

one can infer by analogy that regular behavior is to be expected.

Because of the frequent ease with which reaction rates can be measured as a function of mineral acid concentration, because of the present considerable accuracy of the empirical criterion of mechanism and the probability that it will become more accurate with the passage of time, kinetic response to changing acid concentration deserves a restoration of status as a criterion of mechanism.

**Acknowledgments.**—Financial support from the Office of Ordnance Research, U. S. Army, the National Science Foundation, the John Simon Guggenheim Memorial Foundation and the U. S.

State Department (Fulbright program) is greatly appreciated. The manuscript was written in the Institut für organische Chemie der Universität München by virtue of the hospitality of Professor Rolf Huisgen.

Development of the ideas, arguments and procedures presented in these four papers has benefited from constructive criticism by many chemists. An incomplete list includes the names of E. Bunzel, C. A. Bunton, J. O. Edwards, M. Eigen, E. Grunwald, Sir Christopher Ingold, A. J. Kresge, H. Kuivila, H. Kwart, F. A. Long, K. V. Nahabedian, D. S. Noyce, F. Olsen, W. M. Schubert, C. G. Swain and C. A. Vernon.

[CONTRIBUTION FROM THE PHYSICAL CHEMISTRY LABORATORY OF OXFORD UNIVERSITY, OXFORD, ENG., AND THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY, SCHOOL OF PHARMACY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CALIF.]

## Structure of Salts of N,N-Dimethylacetamide and N,N-Di(*n*)butylacetamide<sup>1</sup>

BY W. D. KUMLER

RECEIVED JUNE 27, 1961

The infrared spectra of N,N-dimethylacetamide, N,N-di(*n*)butylacetamide, their hydrochlorides and deuteriochlorides have been measured. The spectra are interpreted on the assumption that the proton goes to oxygen.

### Introduction

Pauling<sup>2</sup> calculated that the basic dissociation constant of amides would be  $1 \times 10^{-20}$  if the proton goes to nitrogen and commented "the value for the base constant  $1 \times 10^{-20}$  is so small as to be without significance, except to show that the amides do not form salts with acids by adding a proton to the amino group." This calculation did not take into account the inductive effect of the carbonyl group

which should be considered. The  $pK_a$  of  $\text{CH}_3\text{-C}(=\text{O})\text{-NH}_2^+$  can be estimated by analogy to be 5.0 from the

values for acetic acid, 4.76; glycolic, 3.83; acetoacetic, 3.38; ammonium ion, 9.25; and hydroxyammonium ion, 5.96. The corresponding  $K_b$  for

$\text{CH}_3\text{-C}(=\text{O})\text{-NH}_2$  without resonance would be  $10^{-9}$ . Since acetamide has 21 kcal. resonance energy the  $K_b$  of the compound would be  $RT \ln 10^{-9}/21,000 = 10^{-24.3}$ , a smaller value than that above, making N-protonation in amides even more unlikely.

It has been concluded from a number of n.m.r. studies<sup>3-7</sup> that the proton goes mainly on oxygen in agreement with this calculation, but some of these studies<sup>5,7</sup> have found a fast proton ex-

change on nitrogen but with the concentration of the N-protonated species undetectably small.

Other studies using ultraviolet and infrared<sup>8-10</sup> and dissociation constant<sup>11</sup> data have concluded the proton goes on the nitrogen.

Since the previous evidence was on urea or unsubstituted or monosubstituted amides with one or more hydrogens on the nitrogen, it was of interest to measure N-disubstituted amides where only one proton or deuteron would be present in the hydrochloride or deuteriochloride.

### Results

The spectra of N,N-dimethylacetamide and N,N-di(*n*)butylacetamide, together with their hydrochlorides and deuteriochlorides shown in Fig. 1, indicate that the spectra of the salts are quite different from those of the free amides particularly in the 4.0 to 6.5  $\mu$  region. Conclusions from the infrared spectra, including our own, that the proton goes to nitrogen have been based largely on the assumption that the band around 6  $\mu$  in the salts arises from a carbonyl vibration.

While it is probably an oversimplification to consider any single vibration of a pair of atoms in the -CO-NH system as being exclusively re-

(1) Presented in part at the 137th National Meeting of the American Chemical Society at Cleveland, Ohio, April, 1960.

(2) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., Third Edition, 1960, p. 281.

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

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

(5) G. Fraenkel and C. Niemann, *Proc. Natl. Acad. Sci.*, **44**, 688 (1958).

(6) A. Berger, A. Loewenstein and S. Meiboom, *J. Am. Chem. Soc.*, **81**, 62 (1959).

(7) G. Fraenkel and C. Franconi, *ibid.*, **82**, 4478 (1960).

(8) S. Mizushima, T. Simanouti, S. Nagakura, E. Kuratani, M. Tsuboi, H. Baba and O. Fujioka, *ibid.*, **72**, 3420 (1950). We have repeated this work on N-methylacetamide and like these workers find a band at 2695 Å. in 5 N HCl. However, when the compound was carefully purified as reported by Bello (J. Bello, *J. Phys. Chem.*, **60**, 1341 (1956)) no band was found. The band therefore results from an impurity and gives no evidence that the proton is on nitrogen in the salt of N-methylacetamide.

(9) M. Davies and L. Hopkins, *Trans. Faraday Soc.*, **53**, 1563 (1957).

(10) E. Spinner, *Spectrochim. Acta*, **95** (1959), and *J. Phys. Chem.*, **64**, 275 (1960).

(11) J. T. Edward, H. S. Chang, K. Ajatis and R. Stewart, *Can. J. Chem.*, **38**, 1518 (1960).



There are humps on the long wave length side of the bands in the 4.0 to 5.3  $\mu$  region by adding frequencies of some of the longer wave length bands, it seems unlikely that the intensity of these combination bands would be as great as those observed. Also, in N,N-dimethylacetamide itself one can add up low frequency bands in the same way which should give bands in this region if this is a factor, but there is no evidence of any absorption at all in this region in the free amide. Since we know of no reason why the salts should behave differently from the free amide with respect to combination bands, we are at a loss to account for the bands in this region.

There is a new band in the deuteriochloride at 7.72  $\mu$  which evidently arises from the  $-\overset{+}{\text{O}}=\text{D} \leftrightarrow -\text{O}-\text{D}$  bending mode, since the ratio of the frequency of the band that disappeared in the hydrochloride to the frequency of this band is  $1770 \text{ cm.}^{-1} / 1295 \text{ cm.}^{-1} = 1.37$ .

The spectra of N,N-di(*n*)butylacetamide and its hydrochloride and deuteriochloride in the 4.0 to 6.5  $\mu$  region are similar to those of the dimethyl compound. Thus, the free amide has a narrow band at 6.10  $\mu$  due to the carbon absorption and no additional bands down to 4.0  $\mu$ . The hydrochloride has a broad band at 6.05  $\mu$  with shoulders at 6.25 and 6.45  $\mu$ , a band at 5.70  $\mu$ , one at 5.10  $\mu$  with shoulders at 4.80 and 4.25  $\mu$ . The deuteriochloride has a band at 6.05  $\mu$  with shoulders at 6.30 and 6.50  $\mu$ , a band at 5.15  $\mu$  with shoulders at 4.85 and 4.30  $\mu$ . The band at 5.70  $\mu$  in the hydrochloride has virtually disappeared in the deuteriochloride so this can be attributed to the OH band. The whole region from 3.70 to 5.50  $\mu$  in the hydrochloride gives evidence of more absorption than it does in the deuteriochloride so this is attributed to the OH stretch. The shoulders at 6.30 and 6.50  $\mu$  in the spectra of the salts are attributed to the carbon-oxygen stretch in the  $\overset{+}{\text{C}}=\text{OH} \leftrightarrow \text{C}-\text{OH}$  group.

The general similarity of the spectra of the salts of N,N-di(*n*)butylacetamide with that of N,N-

dimethylacetamide in the region 4.0 to 6.5  $\mu$  is a reason for considering that the same kind of protonation, namely O-protonation, is present in both cases.

The greater complexity of the spectra from 7 to 9  $\mu$  in the N,N-di(*n*)butylacetamide and its salts presumably arises from the increased modes possible in the butyl groups compared to methyl.

The strong band at 14.62  $\mu$  in the deuterium salt of N,N-di(*n*)butylacetamide which is not present either in the hydrochloride or the free amide is apparently associated with an  $=\overset{+}{\text{O}}\text{D}$  bending mode, perhaps an out-of-plane mode. There is an indication of a similar band off scale in N,N-dimethylacetamide deuteriochloride for the curve decreased 10 transmittance % units from 14.7 to 15.0  $\mu$ , suggesting a band beyond 15  $\mu$ .

### Experimental

The salts were made by passing dry HCl or dry DCl into a benzene solution of the amide. The salts precipitated and the benzene and excess HCl or DCl were removed under vacuum. The resulting white solids were very hygroscopic. The equivalent weights were determined by quickly removing a portion from a stoppered tube and titrating with base. The equivalent weights are given in Table I.

TABLE I

Compound	Equivalent weight	
	Obsd.	Theor.
N,N-Dimethylacetamide HCl	122	123.4
N,N-Dimethylacetamide DCl	124	124.4
N,N-Di( <i>n</i> )butylacetamide HCl	208	207.8
N,N-Di( <i>n</i> )butylacetamide DCl	207	208.8

An attempt was made to measure the salts in KBr but the spectra always showed the presence of water. By making up mulls in a dry-box kept free of moisture by circulating nitrogen over molecular sieves it was found that spectra using Nujol or perfluorokerosene could be obtained that gave no evidence of the presence of water.

The spectra were measured on a Perkin-Elmer model 21 recording infrared spectrophotometer with a sodium chloride prism.

The author is indebted to Dr. L. E. Sutton, Dr. H. W. Thompson and Dr. G. D. Meakins for use of their laboratory facilities and to them and Dr. L. J. Bellamy for helpful discussions. We also thank Mr. Michael K. Hrenoff for running some of the spectra.