State College, and to his assistants, Mr. C. A. Gamble and Mr. G. H. Hardin, for help in the analytical work.

NEW YORK CITY

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

THE ISOMERIC HYDROXYPHENYLARSONIC ACIDS AND THE DIRECT ARSENATION OF PHENOL.

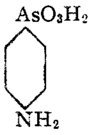
BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

Received June 30, 1919.

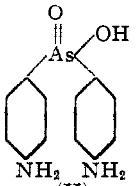
The present study of the action of arsenic acid upon phenol has demonstrated that this reaction is more complicated than has been heretofore assumed. As we shall set forth below, not only is *p*-hydroxyphenylarsonic acid formed in the reaction, but several other related substances as well.

Ehrlich and Bertheim,[1] in establishing the nature of the substance now known as arsanilic acid or *p*-amino-phenylarsonic acid (I), obtained by heating aniline with arsenic acid, drew the analogy between this substance and sulfanilic acid, obtained by a parallel method. As far as has been determined in these reactions, the substituent enters only the position *para* to the amino group. It was then found that the method of direct arsenation was capable of extension to other simple aromatic amines with a free *para* position. Only in the case of a few *para*-substituted arylamines was it possible to force the arsonic acid into the *ortho* position and then only with great difficulty as evidenced by the very poor yields.

Benda,[2] and independently, Pyman and Reynolds[3] later found that this reaction did not stop at the formation of the primary arsonic acid but that this condensed further to an appreciable extent with a second molecule of the amine to form the secondary arsonic acid (II) in which the arsonic acid residue again entered the *para* position in the second arylamine nucleus.



(I).



(II).

The method of direct arsenation has also been extended to include the simpler phenols. According to the method outlined in *D. R. P.* 205616,

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[1] *Ber.*, 40, 3292 (1907).

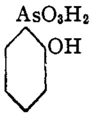
[2] *Ibid.*, 41, 2367 (1908).

[3] *J. Chem. Soc.*, 93, 1184 (1908).

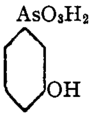
in which phenol, *o*- and *m*-cresol are heated with arsenic acid, substances are obtained in which the arsonic acid residue enters the position *para* to the phenolic group. Further than this the patent does not go; and, as far as we are aware, more recent work has applied the reaction only to the arsenation of resorcin and its monomethyl ether.[1] From previous work, therefore, it would seem that the arsenation of phenolic compounds parallels that of the amines in that only *p*-hydroxy-arsonic acids have thus far been isolated.

In connection with the preparation of *p*-hydroxy-phenylarsonic acid essentially according to the method outlined in *D. R. P.* 205616 we have had the opportunity of studying this reaction more fully. After isolating the *para* acid as the sodium salt, we were struck by the amount of material contained in the mother liquors which showed all the reactions of an aromatic arsonic acid and which obviously contained but relatively negligible amounts of the *p*-hydroxy acid. Furthermore, this mother liquor yielded an intense wine-red color with ferric chloride solution, whereas *p*-hydroxy-phenylarsonic acid gives no such color test. It therefore seemed likely that we were dealing with isomeric hydroxy compounds which were also products of the reaction. Just as the arsenation of aniline has been compared with the sulfonation of this base, it seemed also logical to compare the arsenation of phenol with the sulfonation of this compound. As is well known, depending upon the conditions of sulfonation, varying proportions of both *o*- and *p*-phenolsulfonic acids may be obtained.

Accordingly, in order to learn the properties of both *o*- and *m*-hydroxyphenylarsonic acids (III) and (IV), neither of which had hitherto been described, we prepared these compounds by diazotization of *o*- and *m*-arsanilic acids. Whereas phenol-*m*-arsonic acid resembled the *para* compound in giving no color test with ferric chloride, the phenol-*o*-arsonic acid gave the identical wine-red color observed with the mother liquors from phenol-*p*-arsonic acid.



(III).



(IV).

It was then found possible to isolate a basic barium salt from these mother liquors, which yielded a free acid identical with the hydroxy-compound obtained from *o*-arsanilic acid. The amount of this substance isolated was approximately $^1/_7$ of the yield of *p*-hydroxy-phenylarsonic acid. We hope by varying the conditions of the arsenation to determine

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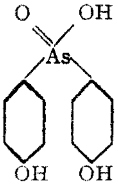
[1] Bauer, *Ber.*, 48, 509 (1915).

whether or not the small yield is due to the migration of the arsonic acid residue from the *o*- to the *p*-position at the elevated temperature employed, a process which has been shown to occur in the sulfonation of phenol. We have not succeeded in isolating a *meta* acid from the mother liquors and it seens hardly likely on theoretical grounds that one should be formed in the arsenation of phenol.

A comparison of the solubilities of the 3 phenolarsonic acids with those of the isomeric arsanilic acids proved interesting. Whereas in the latter series the *ortho* acid is most soluble and the *meta* compound the least soluble, with the former compounds the *o*-hydroxy acid unexpectedly proved to be the least soluble of the three. Thus it can be readily recrystallized from water without serious loss. There is little difference, on the other hand, between the solubilities of the *m*- and *p*-phenolarsonic acids.

We are continuing the study of the *o*- and *m*-hydroxy-phenylarsonic acids and their reduction products, nitro derivatives, etc.

On careful acidification of the mother liquor from the barium salt of the phenol-*o*-arsonic acid we were able to isolate two other substances, both of which gave analytical figures for the secondary dihydroxy-diphenylarsonic acids. These substances differed from one another in melting points and in the fact that in aqueous suspension one gave no color with ferric chloride solution, while the other, lower-melting substance, exhibited the same pronounced wine-red color so characteristic of phenol-*o*-arsonic acid. The higher melting acid possessed the same melting point as the *p,p'*-dihydroxy-diphenylarsonic acid (V), obtained according to Benda[1] by diazotization of *p,p'*-diamino-diphenylarsonic acid, and agreed in other properties with this substance. We therefore conclude that our first substance is identical with Benda's compound.



(V).

The color reaction exhibited by our second substance indicates that it is a secondary *o*-hydroxy-arsonic acid. There are two substances which might possibly be formed in the arsenation of phenol and exhibit the properties of the isolated compound; *o,o'*-dihydroxy-diphenylarsonic acid (VI), and *o,p'*-dihydroxy-diphenylarsonic acid (VII).

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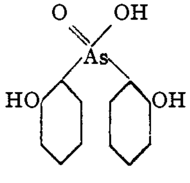
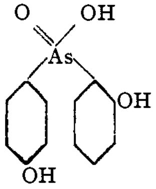
[1] *Loc. cit.*



(VI).



(VII).

Since the secondary arsonic acids no doubt arise from the reaction of a second molecule of phenol with the primary hydroxy-arsonic acids already formed, it is evident that VII could be formed in two ways: by the elimination of water between *o*-hydroxy-phenylarsonic acid and the *para* hydrogen atom of a second phenol molecule, or by the condensation of *p*-hydroxy-phenylarsonic acid with the *ortho* hydrogen of a second phenol molecule. VI, on the other hand, can only be formed from *o*-hydroxy-phenylarsonic acid which is present only in minor amounts. Therefore, since the yield of our second substance was approximately equal to that of the *p,p'* compound recovered, we are inclined to consider Formula VII as the more probable. We are at present attempting to establish the structure of the compound by other means. It also seems very likely that smaller amounts of VI are formed in the reaction and we are continuing the search for this substance.

The formation of the secondary acids extends the analogy to the sulfonation of phenol, since among the products of the latter is found dihydroxy-diphenylsulfone, and is likewise similar to the production of *p,p'*-diamino-diphenylarsonic acid in the arsenation of aniline. The formation of tertiary arsinoxides is likewise suggested, and we shall turn our attention to the possibility of isolating these among the products of the reaction. We shall also extend the study to the arsenation of other phenolic compounds, since similar products should result in the arsenation of the cresols, etc.

Finally, after the present work had long been under way, an article appeared by Conant[1] on the arsenation of phenol for the preparation of *p*-hydroxy-phenylarsonic acid. It will be seen that the conditions employed by us for the interaction of phenol and arsenic acid, with a few exceptions, are similar to those used by him and to those outlined in *D. R. P.* 205616, which, however, specifies "crystalline arsenic acid." However, it is entirely unnecessary in working up the melt to be satisfied with an impure sodium salt such as is isolated by Conant's method. As will be found in the experimental part of the present communication, and as has already been claimed by Kay,[2] it is a simple matter to obtain satisfactory yields of pure sodium *p*-hydroxy-phenylarsonate uncon-

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[1] This Journal, 41, 431 (1919).

[2] *Eng. pat.* 6,322 (1915).

taminated by other salts or by tarry by-products. As a matter of fact, the amount of tar formed in the method we have used is practically negligible and occasioned no difficulty. We are convinced that the direct arsenation of phenol is by far the simplest and most economical method for the preparation of this substance, so important in the manufacture of arsphenamine.

EXPERIMENTAL.

(A) *o*- and *m*-Hydroxy-phenylarsonic Acids.

***o*-Hydroxy-phenylarsonic Acids.**—This substance was isolated in the direct arsenation of phenol as described in Section B, and in order to prove its structure it was also synthesized directly from *o*-arsanilic acid.[1]

11 g. of *o*-arsanilic acid were dissolved in 100 cc. of *N* hydrochloric acid, chilled, and diazotized with 50 cc. of *N* sodium nitrite solution. On standing at room temperature a steady, copious evolution of nitrogen occurred which was completed after an hour by gentle heating. The mixture was boiled with bone black, and the colorless filtrate treated with 50 cc. of *N* sodium hydroxide solution. On concentrating on the water bath the new hydroxy-phenylarsonic acid separated as a crust of long, stout needles. A few drops of dil. hydrochloric acid were added on cooling to insure proper acidity and the acid was filtered off and washed with ice water. The yield was 9.5 g. The acid is very easily soluble in hot water and forms supersaturated solutions on cooling, which rapidly crystallize when rubbed, yielding a mass of rosets of minute, colorless needles. When crystallization occurs slowly, as on concentrating its aqueous solutions, the acid separates as crusts of long, lustrous needles. Contrary to its *p*-isomer, it is rather sparingly soluble in cold water. The solubility relationships, therefore do not parallel those found in the comparison of *o*- and *p*-arsanilic acids, the latter being by far the less soluble.

o-Hydroxy-phenylarsonic acid is readily distinguished from the *para* compound by the color which it gives with ferric chloride solution. Whereas the *p*-isomer gives no color with this reagent even very dilute solutions of the *ortho* acid give a pronounced wine-red color. *m*-Hydroxy-phenylarsonic acid, described below, resembles the *para* compound in giving no color with ferric chloride, so that this reaction may therefore be used to distinguish the *ortho* acid from its isomers.

When rapidly heated to 185°, then slowly, *o*-hydroxy-phenylarsonic acid begins to soften at 185°, but is not completely melted until 196° is reached, then forming a liquid filled with bubbles. It is soluble in methyl or ethyl alcohol and but sparingly so in hot acetone or chloroform. Although difficultly soluble in glacial acetic acid, it dissolves readily on boiling. In alkaline solution, it couples readily with diazotized sulfanilic acid, yielding a bright orange solution. It is readily precipitated from

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[1] THIS JOURNAL, 40, 1583 (1918).

concentrated solutions of its salts by hydrochloric acid, but redissolves on adding an excess. Acetic acid does not readily displace it from its salts.

Subs., 0.3273: $Mg_2As_2O_7$, 0.2298.
Calc. for $C_6H_7O_4As$: As, 34.36. Found: 33.87.

Sodium Salt.—A suspension of the acid in a small amount of hot water was neutralized to litmus with strong sodium·hydroxide solution and then treated with an equal volume of alcohol. The sodium salt, which separated on rubbing, was recrystallized from 50% alcohol, separating on standing in the cold as glistening, hexagonal platelets which contain 4 molecules of water of crystallization when air-dry. The salt is readily soluble in water and gives no immediate precipitates with calcium or barium salts but in the latter case, on rendering alkaline to phenolphthalein, what is probably a basic barium salt separates as rosets of colorless, microscopic needles. The heavy metals cause immediate flocculent precipitates.

Subs., air-dry, 0.7476: loss, 0.1713 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_6H_6O_4AsNa.4H_2O$: H_2O, 23.07. Found: 22.92.
Subs., anhydrous, 0.2846: $Mg_2As_2O_7$, 0.1820.
Calc. for $C_6H_6O_4AsNa$: As, 31.20. Found: 30.87.

***m*-Hydroxy-phenylarsonic Acid.**—This substance was prepared as follows from *m*-arsanilic acid.[1] 11 g. of *m*-arsanilic acid were dissolved in 100 cc. of 10% sulfuric acid, chilled and diazotized with a solution of 3.6 g. of sodium nitrite. The solution was diluted to 250 cc. and warmed to 60°, when a steady evolution of nitrogen occurred. When this had ceased, the sulfuric acid was completely removed with barium hydroxide solution. The filtrate was acidified with acetic acid, heated, and then treated with lead acetate solution as long as a precipitate formed. The lead salt separated at first in amorphous form, but rapidly changed to aggregates of microscopic platelets. After filtering off and washing, it was shaken with an excess of 10% sulfuric acid until completely decomposed. The filtrate from the lead sulfate was in turn treated with barium hydroxide solution until a test portion no longer showed the presence of dissolved barium and sulfate ions. The mixture was then treated with bone black and the clear, colorless filtrate boiled almost to dryness. The oily residue quickly crystallized on rubbing, giving 8 g. of the new arsonic acid. Recrystallized from a small volume of water and chilled to 0°, it separated as aggregates of rhombic crystals which melt slowly from 159° to 173°. It is readily soluble at room temperature in water, methyl and ethyl alcohols, and in boiling acetic acid. It is also somewhat soluble in hot acetone but practically insoluble in chloroform or benzene. It gives no color with ferric chloride solution and couples readily in alkaline solution with diazotized sulfanilic acid, giving a bright orange color.

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[1] THIS JOURNAL, 40, 1583 (1918).

Subs., 0.3045: $Mg_2As_2O_7$, 0.2135.
Calc. for $C_6H_7O_4As$: As, 34.36. Found: 33.84.

Sodium Salt.—A suspension of the acid in a very small amount of hot water was neutralized to litmus with sodium hydroxide solution. Since the salt could not be obtained by the addition of alcohol, it was allowed to evaporate and when almost dry, gradually crystallized in rosets of flat needles. It was too soluble to be recrystallized and acetone precipitated the concentrated aqueous solution as a pasty mass. For analysis this was dried *in vacuo* at 100° over sulfuric acid.

Subs., 0.2854: $Mg_2As_2O_7$, 0.1833.
Calc. for $C_6H_6O_4AsNa$: As, 31.20. Found: 31.00.

A solution of the salt gives no precipitates with barium or calcium salts but insoluble precipitates with those of the heavy metals.

(B) The Arsenation of Phenol.

***p*-Hydroxy-phenylarsonic Acid.**—480 g. of 80% aqueous arsenic acid were boiled in an open flask, allowing the water to escape until the temperature reached 150°. Then 200 g. of molten phenol were poured in at once and an air condenser attached, the flask being then placed in an oil bath, the temperature of which was maintained at 155–60°. The contents of the flask boiled, rendering mechanical stirring unnecessary, and heating was continued for 7 hours. The air condenser acts as an efficient reflux avoiding undue loss of phenol. At the end the somewhat dark-colored liquid, which at first consisted of two layers, was homogeneous. It was diluted with about 2 liters of water, whereupon a small amount of tar precipitated, and, without filtering, a strong, hot solution of barium hydroxide was then added with vigorous stirring until the solution became just neutral to litmus, the unchanged arsenic acid being completely removed as the barium salt, which also efficiently collects the small amount of tar. It is important to avoid an unnecessary excess of barium hydroxide, since if the reaction becomes too strongly alkaline, the hydroxyphenylarsonic acids may also be precipitated. The clear, almost colorless filtrate from the copious barium arsenate precipitate was then treated with just enough sulfuric acid to remove the dissolved barium, a preliminary heating greatly facilitating the subsequent filtration of the barium sulfate. The precipitation is easily followed during the addition of the sulfuric acid by tests with filtered samples, and it is a simple matter to strike the point at which the filtrate no longer gives a test for either barium or sulfuric ion.

The filtrate was next concentrated to about a liter, preferably *in vacuo*, and the *n* neutralized to litmus with sodium hydroxide. The solution of the salts was then concentrated further to small bulk, whereupon a partial crystallization of sodium *p*-hydroxy-phenylarsonate occurred. The mixture was heated until this was redissolved, a very small amount of water added if necessary; and then treated while still hot with several volumes of alcohol until a slight permanent turbidity was reached. On rubbing, the sodium salt quickly crystallized out, and after several hours of thorough chilling it was filtered off and washed with 85% alcohol. The yield averages about 120 g. and the colorless product so obtained is a practically pure sodium *p*-hydroxy-phenylarsonate giving no test for arsenate or sulfate ion and no color with ferric chloride solution. Hence it is seen that contamination with sodium sulfate, as occurs in Conant's method,[1] is an unnecessary complication.

Subs., air-dry, 0.6264: loss, 0.0781 *in vacuo* at 80° over H_2SO_4.
Calc. for $C_6H_6O_4AsNa.2H_2O$: H_2O, 13.04. Found: 12.46.
Subs., anhydrous, 0.2637: $Mg_2As_2O_7$, 0.1708.
Calc. for $C_6H_6O_4AsNa$: As, 31.20. Found: 31.26.

If it is desired to isolate the free *p*-hydroxy-phenylarsonic acid, the filtrate from the barium sulfate is concentrated *in vacuo* without the addition of sodium hydroxide, a thick syrup of a mixture of free arsonic acids being obtained. On dissolving this in several volumes of hot glacial acetic acid, a faintly colored solution is obtained which gradually sets to a thick paste of colorless crystals of *p*-hydroxy-phenylarsonic acid on chilling and rubbing. After standing 24 hours in the refrigerator it is filtered off and washed with small portions of cold glacial acetic acid. The yield of the arsonic acid, which melts at 170–3° with preliminary softening, averages 40 grams.

Subs., 0.2573: $Mg_2As_2O_7$, 0.1850.
Calc. for $C_6H_7O_4As$: As, 34.36. Found: 34.70.

Isolation of the substance as the sodium salt as first described is therefore preferable from the standpoint of yield. We have nothing to add to the properties of the acid and its sodium salt as already recorded in the literature.

***o*-Hydroxy-phenylarsonic Acid.**—The alcoholic mother liquor from the sodium salt of *p*-hydroxy-phenylarsonic acid was concentrated to remove the alcohol and then diluted to about 750 cc. with water. A few drops of this solution gave the intense wine-red color characteristic of *o*-hydroxy-phenylarsonic acid on treating with a drop of ferric chloride solution. The solution was treated with aqueous sodium hydroxide until strongly alkaline to phenolphthalein, and then with an excess of concentrated barium chloride solution. The barium salt of *o*-hydroxy-phenylarsonic acid separated as a heavy powder on rubbing, and an additional small quantity was obtained by heating the filtrate from this to boiling. The combined fractions of the salt were suspended in water and treated with dil. sulfuric acid in slight excess and then the excess of sulfuric acid precipitated by the addition of just enough barium hy-

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[1] *Loc. cit.*

droxide solution so that the filtrate contained neither barium nor sulfate ions. The colorless filtrate was concentrated on the water bath to crystallization, the *o*-hydroxy-phenylarsonic acid separating as a characteristic crust of long, lustrous needles. After thorough chilling, it was filtered off and dried. The yield was 14 g. Recrystallized from hot water it formed flat, colorless needles which gave a wine-red color with ferric chloride solution, and proved identical in all respects with the substance obtained from *o*-arsanilic acid as described above. A mixture of the substances obtained by both methods showed no alteration in the melting point.

Subs., 0.3279: $Mg_2As_2O_7$, 0.2310.
Calc. for $C_6H_6O_4As$: As, 34.36. Found: 34.00.

For further identification, it was converted into the sodium salt, which separated from 50% alcohol as hexagonal, microscopic platelets containing 4 molecules of water of crystallization, just as in the case of the salt prepared from the sample synthesized from *o*-arsanilic acid.

Subs., 0.6372: loss, 0.1475 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_6H_6O_4AsNa.4H_2O$: H_2O, 23.07. Found: 23.15.
Subs., anhydrous, 0.2508: $Mg_2As_2O_7$, 0.1635.
Calc. for $C_6H_6O_4AsNa$: As, 31.20. Found: 31.48.

***p,p'*-Dihydroxy-diphenylarsonic Acid.**—The mother liquor from the barium salt of *o*-hydroxy-phenylarsonic acid was treated with hydrochloric acid until only faintly alkaline and then concentrated to about one liter. The chilled solution was then further treated with 1 : 1 hydrochloric acid, causing the separation of an oily precipitate which partly dissolved on further addition of the acid until definitely acid to congo red. On rubbing, crystallization slowly started, and on continued manipulation the oily precipitate also slowly solidified. After 4 hours' standing, the deposit was filtered off and washed with water. An aqueous suspension gave a wine-red color with ferric chloride due to contamination with another secondary arsonic acid to be described below. On dissolving in hot 50% acetic acid and letting stand in the refrigerator, colorless, prismatic needles separated with a yield of 10 g., melting slowly with effervescence at 250–1° (uncorr.). Benda[1] gives 239° as the melting point of *p,p'*-dihydroxy-diphenylarsonic acid obtained by diazotization of *p,p'*-diamino-diphenylarsonic acid. A sample of this substance prepared by us according to Benda also melted at 250–1° with effervescence, as did a mixture of this substance and that isolated as described above. Other properties were also identical. An aqueous suspension of the pure substance gave no color test with ferric chloride solution. It is practically insoluble in cold water, but dissolves appreciably on boiling and separates on cooling as short, colorless, prismatic needles. It is readily soluble in

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[1] Benda, *Ber.*, 41, 2371 (1908).

hot 50% or 95% alcohol or glacial acetic acid and in cold methyl alcohol, but very sparingly so in ether and acetone. Benzene and chloroform do not dissolve the substance. It is readily soluble in alkali and carbonate solutions and in 10% hydrochloric acid. In alkaline solution, it couples with diazotized sulfanilic acid, yielding an orange solution. There is no doubt that this substance is identical with that described by Benda as dihydroxy-diphenylarsonic acid.

Subs., 0.2573: $Mg_2As_2O_7$, 0.1348.
Calc. for $C_{12}H_{11}O_4As$: As, 25.49. Found: 25.30.

o,p'(?)-**Dihydroxy-diphenylarsonic Acid.**—On standing several hours longer, the aqueous mother liquor from the *p,p'*-arsonic acid gradually deposited heavy aggregates of stout, glistening prisms which increased on rubbing. After about 48 hours, these were filtered off and washed with water. Four g. were obtained, melting at 215–6° with effervescence and giving a deep wine-red color with ferric chloride solution. The mother liquor was treated with sodium acetate solution until neutral to congo red, causing the precipitation of a small amount of resinous material. On standing, crystallization again started and was facilitated by rubbing. An additional 4 g. of material were thus obtained which also melted at 215–6° with effervescence and gave a deep wine-red color with ferric chloride solution. The combined fractions were dissolved in a small volume of hot 50% acetic acid and separated slowly on cooling as short, stout, glistening prisms which melted at 215–7° (uncor.) to a liquid filled with bubbles. Repeated recrystallization did not alter the melting point. A further small quantity of this substance was obtained on concentrating the 50% acetic acid mother liquor obtained in the recrystallization of the previously described *p,p'*-dihydroxy-diphenylarsonic acid and fractional recrystallization of the product so obtained. The compound is appreciably soluble in boiling water and separates on cooling as flat, glistening, prismatic needles. It is somewhat soluble in 50 or 95% alcohol, but quite readily so on boiling. It is also soluble in hot acetic acid and cold methyl alcohol, very sparingly in acetone and ether, and insoluble in benzene and chloroform. It dissolves readily in alkali and carbonate solutions and in 10% hydrochloric acid. In alkaline solution it couples with diazotized sulfanilic acid to yield an orange solution.

Subs., 0.2508: $Mg_2As_2O_7$, 0.1322.
Calc. for $C_{12}H_{11}O_4As$: As, 25.49. Found: 25.43.

The substance is readily distinguished from the *p,p'* isomer by the fact that in aqueous suspension it gives an intense wine-red color with ferric chloride solution, similarly to *o*-hydroxy-phenylarsonic acid. We, therefore, conclude that it is either *o,p'*-dihydroxy-diphenylarsonic acid or the *o,o'* isomer. Since *o*-hydroxy-phenylarsonic acid is now definitely established as a product of the arsenation of phenol, it seems likely that this substance may react with a second molecule of phenol to form the secondary arsonic acid, the arsonic residue entering the position *para* to the hydroxyl groups just as the *p,p'*-hydroxy compound results from the further alteration of *p*-hydroxy-phenylarsonic acid. The yield of the acid also makes it seem probable that we are dealing with the *o,p'*-dihydroxy compound rather than the *o,o'* acid, as well as the additional possibility of its formation by condensation of *p*-hydroxy-phenylarsonic acid with a further molecule of phenol in the *o*-position. It is also probable that the *o,o'*-dihydroxy acid may occur among the reaction products but in such small amount as to render its isolation difficult. We are at present attempting to establish with certainty the identity of the new compound by synthetic means.

NEW YORK CITY.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

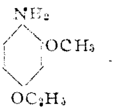
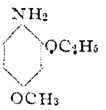
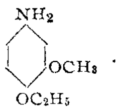
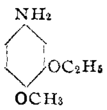
CERTAIN AMINO AND ACYLAMINO PHENOL ETHERS.

BY MICHAEL HEIDELBERGER AND WALTER A. JACOBS.

Received July 5, 1919.

In the course of recent chemotherapeutic studies it was found necessary to prepare as intermediates certain aromatic amines containing hydroxy, methoxy, and ethoxy groups, as well as multiples and combinations of these. While the monosubstituted compounds of this type have been adequately studied there are many gaps in the series of disubstituted amines containing the groups in question, as well as a number of inaccuracies in the descriptions of compounds which have already been prepared. In the present paper we have endeavored to fill some of these gaps and correct those inaccuracies which we have encountered, confining the discussion to certain amines and acylamino derivatives of anisole and phenetole and of the simpler mono- and di-ethers of pyrocatechol and resorcinol.

Of primary interest are perhaps the 4 isomeric methoxy-ethoxy-anilines:

M. P.				
The base...............	27.5–8.5°	22.5°	55°	81.5–2°
Acetamino deriv.........	117.5–8.5	100.5–1	148.5–50	145–6
Chloroacetylamino deriv.	97.5–8	126–7	133–4	135.5–6

Of these the two derived from resorcinol have never been prepared, as far as we have been able to find, while the two amino-pyrocatechol ethers apparently were isolated as their hydrochlorides by Wisinger,[1] who also

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[1] *Monatsh.*, 21, 1013 (1900).