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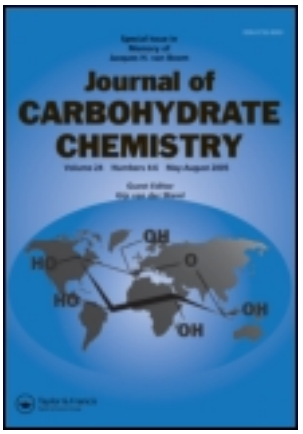

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APPLICATION OF SUGAR PHOSPHONATES FOR THE PREPARATION OF HIGHER CARBON MONOSACCHARIDES

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ABSTRACT

Reaction of sugar derived phosphonates [Sug-C(O)CH_2P(O)$(OMe)_2$] with sugar aldehydes (Sug'-CHO) provides the higher enones of the general formula Sug-C(O)CH=CH-Sug' with the *trans* configuration of the double bond. The phosphonate method is superior to the previously used phosphorane methodology [Sug-C(O)CH=PPh_3 + Sug'-CHO] since sugar phosphonates can be prepared in much higher yields and are much more nucleophilic than corresponding phosphoranes. The sugar enones are reduced to appropriate allylic alcohols with zinc borohydride; the stereoselectivity of this process is >97:3 (with the D-*glycero* isomer predominating) when the carbonyl group is placed at the α-position to the sugar ring. CD spectroscopy was used for the determination of the configuration of higher sugar allylic alcohols.

INTRODUCTION

The synthesis of higher carbon sugars having more than 10 carbon atoms in the chain has gained considerable attention in the past two decades since they are

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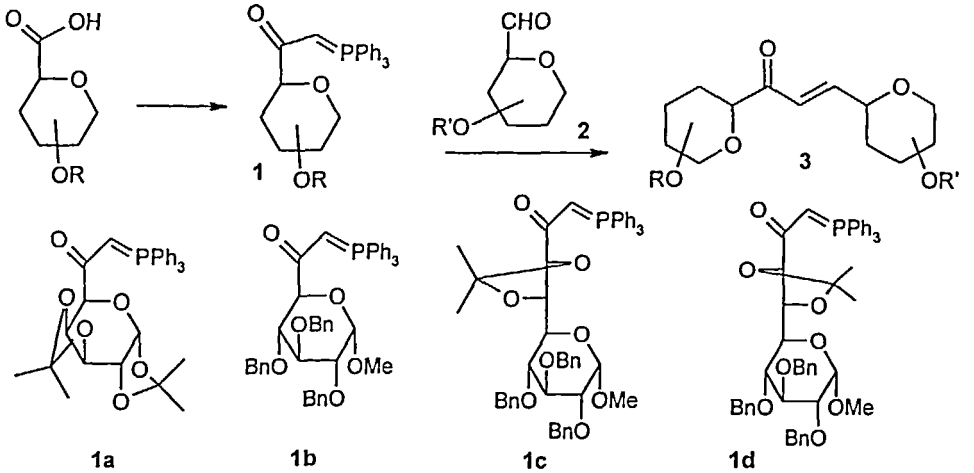
components of some antibiotics (hikizimycin,[2] tunikamycin[3] *etc.*) and might be used as non-metabolisable analogues of disaccharides. Preparation of such compounds can now be accomplished almost routinely,[4] although for a long time it presented a real challenge for organic chemists. Higher carbon sugars can be obtained either by iterative two carbon atoms homologation (as shown by Brimacombe[5]) or more conveniently by coupling of appropriately funtionalized sugar subunits. In the past several years we elaborated a method of such coupling of monosaccharides *via* their terminal C-atoms.[6]

One of the useful methods[7] consists of the reaction of sugar-derived phosphoranes **1** (prepared from appropriate uronic acid) with terminal aldoses **2** (Scheme 1), providing higher sugar enones **3** in which the allylic C_3-bridge can be then converted into a triol system.



Scheme 1. preparation of higher carbon sugars by application of the Wittig methodology

There is, however, a serious disadvantage to this methodology. Sugar phosphoranes are obtained in only moderate yields (*ca.* 50%). Moreover, the higher analogues[8] **1c** and **1d** do not react even with simple aldehydes under standard reaction conditions; the reaction must be performed under high pressure (>10 kbar) in order to obtain appropriate Wittig-type adduct (**1c** + 4 → **5**; Scheme 2).[8] A solution to the high pressure Wittig-type methodology is the replacement of phosphoranes with more nucleophilic phosphonates. The latter can be prepared[8] readily from appropriate methyl

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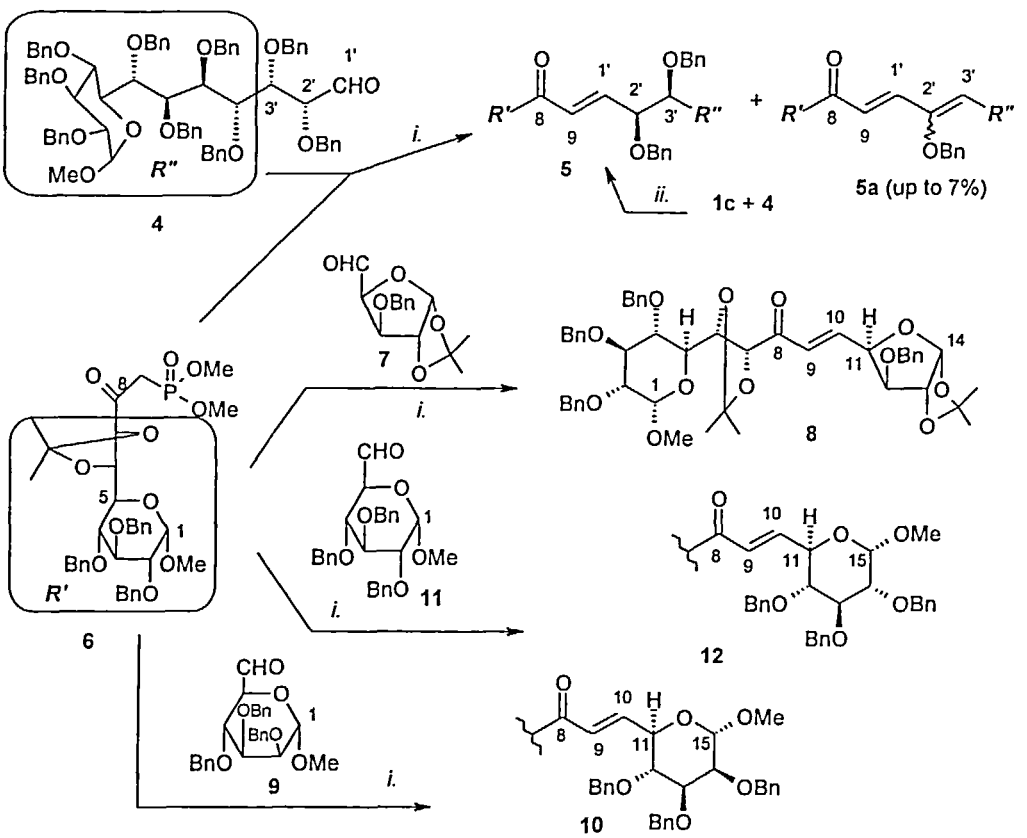
uronates and dimethyl methylphosphonate. Indeed, reaction of phosphonate **6** with the C_{12}-aldehyde **4** afforded the desired C_{21}-monosaccharide precursor **5**; however, partial β-elimination occurred under the slightly basic reaction conditions resulting in formation of the diene **5a** which was isolated in small amounts (see Scheme 2). In this paper application of the phosphonate methodology for the preparation of other higher carbon sugar precursors will be presented.

RESULTS AND DISCUSSION

Reaction of phosphonate **6** with 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranos-5-ulose (**7**) under phase transfer conditions afforded the higher sugar enone **8**



Scheme 2. i. K_2CO_3, 18-crown-6, toluene; ii. 12 kbar.

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in high yield. No β-elimination product (similar to **5a**) was detected in the post-reaction mixture.

Similarly, reaction of **6** with other aldehydes methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranosid-6-ulose (**9**) and methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-ulose (**11**) afforded appropriate higher sugar enones **10** and **12** in high yield. Again, no β-eliminated products were formed in this process (Scheme 2).

In order to convert the three carbon atom bridge (C_8-C_{10}) into a triol system the carbonyl function has to be reduced to an allylic alcohol and the double bond in the latter oxidized either *via* a *cis*-hydroxylation or epoxidation (followed by the opening of the oxirane ring) processes. We have found that zinc borohydride reduces the higher sugar enones (derived from the sugars of the D-configuration) with very high stereoselectivities to alcohols with the *R*-configuration at the newly created stereogenic center. These results may be explained by a cyclic model[7] as shown in Fig. 1. This model works well for higher enones in which the carbonyl group is placed at the α-position to the sugar ring. We plan also to test this model for other, less constrained derivatives such as those arising from the coupling of the C_9-phosphorane **6** with aldehydes.

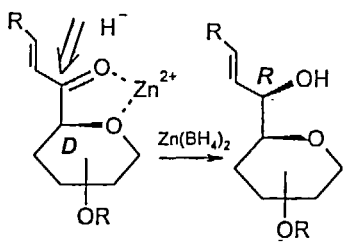
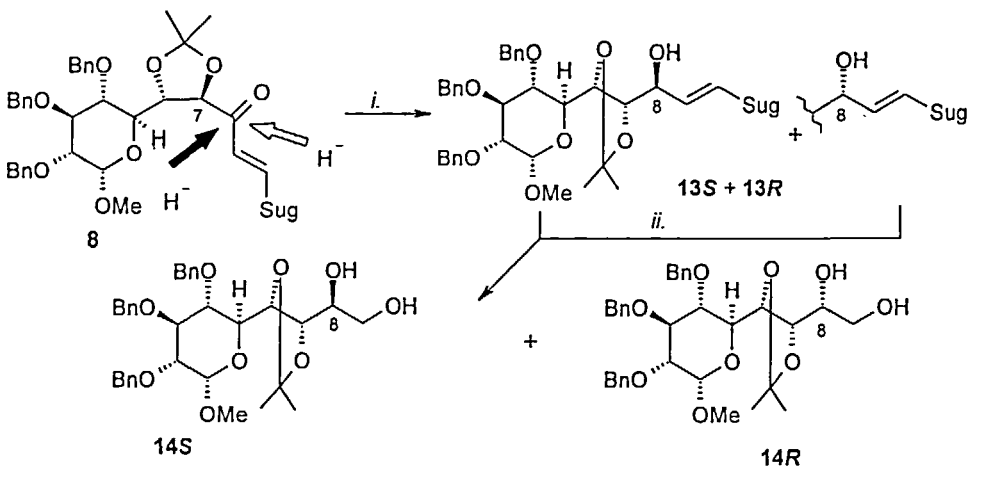


Figure 1.



Scheme 3. *i.* $Zn(BH_4)_2$, ether, 0 °C; *ii.* O_3, CH_2Cl_2, -78 °C, then $NaBH_4$

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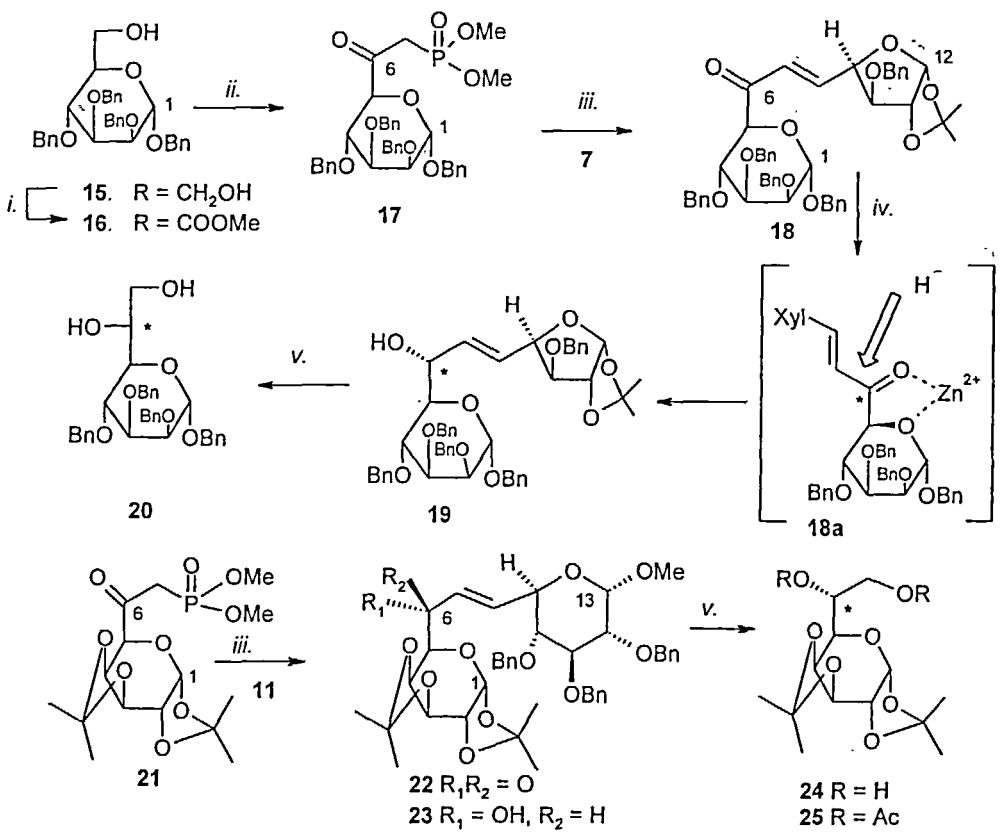
Reduction of ketone 8 with zinc borohydride afforded an inseparable mixture of higher sugar allylic alcohols **13** *S/R* (Scheme 3). The low selectivity in this reaction is not very surprising, since differentiation between the *re* and *si* sides of the carbonyl group in such an open-chain derivative (*e.g.* **8**) even after complexation of the carbonyl and neighboring (α or β) oxygen atoms with Zn^{+2}, is not significant (as compared to compounds with the carbonyl group placed at the α-position to the sugar ring).

To test the validity of our model for other compounds with the carbonyl group at the α-position to the sugar ring two more enones were prepared from phosphonates **17** and **21**[8] respectively (Scheme 4), 3-*O*-benzyl-5-deoxy-5-*C*-[benzyl 2,3,4-tri-*O*-benzyl-7-deoxy-α-D-*manno*-6-ulos-7(*E*)-ylidene]-1,2-*O*-isopropylidene-α-D-xylofuranose (**18**) and methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-*C*-[(*E*) 1,2:3,4-di-*O*-isopropylidene-7-deoxy-α-D-*galacto*-heptopyranosid-6-ulose-7-ylidene]-α-D-*gluco*-hexopyranoside (**22**).



Scheme 4. *i. a.* Jones' reagent. *b.* CH_2N_2; *ii.* $(\text{-})CH_2P(O)(OMe)_2$; *iii.* K_2CO_3, 18-crown-6, toluene; *iv.* $Zn(BH_4)_2$, ether, 0°C; *v.* a.O_3 b. $NaBH_4$

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These enones were reduced with zinc borohydride to the corresponding allylic alcohols **19** and **23** with the *R*-configuration at the newly created chiral center (stereoselectivity > 97:3). The configurations of these alcohols were determined by chemical degradation to known heptose derivatives **20**[9] and **24**,[10] the configuration of the former (**20**) was also verified by the CD spectroscopy (*see* below).

Determination of the configuration of higher allylic alcohols 13, 19 and 23.

In order to determine the configuration at the newly created stereogenic center in alcohols **13*S/R*** (as an inseparable 1:2 mixture of isomers), **18** and **23** were converted into nonose **14*S*** and **14*R*** (Scheme 3) and heptose **20**[9] and **24**[10] (Scheme 4) derivatives, respectively, by ozonolysis of the double bond followed by reduction of the crude ozonide with sodium borohydride. Diol **24** was converted into known diacetate **25** for which the D-*glycero*-configuration at the C6 center was assigned on the basis of ^{1}H NMR data. The significant difference in the chemical shift of the H6-resonance between **25** and its L-*glycero*-isomer (δ = 5.15 and 5.32 ppm respectively)[10] makes possible the precise structural assignment. The configurations of the diols **14*S***, **14*R*** and **20** were assigned on the basis of CD spectroscopic evidence.

The CD spectra of both glycols **14** (***S*** and ***R***) were measured in the form of their chiral molybdenum complexes formed *in situ* with dimolybdenum tetracetate as an auxiliary chromophore. These spectra show two well separated Cotton effects (CEs) between 400 and 300 nm in both cases. As the two diols under investigation represent local enantiomers with regard to the diol unit, their CD spectra display a quasi-mirror image, as expected (Fig. 2). According to the helicity rule operating for molybdenum *in situ* complexes with *vic*-glycols,[11] a positive (negative) CE at around 300 nm corresponds to the positive (negative) torsional angle in the O–C–C–O moiety. For steric reasons, the conformation with an antiperiplanar arrangement of O–C9–C8–C7 unit should be preferred in both cases. This conformational requirement leads to the *R* absolute configurational assignment of C_8 for the glycol with a positive CE at *ca.* 300 nm (glycol **14*R***) and to C_8(*S*) for the glycol with a negative CE in the same region (glycol **14*S***).

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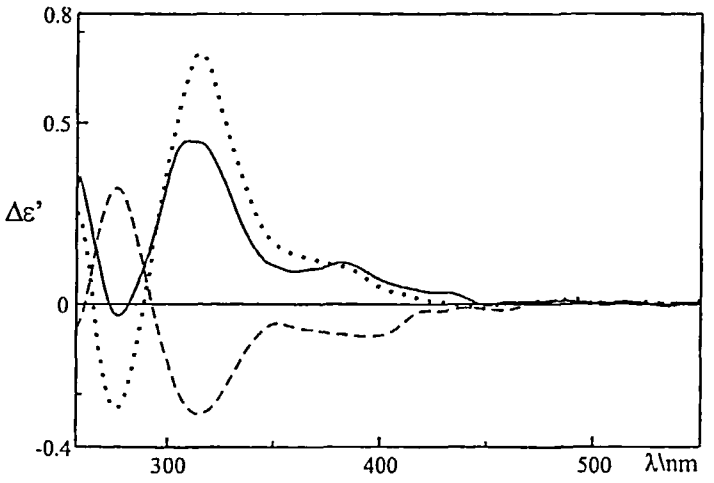

Figure 2: CD spectra of *in situ* Mo-complexes of compounds **14** *R* (——), **14** *S* (– – –) and **20** (· · · ·).

Analogously, the absolute configuration at C6 in compound **20** can be described to be $C_6(R)$ on the basis of the positive sign of the CE at *ca.* 300 nm (Fig. 2).

CONCLUSION

The higher sugar enones are readily prepared by reaction of appropriate phosphonates with aldehydes. The enones in which the carbonyl function is placed at the α-position to the sugar ring can be selectively reduced with zinc borohydride to (*R*)-allylic alcohols what might be explained by a cyclic model involving the complexation of the zinc cation to the carbonyl and α-(ring)-oxygen atoms which fixes the conformation and differentiates significantly both sides of the carbonyl group. The configuration at the newly created stereogenic center can be conveniently assigned from the CD spectra of the molybdenum complexes of their degradation products (diols).

Stereoselectivity is much lower for derivatives in which the C=O grouping is separated from the sugar ring, since in this case the differentiation between the *re* and *si* sides of the molecule is not very significant.

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EXPERIMENTAL

General methods. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AM 500 (ylides **1a-1d** COSY, HETCOR) and Varian Gemini 200 spectrometers (for other products) for solutions in $CDCl_3$ (internal Me_4Si). Mass spectra [LSIMS (*m*-nitrobenzyl alcohol was used as a matrix to which sodium acetate was added)] were recorded with a AMD-604 (AMD Intectra GmbH, Germany) mass spectrometer. Specific rotations were measured with a JASCO P-1020 digital polarimeter for solutions in chloroform (*c* 1). Column chromatography was performed on silica gel (Merck, 70-230 mesh). Organic solutions were dried over anhydrous magnesium sulfate. CD spectra were measured between 650 and 230 nm at room temperature with a JASCO J715 spectropolarimeter using DMSO solutions in cells of 0.2 path length (spectral band width 2 nm, sensitivity 10×10^{-6} or 20×10^{-6} ΔA-unit/nm). Depending on the S/N-ratio the λ-scan speed was 0.2 or 0.5 nm/s. For CD measurements the chiral diol (1 - 3 mg) was dissolved in a stock solution of $[Mo_2(OAc)_4]$ complex (2.5 - 3 mg) in DMSO (5 mL), so that the molar ratio of the stock complex to diol was about 1:0.6 to 1:0.9. As the true concentrations of the individual optically active complexes are not known, apparent Δε' values are given, calculated from the total ligand concentration and assuming 100% complexation. $[Mo_2(OAc)_4]$ and DMSO (Uvasol) were commercially available from Fluka AG and E. Merck, respectively, and were used without further purification.

Spectral data for sugar phosphoranes 1a-1d. These ylides were prepared previously but were not fully characterized; the ^{1}H, ^{13}C, and ^{31}P NMR spectra for all four compounds are listed below.

(1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranuronyl)-(triphenylphosphoranylidene)methane[12] (1a). ^{1}H NMR δ: 5.67 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1), 4.83 (dd, 1H, $J_{3,4}$ = 7.9, $J_{4,5}$ = 2.1 Hz, H-4), 4.63 (dd, 1H, $J_{2,3}$ = 2.2 Hz, H-3), 4.33 (dd, 1 H, H-2), 4.25 (d, 1H, H-5), 1.54, 1.52, 1.38, and 1.32 (4s, 12H, 4×Me); ^{13}C NMR δ: 96.7 (C1), 72.3 (C4), 71.4 (C5), 70.9 (C3), 70.8 (C2); ^{31}P NMR δ: 16.9.

(Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosiduronyl)-(triphenylphosphoranylidene)methane[7] (1b). ^{1}H NMR δ: 4.66 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.18 (dd, 1H, $J_{C,P}$ = 1.0, $J_{4,5}$ = 9.8 Hz, H-5), 4.02 (dd, 1H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 9.4 Hz, H-3), 3.81 (dd, 1H, H-4),

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3.60 (d, 1H, H-2), 3.44 (s, 3 H, OMe); ^{13}C NMR δ: 98.5 (C1), 81.9 (C3), 80.1 (C4), 79.4 (C2), 74.4 (C5), 55.1 (OMe); ^{31}P NMR δ: 15.5.

(Methyl 2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-L-*threo*-α-D-*gluco*-oct-1,5-pyranosid-8-uronyl)-(triphenylphosphoranylidene)methane[8] (1c). ^{1}H NMR δ: 4.62 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.0 (m, 2H, H-3,4), 3.88 (dd, 1H, $J_{4,5}$ = 10.1, $J_{5,6}$ = 1.3 Hz, H-5), 3.55 (dd, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 3.33 (OMe), 1.54 and 1.51 (CMe_2); ^{13}C NMR δ: 97.9 (C1), 82.8 (C3,4), 79.5 (C2), 79.6 (C4) and 77.5 (C-5); ^{31}P NMR δ: 16.9.

(Methyl 2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-D-*threo*-α-D-*gluco*-oct-1,5-pyranosid-8-uronyl)-(triphenylphosphoranylidene)methane[8] (1d). ^{1}H NMR δ: 4.60 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 3.96 (dd, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 3.91 (dd, 1H, $J_{4,5}$ = 9.9, $J_{5,6}$ = 1.5 Hz, H-5), 3.70 (dd, 1H, H-4), 3.57 (dd, 1H, H-2), 3.36 (OMe), 1.48 and 1.45 (CMe_2); ^{13}C NMR δ: 98.3 (C1), 82.2 (C3), 80.0 (C2), 79.1 (C4) and 68.2 (C5); ^{31}P NMR δ: 16.5.

***Dimethyl* (benzyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-heptopyranos-6-ulos-7-yl) phosphonate (17).** To a stirred solution of dimethyl methylphosphonate (1 mL, 9.34 mmol) in dry THF (20 mL) at -78 °C, a solution of BuLi (2.5M in hexane, 3.6 mL) was added and the mixture was stirred under an argon atmosphere at -78 °C for 15 min. A solution of uronate **16** (1.74 g, 3.06 mmol; prepared by the oxidation of alcohol **15** with the Jones'[13] reagent and subsequent reaction with CH_2N_2) in THF (5 mL) was added, stirring was continued for an additional 20 min at -78 °C and the mixture was allowed to reach room temperature. TLC (hexanes - ethyl acetate, 2:1) showed disappearance of a starting material and formation of a new, very polar product. The mixture was partitioned between ethyl acetate and brine, the organic layer was separated, washed twice with water, dried, concentrated, and the crude product was purified by column chromatography (hexanes - ethyl acetate 2:1 to 1:1) to afford **17** as an oil (1.51 g, 75%). $[\alpha]_D$ +22.1°. ^{1}H NMR δ: 4.98 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.31 (d, 1H, $J_{4,5}$ = 9.0 Hz, H-5), 4.12 (dd, 1H, H-4), 3.97 (dd, 1H, $J_{3,4}$ = 8.8, $J_{2,3}$ = 2.8 Hz, H-3), 3.77 (dd, 1H, H-2), 3.73, 3.77 [2d, 6H, $J_{H,P}$ = 11.2 Hz, $P(OC\underline{H}_3)_2$], 3.36 (dd, 1H, $J_{7a,7b}$ = 14.5, $J_{7a,P}$ = 22.0 Hz, H-7a), 3.21 (dd, 1H, $J_{7b,P}$ = 22.1 Hz, H-7b); ^{13}C NMR δ: 197.8 (d, $J_{6,P}$ = 6.8 Hz, C6), 97.4 (C1), 79.2 (C3), 75.8 (C5), 74.8 (C4), 74.2 (C2), 74.6, 72.6, 72.1, 69.3 (4×O$\underline{C}H_2$Ph), 52.7, 52.6 [2d, $J_{C,P}$ = 6.2 and 6.4 Hz,

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$P(O\underline{C}H_3)_2$], 37.7 (d, $J_{7,P}$ = 130.3 Hz, C7); *m/z*: 661.2558 [$M(C_{37}H_{41}O_9P) + H^+$ = 661.2566].

General method for the preparation of higher sugar enones. To a solution of sugar phosphonate (**6**,[8] **17**, **21**[8] 2 mmol) and appropriate sugar aldehyde (**7**, **9**, **11** 2 mmol) in dry toluene (20 mL) anhydrous potassium carbonate (0.4 g) was added followed by a catalytic amount of 18-crown-6 (*ca.* 5% mol; the crown ether can be replaced with more convenient Bu_4NBr without significant changes in the time of the reaction and yields of the products). The heterogeneous mixture was vigorously stirred overnight at room temperature and was partitioned between ether (50 mL) and brine (20 mL). The organic layer was separated, washed with water, dried and concentrated and the product was purified by column chromatography (hexane - ethyl acetate, 5:1 → 3:1).

3-*O*-Benzyl-5-deoxy-5-*C*-[methyl 9-deoxy-2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-L-*threo*-α-D-*gluco*-nonopyranos-8-ulose-9(*E*)-ylidene]-1,2-*O*-isopropylidene-α-D-xylofuranose (8). Prepared from phosphonate **6** and aldehyde **7** in 92% yield. $[\alpha]_D$ -9.6°. ^{1}H NMR δ: 7.00 (dd, 1H, $J_{10,11}$ = 4.6, $J_{9,10}$ = 15.8 Hz, H-10), 6.86 (dd, 1H, $J_{9,11}$ = 1.1 Hz, H-9), 5.99 (d,1H, $J_{13,14}$ = 3.7 Hz, H-14), 4.71 (m, 1H, H-11), 4.60 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.04 (dd, 1H, $J_{3,4}$= 9.5 Hz, H-3), 3.60 (dd, 1H, $J_{4,5}$ = 10.0 Hz, H-4), 3.40 (s, 3H, OMe), 1.49 (6H), 1.32, and 1.26 (2×CMe_2); ^{13}C NMR δ: 198.8 (C=O), 141.9 (C10), 126.3 (C9), 111.8 and 110.8 (2×$\underline{C}Me_2$), 105.0 (C14), 98.7 (C1), 83.1, 82.7, 82.5, 79.8 (double intensity), 79.6, 78.1, 77.6 and 69.7 (9×C), 75.7, 74.7, 73.2, and 72.1 (4×$\underline{C}H_2Ph$), 55.1 (OMe), 26.8, 26.5, 26.2, and 25.8 (2×$C\underline{Me}_2$); *m/z*: 859.3651 [$M(C_{49}H_{56}O_{12}) + Na^+$ = 859.3670].

Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-*C*-[methyl 9-deoxy-2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-L-*threo*-α-D-*gluco*-nonopyranos-8-ulose-9(*E*)-ylidene]-α-D-manno-pyranoside (10). Prepared from phosphonate **6** and aldehyde **9** in 60% yield. $[\alpha]_D$ +45.3°. ^{1}H NMR δ: 7.15 (dd, 1H, $J_{10,11}$ = 4.6, $J_{9,10}$ = 15.9 Hz, H-10), 6.93 (dd, 1H, $J_{9,11}$ = 1.5 Hz, H-9), 3.39 and 3.27 (2×OMe), 1.50 and 1.30 (CMe_2); ^{13}C NMR δ: 199.1 (C=O), 144.9 (C10), 125.3 (C9), 110.8 ($\underline{C}Me_2$), 99.2 and 97.7 (C1,15), 82.6, 80.0, 79.8, 79.6, 78.1, 78.0, 77.7, 74.7, 70.9, and 70.0 (10×C), 75.7, 75.2, 74.8, 73.2, 72.9, and 72.3 (6×$\underline{C}H_2Ph$), 55.1 and 54.9 (2×OMe), 26.6 and 26.0 ($C\underline{Me}_2$); *m/z*: 1043 [$M(C_{62}H_{68}O_{13}) + Na^+$].

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Anal. Calcd for $C_{62}H_{68}O_{13}$: C, 72.92; H, 6.71. Found: C, 72.79; H, 6.90

Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-*C*-[methyl 9-deoxy-2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-L-*threo*-α-D-*gluco*-nonopyranos-8-ulose-9(*E*)-ylidene]-α-D-glucopyranoside (12). Prepared from phosphonate **6** and aldehyde **11** in 72% yield. $[\alpha]_D$ +32.7°. ^{1}H NMR δ: 7.09 (dd, 1H, $J_{10,11}$ = 4.5, $J_{9,10}$ = 15.8 Hz, H-10), 6.85 (dd, 1H, $J_{9,11}$ = 1.1 Hz, H-9), 3.51 (dd, 1H, $J_{1,2}$ = 3.5, $J_{2,3}$ = 9.6 Hz, H-2), 3.39 and 3.34 (2×OMe), 1.51 and 1.28 (CMe_2); ^{13}C NMR δ: 198.9 (C=O), 144.4 (C10), 124.8 (C9), 110.7 ($\underline{C}Me_2$), 98.0 and 97.6 (C1,15), 82.5, 81.7, 81.4, 79.8, 79.6 (double), 78.0, 77.6, 69.6, and 69.5 (10C), 75.7, 75.6, 75.2, 74.6, 73.3, and 73.2 (6×$\underline{C}H_2Ph$), 55.9 and 55.7 (2×OMe), 27.1 and 26.6 ($C\underline{Me}_2$); *m/z*: 1043 [$M(C_{62}H_{68}O_{13}) + Na^+$].

Anal. Calcd for $C_{62}H_{68}O_{13}$: C, 72.92; H, 6.71. Found: C, 72.70; H, 6.89

3-*O*-Benzyl-5-deoxy-5-*C*-[benzyl 2,3,4-tri-*O*-benzyl-7-deoxy-α-D-*manno*-heptopyranosid-6-ulose-7(*E*)-ylidene]-1,2-*O*-isopropylidene-α-D-xylofuranose (18). Prepared from phosphonate **17** and aldehyde **7** in 82% yield. $[\alpha]_D$ +8.5°. ^{1}H NMR δ: 7.05 (dd, 1H, $J_{8,9}$ = 4.7, $J_{7,8}$ = 15.9 Hz, H-8), 6.78 (dd, 1H, $J_{7,9}$ = 1.6 Hz, H-7), 5.96 (d, 1H, $J_{11,12}$ = 3.7 Hz, H-12), 5.00 (d, 1H, $J_{1,2}$ = 2.2 Hz, H-1), 4.20 (dd, 1H, $J_{3,4}$ = 8.9, $J_{4,5}$ = 9.1 Hz, H-4), 3.98 (dd, 1H, $J_{2,3}$ = 2.8 Hz, H-3), 3.92 (d, 1H, $J_{9,10}$ = 3.3 Hz, H-10), 3.80 (dd, 1H, H-2), 1.50 and 1.32 (CMe_2); ^{13}C NMR δ: 199.5 (C=O), 141.2 (C8), 127.5 (C7), 111.8 ($\underline{C}Me_2$), 104.9 (C12), 97.6 (C1), 83.0, 82.7, 79.7, 79.2, 75.9, 75.6, and 74.6 (7×C), 74.8, 72.7, 72.3, 72.1, and 69.5 (5×$\underline{C}H_2Ph$), 26.8 and 26.2 ($C\underline{Me}_2$); *m/z*: 835.3461 [$M(C_{50}H_{52}O_{10}) + Na^+$ = 835.3458].

Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-*C*-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-heptopyranos-6-ulose-7(*E*)-ylidene]-α-D-glucopyranoside (22). Prepared from phosphonate **21** and aldehyde **11** in 80% yield. $[\alpha]_D$ -33.3°. ^{1}H NMR δ: 7.10 (dd, 1H, $J_{8,9}$ = 4.3, $J_{7,8}$ = 15.8 Hz, H-8), 6.89 (dd, 1H, $J_{7,9}$ = 1.3 Hz, H-7), 5.66 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 3.51 (dd, 1H, $J_{11,12}$ = 3.6 Hz, $J_{12,13}$ = 9.7 Hz, H-12), 3.35 (s, 3H, OCH_3), 1.50, 1.35, 1.33, and 1.28 (2×$C\underline{Me}_2$); ^{13}C NMR δ: 196.3 (C=O), 143.0 (C8), 124.8 (C7), 109.6 and 108.8 (2×$\underline{C}Me_2$), 98.0 and 96.3 (C1,13), 81.8, 81.7, 79.6, 73.3, 72.3, 70.6, 70.3, and 69.6 (8×C), 75.8, 75.3, 73.4 (3×CH_2Ph), 55.3 (OMe), 25.9, 25.8, 24.8, 24.2 (2×$C\underline{Me}_2$); *m/z*: 739.3122 [$M(C_{41}H_{48}O_{11}) + Na^+$ = 739.3094].

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Reduction of higher sugar enones with zinc borohydride.

The appropriate enone (**8**, **18**, and **21**; 1.5 mmol) was dissolved in dry diethyl ether (15 mL) and the solution cooled to 0 °C (ice-water bath). A solution of zinc borohydride (4 mL of a *ca.* 0.5M solution in diethyl ether) was added, and the mixture was stirred for 30 min at 0 °C. Excess hydride was decomposed by careful addition of water, the organic layer was separated washed with dilute H_2SO_4, water, dried and concentrated and the crude product was separated by column chromatography (hexane - ethyl acetate, 4:1 → 2:1).

3-*O*-Benzyl-5-deoxy-5-*C*-[methyl 9-deoxy-2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-L-*arabino*- and D-*xylo*-α-D-*gluco*-nonopyranos-9(*E*)-ylidene]-1,2-*O*-isopropylidene-α-D-xylofuranoses (13*S* and 13*R* respectively). These alcohols were obtained (as an inseparable mixture of *S*/*R* stereoisomers in the ratio 1:2; ^{1}H NMR estimation for OMe signals at δ: 3.35 and 3.33 ppm, respectively) by reduction of **8** in 83% yield. *m/z*: 861.3860 [M($C_{49}H_{58}O_{12}$) + Na^+ = 861.3826].

3-*O*-Benzyl-5-deoxy-5-*C*-[benzyl 2,3,4-tri-*O*-benzyl-7-deoxy-D-*glycero*-α-D-*man no*-heptopyranosid-7(*E*)-ylidene]-1,2-*O*-isopropylidene-α-D-xylofuranose (19). Obtained from **18** in 80% yield. $[\alpha]_D$ -11.9°. ^{1}H NMR δ: 5.86-6.12 (m, 3H, $J_{11,12}$ = 3.8 Hz, H-7,8,12), 4.93 (d, 1H, $J_{1,1}$ = 1.7 Hz, H-1), 1.50 and 1.31 (CMe_2); ^{13}C NMR δ: 133.5 and 129.6 (C7,8), 111.3 ($\underline{C}Me_2$), 104.8 (C12), 96.9 (C1), 84.5, 83.5, 81.5, 80.9, 76.2, 75.3, 75.1, and 72.7 (8×C), 75.2, 72.8, 72.7 (double intensity), and 69.6 (5×$\underline{C}H_2Ph$), 22.8 and 26.2 ($C\underline{Me}_2$); *m/z*: 837.3628 [M($C_{50}H_{54}O_{10}$) + Na^+ = 837.3615].

Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-*C*-[7-deoxy-1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-heptopyranos-7(*E*)-ylidene]-α-D-glucopyranoside (23). Obtained from **22** in 64% yield. $[\alpha]_D$ -14.2°. ^{1}H NMR δ: 6.08-5.90 (m, 2H, H-7,8), 5.55 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1), 4.28 (dd, 1H, $J_{2,3}$ = 2.2 Hz, H-2), 3.99 (dd, 1H, $J_{10,11}$ = 9.0 Hz, H-11), 3.46 (dd, 1H, $J_{12,13}$ = 3.5 Hz, $J_{11,12}$ = 9.7 Hz, H-12), 3.37 (s, 3H, OMe), 3.21 (dd, 1H, $J_{9,10}$ = 9.7 Hz, H-10), 1.44 (2×), 1.29, and 1.25 (2×CMe_2); ^{13}C NMR δ: 109.3 and 108.4 (2×$\underline{C}Me_2$), 97.9 and 96.4 (C1,13), 82.6, 81.5, 79.7, 71.6, 71.3, 70.6, 70.4, 70.2, and 68.7 (9×C), 75.6, 74.9, 73.2 (3×CH_2Ph), 55.1 (OMe), 25.9, 25.8, 24.8, 24.1 (2×CMe_2); *m/z*: 741.3289 [M($C_{41}H_{50}O_{11}$) + Na^+ = 741.3251].

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Determination of the configuration of higher sugar allylic alcohols 13, 19 and 23. The appropriate olefin (**13** as a 1:2 mixture of the *S/R* isomers and pure isomers **19** and **23**; 1 mmol each) was dissolved in dichloromethane (20 mL) and methanol (5 mL) and cooled to -78 °C. Ozone was bubbled through the solution until the blue color persisted (*ca.* 15 min). The solution was flushed with oxygen to remove excess ozone (*ca.* 10 min), the solvent was evaporated under vacuum, the crude material was dissolved in methanol (20 mL) and reduced with sodium borohydride (*ca.* 0.1 g) for 1 h. The reaction mixture was worked-up in the usual way and the residue subjected to column chromatography (hexane - ethyl acetate, 3:1 → 1:1). First eluted were the corresponding monoalcohols 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranose or methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside, respectively. Eluted next were the corresponding diols **14*S*** (less polar isomer, 25%) and **14*R*** (50%) as pure isomers from ozonolysis of the **13*S/R*** mixture (in a ratio 1:2), **20** (70% from **19**), or **24** (70% from **23**), characterized as diacetate **25**.

Methyl 2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-L-*arabino*-α-D-*gluco*-nono-1,5-pyranoside (14*S*). ^{1}H NMR δ: 4.81 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 4.03 (dd, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, H-3), 3.83 (dd, 1H, $J_{4,5}$ = 9.9, $J_{5,6}$ = 3.3 Hz, H-5), 3.38 (s, OMe), 1.44 and 1.38 (CMe_2); ^{13}C NMR δ: 109.7 ($\underline{C}Me_2$), 97.9 (C1), 82.2, 80.5, 79.4, 78.8, 77.4, 73.2, and 70.2 (C2,3,4,5,6,7,8), 75.7, 74.5, and 73.3 (3×CH_2Ph), 64.0 (C9), 55.3 (OMe), 27.2 and 27.0 ($C\underline{Me}_2$).

Methyl 2,3,4-tri-*O*-benzyl-6,7-*O*-isopropylidene-D-*xylo*-α-D-*gluco*-nono-1,5-py-ranoside (14*R*). $[\alpha]_D$ -11.9°. ^{1}H NMR δ: 4.57 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.35 (dd, 1H, $J_{6,7}$ = 8.2, $J_{5,6}$ = 3.5 Hz, H-6), 4.21 (d, 1H, $J_{7,8}$ ~0 Hz, H-7), 4.01 (dd, 1H, $J_{2,3}$ = 9.4, $J_{3,4}$ = 9.0 Hz, H-3), 3.83 (dd, 1H, $J_{4,5}$ = 9.9 Hz, H-5), 3.36 (s, OMe), 1.44 and 1.42 (CMe_2). ^{13}C NMR δ: 109.5 ($\underline{C}Me_2$), 97.8 (C1), 82.1, 79.4, 79.2, 78.6, 77.2, 69.6, and 69.4 (C2,3,4,5, 6,7,8), 75.7, 74.6, and 73.2 (3×CH_2Ph), 65.1 (C9), 55.2 (OMe), 27.1 and 26.8 ($C\underline{Me}_2$). *m/z*: 617.2706 [M($C_{34}H_{42}O_9$) + Na^+ = 617.2726].

Benzyl 2,3,4-tri-*O*-benzyl-D-*glycero*-α-D-*manno*-heptopyranoside[9] (20). $[\alpha]_D$ +48.1°. ^{1}H NMR δ: 4.86 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1); ^{13}C NMR δ: 96.9 (C1), 80.4, 76.9, 74.4, 72.6, and 71.4 (C2,3,4,5,6), 62.9 (C7), 75.1, 72.8, 71.9, and 69.0 (4×CH_2Ph).

6,7-Di-*O*-acetyl-1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-galactoheptopyranose (25). ^{1}H NMR δ: 5.50 (dd, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 5.15 (ddd, 1H, $J_{5,6}$ = 8.8 Hz, $J_{6,7a}$ = 4.0 Hz, $J_{6,7b}$ = 2.2 Hz, H-6), 4.62 (dd, 1H, $J_{2,3}$ = 2.6 Hz, $J_{3,4}$ = 7.8 Hz, H-3), 4.59 (dd, 1H, $J_{7a,7b}$ = 12.5 Hz, H-7b), 4.33 (dd, 1H, H-2), 4.25 (dd, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 4.22 (dd, 1H, H-7a), 4.03 (dd, 1H, H-5), 2.07, 2.06 (2×$COCH_3$), 1.55, 1.43, 1.34, 1.32 (2×CMe_2). The H6 resonance for the opposite L-*glycero* isomer δ: 5.32 ppm.[10]

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