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Structure and Reactions of Glycopyranoside Derived Dialdehydes

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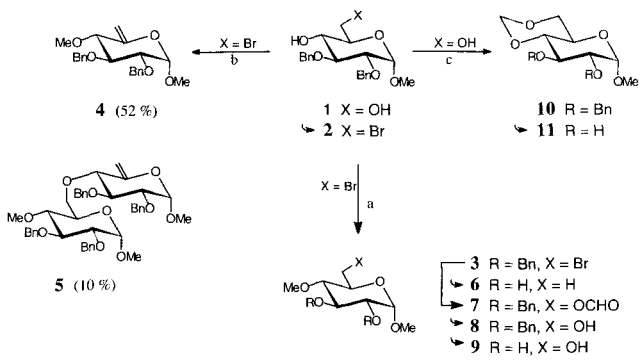
Abstract. Several 4- protected D-glucopyranosides were synthesized and cleaved by sodium metaperiodate. Depending on the protection pattern the resulting dialdehydes showed different types of structures. Predominantly dioxane structures of the hemiacetal or hemialdal type were obtained with preferred *trans* orientation of the *exo* oxygen groups at C-1 and C-2. The dialdehyde derived from methyl 4-*O*-methyl-α-D-glucopyranoside was treated with various C-nucleophiles. A higher reactivity of the aldehyde function at the former C-3 in comparison to C-2 and a special stability of dioxane type structures for glycol cleavage dialdehydes derived was observed.

Glycol cleavage has long been known as a synthetic and especially analytical tool in carbohydrate chemistry. Despite its use there is but incomplete knowledge concerning the structure of the initially obtained dialdehydes [1–6]. With regard to synthetic and property studies of starch based polycarboxylates, the dialdehydes of various model glucosides were analysed using one and two dimensional nmr techniques. The results show the preferred formation of dioxane structures. Further, their reactions with C-nucleophiles were studied to arrive at a better understanding of the chemical behaviour of glycoside derived dialdehydes.

Synthesis of 4-Protected Glucopyranosides

Starting from 4,6-cyclic acetals of methyl glucoside several different glucosides, protected at position 4 were synthesized. The cyclic acetal function was used for temporary blocking in order to get the 2,3-dibenzylated glucoside **1** [7]. Its hydroxy group at position 6 was exchanged with bromine according to Hanessian *et al.* [8] to give compound **2** [9] which was methylated subsequently by treatment with dimethyl sulfate. Whereas the reaction in ethers such as THF or glyme afforded the desired compound **3**, treatment in DMSO gave rise to the formation of exocyclic glycals. In addition to hexenoside **4** the formation of the unusual ether-bridged saccharide dimer **5** was observed. Presumably it resulted from the bromide substitution by the 4-hydroxy group of another sugar molecule. We did not search for further oligomers, since the total yield of sugars was within the expectation.

According to a published procedure [10] the 4-methylated 6-deoxy-glucoside **6** [11] was synthesized from the bromo-deoxy-glucoside **3**. Furthermore, **3** can be transformed into sugar derivative **9** [12] by substitution of the bromide with sodium formiate and subsequent deacylation of the 6-*O*-formyl-glucoside **7**, followed by hydrogenolysis of the intermediate **8**.



Scheme 1 Syntheses of 4-protected methyl glucopyranosides a) NaOH, Me_2SO_4, glyme b) NaOH, Me_2SO_4, DMSO c) CH_2Cl_2, NaOH (aq)

In addition, 4,6-*O*-methylene-glucopyranoside **11** and methyl 4,6-di-*O*-methyl-α-D-glucopyranoside (not shown) [13] were synthesized starting from **1**. Com-

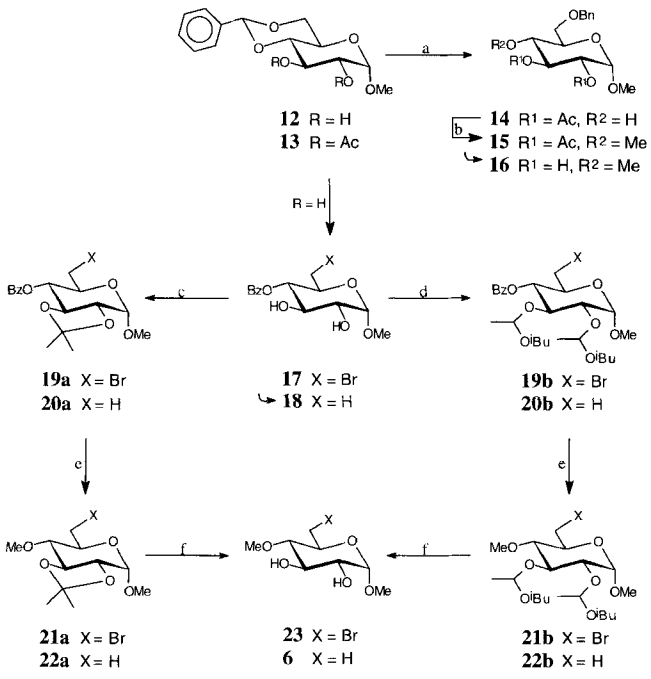
pound **11** was not obtained from methyl α-D-glucopyranoside, but easily prepared by phase transfer reaction of **1** with dichloromethane followed by debenzylation. This compound is quite soluble in water and therefore represents a good alternative to the benzylidene analogue **12** that was previously used in glycol cleavage studies [4].

In another approach the benzylidene blocking group was used not only to realize selective protection at position 2 and 3 but also for special blocking of C-6. This pathway employed oxidative and reductive transformations of the 2-phenyl-1,3-dioxane structure of 4,6-benzylidene protected glucosides such as **12** [14] and **13** [15].

Following Garegg's reduction procedure [16] compound **14** afforded the 4-methylated and 6-benzylated methyl glucoside **16** after methylation and deacetylation. Methylation was done with diazomethane catalysed by boron trifluoride etherate [17, 18]. This procedure proved to be less favourable due to rather low yields. On the other hand reductive benzylidene opening appeared to be superior even for acetylated compounds.

Alternatively, the benzylidene ring may be cleaved by oxidation with NBS [10]. The resulting 4-*O*-benzoyl-6-bromo-6-deoxy-glucoside **17** [10] represents a suitable intermediate for the synthesis of 4-methylated 6-deoxy glucosides **23** and **6** [11]. One of the central steps in this approach is the protection of the hydroxy groups by acid catalyzed vinyl ether addition [19]. The whole sequence may be carried out as a one pot procedure. The two different enol ethers chosen for the blocking gave similar yields, however, the structures of the intermediates showed interesting distinctions. Whereas isobutyl vinyl ether led to the formation of diastereoisomeric bisacetals of the open chain type such as **19b** and **20b**, with 2-methoxypropene 2,3-cyclic isopropylidene derivatives [20] such as **19a** or **20a** were obtained.

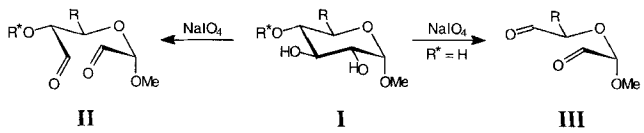
As further starting material for glycol cleavage some other glucosides were synthesized. These include butyl α- and β-D-glucopyranoside [21, 22], methyl 4-*O*-methyl-β-D-glucopyranoside [23] and methyl α-D-quinovoside [24].



Scheme 2 Syntheses of 4- and 6-protected methyl glucopyranosides a) $NaCNBH_3$, HCl; b) CH_2N_2, BF_3 OEt_2; c) H^+, 2-methoxypropene; d) H^+, isobutyl vinyl ether; e) NaOH, Me_2SO_4; f) H^+ aq

Structures of Glucoside-derived Dialdehydes

Glycol cleavage was achieved by sodium metaperiodate in aqueous solution and gave dialdehydes at the former C-2 and C-3 for the 4-protected glucosides (**II**) and at C-2 and C-4 for the sugars having a free 4-OH (**III**), respectively. Structures were determined by one and two dimensional NMR spectroscopy and are predominantly based on the assignment of vicinal coupling constants. As an additional tool the characteristic downfield shift of axial protons having an 1,3-*cis*-positioned oxygen functionality was employed.



Scheme 3

In the case of the 4-protected methyl α- and β-D-glucopyranosides the exclusive formation of an intramolecular hemiacetal was observed. This included the aldehyde at the former C-2 and the 6-hydroxy group, thus leading to dioxane structures **24** (α-glucoside) or **25** (β-glucoside). The conformation of the dioxane ring is $^1C_6$ with the numbering based on the starting material. Regarding the configuration at the hemiacetal center C-2 a 2:1 preference for the *trans*-orientation of the hydroxy group at C-2 and the alkoxy group at the anomeric center was recognized [**24**-*cis*: $J_{1,2}$ = 2.0 Hz; **24**-*trans*: $J_{1,2}$ = 6.0 Hz; **25**-*cis*/**25**-*trans*: $J_{1,2}$ = 0.5/1.5 Hz (ambiguous)]. However, this is only the case in water but in organic solvents the composition of the diastereomers differs.

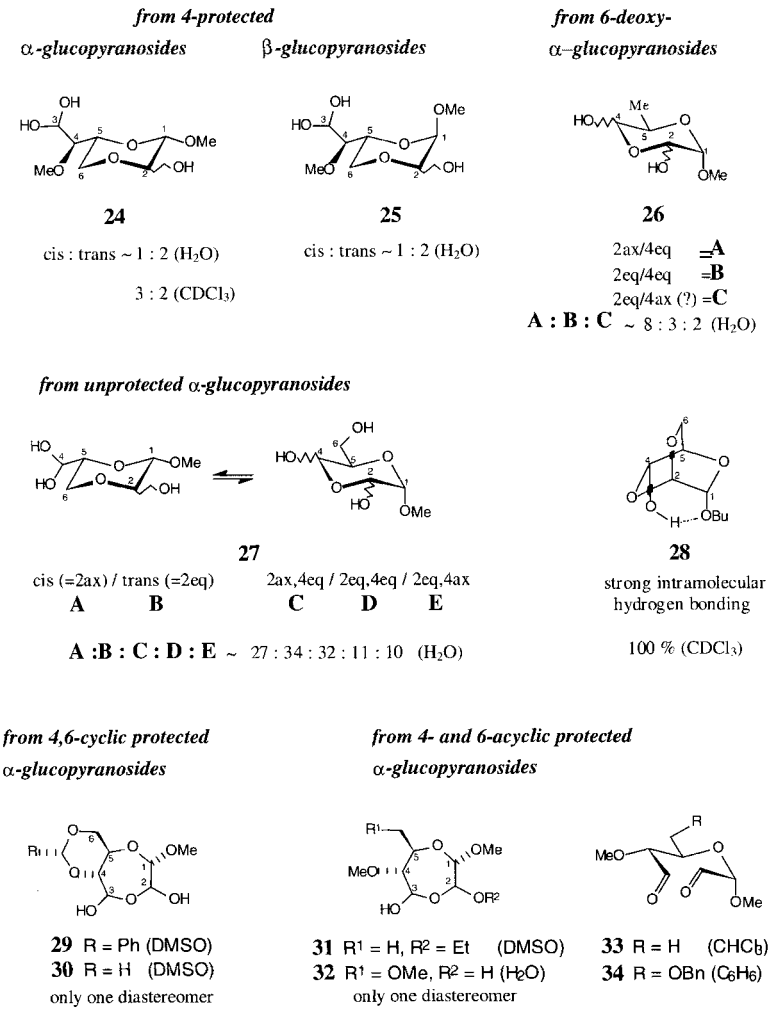
A somehow similar structure was found for the dialdehyde derived from methyl 6-deoxy-α-D-glucopyran-

oside. In this case the dioxane was observed as a hydrated hemialdal connecting the aldehyde centers C-2 and C-4. The conformation may be characterized as $^4C_1$. Structures of that kind were already reported in the literature[1, 2]. The configuration at the hemiacetal centers at C-2 and C-4 was more complex, but as in the hemiacetal derived dioxane the most stable diastereomer **26A** showed a 1,2-*trans* orientation ($J_{1,2}$= 1.0 Hz) of the oxygen containing substituents and is favoured over the *cis* analogous structure **26B** ($J_{1,2}$= 1.5 Hz) with a ratio **26A**:**26B** ≈ 2:1.

Dialdehydes of unprotected glucosides in water formed dioxane rings of the hemiacetal and hemialdal type, such as **27**, analogous to the depicted structures [3]. The hemiacetal type dioxane is slightly favoured. The tentative assignment of the different equilibrating structures in **27** was based on comparison of the NMR spectra with those of **24,** and **26**. *E.g.*, for **27A** and **27B** the 1,2-*cis* and 1,2-*trans* arrangements are obvious from the $J_{1,2}$ coupling constants, 1.5 and 6.0 Hz, respectively, similar to **24**. Similarly, the $J_{1,2}$ values of **27C** (0.5 Hz) and **27D** (1.5 Hz) resemble those found for **26A** and **26B**.

In chloroform solution only one bicyclic structure, **28**, for the butyl α-glucopyranoside derived dialdehyde could be observed. Interestingly, the corresponding periodate cleavage product of butyl β-glucopyranoside showed a more complex NMR spectrum, including about 15% of the free aldehyde which indicates a mixture of various structures. The different behavior of the anomeric dialdehyde glycosides may be explained by a strong hydrogen bridging as shown in scheme 4. In fact, the failure of deuterium exchange in **28** as well as the unusually large coupling constant $J_{4,OH}$ = 13 Hz are notable. The presence of a bicyclic structure for the methyl α-D-glucopyranoside derived dialdehyde **27** may be assumed from the missing carbonyl vibration in the IR. Nonetheless, a bicyclic structure should be hydrolysed in water.

A special case of structure was found for 4- and 6-protected glucoside-derived dialdehydes. For these com-



Scheme 4 Structures of glucoside-derived dialdehydes

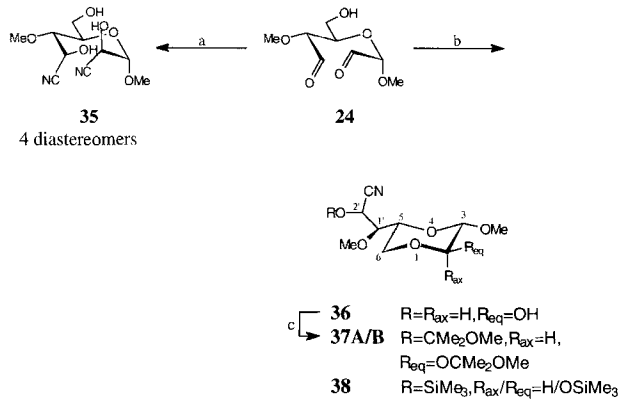
pounds the formation of a dioxane structure is impossible. Previously, the bicyclic structure **29** was reported for the dialdehyde of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside **12** [4]. Remarkable is the exclusive formation of one dioxepane hemialdal diastereomer. Since **29** was poorly soluble in most solvents only DMSO, DMF and pyridine have been reported as practical solvents. It was of interest to check, whether the dioxepane structure would be a general element for 4- and 6-protected glucoside-derived dialdehydes. In fact, the 4,6-*O*-methylene glucopyranoside **11** formed a poorly soluble product **30**, except for the outlined solvents. It may be assumed that the bicyclic structure is favoured and responsible for the solubility. Starting with 4,6-*O*-isopropylidene glucoside no isopropylidene containing dialdehyde could be obtained, which indicated a sensivity to even weak aqueous acidic conditions. A similar reason may be assumed for the low yield (37%) of **30**. In all cases **29** to **32** the 1,4-dioxepane rings adopt chair-type conformations on both ends and the *trans* arrangements of the substitution pattern reflects in the large coupling constants ($J_{1,2}$=6.0, $J_{3,4}$=7.5, $J_{4,5}$=9.5 Hz).

With non cyclic 4- and 6-protected glucosides products were obtained which were soluble in water or chloroform. Whereas only acyclic structures were found in chloroform or benzene, *e.g.* **33** and **34**, the NMR spectrum of the dialdehyde **32** from methyl 4,6-di-*O*-methyl-α-D-glucopyranoside in water appeared to show better correspondence to the dioxepane structure. Nevertheless, in chloroform other structures of partly hydrated aldehydes were present.

The glucoside-derived dialdehyde **29** was reported to form stable monoadducts directly by treatment with alcohols [3, 4, 25]. This behavior was recognized to be also valid for the acyclic protected analogues. Whereas the regioselectivity of the addition could not be specified previously it was shown to occur at C-2 as obvious by a coupling between H-3 and the hydroxy group for **31** in DMSO ($J_{3,OH}$ = 6.5 Hz). The recognized structure is analogous to that one reported for **29** implying again just one diastereoisomer.

Reactions of Glucoside-Derived Dialdehydes with C-Nucleophiles

With respect to model reactions regarding the synthesis of starch derived polycarboxylates, addition of C-nucleophiles to the dialdehyde derivatives were studied. For cyanohydrin synthesis often alkali cyanides in aqueous solution are used [26], and generally the resulting hydroxyamides are finally saponified using acidic conditions at higher temperature. However, this procedure was not applicable to 4-protected glycoside-derived dialdehydes. Treatment with aqueous sodium cyanide did not yield definite products but resulted in complex mixtures, due to some alkaline fragmentation of the glycoside-derived dialdehydes [27].

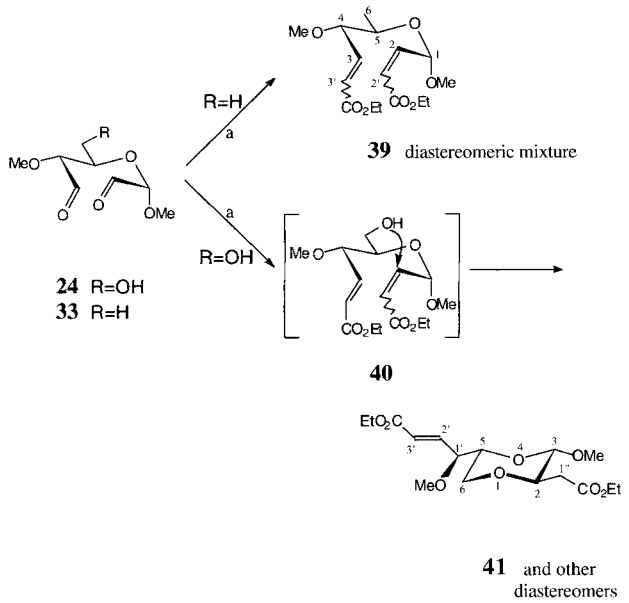


Scheme 5 Hydrocyanation of the dialdehyde obtained from methyl 4-*O*-methyl-α-D-glucopyranoside a) 2.3 equiv. acetone cyanohydrin, cat. NEt_3 b) 1.4 equiv. acetone cyanohydrin, cat. NEt_3/3 equiv. Me_3SiCN, cat. NaCN c) H^+, 2-methoxypropene

Nevertheless, cyanohydrins such as **35** could be synthesized in aprotic organic solvents by transhydrocyanation [28, 29] using acetone cyanohydrin and a catalytic amount of a tertiary amine. An interesting aspect of hydrocyanation of **24** was observed in the regio- and partly stereoselective formation of a monoadduct **36** with just one equivalent of the reagent. The product indicated the stability of the dioxane hemiacetals in glycoside-derived dialdehydes. The crystalline material was poorly soluble in chloroform and showed mutarotation in water. By treatment with 2-methoxypropene **36** was transformed into **37** stereoselectively in the dioxane ring but not at the cyanohydrin center. Due to the sensivity of the compounds and the drastic conditions for nitrile saponification further attempts to transform the cyanohydrines to hydroxycarboxylates failed. The assignment of the configuration at C-2 for the derivative **37** ($J_{2,3}$ = 5.0 Hz) reflected the NMR data of **24** and **27**.

Analogous to hydrocyanation dialdehyde **24** was cyanosilylated according to literature procedures [30–32]. The product was assumed to be the bis-silylated compound **38** due to the similarity of the NMR data – especially the ^{13}C-NMR of **37** and **38**. Interestingly, for **38** the formation of the dioxane ring was not stereospecific in contrast to **37**.

As an alternative for the cyanohydrin synthesis Horner reactions [33, 34, 35, 36] of **24** and its 6-deoxy analogue **33** were studied. Whereas the 6-deoxy structure **39** could be isolated as a mixture of *E/Z*-isomers, the Horner reaction of **24** was followed by an intramo-



Scheme 6 Tandem Horner-oxa-Michael reaction
a) $(EtO)_2POCH_2CO_2Et$, BuLi

lecular oxa-Michael reaction and therefore led directly to the dioxane structure **41**. Some corresponding findings for so called tandem Horner-Michael reactions of hydroxyaldehydes were reported previously [34, 35].

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Experimental

Melting points were determined with a Leitz melting point apparatus and were uncorrected. Specific rotations were measured on a Perkin-Elmer model 241 polarimeter. TLC was performed on silica gel 60 GF_{254} aluminium sheets (E. Merck, Darmstadt, Germany); detection was effected by observation under UV light (254 nm), then spraying with 20% ethanolic sulfuric acid and charring with a heat gun. Column chromatography was conducted with silica gel 60 (0.040–0.063 mm, E. Merck) using the flash procedure. HPLC was run on Nucleosil 100 (5 µm, 250 mm, d 40 mm, 10 mL/min) using Knauer pump 64 and a Knauer differential refractometer. NMR spectra were recorded at 300 *K* in $CDCl_3$ (unless otherwise specified) on Bruker AC 250 (62.89 MHz for ^{13}C) and AMX 400 (100.67 MHz for ^{13}C). Chemical shifts are expressed in ppm downfield from TMS. Spectra in D_2O were calibrated on HDO (4.65 ppm) or internal acetonitrile (1.98 ppm for ^1H, 0.80 ppm for ^{13}C).

Glycol cleavage was achieved in water according to standard conditions [37]. The dialdehydes were isolated by freeze-drying of the reaction solution and extraction of the solid residue with chloroform. In case of the unblocked methyl glucoside the separation was based on the precipitation of barium iodate. The dialdehydes of 4,6-cyclic protected methyl glucosides precipitated during the reaction and were filtered and washed with water, and dried. The crude products were analyzed by one and two dimensional ($^1H^1H$-COSY, $^{13}C^1H$-COSY and J_{res}) NMR spectroscopy.

Methyl 2,3-di-O-benzyl-6-bromo-6-deoxy-α-D-glucopyranoside (**2**)

A cooled solution of **1** [7] (250 mg, 0.67 mmol) and triphenylphosphine (350 mg, 1.3 mmol, 2 equiv.) in dry DMF (10 ml) was treated with NBS (240 mg, 1.3 mmol, 2 equiv.) and heated to 70 °C for 1.5 h. After destillation of the DMF the residue was taken up in chloroform and succinimide was removed by extraction with an aqueous solution of sodium hydrogen carbonate. The product was purified chromatographically using petroleum ether : ethyl acetate 10:1 to furnish 164 mg (65%) of **2** as a pale yellow syrup and 78 mg (25%) of its 4-formiate as a colorless solid. **2**: ^1H NMR: δ/ppm = 7.40–7.26 (m, 10H, Ph-H), 5.03 (d, ^2J=11.5 Hz, Ph–CH_2–A), 4.77 (d, ^2J=11.5 Hz, Ph–CH_2–B), 4.68 (d, Ph–A'), 4.65 (d, Ph–B'), 4.65 (d, $J_{1,2}$=3.5 Hz, H-1), 3.77 (dd, $J_{2,3}$=9.5 Hz, $J_{3,4}$=9.0 Hz, H-3), 3.70 (dd, $J_{5,6A}$=2.5 Hz, $^2J_6$=10.5 Hz, H-6A), 3.76–3.65 (m, H-5), 3.53 (dd, H-2), 3.51 (dd, $J_{5,6B}$=6.0 Hz, H-6B), 3.43 (ddd, $J_{4,5}$=9.5 Hz, $J_{4,OH}$=2.5 Hz, H-4), 3.41 (s, 3H, Me), 2.18 (d, 4-OH). – ^{13}C NMR: δ/ppm = 138.58, 137.88 (2C), 128.72, 128.55, 128.11, 128.07, 128.04, 128.01 (8CH), 98.15 (C-1), 81.00, 79.82 (C-2 ,C-3), 75.40, 73.18 ($2CH_2$), 71.90 (C-4), 69.90 (C-5), 55,42 (C-5), 33.25 (C-6).

Alkaline Treatment of 2 in DMSO

Compound **2** (815 mg, 1.9 mmol) was dissolved in DMSO (25 ml) and treated with freshly powdered sodium hydroxide (700 mg, 17 mmol). After 15 minutes dimethylsulfate (500 µl, 11 mmol) was added to the stirred suspension and stirring was continued for 2 hours. The excess of methylation reagent was destroyed by addition of methanol, and the solvents were removed *in vacuo*. The residue was taken up in dichloro-methane and washed several times with water. Product separation was achieved chromatographically using petroleum ether : ethyl acetate 1:1. Yield 359 mg (52%) of **4** as a yellow oil and 68 mg (10%) of **5** as a yellow syrup.

Methyl 2,3-Di-O-benzyl-6-deoxy-4-O-methyl-α-D-xylo-hex-5-enopyranoside (**4**)

^1H NMR: δ/ppm = 7.43–7.25 (m, 10H, Ph-H), 4.86 (s, 2H, Ph–CH_2–A), 4.82 (d, ^2J=11.5 Hz, Ph–CH_2–B), 4.78 (dd, $^2H_6$= 1.0 Hz, $^4J_{4,6A}$=2.0 Hz, H-6A), 4.69 (dd, $J_{4,6B}$=2.0 Hz, H-6B), 4.67 (d, Ph–CH_2–B'), 4.62 (d, $J_{1,2}$=3.5 Hz, H-1), 3.78 (dd, $J_{2,3}$=9.5 Hz, $J_{3,4}$=9.0 Hz, H-3), 3.64 (ddd, H-4), 3.59, 3.41 (2 s, 2 ×3H, Me), 3.57 (dd, H-2).

Methyl 2,3-Di-O-benzyl-6-deoxy-4-O-(methyl 2,3-di-O-benzyl-4-O-methyl-α-D-glucopyranosid-6-yl)-α-D-xylo-hex-5-enopyranoside (**5**)

^1H NMR: δ/ppm = 7.39–7.26 (m, 20H, Ph-H), 4.93 (d, ^2J=10.5 Hz, Ph–CH_2–A), 4.92 (dd, $^2J_6$=1.0 Hz, $^4J_{4,6A}$=2.0 Hz, H-6A'), 4.89 (d, ^2J = 11.0 Hz, Ph–CH_2–B), 4.86 (d, Ph–CH_2–B'), 4.81 (d, Ph–CH_2–A'), 4.78 (d, ^2J= 12.5 Hz, Ph–CH_2–C), 4.76 (d, ^2J= 12.0 Hz, Ph–CH_2–D), 4.67 (dd, $J_{4,6B}$= 1.5 Hz, H-6B'), 4.64 (d, Ph–CH_2–C'), 4.63 (d, Ph–CH_2–D'), 4.60, 4.59 (2×d, 2H,

$J_{1,2}$ = 3.5 Hz, $J_{1',2'}$ = 3.5 Hz, H-1, H-1'), 3.97–3.86 (m, 2H, H-6), 3.90 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.87 (dd, $J_{2',3'}$ = 9.5 Hz, $J_{3',4'}$ = 9.0 Hz, H-3'), 3.79 (ddd, H-4'), 3.65 (ddd, $J_{4,5}$ = 10.5 Hz, $J_{5,6A}$ = 4.0 Hz, $J_{5,6}$ = 2.5 Hz, H-5), 3.57, 3.47 (2×dd, 2H, H-2, H-2'), 3.45, 3.40, 3.35 (3 s, 3×3H, Me), 3.24 (dd, H-4). – ^{13}C NMR: δ/ppm = 153.39 (C-5'), 138.90, 138.68, 138.22, 138.02 (4C), 128.43–127.51 (16CH), 98.96, 98.02 (C-1, C-1'), 97.06 (C-6'), 81.98, 81.03, 80.25, 79.83, 79.61, 79.42 (C-2, C-3, C-4, C-2', C-3', C-4'), 75.53, 75.49, 73.52, 73.32 ($4CH_2$), 71.31 (C-6), 70.38 (C-5), 60.64, 55.43, 55.23 (Me).

Methyl 6-Deoxy-4-O-methyl-α-D-glucopyranoside (**6**)

A solution of methyl 4-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (**17** [3], 920 mg, 2.5 mmol) in dry toluene (30 ml) was treated with tributylstannane (1.2 ml, 4.5 mmol) and AIPH (80 mg). The mixture was heated to 70 °C for 3 h and the solvent stripped of. Removal of stannanes was achieved by extraction of a solution in acetonitrile with light petroleum. Purification was finished by chromatography using toluene : ethyl acetate 1:1. Yield 700 mg (97%) of methyl 4-*O*-benzoyl-6-deoxy-α-D-glucopyranoside (**18**) as a clear syrup: $[\alpha]_{546}^{21}$ = +131° (c 1.0, chloroform). – ^{1}H NMR: δ/ppm 8.08–8.03, 7.61–7.55, 7.48–7.41 (3m, 2+1+2H, Ph-H), 4.89 (dd, $J_{3,4}$ = 9.5 Hz, $J_{4,5}$ = 9.0 Hz, H-4), 4.79 (d, $J_{1,2}$ = 4.0 Hz, H-1), 3.96 (dq, $J_{5,6}$ = 6.5 Hz, H-5), 3.95 (dd, $J_{2,3}$ = 9.0 Hz, H-3), 3.68 (dd, H-2), 3.47 (s, 3H, Me), 1.24 (d, 3 H, H-6).

Compound **18** (50 mg, 0.18 mmol) was dissolved in dry dichloromethane (5 ml) and treated with 2-methoxypropene (60 µl, 0.6 mmol) and a catalytic amount of pyridinium tosylate (PPTS). The mixture was stirred for 30 minutes and then potassium carbonate and a few drops of water were added for neutralization. The salts were filtered off and the organic layer concentrated to dryness. After solution of the crude **20a** in dry 1,4-dioxane (10 ml) sodium hydroxide (60 mg, 1.5 mmol) was added and the mixture stirred for approximately 2 h before addition of dimethylsulfate (50 µl, 0.53 mmol). After 5 hours the excess of the methylating agent was destroyed by addition of methanol (0.5 ml) and the solvent stripped off. The resulting raw material **22a** was taken up in dichloromethane, washed twice with water and dried over magnesium sulfate. Finally it was dissolved in ethanol, some drops of diluted hydrochloric acid were added and the solvent was removed on a steam bath. Yield 30 mg (88%) of **6** as a colorless solid: *m.p.* 81°C, $[\alpha]_D^{22}$ = 171° (c 1.0, chloroform). – ^{1}H NMR: δ/ppm 4.69 (d, $J_{1,2}$ = 4.0 Hz, H-1), 3.73 (ddd, $J_{2,3}$ = 9.0 Hz, $J_{3,4}$ = 9.0 Hz, $J_{3,OH}$ = 2.0 Hz, H-3), 3.63 (dq, $J_{4,5}$ = 9.5 Hz, $J_{5,6}$ = 6.0 Hz, H-5), 3.58, 3.40 (2s, 2×3H, Me), 3.51 (ddd, $J_{2,OH}$ = 9.5 Hz, H-2), 2.82 (d, 3OH), 2.78 (dd, H-4), 2.29 (d, 2OH), 1.29 (d, 3H, H-6).

$C_8H_{16}O_5$	calcd.:	C 49.99	H 8.38
(192.2)	found:	C 50.01	H 8.39.

Methyl 4,6-O-Methylene-α-D-glucopyranoside (**11**)

Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**1** [15], 5.0 g, 13 mmol) was dissolved in dichloromethane (150 ml) and treated with tetrabutylammonium hydrogen carbonate (7.0 g) and 50% aqueous sodium hydroxide (25.0 g). The mixture was vigorously stirred at room temperature until TLC showed the total absence of the starting material. The organic layer was separated and the aqueous phase extracted twice with dichloromethane. After drying of the organic layer with magnesium sulfate the crude product was purified by chromatography (dichloromethane : acetone = 100:1) to give 2.8 g (55%) of methyl 2,3-di-*O*-benzyl-4,6-*O*-methylene-α-D-glucopyranoside (**10**) [38] as a clear colorless syrup: $[\alpha]_{546}^{21}$ = 94° (c 0.5, chloroform); Lit. [38]: $[\alpha]_D$ +29.3° (c 1.08, chloroform). – ^{1}H NMR: δ/ppm 7.40–7.25 (m, 10H, Ph-H), 5.07 (d, ^2J = 6.0 Hz, CH_2-A), 4.87 (d, ^2J = 11.0 Hz, Ph–CH_2-A), 4.82 (d, Ph–CH_2-A'), 4.81 (d, ^2J = 12.0 Hz, Ph–CH_2-B), 4.65 (d, Ph–CH_2–B'), 4.61 (d, CH_2–B), 4.55 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.11 (dd, $J_{5,6eq}$ = 5.0 Hz, $^2J_6$ = 10.0 Hz, H-6eq), 3.95 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 10.0 Hz, H-3), 3.71 (ddd, $J_{4,5}$ = 9.5 Hz, $J_{5,6ax}$ = 10.0 Hz, H-5), 3.51 (dd, H-2), 3.41 (dd, H-6ax), 3.38 (s, 3H, Me), 3.31 (dd, H-4); Lit. [38] (100 MHz): 7.4–7.2 (m, 10H, Ph-H), 5.03 (d, ^2J = 6.0 Hz, CH_2-ax), 4.80 (s, 2H, Ph–CH_2–A), 4.7 (m, 2H, Ph–CH_2–B), 4.58 (d, $J_{1,2}$ = 1.9 Hz, H-1), 4.52 (d, CH_2-eq), 4.08 (dd, H-2), 3.94 (t, H-3), 3.7 (m, H-5), 3.5 (m, 2 H, H-6), 3.31 (s, 3H, Me).

The debenzylation of **10** was achieved by hydrogenolysis in methanol using 10% palladium on charcoal at 1 bar hydrogen. Yield 1.4 g (quant.) as an amorphous solid: $[\alpha]_{546}^{21}$ +147° (*c* 1.0, chloroform). – ^{1}H NMR: δ/ppm = 5.07 (d, ^2J = 6.0 Hz, CH_2–A), 4.75 (d, $J_{1,2}$ = 4.0 Hz, H-1), 4.62 (d, CH_2–B), 4.14 (dd, $J_{5,6eq}$ = 5.0 Hz, $^2J_6$ = 10.0 Hz, H-6eq), 3.88 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 10.0 Hz, H-3), 3.68 (ddd, $J_{4,5}$ = 10.0 Hz, $J_{5,6ax}$ = 10.0 Hz, H-5), 3.58 (dd not resolved, H-2), 3.47 (dd, H-6ax), 3.43 (s, 3H, Me), 3.40 (bs, OH), 3.22 (dd, H-4), 2.79 (bs, OH).

$C_8H_{14}O_6$	calcd.:	C 46.60	H 6.84
(206.2)	found:	C 46.53	H 6.91.

Methyl 2,3-Di-O-acetyl-6-O-benzyl-α-D-glucopyranoside (**14**)

A solution of methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**13** [15],1.0 g, 2.7 mmol) and sodium cyanoborohydride (1.5 g, 24 mmol) in dry THF (70 ml) containing 3Å molecular sieves was treated with a hydrogen chloride solution in ether until the gas evolution ceased indicating acidic conditions. During the whole process the temperature was held below 10 °C using an ice bath. After 30 minutes the mixture was poured onto water (170 ml) and extracted with dichloromethane. The organic layer was washed with saturated aqueous sodium hydrogen carbonate and dried over sodium sulfate. After chromatographic purification (toluene : ethyl acetate = 2:1) 834 mg (83%) of a pale yellow syrup were isolated: $[\alpha]_D^{22}$ = +99° (*c* 1.0, chloroform). – ^{1}H NMR: δ/ppm = 7.38–7.26 (m, 5H, Ph-H), 5.30 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 8.5 Hz, H-3), 4.91 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.86 (H-2), 4.63 (d, ^2J = 12.0 Hz, Ph–CH_2), 4.57 (d, Ph–CH_2'), 3.86–3.68 (m, 4H, H-4, H-5, H-6A, H-6B), 3.40 (s, 3H, Me), 2.83 (d, $J_{4,OH}$ = 2.5 Hz, 4-OH), 2.09, 2.08 (2 s, 2×3H, Ac).

Methyl 6-O-Benzyl-4-O-methyl-α-D-glucopyranoside (**16**)

Compound **14** (380 mg, 1.0 mmol) was dissolved in dichloromethane (5 ml) and cooled to –78 °C. After treatment with some drops of borontrifluoride etherate an ether solution of diazomethane, freshly prepared from *N*-nitroso-*N*-methyl-urea (1.0 g, 11 mmol), was added stepwise. After gas evolution terminated polymethylene was removed by filtration and the

resulting syrup was fractionated by HPLC (dichloromethane : acetone = 20:1). Yield 128 mg (32%) methyl 2,3-di-*O*-acetyl-6-*O*-benzyl-4-*O*-methyl-α-D-glucopyranoside (**15**) and 78 mg (21%) recovered **14**: $[\alpha]_D^{23}$ = +113° (c 1.0, chloroform). – ^{1}H NMR: δ/ppm = 7.36–7.26 (m, 5H, Ph-H), 5.44 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 4.98 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.83 (dd, H-2), 4.67, 4.55 (2 d, ^2J = 12.0 Hz, Ph–CH_2), 3.76–3.67 (m, 3H, H-5, H-6A, H-6B), 3.48 (dd, $J_{4,5}$ = 9.5 Hz, H-4), 3.38, 3.37 (2s, 2×3H, Me), 2.07, 2.06 (2 s, 2×3H, Ac).

Deacetylation was achieved with a solution of compound **15** (124 mg, 0.32 mmol) in dry methanol (2 ml) and dry ether (2 ml) and treatment with catalytic amounts of sodium methylate. The solution was stirred for 2 h, then acidic ion exchanger was added and removed after some minutes. Yield 98 mg (quant.) of yellow syrupy **16**. – ^{1}H NMR: (CD_3OD) δ/ppm = 7.39–7.24 (m, 5H, Ph-H), 4.65 (d, $J_{1,2}$ = 4.0 Hz, H-1), 4.61, 4.54 (2d, ^2J = 11.5 Hz, Ph–CH_2), 3.72–3.66 (m, 2H, H-6A, H-6B), 3.68 (dd, $J_{2,3}$ = 9.0 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.61 (ddd, H-5, $J_{4,5}$ = 9.5 Hz, $J_{5,6A}$ = 2.5 Hz, $J_{5,6B}$ = 3.5 Hz, H-5), 3.49, 3.38 (2s, 2×3H, Me), 3.40 (dd, H-2), 3.12 (dd, H-4).

Methyl 6-Bromo-6-deoxy-2,3-O-isopropylidene-4-O-methyl-α-D-glucopyranoside (**21a**)

A solution of **17** (5.5 g, 15 mmol) and 2-methoxypropene (3.2 ml, 32 mmol, 2.1 equiv.) in dry dichloromethane (200 ml) was treated with a catalytic amount of PPTS. After 30 minutes potassium carbonate and a few drops of water were added, then the salts filtered off, the organic layer washed with brine, dried over magnesium sulfate and concentrated to dryness. Yield 5.7 g (93%) methyl 4-*O*-benzoyl-6-bromo-6-deoxy-2,3-*O*-isopropylidene-α-D-glucopyranoside (**19a**) as a syrup. This material (14 mmol) was dissolved in 1,4-dioxane (70 ml) and stirred for 1 h over freshly pulverized sodium hydroxide (2.8 g, 70 mmol) before addition of dimethylsulfate (2.5 ml, 27 mmol). Stirring was continued over night and then methanol (5 ml) added to destroy exess of the methylating agent. The solvents were evaporated and the resulting material taken up in dichloromethane and water. Finally the crude product was purified by chromatography using dichloromethane : acetone 20:1 yielding 3.4 g (85%) of **21a** as a clear syrup: $[\alpha]_{546}^{21}$ = 167° (c 1.0, chloroform). – ^{1}H NMR: δ/ppm = 5.07 (d, $J_{1,2}$ = 3.0 Hz, H-1), 4.02 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 10.0 Hz, H-3), 3.76–3.58 (m, 3H, H-5, H-6A, H-6B), 3.55, 3.48 (2s, 2×3H, Me), 3.52–3.45 (m, H-2), 3.,45 (dd, H-4), 1.49, 1.45 (2s, 2×3H, Me).

Glycol Cleavage of **11** *to give* **30**

Compound **11** (100 mg, 0.49 mmol) was dissolved in water and stirred with sodium metaperiodate (110 mg, 0.51 mmol) for 24 h at room temperature. The crystalline material **30** precipitated, was filtered and dried. Yield 40 mg (37%); $[\alpha]_D^{22}$ = +107° (c 1.0, DMSO); *m.p.* 115 °C.

$C_8H_{14}O_7$	calcd.:	C 43.24	H 6.35	
(222.2)	found:	C 43.06	H 6.35.	

Bishydrocyanation of the Dialdehyde Derived from Methyl 4-O-Methyl-α-D-glucopyranoside

A solution of **24** (44 mg, 0.2 mmol) in dichloromethane (250 µl) was treated with acetone cyanohydrin (43 µl, 0.46 mmol, 2.3 equiv.) and triethylamine (10 µl). After 1 day the solvent was evaporated by codestillation with toluene to give **35** (56 mg) as a yellow syrup. – ^{13}C NMR (CD_3OD): δ/ppm = 119.89, 119.02, 118.99, 118.23, 118.19, 118.15 (CN), 103.43, 103.15, 102.85, 102.42 (C-1), 63.97, 63,79, 63.32, 63.30; 63.07, 62.99, 59.98, 58.85 (C-2, C-3), 81.96, 81.74, 81.21, 81.05; 78.01, 78.01, 77.38, 77.38 (C-4, C-5), 60.59, 60.44, 60.30, 60.12 (C-6), 60.01, 60.01, 57.73, 57.44, 56.33, 56.22 (Me).

(2S,3S,5R)-5-[(1R)-2-Cyano-2-hydroxy-1-methoxy-ethyl]-2-hydroxy-3-methoxy-1,4-dioxane (**36**)

A solution of **24** (2 g, 9.7 mmol) in dichloromethane (40 ml) was treated with acetone cyanohydrin (1.25 ml, 13.4 mmol, 1.4 equiv.) and triethylamine (40 µl, 0.03 equiv.). After one day stirring the solid product was removed, washed with dichloromethane and the remainder dried *in vacuo*. Yield 705 mg (32%) of **36**: *m.p.* 179 °C, $[\alpha]_D^{22}$ +49° (c 1.0, water at equilibrium).

$C_9H_{15}NO_6$	calcd.:	C 46.35	H 6.48	N 6.00
(233.2)	found:	C 45.78	H 6.29	N 6.24.

2-Methoxypropylation of **36**

Compound **36** (20 mg, 86 µmol) was dissolved in dry dioxane (2 ml) and treated with 2-methoxypropene (75 µl, 8.9 equiv.) and traces of hydrogen chloride in diethylether. After some minutes potassium carbonate was added and stirring was continued for 10 further minutes. The salts were removed by filtration and the solvent removed *in vacuo* to leave 30 mg (92%) of **37** as a yellow syrup. The NMR analysis showed a diastereomeric ratio of **37A**:**37B** 3:1.

37A: ^{1}H NMR: δ/ppm = 4.68 (d, $J_{1',2'}$ = 2.5 Hz, H-2'), 4.62 (d, $J_{2,3}$ = 5.0 Hz, H-2), 4.21 (d, H-3), 4.10 (dd, $J_{5,6eq}$ = 3.0 Hz, $^2J_6$ = 11.5 Hz, H-6eq), 3.86 (ddd, $J_{5,6ax}$ = $J_{5,1'}$ = 8.0 Hz, H-5), 3.63 (dd, H-6ax), 3.60 (dd, H-1'), 3.63, 3.50, 3.33, 3.26 (4 s, 4×3H, OMe), 1.49, 1.42, 1.40, 1.39 (4 s, 4×3 H, Me). – ^{13}C NMR: δ/ppm = 118.68 (CN), 102.78, 101.84 (C), 100.81 (C-3), 91.87 (C-2), 81.69 (C-1'), 70.86 (C-5), 64.26 (C-6), 61.25 (1'-OMe), 58.70 (C-2'), 50.52, 49.25 (OMe), 26.57, 24.61, 24.58, 24.42 (Me).

37B: ^{1}H NMR: δ/ppm = 4.85 (d, $J_{1',2'}$ = 2.5 Hz, H-2'), 4.57 (d, $J_{2,3}$ = 6.0 Hz, H-2), 4.26 (d, H-3), 4.06 (dd, $J_{5,6}$ = 3.0 Hz, $^2J_6$ = 11.5 Hz, H-6eq), 3.82 (ddd, $J_{5,6ax}$ = 8.0 Hz, H-5), 3.55 (dd, H-6ax), 3.47 (dd, H-1'), 3.56, 3.52, 3.28, 3.27 (4 s, 4×3H, OMe), 1.48, 1.42, 1.40, 1.39 (4 s, 4×3H, Me). – ^{13}C NMR: δ/ppm = 117.46 (CN), 102.64, 101.79 (C), 101.03 (C-3), 92.20 (C-2), 81.97 (C-2'), 71.92 (C-5), 65.31 (C-6), 61.88 (1'-OMe), 60.67 (C-1'), 56.70 (3-OMe), 49.75, 49.25 (OMe), 24.80, 24.56, 24.24 (Me).

Cyanosilylation of the Dialdehyde Derived from Methyl 4-O-Methyl-α-D-glucopyranoside

A solution of **24** (27 mg, 0.13 mmol) in dry chloroform (1.3 ml) was treated with trimethylsilylcyanide (37 µl, 0.3 mmol) and sodium cyanide 18-crown-6 complex (0.5 mg). After stirring overnight the solvent and excess of the reagent were evaporated to give **38** (54 mg) as a pale yellow liquid. – ^{1}H NMR: δ/ppm = 4.50–4.00 (H-1), 4.95–4.35 (H-2), 3.60–3.25 (H-3), 4.80–4.65 (H-4, H-5), 3.85–3.50 (H-6), 3.60–3.40 (Me), 0.07–0.27 ($SiMe_3$). – ^{13}C NMR: δ/ppm = 119.30,

Table 1 Compilation of NMR data [a]) of water soluble glucoside-derived dialdehydes

	24cis	24 trans	25 cis	25 trans	26A	26B	26C	27A	27B	27C
H-1	4.55 (d)	4.23 (d)	4.62 (d)	4.56 (d)	4.50 (d)	4.55 (d)	4.61 (d)	4.57 (d)	4.26 (d)	4.47 (d)
H-2	4.86 (d)	4.43 (d)	4.88 (d)	4.85 (d)	5.05 (d)	5.04 (d)	5.29 (d)	4.84 (d)	4.43 (d)	4.96-4.91
H-3	5.08 (d)	5.04 (d)	5.10 (d)	5.13 (d)	–	–	–	–	–	–
H-4	3.34–3.29	3.34–3.29	3.35 (dd)	3.34 (dd)	5.00 (d)	4.69 (d)	5.02 (d)	3.96-3.91	3.96-3.91	5.11 (d)
H-5	3.95–3.84	3.95–3.84	4.14 (ddd)	4.24 (ddd)	3.83 (dq)	3.69 (dq)	4.16 (dq)	3.72-3.62	3.72-3.62	3.72-3.62
H-6ax/A	3.95–3.84	3.68 (dd)	3.90 (dd)	4.17 (dd)	1.23 (d)	1.20 (d)	1.14 (d)	3.76-3.51	3.57 (dd)	3.80 (dd)
H-6eq/B	3.63–3.53	3.95–3.84	4.03 (dd)	3.66 (dd)	–	–	–	3.76-3.51	3.92 (dd)	3.61-3.52
Me	3.46 (s)	3.47 (s)	3.53 (s)	3.55 (s)	3.45 (s)	3.47 (s)	3.48 (s)	3.46 (s)	3.48 (s)	3.37 (s)
	3.44 (s)	3.44 (s)	3.47 (s)	3.45 (s)	–	–	–	–	–	–
$J_{1,2}$	2.0 Hz	6.0 Hz	1.5 Hz	0.5 Hz	1.0 Hz	1.5 Hz	2.0 Hz	1.5 Hz	6.0 Hz	0.5 Hz
$J_{3,4}$	3.5 Hz	4.0 Hz	4.0 Hz	4.0 Hz	–	–	–	–	–	–
$J_{4,5}$			5.0 Hz	5.0 Hz	8.0 Hz	8.0 Hz	2.5 Hz			7.5 Hz
$J_{5,6A}$		9.5 Hz	10.5 Hz	11.0 Hz	6.5 Hz	6.0 Hz	6.5 Hz		10.0 Hz	10.0 Hz
$J_{5,6B}$			2.5 Hz	2.0 Hz	–	–	–		2.5 Hz	
$^2J_6$		11.5 Hz	12.0 Hz	11.0 Hz	–	–	–		12.0 Hz	11.5 Hz
C-1	99.46	101.84	99.10	99.58	99.71	98.80	99.64			
C-2	88.15	93.31	93.75	90.88	94.51/	96.44/	93.69/			
					94.31	93.72	88.33			
C-3	88.77	88.83	91.11	91.22	–	–	–			
C-4	82.93	82.76	85.28	85.64	94.51/	96.44/	93.69/			
					94.31	93.72	88.33			
C-5	74.00	73.90	68.55	68.88	70.45	69.80	67.54			
C-6	59.05	65.72	68.60	61.30	18.35	17.34	17.68			
Me	60.67	60.61	62.73	62.93	–	–	–			
	56.71	56.96	57.60	57.15	57.82	57.22	57.35			

	27D	27E	32
H-1	4.51 (d)	4.59–4.54	4.56 (d)
H-2	4.96–4.91	5.23 (d)	5.16 (d)
H-3	–	–	4.96 (d)
H-4	4.86 (d)	5.06 (d)	3.70 (dd)
H-5	3.76–3.51	3.76–3.51	4.12 (ddd)
H-6ax/A	3.76–3.51	3.76–3.51	3.76 (dd)
H-6eq/B	3.76–3.51	3.76–3.51	3.68 (dd)
Me	3.40/3.38	3.40/3.38	3.43 (s)
	–	–	3.55 (s), 3.58 (s)
$J_{1,2}$	1.5 Hz	2.0 Hz	4 Hz
$J_{3,4}$	–	–	3.5 Hz
$J_{4,5}$	8.5 Hz	2 Hz	9.0 Hz
$J_{5,6A}$			6.0 Hz
$J_{5,6B}$			6.0 Hz
$^2J_6$			11.0 Hz

[a]) Recorded in D_2O with acetonitrile or HDO as internal standard.

119.29, 118.09, 118.06 (CN), 102.66, 102.42, 100.66, 100.47 (C-1), 94.72, 94.38, 89.58, 89.58 (C-2), 82.77, 82.62, 82.58, 82.40 (C-3), 73.38, 72.00, 71.21, 70.31; 64.44, 63.93, 60.82, 60.32 (C-4, C-5), 65.94, 65.06, 60.13, 60.10 (C-6), 61.53, 61.36, 60.86, 60.41; 57.48, 57.42, 57.35, 57.17 (Me), 2.34 – 0.00 ($SiMe_3$)-Numbering based on starting material.

Horner Reaction with the Dialdehyde **33** *Derived from Glucoside* **6**

A solution of diethylethoxy-carbonylmethanephosphonate (430 µl, 2.1 mmol) in dry THF (6 ml) was treated with butyllithium (15% solution in hexane, 1.25 ml, 2 mmol) while the temperature was maintained at 0 °C. After 2 h the mixture was cooled to –78 °C and a solution of **33** (155 mg, 0.81 mmol) in dry THF (2.5 ml) was slowly added. After an hour the mixture was allowed to warm to room temperature. The solvent was evaporated the residue taken up in dichloromethane and washed with water. Double chromatographic purification (1. light petroleum : ether 2:3; 2. light petroleum:acetone: ether 20:1:1) yielded **39** (135 mg, 50%) as a clear oil: $[\alpha]_{546}^{21}$ = +36° (*c* 4.0, chloroform). – IR (KBr) 1724 cm^{-1} (ester). – ^1H NMR data of the prevailing diastereomer: δ/ppm = 7.12 (dd, $J_{3,3'}$ = 15.5 Hz, $J_{3,4}$ = 6.0 Hz, H-3), 6.30 (d, $J_{1,2}$ = 7.5 Hz, H-1), 6.19 (dd, $J_{2,2'}$ = 11.5 Hz, H-2), 5.69 (d, H-2'), 4.03 (q, J_{Et} = 7.0 Hz, Et–CH_2), 3.91 (dq, $J_{4,5}$ = 5.0 Hz, $J_{5,6}$ = 6.0 Hz, H-5), 3.91 (q, J_{Et} = 7.0 Hz, Et–CH_2), 3.63 (dd, H-4), 3.28, 3.09 (s, 2×3H, Me), 1.16 (d, 3H, H-6), 0.98, 0.92 (t, 2×3H, Et–CH_2). – ^{13}C NMR: δ/ppm = 145.04, 143.51 (C-2, C-3), 123.63, 121.75 (C-2', C-3'), 96.48 (C-1), 83.77 (C-4), 74.32 (C-5), 60.53 (Et–CH_2), 57.85, 53.85 (Me), 15.86 (C-6), 14.24, 14.18 (Et–CH_3).

(2S,3S,5R)-5-[(1'R,2E)-3'-Ethoxycarbonyl-1'-methoxy-allyl]-2-(ethoxy-carbonylmethyl)-3-methoxy-1,4-dioxane (**41**)

A solution of diethyl-ethoxycarbonylmethane phosphonate (425 µl, 2.1 mmol) in dry THF (7 ml) was treated with butyllithium (15% solution in hexane, 1.5 ml, 2.0 mmol) while the temperature was maintained at 0 °C. After 2 h the mixture was cooled to –60 °C and a solution of **24** (168 mg, 0.82 mmol) in dry THF (2 ml) was slowly added keeping the reaction temperature below –40 °C. After several hours the mixture was allowed to warm to room temperature. The solvent was evaporated and the residue taken up in dichloromethane. After washing with water the crude product was chromatographed using light petroleum : ether 2:1 yielding 237 mg of

Table 2 Compilation of NMR data [a]) of glucoside-derived dialdehydes in organic solvents

	24 ***cis***	**24** ***trans***	**28**	**29**	**30**	**31**	**33**	**34**
solvent	chloroform	chloroform	chloroform	DMSO	DMSO	DMSO	chloroform	benzene
H-1	4.48 (d)	4.20 (d)	4.93 (d)	4.28 (d)	4.25 (d)	4.22 (d)	4.61 (d)	4.38 (d)
H-2	4.84 (d)	4.58 (d)	4.96 (d)	4.73 (dd)	4.69 (dd)	4.41 (d)	9.41 (d)	9.19 (d)
H-3	9.71 (d)	9.71(d)	–	4.73 (dd)	4.67 (dd)	4.57 (dd)	9.72 (d)	9.56 (d)
H-4	3.73 (dd)	3.80 (dd)	5.11 (dd)	3.46 (dd)	3.18 (dd)	2.85 (dd)	3.64 (dd)	3.55 (dd)
H-5	4.10–3.95	4.10–3.95	4.01 (ddd)	3.74 (ddd)	3.63 (ddd)	3.66 (ddd)	4.17 (dq)	4.10 (ddd)
H-6ax/A	3.71–3.58	3.71–3.58	4.08 (dd)	3.61 (dd)	3.32 (dd)	3.50–3.39	1.27 (d)	3.53 (dd)
H-6eq/B	4.10–3.95	4.10–3.95	3.83 (dd)	4.11 (dd)	3.98 (dd)	3.50–3.39	–	3.45 (dd)
Me	3.47 (s)	3.48 (s)	–	3.31 (s)	3.30 (s)	3.31 (s)	3.46 (s)	3.06 (s)
2-OH			–	6.87 (d)	6.83 (d)	–	–	–
3-OH			–	6.93 (d)	6.89 (d)	6.88 (d)	–	–
4-OH	–	–	4.39 (d)	–	–	–	–	–
others	3.51 (s, 3H)	3.51 (s, 3H)	0.97–0.89 (3H) 1.47–1.33 (2H) 1.70–1.54 (2H) 3.64–3.57 (1H) 3.97–3.87 (1H)	5.54 (s) 7.45–7.32 (5H)	4.93 (d) 4.52 (d)	3.37 (s, 3H) 3.27 (s, 3H) 3.73 (dq) 3.50–3.39 1.52 (dd)	3.52 (s,3H)	3.07 (s, 3H) 4.20 (s, 2H) 7.39–7.22 (5H)
$J_{1,2}$	1.5 Hz	5.5 Hz	1.5 Hz	6.0 Hz	5.5 Hz	6.0 Hz	2.0 Hz	2.0 Hz
$J_{3,4}$	2 Hz	2 Hz	–	7.0 Hz	7.5 Hz	7.5 Hz	2.0 Hz	1.5 Hz
$J_{4,5}$	7 Hz	7 Hz	2.0 Hz	9.5 Hz	9.0 Hz	10.0 Hz	3.5 Hz	3.5 Hz
$J_{5,6A}$			3.5 Hz	10.0 Hz	10.0 Hz	4.0 Hz	6.0 Hz	6.0 Hz
$J_{5,6B}$			<1.0 Hz	5.0 Hz	5.5 Hz	4.0 Hz		6.0 Hz
$^2J_6$			10.0 Hz	10.0 Hz	10.0 Hz			9.5 Hz
$J_{2,OH}$	–	–	–	6.5 Hz	6.5 Hz	–		
$J_{3,OH}$	–	–	–	6.5 Hz	7.0 Hz	6.5 Hz		
$J_{4,OH}$	–	–	13.0 Hz	–	–	–		
others [b])	–	–	–	–	6.0 Hz	7.0 Hz [c]) 8.5 Hz [c])		
C-1	98.50	101.38	99.16		104.98			102.34
C-2	89.46	93.47	88.71		94.77			201.25
C-3	200.72	200.72	–		98.22			201.25
C-4	84.15	83.99	92.92		83.08			85.85
C-5	72.68/72.27	72.68/72.27	68.66		62.18			77.34
C-6	60.16	60.16	63.77		68.97			68.65
Me	56.93/56.73	56.93/56.73	–		56.00			55.18
others [d])								

[a]) Recorded with internal TMS standard; [b]) Sign of DEPT signals in brackets; [c]) Couplings of ethyl group; [d]) others **24** ***cis*** 59.21 (+), **24** ***trans*** 59.13 (+), **28** 13.76 (+), 19.28 (–), 31.69 (–), 69.03 (–), **30** 93.06 (–), **34** 59.19 (+), 73.54 (–), 128.48 (+), 127.89 (+), 127.74 (+)

a mixture of products as a clear liquid. 35 mg of that oil were further separated by HPLC using light petroleum : acetone 20:1 and 0.2% triethylamine. Yield 20 mg (48%) of **41** as clear oil: $[\alpha]_{546}^{21}$ = +22° (*c* 1.0, chloroform). – ^{1}H NMR: δ/ppm = 6.86 (dd, $J_{1',2'}$=6.0 Hz, $J_{2',3'}$=15.5 Hz, H-2'), 6.07 (dd, $^4J_{1',3'}$= 1.5 Hz, H-3'), 4.22, 4.15 (2q, 2×2H, $^3J_{Et}$=7.0 Hz, Et–CH_2), 4.21 (d, $J_{2,3}$=8.0, H-3), 3.91 (dd, $J_{5,6eq}$=2.5 Hz, $^2J_6$= 11.0 Hz, H-6eq), 3.79 (ddd, $J_{5,1'}$=6.5 Hz, H-1'), 3.70 (ddd, $J_{5,6ax}$= 10.0, H-5), 3.61 (ddd, $J_{2,1''A}$=4.0 Hz, $J_{2,1''B}$=8.5 Hz, H-2), 3.45, 3.33 (2s, 2×3H, Me), 3.44 (dd, H-6ax), 2.63 (dd, $^2J_{1''}$= 15.0 Hz, H-1''A), 2.41 (dd, H-1''B), 1.30, 1.25 (2t, 2×3H, Et–CH_3). – ^{13}C NMR: δ/ppm = 170 (C-4'), 165.90 (C-2''), 144.32 (C-2'), 123.89 (C-3'), 102.06 (C-3), 80.42 (C-1'), 75.89, 74.72 (C-2, C-5), 67.99 (C-6), 60.65, 60.58 (Et–CH_2), 57.95, 56.40 (Me), 36.36 (C-1''), 14.22, 14.18 (Et–CH_3).

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