TABLE I

ARSONIC ACIDS AND ARSENOSO COMPOUNDS DERIVED FROM BENZOYLUREA AND RELATED COMPOUNDS

Compound	Description	M. p., °C.	Yield, %	Formula	As analyses, % Calcd.	As analyses, % Found	N analyses, % Calcd.	N analyses, % Found
R = Arsono								
p-R-benzoylurea	Amorphous (W)	326.5	17	$C_8H_9AsN_2O_5$	26.0	25.6	9.73	9.78
1-(*p*-R-benzoyl)-3-(2-hydroxyethyl)-urea	Rectangular plates (W)	238–238.5 w. dec.	50	$C_{10}H_{13}AsN_2O_6$	22.6	22.5	8.44	8.50
1-(*p*-R-benzoyl)-biur t	Rectangular plates (W)	> 360	17	$C_9H_{10}AsN_3O_6$	22.6	22.7	12.7	12.9
α-(*p*-R-benzamido)-acetamide	Platelets (W)	211–213 w. dec.	5	$C_9H_{11}AsN_2O_5$	24.8	24.7	9.28	9.26
R = Arsenoso								
p-R-benzoylurea	Amorphous	270–271	75	$C_8H_7AsN_2O_3 \cdot H_2O$	27.5	28.0	10.3	10.4
1-(*p*-R-benzoyl)-3-(2-hydroxyethyl)-urea	Amorphous	...	67	$C_{10}H_{11}AsN_2O_4$	25.1	25.2	9.40	9.15
1-(*p*-R-benzoyl)-biuret	Needles (W)	> 360	84	$C_9H_8AsN_3O_4 \cdot 3H_2O$	21.3	21.5	12.0	12.0
p-R-α-toluylurea	Shiny plates (W)	Chars > 272	45	$C_9H_9AsN_2O_3$	28.0	27.5	10.5	9.86
N^{α}-(*p*-R-phenyl)-glycylurea	Amorphous	166–168 w. dec.	75	$C_9H_{10}AsN_3O_3 \cdot 2H_2O$	23.5	23.5	13.2	13.6
α-(*p*-R-benzamido)-acetamide	Rectangular prisms (W)	Chars > 285	65	$C_9H_9AsN_3O_3$	28.0	28.1	10.5	10.5
N-(*p*-R-hippuryl)-glycine	Amorphous	Dec. > 220	75	$C_{11}H_{11}AsN_2O_6 \cdot H_2O$	21.8	21.3	8.14	7.92
N-(*p*-R-hippuryl)-glycine, methyl ester	Amorphous	Chars > 240	30	$C_{12}H_{13}AsN_2O_6 \cdot H_2O$	20.9	20.8	7.83	7.80
α-[α-(*p*-R-benzamido)-acetamido]-acetamide	Rectangular prisms (W)	Chars > 240	50	$C_{11}H_{12}AsN_3O_4 \cdot H_2O$	21.8	21.9	12.3	12.0
β-(*p*-R-benzamido)-propionamide	Needles (W)	283–285 w. dec.	50	$C_{10}H_{11}AsN_2O_4$	26.6	26.6	9.94	9.94
α-Amino-N^{α}-(*p*-R-α-toluyl)-acetamide	Needles (W)	133 w. dec.	50	$C_{10}H_{11}AsN_2O_3 \cdot 2H_2O$	23.6	23.5	8.81	8.40
α-(*p*-R-phenylsulfonamido)-acetamide	Amorphous	193–195 w. dec.	55	$C_8H_9AsN_2O_4S$	24.6	24.4	9.22	8.89

Attempted Preparation of Sulfur Ureas.—In contrast to the behavior of urea, sulfamide[14] did not condense with *p*-nitrobenzoyl chloride when refluxed in benzene for forty-eight hours or in ethyl acetate for twenty-four hours. Potassium sulfamide[15] also failed to condense with either *p*-nitrobenzoyl chloride or *p*-nitrobenzenesulfonyl chloride when refluxed in benzene for forty-eight hours.

The table lists the arsonic acids and arsenoso compounds which were prepared. Recrystallization was done from water (W). Melting points below 200° were taken in a double-walled sulfuric acid bath using Anschütz thermometers with a Bureau of Standards report; no stem correction was made. Melting points above 200° were made in a copper block with a thermometer standardized against the same set of Anschütz thermometers. All analytical results were the average of two or more determinations.

(14) Kindly supplied through the courtesy of Doctor E. F. Degering, Purdue University.

(15) Franklin and Stafford, *Am. Chem. J.*, **28**, 83 (1902).

Acknowledgment.—The authors wish to acknowledge the assistance given by Leon D. Freedman throughout the course of the work.

Summary

A number of arsonic acids and arsenoso compounds containing two or more amide groups on a single side chain have been prepared.

BALTIMORE, MD. RECEIVED OCTOBER 12, 1943

[CONTRIBUTION FROM THE VENEREAL DISEASE RESEARCH AND POSTGRADUATE TRAINING CENTER, UNITED STATES PUBLIC HEALTH SERVICE, JOHNS HOPKINS HOSPITAL]

Arsenoso Compounds Containing Amide Groups[1]

BY G. O. DOAK, H. G. STEINMAN AND HARRY EAGLE

Among the various types of aromatic arsenoso compounds which have been described in previous publications from this Laboratory, those containing amide groups have been of particular interest from the pharmacological viewpoint. The present paper gives the results of further research on this class of compounds.

For the oxidation of tolylarsonic acids and the esterification of the resulting arsonobenzoic acids the methods of Cohen, King and Strangeways[2] were used. The catalytic method of Stevinson and Hamilton[3] was used for the reduction of nitrobenzenearsonic acids to the corresponding amino compounds. Cyanobenzenearsonic acids were prepared and isolated by the method previously described,[4] except that cuprous cyanide was substituted for nickel cyanide. In contrast to the findings of Korczynski and Fandrich[5] with non-arsenated aromatic amines the use of cuprous cyanide gave a larger yield in this particular reaction. The Scheller–Bart reaction[6] was used for the preparation of **4-nitro-, and 5-nitro-*o*-toluenearsonic acids.** While the yields were larger by this procedure as compared to the

(1) Paper VII in the Series Entitled "The Preparation of Phenylarsenoxides."

(2) Cohen, King and Strangeways, *J. Chem. Soc.*, 3236 (1931).

(3) Stevinson and Hamilton, THIS JOURNAL, **57**, 1298 (1935).

(4) Doak, Eagle and Steinman, *ibid.*, **62**, 3010 (1940).

(5) Korczynski and Fandrich, *Compt. rend.*, **183**, 421 (1926).

(6) Scheller, French Patent 624,028, *Chem. Zentr.*, **98**, II, 2229 (1927); Doak, THIS JOURNAL, **62**, 167 (1940).

customary Bart reaction,[7] considerable difficulty was experienced in removing inorganic arsenic. Contrary to the statement of Maschmann[7c] the preparation of 2-arsono-4-nitrobenzoic acid by the oxidation of 2-methyl-5-nitrobenzenearsonic acid did not proceed smoothly and repeated recrystallizations were necessary in order to obtain an analytically pure sample. For the preparation of 2-arsono-5-nitrobenzoic acid the method of Karrer[8] was found preferable to the oxidation of 2-methyl-4-nitrobenzenearsonic acid.

N-Substituted arsenosobenzamides were prepared by the condensation of dichloroarsinobenzoyl chlorides with the appropriate amine as described for the preparation of *p*-arsenoso-N-(2,3-dihydroxypropyl)-benzamide.

Experimental Part

5-Arsenosoisophthalamide.—The Bart reaction applied to 3,5-xylidine gave **3,5-xylenearsonic acid** which was then oxidized with potassium permanganate. An acid **potassium salt of 5-arsonoisophthalic acid, with the composition** $H_2O_3AsC_6H_3(COOH)_2 \cdot KHO_3AsC_6H_3(COOH)_2$, crystallized from solutions strongly acid to congo red. This acid salt, suspended in chloroform, was treated with phosphorus tri- and pentachloride and the reaction mixture added to cold aqueous ammonia. Instead of the expected amide we obtained **5-arsenosoisophthalic acid.** This compound was esterified to **5-arsenosoisophthalic acid, dimethyl ester,** which gave the desired compound when heated with ammonia in a sealed tube at 100° for six hours.

6-Arsenosoisophthalamic Acid.—2-Arsono-5-nitrobenzoic acid[8] on reduction gave **5-amino-2-arsonobenzoic acid.** The Sandmeyer reaction applied to this compound gave **2-arsono-5-cyanobenzoic acid** in impure form. We were unable to obtain an analytically pure sample by repeated recrystallization from either water or alcohol. Oxidation of the slightly impure nitrile with 30% hydrogen peroxide gave **6-arsonoisophthalamic acid.** Reduction gave the desired arsenoso compound.

6-Arsenosoterephthalamic Acid.—2-Arsono-4-nitrobenzoic acid was reduced catalytically to 4-amino-2-arsonobenzoic acid.[7c] By a series of reactions similar to those described above we obtained **2-arsono-4-cyanobenzoic acid, 2-arsonoterephthalamic acid** and finally the desired arsenoso compound.

2-Amino-4-arsenosobenzamide.—This compound has been previously described[9] but the following procedures offer some improvement. The acid potassium salt of 2-nitro-4-arsonobenzoic acid,[2] suspended in chloroform, was treated with phosphorus tri- and pentachlorides. The solvent was removed *in vacuo* and the residue added to cold aqueous ammonia. The resulting **4-arsenoso-2-nitrobenzamide** was oxidized to **4-carbamyl-3-nitrobenzenearsonic acid** with 30% hydrogen peroxide. Catalytic reduction gave 4-carbamyl-*m*-arsanilic acid which was reduced to the arsenoso compound with sulfur dioxide.

The compound was more satisfactorily prepared from the methyl ester of 4-arsenosoanthranilic acid[2] by heating in a sealed tube with aqueous ammonia for sixty hours at 90°.

2-Acetamido-4-arsenosobenzamide.—While this compound was prepared readily by acetylation of 2-amino-4-arsenosobenzamide, we were unable to prepare it by reduction of the corresponding arsonic acid. We were also unable to convert 2-acetamido-4-arsonobenzoic acid to the amide by treatment with phosphorus tri- and pentachlorides, and adding the mixture to ammonia.

4-Arsenososalicylamide.—This compound was obtained by reduction of the corresponding arsonic acid.[2]

5-Arsenososalicylamide.—5-Arsonosalicylic acid[10] esterified with methanol gave **5-arsonosalicylic acid, methyl ester,** which possessed a faint but definite wintergreen odor. Ammonolysis at 100° in a sealed tube resulted in splitting arsenic from the ring. Ammonolysis at 0° for several days gave **3-carbamyl-4-hydroxybenzenearsonic acid.** Reduction of this arsonic acid gave the desired compound.

3-Amino-5-dichloroarsinosalicylamide Hydrochloride.—Esterification of 3-amino-5-arsonosalicylic acid[9] gave 3-amino-5-arsonosalicylic acid, methyl ester. This compound was not purified but added directly at 0° to aqueous ammonia, especially prepared from oxygen free water. After standing for three days the ammonia was removed in a stream of nitrogen and the solution acidified. **5-Carbamyl-4-hydroxy-*m*-arsanilic acid** precipitated.

Anal. Calcd. for $C_7H_9AsN_2O_5$: N, 10.2. Found: N, 10.2.

Reduction in hydrochloric acid solution gave the dichloroarsino hydrochloride compound, m. p. 177–178°.

Anal. Calcd. for $C_7H_7AsCl_2N_2O_2 \cdot HCl \cdot H_2O$: As, 21.3; N, 7.97. Found: As, 21.8; N, 8.07.

As this compound was unstable in alkaline solution the arsenoso compound was not prepared.

***p*-Arsenosobenzimido Ethyl Ether.**—*p*-Cyanobenzenearsonic acid was reduced with sulfur dioxide and hydriodic acid in 12 *N* sulfuric acid and the precipitate treated with sodium bicarbonate solution. The resulting ***p*-arsenosobenzonitrile** (2.5 g.) was suspended in 10 ml. of ether, 0.7 ml. of 95% alcohol added, and the mixture saturated with hydrogen chloride at 0°. After standing two days at 10°, the ***p*-dichloroarsinobenzimido ethyl ether hydrochloride** was filtered off and thoroughly washed with ether. The yield was 53%, m. p. 141°.

Anal. Calcd. for $C_9H_{10}AsCl_2NO \cdot HCl \cdot H_2O$: As, 21.5; N, 4.02. Found: As, 21.3; N, 4.06.

This was hydrolyzed with sodium bicarbonate solution to the arsenoso derivative.

***p*-Arsenoso-N-(2,3-dihydroxypropyl)-benzamide.**—*p*-Dichloroarsinobenzoyl chloride (8.6 g.) in 20 ml. of acetone was added dropwise and with cooling to a solution of 2.8 g. of 3-amino-1,2-propanediol in 100 ml. of 10% sodium carbonate solution. After standing overnight the precipitated arsenoso compound was filtered, washed, and finally recrystallized from 0.1% sodium bicarbonate solution.

***p,p'*-Diarsenoso-1,2-dibenzoylhydrazine.**—Hydrazine hydrate was added to an excess of *p*-dichloroarsinobenzoyl chloride in pyridine and benzene. The compound was purified by dissolving in sodium hydroxide solution and precipitating with acid.

***p*-Arsenoso-N-(2-acetamidoethyl)-benzamide.**—*p*-Dichloroarsinobenzoyl chloride was condensed with glycinonitrile sulfate in sodium carbonate solution and the resulting ***p*-arsenoso-N-(cyanomethyl)-benzamide** recrystallized from 0.1% sodium bicarbonate solution. Oxidation with iodine in sodium bicarbonate solution gave ***p*-(cyanomethyl)-carbamylbenzenearsonic acid.** Neither the arsonic acid nor the arsenoso compound could be reduced to the amine. No reduction occurred with the method of Carothers and Jones.[11] Reduction of the arsonic acid by Hartung's method[12] gave *p*-arsonohippuric acid. Reduction of the arsonic acid employing Raney nickel gave a mixture of amines. When *p*-dichloroarsinobenzoyl chloride was coupled with an excess of ethylenediamine in sodium carbonate solution only ***p,p'*-diarsenoso-N,N'-dibenzoylethylenediamine** was obtained. The desired compound was finally prepared by coupling the acid chloride with N-(2-aminoethyl)-acetamide.[13] The crude material was recrystallized twice from acetic acid and finally from water.

(7) (a) Jacobs, Heidelberger and Rolf, THIS JOURNAL, **40**, 1580 (1918); (b) Karrer, *Ber.*, **48**, 311 (1915); (c) Maschmann, *ibid.*, **57**, 1759 (1924).

(8) Karrer, *ibid.*, **48**, 1058 (1915).

(9) Doak, Steinman and Eagle, THIS JOURNAL, **63**, 99 (1941).

(10) Newberry, Phillips and Stickings, *J. Chem. Soc.*, 3051 (1928).

(11) Carothers and Jones, THIS JOURNAL, **47**, 3051 (1925).

(12) Hartung, *ibid.*, **50**, 3370 (1928).

(13) Hill and Aspinall, *ibid.*, **61**, 822 (1939).

TABLE I

ARSONIC ACIDS AND ARSENOSO COMPOUNDS CONTAINING AMIDE GROUPS

Compound	Description	M. p., °C.	Yield, %	Formula	As analyses, % Calcd.	As analyses, % Found	N analyses, % Calcd.	N analyses, % Found
Arsonic acids								
3,5-Xylenearsonic acid	Needles (W)	222–223	18	$C_8H_{11}AsO_3$	32.6	32.2	...	...
5-Arsonoisophthalic acid, potassium acid salt	Needles (W)	Chars > 300	75	$C_{16}H_{12}As_2KO_{14}$[a]	24.2	24.0	...	...
4-Nitro-*o*-toluenearsonic acid	Needles (W)	240	67[b]	$C_7H_8AsNO_5$	28.7	29.2	5.37	5.39
5-Amino-2-arsonobenzoic acid	Plates (W)	> 360	72	$C_7H_8AsNO_5$	28.7	28.9	5.37	5.36
2-Arsono-5-cyanobenzoic acid	Plates (W)	Dec. > 300	23	$C_8H_4AsNO_5$	27.6	26.0	5.16	5.57
6-Arsonoisophthalamic acid	Rectangular prisms (W)	347.5	57	$C_8H_9AsNO_6$	25.9	25.6	4.85	4.86
5-Nitro-*o*-toluenearsonic acid	Needles (W)	235–236	52[b]	$C_7H_8AsNO_6$	28.7	29.2	5.37	5.38
4-Amino-2-arsonobenzoic acid	Needles (W)	Dec. > 220	94	$C_7H_8AsNO_5 \cdot H_2O$[c]	26.9	26.4	5.02	5.10
2-Arsono-4-cyanobenzoic acid	Needles (W)	Dec. > 351	41	$C_8H_6AsNO_4$	27.6	28.0	5.16	5.18
2-Arsonoterephthalamic acid	Plates (W)	> 360	63	$C_8H_9AsNO_6$	25.9	26.0	4.85	4.95
5-Arsonosalicylic acid, methyl ester	Needles (M)	Softens 193	59	$C_8H_9AsO_6$	27.0	26.8	...	...
3-Carbamyl-4-hydroxybenzenearsonic acid	Needles (W)	Chars > 330	90	$C_7H_8AsNO_6$	28.7	28.6	5.37	5.70
4-Carbamyl-3-nitrobenzenearsonic acid	Rectangular prisms (W)	Chars > 270	60	$C_7H_7AsN_2O_6$	25.8	26.2	9.66	9.72
4-Carbamyl-*m*-arsanilic acid	Plates (W)	Dec. > 230	60	$C_7H_9AsN_2O_4$	28.8	28.5	10.8	10.4
p-[(Cyanomethyl)-carbamyl]-benzenearsonic acid	Rectangular prisms (W)	251–252 w. dec.	100	$C_9H_9AsN_2O_4$	26.4	26.7	9.87	9.91
N-*p*-toluylarsanilic acid	Needles (AA)	> 360	100	$C_{14}H_{14}AsNO_4$	22.3	22.4	4.18	4.32
p-Arsonoterephthalanilic acid	Rosets (AA)	> 360	5	$C_{14}H_{12}AsNO_8$	20.5	20.5	3.84	3.79
N,N'-Terephthaloyldiarsanilic acid	Amorphous	Chars > 250	25	$C_{20}H_{18}As_2N_2O_8$	26.6	26.8	4.96	4.81
N-(*p*-Cyanobenzoyl)-arsanilic acid	Amorphous	> 360	35	$C_{14}H_{11}AsN_2O_4$	21.6	21.7	8.10	8.13
N-(*p*-Carbamylbenzoyl)-arsanilic acid	Needles (W)	> 360	95	$C_{14}H_{13}AsN_2O_4$	20.6	20.6	7.70	7.63
p-(*p*-Nitrophenylthio)-benzenearsonic acid	Yellow needles (A)	291–292	39	$C_{12}H_{10}AsNO_5S$	21.1	21.5	3.95	3.92
p-(*p*-Aminophenylthio)-benzenearsonic acid	Needles (A)	Dec. > 190	67	$C_{12}H_{12}AsNO_3S$	23.1	23.2	4.31	4.00
p-(*p*-Cyanophenylthio)-benzenearsonic acid	Yellow needles (W)	Dec. > 200	32	$C_{13}H_{10}AsNO_3S$	22.4	21.9	4.18	4.25
p-(*p*-Carbamylphenylsulfonyl)-benzenearsonic acid	Needles (W)	310.5	28	$C_{13}H_{12}AsNO_4S$	19.4	19.7	3.64	3.62
R = Arsenoso								
5-R-isophthalic acid	Amorphous (W)	224–225	39	$C_8H_5AsO_5 \cdot 2H_2O$	25.7	25.7	...	...
5-R-isophthalic acid, dimethyl ester	Rectangular prisms (M)	255	86	$C_{10}H_9AsO_5$	26.4	26.6	...	...
5-R-isophthalamide	Glass (W)	Sinters at 75	81	$C_8H_7AsN_2O_3 \cdot H_2O$	27.5	27.7	10.3	9.60
6-R-isophthalamic acid	Hexagonal needles (W)	236.5–237.5	43	$C_8H_8AsNO_4 \cdot H_2O$	27.4	27.6	5.13	5.16
6-R-terephthalamic acid	Rectangular prisms (W)	221.5–222.5	67	$C_8H_8AsNO_4$	29.4	29.5	5.49	5.67
4-R-2-nitrobenzamide	Hexagonal prisms (W)	162–163 w. dec.	60	$C_7H_6AsN_3O_4$	29.3	28.8	10.9	10.9
2-Amino-4-R-benzamide	Hexagonal prisms (W)	177–178	40[d]	$C_7H_7AsN_2O_3 \cdot 1^1/_2H_2O$	29.6	29.6	11.1	10.9
2-Acetamido-4-R-benzamide	Amorphous	263–264 w. dec.	35	$C_9H_9AsN_2O_3 \cdot H_2O$	26.2	26.2	9.80	9.40
4-R-salicylamide	Cubes (A)	> 360	72	$C_7H_8AsNO_3 \cdot H_2O$	30.6	30.1	5.72	5.64
5-R-salicylamide	Needles (W)	222–223	72	$C_7H_8AsNO_3 \cdot {}^1/_2H_2O$	31.7	31.5	5.94	5.87
p-R-benzonitrile	Amorphous	195.5–197.5	52	C_7H_6AsNO	38.8	38.7	7.25	7.03
p-R-benzimido ethyl ether	Amorphous	184.5–185	65	$C_9H_{10}AsNO_2 \cdot H_2O$	29.2	29.8	5.45	5.61
p-R-N-(2,3-dihydroxypropyl)-benzamide	Amorphous (W)	Chars > 250	50	$C_{10}H_{12}AsNO_4$	26.3	26.6	4.92	4.56
p,p'-Di-R-1,2-dibenzoylhydrazine	Amorphous	> 360	60	$C_{14}H_{10}As_2N_2O_4 \cdot 2H_2O$	32.9	33.0	6.14	5.94[e]
p-R-N-(cyanomethyl)-benzamide	Amorphous (W)	Chars > 265	87	$C_9H_7AsN_2O_2$	30.0	30.0	11.2	11.1
p,p'-Di-R-N,N'-dibenzoylethylenediamine	Amorphous	Chars > 320	80	$C_{18}H_{14}As_2N_2O_4 \cdot 2H_2O$	31.0	31.5	5.79	5.62[e]
p-R-N-(2-acetamidoethyl)-benzamide	Amorphous (W)	270–272 w. dec.	85	$C_{11}H_{14}AsN_3O_3$	25.3	25.2	9.47	9.76
p'-R-*p*-carbamylbenzanilide	Amorphous	319	100	$C_{14}H_{11}AsN_2O_3$	22.7	22.7	8.50	8.07

[a] Calcd.: K, 6.31. Found: K, 6.06. [b] These yields are for the Scheller–Bart reaction. For the yields by the customary Bart reaction see ref. 7. [c] Maschmann reports the unhydrated acid; m. p. 120° with dec. The hydrated acid, reported here, was converted to the anhydride on heating. Calcd.: H_2O, 12.9. Loss at 100°, 13.3. [d] Yield by ammonolysis of the corresponding ester. [e] Nitrogen determinations by a micro Dumas procedure.

α-Amino-p-dichloroarsinoacetanilide Hydrochloride.—Reduction of the corresponding arsonic acid[14] in hydrochloric acid gave this dichloroarsine. It could not be successfully hydrolyzed to the arsenoso derivative.

Anal. Calcd. for $C_8H_8AsCl_3N_2O \cdot HCl$: As, 22.6; N, 8.45. Found: As, 22.3; N, 8.45.

p'-Arsenoso-p-carbamylbenzanilide.—By means of the Schotten–Baumann reaction *p*-toluyl chloride was condensed with atoxyl to give **N-p-toluylarsanilic acid.** This compound was oxidized with potassium permanganate in neutral solution, in the presence of magnesium sulfate. From the reaction mixture terephthalic acid was isolated in quantitative yield. According to German Patent 191,548[15] terephthalyl chloride condenses with arsanilic acid to give *p*-arsonoterephthalanilic acid. In several experiments, using various experimental conditions, we obtained a mixture of this compound and **N,N'-terephthaloyldiarsanilic** acid. It was found that the two compounds could be separated by the differential solubilities of their magnesium salts, as described for the separation of a similar mixture in the biphenyl series,[16] but the yield was poor. The desired compound was finally obtained by the following synthesis. *p*-Cyanobenzoic acid (14.7 g.) and 7.9 g. of pyridine were dissolved in 1 liter of absolute ether and the mixture treated with 11.9 g. of thionyl chloride according to the directions of Carré and Libermann.[17] While the resulting *p*-cyanobenzoyl chloride could not be readily separated from pyridine hydrochloride, this was found unnecessary. After removing the solvent the residue was triturated with 43 g. of arsanilic acid and then warmed on the water-bath for one hour. An excess of 10% hydrochloric acid was added and the mixture stirred for one hour to dissolve any unchanged arsanilic acid. The resulting **N-(p-cyanobenzoyl)-arsanilic acid** was purified through its magnesium salt. Oxidation with 30% hydrogen peroxide gave **N-(p-carbamylbenzoyl)-arsanilic acid,** which was reduced to the desired arsenoso derivative.

p-(p-Carbamylphenylsulfonyl)-benzenearsonic Acid.—The Scheller–Bart reaction, applied to *p*-amino-*p'*-nitrodiphenyl sulfide,[18] gave **p-(p-nitrophenylthio)-benzenearsonic acid** which was reduced catalytically to *p*-(*p*-aminophenylthio)-benzenearsonic acid. The Sandmeyer reaction applied to this amine gave *p*-(*p*-cyanophenylthio)-benzenearsonic acid. This nitrile was then oxidized with an excess of 30% hydrogen peroxide in alkaline solution. ***p*-(*p*-Carbamylphenylsulfonyl)-benzenearsonic acid** precipitated when the alkaline solution was acidified. Unfortunately all attempts to reduce this compound to the corresponding arsenoso derivative resulted in partial hydrolysis of the amide group.

The table lists the arsonic acids and arsenoso compounds which are new compounds or are known compounds prepared by a new procedure. Under "description," the letters in parentheses refer to the solvent used for crystallizing: W = water, A = ethyl alcohol, M = methanol and AA = acetic acid. Melting points were taken by the procedure described in paper VI. All analytical results are the average of two or more determinations.

Acknowledgment.—The authors wish to acknowledge the assistance given by Leon D. Freedman throughout the course of the work.

Summary

A number of arsonic acids and arsenoso compounds containing amide groups have been prepared.

(14) Jacobs and Heidelberger, THIS JOURNAL, **41** 1809 (1919).
(15) German Patent 191,548; *Chem. Zentr.*, **79**, I, 779 (1908).
(16) Doak, Eagle and Steinman, THIS JOURNAL, **64**, 1064 (1942).
(17) Carré and Libermann, *Compt. rend.*, **199**, 1422 (1934).
(18) Raiziss, Clemence, Severac and Moetsch, THIS JOURNAL, **61**, 2763 (1939).

BALTIMORE, MARYLAND RECEIVED OCTOBER 12, 1943

[CONTRIBUTION FROM VENEREAL DISEASE RESEARCH AND POSTGRADUATE TRAINING CENTER, UNITED STATES PUBLIC HEALTH SERVICE, JOHNS HOPKINS HOSPITAL.]

Arsonic Acids and Arsenoso Compounds Containing the Azo Linkage[1]

BY G. O. DOAK, H. G. STEINMAN AND HARRY EAGLE

The customary preparation of arsonic acids containing the azo linkage consists in the coupling of diazotized aminoarylarsonic acids with phenols and amines. We have also prepared such compounds by coupling diazo compounds with hydroxyarylarsonic acids and by the application of the Scheller–Bart reaction[2] to aminoazo compounds.

While it has been stated that *o*- and *m*-hydroxybenzenearsonic acids[3] and *m*-arsanilic acid[4] couple with diazo compounds, the only evidence for such a reaction was color formation. Benda[5] obtained only arsenic acid and the corresponding phenylazophenol from *p*-hydroxybenzenearsonic acid and diazo compounds. Lawrence and Hamilton,[6] however, have successfully coupled aminonaphthalenearsonic acids.

In this Laboratory it has been found that diazo compounds couple with *o*- and *m*-hydroxybenzenearsonic acids, the coupling occurring in *para* position to the hydroxy group. Where the para position is blocked, *e. g.*, *p*-hydroxybenzenearsonic acid, the arsonic acid group is partially replaced by the phenylazo group. In addition, however, some coupling occurs in *ortho* position to the hydroxy group. The resulting azoarsonic acid then reacts further with the diazo compound to give the *bis*-(phenylazo)-phenol. The extent to which each of these three reactions occurs depends not only upon the strength of the reactants as coupling agents but is also influenced by the *p*H of the reaction mixture. The results of a series of experiments are given in Table I.

Experimental Part

A. The Coupling of Diazo Compounds with Hydroxyarylarsonic Acids.—The following description illustrates the general procedure that was followed.

(1) Paper VIII in the Series Entitled "The Preparation of Phenylarsenoxides."
(2) Scheller, French Patent 624,028, *Chem. Zentr.*, **98**, II, 2229 (1927); Doak, THIS JOURNAL, **62**, 167 (1940).
(3) Jacobs and Heidelberger, *ibid.*, **41**, 1440 (1919).
(4) Bertheim, *Ber.*, **41**, 1655 (1908).
(5) Benda, *ibid.*, **44**, 3449 (1911).
(6) Personal communication from Dr. Hamilton.