Photoreactions of Alkylated 2-Pyridones

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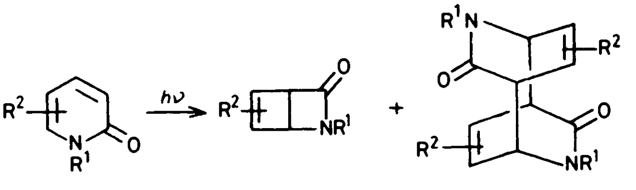
Photoisomerisation and dimerisation reactions in solution have been studied with a series of alkylated 2-pyridones (**1**). The low quantum efficiencies for the photoisomerisation (0.01—0.07) are related to the short-lived singlet excited states (below 1 ns). The effects of temperature, solvent, and substrate concentration were also examined. The photodimerisation reactions of (**1**) are considered to involve preliminary association *via* strong dipole–dipole interaction rather than hydrogen-bonded pairing.

Upon direct irradiation 2-pyridones generally undergo valence isomerisation in dilute solution,[1,2] whereas at higher concentration dimerisation dominates to give mainly 4 + 4 *trans-anti*-dimers.[2,3] 4-Oxygenated 2-pyridones[1,4] and 1-alkenyl-2-pyridones[1,5] tend to undergo highly selective photoisomerisation, and have consequently received attention as useful precursors of the intermediates for β-lactam antibiotic synthesis,[6] as well as potential systems for photochemical energy storage.[5] However, there have been few systematic studies[2,5] on the mechanisms of these reactions, and little information is available yet on structure–photoreactivity relationships;[4] however, the electronic properties have been thoroughly studied recently.[7] In the present investigation the effects of substituent, temperature, concentration, and solvent have been studied using a series of alkylated 2-pyridones, as a preliminary to the elucidation of structural effects and further extension of 2-pyridone photochemistry.

Results

Effects of Substituent and Photolytic Conditions.—Alkylated 2-pyridones (**1**) undergo isomerisation and 4 + 4 dimerisation competitively with each other, on irradiation with 313—334 nm light in ethyl acetate (Scheme 1). Though only a few dimers (**3d**, **e**, **g**, and **h**) were isolated in the present work, the physical properties of the major dimers were consistent with the *trans-anti*-structure (**3**) except for the product from (**1h**); this is the general tendency in 2-pyridone photochemistry.[3] Table 1 lists the yields of the photoisomers (**2**) and the quantum yields (φ) for the photoreaction in 10^{-3}M-solution. The effect of dissolved oxygen is nil; however, oxygenation may occur on irradiation under oxygen with sensitizer.[8] Both the yields of (**2**) and the φ values were independent of the percent conversion up to 60%, since the products do not absorb above 300 nm. The yields of (**2**) vary moderately with substituents: 4-alkylated derivatives (**1d**, **g**, and **h**) show higher yields. Values of φ (%) are generally low and vary relatively little with substituents, except for (**1h** and **f**). On similar photolysis in aqueous solution at 25 °C, the φ values for (**1a**—**j**) were, respectively, 2.6, 2.3, 2.4, 3.6, 2.2, 0.4, 3.5, 5.0, 2.9, and 1.3 (showing a similar trend). While φ is relatively unaffected by solvent properties, the yield of (**2**) varies significantly with solvent (Table 2). Viscous media, including liquid paraffin or glycerine, somewhat depressed the φ value of (**1d**).

Temperature effects have been examined using 1-substituted (**1g**) and 1-unsubstituted 2-pyridones (**1d**) in 10^{-3}M-solution. In ethyl acetate photoisomerisation of (**1d**) occurred in high yield [(**2d**); 94—100%] without dimerisation at any temperature (from —15 to 50 °C), with small variation in φ (0.03—0.04). In hexane, in contrast, remarkable temperature dependence was observed in the yields of (**2d**) and (**3d**) as well as in φ: the yields of (**2d**) and (**3d**), and the φ values, were respectively 0%, 100%, and 0.10 at −15 °C, 26%, 70%, and 0.037 at 1 °C, and 90—100%, 0%, and 0.037—0.05 at 20—50 °C. Similarly the yields of (**2g**) and φ in hexane were respectively 0% and 0.08 at −15 °C, 31% and 0.06 at 1 °C, 43% and 0.04 at 20 °C, 64% and 0.04 at 40 °C, and 67% and 0.04 at 50 °C.



(1) (2) (3)

	a	b	c	d	e	f	g	h	i	j
R^1	H	Me	H	H	H	H	Me	Me	Et	vinyl
R^2	H	H	3-Me	4-Me	5-Me	6-Me	4-Me	4-Bu^t	H	H

Scheme 1.

While low concentrations of (**1**) favour photoisomerisation high concentrations tend to favour photodimerisation (Table 3), analogously to the reported tendency with (**1a** and **b**).[2] However, (**1h**) undergoes selective photoisomerisation even in 0.1M-concentration where (**1d**) and (**1g**) give significant amounts of photodimers. The highly selective photoisomerisation of (**1h**) is similar to that observed with 4-oxygenated 2-pyridones, which give photoisomers without dimers.[1c,4]

U.v. Absorption and Fluorescence Spectra.—The u.v. absorption and fluorescence spectral data are summarized in Table 4. The absorption spectra show little variation with substituents; the fluorescence quantum yields are low and vary moderately. The excited singlet states are very short-lived (0.05—0.8 ns). The room-temperature fluorescence of (**1b**) showed vibrational structure in hexane (10^{-5}M-solution) but became less structured at higher concentrations (above 10^{-3}M). No excimer emission was detected in a room-temperature solution of (**1b**).

Ground-state Composition in Solution.—Ground-state association equilibria may play an important role in partitioning between the unimolecular and bimolecular photoreactions. In the present study the hydrogen-bonded association of 1-unsubstituted 2-pyridones has been examined conveniently by i.r. spectroscopy [*cf.* the study with (**1a**)[7c]], and the potential association of 1-alkylated 2-pyridones *via* dipole–dipole pairing was examined by cryoscopic experiments in benzene. The i.r. spectrum of (**1d**) (0.03M in benzene solution) at room temperature showed a single peak at 1 657 cm^{-1} (C=O in hydrogen-bonded pair); both 1 660 cm^{-1} (hydrogen-bonded) and 1 675 cm^{-1} (not hydrogen-bonded) peaks were observed in ethyl acetate. The pyridone (**1g**) showed only single peaks in benzene (1 668 cm^{-1}) and in tetrahydrofuran (1 670 cm^{-1}). Thus, it is

Table 1. Substituent effects on the photoisomerisation[a]

2-Pyridone	At 25 °C φ(%)	At 25 °C (2) (%)	At 50 °C φ (%)	At 50 °C (2) (%)
(1a)	2.1	95	2.3	91
(1b)	2.1	70	2.4	13
(1c)	2.7	51	1.7	47
(1d)	3.1	100	3.4	100
(1e)	2.5	73	2.3	72
(1f)	1.3	65	0.6	86
(1g)	3.6	100	3.8	72
(1h)	6.7	100	7.2	86
(1i)	1.8	51		
(1j)	3.0	17		

[a] Initial concentration of (1) was 1.0mM, irradiated in ethyl acetate under air with 313—334 nm light. φ Values were unaffected by the dissolved oxygen. Yields of (2) are based on the consumed amounts of (1), and φ is the quantum yield for the consumption of (1) at 30—50% conversion.

Table 2. Solvent effects on the photoisomerisation of (1d)[a]

Solvent	At 25 °C φ (%)	At 25 °C (2d) (%)	At 50 °C φ (%)	At 50 °C (2d) (%)
H_2O	4.2	49	3.9	65
CH_3CN	2.9	81	2.8	100
EtOH	3.2	100	2.9	100
Bu^tOH	3.7	52	3.2	86
THF	3.2	94	2.9	[b]
EtOAc	3.1	100	2.7	100
$CHCl_3$	3.6	71	[b]	[b]
C_6H_6	3.8	48	3.2	79
C_6H_{12}	4.1	100	3.4	100

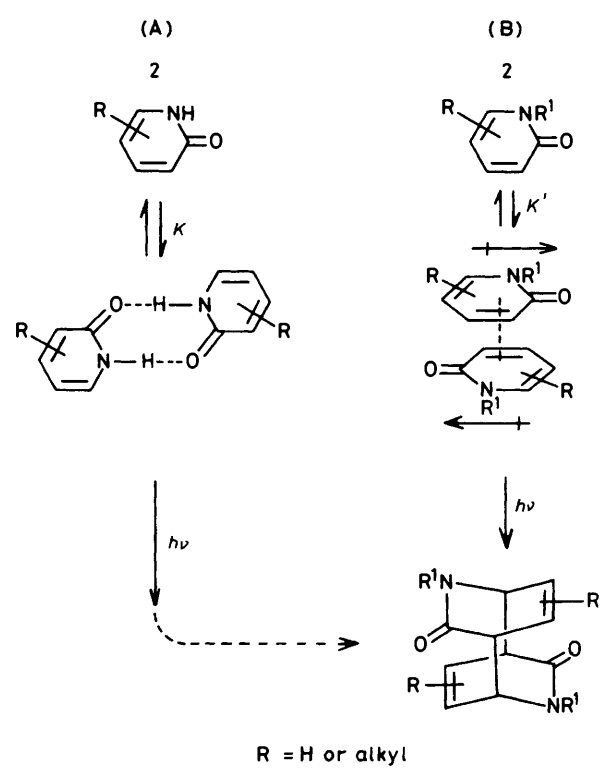
[a] Photolytic conditions and notations are similar to those in Table 1. [b] Not determined.

inferred that 1-unsubstituted 2-pyridones exist mainly as hydrogen-bonded pairs in nonpolar solvents and partly so in polar solvents. On the other hand, the apparent molecular weights of (1b) (*M* 109) in benzene were 166 ± 15 in 0.06M-solution and 177 ± 15 in 0.11M-solution, implying considerable dipole–dipole association (35—50%). In contrast, (1h) (*M* 165) showed no tendency for association: 179 ± 18 at 0.03M in benzene solution and 178 ± 18 in 0.11M-solution.

Table 3. Concentration effects on the yields of (2) and (3)[a]

[2-Pyridone]/M	Solvent	(2) (%)	(3) (%)
(1d) 0.001	Ethyl acetate	100	0
0.01	Water	46	9
0.1	Ethanol	33	29
(1g) 0.001	Ethyl acetate	100	0
0.01	Water	73	1
0.1	Ethanol	16	21
(1h) 0.001	Ethyl acetate	100	0
0.1	Ethanol	100	0
1.0	Ethanol	60	35[b]

[a] Yields of isolated material at nearly complete consumption of (1). [b] Mixture of dimers; the most likely structures are of *trans-anti* (5%) and *trans-syn* (30%) orientation from i.r. and n.m.r. spectra.



Scheme 2.

Discussion

Pre-equilibrium of static bimolecular association may be crucial for photochemical bimolecular processes to occur when the relevant excited states are very short-lived and incapable of effective dynamic collisions during their lifetime. At low temperature, association will be more favoured while dynamic collision will be disfavoured. Thus, the enhanced photodimerisation (or concomitant reduced isomerisation) at low temperature in hexane suggests that the photodimerisation takes place through a pre-equilibrium of association into species such as hydrogen-bonded or dipole–dipole pairs.

The photodimerisation reaction of 1-unsubstituted 2-pyridones can be explained in terms of Scheme 2(A), which includes hydrogen-bonded pairs as precursors. However, photodimerisation can occur with 1-alkylated 2-pyridones which are incapable of bimolecular association *via* hydrogen bonding. Further, the photodimerisation of (1g) is almost as efficient as that of (1d) in 0.1M-solution (Table 3), suggesting a less important role for hydrogen-bonded association (though this should not be ruled out). More likely is Scheme 2(B), which involves bimolecular dipole–dipole association. The large dipole moments of (1), *e.g.* 4.04 D for (1b),[9] may cause significant association, as supported by the cryoscopic experiment with (1b). Scheme 2(B) is also favoured by the general tendency for the major photodimers to be of *trans-anti*-structure;[2,3] Scheme 2(A) would require substantial changes in the structure of the hydrogen-bonded pairs, which should show more marked viscosity dependence than observed. The most likely structure of the major photodimer (1h) (30%) is the *trans-syn*-dimer: its spectra are similar to those of the *trans-anti*-dimer (3h) (5%). That the former is sterically least hindered is implied by a molecular model.

In 10^{-3}M-solution photodimerisation is of minor importance and unimolecular isomerisation occurs with high selectivity. In such dilute solution, the short-lived excited states (τ_s < 1 ns) would be incapable of any bimolecular reactions such as

Table 4. U.v. absorption and fluorescence spectral data

	Absorption[a]	τ_s[b]	Fluorescence[c]	
2-Pyridone	$\lambda_{max.}$/nm (ε/m^2 mol)	ns	$\lambda^f_{max.}$/nm	φ_f
(1a)	222 (914), 294 (737)	0.22	373	0.011
(1b)	224 (993), 295 (905)	0.23	375	0.011
(1c)	225 (582), 292 (709)	0.25	377	0.014
(1d)	224 (626), 289 (735)	0.12	375	0.005
(1e)	226 (847), 301 (625)	0.81	384	0.034
(1f)	224 (705), 300 (761)	0.05	376	0.003
(1g)	225 (465), 291 (567)	0.17	375	0.005
(1h)	223 (485), 291 (544)	0.07	375	0.003
(1i)	225 (662), 296 (595)	0.35	372	0.016
(1j)	310 (621)	1.8	389	0.11

[a] In aqueous solution. [b] Radiative lifetimes estimated from φ_f and u.v. absorption bands in ethyl acetate. [c] Fluorescence quantum yields in ethyl acetate at room temperature, measured using φ_f = 0.55 for quinine sulphate in aqueous 0.5M-sulphuric acid as a standard.

Table 5. Spectral data of the photoproducts[a]

Product	$\nu_{max.}$(CHCl$_3$)/cm^{-1} (C=O)	$\lambda_{max.}$/nm (EtOH) [ε/dm^3 mol^{-1} cm^{-1}]	δ_H(CDCl$_3$) (p.p.m.)	*m/z* (%)
(2c)	1 737	*b*	1.50 (3 H, s), 4.28 (1 H, d, *J* 3 Hz) 6.7 (2 H, m)	*b*
(2d)	1 743	214 [18]	1.84 (3 H, s), 3.98 (1 H, s) 4.21 (1 H, s), 6.1 (1 H, m)	109 (M^+, 50), 80 (35) 66 (100)
(2e)	1 752	213 [19]	1.64 (3 H, s), 3.68 (1 H, s) 3.96 (1 H, t, *J* 2 Hz), 5.94 (1 H, br s)	109 (M^+, 25), 80 (90) 66 (100), 65 (90)
(2f)	1 750	*c*	2.06 (3 H, s), 3.79 (1 H, br s) 6.6 (2 H, m)	*c*
(2g)	1 735	219 [18]	1.61 (3 H, s), 2.50 (3 H, s), 3.35 (1 H, s) 3.39 (1 H, s), 6.0 (1 H, m)	123 (M^+, 40), 94 (25) 82 (35), 66 (100)
(2h)	1 730	219 [18]	1.04 (9 H, s), 2.66 (3 H, s) 3.95 (2 H, s), 6.0 (1 H, s)	165 (M^+, 55), 110 (100), 108 (80), 93 (100), 91 (50), 77 (40)
(3h)	1 644	207 [36]	0.60 (18 H, s), 2.51 (6 H, s) 3.7—4.1 (4 H, m), 6.1 (2 H, d, *J* 5 Hz)[d]	166 (80), 165 (M^+/2, 100) 150 (90), 123 (50), 122 (70)[e]
Product from **(1h)**	1 652	204 [36]	0.92 (18 H, s), 2.80 (6 H, s) 3.6—4.1 (4 H, m), 5.5 (2 H, d, *J* 5 Hz)[d]	330 (M^+, 3), 165 (M^+/2, 100) 166 (100), 150 (60), 123 (25) 122 (30)

[a] Oils except for **(2d)**, m.p. 52—53 °C; and **(3h)**, m.p. 230—231 °C. [b] Darkened during storage for several weeks after isolation. [c] The product had been exhausted. [d] Measured in trifluoroacetic acid. [e] M^+ peak not found.

excimer formation and bimolecular deactivation. The low quantum efficiencies for the photoisomerisation even in the absence of competing bimolecular processes in 10^{-3}M-solution are attributable to the rapid and efficient intramolecular deactivation pathways. Similarly, notable variation in φ, *e.g.* with **(1f)** and **(1h)**, essentially reflects the intramolecular consequences in dilute solution, while the high selectivity for the photoisomerisation of **(1g)** in 0.1M-solution is ascribable to the large steric hindrance in the competing bimolecular processes.

The nature of the rapid deactivation pathways remains unsolved and deserves further systematic investigation.

Experimental

I.r. and n.m.r. spectra were recorded with a Nihon Bunko IRA-1 spectrometer and a Hitachi R-24 spectrometer (60 MHz), respectively. U.v. absorption and emission spectra were measured by means of a Hitachi 200-10 spectrophotometer and a Hitachi 204-Fluorescence spectrometer, respectively. Quantitative t.l.c. was carried out by means of an Iatroscan TH-10 TLC/FID analyser with silica gel rods.

Solvents for the photoreactions were distilled before use. Commercially available 2-pyridone **(1a)** was used after purification by crystallisation (twice); substituted 2-pyridones were prepared according to reported methods: **(1b)**,[10] b.p. 138—145 °C at 4 mmHg; **(1c)**,[3c] m.p. 139—142 °C; **(1d)**,[3c] m.p. 128—129 °C; **(1e)**,[3c] m.p. 180—184 °C; **(1f)**,[3c] m.p. 160—161 °C; **(1g)**,[3c] m.p. 54—55 °C; **(1h)**,[10] m.p. 57—58 °C; **(1i)**,[11] b.p. 105—110 °C at 5 mmHg; **(1j)**,[12] b.p. 120—121 °C at 8 mmHg.

For preparative photoreactions, 2-pyridones (10^{-3}—10^{-2}M in 1 000 ml solution) were irradiated until the reactants were almost consumed, with a 100 or 400 W high-pressure mercury lamp immersed in the reaction vessel. The photodimers **(3)** were isolated as precipitates after condensation; the photoisomers **(2)** were isolated by column chromatography on silica gel with benzene–ethyl acetate as eluant. The physical properties of the new products are listed in Table 5. The m.p.s and ^{1}H n.m.r., i.r., and u.v. spectra of the known products **(2a)**,[1b] **(2b)**,[1] **(2i)**,[3d] **(3d)**,[3c] **(3e)**,[3c] and **(3g)**[3d] were consistent with those in the literature. The spectral patterns of the new products **(2c—h)** and **(3h)** are essentially similar to those of the known products.

Small-scale (usually 10 ml ampoules) photoreactions for quantitative experiments and quantum yield measurements were carried out with a merry-go-round irradiation apparatus. The 313—334 nm light beams were isolated through a filter of aqueous NiSO$_4$ solution. The consumption of **(1)** was determined from the absorption around 300 nm; the amounts of the photoisomers **(2)** or the molar ratios of **(2)** to **(1)** recovered were determined by means of the TLC/FID analyser after removal of solvent followed by extraction of the residues with methanol.

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