

Notes

Acid-Catalyzed Hydrolysis of Acylpyrroles and Their Derivatives

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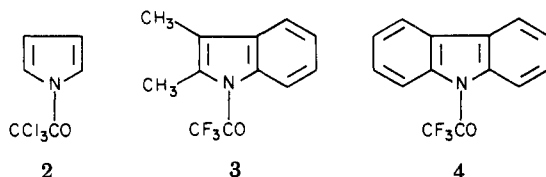
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Acid-catalyzed hydrolyses of carboxylic esters, amides, and related compounds are typically written as involving rate-limiting attack of water upon protonated substrate, and in some cases substrates are sufficiently basic for the extent of their protonation to be measured directly.^{1,2} For example, $pK_a \approx -2$ for protonated aliphatic amides, and rate constants of hydrolysis go through maxima with increasing acidity.²

However, *N*-(trifluoroacetyl)pyrrole (1) is extensively hydrated in water,³ but its hydrolysis is acid catalyzed with a rate maximum at ca. 3 M H_2SO_4 .⁴ These observations were inconsistent with an A2 mechanism of hydrolysis, in which prior protonation of the substrate assists attack of water and were explained on the assumption that a pre-formed *gem*-diol (1a) gave products by a rate-limiting attack of hydronium ion or other acid (Scheme I). Rate-limiting protonation could be on nitrogen or on C-2 of the pyrrole ring.⁵

For other similar substrates, e.g., *N*-(trifluoroacetyl)indole, tetrahydrocarbazole, and *N*-acetylindole, variations of hydrolysis rate with acidity were similar to that for 1, and although these substrates were not extensively hydrated, it seemed that their hydrolyses followed the general reactions shown in Scheme I.

We now report evidence on the acid hydrolysis of *N*-(trichloroacetyl)pyrrole (2), *N*-(trifluoroacetyl)-2,3-dimethylindole (3), and *N*-(trifluoroacetyl)carbazole (4).



These, and similar compounds, are much more readily hydrolyzed than the simple aliphatic amides, and this high reactivity is readily understandable in terms of the reduced carbon-nitrogen conjugation in the acyl pyrroles and indoles.⁴⁻⁸

We also examined general-acid catalysis of the hydrolysis of *N*-(trifluoroacetyl)tetrahydrocarbazole. The hydrolysis in strong acid has been examined.⁵

Results

Reaction in Strong Acid. We observed rate maxima in the acid hydrolyses of 1-3 (Figure 1), and the variation of rate constant with acidity can be fitted to the Bun-

Scheme I

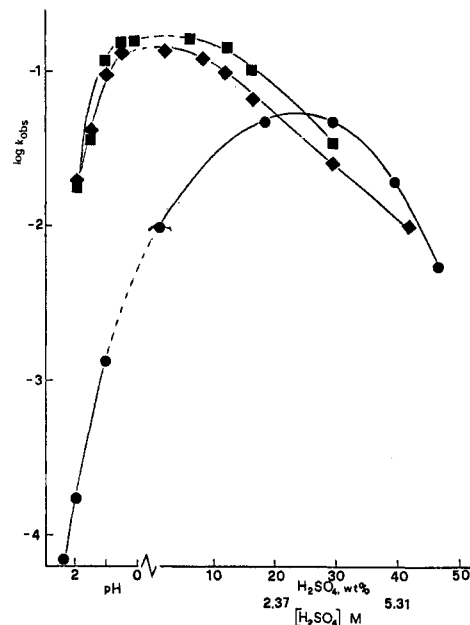
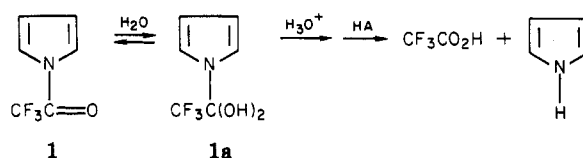


Figure 1. Acid hydrolysis of (●) *N*-(trichloroacetyl)pyrrole, (■) *N*-(trifluoroacetyl)-2,3-dimethylindole, and (♦) *N*-(trifluoroacetyl)carbazole.

Table I. Relation between Reaction Rate and Acidity

substrate ^a	ϕ^b	substrate ^a	ϕ^b
<i>N</i> -CCl ₃ CO-P	1.6	<i>N</i> -CF ₃ CO-C	2.2
<i>N</i> -CF ₃ CO-P	1.7 ^c	<i>N</i> -CF ₃ CO-IME ₂	2.4
<i>N</i> -CF ₃ CO-THC	1.9 ^c	<i>N</i> -CF ₃ CO-I	1.6 ^c

^a P denotes pyrrole; C, carbazole; THC, tetrahydrocarbazole; I, indole; IME₂, 2,3-dimethylindole. ^b Calculated by using H_0' values of: Johnson, C. D.; Katritzky, A. R.; Shapiro, S. A. *J. Am. Chem. Soc.* 1969, 91, 6654. ^c Reference 5.

nett-Olsen equation (eq 1), including the logarithm of water activity to allow for hydration of the substrate.^{9,10}

$$\log k_{\psi} + H_0' - \log a_{H_2O} = \phi(H_0' + \log [H^+]) + \log k_0 \quad (1)$$

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Table II. General-Acid-Catalyzed Hydrolysis of *N*-(Trifluoroacetyl)tetrahydrocarbazole^a

[buffer acid], M	$10^2 k_{\psi}$, s ⁻¹	[buffer acid], M	$10^2 k_{\psi}$, s ⁻¹
0.00	0.90	0.10	1.99
0.05	1.49	0.20	3.51

^a At 25.0 °C, $\mu = 0.30$ (NaCl), and pH 2.00 in H₃PO₄/NaH₂PO₄.

In eq 1 H_0' is Hammett's acidity function for protonation of primary amines, so that ϕ gives information on the effect of acidity on the activity coefficients of the initial and transition states relative to those for protonation of a Hammett base.¹⁰ Our data follow eq 1 and give the values of ϕ in Table I. This table includes ϕ values for hydrolysis of similar substrates reported earlier,⁵ and the similarity of the ϕ values suggests that the hydrolyses are following similar mechanisms. The data can also be fitted reasonably well to the Bunnett equation which involves water activity as one parameter,¹¹ and as for similar reactions,⁵ values of ω are large and positive.

Buffer Catalysis. The hydrolysis of *N*-(trifluoroacetyl)tetrahydrocarbazole is general catalyzed (Table II) as is that of *N*-(trifluoroacetyl)pyrrole.⁵ The magnitude of the buffer effect relative to the rate constant in dilute HCl is very similar for both hydrolyses and is consistent with proton transfer in the rate-limiting step.

Discussion

Our results, together with those reported earlier,⁵ are inconsistent with rate-limiting attack of water upon protonated substrate. They are consistent with rate-limiting protonation of a preformed *gem*-diol or concerted water addition and proton transfer, i.e., reactions follow S_E2(H) rather than A2 mechanisms. As noted earlier, these S_E2(H) mechanisms seem to be typical of acid hydrolyses of weakly basic substrates which contain strongly electron-withdrawing groups which assist hydration but inhibit protonation.¹²

Jencks has pointed out that reactions may take various pathways in order to avoid formation of high-energy intermediates.¹³ With these weakly basic acyl pyrroles and their derivatives, protonated substrates would be high-energy intermediates, whose formation is avoided if hydration is followed by proton transfer.⁵

The values of k_{ψ} at the rate maxima (Figure 1) are very similar for hydrolyses of these substrates and of *N*-(trifluoroacetyl)pyrrole but much larger than for *N*-acetylindole.⁵ The acid concentration at the rate maximum is lower for hydrolyses of the substrates having the bulkiest leaving groups, e.g., carbazole or 2,3-dimethylindole as compared with pyrrole (Figure 1 and ref 5). Increasing the bulk of the heterocyclic moiety decreases the extent of substrate hydration, but steric acceleration may help acid-assisted decomposition of the *gem*-diol with C-N bond breaking. The various pathways for this reaction have been discussed.⁵

Experimental Section

Materials. The preparation of most of the substrates has been described.^{4,14} *N*-(Trichloroacetyl)pyrrole was prepared from the potassium salt of pyrrole in Et₂O by the method described for preparation of the trifluoroacetyl derivative except that we used CCl₃C(O)Cl.⁵ It was purified by distillation in vacuo [81 °C (3 mm)] in 50% overall yield and was further purified by preparative GLC (2 m, silicone SE-30, 10% on Chromosorb at 130 °C). The NMR (CCl₄) δ 7.55 (2 H, m, α -H), 6.25 (2 H, m, β -H) and IR ($\nu_{C=O}$ 1730 cm⁻¹) spectral data were similar to those of the trifluoroacetyl derivative.⁵ Anal. Calcd: C, 33.92; H, 1.89; N, 6.59. Found: C, 33.88; H, 1.91; N, 6.50.

Kinetics. Reactions were followed spectrophotometrically at 25.0 °C in aqueous acid at the following wavelengths: *N*-(trichloroacetyl)pyrrole, 254 nm; *N*-(trifluoroacetyl)-2,3-dimethylindole, -carbazole, and -tetrahydrocarbazole, 255, 270, and 260 nm, respectively.

Substrate concentrations were 10⁻⁵–10⁻⁴ M, and the first-order rate constants, k_{ψ} , s⁻¹, were unaffected by changes in substrate concentration.

Reactions in the pH range were carried out in dilute HCl at an ionic strength of 0.3 (NaCl). We used H₂SO₄ made up by weight, for reactions in moderately concentrated acid. Catalysis by phosphate buffer was examined at a fixed pH at constant ionic strength, 0.3 (NaCl), by using mixtures of acid and sodium salt.

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Unprecedented Oxidative Degradation of Arylethanol and Arylacetic Acids by Means of Active γ -Manganese Dioxide

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Active manganese dioxide is known¹ to be an excellent reagent for the oxidation of primary and secondary allylic and benzylic alcohols to the corresponding carbonyl compounds (aldehydes and ketones).²⁻⁴ Also, some saturated aliphatic alcohols are reported to be oxidized in the same way, though at a lower rate, by this reagent.⁵ The use of manganese dioxide has been also reported as an oxidant for phenols.⁶ Among the various types of active manganese dioxide, γ -manganese dioxide is considered⁷ to be the most reactive form. We report on some observations which indicate that it can oxidize benzylic-type alcohols beyond

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