ening and softening. It is sparingly soluble in cold water, acetic acid, or 50% alcohol, but dissolves more easily in these solvents on boiling.

Subs., 0.1644: (Kjeldahl) 10.9 cc. 0.1 *N* HCl. Subs., 0.3224: $Mg_2As_2O_7$, 0.1644.
Calc. for $C_{10}H_{15}O_4N_2As$: N, 9.27; As, 24.81. Found: N, 9.29; As, 24.61.

NEW YORK, N. Y.

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

AROMATIC ARSENIC COMPOUNDS. III. THE UREIDES AND β-SUBSTITUTED UREIDES OF *N*-ARYLGLYCINE ARSONIC ACIDS.

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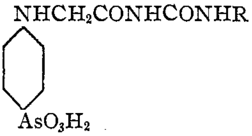
On replacing the amides of chloroacetic acid by the ureide and its β-alkyl or -aryl derivatives in the reaction described in the preceding paper, the ureides and substituted ureides of the arylglycine arsonic acids were obtained,



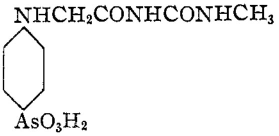
$NHCH_2CONHCONHR$ / AsO_3H_2

in which R may be hydrogen, an alkyl, or an aryl radical.

When chloroacetyl-urea or its simpler β-alkyl derivatives were employed the reaction could be accomplished by boiling in aqueous solution with the sodium salt of the aminoaryl arsonic acid. In the preparation of the β-arylureides of phenylglycine arsonic acid, however, involving the use of the very sparingly soluble chloroacetyl-substituted phenyl-ureas, the reaction proceeded most satisfactorily in 50% alcohol and only after sodium iodide had been added in order to cause the intermediate formation of the more reactive iodoacetyl compounds.

The new arsonic acids of this series resemble in their general properties the amides of the arylglycine arsonic acids, forming colorless crystalline compounds which are on the whole less soluble than the corresponding substances in the amide series. Like the latter they form stable and soluble neutral salts with the alkali metals. The ureide linkage, like that of the amides, is easily ruptured, this often occurring even at room temperature in solutions containing excess fixed alkali. Therefore, it was found important to avoid undue exposure to such conditions during the manipulations employed for the preparation of the sodium salts or in the purification of the acids by solution in alkali and reprecipitation with acids. In the latter case the use of dil. ammonia avoided this danger.

Of the numerous substances of this group which were prepared and studied the methylureide of *N*-phenylglycine-*p*-arsonic acid



has been of special interest since it has been found to exert a definite therapeutic effect in experimental syphilis and trypanosomiasis in rabbits.[1] Interesting biological results were also obtained with the ureide itself, although less striking than those given by the methyl derivative. The biological data will be published elsewhere by Drs. Brown and Pearce.

EXPERIMENTAL.

(A) Derivatives of *p*-Arsanilic Acid.

***N*-(Phenyl-4-arsonic acid)glycine-ureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONH_2$.—44 g. of arsanilic acid, dissolved in 200 cc. of *N* sodium hydroxide solution, and 27 g. of chloroacetyl-urea were boiled under a reflux condenser. After about 15 minutes the reaction product separated. The mixture was heated in a water bath for $^3/_4$ of an hour longer, cooled, and treated with 50 cc. of conc. hydrochloric acid. The crude, washed ureide was dissolved in dil. ammonia and reprecipitated with acetic acid, separating as aggregates of microscopic needles. It is sparingly soluble in boiling water or 50% alcohol and almost insoluble in methyl alcohol. When rapidly heated it sinters slightly above 230° and darkens, but does not melt below 280°

Subs., 0.2959: (Kjeldahl) 27.7 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1445.
Calc. for $C_9H_{12}O_5N_3As$: N, 13.25; As, 23.62. Found: N, 13.12; As, 23.56.

Sodium Salt.—The crude acid obtained above was suspended in a small volume of water and carefully treated with sodium hydroxide until solution was complete and the reaction was neutral to litmus. Addition of too much alkali is to be avoided owing to the danger of hydrolysis. An equal volume of saturated sodium acetate solution was then added, the sodium salt of the arsonic acid separating as well defined hexagonal or diamond-shaped, microscopic platelets. After standing in the refrigerator, the salt was filtered off, washed with a little ice water, and recrystallized from a small volume of hot water. The air-dried salt contains two molecules of water of crystallization and is readily soluble in water. The yield was 30 g. An additional quantity of the arsonic acid was contained in the mother liquors.

Subs., air-dry, 0.3724: loss, 0.0355 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_9H_{11}O_5N_3AsNa.2H_2O$: H_2O, 9.60. Found: 9.53.
Subs., anhydrous, 0.2968: (Kjeldahl) 25.8 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1372.
Calc. for $C_9H_{11}O_5N_3AsNa$: N, 12.39; As, 22.09. Found: N, 12.18; As, 22.31.

Solutions of the sodium salt give precipitates with salts of the heavy metals. The *silver salt* forms colorless, microscopic needles. Magnesia

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[1] Cf. footnote, THIS JOURNAL, 41, 1588–9 (1919).

mixture does not precipitate the solution in the cold but the *magnesium salt* separates on boiling.

***N*-(Phenyl-4-arsonic acid) glycine-methylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHCH_3$.—44 g. of arsanilic acid were dissolved in 200 cc. of *N* sodium hydroxide solution and 30 g. of α-chloroacetyl-β-methyl urea added. The mixture was boiled for one hour, during which the sparingly soluble chloro compound gradually dissolved. The ureide crystallized on cooling, or in some cases during the heating, after which the mixture was acidified to congo red with hydrochloric acid and filtered. The crude substance was dissolved in dil. ammonia and precipitated by acidifying the solution with acetic acid, but this did not always give satisfactory analytical figures. In order to obtain the acid pure it was converted into the sodium salt as described below and this dissolved in water and again acidified with acetic acid. The substance is sparingly soluble in hot water, separating on cooling as long, thin, glistening needles. It is also difficultly soluble in boiling 50% alcohol and is practically insoluble in the usual organic solvents. When rapidly heated to 220°, then slowly, it decomposes at 224–5°.

Subs., 0.1507: (Kjeldahl) 13.5 cc. 0.1 *N* HCl. Subs., 0.3428: $Mg_2As_2O_7$, 0.1590.

Calc. for $C_{10}H_{14}O_5N_3As$: N, 12.69; As, 22.63. Found: N, 12.54; As, 22.40.

Sodium Salt.—The acid was suspended in a small volume of hot water and carefully treated with sodium hydroxide until the solution reacted neutral to litmus, carefully avoiding an excess of alkali owing to the danger of saponification. After filtering and cooling the sodium salt slowly crystallized and after thorough chilling the salt was filtered off and washed with ice water. It was recrystallized from a small volume of water and air dried. The yield was 30 g. The sodium salt separates from water as microscopic platelets containing 7 molecules of water of crystallization, although slight impurities, or the conditions under which it is obtained, are apt to affect the water content. It is quite readily soluble in water, exceptionally so on warming, and easily forms supersaturated solutions. The solution of the sodium salt is not precipitated by magnesia mixture in the cold, but yields a precipitate of the *magnesium salt* on boiling. Heavy metal salts cause insoluble precipitates, the *silver salt* separating as thin, microscopic platelets.

Subs., air-dry, 0.7551: loss, 0.2013 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{10}H_{13}O_5N_3AsNa.7H_2O$: H_2O, 26.30. Found: 26.66.

Subs., anhydrous, 0.1438: 15.0 cc. N (24.5°, 754 mm.). Subs., 0.3041: $Mg_2As_2O_7$, 0.1346.

Calc. for $C_{10}H_{13}O_5N_3AsNa$: N, 11.89; As, 21.22. Found: N, 12.04; As, 21.35.

***N*-(Phenyl-4-arsonic acid)glycine-ethylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_2H_5$.—Treated as described in the case of the methylureide, 3.3 g. of α-chloroacetyl-β-ethyl-urea[1] yielded 4.5 g. of the ethyl-

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[1] THIS JOURNAL, 41, 473 (1919).

ureide arsonic acid. The substance is precipitated from the hot solution of its sodium salt (see below) by acetic acid as plumes of microscopic needles which are very difficultly soluble in hot water or methyl alcohol but more readily so in 50% alcohol. When rapidly heated to 220°, then slowly, it decomposes at 223–5°.

Subs., 0.1415: 15.0 cc. N (26.5°, 757 mm.).
Calc. for $C_{11}H_{16}O_5N_3As$: N, 12.17. Found: 12.03.

Sodium Salt.—An exactly neutral solution of the acid in a small volume of sodium hydroxide solution was treated with several volumes of alcohol. On scratching the salt rapidly separated as a paste of thin, microscopic platelets which were recrystallized from hot 85% alcohol and air dried. As so obtained the salt contained approximately 4.5 molecules of water of crystallization and dissolved readily in water.

Subs., air-dry, 1.0813: loss, 0.1892 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{11}H_{15}O_5N_3AsNa.4.5H_2O$: H_2O, 18.08. Found: 17.50.
Subs., anhydrous, 0.2950: (Kjeldahl) 23.7 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1235.
Calc. for $C_{11}H_{15}O_5N_3AsNa$: N, 11.45; As, 20.42. Found: N, 11.26; As, 20.21.

***N*-(Phenyl-4-arsonic acid)glycine-benzylureide,** p-$H_2O_3AsC_6H_4NHCH_2$-$CONHCONHCH_2C_6H_5$.—4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and 4.6 g. of α-chloroacetyl-β-benzyl urea[1] and 20 cc. of alcohol were added. After 3 hours' boiling, solution was complete and the mixture was chilled, diluted with water, and treated with a slight excess of ammonia. Some insoluble material was filtered off and the filtrate acidified with acetic acid, the benzylureide separating at once. For purification it was again dissolved in dil. ammonia and precipitated by acetic acid. The yield was 2.5 g. Recrystallized from 50% alcohol the acid separated as rosets of delicate needles which, when rapidly heated to 220° and then slowly, decompose at 225°. It is sparingly soluble in boiling water and practically insoluble in methyl alcohol.

Subs., 0.3184: (Kjeldahl) 23.6 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1205.
Calc. for $C_{16}H_{18}O_5N_3As$: N, 10.32; As, 18.39. Found: N, 10.38; As, 18.26.

α-*N*-(Phenyl-4-arsonic acid)aminopropionyl-urea, p-$H_2O_3AsC_6H_4NH$-$CH(CH_3)CONHCONH_2$.—8.8 g. of arsanilic acid dissolved in 40 cc. of *N* sodium hydroxide solution, and 8 g. of α-bromopropionyl-urea were boiled for one hour. The urea gradually dissolved and the arsonic acid rapidly crystallized on cooling, after which the mixture was treated with 20 cc. of 10% hydrochloric acid and filtered. The resulting substance was reprecipitated from its ammoniacal solution by acetic acid in a yield of 7 g. Recrystallized from 50% alcohol it forms aggregates of minute needles which are sparingly soluble in water and methyl alcohol. When rapidly heated to 220°, then slowly, it decomposes at 225–6°.

Subs., 0.1512: 16.7 cc. N (28.0°, 761 mm.). Subs., 0.3142: $Mg_2As_2O_7$, 0.1475.
Calc. for $C_{10}H_{14}O_6N_3As$: N, 12.69; As, 22.63. Found: N, 12.55; As, 22.65.

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[1] *J. Biol. Chem.*, **21**, 152 (1915).

N-**(Phenyl-4-arsonic acid)glycine-phenylureide,** *p*-$H_2O_3AsC_6H_4NH$-$CH_2CONHCONHC_6H_5$.—4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and 4.4 g. of chloroacetyl-phenyl-urea, 4 g. of sodium iodide, and 40 cc. of alcohol were added. After 4 hours' boiling the reaction product was filtered off and dissolved in dil. ammonia. The filtered solution was heated and then treated with an excess of acetic acid, causing the separation of the arsonic acid as feathery aggregates of silky hairs. When rapidly heated to 280° the acid darkens slightly and then melts. It is appreciably soluble in boiling 50% alcohol, separating on cooling as long, fine needles, and is almost insoluble in boiling water or methyl alcohol.

Subs., 0.1422: 13.25 cc. N (19.0°, 749 mm.).
Calc. for $C_{15}H_{16}O_5N_3As$: N, 10.69. Found: 10.73.

Sodium Salt.—The acid was suspended in a small amount of hot water and carefully treated with sodium hydroxide solution until just dissolved. The sodium salt separated on cooling as lustrous leaflets. The crystallization was aided by the addition of saturated sodium acetate solution. After filtration and washing with ice water the salt was recrystallized from 50% alcohol, separating on cooling as flat needles containing 5 molecules of water of crystallization.

Subs., air-dry, 0.9424: loss, 0.1701 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{15}O_5N_3AsNa.5H_2O$: H_2O, 17.83. Found: 18.05.
Subs., anhydrous, 0.3318: (Kjeldahl) 23.9 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1251.
Calc. for $C_{15}H_{15}O_5N_3AsNa$: N, 10.13; As, 18.06. Found: N, 10.09; As, 18.20.

N-**(Phenyl-4-arsonic acid)glycine-4′-acetamino-phenylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4NHCOCH_3$(*p*-).—On boiling 4.4 g. of arsanilic acid dissolved in 20 cc. of *N* sodium hydroxide solution and 20 cc. of alcohol with 5.4 g. of *p*-acetaminophenyl-chloroacetyl-urea[1] and 4 g. of sodium iodide the sparingly soluble halide was gradually replaced by the reaction product. After 4 hours the solid was almost completely soluble in dil. ammonia, and was then filtered off, dissolved in hot dil. ammonia and precipitated from the hot solution by acetic acid. The arsonic acid separated quickly in clusters of flat, microscopic needles which sinter and darken above 240° when rapidly heated and decompose at 265–6°. The acid is almost insoluble in boiling water but is appreciably soluble in hot 50% alcohol, separating on cooling as plumes of long, delicate hairs.

Subs., 0.1654: (Kjeldahl) 14.65 cc. 0.1 *N* HCl.
Calc. for $C_{17}H_{19}O_6N_4As$: N, 12.44. Found: 12.41.

Sodium Salt.—A concentrated neutral solution of the acid in dil. sodium hydroxide was salted out by the addition of saturated sodium acetate solution and recrystallized from a small volume of boiling water to which a few drops of sodium carbonate solution were added in order to prevent

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[1] THIS JOURNAL, 39, 1455 (1917).

the slight hydrolysis of the salt and separation of the acid which otherwise occurred in the hot solution. The salt separated on chilling as woolly masses of flat needles which contained 5 molecules of water of crystallization.

Subs., air-dry, 0.6962: loss, 0.1114 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{17}H_{18}O_6N_4AsNa.5H_2O$: H_2O, 16.02. Found: 16.00.
Subs., anhydrous, 0.3165: (Kjeldahl) 26.7 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1028.
Calc. for $C_{17}H_{18}O_6N_4AsNa$: N, 11.87; As, 15.88. Found: N, 11.82; As, 15.68.

***N*-(Phenyl-4-arsonic acid)glycine-3′-oxyamylamino-phenylureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4NHCOCONH_2$(*m*-).— 4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and 40 cc. of alcohol and boiled with 4.4 g. of sodium iodide and 6.2 g. of *m*-chloroacetyl-uramino-oxanilamide,[1] the sparingly soluble halide being gradually replaced by the reaction product. After 6 hours the solid was filtered off and digested with dil. ammonia. The filtrate from the undissolved material was diluted to 500 cc., heated on the water bath, and treated with an excess of acetic acid. Precipitated in this manner from the hot solution the arsonic acid separated as a micro-crystalline powder which was easily filtered. The yield was 1.3 g. Although almost insoluble in boiling water the acid dissolves appreciably in hot 50% alcohol. When rapidly heated it decomposes at 223–4°.

Subs., 0.1172: 15.2 cc. N (23.5°, 747 mm.). Subs., 0.2563: $Mg_2As_2O_7$, 0.0819.
Calc. for $C_{17}H_{18}O_7N_5As$: N, 14.62; As, 15.64. Found: N, 14.68; As, 15.42.

***N*-(Phenyl-4-arsonic acid)glycine-4′-hydroxyphenylureide,** *p*-H_2O_3As-$C_6H_4NHCH_2CONHCONHC_6H_4OH$(*p*-).—Because of our inability to prepare satisfactorily *p*-hydroxyphenyl-chloroacetyl-urea the arsonic acid was obtained by using the acetate of this substance. 2.2 g. of arsanilic acid were dissolved in 10 cc. of *N* sodium hydroxide solution and boiled for 2 hours with 2.7 g. of *p*-acetoxyphenyl-chloroacetyl-urea,[2] 2 g. of sodium iodide and 20 cc. of alcohol. On cooling the mixture set to a crystalline cake which was disintegrated, filtered, and washed with 50% alcohol. This product, in which the acetoxy group was presumably still intact, was dissolved in cold, dil. sodium hydroxide solution, making definitely alkaline to phenolphthalein in order to saponify the ester group. The solution was immediately filtered and exactly neutralized with acetic acid, for if allowed to stand too long in alkaline solution the glycylurea grouping is apt to be hydrolyzed as well, giving phenylglycine arsonic acid. From this solution the sodium salt described below was obtained. The acid itself was obtained by dissolving the sodium salts in hot water and treating with an excess of acetic acid, separating at once as microscopic needles containing 1.5 molecules of water of crystallization. The an-

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[1] THIS JOURNAL, 39, 1453 (1917).

[2] *Ibid.*, 39, 2441 (1917).

hydrous substance darkens above 200° and sinters and chars at about 250° when rapidly heated, but does not melt up to 280°.

Subs., air-dry, 0.1851: loss, 0.0113 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_6N_3As.1.5H_2O$: H_2O, 6.20. Found: 6.10.
Subs., anhydrous, 0.1726: (Kjeldahl) 12.80 cc. 0.1 *N* HCl.
Calc. for $C_{15}H_{16}O_6N_3As$: N, 10.27. Found: 10.38.

Sodium Salt.—This was obtained from the solution described above, crystallization being facilitated by the addition of saturated sodium acetate solution. The salt separated as nacreous plates, in a yield of only 1.3 g., owing possibly to the destruction of the substance during the saponification of the acetyl group. When recrystallized from 50% alcohol the salt separates as glistening leaflets containing from 4 to 4.5 molecules of water of crystallization. It is fairly readily soluble in water, particularly on warming.

Subs., air-dry, 0.3698: loss, 0.0560 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{15}O_6N_3AsNa.4.5H_2O$: H_2O, 15.81. Found: 15.14.
Subs., anhydrous, 0.2937; (Kjeldahl) 20.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1065.
Calc. for $C_{15}H_{15}O_6N_3AsNa$: N, 9.75; As, 17.39. Found: N, 9.78; As, 17.51.

N-**(Phenyl-4-arsonic acid)glycyl-4-uramino-phenoxyacetamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4OCH_2CONH_2$(*p*-). — In this case, using *p*-chloroacetyluramino-phenoxyacetamide[1] as starting material the reaction mixture behaved as in the preceding examples. After 4 to 5 hours' boiling the mixture was diluted with water, filtered, and the solid suspended in water and treated carefully with dil. sodium hydroxide solution until just alkaline to litmus. The filtrate was exactly neutralized with acetic acid and the *sodium salt* thrown out by the addition of sodium acetate, filtered off, and washed with 20% sodium acetate solution, then with 85% alcohol. Recrystallized from 50% alcohol it separated as aggregates of slightly purplish plates which were practically anhydrous. The salt is fairly readily soluble in water, especially on warming.

Subs., 0.2959: (Kjeldahl) 24.95 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.0929.
Calc. for $C_{17}H_{18}O_7N_4AsNa$: N, 11.48; As, 15.36. Found: N, 11.81; As, 15.16.

On adding acetic acid to a dilute solution of the sodium salt the *arsonic acid* separates slowly as glistening, diamond-shaped platelets which are almost insoluble in boiling water or boiling 50% alcohol. When rapidly heated it decomposes at 243–4° with preliminary sintering and darkening.

Subs., 0.1546: 16.05 cc. N (16.5°, 753 mm.).
Calc. for $C_{17}H_{19}O_7N_4As$: N, 12.02. Found: 12.13.

N-**(Phenyl-4-arsonic acid)glycyl-3-uramino-benzamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4CONH_2$(*m*-).—In the preparation of this substance the sparingly soluble *m*-chloroacetyluramino-benzamide[2] rapidly dis-

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[1] THIS JOURNAL, **39**, 2439 (1917).
[2] *Ibid.*, **39**, 2437 (1917).

solved as the reaction progressed, and the new arsonic acid soon separated. After 2 hours' boiling the solid was dissolved in dil. ammonia, the filtrate diluted to several hundred cc., heated, and then acidified with acetic acid. The arsonic acid separated as a rather voluminous, micro-crystalline powder. 4.2 g. were obtained from 5.2 g. of halide. It is very sparingly soluble in boiling water, but somewhat more soluble in boiling 50% alcohol, from which it separates as sheaves of flat, microscopic needles. When rapidly heated it melts at 213–4° with effervescence and darkening.

Subs., 0.1508: 17.0 cc. N (22.5°, 757 mm.). Subs., 0.3042: $Mg_2As_2O_7$, 0.1066.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.84; As, 17.18. Found: N, 12.97; As, 16.92.

N-(Phenyl-4-arsonic acid)glycyl-4-uramino-benzamide.—Starting with 5.2 g. of p-chloroacetyluramino-benzamide[1] the reaction mixture was boiled for 5 hours. The product obtained was dissolved in dil. ammonia, and the filtrate heated and acidified with acetic acid, the arsonic acid separating as short, microscopic needles. It was further purified by redissolving in dil. ammonia and reprecipitating with acetic acid. The yield was 3.1 g. When rapidly heated the substance darkens above 230° and decomposes at 245°.

Subs., 0.3288: (Kjeldahl) 29.85 cc. 0.1 N HCl; $Mg_2As_2O_7$, 0.1160.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.84; As, 17.18. Found: N, 12.72; As, 17.03.

N-(Phenyl-4-arsonic acid)glycyl-3-uramino-phenylacetamide, p-$H_2O_3AsC_6H_4NHCH_2CONHCONHC_6H_4CH_2CONH_2(m$-$)$:—In this case the reaction mixture, containing 10.8 g. of m-chloroacetyluramino-phenylacetamide,[1] was boiled for 3 hours. On cooling and scratching the arsonic acid separated from the clear solution as a thick, crystalline mass. After filtering, the crude product was dissolved in dil. ammonia and the filtrate treated with acetic acid, the substance gradually separating as a thick mass of needles in a yield of 9.5 g. The arsonic acid is soluble in hot water from which it separates as felted needles. It is also soluble in 50% alcohol and, when rapidly heated, decomposes at 214–6°.

Subs., 0.1460: 15.9 cc. N (23.0°, 754 mm.). Subs., 0.3102: $Mg_2As_2O_7$, 0.1055.
Calc. for $C_{17}H_{19}O_6N_4As$: N, 12.45; As, 16.65. Found: N, 12.47; As, 16.42.

N-(Phenyl-4-arsonic acid)glycyl-4-uraminophenyl acetamide.—The reaction mixture, containing 8.1 g. of p-chloroacetyluramino-phenylacetamide[2] yielded a clear solution after 2 hours' boiling. At the end of 4 hours the solution was cooled and the precipitated solid dissolved by the careful addition of dil. sodium hydroxide solution. After filtering and exactly neutralizing with acetic acid the *sodium salt* was salted out with sodium acetate, filtered off, washed with 85% alcohol, dissolved in a small volume of warm water and treated with an equal volume of alcohol. The sodium salt separated as microscopic, hexagonal platelets containing

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[1] This Journal, **39**, 2438 (1917).

[2] *Ibid.*, **39**, 2439 (1917).

about 2.5 molecules of water of crystallization. The yield of the air-dry salt was 4.5 g.

Subs., air-dry, 0.3606: loss, 0.0330 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{17}H_{18}O_6N_4AsNa.2.5H_2O$: H_2O, 8.71. Found: 9.15.

Subs., anhydrous, 0.1213: 12.8 cc. N (27.0°, 764 mm.). Subs., 0.2059: $Mg_2As_2O_7$, 0.0667.

Calc. for $C_{17}H_{18}O_6N_4AsNa$: N, 11.87; As, 15.88. Found: N, 12.08; As, 15.64.

On adding acetic acid to the hot solution of the sodium salt the *arsonic acid* separated slowly as plumes of delicate needles containing one molecule of water of crystallization. It is very sparingly soluble in boiling water but more readily so in boiling 50% alcohol. The anhydrous substance decomposes at 218–21° when rapidly heated.

Subs., air-dry, 0.6892: loss, 0.0255 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{17}H_{19}O_6N_4As.H_2O$: H_2O, 3.85. Found: 3.70.

Subs., anhydrous, 0.1485: (Kjeldahl) 13.2 cc. 0.1 *N* HCl.

Calc. for $C_{17}H_{19}O_6N_4As$: N, 12.45. Found: 12.44.

(B) Derivatives of *o*-Arsanilic Acid.

***N*-(Phenyl-2-arsonic acid) glycine-ureide.**—4.4 g. of *o*-arsanilic acid[1] were dissolved in 20 cc. of *N* sodium hydroxide solution and boiled $^1/_2$ hour with 2.7 g. of chloroacetyl-urea, the new arsonic acid precipitating after 7 to 8 minutes. The mixture was cooled, acidified to congo red, filtered, and the solid suspended in a little water, treated with an excess of ammonia, and the solution treated with boneblack and filtered. The pale yellow filtrate, heated to boiling and acidified strongly with acetic acid, deposited the ureide as plumes of minute, delicate needles which are almost insoluble in the usual neutral solvents. The yield was 2.5 g. When rapidly heated to 230°, then slowly, it melts and decomposes at 231–2° with preliminary softening and yellowing.

Subs., 0.1535: (Kjeldahl) 14.4 cc. 0.1 *N* HCl. Subs., 0.3396: $Mg_2As_7O_7$, 0.1647.

Calc. for $C_9H_{12}O_5N_3As$: N, 13.25; As, 23.62. Found: N, 13.14; As, 23.41.

***N*-(Phenyl-2-arsonic acid)-glycine-methylureide.**—A solution of 4.4 g. of *o*-arsanilic acid in 20 cc. of *N* aqueous sodium hydroxide solution was boiled 50 minutes with 3.1 g. of α-chloroacetyl-β-methyl-urea, the latter gradually dissolving and the mixture finally setting to an almost solid cake, being then transferred to the water bath and heated $^1/_2$ hour longer. After reprecipitation from dil. ammonia in the usual manner, 2.1 g. of the arsonic acid were obtained as balls of minute needles which are very sparingly soluble in boiling water, alcohol, or methyl alcohol, but dissolve in boiling acetic acid. When rapidly heated to 215°, then slowly, the acid melts and decomposes at 218° with slight preliminary softening and darkening.

Subs., 0.1642: (Kjeldahl) 15.05 cc. 0.1 *N* HCl. Subs., 0.3248: $Mg_2As_2O_7$, 0.1507.

Calc. for $C_{10}H_{14}O_5N_3As$: N, 12.69; As, 22.63. Found: N, 12.84; As, 22.40.

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

(C) Derivatives of *m*-Arsanilic Acid.

***N*-(Phenyl-3-arsonic acid)glycine-ureide.**—This substance was prepared and purified by the method of the preceding experiment, from 4.4 g. of *m*-arsanilic acid,[1] separating gradually as colorless microscopic needles frequently grouped in bundles. The yield was 2.5 g. It is soluble in boiling water and boiling 50% alcohol and separates from the former in rosets of minute needles. It decomposes at 208–9° with preliminary softening.

Subs., 0.1494: 17.2 cc. N (27.0°, 758 mm.). Subs., 0.3038: $Mg_2As_2O_7$, 0.1501.
Calc. for $C_9H_{12}O_5N_3As$: N, 13.25; As, 23.62. Found: N, 13.08; As, 23.84.

***N*-(Phenyl-3-arsonic acid)glycine-methylureide.**—Using 17.5 g. of *m*-arsanilic acid and 13 g. of α-chloroacetyl-β-methyl-urea in the usual manner, the substance suddenly separated after 1/2 hour. 80 cc. of *N* hydrochloric acid solution were added on cooling and the precipitate filtered off and washed with water. The yield was 19 g. Recrystallized as in the preceding examples, the acid melts with decomposition at 213–3.5° when rapidly heated. It is rather sparingly soluble in boiling water or 50% alcohol, separating from the former as rosets of delicate needles.

Subs., 0.1460: 16.1 cc. N (23.5°, 750 mm.). Subs., 0.3273: $Mg_2As_2O_7$, 0.1493.
Calc. for $C_{10}H_{14}O_5N_3As$: N, 12.69; As, 22.63. Found: N, 12.54; As, 22.01.

(D) Derivatives of Substituted Arsanilic Acids.

***N*-(3-Methylphenyl-4-arsonic acid)glycine-ureide.**—16.2 g. of 3-methyl-4-aminophenyl arsonic acid (from *o*-toluidine), were dissolved in 70 cc. of *N* sodium hydroxide solution and boiled with 9.5 g. of chloroacetyl-urea. After 1/2 hour the mixture suddenly crystallized and was cooled, treated with 25 cc. of 10% hydrochloric acid, filtered, and washed. The acid was dissolved in dil. ammonia, and the solution heated and acidified with acetic acid, causing the separation of the ureide as delicate needles. The yield was 11 g. The substance is sparingly soluble in boiling water or boiling 50% alcohol, and decomposes at about 235° when rapidly heated.

Subs., 0.1392: 15.5 cc. N (22.5°, 756 mm.). Subs., 0.3327: $Mg_2As_2O_7$, 0.1544.
Calc. for $C_{10}H_{14}O_5N_3As$: N, 12.69; As, 22.63. Found: N, 12.80; As, 22.40.

Sodium Salt.—The acid was suspended in a small volume of water and sodium hydroxide solution carefully added until solution was complete and the reaction was faintly alkaline to litmus. On warming the solution and adding 2 volumes of alcohol the sodium salt separated as glistening plates containing 2 molecules of water of crystallization. When recrystallized from a small volume of hot water it also separates as the same hydrate.

Subs., air-dry, 0.5114: loss, 0.0460 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{10}H_{13}O_5N_3AsNa.2H_2O$: H_2O, 9.26. Found: 9.00.

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

Subs., anhydrous, 0.1132: 11.4 cc. N (20.0°, 758 mm.). Subs., 0.2586: $Mg_2As_2O_7$, 0.1123.

Calc. for $C_{10}H_{13}O_5N_3AsNa$: N, 11.90; As, 21.22. Found: 11.71; As, 20.96.

***N*-(3-Methylphenyl-4-arsonic acid)glycine-methylureide.**—After one hour 23 g. of 3-methyl-4-aminophenyl arsonic acid as the sodium salt and 15 g. of α-chloroacetyl-β-methyl-urea yielded a solution which set to a thick, crystalline mass on cooling. This was diluted with water and treated with 40 cc. of 10% hydrochloric acid. Reprecipitated from hot dil. ammoniacal solution with acetic acid, the yield was 12 g. The substance is sparingly soluble in hot water but dissolves in boiling 50% alcohol. It separates from the former as hair-like needles and from the latter as radiating masses of minute needles. When rapidly heated it decomposes at 218–9°.

Subs., 0.1326: 14.0 cc. N (24.5°, 756 mm.). Subs., 0.3418: $Mg_2As_2O_7$, 0.1523.

Calc. for $C_{11}H_{16}O_5N_3As$: N, 12.17; As, 21.72. Found: N, 12.07; As, 21.52.

***N*-(2-Hydroxyphenyl-5-arsonic acid)glycine-ureide.**—On boiling a solution of 3.8 g. of 3-amino-4-hydroxyphenyl arsonic acid[1] in 16.5 cc. of *N* sodium hydroxide solution with 4.4 g. of chloroacetyl-urea it suddenly set to a solid, crystalline cake. After another hour on the water bath water was added and the crystalline mass disintegrated and filtered. Reprecipitated from solution in hot, dil. ammonia with acetic acid, the substance separated as flat, minute, almost colorless, glistening needles which contained between 1 and 1.5 molecules of water of crystallization. The yield was 3.3 g. When anhydrous it decomposes at 203–5°.

Subs., air-dry, 0.4214: loss, 0.0257 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_9H_{12}O_6N_3As.H_2O$: H_2O, 5.13. Found: 6.10.

Subs., anhydrous, 0.2946: (Kjeldahl) 26.65 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1380.

Calc. for $C_9H_{12}O_6N_3As$: N, 12.62; As, 22.50. Found: N, 12.68; As, 22.61.

NEW YORK, N. Y.

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

AROMATIC ARSENIC COMPOUNDS. IV.

AROMATIC AMIDES OF *N*-ARYLGLYCINE ARSONIC ACIDS.

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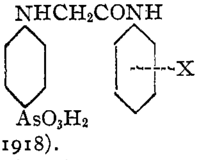
In continuation of the studies described in the preceding papers of this series,[2] we have prepared the arylamides and substituted arylamides of the arylglycine arsonic acids possessing the following general formula:



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[1] THIS JOURNAL, 40, 1590 (1918).

[2] *Ibid.*, 41, 1581, 1587, 1600 (1919).