peaks were identified by a comparison of their retention times with those of a known mixture of phenols. The amount of dienone present in the neutral fraction was found to be 0.04 g. (0.2%) calculated from its absorption in the ultraviolet.

URBANA, ILL.

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, UNIVERSITY OF NORTH CAROLINA]

Base Catalysis of the Reaction of N-Methylaniline with 2,4-Dinitrofluorobenzene. Proof of the Intermediate Complex Mechanism for Aromatic Nucleophilic Substitution[1]

BY J. F. BUNNETT[2] AND JOHN J. RANDALL

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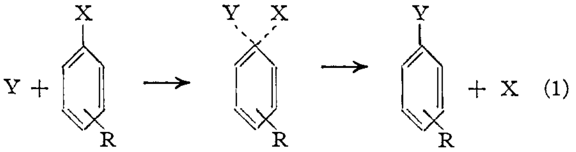
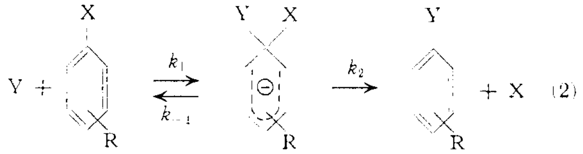
The reaction of N-methylaniline with 2,4-dinitrofluorobenzene is sensitive to base catalysis, whereas reactions with the corresponding chlorine and bromine compounds are not. In ethanol, the catalyzed rate is linearly dependent on potassium acetate concentration. In 60% dioxane–40% water, the catalyzed rate shows less than linear response to hydroxide ion concentration at higher concentrations of the base (Fig. 3). The acetate-catalyzed rate is not depressed by added acetic acid; the reaction is thus *general* base catalyzed. These observations are inconsistent with any form of one-step mechanism for the displacement reaction. They are, however, rationally interpretable in terms of the intermediate complex mechanism shown in Chart I. In combination with other evidence previously published, the present work firmly establishes the intermediate complex mechanism for a large group of aromatic nucleophilic substitution reactions, and makes this mechanism extremely probable for all such reactions.

The mechanism of nucleophilic displacement at aromatic carbon has been a subject of active discussion in recent years. Many chemists have advocated a one-step, SN2-like mechanism which has often been represented as



Others have favored a two-step mechanism involving a metastable intermediate complex. The latter view was strongly advocated by Bunnett and Zahler[3] and has been further supported in recent papers from this Laboratory.

The intermediate complex mechanism is represented by equation 2.



This mechanism predicts second-order kinetics, as commonly observed, and the over-all second-order rate coefficient depends on the rate coefficients of the individual steps

$$k = k_1k_2/(k_{-1} + k_2) \qquad (3)$$

Reactions occurring by this mechanism may be classified according to the relative magnitudes of k_{-1} and k_2: (class A) If $k_2 >> k_{-1}$, that is, if X is expelled from the intermediate complex much faster than Y, equation 3 simplifies to $k = k_1$; the rate is determined by the rate of formation of the intermediate complex. (class B) If $k_{-1} >> k_2$, equation 3 becomes $k = k_1k_2/k_{-1}$; the rate is equal to the equilibrium concentration of the intermediate complex times the rate coefficient (k_2) for its transformation into products. (class C) If k_2 and k_{-1} are of comparable magnitude, equation 3 cannot be simplified; the over-all rate is affected both by the rates of bond-making (k_1) and of bond-breaking (k_2), as well as by k_{-1}.

The case for the intermediate complex mechanism comprises the following principal arguments: 1. The transition state for the one-step, SN2-like mechanism is difficult to rationalize quantum-mechanically, whereas the transition states and intermediate for the intermediate complex mechanism are easily rationalized.[3] 2. Certain highly activated substrates have been observed to form *stable* complexes similar to the intermediate complex in equation 2; it is reasonable that when less activation is present complexes of this sort are also formed though their stability may not be sufficient to permit isolation.[3] 3. In reactions known to involve breaking of a carbon–halogen bond in the rate-determining step, the carbon–fluorine bond is broken very much slower than other carbon–halogen bonds. Yet in many aromatic nuclophilic substitution reaction series, the order of mobility of the halogens is F >> Cl ~ Br ~ I. It is therefore concluded that in such reaction series the C–X bond is not broken in rate-determining steps. This result is incompatible with the SN2-like mechanism,[4] but is agreeably explained in terms of the intermediate complex mechanism, class A, in which the rate is determined by the rate of formation of the intermediate.[5] 4. In reactions of piperidine with several 1-substituted-2,4-dinitrobenzenes,[5] six substituents with first atoms representing five elements were displaced at nearly the same rate.[6] Since there

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[1] Financial assistance from the Office of Ordnance Research, U. S. Army, is gratefully acknowledged. Presented in part at the Southeastern Regional American Chemical Society Meeting, Durham, N. C., November, 1957.

[2] Department of Chemistry, Brown University, Providence, R. I.

[3] J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 297 (1951).

[4] With this exception: the result could be accommodated by an unlikely one-step mechanism in which bond-breaking had made little or no progress at the rate-determining transition state.[5]

[5] J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, THIS JOURNAL, **79**, 385 (1957).

[6] A similar result has been obtained in reactions of sodium thiophenoxide with the same substrates; *cf.* J. F. Bunnett and W. D. Merritt, Jr., *ibid.*, **79**, 5967 (1957).

are ordinarily great differences in the rates of heterolysis of bonds as diverse as C–I, C–O and C–S, the sameness of rate observed indicates that little or no breaking of the old bond had occurred at the rate-determining transition state. Again the result is incompatible with the SN2-like mechanism,[4] but is readily interpreted in terms of the intermediate complex mechanism with $k_2 >> k_{-1}$ (class A).

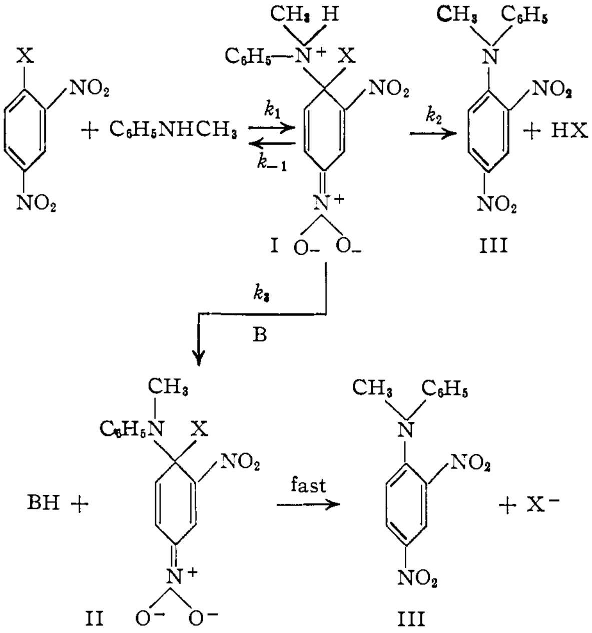
These four arguments constitute a strong case for the intermediate complex mechanism, but some features of the situation call for further attention. One is the unlikely exception, noted in footnote 4, to arguments 3 and 4. Another is a change in the order of mobility of the halogens which accompanies certain changes in the nucleophilic reagent. Thus in contrast to the order of mobility $F >> Cl \sim Br \sim I$ with most alkoxide, mercaptide and amine reagents, the order is $Br > Cl > F$ in reactions of 2,4-dinitrohalobenzenes with potassium iodide in acetone[7] and with N-methylaniline in ethanol or in nitrobenzene.[8]

The fact that the order $Br > Cl > F$ also obtains in SN2 displacements at saturated carbon atoms has been taken[7] as evidence that an SN2-like mechanism prevails in these aromatic substitutions. However, the order $Br > Cl > F$ can also be understood in terms of the intermediate complex mechanism. Consider the case of reagent iodide ion. For displacement of fluorine, in the symbolism of equation 2, one would have $X = F$ and $Y = I$. In this case k_{-1} would be much greater than k_2 because iodide would be split out of the intermediate complex, to regenerate reactants, much faster than fluoride ion would be split out to form products; the decomposition of the intermediate complex is analogous to the first step of an SN1 reaction of a saturated alkyl halide, and in such reactions iodides react much faster than fluorides.[9] Thus in the displacement of fluorine (or chlorine) by iodide, one would have class B of the intermediate complex mechanism in which the rate of breaking of the C–X bond very much enters into determination of over-all reaction rate; the order $Br > Cl > F$ would be expected.

The order $Br > Cl > F$ with reagent N-methylaniline[8] can also be rationalized in terms of the intermediate complex mechanism, class B. The relevant chemical equation is set down in the top line of Chart I. Especially in the case of $X = F$ it is not unreasonable that k_{-1} should greatly exceed k_2, that is, that the N-methylanilino group of I should be expelled to regenerate reactants faster than fluoride ion is expelled to form products.

Scrutiny of structure I suggested an experimental test of this rationalization. There is a hydrogen atom on the ammonium nitrogen atom of I. It seemed that a base (B) ought to be able to remove this hydrogen atom, converting intermediate I to intermediate II from which the expulsion of halide ion should be easy and the expulsion of the N-methylanilide ion difficult. Thus base catalysis was predicted.

CHART I



Base catalysis was found, as shown by the data of Table I. In this table, the following points should be noted: (a) In the absence of added salts the order of halogen mobility is $Br > Cl = F$, in essential agreement with Hammond and Parks although they reported fluorine to be displaced somewhat slower than chlorine. (b) Addition of sodium perchlorate (0.1 M) in each case causes a modest increase in rate (22 to 40%); this is a measure of the normal salt effect on these reactions. (c) Addition of potassium acetate (0.1 M) causes an increase in rate of displacement of bromine or chlorine somewhat less than caused by addition of sodium perchlorate; this also represents a normal salt effect which is smaller in the case of potassium acetate because this salt is more highly ion-paired in ethanol.[10] (d) Added potassium acetate accelerates the displacement of fluorine by 1400%. This acceleration is nearly a hundred times as great as the normal salt effect of potassium acetate would be. The special characteristic of potassium acetate responsible for this 15-fold increase in rate is the basicity of the acetate ion. This is base catalysis.

TABLE I

REACTIONS OF 1-HALO-2,4-DINITROBENZENES WITH N-METHYLANILINE IN ABSOLUTE ETHANOL AT 67.2°

Added salt	Rate coefficient[a] (l. mole^{-1} sec.$^{-1}$ × 10^5) when the halogen is Bromine	Chlorine	Fluorine
None	20.3	7.3	7.3
$KC_2H_3O_2$ (0.104 M)	23.2	9.1	110
$NaClO_4$ (0.104 M)	24.9	10.3	10.2

[a] These data abstracted from Table II.

Acetate ion is a significant nucleophilic reagent and itself displaces fluorine from 2,4-dinitrofluoro-

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[7] J. Cortier, P. J. C. Fierens, M. Gilon and A. Halleux, *Bull. soc. chim. Belg.*, **64**, 709 (1955); P. J. C. Fierens and A. Halleux, *ibid.*, **64**, 717 (1955).

[8] G. S. Hammond and L. R. Parks, THIS JOURNAL, **77**, 340 (1955).

[9] K. A. Cooper and E. D. Hughes, *J. Chem. Soc.*, 1183 (1937); N. B. Chapman and J. L. Levy, *ibid.*, 1677 (1952); W. T. Miller, Jr., and J. Bernstein, THIS JOURNAL, **70**, 3600 (1948).

[10] J. D. Reinheimer, W. F. Kieffer, S. W. Frey, J. C. Cochran and E. W. Barr, *ibid.*, **80**, 164 (1958); S. Winstein and E. Clippinger, *ibid.*, **78**, 2784 (1956).

benzene.[11] Also, it interacts with ethanol to form ethoxide ions which may displace fluorine. A few words therefore need be said about our procedure for determining the rate of reaction with N-methylaniline in the presence of competing nucleophilic reagents. 2,4 - Dinitro - N - methyldiphenylamine (III) is orange whereas 2,4-dinitrofluorobenzene and the products of displacement of fluorine by acetate or ethoxide ion (2,4-dinitrophenetole, 2,4-dinitrophenyl acetate and 2,4-dinitrophenol) are all colorless in acidic medium. Thus, the production of III could be measured directly by photometric analysis. Reactions were set up so as to furnish pseudo-first order kinetics; initial concentrations were as follows: 2,4-dinitrohalobenzene, 2.5×10^{-3} *M;* N-methylaniline, 0.2 *M;* potassium acetate, 0.02 to 0.31 *M*. Good first-order kinetics were observed, as shown by the linearity of plots of $\ln(A_\infty - A)$ *vs.* time; a representative plot is shown in Fig. 1. The slope of such a line is the total first-order rate coefficient for all reactions destroying the substrate; multiplication of the slope by the fractional yield of III (easily determined photometrically) gives the first-order rate coefficient, k_{III}^*, for the reaction of the substrate with N-methylaniline to form III. This procedure is rigorous; the only assumptions involved are that the various competing reactions occur in constant ratio to one another throughout the run, that III is the only colored product formed and that III is not destroyed under the conditions of the experiment. Evidence for the validity of these assumptions with reference to our experiments is discussed in the Experimental section.

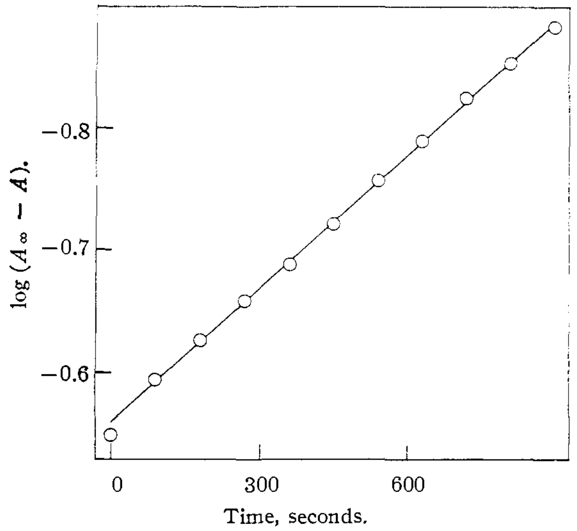

Fig. 1.—Plot of log $(A_\infty - A)$ *versus* time for a typical run in ethanol at 46°. Reaction of 2,4-dinitrofluorobenzene with N-methylaniline, catalyzed by potassium acetate; data from Table VI.

Base catalysis of the reaction of 2,4-dinitro*fluoro*benzene with N-methylaniline having been found, it was next of interest to determine the form of the dependence of catalyzed rate on potassium acetate concentration. The results from a series of runs are summarized in Table II and displayed graphically in Fig. 2. It is apparent that the catalyzed rate is linearly dependent on potassium acetate concentration. In several runs, represented in Fig. 2 by black circles, acetic acid was added as well as potassium acetate and in concentration equal to that of the potassium acetate. *Added acetic acid did not depress the base-catalyzed rate.* Thus, the reaction is general base catalyzed[12]; the catalyzed rate is dependent on the concentration of potassium acetate and not on the concentration of ethoxide ions. (It was shown separately that acetic acid itself does not catalyze the reaction.)

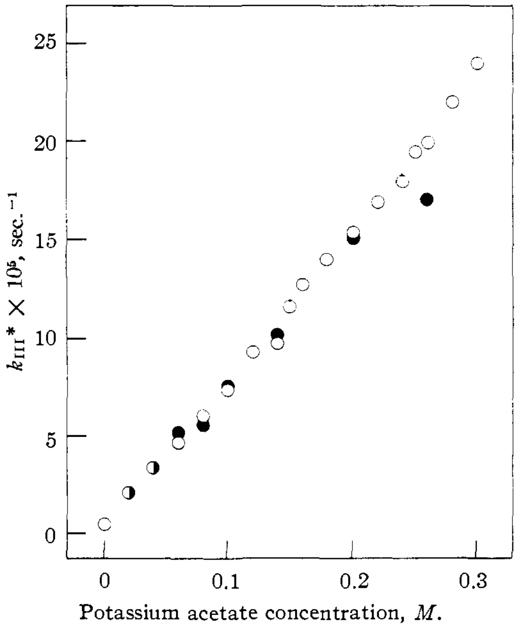

Fig. 2.—Effect of acetate ion on rate of reaction of N-methylaniline with 2,4-dinitrofluorobenzene in ethanol at 46°: open circles, only potassium acetate added; solid circles, acetic acid also present, in concentration equal to that of the potassium acetate; half-filled circles (◑), identical values obtained with or without acetic acid. Several points are mean values from more than one run; see Table II.

This observation of *general* base catalysis has the same significance for the mechanism of amine-induced aromatic nucleophilic substitutions that the observation of zero-order kinetics in certain nitration reactions[13] had in respect to the mechanism of nitration. Just as in nitration the observations of second-order kinetics in sulfuric acid medium and of first-order kinetics in nitric acid were "too normal" to give any specific indication of mechanism[13]; so also the observations of second-order kinetics and of insensitivity to base catalysis in many amine-induced aromatic displacements[14] are too normal to be of themselves of much diagnostic value, being consistent with both the S$_N$2-like and the intermediate complex mechanism. And just as

[11] *Cf.* L. R. Parks, G. S. Hammond and M. F. Hawthorne, This Journal, **77**, 2903 (1955).

[12] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 215.

[13] E. D. Hughes, C. K. Ingold and R. I. Reed, *J. Chem. Soc.*, 2410 (1950).

[14] J. F. Bunnett and K. M. Pruitt, *J. Elisha Mitchell Sci. Soc.*, **73**, 297 (1957).

TABLE II

REACTIONS OF 2,4-DINITROHALOBENZENES WITH N-METHYLANILINE IN ABSOLUTE ETHANOL

Halogen	$[KC_2H_3O_2]_0$, *M*	Other added subtance, *M*	k_{tot} sec.$^{-1}$ × 10^5	Yield of III, %	k_{III}*, sec.$^{-1}$ × 10^{5a}	k_{OR}*, sec.$^{-1}$ × 10^5	k_{OR} × 10^5,^{b} l. mole^{-1} sec.$^{-1}$
Temperature, 67.2°							
Br	...	....	3.75	100	3.75		
Br	...	$NaClO_4$, 0.096	4.61	100	4.61		
Br	0.096	....	4.31	94.8	4.09	0.22	2.4
Cl	...	....	1.35	100	1.35		
Cl	...	$NaClO_4$, 0.096	1.90	100	1.90		
Cl	.096	....	1.67	96.5	1.61	.06	0.6
F	...	....	1.73	77.5	1.34	.39	
F	...	....	1.79	77.7	1.38	.41	
F	...	$NaClO_4$, 0.096	2.32	79.2	1.84	.52	
F	...	$NaClO_4$, .096	2.30	81.8	1.88	.58	
F	...	$NaClO_4$, .096	2.40	81.0	1.94	.54	
F	.096	....	266	8.3	22.1	244	2530
F	.096	....	241	8.1	19.5	222	2400
F	.096	....	247	7.9	19.5	228	2460
Temperature, 46.0°							
F	...	....	0.638	78.8	0.503	0.135	
F	...	$NaClO_4$, 0.0985	0.801	84.0	0.675	0.126	
F	.0197	....	10.1	18.5	1.87	8.2	432
F	.0197	....	10.6	19.8	2.09	8.5	448
F	.0197	$HC_2H_3O_2$, 0.0197	8.82	22.7	2.00	6.82	360
F	.0395	....	18.4	17.1	3.14	15.3	404
F	.0395	....	19.2	18.2	3.50	15.7	414
F	.0395	$HC_2H_3O_2$, 0.0395	16.1	20.5	3.31	12.8	337
F	.0591	....	26.2	16.2	4.25	21.9	385
F	.0591	....	28.0	16.9	4.75	22.3	392
F	.0591	$HC_2H_3O_2$, 0.0591	24.9	20.5	5.11	19.8	348
F	.0790	....	34.1	16.2	5.53	28.6	377
F	.0790	....	37.8	17.1	6.39	31.4	414
F	.0790	$HC_2H_3O_2$, 0.0790	32.6	20.2	5.50	27.1	370
F	.0985	....	46.0	15.7	7.22	38.8	409
F	.0985	....	43.5	15.6	6.78	36.7	387
F	.0985	....	44.5	16.7	7.44	37.1	391
F	.0985	$HC_2H_3O_2$, 0.0985	37.3	19.8	7.39	29.9	315
F	.1182	....	54.7	16.8	9.19	45.5	399
F	.1380	....	61.2	15.7	9.61	51.6	389
F	.1380	$HC_2H_3O_2$, 0.1380	45.6	22.6	10.3	35.3	272
F	.148	....	67.1	17.0	11.4	55.7	391
F	.148	....	70.5	16.5	11.6	58.9	413
F	.158	....	76.5	16.5	12.6	63.9	421
F	.178	....	82.4	16.9	13.9	68.5	401
F	.197	....	89.5	17.1	15.3	74.2	391
F	.208	$HC_2H_3O_2$, 0.208	68.3	22.0	15.0	53.3	267
F	.217	....	100.0	16.7	16.7	83.3	399
F	.236	....	105.3	16.9	17.8	87.5	384
F	.247	....	116.1	16.7	19.4	99.7	420
F	.269	....	120.5	16.5	19.9	100.6	408
F	.269	$HC_2H_3O_2$, 0.269	76.6	22.2	17.0	59.6	229
F	.276	....	128.2	17.1	21.9	106.3	401
F	.296	....	143.0	16.7	23.9	119.1	419
F	.296	....	139.1	15.6	21.7	117.4	413

[a] To calculate k_{III}, the second-order coefficient, divide by the concentration of N-methylaniline: 0.1896 *M* at 46° and 0.1850 *M* at 67.2°. [b] Values corrected for solvent expansion.

in nitration it was the unusual observation of zero-order kinetics in certain reactions that led to a definitive interpretation of nitration mechanism, in amine-induced aromatic displacements it is the unusual observation of *general* base catalysis uniquely of the reaction of N-methylaniline with 2,4-dinitrofluorobenzene that leads to a firm conclusion about mechanism. The conclusion is that the mechanism of this particular reaction is as represented in Chart I, and that in general these reactions occur by the intermediate complex mechanism.

Base catalysis might be supposed to involve interaction of acetate ions with N-methylaniline to form N-methylanilide ions (equation 4) which then attack 2,4-dinitrofluorobenzene very rapidly to form III; such a representation would not lack precedent.[15] The actual displacement of fluorine

$$CH_3COO^- + C_6H_5NHCH_3 \rightleftharpoons C_6H_5NCH_3^- + CH_3COOH \quad (4)$$

by N-methylanilide ion might be supposed to occur by either the SN2-like or the intermediate complex mechanism. This representation of base catalysis would require that N-methylanilide ion react exceedingly fast with 2,4-dinitrofluorobenzene, but not fast enough with the corresponding chloro or bromo compound to significantly affect over-all reaction rate. This is improbable. An even more serious difficulty is that this representation (see equation 4) requires repression of the catalyzed rate by added acetic acid whereas, in fact, added acetic acid does not affect the rate. Nor can it be asserted that N-methylanilide ion formed according to equation 4 is so reactive with 2,4-dinitrofluorobenzene that it reacts forthwith before the reverse of reaction 4 has time to occur, for this would require zero-order kinetics.

The mechanism of Chart I gives a good account of the experimental facts. In this mechanism the base B (in the immediate case acetate ion) removes a proton from intermediate I to form a second intermediate II which rapidly loses halide ion to form product III. That the formation of II is not reversible is shown by the absence of kinetic effect of added acetic acid. The proton abstraction step is thus rate-determining. Alternatively, it is possible that the base effects a concerted elimination leading directly to product III without the intermediacy of II.

At any given base concentration, the rate of reaction is defined by the expression $d(III)/dt = k_{III}$ [substrate] $[C_6H_5NHCH_3]$. With use of the steady state assumption, one can derive

$$k_{III} = \frac{k_1k_2 + k_1k_3[B]}{k_{-1} + k_2 + k_3[B]} \quad (5)$$

If k_{-1} is much greater than k_2 or $k_3[B]$, equation 5 reduces to

$$k_{III} = (k_2 + k_3[B])k_1/k_{-1} \quad (6)$$

Rate is then directly proportional to the concentration of the base B; in the present work this case is exemplified by the potassium acetate-catalyzed reaction with 2,4-dinitrofluorobenzene in ethanol solution (see Fig. 2).

If $k_2 >> k_{-1}$, equation 5 reduces to $k_{III} = k_1$. Regardless of the concentration or catalytic activity of the base B, the reaction is insensitive to base catalysis. This case is exemplified in the present work by the reactions of 2,4-dinitrochloro- and bromobenzenes with N-methylaniline. From the order of halogen mobility in SN1 reactions,[9] Br > Cl >> F, one would expect k_2 to be *much* greater with X = Cl or Br than with X = F. Thus the mechanism of Chart I provides a consistent interpretation of the fact (Table I) that only the displacement of fluorine is base catalyzed.

In a strictly mathematical sense, the following mechanism is also compatible with the kinetics observed

$$(O_2N)_2C_6H_3X + C_6H_5NHCH_3 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (O_2N)_2C_6H_3NH(CH_3)C_6H_5^+ + X^-$$

$$(O_2N)_2C_6H_3NH(CH_3)C_6H_5^+ + \text{solvent} \xrightarrow{k_2} III + \text{solvent}\cdot H^+$$

$$(O_2N)_2C_6H_3NH(CH_3)C_6H_5^+ + B \xrightarrow{k_3} III + BH$$

The first reaction might be a one-step displacement or it might comprise two or more steps. An equation similar to equation 5 could be derived for this mechanism; the most important point of difference would have to do with the fact that here reversal of the first reaction is bimolecular whereas reversal of the first step in Chart I is unimolecular. This mechanism is unacceptable for chemical reasons, as follows: Firstly, in order for this mechanism to explain the linear response of rate to acetate ion concentration (Fig. 2), it would be necessary that $k_{-1}[F^-] >> k_3[CH_3COO^-]$; that is, fluoride ion would have to effect displacement of the N-methylanilino group of $(O_2N)_2C_6H_3NH(CH_3)C_6H_5^+$ *much faster* than acetate ion (in *ca.* 100-fold greater concentration) could remove a proton from the same species. This is most improbable in view of the low nucleophilic reactivity of the fluoride ion and the high rate of proton transfers from positive nitrogen to negative oxygen. Secondly, in order for this mechanism to explain the insensitivity to base catalysis of reactions of 2,4-dinitrochloro- and bromobenzenes with N-methylaniline, it would be necessary that chloride and bromide ions be inactive (as nucleophilic reagents) with a substrate with which fluoride ion reacted with extreme rapidity. Actually, chloride and bromide ions are much stronger nucleophiles than fluoride ion. This mechanism is therefore rejected.

It is necessary to consider whether the one-step, SN2-like mechanism could in any manner account for the experimental facts. Two mechanisms for base catalysis with reference to the SN2-like mechanism, the one involving equilibrium reaction 4 and the other immediately above, already have been ruled out. A conceivable one-step displacement mechanism consistent with general base catalysis is[16]

$$CH_3COO^- + C_6H_5NHCH_3 \rightleftharpoons \underset{IV}{CH_3COO^-\cdot HN(CH_3)C_6H_5}$$

$$\underset{IV}{CH_3COO^-\cdot HN(CH_3)C_6H_5} + (O_2N)_2C_6H_3F \longrightarrow III + F^- + CH_3COOH \quad (7)$$

This mechanism is improbable at best. It requires that the concentration of complex IV, presumably a hydrogen-bonded couple in which N-methylaniline exhibits acidic character, should be unaffected by the addition of acetic acid. It also requires that complex IV should have very high nucleophilic reactivity uniquely for the displacement of fluorine.

Improbable as this mechanism was, a further experimental test seemed desirable. From equation 5, it can be seen that the intermediate complex mechanism predicts that at very high base concentration and/or with a base of very high cata-

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(15) R. L. Betts and L. P. Hammett, THIS JOURNAL, 59, 1569 (1937).

(16) *Cf.* A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 208.

TABLE III

REACTIONS OF 2,4-DINITROHALOBENZENES WITH N-METHYLANILINE IN 60% DIOXANE–40% WATER (BY VOLUME)

Halogen	$[NaOH]_0$, M	Other added substance, M	k_{tot}, sec.$^{-1}$ × 10^5	Yield of III, %	k_{III}^*, sec.$^{-1}$ × 10^{5a}	$k_{OH^-}^*$, sec.$^{-1}$ × 10^5	k_{OH^-} × 10^5 l. mole^{-1} sec.$^{-1}$
			Temperature, 46.0°				
Cl			1.34	100	1.34		
Cl			1.42	100	1.42		
Cl			1.38	100	1.38		
Cl		N-Me-aniline hydrochloride, 0.2	1.42	100	1.42		
Cl	0.02		22.4	5.98	1.34	21.1	1110
Cl	.02		21.9	8.45	1.85	20.0	1050
Cl	.02		19.7	8.45	1.66	18.0	950
Cl	.02		15.3	8.65	1.32	14.0	740
Cl	.02		15.6	8.60	1.34	14.3	760
F			4.45	96.7	4.30	0.15	
F			4.41	96.4	4.25	.16	
F			4.36	98.3	4.28	.08	
F		$NaClO_4$, 0.03	4.37	96.6	4.22	.15	
			Temperature, 0.0°				
F			0.354	94.8	0.335	.019	
F		$KC_2H_3O_2$, 0.03	.502	91.2	.458	.044	
F		$KC_2H_3O_2$, 0.06	.665	88.3	.587	.078	
F	0.005		58.3	1.61	.94	57.4	11,480
F	.005		56.4	1.63	.92	55.5	11,100
F	.0075		105	1.13	1.18	104	13,900
F	.0075		97.5	1.15	1.12	96.4	12,800
F	.010		120	1.01	1.21	119	11,900
F	.0125		124	0.95	1.63	122	9,760
F	.015		213	.925	1.97	211	14,100
F	.0175		181	.82	1.48	180	10,300
F	.02		151	1.21	1.83	150	7,500
F	.02		221	0.79	1.75	209	10,500
F	.0225		230	.84	1.93	228	10,100
F	.025		300	.745	2.28	304	12,200
F	.0275		314	.76	2.38	312	11,300
F	.03		360	.725	2.60	357	11,900

[a] To calculate k_{III}, the second-order rate coefficient, divide by the concentration of N-methylaniline: 0.2 M in all runs.

lytic activity (that is, when $k_3[B]$ is very large) the rate will be insensitive to changes in base concentration. If $k_3[B]$ is much greater than k_{-1}, equation 5 reduces to $k_{III} = k_1$. For a reaction catalyzed by a very active base, a plot of catalyzed rate *versus* base concentration should be curved: the plot should rise linearly at very low base concentration (the region of applicability of equation 6), it should be flat at very high base concentration, and in between its slope should decrease steadily.[17] The curve should be concave downward. On the other hand, one-step, SN2-like displacement according to equation 7 would predict a thoroughly linear variation of rate with base concentration. (This statement involves the provision that a complex of type IV cannot form in massive amounts. This provision is amply met for the situations dealt with in this paper, involving the bases acetate ion and hydroxide ion.)

Catalysis by Hydroxide Ion.—Catalysis by potassium acetate in ethanol (Fig. 2) having been investigated at as high base concentrations as the solubility of potassium acetate would allow and only linear response to base concentration having been observed, it was necessary to change to another system in order to observe curvature in such a plot. Sodium hydroxide was chosen as the new catalyzing base, because a large k_3 value was expected; and 60% dioxane–40% water was chosen as the solvent because hydroxide ion cannot undergo chemical change in this solvent as it can in alcohols.[18] Study of this system was complicated by the very high reactivity of hydroxide ion with 2,4-dinitrofluorobenzene. Because of this complication, it was possible to investigate only a rather narrow range of hydroxide ion concentrations. Results are summarized in Table III.

The rate of displacement of fluorine by N-methylaniline is plotted as a function of hydroxide ion concentration in Fig. 3. The points on the left side of the plot, based on higher yields of III and moderate over-all reaction rates, are considerably more precise than those at the right which are based on low yields of III and inconveniently high over-all rates. The line drawn in Fig. 3 represents linear response to base concentration, and is based on the more precise points at the left of the plot. The points on the right scatter considerably, but it is obvious that they do not group about the line. They fall definitely below. The plot is concave downward as predicted on the basis of the intermediate complex mechanism. The one-step, SN2-like mechanism

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(17) A similar case is encountered in base catalysis of certain diazo coupling reactions; *cf.* H. Zollinger, *Helv. Chim. Acta*, **38**, 1597 (1955).

(18) J. F. Bunnett and G. T. Davis, THIS JOURNAL, **76**, 3011 (1954).

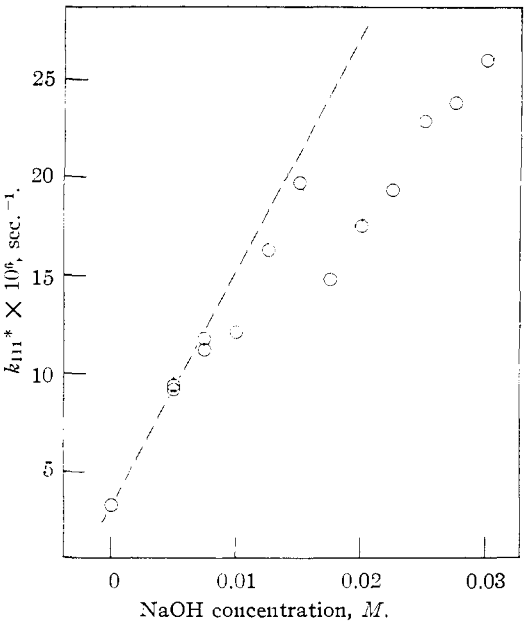

Fig. 3.—Effect of hydroxide ion on rate of reaction of N-methylaniline with 2,4-dinitrofluorobenzene in 60% dioxane–40% water at 0°. The dashed line would represent linear dependence on [OH$^-$], based on values at low [OH$^-$], which are the most accurate.

involving complex IV would have required linear response. Already most improbable, the one-step mechanism fails again on this final test. It is therefore rejected altogether.

General Conclusions.—A set of unusual observations—that the displacement of fluorine but not of chlorine or bromine is based catalyzed, that the reaction is *general* base catalyzed, and that the catalyzed rate is linearly proportional to potassium acetate concentration in ethanol but not linearly dependent on hydroxide ion concentration in aqueous dioxane—have been shown to be consistent with the intermediate complex mechanism of Chart I but incompatible with any variation of the one-step, S$_N$2-like mechanism. The intermediate complex mechanism is thus established for the reactions of the 2,4-dinitrohalobenzenes with N-methylaniline.

Furthermore, these reactions show characteristics similar to other aromatic nucleophilic substitutions for which, as discussed in the introduction to this paper, strong evidence in favor of the intermediate complex mechanism and against the one-step, S$_N$2-like mechanism has been obtained on quite independent grounds. For example, N-methylaniline combines especially fast with 2,4-dinitrofluorobenzene, as compared to the corresponding chloro and bromo compounds, to form a covalent intermediate complex (I) just as other nucleophilic reagents do.[5,19] There is no indication of a discontinuity, of a difference in kind, between the reactions dealt with in the present paper and the reactions in which nitro-activated halogens or other substituents are displaced by piperidine, thiophenoxide ion or methoxide ion or between those and analogous displacements in heterocyclic systems or in aromatic systems not provided with activating substituents. In these many varieties of aromatic nucleophilic substitution, no evidence definitely requiring the one-step, S$_N$2-like mechanism has been found whilst several independent types of evidence incompatible with the S$_N$2-like mechanism and thoroughly consistent with the intermediate complex mechanism have been brought to light. In these circumstances the intermediate complex mechanism must be accepted for aromatic nucleophilic substitution reactions in general.

Miscellaneous Considerations

The Possibility of Nucleophilic Catalysis by Acetate Ion.—It might be supposed that catalysis by potassium acetate involved displacement of fluorine by acetate ion to form 2,4-dinitrophenyl acetate which then was attacked by N-methylaniline to form III. This mechanism of catalysis would be consistent with *general* base catalysis and finds a close analogy in the nucleophilic catalysis of ester hydrolysis observed by Bender and Turnquest.[20] This interpretation was ruled out in the present work by the observation that the reaction of 2,4-dinitrophenyl acetate with N-methylaniline in ethanol did not form III.

Comparison of Uncatalyzed Rates with Literature Values.—The rate coefficients recorded in Table I for the uncatalyzed reactions of the three 2,4-dinitrohalobenzenes with N-methylaniline in ethanol are all higher than reported by Hammond and Parks by factors of 50- to 70-fold. This discrepancy was called to the attention of Professor Hammond, and he has found that an error was made in the calculation of their rate coefficients for reactions in ethanol.[21] The discrepancy is thus resolved.

Competing Reactions; Yields of III.—Potassium acetate in ethanol furnished two nucleophilic reagents, acetate ion and ethoxide ion (formed by interaction of acetate ion with ethanol), to compete with N-methylaniline. Two immediate by-products were expected: 2,4-dinitrophenyl acetate in large amount and 2,4-dinitrophenetole in lesser amount. Efforts to isolate the former from the reaction of potassium acetate with 2,4-dinitrofluorobenzene in ethanol were unsuccessful; only 2,4-dinitrophenol was found. Presumably this is a secondary product resulting from ethanolysis of 2,4-dinitrophenyl acetate.[11]

In potassium acetate–acetic acid catalyzed runs, in which ethoxide ion is suppressed, the rate of formation of by-products (collectively ArOR) is defined: $d[\mathrm{ArOR}]/dt = k_{\mathrm{OAc^-}}[\mathrm{ArX}][\mathrm{CH_3COO^-}]$. From this expression and equation 6, one may then derive an equation relating yield of III to yield of by-products

$$\frac{[\mathrm{III}]}{[\mathrm{ArOR}]} = \frac{k_1(k_2 + k_3[\mathrm{CH_3COO^-}])[\mathrm{C_6H_5NHCH_3}]}{k_{-1}k_{\mathrm{OAc^-}}[\mathrm{CH_3COO^-}]} \qquad (8)$$

When $k_3[\mathrm{CH_3COO^-}] >> k_2$, this equation simplifies to

$$\frac{[\mathrm{III}]}{[\mathrm{ArOR}]} = \frac{k_1k_3}{k_{-1}k_{\mathrm{OAc^-}}}[\mathrm{C_6H_5NHCH_3}] \qquad (9)$$

Under these conditions, the yield of III is independent of base concentration. Such constancy of yield was indeed

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[19] We have shown that the comparatively low uncatalyzed rate of displacement of fluorine by N-methylaniline is due not to slowness of formation of intermediate I when X = F but rather to the circumstance that I reverts to reactants frequently when X = F but not when X = Cl or Br.

[20] M. L. Bender and B. W. Turnquest, THIS JOURNAL, **79**, 1656 (1957).

[21] Professor Hammond writes: "A recheck reveals that the rate constants in Table I (of Hammond and Parks[7] paper[8]) for ethanol solution should be increased by a factor of sixty and that the others are correct as they stand."

observed; the yield of III (Table II) in potassium acetate–acetic acid catalyzed runs was constant at about 21%.

In runs catalyzed by potassium acetate without acetic acid, the rate of formation of by-products is defined

$$d[\text{ArOR}]/dt = k_{\text{OAc}^-}[\text{ArX}][\text{CH}_3\text{COO}^-] + k_{\text{OEt}^-}[\text{ArX}][\text{C}_2\text{H}_5\text{O}^-] \quad (10)$$

Ethoxide ion concentration is actually proportional to the square root of acetate ion concentration,[22] but when the ethoxide term is small compared to the acetate term and when only moderate variations in acetate ion concentration are involved, the second term may not cause much deviation from an over-all linear dependence of by-product formation rate on acetate ion concentration. Under such conditions equation 10 can be simplified to the approximate expression: $d[\text{ArOR}]/dt = k_{\text{OR}}[\text{ArX}][\text{CH}_3\text{COO}^-]$. Expressions analogous to equations 8 and 9 may then be written, the latter being

$$\frac{[\text{III}]}{[\text{ArOR}]} = \frac{k_1 k_3}{k_{-1} k_{\text{OR}}}[\text{C}_6\text{H}_5\text{NHCH}_3] \quad (11)$$

Evidently the conditions necessary for this expression to be valid were fulfilled in our experiments, for the yield of III in potassium acetate-catalyzed runs with 2,4-dinitrofluorobenzene (Table II) was constant at about 16 to 17% at all potassium acetate concentrations.

Equation 9 was derived from equation 6 and is valid only so long as the pre-requisite condition for equation 6, that k_{-1} is much greater than k_2 or $k_3[\text{B}]$, is true. This condition is not satisfied for the hydroxide-catalyzed runs in aqueous dioxane solution, and it therefore is not surprising this in this series the yield of III decreases as hydroxide ion concentration increases (Table III).

Effects of Added Substances on Rates in Aqueous Dioxane.—In Table III, it will be noted that addition of sodium hydroxide does not accelerate the formation of III from N-methylaniline and 2,4-dinitro*chloro*benzene. It is thus indicated that $k_2 \gg k_{-1}$. Bunnett and Pruitt[14] similarly observed non-acceleration by hydroxide ion of reactions of this substrate with aniline and with piperidine.

Added sodium perchlorate has no effect on the rate of reaction of N-methylaniline with 2,4-dinitrofluorobenzene in 60% aqueous dioxane; it is therefore certain that the acceleration caused by added hydroxide ion is no mere salt effect. Added sodium acetate has a small accelerating effect on the same reaction. This no doubt represents base catalysis by the weak base acetate ion.

Dissection of Rate Coefficients.—Equation 5 may be written in the form

$$k_{\text{III}}\frac{(k_{-1} + k_2)}{k_3} + k_{\text{III}}[\text{OH}^-] = \frac{k_1 k_2}{k_3} + k_1[\text{OH}^-] \quad (12)$$

This is an equation in three unknowns: k_1, $(k_{-1} + k_2)/k_3$ and $k_1 k_2/k_3$. When this equation applies, as it does for catalysis by hydroxide ion in aqueous dioxane, these three unknowns can be evaluated from knowledge of k_{III} values at three or more hydroxide ion concentrations. These unknowns have been evaluated from data in Table III; details are given in the Experimental section. Also, by simple algebra the ratios k_2/k_3, k_{-1}/k_3 and k_{-1}/k_2 have been evaluated. The most interesting numbers so obtained are

$$k_1 = 20 \times 10^{-5} \text{ l. mole}^{-1} \text{ sec.}^{-1}$$
$$k_{-1}/k_3 = 0.0205 \text{ mole/l.}$$
$$k_{-1}/k_2 = 14$$

The last figure tells that in the uncatalyzed reaction the intermediate complex (Chart I) reverts to reactants 14 times for every one time it goes on to products. This can also be seen by comparing k_1 with the uncatalyzed k_{III}, 1.67×10^{-5} l. mole^{-1} sec.$^{-1}$; the former is 12 times greater.

Division of k_{-1}/k_3 by the hydroxide ion concentration gives $k_{-1}/k_3[\text{OH}^-]$ which is the ratio of reversion to reactants to base-catalyzed advance to products; with 0.02 *M* hydroxide ion, this ratio is 1.0. In other words, in the presence of 0.02 *M* hydroxide ion half of the intermediate complex goes on to products and half reverts to reactants.

The insensitivity of the reaction of 2,4-dinitro*chloro*benzene with N-methylaniline to base catalysis indicates that for this reaction $k_{\text{III}} = k_1 = 6.9 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ at 46°. By rule-of-thumb, k_1 at 0° may be estimated as 3×10^{-6} l. mole^{-1} sec.$^{-1}$. This figure is only $^1/_{70}$ as great as k_1 for combination of the same amine with 2,4-dinitro*fluoro*benzene.

For potassium acetate catalyzed runs in ethanol, it is possible to evaluate the product, $k_1 k_3/k_{-1}$, from yield data and from knowledge of k_{OAc^-} or k_{OR}. By substitution in equation 9 of 20.5% for [III], 79.5% for [ArOR] and 3.53×10^{-3} l. mole^{-1} sec.$^{-1}$ for k_{OAc^-}, one evaluates $k_1 k_3/k_{-1}$ as 4.5×10^{-3}; by substitution in equation 11 of 17% for [III], 83% for [ArOR] and of 4.04×10^{-3} l. mole^{-1} sec.$^{-1}$ for k_{OR}, the same product is calculated to be 4.0×10^{-3}; and from the slope of the line in Fig. 2 (see equation 6), this product is 3.51×10^{-3} (all in l.^{2} mole^{-2} sec.$^{-1}$ at 46°). The uncatalyzed k_{III}, for reaction of 2,4-dinitrofluorobenzene with N-methylaniline, is $k_1 k_2/k_{-1}$ and at 46° this is 2.65×10^{-5} l. mole^{-1} sec.$^{-1}$. One can then calculate $(k_1 k_3/k_{-1})/(k_1 k_2/k_{-1}) = k_3/k_2 = 150$ l. mole^{-1}. Unfortunately, the data available do not in this case allow calculation of individual rate coefficients or of other rate ratios.

Comparison of Solvents.—The kinetics indicate that, for the reaction of 2,4-dinitrofluorobenzene with N-methylaniline, $k_{-1} >> k_2$ in ethanol whilst in 60% dioxane–40% water k_{-1} is only 14 times as great as k_2. The reaction changes from class B of the intermediate complex mechanism in ethanol to class C in aqueous dioxane. This change in the relative magnitudes of k_{-1} and k_2 is reasonable; k_{-1} relates to a process in which the transition state is less ionic than the reactant (I); k_{-1} would be expected to be smaller in aqueous dioxane, a better solvating solvent, than in ethanol; k_2 relates to a process in which the transition state is more ionic than the reactant (I); k_2 would be expected to be larger in aqueous dioxane than in ethanol. Both changes are in the direction of decreasing the k_{-1}/k_2 ratio with change from ethanol to aqueous dioxane solvent.

As discussed above, there is kinetic evidence that the reactions of typical amines with 2,4-dinitrochlorobenzene proceed by class A of the intermediate complex mechanism ($k_2 >> k_{-1}$).[5,14] The relevant kinetics were investigated in alcoholic or aqueous dioxane solutions. In view of the change in the relative magnitudes of k_{-1} and k_2 discussed in the preceding paragraph, it is conceivable that these reactions of 2,4-dinitrochlorobenzene might experience a sufficient change in the k_{-1}/k_2 ratio to change them, for example, from class A in alcoholic solvents to class C or even class B in a poor solvent for ions such as benzene.

Reactivities with Acetate, Ethoxide and Hydroxide Ions.—The catalyzing bases hydroxide ion and acetate ion are themselves significant nucleophilic reagents and they competed with N-methylaniline for the various substrates. The experimental method used furnishes rate coefficients for these competing reactions.

In Table III, second-order rate coefficients for reactions with hydroxide ion are listed in the far right hand column. For reaction with 2,4-dinitrochlorobenzene, the mean value obtained in the present work, 8.5×10^{-3} l. mole^{-1} sec.$^{-1}$ at 46°, agrees well with the value 7.55×10^{-3} l. mole^{-1} sec.$^{-1}$ extrapolated from direct measurements of Bunnett and Davis.[19] From runs with 2,4-dinitro*fluoro*benzene, a substantially constant value of k_{OH^-} is obtained; there is only random variation with changing hydroxide ion concentration. The mean value is 0.114 l. mole^{-1} sec.$^{-1}$ at 0°; for reaction with the corresponding chloro compound at 0° the coefficient 7.2×10^{-5} l. mole^{-1} sec.$^{-1}$ is extrapolated from data of Bunnett and Davis.[19] Thus fluorine is displaced by hydroxide ion 1600 times faster than chlorine. With sodium methoxide in methanol, 2,4-dinitrofluorobenzene reacts only 880 times faster than 2,4-dinitrochlorobenzene.[23] It is reasonable that the relative mobility of fluorine should be greater with hydroxide than with methoxide ion because hydroxide ion has lower polarizability.[23]

For runs in ethanol, it was operationally convenient to split the total pseudo-first order rate coefficient in each run into k_{III}^*, pertaining to the formation of III, and k_{OR}^*, pertaining to the formation of by-products. Values of both are listed for all runs in Table II. From equation 10, it follows

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(22) $[\text{C}_2\text{H}_5\text{O}^-] = (K_{\text{EtOH}}/K_{\text{HOAc}})^{1/2}[\text{CH}_3\text{COO}^-]^{1/2}$ where K_{EtOH} is the autoprotolysis constant for ethanol, evaluated as 8×10^{-20} by P. S. Danner, THIS JOURNAL, **44**, 2832 (1922); K_{HOAc} is the dissociation constant of acetic acid in absolute ethanol, tabulated as 4.8×10^{-11} mole/l. by E. Grunwald and B. J. Berkowitz, *ibid.*, **73**, 4939 (1951).

(23) J. F. Bunnett, THIS JOURNAL, **79**, 5969 (1957).

that

$$k_{OR}^* = k_{OAc^-}[CH_3COO^-] + k_{OEt^-}[C_2H_5O^-] \quad (13)$$

Since added acetic acid strongly represses ethoxide ion, $k_{OR}^*/[CH_3COO^-]$ should equal k_{OAc^-} in such runs. Values of $k_{OR}^*/[CH_3COO^-]$ are listed in the far right hand column of Table II. It will be noted that for acetic acid-containing runs this value is approximately constant at about 315 × 10^{-5} l. mole^{-1} sec.$^{-1}$ although there is a definite tendency toward lower values at higher potassium acetate–acetic acid concentrations. This downward drift may represent partial combination of acetate ions with acetic acid molecules to form biacetate ions, $CH_3COO^- \cdot HOOCCH_3$. Such combination would be relatively more important at higher concentrations of acetate ion and acetic acid. If so, the $k_{OR}^*/[CH_3COO^-]$ values at lower potassium acetate–acetic acid concentrations are most nearly representative of k_{OAc^-}. The mean value of the first four such values in Table II, 3.54 × 10^{-3} l. mole^{-1} sec.$^{-1}$, therefore appears to be the best value from this work for the rate coefficient for reaction of 2,4-dinitrofluorobenzene with potassium acetate in ethanol at 46°.

For runs lacking acetic acid, $k_{OR}^*/[CH_3COO^-]$ is k_{OR}, the composite coefficient which has already appeared in equation 11. As suggested by yield data, k_{OR} is substantially constant at all potassium acetate concentrations (Table II, far right hand column). There is only random variation. The mean value, 4.04 × 10^{-3} l. mole^{-1} sec.$^{-1}$, should be the sum of k_{OAc^-} plus $k_{OEt^-}[C_2H_5O^-]/[CH_3COO^-]$. By subtraction, the latter term is evaluated as 5.0 × 10^{-4} l. mole^{-1} sec.$^{-1}$. At the typical potassium acetate concentration of $0.15M$ the value of $k_{OEt^-}[C_2H_5O^-]$ is then 7.5 × 10^{-5} sec.$^{-1}$. The concentration of ethoxide ion in 0.15 M potassium acetate solution is calculated[22] to be 1.6 × 10^{-5} M; k_{OEt^-}, the rate coefficient for reaction of 2,4-dinitrofluorobenzene with ethoxide ion in ethanol at 46°, is then 4.7 l. mole^{-1} sec.$^{-1}$. This coefficient has not been determined by direct measurement, but from data of Bevan and Bye[24] the rate coefficient for reaction of this substrate with methoxide ion in methanol at 46° is 46 l. mole^{-1} sec.$^{-1}$. Ethoxide ion in ethanol reacts with 2,4-dinitro*chloro*benzene about three times as fast as does methoxide ion in methanol.[25] Therefore k_{OEt^-} is estimated to be about 138 l. mole^{-1} sec.$^{-1}$. The agreement between the k_{OEt^-} values estimated in these two independent ways is fairly good in view of the many assumptions and approximations involved in the estimates.

In the first part of Table II it will be noted that k_{OR}, for runs with potassium acetate 0.1 M, varies according to the halogen displaced in the order F >> Br > Cl; k_{OR} is about a thousand times greater for displacement of fluorine than for displacement of bromine. As mentioned earlier, this is a not unusual order of halogen mobility in nucleophilic aromatic substitution.

Variation of Uncatalyzed Rate with Amine Concentration.—The reaction of 2,4-dinitrofluorobenzene with N-methylaniline having been found to be base catalyzed, and N-methylaniline being a base, it was of interest to see whether this amine could itself catalyze the reaction. If the reaction were wholly dependent on catalysis by N-methylaniline, it would be kinetically third order (see equation 6). This point was investigated by determining the pseudo-first order rate coefficient, k_{III}^*, at three amine concentrations; data are given Table IV.

TABLE IV

EFFECT OF AMINE CONCENTRATION ON THE RATE OF REACTION OF N-METHYLANILINE WITH 2,4-DINITROFLUOROBENZENE[a]

$[C_6H_5NHCH_3]$, M	$k_{III}^* \times 10^5$, sec.$^{-1}$	$k_{III} \times 10^5$, l. mole^{-1} sec.$^{-1}$
0.0925	0.656	6.06
.185	1.36	6.29
.370	3.39	7.84

[a] Substrate concentration 0.0025 M in each run; conditions, ethanol solution at 67.2°.

It will be noted that the second-order coefficient, $k_{III} = k_{III}^*/[C_6H_5NHCH_3]$, varies only slightly with changing amine concentration; the kinetics are thus a close approximation to second order. The small but steady increase of k_{III} with increasing amine concentration may indicate minor participation of a third-order term (see equation 6) or it may represent the effect of a change in the medium. A change from 0.1 to 0.4 M N-methylaniline is also a change from 1 to 4% of this amine in the medium.

Ross and co-workers[26] recently have found that in the reactions of several amines with 2,4-dinitrochlorobenzene in ethanol or chloroform solution, the second-order rate coefficient rises with increasing amine concentration. For example, the coefficient for reaction with *n*-butylamine in chloroform triples as the amine concentration increases from 0.1 to 1.0 M. The second-order coefficient for the same reaction in ethanol increases 1.5-fold with increase in amine concentration from 0.17 to 0.88 M. This reaction in chloroform also is accelerated by added triethylamine. Similar observations of lesser scope were made some years ago by Brady and Cropper.[27]

Ross and co-workers[26] have shown that their data fit a rate expression involving both a second- and a third-order term. The latter has been tentatively identified as representing base catalysis. Insofar as the reactions in ethanol are concerned, this identification is difficult to accept because of the strong evidence[5,14] that reactions of typical amines with 2,4-dinitrochlorobenzene in alcoholic solvents occur by class A of the intermediate complex mechanism and are insensitive to base catalysis. A general medium effect, which could well be linear with $[RNH_2]$, seems a more likely interpretation. On the other hand, for the reactions in chloroform, as discussed above under "Comparison of Solvents," it is not unreasonable that k_{-1} might approach or exceed k_2, in which case base catalysis would be expected.

Experimental

Materials.—**Dioxane** was purified by the method of Beste and Hammett.[28] It was stored over sodium metal and redistilled from sodium immediately before being used. 60% dioxane–40% water solvent was prepared by mixing three volumes of dioxane with two of water. Commercial **absolute ethanol** was refluxed for at least two hours with 7 g. of sodium metal and 25 g. of ethyl phthalate for each liter of ethanol. It then was distilled and stored in a tightly stoppered bottle protected by a drying tube. The ethanol was checked occasionally by the method of Henle[29] for water content. A positive test (more than 0.05% water) was never obtained although blank tests on samples deliberately contaminated with water supported Henle's claims for his method. Purified **acetic acid** was generously furnished by Mr. F. E. Carevic whose method of purification involved heating commercial acetic acid at reflux with chromic acid overnight, distilling, heating at reflux with acetic anhydride, and finally fractionating through a good column.

N-Methyl-2,4-dinitrodiphenylamine (III) was prepared by heating two equivalents of N-methylaniline with one of 2,4-dinitrochlorobenzene on the steam-bath until the mixture solidified, triturating with water to remove the amine

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(24) C. W. L. Bevan and G. C. Bye, *J. Chem. Soc.*, 3091 (1954).

(25) Reference 3, p. 357.

(26) S. D. Ross and M. Finkelstein, THIS JOURNAL, **79**, 6547 (1957); S. D. Ross and R. C. Petersen, *ibid.*, **80**, 2447 (1958). We thank Dr. Ross for sending us copies of these articles in advance of publication.

(27) O. L. Brady and F. R. Cropper, *J. Chem. Soc.*, 507 (1950).

(28) G. W. Beste and L. P. Hammett, THIS JOURNAL, **62**, 2481 (1940).

(29) F. Henle, *Ber.*, **53**, 719 (1920).

hydrochloride, and recrystallizing several times from an ethanol–acetone mixture; orange crystals of m.p. 169–170° (lit.[30] 166–167.5°) were obtained. **N-Methylaniline** was purified by the method of Hammond and Parks[8]; when pure, it was water-white and boiled at 57° (4 mm.). **2,4-Dinitrofluorobenzene** of b.p. 118–118.5° (2.5 mm.) and m.p. 27.5° was obtained by distillation of a commercial product. **2,4-Dinitrochlorobenzene, 2,4-dinitrobromobenzene, 2,4-dinitrophenol** and **2,4-dinitrophenetole** were commercial products recrystallized. **2,4-Dinitrophenyl acetate**, m.p. 71.5–72°, was prepared as described by Bender and Turnquest.[20]

Definition of Symbols for Rate Coefficients.—k_1, k_{-1}, k_2 and k_3 are defined in Chart I (or equation 2). k_{tot} is the total first-order coefficient for consumption of substrate. $k_{III}{}^*$, $k_{OH^-}{}^*$ and $k_{OR}{}^*$ are, respectively, first-order coefficients for the formation of III, for reaction of the substrate with hydroxide ion and for the reaction of the substrate with the sum of competing nucleophilic reagents; k_{III} is the second-order coefficient for formation of III and k_{OR} an approximate coefficient of second order, defined as $k_{OR}{}^*/[CH_3COO^-]$. k_{OH^-}, k_{OAc^-} and k_{OEt^-} are second-order coefficients for reaction with, respectively, hydroxide, acetate and ethoxide ions.

General Kinetic Procedure and Method of Calculation of Data.—Runs were set up so that N-methylaniline and any added base were in large excess over the substrate; in this way, pseudo-first order kinetics were assured. Aliquots of the reaction mixture were, at various recorded times, combined with a standard volume of excess mineral acid in 50% ethanol; this neutralized the amine and any other bases present, but did not convert III to its conjugate acid. One or more infinity samples were taken after ten half-lives, and were quenched in the standard manner. A mock infinity solution, containing III in the concentration expected on the assumption of a quantitative yield of III, was prepared and a sample of it was quenched in the standard way. The absorbances (A at any time, A_∞ for the experimental infinity sample and $A_{\infty,\,theo}$ for the mock infinity sample)of the various samples were determined by means of a Beckman model B spectrophotometer at 398 mμ.

The slope of a plot of log ($A_\infty - A$) *vs.* time, multiplied by 2.303, gave k_{tot}. Other values were then calculated as

$$\text{yield of III} = 100A_\infty/A_{\infty,\,theo}$$
$$k_{III}{}^* = k_{tot}A_\infty/A_{\infty,\,theo}$$
$$k_{OH^-}{}^* = k_{tot} - k_{III}{}^* \text{ (reactions in aq. dioxane)}$$
$$k_{OR}{}^* = k_{tot} - k_{III}{}^* \text{ (reactions in ethanol)}$$
$$k_{III} = k_{III}{}^*/[C_6H_5NHCH_3]$$
$$k_{OH^-} = k_{OH^-}{}^*/[OH^-]$$
$$k_{OR} = k_{OR}{}^*/[CH_3COO^-]$$

Measurements in 60% Dioxane–40% Water at 0°.—In all runs the concentration of 2,4-dinitrofluorobenzene was approximately 2.5×10^{-3} *M* and of N-methylaniline 0.2 *M*. Each reaction solution had an initial volume of 600 cc., made up as follows: 10 cc. of a standard solution of 2,4-dinitrofluorobenzene in pure dioxane was pipetted into a 250-cc. volumetric flask. In an identical flask was placed 13.02 cc. or 12.84 g. of N-methylaniline and, when desired, an appropriate volume of standard aqueous sodium hydroxide solution. In a 100-cc. volumetric flask was placed an appropriate volume of excess dioxane or water to match in the correct ratio the amounts of these solvents introduced from the standard solutions. All three flasks were filled nearly to the mark with 60% aqueous dioxane and were set in an ice–water-bath; when temperature equilibrium had been reached, each was filled to the mark with chilled solvent. The contents of the second two flasks were combined in a 1000-cc. glass-stoppered flask which was immersed in the bath. The 2,4-dinitrofluorobenzene solution was added as a stopwatch was started, the mixture was swirled, and a 50-cc. aliquot was immediately removed and was combined with a 50-cc. pipetted volume of quenching solution. (Quenching solution was made by combining one liter of 95% ethanol, one liter of water and 200 g. of concentrated sulfuric acid.) Ten or eleven samples were taken at recorded times, usually at one-minute intervals, and an infinity sample was taken after about ten half-lives.

Because the yields of III from 2,4-dinitrofluorobenzene were so low when hydroxide ion was present, the above runs were run at rather high substrate concentration in order that absorbances of significant magnitude might be observed. Under these conditions, the absorbance of the quenched mock infinity sample was so high that it could not be measured directly. After quantitative dilution the absorbance was measured, and the mock infinity absorbance was then calculated. Data from a typical run are displayed in Table V.

TABLE V

SODIUM HYDROXIDE CATALYZED REACTION OF 2,4-DINITROFLUOROBENZENE WITH N-METHYLANILINE IN 60% DIOXANE: 40% WATER AT 0°. A REPRESENTATIVE RUN.

Initial concentrations: $C_6H_3(NO_2)_2F$, 0.00125 *M;* $C_6H_5NHCH_3$, 0.2 *M;* NaOH, 0.0125 *M*

Time, sec.	Absorbance (A)	$A_\infty - A$	log ($A_\infty - A$
0	0	0.080	−1.097
60	0.009	.071	−1.149
120	.016	.064	−1.194
180	.023	.057	−1.244
240	.026	.054	−1.268
300	.032	.048	−1.319
360	.038	.042	−1.377
420	.041	.039	−1.409
480	.044	.036	−1.444
540	.049	.031	−1.509
3600	.080	...	

Measurements in 60% Dioxane–40% Water at 46°.—In all runs the concentration of N-methylaniline was approximately 0.2 *M* and, except in two runs in which it was doubled, the substrate concentration was 5×10^{-4} *M*. In a 100-cc. volumetric flask the desired amount of substrate was placed in the form of an aliquot of a standard solution and the flask was filled to the mark with solvent at thermostat temperature. In a like flask, a weighed quantity of N-methylaniline was placed together with (if desired) a measured volume of a standard solution of sodium hydroxide in water and three-halves this volume of pure dioxane; the flask was diluted to the mark with solvent at thermostat temperature. The contents of the two flasks were combined with vigorous shaking in a 250-cc. glass-stoppered flask at zero time and 10-cc. samples were removed at recorded times. The samples were quenched and diluted to the mark in 100-cc. volumetric flasks; the quenching solution was made by combining 18 g. of concentrated sulfuric acid with 1 l. of water and 1 l. of 95% ethanol.

Measurements in Ethanol.—With the exceptions noted below, the reaction solutions were prepared by combining, at 0°, a weighed amount of N-methylaniline, 10 cc. of a standard solution of substrate and (if used) the necessary amount of a standard solution of potassium acetate or potassium acetate–acetic acid. The mixture was diluted to the mark in a 100-cc. volumetric flask with chilled ethanol; 5-cc. aliquots were pipetted into special reaction tubes which were chilled by ice. (These tubes were about 130 mm. long and about 10 mm. in internal diameter. Each had a male standard taper joint at the top and for each there was a female-jointed cap, and glass hooks near each joint allowed the caps to be bound in place by means of stout rubber bands. The caps fit tightly; there was negligible loss of acetone from such a tube at 67° for three days.) The tubes were capped securely and placed in the thermostat all at once. Tubes were removed at regular intervals, placed in an ice-bath for 10 to 12 seconds, opened, and the contents were poured and rinsed into 100-cc. volumetric flasks which were finally filled to the mark with the quenching solution described immediately above. Data from a typical run are displayed in Table VI and plotted in Fig. 1.

In the two runs with acetic acid concentrations 0.2078 and 0.2702 *M*, the method was the same as for runs in aqueous dioxane at 46°. It was necessary to change because potassium acetate precipitated from the chilled solutions containing acetic acid in such high concentrations.

A single run on the reaction of 2,4-dinitrobromobenzene with N-methylaniline at 67.19° was made with analysis for bromide ion. N-Methylaniline (2.6763 g.) and 2,4-dinitro-

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(30) S. I. Lur'e, *Zhur. Obshchei Khim.*, **22**, 256 (1952); *C. A.*, **47**, **1626g (1953)**.

Table VI

Potassium Acetate-catalyzed Reaction of 2,4-Dinitrofluorobenzene with N-Methylaniline in Absolute Ethanol at 46.0°: A Representative Run

Initial concentrations: $C_6H_3(NO_2)_2F$, 0.00237 *M*; $C_6H_5NHCH_3$, 0.190 *M*; $KC_2H_3O_2$, 0.178 *M*

Time, sec.	Absorbance (A)	$A_\infty - A$	$\log (A_\infty - A)$
0	0	0.285	−0.545
90	0.030	.255	− .593
180	.049	.236	− .627
270	.065	.220	− .658
360	.080	.205	− .688
450	.095	.190	− .721
540	.110	.175	− .757
630	.123	.162	− .790
720	.135	.150	− .824
810	.145	.140	− .854
900	.154	.131	− .883
9000 (∞)	.284	. . .	
9000 (∞)	.286	. . .	

bromobenzene (3.0877 g.) were dissolved in ethanol and the solution was diluted to 250 cc. at 0°. Aliquots (22.5 cc.) were placed in test-tubes which had been constricted near the top and the tubes were sealed by means of a flame. The tubes were placed in the thermostat all at once and removed at recorded times. Each sample was combined with 50 cc. of 0.4 *M* sulfuric acid and bromide ion was determined by potentiometric titration.[19] This run was designed to provide second-order kinetics, and a good linear plot was obtained when the data were calculated by an appropriate expression. The rate coefficient obtained was 2.00×10^{-4} l. mole^{-1} sec.$^{-1}$ (at 67.19°); from photometric measurements (Table II) the same coefficient was 2.03×10^{-4} l. mole^{-1} sec.$^{-1}$.

In calculation of results of runs made up at 0° and run at a higher temperature, an appropriate correction for thermal expansion of the solvent was made.

The possibility of disturbance through reaction of acetic acid with the ethanol solvent to form ethyl acetate was considered. The work of Goldschmidt[31] indicates that this complication was insignificant under the conditions of our experiments.

In the text, it is mentioned that the validity of our photometric method for determination of rate coefficients depends on three assumptions, which are now considered. The assumption that III is not destroyed under the conditions of the reactions is justified by our observation that infinity solutions maintained constant absorbance over many half-lives. The assumption that III is the only colored product formed is reasonable since all the expected by-products are colorless in acid solution; it receives support from the excellent agreement between absorbances of infinity and mock infinity samples from reactions with 2,4-dinitrochloro- and bromobenzenes and from the excellent agreement between the photometric and the titration rate coefficients for reaction with the bromo substrate. Side reactions leading to colored products from the fluoro substrate might be suspected if this compound reacted much slower than the bromo substrate, but actually the fluoro substrate reacted faster in the base-catalyzed reactions. The most probable colored by-products would be azo or azoxy compounds resulting from reduction of nitro groups by alkaline ethanol; however, such reactions are generally insignificant even when much stronger bases than acetate and much higher reaction temperatures are employed. The assumption that the various competing reactions occur in constant ratio throughout the run would be unjustified only if conditions changed during the run in such a way that one reaction diminished or grew in importance with respect to the others. The large excesses of N-methylaniline and of basic catalysts employed assured that conditions remained substantially constant throughout each run.

Detail on "Dissection of Rate Coefficients."—If the hydroxide ion-catalyzed reaction of N-methylaniline with 2,4-dinitrofluorobenzene gives rate coefficient $k_{\mathrm{III,a}}$ at $[\mathrm{OH^-}]_a$, $k_{\mathrm{III,b}}$ at $[\mathrm{OH^-}]_b$ and $k_{\mathrm{III,c}}$ at $[\mathrm{OH^-}]_c$, these values may in turn be substituted into equation 12 to give three simultaneous equations which can be solved for k_1, $(k_{-1} + k_2)/k_3$ and k_1k_2/k_3. One can derive

$$k_1 = \frac{k_{\mathrm{III,b}}[\mathrm{OH^-}]_b - k_{\mathrm{III,a}}[\mathrm{OH^-}]_a - k_{\mathrm{III,c}}[\mathrm{OH^-}]_c - k_{\mathrm{III,a}}[\mathrm{OH^-}]_a\left(\dfrac{k_{\mathrm{III,a}} - k_{\mathrm{III,b}}}{k_{\mathrm{III,a}} - k_{\mathrm{III,c}}}\right)}{([\mathrm{OH^-}]_a - [\mathrm{OH^-}]_c)\left(\dfrac{k_{\mathrm{III,a}} - k_{\mathrm{III,b}}}{k_{\mathrm{III,a}} - k_{\mathrm{III,c}}}\right) - ([\mathrm{OH^-}]_a - [\mathrm{OH^-}]_b)} \qquad (14)$$

Once k_1 is known, $(k_{-1} + k_2)/k_3$ can be evaluated from the expression

$$\frac{k_{-1} + k_2}{k_3} = \frac{k_1([\mathrm{OH^-}]_a - [\mathrm{OH^-}]_b) + k_{\mathrm{III,b}}[\mathrm{OH^-}]_b - k_{\mathrm{III,a}}[\mathrm{OH^-}]_a}{k_{\mathrm{III,a}} - k_{\mathrm{III,b}}} \qquad (15)$$

and finally k_1k_2/k_3 can be evaluated from equation 12 by substitution of a particular pair of k_{III} and $[\mathrm{OH^-}]$ values. Using the values $[\mathrm{OH^-}]_c = 0$, $[\mathrm{OH^-}]_b = 0.005$ and $[\mathrm{OH^-}]_a = 0.02$ and the corresponding k_{III} values (from Table III), one obtains $k_1 = 17 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ whilst from the same information except that $[\mathrm{OH^-}]_a = 0.03$ one obtains 22×10^{-5} l. mole^{-1} sec.$^{-1}$. Then with $[\mathrm{OH^-}]_a = 0.02$, $(k_{-1} + k_2)/k_3$ is 0.023 mole/l. whilst with $[\mathrm{OH^-}]_a = 0.03$ it is 0.022 mole/l. Finally when $[\mathrm{OH^-}]_a$ is 0.02, k_1k_2/k_3 is 4.5×10^{-7} sec.$^{-1}$ whilst with $[\mathrm{OH^-}]_a = 0.03$ it is 1.5×10^{-7} sec.$^{-1}$. The average values for these three "unknowns" are, respectively, 20×10^{-5} l. mole^{-1} sec.$^{-1}$, 0.022 mole/l. and 3×10^{-7} sec.$^{-1}$. By simple arithmetic, k_{-1}/k_3 is then 0.0205 mole/l., k_2/k_3 is 1.5×10^{-3} mole/l. and k_{-1}/k_2 is 14.

Chapel Hill, N. C.

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[31] H. Goldschmidt, *Z. physik. Chem.*, **94**, 233 (1920).