

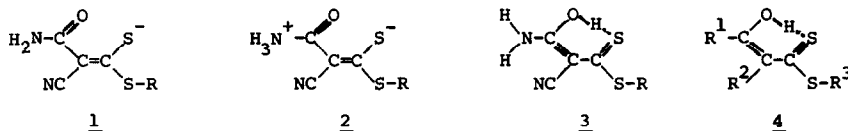
PROTONATION OF AMIDES. O-PROTONATION OF 1-ALKYLTHIO-2-CARBAMOYL-2-CYANOETHYLENE-1-THIOLATES

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The long-lasting discussion of N- versus O-protonation of amides at one point seemed to be resolved in favor of the latter protonation site primarily as a result of the firm evidence obtained from ^1H NMR spectroscopy in strong acids.¹ However, the discussion has recently been reopened by the suggestion² that the site of protonation may shift from O in concentrated to N in dilute acids. In this connection the claim³ that the products obtained by protonation of 1-alkylthio-2-carbamoyl-2-cyanoethylene-1-thiolates (1) are the N-protonated zwitterions (2) attains importance. These protonation products can be isolated as solids⁴ and studied as such or in non-acidic solvents, *i.e.* under conditions suggested to favor N-protonation. The exis-



tence of 2 would provide an example of predominating N-protonation at low acidity of an amide function although the latter in 1 is rendered atypical by virtue of conjugation with the electron donating thiolate group and results obtained with 1 cannot without qualifications be generalized to ordinary amides. However, we have found an alternate interpretation of the data cited as evidence for 2 and both the IR and the ^1H NMR spectra of protonated 1 on closer scrutiny provide conclusive evidence against 2 and strongly suggest the O-protonated, hydrogen bonded tautomer (3) as the observed species. Similarly bonded species (4) have previously been reported as the protonation products of the related 2-acylethylene-1,1-dithiolates.^{5,6}

The proposal of structure 2 was based on the occurrence in the NMR spectrum of protonated 1 (R = Et), recorded in $\text{DMSO}-d_6$, of a broad singlet at $\delta = 7.75$ ppm (3 H) which was assigned

to NH_3^+ . However, this is almost certainly an average signal from all exchanging protons. An increase in the water content of the solvent increased its intensity and shifted it toward higher field.⁷ The rapid exchange of all labile protons is understandable since protonated 1 are strong acids which by conductometry were found to be partially dissociated in DMSO. For slow exchange of the labile protons an entirely different pattern emerged. In addition to one set of signals from the S-alkyl group three different exchangeable protons were observed. For example, the spectrum of protonated 1 ($\text{R} = \text{Pr}^i$), recorded at -30°C in CD_3CN , displayed signals (1 H each) at $\delta = 7.12, 7.20$ and 16.65 ppm. The first two signals were singlets with the broad shape characteristic of N-protons; the last signal appeared as a sharp doublet ($J = 2.5$ Hz) which collapsed into a singlet on irradiation at the low-field NH-signal. A similar pattern was observed at -50° in CH_3OH , at -10° in CDCl_3 , at 10° in C_6D_6 and at 15° in dioxane.

This pattern indicates that 3 is the species observed. Firstly, the low-field signal can be assigned to a proton participating in intramolecular (O-H--S) hydrogen bonding.^{5,6} Secondly, the NMR spectra of protonated acetamide and propionamide in FSO_3H which were convincingly argued to indicate O-protonation showed not only the same specific coupling between the O- and one N-proton but also an identical coupling constant.⁸ Thirdly, the W-configuration of the H-N-C-O-H bonds assumed to be responsible for the observation of long-range coupling⁸ is imposed on 3 by the presence of the hydrogen bond. This configuration places the coupling N-proton close to the cyano group in agreement with the observation of coupling to the N-proton at lower field. Conversely structure 2, even modified to allow intramolecular (N-H--S) hydrogen bonding, can explain neither the observation of three different labile protons nor the coupling pattern.

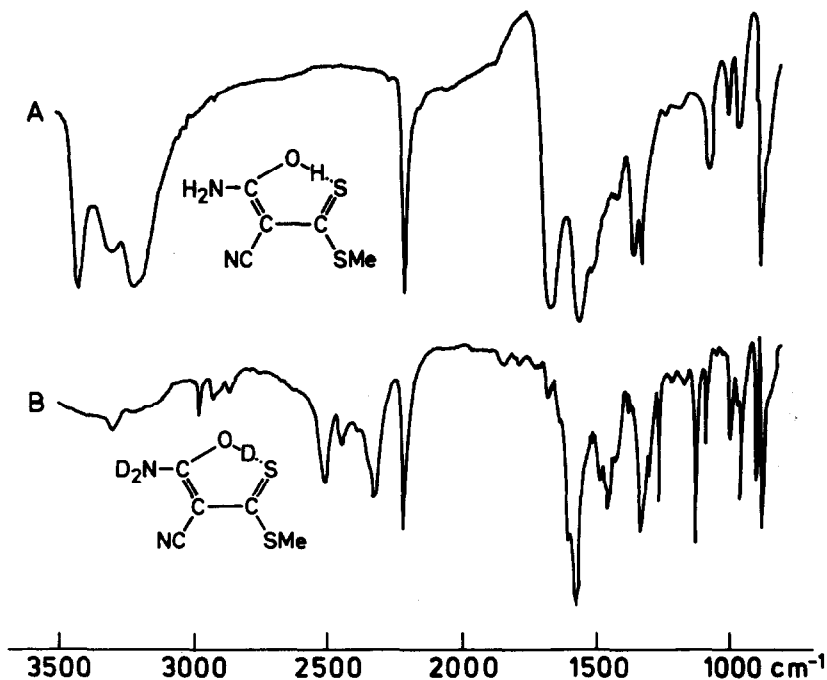
These conclusions are supported by the IR spectra, exemplified by the spectrum of protonated 1 ($\text{R} = \text{Me}$) shown as Fig. A. The bands, 3400(s), 3250(m), 3200(s), ca. 2400-1800(w), 2200(s), 1660(s) and 1550(s) cm^{-1} , of this figure are characteristic for protonated 1.⁹ Exchange of the labile protons with deuterium gave the spectrum shown as Fig. B. This allows the separation of the bands correlated with these hydrogen atoms. The bands at 3400-3200 and 1660 cm^{-1} can be assigned conventionally to an NH₂-group. The weak 2400-1800 cm^{-1} band is also observed in the spectrum recorded in dioxane¹⁰ and is not concentration-dependent. Combined with the position and the broad shape this suggests the origin of the band in a strong,

intramolecular hydrogen bond. The 2200 and 1550 cm^{-1} bands which are almost unaffected by deuteration can be assigned respectively to a conjugated cyano group⁴ and a conjugated C=C bond.⁵

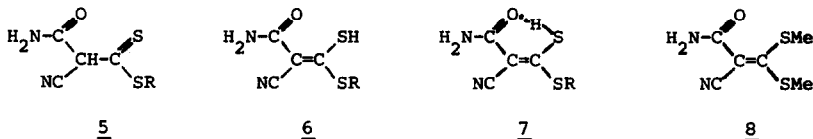
All of these bands can be rationalized in terms of structure 3 and conversely, no characteristic bands absent from the observed spectra are predicted from this structure. Structure 2, on the other hand, should give rise to N-H stretching bands in the 3100-2700 cm^{-1} region instead of the observed bands at 3400-3200 cm^{-1} and to a recognizable C=O band which is definitely not observed. Again here, the introduction of (N-H--S) hydrogen bonding into 2 does not weaken the arguments against this structure.

Two additional tautomers, *viz.* 5 and 6, might be considered as alternatives to 3. Structure 5 was previously rejected as a consequence of the IR evidence for a conjugated cyano group.⁴ A suggestion⁶ of 6 as the observed species was based upon the assignment to SH of a peak at $\delta = 4.87$ ppm in the NMR spectrum of protonated 1 (R = Me) in $\text{CF}_3\text{CO}_2\text{H}$. We ascribe this peak to a decomposition product since we did not observe it in the cold, freshly prepared solution and its subsequent appearance was accompanied by other, irreversible changes in the

FIGURE. IR spectra (recorded in KBr).



spectrum. Direct evidence against 6 or its hydrogen-bonded equivalent (7) is found in the coupling pattern of the NMR spectra and also in the absence of amide I and II IR-bands, since such bands (1670 and 1605 cm^{-1}) are seen in the spectrum of 8 which is a close structural analogue of 6.⁴



In conclusion, the available evidence indicates that 3 is the stable species formed by protonation of 1. This series of compounds thus cannot be taken to support the hypothesis that amides are N-protonated at low acidity.

REFERENCES.

1. R. B. Homer and C. D. Johnson in "The Chemistry of Amides", J. Zabicky, Ed., Interscience Publishers, London (1970), Chapter 3, p. 188.
2. M. Liler, Chem. Comm. 1971 115.
3. M. Yokoyama, Bull. Chem. Soc. Japan 44 1610 (1971).
4. R. Gompper, and W. Töpfl, Chem. Ber. 95 2861 (1962).
5. M. Saquet and A. Thuillier, Bull. Soc. Chim. France 1967 2841.
6. R. Gompper and H. Schaefer, Chem. Ber. 100 591 (1970).
7. The proposal (M. Yokoyama, J. Org. Chem. 36 2009 (1971)) of a zwitterion structure like 2 for the protonated thiocarbamoyl analogues of 1 was based upon the same evidence and is subject to the same criticism as 2.
8. D. M. Brouwer and J. A. van Doorn, Tetrahedron Letters 1971 3339.
9. Compounds 3 (R = Me, Pr, Prⁱ and benzyl) were isolated; these gave satisfactory analytical values and displayed IR spectra very similar to Fig. A.
10. The observation of the characteristic patterns of both the IR spectrum and the NMR spectrum in the same solvent, dioxane, shows that the two types of spectra refer to a single species.