

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Tritylation Experiments in the Sugar Alcohol Series

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For the purposes of another problem under investigation in this Laboratory, we were interested in the tritylation,¹ by the Helferich procedure,² of sugar alcohols of the five and six carbon atom series. By this general reaction of tritylation, followed by acetylation and detritylation, the 2,3,4,5-tetraacetate³ and 2,3,4,5-tetrabenzoate⁴ of *D*-mannitol have been prepared previously. We were able to obtain a monotrityl ether of mannitol as its crystalline pentaacetate by treating an excess of mannitol with trityl chloride. This derivative is of interest because the two terminal positions of mannitol are chemically equivalent.

The methylpentitols offer the interesting case of presenting only one primary hydroxyl group to react with the tritylation reagent and accordingly the 2,3,4,5-tetraacetate of *L*-fucitol was synthesized. The detritylation of trityl-*L*-fucitol tetraacetate presented some difficulty as the Helferich detritylation procedure using hydrogen bromide in glacial acetic acid resulted in the formation of the bromide rather than the free hydroxyl group. This type of behavior was reported previously from this Laboratory⁵ with acyclic derivatives of glucose and galactose. To avoid this bromine replacement, detritylation of this substance was effected with hot dilute acetic acid according to the procedure of Kuhn and co-workers.⁶ Retritylation of the fucitol tetraacetate produced the original trityl-*L*-fucitol tetraacetate and treatment of the tetraacetate with hydrogen bromide yielded the same bromide tetraacetate that was obtained on detritylation by the Helferich procedure. The pentaacetate of *L*-fucitol was also synthesized in crystalline form. In the pentitol series, we have also obtained ditrityl-xylitol triacetate.

The tritylation of dulcitol presents an interesting case. Valentin⁷ reports that dulcitol does not form a trityl compound when treated with a pyri-

dine solution of trityl chloride. We found that a ditrityl compound was formed but that it separated from the reaction mixture as a dipyridinium hydrochloride addition compound. The acidity of this addition compound was sufficient to detritylate the dulcitol when the compound was recrystallized from hot ethanol. The dipyridinium compound was decomposed readily by bases without detritylation and in this manner ditrityl dulcitol was obtained. Ditrityl dulcitol crystallizes from ethanol with one mole of alcohol of crystallization. This behavior of ditrityl dulcitol with pyridine hydrochloride is reminiscent of the behavior of *D*-sorbitol with pyridine, wherein a readily crystallizable pyridine compound is formed.⁸

Acetylation of ditrityl dulcitol yielded the ditrityl dulcitol tetraacetate, from which 1,6-dibromodulcitol tetraacetate was obtained on detritylation with hydrogen bromide in glacial acetic acid. Ditrityl dulcitol formed a dibenzylidene compound without detritylation. In preparing this substance we removed the excess of benzaldehyde by allowing it to oxidize in the air to benzoic acid and removing the latter with a mild alkali.

Experimental

1-Trityl *L*-Fucitol Tetraacetate.—*L*-Fucitol (1.5 g., 1 mol) and 2.6 g. (1 mol) of trityl chloride were dissolved in 20 cc. of warm, dry pyridine and kept at 60° for two days. To the cooled solution was added 18 cc. of acetic anhydride and the solution kept at 45° for twenty-four hours. The product crystallized from the reaction mixture and was recrystallized from ethanol: yield 2.4 g., m. p. 152°, spec. rot. -18° (30°, *c* 1.9, CHCl₃).⁹ A further quantity of the substance (0.6 g.) was obtained by pouring the pyridine mother liquor into ice and water.

Anal. Calcd. for C₆H₉O₅(COCH₃)₄C(C₆H₅)₃: C(C₆H₅)₃, 42.2; CH₃CO, 6.94 cc. 0.1 *N* NaOH per 100 mg. Found: C(C₆H₅)₃ (7), 41.9; CH₃CO, 6.89 cc.

The same product was obtained on acetylation of the trityl-*L*-fucitol of Valentin.⁷

1-Bromo-*L*-fucitol Tetraacetate.—To a solution of 2.5 g. (1 mol) of 1-trityl-*L*-fucitol tetraacetate in 10 cc. of glacial acetic acid was added 2 cc. of a glacial acetic acid solution of hydrogen bromide (4 mols). The precipitated

(1) Trityl = triphenylmethyl.

(2) B. Helferich, P. E. Speidel and W. Toeldte, *Ber.*, **56**, 766 (1923); B. Helferich and J. Becker, *Ann.*, **440**, 1 (1924); B. Helferich, *Z. angew. Chem.*, **41**, 871 (1928), review paper.

(3) F. Micheel, *Ber.*, **65**, 262 (1932).

(4) F. Micheel, *Ann.*, **496**, 77 (1932); A. Müller, *Ber.*, **65**, 1051 (1932).

(5) M. L. Wolfrom, J. L. Quinn and C. C. Christman, *THIS JOURNAL*, **57**, 713 (1935); M. L. Wolfrom and C. C. Christman, *ibid.*, **58**, 39 (1936).

(6) R. Kuhn, H. Rudy and F. Weygand, *Ber.*, **69**, 1546 (1936).

(7) F. Valentin, *Coll. Czechoslov. Chem. Commun.*, **3**, 499 (1931).

(8) H. H. Strain, *THIS JOURNAL*, **56**, 1756 (1934).

(9) All specific rotations are recorded to the D-line of sodium light; 30° is the temperature; *c* is the concentration in g. per 100 cc. of soln., the chloroform used was U. S. P. (United States Pharmacopoeia). All substances were recrystallized to constant rotation and melting point.

trityl bromide was removed by filtration and the filtrate was poured into ice and water. The crystalline precipitate was removed by filtration and recrystallized from ethanol; yield 0.9 g., m. p. 142–143°; spec. rot. -9.8° (22° , c 1.76, CHCl_3).

The compound was readily soluble in glacial acetic acid, chloroform, acetone and hot ethanol. It was practically insoluble in water and petroleum ether.

Anal. Calcd. for $\text{C}_6\text{H}_9\text{O}_4(\text{COCH}_3)_4\text{Br}$: CH_3CO , 10.1 cc. 0.1 *N* NaOH per 100 mg.; Br, 20.1. Found: CH_3CO (Freudenberg method¹⁰), 10.1 cc.; Br, 20.4.

***l*-Fucitol 2,3,4,5-Tetraacetate.**—1-Trityl *l*-fucitol tetraacetate (10 g.) was dissolved in 40 cc. of warm glacial acetic acid and the mixture heated under a reflux condenser. Water (10 cc.) was added in 2-cc. portions and the mixture was refluxed for one hour. Water (50 cc.) was then added, the mixture cooled to room temperature and the separated trityl carbinol (4.3 g., 95%) separated by filtration. The sirup obtained on solvent removal under reduced pressure was taken up in ether and the ether solution was shaken first with a suspension of calcium carbonate in water and finally with water. The dried ether extract (carboraffin) was treated with petroleum ether to incipient opalescence and allowed to stand overnight at icebox temperature; yield 1.2 g., m. p. 92–94°. A second crop (0.7 g., m. p. 92–94°) was obtained from the mother liquor on the addition of more petroleum ether. The substance is readily recrystallized from xylene; m. p. 92–94°, spec. rot. -15° (25° , c 3.0, CHCl_3). The above procedure is essentially the detriptylation procedure of Kuhn, Rudy and Weygand.⁶

The compound crystallizes in elongated prisms from water. It is readily soluble in chloroform, acetone, ethanol, acetic acid, warm ether and warm xylene and is practically insoluble in petroleum ether. It is slightly soluble in cold and fairly soluble in hot water.

Anal. Calcd. for $\text{C}_6\text{H}_{10}\text{O}_5(\text{COCH}_3)_4$: C, 50.3; H, 6.64; CH_3CO , 12.0 cc. 0.1 *N* NaOH per 100 mg. Found: C, 50.5; H, 6.59; CH_3CO , 11.9 cc.

The original 1-bromo-*l*-fucitol tetraacetate was regenerated on treatment of *l*-fucitol tetraacetate (0.25 g.) in glacial acetic acid (8 cc.) with 4 cc. of acetic acid saturated with hydrogen bromide and allowing the mixture to stand for three hours. The crystalline product obtained on pouring the reaction mixture into ice and water was removed by filtration, washed with water and recrystallized from 60% ethanol; yield 0.13 g., m. p. 143° (mixed m. p. unchanged).

***l*-Fucitol Pentaacetate.**—*l*-Fucitol (0.95 g.) was acetylated with pyridine (5 cc.) and acetic anhydride (10 cc.) for sixteen hours at room temperature and the reaction product obtained crystalline on pouring the acetylation mixture into ice and water; yield 2.0 g. (93%), m. p. 126°. The product was recrystallized from ethanol; m. p. 127°, spec. rot. $+20.5^\circ$ (25° , c 3.0, CHCl_3).

The substance crystallizes from ethanol in prisms and is insoluble in petroleum ether, soluble in hot ethanol and is readily soluble in chloroform, acetone and acetic acid.

Anal. Calcd. for $\text{C}_6\text{H}_9\text{O}_5(\text{COCH}_3)_5$: C, 51.0; H, 6.43; CH_3CO , 13.3 cc. 0.1 *N* NaOH per 100 mg. Found: C, 51.1; H, 6.33; CH_3CO , 13.3 cc.

1,6-Ditrityl Dulcitol Dipyridinium Hydrochloride.—Five grams (1 mol) of dulcitol and 16 g. (2 mols) of trityl chloride were added to 30 cc. of dry pyridine. The mixture was shaken intermittently for five days. The dulcitol gradually went into solution and a product precipitated. The product was removed by filtration and washed with pyridine and then with water; m. p. 182–184°, mixed m. p. 172–178° with ditrityl dulcitol (see below) of m. p. 184°. Upon acetylation with pyridine and acetic anhydride the product was converted into ditrityl dulcitol tetraacetate (see below); m. p. 233°, mixed m. p. unchanged. When the product was dissolved in hot ethanol, dulcitol, identified by melting point and mixed melting point, separated on cooling. From the mother liquor trityl ethyl ether (m. p. 83°, mixed m. p. unchanged) was recovered. When the product (odorless) was heated a distinct odor of pyridine was observed.

Anal. Calcd. for $\text{C}_6\text{H}_{12}\text{O}_6[\text{C}(\text{C}_6\text{H}_5)_3]_2[\text{C}_5\text{H}_5\text{N}\cdot\text{HCl}]_2$: Cl, 7.90; HCl, 2.23 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 8.2; HCl, 2.16 cc.

1,6-Ditrityl Dulcitol Ethyl Alcoholate.—The 1,6-ditrityl dulcitol dipyridinium hydrochloride obtained from 5 g. of dulcitol was suspended in 250 cc. of water, 0.1 *N* sodium hydroxide was added until the solution was basic, mechanical stirring was then maintained for two hours and the product removed by filtration and washed with water, yield 18 g.; after two recrystallizations from ethanol, yield 14 g., m. p. 183–184° (slight sintering at 80°).

The compound crystallizes in rectangular prisms from ethanol. It is readily soluble in benzene, moderately so in pyridine, chloroform and hot ethanol and insoluble in water and petroleum ether.

Anal. Calcd. for $\text{C}_6\text{H}_{12}\text{O}_6[\text{C}(\text{C}_6\text{H}_5)_3]_2\text{C}_2\text{H}_5\text{OH}$: $\text{C}(\text{C}_6\text{H}_5)_3$, 68.3; $\text{C}_2\text{H}_5\text{OH}$, 6.46. Found: $\text{C}(\text{C}_6\text{H}_5)_3$, 68.4; $\text{C}_2\text{H}_5\text{OH}$ (loss in weight at 110° under reduced pressure), 6.38; OC_2H_5 , present.

1,6-Ditrityl Dulcitol.—This substance was obtained as a crystalline residue on heating its ethyl alcoholate for sixteen hours at 110° under reduced pressure and over phosphorus pentoxide; yield quantitative, m. p. 183–184°.

Anal. Calcd. for $\text{C}_6\text{H}_{12}\text{O}_6[\text{C}(\text{C}_6\text{H}_5)_3]_2$: $\text{C}(\text{C}_6\text{H}_5)_3$, 73.0; C, 79.2; H, 6.33. Found: $\text{C}(\text{C}_6\text{H}_5)_3$, 72.7; C, 78.9; H, 6.31.

1,6-Ditrityl Dulcitol Tetraacetate.—1,6-Ditrityl dulcitol ethyl alcoholate (2.5 g.) was dissolved in 23 cc. of pyridine, cooled to 0°, 15 cc. of acetic anhydride added slowly and the mixture kept at icebox temperature. In about three hours crystals began to form and crystallization was completed on standing overnight; yield 2.5 g., m. p. 232–234°. Pure material was obtained on recrystallization from trichloroethylene; m. p. 237–238°.

Anal. Calcd. for $\text{C}_{14}\text{H}_{20}\text{O}_{10}[\text{C}(\text{C}_6\text{H}_5)_3]_2$: C, 74.8; H, 6.04; $\text{C}(\text{C}_6\text{H}_5)_3$, 58.3; mol. wt., 838.4. Found: C, 74.3; H, 6.03; $\text{C}(\text{C}_6\text{H}_5)_3$, 58.7; mol. wt. (Rast), 870, 824.

1,6-Dibromodulcitol Tetraacetate.—1,6-Ditrityl dulcitol tetraacetate (4.5 g.) was detriptylated with hydrogen bromide in glacial acetic acid as described previously for the synthesis of 1-bromo-*l*-fucitol tetraacetate, except that the filtrate from the trityl bromide was poured into chloroform (100 cc.) and the chloroform was washed with cold water until free of halogen. The residue obtained on solvent

(10) K. Freudenberg and M. Harder, *Ann.*, **433**, 230 (1923).

removal was triturated with ether and recrystallized several times from ethyl acetate; yield 1.1 g., m. p. 197–198°. The substance was practically insoluble in ether and alcohol but was soluble in chloroform, hot ethyl acetate and hot benzene.

Anal. Calcd. for $C_6H_8O_4(COCH_3)_4Br_2 \cdot CH_3CO$, 8.40 cc. 0.1 *N* NaOH per 100 mg.; Br, 33.57. Found: CH_3CO , 8.38 cc. (Freudenberg method¹⁰); Br, 33.45.

1,6-Ditrityl Dibenzylidene Dulcitol.—1,6-Ditrityl dulcitol (3 g.) was dissolved in 10 cc. of benzaldehyde and 3 to 4 g. of freshly fused zinc chloride was added. The mixture was shaken until the zinc chloride dissolved and kept overnight at room temperature. Chloroform (50 cc.) was then added and the solution washed with water to remove the zinc chloride, dried and placed in a 12-inch (30-cm.) evaporating dish. The solution was heated over a light bulb and dry, warm air was blown over its surface. After about a day there was only a very faint odor of benzaldehyde. The resulting crystalline mass was dissolved in chloroform, washed repeatedly with an aqueous solution of sodium bicarbonate to remove the benzoic acid and finally with water. The crystalline residue obtained on solvent removal from the dried (carboraffin) chloroform solution was recrystallized from trichloroethylene; yield 2.9 g., m. p. 233–234°, optically inactive in chloroform solution for the D-line of sodium light. When the substance was dissolved in concentrated sulfuric acid and diluted with water, a distinct odor of benzaldehyde could be noted.

Anal. Calcd. for $C_{20}H_{20}O_6[C(C_6H_5)_3]_2$: C, 82.6; H, 5.98; $C(C_6H_5)_3$, 57.7. Found: C, 82.4; H, 5.78; $C(C_6H_5)_3$, 57.3.

1,5-Ditrityl Xylitol Triacetate.—Nineteen grams (2 mols) of trityl chloride was added to 5 g. (1 mol) of xylitol sirup in 25 cc. of dry pyridine and the solution was kept at room temperature for four days, whereupon 15 cc. of acetic anhydride was added. In a few hours a crystalline product separated from the reaction mixture. Recrystallization was effected by solution in hot xylene (carboraffin) followed by the addition of ethanol; yield 17 g., m. p. 206°.

Anal. Calcd. for $C_6H_7O_5(COCH_3)_3[C(C_6H_5)_3]_2$: $C(C_6H_5)_3$, 63.8; CH_3CO , 3.94 cc. 0.1 *N* NaOH per 100 mg. Found: $C(C_6H_5)_3$, 63.7; CH_3CO , 3.81 cc.

1-Trityl¹¹-*d*-mannitol Pentaacetate.—Ten grams (2 mols) of dry mannitol, 7.8 g. (1 mol) of trityl chloride and 60 cc. of dry pyridine were heated at 90° for twelve hours, whereupon the solution was cooled and poured in a thin stream into ice and water (2 liters). The precipitated mass hardened on standing at ice box temperature for several hours and was identified as ditrityl mannitol tetraacetate³ on acetylation; yield of ditrityl mannitol tetraacetate 10 g., m. p. 183–184° (mixed m. p. with an authentic specimen unchanged).

(11) Positions 1 and 6 are equivalent.

The aqueous filtrate above was concentrated until a sticky mass separated. This was removed by chloroform extraction and the sirup obtained on solvent removal from the dried extract was acetylated overnight with pyridine (20 cc.) and acetic anhydride (15 cc.). The crystalline product obtained on pouring the acetylation mixture into ice and water was removed by filtration, washed with water, dried and recrystallized from xylene (carboraffin); yield 4 g., m. p. 163–164°, spec. rot. +35.5° (25°, *c* 4, $CHCl_3$).

Anal. Calcd. for $C_6H_8O_6(COCH_3)_5C(C_6H_5)_3$: $C(C_6H_5)_3$, 38.3; CH_3CO , 7.88 cc. 0.1 *N* NaOH per 100 mg. Found: $C(C_6H_5)_3$, 37.9; CH_3CO , 7.92 cc.

We wish to express our indebtedness to the Atlas Powder Co. for furnishing the mannitol used in this investigation and also for preparing the other sugar alcohols from the corresponding aldoses by high pressure, catalytic reduction. We also wish to express our indebtedness to Mr. H. S. Clark for the microcombustion analyses.

Summary

1. The acetates of monotrityl-*d*-mannitol, ditrityl-xylitol, trityl-*l*-fucitol and ditrityl-dulcitol have been synthesized.

2. *l*-Fucitol 2,3,4,5-tetraacetate has been synthesized.

3. Detrylation of trityl-*l*-fucitol tetraacetate and of ditrityl dulcitol tetraacetate with hydrogen bromide in acetic acid resulted in bromine replacement of the trityl groups.

4. *l*-Fucitol 2,3,4,5-tetraacetate on retritrylation produces the original trityl-*l*-fucitol tetraacetate and on treatment with hydrogen bromide the same acetylated bromide is obtained as on detrylation with hydrogen bromide in acetic acid.

5. *l*-Fucitol pentaacetate has been synthesized.

6. On tritylation of dulcitol with pyridine and trityl chloride, a dipyridinium hydrochloride compound of the reaction product is formed, from which the ditrityl dulcitol may be obtained, as a monoethyl alcoholate or in the non-solvated form.

7. Dibenzylidene ditrityl dulcitol has been synthesized.

8. All compounds reported were obtained in crystalline form and were purified to constant rotation and melting point.