

Studies on Chemical Carcinogens. VIII.¹⁾ The Structure-carcinogenicity Relationship among Derivatives of 4-Nitro- and 4-Hydroxyamino-quinoline 1-Oxides (Supplement)²⁾

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(Received August 12, 1968)

The twenty-three compounds related to 4-nitro- and 4-hydroxyamino-quinoline 1-oxides, in addition to forty quinoline derivatives already tested, were tested for carcinogenic activity by the subcutaneous injection in mice. The results were tried to be correlated with chemical and physical properties of the compounds.

Many studies have been reported on the carcinogenic mechanism of 4-nitroquinoline 1-oxide derivatives and a conclusion has become reliable that 4-hydroxyaminoquinoline 1-oxide which is metabolically produced from the 4-nitroquinoline 1-oxide administered, is the proximate carcinogen in the carcinogenesis of 4-nitroquinoline 1-oxide. This conclusion is supported by the following facts.

i) 4-Hydroxyaminoquinoline 1-oxide⁴⁻⁸⁾ and its many substituted derivatives⁹⁾ show similar or more potent carcinogenic activity compared to the parent 4-nitroquinoline 1-oxides.

ii) 4-Nitroquinoline 1-oxide is metabolized to 4-hydroxyaminoquinoline 1-oxide at the site of the injection and the latter is considerably stabilized, resistant to further metabolic changes.¹⁰⁻¹²⁾ This is also shown in metabolism in microorganisms.^{13,14)} The chemical stability of 4-hydroxyaminoquinoline 1-oxide in the reduction process is demonstrated to be considerable in enzymic reduction *in vitro*,^{12,15)} reductions by chemical means,¹⁶⁻²⁰⁾ and also polarographic reduction.^{20,21)}

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- 4) Y. Shirasu and A. Ohta, *Gann*, **54**, 221 (1963).
- 5) Y. Shirasu, *Gann*, **54**, 487 (1963).
- 6) H. Endo and F. Kume, *Gann*, **54**, 443 (1963).
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- 9) Y. Kawazoe, M. Tachibana, K. Aoki, and W. Nakahara, *Biochem. Pharmacol.*, **16**, 631 (1967).
- 10) H. Hoshino, F. Fukuoka, K. Okabe, and T. Sugimura, *Gann*, **57**, 71 (1966).
- 11) T. Sugimura, K. Okabe, and M. Nagao, *Cancer Res.*, **26**, 1717 (1966).
- 12) T. Sugimura, K. Okabe, and H. Endo, *Gann*, **56**, 489 (1965).
- 13) T. Okabayashi, *Chem. Pharm. Bull.* (Tokyo), **10**, 1127 (1962).
- 14) T. Okabayashi and A. Yoshimoto, *Chem. Pharm. Bull.* (Tokyo), **10**, 1221 (1962).
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- 17) E. Ochiai and H. Mitarashi, *Ann. Rept. Itsuu Lab.*, **13**, 19 (1963).
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- 20) Y. Kawazoe and M. Araki, *Chem. Pharm. Bull.* (Tokyo), **16**, 839 (1968).
- 21) M. Tachibana, S. Sawaki, and Y. Kawazoe, *Chem. Pharm. Bull.* (Tokyo), **15**, 1112 (1967).

iii) There are found chemical evidences for importance of the production of 4-hydroxy-aminoquinoline 1-oxide structure in the carcinogenesis of 4-nitroquinoline 1-oxide, as described in ref. 9).²²⁾

This paper adds supplemental data for the structure-carcinogenicity correlation in the carcinogenesis of this class of compounds.

Results and Discussion

Twenty-three derivatives of quinoline 1-oxide were tested for the carcinogenic activity by the subcutaneous injection in mice. The compounds tested were 3-fluoro-4-nitroquinoline 1-oxide (I),¹⁾ 3-chloro-4-nitroquinoline 1-oxide (II),¹⁹⁾ 3-bromo-4-nitroquinoline 1-oxide (III),²³⁾ 3-methyl-4-nitroquinoline 1-oxide (IV),¹⁹⁾ 4,6-dinitroquinoline 1-oxide (V),²⁴⁾ 6-nitro-4-hydroxy-aminoquinoline 1-oxide (VI),¹⁹⁾ 6-*n*-butyl-4-nitroquinoline 1-oxide (VII), 6-*n*-butyl-4-hydroxy-aminoquinoline 1-oxide (VIII), 6-*tert*-butyl-4-nitroquinoline 1-oxide (IX), 6-*tert*-butyl-4-hydroxy-aminoquinoline 1-oxide (X), 6-*n*-hexyl-4-nitroquinoline 1-oxide (XI), 6-*n*-hexyl-4-hydroxy-aminoquinoline 1-oxide (XII), 6-*cyclo*-hexyl-4-nitroquinoline 1-oxide (XIII), 6-*cyclo*-hexyl-4-hydroxyaminoquinoline 1-oxide (XIV), 8-fluoro-4-nitroquinoline 1-oxide (XV),²⁰⁾ 4,4'-dinitro (2,2'-biquinoline) 1,1'-dioxide (XVI),²⁵⁾ 3-hydroxy-4-aminoquinoline 1-oxide (XVII), 3-amino-4-hydroxyquinoline 1-oxide (XVIII), 4-acetamidoquinoline 1-oxide (XIX), 4-hydroxyamino-pyridine 1-oxide (XX),^{16,17)} 3-hydroxyaminoquinoline 1-oxide (XXI),¹⁸⁾ 5-hydroxyamino-quinoline 1-oxide (XXII),²⁰⁾ and O,O'-diacetyl-4-hydroxyaminoquinoline 1-oxide (XXIII).²⁶⁾

TABLE I. Carcinogenic Activity of Quinoline Derivatives and Their Related Compounds on Mice

Compound	Total doses applied	
	1.5 mg/mouse	Increased dose (mg)
3-Fluoro-4-nitroquinoline 1-oxide (I)	—	+ (8.67)
3-Chloro-4-nitroquinoline 1-oxide (II)	—	+ (8.67)
3-Bromo-4-nitroquinoline 1-oxide (III)	+	+
3-Methyl-4-nitroquinoline 1-oxide (IV)	—	— (15.0)
4,6-Dinitroquinoline 1-oxide (V)	—	+ (14.0)
6-Nitro-4-hydroxyaminoquinoline 1-oxide (VI)	+	+
6- <i>n</i> -Butyl-4-nitroquinoline 1-oxide (VII)	+	+
6- <i>n</i> -Butyl-4-hydroxyaminoquinoline 1-oxide (VIII)	+	+
6- <i>tert</i> -Butyl-4-nitroquinoline 1-oxide (IX)	—	—
6- <i>tert</i> -Butyl-4-hydroxyaminoquinoline 1-oxide (X)	—	—
6- <i>n</i> -Hexyl-4-nitroquinoline 1-oxide (XI)	—	—
6- <i>n</i> -Hexyl-4-hydroxyaminoquinoline 1-oxide (XII)	—	—
6- <i>cyclo</i> -Hexyl-4-nitroquinoline 1-oxide (XIII)	—	—
6- <i>cyclo</i> -Hexyl-4-hydroxyaminoquinoline 1-oxide (XIV)	—	—
8-Fluoro-4-nitroquinoline 1-oxide (XV)	+	+
4,4'-Dinitro-2,2'-biquinoline 1,1'-dioxide (XVI)	—	—
3-Hydroxy-4-aminoquinoline 1-oxide (XVII)	—	— (10.78)
3-Amino-4-hydroxyquinoline 1-oxide (XVIII)	—	—
4-Acetamidoquinoline 1-oxide (XIX)	—	— (15.0)
4-Hydroxyaminopyridine 1-oxide (XX)	—	— (5.3)
3-Hydroxyaminoquinoline 1-oxide (XXI)	—	— (15.0)
5-Hydroxyaminoquinoline 1-oxide (XXII)	—	— (15.0)
O,O'-Diacetyl-4-hydroxyaminoquinoline 1-oxide (XXIII)	+	+ (10.5)

22) See pp. 632—635 in ref. (9).

23) T. Okamoto, *Yakugaku Zasshi*, **70**, 376 (1950).

24) E. Ochiai and T. Okamoto, *Yakugaku Zasshi*, **70**, 384 (1950).

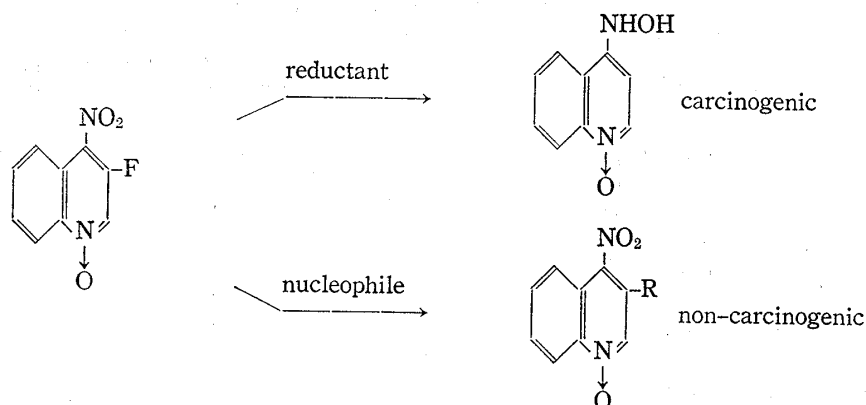
25) F.H. Case and J.M. Lesser, *J. Heterocyclic Chem.*, **3**, 1701 (1966).

26) Y. Kawazoe and M. Araki, *Gann*, **58**, 485 (1967).

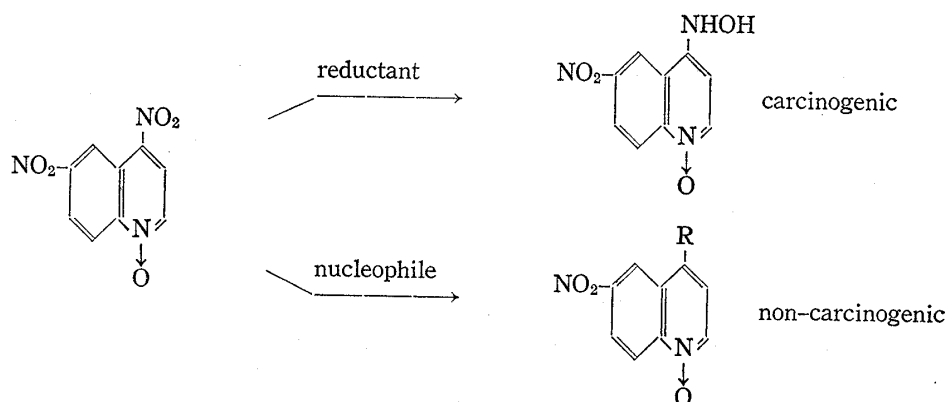
Some of these compounds were new, synthetic procedures being described in the experimental part.

The compounds to be assayed were dissolved in propylene glycol at concentrations ranging from 5 mg to 10 mg per ml of the solvent and injected subcutaneously into the left groin of the mouse in doses of 0.1 ml each, the injections being repeated at the same site until the total doses reached 1.5 mg or more per mouse, as indicated in Table I. Normal ddN female mice were used in groups of 20 for each test. The mice that developed tumors at the site of injections were recorded and submitted to an autopsy at death. The tumors were histologically diagnosed mostly as fibrosarcoma, with small proportions of rhabdomyosarcomas and squamous cell carcinomas. Results are summarized in Table I. The sign “-” is used in Table I when none of the treated mice showed tumors at the end of 300 days after the first injection.

No tumor was induced with 3-methyl-4-nitroquinoline 1-oxide (IV) even when the dosage was raised ten-folds (15 mg/mouse). Among the 3-substituted 4-nitroquinoline 1-oxides, only halogeno derivatives, I, II, and III, induced tumors under the condition shown in Table I. As already suggested in a previous paper,⁹⁾ dehalogenation may take place in a metabolic reduction process to produce carcinogenic 4-hydroxyaminoquinoline 1-oxide. 3-Bromo derivatives (III), which is converted to 4-hydroxyaminoquinoline 1-oxide by chemical reduction procedures in a better yield than other two halogeno derivatives, I and II,⁹⁾ induced tumor at the dosage of 1.5 mg/mouse. 3-Position of fluoro derivative (I) is very reactive toward nucleophiles¹⁾ and the replacement with -SR, -NR₂, etc., may take place in preference to defluorination by hydrogen. This may be the reason why the fluoro derivative (I) requires



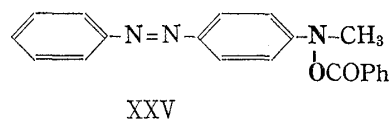
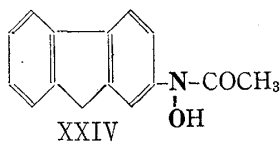
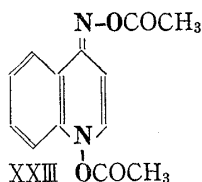
more dosage than the usual for tumor-induction. 4,6-Dinitroquinoline 1-oxide (V) seems to be in the same situation as the fluoro derivative. Thus, the fact that this compound required an increased dosage for tumor-induction, although its hydroxyamino derivative (VI) induced tumor at the usual dosage of 1.5 mg/mouse, may indicate that undesirable nucleophilic replace-



ments of 4-nitro group with $-SR$, $-NR_2$, etc., take place to a remarkable extent ²⁷⁾ competitively with its reductive conversion to carcinogenic 6-nitro-4-hydroxyaminoquinoline 1-oxide.

Some hydroxyamino derivatives (XX, XXI, and XXII) and the related compounds (XVII, XVIII, and XIX) were tested for carcinogenicity. The position isomers of 4-hydroxyaminoquinoline 1-oxide, 3- and 5-hydroxyamino derivatives (XXI and XXII), brought about no effect on mice. 4-Hydroxyaminopyridine 1-oxide (XX), which appears very similar to the quinoline analogue in chemical reactivity, did not induce tumor even at the dosage of 5.3 mg/mouse although fairly severe ulcer was observed at the site of injection. 4-Acetylaminoquinoline 1-oxide (XIX) did not give any effect even with 15.0 mg/mouse, but question still remains that this compound might exert carcinogenic effect by being metabolically converted to the N-hydroxy derivative probably in liver, as demonstrated in the carcinogenesis of acetylaminofluorene.²⁹⁻³¹⁾ In connection with the carcinogenesis of aminonaphthol derivatives, carcinogenic activity was tested of 3-hydroxy-4-aminoquinoline 1-oxide (XVII) and 3-amino-4-hydroxyquinoline 1-oxide (XVIII), taking account of metabolic rearrangement of 4-hydroxyaminoquinoline 1-oxide into 3-hydroxy-4-aminoquinoline 1-oxide (XVII). But no tumor-induction was observed in either case.

O,O'-Diacetyl derivative of 4-hydroxyaminoquinoline 1-oxide, which was once tested by painting on the skin of mouse and reported to be non-carcinogenic,⁵⁾ was re-examined by subcutaneous injection since the activity of this compound may be of great interest in relation to the carcinogenesis of acetamidofluorenes and azo dyes. Thus, the latter two carcinogens are known to be converted into acylhydroxylamine derivatives, XXIV and XXV, as the proximate forms for tumor induction.²⁹⁻³⁴⁾ This diacetate (XXIII) was demonstrated, contrary to the former result, to be carcinogenic.



It is to be noted that this diacetate is so labile in itself that it appears to undergo some unknown reactions in preference to simple hydrolysis. It is very probable that this diacetate is carcinogenic in itself but not converted to carcinogenic 4-hydroxyaminoquinoline 1-oxide *in vivo*. Detail of the reactivity of this acetate will be described in a forthcoming paper.

Another interesting feature was found in the carcinogenesis of this group of compounds. Thus, the carcinogenic activity of 6-alkyl derivatives seems to depend on the size of the alkyl group in the 6-position. 6-*n*-Butyl-4-nitroquinoline 1-oxide (VII) and its corresponding 4-hydroxyamino derivative (VIII) induced tumor at the dosage of 1.5 mg/mouse as well as 6-methyl derivative, whereas neither 6-*tert*-butyl derivatives of 4-nitro nor 4-hydroxyaminoquinoline 1-oxide (IX nor X) brought about any histological change at the site of the injection. 6-*n*- and 6-*tert*-butyl derivatives of 4-nitroquinoline 1-oxide have the same molecular

27) It is known that 4,6-dinitroquinoline 1-oxide undergoes nucleophilic replacement with thioglycolic acid 50 times faster than 4-nitroquinoline 1-oxide.²⁸⁾

28) T. Okamoto and M. Itoh, *Chem. Pharm. Bull.* (Tokyo), **11**, 785 (1963).

29) J. A. Miller, R.B. Sandin, E.C. Miller, and H.P. Rusch, *Cancer Res.*, **15**, 188 (1955).

30) E.C. Miller, J.A. Miller, and H.A. Hartmann, *Cancer Res.*, **21**, 815 (1961).

31) E. Kriek, J.A. Miller, U. Juhl, and E.C. Miller, *Biochemistry*, **6**, 177 (1967).

32) K. Sato, L.A. Poirier, J.A. Miller, and E.C. Miller, *Cancer Res.*, **26**, 1678 (1966).

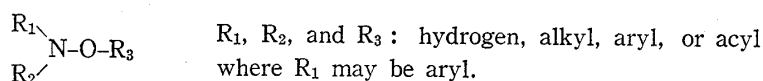
33) L.A. Poirier, J.A. Miller, E.C. Miller, and K. Sato, *Cancer Res.*, **27**, 1600 (1967), and literatures cited therein.

34) G.S. Tranowski, W. Kreis, F.A. Schmid, J.S. Cappuccino, and J.H. Burchenal, *Cancer Res.*, **26**, 1279 (1966).

weight and the very similar chemical properties: the half-wave reduction potential, reactivity toward reducing agents, and spectroscopic data in nuclear magnetic resonance and ultraviolet absorption. In addition, neither 6-*n*-hexyl nor 6-cyclohexyl derivatives induced tumor regardless of the substituent in 4-position, nitro nor hydroxyamino.³⁵⁾ The 4-hydroxyamino derivatives, X, XII, and XIV, are the only examples where carcinogenic activity was not demonstrated among all the 4-hydroxyaminoquinoline 1-oxides so far tested. It may, therefore, be realized that another factor which is playing an essential role in the chemical carcinogenesis should be considered besides the essential chemical reactivity of the compounds for tumor-induction. Thus, attention should be paid to the biological importance of the physical and chemical properties governed by the whole molecule, such as specificity in enzyme reactions, lipophilic-hydrophilic character in passive transport (diffusion) in the living system.

When one takes into account the carcinogenic mechanisms of azo dyes and acetamido-fluorenes, the following general aspect might be realized on the structure-carcinogenicity relationship in this and some other groups of chemical carcinogens.

I) Existence of the following essential functional group for tumor induction



II) Role of the rest of molecule

- a) Electronic and steric effects on the reactivity of the above essential functional group
- b) Biological importance of the physical and chemical properties of the molecule governed by the whole molecule, such as specificity in enzyme reactions, lipophilic-hydrophilic character in interaction with biological substances *in vivo*, etc.

Thus, the structure-carcinogenicity correlation should be considered on the basis of the above three factors and one can try to induce which chemical reaction of hydroxylamines would be essential for tumor-induction. Further investigation is being carried out in our laboratory for correlation of carcinogenic activity with the chemical and physicochemical properties of carcinogenic hydroxylamines.

Experimental

The method for bioassay was described in the part of Results and Discussion. The identifications of the chemical structures of 6-substituted 4-nitroquinoline 1-oxides were performed by nuclear magnetic resonance spectroscopy and polarographic analysis.

6-*n*-Butyl-4-nitroquinoline 1-Oxide—To a solution (warmed at 90°) of 1.5 g of 6-*n*-butylquinoline 1-oxide in 10 ml of 83% H₂SO₄ was added 0.9 g of KNO₃ in small portions under stirring. The reaction mixture was kept standing at this temperature for 3 hr. The reaction mixture was poured into ice water, and extracted with CHCl₃. Chloroform extract was washed with aqueous NaHCO₃ solution and dried over anhydrous Na₂SO₄. After evaporation of the solvent *in vacuo*, the residue was chromatographed through an alumina column, eluted with benzene and then with CHCl₃. From benzene fractions, 0.36 g of 6-*n*-butyl-4-nitroquinoline 1-oxide was obtained as yellow prism. They were recrystallized from ether. mp, 102°. Yield, 20%. About one gram of the starting material was recovered from the CHCl₃ fraction. *Anal.* Calcd. for C₁₃H₁₄O₃N₂: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.20; H, 5.78; N, 11.27.

6-*n*-Butyl-4-hydroxyaminoquinoline 1-Oxide—A mixture of 0.14 g of 6-*n*-butyl-4-nitroquinoline 1-oxide, 1.0 ml of EtOH and 0.5 ml of phenylhydrazine was kept standing at 35° for 3 hr. Addition of 3 ml of ether to the reaction mixture afforded yellow precipitates which were gathered on a filter and washed with ether. They were almost pure 6-*n*-butyl-4-hydroxyaminoquinoline 1-oxide which weighed 0.12 g. mp, 216–217°. Yield, 92%. They were converted into the hydrochloride by recrystallizing from MeOH containing an excess of conc. HCl. mp 169.5–170.5 (decomp.). *Anal.* Calcd. for C₁₃H₁₇O₂N₂Cl: C, 58.10; H, 6.33; N, 10.42. Found: C, 57.94; H, 6.30; N, 10.62.

6-*tert*-Butyl-4-nitroquinoline 1-Oxide—A solution of 1.0 g of 6-*tert*-butylquinoline 1-oxide in 8 ml of 79% H₂SO₄ was warmed at 90°. To this solution was added 0.73 g of KNO₃ in small portions and then

35) Further experiments are now being pursued with increased doses of these compounds.

the mixture was kept standing at this temperature for 2.5 hr. The reaction mixture was poured into ice water and extracted with CHCl_3 . The chloroform extract was washed with aqueous NaHCO_3 and dried with Na_2SO_4 . Chromatographic separation using an alumina column afforded 0.7 g of 6-*tert*-butyl-4-nitroquinoline 1-oxide from benzene fraction, which was recrystallized from MeOH. mp 128—129°. Yield, 56%. *Anal.* Calcd. for $\text{C}_{13}\text{H}_{14}\text{O}_3\text{N}_2$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.22; H, 5.88; N, 11.33.

6-*tert*-Butyl-4-hydroxyaminoquinoline 1-Oxide—A mixture of 0.15 g of 6-*tert*-butyl-4-nitroquinoline 1-oxide, 1 ml of EtOH, and 0.5 ml of phenylhydrazine was warmed at 35° for 3 hr. The same treatment of the reaction mixture as the case of 6-*n*-butyl-4-hydroxyaminoquinoline 1-oxide gave 0.13 g of yellow powder. It was dissolved in conc. HCl-MeOH solution and then ether was added to this solution in small portions. The resulting white crystalline material was recrystallized from acetone. mp 181—181.5° (decomp.). Yield, 93%. *Anal.* Calcd. for $\text{C}_{13}\text{H}_{17}\text{O}_2\text{N}_2\text{Cl}$: C, 58.10; H, 6.38; N, 10.42. Found: C, 57.83; H, 6.42; N, 10.58.

6-*n*-Hexyl-4-nitroquinoline 1-Oxide—A solution of 2 g of 6-*n*-hexylquinoline 1-oxide in 15 ml of 79% H_2SO_4 was warmed at 90°. To this solution was added 1.3 g of KNO_3 in small portions. After the reaction mixture was kept standing at 90° for 3.5 hr, it was poured into ice water and extracted with CHCl_3 . The chloroform layer was washed with NaHCO_3 solution and dried over Na_2SO_4 . 6-*n*-Hexyl-4-nitroquinoline 1-oxide was isolated as yellow scales by alumina column chromatography eluted with benzene, which weighed 0.14 g. It was recrystallized from MeOH. mp 102°. Yield, 6%. *Anal.* Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_3\text{N}_2$: C, 65.57; H, 6.61; N, 10.21. Found: C, 65.39; H, 6.79; N, 10.08.

6-*n*-Hexyl-4-hydroxyaminoquinoline 1-Oxide—A mixture of 60 mg of 6-*n*-hexyl-4-nitroquinoline 1-oxide, 0.5 ml of EtOH, and 0.5 ml of phenylhydrazine was warmed at 80° for 2 min and kept standing at room temperature for 2 hr. The same treatment of the reaction mixture as the case of 6-*n*-butyl-4-hydroxyaminoquinoline 1-oxide gave yellow powder in a quantitative yield. Recrystallization from MeOH containing an excess of conc. HCl afforded the hydrochloride of 6-*n*-hexyl-4-hydroxyaminoquinoline 1-oxide. mp 179.5—180° (decomp.). *Anal.* Calcd. for $\text{C}_{15}\text{H}_{21}\text{O}_2\text{N}_2\text{Cl}$: C, 60.70; H, 7.08; N, 9.43. Found: C, 60.58; H, 7.18; N, 9.61.

6-*cyclo*-Hexyl-4-nitroquinoline 1-Oxide—A solution of 1.0 g of 6-*cyclo*-hexylquinoline 1-oxide in 10 ml of 79% H_2SO_4 was warmed at 90°. To this solution was added 0.65 g of KNO_3 in small portions. After the reaction mixture was kept at the same temperature for 3.5 hr, it was poured into ice water and extracted with CHCl_3 . The chloroform layer was washed with aqueous NaHCO_3 and dried over anhydrous Na_2SO_4 . After evaporation of the solvent *in vacuo*, the residue was chromatographed through an alumina column with benzene and then CHCl_3 . From the benzene fraction, 0.1 g of yellow scales of 6-*cyclo*hexyl-4-nitroquinoline 1-oxide was obtained, which was recrystallized from MeOH. mp 161—162°. Yield, 8%. *Anal.* Calcd. for $\text{C}_{15}\text{H}_{16}\text{O}_3\text{N}_2$: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.03; H, 5.91; N, 10.61. From the chloroform fraction, 0.4 g of the starting material was recovered.

6-*cyclo*-hexyl-4-hydroxyaminoquinoline 1-Oxide—A mixture of 0.15 g of 6-*cyclo*-hexyl-4-nitroquinoline 1-oxide, 0.5 ml of EtOH, and 0.5 ml of phenylhydrazine was warmed at 80° for 2 min and kept standing at room temperature for 2 hr. The same treatment of the mixture as the case of 6-*n*-butyl-4-hydroxyaminoquinoline 1-oxide afforded yellow powder in a quantitative yield. Recrystallization from MeOH containing conc. HCl gave the hydrochloride as white needles. mp 187—188° (decomp.). *Anal.* Calcd. for $\text{C}_{15}\text{H}_{19}\text{O}_2\text{N}_2\text{Cl}$: C, 61.06; H, 6.45. Found: C, 60.47; H, 6.81.

3-Hydroxy-4-aminoquinoline 1-Oxide—Hundred milligram of 3-methoxy-4-aminoquinoline 1-oxide which was derived from 3-methoxy-4-nitroquinoline 1-oxide by catalytic reduction was dissolved in 5 ml of conc. HBr and sealed in a glass tube, which was warmed at 140—150° in an oil bath for 2 hr. After cooling, the resulting white needles was gathered on a filter and washed with a small volume of water. Recrystallization from MeOH gave white needles of the hydrobromide of 3-hydroxy-4-aminoquinoline 1-oxide in a quantitative yield. mp, 229.5° (decomp.). *Anal.* Calcd. for $\text{C}_9\text{H}_9\text{O}_2\text{N}_2\text{Br}$: C, 42.18; H, 3.51; N, 10.93. Found: C, 42.17; H, 3.57; N, 10.83.

Acknowledgement This work was financially supported by a Grand-in-Aid for Cancer Research from the Ministry of Education.