoropyridine (**I**) with potassium pentafluorophenoxide and hence for deviation of the corresponding point from the correlation shown in Fig. 1. Therefore, the specific behavior of compound **XII** in the reaction with **I** (Scheme 5) cannot be attributed to its acidity, since more acidic heptafluoronaphthols **X** and **XI** follow only the fluorine replacement path (Scheme 4) and conform to the Brønsted relation (Fig. 1). On the other hand, 2,3,5,6-tetrafluoro-4-methylphenol (**XIV**), which is structurally similar to pentafluorophenol (**XII**), shows a normal reactivity in keeping with the Brønsted plot (Fig. 1).

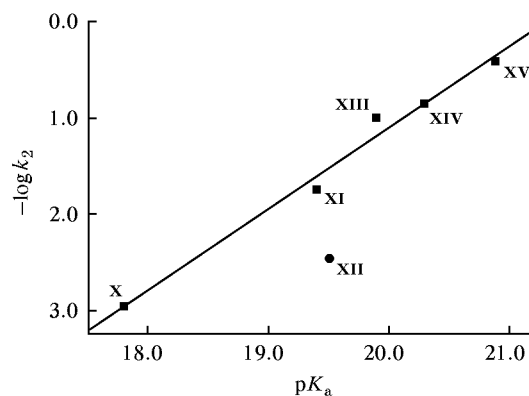
The data in Table 3 also indicate that the relative rate of fluorine replacement (depending on the basicity of aroxide ion) increases as the temperature rises. Moreover, there is a correlation between the Brønsted coefficients  $\beta_{\text{Nuc}}$  (see notes <sup>e</sup>, <sup>f</sup>, and <sup>g</sup> to Table 3) and the reciprocal temperature:  $\beta_{\text{Nuc}} = 1.60 - 223.7/T$  ( $r = 0.997$ ,  $s = 0.004$ ,  $n = 3$ ). The existence of such correlation suggests that at  $\beta_{\text{Nuc}} = 1$  the S<sub>N</sub>Ar reaction mechanism can change to SET at ~100°C for most

reactive nucleophiles (cf. [6]). On the other hand, at  $\beta_{\text{Nuc}} = 0$  the isokinetic temperature is  $-133^\circ\text{C}$ , i.e., it is much lower than the experimental temperature boundary. This fact may be regarded as an evidence that fluorine replacement in pentafluoropyridine (**I**) by the action of aroxide ions is controlled by the entropy factor [7] and is characterized by large values of the preexponential factor  $\log A$  (Table 3). Comparison of  $\log A$  for the reactions of **I** with potassium pentafluorophenoxide ( $\log A = 7.18$ ) and of **II** with fluoride ion ( $\log A = 1.41$ ) indicates a more ordered transition state in the latter reaction. In addition, from the temperature dependence of the rate constant:  $\log k_1 = 1.41 - 214.1/T$  ( $r = 0.996$ ,  $s = 0.004$ ,  $n = 3$ ) it follows that the isokinetic temperature for replacement of the  $\text{C}_6\text{F}_5\text{O}$  group in **II** by fluorine is  $-121.6^\circ\text{C}$ . This value lies considerably lower than the experimental range, indicating again the entropy control of the process. Obviously, the replacement of fluorine by pentafluorophenoxide ion and of  $\text{C}_6\text{F}_5\text{O}$  group by fluoride ion (Scheme 6) is governed by different factors, and this problem requires a more detailed consideration with the aid of quantum-chemical calculations.

The results of PM3 [8] calculations of aryl pyridyl ethers **II**, **III**, **XVII–XX**, and **XXII** are summarized in Table 4. Molecules **II**, **XVII**, **XVIII**, **XX**, and **XXII** are characterized by similar dihedral angles between the aromatic ring planes ( $\theta_A$  and  $\theta_B$ ; cf. [9]), as well as by similar  $\text{O–C}^2$  and  $\text{O–C}^1$  bond lengths between the ether oxygen atom and aryl and pyridine rings. This means that the lone electron pair on the oxygen atom is equally conjugated with both aryl and tetrafluoropyridine rings [10]. Ethers **III** and **XIX** having a nitro group in the *para*-position of the benzene ring are characterized by deviation of that ring from the plane including the oxygen atom. This leads to an appreciable increase of positive charge on the carbon atom attached to oxygen ( $q_{\text{C}^2}$ , Table 4).

Therefore, ethers **III** and **XIX** are more likely to react with fluoride ion at the benzene ring carbon atom with replacement of the tetrafluoropyridyloxy group rather than at the pyridine ring carbon atom with replacement of the aroxy group. However, diaryl ethers **II**, **XVII**, and **XX** having both similar dihedral angles  $\theta_A$  and  $\theta_B$  and similar charges on  $\text{C}^1$  and  $\text{C}^2$  should react with fluoride ion similarly, which contradicts the experimental data. Therefore, the different reactivities of these compounds may be explained in terms of different parameters of the corresponding  $\sigma$ -complexes.

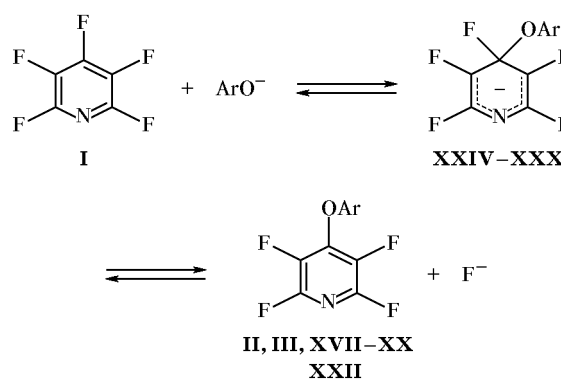
The results of calculation of  $\sigma$ -complexes **XXIV–XXX**, which simulate transition states in the reactions under study, are given in Table 5. The similarity of



**Fig. 1.** Brønsted plots of  $\log k_2$  versus  $\text{p}K_a$  for the reaction of pentafluoropyridine (**I**) with potassium phenoxides and naphthoxides at  $20^\circ\text{C}$ ; the numbers at the points correspond to compound numbers ( $\text{ArOH}$ ) in Tables 1 and 3.

geometric parameters of  $\sigma$ -complexes **XXIV–XXX** (cf. [12]) indicate the absence of specific steric effect of the  $\text{C}_6\text{F}_5\text{O}$  group in  $\sigma$ -complex **XXIV** (Scheme 7).

#### Scheme 7.

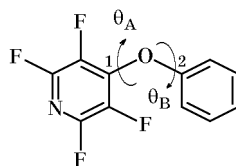


**II**, **XXIV**,  $\text{Ar} = \text{C}_6\text{F}_5$ ; **III**, **XXV**,  $\text{Ar} = 4\text{-NO}_2\text{C}_6\text{H}_4$ ; **XVII**, **XXVI**,  $\text{Ar} = 2\text{-C}_{10}\text{F}_7$ ; **XVIII**, **XXVII**,  $\text{Ar} = 1\text{-C}_{10}\text{F}_7$ ; **XIX**, **XXVIII**,  $\text{Ar} = 3\text{-Cl-4-NO}_2\text{C}_6\text{H}_3$ ; **XX**, **XXIX**,  $\text{Ar} = 4\text{-CH}_3\text{C}_6\text{F}_4$ ; **XXII**, **XXX**,  $\text{Ar} = \text{Ph}$ .

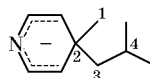
The enthalpies of formation of diaryl ethers **II**, **III**, **XVII–XX**, and **XXII** (Table 4),  $\sigma$ -complexes **XXIV–XXX**, pentafluoropyridine (**I**), aroxide ions, and fluoride ion (Table 5) were used to calculate the heats of complex formation ( $\Delta H_c$ ) according to Scheme 7 (Table 6). The values of  $\Delta H_c$  were calculated by the thermochemical equation

$$\Delta H_c = \Delta H_f^\sigma - [\Delta H_f(\text{E}) + \Delta H_f(\text{Nu}^-)].$$

Here,  $\Delta H_f^\sigma$  is the enthalpy of formation of  $\sigma$ -complex **XXIV–XXX**,  $\Delta H_f(\text{E})$  is the enthalpy of formation

**Table 4.** Some geometric parameters, charges on atoms, and enthalpies of formation of ethers **II**, **III**, **XVII–XX**, and **XXII**, calculated by the PM3 method [8]

Compound no.	Angle, deg		Bond length, Å		Charge on C atoms		$-\Delta H_f$ , kcal/mol
	$\theta_A$	$\theta_B$	C <sup>1</sup> –O	C <sup>2</sup> –O	$q_{C^1}$	$q_{C^2}$	
<b>II</b>	75.8	78.0	1.388	1.391	0.0509	–0.0016	347.3
<b>III</b>	84.1	17.9	1.382	1.388	0.0601	0.1285	147.3
<b>XVII</b>	75.2	77.9	1.387	1.392	0.0532	–0.0067	412.6
<b>XVIII</b>	76.5	76.5	1.387	1.393	0.0535	0.0395	410.8
<b>XIX</b>	89.1	6.8	1.384	1.385	0.0562	0.1418	150.1
<b>XX</b>	77.1	78.5	1.388	1.391	0.0548	0.0015	315.4
<b>XXII</b>	86.0	83.0	1.383	1.404	0.0878	0.0240	139.5

**Table 5.** Dihedral angles C<sup>1</sup>C<sup>2</sup>C<sup>3</sup>C<sup>4</sup> and enthalpies of formation  $\Delta H_f^\sigma$  of  $\sigma$ -complexes **XXIV–XXX**,  $\Delta H_f$  of pentafluoropyridine (**I**) and nucleophiles ArO<sup>–</sup> and F<sup>–</sup>, and charges on the oxygen atoms in ArO<sup>–</sup>, calculated by the PM3 method [8]

Compound no.	C <sup>1</sup> C <sup>2</sup> C <sup>3</sup> C <sup>4</sup> angle, deg	$-\Delta H_f^\sigma$ , kcal/mol	Nucleophile	$H_f$ , kcal/mol	$-q_O$ , a.u.
<b>I</b>	–	181.0	F <sup>–</sup>	59.6 <sup>a</sup>	–
<b>XXIV</b>	180	470.1	C <sub>6</sub> F <sub>5</sub> O <sup>–</sup>	284.0	0.4677
<b>XXV</b>	171.5	271.9	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> O <sup>–</sup>	81.5	0.4857
<b>XXVI</b>	180	535.9	2-C <sub>10</sub> F <sub>7</sub> O <sup>–</sup>	355.6	0.4286
<b>XXVII</b>	176.9	533.5	1-C <sub>10</sub> F <sub>7</sub> O <sup>–</sup>	356.2	0.4230
<b>XXVIII</b>	171.1	275.3	3-Cl-4-NO <sub>2</sub> C <sub>6</sub> H <sub>3</sub> O <sup>–</sup>	90.6	0.4591
<b>XXIX</b>	180	434.7	4-CH <sub>3</sub> C <sub>6</sub> F <sub>4</sub> O <sup>–</sup>	245.4	0.4787
<b>XXX</b>	179	253.5	PhO <sup>–</sup>	44.1	0.5725

<sup>a</sup> Experimental gas-phase enthalpy of formation  $\Delta H_f$  of fluoride ion [11].

of electrophile (compound **I** or **II**, **III**, **XVII–XX**, **XXII**), and  $\Delta H_f(\text{Nu}^-)$  is the enthalpy of formation of nucleophile (ArO<sup>–</sup> or F<sup>–</sup>). The quantities  $\Delta H_c^f$  for the reaction of **I** with aroxide ions and  $\Delta H_c^r$  for the reaction of ethers **II**, **III**, **XVII–XX**, and **XXII** with fluoride ions (Table 6) can be regarded as a measure of the stability of the corresponding  $\sigma$ -complexes **XXIV–XXX**, which is assumed to be proportional to the energy barrier of both reactions (Scheme 7). According to the calculations,  $\Delta H_c^f$  for the reaction of **I** with aroxide ions is linearly related to the charge on

the oxygen atom of the nucleophile:  $\Delta H_c^f = 212.8q_O + 93.5$  ( $r = 0.997$ ,  $s = 0.93$ ,  $n = 7$ ), which corresponds to the observed Brønsted dependence (Fig. 1). Moreover,  $\Delta H_c^f$  correlates with  $\text{p}K_a$  of compounds **X–XVI**:  $\Delta H_c^f = -3.3\text{p}K_a + 60.7$  ( $r = 0.956$ ,  $s = 3.4$ ,  $n = 7$ ), in support of our assumption that the stability of  $\sigma$ -complex is proportional to the energy barrier.

As concerns the reverse reaction of fluoride ion with diaryl ethers (Scheme 7), we cannot explain the unusual lability of the C<sub>6</sub>F<sub>5</sub>O group on the basis of the calculated heats of complex formation  $\Delta H_c^r$ . No

correlation was observed between  $\Delta H_c^r$  and the charge on the carbon atom  $q_C$  in ethers **II**, **III**, **XVII–XX**, and **XXII** (Table 4) or the charge on the oxygen atom  $q_O$  of the departing group  $ArO^-$  (Table 5). Presumably, the transition state (TS) for the reaction of diaryl ether **II** with fluoride ion has a structure essentially different from the structure of TS formed along the path to  $\sigma$ -complex in the reaction of pentafluoropyridine with pentafluorophenoxide ion. It is quite probable that the reactions of diaryl ethers **II**, **III**, **XVII–XX**, and **XXII** with fluoride ion (Scheme 7) are governed by the orbital factor; therefore, the TS structure should be reagent-like [13]. In this case it is necessary to analyze parameters of the lowest unoccupied molecular orbitals (LUMO) of substrates **II**, **III**, **XVII–XX**, and **XXII** (Fig. 2).

Obviously, the LUMO of compound **II** appreciably differs from those of the other diaryl ethers. The main difference is that both benzene and pyridine rings of **II** equally participate in the formation of its LUMO. The lowest unoccupied molecular orbitals of the other ethers are localized at one of the aromatic fragment: on the pyridine ring in compounds **III**, **XIX**, **XX**, and **XXI** or on the naphthalene ring in **XVII** and **XVIII**. The vacant molecular orbital localized on the pyridine ring in **XVII** and **XVIII** has a higher energy (Fig. 2). All the above MOs, except those localized on the naphthalene fragments, are similar; they originate from one component of the degenerate benzene LUMO, namely from  $b_1$ -MO having a  $C_{2v}$  symmetry. The observed differences in localization of LUMOs of aryl pyridyl ethers are likely to result from the energies of the corresponding MOs of the aromatic fragments. We performed quantum-chemical calculations of model  $ArOH$  systems (Table 7), which gave similar energies of vacant  $b_1$ -like MOs for 2,3,5,6-tetrafluoro-4-hydroxypyridine and pentafluorophenol. These data explain delocalization of the LUMO of ether **II** over both aromatic fragments.

A linear relation was revealed between  $\Delta H_c^r$  for  $\sigma$ -complexes **XXIV–XXX** (Table 6) and the energies of LUMOs localized on the pyridine ring in ethers **II**, **III**, **XIX**, **XX**, and **XXII** and high-lying vacant MOs of ethers **XVII** and **XVIII**:  $\Delta H_c^r = -25.7 + 20.7\varepsilon$ ;  $r = 0.976$ ,  $s = 0.9$ ,  $n = 7$ . This correlation suggests orbital control of the formation of  $\sigma$ -complexes in the reaction of fluoride ion with aryl pyridyl ethers. However, the highest occupied molecular orbitals of all  $\sigma$ -complexes **XXIV–XXX** are localized mainly on the pyridine ring (Fig. 2), which should favor elimination of fluoride ion rather than  $ArO^-$  moiety (the latter process requires essential reorganization of the HOMO). Therefore, facile replacement of the

**Table 6.** Heats of formation  $\Delta H_c^f$  and  $\Delta H_c^r$  of  $\sigma$ -complexes **XXIV–XXX** in the reactions of pentafluoropyridine (**I**) with aroxide ions and of ethers **II**, **III**, **XVII–XX**, and **XXII** with fluoride ion (Scheme 7)

Nucleophile $ArO^-$	$\Delta H_c^f$ , <sup>a</sup> kcal/mol	Diaryl ether	$-\Delta H_c^r$ , <sup>b</sup> kcal/mol
2- $C_{10}F_7O^-$	0.70	<b>XVII</b>	63.7
1- $C_{10}F_7O^-$	3.67	<b>XVIII</b>	63.1
$C_6F_5O^-$	-5.1	<b>II</b>	62.8
3-Cl-4- $NO_2C_6H_3O^-$	-3.7	<b>XIX</b>	65.7
4- $CH_3C_6F_4O^-$	-8.3	<b>XX</b>	59.7
4- $NO_2C_6H_4O^-$	-9.3	<b>III</b>	64.9
$PhO^-$	-28.9	<b>XXII</b>	55.0

<sup>a</sup>  $\Delta H_c^f = \Delta H_f^\sigma - [\Delta H_f(C_5F_5N) + \Delta H_f(ArO^-)]$ ; the enthalpies of formation were taken from Table 5.

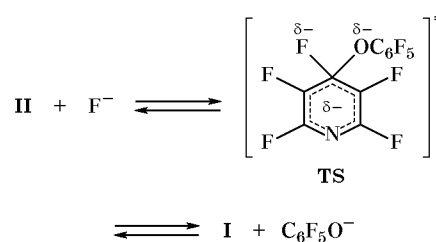
<sup>b</sup>  $\Delta H_c^r = \Delta H_f^\sigma - [\Delta H_f(ArOAr) + \Delta H_f(F^-)]$ ; the enthalpies of formation were taken from Tables 4 and 5.

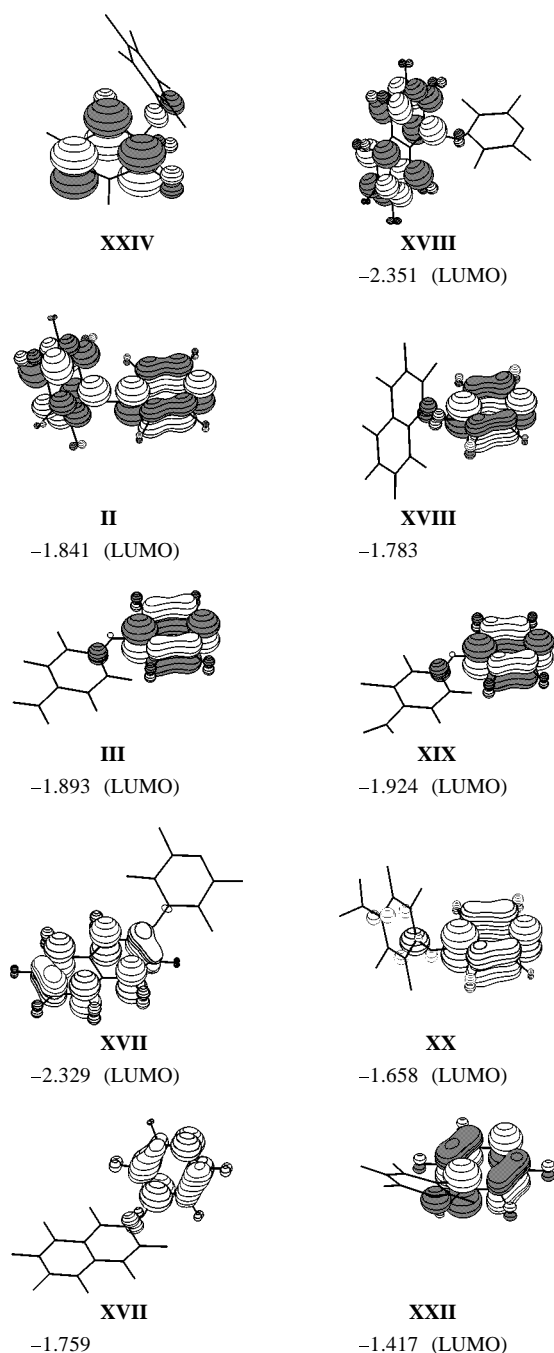
**Table 7.** Energies of low-lying vacant molecular orbitals of compounds **X–XVI** and 2,3,5,6-tetrafluoro-4-hydroxypyridine (**XXXI**)

Comp. no.	Energy $\varepsilon$ , eV		$\Delta\varepsilon(b_1)$
	LUMO	2nd UMO	
<b>X</b>	-2.0063		-0.75
<b>XI</b>	-2.0083		-0.75
<b>XII</b>	-1.3429 ( $a_2$ )	-1.2025 ( $b_1$ )	0.05
<b>XIII</b>	-1.1519 ( $b_1$ )	-0.6669 ( $a_2$ )	0.10
<b>XIV</b>	-0.9754 ( $a_2$ )	-0.8455 ( $b_1$ )	0.41
<b>XV</b>	-1.0807 ( $b_1$ )	-0.4655 ( $a_2$ )	0.18
<b>XVI</b>	0.2908 ( $a_2$ )	0.4119 ( $b_1$ )	1.67
<b>XXXI</b>	-1.3961 ( $a_2$ )	-1.2559 ( $b_1$ )	0

pentafluorophenoxy group in ether **II** by fluoride ion cannot be explained in terms of intermediate formation of  $\sigma$ -complex **XXIV**. Probably, due to delocalized character of the LUMO in **II** the transition state has a structure favoring charge transfer from fluoride ion

**Scheme 8.**





**Fig. 2.** LUMO structures of  $\sigma$ -complexes **XXIV–XXX** with  $\sigma$ -complex **XXIV** as an example; LUMO structures and energies (eV) of ethers **II**, **III**, **XVII–XX**, and **XXII**, according to the PM3 calculations; for ethers **XVII** and **XVIII**, the parameters of higher-energy vacant MOs are also given.

to the departing  $C_6F_5O^-$  group. In this case replacement of the pentafluorophenoxy group may follow a concerted mechanism shown in Scheme 8 (cf. [14]) rather than  $S_NAr$  mechanism involving formation of

$\sigma$ -complex **XXIV** (Scheme 7). Probably, the replacement of  $C_6F_5O$  in compounds **IV** and **VI** (Scheme 5) also occurs by concerted mechanism.

It should be noted that the aroxy group in 4-aroxy-2,3,5,6-tetrafluoropyridine is also readily replaced by the action of sodium methoxide in DMF at 10°C, while analogous reaction with 4-aroxy-pentafluorobenzene almost does not occur under the same conditions [15]. Therefore, the unusual lability of the  $C_6F_5O$  group in ethers **II**, **IV**, and **VI** refers only to their reaction with fluoride ion. We cannot exclude the possibility for ready replacement of  $C_6F_5O$  group by fluorine in other highly electrophilic substrates.

## EXPERIMENTAL

The  $^1H$  and  $^{19}F$  NMR spectra were recorded on a Varian A56/60A instrument at 60 and 56.4 MHz, respectively, using  $CCl_4$  as solvent and TMS ( $^1H$ ) or hexafluorobenzene ( $^{19}F$ ) as internal reference. The IR spectra were measured on a UR-20 spectrometer from 5% solutions in  $CCl_4$  or KBr pellets (0.25%). The reaction mixtures were analyzed by GLC using an LKhM-7A chromatograph (thermal conductivity detector; linear oven temperature programming from 50 to 270°C at a rate of 10 deg/min; 4000×4-mm column packed with 15% of SE-54, SKTFT-803, or SE-30 on W-DMCS or Chromaton-N; carrier gas helium, flow rate 60 ml/min). The components were quantitated by the internal normalization technique and were identified by adding authentic samples.

Quantum-chemical calculations were performed in the PM3 approximation with full geometry optimization using standard MOPAC software [8]; molecular orbitals were simulated using MOLDEN software package [16].

We used commercial 4-nitrophenol (**XV**) (chemically pure grade, mp 112–113°C), phenol (**XVI**) (chemically pure grade, bp 181°C, mp 43°C), pentafluoropyridine (**I**) (bp 83–84°C), dibenzo-18-crown-6 as a complex with acetonitrile, and dibenzo-24-crown-8 (produced by the pilot factory at the Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences). Commercial potassium fluoride and cesium fluoride were dehydrated by calcination and powdered by grinding prior to use. Heptafluoro-1-naphthol (**XI**, mp 103–104°C) [17], heptafluoro-2-naphthol (**X**, mp 124–126°C) [18], 2,3,5,6-tetrafluoro-4-methylphenol (**XIV**, mp 52°C) [19], 3-chloro-4-nitrophenol (**XIII**, mp 121–122°C) [20], and pentafluorophenol (**XII**, bp 144–145°C) [19] were synthesized by known methods. Acetonitrile was purified and dried by the procedure described in [21].



**Table 8.** Melting points, IR spectra, and elemental analyses of compounds **XVII–XXIII**

Comp. no.	mp, <sup>a</sup> °C	IR spectrum, $\nu$ , $\text{cm}^{-1}$		
		C–F	C–O–C	C=C <sub>arom</sub>
<b>XVII</b>	83–84	990 v.s, 1020 s	1095 s, 1130 s	1415 v.s, 1460–1500 br, v.s
<b>XVIII</b>	64–65	995 v.s, 1035 s	1085 s, 1135 s	1480–1515 br, v.s
<b>XIX<sup>b</sup></b>	108–110	985 v.s	1085 v.s	1460–1540 br, v.s
<b>XX</b>	57–58	990 v.s, 1055 v.s	1080 s, 1140 v.s	1490–1520 br, v.s
<b>XXI</b>	91–93	970 s, 1010 s	1085 s, 1140 v.s	1470–1530 br, v.s
<b>XXII</b>	68–70 (5) <sup>c</sup>	985 v.s	1080 v.s	1470–1540 br, v.s
<b>XXIII</b>	54–56	990 v.s	1075 v.s, 1165 s	1460–1510 br, v.s

Compound no.	Found, %				Formula	Calculated, %				$M^d$	
	C	H	F	N		C	H	F	N	found	calcd.
<b>XVII</b>	42.7	–	50.2	2.99	$\text{C}_{15}\text{F}_{11}\text{NO}$	42.9	–	49.9	3.34	425	419
<b>XVIII</b>	42.8	–	50.1	3.24	$\text{C}_{15}\text{F}_{11}\text{NO}$	42.9	–	49.9	3.34	422	419
<b>XIX</b>	40.7	0.79	23.7	8.74	$\text{C}_{11}\text{H}_3\text{ClF}_4\text{N}_2\text{O}_3$	40.9	0.93	23.6	8.68	326	322
<b>XX</b>	44.1	1.04	46.3	4.16	$\text{C}_{12}\text{H}_3\text{F}_8\text{NO}$	43.9	0.91	46.2	4.26	333	329
<b>XXI</b>	46.3	1.31	42.9	2.91	$\text{C}_{19}\text{H}_6\text{F}_{11}\text{NO}_2$	46.6	1.23	42.7	2.86	495	489
<b>XXII</b>	54.0	2.14	31.4	5.89	$\text{C}_{11}\text{H}_5\text{F}_4\text{NO}$	54.3	2.06	31.3	5.76	249	243
<b>XXIII</b>	64.1	3.24	18.1	4.36	$\text{C}_{17}\text{H}_{10}\text{F}_3\text{NO}_2$	64.4	3.15	18.0	4.42	322	317

<sup>a</sup> After recrystallization from petroleum ether (bp 40–70°C).

<sup>b</sup> The IR spectrum also contained the following bands,  $\nu$ ,  $\text{cm}^{-1}$ : 760 m (C–Cl); 1350 v.s, 1590 v.s, 1650 v.s ( $\text{NO}_2$ ).

<sup>c</sup> Boiling point, °C ( $p$ , mm).

<sup>d</sup> Determined by isothermal distillation.

**Reaction of pentafluoropyridine (I) with naphthols X and XI and phenols XIII–XVI in acetonitrile in the presence of KF.** A flask was purged with dry nitrogen and was charged with 0.02 mol of KF, 0.01 mol of compound X, XI, or XIII–XVI, 0.001 mol of dibenzo-18-crown-6, and 15–20 ml of acetonitrile. The mixture was stirred for 10–15 min, and a solution of 0.01 mol of pentafluoropyridine (I) in 5–6 ml of acetonitrile was added. The mixture was heated for 5 h at 80°C while stirring, cooled to room temperature, and poured into 80–100 ml of 5% hydrochloric acid. The organic phase was separated, and the aqueous phase was extracted with diethyl ether (3 × 10 ml). The combined extracts were washed with water (3 × 10 ml) and dried over  $\text{CaCl}_2$ . The solvent was distilled off through a column, and the residue was recrystallized (if solid) or distilled under reduced pressure to isolate products **XVII–XXIII**. The conditions of experiments, and the yields of the products are given in Table 2. Tables 8 and 9 contain the physical constants, elemental analyses, and spectral data of compounds **XVII–XXIII**. Experiments with

ethers **XVII–XX** and **XXII** in the presence of KF were carried out by a similar procedure (Table 2).

**Potassium salts of naphthols X and XI and phenols XII–XV.** Metallic potassium, 0.1 mol, was added in portions to 200–300 ml of anhydrous methanol under stirring at –10 to –20°C in a stream of dry nitrogen. When the metal dissolved completely, a solution of 0.1 mol of appropriate naphthol or phenol in 80–100 ml of methanol was added under stirring over a period of 20–30 min. The mixture was stirred for 60–90 min at 50–60°C, and the solvent was distilled off. The remaining potassium salt was ground and dried for 10–12 h at 95–100°C under reduced pressure (2 mm).

**Kinetic study of the reactions of pentafluoropyridine (I) with potassium naphthoxides and phenoxides.** The reactions were carried out in sealed ampules which were preliminarily purged with dry nitrogen and adjusted to a required temperature (Table 3) with an accuracy of  $\pm 0.2^\circ\text{C}$ . Equimolar amounts of substrate **A** and reagent **B** were taken; their initial concentrations,  $a$  and  $b$ , respectively,

**Table 9.**  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra of compounds **XVII–XXIII**<sup>a</sup>

Compound no.	$^1\text{H}$ NMR spectrum, $\delta$ , ppm	$^{19}\text{F}$ NMR spectrum, $\delta_{\text{F}}$ , ppm								
		2(6)-F	3(5)-F	2'-F	3'-F	4'-F	5'-F	6'-F	7'-F	8'-F
<b>XVII</b> <sup>b</sup>		73.7	8.0	27.3 <sup>c</sup>	27.3	19.7	20.3	11.7	12.5	15.7
<b>XVIII</b> <sup>d</sup>		73.4	8.2	17.0	3.2	18.4	22.4	9.2	10.1	16.3
<b>XIX</b>	7.50 (2'-H), 8.03 (5'-H), 7.40 (6'-H)	74.3	9.2	–	–	–	–	–	–	–
<b>XX</b>	2.26 (Me)	73.4	4.8	4.8	19.5	–	19.5	4.8	–	–
<b>XXI</b>	2.24 (Me)	71.3	5.0 <sup>e</sup>	0.2	19.7	–	19.7	0.2	–	–
			18.4 <sup>f</sup>	–1.2 <sup>g</sup>	7.8 <sup>h</sup>		7.8 <sup>h</sup>	–1.2 <sup>g</sup>		
<b>XXII</b>	7.0 (Ph)	75.9	10.5	–	–	–	–	–	–	–
<b>XXIII</b>	7.12 (Ph)	75.6	6.0 <sup>e</sup>	–	–	–	–	–	–	–
			12.8 <sup>f</sup>							

<sup>a</sup> The signal intensity ratios conformed to the expected values; the fluorine signals of compounds **XVII** and **XVIII** were assigned on the basis of the data in [23].

<sup>b</sup>  $J(1'-\text{F}, 8'-\text{F}) = 70$  Hz,  $J(4'-\text{F}, 5'-\text{F}) = 63$  Hz.

<sup>c</sup> 1'-F.

<sup>d</sup>  $J(4'-\text{F}, 5'-\text{F}) = 62$  Hz.

<sup>e</sup> 5-F.

<sup>f</sup> 3-F.

<sup>g</sup> 2''-F, 6''-F.

<sup>h</sup> 3''-F, 5''-F.

were 0.024–0.032 M. The progress of the reaction was monitored following the concentration of fluoride ion [22] and also (in parallel) by GLC with calibration against an artificial mixture of products. The rate constants were calculated by the second-order equation at  $a = b$ :

$$k = \frac{x}{b(b-x)\tau} = \frac{x}{a(a-x)\tau}, \text{ l mol}^{-1} \text{ s}^{-1},$$

where  $a$  and  $b$  (mol/l) are the initial concentrations of substrate **A** and reagent **B**,  $x$  (mol/l) is the concentration of the product, and  $\tau$  (s) is the reaction time. The rate constants given above were obtained by averaging 3–5 current values which deviated from the average value by no more than 15–20%.

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