The Acid-Catalyzed Nitramine Rearrangement. III. The Nature of the Acid Catalysis[1-3]

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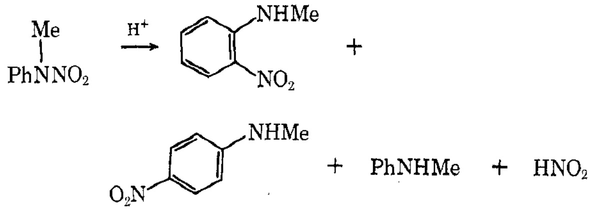
Kinetic studies of the perchloric acid catalyzed rearrangement of three *p*-X-N-nitro-N-methylanilines (X = CH_3O, H, and O_2N) have shown that the reactions are first order in substrate and first order in acid. It was also established that the nitramine rearrangement is subject to specific acid catalysis through (1) the effect of acetic acid–acetate buffers on the isomerization rate of N-methyl-N-phenylnitramine, (2) the influence of the isotopic composition of the solvent on the rate of reaction of the same substrate, and (3) the acidity function correlation of the rate of rearrangement of N-nitro-N-methylaniline in hydrochloric acid or phosphoric acid and of 4,N-nitro-N-methylaniline in perchloric acid. Thus the acid-catalyzed rearrangement of aromatic nitramines involves reversible protonation of the substrate followed by a rate-determining unimolecular reaction of the protonated nitramine.

The mechanism of the acid-catalyzed rearrangement of aromatic nitramines, *e.g.*, eq 1, is of considerable theoretical interest. Product studies[4] and crossover experiments[4b,5] have led some investigators to conclude that the reaction was intramolecular (*i.e.*, the nitro group and aromatic amine moiety never become independent of one another). If this is true, the reaction belongs in the same mechanistic category as the benzidine rearrangement.



(1)

Further information about the mechanism of the nitramine rearrangement should be available from the kinetics of the process and the influence of substrate structural modifications on rate. As a first step, the characterization of the nature of acid intervention is of prime importance. Since acid accelerates the reaction, its concentration must appear in the rate expression. The order of the reaction with respect to acid can be obtained from the dependence of the rate on acid concentration. Although this order can have important mechanistic implications, the nature of this catalysis—general or specific—is probably of greater consequence. If the rearrangement is subject to specific acid catalysis, the rate-determining step follows a reversible protonation so that the rates will reflect not only the ease of protonation, but also the

$$S + HA \overset{\text{fast}}{\rightleftharpoons} A^- + HS^+ \xrightarrow{\text{slow}} \text{products}$$

facility of later bond-breaking or -making processes. In such a situation, the effect of structural changes on rate provides a great deal of information about the nature of bonding changes in the critical steps of a reaction. On the other hand, if the reaction is subject to general acid catalysis, the proton transfer is rate limiting, so that very few deductions about the character of the rearrangement could be made from structural effects on rates.

The first determinations of the nitramine rearrangement rate were made by colorimetric techniques.[5a,6] It was found that the reaction was first order in nitramine, but, because of the necessity for dealing with nonaqueous or highly acidic media for the reaction and because adequate theories and correlations for treating rates measured in these solvent systems were not available, the data and conclusions with respect to the influence of acid were not too meaningful. The rearrangement was found to be faster in acetic acid or aqueous acetic acid solutions than in water containing a similar amount of mineral acid. In 98% acetic acid, the velocity of isomerization was qualitatively related to the strength of the catalyzing acid:[7] $HClO_4 > HCl > H_2SO_4 > HNO_3$. The *apparent* order with respect to mineral acid concentration was found to vary from one to two depending on the solvent.[5a,6] It was concluded that the reaction was subject to general acid catalysis.[8]

In this investigation, the influence of acid strength and concentration on the rearrangement rates of substituted N-methyl arylnitramines (secondary nitramines) was studied. These compounds rearrange much more readily than the simple arylnitramines (primary nitramines) which have been the substrates used in previous researches. Thus it was possible to examine the reaction in dilute aqueous solution and define the order with respect to acid. The nature of the acid catalysis was determined in three different ways.

Results and Discussion

Kinetic Nature.—The data in Table I indicate quite clearly that the aromatic nitramine rearrangement is first order in nitramine concentration and first order in acid concentration. Thus the general kinetic expression for the rate of this reaction is

$$\text{rate} = k[\text{nitramine}][\text{acid}]$$

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[3] This work was supported by Grants G-7345 and GP-1970 from the National Science Foundation.

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TABLE I

RATE CONSTANTS FOR ACID-CATALYZED REARRANGEMENT OF SOME AROMATIC NITRAMINES

$[HClO_4]$,[a] M	10^4k_1, sec^{-1}	10^4k_2, M^{-1} sec^{-1}
A. *p*-Methoxy-N-nitro-N-methylaniline (30.0°)		
0.00200	23.8 ± 0.6	11900 ± 300
0.00100	11.7 ± 0.1	11700 ± 100
B. N-Nitro-N-methylaniline (55.0°)		
0.0200	5.21 ± 0.03	261 ± 2
0.0100	2.68 ± 0.05	268 ± 5
C. *p*-N-Dinitro-N-methylaniline (80.0°)		
1.002	9.99 ± 0.08	10.0 ± 0.1
0.501	5.11 ± 0.04	10.2 ± 0.1

[a] Ionic strength maintained at 1.002 M by addition of $KClO_4$.

Acetic Acid-Acetate Buffers.—The rate of a general acid catalyzed reaction depends on the concentration of the catalyzing acid, while the velocity of a specific acid catalyzed process is determined by the pH of the medium.[9]

N-Nitro-N-methylaniline was rearranged in a series of acetic acid-acetate buffers of differing acid concentration but of constant ionic strength and buffer ratio. Under such conditions, the pH of the medium should remain constant so that the rate of a specific acid catalyzed reaction will be unaffected but the rate of a general acid catalyzed process should increase as the concentration of acid present increases. A temperature of 125° was chosen for this study. At this temperature, the rearrangement in the absence of acid is about half as fast as in the presence of the buffer. A concerted proton transfer-isomerization mechanism (general acid catalyzed process) should be most apparent under conditions favorable to a thermal, uncatalyzed reaction. Even under these extreme conditions, the data (Table II) indicate that the rate is unaffected by changes in acid concentration as long as the buffer ratio (pH) remains constant; and thus a reversible proton transfer to substrate precedes rearrangement.

TABLE II

EFFECT OF BUFFER STRENGTH ON REARRANGEMENT RATE OF N-NITRO-N-METHYLANILINE AT 125°

[HOAc],[a] M	10^4k_1, sec^{-1}	[HOAc],[a] M	10^4k_1, sec^{-1}
0.00[b]	1.93[b]	2.60	3.60
0.20	3.83	3.00	3.76
0.40	4.03	3.60	3.45
1.00	3.77	4.00	3.39
1.60	3.88	4.60	3.44
2.00	3.64		

[a] [HOAc]/[NaOAc] was maintained equal to 2.00 while the ionic strength was kept constant at 2.30 M with KCl. [b] No HOAc or NaOAc was present in this experiment. The ionic strength was 2.30 M (KCl).

Deuterated Solvents.—The nature of acid catalysis may also be ascertained from the rate effect of changes in solvent isotopic composition.[10] Specific acid catalyzed reactions usually proceed faster in deuterated than in normal solvents, while the opposite is true for general acid catalyzed processes. N-Nitro-N-methylaniline was rearranged in aqueous solutions containing varying amounts of heavy water. The results (Table III) are those anticipated for a specific acid catalyzed reaction. In addition, the data are correlated within experimental error by the Nelson-Butler equation,[10a,b] which applies to reactions involving a preliminary equilibrium between the substrate and hydrogen ion.

TABLE III

SOLVENT ISOTOPE EFFECT ON REARRANGEMENT RATE OF N-NITRO-N-METHYLANILINE[a]

D_2O, mol %	10^4k_1, sec^{-1}	k_x/k_0
0.0	9.8 ± 0.5	1.00
25.0	12.3 ± 0.6	1.26
50.0	15.4 ± 0.2	1.57
75.0	20.2 ± 0.7	2.06
100.0	29.0 ± 1.1	2.96

[a] [HCl] or [DCl] = 0.476 M; T = 40.0°.

Concentrated Solutions of Strong Acids.—The rate of a specific acid catalyzed reaction will parallel the tendency of a medium to transfer a proton to a base (*i.e.*, the acidity function) if water is not involved in the rate-limiting step. Most reactions subject to general acid catalysis do not exhibit this behavior.[11] The correlation of rates with acidity functions has been questioned because of the finding that the tendency of a medium to protonate a base varies with the nature of the base.[12] Nevertheless, a reasonable degree of parallelism between reaction rates in a series of media and an acid-base equilibrium process in the same solutions should be a fairly good indication that the rate process involves a reversible protonation preceding the rate-determining step.

The rearrangement rates of N-nitro-N-methylaniline in hydrochloric acid and phosphoric acid solutions and of *p*-N-dinitro-N-methylaniline in perchloric acid solutions were determined. The results are summarized in Table IV. These kinetic data were plotted

TABLE IV

RATES OF REARRANGEMENT OF SOME AROMATIC NITRAMINES IN CONCENTRATED SOLUTIONS OF STRONG ACIDS

[Acid], M	10^4k_1, sec^{-1}	[Acid], M	10^4k_1, sec^{-1}
A. N-Nitro-N-methylaniline (HCl, 30.0°)		B. *p*,N-Dinitro-N-methylaniline ($HClO_4$, 30.0°)	
0.205	1.35	4.19	1.38
0.497	3.45	4.19	1.57
1.008	8.79	4.62	2.33
1.45	16.0	4.64	2.50
1.69	24.6	5.02	4.68
2.08	38.3	5.03	4.82
2.55	59.8	5.45	9.35
2.88	97.3	5.48	7.76
3.35	176	5.84	16.9
(H_3PO_4, 19.0°)		5.93	18.3
1.28	0.322	6.26	35.7
1.83	0.595	6.38	40.6
2.20	0.829	6.73	83.8
2.75	1.49	6.79	81.2
3.11	2.01		
3.67	2.87		
4.58	5.80		
5.42	14.6		

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[9] R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp 124-214.

[10] (a) W. E. Nelson and J. A. V. Butler, *J. Chem. Soc.*, 957 (1938); (b) J. G. Pritchard and F. A. Long, *J. Amer. Chem. Soc.*, **78** 6008 (1956); (c) C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 3207 (1961).

[11] See, however, L. Melander and P. C. Myhre, *Ark. Kemi*, **13**, 507 (1959); F. A. Long and M. A. Paul, *Chem. Rev.*, **57**, 935 (1957).

vs. H_0' and H_0''', the acidity functions defined by primary and tertiary aromatic amines, respectively.[12,13] Straight lines with no apparent curvature were obtained. The slopes are listed in Table V. It is to be noted that use of neither H_0' nor H_0''' leads to the theoretical slope of 1.00 expected for such correlations. This is undoubtedly due to the fact that the protonation equilibria of neither primary nor tertiary amines (which are used to define H_0' and H_0''', respectively) are perfect models for the protonation equilibria of nitramines. The latter must be intermediate in nature.

TABLE V

CORRELATION OF AROMATIC NITRAMINE REARRANGEMENT RATES IN CONCENTRATED SOLUTIONS OF STRONG ACIDS

Nitramine	Acid	H_0' slope[a]	H_0''' slope[a]	w[b,c]
$C_6H_5NMeNO_2$	HCl	1.24	0.91	−4.0
$C_6H_5NMeNO_2$	H_3PO_4	1.20	0.82	−3.3
p-$O_2NC_6H_4NMeNO_2$	$HClO_4$	1.09		−0.7

[a] H_0' and H_0''' values for hydrochloric and phosphoric acids were obtained from ref 12; H_0' values for perchloric acid were obtained from M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957). [b] Log a_{H_2O} values for hydrochloric and perchloric acids were taken from ref 14; log a_{H_2O} values for phosphoric acid were obtained from K. E. Elmore, C. M. Mason, and J. H. Cristensen, *J. Amer. Chem. Soc.*, **68**, 2528 (1946). [c] See ref 14.

Application of Bunnett's equation[14] to the experimental data permits the nitramine rearrangement to be classified according to its nature. The values of w (Table V) for the isomerization of N-nitro-N-methylaniline in hydrochloric or phosphoric acid solutions and of *p*-N-dinitro-N-methylaniline in aqueous perchloric acid indicates that the nitramine rearrangement is one of those reactions in which water does not participate in the rate-determining step either as a nucleophile or a proton-transfer agent. These studies of the rearrangement in concentrated solutions of strong acids demonstrate that the conversion of aromatic nitramines into nitroanilines is subject to specific acid catalysis.

Conclusion

In this paper the acid-catalyzed rearrangement of arylnitramines has been shown to be a second-order reaction—first order in the substrate and first order in the catalyzing acid. Three different tests were employed to determine the nature of the acid catalysis. Although the result from any one of these methods alone could be challenged as inconclusive, the singular conclusion from each of these approaches that the reaction is subject to specific acid catalysis makes the general categorization of the process incontrovertible. The acid-catalyzed aromatic nitramine rearrangement therefore involves reversible protonation of the nitramine followed by a rate-limiting step leading to rearrangement.

Experimental Section

Aromatic Nitramines.—*p*-Methoxy-N-nitro-N-methylaniline, mp 68.1–69.1°, and N-nitro-N-methylaniline, mp 36.6–37.6°, were prepared by sequential alkaline nitration and methylation of *p*-anisidine and aniline, respectively.[15] *p*-N-Nitro-N-methylaniline, mp 138.2–139.5°, was obtained by oxidizing *p*-nitrobenzenediazonium ion to the nitramine[16] and methylating it.[17]

Acids.—Reagent grade hydrochloric, phosphoric, and perchloric acid were diluted with water to the approximate concentrations required for the acidity-function studies.

Deuteriochloric acid was prepared by adding phosphorus pentachloride to 99.9% pure heavy water and distilling the product. A normal hydrochloric acid solution of exactly the same concentration was made by dilution of reagent grade hydrochloric acid. Measured volumes of these two acids were used to prepare the media for kinetics.

The acetic acid–acetate buffer solutions were obtained by mixing different volumetric proportions of 2.50 *M* aqueous potassium chloride and a solution 2.50 *M* in potassium acetate and 5.00 *M* in acetic acid.

Kinetic Measurements.—A volumetric flask was filled almost to the mark with the acid solution and thermostated for 20 min. Sufficient additional acid was then added to adjust the volume to the mark and the flask was then allowed to remain in the thermostat for another 20 min. An aliquot of a dioxane solution of the nitramine was added and the mixture was shaken thoroughly and immediately returned to the thermostat. The concentration of nitramine (*ca.* 10^{-4} *M*) was such that the final visible absorbance of the product was easily and accurately determinable. The maximum concentration of dioxane in any reaction mixture was never over 1%.

From time to time, aliquots of the reaction mixture were withdrawn and the absorbances were determined at the wavelength of maximum extinction (420 mμ for N-nitro-N-methylaniline, 400 mμ for *p*-N-dinitro-N-methylaniline, 470 mμ for *p*-methoxy-N-nitro-N-methylaniline). The optical density at infinite time was approximated by allowing the reaction to proceed for 10 half-lives. First-order rate constants were then calculated in the usual way.

The acid concentrations in the studies involving acidity functions and solvent isotope effects were checked by direct titration of an aliquot of the reaction mixture.

A somewhat different kinetic procedure was necessary in the acetic acid–acetate buffer investigations because of the high temperature. The reactants were mixed as before, but at room temperature. Aliquots of the reaction mixture were then sealed in tubes and plunged into a high-temperature bath. Quenching was accomplished by withdrawing tubes and cooling them rapidly to room temperature.

Registry No.—*p*-Methoxy-N-nitro-N-methylaniline, 22809-78-5; N-nitro-N-methylaniline, 7119-93-9; *p*-N-dinitro-N-methylaniline, 16698-03-6.

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