extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, Na_2CO_3 solution, and water, dried (Na_2SO_4), and evaporated to dryness. Crystallization of the residue from ether gave 259 mg. of crystals, which were recrystallized from CH_2Cl_2–MeOH to yield 2-oxo thiazolino compound (XII), m.p. 291～293° (decomp.). $[\alpha]_D^{27}$ $-6.6\pm2°$ (c=0.950). *Anal.* Calcd. for $C_{22}H_{31}O_3NS$: C, 67.83; H, 8.02; N, 3.60; S, 8.23. Found: C, 67.75; H, 8.11; N, 3.57; S, 8.23. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3403, 3207, 1700, 1674. UV λ_{max}^{EtOH} 280 mμ (ε 120). ORD (in dioxane): $[\alpha]_{700}$ +50, $[\alpha]_{375}$ +150, $[\alpha]_{316}^{peak}$ +1506, $[\alpha]_{270}^{inf.}$ −3500, $[\alpha]_{250}$ −5200. NMR (τ): (18-H) 9.36, (19-H) 8.85, (21-H) 7.88, (6β-H) 6.64 multiplet ($W_H\approx24$ c.p.s.), (4-CH_2) AB type quartet at 6.65, 6.92, 7.38, and 7.65. $|J_{AB}|\approx16$ c.p.s., (NH) 2.60.

The mother liquor was evaporated to dryness. The residue (273 mg.) was dissolved in benzene and chromatographed over Al_2O_3 (7 g.). The material eluated with benzene was crystallized from ether–petr. ether to give 151 mg. (31.9%) of progesterone, m.p. 120～122°. The eluate with benzene–ether (9:1) was crystallized from ether to yield 14 mg. of XII. Combined yield of XII, 273 mg., 46.7%.

We are indebted to Dr. Kuriyama for the measurements and discussion of ORD and CD curves and to Dr. Tori for the measurements of NMR spectra.

Summary

Dehydration of 5α-hydroxy-6β-thiocyanato-5α-pregnane-3,20-dione with hydrochloric acid and with sodium methoxide, respectively, was studied. The former reagent gave 6α-thiocyanatoprogesterone and 2-chloro-2-thiazolino compound, whilst sodium methoxide yields 6α-hydroxyprogesterone.

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UDC 547.831.1.07; 547.833.1.07; 541.144

151. Masayuki Ishikawa, Sachiko Yamada, Hiromichi Hotta, and Chikara Kaneko: Photochemistry of the N-Oxides of Azanaphthalene and Their Substituted Derivatives.*1

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As has been reported in our communication,[1] ultraviolet irradiation of quinaldine 1-oxide in methanolic solution gave rise to N-methylcarbostyril (I), 3-methylcarbostyril (II), and N-acetylindole (III), in respective yields of 16, 22, and 10% together with a small amount (less than 5%) of quinaldine. Considering this observation, together with our[1] and other experimental results[2] on the photochemical alteration of aromatic N-oxides to the corresponding amide-type compounds, we have postulated the mechanism shown in Chart 1 for the formation of these rearrangement products. Plausibility of the formation of three-membered ring intermediates such as IV in the photochemical alteration of aromatic N-oxides to the corresponding amide-type

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*1 This work was presented at International Conference of Photochemistry, Tokyo (August, 1965). cf. p. 179 of its abstracts.

*2 Bunkyo-ku, Tokyo (石川正幸, 山田幸子, 堀田弘道, 金子主税).

[1] M. Ishikawa, S. Yamada, C. Kaneko: This Bulletin, **13**, 747 (1965).

[2] *a*) O. Buchardt: Acta Chem. Scand., **17**, 1461 (1963). *b*) G.B. Brown, G. Levin, S. Murphy: Biochemistry, **3**, 880 (1964). *c*) F. Cramer, G. Schlingloff: Tetrahedron Letters, **1964**, 3201.

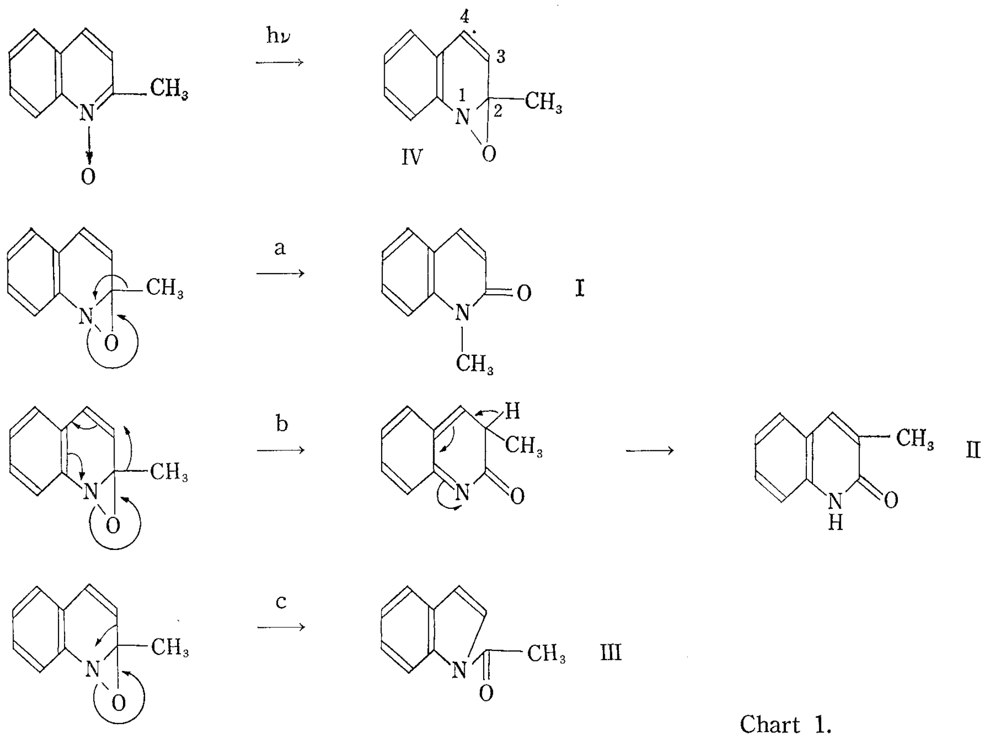

Chart 1.

compounds has also been suggested by several workers[2~5)] mainly from analogy with the well-settled photochemical conversion of nitrone→oxazirane→amide in the aliphatic series.[6)] To investigate the scope and further clarification of the mechanism of this rearrangement, the reaction was carried out with a variety of substituted quinoline, isoquinoline, and phenanthridine N-oxides, and the present paper deals with the results which seem to support the postulated mechanism.

For the convenience of exposition, the photochemistry of substituted quinoline 1-oxides will be discussed at first. The products obtained from the above reaction are shown in Table I.

In all cases, the products obtained were consistent with the postulated mechanism. Thus, quinoline 1-oxides having no substituents in 2-position underwent rearrangement mainly to the corresponding carbostyrils on irradiation in methanol solution. This could be due to the weaker nature of C_2-H bond compared to C_2-C_3 bond in the supposed oxazirane intermediates.[*3] It is worth noting that Buchardt, *et al.* in their recent paper[5)] reported the formation of the corresponding carbostyrils as the only detectable rearrangements products by photo-irradiation of quinaldine and lepidine 1-oxides under the reaction conditions essentially similar to ours. In our experiments, however, the corresponding indole-type compounds have also been isolated from the reaction mixtures of both N-oxides as shown in Table I.

2-Substituted quinoline 1-oxides, on the other hand, produced indole derivatives in comparatively high yields. The marked increase of the yields of indole derivatives in the 2-substituted series than those in unsubstituted series is understandable, if one considers the comparable strength of C_2-CH_3 bond to that of C_2-C_3 bond in the corresponding oxaziranes (such as Ⅳ) of the former series. Application of this reaction

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[*3] Most of the oxaziranes derived from nitrones are known to be unstable, and it is known that this stability is markedly affected by the nature of substituents.[6)]

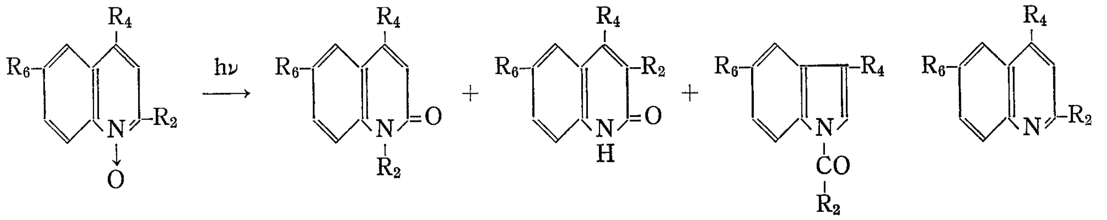
3) J.K. Landquist: J. Chem. Soc., **1953**, 2830.

4) E.C. Taylor, B. Furth, M. Pfau: J. Am. Chem. Soc., **87**, 1400 (1965).

5) O. Buchardt, J. Becher, Chr. Lohse: Acta Chem. Scand., **19**, 1120 (1965).

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

TABLE I. Irradiation of Quinoline 1-Oxides in Methanol Solution[a,b]



	N-Oxide	Rearrangement products		Simple deoxygenated product
		Amide-type compound	Indole-type compound	
2-Unsubstituted series	$R_{2,4,6}=H$[g]	carbostyril[5][f] m.p. 192~193° (60~70)	N-formylindole[c] (2.5)	m.p. 196~197°[e] (5~6)
	$R_4=CH_3$, $R_{2,6}=H$[g]	4-methylcarbostyril[5] m.p. 220~222° (70~75)	skatole[d] m.p. 94~95° (5)	m.p. 207~208°[e] (1~2)
	$R_4=Cl$, $R_{2,6}=H$[h]	4-chlorocarbostyril[7] m.p. 252~254° (75~80)	±	m.p. 213~215°[e] (2~3)
	$R_4=OCH_3$, $R_{2,6}=H$[h]	4-methoxycarbostyril[8] m.p. 254~256° (60~70)	±	m.p. 39~40° (4~5)
	$R_6=OCH_3$, $R_{2,4}=H$[g]	6-methoxycarbostyril[9][f] m.p. 215~217° (50~55)	±	m.p. 213~215°[e] (5)
2-Substituted series	$R_2=CH_3$, $R_{2,6}=H$[g]	N-methylcarbostyril[1][f] m.p. 75~76.5° (16)	N-acetylindole[1][c,e] m.p. 98~99° (10)	m.p. 191~193°[e] (4~5)
		3-methylcarbostyril[1] m.p. 238~239° (22)		
	$R_{2,4}=CH_3$, $R_6=H$[g]	4,N-dimethylcarbostyril[10] m.p. 135~136° (20)	skatole[d] m.p. 94~95° (6~7)	m.p. 194~196°[e] (7~8)
		3,4-dimethylcarbostyril[11] m.p. 268~269° (14~15)		

a) Irradiation was carried out as described in the experimental part of this paper.
b) The numbers in parentheses designate the yield of the corresponding products.
c) The purity of the compounds was checked by gas-phase chromatography. Indole was obtained from them by alkaline hydrolysis.
d) The isolated product was skatole, and no corresponding acyl derivatives were obtained.
e) This compound was identified as its picrate. The melting point corresponds to that of its picrate.
f) Prolonged irradiation in methanol resulted in dimerization of the compounds. The dimer of carbostyril, m.p. 279~283°, $C_{18}H_{14}O_2N_2$ (from dimethylformamide); the dimer of N-methylcarbostyril, m.p. 215~216°, $C_{20}H_{18}O_2N_2$ (from methanol); the dimer of 6-methoxycarbostyril, m.p. 268~269°, $C_{20}H_{18}O_4N_2$ (from dimethylformamide). The structures of the dimers of carbostyril and N-methylcarbostyril were elegantly elucidated by Buchardt.[12] In present authors' observation, only 3,4-unsubstituted carbostyrils tend to dimerize by irradiation in methanol.
g) N-Oxide was prepared by the method of Ochiai.[13]
h) N-Oxide was prepared from 4-nitroquinoline 1-oxide by the method described by Ochiai.[13]

to isoquinoline 2-oxides was also carried out and the results are shown in Table Ⅱ.

The products could be predicted correctly if we assume the formation of oxaziranes (V), having 1,2-epoxy-1,2-dihydroisoquinoline skeleton as intermediates. Another formulation of oxaziranes, namely, (Ⅵ) having 2,3-epoxy function, should be avoided by the fact that no 3-oxo compounds were detected in the reaction products. The noteworthy fact in the photochemical reaction of isoquinoline series is that formation

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7) C. Kaneko: This Bulletin, 8, 286 (1960).
8) F. Arndt, L. Ergener, O. Kutli: Ber., **86**, 951 (1953).
9) L. Gattermann: Ber., **27**, 1936 (1894).
10) L. Knorr: Ann., **236**, 69 (1886).
11) *Idem*: *Ibid.*, **245**, 357 (1888).
12) O. Buchardt: Acta Chem. Scand., **18**, 1389 (1964).
13) E. Ochiai: J. Org. Chem., **18**, 534 (1953).
14) E. Ochiai, M. Ikehara: This Bulletin, **3**, 454 (1955).
15) M. M. Robison, L. Robison: J. Org. Chem., **21**, 1337 (1957).
16) E. Bamberger, W. Frew: Ber., **27**, 198 (1894).

Table II. Irradiation of Isoquinoline 2-Oxides in Methanol Solution[a,b]

N-Oxide	Rearrangement products		Simple deoxygenated compound
	Amide-type compound	Indole-type compound	
Isoquinoline 2-oxide[g]	isocarbostyril[14] m.p. 206~208° (60~70)	—[i]	m.p. 222~223°[e] (4~5)
3-Methylisoquinoline 2-oxide[g]	3-methylisocarbostyril[15] m.p. 209~210° (65~75)	—[i]	m.p. 196~197°[e] (4~5)
1-Methylisoquinoline 2-oxide[g]	N-methylisocarbostyril[16] m.p. 39~40° (35~45)	—[i]	m.p. 209~210°[e] (8~10)

a~h) c.f. Footnotes to Table I.

i) The indole-type compounds could not be detected even by gas-chromatography of the concentrated reaction mixture.

of any detectable amount of the corresponding indole-type compounds had not been detected in the reaction products. Thus, the fate of the oxaziranes (V) derived from photo-irradiation of isoquinoline 2-oxides in protic solvents[*4] may be formulated as in Chart 2.

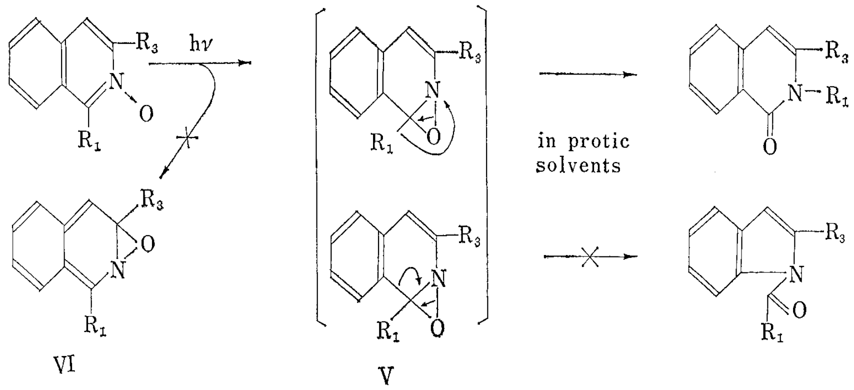

Chart 2.

The extention of this reaction was tried with phenanthridine 5-oxide and its 6-methyl derivative and the results are given in Table III. The results obtained for the former compound was almost the same as that reported by Taylor, *et al.*,[4] except the formation of phenanthridine which was not detected in their experiment.[*5] Here again, there was no indication for the formation of the corresponding carbazole derivatives.

As a conclusion, the following assumptions seem to be plausible. (i) Aromatic N-oxides are transformed to the corresponding oxaziranes *via* photo-excited states. (ii) The oxaziranes, when they are unstable, undergo various reactions (such as course a, b, and c, etc.) to give rise to rearrangement products. (iii) If no precautions were taken to avoid the presence of air in the irradiated mixture, simple deoxygenation

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[*4] The change of solvent from methanol to other protic solvents (such as ethanol, water, etc.) did not affect the kind and ratio of the products. However, the use of non-protic solvents for these photo-reactions produced a marked change. Details of these reactions will be published soon.

[*5] As seen from the results shown in Tables I~III, formation of simple deoxygenation products occurs without exception. In the present authors' opinion, this formation is due to the presence of a small amount of air in the reaction mixture during irradiation. As no precautions are taken to avoid the presence of air in Taylors' and our experiments, we believe that Taylors' products should also contain phenanthridine.

17) R.A. Heacock, D.H. Hey: J. Chem. Soc., **1952**, 1508.

TABLE III. Irradiation of Phenanthridine 5-Oxides in Methanol Solution[a,b]

N-Oxide	Rearrangement product (Phenanthridones)	Simple deoxygenated compound (Phenanthridines)
Phenanthridine 5-oxide[g]	phenanthridone[4] m.p. 290~292° (80~85)	m.p. 104° m.p. 238~240°[e] (4~5)
6-Methylphenanthridine 5-oxide[g,j]	N-methylphenanthridone[17] m.p. 105~108° (90)	m.p. 83.5~84.5° m.p. 233~235°[e] (1~2)

a~h) c.f. Footnotes to Table I.
j) Complete absence of the formation of acetylcarbazole in the irradiated mixture was assured by gas-phase chromatography.

reaction[*6,18,19] occurs competitively with (i). It is also a photochemical reaction, but the excited species responsible for the deoxygenation reaction is not necessarily the same as those of (i).

Experimental

All melting points were measured by capillary and are uncorrected. Infrared spectra were recorded either on a Nihon Bunkō Infracord, or its model DS-301 double-beam spectrophotometer. Ultraviolet spectra were recorded on a Hitachi model EPS-2 UV spectrophotometer. Nuclear magnetic resonance spectra were recorded on a JNM-3H-60 with tetramethylsilane as internal reference. 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. Satisfactory analyses were obtained for all the rearrangement products listed in Tables I, II, and III, except for N-formylindole. These results are shown in Table IV. The structure of the last compound was consistent with its spectra (UV and IR) and was confirmed by its successful conversion to indole by alkaline hydrolysis.

TABLE IV. Elemental Analysis of the Rearrangement Products

Products	Molecular composition	Calculated			Found			Notes
		C	H	N	C	H	N	
Carbostyril	C_9H_7ON	74.47	4.86	9.65	74.60	4.90	9.80	
4-Methylcarbostyril	$C_{10}H_9ON$	75.45	5.70	8.80	75.43	5.72	8.78	
4-Chlorocarbostyril	C_9H_6ONCl	60.22	3.30	7.80	60.52	3.55	7.69	
4-Methoxycarbostyril	$C_{10}H_9O_2N$	68.56	5.18	8.00	68.43	5.22	7.81	
6-Methoxycarbostyril	〃	68.56	5.18	8.00	68.60	5.23	7.83	
N-Methylcarbostyril	$C_{10}H_9ON$	75.45	5.70	8.80	75.45	5.75	8.79	
3-Methylcarbostyril	〃	75.45	5.70	8.80	75.49	5.70	8.78	
4,N-Dimethylcarbostyril	$C_{11}H_{11}ON$	76.27	6.40	8.09	76.13	6.44	7.99	
3,4-Dimethylcarbostyril	〃	76.27	6.40	8.09	76.20	6.38	8.00	
Isocarbostyril	C_9H_7ON	74.47	4.86	9.65	74.23	5.00	9.53	
3-Methylisocarbostyril	$C_{10}H_9ON$	75.45	5.70	8.80	75.52	5.79	8.69	
1-Methylisocarbostyril	〃	75.45	5.70	8.80	75.30	5.90	8.60	
Phenanthridone	$C_{13}H_9ON$	79.98	4.65	7.17	80.22	4.75	7.03	
5-Methylphenanthridone	$C_{14}H_{11}ON$	80.36	5.30	6.69	80.36	5.30	6.50	
Skatole	C_9H_9N	82.40	6.92	10.68	82.45	7.01	10.49	
Indole	C_8H_7N	82.02	6.02	11.96	81.93	6.21	12.01	
N-Acetylindole	$C_{16}H_{12}O_8N_4$	49.47	3.12	14.43	49.36	3.16	15.06	analyzed as picrate
N-Formylindole	C_9H_7ON							$\nu_{CO}(CHCl_3)=1712\ cm^{-1}$

[*6] This type of photochemical reaction has been recorded for pyridine 1-oxides in the gas phase,[18] as well as for purine N-oxides[2b,2c] and 4-nitroquinoline 1-oxide[19] in solution.

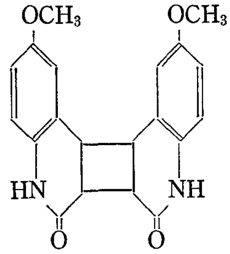
18) N. Hata, *et al.*: J. Chem. Phys., **36**, 2072 (1962); *Idem*: Bull. Chem. Soc. Japan, **34**, 1440, 1445 (1961).

19) T. Kosuge, *et al.*: Yakugaku Zasshi, **85**, 66 (1965).

i) General Procedure for Photochemical Reactions——A solution of 200 ml. of methanol containing 2 g. of N-oxide is placed in a glass cylinder. A high pressure 100-W Hanovia mercury arc is then immersed in the solution. The reaction is followed by the periodical injection of a sample of the solution into the gas-phase chromatograph, and the irradiation is continued until all of the N-oxide is consumed in the irradiated mixture. No precautions are taken to avoid the presence of a small amount of air in the solution in these reactions. The reaction mixture is stirred during irradiation. Under this condition, the reaction takes 13～20 hr. for all the N-oxides described. The solution is then evaporated under reduced pressure at room temperature. Trituration of the residue with ether (or acetone) results in precipitation of amide-type compounds having hydrogen on ring nitrogen, which are recrystallized from appropriate solvents. After evaporation of the solvent from combined mother liquors, the residue is chromatographed on silica gel. Elution with hexane-ether gives indole derivatives and N-methylamide-type products in that order. Elution with ether gives deoxygenated products, and finally with $CHCl_3$ containing 5% of methanol, gives the additional NH-amide-type compounds. These procedures give results shown in Tables I, II, and III. The purity of each products was assured by gas-phase chromatography. The mixed melting point determination with authentic samples confirmed the identities of all the rearrangement products.

ii) Irradiation of 6-Methoxyquinoline 1-Oxide for 48 Hours——One gram of the N-oxide was irradiated as in (i). The precipitated crystals (630 mg.) were separated from the concentrated irradiation mixture by filtration. A small sample was recrystallized from dimethylformamide to colorless plates, m.p. 268～269°. *Anal.* Calcd. for $C_{20}H_{18}O_4N_2$: C, 68.56; H, 5.18; N, 8.00. Found : C, 68.33; H, 5.31; N, 7.89. IR ν_{max}^{KBr} cm^{-1} : 3270 w, 3180 w, 3040 w, 2920 w, 1724 vs, 1621 (shoulder) m, 1616 w, 1502 s, 1460 w, 1415 w, 1375 m, 1298 w, 1265 m, 1241 s, 1190 w, 1160 m, 1131 w, 1113 w, 1038 m, 965 w, 940 w, 908 w, 855 w, 841 m, 818 m, 810 m, 772 w, 736 w, 721 w. UV $\lambda_{max}^{95\%\ EtOH}$ mμ (log ε) : 266 (4.40), 310 (3.74). NMR (in trifluoroacetic acid) : 2.93～3.18 τ (6H, multiplet due to aromatic protons), 5.87 τ (4H, broad singlet due to aliphatic protons) and 6.05 τ (6H, singlet due to protons on methoxy-group).

The solvent was evaporated from the filtrate and the residue, by treatment as in (i), gave 50 mg. of 6-methoxyquinoline (picrate, m.p. 213～215°) and 40 mg. of 6-methoxycarbostyril (m.p. 215～217°). Structure of the first product is consistent with VII. The basic structure of VII is the same with the dimer of carbostyril, whose structure has been elegantly elucidated recently by Buchardt.[12]



VII

We thank Dr. Y. Kawazoe and Miss M. Ohnishi at the National Cancer Center, Tokyo, for the measurement of NMR spectra.

Summary

As previously reported,[1] three rearrangement products were obtained on irradiation of quinaldine 1-oxide in methanol solution. To investigate the scope and further clarification of the mechanism of this rearrangement, the reaction has been extended to a variety of substituted azanaphthalene N-oxides and some phenanthridine N-oxides. The results obtained seem to support the postulated mechanism,[1] namely, the photochemical formation of a three-membered ring intermediate (such as IV in the case of quinoline 1-oxides) and its subsequent thermal rearrangement to the final products.

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