First Evidence for Hydration of Amides. Hydration of *N*-Trifluoroacetylpyrrole

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Summary ^1H n.m.r. and u.v. spectral data provide evidence for the appreciable hydration of *N*-trifluoroacetylpyrrole in aqueous solution; the hydrate detected represents a tetrahedral intermediate in the hydrolysis of the title compound.

IN aqueous solution aldehydes and ketones have been shown to be extensively hydrated,[1] electron withdrawing substituents strongly favouring the *gem*-diol form $RCH(OH)_2$.[1,2] In contrast, experimental evidence shows little support for the hydration of amides, and the evaluation of free energies of formation of the species $RC(OH)_2NMe_2$[3] (*ca.* +20 kcal mol^{-1}) strongly suggests that simple amides are hydrated to only a very small extent.

During our studies on the hydrolysis of *N*-acylpyrroles we obtained evidence for a detectable amount of hydration of an amide; *i.e.* *N*-trifluoroacetylpyrrole (**1**).†

† This was prepared in low yield by action of trifluoroacetic anhydride on the sodium salt of pyrrole in anhydrous diethyl ether.

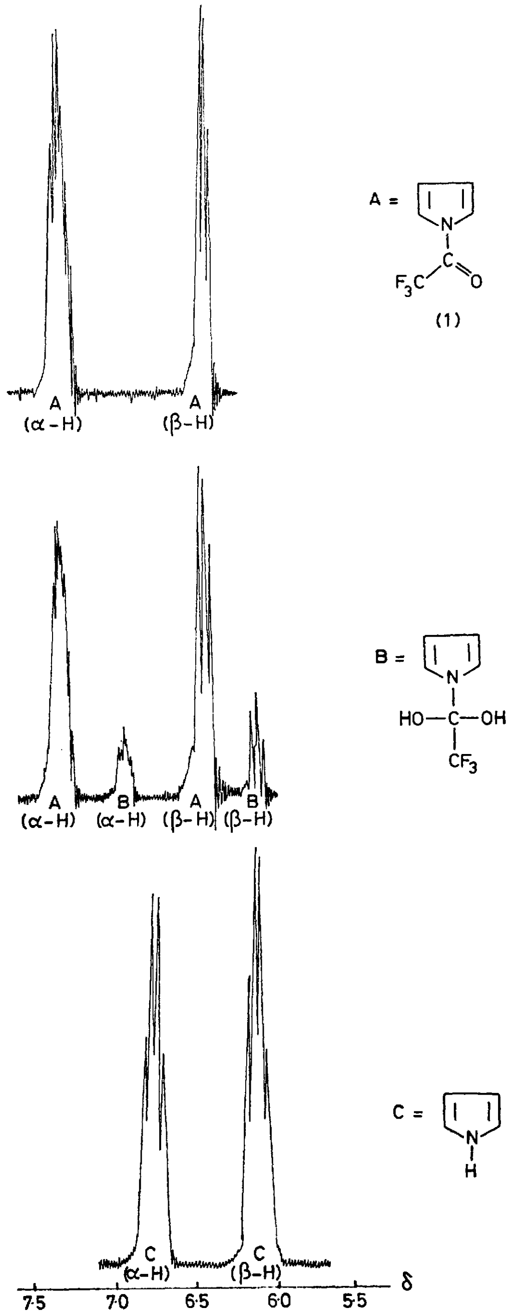

FIGURE. Variation of the n.m.r. spectrum of *N*-trifluoroacetylpyrrole (**1**): A, in MeCN; B, in 17% H_2O–MeCN(v/v); C, after complete hydrolysis (≡ pyrrole).

The ^1H n.m.r. spectrum, on a JEOL C-60HL instrument, of (**1**) in MeCN consists of two signals, δ 7·45 (2H, m, α-H) and 6·51 (2H, m, β-H). In a mixture of 17% H_2O–MeCN (v/v) under acidic conditions (pH 3·5), where hydrolysis is very slow ($t_{1/2}$ 2 h), the spectrum consists of two multiplets at δ 7·45 and 6·51; in addition two more signals appear at δ 7·02 (2H, m, α-H) and 6·16 (2H, m, β-H), which are not attributable to pyrrole since the spectrum of pyrrole under these conditions consists of two signals at δ 6·78 (2H, m, α-H) and 6·16 (2H, m, β-H) (Figure). We have assigned these additional lines to the hydrated form of (**1**). The α-H protons appear to be less deshielded than in the unhydrated form and this is to be expected based on the effect of *N*-substituents on the chemical shift[5] [–$COCF_3$ being a stronger electron withdrawing group than –$C(OH)_2CF_3$]. The β-H protons have the same chemical shift as the corresponding pyrrole hydrogens because they are (again as expected[4]) not affected by *N*-substitution.‡

From the areas of the absorption peaks of the unhydrated and the hydrated forms we obtained $K_d = 25$ mol l^{-1} (the dissociation constant has been calculated considering the mole fraction of water).

Analogous information on the hydration of (**1**) has been obtained from u.v. spectroscopy. In MeCN where the unhydrated form predominates, we observe an absorption maximum at 246 nm, which shows the expected strong bathochromic shift with respect to unsubstituted pyrrole.[5] In H_2O–MeCN mixtures hydration causes a decrease in intensity of the absorption at 246 nm and a further band appears at 206 nm. The latter resembles the corresponding band in the spectrum of pyrrole, but it cannot be due to pyrrole itself since under these conditions no appreciable hydrolysis occurs as shown by the n.m.r. data. The assumption that, at 246 nm, the molar absorbance of the hydrated form is negligible[6] and that in MeCN hydration is irrelevant (see n.m.r. results) allowed us to calculate $K_d = 20$ mol l^{-1} in 17% H_2O–MeCN (v/v). The agreement between the values obtained from the two different approaches supports the rough assumptions made throughout in calculating dissociation constants.[6] It is interesting that the value of K_d for the hydrated form is comparable with that of acetaldehyde hydrate (K_d *ca.* 50)[1] but it is higher than that of $\alpha\alpha\alpha$-trifluoroacetophenone hydrate (K_d *ca.* 1).[6] These results show the importance of structural effects in favouring hydration of the carbonyl unit.

Moreover, although the mechanism of the hydrolysis of (**1**) is somewhat unusual with respect to that of other amides,[7] this work represents the first experimental evidence for the existence of a simple tetrahedral intermediate in the acid-catalysed hydrolysis of amides.

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‡ The spectrum of the mixture after partial hydrolysis shows distinct peaks due to the α-H of the hydrate and of pyrrole.

[1] R. P. Bell, *Adv. Phys. Chem.*, 1966, **4**, 1.
[2] S. Patai, 'The Chemistry of the Carbonyl Group,' Vol. II, Interscience, London, 1970, p. 1.
[3] J. P. Guthrie, *J. Amer. Chem. Soc.*, 1974, **96**, 3608.
[4] R. A. Jones, T. Mc. L. Spotswood, and (in part) P. Cheuychut, *Tetrahedron*, 1967, **23**, 4469.
[5] R. A. Jones, *Adv. Heterocyclic Chem.*, 1970, **11**, 383.
[6] W. J. Scott and P. Zuman, *J.C.S. Faraday I*, 1976, 1192.
[7] A. Cipiciani, P. Linda, and G. Savelli, Atti del IX Congresso di Chimica Organica, Salsomaggiore, 1976, **73**, and unpublished results.