Photochemical Studies

V. The Photochemistry of Some 2-Methyl Substituted Quinoline N-Oxides

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The photolysis of five 2-methylquinoline N-oxides have been investigated. Irradiation of solutions of the N-oxides or their hydrates in ether or benzene containing water yielded in each case as the main product either the expected N-acetyl-2-hydroxy-2,3-dihydroindoles (II) or the tautomeric oxo-compounds (III). Nuclear magnetic resonance spectroscopic data indicates the existence of an equilibrium between the ring structure II and the open structure III. In each photolysis was detected as a minor component the parent quinoline, and in four cases an oxo-compound with less carbon atoms than the starting material. Minor amounts of some other compounds were also found.

In a recent communication,[1] we described the photochemical conversion of 2-methylquinoline N-oxide (Ia) dihydrate to a mixture of N-acetyl-2-hydroxy-2,3-dihydroindole (IIa), N-acetylindole (VIa) and 2-methylquinoline (IVa), with IIa as the main product.

Apparently no simple derivatives of II with a hydrogen atom in the 3-position are known and it would probably be difficult to prepare such compounds by other methods due to their instability (*i.e.* loss of water) towards acids and heating as well as their sensitivity towards bases.

Thus, it seemed of interest to examine this photochemical reaction further, both with regard to its preparative value and its mechanism.

IRRADIATIONS

By repeating the photolysis of Ia hydrate in ether or benzene solution, we found the expected IIa, IVa, and VIa. Furthermore small amounts of 3-methylcarbostyril (VIIIa) and *o*-acetamidobenzaldehyde (Va) were isolated. Thin-layer chromatography (TLC) of the crude reaction product revealed the existence of several other compounds in minor amounts.

When a potassium bromide pellet of Ia hydrate was irradiated, it was found by infrared spectroscopy that impure IIa was formed.[2] This led us to irradiate Ia hydrate in the solid form to prepare IIa, but this method gave a poor yield.

The photolysis of 2,3-dimethylquinoline *N*-oxide (Ib) in ether containing some water gave a mixture of products. These were separated by preparative layer chromatography (PLC). The main fraction was a crystalline compound which was identified as *o*-acetamidophenylacetone (IIIb). Small amounts of 2,3-dimethylquinoline (IVb) and *o*-acetamidobenzaldehyde (Va) were also found.

The irradiation of 2,4-dimethylquinoline *N*-oxide (Ic) in benzene containing water yielded an oil which was separated by column chromatography into skatole (VIIc), *N*-acetylskatole (VIc), *o*-acetamidoacetophenone (Vc) and, as the main product, *N*-acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (IIc). Furthermore, a small amount of 3,4-dimethylcarbostyril (VIIIc) was isolated, and 2,4-dimethylquinoline (IVc) was detected by TLC.

The photolysis of 2,3,4-trimethylquinoline *N*-oxide (Id) in ether containing water gave, after evaporation of the solvent, an oil which was separated by PLC into four crystalline compounds. These were identified as 2,3,4-trimethylquinoline (IVd), *o*-acetamidoacetophenone (Vc), and as the major product 3-(*o*-acetamidophenyl)-2-butanone (IIId). The fourth compound was not identified.

Photolysis of 2-methyl-6-methoxyquinoline *N*-oxide (Ie) hydrate in benzene and separation of the reaction product by PLC yielded two crystalline fractions, one identified as *N*-acetyl-2-hydroxy-5-methoxy-2,3-dihydroindole (IIe), the other as the parent quinoline (IVe).
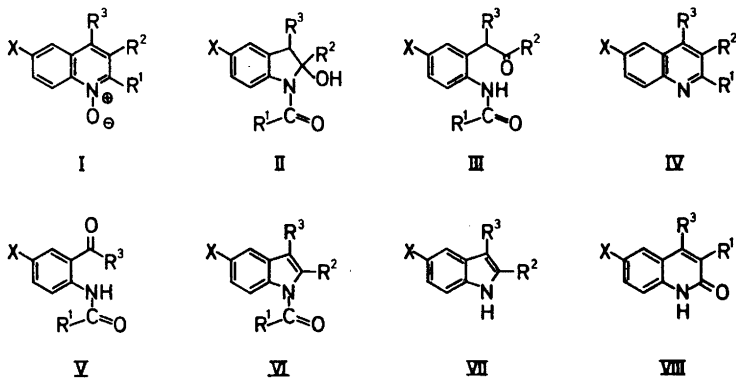
a : R^1=CH$_3$, R^2=R^3=X=H

b : R^1=R^2=CH$_3$,R^3=X=H

c : R^1=R^3=CH$_3$,R^2=X=H

d : R^1=R^2=R^3=CH$_3$,X=H

e : R^1=CH$_3$,R^2=R^3=H,X=OCH$_3$

IDENTIFICATION OF PRODUCTS

The identification of IIa by chemical and spectroscopical methods has already been described,[1] however, without the experimental details which are given in this paper.

The new compounds, IIIb, IIc, IIId, and IIe, are assigned their structures on the evidence of their elemental analysis and on their spectral data.

A. Ultraviolet spectra (Table 1): The ultraviolet spectra of IIa, IIc and IIe are compared with the spectra of 3,4-dihydrocarbostyril and *N*-methyl-3,4-dihydrocarbostyril.[3] This clearly demonstrates that the conjugation in IIa, IIc, and IIe is diminished compared to the starting materials, the spectra of which are also seen in Table 1.

The ultraviolet spectra of IIIb and IIId are quite different from those of the starting materials as well as from those of IIa, IIc, and IIe.

Table 1. Long wavelength ultraviolet absorption spectra. Solvent 96 % ethanol.

Compound	λ_{max} mμ	log ε	λ_{max} mμ	log ε	λ_{max} mμ	log ε
2-Methylquinoline *N*-oxide (Ia)	319	3.99	329sh	3.94		
2,3-Dimethylquinoline *N*-oxide (Ib)	317	3.87	337sh	3.76		
2,4-Dimethylquinoline *N*-oxide (Ic)	323	3.98	333sh	3.93		
2,3,4-Trimethylquinoline *N*-oxide (Id)	323	3.88	338sh	3.81		
2-Methyl-6-methoxyquinoline *N*-oxide (Ie)	315	3.89	333sh	3.63	348sh	3.49
N-Acetyl-2-hydroxy-2,3-dihydroindole (IIa)	248	4.14	279	3.55	285	3.48
N-Acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (IIc)	248	4.19	278	3.56	285	3.51
N-Acetyl-2-hydroxy-5-methoxy-2,3-dihydroindole (IIe)	254	4.24	293	3.58	303sh	3.47
o-Acetamidophenylacetone (IIIb)	227sh	3.79				
3-(*o*-Acetamidophenyl)-2-butanone (IIId)	226	3.80				
2,3-Dihydrocarbostyril	249	4.14	277sh	3.43	287sh	3.07
N-Methyl-2,3-dihydrocarbostyril	250	4.01	275sh	3.37	283sh	2.88

Table 2. Infrared absorptions (in KBr).

Compound	CO cm⁻¹	OH cm⁻¹	NH cm⁻¹
N-Acetyl-2-hydroxy-2,3-dihydroindole (IIa)	1640[a]	3355	
N-Acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (IIc)	1645[a]	3365	
N-Acetyl-2-hydroxy-5-methoxy-2,3-dihydroindole (IIe)	1640[b]	3270	
o-Acetamidophenylacetone (IIIb)	1720 1670		3330
3-(*o*-Acetamidophenyl)-2-butanone (IIId)	1720 1665		3330

[a] Center of two absorptions *ca.* 10 cm⁻¹ apart.
[b] Another weaker absorption is found *ca.* 10 cm⁻¹ towards lower frequencies.

B. Infrared spectra (Table 2): The infrared spectra of the new compounds all show the presence of a strong band in the region 3270—3370 cm⁻¹. This band is assigned to the OH absorption in IIa, IIc and IIe, and to the NH absorption in IIIb and IIId. In the spectra of IIa, IIc, and IIe are found a narrow doublet situated between 1630 cm⁻¹ and 1650 cm⁻¹, the spacing being *ca.* 10 cm⁻¹. These bands are assigned to the amide I absorption. According to Bellamy,[4] the amide I band is usually found near 1690 cm⁻¹ in tertiary amides with a phenyl group on the nitrogen atom. The displacement of the center of the doublets towards lower frequencies is probably due to hydrogen bonding. The occurrence of two close bands may be due to the presence of intramolecular as well as intermolecular hydrogen bonding. In the spectra of IIIb and IIId, one similar band is found near 1660 cm⁻¹ which is also assigned to the amide I absorption, but in these spectra an additional strong band is found near 1720 cm⁻¹ which is assigned to the CO absorption of an open chain ketone.[5]

C. Nuclear magnetic resonance spectra (Table 3): The NMR-spectrum of IIa (Fig. 1) is in excellent agreement with the assigned structure. The aromatic protons were observed at 2.00 τ (1H) and at 2.9 τ (3H). The signal at 2.00 τ, which occurs as a doublet with $J = 8$ cps, must be due to the proton in the 7-position. The shift of 0.9 τ is indicative of the electronegative character of the nitrogen atom and the magnitude of the coupling is typical for that of *ortho*-protons.[6] The signal due to the hydroxyl protons varied with the content of water in the sample. A very dry sample showed coupling between the hydroxyl proton and the aliphatic proton in the 2-position. Under these conditions, the hydroxyl proton appeared as a doublet at 3.5 τ ($J = 7$ cps), while the signal at 4.16 τ appeared as a triplet (the latter spectrum was recorded

Table 3. Nuclear magnetic resonance spectra.^a

Compound	Amide protons	Aromatic protons	Aliphatic methylene and methine protons		Acetyl protons	Other methyl protons
N-Acetyl-2-hydroxy-2,3-dihydroindole (IIa)^b		2.00, d, J=8, 1H; 2.9, m, 3H	4.16, d, J=7, 6.62, dd, J₁=7, J₂=17, 7.15, d, J=17,	1H 1H 1H	7.72, s, 3H	
cis-N-Acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (IIc')^b		1.84, d, J=8, 1H; 2.7, m, 3H	4.18, d, J=7, 6.55, quin, J₁=7, J₂=7,	1H 1H	7.60, s, 3H	8.54, d, J=7, 3H
trans-N-Acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (IIc'')^b		1.84, d, J=8, 1H; 2.7, m, 3H	4.53, s, 6.79, q, J=7,	1H 1H	7.60, s, 3H	8.69, d, J=7, 3H
N-Acetyl-2-hydroxy-5-methoxy-2,3-dihydroindole (IIe)^c		2.09, d, J=8, 1H; 3.19, m, 2H	4.18^d, d, J=7, 6.6^e, dd, J₁=7, J₂=17, 7.18, d, J=17,	1H 1H 1H	7.73, s, 3H	6.28, s, 3H
o-Acetamidophenylacetone (IIIb)^c	0.75, s, 1H	2.8, m, 4H	6.23, s,	2H		7.92, s, 3H; 7.98, s, 3H
3-(o-Acetamidophenyl)-2-butanone (IIId)^c	0.45, s, 1H	2.8, m, 4H	5.93, q, J=7,	1H	7.93, s, 3H	8.05, s, 3H; 8.76, d, J=7, 3H

^{a} All spectra were recorded in hexadeuteriodimethylsulfoxide (DMSOd_6). Chemical shifts are in τ-units, s = singlet, d = doublet, q = quartet, quin = quintet, m = multiplet, dd = doublet of doublets. The absorption from water and hydroxylic protons is excluded.
^{b} Recorded at 100 Mc/s with tetramethylsilane (TMS) as external reference.
^{c} Recorded at 60 Mc/s with TMS as internal reference.
^{d} Poorly resolved.
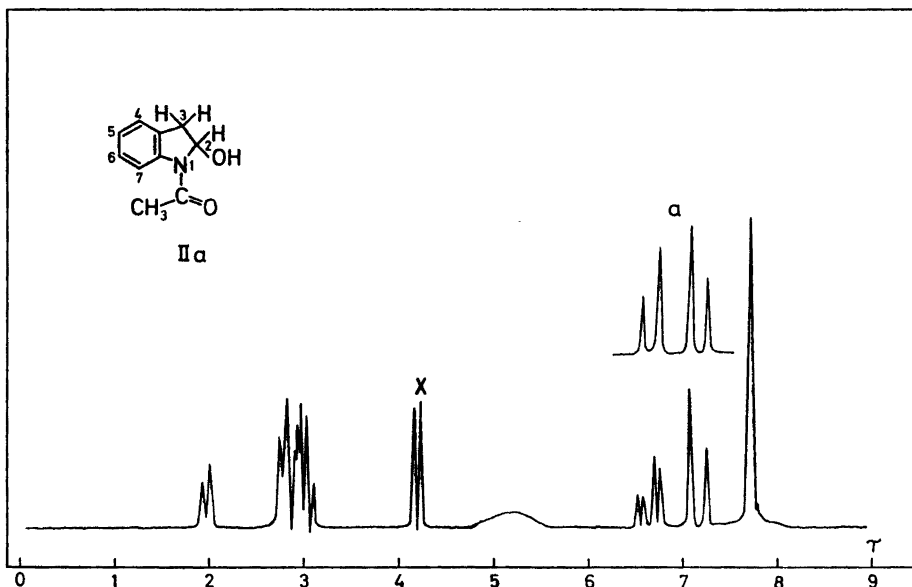^{e} Partly covered by the H_2O—OH signal.

Fig. 1. 100 Mc/s NMR-spectrum of IIa in DMSOd_6 with TMS as external reference (Table 3).
a) Double resonance at X.

at 60 Mc/s). With a small content of water in the sample solution the aliphatic protons appear as a doublet at 4.16 τ ($J = 7$ cps, 1H), a doublet of doublets at 6.62 τ ($J_1 = 7$ cps, $J_2 = 17$ cps, 1H), and a doublet at 7.15 τ ($J = 17$ cps, 1H). This corresponds to an ABX-system, with $J_{AB} = 17$ cps, $J_{AX} = 7$ cps and $J_{BX} = 0$. The magnitude of the coupling constants is in agreement with theory, the geminal coupling constant being 17 cps,* the vicinal coupling constants 7 cps and 0 cps, respectively. A coupling constant of 7 cps corresponds to an angle of approximately 20°, the coupling constant 0 cps to an angle of approximately 80° or 100° between the vicinal protons.[8] The frequencies lie in the expected range.[9] With spin decoupling at X, the geminal protons appear as an AB-system (Fig. 1).

The 60 Mc/s NMR-spectrum of IIc in hexadeuteriodimethylsulfoxide shows the same pattern as the spectrum of IIa in the aromatic region but the remainder of the spectrum was, at first glance, confusing. It consists of a broad doublet at 4.3 τ and a singlet at 4.6 τ (1H), a multiplet at 6.0—7.2 τ (1H), acetyl protons at 3.70 τ (3H), and a triplet centered at 8.75 τ (3H). The triplet can only be explained as a merging of two doublets of different intensities, since the peak at highest field is more intense than the peak at lowest field.

The recording of this spectrum led to an examination of the sample by TLC, since the spectrum indicated that the sample consisted of more than one compound. The TLC-plate, however, showed only one spot.

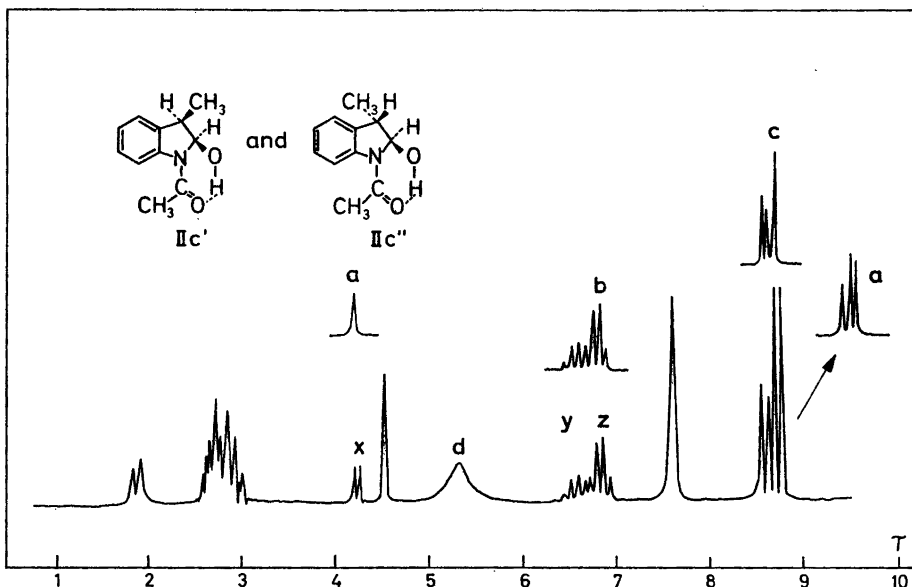
* Only the numerical value is considered here.[7]

Fig. 2. 100 Mc/s NMR-spectrum of IIc in DMSOd_6 with TMS as external reference
(Table 3).

a) Double resonance at Y.
b) » » » X.
c) » » » Z.
d) Signal from H_2O and $-OH$.

By recording at 100 Mc/s (Fig. 2, Table 3), the higher resolving power and the change of pattern enabled us to interpret the spectrum.

We believe that IIc, when dissolved, rapidly forms an equilibrium mixture of the two diastereoisomeric compounds IIc′ and IIc″ with a, possibly very shortlived, open form IIIc as intermediate. The spectrum shows that
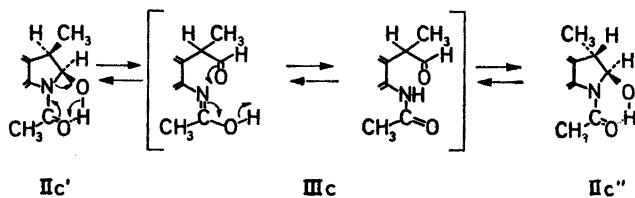
the concentration of IIc″ is approximately twice the concentration of IIc′ in the sample solution. From Fig. 2, it is seen that IIc′ shows a signal at 4.18 τ (doublet, $J = 7$ cps, 1H), at 6.55 τ (quintet, partly obscured, $J_1 = 7$ cps, $J_2 = 7$ cps, 1H) and at 8.54 τ (doublet, $J = 7$ cps, 3H). This is in good agreement with a *cis* configuration for the 2,3-hydrogen atoms. IIc″ shows a signal at 4.53 τ (singlet, 1H), at 6.79 τ (quartet, partly obscured, $J = 7$ cps, 1H)

and at 8.69 τ (doublet, $J = 7$ cps, 3H). This agrees with the postulated *trans* configuration. No sign of two compounds is found in the signal from the aromatic protons, and only one peak is found in the signal from the acetyl protons.

The assignments were confirmed with double resonance experiments (Fig. 2). With spin decoupling at Y, the doublets at 4.18 τ (X) and 8.54 τ coalesced to singlets. By spin decoupling at X, the pattern at Y was simplified to a quartet, partly obscured, while spin decoupling at Z simplified the doublet at 8.69 τ to a singlet.

The NMR-spectrum of IIe showed the expected pattern (Table 3).
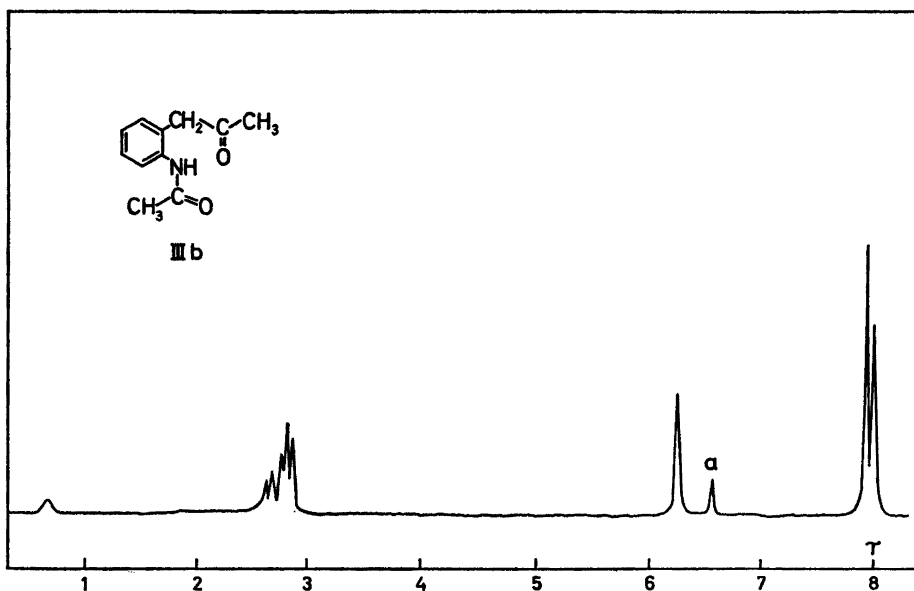

Fig. 3. 60 Mc/s NMR spectrum of IIIb in DMSOd_6 with TMS as internal reference (Table 3). The peak a became more intense on addition of water, while the remainder of the spectrum was unchanged.

The NMR-spectra of IIIb and IIId (Fig. 3—4) indicate that these compounds exist in the open forms in the sample solutions.

D. Chemical evidence: Only compound IIa has been subjected to chemical examination. In our preliminary communication,[1] we described the acid hydrolysis, the pyrolysis, and the oxidative degradation of IIa. The details of this work is described in the experimental section of this paper. Furthermore, we have isolated two compounds from the bromination of an aqueous solution of IIa. The major product is believed to be *N*-acetyl-5-bromo-2-hydroxy-2,3-dihydroindole while the minor product probably is the 5,7-dibromo derivative of IIa.
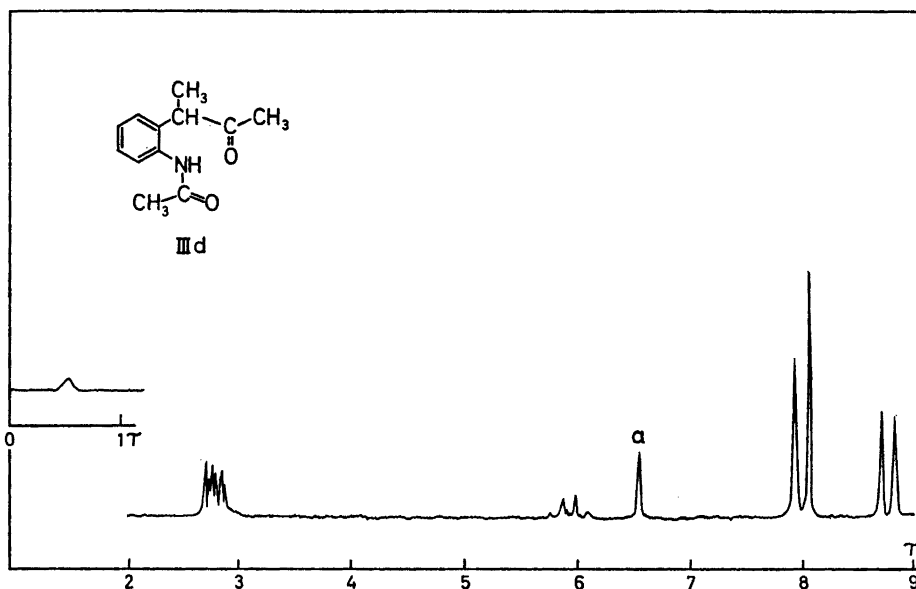
Fig. 4. 60 Mc/s NMR spectrum of IIId in DMSOd_6 with TMS as internal reference (Table 3). The peak a became more intense on addition of water, while the remainder of the spectrum was unchanged.

The minor products (IVa—e, Va, Vc, VIa, VIc, VIIc, VIIIa, VIIIc) which were formed by the irradiations, were identified by comparison with authentic samples (see the experimental section).

E. Further experiments to clarify the ring-chain tautomerism of IIa and IIc: In order to observe any resonance from aldehydic protons, the 60 Mc/s spectra of IIa and IIc in hexadeuteriodimethylsulfoxide were recorded, using the Varian C 1024 computer, in the region 0—1 τ. Nothing was observed even after 1000 scans. It may thus be concluded that the aldehydic form, if present, exists only in very small concentration.

Table 4. Temperature and solvent dependence of the *cis-trans*-ratio of IIc measured by nuclear magnetic resonance spectroscopy.[a]

Solvent	(CD$_3$)$_2$SO					CDCl$_3$[b]	(CD$_3$)$_2$CO
Temp.	25°	35°	50°	75°	100°	25°	25°
cis:trans	1:1.9	1:2.0	1:2.0	1:2.1	1:2.4	1:2.4	1:2.0

[a] The ratio was found by measuring the height of the peaks in the signal from the methyl group at high field (60 Mc/s).
[b] In CDCl$_3$ the signal occurred as two doublets.

It seems improbable, however, that the highly crystalline IIc exists as a 2:1 mixture in the solid form (m.p. 123—124°), and it was not possible by TLC to observe more than one spot. To observe a possible temperature effect on the *cis-trans* ratio of IIc, its NMR-spectrum was recorded at different temperatures. By measuring the intensity of the peaks in the signal from the methyl protons, a slight temperature effect was observed. By recording the spectrum of IIc in different solvents, a similar small change in the intensity ratio was observed (Table 4).

On the evidence given, *vide supra*, it is concluded that compounds with the general formula II exist in equilibrium with the open forms III. Similar ring-chain tautomerizations are known. [10]

II   III
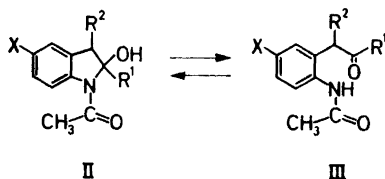
When $R^1 = CH_3$, the open form is the preferred, while when $R^1 = H$, the cyclic form is the preferred.

## DISCUSSION AND SOME PRELIMINARY EXPERIMENTS

Considering the recent paper by Kaneko, Yamada and Ishikawa,[11] describing the formation of oxaziridines by the photolysis of some quinoline *N*-oxides and isoquinoline *N*-oxides, it is reasonable to anticipate the same type of intermediate in the presently considered reactions. A preliminary experiment was performed supporting this contention. When 2,4-dimethylquinoline *N*-oxide (Ic) was photolyzed in benzene solution, under very dry conditions,

I   IX   X   XI

XI   XII   XIII   XIV

XIV   III   II
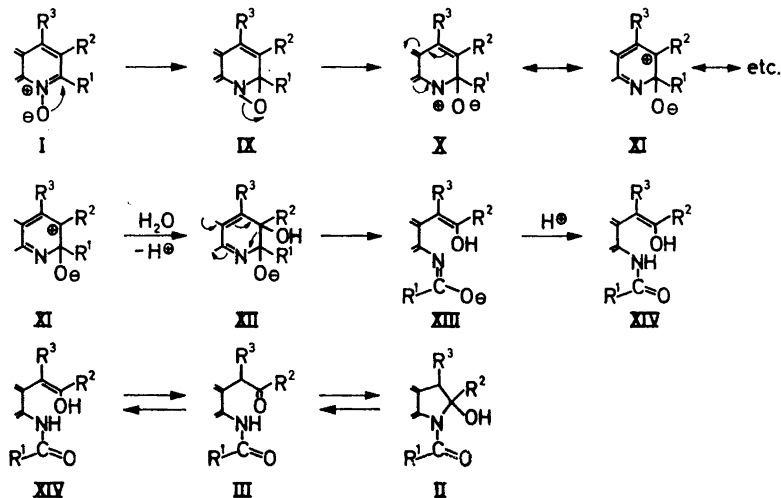
it was found by TLC that only one compound was formed. When the solvent was removed and the oily residue exposed to the atmosphere it quickly decomposed to a mixture of products.*

The oxaziridines are then either further photolyzed, or react thermally or a combination of both take place. A tentative reaction scheme for these degradations is suggested, (see p. 2476).

The oxaziridines (IX), by heterolytic cleavage, form the dipolar intermediate X—XI. In non-polar solvents with only a small content of water, nucleophilic attack of water in the 3-position of XI forms XII. Opening of the ring with subsequent protonization to XIV, followed by tautomerization, account for the formation of the ring-chain tautomers III—II.
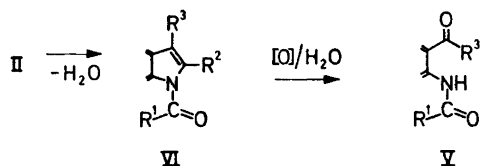
By dehydration, II forms the N-acylindole (VI) very easily, and it is well known[12] that indoles can be oxidized to o-acylaminobenzaldehydes or the corresponding phenones (V). In the described experiments, the irradiated solutions were not flushed with nitrogen to exclude small amounts of oxygen, and at least part of the oxidation may be due to this. However, deoxygenation of the quinoline N-oxides during photolysis always takes place. By irradiating a benzene solution of Ic, with exclusion of oxygen, no sign of the oxidation was observed. If Ic was irradiated in benzene solution under a continuous stream of oxygen, extensive degradation took place. The formation of small amounts of skatole (VIIc) from Ic during irradiation must be due to hydrolysis of initially formed N-acetylskatole (VIc).

By irradiating samples of N-acetylindole under different conditions, no addition of water was noted. This indicates that the N-acylindoles must be formed by dehydration of II.

The formation of isomeric carbostyrils as the major products in the photolysis of quinoline N-oxides in aqueous and alcoholic solutions[2,13-14] could be explained by assuming that, in these solvents, ions are stabilized by solvation. The longer lifetime of the ions enhances the possibility of the rearrangements shown below.
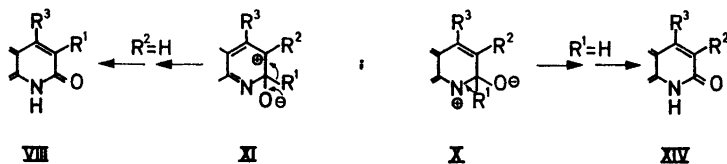
* Attempts to isolate and identify the oxaziridine rings from aryl- and alkylquinoline N-oxides and quinoline N-oxide itself are presently in progress in our laboratory.

By assuming the same ion as intermediate, the formation of N-methyl-carbostyril in the photolysis of IIa in methanolic solution [14] could be rationalized.

It is interesting to note, that Streith and Sigwald [15] have found that pyridine N-oxide and α-picoline N-oxide rearrange to the corresponding 2-formylpyrroles. These results are consistent with the suggested mechanism.
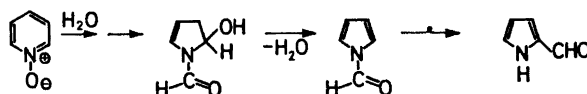
The rearrangement of N-acylpyrroles to 2-acylpyrroles is well known.[16]

EXPERIMENTAL

Microanalyses were carried out in the microanalysis department of this laboratory by Mr. Preben Hansen and his staff.

Melting points (uncorrected) were determined on a Reichert melting point microscope.

Infrared spectra for identification were recorded on a Perkin Elmer "Infracord", infrared spectra for analytical purposes on a Perkin Elmer model 337, grating infrared spectrophotometer. Ultraviolet spectra were recorded on a Perkin Elmer model 137 UV spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian A 60 or a Varian HA 100. Some of the nuclear magnetic resonance spectra were recorded using a time averaging computer, Varian model C 1024, with the A 60 model.

Methods of irradiation. A. The light source was a medium pressure mercury lamp (Hanovia Q-81), equipped with a pyrex cooling mantle, placed in the center of the reaction vessel. Frequently, a brown precipitate, which formed on the surface of the cooling mantle, was removed. B. Here, the irradiations were carried out analogously to method A with the exception that a more powerful lamp was used (Hanovia Q-700). C. The samples to be irradiated (in pyrex flasks) were placed 30—40 cm from the light source (a Hanovia Q-700 equipped with a reflector).

In all experiments, the irradiations were followed by TLC, and irradiation discontinued as soon as no more N-oxide could be detected. The temperature during irradiations varied from 15—25°.

Preparative layer chromatography (PLC). The method described by Halpaap [17] was employed. The plates were 40 × 60 cm. The thickness of the layer (kieselgel PF_{254}, Merck) varied from 1.5 to 2.5 mm. The plates were developed 2—5 times with a mixture of benzene-acetone-ethyl acetate in the ratio 50:10:1. The fractions were isolated by extraction four times with acetone, ethyl acetate, or ethanol.

Thin layer chromatograms (TLC). These were run on 8 × 10 cm plates with a 0.25 mm layer of kieselgel (HF_{254}, Merck). The plates were visualized with UV light or sprayed with Dragendorff's reagent.

Quinolines. IVa, IVc, and IVe were commercially available while IVb was prepared according to Ref. 18 and IVd according to Ref. 19.

Quinoline N-oxides. These were prepared by the method described in a previous paper [2] (Table 5).

Irradiations of 2-methylquinoline N-oxide (Ia) dihydrate. 1. A solution of 2-methylquinoline N-oxide dihydrate (5.00 g) in benzene (4 l), was irradiated for 34 h after method A. The benzene was evaporated at *ca.* 40°, and the resulting brown oil chromatographed on aluminium oxide (300 g). This gave by elution with benzene and benzene-ethyl acetate (4:1) a series of oily fractions which consisted mainly of N-acetylindole (VIa), with 2-methylquinoline (IVa) and several other components in minor amounts. N-Acetylindole was identified by the identity of its infrared spectrum with that from an authentic sample, and IVa was identified by TLC. In a later experiment, we were able to identify one of the minor components as *o*-acetamidobenzaldehyde (Va) by the identity of its

Table 5. Quinoline N-oxides.

Compound	Yield %	M.p.	% C		% H		% N	
			Found	Calc.	Found	Calc.	Found	Calc.
2,3-Dimethylquinoline N-oxide (Ib)	70	130—31°	76.08	76.27	6.35	6.40	8.34	8.09
2,4-Dimethylquinoline N-oxide (Ic)	74	118—20°	76.35	76.27	6.47	6.40	8.15	8.09
2,3,4-Trimethylquinoline N-oxide (Id)	95	168—70°	76.81	76.97	6.74	7.00	7.33	7.48
2-Methyl-6-methoxyquinoline N-oxide (Ie), 1 ¼ H₂O.	76	154—56°	62.41	62.42	6.31	6.48	6.70	6.62

infrared spectrum with that from an authentic sample.[20] Elution with ethyl acetate yielded a crystalline fraction (3.00 g, 66 %) of N-acetyl-2-hydroxy-2,3-dihydroindole (IIa). Recrystallization of IIa from ethanol-water, with subsequent sublimation at 150°/0.05 torr raised the melting point to 157—159°. For elemental analysis and m.w., see Ref. 1. In a later experiment, it was found that further elution with ethanol yielded 3-methylcarbostyril (VIIIa) (identified by the identity of its infrared spectrum with that from an authentic sample [3]).

2. 2-Methylquinoline N-oxide dihydrate (0.50 g), finely powdered, was placed in a 500 ml pyrex flask. The N-oxide was continuously stirred with a magnetic stirrer, and irradiated after method C for 20 h. From the dark semicrystalline reaction mixture was obtained 50 mg IIa by sublimation at 0.5 torr.

Irradiation of 2,3-dimethylquinoline N-oxide (Ib). A solution of Ib (673 mg) in benzene containing water (1.0 l) was irradiated after method A for 14 h. The benzene was removed *in vacuo* and the resulting oil, which showed four spots by TLC, separated by PLC. This chromatogram yielded: Fraction 1, 32 mg of an oil. This non-polar fraction was found in most experiments when the normal grade pure commercial benzene was used as solvent and consists of high molecular hydrocarbons. Fraction 2, 111 mg, consisted of o-acetamidobenzaldehyde (Va), identified by infrared spectroscopy. Fraction 3, 83 mg oil, the infrared spectrum of which showed absorption from Va, with some characteristic lines from 2,3-dimethylquinoline (IVb) superimposed. Fraction 4, 528 mg (71 %) of crystalline o-acetamidophenylacetone (IIIb). After several recrystallizations from benzene, the melting point of IIIb was raised to 135—137°. (Found: C 68.75; H 6.70; N 7.53. Calc. for C₁₁H₁₃NO₂: C 69.09; H 6.85; N 7.33).

Irradiation of 2,4-dimethylquinoline N-oxide (Ic). 2,4-Dimethylquinoline N-oxide (7.00 g) dissolved in benzene saturated with water (10 l) was irradiated for 18 h according to method B. The solvent was evaporated and the remaining oil chromatographed on aluminium oxide (300 g) (Table 6).

o-Acetamidoacetophenone (Vc) was identified by its elemental analysis (Found: C 67.85; H 6.22; N 7.92. M.w. (mass spectrometric) 177. Calc. for C₁₀H₁₁NO₂: C 67.78; H 6.26; N 7.91. M.w. 177), and the identity of its infrared spectrum with that of an authentic sample.[21] The total yield of crude Vc was 1.42 g (20 %).

N-Acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (IIc) was identified by its infrared, ultraviolet and nuclear magnetic resonance spectra, *vide supra*, and its elemental analysis. Recrystallization of IIc, once from ethyl acetate and once from benzene, raised the melting point to 123—124°. (Found: C 68.85; H 6.67; N 7.47. Calc. for C₁₁H₁₃NO₂: C 69.09; H 6.85; N 7.33). The total yield of crude IIc was 3.79 g (49 %). By TLC of the crude product, a spot corresponding to 2,4-dimethylquinoline (IVc) was found.

Table 6. Chromatogram of the products from the photolysis of Ic.

Fraction	Eluent	Weight	Compounds
1 — 6	Petroleum ether-benzene	oil *ca.* 0.5 g	High molecular hydrocarbon [a]
7	Benzene	cryst. 230 mg	*o*-Acetamidoacetophenone (Vc)
8	Benzene-ethyl acetate 4:1	oil 670 mg	Vc, Skatole (VIIc), *N*-acetylskatole (VIc) [b]
9 — 13	Benzene-ethyl acetate 4:1	cryst. 920 mg	Vc
14 — 15	Benzene-ethyl acetate 3:2	oil 250 mg	Vc, *N*-Acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (IIc) [c]
16 — 17	Benzene-ethyl acetate 1:4	cryst. 1.54 g	IIc
18 — 23	Ethyl acetate	cryst. 1.60 g	IIc
24 — 25	Ethanol	cryst. 540 mg	IIc
26	Ethanol	oil 630 mg	IIc, 3,4-Dimethylcarbostyril (VIIIc)[d],[e]
27	Ethanol	cryst. 130 mg	VIIIc [e]
28	Ethanol	oil 330 mg	Unidentified products

[a] This fraction was found in most experiments, where commercial benzene was used as solvent.

[b] Rechromatography of fraction 8 showed that it mainly consisted of Vc. The existence of VIc and VIIc was inferred by TLC.

[c] The infrared spectrum of the oil showed lines from Vc, with lines from IIc superimposed.

[d] The infrared spectrum from this oil showed lines from both IIc and VIIIc.

[e] The infrared spectrum from fraction 27 was identical with the infrared spectrum of an authentic sample of 3,4-dimethylcarbostyril.[22]

Irradiation of 2,4-dimethylquinoline N-oxide (Ic), in the absence of oxygen. Benzene, containing water, was flushed with deoxygenated nitrogen for 30 min. A solution of Ic (1.00 g) in the pre-deoxygenated benzene (1.0 l) was irradiated for 8 h after method A, under continuous flushing with deoxygenated nitrogen. After removal of the benzene *in vacuo* the remaining oil was separated by PLC into two major fractions. Fraction 1 consisted of skatole (VIIc) (290 mg) and fraction 2 consisted of *N*-acetyl-2-hydroxy-3-methyl-2,3-dihydroindole (615 mg). One of the minor fractions (5 mg) consisted of 2,4-dimethylquinoline (IVe), but no *o*-acetamidoacetophenone was found.

Irradiation of 2,4-dimethylquinoline N-oxide (Ic) with excess of oxygen. A solution of Ic (1.00 g) in benzene (1.0 l) was irradiated for 8 h after method A. During the irradiation, the solution was continuously flushed with oxygen. TLC on the reaction product revealed that it consisted of a very complicated mixture, which was not further examined.

Irradiation of 2,4-dimethylquinoline N-oxide (Ic) in anhydrous benzene. A solution of Ic (1.00 g) in anhydrous benzene (1.0 l) was irradiated after method C for 48 h. TLC of the reaction mixture showed only one spot. By evaporation of the solvent, an oil remained, which, however, showed five spots by TLC. Attempts to identify the preformed species are in progress.

Irradiation of 2,3,4-trimethylquinoline N-oxide (Id). 2,3,4-Trimethylquinoline *N*-oxide (2.00 g) in benzene, containing water (250 ml), was irradiated for 140 h after method C. The solvent was evaporated, and the remaining yellow oil was separated in six fractions by PLC. Fraction 1, 14 mg impurities from the benzene. Fraction 2, 46 mg oil, unidentified. Fraction 3, 29 mg crystalline material which was identified as *o*-acetamido-acetophenone (Vc) by infrared spectroscopy. Fraction 4, 14 mg crystalline material, not yet identified. Fraction 5, 83 mg crystalline material, was identified as 2,3,4-trimethyl-quinoline (IVd) by infrared spectroscopy. Fraction 6, 400 mg of a yellow oil, was crystallized after several cycles of cooling to *ca.* −60° with subsequent slow warming to room temperature. The latter fraction was recrystallized three times from ether-benzene (the separation of the crystals from the solution required several days at −20°) to give a product with m.p. 76−78°. This was identified as 3-(*o*-acetamidophenyl)-2-butanone (IIId). (Found: C 69.95; H 7.20; N 6.73. Calc. for $C_{12}H_{15}NO_2$: C 70.22; H 7.37; N 6.82). The total yield of IIId was 18 %. In a later experiment IIId was obtained in 65 % yield.

Irradiation of 2-methyl-6-methoxyquinoline N-oxide (Ie), 1 1/4 H_2O. A solution of Ie, 1 1/4 H_2O (700 mg) in ether (1.0 l) was irradiated after method A for 8 h. The solvent was evaporated and the resulting oil separated by PLC into 300 mg 2-methyl-6-methoxy-quinoline (IVe), identified by infrared spectroscopy, and 230 mg (34 %) *N*-acetyl-2-hydroxy-5-methoxy-2,3-dihydroindole (IIe). Recrystallization of IIe two times from benzene raised the m.p. to 138−140°. (Found: C 63.35; H 6.28; N 6.71. Calc. for $C_{11}H_{13}NO_3$: C 63.75; H 6.32; N 6.76).

Irradiation of N-acetylindole (VIa). By irradiating VIa after method A in ether or benzene containing small amounts of water, with subsequent chromatographic analysis, no IIa was detected.

Pyrolysis of IIa. *N*-Acetyl-2-hydroxy-2,3-dihydroindole (IIa) (100 mg) was heated over phosphorus pentoxide at 165° for 3 h. The remaining oil, which showed only one spot by TLC, was identified as *N*-acetylindole by the identity of its infrared spectrum with that of an authentic sample, and by the identity of its mass spectrum with that of *N*-acetylindole.[1]

Hydrolysis of IIa. Compound IIa (404 mg) was treated with 0.4 N hydrochloric acid (100 ml) for 1 h at 80°. The resulting suspension was extracted with ether, the ethereal solution washed five times with water and two times with saturated sodium chloride solution. The ethereal solution was filtered through anhydrous magnesium sulfate and the ether removed by evaporation. The remaining oil (390 mg) was chromatographed on florisil (15 g). This yielded 21 mg of crystalline compound, the infrared spectrum of which was identical with that of authentic indole, some impure oily fractions, and 194 mg pure *N*-acetylindole identified by infrared spectroscopy.

Oxidation of IIa. Compound IIa (300 mg) was dissolved in N sodium hydroxide. To this solution was added potassium permanganate (400 mg) and the reaction mixture stirred for 20 h at room temperature. After being acidified with a slight excess of hydrochloric acid, the solution was extracted with ether (250 ml). The extract was dried over anhydrous magnesium sulfate, filtered, and the ether removed *in vacuo*. This yielded 190 mg colourless crystals which, after several recrystallizations from ethyl acetate, melted at 154−156°. The IR-spectrum of this compound was identical with the IR-spectrum of an authentic sample of *o*-acetamidophenylactic acid.

Preparation of o-acetamidophenylacetic acid. The synthesis of this compound according to the method described by Snida[23] resulted in a very low yield of highly impure product, the infrared spectrum of which, however, was somewhat similar to that of pure *o*-acetamidophenylacetic acid. Pure *o*-acetamidophenylacetic acid (m.p. 155−156°, after solidifying again, the m.p. was 159−161°) was prepared by acetylating *o*-amino-phenylacetic acid with acetic anhydride.[24] (Found: C 62.05; H 5.96; N 7.19. Calc. for $C_{10}H_{11}NO_3$: C 62.16; H 5.74; N 7.25). *o*-Aminophenylacetic acid was prepared from *o*-nitrophenylacetic acid[25] and from oxindole.[26]

Treatment of IIa with bromine. Compound IIa (100 mg) was dissolved in hot water (12 ml). To the 60−70° hot aqueous solution was added aqueous bromine until a slight colour remained. The addition of bromine caused an oil to separate which crystallized on cooling. The crystals were isolated (118 mg). After three recrystallizations from ethanol-water and one from benzene-ethanol, was isolated 52 mg of a compound with m.p. 163−166°. (Found: C 46.81; H 3.98; N 5.70; Br 31.23. Calc. for $C_{10}H_{10}BrNO_2$: C 46.87;

H 3.90; N 5.47; Br 31.25). On the basis of its infrared spectrum which shows an OH absorption at 3400 cm^{-1}, and a C=O absorption at 1645 cm^{-1} and its ultraviolet spectrum which is very similar to that of II (λ_{max}^{EtOH} = 253, 285, 295; log ε = 4.30, 3.67, 3.60) *vide supra*, it is believed to be *N*-acetyl-2-hydroxy-5-bromo-2,3-dihydroindole. In another experiment with 200 mg IIa, was isolated 6 mg of another compound which, after two recrystallizations from ethanol, melted at 189−191°. On the basis of its infrared spectrum which also shows the characteristic OH and C=O absorptions (3300 cm^{-1}, 1655 cm^{-1}), and its ultraviolet spectrum (λ_{max}^{EtOH} = 254, 286, 295; log ε = 4.20, 3.40, 3.25), we infer that it is a dibromo derivative of IIa, *i.e.* *N*-acetyl-2-hydroxy-5,7-dibromo-2,3-dihydroindole.

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