

PHOTOCHEMISTRY OF 2- AND 4-BENZOYLPYRIDINE *N*-OXIDES

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Summary

Deoxygenation to the corresponding pyridine is the main process in the irradiation of 2-benzoylpyridine *N*-oxide (1) and the 4-isomer (2), and in the case of *N*-oxide 1 is accompanied by minor isomerization to 2-hydroxyphenyl 2-pyridylketone. The results of experiments on the solvent and oxygen effect and those for sensitization support the operation of a triplet mechanism for the deoxygenation process. The ordering of the excited states in these molecules and the relevance of the present results in the general framework of *N*-oxide photochemistry are discussed.

1. Introduction

After some initial discussion, there is now general agreement that the photorearrangement of heterocyclic *N*-oxides is a singlet state reaction [1, 2]. As for photodeoxygenation to the corresponding base, which is often but not always observed as a minor process besides rearrangement, opinions are less uniform. There is some indication that deoxygenation is a triplet reaction, *e.g.* triplet sensitization of deoxygenation, not rearrangement, has been reported in a few cases [3, 4]. In other cases, however, there is evidence that both processes originate from the same excited state, and deoxygenation involves some "oxidizing" species formed as an intermediate during the rearrangement, such as an oxaziridine, an "oxene" or a diradical [5 - 7]. In other instances, there has been speculation on the multiplicity of the reactive excited state on the basis of the effect of dissolved oxygen on these reactions. The effect is adverse to deoxygenation in some cases [8, 9], but is favourable [10] in other cases and is not probatory *per se*.

The mechanism of this reaction is interesting, and more so because photochemical oxygen transfer from *N*-oxides has been taken as a model for some biochemical oxidations [6], although in most cases deoxygenation remains a minor pathway unless good oxygen acceptors are present [4, 5, 11]. Furthermore, the spectroscopic evidence for the identification of the triplet is scarce. We reasoned that a way of obtaining more revealing evidence would be to "force" the *N*-oxides into the triplet manifold.

With this aim, we investigated the photochemistry of 2- and 4-benzoylpyridine *N*-oxides (1 and 2).

2. Experimental details

The *N*-oxides 1 and 2 were prepared by reaction of the corresponding pyridines with peracetic acid [12] and purified by repeated recrystallization.

Preparative irradiations were carried out on about 10^{-2} M solutions of the *N*-oxides by means of a Hanau TNN 20 W low pressure mercury arc. After consumption of 50% - 80% of the starting material, the solution was evaporated and chromatographed on silica gel, eluting with cyclohexane-ethyl acetate-chloroform mixtures. Apart from the pyridines and products arising from their further reaction, the only product isolated from 1 was 2-hydroxyphenyl 2-pyridinyl ketone (4). This compound was obtained as colourless needles (melting point, 53 - 54 °C) from cyclohexane. Analysis gave the following results. Found, C 72.53%, H 4.61%, N 6.89%; calculated for $C_{12}H_9NO_2$, C 72.35%, H 4.55%, N 7.03%. NMR, δ 6.9 (t, 1H), 7.07 (d, 1H), 7.4 - 7.6 (m, 2H), 7.9 - 8.2 (m, 3H), 8.75 (d, 1H). IR, 1640 and 1585 cm^{-1} . UV (EtOH), 271 nm ($\log \epsilon = 4.18$), 345 nm (3.65), no change with dilute acids; in the presence of bases 265 nm (4.17), 393 nm (3.88). Synthesis of this compound has been previously reported [13].

Irradiations for quantum yield measurements were carried out on about 10^{-3} M solutions of *N*-oxides in spectrophotometric cuvettes on an optical bench fitted with a low pressure mercury arc or a high pressure Osram 200 W mercury arc with a suitable interference filter. The reaction was followed by absorption spectroscopy and HPLC (Waters instrument, μ -Corasil column, cyclohexane-ethyl acetate mixture as above). The light flux was determined by ferrioxalate actinometry (about 10^{-7} einsteins $min^{-1} cm^{-2}$).

Deaeration was effected either by flushing with purified nitrogen or by repeated freeze-pump-thaw cycles.

Absorption spectra were determined by means of a Cary 19 spectrophotometer and luminescence spectra were recorded by means of an Aminco-Bowman MPF instrument with a phosphorescence attachment when appropriate.

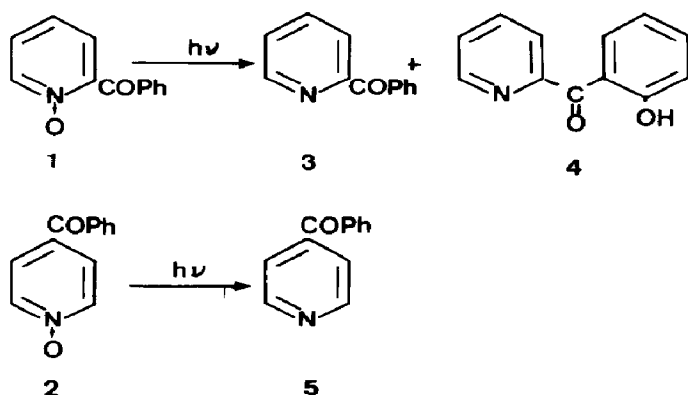
3. Results and discussion

Preparative irradiation (Table 1, Scheme 1) of 1 in benzene, ethanol and water, followed by chromatographic separation, yields the corresponding pyridine (3) and a crystalline compound isomeric with the starting material which was identified as 4 on the basis of its analytic and spectroscopic properties (see Section 2). Similar irradiation of 2 mainly yields 4-benzoylpyridine (5). Under these conditions the material balance is low,

TABLE 1

Preparative results from the irradiation of *N*-oxides 1 and 2

Starting material	Solvent	Product (yield %)
1	Benzene	3 (15), 4 (20)
1	Ethanol	3 (22), 4 (11)
2	Benzene	5 (32)
2	Ethanol	5 (32)
2	Water	5 (10)



Scheme 1.

owing to the formation of tars and small amounts of minor products. Low conversion (20% or below) experiments and high performance liquid chromatography (HPLC) determination clearly show that the pyridines (3 and 5) are the primary products (about 70% yield of 3 from 1 and about 80% yield of 5 from 2), and that they are later converted to complex mixtures. Separate irradiation of the pyridines in fact yields similar mixtures. This is expected in view of the photolability of these compounds, which is a known phenomenon, although not yet completely accounted for as far as product isolation is concerned [14].

Of the two processes observed for *N*-oxide 1, oxygen migration to the neighbouring benzene ring has a precedent in the formation of 2-hydroxyphenyl-2-pyridylmethane from 2-benzylpyridine *N*-oxide [15] and might be explained through the formation of an intermediate six-membered ring (6).

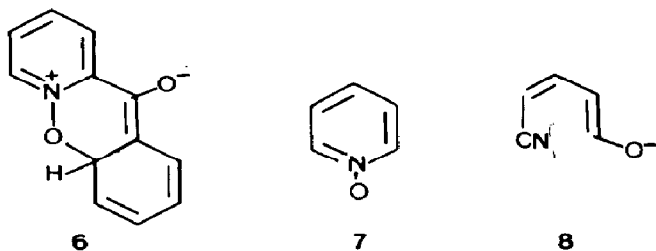


TABLE 2

Quantum yield for the photochemical reaction (low conversion) of *N*-oxides 1, 2 and 7

	1		2		7
	<i>N</i> ₂	<i>Air</i>	<i>N</i> ₂	<i>Air</i>	<i>Air</i>
Cyclohexane	0.022	0.02	0.068	0.035	0.31
Ethanol	0.011	0.011	0.21	0.013	0.2
Water	0.005	0.0045	0.01	0.003	0.2

TABLE 3

Absorption spectra for *N*-oxides 1 and 2

Substrate	Solvent	λ_{\max} (nm) (log ϵ)
1	Cyclohexane	304 (sh, 3.72), 255 (4.25)
1	Ethanol	258 (4.27)
1	Water	258 (4.28)
2	Cyclohexane	342 (sh, 4.16), 333 (4.24), 255 (3.93), 236 (4.12)
2	Ethanol	304 (4.25), 228 (3.97)
2	Water	293 (4.13), 220 (3.97)

As for the deoxygenation process, this is much more efficient than usually observed. The parent pyridine *N*-oxide (7) undergoes ring cleavage, yielding the anion 8 in basic media and tars in neutral media, and pyridine is virtually not formed [16]. As for substituted pyridine *N*-oxides, deoxygenation is limited to several per cent, with a few exceptions (23% from 2-cyanopyridine *N*-oxide [17]). Furthermore, in the present case the efficiency of the photodeoxygenation clearly follows the trend of the hydrogen-donating ability of the solvents, and as far as *N*-oxide 2 is concerned is strongly decreased by dissolved oxygen (by a factor of 2 - 15, a much larger effect than that observed in the cases mentioned above).

A further difference is observed in the quantum yields of reaction for these compounds (Table 2). Values between 0.003 and 0.03 are obtained, reaching 0.21 only with *N*-oxide 2 in degassed ethanol, in sharp contrast to the value observed for unsubstituted pyridine *N*-oxide (Table 2) and in general for other *N*-oxides, which typically ranges from 0.2 to 0.3 [1].

As for spectroscopic evidence, the absorption spectrum of the 2-benzoyl *N*-oxide 1 does not greatly differ from that of the corresponding pyridine (3). An $n\pi^*$ absorption is revealed by a shoulder at 304 nm in cyclohexane and disappears under the strong absorption at about 260 nm in polar solvents (Table 3). The spectrum of the 4-benzoyl *N*-oxides is red shifted with respect to the pyridines and to *N*-oxide 1, as here the N \rightarrow O group does not hinder the coplanarity of the molecule. In this case the lower energy band is intense and undergoes about a 50 nm shift in going from water to cyclohexane (see Fig. 1). It is probably more appropriate here to speak of an internal charge transfer state rather than an $n\pi^*$ absorption,

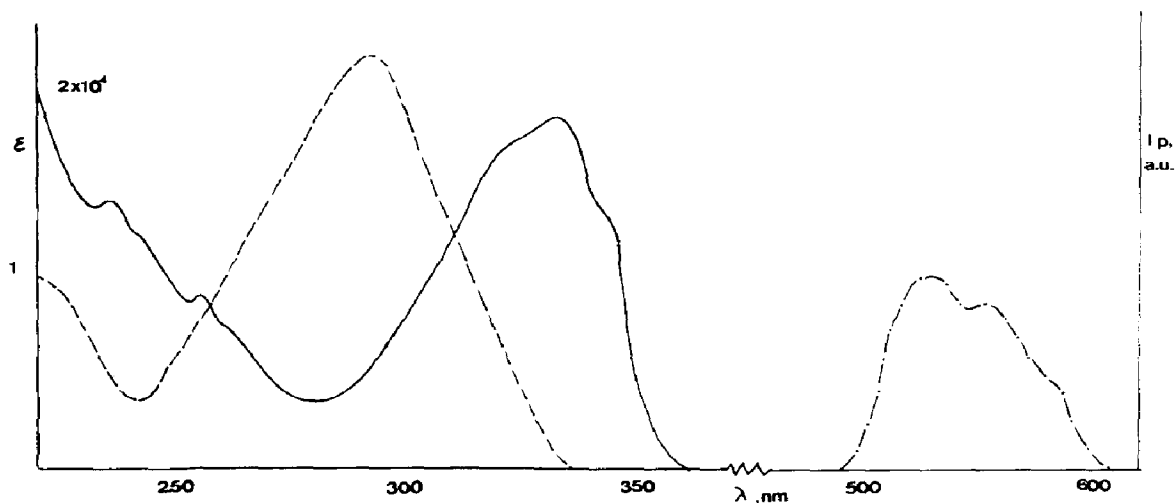
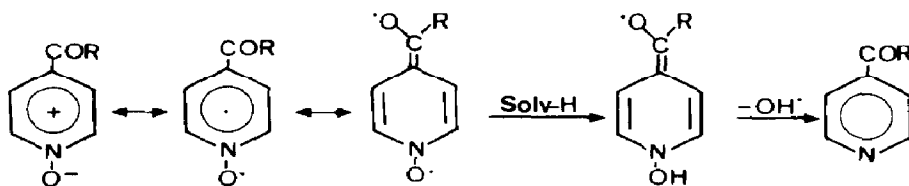


Fig. 1. Electronic spectrum of 2 in cyclohexane (—) and in water (---), and uncorrected phosphorescence spectrum in ether-pentane-alcohol at 77 K, $\lambda_{\text{ex}} = 315$ nm (— · —) (the intensity is less than 1% of that of 4-benzoylpyridine under similar conditions).

analogously to the case of 4-aminobenzophenone and its derivatives. The greater importance of zwitterionic mesomeric formulae (see Scheme 2) in the ground state causes the observed solvent effect.



Scheme 2.

No fluorescence is detected from either *N*-oxide, but a weak phosphorescence is observed in the case of compound 2 at 77 K in ether-pentane-ethanol glass (onset at 503 nm, 56.8 kcal mol⁻¹). The emission has rudimentary fine structure, in contrast with the strong and structured emission from the corresponding pyridines 3 and 5. Phosphorescence from *N*-oxides had been previously reported only for isoquinoline *N*-oxide [18], while a weak electron paramagnetic resonance signal had been reported for the quinoline *N*-oxide triplet state [19].

Sensitization experiments were carried out, and they showed that compound 2 was efficiently deoxygenated when irradiated in the presence of diacetyl (9, light absorbed by the latter). Conclusions from the experiments in ethanol are not unambiguous, as 9 is consumed under these conditions and the possibility of chemical sensitization remains. In cyclohexane there is clear indication for triplet energy transfer, as 9 does not react and its phosphorescence (not its fluorescence) is completely quenched by 2.

It is apparent from the present results that the benzophenone chromophore promotes efficient intersystem crossing to the triplet states of *N*-oxides 1 and 2. Ring cleavage or other singlet state processes are no longer observed, and thus their efficiency has been reduced by at least two orders of magnitude. This is in accord with the idea that k_{isc} is near to that for benzophenone (10^{11} s^{-1}) and that intersystem crossing competes with the singlet state chemistry (k_r is legitimately expected to be about 10^9 s^{-1} by comparison with isoquinoline *N*-oxide [20]). The analogy with sensitized experiments and the influence of oxygen and the solvent suggest that the triplet state is also responsible for the reactions observed on direct irradiation. Both the observed reaction and the phosphorescence characteristics show that excitation is not localized on the C=O chromophore, but indicate that it imparts radical character to the N → O group. This causes both intramolecular attack on the phenyl ring and hydrogen abstraction from the solvent (not as efficient as observed with triplet benzophenone, probably owing to a much lower lifetime).

In conclusion, this work supports both the notion that there is a triplet pathway to deoxygenation for *N*-oxides (although of course there might be a singlet pathway in different cases) and the generalization that triplet reactions are unimportant for *N*-oxides (or at least for pyridine and azanaphthalene *N*-oxides, the situation being somewhat different for higher members of the series [1]) as intersystem crossing is generally slow in comparison with the high rate of reaction of the singlet excited state. There are exceptions to this generalization, and the presently considered benzoylpyridine *N*-oxides do in fact show behaviour completely different from that of the related *N*-oxides.

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