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SHORT COMMUNICATIONS

Reaction of 2,4-Dibromoquinoline with Hydrogen Chloride

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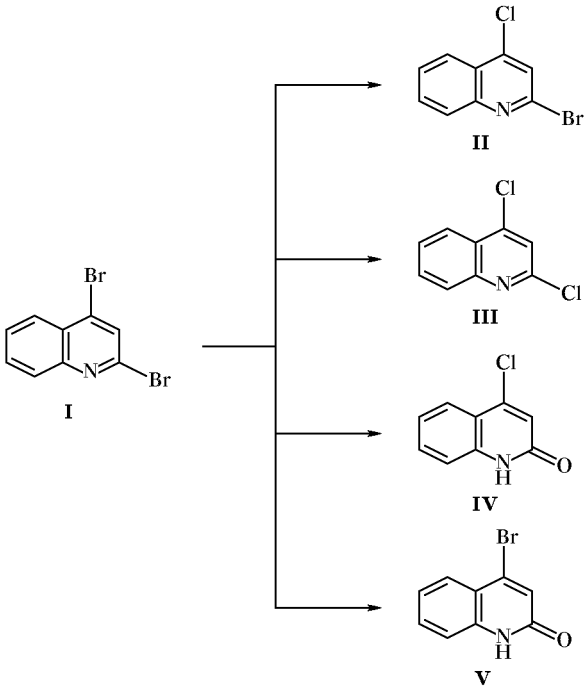
It is known that nucleophilic aromatic substitution in nitrogen-containing heterocycles by the action of such weak nucleophiles as halide ions is very difficult to occur, even when the heteroring is activated by *N*-oxide moiety. For example, replacement of nitro group in heteroaromatic *N*-oxides requires severe conditions: heating with concentrated hydrohalic acids at the boiling boint or using acetyl or phosphinoyl halides [1]. According to the recent data, S_N reactions of 4-nitroquinoline *N*-oxide in aprotic solvents are favored by formation of molecular complexes with π-(tetracyanoethylene) [2] and especially *v*-acceptors (H^+, BF_3, $AlCl_3$) [3]. As a result, the corresponding products are formed in quantitative yield under mild conditions.

Scheme 1.



We have found that the same method for activation of S_NAr can be applied to substitution in the quinoline ring having no *N*-oxide moiety. The structure of the products obtained from 2,4-dibromo-, 2-bromo-4-chloro-, and 2,4-dichloroquinolines **I**–**III** depends on the conditions. The reaction of dibromoquinoline **I** with HCl in acetonitrile gave product **III** as a result of replacement of both bromine atoms by chlorine. When gaseous hydrogen chloride was passed through a solution of 2,4-dibromoquinoline in acetonitrile, monosubstitution product **II** was formed quickly and quantitatively. On prolonged reaction, compound **II** was slowly (by 35% in 4 h) converted into dichloro derivative **III**. The same reaction in chloroform gave only 2-bromo-4-chloroquinoline (**II**) in quantitative yield. No halogen replacement occurred on passing gaseous hydrogen chloride through a solution of **I** in hexane, but 2,4-dibromoquinoline hydrochloride was quantitatively formed. Thus, by varying the solvent polarity we can obtain in quantitative yield 2,4-dibromoquinoline hydrochloride and the corresponding mono- or dichloro analogs.

Conditions and results of S_N reactions of 2,4-dibromoquinoline

Acid	Temperature, °C	Solvent	Product,[a] yield (%),[b] time
HCl (concd.)	65	CH_3CN	**III**, 98, 30 min, or **IV**, 98, 72 h
HCl (concd.)	20	CH_3CN	**III**, 94, 20 h
HCl (gas)	20	$CHCl_3$	**II**, 94, 60 min
HCl (gas)	20	CH_3CN	**II**, 98, 5 min, or **III**, 96, 24 h
$HClO_4$	65	CH_3CN	**V**, 81, 72 h

[a] The ^1H NMR, IR, and UV spectra and melting points of the were consistent with published data [4].

[b] Yield of the isolated product.

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Prolonged heating (for 3 days at 65°C or for 10 h at 80°C) of compound **I** in acetonitrile with HCl or HBr or of compounds **I**–**III** with HCl leads to almost quantitative formation of 4-chloro-2-hydroxyquinoline (**IV**) or 4-bromo-2-hydroxyquinoline (**V**), respectively.

Method A. A mixture of 0.5 mmol of 2,4-dibromoquinoline and 0.2 ml of concentrated acid in 1.5 ml of acetonitrile was kept under conditions specified in table. When the reaction was complete (HPLC), the mixture was evaporated to dryness, the residue was treated with a saturated solution of sodium carbonate to pH ~8 and extracted with chloroform, the extract was dried over anhydrous Na_2CO_3, and the solvent was removed under reduced pressure.

Method B. Gaseous hydrogen chloride was passed through a solution of 0.5 mmol of 2,4-dibromoquinoline in 1.5 ml of chloroform or acetonitrile. The mixture was then treated by the procedure described above in method *A*.

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