[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Acid–Base Reactions in Non-water-like Solvents: Sulfuric Acid in Nitromethane[1]

BY HUGO VAN LOOY[2] AND LOUIS P. HAMMETT

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In the solvent nitromethane the reaction of sulfuric acid (HA) with an indicator (I) of the nitroaniline type can be completely accounted for by the following processes: $\mathrm{I} + \mathrm{HA} \rightleftarrows \mathrm{IH}^+{\cdot}\mathrm{A}^-$ and $\mathrm{I} + 3\mathrm{HA} \rightleftarrows \mathrm{IH}^+{\cdot}\mathrm{A(HA)_2}^-$, the ion pairs $\mathrm{IH}^+{\cdot}\mathrm{A}^-$ and $\mathrm{IH}^+{\cdot}\mathrm{A(HA)_2}^-$ having the same light absorption as the free ion IH^+. The effect of the added salt pyridinium bisulfate is to decrease the apparent acidity by an amount only a little greater than would result from the reaction $\mathrm{PyH}^+{\cdot}\mathrm{A}^- + 2\mathrm{HA} \rightleftarrows \mathrm{PyH}^+{\cdot}\mathrm{A(HA)_2}^-$ where PyH^+ is pyridinium ion. It appears that the reaction of one molecule of acid with one molecule of base as it is observed in water-like solvents requires as an indispensable factor the solvation of the anion, presumably by hydrogen bonding between the acidic hydrogen of the solvent and the unshared electrons of the anion, and that in the absence of solvent molecules with the necessary properties the transfer of the proton from the acid to the base may take place only if an additional molecule or molecules of the acid are drafted to perform the function fulfilled by the solvent in water-like systems. It appears further that in non-water-like solvents, even when the dielectric constant is as high as 38, ion-pairs of high stability are formed when the structures involved permit strong hydrogen bonding between cation and anion.

The predominant influence which has been attributed to the dielectric constant of the solvent in discussions of the properties of electrolytes has made the peculiar chemistry of acid–base reactions in solvents like benzene[3] and acetic acid[4] seem an excusable deviation from the classical picture which was derived from the study of reactions in water. It tends however to obscure rather than to clarify the unexpected behavior of such reactions in the solvent nitromethane[5] because this solvent has a dielectric constant of 38 (at 25°) whereas methanol with a constant of 32 is a solvent in which acid–base reactions have shown no unexpected deviations from water-like behavior.[6] The key to the problem appeared with the recognition by Rosetta Natoli Reusch[7] that the Smith and Hammett results, which she verified in principle and extended, can only be understood in terms of the reaction of one molecule of a simple basic indicator I with more than one molecule of the strong acid HA, typically for instance by the process

$$\mathrm{I} + 2\mathrm{HA} \rightleftarrows \mathrm{IH}^+ + \mathrm{AHA}^- \qquad (1)$$[8]

The clear implication is that the reaction of one molecule of acid with one molecule of base as it is observed in water-like solvents requires as an indispensable factor the solvation of the anion, presumably by hydrogen bonding between the acidic hydrogen of the solvent and the unshared electrons of the anion. In the absence of solvent molecules with the necessary properties the transfer of the proton from the acid to the base may require the drafting of an additional molecule or molecules of the acid to perform the function fulfilled by the solvent in water-like systems. The present investigation, which covers a wider range of acid concentrations, makes it possible to give greater precision to this interpretation.

Experimental

Materials.—The purification of nitromethane is a critical problem, because of a variability in the properties of electrolytes in this solvent which apparently depends upon the history of the solvent sample and which has been noted by others as well as in previous work from this Laboratory. All of the results reported in this article were obtained with solvent purified as follows. About 150 ml. of concentrated sulfuric acid for each liter of nitromethane was mixed with the solvent and the mixture was allowed to stand for one or two days. The solvent then was washed with water, treated with sodium carbonate and washed again. It was kept over anhydrous magnesium sulfate for several days, then filtered and stored over Drierite. Before use it was distilled in two to three-liter lots through a 1-meter bead column. The forerun contained a water–nitromethane azeotrope and a fraction containing hydrogen cyanide. The middle cut, which was used in our experiments boiled at 101° at 760 mm.; its refractive index was 1.37975 at 25°; and its density was 1.127. A vapor phase chromatogram showed the presence of nitroethane. Karl Fischer titration indicated less than 0.001 *M* water. This titration when applied to samples to which known amounts of water had been added reproduced closely the amount added.

Other methods of purification which were tried included distillation from phosphorus pentoxide, from sulfuric acid or from boric acid followed by fractional distillation at atmospheric or at reduced pressure. These were all rejected in favor of the method of the previous paragraph, the criterion being the quality of the results obtained with the less acidic indicators (4-chloro-2-nitroaniline and 2,4-dichloro-6-nitroaniline), *i.e.*, with sulfuric acid concentrations below 0.1 *M*. The preferred method gave solutions with higher values of the indicator ratio $[\mathrm{IH}^+]/[\mathrm{I}]$ and a smaller spread (0.2 in the logarithm) between values obtained with successive batches of solvent. The data reported in this article were obtained with three batches of solvent which gave closely agreeing results; which gave the highest average values of the indicator ratio at a given acid concentration; and which showed no tendency for the light absorption of solutions containing acid and indicator to change with time. The difficulty with lack of reproducibility was much less serious with solutions of higher acid concentrations, in which the indicator 6-bromo-2,4-dinitroaniline was used. The data reported for this indicator were obtained with six out of the seven batches of solvent prepared. For some unknown reason the other batch gave inconsistent results.

The other materials were purified by usual methods, particular attention being given to the indicators. All water sensitive materials were carefully protected from the air, and all transfers of materials were made and all solutions prepared in an effective drybox.

Apparatus.—Measurements of light absorption were made in a Beckman DU spectrophotometer modified so as to permit temperature control to within 0.1° and to protect the cell windows against condensation of moisture at low temperatures. Solution temperatures in the spectropho-

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[2] Belgian–American Educational Foundation Graduate Fellow 1955–1956.

[3] V. K. LaMer and H. C. Downes, THIS JOURNAL, **55**, 1840 (1953).

[4] I. M. Kolthoff and S. Bruckenstein, *ibid.*, **78**, 1 (1956); S. Bruckenstein and I. M. Kolthoff, *ibid.*, **78**, 10 (1956).

[5] L. C. Smith and L. P. Hammett, *ibid.*, **72**, 301 (1950).

[6] I. M. Kolthoff and L. S. Guss, *ibid.*, **60**, 2516 (1938); **61**, 330 (1939).

[7] R. Natoli, Ph.D. Dissertation Columbia University, 1955, published by University Microfilms, Publication 21809.

[8] The same conclusion has been reached independently by Y. Pocker, *J. Chem. Soc.*, 240 (1958).

tometer were measured by a thermistor placed in the cell just outside the light path.

Procedure.—Solutions containing sulfuric acid at concentrations ranging from 0.002 to 1.1 *M*, with or without small additions of pyridinium bisulfate or of water, and indicator at a concentration in the neighborhood of 1 × 10^{-4} *M* were measured with a slit width of 0.15 mm. at a suitable wave length. For 4-chloro-2-nitroaniline and 2,4-dichloro-6-nitroaniline this was 410 mμ, which corresponds to the maximum in the absorption band; for 2,4-dinitroaniline and 6-bromo-2,4-dinitroaniline it was 400 mμ, which is close to the maximum at 390, but outside the region of absorption by the solvent.

It was found that none of these indicators absorbs at the wave length used when it is in the acid form IH^+, and that Lambert's law holds for the base form I of all of them at concentrations from 10^{-5} to 3 × 10^{-4} *M*. With 6-bromo-2,4-dinitroaniline, with which no appreciable concentration of IH^+ appears at acid concentrations below 0.1 *M*, it was found that the absorption of the indicator was independent of acid concentration at concentrations below 0.1 *M* and that pyridinium bisulfate at the concentrations used in our experiments had no effect upon the absorption of the basic form of the indicator.

Results

The colorimetrically determined values of the indicator ratio $[IH^+]/[I]$ for the four nitroaniline indicators in solutions of sulfuric acid in nitromethane at 25° are reported in Fig. 1. From these results and the value −1.03[9] for the *pK* of 4-chloro-2-nitroaniline the *pK* values of the other indicators are estimated as: 2,4-dichloro-6-nitroaniline, −3.34; 2,4-dinitroaniline, −4.17; 6-bromo-2,4-dinitroaniline, −6.46. The best values of Paul and Long, which are based upon the behavior in water–strong acid mixtures, are −3.32, −4.53 and −6.71. The differences between the two series of values are no larger than those frequently found in similar comparisons.[9] With these values of the acidity constants of the indicators the data of Fig. 1 have been translated into the plot of the acidity function H_0 against the logarithm of the concentration of sulfuric acid shown in the upper curve of Fig. 2. The other curves in this figure represent values obtained in similar fashion for solutions containing specified small concentrations of the salt pyridinium bisulfate. Figure 3 shows in the same way the effect upon the acidity function of sulfuric acid solutions of specified concentrations of water.

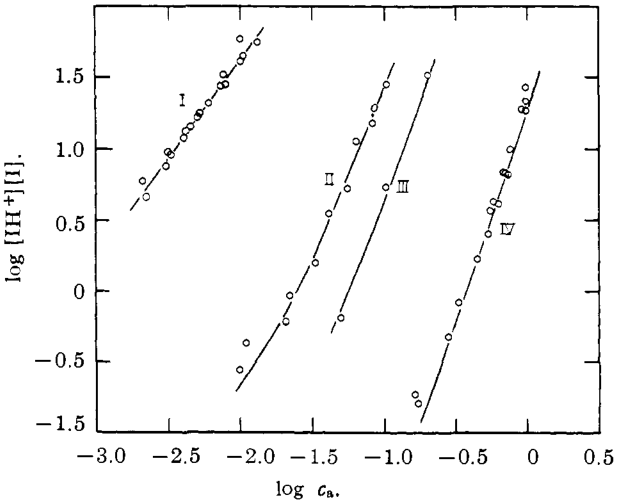

Fig. 1.—Plots of the logarithm of the indicator ratio, $[IH^+]/[I]$, against the logarithm of c_a, the concentration of sulfuric acid in the solvent nitromethane at 25°. The indicators are: I, 4-chloro-2-nitroaniline; II, 2,4-dichloro-6-nitroaniline; III, 2,4-dinitroaniline; IV, 6-bromo-2,4-dinitroaniline. The indicator concentration is between 1.17 × 10^{-4} *M* and 1.23 × 10^{-4} *M* except in the case of dinitroaniline where it is 0.642 × 10^{-4} *M*.

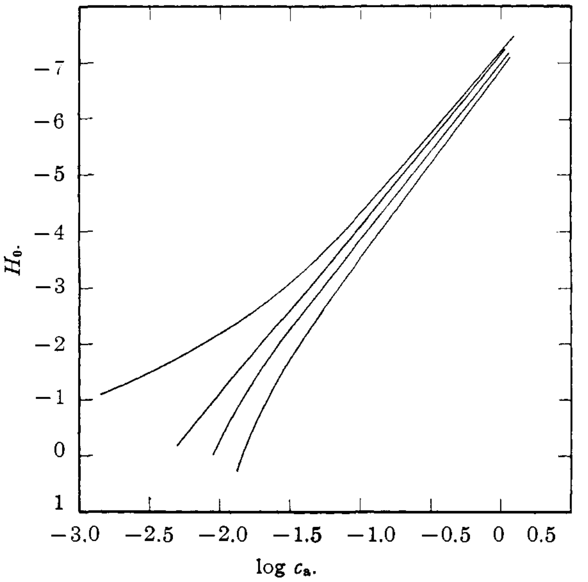

Fig. 2.—Plots of the acidity function H_0 against the logarithm of c_a the molar concentration of sulfuric acid in nitromethane at 25°: top curve, acid and indicator alone; 2nd from top, 0.0048 *M* pyridinium bisulfate added; 3rd from top, 0.0096 *M* pyridinium bisulfate added; bottom curve, 0.0192 *M* pyridinium bisulfate added.

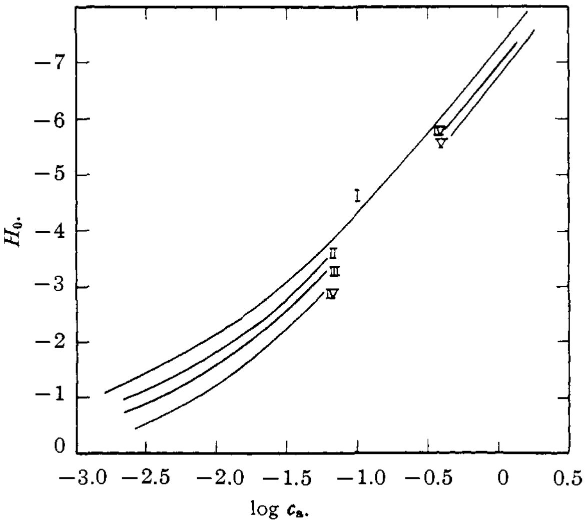

Fig. 3.—Plots of the acidity function H_0 against the logarithm of c_a, the molar concentration of sulfuric acid in nitromethane at 25°: I, acid and indicator alone; II, 0.011 *M* water added; III, 0.0225 *M* water added; IV, 0.045 *M* water added; V, 0.090 *M* water added.

Over the narrower range of acid concentrations employed by Dr. Reusch[7] the results reported above are in rather good agreement with hers, allowance

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[9] M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957).

being made for our use of Paul and Long's revised value of the acidity constant of 4-chloro-2-nitroaniline. There is however an as yet unexplained discrepancy between the present results and the earlier ones with respect to the effect of temperature. Our data indicate a parallel displacement of the plot for sulfuric acid solutions toward lower values of the indicator ratio which averages 0.15 unit in the logarithm for each 10 degree increase in temperature. This was found both with 4-chloro-2-nitroaniline and with 2,4-dichloro-6-nitroaniline and over the range from 11.4 to 39.5°.

For three of the indicators we investigated the effect of the titer concentration c_i of the indicator on the indicator ratio. The results are reported in Table I. The figures in parentheses for the bromodinitro indicator have been calculated to a fixed acid concentration of 0.400 *M*.

TABLE I

EFFECT OF INDICATOR CONCENTRATION

10^4c_i	10^3c_a	$\log [IH^+]/[I]$
	4-Chloro-2-nitroaniline	
0.294	5.31	0.66
.589	5.31	.64
.883	5.31	.61
1.18	5.31	.54
0.59	1.149	1.07
1.17	1.149	1.05
1.76	1.149	1.03
2.34	1.149	1.01
3.51	1.149	0.97
4.68	1.149	0.92
	2,4-Dichloro-6-nitroaniline	
0.295	53.1	−0.20
.59	53.1	− .16
.885	53.1	− .17
1.18	53.1	− .20
1.77	53.1	− .20
2.36	53.1	− .22
	6-Bromo-2,4-dinitroaniline	
0.3	389.4	−0.47 (−0.44)
0.6	412.0	− .45 (− .49)
1.8	400.4	− .42 (− .43)
2.4	399.6	− .41 (− .43)
3.6	433.8	− .21 (− .32)

Because the indicator data point so strongly toward extensive ion association of the indicator salts we have investigated the conductance of the salt pyridinium bisulfate in nitromethane. The solvent had a conductance of 3.41×10^{-7}. The results are presented in Table II. Applying the Shedlovsky extrapolation formula[10] in the theory of Fuoss and Kraus[11] one obtains $\Lambda_0 = 142$ and $K = 1.7 \times 10^{-3}$. The degree of dissociation of the ion pairs calculated from these figures ranges from 0.55 for a 0.003 *M* solution of the salt to 0.85 for a 0.000068 *M* solution.

Conclusions

These are extremely acidic solutions; this would indeed be expected from the very low basicity of nitromethane, which is only slightly ionized as a solute in dilute solution in the solvent sulfuric acid.[12] As was the case in previous work on strong acids in the solvent nitromethane plots of acidity function against the logarithm of the acid concentration show unexpectedly steep slopes.

Considering first the region of acid concentration above 0.1 *M*, the only possible interpretation appears to be a reaction of one molecule of indicator I with three molecules of acid HA according to

$$I + 3HA \rightleftarrows IH^+ \cdot A(HA)_2^- \qquad (2)$$

the product being an ion-pair which has the same light absorption as the free ion IH^+. For this reaction it is shown easily that r, the observed ratio of the sum of the concentrations of all acid forms of the indicator to the concentration of the base form, is given by

$$r = K_3c_a^3 \qquad (3)$$

K_3 being the equilibrium constant of reaction 2, provided, as is the actual case, that the indicator concentration c_i is much less than the acid concentration c_a. This equation predicts a slope of 3 for a plot of $\log r$ against $\log c_a$ and consequently a slope of −3 for a plot of H_0 (which equals $pK_a - \log r$) against $\log c_a$. Least squares treatment of our data over the range from 0.1 to 1 *M* gives a slope of −2.94.

The evidence is strongly against any significant dissociation of the ion pair into the ions IH^+ and $A(HA)_2^-$. If there were appreciable dissociation with an equilibrium constant K_i the equation

$$K_3\frac{c_a^3}{r} = 1 + \frac{1}{2}\frac{K_i(1+r)}{c_ir} - \sqrt{\left\{\frac{K_i(1+r)}{2c_ir}\right\}^2 + \frac{K_i(1+r)}{c_ir}} \qquad (4)$$

would apply, and r would vary with c_i, which the data of Table I show is contrary to fact in this region of acid concentration. The conclusion is further supported by the fact that the difference in the pK values of the two indicators used in this region is close to the difference observed in strong aqueous acid solutions (2.29 against 2.18). Furthermore the acidity of a solution in which considerable dissociation of the ion pair existed would be affected much more largely by the addition of a salt with an ion in common, such as pyridinium bisulfate, than is the case in this region of acid concentration.

At lower acid concentrations new phenomena appear. With solutions containing no added salt the slope of the plot decreases sharply at acid concentrations below 0.1 *M*, and the data can be fitted closely by supposing that the reaction

$$I + HA \rightleftarrows IH^+ \cdot A^- \qquad (5)$$

accompanies reaction (2). With K_1 as the equilibrium constant of reaction 5 and assuming no dissociation of the ion-pairs we have then

$$r = K_1c_a + K_3c_a^3 \qquad (6)$$

and

$$H_0 = -\log K_a\,(K_1c_a + K_3c_a^3) \qquad (7)$$

Thus with $K_aK_1 = 1.23 \times 10^4$ and $K_aK_3 = 1.78 \times 10^7$ we have the agreement between calculated

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(10) T. Shedlovsky, *J. Franklin Inst.*, **225**, 739 (1938).

(11) R. M. Fuoss and C. A. Kraus, THIS JOURNAL, **55**, 476 (1933).

(12) R. J. Gillespie, *J. Chem. Soc.*, 2547 (1950).

TABLE II

CONDUCTANCE OF PYRIDINIUM BISULFATE SOLUTIONS IN NITROMETHANE

10^3c	2.9725	1.5446	1.2448	1.0507	0.6737	0.3533	0.1743	0.0683
Λ	31.18	41.83	44.85	47.44	55.43	66.88	79.98	88.15

TABLE III

OBSERVED AND CALCULATED ACIDITY FUNCTIONS

log c_a	0	−0.5	−1.0	−1.5	−2.0	−2.5
H_0 (obsd.)	−7.24	−5.75	−4.32	−3.06	−2.14	−1.45
H_0 (calcd.)	−7.25	−5.75	−4.28	−2.98	−2.12	−1.60

TABLE IV

EFFECT OF SALT UPON THE APPARENT CONCENTRATION OF AVAILABLE ACID

C_a	C_s	[HA]	Δ[HA]	C_a	C_s	[HA]	Δ[HA]
0.016	0.0048	0.005	0.011	0.1	0.0048	0.081	0.019
	.0096	.002	.014		.0096	.067	.033
					.0192	.048	.052
0.04	.0048	.025	.015	0.4	.0048	.360	.040
	.0096	.018	.022		.0096	.320	.080
	.0192	.010	.030		.0192	.282	.118

and observed value of the acidity function shown in Table III. The equation

$$H_0 = -\log K_a(K_1c_a + K_2c_a^2 + K_3c_a^3) \qquad (8)$$

fits the data as well as (7) but not significantly better.

In the experiments at low acid concentrations with the indicator 4-chloro-2-nitroaniline a weak but probably real dependence of r upon indicator concentration is observed (Table I), although there is no evidence for such an effect at higher acid concentrations where indicators of more negative pK value were employed. According to eq. 4 (or to the similar equation with K_1c_a/r on the left side and an identical right side which should apply at low acid concentrations) r can be a function of c_i only in so far as the right side of the equation differs from unity. For any given value of the ratio K_i/c_i the difference will be greater the greater the value of the quantity $(1 + r)/r$, *i.e.*, the smaller the value of r. In fact however the only measurements which show an appreciable dependence of r on c_i involve high rather than low values of r. This effect is possibly spurious since it appears only with low values of c_a where the experimental uncertainty is greatest. If it is not the dissociation constant K_i must be greater for the salts of the least acidic indicator than for the more acidic ones. Such a relationship would be consistent with the fact that the dissociation constant of pyridinium bisulfate is about 10^{-3} while that for the indicator salts cannot in any case be more than 10^{-5}. With a pK of 5.6 pyridinium ion is much less acidic than the conjugate acids of any of our indicators. The relationship is also consistent with existing evidence for strong hydrogen bonding between anions and cations of the structure R_3NH^+ in the solvent nitrobenzene[13]; with the normal and expected increase in the strength of hydrogen bonding with increasing acidity of the hydrogen donor; and with the fact that the quaternary salt tetramethylammonium bromide, in which no hydrogen bonding of this kind is possible, has a dissociation constant of 0.02 in the solvent nitrobenzene,[14] whose lower dielectric constant (35 compared with 38) would tend toward lower rather than higher dissociation of salts.

The addition of a salt such as pyridinium bisulfate must decrease the concentration of free acid by reactions such as

$$PyH^+{\cdot}A^- + 2HA \rightleftharpoons PyH^+{\cdot}A(HA)^- \qquad (9)$$

complicated by the dissociation of both the ion pairs. The decrease in acid concentration must then decrease the value of r. In the specific case of a solution containing no salt for which $c_a = 0.1$, $c_i = 1.2 \times 10^{-4}$ and $H_0 = -4.33$, the actual concentration of free acid may be taken to be 0.1. Addition of 0.0192 M salt increases the observed value of H_0 to -3.55. From the graph it appears that an identical increase in H_0 could have been obtained by decreasing c_a and consequently [HA] to 0.048 without the addition of any salt. The effect of the addition of the salt upon the value of r is therefore the same as the removal from the solution of 0.052 mole per liter of acid, an amount which is 2.7 times the quantity of added salt. Figures obtained in this way for other representative cases are listed in Table IV, in which the column headed [HA] is the actual molar concentration of acid and the column headed Δ[HA] is the calculated change in the concentration of uncombined acid resulting from the addition of the salt. These calculated changes are generally more than twice the concentration of the salt, but hardly by a larger factor than can be expected from the uncertainties connected with the small magnitude of the total effect of the salt upon the acidity in all but the lowest acid concentrations. If in fact the indicator salt is partially dissociated repression of the dissociation by the added salt would increase the total effect in the observed direction.

The effect of water at the higher acid concentrations is about the same as that of the pyridinium salt. At low acid concentrations, however, water has a considerably smaller effect than the salt. This may be taken to indicate that the reaction

$$H_2O + H_2SO_4 \rightleftharpoons OH_3^+{\cdot}HSO_4^- \qquad (10)$$

is incomplete at low acid concentrations but becomes essentially complete at acid concentrations greater than about 0.1 M.

Our finding that salt formation between an amine base and a strong acid may involve more than one mole of acid per mole of base finds strong support in the discovery by Brown and Holmes[15] that in the solvent nitrobenzene salts of 2-alkylpyridines with the strong acid methanesulfonic acid react with excess methanesulfonic acid by a process which is accompanied by a considerable heat evolution. This process occurs with salt concentrations of the order of 0.08 M and the heat evolution does not cease when one additional mole of acid has been added. In the solvent nitro-

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[13] (a) W. F. K. Wynne-Jones, *J. Chem. Soc.*, 795 (1931); (b) E. G. Taylor and C. A. Kraus, THIS JOURNAL, **69**, 1731 (1947).

[14] H. Sadek and R. M. Fuoss, *ibid.*, **76**, 5905 (1954).

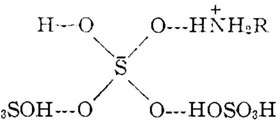
[15] H. C. Brown and R. R. Holmes, *ibid.*, **77**, 1727 (1954).

methane Pocker[8] has presented good evidence for the stability of the ClHCl$^-$ ion.

Because the hydrofluoride ion FHF$^-$ is so familiar even to an aquocentric chemistry, ClHCl$^-$ does not seem as difficult to accept as the combination of bisulfate ion with additional acid molecules which our results require. The principle is not in fact new, we suppose that the hydrogen atom of the acid bonds with unshared electrons on the oxygen atoms in the bisulfate ion in the same way that the hydrogen atoms in HF bond with unshared electrons in the fluoride ion. It is true that the oxygen atoms in the bisulfate ion can have only very weakly basic properties, but it is also true that the hydrogen atoms in sulfuric acid are extremely acidic, and hydrogen bonding depends as much on the acidity of the hydrogen donor as it does on basicity of the acceptor.

It seems necessary then to conclude that the remarkably non-water-like quality of the chemistry of acid–base reactions in nitromethane should be attributed to the lack of hydrogen bonding donor properties of this solvent, and that conversely the familiar properties of acid–base systems in water-like solvents must be attributed much more to the quality of these solvents as hydrogen bonding donors and much less to their relatively high dielectric constants than has usually been the case.[16]

Our picture of the indicator salt in solutions of sulfuric acid of concentration over 0.1 *M* would in fact be



and we expect the stability of similar structures to be an important factor in the chemistry of all solvents which lack the hydrogen bonding donor properties of water and of other solvents which, like water, contain relatively acidic hydrogen atoms. Because of the close parallelism which often exists[17] between the equilibrium of the salt, formation of indicators and the rates of acid-catalyzed reactions, we expect also that the rates of acid-catalyzed reactions in non-water-like solvents will frequently depend upon a higher power than the first of the acid concentration and that such reactions will often be retarded by the addition of "neutral" salts even though a catalysis by the lyonium ion is out of the question.[18]

[16] See however ref. 13.

[17] Recently reviewed by F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 935 (1957).

[18] Such a retardation is observed in the effect of tetramethylammonium *p*-nitrobenzoate on the mutarotation catalyzed by *p*-nitrobenzoic acid of tetramethylglucose in nitromethane; E. L. Blackall and A. M. Eastham, THIS JOURNAL, **77**, 2184 (1955).

NEW YORK, N. Y.

[CONTRIBUTION FROM THE LABORATORY OF THEORETICAL CHEMISTRY, THE UNIVERSITY OF PARIS]

On the Hydrogenation of Purines[1]

BY T. NAKAJIMA AND B. PULLMAN

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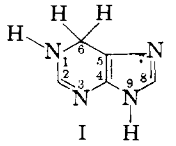
The reduction of purine hydrochloride under one atmosphere of hydrogen in the presence of palladium–charcoal catalyst at room temperature, and the inertness under the same conditions of purine and the biological purines: adenine, guanine and xanthine, are interpreted in terms of the relatively great value of the free valence—and correlatively small value of the radical localization energy—of carbon 6 of purine hydrochloride.

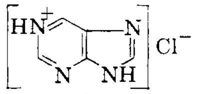
We have studied in a series of recent publications the electronic structure of purines in relation to their chemical and physicochemical properties[2-4] and with the principal object of establishing a correlation between the structure and the antitumor activity of purine antimetabolites.[5] This note is concerned with the interpretation of some recent observations on the hydrogenation of purines.

Bendich[6] has shown that *purine hydrochloride* may be reduced under one atmosphere of hydrogen in the presence of 5% palladium–charcoal catalyst at room temperature. The product obtained has been considered tentatively to be 1,6-dihydropurine (I). *Purine itself* does not reduce under these conditions and neither do the "biological" purines: adenine, guanine and xanthine.

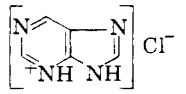


I

There are three possible structures for purine hydrochloride with the proton attached, respectively, to N_1, N_3 or N_7. Following our theoretical investigation on the position of the most basic nitrogen on the skeleton of purine, it is the structure II which is the most probable.[3,4]



II



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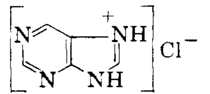

IV

[1] Supported by Public Health Service Grant C-3073.

[2] A. Pullman and B. Pullman, *Bull. soc. chim. France*, **25**, 766 (1958).

[3] A. Pullman, *ibid.*, **25**, 641 (1958).

[4] T. Nakajima and B. Pullman, *ibid.*, **25**, 502 (1958).

[5] B. Pullman and A. Pullman, *ibid.*, **25**, 973 (1958), and in press.

[6] A. Bendich in "The Chemistry and Biology of Purines," A. Ciba Foundation Symposium, Churchill Ltd., London, 1957, p. 308.