1013. *The* S_N *Mechanism in Aromatic Compounds. Part XXXI.*[1] *The Reactions of Thiomethoxide Ion in Methanol with Some Fluoro- and Iodo-nitrobenzenes*

By J. Miller and (Miss) K. W. Wong

A novel pattern of reactivity and of Arrhenius parameters in the reactions of thiomethoxide ion in methanol with *p*-fluoro- and *p*-iodo-nitrobenzene, and 1-fluoro- and 1-iodo-2,4-dinitrobenzene, was predicted in a recent Paper, and regarded as a consequence of a close balance in energy levels of two transition states in a mechanism involving an intermediate complex. The relative and absolute values predicted are now confirmed by experiment.

The E_{act} difference between fluoro- and iodo-compounds is less in the *p*-nitro-compounds than is usual in activated aromatic S_N reactions, but has the typical value in the 2,4-dinitro-compounds. Reduced reactivity of the iodo-compounds with thiomethoxide ion, associated with low values of S_{act}, and regarded as steric in origin, then render the relative fluorine/iodine mobility about normal for the *p*-nitro-compounds, and very high for the 2,4-dinitro-compounds.

In a recent Paper,[2] Miller made energy calculations for a number of anion–dipole aromatic nucleophilic substitutions, including reactions of thiomethoxide ion with some halogeno-nitrobenzenes. The concept of an intermediate complex was utilised, and data for bond energies, electron affinities, and solvation energies, together with an allowance for electronic reorganisation were used in calculations. Brief comment was also made about factors affecting the entropy of activation.

A novel pattern of reactivity and the corresponding Arrhenius parameters was predicted and is now fully confirmed. A further prediction about the E_{act} component of relative reactivity of thiomethoxide and methoxide ions with these substrates is shown to be partly correct.

Experimental

Materials.—The halogen compounds were made by standard procedures, and purified. Solid sodium thiomethoxide was prepared by Plieninger's method,[3] involving reaction of methanethiol with sodium methoxide, and addition of toluene.

Products.—The known thioethers were produced, free from by-products except in one reaction. In reaction between thiomethoxide and 1-iodo-2,4-dinitrobenzene the products react to give diaryl sulphide and disulphide (and methyl iodide). This tendency of heavy nucleophiles to be relatively more effective in aliphatic than aromatic S_N reactions has been referred to by Miller.[2] This subsequent reaction did not prevent good second-order kinetics from being followed for well over one half-life.

Kinetic Procedure.—Runs were carried out with equimolar proportions of the aromatic halogeno-compound and sodium thiomethoxide in absolute methanol. Good second-order rate constants (k_2) were obtained by graphical plots. With the iodo-compounds, iodide ion was estimated potentiometrically. With *p*-fluoronitrobenzene, thiomethoxide was estimated potentiometrically by acid–base procedures, and fluoride ion by the potentiometric procedure of O'Donnell and Stewart.[4] The reaction with 1-fluoro-2,4-dinitrobenzene, which is fast even at low temperatures, was followed by a conductivity procedure after calibration curves at various temperatures were constructed.

Ordinary thermostats were used except for the reaction with 1-fluoro-2,4-dinitrobenzene. For this, a large Dewar flask was used with the reaction vessel described earlier [5] plus an electrode system. This was immersed in well-cooled solid carbon dioxide–acetone mixtures to which a

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[1] Part XXX, Chan Tin-Lock, J. Miller, and F. Stansfield, *J.*, 1964, 1213.
[2] J. Miller, *J. Amer. Chem. Soc.*, 1963, **85**, 1628.
[3] H. Plieninger, *Chem. Ber.*, 1950, **83**, 266.
[4] T. A. O'Donnell and D. F. Stewart, *Analyt. Chem.*, 1961, **33**, 337.
[5] J. Miller and K. W. Wong, *Austral. J. Chem.*, 1965, **18**, 117.

suitable amount of fresh acetone was added. Sufficient time was then left for the reaction vessel and bath to equilibrate. Reactants were then allowed to mix, and condvctivity readings taken then and at suitable times thereafter. The capacity and insulation of the system, and short times of reaction, ensured that temperatures remained constant to within 0·5°, but were reported only to the nearest 0·5°. The large number of points in the Arrhenius plot compensate for this, and lead to a precision comparable with that for the other compounds, *viz.*, E_{act} $\pm 0{\cdot}3$ kcal. Kinetic and derived data for all the compounds are given in Tables 1 and 2. An example of the short runs with 1-fluoro-2,4-dinitrobenzene is given as Figure 1, and of a run with

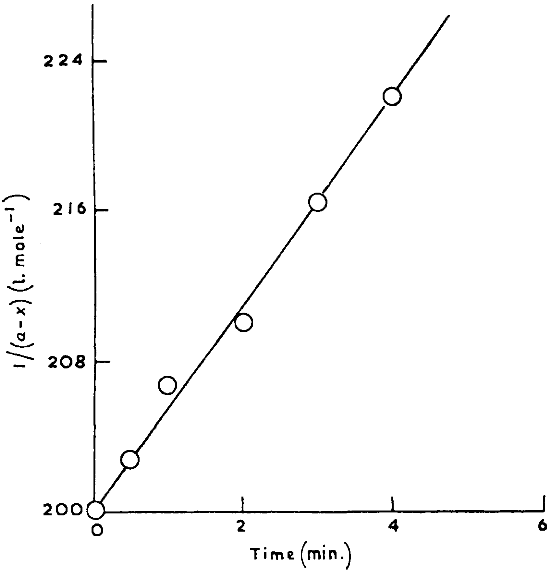

FIGURE 1. Reaction between sodium thiomethoxide and 1-fluoro-2,4-dinitrobenzene in absolute methanol at −75°

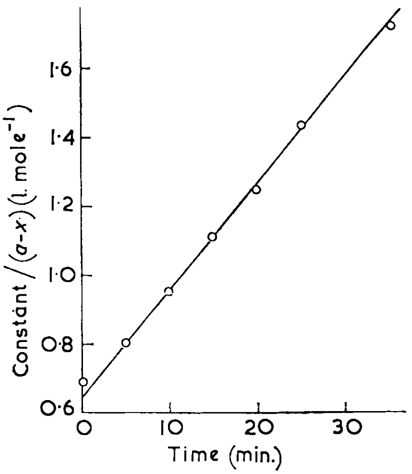

FIGURE 2. Reaction between sodium thiomethoxide and *p*-fluoronitrobenzene in absolute methanol at 61°

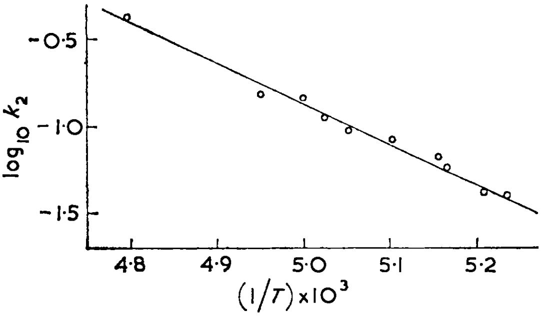

FIGURE 3. Arrhenius plot for the reaction between sodium thiomethoxide and 1-fluoro-2,4-dinitrobenzene in absolute methanol

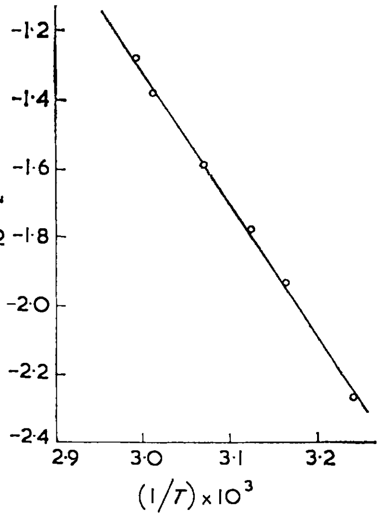

FIGURE 4. Arrhenius plot for the reaction between sodium thiomethoxide and *p*-fluoronitrobenzene in absolute methanol

p-fluoronitrobenzene as Figure 2. The Arrhenius plots for these compounds are given as Figures 3 and 4.

TABLE 1

Experimental rate constants k_2 (l. mole^{-1} sec.$^{-1}$, at temperatures shown in parentheses) for reaction of SMe$^-$/MeOH with some halogenonitrobenzenes

Substituents			
1-F, 4-NO_2	1-I, 4-NO_2	1-F, 2,4-$(NO_2)_2$ *	1-I, 2,4-$(NO_2)_2$
$5·93 \times 10^{-3}$ $5·93 \times 10^{-3}$ (35·2°)	$3·33 \times 10^{-4}$ $3·40 \times 10^{-4}$ (93·0°)	$3·90 \times 10^{-2}$ (−82·0°)	$8·63 \times 10^{-3}$ $8·63 \times 10^{-3}$ (36·0°)
$1·16 \times 10^{-2}$ $1·18 \times 10^{-2}$ (43·1)		$4·18 \times 10^{-2}$ (−81·0)	
$1·64_5 \times 10^{-2}$ (47·1)	$6·66 \times 10^{-4}$ (102·6)	$5·59 \times 10^{-2}$ (−79·5)	$8·75 \times 10^{-3}$ (37·0)
$2·52 \times 10^{-2}$ $2·52 \times 10^{-2}$ (52·6) $2·52 \times 10^{-2}$	$1·04 \times 10^{-3}$ $1·04 \times 10^{-3}$ (107·4)	$6·39 \times 10^{-2}$ (−79·0)	$1·37 \times 10^{-2}$ $1·37 \times 10^{-2}$ (42·1)
$4·11 \times 10^{-2}$ (58·7)	$2·31 \times 10^{-3}$ $2·32 \times 10^{-3}$ (121·2)	$8·00 \times 10^{-2}$ (−77·0) $9·17 \times 10^{-2}$ (−75·0)	$2·24 \times 10^{-2}$ $2·33 \times 10^{-2}$ (49·1)
$5·13 \times 10^{-2}$ $5·15 \times 10^{-2}$ (61·0)	$4·27 \times 10^{-3}$ $4·27 \times 10^{-3}$ (130·3)	$1·13 \times 10^{-1}$ (−74·0) $1·40 \times 10^{-1}$ (−73·0) $1·48 \times 10^{-1}$ (−71·0) $4·30 \times 10^{-1}$ (−64·5)	$3·09 \times 10^{-2}$ $3·23 \times 10^{-2}$ (55·0) $3·33 \times 10^{-2}$

* Owing to difficulty in control, the temperatures for this compound are assumed constant to only 0·5°.

TABLE 2

Data for reaction of SMe$^-$/MeOH with some halogenonitrobenzenes at 0°

		E_{act}		$\log_{10} B$			
Substituents	k_2 (l. mole^{-1} sec.$^{-1}$)	Expt.	Calc.	Expt.	Predicted	Expt. S_{act}	F/I mobility
1-F, 4-NO_2	$1·29 \times 10^{-4}$	17·9	17·5	$10·4_5$	Normal	−12·5	3720 [a]
1-I, 4-NO_2	$3·47 \times 10^{-8}$	19·7	19·5	8·3	Low	−22·4	1
1-F, 2,4-$(NO_2)_2$	$1·51_5 \times 10^2$	$10·4_5$	10·5	$10·5_5$	Normal	−12·1	372,000 [b]
1-I, 2,4-$(NO_2)_2$	$4·07 \times 10^{-4}$	14·3	14·5	$8·0_5$	Low	−23·5	1

[a] F/I mobility with OMe$^-$/MeOH at 0° = 2550 [5] and this is due to the E_{act} difference alone. The F/I mobility with SMe$^-$/MeOH at 0° due to the E_{act} difference alone = 27·5. [b] F/I mobility with OMe$^-$/MeOH at 0° = 5780 [5] and this is due to the E_{act} difference alone. The F/I mobility with SMe$^-$/MeOH at 0° due to the E_{act} difference alone = 1200.

RESULTS AND DISCUSSION

Figure 5 gives the calculated potential energy–reaction co-ordinate profiles for the reaction of thiomethoxide ion in methanol with the four substrates, *viz.*, *p*-fluoro- and *p*-iodo-nitrobenzenes, and 1-fluoro- and 1-iodo-2,4-dinitrobenzenes. These may be compared with the experimental E_{act} values shown in Tables 1 and 2, and the corresponding values for methoxide ion in methanol—a typical reagent for activated aromatic S_N reactions—from earlier data,[6,7] now completed with reliable measurements with 1-fluoro-2,4-dinitrobenzene.[5] In the reaction with *p*-fluoronitrobenzene, the prediction is that formation of the second transition state (T.St.2) is rate-limiting, but the difference between T.St.2 and T.St.1 is only 2 kcal., whereas in comparison with the reaction with *p*-iodonitrobenzene, T.St.1 for the fluoro-compound is 4 kcal. less, due to the electronegative fluorine (the α-effect [2]) facilitating bond formation. Thus, the high mobility of fluorine relative to iodine (and other halogens), normally a consequence of a reduction in E_{act} only of about 4 kcal., is modified to an E_{act} difference of only 2 kcal. The mobility ratio at 0° in this pair of compounds, due to the E_{act} difference alone, is only 27·5, whereas with methoxide at 0° it is 2550.[5,6] However, due, it was suggested,[2] to steric factors operating when neither entering nor replaced group is attached by a first-row element, the entropy of activation is low in such cases,* and therefore for the reaction with the iodo- but not the

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* In private discussion, Professor S. Winstein has suggested alternatively that this may be a solvation effect.

[6] G. P. Briner, M. Liveris, P. G. Lutz, and J. Miller, *J.*, 1954, 1265.

[7] A. L. Beckwith, G. D. Leahy, and J. Miller, *J.*, 1952, 3552.

fluoro-compound. The free-energy difference in reactivity should thus be restored to around the normal value. This, too, is observed, for the free-energy relative mobility is 3720 compared with 2550 at 0° for methoxide. The absolute values of E_{act} were also predicted. Both with respect to E_{act} and S_{act} the predictions are now fully confirmed (Table 2).

The reaction with 1-fluoro-2,4-dinitrobenzene differs from that with *p*-fluoronitrobenzene in that energies of initial and final states are raised relative to that of the corresponding intermediate complex. In relation to the bond dissociation energy–thermicity curve used to compute T.St. levels relative to initial and final states and intermediate complex, the effect is to raise T.St.1 relative to T.St.2; and it is predicted for the reaction with 1-fluoro-2,4-dinitrobenzene that T.St.1 and T.St.2 are equal. Thus, the normal high mobility of fluorine relative to iodine, due to an α-effect of 4 kcal. in E_{act}, is expected, but with a further increase in the overall free energy mobility due to a low S_{act} value for the reaction with 1-iodo-2-4-dinitrobenzene. This is what is observed. As regards the E_{act} difference alone, the F/I mobility at 0° is 1200 compared with 5780 for methoxide, whilst the overall free-energy relative mobility is 372,000. This is far higher than any value of F/I mobility previously found. The absolute values of E_{act} were also predicted. Both with respect to E_{act} and S_{act} the predictions are now fully confirmed (Table 2).

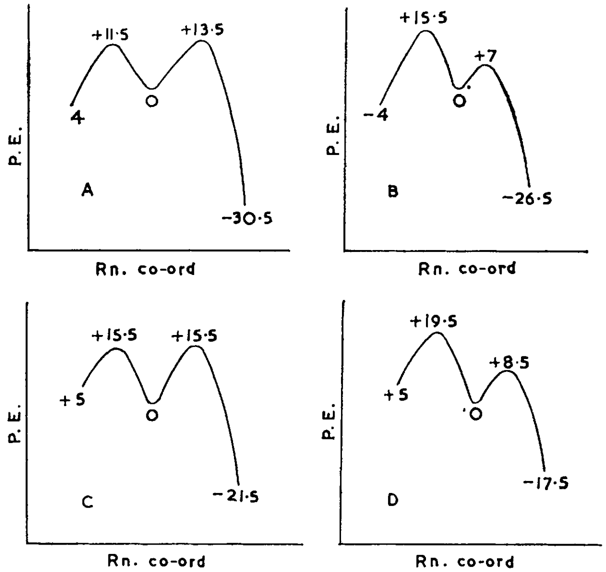

FIGURE 5. Potential energy–reaction co-ordinate profiles for reaction of thiomethoxide ion, in methanol, with

(A) *p*-fluoronitrobenzene,
(B) *p*-iodonitrobenzene,
(C) 1-fluoro-2,4-dinitrobenzene,
(D) 1-iodo-2,4-dinitrobenzene

TABLE 3

Activation energies and differences between OMe^- and SMe^- in MeOH in reaction with halogenonitrobenzenes

	Compound	*p*-Fluoro-nitrobenzene	*p*-Iodo-nitrobenzene	1-Fluoro-2,4-dinitrobenzene	1-Iodo-2,4-dinitrobenzene
E_{act} Calc.	OMe^-	21	25	15	19
	SMe^-	17·5	19·5	10·5	14·5
	ΔE_{act}	3·5	5·5	4·5	4·5
E_{act} Found	OMe^-	21·2	25·0	13·5	$18{\cdot}9_5$
	SMe^-	17·9	19·7	$10{\cdot}4_5$	14·3
	ΔE_{act}	3·3	5·3	$3{\cdot}0_5$	$4{\cdot}6_5$

The other prediction made,[2] *viz.*, that as far as E_{act} values are concerned, a lower SMe^-/OMe^- nucleophilicity ratio is expected for reactions with *p*-fluoronitrobenzene than for reactions with the other three substrates is now seen to be only partly true. The experimental details are given in Table 3. It will be seen that the predicted E_{act} and ΔE_{act} values are confirmed to within a fraction of a kcal. for three pairs but not for the fourth. In fact, the predicted and experimental values agree to within a fraction of a kcal. for seven of the eight reactions, but differ by 1½ kcal. for the reaction of methoxide with 1-fluoro-2,4-dinitrobenzene. Even this is quite reasonable agreement,* but it upsets the rather delicate distinction referred to, so that experimentally the ΔE_{act} values are lower for *both* fluoro-compounds than for either of the iodo-compounds.

Conclusions.—The data presented, together with earlier work, support the following general picture regarding activated aromatic nucleophilic substitutions.

(i) *With first-row nucleophiles in protic solvents.* The typical aromatic mobility pattern,[5-7,9-11] with F > I (ratio *ca.* 10^3), will be found, due to an electronegativity effect (α-effect) resulting in difference in E_{act} alone.

(ii) *With thiomethoxide ion, and any similar borderline reagent, in protic solvents.* (*a*) The typical aromatic mobility pattern will be found with substrates of moderate reactivity, due to the combination of a lesser E_{act} difference plus a heavy nucleophile steric interaction depressing S_{act} for displacement of larger groups. (*b*) An enhanced aromatic mobility pattern F > I (ratio *ca.* 10^5) will be found with reactive substrates, due to the full electronegativity effect, lowering E_{act}, *plus* the heavy nucleophile interaction affecting S_{act}. (*c*) It is to be expected that with low-reactivity substrates there will be a tendency towards the reverse mobility pattern F < I (see below).

(iii) *With heavy nucleophiles in protic solvents.* The reverse of the typical aromatic mobility pattern F < I (ratio *ca.* 10^{-2} to 10^{-3}) will be found as the typical result, due to formation of the second transition state (T.St.2), *i.e.*, the bond-breaking process, as the rate-limiting step, with T.St.2 higher for fluoro-compounds than the rate-limiting T.St.1 for corresponding iodo- and other similar compounds. The difference is large enough to counterbalance the heavy nucleophile interaction.

UNIVERSITY OF HONG KONG, DEPARTMENT OF CHEMISTRY,
HONG KONG, B.C.C.

[*Received, February* 26*th*, 1965.]

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* Murto [8] used Miller's method of calculation [2] for this reaction, but made an error in doing so, and gave the incorrectly predicted value of $E_{act} = 16{\cdot}5$ kcal.

[8] J. Murto, *Acta Chem. Scand.*, 1964, **18**, 1029.

[9] J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, 1951, **49**, 273.

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[11] J. F. Bunnett, E. W. Garbisch, and K. M. Pruitt, *J. Amer. Chem. Soc.*, 1957, **79**, 385.