THE ACTION OF PYRIDINE ON DULCITOL HEXANITRATE[1]

By G. G. McKeown and L. D. Hayward

ABSTRACT

A pyridine solution of dulcitol hexanitrate evolved gas and became highly colored when warmed to 50°C.; dilution with water caused the precipitation of 67% of the theoretical amount of a dulcitol pentanitrate. The product was characterized as D,L-galactitol-1,2,4,5,6-pentanitrate by methylation to a monomethyl dulcitol pentanitrate, denitration of the latter, and periodate oxidation of the monomethyl dulcitol obtained. The hexitol derivatives were all obtained in a pure crystalline form. The significance of the data now available on the selective partial denitration by pyridine of hexitol hexanitrates is briefly discussed.

INTRODUCTION

In a previous research (5) it was shown that excess pyridine at 35°C. selectively removed the third (or equivalent fourth) nitrate group from D-mannitol hexanitrate to give D-mannitol-1,2,3,5,6-pentanitrate in 73% yield. This reaction was first described in 1903 by Wigner (14) who also reported a good yield of a mannitol pentanitrate from the action of alcoholic pyridine on mannitol hexanitrate. Wigner also nitrated dulcitol (I) to obtain a hexanitrate melting at "about 95°" (3, 4, 13) and found that alcoholic pyridine had almost no effect on this product even at the boiling point. Warming a solution of the dulcitol hexanitrate in pure pyridine, however, caused a reaction accompanied by evolution of a gas, and, on pouring the reaction mixture into water, Wigner obtained a crystalline product which "sintered at 71° and melted at about 75°" after three recrystallizations from aqueous alcohol. Analysis indicated this product to be a dulcitol pentanitrate.

In the present research Wigner's results were confirmed and the dulcitol pentanitrate was characterized as the racemic D- and L-galactitol-1,2,4,5,6-pentanitrate (III) by a series of reactions parallel to that previously described (5) for the characterization of D-mannitol-1,2,3,5,6-pentanitrate.

Dulcitol hexanitrate (D- or L-galactitol-1,2,3,4,5,6-hexanitrate) (II) was prepared in 92% yield by direct nitration of dulcitol (galactitol) (I) with nitric–sulphuric acid mixture, and the pure, crystalline, optically inactive compound melted at 98–99°C. and had the correct nitrate nitrogen content. Hydrogenolysis of a sample of the hexanitrate produced dulcitol quantitatively (5, 6). The hexanitrate dissolved readily in pure pyridine at 30°C. to give an initially colorless solution which became orange-colored in five minutes. No gas evolution was observed until the solution was warmed to 50°C., whereupon an exothermic reaction commenced, brown fumes were observed in the open vessel, and fine, colorless, needle-like crystals appeared on the inner walls of the flask above the solution. The vigorous reaction subsided within a few minutes and after 24 hr. the dark-red solution was poured into

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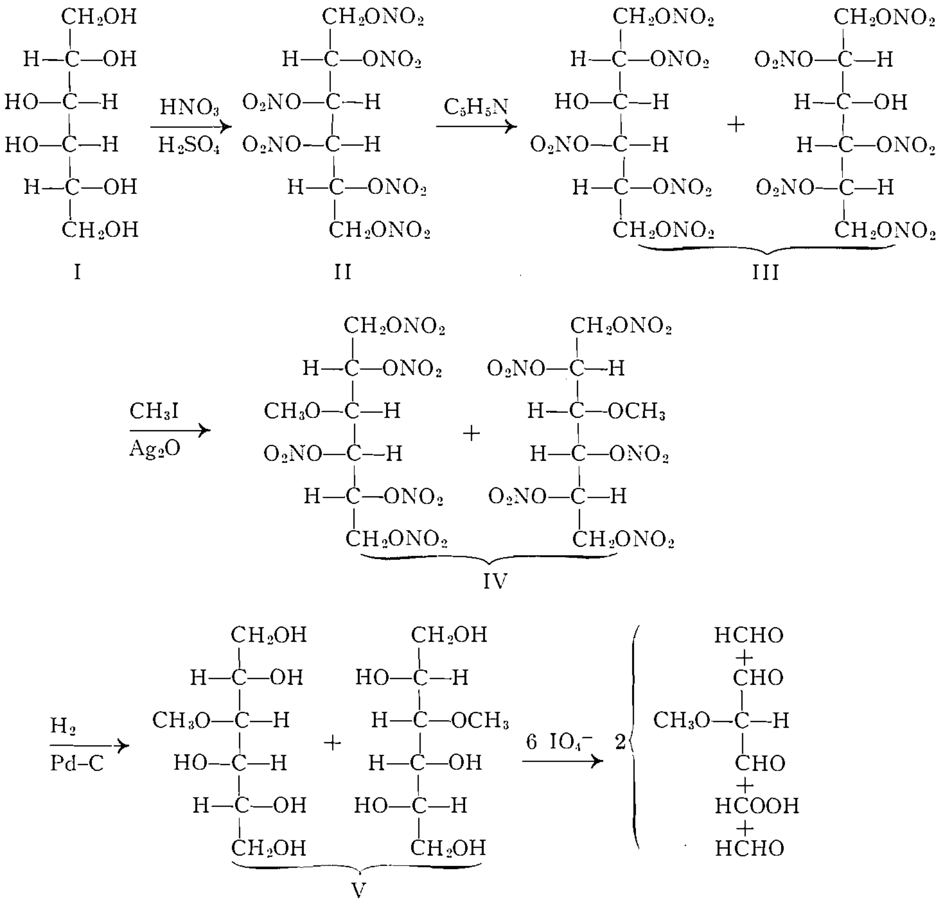
water which caused the separation of crystalline dulcitol pentanitrate (III) in 63–72% yield. The pure pentanitrate melted at 85–86°, was optically inactive, and did not reduce Fehling's solution (13). Hydrogenolysis again gave a nearly quantitative yield of dulcitol thus proving that the pyridine caused no structural or configurational changes in the hexitol skeleton. The pentanitrate was stable to the further action of pyridine under conditions which caused the partial denitration of the hexanitrate.



I II III IV V

II or III $\xrightarrow{H_2,\ Pd\text{-}C}$ I (quantitative) III + C_5H_5N $\longrightarrow$ 94% recovery

V $\xrightarrow[H_2SO_4]{HNO_3}$ IV (75%) IV + C_5H_5N $\longrightarrow$ 89% recovery

Methylation of the pentanitrate gave a 67% yield of a new methyl dulcitol pentanitrate (IV), m.p. 99–100°C., with correct methoxyl and nitrogen analyses and this compound was also stable to pyridine at room temperature. Catalytic hydrogenolysis of the methylated pentanitrate yielded a crystalline monomethyl dulcitol (V) melting at 149–150°. A sample of (V) was renitrated with mixed acids at −10°C. to give a 75% yield of the original methyl dulcitol pentanitrate (IV).

A literature search revealed no previous report of monomethyl derivatives of dulcitol and, apart from an independent synthesis, periodate oxidation appeared to be the most reliable means of locating the position of the methyl group. Taking account of the meso configuration of dulcitol our monomethyl hexitol was one of three possible compounds: a racemate of (1) D- and L-1-*O*-methyl galactitol, (2) D- and L-2-*O*-methyl galactitol, or (3) D- and L-3-*O*-methyl galactitol. The theoretical behavior of these compounds toward periodate oxidation is summarized in Table I.

TABLE I

THEORETICAL PRODUCTS OF THE PERIODATE OXIDATION OF HEXITOL MONOMETHYL ETHERS

	Position of OCH_3 group	Periodate consumed (moles)	Oxidation products (moles)		
			HCHO	HCOOH	Other
Case 1	1 or 6*	4	1	3	CHO | CH_2OCH_3
Case 2	2 or 5*	3	1	2	CH_2OH | $H—C—OCH_3$ | CHO
Case 3	3 or 4*	3	2	1	CHO | $H—C—OCH_3$ | CHO

**Pairs of structural isomers although each compound has a unique configuration. Of the mannitol and iditol derivatives only one compound of the* D-*configuration and one of the* L-*configuration can exist in each case. For dulcitol and allitol derivatives the pair in each case is racemic.*

Oxidation of the monomethyl dulcitol with aqueous sodium periodate at room temperature showed a consumption of 4.9 moles of oxidant with the production of 2.1 moles of formic acid and 2.0 moles of formaldehyde per mole of methyl ether. Dulcitol under the same conditions gave the nearly theoretical values of consumption of oxidant (4.95 moles), formic acid (3.68 moles), and formaldehyde (1.98 moles). Comparison of the results for the monomethyl dulcitol with Table I showed Case 1 to be ruled out and that either Case 2 or Case 3 could have given these values if an additional oxidation requiring 2 moles of oxidant occurred with the concomitant formation of an extra mole of formaldehyde or of formic acid respectively. The rate of the periodate oxidation was therefore studied to determine the possibility of "overoxidation" at room temperature. The rates of oxidant consumption, and aldehyde and acid production at 23°C. for the monomethyl dulcitol (Fig. 1, Curves A, B, and C) indicated a rapid initial consumption of 3 moles of oxidant producing 2 moles of formaldehyde and approximately 1 mole of formic acid. The results at this stage conformed to Case 3. An hour later the aldehyde value was the same but the amount of formic acid had increased to 2 moles and that of oxidant consumed to 5. A rate reaction run at 0°C. (Fig. 1, Curve D) in order to slow or halt the overoxidation clearly showed the rapid initial formation of 1 mole of formic acid followed by a slower secondary oxidation in which further quantities of acid were produced to the final total of 2.0 moles of acid at 11 hr. These data indicated Case 3 to be involved and that the dialdehyde formed (Table I) in the first stages of the oxidation was oxidized further to produce a mole of formic or other acid. A similar reaction of the dialdehyde of malonic acid (VII) was reported by Huebner, Ames, and Bubl (7) in which 3 moles of formic acid was produced with oxidant consumption of 3 moles. The methyl ester of glyoxylic acid (VI) presumably formed in Case 3 could be expected to be comparatively stable to further oxidation. The unique correlation of the periodate oxidation data was for the monomethyl dulcitol to be the racemate,

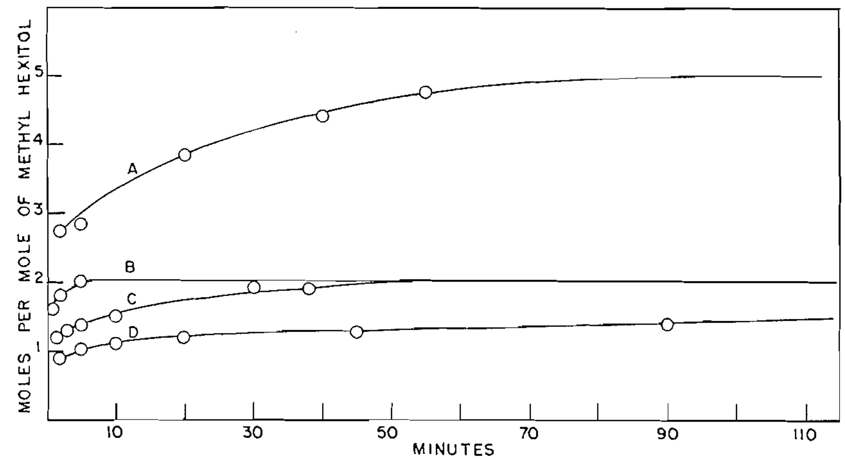
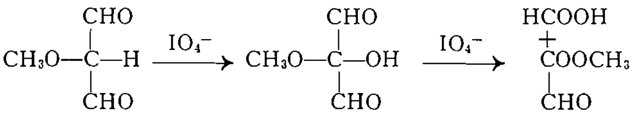
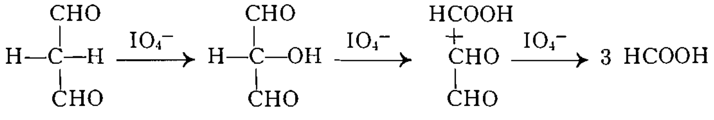


FIG. 1. Periodate oxidation of 3-*O*-methyl-D,L-galactitol.
A: Periodate consumption at 23°C.
B: Formaldehyde production at 23°C.
C: Formic acid production at 23°C.
D: Formic acid production at 0°C.



$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{CH_3O{-}C{-}H}\\|\\\mathrm{CHO}\end{array}\xrightarrow{\mathrm{IO_4^-}}\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{CH_3O{-}C{-}OH}\\|\\\mathrm{CHO}\end{array}\xrightarrow{\mathrm{IO_4^-}}\begin{array}{c}\mathrm{HCOOH}\\+\\\mathrm{COOCH_3}\\|\\\mathrm{CHO}\end{array}$$

VI



$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{H{-}C{-}H}\\|\\\mathrm{CHO}\end{array}\xrightarrow{\mathrm{IO_4^-}}\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{H{-}C{-}OH}\\|\\\mathrm{CHO}\end{array}\xrightarrow{\mathrm{IO_4^-}}\begin{array}{c}\mathrm{HCOOH}\\+\\\mathrm{CHO}\\|\\\mathrm{CHO}\end{array}\xrightarrow{\mathrm{IO_4^-}}3\ \mathrm{HCOOH}$$

VII

3-*O*-methyl-D- and L-galactitol (V), and hence the structures and configurations of the compounds (III) and (IV) which preceded it were also established.

The reactions of mannitol and dulcitol hexanitrates with pyridine were analogous and consisted in the replacement of a nitric acid ester group by hydrogen at the 3 (or equivalent 4) position in about 70% of the hexanitrate molecules. No inversion of configuration occurred at the asymmetric center attached to the nitrate group and it may therefore be assumed that the O—N bond was cleaved through some type of nucleophilic attack of pyridine on the nitrate nitrogen (1, 2).

The selectivity of the reaction for one particular nitrate group among six in each molecule is intriguing. To test the hypothesis that this group must occupy a unique spatial environment we plan to treat the nitrates of other polyols with pyridine. Urbanski and Kwiatkowska (12) reported partial denitration of sorbitol hexanitrate when it was heated with alcoholic pyridine; however, the viscous product was not characterized.

EXPERIMENTAL

Materials and Methods

Since dulcitol hexanitrate and its partially nitrated derivatives are explosives (11), the scale of the preparations was restricted to 5 gm. or less and all evaporations were under reduced pressure with bath temperatures not exceeding 50°C.

Pure dulcitol (galactitol (I)) (m.p. 187–188°, optically inactive) (8) when nitrated with fuming nitric and concentrated sulphuric acids at −10°C., as described by Bechamp (3) and Patterson and Todd (9), gave a 92% yield of the crystalline dulcitol hexanitrate (II). After recrystallization from aqueous ethanol the colorless, needle-like crystals of hexanitrate were optically inactive and melted at 98–99°C. (corr.). The melting point was not altered by further recrystallizations. Previous workers (3, 13, 14) reported a melting point of 95°C. Found: N (nitrometer), 18.4, 18.8%. Calc. for $C_6H_8(NO_3)_6$: N, 18.6%. Hydrogenolysis of 0.685 gm. of the hexanitrate over palladized charcoal at 20–30 p.s.i. and room temperature as previously described (5, 6) yielded 0.289 gm. of crude product. Recrystallization from aqueous ethanol gave thick, colorless crystals melting at 185–187°C. A mixed melting point with authentic dulcitol showed no depression.

The analytical procedures for nitrate nitrogen, methoxyl, and periodate oxidation products were previously described (5, 6, 10).

Action of Pyridine on Dulcitol Hexanitrate

A 500 ml. Erlenmyer flask containing 3.11 gm. of pure dry dulcitol hexanitrate was immersed in a water-bath at 30°C. The hexanitrate dissolved immediately on addition of 25 ml. of pyridine (B.D.H. analytical reagent grade) to form a clear, colorless solution which became orange-colored within five minutes. No further change was observed until the water-bath was heated to 50°C. when the solution rapidly evolved small bubbles of gas and fine, colorless crystal-needles appeared on the neck of the flask. After the first vigorous reaction had subsided, the now dark-red solution was allowed to stand at room temperature for 24 hr. and was then poured with stirring into

300 ml. of water. The colorless sirup which separated crystallized readily and was recovered on a glass filter, washed thoroughly with water, and dried to constant weight *in vacuo*; yield 1.81 gm. (65%). Yields obtained in similar denitrations were 63, 65, 69, and 72%. Recrystallization of the product from aqueous ethanol, ether – petroleum ether, or carbon tetrachloride yielded colorless needles of pure dulcitol pentanitrate (D,L-galactitol-1,2,4,5,6-pentanitrate) (III); m.p. 85–86°C., optically inactive, soluble in alcohol, ether, benzene, and chloroform, insoluble in water and petroleum ether. The pentanitrate did not reduce Fehling's solution (13, 14). Found: N (nitrometer), 16.9, 17.0%. Calc. for $C_6H_8(OH)(NO_3)_5$: N, 17.2%.

A sample of the dulcitol pentanitrate (0.63 gm.) when treated with pyridine (4.0 ml.) under the conditions which caused denitration of the hexanitrate produced no gas, although the solution became dark-red in color. Unchanged pentanitrate, 0.59 gm. (94%), was recovered when the solution was worked up as described above. A 0.240 gm. sample of dulcitol pentanitrate yielded 0.110 gm. (100%) of crude dulcitol when hydrogenolyzed as described for the hexanitrate. The pure product melted at 185–188°C. and caused no depression in the melting point of pure dulcitol.

*Methyl Dulcitol Pentanitrate (3-O-Methyl-*D,L*-galactitol-1,2,4,5,6-pentanitrate) (IV)*

Dulcitol pentanitrate, 0.730 gm., was dissolved in 11 ml. of methyl iodide and 4 ml. of methanol and treated with 5 gm. of Drierite and 5 gm. of freshly-prepared silver oxide. After being refluxed for nine hours the mixture was filtered and the solids washed with dry acetone. Evaporation of the filtrate and washings and recrystallization of the colorless solid residue from aqueous ethanol yielded 0.508 gm. (67%) of monomethyl dulcitol pentanitrate (3-*O*-methyl-D,L-galactitol-1,2,4,5,6-pentanitrate) (IV); m.p. 99–100°C., soluble in alcohol, ether, acetone, and dioxane, insoluble in water. Found: N, 16.6, 16.5%; OCH_3, 7.34, 7.37%. Calc. for $C_6H_8(OCH_3)(NO_3)_5$: N, 16.6%; OCH_3, 7.37%. A sample of the methylated dulcitol pentanitrate was recovered unchanged in 89% yield from a pyridine solution after two days at room temperature.

*Monomethyl Dulcitol (3-O-Methyl-*D,L*-galactitol) (V)*

Monomethyl dulcitol pentanitrate, 1.42 gm., dissolved in 30 ml. dioxane diluted with 45 ml. ethanol and 5 ml. of water was hydrogenated at room temperature over 1 gm. of palladized charcoal at 45 p.s.i. After one hour the pressure became constant and the solution was free of nitrate by the diphenylamine test. The catalyst was filtered off, and evaporation of the solution left a colorless crystalline product. Recrystallization from boiling absolute alcohol gave 0.552 gm. (83%) of thick, colorless crystals; m.p. 149–150°C. Recrystallization from isoamyl alcohol or from water yielded the same product. Found: OCH_3, 16.1, 16.0%. Calc. for $C_6H_8(OCH_3)(OH)_5$: OCH_3, 15.8%. The monomethyl dulcitol did not react with Fehling's solution or bromine water.

Nitration of a sample of the monomethyl dulcitol with sulphuric–nitric acid mixture gave a 75% yield of the original 3-*O*-methyl-D,L-galactitol-

1,2,4,5,6-pentanitrate, identified by a mixed melting point and methoxyl analysis. Found: OCH_3, 7.39, 7.20%.

Periodate Oxidation of Monomethyl Dulcitol (*3-O-Methyl*-D,L-*galactitol*) (*V*)

Forty to fifty milligram samples of the monomethyl dulcitol were oxidized with aqueous sodium periodate solution by procedures previously described (6) which revealed the amount of periodate consumed and the amounts of formic acid and formaldehyde formed. At room temperature the amounts of formic acid obtained per mole of methyl dulcitol were 1.20, 1.30, 1.38, 1.51, 1.91, 2.06, and 2.11 moles after 1.5, 3, 5, 10, 38, 130, and 900 min. respectively. At 960 min. 4.93 moles of periodate had been consumed and at 1020 min. the formaldehyde production was found to be 1.98 moles. In two other runs under the same conditions the consumption of 2.76, 2.83, 3.86, 4.43, and 4.77 moles of periodate at 2, 5, 20, 40, and 55 min. was observed while the molar production of formaldehyde amounted to 1.61, 1.81, 2.02, 1.92, and 1.98 after 1, 2, 5, 30, and 1020 min. Oxidation of pure dulcitol under the same conditions formed 3.53, 3.63, and 3.68 moles of formic acid after 5, 15, and 25 hr. At 25 hr. the periodate consumption was found to be 4.95 moles and formaldehyde production 1.98 moles.

An oxidation of methyl dulcitol conducted in an ice bath revealed formic acid production as 0.91, 1.04, 1.12, 1.20, 1.27, 1.40, 1.70, 2.06, and 2.11 moles after 2, 5, 10, 20, 45, 90, 300, 660, and 1440 min.

The data for the oxidation of the monomethyl dulcitol are plotted in Fig. 1; theoretical values for the different structural isomers are listed in Table I.

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