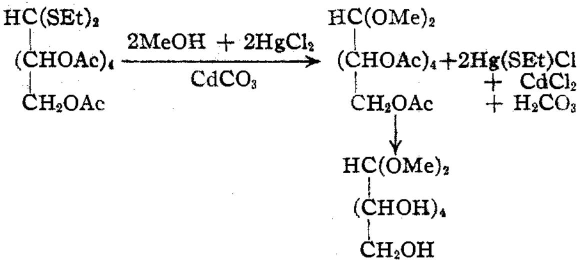
[Contribution from the Chemical Laboratory of The Ohio State University]

Acetals of Galactose and of Dibenzylideneglucose

By M. L. Wolfrom, Leo J. Tanghe, R. W. George and S. W. Waisbrot

The synthesis of (2,3,4,5)-dibenzylideneglucose diethyl mercaptal has been reported from this Laboratory.[1] Since Pacsu[2] had obtained oxygen glycosides on demercaptalation of non-substituted sugar mercaptals in alcoholic solution, it was anticipated that demercaptalation of this dibenzylideneglucose, with the sixth position open, would produce a glucoheptanoside. The alpha and beta forms of methyl galactoheptanoside have been reported by Micheel and co-workers.[3] Demercaptalation in the presence of cadmium carbonate[4] was required in order to protect the sensitive benzylidene groups from the hydrogen chloride produced in the demercaptalation reaction. Under these conditions, the expected dibenzylidene glucoheptanoside was not obtained, but, instead, the dibenzylideneglucose acetal was formed. This result suggested that application of the same reaction conditions to the fully acetylated sugar mercaptals should yield the corresponding acetals and this objective was realized in the galactose structure.

Montgomery, Hann and Hudson[5] have reported the synthesis of the dimethyl acetal of *d*-arabinose from the alpha and beta forms of methyl arabinopyranoside triacetate, through the application of a series of novel reactions discovered by them for the arabinose structure. The results herein reported would seem to indicate that the demercaptalation reaction should be of general application and its extension to other sugar structures is in progress.



$$\begin{array}{l} HC(SEt)_2 \\ \vert \\ (CHOAc)_4 \\ \vert \\ CH_2OAc \end{array} \xrightarrow[CdCO_3]{2MeOH + 2HgCl_2} \begin{array}{l} HC(OMe)_2 \\ \vert \\ (CHOAc)_4 \\ \vert \\ CH_2OAc \end{array} \begin{array}{r} +2Hg(SEt)Cl \\ + CdCl_2 \\ + H_2CO_3 \end{array} \longrightarrow \begin{array}{l} HC(OMe)_2 \\ \vert \\ (CHOH)_4 \\ \vert \\ CH_2OH \end{array}$$

Experimental[6]

Dibenzylidene-*d*-glucose Diethyl Acetal 6-Benzoate.—Dibenzylideneglucose diethyl mercaptal 6-benzoate[1] (2.8 g., 1 mol) and finely powdered cadmium carbonate (3 g.) were added to 50 cc. of absolute ethanol and the mixture heated to 70–80° while stirring with a mercury-sealed stirrer. Mercuric chloride (8.2 g., 6 mols), dissolved in 15 cc. of warm, absolute ethanol, was added rapidly in one portion. The mixture was stirred for one hour at 70–80°, during which time an additional 1 g. of cadmium carbonate was added in 0.3-g. portions. The reaction mixture was filtered while still hot and the residue was washed with a small amount of hot ethanol. The filtrate was transferred to a separatory funnel containing 200 cc. each of chloroform and water, the chloroform layer was washed repeatedly (six times) with 50 cc. of water until chloride-free, and was then dried overnight with anhydrous calcium sulfate (Drierite) and cadmium carbonate. The chloroform was removed at room temperature under diminished pressure, leaving a pasty, crystalline mass. To this was added gradually 30 cc. of a mixture of ethyl ether (1 part) and low-boiling ligroin (5 parts). After cooling at 0°, the product was removed by filtration and washed with a mixture of ether and ligroin. The product was free from sulfur at this point.

Pure material was obtained on recrystallization from 20 to 25 parts of 95% ethanol; yield 1.1 g.; m. p. 141–143°; $[\alpha]^{26}$ + 14° (*c*, 4; $CHCl_3$).[7] The substance was practically insoluble in water; was slightly soluble in warm ligroin; moderately so in hot ethanol, and was soluble in other common organic solvents.

Anal. Calcd. for $C_6H_7O_5(OC_2H_5)_2(C_6H_5CO)(C_6H_5CH)_2$: OC_2H_5, 16.86; C_6H_5CO, 19.7; C_6H_5CH, 33.7. Found: OC_2H_5, 16.76; C_6H_5CO, 20.1; C_6H_5CH, 33.6; S, absent.

All benzoyl determinations were performed by refluxing the sample for three hours with 10 cc. (5-fold excess) of 0.5 *N* sodium ethylate and back-titrating with standard acid. The method of Alberda van Ekenstein and Blanksma[8] was employed for the benzylidene determinations.

(2,3,4,5)-Dibenzylideneglucose Diethyl Acetal.—(2,3,4,5)-Dibenzylideneglucose diethyl mercaptal[1] (4.6 g.) was treated with mercuric chloride and cadmium carbonate in ethanol solution, as described for the synthesis of dibenzylideneglucose diethyl acetal 6-benzoate. The crude product was recrystallized from 50% ethanol; yield 1.0 g. Pure material was obtained on recrystallization from isopropyl ether (70 parts) or from 50% ethanol (25 parts); m. p. 133–135°; $[\alpha]^{25}$ + 16° (*c*, 4; $CHCl_3$). The substance crystallized in long, fibrous needles, was practically insoluble in water, and was soluble in the common organic solvents, except ligroin.

---

[1] M. L. Wolfrom and Leo J. Tanghe, This Journal, **59**, 1597 (1937).

[2] E. Pacsu, *Ber.*, **58**, 511 (1925).

[3] F. Micheel and F. Suckfüll, *Ann.*, **502**, 85 (1933); *ibid.*, **507**, 138 (1933); *Ber.*, **66**, 1957 (1933); F. Micheel and W. Spruck, *ibid.*, **67**, 1665 (1934).

[4] M. L. Wolfrom, This Journal, **51**, 2188 (1929).

[5] Edna M. Montgomery, R. M. Hann and C. S. Hudson, *ibid.*, **59**, 1124 (1937).

[6] The experimental work on the dibenzylidene glucose derivatives was performed by Leo J. Tanghe.

[7] All rotations are recorded to the D-line of sodium light.

[8] W. Alberda van Ekenstein and J. J. Blanksma, *Rec. trav. chim.*, **25**, 153 (1906).

Anal. Calcd. for $C_6H_8O_5(OC_2H_5)_2(C_6H_5CH)_2$: OC_2H_5, 20.93; C_6H_5CH, 41.9. Found: OC_2H_5, 20.6; C_6H_5CH, 40.3; S, absent.

(2,3,4,5)-Dibenzylideneglucose diethyl acetal could also be prepared by debenzoylation of its 6-benzoate. The crystalline precipitate (0.33 g.) obtained on refluxing the latter (0.46 g.) with 0.5 *N* sodium ethylate solution for three hours was recrystallized from isopropyl ether and was identified by melting point, mixed melting point and rotation.

Rebenzoylation of (2,3,4,5)-dibenzylideneglucose diethyl acetal (0.10 g.) with pyridine (2 cc.) and benzoyl chloride (0.15 cc.) by heating at 40° for three hours, produced the corresponding 6-benzoate (0.08 g.), identified, after ethanol recrystallization, by melting point, mixed melting point and rotation.

Dibenzylidene-*d*-glucose Dimethyl Acetal 6-Benzoate.—The method of synthesis used for this substance was the same as that described for the corresponding diethyl acetal, but using absolute methanol and working at a temperature of 65–70°. The crude material was recrystallized from 95% ethanol; yield 2.5 g. from 5.7 g. of dibenzylideneglucose diethyl mercaptal 6-benzoate. Pure material was obtained on recrystallization from 15 parts of 95% ethanol; m. p. 156–159°, softening at 142°; $[\alpha]^{24}$ + 14° (*c*, 4; $CHCl_3$). The solubilities of the substance were similar to those of the corresponding diethyl compound.

Anal. Calcd. for $C_6H_7O_5(OCH_3)_2(C_6H_5CO)(C_6H_5CH)_2$: OCH_3, 12.25; C_6H_5CO, 20.75; C_6H_5CH, 35.6. Found: OCH_3, 12.33; C_6H_5CO, 20.3; C_6H_5CH, 35.9; S, absent.

***d*-Galactose Diethyl Acetal Pentaacetate.**—Galactose diethyl mercaptal pentaacetate[9] (10 g., 1 mol) and finely powdered cadmium carbonate (12 g.) were added to 100 cc. of absolute ethanol and the mixture heated to 70–80° while stirring with a mercury-sealed stirrer. Mercuric chloride (32.8 g., 6 mols), dissolved in 80 cc. of warm, absolute ethanol, was added rapidly in one portion. The mixture was stirred for five hours at 70–80°, with occasional additions of fresh cadmium carbonate. The reaction mixture was filtered hot and the residue was washed with warm ethanol. The filtrate was transferred to a separatory funnel containing 300 cc. each of chloroform and water, the chloroform layer was washed repeatedly (seven times) with 100-cc. portions of water until chloride free, and was then dried overnight with anhydrous calcium sulfate (Drierite) and cadmium carbonate. The chloroform was removed at room temperature under diminished pressure, leaving a solid crystalline mass. This was triturated with 50% methanol, filtered and recrystallized from hot 50% ethanol; yield 5.4 g.; m. p. 79°; $[\alpha]^{30}$ +17.5° (*c*, 4; $CHCl_3$). Further recrystallization did not alter these constants. The substance crystallized in elongated prisms and was practically insoluble in water and was soluble in the common organic solvents, including warm heptane. It did not reduce Fehling's solution.

Anal. Calcd. for $C_6H_7O_5(OC_2H_5)_2(CH_3CO)_5$: OC_2H_5, 19.40; CH_3CO, 10.76 cc. 0.1 *N* NaOH per 100 mg. Found: OC_2H_5, 19.49; CH_3CO, 10.78 cc.; S, absent.

***d*-Galactose Diethyl Acetal.**—Galactose diethyl acetal pentaacetate was deacetylated essentially according to the deacetylation procedure described by Montgomery, Hann and Hudson[5] for *d*-arabinose dimethyl acetal tetraacetate. Galactose diethyl acetal pentaacetate (5.4 g.) was dissolved in 35 cc. of absolute methanol, cooled to 0°, 2 cc. of 0.7 *N* barium methylate added, and the mixture kept at 0° overnight. The product crystallized from the reaction mixture; yield 1.9 g.; m. p. 127–128°; $[\alpha]^{20}$ +15° (*c*, 4; H_2O). Further recrystallization from absolute ethanol did not alter these constants. The substance crystallized in elongated prisms. It was soluble in water, alcohol and hot acetone and was practically insoluble in ether, chloroform and benzene. It reduced Fehling's solution only after acid hydrolysis.

Anal. Calcd. for $C_6H_{12}O_5(OC_2H_5)_2$: C, 47.24; H, 8.72; OC_2H_5, 35.44. Found: C, 47.12; H, 8.76; OC_2H_5, 35.56.

***d*-Galactose Dimethyl Acetal Pentaacetate.**—This substance was synthesized according to the procedure described for the corresponding ethyl compound, but using absolute methanol and working at a temperature of 60–70°. The product crystallized readily and was obtained pure on recrystallization from methanol; m. p. 128–129°; $[\alpha]^{20}$ +16° (*c*, 4; $CHCl_3$). The substance crystallized in elongated prisms and exhibited solubilities similar to those of the corresponding ethyl derivative. It did not reduce Fehling's solution.

Anal. Calcd. for $C_6H_7O_5(OCH_3)_2(CH_3CO)_5$: OCH_3, 14.22; CH_3CO, 11.48 cc. 0.1 *N* NaOH per 100 mg. Found: OCH_3, 14.10; CH_3CO, 11.40 cc.; S, absent.

***d*-Galactose Dimethyl Acetal.**—This substance was synthesized from its pentaacetate as described for the corresponding ethyl compound. It was obtained crystalline on removal of the methanol solvent and was obtained pure on recrystallization from methanol by the addition of ether; m. p. 122–123°; $[\alpha]^{28}$ +16° (*c*, 2; H_2O). The substance crystallized in elongated prisms and exhibited solubilities similar to those of the corresponding ethyl derivative. It reduced Fehling's solution only after acid hydrolysis.

Anal. Calcd. for $C_6H_{12}O_5(OCH_3)_2$: C, 42.47; H, 8.02; OCH_3, 27.44. Found: C, 42.45; H, 7.99; OCH_3, 27.87.

Reacetylation of this substance with pyridine and acetic anhydride produced the previously described pentaacetate of melting point 128–129°.

Acknowledgment is made to Mr. Howard S. Clark for the recorded semi-micro combustion analyses.

Summary

1. Demercaptalation of *d*-galactose diethyl mercaptal pentaacetate with mercuric chloride and cadmium carbonate in methanol solution yielded the crystalline *d*-galactose dimethyl acetal pentaacetate.

2. Application of the above reaction conditions to (2,3,4,5)-dibenzylidene-*d*-glucose diethyl mercaptal produced the crystalline (2,3,4,5)-dibenzylidene-*d*-glucose dimethyl acetal.

3. The dimethyl and diethyl acetals (and their

---

(9) M. L. Wolfrom, THIS JOURNAL, **52**, 2464 (1930).

pentaacetates) of *d*-galactose have been synthesized in crystalline form.

4. The dimethyl and diethyl acetals of (2,3,4,5)-dibenzylidene-*d*-glucose 6-benzoate have been synthesized in crystalline form.

COLUMBUS, OHIO RECEIVED NOVEMBER 19, 1937

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Ortho-Arsenated Phenoxyalkanols

BY STEPHEN B. BINKLEY[1] AND CLIFF S. HAMILTON

This investigation deals with a series of arsenated phenylglycol ethers formed by condensing *o*-nitrophenol with propylene chlorohydrin, reducing to the corresponding amine, and introducing the arsono group by means of the Bart[2] reaction. *o*-Hydroxyphenylarsonic acid would not condense with propylene chlorohydrin.

Nitration of α-methyl-β-2-arsonophenoxyethanol at 0° for three hours with two molecular proportions of fuming nitric acid (sp. gr. 1.50) introduced one nuclear nitro group and esterified the alcoholic hydroxyl group. The nitration product, α-methyl-β-2-arsono-4-nitrophenoxyethyl nitrate, when hydrolyzed by refluxing with 3-N hydrochloric acid, yielded α-methyl-β-2-arsono-4-nitrophenoxyethanol, which was then reduced catalytically to the amine. 2-β-Hydroxy-*n*-propoxyphenylarsonic acid and 5-amino-2-β-hydroxy-*n*-propoxyphenylarsonic acid were reduced to the corresponding oxides by reduction with sulfurous acid, employing hydriodic acid as a catalyst.

The arseno derivatives were obtained by reduction of the corresponding arsonic acids with hypophosphorous acid.

Attempts to oxidize the secondary alcohol group to the corresponding ketone were unsuccessful.

Experimental

α-Methyl-β-2-nitrophenoxyethanol.—To a suspension of 177 g. of the potassium salt of *o*-nitrophenol in 400 cc. of 95% ethyl alcohol was added 85 cc. (1 mol. eq.) of propylene chlorohydrin and the mixture was refluxed (for twenty-four hours) until the potassium salt of *o*-nitrophenol did not separate on cooling. After removal of the potassium chloride by filtration and the alcohol by distillation, the residue was acidified to congo red paper with dilute hydrochloric acid and steam distilled until all the *o*-nitrophenol had been removed. The product which remained as a heavy oil was separated, washed with 300 cc. of water in 100 cc. portions, dried over calcium chloride and distilled at reduced pressures.

α-Methyl-β-2-aminophenoxyethanol.—Ninety grams of α-methyl-β-2-nitrophenoxyethanol was dissolved in 200 cc. of tech. methyl alcohol and reduced with molecular hydrogen at 30 pounds (2 atm.) pressure in the presence of Raney[3] catalyst. After the reduction was complete the catalyst was filtered off, 100 cc. of water added to the filtrate, and the alcohol removed by distillation. On cooling the amine separated as an oil which soon solidified; it was purified by recrystallization from water.

TABLE I

Name	Yield, %	B. p., °C.	Formula	N analyses, % Calcd.	N analyses, % Found
α-Methyl-β-2-nitrophenoxyethanol	65	223–225 25 mm.	$C_9H_{11}O_4N$	7.14	7.35
α-Methyl-β-2-aminophenoxyethanol	95	75 m. p.	$C_9H_{13}O_2N$	8.48	8.62

α-Methyl-β-2-arsonophenoxyethanol and its Sodium Salt.—Eighty-five grams of α-methyl-β-2-aminophenoxyethanol was added to a mixture of 125 cc. of hydrochloric acid (sp. gr. 1.18), 1 liter of water, and 500 g. of ice, and diazotized with 35 g. of sodium nitrite in 500 cc. of water; time, thirty minutes; temperature, <5°. After diazotization 85 cc. of 6 *N* sodium hydroxide was added dropwise. The cold diazonium solution was added with vigorous stirring to a mixture of 80 g. of arsenic trioxide dissolved in 250 cc. of 6 *N* sodium hydroxide, 2 liters of water, 1 kg. of ice, and 5 g. of copper sulfate. The mixture was stirred for an hour, filtered through a charcoal mat, and evaporated to about 700 cc. The solution was made just acid to litmus paper, decolorized with charcoal, acidified to congo red paper and evaporated to dryness. The dry residue was extracted with 800 cc. of isopropyl alcohol in 200-cc. portions and the extract neutralized to litmus with 6 *N* sodium hydroxide. The monosodium salt of α-methyl-β-2-arsonophenoxyethanol separated on stirring and cooling. The product was dissolved in 150 cc. of water, decolorized with charcoal, and acidified to congo red paper. The free acid separated in tiny white plates.

When the acid was dissolved in sufficient 2 *N* sodium hydroxide to give a solution neutral to litmus paper and was added slowly to cold acetone the monosodium salt separated as white granules.

α-Methyl-β-4-nitro-2-arsonophenoxyethyl Nitrate.—The monosodium salt of α-methyl-β-2-arsonophenoxyethanol (20 g.) was stirred with 60 cc. of nitric acid (sp. gr. 1.50) for three hours. The product was precipitated by pouring into cold water.

α-Methyl-β-4-nitro-2-arsonophenoxyethanol.—α-Methyl-β-4-nitro-2-arsonophenoxyethyl nitrate (20 g.)

---

[1] Parke, Davis and Company Fellow.

[2] Bart, *Ann.*, **429**, 55 (1922).

[3] Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).