TABLE 7

CRITICAL VOLUMES (cc.)

	$n = 6$	(Walter)	Observed
Neon	43.48	49.0	41.74
Argon	77.69	78.7	75.26
Krypton	88.32	81.0	...
Xenon	113.52	112.0	113.8

The critical properties above were calculated algebraically in the usual way, using

$$\left(\frac{\partial A}{\partial V}\right)_T = -p, \left(\frac{\partial p}{\partial V}\right)_T = 0, \left(\frac{\partial^2 p}{\partial V^2}\right)_T = 0.$$

The method of significant structures thus leads to a simple and surprisingly successful reduced equation of state for normal liquids. The deviations from experiment, particularly in the pressure, are such as would arise from insufficient account of clusters of molecules in the saturated vapor. Such clusters are known to exist. Extension of our partition function to abnormal liquids and to metals and molten salts are in progress along lines that have previously been found successful, using the Walter-Eyring partition function.

The authors wish to express appreciation to the National Science Foundation and one of them (N. H.) to the Research Corporation for their generous support.

[1] R. H. Ewell and H. Eyring, *J. Chem. Phys.*, **5**, 726, 1937.
[2] Ralph Livingston, private communication.
[3] J. Walter and H. Eyring, *J. Chem. Phys.*, **9**, 393, 1941.
[4] H. Eyring, J. Walter, and A. E. Stearn, in *Surface Chemistry*, (Washington, D. C.: American Association for the Advancement of Science, 1943), No. 21, p. 88.

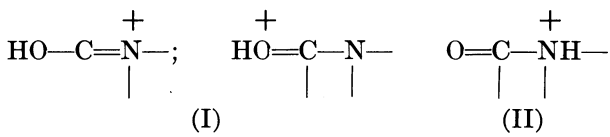
THE MODE OF PROTONATION OF AMIDES

BY GIDEON FRAENKEL AND CARL NIEMANN

GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY,* PASADENA, CALIFORNIA

Communicated May 16, 1958

The relative basicities of oxygen versus nitrogen in amides is a problem which has not been satisfactorily resolved. However, it might be anticipated from considerations of resonance and structural parameters that in strongly acidic solutions the proton will attach to oxygen rather than to nitrogen, to give I rather than II:



(I) (II)

It is generally recognized that amides are monoprotonated in 100 per cent sulfuric acid. For example, O'Brien and Niemann[1] reported *i*-factors of 2.0, 2.7, 2.0,

TABLE 1

CHEMICAL SHIFTS OF AMIDES IN VARIOUS MEDIA*

RCONR₁R₂	SOLVENT	SHIFT				SPLITTING
		Solvent	RCO	NR_1R_2	$\Delta\nu$†	NR_1R_2
$HCON(CH_3)_2$	Pure liquid	...	−117.7	85.9‡	203.6	6.9
				92.0		
	H_2O	2.4	−125.9	75.1‡	201.1	6.7
				81.8		
	12 *M* HCl	−122.1	−143.9	59.5‡	203.4	5.9
				65.4		
	48% HBr	−95.7	−154.6	48.2‡	202.7	5.7
				53.9		
	98% H_2SO_4	−271.3	−141.1	51.0‡	192.1	4.7
				55.7		
	100% D_2SO_4	−280.5§	−144.9	49.4‡	194.3	4.6
				54.0		
$CH_3CON(CH_3)_2$	H_2O	5.9	106.8	68.0‡	38.7	6.0
				74.0		
	D_2O	...	106.8	68.0‡	38.7	6.0
				74.0		
	4 *M* Na_2SO_4 in H_2O	−4.4	98.8	60.4‡	38.4	5.8
				66.2		
	10 *M* $HClO_4$	−85.1	90.6	58.2	33.3	..
	5 *M* $HClO_4$	−24.3	98.8	64.2	34.6	..
	3 *M* $HClO_4$	−15.3	101.8	67.4	34.4	..
	1 *M* $HClO_4$	−3.6	105.4	69.3	36.1	..
$(CH_3)_2CHCON(CH_3)_2$	Pure liquid	..	113.9‡, ‖	76.1‡	..	8.1
			120.9	84.2	..	..
			152.7‡, #	..	..	..
			158.8	..	..	..
	100% H_2SO_4	−261.6	137.6‡, #	53.0‡	..	3.0
			124.9	56.0	..	
	100% D_2SO_4	−281.5§	135.3‡, #	49.0‡	..	2.7
			128.9	51.7	..	
$C_3H_5CON(CH_3)_2$	Pure liquid	...	162.5‡, **	65.3‡	...	10.6
			169.1	75.9	..	..
			109.4††, ‖	..	..	..
			115.7	..	..	..
			122.1	..	..	..
			127.6	..	..	..
			134.1	..	..	..
			140.6	..	..	..
	100% H_2SO_4	−267.5	134.0‡, **	45.0‡	..	7.3
			128.8	52.3		
$CH_3CONHCH_3$	Pure liquid	...	124.7	93.5‡	−118.3‡‡	4.0
				97.5		
	H_2O	1.8	113.4	82.5‡	..	3.8
				86.3	..	
	D_2O	3.6§	113.3	83.4	..	
	0.1 *M* HCl	...	95.4	69.4	..	
	0.1 *M* NaOH	...	111.0	81.9	..	
	60% $HClO_4$	−85.1	96.5	71.4	..	
	1% $HClO_4$	−5.2	112.1	82.1	..	
	100% H_2SO_4	−271.9	87.7	69.7‡	−144.8‡‡	4.2
				65.5	...	
	100% D_2SO_4	−286.5§	84.7	55.9	..	
CH_3CONH_2	H_2O	5.0	112.8	..	−98.0‡‡	
	100% H_2SO_4	−289.7	87.4	..	−147.9‡‡	

* In cycles from H_2O at 40 megacycles.
† Intramolecular chemical shift between N-methyl hydrogens and hydrogens of R group except where otherwise noted.
‡ Doublet.
§ Hydrogen of exchange and/or impurity.
‖ Methine hydrogen.
Methyl hydrogens.
** Methylene hydrogens.
†† Sextuplet.
‡‡ N-H chemical shift.

2.9, and 1.9 for benzamide, glycinamide, trichloroacetamide, benzoylglycinamide, and phthalimide, respectively, in this solvent. Similarly, in this study we have found the *i*-factors of N,N-dimethylformamide, N,N-dimethylacetamide, and acetamide to be 2.1, 2.1, and 2.0, respectively. Thus the problem is to locate the locus of protonation in singly protonated primary, secondary, and tertiary amides.

Tertiary Amides.—It was thought that one might determine the site of protonation of a representative tertiary amide by examining the nuclear magnetic resonance (n-m-r) spectra of N,N-dimethylformamide in strongly acidic solutions. The pure liquid compound, as well as solutions of it in carbon tetrachloride and in water, has an n-m-r spectrum of three lines, one for the formyl hydrogen and a doublet for the methyl hydrogens. This splitting has been traced to a chemical shift between the methyl groups which results from hindered rotation about the carbon-nitrogen bond considered in I and II.[2] In strong acids, if the proton attached to oxygen one might expect retention of the methyl doublet since the carbon-nitrogen bond would still have considerable double-bond character as indicated in I. On the other hand, protonation on nitrogen should yield free rotation about the carbon-nitrogen bond and therefore collapse of the doublet. In fact, the methyl splitting of N,N-dimethylformamide was preserved in a variety of strong acids, e.g., 12 *M* HCl, 48 per cent HBr, 0.1–10 *M* $HClO_4$, including 100 per cent H_2SO_4 and D_2SO_4 (cf. Table 1).[3]

It might be argued, in the case of the hydrogen acids, that N-protonation had occurred, the N-H proton splitting the methyl hydrogens by spin-coupling. Deuterium couples very weakly,[4] especially through nitrogen.[5] Accordingly, the n-m-r spectrum of N,N-dimethylformamide was observed in 100 per cent D_2SO_4. The magnitude of the methyl splitting in this as well as in all other media tried was relatively constant throughout. Whereas the absolute positions of the peaks varied from one solvent to the next, the difference between the chemical shift of formyl hydrogen and the methyl hydrogens was substantially constant, indicating that the methyl hydrogens and the formyl hydrogen were equidistant from the center of charge on the molecule. The behavior of N,N-dimethylcyclopropylcarboxamide and N,N-dimethylisobutyramide also fell into this pattern. The methyl doublet of N,N-dimethylacetamide collapses reversibly in acidic solutions, from 0.1 *M* $HClO_4$ upward (cf. Table 1).

Secondary Amides.—The n-m-r absorption spectrum of N-methylacetamide in the liquid state, in nonpolar media, and in water at pH 7 consists of three peaks, a singlet for acetyl methyl and a doublet for the N-methyl hydrogens, which collapses to a singlet in the presence of most acids and bases and in D_2O. The effect of the first two types of solvents has been traced to a rapid exchange between N-H and solvent, i.e., the relaxation time for the N-methyl proton spins must exceed the half-life of N-H exchange.[5, 6] Since deuterium spin-couples but weakly,[4] N-deutero-N-methylacetamide would be expected to yield a single peak for the N-methyl hydrogens. The N-H peak itself is weak and quadrupole-broadened and is observable only in the pure compound.

In 96–100 per cent H_2SO_4 the methyl doublet returns, as does the N-H absorption. The doublet peaks are of equal amplitude with about the same separation as in the pure liquid. In D_2SO_4 the N-methyl doublet again collapses.

The above results again are consistent with O-protonation. There can be only

one proton on nitrogen, the other must be on oxygen. Acetylglycine shows the same behavior. It can also be concluded that the bisulfate ion is a poor base for exchanging the N-H proton of secondary amides in sulfuric acid.

Primary Amides.—The N-H proton magnetic resonance absorption of acetamide has been observed in saturated aqueous solutions at pH 7 and in 100 per cent sulfuric acid. Here, also, exchange of the N-H proton in sulfuric acid appears to be slow in comparison with its relaxation time. By measuring the areas under the absorption peaks it has been possible tentatively to assign O-protonation of acetamide in 100 per cent sulfuric acid. This interpretation is in accord with that of Hantzch, based upon ultraviolet spectroscopy,[7] and that of Huisgen and Brade,[8] based upon potentiometric pK determinations.

Experimental.—All spectra were determined with the Varian 4300 B, 40-mc., 9,400-gauss n-m-r spectrometer, equipped with spinner and superstabilizer. Samples were sealed in 5-mm. o.d. Pyrex tubes. Chemical shifts were calibrated by a combination of the method of side bands[9] and the use of toluene markers in capillary tubes as secondary standards. The cryoscopic measurements in 100 per cent sulfuric acid were conducted as described by O'Brien and Niemann.[1] The N,N-dimethylcyclopropylcarboxamide was kindly supplied by Mr. David Schuster. All other materials were obtained by the purification of samples of commercial origin.

The authors are indebted to Professor J. D. Roberts for his assistance during the course of this investigation.

* Contribution No. 2337.

[1] J. L. O'Brien and C. Niemann, *J. Am. Chem. Soc.*, **79**, 1386, 1957.

[2] H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228, 1956.

[3] This phenomena has also been observed by Dr. W. D. Phillips, of the Central Research Department, E. I. du Pont de Nemours and Co., Wilmington, Delaware.

[4] E. R. Andrew, *Nuclear Magnetic Resonance* (Cambridge: Cambridge University Press, 1956), p. 145.

[5] G. Fraenkel, unpublished observations.

[6] H. S. Gutowsky, private communication.

[7] A. Hantzsch, *Ber.*, **64**, 661, 1931.

[8] R. Huisgen and H. Brade, *Ber.*, **90**, 432, 1957.

[9] J. T. Arnold and M. E. Packard, *J. Chem. Phys.*, **19**, 1608, 1951.

---

*OCCURRENCE OF CHROMOSOMAL ABERRATIONS IN PRE-SPERMATOCYTIC CELLS OF IRRADIATED MALE MICE**

BY A. B. GRIFFEN

ROSCOE B. JACKSON MEMORIAL LABORATORY, BAR HARBOR, MAINE

Communicated by C. C. Little, May 23, 1958

In both insects and mammals, only sperm which are mature at the time of irradiation are considered to form F_1 individuals, which bear major chromosome aberrations and particularly translocations. In the male mouse there is an initial period of approximately 1 month after the irradiation during which fertility remains good; offspring sired during this period bear appreciable numbers of genetic effects,