729. *Nucleophilic Displacement of Fluorine from Organic Compounds. Part I. Kinetics of the Reactions of* 1-*Fluoro*-2 : 4-*dinitrobenzene with Primary Aromatic Amines.*

By N. B. Chapman and R. E. Parker.

The Arrhenius parameters for the reactions of 1-fluoro-2 : 4-dinitrobenzene with primary aromatic amines in 99·8% ethanol have been determined. The energy of activation is ~5000 cals. less than for the corresponding reactions of chloro- and bromo-compounds, and $\log_{10} A$ is 1·3—3·0 units less. This is ascribed mainly to an accentuated increase in solvation of the transition state in the reactions of the fluoro-compound. The fluoro-compound consumes only one mole of amine per mole and reacts ~100—200 times as fast as the chloro-compound at 30°, and ~20—70 times as fast at 50°. The mechanism of the reaction and values of the Arrhenius parameters are discussed, with special reference to a theory advanced by Berliner, Quinn, and Edgerton (*J. Amer. Chem. Soc.*, 1950, **72**, 5305) for analogous reactions of halogenonitronaphthalenes.

The kinetics of nucleophilic displacement of fluorine from organic compounds have not been much investigated, possibly because many organic fluorides apparently react very slowly with nucleophilic reagents. However, the kinetics of the reactions of 2-fluoroethanol with hydroxide ions have been examined (McCabe and Warner, *J. Amer. Chem. Soc.*, 1948, **70**, 4031) and the reactions of *n*-amyl, *cyclo*hexyl, and *tert.*-amyl fluorides, among others, with ethoxide ions have been recently studied in these laboratories (unpublished work by J. L. Levy). Aromatic fluoro-compounds of suitable structure react smoothly and relatively rapidly even with weakly nucleophilic reagents such as aromatic amines : 1-fluoro-2 : 4-dinitrobenzene is typical of these compounds, and for that reason has been chosen for study. The kinetics of the reactions of halogeno-2 : 4-dinitrobenzenes with amines have been the subject of a fair amount of investigation by Blanksma and Schreinemachers (*Rec. Trav. chim.*, 1933, **52**, 428), Singh and Peacock (*J.*, 1935, 1410; *J. Phys. Chem.*, 1936, **40**, 669), and Brady and Cropper (*J.*, 1950, 507). The present paper records the results of the first investigation of the kinetics of such reactions when the displaced halogen is fluorine, with the object of elucidating the causes of the relatively high rates of reaction.

Primary aromatic amines have been chosen as nucleophilic reagents for three main reasons : (*a*) the corresponding reactions of these amines with 1-chloro-2 : 4-dinitrobenzene have been thoroughly studied by Singh and Peacock (*loc. cit.*) and by van Opstall (*Rec. Trav. chim.*, 1933, **52**, 901); (*b*) the reactions can be studied by bromometric determination of the unchanged amine for a suitable range of amines, whereas the determination of fluoride ion, in contrast to that of other halide ions, is not well adapted to kinetic studies; (*c*) there was reason to believe, by analogy with Singh and Peacock's work (*loc. cit.*), that the reactions of the different amines, appropriately chosen, would have nearly the same entropies of activation, thus simplifying the interpretation of the results.

Additional interest attaches to the behaviour of 1-fluoro-2 : 4-dinitrobenzene since it has found a valuable application in " labelling " free amino-groups in proteins before hydrolysis (Sanger, *Biochem. J.*, 1945, **39**, 507; 1946, **40**, 261; 1948, **42**, 287). 1-Fluoro-2 : 4-dinitrobenzene owes its use in the above way to the remarkable ease with which the fluorine is displaced—this property has also been exploited in a preparative way by Whalley (*J.*, 1950, 2241) to convert alcohols into the corresponding 2 : 4-dinitrophenyl ethers by the action of 1-fluoro-2 : 4-dinitrobenzene in the presence of *tert.*-amines. Rarik, Brewster, and Dains (*J. Amer. Chem. Soc.*, 1933, **55**, 1289) employed *p*-fluoronitrobenzene similarly.

For kinetic studies with nucleophilic reagents Lulofs (*Rec. Trav. chim.*, 1901, **20**, 292) chose alkoxide ions, whereas Singh and Peacock, van Opstall, and Blanksma and Schreinemachers (*locc. cit.*), and Rheinlander (*J.*, 1923, 3099) used either aliphatic or aromatic amines or ammonia. The most relevant of these results for our purposes are those of Singh and Peacock, and of van Opstall, and we shall return to these in the discussion. Le Roux, Lu, Sugden, and Thomson (*J.*, 1945, 586) and Bennett and Vernon (*J.*, 1938, 1783) have studied the simplest of all nucleophilic displacements with these compounds, *viz.*, when the reagent is a halide ion, either isotopically distinguished from, as in the former case, or chemically different from, the halogen present in the organic compound, as in the latter case. However, no reactions in which fluorine is displaced, nor yet when it is the attacking reagent, have so far been studied.

The Arrhenius parameters for the reactions of 1-fluoro-2 : 4-dinitrobenzene with a series of primary aromatic amines in 99·8% ethanol are now presented. It has been possible to formulate a mechanism for the reactions and to suggest the causes of the observed reaction velocities, relative to those of other analogous halogeno-compounds. A brief preliminary account of this work has already been given (Chapman, Parker, and Soanes, *Chem. and Ind.*, 1951, 148).

EXPERIMENTAL.

(M. p.s are uncorrected.)

Materials.—1-Fluoro-2 : 4-dinitrobenzene, m. p. 26·5—27·0°, was prepared by Cook and Saunders's method (*Biochem. J.*, 1947, **41**, 558). After fractionation at 2 mm. the product was crystallised to constant m. p. from absolute ethanol.

The amines were all purified by crystallisation of their acetyl derivatives, followed by fractionation or crystallisation of the free bases (cf. Singh and Peacock, *loc. cit.*). The m. p.s of the acetyl derivatives and of the solid amines agreed with those given by these authors.

The hydrofluorides of aniline and *m*-bromoaniline were prepared by dropwise addition of 40% (wt.) hydrofluoric acid (6 g.) to a stirred solution of the amine (0·2 mol.) in absolute ethanol (10 c.c.) at 0°. The precipitated hydrofluorides were filtered off, sucked dry, well washed with benzene, and allowed to dry in the air. Thus were obtained aniline hydrofluoride (Found : $C_6H_5{\cdot}NH_2$, 70·5; HF, 15·2. Calc. for C_6H_7N,HF,H_2O : $C_6H_5{\cdot}NH_2$, 71·0; HF, 15·3%) and *m*-bromoaniline hydrofluoride (Found : *m*-$C_6H_4Br{\cdot}NH_2$, 82·0; HF, 13·5%. These figures were reproducible but do not correspond to any integral formula). Both the products deteriorated on storage and were freshly prepared before use.

The ethanol was purified by drying the commercial absolute product by Lund and Bjerrum's method (*Ber.*, 1931, **64**, 210) and fractionating the product. The water content of the ethanol was determined by the Karl Fischer reagent as modified by Smith, Bryant, and Mitchell (*J. Amer. Chem. Soc.*, 1939, **61**, 2407), and water was added to give 99·80% (by wt.) ethanol.

Thermostats.—A well-stirred mixture of crushed ice and water gave a steady temperature of 0·10°. For the higher temperatures the usual arrangement was employed : temperatures were steady to ±0·05°.

Procedure.—A solution (15 c.c.) of 1-fluoro-2 : 4-dinitrobenzene in 99·80% ethanol of definite concentration, about 0·020M., at thermostat temperature was added to a similar solution (10 c.c.) of amine, about 0·125M., in each of several 25-c.c. stoppered graduated flasks already in the thermostat. At known intervals the contents of a flask were poured into a mixture of benzene (50 c.c.) and concentrated hydrochloric acid (25 c.c.). This stopped the reaction by converting all the free amine into its hydrochloride. The flask was washed twice with distilled water, and the washings were added to the benzene–acid mixture. The benzene layer, containing unchanged fluorodinitrobenzene and most of the substituted diphenylamine produced, was separated and washed twice with water.

The residual amine in the combined aqueous layers was determined bromometrically following Day and Taggart's procedure (*Ind. Eng. Chem.*, 1928, **20**, 545). The excess of bromate–bromide solution never exceeded about 3 c.c. of 0·1N-solution. Under these conditions it was shown that none of the other substances possibly present, particularly ethanol, interferes. With larger excesses of bromate–bromide solution ethanol is oxidised. In all cases the accuracy of the procedure was checked by carrying out a blank. In some cases the initial amine concentration determined in this way differed from that calculated from the weight of amine, by up to 0·5%, and the concentration determined by titration was then used to calculate the rate constants given below.* As a further check the amount of free amine left after "infinite" time was determined. This usually corresponded to between 99·0% and 100% reaction.

Products.—2 : 4-Dinitrodiphenylamine and its various derivatives were isolated and characterised by their m. p.s.

RESULTS.

The reactions with aniline and with *m*-bromoaniline, both at 30°, were each carried out at three different initial concentrations, and by application of the differential method of determining orders (Laidler, "Chemical Kinetics," New York, 1950, p. 14), were shown to be of the first order with respect both to the fluoro-compound and to the amine. This was assumed to hold for the other cases also, as they all obeyed the second-order rate law given below.

By comparing the velocity coefficients assembled in Table I it was concluded that the reactions are represented by the equation

$$Ar{\cdot}NH_2 + Ar'F = Ar{\cdot}NHAr' + HF$$

Under the conditions of our experiments the liberated hydrogen fluoride does not apparently fix the amine and render it incapable of reaction (cf. Singh and Peacock's results with 1-chloro-2 : 4-dinitrobenzene, *loc. cit.*) since the amine hydrofluorides react almost as rapidly as the free amines.

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* In a preliminary report of this work (Chapman, Parker, and Soanes, *loc. cit.*) the rate constants were calculated by using initial amine concentrations calculated from the weight of amine. This explains the slight discrepancies.

The rate law is therefore

$$dx/dt = k(a - x)(b - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

giving

$$k = \frac{2{\cdot}303}{t(a - b)}\log_{10}\frac{b(a - x)}{a(b - x)}$$

where a = initial concentration of amine and b = initial concentration of fluorodinitrobenzene.

TABLE I.

k is in l. mole^{-1} sec.$^{-1}$.

Reagent	Temp.	$k \times 10^4$	Reagent	Temp.	$k \times 10^4$
Aniline	40°	122	*m*-Bromoaniline	30°	2·04
Aniline hydrofluoride	40	114	*m*-Bromoaniline hydrofluoride	30	1·85

TABLE II.

Aniline. 0·0503M-NH_2Ph, 0·0125M-$C_6H_3F(NO_2)_2$; 30°.

Time (secs.)	242	902	1908	3661	8032	17 hrs.
Decompn., %	9·60	31·44	53·84	75·28	93·46	99·36
10^4k	84·0	86·9	87·3	86·1	81·1	

Mean k = 85·1 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

m-*Toluidine.* 0·0497M-$NH_2{\cdot}C_6H_4Me$, 0·0125M-$C_6H_3F(NO_2)_2$; 20°.

Time (secs.)	802	1094	1364	1632	1919	2224
Decompn., %	31·63	40·34	47·12	52·96	58·63	62·94
10^4k	99·6	100·6	100·7	100·6	101·2	99·1

Mean k = 100·3 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

p-*Chloroaniline.* 0·0497M-$NH_2{\cdot}C_6H_4Cl$, 0·0125M-$C_6H_3F(NO_2)_2$; 40°.

Time (secs.)	4333	6615	18,377	30,660	124 hrs.
Decompn., %	28·16	38·88	71·12	86·16	100·6
10^4k	16·0	15·8	15·3	15·2	—

Mean k = 15·6 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

p-*Bromoaniline.* 0·0499M-$NH_2{\cdot}C_6H_4Br$, 0·0125M-$C_6H_3F(NO_2)_2$; 30°.

Time (secs.)	2687	10,115	19,980	40,440	89,700	127 hrs.
Decompn., %	9·59	30·06	48·92	72·58	92·65	99·92
10^4k	7·62	7·39	7·25	7·23	7·00	—

Mean k = 7·30 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

m-*Chloroaniline.* 0·0492M-$NH_2{\cdot}C_6H_4Cl$, 0·0125M-$C_6H_3F(NO_2)_2$; 20°.

Time (mins.)	1225	1345	1496	2667	3142	4035
Decompn., %	37·04	39·92	43·44	61·60	67·76	75·44
10^4k	1·35	1·36	1·38	1·34	1·36	1·34

Mean k = 1·36 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

m-*Bromoaniline.* 0·0495M-$NH_2{\cdot}C_6H_4Br$, 0·0126M-$C_6H_3F(NO_2)_2$; 40°.

Time (mins.)	118·3	385·7	1072	1469	2840	340 hrs.
Decompn., %	10·33	29·55	60·29	71·17	89·28	98·01
10^4k	3·14	3·19	3·19	3·21	3·14	—

Mean k = 3·17 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

Aniline hydrofluoride. 0·0247M-NH_2Ph,HF,H_2O, 0·0125M-$C_6H_3F(NO_2)_2$; 40°.

Time (secs.)	348	1317	2709	5150	11,248	46 hrs.
Decompn., %	8·99	29·70	48·48	68·06	87·64	99·52
10^4k	109	114	115	118	112	—

Mean k = 114 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

m-*Bromoaniline hydrofluoride.* 0·0257M-$NH_2{\cdot}C_6H_4Br,1{\cdot}4HF,0{\cdot}5H_2O$, 0·0125M-$C_6H_3F(NO_2)_2$; 30°.

Time (mins.)	926	1403	2383	2836	3822	5692
Decompn., %	24·24	31·84	46·24	49·76	58·08	67·04
10^4k	2·07	1·94	1·94	1·83	1·78	1·59

Mean k = 1·86 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

Mean deviation from mean 6·7%.

Except for the amine hydrofluorides (where solubilties were too low) $a = 4b$, ensuring that, so far as possible, the results are comparable with those of Singh and Peacock. It was not possible to work at the same absolute concentrations, owing to the high rates of the reactions under investigation.

Detailed results are given above for a few cases (Table II), and all the results are summarised in Table III. The mean deviation from the mean is always less than 3%, except for *m*-bromoaniline hydrofluoride (about 6%). In this case the values of *k* fall with time and it is evident that a simple second-order law is not obeyed over the whole reaction. However, the rate over the first 50% of the reaction is nearly as large as that of the reaction with *m*-bromoaniline.

TABLE III.

Amine	*a*	*b*	$10^4k^{0\cdot1}$	10^4k^{20}	10^4k^{25}	10^4k^{30}	10^4k^{40}	*E* (cals.)	$\log_{10} A$
Aniline	0·05	0·0125	27·1	60·1	72·0	85·7	122	6400	2·55
	0·025	0·0125	—	—	—	85·5	—	—	—
	0·05	0·025	—	—	—	88·7	—	—	—
m-Toluidine	0·05	0·0125	—	99·2	—	142	203	6550	2·88
p-Chloroaniline	0·05	0·0125	—	6·39	—	10·0	15·5	8100	2·82
p-Bromoaniline	0·05	0·0125	—	4·57	—	7·25	11·1	8100	2·69
m-Chloroaniline	0·05	0·0125	—	1·37	—	2·24	3·54	8700	2·60
m-Bromoaniline	0·05	0·0125	—	1·27	—	2·06	3·21	8500	2·43
	0·025	0·0125	—	—	—	2·04	—	—	—
	0·05	0·025	—	—	—	2·09	—	—	—
Aniline hydrofluoride	0·025	0·0125	—	—	—	—	114	—	—
m-Bromoaniline hydrofluoride	0·025	0·0125	—	—	—	1·85	—	—	—

a and *b* are initial (molar) concentrations of amine and fluorodinitrobenzene respectively.

Mean values of *k* are from several experiments. *k* and *A* are l. mole^{-1} sec.$^{-1}$.

DISCUSSION.

Velocity coefficients and Arrhenius parameters for the reactions of the corresponding fluoro-, chloro-, and bromo-compounds are assembled in Table IV. The results of Singh and Peacock, of Rheinlander, and of van Opstall have been recalculated in terms of mole/l. and seconds, and for 50° where necessary. Our own results have also been extrapolated to 50°, the only temperature used by Rheinlander. Different authors have used slightly different solvents: we have used 99·8% (by wt.) ethanol, Rheinlander 99·16% (by vol.). Changes in water content in the medium of less than 1% do not increase velocity coefficients by more than 10% and only Rheinlander's results need correction on this account. Minor inconsistencies also arise because of varying initial concentrations, but neither these nor the solvent differences alter the main features of the assembled results.

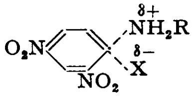
TABLE IV.

Amine	1-Fluoro-2 : 4-dinitrobenzene			1-Chloro-2 : 4-dinitrobenzene			1-Bromo-2 : 4-dinitrobenzene			1-Iodo-2 : 4-dinitrobenzene
	10^4k^{50}	*E*	$\log_{10} A$	10^4k^{50}	*E*	$\log_{10} A$	10^4k^{50}	*E*	$\log_{10} A$	10^4k^{50}
Aniline	168	6400	2·55	2·69	11,200	4·0	4·05	11,200	4·2	—
	—	—	—	2·74	10,400	3·5	—	—	—	—
	—	—	—	2·98	—	—	4·51	—	—	1·31
m-Toluidine ...	282	6550	2·88	3·91	11,600	4·4	5·59	11,600	4·6	—
				3·72	10,800	3·9	—	—	—	—
p-Chloroaniline	23·1	8100	2·82	0·632	12,300	4·1	—	—	—	—
p-Bromoaniline	16·6	8100	2·69	0·544	14,600	5·6	—	—	—	—
m-Chloroaniline	5·46	8700	2·60	0·197	13,000	4·1	—	—	—	—
m-Bromoaniline	4·90	8500	2·43	0·219	15,100	5·5	—	—	—	—

k and *A* in 1 mole^{-1} sec.$^{-1}$. *E* in cals. (accurate to ± 500 cals.).
A is accurate to ±0·3 unit.
Singh and Peacock (*loc. cit.*) used $a = 0{\cdot}4$M., $b = 0{\cdot}1$M. in absolute ethanol.
Van Opstall (*loc. cit.*) used $a = 0{\cdot}08$M., $b = 0{\cdot}04$M. in absolute ethanol.
Rheinlander (*loc. cit.*) used $a = 0{\cdot}1$M., $b = 0{\cdot}1$M. in 99·16% (by vol.) ethanol.
(*a* and *b* have the same significance as in Table II.)

The first major difference between the fluoro-compound and the other halides lies in the stoicheiometry of the reaction. Whereas the fluoro-compound consumes only one mole of amine per mole, the others consume two moles by virtue of the formation of stable salts by the hydrogen halide generated. The amine hydrofluorides may be ethanolysed under our experimental conditions, or it may be that they are readily dissociated hydrogen-bonded complexes rather than true salts. Whatever their nature, the critical fact is that they appear to react almost as readily with 1-fluoro-2 : 4-dinitrobenzene as do the free amines. This is exemplified in Table I. Moreover the reactions obey the rate law $dx/dt = k_2(a - x)(b - x)$ much better than the law $dx/dt = k_2(a - 2x)(b - x)$.

Inspection of Table IV reveals that for the reactions of these amines with the chloro- and bromo-compounds, the Arrhenius parameters are the same within experimental error, but for the reactions of the fluoro-compound both the experimental energy of activation, *E*, and the non-exponential term, *A*, are strongly diminished, *viz.*, by about 5000 cals. and $10^{1\cdot3}$—$10^{3\cdot0}$ units respectively. The velocity coefficients for the reactions of the fluoro-compound are some 20—70 times greater than for the other halides, and it is clear that the diminution in *A* is more than offset by the increase in $e^{-E/RT}$. If it is assumed for the present that the reaction pursues a simple bimolecular course (cf. Brady and Cropper, *loc. cit.*) corresponding directly to second-order kinetics, the dipolar transition state may be represented by :



(X = F, Cl, or Br)

We may deduce that the relatively low values of *A* (low values of the entropy of activation) are caused mainly by an increase of solvation in the transition state relative to the uncharged initial state, and that this increase is most marked when X = F (cf. Bell, *J.*, 1943, 632). Thus it is solvation that makes possible the remarkably low energy of activation observed with the fluoro-compound. Moreover, the increased reaction velocity in aqueous ethanol, a solvent of higher " solvating power " than pure ethanol, is readily understood in terms of Hughes and Ingold's theory of solvent action (*Trans. Faraday Soc.*, 1941, **37**, 608). This critically important increased solvation of the transition state is readily intelligible in terms of the small size of the fluoride ion and its comparatively large solvation energy. Thus the ionic radii of the fluoride, chloride, and bromide ions are 1·36, 1·81, and 1·95 Å respectively (Pauling, " The Nature of the Chemical Bond," Ithaca, 1945, p. 346). The heats of solution of fluoride, chloride, and bromide ions in water are 97,000, 65,000, and 57,000 cals./g.-ion respectively (Bernal and Fowler, *J. Chem. Physics*, 1933, **1**, 538). Mishchenko (*Acta Physicochim. U.R.S.S.*, 1935, **3**, 693) has shown that the heats of solution of ions in methanol and ethanol are of the same order as in water, so we may take Bernal and Fowler's values as giving an approximate measure of the different solvation energies (cf. A. G. Evans, *Trans. Faraday Soc.*, 1946, **42**, 724). The sharp divergence of behaviour between the fluoro-compound and other halides should be much less marked in weakly solvating solvents, but more marked in strongly solvating solvents, a subject which we hope to investigate in due course.

Berliner, Quinn, and Edgerton (*J. Amer. Chem. Soc.*, 1950, **72**, 5305) have suggested that reactions of the 1-halogeno-2-nitro- and 2-halogeno-1-nitro-naphthalenes, very similar to those at present under discussion, occur by a two-stage mechanism :

$$\mathrm{RX} + \mathrm{NHR'_2} \rightleftharpoons \text{Complex} \quad . \ . \ . \ . \ . \ . \ . \ . \ . \ . \quad \text{(i)}$$

$$\text{Complex} \longrightarrow \mathrm{NRR'_2} + \mathrm{X^-} \quad . \ . \ . \ . \ . \ . \ . \ . \ . \quad \text{(ii)}$$

where X = Cl or Br. These authors studied pseudo-unimolecular reactions, using piperidine both as reagent and solvent. Consequently their results yield no information about how the rate of reaction depends on the concentration of piperidine. However, the results recently published by us (Chapman, Parker, and Soanes, *loc. cit.*) for *o*- and *p*-halogenonitrobenzenes make it very probable that the reactions studied by Berliner *et al.* would show second-order kinetics under suitable conditions.

The complex in equation (i) is formulated as in Fig. 1, with apparently a true covalency between N and $C_{(1)}$. A proton must also have been lost from the nitrogen, but this is not likely to have kinetic significance. This formulation presents certain steric difficulties. It requires that the nitro-group shall be coplanar with the rings. With picryl iodide it is known (Huse and Powell, *J.*, 1940, 1398) that the *o*-nitro-group is nearly perpendicular to the ring, and with other *o*-halogenonitrobenzenes or 1-halogeno-2-nitro- or 2-halogeno-1-nitro-naphthalenes, geometrical considerations make a similar conclusion probable, although there appears to be no critical experimental evidence available. To the extent that the nitro-group is not coplanar with the ring, it will be " imperfectly conjugated " with the ring, thus raising the energy of the complex. In the formation of complexes between *o*-chloronitrobenzene or 1-chloro-2 : 4-dinitrobenzene and aromatic amines, the weight of evidence seems to be against covalent-bond formation (cf. Hammick *et al.*, *J.*, 1940, 1539). There seems to be no positive evidence for such bond formation with piperidine, nor apparently has any such complex been isolated.

Berliner *et al.* assume that " the formation of the intermediate is probably a rapid process," with " the breaking of the carbon–halogen bond the slow, rate-determining step." If, as seems probable, these reactions would show second-order kinetics in dilute solution, then the first step would under these conditions also be reversible, and be in fact reversed. However, in an excess of piperidine the first step may go rapidly to completion and not in fact be reversed. In this case the second step would be truly rate-determining. In the former case the overall rate would be determined by the velocity of the second step and the position of equilibrium in the first step. The ready displacement of fluorine might then be ascribed to its great electronegativity and consequent ease of anionisation. The following considerations seem to us, however, to cast grave doubts on the two-stage mechanism.

A second nitro-group in the *ortho*- or *para*-position to the halogen in *o*- or *p*-halogenonitrobenzene or 1-halogeno-2- or -4-nitronaphthalene greatly facilitates nucleophilic displacement of the halogen. Thus in the benzene series, reactions of piperidine with *o*- and *p*-chloronitrobenzene in dilute solution in 99·8% ethanol have been shown in these laboratories (Chapman *et al.*, *loc. cit.*) to have energies of activation of ~18,000 cals. whereas the corresponding value for 1-chloro-2 : 4-dinitrobenzene is ~10,000 cals. (Brady *et al.*, *loc. cit.*). The entropy factors differ very little. In the naphthalene series van Opstall (*Rec. Trav. chim.*, 1933, **52**, 901) has shown that 1-chloro-2 : 4-dinitronaphthalene reacts with amines about 200 times as fast as 1-chloro-2 : 4-dinitrobenzene, which itself reacts faster than 1-chloro-2-nitro- or 2-chloro-1-nitro-naphthalene with piperidine. An electron-wthdrawing group such as NO_2 could hardly act by facilitating ionisation of the halogen. In our view it almost certainly acts by diminishing the repulsive energy between the attacking nucleophilic reagent and the halogeno-compound (cf. Glasstone, Laidler, and Eyring, "Theory of Rate Processes," New York, 1941, pp. 452 *et seq.*) in a typical bimolecular process. It seems to us, therefore, that even in the presence of an excess of piperidine, stage (ii) in Berliner's mechanism cannot be truly rate-determining. We may add that Lindemann and Pabst (*Annalen*, 1928, **462**, 24) have provided convincing experimental evidence that, in the reactions of 1-chloro-2 : 4-dinitrobenzene with aromatic amines, where complexes can be isolated, such complexes are not intermediates in the reaction. In these circumstances we prefer, for our own reactions, a one-stage bimolecular substitution process, with the probability that this mechanism is universal for this class of reaction (cf. Brady *et al.*, *loc. cit.*). The Arrhenius parameters of the reactions may be qualitatively understood, as we have seen, in terms of such a mechanism and the structure of the corresponding transition state.

FIG. 1.

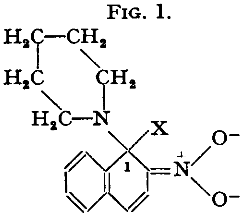
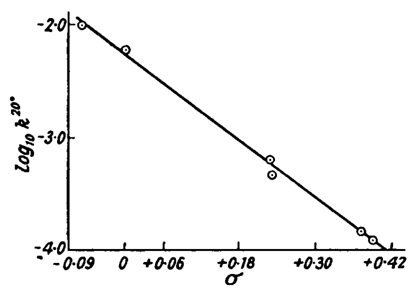


FIG. 2.

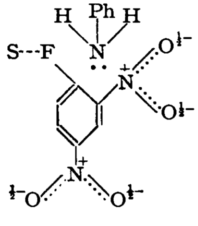


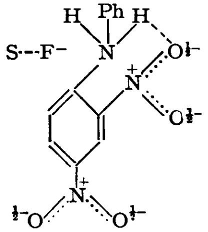
Despite the existence of a bulky nitro-group *ortho* to the seat of substitution it is unlikely that steric compression energies contribute to the observed energies of activation. Preliminary calculations on a reasonable model of the transition state (Chapman, to be published) show that such compressions are small and vary little with change of halogen. It is true that they are least when fluorine is the halogen. Also the conjugation (p. 3305) of the *o*-nitro-group with the ring will be at a maximum when the halogen is fluorine, because of its small size. Both these factors may facilitate the reaction.

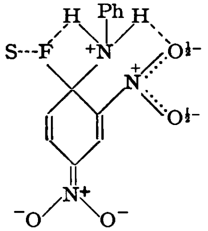
We have also considered the possibility that variation in the dipole–dipole interaction energy may be responsible for the observed variations in E as the halogen is varied. However, the dipole moments of 2 : 4-$(NO_2)_2C_6H_3X$ vary very little : μ = 3·5, 3·0—3·3, and 3·1 ± 0·1D when X = F, Cl, and Br respectively (*Trans. Faraday Soc.*, 1934, **30**, lxxviii). It does not seem likely that the equilibrium distance between the dipoles in the transition state, to which the interaction energy is very sensitive, will differ very greatly according to the nature of X, being largely determined by the structures of the reacting molecules as a whole. We therefore conclude tentatively that dipole–dipole interaction does not alter very much in the different reactions under consideration.

Fig. 2 shows that, as for the chloro- and bromo-compounds, these reactions of the fluoro-compound obey to a fair degree of approximation the Hammett σ–ρ relation (Hammett,

" Physical Organic Chemistry," New York, 1941, p. 184). The straight line has a slope $-4{\cdot}245$ for 20°, and similar lines have slopes $-4{\cdot}180$ for 30°, and $-4{\cdot}006$ for 40°, thus defining the ρ values for this reaction for these three temperatures. The variation of velocity coefficients with the structure of the amine, a subject in which we are not primarily interested here, is broadly in accordance with expectations based on their structure and basic strength. In our view, a formula of the intermediate complex of the type suggested by Berliner *et al.* represents one extreme configuration of the transition state, which may be specified as a hybrid of several configurations, thus :







We include a proton in our formulation but the loss of it is kinetically insignificant. We have deliberately excluded *o*-quinonoid stuctures because of doubts about the coplanarity of the *o*-nitro-group with the ring. We also include, in our formulation of the transition state, electrostatic interactions (represented by broken lines) between (*a*) amino-hydrogen and nitro-oxygen, (*b*) amino-hydrogen and fluorine, and (*c*) fluorine and solvent (S represents several solvent molecules). We specify the solvent interaction to be with fluorine because of its special importance for this case, although we envisage the whole of the transition state as being solvated. It seems to us that there can be little doubt of the operation of this solvation factor : factors (*a*) and (*b*) we put forward more tentatively (cf. a similar suggestion by Gold and Whittaker, *J.*, 1951, 1188, for electrophilic substitution) and hope to devise experiments to test these ideas. Factor (*a*) could operate whatever the halogen, whereas factor (*b*) would only be expected to be appreciable when the halogen is fluorine. The latter, therefore, may be an additional factor (besides the increased solvation discussed above) tending to produce a lower energy and entropy of activation for the fluoro-compound.

We hope to extend this work to include *p*-fluoronitrobenzene and 1-fluoro-2 : 4-dinitronaphthalene and possibly fluoromononitronaphthalenes, as well as giving attention to variation of solvent.

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