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A NEW SYNTHESIS OF L-ASCORBIC ACID FROM D-GALACTOSE

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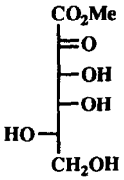
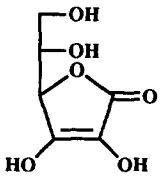
Key Words: 2,6-Anhydro-3-deoxy-hex-2-enonic acids; hex-2-ulopyranosonates; eliminations; conformations.

Abstract. *- 1,5-Anhydro-D-galactitol, easily available from D-galactose, was selectively protected in positions 2, 3 and 4 and converted into 5-O-acetyl-2,6-anhydro-3-deoxy-L-*threo*-hex-2-enonic acid methyl ester, which, on reaction with MCPBA in acetic acid gave 2,5-di-O-acetyl-α-L-*lyxo*-hex-2-ulopyranosonic acid methyl ester. Reaction of the latter with sodium methoxide produced sodium L-ascorbate in high yield. Several side-reactions and the conformations of some of the intermediates are also discussed.*

Among natural products, L-ascorbic acid certainly has been one of the most extensively investigated targets of synthetic organic chemists, owing to its great industrial importance as a vitamin, a drug, a presumed prophylactic agent, an antioxidant, etc. A huge number of synthetic approaches[1] to vitamin C have therefore been proposed since Reichstein's first synthesis of 1933.[2] Apart from a few build-up sequences, mainly of historical interest, starting from L-threose, L-lyxose, or L-xylose, most of these syntheses use as the starting material D-glucose, the hydroxymethylene groups in positions 2 and 3 of which provide, in the great majority of cases, the chiral L-*threo* 4,5-moiety of L-ascorbic acid through countless alternative pathways involving chemical and/or microbiological steps. Strangely enough, D-galactose, having the same configuration at positions 2 and 3 as D-glucose, has been completely neglected as the starting material for L-ascorbic acid syntheses. The nearest to it is a sequence, starting from pectin, which is converted into D-galacturonic acid, *via* enzymic hydrolysis, followed by its transformation into methyl L-*lyxo*-hex-2-ulosonate (**1**), and further into L-ascorbic acid (**2**) with an overall yield of about 3%.[3]



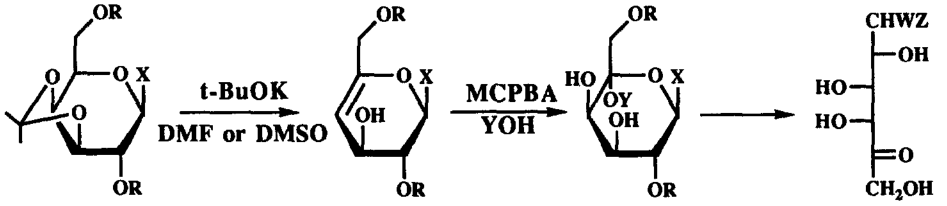
1



2

We have been interested during the last few years in the use, as versatile reaction intermediates, of the unsaturated sugar derivatives of types **5** (4-deoxy-α-L-*threo*-hex-4 enopyranosides) and **6** (2,6-anhydro-3-

deoxy-L-*threo*-hex-2-enitols), which are readily available, respectively, from 3,4-*O*-isopropylidene-β-D-galactopyranosides (3)[4] and from 1,5-anhydro-3,4-*O*-isopropylidene-D-galactitols (4)[5]. They can be converted by *m*-chloroperoxybenzoic acid (MCPBA), in the presence of appropriate nucleophiles (alcohols, acyloxy anions) into the adducts of types **7** and **8**, which on deprotection by acid hydrolysis or hydrogenolysis lead to L-*arabino*-hexose-5-ulose (**9**)[6] and L-tagatose (**10**)[5], or their derivatives. These reaction sequences therefore formally correspond to selective oxidations in position 5 of D-galactose or *meso*-galactitol.



3: X=OMe
4: X=H

5: X=OMe
6: X=H

7: X=OMe; Y=Alk, Ac
8: X=H; Y=Alk, Ac

9: WZ = O
10: WZ=H, OH

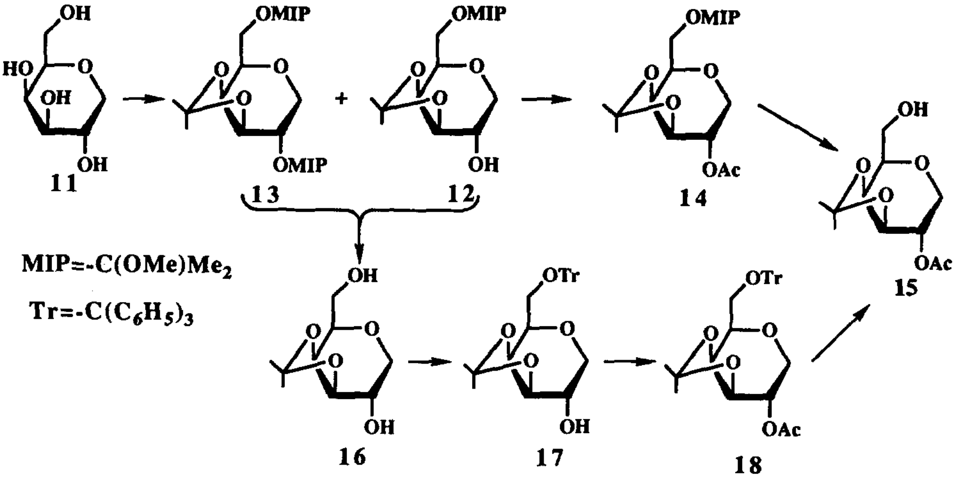
One possible use of these reactions appeared to be in the conversion of D-galactose into L-ascorbic acid. If the sequence **3** → **9** was chosen, this required selective reduction of the aldehydo group of **9** to hydroxymethyl and oxidation at C-6, followed by esterification to obtain the immediate precursor **1**. If the sequence **4** → **10** was followed, only the oxidation/esterification steps were required at some stage. We chose the latter approach that appeared simpler.

RESULTS AND DISCUSSION

1,5-Anhydro-D-galactitol (**11**) was prepared from tetra-*O*-acetyl-D-galactopyranosyl bromide, by reduction with tributyltin hydride, followed by Zemplen methanolysis.[7] Its conversion into the ester **1** required appropriate protection, which had to be different depending on which of several alternative pathways was chosen. The sequence of the three key steps, elimination to give the 4,5-unsaturated intermediate, its oxidation with peroxyacid to produce the 5-*O*-substituted adduct, and oxidation at position 6 to form the carboxylic group, did not necessarily have to follow this order. We chose to perform the last of these operations first, since it was expected that, in the presence of an aldehydic or carboxylic functionality, conjugation would greatly favour a subsequent elimination.

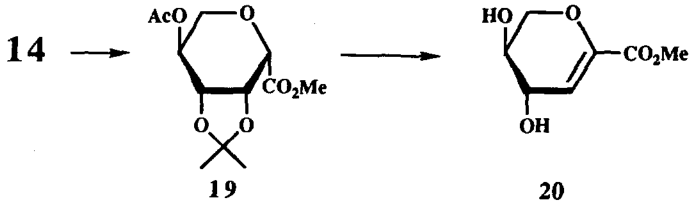
We had previously reported in preliminary form[5] that a dilute solution of **11** in 2,2-dimethoxypropane is converted into a mixture of the bis-acetal **12** (50%) and the tris acetal **13** (40%), which are easily separated by flash-cromatography. This reaction is much less selective with **11** than with the configurationally analogous β-D-galactopyranosides, which form the corresponding bis-acetals in over 90% yield,[8] obviously because of the smaller hindrance around 2-OH of **11** in the absence of the anomeric group. Acetylation of **12** to **14**, followed by selective deprotection from the highly labile mixed acetal group at position 6, produced **15**, which has the right protection for oxidation at this position.

A more complete conversion of **11** into **15** was achieved by selective deprotection of the crude mixture of **12** and **13** to 1,5-anhydro-3,4-*O*-isopropylidene-D-galactitol (**16**), followed by tritylation to **17**, acetylation to **18**, and hydrogenolytic detritylation, to give **15** in 73% overall yield from **11**.



Several methods were investigated for the conversion of **14** or **15** into the ester **19**. A recent report[9] on the direct high yield conversion into the methyl ester of a D-galactopyranoside analogue of **14** by oxidation with Jones reagent (deprotection in 6 immediately occurs in the acidic medium), followed by esterification with methyl iodide under phase transfer conditions, made this approach promising for application to **14**. However, under the reported conditions, only 30% of the desired ester **19** was obtained, accompanied by recovered **15** and by non-identified products of more extensive oxidation. Apparently the acidity of the medium (H_2SO_4) causes removal not only of the labile 6-OH protection, but in part also of the more stable 3,4-*O*-isopropylidene one, with consequent over-oxidation of the substrate.

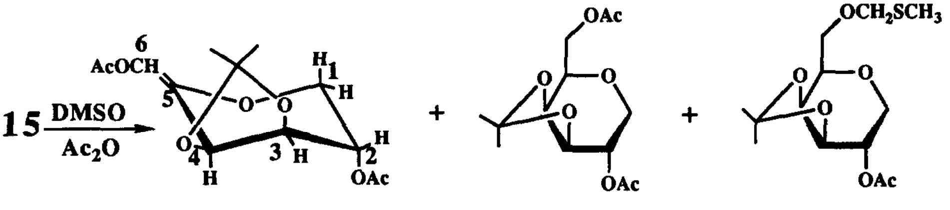
Treatment of **19** with sodium methoxide in methanol produced methanolysis of the acetyl group and elimination of acetone to give the unsaturated ester **20**. This very facile elimination reaction has previously been observed for D-galactopyranosiduronic ester analogues of **19**.[10]



The oxidation of **15** with DMSO in acetic anhydride,[11,12] a mild procedure often employed in the carbohydrate field for the conversion of primary and secondary alcoholic functions into the corresponding aldehydes and ketones, was investigated next, with an essentially negative result.

The only product related to the expected aldehyde that was isolated from the reaction was the corresponding enol acetate **21** (25% yield), accompanied by the diacetate **22** (40%) and by the 6-*O*-methylthiomethyl derivate **23** (13%), a Pummerer rearrangement product frequently encountered in this type of oxidations.[11]

The structure of **21** as 2,6-di-*O*-acetyl-3,4-*O*-isopropylidene-L-*arabino*-hex-5-enitol clearly resulted from its ^1H and ^{13}C NMR spectra, which also showed that it exists in an approximately $^5C_2$ (L) conformation on the basis of the low values of all vicinal coupling constants (between 1.28 and 2.74 Hz), except $J_{3,4}$, the value of which (7.10 Hz) points to a significant flattening of the C(2)-C(3)-C(4)-C(5) dihedral angle, that can be attributed to the presence of the fused dioxolane ring and to the sp^2 hybridation at C(5). A significant long-range coupling (J=2.17 Hz) between H(3) and H(1eq) and a smaller one (0.57 Hz) between H(2) and H(4) provided further confirmation of the conformation of **21**. Literature references[13] to similar compounds of the L-*xylo* and D-*arabino* series report NMR and X-ray diffraction evidence that diastereomers with Z configuration around the double bond exist in solution as equilibria between $^5C_2$ and $^2C_5$ conformers, whereas the corresponding E forms are exclusively in the $^5C_2$ form. Although we did not establish whether our compound **21** has the E or Z configuration, the fact that it adopts the $^5C_2$ form may hint to its being the E diastereomer.

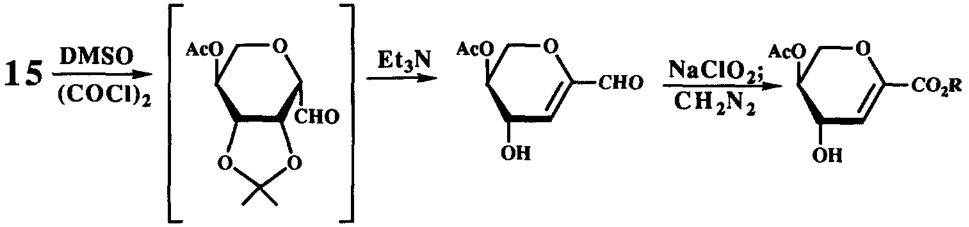


21
$^5C_2$ (L)

22

23

A third approach to the oxidation of **15**, the Swern method[11] employing oxalyl chloride and DMSO, proved to be definitely better than the other two. Under these conditions, with addition of the triethylamine at the end of the reaction, the unsaturated aldehyde **25** was obtained in 80% yield. Its oxidation with sodium chlorite[14] gave the corresponding acid **26**, which was converted into the ester **27** with diazomethane in an overall yield of 69% from **15**.



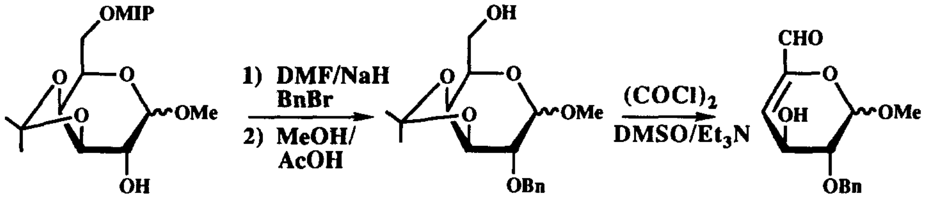
24

25

26: R=H
27: R=Me

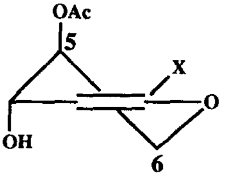
The conversion of **15** into **25** obviously involves an elimination of acetone from the intermediate saturated aldehyde **24**, which is similar to the *t*-BuOK promoted transformation of **3** and **4** into **5** and **6**. The presence of the aldehydo group makes, as expected, the formation of the adjacent carbanion and the subsequent cleavage of the C(4)-*O* axial bond particularly facile, so that triethylamine is sufficiently basic to promote elimination. A similar oxidation-elimination had been observed in the treatment of methyl 2,3,4-tri-*O*-acetyl-D-glucopyranoside with DMSO/SO_3/pyridine.[15] On the other hand oxidations in positions 6 with DMSO/$(COCl)_2$/Et_3N of 3,4-*O*-isopropylidene[16] or 3,4-*O*-cyclohexylidene derivatives[17] of D-galactopyranosides have been reported to give the corresponding saturated aldehydes in high yields.

Since it appeared unlikely that the absence of the anomeric substituent could be the cause of the facile elimination reaction during the Swern oxidation of **15**, we applied the same method to the α and β anomers of the D-galactopyranoside derivative **29**, obtained by benzylation and selective deprotection of α- and β-**28**. The β-anomer was converted into the unsaturated aldehyde α-**30** in 90% yield, whereas the formation of β-**30** from α-**29** was only partial (about 50%), and some of the saturated 3,4-*O*-isopropylidene aldehyde was also present in the reaction product. It may be mentioned that in the case of D-galactopyranosides of type **3** only β-anomers were readily converted by *t*-BuOK in DMF into the 4-deoxy-α-L-*threo*-hex-4-enopyranosides **5**, whereas the corresponding α-anomers were totally resistant to this treatment.[4]

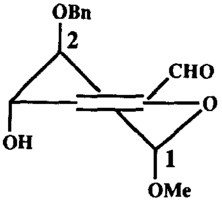


28 **29** **30**

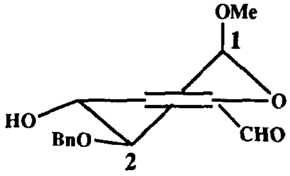
As shown by their H-H coupling constants compounds **25-27** exhibit a high preference for the $^{5}H_{6}$ (L) half-boat conformation with axial and pseudo-axial substituents in position 4 and 5, and compound α-**30** for the structurally analogous $^{1}H_{2}$ (L) diaxial-pseudo-diaxial form, whereas β-**30** prevalently exists in the $^{2}H_{1}$ (L) form. This is in accordance with previous observations on the corrisponding compounds with CH_2OH in place of CHO or COOR, the 2,6-anhydro-3-deoxy-L-*threo*-hex-2-enitols[5] (such as **6**) and the 4-deoxy-α-L-threo-hex-4-enopyranosides (such as **5**)[4] on one hand, and the corrisponding β forms[18] (anomers of **5**) on the other, which show inverted conformational preferences. It can thus be stated that the conformational situation is indipendent of the nature of the group that is adjacent to the double bond: be it CH_2OH, CHO, COOH or COOMe the very similar values of ring proton coupling costants clearly point to almost identical conformations.



25-27
$^{5}H_{6}$ (L)

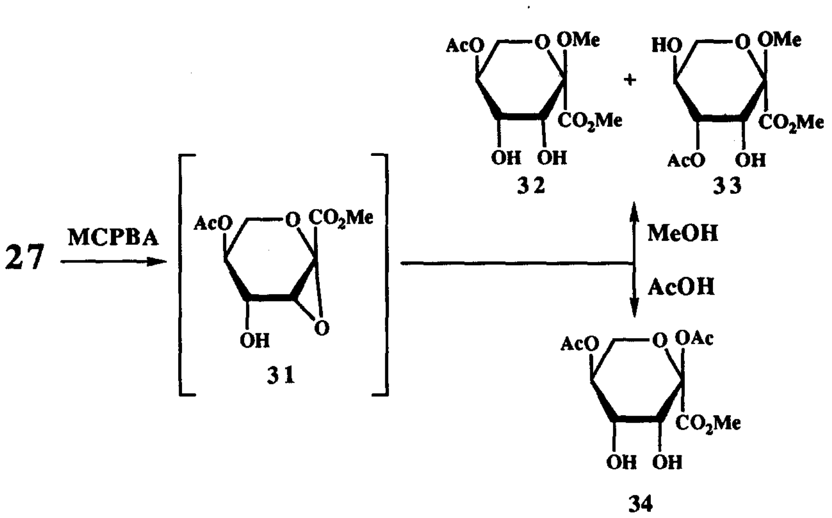


α-30
$^{1}H_{2}$ (L)



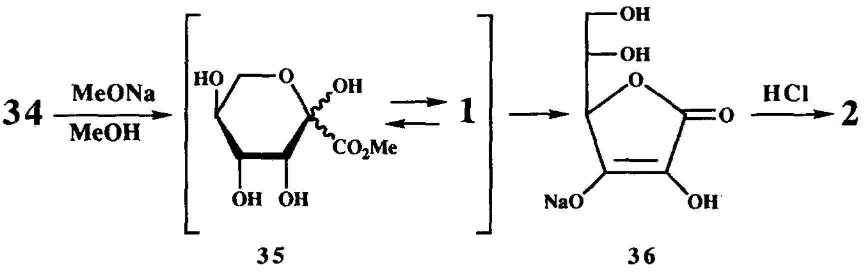
β-30
$^{2}H_{1}$ (L)

Further elaboration of the unsaturated ester **27** into L-ascorbic acid required the introduction of a hydroxy group at position 3 and of an equivalent of a carbonyl group in position 2. This was achieved by the reaction with MCPBA in a nucleophilic solvent, as in the conversion of **5** or **6** into **7** and **8**. When methanol was used as the solvent the adduct **32** was obtained in 78% yield, accompanied by the acyl shift product **33** (15%). When the peroxyacid reaction was conducted in acetic acid, the adduct **34** was formed in 78% yield.



Compounds **32-34** derive from nucleophilic opening of the intermediate labile epoxide **31** and their structure and $^2C_5$ (L) conformation are clearly shown by their NMR spectra. The only point which does not immediately result from their proton spectra is the configuration at C(2), which can however be confidently assumed to be α-L, on the basis of the fact that in all previously studied cases of reactions of this type anti opening of the epoxide ring has been proven beyond doubt. Furthermore, the moderately negative values of the specific rotations of **32-34** are in good agreement with those found for α-L-hexos-2-ulopyranose derivatives, including some hex-2-ulopyranosidonic esters very closely related to the compounds under discussion.[19]

Compound **32-34** are masked forms of methyl L-*lyxo*-hex-2-ulosonate (**1**) and are well suited for being converted into L-ascorbic acid (**2**) through suitable deprotection with acidic and/or basic reagents. Although it should be possible to transform the **32**+**33** mixture directly into **2** under acid conditions promoting complete deprotection and lactonization, some difficulties were envisaged in view of the different nature of the three groups to be removed (*O*-acetyl, methyl ester and methyl glycoside), and actually encountered in preliminary experiments. On the other hand, a single treatment of compound **34** with sodium methoxide in methanol converted it in almost quantitative yield into sodium L-ascorbate (**36**), through methanolysis of the two *O*-acetyl groups, producing **35**, the pyranosic form of **1**, followed by lactonization, enolization and salt formation. Neutralization with hydrogen chloride in methanol gave L-ascorbic acid (**2**), for which the ^{13}C NMR spectrum of the crude product provided proof of the absence of significant amounts of side-products.



This new synthesis of the vitamin C, although certainly not competitive with industrial methods involving microbiological steps, is simpler than most of the known non-enzymatic approaches from which it differs by having D-galactose as the starting material. It can find some uses in the preparation of non-natural analogues or derivatives of ascorbic acid.

Experimental

Melting points were determined with a Kofler apparatus and are uncorrected. Optical rotations were measured on (1.0±0.1)% solutions in $CHCl_3$ at 20±2°C on a Perkin-Elmer 241 polarimeter. ^1H NMR spectra (internal Me_4Si) were recorded with a Bruker AC 200 instrument at 200 MHz. First order spectral analysis was performed whenever possible, otherwise spectra were simulated with PANIC (Bruker) computer program. Chemical shift and J coupling values were confirmed, when necessary, with COSY or J-RES experiments. In some cases signal overlapping prevented a complete analysis. ^{13}C NMR spectra were recorded with the same spectrometer at 50 MHz. Assignments were made with the aid of DEPT and HETCOR experiments. All reactions were followed by TLC on Kieselgel 60 F_{254} with detection by UV light or with ethanolic 10% phosphomolybdic or sulphuric acid and heating. Kieselgel 60 (Merck, 70-230 or 230-400 mesh) was used for column and flash chromatography. Solvents were distilled and stored over 4Å molecular sieves activated by heating for at last 24 h at 400° C. All reactions were conducted under argon.

1,5-Anhydro-3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-D-galactitol (12); 1,5-anhydro-3,4-*O*-isopropylidene-2,6-di-*O*-(1-methoxy-1-methylethyl)-D-galactitol (13). A suspension of 1,5-anhydro-D-galactitol[7] (**11**, 1 g, 6.1 mmole) in 2,2-dimethoxypropane (61 ml), containing 10-camphorsulfonic acid (30 mg) was stirred at room temperature. The compound slowly dissolved and after 48 h TLC showed that a stationary situation had been reached with the formation of two products. Triethylamine (0.5 ml) was added, the solution was evaporated *in vacuo*, and the residue subjected to flash chromatography (elution with 1:1 hexane/AcOEt, containing 0.1% Et_3N) to yield compounds **13** (842 mg, 40%) and **12** (849 mg, 50%).

Compound 12: R_f 0.20 (1:1 hexane/AcOEt), m.p. 138-140°C (from AcOEt/hexane), $[\alpha]_D$ + 39.5°, ^1H NMR (CD_3CN) δ: 1.28 (s, 9 H, 2 MIP Me + 1 dioxolane Me); 1.43 (s, 3 H, dioxolane Me); 3.01 (dd, 1 H, $J_{1',2}$ 10.12 Hz, H-1'); 3.14 (s, 3 H, OMe); 3.45 (dd, 1 H, $J_{5,6'}$ 7.42 Hz, H-6'); 3.53 (dd, 1 H, $J_{6,6'}$ 10.01 Hz, H-6); 3.60 (ddd, 1 H, $J_{2,3}$ 7.09 Hz, H-2); 3.73 (ddd, 1 H, $J_{5,6}$ 4.64 Hz, H-5); 3.77 (dd, 1 H, $J_{1,2}$ 5.33 Hz, $J_{1,1'}$ 11.02 Hz, H-1); 3.88 (dd, 1 H, $J_{3,4}$ 5.55 Hz, H-3); 4.15 (dd, 1 H, $J_{4,5}$ 2.15 Hz, H-4). ^{13}C NMR (CD_3CN) δ: 23.64 (2 MIP Me); 25.43 and 27.35 (2 dioxolane Me); 47.68 (OMe); 60.57 (C-6); 67.98 (C-1); 68.76 (C-2); 73.80 (C-4); 75.18 (C-5); 78.90 (C-3); 99.71 (MIP*C*Me_2); 108.84 (dioxolane *C*Me_2). Anal. Calcd. for $C_{13}H_{24}O_6$: C, 56.5%; H, 8.8%. Found: C, 56.0%; H, 8.6%.

Compound 13: R_f 0.68 (1:1 hexane/AcOEt), m.p. 50-51°C (from hexane), $[\alpha]_D$ +36.4°, ^1H NMR (CD_3CN) δ: 1.28 (1 s, 9 H, 2 6-MIP Me + 1 dioxolane Me); 1.29 and 1.32 (2 s, 6 H, 2 2-MIP Me); 1.45 (s, 3 H, 1 dioxolane Me); 3.03 (dd, 1 H, $J_{1',2}$ 9.97 Hz, H-1'); 3.14 (s, 3 H, 6-MIP OMe); 3.18 (s, 3 H, 2-MIP OMe); 3.45 (dd, 1 H, $J_{5,6'}$ 7.36 Hz, H-6'); 3.52 (dd, 1 H, $J_{6,6'}$ 10.02 Hz, H-6); 3.72 (ddd, 1 H, $J_{5,6}$ 4.64 Hz, H-5); 3.75 (ddd, 1 H, $J_{2,3}$ 7.31 Hz, H-2); 3.89 (dd, 1 H, $J_{1,2}$ 5.33 Hz, $J_{1,1'}$ 11.09 Hz, H-1); 3.93 (dd, 1 H, $J_{3,4}$ 5.48 Hz, H-3); 4.16 (dd, 1 H, $J_{4,5}$ 2.14 Hz, H-4). ^{13}C-NMR (CD_3CN) δ: 23.64 and 23.66 (2 6-MIP Me); 24.57 and 25.10 (2 2-MIP Me); 25.51 and 27.13 (2 dioxolane Me); 47.68 (6-MIP OMe); 48.47 (2-MIP OMe); 60.56 (C-6); 67.42 (C-1); 68.53 (C-2); 74.04 (C-4); 75.09 (C-5); 77.75 (C-3); 99.69 (6-MIP *C*Me_2); 100.47 (2-MIP *C*Me_2); 108.75 (dioxolane *C*Me_2). Anal. Calcd. for $C_{17}H_{32}O_7$: C, 58.6%; H, 9.3%. Found: C, 58.1%; H, 9.0%.

2-*O*-Acetyl-1,5-anhydro-3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-D-galactitol (14). A solution of **12** (2 g, 7.25 mmole) in pyridine (70 ml) and acetic anhydride (35 ml) was left 24 h at room temperature, then coevaporated three times with toluene and the residue was purified by chromatography on silica gel (eluant 3:2 hexane/AcOEt + 0.1% Et_3N) to give **14** in 94% yield. R_f 0.60 (1:1 hexane/AcOEt), $[\alpha]_D$ +53.5°, ^1H NMR (CD_3CN) δ: 1.29 (s, 9 H, 2 MIP Me + 1 dioxolane Me); 1.44 (1 s, 3 H, 1 dioxolane Me); 2.02 (s, 3 H, OAc); 3.14 (dd, 1 H, $J_{1'2}$ 9.92 Hz, H-1'); 3.15 (s, 3 H, MIP OMe); 3.48 (dd, 1 H, $J_{5,6'}$ 7.25 Hz, H-6'); 3.55 (dd, 1 H, $J_{6,6'}$ 10.01 Hz, H-6); 3.79 (ddd, 1 H, $J_{5,6}$ 4.83 Hz, H-5); 3.89 (dd, 1 H, $J_{1,2}$ 5.23 Hz, $J_{1,1'}$ 11.28 Hz, H-1); 4.13 (dd, 1 H, $J_{3,4}$ 5.63 Hz, H-3); 4.24 (dd, 1 H, $J_{4,5}$ 2.08 Hz, H-4); 4.80 (dd, 1 H, $J_{2,3}$ 7.10 Hz, H-2). ^{13}C NMR (CD_3CN) δ: 21.08 (*Me*CO); 24.66 (2 MIP Me); 26.29 and 28.10 (2 dioxolane Me); 48.72 (MIP OMe); 61.42 (C-6); 65.58 (C-1); 71.69 (C-2); 74.81 (C-4); 75.98 (C-3); 76.21 (C-5); 100.78 (MIP *C*Me_2); 110.37 (dioxolane *C*Me_2); 171.03 (Me*C*O). Anal. Calcd. for $C_{15}H_{26}O_7$: C, 56.6%; H, 8.2%. Found: C, 56.6%; H, 8.1%.

1,5-Anhydro-3,4-*O*-isopropylidene-D-galactitol (16). The crude product (1g) from the reaction of **11** with 2,2-dimethoxypropane was dissolved in a 10:1 methanol/water mixture (50 ml) containing acetic acid (0.1 g) and the solution was heated at 50° C for 30 min. After addition of Et_3N (0.2 ml), evaporation *in vacuo* , two coevaporations of the residue with toluene (2 x 10 ml) and chromatography on silica gel (AcOEt as eluant) the acetonide **16** was obtained in 94% yield. R_f 0.27 (AcOEt), m.p. 92-93° C (from AcOEt/hexane), $[\alpha]_D$ +73.0°, ^1H NMR (CD_3CN/D_2O) δ: 1.28 and 1.43 (2 s, 6 H, 2 dioxolane Me); 3.02 (dd, 1 H, $J_{1',2}$ 10.01 Hz, H-1'); 3.55-3.67 (m, 4 H, a HETCOR experiment assigns H-6,6' at δ 3.60 and 3.63, H-2 at δ 3.62 and H-5 at δ 3.66); 3.79 (dd, 1 H, $J_{1,2}$ 5.31 Hz, $J_{1,1'}$ 11.00 Hz, H-1); 3.88 (dd, 1 H, $J_{3,4}$ 5.61 Hz, $J_{2,3}$ 7.02 Hz, H-3); 4.16 (dd, 1 H, $J_{4,5}$ 1.83 Hz, H-4). ^{13}C NMR (CD_3CN/D_2O) δ: 25.42 and 27.28 (2 dioxolane Me); 61.64 (C-6); 67.95 (C-1); 68.75 (C-2); 73.54 (C-4); 76.56 (C-5); 78.88 (C-3); 108.84 (dioxolane *C*Me_2). Anal. Calcd. for $C_9H_{16}O_5$: C, 52.9%; H, 7.9%. Found: C, 52.1%; H, 7.8%.

1,5-Anhydro-3,4-*O*-isopropylidene-6-*O*-trityl-D-galactitol (17). A solution of **16** (500 mg, 2.45 mmole), trityl chloride (1.35 g, 4.9 mmole) and 4-dimethylaminopyridine (70 mg, 0.57 mmole) in dry pyridine (6 ml) was stirred at room temperature for 48 h. Coevaporation with toluene *in vacuo* and chromatography on silica gel (1:1 hexane/AcOEt) gave **17** (960 mg, 88% yield). R_f 0.61 (1:1 hexane/AcOEt), m.p. 61-63°C (from AcOEt/hexane), $[\alpha]_D$ +11.7°, ^1H NMR ($CDCl_3$) δ: 1.38 and 1.48 (2 s, 6 H, 2 dioxolane Me); 3.08 (dd, 1 H, $J_{1,2}$ 10.10 Hz, $J_{1,1'}$ 10.93 Hz, H-1); 3.35 (dd, 1 H, $J_{5,6}$ 6.41 Hz, H-6); 3.41 (dd, 1 H, $J_{5,6'}$ 6.51 Hz, $J_{6,6'}$ 9.11 Hz, H-6'); 3.70-3.99 (m, 4 H, H-1', H-2, H-3 and H-5); 4.30 (dd, 1 H, $J_{3,4}$ 5.41 Hz, $J_{4,5}$ 2.15 Hz, H-4); 7.22-7.34 (m, 9 H, aromatic); 7.42-7.49 (m, 6 H, aromatic). ^{13}C NMR ($CDCl_3$) δ: 26.21 and 28.18 (2 dioxolane Me); 62.77 (C-6); 68.14 (C-1); 69.62 (C-2); 73.61 (C-4); 75.50 (C-5); 79.35 (C-3); 86.71 (*C*Ph_3); 109.63 (dioxolane *C*Me_2); 126.96 (*para* C); 127.73 and 128.69 (*ortho* and *meta* C); 143.85 (ipso *C*). Anal. Calcd. for $C_{28}H_{30}O_5$: C, 75.3%; H, 6.8%. Found: C, 75.0%; H, 6.5%.

2-*O*-Acetyl-1,5-anhydro-3,4-*O*-isopropylidene-6-*O*-trityl-D-galactitol (18). Acetylation of **17** as described for the preparation of **14** gave, after chromatography on silica gel **18** in 95% yield. R_f 0,40 (4:1 hexane/AcOEt), m.p. 58-60°C (from hexane), $[\alpha]_D$ +23,6°, ^1H NMR ($CDCl_3$) δ: 1.37 and 1.50 (2 s, 6 H, 2 dioxolane Me); 2.08 (s, 3 H, OAc); 3.12 (dd, 1 H, $J_{1,2}$ 9.64 Hz, $J_{1,1'}$ 11.29 Hz, H-1); 3.37 (dd, 1 H, $J_{5,6'}$ 6.32 Hz, H-6'); 3.41 (dd, 1 H, $J_{6,6'}$ 10.31 Hz, H-6); 3.73 (ddd, 1 H, $J_{5,6}$ 6.42 Hz, H-5); 4.01 (dd, 1 H, $J_{1',2}$ 5.25 Hz, H-1'); 4.14 (dd, 1 H, $J_{3,4}$ 5.62 Hz, H-3); 4.34 (dd, 1 H, $J_{4,5}$ 2.05 Hz, H-4); 4.94 (ddd, 1 H, $J_{2,3}$ 6.99 Hz, H-2); 7.22-7.34 (m, 9 H, aromatic); 7.43-7.49 (m, 6 H, aromatic). Anal. Calcd. for $C_{30}H_{32}O_6$: C, 73.7%; H, 6.6%. Found: C, 73.6%, H, 6.5%.

2-*O*-Acetyl-1,5-anhydro-3,4-*O*-isopropylidene-D-galactitol (15). Method a: Compound **14** was selectively deprotected by the method described above for the preparation of **16** to give, after chromatography on silica, **15** in 95% yield. **Method b**: A solution of **18** (880 mg, 1.80 mmole) in MeOH (40 ml) was subjected to hydrogenation in the presence of 10% Pd/C at room temperature and pressure. After 90 min the calculated amount of hydrogen had been absorbed. Filtration over Celite^R, evaporation and chromatography on silica gel (1:1 hexane/AcOEt) gave **15** (400 mg, 92% yield). R_f 0.21 (1:1 hexane/AcOEt), m.p. 84-85°C (from AcOEt/hexane), $[\alpha]_D$ +82.8°, ^1H NMR (CD_3CN) δ: 1.30 and 1.44 (2 s, 6 H, 2 dioxolane Me); 2.02 (s, 3 H, OAc); 3.14 (dd, 1 H, $J_{1,2}$ 9.87 Hz, H-1); 3.60 (m, 2 H, $J_{5,6'}$ 6.55 Hz, $J_{5,6}$ 5.32 Hz, H-6 and H-6'); 3.72 (ddd, 1 H, $J_{4,5}$ 1.97 Hz, H-5); 3.90 (dd, 1 H, $J_{1,1'}$ 11.28 Hz, H-1'); 4.14 (dd, 1 H, $J_{2,3}$ 7.08 Hz, H-3); 4.24 (dd, 1 H, $J_{3,4}$ 5.67 Hz, H-4); 4.79 (ddd, 1 H, $J_{1',2}$ 5.26 Hz, H-2). ^{13}C-NMR (CD_3CN) δ: 21.13 (*Me*CO); 26.34 and 28.08 (2 dioxolane Me); 62.32 (C-6); 65.64 (C-1); 71.79 (C-2); 74.60 (C-4); 76.27 (C-3); 77.46 (C-5); 110.52 (dioxolane *C*Me_2); 171.39 (Me*C*O). Anal. Calcd. for $C_{11}H_{18}O_6$: C, 53.7%; H, 7.4%. Found: C, 52.9%; H, 6.9%.

Methyl 5-*O*-acetyl-2,6-anhydro-3,4-*O*-isopropylidene-L-galactonate (19). A solution of compound **14** (636 mg, 2.0 mmole) in acetone (30 ml) and CH_2Cl_2 (20 ml), cooled at O°C was treated dropwise with CrO_3 (420 mg, 4.2 mmole) in 2 *N* H_2SO_4 (2 ml). After 3 h the starting material had disappeared (TLC). Ethanol (10 ml) was added at 0°C and after stirring for 30 min and filtration through Celite^R, the solution was concentrated *in vacuo* to 100 ml, neutralized with solid $NaHCO_3$, dried on $MgSO_4$, and evaporated to dryness *in vacuo*. The residue was taken up in CH_2Cl_2 (30 ml), water (15 ml), methyl iodide (1.5 ml) and Bu_4NBr (0.7 g) were added and the suspension was vigorously stirred at room temperature for 20 h. After filtration through Celite^R the organic phase was separated, the aqueous one was washed with CH_2Cl_2 (4 x 30 ml), the combined organic phases were dried ($MgSO_4$) and evaporated to dryness. The residue was dissolved in the minimum amount of CH_2Cl_2 and ether was added to precipitate the quaternary ammonium bromide. After filtration, chromatography on silica gel (1:1 hexane/AcOEt) allowed to separate the ester **19** (165 mg, 30% yield) from compound **15** (150 mg, 30%) and other unidentified side-products.

Compound 19: R_f 0.41 (1:1 hexane/AcOEt), m.p. 137-138°C (from AcOEt/hexane), $[\alpha]_D$ +21.1°, ^1H NMR (CD_3CN) δ: 1.30 and 1.43 (2 s, 6 H, 2 dioxolane Me); 2.03 (s, 3 H, OAc); 3.31 (dd, 1 H, $J_{5,6'}$ 8.38 Hz, H-6'); 3.72 (s, 3 H, OMe); 4.02 (dd, 1 H, $J_{6,6'}$ 11.59 Hz, $J_{5,6}$ 5.06 Hz, H-6); 4.26 (dd, 1 H, $J_{3,4}$ 5.96 Hz, H-4); 4.43 (d, 1 H, $J_{2,3}$ 2.39 Hz, H-2); 4.54 (dd, 1 H, H-3); 4.84 (ddd, 1 H, $J_{4,5}$ 6.34 Hz, H-5). ^{13}C NMR (CD_3CN) δ: 21.06 (*Me*CO); 26.04 and 27.64 (2 dioxolane Me); 52.58 (OMe); 65.20 (C-6); 70.41 (C-5); 74.75 (C-2 and C-3); 75.31 (C-4); 110.83 (dioxolane *C*Me$_2$); 169.20 (MeCO); 170.85 (C-1). Anal. Calcd. for $C_{12}H_{18}O_7$: C, 52.6%; H, 6.6%. Found: C, 52.2%; H, 6.5%.

Methyl 2,6-anhydro-3-deoxy-L-*threo*-hex-2-enonate (20). A solution of compound **19** (274 mg, 1 mmole) in methanol (30 ml) containing sodium methoxide (1.5 mmole) was left at room temperature for 1 h. After neutralization with acetic acid, elimination of the solvent *in vacuo* and chromatography of the residue on silica gel (AcOEt) compound **20** was obtained as a syrup (164 mg, 94% yield). R_f 0.44 (AcOEt), $[\alpha]_D$ +129.6°, ^1H NMR (CD_3CN) δ: 3.73 (s, 3 H, OMe); 3.65 (dddd, 1 H, $J_{3,5}$ 1.20 Hz, H-5); 3.91 (dd, 1 H, $J_{5,6'}$ 2.26 Hz, H-6'); 3.92 (ddd, 1 H, $J_{4,5}$ 3.0 Hz, $J_{4,6}$ 1.43 Hz, H-4); 4.02 (ddd, 1 H, $J_{6,6'}$ 11,48 Hz, $J_{5,6}$ 4.45 Hz, H-6); 5.94 (dd, 1 H, $J_{3,4}$ 4.59 Hz, H-3). ^{13}C NMR (CD_3CN) δ: 52.77 (OMe); 65.40 (C-6); 67.57 (C-4); 68.43 (C-5); 110.60 (C-3); 145.32 (C-2); 163.77 (C-1). Anal. Calcd. for $C_7H_{10}O_5$: C, 48.3%; H, 5.8%; Found: C, 47.9%; H, 6.0%.

Oxidation of 15 with DMSO/Ac$_2$O: 2,6-di-*O*-acetyl-1,5-anhydro-3,4-*O*-isopropylidene-L-*arabino*-hex-5-enitol (21); 2,6-di-*O*-acetyl-1,5-anhydro-3,4-*O*-isopropylidene-D-galactitol (22); 2-*O*-acetyl-1,5-anhydro-3,4-*O*-isopropylidene-6-*O*-methylthiomethyl-D-galactitol (23). A solution of compound **15** (246 mg, 1 mmole) in DMSO (2.3 ml) and Ac_2O (0.7 ml) was stored at room temperature for 60 h. Water (5 ml) was added and the product was extracted with CH_2Cl_2. Evaporation and chromatography on silica gel (1:1 hexane/AcOEt) gave, in the order, products **22** (115 mg, 40%), **21** (72 mg, 25%) and **23** (27 mg, 13%).

Compound 21: R_f 0.81 (9.5:0.5 CH_2Cl_2/acetone), $[\alpha]_D$ +31.8°, ^1H NMR ($CDCl_3$) δ: 1.36 and 1.53 (2 s, 6 H, 2 dioxolane Me); 2.10 and 2.21 (2 s, 6 H, 2 OAc); 4.14 (ddd, 1 H, $J_{6,6'}$ 12.11 Hz, $J_{4,6}$ 2.17 Hz, $J_{5,6}$ 2.74 Hz, H-6); 4.24 (ddd, 1 H, $J_{3,4}$ 7.10 Hz, $J_{4,5}$ 1.73 Hz, H-4); 4.37 (dd, 1 H, $J_{5,6'}$ 1.28 Hz, H-6'); 4.56 (ddd, 1 H, $J_{1,3}$ 0.2 Hz, H-3); 4.81 (dddd, 1 H, $J_{3,5}$ 0.57 Hz, H-5); 6.87 (d, 1 H, H-1); ^{13}C-NMR ($CDCl_3$) δ: 20.64 and 20.94 (2 *Me*CO); 23.98 and 26.60 (2 dioxolane Me); 62.65 (C-6); 69.31 (C-4); 70.89 (C-3); 71.91 (C-5); 109.63 (dioxolane *C*Me$_2$); 119.15 (C-1); 133.05 (C-2); 167.32 and 169.78 (2 MeCO). Anal. Calcd. for $C_{13}H_{18}O_7$: C, 51.9%; H, 6.4%. Found: C, 51.4%; H, 6.2%.

Compound 22: R_f 0.59 (1:1 hexane/AcOEt), m.p. 87-92°C (from AcOEt/hexane), $[\alpha]_D$ +70.8°, ^1H NMR (CD_3CN) δ: 1.30 and 1.45 (2 s, 6 H, 2 dioxolane Me); 2.01 and 2.02 (2 s, 6 H, 2 OAc); 3.18 (dd, 1 H, $J_{1',2}$ 9.54 Hz, H-1'); 3.91 (ddd, 1 H, $J_{5,6}$ 4.53 Hz, H-5); 3.92 (dd, 1 H, $J_{1,2}$ 5.20 Hz, $J_{1,1'}$ 11.40 Hz, H-1); 4.13 (dd, 1 H, $J_{5,6'}$ 7.33 Hz, H-6'); 4.20 (dd, 1 H, $J_{3,4}$ 5.74 Hz, H-3); 4.21 (dd, 1 H, $J_{6,6'}$ 11.60 Hz, H-6); 4.25 (dd, 1 H, $J_{4,5}$ 2.08 Hz, H-4); 4.81 (ddd, 1 H, $J_{2,3}$ 6.75 Hz, H-2). ^{13}C NMR (CD_3CN) δ: 20.95 and 21.08 (2 *Me*CO); 26.27 and 27.97 (2 dioxolane Me); 64.63 (C-6); 65.47 (C-1); 71.30 (C-2); 74.28 (C-4); 74.46 (C-3); 76.01 (C-5); 110.67 (dioxolane *C*Me$_2$); 170.97 and 171.45 (2 Me*C*O). Anal. Calcd. for $C_{13}H_{20}O_7$: C, 54.2%; H, 7.0%. Found: C, 53.7%; H, 7.3%.

Compound 23: R_f 0.74 (9.5:0.5 CH_2Cl_2/acetone); $[\alpha]_D$ +13.3°, ^1H NMR (CD_3CN) δ: 1.30 and 1.44 (2 s, 6 H, 2 dioxolane Me); 2.02 (s, 3 H, OAc); 2.10 (s, 3 H, SMe); 3.15 (dd, 1 H, $J_{1',2}$ 9.80 Hz, H-1'); 3.61 (dd, 1 H, $J_{5,6'}$ 7.53 Hz, H-6'); 3.71 (dd, 1 H, $J_{6,6'}$ 10.28 Hz, H-6); 3.87 (ddd, 1 H, $J_{5,6}$ 4.43 Hz, H-5); 3.90 (dd, 1 H, $J_{1,2}$ 5.24 Hz, $J_{1,1'}$ 11.34 Hz, H-1); 4.14 (dd, 1 H, $J_{3,4}$ 5.68 Hz, H-3); 4.23 (dd, 1 H, $J_{4,5}$ 2.08 Hz, H-4); 4.65 and 4.69 (AB system, 2 H, J_{AB} 11.43 Hz, S*CH*$_2$); 4.80 (ddd, 1 H, $J_{2,3}$ 6.97 Hz, H-2). ^{13}C NMR (CD_3CN) δ: 13.73 (SMe); 21.08 (*Me*CO); 26.32 and 28.07 (2 dioxolane Me); 65.56 (C-1); 68.10 (C-6); 71.56 (C-2); 74.71 (C-4); 75.40 (C-3); 75.90 (SCH_2); 76.15 (C-5); 110.43 (dioxolane *C*Me$_2$); 170.99 (MeCO).

5-*O*-Acetyl-2,6-anhydro-3-deoxy-L-*threo*-hex-2-enose (25). To oxalyl chloride (0.70 ml, 8 mmole) in dry CH_2Cl_2 cooled at -60°C, a solution of dry DMSO (1.4 ml, 20 mmole) in CH_2Cl_2 (10 ml) was added drop-wise under stirring, followed, after 2 min, by one of compound **15** (1.97 g, 8.0 mmole) in the same solvent (10 ml). Stirring was continued for 30 min at -60°C, Et_3N (5 ml) was slowly added, and, after the mixture had reached room temperature, addition of water (30 ml) separation of the organic phase, extraction of the aqueous one with CH_2Cl_2 (3 x 30 ml), washing the combined organic layers with saturated NaCl, drying with $MgSO_4$, evaporation and chromatography over silica gel (1:1 hexane/AcOEt) gave **25** as an oil (1.19 g, 80% yield). R_f 0.33 (9:1 CH_2Cl_2/acetone), $[\alpha]_D$ +104,3°, ^1H NMR (C_6D_6) δ: 1.53 (s, 3 H, OAc); 3.69 (dd, 1 H, $J_{5,6'}$ 1.96 Hz H-6'); 3.83 (ddd, 1 H, $J_{4,5}$ 2.91 Hz, $J_{4,6}$ 1.62 Hz, H-4); 3.90 (ddd, 1 H, $J_{6,6'}$ 12.10 Hz,

$J_{5,6}$ 3.52 Hz, H-6); 4.71 (dddd, 1 H, $J_{3,5}$ 1.42 Hz, H-5); 5.28 (dd, 1 H, $J_{3,4}$ 4.82 Hz, H-3); 8.84 (s, 1 H, H-1); ^{13}C NMR (C_6D_6) δ: 20.38 (*Me*CO); 62.01 (C-4); 63.79 (C-6); 70.06 (C-5); 116.93 (C-3); 152.53 (C-2); 170.12 (Me*C*O); 186.86 (C-1). Anal. Calcd. for $C_8H_{10}O_5$: C, 51.6%; H, 5.4%. Found: C, 51.0%; H, 5.6%.

5-*O*-Acetyl-2,6-anhydro-3-deoxy-L-*threo*-hex-2-enonic acid (26). A solution of compound **25** (600 mg, 3.22 mmole) and 2,3-dimethyl-2-butene (chlorine scavenger[14], 1.8 ml) in *t*-BuOH (18 ml) was cooled at 0°C and treated with a solution of 80% $NaClO_2$ (0.4 g, 3.52 mmole) and $NaH_2PO_4 \cdot 2H_2O$ (0.4 g) in water (4 ml). After 3 h at room temperature, **25** had disappeared and the solvent was eliminated *in vacuo*, water (20 ml) was added to the residue, the solution was brought to pH 2 with 2 N HCl, the product was extracted with AcOEt (5 x 50 ml), the organic layer was dried over $MgSO_4$ and evaporated *in vacuo* to give a residue that was practically pure **26** (604 mg, 93% yield). R_f 0.28 (10:7 AcOEt/MeOH), m.p. 96-110°C (from hexane/AcOEt); $[\alpha]_D$ +146° (MeOH), ^{1}H NMR (CD_3CN) δ: 2.00 (s, 3 H, OAc); 4.00 (dd, 1H, $J_{5,6'}$ 1.75 Hz. H-6'); 4.03 (ddd, 1 H, $J_{4,5}$ 3.0 Hz, $J_{4,6}$ 1.67 Hz, H-4); 4.21 (ddd, 1 H, $J_{6,6'}$ 12.17 Hz, $J_{5,6}$ 3.34 Hz, H-6); 4.81 (dddd, 1 H, $J_{3,5}$ 1.48 Hz, H-5); 6.04 (dd, 1 H, $J_{3,4}$ 4.87 Hz, H-3). ^{13}C NMR (CD_3CN) δ: 21.07 (*Me*CO); 61.07 (C-4); 64.80 (C-6); 70.13 (C-5); 110.09 (C-3); 145.39 (C-2); 163.85 (C-1); 171.01 (Me*C*O).

Methyl 5-*O*-acetyl-2,6-anhydro-3-deoxy-L-*threo*-hex-2-enonate (27). A solution of **26** (300 mg, 1.48 mmole) in AcOEt was treated drop-wise with CH_2N_2 in ether until a persistent yellow colour was observed. After decomposition of excess CH_2N_2 with a few drops of acetic acid and evaporation *in vacuo*, the residue was purified by chromatography on silica gel (1:1 hexane/AcOEt) to yield **27** (294 mg, 92%) as syrup. R_f 0.33 (1:1 hexane/AcOEt); $[\alpha]_D$ +118°, ^{1}H NMR (CD_3CN) δ: 1.99 (s, 3 H, OAc); 3.75 (s, 3 H, OMe); 3.98 (dd, 1 H, $J_{5,6'}$ 1.80 Hz, H-6'); 3.99 (ddd, 1 H, $J_{4,5}$ 2.77 Hz, $J_{4,6}$ 1.75 Hz, H-4); 4.20 (ddd, 1 H, $J_{6,6'}$ 12.25 Hz, $J_{5,6}$ 3.21 Hz, H-6); 4.79 (dddd, 1 H, $J_{3,5}$ 1.44 Hz, H-5); 6.01 (dd, 1 H, $J_{3,4}$ 4.97 Hz, H-3). ^{13}C NMR (CD_3CN) δ: 21.07 (*Me*CO); 52.88 (OMe); 61.86 (C-4); 64.81 (C-6); 70.17 (C-5); 109.83 (C-3); 145.70 (C-2); 163.51 (C-1); 170.83 (Me*C*O). Anal. Calcd. for $C_9H_{12}O_6$: C, 50.0%; H, 5.6%. Found: C, 49.9%; H, 5.8%.

Methyl 2-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (α-29). 60%NaH in mineral oil (570 mg, 14.2 mmole) was washed with hexane (3 x 30 ml), suspended in dry DMF (10 ml), cooled at 0°C and treated with compound **α-28**[20] (490 mg, 1.60 mmole) in DMF (12 ml). After stirring 15 min at 0°C and 30 min at room temperature, the mixture was cooled again at 0°C, and benzyl bromide (0.4 ml, 3.3 mmole) was added and stirring was continued for 15 min at 0°C and 2 h at room temperature. After decomposition of excess NaH by careful addition of MeOH most of the solvents were evaporated *in vacuo*, the residue was taken up with 20 ml of ice-cold water, the product was extracted with CH_2Cl_2 (4 x 30 ml), the organic phase was dried ($MgSO_4$), the solvent evaporated and the residue taken up in 10:1 MeOH/H_2O (20 ml) containing 5 drops of acetic acid. After 10 min Et_3N (5 drops) was added, the solution was evaporated *in vacuo* and the residue coevaporated twice with toluene. Chromatography of the residue on silica gel (1:1 hexane/AcOEt) gave α-**29** as on oil (435 mg, 84% yield). R_f 0.29 (1:1 hexane/AcOEt), $[\alpha]_D$ +95.7°, ^{1}H NMR (CD_3CN) δ: 1.28 and 1.36 (2 s, 6 H, 2 dioxolane Me); 3.33 (s, 3 H, OMe); 3.48 (dd, 1 H, $J_{2,3}$ 7.59 Hz, H-2); 3.64 (m, 1 H, H-6'); 3.67 (m, 1 H, H-6); 3.92 (m, 1 H, H-5); 4.18 (m, 1 H, $J_{3,4}$ 5.43 Hz, H-3); 4.22 (m, 1 H, $J_{4,5}$ 1.55 Hz, H-4); 4.65 and 4.69 (AB system, 2 H, $J_{A,B}$ 12.03 Hz, benzylic CH_2); 4.76 (d, 1 H, $J_{1,2}$ 3.54 Hz, H-1); 7.29-7.38 (m, 5 H, aromatic). ^{13}C NMR (CD_3CN) δ: 26.63 and 28.42 (2 dioxolane Me); 55.51 (OMe); 62.36 (C-6); 68.78 (C-5); 72.55 (benzylic CH_2); 72.55 (C-4); 76.65 (C-2); 78.10 (C-3); 98.62 (C-1); 109.67 (dioxolane *C*Me_2); 128.50 (*para* C); 128.78 and 129.82 (*ortho* and *meta* C); 139.62 (*ipso* C). Anal. Calcd. for $C_{17}H_{24}O_6$: C, 63.0%; H, 7.4%. Found: C, 62.5%; H, 7.2 %.

Methyl 2-*O*-benzyl-3,4-*O*-isopropylidene-β-D-galactopyranoside (β-29). This compound was prepared starting from **β-28**[20], as described for **α-29** in 88% yield, R_f 0.42 (2:3 hexane/AcOEt), m.p. 90-92°C (from AcOEt/hexane), $[\alpha]_D$ +46,8°, ^{1}H NMR (CD_3CN) δ: 1.29 and 1.34 (2 s, 6 H, 2 dioxolane Me); 3.27 (m, 1 H, $J_{2,3}$ 6.62 Hz, H-2); 3.49 (s, 3 H, OMe); 3.73 (m, 1 H, H-6'); 3.75 (m, 1 H, H-6); 3.78 (m, 1 H, H-5); 4.12 (m, 1 H, $J_{3,4}$ 5.64 Hz, H-3); 4.15 (dd, 1 H, $J_{4,5}$ 1.14 Hz, H-4); 4.22 (d, 1 H, $J_{1,2}$ 8.11 Hz, H-1); 4.72 and 4.76 (AB system, 2 H, $J_{A,B}$ 11.92 Hz, benzylic CH_2); 7.28-7.39 (m, 5 H, aromatic). ^{13}C NMR (CD_3CN) δ: 26.60 and 28.22 (2 dioxolane Me); 56.85 (OMe); 62.30 (C-6); 73.83 (benzylic CH_2); 74.32 (C-5); 74.77 (C-4); 79.92 (C-3); 81.16 (C-2); 104.48 (C-1); 110.30 (dioxolane *C*Me_2); 128.34 (*para* C); 128.81 and 129.11(*ortho* and *meta* C); 139.83 (*ipso* C). Anal. Calcd. for $C_{17}H_{24}O_6$: C, 63.0%; H, 7.4%. Found: C, 62.6%; H, 7.0%.

Methyl 2-*O*-benzyl-4-deoxy-β-L-*threo*-hex-4-enodialdo-1,5-pyranoside (β-30). Compound **α-29** was oxidized by the Swern method under the conditions described above for the conversion of **15** into **25**. The crude product was subjected to chromatography on silica gel (1:1 hexane/AcOEt) to give **β-30** in 50% yield. A second fraction was also isolated, which on the basis of NMR data appeared to be essentially methyl 2-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactodialdo-1,5-pyranoside, but was not further investigated. Compound **β-30** is a syrup, R_f 0. 38 (7:3 hexane/AcOEt), $[\alpha]_D$ +191°, ^{1}H NMR (CD_3CN) δ: 3.41 (s, 3 H, OMe); 3.61 (dd, 1 H, $J_{2,3}$ 8.08 Hz, H-2); 3.77 (d, 1 H, $J_{3,OH}$ 5.81 Hz, OH-3); 4.47 (ddd, 1 H, $J_{3,4}$ 2.90 Hz, H-3); 4.68 and 4.74 (AB system, 2 H, $J_{A,B}$ 11.85 Hz, benzylic CH_2); 5.10 (d, 1 H, $J_{1,2}$ 2.53 Hz, H-1); 5.90 (d, 1 H, H-4); 7.32-7.40 (m, 5 H, aromatic); 9.19 (s, 1 H, CHO). ^{13}C NMR (CD_3CN) δ: 57.04 (OMe); 66.13 (C-3); 73.30 (benzylic CH_2); 78.82 (C-2); 100.27 (C-1); 124.53 (C-4); 128.63 (*para* C); 128.81 and 129.27 (*ortho* and *meta* C); 139.39 (*ipso* C); 149.07 (C-5); 187.70 (C-6). Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.6%; H, 6.1%. Found: C, 63.2%; H, 5.9%.

Methyl 2-*O*-benzyl-4-deoxy-α-L-*threo*-hex-4-enodialdo-1,5-pyranoside (α-30). Swern oxidation of **β-29** under the same conditions as above gave **α-30** in 90% yield, as a syrup, R_f 0.45 (1:1 hexane/AcOEt), $[\alpha]_D$ -42.1°, ^{1}H NMR (CD_3CN) δ: 3.31 (d, 1 H, $J_{3,OH}$ 9.37 Hz, OH-3); 3.43 (s, 3 H, OMe); 3.72 (ddd, 1 H, $J_{2,3}$ 3.15 Hz, $J_{2,4}$ 1.14 Hz, H-2); 4.17 (m, 1 H, $J_{3,4}$ 4.43 Hz, H-3); 4.66 and 4.72 (AB system, 2 H, $J_{A,B}$ 11.59 Hz, benzylic CH_2); 5.20 (dd, 1 H, $J_{1,2}$ 3.58 Hz, $J_{1,3}$ 1.07 Hz, H-1); 6.06 (dd, 1 H, H-4); 7.35 (m, 5 H, aromatic); 9.23 (s, 1 H, CHO). ^{13}C NMR (CD_3CN) δ: 56.90 (OMe); 64.54 (C-3); 73.00 (benzylic CH_2); 77.53 (C-2); 100.55 (C-1); 123.13 (C-4); 128.71 (*ipso* C); 128.82 and 129.29 (*ortho* and *meta* C); 139.07 (*ipso* C); 148.59 (C-5); 188.29 (C-6). Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.6%; H, 6.1%. Found: C, 63.1%; H, 5.8%.

Methyl 5-*O*-acetyl- and 4-*O*-acetyl-α-L-*lyxo*-hex-2-ulopyranosidonic acid methyl esters (32 and 33). A solution of compound **27** (285 mg, 1.32 mmole) in MeOH (6 ml) was cooled at 0°C and 83% MCPBA (548 mg, 2.64 mmole) in MeOH (5 ml) was added drop-wise. After 4 h the starting material had disappeared (TLC), saturated $NaHCO_3$ was used to neutralize the solution, the solvent was eliminated *in vacuo*, water (5 ml) was added, the product was extracted with CH_2Cl_2 (4 x 30 ml) and, after evaporation and drying, the residue was chromatographed on silica gel (4:1 AcOEt/hexane) to give **32** (273 mg, 78%) and **33** (40 mg, 12%).

Compound 32: R_f 0.29 (1:4 hexane/AcOEt), m.p.190-192°C (from AcOEt/hexane), $[\alpha]_D$ -26.1°, ^{1}H NMR (CD_3CN) δ: 2.02 (s, 3 H, OAc); 3.13 (s, 3 H, 2-OMe); 3.29 (dd, 1 H, $J_{5,6'}$ 10.75 Hz, H-6'); 3.74 (s, 3 H, COO*Me*); 3.79 (dd, 1 H, $J_{4,5}$ 9.55 Hz, H-4); 3.82 (dd, 1 H, $J_{6,6'}$ 10.80 Hz, $J_{5,6}$ 5.75 Hz, H-6); 3.98 (d, 1 H, $J_{3,4}$ 3.47 Hz, H-3); 4.90 (ddd, 1 H, H-5). ^{13}C NMR (CD_3CN) δ: 21.10 (*Me*CO); 51.77 (2-OMe); 52.94 (COO*Me*); 60.83 (C-6); 69.47 (C-4); 69.58 (C-5); 72.59 (C-3); 101.90 (C -2); 168.25 (MeCO); 171.48 (*C*OOMe). Anal. Calcd. for $C_{10}H_{16}O_8$: C, 45.5%; H, 6.1%. Found: C, 45.4%; H, 5.9%.

Compound 33: R_f 0,26 (4:1 hexane/AcOEt). ^{1}H NMR (CD_3CN) δ: 2.06 (s, 3 H, OAc); 3.15 (s, 3 H, 2-OMe); 3.33 (dd, 1H, $J_{5,6'}$ 10.48 Hz, H-6'); 3.72 (s, 3 H, COO*Me*); 3.78 (dd, 1 H, $J_{6,6'}$ 10.84 Hz, $J_{5,6}$ 5.85 Hz, H-6); 3.96 (ddd, 1 H, $J_{4,5}$ 9.83 Hz, H-5); 4.06 (d, 1 H, $J_{3,4}$ 3.23 Hz, H-3); 4.80 (dd, 1 H, H-4). ^{13}C NMR (CD_3CN) δ: 21.28 (*Me*CO); 51.32 (2-OMe); 52.50 (COO*Me*); 64.08 (C-5); 64.19 (C-6); 70.24 (C-3); 75.33 (C-4); 102.00 (C-2); 168.28 (MeCO); 171.43 (*C*OOMe).

Methyl 2,5-di-*O*-acetyl-α-L-*lyxo*-hex-2-ulopyranosonate (34). A solution of compound **27** (710 mg, 3.39 mmole) in glacial acetic acid (33 ml) was treated at 15°C under stirring with 83% MCPBA (7.0 mmole). After 6 h the solvent was evaporated *in vacuo*, the residue was neutralized with saturated $NaHCO_3$ and extracted with CH_2Cl_2. Chromatography over silica gel (7:3 AcOEt/hexane) gave **34** (720 mg, 75% yield). R_f 0.3 (4:1 AcOEt/hexane), m.p. 189-192°C (from AcOEt/hexane); $[\alpha]_D$ -36,7° (*c* 0.55, MeOH), ^{1}H NMR (CD_3CN) δ: 2.04 and 2.07 (2 s, 6 H, 2 OAc); 3.43 (dd, 1 H, $J_{5,6'}$ 10.74 Hz, H-6'); 3.70 (s, 3 H, OMe); 3.90 (dd, 1 H, $J_{6,6'}$ 11.08 Hz, $J_{5,6}$ 5.72 Hz, H-6); 3.93 (dd, 1 H, $J_{4,5}$ 9.78 Hz, H-4); 3.99 (d, 1 H, $J_{3,4}$ 3.44 Hz, H-3); 4.96 (ddd, 1 H, H-5). ^{13}C NMR (CD_3CN) δ: 20.77 and 21.09 (2 *Me*CO); 53.09 (OMe); 62.35 (C-6); 69.01 (C-4); 69.22 (C-5); 72.39 (C-3); 98.67 (C-2); 167.35 and 169.21 (2 MeCO); 171.39 (COOMe). Anal. Calcd. for $C_{11}H_{16}O_9$: C, 45.2%; H, 5.5%. Found: C, 45.1%; H, 5.1%.

L-Ascorbic acid (2). Compound **34** (1.00 g, 3.42 mmole) was added to a 0.300 *M* solution of MeONa in MeOH (17.1 ml, 5.13 mmole). After 20 min stirring at room temperature a 0.300 *M* solution of HCl in dry MeOH (17.1 ml) was added and the solvent was evaporated *in vacuo*. A ^{13}C NMR spectrum of the residue showed that, apart from trace amounts of impurities, the residue contained L-ascorbic acid as the only organic product. It was separated from NaCl by extraction with hot absolute ethanol to give, after evaporation, practically pure L-ascorbic acid (560 mg, 93%), R_f 0,19 (5:1 AcOEt/MeOH), m.p. 184-187°C, dec. (sealed capillary), $[\alpha]_D$ +45° (MeOH); lit[21]: m.p. 190°C , dec., $[\alpha]_D$ +49° (MeOH), ^{1}H NMR (CD_3CN/D_2O) δ: 3.60 (m, 2 H, H-6 and H-6'); 3.90 (ddd, 1 H, $J_{5,6}$ 6.28 Hz, $J_{5,6'}$ 6.96 Hz, H-5); 4.78 (d, 1 H, $J_{4,5}$ 1.91 Hz, H-4). ^{13}C NMR (CD_3CN / D_2O) δ: 62.93 (C-6); 69.81 (C-5); 76.66 (C-4); 118.97 (C-2); 154.97 (C-3); 173.23 (C-1). These spectra were identical to those obtained with a commercial sample of pure L-ascorbic acid.

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