KINETIC STUDIES OF [4*n*+2]π-THERMAL CYCLODIMERIZATION OF 1-(3-PYRIDAZINYL)-3-OXIDOPYRIDINIUM BETAINES

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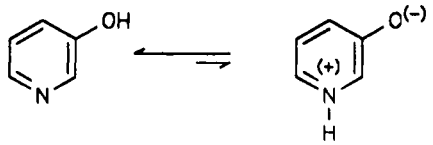
The reactivity of the base induced cyclodimerization of 1-(6-arylpyridazin-3-yl)-3-oxidopyridinium chlorides in a pericyclic process have been investigated kinetically at λ 380 nm. The reaction was found to be second order with respect to the liberated betaine and zero order with respect to the base. On the other hand dedimerization (monomer formation) was found to be first order). It was shown that dimerization is favoured at low temperature, whereas dedimerization process is favoured at relatively high temperature (ca 70 °C). Solvent effects on the reaction rate have been found to follow the order ethanol > chloroform ≈ 1,2-dichloroethane. Complete dissociation was accomplished only in 1,2-dichloroethane at ca 70 °C. The thermodynamic activation parameters have been calculated by a standard method. Thus, $\Delta G^{\neq}$ has been found to be independent on substituents and solvents. The high negative values of $\Delta S^{\neq}$ supports the cyclic transition state which is in favour with the concerted mechanism. MO calculations using SCF–PPP approximation method indicated low HOMO–LUMO energy gap of the investigated betaines.

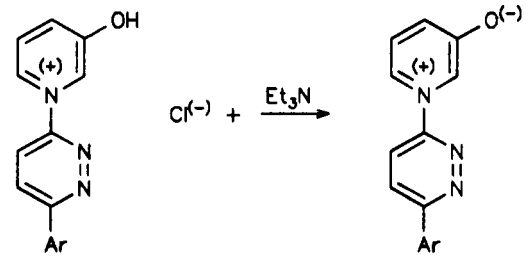
3-Hydroxypyridine (*I*) and its 1-substituted 3-oxidopyridinium betaines fall into the class of azomethine yields, which are octet stabilized 1,3-dipoles without an orthogonal double bond. Consequently these compounds mainly undergo 1,3-dipolar cycloadditions across their endocyclic atoms to give bicyclic adducts[1,2]. Katritzky, Dennis and Takenchi[3,4] claimed that the 1,3-dipolar character of 1-substituted-3-oxidopyridinium betaines is directly proportional to the electron-withdrawing properties of the 1-substituents.



The ready formation of the dimeric compounds (*IVa*, *IVb*) from 1-(6-phenyl) and 1-[6-(4-tolylpyridazin-3-yl)]-3-oxidopyridinium betains is indicative of small HOMO–LUMO energy gap for the monomeric system. The enhanced reactivity of 1-(6-arylpy-

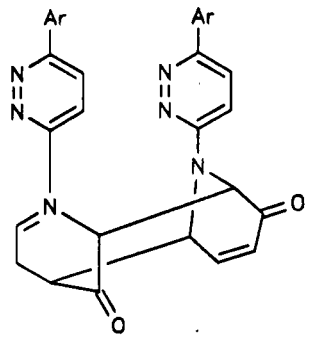
ridazin-3-yl)-3-oxidopyridinium betaines of the type (*IIIa*, *IIIb*) towards a range of 2π- and 4π-1,3-dipolarophiles[5-7] has encouraged us to correlate the reactivity of such betaines quantitatively by kinetic methods to see to what extent the 1-(6-arylpyridazin-3-yl) as 1-azaheteroaryl substituent (i.e. system with two annular nitrogen atoms at 2- and 3-positions in the 1-aryl substituent) agrees with the previously reported 1-azaheteroaryl betaines[3,8] where the annular atoms are located at the alternant 2,4 and 6 positions in the 1-aryl substituent.

The stable 1-(6-arylpyridazin-3-yl)-3-hydroxypyridinium chlorides (*IIa*, *IIb*) are considered to be convenient sources of the corresponding unstable 1-(6-arylpyridazin-3-yl)-3-oxidopyridinium betaines (*IIIa*, *IIIb*). Thus, treatment of 1-(6-arylpyridazin-3-



II *III*

a, Ar = C_6H_5
b, Ar = $CH_3-C_6H_4$



IV

SCHEME 1

yl)-3-hydroxypyridinium chlorides (*IIa*, *IIb*) with triethylamine in 1,2-dichloroethane at room temperature afforded the corresponding dimers (*IVa*, *IVb*). The formation of the dimer (*IVa*) was monitored by the infrared technique where the two carbonyls absorption bands (at 1 720 cm^{-1} (non-conjugated C=O) and 1 680 cm^{-1} (conjugated C=O) gradually appeared. However, pure samples of the dimers for further characterization could not be isolated due to their instability (see Scheme 1).

EXPERIMENTAL

UV-VIS spectra were recorded on a Pye–Unicam SP 1800 recording spectrophotometer, while all the kinetic measurements were recorded on SP 6-200 Pye–Unicam Spectrophotometer, equipped with thermostatted unit. Infrared spectra were recorded on Perkin–Elmer model 180.

All reagents were of analytical grade unless otherwise specified. Ethanol b.p. 78 °C was dried by magnesium iodide method[9].

1-(6-Phenylpyridazin-3-yl)-3-hydroxypyridinium chloride, m.p. 234 – 235 °C (ref.[5]) and 1-[6-(4-tolylpyridazin-3-yl)-3-hydroxypyridinium chloride, m.p. 251 – 253 °C were prepared according to refs[6,7].

Kinetic Procedure

The ultraviolet and visible spectra of 1-(6-phenyl-pyridazin-3-yl)-3-hydroxypyridinium chloride, triethylamine and the product in 1,2-dichloroethane, ethanol and chloroform were determined and the analytical wavelength was then chosen as shown in Fig. 1. Freshly prepared samples of 1-[6-phenylpyridazin-3-yl)]-3-hydroxypyridinium chloride and triethylamine were allowed to stand for 30 min in thermostat at the required temperature 20 – 40 °C.

Aliquots of 5, 6 and 7 ml of 1-(6-phenylpyridazin-3-yl)-3-hydroxypyridinium chloride were transferred to test tubes each containing 2.0 ml of triethylamine diluted with appropriate solvent to 10 ml. Addition of triethylamine marks the zero time of reaction. A portion of the reaction mixture was immediately transferred to 1.0 cm quartz cell placed in the thermostatted cell compartment of the spectrophotometer. The absorbance (A) at λ 370 or λ 380 nm (according to the solvent used) was recorded as a function of time (t), against a blank without triethylamine.

From the absorbance time curves, the initial slope (dA/dt), initial rates, rate constants and thermodynamic activation parameters were calculated by standard methods[10].

The same procedure has been carried out for 1-[6-(4-tolyl-pyridazin-3-yl)-3-yl)-3-hydroxypyridinium chloride.

RESULTS AND DISCUSSION

The kinetics of the thermally allowed $[4n+2]\pi$-cyclodimerization of 1-(6-arylpyridazinyl)-3-oxidopyridinium betaines (*IIIa*, *IIIb*) have been investigated in different solvents, namely 1,2-dichloroethane, ethanol and chloroform. The rate of cyclodimerization and the rate of dedimerization (monomer formation) appears to depend upon two main factors: (i) Experimental conditions such as, concentration, temperature and solvent. (ii) Substituent and steric effects and energy separation of the interacting frontier molecular orbitals of the betaine (HOMO–LUMO energy gap).

Kinetics and Mechanism of the Reaction

The effect of concentration of both reactants 1-(6-phenylpyridazin-3-yl)-3-hydroxypyridinium chloride (*IIa*) and triethylamine of reaction rate in different solvents have been investigated to determine the order on reaction using the differential method suggested by Van't Hoff[10]. The kinetic data compiled in Tables I and II and Fig. 2 show clearly that the reaction is second order with respect to 1-(6-phenylpyridazin-3-yl)-3-hydroxypyridinium chloride and zero order with respect to triethylamine. The order of reaction of 1-[6-(4-tolylpyridazinc-3-yl)]-3-hydroxypyridinium chloride investigated by similar method and has been also found to be second order as shown in Table I, Fig. 2.

The reaction between 1-(6-phenylpyridazin-3-yl)-3-hydroxypyridinium chloride (*IIa*) or 1-[6-(4-tolylpyridazin-3-yl)]-3-hydroxypyridinium chloride (*IIb*) with triethylamine at (20 – 40 °C) in all solvents used, shows clearly one absorption band in the visible at 370 – 380 nm, assignable for the dimer (*IV*). However, if the reaction is carried out at higher temperature, e.g. 70 °C, in 1,2-dichloroethane, different behaviour has been observed. The absorption band at 380 nm gradually disappeared at the expense of the appearance of a new absorption band at 480 nm, accompanied by change in colour from

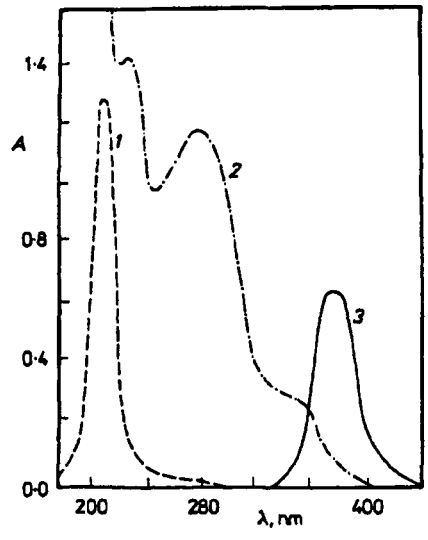


FIG. 1

Absorption spectra of *1* 0.6 mM triethylamine; *2* 0.8 mM 1-(6-phenylpyridazin-3-yl)-3-hydroxypyridinium chloride (*IIa*); *3* reaction product in 1,2-dichloroethane at 40 °C

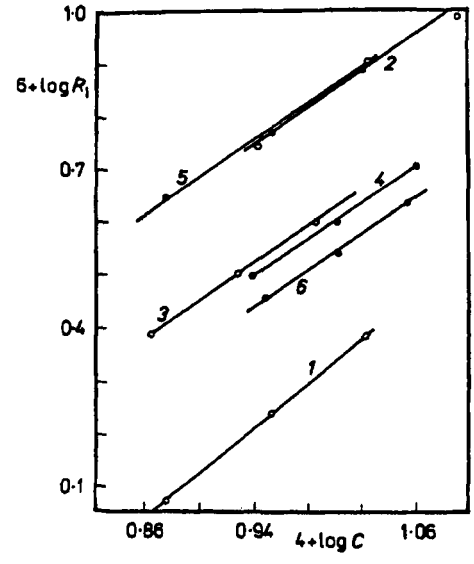


FIG. 2

Logarithmic relationship of initial rates vs initial concentrations for *IIa* 1,2,3 and for *IIb* 4,5,6 via their interaction with 11.6 mM triethylamine at 40 °C, in 1,2-dichloroethane, ethanol, and chloroform, respectively

yellow to a pale pink which may be attributed to the dissociation of dimer to monomer (cf. Scheme 1).

The rate of thermal dissociation of dimer *IVa* (at 380 nm) and the rate of formation of monomer *IIIa* (at 480 nm) in 1,2-dichloroethane at 70 °C, at different concentrations of the *IIIa* presursor, 1-(6-phenylpyridazin-3-yl)-3-hydroxypyridinium chloride (*IIa*), have been measured to determine the order of the reaction as indicated previously by the differential method[10].

The results compiled in Table III indicate that the dissociation of the dimer *IVa* is first order, as follows both from the rate of disappearance of the dimer *IVa* and from the rate of formation of the monomer *IIIa*. This manifests the irreversibility of the reaction at this temperature. The isosbestic point shown in Fig. 3 indicates the presence of two equilibrated compounds where that the dimer is converted into monomer without any long-lived intermediate formation[11].

TABLE I
Initial rates (R_i) and the order (n) of reaction of *IIa* and *IIb* with 11.6 mM triethylamine in different solvents at 40 °C

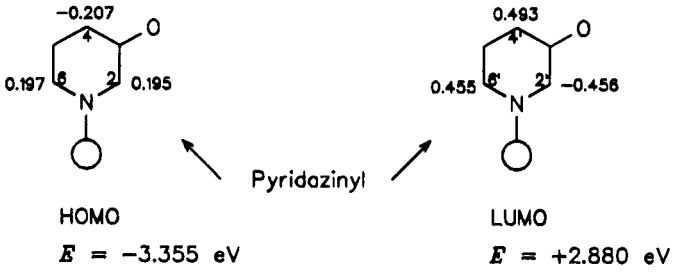
Substrate	Solvent λ, nm[a]	Concentration 10^4 mol l^{-1}	$10^6 R_i$ mol l^{-1} S^{-1}	n
IIa	ethanol	8.75	5.54	1.81
	370	10.50	8.39	
		12.25	10.21	
IIa	1,2-dichloroethane	7.50	1.20	2.1
	380	9.00	1.74	
		10.50	2.45	
IIa	chloroform	7.26	2.47	1.83
	380	8.47	3.21	
		9.68	4.01	
IIb	ethanol	7.50	4.53	1.83
	370	9.00	5.91	
		10.50	8.02	
IIb	1,2-dichloroethane	8.61	3.21	1.85
	380	10.04	4.00	
		11.48	5.20	
IIb	chloroform	8.82	2.91	1.90
	380	10.08	3.53	
		11.34	4.36	

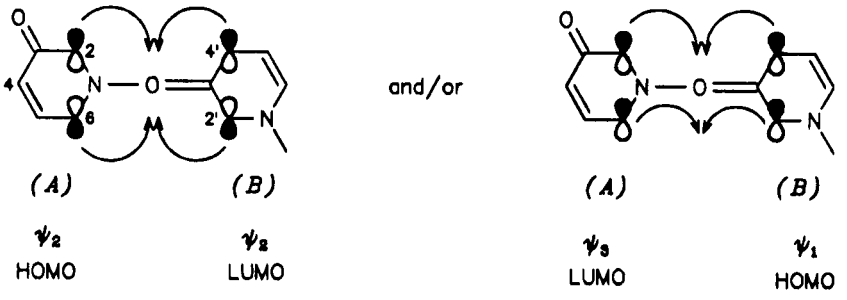
[a] Monitoring wavelength.

On the other hand if the temperature was decreased slowly the pink colour of betaine *IIIa* changed back to yellow indicating dimer formation. High reactivity of the betaine *IIIa*, seems to be in good agreement with observations reported earlier[12]. The activation parameters have been calculated by the standard method[10]. The value of $\Delta G^{\neq}$ was found to be independent on substituents and solvents. The high negative values of $\Delta S^{\neq}$ support the cyclic transition state which is in accord with concerted mechanism.

Frontier Molecular Orbital Calculations

MO calculations of the coefficients of the 1-(6-arylpyridazin-3-yl)-3-oxidopyridinium betaine (*IIIa*) were performed using the SCF–PPP method[13,14]. The data are depicted in Scheme 2. Moreover, the electronic transition energies and the probabilities were calculated using configuration interaction procedure involving the three highest occupied and the three lowest unoccupied MO'S (cf. Scheme 2).





SCHEME 2

TABLE II
Initial rates (R_i) and the order of reaction (n) with respect to triethylamine (TEA) via their interaction with use commercial symbols (*IIa*, *IIb*) at 40 °C

Substrate	Solvent λ, nm[a]	Concentration 10^4 mol l^{-1}	TEA 10^3 mol l^{-1}	$10^6 R_i$ mol l^{-1} S^{-1}	n
IIa	ethanol	8.75	11.6	5.54	0
	370	8.75	17.4	5.50	
		8.75	23.2	5.51	
IIa	1,2-dichloroethane	9.00	11.6	1.74	0
	380	9.00	17.4	1.74	
		9.00	23.2	1.70	
IIa	chloroform	8.47	11.6	3.21	0
	380	8.47	17.4	3.20	
		8.47	23.2	3.24	
IIb	ethanol	7.50	11.6	4.50	0
	370	7.50	17.4	4.53	
		7.50	23.2	4.51	
IIb	1,2-dichloroethane	10.04	11.6	4.00	0
	380	10.04	17.4	4.00	
		10.04	23.2	4.20	
IIb	chloroform	10.08	11.6	3.53	0
	380	10.08	17.4	3.50	
		10.08	23.2	3.54	

[a] Monitoring wavelength.

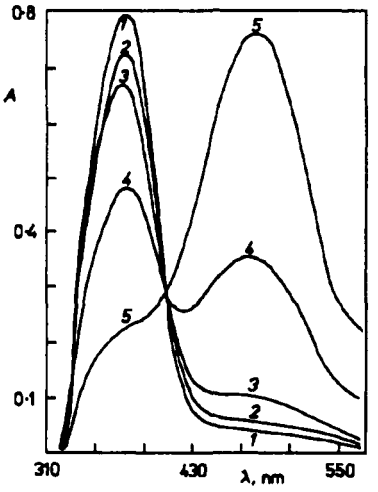


FIG. 3
The effect of time (120 min) on the absorption spectra of the reaction products, due the interaction of 1.05 mM *IIa* with 11.6 mM triethylamine in 1,2-dichloroethane at 70 °C

The reaction is considered to occur between the 2,6-positions of one molecule (4π-1,3 dipole) and the 2',4' positions of the second molecule (2π-1,3-dipolarophile) in a suprafacial–suprafacial interaction to give the dimeric cycloadduct. 1-(6-Arylpyridazin-3-yl)-3-oxidopyridinium acts as 4π-1,3-dipole across 2,6-positions and can be considered as an aza-allyl anion (*A*), whereas it may act as 2π-1,3-dipolarophile across 2',4' positions which can be considered as an allyl cation (*B*) both having the following sets of molecular orbitals ψ_1, ψ_2, ψ_3 (*A*) with 4π–electrons, where ψ_2 represent the HOMO and ψ_3 the LUMO. Meanwhile, (*B*) with 2π-electrons only has ψ_1 as the HOMO and ψ_2

TABLE III
Initial rates (R_i) of dimer decomposition and monomer formation for the reaction of 11.6 mM triethylamine with various molar concentrations of *IIa* in 1,2-dichloroethane at 70 °C

Concentration 10^4 mol l^{-1}	λ^a nm	$10^6 R_i$ mol l^{-1} S^{-1}	n
7.50	380	1.30	0.97
9.00		1.60	
10.50		1.79	
7.50	480	1.31	1.00
9.00		1.62	
10.50		1.77	

[a] Monitoring wavelength.

TABLE IV
Rate constants and activation parameters for the reaction of *IIa* and *IIb* with 11.6 mM triethylamine in different solvents

Substrate	Solvent	k_2, l mol^{-1} s^{-1}			$\Delta E^{\neq}$	$\Delta H^{\neq}$ kJ mol^{-1}	$\Delta G^{\neq}$	$\Delta S^{\neq}$ J K^{-1} mol^{-1}
		293 K	303 K	313 K				
IIa	1,2-dichloroethane	0.88	1.36	2.14	35.11	32.60	82.34	-149.64
IIa	chloroform	2.84	3.54	4.47	20.90	14.21	80.67	-199.80
IIa	ethanol	4.93	5.71	7.60	14.21	11.70	79.00	-202.31
IIb	1,2-dichloroethane	2.63	3.30	4.33	18.39	15.88	80.67	-194.37
IIb	chloroform	2.52	3.15	3.74	17.55	15.04	80.67	-198.13
IIb	ethanol	5.30	6.50	7.30	15.46	12.54	79.00	-199.80

as the LUMO. The FMO calculation predicts that both HOMO of (*A*) (i.e. ψ_2) and LUMO (*A*) ψ_3 and HOMO (*B*) ψ_1 modes of interaction are thermally allowed suprafacial–suprafacial processes, in accord with the observed results.

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