

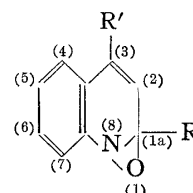
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Three-membered Ring System with Two Hetero Atoms. I.*¹
Synthesis of 1a*H*-Oxazirino[2,3-*a*]quinoline Derivatives.*²

We wish to report the photochemical preparation of three novel compounds, I, II, and III, having 1a*H*-oxazirino[2,3-*a*]quinoline skeleton, which are representative of a new class of heterocyclic compounds.

Irradiation*³ of 4-methyl-2-cyanoquinoline 1-oxide*^{4,1)} (IV) in absolute methanol, using a 100-W Hanovia high pressure mercury lamp as a light source (Pyrex filter was used to eliminate light of wavelength shorter than 300 mμ), followed by removal of solvent under reduced pressure, produced a pale yellow solid. Two products, I, m.p. 66~67.5° (from hexane), C₁₁H₈ON₂, [mol.wt*⁶(found) : 189; UV λ_{max}^{95% EtOH} mμ(log ε) : 239 (4.42), 315 (3.58); IR*⁶ ν_{max}^{KBr} cm⁻¹: 2205 vw, 1658m, 1640m, 1598w, 1485w, 1441m, 1383w, 1367w, 1280~1290w,



1243m, 1207w, 1143s, 1125s, 1080m, 1065m, 1045vw, 1033w, 992m, 950w, 877w, 841w, 800m, 757s] and V, m.p. 97~98° (from methanol), C₁₁H₈N₂, were obtained in 85% and 5% yields after separation by chromatography on silica gel. The minor product (V) was identified with 2-cyanolepidine through mixed melting point determination with the authentic specimen²⁾. The nuclear magnetic resonance (NMR) spectrum*⁷ of the former compound (I) showed absorptions at 2.7~2.8τ (4H, multiplet due to aromatic protons), 3.89τ (1H, quartet due to olefinic proton), and 8.05τ (3H, doublet due to methyl protons). The assignment of each signal is given in Table I. Formula (I) is the only structure consistent with these data. This fact fits well and gives strong support to the postulation that the corresponding oxaziranes may be the intermediates of the photochemical conversion of azanaphthalene N-oxides to the corresponding amides³⁾ and other rearrangement products⁴⁾. The structure of I was not inconsistent with its facile conversion to skatole derivatives. On prolonged boiling in aqueous methanol in nitrogen atmosphere, I produced VI, m.p. 95° (from hexane), C₉H₉N, [UV λ_{max}^{95% EtOH} mμ(log ε) : 224(4.58),

I : R' = CH₃, R = CN
 II : R' = H, R = CN
 III : R' = H, R = phenyl

*¹ This paper forms Part IV of "Studies on the N-Oxides of π-Deficient N-Heteroaromatics" by C. Kaneko. Part III : C. Kaneko, S. Yamada, I. Yokoe : Rept. Res. Inst. Dental Materials, Tokyo Medico-Dental University, **2**, 475 (1963).

*² All melting points were measured by capillary and are uncorrected. Satisfactory analyses were obtained for all the compounds described. All the products, as well as the reaction mixtures, were examined by gas-phase chromatography to check their purity and identity. Gas-phase chromatography was conducted on the following conditions : Apparatus, Shimadzu GC-1B, HID-1; column, 6 mm./150 cm.; 1% SE-30 on Chromosorb-W; column temp., 182.5°; flash heater temp., 240°; N₂ pressure 2 kg. 30 ml./min.; H₂ pressure, 0.8 kg. 35 ml./min. The retention time under the above conditions were as follows : I; 1.13, II; 0.87, III; 4.14, IV; 6.24, V; 1.52, VI; 0.66, VII; 4.04, VIII; 1.49.

*³ Irradiation was continued until N-oxides were no longer detected in the reaction mixture by gas chromatography, and no precautions were taken to avoid the presence of a small amount of air in the irradiated mixture.

*⁴ This N-oxide, m.p. 183~185° (from acetone), C₁₁H₈ON₂, was prepared from 2-cyanolepidine by Ochiai's method.¹⁾ [cf. 1) E. Ochiai : J. Org. Chem., **18**, 534 (1953).]

*⁵ Molecular weights were determined by the Rast method.

*⁶ The letters, w, m, s, and vs, occurring after frequencies indicate the intensity of the absorption as weak, medium, strong, and very strong, respectively, throughout this communication.

*⁷ Nuclear magnetic resonance spectra were all obtained in deuteriochloroform solution on a JNM-3H-60 spectrometer operated at 60 Mc. The chemical shifts are given in τ-unit. The authors are very grateful to Dr. Y. Kawazoe and Miss M. Ōnishi at the National Cancer Center, Tokyo, for taking these spectra.

2) F. Feely, E. M. Beavers : J. Am. Chem. Soc., **81**, 4004 (1959).

3) O. Buchardt, J. Bocher, Chr. Lohse : Acta Chem. Scand., **19**, 1120 (1965), and papers cited therein.

4) M. Ishikawa, S. Yamada, C. Kaneko : This Bulletin, **13**, 747 (1965), and papers cited therein.

283(3.78)] in ca. 50% yield after solvent evaporation and isolation by chromatography on alumina. The infrared and ultraviolet absorption spectra of VI were identical with those of skatole and the mixed melting point determination definitely confirmed their identity. The most plausible formulation of this transformation is shown in Chart 1.

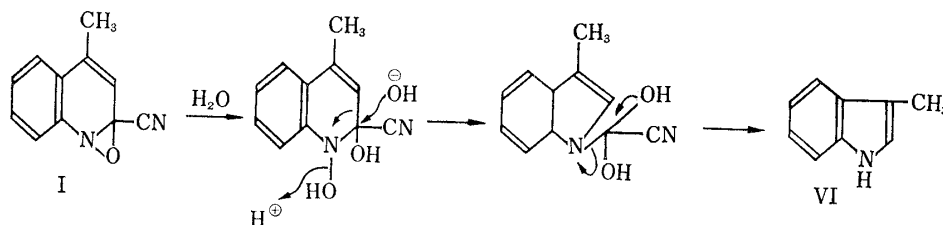


Chart 1.

Lithium aluminum hydride reduction of I in ether gave rise to a basic oil [picrate, m.p. 207~209° (decomp.), C₁₇H₁₇O₇N₅] as a sole product. On treatment of this oil with acetic anhydride, a neutral crystalline compound (VII), m.p. 89~91° (from ether), C₁₃H₁₆ON₂, [UV λ_{max}^{95% EtOH} mμ(log ε): 228(4.34), 292(3.79); IR ν_{max}^{KBr} cm⁻¹: 3315m, 1640s, 1545s, 735m] was obtained in quantitative yield. The similarity of UV spectrum of this compound (VII) with that of skatole indicated that VII should have the indole skeleton. It follows that VII is the monoacetate of N-(2-aminoethyl) skatole. The NMR spectrum*⁷ of VII [2.47τ, broad singlet(1H); 2.79τ, multiplet(4H); 3.19τ, singlet(1H); 5.84τ, triplet(2H); 6.94τ, triplet(2H); 7.70τ, singlet(3H), and 8.19τ, singlet(3H)] fits well with the proposed structure. These experiments confirmed that the direct reduction product was N-(2-aminoethyl) skatole. Two reactions mentioned above seem to demonstrate the utility of these photochemically prepared oxaziranes (I~III) as key intermediates in preparation of indole derivatives from quinoline derivatives.

Though this compound (I) is quite stable in most of the organic solvents in a dark room*⁸, irradiation of methanol solution of I with 253.7 mμ light*⁹ induced an interesting photochemical reaction. Under this condition, I was quantitatively converted to VIII, m.p. 104~106° (from hexane), C₁₀H₈N₂, [mol. wt. (found) 161*⁵; UV λ_{max}^{95% EtOH} mμ(log ε): 226.5 (4.56), 287 (4.24); IR ν_{max}^{KBr} cm⁻¹: 3285m, 2212m, 736m; NMR*⁷ spectrum: 2.3~3.0τ (4H, multiplet), 7.55τ (3H, singlet) and 1.4τ (1H, broad singlet, which disappeared on addition of CH₃OD)]. The structure of this compound (VIII) was elucidated as 2-cyanoskatole through its conversion to 2-carboxyskatole (IX), m.p. 165~167° (from benzene), C₁₀H₉O₂N, by alkaline hydrolysis. Identity of the latter compound with an authentic sample⁵ of IX was assured by mixed melting point determination. The mechanism of this interesting photo-alteration of I, together with those of its related oxaziranes (II, III), will be reported in near future.

Irradiation of 2-cyano⁶- and 2-phenyl-quinoline⁷ 1-oxides under similar conditions with that of IV, followed by similar work-up produced the corresponding oxaziranes, II, m.p. 65~66° (from hexane), C₁₀H₈ON₂, [UV λ_{max}^{95% EtOH} mμ(log ε): 240(4.51), 322(3.56); IR ν_{max}^{KBr} cm⁻¹: 2205vw, 1657m, 1632m, 1593w, 1484w, 1446m, 1382w, 1302w, 1265~1280vw, 1219m, 1208m, 1140s, 1002m, 947w, 919w, 871w, 855w, 833w, 812m, 759s, 706vw] and III, m.p. 67~67.5° (from hexane), C₁₃H₁₁ON, [UV λ_{max}^{95% EtOH} mμ(log ε): 251.5(4.59), 317(3.83); IR ν_{max}^{KBr} cm⁻¹: 1662m, 1630m, 1595w, 1484w, 1446m, 1350w, 1311w, 1278w, 1250m, 1220vw, 1206w,

*⁸ In protic solvents, I and its related oxaziranes are rather unstable, and, in an elevated temperature, slowly changed to other products. The full detail of these reactions will be published separately.

*⁹ The light source was a 6-W low-pressure mercury arc, manufactured by Osawa Denki Co.

5) E. Camps : Ber., **32**, 3228 (1900).

6) J. Druey, H. V. Daeniker : Helv. Chim. Acta, **41**, 2148 (1958).

7) A. Risalti : Ricerca Sci., **24**, 2351 (1954) [Chem. Abst., **49**, 15902 (1955)].

1192m, 1111m, 1041m, 1035m, 1022m, 983w, 929w, 775m, 767w, 750m, 691m] in high yields, together with small amounts of deoxygenated products. Similarity in the UV spectra of I, II, and III strongly suggested the existence of a common chromophore in these three compounds. The NMR spectra of II and III together with the assignments are shown in Table I, and these are consistent with the proposed structures, II and III.

TABLE I. Nuclear Magnetic Resonance Spectra*7,a) of Oxaziranes

Compounds	-CH ₃	Aromatic protons	Olefinic protons	Ratio
I	8.05 ^{b)} J=3	2.65~2.84 ^{c)}	3.89 ^{d)} J=3	3:4:1
II	—	2.75~3.15 ^{c)}	4.07, ^{b)} 4.28 ^{b)} J=6 J=6	4:1:1
III	—	1.8~2.03, ^{c)} 2.5~3.0 ^{c)}	3.72, ^{b)} 4.03 ^{b)} J=6 J=6	2:7:1:1

a) Coupling constants are given in c.p.s.
b) Center of doublet.

c) Multiplet.
d) Center of quartet.

Preliminary studies on these oxazirane compounds (I~III) indicated that these compounds are quite stable either in their solid state or in non-polar solvents, even at elevated temperature. Strong contrast of these oxaziranes derived from aromatic N-oxides with those⁸⁾ derived from aliphatic nitrones is the lack of oxidizing ability of the former compounds. Thus, I to III do not liberate iodine from potassium iodide. Another feature of these compounds is their susceptibility to cationic reagents. So far we have found many interesting reactions of these compounds using a variety of cationic reagents. A detailed study of the chemical reactions of these novel heterocyclic compounds will be reported in near future.

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8) J.S. Splitter, M. Calvin: J. Org. Chem., **30**, 3427 (1965) and references cited therein.

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Autoxidation of Quinoline N-Oxide

In this paper the authors wish to report a new type of reaction that quinoline 1-oxide (I) is autoxidized in the presence of potassium *tert*-butoxide to afford 1-hydroxycarbostyryl (II) and 2,2'-biquinoline (III), accompanied with a mono N-oxide (IV) of III.

When quinoline 1-oxide (I) was heated with an equimolar amount of potassium *tert*-butoxide in *tert*-butanol at 70° for 9 hr. with bubbling of oxygen, three kinds of compounds (II, m.p. 190°, III, m.p. 193° and IV, m.p. 170°) were obtained as the main reaction products in 41%, 34% and 10% yields respectively. In addition to these, carbostyryl (V) was detected in a very poor yield (0.6%), accompanied by the recovery (5%) of the