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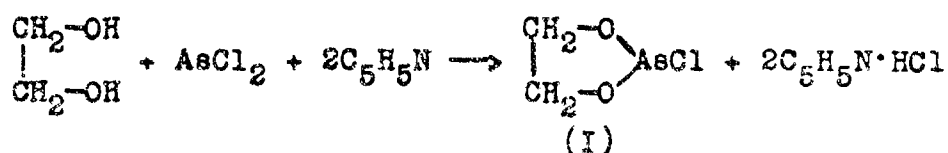
Translated from Zh. Obshchei Khim. SSSR, 23 (1953), 8, 1323-1330.

ON THE ESTERS OF ETHYLENE GLYCOL-ARSENOUS ACID

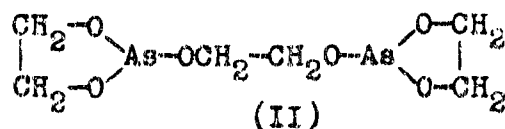
Gil'm Kamai and Z. L. Khisamova

Detailed studies of the cyclic derivatives of arsenous acid were begun at our laboratory in 1950 [1-2]. The cyclic esters of ethylene-glycol-arsenous acid have not previously been studied by anyone. In the present communication we report our results from the study of the chloroanhydride and the mixed esters of ethylene-glycol-arsenous acid, containing a five-membered ring.

By reacting an equimolecular quantity of arsenic trichloride with ethylene glycol in an absolute ether medium in the presence of anhydrous pyridine, we synthesized the cyclic chloroanhydride of ethylene-glycol arsenous acid (I)* as the principal reaction product, according to the equation:



It was also brought out that in this reaction there is formed, beside the chloroanhydride, the full ethylene-glycol ester of arsenous acid (II)**:



An experiment on the reaction between the chloroanhydride of ethylene-glycol-arsenous acid and ethylene glycol in the presence of pyridine in an absolute ether medium led to a similar final result. Thus it was demonstrated that the

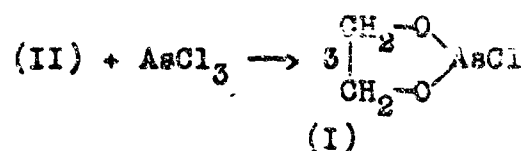
* Can be named 2-chloro (1:3 dioxo-2-arsenacyclopentane).
(G. A. Grant)

** Can be named 1,2-bis-2- (1:3 dioxo-2-arsenacyclopentany) ethylene glycolate. (G. A. Grant)

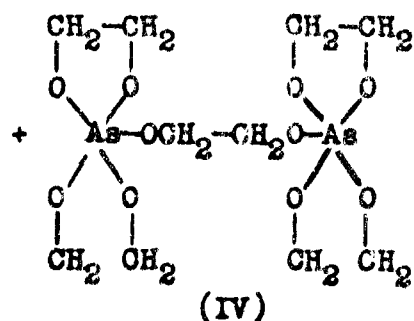
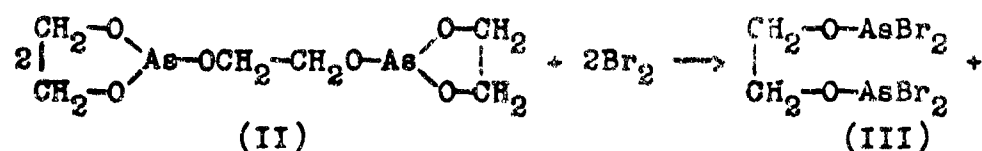
ester (II) is formed through a secondary reaction.

The full * ethylene glycol ester of arsenous acid (II) is also produced in very good yields (in the neighborhood of 89-92%) by the direct reaction of arsenous oxide with ethylene glycol at a temperature of 140-150°C. This reaction is reversible: with an excess of water the ester is completely hydrolysed, forming arsenous oxide and ethylene glycol.

When an equimolecular quantity of arsenic trichloride reacts with (II), there is an almost quantitative formation of the chloroanhydride of ethylene-glycol-arsenous acid (I), according to the equation



The ethylene glycol ester of arsenous acid (II) does not react when heated with methyl iodide; it does not combine with sulfur and copper monobromide. Its bromination reaction takes a quite unusual course. Instead of the expected combination with two molecules of bromine, what happens in this reaction is that only half of the calculated quantity combines; that is, one molecule of bromine reacts with one molecule of II. There takes place an interesting conversion with a complex regrouping of radicals. We have previously given the following scheme for the reaction course: [1]



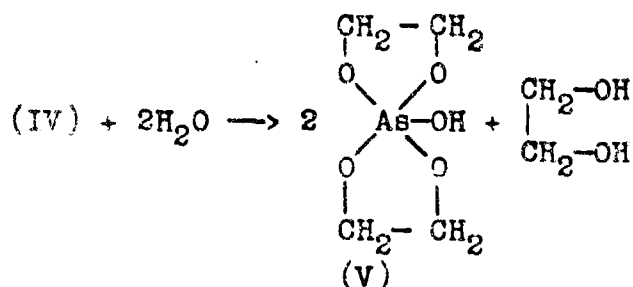
* Full ester = di-ester.

The formation of the bromoanhydride (III), * under the given conditions, has been experimentally demonstrated. This bromoanhydride is a liquid of greenish color with a mustard-like odor and a boiling point of 86°C at 11 mm of mercury.

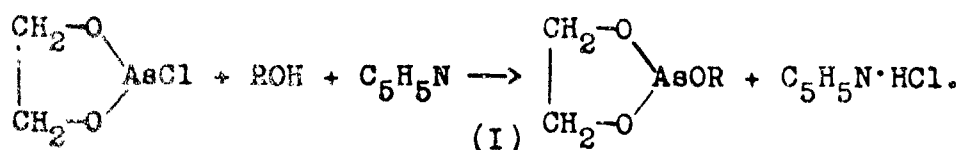
The second compound of pentavalent arsenic isolated by us ... shiny crystals of melting point 127°C ... dissolves well in many organic solvents and in water; it does not hydrolyse when cold. The aqueous solution has an acid reaction and may be titrated with a 0.1 n solution of NaOH.

We now doubt the hypothetical structure given by us previously {1} for substance (IV). Further research has indicated that this substance is the diethylene-glycol-arsenous acid (V) described by Englund {3}. However, in contrast to Englund's preparation, ours has a melting point of 127°, not 120°; the molecular weight as found by Rast's method is not doubled; in a bromoform solution it actually is close to the doubled value.

The formation of diethylene-glycol-arsenous acid very likely takes place by way of hydrolysis of the hypothetical compound (IV) shown above:



By reacting the chloroanhydride of ethylene-glycol-arsenous acid (I) with the corresponding absolute alcohols in the presence of pyridine in an ethyl ether medium, we synthesized the several mixed esters of ethylene-glycol-arsenous acid according to the following scheme:



In this way we separated the methyl, ethyl, n-propyl, n-butyl, n-hexyl, n-heptyl, n-octyl, nonyl, phenyl and cyclohexyl esters of ethylene-glycol-arsenous acid.

Under the action of water, the said esters decompose rather easily, with liberation of heat and formation of the

* Can be named (1:1', 6:6' tetrabromo-1:6 arsena)-2:5 dioxahexane. (G. A. Grant) - 3 -

37.5 g of ethylene glycol, 87.3 g of anhydrous pyridine and 400 ml of dry ether.

While stirring and keeping the flask cool externally with ice-water, we added to the mixture, drop by drop, 100 g of arsenic trichloride. After the whole of the arsenic trichloride had been added, the refrigeration was stopped and the reaction-mixture heated over a water bath for a period of one hour; then it was allowed to stand overnight. Next day the ether solution was separated from the precipitate by decantation, and the precipitate was washed three times with absolute ether. After driving off the solvent, we subjected the filtrate to vacuum distillation, with the result that the following fractions were separated at 11 mm:

- 1) boiling point 70-76°C, quantity 61.3 g.
- 2) boiling point 76-160°C, quantity 6.5 g.
- 3) boiling point 160-195°C, quantity 10.3 g.

Repeating the distillation, we separated from the first fraction a substance of boiling point 71-72°C at 11 mm, and melting point 44-45°C.

Found %: As 44.10, Cl 20.95. $C_2H_4O_2AsCl$.

Calculated %: As 44.05, Cl 20.82.

The cyclic chloroanhydride of ethylene-glycol-arsenous acid, here separated, is in the form of white shiny crystals of needle type, easily soluble in ether, benzene, toluene, dichloroethane and dioxane. This chloroanhydride is instantaneously hydrolysed by water, with liberation of heat and formation of As_2O_3 (found %: As 75.21; calculated %: As 75.73).

From the third high-boiling-point fraction, we obtained a substance with boiling point 166-167°C at 4 mm (I'), a colorless viscous liquid:

d_4^{20} 1.8951; n_D^{20} 1.5433; MR_D 56.18; calculated 56.61.

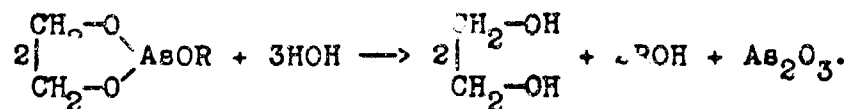
Found %: As 45.28. $C_6H_{12}O_6As_2$

Calculated %: As 45.40.

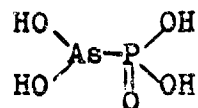
Production of the Full Ethylene Glycol Ester of Arsenous Acid (II).

1) From the chloroanhydride of ethylene-glycol-arsenous acid. To a solution of 4.8 g of ethylene glycol and 10.4 g of

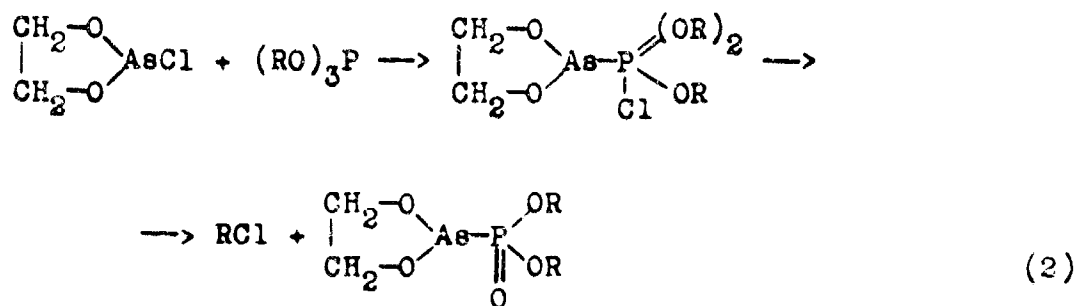
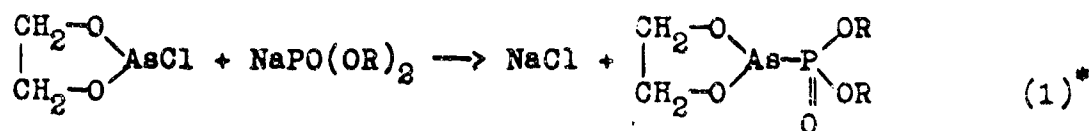
corresponding alcohol, ethylene glycol and arsenous oxide (As_2O_3).



With the intention of producing a derivative of the hypothetically postulable acid:



we made attempts to bring about reactions (1) and (2), but these attempts turned out unsuccessful.



EXPERIMENTAL PART

Production of the Chloroanhydride of Ethylene-glycol-arsenous Acid (I).

In a round-bottomed flask provided with a reflux condenser, a mechanical stirrer and a dropping funnel, we placed

* Can be named 1:2-dioxa-2-arsenapentyl phosphonate. (G. A. Grant.)

pyridine in 200 ml of dry ether we added, with mechanical stirring and refrigeration, the chloroanhydride of ethylene-glycol-arsenous acid. After removal of the pyridine chloride the filtrate was subjected to distillation. The principal fraction had a boiling point of 166-167°C at 4 mm.

2) From arsenous oxide and ethylene glycol. In an Arbuzov distillation-flask, we took 60 g of arsenous oxide and 86.4 g of ethylene glycol. The flask was heated on an oil bath at 140-150°C for 30 minutes, with a water-jet pump to get rid of the water liberated in the reaction. After removal of the water under vacuum and by a double distillation, we had a fraction of boiling point 160-161°C at 2 mm; quantity 80.2 g (92.4%).

Found %: As 45.47, 45.66. $C_6H_{12}O_6As_2$.

Calculated %: As 45.40.

Reaction of arsenic trichloride with the full ethylene glycol ester of arsenous acid. In a round-bottomed flask with a reflux condenser and a dropping funnel, we placed 15 g of the full ethylene glycol ester of arsenous acid. Then we dripped in 6 g of arsenic trichloride. With this completed, we heated the flask on an oil bath for 30 minutes. After cooling, the reaction mixture was distilled in vacuo. The principal fraction had a boiling point of 66-67°C at 9 mm, and a melting point 44-45°C.

Found %: As 43.98; Cl 20.67. $C_2H_4O_2AsCl$.

Calculated %: As 44.05; Cl 20.82.

Saponification of ester (II). In a round-bottomed flask under a reflux condenser, we boiled 2.5 g of the ethylene-glycol ester of arsenous acid in 50 ml of water for 1 hour. The white precipitate which formed was found to be arsenous oxide.

Found %: As 75.62. As_2O_3 .

Calculated %: As 75.73.

Action of bromine on ester (II). To 51 g of the ester, dissolved in carbon tetrachloride, we added 28 g of bromine through a dropping funnel. The reaction flask was externally cooled with snow. Each drop of bromine produced an energetic reaction with evolution of heat. The bromination was continued until a faint yellow coloration appeared. Upon standing, needle-shaped crystals were precipitated from the solution. Next day the crystals were filtered out, pressed dry, and washed with carbon tetrachloride. The filtrate was distilled in vacuo. A principal fraction was obtained which had a boiling point of 86°C at 11 mm; quantity 32.2 g. The substance thus separated was a liquid faintly tinged with green, having a mustard odor and a lacrymatory effect.

d_4^{20} 1.6079; d_4^{20} 2.5668; n_D^{20} 1.6568.

Found %: As 28.38, 28.41; Br 60.39. $C_2H_4O_2As_2Br_4$.

Calculated %: As 28.30; Br 60.36.

Next, the needle-shaped crystals of (V) produced by us were repeatedly recrystallized from hot toluene. Shining white needles of melting point $127^{\circ}C$, soluble in toluene, benzene, dioxane, acetone, chloroform, ethyl alcohol and water; poor solubility in ether. The aqueous solution has an acid reaction (congo red turns strongly blue).

Found %: As 35.62, 35.63. $C_4H_9O_5As$.

Calculated %: As 35.42.

0.2255 g of substance: 10.75 ml of 0.1 n. NaOH.
Found: equimolecular weight 210.82. Found: M 210.41, 211.25 (by Rast's method); 378.4, 375.6 (cryoscopically, in bromoform). $C_4H_9O_5As$. Calculated: M 212.03.

Reacting 1.5 g of brucine in methyl alcohol solution with 0.807 g of diethylene-glycol-arsenous acid (V), we obtained a salt with melting point about $204^{\circ}C$, in agreement with England's findings [3].

Found %: As 11.82, 11.63. $C_{23}H_{26}O_4N_2(C_2H_4O_2)_2AsOH \cdot CH_3OH$.

Calculated %: As 11.75.

Production of the Methyl Ester of Ethylene-glycol-arsenous Acid.

To a solution, chilled to $0^{\circ}C$, of 3.6 g of methyl alcohol, 9.2 g of anhydrous pyridine and 250 ml of absolute ethyl ether we added, by means of a dropping funnel, 20 g of the chloroanhydride of ethylene-glycol-arsenous acid (I) dissolved in 50 ml of ethyl ether. After the whole of the chloroanhydride had been poured in, the mixture was heated over a water bath for one hour. Next day we filtered off the precipitate of pyridine chloride and washed three times with dry ether. After the solvent was driven off, the remaining liquid was distilled in vacuo. We obtained a fraction of boiling point $80-81^{\circ}C$ at 11 mm, quantity 8.6 g. The methyl ester of ethylene-glycol-arsenous acid is an easily mobile liquid. Water easily hydrolyses it, with formation of arsenous oxide.

Production of other esters of ethylene-glycol-arsenous acid. These were produced by the method described, starting from the corresponding alcohols, plus 9.2-9.3 g of dry pyridine and

20 g of the chloroanhydride of ethylene-glycol-arsenous acid (I) in 200-300 ml of ethyl ether.

The esters thus obtained are colorless liquids (from the hexyl ester onward, they are of a viscous consistency), without odor (except for the nonyl ester, which has a pleasant smell).

Data on the esters obtained are given in the Table.

Experiment on the Reaction between the Methyl Ester of Ethylene-glycol-arsenous Acid and Methyl Iodide.

5 g of the methyl ester of ethylene-glycol-arsenous acid and 8 g of methyl iodide were heated over a water bath in a flask with a reflux condenser for a period of six hours. Distillation then separated and recovered for us (according to boiling point data and index of refraction) the starting substances. We were unable to isolate any other individual substances.

Action of Bromine on the Ethyl Ester of Ethylene-glycol-arsenous acid.

In a round-bottomed flask of 50 ml capacity, we took 5 g of the ethyl ester of ethylene-glycol-arsenous acid and 20 ml of carbon tetrachloride, and then added 4.4 g of bromine with a dropping funnel. Intense heating was observed. The carbon tetrachloride was distilled off at atmospheric pressure. The remaining liquid was then distilled under vacuum. The principal fraction boiled at 72-73°C at 14 mm.

The product of this reaction is a heavy liquid, slightly tinged with yellow.

d_4^{20} 2.2152; d_4^{20} 2.1767; n_D^{20} 1.5880.

Found %: As 22.09; Br 46.69; $C_4H_9O_3AsBr_2$.

Calculated: As 22.04; Br 47.03.

Reaction Between the Chloroanhydride of Ethylene-glycol-Arsenous Acid and the Butyl Ester of Phosphorous Acid.

In a round-bottomed flask with a reflux condenser and a dropping funnel, we took 15 g of tributyl phosphite, dissolved in 200 ml of ethyl ether. Refrigerating to -13°C (with ice and salt) we added, drop by drop, 10.3 g of the chloroanhydride of ethylene-glycol-arsenous acid, diluted to one-half with ether. The reaction proceeded very energetically. The reaction-mixture at first became markedly yellow, and then began to turn brown. Upon standing, a precipitate of red phosphorus was formed. The precipitate was filtered out, and the filtrate subjected to distillation. After removal of the ether at atmospheric pressure, we obtained a fraction boiling at $117-120^{\circ}\text{C}$ (d_4^{20} 0.8099, n_D^{20} 1.4015), which is right for butyl alcohol. Upon further distillation in vacuo we obtained another fraction, of boiling point 140°C at 5 mm: d_4^{20} 1.1185, n_D^{20} 1.4333. The substance contains arsenic and phosphorus, but speedily decomposes with formation of a black precipitate.

Reaction Between the Chloroanhydride of Ethylene-glycol-arsenous Acid and the Na-Derivative of Diethyl-phosphorous Acid.

In the reaction flask we took 200 ml of dry ethyl ether and 4.1 g of metallic sodium. To this we added, by means of a dropping funnel, 24.5 g of diethyl-phosphorous acid.

To the Na-derivative of diethyl-phosphorous acid we added, drop by drop and with external refrigeration, 30 g of the chloroanhydride of ethylene-glycol-arsenous acid, diluted to one-half with ether. As the dropping continued, the flask contents at first turned yellow, and finally took on a brick-red color. The precipitate ... sodium chloride ... was filtered out; its net weight after drying was 9.9 g (10.3 g are theoretically required). Upon distillation in vacuo, a strong decomposition takes place. We did not succeed in isolating any individual substances.

CONCLUSIONS

1) It was established that by reacting ethylene glycol with arsenic trichloride in an absolute ether medium in the presence of pyridine, we may obtain the chloroanhydride of ethylene-glycol-arsenous-acid and the full ethylene glycol ester of arsenous acid.

2) A simple and convenient method was worked out for producing the ethylene-glycol ester of arsenous acid by way of the reaction of ethylene glycol with arsenous oxide.

3) The bromination of the ethylene-glycol ester of arsenous acid was studied. By this reaction, the bromoanhydride, with structure $[-CH_2OAsBr_2]_2$, and diethylene-glycol-arsenous acid were isolated.

4) The cyclic mixed esters of structure $\begin{array}{c} CH_2-O \\ | \\ CH_2-O-AsOR \end{array}$ were synthesized, and their properties and reactions have been described.

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- [2] G. KAMAI and N. A. CHADAYEVA, Dok. Akad. Nauk SSSR, 81, 857 (1951).
- [3] Englund, J. pr. Ch., (2) 120, 179 (1928).

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Esters of ethylene-glycol-arsenous acid

Ester	Formula of ester	Alcohol used in reaction (in g)	Yield of ester (in g)	Boiling point (in °C)	Pressure (in mm)	d_4^{20}	d_4^{20}	n_D^{20}	MR _D found	MR _D calculated	Content of As (in %) found	Content of As (in %) calculated
Methyl ester	$C_3H_7O_3As$	3.8	8.6	50-51	11	1.6453	1.6310	1.4935	29.25	29.41	44.72	45.09
Ethyl ester *	$C_4H_9O_3As$	9.5	19	61-62	11	1.5031	1.4784	1.4798	34.50	34.03	41.54	41.61
n-propyl ester	$C_5H_{11}O_3As$	7	-	74-75	12	1.4188	1.3923	1.4752	39.33	38.64	38.85	38.50
n-butyl ester	$C_6H_{13}O_3As$	8.7	11	93	15	1.4024	1.3764	1.4785	42.82	43.23	36.31	36.00
n-hexyl ester	$C_8H_{17}O_3As$	12	17	120-121	10	1.3033	1.2813	1.4742	51.85	52.49	31.63	31.72
n-heptyl ester	$C_9H_{19}O_3As$	13.7	21.8	130-131	11	1.2671	1.2465	1.4736	56.37	57.14	29.80	29.94
n-octyl ester **	$C_{10}H_{21}O_3As$	15.2	14	110	2	1.2449	1.2250	1.4737	61.44	61.73	28.41	28.34
n-nonyl ester	$C_{11}H_{23}O_3As$	17	15.6	117-118	2	1.2240	1.2041	1.4748	-	-	27.33	27.03
cyclohexyl ester***	$C_6H_{15}O_3As$	5.8	-	118	11	1.4270	1.4044	1.5070	-	-	31.84	32.00
phenyl ester	$C_6H_5O_3As$	11	6.3	143-144	12	1.5687	1.5440	1.5716	-	-	32.70	32.85

* 16.4 g of pyridine and 35 g of the chloroanhydride (I) reacted.

** 6.7 g of pyridine reacted.

*** 6.9 g of pyridine and 15 g of the chloroanhydride (I) reacted.