[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEBRASKA]

THE ACTION OF ALKYL CHLOROCARBONATES ON AMINO-ARYLARSONIC ACIDS[1]

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The action of alkyl chlorocarbonates on amino-arylarsonic acids has been but little studied. 3-Carbethoxy-amino-phenylarsonic acid,[2] and 4-carbethoxy-amino-phenylarsonic acid,[3] have both been prepared as intermediates, the chlorocarbonates being added simply to protect the amino group.

The object of this research was to study more fully the action of various alkyl chlorocarbonates on arylarsonic acids with one or two amino groups, and in one case, both an amino and an hydroxyl group, attached to the benzene ring. Methyl, ethyl, propyl, *iso*propyl, butyl and *iso*butyl chlorocarbonates were condensed with *p*-arsanilic acid, *m*-arsanilic acid, 3-amino-4-methyl-phenylarsonic acid, 3,4-diamino-phenylarsonic acid and 3-amino-4-hydroxy-phenylarsonic acid. The activity of the alkyl chlorocarbonates decreased slightly as their carbon content increased.

Condensation was effected by dissolving the amino-arylarsonic acid in a slight excess of *N* sodium carbonate and adding slowly a slight excess of the chlorocarbonate. The products were, for the most part, colorless crystals. Their melting points decreased with an increase in the length of the carbon chain of the alkyl chlorocarbonates. The products formed by condensation with *iso*alkyl chlorocarbonates had slightly higher melting points than those formed with the straight chain alkyl chlorocarbonates. Practically all were soluble in cold alcohol, insoluble in chloroform, benzene and ether, with decreasing solubilities in cold water as the carbon content of the alkyl chlorocarbonate increased. In hot water all were soluble.

The condensation products were analyzed by Ewins' method[4] with the slight modification that the iodine used for titration was standardized against a blank to which a known amount of arsenious oxide had been added.

Experimental Part

Preparation of Amino-arylarsonic Acids. *p*-Arsanilic Acid.—The method of Cheetham and Schmidt[5] with slight modification was followed. The time of heating was four hours instead of 12 hours and the contents of

[1] Constructed from a thesis submitted by Caryl Sly in partial fulfilment of the requirements for the degree of Master of Science at the University of Nebraska.

[2] Farb. Meister, Lucius and Bruning, Ger. pat. 256,343, **1911.**

[3] Adam, Ger. pat. 232,879, **1909.**

[4] Ewins, *J. Chem. Soc.*, **109,** 1356 (1916).

[5] Cheetham and Schmidt, THIS JOURNAL, **42,** 828 (1920).

the reaction flask were mechanically stirred throughout the procedure. A yield of 26% of the calculated amount was obtained.

m-**Arsanilic Acid.**—This was prepared in three steps by making phenylarsonic acid, nitrating this and reducing the 3-nitro-phenylarsonic acid.

Phenylarsonic acid was prepared by the method of Palmer and Adams;[6] yield, 45%.

In the preparation of 3-nitro-phenylarsonic acid, the method of Michaelis,[7] with a slight modification, was used. The modification consisted in neutralizing some of the acid of the nitrating mixture with sodium hydroxide solution. Fifty g. of phenylarsonic acid was slowly added to a mixture of 135 cc. of concd. sulfuric acid and 135 cc. of red, fuming nitric acid at 15°. One hundred and eighty g. of sodium hydroxide was dissolved in 250–300 cc. of water and 1 kg. of ice added. The nitrated mixture was then cautiously added to the caustic solution. On cooling the mixture and scratching the sides of the beaker, yellow crystals were deposited; yield, 75%.

Reduction of the 3-nitro-phenylarsonic acid to the corresponding amino-phenylarsonic acid (*m*-arsanilic acid) was effected by the method of Johnson and Adams;[8] yield, 48%.

3-Amino-4-methyl-phenylarsonic Acid.—The corresponding nitro compound was reduced by the method of Johnson and Adams;[8] yield, 37%.

3-Amino-4-hydroxy-phenylarsonic Acid.—Again the corresponding nitro compound was reduced. In this case the method of Christiansen[9] was used; yield, 66%.

Preparation of Alkyl Chlorocarbonates

Following the procedure of Rose[10] the alcohol used was placed in a slender glass cylinder and cooled to 5°. Phosgene, first dried by passing through concd. sulfuric acid, was then passed in a slow stream through the cold alcohol. When the reaction was complete, as indicated by the fact that the phosgene bubbled through the alcohol unchanged, the reaction mixture was transferred to a separatory funnel and washed several times in ice water. The alkyl chlorocarbonate separated as the lower layer. This was drawn off and subjected to fractional distillation. The time required for a complete reaction, using methyl and ethyl alcohol, was one hour. In the case of all the other alcohols used, approximately two hours was necessary. The phosgene was then bubbled into the alcohols at room temperature. The time required for the reaction was cut in half, but the yields also decreased 10 to 25%.

[6] Palmer and Adams, THIS JOURNAL, **44,** 1361 (1922).

[7] Michaelis, *Ann.*, **320,** 321 (1902).

[8] Johnson and Adams, THIS JOURNAL, **45,** 1307 (1923).

[9] Christiansen, *ibid.*, **43,** 2208 (1921).

[10] Rose, *Ann.*, **205,** 229 (1880).

TABLE I

BOILING POINTS AND YIELDS OF ALKYL CHLOROCARBONATES

Alkyl	Methyl	Ethyl	Propyl	*iso*Propyl	Butyl	*iso*Butyl
B. p., °C.	71.4	93	115	103	142	128.8
Yield, %	25	50	42	40	35	35

Preparation of Carbo-alkoxy-amino-arylarsonic Acids

One molecular equivalent of the mono-amino-arylarsonic acid was dissolved in a slight excess of *N* sodium carbonate solution; 1.5 molecular equivalents of either the methyl or ethyl chlorocarbonate were then added, at room temperature, drop by drop, while the liquid was constantly shaken. The reaction mixture was kept slightly alkaline during the addition. After

TABLE II

CARBO-ALKOXY-AMINO-ARYLARSONIC ACIDS

Name and formula -Phenylarsonic acid	Yield %	M. p. °C. (Uncorr.)	Analyses: Subs. G.	0.0518 *N* I_2 Cc.	% As Calcd.	% As Found
4-Carbomethoxy-amino- $CH_3OCONHC_6H_4AsO_3H_2$	91	>250	0.2001	28.06	27.27	27.18
3-Carbomethoxy-amino- $CH_3OCONHC_6H_4AsO_3H_2$	90	Decomp. 231	.2015	28.10	27.27	27.07
3-Carbomethoxy-amino-4-methyl- $CH_3OCONHC_6H_3(CH_3)AsO_3H_2$	87	191–193	.2022	27.15	25.25	26.04
3-Carbomethoxy-amino-4-carbo-methoxy-hydroxy- $(CH_3OCONH)(CH_3OCOO)C_6H_3AsO_3H_2$	87	172–174	.2033	20.96	21.49	21.46
3,4-Dicarbomethoxy-amino- $(CH_3OCONH)_2C_6H_3AsO_3H_2$	65	>250	.2003	22.39	21.55	21.70
4-Carbethoxy-amino- $C_2H_5OCONHC_6H_4AsO_3H_2$	90	>250	.2026	27.00	25.95	25.86
3-Carbethoxy-amino- $C_2H_5OCONHC_6H_4AsO_3H_2$	80–85	180	.2024	27.10	25.95	26.00
3-Carbethoxy-amino-4-methyl- $C_2H_5OCONHC_6H_3(CH_3)AsO_3H_2$	87	181	.2080	26.50	24.75	24.73
3-Carbethoxy-amino-4-carbethoxy-hydroxy- $(C_2H_5OCONH)(C_2H_5OCOO)C_6H_3AsO_3H_2$	51	165	.2020	20.80	19.89	19.99
3,4-Di-carbethoxy-amino- $(C_2H_5OCONH)_2C_6H_3AsO_3H_2$	78	187	.2054	21.00	19.94	19.84
4-Carbopropoxy-amino- $CH_3(CH_2)_2OCONHC_6H_4AsO_3H_2$	85–90	>250	.2026	25.90	24.76	24.78
3-Carbopropoxy-amino- $CH_3(CH_2)_2OCONHC_6H_4AsO_3H_2$	35	117	.2068	26.40	24.76	24.77
3-Carbopropoxy-amino-4-methyl- $CH_3(CH_2)_2OCONHC_6H_3(CH_3)AsO_3H_2$	90	150–151	.2027	24.80	23.66	23.74
3-Carbopropoxy-amino-4-carbo-propoxy-hydroxy- $CH_3(CH_2)_2OCONH(CH_3-(CH_2)_2OCOO)C_6H_3AsO_3H_2$	55–60	133–134	.2044	19.38	18.52	18.41

TABLE II (*Concluded*)

Name and formula -Phenylarsonic acid	Yield %	M. p. °C. (Uncorr.)	Analyses: Subs. G.	0.0518 *N* I_2 Cc.	% As Calcd.	% As Found
3,4-Dicarbopropoxy-amino- $(CH_3(CH_2)_2OCONH)_2C_6H_3AsO_3H_2$	52	165–166	.2026	19.40	18.56	18.58
4-Carbo-*iso*propoxy-amino- $(CH_3)_2CHOCONHC_6H_4AsO_3H_2$	85	>250	.2046	26.20	24.76	24.84
3-Carbo-*iso*propoxy-amino- $(CH_3)_2CHOCONHC_6H_4AsO_3H_2$	45	144–145	.2030	25.83	24.76	24.68
3-Carbo-*iso*propoxy-amino-4-methyl- $(CH_3)_2CHOCONHC_6H_3(CH_3)AsO_3H_2$	83	179	.2059	24.95	23.66	23.51
3-Carbo-*iso*propoxy-amino-4-carbo-*iso*propoxy-hydroxy- $((CH_3)_2CHOCONH)((CH_3)_2CHOCOO)$- $C_6H_3AsO_3H_2$	70	154–155	.2065	19.65	18.52	18.47
3,4-Di-carbo-*iso*propoxy-amino- $((CH_3)_2CHOCONH)_2C_6H_3AsO_3H_2$	50	177	.2026	19.50	18.56	18.67
4-Carbobutoxy-amino- $CH_3(CH_2)_3OCONHC_6H_4AsO_3H_2$	85–90	>250	.2000	24.27	23.66	23.56
3-Carbobutoxy-amino- $CH_3(CH_2)_3OCONHC_6H_4AsO_3H_2$	40	83–84	.2002	24.38	23.66	22.63
3-Carbobutoxy-amino-4-methyl- $CH_3(CH_2)_3OCONHC_6H_3(CH_3)AsO_3H_2$	40–50	143–144	.2050	23.88	22.66	22.61
3-Carbobutoxy-amino-4-carbobutoxy-hydroxy- $(CH_3(CH_2)_3OCONH)(CH_3(CH_2)_3$ $OCOO)C_6H_3AsO_3H_2$	40	143	.2038	18.11	17.32	17.25
3,4-Dicarbobutoxy-amino- $(CH_3(CH_2)_3OCONH)_2C_6H_3AsO_3H_2$	80–85	197–198	.2017	18.00	17.36	17.33
4-Carbo-*iso*butoxy-amino- $(CH_3)_2CHCH_2OCONHC_6H_4AsO_3H_2$	90	>250	.2030	24.76	23.66	23.68
3-Carbo-*iso*butoxy-amino- $(CH_3)_2CHCH_2OCONHC_6H_4AsO_3H_2$	50	142–143	.2020	24.64	23.66	23.70
3-Carbo-*iso*butoxy-amino-4-methyl- $(CH_3)_2CHCH_2OCONHC_6H_3(CH_3)$ AsO_3H_2	70	162	.2017	23.88	22.66	22.80
3-Carbo-*iso*butoxy-amino-4-carbo-*iso*butoxy-hydroxy- $((CH_3)_2CHCH_2OCONH)((CH_3)_2$ $CHCH_2OCOO)C_6H_3AsO_3H_2$	55	142–143	.2011	19.84	17.32	17.30
3,4-Dicarbo-*iso*butoxy-amino- $((CH_3)_2CHCH_2OCONH)_2C_6H_3AsO_3H_2$	50–60	172	.2012	17.95	17.36	17.33

one-half hour, the solution was made acid to congo red with concd. hydrochloric acid, the precipitate filtered, dried and analyzed.

In the case of the 3,4-diamino-phenylarsonic acid, 2.5 molecular equivalents of either the methyl or the ethyl chlorocarbonate were added. The rest of the procedure remained the same as for the mono-amino compounds.

When working with propyl, *iso*propyl, butyl and *iso*butyl chlorocar-

bonates, for one molecular equivalent of the arsonic acid but slightly more than one or two molecular equivalents of the chlorocarbonates were added. When too great an excess was added, an oil, instead of crystals, was obtained upon acidification. Likewise when the reaction mixture was acidified too rapidly or too strongly, an oil formed. It was found best to make the solution barely acid with hydrochloric acid and then allow it to stand for several hours. At the end of this period more hydrochloric acid was cautiously added, to insure slow precipitation. Once an oil had formed it was almost impossible to obtain crystals. Upon standing several days the oil changed to a cake, which consistently showed by analysis too great arsenic content. The *m*-arsanilic acid, 3,4-diamino-phenylarsonic acid and the 3-amino-4-hydroxy-phenylarsonic acid showed a greater tendency to form oils than the others. In any case, when the precipitation was complete a moderate excess of hydrochloric acid was added to dissolve any unchanged amino-arylarsonic acid, since all of the products were but slightly soluble under these conditions.

The products were obtained in 80–90% yields for the methyl and ethyl chlorocarbonates. The other alkyl chlorocarbonates gave similar results with *p*-arsanilic acid and 3-amino-4-methyl-phenylarsonic acid, but with the other phenylarsonic acids the yields dropped to 50–60% of the calculated amounts.

Summary

1. The action of various alkyl chlorocarbonates on amino-arylarsonic acids has been studied.

2. Methyl, ethyl, propyl, *iso*propyl, butyl and *iso*butyl chlorocarbonates were condensed with *p*-arsanilic acid, *m*-arsanilic acid, 3-amino-4-methyl-phenylarsonic acid, 3,4-diamino-phenylarsonic acid, and 3-amino-4-hydroxy-phenylarsonic acid; and the products have been isolated and identified.

3. The products were, for the most part, colorless crystals. Their melting points decreased as the length of the carbon chain of the alkyl chlorocarbonates increased, the *iso* compounds having slightly higher melting points than the corresponding straight-chain compounds.

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