[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Iodination of Phenol under Anhydrous Conditions[1]

BY W. H. HUNTER AND THEODORE T. BUDROW

Pure phenol does not react with iodine to any appreciable extent. However, in alkaline aqueous solution, the reaction proceeds rapidly and it has been shown in this Laboratory[2] that alkali salts of *sym*-trihalogenated phenols react with iodine, either in aqueous solution or under anhydrous conditions, to form amorphous substances which have the composition $(C_6H_2X_2O)_n$.

In 1883, Schall[3] prepared what he believed to be anhydrous sodium phenolate, by drying the salt in a current of hydrogen at 300°. This material upon treatment with dry iodine in anhydrous carbon disulfide yielded *o*-iodophenol together with smaller amounts of the di- and triiodophenols. A similar reaction was carried out by Birnbaum and Reinherz,[4] who treated silver salicylate with iodine without the use of solvent, obtaining mono- and diiodosalicylic acids and also free salicylic acid. Later, Coffman,[5] on the basis of a study of the iodination of phenols in aqueous solution, reached the conclusion that in all methods of iodinating phenols, the active iodinating agent is not free iodine, but hypoiodous acid. He applied this hypothesis to all the known methods of iodination and was able to show that, when water is the solvent, iodination is dependent upon the presence of HOI. However, in order to account for the results of Schall and of Birnbaum and Reinherz, he was forced to postulate that completely anhydrous conditions were not obtained and that the small amount of water present was sufficient to give the necessary HOI concentration.

The present work was done to repeat Schall's reaction under as nearly anhydrous conditions as possible, in the hope that the work would throw some light on the mechanism of the phenol reactions studied by Hunter and co-workers, and, incidentally, to test Coffman's theory of iodination.

Preliminary experiments in preparing sodium phenolate from sodium hydroxide and phenol showed that the water of the monohydrate ($C_6H_5ONa \cdot H_2O$) is extremely difficult to remove and that it is doubtful that the monohydrate can be successfully dehydrated by heating in hydrogen, at least not without the occurrence of side decompositions.

To prepare anhydrous phenolate, it was decided to use a method in which no water of reaction is formed and thus avoid the formation of the

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(1) The work described in this paper constituted part of a thesis submitted to the Graduate Faculty of the University of Minnesota by Theodore T. Budrow, in partial fulfilment of the requirements for the degree of Doctor of Philosophy in 1928. This paper was prepared by the junior author after the death of Dr. Hunter.—L. I. SMITH.

(2) Hunter and Woollett, THIS JOURNAL, **43**, 135 (1921); Hunter and Seyfried, *ibid.*, **43**, 151 (1921); Woollett, *ibid.*, **38**, 2474 (1916).

(3) Schall, *Ber.*, **16**, 1897, 1902 (1883); **20**, 3363 (1889).

(4) Birnbaum and Reinherz, *ibid.*, **15**, 456 (1882).

(5) Coffman, *J. Chem. Soc.*, **115**, 1040 (1919).

hydrate. The method selected comprised treating oxide-free sodium with an anhydrous xylene solution of pure phenol.

The purified sodium was melted under the xylene and, in order to ensure complete reaction, a large excess of phenol was added. Stirring the reaction mixture for about six hours at 100–120° was sufficient to bring about complete reaction of the metal. The white, flocculent sodium phenolate settled out rapidly if allowed to stand.

The iodine (purified by repeated sublimations and stored in a desiccator over phosphorus pentoxide or sulfuric acid) was added (in some cases as the solid and in others in anhydrous xylene solution) to the phenolate suspension with rapid stirring until the addition of a small portion caused a permanent pink color. The reaction was practically instantaneous, regardless of the quantity of iodine added at a time, until approximately 0.8 mole of iodine had reacted; the reaction then gradually became slower. The addition of iodine was accompanied by the development of a blue color, and when the mixture was filtered after completion of the reaction, this blue substance was found to be adsorbed or occluded by the precipitated sodium iodide. It was insoluble in ethyl alcohol, ether, benzene or xylene but was decomposed when the iodide was dissolved in water.

A quantitative investigation of the reaction showed that approximately one mole of iodine (average of eight expts., 0.95) reacts with one mole of phenolate and that one-half of the iodine (average of eight expts., 0.52) reacts to form sodium iodide.

The reaction products consisted mainly of *o*-iodophenol, with small amounts of diiodophenol and triiodophenol. It was thought that some phenoxyphenol might be formed in accordance with the reaction

$$C_6H_5ONa + C_6H_4IOH \longrightarrow C_6H_4(OC_6H_5)OH + NaI$$

but this compound could not be found in the reaction mixture, although a very small amount of a light yellow, odorless, crystalline substance, melting at 116–118°, was isolated. This was not phenolic, as it was not attacked by any concentration of sodium hydroxide, and it did not contain halogen. It was not identified.

The reaction between iodine and phenolate in anhydrous xylene was very rapid. Actually, in two experiments where this was roughly measured, the reaction was practically instantaneous until 86–88% of the iodine had been added.[6] This behavior was then compared with that in aqueous solution by adding measured quantities of a 0.5 molar solution of iodine in potassium iodide solution to a 2 molar solution of sodium phenolate containing 100% excess of free phenol and noting the time required to discharge the iodine color. These concentrations of reactants were selected as the approximate concentrations occurring in most of the experiments with the xylene solutions previously described. The results

(6) That is, percentage of total I_2 required to react with C_6H_5ONa to form monoiodophenol.

again indicated that the reaction was practically instantaneous until about 85% of the iodine had been added.

These data indicated that the reaction of iodine with sodium phenolate occurs as rapidly under anhydrous conditions as in aqueous solution. Now, according to Coffman's explanation of the anhydrous reaction, it must be supposed that a small amount of water which may have been present served to permit the formation of sufficient hypoiodous acid to iodinate the phenol. Since the anhydrous reaction is heterogeneous, if it actually occurred on account of the presence of a minute amount of water, it could not go as rapidly as the iodination in aqueous solution. Hence, it may be concluded that whether or not Coffman's theory of iodination is correct for the reaction in aqueous solutions, it does not explain the iodination of phenol under anhydrous conditions.

Experimental

In all experiments the sodium was purified according to the method of Lewis and Kraus.[7] The molten sodium ran from a capillary directly into dry xylene in an atmosphere of hydrogen. The weight of the purified sodium was obtained by weighing the tube to which the capillary was sealed before and after the operation. Meanwhile, the reaction apparatus had been dried carefully, dry xylene introduced therein, and all air displaced by dry hydrogen. The vessel containing the purified sodium under xylene was quickly disengaged from the sodium purification apparatus and the contents poured into the reaction vessel, which was momentarily opened for this purpose. During this operation a positive hydrogen pressure of a few inches of mercury was maintained in the reaction vessel to reduce the chances of the entrance of air. After the introduction of the sodium the reaction apparatus was further swept with hydrogen to remove any traces of air which may have entered. No perceptible tarnishing of the sodium occurred during these operations. The xylene was then heated to about 100° and a solution of pure phenol in dry xylene was run in with agitation. The phenol was purified by several fractionations, the last distillation having been carried out in an atmosphere of dry, oxygen-free hydrogen.

In these experiments the amount of sodium finally appearing as sodium iodide (determined by the Volhard analysis) checked with reasonable closeness to the original weight of the metal. Hence, it was decided to dispense with the weighing of the sodium and rely entirely on the analysis of the sodium iodide residue to determine the amount of sodium which reacted. This permitted the entire series of operations to be carried out without opening the reaction vessel.

A two-necked round-bottomed flask served as the reaction vessel. One neck carried a mercury-seal stirrer, inlet and outlet tubes for hydrogen and a separatory funnel. The other opening accommodated a glass tube 12 cm. × 2 cm. which was terminated by a 5 cm. × 0.4 mm. capillary. The sodium was melted in this tube by means of the boiling xylene contained in the reaction vessel and was then forced through the capillary by means of purified hydrogen. After the sodium had been introduced, the phenol solution and later the iodine solution were introduced by means of the separatory funnel.

Summary

1. The action of iodine upon sodium phenolate has been studied under anhydrous conditions.

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(7) Lewis and Kraus, THIS JOURNAL, **32**, 1461 (1910).

2. Iodination proceeds very rapidly under these conditions, in fact practically as fast as in the presence of water.

3. The explanation of Coffman which requires that the active iodinating agent is not free iodine but hypoiodous acid may or may not be correct for the reaction in aqueous solutions, but it does not account for iodination under anhydrous conditions.

MINNEAPOLIS, MINNESOTA RECEIVED DECEMBER 5, 1932
PUBLISHED MAY 6, 1933

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE UNIVERSITY OF IOWA]

Behavior of Mixed Halogenated Phenols in the Zincke Method of Nitration[1]

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Zincke and others[2] proved that when a brominated phenol or cresol is treated with nitrous acid, bromine or a hydrogen atom in a favorable position as respects hydroxyl may be replaced by the nitro group. Raiford and collaborators[3] have shown that when both ortho and the para positions are occupied by bromine isomeric *o*- and *p*-mononitrohalogenated derivatives may be obtained in this way in a single experiment. Chlorine compounds are much less reactive[4] and on this account compounds containing bromine and chlorine in the same molecule have been studied. The relative positions of these substituents have been varied in order to learn if replacement can occur in positions other than ortho and para, and whether chlorine can be replaced at all by the Zincke method.

Nitration of 2-bromo-4-chlorophenol (2) replaced the ortho hydrogen atom to give the 6-nitro compound (1). When the isomer, 2-chloro-4-bromophenol (10), was used, the ortho hydrogen was again displaced from one portion and the para bromine atom from another, giving a mixture of products (9) and (11). The isomeric monobromodichlorophenols, (3) and (6), lost bromine from the ortho and para positions, respectively, and gave the corresponding 2- and 4-nitrodichloro compounds, (4) and (7). Of the monochlorodibromo compounds (5) and (12), the first lost an ortho bromine atom to give the 6-nitro product (1), while the second gave a mixture of the 4-nitro (8) and the 6-nitro (11) derivatives.

With the cresols similar results were obtained. From *o*-cresol (CH_3 = 2) there were prepared the isomeric compounds (13) and (15) in which chlorine occupies the ortho and para positions, respectively, with bromine

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(1) From the thesis submitted in partial fulfilment of the requirements for the Ph.D. degree in the University of Iowa.

(2) Zincke, *J. prakt. Chem.* [2], **61**, 56 (1900); Dahmer, *Ann.*, **333**, 353 (1904).

(3) Raiford, THIS JOURNAL, **44**, 158 (1922).

(4) Raiford and Heyl [*Am. Chem. J.*, **43**, 397 (1910)] and Raiford [*ibid.*, **46**, 425 (1911)] failed to replace chlorine in *sym*-trichlorophenol and *m*-cresol by this method.