ture (benzene–ethanol, 500:1 by vol.). The extruded column was streaked with a freshly prepared solution of alkaline potassium permanganate (0.1 g. of potassium permanganate, 1.0 g. of sodium hydroxide and 10 ml. of water). Four zones were detected and subsequently eluted from the sectioned adsorbent with acetone. The locations and yields of material from these zones were as follows: top zone, 0–5 mm. (distance from the top of the column), 53 mg.; zone one, 34–42 mm., 93 mg.; zone two, 54–65 mm., 93 mg.; zone three, 83–113 mm., 276 mg.; interzone one, 5–34 mm., 71 mg.; and interzone two, 113–132 mm., 3 mg. The total yield was 589 mg. The material in zone three crystallized. This material (200 mg.) was rechromatographed on a Magnesol column with 100 ml. of benzene–1-butanol (500:1 by vol.) as developer. The column was extruded, streaked, and eluted in the manner described previously. The zone material crystallized; yield 192 mg., m.p. 106–109° uncor. An X-ray powder diffraction pattern of the crystalline derivative was obtained using filtered CuKα radiation. The resulting pattern was compared and found to be identical with that of an authentic sample of α-D-glycopyranose pentaacetate.[27]

The Irradiation of Methyl α-D-Glucopyranoside.—Powdered samples of methyl α-D-glucopyranoside[28] were subjected to 1 to 8 intermittent dosages of irradiation, each of 13 megareps. During irradiation the samples were cooled by an ice–water-bath. The irradiated samples were dried under reduced pressure over phosphorus pentoxide at 20–25° for a period of 2 weeks. The degree of apparent hydrolysis (based on conversion to glucose) was determined by the copper-reduction method of Somogyi[21] (Fig. 3).

Samples of 50% aqueous mixtures of methyl α-D-glucopyranoside were irradiated as described above. Lyophilization of the irradiated samples yielded thin, brittle films which were ground into powders and dried under reduced pressure over phosphorus pentoxide at 20–25°. The degree of apparent hydrolysis was determined as described above and the data plotted in Fig. 3.

A descending paper chromatogram was made of two samples of irradiated methyl α-D-glucopyranoside in order to test for the presence of sugars. One of the two samples had been irradiated as a powder while the other had been irradiated as a 50% aqueous solution. Both samples had received 104 megareps of cathode irradiation while being cooled by an ice-water-bath. Aqueous solutions (2%) were prepared from the dried, irradiated samples and applied to a paper chromatogram according to previous directions. The chromatogram was developed for 40 hr. with 1-butanol–ethanol–water (40:11:19 by vol.), air-dried, and sprayed with *p*-anisidine hydrochloride. An examination of the developed paper chromatogram (Table II) revealed a single spot which was found to have an R_g-value[29] of unity.

Calculation of *G*-Values.—The *G*-values (the number of molecules decomposed per 100 e.v. of energy absorbed) were calculated as

$$G = \frac{(\text{fraction of sugar hydrolyzed})(6.02 \times 10^{23})(100)}{(\text{mol. wt. sugar})(\text{dose in megareps})(56 \times 10^{18}\ \text{e.v./g.-megareps})}$$

Acknowledgment.—The assistance of Dr. D. S. Miyada in preparing this manuscript is acknowledged.

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[27] M. L. Wolfrom and H. B. Wood, This Journal, **71**, 3175 (1949).

[28] A product of the Corn Products Refining Co., Argo, Illinois. This material was recrystallized from ethyl alcohol before use.

[29] A ratio of the relative mobility of the substance to D-glucose.

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

2,4-Dinitrophenyl Ethers of the Alditols[1]

By M. L. Wolfrom, B. O. Juliano, Madeline S. Toy and A. Chaney

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The facile formation of the fully substituted 2,4-dinitrophenyl ethers of a number of alditols and of *myo*-inositol has been demonstrated. These stable, crystalline derivatives possess sharp, characteristic melting points. Although several alternate methods for their preparation were explored, the method of choice involves the room temperature reaction of 2,4-dinitrofluorobenzene with the polyhydroxy compound in *N,N*-dimethylformamide solution in the presence of triethylamine.

Although the 2,4-dinitrophenyl ethers of a great number of monohydric alcohols and phenols have been described,[2,3] very little effort has been directed to the preparation of similar fully substituted derivatives of the polyhydric alcohols. Whalley[3] prepared the bis-(2,4-dinitrophenyl) ether of ethylene glycol, and the mono-(2,4-dinitrophenyl) ethers of ethylene glycol and glyceritol were synthesized by Blanksma and Fohr.[4] The extension of similar techniques to the preparation of fully substituted 2,4-dinitrophenyl ethers of polyhydroxy substances was undertaken in the hope that crystalline derivatives, useful for identification, would result or that the reagent of choice, 2,4-dinitrofluorobenzene, might exhibit selective reactivity toward different types of hydroxyl groups.

The reaction of a number of polyhydric alcohols (Table I) with 2,4-dinitrofluorobenzene dissolved in *N,N*-dimethylformamide occurred readily at room temperature. The addition of a base, triethylamine (preferable), alkali carbonate or bicarbonate was necessary. Otherwise, no ether derivative could be detected, even after extended reaction times, and the polyhydric alcohol could be recovered in high yield. The use of a 10% molar excess of 2,4-dinitrofluorobenzene sufficed to produce the fully substituted pure alditol ethers in 20 to 80% yields. Larger molar excesses of reagent would undoubtedly improve these yields but the reagent is relatively expensive. Slightly lower yields were obtained when the inorganic bases were employed. These bases reacted with the 2,4-dinitrofluorobenzene to form the alkali 2,4-dinitrophenoxide and were less effective than the tertiary amine in promoting the dissolution of the alditol. If the relative amount of 2,4-dinitrofluorobenzene and the reaction time were increased, equally good yields resulted on employing the

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[1] This work was carried out under contract between the Ordnance Corps (DA-33-019-ord-2025) and The Ohio State University Research Foundation (Project 675). The support of the supervising agency, the Ballistic Research Laboratories of Aberdeen Proving Ground, Md., and the inspiration of Dr. L. P. Kuhn are gratefully acknowledged. Preliminary communication: *Abstracts Papers Am. Chem. Soc.*, **134**, 11D (1958).

[2] J. D. Reinheimer, J. P. Douglass, H. Leister and Martha B. Voelkel, *J. Org. Chem.*, **22**, 1743 (1957); J. J. Blanksma and P. W. M. van der Weyden, *Rec. trav. chim.*, **59**, 629 (1940).

[3] W. B. Whalley, *J. Chem. Soc.*, 2241 (1950).

[4] J. J. Blanksma and P. G. Fohr, *Rec trav chim.*, **65**, 711 (1946).

TABLE I

POLYHYDROXY ALCOHOL 2,4-DINITROPHENYL ETHERS

Ether	Composition found, %[a] C	H	N	Powder pattern[b]	M.p., °C.[c]	$[\alpha]^{25}\mathrm{D}$[d]	Yield,[e] %
Tris-*O*-(2,4-dinitrophenyl)-glyceritol	42.39	2.28	14.44	4.46, 3.61, 5.23	182–183	.....	70
Tetrakis-*O*-(2,4-dinitrophenyl)-erythritol	42.63	2.45	14.31	3.57, 6.39, 5.58	280–281	.....	55
Pentakis-*O*-(2,4-dinitrophenyl)-D-arabinitol	...	..	14.15	7.42, 4.69, 3.75	148–150	−19.6°	40
Pentakis-*O*-(2,4-dinitrophenyl)-L-arabinitol	...	..	14.32	7.40, 4.68, 3.74	147–149	+18.2	45
Pentakis-*O*-(2,4-dinitrophenyl)-xylitol	42.60	2.42	14.31	13.0, 9.17, 3.67	151–153[f]	.....	71
Hexakis-*O*-(2,4-dinitrophenyl)-galactitol	...	..	13.95	6.13, 13.3, 4.09	326–328[g]	.....	70[h]
Hexakis-*O*-(2,4-dinitrophenyl)-D-glucitol	...	..	14.31	Amorphous	160–162	− 5.45	20
Hexakis-*O*-(2,4-dinitrophenyl)-D-mannitol	42.51	2.55	14.26	7.58, 5.10, 4.02	301–302[g]	− 5.54	81[i]
Hexakis-*O*-(2,4-dinitrophenyl)-*myo*-inositol	...	..	14.30	1.77, 2.65, 3.36	338–340[g]	.....	30[j]

[a] The calculated values for all of these derivatives are C, 42.75 ± 0.04; H, 2.31 ± 0.08; N, 14.26 ± 0.02. [b] The X-ray powder diffraction patterns were obtained (camera diameter, 114.59 mm.) using FeKα radiation. The calculated interplanar spacings (Å.) of the three strongest lines are cited in the order of their intensity except for the *myo*-inositol derivative for which the three lines cited were chosen empirically because the pattern was of poor contrast. [c] Melting points were taken with a Fisher–Johns apparatus. [d] The rotations were determined in *N*,*N*-dimethylformamide solution (*c* 1) with a Rudolph photoelectric polarimeter (model 200). [e] These yields are for pure ether; crude yields were nearly 100% in all cases; reaction conditions 24 hr. at room temperature using triethylamine catalyst; see Experimental section. [f] Dimorphous, solidification occurred at higher temperatures and final m.p. of 250–251° was observed. [g] Decomposition point. [h] Reaction time of 96 hr. was used because of the low solubility of galactitol in the reaction media. [i] This experiment employed 15 g. of D-mannitol; 1.0 g. of the alditol was taken in the others. [j] Reaction at 100° for 8 hr.

inorganic bases. If the reaction mixtures were heated, increased rates resulted but the isolation of the desired product was hampered by the formation of oily by-products.

The D-glucitol derivative was amorphous and the glyceritol triether had a light yellow color. Otherwise, the 2,4-dinitrophenyl ethers prepared (Table I) were white, sharp melting, crystalline solids and afforded well defined X-ray powder diffraction patterns. The infrared absorption spectra of the alditol 2,4-dinitrophenyl ethers (example, Fig. 1) were very similar. The differences were insufficient to permit use for identification of the parent alditol. In all cases, the absence of hydroxyl absorption confirmed the assignment of complete substitution indicated by the analytical data (Table I). The relative ease of formation of these completely substituted ether derivatives is in striking contrast to the difficulties encountered in the methylation of the alditols. Repeated treatments with the common methylating reagents are usually required to produce the fully substituted ethers.[5] The reasons for the contrast must rest in the nature of the carbon–fluorine bond in 2,4-dinitrofluorobenzene The courses of certain related aromatic nucleophilic displacement reactions have been investigated extensively by Bunnett.[6]

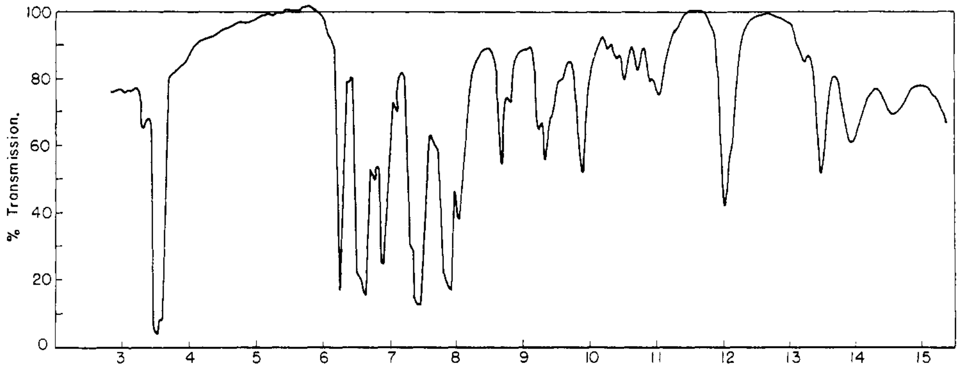

Fig. 1.—Infrared absorption spectrum of hexakis-*O*-(2,4-dinitrophenyl)-D-mannitol (Nujol mull).

Under the same conditions employed with 2,4-dinitrofluorobenzene, 2,4,6-trinitrofluorobenzene failed to afford the corresponding 2,4,6-trinitrophenyl ethers. When the inorganic bases were used to catalyze the reaction, the alkali salt of 2,4,6-trinitrophenol was the only product isolated (95% yields). If triethylamine was used as catalyst, no crystalline derivatives were isolated. Triethylamine apparently forms a stable complex with 2,4,6-trinitrofluorobenzene which cannot react with hydroxyl groups. Although similar complex formation occurs with 2,4-dinitrofluorobenzene, the complex appears to be less stable and ether formation is possible.

Further investigations of the 2,4-dinitrophenyl ethers of the carbohydrates are contemplated, with emphasis on their chemical reactions, especially those with bases. Several simple 2,4-dinitrophenyl ethers have been cleaved with hydrazine,[6a] hydroxylamine,[6] methylamine[4] and other amines.[7]

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(5) F. J. Bates and associates, "Polarimetry, Saccharimetry and the Sugars," Circular 440, United States Government Printing Office, Washington, D. C., 1942, p. 506.

(6) J. F. Bunnett, THIS JOURNAL, **79**, 5969 (1957); *Quart. Revs.* (*London*), **12**, 5 (1958).

(6a) W. Borsche, *Ber.*, **56B**, 1488, 1494 (1923).

(7) M. Zahn and R. Kocklãuner, *Z. anal. Chem.*, **141**, 183 (1954).

The fate of the original alcohol component of the ether has not been defined in these examples.

Experimental

Materials.—The polyhydric alcohols were all commercially available products. The reaction solvent, *N,N*-dimethylformamide, and the triethylamine were fractionally distilled commercial samples (b.p. 149–150° and 89.0°, respectively). The 2,4-dinitrofluorobenzene was used without purification as obtained from the Pierce Chemical Co., Rockford, Ill. The 2,4,6-trinitrofluorobenzene was prepared by the method of Vogel and Henne.[8]

Preparation and Properties of 2,4-Dinitrophenyl Ethers.—Examples are given of the various techniques employed in the derivatization of the polyhydric alcohols. Complete data on yields, melting points, analyses and X-ray powder diffraction patterns[9] are given in Table I; a representative infrared absorption spectrum is given in Fig. 1. The 2,4-dinitrophenyl ethers of the polyhydric alcohols were insoluble in water, diethyl ether, ethanol, benzene, chloroform, carbon tetrachloride, pyridine, ethyl acetate and acetic acid. These ethers were soluble (with wide variations in degree) in acetone, *N,N*-dimethylformamide, nitrobenzene and dimethyl sulfoxide. Their solutions showed a slight yellow color. On pouring solutions of the ethers in concd. sulfuric or nitric acids into water the ethers were recovered unchanged. Although the ethers were stable under most conditions, low order detonations resulted on heating in a direct flame or on striking them with a hammer on steel.

Tetrakis-*O*-(2,4-dinitrophenyl)-erythritol.—Erythritol (11 mmoles) was added to a stirred suspension of 10 g. of potassium carbonate powder in 50 ml. of *N,N*-dimethylformamide containing 75 mmoles of 2,4-dinitrofluorobenzene. After stirring for 40 hr., the insoluble salts were removed by filtration and washed with added solvent. The blood-red filtrate and washings were diluted with 1 liter of benzene. The yellow-orange precipitate was collected and washed with ethanol and hot water. The powder was dried (110°) and dissolved in a minimum of warm acetone. After treatment with activated carbon, the solution was concentrated and benzene added. Cooling afforded crystals which were recrystallized in the same manner to give a white product; yield 4.1 g.

If the 2,4-dinitrofluorobenzene was replaced by equimolar amounts of either 2,4,6-trinitrofluorobenzene or its chloro analog, the only product isolated was potassium 2,4,6-trinitrophenoxide in high yield. Potassium 2,4-dinitrophenoxide could also be isolated in low yield from the water washings of the 2,4-dinitrofluorobenzene crude reaction product.

Hexakis-*O*-(2,4-dinitrophenyl)-D-mannitol.—D-Mannitol, 15 g., was added to a mixture of 75 ml. of triethylamine, 75 ml. of 2,4-dinitrofluorobenzene and 180 ml. of *N,N*-dimethylformamide. After stirring for 24 hr. at room temperature, the reaction mixture (a deep red solution) was acidified with dilute hydrochloric acid, diluted to 1 liter with water and cooled. The hard mass of precipitate was separated by decantation and washed with water before drying. The dry solid was extracted twice with small volumes of cold acetone, once each with hot ethanol and hot water. After drying again, the solid was dissolved in hot *N,N*-dimethylformamide, treated with activated carbon, and benzene added (hot) until crystallization ensued. Cooling, followed by the further addition of benzene, afforded 79 g. of slightly yellow crystals, hexakis-*O*-(2,4-dinitrophenyl)-D-mannitol. The analytical sample was crystallized once more from acetone–benzene.

If 2,4,6-trinitrofluorobenzene was substituted for the dinitro analog in the above process, an intensely black mixture resulted which did not afford any solid material when processed as above or by various alternate methods. If no base was added to the reaction mixture, no reaction occurred (72 hr.) and the D-mannitol could be recovered in 85% yields by filtration. The filtrate failed to produce turbidity on addition to water. Substitution of 2,4-dinitrochlorobenzene for the fluoro analog resulted in extremely low yields of the desired fully etherified derivatives. No reaction was observed with 4-nitrofluorobenzene.

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[8] G. Vogel and A. Henne, unpublished work.

[9] A complete tabulation of these data is presented in the M. Sc. Thesis of B. O. Juliano, The Ohio State University, 1958.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

The Acid-catalyzed Anomerization of Acetylated Aldopyranoses[1]

BY WILLIAM A. BONNER

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Three acetylated aldohexopyranoses, an acetylated 6-deoxyaldohexopyranose and three acetylated aldopentopyranoses have been studied from the viewpoint of their sulfuric acid-catalyzed anomerization in 1:1 acetic acid–acetic anhydride solvent. In each case the rate of anomerization has been found to be approximately first order in sulfuric acid concentration and first order in acetylated aldopyranose concentration. Acetylated aldopentopyranoses have been found to anomerize 8-25 times as rapidly as acetylated aldohexopyranoses, a feature which can be rationalized by steric shielding of the anomeric center by the C5 acetoxymethyl groups in the latter series. Several tentative generalizations regarding the effect of stereochemical configuration on the anomerization rates of acetylated aldohexoses and aldopentoses are pointed out. The equilibrium constant for each acetylated aldopyranose anomerization has been estimated, and it has been found that the predominant anomer at equilibrium may be qualitatively predicted by application of the Hassel–Ottar effect.

Introduction

Although the action of Lewis acids in mixtures of acetic acid and acetic anhydride on acetylated β-D-aldopyranoses has been widely used[2] as a synthetic tool for the general preparation of poly-*O*-acetyl-α-D-glycopyranoses, relatively little attention has been paid to the fundamental mechanism of this anomerization reaction. In 1951, we published[3] the results of a rather detailed kinetic study of the sulfuric acid-catalyzed anomerization of the penta-*O*-acetyl-D-glucopyranoses, (a) pointing out the approximately linear relationship between anomerization rate and acid concentration, (b) indicating the absence of a salt effect in the anomerization, (c) studying the effect of solvent composition, particularly with respect to acetic anhydride concentration, on the rate of anomerization, (d) demonstrating the specificity of the anomerization process for the anomeric center and (e) suggesting a mechanism for anomerization consisting essentially of an SN2 attack by the conjugate acid of acetic anhydride on the anomeric carbon. In 1953, Painter disclosed[4] the results of a similar study

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[1] We are indebted to the Quaker Oats Co. for their generous support of a portion of this research.

[2] *Cf.* ref. 3 for a number of specific examples.

[3] W. A. Bonner, THIS JOURNAL, **73**, 2659 (1951).

[4] E. P. Painter, *ibid.*, **75**, 1137 (1953).