Alditol Arsenite Esters[1]

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As one phase of a program initiated to explore the preparation of various partially nitrated alditols, the use of the cyclic arsenite esters of the alditols as possible intermediates appeared attractive. Although efforts to this end are not complete, a report on the preparation of several crystalline carbohydrate arsenites seems warranted at this time.

The cyclic arsenite esters of glycerol,[2–4] erythritol,[5] and pentaerythritol[5,6] have been described; only the last was isolated in crystalline form. Although the method of choice for the preparation of these compounds appears to be the reaction between arsenic trioxide and the polyhydroxy material under conditions which permit the removal of the water formed, other methods[4] have been described. More recently the use of arsenic trichloride has been suggested.[7]

Following Pascal and Dupire,[4] glycerol arsenite was prepared and on sublimation was found to afford a crystalline hygroscopic product (m.p. 66–70°) which appears to be the monomeric arsenite in contrast to the polymeric glassy solid described by the earlier workers.[4]

The crystalline diarsenite esters of D-mannitol (m.p. 226–227°) and galactitol (m.p. 266–267°) are reported for the first time. These monomeric derivatives were prepared by reaction of the alditol with arsenic trioxide in boiling dioxane with the water produced being removed by fractional distillation of the dioxane-water azeotrope. The reaction was found to be strongly catalyzed by mineral acid. Although these crystalline diarsenites are stable for short periods when exposed to moist air, the compounds must be considered quite sensitive toward hydrolysis by water. The positions of attachment of the cyclic arsenic rings to the hexitol chains have not been elucidated.

Attempts were made to prepare crystalline arsenites of 1,2,4-trihydroxybutane, erythritol, DL-threitol, xylitol, ribitol, and D-glucitol. In each case, the evolution of water and the solution of the arsenic trioxide in the dioxane indicated that reaction occurred but only sirups or glassy solids were obtained when the products were isolated.

EXPERIMENTAL

Glycerol arsenite. Arsenite trioxide (19.8 g.) and glycerol (glycerol, 18.4 g.) were placed in a flask and covered with 200 ml. of toluene. The mixture was refluxed and the water collected in a Dean and Stark receiver.[8] After 8 hr. of refluxing, distillation of the toluene gave a colorless, very viscous sirup which partially sublimed on heating to 120–140° at 0.3 mm. The sublimate was resublimed under similar conditions resulting in large, very hygroscopic crystals firmly affixed to the condensing surface; m.p. 66–70°.

Anal. Calcd. for $C_3H_5AsO_3$: As, 45.7. Found: As, 45.7.

D-*Mannitol diarsenite.* A mixture of D-mannitol (4.55 g., 25 mmoles), arsenic trioxide (4.95 g., 25 mmoles), dioxane (150 ml., peroxide-free), and concd. hydrochloric acid (0.25 ml.) were heated in a flask fitted with a fractionating column. When the temperature at the column head fell below the boiling point of dioxane, distillate was collected. Complete solution resulted after about 15 min. and the evolution of water ceased after 1 hr. The resulting solution was concentrated to dryness and the solid residue was dissolved in 200 ml. of chloroform. Concentration to a volume of 50 ml. initiated crystallization which was completed at 5°. Decantation of the liquid and drying gave a crude product; yield 6.9 g., m.p. 200–220°. The material that was insoluble in 75 ml. of refluxing chloroform was discarded. Cooling afforded crystalline hygroscopic material; yield 4.1 g. (50%) m.p. 224–225°. The analytical sample was obtained by two additional crystallizations from chloroform; m.p. 226–227°, $[\alpha]^{26}_{D}$ −72° (*c* 0.7, dioxane), infrared absorption[9]: 12.28 (95%), 9.52, 13.52B, 9.45, 9.92, 9.25, 9.96, 9.74, 15.65B, 10.65, 10.71, 12.07, 9.09 (50%), 11.86, 11.49, 10.52, 11.43, 7.45, 15.08B, 3.45, 8.90, 11.22, 3.38, 11.29, 14.15B, 10.34, 3.41, 10.24, 7.58, 7.76, 7.88, 8.31, 7.93, 7.66, 7.34, 8.22, 6.83 (5%). The substance sublimed readily at 170° and 0.1 mm.

Anal. Calcd. for $C_6H_8As_2O_6$: C, 22.11; H, 2.47; As, 46.0; mol. wt., 326. Found: C, 22.06; H, 2.41; As, 46.1; mol. wt., 350 (Rast).

Galactitol diarsenite. This preparation was carried out in the same manner as described above except that the D-mannitol was replaced by galactitol (dulcitol). The water removal was complete after 3 hr. (50 ml. of distillate). Cooling of the reaction mixture to room temperature completed precipitation of the slightly hygroscopic product, galactitol diarsenite; yield 7.1 g. (87%), m.p. 266–267°; infrared absorption[9]: 9.72 (95%), 10.72, 10.21, 9.87, 13.32, 14.72, 11.46, 15.60B, 9.07, 3.38 (50%), 3.46, 6.82, 12.60, 8.01, 7.88, 8.30, 8.25, 7.33, 6.92 (5%). Although the substance sublimes readily at 170° and 0.1 mm., the analytical sample was obtained by recrystallization twice from dioxane (melting point unchanged).

Anal. Calcd. for $C_6H_8As_2O_6$: C, 22.11; H, 2.47; As, 46.0. Found: C, 21.75; H, 2.60; As, 45.9.

Arsenite esters of other polyhydroxy alcohols. Application of the methods used for making the hexitol arsenites to 1,2,4-trihydroxybutane, erythritol, DL-threitol, xylitol, ribitol, and D-glucitol resulted in the evolution of water and dissolution of the arsenic trioxide. However, all efforts to isolate crystalline products failed. No sublimation products could be obtained from the ribitol and D-glucitol reaction products; a solid obtained from the xylitol reaction decomposed in

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(9) Wave lengths in microns corrected to polystyrene standard; potassium bromide pellets; Baird Model B instrument. The percentages record the absorbance and the sequence is from the strongest to the weakest; B signifies a broad peak.

moist air. Efforts to prepare monoacyl derivatives of the glassy erythritol arsenite followed by hydrolysis of the arsenic function afforded mixtures which were not separated.

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A New Synthesis of the Benzothiazole and Benzoxazole Rings

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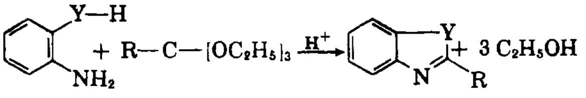
In an attempt to prepare a series of 2-(*N*-alkylamino)benzenethiols, ethyl orthoformate was treated with 2-aminobenzenethiol in a manner similar to that reported in *Organic Syntheses*[1] for the preparation of secondary amines. Although our attempt did not produce the desired product, we did discover a convenient method of preparing 2-substituted benzothiazole and benzoxazole rings (Table I) in 75–85% yields.

Table I lists the compounds prepared by treating 2-aminobenzenethiol or 2-aminophenol with the corresponding ortho-esters.

TABLE I

2-SUBSTITUTED BENZOTHIAZOLE AND BENZOXAZOLE COMPOUNDS



	Y	R	B.P. (mm.)[a] of Heterocycle	
1	S	H	183	(754)
2	S	CH_3	151	(15)
3	S	C_2H_5	132	(18)
4	O	H	182	(753)
5	O	CH_3	91	(18)
6	O	C_2H_5	129	(23)

[a] The physical properties of these compounds were in close agreement with those reported in the literature (Beilstein).

All of the above compounds were prepared according to the following procedure used for the synthesis of benzothiazole.

EXPERIMENTAL

In a 100 ml. round bottomed flask were placed 22 g. (0.17 mole) of 2-aminobenzenethiol, 37 g. (0.25 mole) of ethyl orthoformate, and 0.7 g. (0.007 mole) of concd. sulfuric acid. To the flask was attached a Vigreux column surmounted with a distillation head. The flask was heated in an oil bath and after the temperature reached 115–130° the ethanol began to distill. Heating was continued until the temperature reached 170–180°, at which time all of the ethanol and some yellow material had been removed (*ca.* 1 hr.). About 31 ml. of ethanol was collected. The reaction mixture was kept in the oil bath at 175–185° for an additional 45 min., after which time it was cooled and the product distilled under vacuum.

Anal. Calcd. for C_7H_5NS: C, 62.19; H, 3.73. Found: C, 62.45; H, 3.41.

The infrared spectrum of benzothiazole was identical with that obtained from a commercial product.

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Reaction of Tertiary Mercaptans with Sulfur

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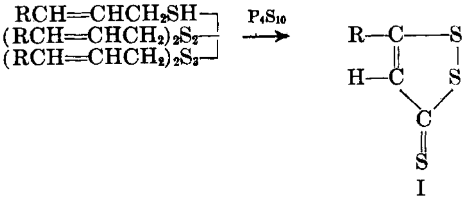
The interesting pseudoaromatic 1,2-dithiole-3-thiones have been prepared by the reaction of sulfur and/or phosphorus pentasulfide with aldehydes,[1] methyl substituted olefins or olefins easily converted to methyl substituted derivatives,[2,3] diolefins,[3] and unsaturated carbonyl compounds.[4] There are also scattered references to the synthesis of these systems from sulfur compounds. Allylic thiols, disulfides, and trisulfides[4] are reported to yield 5-alkyl-1,2-dithiole-3-thiones, I.



I

Wessely and Siegel[5] have reported low yields of thiones by reaction of sulfur with saturated aliphatic sulfides, disulfides and polysulfides. These workers have suggested a cleavage of the sulfide linkage as an initial intermediate on the route to the thione as well as to higher molecular weight products.

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