Tetrahedron Letters No. 36, pp 3167 - 3170, 1977. Pergamon Press. Printed in Great Britain.

PROTONATION STUDIES ON N-METHYLHYDROXAMIC ACIDS

A.M.Lobo*, S.Prabhakar and M.T.C.Fonseca
Department of Chemistry, Universidade Nova de Lisboa,
I.N.S.A., Lab 3L48, Av.Pe.Cruz, Lisboa, Portugal
and A.M.B.Rodriguez
Faculty of Pharmacy, Av.Forças Armadas, Lisboa, Portugal

(Received in UK 21 June 1977; accepted for publication 14 July 1977)

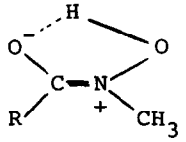
The site of protonation of hydroxamic acids has been the subject of some speculation, since there are at least two basic centres in these molecules which can be protonated: the carbonyl oxygen and the nitrogen atom.[1-3] The ^1H n.m.r. spectrum of hydroxamic acid (1)[4] in $CDCl_3$ showed clearly the presence of the cis*[1] (7) and the trans (7a) forms arising from restricted rotation about the C-N bond. This barrier has been found to be -16.4 kcal/mole. The spectrum of (1) in sulphuric acid (< 2.5 M) contained two N-methyl and two formyl signals as in $CDCl_3$, attributed to (7) and (7a).*[2] At higher concentrations of acid (3 M to ca. 13 M) the two N-methyl signals collapsed to a singlet attributable to the presence of significant concentrations of the N-protonated form (8). No splitting of the N--methyl signal was seen due to rapid exchange with the medium. At concentrations of sulphuric acid above 13 M there were two sets of signals, for the N-methyl and the formyl protons, an observation that is rationalized on the basis of O-protonation leading to species (9) and (9a) (cf. Table). Furthermore the low temperature (below -70°C) spectrum of (1) in FSO_3H showed considerable broadening of the formyl signals, due to coupling with the proton in the carbonyl oxygen.[7]

Table. ^1H n.m.r. chemical shifts of the N-methyl group of $RCON(OH)CH_3$, in conc. H_2SO_4, 33°C

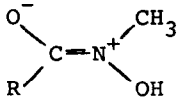
no.	R	τ*	
(1)	H	6.60 (s)	6.70 (bs)
(2)	CH_3	6.28 (s)	6.37 (q, J 0.7 Hz)
(3)	$CH(CH_2)_5$	6.22 (s)	6.33 (s)
(4)	$C(CH_3)_3$	6.33 (s)	6.53 (s)
(5)	C_6H_5	6.20 (bs)	
(6)	p-CH_3-C_6H_5	6.20 (bs)	

*Relative to an external reference of TMS.

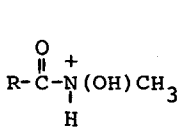
Compounds (2)[8], (3) and (4)[9] in sulphuric acid (0.5 to 13 M) do not exhibit signals which could be indicative of the presence of (9) and (9a) since only one singlet for the N-methyl resonance was observed in their ^{1}H n.m.r. spectra. However at higher acidities two distinguishable N-methyl resonances were detected and attributed to species (9) and (9a) (see Table). Simple dilution of the solutions regenerated the original spectra. These observations are consistent with a changeover in the protonation site of these hydroxamic acids, from nitrogen to oxygen, similar to the one previously observed for amides and attributed to the different solvation requirements of the N-protonated versus the O-protonated species.[10] It is known that above 60% sulphuric acid the activity of water decreases very sharply and that this might render the N-protonated cation more unstable than the O-protonated one.[10]



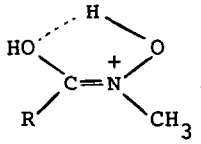
(7)



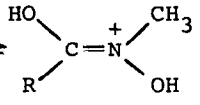
(7a)



(8)



(9)



(9a)

The protonation behaviour of (5)[11] and (6)[12] was less clear cut in that their n.m.r. spectra showed only one set of n.m.r. signals throughout the whole region of sulphuric acid concentration studied (o.5 to 18 M), namely a singlet for the N-methyl protons resonance. However the ultraviolet spectra obtained for (6) in different acid concentrations were illuminating since substantial changes were observed between 60% (λ_{max} 254 nm, ε 12,400) and 96% H_2SO_4 (λ_{max} 264 nm, ε 13,600).*[3] This bathochromic shift can again be rationalized in terms of a change in the protonation site from nitrogen to oxygen as has also been observed for benzamide under similar conditions.[14]

Acknowledgment. We thank the Foundation Calouste Gulbenkian for financial support and for award of a student research grant (to A.M.B.R.), and Dr.J.G.Tillet (University of Essex) for his interest in this work.

References and Footnotes

*1 The cis form refers here to the relative positions of the substituents R and the N-methyl group.

*2 The sigmoid curve obtained by plotting the N-methyl chemical shifts (relative to trimethylammonium) against the amide acidity function[5], H_A, showed the absence of any appreciable protonation in this region of acidity. The pK_A values for all compounds studied by this n.m.r. method[6] fell within the range of (-1) to (-3).

*3 A similar chromophore ($\lambda_{max}^{CH_3CN}$ 263 nm, ε 12,000) was found for the BF_2--hydroxamate complex of (6). Japanese workers[13] also found a chromophore with a λ_{max} 265 nm, in the solutions of boric acid and benzohydroxamic acid, which they attributed to the presence of the imidol form.

1. L.Bauer and O.Exner, Angew.Chem.internat.Edit., 13, 376 (1974).

2. A.J.Buglass, K.Hudson and J.G.Tillet, J.Chem.Soc. B, 123 (1971).

3. A.Ahmad, J.Socha and M.Večeřa, Coll. Czech.Chem.Comm., 39, 3293 (1974).

4. W.Walter and E.Schaumann, Liebigs Ann.Chem., 743, 154 (1971).

5. K.Yates and J.B.Stevens, Can.J.Chem., 42, 1957 (1964).

6. P.Bonvicini, A.Levi, V.Lucchini, G.Modena and G.Scorrano, J.Amer.Chem.Soc., 95, 5960 (1973).

7. W.E.Stewart and T.H.Siddall, Chem.Rev., 70, 517 (1970).

8. O.Exner, Coll.Czech.Chem.Comm., 16, 266 (1951).

9. J.D.Aubort and R.F.Hudson, J.C.S.Chem.Comm., 1378 (1970).

10. M.Liler, J.C.S.Chem.Comm., 115 (1971).

11. R.E.Plapinger, J.Org.Chem., 24, 802 (1959).

12. W.B.Ankers, D.B.Bigley, R.F.Hudson and J.C.Thurman, Tetrahedron Lett., 4539 (1969).

13. K.Kobashi, N.Terashima and J.Hase, Chem.Pharm.Bull. (Japan), 21, 2303 (1973).

14. M.Liler, J.C.S.Perkin II, 71 (1974).