

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLLEGE OF LIBERAL ARTS,
NORTHWESTERN UNIVERSITY]

THE DIRECT ARSONATION OF BENZENE DERIVATIVES

BY CLIFF S. HAMILTON AND CLIFFORD G. LUDEMAN

RECEIVED APRIL 21, 1930

PUBLISHED AUGUST 5, 1930

The methods of Bart¹ and Béchamp² constitute at present the only practicable means of introducing arsenic into the benzene ring. In 1921, Rosenmund³ reported the preparation of phenylarsonic acid and *o*-carboxyphenylarsonic acid from *o*-bromobenzene and *o*-bromobenzoic acid, respectively, by treatment with tripotassium arsenite, and in 1923 Albert and Schulenberg⁴ patented the preparation of mixed aromatic-aliphatic arsonic acids by replacement of nucleus-substituted halogens with sodium arsenite. This investigation was started with the idea of extending the method of Rosenmund and in this work activated aryl halides were used.

Rosenmund's synthesis of *o*-carboxyphenylarsonic acid was confirmed, though his directions were incomplete, and the synthesis of *p*-acetophenone-arsonic acid as prepared by Albert and Schulenberg was confirmed with difficulty. In the preparation of *p*-carboxyphenylarsonic acid the yields were always quite low and hydrolysis products predominated. Low temperatures and a long reaction time produced the best yields. *p*-Hydroxybenzoic acid was generally isolated and phenol in increasing amounts was obtained with increased reaction temperatures.

The preparation of *o*-phenylenediarsonic acid from *o*-bromophenylarsonic acid resulted in good yields and its identity was established by the preparation of *o*-phenylenediarsine oxychloride according to the method of Kalb.⁵ Phenol was obtained in considerable amounts as a by-product, yet boiling solutions of alkali did not convert *o*-bromophenylarsonic acid or *o*-phenylenediarsonic acid to phenol or other hydrolysis products.

Attempts to prepare various nitrophenylarsonic acids were unsuccessful. When *o*-chloronitrobenzene was used as the starting material it was always reclaimed unchanged. Using *o*-bromonitrobenzene, partial hydrolysis occurred at 105°, while if the reaction mixture consisting of *o*-bromonitrobenzene and an excess of 50% trisodium arsenite solution was refluxed vigorously for twenty-four hours, a small amount of an arsonated product was obtained as evidenced by the arseno-test. This was contrary to the findings of Loesner.⁶ In the attempt to prepare *p*-nitrophenylarsonic acid from *p*-bromonitrobenzene, 45% of the calculated amount of 4,4-dibromo-

¹ Bart, *Ann.*, **429**, 55 (1922).

² Béchamp, *Compt. rend.*, **50**, 870 (1860); **51**, 356 (1860).

³ Rosenmund, *Ber.*, **54**, 438 (1921).

⁴ Albert and Schulenberg, German Patent 468,403 (1923).

⁵ Kalb, *Ann.*, **423**, 39 (1921).

⁶ Loesner, *J. prakt. Chem.*, [2] **50**, 564 (1894).

azoxybenzene was produced. Only a small amount of material was obtained which gave a positive arseno-test, but no products could be identified. In the study of 2,4-dinitrochlorobenzene the results of Balaban,⁷ who reported the formation of the corresponding phenol, were confirmed rather than the production of 2,4-dinitrophenetole as published by Nijk.⁸ Attempts to prepare *p*-sulfophenylarsonic acid from *p*-bromobenzene sulfonic acid were unsuccessful. The reaction was tried at various temperatures up to 160° at which point a small amount of material giving a positive arseno-test resulted.

Experimental

***o*-Carboxyphenylarsonic Acid (*o*-Benzarsonic Acid).**—A mixture of 20 g. (0.1 mole) of *o*-bromobenzoic acid, 63 cc. of 10% potassium hydroxide solution, 20 cc. of ethyl alcohol, 40 cc. of 50% tripotassium arsenite solution and a little freshly reduced copper was refluxed at 90 to 95° for twelve hours with constant stirring. The reaction mixture was filtered hot to remove copper, made acid to congo red paper with 20 cc. of concd. hydrochloric acid and evaporated to dryness on a steam cone. The resulting residue was extracted with absolute methanol; the methanol extract was evaporated to dryness and the residue washed with ether to remove salicylic acid and unchanged *o*-bromobenzoic acid. The ether-washed residue was twice recrystallized from hot water after decolorization with bone black; yield, 10.1 g., 41% of the calcd. amount.

Anal. Subs., 0.2460, 0.2460: 40.00, 39.95 cc. of 0.05 *N* KBrO₃. Calcd. for C₆H₄(COOH)AsO(OH)₂: As, 30.47. Found: As, 30.47, 30.44.

Optically, *o*-carboxyphenylarsonic acid consists of positive biaxial crystals having a very small optic angle. The indices of refraction are $\alpha = 1.615$ and $\beta =$ a little more than 1.620 with sodium light.

***p*-Acetophenone-arsonic Acid.**—A solution of 3 g. (0.015 mole) of *p*-bromoacetophenone in 21 cc. of 95% ethyl alcohol and a solution of 6.75 g. (0.028 mcl.) of tripotassium arsenite in 21 cc. of water was heated in a sealed tube at 165 to 170° for twelve hours. The contents of the tube were removed by washing with hot water and then hot alcohol, and the whole was made acid to congo red paper with 5 cc. of concd. hydrochloric acid. After cooling, the unchanged *p*-bromoacetophenone and some precipitated arsenious oxide were removed by filtration and the filtrate was then evaporated to dryness on a steam cone. Isolation and purification of the product was carried out as outlined under *o*-carboxyphenylarsonic acid.

Anal. Subs., 0.2025: 33.0 cc. of 0.05 *N* KBrO₃. Calcd. for CH₃COC₆H₄AsO(OH)₂: As, 30.72. Found: As, 30.54.

***p*-Carboxyphenylarsonic Acid (*p*-Benzarsonic Acid).**—The amounts of materials and the procedure in this preparation were the same as those used in the preparation of *o*-carboxyphenylarsonic acid except that *p*-bromobenzoic acid was used in place of the ortho compound and the temperature was 89 to 93° for forty-eight hours; yield, 1.14 g., 4.6% of the calcd. amount.

Anal. Subs., 0.2005, 0.20055: 32.6, 32.55 cc. of 0.05 *N* KBrO₃. Calcd. for C₆H₄(COOH)AsO(OH)₂: As, 30.47. Found: As, 30.47, 30.43.

Optically, *p*-carboxyphenylarsonic acid consists of positive biaxial crystals having a large optic angle. The crystals were incorrectly orientated for an accurate determination of the indices of refraction with the means at hand.

⁷ Balaban, *J. Chem. Soc.*, 569 (1926).

⁸ Nijk, *Rec. trav. chim.*, **41**, 461 (1922).

o-Phenylenediarsonic Acid.—A solution of 14 g. (0.05 mole) of *o*-bromophenylarsonic acid in 3.7 cc. (0.05 mole) of 50% potassium hydroxide and 17 cc. (0.07 mole) of 50% trisodium arsenite solution was refluxed at 110° for forty-eight hours. The reaction mixture was made acid to congo red paper with an excess of concd. hydrochloric acid and the solution steam distilled; the distillate yielded 0.6 g. or 14.3% of the calculated amount of phenol on extraction with ether. The phenol so obtained boiled at 180°, gave the tribromo derivative melting at 93° with bromine water, and gave a negative bromine test on sodium fusion. The residue from the steam distillation was cooled and filtered. The precipitate after washing with absolute methanol was dissolved in an excess of concd. ammonium hydroxide and the resulting solution treated with 7 cc. of 30% hydrogen peroxide; the excess of ammonia and hydrogen peroxide was removed by boiling, and the diarsonic acid obtained by reprecipitation weighed 7.09 g. Two small crops of crystals obtained from the mother liquor resulting from the steam distillation and from the methanol washings weighed 0.15 and 0.21 g., respectively; total yield, 7.45 g., 45.7% of the calcd. amount.

Anal. Subs., 0.1778, 0.2712: 35.65, 66.4 cc. of 0.05 *N* KBrO₃. Calcd. for C₆H₄(AsO(OH)₂)₂: As, 45.99. Found: As, 45.85, 45.88.

The identity of the substance was further established by preparation of *o*-phenylenediarsine-oxychloride according to the directions of Kalb.⁹ One gram of the diarsonic acid was dissolved in 15 cc. of concentrated hydrochloric acid, treated with 0.5 g. of potassium iodide, and sulfur dioxide passed through the solution for thirty minutes, during which time crystals of *o*-phenylenediarsine-oxychloride separated. Recrystallization from dilute ethyl alcohol gave crystals which melted at 150°.

Note.—Copper was used as a catalyst at times though its advantages are of doubtful nature. A number of reactions were run without its use and were apparently as good as those run using it; no study of its catalytic properties was made.

The method of arsenic analysis was the potentiometric titration of a digested sample in the presence of an excess of sulfuric acid with potassium bromate, as developed by Cislak and Hamilton, *THIS JOURNAL*, **52**, 638 (1930).

Summary

1. Rosenmund's synthesis of *o*-carboxyphenylarsonic acid and Albert and Schulenberg's synthesis of *p*-acetophenone-arsonic acid were confirmed.

2. *p*-Carboxyphenylarsonic acid and *o*-phenylenediarsonic acid were prepared for the first time by this method, though they have been synthesized previously by other methods.

3. The arseno-test, which consists of warming a saturated solution of an arsonic acid with hypophosphorous acid, seems to be specific for arsonic acids and to be quite sensitive. Its use gave qualitative evidence (together with other considerations) for the formation in small amounts of *p*-sulfophenylarsonic acid and some unidentified reduced *o*- and *p*-nitrophenylarsonic acids.

LINCOLN, NEBRASKA

⁹ Kalb, *Ann.*, **423**, 39 (1921).