Pyrylium-mediated Transformations of Natural Products. Part 2.[1] Reaction of 4-(4-Methoxy-3-sulphophenyl)-2,6-bis-(4-sulphophenyl)-pyrylium Perchlorate with Primary Amines

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The title pyrylium cation reacts with amines in aqueous solution to give mixtures of divinylogous amide and pseudobase. The two products are formed by kinetic control in quantities which then slowly come to equilibrium. Further pyridinium ion is formed slowly from pseudobase. The divinylogous amide cyclises to pyridinium ion. Kinetic rate constants are described for reactions with lysine and other typical primary amines. With s-butylamine appreciable quantities of the 2*H*-pyran are formed.

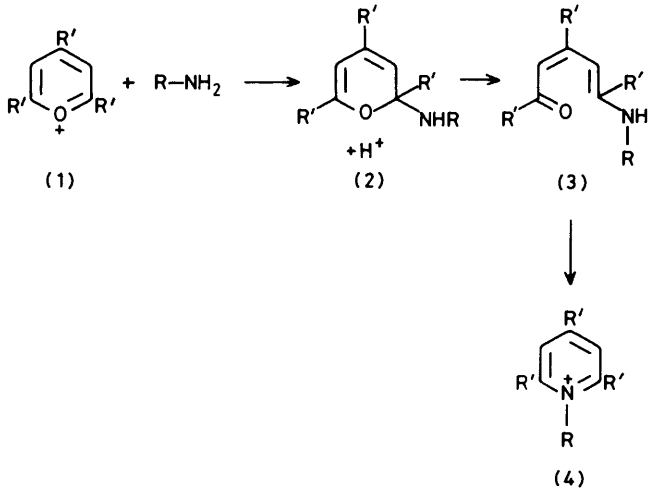
In 1910 A. Baeyer reported [2] the first pyrylium ion to pyridine conversion, by treatment with ammonia. Primary amines, pyridinium salts,[3] and the amino groups of hydrazines, hydroxylamines, and hydrazides also react.[4] The *N*-substituent of pyridinium salts undergoes nucleophilic or free radical displacement.[5]

The aim of this series of papers is to develop a method for the selective transformation of primary amino groups present in water-soluble natural products such as polypeptides. In the preceding paper a prototype water-soluble pyrylium ion was described.[1] We now examine the reactions of this pyrylium ion with simple primary amines. Lysine is chosen as a model for the primary amino groups of many natural products and its behaviour is compared with that of other primary amines.

Previous Studies on the Pyrylium–Pyridinium Transformation.—Reaction of a pyrylium ion with an amine initially gives a 2*H*-pyran.[3] This intermediate is generally only isolable when a secondary amine is used.[6,7] With NH_3 or a primary amine, the 2*H*-pyran ring spontaneously opens; however in recent studies 2*H*-pyrans were detected by ^{13}C n.m.r. in reactions of sterically crowded pyrylium ions with primary amines.[8,9]

An open-chain intermediate was isolated in 1958 from the reaction of 2,4,6-triphenylpyrylium ion and cyclohexylamine.[10] Since then similar intermediates have been obtained or detected from reactions of NH_3 [11] and primary [8,12–14] and secondary amines [8,9,13–15] with pyrylium ions. These intermediates have been variously considered to be: (i) a tautomeric mixture of the divinylogous amide (3) and an imino-enol; [10,12] (ii) an imino-enol; [11] (iii) the zwitterionic form of the divinylogous amide.[15] Recent ^{13}C n.m.r. studies have shown that the divinylogous amide is the stable tautomer.[8,13] The kinetics of pyridinium ion formation in organic solvents have also been studied,[14] and Scheme 1 summarizes the accepted mechanism.[3]

Preparation of Pyridinium Salts.—The reaction of the pyrylium ion (5) with the amines given in Scheme 2 was carried out preparatively to check the synthetic utility of (5) and to obtain authentic samples for the kinetic studies. Spectral data (u.v., and ^1H and ^{13}C n.m.r.) (Tables 1—3) and elemental analyses were in accord with the expected structures except with s-butylamine. In particular the ^{13}C n.m.r. spectra demonstrate that the ω-amino group of lysine reacts.



Scheme 1.

Table 1. U.v. data for compounds (7a—c, e, and f) and (8d) in aqueous solution

Compound	$\lambda_{max.}$/nm ($\varepsilon_{max.}$/l mol^{-1} cm^{-1})
(7a)	223 (36 000), 340 (26 800), 408 (4 600)
(7b)	222 (35 800), 337 (25 000)
(7c)	222 (39 600), 343 (29 000)
(7e)	220sh (40 500), 246sh (22 200), 345 (31 600)
(7f)	222sh (33 200), 354 (30 600)
(8d)	221 (16 600), 259 (8 860)

Reaction of the Pyrylium Ion (5) *with s-Butylamine.*—The reaction of s-butylamine with the pyrylium ion (5) gave (in contrast to the other primary amines) the 2*H*-pyran (8d), as indicated by the chemical and spectral properties. Similar intermediates have been detected when steric crowding at C-2(6) of the 2*H*-pyran prevented ring opening.[8,9]

The formation of the pyrylium ion (5) was observed by u.v. when a solution of the 2*H*-pyran (8d) was acidified with conc. HCl. The ^{13}C n.m.r. spectrum (Table 3) lacked the characteristic carbonyl peaks of the pseudobase (9).[1] Peak assignments for the 2*H*-pyran (8d) are in accord with previous reports for 2*H*-pyrans: [8] the signals due to C-1′, -3′, and -5′ in the phenyl ring attached to C-6 of the pyran are shifted 0.3—1.1 p.p.m. downfield as compared with the same carbon atoms in the phenyl ring attached to C-2; however C-2′ and

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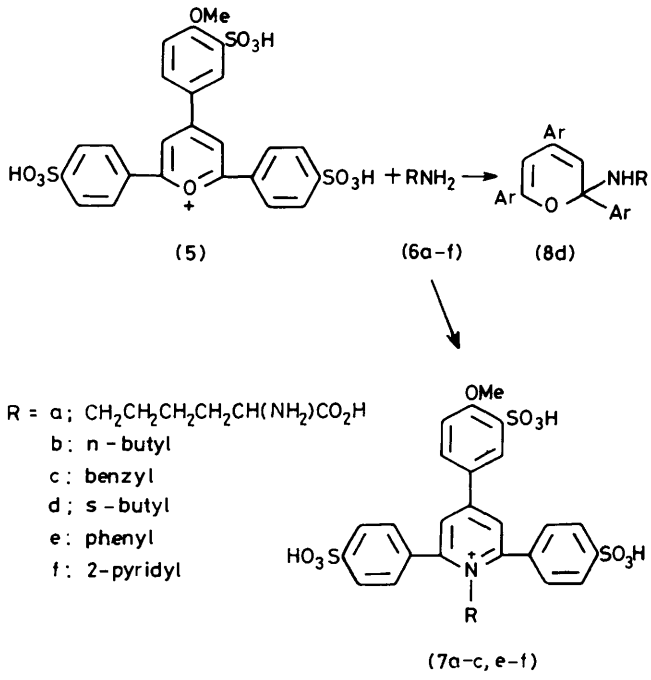
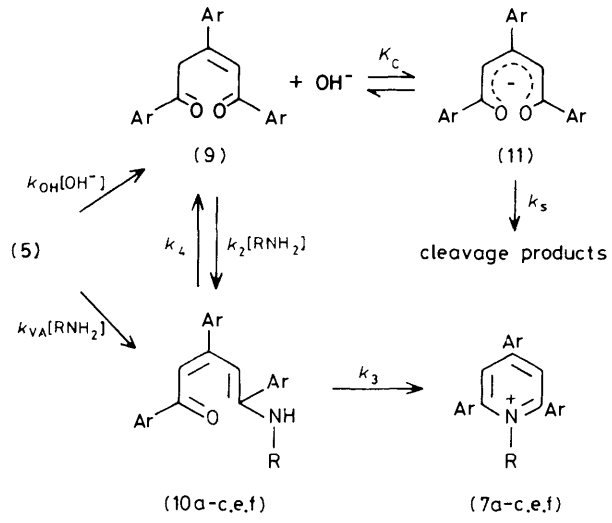


Scheme 2.



Scheme 3. For designation of R, see Scheme 2

-6′ of the phenyl ring attached to C-6 of the pyran show upfield shifts of 1.7 p.p.m. These changes are associated with differences in the hybridisation of C-2 and C-6 in the 2*H*-pyran. There is some uncertainty in the assignment of peaks attributed to C-3 in the 2*H*-pyran and C-5′ in the phenyl group attached to C-4 of the 2*H*-pyran. Values of 108.9—115.0 p.p.m. have been reported for the C-3 of 2*H*-pyrans [8] and the calculated * chemical shift for C-5′ was 115.6.

Reaction of the Pyrylium Ion (5) *with Lysine.*—Previous observations suggested that contact of a pyrylium ion with an amine in water or ethanol generally resulted in hydrolysis of the cation.[10,14,15] The pseudobase formed (a 1,5-diene-2-one) then reacted slowly [13] with amine to give the pyridinium salt. Addition of a solution of the pyrylium ion (5) in 0.01N-HCl to a buffer of pH 10.1 containing the amine substantially changed this pattern (for reasons discussed later). After the two solutions were mixed no trace of the characteristic absorbance [1] (407 nm) of the pyrylium ion (5) could be detected by u.v.–visible spectroscopy. A new absorption band appeared at *ca.* 480 nm whose magnitude depended on the concentration of amine present (at constant pH). The rate at which the 480 nm absorption decreased and the nature of the products formed also depended on amine concentration: the corresponding pyridinium ion was formed at high lysine concentrations (≥0.1M); whereas low lysine concentrations gave the pseudobase (9) of the pyrylium ion (5). [The presence of (9) was confirmed by acidifying the reaction mixture and regenerating the pyrylium ion.[1,17]] The pseudobase (9) then reacted slowly with amine to give the pyridinium salt (7). It is proposed that the initially observed intermediate was the corresponding divinylogous amide (10). These amides

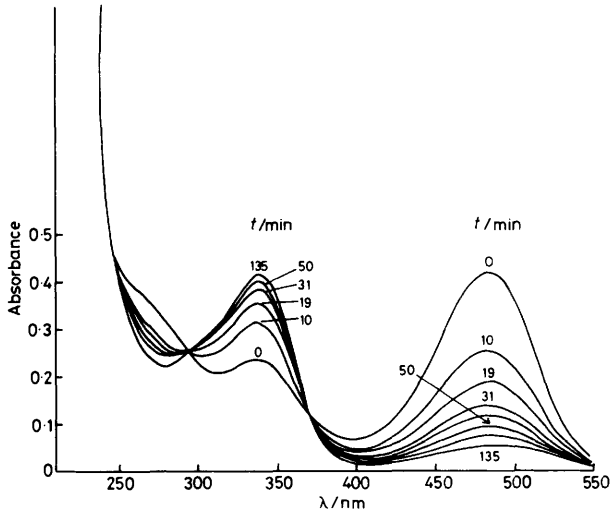


Figure 1. Scanning u.v. study of the reaction of the pyrylium ion (5) (2 × 10^{-5}M) with lysine (0.022M) at pH 10.07 and 25 °C in water

(10) absorb in this region [14] and have been detected in cognate studies in organic solvents.[8,9,14]

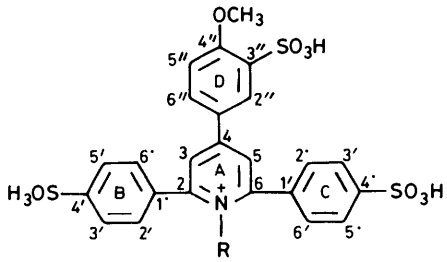
We shall show that the reaction of (5) with lysine and other amines is consistent with the mechanism of Scheme 3.

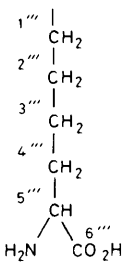
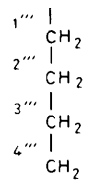
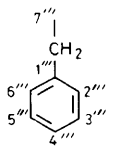
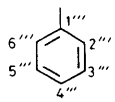
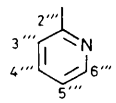
Figure 1 illustrates what occurred when a solution of the pyrylium ion (5) in 0.01N-HCl was added to a buffer at pH 10.1 containing lysine [ratio 1 400 : 1 lysine to (5)]. No absorption for the pyrylium ion (5) was detected, but a new band attributed to the divinylogous amide (10a) appeared at 483 nm. The initial absorbance at 483 nm was greater the greater the lysine concentration, and a maximum value was obtained where essentially all the pyrylium ion (5) had been converted into divinylogous amide (10a). The band at 483 nm decreased with time to give the characteristic pyridinium salt (7a) band at 338 nm (Figure 1). The pseudobase (9) absorbs at 339 nm,[1] but upon acidification [1,17] no absorption at 407 nm appeared for the pyrylium ion (5), thus eliminating (9) as a possible product.

The formation of the pyridinium ion (7a) was a biphasic process (Figure 2). Individual pseudo-first-order rate constants were calculated by the subtraction method [18] using equation

* The chemical shift for C-5′ was calculated from the equation $\delta_C = \delta_{PhH} + \Sigma\Delta\delta_{sub}$, where δ_C is the chemical shift of the appropriate carbon atom, δ_{PhH} = 128.5 p.p.m. (chemical shift of benzene [16]) and $\Delta\delta_{sub}$ is the change in chemical shift associated with the presence of the substituent in the phenyl ring.[16] In the calculation it was assumed that the 2*H*-pyran behaved as a vinyl group.

Table 2. ^{13}C N.m.r. data (δ) for pyridinium ions (7a—c, e, and f)



	(7a)	(7b)	(7c)	(7e)	(7f)
Ring A					
2,6-C	155.9	155.9	156.6	150.8	150.6
3,5-C	126.3	126.3	126.5	126.3	127.3
4-C	154.4	154.2	155.4	160.9	157.2
Rings B and C					
1′-C	135.7	135.8	135.7	145.3	145.6
2′,6′-C	130.7	130.6	130.4	129.2	129.5
3′,5′-C	127.2	127.2	127.2	125.8	126.5
4′-C	146.2	146.1	146.1	139.1	140.9
Ring D					
1″-C	125.2	125.3	125.3	134.6	134.8
2″-C	134.2	129.0	129.8	124.1	125.6
3″-C	132.5	132.5	129.2	129.9	131.0
4″-C	160.7	160.6	160.9	156.1	155.4
5″-C	114.6	114.6	114.7	114.7	114.7
6″-C	135.0	134.2	134.3	132.7	132.7
OCH_3	57.2	57.2	57.3	57.3	57.3
R =					
1‴-C	53.5	55.3	133.3	135.9	
2‴-C	29.2	32.0	127.2	126.3	149.7 [a]
3‴-C	21.8	19.4			124.9
4‴-C	24.7	12.7	132.5	131.1	135.2
5‴-C	53.0				125.4
6‴-C	172.1		127.2	126.3	150.6 [a]
7‴-C			59.1		

[a] Tentative assignment.

(i) (Table 4), where k_{obs} is the rate constant for formation of

$$A_t = A_{0.1}\,e^{-k_{obs}t} + A_{0.2}\,e^{-k't} \qquad \text{(i)}$$

pyridinium from divinylogous amide, k' is the rate constant for the formation of pyridinium from pseudobase, A_t is the total absorbance at 483 nm, $A_{0.1}$ is the absorbance of divinylogous amide at $t = 0$ at 483 nm, and $A_{0.2}$ is the absorbance of the anion [1] of pseudobase (9) at 483 nm and $t = 0$. The decrease in anion absorbance is directly proportional to the rate of conversion of pseudobase (9) into pyridinium ion (7a); therefore, the rate constant obtained from the disappearance of the anion is identical with that for the conversion of pseudobase (9) into pyridinium ion (7a). Experiments starting with the pseudobase (9) (see next section) confirmed that the rate constant for formation of the pyridinium ion (7a) from the pseudobase (9) was essentially identical with k' obtained from equation (i), starting with the pyrylium ion (5).

Extrapolation of the slow portion of the curve in Figure 2 gives the anion concentration at $t = 0$. (This is actually the stoicheiometric concentration of anion which is the sum of anion and pseudobase concentrations at pH 10.1.) In the same manner anion absorbance (concentration) can be determined at any point in the reaction path and by difference the divinylogous amide absorbance at 483 nm. Plots of $\ln(A - A_\infty)$ *versus* time for the disappearance of divinylogous amide and anion gave k_{obs} and k' respectively.

The rate constant k_{obs} depended on lysine concentration (Figure 3) according to equation (ii),[19] where k_3 is the rate

Table 3. ^{13}C Chemical shifts (δ) of the 2*H*-pyran (8d)

2*H*-Pyran		2-Aryl [a]		6-Aryl [a]		4-Aryl [a]		1″ 2″ 3″ 4″ $CH_3CHCH_2CH_3$	
		1′	141.6	1′	142.7	1′	131.7	1″	28.0
2	104.2	2′, 6′	129.9 [b]	2′, 6′	128.1	2′	130.6 [b]	2″	50.1
3	113.5 [b]	3′, 5′	126.0	3′, 5′	126.3	3′	130.2 [b]	3″	34.8
4	136.8	4′	145.4	4′	145.8	4′	157.3	4″	18.1
5	93.0					5′	113.5 [b]		
6	147.1					6′	130.8		
						OCH_3	56.9		

[a] $0 \leqslant \Delta(\text{abs} - \text{calc}) \leqslant |1.71|$ p.p.m. [b] Tentative assignments.

Table 4. Rate constants for reaction of the pyrylium ion (5) with lysine determined at pH 10.1 and 25.0 ± 0.1 °C

[lysine]/mol l^{-1}	$10^4\ k'/s^{-1}$	$10^4\ k_{obs}/s^{-1}$	$10^4\ k_2/s^{-1}$	$10^4\ k_4/s^{-1}$	A_0	10^5[pseudobase]/mol l^{-1}	10^5[divinylogous amide]/mol l^{-1}
0.001	0.51	21.22	0.003	0.014	0.424	1.68	0.32
0.005	0.46	11.72	0.02	0.018	0.482	1.19	0.81
0.025	0.41	7.83	0.08	0.014	0.571	0.46	1.54
0.05	0.49	7.31	0.17	0.015	0.586	0.33	1.67
0.1	0.64	6.54			0.580	0.26	1.74
0.25	1.38	6.76			0.607		
0.5	2.87	8.47			0.591		

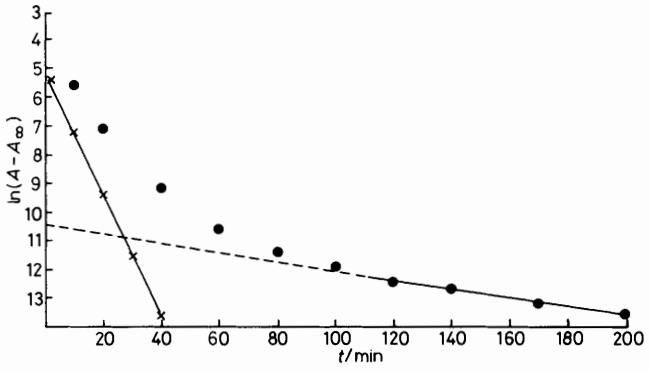


Figure 2. Biphasic plot of $\ln(A - A_\infty)$ *versus* time for reaction of the pyrylium ion (5) (2×10^{-5}M) with lysine (0.028M) at pH 10.08 and 25 °C in water

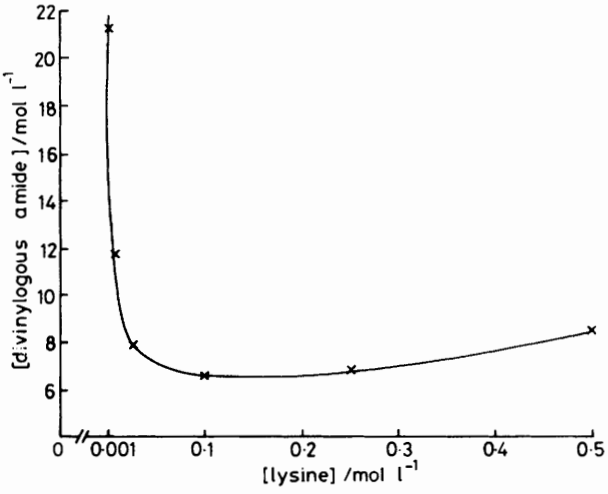


Figure 3. Rate of disappearance of divinylogous amide (10a) *versus* [lysine]

of conversion of divinylogous amide (10a) into pyridinium ion (7a) and K_v = [divinylogous amide]/[lysine][pseudobase]. Equation (ii) was transformed into equation (iv), and a plot

$$k_{obs} = k_3(1 + K_v/[\text{lysine}]) \quad \text{(ii)}$$

$$k_{obs} = k_3 + k_3K_v/[\text{lysine}] \quad \text{(iii)}$$

$$k_{obs}[\text{lysine}] = k_3[\text{lysine}] + k_3K_v \quad \text{(iv)}$$

of k_{obs}[lysine] *versus* [lysine] gave a good straight line (r = 0.9986) whose intercept was k_3K_v and slope k_3. Values of k_3 and K_v are in Table 5.

Previous kinetic studies indicated that OH^- and primary amines react with pyrylium ions to give in each case a 2*H*-pyran which quickly ring opens to a pseudobase [1,3] or a divinylogous amide, respectively.[14] The initial ratio of pseudobase and divinylogous amide formed is determined by the relative rates of attack of OH^- and primary amine on the pyrylium ring. The total concentration of pseudobase and anion derived from attack of OH^- on the pyrylium ion (5) was obtained by extrapolation (see before).

The initial concentration of divinylogous amide is obtained by subtracting this concentration from the initial concentration of pyrylium ion (5). The relative rate (k_{VA}/k_{OH}) of formation of (10a) with respect to (9) was determined as 0.13 (Table 5) using equations (v)—(vii). Here, K_a' is the acidity constant of lysine corrected for the ionic strength of the buffer used.[20]

$$[\text{lysine}] = [\text{lysine}]_{stoich}(K_a' + [H^+])/K_a' \quad \text{(v)}$$

$$\frac{[VA]}{[PB]} = \frac{k_{VA}[\text{lysine}]}{k_{OH}[OH^-]} \quad \text{(vi)}$$

$$\frac{k_{VA}}{k_{OH}} = \frac{[VA][OH^-]}{[PB][\text{lysine}]} \quad \text{(vii)}$$

An equilibrium exists between divinylogous amide (10a) and pseudobase (9). Their respective initial concentrations are kinetically determined as already noted. Reaction of (5) with amine (k_{VA}[lysine]) was much faster than with hydroxide (k_{OH}[OH]). At low amine concentrations this resulted in a

Table 5. Comparison of kinetic data for reaction of the pyrylium ion (5) and/or the pseudobase (9) with different amines at pH 10.1 and 25.0 ± 0.1 °C

Amine	k_{VA}/k_{OH}	$10^4 k_3/s^{-1}$	$10^3 K_V$/mol l^{-1}	$10^4 k_B$/l $mol^{-1} s^{-1}$	$10^4 k_S/s^{-1}$
Lysine	0.130	6.36	4.50	3.34 ±0.25	0.54 ±0.08
n-Butylamine	0.181	40.44	10.73	7.83 ±0.93	0.09 ±0.32
Benzylamine	0.047	20.45	5.07	1.16 ±0.26	0.63 ±0.25
Aniline	0.043	*ca.* 1 000			0.54 [a] ±0.17
2-Aminopyridine	*ca.* 0.001	*ca.* 700			0.37 [a] ±0.08

[a] Average values.

Table 6. Observed rate constants [a] for reaction of pseudobase with lysine

pH	$10^5 k'/s^{-1}$ [b]	Conc. of [lysine]/mol l^{-1}	$10^4 k'/s^{-1}$ [c]
8.38	0.71 [d]	0.028	0.61
9.15	1.93	0.1	0.89
9.36	2.21	0.4	1.90
9.99	5.96	0.5	2.31
10.13	5.36		
10.92	6.81		

[a] Correlation coefficients for all observed rate constants are $0.998 \leqslant r \leqslant 1.000$. [b] [Lysine] 0.1 mol l^{-1}. [c] pH 10.1. [d] Reaction under these conditions has biphasic character and $k_{fast} = 5.30 \times 10^{-4}\ s^{-1}$.

metastable state in which the concentration of divinylogous amide (10a) was higher than indicated by K_V. Equilibrium was established by the conversion of (10a) into pseudobase. When [lysine] > K_V there is little difference between the kinetic (initial concentration) and equilibrium concentrations of divinylogous amide. The rate-determining step from equation (ii) for pyridinium ion formation is then the cyclisation of the divinylogous amide (k_3). The reactions of pseudobase will be discussed in the next section.

Figure 3 indicated that as the concentration of lysine increased the rate levelled off following equation (ii). For lysine concentrations higher than 0.1M, k_{obs} began to increase. Possibly another process occurs: divinylogous amide could react further with lysine to give a dianil. Such intermediates are known to cyclise to give a pyridinium compound and an amine fragment.[21] This reaction was not explored further.

Reaction of Pseudobase with Lysine.—Solutions of the pseudobase (9) were prepared by dissolving the pyrylium ion (5) in buffers of appropriate pH.[1] This solution was then added to a buffer containing lysine. The reaction was followed by adding a sample of the reaction mixture to a buffer of pH 11 and thus converting unchanged pseudobase (9) into its anion (11). Changes in the anion absorbance (487 nm) were used to determine the rate of disappearance of (9).

In Figure 4 and Table 6 can be seen the results of studying the reaction between pH 8.38 and 10.92 and maintaining the stoicheiometric concentration of lysine at 0.1M. A maximum value was obtained when pK_a(lysine) > pH. At constant pH (10.1) the rate depended on the lysine concentration as equation (viii) (Figure 5), where k_B is the second-order rate constant of formation of divinylogous amide (10a)

$$k' = k_S + k_B[\text{lysine}] \qquad \text{(viii)}$$

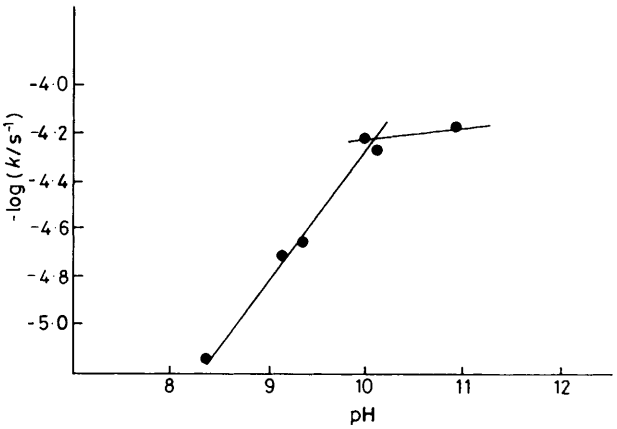


Figure 4. log k_{obs} *versus* pH for reaction of pyrylium ion (5) (5×10^{-4}M) with constant stoicheiometric concentration of lysine (0.1M)

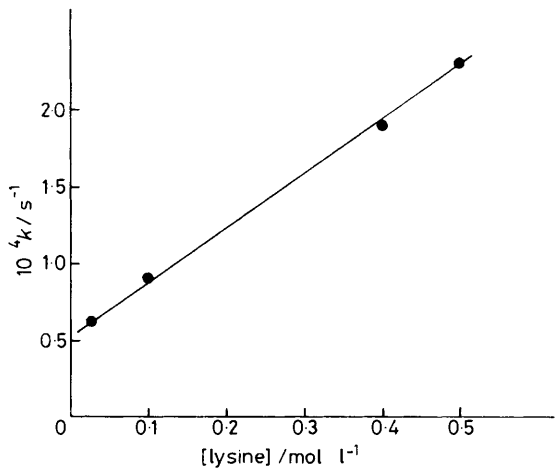
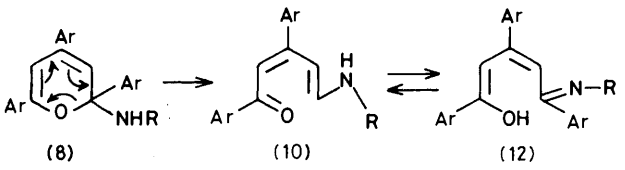


Figure 5. Rate of pseudobase (9) disappearance *versus* [lysine]

and k_S is the rate constant of alkaline cleavage of pseudobase (9). The latter process has been previously described [1] and depends only on the concentration of OH^-. Conversion of pseudobase (9) into divinylogous amide (10a) (k_2) was *ca.* 1/20th as fast as the conversion of (10a) into pyridinium ion (7a) (k_3).

Comparison of the foregoing results with those in the previous section indicated that the rate of pyridinium ion



Scheme 4.

formation depended on the relation between K_v and [lysine]. If $K_v >$ [lysine] the rate-determining step was cyclisation of divinylogous amide (10a) and pyridinium ion formation was fast when $K_v <$ [lysine] the rate-determining step was formation of (10a).

The rate of conversion of divinylogous amide into pseudobase at low lysine concentration was found to be 1.5×10^{-6} s^{-1} (Table 4), calculated by equation (ix) (see Scheme 3).

$$K_v k_2/[\text{lysine}] = k_4 \qquad \text{(ix)}$$

Comparison of Reactivity of Primary Amines with the Pyrylium Ion (5).—Examples of the following three classes of primary amines were studied: primary alkylamines, secondary alkylamines, and aromatic amines. As noted previously all the amines except s-butylamine were converted into their respective pyridinium salts in a process similar to that described for lysine, and the kinetic data of Table 5 were obtained as described for lysine.

Aliphatic amines (6b and c) behaved quite similarly to lysine (6a) and there was no apparent trend in their respective values of k_{VA}/k_{OH}, k_3, and K_v. This reflects their similar basicities and nucleophilicities. The formation of pyridinium ion from the aromatic amines, aniline (6e) and 2-aminopyridine (6f), was much faster than when aliphatic amines were used. In an analogous ^{13}C n.m.r. study ([$^2H_6$]Me_2SO) of the formation of a pyridinium cation from 2,4,6-triphenylpyrylium ion and aniline, the pyridinium salt formed rapidly and no divinylogous amide was detected.[13] Similar results were obtained in a preparative study.[9] It is particularly surprising that the pyridinium ion (7f) was formed so quickly when 2-aminopyridine (6f) was used. Its low value of k_{VA}/k_{OH} is in accord with the known poor nucleophilic character of the amino group in (6f).

A likely reason for the fast ring closing (k_3) is the nature of the tautomer found in solution. ^{13}C N.m.r. studies have indicated that for aliphatic amines the most stable tautomer is the divinylogous amide.[8,13] For the divinylogous amide from an aromatic amine such as (6e) or (6f), conjugation of the aromatic ring with the open chain should favour a larger concentration of the imino-enol tautomer. This tautomer could then undergo rapid electrocyclic ring closure. Analogous intermediates have been reported to undergo such electrocyclic processes.[22-25] The divinylogous amide (3) is the product formed initially by the electrocyclic ring opening of the 2*H*-pyran.[3] The foregoing discussion implies that when an aliphatic amine is used the conversion of divinylogous amide (10) into imino-enol (12) is the rate-determining step in the sequence from pyrylium ion (5) to pyridinium ion (7). Interestingly in the first studies of the pyrylium–pyridinium transformation ammonia was used. Here too the imino-enol would be expected to be more stable and formation of pyridine in this case is very fast.[2]

Comparison of Reactivity of Primary Amines with the Pseudobase (9).—The pseudobase (9) undergoes two processes in the presence of amines at pH 10.1 [equation (viii)]: cleavage (k_S) [1] and conversion into pyridinium ion (k_B). The values of k_S determined [equation (viii)] for all amines, except s-butylamine, are the same within experimental error. A similar value (0.47×10^{-4} s^{-1}) is obtained for the rate of cleavage of pseudobase (9) at pH 10.1 and in the absence of amine.

Cleavage of the pseudobase [1] (9) is the only reaction observed when aromatic amines (aniline and 2-aminopyridine) are used. No amine-concentration-dependent process is observed.

The rate constants (k_B) for the reaction of pseudobase (9) with aliphatic amines to give pyridinium salts are similar (Table 5). As noted previously this reflects their similar nucleophilic characters. Aromatic amines (6e and f) are not sufficiently nucleophilic to compete successfully with nucleophilic attack of OH^- on the carbonyl groups of the pseudobase (9).[1,26] This latter process results in cleavage of (9).[1]

Conclusions

The pyrylium ion (5) can be converted into the pyridinium ion (7) both on a preparative scale and at u.v. concentrations by the addition of acidic solutions of (5) to amine buffers. Amines react faster with (5) than with its pseudobase (9), as in organic solvents.[13]

Surprisingly, the less nucleophilic aromatic amines react faster than aliphatic amines with the pyrylium ion (5) to give the pyridinium ion (7). This is attributed to a difference in tautomeric composition, *i.e.* a predominant divinylogous amide (10) when aliphatic amines are used and somewhat more imino-enol (12) with aromatic amines. The imino-enol cyclises by an electrocyclic process.[22-25] When aliphatic amines are used tautomerisation of the initially formed divinylogous amide to the imino-enol is the rate-determining step.

An equilibrium exists between divinylogous amide (10), pseudobase (9), and amine (6) in H_2O.

Subsequent papers in this series examine the influence of pyrylium ion structure on the rate of pyridinium ion formation.

Experimental

U.v. spectra were recorded with a Perkin-Elmer 330 and a Pye Unicam 8-200 instrument and i.r. spectra with a Perkin-Elmer 293B spectrometer. A Varian EM 360 spectrometer was used for recording ^1H n.m.r. spectra and a JEOL FX 100 instrument for ^{13}C n.m.r. spectra. Elemental analyses were carried out by Atlantic Microlab Inc., Atlanta, Georgia. M.p.s were determined with a Bristolscope microscopic hot state. The u.v. and ^{13}C n.m.r. data for the compounds under study are summarised in Tables 1 and 2.

Preparation of Pyridinium Salts (7b, e, *and* f).—The pyrylium salt (5) (1.358 g, 2 mmol) was added to an amine (8 mmol) in water (10 ml) and the reaction mixture was stirred at 25 °C for 15 h. Acetone (60 ml) was added and the mixture was kept 12 h at 5 °C. The crystals were filtered off, recrystallised from methanol–acetone (3 : 1) and dried at 1 Torr and 25 °C over P_2O_5 to give: 1-*butyl*-4-(4-*methoxy*-3-*sulphophenyl*)-2,6-*bis*-(4-*sulphophenyl*)*pyridinium perchlorate* (7b) pale yellow microcrystals (44%), m.p. > 350 °C [Found: C, 45.7; H, 3.9. $C_{28}H_{28}ClNO_{14}S_3$ (734.2) requires C, 45.8; H, 3.8%]; $\nu_{max.}$ ($CHBr_3$ mull) 3 050, 1 595, 1 495, 1 440, 1 420, and 1 140 cm^{-1}; δ (D_2O) 0.4—1.8 (7 H, m, $CH_2CH_2CH_3$), 4.2—4.7 (2 H, m, N^+CH_2), 4.05 (3 H, s, OCH_3), and 7.3—8.6 (13 H, arom., m); 4-(4-*methoxy*-3-*sulphophenyl*)-1-*phenyl*-2,6-*bis*-(4-*sulphophenyl*)*pyridinium perchlorate* (7e) pale beige microcrystals (1.20 g, 84.8%), m.p. > 350 °C [Found: C, 46.6; H, 3.1. $C_{30}H_{26}ClNO_{15}S_3$ (772.2) requires C, 46.7; H, 3.4%]; $\nu_{max.}$ ($CHBr_3$ mull) 3 020, 1 595, 1 440, 1 360, and 1 140 cm^{-1};

δ (D_2O) 4.05 (3 H, s, OCH_3) and 6.9—8.6 (18 H, arom., m); 4-(4-*methoxy*-3-*sulphophenyl*)-1-(2-*pyridyl*)-2,6-*bis*-(4-*sulphophenyl*)*pyridinium perchlorate* (7f), yellow microcrystals (1.17 g, 82.5%), m.p. > 350 °C [Found: C, 45.9; H, 3.0. $C_{29}H_{23}ClN_2O_{14}S_3$ (755.2) requires C, 46.1; H, 3.1%]; $\nu_{max.}$ ($CHBr_3$ mull) 3 020, 1 595, 1 495, 1 445, 1 360, and 1 140 cm^{-1}; δ (D_2O) 4.05 (3 H, s, OCH_3) and 7.3—8.7 (17 H, arom., m).

1-(5-*Amino*-5-*carboxypentyl*)-4-(4-*methoxy*-3-*sulphophenyl*)-2,6-*bis*-(4-*sulphophenyl*)*pyridinium* (7a).—The pyrylium salt (5) (1.358 g, 2 mmol) was added to lysine monohydrochloride (0.731 g, 4 mmol) and $NaHCO_3$ (1.344 g, 16 mmol) in water (10 ml). The mixture was stirred at 25 °C for 20 h, then acidified with 70% $HClO_4$ to pH 1 and evaporated at 50 °C and 20 Torr to half its volume. Acetone (60 ml) was added and the mixture was kept 12 h at 5 °C. The precipitate was recrystallised from methanol–acetone (3 : 1) and dried at 1 Torr and 25 °C over P_2O_5 to give yellow microcrystals (0.55 g, 39%), m.p. 320 °C (decomp.) [Found: C, 46.9; H, 4.5, of the zwitterion trihydrate. $C_{30}H_{36}N_2O_{15}S_3$ (760.8) requires C, 47.4; H, 4.8%]; $\nu_{max.}$ ($CHBr_3$ mull) 3 700—2 800, 1 750, 1 595, 1 500, 1 460, and 1 145 cm^{-1}; δ (D_2O) 1.7—2.2 (7 H, m, $[CH_2]_3CH$), 3.7—4.7 (4 H, m, NH_2, NCH_2), 3.95 (3 H, s, OCH_3), and 7.2—8.7 (13 H, arom., m).

1-*Benzyl*-4-(4-*methoxy*-3-*sulphophenyl*)-2,6-*bis*-(4-*sulphophenyl*)*pyridinium* (7c).—The pyrylium salt (5) (1.358 g, 2 mmol) was added to benzylamine (0.857 g, 8 mmol) and $NaHCO_3$ (0.672 g, 8 mmol) in water (10 ml). The mixture was stirred at 25 °C for 24 h, then extracted with ether (3 × 20 ml). The aqueous layer was acidified with 70% $HClO_4$ to pH 1 and evaporated at 50 °C and 20 Torr to 5 ml. Acetone (60 ml) was added and the mixture was kept 12 h at 5 °C. The acetone layer was decanted and a semi-solid precipitate was crystallised from ethanol to give pale yellow microcrystals (0.8 g, 58%), m.p. > 350 °C [Found: C, 51.1; H, 3.9, of the zwitterion trihydrate. $C_{31}H_{31}NO_{13}S_3$ (721.8) requires C, 51.6; H, 4.3%]; $\nu_{max.}$ ($CHBr_3$ mull) 3 020, 1 595, 1 495, 1 455, 1 370, and 1 140 cm^{-1}; δ (D_2O) 4.15 (3 H, s, OCH_3), 6.6 (2 H, br s, CH_2), and 7.4—9.7 (18 H, arom., m).

4-(4-*Methoxy*-3-*sulphophenyl*)-2-(*s-butylamino*)-2,6-*bis*-(4-*sulphophenyl*)-2H-*pyran* (8d).*—The pyrylium salt (5) (1.358 g, 2 mmol) was added to s-butylamine (0.585 g, 8 mmol) in water (10 ml) and the mixture was stirred at 25 °C for 120 h. Acetone (60 ml) was added and the mixture was kept 12 h at 5 °C. The crystals were filtered off, recrystallised from methanol–acetone (3 : 1) and dried at 1 Torr and 25 °C over P_2O_5 to give pale yellow microcrystals (0.59 g, 46%), m.p. 350 °C; $\nu_{max.}$ ($CHBr_3$ mull) 3 020, 1 605, 1 560, 1 495, 1 380, 1 135m, 1 035, and 1 010 cm^{-1}; δ (D_2O) 0.9 (3 H, t, CH_3CH_2), 1.25 (3 H, d, CH_3CH), 1.5 (2 H, m, CH_2), 3.7—4.1 (1 H, m, NCH), 4.0 (3 H, s, OCH_3), and 6.5—8.4 (13 H, m, arom.).

Kinetic Procedure.—Method A. The pyrylium salt (5) (8.5 mg) was dissolved in a buffer solution (5 ml) and after 5 min was mixed with a buffered solution of the appropriate amine and diluted with buffer to 25 ml. The reaction mixture was thermostatted to 25.0 ± 0.1 °C. At appropriate times 1 ml samples were withdrawn and diluted to 25 ml with a buffer of pH 11.0. Reactions were followed by monitoring the disappearance of the characteristic absorbance [1] at 487 nm of the anionic form of the pseudobase (9).

Method B. A 0.005M stock solution of the pyrylium salt (5) was prepared in 0.01N-HCl. Reactions were initiated by injecting 10 μl of a stock solution of (5) with a Hamilton syringe into a thermostatted (25.0 ± 0.1 °C) u.v. cell containing 2.5 ml of a buffered amine solution. Reactions were followed by monitoring the disappearance of the characteristic absorbance of the divinylogous amide at *ca.* 480 nm.

In both these methods pseudo-first-order rate constants were obtained from the slope of the straight line obtained from a plot of $\ln(A - A_\infty) = f(t)$ ($r > 0.998$).

* The 2*H*-pyran (8d) could not be obtained analytically pure, but was identified on the basis of ^1H and ^{13}C n.m.r. spectra (Table 3).

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