INFLUENCE OF SUBSTITUENTS ON THE CHEMICAL SHIFTS OF FLUORINE

IN 2- AND 3-FLUOROSUBSTITUTED PHENYL BENZYL ETHERS

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For a study of the structure of organometallic derivatives of tautomeric systems in solution by the NMR method, a new approach, based on a comparison of the transmission capacity (TC) of organometallic derivatives of systems containing a label (19 F) at the aromatic C atom, for example,

$$Ar_{n}M - X - Y = ZC_{6}H_{4}F \rightleftharpoons X = Y - Z$$

 $(Ar_nM represents monovalent organometallic groups; X and Z are cation-acceptor sites; Y is the molecular skeleton) with the TC of arylalkyl derivatives of the corresponding systems, possessing a fixed structure$

$$C_6H_4F$$

ArCH₂-X-Y=Z-C₆H₄F or X=Y-Z-CH₂Ar

within the framework of the ¹⁹F NMR method, is potentially possible. This approach is based on the existence of a relationship between the distance of the indicator F atom from the variable substituent and the effectiveness of the transmission of the electronic effect of the latter to it. A necessary condition for such an investigation is the presence of systematic quantitative data on the TC of binuclear bridge groups (BBG) of the Q-X type (where Q is an atom of a heavy nontransition metal or carbon, while X is a heteroatom) [1-3].

To evaluate the potential prospects of the indicated approach it was necessary to determine what type of fluoroalkyl groups can be used as indicator groups. In view of this, it seemed advisable to obtain quantitative data on the sensitivity of the shielding of F in various positions of the indicator group C_6H_4F relative to the electronic influence of the variable substituents (EIS) both in organometallic systems and in their carbon analogs.

The present work is devoted to an investigation of the problem posed on the example of organic objects - substituted aryl benzyl ethers, the selection of which was due to the fact that the phenolic structural element is contained in various tautomeric and potentially tautomeric systems, such as nitrosophenols, arylazophenols, indophenols, and hydroxy-N-heterocycles. Moreover, there are now data available on the effectiveness of the transmission of EIS in the system $ArCH_2OC_5H_4F-4$ (I) [4].

To determine the sensitivity of the shielding of fluorine in the 3 and 2 positions of the indicator aromatic ring to the influence of the variable substituents in the aromatic group separated from the indicator by BBG CH_2-O , two series of substituted aryl benzyl ethers $ArCH_2OC_6H_4F-3$ (IIa-i) and $ArCH_2OC_6H_4F-2$ (IIIa-j) were synthesized, where $Ar = 4-MeOC_6H_4$ (a), $4-MeC_6H_4$ (b), $3-MeC_6H_4$ (c), Ph (d), $4-ClC_6H_4$ (e), $4-FC_6H_4$ (f), $3-FC_6H_4$ (g), $3-CF_3C_6H_4$ (h), $3,4-Cl_2C_6H_3$ (i), $4-NO_2C_6H_4$ (j). For these compounds we determined the chemical shifts of fluorine (CSF) relative to PhF in PhC1 (Table 1). A positive sign of the CSF corresponds to a strong-field shift.

From the data of Table 1 it follows that transition from electron-donor to electronacceptor substituents in the series of compounds (II) is accompanied by successive unshielding of the indicator nucleus F; however, the range of variation of the CSF is extremely small (~ 0.4 ppm).

A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 6, pp. 1300-1304, June, 1985. Original article submitted February 15, 1984.



Fig. 1. Dependence of the chemical shifts of ¹⁹F in 2-fluorosubstituted phenyl benzyl ethers in PhCl on the inductive constants of aromatic substituents: 1) 4-MeOC₆H_u; 2) 4-MeC₆H₄; 3) 3-MeC₆H₄; 4) Ph; 5) 4-FC₆H₄; 6) 4-ClC₆H₄; 7) 3-CF₃C₆H₄; 8) 3,4-Cl₂C₆H₃; 9) 4-NO₂C₆H₄.

TABLE 1. Values of the CSF of (II) and (III) Relative to C_6H_5F in PhCl (ppm)

Compound	CSF	Compound	CSF
(IIa) (IIb) (IIc) (Ild) (Ile) (Ilf) (IIg) (IIg) (IIh) (IIi)	$\begin{array}{c} -1,35\\ -1,35\\ -1,44\\ -1,39\\ -1,58\\ -1,66\\ -1,49\\ -1,64\\ -1,81\\ \end{array}$	(IIIa) (IIIb) (IIIc) (IIId) (IIIe) (IIIf) (IIB) (IIB) (IIIb) (IIIj)	20,86 20,91 20,93 20,94 20,81 20,83 20,88 20,78 20,71 20,86

In series (III) virtually no correlation at all is observed between the CSF and the electronic properties of the substituents. An illustration of this is Fig. 1, which provides evidence of the existence of a random dependence of the CSF of (III) on the σ° constants of the substituted aryl groups [5]. Statistical treatment of the data obtained on the CSF for (II) [CSF (II) = $(-0.50 \pm 0.22)\sigma^{\circ} - 1.44$, S = 0.77, r = 0.891] showed that in the series of compound (II), likewise no "approximate" (in Jaffe's terms, 0.950 > r > 0.900 [6]) correlation is observed between the CSF and σ° . However, for series (II) there is a rather clear correlation between the changes in the CSF and the electronic nature of the substituents in the aromatic radical. At the same time, it should be noted that the correlation of the CSF of (II) with the CSF of (I) is satisfactory [CSF (II) = (0.45 ± 0.17) ; CSF (I) -6.24, S = 0.068, r = 0.917]. Thus, generalizing the data obtained and the results of [4], we can conclude that the CSF correctly reflects the EIS in fluorosubstituted aryl benzyl ethers only when the indicator atom is in the 4 position of the benzene ring with respect to the ArCH₂O group [CSF (I) = $(1.17 \pm 0.09)\sigma^{\circ} + 10.72$, S = 0.037, r = 0.996]. In this sense the 3- and 2-fluorophenyl indicators are uninformative inthis case, since other factors in addition to the EIS make a substantial contribution to the shielding of F, and they are dominant for o-fluorophenyl-substituted ethers.

One of the possible causes of the observed situation might be short-range and long-range field effects of the substituents, associated with differences in the conformational behavior of the investigated compounds. In view of the absence of data in the literature on the conformation of phenyl benzyl ether or its derivatives, we analyzed the possible conformations of the investigated substituted phenyl benzyl ethers on molecular models. It was discovered that the distance between the substituent and the indicator F atom may be changed as a result of free rotation around the $C_{al}-C_{ar}$, $C_{al}-O$, and $O-C_{ar}$ bonds. Thus, as a result of rotation around the $C_{al}-O$ bond, two extreme conformations of the S-cis (A) and S-trans

Compound	Yield, %	Temp., °C		20	Found/calc., %	
		mp*	bp (p, mm Hg)	n _D	C	H
4-MeOC ₆ H ₄ CH ₂ OC ₆ H ₄ F-3	55	27-30	200–202 (12)		$\begin{array}{c c} \hline 72,36\\ \hline 72,40 \end{array}$	$\tfrac{6,14}{5,64}$
$4\text{-}MeC_6H_4CH_2OC_6H_4F\text{-}3$	85	46-47		-	77,67	$\frac{5,87}{6,06}$
$3-MeC_6H_4CH_2OC_6H_4F-3$	90		144146 (4)	1,5430	77,7 <u>1</u> 77,75	<u>6,03</u> 6,06
$4\text{-}FC_6H_4CH_2OC_6H_4F\text{-}3$	60	-	109–113 (1–2)	1,5350	$\frac{70,58}{70,90}$	4,55
$3-FC_6H_4CH_2OC_6H_4F-3$	85	-	114–116 (1)	1,5412	$\frac{70,84}{70,90}$	$\tfrac{4,38}{4,58}$
3-CF ₃ C ₆ H ₄ CH ₂ OC ₆ H ₄ F-3	42	-	124-130 (1)	1,5054	<u>61,69</u> <u>62,22</u>	$\frac{3,80}{3,73}$
$3,4-Cl_2C_6H_3CH_2OC_6H_4F-3$	40	3436	184–185 (5)	-	57,46	$\frac{3,59}{3,34}$
$4\text{-}MeOC_6H_4CH_2OC_6H_4F\text{-}2$	80	70-71	-	-	$\frac{72,05}{72,40}$	$\frac{5,37}{5,64}$
$4\text{-}MeC_6H_4CH_2OC_6H_4F\text{-}2$	85	54-55	-	-	$\frac{77,59}{77,75}$	6,03
$3-MeC_6H_4CH_2OC_6H_4F-2$	85	-	155–159 (9)	1,5565	$\frac{77,49}{77,75}$	<u>6,07</u> 6,06
$4\text{-}\mathrm{FC}_6\mathrm{H}_4\mathrm{CH}_2\mathrm{OC}_6\mathrm{H}_4\mathrm{F}\text{-}2$	60	35-37	-		70,84 70,90	$\frac{4,50}{4,58}$
$4-ClC_6H_4CH_2OC_6H_4F-2$	50	52-53	-		$\frac{65,88}{65,96}$	$\begin{array}{c} \underline{4,23} \\ \underline{4,26} \end{array}$
$3-FC_6H_4CH_2OC_6H_4F-2$	90	-	114-116 (1-2)	1,5400	70,66	$\frac{4,43}{4,58}$
$3-CF_3C_6H_4CH_2OC_6H_4F-2$	35	-	120-122 (1)	1,5055	$\tfrac{62,09}{62,22}$	$\frac{3,57}{3,73}$
$3,4\text{-}\mathrm{Cl_2C_6H_3CH_2OC_6H_4F-2}$	80	51-52		-	$\frac{57,54}{57,57}$	$\frac{3,26}{3,34}$
$4\text{-NO}_2C_6H_4CH_2OC_6H_4F\text{-}2$	85	77-78	-	-	$\frac{62,92}{63,16}$	$\frac{3,70}{4,08}$
4-ClC ₆ H ₄ CH ₂ OC ₆ H ₄ F-3	31	-	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	1,5664	<u>66,03</u> <u>65.96</u>	4,13
$C_6H_5CH_2OC_6H_4F$ -3	75	42-43	-	-	$\frac{76,88}{77,21}$	5,46

TABLE 2. Analytical Data and Physical Properties of the Compounds Synthesized

*From MeOH.

(B) types, respectively, may arise, with minimum and maximum distances between the substituents X and F:



Then for (A) the CSF should naturally be determined not only by the EIS, but also by the influence of short-range field effects of the C-X bond. An analysis of the models showed that these factors should be most effective in the case of the $p-FC_6H_u$ group. However, the experimental data obtained earlier [4] on the existence of a good correlation between

the CSF of (I) and the parameters σ° (r = 0.996) suggest that probably conformation (B) is preferential for the investigated aryl benzyl ethers.

Then if we take conformation (B) as the basis, it is evident that for series (I) the distances between X and F are fixed and are not changed in the presence of any rotations around the $C_{al}-C_{ar}$ and $C_{ar}-O$ bonds. In contrast to this, for the m series (II), transition from S-trans-S-trans (C) to S-cis-S-trans-S-trans (D), or S-trans-S-trans-S-cis (E) conformations as a result of free rotation around the $C_{ar}-O$ or $C_{al}-C_{ar}$ bonds may lead to a decrease in the distance between 3-F and 3-X (the most unfavorable case) from 12 to 9.5 or 10 Å, respectively.

Thus, the absence of a good correlation between the CSF of (II) and σ° and the existence of a positive correspondence of the variation of these quantities, in all probability, may be associated with the different population of the conformations (D) and (E) and the influence on the shielding of m-F not only of the polar effect of substituents at the bonds or a π -polarization effect [7] but also a direct field effect of the substituent [8].

For the o series (III), transition from (C) to (D) or (E) is accompanied by approximately the same changes in the distances between o-F and p-X ($\sim 2-2.5$ Å) as for the m series (II). Consequently, under the action of this factor alone, for (III) the same principles should have been observed as for (II). The absence of a dependence of the CSF of (III) on σ° is evidence that in this case conformational factors are not dominant. The most probable cause of this is direct electrostatic interaction through space between the electron shells of F and O. Thus, the introduction of a substituent into the benzyl radical, as a result of transmission of its influence along the bonds, should change the electron density both on the O atom and on the F atom. However, as a result of electrostatic interaction through space, the change in the electron density on the O atom should prevent its analogous change on the F atom and equalize the electronic influence of the substituent transmitted along the bonds.

On the basis of the results obtained we can conclude that strictly quantitative data on the effectiveness of the transmission of the EIS in fluorophenyl benzyl ethers can be obtained only when the indicator group $4-FC_6H_4$ is used.

EXPERIMENTAL

The ¹⁹F-{¹H} NMR spectra were obtained on a Tesla BS-497 spectrometer (working frequency 94.075 MHz) at 25°C for dilute solutions (concentration 0.2 M). The experimental error in the determination of the CSF was ± 0.01 ppm. The solvents were purified according to the standard procedures.

Substituted fluorophenyl benzylethers (II) and (III) were produced by the reaction of sodium fluorophenolates with corresponding substituted benzyl chlorides. The (III) described in the literature [9] were identified according to their melting or boiling points and n_D^{20} . The constants and data of analysis for the new compounds are cited in Table 2. Typical examples of the synthesis of the compounds are given below.

<u>3-Fluorophenyl 4-Fluorobenzyl Ether (IIf)</u>. To a solution of 0.01 mmole sodium 3-fluorophenolate [from 1.12 g (0.01 mmole) 3-fluorophenol and 0.23 g (0.01 g-atom) Na] in 50 ml abs. C_2H_5OH we added a solution of 1.44 g (0.01 mmole) of 4-fluorobenzyl chloride in 30 ml of abs. C_2H_5OH and boiled with a reflux condenser for 2 h. The solvent was evaporated under vacuum, the residue dissolved in ether, washed with H_2O and witha weak solution of NaOH, and dried with Na₂SO₄. After redistillation under vacuum we obtained 1.32 g of a colorless liquid with bp 114-116°C (1 mm), n_D^{20} 1.5412.

CONCLUSIONS

1. The ${}^{19}F-{}^{1}H$ NMR spectra of a series of substituted 3- and 2-fluorophenyl benzyl ethers were investigated.

2. With respect to the effectiveness of the transmission of electronic influences of the substituents in the benzene group on the indicator fluorine atom in fluorophenyl benzyl ethers, the 3-fluorophenyl group is less informative than the 4-fluorophenyl group, while the 2-fluorophenyl group gives no information.

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INFLUENCE OF SUBSTITUENTS ON THE CHEMICAL SHIFT OF FLUORINE IN CERTAIN FLUOROSUBSTITUTED ARYLPHENYLMERCURY COMPOUNDS AND N-ARYLMERCURY DERIVATIVES OF BENZENESULFONANILIDE

UDC 541.124:543.422.25:547.559.49'161

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Earlier [1], in a ¹⁹F NMR investigation of the electronic influence of substituents (EIS) on the chemical shifts of fluorine (CSF) in fluorosubstituted phenyl benzyl ethers $ArCH_2OC_6H_4F-4$ (2), (3), it was established that with respect to the effectiveness of the transmission of the EIS in the benzyl group to the indicator fluorine atom, the 3-fluorophenyl group is less informative than the 4-fluorophenyl group, whereas the CSF in the 2-fluorophenyl group is virtually independent of the nature of the substituent. In accordance with this, it seemed interesting to determine the degree of generality of the principles detected for structurally similar organic and organometallic compounds, and also to compare the behavior of mono- and binuclear bridge systems in this sense.

To determine the relative sensitivity of the shielding of F in various positions of the indicator fluorophenyl group to the EIS in an aromatic ring, separated from the indicator by a mono- or binuclear bridge group, in the present work we investigated the following series of model compounds: $ArHgC_6H_4F-3$ (Ia-k), $ArHgC_6H_4F-2$ (IIa, c, d, e, h), $ArHgN(SO_2Ph)C_6H_4F-3$ (IIIa, c, e, f, i, k), and $ArHgN(SO_2Ph)C_6H_4F-2$ (IVa-f, h, k), where $Ar = 4-Me_2NC_6H_4$ (a), $4-MeOC_6H_4$ (b), $4-MeC_6H_4$ (c), Ph (d), $4-ClC_6H_4$ (e), $4-FC_6H_4$ (f), $3-ClC_6H_4$ (g), $3-CF_3C_6H_4$ (h), $3,4-Cl_2C_6H_3$ (i), $3,5-Cl_2C_6H_3$ (j), and $3,4,5-Cl_3C_6H_2$ (k), for which the CSF were determined with respect to PhF in PhC1 (Table 1). A positive sign of the CSF corresponds to a strong-field shift.

In connection with the tendency for symmetrization of nonsymmetrical arylmercury compounds, the compounds of type (I) and (II) were generated in solution by exchange reactions $Ar_2Hg + Hg(C_6H_4F-3(2))_2 \rightleftharpoons ArHgC_6H_4F-3(2)$

which, as was established, are slow in the NMR time scale.

From the data (see Table 1) it follows that for both the 3-fluorophenyl-substituted series of compounds (I) and (III) the changes in the CSF corresponds to the nature of the substituents in Ar. However, the range of variation of the CSF of (III) (~ 0.5 ppm) is somewhat smaller than for (I) (~ 0.75 ppm). For series (II) the electron-donor group Me₂N has the same influence on the CSF as H, while the transition to acceptor substituents is accompanied by a

A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 6, pp. 1305-1308, June, 1985. Original article submitted February 15, 1984.

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