that of meteoric chlorine is $35.458_0 \pm 0.000_5$. The mean of the best results on terrestrial chlorine is $35.457_4$, which is identical with the mean of the first five determinations with meteoric chlorine, that is, those made upon the original highly purified hydrogen chloride obtained from the chlorine of the meteorite.

3. Terrestrial chlorine of non-marine origin is found to have the same atomic weight as that obtained from the sea.

4. Silver may be converted into silver chloride in quartz flasks with long necks without the loss of any material essential to the exact determination of the ratio of the weights of the two substances, and in such a way that aside from air, nothing but pure silver chloride is left in the flask. The mean of all of the ratios of silver chloride to silver is found to be $1.32867_7 \pm 0.00000_2$. The average values from each set of seven determinations varied from the others only in the seventh significant figure.

5. The identity of the atomic weights of meteoric chlorine, and of chlorine of non-marine and marine origin is further evidence in favor of the theory of Harkins that the relative abundance of isotopes is most largely conditioned by the relative stability of the isotopes, that is their stability with regard to the different types of both disintegration and formation and also by the abundance of the atomic species from which they are formed.

CHICAGO, ILLINOIS

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

# A STUDY OF 3,4-DIAMINO-PHENYLARSONIC ACID AND SOME OF ITS DERIVATIVES

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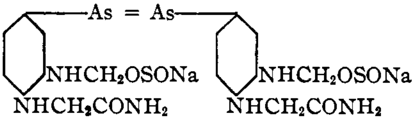
The present study was undertaken with a view to the synthesis of a new arsenical which would combine structural features of the important drugs Neoarsphenamine, "Ehrlich 914," and Tryparsamide, namely, the sodium formaldehyde sulfoxylate derivative of 3,3′-diamino-4,4′-di-N-glycylamide-arseno-benzene.



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[1] This research was carried out under a grant from the Public Health Institute of Chicago. Certain of the substances obtained are being tested pharmacologically under similar grants at the University of Wisconsin and the Wisconsin Psychiatric Institute under the direction of Drs. A. S. Loevenhart and W. F. Lorenz.

Before preparing this substance, it was necessary to make two preliminary studies, one of the nature of the reaction by which the amino-arsonic acids lose water at slightly elevated temperatures, and the other on the reactivity of the amino groups in such arsonic acids, to various reagents. The first of these studies was shown to be necessary by the earlier discovery that the loss of water from such acids takes place more easily than might be expected. Since the steps of the desired synthesis were followed by means of arsenic determinations, it was necessary to determine the conditions of the loss of water. It was found that between 100° and 140°, the temperature varying with the acid, and at 10 mm. pressure, the following reaction takes place: $H_2AsO_3.C_6H_4R \longrightarrow O_2As.C_6H_4R + H_2O$.

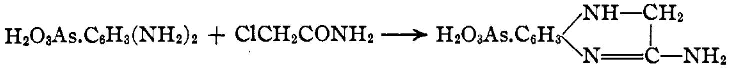
The reactivity of the amino groups in the diamino-phenylarsonic acid was then studied by means of the reactions with acid halides, chlorocarbonates, and C-chloro-amides. In general acid chlorides react with both groups in 3,4-diamino-phenylarsonic acid. Acetyl and propionyl chlorides are noteworthy exceptions, reacting with one amino group only.

Chlorocarbonates react normally with both amino groups in the diamino acid. Oxalyl chloride gives 2,3-dihydroxy-6-arsono-quinoxaline while ethyl malonate yields a seven-membered ring as follows: $H_2O_3As.C_6H_3(NH_2)_2 + CH_2(COOC_2H_5)_2 \longrightarrow H_2O_3As.C_6H_3 < (NHCO)_2 > CH_2 + 2C_2H_5OH$.

Diamino-phenylarsonic acid affords few solvents for condensation purposes, methyl alcohol being the best. In the presence of mineral acids, however, 2,3-di(dimethylamino)-phenylarsonic acid is formed, by reaction with the methyl alcohol itself.

Halogenated amides react in two ways, although the second reaction predominates.

$$H_2O_3As.C_6H_3(NH_2)_2 + ClCH_2CONH_2 \longrightarrow H_2O_3As.C_6H_3(NH_2)NHCH_2CONH_2$$



$$H_2O_3As.C_6H_3(NH_2)_2 + ClCH_2CONH_2 \longrightarrow H_2O_3As.C_6H_3\begin{cases} NH-CH_2 \\ N=C-NH_2 \end{cases}$$

The product of the first reaction above, namely, aminotryparsamide, gave on refluxing in water solution with sodium formaldehyde sulfoxylate, the desired arseno derivative of sulfoxylated amino-tryparsamide.

## Experimental Part

### The Effect of Drying on the Arsonic Acid Group

The uniform procedure in this Laboratory has been to dry all samples to constant weight in a vacuum drier jacketed with boiling xylene at 10 mm. pressure and containing phosphorus pentoxide.

Under these conditions the compounds listed in Table I lose a molecule of water.

The magnesium salts of these compounds did not lose water when heated

TABLE I

EFFECT OF HEAT ON THE FREE ARSONIC ACID GROUP

| Compound | Percentage of As<br>Calcd. for cpd. as listed, % | <br>Calcd. for cpd. listed less $H_2O$, % | Found, % |
|---|---|---|---|
| $H_2O_3As.C_6H_4NH_2$ | 34.5 | 37.7 | (a) 37.21 |
| | | | (b) 37.97 |
| $H_2O_3As.C_6H_3(NH_2)NHCOC_6H_4COOH$ | 19.7 | 20.7 | (a) 20.05 |
| | | | (b) 20.55 |
| $H_2O_3As.C_6H_3(NHCO)_2CH_2$ | 25.0 | 26.6 | (a) 26.65 |
| | | | (b) 26.55 |

to constant weight under the same conditions, showing the loss to take place from the arsonic group. For example, $MgO_3As.C_6H_3(NHCOC_6H_4COOH)_2$ analyzed, after being heated, as follows.

*Anal.* Subs., 0.1066, 0.1044: 8.27, 7.96 cc. of 0.0480 *N* iodine soln. Calcd. for $C_{22}H_{15}O_9N_2AsMg$: As, 13.68. Found: 13.97, 13.73.

To establish further the conditions of this loss, arsanilic acid was dried to constant weight in a vacuum desiccator over calcium chloride at 20°. At the end of 168 hours the analysis was as follows, showing no loss of water.

*Anal.* Subs., 0.1197, 0.0946: 23.22, 18.21 cc. of 0.0480 *N* iodine soln. Calcd. for $C_6H_8O_3NAs$: As, 34.55. Found: 34.96, 34.65.

A sample of arsanilic acid dried to constant weight in a vacuum drier at 139° became constant in seven hours with loss of water.[2]

*Anal.* Subs., 0.1684, 0.1071: 35.48, 22.20 cc. of 0.0480 *N* iodine soln. Calcd. for $C_6H_6O_2NAs$: As, 37.7. Found: 37.9, 37.3.

The calculated loss in weight equivalent to a molecule of water is 8.3%. That found was 8.2%.

In order to establish that the loss of water was from the arsonic group as such, rather than between the arsonic group and the amino group, *N*-dimethylarsanilic acid was prepared and dried to constant weight at 20°, 100° and 140°, respectively, with the following results. At 20° and 100° no loss in weight occurred. The samples dried at 20° and 140° analyzed, respectively, as follows.

*Anal.* Subs., 0.1125, 0.1143: 28.50, 28.76 cc. of 0.0322 *N* iodine soln. Calcd. for $C_8H_{14}O_3NAs$: As, 30.61. Found: 30.60, 30.40.

Subs., 0.1330, 0.1219: 36.14, 33.08 cc. of 0.0322 *N* iodine soln. Calcd. for $C_8H_{12}O_2NAs$: As, 33.04. Found: 32.83, 32.78.

This experiment shows that between 100° and 140° the arsonic group loses a molecule of water.

A similar study was carried out on amino-arsanilic acid (3,4-diamino-phenylarsonic acid) with somewhat different results.

A sample dried over calcium chloride at atmospheric pressure and 20° came to constant weight in 24 hours and analyzed as follows.

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[2] Raiziss and Gavron, "Organic Arsenical Compounds," Chemical Catalog Co., **1924**, p. 277.

*Anal.* Subs., 0.2234, 0.1917: 37.79, 33.05 cc. of 0.0480 *N* iodine soln. Calcd. for $C_6H_9O_3N_2As.{}^1/_2H_2O$: As, 31.1. Found: 30.45, 31.03.

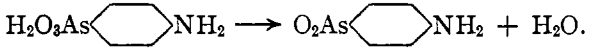
The results show the presence of one-half molecule of water as given by Morgan.[3]

Dried at 10 mm. and 140° over phosphorus pentoxide, the sample attained constant weight in 22 hours and analyzed for the loss of two molecules of water.

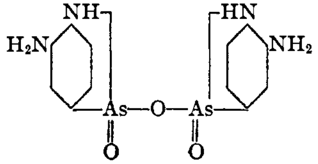
Subs., 0.1222, 0.1586: 25.00, 32.26 cc. of 0.0480 *N* iodine soln. Calcd. for $C_6H_5ON_2As.{}^1/_2H_2O$: As 36.59. Found: 36.82, 36.61.

The calculated loss in weight for two molecular equivalents of water would be 14.9%. That found is 15.4%.

Pope[4] has shown that $\beta$-chlorovinylarsonic acid loses water on being heated at 110–120° according to the following reaction, $ClCH_2CH_2AsO_3H_2 \longrightarrow ClCH_2CH_2AsO_2$. This fact has been confirmed in this Laboratory. It would be suspected that the reaction is the same in the case of arsanilic acid.



The behavior of amino-arsanilic acid may be explained by assuming that a molecule of water binds two molecules together to give an ortho-pyro acid with three hydroxyls on each arsenic atom. Possibly the half molecule of water which crystallizes with the acid and persists at 140°, represents a binding through the nitrogen as a substituted nitrogen oxide. The loss of two molecules of water for each arsenic atom would necessarily involve an amino group. Inasmuch as a half molecule of water would make a difference of 1.6% in the arsenic analysis there is no difficulty in detecting accurately such a loss. The final result might be indicated by the following formula.



**The Preparation of Amino-arsanilic Acid.**—This compound was prepared in three steps from arsanilic acid. Oxalyl-arsanilic acid was prepared and nitrated in 90% yields according to the method of Bertheim.[5] The reduction was carried out in 60% yields, following the method of Jacobs and Heidelberger[6] as modified in this Laboratory.

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[3] Morgan, "Organic Compounds of Arsenic and Antimony," Longmans Green and Company, London, **1918**, p. 196.

[4] Mann and Pope, *J. Chem. Soc.*, **121**, 1755 (1922). Compare also Ref. **2**, pp. 241, 242, 252.

[5] Bertheim, *Ber.*, **44**, 3092 (1911).

[6] Jacobs and Heidelberger, THIS JOURNAL, **40**, 1581 (1918).

## Reactions with Aliphatic Acid Chlorides

**4-Chloro-acetylaminophenylarsonic Acid,**[7] $H_2O_3As.C_6H_4NHCOCH_2Cl$.—The method of Jacobs and Heidelberger[8] for the preparation of chloro-acetanilides was here applied to the type of reaction described above.

Five g. of arsanilic acid was dissolved in 25 g. of glacial acetic acid and 25 g. of a saturated solution of sodium acetate. To this solution 4 g. of chloro-acetyl chloride was added and after the reaction was complete the solution was allowed to stand overnight for complete precipitation. The product was purified by dissolving in dil. sodium hydroxide solution and precipitating with hydrochloric acid. The compound melted correctly at 290°. 4-Propionylaminophenylarsonic acid, $H_2O_3As.C_6H_4NHCOC_2H_5$, is prepared from arsanilic acid and propionyl chloride as described above. The product was purified thrice by dissolving it in sodium hydroxide and precipitating with hydrochloric acid. The yield of purified product was 2 g., or 32%. The compound does not melt when heated to 260°.

*Anal.* Subs., 0.2116, 0.1082: 28.52, 14.63 cc. of 0.0557 *N* iodine soln. Calcd. for $C_9H_{12}O_4NAs$: As, 27.5. Found: 28.12, 28.22.

As this method proved of limited application, owing to the solubility of the product in the reaction mixture, the method used in all of the succeeding experiments is a modified Schotten-Baumann. Unless otherwise specified, the experimental method was in every case the same. That is, 4 g. (1 molecular equivalent) of arsanilic acid or amino-arsanilic acid was dissolved in an equivalent amount of *N* sodium hydroxide solution to give the monosodium salt. The solution was placed in a 200cc. round-bottom Pyrex flask and stirred vigorously. An ice–hydrochloric-acid mixture kept the temperature of the solution at its freezing point. The acid chloride was then added drop by drop through a small funnel (1.5 molecular proportions when working with arsanilic acid and 2.5 proportions when working with amino-arsanilic acid) and at the same time sufficient 12 *N* sodium hydroxide solution was added through another funnel to keep the solution basic. The first indication of an acid reaction mixture is the formation of the free acid on the walls of the flask. Stirring was continued for one hour after the reaction seemed complete. The solution was then filtered and replaced in the flask. Hydrochloric acid was added to the cold solution during stirring until the mixture was normal with respect to free hydrochloric acid. Sufficient water was added to keep the precipitate from caking. Usually the volume was not more than 50–75 cc., but in the case of some of the nitrobenzoyl derivatives the volume was 500–1000 cc. Precipitation twice more in the manner described was usually sufficient to obtain an excellent analysis.

**Reaction with Chlorocarbonates.**—The general method of preparing anilides from acid chlorides was found to be applicable to chloro-carbonates. As with most of the acid chlorides, both amino groups of amino-arsanilic acid were found to react.

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[7] Ref. 2, p. 291.

[8] Jacobs and Heidelberger, THIS JOURNAL, **39**, 1441 (1917).

**Reaction with Aromatic Acid Chlorides.**—The reaction was carried out as in the previous experiments in those cases in which the acid chloride was a liquid. If not a liquid the acid chloride was dissolved in twice its weight of benzene and the reaction carried out in the same manner. The benzene layer could easily be separated after the reaction was complete. The precipitate tended to become gelatinous and pass through the paper in some cases but prolonged, vigorous stirring broke up the jell structure. The nitrobenzoic acid formed in the reaction was extracted by means of ether. This process was not complete in the experiments in which *p*-nitrobenzoyl chloride was used. However, the analysis clearly indicated that a reaction had taken place with both arsanilic acid and amino-arsanilic acid. In the latter case both amino groups reacted.

Table II

Derivatives of Phenylarsonic Acid

| Derivative | Formula | Yield, % | Analyses, % Calcd. | Analyses, % Found |
|---|---|---|---|---|
| 4-Valerylamino | $H_2O_3As.C_6H_4NHCOC_4H_9$ | 59. | 24.87 | 24.85, 25.05 |
| 4-Phenylacetylamino | $H_2O_3As.C_6H_4NHCOCH_2C_6H_6$ | 81. | 22.42 | 22.48, 22.57 |
| 3-Amino-4-acetylamino[a] | $H_2O_3As.C_6H_3(NH_2)NHCOCH_3$ | 74. | 27.37 | 27.66, 28.01 |
| 3-Amino-4-propionylamino[b] | $H_2O_3As.C_6H_3(NH_2)NHCOC_2H_5$ | 40. | 26.04 | 26.23, 26.20 |
| 3,4-Di-valerylamino | $H_2O_3As.C_6H_3(NHCOC_4H_9)_2$ | 44. | 18.80 | 18.96, 18.87 |
| 3,4-Di-chloro-acetylamino | $H_2O_3As.C_6H_3(NHCOCH_2Cl)_2$ | 49. | 18.42[c] | 18.63, 18.59 |
| 3,4-Di-phenylacetylamino | $H_2O_3As.C_6H_3(NHCOCH_2C_6H_5)_2$ | 62. | 16.06 | 16.14, 16.12 |
| 3,4-Di-benzoylamino | $H_2O_3As.C_6H_3(NHCOC_6H_5)_2$ | 53. | 17.05 | 17.42, 17.41 |
| 3,4-Di-phthalylamino | $H_2O_3As.C_6H_3(NHCOC_6H_4COOH)_2$ | 16.5 | 14.20 | 14.28, 14.25 |
| 4-Carbopropyl-oxyamino | $H_2O_3As.C_6H_4NHCO_2C_3H_7$ | 81. | 24.82 | 24.94, 24.98 |
| 4-Carbobutyl-oxyamino | $H_2O_3As.C_6H_4NHCO_2C_4H_9$ | 43. | 23.81 | 23.94, 23.91 |
| 3,4-Di-carbo-ethoxyamino[d] | $H_2O_3As.C_6H_3(NHCO_2C_2H_5)_2$ | 23. | 19.95 | 20.21, 20.22 |
| 3,4-Di-carbopropyloxyamino | $H_2O_3As.C_6H_3(NHCO_2C_3H_7)_2$ | 57. | 18.57 | 19.01, 19.06 |
| 3,4-Di-carbobutyloxyamino[f] | $H_2O_3As.C_6H_2(NHCO_2C_4H_9)_2$ | 13.6 | 17.36 | 17.45, 17.51 |

[a] M. p., 265–267°.
[b] M. p., 230–235°.
[c] Chlorine.
[d] M. p., 192–192.5°.
[e] Decomp., 249–253°.
[f] Decomp., 185–187°.

The *p*-amino group is assumed to be the more reactive.

## Compounds Related to Tryparsamide

The compounds discussed under this section were prepared in the same manner as was tryparsamide.[9] Two variations were introduced, in that amino-arsanilic acid was substituted for arsanilic acid, and in another experiment bromomalonamide was substituted for chloro-acetamide. In the first case it was found that chloro-acetamide reacts with but one amino group. However, when the conditions of the experiment are not carefully controlled a secondary reaction takes place between the carbonyl group and the amino group on the ring, which are in the 1,6 position, giving a quinoxaline. In any event, the second reaction takes place to a slight extent. This quinoxaline no longer has an amide group, does not liberate ammonia when heated with a caustic alkali, has a different decomposition point, and gives an arsenic analysis more than 1.5% higher

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[9] Jacobs and Heidelberger, This Journal, **41**, 1589 (1919).

than the first compound. The ammonium salt and two derivatives also indicate the same structure. Bromomalonamide was found to behave in the same manner with amino-arsanilic acid, giving a disubstituted quinoxaline. The reaction is analogous to the preparation of a quinoxaline from ω-bromo-acetophenone and *o*-phenylenediamine[10] or amino-arsanilic acid.[11] However the reaction with a halogenated amide is not recorded in the literature and is a new method of preparing quinoxalines containing an amino group.

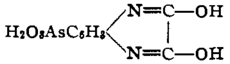
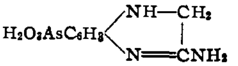
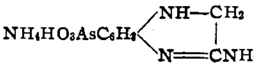
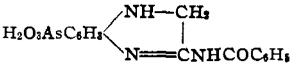
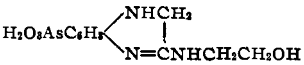
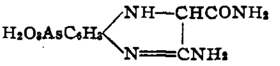
**N-(Phenyl-1-amino-4-arsonic Acid)glycine-amide,** $H_2O_3AsC_6H_3(NH_2)NHCH_2CONH_2$, was prepared by dissolving 75 g. of amino-arsanilic acid in 12.4 g. of sodium hydroxide dissolved in 310 cc. of water. The solution was warmed slightly to complete solution and filtered; 58.2 g. of chloro-acetamide was then added and the mixture refluxed on an air-bath for 45 minutes. The clear solution was filtered and acidified with 23.3 cc. of concd. hydrochloric acid. After some time and with scratching, crystallization commenced. The product was crystallized once under the same conditions; yield, 55 g., or 62%, of a light gray powder. The analytical results were high, due probably to the presence of some quinoxaline. When heated, the compound began to darken at 215° but melted with decomposition at 234–241°. This range probably indicates the presence of some quinoxaline.

*Anal.* Subs., 0.1270, 0.1126: 16.30, 14.40 cc. of 0.0549 *N* iodine soln. Calcd. for $C_8H_{12}O_4N_3As$: As, 26.0. Found: 26.43, 26.33.

In Table II of arsonoquinoxalines, 2,3-dihydro-6-arsonoquinoxaline is prepared from oxalyl chloride and amino-arsanilic acid. 1,2-Dihydro-3-amino-6-arsonoquinoxaline is prepared like *N*-(phenyl-1-amino-4-arsonic acid)glycine-amide, using about 25% more alkali. Longer heating or

Table III

Derivatives of Arsonoquinoxaline

| Name | Formula | Yield, % | Analyses, % Calcd. | Found |
|---|---|---|---|---|
| 2,3-Dihydroxy-6- |  $H_2O_3AsC_6H_3\left\langle\begin{matrix}N{=}C{-}OH\\ \vert\\ N{=}C{-}OH\end{matrix}\right.$ | 32 | 26.22 | 26.06, 26.10 |
| 1,2-Dihydro-3-amino-6-[a] |  $H_2O_3AsC_6H_3\left\langle\begin{matrix}NH{-}CH_2\\ \vert\\ N{=}CNH_2\end{matrix}\right.$ | .. | 27.68 | 27.79, 27.76 |
| 1,2-Dihydro-3-amino-6-ammonium[b] |  $NH_4HO_3AsC_6H_3\left\langle\begin{matrix}NH{-}CH_2\\ \vert\\ N{=}CNH_2\end{matrix}\right.$ | 21 | 26.04 | 26.27, 26.18 |
| 1,2-Dihydro-3-benzoylamino-6-[c] |  $H_2O_3AsC_6H_3\left\langle\begin{matrix}NH{-}CH_2\\ \vert\\ N{=}CNHCOC_6H_5\end{matrix}\right.$ | 45 | 20.00 | 20.29, 20.17 |
| 1,2-Dihydro-3-hydroxyethylamino-6- |  $H_2O_3AsC_6H_3\left\langle\begin{matrix}NHCH_2\\ \vert\\ N{=}CNHCH_2CH_2OH\end{matrix}\right.$ | 34 | 23.81 | 24.41, 24.50 |
| 1,2-Dihydro-2-formamide-3-amino-6- |  $H_2O_3AsC_6H_3\left\langle\begin{matrix}NH{-}CHCONH_2\\ \vert\\ N{=}CNH_2\end{matrix}\right.$ | 17.2 | 23.89 | 23.98, 23.95 |

[a] M. p., 226°. [b] Decomp., 200°. [c] M. p., 234°.

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[10] *Ber.*, **41**, 2350 (1908).

[11] Cramer, unpublished work done in this Laboratory.

recrystallization of the glycine amide in an excess of alkali will cause it to go over into the quinoxaline. 1,2-Dihydro-3-benzoylamino-6-arsonoquinoxaline is prepared from the quinoxaline with benzoyl chloride. 1,2-Dihydro-3-hydroxyethylamino-6-arsonoquinoxaline is prepared by allowing the amino-quinoxaline, dissolved in sodium hydroxide, to stand for several days at 30° with an excess of ethylene oxide, and occasionally shaking the mixture. Bromomalonamide, when refluxed for two hours with amino-arsanilic acid, following the method of tryparsamide preparation, yields 1,2-dihydro-2-formamide-3-amino-6-arsonoquinoxaline.

**The Arseno Derivative of Sulfoxylated Amino-tryparsamide,** $[=AsC_6H_3(NHCH_2CONH_2)NHCH_2OSONa]_2$, is prepared by refluxing on a water-bath during occasional shaking 4 g. of amino-triparsamide with 8 g. of sodium formaldehyde sulfoxalate. A precipitate forms during the first half hour, which may be filtered off in an atmosphere of carbon dioxide. This appears to be the arseno compound with but one amino group condensed with the sodium formaldehyde sulfoxylate.

*Anal.* Subs., 0.1189, 0.1706: 16.95, 24.42 cc. of 0.0478 *N* iodine soln. Calcd. for $C_{17}H_{21}O_4N_6SAs_2Na$: As, 25.95. Found: 25.56, 25.66.

As the refluxing is continued the solution becomes practically clear. At the end of 15 hours the solution is cooled and filtered drop by drop, during stirring, into 300 cc. of alcohol. The arseno derivative precipitates as a fine, light yellow powder which may be filtered off and dried in the air without change; yield, 3.5 g., or 75%. The crude product is about 3% low in arsenic, probably due to the presence of inorganic material or alcohol of crystallization. Fractional precipitation in which the first product precipitated is discarded and only a small part in the middle is taken gives a correct analysis. The compound is a light yellow powder, unchanged by contact with the air. When it is heated no change is observed below 260°. The compound is readily soluble in water and gives the indigo-carmine test for the sulfinic acid group.

*Anal.* Subs., 0.1198, 0.1085: 14.00, 12.80 cc. of 0.0504 *N* iodine soln. Calcd. for $C_{18}H_{22}O_6N_6S_2As_2Na_2$: As, 22.1. Found: 22.08, 22.29.

A sample of the crude material which was low in arsenic was analyzed for sulfur. The fact that the results of this analysis were high would indicate that the contamination was due to sulfates.

*Anal.* Subs., 0.2476, 0.2203: $BaSO_4$, 0.1712, 0.1578. Calcd. for $C_{18}H_{22}O_6N_6S_2Na$: S, 9.42. Found: 9.50, 9.83.

**N-(4-Arsonophenyl)-aminomalonamide,** $H_2O_3AsC_6H_4NHCH(CONH_2)_2$, is prepared in the same manner as is tryparsamide, starting with bromomalonamide.[12] After about two hours' refluxing the reaction mixture suddenly gave a heavy precipitate. The yield of recrystallized material was 3 g., or 57%. When this substance was heated to 260° no change was observed.

*Anal.* Subs., 0.1141, 0.1182: 13.17, 13.73 cc. of 0.0556 *N* iodine soln. Calcd. for $C_9H_{12}O_5N_3As$: As, 23.66. Found: 24.03, 24.21.

## Miscellaneous Reactions

**Malonylamino-arsanilic oxide,** $O_2AsC_6H_3<(NHCO)_2>CH_2$, is prepared by refluxing malonic ester with amino-arsanilic acid.

Four g. of amino-arsanilic acid, 6 g. of malonic ester and 40 cc. of absolute methyl

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[12] *J. Chem. Soc.*, **119**, 364 (1921).

alcohol were refluxed for four hours and the mixture was then allowed to stand. On evaporation 2 g. of a light red material was obtained, which is a 26% yield. This was purified by solution in glacial acetic acid, filtration and precipitation with ether, to give a bright red powder. The sample was dried to constant weight at 139° losing water from the arsonic group.

*Anal.* Subs., 0.1194, 0.1068: 17.62, 15.70 cc. of 0.0481 *N* iodine soln. Calcd. for $C_9H_7O_4N_2As$: As, 26.60. Found: 26.65, 26.55.

**4-Phthalylamino-3-aminophenylarsonic Acid,** $H_2O_3AsC_6H_3(NH_2)NHCOC_6H_4$-COOH.—Sixteen g. of amino arsanilic acid and 12 g. of phthalic anhydride were dissolved in 40 cc. of absolute methyl alcohol and the solution was refluxed for four hours. The mother liquor was evaporated and scratched and the precipitate thus obtained recrystallized from absolute methyl alcohol; yield, 3.8 g., or 15%. When heated, the material seemed to lose volume at 203–207° and then to increase in volume at 240–245°. No further change took place up to 260°.

*Anal.* Subs., 0.0995, 0.1094: 11.94, 13.45 cc. of 0.0430 *N* iodine soln. Calcd. for $C_{14}H_{13}O_6N_2As$: As, 19.73. Found: 19.38, 19.86.

**1,2-Di-(N,N-dimethylamino)-4-arsonobenzene,** $H_2O_3AsC_6H_3[N(CH_3)_2]_2$.—In attempting to obtain a condensation between carboxyl groups and amino-arsanilic acid a uniform product was obtained which appeared to be tetramethyl-amino-arsanilic acid. Four g. of amino-arsanilic acid was therefore dissolved in 44 cc. of absolute methyl alcohol and the solution refluxed for 34 hours with 3.6 cc. of concd. hydrochloric acid. A light pink precipitate formed which was filtered off, washed, and dried to constant weight at 20°.

*Anal.* Subs., 0.1611, 0.1664: 20.65, 21.60 cc. of 0.0549 *N* iodine soln. Calcd. for $C_{10}H_{17}O_3N_2As$: As, 26.04. Found: 26.38, 27.73.

## Summary

1. Between 100° and 140° at 10 mm. pressure, over phosphorus pentoxide the free arsonic group in arsanilic acid and related compounds loses water.

2. The reaction of the amino groups in arsanilic and amino-arsanilic acids with acid chlorides, chlorocarbonates and chloro-amides has been studied and a number of new organic arsenic compounds prepared.

3. The sulfoxylate derivative of 3,3′-diamino-4,4′-di-N-glycylamido-arsenobenzene has been synthesized as a possible arsenical drug.

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