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# Organic Photochemical Reactions. VII.[1] Photolysis of 1-Benzyl-2-ethylbenzimidazole 3-Oxide

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It is suggested that photolysis of 1-benzyl-2-ethylbenzimidazole 3-oxide (I) involves two different pathways; one goes *via* an oxaziridine intermediate (VI) formed from the excited singlet state; and the other is deoxygenated *via* the excited triplet state, enhanced by the presence of benzophenone or anthraquinone. Deoxygenation of several aromatic *N*-oxides is shown to be effected by anthraquinone.

A number of works dealing with photolysis of aromatic amine N-oxides have been reported recently.[3] Except for simple deoxygenation processes, the photolyses were shown to proceed *via* an oxaziridine intermediate. Recent evidence has suggested that in the primary photochemical reaction of pyridine N-oxides, deoxygenation involves the excited triplet state;[4] whereas reactions *via* the oxaziridine intermediate involve the excited singlet state.[4] In

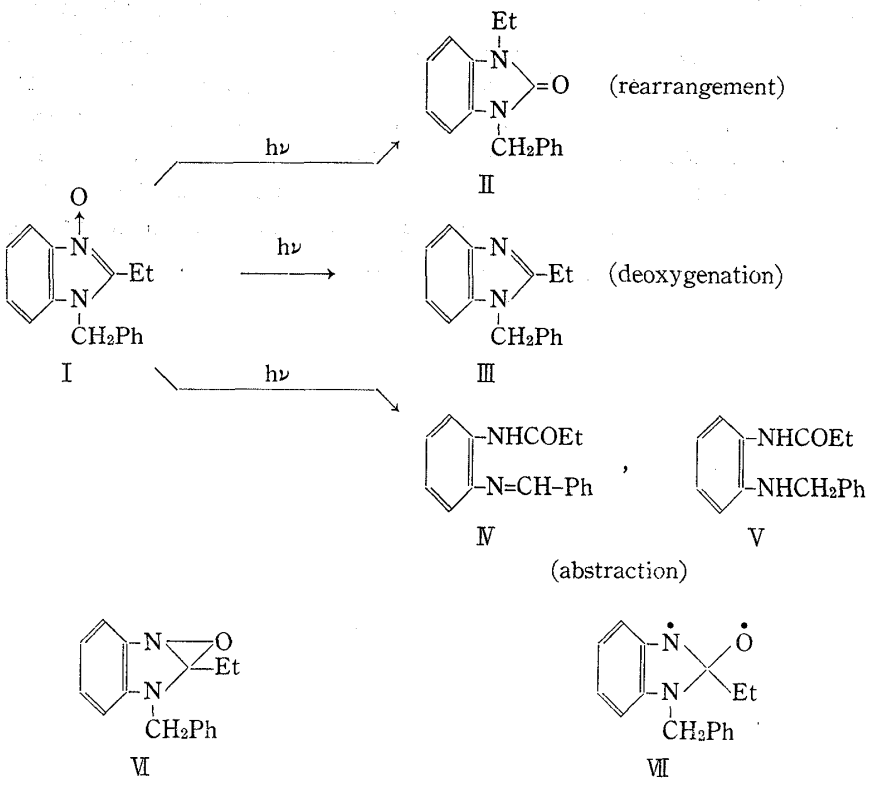


Chart 1

1) Part VI: M. Ogata, H. Matsumoto, and H. Kano, *Tetrahedron*, **25**, 5205 (1969).
2) Location: *Fukushima-ku, Osaka.*
3) C. Kaneko, *J. Synthe. Org. Chem.* (Japan), **1968**, 758.
4) *a*) K. Koyano and I. Tanaka, *J. Phys. Chem.*, **69**, 2545 (1965); *b*) T. Hata, Presented at Symposium on Photochemistry, Japan, in Sendai, October 1968; *c*) P.L. Kumler and O. Buchardt, *Chem. Commun.*, **1968**, 1321.

view of these communications, we now report our observation of the phtolysis of benzimidazole N-oxides.

Irradiation of 1-benzyl-2-ethylbenzimidazole 3-oxide (I) in methanol through a pyrex filter gave mainly 1-benzyl-3-ethyl-2-benzimidazolinone (II), together with small amounts of the deoxygenated product (III) and N-benzylidene-N'-propionyl-O-phenylenediamine (IV). Photolysis of I in dioxane under similar conditions gave IV as the major product, accompanied by small amounts of III and N-benzyl-N'-propionyl-O-phenylenediamine (V). At a low temperature (−58°), the photolysis in methanol gave only IV (18.4%), with a 54.8% recovery of I.

The above results are rationalized by assuming that an initially formed oxaziridine intermediate (VI) undergoes ionic rearrangement to II in a protic solvent at room temperature, while in an aprotic solvent, or at a low temperature even in a protic solvent, the N–O bond of VI undergoes homolysis (probably photochemically) to give a biradical (VII), which subsequently rearranges to IV or V through hydrogen abstraction from the benzyl group or from the solvent used. The ionic path may proceed thermally as well as photochemically.

Table I. Photolysis of I in Various Conditions[a)]

| Sensitizer (mol. eq.) ($E_T$ kcal) | Solvent | Product (%) II | III | IV | V | Intensity of fluorescence |
|---|---|---|---|---|---|---|
| — | MeOH | 71.4 | 1.1 | 0.8 | — | standard (100%) |
| Acetophenone (2) (~74) | MeOH | 61.7 | 4.8 | — | — | 62% |
| Benzophenone (2) (~69) | MeOH | 19.8 | 49.4 | — | — | 32% |
| Anthraquinone (0.2) (~62) | MeOH | 4.2 | 79.5 | — | — | 16% |
| Fluorenone (2) (~53) | MeOH | 55.5 | trace | — | — | 43% |
| — | dioxane | — | 4.4 | 41.2 | 2.9 | standard (100%) |
| Anthraquinone (2) (~69) | dioxane | — | 36.1 | 8.8 | 6.2 | 4% |

*a)* at room temperature

In the presence of triplet sensitizers such as anthraquinone or benzophenone, the photochemical deoxygenation was strongly enhanced in both protic and aprotic solvents, whereas the presence of acetophenone or fluorenone had no effect (Table I). Since the ultraviolet (UV) spectrum of a solution of I and anthraquinone showed an additive absorption-curve for the individual components, absorption by a I-anthraquinone complex cannot be significant. Moreover, the fact that the presence of acetophenone, which has the highest triplet energy of the four ketones, does not affect the deoxygenation, suggests that neither anthraquinone nor benzophenone is acting here as a photosensitizer in the usual sense.

$$\mathrm{I} \xrightarrow{h\nu} \mathrm{I}^{*1}$$

$$\mathrm{I}^{*1} + \text{ketone} \longrightarrow \mathrm{I} + \text{ketone}^{*1}$$

$$\text{ketone}^{*1} \xrightarrow[\text{crossing}]{\text{instersystem}} \text{ketone}^{*3}$$

$$\text{ketone}^{*3} + \mathrm{I} \longrightarrow \text{ketone} + \mathrm{I}^{*3}$$

$$\mathrm{I}^{*3} \longrightarrow \mathrm{III}$$

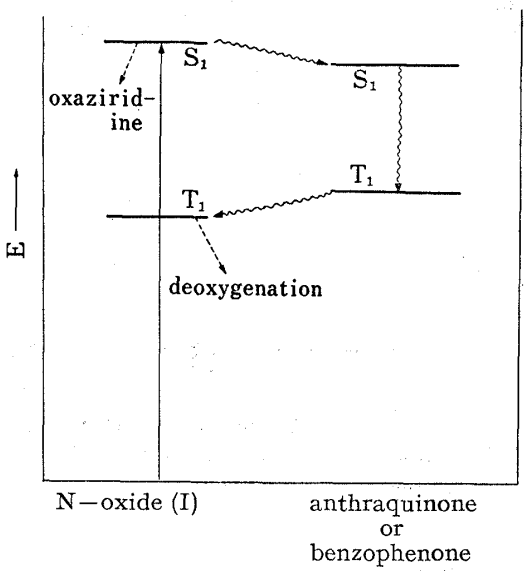


Fig. 1. The Relationships among the Low-lying excited States of N-Oxide (I) and Anthraquinone (Benzophenone) (the double energy transfer)

We propose, therefore, that the deoxygenation reaction effected by anthraquinone or benzophenone involves a double intermolecular energy transfer: the first energy transfer occurs from the excited singlet state of I to the ketones as a singlet excitation, and after intersystem crossing, the triplet state energy of the ketone returns to I as triplet energy.[5]

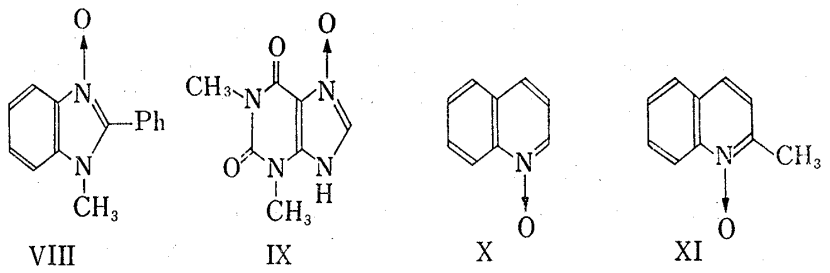


Chart 2

Table II. Deoxygenation of N-Oxides[a]

| N-Oxide | Anthraquinone (mol. eq.) | Yield of deoxygenated amine (%) |
|---|---|---|
| (VIII) | — | trace |
| (VIII) | 0.2 | 22.6 |
| (IX)[7] | — | recovery |
| (IX)[7] | 0.2 | 34.1 |
| (X)[3] | — | 1.9 |
| (X)[3] | 0.1 | 6.6 |
| (XI)[3] | — | 12.9 |
| (XI)[3] | 0.2 | 31.6 |

a) methanol solution at room temperature

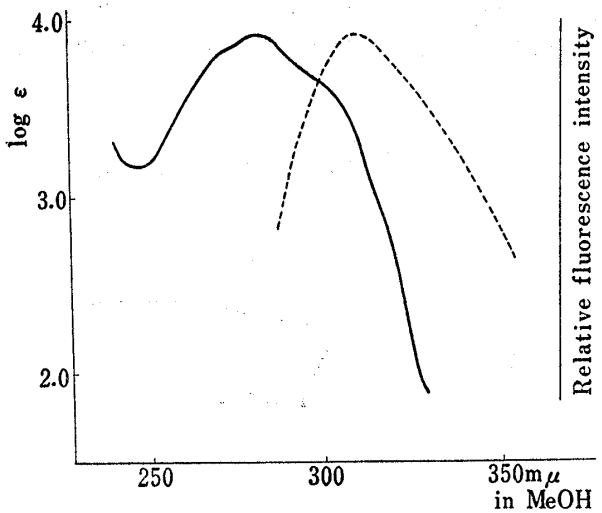


Fig. 2. Ultraviolet Spectra of 1-Benzyl-2-ethylbenzimidazole 3-Oxide (I) (—) and Its Fluoresence (····)

A similar mechanism was proposed by Hammond, *et al.* for the photodimerization of coumarin effected by benzophenone.[6]

Evidence for energy transfer from I*1 to ketone was obtained by the following experiment. Irradiation of a methanol solution of I gave a fluorescence ($\lambda_{max}$ 310 mμ) which was strongly quenched by benzophenone or anthraquinone, as shown in Table I.

Analogous deoxygenation effected by anthraquinone was observed with 1-methyl-2-phenylbenzimidazole 3-oxide(VIII), theophylline 7-oxide[7] (IX), quinoline N-oxide[3] (X), and quinaldine N-oxide[3] (XI). The yield of deoxygenated products are shown in Table II.

5) In the absence of the ketones, the formation of III would involve the following mechanisms: (I)→(I)*1→(I)*3→(III).
6) G.S. Hammond, C.A. Stout, and A.A. Lamola, *J. Am. Chem. Soc.*, **86**, 3103 (1964).
7) H. Goldner, G. Dietz, and E. Carstens, *Ann.*, **691**, 233 (1966).

## Experimental

All melting points were taken on a Kofler hot-stage and are uncorrected. The light source for the photolysis was a high pressure Hg arc lamp with pyrex filter. During irradiation a steady stream of argon was bubbled through the solution.

**N-Benzyl-N-propionyl-O-nitroaniline**——A mixture of N-benzyl-O-nitroaniline (15.0 g) and $(EtCO)_2O$ (15.0 ml) was refluxed for 19 hr. The resulting solution was neutralized with aq. $NH_4OH$, and extracted with $CH_2Cl_2$. The $CH_2Cl_2$ layer was separated, dried over $Na_2SO_4$, and evaporated to give a yellow oil (15.3 g), bp 197—202° (1 mmHg). *Anal.* Calcd. for $C_{16}H_{16}O_3N_2$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.50; H, 5.64; N, 10.05.

**1-Benzyl-2-ethylbenzimidazole 3-Oxide (I)**——A solution of N-benzyl-N-propionyl-O-nitroaniline (15.0 g) in 2% EtOH–HCl (650 ml) was shaken in a $H_2$ stream over Pt ($PtO_2$, 1.5 g), $H_2$ being absorbed within about 35 min. The catalyst was removed by filtration and washed with EtOH. The filtrate was concentrated and the residual oil was neutralized with aq. $K_2CO_3$ solution ($K_2CO_3$, 74.5 g; $H_2O$, 370 ml). The resulting solution was extracted with $CHCl_3$. The $CHCl_3$ layer was dried over $Na_2SO_4$ and evaporated, and AcOEt was added to the residual oil to give colorless crystals (7.9 g). Recrystallization from benzene gave colorless needles, mp 135—136°. *Anal.* Calcd. for $C_{16}H_{16}ON_2$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.19; H, 6.54; N, 10.74.

**1-Benzyl-3-ethyl-2-benzimidazolinone (II)**——A mixture of N-benzyl-O-phenylenediamine[8] (2.84 g) and urea (1.05 g) was heated at 180° for 19 hr. EtOH was added to the residue, and the product was collected by filtration (2.65 g). Recrystallization from EtOH gave 1-benzyl-2-benzimidazolinone, colorless needles (2.22 g, mp 204—207°). A mixture of 1-benzyl-2-benzimidazolinone (1.0 g) in aq. NaOH (10%, 3 ml) and EtJ (20 ml) was refluxed for 3 hr. The resulting solution was concentrated, and neutralized with 6N HCl. The separated oil was extracted with ether. The ether solution was dried over $Na_2SO_4$ and evaporated, and the residual oil was chromatographed on neutral alumina to give II, 301 mg, (mp 73—76°). This was recrystallized from isopropyl ether to colorless prisms, mp 83—84°. *Anal.* Calcd. for $C_{16}H_{16}ON_2$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.43; H, 6.43; N, 11.05.

**1-Benzyl-2-ethylbenzimidazole (III)**——A solution of N-benzyl-N-propionyl-O-nitroaniline (4.1 g) in EtOH (50 ml) was shaken in $H_2$ stream over Pt ($PtO_2$, 300 mg), $H_2$ being absorbed within about 30 min. The catalyst was removed by filtration and washed with EtOH. The filtrate was concentrated and the residual oil was dissolved in 4N HCl (30 ml), then heated on a water bath for 1 hr. The resulting solution was neutralized with aq. $K_2CO_3$ solution, and extracted with ether. The ether layer was evaporated to give an oil, bp 171—172° (0.2 mmHg), which was solidified by cololing to colorless crystals. Recrystallization from isopropyl ether gave colorless needles, mp 56°. *Anal.* Calcd. for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83; N, 11.86. Found: C, 81.07; H, 7.00; N, 11.76.

**N-Benzylidene-N′-propionyl-O-phenylenediamine (IV)**——A solution of N-propionyl-O-nitroaniline (500 mg) in EtOH (30 ml) was shaken in a $H_2$ stream over Pt ($PtO_2$, 50 mg). The catalyst was removed by filtration. The filtrate was concentrated, and a mixture of benzaldehyde (330 mg) and $K_2S_2O_8$ (660 mg) was added to the residual oil, then heated on a water bath for 1 hr. The resulting product was extracted with $CH_2Cl_2$, the $CH_2Cl_2$ layer was washed with $H_2O$, dried over $Na_2SO_4$, then evaporated. The residue was crystallized from isopropyl ether to pale yellow crystals (84 mg, mp 123—125°). This was recrystallized from isopropyl ether to pale yellow scales, mp 126—127°. *Anal.* Calcd. for $C_{16}H_{16}ON_2$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.30; H, 6.44; N, 10.94.

**N-Benzyl-N′-propionyl-O-phenylenediamine (V)**——A mixture of IV (30 mg) and $NaBH_4$ (60 mg) in EtOH (2 ml) was heated on a water bath at 60° for 1 hr. After addition of AcOH, the resulting solution was extracted with $CH_2Cl_2$. The $CH_2Cl_2$ layer was separated, washed with $H_2O$, dried over $Na_2SO_4$, and evaporated. The residue was recrystallized from AcOEt to give colorless needles, 13 mg, mp 147°. *Anal.* Calcd. for $C_{16}H_{18}ON_2$: C, 75.56; H, 7.13; N, 11.02. Found: C, 75.32; H, 6.81; N, 11.28.

**Photolysis of 1-Benzyl-2-ethylbenzimidazole 3-Oxide (I)**——A) In MeOH at Room Temperature: A solution of I (1.26 g) in MeOH (400 ml) was irradiated for 2.5 hr. The solvent was evaporated and the residue was chromatographed on neutral alumina (activity IV). Elution with benzene gave IV (1 mg, 0.8%) and II (899 mg, 71.4%). Elution with benzene–$CH_2Cl_2$ (1:1) gave III (14 mg, 1.1%). These compounds were identical with authentic samples by comparison of their IR spectra.

B) In Dioxane at Room Temperature: A solution of I (1.26 g) in dry dioxane (400 ml) was irradiated for 2.5 hr. The reaction mixture was treated in the same way as described above. IV (519 mg, 41.2%), III (52 mg, 4.4%) and V (37 mg, 2.9%) were obtained. These compounds were identical with authentic samples by comparison of their IR spectra.

C) In MeOH at −58°: A solution of I (500 mg) in MeOH (50 ml) was irradiated at −58° (Dry Ice–$CHCl_3$) for 5 hr. The reaction mixture was treated in the same way as described above. IV (92 mg, 18.4%) was obtained along with recovery of I (274 mg, 54.8%).

8) F. Kehrmann, *Ann.*, **290**, 247 (1896).

D) Presence of Acetophenone in MeOH: A solution of I (1.26 g, 0.005M) and acetophenone (1.21 g, 0.01M) in MeOH (400 ml) was irradiated for 2.5 hr. The reaction mixture was treated in the same way as described above. Acetophenone [0.86 g, 71.1%, elution with petr. ether–benzene (1:1)], II (715 mg, 57.2%, elution with benzene) and II+III [110 mg, ratio 48:52, by gas chromatography (Temperature 150°, column 5% SE-30), II (4.5%), III (4.8%), elution with benzene-benzene–$CH_2Cl_2$ (1:1)] were obtained.

E) Presence of Benzophenone in MeOH: A solution of I (1.26 g, 5 mM) and benzophenone (1.82 g, 10 mM) in MeOH (300 ml) was irradiated for 2.5 hr. The reaction mixture was treated in the same way as described above. Benzopinacol (406 mg), benzophenone (223 mg) [total; 34.1%, elution with petr. ether-petr. ether–benzene (1:1)], and II+III [832 mg, ratio 30:70, by gas chromatography II (19.8%), III (49.4%)] were obtained.

F) Presence of Anthraquinone in MeOH: A solution of I (1.26 g, 5 mM) and anthraquinone (210 mg, 1 mM) in MeOH (400 ml) was irradiated for 2.5 hr. Anthraquinone (7 mg, 3.3%, elution with benzene) and II+III [989 mg, ratio 5:95, by gas chromatography, II (4.2%), III (79.5%), elution with benzene–$CH_2Cl_2$] were obtained.

G) Presence of Fluorenone in MeOH: A solution of I (756 mg, 3 mM) and fluorenone (1.08 g, 6 mM) in MeOH (400 ml) was irradiated for 2.5 hr. The reaction mixture was treated in the same way as described above. Fluorenone [1.02 g, 94.4%, elution with petr. ether. ether–benzene (1:1)] and II (420 mg, 55.5%, elution with benzene) were obtained.

H) Presence of Anthraquinone in Dioxane: A solution of I (1.26 g, 5 mM) and anthraquinone (210 mg, 1 mM) in dioxane (400 ml) was irradiated fof 2.5 hr. Anthraquinone (13 mg, 6.2,% elution with benzene), IV (110 mg, 8.8%, elution with benzene), III (432 mg, 36.1%, elution with benzene) and V (78 mg, 6.2%, elution with $CH_2Cl_2$) were obtained.

**1-Methyl-2-phenylbenzimidazole 3-Oxide (VIII)**——A solution of N-methyl-N-propionyl-O-nitroaniline (30.0 g) in 1.7% EtOH–HCl (900 ml) was shaken in a $H_2$ stream over Pt ($PtO_2$, 3.0 g), $H_2$ being absorbed within about 1 hr. The catalyst was removed by filtration. The filtrate was concentrated and neutralized with aq. $K_2CO_3$ solution (20%, 610 ml) and then extracted with $CHCl_3$. The $CHCl_3$ layer was evaporated and the residue was recrystallized from AcOEt–$CH_2Cl_2$ to give pale yellow plates, 18.3 g, mp 173—176°. *Anal.* Calcd. for $C_{14}H_{12}ON_2$: C, 74.99; H, 5.38; N, 12.49. Found: C, 74.94; H, 5.43; N, 12.49.

**1-Methyl-2-phenylbenzimidazole**——A solution of N-methyl-N-benzoyl-O-nitroaniline (1.5 g) in MeOH (50 ml) was shaken in a $H_2$ stream over Pt ($PtO_2$, 300 mg), $H_2$ being absorbed within about 30 min. The catalyst was removed by filtration. The filtrate was concentrated and the residual oil was dissolved in 6N HCl (5 ml), then heated on a water bath for 1 hr. The resulting solution was neutralized with aq. $Na_2CO_3$, and extracted with $CHCl_3$. The $CHCl_3$ layer was evaporated and the residue was recrystallized from isopropyl ether to colorless prisms, mp 94—95°. *Anal.* Calcd. for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45. Found: C, 81.02; H, 5.73; N, 13.27.

**Photolysis of 1-Methyl-2-phenylbenzimidazole 3-Oxide (VIII)**——A) In MeOH: A solution of VIII (1.12 g) in MeOH (400 ml) was irradiated for 2 hr. The solvent was evaporated and the residue was chromatographed on neutral alumina (activity IV). Elution with benzene–$CH_2Cl_2$ (1:1) gave amorphous powder (no N–Me signal in NMR spectrum). This product was added to a solution of $NaBH_4$ (1.74 g) in EtOH (50 ml) and heated at 60° for 1 hr. After addition of AcOH (0.2 ml), the resulting solution was extracted with $CH_2Cl_2$. The $CH_2Cl_2$ layer was separated, washed with $H_2O$, dried over $Na_2SO_4$, and evaporated. The residue was chromatographed on neutral alumina (activity IV). Elution with benzene gave N-methyl-N′-benzoyl-O-phenylenediamine (190 mg, 16.8%) which was prepared from N-methyl-O-phenylenediamine and benzoyl chloride in aq. NaOH solution. Elution with benzene–$CH_2Cl_2$ (3:1) gave N-benzoyl-O-phenylenediamine (381 mg, 32.8%) which was identical with a sample prepared by catalytic hydrogenation of N-benzoyl-O-nitroaniline in the presence of Pt in EtOH.

B) Presence of Anthraquinone in MeOH: A solution of VIII (1.12 g, 5 mM) and anthraquinone (208 mg, 1 mM) in MeOH (400 ml) was irradiated for 2 hr. The reaction mixture was treated in the same way as described above. Anthraquinone (84 mg, 40.4%, elution with petr. ether), 1-methyl-2-phenylbenzimidazole (235 mg, 22.6%, elution with benzene–petr. ether (1:1)], and N-methyl-N′-benzoyl-O-phenylenediamine (5 mg, 0.4% elution with benzene–petr. ether (1:1)] were obtained.

**Photolysis of Theophylline 7-Oxide (IX)**——A) In MeOH: A solution of theophylline 7-oxide[7] (300 mg) in MeOH (100 ml) was irradiated for 2 hr. The starting material was recovered.

B) Presence of Anthraquinone in MeOH: A solution of IX (300 mg, 1.5 mM) and anthraquinone (63 mg, 0.3 mM) in MeOH (100 ml) was irradiated for 2 hr. The solvent was evaporated and the residue was washed with $CH_2Cl_2$ to give theophylline (53 mg, 19.3%). The filtrate was chromatographed on neutral alumina (activity IV). Elution with $CH_2Cl_2$ gave anthraquinone (36 mg, 57.1%). Elution with $CH_2Cl_2$–MeOH (20:1) gave theophylline (41 mg, 14.9%).

**Photolysis of Quinoline N-Oxide (X)**——A) In MeOH: A solution of X (2.0 g) in MeOH (300 ml) was irradiated for 3 hr. The solvent was evaporated, and the residue was washed with benzene to give carbostyril (905 mg, 45.3%). The filtrate was chromatographed on neutarl alumina (activity IV). Elution with benzene gave quinoline (38 mg, 1.9%). Elution with $CH_2Cl_2$–MeOH (9:1) gave carbostyril (320 mg, 16.0%).

B) Presence of Anthraquinone in MeOH: A solution of X (2.0 g, 14 mM) and anthraquinone (200 mg, 1 mM) in MeOH (300 ml) was irradiated for 3 hr. The reaction mixture was treated in the same way as described above. Elution with benzene gave anthraquinone (80 mg), and quinoline (118 mg, 6.6%). Elution with $CH_2Cl_2$–MeOH (9:1) gave carbostyril (985 mg, 49.3%).

**Photolysis of Quinaldine N-Oxide (XI)**[3b]——A) In MeOH: A solution of XI (2.0 g) in MeOH (300 ml) was irradiated for 2.5 hr. The solvent was evaporated, and the residue was washed with AcOEt to give 3-methylcarbostyril (208 mg, 10.4%), and the filtrate was chromatographed on neutral alumina (activity IV). Elution with benzene gave quinaldine (222 mg, 12.9%). Elution with benzene–$CH_2Cl_2$ (1:1) gave N-methylcarbostyril (290 mg, 14.5%). Elution with $CH_2Cl_2$–MeOH (9:1) gave 3-methylcarbostyril (65 mg, 3.3%). These compounds were identical with an authentic sample by comparison of their IR spectra.

B) Presence of Anthraquinone in MeOH: A solution of XI (2.0 g, 14 mM) and anthraquinone (130 mg, 0.6 mM) in MeOH (400 ml) was irradiated for 2.5 hr. The reaction mixture was treated in the same way as described above. Quinaldine (632 mg, 31.6%), N-methylcarbostyril (226 mg, 11.3%) and 3-methylcarbostyril (209 mg, 10.5%) were obtained.

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