pentaacetates) of *d*-galactose have been synthesized in crystalline form.

4. The dimethyl and diethyl acetals of (2,3,4,5)-dibenzylidene-*d*-glucose 6-benzoate have been synthesized in crystalline form.

COLUMBUS, OHIO RECEIVED NOVEMBER 19, 1937

---

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

# Ortho-Arsenated Phenoxyalkanols

BY STEPHEN B. BINKLEY[1] AND CLIFF S. HAMILTON

This investigation deals with a series of arsenated phenylglycol ethers formed by condensing *o*-nitrophenol with propylene chlorohydrin, reducing to the corresponding amine, and introducing the arsono group by means of the Bart[2] reaction. *o*-Hydroxyphenylarsonic acid would not condense with propylene chlorohydrin.

Nitration of α-methyl-β-2-arsonophenoxyethanol at 0° for three hours with two molecular proportions of fuming nitric acid (sp. gr. 1.50) introduced one nuclear nitro group and esterified the alcoholic hydroxyl group. The nitration product, α-methyl-β-2-arsono-4-nitrophenoxyethyl nitrate, when hydrolyzed by refluxing with 3-N hydrochloric acid, yielded α-methyl-β-2-arsono-4-nitrophenoxyethanol, which was then reduced catalytically to the amine. 2-β-Hydroxy-*n*-propoxyphenylarsonic acid and 5-amino-2-β-hydroxy-*n*-propoxyphenylarsonic acid were reduced to the corresponding oxides by reduction with sulfurous acid, employing hydriodic acid as a catalyst.

The arseno derivatives were obtained by reduction of the corresponding arsonic acids with hypophosphorous acid.

Attempts to oxidize the secondary alcohol group to the corresponding ketone were unsuccessful.

## Experimental

**α-Methyl-β-2-nitrophenoxyethanol.**—To a suspension of 177 g. of the potassium salt of *o*-nitrophenol in 400 cc. of 95% ethyl alcohol was added 85 cc. (1 mol. eq.) of propylene chlorohydrin and the mixture was refluxed (for twenty-four hours) until the potassium salt of *o*-nitrophenol did not separate on cooling. After removal of the potassium chloride by filtration and the alcohol by distillation, the residue was acidified to congo red paper with dilute hydrochloric acid and steam distilled until all the *o*-nitrophenol had been removed. The product which remained as a heavy oil was separated, washed with 300 cc. of water in 100 cc. portions, dried over calcium chloride and distilled at reduced pressures.

**α-Methyl-β-2-aminophenoxyethanol.**—Ninety grams of α-methyl-β-2-nitrophenoxyethanol was dissolved in 200 cc. of tech. methyl alcohol and reduced with molecular hydrogen at 30 pounds (2 atm.) pressure in the presence of Raney[3] catalyst. After the reduction was complete the catalyst was filtered off, 100 cc. of water added to the filtrate, and the alcohol removed by distillation. On cooling the amine separated as an oil which soon solidified; it was purified by recrystallization from water.

TABLE I

| Name | Yield, % | B. p., °C. | Formula | N analyses, % Calcd. | N analyses, % Found |
|---|---|---|---|---|---|
| α-Methyl-β-2-nitrophenoxyethanol | 65 | 223–225 25 mm. | $C_9H_{11}O_4N$ | 7.14 | 7.35 |
| α-Methyl-β-2-aminophenoxyethanol | 95 | 75 m. p. | $C_9H_{13}O_2N$ | 8.48 | 8.62 |

**α-Methyl-β-2-arsonophenoxyethanol and its Sodium Salt.**—Eighty-five grams of α-methyl-β-2-aminophenoxyethanol was added to a mixture of 125 cc. of hydrochloric acid (sp. gr. 1.18), 1 liter of water, and 500 g. of ice, and diazotized with 35 g. of sodium nitrite in 500 cc. of water; time, thirty minutes; temperature, <5°. After diazotization 85 cc. of 6 *N* sodium hydroxide was added dropwise. The cold diazonium solution was added with vigorous stirring to a mixture of 80 g. of arsenic trioxide dissolved in 250 cc. of 6 *N* sodium hydroxide, 2 liters of water, 1 kg. of ice, and 5 g. of copper sulfate. The mixture was stirred for an hour, filtered through a charcoal mat, and evaporated to about 700 cc. The solution was made just acid to litmus paper, decolorized with charcoal, acidified to congo red paper and evaporated to dryness. The dry residue was extracted with 800 cc. of isopropyl alcohol in 200-cc. portions and the extract neutralized to litmus with 6 *N* sodium hydroxide. The monosodium salt of α-methyl-β-2-arsonophenoxyethanol separated on stirring and cooling. The product was dissolved in 150 cc. of water, decolorized with charcoal, and acidified to congo red paper. The free acid separated in tiny white plates.

When the acid was dissolved in sufficient 2 *N* sodium hydroxide to give a solution neutral to litmus paper and was added slowly to cold acetone the monosodium salt separated as white granules.

**α-Methyl-β-4-nitro-2-arsonophenoxyethyl Nitrate.**—The monosodium salt of α-methyl-β-2-arsonophenoxyethanol (20 g.) was stirred with 60 cc. of nitric acid (sp. gr. 1.50) for three hours. The product was precipitated by pouring into cold water.

**α-Methyl-β-4-nitro-2-arsonophenoxyethanol.**—α-Methyl-β-4-nitro-2-arsonophenoxyethyl nitrate (20 g.)

---

[1] Parke, Davis and Company Fellow.

[2] Bart, *Ann.*, **429**, 55 (1922).

[3] Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

TABLE II

| | Name | Crystalline form | Yield | M. p., °C. | Formula | As analyses, %[a] Calcd. | As analyses, %[a] Found |
|---|---|---|---|---|---|---|---|
| 1 | α-Methyl-β-2-arsonophenoxyethanol | Colorless plates | 15 | 167 | $C_9H_{13}O_5As$ | 27.15 | 27.12 |
| 2 | Sodium salt of 1 | Colorless granules | 94 | ... | $C_9H_{12}O_5AsNa$ | 25.14 | 25.05 |
| 3 | 2-β-Hydroxy-*n*-propoxyphenylarsenious oxide | Amorphous | 55 | 115–120 | $C_9H_{11}O_3As$ | 30.96 | 30.78 |
| 4 | α-Methyl-β-4-nitro-2-arsonophenoxyethyl nitrate | Colorless needles | 78 | 186 | $C_9H_{11}O_9N_2As$ | 20.47 | 20.55 |
| 5 | α-Methyl-β-4-nitro-2-arsonophenoxyethanol | ........ | 85 | 165–167 | $C_9H_{12}O_7NAs$ | 23.34 | 23.22 |
| 6 | α-Methyl-β-4-amino-2-arsonophenoxyethanol | Colorless needles | 80 | ... | $C_9H_{14}NAs \cdot 2H_2O$ | 22.92 | 22.98 |
| 7 | 6 Anhydrous | ........ | .. | 184 | $C_9H_{14}O_5NAs$ | 25.74 | 25.68 |
| 8 | Sodium salt of 6 | ........ | 90 | ... | $C_9H_{13}O_5NAsNa$ | 23.94 | 23.58 |
| 9 | 5-Nitro-2-β-hydroxy-*n*-propoxyphenylarsenious oxide | Amorphous | 90 | 152–154 | $C_9H_{10}O_5NAs$ | 26.13 | 26.05 |
| 10 | 5-Amino-2-β-hydroxy-*n*-propoxyphenylarsenious oxide | Amorphous | 50 | 125–128 | $C_9H_{12}O_3NAs$ | 29.16 | 29.06 |
| 11 | Arseno-2,2′-di-α-methyl-β-phenoxyethanol | Powder | 82 | 121–124 | $C_{18}H_{22}O_4As_2$ | 33.15 | 33.08 |

[a] See Cislak and Hamilton, THIS JOURNAL, **52**, 638 (1930).

was hydrolyzed by refluxing for two hours with 75 cc. of 3 *N* hydrochloric acid. By filtering the solution, neutralizing the excess acid with 6 *N* sodium hydroxide until the solution was just acid to congo red paper, evaporating on a water-bath until salt started to separate, and cooling to 0°, the product was obtained as a heavy oil which was purified by dissolving the dried product in acetone and precipitating by addition of dry isopropyl ether.

**α-Methyl-β-4-amino-2-arsonophenoxyethanol and its Sodium Salt.**—To a solution of α-methyl-β-4-nitro-2-arsonophenoxyethanol (10 g.) in 100 cc. of water which had been boiled for a few minutes to remove the last traces of nitrite was added sufficient sodium carbonate to give a solution which was exactly neutral to litmus. The solution was shaken in a shaking apparatus with 3 g. of Raney[8] catalyst while hydrogen gas was introduced under 40 pounds (2.6 atm.) pressure. When the reduction was complete, as indicated by the pressure drop, the mixture was filtered free of catalyst, cooled to 0°, and sufficient 6 *N* hydrochloric acid added to make the solution neutral to congo red paper. For further purification the product was recrystallized from 75 cc. of water. The product was quite sensitive to air oxidation, especially in warm aqueous neutral or alkaline solution. When the amine was dried over calcium chloride it was obtained as the dihydrate, while drying at 60° in a vacuum oven gave the monohydrate, and drying at 110° gave the anhydrous product.

A neutral solution was prepared by dissolving 10 g. of the pure amine and 1.8 g. of anhydrous sodium carbonate in 25 cc. of water. When this was poured slowly with stirring into 500 cc. of cold, dry acetone the monosodium salt was obtained.

**5-Amino-2-β-hydroxy-*n*-propoxyphenylarsenious Oxide.**—A solution of 15 g. of α-methyl-β-4-amino-2-arsonophenoxyethanol in 40 cc. of 1.5 *N* hydrochloric acid containing 0.8 g. of potassium iodide was saturated with sulfur dioxide; time five hours. The oxide was precipitated from the cold solution by neutralizing to litmus paper with concentrated ammonium hydroxide and saturating the solution with salt. The product was purified by drying at 45°, for forty-eight hours, dissolving in 15 cc. of absolute ethyl alcohol, adding 50 cc. of absolute diethyl ether, filtering and evaporating the filtrate to dryness.

**2-β-Hydroxy-*n*-propoxyphenylarsenious Oxide.**—Ten grams of α-methyl-β-2-arsonophenoxyethanol dissolved in 60 cc. of 1 *N* hydrochloric acid containing 0.3 g. of potassium iodide was reduced with sulfur dioxide. The product separated as a sticky mass which was purified by dissolving in 3 *N* sodium hydroxide and reprecipitating at 0° with 1 *N* hydrochloric acid.

## Summary

α-Methyl-β-2-arsonophenoxyethanol was prepared, by means of the Bart[2] reaction, from α-methyl-β-2-aminophenoxyethanol. Nitration with nitric acid (sp. gr. 1.50) gave α-methyl-β-4-nitro-2-arsonophenoxyethyl nitrate which was hydrolyzed with 3 *N* hydrochloric acid to give the mononitro compound. α-Methyl-β-2-arsono-4-aminophenoxyethanol was obtained by reducing the corresponding nitro compound. Arseno-2,2′-di-α-methyl-β-phenoxyethanol was prepared from the corresponding arsonic acid by reduction with hypophosphorous acid. 2-β-Hydroxy-*n*-propoxyphenylarsenious oxide, 5-nitro- and 5-amino-2-β-hydroxy-*n*-propoxyphenylarsenious oxides were prepared from the corresponding arsonic acids by reduction with sulfur dioxide using hydriodic acid as the catalyst.

LINCOLN, NEBRASKA RECEIVED NOVEMBER 26, 1937