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

CONDENSATION PRODUCTS OF AMINO-ARSANILIC ACID[1]

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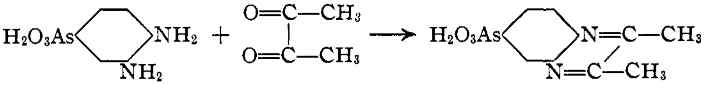
As part of a general plan for the synthesis of organic compounds containing arsenic the preparation of arsenated quinoxalines was undertaken for the reason that arsenated heterocyclic compounds containing nitrogen have received but scant study as possible therapeutic agents.[3] The recognized necessity of nitrogen in the form of free or modified amino groups in arsenical drugs gives the subject of nitrogen in other forms in such compounds special interest.

Amino-arsanilic acid prepared by the method of Bertheim as modified in this Laboratory was condensed with various compounds containing the 1,2-diketone grouping. The range of suitable solvents for such condensations is limited owing to the limited solubility of amino-arsanilic acid itself. In most instances absolute methyl alcohol was used, although more recently the higher-boiling glycol and glycerol have been found effective.[4]

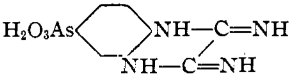
In most instances only sufficient derivatives of each condensation product were prepared to establish its structure.

The substances studied may be roughly divided into two classes. First are the arsenated quinoxalines obtained from amino-arsanilic acid and substances of the general type of 1,2-diketones. The reaction with diacetyl is typical of these.

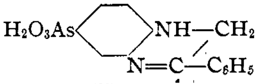


Similar reactions and products were obtained with benzil and its *m*-nitro, *p*-methoxy, *p*-ethoxy and *p*-dimethylamino derivatives as well as with piperil and furil.

Cyanogen adds to the diamino compound to give a di-imino-dihydroquinoxaline (I). ω-Bromo-acetophenone condenses to form a phenyl-dihydro-quinoxaline (II). No method has been found to determine the position of the phenyl group in the quinoxaline ring.



I



II

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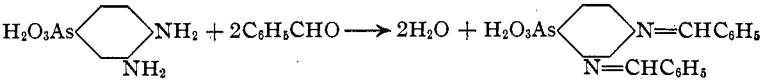
[1] This research was carried out under a grant from the Research Board of the Public Health Institute. Some of the compounds are being studied pharmacologically under a similar grant at the University of Wisconsin under the direction of Dr. A. S. Loevenhart.

[2] The condensation products of amino-arsanilic acid with certain aldehydes were prepared in this Laboratory by Mr. E. A. Larson.

[3] Baxter and Fargher, *J. Chem. Soc.*, **115**, 1372 (1919).

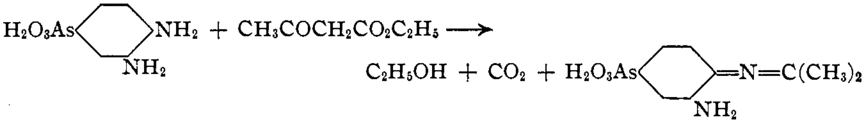
[4] Unpublished results obtained by Mr. E. B. Kester of this Laboratory.

The second type of product studied involves the condensation of monocarbonyl compounds to form arsenated Schiff's bases. The action of benzaldehyde is typical here.



Similar reactions and products were obtained with aldol, crotonic aldehyde, benzaldehyde, *o*- and *p*-anisaldehyde, and piperonal.

Ethyl aceto-acetate gives an unexpected reaction, the product being a condensation product of one molecule of the amino acid with one of acetone. This product cannot be obtained directly from acetone.



No method has been found to determine which amino group is involved in the reaction.

A reaction which falls under neither of the main classes is the action of chloro-acetamide on amino-arsanilic acid. This was carried out with the hope of obtaining a substance of pharmacological properties analogous to those of the related substance obtained from arsanilic acid and chloroacetamide (Tryparsamide).[5] One amino group reacts readily to give the grouping —$NHCH_2CONH_2$. Experiments are now being carried on to determine which amino group is involved in the reaction.

A paper will shortly appear covering work similar to that of the present paper but carried out with various carbohydrates and their derivatives. These reactions give new types of arsenicals containing an aromatic arsonic acid group, a nitrogen ring, and a carbohydrate residue.

Experimental Part

Preparation of Amino-arsanilic Acid (3,4-Diamino-phenyl-arsonic Acid).—The 3,4-diamino-phenyl-arsonic acid used in this research was prepared by the method of Bertheim.[6] Yields of 75–95% of the oxalylarsanilic acid were obtained depending upon the purity of the arsanilic acid used. In the nitration a yield of 68–78% was obtained but Bertheim's method of reduction with sodium hyposulfite ($Na_2S_2O_4$) gave poor results. The general method of Jacobs and Heidelberger[7] for the reduction of nitroarsonic acids by means of ferrous hydroxide was applied with good results. It was carried out as follows.

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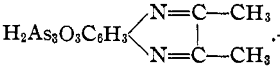
[5] (a) Jacobs and Heidelberger, This Journal, **41**, 1589 (1919). For full list of references see (b) Brown and Pearce, *J. Am. Med. Assoc.*, **82**, 5 (1924).

[6] Bertheim, *Ber.*, **44**, 3094 (1911).

[7] Jacobs, Heidelberger and Rolf, This Journal, **40**, 1581 (1918). Benda, *Ber.* **47**, 1006, 1316 (1914).

To a solution of 340 g. of hydrated ferrous chloride ($FeCl_2.4H_2O$) in 1250 cc. of water in a 3-liter flask, a 25% solution of sodium hydroxide was added in small portions until a strong alkaline reaction was obtained after the mixture had been shaken for several minutes. A solution of 61.5 g. of the acid in 250 cc. of 12% sodium hydroxide solution was poured into the alkaline ferrous hydroxide solution, the mixture shaken for ten to fifteen minutes and filtered through a large Büchner funnel. This is a very slow process and was usually arranged to continue overnight. The filtrate was nearly neutralized with hydrochloric acid and concentrated to about 250 cc. under a vacuum. It was filtered from sodium chloride and acidified to congo red with hydrochloric acid. When the sides of the vessel were scratched the 3,4-diamino-phenyl-arsonic acid precipitated immediately as a dark brown, crystalline powder. It was collected on a filter and the filtrate saved for recovery of a further amount of the amino-arsanilic acid.

The mud of ferrous and ferric hydroxides was extracted again with about 500 cc. of 25% sodium hydroxide solution and treated as described above. The first mother liquor was added before concentration under reduced pressure. The two crops of crystals amounted to 36 g. and 5 g. The product was dissolved in 350 cc. of water, treated with boneblack and filtered hot. It precipitated in tufts of brown crystals which melted at 159–160° with decomposition; yield, 33 g., or 60.7%.



2,3-Dimethyl-quinoxaline-6-arsonic Acid, $H_2As_3O_3C_6H_3\left\langle\begin{array}{l}N{=}C{-}CH_3\\ \quad\ \ |\\ N{=}C{-}CH_3\end{array}\right.$.—This compound was prepared by treating 5 g. of amino-arsanilic acid, in 100 cc. of absolute alcohol, with 2 g. of diacetyl and refluxing the materials for four hours. As no precipitate formed after long standing, the solution was concentrated to a small volume, and twice its volume of water added. A bluish precipitate separated, which after two recrystallizations from hot water, to which bone black was added, gave 2.5 g. of shiny pink flakes, a yield of 42%. This compound, melting with decomposition at 212–215°, is quite soluble in methyl alcohol and difficultly soluble in water.

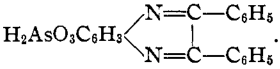
Anal. Subs., 0.1507, 0.1593: 30.60, 32.60 cc. of 0.03458 *N* iodine soln. Subs., 0.2077, 0.2466: 12.25, 14.94 cc. of 0.1173 *N* HCl. Calc. for $C_{10}H_{11}O_3N_2As$: N, 9.92; As, 26.55. Found: N, 9.62, 9.94; As, 26.35, 26.54.

2,3-Di-imino-1,4-dihydro-quinoxaline-6-arsonic Acid, I.—Five g. of amino-arsanilic acid was dissolved in 60 cc. of absolute methyl alcohol and cyanogen was passed slowly into the warm solution for two hours. The solution was placed in a small crystallizing dish and the oily residue after evaporation was treated with absolute ethyl alcohol until all of the product had been converted to an orange-colored powder. The product was recrystallized from ethyl alcohol and dried at 85°; yield, 2.1 g., or 36%; m. p. (decomp.), 200–205°. It is quite soluble in water or methyl alcohol and difficultly soluble in ethyl alcohol.

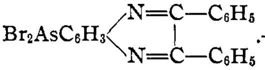
Anal. Subs., 0.1143, 0.1114: 13.65, 13.35 cc. of 0.0587 *N* iodine soln. Calc. for $C_8H_9O_3N_4As$: As, 26.39. Found: 26.30, 26.39.

3-Phenyl-1,2-dihydro-quinoxaline-6-arsonic Acid, II.—Five g. of amino-arsanilic acid was dissolved in 50 cc. of absolute methyl alcohol, and 4.1 g. of bromo-acetophenone added. The solution was refluxed for 16 hours, filtered and concentrated to one-half its volume. After standing in the cold for 24 hours, a mass of orange-colored crystals had formed on the sides of the container. The product was filtered off, the residue washed with a small amount of ethyl alcohol and recrystallized from methyl alcohol; yield, 2.7 g., or 38%. It did not melt below 250°. It is soluble in methyl alcohol, ethyl alcohol, dil. alkali and difficultly soluble in water. Chloro-acetophenone did not condense with amino-arsanilic acid under similar conditions.

Anal. Subs., 0.1212, 0.1230: 12.45, 12.50 cc. of 0.0583 *N* iodine soln. Calc. for $C_{14}H_{13}O_3N_2As$: As, 22.72. Found: 22.45, 22.39.

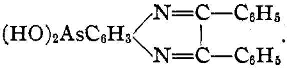
2,3-Diphenyl-quinoxaline-6-arsonic Acid,  $H_2AsO_3C_6H_3\left\langle\begin{matrix}N=C-C_6H_5\\ |\\ N=C-C_6H_5\end{matrix}\right.$.—To a solution of 12.5 g. of amino-arsanilic acid in 100 cc. of boiling methyl alcohol was added 10 g. of benzil (an equimolecular quantity). After this solution had been refluxed on a water-bath for 30 minutes a white solid appeared, which soon thickened the entire solution. The refluxing was continued for one and a half hours. After cooling the product, it was filtered and the residue dried on a porous plate; yield, 13 g., of a white or slightly yellow substance, or 64%. The product was purified by solution in sodium hydroxide solution and reprecipitation with hydrochloric acid. It is insoluble in alcohol and ether and slightly soluble in acetic acid.

Anal. Subs., 0.2089, 0.1298: 24.00, 14.75 cc. of 0.0432 *N* iodine soln. Subs., 0.2182, 0.1987: 9.50, 8.72 cc. of 0.10957 *N* HCl. Calc. for $C_{20}H_{15}O_3N_2As$: N, 6.89; As, 18.47. Found: N, 6.68, 6.73; As, 18.61, 18.41.

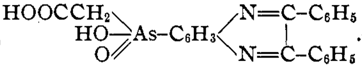
2,3-Diphenyl-quinoxaline-6-arsenious Bromide,  $Br_2AsC_6H_3\left\langle\begin{matrix}N=C-C_6H_5\\ |\\ N=C-C_6H_5\end{matrix}\right.$.—To 8.5 g. of 2,3-diphenyl-quinoxaline-6-arsonic acid was added 100 cc. of acetic acid, the mixture heated to boiling and an excess of a 50% solution of hydrobromic acid added. The acetic acid solution became clear immediately, but was colored due to the liberation of bromine. In a few minutes the bromide precipitated as shiny, yellow plates; yield, 8.8 g., or 83%. The product was recrystallized by solution in absolute alcohol and the addition of acetic acid. It is slightly soluble in acetic acid and benzene, and very soluble in alcohol; m. p., 232°.

Anal. Subs., 0.1575, 0.1673: AgBr, 0.1172, 0.1219. Calc. for $C_{20}H_{13}N_2AsBr_2$: Br, 31.00. Found: 31.67, 31.01.

The iodide could not be prepared from the arsonic acid by similar treatment with hydriodic acid, tars always resulting, but both the iodide and chloride were prepared from the oxide by solution in acetic acid and the addition of the corresponding halogen acid. The 2,3-diphenyl-quinoxaline-6-arsenious chloride melts at 185–187°.

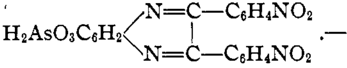
2,3-Diphenyl-quinoxaline-6-arsenious Acid,  $(HO)_2AsC_6H_3\left\langle\begin{matrix}N=C-C_6H_5\\ |\\ N=C-C_6H_5\end{matrix}\right.$.—To a solution of 8.8 g. of 2,3-diphenyl-quinoxaline-6-arsenious bromide in 50 cc. of 95% alcohol was added a 10% solution of sodium carbonate until the volume was approximately 300 cc. The white precipitate which formed was dissolved by the addition of a little concd. sodium hydroxide solution. From the clear, strongly alkaline solution the oxide was precipitated as a white, mushy precipitate on acidification with dil. sulfuric acid. The mixture was filtered, and the solid washed and dried; yield, 7.0 g., or 82%.

Anal. Subs., 0.1830, 0.1364: 19.40, 14.73 cc. of 0.0472 *N* iodine soln. Subs., 0.1641, 0.1580: 7.29, 6.84 cc. of 0.120 *N* HCl. Calc. for $C_{20}H_{15}O_2N_2As$: N, 7.15%; As, 19.23. Found: N, 7.46, 7.28; As, 18.77, 19.11.

2,3-Diphenyl-quinoxaline-6-arsino-acetic Acid,  $\begin{matrix}HOOCCH_2\\ HO\\ O\end{matrix}\!\!>\!As-C_6H_3\left\langle\begin{matrix}N=C-C_6H_5\\ |\\ N=C-C_6H_5\end{matrix}\right.$.—Two g. of 2,3-diphenyl-quinoxaline-6-arsenious oxide was treated with 25 cc. of 12 *N* sodium hydroxide solution and just enough alcohol was added to effect solution. The oxide is not sufficiently soluble in strong alkali to bring about this reaction without addition of alcohol. To the solution was added a solution of 1.0 g. of chloro-acetic acid in 5 cc. of 6 *N* sodium hydroxide solution.[8] After the mixture had stood overnight a small quantity of fine needles had separated; the mixture was then acidified to phenolphthalein with hydrochloric acid, filtered from the small amount of precipitated material and the filtrate acidified to congo red paper. The bulky, white precipitate was collected on a filter, dried and recrystallized from 50% acetic acid; yield, 1.0 g., or 45%, of small white needles; m. p., 122–125°, with evolution of gas.

Anal. Subs., 0.1410, 0.1059: 11.60, 8.60 cc. of 0.05568 *N* iodine soln. Subs., 0.1684, 0.2088: 6.28, 7.66 cc. of 0.1163 *N* HCl. Calc. for $C_{22}H_{17}O_4N_2As$: N, 5.74; As, 16.72. Found: N, 5.98, 6.08; As, 17.17; 16.95.

***m,m'*-Dinitro-2,3-diphenyl-quinoxaline-4-arsonic Acid,**



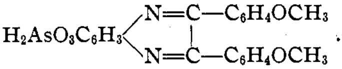
$H_2AsO_3C_6H_2\Big\langle\begin{matrix}N{=}C{-}C_6H_4NO_2\\ |\\ N{=}C{-}C_6H_4NO_2\end{matrix}$

.—A mixture of 2.3 g. of amino-arsanilic acid and 3 g. of dinitro-benzil melting at 110–111°, and prepared according to the method of Barnett and Kay,[9] together with 130 cc. of absolute methyl alcohol was refluxed for seven hours. The reaction mixture was concentrated to 50 cc., cooled and poured into 100 cc. of cold water. The precipitate found was recrystallized from 40% alcohol and dried to constant weight under reduced pressure at 100°; yield of pure compound, 3.5 g., or 75%.

The compound, which does not melt below 230°, is a white powder, insoluble in water but soluble in alkali forming a deep red solution.

Anal. Subs., 0.0971, 0.1087: 8.95, 10.05 cc. of 0.04307 *N* iodine soln. Subs., 0.4352, 0.2906: 30.00, 20.51 cc. of 0.1146 *N* HCl. Calc. for $C_{20}H_{13}O_7N_4As$: As, 15.11; N, 11.29. Found: As, 14.88, 14.92; N, 11.06, 11.32.

2,3-Di(*p*-methoxyphenyl)quinoxaline-6-arsonic Acid,



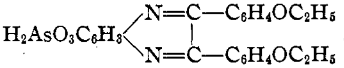
$H_2AsO_3C_6H_3\Big\langle\begin{matrix}N{=}C{-}C_6H_4OCH_3\\ |\\ N{=}C{-}C_6H_4OCH_3\end{matrix}$

.—Anisil was prepared in 30% yield from oxalyl chloride and anisole, in carbon disulfide solution, in the presence of aluminum chloride, according to Staudinger.[10] The product melts at 131–133°, instead of 95° as given in Beilstein.

The quinoxaline was prepared by treating 4.6 g. of amino-arsanilic acid in 50 cc. of methyl alcohol with 5.4 g. of anisil and refluxing the solution for about six hours. On cooling the product, some yellow needles of unchanged anisil crystallized. These were removed by filtration, and after scratching the vessel and allowing the solution to stand for two hours the arsenic compound precipitated as a yellowish, crystalline mass; yield, 5.8 g., or 61%. The product was dissolved in dil. sodium hydroxide solution and reprecipitated by acidifying to congo red paper with hydrochloric acid. Upon recrystallization from hot acetic acid the compound formed light yellow needles, easily soluble in hot acetic acid, slightly soluble in alcohol. A sample was dried in the oven at 125–130° for eight hours for the analyses.

Anal. Subs., 0.1259, 0.1602: 11.18, 14.00 cc. of 0.0472 *N* iodine soln. Subs. 0.1329, 0.1785: 4.79, 6.42 cc. of 0.1173 *N* HCl. Calc. for $C_{22}H_{19}O_5N_2As$: N, 6.01; As, 16.09. Found: N, 5.92, 5.91; As, 15.72, 15.82.

2,3-Di(*p*-ethoxyphenyl)quinoxaline-6-arsonic Acid,



$H_2AsO_3C_6H_3\Big\langle\begin{matrix}N{=}C{-}C_6H_4OC_2H_5\\ |\\ N{=}C{-}C_6H_4OC_2H_5\end{matrix}$

.—Phenetil may be obtained as follows by Staud-

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[8] G. Meyer, *Ber.*, **16**, 1440 (1883). Adams and Quick, THIS JOURNAL, **44**, 805 (1922).

[9] Barnett and Kay, *Chem. News*, **125**, 57 (1922).

[10] Staudinger, *Ber.*, **45**, 1594 (1912).

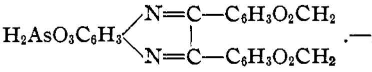
inger's[10] method which is superior to that of Vorländer[11] who used phenetole, cyanogen and aluminum chloride.

To a well-cooled solution of 17 g. of phenetol and 6 g. of oxalyl chloride in 50 cc. of carbon disulfide was added 15 g. of anhydrous aluminum chloride. After two hours the mixture was refluxed for 30 minutes on a water-bath, and then poured into a beaker of crushed ice and hydrochloric acid when the phenetil separated as a red, sticky mass. It was filtered dry on a Büchner funnel and washed with a little sodium carbonate solution. The product, obtained in good yield as small, white needles from chloroform and alcohol, melted at 150–151°.

A mixture of 3.5 g. of amino-arsanilic acid with 50 cc. of glacial acetic acid was heated to boiling and 4 g. of phenetil added. The clear solution was refluxed for one-half hour. On cooling the solution the condensation product crystallized in beautiful, yellow, needle-like crystals; yield, 5.5 g., or 84%. This product was purified for analysis by dissolving it in dil. sodium hydroxide solution, reprecipitating with hydrochloric acid and subsequently recrystallizing the precipitate from glacial acetic acid. The pure compound is light yellow and easily soluble in hot acetic acid and methyl alcohol. The product was dried at 125–130° for eight hours for analysis.

Anal. Subs., 0.1798, 0.1279: 15.75, 10.92 cc. of 0.0472 *N* iodine soln. Subs., 0.2153, 0.2366: 7.23, 8.00 cc. of 0.1173 *N* HCl. Calc. for $C_{24}H_{23}O_5N_2As$: N, 5.67; As, 15.18. Found: N, 5.52, 5.55; As, 15.11, 15.51.

2,3-Di(3,4-methylenedioxyphenyl)quinoxaline-6-arsonic Acid,

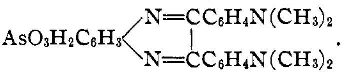


$H_2AsO_3C_6H_3\left\langle\begin{array}{l}N{=}C{-}C_6H_3O_2CH_2\\ \quad |\\ N{=}C{-}C_6H_3O_2CH_2\end{array}\right.$

.—A solution of 4.6 g. of amino-arsanilic acid and 6 g. of piperil in 75 cc. of glacial acetic acid was refluxed for 30 minutes. The reaction product then precipitated as a yellow, crystalline powder when the mixture was cooled and the walls of the vessel were scratched; yield, 9.2 g., or 92%. The product is soluble in acetic acid and methyl alcohol. It was recrystallized twice from glacial acetic acid for analysis.

Anal. Subs., 0.1851: 15.5 cc. of 0.0472 *N* iodine soln. Calc. for $C_{22}H_{15}O_7N_2As$: As, 15.17. Found: 14.82.

2,3-Di(*p*-dimethylaminophenyl)quinoxaline-6-arsonic Acid,

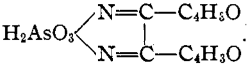


$AsO_3H_2C_6H_3\left\langle\begin{array}{l}N{=}CC_6H_4N(CH_3)_2\\ \quad |\\ N{=}CC_6H_4N(CH_3)_2\end{array}\right.$

.—Four g. of tetramethyldiamino-benzil was dissolved in 150 cc. of glacial acetic acid and a solution of 3 g. of amino-arsanilic acid in 50 cc. of glacial acetic acid added. After the material had been boiled for one hour the resulting brown precipitate was collected and recrystallized twice from methyl alcohol; yield of yellow powder, 5 g., or 45%. It is soluble in dil. alkali, difficultly soluble in methyl alcohol, insoluble in water and does not melt below 260°.

Anal. Subs., 0.1298, 0.1195: 12.25, 11.13 cc. of 0.04402 *N* iodine soln. Calc. for $C_{24}H_{25}O_3N_4As$: As, 15.23. Found: 15.56, 15.36.

2,3-Difuryl-quinoxaline-6-arsonic Acid,



$H_2AsO_3\left\langle\begin{array}{l}N{=}C{-}C_4H_3O\\ \quad |\\ N{=}C{-}C_4H_3O\end{array}\right.$

.—A solution of 2.8 g. of amino-arsanilic acid and 2 g. of furil (one molecular equivalent) in 25 cc. of absolute methyl alcohol was refluxed for three hours. The light brown precipitate which formed on cooling the solution was freed from amino-arsanilic with great difficulty, namely, only after further refluxing a solution of it in absolute methyl alcohol containing a small amount of furil, followed by recrystallization of the solid product thrice

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[11] Vorländer, *Ber.*, **44**, 2464 (1911).

from absolute methyl alcohol. The substance did not melt below 250° and was dried to constant weight at 100° for analysis.

Anal. Subs., 0.0885, 0.0660: 10.75, 8.10 cc. of 0.04239 *N* iodine soln. Calc. for $C_{16}H_{11}O_5N_2As$: As, 19.42. Found: 19.50, 19.30.

4-Dimethylmethylene-amino-3-aminophenyl-arsonic Acid, $AsO_3H_2C_6H_3[N{=}C(CH_3)_2]$ (NH_2).—A solution of 1 g. of amino-arsanilic acid in 30 cc. of absolute methyl alcohol mixed with 1 cc. of aceto-acetic ester was refluxed for four hours. The precipitate was collected on a filter the next morning and dried to constant weight at 110°; yield, 1 g., or 88%. The compound does not melt below 260°. The reaction, $AsO_3H_2C_6H_3(NH_2)_2 + CH_3COCH_2COOC_2H_5 = AsO_3H_2C_6H_3(NH_2)[N = C(CH_3)_2] + C_2H_5OH + CO_2$, appears to take place as the substance gives analytical values for the condensation product of acetone and amino-arsanilic acid. Carbon dioxide was evolved; its presence was proved by a test with barium hydroxide solution. Acetone could not be condensed directly with amino-arsanilic acid.

Anal. Subs., 0.1107, 0.1267: 16.78, 19.25 of 0.04818 *N* iodine soln. Calc. for $C_9H_{13}N_2O_3As$: As, 27.55%. Found: 27.43, 27.42.

1,2-Di(3-hydroxybutyleneamino)benzene-4-arsonic Acid, $AsO_3H_2C_6H_3(N{=}CHCH_2CHOHCH_3)_2$.—A solution of 5 g. of amino-arsanilic acid in 60 g. of absolute methyl alcohol mixed with 4 g. of aldol was filtered and refluxed for 12 hours. Concentrating the solution to one-half its volume produced no precipitate. The solution was evaporated to dryness and the dark, oily residue treated with absolute ethyl alcohol until all the oily substance had been converted to a brown powder. A mixture of this substance was refluxed and the residue separated in absolute ethyl alcohol and dried at 100° under reduced pressure; yield, 2 g., or 26% of a white crystalline product melting below 260°. It is soluble in methyl alcohol, water and dil. alkali and slightly soluble in ethyl alcohol.

Anal. Subs., 0.1064, 0.1120: 18.10, 19.10 cc. of 0.03223 *N* iodine soln. Calc. for $C_{14}H_{21}O_5N_2As$: As, 20.15. Found: 20.56, 20.61.

3,4-Di(crotonalamino)phenyl-arsonic Acid, $H_2AsO_3C_6H_3(N{=}CH{-}CH{=}CHCH_3)_2$.—A solution of 5 g. of amino-arsanilic acid in 60 cc. of absolute methyl alcohol was mixed with 4 cc. of crotonic aldehyde and the mixture was refluxed for four hours, the color of the solution changing to deep red. The solution was filtered and diluted with water until it became slightly cloudy. After it had stood in the cold for 24 hours, a grayish powder had precipitated. The substance was purified by dissolving it in methyl alcohol and precipitating with water as in the first procedure. The product, which does not melt below 260°, was dried to constant weight at 100°; yield, 2.7 g., or 39%.

Anal. Subs., 0.1138, 0.1133: 23.30, 23.10 cc. of 0.02881 *N* iodine soln. Calc. for $C_{14}H_{17}O_3N_2As$: As, 22.30. Found: 22.13, 22.02.

3,4-Dibenzalamino-phenyl-arsonic Acid, $AsO_3H_2C_6H_3(N{=}CHC_6H_5)_2$.—Twenty g. of benzaldehyde was slowly added to 23 g. of diamino-arsanilic acid dissolved in 300 cc. of absolute methyl alcohol and the mixture boiled gently under a reflux condenser for eight hours. A small quantity of yellow precipitate formed during refluxing and was removed. As the filtrate cooled, a clear gelatinous mass formed. This was warmed until it liquefied and then was poured into 1 liter of water. The yellow product which formed was best purified by repeating the treatment with alcohol and water two or three times, washing the precipitate thoroughly with water; yield of air-dried substance, 18 g., or 28%. It is insoluble in water but readily soluble in alcohol and alkali. It does not melt below 250°.

Anal. Subs., 0.1826, 0.1366: 27.70, 20.55 cc. of 0.03245 *N* iodine soln. Calc. for $C_{20}H_{17}O_3N_2As$: As, 18.37. Found: 18.44, 18.30.

The yellow precipitate formed during refluxing could not be adequately purified but the analytical results obtained approximated closely to those for the condensation product of one molecule of benzaldehyde with one molecule of amino-arsanilic acid.

4-(*o*-Methoxybenzalamino)-3-aminophenyl-arsonic Acid, $AsO_3H_2C_6H_3(NH_2)(N{=}CH C_6H_4OCH_3)$.—*o*-Methoxy-benzaldehyde (2.8 g.) is added to amino-arsanilic acid (4.68 g.) dissolved in absolute methyl alcohol (70 cc.) and the mixture refluxed for two hours. The light brown precipitate formed as the mixture cools is collected on a filter and purified by recrystallization from absolute methyl alcohol; yield, 2 g., or 28%. The product is a white powder soluble in alcohol and in alkali, but insoluble in water. It does not melt below 250°.

Anal. Subs., 0.1099, 0.1688: 14.65, 22.65 cc. of 0.04307 *N* iodine solution. Calc. for $C_{14}H_{15}O_4N_2As$: As, 21.41. Found: 21.52, 21.66.

Variations of the procedure described above failed to effect a condensation of two molecular equivalents of the aldehyde and one of amino-arsanilic acid.

The corresponding 4-(*p*-methoxybenzalamino)-3-aminophenyl-arsonic acid can be obtained in somewhat larger yield by substituting anisaldehyde in the procedure described above. The product is indistinguishable from the above compound except that it is yellow.

Anal. Subs., 0.4703, 0.1892: 81.85, 33.30 cc. of 0.03245 *N* iodine soln. Calc. for $C_{14}H_{15}O_4N_2As$: As, 21.41. Found: 21.15, 21.40.

4-Piperonalamino-3-aminophenyl-arsonic Acid, $AsO_3H_2C_6H_3(NH_2)_2(N{=}CHC_6H_3\text{-}O_2CH_2)$.—This compound was prepared by refluxing for four hours 9 g. of piperonal dissolved in 20 cc. of absolute methyl alcohol and adding to 4.6 g. of amino-arsanilic acid dissolved in 80 cc. of absolute methyl alcohol. The light brown precipitate which formed was filtered off and repeatedly ground in an agate mortar with absolute methyl alcohol, filtered off and washed. The product is insoluble in water but soluble in ethyl alcohol and alkali. It was dried at 100° under reduced pressure to constant weight for analysis.

Anal. Subs., 0.2379, 0.1374: 30.10, 17.30 cc. of 0.04307 *N* iodine soln. Calc. for $C_{14}H_{13}O_5N_2As$: As, 20.59. Found: 20.42, 20.33.

4-Aceto-amido-amino-3-aminophenyl-arsonic Acid, $AsO_3H_2C_6H_3(NHCH_2CONH_2)(NH_2)$.—A solution of 5 g. of amino-arsanilic acid in 20 cc. of *N* sodium hydroxide solution was mixed with 2 g. of chloro-acetamide and the mixture was refluxed for three hours, filtered, cooled and 1.5 cc. of concd. hydrochloric acid added. A grayish substance formed and was purified by crystallization from hot water as fine needles; yield, 3.5 g., or 58%. The product decomposed at 220–232°. For analysis the product was dried at 100° under reduced pressure.

Anal. Subs., 0.1880, 0.1117: 23.83, 14.25 cc. of 0.05568 *N* iodine soln. Calc. for $C_8H_{12}O_4N_3As$: As, 25.94. Found: 26.43, 26.62.

Summary

1. A series of arsenated ring compounds have been prepared with a view to determining the effect of ring nitrogen in arsenic drugs.

2. 1,2-Diamino-benzene-4-arsonic acid has been condensed with various compounds of the nature of 1,2-diketones, and with certain aldehydes.

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