1-methyl-1-(4-methyl-2-quinolyl) hydrazine picrate, 35356-64-0; 3-amino-1,9-dimethyl-s-triazolo[4,3-a]-quinolinium bromide, 35356-65-1; compound of mp 203–204°, 35427-27-1.

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The Mechanism of the Benzidine Rearrangement. II.[1,2] The Rearrangement of N-Acetylhydrazobenzene

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In concentrated perchloric acid–sodium perchlorate solutions, N-acetylhydrazobenzene undergoes an intramolecular rearrangement to N-acetylbenzidine. The rate of rearrangement has a first-order dependency on the Hammett acidity, H_0, and is subject to a small solvent isotope effect, $k_{H_2O}/k_{D_2O} = 1.27$. A small but reproducible substrate isotope effect is observed on the rate of rearrangement of the ring perdeuterated material, $k_H/k_D = 1.07$. On the basis of these observations it is concluded that the rearrangement is clearly a manifestation of the benzidine rearrangement, that the mechanism of rearrangement involves a single proton transfer in an equilibrium established prior to the rate-limiting process, and that both the solvent deuterium isotope effect and the substrate deuterium isotope are secondary isotope effects. Arguments are given in favor of a pathway involving a rate-limiting heterolysis of the nitrogen–nitrogen σ bond following the preequilibrium proton transfer. The electron-withdrawing, inductive effect of the N-acetyl substituent is envisaged to usurp the catalytic role of the second proton in the acid-catalyzed rearrangement of hydrazobenzene. The driving force for bond heterolysis and rearrangement is a cumulation of the repulsion between the N-acetyl group and the protonated N′-amino nitrogen, and incipient bonding of a π-complex type. The reaction of N-acetylhydrazobenzene to give benzidine (and presumably diphenyline) in dilute acid solutions probably proceeds *via* slow hydrolysis to hydrazobenzene, followed by rapid rearrangement to the observed product(s).

The research described in this series on the mechanism of the benzidine rearrangement was incepted with the intention of investigating the nature of the transient bonding forces responsible for imparting *intra*molecularity to the transformation. Accordingly, structural analogs of hydrazobenzene have been prepared and investigated with the expectation that the mode of rearrangement of these compounds will provide evidence which will aid in defining the energetics of the rate-limiting and the product-forming stages of the reactions.

The first paper in this series[1] reports evidence for the formation of N-acetyl-O,N-diphenylhydroxylamine as a transient intermediate in the reaction of N-acetyl-N-phenylhydroxylamine with diphenyliodonium hydroxide. The N-acetyl-O,N-diphenylhydroxylamine thus produced was found to undergo a spontaneous, intramolecular rearrangement to 4′-hydroxy-4-acetamidobiphenyl and traces of 2′-hydroxy-4-acetamidobiphenyl. The spontaneity of this benzidine-like rearrangement in the absence of acid catalysis was rationalized as resulting from the combination of the electron-withdrawing effect of the N-acetyl substituent with the greater electronegativity of the O-phenyl oxygen as compared to nitrogen, which together simulate the electronic characteristics of the diprotonated hydrazobenzene cation.

In this paper there is described a mechanistic study of the acid-catalyzed rearrangement of N-acetylhydrazobenzene which was carried out with the intention of examining the possibility that the N-acetyl function can act as an internal general acid catalyst in such processes generally.

Experimental Section

Melting and boiling points are uncorrected. Pmr spectra were recorded with a Varian A-60 spectrometer and ir spectra with a Perkin-Elmer 21 spectrometer.

Instrumentation.—All kinetic measurements were performed with a Zeiss PMQ-II spectrophotometer equipped with a thermostated cell compartment and cell holder. The mass spectrometer analyses were carried out on an Atlas CH-4 mass spectrometer, by recording the cracking pattern and the detail in the molecular weight region at low ionization potentials.

Materials.—The concentrated perchloric acid (70–72%) and sodium perchlorate (analytical grade) used were the commercially available materials, as were deuterium oxide, sulfuric acid-d_2 (99.6 atom % D), and benzene-d_6 (99.5 atom % D). Perchloric acid-d_1 and nitric acid-d_1 were prepared from the corresponding anhydrous sodium salts according to the procedures described for the isotopically normal materials.[4]

N-Acetylhydrazobenzene was prepared after the method of Goldschmidt and Euler. The crude product was recrystallized from chloroform, mp 162–163° (reported[5] mp 159°).

2,3,4,5,6,2′,3′,4′,5′,6′-Decadeuterio-N-acetylhydrazobenzene was prepared by the nitration of benzene-d_6 with nitric acid-d_1 and sulfuric acid-d_2 followed by reduction of the resulting nitrobenzene-d_5 (99.5 atom % deuterium content by nmr) with zinc dust in alcoholic sodium hydroxide and acylation with acetic anhydride.[5] Each step was carried out according to the usual procedures employed for the isotopically normal materials. The resulting ring perdeuterio-N-acetylhydrazobenzene, mp 162–163°, gave pmr and ir spectra which indicated a high degree of ring deuterium content.

The Acid-Catalyzed Reaction of N-Acetylhydrazobenzene in Ethanol–Water Solution.—N-Acetylhydrazobenzene, 1.00 g (4.43 mmol), dissolved in 75 ml of ethanol and 10 ml of concentrated hydrochloric acid, gave, after standing at room temperature for 24 hr, a white, crystalline precipitate. This material was collected by vacuum filtration, redissolved in water, and neu-

(1) This work was done in partial fulfillment of the requirements for the Ph.D. degree by Michael F. Dunn. First paper in this series: J. R. Cox, Jr., and M. F. Dunn, *Tetrahedron Lett.*, 985 (1963).

(2) The authors gratefully acknowledge the support of this work by the National Science Foundation under Grant GP-1576.

(3) To whom inquiries should be addressed at the University of Houston.

(4) G. Brauer, Ed., "Handbook of Preparative Inorganic Chemistry," 2nd ed, Academic Press, New York, N. Y., 1963, pp 318, 491.

(5) S. Goldschmidt and K. Euler, *Chem. Ber.*, **55**, 616 (1922).

tralized to *ca.* pH 8 by the addition of dilute sodium hydroxide. The soft, white solid which separated was extracted into ether. Evaporation of the extract yielded 0.55 g (62% of theory) of a glistening, almost white solid, mp 123–124°, which exhibited an infrared spectrum superimposable upon that of authentic benzidine. Kinetic studies on the rate of hydrolysis of *N*-acetylbenzidine indicate that only a small amount of the benzidine produced could have resulted from the hydrolysis of *N*-acetylbenzidine.

The Rearrangement of *N*-Acetylhydrazobenzene in Concentrated Mineral Acid.—Treatment of *N*-acetylhydrazobenzene, 1.00 g (4.43 mmol), with 10 ml of 60% perchloric acid yielded immediately a dark, greenish-brown solution. Dissolution was accompanied by the evolution of considerable heat. This solution was cooled in ice and neutralized by the careful addition of sodium hydroxide. The tan solid which separated was recrystallized from hot ethanol, yielding an almost white, crystalline material, mp 202–203° dec, shown to be identical with authentic *N*-acetylbenzidine (reported[6] mp 199° dec) by mixture decomposition point, which was undepressed, and by comparison of ir spectra, which were superimposable: yield 0.83 g (83% of theory). Ether extraction of the aqueous filtrate followed by evaporation gave approximately 0.1 g of an oily, brown residue which was not identified.

The Mixed Rearrangement of Perdeuterio- and Isotopically Normal *N*-Acetylhydrazobenzene.—*N*-Acetylhydrazobenzene, 0.1000 g (0.443 mmol), and perdeuterio-*N*-acetylhydrazobenzene, 0.1394 g (0.591 mmol), were ground to fine powders and thoroughly mixed. The mixture was added to a 50-ml flask containing 25 ml of 6.01 formal (*F*) perchloric acid. Solution was brought about by placing the mixture on the surface of the ground glass joint of the flask and mulling with perchloric acid by grinding a stopper in the joint. The resulting mull was then washed into the flask with more acid. This method for effecting solution was employed to avoid the marked tendency of the material to form cakes which do not dissolve readily in the acid medium. Addition was completed in 15 min. The resulting mixture was stirred for 80 min, during which time a precipitate of insoluble *N*-acetylbenzidinium perchlorate formed. The collected precipitate was dispersed in 25 ml of distilled water and neutralized with anhydrous sodium carbonate. The resulting precipitate of *N*-acetylbenzidine was recovered after vacuum drying in a yield of 0.1840 g (77% of theory). This material was recrystallized from methanol and sublimed, 160–170° (0.05 mm), yielding white crystals (as star clusters), mp 205.4–206.4°. The analysis of the mass spectrum of this mixture is given in Table II.

Ring perdeuterio-*N*-acetylhydrazobenzene, by itself, was rearranged under the same conditions. On work-up, the crude rearranged material was obtained in a yield of 91.5% of theory. Analysis of the mass spectrum of this material indicated at least 98.8% ring deuterium content; see Table II.

Kinetic Studies.—The conversion of *N*-acetylhydrazobenzene to benzidine in 30% methanol–water was studied in solutions of perchloric acid maintained at a constant ionic strength of 1.08 with added sodium perchlorate. Rate measurements were made by following the change in optical density at 235 mμ (the absorption maximum for *N*-acetylhydrazobenzene) and at 280 mμ (the absorption maximum for benzidine) of neutralized aliquots withdrawn at various time intervals from a solution thermostated at 30 ± 0.1 or 60.0 ± 0.1°, depending on the particular experiment. Rearrangement of hydrazobenzene under the same conditions gave a product mixture having a uv spectrum identical with that of the product mixture obtained from *N*-acetylhydrazobenzene by the procedure described above.

Rate studies of the rearrangement of *N*-acetylhydrazobenzene to *N*-acetylbenzidine were carried out in concentrated perchloric acid–sodium perchlorate solutions 6.0 in total ionic strength. Stock solutions were prepared by the dilution of the appropriate amounts of sodium perchlorate and standardized concentrated perchloric acid to the desired concentrations, according to Harbottle.[7] Individual kinetic runs were then performed by adding an appropriate amount of *N*-acetylhydrazobenzene to a 5-ml aliquot of the stock solution. Solution was effected by vigorously shaking for about 20 sec. The quartz cuvette then was filled from a capillary eye dropper to avoid including any undissolved particles. Changes in optical density corresponding to the appearance of *N*-acetylbenzidinium ion (λ_{max} 268 mμ, ϵ_{max} 1.84 × 10^4) were measured as a function of time. The absorbance of the solution at 236.6 mμ was found to be invariant during the course of a kinetic run. No spectrophotometric evidence could be found for the formation of products other than *N*-acetylbenzidine during the period of time required for completion of a kinetic run. However, prolonged observations at 268 mμ indicate that the product undergoes a slow hydrolysis.

Results

Under preparative conditions (see Experimental Section), benzidine was isolated in 62% of theory from *N*-acetylhydrazobenzene in ethanol–dilute hydrochloric acid. In methanol–water solutions of dilute perchloric acid (Table I) *N*-acetylhydrazobenzene affords a product mixture with uv spectrum identical with that obtained from the rearrangement of hydrazobenzene under the same conditions. Thus, benzidine (and presumably diphenyline) are the products of the reaction of *N*-acetylhydrazobenzene under conditions of dilute aqueous (or alcoholic) hydrochloric or perchloric acid catalysis, in good agreement with the findings of Vecera, *et al.*[8]

TABLE I

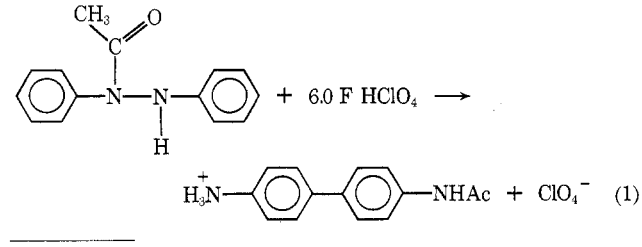
THE ACID-CATALYZED REACTION OF *N*-ACETYLHYDRAZOBENZENE TO BENZIDINE IN 30% METHANOL–WATER SOLUTIONS

Temp,[a] °C	[H⁺] $HClO_4$	$NaClO_4$	k_h,[b] hr^{-1}	$t_h^{1/2}$, hr	k_h/[H⁺]	k_b,[b] hr^{-1}	$t_b^{1/2}$, hr	k_b/[H⁺]
30.0	1.080	0.000	0.040	17	0.035	0.038	18	0.035
30.0	0.753	0.227	0.025	28	0.033	0.025	28	0.033
30.0	0.540	0.520	0.020	35	0.037	0.019	37	0.035
30.0	0.374	0.706	0.015	46	0.040	0.016	42	0.044
60.0	1.080	0.000	0.59	1.2	0.54	0.58	1.2	0.53

[a] The temperature was controlled within ±0.1°. [b] The rate constant k_h is the apparent rate of disappearance of *N*-acetylhydrazobenzene and k_b is the apparent rate of formation of benzidine.

The spectrophotometric kinetic studies summarized in Table I demonstrate that the rate of disappearance of *N*-acetylhydrazobenzene and the rate of appearance of benzidine are experimentally identical. The reaction is found to follow second-order kinetics (first order with respect to stoichiometric acidity and first order with respect to *N*-acetylhydrazobenzene). Comparison of the relative rates of this process at 30.0 and 60.0° allows estimation of the apparent energy of activation, 18 kcal mol^{-1}.

In contrast, the reaction of *N*-acetylhydrazobenzene under conditions of concentrated mineral acid catalysis gives the product *N*-acetylbenzidine in nearly quantitative yield (see Experimental Section) according to eq 1. This finding is in good agreement with the observations of Pongratz and Scholtis on the composition of the re-



(1)

(6) H. Schmidt and G. Schultz, *Chem. Ber.*, **12**, 489 (1879).
(7) G. Harbottle, *J. Amer. Chem. Soc.*, **73**, 4024 (1951).
(8) M. Vecera, J. Petranek, and J. Gasparic, *Collect. Czech. Chem. Commun.*, **22**, 1063 (1957).

TABLE II

THE MASS SPECTRA OF THE PRODUCTS FROM THE REARRANGEMENTS OF 2,3,4,5,6,2′,3′,4′,5′,6′-DECADEUTERIO-*N*-ACETYLHYDRAZOBENZENE AND *N*-ACETYLHYDRAZOBENZENE IN 6.01 *F* $HClO_4$

	Relative peak intensities		
Material	226	230	234
Isotopically normal	248	~2	~2
Authentic perdeuterio	8		675
Rearrangement mixture (42.1% protio and 57.9% perdeuterio)	348	~0.75	498

arrangement products in concentrated hydrochloric acid.[9]

The presumed *intra*molecularity of this process was tested by mass spectrometric analysis of the products resulting from rearrangement of an approximately equimolar mixture of ring perdeuterio- and isotopically normal *N*-acetylhydrazobenzene in 6 *F* perchloric acid. If rearrangement is intramolecular, then the mass spectrum of the products should exhibit only parent peaks corresponding to the isotopically normal and to the octadeuterio materials (*m/e* 226 and 234, respectively). The peak at *m/e* 230 (the mass corresponding to the parent peak of the cross product) is a direct measure of *inter*molecular recombination. Table II summarizes the results of this experiment. *These data clearly demonstrate that no more than 0.2% of the products can be accounted for via an intermolecular pathway.* Exchange of ring-substituted deuterium with solvent hydrogen under the same conditions of rearrangement was found not to be significant. Deuterium-labeled *N*-acetylbenzidine obtained *via* rearrangement of ring perdeuterated *N*-acetylhydrazobenzene in isotopically normal perchloric acid contained at least 98.8% ring-bound deuterium (measured as the *m/e* 234/233 ratio, Table II).

Kinetic investigation of the rearrangement was carried out in the aqueous perchloric acid–sodium perchlorate system of Harbottle.[7] This system, in which the total perchlorate ion concentration is maintained at 6.0 *F*, was chosen for the advantage it provides in the linearity of its Hammett acidity function (H_0) over the range 2–6 *F* perchloric acid. Additional advantages are derived from a low water activity and an acidity range that gives convenient rearrangement rates at easily accessible temperatures.

The kinetics of rearrangement were measured by following directly the uv spectral changes accompanying the appearance of *N*-acetylbenzidinium ion. The results of these measurements are presented in Table III. Apparent first-order kinetics were found over greater than 90% completion of reaction. *A plot of H_0 vs. log k_{app} (Figure 1) gives a linear correlation with a slope near unity (slope 0.833).* The corresponding plot of log $[HClO_4]$ *vs.* log k_{app} gives a nonlinear correlation (Figure 2).

The solvent deuterium isotope effect upon the rate of rearrangement was determined by comparing rates in isotopically normal and deuterium oxide–perchloric acid-d_1 solutions, both 6.01 *F* in perchloric acid. The ratio of rates obtained, $k_{H_2O}/k_{D_2O} = 1.27$, reflects a 20% rate decrease for the deuterated solvent system.

(9) A. Pongratz and K. Scholtis, *Chem. Ber.*, **75**, 138 (1942); see also D. W. Davies and D. L. Hammick, *J. Chem. Soc.*, 475 (1954).

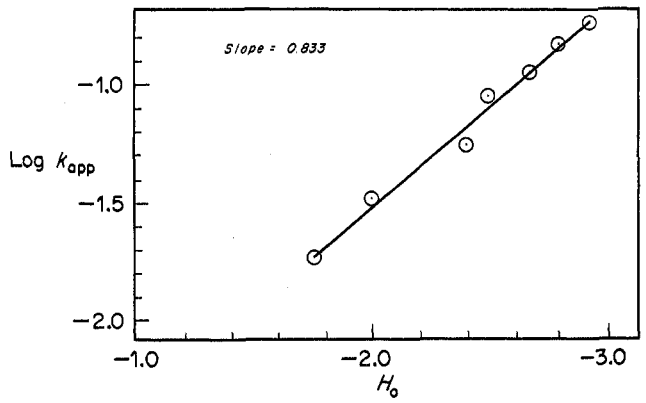


Figure 1.—H_0 *vs.* log k_{app} for the rearrangement of *N*-acetylhydrazobenzene in solutions of perchloric acid–sodium perchlorate 6 *F* in perchlorate ion.

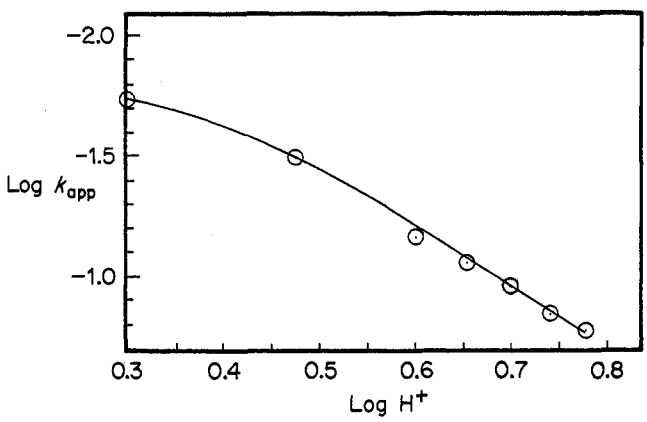


Figure 2.—Log H^+ *vs.* log k_{app} for the rearrangement of *N*-acetylhydrazobenzene in solutions of perchloric acid–sodium perchlorate 6 *F* in perchlorate ion.

TABLE III

THE ACID-CATALYZED REARRANGEMENT OF *N*-ACETYLHYDRAZOBENZENE TO *N*-ACETYLBENZIDINE IN CONCENTRATED PERCHLORIC ACID–SODIUM PERCHLORATE

Temp,[a] °C	$[HClO_4]$, *F*	$[NaClO_4]$, *F*	$-H_0$	h_0[b]	k_{app},[c] min^{-1}	$t_{1/2}$, min	k_{app}/h_0 × 10^4	$k_{app}/[H^+]$ × 10^2
30.0	6.01	0.00	2.92	832	0.175	3.96	2.10	2.92
30.0	5.50	0.50	2.78	605	0.143	4.84	2.36	2.60
30.0	5.00	1.00	2.64	437	0.110	6.30	2.51	2.20
30.0	4.50	1.50	2.49	302	0.0872	7.95	2.89	1.94
30.0	4.00	2.00	2.40	218	0.0548	11.9	2.68	1.46
30.0	3.00	3.00	2.00	108	0.0321	21.6	2.97	1.07
30.0	2.00	4.00	1.76	53	0.0184	37.1	3.47	0.92
20.0	6.01	0.00	2.92	832	0.0467	14.8		
20.0	5.00	1.00	2.64	437	0.0284	24.4		

[a] The temperature was controlled to ±0.1°. [b] These values were obtained from the relationship $H_0 = -\log h_0$. [c] The reproducibility of k_{app} was 0.005 min^{-1}.

This decrease is considerably greater than the experimental error (*ca.* 5%) involved in the rate determinations.

A small but reproducible substrate deuterium isotope effect ($k_H/k_D = 1.07$) on the rate of rearrangement of the ring perdeuterio *N*-acetylhydrazobenzene was observed. To ensure that this decrease in rate did not result from a systematic experimental error, alternate kinetic runs on the isotopically normal and perdeuterio materials were carried out using the same stock solution of acid. Kinetic runs carried out in this way consistently gave a larger rate constant for the isotopically normal material.

Discussion

We define the term "benzidine rearrangement" to mean the intramolecular transformations of hydrazoaromatic compounds and their isoelectronic analogs, including, but not limited to, those processes which occur under protonic and Lewis acid catalysis. The mass spectral studies presented herein unequivocally demonstrate the intramolecularity of the acid-catalyzed rearrangement of *N*-acetylhydrazobenzene, and it is, therefore, a manifestation of the benzidine rearrangement in the sense of our definition.

The finding that the rate of rearrangement has a first-order dependency on the Hammett acidity (H_0) of the concentrated perchloric acid–sodium perchlorate mixtures is good evidence for a mechanism involving *a single proton transfer prior to the rate-determining step.*[10]

A growing number of examples of the benzidine rearrangement exhibit either a first-order dependency on Hammett acidity or an apparent order which varies between one and two with increasing acidity. Examples in which the apparent order in H_0 varies with the acidity are found to behave according to the rate expression $v = k(\text{hydrazo})(H_0) + k'(\text{hydrazo})(H_0)$,[2] the expression derived for a mechanism involving two parallel pathways for rearrangement that differ only in the respective hydrogen ion dependencies.[12] Banthorpe and O'Sullivan, reasoning from the considerable body of evidence that the transition state of the benzidine rearrangement is highly polar, predicted[13] that either electron-releasing or electron-withdrawing substituents in hydrazobenzene might lower the kinetic order in protons of its rearrangement. Most of the examples encountered previously have been substituted with electron-releasing substituents, some being first order in protons[11,14-17] and some, transitional.[18-22] One previous example of transitional kinetics[23] and one of first-order proton dependence[24] in which electron-withdrawing substituents were present have been reported. As Banthorpe and O'Sullivan point out,[13,24] these substituents greatly reduce both the base strength of the hydrazobenzene molecule and the absolute rate of its rearrangement. *N*-Acetylhydrazobenzene provides the first example of confinement to a one-proton process in which the ring is not substituted. The *N*-acetyl substituent also decreases the basicity of the hydrazobenzene as well as the rate of rearrangement.

The absence of the equilibrium protonation isotope effect on the rate of rearrangement in D_2O solutions observed for other examples of the benzidine rearrangement[11] could not have been predicted. However, it has been found experimentally that D_0, the Hammett acidity function of sulfuric acid-d_2, is numerically the same as H_0 for solutions of the same acid concentration.[25] Hence, the deuterium-donating ability of concentrated sulfuric acid-d_2 is numerically the same as the proton-donating ability of isotopically normal sulfuric acid.

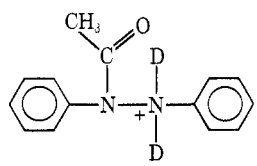
The observation that D_0 and H_0 are equivalent is rationalized in the following way. Equilibrium isotope effects arise from differences in the equilibrium constants, respectively, for protonation and deuteration according to eq 2 and 3, where B is a moderately weak base.

$$H_2SO_4 + B \overset{K_H}{\rightleftharpoons} BH^+ + HSO_4^- \quad (2)$$

$$D_2SO_4 + B \overset{K_D}{\rightleftharpoons} BD^+ + DSO_4^- \quad (3)$$

However, as the base strength of B decreases, the ratio K_H/K_D approaches unity[26] because the difference between the zero point vibrational energies of BH^+ and BD^+ becomes a smaller percentage of the total ground state energy difference (as measured by K_H or K_D) between B and its conjugate acid.

The decreased rate in perchloric acid-d_1 then becomes understandable as a secondary isotope effect if one assumes that (a) the ratio K_D/K_H for the formation of the conjugate acid of *N*-acetylhydrazobenzene is close to unity; (b) the rearranging species in D_2O–perchloric acid-d_1 is the conjugate acid of *N*-acetyl-*N*-deuteriohydrazobenzene (**1**); and (c) the rate-determining step of



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the rearrangement is N–N bond scission. Although no perfect analog of this system has been found by the authors in the literature, α-deuterium substitution at an aliphatic carbon regularly reduces the rate of solvolysis of halides by a degree of magnitude very similar to that measured in this work.[27,28]

Secondary isotope effects which arise from deuterium substitution at a site remote from the reaction center are well known.[29] The small but reproducible substrate isotope effects on the rate of rearrangement of ring perdeuterio-*N*-acetylhydrazobenzene clearly belong to the category of secondary isotope effects. This observation is the first report of a secondary isotope effect on the rate-limiting step of an acid-catalyzed benzidine rearrangement in which the effect arose from ring deuterium substitution. Since all available evidence pinpoints the N–N cleavage as rate limiting, the isotope effect therefore attaches to this process.

Various mechanisms have been suggested for the benzidine rearrangement. Of these, the two leading

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(11) D. V. Banthorpe, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 2386 (1962).
(12) D. A. Blackadder and C. Hinshelwood, *ibid.*, 2898 (1957).
(13) D. V. Banthorpe and M. O'Sullivan, *J. Chem. Soc. B*, 615 (1968).
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(15) W. N. White and E. E. Moore, *J. Amer. Chem. Soc.*, **90**, 526 (1968).
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(17) D. V. Banthorpe, A. Cooper, and C. K. Ingold, *ibid.*, 609 (1968).
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(19) D. V. Banthorpe, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 2418 (1962).
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(21) D. V. Banthorpe, C. K. Ingold, J. Roy, and S. M. Somerville, *ibid.*, 2436 (1962).
(22) D. V. Banthorpe, C. K. Ingold, and J. Roy, *J. Chem. Soc. B*, 64 (1968).
(23) D. V. Banthorpe, C. K. Ingold, and M. O'Sullivan, *ibid.*, 624 (1968).
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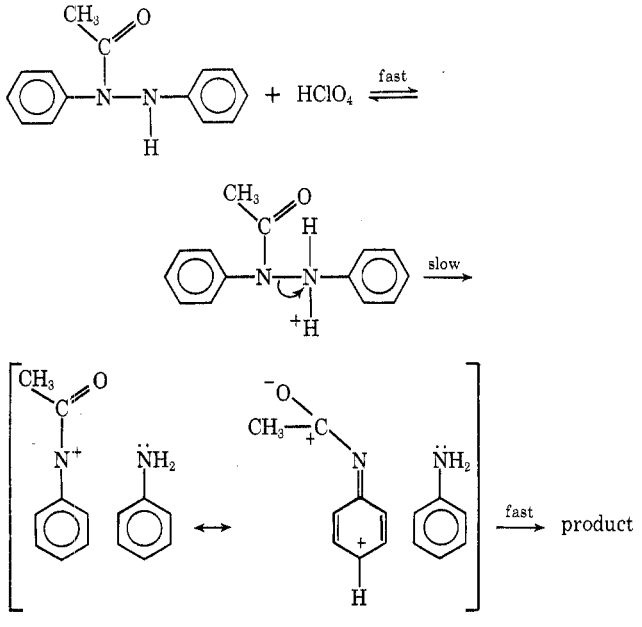
(25) E. Hogfelt and J. Bigeleisen *J. Amer. Chem. Soc.*, **82**, 15 (1960).
(26) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 187.
(27) E. A. Halevi, "Progress in Physical Organic Chemistry," Vol. 1, Interscience, New York, N. Y., 1963, pp 171–173.
(28) V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr, and G. Lamaty, *J. Amer. Chem. Soc.*, **90**, 418 (1968).
(29) Reference 27, pp 200–204.

contenders are the "polar transition state" mechanism[30,31] and the "π-complex intermediate" mechanism.[32] Shine has recently made a critical review of these and other suggestions.[33] Since the experimental evidence does not provide unambiguous criteria for defining all of the mechanistic features, the proposed pathways rely heavily on intuitive arguments which at times take on polemic overtones. These controversies have served to obscure the fundamentally important evidence that the rate-limiting process differs from the product-forming process. The rate-limiting step is strongly influenced by polar factors, suggesting substantial charge separation in the transition state. The structures of the various products formed suggest a geometry for the intermediate in which the rings are roughly parallel and are free to rotate relative to each other about an axis perpendicular to the planes of the rings. This orientation would not be required, in the transition state or in an intermediate, by ionic bonding. Hence, the transition state for the rate-limiting process leads to a metastable intermediate from which products are formed over a separate transition state.

The free energy of activation for the rate-limiting process may be lowered either by raising the free-energy content of the ground state or by lowering the free-energy content of the transition state, or by a combination of both. Proponents of the "polar transition state" theory have characteristically focused on the former,[13,30,31] while proponents of the "π-complex intermediate" have focused on considerations of bonding in the intermediate, since multicenter bonding, with or without a strong charge-transfer component, may readily be envisioned to play the major role in the stabilization of this structure, which is a π complex in Dewar's terminology.[32] The essence of the controversy seems to concern the degree to which bonding similar to that in the proposed intermediate lowers the energy of the transition state leading to the intermediate. That is, how much of the "driving force" for the rate-limiting step of the reaction is due to lowering of the free energy of the transition state by virtue of the stabilization of the presumed, intermediate π complex? Although at present no method has been made available, either experimental or theoretical, by which the intermediate can be characterized—a necessary step in the definition of the energy surface on which it resides—it is still instructive to consider energetic factors which arise from bond breaking.

Protonation of one or both nitrogens of an hydrazobenzene greatly facilitates its rearrangement. In most previous examples of hydrazobenzenes which rearrange at a detectable rate upon monoprotonation, at least one ring has been substituted so as to make it more effective than a phenyl ring in stabilizing a positive charge. Such substitution being absent, diprotonation is required, unless other factors contribute to N–N bond polarization.[13,24]

The observation reported herein that ring protons are not exchanged with solvent during the rearrangement, taken with the demonstrated equilibrium protonation process, clearly defines both protonation sites as the nitrogen atoms and not the unsubstituted carbon atoms of the rings. Relief in the transition state of the coulombic repulsion generated by the protonation clearly contributes significantly to the energetics of the process. Breslow and McNelis[34] observed that the repulsion between the dipole of the carbonyl group and the positively charged nitrogen atom of 2-acetylthiazolinium salts greatly facilitated nucleophilic addition to the carbonyl carbon, resulting in acyl–carbon bond cleavage. We believe that the carbonyl function of N′-protonated *N*-acetylhydrazobenzene similarly facilitates N–N bond cleavage. Since the rate of cleavage of the bond to nitrogen in an N-substituted anilide is sensitive to the ability of the leaving group to stabilize a negative charge,[35] we believe that the bond breaking is heterolytic in nature. We envision the sequence surrounding the rate-limiting step as follows.



The bracketed intermediate should certainly possess considerable stabilization from multicenter bonding, and in it the positive charges have been effectively delocalized. The balance of the repulsive and the bonding forces which operate in the transition state is undefined at present, but we believe both of them to contribute to lowering the free energy of activation. This model accommodates and explains the first-order dependency on H_0, in that the *N*-acetyl substituent usurps the catalytic role of the second proton in the usual benzidine rearrangement. It also is an isoelectronic analog of *N*-acetyl-*O*,*N*-diphenylhydroxylamine, which rearranges with great facility.[1] In highly symmetrical molecules such as hydrazobenzene itself, bonding in the transition state may have less of a charge-transfer component, and therefore less polarity, than in unsymmetrical systems such as ours. Description of the bonding in this series of metastable structures remains a fascinating challenge to the theoretical chemist.

(30) D. V. Banthorpe, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 2864 (1964).

(31) D. V. Banthorpe, *Chem. Rev.*, **70**, 295 (1970).

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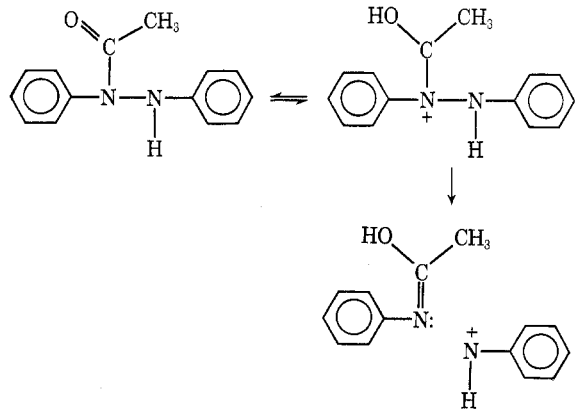
(33) H. J. Shine in "Mechanisms of Molecular Migrations," Vol. 2, B. S. Thyagarajan, Ed., Wiley, New York, N. Y., 1969, p 191.

(34) R. Breslow and E. McNelis, *J. Amer. Chem. Soc.*, **82**, 2394 (1960).

(35) Rearrangement of *O*,*N*-diacyl-*N*-phenylhydroxylamines has been found to have a strong dependency on the leaving group: M. F. Dunn, Ph.D. Thesis, Georgia Institute of Technology, 1966. See also ref 1.

The alternate possibility that heterolytic scission of the N–N bond occurs in the opposite sense, that is,



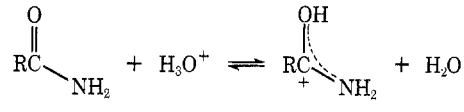
is not totally excluded by the work reported herein, but is inconsistent with the growing body of evidence that heterolysis of an electronegative substituent on nitrogen in a substituted anilide readily occurs to afford an *N*-acylnitrenium cationoid fragment.[1,35,36] This theme will be developed in subsequent papers.

The recent proposal[37] by Allan that the benzidine rearrangement occurs *via* a species protonated at C-1 and nitrogen of one ring of hydrazobenzene may be ruled out on several grounds. (1) Electronic considerations suggest that C-1 is a very weakly basic position. (2) Consideration of models shows that the stereochemical problem is not greatly diminished by this pathway. (3) Protonation of C-1 and the adjacent nitrogen offers little driving force for heterolytic N–N bond breaking; yet this factor is known to be prominent in the energetics of the process. (4) The model cannot successfully be extended to the work reported herein.

The detailed course of the rearrangement in dilute acid which is accompanied by hydrolysis is less clearly established. The H_0 of 1.080 *F* perchloric acid in 30% aqueous methanol has not been established, but it may be approximated from the data of Yates and Wai[38] to be about −0.4. It should be noted that addition of 5 *F* $NaClO_4$ to 1 *F* $HClO_4$ lowers the activity of water in the solution[39] and increases the Hammett acidity, thereby making the H_0 more negative by about one (logarithmic) unit.[7] Thus, although the rate of rearrangement in 2 *F* $HClO_4$–4 *F* $NaClO_4$ solution at first appears to have been abnormally accelerated over that in 1 *F* $HClO_4$, the acceleration is due in large measure to the increased acidity of the medium. Extrapolation of the rates measured in solutions 6 *F* in electrolyte to an H_0 of −0.4 suggests that the rate of rearrangement of acetylhydrazobenzene in 1 *F* $HClO_4$ *without* added salt should be about 1.3×10^{-3} min^{-1}. The measured rate of conversion of acetylhydrazobenzene to deacylated rearrangement products is about one-half this calculated rate, 6.6×10^{-4} min^{-1}. Although the extrapolation may be faulty, the possibility of rearrangement followed by deacylation is not grossly inconsistent with the predicted magnitudes of the rearrangement in dilute acid.

Other considerations favor slow deacylation followed by rearrangement, however. (1) *N*-Acetylbenzidine is deacylated under the reaction conditions only about as rapidly as the overall conversion occurs, and it should have been readily detectable in the solution if it had been formed as an intermediate. Although a search was made for it, none was found. In contrast, hydrazobenzene rearranges very rapidly in acid solutions of the concentrations used, and could not have been detected, if formed. (2) Although the rearrangement product in the presence of concentrated electrolytes was exclusively *N*-acetylbenzidine, in dilute solution products other than benzidine were formed. Hydrazobenzene is known to afford considerable diphenyline under these conditions. (3) The rate of the benzidine rearrangement is known[11] to have a large, positive salt effect. The extrapolation of the rate of rearrangement of *N*-acetylhydrazobenzene ignored any possible salt effect, and may have given much too high a predicted rate on that account.

If indeed the reaction in dilute acid proceeds *via* a rate-limiting deacylation, perhaps the most surprising feature of the work reported here is the relative response of the rates of amide hydrolysis and rearrangement to the acidity of the solutions. It has been known for many years that the rate of acid-catalyzed hydrolysis of amides passes through a maximum with increasing acid concentration and then falls as the concentration of acid is further increased.[40] The conjugate acid species of an ordinary amide which is favored at equilibrium is protonated on oxygen



and this species is almost certainly the intermediate in the acid-catalyzed hydrolysis of amides. Yates and Stevens[41] have compared literature data on amide hydrolysis from many sources with acidity functions developed for amides,[42] and have correlated the rate–acidity dependence of acid-catalyzed amide hydrolysis with the water activity of the reaction medium. Several treatments suggest that the transition state contains three molecules of water. The rate of hydrolysis is, therefore, reduced in concentrated solutions in which the water activity is low.

Since conjugate acids other than that which participates in the hydrolysis are present in equilibrium with that species at concentrations proportional to the acidity of the medium, the postulated change in mechanistic course appears consistent with competition of two pathways involving two conjugate acid species. This formulation requires, however, that the conjugate acid species which rearranges be that which is present at equilibrium in smaller amount than that which undergoes hydrolysis. *A priori* the unacylated nitrogen would seem to be the most basic site in *N*-acetylhydrazobenzene; yet the N-protonated conjugate acid is the species we believe to be responsible for rearrangement.

In summary, the weight of the evidence seems to us to point to a pathway in dilute acid of rate-limiting

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(37) Z. J. Allan, *Tetrahedron Lett.*, 4225 (1971).
(38) K. Yates and H. Wai, *J. Amer. Chem. Soc.*, **86**, 5408 (1964).
(39) Yates and Wai[38] have shown that the H_0 of concentrated aqueous solutions of strong acids is a remarkably consistent function of water activity.
(40) V. K. Krieble and K. A. Holst, *J. Amer. Chem. Soc.*, **60**, 2976 (1938).
(41) K. Yates and J. B. Stevens, *Can. J. Chem.*, **43**, 529 (1965).
(42) K. Yates and J. C. Riordan, *ibid.*, **43**, 2328 (1965).

deacylation followed by rapid rearrangement. Verification of this hypothesis must await detailed kinetic and product studies in regions of intermediate acidity and salt concentrations.

Registry No.—*N*-Acetylhydrazobenzene, 22293-38-5; 2,3,4,5,6,2′,3′,4′,5′,6′-decadeuterio-*N*-acetylhydrazobenzene, 36358-15-3; *N*-acetylbenzidine, 3366-61-8; benzidine, 92-87-5.

Electron Impact Induced Stereospecific Hydrocarbon Fragmentations. Mass Spectrometric Determination of the Configuration at C-5 in Steroidal Hydrocarbons[1]

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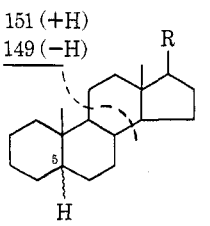
The mass spectra of C-17 side chain bearing steroidal hydrocarbons exhibit stereospecific fragmentation reactions which are diagnostic for the configuration at C-5. The resulting fragment ions are most probably derived from a D-seco molecular ion which is formed by the facile cleavage of the 13–17 bond in the presence of the C-17 side chain. Consequently, these stereospecific reactions are absent in the spectra of C-5 epimeric androstanes which lack the side chain. The cleavage patterns and fragmentation mechanisms of these reactions were studied with the aid of substituent and deuterium labeling techniques and metastable peak analysis. This study lead to the discovery of a site-specific hydrogen transfer from C-12 in association with the formation of the diagnostically important *m/e* 151 ion. The synthesis of the various labeled compounds is described.

Initial recognition of mass spectroscopy as an indispensable tool in structure elucidation originates from hydrocarbon chemistry. Its value in two-dimensional structure elucidation is well established, but generally in this field mass spectroscopy provides very little steric information. In a recent review of the stereoisomeric effect on the mass spectra of hydrocarbons, Meyerson and Weitkamp[2] concluded that the spectra of hydrocarbon stereoisomers, unlike those of many functional group containing species, show no clear evidence of stereospecific reactions. Similarly, careful analysis of the mass spectra of the various 1-methyl- and 2-methyldecalins by the same authors revealed only very modest differences between these stereoisomers.[3] Correlation does exist, for example, between the relative intensity of the $M^+ - CH_3$ fragment ions and the relative stability of the molecules, but these spectral variations are very sensitive to experimental conditions, and they are meaningful only in comparative studies.

Extraction of the maximum amount of structural information (including stereochemistry) from the mass spectrum of a compound is especially important in gc–mass spectroscopy, which can be used to analyze submilligram amounts of complex mixtures. The structure elucidation of the components in such mixtures depends largely on the interpretation of the fragmentation patterns. The importance of reliable interpretations is, therefore, obvious in fields such as natural product chemistry and biological research, where scarcity of the material, or complexity of the mixture, often preclude the application of other physical or chemical techniques.

During the course of earlier detailed examination of the fragmentation mechanisms of steroidal hydrocarbons,[4,5] it was noted that the C-5 epimeric preganes (III and IV) exhibit a significant difference in the relative intensities of the *m/e* 149 and 151 ions.[4] To test for the generality of this fragmentation as a diagnostic feature for the stereochemistry at the A/B ring junction, we examined the mass spectra of the three most important C-5 epimeric hydrocarbon pairs, androstanes (I and II, Figures 1 and 2), pregnanes (III and IV, Figures 3 and 4), and cholestanes (V and VI, Figures 5 and 6) under various experimental conditions. It was found that the characteristic features in the *m/e* 147–153 region of the spectrum provide unequivocal differentiation between the 5α and 5β epimers of C-17 side chain bearing hydrocarbons (see Figures 3–6). This mass range is dominated by an intense *m/e* 149 ion in the spectra of 5α steroids while two significant peaks (*m/e* 149 and 151) are characteristic for the 5β epimers. This difference, however, is not apparent in the mass spectra of 5α- and 5β-androstanes (I and II), which consist of the tetracyclic nucleus only without any side chain at C-17 (compare Figures 1 and 2).



I, 5α; R = H
II, 5β; R = H
III, 5α; R = C_2H_5
IV, 5β; R = C_2H_5
V, 5α; R = C_8H_{17}
VI, 5β; R = C_8H_{17}

The stereoisomeric effect on the fragmentations of these hydrocarbons is of considerable practical as well as theoretical interest. Its practical significance has been clearly demonstrated[6] by the recent studies of the constituents of Green River shale and California petro-

(1) Presented in part at the Pacific Conference on Chemistry and Spectroscopy, Anaheim, Calif., Oct 1971.

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(3) S. Meyerson and A. W. Weitkamp, *ibid.*, **2**, 603 (1969).

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