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NON-EQUIVALENCE OF N-H PROTONS AND CONFIGURATION OF PROTONATED AMIDES

D. M. Brouwer and J. A. van Doorn

Koninklijke/Shell-Laboratorium, Amsterdam, The Netherlands
(Shell Research N. V.)

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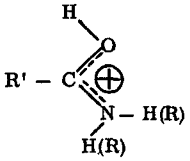
It has long been known that amides are protonated on the oxygen and that there is a high barrier to rotation around the C-N bond owing to its having a partial double-bond character[1].



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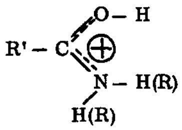

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The non-equivalence of the two N-R groups in protonated N,N-dialkyl amides has been firmly established by PMR spectroscopy[1]. Concerning the non-equivalence of the N-H protons in N-unsubstituted amides, there has so far been only one report in the literature. Gillespie and Birchall[2] observed a doublet splitting in the N-H resonance peak of protonated acetamide in FSO_3H at -80°, which they attributed to the expected non-equivalence, but no definite proof was given. No separated N-H peaks were observed with formamide[2] and benzamide[3]. For protonated amides, unlike many other carboxylic compounds[1], the configuration around the partially double C-OH bond (structure A or B) has not yet been established.

We have now obtained definitive proof of the non-equivalence of the two N-H protons in a number of protonated aliphatic amides,and - from the presence of a four-bond (H-N-C-O-H) coupling - information on the configuration of these protonated amides and protonated N-methylacetamide.

TABLE I

PMR SPECTROSCOPIC DATA OF PROTONATED AMIDES[a]

Amide	Chemical shift and multiplicity[b]		
	OH	NH	Other groups
1. CH_3-$CONH_2$	9.87	8.20; 8.09[c]	CH_3 : 2.68
	(d, 2.5)	(br) (br)	
2. CH_3CH_2-$CONH_2$	9.80	8.17	CH_3 : 1.45 (t, 7.2)
	(d, 2.5)	(br)	CH_2 : 2.97 (q, 7.2)
3. $(CH_3)_2CH$-$CONH_2$	9.74	8.10	CH_3 : 1.46 (d, 7.5)
	(d, 2.0)	(br)	CH : 3.10 (sept, 7.5)
4. $(CH_3)_3C$-$CONH_2$	9.67	8.22; 8.05[c]	CH_3 : 1.52
	(d, 1.5)	(br) (br)	
5. CH_3-$CONHCH_3$	9.72	8.19	NCH_3: 3.24 (d, 4.5)[d]
	(d, 2.5)	(br)	CH_3 : 2.60

a. Measured in FSO_3H/SbF_5 (molar ratio 1/1) diluted with SO_2 at -80°.

b. Chemical shifts in ppm from TMS, measured with tetramethylammonium ion ($\delta = 3.20$) as internal reference. Coupling constants in Hz.

c. Downfield signal broader and lower than upfield signal.

d. Coupling with NH confirmed by double resonance.

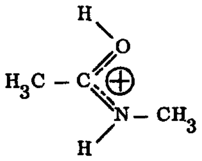
The PMR spectrum of protonated acetamide (1) in FSO_3H-SbF_5-SO_2 at 80° contains two N-H peaks (Table I), the distance between which (in Hz) is field-dependent, and an O-H doublet, the splitting of which is field-independent. Both N-H peaks are broadened owing to the interaction of the protons with the ^{14}N nucleus[4], but the low-field peak is markedly lower and broader than the high-field peak. Double-resonance measurements confirmed that this additional broadening is due to spin-spin coupling between the O-H and low-field N-H protons. These observations definitely prove the non-equivalence of the N-H protons.

The substantial four-bond coupling (2.5 Hz) between the O-H and low-field N-H protons strongly indicates the favourable W-path coupling[5], which means that 1 has configuration A, with the O-H as well as the low-field N-H protons in the "outer" positions, and not configuration B, with the O-H proton in the "inner" position. This preferred configuration is in keeping with that found for protonated carboxylic acids[1], where the configuration with both O-H protons in the inner positions is energetically unfavourable.

Separated N-H resonances as well as the doublet splitting of the OH peak were also observed with the protonated amide of pivalic acid, 4 (Table I). The protonated amides of propionic and isobutyric acid gave no separated N-H peaks, but the doublet splitting of the O-H peaks was still present, demonstrating the non-equivalence of the N-H protons.

The presence of the H-N-C-O-H coupling in the case of 4 shows that even if R' = t-butyl the hydroxyl proton is still in the "outer" position, i.e. *syn* with respect to the bulky alkyl group. (In accordance with this is the observation that the OH shielding decreases very regularly from 1 to 2 to 3 to 4, without showing a jump between 3 and 4.) This result lends support to the conclusion[6] that in protonated pivalic acid one of the hydroxyl protons still occupies the "outer" position.

The four-bond coupling was also observed in the spectrum of protonated N-methylacetamide (5), from which we conclude that the preferred configuration of 5 is that with the N-CH_3 group in the inner position:



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