Table V shows the final equilibrium when β-glucose pentaacetate was anomerized in acetic acid purified by a single distillation. Rotations are in arbitrary units.

As a practical procedure one ml. of acetic anhydride was added to 100 ml. of purified acetic acid in most of the runs. The catalyst was prepared by dissolving anhydrous silver perchlorate in dry acetic acid and precipitating the silver with a stream of dry hydrogen chloride. A stream of dry nitrogen through the warmed solution removed the excess hydrogen chloride. Perchloric acid in acetic acid was determined by titration with potassium acid phthalate.[25]

TABLE V

EQUILIBRIUM ROTATION IN ACETIC ACID SOLUTIONS

H_2O added, ml./100 ml.	Acetic anhydride added, ml./100 ml.	Rotation
None		11.2
0.4		10.1
1.0		9.7
2.0		9.6
None	2	11.5
None	5	11.5

Most rates given at 0.1 *M* perchloric acid were calculated assuming the rate first order in acid as reported in acetic acid–acetic anhydride mixtures.[5] This has been found true by checking several solvent mixtures at two concentrations of acid. When the points were on a straight line through the origin it was assumed calculation to any concentration was justified. In Table VI results in a solvent low in acetic acid are given.

TABLE VI

DEPENDENCE OF RATE ON $HClO_4$ CONCENTRATION AT LOW ACETIC ACID

$(AcOH)_2$, *M*	SOAc, *M*	$HClO_4$, *M*	$k_1 + k_1$, min.$^{-1}$ Found	$k_1 + k_1$, min.$^{-1}$ Calcd. to 0.1 *M* $HClO_4$
0.103	0.0513	0.0009	0.0083	0.92
.103	.0513	.0018	.0163	.91
.103	.0513	.0036	.0324	.90
.103	.0513	.0054	.0476	.88

Methylene dichloride was the other solvent.

When concentrations are given in % by volume, the measured volumes were mixed and the total volume assumed to be the sum. When concentrations are expressed as molar, solutions were made up to measured volumes.

DAVIS, CALIF.

---

[25] J. S. Fritz, "Acid–Base Titration in Nonaqueous Solvents," G. Frederick Smith Chemical Co., Columbus, Ohio, 1952.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Derivatives of D-Mannitol 1,2,3,5,6-Pentanitrate[1]

BY M. L. WOLFROM, E. P. SWAN, K. S. ENNOR AND A. CHANEY

RECEIVED MAY 2, 1959

The synthesis and reactions of several organic acid (acetic, propionic and benzoic) esters of D-mannitol 1,2,3,5,6-pentanitrate are described. Polymerization of 3-*O*-acryloyl-D-mannitol pentanitrate was effected only with considerable difficulty. The catalytic reduction of these materials under neutral or basic conditions promoted migration of the various acyl functions from carbon three to one; no migration was observed under acidic conditions. Several new ether derivatives, 1-*O*-methyl-D-mannitol pentanitrate, 3-*O*-*n*-propyl-D-mannitol and 3-*O*-allyl-D-mannitol pentanitrate, are described; polymerization of the last was not effected. The interesting conversion of 1,6-dichloro-1,6-dideoxy-D-mannitol, by the action of silver nitrate, to 1,4:3,6-dianhydro-D-mannitol 2,5-dinitrate has been discovered.

This Laboratory has been concerned with the synthesis of nitrated polymers through the direct addition polymerization of suitably substituted ethylenic monomers. The required nitrated monomers may be obtained by two routes. An unsaturated polyhydric substance may be nitrated under appropriate conditions to afford an unsaturated polynitrate.[2–4] The alternate route, of major importance in the current report, concerns the formation of unsaturated derivatives from a partially nitrated polyhydric alcohol.

Conversion of D-mannitol hexanitrate to D-mannitol 1,2,3,5,6-pentanitrate, in 70% yield, has been effected by treatment with pyridine[5] and ammonium carbonate in aqueous acetone.[6] We have found that the latter method was more convenient for conducting the denitration on a fairly large scale, since it did not require exhaustive drying of the explosive hexanitrate. Good reproducible yields (78%) were obtained when the reaction was carried out at 0 to 8°; at higher temperatures, considerable decomposition resulted. Reaction of allyl bromide with D-mannitol 1,2,3,5,6-pentanitrate in tetrahydrofuran, in the presence of silver oxide and anhydrous calcium sulfate, afforded a 3% yield of 3-*O*-allyl-D-mannitol pentanitrate. Larger amounts of this material were obtained (71% yield) by nitration of 3-*O*-allyl-D-mannitol with absolute nitric acid in acetic anhydride, following the general method described by Honeyman and Morgan.[7]

Good yields (72%) of crystalline 3-*O*-acryloyl-D-mannitol pentanitrate resulted from the reaction of acryloyl chloride with D-mannitol 1,2,3,5,6-pentanitrate dissolved in acetonitrile containing N,N-dimethylaniline. When the aniline derivative was replaced by pyridine, isolation of the product was not possible. Application of this method to the synthesis of 3-*O*-methacryloyl-D-mannitol pentanitrate resulted in a sirup which has not crystallized but readily afforded a hard polymer on exposure to light and air. Only low molecular weight, gummy polymers have been obtained from the action of dibenzoyl peroxide on 3-*O*-acryloyl-D-mannitol pentanitrate and under the same condi-

---

[1] This work was carried out under Contract DA-33-019-ord-2025, between the Ballistic Research Laboratories of Aberdeen Proving Ground, Md., and The Ohio State University Research Foundation (Project 675). Preliminary communication: *Abstracts Papers Am. Chem. Soc.*, **135**, 8D (1959).

[2] G. Desseigne, *Bull. soc. chim. France*, [5] **13**, 98 (1946).

[3] R. Evans and J. A. Gallaghan, THIS JOURNAL, **75**, 1248 (1953).

[4] L. Fishbein and J. A. Gallaghan, *ibid.*, **78**, 1218 (1956).

[5] L. D. Hayward, *ibid.*, **73**, 1974 (1951).

[6] D. E. Elrick, N. S. Marans and R. F. Preckel, *ibid.*, **76**, 1373 (1954).

[7] J. Honeyman and J. W. W. Morgan, *Chem. & Ind.* (*London*) 1035 (1953).

tions, 3-*O*-allyl-D-mannitol pentanitrate has failed to polymerize. Further investigation of this problem is being undertaken.

Treatment of 3-*O*-acryloyl-D-mannitol pentanitrate with hydrogen and palladium-on-charcoal afforded a crystalline D-mannitol monopropionate, in high yield. Nitration of this compound yielded a hitherto unreported pentanitrate. The melting point, specific rotation and infrared absorption spectrum of this compound were different from those of the known 3-*O*-propionyl-D-mannitol pentanitrate.[6] The *O*-propionyl-D-mannitol pentanitrate was characterized through removal of the propionate group by treatment with sodium hydroxide, followed by methylation with methyl iodide and silver oxide. The product was the hitherto unreported crystalline 1-*O*-methyl-D-mannitol pentanitrate which subsequently was obtained by nitration of 1-*O*-methyl-D-mannitol. It follows that during the hydrogenation of 3-*O*-acryloyl-D-mannitol pentanitrate, the acyl group migrated from C3 to C1.

The above migration is probably a general reaction, since hydrogenation of 3-*O*-acetyl-, 3-*O*-benzoyl- and 3-*O*-propionyl-D-mannitol pentanitrate, under the same conditions, afforded crystalline 1-*O*-acetyl-D-mannitol,[8] 1-*O*-benzoyl-D-mannitol and 1-*O*-propionyl-D-mannitol, respectively. In some cases, high and reproducible yields were obtained only after treating the hydrogenated mixture with a trace of aqueous sodium hydroxide, the migration of the acyl group taking place under the influence of traces of alkali. These are interesting examples of the well established migration of acyl groups in partially substituted carbohydrates.[9,10] The addition of excess benzoic acid to the reduction mixtures prior to addition of the catalyst prevented the rearrangement. The resulting non-crystalline 3-*O*-acyl-D-mannitols afforded the original 3-*O*-acyl-D-mannitol pentanitrates on renitration.

The action of silver nitrate on 1,6-dichloro-1,6-dideoxy-D-mannitol[11] in boiling acetonitrile solution has been shown to produce 1,4:3,6-dianhydro-D-mannitol 2,5-dinitrate[12] as the major reaction product. A similar reaction has been reported for 1,6-dibenzoyl-D-mannitol on heating with *p*-toluenesulfonic acid in acetylene tetrachloride.[13] Since the nitrate group is non-participating[14] and probably does not migrate,[15] the isomannide dinitrate probably arises by elimination of hydrogen chloride to form 1,4:3,6-dianhydro-*O*-mannitol which is subsequently nitrated by the nitric acid generated from the silver nitrate by the hydrogen chloride.

Attempts to prepare various monohydroxy pentanitrates of D-mannitol by the treatment of the available acyl pentanitrate derivatives with different bases have been inconclusive. In most cases, the unchanged starting materials were recovered. More vigorous conditions resulted in the loss of both nitrate and acyl functions. The acyl pentanitrates appear to be quite stable to treatment with acidic materials.

In addition to the several new D-mannitol derivatives mentioned above, the catalytic reduction of both 3-*O*-allyl-D-mannitol and its pentanitrate derivative produced 3-*O*-*n*-propyl-D-mannitol. This compound was also obtained, in lower yield, from 3-*O*-allyl-D-mannitol pentanitrate on treatment with hydrazine hydrate in boiling ethanol.[16]

Experimental

Preparation of D-Mannitol 1,2,3,5,6-Pentanitrate.—D-Mannitol hexanitrate[17] (90 g., m.p. 102–107°) was converted into D-mannitol 1,2,3,5,6-pentanitrate through the method of Elrick, Marans and Preckel,[6] which was modified by conducting the reaction at 0 to 8°; yield 63 g. (78%), m.p. 81–82°.

3-*O*-Allyl-D-mannitol Pentanitrate. (a) **From 3-*O*-Allyl-D-mannitol.**—An amount of 11.1 g. (0.05 mole) of 3-*O*-allyl-D-mannitol[18] was added in small portions, with shaking, to a solution of 16 ml. (0.38 mole) of absolute nitric acid in 45 ml. of acetic anhydride at 0 to 4°. After 4 min. at room temperature, the solution was poured into ice and water containing potassium carbonate. The resulting crude precipitate, which rapidly solidified, was filtered, washed with dilute aqueous potassium carbonate and with water and dried; yield 21.3 g. (94%). Recrystallization from 90% ethanol afforded clustered needles; yield 16.1 g. (71%), m.p. 72–72.5°, $[\alpha]^{21}\mathrm{D}$ +40° (*c* 4.560, chloroform).

Anal. Calcd. for $C_9H_{13}N_5O_{16}$: C, 24.17; H, 2.93; N, 15.70. Found: C, 23.96; H, 3.03; N, 15.85.

(b) **From D-Mannitol 1,2,3,5,6-Pentanitrate.**—Allyl bromide (3.3 ml.) was added, over a period of 15 min., to a stirred suspension of 1 g. of D-mannitol 1,2,3,5,6-pentanitrate, 5.6 g. of silver oxide and 5.1 g. of anhydrous calcium sulfate in 20 ml. of boiling tetrahydrofuran. The mixture was boiled under reflux for 3 hr. and the solids were filtered and washed with ethanol. The combined filtrate and washings were decolorized with activated carbon and then evaporated to a yellow sirup. Treatment of this with ethanol gave needles; yield 0.03 g. (3%), m.p. 70–71°, undepressed on admixture with the sample prepared by method **a**, $[\alpha]^{23}\mathrm{D}$ +39° (*c* 1.141, chloroform).

3-*O*-Acryloyl-D-mannitol Pentanitrate.—To a solution of 25.0 g. (61 mmoles) of D-mannitol 1,2,3,5,6-pentanitrate and 25.0 ml. (198 mmoles) of N,N-dimethylaniline in 100 ml. of acetonitrile at 0° was added 20 ml. (245 mmoles) of pure (critical) acryloyl chloride.[19] The green solution obtained was stirred at 0° for 24 hr. before being poured into ether and water (500 ml. each). After shaking, the water layer was discarded and the ether layer was washed with water, 5% hydrochloric acid, saturated aqueous sodium bicarbonate and water (two times each with 300 ml.). A small amount of ethanol was added to the ether layer before concentration to a sirup which was dissolved in ethanol and decolorized. The nearly colorless filtrate was heated to 50° and water was added to opalescence whereupon slow cooling (finally to 0°) afforded 3-*O*-acryloyl-D-mannitol pentanitrate; yield 20.3 g. (72%), m.p. 65–66°, $[\alpha]^{21}\mathrm{D}$ +49° (*c* 3.2, acetonitrile).

Anal. Calcd. for $C_9H_{11}N_5O_{17}$: C, 23.43; H, 2.39; N, 15.19. Found: C, 23.58; H, 2.50; N, 15.25.

Following a modification of the general method of Brewster and Ciotti[20] for the acylation of hydroxyl groups, the

---

(8) B. Lindberg, *Acta Chem. Scand.*, **7**, 1119 (1953).

(9) E. Pacsu, *Advances in Carbohydrate Chem.*, **1**, 109, 113 (1945).

(10) M. L. Wolfrom, A. Thompson and M. Inatome, This Journal, **79**, 3868 (1957).

(11) A. Siwoloboff, *Ann.*, **233**, 368 (1886).

(12) S. E. Forman, C. J. Carr and J. C. Krantz, Jr., *J. Am. Pharm. Assoc.*, **30**, 132 (1941).

(13) P. Brigl and H. Grüner, *Ber.*, **66**, 1945 (1933); **67**, 1582 (1934).

(14) L. Fishbein, This Journal, **79**, 2959 (1957); S. J. Cristol and B. Franzus, *ibid.*, 2488.

(15) J. Honeyman and J. W. W. Morgan, *J. Chem. Soc.*, 3660 (1955); these authors report the single example of a possible migration of a nitrate group.

(16) K. S. Ennor and J. Honeyman, *ibid.*, 2586 (1958).

(17) Supplied by Atlas Powder Company, Wilmington, Delaware.

(18) P. Bladon and L. N. Owen, *J. Chem. Soc.*, 591 (1950); in our hands, omission of the distillation of the intermediate, 3-*O*-allyl-1,2:5,6-di-*O*-isopropylidene-D-mannitol, resulted in improved yields (65% over-all for the two steps).

(19) G. H. Stempel, Jr., R. P. Cross and R. P. Mariella, This Journal, **72**, 2299 (1950).

(20) J. H. Brewster and C. J. Ciotti, Jr., *ibid.*, **77**, 6214 (1955).

same substance was obtained in lower yield. Thus, 8.1 g. (20 mmoles) of D-mannitol 1,2,3,5,6-pentanitrate was dissolved in 50 ml. of acetonitrile and cooled to 0°. While stirring, 4 ml. (60 mmoles) of acrylic acid, 10 ml. (100 mmoles) of triethylamine and 4 ml. (31 mmoles) of benzenesulfonyl chloride were added successively. The mixture was stirred for 24 hr. at room temperature before the acrylate was isolated in the manner described above; yield 4.4 g. (49%), m.p. 62–63°. An additional recrystallization afforded pure material which had the same optical rotation as the product obtained above and did not depress its melting point. Attempts to obtain the acrylate from reaction systems that employed acryloyl chloride with pyridine as the base were complicated by the formation of intractable products.

Attempted Preparation of 3-*O*-Methacryloyl-D-mannitol Pentanitrate.—Methacryloyl chloride was substituted for the acryloyl chloride in the method detailed above. Except for extension of the reaction time to 48 hr. at 0°, the reaction and isolation of product were identical. However, the impure sirup obtained (40% yield) on evaporation of the final ethereal solution has not been crystallized and, during attempts to obtain crystalline material, the product polymerized spontaneously to a hard solid.

Polymerization Studies. (a)—A tube containing 1.15 g. of molten 3-*O*-acryloyl-D-mannitol pentanitrate and 1 mg. of dibenzoyl peroxide was partially evacuated and maintained at 80 to 85° for 3 hr. The reaction mixture was extracted repeatedly with boiling ethanol; the residue was a yellow gum with an intrinsic viscosity of 0.08 in acetone solution; yield 0.52 g. (45%).

(b).—Molten 3-*O*-allyl-D-mannitol pentanitrate was kept at 80° either in air or under a current of oxygen for 24 hr. In each case, starting compound was recovered unchanged; yield 91%, after recrystallization from 90% ethanol.

(c).—A solution of 2 g. of 3-*O*-allyl-D-mannitol pentanitrate and 0.2 g. of dibenzoyl peroxide in 10 ml. of benzene was boiled under reflux for 24 hr. The unchanged monomer was then recovered; yield 73%.

(d).—A solution of 1 g. of 3-*O*-allyl-D-mannitol pentanitrate and 0.1 g. of Luperox Number 6[21] in 25 ml. of ethanol was kept at 65° for 21 hr. Concentration of the solution gave unchanged compound; yield 85%.

Hydrogenation of 3-*O*-Acryloyl-D-mannitol Pentanitrate.—A solution of 2.0 g. of 3-*O*-acryloyl-D-mannitol pentanitrate in 200 ml. of abs. ethanol was hydrogenated in the Parr apparatus at 3 atm. for 6 hr. using 0.1 g. of 10% palladium-on-charcoal.[22] The catalyst was filtered, washed with ethanol, and the combined filtrate and washings were evaporated. The residual solid was recrystallized from ethanol–ethyl acetate to give 1-*O*-propionyl-D-mannitol; yield 0.83 g. (81%), m.p. 110–112°. Recrystallization from ethanol afforded pure product, m.p. 115–116.5°, $[\alpha]^{25}_{D}$ +4.2° (*c* 4.085, water).

Anal. Calcd. for $C_9H_{18}O_7$: C, 45.37; H, 7.62. Found: C, 45.19; H, 7.56.

1-*O*-**Propionyl-D-mannitol Pentanitrate.**—1-*O*-Propionyl-D-mannitol (2.38 g.) was nitrated by the procedure employed for 3-*O*-allyl-D-mannitol, except that ice and water were used in place of aqueous potassium carbonate for the isolation and washing of the crude product; yield 4.26 g. (92%).

Recrystallization from ethanol afforded clustered needles; yield 3.29 g. (71%), m.p. 126–127°, $[\alpha]^{26}_{D}$ +28.6° (*c* 3.912, acetone).

Anal. Calcd. for $C_9H_{13}N_5O_{17}$: C, 23.33; H, 2.83; N, 15.12. Found: C, 23.32; H, 2.71; N, 15.06.

Characterization of 1-*O*-Propionyl-D-mannitol Pentanitrate.—A solution of 0.24 g. (6 mmoles) of sodium hydroxide in 0.6 ml. of water was added to 0.93 g. (2 mmoles) of 1-*O*-propionyl-D-mannitol pentanitrate in 6 ml. of acetone and 2 ml. of methanol at 0°. The brown reaction mixture was left at room temperature for 20 min. and was then evaporated. Chloroform and water were added to the residue and, after shaking, the water layer was discarded. The chloroform layer was dried over anhydrous magnesium sulfate and then evaporated to a colorless sirup. Silver oxide (2 g.) was added in portions to a suspension of the sirup in 8 ml. of boiling methyl iodide. The mixture was boiled for 8 hr. and the silver residue was filtered, washed with acetone, and the combined filtrate and washings were evaporated. Treatment of the residue with methanol afforded needles of 1-*O*-methyl-D-mannitol pentanitrate; yield 0.11 g. (13%), m.p. 112–113°, alone or on admixture with the sample prepared as described below, $[\alpha]^{25}_{D}$ +30.7° (*c* 2.014, acetone).

Anal. Calcd. for $C_7H_{11}N_5O_{16}$: C, 19.96; H, 2.63; N, 16.63. Found: C, 19.88; H, 2.62; N, 16.38.

Preparation of 1-*O*-Methyl-D-mannitol.—Sucrose was converted to 2,3:4,5-di-*O*-isopropylidene-D-fructopyranose[23]; yield 57%, m.p. 98–99°.

This compound was methylated, in tetrahydrofuran solution, with dimethyl sulfate and sodium hydroxide by the general methylation procedure of Falconer and Adams[24] to give 1-*O*-methyl-2,3:4,5-di-*O*-isopropylidene-D-fructopyranose; yield 86%, m.p. 48–48.5°. Glen, Myers and Grant[23] report m.p. 48–48.5°.

Hydrolysis of this compound with 0.1 *N* sulfuric acid afforded 1-*O*-methyl-D-fructose[25] as a sirup which was boiled with Raney nickel in 70% ethanol to give 1-*O*-methyl-D-mannitol[25]; yield 19%, m.p. 121–122°. Bayne and Wildy[25] record m.p. 119°.

1-*O*-**Methyl-D-fructose 2,4-Dinitropyenylhydrazone.**—A solution of equimolecular amounts of 1-*O*-methyl-D-fructose and 2,4-dinitrophenylhydrazine in abs. ethanol was refluxed for 3 hr. and the product obtained on cooling was filtered and recrystallized twice from ethyl acetate–*n*-hexane; m.p. 185–187°.

Anal. Calcd. for $C_{13}H_{18}N_4O_9$: C, 41.71; H, 4.85; N, 14.97. Found: C, 41.87; H, 4.99; N, 14.90

1-*O*-**Methyl-D-mannitol Pentanitrate.**—Nitration of 3.51 g. of 1-*O*-methyl-D-mannitol by the procedure employed to make 3-*O*-allyl-D-mannitol pentanitrate afforded a crude solid; yield 6.28 g. (83%). This product was recrystallized from aqueous methanol as needles; yield 4.99 g. (66%), m.p. 112–113°, $[\alpha]^{24}_{D}$ +30.7° (*c* 4.333, acetone).

Preparation of 3-*O*-Acetyl-D-mannitol Pentanitrate.—A solution of 48.8 g. (0.12 mole) of D-mannitol 1,2,3,5,6-pentanitrate and 18.4 g. (0.18 mole) of acetic anhydride in 80 ml. of pyridine was kept at 0° for 13 hr. The reaction solution was poured into ice and water and the resulting solid was washed with water and then recrystallized from aqueous methanol to give clustered needles; yield 48.0 g. (89%), m.p. 83–84°, $[\alpha]^{20}_{D}$ +56.6° (*c* 2.11, chloroform). Elrick, Marans and Preckel[6] report m.p. 77–78° on the product obtained by reaction of D-mannitol 1,2,3,5,6-pentanitrate with acetyl chloride.

Anal. Calcd. for $C_8H_{11}N_5O_{17}$: C, 21.39; H, 2.47; N, 15.59. Found: C, 21.36; H, 2.36; N, 15.42.

Preparation of 3-*O*-Propionyl-D-mannitol Pentanitrate.—The above procedure was employed with propionic anhydride in place of acetic anhydride. The product was recrystallized from aqueous methanol to afford clustered needles; yield 82%, m.p. 71–72°, $[\alpha]^{25}_{D}$ +56.5° (*c* 3.12, chloroform). Elrick, Marans and Preckel[6] report m.p. 65–68° on the product obtained by reaction of D-mannitol 1,2,3,5,6-pentanitrate with propionyl chloride.

Anal. Calcd. for $C_9H_{13}N_5O_{17}$: C, 23.33; H, 2.83; N, 15.12. Found: C, 23.22; H, 2.80; N, 14.90.

Hydrogenation of 3-*O*-Acetyl-D-mannitol Pentanitrate.—A solution of 6.0 g. of 3-*O*-acetyl-D-mannitol pentanitrate in 250 ml. of abs. ethanol was hydrogenated in the Parr apparatus at 3 atm. for 4 hr. using 0.3 g. of 10% palladium-on-charcoal.[22] The solution was filtered and the filtrate was evaporated to a solid which was dissolved in 35 ml. of 0.005 *N* aqueous sodium hydroxide and this solution was left for 14 hr. at room temperature and then evaporated. The residue was repeatedly dissolved in abs. ethanol and the solution was evaporated to remove traces of moisture. Recrystallization from ethanol afforded 1.74 g. of 1-*O*-acetyl-D-mannitol., m.p. 120–122°. The mother liquor was evaporated to a sirup which was treated with 35 ml. of 0.005 *N* aqueous sodium hydroxide, as described above. This afforded 0.62 g. of 1-*O*-acetyl-D-mannitol, m.p. 120–122°; total yield

---

[21] An organic peroxide, a product of Wallace and Tiernan, Inc., Buffalo 5, N. Y.

[22] Mathieson, Coleman and Bell Division of the Mathieson Co., Inc., Norwood, Ohio.

[23] W. L. Glen, G. S. Myers and G. A. Grant, *J. Chem. Soc.*, 2568 (1951); M. L. Wolfrom, W. L. Shilling and W. W. Binkley, THIS JOURNAL, **72**, 4544 (1950).

[24] E. L. Falconer and G. A. Adams, *Can. J. Chem.* **34**, 338 (1956).

[25] S. Bayne and J. Wildy *J. Chem. Soc.*, 1147 (1954).

2.36 g. (79%). The melting point of this product was undepressed on admixture with an authentic sample (m.p. 123–124°) kindly supplied by Dr. B. Lindberg, $[\alpha]^{24}$D +4.8° (*c* 6.809, water). Lindberg[8] reports m.p. 124–125°, $[\alpha]^{20}$D +5° (*c* 2, water). Variable and unreproducible results were obtained on omission of the above treatment with mild alkali.

1-*O*-Acetyl-D-mannitol Pentanitrate.—Nitration of 2.24 g. of 1-*O*-acetyl-D-mannitol by the method described for the preparation of 1-*O*-propionyl-D-mannitol pentanitrate afforded a crude solid; yield 4.24 g. (93%). This was recrystallized from ethanol–acetone to provide a pure product; yield 3.31 g. (74%), m.p. 147–148°, $[\alpha]^{24}$D +31° (*c* 2.25, acetone).

Anal. Calcd. for $C_8H_{11}N_5O_{17}$: C, 21.39; H, 2.47; N, 15.59. Found: C, 21.38; H, 2.69; N, 15.69.

This pentanitrate (1.5 g.) was carried through the sequence of reactions employed for the preparation of 1-*O*-methyl-D-mannitol pentanitrate from 1-*O*-propionyl-D-mannitol pentanitrate; 0.19 g. (14%) of the methyl derivative was obtained.

Hydrogenation of 1-*O*-Acetyl-D-mannitol Pentanitrate.—One gram of 1-*O*-acetyl-D-mannitol pentanitrate was hydrogenated by the procedure employed for 3-*O*-acetyl-D-mannitol pentanitrate, except that the treatment with alkali was omitted. The product was 1-*O*-acetyl-D-mannitol; yield 0.39 g. (78%), m.p. 123–124°, alone or on admixture with an authentic sample, $[\alpha]^{25}$D +4.9° (*c* 5.16, water.).

Hydrogenation of 3-*O*-Propionyl-D-mannitol Pentanitrate.—The reaction was carried out as described for 3-*O*-acetyl-D-mannitol pentanitrate. The crude product had m.p. 105–107°, yield 77%. Recrystallization from ethanol afforded pure 1-*O*-propionyl-D-mannitol, m.p. 115–116°, $[\alpha]^{23}$D +4.2° (*c* 4.27, water).

3-*O*-*n*-Propyl-D-mannitol. (a).—Hydrogenation of 10 g. of 3-*O*-allyl-D-mannitol pentanitrate by the procedure used above in the reductive denitration of 1-*O*-acetyl-D-mannitol pentanitrate afforded 3-*O*-*n*-propyl-D-mannitol as a solid which was recrystallized from ethanol; yield 4.1 g. (82%), m.p. 140–141°, $[\alpha]^{19}$D +21° (*c* 3.76, water).

Anal. Calcd. for $C_9H_{20}O_6$: C, 48.20; H, 8.99. Found: C, 48.37; H, 8.92.

(b).—Four grams of 3-*O*-allyl-D-mannitol was treated as in method **a** to provide a crude product; yield 3.7 g. (92%), m.p. 131–136°. Recrystallization from ethanol and then water afforded the pure compound, m.p. 140–141° alone or on admixture with the previous sample.

(c).—A solution of 1.79 g. (4 mmoles) of 3-*O*-allyl-D-mannitol pentanitrate and 2.0 g. (40 mmoles) of 100% hydrazine hydrate in 20 ml. of ethanol was boiled under reflux for 90 min. The solution was then boiled with Raney nickel for 15 min., filtered and the filtrate was evaporated to a solid. Recrystallization from ethanol afforded 3-*O*-*n*-propyl-D-mannitol; yield 0.44 g. (49%), m.p. 139–140°, undepressed on admixture with the previous sample.

3-*O*-Benzoyl-D-mannitol Pentanitrate.—Benzoyl chloride (25 ml.) was cooled to 0° and 8.0 g. of solid D-mannitol 1,2,3,5,6-pentanitrate was added slowly under stirring. Stirring was maintained at room temperature for 30 hr. and the solution was then poured into 350 ml. of saturated aqueous sodium bicarbonate. The aqueous mixture was stirred for 24 hr. and then extracted with chloroform. The chloroform solution was washed repeatedly with saturated aqueous sodium bicarbonate and subsequently with water. The sirup obtained on chloroform removal was dissolved in warm aqueous ethanol. Cooling afforded an oil which crystallized on standing for six weeks at 5°; yield 4.1 g. (45%), m.p. 64.0–64.5° after another crystallization from ethanol–water, $[\alpha]^{19}$D +60° (*c* 5.23, ethanol).

Anal. Calcd. for $C_{13}H_{13}N_5O_{17}$: C, 30.54; H, 2.56; N, 13.70. Found: C, 30.65; H, 2.71; N, 13.86.

Hydrogenation of 3-*O*-Benzoyl-D-mannitol Pentanitrate.—This reduction was carried out with 2.3 g. of the benzoate ester employing the method (without alkali treatment) used for the aliphatic acyl derivatives. There was obtained a white crystalline substance; yield 1.05 g. (82%). Pure material was obtained on recrystallization from ethanol–ether, m.p. 121–122°, $[\alpha]^{16}$D +9° (*c* 5.22, ethanol).

Anal. Calcd. for $C_{13}H_{18}O_7$: C, 54.54; H, 6.34. Found: C, 54.60; H, 6.19.

Since nitration of this material afforded (below) a pentanitrate convertible to 1-*O*-methyl-D-mannitol pentanitrate, this substance is 1-*O*-benzoyl-D-mannitol.

1-*O*-Benzoyl-D-mannitol Pentanitrate.—The 1-*O*-benzoyl-D-mannitol (0.5 g.) was added to 25 ml. of cold absolute nitric acid. The solution was stirred for 2 hr. at 0° and poured into water. The aqueous mixture was extracted with ether and the ether extract was washed successively with water, saturated aqueous sodium bicarbonate and again with water. Evaporation of the ether afforded a sirup which was dissolved at room temperature in aqueous ethanol. Cooling produced an oil which slowly crystallized. Two crystallizations from aqueous ethanol gave pure 1-*O*-benzoyl-D-mannitol pentanitrate; yield 0.08 g. (9%), m.p. 82–83°, $[\alpha]^{23}$D +49° (*c* 1.47 ethanol). This nitrate depressed the melting point of 3-*O*-benzoyl-D-mannitol pentanitrate.

Anal. Calcd. for $C_{13}H_{13}N_5O_{17}$: C, 30.54; H, 2.56; N, 13.70. Found: C, 30.33; H, 2.59; N, 13.72.

An additional quantity (0.8 g.) of the 1-*O*-benzoyl-D-mannitol pentanitrate was prepared and converted to 1-*O*-methyl-D-mannitol pentanitrate as described for the characterization of 1-*O*-propionyl-D-mannitol pentanitrate; yield 29%.

Catalytic Reduction Under Acidic Conditions.—Reduction of the 3-*O*-acetyl-, 3-*O*-propionyl- and 3-*O*-benzoyl-D-mannitol pentanitrates under conditions equivalent to those described above, except that benzoic acid (weight equal to nitrate taken) was added to the mixture prior to reduction, afforded sirups (85–90% yields) that failed to crystallize. These were shown to be the corresponding 3-*O*-acyl-D-mannitol derivatives by nitration with absolute nitric acid in acetic anhydride. The original 3-*O*-acyl-D-mannitol pentanitrates were recovered in 75 to 80% yields.

1,4:3,6-Dianhydro-D-mannitol 2,5-Dinitrate.—A suspension of 10 g. of 1,6-dichloro-1,6-dideoxy-D-mannitol[11] in acetonitrile (75 ml.) was stirred and 40 g. of silver nitrate in 50 ml. of acetonitrile was added. The mixture was refluxed for 80 hr., cooled and filtered from the insoluble material. The solid was a mixture of silver chloride (51%) and unreacted starting material (35%) which latter was isolated by hot water extraction and crystallization (on cooling). The filtrate was poured into ether and water (200 ml. each) and the resulting ether layer was extracted five times with an equal volume of water. The sirup obtained on evaporation of the ether was dissolved in warm ethanol and water was added to incipient turbidity; yield 3.1 g. (29%) of 1,4:3,6-dianhydro-D-mannitol 2,5-dinitrate, m.p. 66–67° undepressed on addition of authentic material,[12] $[\alpha]^{22}$D +304° (*c* 0.5, acetonitrile). Further identification was effected by reduction with hydrogen over 10% palladium-on-charcoal which afforded 1,4:3,6-dianhydro-D-mannitol; yield 87%, m.p. 87–88° unchanged on addition of an authentic sample.[26]

Preparation of 1,6-Dichloro-1,6-dideoxy-D-mannitol Tetranitrate.—This compound, first reported over eighty years ago,[27] was prepared by modern methods. An amount of 2.0 g. of 1,6-dichloro-1,6-dideoxy-D-mannitol[11] was added to abs. nitric acid (40 ml.) at 0°. The heterogeneous mixture was stirred (0°) for 2 hr. and was then poured into ice and water (300 ml.). The precipitated solid was filtered, washed with water and crystallized twice from acetone–water; yield 1.4 g. (31%), m.p. 145–146° (145°[27]), $[\alpha]^{25}$D +18° (*c* 1.0, acetonitrile).

Anal. Calcd. for $C_6H_8Cl_2N_4O_{12}$: C, 18.06; H, 2.02; Cl, 17.77; N, 14.04. Found: C, 18.23; H, 2.37; Cl, 17.73; N, 13.84.

Reduction of this tetranitrate with hydrogen over palladium-on-charcoal afforded 1,6-dichloro-1,6-dideoxy-D-mannitol in 91% yield.

Action of Acids and Bases on Various Derivatives of D-Mannitol 1,2,3,5,6-Pentanitrate.—The reaction of pyridine,[5] aqueous acetone containing ammonium carbonate[6] or sodium hydroxide in aqueous acetone with 3-*O*-allyl- and the 3-*O*-acyl derivatives of D-mannitol 1,2,3,5,6-pentanitrate was investigated. In every case, the only crystalline products obtained were the respective starting materials in 40–80% yields. In addition, varying amounts of non-crystallizable materials were obtained. Since these attempts did not appear to afford either new partially substituted D-mannitol derivatives or the known pentanitrate, as specific high yield reaction products, no further investigation was undertaken. Similar results were reported[5] for 3-*O*-methyl-D-mannitol pentanitrate.

---

(26) A. Fauconnier, *Bull. soc. chim. France*, [2] **41**, 119 (1884).

(27) G. Bouchardat, *Ann. chim. phys.*, [5] **6**, 126 (1875).

D-Mannitol hexanitrate was treated with either triethylamine or N,N-dimethylaniline following the Hayward pyridine denitration technique.[5] Triethylamine effected a vigorous reaction that teminated in a fire. Dilution of the system with acetonitrile was employed to moderate the reaction but no crystalline products were obtained. In contrast, N,N-dimethylaniline diluted with acetonitrile afforded D-mannitol hexanitrate in 60% yield as the only crystalline product. In view of the diversity of the two bases (above) which effect the denitration in high yield, these results are surprising.

Solutions of either 3-*O*-allyl- or 3-*O*-propionyl-D-mannitol in ethanol containing twice their weight of *p*-toluenesulfonic acid were stirred at room temperature for 20 hr. Cooling and adding water in each case afforded the unchanged starting material quantitatively.

Columbus 10, Ohio

[Contribution from the Department of Chemistry of The Ohio State University]

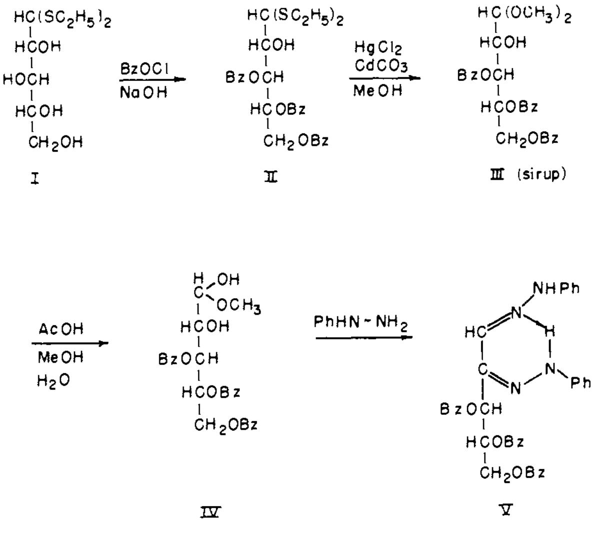
3,4,5-Tri-*O*-benzoyl-D-xylose Dimethyl Acetal[1]

By M. L. Wolfrom and Walter von Bebenburg

Received May 28, 1959

D-Xylose diethyl dithioacetal was partially benzoylated to form a tribenzoate followed by successive conversion of the diethyl dithioacetal to the dimethyl acetal tribenzoate and the methyl hemiacetal tribenzoate. The latter substance produced a phenylosazone, without loss of benzoyl groups, identical with the product of benzoylation of D-xylose phenylosazone, indicating that carbon two in the members of this series was unbenzoylated.

3,4,5,6-Tetra-*O*-benzoyl-D-glucose diethyl dithioacetal[2] has been prepared by the partial benzoylation of D-glucose diethyl dithioacetal. The free hydroxyl group was substituted by a thioethoxyl group[3] which after demercaptalation and debenzoylation[4] produced D-*arabino*-hexose (D-glucose) phenylosazone indicating that the unsubstituted hydroxyl group was on carbon two. Since the pentose D-xylose possesses the same configuration as D-glucose for the two centers below the carbonyl group, it was considered that the extension of this reaction to D-xylose would be feasible. D-Xylose diethyl dithioacetal (I) was partially benzoylated to produce 3,4,5-tri-*O*-benzoyl-D-xylose diethyl dithioacetal (II). The diethyl dithioacetal (II) was converted[5] successively to the sirupy dimethyl acetal III, the crystalline methyl hemiacetal IV and the crystalline phenylosazone without loss of a benzoyl group, indicating that the free hydroxyl group is at carbon two.



Bz = benzoyl; Ph = phenyl

Acknowledgment.—The counsel and assistance of Doctors F. Shafizadeh and A. Thompson is gratefully acknowledged.

Experimental

3,4,5-Tri-*O*-benzoyl-D-xylose Diethyl Dithioacetal (II).—D-Xylose diethyl dithioacetal[6] (I, 90 g., 0.35 mole) was dissolved at 0° in 1500 ml. of 2 *N* sodium hydroxide. A solution of 160 g. (1.15 mole) of benzoyl chloride in 600 ml. of chloroform was added portionwise with vigorous stirring and cooling in an ice–salt-bath so that the temperature did not exceed 10°. After the addition, stirring was continued for 30 min. The chloroform layer was washed several times with water and dried with anhydrous sodium sulfate. The chloroform was evaporated under reduced pressure and the sirupy residue was dissolved in 500 ml. of hot ethanol and 150 ml. of water added. Fine needles separated and after standing for 24 hr. at room temperature, the mixture had completely solidified. The compound was recrystallized thrice from ethanol–water; yield 58 g. (29%), m.p. 138–140°, $[\alpha]^{20}\text{D}$ +6° (*c* 3, chloroform).

Anal. Calcd. for $C_{30}H_{32}O_7S_2$: C, 63.34; H, 5.67; S, 11.28. Found: C, 63.27; H, 5.61; S, 11.38.

3,4,5-Tri-*O*-benzoyl-*aldehydo*-D-xylose Methyl Hemiacetal (IV).—3,4,5-Tri-*O*-benzoyl-D-xylose diethyl dithioacetal (II, 10 g., 0.176 mole) was dissolved in 120 ml. of dry methanol in which 25 g. of dry cadmium carbonate was suspended and the mixture was heated to boiling. A solution of 45 g. of mercuric chloride in 100 ml. of methanol was added in portions with vigorous stirring. The mixture was refluxed for 4 hr. with the occasional addition of small amounts of cadmium carbonate. The solution was filtered into a flask containing 5 g. of cadmium carbonate, and the filtrate was evaporated to dryness under reduced pressure. The residue was extracted several times with chloroform. The combined chloroform extract was washed with potassium iodide solution, and water, dried with sodium sulfate and evaporated under reduced pressure to a sirup. This colorless sirup contained no sulfur and failed to crystallize after six months. This sirupy 3,4,5-tri-*O*-benzoyl-D-xylose dimethyl acetal (III, 2 g.) was dissolved in 100 ml. of methanol to which 1 ml. of acetic acid and 10 ml. of water were added, and the solution refluxed for 3 hr. A 50-ml. portion of this solution was diluted with 30 ml. of water. After standing overnight, crystalline material separated and was recrystallized twice from methanol; yield 750 mg., m.p. 131°, $[\alpha]^{30}\text{D}$ + 24 → −18° (*c* 0.7, methanol, 42 hr.).

---

(1) Supported by Grant No. CY-3232 from the Department of Health, Education and Welfare, Public Health Service, National Institutes of Health, Bethesda 14, Md.

(2) P. Brigl and H. Mühlschlegel, *Ber.*, **63**, 1551 (1930).

(3) P. Brigl, H. Mühlschlegel and R. Schinle, *ibid.*, **64**, 2921 (1931).

(4) P. Brigl and R. Schinle, *ibid.*, **65**, 1890 (1932).

(5) M. L. Wolfrom, L. J. Tanghe, R. W. George and S. W. Waisbrot, This Journal, **60**, 132 (1938).

(6) M. L. Wolfrom, Mildred R. Newlin and E. E. Stahly, *ibid.*, **53** 4379 (1931).