[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

The Aldehyde Oxidation of Toluenearsonic Acids

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Recently, Scott and Hamilton[2] used the Bart reaction in the preparation of 4-formyl-2-nitrobenzenearsonic acid and *m*-formylbenzenearsonic acid. Applying Thiele and Winter's method,[3] they oxidized *p*-toluenearsonic acid to *p*-formylbenzenearsonic acid, obtaining a small yield. The preparation of *p*-formylbenzenearsonic acid and several ketone arsonic acids has been claimed in patents granted to Margulies[4] and again in others granted to Albert.[5] Margulies patented the derivatives of 4-formyl-2-nitrobenzenearsonic acid and 4-formyl-2-hydroxybenzenearsonic acids,[6] while Albert[7] also has been granted a patent for the latter. Streitwolf and Fehrle have been given a patent[8] covering the thiosemicarbazones of several acetyl- and formylbenzenearseno compounds, in which the authors claim that the compounds can be made either by reducing the arsonic acid to the formylarseno compound and then preparing the thiosemicarbazone, or by first preparing the thiosemicarbazone of the aldehyde arsonic acid and subsequently reducing it. Quite recently Gibson and Levin[9] have recorded the preparation of a number of derivatives of *p*-formylbenzenearsonic acid.

The amino aldehydes, which are the starting compounds in the previous methods of preparing aldehyde arsonic acids, are costly and difficult to prepare. They tend to react with themselves, forming "Schiff bases," and are diazotized and coupled with arsenite with difficulty. The direct method of Rosenmund[10] in which an aryl halide is treated with tripotassium arsenite, has been applied to produce certain ketone arsonic acids in a patent granted to Albert and Schulenberg.[11] It has been shown, however, by Hamilton and Ludeman[12] that the reaction leaves much to be desired. This investigation was undertaken, therefore, to ascertain if the oxidation of the toluenearsonic acids would afford a simple and easier method of preparing aldehyde arsonic acids.

The three isomeric toluenearsonic acids were oxidized with manganic oxide in sulfuric acid solution to the corresponding formylbenzenearsonic acids and isolated as the nitrophenylhydrazones. Manganese dioxide gave

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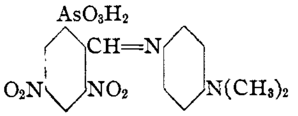
(1) Parke, Davis and Co. Fellow.
(2) Scott and Hamilton, THIS JOURNAL, **52**, 4122 (1930).
(3) Thiele and Winter, *Ann.*, **311**, 355 (1900).
(4) Margulies, French Patent 562,460 (1923).
(5) Albert, German Patent 459,648 Kl_0 12 (1917).
(6) Margulies, British Patent 220,668 (1923); Swiss Patent 111,939 (1922).
(7) Albert, Canadian Patent 280,834 (1928).
(8) Streitwolf and Fehrle, U. S. Patent 1,785,660 (1930).
(9) Gibson and Levin, *J. Chem. Soc.*, 2388 (1931).
(10) Rosenmund, *Ber.*, **54**, 438 (1921).
(11) Albert and Schulenberg, German Patent 468,403 (1923).
(12) Hamilton and Ludeman, THIS JOURNAL, **52**, 3284 (1930).

similar yields with *o*-toluenearsonic acid but no unused arsonic acid could be recovered, whereas with the manganic oxide considerable amounts of the toluenearsonic acids were recoverable.

It was found necessary to maintain a high acidity in the precipitation of the substituted hydrazones of aldehydes formed by oxidation with the oxides of manganese, since, if the strongly acid solutions were neutralized or partly neutralized, manganous salts of the arsonic acids precipitated.

The oxidation with chromic anhydride, as carried out by Scott and Hamilton,[2] was repeated with increased yields, but in the case of the *p*-toluenearsonic acid, ether extraction was the only successful method for separating the arsonic acid from the chromium. Metal salts of the arsonic acid, as well as the insoluble derivatives of the reactive aldehyde group, all contained chromium, which could not be precipitated, while precipitation of the chromium as chromic hydroxide was carried out only with difficulty and when accomplished it was found that most of the organic matter was carried down in the precipitate. When *o*-toluenearsonic acid was so oxidized, the aldehyde was precipitated from the reaction mixture as the *p*-nitrophenylhydrazone, and although it contained chromium as an impurity, it could be purified.



N - (2 - Arsono - 4,6 - dinitrobenzal) - N′,N′ - dimethyl - *p* - diaminobenzene was prepared by heating 2-methyl-3,5-dinitrobenzenearsonic acid with *p*-nitrosodimethylaniline and sodium carbonate in alcohol, after the method of Sachs and Kempf[13] for the preparation of N-(2,4-dinitrobenzal)-N′,N′-dimethyl-*p*-diaminobenzene. This reaction opens the way to the preparation of derivatives of 2-formyl-3,5-diaminobenzenearsonic acid, since it should be possible to hydrolyze the condensation product to give 2-formyl-3,5-dinitrobenzenearsonic acid, and to convert this to some stable derivative, for example, the semicarbazone. This semicarbazone could then be reduced to the semicarbazone of 2-formyl-3,5-diaminobenzenearsonic acid. Work on the hydrolysis of the condensation product is now being carried out. In the course of this investigation, two new substituted toluenearsonic acids, 2-methyl-3,5-dinitrobenzenearsonic acid and 2-methyl-3,5-diaminobenzenearsonic acid were prepared, the first for the condensation reaction and the second to confirm the first.

Several of the oxidation methods, which were attempted, did not give aldehydes, among these being Étard's method[14] using chromyl chloride, cerium dioxide in sulfuric acid solution, lead dioxide, and sodium hypochlorite in the presence of nickel salts. Amyl nitrite, which, according to a patent,[15] reacts with *o*- and *p*-nitrotoluene to give the oxime of *o*-

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(13) Sachs and Kempf, *Ber.*, **35**, 1226 (1902).

(14) Étard, *Ann. chim. phys.*, [V] **22**, 218 (1881).

(15) Meister Lucius and Bruning, German Patent 107,095 (1898).

and *p*-nitrobenzaldehyde, did not react with either the sodium salt of 2-methyl-5-nitrobenzenearsonic acid, or that of 4-methyl-3-nitrobenzenearsonic acid.

Modification of the analytical method of Cislak and Hamilton,[16] which was used to determine arsenic in this work, was found necessary, since the method failed to give accurate results, due to the sulfur dioxide which remained dissolved in the sulfuric acid unless the digestions were diluted at just the right temperature. This chance of error in the method was eliminated by diluting the digestions to 125 cc., returning the Kjeldahl flask to the flame and boiling briskly for fifteen to thirty seconds.

Experimental

Oxidation of the Isomeric Toluenearsonic Acids with Manganic Oxide.—The proportions used in the oxidations in diluted sulfuric acid were: 1 part manganic oxide, 1 part arsonic acid, and 6 parts of the sulfuric acid solution, by weight. In the oxidations carried out in concentrated sulfuric acid, 1 part manganic oxide, 1 part arsonic acid and 3.6 parts of concentrated sulfuric acid were used. The manganic oxide was mixed with the sulfuric acid solution in an ice cooled flask, and the arsonic acid added. The flask was placed in the water-bath at the desired temperature and stirred until the disappearance of the dark brown color indicated that the manganic oxide was nearly all reduced. The addition of the oxide and of the arsonic acid to the concentrated sulfuric acid was made very slowly with rapid stirring and good cooling, and the smooth brown paste placed in the refrigerator, where it hardened to a firm cake. (If these precautions are not observed, the mixture grows hot, swells and hardens too rapidly, with a lowering of the yield.) After twenty-four hours the flask was removed from the refrigerator and placed in the water-bath. Its contents could not be stirred. All reactions were continued for ten hours unless the oxide was reduced before that time, except those in concentrated sulfuric acid at room temperature, which were allowed to stand for seven days at the temperature of the laboratory.

In all cases, when the flask was removed from the water-bath, the contents were diluted with water until the concentration of sulfuric acid was 30–40%, and the unused manganic oxide filtered off and washed well with boiling water. The combined filtrate and washings were diluted with water until there was 30 cc. for each cubic centimeter of sulfuric acid originally present. The solution was filtered and treated with *p*-nitrophenylhydrazinehydrochloride solution until no more precipitate would form, allowed to stand for an hour and the practically pure nitrophenylhydrazone filtered off, washed and dried at 105°.

The unused manganic oxide from each oxidation was washed with ether, *N* sodium hydroxide solution, 10% sulfuric acid solution, and finally with water before drying. The unused toluenearsonic acid from each oxidation was dissolved in 40 cc. of dilute sodium carbonate solution, filtered and reprecipitated with hydrochloric acid.

The concentration of sulfuric acid was varied from 30 to 96% and the temperature varied from room temperature to the boiling point of the solution, except in the case of the 96% sulfuric acid which was not heated above 100°. The best average yield of *o*-formylbenzenearsonic acid was 24.8%, allowing for the recovered *o*-toluenearsonic acid, and was obtained using 96% sulfuric acid at room temperature. The greatest yield of *p*-formylbenzenearsonic acid was 11.8%, allowing for the recovered *p*-toluenearsonic acid, and was obtained using 96% sulfuric acid at 80°, while the best yield of *m*-toluene-

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

arsonic acid was 7.4%, taking into consideration the recovered *m*-toluenearsonic acid, and was obtained using 40% sulfuric acid at the temperature of a boiling water-bath.

The *p*-Nitrophenylhydrazones.—The *p*-nitrophenylhydrazone of *p*-formylbenzenearsonic acid precipitated as orange flocks which coagulated to a yellow solid, insoluble in water and in ordinary organic solvents, but could be recrystallized with difficulty from glacial acetic acid. It was purified by making the solution of its sodium salt just faintly acid to litmus paper, and filtering, then acidifying the filtrate to Congo red paper with hydrochloric acid; m. p. > 250°.

Anal. Calcd. for $C_{13}H_{12}O_5N_3As$: As, 20.53. Found: As, 20.53, 20.50.

The *p*-nitrophenylhydrazone of *o*-formylbenzenearsonic acid precipitated as orange flocks which coagulated slowly at room temperature, rapidly at 60°, to a yellow solid. It was insoluble in water, but could be recrystallized from a large volume of alcohol as yellow needles; m. p. 201.5°, corr.

Anal. Calcd. for $C_{13}H_{12}O_5N_3As$: As, 20.53. Found: As, 20.45, 20.49.

The *p*-nitrophenylhydrazone of *m*-formylbenzenearsonic acid was an orange solid and was purified by reprecipitation from a solution of its sodium salt. It was but little soluble in organic solvents; m. p. > 250°.

Anal. Calcd. for $C_{13}H_{12}O_5N_3As$: As, 20.53. Found: As, 20.52, 20.58.

Phenylhydrazone of *o*-Formylbenzenearsonic Acid.—In addition to the *p*-nitrophenylhydrazone used to determine the yields, a new compound, the phenylhydrazone, was prepared as follows. Twelve grams of *o*-toluenearsonic acid was oxidized with manganic oxide and sulfuric acid and after removing the unused oxide from the mixture, the remaining solution was treated with concentrated ammonium hydroxide solution until a trace of permanent precipitate formed. A solution of phenylhydrazine hydrochloride, containing 2 g. of phenylhydrazine, was then added whereupon the phenylhydrazone precipitated as a yellow solid. This was suspended in 20 cc. of warm water and dissolved by adding sodium carbonate. The solution was neutralized with acetic acid, cooled in ice, and the sodium salt of the phenylhydrazone of *o*-formylbenzenearsonic acid precipitated as shining scales. These were filtered off, sucked as dry as possible (but not washed), dissolved in 300 cc. of water, filtered and the solution made acid to Congo red paper to precipitate the arsonic acid. This was filtered off and dried in a vacuum desiccator over phosphorus pentoxide; yield, 2.1 g. (11.8%). The substance darkened when dried at 105°, and decomposed between 131 and 137°, depending on the rapidity of heating. It crystallized from hot alcohol as small yellow prisms.

Anal. Calcd. for $C_{13}H_{13}O_3N_2As$: As, 23.42. Found: As, 23.45, 23.44.

Oxidation of *o*-Toluenearsonic Acid with Manganese Dioxide.—Five grams of manganese dioxide with 8.3 g. of *o*-toluenearsonic acid was refluxed with 50 g. of 40% sulfuric acid solution for ten hours. The unused manganese dioxide was filtered off and washed thoroughly with boiling water. The filtrate and washings were combined, diluted to 300 cc. and treated with *p*-nitrophenylhydrazine hydrochloride solution until no more precipitate formed. The *p*-nitrophenylhydrazone of *o*-formylbenzenearsonic acid was filtered, washed and dried at 105°, then over phosphorus pentoxide; yield, 0.8 g. (6%). A similar oxidation using 10 g. of manganese dioxide gave 0.7 g. (7%). Two reactions were carried out in bomb tubes. Both tubes contained 8.3 g. of *o*-toluenearsonic acid, 5 g. of manganese dioxide and 50 g. of 40% sulfuric acid solution and were heated for ten hours, one at 140° and the other at 155°. The first gave 0.35 g. (3%), the second gave 0.65 g. (7%).

The filtrates, from which the *p*-nitrophenylhydrazone was taken, were decolorized with activated charcoal and concentrated to about one-third their former volume. On cooling, there was formed a small quantity of white needles which did not melt below

260°. These portions of needles were combined and recrystallized from hot water, and proved to be *o*-benzarsonic acid.

Oxidation of *p*-Toluenearsonic Acid with Chromic Acid Anhydride.[17]—Thirty grams of *p*-toluenearsonic acid was dissolved in a solution of 120 cc. of acetic anhydride, 120 cc. of glacial acetic acid and 27 cc. of concentrated sulfuric acid, in a 500-cc. wide-mouthed flask, through the stopper of which passed a stirrer, thermometer and addition tube. The flask was cooled in ice and 24 g. of chromic acid anhydride added in small portions over a period of ninety minutes. The temperature was held at 5–10°, and the mixture stirred vigorously during the addition and for forty-five minutes thereafter. The reaction mixture was then scraped into 300 g. of ice, dissolved and allowed to come to room temperature. The solution was extracted with one 400-cc. and three 100-cc. portions of ether. The aqueous layer was treated several times by alternately adding 15 cc. of glacial acetic acid and extracting it with 75 cc. of ether. The ether extract was concentrated under reduced pressure to 100 cc., diluted with water to 250 cc., and again concentrated to 100 cc. It was then nearly neutralized with 6 *N* sodium hydroxide solution and filtered. The filtrate contained the *p*-formylbenzenearsonic acid, and from such solutions the derivatives described below were prepared. *p*-Nitrophenylhydrazone of *p*-formylbenzenearsonic acid was obtained in yields of 12% from the concentrated extract resulting from the oxidation of 15.8 g. of *p*-toluenearsonic acid. Phenylhydrazone of *p*-formylbenzenearsonic acid was obtained in 8% yields from the concentrated extract produced by the oxidation of 30 g. of *p*-toluenearsonic acid. One and two-tenths grams (5.7%) of the semicarbazone of *p*-formylbenzenearsonic acid[18] was obtained from the concentrated extract obtained by the oxidation of 15.8 g. of the arsonic acid.

Oxidation of *o*-Toluenearsonic Acid with Chromic Acid Anhydride.—Fifteen grams of *o*-toluenearsonic acid was oxidized by the method outlined for the para isomer, and the reaction mixture scraped into 200 g. of ice and dissolved. The solution was diluted to 500 cc. and allowed to come to room temperature, then treated with 60 cc. of *p*-nitrophenylhydrazine hydrochloride solution containing 2 g. of *p*-nitrophenylhydrazine. The yellow precipitate was filtered, washed, warmed with dilute sodium carbonate solution, and the insoluble part filtered off and dissolved in 10 cc. of concentrated sulfuric acid in an ice-bath. The sulfuric acid solution was poured into 300 cc. of water, whereupon a yellow precipitate in a green solution was formed. This was filtered, the precipitate washed and dissolved in dilute sodium carbonate solution, which was then combined with the original sodium carbonate filtrate. The resulting solution was made just acid to litmus paper and treated with activated charcoal while hot, then acidified to Congo red paper. The *p*-nitrophenylhydrazone of *o*-formylbenzenearsonic acid precipitated as a yellow solid; yield, 1.0 g. (4%).

2-Methyl-3,5-dinitrobenzenearsonic Acid.—Using the method of Karrer,[19] 2-methyl-5-nitrobenzenearsonic acid was prepared, and 30 g. of the carefully dried product dissolved in 60 cc. of fuming sulfuric acid (20% excess sulfur trioxide) in a 200-cc. flask. To this solution 22.5 cc. of red fuming nitric acid (sp. gr. 1.6) was added in small portions. A vertical tube 70 cm. long was fitted to the flask with a ground-glass connection and the flask placed over a boiling water-bath. The water level was held just below the bottom of the flask, which rested on the rings that covered the bath. The solution was stirred through the tube and heated for four hours, then poured over six volumes of crushed ice. The 2-methyl-3,5-dinitrobenzenearsonic acid precipitated as white crystals. It was filtered off, washed with a little water, then suspended in 200 cc. of water, and concentrated ammonium hydroxide solution added with warming until all dissolved. The solution was made just acid to litmus paper with hydrochloric acid, and filtered

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[17] Scott and Hamilton, THIS JOURNAL, **52**, 4122 (1930).

[18] Gibson and Levin, *J. Chem. Soc.*, 2388 (1931).

[19] Karrer, *Ber.*, **48**, 311 (1915).

warm through a mat of activated charcoal, and the filtrate acidified to Congo red paper. The substance precipitated as needles; yield, 23–24 g. (65–68%) of almost pure material, which was used in this form; m. p. 201–203°. The substance crystallized in two interconvertible forms. When a hot solution was cooled rapidly, the product consisted of hexagonal plates, frequently elongated to needles, but when a cold neutral solution of the sodium salt was acidified slowly with hydrochloric acid, the plates were rectangular. The rectangular plates could also be produced by seeding a hot solution and cooling it slowly.

Anal. Calcd. for $C_7H_7O_7N_2As$: N, 9.15; As, 24.50. Found: N, 9.45; As, 24.58, 24.55.

Ammonium Salt of 2-Methyl-3,5-dinitrobenzenearsonic Acid.—Eight grams of 2-methyl-3,5-dinitrobenzenearsonic acid was suspended in 60 cc. of water and concentrated ammonium hydroxide solution added with warming until all dissolved. The solution was then just neutralized with hydrochloric acid and cooled. Scratching the beaker with a glass rod, or seeding, caused the ammonium salt to precipitate as rhomboidal scales which were filtered off, washed with 10 cc. of water and dried at 105°. They were soluble in water and the aqueous solution gave back the 2-methyl-3,5-dinitrobenzenearsonic acid when acidified to Congo red paper with hydrochloric acid.

Anal. Calcd. for $C_7H_{10}O_7N_3As$: As, 23.20. Found: As, 23.11, 23.17.

2-Methyl-3,5-diaminobenzenearsonic Acid and its Sodium Salt.—Ten grams of 2-methyl-3,5-dinitrobenzenearsonic acid gave 3 g. (37%) of the corresponding diamino compound when reduced by the ferrous hydroxide method of Jacobs, Heidelberger and Rolf.[20] The product was precipitated as fine needles, soluble in 3 *N* hydrochloric acid solution, but insoluble in water.

Anal. Calcd. for $C_7H_{11}O_3N_2As$: As, 30.46. Found: As, 30.50, 30.48.

The sodium salt was prepared by dissolving the acid in dilute sodium carbonate solution and neutralizing the solution to litmus paper with hydrochloric acid. The sodium salt, separating as a yellow solid, was filtered off, washed with a little alcohol and dried at 105°.

Anal. Calcd. for $C_7H_{10}O_3N_2AsNa$: As, 27.96. Found: As, 28.07, 28.10.

N-(2-Arsono-4,6-dinitrobenzal)-N′,N′-dimethyldiaminobenzene.—Twenty-five grams of 2-methyl-3,5-dinitrobenzenearsonic acid and 10 g. of anhydrous sodium carbonate were placed in a 500-cc. flask with a mixture of 75 cc. of ethyl alcohol and 75 cc. of methyl alcohol. The flask was fitted with a reflux condenser and the contents refluxed on a water-bath. Carbon dioxide was evolved. After fifteen minutes refluxing, the flask was removed and 10.8 g. of *p*-nitrosodimethylaniline added, then returned to the bath and refluxed for two hours. The color of the solution changed from green to dark brown. The flask was again removed and the contents poured into an evaporating dish, where the alcohol was allowed to evaporate at 30–35°. The black solid which remained was dissolved in 300 cc. of water and a small amount of insoluble material filtered off on a mat of activated charcoal. The deep red-brown filtrate was then treated with glacial acetic acid until it was definitely acid to litmus paper and a black precipitate formed, which was filtered off and air dried; wt. 19 g. It was dissolved in dilute sodium carbonate solution and filtered, then reprecipitated as before with acetic acid. This solution and reprecipitation was repeated two more times, with a final yield of 4.7 g. (13%), air dried. The product was bulky and gelatinous when freshly precipitated, and was difficult to wash on the filter. It was therefore placed in a flask with 100 cc. of water and stirred rapidly with a mechanical stirrer for one-half hour, then filtered again. When dry, its volume always diminished greatly. It was ground in a

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[20] Jacobs, Heidelberger and Rolf, THIS JOURNAL, **40**, 1580 (1918).

mortar until all would pass through a 100-mesh screen and the sifted material dried several days in a vacuum desiccator over phosphorus pentoxide.

The condensation product was black, but when the solution dried it left a purple film. It was soluble in 2 *N* hydrochloric acid, giving a red solution. When the substance was boiled with water, acetic acid, ethyl or methyl alcohol, the liquid was colored deep purple, although it was not sufficiently soluble in these solvents for recrystallization.

Anal. Calcd. for $C_{15}H_{15}O_7N_4As$: As, 17.09. Found: As 16.85, 16.70.

Summary

1. The three isomeric formylbenzenearsonic acids have been prepared by oxidation of the corresponding toluenearsonic acid, using manganic oxide and sulfuric acid solutions, and manganese dioxide and sulfuric acid solution. The aldehydes were isolated as insoluble derivatives of the carbonyl group.
2. The oxidation of *p*-toluenearsonic acid, as carried out by Scott and Hamilton, has been repeated with increased yield of the *p*-nitrophenylhydrazone and the method applied to the oxidation of *o*-toluenearsonic acid.
3. Derivatives of a new arsonic acid, *o*-formylbenzenearsonic acid, have been prepared.
4. Two new arsonic acids, 2-methyl-3,5-dinitrobenzenearsonic acid and 2-methyl-3,5-diaminobenzenearsonic acid, have been described.
5. 2-Methyl-3,5-dinitrobenzenearsonic acid has been condensed with *p*-nitrosodimethylaniline to produce N-(2-arsono-4,6-dinitrobenzal)-N',N'-dimethyl-*p*-diaminobenzene. This is a new way of preparing derivatives of an aldehyde arsonic acid.
6. An improvement in the potentiometric titration method for the determination of arsenic has been made.

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