

alcohol (10 wt. %). This unknown compound was probably a condensation product from *p-tert*-butylphenol, but the infrared spectrum of this fraction showed no bands due to functional groups other than the hydroxyl group in *tert*-butylcyclohexanol. This alcohol was characterized by preparing its phenylurethan derivative (m.p. 161–163°). One conclusion that can be drawn from the data is that the tertiary butyl group was not cleaved from the ring during

hydrogenation since neither cyclohexane nor cyclohexanol was found in the products.

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[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT LABORATORIES OF THE ETHYL CORPORATION]

## Convenient Syntheses of *p*-Bromo- and *p*-Aminophenol

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Convenient syntheses are described for preparing *p*-bromophenol in high yield and high purity and for *p*-aminophenol in high yield. Possible mechanisms for the copper sulfate-catalyzed ammonolysis of *p*-halophenols are discussed.

While investigating the synthesis of *p*-aminophenol from phenol *via p*-bromophenol, several interesting observations were made. It was found that the bromination of phenol by the *Organic Syntheses* procedure,<sup>1</sup> using equimolecular amounts of phenol and bromine in ethylene dichloride instead of carbon disulfide, gave an 83% yield of crude *p*-bromophenol containing as much as 12% 2,4-dibromophenol.<sup>2</sup> Variations in the rate of addition of the bromine solution, stirring, dilution, temperature (–5 to +5°), or dryness of the ethylene dichloride solvent gave little or no improvement in the conversion beyond 72% pure *p*-bromophenol. However, use of a 20% or greater excess of phenol resulted in a substantial decrease in the amount of 2,4-dibromophenol and a corresponding increase in the conversion and purity of *p*-bromophenol. The procedure developed here was found to be very convenient not only because of the high conversion to *p*-bromophenol but because of the ease of obtaining high purity *p*-bromophenol.

It is of interest to note that there was a direct correlation between the amount of 2,4-dibromophenol and the amount of unreacted phenol in the experiments where equimolecular amounts of phenol and bromine were used. Moreover, the ortho and meta isomers were in every case present to the extent of less than 1–2% and showed no variation with the amount of 2,4-dibromophenol formed. This indicates that the 2,4-dibromophenol was formed almost exclusively from *p*-bromophenol.

Although the aminolysis of *p*-bromophenol with methylamine has been reported,<sup>3</sup> the corresponding

reaction with ammonia apparently has not been. References were found, however, to the ammonolysis of *p*-chlorophenol. In one reference<sup>4</sup> the conditions given involved reaction at 140° for 12 hr. in the presence of catalytic amounts of copper sulfate (no yield given), whereas in the other reference<sup>5</sup> the optimum conditions involved reaction of one volume *p*-chlorophenol with 4 volumes of 33% aqueous ammonia containing 16% copper sulfate at 185° for 3 hr. to produce an 82% yield of *p*-aminophenol. Since *p*-bromophenol reacts much more readily with methylamine than does *p*-chlorophenol, it appeared that considerably milder ammonolysis conditions could be used for the *p*-bromophenol than those reported for *p*-chlorophenol.

The initial ammonolysis experiments with *p*-bromophenol were therefore conducted in the presence of catalytic amounts of copper sulfate at 25° to 60°. It was found that no significant reaction occurred. Consequently, it appears that there is a considerable difference in the reactivity of ammonia and methylamine towards *p*-halophenols, possibly even more than would correspond to their relative basicities (which differ by a factor of about 30). Some experiments were then conducted in the presence of relatively large quantities of copper sulfate (0.34 mole per mole *p*-bromophenol) as specified in one of the references for the ammonolysis of *p*-chlorophenol. At 65 to 140° the conversion to *p*-aminophenol was at best only 39%, and at 140° appreciable tar formation also occurred. Use of milder conditions in the presence of catalytic amounts of copper sulfate was therefore indicated.

A reaction variable study gave the following results: (1) The yield of *p*-aminophenol from *p*-bromophenol increased appreciably from 25° to 120° and

(1) R. Adams and C. S. Marvel, *Org. Syntheses*, Coll. Vol. I, 128, (1941).

(2) 2,4-Dibromophenol and *p*-bromophenol boil within one degree at the distillation pressures used. The components were determined by infrared analyses.

(3) F. R. Bean (to Eastman Kodak) U. S. Patent 2,397,911, Apr. 9, 1946.

(4) German Patent 205,415, Dec. 31, 1907. Akt.-Ges. für Anilin-Fabrikation, Berlin.

(5) A. I. Kipriyanov, G. I. Kipriyanov, and M. Dashevskii, *Ukrain. Khim. Zhur.*, 7 Wiss. Tech. Abt. 87–93 (1932).

decreased somewhat at temperatures above 140° due to side reactions; (2) the yield increased with an increase in the copper sulfate concentration up to a certain point and then decreased due to tar formation; (3) the yield increased with an increase in the ammonia concentration; and (4) the yield decreased somewhat in the presence of an equivalent of sodium hydroxide per equivalent of *p*-bromophenol. The best results were obtained by using 6–9 moles aqueous ammonia per mole *p*-bromophenol in the presence of 0.04 mole copper sulfate at 120° for 4 hr. or at 140° for 1.5–2.0 hr. These conditions resulted in a 62–66% yield of *p*-aminophenol isolated directly by filtration of the reaction mixture. It was estimated from solubility data that an additional 12–15% yield of *p*-aminophenol was present in the filtrate. The over-all yield of *p*-aminophenol (not allowing for recoverable *p*-bromophenol) was 74–81%.

*Mechanism of the ammonolysis reaction.* Although this study was not directed at determining the mechanism of the copper sulfate catalyzed ammonolysis of *p*-halophenol it is of interest to consider various mechanisms which are consistent with the observed facts. The ammonolysis of *p*-halophenols may be classified as an unactivated aromatic nucleophilic substitution reaction.<sup>6</sup> There are at least three types of mechanisms which have been advanced or in some cases pretty well established for reactions which may be so classified. (1) S<sub>N</sub>1, such as the hydrolysis of diazonium salts<sup>7</sup> and the saponification of aryl halides at high temperatures,<sup>8</sup> (2) *cine* substitutions via a "benzyne" intermediate, such as the reaction of aryl halides with sodium amide in liquid ammonia,<sup>9</sup> and (3) S<sub>N</sub>2, via a copper complex, such as the Ullmann and Sandmeyer reactions.<sup>6</sup> From the observed facts it would appear that the ammonolysis reaction in question bears the closest resemblance mechanistically to the latter type reactions. Although it resembles in certain respects the reactions of aryl halides with aqueous base at high temperatures, its apparent dependence upon the ammonia and catalyst concentrations, and the apparent lesser reactivity of the phenolate ion appears to rule out the S<sub>N</sub>1 mechanism. The fact that only the normal substituted product is here obtained rules out the "benzyne" intermediate type of mechanism.<sup>10</sup>

(6) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 273 (1951).

(7) M. L. Crossely, R. H. Kienle, and C. H. Benbrook, *J. Am. Chem. Soc.*, **62**, 1400 (1940).

(8) W. J. Hale and E. C. Britton, *Ind. Eng. Chem.*, **20**, 114 (1928).

(9) J. D. Roberts, *et. al.*, *J. Am. Chem. Soc.*, **75**, 3290 (1953); **78**, 601–614 (1956).

There are at least three mechanisms which are consistent with the observed facts on the copper sulfate catalyzed ammonolysis of *p*-halophenols: (1) A termolecular mechanism involving "push" by ammonia and "pull" by cupric or copper amino ions on bromine; (2) a two-step reaction involving formation of a loose complex between the bromo substituent and the cupric or copper amino ions, followed by displacement of bromide by ammonia; and (3) a two-step reaction involving a fast reversible formation of a  $\pi$  complex between the halophenol and cupric or copper amino ion followed by a rate determining displacement of bromide ion from the  $\pi$  complex by ammonia. At present there are insufficient data available to clearly distinguish between these mechanisms.

#### EXPERIMENTAL

For brevity, only the best procedures developed are described.

*p*-Bromophenol. To a solution of 113 g. (1.2 moles) of phenol in 240 ml. of ethylene dichloride was added dropwise a solution of 160 g. (1.0 mole) of bromine and 105 ml. of ethylene dichloride at 0° over a period of 160 min. The mixture was stirred an additional 0.5 hr. at 0°, and then the ethylene dichloride was stripped at atmospheric pressure, b.p. 81–83°. The excess phenol and product were then rectified through an 18-in. heated Vigreux column at 15 mm. The *p*-bromophenol distilled at 120–122°/15 mm., 161 g. m.p. 63–65°<sup>11</sup> lit.<sup>1</sup> 63°, (93% yield, based on bromine) and is 98% pure (based on infrared analyses).

*p*-Aminophenol. *p*-Bromophenol (34.6 g., 0.2 mole) was dissolved in a solution of 2 g. of copper sulfate pentahydrate (0.008 mole) dissolved in 10 ml. of water and 120 ml. of concentrated ammonium hydroxide (28–30%, 1.8 moles) at 30–35°. Below this temperature there was a tendency for a precipitate to form. The mixture was then transferred to a 250-ml. Magne-Dash autoclave which was assembled and then heated rapidly to 140°. The temperature was maintained at 140° for 80–120 min. The bomb was then cooled with an air jet. The bomb was opened and the contents cooled to 0° and filtered (15.6 g. black solid). The product was slurried with 15–20 ml. of water, filtered, reslurried with 15–20 ml. of ether, and filtered again. The yield of dry *p*-aminophenol was 14.7 g., 63% (based on *p*-bromophenol) and 93% pure (based on nitrogen analysis), m.p. 180–183° dec. Recrystallization of 3 g. of this product from 80 ml. of boiling water and 1 g. of activated charcoal in the presence of 0.2 g. of sodium hydrosulfite gave 2.1 g. of light gray solid, m.p. 184–186° dec., lit.<sup>12</sup> 184–186° dec. (70% recovery, 98% pure or better, based on nitrogen analysis).

Alternate conditions giving about the same results involve reaction at 120° for 225 min. The pressure developed at 120° was about 90 p.s.i.g., whereas at 140° it was about 165 p.s.i.g., using the same amount of reactants.

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(10) The reaction of *p*-halophenols with amines in the presence of copper catalysts in anhydrous media or with liquid ammonia would be of interest in this connection.

(11) All melting points are uncorrected.

(12) Beilstein XIII-427, N. V. Sidgwick, and R. K. Calow, *J. Chem. Soc.*, **125**, 522 (1924).