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APPROACHES TO HIGHER-CARBON SUGARS*, BASED ON THE USE OF SUGAR-DERIVED, STABILIZED WITTIG REAGENTS

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ABSTRACT

1-(1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranuronyl)imidazole, obtained by treating the corresponding diacetal of α-D-galactopyranuronic acid with 1,1-carbonyldiimidazole, reacts with methylenetriphenylphosphorane to give (1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranuronyl)-(triphenylphosphoranylidene)methane (**3**) as a crystalline, stable Wittig reagent. Compound **3** reacts with aldehydo sugars to provide α,β-unsaturated ketones, preponderantly as the *E* isomers. The α,β-unsaturated ketones react with lithium dimethyl cuprate to afford an ~3:1 mixture of the 1,4-addition products, and with methylmagnesium chloride to give a 12:1 mixture of the tertiary allylic alcohols methyl 5-deoxy-5-*C*-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-6-*C*-methyl-D(and L)-*glycero*-α-D-*galacto*-heptos-7(*E*)-ylidene]-2,3-*O*-isopropylidene-β-D-ribofuranoside, which undergoes an oxidative rearrangement when treated with pyridinium chlorochromate.

INTRODUCTION

Higher-carbon sugars[1] and many macrolides[2] share the common feature of having a backbone of more than six carbon atoms, studded with methyl or hydroxyl groups, or both, and so the challenges presented by both classes of molecule are in many respects similar. The seminal studies of Hanessian and co-workers in this area, based on the "chiron" approach[3], are well known. We recently described a concept termed[4] "pyranosidic homologation" in which a pyranose core is elaborated into interlocking dipyranose[4b,4c] and tripyranose[4a] systems that respectively provide arrays containing between eight and twelve contiguous, chiral centers.

We now outline an alternative approach to the synthesis of higher-carbon sugars, pseudo or authentic, that employs Wittig methodology.

The combination of a carbohydrate-derived Wittig reagent with an aldehydo

*Because of their resemblance to disaccharides, products are named as *x*-deoxy-*x*-(*C*-glycosyl)glycose derivatives, and their carbon atoms are numbered accordingly.

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sugar for the synthesis of higher-carbon sugars was applied by Secrist and co-workers[5] in a landmark synthesis of hikizimycin. The event was remarkable, in that, despite being "unstabilized", the reagent could be generated from the phosphonium salt precursor without elimination of the β-oxygen atom*. Furthermore, because of the basicity of such unstabilized reagents, carbohydrate *electrophiles* frequently undergo β-eliminations during the reaction[7]. Thus, *both* partners in the condensation are prone to β-elimination and, not surprisingly, the favorable outcome achieved by Secrist and Wu[5] required the use of very precise reaction-conditions.

The reaction of stabilized Wittig reagents with carbohydrate aldehydes or hemiacetals for extending the carbon chain was pioneered by Russian workers[8], and this methodology provides a popular route for the preparation of *C*-glycosyl compounds[9]. Normally, stabilized Wittig reagents react readily with carbohydrate substrates, because the carbonyl groups are usually very electrophilic by virtue of the β-oxygen atom(s). Hence β-eliminations are not a problem.

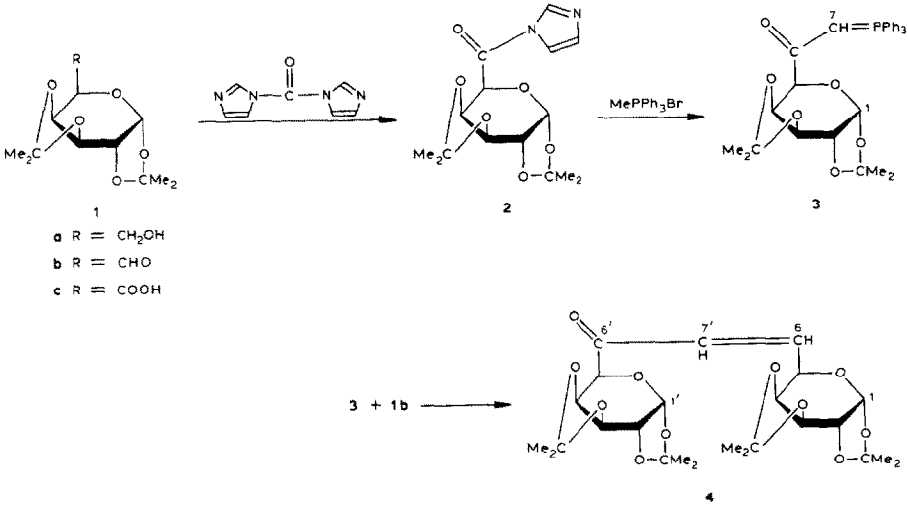
Accordingly, we decided to examine a procedure for connecting two sugars by means of stabilized-Wittig methodology. The procedure promised to be valuable, because (*a*) the two partners could be normal, or modified, sugars, (*b*) the methods involved should be tolerant of a wide variety of functional groups, (*c*) the connecting link between the two sugar nuclei (see **4**, for example) is a versatile synthon, and (*d*) some degree of asymmetric induction, by both sugar residues, on the reactions of the enone could be anticipated.

RESULTS AND DISCUSSION

On reaction with 1,1-carbonyldiimidazole according to the procedure of Staab[10], the uronic acid **1c**, readily prepared[11] from the diacetal **1a**, gave the imidazolide **2** as a stable, crystalline compound. Addition of **2** to methylenetriphenylphosphorane as described by Bestmann[12] afforded the Wittig reagent **3** as another stable, crystalline compound (in 73% yield). Compound **3** survived purification by column chromatography, and could be stored indefinitely in a refrigerator. The conversion of **1c** into **3** in one flask, without isolation of imidazolide **2**, resulted in a much improved, overall yield (68% *versus* 40%). The molecular ion for **3** could not be detected in its mass spectrum, but there were observed daughter ions that were in accord with the fragmentation pattern expected (see the Experimental section).

The reaction of phosphorane **3** with 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose[13] (**1b**) in refluxing benzene afforded only a moderate yield (52%) of a single condensation-product. Assignment as **4** followed from the mass-spectrometric data, which contained the molecular ion and daughter ions consistent

*Note may be taken of the special approach[6] for preparation of such β-oxygenated ylids as $Ph_3P{=}CHCH(OR)_2$



1
a R = CH_2OH
b R = CHO
c R = COOH

2

3

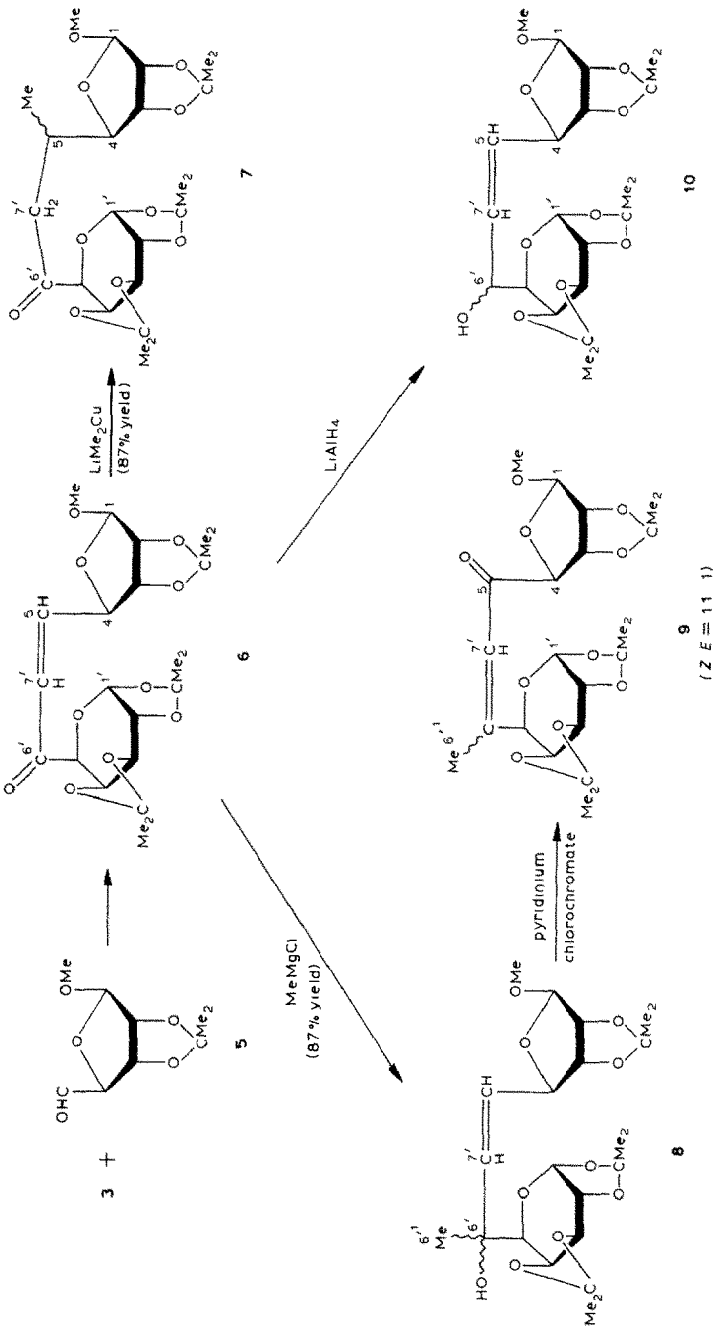
4

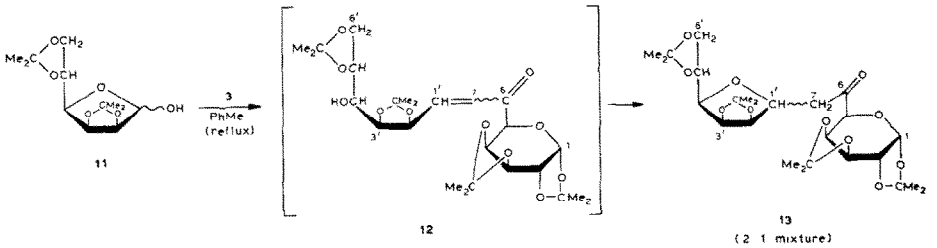
with cleavage of the C-6′–C-7′ and C-5′–C-6′ bonds (see the Experimental section). I.r. bands at 1680 and 1620 cm^{-1} revealed the α-enone chromophore. The orientation in **4** was tentatively assigned as *E*, as would be expected[8,9], and by comparison with **6** (see later). Unfortunately, the alkenic protons overlapped in the ^{1}H-n.m.r. spectrum, so that the orientation could not be assigned on the basis of the coupling constant.

A comparable product, **6** was obtained from methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanoside[14] (**5**), but the yield (78%) was significantly higher. Mass-spectrometric (see the Experimental section) and also i.r. data were appropriate for structure **6**. The ^{1}H-n.m.r. spectrum was more revealing in the case of **6** than of **4**. Thus, the presence of a single methoxyl signal in the 400-MHz spectrum suggested that **6** could be confidently assigned as a single geometric isomer, and the readily determined value for $J_{5,7'}$ (15.87 Hz) seen in the signals for H-7′ (6.57 p.p.m.) indicated the *E* isomer.

We decided to conduct some transformations on **6**, in order to ascertain the level of stereoselectivity that could be induced in reactions of the α,β-unsaturated portion. Reaction with lithium dimethyl cuprate gave, in 87% yield, the conjugate-addition product **7**, whose 250-MHz, ^{1}H-n.m.r. spectrum showed that it was a 3:1 mixture of the C-5 epimers. These were not resolved in a variety of chromatographic systems, but the composition of the mixture was apparent from the methoxyl signals for the major and minor isomers, at 3.29 and 3.37 p.p.m., respectively. Similarly, the signal of the C-5 methyl group appeared as a doublet at 0.93 and 1.03 p.p.m. The high-resolution mass spectrum of **7** was consistent with the structure expected (see the Experimental section).

Reaction of **6** with methylmagnesium chloride led to an 87% yield of the 1,2-adduct **8** as a 12:1 mixture of epimers (judging from the methoxyl signals at 3.30 and 3.31 p.p.m., respectively). In order to probe further the tolerance of the


3 +
5
6
7
8
9
(Z E = 11 1)
10
LiMe2Cu
(87% yield)
MeMgCl
(87% yield)
LiAlH4
pyridinium
chlorochromate



three-carbon bridge for manipulations, these tertiary alcohols **8** were subjected to an oxidative rearrangement. Thus, treatment of **8** with pyridinium chlorochromate in refluxing benzene[15] did effect the expected rearrangement, as the formation of the α-enone was readily determined by the appearance of a u.v.-active product in t.l. chromatograms. However, the reaction had to be interrupted after 2 h, even though an appreciable proportion of starting material remained, because of t.l.c. evidence for degradation of the product. Compound **9** was isolated by preparative-layer chromatography, and its 400-MHz, ^{1}H-n.m.r. spectrum was recorded. Signals for two vinyl methyl groups were observed in the spectrum, a singlet at 2.16 p.p.m. and a doublet at 2.26 p.p.m. (J_{H,CH_3} 0.66 Hz) in 53 and 47% proportion, respectively. The former was assigned as the *Z* isomer, as the methyl group of the *E* isomer would be expected to resonate at lower field, owing to the deshielding effect of the adjacent carbomethylidene group. A precedent for the assignment was found in related structures whose methyl groups resonate at 2.00 and 2.20 p.p.m. respectively[16].

The results from the oxidative rearrangement indicated that the process is not stereospecific, *i.e.*, the composition of the tertiary alcohol mixture **8** is not reflected in the composition of the geometric isomers **9**. Reduction of enone **6** with lithium aluminum hydride gave a mixture of the epimeric C-6′ alcohols **10**. The composition of the mixture was apparent from the 250-MHz, ^{1}H-n.m.r. spectrum, which showed H-7′ of the isomers as doublets at 5.97 ($J_{5,7'}$ 15.48 Hz) and 5.73 p.p.m. ($J_{5,7'}$ 15.0 Hz) in the ratio of 2.6:1. The methoxyl signals for both isomers were also seen, although they were not clearly resolved.

The reaction of phosphorane **3** with a sugar hemiacetal was also investigated. Equimolar amounts of **3** and 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**11**) were heated in refluxing toluene. A product was isolated crystalline, which proved to be a 2:1 mixture of the isomers **13**, based on the intensities of the signals for the anomeric (H-1) and the C-7 methylene protons. All efforts to isolate the partly acyclic intermediate **12** were unsuccessful.

EXPERIMENTAL

General. — Melting points were determined in capillary tubes, using a Büchi Model 510 apparatus, and are uncorrected. Elemental analyses were performed either by Guelph Chemical Labs. (Guelph, Ontario) or by Dr. F. Kasler (Depart-

ment of Chemistry, University of Maryland). Optical rotations were determined with a Perkin–Elmer 241 polarimeter. T.l.c. was performed on Silica Gel HF-254 (0.2-mm layers) containing a fluorescent indicator (Merck, 5539), with detection by u.v. (254 nm) or charring with sulfuric acid. Column chromatography was effected on silica gel (Merck 70–230 mesh A.S.T.M. or 230–400 mesh A.S.T.M.). ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si), unless otherwise stated, with a Varian XL-100, Bruker WM-250, or Bruker WH-400 spectrometer. Coupling constants were measured directly from the spectra, or calculated from the peak listings. I.r. spectra of films or solutions were recorded with either a Beckman IR-10 or a Perkin–Elmer 298 spectrometer. Low-resolution mass spectra were recorded with a Hitachi–Perkin–Elmer RMH-2 instrument, and high-resolution mass spectra, with a VG-7070F instrument.

1-(1,2:3,4-Di-O-isopropylidene-α-D-galactopyranuronyl)imidazole (**2**). — 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranuronic acid[11] (**1c**; 1.65 g, 6.0 mmol) was dissolved in dry tetrahydrofuran (10 mL) and 1,1-carbonyldiimidazole (1.04 g, 6.41 mmol) was added with stirring. After evolution of CO_2 had ceased (~15 min), the mixture was diluted with dry ether (30 mL) and left to crystalline at 0°. The crystals were collected, washed with dry ether, and dried, to give 1.123 g (58%) of product **2**; m.p. 149–151°, $[\alpha]_D^{20}$ −65.2° (*c* 0.25, chloroform); ^{1}H-n.m.r. (250 MHz): δ 1.30, 1.33, 1.40, 1.50 (4 s, 12 H, 4 isopropylidene CH_3), 4.28–4.82 (m, 3 H, H-2,3,4), 5.63 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), and 6.92, 7.53, and 8.40 (imidazole).

Anal. Calc. for $C_{15}H_{20}N_2O_6$: C, 55.55; H, 6.21; N, 8.64. Found: C, 54.91; H, 6.19; N, 8.48.

(1,2:3,4-Di-O-isopropylidene-α-D-galactopyranuronyl)-(triphenylphosphoranylidene)methane (**3**). — (*a*) Methyltriphenylphosphonium bromide (1.16 g, 3.25 mmol) was suspended in benzene (100 mL) under argon at room temperature, and 2.5M butyllithium (1.33 mL, 3.33 mmol) was added. After the resulting mixture had been stirred for 30 min, a solution of the imidazolide **2** (500 mg, 1.54 mmol) in benzene (40 mL) was added dropwise, and the mixture was stirred for 2 h at room temperature, when the reaction was found to be complete (t.l.c.). A solution of ammonium chloride (50 mL) was added, and the benzene layer was separated, washed with water, dried, and evaporated. The residue was subjected to column chromatography using 1:1 (v/v) petroleum ether–ethyl acetate, to give 599 mg (73%) of the phosphorane **3** as a crystalline material, m.p. 110–118°. Recrystallization from ethyl acetate–petroleum ether gave pure **3**.

(*b*) To a solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranuronic acid (**1c**; 1.65 g, 6.0 mmol) in tetrahydrofuran (10 mL) was added 1,1-carbonyldiimidazole (1.04 g, 6.41 mmol). After 15 min, when evolution of carbon dioxide had ceased, the mixture was added to the Wittig reagent generated from methyltriphenylphosphonium bromide (7.1 g, 19.9 mmol) and 2.5M butyllithium (7.4 mL, 18.5 mmol) in benzene under argon at room temperature. Isolation of the product, **3**, as described in (*a*) afforded 2.166 g (68%, based on acid **1c**); m.p. 119–121°, $[\alpha]_D^{23}$ −113.6° (*c* 0.25, chloroform); ^{1}H-n.m.r. (250 MHz): δ 1.30, 1.33, 1.45, 1.50

(4 s, 12 H, 4 isopropylidene CH_3), 4.22 (bs, 1 H, H-5), 4.31 (dd, 1 H, $J_{1,2}$ 5.2, $J_{2,3}$ 3.0 Hz, H-2), 4.60 (dd, 1 H, $J_{3,4}$ 8.0 Hz, H-3), 4.82 (dd, 1 H, $J_{4,5}$ 2.0 Hz, H-4), 5.67 (d, 1 H, H-1), and 7.30–8.03 (m, 16 H, aromatic and C*H*=PPh_3).

Anal. Calc. for $C_{31}H_{33}O_6P$: C, 69.90; H, 6.25. Found: C, 71.00; H, 6.18.

*6-Deoxy-6-*C*-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galacto-heptopyranos-6-ulose-7(*E*)-ylidene]-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**4**). — The phosphorane **3** (450 mg, 846 μmol) and 1,2:3,4-di-*O*-isopropylidene-α-*D*-*galacto*-hexodialdo-1,5-pyranose[13] (**1b**; 258 mg, 1.0 mmol) were dissolved in benzene (20 mL), and the solution was boiled under reflux for 24 h. T.l.c. (1:1 EtOAc–petroleum ether) then showed only traces of the starting materials, and the formation of new compounds (less polar, and less visible under u.v. light). The product **4** was isolated as an oil (225 mg, 52%); ^{1}H-n.m.r. (100 MHz): δ 1.33–1.50 (singlets, 24 H, 8 isopropylidene CH_3), 5.58 and 5.65 (2 d, 2 H, *J* ~5 Hz, anomeric protons), and 6.95 (overlapping alkenic protons); $\nu_{max}^{CHCl_3}$ 1680 and 1620 cm^{-1} (unsaturated ketone); *m/z* 512 (M^+), 497 (M − CH_3), 454 (M − Me_2CO), 256 (cleavage at C-6′–C-7′), and 229 and 283 (cleavage at C-5′–C-6′).

Anal. Calc. for $C_{25}H_{36}O_{11}$: C, 58.56; H, 7.08. Found: C, 58.21; H, 6.98.

*Methyl 5-deoxy-5-*C*-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galacto-hepto-pyranos-6-ulose-7(*E*)-ylidene]-β-*D*-ribofuranoside* (**6**). — The phosphorane **2** (1.86 g, 3.5 mmol) and methyl 2,3-*O*-isopropylidene-β-*D*-*ribo*-pentodialdo-1,4-furanoside[14] (**5**; 710 mg, 3.8 mmol) were dissolved in toluene (15 mL), and the solution was boiled under reflux. After 1 h, t.l.c. (1:1 EtOAc–petroleum ether) showed the disappearance of the starting materials, and the formation of a new, u.v.-active syrup; column chromatography with 3:7 EtOAc–petroleum ether afforded 1.25 g (78%) of **6**; $[\alpha]_D^{23}$ −106° (*c* 2.2, chloroform); ^{1}H-n.m.r. (400 MHz): δ 1.454, 1.446, 1.377, 1.292, 1.257, 1.257 (6 s, 18 H, 6 isopropylidene CH_3), 3.35 (s, 3 H, OCH_3), 4.30 (d, 1 H, $J_{4',5'}$ 1.95 Hz, H-5′), 4.37 (dd, 1 H, $J_{2',3'}$ 2.44 Hz, H-2′), 4.53–4.64 (m, 4 H, H-2,3,3′,4′), 4.74 (d, 1 H, $J_{4,5}$ 6.59 Hz, H-4), 4.980 (s, 1 H, H-1), 5.611 (d, 1 H, $J_{1',2'}$ 5.127 Hz, H-1′), 6.575 (q, 1 H, $J_{5,6}$ 15.869 Hz, H-6), and 6.848 (dd, 1 H, H-5); $\nu_{max}^{CHCl_3}$ 1680 and 1610 cm^{-1} (unsaturated ketone); *m/z* 456 (M^+), 441 (M − CH_3), 398 (M − Me_2 − CO), 229 and 227 (cleavage at C-5′–C-6′), and 199 (227 − CO).

Anal. Calc. for $C_{22}H_{32}O_{10}$: C, 57.87; H, 7.07. Found: C, 57.50; H, 6.82.

Reaction of enone **6** *with methyllithium to give* **7**. — Methyllithium (1.4M; 0.37 mL, 0.52 mmol) was added to a suspension of copper(I) iodide (49 mg, 0.26 mmol) in dry ether (3 mL) at 0°. The resulting clear, colorless solution was stirred for 10 min, and a solution of **6** (10 mg, 22 μmol) in dry ether (1 mL) was added through a syringe. The mixture was stirred for 20 min at 0°, poured into saturated ammonium chloride solution (3 mL), the mixture extracted with ether, and the extract washed with ammonium chloride solution until the blue color in the aqueous layer had disappeared, and then with sodium chloride solution. Column chromatography with 3:7 EtOAc–petroleum ether afforded 9 mg (87%) of material found to be a 3:1 mixture of the C-5 isomers of methyl 5-*C*-(*RS*)-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-*galacto*-heptopyranos-6-ulose-7-yl]-5,6-dideoxy-β-*D*-*ribo*-hexo-

furanoside (**7**); ^{1}H-n.m.r. (250 MHz): δ 0.93 (d, 3 H, J 7.0 Hz, CH_3-5, minor isomer), 1.03 (d, 3 H, J 7.0 Hz, CH_3-5, major isomer), 1.20–1.55 (m, 18 H, 6 isopropylidene CH_3), 2.40–2.55 (m, 1 H, H-5), 2.74 (bABq, 2 H, J_{AB} 18 Hz, $\Delta\delta$ 0.03 p.p.m., C-7′-CH_2, major isomer), 3.04 (bABq, 2 H, J_{AB} 18 Hz, $\Delta\delta$ 0.02 p.p.m., C-7′-CH_2, minor isomer), 3.29 (s, 3 H, OCH_3, minor isomer), 3.37 (s, 3 H, OCH_3, major isomer), 4.16 (d, 1 H, $J_{4',5'}$ 2.0 Hz, H-4′, minor isomer), 4.19 (d, 1 H, $J_{4',5'}$ 2.0 Hz, H-4′, major isomer), 4.35 (dd, 1 H, $J_{2',3'}$ 2.7 Hz, H-2′), 4.52–4.68 (m, 5 H, H-2,3,4,3′,4′), 4.80 (bs, 1 H, H-1, minor isomer), 4.82 (bs, 1 H, H-1, major isomer), and 5.64 (d, 1 H, $J_{1',2'}$ 5.2 Hz, H-1′); $\nu_{max}^{CHCl_3}$ 1720 cm^{-1}; *m/z* 457 (M^+ − 15), 425 (M − 15 − MeOH), 243, 229, 171, and 71; *m/z* 457.2067 (M^+ − 15). Calc. for $[C_{13}H_{36}O_{16}CH_3]$, 457.2073.

Reaction of enone **6** *with methylmagnesium chloride to give* **8**. — Methylmagnesium chloride (2.8M in THF; 0.02 mL, 5.6 μmol) was added to a solution of the α-enone **6** (10 mg, 22 μmol) in ether (2 mL) at 0°. After stirring for 20 min at 0°, saturated ammonium chloride solution (1 mL) was added, and the product was isolated in the usual way, to afford 9 mg (87%) of material which was shown to be a 12:1 mixture of the isomers of methyl 5-deoxy-5-*C*-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-6-*C*-methyl-D-(or L-)*glycero*-α-D-*galacto*-heptos-7(*E*)-ylidene]-2,3-*O*-isopropylidene-β-D-ribofuranoside (**8**); $[\alpha]_D^{23}$ −49.33° (*c* 0.9, chloroform); ^{1}H-n.m.r. (250 MHz): δ 1.20–1.52 (m, 21 H, 6 isopropylidene CH_3 and CH_3-6′), 3.30 (s, 3 H, OCH_3, major isomer), 3.31 (s, 3 H, OCH_3, minor isomer), 3.50 (d, 1 H, $J_{2,3}$ 1.5 Hz, H-3), 3.89 (bs, 1 H, H-5′), 4.36 (dd, 1 H, $J_{1',2'}$ 5, $J_{2',3'}$ 3 Hz, H-2′), 4.43 (dd, 1 H, $J_{3',4'}$ 8, $J_{4',5'}$ 1.7 Hz, H-4′), 4.55 (dd, 1 H, H-3′), 4.58–4.64 (m, 2 H, H-2 and O*H*), 4.67 (bd, 1 H, $J_{4,5}$ 8 Hz, H-4), 4.97 (s, 1 H, H-1), 5.65 (d, 1 H, H-1′), 5.79 (d, 1 H, $J_{5,7'}$ 15 Hz, H-7′), and 5.92 (dd, 1 H, H-5).

Oxidative rearrangement of the tertiary allylic alcohols **8**. — To a solution of the mixture of allylic alcohols **8** (60 mg, 0.13 mmol) in benzene (5 mL) were added pyridinium chlorochromate (166 mg) and sodium acetate (65 mg), and the solution was boiled under reflux. T.l.c. gave evidence of a u.v.-active product, but, after 2 h, it was apparent that the material was decomposing, and the reaction was interrupted. The product, namely, methyl 5-*C*-(6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-6-*C*-methyl-α-D-*galacto*-hept-6-enopyranose-7-yl)-2,3-*O*-isopropylidene-β-D-ribofuranosid-5-ulose acid (**9**), was isolated by preparative-layer chromatography with 4:1 petroleum ether–ethyl acetate; ^{1}H-n.m.r. (250 MHz): δ 2.16 (d, 3 H, J_{H,CH_3} 0.663, *Z*-CH_3), 2.26 (s, 3 H, *E*-CH_3), 5.61 (m, 1 H, H-7′), and 5.65 (m, 1 H, H-1′); *E*:*Z* = 43:57.

Reduction of enone **6** *with lithium aluminum hydride*. — Lithium aluminum hydride (20 mg) was added to a solution of enone **6** (106 mg) in dry ether (5 mL). After 1 h, the product was isolated in the usual way, affording methyl 5-deoxy-5-*C*-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-D(or L)-*glycero*-α-D-*galacto*-heptos-7(*E*)-ylidene]-2,3-*O*-isopropylidene-β-D-ribofuranoside (**10**) as a mixture (87 mg, 80%) of epimers in the ratio of ~2.6:1; ^{1}H-n.m.r. (250 MHz): δ 1.20–1.50 (m, 18 H, 6 isopropylidene CH_3), 3.00 (s, 3 H, O*C*H_3, major isomer), 3.31 (s, 3 H, O*C*H_3,

minor isomer), 3.50 (d, 1 H, $J_{2,3}$ 1.5 Hz, H-3), 4.36 (dd, 1 H, $J_{1',2'}$ 5, $J_{2',3'}$ 3 Hz, H-2'), 4.43 (dd, 1 H, $J_{3',4'}$ 8, $J_{4',5'}$ 1.7 Hz, H-4'), 4.55 (dd, 1 H, H-3'), 4.59–4.64 (m, 2 H, H-2 and O*H*), 4.67 (bd, 1 H, $J_{4,5}$ 8 Hz, H-4), 4.93 (s, 1 H, H-1), 5.65 (d, 1 H, H-1'), 5.76 (d, 1 H, $J_{5,7'}$ 15 Hz, H-7'), and 5.95 (dd, 1 H, H-5); *m/z* 458 (M^+), 443 (M − CH_3), 400 (M − Me_2CO), and 458.2582 (M^+). Calc. for $C_{22}H_{34}O_{10}$, 458.2600.

*Reaction of 2,3:5,6-di-*O*-isopropylidene-*D*-mannofuranose* (**11**) *with phosphorane* **3**. — A toluene solution (10 mL) containing the phosphorane **3** (106.4 mg, 0.2 mmol) and 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**11**; 52 mg, 0.2 mmol) was boiled under reflux for 20 h, when t.l.c. showed the formation of a product less polar than either reactant. The compound was isolated by chromatography with 1:4 ethyl acetate–petroleum ether. Crystalline material (70 mg) was obtained from benzene–petroleum ether; m.p. 125–137°; the ^{1}H-n.m.r. spectrum showed it to be a 2:1 mixture of isomers of 7-*C*-(1,4-anhydro-2,3:5,6-di-*O*-isopropylidene-D-mannitol-1-yl)-7-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hepto-pyranos-6-ulose (**13**). For this mixture, ^{1}H-n.m.r. (250 MHz): δ 2.74 (dd, 1 H, J_{gem} 17, $J_{1',7a}$ 6.5 Hz, H-7a, minor isomer), 2.86 (dd, 1 H, $J_{1',7b}$ 6.5 Hz, H-7b, minor isomer), 2.97 (dd, 1 H, J_{gem} 18, $J_{1',7a}$ 7.5 Hz, H-7a, major isomer), 3.18 (dd, 1 H, $J_{1'7b}$ 5.8 Hz, H-7a, major isomer), 3.42–3.51 (m, 1 H, H-1', major isomer), 3.66–3.72 (m, 1 H, H-1', minor isomer), 5.34 (bs, 1 H, H-5, minor isomer), 5.36 (bs, 1 H, H-5, major isomer), 5.59 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1, minor isomer), and 5.61 (d, 1 H, $J_{1,2}$ 4.5 Hz, major isomer); *m/z* 514 (M^+), 499 (M − CH_3), and 456 (M − Me_2 − CO). Calc. for $C_{25}H_{38}O_{11}$: 514.2962. Found: 514.2970.

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