Effect of Poly(diallyldimethylammonium Chloride) and of Poly(ethyleneimine) on the Esterolysis of 8-Acetoxyquinoline

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The esterolysis of 8-acetoxyquinoline (8-AQ) in aqueous solution in the presence of an excess of poly(diallyldimethylammonium chloride) (PDDA) or poly(ethyleneimine) (PEI) was investigated at 30 °C. In the presence of PDDA hydrolysis takes place and the polyion does not affect the rate of the reaction. In the presence of PEI the ester undergoes aminolysis and saturation kinetics are observed. The pH dependence of k_{obs}, the apparent first-order rate constant of esterolysis, can be explained on the basis of the pH dependence of pK_{app} and of the degree of ionization of PEI. A Brønsted relationship has already been found for the aminolysis of 8-AQ with primary and secondary amines of low molecular weight. By extending this relationship to the reaction between the polymeric amino-groups in PEI and 8-AQ, we can quantitatively predict the pH dependence of k_{obs} under saturation conditions, provided that the proper values of pK_{app} of the amino-groups are considered.

Polyelectrolytes can change the rates of reaction of organic and inorganic substrates by electrostatic or by hydrophobic interactions.[1-5] For reactions involving ionic substrates the effect of a charged polymer depends largely on its electrostatic potential and on the ionic atmosphere surrounding the polymer in solution.[3,4] When the substrate has no charge, an interaction is still possible provided the structure of the substrate and of the polyelectrolyte allows the existence of apolar, charge transfer, or hydrogen bond interactions.

Polyelectrolytes such as poly(diallyldimethylammonium chloride) (PDDA) (1), have no specifically reactive groups other than the quaternary nitrogen groups, while others such as poly(ethyleneimine) (PEI) (2) have amino groups which, depending on pH, may act as nucleophiles on a substrate.

This paper reports an investigation of the effects of PDDA and PEI on the esterolysis of 8-acetoxyquinoline (8-AQ). Hydrolysis and aminolysis of this ester have been extensively studied by others [6-8] and by us.[9,10]

Hydrolysis of 8-AQ in buffered aqueous solutions at 30 °C and ionic strength 1 has been explained in terms of an acid-catalysed and of spontaneous water hydrolysis of the protonated substrate (within the pH range 0.8—3) and of the reaction of the unprotonated substrate with water (pH 3—8) and with OH^- (over pH 8). The pH–log rate profile is shown in Figure 1.

The mechanism of the water reaction in the plateau region has been interpreted as an intramolecular general base-concerted catalysis by the quinoline nitrogen, according to the rate-determining step represented in (3).

Aminolysis of 8-AQ with monomeric primary and secondary amines has been reported to follow the simple rate law (1)

$$v = k_N[N_f][8\text{-AQ}] \quad (1)$$

where N_f is the unprotonated amine and k_N is the second-order rate constant. There follows at 30 °C and ionic strength 1 the Brønsted catalysis law (2) where K_a is the dissociation

$$\log k_N = 0.68\ pK_a - 6.92\ (k_N/l\ mol^{-1}\ s^{-1}) \quad (2)$$

constant of the protonated amine.

The mechanism of aminolysis with primary and secondary amines has been argued to be based on a rate-determining deprotonation of a $T^{\pm}$ intermediate as in (4),[10] rather than on a concerted intramolecular base-catalysed attack of the amine, similar to the water reaction.[7]

From the above-mentioned results we can express the rate constant for the simultaneous reactions of hydrolysis and aminolysis at pH > 4 in the form (3).

$$\frac{v}{[8\text{-AQ}]} = k_{obs} = k_{H_2O}[H_2O] + k_{OH}[OH^-] + k_N[N_f] \quad (3)$$

Since the quinoline nitrogen in 8-AQ has pK_a 3.3 (see ref. 9) one can safely assume that the substrate participates in the unprotonated form.

Experimental

Materials.—8-AQ was prepared according to ref. 7. PDDA was obtained from Polyscience. Careful titration with $AgNO_3$ gave a molecular weight of 197 for chloride ion. The absolute concentration was 14.6% by weight.

PEI was Polymin P from B.D.H. Titration with 1N- or 2N-HCl gave a molecular weight of 59 for ionic nitrogen. The absolute concentration of 47.6% by weight was determined by differential refractometry (Brice Phoenix model BP 2000 V) at 25 °C using the refractive increment $dn/dc = 0.216$ (ml/g) for Na_D light (λ 589 nm), found elsewhere.[11] A coincident value was obtained by freeze-drying.

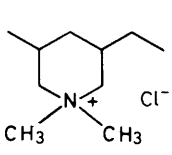
Other reagents were from Merck or Carlo Erba. Water was distilled over $KMnO_4$.

Potentiometric Titrations.—The potentiometric titration of PEI at various concentrations in the range 0.02—0.4 monomol l^{-1} was performed in a thermostatted (30 ± 0.1 °C) polarographic cell, fitted with a microsyringe burette. Measurements of pH were made with an Ingold HA 405 combined glass electrode connected to a Knick pH meter model 603. The glass electrode was standardised with phosphate, phthalate, and borate buffers at 30 °C.[12] Duplicate titrations gave an error of ±0.03 in the pH values.

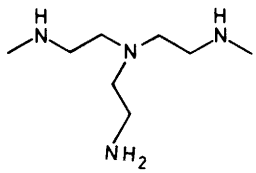
The ionization degree $\alpha = [\overset{+}{N}H]/[PEI_{tot}]$ at any pH was calculated from electroneutrality conditions according to ref. 13. pK_w 13.84 at 30 °C was taken from ref. 14. The values of pK_{app} at each pH were calculated from the Henderson–Hasselbalch equation (5). Results are reported in Tables 1 and 2.

$$\alpha = \frac{[H_{add}^+] - a_{H^+} + [OH_f^-]}{[PEI_{tot}]} \quad (4)$$

$$pK_{app} = pH - \log [(1 - \alpha)/\alpha] \quad (5)$$



(1)



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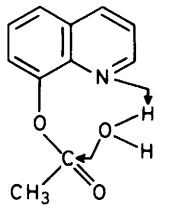

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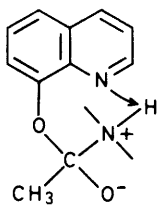


(4)

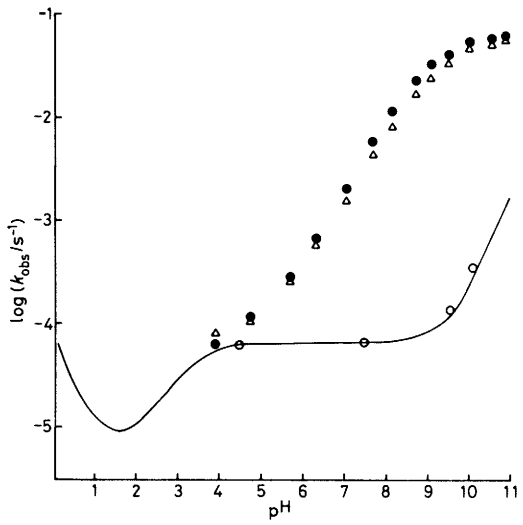


Figure 1. pH–log $k_{obs.}$ profile for the esterolysis of 8-acetoxyquinoline at 30 °C. Hydrolysis in aqueous buffered solutions (——).[9] Hydrolysis in the presence of 0.08 monomol l^{-1} PDDA (○). Esterolysis in the presence of 0.4 monomol l^{-1} PEI: (●) observed values, (△) expected values (see Table 1)

Kinetics.—Kinetic runs were carried out directly in a Perkin-Elmer model 402 u.v. spectrophotometer, equipped with a brass cell holder through which water at 30 °C was circulated. Buffer solutions contained: (i) PDDA (0.03—0.08 monomol l^{-1}) in 0.015M-acetate (pH 4.49), 0.05M-phosphate (pH 7.50), or 0.008M-carbonate (pH 9.60 and 10.10) carriers; (ii) PEI (0.005—0.5 monomol l^{-1}) with added 2N-HCl up to the desired pH.

A stock solution of 8-AQ (2.67×10^{-2} mol l^{-1}) was prepared in 50% v/v dioxane–water. The stock solution (30 μl) was added to a prethermostatted cell containing buffer (3 ml). The initial concentration of ester was 2.67×10^{-4} mol l^{-1} in 0.5% dioxane–water.

The kinetic measurements were performed by following the disappearance of the ester by recording the optical density at 288 nm. At alkaline pH values the appearance of 8-hydroxyquinoline was followed, recording the O.D. at 325 nm.

The pseudo-first-order rate constants were calculated from the slope of plots of $2.303 \log (O.D._{\infty} - O.D._{o})/(O.D._{\infty} - O.D._{t})$ *versus* time, by a least-squares routine.

Reactions were followed for at least two half-lives and were invariably found to be apparently first order. The reproducibility was within 3—5%. In the course of the runs a maximum drift of ±0.06 pH units was observed.

Reaction Products.—In experiments carried out in the presence of PDDA, 8-hydroxyquinoline was identified in the solution by comparing its u.v. spectrum with that of an authentic sample.

In experiments in the presence of PEI acetic acid was quantitatively determined in order to discriminate between hydrolysis and aminolysis. In the first case free acid is expected in an amount equivalent to that of 8-hydroxyquinoline. In the second case the acid could be retained by PEI by formation of acetyl derivatives of primary and secondary amino-groups.

2.2×10^{-4}M-8-AQ and 2.2×10^{-3} monomol l^{-1} PEI (total 5 ml) at pH 7.6 were reacted at 40 °C for 30 min. 8-Hydroxyquinoline precipitated and it was collected by centrifugation. The yield was 82% of the theoretical amount. The dissolved portion was recovered to a total extent of 96% by ion exchange chromatography on Amberlist 29 (Carlo Erba) using 50% ethanol–water as eluant. In parallel runs the solution collected after centrifugation was acidified to pH 1 with hydrochloric acid and then submitted to g.l.c. on a glass column filled with Poropak QS 80—100 mesh. 7% of the theoretical amount of acetic acid was recovered. A recovery of 95% was obtained in comparable experiments with added acetic acid.

Results and Discussion

Apparent first-order rate constants for the hydrolysis of 8-AQ in the presence of 0.08 monomol l^{-1} PDDA were 6.79×10^{-5} s^{-1} at pH 4.49, 6.85×10^{-5} s^{-1} at pH 7.50, 2.02×10^{-4} s^{-1} at pH 9.60, and 4.03×10^{-4} s^{-1} at pH 10.10. The points fit the pH–log rate profile of the hydrolysis in buffered water solution at $\mu = 1$ found in the absence of polyelectrolytes (Figure 1).

The ineffectiveness of PDDA on the hydrolysis of 8-AQ reveals the absence of any electrostatic or lipophilic interaction affecting the reaction rate.

The results obtained in the presence of PEI are quite different. The experimental evidence that PEI can be acetylated in the reaction suggests that an aminolysis, rather than a hydrolysis, takes place.

There is strong evidence that PEI is a branched polyelectrolyte with a compact structure, in which primary, secondary, and tertiary amino-groups are present.[15,16] Therefore the sites of the reaction are not uniform. Moreover the most relevant feature of the dissociation equilibrium of PEI is the change in the apparent dissociation constant (K_{app}) with the degree of dissociation, due to the neighbouring interactions between charged and uncharged groups along the polymer network.[13,17,18]

We titrated our sample of PEI to determine the dissociation constant and the ionization degree as a function of pH and of the total concentration of the polymer. Results are close to those reported for similar conditions by others.[13] From values reported in Table 1 it is clear that an increase in the pH leads to a rather large increase of pK_{app} and to a relatively small decrement of the degree of ionization.

A more detailed analysis of the dependence of $[N_f]$, $[\overset{+}{N}H]$, and pK_{app} on the total concentration of PEI at pH 6.40, 7.50, and 8.50 is reported in Table 2. The data show that an increase of the total concentration of the polymer at a fixed pH is accompanied by an increase of the degree of ionization $\alpha = ([\overset{+}{N}H]/[PEI_{tot}])$ at alkaline pH.

Table 1. pH Dependence of pK_{app} and free amino-group concentration of PEI. Apparent first-order rate constants of the esterolysis of 8-acetoxyquinoline in the presence of PEI at 30 °C [a]

pH	pK_{app} [b]	$[N_f]$ [c]	$10^4 k_{obs}/s^{-1}$ Found	$10^4 k_{obs}/s^{-1}$ Expected [d]
3.96	4.39	0.108	0.61	0.80
4.76	5.10	0.126	1.18	1.12
5.69	5.92	0.148	2.67	2.58
6.32	6.51	0.156	6.43	5.69
7.07	7.10	0.192	21.0	16.3
7.75	7.65	0.223	62.8	43.3
8.17	8.01	0.236	119	80.2
8.73	8.32	0.288	237	166
9.09	8.50	0.320	341	233
9.51	8.70	0.348	418	346
10.05	8.86	0.376	538	481
10.58	8.89	0.392	548	528
10.89	8.94	0.395	570	583

[a] [8-AQ] 2.67×10^{-4}M; [PEI] 0.4 monomol l^{-1}. [b] Calculated by equation (5). [c] $[N_f] = (1 - \alpha)[PEI_{tot}]$, calculated from equation (4). [d] From equations (2) and (3), with $k_{H_2O}[H_2O]$ 6.75×10^{-5} s^{-1} and k_{OH} 1.22 l mol^{-1} s^{-1}.

Table 2. Concentration of free and protonated amino-groups and pK_{app} of PEI determined from titration curves at 30 ± 0.1 °C

pH	PEI_{tot} [a]	$[N_f]$ [b]	$[\overset{+}{N}H]$ [b]	pK_{app} [c]
6.40	0.02	0.0089	0.0111	6.50
	0.05	0.0203	0.0297	6.56
	0.10	0.0418	0.0582	6.54
	0.15	0.060	0.090	6.57
	0.25	0.108	0.142	6.54
	0.40	0.172	0.228	6.56
7.50	0.02	0.0127	0.0073	7.26
	0.05	0.0296	0.0204	7.38
	0.10	0.0564	0.0436	7.41
	0.15	0.080	0.070	7.44
	0.25	0.136	0.144	7.43
	0.40	0.212	0.188	7.45
8.50	0.02	0.0166	0.0034	7.82
	0.05	0.039	0.011	7.93
	0.10	0.0758	0.0242	8.01
	0.15	0.108	0.042	8.05
	0.25	0.178	0.072	8.12
	0.40	0.274	0.126	8.16

[a] Monomol l^{-1}. [b] Calculated from equation (4). [c] Calc. from equation (5).

These data are useful in the interpretation of the dependence of the rate of the reaction of 8-AQ on the concentration of the polymer and on pH.

Experiments performed at 30 °C at pH 6.40, 7.50, and 8.50 showed that the apparent first-order rate constant of the esterolysis of 8-AQ is enhanced by increasing the total concentration of PEI (Figure 2). The saturation trend of the curves suggests the presence of association phenomena. The data were therefore analysed according to the reaction scheme (6)

$$C + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CS \xrightarrow{k_{cat}} P_1 + P_2 \qquad (6)$$

where C is the polymer, S is 8-AQ, CS is an association compound, and P_1 and P_2 denote acetylated PEI and 8-hydroxyquinoline, respectively.

Since initially an excess of polymer is present over the substrate ($[C_o] \gg [S_o]$) equation (7) obtains where $[S_f] = [S] + [CS]$. Supposing $k_{-1} \gg k_{cat}$, equation (8) results where

$$v = k_{obs}[S_f] \qquad (7)$$

$$k_{obs} = \frac{k_{cat}K_b[C_o]}{1 + K_b[C_o]} \qquad (8)$$

$K_b = k_1/k_{-1}$. Equation (8) can be reorganised as (9) and the

$$\frac{1}{k_{obs}} = \frac{1}{k_{cat}} + \frac{1}{k_{cat}K_b[C_o]} \qquad (9)$$

treatment of experimental data by the least-squares method showed the good fit of $1/k_{obs}$ to a straight line. Values of k_{cat}, K_b, and the correlation coefficients are reported in Table 3.

Clearly the binding constant K_b decreases upon increasing the pH, but k_{cat} increases. Moreover, since a lower pH implies a lower pK_{app} of the protonated amino-groups of PEI, we may infer an association, of unknown origin, of the substrate with the protonated polymer.

The addition of KCl slows down the rate of the reaction. At pH 7.5 and at a PEI concentration of 0.05—0.4 monomol l^{-1}, the values of the rate constants in the presence of 0.24M-KCl are reduced to 40% and 11%, respectively, of the values observed without added salt.

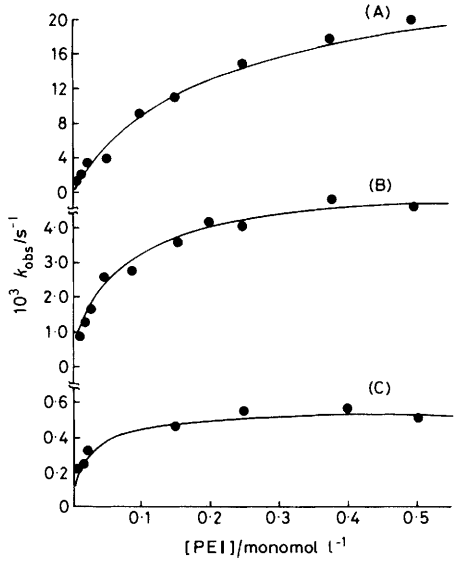
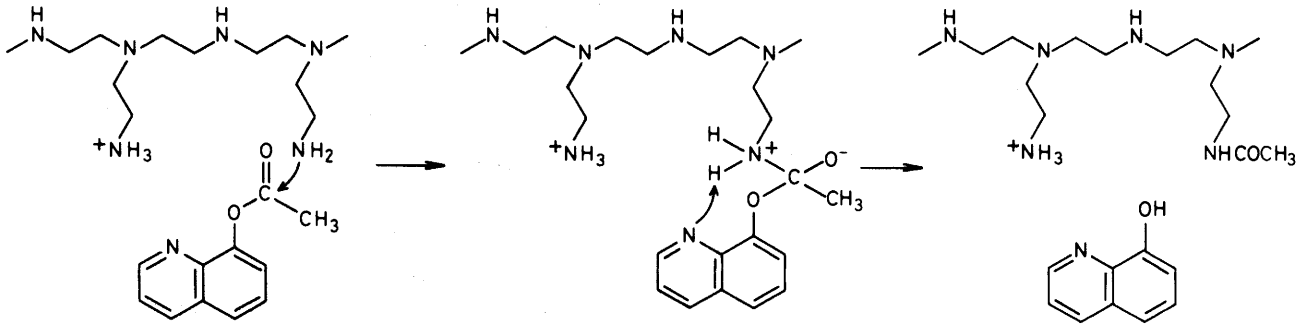


Figure 2. Dependence of the apparent first-order rate constant (k_{obs}) on the PEI concentration at 30 °C: (A) at pH 8.50, (B) at pH 7.50, (C) at pH 6.40. The solid lines were calculated from equation (8) and from the data in Table 3

Table 3. Kinetic parameters for esterolysis of 8-acetoxyquinoline in the presence of PEI at 30 °C [a]

pH [b]	k_{cat}/s^{-1}	K_b/l mol^{-1}	r [c]
8.50	2.0×10^{-2}	6.4	0.998
7.50	4.3×10^{-3}	20.5	0.995
6.40	5.3×10^{-4}	49.0	0.981

[a] [8-AQ] 2.67×10^{-4}M, $[PEI_{tot}]$ 0.005—0.5 monomol l^{-1}. [b] ±0.05. [c] Correlation coefficient for equation (9).



Scheme.

It is known that pK_{app} of PEI increases in the presence of NaCl.[13] This salt does not induce conformational changes in the PEI network.[13] It is reasonable to expect similar behaviour by KCl. However, an increase in pK_{app} of PEI would enhance the reaction rate. The opposite effect is observed. The result can be ascribed to a decrease of the polymer–substrate interactions by charge shielding.

The reactivity of the association compound is expressed by k_{cat}. It increases with pH, reflecting the relative availability of amino-groups as well as their nucleophilicity, and this is in the direction expected on the basis of the values of $[N_f]$ and of pK_{app} reported in Tables 1 and 2.

It should be noted that at least at pH 8.50, owing to the change of pK_{app} with the total concentration of PEI, the value of k_{cat} can be considered as a combination of several values.[19]

A deeper insight into the significance of k_{cat} and into the possible mechanism of the reaction comes from consideration of the pH dependence of the reaction rate. The sigmoidal pH dependence of log rate, represented by the points in Figure 1, looks at first glance like the one expected for a nucleophilic amine. However, keeping in mind the results of the titration curves of PEI, the variation of log k_{obs} with pH could depend far more on the variation of pK_{app} of the amino-groups than on the variation of their concentration.

In order to compare the behaviour of 8-AQ with PEI with that observed with monomeric amines having similar pK_a, we calculate the values of k_{obs} that can be predicted on the basis of pK_{app} of the amino-groups of PEI. We chose pK_{app} instead of pK_o (pK_a at α 0) because, since it is a function of the charge on the polyion, it should thus correlate with nucleophilicity.[20]

Temporarily disregarding the association of the substrate with PEI, we express the concentration of the polymer as monomoles of free amino-groups at each pH, according to the data collected in Table 1 for [PEI] 0.4 monomol l^{-1}. From Table 1 we take the respective values of pK_{app} at each value of pH. By inserting these data in equation (2) we derive k_N. The values of k_{obs} at each pH are then calculated by equation (3). Comparison of calculated and experimental values of k_{obs} is made in Figure 1 and Table 1.

The rather good agreement between the two sets of values is not to be considered fortuitous in spite of the arbitrary choice of the concentration of PEI and the different kinetic laws involved in the two underlying processes [equations (3) and (8)]. Actually the PEI concentration of 0.4 monomol l^{-1} falls at the limit of the saturation conditions (Figure 2) and the substrate can be considered almost fully associated with the polymer.* According to equation (12), k_{obs} would then not differ so much from k_{cat}. The latter could depend on pK_{app} of the free amino-groups of PEI in the same way as k_N depends on pK_a of primary and secondary amines in the bimolecular process [equation (2)].

Consequently a similar mechanism could also be expected.

In conclusion, the changing of the nucleophilicity of the amino-groups of PEI by changing pH gives a good account of the sigmoidal shape of the pH–log rate profile, provided that the proper pK_{app} values are considered.

Extending the mechanism already advanced for the aminolysis of 8-AQ with monomeric primary and secondary amines to the present case, the esterolysis of 8-AQ in the presence of PEI could first involve an association of the substrate with the polyion. Aminolysis would then follow, having as rate-determining step the breakdown of a $T^{\pm}$ intermediate, catalysed by the quinoline nitrogen, as in the Scheme. The proximity of the amino-groups participating in the reaction is assumed for sake of simplicity in the Scheme. Groups far apart may also react if suitably placed in the network of the polymer. The contribution of the tertiary amino-groups in PEI is not important, as monomeric tertiary amines are *ca.* 100 times less reactive than primary and secondary amines in the reaction with 8-AQ.

* At a PEI total concentration of 0.02 monomol l^{-1}, well below the saturation conditions, the calculated values of k_{obs} are lower than those experimentally determined.

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