for K_2) and suggests the possibility that the dimer in solution is essentially the same as the gas phase dimer and may not have the loosely-bound electrons postulated by the expanded-orbital model.

Acknowledgments.—The authors wish to thank Dr. Andrew Timnick for his advice concerning instrumentation and also wish to acknowledge the financial assistance received from the U. S. Atomic Energy Commission.

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Protonation of Amides[1]

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Evidence from cryoscopic measurements is presented that N,N-dimethylformamide (DMF), N,N-dimethylacetamide (DMA), N-methylacetamide (NMA) and acetamide are monoprotonated in 100% sulfuric acid. The n.m.r. spectra of a wide variety of amides in acid solution have been investigated. It is concluded that all materials examined protonate predominantly on oxygen. In aqueous acid solution proton exchange on nitrogen has been detected, the concentration of N-protonated species being too small to measure. A more precise method for calculating barriers to rotation for DMF is described and the values found for pure DMF and protonated DMF are 9.6 ± 1.5 and 12.7 ± 1.5 kcal./mole, respectively. The rate of exchange protolysis on nitrogen of DMA is first order in (DMA) and (H^+) with a rate constant of 400 M^{-1} sec.$^{-1}$. The activation energy for this process for 0.4 M DMA in 6 M aqueous HCl is 7 ± 0.5 kcal./mole.

Introduction

The question as to whether amides protonate on oxygen or nitrogen has remained open for many years.[3-5] Of the two possibilities for a protonated amide, I and II, considerations of resonance[6] should favor I.

I II

Fraenkel and Niemann[7] have examined qualitatively the n.m.r. spectra of several amides in acidic media. Berger, Loewenstein and Meiboom[8] studied the exchange protolysis of N-methylacetamide in acid and basic solutions using n.m.r. techniques. They both concluded that amides protonate chiefly on oxygen.

It is the purpose of this investigation to elucidate the site of protonation of amides and also to study the attendant changes in structure which occur when an amide is protonated. The technique of n.m.r. was chosen because we anticipated the n.m.r. spectra of O- and N-protonated amides, I and II, respectively, to be clearly differentiable.[9] For any N,N-dimethylcarboxamide four possibilities may be recognized: (1) N-protonation, II, with slow proton exchange on nitrogen should yield free rotation about the central C–N bond. The n.m.r. spectrum of the N-methyl groups would consist of a doublet due to spin-coupling between the NH and NCH_3 protons, respectively, and a broad line for NH. In the presence of D_2SO_4 the doublet would nearly collapse since $J_D/J_H = 1/7$. (2) N-protonation with fast exchange of protons on nitrogen would produce a single line for the N-methyl resonance. (3) O-protonation, I, with slow exchange of protons on oxygen would produce a chemical shift between the two N-methyl groups, as in the case of pure N,N-dimethyl amides,[10,11] and a single line for OH. (4) O-protonation with fast exchange of protons on oxygen would yield the same spectrum for the N-methyl groups but no OH line. Similar considerations may be applied to other amides.

The manner in which chemical shifts and spin coupling constants in simple amides change when the amide is protonated will reflect differences in electronic configuration for the two species as well as the kinetics of exchange protolysis in acid solution.

In conjunction with these studies we have determined the degree of protonation of several amides in 100% sulfuric acid by means of cryoscopic measurements.

Experimental

Materials.—All liquids were fractionally distilled before use. Their purity was determined and in certain cases improved by vapor phase chromatography through the "Aerograph" Gas Chromatographic Instrument, Wilkens Instrument Research, Inc.

The compounds N,N-dimethylacetamide, N,N-dimethylpropionamide, N,N-dimethylbutyramide, N-methylacetamide and N-methylformamide were obtained from Eastman Kodak Co. Mr. David Schuster kindly donated samples of N,N-dimethylcyclopropanecarboxamide and N,N-dimethylisobutyramide.

i-Factors.—Cryoscopic measurements in sulfuric acid were conducted as described by O'Brien and Neimann,[12] our technique differing only in that liquid samples were introduced into the apparatus from a 1 cc. syringe which was weighed before and after.

Spectrometer.—All spectra were determined with the Varian High Resolution n.m.r. Spectrometer equipped

(1) Supported in part by U. S. Public Health Service, Grants No. RG 3823 and A 2145.

(2) Arthur A. Noyes Fellow 1958–1959.

(3) A. Hantzsch, *Ber.*, **64**, 661 (1931).

(4) A. R. Goldfarb, A. Mele and N. Gutstein, THIS JOURNAL, **77**, 6194 (1955).

(5) S. Mizushima, T. Simanouti, S. Nagakura, M. Tsuboi and O. Fujioka, *ibid.*, **72**, 3490 (1950).

(6) L. Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, New York, 1948, p. 207.

(7) G. Frankel and C. Niemann, *Proc. Natl. Acad. Sci. U. S.*, **44**, 688 (1958).

(8) A. Berger, A. Loewenstein and S. Meiboom, THIS JOURNAL, **81**, 62 (1959).

(9) W. D. Phillips, Research Department, Du Pont de Nemours, Delaware, has worked along similar lines (private communication).

(10) W. D. Phillips, *J. Chem. Phys.*, **23**, 1363 (1955).

(11) H. S. Gutowsky and C. H. Holm, *ibid.*, **25**, 1228 (1956).

(12) J. L. O'Brien and C. Niemann, THIS JOURNAL, **73**, 4264 (1951).

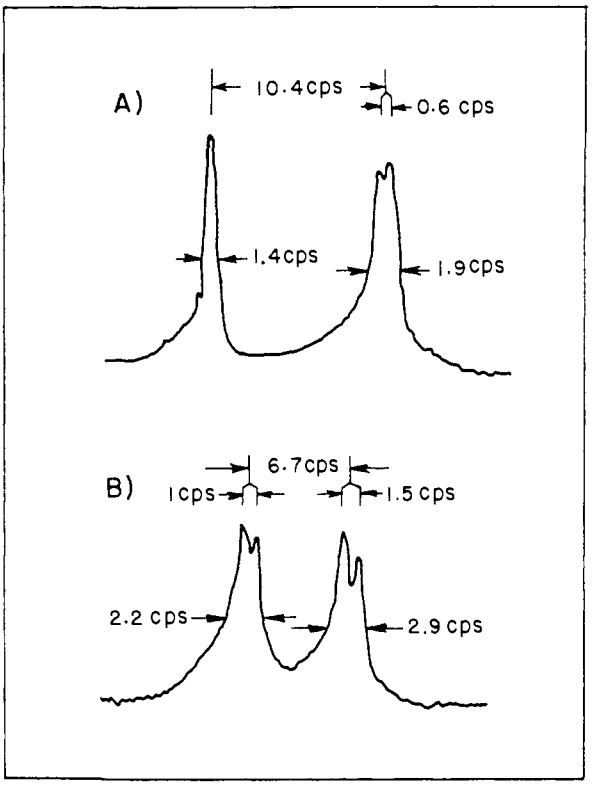


Fig. 1.—N.m.r. spectra of N-methyl protons in DMF, 60 Mc., 29°: A, DMF pure; B, 0.4 *M* DMF in 100% H_2SO_4. The magnetic field increases from left to right.

with Super-stabilizer, spinner and R. F. units for 40 and 60 Mc. Chemical shifts were calibrated by the method of side-band audio-modulation,[13] with an accuracy of ±0.1 c.p.s. Benzene was used as the external standard. The variable temperature insert used in this work will be described elsewhere.[14]

Kinetic Experiments.—Line-shapes for the collapsing n.m.r. multiplets were determined as a function of temperature. Before and after each measurement, in order to monitor the homogeneity of the field, the T_2 for the lines of contained cyclohexane, when used as an internal reference, or H^+ in the sulfuric acid solutions was determined by measuring the decay of the "wiggles" on rapid passage using a Sanborn recorder. The T_2 for the H^+ line in sulfuric acid is found to be unchanged by addition of N,N-dimethylformamide and is not considered to be exchange-broadened. In the experiments with N,N-dimethylacetamide, measurement of the C-methyl proton line width served the same purpose. Corrections were applied to the data for variations in field homogeneity, as described in Appendix A.

Results and Discussion

Cryoscopic Measurements.—It has already been established that simple amides are monoprotonated in 100% sulfuric acid.[15] Similarly we have found the *i*-factors in 100% sulfuric acid of N,N-dimethylacetamide, N,N-dimethylformamide, N-methylacetamide, N-methylformamide and acetamide to be all 2.00.

N,N-Dimethylformamide, DMF.—The n.m.r. spectrum of DMF consists of two narrow doublets for the methyl groups shown in Fig. 1A and an unresolved band for the CH proton (not shown in Fig. 1A). The main splitting is field dependent and has been traced to hindered rotation about the central C–N bond in the molecule.[10,11] The small doublets arise from coupling between the formyl and methyl hydrogens. The origin of these splittings has been verified by the use of $DCON(CH_3)_2$.[16]

The chemical shift between the methyl groups is somewhat dependent on the solvent and is retained in a wide variety of acids at room temperature, including 100% H_2SO_4 and 100% D_2SO_4, see Table I.

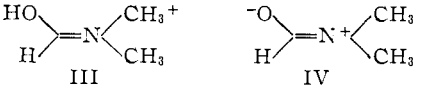
Figure 1B illustrates the methyl proton resonance pattern of a 0.4 *M* solution of DMF in 100% sulfuric acid, $DMFH^+$. Compared to pure DMF,[17] the *cis* and *trans* coupling constants between the formyl and methyl protons increase from 0.5 to 1.2 and from 0.75 to 1.7, c.p.s., respectively. No separate OH or NH line could be detected. As DMF, has been found to be monoprotonated in 100% sulfuric acid, these results clearly imply that in acid solution at room temperature DMF *protonates chiefly on oxygen.* At the same time protons are exchanging rapidly between the oxygen of DMF and the solvent.

Hindered Rotation in Protonated and Pure DMF.—As the temperature of the sulfuric acid solution of DMF is increased the two N-methyl doublets collapse into a single line at 130°. There is no evidence that the DMF has decomposed under these conditions since the n.m.r. spectrum is reversible with temperature. Furthermore fresh samples were used for each experiment.

The mean lifetime, τ, between interconversions of the two methyl groups was determined at several temperatures using a modified procedure based on the methods of Gutowsky and co-workers,[18] and Grunwald, Loewenstein and Meiboom,[19] see Appendix B.

The temperature dependence of the rate of internal rotation of 0.4 *M* DMF in 100% sulfuric acid and, for comparison, that of pure DMF are shown in Fig. 2. The results are listed in Table II.

It is evident that the activation energies in Table II represent barriers to rotation. It seems reasonable for the barrier in protonated DMF to exceed that of pure DMF since the resonance form III would be more important in stabilizing protonated DMF than would IV in stabilizing DMF. The increase in the formyl-methyl proton coupling constants in protonated DMF compared to DMF also indicates that stiffening of the central C–N bond has taken place.



However, concerning protonated DMF, it might still be argued that chemical exchange steps such

(13) J. T. Arnold and M. E. Packard, *J. Chem. Phys.*, **19**, 1608 (1951).

(14) C. Franconi and G. Fraenkel, *Rev. Sci. Instr.*, in press (1960).

(15) J. L. O'Brien and C. Niemann, THIS JOURNAL, **79**, 1386 (1957).

(16) R. A. Ogg and C. Franconi, unpublished results.

(17) In Fig. 1A only one N-methyl resonance is split. The spectrum was taken under the average conditions of field homogeneity (T_2 = 0.7 sec. for the water line) found at 60 Mc. Both doublets are more easily resolvable at 40 Mc.

(18) H. S. Gutowsky, D. McCall and C. P. Slichter, *J. Chem. Phys.*, **21**, 279 (1953); H. S. Gutowsky and A. Saika, *ibid.*, **21**, 1688 (1953).

(19) E. Grunwald, A. Loewenstein and S. Meiboom, *ibid.*, **27**, 1067 (1957).

TABLE I

CHEMICAL SHIFTS AND SPIN-COUPLING CONSTANTS FOR N-SUBSTITUENT GROUPS, $N\langle^{R_1}_{R_2}$, IN AMIDES, 29°

Compound	Solvent	Concn., M	δ	$J_{R_1R_2}$, c.p.s.	δ^a
DMF[b]	Pure	..	0.172		4.111, 3.939
DMF	48% HBr	0.6	.143		3.139, 2.996
DMF	100% H_2SO_4	.4	.118		3.184, 3.066
DMF	100% D_2SO_4	.4	.115		3.141, 3.026
DMA[b]	Pure	..	.150		3.641, 3.491
DMA	10 M $HClO_4$	.5			3.246
DMA	100% H_2SO_4	.5			3.104
DMA	100% D_2SO_4	.5			3.126
$(CH_3)_2CHCON(CH_3)_2$[b,d]	Pure	..	.202		3.896, 3.694
$(CH_3)_2CHCON(CH_3)_2$	100% H_2SO_4	.4	.075		3.191, 3.116
$(CH_3)_2CHCON(CH_3)_2$	100% D_2SO_4	.4	.068		3.084, 3.016
$(CH_2)_2CHCON(CH_3)_2$[b,d]	Pure	.4	.265		3.644, 3.379
$(CH_2)_2CHCON(CH_3)_2$	100% H_2SO_4	.4	.183		3.099, 2.916
$(CH_2)_2CHCON(CH_3)_2$	100% D_2SO_4	.4	.183		3.104, 2.921
$CH_3CH_2CON(CH_3)_2$[c]	Pure	.4	.123		3.875, 3.772
$CH_3CH_2CON(CH_3)_2$	100% H_2SO_4	.4	.071		3.098, 3.027
$CH_3CH_2CON(CH_3)_2$	100% H_2SO_4	.4	.070		3.102, 3.032
$CH_3CH_2CH_2CON(CH_3)_2$[c]	Pure	..	.188		3.932, 3.744
$CH_3CH_2CH_2CON(CH_3)_2$	100% H_2SO_4	.4	.054		3.130, 3.076
$CH_3CH_2CH_2CON(CH_3)_2$	100% D_2SO_4	.4	.055		3.137, 3.082
NMA[b]	Pure	..		4.0	4.229, 4.129
NMA[b]	100% H_2SO_4	.4		4.2	3.543, 4.429
$HCONHCH_3$[c]	Pure	..		4.8	4.164, 4.104
$HCONHCH_3$	0.1 M HCl	.4			3.569
$HCONHCH_3$	0.1 M NaOH	.4			3.782
$HCONHCH_3$	100% H_2SO_4	.4		5.2	3.219, 3.133

[a] Chemical shifts in p.p.m. from benzene as external reference standard, using 1 mm. Pyrex capillary tube concentric to sample tubes. [b] Spectra determined at 40 Mc. [c] Spectra determined at 60 Mc. [d] Data taken from reference 7.

as proton exchange on nitrogen, (a), or nucleophilic additions across the carbonyl group, (b), increase the rate of rotation about the central

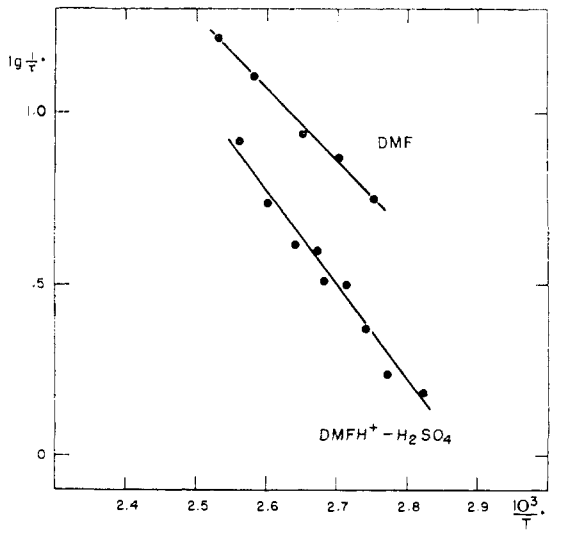


Fig. 2.—Temperature dependence of mean lifetime, τ, between successive rotations of N-methyl proton groups in pure DMF and 0.4 M DMF in 100% H_2SO_4, determined at 60 Mc.

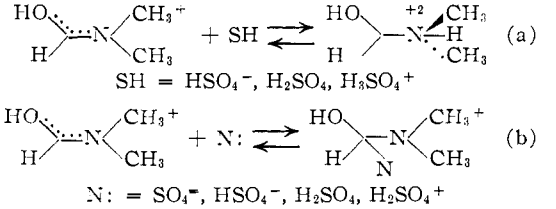
C–N bond in the molecule. These two possibilities can be minimized since coulombic considerations render a second protonation unlikely and the species $H_2SO_4^-$, $SO_4^=$, $H_3SO_4^+$ and HSO_4 are recognized to be extremely poor nucleophiles.[20] Furthermore the barrier of protonated DMF exceeds that of pure DMF by 3 kcal. mole^{-1}.

TABLE II[a]

N.M.R. PARAMETERS AND RESULTS FOR DMF AND $DMFH^+$ IN SULFURIC ACID

	$\delta\omega$[c] rad./sec.	T_2,[b] sec.	A, sec.$^{-1}$	ΔE kcal./mole
DMF pure	33 ± 0.5	0.5	3.4×10^6	9.6 ± 1.5
0.4 M DMF in 100% H_2SO_4	21 ± 0.5	0.5	1.0×10^8	12.7 ± 1.5

[a] Determined at 60 Mc. [b] Transverse relaxation time of single component of collapsing quadruplet. [c] Half the chemical shift between the two N-methyl proton resonances at low rate of rotation.



Collectively these considerations show our value of 12.7 kcal. mole^{-1} to be the minimum barrier to rotation of protonated DMF only to the extent that chemical exchange processes might cause the observed barrier to be lower than the absolute barrier.

(20) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, New York, 1953, p. 202.

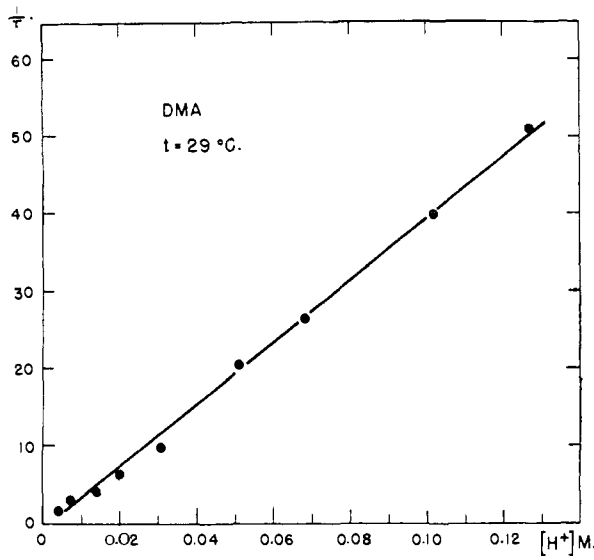
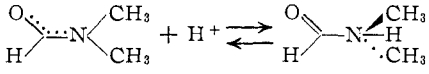


Fig. 3.—Mean lifetime of the N-methyl protons in DMA as a function of hydrogen ion concentration, determined at 60 Mc. DMA concentrations are from left to right: 0.1, 0.2, 0.3, 0.5, 0.8, 0.2, 0.4, 0.8 and 1.1 M, respectively.

DMF in Aqueous Acid Solution.—Qualitative experiments show that when solutions of 0.4 M DMF in 5 N aqueous HBr, HCl and $HClO_4$ are warmed to 43° the methyl proton resonance quadruplets collapse into a single line. Different anions show very little effect on this process. These spectra are temperature reversible within 12 hr. After long periods slow hydrolysis of the amide becomes evident. Since the rates of rotation of pure and protonated DMF are too slow to contribute at this temperature, the effect can be chiefly ascribed to fast proton exchange on nitrogen, (c), the concentration of N-protonated species being extremely low.



(c)

N,N-Dimethylacetamide, DMA.—The N-methyl doublet of DMA collapses reversibly in acid solution below pH 2 at 29°. This collapse has been examined in the pH range 2.4 to 0.9 with (DMA) = 0.1 to 1.1 M in aqueous hydrochloric acid.

The pH dependence for $1/\tau$ is shown in Fig. 3 to fit the relationship

$$\frac{1}{\tau} = 4 \times 10^2 (H^+) \text{ sec.}^{-1} \qquad (1)$$

Following Grunwald, Meiboom and Loewenstein[21] $1/\tau$ is defined in equation 2 where (A)

$$\frac{1}{\tau} \equiv \frac{1}{A}\frac{d(A)}{dt} \qquad (2)$$

indicates the amide concentration.

It has also been found that when strongly acidified solutions of DMA are cooled the N-methyl doublet reappears. The same effect can be accomplished at room temperature by adding dioxane[8] to the acidified DMA solutions. The N-methyl line shape of a 0.5 M solution of DMA in 6 M aqueous hydrochloric acid was then investigated as a function of temperature between − 20 and + 30°C, see Appendix A. The results follow the exponential temperature dependence

$$\frac{1}{\tau} = 1.1 \times 10^7 e^{-(7.3 \pm 0.5) \times 10^3/RT} \qquad (3)$$

The second order rate constant for proton exchange on DMA is very close to the value of 380 M^{-1} sec.$^{-1}$ determined by Berger, Loewenstein and Meiboom for the analogous step with N-methylacetamide. At lower temperatures the exchange protolysis of DMA is slowed down. Thus the solution of DMA in HCl showed an activation energy of 7.3 kcal. mole^{-1}. The frequency factor is probably a function of the hydrogen ion activity. It was not possible to perform the equivalent experiment with a solution of DMA in 100% sulfuric acid since viscosity of the acid ruled out suitable resolution of the N-methyl doublet. The results nevertheless show that DMA protonates predominantly on oxygen.

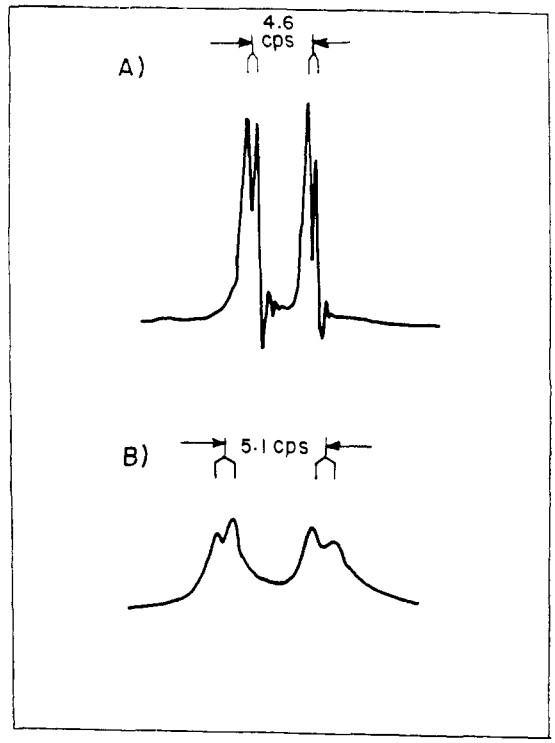


Fig. 4.—N.m.r. spectra for N-methyl protons in NMF: A, Pure NMF; B, 0.4 M NMF in 100% H_2SO_4, determined at 60 Mc., 29°. The magnetic field increases from left to right.

Other Tertiary Amides.—The n.m.r. spectra of several other N,N-dimethylamides have been investigated in acid solution, see Table I. They all behave similarly to DMF.

N-Methylformamide, NMF.—The n.m.r. absorption of NMF consists[16] of a single unresolved line for CH, a broad band for NH, beneath the CH line, and a quadruplet for NCH_3, which is shown separately in Fig. 4. The main splitting is due to coupling between NH and CH_3, while the narrow doublets arise from coupling between formyl and methyl protons. This pattern of lines collapses

(21) E. Grunwald, H. Loewenstein and S. Meiboom, *J. Chem. Phys.*, **27**, 630 (1957).

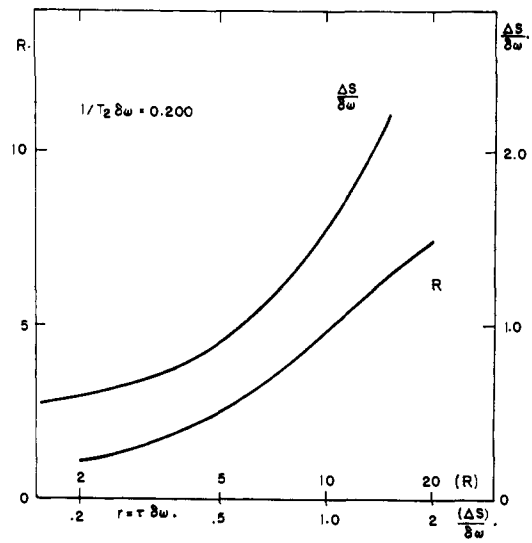


Fig. 5.—Theoretical plots of ΔS and R as a function of τ. Symbols are defined below Table II and Appendix A.

into a single unresolved line in the presence of D_2O, weak acids and weak bases while the NH absorption disappears.

In 100% sulfuric acid the N-methyl splittings return. Comparing this result with pure NMF, the formyl-methyl proton coupling constant increases from 0.4 to 1.1 c.p.s., see Fig. 4A and B.

The site of protonation of N-methylamides may be determined from our data by a line of reasoning similar to that applied above for N,N-dimethylamides. The spectrum of protonated NMF in sulfuric acid is very similar to that of pure NMF; and, as no separate OH line could be found, the results are quite consistent with *O-protonation* together with fast proton exchange on oxygen.

The increase in the formyl-methyl portion coupling constant between NMF and its conjugate acid follows that found for DMF. Possibly the increased double bond character in the two protonated species may account for the change in coupling constants.

By analogy to the results of Berger, Loewenstein and Meiboom with N-methylacetamide,[8] collapse of the N-methyl proton multiplet of NMF in the presence of weak acids and bases may be ascribed to proton exchange processes on nitrogen.

N-Methylacetamide, NMA.—The results for NMA are very similar to those found for NMF; that is, the spectrum of protonated NMA in sulfuric acid closely resembles that of the pure material.

Acetamide.—The NH_2 band of acetamide is broadened by nitrogen quadrupole relaxation as well as proton–nitrogen spin coupling, and the absorption can be observed when the material is dissolved in water *p*H 7 and 100% sulfuric acid. In the latter solvent the ratio of peak areas CH_3/NH_2 is closely 3/2. This finding is confirmed by recent X-ray[22] and neutron[23] diffraction studies of

(22) E. W. Hughes and W. Takei, Report of the Division of Chemistry and Chemical Engineering, California Institute of Technology, 1956–1957, p. 36.

(23) S. W. Peterson and J. E. Worsham, Program and Abstracts, Annual Meeting, American Crystallographic Association, July 19–24, 1959, p. 41.

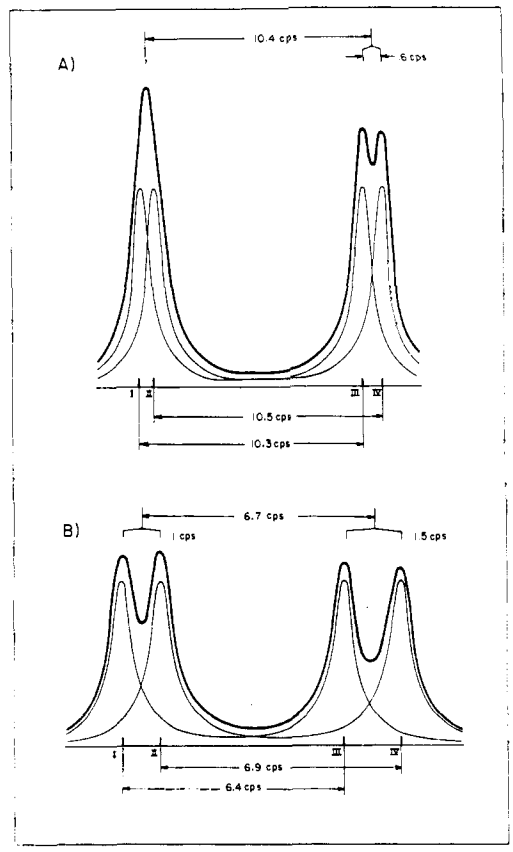


Fig. 6.—Theoretical envelopes for the N-methyl proton resonance of DMF, 60 Mc., 29°: A, Pure DMF; B, 0.4 *M* DMF in 100% H_2SO_4 to fit the experimental spectra of Fig. 1.

the structure of crystalline acetamide hemihydrochloride which establish the acid proton to be located equidistantly on a line between two carbonyl oxygen atoms.

General Considerations

It has been found that the n.m.r. spectra of protonated amides resemble those for the pure amides and in each case this observation is closely in accord with *O-protonation*.

Qualitatively the criteria for hydrogen bonding of amides should follow those found for protonation, hydrogen bonding to oxygen being more favorable than to nitrogen. Similarly an increased barrier to rotation should be found for H-bonded amides over non-associated species.

Intramolecular hydrogen bonding in proteins is assumed to be partially responsible for maintaining the geometrical integrity necessary for biological activity. In addition to holding the system in a specific shape the hydrogen bonds could also strengthen the individual amide linkages which are associated, by analogy with our results.

Appendix A

The collapse of the N-methyl doublet of DMA has been correlated with the mean lifetime, τ, of the N-methyl protons between successive rotations. Theoretical line shapes for such a collapsing doublet have been evaluated from

numerical solutions[24] of Gutowsky's[18] equations for exchange.

In this work τ has been determined for the different solutions studied by comparing experimental line shapes with theoretical ones[24] plotted in Fig. 5.

The parameters of the collapsing doublet used were R, the ratio of maximum to minimum amplitudes and Δs, the width of the collapsed doublet at half amplitude. In these calculations the independent parameters $\delta\omega$ = 32.3 rad. sec.$^{-1}$ and T_2 = 0.17 sec., defined below Table II, were obtained from an aqueous solution of DMA, *p*H 7 at 29°, since it was impossible to reach a low rate of rotation with a solution of DMA in 6 *M* hydrochloric acid before the solution froze. T_2 was evaluated from the line width at half amplitude of the N-methyl components in the absence of exchange.

Corrections for the variation of magnetic field homogeneity were applied by using theoretical curves for different values of T_2.

Appendix B

The values for the activation energies for rotation of DMF and $DMFH^+$ obtained by the methods of Gutowsky[18] or that of Meiboom[19] see Appendix A, are strongly dependent upon the correct choice of the natural line widths of the collapsing lines; furthermore, these lines are assumed not to be multiplets.

Actually the spectra of DMF and $DMFH^+$ show spin-coupling between the N-methyl and formyl protons in both molecular species, and the coupling constants are different in the two cases, the N-methyl resonances at higher fields showing the larger splittings which are assumed to be associated with the methyl groups *trans*[25] to the formyl protons. Any attempt to evaluate activation energies for these species, using as line widths the experimentally determined values, may fail to give the correct values.

It should not be assumed that a given spin-spin multiplet can be well represented by an envelope line unless the multiplet components are broad enough to cancel the structure. For this reason the standard procedure[18,19] for evaluating exchange rates from collapsing single lines has been modified by taking the extra splitting into account.

It is assumed that during an interconversion the spin states of the methyl proton groups do not change, that is, the lower field components of each doublet (lines I and III in Fig. 7), being generated by the same spin states, collapse into one another as do the high field components (lies II and IV in Fig. 6). The over-all process of averaging the resonance line positions is considered as due to the independent collapse of each doublet, the experimental shape being illustrated in Fig. 6 where the spectra of DMF and $DMFH^+$ are reproduced by superposing theoretical line shapes of two simple collapsing doublets[24] using the experimental chemical shift and spin coupling constants. At elevated temperatures these multiplets should collapse into a narrow doublet, being the average of the *cis* and *trans* methyl-formyl proton coupling constants, respectively. Actually our conditions at 200° precluded such resolution.

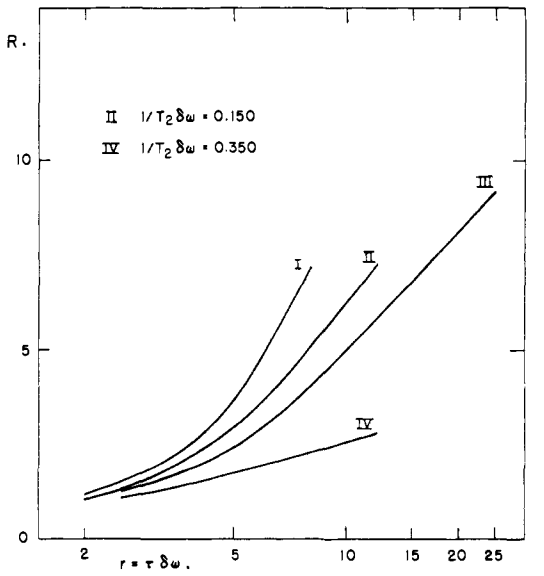


Fig. 7.—Theoretical plots of R for DMF and $DMFH^+$ under different assumptions as a function of τ, see Appendix B.

These theoretical envelopes for the two collapsing doublets have been constructed graphically for several rates of interconversion. Plots of the ratio R, average maximum to central minimum amplitudes, as a function of the mean lifetime thus obtained for DMF and $DMFH^+$ are shown in Fig. 7. Curves II and IV in Fig. 9 refer to the treatment for a simple collapsing doublet for DMF and $DMFH^+$, respectively, where formyl-methyl proton coupling has been neglected. The striking difference between these curves and the ones obtained by taking into account the extra splittings, I for DMF and III for $DMFH^+$, shows the assumption that the doublet can be well represented by a Lorentian line to have severe limitations. The difference starts to be unimportant only when the broadening of the multiplet components exceeds the multiplet splitting.

The remaining procedure follows that for DMA described in Appendix A.

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