Table VII. Nmr Data. Isolated 2,4-Lutidine from Decomposition of **6** in Na_2CO_3–D_2O

Shift in CCl_4, ppm	Pattern	Relative area	Assignment
8.2	d (broad)	0.3	Ortho H
6.8	m	2.0	Meta H's
2.42	s (broad)	1.9	Ortho Me
2.25	s (broad)	2.3	Para Me

2,4-lutidine that is isolated from the decomposed adduct **6** in Na_2CO_3–D_2O contains a substantial amount of deuterium not only within the methyl groups, but also at the ortho position. Ring hydrogens of adducts of 2,6-lutidine *N*-oxide have shown no such propensity toward H–D exchange, but it is not surprising that such exchange is seen in this case. It already has been documented that ortho hydrogens of pyridinium salts undergo such exchange at a rate that is two orders of magnitude greater than the exchange rate of meta hydrogens, and three orders of magnitude greater than the rate of exchange of the para hydrogen.[36–38]

Acknowledgment. The authors thank the U. S. Public Health Service for financial support under research grants CA-7174, CA-7803, and CA-10439 of the National Cancer Institute. The authors also thank Drs. David R. Dalton and John R. Williams for helpful discussions, and the Reilly Tar and Chemical Co. for providing samples of some amines and amine oxides.

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Demonstration of Intermediates in the Hydrolysis of 4-Ethoxypyrylium Salts

G. Salvadori and A. Williams*

Contribution from the Chemical Laboratories, University of Kent, Canterbury, Kent, England. *Received September 14, 1970*

Abstract: The formation of open chain diketone intermediates has been demonstrated during the hydrolysis of 4-ethoxypyrylium salts. Reaction occurs at both $C_{2(6)}$ and C_4 positions to yield open chain diketone and 4-pyrone, respectively; the diketone (a vinyl ether) hydrolyzes and cyclizes to give the 4-pyrone. The yield of 4-pyrone is stoichiometric and oxygen-18 and deuterium isotope experiments show that at low pH the direct mechanism (attack at C_4) predominates but at high pH the diketone intermediate ($C_{2(6)}$ attack) is predominantly involved. The maximal concentration of intermediate varies with pH according to an equation derived from the proposed theoretical mechanism and can be accurately predicted using rate constants reported here. The rate constant for decomposition of pyrylium salt is given by the equation $k_a = k_0 + k_B[B] + k_{OH}[OH^-] + k_{H_2O}/(1 + a_H/K_a)$. The ionization term in the equation can arise from the pH-dependent partitioning of a cyclic hemiacetal intermediate between pyrylium salt and diketone intermediate. Decomposition of the diketone intermediate to give 4-pyrone is specific acid catalyzed (the existence of a preequilibrium protonation is supported by an inverse deuterium isotope effect) and is rate determining at high pH but as the pH decreases the formation of diketone becomes rate determining. However, the latter rate constant decreases with decreasing pH and a pH-independent direct attack of water at C_4 becomes predominant (k_0); the rate constant for 4-pyrone production (k_b) therefore exhibits a plateau region at low pH. The diketone intermediate is shown to yield 2,6-dimethyl-4-pyrone *via* a pathway not including diacetylacetone.

4-Alkoxypyrylium salts were first synthesized over 50 years ago[1] and their lability to water and alcohols is a well-known property.[2,3] However, no mechanistic studies of the hydrolysis reaction have yet been reported. Calculation of the electron density in the pyrylium nucleus indicates that the $C_{2(6)}$ position is favored for nucleophilic addition;[4] however, recrystallization of the 4-methoxypyrylium salt from ethanol yields the 4-ethoxy salt[2] and when treated with water the latter yields the 4-pyrone.[3] Attack of hydroxide and water at C_2 is observed in other pyrylium salts with ring opening.[5]

Experimental Section

Materials. Oxygen-18 enriched water (1.7% ^{18}O; 0.122% ^{17}O) was obtained from Yeda Research and Development Co. at the Weizmann Institute. 2,6-Dimethyl-4-pyrone was prepared according to Otha and Kato.[6] The pyrone had mp 132–133° (lit.[6] mp 130°); uv max (phosphate buffer, pH 6) 250 nm (ϵ 15,150). 2,6-Dimethyl-4-ethoxypyrylium tetrafluoroborate was prepared according to Meerwein.[7] The material had mp 90° (lit.[10] mp 90–91°); uv max (phosphate buffer, pH 6), 248 nm (ϵ 16,700), (CH_3CN), 247 nm (ϵ 12,000).

4-Pyrone was prepared according to Willstätter and Pummerer[8] by the decarboxylation of chelidonic acid. The product had bp 107–108° (15 mm) (lit.[8] bp 97° (13 mm)); mp 31–33°; uv max (CH_3CN), 243 nm (ϵ 10,150).

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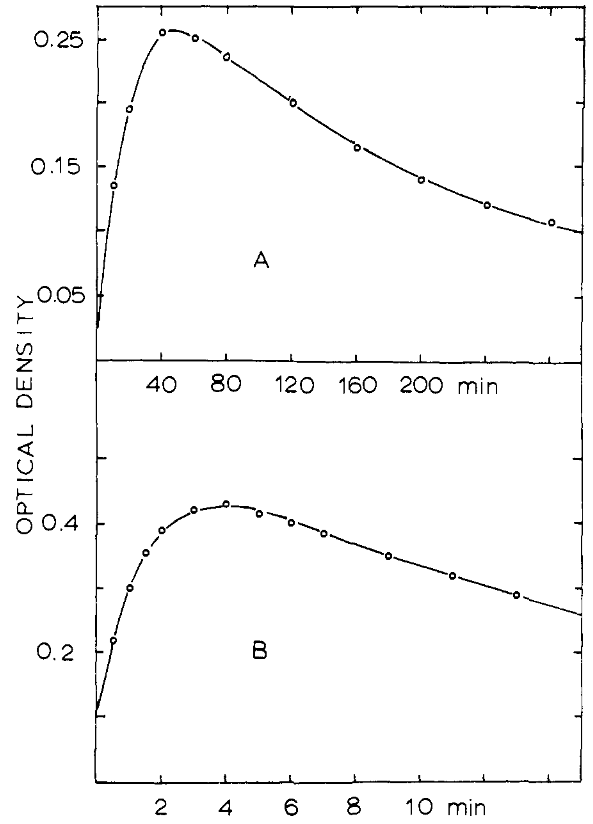

Figure 1. Kinetic demonstration of a third species in the hydrolysis of 2,6-dimethyl-4-ethoxypyrylium tetrafluoroborate (A, 285 nm, pH 5.0, 50°) and of 4-ethoxypyrylium tetrafluoroborate (B, 270 nm, pH 3.5, 25°). Lines are theoretical, see text.

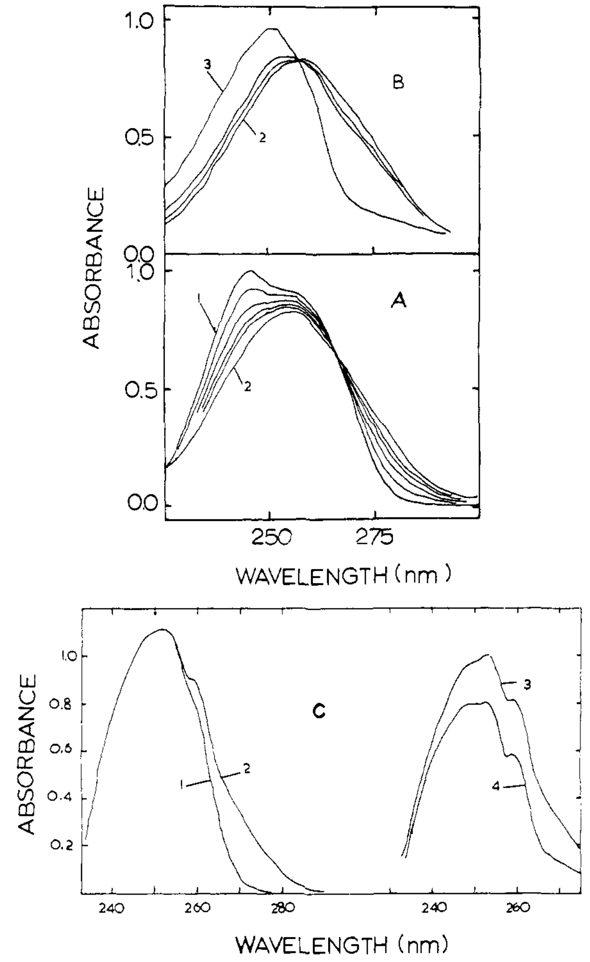

Figure 2. Spectrum scan of interconversion: (A) 2,6-dimethyl-4-ethoxypyrylium tetrafluoroborate (1) into intermediate (2), substrate concentration 0.6 × 10^{-4} *M*, pH 5.5, 50°, 0.1 *M* ionic concentration, scanning interval 4 min; (B) intermediate (2) into 2,6-dimethyl-4-pyrone (3), conditions identical with A, scanning time 1 hr, final scan after 2 days; (C) 4-ethoxypyrylium tetrafluoroborate (1) into intermediate (2), 4-pyrone (4) is the final product; (3) represents an intermediate scan, substrate concentration, 0.94 × 10^{-4} *M*, pH 3.5, 25°, 0.1 *M* ionic concentration; the transformation 1-2 was very fast, and the transformation 2-4 was slower; individual scanned spectra are not included here for the sake of clarity.

4-Ethoxypyrylium tetrafluoroborate (parent salt) was prepared according to Meerwein.[7] The product separated as an oil from dichloromethane and did not crystallize in spite of several attempts of treatment with petroleum ether at −70°. The product had ir max (neat) 1640 (C=C), 1000–1100 cm^{-1} (broad, COC); uv max (CH_3CN) 248 nm (ε 10,640); nmr (neat) τ 1.25 (d, 2, 6 Hz, ring proton), 2.70 (d, 2, 6 Hz, ring proton), 5.6 (q, 2, 7 Hz, CH_2CH_3), 8.8 (t, 3, 7 Hz, CH_2CH_3). *Anal.* Calcd for $C_7H_9BF_4O_2$: C, 39.66; H, 4.28; F, 35.86. Found: C, 39.56; H, 4.41; F, 35.78.

At pH 6 and 50° the intermediate (4-ethoxy-3-heptene-2,6-dione) has a half-life of about 17 hr and was extracted from the cooled reaction mixture (10^{-2} *M*) with chloroform after allowing pyrylium salt to react for 15 min. The extract was dried, evaporated, and the yellow oil produced had ir (liquid film) 1720, 1675, 1590 cm^{-1}; uv max (CH_3CN) 252 nm (ε 15,000), (H_2O) 257 nm (ε 14,000); nmr τ 5.24 (s, 1, =CH-), 6.15 (s, 2, $-CH_2-$), 5.8, 5.9, 6.03, 6.15 (q, 2, $-CH_2CH_3$), 7.75, 7.85 (6, $-CH_3$), 8.5, 8.6, 8.7 (t, 3, $-CH_2CH_3$). *Anal.* Calcd for $C_9H_{14}O_3$: C, 63.5; H, 8.25. Found: C, 63.4; H, 8.4. The oil solidified to a low-melting solid on keeping in the freezer for 1 week. When the reaction was repeated in deuterium oxide the oil was identical in all respects with the previous one except that the nmr absorption at τ 6.15 was considerably reduced.

Diacetylacetone was prepared by the method of Collie[9] and had mp 45° (lit.[9] mp 49°).

Other materials were as described in the accompanying paper[5] as were the methods and kinetics. Mass spectra (used in ^{18}O estimation) were recorded on an A.E.I. M.S. 902 spectrometer.

Results

Demonstration of an Intermediate. The reaction of 4-ethoxypyrylium salts with water buffered in the neutral region was followed by repetitive scanning of the uv spectrum from 300 to 200 nm. 4-Pyrone was produced in 100 ± 2% yield as judged from the extinction coefficients over the pH ranges 0–9.2 and 1.6–6.6 for 2,6-dimethyl and parent 4-ethoxypyrylium salts, respectively. A close examination of the repetitive uv scans for both pyrylium salts revealed the existence of two reactions: a fast conversion of pyrylium salt to an "intermediate" followed by a slower conversion of "intermediate" to 4-pyrone. The formation of the "intermediate" species is illustrated in Figure 1 for the hydrolysis of 2,6-dimethyl-4-ethoxypyrylium and the parent salt. The parent salt showed no well-defined isosbestic points during hydrolysis. Inspection of Figure 2 reveals excellent isosbestic points between 2,6-dimethyl-4-ethoxypyrylium salt and "intermediate" and between "intermediate" and 2,6-dimethyl-4-pyrone. The sharpness of the isosbestic wavelengths indicates that for the 2,6-dimethyl salt hydrolysis involves only one intermediate species opaque to the uv. At 267 nm (the isosbestic wavelength between 2,6-dimethylpyrylium salt and "intermediate") an induction period in the production of pyrone is observed (Figure 3) showing that production of 2,6-dimethyl-4-pyrone must proceed *via* the "intermediate." A similar conclusion

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(9) J. N. Collie and A. A. B. Reilly, *J. Chem. Soc.*, 1984 (1922).

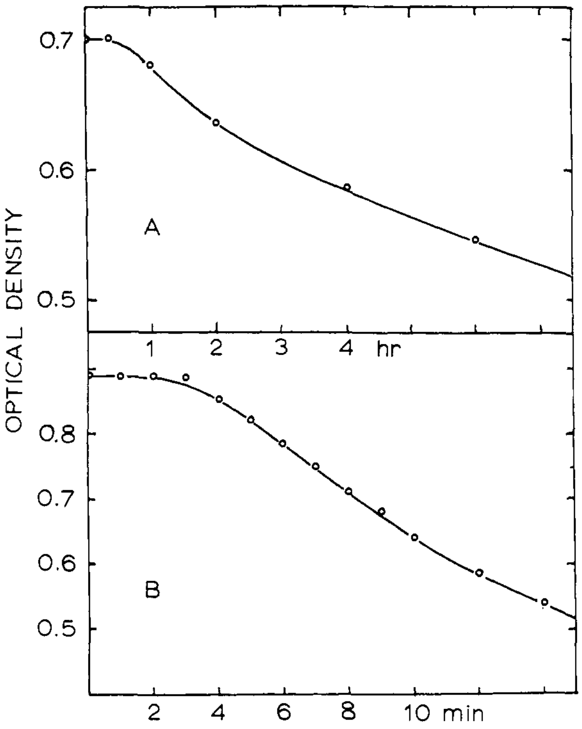
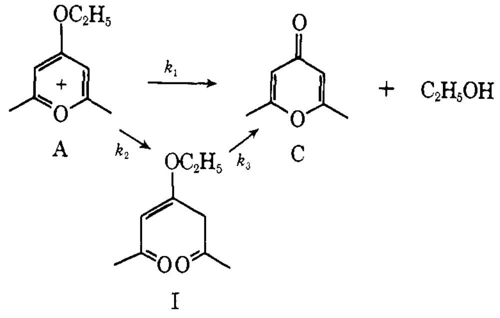


Figure 3. Demonstration of induction periods in the hydrolysis of 2,6-dimethyl-4-ethoxypyrylium tetrafluoroborate (A, pH 6.1, 267 nm, 50°) and of 4-ethoxypyrylium tetrafluoroborate (B, pH 3.5, 252 nm, 25°). Lines are theoretical (see text).

is drawn from the induction period observed at 252 nm where parent pyrylium salt and intermediate have identical absorptions (Figure 3). The progress curves (Figures 1 and 3) were predicted from the kinetic parameters for formation and decomposition of intermediate (see later on in Table IV) using equations derived from Frost and Pearson[10] and the appropriate extinction coefficients for A, I, and C (see Chart I). The coexistence of a by-pass mechanism is not ruled out.

Chart I



Nature of the Intermediates. The physical characteristics of the intermediate from the 2,6-dimethylpyrylium cation indicate that it has the structure 4-ethoxy-3-heptene-2,6-dione. It is likely from the nmr evidence that the isolated material is only one of the possible geometric isomers and this is probably the cis form.[11] By analogy it is assumed that the intermediate in the hydrolysis of 4-ethoxypyrylium tetrafluoroborate is 3-ethoxy-2-pentene-1,5-dione.

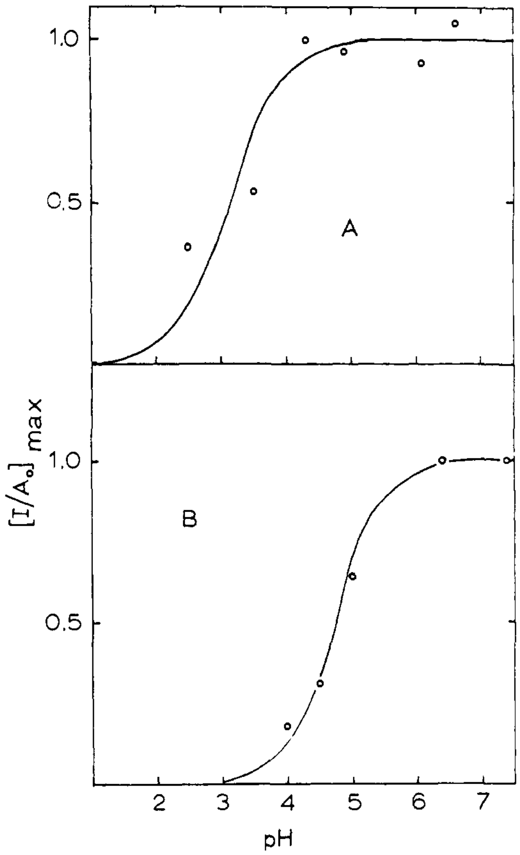


Figure 4. pH dependence of the maximal concentration of intermediate: A, 4-ethoxypyrylium tetrafluoroborate, 25°, 270 nm; B, 2,6-dimethyl-4-ethoxypyrylium tetrafluoroborate, 50°, 285 nm. Lines are theoretical from eq 1 and parameters from Table IV.

Overall Mechanism. The kinetic parameters show that above pH 5 the rate of hydrolysis of the intermediate is less than its rate of formation for both pyrylium salts so that the formation of intermediate is stoichiometric. Figure 4 demonstrates that the maximal intermediate concentration varies as a function of pH and these results could indicate a change in rate-limiting step as the pH is lowered. Hydrolysis of the 2,6-dimethyl-4-ethoxypyrylium salt at pH 4 in water enriched with oxygen-18 yields a 4-pyrone which has only one labeled oxygen (the accuracy of the experiment was ±20%). Furthermore, contrary to results above pH 6, deuterium is not exchanged at the $C_{3(5)}$ positions during hydrolysis in heavy water at pD 4. Thus the ring stays intact in the low pH range but opens in the high pH range. The most sensible explanation of these phenomena is that the direct mechanism (k_1) is favored at low pH and the indirect at high pH. Chart I enables the maximal concentration of intermediate (during reaction) to be predicted (see Figure 4) using the rate constants derived later and eq 1, where $k_1 = k_0$, $k_3 = k_{\mathrm{H_3O^+}}[a_\mathrm{H}]$,

$$\frac{[\mathrm{I}]}{[\mathrm{A_0}]} = \left[\frac{k_2}{(k_1 + k_3)}\right]^{k_2/(k_1 + k_2 + k_3)} \qquad (1)$$

$k_2 = k_{\mathrm{H_2O}}/(1 + a_\mathrm{H}/K_\mathrm{a}) + k_\mathrm{OH}[\mathrm{OH}]$. As pH decreases k_2 becomes less than k_3 and a changeover in predominant mechanism also occurs because k_2 becomes less than k_1.

Consumption of Pyrylium Salt (k_a). The disappearance of 2,6-dimethyl-4-ethoxypyrylium salt was fol-

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[10] A. A. Frost and R. G. Pearson, "Kinetics and Mechanisms," 2nd ed, Wiley, New York, N. Y., 1961, p 166.

[11] A previous report [G. Salvadori and A. Williams, *Chem. Commun.*, 775 (1968)] identified this intermediate as the 4,4′-adduct owing to a misinterpretation of the fact that at low pH no solvent deuterium exchanges with a ring proton; an open chain intermediate was therefore not considered possible. The present report demonstrates deuterium exchange at neutral pH.

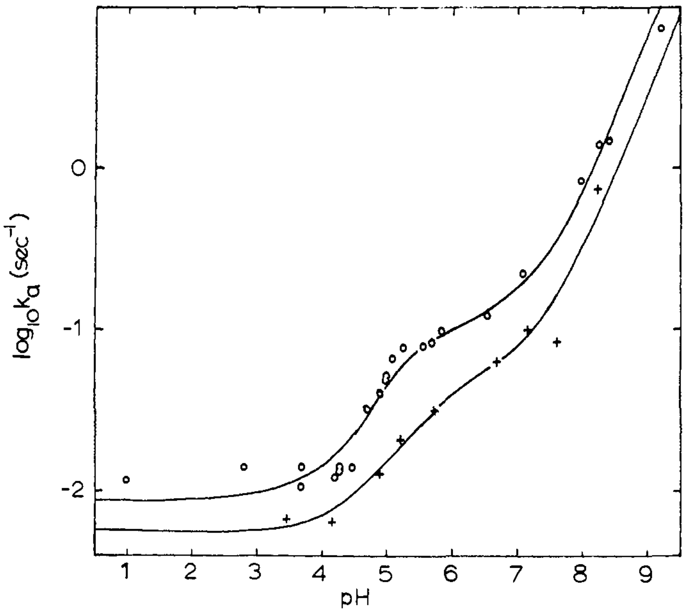


Figure 5. pH dependence of the rate constant for depletion of 2,6-dimethyl-4-ethoxypyrylium tetrafluoroborate (k_a), 50°, 0.1 M ionic concentration: ○, H_2O solvent; +, D_2O solvent. Lines are theoretical from eq 2 and parameters from Table IV.

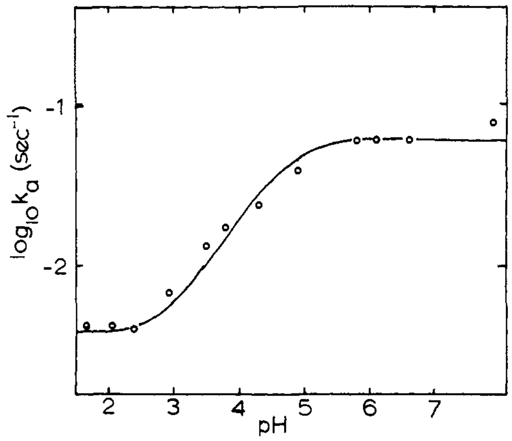


Figure 6. pH dependence of the rate constant for depletion of 4-ethoxypyrylium tetrafluoroborate (k_a), 25°, 0.1 M ionic concentration. Lines are theoretical from eq 2 and parameters from Table IV.

lowed at 255 nm (the isosbestic wavelength between diketone intermediate and 2,6-dimethyl-4-pyrone). No isosbestic wavelengths existed between the dialdehyde intermediate and 4-pyrone but pyrylium salt and intermediate had the same absorbance in the region 252–235 nm. A wavelength above 252 nm was used to follow the overall kinetics; the trace (for parent salt) involved essentially two first-order portions (consisting of formation and decomposition of intermediate) and as the pH was lowered the two-phase kinetics changed to one phase in this wavelength region. Identical rates were observed at all wavelengths below pH 3. All the kinetic results refer to 0.001 M buffer concentration where the effect of general base catalysis by buffer is negligible for the parent pyrylium salt. The variation with pH of the rate constant for disappearance of the 4-ethoxypyrylium salts is shown in Figures 5 and 6 (Tables I, II, and III) and fits eq 2. Individual rate constants

$$k_a = k_0 + k_{H_2O}/(1 + a_H/K_a) + k_B[B] + k_{OH}[OH] \quad (2)$$

calculated assuming eq 2 are collected in Table IV.

General Base Catalysis. The base term in eq 2 was observed for both 2,6-dimethyl- and parent 4-ethoxypyrylium salts (Table V). Acetic acid was shown to have no effect on k_a (Table V) and it was assumed that the other acids also had no effect. It was shown earlier that at low pH the predominant mechanism for decomposition is directly to 4-pyrone while at high pH it is

Table I. Rate Constants for the Hydrolysis of 2,6-Dimethyl-4-ethoxypyrylium Tetrafluoroborate[a]

Buffer	pH	$k_a \times 10^4$, sec^{-1}	$k_b \times 10^4$, sec^{-1}
HCl	1.0	1.92	
Citrate	2.8	2.33	2.33
Acetate	3.67	2.33,[b] 1.77	2.33, 2.30[b]
	4.17	2.0,[b] 2.0	2.0
	4.27	2.28,[b] 2.33	2.28
	4.47	2.17,[b] 2.17	2.17
	4.67	5.27	
	4.72		1.65,[d] 1.60[e]
	4.87	6.64	
	4.97	8.25, 8.40	1.42[c]
	5.07	10.6	0.885,[i] 0.935,[j] 0.870[k]
	5.23	12.8	
	5.52	12.8	
	5.62		0.242
	5.67	13.8	0.276, 0.284[l]
	5.82	16.2	
Phosphate	6.16		0.0965,[f] 0.102[g]
	6.31		0.0985
	6.51	20.0	
	6.86		0.0416
	7.06	36.8	
	7.96	136	
Borate	8.23	232	
	8.38	242	
	9.18	1200 (184[h])	

[a] 0.1 M ionic concentration, 0.001 M buffer, 50°, k_a from measurements at 255 nm, k_b from 267 nm. [b] 267 nm. [c] 0.5 M ionic concentration. [d] 0.005 M acetate. [e] 0.05 M acetate. [f] 0.0455 M phosphate. [g] 0.00455 M phosphate. [h] 25°. [i] 0.0285 M acetate. [j] 0.0171 M acetate. [k] 0.0028 M acetate. [l] Rate constant for hydrolysis of the intermediate.

Table II. Effect of Deuterium Oxide Solvent on Hydrolysis of 2,6-Dimethyl-4-ethoxypyrylium Tetrafluoroborate[a]

pD	$k_a \times 10^4$, sec^{-1}	pH	$k_a \times 10^4$, sec^{-1}	k_H/k_D
3.47	1.15			
4.17	1.05			
4.87	2.1			
5.17	3.52			
5.71	5.27 (k_b = 0.305)	5.71	(k_b = 0.27)	0.88
6.66	10.6			
7.16	16.7			
7.61	13.8, 20,[b] 26.2[c]	7.61	38.7,[b] 49.0[c]	*d*
8.23	122	8.23	232	

[a] 0.1 *M* ionic concentration, 50°, 0.001 *M* buffer concentration. [b] $[D(H)PO_4^{2-}]$ = 0.025 *M*. [c] $[D(H)PO_4^{2-}]$ = 0.05 *M*. [d] $k_{HPO_4^{2-}} = 4.17 \times 10^{-2}\ M^{-1}\ sec^{-1}$, $k_{DPO_4^{2-}} = 2.58 \times 10^{-2}\ M^{-1}\ sec^{-1}$.

Table III. The Hydrolysis of 4-Ethoxypyrylium Tetrafluoroborate[a]

Buffer	pH	$k_a \times 10^2$, sec^{-1} 25°	$k_a \times 10^2$, sec^{-1} 45°	$k_b \times 10^2$, sec^{-1} 25°	$k_b \times 10^2$, sec^{-1} 45°
Oxalate	1.60				1.66[b]
	1.65	0.42[b]	1.68[b]	0.42	
	2.05	0.418[b]	1.67[b]	0.42	1.73
Citrate	2.4	0.4	1.60[b]	0.40	1.58
	2.92	0.675			0.93
	3.20			0.20	0.90
	3.50	1.31	5.25	0.155	0.88
Acetate	3.8	1.67	6.7	0.079	
	4.3	2.36		0.02	0.147,[c] 0.144,[d] 0.158[e]
	4.9	3.85		0.008	0.039
	5.8	5.76			0.0076
Phosphate	6.1	5.9			
	6.6	5.9			0.0031
	7.9	7.7			

[a] 0.1 *M* ionic concentration, k_a measured at 270 nm, k_b at 260 nm, 0.001 *M* buffer concentration. [b] 252 nm. [c] 0.00655 *M* acetate. [d] 0.00113 *M* acetate. [e] 0.0131 *M* acetate.

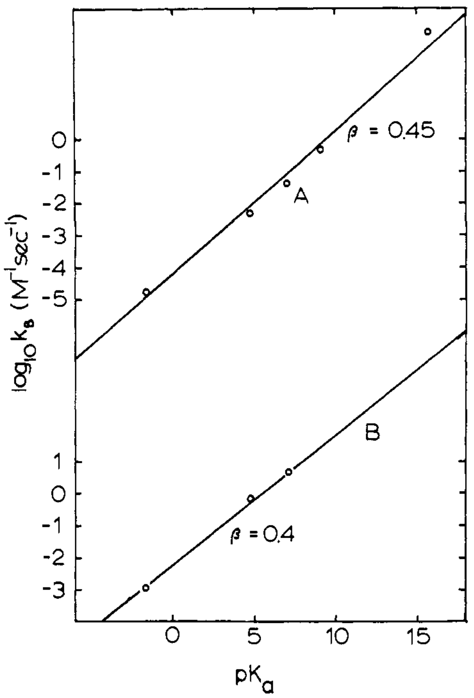


Figure 7. Plot of log k_B *vs.* the pK_a of the conjugate acid of base. Lines are arbitrary, A refers to 2,6-dimethyl-4-ethoxypyrylium cation (50°), and B refers to the 4-ethoxypyrylium cation (25°). Data are from Table VI; the data have not been corrected statistically.

Table IV. Collection of Kinetic Parameters for Hydrolysis of 4-Ethoxypyrylium Salts

	k_0 $\times 10^4$, sec^{-1}	k_{H_2O} $\times 10^4$, sec^{-1}	K_a $\times 10^6$, *M*	k_{OH} $\times 10^{-5}$, M^{-1} sec^{-1}	$k_{H_3O^+}$,[a] M^{-1} sec^{-1}
		2,6-Dimethyl-4-ethoxypyrylium tetrafluoroborate			
H_2O	1.5 ± 0.1	18.0 ± 1	4.5 ± 0.5	1.8 ± 0.05	14 ± 1[d]
D_2O	0.9 ± 0.1	7.5 ± 0.5	2.7 ± 0.3	6.0 ± 0.5	15.8[b]
		4-Ethoxypyrylium tetrafluoroborate			
H_2O	0.4 ± 0.05	6.0 ± 0.5	3.2 ± 0.5		5.0[c]

[a] Obtained from the pH-dependent values for k_b. [b] Derived from the ratio k_b^H/k_b^D at pH (D) 5.71 (Table II). [c] 35 M^{-1} sec^{-1} at 45°. [d] This value is identical with that obtained directly for the hydrolysis of 4-ethoxy-3-heptene-2,6-dione. Pseudounimolecular rate constant was proportional to a_H from 10^{-6} to 0.2 *M*.

via an open chain intermediate. Thus k_0 in eq 2 refers to the direct mechanism while $k_{H_2O}/(1 + a_H/K_a)$ and the hydroxide terms refer to the indirect mechanism. The general base catalytic terms are collected in Table VI and it is assumed that all the terms of eq 2 except k_0 refer to the indirect mechanism. The reason for this is given later; the plot k_B *vs.* the pK_a of the conjugate acid is given in Figure 7 for 2,6-dimethyl and parent salts.

Formation of Pyrone (k_b). The formation of pyrone was followed at the isosbestic wavelength between pyrylium salt and intermediate (267 nm for 2,6-dimethyl derivative) and at 252 nm for the parent salt. In the case of the parent salt the rate constant derived from the second phase of the two reactions measured at 260 nm also gave the rate of decomposition of intermediate. This rate constant was not affected by ionic strength or by general acids or bases in the pH-dependent range. The pH dependencies are shown in Figures 8 and 9 (Tables I-III) and at high pH's k_b is specific acid catalyzed. A plateau region is observed at low pH's and this represents the more efficient (at these pH's) direct pathway (k_0).

In the pH-dependent region the rates of hydrolysis of 4-ethoxy-3-heptene-2,6-dione and of 2,6-dimethyl-4-ethoxypyrylium salt were identical. The vinyl ether of the dimethylpyrylium salt hydrolyzed faster (Tables I and IV) than the reactant salt in the region where k_b was pH independent (pH 3.67). The rate constants k_a and k_b were identical in the pH-independent region for both parent and 2,6-dimethylpyrylium salts. The solid lines in Figures 8 and 9 were calculated assuming the mechanism of Chart I.

Discussion

Mechanism of Hydrolysis. Good evidence has been presented to show that two mechanisms exist for the hydrolysis of 4-ethoxypyrylium salts: one involving a

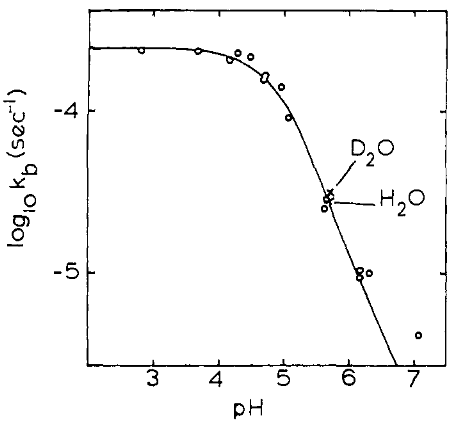


Figure 8. Production of 2,6-dimethyl-4-pyrone as a function of pH. Line is theoretical (see text), data from Table I (50°, 0.1 M ionic concentration).

diketone intermediate and a direct mechanism with no ring opening proceeding *via* a 4,4′ σ complex. Reports of analogous reactions[12] support the coexistence of the latter mechanism.

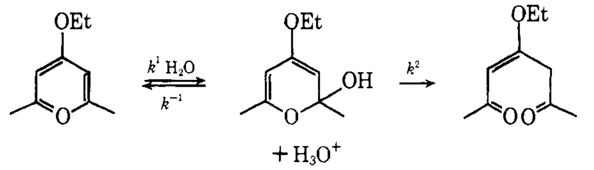
Table V. Effect of Buffer Concentration on k_a for the 4-Ethoxypyrylium Salts[a]

Buffer	pH	$k_a \times 10^4$, sec^{-1}	Base concn, M	k_B, M^{-1} sec^{-1}
	2,6-Dimethyl-4-ethoxypyrylium salt (50°)			
Acetate	5.55	0.167	0.086	
	5.55	0.157	0.057	0.494×10^{-2}
	5.55	0.137	0.025	
Acetate	4.7	0.0815	0.050	
	4.7	0.0675	0.025	0.500×10^{-2}
	4.7	0.0625	0.01	
Borate	8.28	2.35	0.011	0.625
	8.28	1.75	0.001	
	8.93	7.80	0.0370	0.625
	8.93	5.75	0.0045	
	4-Ethoxypyrylium tetrafluoroborate (25°)			
Acetate	3.8	2.3	0.01	
	3.8	2.06	0.005	0.64
	3.8	1.67	0.001	
Phosphate	6.1	8.4	0.0052	
	6.1	7.16	0.0026	4.82
	6.1	6.15	0.00052	

[a] 0.1 M ionic concentration.

The indirect pathway involves a vinyl ether open chain intermediate and is predominant at neutral and alkaline pH's where the ionization and hydroxide terms become predominant. We ascribe the ionization term (see a similar reaction[5]) to the kinetics arising from a process (Chart II) involving the pH-dependent partitioning of a cyclic hemiacetal intermediate between reactant and open chain diketone.

Chart II



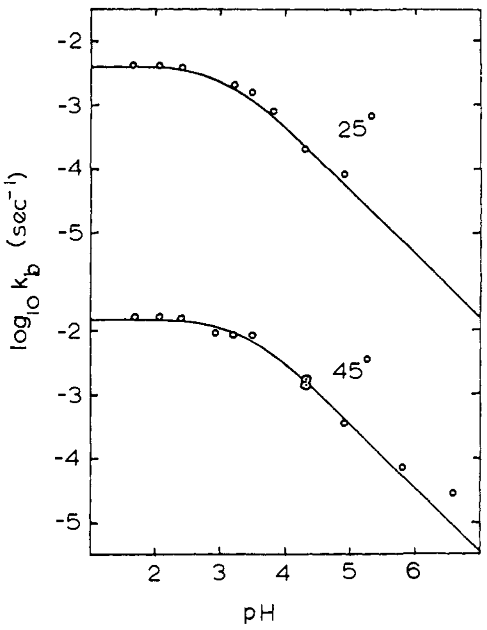


Figure 9. Production of 4-pyrone as a function of pH. Lines are theoretical (see text), data from Table III.

Table VI. General Base Catalytic Terms for k_a[a]

Base	pK_a[b]	k_B, M^{-1} sec^{-1}
2,6-Dimethyl-4-ethoxypyrylium salt (50°)		
Water	−1.7	3.33×10^{-5}[c]
Acetate	4.7	4.94×10^{-3}
Phosphate dianion	7.0	3.83×10^{-2}
Borate	9.0	6.25×10^{-1}
Hydroxide	15.7	184
DPO_4^{2-} (in D_2O)		2.58×10^{-2}
4-Ethoxypyrylium salt (25°)		
Water	−1.7	1.08×10^{-3}
Acetate	4.7	0.64
Phosphate dianion	7.0	4.82

[a] 0.1 M ionic concentration. [b] "Handbook of Chemistry and Physics," 46th ed, The Chemical Rubber Publishing Co., Cleveland, Ohio, 1965–1966. [c] Calculated from k_{H_2O} using $[H_2O] = 55\ M$.

The excellent fit of the general base terms (including k_{H_2O}) to a Brønsted equation (Figure 7) confirms that the terms arise from the same (indirect) mechanism and that k_B and k_{OH} contain little if any of a term representing the direct mechanism. There is no reason why the direct mechanism should not be base catalyzed and a few studies in the appropriate pH region show this assertion to be correct.

The value of the Brønsted β (0.45 for the 2,6-dimethyl and 0.40 for the parent pyrylium salt) suggests that the proton is only partially removed from the oxygen of water in the transition state. The value of the deuterium oxide solvent isotope effect on the general base terms (see Tables IV and VI) confirms this and is of the order of 1-2 for water and phosphate. The inverse effect for hydroxide ion can be explained by the higher basicity of deuteroxide ion than hydroxide ion.[13] The deuterium isotope effect on the ionization term $K_a^H/$

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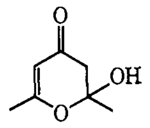
K_a^D = 1.7 for the 2,6-dimethylpyrylium salt is roughly that expected for an acid of comparable acidity.[14]

Formation of 4-Pyrone. The identity of the acid plateau rate constant ($k_a = k_0 \sim$ Figures 5 and 6) with the rate constant for the rate of formation of 4-pyrone (k_b) in the plateau region and the identity of the *pH-dependent* rate constant for the latter reaction with that for the hydrolysis of the isolated intermediate is good evidence for the changeover in rate-limiting step and mechanism. The plateau region for k_b corresponds to the direct reaction of water at the 4 position which is predominant because although the acid-catalyzed hydrolysis of the intermediate is larger than its rate of formation at this pH (Table IV) the latter is much less than the direct rate.

The hydrolysis of intermediate to give diacetylacetone which then cyclizes to 2,6-dimethyl-4-pyrone is not a valid mechanism since the bimolecular acid-catalyzed rate constant for the latter reaction is 1.36 × 10^{-4} M^{-1} $\sec^{-1}$ (45°) which does not support the overall rate constant from intermediate (14 $\sec^{-1}$, see Table IV). Mechanisms involving the intermediates shown are probably not valid since models of their dehydration[15] also have rate constants ($\sim 10^{-5}$ M^{-1} $\sec^{-1}$ at 25°) insufficient to sustain the observed rate constant. The mechanism of Chart III is suggested as a possible candidate and work of Pocker and Hill[16] on the rearrangement of 1-phenyl-3-methylallyl alcohol (an analog of the penultimate step) suggests that the rearrangement step could be rate controlling. The inverse deuterium isotope effect (Table IV) supports the preequilibrium protonation of the diketone.



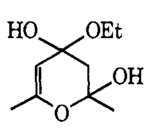
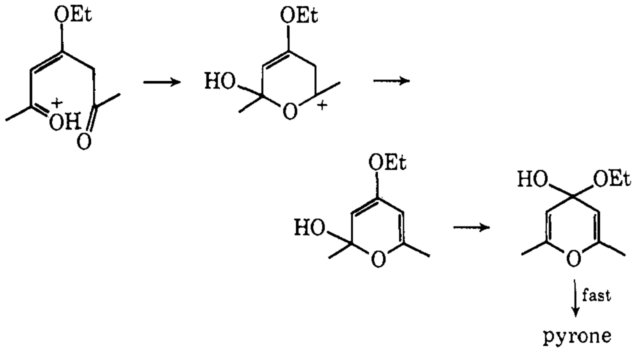


Chart III



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(14) R. P. Bell, "The Proton in Chemistry," Methuen, London, 1959, p 188.

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The Hydrolysis of Pyrylium Salts. Kinetic Evidence for Hemiacetal Intermediates

A. Williams

Contribution from the Chemical Laboratory, University of Kent, Canterbury, Kent, England.
Received September 14, 1970

Abstract: The hydrolyses of 2,4,6-triphenylpyrylium tetrafluoroborate, 2,4,6-trimethylpyrylium perchlorate, and 2-methyl-4,6-diphenylpyrylium chloride (to yield diketones) were measured over a range of pH, buffer concentration, and in deuterium oxide solvent. The rate constant for the forward reaction in each case obeyed the empirical equation $k_f = k_{H_2O}/(1 + a_H/K_a) + k_{OH}[OH] + k_B[B]$. The titration term is judged to arise from the pH-dependent partitioning of a cyclic hemiacetal intermediate formed by reaction of water at the C_2 position. The attack of water on the 2-methyl-4,6-diphenylpyrylium cation proceeds at the 2 position and the product is shown to be the 1,3-diphenyl-2-hexene-1,5-dione.

The formation of pseudobases from pyrylium salts and aqueous media is a well-known phenomenon[1] and probably involves a cyclic hemiacetal intermediate but evidence for this mechanism is indirect.[2] The structures of the final hydrolysis products are now known not to include the hemiacetal adduct except where this or its vinylog cannot react further.[2c] Berson[1a] showed that the pseudobase from the 2,4,6-triphenylpyrylium cation was the diketone and not the keto enol.

Experimental Section

Materials. Deuterium oxide (99.7%) was obtained from Prochem Ltd., U.K. Deuterium oxide buffers were prepared directly from heavy water and protium buffer. For example, 0.1 *M* disodium hydrogen phosphate will exchange in heavy water to give 0.05 *M* water, a dilution of the heavy water which is negligible for the purposes of our experiments. pD was calculated from the

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(1) (a) J. A. Berson, *J. Amer. Chem. Soc.*, **74**, 358 (1952); (b) W. Dilthey, *J. Prakt. Chem.*, **94**, 53 (1916); **95**, 107 (1917); **101**, 177 (1920); (c) W. Dilthey and T. Böttler, *Ber.*, **52**, 2040 (1919); (d) H. R. Hensel, *Justus Liebigs Ann. Chem.*, **611**, 97 (1958); (e) J. J. Basselier, *Ann. Chim. (Paris)*, **6**, 1131 (1961); (f) G. Rio and Y. Fellion, *Tetrahedron Lett.*, 1213 (1962).

(2) (a) K. Dimroth and K. H. Wolf, "Newer Methods of Preparative Organic Chemistry," W. Foerst, Ed., Academic Press, New York, N. Y., 1964, p 357; (b) M. Gomberg and L. H. Cone, *Justus Liebigs Ann. Chem.*, **370**, 142 (1909); (c) S. Wawzonek, "Heterocyclic Compounds," R. C. Elderfield, Ed., Wiley, New York, N. Y., 1951, p 463 ff; (d) see ref 2c, p 316 ff; (e) D. W. Hill and R. R. Melhuish, *J. Chem. Soc.*, 1163 (1935).