Kinetics of Reactions of Aniline and *n*-Butylamine with 2,4-Dinitrofluorobenzene. Search for Evidence of Catalysis by Bases[1]

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Second-order rate coefficients for reactions of 2,4-dinitrofluorobenzene with n-butylamine in methanol and with aniline in methanol, t-butyl alcohol, and 60% dioxane–40% water are at most mildly augmented by addition of bases. The bases studied were variously the amines themselves, potassium acetate, and sodium hydroxide. These reactions are judged to occur by the intermediate complex mechanism with the first step rate limiting. The true chemical character of these mild accelerations is not clear.

Many reactions of amines with nitro-activated halobenzenes and related substrates have been described as base catalyzed. That is, the second-order rate coefficient (first order in substrate, first order in amine) has been found to be augmented by increase in amine concentration or by addition of other bases. However, not all such reactions are accelerated by bases, and the incidence of such kinetic effects is imperfectly understood. Also, there is some controversy as to their interpretation.

When such effects have been observed, they have mostly conformed to the mathematical form

$$k_A = k' + k''[B] \qquad (1)$$

where k_A is the observed, second-order rate coefficient and k' and k'' are, respectively, second- and third-order coefficients. The extent of acceleration by bases is conveniently expressed as k''/k', which represents the relative magnitudes of the accelerated and unaccelerated parts of the reaction at 1 *M* base concentration.[2,3]

A striking feature is that many reactions are but mildly accelerated by bases while others are strongly catalyzed. "Mildly" accelerated reactions include those of several amines with 2,4-dinitrochlorobenzene in chloroform or ethanol,[2] for which k''/k' varies from 0.21 to 4.6, and those of piperidine with *p*-fluoronitrobenzene in several polar solvents,[4] for which k''/k' is less than 3.2. Reactions of 2,4-dinitrochlorobenzene with amines *in benzene solution* are at most mildly accelerated by excess amine,[5,6] but those of 2,4-dinitrofluorobenzene,[5,6] and *p*-fluoronitrobenzene[4] are so strongly dependent on amine catalysis that they are essentially second-order in amine except at very low amine concentrations.[5] Reactions of 2,4-dinitrofluorobenzene with N-methylaniline are strongly catalyzed by oxyanion bases[7]; k''/k' is 150 for the acetate-catalyzed reaction in ethanol and 350 for the hydroxide-catalyzed reaction[8] in 60% dioxane–40% water. However, reactions of 2,4-dinitrochlorobenzene with amines are so weakly affected by hydroxide and acetate ions that the acceleration, if there is any, is scarcely larger than experimental error.[7,9,10]

In the present research, we have sought evidence of base catalysis in reactions of 2,4-dinitrofluorobenzene with *n*-butylamine and with aniline in three solvents.

Experimental

Solvents. Methanol was purified by the magnesium method.[11] Dioxane was purified by the method of Fieser[11] and was stored over lithium aluminum hydride, from which it was distilled as needed. The solvent "60% dioxane–40% water" was obtained by mixing three volumes of purified dioxane with two volumes of boiled distilled water. *t*-Butyl alcohol was fractionally distilled through an 80-cm. column packed with glass helices; the fraction collected had m.p. 25.66°.

Reactants and Products. 2,4-Dinitrofluorobenzene of m.p. 24.0–25.4° was used. N-(*n*-Butyl)-2,4-dinitroaniline, m.p. 90.5–91.5°, and 2,4-dinitrodiphenylamine, m.p. 156.5–157.5°, were prepared and purified by standard methods. A commercial sample of *n*-butylamine was distilled from zinc dust and solid potassium hydroxide, b.p. 77.0–77.3°. *n*-Butylamine hydrochloride was recrystallized from absolute ethanol (with diethyl ether), m.p. 212.5–213.5°. Aniline was twice distilled from potassium hydroxide and zinc dust. Aniline hydrochloride was recrystallized from absolute ethanol, m.p. 197–198°.

Kinetic Procedure. In all runs, the substrate concentration was much less than that of the amine or base, and pseudo-first-order kinetics were obtained. Reactions were followed by photometric analysis, after Bunnett and Randall.[7] Data were treated according to the general procedure of Bunnett and Randall.

Results

The rate of reaction of *n*-butylamine with 2,4-dinitrofluorobenzene (ArF) in methanol solution was determined at several amine concentrations. *n*-Butyl-

(1) (a) Supported, in part, by the National Science Foundation; (b) abstracted from the Ph.D. Thesis of R. H. Garst, Brown University, June 1964; *Dissertation Abstr.*, **25**, 4404 (1965).

(2) S. D. Ross in "Progress in Physical Organic Chemistry," Vol. 1, S. G. Cohen, A. Streitwieser, Jr., and R. W. Taft, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 31.

(3) The units of k''/k' are l./mole.

(4) H. Suhr, *Ber. Bunsenges. physik. Chem.*, **67**, 893 (1963).

(5) F. Pietra and A. Fava, *Tetrahedron Letters*, 1535 (1963); F. Pietra, *ibid.*, 745 (1965).

(6) H. Zollinger and C. Bernasconi, *ibid.*, 1083 (1965).

(7) J. F. Bunnett and J. J. Randall, *J. Am. Chem. Soc.*, **80**, 6020 (1958).

(8) This figure is based on the initial slope.

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

(10) S. D. Ross, *J. Am. Chem. Soc.*, **80**, 5319 (1958).

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

amine hydrochloride (0.01 M) was present in all runs, to repress complications due to methoxide ion,[12] and formation of N-(n-butyl)-2,4-dinitroaniline was quantitative. Results are set forth in Table I. The second-order rate coefficient, k_A,[13] is seen to change

Table I. Reaction of n-Butylamine with 2,4-Dinitrofluorobenzene in Methanol at 0.0°[a]

$[ArF]_0$, M	$[C_4H_9NH_2]$, M	$k_\psi \times 10^4$, sec.$^{-1}$	$k_A \times 10^2$, l. mole^{-1} sec.$^{-1}$
5.25×10^{-5}	0.0005	0.370	7.40[b]
...	0.0010	0.736	7.36[b]
...	0.0025	1.80	7.21[c]
1.01×10^{-3}	0.0100	7.12	7.12[b]
...	0.0250	18.9	7.56
1.04×10^{-3}	0.0250	19.9	7.96[b]
...	0.1000	80.5	8.05[d]

[a] $[C_4H_9NH_3^+Cl^-]$ 0.01 M in all runs. [b] Average of two runs. [c] Average of three runs. [d] Average of four runs.

very little as the amine concentration is varied 200-fold. There is a slight rise in k_A as amine concentration increases, but it is not much greater than experimental error. By linear regression analysis, k' is 7.3×10^{-2} l. mole^{-1} sec.$^{-1}$ and k'' is 9.0×10^{-2} l.^{2} mole^{-2} sec.$^{-1}$ (see eq. 1). The standard deviation in k'' is 2.8×10^{-2} l.^{2} mole^{-2} sec.$^{-1}$, about 30% of k''. k''/k' is 1.2; thus, another "mild" acceleration is evident in these data.

The reaction of ArF with aniline in methanol solution was also studied at several amine concentrations. Results are displayed in Table II. The second-order

Table II. Reaction of Aniline with 2,4-Dinitrofluorobenzene in Methanol at 29.4°[a]

$[C_6H_5NH_2]$, M	$10^5 k_\psi$, sec.$^{-1}$	$10^3 k_A$, M^{-1} sec.$^{-1}$
0.0005	0.63 ± 0.01[b]	12.6 ± 0.2
0.0010	1.14 ± 0.02[b]	11.4 ± 0.2
0.0100	8.47 ± 0.09[c]	8.47 ± 0.09
0.100	87.8 ± 1.3[d]	8.78 ± 0.13

[a] Initial concentrations (all runs): ArF, 5.00×10^{-5} M; aniline hydrochloride, 0.001 M. [b] Average of two runs. [c] Average of four runs; average deviation given. [d] Average of three runs.

rate coefficient, k_A, was found to *decrease* about 30% as aniline concentration increased from 0.0005 to 0.01 M. Similar effects were observed by Ross and Kuntz[14] in the reactions of 2,4-dinitrochlorobenzene with aniline in ethanol and in 50% ethanol-50% ethyl acetate. They held molecular compound (charge-transfer complex) formation to be responsible, and we suggest the same interpretation for the present case. The small increase in k_A between 0.01 and 0.1 M aniline (Table II) is interesting because complex formation ought further to depress k_A; this suggests that an accelerating influence of aniline is also at play.

The effects of neutral and basic salts on the rate of the ArF–aniline reaction in methanol were studied; results are presented in Table III. Although lithium chloride, sodium perchlorate, and aniline hydrochloride all affected reaction rate to about the same small extent, the effect of 0.1 M potassium acetate was to increase k_A about 65%. At 0.2 M, the effect of potassium acetate was still greater, and addition of acetic acid in equal concentration did not diminish it. This effect corresponds to a k''/k' ratio of about 5 or 6 (see eq. 1). Though appreciable, it is mild compared to the strong effect of potassium acetate on the reaction of ArF with N-methylaniline in ethanol, for which k''/k' is 150.[7]

The effect of sodium hydroxide on the reaction of ArF with aniline in 60% dioxane–40% water was next studied. Results are shown in Table IV, which comprises two series of runs. In one series (upper part of table), sodium hydroxide concentration was varied without addition of other electrolytes. In the other series (lower part), [NaOH] was varied but total electrolyte concentration was held constant, but for two runs, at 0.2 M by addition of sodium chloride as required.

With or without compensation by sodium chloride, k_A was mildly augmented by increase of [NaOH] to 0.2 M; the effect corresponds to k''/k' of about 2. In contrast, k''/k' for the hydroxide-catalyzed reaction of ArF *with N-methylaniline* in the same solvent is about 350.[7]

The experiments in Table IV also provide values for k_{OH}, the second-order coefficient for reaction of ArF with sodium hydroxide to form 2,4-dinitrophenol. When sodium hydroxide was the only electrolyte present, k_{OH} was depressed by increase of [NaOH]. However, at constant electrolyte concentration k_{OH} varied only randomly. This suggests that the hydroxydefluorination reaction is cleanly second order, and that the fall in k_{OH} with rise in [NaOH] in the upper part of Table IV is due to a negative salt effect.

From measurements on the competitive reactions of ArF with N-methylaniline and hydroxide ion in 60% dioxane–40% water at 0°, Bunnett and Randall[7] determined the second-order rate coefficient for reaction with hydroxide ion (k_{OH}) to be 0.114 l. mole^{-1} sec.$^{-1}$; their measurements were made at low sodium hydroxide ion concentrations (<0.03 M) in the absence of any other electrolytes. In our experience (Table IV, upper part), k_{OH} for the same reaction at 0.05 M sodium hydroxide concentration in the absence of other electrolytes is 0.112 l. mole^{-1} sec.$^{-1}$. The average value of k_{OH} at 0.2 M total electrolyte concentration is 0.064 l. mole^{-1} sec.$^{-1}$.

The reaction of aniline with ArF in t-butyl alcohol solution was also studied. Results are given in Table V. k_A was found to increase steadily with aniline concentration. By linear regression analysis, k' (intercept) is 2.64×10^{-3} l. mole^{-1} sec.$^{-1}$ and k'' (slope) is 6.9×10^{-3} l.^{2} mole^{-2} sec.$^{-1}$; k''/k' is 2.6. This is another instance of "mild" acceleration. It is interesting that, in contrast to the reaction in methanol (Table II),

(12) J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, *J. Am. Chem. Soc.*, 79, 385 (1957).

(13) Rate coefficients are symbolized: k_ψ, pseudo-first-order coefficient for the sum of all reactions consuming the substrate, ArF; k_A^*, pseudo-first-order coefficient for formation of dinitrophenylamine product (k_A^* = (fractional yield of amine product) $\times k_\psi$); k_A, second-order coefficient for formation of dinitrophenylamine product ($k_A = k_A^*$/[amine]); k_{OH}^* (in reactions containing OH^-), pseudo-first-order coefficient for reaction of ArF with OH^- ($k_{OH}^* = k_\psi - k_A^*$); k_{OH}, second-order coefficient for reaction of ArF with OH^- ($k_{OH} = k_{OH}^*/[OH^-]$); k_{OR}^* (for reactions in methanol containing potassium acetate), pseudo-first-order coefficient for sum of side reactions ($k_{OR}^* = k_\psi - k_A^*$).

(14) S. D. Ross and I. Kuntz, *J. Am. Chem. Soc.*, 76, 3000 (1954).

Table III. Kinetics of Reaction of Aniline with 2,4-Dinitrofluorobenzene in Methanol at 29.4° in the Presence of Diverse Salts[a]

Salt	[Salt], M	$k_\psi \times 10^3$, sec.$^{-1}$	Yield, %	$k_A^* \times 10^3$, sec.$^{-1}$	$k_A \times 10^2$, l. mole^{-1} sec.$^{-1}$	$k_{OR}^* \times 10^4$, sec.$^{-1}$
$C_6H_5NH_3^+Cl^-$	0.0010	0.887	100.0	0.887	0.887	...
$KC_2H_3O_2$	0.100	2.12	68.8	1.46	1.46	6.6[b]
$KC_2H_3O_2$	0.200	2.46	71.1	1.74	1.74	7.2
$KC_2H_3O_2$[c]	0.200	2.14	89.6	1.90	1.90	2.4
LiCl	0.100	1.10[d]	89.6	...	...	...
$NaClO_4$	0.100	0.926[d]	93.3	...	...	...

[a] Initial concentrations: ArF, 5×10^{-5} M; $C_6H_5NH_2$, 0.1 M. [b] Average of three runs. [c] Acetic acid, 0.20 M, was also present. [d] k_{obsd} was calculated using a theoretically calculated A_∞.

Table IV. Reaction of Sodium Hydroxide and Aniline with 2,4-Dinitrofluorobenzene in 60% Dioxane–40% Water at 0.0°[a]

$[NaOH]_0$, M	[NaCl], M	$k_\psi \times 10^3$, sec.$^{-1}$	Yield, %	$k_A^* \times 10^3$, sec.$^{-1}$	$k_A \times 10^3$, l. mole^{-1} sec.$^{-1}$	$k_{OH}^* \times 10^3$, sec.$^{-1}$	$k_{OH} \times 10^2$, l. mole^{-1} sec.$^{-1}$
Nil[b]		1.27[c]	100.0	1.27	6.35	...	...
0.0513		6.94	19.1	1.33	6.63	5.61	11.2
0.0966		10.2[c]	14.8[c]	1.50	7.52	8.72	9.02
0.100		10.9	13.4	1.46	7.30	9.43	9.43
0.200		16.3[d]	11.2[d]	1.83	9.12	14.5	7.25
Nil	0.200	1.46	100.0	1.46	7.32	...	...
0.040	0.160	4.42	41.3	1.83	9.15	2.59	6.48
0.050	0.150	4.30	39.1	1.68	8.40	2.62	5.24
0.067	0.100	6.18[c]	29.9[c]	1.85	9.25	4.34	6.51
0.100	0.100	8.54	22.6	1.93	9.65	6.61	6.61
0.120	0.080	9.21	20.2	1.86	9.30	7.35	6.13
0.150	0.050	11.5	17.7	2.03	10.2	9.46	6.30
0.180	0.020	13.6	14.9	2.03	10.2	11.6	6.46

[a] Initial concentrations: ArF, 0.001 M; $C_6H_5NH_2$, 0.2 M, except as otherwise noted. [b] $[ArF]_0$ 4.05×10^{-5} M. [c] Average of two runs. [d] Average of three runs.

Table V. Reaction of Aniline with 2,4-Dinitrofluorobenzene in 2-Methyl-2-propanol at 29.4°[a]

$[C_6H_5NH_2]$, M	$k_\psi \times 10^5$, sec.$^{-1}$	$k_A \times 10^3$, l. mole^{-1} sec.$^{-1}$
0.00198	0.506	2.55
0.00497	1.39	2.79
0.0099	2.78	2.80
0.0197	5.56	2.82
0.0502	15.3	3.04
0.0602	17.4	2.90
0.0702	21.6	3.09
0.0996	33.0	3.31
0.1500	51.1	3.40
0.2002	82.3	4.12
0.1997	82.8	4.14

[a] $[ArF]_0$ 1.01×10^{-4} M in all runs.

no deceleration of the sort ascribed to charge-transfer complex formation is evident in t-butyl alcohol. Ross and Kuntz[14] found no evidence for such an effect in rates of reaction of aniline with 2,4-dinitrochlorobenzene in ethyl acetate solution.

Discussion

We have found the second-order rate coefficients for reactions of 2,4-dinitrofluorobenzene with n-butylamine in methanol, and with aniline in methanol, t-butyl alcohol, and 60% dioxane–40% water, to be at most mildly augmented by addition of bases. In the symbolism of eq. 1, the largest k''/k' ratio observed was about 5 or 6.

Though these and similar mild accelerations observed by other authors have the mathematical form appropriate for base catalysis, it is not clear that description of the acceleration as base catalysis is chemically warranted. Strong bases like hydroxide ion are scarcely more effective, or are even less effective, than rather weak bases like amines. And effects of similar character are caused by substances such as nitro compounds, sulfoxides, and sulfones which do not normally display basic character in alcoholic solvents.[2]

If the argument that these accelerations are not due to medium effects is accepted,[2] the k'' term in eq. 1 must represent inclusion of the accelerating species in the rate-limiting transition state. But that it functions as a base in the transition state does not necessarily follow. The true character of these accelerations remains unclear.

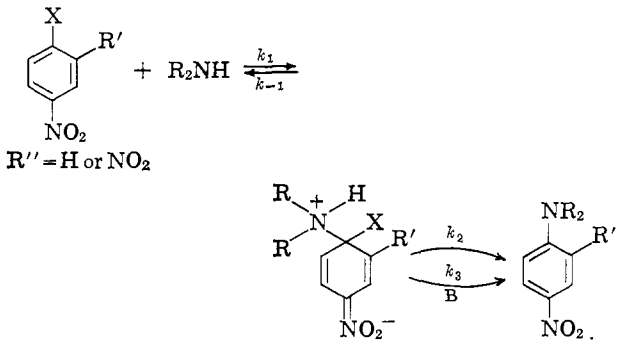
Ross[2] and Suhr[4] have identified these mild accelerations as base catalysis. They consider them to represent catalysis of the second step of the intermediate complex mechanism of substitution.[15] In this scheme, it is visualized that progression from intermediate complex to products may occur either uncatalyzed (k_2) or with catalysis by base (k_3). Bunnett and Randall[7] showed that, if $k_{-1} >> (k_2 + k_3[B])$, the reaction should manifest base catalysis according to the law

$$k_A = k_1k_2/k_{-1} + (k_1k_3/k_{-1})[B] \qquad (2)$$

This has the same mathematical form as eq. 1, and

(15) J. F. Bunnett, *Quart. Rev.* (London), **12**, 1 (1958).

k''/k' represents k_3/k_2 if this chemical interpretation is correct.



The present results cast considerable doubt on this interpretation of the mild accelerations. For hydroxide ion accelerated reactions with ArF in 60% dioxane–40% water, k''/k' is about 2 for aniline and about 350 for N-methylaniline. If both accelerations were due to base catalysis of the second step of the intermediate complex mechanism, changing the amine from aniline to N-methylaniline must have caused a great increase in the sensitivity of the fluoride ejection step to catalysis by base. But this is unreasonable; in both cases this step is concerned with elimination of HF from very similar intermediates, and sensitivity to base catalysis ought to be nearly the same.

A more satisfactory interpretation is that the fluoride ejection step is rate limiting only with N-methylaniline, and that formation of the intermediate complex is rate determining in the aniline reaction. It is reasonable that k_{-1} should be much greater with N-methylaniline than with aniline because of the bulk of the methyl group and consequent steric strain in the intermediate complex. The data indicate that k_{-1} is so much greater in the case of N-methylaniline as to change the rate-limiting step of the mechanism.

For this reason and in consideration of factors discussed by Bunnett and Randall,[7] we judge that the first step of the intermediate complex mechanism is rate limiting in all the reactions studied in the present work, in reactions of 2,4-dinitrochlorobenzene with amines in alcoholic and water–dioxane solvents, and in the mildly accelerated ($k''/k' < 5$) reactions of *p*-fluoronitrobenzene with piperidine reported by Suhr.[4]

In response to a referee's comments, we elaborate the basis of our judgment. When $(k_2 + k_3[B]) \gg k_{-1}$, a situation most apt to be encountered with good leaving groups, formation of the intermediate complex is rate determining. The reaction is immune to base catalysis, except as this first step may be catalyzed by base. In contrast, base catalysis in manifestation of eq. 2 is expected if the leaving group is one which does not separate rapidly from carbon (causing k_2 and $k_3[B]$ to be small) and/or if the solvent and other factors cause k_{-1} to be large.

The actual incidence of strong acceleration by bases ($k''/k' > 50$) matches these expectations. Strong acceleration has never been observed in reactions of 2,4-dinitrochloro- or -bromobenzene, which have very good leaving groups. Strong acceleration has been observed in reactions of piperidine with 2,4-dinitroanisole[1b,16] and 2,4-dinitrodiphenyl ether[16,17] which have poor leaving groups. 2,4-Dinitrofluorobenzene appears to represent a borderline case in which the relative magnitudes of k_{-1} and $(k_2 + k_3[B])$ are governed by factors, such as the solvent and the bulkiness of the amine, which especially affect k_{-1}.

It is consistent with this interpretation that reactions insensitive to base catalysis are among those for which scarcely any kinetic "element effect" in the leaving group is observed.[9,12] This is independent evidence that leaving group expulsion is not rate limiting.

Kirby and Jencks[18] have suggested that the mild accelerations of reactions "in which the first step ... is probably rate determining" may represent base catalysis of the first step of the intermediate complex mechanism. We do not feel that this possibility can be altogether excluded. But it must indeed be a strange type of base catalysis when hydroxide ion, amines, and nitro compounds are nearly equally effective as catalysts.

Acknowledgment. We thank Dr. Kevork V. Nahabedian for discussions and counsel.

(16) J. F. Bunnett and C. Bernasconi, manuscript in preparation.
(17) J. F. Bunnett and R. H. Garst, *J. Am. Chem. Soc.*, **87**, 3879 (1965).
(18) A. J. Kirby and W. P. Jencks, *ibid.*, **87**, 3217 (1965).