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Investigations into the nitric acid mediated dehalonitration of halophenols

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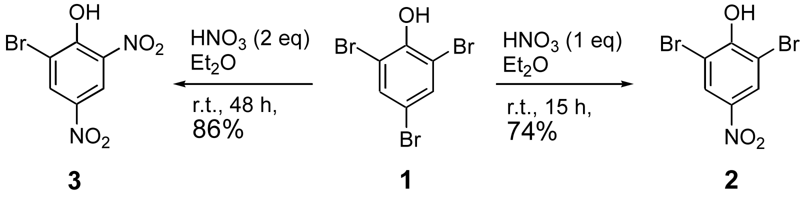
Abstract—A reaction of nitric acid with bromophenols and iodophenols results in substitution of the halogen with a nitro group. The study indicates moderate reactivity for bromophenols and iodophenols, while chlorophenols were found to be sluggish in this reaction.

In recent years there has been considerable interest in exploring the possibility of using aromatic bromides as protecting groups in synthetic organic chemistry.[1,2] This notion is aided by the easy accessibility of several aromatic bromo compounds as well as their high reactivity for substitution reactions. One such reaction is electrophilic debromination, brought about using hydrobromic acid (HBr) in the presence of a suitable bromine scavenger. Due to the considerable potential of this subject, we were interested in studying the reaction of halophenols, in general, with other electrophiles and present our findings on the specific reaction with nitronium ions in this communication. This reaction is similar to the investigations reported by Zincke[3] and others[4,5] when bromophenols were exposed to the source of nitronium ion or sodium nitrite,[6] resulting in the formation of the corresponding nitrophenols.

The reaction of 2,4,6-tribromophenol **1** with one equivalent of concentrated nitric acid under ambient conditions furnished a single product which was identified as 4-nitro-2,6-dibromophenol **2**, while the same reaction with two equivalents of nitric acid resulted in the formation of 2-bromo-4,6-dinitrophenol **3**, as shown in Eq. (1). The substitution of bromine is selective in **1** where the *para*-bromine was substituted by a nitro group. Similarly, when **1** was exposed to two equivalents of nitric acid, the substitution of the second bromine at the *ortho* position was achieved, albeit more slowly, to give **3**, in good yield, as a single product.

It is known in the literature[7,8] that in concentrated nitric acid the equilibrium outlined in Eq. (2) is present, providing a source of nitronium ions. The subsequent reaction of a nitronium ion with **1** gives intermediate **4**, which loses a bromonium ion to give the nitrophenol **2** as shown in Eq. (3).



(1)

Keywords: dehalonitration; halophenols; nitrophenols; nitric acid.

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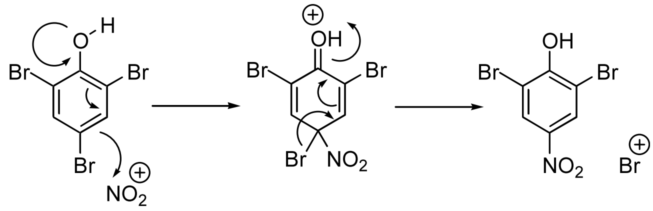
$$HNO_3 + HNO_3 \xrightleftharpoons{4\,\%} H_2O + NO_3^{\ominus} + \boxed{NO_2^{\oplus}} \qquad (2)$$



1 **4** **2** (3)

The reaction of tetrabromobisphenol **5** with two equivalents of nitric acid gave the dinitro product **6** as the major product, where one bromine from each aromatic ring had been substituted, Eq. (4). In this reaction along with **6** a small amount of a mononitro product, resulting from a monosubstitution was also isolated.

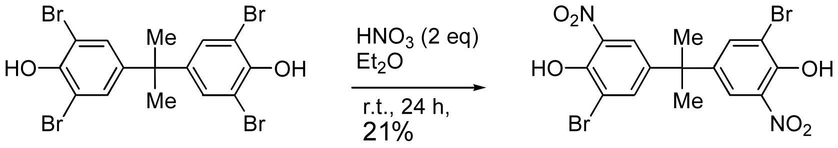
We examined the reaction of nitric acid with 1-halo-2-naphthols to compare the reactivity of three different derivatives. The reaction of 1-chloro-2-naphthol **7** did not furnish the substitution product **8**, instead nitration took place at other positions. We isolated the major product and identified it as 6-nitro-1-chloro-2-naphthol **9**. However, the reaction of 1-bromo-2-naphthol **10** with nitric acid gave the expected substitution product **8**, albeit in low yield. The other product isolated was identified as **11** by the usual spectral and analytical methods. The reaction of 1-iodo-2-naphthol **12** gave mainly **8** in a good isolated yield. The higher conversions of iodophenols to nitrophenols compared to other halophenols could be because the iodonium ion is a better leaving group. Reaction of 2-naphthol **13** under identical reaction conditions furnished **8** in only 32% yield as the main product (Chart 1).

Further exploration of the reaction of nitric acid with other substrates such as 4-bromoanisole, 4-iodoanisole, 1-bromo-2-methoxynaphthalene, 1-iodo-2-methoxynaphthalene and 4-iodo acetanilide did not result in the substitution of the halogen by a nitro group nor nitration at other positions. This result indicates the necessity of having a free hydroxyl group for this transformation which fits in with the mechanism suggested in Eq. (3).

Thus we present our findings on the reactions of concentrated nitric acid with halophenols which forms nitrophenols under simple reaction conditions.

Standard reaction conditions

Reaction of 1-iodo-2-naphthol: To a solution of 1-iodo-2-naphthol (0.27 g, 1 mmol) in diethyl ether (15 mL) at



5 **6** (4)

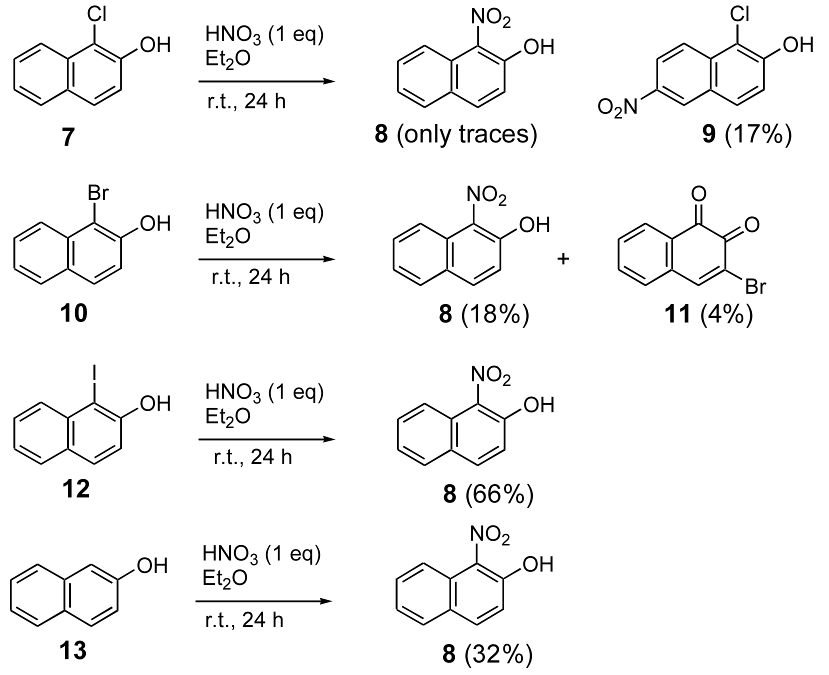


Chart 1.

ambient temperature was added concentrated nitric acid (0.09 mL of 70% aq., 1 mmol) and the reaction mixture was stirred. After 24 h, the mixture was diluted with fresh diethyl ether (35 mL), washed with water, dried over anhydrous sodium sulphate and concentrated. The pure 1-nitro-2-naphthalene was separated by a short column over silica gel (3% ethyl acetate in hexane) as yellow crystals (0.125 g; 66%), and its structure was confirmed by melting point and NMR analysis as well as by comparison by thin layer chromatography with an authentic sample.

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