

An Investigation of Some Nucleophilic Substitutions in the Benzene Ring

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The electronic theory of aromatic substitutions represents groups such as the nitro, the carboxyl, the carbonyl, the cyano, and the sulfone group as withdrawing electrons from the benzene ring, particularly from the meta positions. This theory is corroborated by well-known substitutions of electrophilic reagents such as the halogens, nitric acid, and sulfuric acid in the meta position to these groups. These substitutions occur with considerable more difficulty than with unsubstituted benzene.

The same theory predicts that nucleophilic reagents such as sodium hydroxide, sodium cyanide, and sodiumamide will react with nitrobenzene, benzoic acid, acetophenone, benzonitrile, and diphenylsulfone in the ortho or para position with more ease than in the case of unsubstituted benzene. A few reactions of this kind have been reported in the literature. Wohl (3) found that *o*- and traces of *p*-nitrophenol were formed when nitrobenzene reacted with dry powdered potassium hydroxide. Tschitschibabin (2) obtained 2-pyridone by passing pyridine vapors over dry potassium hydroxide at 300-350° C. Barts and Schreder (1) obtained phloroglucinol by the

fusion of phenol or resorcinol with potassium hydroxide. 2-aminopyridine is commonly prepared by the action of sodiumamide and pyridine.

The purpose of this investigation was to study nucleophilic substitutions of aromatic compounds in order to find optimum conditions for the reactions. In order to give greater impetus to a nucleophilic substitution, compounds containing two or more electron-attracting groups were chosen for study. These compounds were 3-nitrobenzoic acid, 3, 5-dinitrobenzoic acid, 3-nitroacetophenone, 3-nitrobenzotrile, and 3-nitrodiphenylsulfone. The greatest emphasis in this investigation was on hydroxylation, but a few attempts to achieve amination and cyanation by nucleophilic substitution were made. Variations made in experimental conditions included dry fusion and use of solvents such as water, benzene, diethylene glycol, and liquid ammonia. Oxidizing agents in the form of hydrogen peroxide and atmospheric oxygen were used in some experiments in the hope that they would promote nucleophilic substitutions.

EXPERIMENTAL

The following typical runs illustrate the experimental conditions used:

A. DRY FUSION. One-half gram of potassium hydroxide and 1.5 gm. of 3-nitroacetophenone were heated for one-half hour at 150° C. The ketone melted and formed a dark-brown viscous solution. The cooled reaction mixture was suspended in 50 ml. of water and acidified; a brown solid settled out. The product after recrystallization from ethanol melted at 79° C. The melting point of a mixture of this solid with some of the original ketone was also 79° C. Both the aqueous filtrate from the reaction mixture and the mother liquor from the recrystallization of the solid gave a negative test for a phenolic hydroxyl group when tested with ferric chloride solution.

B. DIETHYLENE GLYCOL AS THE SOLVENT. Eight and four-tenths grams of potassium hydroxide was added to 150 ml. of diethylene glycol and the mixture was heated to 150° C. The potassium hydroxide dissolved completely, giving an orange solution. Eight grams of 3-nitrobenzoic acid dissolved in 55 ml. of diethylene glycol was added to the above mixture. The reaction mixture darkened at once and in a short time was dark brown. After the solution had refluxed for two hours it was set aside to cool. The cooled reaction mixture consisted of an extremely dark brown viscous solution with a black solid mass in the bottom of the flask. No identifiable material could be separated from the mixture.

C. LIQUID AMMONIA AS THE SOLVENT. Seven-tenths gram of potassium metal was added to approximately 30 ml. of liquid ammonia contained in a Dewar flask surrounded by an acetone-dry ice bath. Nickel oxide and ferric nitrate were added in minute amounts to catalyze the formation of potassium amide. The solution turned deep blue upon the addition of the potassium. The blue color disappeared slowly and was replaced with a light brown precipitate. One gram of 3-nitroacetophenone was added to this mixture. The mixture became red for a short time, but quickly deepened to dark brown. The liquid ammonia was allowed to evaporate over a period of six hours. A black metallic residue remained in the reaction vessel. The residue was extracted with acetone several times. No products could be isolated from the acetone. The solid residue showed little change upon strong ignition.

DISCUSSION

No evidence of nucleophilic substitution in the benzene nucleus was obtained under the conditions used in this investigation. New substances were found in two cases: white needle-like crystals from the dry fusion of sodium hydroxide and 3-nitrobenzoic acid, and colored crystals from the reaction of sodium hydroxide and 3-nitrobenzoic acid with diethylene glycol

as the solvent. In both cases, the yields were too small to permit complete characterization of these substances.

In general, the balance of the runs resulted in either complete decomposition of the reactants or recovery of the unchanged organic reactant in good yields. Further work is needed to establish experimental conditions necessary for nucleophilic substitutions.

LITERATURE CITED

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