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The hydroxide ion catalyzed hydrolysis of a series of *N*-acylcarbazoles has been studied in water at 25°. Both the rate constants of formation of the tetrahedral intermediate and of its collapse to products are strongly increased by alkyl group branching in the acyl portion.

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Steric effects have been largely studied to provide useful information on the mechanism of the hydrolysis of amides.

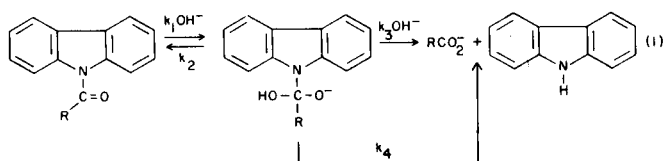
Fife (1) has reported that the rate of hydroxide-catalyzed hydrolysis of *N*-trimethylacetylimidazole is 1.7 times faster than the corresponding rate for *N*-acetylimidazole and equal to that for *N*-propionylimidazole. The steric acceleration has been attributed at least in part (1,2) to a destabilization of the molecular ground state of *N*-trimethylacetylimidazole caused by a loss of resonance energy due to the forcing of the carbonyl group out of coplanarity with the imidazole ring. This behaviour is in contrast with the ten-fold deceleration observed in the rate of alkaline hydrolysis for trimethylacetamide with respect to acetamide (3,4).

Recently we established through a C-13 study that in *N*-trimethylacetylcarbazole, the carbonyl group plane forms an angle of 75° with the carbazole ring (5).

Since this substrate appears to be particularly interesting to test the influence of the non-coplanarity of the carbonyl group and the heterocyclic ring on the hydrolytic behaviour, we studied the alkaline hydrolysis in water of a series of *N*-acylcarbazoles.

#### Results and Discussion.

The mechanism of the basic hydrolysis of *N*-acylcarbazole can be represented by the following scheme of reaction (eq. (1))



and equation (2) represents the rate law for that mechanistic scheme

$$k_{\text{obsd}} = \frac{k_1 k_4 [\text{OH}^-] + k_1 k_3 [\text{OH}^-]^2}{k_2 + k_4 + k_3 [\text{OH}^-]} \quad (2)$$

Plots of  $k_{\text{obsd}}/[\text{OH}^-]$  vs.  $[\text{OH}^-]$  in the range of  $[\text{OH}^-]$   $0.9 + 12.0 \times 10^{-3} M$  are typically curved for all the substrates examined, confirming the postulated mechanism

and showing that at low base concentration the hydrolysis is mainly second order in hydroxide ion, while at high base concentration it is largely first order in hydroxide ion.

The rate constants for the single steps calculated as described in the preceding paper are reported in Table I. The statistical treatment showed that  $k_4$  (the rate constants for the water-catalyzed decomposition of the tetrahedral intermediate) is negligible for all substrates.

From the data of Table I it can be seen that increasing the number of methyl groups at the  $\alpha$ -carbon atoms of the acyl moiety it results in large acceleration, both the  $k_1$  and  $(k_1/k_2)k_3$  being increased. The rate of formation of the intermediate ( $k_1$ ) is increased by a factor of about 30 going from the acetyl to the trimethylacetyl group showing that steric factors affecting the noncoplanarity of the C=O group in respect to the carbazole ring, with the consequent relative loss of the ground state stabilization in the series, plays an important role in determining the reactivity of these compounds.

This factor is probably not the only one concerned in the observed effect, since different solvation in the ground state and in the transition state can be important in highly hydrophobic substrate as *N*-trimethylacetylcarbazole.

Even more striking appears the importance of steric effects on the collapse of the intermediate to the product. In fact the methylpropionyl group increases by a factor of about 30 the rate of decomposition of the intermediate. The acceleration caused by the trimethylacetyl group is even greater (about 60 times).

In this case the greater facilitation in the rate can be ascribed to a relief of steric hindrance in the decomposition of the overcrowded tetrahedral intermediate.

A final comment relative to the importance of the transition state structure is reserved to the different magnitude of steric effects in amide and ester hydrolysis in strongly alkaline solution. Propionate ethyl ester undergoes hydrolysis at a rate 100 times higher than trimethylacetate ethyl ester (6,7), while propionamide is hydrolyzed only 8-9 times easier than trimethylacetamide (3,4). This behaviour is probably due to substantially different transition state structures for the two different classes of compounds. Different solvation patterns and a difference in importance of bond-making may be suggested as factors.

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Table I.

Rate Constants for the Hydroxide-Catalyzed Hydrolysis of *N*-Acylcarbazoles  
in Water at  $25.0 \pm 0.1^\circ$  ( $\mu = 0.2$  Added Sodium Chloride) (a,b)

<i>N</i> -Acyl group	$k_1$ ( $M^{-1} \text{ sec}^{-1}$ )	$k_{rel}$	$\frac{k_1}{k_2} k_3$ ( $M^{-2} \text{ sec}^{-1}$ )	$k_{rel}$	$\frac{k_3}{k_2}$ ( $M^{-1}$ )
Acetyl	$0.75 \pm 0.01$	1.0	$256.4 \pm 5.0$	1.0	341.8
Propionyl	$1.50 \pm 0.02$	2.0	$481.4 \pm 15$	1.9	320.9
Methylpropionyl	$3.73 \pm 0.03$	5.0	$6915 \pm 162$	27	1854
Trimethylacetyl	$24.2 \pm 0.2$	32	$14270 \pm 189$	56	589.0

(a) Error limits are standard deviations. (b) Rate constants were determined from 160 kinetic runs under first order conditions.

## EXPERIMENTAL

The synthesis of the compounds has been described elsewhere (5). Kinetic runs, product analysis and data treatment were carried out as described in the preceding paper. Monitoring wavelength expressed in nm are the following: *N*-acetylcarbazole (270), *N*-propionylcarbazole (268), *N*-methylpropionylcarbazole (268), *N*-trimethylacetylcarbazole (272).

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