catalyst. In the lower concentrations the aluminum chloride is not present as such but as a complex with the ethoxide and if the ester reaction is inhibited by alcohol no polymerization takes place. Aluminum ethoxide is thus an "anticatalyst" for the polymerization reaction under these conditions. The reaction takes place in a homogeneous system and is not dependent upon colloidal solutions.

Three moles of water react quantitatively with one mole of catalyst and destroy its catalytic activity.

The temperature coefficient of the reaction in xylene is approximately 1.30 for a rise of 10° in the vicinity of room temperatures.

The patent claims in regard to the use of camphor and the conversion of the catalyst to an "active form" by melting are baseless except in so far as melting destroys a film of hydrated alumina and hence increases the rate of solubility.

The study of this reaction is being continued. The correlation of the results with those obtained with other reactions of aldehydes and an interpretation of them will be given in a later paper.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

ALIPHATIC ARSENO COMPOUNDS. I

ARSENO-ACETIC ACID AND TETRA-ARSENO-ACETIC ACID

BY CHARLES SHATTUCK PALMER[1]

RECEIVED AUGUST 11, 1923

Aliphatic arsenicals such as "arrhenal"[2] and "mon-arsone"[3] have found a limited application in therapy, but the superiority of the aromatic arsenic compounds seems to have been accepted as definitely proved. In

---

[1] National Research Fellow in Chemistry.

[2] (a) Sodium methylarsonate, $CH_3AsO_3Na_2$. (b) Meyer, *Ber.*, **16**, 1440 (1883). (c) Klinger and Kreutz, *Ann.*, **249**, 149 (1888). (d) Gautier, *Compt. rend.*, **134**, 329 (1902). (e) Astruc, *ibid.*, **134**, 660 (1902). (f) Adrian and Trillat, *ibid.*, **134**, 1231 (1902). (g) D'Emilio, Jr., *Boll. Chim. Farm.*, **41**, 633 (1902); *Chem. Zentr.*, **1902**, II, 1277. (h) Mouneyrat, *Compt. rend.*, **136**, 696 (1903). (i) Auger and Billy, *ibid.*, **137**, 925 (1903). (j) Dehn, *Am. Chem. J.*, **33**, 136 (1906); THIS JOURNAL, **28**, 347 (1906). (k) Moore, Nierenstein and Todd, *Ann. Trop. Med.*, **2**, 269 (1908). (l) Castelli, *Arch. Schiffs Tropen-Hyg.*, **16**, 605 (1913). (m) Fabrel, *Bull. sci. pharmacolog.*, **20**, 337 (1913). (n) Launoy, *Compt. rend. soc. biol.*, **81**, 164 (1918). (o) Voegtlin and Smith, *J. Pharmacol.*, **15**, 475 (1920); **16**, 449 (1921). (p) Quick with Adams, THIS JOURNAL, **44**, 805 (1922).

[3] Sodium ethylarsonate, $C_2H_5AsO_3Na_2$. (a) La Coste, *Ann.*, **208**, 34 (1881). Ref. 2j. (b) Valeur and Delaby, *Bull. soc. chim.*, [4] **27**, 366 (1920). Ref. 2o. (c) Wright, Kennell and Hussey, *Med. Record*, **97**, 607 (1920). (d) Nichols, *J. Am. Med. Assoc.*, **76**, 1335 (1921). (e) Council on Pharmacy and Chemistry, *ibid.*, **76**, 1781 (1921). Ref. 2p.

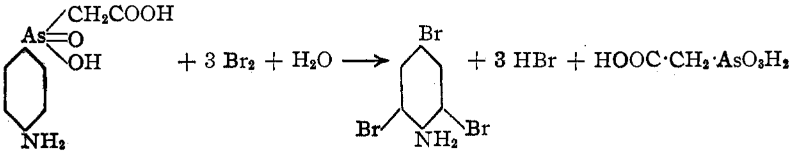
view of the great number of aromatic derivatives containing the arseno linkage, —As=As—, which have been subjected to pharmacological investigation, it is surprising that no water-soluble aliphatic arseno compound has yet been recorded in the literature. The preparation of such an aliphatic arseno compound would provide further means for determining the relative efficiency in comparison with the aromatic series for the treatment of diseases caused by trypanosomes or spirochetes. An opportunity to fill this gap in our knowledge has now been afforded by the synthesis of arseno-acetic acid according to the following equations.

$$NaOOC{\cdot}CH_2Cl + Na_3AsO_3 \longrightarrow NaCl + NaOOC{\cdot}CH_2{\cdot}AsO_3Na_2 \qquad (1)$$

$$2\ HOOC{\cdot}CH_2{\cdot}AsO_3H_2 + 4\ H_3PO_2 \longrightarrow HOOC{\cdot}CH_2As{=}As{\cdot}CH_2COOH + 4\ H_3PO_3 + 2\ H_2O \qquad (2)$$

The only aliphatic arseno compounds previously known were arsenomethane and arseno-ethane which were prepared by Auger[4] by reduction of the corresponding arsonic acids with hypophosphorous acid. Arsenomethane is a yellow oil which polymerizes readily to a brown-black solid.[5] Cryoscopic determinations of molecular weight indicate the dimeric form, $(CH_3As{=}AsCH_3)_2$, but the compound gives several reactions which show the presence of the arseno linkage. Arsenomethane in the form of a red solid polymer was probably the product of the action of methylarsine on methylarsine oxide.[6] So obscure has the series of aliphatic arseno compounds remained that the latest edition of Beilstein does not include it in the classification, Auger's work appearing under methylarsonic acid.[7]

Arsono-acetic acid, the reduction of which leads to arseno-acetic acid, was first prepared by Ehrlich and Bertheim,[8] who treated *p*-aminophenylarsino-acetic acid with bromine water.



(3)

The tribromo-aniline was filtered off and the filtrate boiled with magnesia mixture, whereupon magnesium arsono-acetate precipitated. The ease with which sodium chloro-acetate reacts with the sodium salts of primary aromatic arsine oxides

---

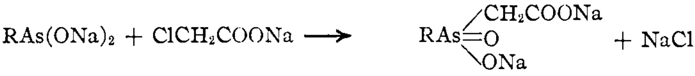
[4] Auger *Compt. rend.*, **138**, 1705 (1904).

[5] Ref. 4. Bougault, *J. pharm. chim.*, [6] **17**, 97 (1903).

[6] Dehn, *Am. Chem. J.*, **40**, 108 (1908).

[7] Beilstein-Prager-Jacobson, "Handbuch der Organischen Chemie," Springer, Berlin, **1922**, Vol. IV.

[8] Ehrlich and Bertheim, *Ber.*, **43**, 926 (1910).

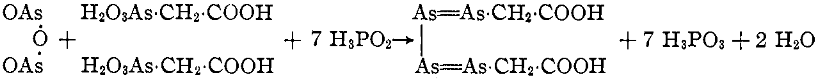


$$RAs(ONa)_2 + ClCH_2COONa \longrightarrow RAs\begin{matrix}\diagup CH_2COONa\\ =O\\ \diagdown ONa\end{matrix} + NaCl^{9} \qquad (4)$$

led to the supposition that it would react with sodium arsenite as well. It has now been found that sodium chloro-acetate can be converted quantitatively into arsono-acetic acid merely by allowing it to react in aqueous solution for two hours with a 100% excess of sodium arsenite. On account of the extreme solubility of the product, it is best isolated as the barium salt.

To prepare arseno-acetic acid, barium arsono-acetate is stirred with hot aqueous sodium sulfate, barium sulfate filtered off, and the cold filtrate treated with sulfuric acid and sodium hypophosphite. On long standing in the cold there results an excellent yield of arseno compound. If the reaction mixture is heated even at a temperature as low as 50°, there is decomposition with formation of inorganic arsenic and the product is badly contaminated with polyarsenide as a result. When pure, arseno-acetic acid consists of yellow needles, which decompose above 200° without melting, and are insoluble in water and common organic solvents, but readily soluble in pyridine and in dilute aqueous alkali hydroxides and carbonates.

Aromatic polyarsenides have been prepared by the simultaneous reduction of aromatic arsonic acids and arsenious acid.[10] In a similar manner reduction of one molecular equivalent of arsenic trioxide and two of arsono-acetic acid leads to the formation of the bright vermilion-red polyarsenide, tetra-arseno-acetic acid:



$$\begin{matrix}OAs\\ \dot{O}\\ OAs\end{matrix} + \begin{matrix}H_2O_3As\cdot CH_2\cdot COOH\\ \\ H_2O_3As\cdot CH_2\cdot COOH\end{matrix} + 7\,H_3PO_2 \rightarrow \begin{matrix}As{=}As\cdot CH_2\cdot COOH\\ |\\ As{=}As\cdot CH_2\cdot COOH\end{matrix} + 7\,H_3PO_3 + 2\,H_2O \qquad (5)$$

In solubility and in behavior toward heat this compound closely resembles arseno-acetic acid.

The sodium salts of arseno-acetic and tetra-arseno-acetic acids are precipitated from aqueous solution by addition of alcohol. Pharmacological tests on these salts are being performed by Professor H. G. Barbour of the University of Louisville, who will publish the results elsewhere.

The preparation of homologs and derivatives of the substances described in this communication, including aliphatic-aromatic arseno compounds, is now in progress. A similar series derived from the chlorohydrins will also be made.

---

[9] Ref. 8, p. 925. Bertheim, *Ber.*, **48**, 350 (1915). Ref. 2 p. Lewis and Cheetham, This Journal, **45**, 514 (1923).

[10] German pat., 270,254. Fargher, *J. Chem. Soc.*, **117**, 865 (1920). Christiansen, This Journal, **43**, 373 (1921); **45**, 1807, 2182 (1923).

Experimental Part

Arsono-acetic Acid,[11] $H_2O_3As{\cdot}CH_2{\cdot}COOH$.—The second reference contains a description of the preparation of arsono-acetic acid from sodium arsenite and sodium chloro-acetate. Using the reagents in the proportion stated in this patent only one-third of the chloro-acetic acid and one-half of the arsenic trioxide are converted into calcium arsono-acetate. The melting point of the free acid is given as 152°, and of the ethyl ester as 94–95°.

The author of the present paper performed his original experiment with sodium arsenite and sodium chloro-acetate in September, 1920, and this method of synthesis was indicated in an application filed with the Research Fellowship Board, National Research Council, in February, 1921.

A solution of 99 g. of arsenic trioxide and 160 g. of sodium hydroxide in 300 cc. of water is cooled to room temperature; of this a 1cc. portion is then titrated with iodine according to the common volumetric method for the determination of arsenic. In the sodium arsenite solution is dissolved 47.25 g. of chloro-acetic acid (50% of the calculated quantity) and the strongly exothermic reaction begins. At the end of two hours a second 1cc. portion of the reaction mixture is removed and titrated. The result indicates that approximately one-half of the sodium arsenite has disappeared. The solution is acidified with glacial acetic acid, avoiding an excess, and cooled. Most of the remaining arsenic trioxide precipitates and is filtered off. The filtrate is poured into a solution containing 185 g. of crystallized barium chloride in 500 cc. of warm water. Barium arsono-acetate, $Ba(OOC.CH_2.AsO_3Ba)_2.6^1/_2H_2O$, immediately forms as a white, finely divided precipitate. It is filtered on a 15cm. Büchner funnel, washed thoroughly with water and dried on plates. The precipitated product is quite pure, but it can be recrystallized from a large volume of boiling water, in which it is sparingly soluble, as fine, feathery, colorless needles. The yield is almost quantitative (between 220 and 230 g.).

Analyses. Subs., 0.1542, 0.3587: loss at 110°, 0.0203, 0.0464. Calc. for $C_4H_4O_{10}As_2Ba_3.6^1/_2H_2O$: H_2O, 13.13. Found: 13.16, 12.93.

Dried subs., 0.2789, 0.1410: 18.5, 9.3 cc. iodine (1 cc. = 0.00293 g. As). Dried subs., 0.2151, 0.3594: $BaSO_4$, 0.1922, 0.3226. Calc. for $C_4H_4O_{10}As_2Ba_3$: As, 19.38; Ba, 53.23. Found: As, 19.43, 19.32; Ba, 52.59, 52.82.

The necessity for using an excess of sodium arsenite is shown by an experiment with reagents as indicated theoretically in Equation 1. After the reaction mixture had stood for 4 hours it was demonstrated by iodine titration that 49% of the original sodium arsenite remained. No change was produced by 18 hours' refluxing. At this point one additional molecular equivalent of chloro-acetic acid and of sodium hydroxide were dissolved in the solution. After 4 additional hours of refluxing, 46% of the sodium arsenite had still failed to react.

Sodium arsono-acetate is prepared by adding 89.1 g. of barium arsono-acetate to a solution of 42.5 g. of anhydrous sodium sulfate in 200 cc. of hot water. The mixture is digested for 1 hour at 100° and frequently stirred. The barium sulfate is then filtered off and the filtrate concentrated on the steam-bath. Sodium arsono-acetate is obtained in several fractions having a combined weight of 47.8 g. (calc., 50.0 g.). This product contains a slight impurity of sodium sulfate, from which it is completely freed by one or two recrystallizations. In final form sodium arsono-acetate is a white, microcrystalline

---

[11] Ref. 8. Huisman, Callsen and Grüttefien, U. S. pat. 1,445,685, Feb. 20, 1923; *C. A.*, **17,** 1534 (1923); Austrian pat. 93,325; Swiss pat. 97,977; *Chem. Zentr.*, **1923,** IV, 721.

powder that readily dissolves in cold water to give a solution which reacts alkaline to litmus.

Analyses. Subs., 0.5544: loss at 110°, 0.0000. Subs., 0.1913, 0.1389: 19.3, 14.0 cc. iodine (1 cc. = 0.00293 g. As). Subs., 0.1729, 0.1729: Na_2SO_4, 0.1455, 0.1491. Calc. for $C_2H_2O_5AsNa_3$: As, 30.00; Na, 27.60. Found: As, 29.56, 29.53; Na, 27.24, 27.92.

Isolation of free arsono-acetic acid from the original reaction mixture after precipitation of the excess of arsenic trioxide is not very satisfactory, since the acid is separated from the various inorganic by-products of the reaction only by a long and inefficient process of fractional crystallization in which the solvent is gradually changed from water to alcohol. The acid is more readily obtained from the barium salt. A mixture of 22.5 g. of powdered barium arsono-acetate and 100 cc. of water containing 5 cc. of sulfuric acid (d., 1.84) is mechanically stirred at room temperature for several hours. Barium sulfate is removed by filtration and the filtrate concentrated in a vacuum over sulfuric acid in the cold. At very small volume crystallization commences. Twenty-five cc. of absolute alcohol is stirred with the mixture of crystals and viscous liquor and the insoluble, inorganic, arsenic containing material filtered off. To the filtrate 25 cc. of ligroin is added and the mixture concentrated at room temperature as before. Arsono-acetic acid now crystallizes, is filtered off, washed with ligroin and dried on a tile. The product consists of colorless, shining plates; m. p., 152° (loss of gas). It is very soluble in water and alcohol, sparingly soluble in hot glacial acetic acid, practically insoluble in ligroin, benzene, acetone, chloroform or ethyl acetate.

Analyses. Subs., 0.1778, 0.1475: 24.5, 20.3 cc. iodine (1 cc. = 0.00293 g. As). Calc. for $C_2H_5O_5As$: As, 40.76. Found: 40.37, 40.32.

Heating during the preparation of arsono-acetic acid as outlined above is inadvisable. Apparently the arsono group is split off very easily when arsono-acetic acid is in hot mineral acid solution and, unless heating is avoided, the isolation of the acid becomes difficult or impossible.

Arseno-acetic Acid, $HOOC{\cdot}CH_2{\cdot}As{=}As{\cdot}CH_2{\cdot}COOH$.—A solution of 12.5 g. of sodium arsono-acetate and 30 g. of sodium hypophosphite ($NaH_2PO_2.H_2O$) in 150 cc. of 15% sulfuric acid is allowed to stand in the cold. After two days the yellow precipitate is filtered off, washed several times with water and dried in a vacuum over sulfuric acid. When dried in air the product darkens slightly, due undoubtedly to oxidation. The filtrate is allowed to stand as before and, after two additional two-day periods, the reaction is practically complete; total yield, 6.2 g. (calc., 6.7 g.). Arseno-acetic acid forms minute yellow needles which begin to decompose at about 205°, but do not melt below 260°. It is insoluble in water and common organic solvents, but readily soluble in pyridine, dil. sodium hydroxide, and dil. sodium carbonate solutions. Usually at least one of the fractions will be found to be analytically pure and the rest nearly so.

Analyses. Subs., 0.1023, 0.1444: 19.5, 27.5 cc. iodine (1 cc. = 0.00293 g. As). Calc. for $C_4H_6O_4As_2$: As, 55.96. Found: 55.86, 55.80.

For the preparation of arseno-acetic acid on a larger scale it is convenient to warm the wet, freshly filtered barium arsono-acetate prepared as described above with sodium sulfate solution and to treat the filtrate from barium sulfate with sulfuric acid and sodium hypophosphite in the cold. Yields of 80–90% calculated from the chloro-acetic acid are obtained. In one run the reaction mixture was heated at 50–55° and the reduction completed in 8 hours. The orange-colored product was found to contain over 70% of arsenic. Evidently the decomposition already noted had taken place and simultaneous reduction of the arsonic acid with an inorganic arsenic compound gave a mixture composed principally of polyarsenide. In the cold this formation of inorganic arsenic is largely prevented, but even at this low temperature later fractions of material may contain a small quantity of tetra-arseno-acetic acid.

A solution of 3.35 g. of arseno-acetic acid in 25 cc. of 5% sodium hydroxide is filtered and 75 cc. of 95% alcohol added. A yellow oil precipitates which, after several hours' standing, crystallizes in rosets composed of very fine needles. These are filtered off, washed repeatedly with 95% alcohol and dried in a vacuum over sulfuric acid; weight, 3.7 g. The salt is then in the form of a light yellow-brown powder which retains some solvent, probably alcohol, and must be dried to constant weight at 110° before analysis. Disodium arseno-acetate is readily soluble in water, giving a clear yellow solution which reacts slightly alkaline to litmus.

Analyses. Subs., 0.1257, 0.2081: 20.5, 34.0 cc. iodine (1 cc. = 0.00293 g. As). Subs., 0.1665, 0.2201: Na_2SO_4, 0.0768, 0.1045. Calc. for $C_4H_4O_4As_2Na_2$: As, 48.08, Na, 14.74. Found: As, 47.78, 47.87; Na, 14.93, 15.37.

Tetra-arseno-acetic Acid, $HOOC{\cdot}CH_2{\cdot}As{=}As{-}As{=}As{\cdot}CH_2{\cdot}COOH$.—Arsono-acetic acid is prepared from sodium arsenite and sodium chloro-acetate in a run just half the size of that described above. As soon as the reaction is complete, 150 g. of sulfuric acid (d., 1.84) and 100 g. of sodium hypophosphite are dissolved in the solution. After three hours a mixture of arsenic trioxide and sodium sulfate containing a little highly-colored organic arsenic compound is filtered off, and the filtrate is allowed to stand in the cold. A bright red precipitate gradually forms, which is filtered off at 3- to 4-day intervals, washed several times with water and dried in a vacuum over sulfuric acid. Drying in air causes the exposed surface to blacken. Altogether, five fractions are obtained, most of which are fairly pure; total yield, 25.6 g. Heating increases the rate of reaction but tends to produce an impure product. Tetra-arseno-acetic acid is a bright vermilion-red, microcrystalline powder, which begins to decompose at about 180°, but does not melt below 250°. The solubilities are closely similar to those of arseno-acetic acid.

Analyses. Subs., 0.1360, 0.1926: 33.1, 46.9 cc. iodine (1 cc. = 0.00293 g. As). Calc. for $C_4H_6O_4As_4$: As, 71.77. Found: 71.31, 71.37.

Seven g. of tetra-arseno-acetic acid is dissolved in 50 cc. of 5% sodium hydroxide solution. On addition of 50 cc. of 95% alcohol, a thick, dark oil is precipitated. The dilute alcohol is decanted, the residue redissolved in 50 cc. of water and an equal volume of 95% alcohol added. The precipitate can now usually be obtained crystalline. It is filtered off, washed with 50% alcohol and dried in a vacuum over sulfuric acid; weight, 6.4 g. Monosodium tetra-arseno-acetate is a red-brown powder which is considerably less soluble in water than disodium arseno-acetate. The solution is dark colored and reacts practically neutral to litmus, with possibly a slight tendency toward alkalinity. It is noteworthy that a monosodium salt is formed in spite of use of an excess of sodium hydroxide.

Analyses. Subs., 0.1090, 0.1232: 25.4, 28.8 cc. iodine (1 cc. = 0.00293 g. As) Subs., 0.1784, 0.1578: Na_2SO_4, 0.0312, 0.0286. Calc. for $C_4H_5O_4As_4Na$: As, 68.18; Na, 5.23. Found: As, 68.28, 68.49; Na, 5.66, 5.87.

Summary

1. Action of a 100% excess of sodium arsenite on sodium chloro-acetate gives a quantitative yield of arsono-acetic acid.

2. Reduction of arsono-acetic acid with hypophosphorous acid produces arseno-acetic acid.

3. By simultaneous reduction of one molecular equivalent of arsenic

trioxide and two of arsono-acetic acid the polyarsenide, tetra-arseno-acetic acid, is obtained.

4. Water-soluble sodium salts of the above acids are readily prepared.
5. Analogous series derived from various halogen acids and halohydrins are now being synthesized in this Laboratory.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE USE OF PLATINUM OXIDE AS A CATALYST IN THE REDUCTION OF ORGANIC COMPOUNDS. IV. REDUCTION OF FURFURAL AND ITS DERIVATIVES[1]

BY W. E. KAUFMANN[2] WITH ROGER ADAMS

RECEIVED AUGUST 15, 1923

The commercial development of furfural during recent years and its remarkable cheapness has led to many investigations for new uses. This communication describes the results obtained on the catalytic reduction of furfural and a number of its simple derivatives. The reduction is of interest not only because the products might be of practical importance, but also because there has been very little work done on the reduction of compounds of the furane series. Moreover, furfural itself is a different type of aldehyde from those which have thus far been reduced with the use of platinum oxide[3] as a catalyst and ferrous chloride as an activating agent.

The first work on the reduction of furfural was published in 1906 by Padoa and Ponti[4] who passed the vapors of furfural with hydrogen over a nickel catalyst at 190°. The primary product of the reduction was furyl alcohol. Further reduction always took place and from the mixture of reaction products it was possible to isolate methyl-2-furane, methyl-2-tetrahydrofurane and pentanol-2. It may thus be seen that rupture of the ring took place during reduction, though to only a very slight extent. The same authors reported that when they used a temperature of 270° the decomposition yielded in addition furane and carbon monoxide.

Law[5] studied the electrolytic reduction of furfural in the presence of alkali and acid but, with the exception of a small amount of furyl alcohol when the acid solution was used, only resins were obtained.

Pringsheim and Noth[6] reduced furfural by passing the vapors with hydrogen over

---

[1] Part of the chloroplatinic acid used in this investigation was purchased with the aid of a grant from the Bache Fund of the National Academy of Sciences. For this aid the authors are greatly indebted.

[2] This communication is an abstract of a thesis submitted by W. E. Kaufmann in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[3] (a) Voorhees and Adams, THIS JOURNAL, **44**, 1397 (1922). (b) Carothers and Adams, **45**, 1071 (1923). (c) Adams and Shriner, **45**, 2171 (1923).

[4] Padoa and Ponti, *Atti. R. accad. Lincei*, **15**, [5] 610 (1906); *Gazz. chim. ital.*, **37**, [2] 105 (1907).

[5] Law, *J. Chem. Soc.*, **89**, 1517 (1906).

[6] Pringsheim and Noth, *Ber.*, **53**, 114 (1920).