

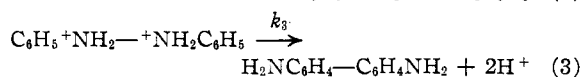
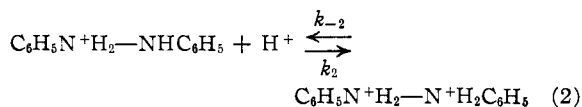
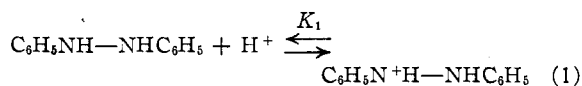
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Mechanism of the Benzidine Rearrangement. II. General Acid Catalysts¹⁻³BY MENDEL D. COHEN⁴ AND GEORGE S. HAMMOND

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The rate of the acid-catalyzed benzidine rearrangement varies with the concentration and nature of undissociated acid present, at constant *pH* meter reading and constant ionic strength. The rearrangement is, thus, subject to general acid catalysis. The transition state must, therefore, consist of an hydrazobenzene molecule, two protons and an anion. The slow step is probably the second proton transfer. This conclusion is supported by the properties of the compound believed to be hydrazobenzene dihydriodide.

In the previous paper³ it was shown that at constant ionic strength the rate of the mineral acid catalyzed benzidine rearrangement varies with the square of the hydrogen ion concentration. It was suggested that a possible reaction path is



Although proton transfer between nitrogen and hydroxylic solvents is usually very rapid, it is conceivable that step (2) is slow because of the initial positive charge on the monoconjugate acid of hydrazobenzene.

It has been known for many years that the rearrangement is catalyzed by acids which are only partially dissociated in solution. It has not been established, previously, whether undissociated acid can serve as catalyst. If such acid can catalyze the rearrangement, and if step (2) is the slow one, the pseudo-unimolecular rate constant would be of the form

$$k = k_{\text{H}^+} [\text{H}^+]^2 + K_1 [\text{H}^+] \sum_i k'_i [\text{HA}_i] \quad (4a)$$

where the HA_i 's are the various undissociated acid species. At constant hydrogen ion concentration this equation reduces to

$$k = c + \sum_i k_i [\text{HA}_i] \quad (4b)$$

where c is a constant. Thus, if the second step involves a slow proton transfer from HA_i to the monoconjugate acid of hydrazobenzene, the rate would be dependent on the nature and concentration of HA_i .

The experimental method employed in testing for general acid catalysis consisted of a determination of the effects of the nature and concentration of undissociated acid on the rearrangement rate, under conditions of constant ionic strength and

constant *pH* meter reading. An alternative method for determining the slow step would be to isolate the various steps and to compare their rates with that of the over-all rearrangement. Pongratz⁵ and co-workers have reported the preparation of hydrazobenzene dihydriodide and showed that solution of the compound led to the formation of benzidine. Thus, it seems possible, if k_{-2} is not too large, to isolate step (3).

Carlin, Nelb and Odioso⁶ have confirmed the second-order hydrogen ion dependence of rearrangement catalyzed by mineral acid. In addition they isolated a compound which they believe to be the dihydrochloride of hydrazobenzene and which, they suggested, is so unstable that it rearranges in the solid state. Hughes and Ingold^{7,8} have misinterpreted the results of Hammond and Shine, and state that step (3) is rate-determining. They argue, very nicely, that the uncertainty involved in electron position during the actual rearrangement is so large as to cause an appreciable stabilization of the transition state. Although such stabilization of the transition state for step (3) undoubtedly occurs, Hammond and Shine did not show that this transition state is the highest energy configuration for the over-all rearrangement, which involves steps (1), (2) and (3).

Experimental Methods and Results

Reagents.—Bindschelder's green was prepared by a modification of the method of Wieland.⁹ It was found that if the product is washed repeatedly with anhydrous alcohol and then with ether, vacuum dried and stored in a desiccator, it is stable indefinitely as a solid and decomposes only very slowly in aqueous solution. Two hundred and fifty ml. of an approximately 0.01 *M* aqueous solution was prepared prior to each run.

Titanous chloride (*ca.* 0.01 *M*) was used as stock solution. A nitrogen atmosphere was maintained in the stock bottle and in the attached automatic buret.

Hydrazobenzene was prepared according to Hickinbottom.¹⁰ It was recrystallized from petroleum ether (fraction boiling 65–100°) immediately before use; m.p. 129.0–129.5° (uncor.).

Lithium perchlorate (anhydrous) was prepared by the method described by Roberts and Watanabe.¹¹

Styphnic acid was prepared by the method of Hickinbottom.¹⁰ Other acids were used as supplied by the manufacturer.

(5) A. Pongratz, S. Böhmert-Süss and K. Scholtis, *Ber.*, **77**, 651 (1944).

(6) R. B. Carlin, R. G. Nelb and R. C. Odioso, *THIS JOURNAL*, **73**, 1002 (1951).

(7) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 1638 (1950).

(8) E. D. Hughes and C. K. Ingold, *Quart. Revs. (London)*, **6**, 34 (1952).

(9) H. Wieland, *Ber.*, **48**, 1087 (1915).

(10) W. J. Hickinbottom, "Reactions of Organic Compounds," Longmans Green and Co., London, 1948, p. 119.

(11) J. D. Roberts and W. Watanabe, *THIS JOURNAL*, **72**, 4869 (1950).

(1) Abstracted from a thesis submitted by Mendel D. Cohen in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate College, Iowa State College, 1952.

(2) Presented, in part, before the Division of Organic Chemistry at the Milwaukee Meeting of the American Chemical Society, April 1, 1952.

(3) Paper I, G. S. Hammond and H. Shine, *THIS JOURNAL*, **72**, 220 (1950).

(4) U. S. Public Health Predoctoral Fellow, 1950–1952.

turers. Sodium salicylate, phosphate and formate were obtained commercially. Other salts were prepared by the action of sodium ethoxide on the corresponding acids.

The action of methyl iodide on hydrazobenzene⁸ at room temperature and under a nitrogen atmosphere was utilized in an attempted preparation of hydrazobenzene dihydroiodide. A yellow solid was separated and unchanged hydrazobenzene extracted with ether. It was not possible to establish unequivocally the nature of the product. It decomposes, on heating, over a five-degree range, 170–175° (uncor.), whereas Pongratz's product decomposed at 210°. No suitable solvent was found for recrystallization, hydroxylic solvents being avoided for fear of inducing rearrangement. The product is soluble in water and in ethanol, but is insoluble in acetone. Potentiometric titration with silver nitrate¹² gave an iodide content of 53.9%, as compared with the calculated value of 57.8%. By titration with base in aqueous solution, the equivalent weight as an acid was found to be 254, while the calculated equivalent weight is 220. Only one end-point was observed in this titration. This suggests that, if the compound is the salt of a dibasic acid, either the second end-point is not observable in water or the two pK values are of similar magnitudes. This is certainly not the case for the diacid from hydrazobenzene. However, the two amino groups in benzidine are of similar basicity, the basic pK 's being 9.03 and 10.25. It would seem, then, that at least at the end of the titration the main species in solution is benzidine. Further, an approximately 0.002 M solution of the compound in water has a pH of 4.90. If the acid present in solution is the diconjugate acid of hydrazobenzene, which must be a strong acid, the pH would be expected to be much lower.

An attempt was made to titrate the compound, dissolved in ethanol, with aqueous Bindschedler's green. The initial rate of decolorization was rapid, but this rate soon decreased markedly. After only one-quarter of the theoretical amount of the dye had been added, no fading was observed in a period of one hour.

The spectra of this compound and of some structurally related compounds were obtained, using mulls in Nujol or hexachlorobutadiene, with a Baird Infrared Recording Spectrophotometer.¹³ The long wave length portion of the spectrum of the compound shows strong similarities with that of hydrazobenzene. Since the C–H frequencies in this range are very sensitive to the number and position of substituents on the benzene rings, this is evidence that the aromatic rings in these two compounds are similarly substituted.¹⁴ A weak absorption peak at 3.9 μ suggests a quaternary nitrogen. Beyond this there is no clear evidence for the diconjugate acid structure since the spectral characteristics of the bond between two positively charged nitrogen atoms are not known. The absence of an absorption maximum in the region of 7.0–7.5 μ , when a hexachlorobutadiene mull is used, indicates the absence of terminal methyl groups. Thus there is nothing to indicate contamination of the dihydroiodide by the corresponding tetramethyl iodide.

The product was examined under a polarizing microscope.¹⁵ With all mounting media evidence was found for non-uniformity in the sample. However, crystals of one type form the bulk of the material and these crystals were found to be internally homogeneous. Their measured properties are: habit, prismatic; extinction, parallel; elongation, negative; refractive indices, 1.75 \pm 0.01, 1.65 \pm 0.01. The crystal-line system is probably tetragonal. When the compound was mounted in methylene iodide a change of crystal type with time was observed.

Benzidine dihydroiodide was prepared by the following procedure. Technical grade benzidine (Matheson Co.) was recrystallized three times from water, twice with decolorizing carbon. The resultant benzidine, which melted at 124.7–125.0° (uncor.), was dissolved in ether into which was then passed hydrogen iodide vapor. A flocculent, light yellow precipitate formed immediately. This was separated by filtration and dried. The salt does not melt

or decompose below 300°. It was found to be opaque in any amount under the microscope, and to disintegrate to a granular powder.

Kinetic Procedure and Analytical Technique.—The analytical method was essentially that of Dewar.¹⁶ All rates were measured for rearrangement at 55.1 \pm 0.06°. The reaction vessel consisted of a 250-ml. standard-taper flask with an indentation, below the neck, into which the hydrazobenzene was placed. The acid solution was placed in the flask, the air flushed out with nitrogen and the glass stopper inserted. The vessel was immersed in the thermostat for an hour before the run was begun by solution of the hydrazobenzene by vigorous shaking. About one minute was required for complete solution. The reaction vessel was equipped with an outlet tube which was kept closed by a small rubber stopper. Aliquots were removed through this stopper by use of a graduated hypodermic syringe.

For each rate determination a plot was made of the logarithm of the volume of titanous chloride (equivalent to the hydrazobenzene in the aliquot) against time after solution. The best straight line through the points was calculated by the method of least squares. The pseudo-first order rate constant was calculated from the slope of this line. Between six and ten points were obtained in each run.

Since disproportionation of hydrazobenzene into azobenzene and aniline occurs under certain conditions, several blank runs were made. A solution of hydrazobenzene in ethanol-water, with added salt but in the absence of acid, was placed in the thermostat. After an hour, aliquots were withdrawn at intervals and treated as in the usual rate determinations. No change in the concentration of hydrazobenzene was observed over a further one-hour period.

Concentrations of acid catalysts were determined by potentiometric titration with standard sodium hydroxide solution. Salt purities, when required, were determined by potentiometric titration with perchloric acid in glacial acetic acid.¹⁷

Variation of Reaction Rate with Change of Acid Catalyst.

—The first test for general acid catalysis consisted of an investigation of whether or not the rate depends on the nature of the acid present, under conditions of constant ionic strength and constant pH meter reading.

Solutions of acid catalyst, sodium ethoxide and lithium perchlorate, all in the same solvent, were prepared. The latter two solutions were of the same concentration. The acid was partially neutralized by addition of the sodium ethoxide. Lithium perchlorate solution was then added and the apparent pH measured with a Beckmann model G pH meter. The same initial volume of acid was taken for all runs. The total volume of sodium ethoxide and lithium perchlorate solutions was kept the same throughout, thus maintaining constant ionic strength. A series of runs was made with each acid, the catalysts differing from run to run in a series in that different amounts of sodium ethoxide were added. Thus the pH meter reading is a measure of the degree of neutralization of the acid and each run in a series corresponds to a different hydrogen ion concentration.

The catalytic acids used in this study were phosphoric, chloroacetic, styphnic and formic acids. The runs with styphnic acid gave non-linear plots, possibly due to complexation with the hydrazobenzene, so rate constants were not obtained. The solvent used was 66%, by weight, aqueous ethanol and the total salt concentration was maintained at 0.013 molar.

In the investigation of catalysis by chloroacetic acid some difficulty was caused by the slow conversion of the acid, in stock solution, into glycolic acid and hydrogen chloride. For this reason the acid solution was utilized as soon after preparation as possible. The pH of an aliquot of this freshly prepared solution was found to remain constant when the aliquot was held at 55° for an hour, and the resultant solution gave no turbidity with silver nitrate.

During the runs with phosphoric acid a brown solid separated out. This solid was identified as benzidine phosphate. For this reason duplicate runs were made, with and without addition of solid benzidine phosphate. No appreciable difference in rate was found.

The results of this study are represented graphically in Fig. 1. The conditions are summarized in Table I. It is

(12) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1946, p. 507.

(13) Thanks are extended to Mr. R. M. Hedges for these studies.

(14) See, for example, N. B. Colthup, *J. Optical Soc. Am.*, **40**, 397 (1950).

(15) Thanks are extended to Mr. S. Flikkema for this work.

(16) M. J. S. Dewar, *J. Chem. Soc.*, 777 (1946).

(17) J. S. Fritz, *Anal. Chem.*, **22**, 1028 (1950).

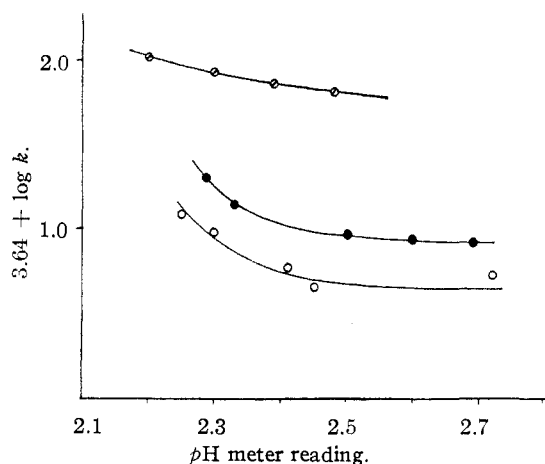


Fig. 1.—Logarithm of rate as a function of pH: phosphoric \ominus ; chloroacetic \bullet ; formic \circ .

seen that, at any one pH meter reading, there is a large variation in rate from acid to acid.

TABLE I
CONDITIONS AND PROBABLE ERRORS OF THE RATE DETERMINATIONS

Acid	Concentration ^a (molar)	Probable error ^b (max.), %	Probable error ^b (av.), %
Chloroacetic	1.12	7.8	2.7
Formic	1.61	3.9	2.6
Phosphoric ^c	0.57	4.0	0.7

^a Concentration of acid before neutralization. ^b The probable error was calculated for each run and expressed as a percentage of the rate constant. ^c In calculation of the amount of lithium perchlorate to be added it was assumed that, at the low degrees of neutralization involved, only univalent ions were present.

Variation of Rate with Concentration of Undissociated Acid.—The second test consisted of a study of whether or not Hammett's¹⁸ criterion for general acid catalysis applies to the rearrangement. The solutions were buffered by use of an acid and its sodium salt. The ratio of acid to salt was constant throughout a series, but the absolute amount of acid varied from run to run. Constant ionic strength was maintained by adding the calculated amount of potassium chloride. The effectiveness of the buffer action was checked by measuring the pH of each solution before use. A variation in rate from run to run in a series, under these conditions, indicates a dependence on the concentration of undissociated acid.

The acids used in this section of the work were formic, glycolic, chloroacetic, salicylic and cyanoacetic. The available concentration ranges were limited by the requirement of maintaining a constant pH. The solvent used throughout was 50%, by weight, aqueous ethanol and all runs were made at a pH meter reading of 2.33 ± 0.06 . The rate corresponding to zero concentration of undissociated acid, and, therefore, due to catalysis by hydrogen ion alone, was obtained from runs employing hydrochloric acid-potassium chloride solutions of the same apparent pH and ionic strength. The total salt concentration was 0.05 molar throughout. The results are represented graphically in Fig. 2, which shows that the rate is dependent on both the concentration and the nature of the catalytic acid.

The catalytic effect of each acid can be represented, approximately, by a linear increase of rate with concentration of acid, with a positive deviation at high concentrations. The slopes of the linear portions have been taken as a measure of the catalytic constants of the various acids. Thus, for a point on the linear section of the curve of rate against acid concentration, the specific rate constant k at the given hydrogen ion concentration is given by

(18) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 221.

$$k \text{ (min.}^{-1}\text{)} = 0.0014 + k_1[\text{HA}] \quad (5)$$

where the k_1 's are the catalytic constants. These constants are listed in Table II. Comparison of equations (4a) and (5) shows that the k_1 's include a constant factor $K_1[\text{H}^+]$.

TABLE II

Acid	Catalytic constant ^a
Formic	0.0027 ± 0.0003
Glycolic	$.0081 \pm .0005$
Chloroacetic	$.0133 \pm .0010$
Salicylic	$.0162 \pm .0010$
Cyanoacetic	$.0368 \pm .0064$

^a Concentrations are expressed as molarities, and rates in min.^{-1} .

Attempted Application of the Brønsted Relation.—Many reactions which are subject to general acid catalysis have been found to satisfy the Brønsted relation¹⁹

$$\log k_1 = G + x(pK_1) \quad (6)$$

where application is confined to a single reaction of one substrate, and the various acids HA_1 are all of the same charge type.

A plot was made of the logarithms of the catalytic constants, listed in Table II, against the pK values of the acids in water at 25°. A similar plot was made using the pK 's of the acids in 50% aqueous ethanol, approximate values of which are reported in the literature.^{20,21} In neither case was a linear relation found.

Attempted Isolation of the Rearrangement Step.—Since the diconjugate acid of hydrazobenzene might be the species which actually rearranges, an attempt was made to prepare that acid and to compare its rate of rearrangement with that of the over-all reaction. That the diconjugate acid is, indeed, the product of the reaction of methyl iodide and hydrazobenzene at room temperature has not been established. All the measured properties suggest, however, that at least part of the product is the dihydriodide, which rearranges rapidly on the addition of a trace of water.

Discussion

The experimental conditions were so chosen that the rate of rearrangement due to hydrogen ion catalysis would be relatively small. In addition, the use of buffers should maintain a constant rate. However, because of the nature of the medium used, the meaning of constant pH meter reading is not unambiguous. Dole²² has suggested that the error exhibited by a glass electrode is constant when the activity of the water in the solution is a constant. This would be, approximately, the case for the solutions used in this study. Further, the large variation in rate found with strong acids, such as cyanoacetic, where small concentrations were employed, indicates that the variation is not due to changes in hydrogen ion activity. Thus the factors causing the change in rate must be the nature and concentration of undissociated acid.

Because of the nature of the analytical technique, the rates measured were those of disappearance of hydrazobenzene and, probably, of its first conjugate acid. The results are, nevertheless, interpretable in terms of the rates of formation of both benzidine and diphenylene, since Carlin⁶ has shown that the rates of formation of both these com-

(19) J. N. Brønsted and K. Pedersen, *Z. physik. Chem.*, **108**, 185 (1924).

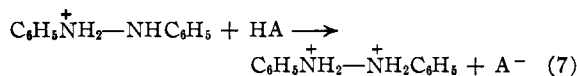
(20) L. J. Minnick and M. Kilpatrick, *J. Phys. Chem.*, **43**, 259 (1939).

(21) H. S. Harned and R. S. Done, *THIS JOURNAL*, **63**, 2579 (1941), and other references cited therein.

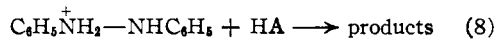
(22) M. Dole, *ibid.*, **54**, 3095 (1932).

pounds have the same hydrogen ion dependence and the same activation energies.

Considering, for the moment, the range in which the rate is proportional to the acid concentration, the kinetics can be explained in terms of a rapid equilibration, as in (1), followed by the slow step

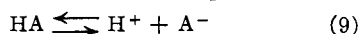


and then fast rearrangement (3). This cannot be kinetically differentiated from a sequence involving the concerted process



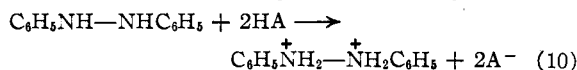
Such a concerted process is considered with disfavor, however. All the work with salts of the diconjugate acid of hydrazobenzene suggests that that acid rearranges rapidly. It might be suggested that the diacid re-equilibrates with the monoacid, which then rearranges in a concerted process. Such a sequence would not, however, be more rapid than the over-all process (1) and (8). Further, if the process is concerted then the energies of activation would, in all probability, be different for the formation of benzidine and diphenylene. It is therefore suggested that the diconjugate acid is a true intermediate, and that the configuration of highest potential energy is passed through prior to the formation of that acid.

Because of the existence of the equilibrium

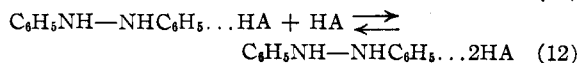
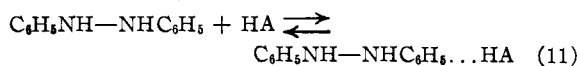


one cannot distinguish between the participation of HA and of H⁺ and A⁻ in the rate-determining step. Thus, this step could be either the transfer of a proton from HA, or the transfer of a solvated proton with simultaneous participation of A⁻ at some other point in the complex.

The positive deviations from linearity observed with all acids (Fig. 2) may be due to true or apparent changes in the stoichiometry of the reaction. Thus the deviations might be caused by a slow step



which becomes of importance at high acid concentrations. The same kinetic results would be obtained for a sequence such as



where the dotted lines indicate some form of complexation. Neither of these reaction paths is considered probable. It is suggested, therefore, that no true change in stoichiometry is involved and that the deviations are due to an alteration in some property of the solvent, such as its dielectric constant. It is of interest to note that plots of rate against the square of the acid concentration approach linearity only in one case, that of glycolic acid. Approximate catalytic constants, calculated from these plots, do not obey the Brønsted relation.

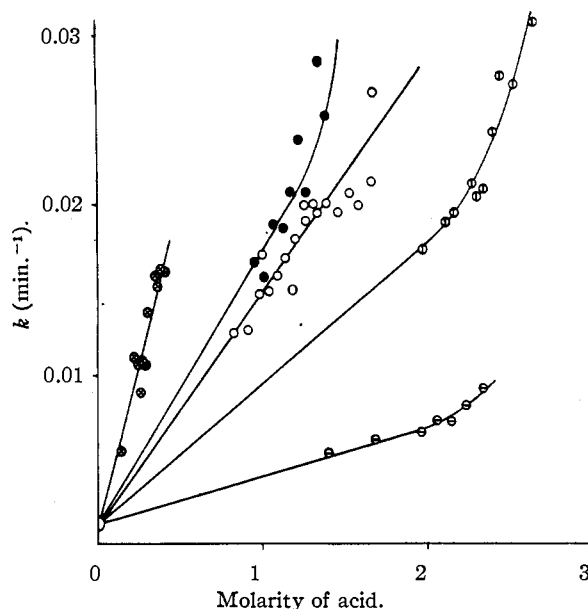


Fig. 2.—Rate as a function of molarity of acid at constant *pH*: cyanoacetic ⊙; salicylic ●; chloroacetic ○; glycolic ⊙; formic ⊖.

Not enough acids were utilized in this study to enable an analysis of the deviations from linearity when application of the Brønsted relation is attempted. It is noted, however, that the failure to find this relation satisfied is not surprising. The measurement of *pK*'s of acids utilizes the transfer of a proton from the acid to neutral solvent. In the benzidine rearrangement, on the other hand, the rate-determining proton transfer takes place to a positively charged molecule. One might expect, then, to find a correlation of the rates with the H⁺ values²³ of the solutions.

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(23) L. P. Hammett, *Chem. Revs.*, **16**, 67 (1935).