Structure, and Infrared and Ultraviolet Spectra of Protonated Dimethylacetamide

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The *X*-ray crystal structure of the title compound was determined by the heavy-atom method from diffractometer data and refined to *R* 0.052 for 621 independent reflections. Crystals of *NN'*-dimethylacetamide hydrochloride (*NN'*-dimethylacetamidonium chloride) are monoclinic, space group $P2_1$ with $Z = 2$ in a unit cell of dimensions $a = 7.343(7)$, $b = 6.890(7)$, $c = 6.765(7)$ Å, $\beta = 97.2(1)°$. A difference-Fourier synthesis revealed the site of protonation of the amide to be the oxygen atom, confirming much indirect evidence. The i.r. spectrum for dichloromethane solution shows an absorption band at 1 670 cm^{-1}, not present in that of the amide base, and assigned to ν(C–N). The u.v. spectrum for dichloromethane solution shows two weak absorption bands at 360 and 315 nm, whereas in aqueous solution there is only a single weak absorption band at 330 nm. Upon acidification of the aqueous solution, the u.v. spectrum of the protonated amide became identical with that obtained for dichloromethane solution.

AMIDES can be protonated potentially at either the carbonyl oxygen atom or the nitrogen. The partial double-bond character of the peptide linkage $\mathrm{N}\overset{\cdots}{-}\mathrm{C}\overset{\cdots}{-}\mathrm{O}$ makes the oxygen atom the site of a partial negative charge. It would therefore be expected that cations interact with amides *via* the carbonyl oxygen atom, and in fact, most experimental results have been interpreted in favour of protonation at oxygen.[1,2] I.r. spectral evidence has indicated that small cations such as lithium interact strongly with amides through the carbonyl oxygen,[3,4] Perhaps the most direct evidence for oxygen protonation has been the observation of ^{1}H n.m.r. signals from the attached hydrogen atom.[5] *X*-Ray analysis of the solid hydrochloride of *NN'*-dimethylacetamide clearly has shown the site of the attached proton to be oxygen, and we have interpreted the i.r. and u.v. spectra in terms of this structure.

EXPERIMENTAL

The *NN'*-dimethylacetamidonium chloride crystals were obtained by passing hydrogen chloride through pure *NN'*-dimethylacetamide. The reaction is exothermic and small crystals which quickly formed were recrystallized from dichloromethane. Although the salt is hygroscopic it appeared to be stable in aqueous solutions, in contrast to the hydrochloride of formamide which readily hydrolyses. Crystals were transferred to *X*-ray tubes in a dry box.

X-Ray data collection was carried out on a Siemens AED atomatic single-crystal diffractometer equipped with a digital computer, scintillation counter, and pulse-height analyser. Nickel-filtered Cu-K_α radiation was used. The θ—2θ mode with the five-measurement technique was employed (Siemens AED manual, vol. 7). A fixed symmetrical scan range of 60° from the computed Cu-K_α peak was used. Intensity data were collected for the independent reflections up to 60°. The intensity of a standard reflection measured at regular intervals to monitor crystal stability and crystal orientation remained essentially constant (within 5%) throughout the run. A total of 731 independent reflections were collected, of which 110 were not considered, having intensities $I < 3\sigma(I)$. Data were corrected for Lorentz and polarization effects, but not for absorption because of the small size of the crystals used.

I.r. spectra were recorded on a Beckman 4250 i.r. spectrophotometer using calcium fluoride cells (Barnes Engineering). U.v. spectra were recorded on a Cary 14 spectrophotometer with quartz cells. Solutions of the amide salt in dichloromethane were made up in a dry box.

X-Ray Analysis.—Crystal data. $C_4H_{10}ClNO$, $M = 123.45$. Monoclinic, $a = 7.343(7)$, $b = 6.890(7)$, $c = 6.765(7)$ Å, $\beta = 97.2(1)°$, $U = 339.5$ Å^3, $D_m = 1.20$, $Z = 2$, $D_c = 1.207$. Space group $P2_1$. Cu-K_α radiation, $\lambda = 1.541\,8$ Å; $\eta(\text{Cu-}K_\alpha) = 6.485\,9 \times 10^7$ cm^{-1}.

Single crystals of *NN'*-dimethylacetamidonium chloride suitable for *X*-ray diffraction analysis were obtained as already described. Preliminary Weisenberg rotation photographs indicated the monoclinic system and the systematic absence of the reflections 0*k*0 with *k* odd suggest the $P2_1$ or the $P2_1/m$ space groups. The value of D_m indicated that only two formula units, $C_4H_{10}NOCl$, are contained in the unit cell (see Figure 1). If the molecule is planar and lies in the mirror plane with hydrogen atoms symmetrically distributed with respect to the mirror plane of the molecule, the space group should be $P2_1/m$, otherwise it is $P2_1$. Lattice constants together with their estimated standard deviations were determined from a least-squares refinement[6] of the setting angles (θ, φ) of twelve high-angle reflections on an automated diffractometer by use of Cu-K_α radiation.

The structure was solved by the heavy-atom method. The position of the chlorine atom was obtained from the Harker section of the Patterson map, and its co-ordinates refined in the space group $P2_1/m$ with two cycles of full-matrix least-squares (*R* 0.46). In the subsequent Fourier synthesis the positions of all the non-hydrogen atoms of the molecule were distinctly located. They nearly correspond to a planar molecule (small deviations were however already evident).

At this stage two refinements were carried out in the two possible space groups $P2_1$ and $P2_1/m$ (in this latter case the co-ordinates of the atoms were adjusted to give a completely planar molecule). At convergence, after a few cycles of full-matrix least-squares, the resulting *R* factor was much higher for space group $P2_1/m$ (0.093) with the molecule fully planar and lying on the mirror plane, than that obtained in space group $P2_1$ (0.075) in which the crystallographic planarity of the molecule did not necessarily need to be maintained. According to the Hamilton test,[7] these *R* values in the two space groups enable rejection at a significance level <0.005 the hypothesis that the space group is actually $P2_1/m$.

RESULTS AND DISCUSSION

The first four peaks in the subsequent difference-Fourier synthesis clearly corresponded to the positions of four hydrogen atoms linked to the oxygen and C(4) atoms. The positions of the three hydrogen atoms linked to C(4) corresponded to the staggering of the C–H bonds with respect to the C(1)–O bond.

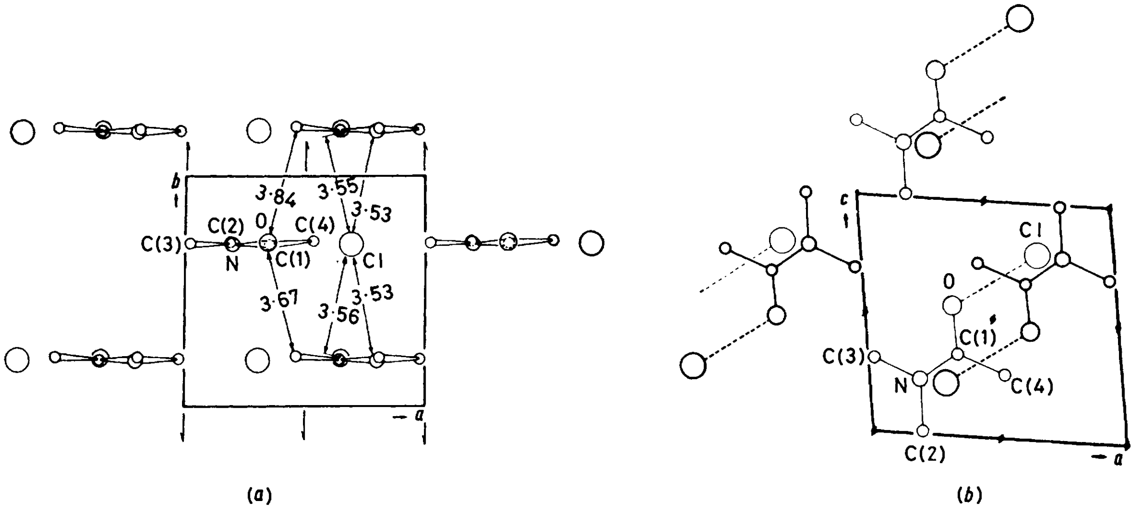

FIGURE 1 Mode of packing of the molecules in the crystal as viewed down (*a*) the *c* and (*b*) the *b* axis. Some of the shorter interatomic contacts are given

Indications on the possible positions of the other hydrogen atoms, those linked to the C(2) and C(3) atoms, were obtained from much smaller peaks of the same difference-Fourier. Even though the C–H distances were rather long (1.4 Å), the stereochemistry seemed reasonable since in both methyl groups one hydrogen was lying almost in the plane of the molecule, while the others were one above and one below that plane. The positional parameters of these six hydrogen atoms were therefore obtained from the previously mentioned difference-Fourier peaks by moving along the C · · · H vector to the predetermined distance of 1.0 Å. All parameters were refined in the last three cycles including those involving hydrogen atoms. The refinement was ended when the maximum shifts in the atomic coordinates and anisotropic thermal factors of the non-hydrogen atoms were $<0.3\sigma$. The final R value was 0.052. Final atom parameters, together with their estimated standard deviations, are reported in Table 1.

TABLE 1

Final atom parameters, with estimated standard deviations in parentheses

	x/a	y/b	z/c
Cl	0.696 3(1)	0.699 7(0)	0.779 9(1)
N	0.200 9(4)	0.699 2(11)	0.228 8(5)
O	0.347 5(3)	0.703 0(14)	0.535 6(4)
C(1)	0.354 8(5)	0.698 8(12)	0.344 1(5)
C(2)	0.196 4(7)	0.704 7(18)	0.009 9(6)
C(3)	0.027 5(6)	0.695 7(18)	0.308 4(8)
C(4)	0.534 3(6)	0.715 8(14)	0.269 4(6)
H(1)[C(2)]	0.061(6)	0.696(21)	−0.044(7)
H(2)[C(2)]	0.262(1)	0.581(11)	−0.021(11)
H(3)[C(2)]	0.257(1)	0.810(12)	0.013(12)
H(1)[C(3)]	0.036(6)	0.653(9)	0.448(7)
H(2)[C(3)]	−0.056(12)	0.604(14)	0.249(12)
H(3)[C(3)]	−0.051(9)	0.800(11)	0.260(10)
H(1)[C(4)]	0.631(7)	0.757(8)	0.363(7)
H(2)[C(4)]	0.548(9)	0.590(10)	0.203(9)
H(3)[C(4)]	0.542(11)	0.816(13)	0.206(12)
H(O)	0.459(6)	0.729(10)	0.607(6)

In the final stages of the refinement process, the weighting scheme of ref. 8 was followed.

Figure 2 depicts the molecular model viewed perpendicular to the molecular plane, and shows all relevant bond lengths and angles. With the exceptions of the chlorine atom and some of the hydrogen atoms the molecule is essentially planar. Distances of relevant atoms from the least-squares plane passing through the six heavy atoms are given in Table 2.

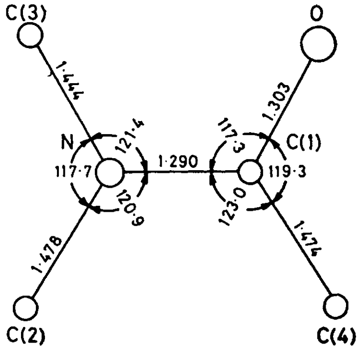

FIGURE 2 Molecular model of the *NN'*-dimethylacetamidonium cation showing bond lengths and angles; estimated standard deviations are 0.006 Å and 0.5°. Internal rotation angles about N–C(1) are: C(3)–N–C(1)–O −3, C(3)–N–C(1)–C(4) 184, C(2)–N–C(1)–O 177, C(2)–N–C(1)–C(4) 4, and C(2)–N–C(1)–O 177°

The molecular plane is inclined with respect to the plane *ac* by 2°. The C(1)–O bond length (1.30 Å) is larger than the typical C–O double bond, which in amides is 1.23 Å.[9] On the other hand, the C(1)–N bond length (1.29 Å) is much shorter than that (1.33 Å) usually found in amides.[9] The Cl···O distance (2.86 Å) indicates the presence of a strong hydrogen bond between these two atoms. This evidence clearly points to the existence of the enolic cation $Me_2N^+{:}C(OH)Me$ as being by far the major contributor in the solid state. The ions in the crystal lattice are held together by electrostatic interactions and hydrogen bonds as shown in Figure 1. Final atom parameters (fractional coordinates and thermal factors) together with their estimated standard deviations are listed in Supplementary Publication No. SUP 22596 (5 pp.).*

TABLE 2

Atomic distances (Å) from the molecular plane passing through N, O, C(1)—(4)

Equation of plane (referred to orthogonal axes):

$$0.0343x - 0.9993y - 0.0118z - 4.8004 = 0$$

Distances: N 0.012, O −0.011, C(1) 0.041, C(2) −0.003, C(3) −0.016, C(4) −0.023, Cl 0.074, HO −0.17, H(1)[C(2)] 0.03, H(2)[C(2)] 0.87, H(3)[C(2)] −0.71, H(1)[C(3)] 0.26, H(2)[C(3)] 0.60, H(3)[C(3)] −0.75, H(1)[C(4)] −0.29, H(2)[C(4)] 0.85, H(3)[C(4)] −0.70

The i.r. spectrum of the solid hydrochloride in a potassium bromide pellet was identical with that for solutions of dimethylacetamidonium chloride in polar organic solvents such as dichloromethane and nitromethane. Since the *X*-ray analysis indicated the solid to be *O*-protonated, it was assumed that the solution spectrum was representative of the *O*-protonated molecule. This spectrum was similar to that of dimethylacetamide in dichloromethane, the most obvious difference being in the 1 600—1 700 cm^{-1} region. The i.r. spectrum of dimethylacetamide in this region exhibited a strong carbonyl stretching band at 1 640 cm^{-1}, whereas that of dimethylacetamidonium chloride had an asymmetric band centred at 1 670 cm^{-1}. This asymmetry could well be due to some free amide present in the solution. When the *NN'*-dimethylacetamide was protonated with DCl, the band at 1 670 cm^{-1} was not shifted, ruling out the possibility that this absorption band was due to an O–H (or O–D) bend. I.r. absorption bands in this region have also been observed in aliphatic Schiff bases (RCH:NR) and oximes (>C:N·OH) and have been attributed to the C=N stretch.[10-12] The i.r. spectrum of the protonated amide in D_2O was surprising in that the 1 670 cm^{-1} band was still present. However, a new absorption band at 1 610 cm^{-1} appeared, which is characteristic of *NN'*-dimethylacetamide in D_2O. When the pH of the solution was increased, the intensity of the absorption band at 1 670 cm^{-1} decreased and that of the band at 1 610 cm^{-1} increased. When the pH of the solution was decreased the converse occurred. These spectra are illustrated in Figure 3. Clearly these two absorption bands represent species obeying the equilibrium:

$$D_2O + DMAH^+ \rightleftharpoons DMA + D_2HO^+$$

Similar observations have also been made for *N*-methylacetamidonium chloride solutions in D_2O. Combelas *et al.*[12] have reported an i.r. and Raman spectroscopic investigation on *NN'*-dimethylformamide, and their results are in agreement with ours; they also assign an absorption band around 1 720 cm^{-1} to ν(C=N).

The u.v. spectrum of the protonated amide in dichloromethane in the region 400—200 nm showed two weak absorption bands at 360 and 315 nm and a strong band beginning at *ca.* 280 nm, continuing to the limit of the spectrometer. This latter absorption band may be due to the intense π–π* absorption of free amide which could be present in small quantities. The two weak absorption bands were considered to be characteristic of the *O*-protonated dimethylacetamide. The u.v. spectrum of dimethylacetamide over the same region shows only the broad intense π–π* transition beginning at *ca.* 300 nm and continuing to the limit of the spectrometer.

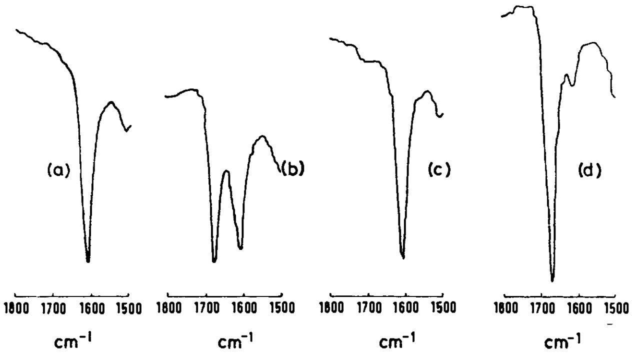

FIGURE 3 (a) I.r. spectrum of *NN'*-dimethylacetamide in D_2O. The ν(C=O) absorption band is shifted to 1 610 cm^{-1} through hydrogen-bonding with solvent. (b) Spectrum of the protonated amide showing the ν(C=N) stretch absorption at 1 670 and the ν(C=O) stretch absorption at 1 610 cm^{-1} in D_2O. (c) As pH is increased the ν(C=O) absorption band becomes predominant. (d) As pH is decreased, the ν(C=N) stretch absorption becomes predominant

The u.v. spectrum of an aqueous solution of the protonated *NN'*-dimethylacetamide showed only a single weak absorption band at 330 nm and a strong band beginning at *ca.* 280 nm. However, when the solution was acidified with hydrochloric acid, the spectrum obtained was characteristic of that observed when the hydrochloride salt was dissolved in dichloromethane. When the solution was made basic, the u.v. spectrum resembled that of an aqueous solution of *NN'*-dimethylacetamide, exhibiting only the intense π–π* band at 280 nm. These three u.v. spectra are illustrated in Figure 4. Depending upon the pH, there can be three different species present in the aqueous solution to greater or lesser extents. The *n*–π* transition in the carbonyl group of amides occurs at shorter wavelengths than in that of acetone owing to destabilization of the excited π* level by resonance in the molecule.[13] The weak band observed at 330 nm in the u.v. spectrum of an aqueous solution of the protonated amide is probably the *n*–π* transition due to small amounts of the *N*-protonated species. If the molar absorptivity of the *n*–π* absorption of the *N*-

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protonated amide is similar to that of acetone, then a Beer's law calculation indicates only *ca.* 0.1% of the salt to be present in the *N*-protonated form; a similar conclusion was expressed by Benderly and Rosenheck.[14]

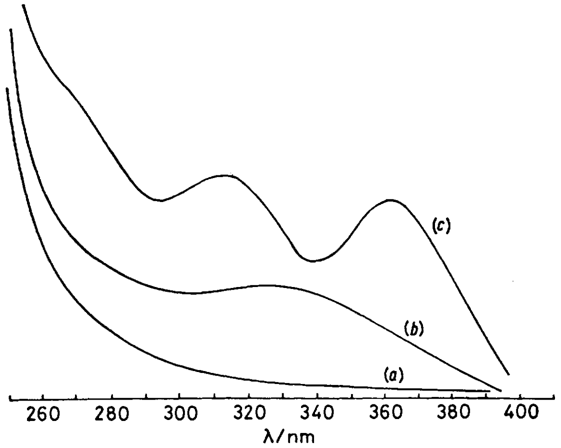

FIGURE 4 (*a*) U.v. spectrum of an aqueous solution of the free amide. The band beginning at 280 mn is the intense π–π^* transition. (*b*) An aqueous solution of the protonated amide shows the weak n–π^* absorption band due to small equilibrium amounts of the nitrogen protonated base. (*c*) At lower pH values, the spectrum is characteristic of the oxygen-protonated cation and is identical with that of the protonated amide in dichloromethane

The site of protonation of amides has been investigated by n.m.r. spectroscopy[5,15,16] and the results were all interpreted in favour of *O*-protonation. Our n.m.r. data for dimethylacetamide hydrochloride in dichloromethane showed a sharp singlet resonance at 12 p.p.m. downfield from tetramethylsilane, typical of an acidic proton. Liler[17,18] has investigated the u.v. spectra of benzamide in sulphuric acid solutions and his conclusions about the site of protonation are in qualitative agreement with ours. In the solid state, in non-aqueous solutions, and aqueous solutions at low pH the *O*-protonated form is the dominant one. In the higher pH range some *N*-protonation is evident.

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