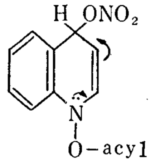
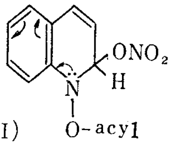
UDC 547.821-31+547.831-31

Bromination of Pyridine and Quinoline 1-Oxides

Ochiai and Kaneko[1] found that application of acyl nitrate to quinoline 1-oxide in chloroform or dioxane resulted in introduction of nitro group into 3- and 6-positions of the quinoline ring and they concluded that this reaction proceeded with electrophilic substitution of the quinoid-type intermediate (I or II), followed by liberation of the acyl nitrate component.[2] In order to find other electrophilic substitutions that progress by the same mechanism, bromination of pyridine and quinoline 1-oxides was examined. During the progress of this work, a report appeared on the bromination of pyridine-type heterocycles under the same idea[3] and, therefore, some results obtained to date are presented here, although this work has not been completed as yet.



(I)



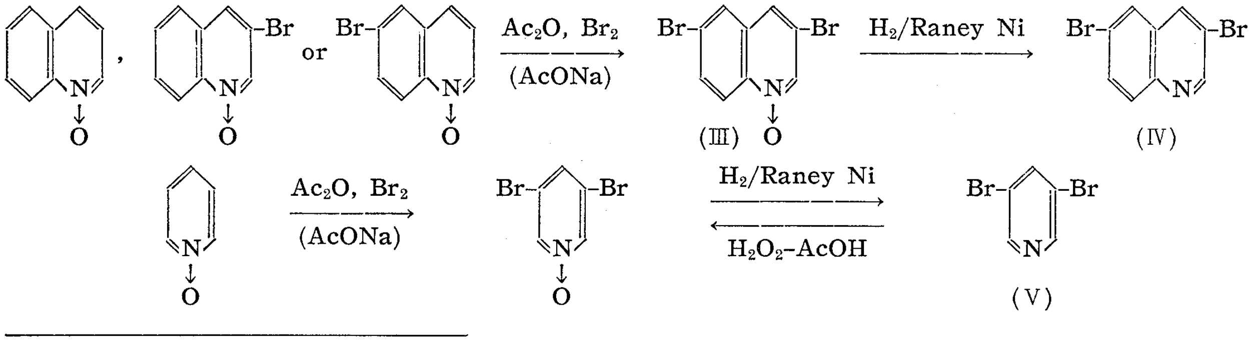
(II)

acyl=Bz or Ac

A solution of 1.45 g. of quinoline 1-oxide dissolved in 1.3 g. of Ac_2O was boiled in $CHCl_3$ with 4 g. of Br_2 and 1.6 g. of AcONa for 3 hr. under reflux, the reaction mixture was cooled, and basified with K_2CO_3-Na_2SO_3 mixture. This was extracted with $CHCl_3$, the extract was washed with 5% HCl, and crystals (III) were obtained from the $CHCl_3$ layer, a small amount of the starting compound being recovered from the HCl layer. Recrystallization of (III) from MeOH gave pale brown scaly crystals of m.p. 199~200° (*Anal.* Calcd. for $C_9H_5ONBr_2$: C, 35.64; H, 1.65; N, 4.62. Found : C, 35.95; H, 1.79; N, 4.76), corresponding to dibromoquinoline 1-oxide or dibromo-hydroxyquinoline. Its infrared spectrum lacked the absorption bands for hydroxyl and carbonyl groups but exhibited an absorption for aromatic amine oxide at 1212 cm^{-1}, from which an N-oxide compound is assumed.

Reduction of (III) in methanol with Raney Ni as catalyst in H_2 atmosphere, at ordinary temperature and pressure, resulted in absorption of 1 mole of hydrogen and produced 3,6-dibromoquinoline (IV) (*Anal.* Calcd. for $C_9H_5NBr_2$: C, 37.63; H, 1.74; N, 4.88. Found: C, 37.40; H, 1.75; N, 4.81). Consequently, (III) is 3,6-dibromoquinoline 1-oxide and its yield was ca. 60%.

Bromination of 3-bromoquinoline 1-oxide and 6-bromoquinoline 1-oxide by the same procedure afforded (III) in respective yield of 26% and 40%.



(III) (IV) (V)

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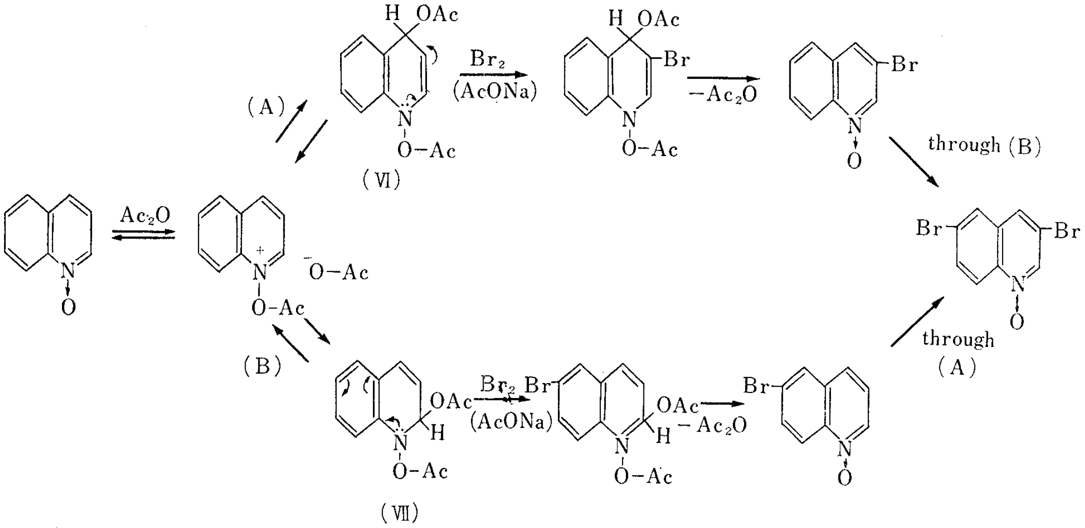
[1] E. Ochiai, C. Kaneko : This Bulletin, **5**, 56 (1957).

[2] *Idem* : *Ibid.*, **7**, 267 (1959).

[3] E. E. Garcia, C. V. Greco, I. M. Hunsberger : J. Am. Chem. Soc., **82**, 4430 (1960).

3,5-Dibromopyridine 1-oxide,[4] m.p. 143～144°, was obtained from pyridine 1-oxide in exactly the same manner in ca. 35% yield (*Anal.* Calcd. for $C_5H_3ONBr_2$: C, 23.72; H, 1.19; N, 5.53. Found : C, 23.84; H, 1.23; N, 5.72). Its structure was proved by its reduction to 3,5-dibromopyridine (V) and its formation from (V) by N-oxidation.

This reaction is considered to progress by the same mechanism as in the case of nitration of quinoline 1-oxide[2] and pyridine 1-oxide[5] by acyl nitrate reported by Ochiai and Kaneko. In this reaction, acetic anhydride adds to the amine oxide to form the *o*- or *p*-quinoid-type intermediates (VI and VII), which undergo bromination by bromine, and liberation of acetic anhydride component takes place. In both cases of quinoline and pyridine 1-oxides, monobromo compound has not been isolated and only the dibromo compound is obtained, which differs markedly from the result of nitration and this point requires further detailed examination.



This type of reaction is expected to make a great progress as electrophilic substitution reaction of aromatic amine oxides and great interest is being felt on how the reaction would be affected by the nature of reactants and change in reaction conditions. These points are now being examined.

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[4] H. J. den Hertog, C. H. Hemkens, K. Dilz : Rec. trav. chim., **72**, 296 (1953).
[5] E. Ochiai, C. Kaneko : This Bulletin, **8**, 28 (1960).