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Reactions of 3-Nitroquinoline Derivatives with Sodium Hypobromite

Most aromatic nitro compounds are very sensitive to nucleophilic reagents (*e.g.*, RO^-, R_2NH, CN^-, *etc.*), with which they can form the Meisenheimer-type σ-complex.[1] As this complex has an anionic character, it is expected that the attack of electrophilic reagents (*e.g.*, Br^+, Cl^+, *etc.*) can take place on anionic positions in this complex. In this communication, we wish to report that the reaction of 3-nitroquinoline (I) and its derivatives in KOH–MeOH with aqueous NaOBr gave interesting results.

I (0.01 mole) in MeOH (100 ml) and 10% aqueous NaOBr (0.12 mole, 130 ml) were simultaneously added with stirring to a solution of KOH (0.03 mole) in MeOH (50 ml) at 0—5°, and the reaction mixture was allowed to stand for 2 hr at 0—5°. A mixture of products was chromatographed over silica gel and afforded 3-bromo-4-methoxyquinoline (IIa, 0.84%), 3-bromo-2,4-dimethoxyquinoline (IIIa, 19.6%), 3,6-dibromo-2,4-dimethoxyquinoline (IIIb, 7.0%), 3,6,8-tribromo-2,4-dimethoxyquinoline (IIIc, 4.6%), 2,4-dimethoxy-3-nitroquinoline (IVa, 0.94%), and 6-bromo-2,4-dimethoxy-3-nitroquinoline (IVb, 0.45%). When the reaction was carried out at 37—40°, it gave IIa (5.9%), 3,6,8-tribromo-4-methoxyquinoline (IIb, 0.13%), IIIa (3.4%), IIIb (0.11%), IIIc (0.29%), 2,4,6-tribromoaniline (Va, 3.6%), and 2,4,6-tribromo-3-methoxyaniline (Vb, 0.19%). In the case of the reaction temperature at −40——37°, the products were IIIa (4.5%), IIIb (18.6%), IIIc (1.7%), IVa (0.78%), and IVb (3.6%). These products are shown in Chart 1.

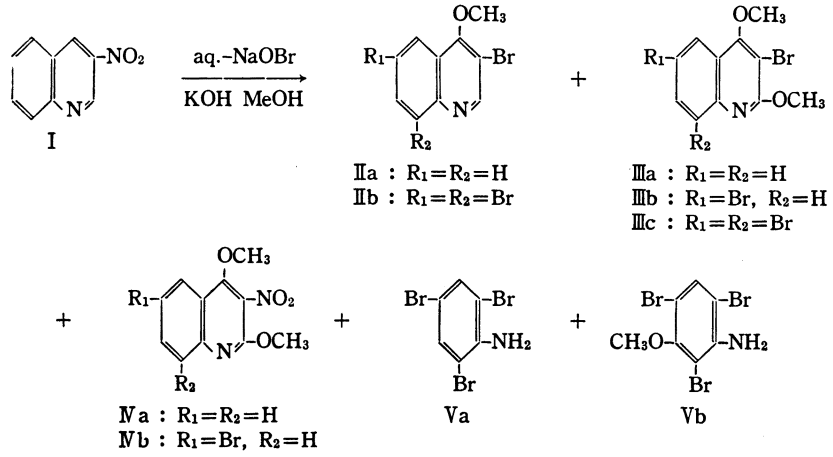

Chart 1

Similar reaction of 2-methoxy-3-nitroquinoline (VI) gave IIIa and IVa in respective yield of 59.2% and 17.5% (Chart 2). In this case, however, the bromination products (IIIb, c, and IVb) were not obtained at all. On the other hand, the same reaction of IVa gave 3-bromo-3,4-dihydro-2,4,4-trimethoxy-3-nitroquinoline (VII) (Chart 2), mp 103—104°; IR ν_{max}^{KBr} cm^{-1}: 1650 (C=N), 1565, 1335 (NO_2); NMR (in $CDCl_3$) δ: 4.06 (3H, s, C_2-OCH_3), 3.30 (3H, s) and 3.42 (3H, s); $C_4\langle^{OCH_3}_{OCH_3}$, 7.2—7.8 (4H, m, C_{5-8}-H).

From these results, it is presumed that this reaction is a combination of addition and elimination. The mechanism of the reaction of VI is shown in Chart 3.

1) R. Foster and C.A. Fyfe, *Rev. Pure and Appl. Chem.*, **16**, 61 (1966).

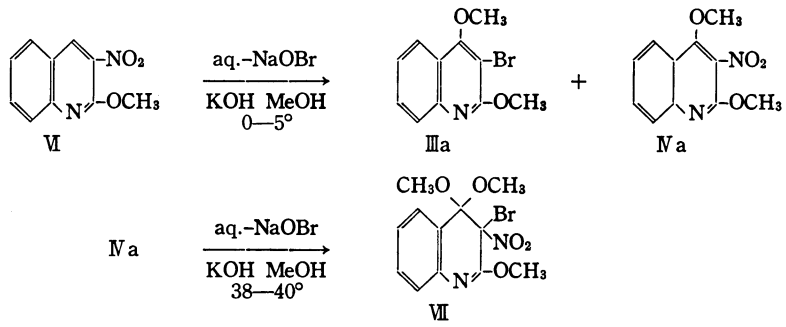

Chart 2

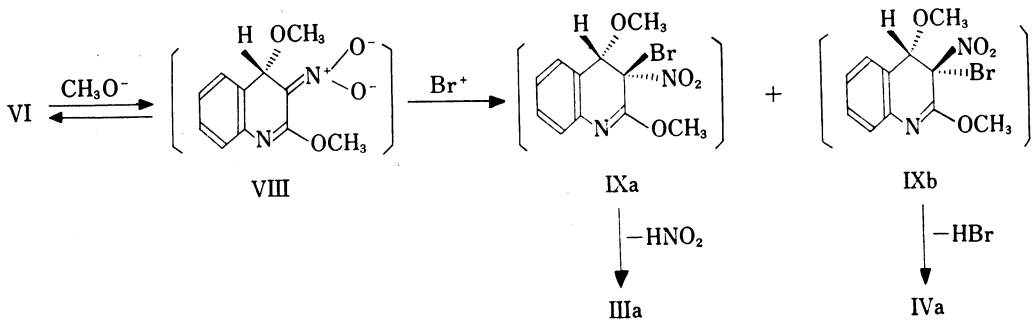

Chart 3

As the first step, the Meisenheimer-type σ-complex (VIII) would be formed by the addition of a methoxide anion (CH_3O^-) to the 4-position of VI in an alkaline medium, and brominated at the carbon atom carrying the nitro group. At the stage of the bromination of VIII, two ways are possible. Br^+ would be preferentially introduced from the side opposite to the 4-CH_3O group in VIII, thus forming the intermediate IXa. On the other hand, the intermediate IXb would be scarcely formed because of the steric hindrance of 4-CH_3O group. IIIa should be obtained from IXa by the *trans* elimination of HNO_2. Similarly, IVa should be obtained from IXb by the *trans* elimination of HBr.

The reaction of 2,4- or 2,3-dinitroaniline with aqueous NaOCl has been reported.[2] Although its mechanism was postulated as resulting from a concerted process involving synchronous attack of ClO^-, it has still not been elucidated. Now, we wish to propose that an addition-elimination mechanism can occur in the reaction of 3-nitroquinoline derivatives with NaOBr.

A similar reaction occurred with other nitroquinolines, 4-, 5-, 6-, and 8-nitroquinoline, and 3-nitropyridine. Details of these reactions and mechanism will be published in the near future.

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2) F.B. Mallory and S.P. Varimbi, *J. Org. Chem.*, **28**, 1656 (1963); F.B. Mallory, C.S. Wood, and B.M. Hurwitz, *ibid.*, **29**, 2605 (1964).