1,3-Dipolar Character of Six-membered Aromatic Rings. Part XXIX.[1] Kinetic Rates and Equilibria for the Addition of 2π-Electron Addends to 3-Oxidopyridinium Betaines

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The rates of addition of methyl acrylate to 1-substituted 3-oxidopyridiniums increase with the electron-withdrawing power of the substituent: Me < CH_2Ph < Ph < 4,6-dimethylpyrimidin-2-yl. The rates of addition of vinyl compounds, $CH_2{:}CHR$ to 1-(pyrimidin-2-yl)-3-oxidopyridinium increase in the series R = OBu^n < Ph < CN < 4-pyridyl < CO_2Me. Rates of addition of methyl acrylate to the pyrimidinyl betaine are but little affected by solvent polarity.

PREPARATIVE aspects of the cycloadditions of 2π-, 4π-, and 6π-electron addends to 3-oxidopyridiniums and other heteroaromatic betaines have been reported in earlier papers of this series.[2] We have now investigated the kinetic rates of the reactions of the five betaines (1)—(5) with the dipolarophiles (6)—(10). In all cases, the reactions were followed by the disappearance of the characteristic betaine absorption in the region 330—370 nm (Table 1). Most reactions proceeded at convenient rates in the temperature range 20—85 °C under pseudo-first-order conditions when the betaine was present at concentration suitable for u.v. study and the dipolarophile in at least 500 times greater concentration. The reactions proceeded to equilibrium and we were able to determine equilibrium constants.

TABLE 1

Wavelength maxima and molecular extinction coefficients for the ' betaine band ' near 350 nm (EtOH as solvent)

Betaine	(1)	(2)	(3)	(4)	(5)
$\lambda_{max.}$/nm	333	333	342	367	336
ε/l mol^{-1} cm^{-1}	5 500	5 200	5 400	4 400	4 300

As previously reported, the pyrimidinyl betaine (4) is dimerised in the solid state and in concentrated solution. In solution at low concentration, the monomer is favoured at equilibrium: after heating for 30 min at 60 °C and cooling, no dimer remained and the Beer–Lambert law was followed. Solutions of all the betaines were stable at the maximum temperature used for many hours.

EXPERIMENTAL

Preparation of Betaines.—(i) 1-*Methyl*-3-*oxidopyridinium*.[3] 3-Hydroxy-1-methylpyridinium iodide (2.4 g) in MeOH (15 ml) was added to KOH (5 g) in MeOH (50 ml). The solution was evaporated and the betaine extracted from the residue with $CHCl_3$ (3 × 20 ml). The dried (Na_2SO_4) extracts were evaporated to give the betaine as a syrup; it was characterised by the u.v. spectrum (Table 1). It is unstable in air and was kept as a solution in EtOH.

(ii) 1-Benzyl-3-oxidopyridinium was similarly prepared from 1-benzyl-3-hydroxypyridinium bromide.[4]

(iii) 3-Oxido-1-phenylpyridinium was prepared in EtOH solution from the HCl salt using Amberlite IRA 401 (*cf.* ref. 5).

(iv) 1-(4,6-*Dimethylpyrimidin*-2-*yl*)-3-*oxidopyridinium*. The dimer[6] was utilised, m.p. 160—161 °C (lit.,[6] 160—161 °C) for the solvents EtOH, Bu^tOH, H_2O, and $(CH_2{\cdot}OH)_2$; de-dimerisation was effected by heating at 60 °C for 30 min as shown by the disappearance of the dimer band at *ca.* 265 nm and complete formation of the monomer band near 370 nm. However in $CHCl_3$, the de-dimerisation was slow and incomplete; therefore we used a more concentrated monomer solution in EtOH and diluted with $CHCl_3$; no significant re-dimerisation had taken place after 2 h in the mixed solvent.

(v) 1-*Methyl*-3-*oxido*-5-*phenylpyridinium*, m.p. 39—40 °C (lit.,[7] 39—40 °C), was kindly provided by Dr. R. Rittner.

Spectrophotometric Method.—The appropriate quantity of dipolarophile (to give solution 0.01—2 mol l^{-1}) was weighed into a volumetric flask and the volume made up with the prepared betaine solution. The solution was then transferred to a 1 cm cell of a Beckmann DK2A or DBG or Cecil CE292 instrument and thermostatted at ± 0.2 °C. The absorbance at $t = 0$ was obtained by extrapolation. Both the de-dimerisation and the cycloaddition kinetics were in the absence of direct sunlight, as the ethanolic monomer solution appeared to be photosensitive.

Kinetic Method.—We applied the Kezdy–Swinbourne method.[8] Each reaction was followed at constant temperature, and values of the absorbance at time t (A_t) were plotted against the absorbance at time $t + \Delta t[A_{(t+\Delta t)}]$. This gave straight lines of which the correlation coefficients were > 0.999. The value of A_∞ (the absorbance at equilibrium) is given by the intersection of this line with a line at 45° passing the origin.[8] The second-order rate constant, k, for the reaction of betaine with dipolarophile is now given[8] by equation (1). Here [D] is the concentration of the dipolarophile (in large excess), ρ is the slope of the $A_t/A_{(t+\Delta t)}$ plot described above and A_0 is the initial absorbance.

$$k = \frac{1}{[D]} \cdot \frac{2.303 \log\rho}{\Delta t} \cdot \frac{A_0 - A_\infty}{A_0} \qquad (1)$$

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[1] Part XXVIII, N. Dennis, A. R. Katritzky, E. Lunt, M. Ramaiah, R. L. Harlow, and S. H. Simonsen, *Tetrahedron Letters*, 1976, 1569.

[2] For a review see N. Dennis, A. R. Katritzky, and Y. Takeuchi, *Angew. Chem. Internat. Edn.*, 1976, **15**, 1.

[3] L. Paoloni, M. L. Tosato, and M. Cignitti, *Theor. Chim. Acta*, 1969, **14**, 221.

[4] *Cf.* J. Banerji, N. Dennis, J. Frank, A. R. Katritzky, and T. Matsuo, *J.C.S. Perkin I*, in the press.

[5] N. Dennis, A. R. Katritzky, and S. K. Parton, *J.C.S. Perkin I*, in the press.

[6] Part XX, N. Dennis, B. Ibrahim, and A. R. Katritzky, *J.C.S. Perkin I*, in the press.

[7] *Cf.* N. Dennis, A. R. Katritzky, and R. Rittner, *J.C.S. Perkin I*, in the press.

[8] E. S. Swinbourne, ' Analysis of Kinetic Data,' Nelson, London, 1971.

Activation and Thermodynamic Parameters.—The activation parameters were obtained from measurements of k at various temperatures and application of equation (2). Values of ΔH^* and ΔS^* were calculated from ΔE_a using equations (3) and (4). Equilibrium parameters were obtained from equations (5) and (6).

$$\log k = \log A - \Delta E_a/2.303RT \qquad (2)$$

$$\Delta H^* = \Delta E_a - RT \qquad (3)$$

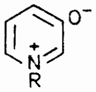
$$\Delta S^* = 4.576 \log (A/T) - 49.21 \qquad (4)$$

$$K = \frac{A_0 - A_\infty}{A_\infty} \cdot \frac{1}{[\mathrm{D}]} \qquad (5)$$

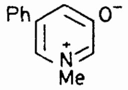
$$2.303\, RT \log K = -\Delta H + T\Delta S \qquad (6)$$

RESULTS AND DISCUSSION

Cycloaddition of Betaines with Methyl Acrylate.—Rate constants for the forward and reverse cycloadditions of the betaines (1)—(5) with methyl acrylate in ethanol solution for a range of temperatures are given in Table 2, together with the equilibrium constants. The thermodynamic parameters derived from these kinetic data are given in Table 3. Two trends are immediately apparent. (i) The rates of cycloaddition increase with the electron-withdrawing effect of the 1-substituent: Me (1) ≈ CH_2Ph (2) < Ph (3) < pyrimidin-2-yl (4). This confirms the results of preparative observations,[6] although the differences in rate now noted are less than were expected.



(1) R = Me
(2) R = CH_2Ph
(3) R = Ph
(4) R = 4,6-dimethylpyrimidin-2-yl



(5)

$CH_2{=}CHX$

(6) X = CO_2Me
(7) X = CN
(8) X = 4-pyridyl
(9) X = Ph
(10) X = OBu^n

TABLE 2

Rate constants k [a] and k' [b] and equilibrium constants K [c] for the cycloaddition of betaines (1)—(5) to methyl acrylate (EtOH solution)

(1)

t/°C	$k \times 10^6$	$k' \times 10^6$	K
29.8	0.345	1.4	0.24
40.4	0.995	3.7	0.27
50.9	2.63	13.2	0.20
58.5	5.85	41.8	0.14
70.5	14.07	108.2	0.13

(2)

t/°C	$k \times 10^6$	$k' \times 10^6$	K
30	0.35	0.3	1.22
41.4	1.24	1.6	0.76
49.9	2.87	4.5	0.64
60.1	7.37	12.2	0.6
70.5	19.82	45	0.44

(3)

t/°C	$k \times 10^5$	$k' \times 10^6$	K
47.6	0.63	0.84	7.5
52.4	1.07	1.7	6·3
61	2.12	3.4	6.3
70	4.74	11.3	4.2
75	6.49		[d]
80	9.14		[d]
85	13.51		[d]

(4)

t/°C	$k \times 10^4$	$k' \times 10^6$	K
20.1	0.58		
27	1.24		
33.5	2.46		
42.8	4.45		
51.4	10.64	1.6 [e]	*ca.* 650 [e]
60.5	20.99		
68	31.34	5.7 [e]	*ca.* 550 [e]

(5)

t/°C	$k \times 10^5$	$k' \times 10^5$	K
28.5	0.29	0.03	10.0
40.4	0.97	0.17	5.7
49.9	2.28	0.55	4.12
59.9	5.37	1.75	3.07
71.1	12.94	4.78	2.71

[a] Rate constants for the cycloaddition reaction in l mol^{-1} s^{-1}. [b] Rate constants for the retrocycloaddition reaction in s^{-1}; $k' = k/K$. [c] l mol^{-1}. [d] K was not measured for $t > 70$ °C because the determination could not be carried out in the cell. [e] Approximate values owing to errors in A_∞ [equation (5)].

TABLE 3

Thermodynamic parameters for the cycloaddition of the betaines (1)—(5) to methyl acrylate (EtOH solution) [a]

	(1)	(2)	(3)	(4)	(5)
E_a/kcal mol^{-1}	19.1 ± 0.9	20.5 ± 0.4	18.4 ± 0.7	16.6 ± 0.9	18.4 ± 0.4
ΔH^*_{298}/kcal mol^{-1}	18.5 ± 0.9	19.9 ± 0.4	17.8 ± 0.7	16.0 ± 0.9	17.8 ± 0.4
ΔS^*_{298}/cal mol^{-1} K^{-1}	−27.2 ± 2.8	−22.5 ± 1.3	−26.8 ± 4.3	−23.2 ± 6.4	−25 ± 1
ΔH/kcal mol^{-1}	−3.6 ± 2.5	−4.8 ± 1.6	−5.0 ± 3.5	*ca.* −2.0	−6.4 ± 1.7
ΔS/cal mol^{-1} K^{-1}	−15 ± 7	−15.6 ± 4.9	[b]	[b]	−17 ± 5.3
E'_a/kcal mol^{-1}	23.0 ± 2.8	25.1 ± 2.0	[b]	[b]	24.7 ± 1.8
$\Delta H'^*_{298}$/kcal mol^{-1}	22.4 ± 2.8	24.5 ± 2.0	[b]	[b]	24.1 ± 1.8
$\Delta S'^*_{298}$/cal mol^{-1} K^{-1}	[b]	−15.6 ± 5	[b]	[b]	−17 ± 5.3

[a] Confidence levels 90%. [b] Significant values cannot be obtained owing to errors in K.

A 5-phenyl substituent (5) also increases the rate significantly. (ii) The equilibrium constants for cycloadduct formation increase very strongly in the same sense Me ≈ CH_2Ph < Ph < pyrimidin-2-yl. It is the combination of these rate and equilibrium effects, and particularly the latter, which renders the pyrimidin-2-yl compound so useful[9] in the preparative cycloadditions. In all cases, rate constants for both forward and backward reactions increase with temperature, but the increase is greater for the dissociation and thus the equilibrium constants for adduct formation decrease with temperature. This observation confirms the experience in preparative work that low temperatures favour adduct formation.

Thermodynamic parameters for these reactions are recorded in Table 3. Entropies of activation for the reverse reactions are less negative than those for the forward reactions, as expected.

TABLE 4

Solvent effect on the rate constants for the cycloaddition of the betaine (4) to methyl acrylate at 50 ± 0.5 °C

Solvent	10^3k/l mol^{-1} s^{-1}	Kosower Z-values
$CHCl_3$ [a]	2.74	63.2
Bu^{t}OH	3.98	71.3
EtOH	0.88	79.6
$(HOCH_2)_2$	0.98	85.1
H_2O	1.18	94.6

[a] Plus 2.5% of ethanol. [b] E. M. Kosower, 'An Introduction to Physical Organic Chemistry,' Wiley, New York, 1968, p. 301.

Solvent Effects on Rates.—As demonstrated by Table 4, the solvent effect on the reaction of the betaine (4) with methyl acrylate is small, and the reactions show no clear trend with solvent polarity. This finding is expected for concerted cycloaddition reactions.

Effect of Dipolarophile Structure on Rates.—Finally, we have determined (Table 5) the rates of addition of a variety of monosubstituted ethylenes to the betaine (4). As expected from preparative observations, the rates increase with the electron-withdrawing character of the substituent, although again the differences are less than we expected. We plan to carry out MO calculations to test the predictive power of FMO theory in these reactions.

TABLE 5

Reaction constants for the cycloadditions of 1-(4,6-dimethylpyrimidin-2-yl)-3-oxidopyridinium with dipolarophiles (CH_2=CHX) in EtOH at 42 °C

X	OBu^n	Ph	4-Pyridyl	CN	CO_2Me
10^4k/l mol^{-1} s^{-1}	0.56	0.92	1.60	1.26	4.45

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[9] Part XXI, N. Dennis, B. Ibrahim, and A. R. Katritzky, *J.C.S. Perkin I*, in the press.