Photorearrangement of Quinoline 1-Oxides: Relevance of Ground and Excited State Basicity and Effect of Heavy Atom Quenchers

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The photoisomerization of some quinoline 1-oxides to 2-quinolones has been studied in aqueous solution as a function of pH. Ground state p*K* values have been measured. There is a decrease in quantum yield of reaction for the protonated molecules. Evidence is given for the setting up of a prototropic equilibrium in the excited state of 4-methoxyquinoline 1-oxide. Fluorescence and reaction quenching by inorganic anions, together with emission spectra at low temperature, showed that the protonated molecule is sensitive to a heavy atom effect. Taken together, the results indicate that the photoisomerization occurs from the n,π^* singlet state of the non-protonated molecule.

AROMATIC amine 1-oxides are known to undergo various kinds of photoreactions: intramolecular rearrangement to hydroxy-derivatives, ring contraction, enlargement or opening, deoxygenation, *etc.* The product distribution varies considerably with the structure of the 1-oxide and the nature of the solvent.[1]

We have previously reported the results obtained for the photoisomerization of the quinoline 1-oxide (QNO) in dilute aqueous solution,[2] where 2-quinolone is the main product. The quantum yield for this photorearrangement was found to decrease with decrease in pH, corresponding to the p*K* value. Low temperature emission spectra showed that the base is only fluorescent, whilst the conjugate acid is phosphorescent as well as fluorescent, with a triplet life-time intermediate between that expected for an n,π^* and a π,π^* triplet state. Triplet sensitization gave no detectable quantity of 2-quinolone. These findings suggest a singlet mechanism, probably involving the unprotonated n,π^* state.

To obtain further information on the photoisomerization mechanism, the study has been extended to some substituted quinoline 1-oxides.

An interesting example of a close association between proton transfer rate and overall photochemical mechanism is afforded by the investigation of the photochemical and -physical behaviour of 4-CH_3O-QNO.

From low temperature phosphorescence measurements, an increase of spin–orbit coupling was observed in the presence of heavy anions. This finding and the fluorescence quenching by the same anions afford further support for the previously proposed suggestion of a singlet mechanism for the photoisomerization.

EXPERIMENTAL

Materials.—The compounds studied were 4-methoxy-, 4-methyl-, 4-chloro-, and 4-bromo-quinoline 1-oxide. They were prepared and purified by standard procedures,[3,4] starting from 4-nitroquinoline 1-oxide, obtained as suggested by Ochiai.[5] Their purity was checked by m.p.s and u.v. absorption spectra.[3b,c,6] The corresponding 2-quinolones were prepared photochemically, following Buchardt.[3b,7] For 4-methoxy-2-quinolone, the preparation was also carried out by a non-photochemical method.[8] The quinolones were purified by chromatography on alumina and their purity checked by m.p.s and u.v. absorption spectra.[7]

Ground state p*K* values were determined by absorption spectrophotometry at 25°; Britton buffers were used from pH 7 to 2 and HCl solutions for the lowest pH values. Solute concentrations were of the order of 5×10^{-5}M. A Sargent PXB pH-meter with a glass electrode was employed. Absorption spectra were registered on an Optica CF4-DR double beam spectrophotometer and a Unicam SP 500/2 single beam spectrophotometer.

Room temperature fluorescence measurements were performed on a CGA DC-3000 and a Hitachi–Perkin-Elmer MPF-3 spectrophotofluorimeters. Fluorescence–pH curves were obtained by excitation at different wavelengths (320—360 nm); readings were made as quickly as possible to avoid photoisomerization of QNOs and the consequent interference of the intense fluorescence of the quinolones.

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[1] G. G. Spence, E. C. Taylor, and O. Buchardt, *Chem. Rev.*, 1970, **70**, 231.

[2] G. Favaro, *Mol. Photochem.*, 1970, **2**, 323.

[3] (*a*) M. Colonna and A. Risaliti, *Ann. Chim.* (*Italy*), 1954, **44**, 1029; (*b*) O. Buchardt, J. Becher, and Chr. Lohse, *Acta Chem. Scand.*, 1965, **19**, 1120; (*c*) T. Okamoto, H. Hayatsu, and Y. Baba, *Chem. and Pharm. Bull.* (*Japan*), 1960, **8**, 892.

[4] E. Ochiai, 'Aromatic Amine Oxides,' Elsevier, London, 1967.

[5] E. Ochiai, *J. Org. Chem.*, 1953, **18**, 534.

[6] M. Colonna, *Boll. sci. Fac. Chim. ind. Bologna*, 1957, **15**, 1.

[7] O. Buchardt, P. L. Kumler, and Chr. Lohse, *Acta Chem. Scand.*, 1969, **23**, 159.

[8] Y. Tanaka, *Bull. Chem. Soc. Japan*, 1956, **29**, 44.

Low temperature luminescence spectra were recorded on the Hitachi–Perkin-Elmer fluorimeter, at liquid nitrogen temperature, in neutral and acidic (H_0 −2) ice matrices. Solute concentrations were of the order of 10^{-5}M.

The quantum yield determinations were run at room temperature (*ca.* 22°), at pH 5.5 and H_0 −1, and, for the 4-methoxy-derivative, in the whole range from pH 7 to H_0 −4. For measurements in acidic medium (pH 2 to H_0 −4) $HClO_4$ solutions were employed. The irradiations were carried out at 313 nm and, in some cases, at 366 nm, using Osram HBO 200 high pressure mercury lamp, with Balzers interference filters. In the concentration range of solute used (10^{-4}M; 4 cm cell path) the incident light was totally absorbed by the QNOs. The extent of the isomerization was followed up to 10—15% conversion in order to minimize the absorbance by the photoproduct 2-quinolone at the irradiation wavelengths. Under these conditions no side product was detected. The analysis was performed by u.v. spectrophotometry in the region 260—360 nm. Ferrioxalate actinometry was employed. The quantum yield values (ϕ), reported in Table 2, were averaged over 3—5 independent runs, with a mean deviation $\leqslant$5%.

RESULTS AND DISCUSSION

Absorption Spectra and Basicities.—Lower energy absorption maxima in water for the basic and acidic forms of quinoline 1-oxides are reported in Table 1.

TABLE 1

Lower energy absorption maxima for substituted quinoline 1-oxides (QNO) in both basic and acidic forms, and basicities in the ground (p*K*) and excited (p*K**) states, in aqueous solution at 25°

Compound	Base $\lambda_{max.}$/nm (log ε)	Acid $\lambda_{max.}$/nm (log ε)	p*K*	p*K* *
QNO	335 (3.78)	318 (3.80)	0.80	−3
4-CH_3-QNO	338 (3.85)	316 (3.84)	1.71	−2.6
4-CH_3O-QNO	333 (3.89)	313 (3.83)	2.63	−1.8
4-Cl-QNO	344 (3.94)	322 (3.90)	0.62	−3.6
4-Br-QNO	344 (3.97)	322 (3.92)	0.38	−3.8

Absorption spectra are very similar, as regards the spectral region and the vibrational structure. This similarity indicates that substitution does not greatly change the electronic configuration. Protonation produces a blue shift, while a lowering of solvent polarity causes a shift to the red (*ca.* 30 nm from water to n-hexane). Although the substituent effect is very small, a red shift can be observed for electron-attracting substituents.

While solvent, protonation and substituent effects are as expected for an n,π^* excited state, the high values of the extinction coefficients indicate rather a π,π^* excited state. This may be related to the occurrence of highly polar structures in the ground state, implying stronger electrostatic interactions with the solvent than in the excited π,π^* state. Thus, a blue shift for the π,π^* transition can take place in polar solvents. The absorption spectra of QNOs can, therefore, be considered to be intermolecular charge transfer in character.[4] However, a low energy n,π^* transition may be submerged in the long wavelength tail of the much more intense π,π^* one.

Before considering the experimental results on the photochemical behaviour of these molecules, attention should be drawn to the basicity values reported in Table 1.

The effect of substituent on the p*K* is of the order expected, as shown in Figure 1 where the corresponding Hammett-type plot has good linearity (correlation coefficient *R* 0.995). In Figure 1, p*K* values for 2-CH_3-QNO (1.47) and 4-NO_2-QNO (−1.46) are also included, together with the value from the literature[9] for 4-CN-QNO. The substituent constants used, σ_{PyNO}, are those determined by Nelson for pyridine 1-oxides.[10] The slope of the plot, 2.2, is very close to that reported for pyridine 1-oxides (2.1),[11] indicating the same electronic transmission in the pyridine and quinoline rings. The σ_{PyNO} value for the *ortho* position has been calculated by Nelson's procedure, using the pK_a of 2-methylpyridine 1-oxide reported in ref. 4.

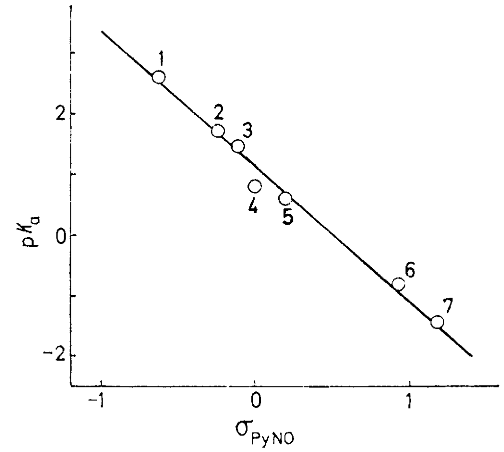

FIGURE 1 Correlation of p*K* with σ_{PyNO} for some substituted quinoline 1-oxides: 1, 4-CH_3O; 2, 4-CH_3; 3, 2-CH_3; 4, 4-H; 5, 4-Cl; 6, 4-CN; 7, 4-NO_2

Approximate values for the acidity constants in the first excited singlet state (p*K**) were determined by the Förster cycle from spectroscopically measured energy levels. Only absorption spectra were used for this calculation (except for 4-CH_3O-QNO), due to the lack of reliable fluorescence data. In fact, the high photoreactivity and very low fluorescence quantum yields do not allow the emission spectra to be recorded, since the intense emissions of the photoproduced quinolones mask those of the QNOs. The calculated p*K** values indicate a decrease of basicity in the excited state (Δp*K* *ca.* 4).

Proton transfer in the excited state may be an important factor in determining the course and the yield of a photochemical reaction. However, when the proton transfer rate in the excited state is low, the ground state equilibrium determines the photochemical behaviour.

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[9] J. H. Nelson, L. C. Nathan, and R. O. Ragsdale, *Inorg. Chem.*, 1968, **7**, 1840.

[10] J. H. Nelson, R. G. Garvey, and R. O. Ragsdale, *J. Heterocyclic Chem.*, 1967, **4**, 591.

[11] H. H. Jaffé and G. O. Doak, *J. Amer. Chem. Soc.*, 1955, **77**, 4441.

This investigation of the effect of pH on the photochemical rearrangement of QNOs to quinolones affords an interesting example of how a change in substituent can effect the proton transfer rate and therefore the overall quantum yield.

Photorearrangement Quantum Yields.—The experimental quantum yields (ϕ) for the photoisomerization are reported in Table 2 at two pH values, where either the basic form (pH 5.5), or the acidic form (H_0—1), only are present in the ground state, as inferred from the pK values in Table 1.

TABLE 2

Experimental quantum yield values for substituted quinoline 1-oxides (QNO) in their acidic and basic forms

	ϕ	
Compound	Base	Acid
QNO	0.24	0.02
4-CH_3-QNO	0.23	0.04
4-CH_3O-QNO	0.28	0.20
4-Cl-QNO	0.22	0.02
4-Br-QNO	0.20	

Quantum yields for the bases are very similar to one another. However, the small differences observed appear to indicate that the reaction is favoured by increasing the electron density at the reaction centre. On the other hand, if the reaction, as we believe, proceeds from a singlet excited state, the largest difference observed for 4-Br-QNO may be related to an increase in the intersystem crossing rate by the heavy atom effect.

The trend of the photoisomerization quantum yield with the pH is similar to that observed for the unsubstituted compound,[2] that is, the quantum yield decreases with decreasing pH, with the maximum change corresponding to the ground state pK.

4-*Methoxyquinoline* 1-*Oxide*.—Particular attention should be drawn to the behaviour of the methoxy-derivative in acidic solution, which is different from that of the other compounds. While a drop to very low quantum yield is generally observed at H_0 —1, for 4-CH_3O-QNO only a small decrease was found at the pH corresponding to the ground state pK, the quantum yield remaining high (0.2) in acidic medium.

For QNO it was previously proposed that the reactive state was the unprotonated excited singlet,[2] considering the effect of pH and the absence of photosensitization by triplet donors. Given that pK* in the excited state (—2.4) is lower than in the ground state (0.8), the appearance of appreciable re-equilibration in the excited state by re-establishing the reactive base would hinder any drastic reduction of the quantum yield.

On the other hand, the behaviour of 4-CH_3O-QNO suggests that for this compound partial proton release can occur before isomerization, in solutions of pH lower than the ground state pK. Therefore, a more detailed investigation was carried out, extending the quantum yield and fluorescence measurements down to H_0 —4. This investigation required a preliminary analysis of the effect of ionic strength on the photoreaction. It was found that this effect depends on the nature of the anions, in the acidic solutions, but is entirely negligible in neutral solutions. At H_0 —1, the reaction is quenched by Br^-, less by Cl^-, whilst ClO_4^- ions are inefficient as quenchers. Therefore, $HClO_4$ solutions were used in the acidic region. The quantum yields for the disappearance of 4-CH_3O-QNO are plotted in Figure 2 from pH 7.4 to H_0 —4. Due to the fairly intense fluorescence emission from both the acidic and basic forms, it was possible to study the fluorimetric behaviour of 4-CH_3O-QNO as a function of pH. The results, plotted in Figure 2, were obtained by excitation at 320 nm and following the emission intensity at 420 nm. At this excitation wavelength both basic and acidic forms have the same extinction coefficient, while at 420 nm emission from acid prevails due to its higher quantum yield. The first inflection point corresponds to the ground state pK, while from the second inflection point a pK* of —1.5 can be obtained for the first excited singlet state, in fairly good agreement with that calculated by the Förster cycle (—1.8), also taking into account the effect of the ionic strength, which should somewhat enhance the experimental value. However, it must be underlined that evaluation of pK* from the mid-point of the fluorescence titration curve does not give reliable values when the lifetimes of the protonated and unprotonated excited states are very different.[12]

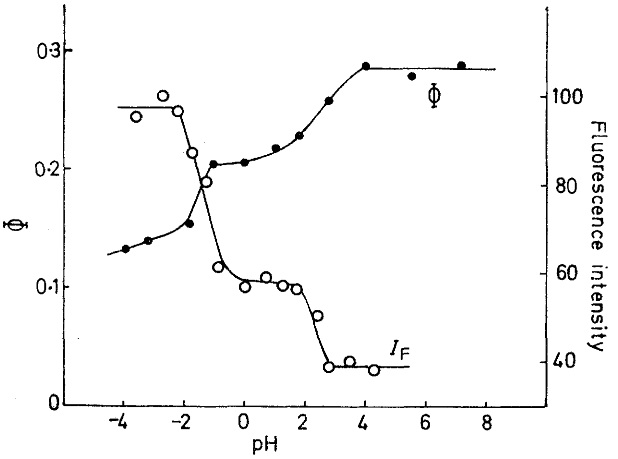

FIGURE 2 Photoisomerization quantum yields (Φ; ●) and fluorescence intensities (I_F; $\lambda_{exc.}$ 320 nm; λ_{emis} 420 nm; ○) of 4-CH_3O-QNO as a function of pH

A comparison between photoreaction quantum yield and fluorescence intensity, both as a function of pH, leads us to the conclusion that 4-CH_3O-QNO, when irradiated in acidic solution, undergoes rapid deprotonation [equilibrium (1)] in the first excited singlet state

$$4\text{-}CH_3O\text{-}QNOH^{+*} + H_2O \rightleftharpoons 4\text{-}CH_3O\text{-}QNO^{*} + H_3O^{+} \quad (1)$$

before rearranging. As long as the irradiation is performed on the basic form (pH >3.5), photoisomerization occurs with a quantum yield very near to those found for the other QNO-derivatives. When the acidic

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[12] (*a*) A. R. Watkins, *J.C.S. Faraday I*, 1972, 28; (*b*) D. M. Rayner and P. A. H. Wyatt, *J.C.S. Faraday II*, 1974, 945.

form is 100% in the ground state, the fast proton release in the excited state partially renews the base, the percentage of which (*ca.* 70%) accounts for the quantum yield in this pH range. The approximate calculation of the equilibrated base was performed assuming the excited protonated form to be unreactive, as was found for the other derivatives. For 4-CH_3O-QNO, the photoisomerization limiting yield of acidic form cannot be obtained, since the course of the reaction changes in very acidic solution ($H_0 < pK^*$), where the spectra show that the photoproduct is no longer 4-methoxy-2-quinolone. Nevertheless, the coupling of the second inflection in the ϕ and I_F against H_0 curves is still significant, since it indicates a close association between the photoreactivity and proton transfer process in the excited state.

Heavy Atom Effect.—We previously reported that phosphorescence emission from protonated QNO occurs in H_2O–HCl matrices.[2] A more careful investigation of the luminescence behaviour at low temperature, extended also to substituted QNOs, showed that the occurrence of phosphorescence from the acidic forms can be related to the heavy atom effect of the anion. In fact, the phosphorescence to fluorescence intensity ratio (I_P/I_F) noticeably increases by using HBr instead of HCl as acidifying agent, whilst it is vanishingly low with $HClO_4$. Figure 3 presents the emission spectra of 4-CH_3O-QNO in $HClO_4$(1), HCl(2), and HBr(3) at the same H_0 value (−2), normalized on the fluorescence maximum. The observed phosphorescence to fluorescence intensity ratios (evaluated approximately from the intensities read at the emission maxima) are in the order: $<10^{-2}$(1), 0.2(2), 3(3). Although these ratios are probably under-estimated since the spectra were not corrected, they at least give a qualitative information of the external heavy atom effect. Similar results were obtained for the other derivatives. Triplet energies of $QNOH^+$, evaluated in HBr solution, are reported in Table 3. The effect of the substituent on the triplet energies, as well as the magnitude of the triplet–singlet energy gaps (4 000—8 000 cm^{-1}) give no precise indication on the nature of the triplet state. In fact, the effect of substituent is that expected for an n,π^* state, but the bromine derivative does not fit this trend, and, moreover, the triplet–singlet energy gaps are intermediate between those expected for n,π^* and π,π^* states.[13]

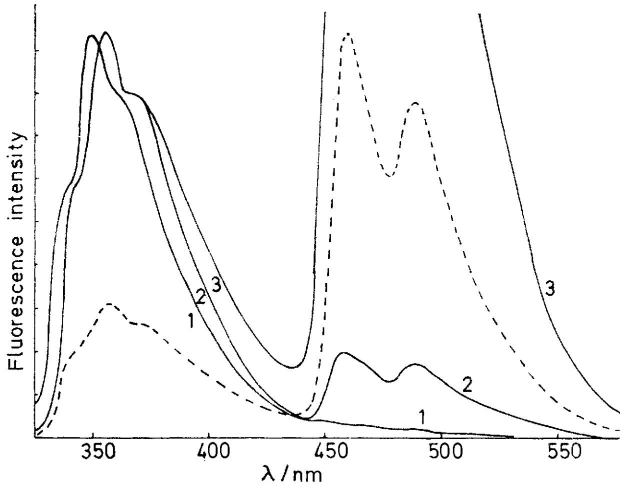

FIGURE 3 Uncorrected emission spectra of 4-CH_3O-QNO in acidic solutions (H_0—2) at 77 K: 1, $HClO_4$; 2, HCl; 3, HBr. The emissions are normalized on the fluorescence band maximum. Broken line refers to emission from HBr solution when instrumental sensitivity is reduced to 1/3

TABLE 3

Triplet energies for protonated quinoline 1-oxides ($QNOH^+$), measured in HBr–water matrix at 77 K

Compound	E_T/kcal mol^{-1}
$QNOH^+$	58.5
4-CH_3-$QNOH^+$	59.5
4-CH_3O-$QNOH^+$	62.0
4-Cl-$QNOH^+$	57.0
4-Br-$QNOH^+$	62.0

Interestingly, 4-Br-QNO exhibits a fairly intense phosphorescence emission also in $HClO_4$ solution (I_P/I_F *ca.* 0.2), showing that the phosphorescence of $QNOH^+$ is also sensitive to the internal heavy atom effect.

An internal, as well as external, heavy atom effect has been taken as a diagnostic test for the nature of the excited state, since it is expected to be high for π,π^* states and low or altogether negligible for the n,π^* states.[13]

The behaviour of the protonated QNOs resembles that of molecules having low-lying π,π^* states. Since neither phosphorescence emission, nor fluorescence quenching have been observed for the bases with Br^- or Cl^- in the solvent environment and phosphorescence was undetectable in neutral solution for the bromine-derivative too, it can be suggested that low-lying n,π^* and π,π^* states invert their positions on protonation. This is reasonable since, as the proton-donating ability of the solvent increases, the n,π^* states should shift considerably to the blue. Therefore, the decrease in quantum yield with decrease in pH may be interpreted as due to the replacement of the reactive n,π^* state of the base with the unreactive π,π^* state for the acid as the lowest one.

The effect of the heavy atom can be checked at room temperature also, for 4-CH_3O-QNO, since this compound presents a particularly favourable situation where simultaneous quenching of photoreaction and fluorescence by inorganic anions can be observed in acidic solution. The photoreaction and fluorescence quenching, both not observed with ClO_4^- anions, run parallel in the presence of Br^-, with a Stern–Volmer slope of 1.2. With Cl^- as quencher, the slopes are very low and difficult to evaluate; however, the quenching effect is still present.

Fluorescence quenching by inorganic anions can be

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[13] S. P. McGlynn, T. Azumi, and M. Kinoshita, 'Molecular Spectroscopy of the Triplet State,' Prentice-Hall, Englewood Cliffs, 1969.

explained by assuming the operation of two mechanisms: (1) electron transfer to the fluorescent species by inorganic anions, or (2) an external heavy atom effect, in which the inorganic anion increases the population of the triplet state *via* spin–orbit coupling.[14]

The increase in phosphorescence does not allow the two mechanisms to be distinguished, since it can be due to both a ' normal ' heavy atom effect or to induced intersystem crossing by the complex formation.

Conclusions.—That fluorescence and photoisomerization quantum yields of $4\text{-CH}_3\text{O-QNOH}^+$ are affected to the same extent by inorganic anions is not sufficient evidence to sustain the conclusion that the reaction occurs in the fluorescent state. However, considered together with the absence of triplet sensitization, quenching effects and phosphorescence enhancement by inorganic anions leave no doubt that the singlet state is responsible for the photorearrangement. Moreover, since the protonated excited molecule is practically unreactive, the quenching of reaction by inorganic anions arises from competition between the crossing to the triplet state and proton releasing process, yielding the isomerizable basic species.

The results of this work support the previously proposed suggestion that a singlet mechanism is responsible for the isomerization of QNOs to 2-quinolones in aqueous solution. The heavy atom effect indicates that the probable lowest excited state is an n,π^* state for the bases and a π,π^* one for the acidic forms. Thus, we can conclude that only the n,π^* state is isomerizable.

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[14] R. Beer, K. M. Davis, and R. Hodgson, *Chem. Comm.*, 1970, 840.