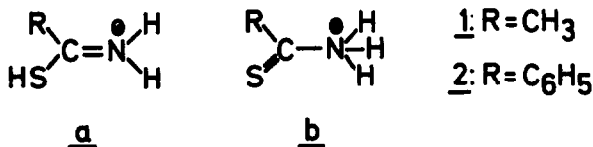


ON THE STRUCTURE OF THIOAMIDES AND THEIR DERIVATIVES, XXVII ¹⁾
THE SITE OF PROTONATION IN PRIMARY THIOAMIDES

Wolfgang Walter ^{*}, Marcia Franzen Sieveking, and Ernst Schaumann
Institute for Organic and Biochemistry, University of Hamburg,
2000 Hamburg 13, Papendamm 6

(Received in UK 3 January 1974; accepted for publication 28 January 1974)

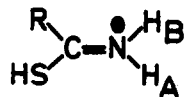
Although the protonation of amides has been the subject of extensive investigation ²⁾, little work has been done on the related thioamides ³⁾. It has been concluded from the chemical shift of a new peak in the spectra of thioacetamide and thioacetanilide recorded in fluorosulfonic acid that thioamides are protonated on the sulfur (a) rather than the nitrogen atom (b) ⁴⁾. Studies on ¹⁵N-acetamide in the same acid have provided conclusive proof that in this medium the amide is protonated on the oxygen atom ^{5),6)}. In order to substantiate the findings of the earlier workers on the site of protonation of thioamides a study of the spectra of ¹⁵N-thioacetamide (1) and ¹⁵N-thio-benzamide (2) in the presence of the very strong trifluoromethanesulfonic acid has been undertaken.



A comparison of the spectra of the two thioamides in the mixed solvent deuteriochloroform/trideuteronitromethane (1:1 v/v) without and with the addition of trifluoromethanesulfonic acid is found in the table. In both compounds the NH peaks move downfield on the addition of acid as to be expected from the decrease in electronic density in the molecule with protonation.

The geminal coupling of the nitrogen protons is unresolvable in the cations, a phenomenon also found with ^{15}N -acetamide ⁶).

Table: NMR spectra of the protonated cations of ^{15}N -thioacetamide and ^{15}N -thiobenzamide at 38°C (δ ppm relative to TMS as internal standard, J in Hz) in $\text{CDCl}_3/\text{CD}_3\text{NO}_2$ (1:1 v/v)



	R=CH ₃		R=C ₆ H ₅	
	without CF ₃ SO ₃ H	with CF ₃ SO ₃ H	without CF ₃ SO ₃ H	with CF ₃ SO ₃ H
δ_{CH_3}	2.50	2.79	--	--
δ_{H_A}	7.32	9.60	8.47	9.83
δ_{H_B}	7.08	9.74	8.18	10.13
δ_{SH}	--	5.92 (br)	--	6.37 (br)
$^2J_{\text{H}_A-\text{H}_B}$	4	--	3.2	--
$^1J_{^{15}\text{N}-\text{H}_A}$	92	94.6	93	94.5
$^1J_{^{15}\text{N}-\text{H}_B}$	91	94.6	90.5	95.5
$^3J_{^{15}\text{N}-\text{SH}}$	--	2.8*	--	2.0*
$^3J_{^{15}\text{N}-\text{CH}_3}$	2	2.9	--	--
$^4J_{\text{H}_A-\text{CH}_3}$	--	0.9	--	--

* Observable on cooling (-10° to -15°C)

A new peak appears in the spectra of both 1 and 2 at δ 5.92 and δ 6.37 ppm respectively. On cooling the peaks become sharper and by -15° both are split into doublets. A coupling constant of 2.8 Hz for 1 and 2.0 Hz for 2 is

consistent for a proton separated by three bonds from the ^{15}N -nucleus as in structure a and not for one directly attached as in b ⁷⁾. Further evidence for the site of protonation being sulfur is that in ^{14}N -heteronuclear double resonance experiments with protonated thioacetamide this new peak remains unchanged. There is also an increase in the ^{15}N -H coupling constants in the cations of 1 and 2 indicating an increase in s character in the NH bond and an increase in the ^{15}N -CH₃ coupling constant in the cation of 1 in agreement with an increase in the double bonding character of the CN bond ⁷⁾. Such increases in the coupling constants can best be explained by a protonation on sulfur as shown in structure a. However, evidence presented on the catalytic effects of acid on the isomerisation of thioamides ⁸⁾ indicates that a small equilibrium amount of b, not detectable in the NMR spectra of the thioamides in concentrated strong acid solutions, cannot be ruled out.

It has already been possible with the help of the benzene dilution method in ^{14}N -heteronuclear double resonance experiments of thioacetamide to assign the low-field and high-field NH-resonances to the protons cis and trans to the sulfur respectively ⁹⁾. In the same study it was also found that in contrast to the amides the protons cis to the sulfur in ^{15}N -thioacetamide and ^{15}N -thiobenzamide show a larger $^1J_{^{15}\text{N-H}}$ -coupling constant than the trans. An analogous assignment of the low-field and high-field NH-resonances of the cations using the same criterium is made difficult by the fact that on protonation the two $^1J_{^{15}\text{N-H}}$ -coupling constants become practically identical.

However, an assignment is suggested by the observed allylic coupling between the CH₃- and NH-protons in protonated 1. The high-field NH-peaks are broadened in this cation, and the methyl resonance, which is already split by coupling with the ^{15}N -nucleus, is further split to give two doublets. By double irradiation of the NH-protons in the ^{14}N -thioacetamide cation the methyl doublet becomes a singlet meaning there is coupling between the two groups. Expansion of the methyl resonance and the high-field NH-resonance in the ^{15}N -cation gives a coupling constant of 0.9 Hz. Since it has been found that for this type of allylic coupling in amides ^{10),11)} and their cations ¹²⁾ the trans coupling

is larger than the *cis*, it would seem that in the cation the high-field resonance must be assigned to the proton *cis* to the sulfur (table). The same broadening of the peak which in the unprotonated compound is assigned to the nitrogen proton *trans* to the carbonylheteroatom has been observed for acid solutions of ^{15}N -acetamide ⁶). The explanation given by Liler ⁶) for this broadening of a *cis* allylic coupling would seem in light of the literature on amides questionable. The possibility of the reversal of the anisotropic effect of the sulfur group on protonation suggested by us is supported by investigations on the cations of secondary thioamides where the difference in amounts of E- and Z-isomers allows a definite assignment of the alkyl peaks ¹³).

The temperature dependent spectra of ^{15}N -thiobenzamide (2) and its cation provide still further evidence for a protonation of thioamides on sulfur. 2 has a barrier to rotation around the CN-bond (ΔG^\ddagger) of 17.9 kcal/mol ($\Delta\nu = 23.5$ Hz, $T_c = 78^\circ$) in pentadeuteronitrobenzene/nitromethane (8:1 v/v). With the addition of trifluoromethanesulfonic acid the barrier to rotation increases to above 19.4 kcal/mol ($\Delta\nu = 17$ Hz, $T_c > 102^\circ$, decomposition). This increase in ΔG^\ddagger in the cation is only to be expected when the proton resides on sulfur as in structure a.

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