most promising results were obtained with the petroleum ether solvent (above), but they could not be duplicated readily because of the volatility of the solvent and the formation of double fronts.

The tetra-*O*-methyl sugar fraction had $[\alpha]^{25}\text{D}$ +33° (*c* 2, H_2O) which indicated a 1:1 ratio of the two tetra-*O*-methylhexoses. The mixture (0.25 g.) was dissolved in 3 ml. of ethanol and refluxed for 6 hours with 0.2 ml. of aniline. The odor of aniline was still apparent, so 2 microliters of concd. HCl was added and the mixture refluxed briefly and allowed to stand overnight. It was evaporated to a sirup and extracted with a few ml. of ether. Petroleum ether was added to the ether solution until it became turbid and an oil formed. Crystals formed upon slow evaporation of the decanted supernatant solution and were recrystallized from an ether–petroleum ether mixture; m.p. and mixed m.p. with an authentic specimen of the N-phenylglycosylamine of 2,3,4,6-tetra-*O*-methyl-D-mannose was 143–144° (lit.[49] m.p. 144–145°).

(f) 2,3,4,6-Tetra-*O*-methyl-D-Glucose (R_g 1.00, solvent C).—The mother liquors from the above crystallization of the tetramethylmannose were evaporated and the solid residue recrystallized from petroleum ether. Only enough material was available for a single m.p. determination. The crystals melted at 134–136° which corresponded to the literature[50] value (137–138°) of the m.p. of the N-phenylglycosylamine of 2,3,4,6-tetra-*O*-methyl-D-glucose.

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SHELTON, WASH.

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[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DEPARTMENT, U. S. NAVAL POWDER FACTORY]

The Reaction of Sodium Borohydride with Glycosyl Nitrates as Compared to its Reaction with the Nitrate Esters of the Primary and Secondary Alcohol Groups of Sugars[1]

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It has been found that sodium borohydride will reduce 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl nitrate and 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl nitrate at room temperature to yield the corresponding 1,5-anhydro alcohol. The nitrate esters of the primary and secondary alcohol groups of a sugar were not reduced.

Numerous studies on the chemistry of the nitrate esters of the sugars indicate that the reactions that any particular nitrate ester will undergo depend upon the position of the ester in the sugar molecule, other chemical groups present and also perhaps the stereochemical configuration of the sugar. When methyl 4,6-*O*-ethylidene-β-D-glucopyranoside 2,3-dinitrate reacts with sodium iodide in acetone the 2-nitrate group is replaced by hydroxyl while the 3-nitrate group is not attacked.[2] Similarly, dimethylamine will replace the 3-nitrate group in 6-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose 3,5-dinitrate with a hydroxyl group but will not replace the 5-nitrate group.[3] Pyridine is also known to be selective in its reaction with nitrate groups. Only the 3- and 4-nitrate groups are replaced by hydroxyl groups when either galactitol or D-mannitol hexanitrate[4] is treated with pyridine. The action of acidic and alkaline conditions has also been investigated[5] and it would seem that although extensive degradation usually occurs, acidic or alkaline conditions are selective in their action on sugar nitrates. Reducing agents, such as zinc and acetic acid[6] and sodium amalgam,[7] have been used to reduce the nitrate group to the parent alcohol. Catalytic hydrogenation[8] is not considered to be selective in the reduction of nitrate esters. It is impossible to be certain of this, however, since the reported reductions have been carried out over extended periods of time and hence any preferential reaction with specific nitrate groups might not become apparent, particularly if selectivity is due to differences in the rates of reaction with specific nitrate groups.

Lithium aluminum hydride, although it readily reduces simple nitrate esters,[9] shows some indication of selectivity in the sugar series. Methyl 4,6-*O*-propylidene-α-D-glucopyranoside 2,3-dinitrate on reduction yielded 19% of the 3-nitrate but none of the 2-nitrate.[10] Similarly the reduction of methyl 4,6-*O*-ethylidene-β-D-glucopyranoside 2,3-dinitrate on treatment with lithium aluminum hydride yielded 3% of the 3-nitrate.[11]

Since sodium borohydride is in general more selective in its action than lithium aluminum hydride[12] it was suspected that sodium borohydride might show more selectivity in its reaction with nitrate esters of sugars. Knowledge of such selectivity in the reduction of nitrate groups could not only be applied to the synthesis of a particular sugar nitrate but

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[1] Published with the permission of the Bureau of Ordnance, Navy Department. The opinions and conclusions are those of the authors.

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could also assist in the identification of unknown sugar nitrates that might form, for example, during the acid or alkaline degradation of cellulose nitrate.

Initial experiments were performed to determine whether or not there was a difference in the ability of sodium borohydride to reduce the nitrate esters of the primary and secondary alcohol groups of the sugars and a glycosyl nitrate.

Accordingly, 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl nitrate was prepared by treating penta-*O*-acetyl-β-D-glucopyranose with fuming nitric acid.[13] The nitrate was then reduced with sodium borohydride in aqueous dioxane. Since no attempts were made to purify the sodium borohydride and the reaction of the aqueous dioxane solution was quite alkaline and hence could conceivably cause some deacetylation, the products of the reduction, after removal of the solvent by distillation under reduced pressure, were reacetylated. The reacetylated material was chromatographed[14] and found to consist of a major zone representing the major portion of the material which was identified as the tetraacetate of polygalitol (1,5-anhydro-D-glucitol).

2,3,4-Tri-*O*-acetyl-β-L-arabinopyranosyl nitrate was prepared by treating 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide with 99.6% nitric acid in the manner used for the preparation of the corresponding derivative of D-glucose.[13] The compound which we have not been able to find reported in the literature was nicely crystalline and melted at 95°. The large rotation (+199° in chloroform) indicates the β-configuration. Treatment of the 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl nitrate with sodium borohydride again led to the formation of the anhydro alcohol (1,5 anhydro-2,3,4-tri-*O*-acetyl-D-arabinitol).

The nitrate ester of a primary alcohol (methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside 6-nitrate) was not reduced upon treatment with sodium borohydride.

In order to study the action of sodium borohydride on the nitrate esters of secondary alcohols, apart from any possible influence of a nitrate ester on an adjacent primary alcohol group, 1,6-di-*O*-benzoyl-D-mannitol 2,3,4,5-tetranitrate was prepared by nitrating[15] 1,6-di-*O*-benzoyl-D-mannitol. 1,6-Di-*O*-benzoyl-D-mannitol 2,3,4,5-tetranitrate, which we were not able to find reported in the literature, was nicely crystalline and melted at 157°. After treatment with sodium borohydride the compound was recovered unchanged.

While it is recognized that the reduction of additional similar compounds should be investigated, it would seem at present that although glycosyl nitrates are reduced readily by sodium borohydride at room temperature, the nitrate esters of the primary and secondary alcohol groups in the sugar chain are not attacked.

The formation of the anhydro sugar alcohol by the reduction of the glycosyl nitrate may be analogous to the reduction of glycosyl bromides with lithium aluminum hydride.[16]

Experimental

Reduction of 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl Nitrate with Sodium Borohydride.—2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl nitrate was prepared from penta-*O*-acetyl-β-D-glucopyranose and 99.6% white, fuming nitric acid.[13]

An amount of 10 g. of the nitrate, 4 g. of sodium borohydride, 50 ml. of water and 50 ml. of *p*-dioxane was placed in a 250-ml. erlenmeyer flask, equipped with a mechanical stirrer and cooled one hour with ice-water. The mixture was stirred overnight at room temperature and then filtered, neutralized with glacial acetic acid and concentrated to dryness under reduced pressure. The residue was acetylated with 60 ml. of pyridine and 40 ml. of acetic anhydride and processed in the usual manner resulting in 5.1 g. of sirup. It had first been determined that 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl nitrate could be recovered unchanged from a pyridine solution.

The sirup was chromatographed, following the general directions of McNeely, Binkley and Wolfrom.[14] The sirup (5.1 g.) was dissolved in a small amount of benzene and placed on a Magnesol[17]–Celite[18] (5:1 by wt.) column (250 mm. × 75 mm.) and developed with 1500 ml. of a mixture of benzene and *t*-butyl alcohol (100:1 by volume). After the column was extruded and streaked with indicator (1% potassium permanganate in 10% sodium hydroxide),[14] two zones appeared. They were numbered from the bottom to the top of the column. Zone I, located 160–190 mm. from the top, was eluted with acetone and evaporated to a sirup (0.8 g.) under reduced pressure. The sirup did not crystallize.

Zone II, located 30–160 mm. from the top, was eluted with acetone, the eluate evaporated to a sirup (2.87 g.) and crystallized from a chilled ether–petroleum ether (b.p. 30–60°) solution; m.p. 62–100°. The crystals were washed with ether, retaining 0.04 g. of crystals, m.p. 95–97°, unchanged on admixture with D-glucitol hexaacetate. The ether solution was concentrated to a sirup, which was crystallized from a chilled ether solution; yield 1.37 g., m.p. 64–66°, $[\alpha]^{25}\mathrm{D}$ +42° ($CHCl_3$, *c* 3). The values for polygalitol tetraacetate (1,5-anhydro-D-glucitol tetraacetate) are m.p. 65–67° and 74–75°[19] (the substance is dimorphous), $[\alpha]^{25}\mathrm{D}$ +38.9°.

Anal. Calcd. for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07; CH_3CO, 12.04 ml. of 0.1 *N* NaOH per 100 mg. Found: C, 50.89; H, 6.08; CH_3CO, 12.00 ml.

The acetate was deacetylated by dissolving 0.8 g. of the substance in 20 ml. of methanol and adding 6 ml. of 0.2 *N* sodium methoxide to the solution. After a half-hour the solution was passed over Amberlite IR-120[20] and Duolite A-4.[21] The aqueous solution was concentrated to dryness under reduced pressure and the residue was crystallized from methanol; yield 0.24 g., m.p. 139–141°, $[\alpha]^{25}\mathrm{D}$ +43.5° (H_2O, *c* 1), in agreement with the published values for polygalitol.[19] The compound showed no depression in melting point on admixture with an authentic sample of polygalitol.

Preparation of 2,3,4-Tri-*O*-acetyl-β-L-arabinopyranosyl Nitrate.—2,3,4-Tri-*O*-acetyl-β-L-arabinopyranosyl bromide[22] was treated with 99.6% nitric acid, following the general directions of Koenigs and Knorr devised for the preparation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl nitrate.

An ice-cold solution of 200 ml. of chloroform–99.6% nitric acid solution (1:1 by vol.) was added to 5 g. of 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide dissolved in 30 ml. of chloroform. After 5 minutes, the solution was washed

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[21] A product of the Chemical Process Co., Redwood City, Calif.

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successively with ice water, sodium acetate, sodium bisulfite, sodium bicarbonate solutions and finally with ice-water. The chloroform solution was dried and concentrated under reduced pressure. The sirup crystallized from ether solution; yield 3.96 g., m.p. 95°, $[\alpha]^{25}\mathrm{D}$ +199° ($CHCl_3$, *c* 6).

Anal. Calcd. for $C_{11}H_{15}O_{10}N$: C, 41.13; H, 4.70; N, 4.36. Found: C, 40.90; H, 4.66; N, 4.20.

Reduction of 2,3,4-Tri-*O*-acetyl-β-L-arabinopyranosyl Nitrate.—2,3,4-Tri-*O*-acetyl-β-L-arabinopyranosyl nitrate (10 g.) was treated with sodium borohydride in the same manner as 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl nitrate. The sirup (3.42 g.) was chromatographed as described previously. Zone I, located 105–130 mm. from the top of the column, was eluted with acetone, evaporated to a sirup and crystallized from a cold ether–petroleum ether solution; yield 0.09 g. No further work was done on this material.

Zone II, located 20–60 mm. from the top, was eluted with acetone, evaporated to a sirup and crystallized from a cold ether–petroleum ether solution; yield 0.83 g. After recrystallization, the melting point was 50–52° and $[\alpha]^{25}\mathrm{D}$ +73.6° ($CHCl_3$, *c* 1.7). The melting point of 1,5 anhydro-2,3,4-tri-*O*-acetyl-D-arabinitol is 58°. Its rotation is −74.2° ($CHCl_3$).[23]

In another experiment, 6.36 g. of sirup, obtained from 10 g. of the nitrate, was chromatographed as described previously. Zone I, located 100–200 mm. from the top, yielded 0.5 g. of crystals from ether–petroleum ether solution. Zone II, located 45–100 mm. from the top, yielded 0.5 g. of crystals from ether–petroleum ether solution.

The crystals were combined and rechromatographed, as described previously. Zone I, located 80–100 mm. from the top, yielded 0.8 g. of crystals, m.p. 49–52° after several recrystallizations from ether–petroleum ether (b.p. 30–60°). Zone II, located 30–75 mm. from the top, yielded 0.20 g. of crystals from ether–petroleum ether solution. Its melting point was 74–75°, unchanged on admixture with a known sample of penta-*O*-acetyl-L-arabinitol.

The substance (0.4 g.) melting at 50–52° was deacetylated in the usual manner. The sirup was crystallized from an ethanol–ethyl acetate solution; yield 0.1 g., m.p. 95–96°, $[\alpha]^{25}\mathrm{D}$ +101° (H_2O, *c* 1.8). The accepted values for 1,5-anhydro-D-arabinitol are m.p. 96–97°, $[\alpha]^{25}\mathrm{D}$ −98.6° (H_2O).[23]

Attempted Reduction of Methyl 2,3,4-Tri-*O*-acetyl-α-D-glucopyranoside 6-Nitrate.—An amount of 5 g. of methyl-2,3,4-tri-*O*-acetyl-α-D-glucopyranoside 6-nitrate,[24] 25 ml. of *p*-dioxane, 25 ml. of water and 2 g. of sodium borohydride were combined and stirred at ice-water temperature for 8 hours and at room temperature overnight. Then the mixture was filtered, neutralized with glacial acetic acid and concentrated to dryness under reduced pressure. The residue was acetylated with 30 ml. of pyridine and 20 ml. of acetic anhydride. After 18 hours, the mixture was poured into ice-water. Crystals appeared which were filtered and recrystallized from ethanol; yield 4.51 g., m.p. 112°, unchanged on admixture with the starting material.

Preparation of 1,6-Di-*O*-benzoyl-D-mannitol 2,3,4,5-Tetranitrate.—1,6-Di-*O*-benzoyl-D-mannitol 2,3,4,5-tetranitrate was prepared by adding a cold solution of nitrating mixture consisting of 10 ml. of 99.6% nitric acid in 20 ml. of acetic anhydride[15] to 5 g. of 1,6-di-*O*-benzoyl-D-mannitol[25] dissolved in 10 ml. of chloroform and kept at ice-water temperature. After 10 minutes, the solution was poured into ice-water. Crystals which appeared were filtered and recrystallized from hot ethanol; yield, 2.3 g., m.p. 157°, $[\alpha]^{25}\mathrm{D}$ +29.7° ($CHCl_3$, *c* 0.5).

Anal. Calcd. for $C_{20}H_{18}O_{16}N_4$: C, 42.12; H, 3.21; N, 9.82. Found: C, 42.36; H, 3.21; N, 9.62.

When the compound was reduced catalytically with hydrogen in the presence of palladium-on-charcoal[8] it yielded 1,6-di-*O*-benzoyl-D-mannitol.

Attempted Reduction of 1,6-Di-*O*-benzoyl-D-mannitol 2,3,4,5-Tetranitrate with Sodium Borohydride.—An amount of 5 g. of 1,6-di-*O*-benzoyl-D-mannitol 2,3,4,5-tetranitrate, 45 ml. of *p*-dioxane, 25 ml. of water and 2 g. of sodium borohydride were combined and stirred at ice-water temperature. After 6 hours, the mixture was filtered, neutralized with glacial acetic acid and refiltered. The filtrate was concentrated to dryness under reduced pressure below 40°. The residue was filtered with the aid of water and the residue was crystallized from hot ethanol; yield 3.61 g. (crude, after recrystallization the yield was 2.0 g.), m.p. 157° unchanged on admixture with the starting material.

Acknowledgment.—We wish to thank Dr. N. K. Richtmyer for the sample of polygalitol and Mrs. P. P. Wheeler for the elementary analyses.

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[Contribution from the Chemical Laboratories of Northwestern University]

Nitrocoumarans

By Charles D. Hurd and Rostyslaw Dowbenko[1]

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A number of alkyl substituted coumarans have been nitrated to give dinitrocoumarans. A phenyl substituted coumaran yielded a trinitro compound. Degradation of the nitration product of 2-methylcoumaran afforded evidence that the nitro groups were in the 5,7-positions.

In connection with other work[2] done in these laboratories a need arose for crystalline, easily accessible derivatives of alkyl and aryl substituted coumarans (2,3-dihydrobenzofurans) suitable for their characterization. Nitro derivatives seemed appropriate for this purpose. Curiously enough the literature has very little to say about nitration of coumarans or rules of orientation in this reaction.

Nitrocoumarans as a class of compound are virtually unknown. The only examples of nitration of coumarans are those reported by Arnold and McCool[3] and by Chatelus.[4] Arnold and McCool nitrated 5-acetamido-2-methylcoumaran expecting to obtain 5-acetamido-2-methyl-6-nitrocoumaran, but they obtained the 4-nitro derivative instead; on nitration of coumaran itself Chatelus obtained a dinitrocoumaran. The same author also nitrated chroman to obtain a dinitrochroman. He considered 6,8-dinitrochroman and 5,7-dinitrochroman as possible structures and preferred the former because of analogy to the nitration of tetralin. Assignment of structure to the nitration product of coumaran as 5,7-dinitrocoumaran then was made

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