

The structure of protonated amides and ureas and their thio analogues

M. J. JANSSEN

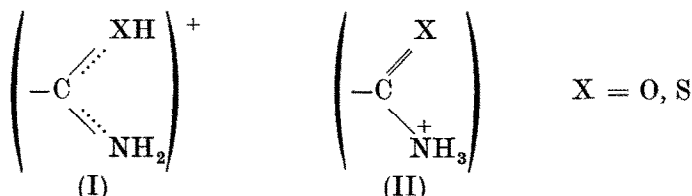
Institute for Organic Chemistry T.N.O., Utrecht, Holland

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Abstract—The electronic absorption spectra were studied of protonated thioamides and thio-ureas, as well as the infra-red spectra of alkylated acetamide, thioacetamide, urea and thiourea and their hydrochlorides. All results consistently show that the proton is normally attached to the oxygen (or sulphur) atom. Earlier data pointing to the existence of the ammonium structure are reinterpreted. The resonance within these molecules appears to be the decisive factor in determining the site of protonation.

Introduction

THE mode of protonation of amides and urea has been discussed frequently during the past decades. In principle two structures are possible: the oxonium (or sulphonium) form (I) and the ammonium form (II).



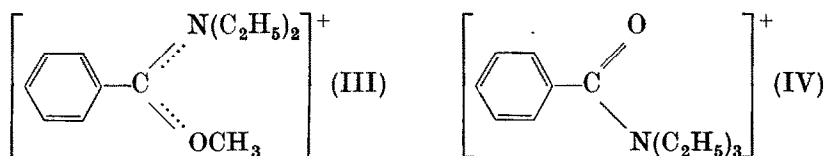
On theoretical grounds [1] structure (I) is to be preferred, since here the resonance in the amide group is preserved, but experimental evidence is still conflicting. Three approaches have been used in this field, namely, nuclear magnetic resonance spectra, vibration spectra and, for sulphur compounds, electronic absorption spectra.

The first technique shows that rotation around the C—N bond is restricted, which points to the oxonium structure [2–5]. This interpretation has been criticized by SPINNER [6] but it is doubtful whether his model is able to account for the high value of the rotation barrier found [5].

Evidence from vibration spectra generally has been interpreted in terms of nitrogen protonation in several amides, urea and thiourea [7–9]. The absence of OH (or SH) vibrations and the shift of the carbonyl-stretching vibration towards

- [1] R. HUISGEN and H. BRADE, *Chem. Ber.* **90**, 1432 (1957).
- [2] G. FRAENKEL and C. NIEMANN, *Proc. Natl. Acad. Sci. U.S.* **44**, 688 (1958).
- [3] A. BERGER, A. LOEWENSTEIN and S. MEIBOOM, *J. Am. Chem. Soc.* **81**, 62 (1959).
- [4] J. A. DUFFY and J. A. LEISTEN, *J. Chem. Soc.* 853 (1960).
- [5] G. FRAENKEL and C. FRANCONI, *J. Am. Chem. Soc.* **82**, 4478 (1960).
- [6] E. SPINNER, *J. Phys. Chem.* **64**, 275 (1960).
- [7] C. G. CANNON, *Mikrochim. Acta* 555 (1955).
- [8] M. DAVIES and L. HOPKINS, *Trans. Faraday Soc.* **53**, 1563 (1957).
- [9] E. SPINNER, *Spectrochim. Acta* **15**, 95 (1959).

higher frequency are both considered arguments for structure (II). On the other hand, GOMPPER and ALTREUTHER [10] synthesized both ions (III) and (IV) in which structures (I) and (II) are fixed and found strong absorption bands at 1640 cm^{-1} for (III) and at $1783/1724\text{ cm}^{-1}$ for (IV). These values, compared with the frequencies of the carbonyl bands of N-diethylbenzamide (1630 cm^{-1}) and benzamidium perchlorate (1654 cm^{-1}), strongly favour the oxonium form for the latter compound.



Electronic absorption spectra above $200\text{ m}\mu$, finally, are only exhibited by the thiocarbonyl compounds. Nearly all of these show a weak long-wavelength band or shoulder which represents an $n \rightarrow \pi^*$ transition [11]. This band disappears in concentrated acids which is to be expected when the proton is attached to the sulphur atom, but N-protonation is not likely to shift this band to shorter wavelengths (cf. below). Even here evidence is not unequivocal, for HOSOYA *et al.* [12] conclude that the ammonium form exists for protonated thioacetamide because of the similarity of the spectrum of the latter with a simple thioketone (thiocamphor). This similarity exists only in the high-intensity band, however, because the thioacetamide ion does not show the $n \rightarrow \pi^*$ transition which is responsible for the red colour of thioketones.

In the present study an attempt is made to remove these discrepancies by studying closely the electronic and vibration spectra. It appears that all major facts are in agreement with the existence of the oxonium (sulphonium) structure in protonated amides, ureas and their sulphur analogues. Only in cases in which the resonance within these groups is sterically hindered will the proton be attached to the nitrogen atom.

Experimental

Materials

All compounds were prepared and purified in this institute by standard techniques and checked by analysis and determination of physical constants.

Hydrochlorides were obtained by the reaction of the compounds with dry HCl gas, except O-methylisourea hydrochloride and S-methylisothioacetamide HCl which were available as such. In the other cases an equimolar quantity of HCl (checked by weighing) was introduced either directly or by removing an excess *in vacuo*.

Upon treatment with HCl tetramethylurea and NNN'-S-tetramethylisothiurea remain liquids and were measured as films of ca. $10\text{ }\mu$. In both cases the stoichiometrical quantity of HCl was present within 5 per cent. Dimethylacetamide solidifies on treatment with HCl and was measured in KBr disks with 7 per cent excess HCl. The solid compounds NN'-diethylurea, dimethylthioacetamide and tetramethylthiurea liquified on treatment with HCl but an excess HCl was always present at the time the solid had disappeared. With suction both the first two substances mentioned above could be obtained as 1:1-adducts, the former being a liquid, the latter a solid. They were measured as a film and in KBr, respectively. With tetramethylthiurea, however, the liquid 1:1-adduct proved unstable and changed spontaneously into a mixture

[10] R. GOMPPER and P. ALTREUTHER, *Z. anal. Chem.* **170**, 205 (1959).

[11] (a) M. J. JANSSEN, *Rec. trav. chim.* **79**, 454 (1960); (b) M. J. JANSSEN, *Ibid.* **79**, 464 (1960)

[12] H. HOSOYA, J. TANAKA and S. NAGAKURA, *Bull. Chem. Soc. Japan* **33**, 850 (1960).

of (solid) tetramethylthiourea and a liquid which must consist of tetramethylthiourea with excess HCl. It was only possible to obtain a uniform sample by applying about 50 per cent excess HCl. The spectrum, taken as a film, fortunately appeared independent of the excess HCl except for a general region of absorption between 2000 and 800 cm^{-1} .

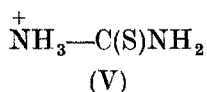
Spectra

Ultra-violet spectra were taken with a Beckman DU spectrophotometer with photomultiplier. A concentration range from 10^{-2} to 5×10^{-5} M was used and the spectra were measured from 220 $\text{m}\mu$ upwards till the most concentrated solution did not absorb any more. Infra-red spectra were measured with the Perkin-Elmer model 137 Infracord (NaCl optics). Spectra of films of liquid hydrochlorides were taken in cells with a path length of about 10 μ . The parts of the cell that were in contact with the samples were constructed of noble metals, the filling tube being made of silver and the spacer of gold. Potassium bromide disks were made in the normal manner, exposure to air being limited as much as possible by manipulating rapidly and whenever possible in closed and dry systems. The appearance of water bands in the spectrum could not be prevented entirely, but only spectra in which they were weak were used. Moreover, the spectra of tetramethylurea and tetramethylthiourea and their hydrochlorides were taken on a Perkin-Elmer model 221 in order to study the 3 μ region more closely.† The results given at present, however, contain only the information obtained with the model 137 Infracord.

Results

A. Ultra-violet spectra

The ultra-violet absorption characteristics of some thio compounds are given in Table 1. Thioamides and thiourea exist in concentrated sulphuric acid in their monoprotonated form, the iso-derivatives are much stronger bases. The similarity between the spectra of protonated thioacetamide and thiourea and those of the corresponding iso-compounds is obvious. As can be expected the low-intensity ($n \rightarrow \pi^*$) band is no longer present. Although no spectra are available of compounds in which the nuclei are fixed in the arrangement (II) they can be readily estimated since it is known that substituents which exert mere inductive effects influence the position of absorption maxima only slightly. Therefore the spectrum of the hypothetical ion (V) should resemble that



of thioacetamide except for small shifts due to the $-I$ effect of the ammonium group. On theoretical grounds [13, 14] this effect is expected to shift the $n \rightarrow \pi^*$ transition to longer wavelengths.‡ The direction of the shift of the high-intensity band is not so easily predicted, but in any case it should be small. Thus the spectrum of (V) is expected to consist of a band at about 300 $\text{m}\mu$ ($\log \epsilon \cong 2$) and a band around 240 $\text{m}\mu$ ($\log \epsilon \cong 4$). The absence of both bands in protonated thiourea therefore is incompatible with nitrogen protonation.

† These spectra were taken at the Analytical Institute T.N.O., Rijswijk. The author is indebted to Mr. J. H. L. ZWIERS for placing this instrument at his disposal.

‡ This is also demonstrated by the low-intensity bands of dimethyltrithiocarbonate and bis-(trifluoromethyl)trithiocarbonate, the maxima being at 429 and 458 $\text{m}\mu$, respectively [15].

[13] F. GERSON and E. HEILBRONNER, *Helv. Chim. Acta* **42**, 1877 (1959).

[14] M. J. JANSSEN, Thesis, Utrecht (1959).

[15] F. CHALLENGER, E. A. MASON, E. C. HOLDSWORTH and R. EMMOTT, *J. Chem. Soc.* 292 (1953).

The same argument may be given for the other structures; in the case of thioacetamide the expected spectra being either that of the isothioamide or of a thioketone. Although a band is reported for thiocamphor at 240 $m\mu$ [16] but not for cyclohexanethione [11b], a band at the same wavelength appears in the isothioacetamidium ion, so that only the behaviour of the low-intensity band is indicative here. The absence of the $n \rightarrow \pi^*$ transition decides in favour of the sulphonium structure.

Table 1. Ultra-violet absorption spectra of some thione derivatives

Formula	Compound	Maxima of un-ionized molecule			Maxima of conjugate acid		
		Solvent	λ_{\max} ($m\mu$)	$\log \epsilon$	Solvent	λ_{\max} ($m\mu$)	$\log \epsilon$
$\text{CH}_3\text{C}(\text{S})\text{NH}_2$	Thioacetamide*	96% ethanol	327 266	1.72 4.10	96% H_2SO_4	234	4.16
$(\text{H}_2\text{N})_2\text{CS}$	Thiourea*	96% ethanol	280 \dagger 242	2 4.11	96% H_2SO_4	only end absorption	
$(\text{CH}_2)_6\text{CS}$	Cyclohexanethione*	96% ethanol	495	—			
$\text{CH}_3\text{C}(\text{NH})\text{SCH}_3$	S-methylisothioacetamide \dagger	—			0.01 N H_2SO_4	240	3.99
$\text{H}_2\text{NC}(\text{NH})\text{SCH}_3$	S-methylisothio-urea \dagger				0.01 N H_2SO_4	only end absorption	

* Ref. [11].

 \dagger Present work. \ddagger Inflexion.

The spectra of several derivatives, e.g. methylated thioamides, methylated thiourea, thionocarbamates and dithiocarbamates all show similar behaviour upon protonation [11a]. It appears that generally in molecules containing the thioamide unit, proton addition occurs to the sulphur atom rather than to the nitrogen atom.

B. Infra-red spectra

As mentioned above, three arguments from vibrational spectral data are given [7–9] as evidence for the existence of the ammonium form for the conjugate acids of amides, urea and thiourea; namely

- (1) The presence of additional NH vibrations.
- (2) The absence of OH (and SH) vibrations.
- (3) The displacement of the carbonyl-stretching band to higher frequencies.

(1) The behaviour of the NH stretching vibrations has been studied on primary [9] and secondary [7] amides as well as on urea [8, 9] and thiourea [9]. In all these molecules the pattern of the NH bands already present may easily confuse the interpretations, especially in such highly hydrogen-bonded structures as exist in hydrochlorides. In this study the spectra of fully methylated (thio)acetamide and

[16] S. KATAGIRI, Y. AMAKO and H. AZUMI, *Symposium on Structural Chemistry, Kyoto* (1958), cited by HOSoya *et al.* [12].

(thio)urea were measured together with those of the hydrochlorides. The hydrochlorides were obtained by the reaction of the bases with HCl gas. In the spectra no

Table 2. Infra-red absorption bands between 3500 and 1450 cm^{-1} of N-dimethylacetamide, N-dimethylthioacetamide and their hydrochlorides

Dimethylacetamide (film)	Dimethylacetamide HCl (in KBr)	Dimethylthioacet- amide (in KBr)	Dimethylthioacet- amide HCl (in KBr)
3260 vw 2980 w 2920 s	3425 w 2930 vw* 2675 vw* 2590 vw* 2530 vw* 2475 vs, b 2280 vw*	2930 m	3420 w 2980 w
2125 vw			2180 s, b 2025 w 1940 s, b
1740 w 1639 vs 1546 w 1493 s	1765 w 1692 vs 1653 vw 1605 vw 1471 s	1725 vw 1670 vw 1535 vs	1700 vw 1623 vs 1565 w

* Small peaks on sides of broad strong absorption band at 2475 cm^{-1} .

Table 3. Infra-red absorption between 3500 and 1450 cm^{-1} of tetramethylurea, tetramethylthiourea and their hydrochlorides

Tetramethylurea (film)	Tetramethylurea HCl (film)	Tetramethylthiourea (KBr)	Tetramethylthiourea HCl (film)*
3000 vw 2940 s 2880 s 2110 vw 1875 vw 1645 vs 1560 w 1497 vs 1458 m	2940 m 2400–2100 s, vb 1755 s 1635 vs 1538 s 1465 m	2940 m 1750 vw 1499 vs 1461 s	2940 m 2200–1800 s, vb 1600 vs 1545 m 1495 s 1460 s

* Excess HCl, see Experimental; spectrum of hydrobromide (likewise with excess) is identical with that of the hydrochloride given.

bands were present of the parent compounds when an equimolar amount of HCl was bound.†

That the 1:1-adducts are formed was checked in some cases by applying a short measure of HCl: bands of the parent molecules appeared in these experiments. An excess of HCl only gave stronger general absorption between 2000 and 800 cm^{-1} . The frequencies of the absorption bands are tabulated in Tables 2 and 3.

† In one case an excess of HCl was inevitable; see Experimental.

In all structures the only bands above 2500 cm^{-1} are the CH stretching frequencies at about 2900 cm^{-1} . In order to be certain that no confusion is possible between CH and NH vibrations the spectra were taken of NNN'S-tetramethylisothiourea (VI) and its HCl adduct (Table 4). Here the proton can only add to the nitrogen

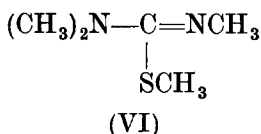


Table 4. Infra-red absorption bands between 3500 and 1450 cm^{-1} of NNN'S-tetramethylisothiourea and its hydrochloride

Tetramethylisothiourea (film)	Tetramethylisothiourea HCl (film)
3210 w	
3000 vw	3120 w
2940 vs	2980
2860 s	2940 } vs, b
2790 vw	2850 }
2625 vw	
2227 vw	
2123 vw	
2037 vw	2000 w
1938 vw	
1610 vs	1608 vs
1471 w	1540 w
1450 s	1495 m

atom. In this case on protonation a very strong set of NH vibrations appear from 3100 to 2800 cm^{-1} , which is easily distinguished from the CH vibrations because of its much greater intensity and different shape (Fig. 1). From the figure and the tables it appears that the amides and ureas studied form no NH bonds on protonation.

(2) In the discussion of the absence of OH and SH stretching vibrations it was presumed that these bands had to be found near their normal frequencies, 3500 and 2500 cm^{-1} , respectively. However, large displacements may be expected because of extensive hydrogen bonding and the polar character of these bonds in protonated carbonyl or thiocarbonyl groups. Except for the CH (and NH) bands already covered no absorption bands other than very weak ones are found in the neutral (thio)amides and (thio)ureas in the region between 3500 and 1800 cm^{-1} . In the hydrochlorides, however, strong broad bands occur at about 2500 cm^{-1} for the oxygen compounds and at about 2100 cm^{-1} for the sulphur derivatives. In the spectrum of tetramethylthiuronium bromide the band occurs at exactly the same position as in the chloride. No bands are present in the spectra of several iso-derivatives so that no NH vibration is involved.

On these grounds the assignment of this band to OH and SH vibrations, strongly displaced by hydrogen bonding, seems reasonable. The absorption is intensified by a very broad absorption region when an excess HCl is present.

(3) Finally, an analysis has to be made of the behaviour of the carbonyl vibration upon protonation. Earlier studies [10] already have shown that a strong carbonyl-like band is present at 1640 cm^{-1} in compound (III) where no real carbonyl group exists in the molecule. From Tables 2 and 3 it appears that all hydrochlorides show strong bands between 1800 and 1600 cm^{-1} no matter whether the parent molecule is a carbonyl or a thiocarbonyl compound. Also in tetramethylisothiurea

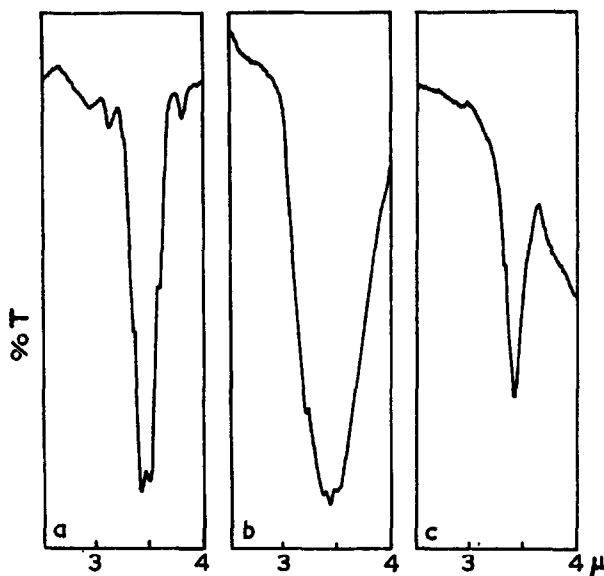


Fig. 1. CH stretching region of: (a) NNN'S-tetramethylisothiurea; (b) NNN'S-tetramethylisothiurea-HCl; and (c) tetramethylthiurea-HCl; all as pure liquids, thickness 0.012 mm .

(Table 4), either neutral or protonated, a similar band occurs. Obviously this band need not at all be connected with a carbonyl frequency. On the other hand, if protonation is supposed to occur at the oxygen or sulphur atom, the resulting structures of all compounds just mentioned have one feature in common, namely the existence of CN bonds with at least partial double bonding. The band belonging to the stretching vibration of the $\text{C}=\text{N}$ bond occurs at only slightly lower frequencies than the $\text{C}=\text{O}$ vibration, viz. around 1670 cm^{-1} [17, 18] and may have comparable intensities especially when heteroatoms are attached to the imide carbon atom [19]. The frequency is found to be somewhat lower in the latter structures (1600 – 1650 cm^{-1}). Quaternization of the nitrogen results generally in a slight shift to higher frequencies [18]. Molecules with the elements $\text{N}-\text{C}=\text{N}$ and $\text{N}_2\text{C}=\text{N}$ (i.e. containing the amidine or guanidine group) and their conjugate acids have asymmetrical $\text{N}-\text{C}-\text{N}$ stretching modes in the same region both as neutral compounds and as ions [20, 21].

[17] L. J. BELLAMY, *The Infrared Spectra of Complex Molecules* (2nd Ed.) p. 267. Methuen, London (1958).

[18] J. FABIAN, M. LEGRAND and P. POIRIER, *Bull. soc. chim. France* 1499 (1956).

[19] J. FABIAN and M. LEGRAND, *Bull. soc. chim. France* 1461 (1956).

[20] M. DAVIES and A. E. PARSONS, *Z. physik. Chem. (Frankfurt)* (N.F.) **20**, 34 (1959).

[21] W. J. JONES, *Trans. Faraday Soc.* **55**, 524 (1959).

In Table 5 the frequencies of this type of stretching vibrations in several molecules are compared with the bands found in the present study. When NH_2 groups are present interaction between the band under discussion and the bending vibration of this group complicates the picture. Nevertheless even in these cases we may estimate the unperturbed value of the stretching vibration since it is reasonable to assume that the interaction will shift the latter band 20–50 cm^{-1} to higher

Table 5. Strong absorption bands in the 1600–1800 cm^{-1} region in various compounds containing $\text{C}=\text{O}$ and $\text{C}=\text{N}$ groups

Compound	Structure	Vibration frequencies		Source
		of neutral molecules	of conjugate acids	
Acetamidine	$\text{CH}_3\text{C}(\text{NH})\text{NH}_2$	1650, 1608	1684	[20]
Acetamide	$\text{CH}_3\text{C}(\text{O})\text{NH}_2$	1675	1718	[9]
N-Dimethylacetamide	$\text{CH}_3\text{C}(\text{O})\text{N}(\text{CH}_3)_2$	1639	1692	This work
N-Dimethylthioacetamide	$\text{CH}_3\text{C}(\text{S})\text{N}(\text{CH}_3)_2$	—	1623	This work
S-Methylisothioacetamide	$\text{CH}_3\text{C}(\text{NH})\text{SCH}_3$		1610	This work
NNS-Trimethylisothioacetamidium iodide	$\text{CH}_3\text{CSCH}_3^+$ \parallel $\text{N}(\text{CH}_3)_2$		1607	*
Guanidine	$(\text{H}_2\text{N})_2\text{CNH}$	1660, 1603	1650	[21]
Urea	$(\text{H}_2\text{N})_2\text{CO}$	1679, 1627	1700, 1642, 1625	[9]
Thiourea	$(\text{H}_2\text{N})_2\text{CS}$	1611	1644	[9]
Tetramethylurea	$[(\text{CH}_3)_2\text{N}]_2\text{CO}$	1645	1755, 1635	This work
Tetramethylthiourea	$[(\text{CH}_3)_2\text{N}]_2\text{CS}$	—	1600	This work
O-Methylisourea	$\text{H}_2\text{NC}(\text{NH})\text{OCH}_3$		1685	This work
NNN'S-Tetramethylisothiurea	$(\text{CH}_3)_2\text{NC}(\text{NCH}_3)\text{SCH}_3$	1610	1608	This work

* J. D. S. GOULDEN, *J. Chem. Soc.* 997 (1953).

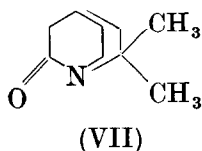
frequencies. From the table it is obvious that the frequencies of the bands of the hydrochlorides studied fit nicely in the pattern of other imide-containing structures. It seems that the alleged carbonyl bands of the conjugate acids may well arise from a stretching mode, in which the $\text{C}=\text{N}$ group plays the dominant role. There is one compound, viz. tetramethylurea-HCl, in which an extra band occurs at a frequency higher than normal. A possible reason for this behaviour will be given below.

Summarizing the evidence from infra-red spectra we may state that in the spectra of the hydrochlorides of methylated (thio)urea and (thio)acetamide no NH bands appear, that a broad absorption region between 2500 and 2000 cm^{-1} may be assigned to an OH or SH absorption band and that the upward displacement of the carbonyl band may alternatively be explained as the replacement of the $\text{C}=\text{O}$ band by a $(\text{X}-)\text{C}=\text{N}$ band. These results indicate that infra-red spectra are consistent with the oxonium (or sulphonium) structure (I).

In order to find out whether or not the evidence is also compatible with structure

(II), we have to make an estimate of the spectrum of the latter. The behaviour of the NH and OH bands is only of limited use, since the unknown effects of hydrogen bonding may shift these bands all the way from 3500 cm^{-1} to 2500 cm^{-1} . It is illustrative, however, that the hydrochloride of tetramethylisothiurea shows NH bands at about 3000 cm^{-1} . On the other hand the carbonyl stretching frequency of amides and urea in which the nitrogen atom is protonated may be estimated fairly accurately. In the case of dimethylacetamide for example we should expect (i) this band to be shifted to the acetone frequency ($\sim 1720\text{ cm}^{-1}$) because of the loss of resonance and, (ii) a further shift to higher frequencies because of the presence of the powerful inductive $^+\text{NH}_3$ substituent.

The extent of the latter shift may be estimated by comparing the inductive substituent constants [22] of this group and, for example, CF_3 , and by considering the shift of the latter substituent which is about 50 cm^{-1} [23]. Thus the $^+\text{NH}_3$ substituent may be supposed to give an upward shift of at least 80 cm^{-1} which would result in absorption around 1800 and 1760 cm^{-1} for amides and urea, respectively, when protonated at the nitrogen. This is in excellent agreement with the value found for the N-triethylbenzamide cation (IV) which absorbs at 1783 cm^{-1} and also for the hydrochloride of the non-mesomeric amide 2:2-dimethylquinuclidone-6 (VII) (1799 cm^{-1}) [24]. In the latter case it is also clear that the effect of hydrogen bonding on the carbonyl band is not very large.



We may conclude that the hydrochlorides of amides, ureas and similar molecules may show a strong absorption band either at about 1800 cm^{-1} in which case the ammonium structure (II) is present, or at about 1700 cm^{-1} in which case we may describe the band as mainly concerned with the C—N stretching vibrations in oxonium salts (I).

Thus the observed bands at 1670 cm^{-1} for urea nitrate [8] and at 1700 cm^{-1} in urea hydrochloride [9] actually point to protonation at the oxygen rather than at the nitrogen atom.

Discussion

From the foregoing sections it appears that the evidence from infra-red spectra, nuclear magnetic resonance spectra and electronic absorption spectra all indicate that in urea and amides the proton is normally attached to the oxygen atom and in thiourea and thioamides to the sulphur atom.

Earlier SPINNER [9] concluded the absence of resonance in this type of molecules on the basis of the existence of the ammonium form in the hydrochlorides.

[22] R. W. TAFT, JR., *Steric Effects in Organic Chemistry* (Edited by M. S. NEWMAN) Table XII, p. 619. Wiley, New York (1956).

[23] R. NORMAN JONES and C. SANDORFY *Chemical Applications of Spectroscopy. Technique of Organic Chemistry* (Edited by W. WEST) Vol. IX, Table 37, p. 444. Interscience, New York (1956).

[24] H. PRACEJUS, *Chem. Ber.* **92**, 988 (1959).

In the light of the present reinterpretation, however, a new analysis of this phenomenon is necessary. Since the compounds are very weak bases— pK values of their conjugate acids range from -2 to 0 —the basicity of the nitrogen atom is very small indeed. Actually we may estimate an upper limit for the basicity of this atom; expressed in pK of the conjugate acid this becomes $pK < -2$. This means a decrease of at least 12.5 units with regard to normal amines. The inductive effect has been shown [24] to account for a decrease of only 5.5 units in amides, so that the remaining lowering, which may be roughly put equal to 10 kcal/mole, should be due to the mesomeric effect. This value is therefore the lower limit for the resonance energy of amides and thioamides and, with a similar reasoning, twice this value should represent the lower limit for the resonance energy of (thio)urea. The results of experimentally determined resonance energies, e.g. around 30 kcal/mole for urea [25] and 27 kcal/mole for thiourea [26] are in agreement with this analysis.

In recent publications [27–29] the importance of hybridization is stressed. It appears that in conjugated hydrocarbons several phenomena—such as bond shortening and “resonance energy”—which are usually explained by electron delocalization, may as well result from changes in hybridization. Although DEWAR and SCHMEISING [27] explicitly exclude molecules in which more than one unexcited structure can be written, it is of interest to see whether the same ideas apply to the molecules under study.

There is strong evidence that in urea [30, 31] and thioacetamide [32] the NH_2 groups are coplanar with the NCO or NCS plane so that the nitrogen atom exists in the sp^2 -hybridization state. The $C-N$ distance in these molecules has been found to be 1.33 Å. If this should be the normal Csp^2-Nsp^2 distance an amazingly large shortening of 0.14 Å has to be assumed (for Csp^2-Csp^2 the shortening is 0.08 Å).

Moreover, it is not *a priori* clear why the nitrogen atom becomes sp^2 -hybridized. In aniline the NH_2 group is likewise attached to an sp^2 -carbon atom, but it does not attain the planar configuration.

On the whole, therefore, it is felt that hybridization effects cannot explain the behaviour of molecules containing the amide or thioamide unit. The close structural relation between amides and carboxylate ions makes it probable that delocalization in the former molecules is important.

When for some reason the mesomerism in an amide or in one half of a urea molecule is hindered, however, we may expect protonation at the nitrogen atom. This will mostly occur because of steric requirements as in (VII). Earlier [11a] it was deduced from the electronic spectrum of tetramethylthiourea, that here steric hindrance of mesomerism occurs. The same may be expected in tetramethylurea and therefore in this molecule the probability of N -protonation is enhanced. In fact a strong band at 1755 cm^{-1} is observed in the hydrochloride of this molecule in addition to the still stronger band at 1635 cm^{-1} . It seems that this band belongs to

[25] G. W. WHELAND, *Resonance in Organic Chemistry* p. 100. Wiley, New York (1955).

[26] ST. SUNNER, *Act. Chem. Scand.* **9**, 847 (1955).

[27] M. J. S. DEWAR and H. N. SCHMEISING, *Tetrahedron* **5**, 166 (1959).

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the N-protonated form which exists in equilibrium with the O-protonated form. The N—H bands, however, that should accompany the N-protonated form could not be clearly distinguished from the C—H vibrations in the 3000 cm^{-1} region. Therefore only a small percentage of the hydrochloride may consist of the ammonium salt. In tetramethylthiourea the possible existence of the ammonium next to the sulphonium structure can only be inferred from the NH stretching vibrations. Analysis of the appropriate region did not yield any clear indication of bands that could not be ascribed to C—H vibrations. For definite conclusions more work is necessary. Further study on similarly crowded molecules is at present in progress.

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