

- (11) Our detection ability would reveal <0.1% yield of such products.
 (12) These work-up procedures are simple compared with those described for hydroboration sequences in which mixtures of products can be obtained and in which a final reduction step is necessary to generate the aldehyde; see, for example, H. C. Brown, "Boranes in Organic Chemistry," Cornell University Press, Ithaca, N.Y., 1972, Chapter XVII.
 (13) For example, see U. Belluco, G. Deganello, R. Pietropaolo, and P. Ugugliati, *Inorg. Chim. Acta, Rev.*, **4**, 7 (1970), and references cited therein.
 (14) Similar reactions occur for Ti analogs; see J. X. McDermott and G. M. Whitesides, *J. Amer. Chem. Soc.*, **96**, 947 (1974).
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 (16) For example, see K. M. Nicholas and M. Rosenblum, *J. Amer. Chem. Soc.*, **95**, 4449 (1973).
 (17) C. W. Bird, "Transition Metal Intermediates in Organic Synthesis," Academic Press, New York, N.Y., 1966, Chapter 6 and 7.
 (18) For example, see R. A. Schunn, *Inorg. Chem.*, **9**, 2567 (1970).
 (19) NOTE ADDED IN PROOF. Yields of carboxylic acids or esters produced from **3** can be substantially improved by treatment of **3** with NBS (to give the acyl bromide) followed by water or alcohols, respectively.

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Received September 6, 1974

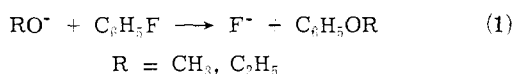
Gas Phase Nucleophilic Reactions of Aromatic Systems

Sir:

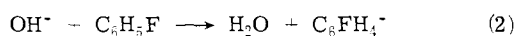
Gas phase ion-molecule reactions have attracted the attention of a wide range of chemists as a means to investigate the interplay of structure and reactivity in the absence of a solvent. A particular point of interest along these lines, and as yet little explored, is to what extent substituent effects observed in solution can be regarded as a true manifestation of intrinsic behavior.¹

Nucleophilic displacement of halides in aromatic systems provide a particularly good case for a direct comparison of substituent effects in solution and in the gas phase. These reactions are known to be subject to dramatic rate enhancements in solution in the presence of electron attracting groups.^{2,3} In an extreme case, acceleration factors of 10⁸ have been reported for polyfluoro compounds with respect to the monofluoro species.^{4,5} In the gas phase, the present communication shows that attack by alkoxide ions on fluoro-substituted benzenes gives rise to a fast ion-molecule reaction leading to a substituted phenoxide ion. Icr techniques have been used to study these processes.⁶

Methoxide and ethoxide ions react slowly with fluorobenzene in the gas phase *via* reaction 1. (See Table I.) Hydrox-

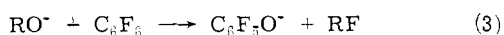


ide ions in turn undergo preferentially the acid-base reaction (2). Observation of C₆FH₄⁻ as originating *only* from



OH⁻, and the inability to detect F⁻ by collision induced decomposition,⁷ is taken as partial support against a benzyne mechanism for reaction 1.

When these same nucleophiles are used with hexafluorobenzene, fluoride displacement suffers no appreciable acceleration. Reaction 3 is found instead to be fast and to



yield a somewhat unexpected product.⁸ Typical rate constants for these reactions are shown in Table I, whereas the

Table I

Reaction	10 ¹⁰ k, cm ³ /mol sec
CH ₃ O ⁻ + C ₆ H ₅ F → F ⁻ + C ₆ H ₅ OCH ₃	0.4
CH ₃ O ⁻ + C ₆ F ₆ → C ₆ F ₅ O ⁻ + CH ₃ F	16
F ⁻ + C ₆ F ₅ OCH ₃	0.4 ^a
<i>i</i> -C ₃ H ₇ O ⁻ + C ₆ F ₆ → C ₆ F ₅ O ⁻ + C ₃ H ₇ F	14
CH ₃ O ⁻ + C ₆ F ₅ H → C ₆ F ₅ O ⁻ + CH ₃ OH	13
<i>i</i> -C ₃ H ₇ O ⁻ + C ₆ F ₅ H → C ₆ F ₅ O ⁻ + C ₃ H ₇ OH	10

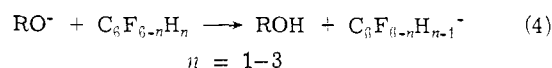
^a See text. The actual rate constant may be considerably lower than this value.

Table II. *k*_{aa}/*k*_{bb} for Difluorobenzenes

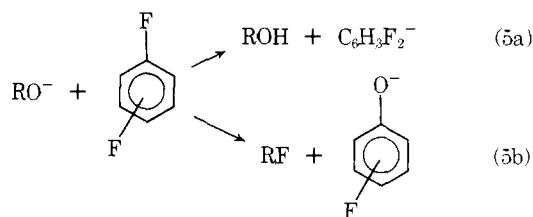
RO ⁻	Ortho	Meta	Para
CH ₃ O ⁻	3.2	10	46
C ₂ H ₅ O ⁻	1.1	8.2	1.5
<i>i</i> -C ₃ H ₇ O ⁻	0.14	19	0.51

rate constant for production of F⁻ is estimated as an upper limit, since it cannot be detected under the conditions used to measure *k*₃.

Reactions of partially fluorinated benzenes with alkoxide ions are helpful to understand under what conditions the three reactivity channels are operative. Pentafluorobenzene, 1,2,3,4-tetrafluorobenzene, and 1,3,5-trifluorobenzene yield exclusively the conjugate base of these aromatics. Upper limits estimated for fluoride displacement show again no substantial rate enhancement over reaction 1.



The formation of phenoxide ion finally becomes competitive in some of the difluorobenzene isomers. In this case,

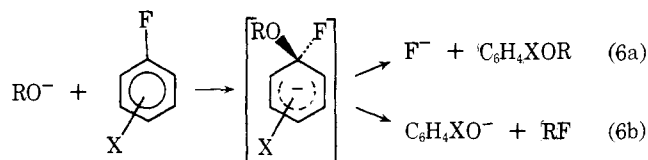


relative rate constants are much more important than absolute values, and can be determined accurately because of the proximity in mass number of the products. (See Table II.) Since these relative rate constants will depend strongly on the relative acidities of the alcohols and the difluorobenzenes, appropriate mixtures of the alkyl nitrite, the difluorobenzenes, and the alcohol can be used to establish the preferred direction of reaction (5a) by double resonance techniques.⁹ The acidity order determined in this fashion is *m*-C₆H₄F₂ > *i*-C₃H₇OH > *o*-C₆H₄F₂ > C₂H₅OH ≥ *p*-C₆H₄F₂ > CH₃OH. Fluoride displacement is again unimportant in the difluorobenzenes.

These examples allow some conclusions to be made: (a) gas phase nucleophilic attack on the ring is feasible only when the acidity of the aromatic compounds is less or comparable to that of the alcohol;¹⁰ (b) electron-attracting substituents¹¹ do not speed up halide displacement as in solution but do accelerate the overall reactivity of the aromatic substrate through a new pathway which leads to a substituted phenoxide.

While the first conclusion is not surprising in view of recent observations in ion-molecule reactions,^{12,13} the formation of a phenoxide ion as opposed to F⁻ is indeed remarkable. The preference for the phenoxide ion formation can be

rationalized by a Meisenheimer-type intermediate. Appreciable stabilization of the postulated intermediate may be



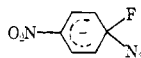
achieved through an inductive effect for X = F, Cl, or by charge delocalization for X = NO₂. A longer lived species¹⁴ might then undergo bond reorganization along the energetically preferred channel.^{15,16}

The mechanistic aspects of these reactions are presently under further study to establish the general reactivity of aryl halides.

Acknowledgment. We thank Dr. Simon Campbell for bringing the hexafluorobenzene problem to our attention. This research was made possible by the support of the Conselho Nacional de Pesquisas of Brazil and a FAPESP scholarship (S.M.J.B.).

References and Notes

- (1) For earlier work concerning substituent effects in ion-molecule reactions, see (a) R. C. Dunbar, J. Shen, and G. A. Olah, *J. Amer. Chem. Soc.*, **94**, 6862 (1972); (b) F. Cacace and E. Possagno, *ibid.*, **95**, 3397 (1973); (c) R. C. Dunbar, J. Shen, E. Melby, and G. A. Olah, *ibid.*, **95**, 7200 (1973).
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- (3) J. Miller, "Aromatic Nucleophilic Substitution," Elsevier, Amsterdam, 1968, Chapter 4, pp 61-132.
- (4) J. Miller and H. W. Yeung, *Aust. J. Chem.*, **20**, 379 (1967).
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- (6) The experimental details were similar to those described by L. K. Blair, P. C. Isolani, and J. M. Riveros, *J. Amer. Chem. Soc.*, **95**, 1057 (1973). Alkoxide ions were generated in the kinetic experiments by low energy electrons (1.5 eV). Rate constants were determined according to S. E. Buttrill, Jr., *J. Chem. Phys.*, **50**, 4125 (1969), with simultaneous ejection of trapped thermal electrons. Residence times are probably poorly defined in these cases, and rate constants are not believed to be better than 25% accurate. Pressure measurements were carried out as in W. T. Huntress, Jr., and R. F. Pinizzotto, Jr., *J. Chem. Phys.*, **59**, 4742 (1973). The ionic spectra of the fluorobenzenes, both positive and negative, show no detectable impurities, or conflicting mass peaks.
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- (8) In reaction 3, 4, and 5, R = CH₃, C₂H₅, and *t*-C₃H₇.
- (9) J. I. Brauman and L. K. Blair, *J. Amer. Chem. Soc.*, **90**, 5636 (1968); **90**, 6561 (1968); **92**, 5986 (1970); **93**, 3911 (1971).
- (10) The word comparable is used because alkoxide ions generated from nitrites can undergo slightly endothermic reactions. However, Δ*H* must be ≤ 2 kcal/mol: P. C. Isolani, Ph.D. Thesis, University of Sao Paulo, 1974, p 65.
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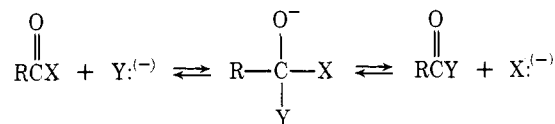
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Received July 29, 1974

Alkoxide Adduct of an Amide. Mean Lifetime of an Intimate Ion Pair

Sir:

The general mechanism by which nucleophiles interconvert carboxylic acids and their derivatives is now believed to involve a tetrahedral intermediate.¹⁻³ With the exception of

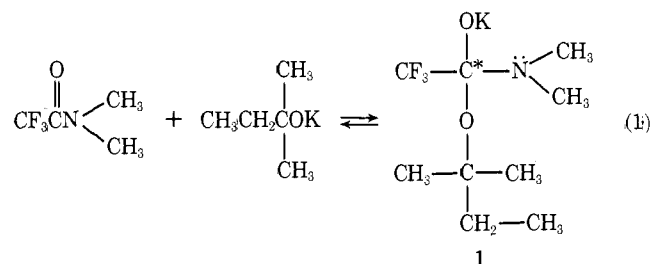


perfluoro derivatives⁴ and special cyclic systems⁵⁻⁷ where intermediates have been isolated, in most of this research the concentrations involved are so low that evidence about tetrahedral intermediates can only be inferred from kinetic and isotope exchange data.¹⁻³

Herein, we report the first direct nmr spectroscopic observation of a potassium alkoxide adduct of *N,N*-dimethyltrifluoroacetamide which provides detailed information of structure and at the same time some estimate of the mean lifetime of an intimate ion pair in a hydrocarbon medium.

Employing as precedent Bender's observation in 1953 that esters and amides of perfluoroacids form isolable tetrahedral adducts with alkoxides,⁴ we anticipated that a tertiary amide of a perfluoroacid would form similar adducts.

When *N,N*-dimethyltrifluoroacetamide is added to a solution of potassium *tert*-amyloxide (made up to be ca. 1 *M* in each constituent) in methyl cyclohexane or isoctane, the resulting solution gives the *N*-methyl nmr absorption shown in Figure 1. Alkoxide resonance in this solution is obscured by the solvent. The *N*-methyl proton resonance consists of two closely spaced quartets for the free amide (indicating slow internal rotation) and a sharp single line ascribed to the adduct **1**. This line disappears when water is added to the solution. Only the amide and *tert*-amyl alcohol are obtained on hydrolysis, and there is no evidence for dimethylamine. Also these results show equilibrium **1** to be slow on the nmr time scale.



As the temperature of the sample containing the reaction mixture (**1**) is lowered, the *N*-methyl resonance of **1**, Figure 1, progressively broadens and finally splits into an equal doublet of separation 2 Hz by -50°. Careful inspection of the shift with respect to internal standards and of the line-shape itself reveals that these effects come from an exchange process. Tentatively, we propose the magnetic nonequivalence of the *N*-methyls of **1** to come from the asymmetry at the central carbon (starred) and its averaging due to inversion at nitrogen, that is the inversion rate at nitrogen is on the nmr time scale -50 to +10°. Comparison of experimental and theoretical line shapes^{8,9} shows the first-order rate constant for inversion to be 2.3 sec⁻¹ at -17°. Considering that most acyclic amines invert at rates many orders of magnitude faster than this¹⁰ around 0°, some special effect must be inhibiting inversion in **1**. That effect is most likely the bidentate chelation of nitrogen and oxygen with potassium ion (**2**). Then it would appear that the rate of in-