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Studies on Tertiary Amine Oxides. LXI.[1] Some Reactions of 2-Phenylquinoline 1-Oxide and Its Derivatives

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The orientation of nitration of 2-phenylquinoline 1-oxide (**1**) with potassium nitrate and sulfuric acid was found to be principally governed by the concentration of sulfuric acid independently of the reaction temperature. Thus, whereas the reaction in concentrated sulfuric acid gave 3'-nitro derivative (**3**) as the main product, the use of 70—75% sulfuric acid was favorable for the formation of 4-nitro derivative (**2**). Further nitration of **2** and **3** readily produced 3',4-dinitro compound (**4**). The Reissert-Henze reaction of 2-(4-methoxyphenyl)quinoline 1-oxide (**7**) afforded 1-benzoyloxy-4-cyano-1,4-dihydroquinoline (**12**) besides 4-cyano (**9**), 6-benzoyloxy- (**10**) and 8-benzoyloxy-quinolines (**11**). From the reaction of 2-(4-nitrophenyl)quinoline 1-oxide (**8**), the corresponding 1,4-dihydroquinoline (**15**) was also isolated together with 6- and 3-benzoyloxyquinolines (**13** and **14**). The mechanism of the formation of benzoyloxy derivatives was discussed.

Keywords——nitration; Reissert-Henze reaction; nucleophilic reaction; N-benzoyloxyquinolinium chlorides; 1,2-dihydroquinoline; 1,4-dihydroquinoline; acyloxy migration

An earlier paper[3] of this series has described that nitration of 2-phenylquinoline 1-oxide (**1**) gives 4-nitro derivative (**2**) under some conditions and the reaction of **1** with benzoyl chloride and aqueous potassium cyanide (the Reissert–Henze reaction[4]) affords 4-cyano- (10%), 6-benzoyloxy- (25%) and 8-benzoyloxy-2-phenylquinolines (8%). However, nitration of **1** was shown to be affected subtly by reaction conditions and the correlation between the reaction conditions and the direction of nitration was not established. As for the formation mechanism of the 6- and 8-benzoyloxy derivatives, the possibility of course c) shown in Chart 2 was suggested besides the generally accepted course b).

The present work was carried out to explore these aspects in some detail and the following results were obtained.

Nitration of 2-Phenylquinoline 1-Oxide (1)

It has been previously found that whereas treatment of **1** (1.1 g) in concentrated sulfuric acid (d=1.84, 2 ml) with concentrated nitric acid (d=1.38, 0.5 g) at 60—70° for 1 hour did give 2-phenyl-4-nitroquinoline 1-oxide (**2**) in 55% yield, the reaction was markedly sensitive to reaction conditions; for example, another run under practically the same conditions using somewhat larger amounts of reactants gave no **2** but only a dinitro derivative (mp *ca.* 210°) accompanied by the recovery of **1**. Taking into account of the temperature effect in nitration of quinoline 1-oxides,[5] some conditions were examined but the reporducible conditions could not be established at that time.

In a while after the completion of this study, one of the authors (M. H.) and Nagayoshi[6] have re-examined nitration of 6-substituted quinoline 1-oxides with potassium nitrate and

1) Part LX: H. Noda, K. Narimatzu, and M. Hamana, *Yakugaku Zasshi*, **96**, 1417 (1976).
2) Location: *Maidashi, Higashi-ku, Fukuoka, 812, Japan.*
3) M. Hamana and K. Shimizu, *Yakugaku Zasshi*, **86**, 59 (1966).
4) M. Henze, *Ber.*, **69**, 1566 (1936).
5) *a*) E. Ochiai and T. Okamoto, *Yakugaku Zasshi*, **70**, 384 (1950); *b*) T. Okamoto, *ibid.*, **71**, 727 (1951); *c*) E. Ochiai and K. Satake *ibid.*, **71**, 1078 (1951).
6) M. Hamana and T. Nagayoshi, *Chem. Pharm. Bull.* (Tokyo), **14**, 319 (1966).

sulfuric acid and revealed that the orientation of reaction was more markedly dependent upon the concentration of sulfuric acid rather than the reaction temperature: the use of the acid of somewhat lower concentrations (75—85%) was shown to be most effective for the formation of 4-nitro derivatives, the temperature effect being noticed only to a small extent. Therefore, we re-examined nitration of **1** with potassium nitrate and sulfuric acid by varing the concentratoin of the acid as well as the reaction temperature .

When **1** was retated with potassium nitrate (1.1 equiv.) in 80—95% sulfuric acid at 0—5°, room temperatures or 60—70°, 2-(3-nitrophenyl)quinoline 1-oxide (**3**), yellow needles, mp 198°, was obtained always as the main product (27—78%) accompanied with a small amount of 2-(3-nitrophenyl)-4-nitroquinoline 1-oxide (**4**), yellow needles, mp 212°, in some cases. On the other hand, 2-phenyl-4-nitroquinoline 1-oxide (**2**), yellow needles, mp 137°, was produced as the main product (19—38%) by employment of 70—75% sulfuric acid, and **3** or **4** was isolated as a minor product in a few cases (Table I).

Table I. Nitration of 2-Phenylquinoline 1-Oxide (**1**)

Concentration of H_2SO_4 (%)	Amopunt of KNO_3 (eq.)	Reaction conditions		Products (yield, %)			Recov. 1 (%)
		temp.	time (hr)	**2**	**3**	**4**	
95	1.1	R.T.	24	—	72	—	—
90	1.1	0—5°	24	—	75	—	—
	1.1	R.T.	24	—	36	—	—
85	1.2	R.T.	24	—	66	5	—
	1.2	60—70°	1	—	27	—	13
80	1.2	R.T.	24	—	78	6	—
	1.1	0—5°	96	—	30	3	—
75	1.2	R.T.	144	25	—	—	27
	1.1	R.T.	384	37	18	—	—
	1.1	60—70°	1	38	—	—	16
	1.1	60—70°	10	28	18	—	—
	1.1	60—70°	2	23	—	1	23
70	1.1	R.T.	504	19	—	—	36

R.T.: room temp.

The structure assignment of these products was based on the following reactions. Compound **3** was deoxygenated with phosphorus trichloride to 2-(3-nitrophenyl)quinoline (**5**) followed by conversion to the corresponding methopicrate (**6**), which was proved identical with an authentic sample prepared from 2-phenylquinoline methosulfate by the method of Le Fevre and Mathur.[7] Treatment of **2** with phosphorus thichloride gave 2-phenyl-4-chloroquinoline as described in the previous paper[3,8] and **2** was shown to be identical with a sample obtained from 4-nitroquinoline 1-oxide and benzoylperoxide by the method of Kosuge, *et al.*[9] The dinitro derivative **4** was found to be identical with an unidentified dinitro compound briefly mentioned in the previous paper,[3] and it was found to be obtained by nitration of either **2** or **3** with potassium nitrate in 90% sulfuric acid. These reactions are shown in Chart 1.

The mono-nitration of 2-phenylquinoline[7] and 2-phenylpyridine[10] have been reported to occur at the 3- or 4-position of the respective 2-phenyl groups. Hands and Katritzky[11] have shown that nitration of 2-phenylpyridine 1-oxide with concentrated nitric and sulfuric

7) J.R. Wood, Le Fevre, and F.C. Mathur, *J. Chem. Soc.*, **1930**, 2236.
8) A. Risalti, *Ricerca Sci.*, **24**, 2351 (1954).
9) T. Kosuge, K. Adachi, M. Yokota, and T. Nakao, *Yakugaku Zasshi*, **85**, 66 (1965).
10) R. Forsynth and F.L. Pyman, *J. Chem. Soc.*, **1926**, 2912.
11) A.R. Hands and A.R. Katritzky, *J. Chem. Soc.*, **1958**, 1754.

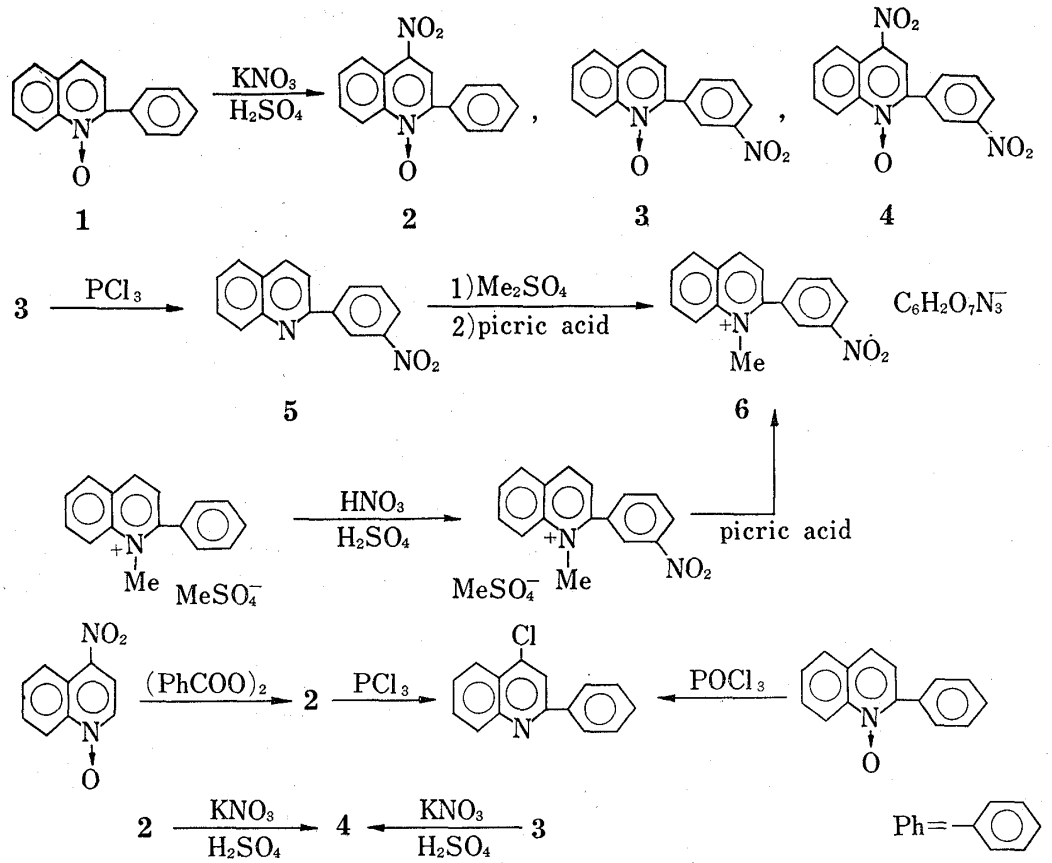

Chart 1

acids also affords 2-(3- or 4- nitrophenyl)pyridine 1-oxide although the ratio of 3- to 4- nitrophenyl derivative slightly differs from that observed in nitration of 2-phenylpyridine. It was further confirmed in our laboratory that comparable nitration of 2-phenylpyridine 1-oxide with potassium nitrate and sulfuric acid under various conditions did not afford 4-nitro derivative at all.[12]

The above-mentioned results apparently indicate that the orienting effect of the N-oxide function operates in nitration of **1** under some conditions, especially those using 70—75% sulfuric acid, and the concentration of sulfuric acid is a more important factor than the reaction temperature for γ-nitration of **1**; however the optimum conditions for the preparation of **2** were established. It is not unexpectedly that the electron-donating effect of the N-oxide function in **1** cannot extend to 2-phenyl side chain, but the difference between behavior of 2-phenylquinoline 1-oxide and that of 2-phenylpyridine 1-oxide towards nitration is noticeable.

The Reissert-Henze Reaction of 2-(4-Methoxyphenyl)-quinoline 1-Oxide (7) and 2-(4-Nitrophenyl)quinoline 1-Oxide (8)

The formation of 2-phenyl-4-cyanoquinoline in the Reissert-Henze reaction[4] of **1** can be explained by course a) shown in Chart 2, which involves the formation of 1,4-dihydroquinoline intermediate (**A**) followed by elimination of benzoic acid from **A**. According to the generally accepted mechanism for nucleophilic substitution at the β- or/and the corresponding positions in the reaction of acyl-adduct of aromatic N-oxide,[13] the formation of

12) H. Muro's experiment.
13) *a*) E. Ochiai, "Aromatic Amine Oxides," Elsevier Publishing Co., Amsterdam, 1967, Chapter 7; *b*) A.R. Katritzky and J.M. Lagowski, "Chemistry of the Heterocyclic N-Oxides," Academic Press, London and New York, 1971, Chapter III-4.

3-, 6- and 8-benzoyloxy derivatives of 2-phenylquinoline from **1** should be considered to follow course b), in which the extrusion of benzoyloxy group from the 1,4-dihydroquinoline intermediate **A** and the concerted rearrangement of the benzoyloxy anion are the crucial steps. However as pointed out in the previous paper,[3] there might be well considered an alternative course c) involving another 1,2-dihydroquinoline intermediate (**B**) formed by the participation of 2-phenyl group. In order to explore which course of b) and c) is more likely, the reaction was examined with 2-(4-methoxyphenyl)-quinoline 1-oxide (**7**) and 2-(4-nitrophenyl) quinoline (**8**).

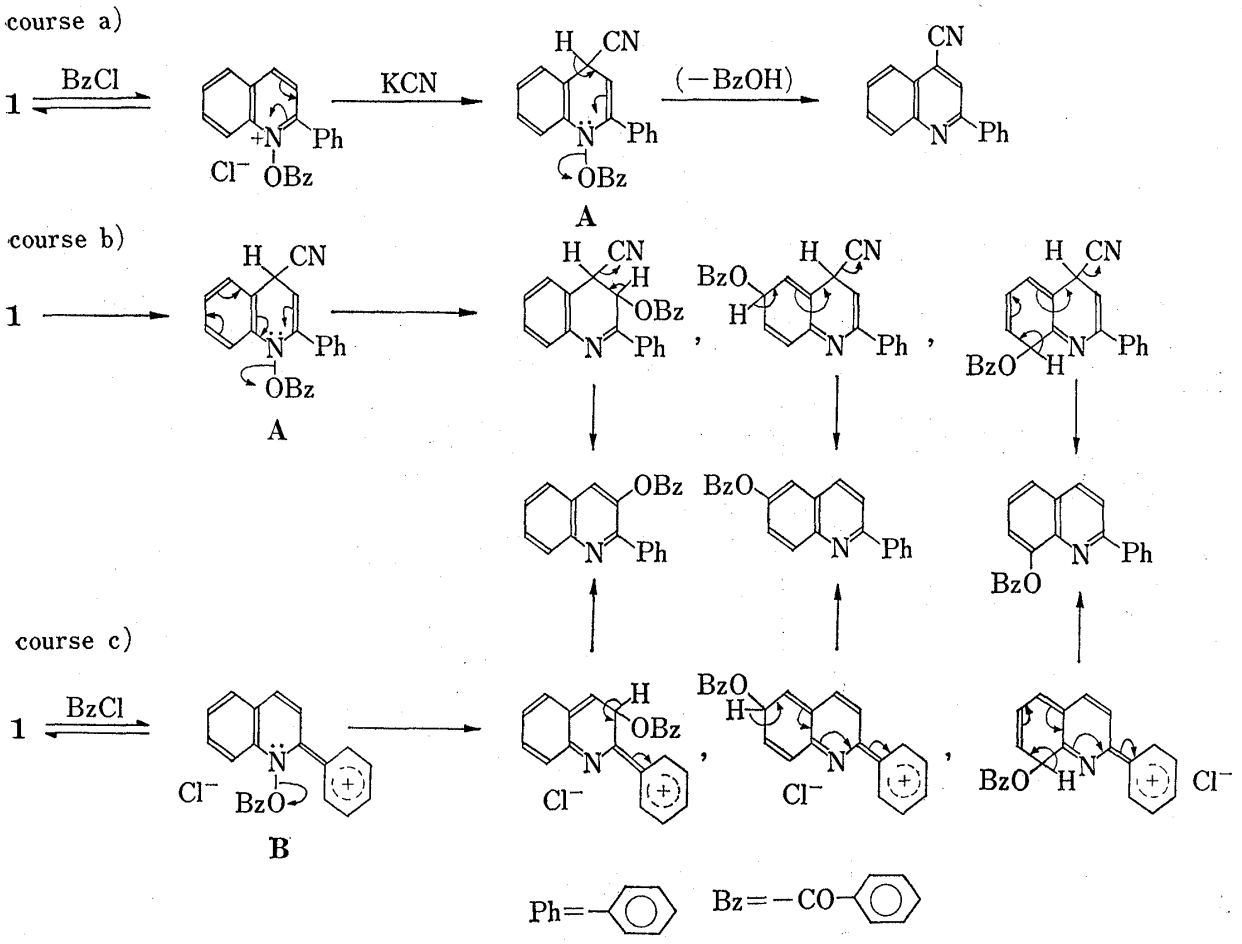

Chart 2

At first the reaction of **7** was examined in some detail under several conditions. Aqueous potassium cyanide (*ca.* 3 equiv.) and benzoyl chloride (*ca.* 1.4 equiv.) were successively added with stirring to an ice-cooled solution of **7** in chloroform, and the reactants were allowed to react under the respective conditions shown in Table II. Thus, in addition to 4-cyano (**9**) and two benzoyloxy derivatives (**10** and **11**), a 1,4-dihydroquinoline (**12**) was isolated in all cases (Table II and Cahrt 3).

The structure of **9** was unequivocally confirmed by direct comparison with an authentic sample of 2-(4-methoxyphenyl)-4-cyanoquinoline prepared by the reaction of isatin and *p*-methoxyacetophenone[14] followed by conversion[15] of the 4-quinolinecarboxylic acid thus formed. Hydrolysis of **10** and **11** with hydroiodic acid yielded 2-(4-hydroxyphenyl)-6-

14) H.C. Lindwall and J.S. Maclember, *J. Am. Chem. Soc.*, **54**, 4739 (1932).
15) C.S. Miller, "Organic Syntheses," Coll. Vol. III, ed. by E.C. Horning, John Wiley, and Sons, Inc., New York, 1955, p. 646.

Table II. Reaction of 2-(4-Methoxyphenyl)quinoline 1-Oxide (7) with KCN in the Presence of Benzoyl Chloride

Reaction conditions		Products (%)			
temp.	time	9	10	11	12
room temp.	overnight	—	27	—	10
room temp.	4 hr	0.5	31	—	9
room temp.	5 hr	1	25	—	7
0°	0.5 hr	0.5	52	17	9
0°	1 hr	—	28	9	8

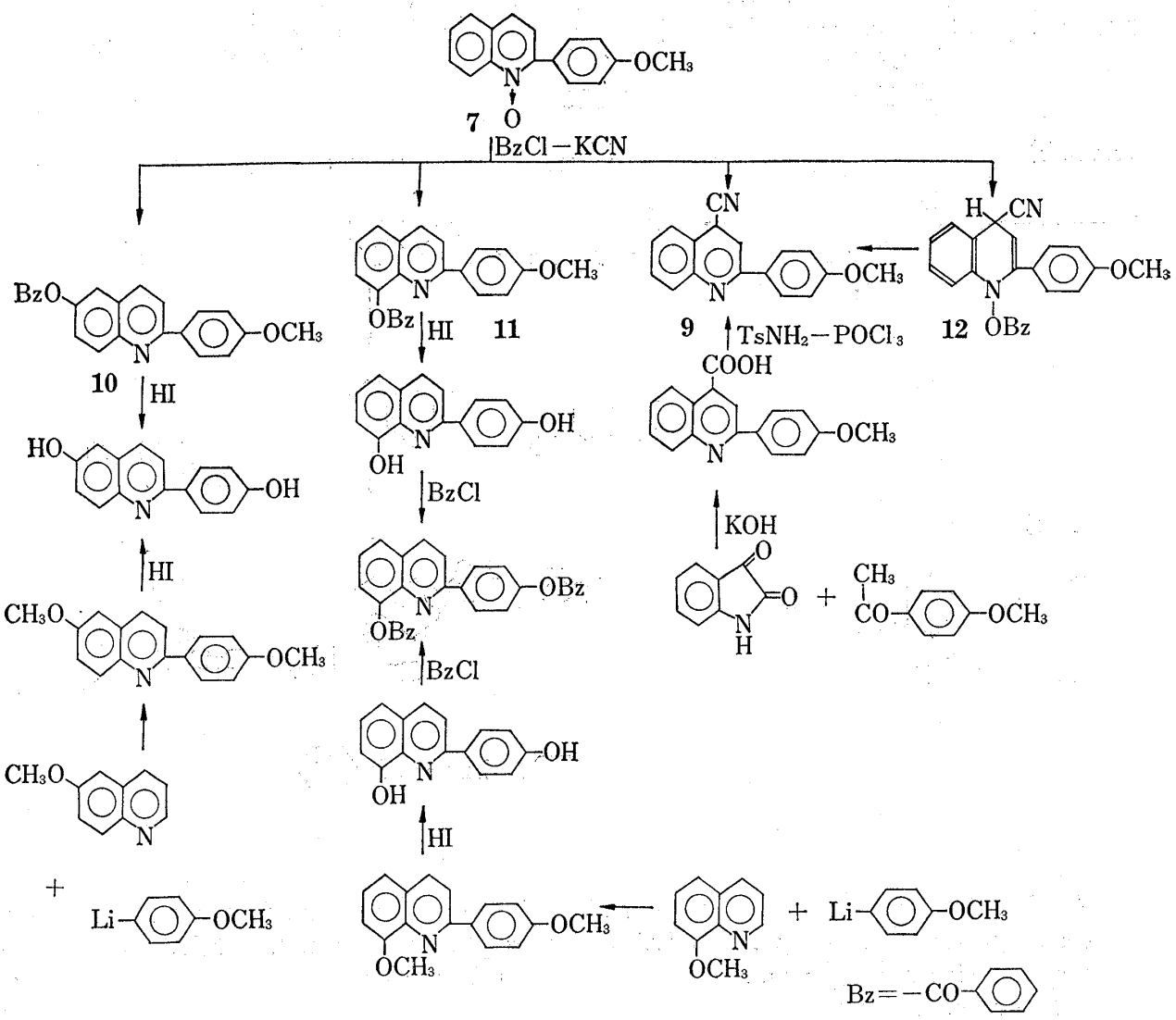

Chart 3

quinolinol and -8-quinolinol, respectively. The identify of these dihydroxyquinolines was confirmed by another synthetic routes formulated in Chart 3.

Product **12** gave analytical values in agreement with the empirical formula $C_{24}H_{18}O_3N_2$. The infrared (IR) spectrum displayed a band characteristic of carbonyl group of $\gg$N-O-COR[16] at 1736 cm^{-1} although no absorption due to cyano group was observed. The nuclear magnetic resonance (NMR) spectrum showed methyl protons of methoxy group as a singlet at τ 6.02

16) Ch. Kaneko, *Yakugaku Zasshi*, **79**, 428 (1959).

and fifteen protons as a complex multiplet at τ 3.3—1.4 in aromatic region, among which a one-proton doublet at τ 3.12 may be reasonably assigned to a 4-proton of 1,4-dihydroquinoline nucleus. Further, the mass spectrum showed the parent peak at *m/e* 382 and the following characteristic peaks at *m/e* 356 (M^+-CN), 355 (M^+-HCN), 277 ($M^+-COC_6H_5$), 261 ($M^+-OCOC_6H_5$), 234 ($M^+-OCOC_6H_5-HCN$) and 105 (C_6H_5CO). Thus the 1,4-dihydroquinolin estructure, 1-benzoyloxy-2-(4-methoxyphenyl)-4-cyano-1,4-dihydroquinoline, was reasonably assigned to product **12**. Heating **12** with 10% hydrochloric acid in ethanol resulted in elimination of a component of benzoic acid to give the 4-cyanoquinoline **9** in 36% yield, although decomposition of **12** occurred to some extent. While no change was noticed when a chloroform solution of **12** was passed through a basic alumina column, **12** was converted into an indefinite acid amide upon treatment with 10% potassium hydroxyde under reflux for 7 hours. Thus **12** was disclosed to be rather fairly stable and transformation into 6- or 8-benzoyloxy derivative (**10** or **11**) could not be effected in spite of attempts under various conditions.

Subsequently, 2-(4-nitrophenyl)quinoline 1-oxide **8** was similarly treated with aqeous potassium cyanide and benzoyl chloride with ice-cooling and stirring for 2 hours, and three product, **13**, **14** and **15**, were obtained in 19, 29 and 5% yields, respectively (Chart 4).

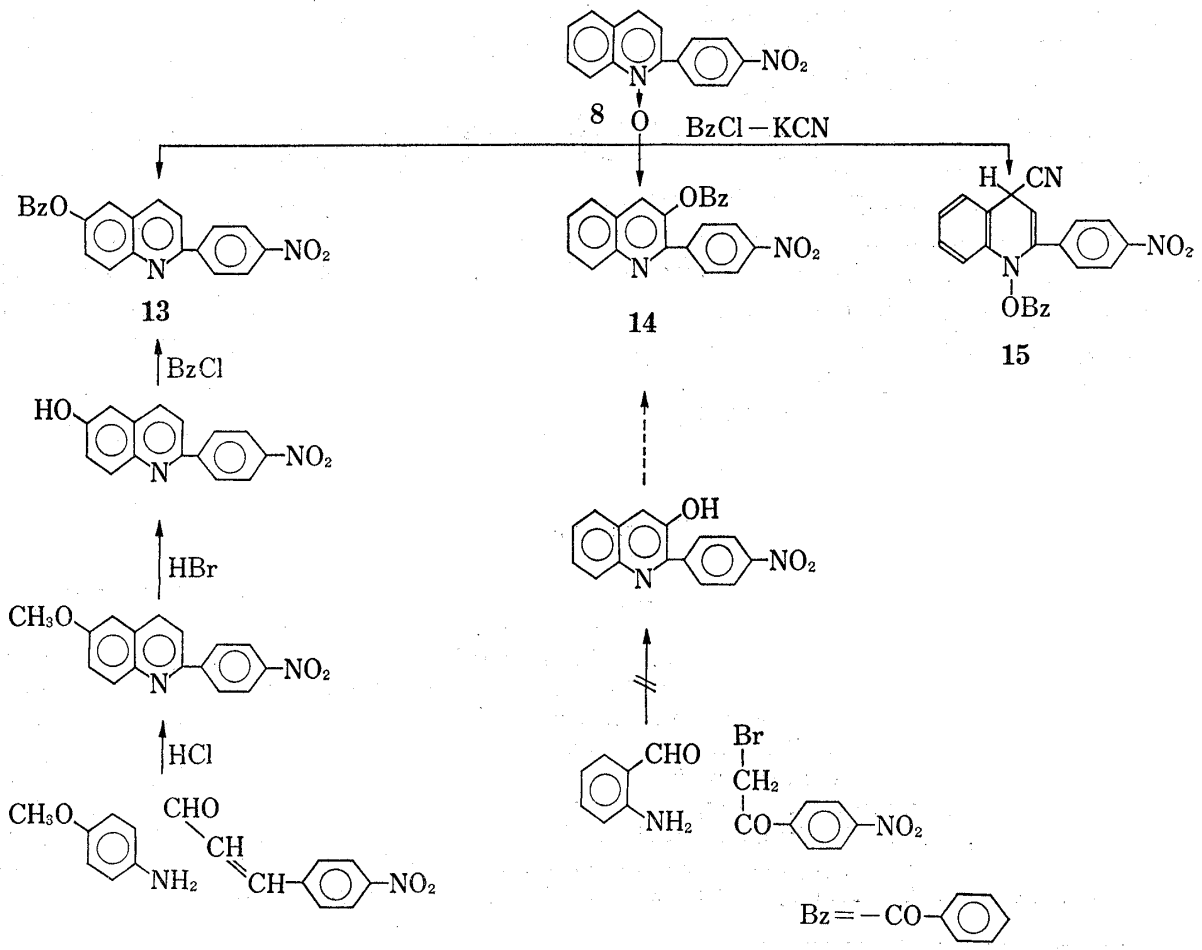

Chart 4

Their elemental analyses and IR spectra indicated that both **13** and **14** were benzoyloxy derivatives of 2-(4-nitrophenyl)quinoline. Product **13** was identified as 6-benzoyloxy derivative by unequivocal synthesis[17] formulated in Chart 4. Although the synthesis of 2-(4-

17) M.V. Miller and F. Kinkelin, *Ber.*, **20**, 1919 (1887).

nitrophenyl)-3-quinolinol from *o*-aminobenzaldehyde and *p*-nitrophenacyl bromide according to the Friedlender method[18] was unsuccessful, **14** was proved not identical with an authentic sample of 2-(4-nitrophenyl)-8-benzoyloxyquinoline prepared starting from *o*-anisidine and *p*-nitrocinnamaldehyde in the same way as the synthesis of **13**. Therefore **14** was assigned 2-(4-nitrophenyl)-3-benzoyloxyquinoline.

Product **15** has an empirical formula $C_{23}H_{15}O_4N_3$, and the IR spectrum exhibited bands at 2200 and 1741 cm^{-1} respectively attributable to a cyano and a characteristic carbonyl groups besides those of nitro group at 1530 and 1349 cm^{-1}. The mass spectrum showed molecular ion at *m/e* 397 and the following characteristic peaks at *m/e* 371 (M^+-CN), 370 (M^+-HCN), 276 ($M^+-OCOC_6H_5$), 275 ($M^+-C_6H_5COOH$), 250 ($M^+-OCOC_6H_5$-CN) and 229 ($M^+-C_6H_5COOH$-NO_2); this fragment pattern bears close resemblance to that of the spectrum of **12**. Thus 1-benzoyloxy-2-(4-nitrophenyl)-4-cyano-1,4-dihydroquinoline was reasonably assigned to **15**.

Contrary to the expectation that reactions of **7** and **8** might provide some evidence for the mechanism of the formation of benzoyloxy derivatives, there was not obtained any clear-cut correlation between the nature of the 4-substituent of 2-phenyl side chain and the proportions of the products. It is difficult at present to explain reasonably the differences among reactions of **1**,[3] **7** and **8** in terms of the polarizations of the respective 2-phenyl side chains.

However, it is quite significant that the 1,4-dihydroquinoline,[19] **12** and **15**, were isolated as fairly stable species from reactions of **7** and **8**, respectively; their stability may be probably due to the participation of 2-phenyl groups.

The fact that the 1,4-dihydroquinolines, **12** and **15**, could not be transformed into any benzoyloxy derivative in spite of various examinations appears to rule out the possibility of the formation of benzoyloxy derivatives by course b). Although the detailes of the mechanism have not been established, course c) seems more probable than course b) for the formation of benzoyloxy derivatives. It seems not unreasonable that the inherent plarizability of 2-phenyl nucleus itself promotes the reaction through course c) but the polar effect of the 4-substituent is not substantially transmitted to the quinoline ring; such phenomena are noticed in many cases such as nitration of biphenyl derivatives.[20] This assumption is apparently more-reasonable with respect to the mechanism of the previously reported Reissert-Henze reaction of 2,4-diphenylquinoline 1-oxide.[3]

Experimental[21]

Nitration of 2-Phenylquinoline 1-Oxide (1)——General Procedure: The concentration of H_2SO_4, the reaction temperature and the reaction time are given in Table I. To a solution of **1** (1.1 g) in H_2SO_4 (6 ml) was added KNO_3 (0.55 g, 1.1 equiv. or 0.60 g, 1.2 equiv.) by portions at the constant temperature, and the whole was kept at the same temperature for the given period. The reaction mixture was poured onto ice-water, made alkaline with Na_2CO_3 and extracted with $CHCl_3$. The extract was evaporated and the residue was chromatographed on alumina with CCl_4, benzene and $CHCl_3$. The CCl_4 eluate gave two fractions; the first was **1** and the second one was recrystallized from acetone to yield 2-(3-nitrophenyl)-4-nitroquinoline 1-oxide (**4**), yellow needles, mp 212°. *Anal.* Calcd. for $C_{15}H_9O_5N_3$: C, 57.88; H, 2.91; N, 13.50. Found: C, 58.02; H, 3.00; N, 13.18. The fraction eluted with benzene was recrystallized from MeOH to give 2-phenyl-4-nitroquinoline 1-oxide (**2**), yellow needles, mp 137°, which was identical with a sample prepared by the method of Kosuge, *et al.*[9] IR ν_{max}^{Nujol} cm^{-1}: 1525, 1320 (NO_2), 1298 (N→O). The last fraction eluted with

18) P. Friedlender, *Ber.*, **15**, 2572 (1882).
19) See the following references for the isolation of analogous dihydroquinolines. *a*) M. Hamana and K. Funakoshi, *Yakugaku Zasshi*, **80**, 1031 (1960); *b*) T. Yoshikawa, *Yakugaku Zasshi*, **81**, 1061 (1961); *c*) M. Hamana and I. Kumadaki, *Chem. Pharm. Bull.* (Tokyo), **18**, 1742 (1970).
20) *a*) F. Bell and J. Kenyon, *J. Chem. Soc.*, **1926**, 2707; *b*) *Idem*, *ibid.*, **1926**, 3048; *c*) H.G. Gull and E.E. Turner, *J. Chem. Soc.*, **1929**, 491.
21) Melting points are uncorrected. NMR spectra were run on JNM-3H-60 spectrometer using TMS as an internal standard. Mass spectra were recorded at 75 eV on a JMS-OISG spectrometer.

benzene–$CHCl_3$ was recrystallized from EtOH–acetone to give 2-(3-nitrophenyl)quinoline 1-oxide (**3**), yellow needles, mp 198°. IR ν_{max}^{Nujol} cm^{-1}: 1537, 1350 (NO_2), 1204 (N→O). *Anal.* Calcd. for $C_{15}H_{10}O_3N_2$: C, 67.66; H, 3.79; N, 10.52. Found: C, 67.25; H, 3.68; N, 10.85.

2-(3-Nitrophenyl)-4-nitroquinoline 1-Oxide (4)——1) To an ice-cooled solution of **3** (0.1 g) in 90% H_2SO_4 (2 ml) was added KNO_3 (0.05 g) by portions, and the reactants were kept at room temperatures for 24 hr. The reaction mixture was poured onto ice-water, made alkaline with Na_2CO_3 and extracted with $CHCl_3$. The extract residue was chromatographed on alumina with CCl_4 and the effluent was recrystallized from acetone to give 0.03 g (26%) of **4**.

2) A similar treatment of **2** gave **4** in 97% yield; chromatography was not needed.

2-Phenyl-4-chloroquinoline——A solution of **2** (0.5 g) and PCl_3 (2 ml) in $CHCl_3$ (8 ml) was refluxed for 3 hr to give 0.26 g (40%) of 2-phenyl-4-chloroquinoline, colorless needles, mp 57° (aq. MeOH), which was identical with an authentic sample prepared from 2-phenylquinoline 1-oxide and $POCl_3$.[8]

2-(3-Nitrophenyl)quinoline (5)——A solution of **3** (1.0 g) and PCl_3 (4 ml) in $CHCl_3$ (30 ml) was refluxed for 1 hr. The reaction mixture was poured onto ice-water, made alkaline with Na_2CO_3 and extracted with $CHCl_3$ to give 0.65 g (61%) of **5**, colorless needles, mp 121° (aq. MeOH). IR ν_{max}^{Nujol} cm^{-1}: 1528, 1345 (NO_2). *Anal.* Calcd. for $C_{15}H_{10}O_2N_2$: C, 71.99; H, 4.03; N, 11.20. Found: C, 71.78; H, 4.23; N, 10.83.

2-(3-Nitrophenyl)quinoline Methopicrate (6)——A solution of **5** (0.2 g) and Me_2SO_4 (5 ml) in anhyd. benzene (5 ml) was refluxed for 2 hr. After cooling, deposited solid was filtered and mixed with aq. NH_4OH, and to this was added a saturated aq. solution of picric acid to yield precipitates, which were recrystallized from 95% EtOH to give 0.06 g (12%) of **6**, yellow granules, mp 183°. It was identical with an authentic sample prepared by the method of Le Fevre and Mathur.[7] *Anal.* Calcd. for $C_{16}H_{13}O_2N_2 \cdot C_6H_2O_7N_3$: C, 53.55; H, 3.06; N, 14.20. Found: C, 53.52; H, 3.11; N, 13.97.

2-(4-Methoxyphenyl)quinoline——To a suspension of Li (5.0 g) in anhyd. ether (200 ml) was added dropwise 4-bromoanisole (60 g) with stirring, and the whole was refluxed for 2 hr to give a solution. To this was added dropwise quinoline (30 g) with ice-cooling and stirring, and stirring was continued at room temperature for 2 hr. Water was added to the reaction mixture with cooling, and the ether layer was separated and dried with K_2CO_3. The ether solution was evaporated and the residue was boiled in nitrobenzene (250 ml) for 30 min. Addition of 50% (v/v) H_2SO_4 gave 2-(4-methoxyphenyl)quinoline sulfate. Neutralization of the salt with NaOH in a small amount of H_2O deposited solid, which was recrystallized from EtOH to give 25 g (46%) of 2-(4-methoxyphenyl)quinoline, bright colorless plates, mp 125°. IR ν_{max}^{Nujol} cm^{-1}: 1253 (OCH_3).

2-(4-Methoxyphenyl)quinoline 1-Oxide (7)——To a solution of 2-(4-methoxyphenyl)quinoline (5.0 g) in benzene (20 ml) was gradually added a mixture of 30% H_2O_2 (6 ml) and Ac_2O (6 ml), and the whole was refluxed for 21 hr. The reactants were concentrated under reduced pressure, made alkaline with Na_2CO_3 and extracted with $CHCl_3$. The extract residue was chromatographed on alumina with $CHCl_3$, and the effluent was recrystallized from AcOEt to give 3.3 g (62.5%) of **7**, yellowish prisms, mp 130°. IR ν_{max}^{Nujol} cm^{-1}: 1208 (N→O). *Anal.* Calcd. for $C_{16}H_{13}O_2N$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.24; H, 5.47; N, 5.64.

The Reissert-Henze Reaction of 2-(4-Methoxyphenyl)quinoline 1-Oxide (7)——To an ice-cooled solution of **7** (1.0 g) in $CHCl_3$ (2 ml) was added an aq. solution (0.5 ml) of KCN (0.8 g) and then PhCOCl (0.8 g) with stirring. The mixture was stirred at 0° or room temperatures for the given period in Table II. The $CHCl_3$ layer was separated and evaporated to give solid residue which was treated with a small amount of CCl_4. A fraction insoluble in CCl_4 was recrystallized from MeOH–acetone to give 2-(4-methoxyphenyl)-6-benzoyloxyquinoline (**10**), colorless plates, mp 170°. IR ν_{max}^{Nujol} cm^{-1}: 1730 (C=O), 1280 (OCH_3). *Anal.* Calcd. for $C_{23}H_{17}O_3N$: C, 77.73; H, 4.82; N, 3.94. Found: C, 77.82; H, 4.83; N, 4.24.

The CCl_4 filtrate was evaporated and the residue was chromatographed on alumina with CCl_4 and $CHCl_3$. The CCl_4 eluate gave 1-benzoyloxy-2-(4-methoxyphenyl)-4-cyano-1,4-dihydroquinoline (**12**), yellow needles, mp 180° (EtOH–acetone). IR ν_{max}^{Nujol} cm^{-1}: 1736 (C=O), 1260 (OCH_3). NMR ($CDCl_3$) τ: 6.02 (3H, s, OCH_3), 3.12 (1H, d, C_4–H), 3.3—1.4 (14H, m, aromatic protons). UV λ_{max}^{EtOH} (log ε): 234.5 (4.735), 289 (4.662), 315 (4.557), 378 (4.079). Mass Spectrum *m/e*: 382 (M^+), 356 (M^+-CN), 355 (M^+-HCN), 277 ($M^+-COC_6H_5$), 261 ($M^+-OCOC_6H_5$), 234 ($M^+-OCOC_6H_5-HCN$), 105 (C_6H_5CO). *Anal.* Calcd. for $C_{24}H_{18}O_3N_2$: C, 75.38; H, 4.74; N, 7.33. Found: C, 75.32; H, 4.82; N, 7.46.

Elution with CCl_4–$CHCl_3$ afforded two fractions. The first was recrystallized from EtOH to give 2-(4-methoxyphenyl)-8-benzoyloxyquinoline (**11**), colorless plates, mp 107°. IR ν_{max}^{Nujol} cm^{-1}: 1736 (C=O), 1228 (OCH_3). *Anal.* Calcd. for $C_{23}H_{17}O_3N$: C, 77.73; H, 4.82; N, 3.94. Found: C, 77.84; H, 4.95; N, 4.22. The second fraction contained an additional **10** and 2-(4-methoxyphenyl)-4-cyanoquinoline (**9**). The former was isolated by recrystallization from EtOH–acetone and **9** was obtained from the mother liquor. Product **9**: colorless needles, mp 173—175°. IR ν_{max}^{Nujol} cm^{-1}: 2245 (CN), 1255 (OCH_3). *Anal.* Calcd. for $C_{17}H_{12}ON_2$: C, 78.44; H, 4.65; N, 10.76. Found: C, 78.29; H, 4.80; N, 10.69.

2-(4-Hydroxyphenyl)-6-quinolinol——A suspension of **10** (0.50 g) in 57% HI (10 ml) was refluxed for 3 hr. The reaction mixture was made alkaline with 10% NaOH and extracted with a small amount of ether to remove the unchanged **10**. Passing CO_2 gas through the resultant clear solution deposited solid, which was recrystallized from aq. EtOH to give 0.30 g (84%) of 2-(4-hydroxyphenyl)-6-quinolinol, brownish

needles, mp 257°. It was proved identical with a sample obtained from 2-(4-methoxyphenyl)-6-methoxyquinoline. IR ν_{max}^{Nujol} cm^{-1}: 3550, 3260 (OH). *Anal.* Calcd. for $C_{15}H_{11}O_2N \cdot H_2O$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.70; H, 5.44; N, 5.74.

2-(4-Benzoyloxyphenyl)-8-benzoyloxyquinoline——In the same way as the above experiment, **11** (0.2 g) was hydrolyzed to the corresponding dihydroxy derivative, which was subsequently treated with PhCOCl in pyridine to give 0.15 g (59%) of 2-(4-benzoyloxyphenyl)-8-benzoyloxyquinoline, colorless granules, mp 163° (AcOEt). IR ν_{max}^{Nujol} cm^{-1}: 1740 (C=O). *Anal.* Calcd. for $C_{29}H_{19}O_4N$: C, 78.19; H, 4.30; N, 3.14. Found: C, 77.91; H, 4.34; N, 3.36.

Conversion of 12 to 9——A mixture of **12** (0.2 g), EtOH (5 ml) and 10% HCl (5 ml) was refluxed on a water bath for 1 hr. The cooled reactants were made alkaline with 10% NaOH to deposit precipitates, which were purified by chromatography on alumina with CCl_4–$CHCl_3$ and then recrystallized from EtOH to give 0.06 g (36%) of **9**, mp 172°. From the alkaline solution, 0.01 g (16%) of benzoic acid and 0.03 g (38%) of *p*-anisidic acid, mp 184—185°, were isolated.

2-(4-Methoxyphenyl)-6-methoxyquinoline and 2-(4-Hydroxyphenyl)-6-quinolinol——1) 2-(4-Methoxyphenyl)-6-methoxyquinoline was prepared from 6-methoxyquinoline and *p*-anisyl lithium in the similar manner as the case of 2-(4-methoxyphenyl)quinoline: colorless plates, mp 180° (AcOEt), 53%. IR ν_{max}^{Nujol} cm^{-1}: 1253 (OCH_3). *Anal.* Calcd. for $C_{17}H_{15}O_2N$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.91; H, 5.50; N, 5.24.

2) A suspension of 2-(4-methoxyphenyl)-6-methoxyquinoline (0.5 g) in 57% HI (10 ml) was refluxed for 4 hr to give 0.35 g (63%) of 2-(4-hydroxyphenyl)-6-quinolinol, brownish needles, mp 257—258° (decomp.) (aq. EtOH).

2-(4-Methoxyphenyl)-8-methoxyquinoline and 2-(4-Hydroxyphenyl)-8-quinolinol——1) 2-(4-Methoxyphenyl)-8-methoxyquinoline was similarly prepared in 55% yield; colorless needles, mp 115—116° (AcOEt). IR ν_{max}^{Nujol} cm^{-1}: 1250—1260 (OCH_3). *Anal.* Calcd. for $C_{17}H_{15}O_2N$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.58; H, 5.78; N, 4.89.

2) 2-(4-Hydroxyphenyl)-8-quinolinol was similarly obtained by HI hydrolysis of the corresponding dimethoxy derivative, but was difficult to crystallize. Therefore, it was derived to the corresponding dibenzoate, colorless granules, mp 163° (AcOEt).

2-(4-Nitrophenyl)quinoline 1-Oxide (8)——To a solution of 2-(4-nitrophenyl)quinoline (1.0 g) in benzene (5 ml) was gradually added a mixture of 30% H_2O_2 (1 ml) and Ac_2O (1 ml), and the whole was refluxed for 24 hr. The reaction mixture was concentrated under reduced pressure, ether was added and precipitated crystals were filtered followed by recrystallization from MeOH to give 0.70 g (66%) of **8**, yellow needles, mp 225—226°. IR ν_{max}^{Nujol} cm^{-1}: 1518, 1348 (NO_2), 1217 (N→O). *Anal.* Calcd. for $C_{15}H_{10}O_3N_2$: C, 67.66; H, 3.79; N, 10.52. Found: C, 67.39; H, 3.73; N, 10.12.

The Reissert-Henze Reaction of 2-(4-Nitrophenyl)quinoline 1-Oxide (8)——To an ice-cooled solution of **8** (1.0 g) in $CHCl_3$ (30 ml) was added aq. solution (5 ml) KCN (0.8 g) and then PhCOCl (0.8 g) with stirring. The mixture was stirred with ice-cooling for 2 hr. The $CHCl_3$ layer was separated, washed with aq. solution of Na_2CO_3 and evaporated. The residue was treated with CCl_4, and an insoluble fraction was separated from the CCl_4 solution. This insoluble solid was recrystallized from a large amount of AcOEt to give 0.21 g (15%) of 2-(4-nitrophenyl)-6-benzoyloxyquinoline (**13**), colorless crystals, mp 222°. IR ν_{max}^{Nujol} cm^{-1}: 1742 (C=O), 1518, 1342 (NO_2). *Anal.* Calcd. for $C_{22}H_{13}O_4N_2$: C, 71.35; H, 3.81; N, 7.56. Found: C, 71.20; H, 3.88; N, 7.71. The fraction remained in the mother liquor was recrystallized from a small amount of AcOEt to give 0.43 g (31%) of 2-(4-nitrophenyl)-3-benzoyloxyquinoline (**14**), colorless needles, mp 216°. IR ν_{max}^{Nujol} cm^{-1}: 1742 (C=O), 1518, 1342 (NO_2). *Anal.* Calcd. for $C_{22}H_{13}O_4N_2$: C, 71.35; H, 3.81; N, 7.56. Found: C, 71.06; H, 3.89; N, 7.56. The CCl_4 solution was passed through an alumina column and the effluent was recrystallized from EtOH–acetone to give 0.06 g (4%) of 1-benzoyloxy-2-(4-nitrophenyl)-4-cyano-1,4-dihydroquinoline (**15**), orange needles, mp 181—182°. IR ν_{max}^{Nujol} cm^{-1}: 2200 (C=N), 1741 (C=O), 1530 and 1349 (NO_2). UV λ_{max}^{EtOH} nm (log ε): 231 (4.679), 282 (4.766) and 410 (4.729). Mass Spectrum *m/e*: 397 (M^+), 371 (M^+—CN), 370 (M^+—HCN), 276 (M^+—$OCOC_6H_5$), 275 (M^+—C_6H_5COOH), 250 (M^+—$OCOC_6H_5$–CN), 229 (M^+—C_6H_5-COOH–NO_2). *Anal.* Calcd. for $C_{23}H_{15}O_4N_3$: C, 69.51; H, 3.81; N, 10.50. Found: C, 69.30; H, 3.99; N, 10.25.

2-(4-Nitrophenyl)-6-benzoyloxyquinoline (13)——1) A mixture of powdered *p*-anisidine (4.0 g), 4-nitrocinnamaldehyde (5.0 g) and conc. HCl (10 ml) was refluxed at 150—160° for 3 hr. The reaction mixture was extracted with hot HCl–EtOH (1: 1 v/v), and the extract was filtered to remove insoluble substances and evaporated to dryness under reduced pressure. The residue was treated with NH_4OH and extracted with $CHCl_3$. The extract residue was chromatographed on alumina with CCl_4–$CHCl_3$ to give 0.7 g (7.8%) of 2-(4-nitrophenyl)-6-methoxyquinoline, yellow granules, mp 156—157° (AcOEt). IR ν_{max}^{Nujol} cm^{-1}: 1515 and 1338 (NO_2). *Anal.* Calcd. for $C_{16}H_{12}O_3N_2$: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.41; H, 4.29; N, 10.17.

2) A suspension of 2-(4-nitrophenyl)-6-methoxyquinoline (0.3 g) in 47% HBr (5 ml) was refluxed for 3 hr. The reaction mixture was neutralized with 10% NaOH and the deposited solid was recrystallized from aq. EtOH to give 0.2 g (60%) of 2-(4-nitrophenyl)-6-quinolinol, yellow crystals, mp 199—201°. IR ν_{max}^{Nujol} cm^{-1}: 3150 (OH), 1515 and 1340 (NO_2). This was treated with PhCOCl in pyridine to give the 6-benzoate **13**, mp 222°.