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THE FORMATION OF INDOLE DERIVATIVES IN THE PHOTOLYSIS OF QUINOLINE N-OXIDES.[x]

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The photochemically induced formation of N-acetyl-2-hydroxy-2,3-dihydroindoles (XII, $R^1 = CH_3$) in tautomeric equilibrium with the corresponding oxo-compounds (XI, $R^1 = CH_3$), from a series of 2-methylquinoline N-oxides (V), has recently been described (1,2). We wish to report that a similar reaction is also found in the photolysis of quinoline N-oxides without substituents in the 2-position.

The quinoline N-oxide hydrates (I), dissolved in benzene or ether were irradiated (Hanovia Q-81 or Q-700, Pyrex filter) until no more starting material could be detected by

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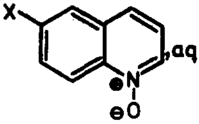
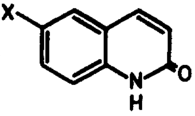
[x] This paper is no. VI in the series (Photochemical Studies").

thin-layer chromatography (Table 1).



I



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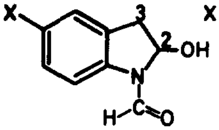
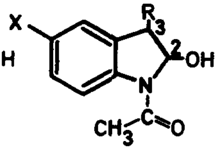


III



IV

I-IIIa. X = H

I-IIIb. X = CH_3

I-IIIc. X = OCH_3

IVa. R = H, X = H

IVb. R = CH_3, X = H

IVc. R = H, X = OCH_3

Table 1.

Irradiation of Quinoline N-Oxides.

Starting material	Solvent	Major products isolated[a]	
Ia, $2H_2O$	Ether	IIa (30%)	IIIa (50%)
Ib, 1 1/4 H_2O	Ether	IIb (30%)	IIIb (33%)
Ic, $2H_2O$	Benzene	IIc (45%)	IIIc (11%)

[a] In most photolyses, one or more further compounds were isolated in minor quantities.

The carbostyrils (II)[x], which precipitated during irradiation, were isolated by filtration and the indole derivatives (III) were isolated by preparative layer chromatography of the filtrates, after evaporation of the solvents.

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[x] The infrared spectra of the carbostyrils were identical with the infrared spectra of authentic samples.

The N-formyl-2-hydroxy-2,3-dihydroindoles (III) were identified by elemental analysis (Table 2), and by the similarity of their ultraviolet spectra with those of the previously described N-acetyl-2-hydroxy-2,3-dihydroindoles (IV) (Table 3). The infrared spectra are also in good agreement with the assigned structures. They show the expected OH absorption in the region 3210-3370 cm^{-1}, and the expected amide I band in the region 1640-1670 cm^{-1} (Table 3).

TABLE 2.

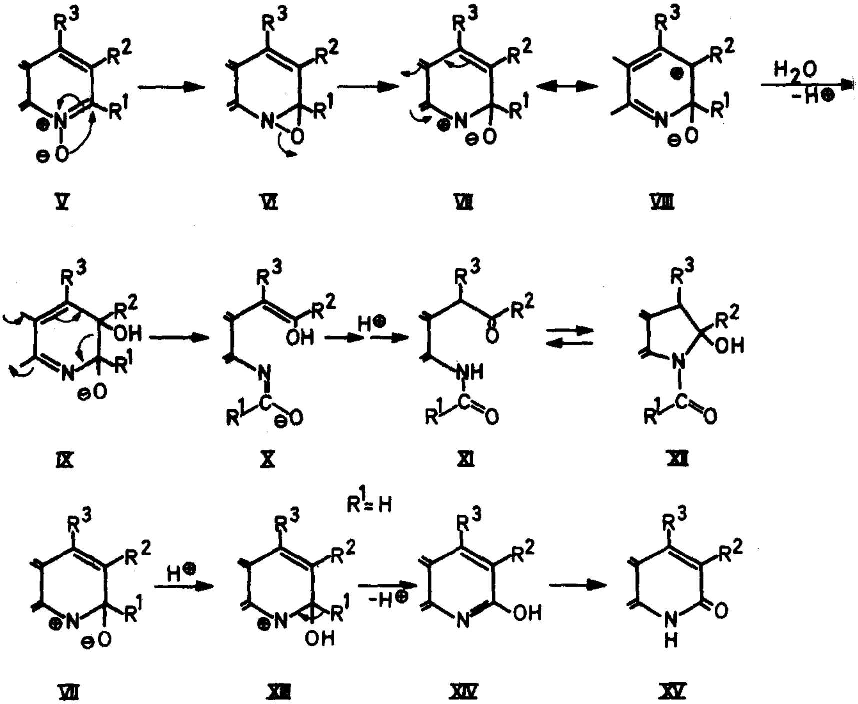
Elemental Analysis and Melting Points.

Compound	M.p.	% C Found	% C Calc.	% H Found	% H Calc.	% N Found.	% N Calc.
IIIa	113-16°	66.05	66.24	5.33	5.56	8.66	8.56
IIIb	108-9°	67.80	67.78	6.10	6.26	7.93	7.91
IIIc	151-52°	62.35	62.13	5.79	5.74	7.43	7.25

The nuclear magnetic resonance spectra support the assigned structures (Table 4). However, superimposed on the pattern from the N-formyl-2-hydroxy-2,3-dihydroindoles is found another pattern, the intensity of which is ca. 2-10 % of the main pattern. The reason for the occurrence of this extra pattern is not yet clearly understood.

From Table 4, it is seen that the nuclear magnetic resonance signals from the aliphatic ring protons in the presently described N-formyl compounds compares very well with the spectra of the previously described N-acetyl compounds (1,2).

The following reaction mechanism is suggested for the formation of the two main products:



The formation of oxaziridines (VI) in the photolysis of quinoline N-oxides has been found in some cases (3), and it seems reasonable to anticipate these substances as the preliminary products in the present photolyses. The next step is thought to be a heterolytic cleavage of VI, possibly photochemically induced, to form the dipolar ion VII-VIII. In non polar solvents, this ion is rapidly attacked by water, with formation of IX, which rearranges to X. Protonization of X with subsequent tautomerization account for the formation of XI and XII. If R^2 is a methyl group, XI is the more stable while R^2 = H makes XII the preferred form (2). Some evidence for an equilibrium between the two forms have been found (2).

TABLE 3.

Ultraviolet Spectra in 96% EtOH. Infrared Spectra in KBr.

Compound	λmax mμ logε	λmax mμ logε	λmax mμ logε	C=O cm^{-1}	OH cm^{-1}
IIIa	248 4.13	278 3.61	287 3.60	1665	3215
IIIb	253 4.16	286 3.58	293 3.58	1670	3210
IIIc	257 4.12	294 3.58	303sh 3.51	1675	3355
IVa	248 4.14	279 3.55	285 3.48	1640	3355
IVb	248 4.19	278 3.56	285 3.51	1645	3365
IVc	254 4.24	293 3.58	303sh 3.47	1640	3270

If the irradiations are performed in solvents like ethanol or water, the better solvating effect of these stabilize the ions VII-VIII and XIII, thus facilitating the formation

TABLE 4.

Nuclear Magnetic Resonance Spectra [a]

Compound	$\mathrm{N{-}\overset{\overset{O}{\|}}{C}{-}H}$	H(2)	$H_A(3)$	$H_B(3)$
IIIa^b	1.29τ	Doublet 4.05τ J = 7 cps	Doublet of doublets 6.50τ J_1= 7 cps, J_2= 17 cps	Doublet 7.05τ J = 17 cps
IVa^b		Doublet 4.16τ J = 7 cps	Doublet of doublets 6.62τ J_1= 7 cps, J_2= 17 cps	Doublet 7.15τ J = 17 cps
IIIb^c	1.40τ	Doublet^d 4.18τ J = 7 cps	Doublet of doublets^e 6.60τ J_1= 7 cps, J_2= 17 cps	Doublet 7.18τ J = 17 cps
IIc^c	1.33τ	Doublet^f 4.18τ J = 7 cps	Doublet of doublets 6.60τ J_1= 7 cps, J_2= 17 cps	Doublet 7.20τ J = 17 cps
IVc^c		Doublet^f 4.18τ J = 7 cps	Doublet of doublets 6.62τ J_1= 7 cps, J_2= 17 cps	Doublet 7.18τ J = 17 cps

a. Solvent used was DMSOd_6.

b. 100 Mc/sec with TMS as external reference.

c. 60 Mc/sec with TMS as internal reference.

d. Each peak in this doublet was further split to a partly resolved doublet with J = 2 cps.

e. Partly obscured by impurity (?).

f. Poorly resolved.

of XV. The photoinduced rearrangements of 2-methylquinoline *N*-oxide to 3-methylcarbostyril (4) and of 2,4-dimethylquinoline *N*-oxide to 3,4-dimethylcarbostyril (5) in aqueous solution can also be explained by assuming the formation of VII-VIII (5). The poor yield of IIIc is in accordance with the suggested mechanism. The CH_3O-group will stabilize the ions VII-VIII and XIII by direct conjugation. This will give an increased yield of IIc, and retard the formation of IIIc.

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