

Search for Acid Catalysis of the Reaction of Thiophenoxide Ion with 2,4-Dinitrofluorobenzene¹

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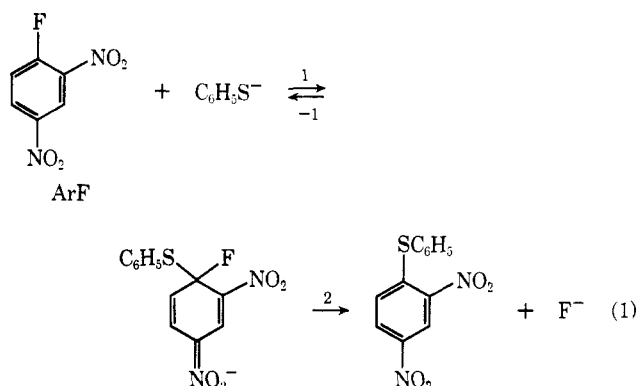
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In five different kinds of systems designed to elicit evidence of acid catalysis of the reaction named in the title, no evidence of such catalysis has been found. No evidence was found either of general acid catalysis or of a thiophenol term in the rate law; the latter would appear if there were catalysis by the solvated proton. Inasmuch as the separation of fluoride ion from carbon is known to respond to catalysis by acids, we conclude that the first step of the intermediate complex mechanism is rate limiting for this reaction. This conclusion is contrary to one reached by other workers on the basis of thermochemical calculations.

In recent years the two-step, intermediate complex mechanism of aromatic nucleophilic substitution² has become generally accepted, and attention has turned increasingly toward defining the energy profiles for reactions involving various nucleophiles, leaving groups, substituents, or solvents. In part this objective has been approached experimentally, for example, by studying the incidence of base catalysis in reactions involving amine reagents, which gives information as to whether the first or second step is rate limiting.³

Miller⁴ has approached this general problem in a different way, namely, by estimation from thermochemical data of the relative energy levels of reactants, intermediates, transition states, and products. As to the transition states (one preceding and one following the intermediate), his method requires assumptions as to the fraction of the bond dissociation energy which must be supplied to attain either transition state from the intermediate, assumptions which are made with respect to the Hammond postulate.⁵ His treatment resembles in some respects that used by Hudson⁶ to deal with other problems of reaction energetics. Miller's thermochemical predictions have been upheld by later experimental determinations in some cases but not in all.⁷

Having had some prior experience⁸ with the reaction of sodium thiophenoxide with 2,4-dinitrofluorobenzene (eq 1), we were interested in Miller's conclusion⁹



(1) This investigation was supported by Public Health Service Research Grant No. GM 14647 from the National Institute of General Medical Sciences.

(2) J. F. Bunnett, *Quart. Rev.* (London), **12**, 1 (1958); A. J. Kirby and W. P. Jencks, *J. Amer. Chem. Soc.*, **87**, 3217 (1965); J. F. Bunnett and R. H. Garst, *ibid.*, **87**, 3879 (1965); C. R. Hart and A. N. Bourns, *Tetrahedron Lett.*, 2995 (1966).

(3) J. F. Bunnett and C. Bernasconi, *J. Amer. Chem. Soc.*, **87**, 5209 (1965); C. Bernasconi and H. Zollinger, *Helv. Chim. Acta*, **49**, 103 (1966); F. Pietra and A. Fava, *Tetrahedron Lett.*, 1535 (1963); C. F. Bernasconi, *J. Org. Chem.*, **32**, 2947 (1967); J. F. Bunnett and R. H. Garst, *ibid.*, **33**, 2320 (1968).

that step 2, involving expulsion of fluoride ion from the intermediate complex, is rate limiting. This was contrary to the judgment of Bunnett and Merritt,⁸ which was based on leaving-group effects.

Inasmuch as the separation of fluoride ion from carbon is known to be susceptible to catalysis by acids,¹⁰ it is possible to decide on experimental grounds which step of eq 1 is rate limiting.¹¹ If the first step is rate limiting, the over-all reaction should follow a simple second-order rate law, first order in 2,4-dinitrofluorobenzene (symbolized ArF) and first order in thiophenoxide ion. But, if the second step is rate limiting, the rate law should include terms representing catalysis by the solvated proton and/or general acids.

If the second step were general acid catalyzed, the over-all rate should in part be proportional to $[\text{ArF}] \cdot [\text{C}_6\text{H}_5\text{S}^-][\text{HA}]$, where HA is a general acid. If it were catalyzed by the solvated proton, proportionality in part to $[\text{ArF}][\text{C}_6\text{H}_5\text{S}^-][\text{H}^+]$ or, rather, to $[\text{ArF}] \cdot [\text{C}_6\text{H}_5\text{SH}]$ would be expected.¹² A solvent-catalyzed term would also be conceivable.

Experimental Section

Materials.—2,4-Dinitrofluorobenzene (Aldrich Reagent) was distilled at reduced pressure, mp 28°, bp 96° (0.3 mm) and 297–298° (760 mm). Thiophenol (Aldrich Reagent) was distilled at reduced pressure, bp 55–56° (9 mm), and stored in a desiccator under nitrogen atmosphere. Reagent grade methanol was further purified by the magnesium method.¹³ Acetic acid (Allied Reagent, ACS), sodium acetate (Matheson Coleman and Bell reagent), chloroacetic acid (Baker Analyzed reagent), tetrapropylammonium bromide (Eastman Kodak, White Label), and lithium chloride (Matheson Coleman and Bell reagent) were used without further purification. *p*-Toluenesulfonic acid (Baker Analyzed reagent) was purified with chloroform after Perron.¹⁴ *N*-Methylpiperidine (Aldrich reagent) was refluxed over sodium for 2 hr and distilled over sodium; bp 106–107°.

(4) J. Miller, *J. Amer. Chem. Soc.*, **85**, 1628 (1963); D. L. Hill, K. C. Ho, and J. Miller, *J. Chem. Soc., B*, 299 (1966).

(5) G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955).

(6) R. F. Hudson, *Chimia (Aarau)*, **16**, 173 (1962).

(7) C. F. Bernasconi, *J. Amer. Chem. Soc.*, **90**, 4982 (1968), summarizes several cases from his own work and from work of other investigators.

(8) J. F. Bunnett and W. D. Merritt, Jr., *ibid.*, **79**, 5967 (1957).

(9) K. C. Ho, J. Miller, and K. W. Wong, *J. Chem. Soc., B*, 310 (1966).

(10) W. T. Miller, Jr., and J. Berstein, *J. Amer. Chem. Soc.*, **70**, 3600 (1948); N. B. Chapman and J. L. Levy, *J. Chem. Soc.*, 1677 (1952); C. W. L. Bevan and R. F. Hudson, *ibid.*, 2187 (1953); A. K. Coverdale and G. Kohnstam, *ibid.*, 3806 (1960); C. G. Swain and R. E. T. Spalding, *J. Amer. Chem. Soc.*, **82**, 6104 (1960).

(11) Cf. K. B. Lam and J. Miller, *Chem. Commun.*, 642 (1966).

(12) A good example of kinetic dependence on $[\text{ArSH}]$ which in all probability represents H^+ catalysis of reaction with ArS^- nucleophile has been reported by G. Illuminati, P. Linda, and G. Marino, *J. Amer. Chem. Soc.*, **89**, 3521 (1967).

(13) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed, D. C. Heath and Co., Boston, Mass., 1941, p 360.

(14) R. Perron, *Bull. Soc. Chim. Fr.*, 966 (1952).

piperidinium chloride was prepared by passing hydrogen chloride into an ethereal solution of N-methylpiperidine; it was crystallized twice from methanol; mp 207–208° (lit.¹⁵ 211–212°).

Chloroacetic acid–sodium chloroacetate buffer was prepared by combining a measured volume of standard sodium methoxide solution with twice the molar amount of chloroacetic acid. The other buffer solutions were prepared by combining weighed amounts of the various compounds. 2,4-Dinitrophenyl phenyl sulfide was available in the laboratory; it was crystallized from methanol; mp 120–121°. The uv and visible spectra of 2,4-dinitrofluorobenzene and 2,4-dinitrophenyl phenyl sulfide in methanol were determined in a Cary Model 14 spectrophotometer. The fluoro compound has maxima at 217 m μ (ϵ 12,000) and at 290 m μ (ϵ 6900) and the sulfide at 215 m μ (ϵ 19,500), 242 (sh), 265 (sh), and 328 m μ (ϵ 10,100).

Kinetic Procedures.—Three techniques were used, depending on the rate of the reaction being measured. In all three, the increase of absorbance at 400 m μ due to 2,4-dinitrophenyl phenyl sulfide was measured. The "infinity" absorbances agreed with those expected for quantitative conversion to that product.

The runs in Table IX were conducted by dispensing aliquots of the reaction solution into ampoules which were then sealed and immersed all at once in the thermostat bath. In preparing the reaction solutions, the required thiophenol was weighed under nitrogen, and the ampoules were flushed with nitrogen before being sealed. From 12 to 15 ampoules were used per run. Absorbances were measured in a Cary Model 14 spectrophotometer.

The runs in Table II were followed by direct observation of the absorbance of the reacting solution in the thermostated cell compartment of a Gilford spectrophotometer. The cuvettes were flushed with nitrogen before and after introduction of the reaction solution. Absorbance was recorded automatically at selected times.

The runs in Tables I and III–VIII were performed in a Durrum–Gibson stopped-flow kinetics spectrophotometer, the essential features of which are those described by Gibson and Milnes.¹⁷

All runs afforded linear plots of $\log(A_\infty - A_t)$ vs. time; k_ψ values were reckoned as -2.3 times the slope as calculated by the least-squares method.

Results and Discussion

The reaction of thiophenoxide ion with 2,4-dinitrofluorobenzene is fast. In the earlier work of Bunnett and Merritt,⁸ its rate could be measured only at 0° and then only by employing both the nucleophile and the substrate at very low concentrations. Ho, Miller, and Wong⁹ used higher concentrations of reactants but experimental temperatures in the very low range of -82 to -65° . In the present work rates were determined at 25° under concentration conditions typical for experiments designed to afford pseudo-first-order kinetics, and the exceedingly rapid reaction rate was measured in a stopped-flow kinetics spectrophotometer.

The rate coefficients determined in four runs with constant thiophenoxide ion concentration but different thiophenol concentrations are presented in Table I. It should be noted that excess thiophenol has no discernible effect on reaction rate. These data suggest but do not prove the absence of a thiophenol term in the rate law. The reactivity of thiophenol conceivably may escape notice when it is in competition with a substantial concentration of the enormously reactive thiophenoxide ion. However, the possibility that reaction with thiophenoxide ion is catalyzed by thiophenol as a general acid is firmly denied by the data of Table I. An aspect of these data of general value is that they serve to establish the second-order rate

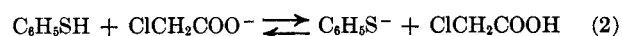
TABLE I
REACTION OF 2,4-DINITROFLUOROBENZENE WITH
SODIUM THIOPHENOXIDE IN METHANOL AT 25.0°.
INFLUENCE OF THE THIOPHENOL CONCENTRATION^a

[C ₆ H ₅ SH], M	k_ψ , sec ⁻¹	k_A , l. mole ⁻¹ sec ⁻¹
Nil	10.44	785
0.0196	10.24	770
0.0695	10.44	785
0.225	10.44	785
		Average 780

^a [ArF]₀, 5.60×10^{-4} M; [C₆H₅SNa], 1.33×10^{-2} M.

coefficient, 780 l. mole⁻¹ sec⁻¹ at 25.0°, for the reaction of our principal interest.

Table II summarizes a series of runs performed in the presence of a constant concentration of a 1:1 chloroacetate buffer and varying concentrations of thiophenol. In these runs a small concentration of thiophenoxide ion was present owing to interaction with chloroacetate ion (eq 2). The amount is controlled by



the equilibrium constant of eq 2, but is linearly proportional to the concentration of thiophenol. The fact that $k_\psi/[\text{C}_6\text{H}_5\text{SH}]$ is constant while thiophenol concentration is varied tenfold affirms (a) the lack of a discernible thiophenol term in the rate law and (b) the lack of a term proportional to $[\text{C}_6\text{H}_5\text{S}^-][\text{C}_6\text{H}_5\text{SH}]$, which would represent general acid catalysis by thiophenol. The data of Table II are a more sensitive test for a thiophenol term than those of Table I.

TABLE II
REACTION OF 2,4-DINITROFLUOROBENZENE WITH
THIOPHENOXIDE ION IN METHANOL AT 25.0°.
INFLUENCE OF THE THIOPHENOL CONCENTRATION
IN A BUFFERED SYSTEM^a

$10^2[\text{C}_6\text{H}_5\text{SH}]$, M	10^3k_ψ , sec ⁻¹	$k_\psi/[\text{C}_6\text{H}_5\text{SH}]$, l. mole ⁻¹ sec ⁻¹
0.95	1.8	0.190
1.60	3.3	0.206
3.80	7.8	0.205
6.0	12.0	0.200
10.0	20.0	0.200

^a [ArF]₀, 5.72×10^{-4} M; buffer: [chloroacetic acid] = [sodium chloroacetate] = 0.01 M.

In Table III, some runs at constant thiophenol concentration and varying concentration of 1:1 acetate buffer are summarized. Again a small concentration of thiophenoxide ion is provided by an equilibrium analogous to that of eq 2. The fact that the pseudo-first-order rate coefficient, k_ψ , is substantially constant

TABLE III
INFLUENCE OF THE ACETATE BUFFER CONCENTRATION
ON THE REACTION OF 2,4-DINITROFLUOROBENZENE
WITH THIOPHENOXIDE ION IN METHANOL AT 25.0°^a

[CH ₃ COOH], ^b M	[LiCl], M	10^3k_ψ , sec ⁻¹	pK _{H₃OAc} ^c
0.010	0.090	7.47	9.57
0.010	0.090	7.47	9.57
0.020	0.080	7.88	9.59
0.050	0.050	7.64	9.58
0.050	0.050	7.82	9.59

^a [ArF]₀, 5.72×10^{-4} M; [C₆H₅SH], 9.72×10^{-3} M. ^b [CH₃COONa] = [CH₃COOH] in all runs. ^c For discussion of the pK_{H₃OAc}, see accompanying paper.²³

(15) A. P. Phillips and J. Mentha, *J. Amer. Chem. Soc.*, **77**, 6393 (1955).

(16) R. W. Bost, J. O. Turner, and R. D. Norton, *ibid.*, **54**, 1985 (1932).

(17) Q. H. Gibson and L. Milnes, *Biochem. J.*, **91**, 161 (1964).

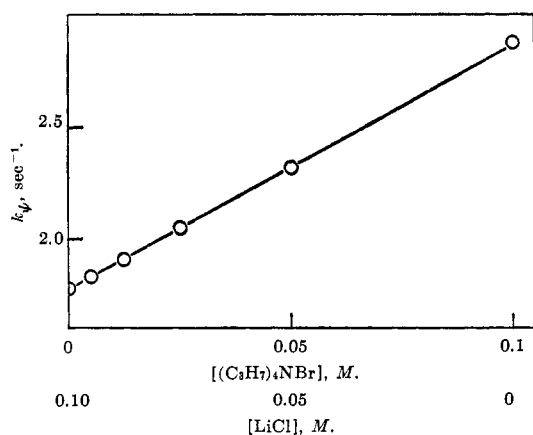


Figure 1.—Rate of reaction of ArF with thiophenoxide ion provided by thiophenol in N-methylpiperidine-N-methylpiperidinium chloride buffer (0.01 M), as affected by changing the nonreacting salt present from LiCl to tetrapropylammonium bromide. Data of Table VI.

shows the absence of general acid catalysis by acetic acid. The minor trend in k_p is not much greater than experimental error, and if real may stem from LiCl having a different salt effect than sodium acetate.

It seemed possible that for coulombic reasons a cationic general acid might be more effective than a neutral one, and therefore the influence of varying 1:1 N-methylpiperidine:N-methylpiperidinium chloride buffer concentration at fixed thiophenol concentration was explored, with LiCl present as needed to maintain constant salt concentration. Results are shown in Table IV. In this case there is a clear trend: the rate increases with increase in buffer concentration. This suggests general acid catalysis by the N-methylpiperidinium ion, but the possibility that it represents a difference in specific salt effects by N-methylpiperidinium chloride and LiCl must also be considered.

TABLE IV
REACTION OF 2,4-DINITROFLUOROBENZENE WITH THIOPHENOXIDE ION IN METHANOL AT 25.0°. INFLUENCE OF N-METHYLPIPERIDINE-N-METHYLPIPERIDINIUM CHLORIDE BUFFER CONCENTRATION WITH COMPENSATION BY LITHIUM CHLORIDE^a

[NMP], ^b M	[LiCl], M	k_p , sec ⁻¹	$10^{10}K_a$, ^c M
0.010	0.09	1.06 ± 0.01	2.31
0.020	0.08	1.25 ± 0.03	1.96
0.050	0.05	1.58 ± 0.02	1.55
0.100	0.00	2.21 ± 0.16	1.11

^a [ArF]₀, 5.72×10^{-4} M; [C₆H₅SH]₀, 1.18×10^{-2} M. ^b NMP stands for N-methylpiperidine; [NMP·HCl] = [NMP] in all runs; each entry is the average of two runs. ^c K_a is the acid dissociation constant of N-methylpiperidinium ion; for discussion see the accompanying paper.²³

As a test of the possibility that the salt effects of LiCl and a salt with a large organic cation might be different, a series of runs was performed with constant sodium thiophenoxide concentration and variable concentrations of tetra-*n*-propylammonium bromide and LiCl, but constant total salt concentration. These runs are summarized in Table V. There is indeed a small effect of the organic salt to accelerate the substitution as compared to the effect of LiCl, but the effect is quantitatively insufficient to account for the trend of the k_p values in Table IV.

TABLE V
REACTION OF 2,4-DINITROFLUOROBENZENE WITH SODIUM THIOPHENOXIDE IN METHANOL AT 25.4°. INFLUENCE OF TETRAPROPYLAMMONIUM BROMIDE vs. LITHIUM CHLORIDE^a

[(C ₂ H ₅) ₄ NBr], M	[LiCl], M	k_p , sec ⁻¹	k_A , l. mole ⁻¹ sec ⁻¹
0.004	0.100	7.85 ± 0.09 ^b	785
0.010	0.096	7.80 ± 0.15 ^c	780
0.050	0.090	7.92 ± 0.01 ^c	792
0.100	0.050	9.06 ± 0.10 ^c	906
0.100	0.000	9.70 ± 0.30 ^c	970

^a [ArF]₀, 5.50×10^{-4} M; [C₆H₅SNa]₀, 1.00×10^{-2} M. ^b Average of three runs. ^c Average of two runs.

The over-all rate coefficients in Table IV are, however, composite, each being the product of an equilibrium constant (for dissociation of thiophenol to thiophenoxide ion) and a rate coefficient (for the actual substitution). The possibility of a differential salt effect on the dissociation was therefore also explored. A series of runs was carried out with constant thiophenol concentration, constant concentration of 1:1 N-methylpiperidine:N-methylpiperidinium chloride buffer and variable concentrations of tetra-*n*-propylammonium bromide and LiCl, but constant total salt concentration. As shown in Table VI and also in Figure 1, there was a steady rise in reaction rate as the organic salt took the place of LiCl. The rates in Table VI are also composite of equilibrium and kinetic effects, just as those in Table IV are, but the magnitude of the kinetic differential salt effect is known from the data of Table V. Inasmuch as the over-all rate increase in Table VI (63%) is greater than in Table V (23%), a differential salt effect on the acid-base equilibrium is demonstrated.

TABLE VI
REACTION OF 2,4-DINITROFLUOROBENZENE WITH THIOPHENOXIDE ION IN METHANOL AT 25.0°. INFLUENCE OF TETRAPROPYLAMMONIUM BROMIDE vs. LITHIUM CHLORIDE AT CONSTANT BUFFER CONCENTRATION^a

[(C ₂ H ₅) ₄ NBr], M	[LiCl], M	k_p , sec ⁻¹
0.005	0.100	1.77 ± 0.06
0.0125	0.095	1.83 ± 0.04
0.025	0.087	1.91 ± 0.04
0.050	0.075	2.05 ± 0.02
0.100	0.050	2.32 ± 0.04
0.100	0.000	2.88 ± 0.04

^a [ArF]₀, 5.50×10^{-4} M; [C₆H₅SH]₀, 1.47×10^{-2} M; [N-methylpiperidine] = [N-methylpiperidine hydrochloride] = 0.01 M.

The genesis of this effect is probably favorable London dispersion force interactions between the high polarizability thiophenoxide ion and the organic cation of rather high polarizability. The effects of London forces on acid-base equilibria have been discussed by Grunwald and Price.¹⁸

It was therefore to be expected that in a set of runs analogous to those of Table IV, but with tetra-*n*-propylammonium bromide as the compensating electrolyte instead of LiCl, the kinetic effect of changing the buffer concentration would be much reduced. In fact, as shown in Table VII, there was at most a very small effect; the rate pattern might also be described

as random variation. It is thus evident that tetra-*n*-propylammonium bromide affects over-all substitution rate to approximately the same extent as *N*-methylpiperidinium chloride does. The trend in Table IV therefore does not warrant interpretation as general acid catalysis of the substitution.

TABLE VII

REACTION OF 2,4-DINITROFLUOROBENZENE WITH THIOPHENOXIDE ION IN METHANOL AT 25.0°. INFLUENCE OF *N*-METHYLPYPERIDINE-*N*-METHYLPYPERIDINIUM CHLORIDE BUFFER CONCENTRATION WITH COMPENSATION BY TETRAPROPYLAMMONIUM BROMIDE^a

[NMP], ^b <i>M</i>	[(C ₄ H ₇) ₄ NBr], <i>M</i>	<i>k</i> _ψ , sec ⁻¹
0.005	0.095	2.90 ± 0.20 ^c
0.0125	0.087	3.05 ± 0.01 ^d
0.025	0.075	3.42 ± 0.02 ^c
0.050	0.050	3.52 ± 0.04 ^c
0.100		3.07 ± 0.02 ^d

^a [ArF]₀, 5.50 × 10⁻⁴ *M*; [C₆H₅SH], 1.43 × 10⁻² *M*. ^b See footnote *b*, Table IV. ^c Average of three runs. ^d Average of two runs.

A series of runs like those of Table VII was also performed in the solvent water-methanol (96:4). Results are listed in Table VIII. There was only random variation of rate as buffer concentration changed 20-fold. Again there is no evidence for general acid catalysis.¹⁹

TABLE VIII

REACTION OF 2,4-DINITROFLUOROBENZENE WITH THIOPHENOXIDE ION IN WATER-METHANOL (96:4) AT 25.8°. INFLUENCE OF *N*-METHYLPYPERIDINE-*N*-METHYLPYPERIDINIUM CHLORIDE BUFFER CONCENTRATION WITH COMPENSATION BY TETRAPROPYLAMMONIUM BROMIDE^a

[NMP], ^b <i>M</i>	[(C ₄ H ₇) ₄ NBr], <i>M</i>	<i>k</i> _ψ , sec ⁻¹
0.005	0.095	0.978 ± 0.018 ^c
0.0125	0.087	0.996 ± 0.029 ^d
0.025	0.075	0.981 ± 0.026 ^d
0.0625	0.0375	0.975 ± 0.002 ^d
0.100		0.966 ± 0.005 ^d

^a [ArF]₀, 2.25 × 10⁻⁴ *M*; [C₆H₅SH], 1.92 × 10⁻³ *M*. ^b See footnote *b*, Table IV. ^c Average of four runs. ^d Average of two runs.

Although the data of Tables I and II gave no indication of a term in the rate law proportional to thiophenol concentration, a more rigorous search for such a term was conducted by carrying out the reaction in the presence of a strong acid, *p*-toluenesulfonic acid (PTS). Such a strong acid strongly represses dissociation of thiophenol to thiophenoxide ion, but the latter is so reactive that its reaction with 2,4-dinitrofluorobenzene is nevertheless measurable. The experiments performed are summarized in Table IX.

If eq 3 and 4 both obtain, the pseudo-first-order rate coefficient, *k*_ψ, should depend on thiophenol and sol-

$$K_{\text{PthSH}} = [\text{C}_6\text{H}_5\text{S}^-][\text{H}^+]/[\text{C}_6\text{H}_5\text{SH}] \quad (3)$$

$$-d[\text{ArF}]/dt = k_{\psi}[\text{ArF}] = k_A[\text{ArF}][\text{C}_6\text{H}_5\text{S}^-] \quad (4)$$

$$k_{\psi} = k_A K_{\text{PthSH}}[\text{C}_6\text{H}_5\text{SH}]/[\text{H}^+] \quad (5)$$

(19) The rate coefficient for reaction of ArF with sodium thiophenoxide in water-methanol (96:4) at 25° was determined to be 512 l. mole⁻¹ sec⁻¹. From this value and the data in Table VIII, it is evident that the thiophenol was essentially fully dissociated under the experimental conditions employed, as was anticipated from the pH's of thiophenol and *N*-methylpiperidine in water.

TABLE IX

REACTION OF 2,4-DINITROFLUOROBENZENE WITH THIOPHENOXIDE ION IN METHANOL AT 25.0° IN THE PRESENCE OF *p*-TOLUENESULFONIC ACID (PTS)^a

10 ⁴ [PTS], <i>M</i>	[LiCl], <i>M</i>	10 ⁴ <i>k</i> _ψ , sec ⁻¹	10 ⁴ <i>k</i> _ψ [PTS], <i>M</i> sec ⁻¹	<i>pK</i> _{PthSH} ^b
1.36	0.10	19.39	2.64	10.56
3.44	0.10	6.972	2.40	10.58
13.6	0.10	1.653	2.25	10.59
1.36	0.01	8.222	1.12	10.91
3.44	0.0097	3.167	1.09	10.92
13.6	0.0086	0.7944	1.08	10.92

^a [ArF], 5.72 × 10⁻⁴ *M*; [C₆H₅SH], 0.117 *M*. ^b See accompanying paper²³ for discussion of *pK*_{PthSH} values.

ated proton concentrations as shown in eq 5. At constant thiophenol concentration, the product, *k*_ψ·[H⁺], should be constant.

The experiments of Table IX involve throughout a constant thiophenol concentration, 0.117 *M*. In the first set of three experiments, LiCl is present at the constant level of 0.10 *M* and *p*-toluenesulfonic acid concentration is varied tenfold, from 1.36 × 10⁻⁴ to 1.36 × 10⁻³ *M*. The product, *k*_ψ[PTS], decreases somewhat with increase in concentration of the strong acid. In the second set of three experiments, LiCl is present at a lower concentration level, approximately 0.01 *M*, but adjusted to maintain total electrolyte concentration constant at 0.01 *M*. *p*-Toluenesulfonic acid concentration is varied as in the first set. In the second set, the product, *k*_ψ[PTS], is constant within experimental error.

If there were a thiophenol term in the rate law, eq 5 would need to be replaced by eq 6. The product,

$$k_{\psi} = k_A K_{\text{PthSH}}[\text{C}_6\text{H}_5\text{SH}]/[\text{H}^+] + k^{\circ}[\text{C}_6\text{H}_5\text{SH}] \quad (6)$$

*k*_ψ[H⁺], would obviously increase with increase of solvated proton concentration to the extent that the thiophenol term contributed. The experimental fact that this product is constant (the lower set of three experiments in Table IX) or that it slightly decreases (the upper set of three) shows that the thiophenol term, if there is one, makes no detectable contribution to the reaction rate.

The preceding paragraph involves the implicit assumption that *p*-toluenesulfonic acid is fully dissociated in methanol at the concentrations employed. In view of the fact that the highest concentration used was only 1.36 × 10⁻³ *M*, this seems a reasonable assumption. If this assumption were not valid, relatively less dissociation would occur at the highest concentration of this acid than at the lowest, repression of thiophenol ionization would be less at the highest *p*-toluenesulfonic acid concentration, and the product, *k*_ψ[PTS], would increase as the concentration of the strong acid increased. The fact that this product remains constant or decreases somewhat demonstrates that the assumption is valid.

The difference in the product, *k*_ψ[PTS], between the first and second sets of experiments in Table IX is attributed to a salt effect on the rate and/or equilibrium constants involved. The cause of the moderate decrease in the product, *k*_ψ[PTS], within the first set is not evident.

Conclusions.—In five different kinds of systems, we have sought evidence for acid catalysis of the reaction

of thiophenoxide ion with 2,4-dinitrofluorobenzene. But in no case was any evidence of such catalysis found. There was no evidence of catalysis by general acids and no evidence of a thiophenol term, which would represent catalysis by the solvated proton.

Inasmuch as the separation of fluoride ion from carbon is known to respond to catalysis by acids, it follows straightforwardly that separation of fluoride ion from carbon is not involved in the rate-limiting step of this reaction. Therefore the first step of the mechanism shown in eq 1 is rate limiting.

This straightforward conclusion can be accepted, however, only after certain subtle features of the system have been considered. The compounds whose solvolysis is known to be catalyzed by acids are stable substances, and it is likely that the transition states for separation of fluoride ion from carbon involve a large extent of C-F bond rupture. In view of the high basicity of the fluoride ion, the energetic advantages of associating the departing fluoride ion with a proton are obvious.

But the intermediate in eq 1 is not a stable substance. The transition state for ejection of fluoride ion from it is therefore likely to involve a lesser degree of rupture of the C-F bond, and a lesser degree of association of a proton with it. In terms of the Brønsted catalysis law, a lower α value should be associated with step 2 of eq 1 than, say, with alkyl fluoride solvolyses. Indeed, if ejection of fluoride ion from the intermediate occurs with exceptional ease, not only general acid catalysis but even catalysis by the solvated proton may be undetectable. On this reasoning it might be contended that separation of fluoride ion from the intermediate would not necessarily require acid catalysis, and therefore that our data do not compel the straightforward conclusion drawn above.

The flaw in this hypothetical contention is that if fluoride ion separates with such exceeding ease from the intermediate, then expulsion of fluoride ion should occur faster than expulsion of thiophenoxide ion, in which case the first step of eq 1 is rate limiting. If the second step is to be rate limiting, there must be an appreciable energetic barrier to separation of fluoride ion from carbon, and in that case its separation should be acid catalyzed. The straightforward conclusion that the first step of eq 1 is rate limiting thus survives scrutiny.²⁰

(20) A referee comments that the conclusion of Ho, Miller, and Wong,⁹ that the second step is rate limiting, is extremely implausible on its face. We quote him: "To claim that the second step of the reaction in question

Inasmuch as Ho, Miller, and Wong⁹ had concluded from thermochemical calculations that the second step of eq 1 is rate limiting, the present results require reconsideration of the basis of those calculations. In their discussion of the results of those calculations, Ho, Miller, and Wong put considerable emphasis on a report from their own laboratory²¹ that thiomethoxide ion is about 3700 times as reactive with *p*-fluoronitrobenzene as with *p*-iodonitrobenzene. However, the same reactions have more recently been studied by Di Nunno and Todesco,²² who report the reactivity difference to be less than sixfold. The latter authors did not redetermine activation parameters; they should be redetermined, in order to verify the excellent agreement between calculated and experimental activation enthalpies reported by Ho, Miller, and Wong.^{9,21}

Although the one-step, S_N2-like mechanism for activated aromatic nucleophilic substitution is seldom advocated any more, we note in passing that it also would call for the reaction of present interest to be catalyzed by acids. These experiments thus constitute further evidence against the one-step mechanism.

Our experimental results contribute incidentally to another topic in solution kinetics. The data of Tables IV-VII demonstrate that the kinetic effects of salts in methanol solution may be quite different from one another, and that "constant ionic strength" even at the modest level of 0.1 *M* is no guarantee of equality of salt effects in this solvent.

Finally, the data of Tables II-IV and IX contain information as to the acid dissociation constants of thiophenol, acetic acid, chloroacetic acid, and *N*-methylpiperidinium ion in methanol. Use of this reaction for the determination of *pK*_a values is developed in the accompanying paper.²³

Registry No.—Thiophenoxide ion, 13133-62-5; 2,4-dinitrofluorobenzene, 70348.

is rate controlling is to claim that the S_N1 reactivity of a certain α -arylthio fluoride is less than that of the corresponding α -fluoro thiophenoxide. Inasmuch as the S_N1 reactivity of fluorides is much greater than that of thiophenoxides and inasmuch as α -ArS substituents increase S_N1 reactivity whereas α -F substituents decrease S_N1 reactivity, this claim seems quite unacceptable. The preceding two sentences, suitably amplified, seem to me to be a better argument against the interpretation of Miller, *et al.*, than is the work of the present manuscript." We agree with this referee's theoretical analysis, but we feel that experimental evidence is ultimately more decisive.

(21) J. Miller and K. W. Wong, *J. Chem. Soc.*, 5454 (1965).

(22) L. Di Nunno and P. E. Todesco, *Tetrahedron Lett.*, 2899 (1967).

(23) J. F. Bunnett and N. S. Nudelman, *J. Org. Chem.*, **34**, 785 (1969).