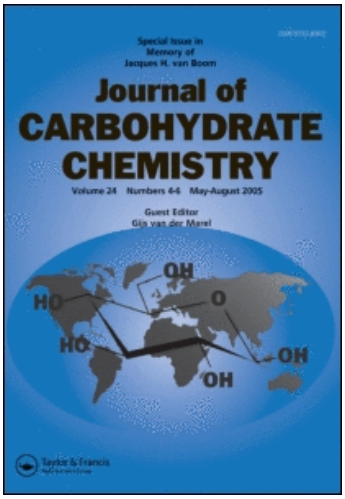

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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To cite this Article Dawe, Robert David and Fraser-reid, Bert(1982) 'The Synthesis and Reactions of Some 3-C-Hethyl Glycals', Journal of Carbohydrate Chemistry, 1: 1, 21 — 35
To link to this Article: DOI: 10.1080/07328308208085076
URL: http://dx.doi.org/10.1080/07328308208085076

J. CARBOHYDRATE CHEMISTRY, 1(1), 21-35 (1982)

THE SYNTHESIS AND REACTIONS OF SOME 3-C-METHYL GLYCALS

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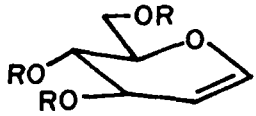
Received February 22, 1982

ABSTRACT

Hex-1-ene-1,5-anhydro-3-uloses, which are easily prepared from glycals, allow for ready introduction of an alkyl group at C3 via 1,2-addition of an organolithium reagent, the stereochemistry of the addition being dependent upon the C4-OH protecting group. The resulting tertiary alcohols are highly reactive, and produce furan derivatives in the presence of mild acids. Quenching of the methyllithium addition with acetic anhydride affords the tertiary acetates, which undergo hydrolytic rearrangement to pseudoglycals and the Ferrier reaction to 3-C-methylhex-2-enopyranosides.

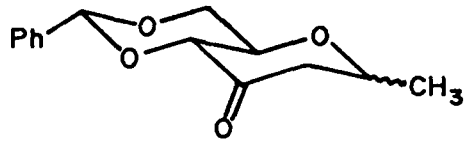
3,4,6-Tri-O-acetyl-D-glucal (1a) has been a fascinating substance since its discovery in 1913 by Emil Fischer,[1] and it has proven to be an excellent starting material for various syntheses of modified sugars. Particularly noteworthy in this regard is its utility for the synthesis of hex-2-enopyranosides[2] (and, from thence, hex-3-enopyranosides)[3] which relies upon the Ferrier reaction,[4] an extremely simple, stereoselective, and efficient process. We recently showed how the Ferrier reaction could be adapted to the preparation of pyranoses bearing an alkyl branch at C1.[5] In this context, alkyl branching can be introduced relatively readily at C1,[5,6] C2,[7] and C4,[8] but not at C3[9] of the pyranose ring and we



1

a R = Ac

b R = H



2

wondered whether triacetyl glucal could be utilized for this purpose. In this report, we describe some recent studies in our laboratories through which this objective has been realized.

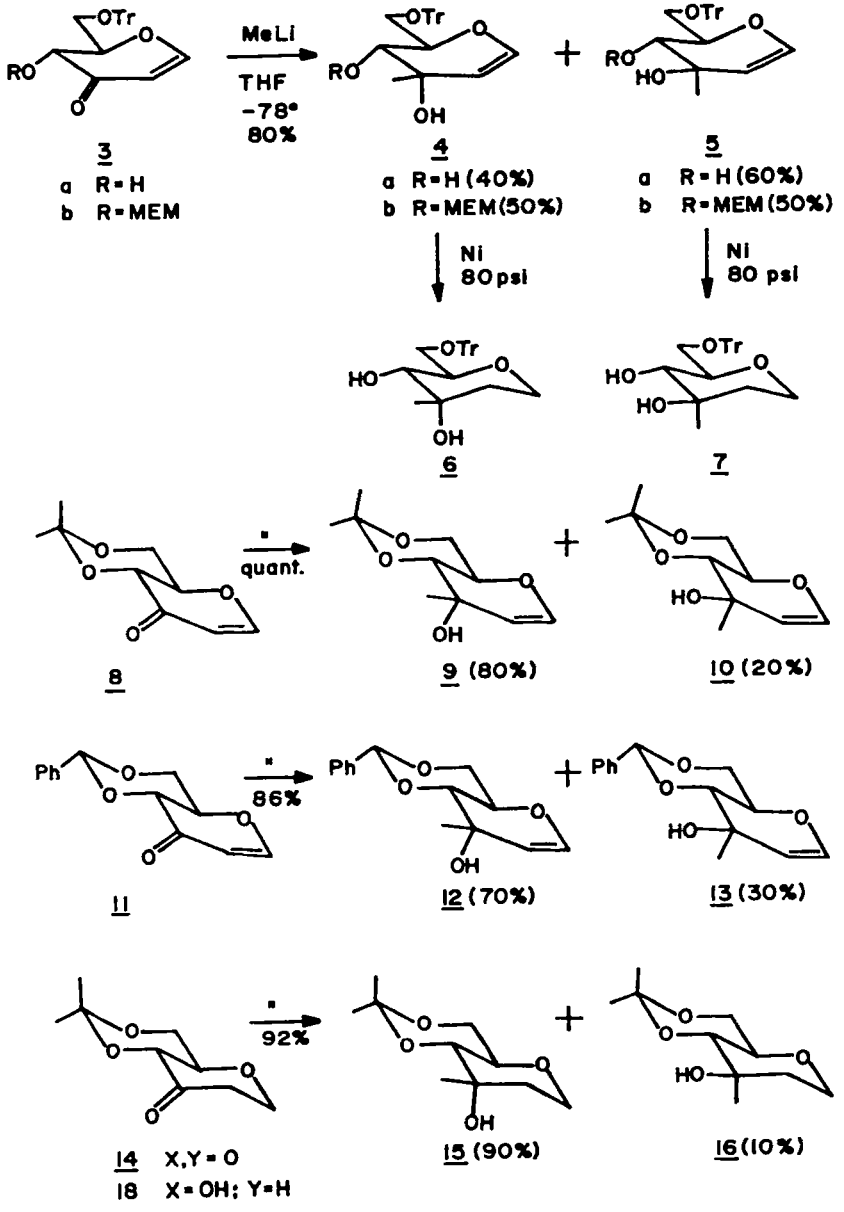
Since C3 of 1 is an allylic site it should, theoretically, be relatively simple to displace an activated hydroxyl group with a carbon nucleophile; however, Guthrie[10] has reported much difficulty in the preparation and handling of 3-O-sulfonate esters of glycals, and hence substrates of this type were not appealing. We therefore decided to examine the enones 3, 8, and 11, whose ready preparation from glucal (1b) has been demonstrated by Collins[11] and our group.[12] In an earlier study,[13] we had found that these β-alkoxyenones reacted poorly with lithium dimethylcuprate to give low yields of conjugate addition products 2. We now wished to investigate the possibility of 1,2-addition to these substances.

Addition of excess methyllithium to the 6-O-trityl-enone 3a led to the formation of two compounds. The ^{1}H NMR spectrum of the crude product mixture showed the presence of olefinic protons as well as two methyl singlets, at δ 1.27 and 1.39 ppm in the ^{1}H NMR spectrum, these data ruling out conjugate addition products of type 2. Both sets of signals were sufficiently resolved in the spectrum for us to determine that the ratio of the isomers was 3:2.

The two compounds could be separated by careful silica gel chromatography, but prolonged residence on the column resulted in lower recovery (vide infra). It was thereby shown that the more polar product was predominant.

To facilitate assignment of configuration by ^{1}H NMR analysis, it was decided to saturate the double bond, since we would then be

Scheme 1

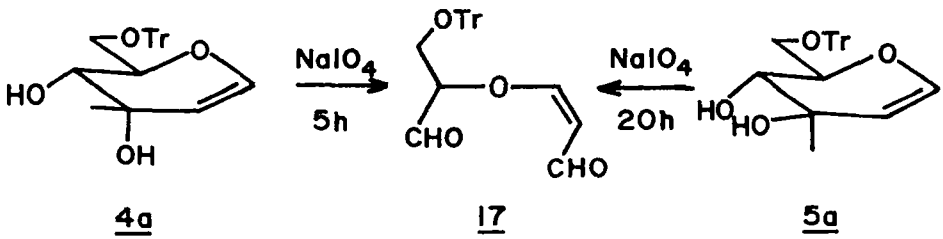


dealing with chair rather than half-chair conformations. Catalytic hydrogenation proved to be unexpectedly difficult. Thus, the use of palladium or platinum catalysts in a variety of solvents, left the olefin unaffected, even at pressures as high as 100 psi! However success was had with freshly prepared Raney nickel in ethanol at 80 psi, by which compounds 6 and 7 were produced cleanly, there being no sign of adverse nickel-induced aberrent reactions, such as reported by Koch and Stuart.[14]

The ^{13}C NMR spectra of the epimers were examined and it was found that the methyl resonances occurred at 19.23 and 27.07 ppm for the major and minor components, respectively. Eliel and Pietrusiewicz[15] have established that, for epimeric substances, an axial methyl carbon atom resonates at higher field than the equatorial, owing to the shielding effect of the syn-axial C5 hydrogen. On this basis we assigned the structure of the major and minor isomers as 6 and 7, respectively. We sought confirmation of these assignments by proton nOe experiments, but the results were not conclusive.

We therefore turned to chemical proof based on the fact that cis-diols are cleaved more readily than trans by sodium metaperiodate. Thus when 4a and 5a were treated with this reagent in aqueous methanol and monitored by TLC, the former began to react within one minute, while the latter was unchanged after twenty minutes. Complete reaction was obtained with 4a in five hours, while 5a required 20 hours. The product from both diols was presumably the same, namely 17, although this material was not isolated.

Scheme 2



4a 17 5a

The formation of 5a as the major isomer was unexpected in that models of 3a suggested that the reagent would approach preferentially from the β-face. The unprotected 4-OH, which would exist as an oxyanion during the reaction, could have been responsible for these unexpected effects, and we therefore decided to examine the 4-O-methoxy-ethoxymethyl derivative yield, but the ratio of the products, 4b and 5b, was 1:1 - not dramatically different from the 3:2 ratio obtained with 3a.

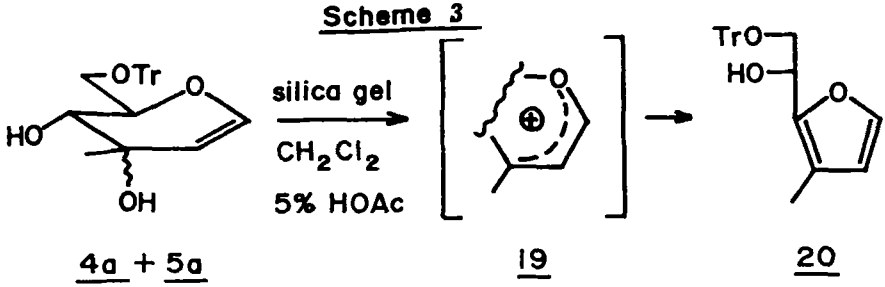
Other protected forms of the enone were therefore examined. The acetonated derivative 8 gave a 4:1 mixture of products 9 and 10, which was separated by column chromatography. The C3 configuration of each product was determined by saturation of the double bond and conversion to the already determined 6-O-trityl derivatives 6 and 7, respectively, using standard transformations. It was thereby shown that the major product from 8 was 9. Similarly, the benzylidene analogue 11 gave an 86% yield of 12 and 13 in the ratio 7:3, the identity of the products being determined by direct ^{1}H NMR comparisons with the acetonides 9 and 10.

The work of Miljkovic has shown that chelation could have dramatic effects upon the stereochemical course of reactions of organometallics with α-alkoxy-ketones of carbohydrate origin,[16] and a similar result has been reported by Still in connection with alicyclic systems.[17] However the addition of methylmagnesium iodide to the acetonide 8 gave a complex mixture containing 1,2 and 1,4-adducts among the products. Grignard reagents were therefore not examined further.

It was surmised that the half-chair conformation might have been somehow responsible for the unexpected stereochemical course observed. Accordingly, it was decided to examine the corresponding saturated ketone 14; however, preparation of 14 from 8 proved more difficult than expected. Thus, hydrogenation of 8 using palladium on carbon led to saturated alcohols. The preferred route to 14 from 1b therefore involved hydrogenation of glucal followed by acetonation to give 18 and then oxidation, the P_2O_5-DMSO/Et_3N mixture of Chittenden[18] being the reagent of choice for the oxidation step.

Treatment of 14 with methyllithium gave a mixture of tertiary alcohols 15 and 16, in the ratio 9:1 (GlC estimation). Thus the

Scheme 3



4a + 5a 19 20

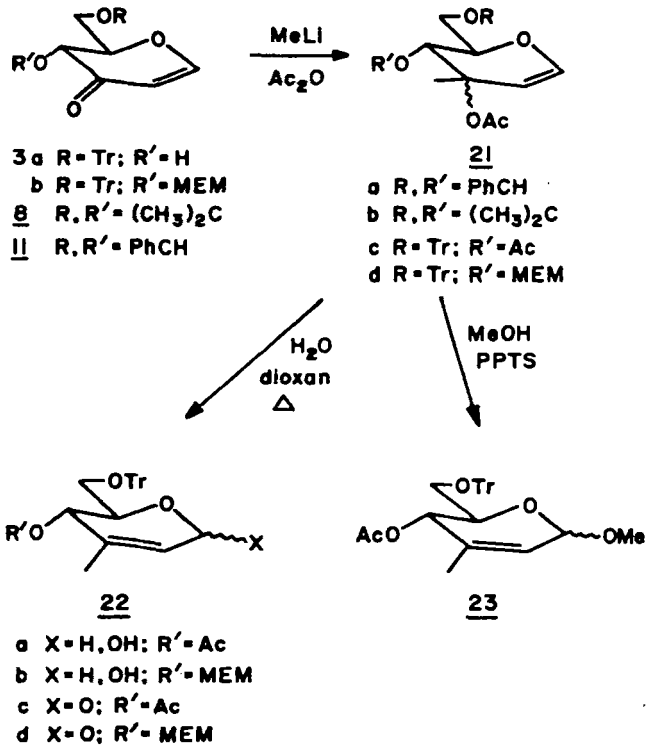
change in conformation in going from enone 8 to ketone 14 caused only a modest enhancement of stereoselectivity in the addition of methyllithium.

We subsequently investigated the chemistry of the C-methyl-glycals shown in Scheme 1. These compounds may be viewed either as allylic tertiary alcohols or as vinylogous hemiacetals, and either description implies that they would be highly reactive. Accordingly, exposure of the mixture (4a + 5a) to silica gel in methylene chloride containing 5% acetic acid for 36 hours, led cleanly to the furan 20 (Scheme 3), which notably retained the trityl group. This transformation finds precedent in some early work of Horton and co-workers.[19] This reactivity is fully rationalized by means of an allylic oxo-carbonium ion intermediate 19.

In view of the high reactivity of (6 + 7), these C-methyl glycals should readily undergo pseudoglycal formation,[18] as well as the related Ferrier reaction,[4] and in order to test these hypotheses, the tertiary acetates 21 were required. Not surprisingly, the tertiary alcohols (for example 4, 9, or 12) resisted acetylation using acetic anhydride and pyridine with or without 4-(N,N-dimethylamino)pyridine as a catalyst; however, when the reaction of enones 3, 8, or 11 with methyllithium was quenched at -40° with a slight excess of acetic anhydride (Scheme 4), the tertiary acetates 21 were obtained in virtually quantitative yields.

When the benzylidene acetate 21a was boiled in aqueous dioxane,[19] gross decomposition ensued as evident from the odor of liberated benzaldehyde. The acetonide 21b fared no better. However the tritylated diacetate 21c and ether 21d gave moderate to good yields of the pseudoglycals 22a and 22b, respectively. Oxidation

Scheme 4



with pyridinium dichromate then afforded lactones 22c and 22d, respectively.

The corresponding glycosidation (Ferrier reaction)[4] of 21c with methanol was carried out using pyridinium p-toluenesulfonate as catalyst. The αβ hex-2-enopyranoside 23 was obtained as an unresolved mixture. The ^{1}H NMR spectrum showed clearly the two methoxyl groups.

Further chemical transformations of the C-methyl glycals (Scheme 2) and pseudoglycal systems (Scheme 4) are underway and will be reported in due course.

EXPERIMENTAL

General Procedures. Melting points were determined in capillary tubes in a Büchi Model 510 apparatus and are uncorrected.

Elemental analyses were performed by Guelph Chemical Labs, Guelph, Ontario, and Dr. F. Kasler, Department of Chemistry, University of Maryland. ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$, (Varian T-60, EM-360, XL-100, HR-220 or HR-360, Brucker WP-80, or WH-400) and IR spectra using a Beckman IR 10 or Perkin Elmer 298 spectrometer. Low resolution MS were obtained on Hitachi/Perkin-Elmer RMH-2 and HRMS on a VG 7070F. TLC was carried out on silica gel plates (E. Merck, CAT. 5539) with ethyl acetate-petroleum ether (30°-60°) mixtures as follows: A (50:50), B (20:80), C (33:67), or D methanol-methylene chloride (10:90). Preparative layer chromatography was done using glass plates (20 cm x 20 cm) coated with silica gel (PF-254, E. Merck) and the above mentioned solvent systems, and column chromatography was carried out using silica gel (E. Merck 70-230 mesh A.S.T.M. or 230-400 mesh A.S.T.M.).

1,5-Anhydro-2 deoxy-3-C-methyl-6-O-trityl-D-ribo-hex-1-enitol (4a) and 1,5-Anhydro-2-deoxy-3-C-methyl-6-O-trityl-D-arabino-hex-1-enitol (5a). 1,5-Anhydro-2-deoxy-6-O-trityl-D-erythro-hex-1-ene-3-ulose 3a[12] (210 mg, 0.54 mmol) was dissolved in tetrahydrofuran (25 mL), cooled under argon to -78°, and methyllithium (~ 3 equivalents) was added. The reaction mixture was allowed to warm up to room temperature and then poured into water. The aqueous layer was saturated with sodium chloride and extracted with diethyl ether, and the combined organic extracts were dried over sodium sulfate and concentrated under vacuum. Preparative layer chromatography using solvent system A afforded 4a (70 mg, 32%) and 5a (104 mg, 48%).

For 4a: TLC: R_f 0.62 (A); $[\alpha]_D^{20}$ +71.2° (c, 2.77 in $CHCl_3$); IR (neat) 3400 cm^{-1} (OH), 1645 cm^{-1} (C=C); ^{1}H NMR: δ 1.39 (s, 3, CH_3), 2.0 (bs, 1, OH), 2.7 (bd, 1, OH), 3.3-4.0 (m, 4, H4, H5, H6, H6'), 4.80 (d, 1, $J_{1,2}$ = 10, H2), 6.40 (d, 1, H1), 7.5 (m, 15, aromatic).

For 5a: TLC: R_f 0.43 (A); $[\alpha]_D^{20}$ 6.50°(c, 1.37 in $CHCl_3$); IR (neat) 3400 cm^{-1} (OH), 1650 cm^{-1} (C=C); ^{1}H NMR: δ 1.27 (s, 3, CH_3), 2.2 (bs, 2, 2 x OH), 3.1-4.1 (m, 4, H4, H5, H6, H6'), 4.63 (d, 1, $J_{1,2}$ = 8, H2), 6.2 (d, 1, H1), 7.4 (m, 15, aromatic).

1,5-Anhydro-2-deoxy-3-C-methyl-6-O-trityl-D-ribo-hexitol (6). The glycal 4a (132 mg, 0.328 mmol) was dissolved in ethanol (25 mL) with a catalytic amount of Raney nickel and shaken under hydrogen (80 psi) for 24 h. The reaction mixture was filtered through Celite

and concentrated to a clear oil (130 mg, 98%) which was purified by preparative layer chromatography (D) yielding 6 as a white solid (93 mg, 70%) having the following characteristics: mp 137° (recrystallized from petroleum ether); TLC: R_f 0.38 (D); $[\alpha]_D^{23}$ -53.2° (c, 0.164 in $CHCl_3$); IR ($CHCl_3$) 3460 cm^{-1} (OH); ^1H NMR: δ 1.25 (s, 3, CH_3), 1.50-1.80 (m, 2, H2, H2'), 2.6 (bs, 2, 2 x OH), 3.12-3.90 (m, 6, H1, H1', H4, H5, H6, H6'), 7.1-7.6 (m, 15, aromatic). ^{13}C NMR: δ 27.071 (CH_3). Anal. Calcd for $C_{26}H_{28}O_4$: C, 77.19; H, 6.98. Found: C, 77.45; H, 7.22.

The glycal 9 (44 mg, 0.22 mmol) was hydrogenated as described in part (a) to give the dihydro analogue 15, 37 mg, R_f 0.32 (B). The material was dissolved in methanol (20 mL) and 3 drops of methanolic hydrogen chloride (12%) were added and then stirred at room temperature for 15 min. Evaporation afforded a white solid (29 mg) R_f 0.38 (D), which was treated with excess trityl chloride and pyridine for 36 h. Work up in the usual way afforded 6 identical with the material obtained in part (a).

1,5-Anhydro-2-deoxy-3-C-methyl-6-O-trityl-D-arabino-hexitol, (7). (a) The glycal 5a (183 mg, 0.454 mmol) was hydrogenated as described above for 4a to yield 7 (180 mg, 98%) as a clear oil. TLC: R_f 0.37 (A); $[\alpha]_D^{22}$ -11.4° (c, 0.832 in $CHCl_3$); IR (neat) 3410 cm^{-1} (OH); ^1H NMR: δ 1.25 (s, 3, CH_3) 1.52-1.97 (m, 2, H2, H2'), 2.83 (bs, 2, 2 x OH), 3.02-3.97 (m, 6, H1, H1', H4, H5, H6, H6'), 7.2-7.6 (m, 15, aromatic); ^{13}C NMR (25.2 MHz) δ 19.233 (CH_3). HRMS Calcd for $C_{26}H_{28}O_4(M^+)$: 404.221. Found: m/z 404.199 (Δ, 5.5 ppm).

(b) Compound 10 was hydrogenated over Raney nickel as described above and the dihydro product 16, R_f 0.27 (B), was converted into the trityl derivative 7 as described in the preceding section for the epimer 9. The products from parts (a) and (b) were identical.

2-Deoxy-4-O-(β-methoxy-ethoxymethyl)-6-O-trityl-D-erythro-hex-1-enopyran-3-ulose (3b).

The hydroxyenone 3a[12] (1.688 g, 4.37 mmol) was dissolved in dry methylene chloride (30 mL). N,N-Diisopropylethylamine (1.5 mL, 8 mmol), and β-methoxyethoxymethyl (MEM) chloride (0.90 mL, 8 mmol) were added to the stirred solution. After 36 h the reaction mixture was poured into diethyl ether and washed successively with aqueous sodium bicarbonate, water and brine. The organic solution was dried over sodium sulfate and concentrated to a yellow oil. Column chromatography (sol-

vent C) on the residue yielded the title compound as a colorless oil (1.6 g, 77%). The following characteristics were observed for compound 3b: TLC: R_f 0.47 (C); $[\alpha]_D^{25}$ +142° (c, 1.12 in $CHCl_3$); IR (neat) 1690 cm^{-1} (C=O); ^1H NMR: δ 3.3-3.9 (m, 9, OCH_3, OCH_2CH_2O, H6, H6'), 4.52 (bs, 2, H4, H5), 4.85 (s, 2, $-OCH_2O-$), 5.48 (d, 1, $J_{1,2}$ = 6, H2), 7.2-7.7 (m, 16, H1, aromatic).

1,5-Anhydro-2-deoxy-4-O-(β-methoxyethoxymethyl)-3-C-methyl-6-O-trityl-D-ribo-hex-1-enitol (4b), and 1,5-Anhydro-2-deoxy-4-O-(β-methoxyethoxymethyl)-3-C-methyl-6-O-trityl-D-arabino-hex-1-enitol (5b). Compound 3b (106 mg, 0.223 mmol) was treated with methyllithium as described above for 3a. Preparative layer chromatography afforded 4b (41 mg, 41%) and 5b (58 mg, 53%).

For 4b: TLC: R_f 0.38 (A); $[\alpha]_D^{20}$ 41.3° (c, 1.5, in $CHCl_3$); IR (neat) 3450 cm^{-1} (OH), 1650 cm^{-1} (C=C); ^1H NMR: δ 1.57 (2, 3, CH_3), 2.9-4.0 (m, 12, H4, H5, H6, H6', OH, OCH_3, OCH_2CH_2O), 4.3-4.8 (m, 3, H2, OCH_2O), 6.5 (d, 1, $J_{1,2}$ = 6, H1), 7.1-7.7 (m, 15, aromatic).

For 5b: mp 125-127°; TLC R_f 0.57 (A); $[\alpha]_D^{20}$ 37.9° (c, 1.50 in $CHCl_3$); IR ($CHCl_3$) 3450 cm^{-1} (OH), 1655 cm^{-1} (C=C); ^1H NMR: δ 1.30 (s, 1, CH_3), 3.0-4.9 (m, 15, H2, H4, H5, H6, H6', OH, OCH_3, OCH_2O, OCH_2CH_2O), 6.40 (d, 2, $J_{1,2}$ = 6.0, H1), 7.1-7.7 (m, 15, aromatic). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.44; H, 6.99. Found: C, 73.51; H, 7.04.

1,5-Anhydro-2-deoxy-4,6-O-isopropylidene-3-C-methyl-D-ribo-hex-1-enitol (9) and 1,5-Anhydro-2-deoxy-4,6-O-isopropylidene-3-C-methyl-D-arabino-hex-1-enitol (10). Compound 8 (214 mg, 1.16 mmol) was treated with methyllithium as described above for 3a. GLC analysis of the oily product (230 mg, 99%) indicated a 4:1 mixture and chromatography on a silica gel column using ethyl acetate-petroleum ether (85:15) afforded 9 (139 mg, 60%) and 10 (46 mg, 20%).

For 9: mp 71-72° (recrystallized from petroleum ether); TLC R_f 0.43 (B); $[\alpha]_D^{20}$ 114° (c, 2.24 in $CHCl_3$); IR ($CHCl_3$) 3400 cm^{-1} (OH), 1640 cm^{-1} (C=C); ^1H NMR: δ 1.35 (s, 3, CH_3), 1.47 (s, 3, CH_3), 1.55 (s, 3, CH_3), 2.4 (bs, 1, OH), 3.5-4.15 (m, 4, H4, H5, H6, H6'), 4.85 (d, 1, $J_{1,2}$ = 6, H2), 6.35 (d, 1, H1). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.96; H, 8.06. Found: C, 60.02; H, 8.31.

For 10: TLC R_f 0.30 (B); $[\alpha]_D^{20}$ 38.7° (c, 0.372 in $CHCl_3$); IR (neat) 3450 cm^{-1} (OH), 1645 cm^{-1} (C=C); ^1H NMR: δ 1.38 (s, 3, CH_3), 1.45 (s, 3, CH_3), 1.54 (s, 3, CH_3), 1.92 (bs, 1, OH), 3.7-4.1 (m,

4, H4, H5, H6, H6'), 4.74 (d, 1, $J_{1,2}$ = 6.1, H2), 6.19 (d, 1, H1); MS m/z 200 (M^+).

1,5-Anhydro-4,6-O-benzylidene-2-deoxy-3-C-methyl-D-ribo-hex-1-enitol (12) and 1,5-anhydro-4,6-O-benzylidene-2-deoxy-3-C-methyl-D-arabino-hex-1-enitol (13). The enone 11[12] (125 mg, 0.539 mmol), dissolved in tetrahydrofuran (20 mL), was treated with methyllithium in the usual way to afford the title compounds (115 mg, 86%). ^{1}H NMR indicated that 13 and 14 were present in a ratio of 7:3. Preparative layer chromatography (C) was only partially successful, affording the major component 12 pure as an oil (36 mg, 27%).

For compound 12: TLC R_f 0.52 (C); $[\alpha]_D^{22}$ +89° (c, 0.26 in $CHCl_3$); IR (neat) 3440 cm^{-1} (OH), 1640 cm^{-1} (C=C); ^{1}H NMR: δ 1.38 (s, 3, CH_3), 2.3 (bs, 1, OH), 3.5-4.6 (m, 4, H4, H5, H6, H6'), 4.85 (d, 1, $J_{1,2}$ = 6, H2), 5.65 (s, 1, PhCH), 6.35 (d, 1, H1), 7.45 (m, 5, aromatic).

The minor component 13 could not be obtained free from the major isomer, but the following data were ascribed to this compound: TLC R_f 0.45 (C); ^{1}H NMR (80 MHz) δ 1.42 (s, CH_3), 4.78 (d, J = 6, H2), 5.55 (s, PhCH), 6.20 (d, H1).

1,5-Anhydro-2-deoxy-4,6-O-isopropylidene-D-arabino-hexitol (18). Triacetyl D-glucal 1a (10 g, 37 mmol) was dissolved in methanol (200 mL) and to the solution was added anhydrous sodium carbonate. After stirring at room temperature for 5 h the reaction was filtered. A catalytic amount of Raney nickel was added to the filtrate, and the mixture was shaken under hydrogen (85 p.s.i.) for 18 h. The reaction mixture was filtered through Celite and concentrated and the resulting oil was treated with dimethoxypropane (ca. 20 mL) in acetone (100 mL) containing a catalytic amount of p-toluenesufonic acid. After 2h a small amount of triethylamine was added to neutralize the acid and evaporation of the volatile materials gave the title compound as a clear oil (5.5 g, 79%).

Compound 18 had the following characteristics: TLC R_f 0.48 (D); $[\alpha]_D$ -19.8° (c, 4.02 in $CHCl_3$); IR (neat) 3450 cm^{-1} (OH); ^{1}H NMR: δ 1.25 (s, 3, CH_3), 1.35 (s, 3, CH_3), 1.6-2.0 (m, 2, H2, H2'), 3.0 (bs, 1, OH), 3.1-4.0 (m, 7, H1, H1', H3, H4, H5, H6, H6').

1,5 Anhydro-2-deoxy-4,6-O-isopropylidene-D-erythro-hex-3-ulose (14). The alcohol 18 (1.109 g, 5.97 mmol) was dissolved in dimethylformamide (5 mL). Dimethyl sulfoxide (1.9 g, 24 mmol) and phosphorus

pentoxide (0.85 g, 6 mmol) were added and the mixture stirred at 65° for 2 h. After cooling the reaction mixture was diluted with methylene chloride (ca. 100 mL). The methylene chloride solution was washed with water until the washings were neutral. The organic layer was dried and concentrated to a brown oil (410 mg, 37%), which was homogeneous by TLC (A).

A small portion of the material was purified by column chromatography. A purified sample of compound 14 gave the following: TLC R_f 0.51 (A); $[\alpha]_D^{24}$ 25.4° (c, 1.83 in $CHCl_3$); IR (neat) 1735 cm^{-1} (C=O); ^1H NMR: δ 1.40 (s, 3, CH_3), 1.50 (s, 3, CH_3), 2.50-2.70 (m, 2, H2, H2'), 3.3-4.5 (m, 6, H1, H1', H4, H5, H6, H6').

1,5-Anhydro-2-deoxy-4,6-O-isopropylidene-3-C-methyl-D-ribo-hexitol (15), and 1,5-Anhydro-2-deoxy-4,6-O-isopropylidene-3-C-methyl-D-arabino-hexitol (16). Ketone 14 (35 mg, 0.19 mmol) was treated with methyllithium as described above for 3, to afford two tertiary alcohols (35 mg, 92%) in the ratio 9:1 (GLC). TLC (B) comparisons with the dihydro products of 9 and 10 (vide supra) showed that major and minor components were 15 and 16 respectively.

1-C-(3-Methylfuran-2'-yl)-2-O-trityl-1R-ethanediol (20). A mixture of the diols 6 and 7 (300 mg, 0.75 mmol) was dissolved in methylene chloride (10 mL). Acetic acid (0.5 mL) and a small amount of silica gel were added and the mixture was stirred at room temperature for 36 h. The reaction mixture was neutralized with sodium bicarbonate, filtered, concentrated and purified by preparative layer chromatography (B) yielding the title compound as a clear oil (200 mg, 69%) having the following characteristics: TLC R_f 0.58 (B); $[\alpha]_D$ +8.8° (c, 0.25 in $CHCl_3$); IR (neat) 3400 cm^{-1} (OH); ^1H NMR: δ 2.00 (bs, 3, CH_3), 2.55 (bs, 1, OH), 3.2-3.7 (m, 2, H2, H2a), 4.83 (dd, 1, $J_{1,2}$ = 5, $J_{1,2a}$ = 7, H1), 6.2 (bd, 1, $J_{4',5'}$ = 3, H4'), 7.2-7.7 (m, 16, H5', aromatic).

Acetylated Glycals 21 (a, b, c and d). The title acetates were prepared from enones 3, 8 and 11 by addition of methyllithium at -78° as described above. The solution was allowed to warm up to -40° and excess acetic anhydride which had been stored over barium carbonate was added. The mixture was allowed to warm up to room temperature and then worked up in the usual way.

4-O-Acetyl-2,3-dideoxy-3-C-methyl-6-O-trityl-D-erythro-hex-2-enopyranose (22a). The diacetate 21c (180 mg, 0.38 mmol) in dioxane

(10 mL) was added to boiling water (40 mL) containing a small amount of hydroquinone the reaction being carried out in the dark under argon. After refluxing for 20 min. the solution was cooled rapidly by the addition of ice and then extracted with methylene chloride to afford an oil (160 mg). Preparative layer chromatography (B) yielded 2a: TLC R_f 0.30 (C); $[\alpha]_D^{22}$ -8.83° (c, 1.97 in $CHCl_3$); IR (neat) 3420 cm^{-1} (OH), 1745 (C=O); ^1H NMR δ 1.80 (bs, 3, CH_3), 2.2 (s, 3, CH_3CO), 2.6 (bs, 1, OH), 3.0-3.5 (m, 2, H6, H6'), 3.9-4.2 (m, 1, H5), 5.0-6.0 (m, 3, H1, H2, H4), 7.2-7.7 (m, 15, aromatic).

4-O-Acetyl-2,3-dideoxy-3-C-methyl-6-O-trityl-D-erythro-hex-2-enono-1,5-lactone (22b). The pseudoglycal 22a (550 mg, 1.12 mmol) was oxidized with pyridinium dichromate. After purification by column chromatography (C), compound 22b was obtained as a white crystalline solid (220 mg, 46%) having the following characteristics: mp 148.3-148.8° (recrystallized from MeOH); $[\alpha]_D^{20}$ + 117°(c, 0.443 in $CHCl_3$) TLC R_f 0.37 (C); IR (neat) 1645 cm^{-1} (acetate and lactone C=O); ^1H NMR 1.95 (d, 3, $J_{CH_3,H-2}$ = 0.7, CH_3), 2.07 (s, 3, CH_3CO), 3.30 and 3.48 (AB of ABX, 2, $J_{5,6} = J_{5',6'} = 4$, $J_{6,6'} = 9$, H6, H6'), 4.53 (ddd, 1, $J_{4,5}$ = 4.5, H5), 5.70 (d, 1, H4), 5.94 (bs, 1, H2), 7.15-7.7 (m, 15, aromatic).

Anal. Calcd for $C_{27}H_{26}O_5$: C, 75.31; H, 6.09. Found: C, 75.58; H, 5.78.

Methyl-4-O-Acetyl-2,3-dideoxy-3-C-methyl-6-O-trityl-αβ-D-erythro-hex-2-enopyranosides (23). The diacetate 21c (105 mg, 0.22 mmol) was dissolved in absolute methanol (10 mL). A catalytic amount of pyridinium p-toluenesulfonate was added and the reaction mixture allowed to stand at room temperature until completion (48 h). A small amount of sodium bicarbonate was added and methanol was removed. The residue was taken up in methylene chloride, washed with water, dried and concentrated to a clear oil. This material was subjected to column chromatography (B) yielding the title compounds 23 as an inseparable mixture (87 mg, 86%) having the following characteristics: TLC R_f 0.54 (B); IR (neat) 1745 cm^{-1} (OAc); ^1H NMR: δ 1.63 (d, 3, $J_{CH_3,H-2}$ 2, CH_3), 1.85 (s, 3, CH_3CO), 3.05-3.35 (m, 2, H-6, H-6'), 3.38 (s, 0.5, OCH_3), 3.50 (s, 2.5, OCH_3), 4.02 (ddd, 1, $J_{4,5}$ = 9, $J_{5,6} = J_{5,6'}$ = 5, H5). 4.93 (bs, 1, H1), 4.30 (d, 1, H4), 4.60 (m, 1, H2), 7.1-7.65 (m, 15, aromatic).

Anal. Calcd for $C_{29}H_{30}O_5$: C, 75.96; H, 6.59. Found: C, 75.78; H, 6.48.

ACKNOWLEDGMENTS

We wish to thank the Natural Sciences and Engineering Research Council for a scholarship (RDD) and for support for this work.

REFERENCES AND FOOTNOTES

1. E. Fischer and C. Zach, Sitzungsber. Kgl. Preuss. Akad. Wiss., 16, 311 (1913); E. Fischer, Chem. Ber., 47, 196 (1914); E. Fischer, M. Bergmann, and H. Schotte, ibid., 53, 509 (1920).

2. S. Laland, W.G. Overend, and M. Stacey, J. Chem. Soc. C., 738 (1950); M. Bergmann, Justus Liebigs Ann. Chem., 443, 223 (1925).

3. R. J. Ferrier and N. Vethaviyasar, J. Chem. Soc. Perkin Trans. I, 1791 (1973); R. D. Guthrie and G. J. Williams, ibid., 2619 (1972).

4. R. J. Ferrier, Advan. Carbohydr. Chem. Biochem., 24, 199 (1954).

5. R. D. Dawe and B. Fraser-Reid, J. Chem. Soc. Chem. Commun., 1180 (1981).

6. For some recent examples see references 1-6 in reference 5 above.

7. (a) T. D. Inch and G. J. Lewis, Carbohyd. Res., 15, 1 (1970); (b) N. Richards and L. F. Wiggins, J. Chem. Soc., 2442 (1953); (c) D. R. Hicks and B. Fraser-Reid, Can. J. Chem., 53, 2017 (1975); (d) M. Miljkovic and D. Glisin, J. Org. Chem., 40, 3357 (1975).

8. N. K. Kochetkov, A. F. Sviridov and M. S. Eermolenko, Tetrahedron Lett., 22, 4319 (1981); M. B. Yunker, D. E. Plaumann, and B. Fraser-Reid, Can. J. Chem., 55, 4002 (1977).

9. See (7c) also K. Heyns and J. In Park, Chem. Ber., 109, 3262 (1976); L. L. Box, V. G. S. Box and E. V. E. Roberts, Heterocycles, 14, 1269 (1980).

10. I. D. Blackburne, A. R. Burfitt, P. F. Fredericks and R. D. Guthrie, "Some Aspects of the Chemistry of D-Glucal" in "Synthetic Methods for Carbohydrates", H. S. El Khadem, Ed.; ACS, Washington, D.C., 1976, Vol. 39, Chapter 7.

11. P. M. Collins, P. Gupta, and R. Iyer, J. Chem. Soc. C., 1670 (1972); P. M. Collins, Carbohydr. Res., 11, 125 (1969); P. J. Benyon, P. M. Collins, P. T. Doganges, and W. G. Overend, J. Chem. Soc. C, 1131 (1966).

12. B. Fraser-Reid, D. L. Walker, S. Y-K. Tam, and N. L. Holder, Can. J. Chem., 51, 3950 (1975).

13. D. L. Walker, B. Fraser-Reid, and J. K. Saunders, J. Chem. Soc. Chem. Commun., 319 (1974).

14. H. J. Koch and R. S. Stuart, Carbohydr. Res., 67, 341 (1979).

15. E. L. Eliel and K. M. Pietrusiewicz, in "Topics in ^{13}C NMR Spectroscopy", G. C. Levy, Ed.; John Wiley and Sons, New York, 1979, Chapter 3: "^{13}C NMR of Nonaromatic Heterocyclic Compounds".

16. M. Miljkovic, M. Gligorijevic, T. Satoh, and D. Miljkovic, J. Org. Chem., 39, 1379 (1974).

17. W. C. Still and J. H. McDonald, Tetrahedron Lett., 21, 1031 (1980).

18. G. J. F. Chittenden, Carbohydr. Res., 15, 101 (1970).

19. E. Albano, D. Horton and T. Tsuchiya, ibid., 2, 349 (1966).

20. S. Y-K. Tam and B. Fraser-Reid, ibid., 45, 29 (1975).