J = 9 Hz) [the aryl protons of two 2-(2-methoxyethoxy)-5-nitrophenyl groups], 4.5–4.2 (4 H, m, 2 OCH_2), 4.0–3.6 (4 H, m, 2 CH_2OMe), 3.50 (3 H, s, OCH_3), 3.22 (3 H, s, OCH_3), 7.81 (1 H, s, =CHC=N), 6.54 (1 H, s, =CHC=O), 1.18 (9 H, s, $C(CH_3)_3$). Anal. Calcd for $C_{28}H_{32}N_4O_{13}S_2$: C, 48.27; H, 4.63; N, 8.04. Found: C, 47.77; H, 4.56; N, 7.83.

The compounds **11d** and **16b** were identical with the samples described above.

Heterogeneous Hydrolysis of 10b and 10d with Aqueous NaOH/AcOEt. Determination of the Yields of the Products. To a solution of 49.98 mg of **10b** (or 53.36 mg of **10d**) in ethyl acetate (5 mL) was added 2 N (or 4 N) sodium hydroxide (10 mL) at room temperature. The mixture was stirred for 1 h at room temperature, diluted with ethyl acetate (5 mL), and then neutralized with 15 mL of aqueous acetic acid (AcOH, 1 mL, and water, 200 mL). After addition of 1,4-di-*tert*-hexyl-2,5-dimethoxybenzene (49.21 mg, as an internal standard), ethyl acetate (15 mL), and sodium chloride (2.5 g), the organic layer was separated and subjected to HPLC determination [using a μ-Bondapak C-18 as a column and $MeCN-H_2O$ (93:7) as an eluent]. Retention times (in minutes) of the components were as follows: **15a** (1.93), **16a** (2.91), **14** (4.07), the standard (7.79) and **11b** (11.41); **15b** (2.32), **16b** (3.15), **14** (4.09), the standard (7.80), and **11d** (15.25). The results are given in Table I.

Oxidation–Hydrolysis of 9b and 9d with Potassium Hexacyanoferrate(III) under Alkaline Conditions. A solution of potassium hexacyanoferrate(III) (0.220 g, 6.44×10^{-4} mol) in 2 N sodium hydroxide (20 mL) was added to a solution of **9b** (0.100 g) and 1,4-di-*tert*-butyl-2,5-dimethoxybenzene (0.0764 g, an internal standard) in ethyl acetate (10 mL). The mixture was stirred for 1 h at room temperature, diluted with ethyl acetate (40 mL), and quenched with 30 mL of aqueous acetic acid (AcOH, 1 mL, and water, 200 mL). After addition of sodium chloride (5.0 g), the organic layer was separated and subjected to HPLC analysis.

The reaction of **9d** was effected under the same conditions. The results are collected in Table I.

Reaction of 10b and 10d with *N*-Ethyl-*N*-[2-(methanesulfonamido)ethyl]-2-methylbenzene-1,4-diamine (17). A solution of **17** (0.60 g, 2.21 mmol) in ethyl acetate (100 mL) was added to a solution of **10b** (1.00 g, 1.61 mmol) in ethyl acetate (200 mL) at room temperature. The mixture was stirred for 1.5 h during which its color changed from yellow to blue. The organic layer was separated, washed with diluted hydrochloric acid and then water, and dried over anhydrous sodium sulfate. After removal of the solvent, the residual solid was recrystallized from methanol. The crystals of **19** (0.5 g) had a melting point of 132–134 C: FDMS, m/e 649 (M); VS (AcOEt) λ_{max} 634 nm (ϵ 21400). Anal. Calcd for $C_{28}H_{35}N_5O_9S_2 \cdot H_2O$: C, 50.35; H, 5.58; N, 10.48. Found: C, 50.46; H, 5.38; N, 10.55.

No indoaniline dye was formed by the reaction of **10d** with **17**.

Reaction between 20a and 17 in the Presence of 10d. A solution of **17** (1.02 g, 3.75 mmol) in ethyl acetate (1 L) was added to a solution of **10d** (0.50 g, 0.75 mmol) and **20a** (0.41 g, 0.75 mmol) in ethyl acetate (1 L). The mixture was stirred at room temperature for 1 h. The yield of the cyan dye **21** from **20a** and **17** was 69% as monitored by visible spectroscopy. The solvent was removed by a rotary evaporator, and the residue was separated with a silica gel column (chloroform–ethyl acetate (1:1) as an eluent). The fractions of the cyan dye **21** were collected, and the solid obtained was recrystallized from methanol. This was identified with the sample described below.

Reaction between **20b** and **17** in the presence of **10d** afforded the same cyan dye in 24% yield.

Synthesis of the Cyan Dye 21. Oxidative Coupling between 20 and 17 with Ammonium Persulfate. To a solution of **20a** (2.0 g, 3.7 mmol) in ethyl acetate (50 mL) and ethanol (25 mL) were added an aqueous solution (40 mL) of sodium carbonate (5.0 g), the developer **17** (1.92 g, 4.4 mmol), and then an aqueous solution (20 mL) of ammonium persulfate (1.25 g, 5.50 mmol). The mixture was stirred for 2 h at room temperature. The organic layer was separated, washed with water, and then dried over anhydrous sodium sulfate. After the removal of the solvent, the residue was purified by column chromatography. The fractions of the cyan dye **21** were collected and condensed. The solid obtained was recrystallized from methanol: 0.50 g (20%); mp 98–101 °C; EIMS, m/e 678 (M), 570 ($M - CH_2NHSO_2CH_3$), 438 ($M - C_{16}H_{33}NH$); VS (AcOEt) λ_{max} 654 nm (ϵ 26000). Anal. Calcd for $C_{39}H_{58}N_4O_4S$: C, 68.99; H, 8.61; N, 8.26. Found: C, 69.16; H, 8.78; N, 8.34.

Acknowledgment. The expert technical assistance of Mr. Kazuharu Hattori is gratefully acknowledged.

Registry No. **6a**, 66481-29-6; **6b**, 77406-46-3; **7a**, 84011-43-8; **7c**, 84011-44-9; **7d**, 78819-49-5; **8a**, 84011-45-0; **8c**, 84011-46-1; **8d**, 78819-50-8; **9a**, 78826-17-2; **9b**, 69920-07-6; **9c**, 84011-47-2; **9d**, 84011-48-3; **10a**, 78826-15-0; **10b**, 78826-16-1; **10c**, 84011-49-4; **10d**, 84011-50-7; **11b**, 84011-51-8; **11c**, 36122-03-9; **11d**, 84011-52-9; **12a**, 78826-18-3; **12b**, 78826-19-4; **12c**, 84011-53-0; **12d**, 84011-54-1; **14**, 78826-20-7; **15a**, 84011-55-2; **15b**, 84011-56-3; **16a**, 78826-21-8; **16b**, 84011-57-4; **17**, 92-09-1; **19**, 84011-58-5; **20a**, 76379-54-9; **20b**, 74918-83-5; **21**, 84011-59-6; 2-(2-methoxyethoxy)-5-nitrobenzenesulfonyl chloride, 69920-06-5; 1-bromohexadecane, 112-82-3.

Gas-Phase Reactions of Anions with 2-, 3-, and 4-Fluoroanisole

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The gas-phase reactions between some anions (NH_2^-, OH^-, and RO^-) and 2-, 3-, and 4-fluoroanisole have been studied by Fourier transform ion cyclotron resonance (FT-ICR). The main reactions are proton transfer, S_N2 substitution, and nucleophilic aromatic substitution leading to a F^- ion–molecule complex. The competition between proton transfer and nucleophilic displacement reactions has been probed by hydrogen–deuterium exchange reactions of the conjugate bases of 2-, 3-, and 4-fluoroanisole. In the 2- and 4-fluoroanisole cases exchange of the aryl hydrogen atoms *and* exchange of the hydrogen atoms of the methyl group are observed. A possible mechanism accounting for the exchange occurring at the methyl group is discussed.

There is growing interest in studying reactions between anions and molecules in the absence of solvents.[1,2] Detailed investigations of the mechanisms of gas-phase ion–molecule reactions have revealed that loose ion–molecule complexes held together by ion–dipole/ion–induced dipole interactions are formed before real chemical bonding oc-

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[1] (a) Nibbering, N. M. M. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 297–306. (b) Nibbering, N. M. M. In "Kinetics of Ion–Molecule Reactions"; Ausloos, P., Ed.; Plenum Press: New York, 1979; NATO ASI Vol. B40, pp 165–197.

[2] DePuy, C. H.; Bierbaum, V. M. *Acc. Chem. Res.* **1981**, *14*, 146–153.

curs.[3] Furthermore, there is increasing evidence that loose ion–molecule complexes formed by primary reactions can be sufficiently long lived to allow secondary reactions to occur before separating.[4,5] We have shown recently that in gas-phase reactions between various nucleophiles and some alkyl pentafluorophenyl ethers, F^- ion–molecule complexes are formed which play a decisive role in the formation of the final products.[5] These F^- ion–molecule complexes are formed by nucleophilic aromatic substitution taking place at the fluorine-bearing carbon atoms, but any information with regard to the site of nucleophilic attack relative to the methoxy substituent could not be obtained.

It is of central importance to gain insight into the competition between different channels which may be operative in gas-phase reactions between ions and molecules. For example, it has been concluded that exothermic proton transfer prevented nucleophilic aromatic substitution in gas-phase systems composed of alkoxides and difluorobenzenes.[6] We have observed in the cases of alkyl pentafluorophenyl ethers that nucleophilic aromatic substitution is favored over S_N2 substitution on the methyl group in the $C_6F_5OCH_3$ system[5] and over E_2 elimination at the ethyl group in the $C_6F_5OCH_2CH_3$ system.[7]

The present paper describes gas-phase reactions between anions and 2-, 3-, and 4-fluoroanisole. These compounds have been chosen partly to obtain information on the influence of the methoxy group on the nucleophilic aromatic substitution occurring at the fluorine-bearing carbon atom and partly to gain insight in the competition between processes such as proton transfer, S_N2 substitution, and nucleophilic aromatic substitution. The systems have been studied by Fourier transform ion cyclotron resonance (FT-ICR).[8]

Experimental Section

Experiments were performed by using the homemade Fourier transform ion cyclotron resonance (FT-ICR) spectrometer.[9,10] The sum of the partial pressures of the 2-, 3-, and 4-fluoroanisole, H_2O, and ROH (pressure ratio 1:1:1) was kept normally below 10^{-4} Pa. The partial pressure of D_2O for studying hydrogen–deuterium-exchange reactions was in some cases 2 times higher than the partial pressure of the 2-, 3-, and 4-fluoroanisoles. The pressures were measured only approximately on an uncalibrated ionization gauge placed in the side arm of the main pumping line.

General Procedure. The general operating procedure for our instrument has been described previously.[5,11,12] The OH^- and NH_2^- ions were generated by dissociative resonance capture of electrons with kinetic energies of 6 (H_2O, OH^- is formed via H^-) and 5 eV (NH_3). No primary negative ions from the 2-, 3-, and 4-fluoroanisoles were observed.

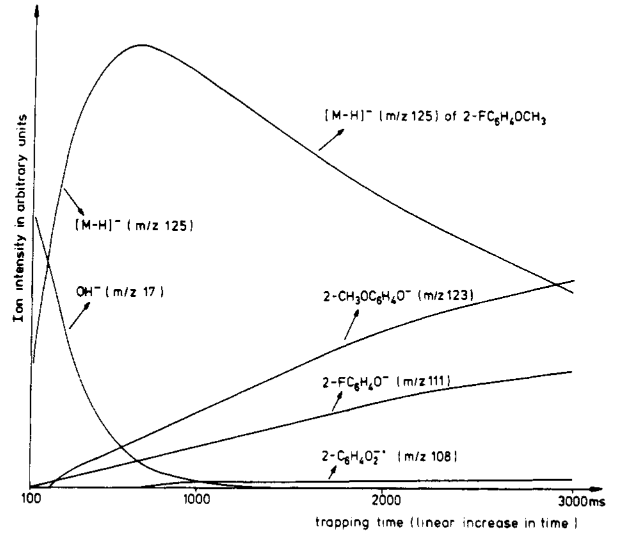

Figure 1. Intensities of reactant and product ions in the 2-fluoroanisole/OH^-/H_2O system followed as a function of trapping time. The trapping time was linearly increased from 100 to 3000 ms in 30 steps. The total ion current was stable in this case. The experimental conditions were as follows: $P(2\text{-}FC_6H_4OCH_3) = 4 \times 10^{-5}$ Pa; $P(H_2O)$ 7×10^{-5} Pa; magnetic field strength, 1.4 T; electron energy, 6 eV; emission current, 600 nA; recording of m/z 12–250 (see ref 5, 11, and 12).

The alkoxides were generated by exothermic proton transfer with OH^- as the base. The OH^- ions were ejected subsequently from the cell by a radio frequency (rf) pulse with an amplitude of 7.1 V_{p-p} and a duration of 20 ms. Product ions from reaction between OH^- and the 2-, 3-, and 4-fluoroanisole were ejected with a second rf pulse having an amplitude of 5 V_{p-p} and a duration of 20 ms. In all cases ejection experiments were used to establish the relationship between a precursor ion and its product ion(s).[12,13] Ejection of the alkoxide ions was achieved with an rf pulse (amplitude 2.5–7.1 V_{p-p}, duration 20 ms) starting after the ejection of the product ions from reaction between OH^- and 2-, 3-, and 4-fluoroanisole. Continuous ejection of a product ion, mostly the $[M - H]^-$ of the 2-, 3-, or 4-fluoroanisole, during the trapping time was carried out with an rf pulse of amplitude 0.9–2.5 V_{p-p}. Normally, this pulse did not remove completely the ^{13}C isotope peak of the $[M - H]^-$ ion from the spectra.

Materials. Most of the chemicals used were commercially available. The 2-, 3-, and 4-fluoroanisoles were purchased from Aldrich and used without further purification. Their identity was checked by ^1H NMR. $2\text{-}FC_6H_4OCD_3$, $3\text{-}FC_6H_4OCD_3$, and $4\text{-}FC_6H_4OCD_3$ (>99% d_3) were prepared by a Williamson ether synthesis carried out under mild conditions such as in acetone by using CO_3^{2-} as the base[14] and purified by preparative GC before use (column type OV-225, temperature 100–130 °C).

Results

The NH_2^-, OH^-, and RO^- (R = alkyl) ions react with 2-, 3-, and 4-fluoroanisole predominantly by proton transfer, S_N2 substitution on the methyl group, and nucleophilic aromatic substitution at the fluorine bearing carbon atom. The occurrence/nonoccurrence and apparent relative importance of these reaction channels are summarized in Table I (see also Figure 1). Other reactions such as IPSO substitution on the carbon atom substituted with the methoxy group and formation of a $C_6H_4F^-$ ion are observed in some cases to a minor extent.

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Table I. Occurrence/Nonoccurrence and Apparent Relative Importance[a] of Reaction Channels in the Anion/2-, 3-, and 4-Fluoroanisole Systems

anion	trapping time,[b] ms	reaction channel: proton transfer	reaction channel: S_N2	reaction channel: attack on fluorine-bearing carbon atom[c]	% conversion into products[d]
		$2\text{-}FC_6H_4OCH_3$			
NH_2^-	500	1.00			100
OH^- 1	1000	0.78	0.09	0.13	100
2	6500	0.12	0.29	0.59	100
CH_3O^-	500		0.74	0.26	50
$CH_3CH_2O^-$ [e]	6500		0.52	0.48	100
$CH_3CH_2CH_2O^-$ [e]	6500		0.54	0.46	88
$(CH_3)_2CHO^-$ [e]	6500		0.67	0.33	56
$(CH_3)_3CCH_2O^-$ [f]	6500		0.69	0.31	47
F^-	1000		1.00		100
		$3\text{-}FC_6H_4OCH_3$			
NH_2^-	500	1.00			100
OH^-	6500	0.91	0.09		100
CH_3O^-	6500	0.57	0.43		100
$CH_3CH_2O^-$ [e]	6500	0.35	0.61	0.04	90=
$CH_3CH_2CH_2O^-$ [e]	6500	0.07	0.85	0.08	83
$(CH_3)_2CHO^-$ [g]	6500	0.12	0.78	0.10	
$(CH_3)_3CCH_2O^-$ [f]	6500		1.00		32
		$4\text{-}FC_6H_4OCH_3$			
NH_2^-	500	1.00			100
OH^-	6500	0.77	0.23		100
CH_3O^-	6500		1.00		100
$CH_3CH_2O^-$ [e]	6500		1.00		59

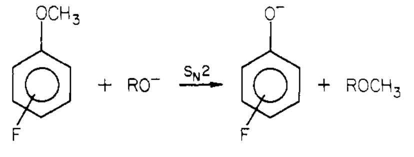
[a] Normalized to 1.00. [b] The trapping time is defined as the time delay between the start of the electron beam pulse and the start of the excitation pulse. [c] See the text and Table III. In the 3-fluoroanisole case the only observable product ion from this process is the $3\text{-}CH_3OC_6H_4O^-$ ion (*m/z* 123). [d] Conversion into products at a total pressure of approximately 10^{-4} Pa. [e] An $[M - 3]^-$ ion of the alcohol is observed (see: Caldwell, G.; Bartmess, J. E., *Int. J. Mass Spectrom. Ion Phys.* **1981**, *40*, 269–274. Boand, G.; Houriet, R.; Gäumann, T. *Adv. Mass Spectrom.* **1980**, *8*, 238–245). This ion constitutes in most cases 10–15% of the total ion current, but has been omitted from the calculation of the conversion into products. [f] An ion corresponding to $RO^- \cdots HOR$ is observed (see: Caldwell, G.; Bartmess, J. E. *J. Phys. Chem.* **1981**, *85*, 3571–3577). Under the conditions used this ion constitutes 25–40% of the total ion current but has been omitted from the calculation of the conversion into products. [g] The $[M - 3]^-$ ion of the alcohol is the major ion observed at the trapping time used.

Acidities. From bracketing experiments the following qualitative acidity order has been established: C_6H_6[15] < H_2O[16] < $C_6H_5OCH_3$[17] < C_6H_5F[17] < $2\text{-}FC_6H_4OCH_3 \approx 4\text{-}FC_6H_4OCH_3$ < CH_3OH[16] < $3\text{-}FC_6H_4OCH_3$ < CH_3SOCH_3.[16] A more accurate determination of the gas-phase acidity of 2-, 3-, and 4-fluoroanisoles is hampered by competitive processes and lack of compounds with a well-known gas-phase acidity between that of H_2O and CH_3OH.

Hydrogen-Deuterium Exchange Reactions. The qualitative gas-phase acidity data refer to the most acidic site within the 2-, 3-, and 4-fluoroanisole molecules. Hydrogen-deuterium exchange reactions with D_2O reveal that the $[M - H]^-$ ions (*m/z* 125) of 2- and 4-fluoroanisole can exchange up to 6 hydrogen atoms with deuterium atoms (see Discussion). The $[M - H]^-$ ion (*m/z* 125) from 3-fluoroanisole exchanges up to three hydrogen atoms with deuterium atoms when formed in the presence of D_2O. This behavior is in agreement with the observation that 3-fluoroanisole is more acidic in the gas phase than 2-fluoroanisole and 4-fluoroanisole. Low-resolution product ion spectra of the 2-, 3-, and 4-fluoroanisole/OD^-/D_2O systems are given in Figure 2.

Formation of $C_6H_4F^-$. When a strong gas-phase base such as NH_2^- reacts with 2-, 3-, and 4-fluoroanisole a $C_6H_4F^-$ ion (*m/z* 95) is formed (see Discussion). The abundance of the $C_6H_4F^-$ ion relative to that of the $[M - H]^-$ ion of the 2-, 3-, or 4-fluoroanisole is approximately 15% at trapping times around 100 ms. The $[C_6H_4F^-]$ decreases, however, with increasing trapping time because the 2-, 3-, and 4-fluoroanisoles are more acidic than fluorobenzene in the gas phase.

S_N2 Substitution. S_N2 substitution on the methyl group is observed for OH^- and RO^- (R = alkyl) but is negligible for NH_2^- (eq 1; Table I). In the 2-, 3-, and 4-fluoroanisole/OD^-/D_2O systems incorporation of deuterium atoms in the 2-, 3-, and 4-fluorophenoxide ions is observed (see Figure 2). For the 2- and 4-fluoroanisoles up to four deuterium atoms and for 3-fluoroanisole up to two deuterium atoms are incorporated in the corresponding fluorophenoxide ions. Furthermore, continuous ejection of the $[M - H]^-$ ions formed in the 2-, 3-, and 4-fluoroanisole/OH^-/H_2O systems and in the 3-fluoroanisole/CH_3O^-/CH_3OH system during the trapping time reduces the abundance of the product ion from the S_N2 substitution. In the 3-fluoroanisole/RO^-/ROH [R = CH_3CH_2, $CH_3CH_2CH_2$, $(CH_3)_2CH$] systems, where proton transfer is reversible, continuous ejection of the $[M - H]^-$



(1)

m/z 111

R = H, alkyl

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(15) Bohme, D. K.; Lee-Ruff, E.; Young, L. B. *J. Am. Chem. Soc.* **1972**, *94*, 5153–5159.

(16) The ΔH_{acid} values can be found in: Bartmess, J. E.; McIver, R. T., Jr. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 1 and 2, Chapter 11, pp 87–121.

(17) Unpublished results.

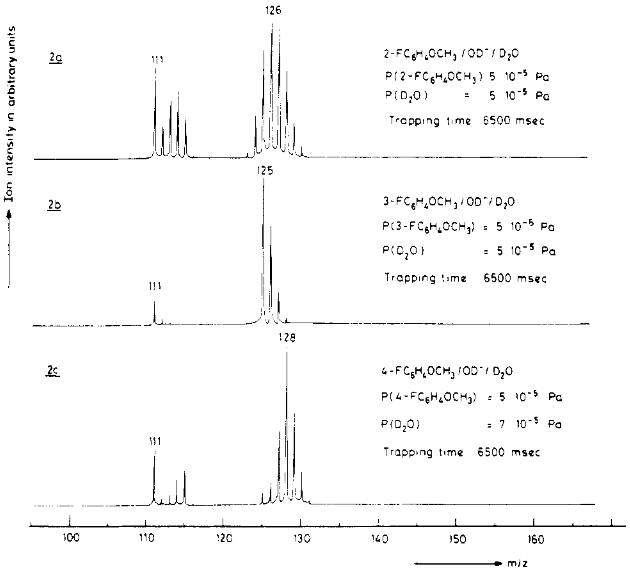


Figure 2. Low-resolution spectra of the 2-, 3-, and 4-fluoroanisole/OD^-/D_2O systems. The ions with *m/z* 111–115 are the S_N2 substitution product ions. The ions with *m/z* 125–131 are the conjugate bases of the 3- and 4-fluoroanisole. The *m/z* 131 ion in the case of 4-fluoroanisole can be seen more clearly at elevated pressures. The ions with *m/z* 123–130 in the 2-fluoroanisole case are mostly the product ions from nucleophilic aromatic substitution at the fluorine bearing carbon atom. This can be seen from the 2-fluoroanisole/OH^-/H_2O system where the abundance of the $[M - H]^-$ ions (*m/z* 125) relative to that of the $2\text{-}CH_3OC_6H_4O^-$ ions (*m/z* 123) is around 15% under similar pressure conditions. The experimental conditions were as follows: magnetic field strength, 1.4 T; emission current, 600 nA; electron energy, 6 eV; recording of *m/z* 85–250.

Table II. IPSO vs. S_N2 Substitution in the $^{18}OH^-$/2-, 3-, and 4-Fluoroanisole Systems[a]

system	% substitution S_N2 ($C_6H_4FO^-$)	IPSO ($C_6H_4F^{18}O^-$)
$2\text{-}FC_6H_4OCH_3$	87 ± 2	13 ± 2
$3\text{-}FC_6H_4OCH_3$	~99	~1
$4\text{-}FC_6H_4OCH_3$	93 ± 2	7 ± 2

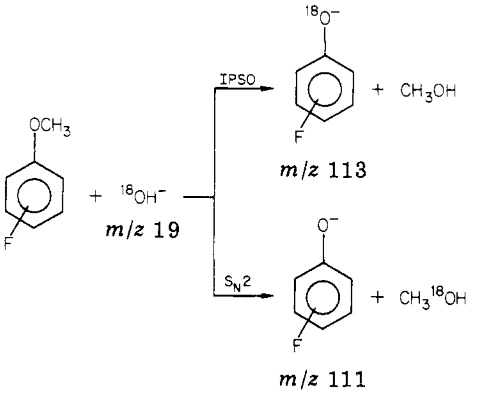
[a] Normalized to 100%; trapping time 6500 ms.

ions results in a decrease in the abundance of the S_N2 product ions.

IPSO Substitution. IPSO substitution on the carbon atom substituted with the methoxy group occurs to a minor extent for OH^- (Table II).[18] This process leads to the same products as the S_N2 substitution, but distinction can be achieved with the use of $^{18}OH^-$ as shown in eq 2 and 3. The $C_6H_4F^{18}O^-$ ion, however, cannot be observed when the $[M - H]^-$ ion of the 2-, 3-, and 4-fluoroanisole is ejected continuously from the cell.

Attack on the Fluorine-Bearing Carbon Atom. Nucleophilic aromatic substitution on the fluorine-bearing carbon atom is only important in the 2-fluoroanisole case (Table I). It is observed to a minor extent in some of the 3-fluoroanisole systems, but it is completely absent in the 4-fluoroanisole case (Table I). The apparently relative abundance of the various product ions arising from this reaction channel in the 2-fluoroanisole systems are given in Table III.

Attack of OH^- on the fluorine-substituted carbon atom leads to formation of a $2\text{-}CH_3OC_6H_4O^-$ ion (*m/z* 123). This ion incorporates up to seven deuterium atoms in the OD^-/D_2O system (see Figure 2a). Furthermore, $[2\text{-}CH_3OC_6H_4O^-]$ decreases to almost zero when the $[M - H]^-$ ion (*m/z* 125) of the 2-fluoroanisole is ejected continuously from the cell during the trapping time (see Experimental Section and Figure 1).

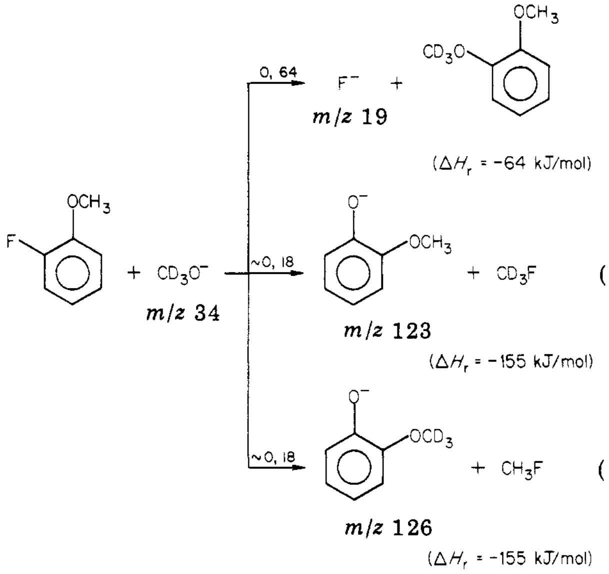


(2)

(3)

The $2\text{-}CH_3OC_6H_4O^-$ formed in the OH^-/H_2O system loses a methyl radical to a small extent (~2%) to form the radical anion of *o*-benzoquinone (*m/z* 108). In agreement with its assigned elemental composition, the *m/z* 108 ion shifts to *m/z* 110 in the $^{18}OH^-/H_2{}^{18}O$ system.

The possible products arising from initial attack on the fluorine-bearing carbon atom in the 2-fluoroanisole molecule are given in eq 4 and 5a,b for the case of CD_3O^-. The ΔH_r values have been calculated for CH_3O^- as the reactant ion.[19] The ratio of $[2\text{-}CH_3OC_6H_4O^-]$ and $[2\text{-}CD_3OC_6H_4O^-]$ is unity within experimental error. The generated F^- ion reacts with 2-fluoroanisole by S_N2 substitution (Table I). This obscures the results in Table I and prevents determination of the amount of F^- ion vs. $2\text{-}CH_3OC_6H_4O^-$ ion produced by the nucleophilic aromatic substitution process. All attempts to observe F^- as an ionic product in the other 2-fluoroanisole/RO^-/ROH systems have failed. In



(4)

(5a)

(5b)

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[18] Kleingeld, J. C.; Nibbering, N. M. M. *Tetrahedron Lett.* **1980**, *21*, 1687–1690.

[19] (a) ΔH_f ($2\text{-}FC_6H_4OCH_3$) = −266.6 kJ/mol, and ΔH_f ($2\text{-}CH_3OC_6H_4OCH_3$) = −230.2 kJ/mol, as calculated on the basis of group additivity rules (no ortho corrections): Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley: New York, 1976. (b) $\Delta H_f(CH_3F)$ = −233.9 kJ/mol, and $\Delta H_f(F^-)$ = −251.2 kJ/mol from: Rosenstock, H. M.; Draxl, K.; Steiner, B. W.; Herron, J. T. *J. Phys. Chem. Ref. Data, Suppl.* **1977**, *6*, 1. (c) $\Delta H_f(CH_3O^-)$ = −150.7 kJ/mol from ref 16. (d) $\Delta H_f(2\text{-}CH_3OC_6H_4O^-)$ = −338.6 kJ/mol, as calculated on the assumption that $\Delta H_{acid} = \Delta G_{acid}(2\text{-}CH_3OC_6H_4OH)$ = 1448 kJ/mol taken from: McMahon, T. B.; Kebarle, P. *J. Am. Chem. Soc.* **1977**, *99*, 2222–2230. This approximation is subject to a quite large error but does not change any conclusions reached.

Table III. Relative Importance of Product Ions Arising from Nucleophilic Attack on the Fluorine Substituted Carbon Atom in the 2-Fluoroanisole Molecule[a]

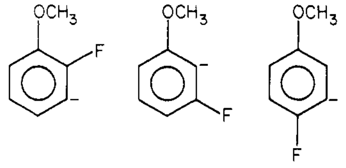
	reattack of the F^- ion by[b]			
anion	proton transfer ($2\text{-}CH_3OC_6H_4O^-$)	E2 ($2\text{-}CH_3OC_6H_4O^-$)	S_N2 ($2\text{-}ROC_6H_4O^-$)[d]	formation of F^- ion[c]
OH^-	1.00			
CH_3O^-			0.39	0.61
CD_3O^-			0.18/0.18[e]	0.64
$CH_3CH_2O^-$		0.97	0.03	
$CH_3CH_2CH_2O^-$		0.96	0.04	
$(CH_3)_2CHO^-$		1.00		
$(CH_3)_3CCH_2O^-$			1.00[f]	

[a] Normalized to 1.00. See Table I for experimental conditions. [b] See text. [c] See text and eq 4. [d] R = alkyl. [e] R = CH_3 and CD_3; see eq 5a,b. [f] R = $(CH_3)_3CCH_2$.

the $(CH_3)_3CCH_2O^-$ case a small amount of possibly generated F^- might not be observable due to reaction with either 2-fluoroanisole (see Table I) or with $(CH_3)_3CCH_2OH$ by proton transfer.[20]

Discussion

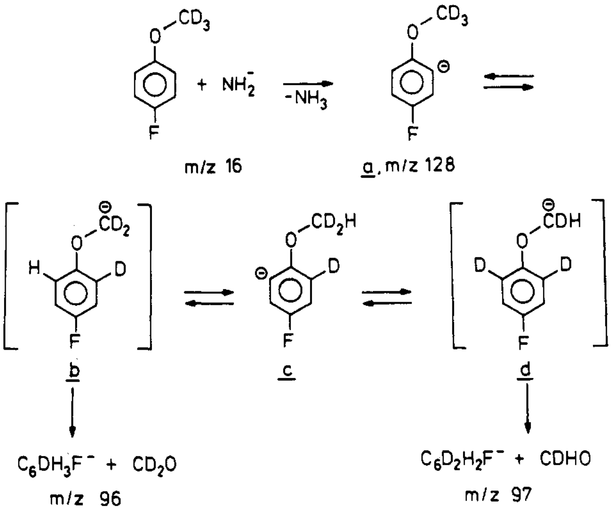
Acidities. The acidity order found (vide supra) refers to the most acidic site within the molecules[21] and permits the conclusion that both the methoxy group and the fluorine atom stabilize the localized negative charge. The more electronegative fluorine atom will contribute more to this stabilization, so that the most stable structures of the conjugate bases of 2-, 3-, and 4-fluoroanisole are expected to be as shown below. The stabilization of the



localized negative charge by the fluorine atom and the methoxy group arises through combined inductive and field effects as seen in the σ_I substituent constant and the value of the $\mathcal{F}$ parameter in the Swain–Lupton equation for F ($\sigma_I = 0.50$, $\mathcal{F} = 0.71$) and for CH_3O ($\sigma_I = 0.27$, $\mathcal{F} = 0.41$).[22] The maximum stabilization arises when the charge is in the 2-position with respect to both substituents as seen in the higher gas-phase acidity of 3-fluoroanisole compared to those of 2- and 4-fluoroanisole.

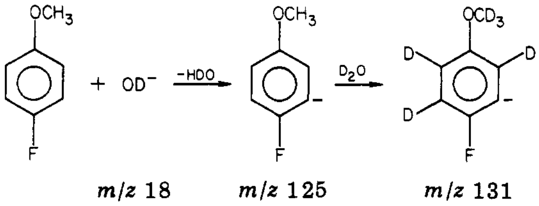
Formation of the $C_6H_4F^-$ Ion. The NH_2^- ion reacts with 2-, 3-, and 4-fluoroanisole by proton transfer and formation of the conjugate base of fluorobenzene. Reaction between NH_2^- and $4\text{-}FC_6H_4OCD_3$ results in the $[M - H]^-$ ion (*m/z* 128) and the product ions $C_6DH_3F^-$ (*m/z* 96) and $C_6D_2H_2F^-$ (*m/z* 97). The ratio $[C_6DH_3F^-]$ to $[C_6D_2H_2F^-]$ is unity within experimental error. The same result is obtained when NH_2^- reacts with $3\text{-}FC_6H_4OCD_3$. In the $2\text{-}FC_6H_4OCD_3$ case only the $C_6DH_3F^-$ ion (*m/z* 96) and the $[M - H]^-$ ion (*m/z* 128) are formed. The proposed mechanism accounting for formation of $C_6DH_3F^-$ and $C_6D_2H_2F^-$ is shown in Scheme I.

Scheme I. Proposed Mechanism for Formation of the $C_6DH_3F^-$ and $C_6D_2H_2F^-$ Ions in the $4\text{-}FC_6H_4OCD_3/NH_2^-/NH_3$ System



The important observation here is that there is an equilibration between the three deuterium atoms of the methyl group and the ortho hydrogen atom prior to the loss of formaldehyde. The intermediate carbanion (ion b or d in Scheme I) must live sufficiently long to allow this equilibration before fragmentation into $C_6DH_3F^-$ and $C_6D_2H_2F^-$ occurs.

Hydrogen–Deuterium Exchange Reactions. Hydrogen–deuterium exchange reactions between anions and deuterated reagents have proven to be a valuable method in probing mechanisms of ion–molecule reactions and structures of ions in the gas phase[23,24] and in solving analytical problems.[25] In this study exchange of up to six hydrogen atoms with deuterium atoms is observed when the conjugate bases of 2- and 4-fluoroanisole are formed in the presence of D_2O (see Figure 2 and Competition between Reactions Channels). This can only mean that the aryl hydrogen atoms *and* the hydrogen atoms of the methyl group participate in the exchange reactions (eq 6).



(6)

Following the hydrogen–deuterium-exchange reactions of the conjugate base of 4-fluoroanisole as a function of

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[20] HF (ΔH_{acid} = 1555 kJ/mol) is only slightly more acidic in the gas phase than $(CH_3)_3CCH_2OH$ (ΔH_{acid} = 1556 kJ/mol) (see ref 16).

[21] For a solution chemistry study on the relative acidity of the 2-, 3-, and 4-positions in some substituted benzenes, see: Hall, G. E.; Piccolini, R.; Roberts, J. D. *J. Am. Chem. Soc.* **1955**, *71*, 4540–4543.

[22] (a) The σ_I values have been taken from: Hine, J. "Structural Effects on Equilibria in Organic Chemistry"; Wiley: New York, 1975. (b) The $\mathcal{F}$ values have been taken from: Swain, G. C.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328–4337.

[23] (a) Stewart, J. H.; Shapiro, R. H.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 7650–7653. (b) DePuy, C. H.; Bierbaum, V. M.; King, G. K.; Shapiro, R. H. *Ibid.* **1978**, *100*, 2921–2922. (c) Squires, R. R.; DePuy, C. H.; Bierbaum, V. M. *Ibid.* **1981**, *103*, 4256–4258.

[24] Noest, A. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1980**, *102*, 6427–6429.

[25] Hunt, D. F.; Sethi, K. S. *J. Am. Chem. Soc.* **1980**, *102*, 6953–6963.

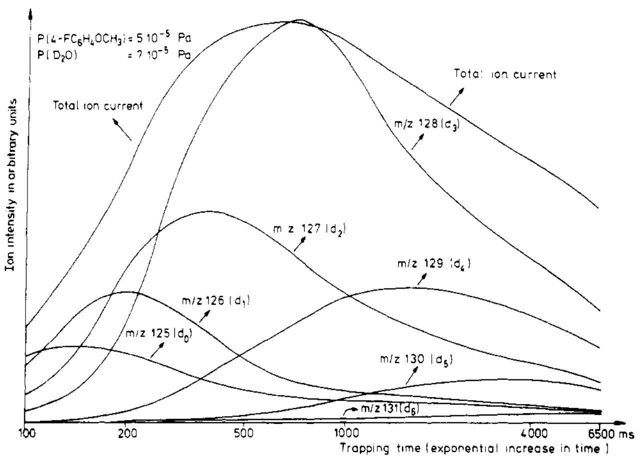


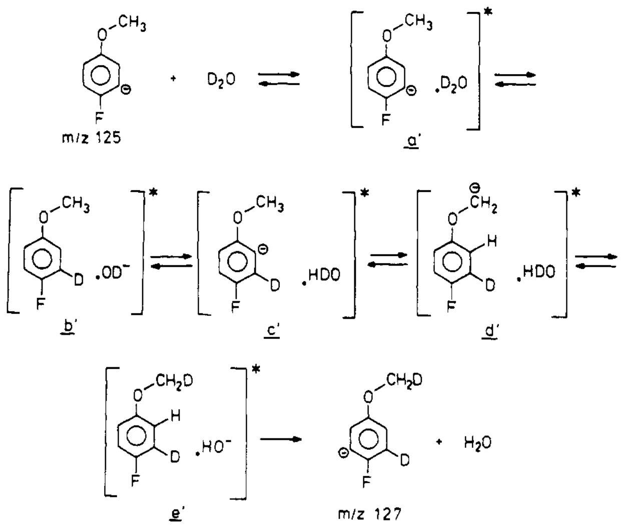
Figure 3. Hydrogen–deuterium exchange reactions of the [M – H]$^-$ ion from 4-fluoroanisole followed as a function of trapping time. The trapping time was increased exponentially from 100 to 6500 ms in 35 steps. The number of incorporated deuterium atoms has been indicated in parentheses. The total ion current increases initially since OD$^-$ is not being detected. The decrease in total ion current at longer trapping times indicates ion loss from the cell probably promoted by the high pressures. The experimental conditions were as follows: $P(4\text{-}FC_6H_4OCH_3) = 5 \times 10^{-5}$ Pa; $P(H_2O) = 7 \times 10^{-5}$ Pa; magnetic field strength, 1.4 T; electron energy, 6 eV; emission current, 600 nA; recording of m/z 85–250.

trapping time (Figure 3) shows that the two types of hydrogen atoms exchange with different rates. Exchange reactions in the conjugate base of 4-FC$_6$H$_4$OCD$_3$ with either H$_2$O or D$_2$O reveal that the aryl hydrogen atoms exchange at a much higher rate than the methyl hydrogen atoms. Similar experiments with the conjugate base of 3-FC$_6$H$_4$OCD$_3$ prove that only aryl hydrogen atoms undergo exchange.

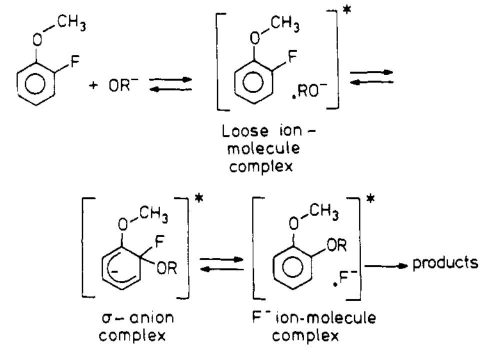
It has been concluded that for exchange of different types of hydrogen atoms within a carbanion the difference in acidity of the hydrogen atoms should be less than 80 kJ/mol.[23c] The gas-phase acidity of the aryl hydrogen atoms in the 4-fluoroanisole molecule can be placed at ~1616 kJ/mol (see Results). This could imply that the upper limit for the gas-phase acidity of the methyl hydrogen atoms is ~1700 kJ/mol.

The results from the reaction between NH$_2^-$ and 2-, 3-, and 4-FC$_6$H$_4$OCD$_3$ show that proton transfer only occurs from the ring positions. The exothermicity associated with this process is apparently large enough that an intramolecular deuteron transfer leading to a short-lived primary carbanion can take place (see Scheme I). Although no C$_6$H$_4$F$^-$ ions are formed in the reaction with OH$^-$, this might lend partial support to the most simple rationalization of the hydrogen–deuterium exchange of the methyl hydrogen atoms, which is as follows: Part of the excess internal energy of about 40–80 kJ/mol gained upon formation of the ion–molecule complex of the conjugate base of 4-fluoroanisole and D$_2$O may drive endothermic proton transfers between these species and an unfavored *intramolecular* proton transfer from the methyl group to the deprotonated 2-position of the aromatic ring. This has been visualized in Scheme II.

Scheme II. Proposed Mechanism for the Exchange of the Hydrogen Atoms on the Methyl Group with Deuterium Atoms in the 4-Fluoroanisole/OD$^-$/D$_2$O System



Scheme III. Formation of the F$^-$ Ion-Molecule Complex



Nucleophilic Aromatic Substitution. Gas-phase nucleophilic aromatic substitutions have received rather limited attention.[5,6,18,26] The presently known examples can best be described as proceeding by the addition–elimination pathway, that is the S$_N$Ar mechanism.[27] Although the methoxy group retards nucleophilic aromatic substitutions in solution,[27a] attack on the fluorine-bearing carbon atom is nearly equally as important as the S$_N$2 substitution in the 2-fluoroanisole systems (Table I). In the 3- and 4-fluoroanisole systems nucleophilic aromatic substitution either occurs only to a very minor extent or does not occur at all (Table I).

The fluorine-substituted carbon atom will have the highest electropositive character in the 2-fluoroanisole molecule since the inductive and field effects operate more effectively from the 2-position with respect to the fluorine atom. The situation for the carbon atom substituted with the methoxy group will be similar, of course.

The high amount of nucleophilic aromatic substitution observed in the 2-fluoroanisole systems (Table I; see also Table II for IPSO substitution) can then be explained with the assumption that the coulombic interaction between the nucleophile and the electropositive center is the controlling factor in the reaction. The electropositive character of the fluorine-bearing carbon atom will be decreased in the 3- and 4-fluoroanisoles. The energy barrier toward nucleophilic attack on this carbon atom might be raised therefore,

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(26) (a) Bowie, J. H.; Stapleton, B. J. *Aust. J. Chem.* **1977**, *30*, 795–800. (b) Bruins, A. P.; Ferrer-Correia, A. J.; Harrison, A. G.; Jennings, K. R.; Mitchum, R. K. *Adv. Mass Spectrom.* **1977**, *7*, 355–358. (c) Dzidic, I.; Carroll, D. I.; Stilwell, R. N.; Horning, E. C. *Anal. Chem.* **1975**, *77*, 1308–1312.

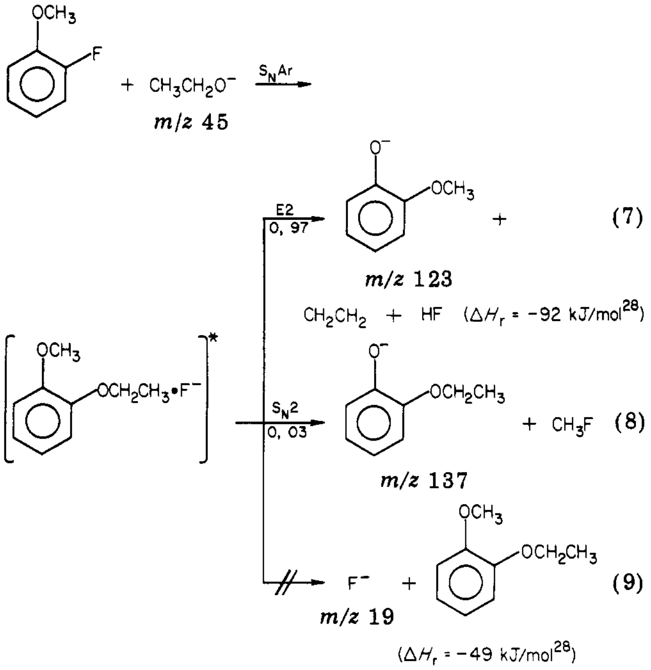
(27) (a) Miller, J. "Aromatic Nucleophilic Substitution"; Elsevier: Amsterdam, 1968. (b) Bernasconi, C. F. *Chimia* **1980**, *34*, 1–11.

(28) $\Delta H_f(2\text{-}CH_3OC_6H_4OCH_2CH_3) = -263.6$ kJ/mol, as calculated on the basis of group additivity rules (no ortho correction) (see ref 19a). $\Delta H_f(HF) = -271.3$ kJ/mol, and $\Delta H_f(CH_2CH_2) = 52.3$ kJ/mol from ref 19a. $\Delta H_f(CH_3CH_2O^-) = -198.9$ kJ/mol from ref 16.

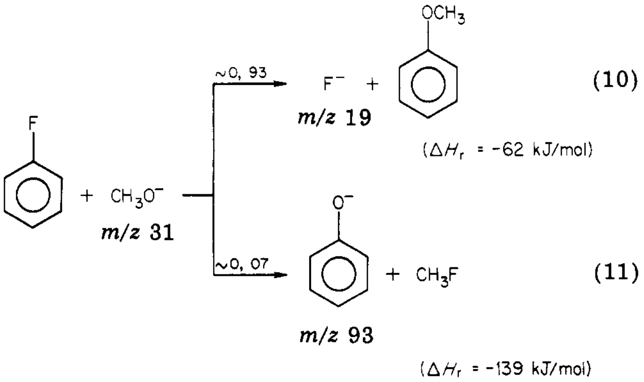
and S_N2 substitution on the methyl group occurs instead (Table I).

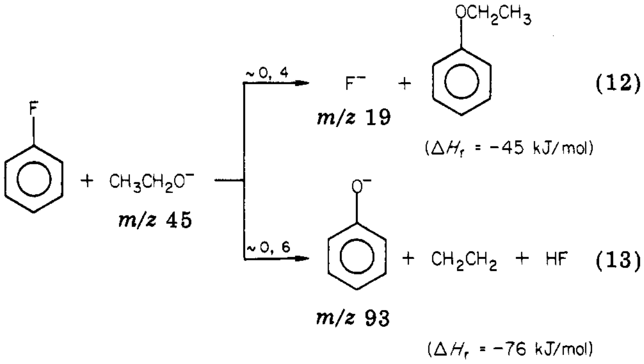
In the alkyl pentafluorophenyl ether systems attack on the fluorine-substituted carbon atom was shown to lead to formation of an F^- ion–molecule complex whose lifetime was long enough to allow reattack by the displaced F^- ion upon the newly formed molecule.[5] The results given in Table III (see also eq 4 and 5a,b) show also that F^- ion–molecule complexes are formed in the case of 2-fluoroanisole as a consequence of nucleophilic attack on the fluorine bearing carbon atom. The mechanism accounting for formation of these complexes is shown in Scheme III and has been discussed previously in detail for the alkyl pentafluorophenyl ether systems.[5]

In most of the 2-fluoroanisole systems all the final product ions arise from reattack of the displaced F^- ion, which reacts by either proton transfer, S_N2 substitution, or E2 elimination (Table III). In the 2-fluoroanisole/CH_3O^- system both F^- and $2\text{-}CH_3OC_6H_4O^-$ ions are produced (see eq 4 and 5a,b). The latter ion is formed by an S_N2 substitution occurring within the F^- ion–molecule complex. E2 elimination occurs preferentially in this complex when the primary reactant ion contains β-hydrogen atoms (eq 7–9; see Table III). No F^- ions are observed, although reaction 9 is exothermic. Reattack of the F^- ion by E2 elimination is favored by an increase in entropy.



When C_6H_5F is used instead of 2-fluoroanisole, reaction with CH_3O^- and $CH_3CH_2O^-$ leads under our experimental conditions to the products given in eq 10–13.[29] The ΔH_r values of these reactions can be seen not to be greatly different from the values for the similar reactions in the 2-fluoroanisole system.[30]





These observations illustrate several points. First, it is important to stress that the competition between reaction channels available for an ion–molecule complex can be described by the RRKM theory only, if the nonfixed energy is completely randomized within the complex and if all microscopic pathways leading to products have an equal probability.[31]

Applying the RRKM theory in a qualitative way to the present situation, the dissociation of the F^- ion–molecule complex can be described as proceeding through a loose transition state, whereas reattack, for example by S_N2 substitution, will involve a tight transition state. In the 2-fluoroanisole/CH_3O^- system dissociation (eq 4) can be seen to dominate over reattack by S_N2 substitution (eq 5). In the 2-fluoroanisole/$CH_3CH_2O^-$ system, where reattack by E2 elimination is possible, dissociation into F^- as an ionic product is apparently absent (Table III and eq 7 and 8).

If the rates of dissociation of the F^- ion–molecule complexes are assumed to be comparable in the two cases, this would indicate that the E2 elimination forming the $2\text{-}CH_3OC_6H_4O^-$ ion in the $CH_3CH_2O^-$ case competes more effectively with this dissociation than the S_N2 substitution forming the same ion in the CH_3O^- case. This can be explained by a "looser" structure and/or a lower energy of the transition state in the E2 elimination compared to that in the S_N2 substitution. Although more detailed knowledge concerning the potential energy surface describing the elimination reaction is necessary to determine which factor will be more important, the result is a further confirmation of the facility of E2 eliminations compared to S_N2 substitution in gas-phase ion–molecule reactions.[4b,5,18]

In the fluorobenzene/$CH_3CH_2O^-$ system the competition between dissociation of the F^- ion–molecule complex and

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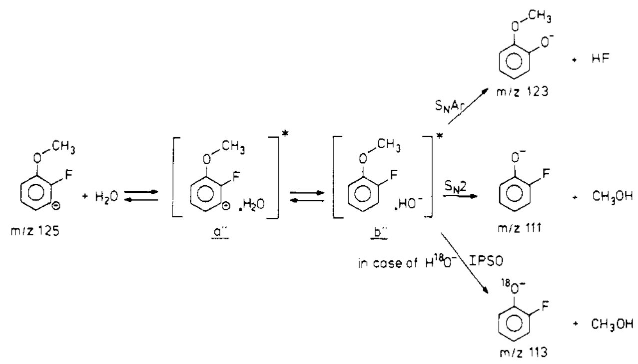
(29) These results are in some contradiction with those presented in ref 6. The discrepancy might be due to improved instrumentation in the present case. The present experiments were carried out under similar conditions as for the 2-, 3-, and 4-fluoroanisoles. The trapping time was 6500 ms. Conversion into products at a total pressure of about 10^{-4} Pa was approximately 65% for CH_3O^- as reactant ion and around 25% for $CH_3CH_2O^-$. In the last case a $[M - 3]^-$ ion of the alcohol was observed. This ion constituted approximately 36% conversion, but has been omitted from the calculation of conversion into products (see also notes to Table I). The amount of F^- ion produced might be higher than that given if the $[M - 3]^-$ ion arises through pyrolysis of CH_3CH_2OH leading to CH_3CHO (see notes to Table I).

(30) $\Delta H_f(C_6H_5F) = -113.4$ kJ/mol, and $\Delta H_f(C_6H_5OCH_3) = -75.3$ kJ/mol. $\Delta H_f(C_6H_5OCH_2CH_3) = -106.3$ kJ/mol, as taken from: Benson, S. W.; Cruickshank, F. R.; Golden, D. M.; Haugen, G. R.; O'Neal, H. E.; Rodgers, A. S.; Shaw, R.; Walsh, R. *Chem. Rev.* **1969**, *69*, 279–324. $\Delta H_f(C_6H_5O^-) = -169.5$ kJ/mol from ref 16.

(31) Robinson, P. J.; Holbrook, K. A. "Unimolecular Reactions"; Wiley-Interscience: New York, 1972.

Scheme IV. Indirect S_NAr, S_N2, and IPSO Substitution in the 2-Fluoroanisole/OH^-/H_2O System



reattack by E2 elimination is changed. This could be explained by a slightly higher transition-state energy for the E2 elimination caused by a change in leaving group from $2\text{-}CH_3OC_6H_4O^-$ to $C_6H_5O^-$. However, it should be pointed out that there will only be a real competition between dissociation of the F^- ion-molecule complex and the various modes of reattack by F^- when the lifetime of the F^- ion-molecule complex is sufficiently long to randomize the energy within the complex. This again will be determined by the detailed dynamics of the reaction forming the F^- ion-molecule complex and the magnitude of the ion-dipole/ion-induced dipole interactions between the F^- ion and the molecule.

Competition between Reaction Channels. Exothermic transfer of a proton to small anions having localized charges has been observed to occur essentially with a rate equal to the collision rate in gas-phase ion-molecule systems.[32] The intervention of an intrinsic energy barrier toward reaction has been documented for gas-phase S_N2 substitution[3a,33] and has been used also to explain the low reaction efficiency of several exothermic S_N2 substitutions.[3a] In gas-phase ion-molecule reactions, where exothermic proton transfer is occurring, one might therefore expect that this reaction completely suppresses a possible S_N2 substitution[34] irrespective of whether the latter process has a higher exothermicity.

The present results prove that proton transfer to the reactant ion precedes S_N2 substitution (to a large extent), IPSO substitution, and nucleophilic attack on the fluorine-bearing carbon atom. Scheme IV illustrates this for the 2-fluoroanisole/OH^-/H_2O system (see also Figure 1).

Within complex b″, which has insufficient energy to dissociate, there is a competition between a proton transfer reaction leading back to a″ and nucleophilic displacement reactions. The exothermic proton transfer leading to a″ will be faster than the nucleophilic substitutions as envisaged in the high amount of deuterium incorporation in the product ions (see Figure 2). The incorporation of up to seven deuterium atoms within the $2\text{-}CH_3OC_6H_4O^-$ ion can only mean that the conjugate base of 2-fluoroanisole can exchange all the hydrogen atoms with deuterium atoms. From the bracketing experiments the initial proton transfer in the 2-fluoroanisole/OH^-/H_2O system can be seen to occur with a maximal ΔH_r of −49 kJ/mol. The S_N2 substitution reaction (eq 3) with OH^- can be calculated to have a ΔH_r of around −185 kJ/mol.[35] The heat of reaction, ΔH_r, of the reaction in which $2\text{-}CH_3OC_6H_4O^-$ is formed can be calculated to be approximately −206 kJ/mol.[35] This means that the initial proton transfer forming the conjugate base of 2-fluoroanisole is kinetically favored. The conjugate base undergoes reactions to form the thermodynamically more stable products (see Figure 1). The important aspect of these results is that, although the initial proton transfer is essentially irreversible, the formation of complex a″ in Scheme IV is associated with a gain in nonfixed energy sufficiently large to carry out an endothermic proton transfer followed by nucleophilic displacement reactions. This situation applies equally well to the 4-fluoroanisole/OH^-/H_2O and 3-fluoroanisole/CH_3O^-/CH_3OH systems. In the 3-fluoroanisole/RO^-/ROH cases, where formation of the conjugate base of 3-fluoroanisole is reversible, there will be an increase in the abundance of the more slowly formed products with increasing trapping time.

Increasing the acidity difference between the substrate and the conjugate acid of the reactant ion causes a higher endothermicity for formation of a complex equivalent to b″ in Scheme IV. This will be the case in the 3-fluoroanisole/OH^-/H_2O system, which explains the smaller amount of S_N2 substitution (Table I), the minor amount of deuterium atoms incorporated in the S_N2 product ion (Figure 2), and the very minor amount of IPSO substitution in this system (Table II). This situation is also met in the fluoroanisole/NH_2^-/NH_3 systems, where only proton transfer and formation of $C_6H_4F^-$ are observed.

In view of the proposed mechanism accounting for the hydrogen-deuterium exchange occurring at the methyl group (Scheme II) and the observation that part of the S_N2 substitution takes place as outlined in Scheme IV, reaction between 2- or $4\text{-}FC_6H_4OCD_3$ and OH^-/H_2O could be expected to lead to incorporation of deuterium atoms in the S_N2 product ion. This is not observed in these cases.[36] The larger acidity difference between 2- or 4-fluoroanisole and H_2O (see Acidities) is likely to increase the rate of dissociation of complex a′ or c′ (Scheme II) and a″ (Scheme IV) and cause back-reaction from b′ to a′ (Scheme II) and also from b″ to a″ (Scheme IV) to be exceedingly fast compared to the S_N2 substitution occurring within the ion-molecule complexes.

Conclusions

The dominant reactions between anions and 2-, 3-, and 4-fluoroanisole in the gas phase are proton transfer, S_N2 substitution, and nucleophilic aromatic substitution. Hydrogen-deuterium-exchange reactions between the conjugate bases of 2-, 3-, and 4-fluoroanisole and D_2O show in the cases of 2- and 4-fluoroanisole that exchange of the aryl hydrogen atoms *and* the methyl hydrogen atoms occurs. The mechanism of the exchange of the methyl hydrogen atoms is likely to be a slow intramolecular process leading to a short-lived primary carbanion which rapidly abstracts a deuteron from the D_2O present in the ion-molecule complex.

Exothermic proton transfer to the reactant ion is kinetically favored. Nucleophilic displacement reactions

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[32] Mackay, G. I.; Betowski, L. D.; Payzant, J. D.; Schiff, H. I.; Bohme, D. K. *J. Chem. Phys.* **1976**, *80*, 2919–2922.

[33] Riveros, J. M.; Breda, A. C.; Blair, L. K. *J. Am. Chem. Soc.* **1973**, *95*, 4066–4067.

[34] Beauchamp, J. L. In "Interactions between Ions and Molecules"; Ausloos, P., Ed.; Plenum Press: New York, 1974; NATO ASI Vol. B6, pp 413–444.

[35] $\Delta H_f(OH)^-$ = −137.4 kJ/mol from ref 19b. $\Delta H_f(CH_3OH)$ = −200.9 kJ/mol from ref 19a. $\Delta H_f(2\text{-}FC_6H_4O^-)$ = −387.6 kJ/mol, as calculated on the assumption that $\Delta H_{acid} = \Delta G_{acid}(2\text{-}FC_6H_4OH)$ = 1436 kJ/mol (see ref 19d).

[36] Preliminary experiments with $C_6H_5OCD_3$ and OH^- (generated either via reaction between $O^{-\cdot}$ and *n*-hexane or from H_2O) indicate that one and two deuterium atoms can be incorporated in the S_N2 substitution product ion. Kleingeld, J. C. Thesis at the University of Amsterdam, to be submitted for publication.

occur even in systems where the initial proton transfer is irreversible in a classical sense. This can be explained by a gain in nonfixed energy when the ion approaches the molecule which is sufficient to drive an endothermic proton transfer and to overcome the energy barrier toward nucleophilic displacement. Nucleophilic aromatic substitution at the fluorine bearing carbon atom is only important compared to S_N2 substitution in the 2-fluoroanisole case. This can be taken as an indication that the controlling factor in the reaction is the interaction between the entering nucleophile and the electropositive fluorine-substituted carbon atom.

Attack on the fluorine-bearing carbon atom in the 2-fluoroanisole leads to formation of an F^- ion–molecule complex whose lifetime is long enough to allow reattack on the newly formed molecule. The results obtained further confirm the importance of relatively long-lived ion–molecule complexes formed by primary reactions in gas-phase ion–molecule systems.

Acknowledgment. We thank the Netherlands Organization for Pure Research (SON/ZWO) for financial support.

Registry No. 2-$FC_6H_4OCH_3$, 321-28-8; 3-$FC_6H_4OCH_3$, 456-49-5; 4-$FC_6H_4OCH_3$, 459-60-9; NH_2^-, 17655-31-1; OH^-, 14280-30-9; CH_3O^-, 3315-60-4; $CH_3CH_2O^-$, 16331-64-9; $CH_3CH_3CH_2O^-$, 26232-83-7; $(CH_3)_2CHO^-$, 15520-32-8; $(CH_3)_3CCH_2O^-$, 55091-58-2; F^-, 16984-48-8; CD_3O^-, 51679-31-3.

Reactions of Aryl Diazonium Salts and Alkyl Arylazo Ethers. 9.[†] Studies of the Carbanionic and Free Radical Mechanisms of Dediazoniation of Substituted 2-Chlorobenzenediazonium Salts

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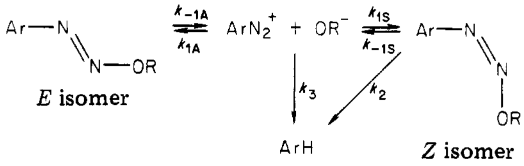
Rate constants for both the decomposition and the *Z–E* interconversion of some substituted 2-chlorophenylazo ethyl ethers in ethanol are reported. In addition, product studies of the decomposition of (2-chlorophenyl)azo methyl ether in the presence of 1,1-diphenylethene and di-*tert*-butyl nitroxide were carried out. On the basis of these results, mechanisms for both anionic and free radical dediazoniation in the basic alcoholic solvents are proposed. A common intermediate, the aryl diimide, formed as a result of hydride ion abstraction from alkoxide ions by the electrophilic terminal nitrogen of the diazonium salt, is proposed for both the anionic and the free radical mechanisms of dediazoniation. The anionic mechanism results from proton abstraction from the aryl diimide by the alkoxide ion. The free radical mechanism results from hydrogen atom abstraction from the aryl diimide by free radicals in solution.

When an aromatic diazonium salt is dissolved in a basic alcoholic solution, the major initial product is the alkyl (*Z*)-arylazo ether.[1,2] This *Z* isomer is, however, unstable, and subsequently it is converted either to the more thermodynamically stable *E* isomer or to the dediazoniation product (ArH, Scheme I).

It has previously been shown that the dediazoniation process can involve either free radical or anionic intermediates.[3] For example reaction in monodeuteriomethanol (CH_3OD) gives rise to deuterated products (ArD) if the reaction involves aryl anion intermediates whereas nondeuterated products (ArH) are formed by the radical mechanism.[3]

The mechanism in a given case depends on the base concentration[3] and on the substituent on the aromatic ring.[3] For all compounds studied to date, reaction of equimolar amounts of diazonium and alkoxide ions result in dediazoniation by the free radical mechanism. In the presence of an excess of alkoxide ions the mechanism depends on the substituent on the aromatic ring. For compounds carrying electron-donating or only weakly electron-withdrawing substituents (e.g., 4-OMe, 4-Me, unsubstituted, or 4-F), the free radical mechanism is observed.[3] For compounds carrying more strongly electron-withdrawing substituents (e.g., 2-Cl, 3-Cl, and 3-NO_2), the ionic mechanism becomes important.[3] In what might be considered the extreme case, compounds carrying either a 2-NO_2 or a 4-NO_2 substituent, reaction by a radical mechanism is observed.[3] It is of interest to determine why the mechanism changes as the substituent is changed. In an attempt to cast some light onto this problem it is necessary to determine for each mechanism whether dediazoniation occurs directly on the *Z* ether or whether prior ionization to the free diazonium ion is required.

Scheme I



From studies of the effect of the solvent on the rate of dediazoniation it had previously been concluded that dediazoniation occurs on the (*Z*)-arylazo ether.[1,4] It was found that reactions involving ionization of alkyl arylazo ethers [k^{-1A}, k^{-1S}, and k_{Z-E}(interconversion)] occur much faster in more polar solvents (e.g., methanol) than in less polar solvents (e.g., ethanol).[1,4] Since the rate of dediazoniation was found to be slightly faster in ethanol than

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