[Chem. Pharm. Bull. 15(4) 474~480 (1967)]

UDC 547.821.2.07 : 547.831.1.07

59. Masatomo Hamana and Hiroshi Noda: Reactions of Aromatic N-Oxides with Enamines of Cyclohexanone in the Presence of Acylating Agents (3).*1 Reactions of Chloro- and Hydroxy-pyridine and -quinoline N-Oxides.*2

(*Faculty of Pharmaceutical Sciences, Kyushu University**3)

The reactions of 2- and 4-chloro or -hydroxy derivatives of pyridine and quinoline N-oxides with morpholine enamine of cyclohexanone in the presence of an acylating agent were examined. From N-oxides of 4-chloroe derivatives (I, II), 2-(4-chloro-2-pyridyl and -quinolyl)cyclohexanone (III, IV) were obtained in good yields. 2-Chloropyridine 1-oxide gave 2-(2-chloro-4-pyridyl)cyclohexanone (X) as the main product accompanied by a few percent of the 6-pyridyl compound (IX). Similarly 2-chloroquinoline 1-oxide (XII) yielded 2-(2-chloro-4-quinolyl)cyclohexanone (XIII) as a sole product, no displacement of 2-chloro atom being detectable. The reaction of 4-quinolinol 1-oxide (XV) led to the formation of 2-(4-hydroxy-3-quinolyl)cyclohexanone (XVI), accompanied by small amounts of by-products.

(Received May 26, 1966)

As a continuation of our research*1,1) on the reaction between aromatic N-oxides and enamines, 2- and 4-chloro or -hydroxy derivatives of pyridine and quinoline N-oxides were applied to morpholine enamine of cyclohexanone in the presence of an acylating agent.

Reactions of Chloro Derivatives

The general procedures were essentially the same as those reported previously.*1,1) For example, 1.2 equivalents of benzoyl chloride were added dropwise to an ice-cooled solution of 4-chloropyridine 1-oxide (I) and 2.0 equivalents of morpholine enamine of cyclohexanone in chloroform and the reaction was allowed to proceed for 3 days at room temperature. Treatment of the reaction mixture with 20% hydrochloric acid gave 2-(4-chloro-2-pyridyl)cyclohexanone (III), a ylleow oil of b.$p_{0.17}$ 125~127°,in a good yield of 87%.

A similar reaction of 4-chloroquinoline 1-oxide (II) gave rise to 2-(4-chloro-2-quinolyl)-cyclohexanone (IV) of m.p. 97~99° in 78.1% yield.

Structures of III and IV were established by their elemental analyses and by their conversions upon catalytic reduction over palladium-carbon to the known 2-(2-pyridyl)-[1] and 2-(2-quinolyl)cyclohexanone[1] (V and VI), respectively. Further, the chloro atom of IV was shown to be readily replaced with ethoxyl group by the action of sodium ethoxide to yield 2-(4-ethoxy-2-quinolyl)cyclohexanone (VII), yellow needles of m.p. 151~152°. The ultraviolet and infrared spectra of IV and VII demonstrate that both compounds predominantly exist as chelated-enol forms (IV′ and VII′, respectively) in the same way as in VI[1].

Subsequently the reactions of 2-chloro derivatives were examined. When 2-chloro-pyridine 1-oxide (VIII) was treated under comparable condition with the morpholine enamine and benzoyl chloride for 3 days, and the resulted reaction mixture was thoroughly shaken with water instead of treating with hydrochloric acid, there was obtained a mixture of three kinds of products. Separation and purification of these

*1 Part (2). M. Hamana, H. Noda: This Bulletin, **14**, 762 (1966).

*2 Part XXX of the series on "Studies on Tertiary Amine Oxides." For paper XXIX see Yakugaku Zasshi, **86**, 1090 (1966).

*3 Katakasu, Fukuoka (浜名政和, 野田浩司).

1) M. Hamana, H. Noda: This Bulletin, **13**, 912 (1965).

products were performed by distillation under a reduced pressue (a fraction of b.$p_{0.17}$ 135~160° was collected) and by subsequent chromatography on alumina using carbon tetrachloride, benzene and chloroform to afford 2-(6-chloro-2-pyridyl)cyclohexanone (IX, 2.9%), 2-(2-chloro-4-pyridyl)cyclohexanone (X, 50.8%) and N-benzoylmorpholine.[2] Both IX and X were pale yellow oils and formed the corresponding oximes of the same empirical formula $C_{11}H_{13}ON_2Cl$ (m.p. 166~167.5° and 157~158°); they were catalytically reduced to 2-(2-pyridyl)-[1] (V) and 2-(4-pyridyl)cyclohexanone[1,3] (XI), respectively.

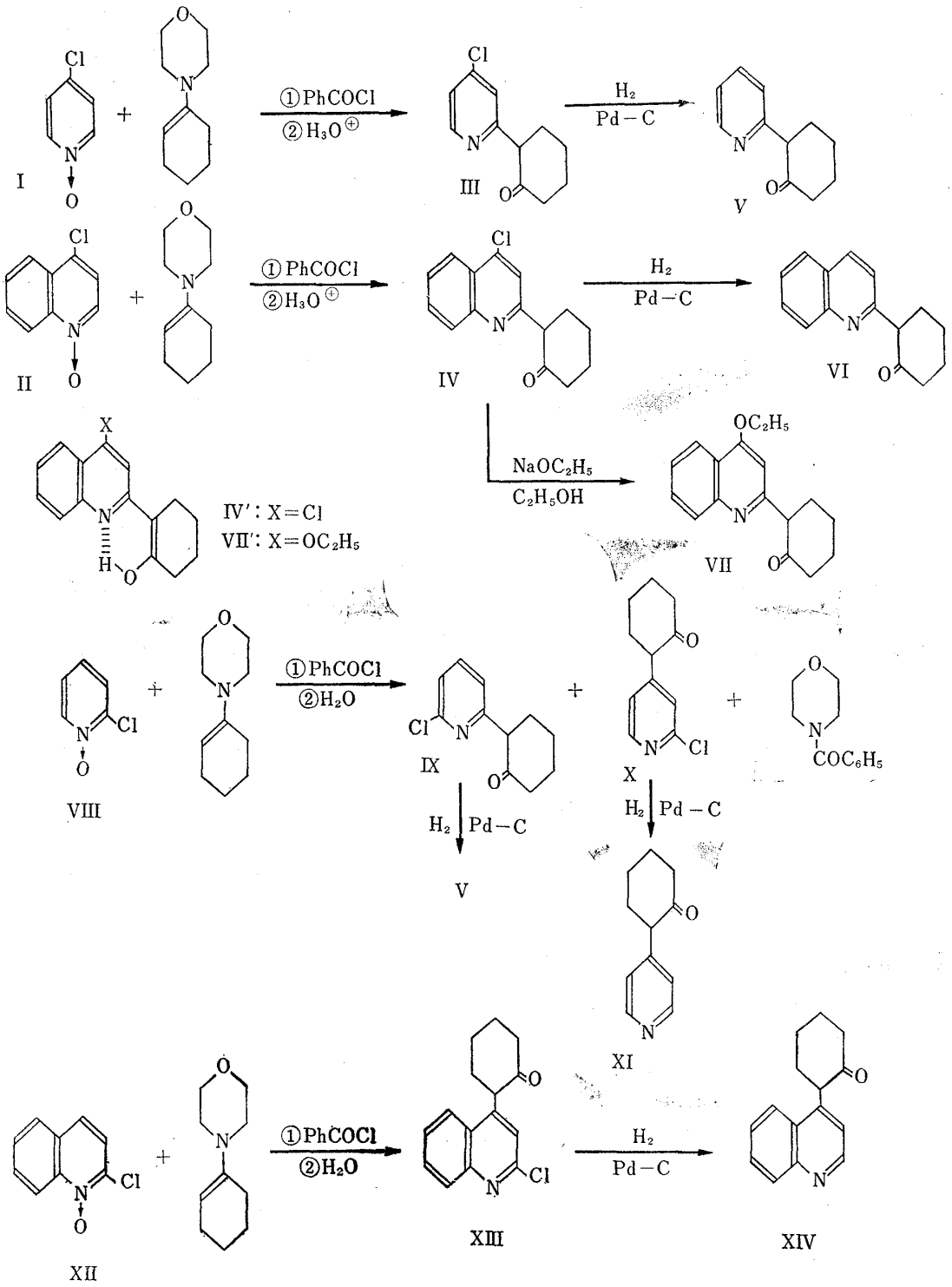


Chart 1.

2) L. Knorr : Ann., **301**, 7 (1898).

The reaction of 2-chloroquinoline 1-oxide (XII) progressed also smoothly and resulted in the exclusive formation of 2-(2-chloro-4-quinolyl)cyclohexanone (XIII) in 54% yield as the outcome of nuclear substitution, no displacement of 2-chloro atom being detectable. The product, XIII, showed the ultraviolet spectrum closely similar to that of 2-chlorolepidine and was transformed by catalytic reduction into 2-(4-quinolyl)cyclohexanone (XIV).[1)]

These results are shown in Chart 1.

Kuehne[4)] has reported that 2-chloroquinoline reacts with pyrrolidine enamine of cyclohexanone to give not 2-(2-quinolyl)cyclohexanone but instead 2-pyrrolidinoquinoline in an unsatisfactory yield. Further, as described in a previous paper, heating of 4-chloroquinoline 1-oxide with the morpholine enamine in dioxane merely resulted in formation of 4-morpholinoquinoline.[1)] Together with these facts, the results mentioned above demonstrate that neither the α- or γ-chloro atom activated by nuclear nitrogen of pyridine ring nor that activated by more electron-attracting N-oxide function is capable of undergoing nucleophilic substitution with the enamine; furthermore, the derivation of N-oxide function to $\overset{\oplus}{\text{N}}$-O-acyl group has no substantial effect in enhancing the reactivity of the chloro atom toward the reaction. On the contrary, it is made clear that the nucleophilic attack of the enamine on the acyl-adduct of aromatic N-oxide by the addition-elimination mechanism proceeds very readily, and it occurs not only at the α-position but also at the γ-position to the N-oxide group.

Since the reaction of 2-chloro derivatives, VIII and XII, leads to the introduction of cyclohexanone in the 4-position of pyridine ring in fairly good yields and also the products easily undergo dehalogenation by catalytic reduction, this route would be promising for the synthesis of 4-substituted derivatives.

Reactions of Hydroxy Derivatives

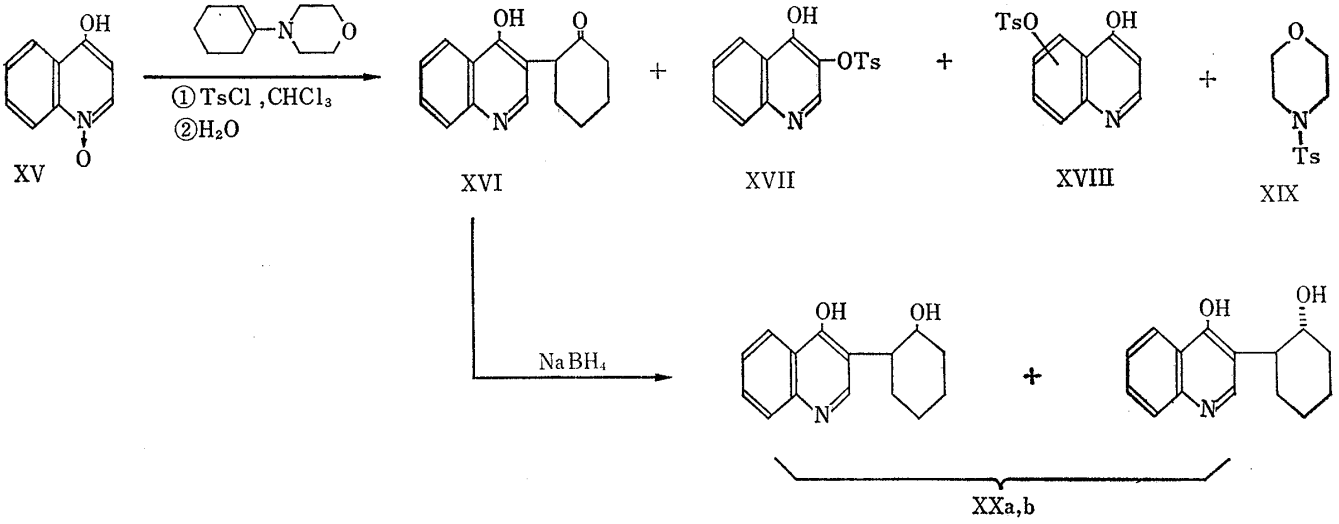
A suspension of 4-quinolinol 1-oxide (XV) in chloroform was vigorously stirred under ice-cooling with the morpholine enamine (3 equiv.) and tosyl chloride (1.2 equiv.) for 3 hours and the reaction mixture was kept overnight at room temperature. As described in the case of 2-chloropyridine 1-oxide, the reaction mixture was treated with water, followed by extracting with chloroform, and the mixture of crude products was subjected to chromatography on alumina using benzene and chloroform-ethanol (9:1) to give 2-(4-hydroxy-3-quinolyl)cyclohexanone (XVI, m.p. 235~236°, 30.5%), 3-tosyloxy-4-quinolinol (XVII, m.p. 238~240°, 11.7%), an isomer of XVII (XVIII, m.p. 250~251°, 2.9%) and N-tosylmorphine[5)] (XIX, 10.7%).

From its analytical values and infrared absorption spectrum ($\nu_{C=O}$ 1715, 1637 cm^{-1}), XVI was assumed to be a (4-hydroxyquinolyl)cyclohexanone. Reduction of XVI with sodium borohydride in ethanol gave rise to two kinds of alcohols of the same empirical formula $C_{15}H_{17}O_2N$ (XXa, m.p. 217~219° and XXb, m.p. 277~278°) though in poor yields (17.5 and 8.1%, respectively). Although there are slight differences between their infrared spectra, their ultraviolet spectra are qiute similar not only each other but also to that of XVI. Therefore, they were most probably considered to be a pair of diastereoisomeric (4-hydroxyquinolyl)cyclohexanols corresponding to XVI. On heating XXa, an isomer obtained in a relatively larger amount, with selenium at 310~330° for 2 hours, we obtained the known 3-phenyl-4-quinolinol (XXI), which was identified as it by direct comparison with an authentic specimen prepared by another method.[6)]

3) W. von E. Doering, W. E. McEwen: J. Am. Chem. Soc., **73**, 2104 (1951).
4) M. E. Kuehne: J. Am. Chem. Soc., **84**, 837 (1962).
5) J. Sand: Ber., **34**, 2908 (1901).
6) W. Wislicenus, K. Börner, P. Kurtz, E. A. Bilhuber: Ann., **413**, 206 (1917).

Consequently, XVI was unequivocally shown to be 2-(4-hydroxy-3-quinolyl)cyclohexanone.

The structure of 3-tosyloxy-4-quinolinol (XVII) was established by comparing it with an authentic sample prepared by the known method.[7] Another tosyloxy compound, XVIII, is presumably considered to be 6- or 8-tosyloxy-4-quinolinol from its empirical formula, infrared spectrum and also from the reaction mode of analogous compounds,[7] but detailed structure has not been elucidated yet.



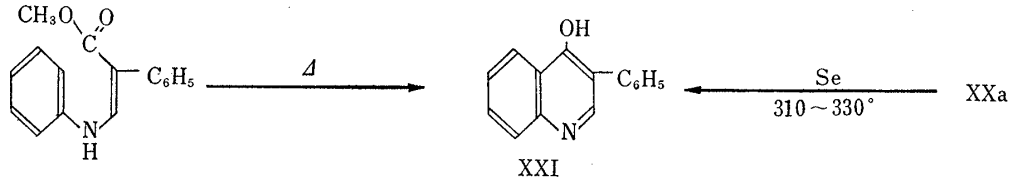


Chart 2.

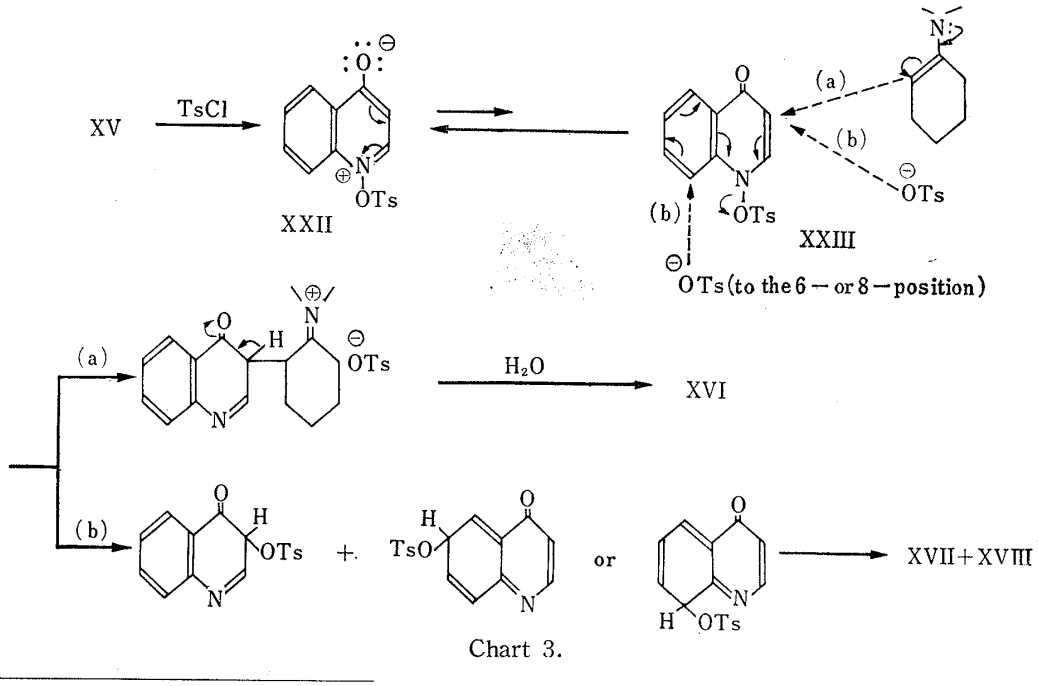


Chart 3.

7) M. Hamana, K. Funakoshi : Yakugaku Zasshi, **84**, 28 (1964).

The reaction of XV with the enamine should be considered to be initiated by the attack of tosyl chloride on XV in the same manner as reported previously.*[1,1] In this case the tosylated product of XV is N-tosyloxy betaine (XXII) as pointed out by infrared examination of acyl derivatives of XV.[8] The subsequent courses may be rationalized by the following reaction sequence (Chart 3).

Cleavage of tosyloxy anion from the quinolone (XXIII), derived from XXII, would cause the electron deficiency at the 3-, 6- and 8-positions of the quinoline ring. Thus, nucleophilic attack by the enamine at the 3-position, followed by a proton shift and hydrolysis affords the product XVI (course a). Formation of XVII and XVIII may be similarly explained by the course b. The course a is neccessarily intermolecular, but it is not clear whether elimination of tosyloxy group from XXIII and nucleophilic attack by the enamine is a two-step process or a synchronous one. The detailed mechanism of the apparent rearrangement of tosyloxy group also remains to be explored.

Although there are reported a number of reactions[7,9] of aromatic N-oxide with acylating agent in which substiution occurs at the β-position to N-oxide function or/ and the corresponding ones accompanied by extrusion of acyloxy group bound to nitrogen, no example can be found which leads to the introduction of a carbon-substituent into the above-mentioned position. From this point of view, the formation of XVI is very noticeable for both the theoretical and preparative implications.

Attempted substitution of 4-hydroxypyridine 1-oxide or 1-hydroxycarbostyril with enamine of cyclohexanone, under various conditions, was unsuccessful and resulted in only formation of N-acyl derivatives of the basic moiety of enamine, *e.g.* N-tosylmorpholine. No expected product was obtained from the reaction of 1-tosyloxy-2-pyridone or 1-tosyloxycabostyril, too. The latter compound underwent the different reactions to yield various product including C-toyloxycarbostyrils, carbostyril and 1-hydroxycarbostyril, depending upon nature of reagents. These results will be reported in another paper.

Experimental*4

Reaction of 4-Chloropyridine 1-Oxide (I) with Morpholine Enamine of Cyclohexanone——To an ice-cooled solution of I (1.3 g.) and the morpholine enamine (3.68 g.) in $CHCl_3$ (10 ml.), PhCOCl (1.69 g.) was added dropwise with stirring and the whole was kept standing at room temperature for 3 days. The dark orange mixture was poured into 20% HCl (20 ml.) and left standing overnight with occasional shaking. It was then concentrated under reduced pressure (below 45° of bath-temp.), washed with benzene-ether mixture, basified with solid K_2CO_3 and extracted with $CHCl_3$. Evaporation of the solvent left an oil, which was distilled *in vacuo* to give 1.81 g. of 2-(4-chloro-2-pyridyl)cyclohexanone (III), a deep yellow oil, $b.p_{0.17}$ 125～127°. Picrate: m.p. 172～174°(EtOH). *Anal.* Calcd. for $C_{11}H_{12}ONCl \cdot C_6H_3O_7N_3$: C, 46.52; H, 3.42; N, 12.77. Found: C, 46.82; H, 3.58; N, 12.91.

Catalytic Reduction of 2-(4-Chloro-2-pyridyl)cyclohexanone (III)——A solution of III (0.84 g.) in MeOH (30 ml.) was hydrogenated at ordinary temperature and pressure over 9% Pd-C (0.22 g.). After uptake of 1 equivalent of hydrogen, the filtered and concentrated solution was treated with Na_2CO_3 solution and extracted with $CHCl_3$. The dried extract on evaporation gave 0.64 g. (91.4%) of 2-(2-pyridyl)cyclohexanone (V), $b.p_{0.03}$ 130°(bath-temp.). Picrate: m.p. 159～160°(EtOH), undepressed on admixture with a sample obtained before.[1]

Reaction of 4-Chloroquinoline 1-Oxide (II) with Morpholine Enamine of Cyclohexanone——The reaction of II (0.9 g.) with the morpholine enamine (1.84 g.) and PhCOCl (0.87 g.) in $CHCl_3$ (5 ml.) was carried out as described for I. Recrystallization of the crude product from MeOH gave 0.84 g. of 2-(4-chloro-2-quinolyl)-cyclohexanone (IV), red needles, m.p. 97～99°. The methanolic mother liquor was evaporated and the residue was purified by chromatography in benzene on alumina to afforded additional 0.173 g. of IV. *Anal.* Calcd.

*4 All melting and boiling points are uncorrected.

8) Ch. Kaneko: *Ibid.*, **79**, 428 (1959).

9) *a*) E.Ochiai: Ann. Rept. ITSUU Lab. (Tokyo), **12**, 43 (1962). *b*) S. Oae, T. Kitao: Kagaku to Kogyo, **16**, 762 (1963). *c*) References quoted in 7).

for $C_{15}H_{14}ONCl$: C, 69.36; H, 5.39; N, 5.39. Found: C, 69.43; H, 5.47; N, 5.59. UV λ_{max}^{EtOH} mμ (log ε): 216 (4.57), 282.5 (4.16), 302 (4.01), 332 (3.81), 337 (3.72), 440 (3.60).

Catalytic Reduction of 2-(4-Chloro-2-quinolyl)cyclohexanone (IV)——Catalytic reduction of IV (0.56 g.) with hydrogen and 10% Pd-C (0.1 g.) in MeOH (40 ml.) gave 0.33 g. of 2-(2-quinolyl)cyclohexanone (VI), m.p. 117~119°.[1]

Reaction of 2-(4-Chloro-2-quinolyl)cyclohexanone (IV) with Sodium Ethoxide——A mixture of IV (1.04 g.) and NaOEt-EtOH (Na 0.14 g., EtOH 30 ml.) was refluxed on a water-bath for 3 hr., the color of solution turning from red to deep yellow during a period of 2 hr. After cooling, NaCl deposited was filtered off, and the filtrate was weakly acidified with conc. HCl and concentrated under reduced pressure. The residue was made alkaline with 10% NaOH and extracted with $CHCl_3$. The $CHCl_3$ extract on evaporation gave a solid, which was recrystallized from MeOH to afford 0.93 g. (86%) of 2-(4-ethoxy-2-quinolyl)cyclohexanone (VII), yellow needles, m.p. 151~153°. *Anal.* Calcd. for $C_{17}H_{19}O_2N$: C, 75.18; H, 7.11; N, 5.20. Found: C, 75.54; H, 6.89; N, 5.43. UV λ_{max}^{EtOH} mμ (log ε): 216 (4.65), 292.5 (4.29), 324 (4.12), 415 (4.22).

Reaction of 2-Chloropyridine 1-Oxide (VIII) with Morpholine Enamine of Cyclohexanone——To an ice-cooled solution of VIII (2.95 g.) and the enamine (8.42 g.) in $CHCl_3$ (10 ml.), PhCOCl (3.85 g.) was added dropwise with stirring. After standing for 3 hr. at room temperature, the reaction mixture was occasionally shaken with water (20 ml.) and kept standing overnight. The aqueous layer was made alkaline with solid K_2CO_3, separated from the $CHCl_3$ layer and extracted with $CHCl_3$. The combined $CHCl_3$ solution on evaporation gave an oily mixture of $b.p_{0.17}$ 135~160°, which was chromatographed on alumina using CCl_4, benzene and then $CHCl_3$ for elution. The first fraction afforded 0.137 g. of 2-(6-chloro-2-pyridyl)cyclohexanone (IX), a pale yellow oil, which formed an oxime, colorless needles, m.p. 166~167.5°(isopropyl ether). *Anal.* Calcd. for $C_{11}H_{13}ON_2Cl$: C, 58.79; H, 5.83; N, 12.47. Found: C, 58.36; H, 5.82; N, 12.40. The second gave 1.91 g. of 2-(2-chloro-4-pyridyl)cyclohexanone (X), a yellow oil. Oxime: colorless needles, m.p. 157~158°(isopropyl ether). *Anal.* Calcd. for $C_{11}H_{13}ON_2Cl$: C, 58.79; H, 5.83; N, 12.47. Found: C, 58.46; H, 5.73; N, 12.27. The third fraction gave 1.64 g. of N-benzoylmorpholine, colorless pillars, m.p. 74~76° (petr. benzin).[2] *Anal.* Calcd. for $C_{11}H_{13}O_2N$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.42; H, 6.75; N, 7.32.

Catalytic Reduction of 2-(6-Chloro-2-pyridyl)- (IX) and 2-(2-Chloro-4-pyridyl)cyclohexanone (X)——1) IX (0.06 g.) was reduced catalytically with hydrogen and 10% Pd-C (0.055 g.) in MeOH (10 ml.) to give 0.05 g. of a yellow oil (V), which was proved to be identical with an authentic sample of 2-(2-pyridyl)-cyclohexanone[1] by comparison of their IR spectra and by admixture of their picrates.

2) Catalytic reduction of X (1.2 g.) was carried out with 8% Pd-C (0.26 g.) in MeOH (20 ml.). The basic product was distilled under reduced pressure, $b.p_{0.32}$ 150~160°(bath-temp.), followed by recrystallization from *n*-hexane to afford 0.9 g. of 2-(4-pyridyl)cyclohexanone, colorless needles, m.p. 106~108.5°, which was shown identical with an authentic sample.[1,3] *Anal.* Calcd. for $C_{11}H_{13}ON$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.02; H, 7.34; N, 7.75.

Reaction of 2-Chloroquinoline 1-Oxide (XII) with Morpholine Enamine of Cyclohexanone——To an ice-cooled solution of XII (1.8 g.) and the enamine (3.34 g.) in $CHCl_3$ (30 ml.), PhCOCl (1.59 g.) was added dropwise with stirring. After standing for 3 days at room temperature, the reaction mixture was shaken with water (30 ml.) for 3 hr., basified with solid K_2CO_3 and the aqueous layer was separated and extracted with $CHCl_3$. The combined $CHCl_3$ solution was evaporated, and the residue was chromatographed on alumina using benzene and ether for elution. The first eluate afforded 1.43 g. of 2-(2-chloro-4-quinolyl)cyclohexanone (XIII), colorless prisms, m.p. 100~101°(petr. benzin). UV λ_{max}^{EtOH} mμ (log ε): 235 (4.60), 285 (3.66), 292 (3.64) (inflec.), 306 (3.58), 320 (3.60).*5 *Anal.* Calcd. for $C_{15}H_{14}ONCl$: C, 69.36; H, 5.39; N, 5.39. Found: C, 69.42; H, 5.56; N, 5.73. Oxime: m.p. 162~163°(MeOH-H_2O). *Anal.* Calcd. for $C_{15}H_{15}ON_2Cl$: C, 65.57; H, 5.50; N, 10.20. Found: C, 65.68; H, 5.67; N, 10.20. The second eluate gave 0.9 g. of N-benzoyl-morpholine,[5] m.p. 74~76°(petr. benzin).

Catalytic Reduction of 2-(2-Chloro-4-quinolyl)cyclohexanone (XIII)——Catalytic reduction of XIII (0.7 g.) with hydrogen and 14% Pd-C (0.15 g.) in MeOH (100 ml.) yielded 0.4 g. (65.6%) of 2-(4-quinolyl)cyclohexanone (XIV), m.p. 127~128°, undepressed on admixture with an authentic sample.[1]

Reaction of 4-Quinolinol 1-Oxide (XV) with Morpholine Enamine of Cyclohexanone——To an ice-cooled suspension of XV (1.75 g.) and the enamine (5.01 g.) in $CHCl_3$ (30 ml.) was added TsCl (2.29 g.) in small portions under stirring. After strring was continued for further 3 hr., the mixture was kept standing overnight at room temperature, and then vigorously shaken with water (30 ml.) for 3 hr., and the aqueous layer was separated and extracted with $CHCl_3$. The combined $CHCl_3$ solution was dried and evaporated. The residue was treated with a small amount of ether followed by standing overnight to afford a solid, which was recrystallized from EtOH to give 0.13 g. of 3-tosyloxy-4-quinolinol (XVIII), colorless needles, m.p. 238~240°, undepressed on admixture with an authentic sample.[7]. The mother liquor was evaporated and the residue was taken up in as possible as small amount of $CHCl_3$. The $CHCl_3$ solution was poured onto alumina column and eluted with benzene and then $CHCl_3$-EtOH (9:1) mixture. From the benzene eluents

*5 UV spectrum of 2-chlorolepidine, λ_{max}^{EtOH} mμ (log ε): 232 (4.71), 280 (3.68), 292.5 (3.60) (inflec.), 305 (3.56), 319 (3.64).

0.31 g. of N-tosylmorpholine (XIX) was obtained; colorless pillars, m.p. 147~148.5°.[5] *Anal.* Calcd. for $C_{11}H_{15}O_3NS$: C, 54.77; H, 6.22; N, 5.83. Found: C, 54.79; H, 6.37; N, 5.65. The first fraction eluted with $CHCl_3$-EtOH mixture gave an additional 0.27 g. of XIX, and the second was recrystallized from MeOH to afford 0.61 g. of 2-(4-hydroxy-3-quinolyl)cyclohexanone (XVI), m.p. 235~236°. UV λ_{max}^{EtOH} mμ (log ε): 212 (4.50), 238.5 (4.39), 242 (4.40), 247.5 (4.36) (inflec.), 291.5 (3.60), 323 (4.07), 336 (4.10). *Anal.* Calcd. for $C_{15}H_{15}O_2N$: C, 74.66; H, 6.27; N, 5.81. Found: C, 74.67; H, 6.40; N, 5.82. Oxime: colorless leaflets, m.p. 242~243° (MeOH). *Anal.* Calcd. for $C_{15}H_{16}O_2N_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.08; H, 6.27; N, 10.89. The third fraction yielded 0.1 g. of x-tosyloxy-4-quinolinol (XVIII), m.p. 250~251° (EtOH). *Anal.* Calcd. for $C_{16}H_{13}O_4NS$: C, 60.94; H, 4.16; N, 4.44. Found: C, 60.61; H, 4.11; N, 4.94.

Conversion of 2-(4-Hydroxy-3-quinolyl)cyclohexanone (XVI) to 3-Phenyl-4-quinolinol (XXI)——1) Reduction of XVI with $NaBH_4$: A solution of XVI (1.3 g.) and $NaBH_4$ (0.31 g.) in anhyd. EtOH (150 ml.) was refluxed for 4 hr. The solvent was disttiled off *in vacuo*, and the residue was treated with water, acidified with 10% HCl and basified again with solid $NaHCO_3$, and extracted with $CHCl_3$. The $CHCl_3$ extract on evaporation afforded a solid which was recrystallized from AcOEt-petr. ether to give 0.23 g. of colorless crystals (XXa), m.p. 217~219°. UV λ_{max}^{EtOH} mμ (log ε): 212 (4.53), 239 (4.48), 243 (4.48), 248 (4.45) (inflec.), 292.5 (3.55), 325.5 (4.12), 339.5 (4.17). *Anal.* Calcd. for $C_{15}H_{17}O_2N$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.42; H, 6.95; N, 6.13. The residue undissolved in $CHCl_3$ was recrystallized from MeOH to yield 0.11 g. of colorless crystals (XXb), m.p. 277~278°. UV λ_{max}^{EtOH} mμ (log ε): 212 (4.48), 239 (4.44), 243 (4.44), 248 (4.31) (inflec.), 292.5 (3.54), 325.5 (4.07), 339 (4.09). *Anal.* Calcd. for $C_{15}H_{17}O_2N$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.31; H, 7.34; N, 5.86. 2) Selenium Dehydrogenation of XXa: A mixture of XXa (0.174 g.) and Se (0.7 g.) was heated at 310~330° for 2 hr., cooled and extracted with hot MeOH. The crude product was recrystallized from MeOH to give 0.04 g. of pale yellow prisms (XXI), m.p. 252~253°, which were proved to be identical with an authentic sample of 3-phenyl-4-quinolinol prepared from another route[6] by admixture and by comparison of thier IR spectra. *Anal.* Calcd. for $C_{15}H_{11}ON$: C, 81.45 H, 5.01; N, 6.33. Found: C, 81.06; H, 4.96; N, 6.23.

A part of expenses for this work was defrayed by the Grant-in-Aid for Scientific Research from the Ministry of Education, which is gratefully acknowledged. Thanks are also due to Messrs. M. Shido, K. Ishimura, Y. Inoue, Miss Y. Takahashi and Miss T. Tahara for elemental analysis, to Mr. H. Matsui and Miss K. Soeda for the measurement of IR and UV absorption spectra, and to Mr. J. Uchida for technical assistance.