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DOUBLE STEREODIFFERENTIATING DREIDING-SCHMIDT REACTIONS

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Summary.- Spiroanellated carbohydrate-derived α-methylene-γ-butyrolactones with an additional stereogenic centre in the β-position of the anellated lactone ring and spiroanellated α-alkylidene-γ-butyrolactones were obtained in a stereoselective manner by *Dreiding-Schmidt* reactions of the deoxy-uloside **1** or of 2,3-*O*-isopropylidene-D-erythronolactone (**2**) with the corresponding (*Z*) alkyl-2-bromomethyl-2-alkenoates in the presence of the highly reactive zinc-silver/graphite surface compound.

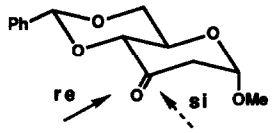
Introduction.- Numerous natural products containing α-alkylidene- especially α-methylene- γ-butyrolactone moieties have been discovered during the past ten years.[1] Many of them like the sesquiterpene derivatives have shown quite promising antineoplastic, phytotoxic and anti-bacterial activities whereas other compounds of this class cause serious allergenic reactions.[1, 2] Due to the extreme pharmaceutical potential of these compounds quite a number of different approaches have been devised for the synthesis of these target molecules, among them cyclisation reactions of 4-hydroxy-2-methylene-butyric acids [3] and of 4-hydroxy-2-methylene-pentenoates [4], *Bayer-Villiger* oxidations [5] of 2-methylene-cyclobutanones, carbonylations [6] as well as methylenations of suitable precursors [7] and metal-assisted reactions of carbonyl compounds.[8] A majority of these approaches on the whole however, are restricted in their application and only a few can seldom be used for synthetic transformations of carbohydrate

derived compounds; a fact which is either due to tedious synthetic schemes for the preparation of the respectable starting materials or more often to functional group incompatibility of the method.

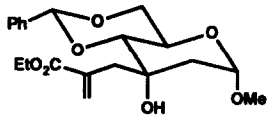
Despite first promising reports on the successful action of carbohydrate derived α-methylene-γ-butyrolactones as successful inhibitors of sulfhydryl enzymes [9] their number remained small over the years up to now due to these synthetic problems.

Many of these compounds [10,11] have been prepared by *Dreiding* [12] *-Schmidt* reactions; [10, 13] however, these zinc-mediated reactions between the carbohydrate derived carbonyl compounds and alkyl 2-bromomethyl-acrylates, when performed under classical conditions afforded the target molecules in only low yields and nearly without any stereoselectivity.[14] Yields and stereoselectivity can significantly be improved by using the highly reactive zinc-silver/graphite surface compound whose usefulness has already been shown in *Reformatsky* reactions [15] and simple *Dreiding-Schmidt* reactions.[11] Thus, the use of this highly active form of zinc metal has allowed an extension of the method even for chain elongating and branching of ulosides [16] and of aldonolactones.[17] Despite these improvements no attempts are known to synthesize either spiroanellated carbohydrate-derived α-methylene-γ-butyrolactones with an additional stereogenic centre in the β-position of the anellated lactone ring or of α-alkylidene- (other than methylene) γ-butyrolactones.

Results and Discussion.- Reaction of the deoxyuloside, methyl-4,6-*O*-benzylidene-2-deoxy-α-D-erythro-hex-3-ulopyranoside (**1**), [18] with ethyl (2-bromomethyl) acrylate (**4**) [19] and zinc-silver/graphite at -78° resulted in the formation of 95% of chain elongated methyl 4,6-*O*-benzylidene-2-deoxy-3-*C*-(2-ethoxycarbonyl-2-propenyl)-α-D-*ribo*-hexopyranoside (**3**). The stereospecific formation of this *ribo*-configured product can be rationalized by a kinetically controlled equatorial attack onto the *re*-face of the carbonyl group, since an axial attack is strongly hindered by the axial-oriented anomeric methoxy group. The IR spectrum of **3** is characterized by signals at ν= 1715 cm^{-1} (C=O) and 1630 cm^{-1} (C=C) and a broad signal at ν= 3500 cm^{-1} which indicates the presence of a hydroxy group and of linear branching instead of the formation of an anellated ring. Attempts of either acid or base catalysed cyclisations of **3** failed.



1



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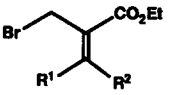
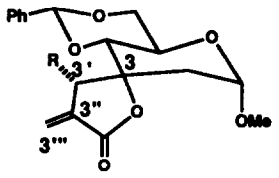
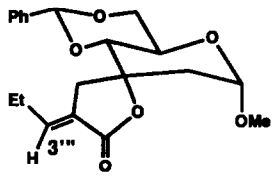


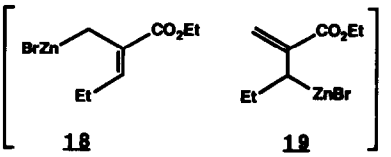
4 ($R^1 = R^2 = H$)
5 (R^1 = Me, $R^2 = H$)
8 (R^1 = Et, $R^2 = H$)



6 (R = Me)
9 (R = Et)



10

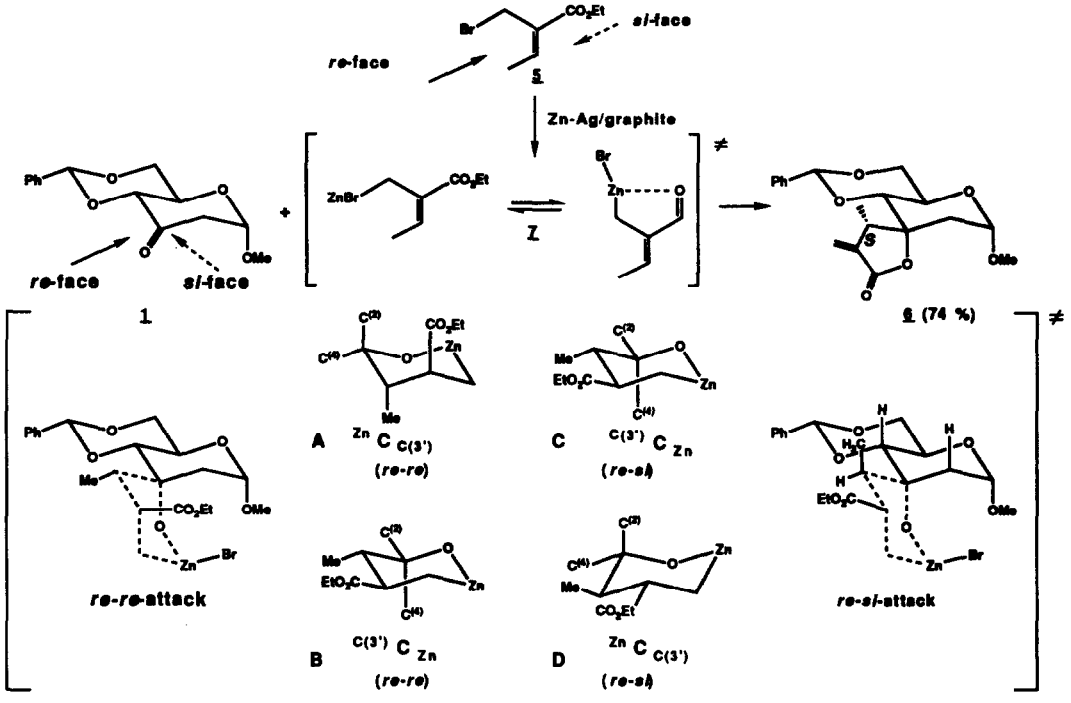


18 19

The reaction of alkyl-3-alkyl-2-(bromomethyl)-propenoates with zinc is known to give fairly stable organozinc species; it has already been shown by spectroscopic evidence that only the isomers possessing the (*Z*)-configuration are formed which are additionally stabilized by a strong chelation between the zinc metal and the carbonyl oxygen of the ester.[20] Thus, **1** afforded on addition to ethyl (*Z*)-2-bromomethyl-2-butenoate [21] (**5**) a slow reaction at -30° leading to the exclusive formation of syrupy **6** which was obtained in 74% yield after chromatographic work up of the reaction mixture. Contrary to the reaction of **1** with **4** no significant reaction was observed at temperatures below -60°.

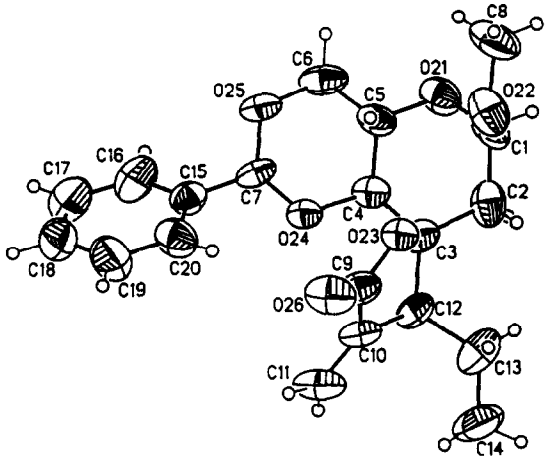
6 is characterized in its IR spectra by absorptions at ν= 1770 (C=O) and 1665 (C=C) cm^{-1} but also by the absence of absorptions at ν >3500 cm^{-1}, hence indicating the absence of an hydroxy function and thus suggesting the presence of the desired spiroanellated butyrolactone ring. **6** is formed by an attack of the *re*-face of the organozinc intermediate **7** onto the *re*-face of the carbonyl moiety. Inspection of *Dreiding* models revealed that the transition state **A** ($^{Zn}C_{C(3')}$) resulting from this *re-re* attack shows only minor steric interactions with the substituents of the uloside; the transition states **B-D**, however, possess such interactions, i.e. in **B** ($^{C(3')}C_{Zn}$, also from an *re-re*-attack) and in **D** ($^{Zn}C_{C(3')}$, *re-si*) steric interactions between the methyl substituent at C(3') and H_{ax}-C(2) and H_{ax}-C(4) are found whereas in **C** ($^{C(3')}C_{Zn}$, *re-si*) steric hinderance between the ester moiety and the 4,6-*O*-benzylidene acetal is observed. Hence, the formation of

the product should rather follow this pathway *via* the six-membered chair-like transition state **A** leading finally to **6** which possesses a (*S*)-configuration at C(3').



Unfortunately, ^{1}H-NOE measurements did not allow an unambiguous verification of this assignment. With the aim to achieve a suitable crystalline derivative both in order to ascertain this preliminary assignment and to generalize these assumptions **1** was allowed to react with (*Z*)-2-bromomethyl-2-pentenoate (**8**) [22] in the presence of the zinc-silver/graphite. The reaction was even slower as compared to the reaction of **5** but came to its completion within 1 h at room temperature. After chromatographic work up two crystalline products **9** (83 %) and **10** (10 %) were obtained. In addition, small amounts of known 2,5-dipropylidene-hexanedioic-acid diethyl ester [20] resulting from a *Wurtz* type dimerization of the intermediary organozinc species were also isolated. This result is in excellent agreement with the previously reported estimated heat of dimerization of the intermediary organozinc compound.[20] The spectra of **9** are very similar to those of **6** and differ only in the presence of an ethyl group at C(3') in **9** instead of a methyl

substituent as in **6**. This can be regarded as a good indication, that **6** and **9** have the same configuration at C(3) and C(3'). Since ^{1}H-NOE experiments again failed to give an unambiguous proof of the correct absolute configuration of the two newly created stereogenic centres, suitable crystals were grown and submitted to a single crystal X-ray analysis.[23] The X-ray analysis of **9** gave proof of the (*S*)-configuration at C(3'). The carbohydrate skeleton as well as the anellated ring showed no anomalies (*cf* Tab. 1 and Tab. 2) neither in the bond lengths nor in the bond angles as compared to compounds of similar structure.



P $2_12_12_1$, No 19

a = 9.731(2)Å

b = 10.136(3)Å

c = 19.440(4)Å

Z = 4; V = 1917.4(8) Å^3

ORTEP-drawing of **9**

Tab. 1: Selected bond lengths (Å) of **9**:

C(1)-C(2)	154.5(10)	C(10)-C(11)	131.7(8)	O(23)-C(3)	146.1(6)
C(2)-C(3)	152.8(9)	C(10)-C(12)	148.3(7)	O(23-C(9)	136.2(7)
C(3)-C(4)	150.2(8)	C(12)-C(13)	155.6(10)	O(24)-C(4)	141.9(7)
C(3)-C(12)	155.6(7)	C(13)-C(14)	142.1(12)	O(24)-C(7)	140.3(6)
C(4)-C(5)	151.8(7)	O(21)-C(1)	139.6(10)	O(25)-C(6)	144.3(8)
C(5)-C(6)	146.6(9)	O(21)-C(1)	141.1(9)	O(25)-C(7)	140.8(6)
C(7)-C(15)	148.1(8)	O(21-C(5)	142.5 (8)	O(26)-C(9)	120.0(7)
C(9)-C(10)	145.3(8)	O(22)-C(8)	145.2(10)		

Tab. 2: Selected bond angles (°) of **9**:

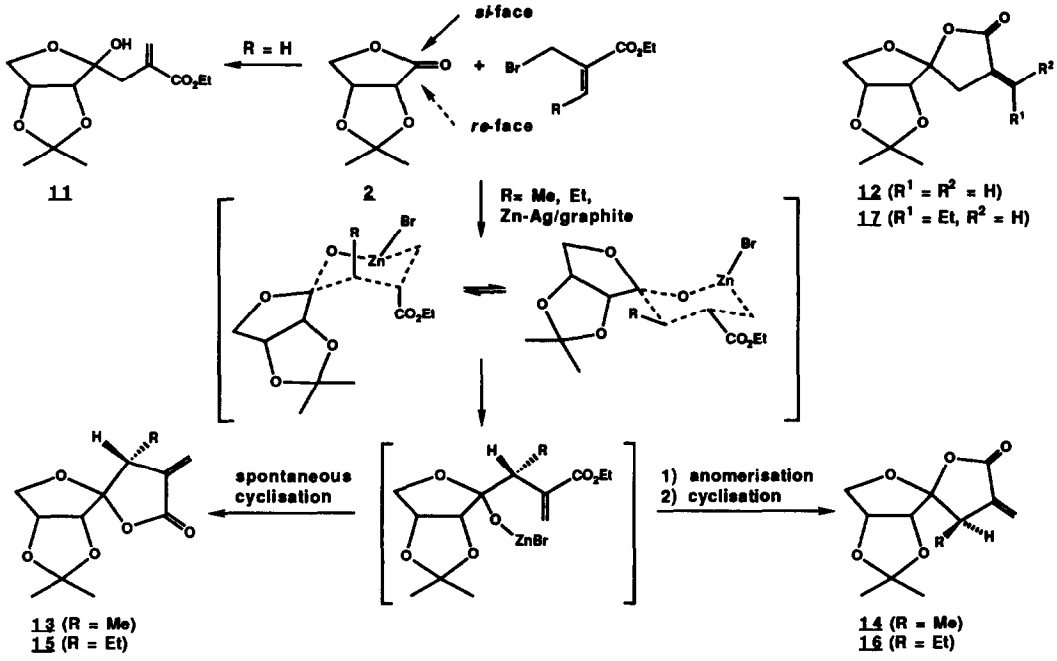
C(1)-C(2)-C(3)	114.5(5)	C(7)-C(15)-C(16)	118.0(3)	O(23)-C(3)-C(2)	109.3(4)
C(1)-O(21)-C(5)	111.3(5)	C(7)-C(15)-C(20)	122.0(3)	O(23)-C(3)-C(4)	107.2(4)
C(1)-O(22)-C(8)	111.3(6)	C(9)-C(10)-C(11)	122.6(5)	O(23)-C(9)-C(10)	110.0(5)
C(2)-C(3)-C(4)	109.0(4)	C(9)-C(10)-C(12)	107.3(4)	O(23)-C(9)-O(26)	120.0(5)
C(2)-C(3)-C(12)	115.6(5)	C(10)-C(12)-C(13)	110.6(5)	O(24)-C(4)-C(3)	111.1(4)
C(3)-C(4)-C(5)	111.2(59	C(11)-C(10)-C(12)	130.1(5)	O(24)-C(4)-C(5)	108.5(4)
C(3)-C(12)-C(10)	101.2(4)	C(12)-C(13)-C(14)	117.5(7)	O(24)-C(7)-C(15)	109.8(4)
C(3)-C(12)-C(13)	112.6(5)	O(21)-C(1)-O(22)	113.3(6)	O(24)-C(7)-O(25)	110.7(4)
C(3)-O(23)-C(9)	109.1(4)	O(21)-C(1)-C(2)	113.3(6)	O(25)-C(6)-C(5)	107.6(4)
C(4)-C(3)-C(12)	111.6(4)	O(21)-C(5)-C(4)	109.3(5)	O(25)-C(7)-C(15)	106.8(4)
C(4)-C(5)-C(6)	110.7(5)	O(21)-C(5)-C(6)	108.5(4)	O(26)-C(9)-C(10)	129.9(5)
C(4)-O(24)-C(7)	113.2(3)	O(22)-C(1)-C(2)	107.7(6)		
C(6)-O(25)-C(7)	111.3(4)	O(23)-C(3)-C(12)	103.7(4)		

The second product of this reaction **10** is characterized in the IR spectra by absorptions at ν= 1760 (C=O) and 1695 (C=C) cm^{-1} and again by the lack of any OH absorptions above 3500 cm^{-1}. In the ^{1}H-NMR spectra only one signal of an olefinic proton (δ = 6.64 ppm) is found. ^{1}H-NOE experiments show a close vicinity of H-C(3') and $H_{A,B}$-C(3"") and a lack of NOE effects between H-C(3"") to H-C(3') thereby indicating a *cis*-relationship between H-C(3"") and the CO-moiety of the butyrolactone ring; this corresponds well with the chemical shift of the olefinic proton as compared to simple model compounds.[24]

To exploit the scope and limitations of this reaction, the reaction of an aldonolactone has been investigated in more detail inasmuch as aldonolactones have previously been shown to be valuable starting materials for the straightforward synthesis of chain-elongated higher monosaccharides.[11]

Thus, reaction of 2,3-*O*-isopropylidene-D-erythronolactone (**2**), easily obtained by degradation of D-isoascorbic acid subsequently followed by isopropylidenation, [25] with ethyl (2-bromo-

methyl)acrylate (**4**)[19] and zinc-silver/graphite resulted in the formation of chain-extended ethyl 2,3-dideoxy-5,6-*O*-isopropylidene-2-*C*-methylene-β-D-erythro-4-heptulofuranosonate (**11**) in 92% yield. **11** is characterized by its broad OH absorption in the IR spectrum at ν=3440 cm^{-1}; the protons of the C(2) methylene group appear as doublets at δ=5.83 and δ=6.28 ppm each showing a geminal coupling constant of 1.3 Hz. No cyclisation of **11** to the corresponding spiroanellated α-methylene-γ-butyrolactone **12** took place during the reaction. Attempts of either acid or base catalysed cyclisations of **11** failed or resulted in huge deterioration of **11** and its polymerisation.



However, at room temperature **2** afforded on its reaction (3 h) with ethyl (*Z*)-2-bromomethyl-2-butenoate (**5**) [21] and zinc-silver/graphite two products **13** and **14** in 30 and 9% yield, respectively. **13** and **14** showed in their IR spectra strong absorptions at ν= 1776/1785 (C=O) and 1720/1720 (C=C) cm^{-1}. Since neither an OH absorption was detected for both compounds in their IR or ^{1}H-NMR spectra nor ethyl ester moieties were found in their corresponding ^{1}H- and ^{13}C-NMR spectra the α-alkylidene-γ-butyrolactone moiety has to be spiroanellated to the

anomeric centre of the carbohydrate; **13/14** differ only in the absolute configuration at the anellation point since *Dreiding-Schmidt* reactions are well known to proceed (*Z*)-selective *via* a chair-like six-membered transition state.[26]

The formation of **13** can be explained by a spontaneous cyclisation of an intermediary zinc alcoholate, probably caused by the presence of zinc bromide acting as a Lewis acid catalyst. **14** is formed, however, after protonation of the zinc alcoholate followed by anomerization *via* the corresponding acyclic keto alcohol to the thermodynamically more stable β-anomer. Thus, **14** afforded upon treatment with methanol in the presence of catalytic amounts of *p*-TsOH, albeit in very low yield, **13** and large amounts of polymeric material, whereas **13** did not upon similar treatment form any **14** which can be accounted for the higher thermodynamic stability of **14** which is also predicted by semi-empirical AM1 calculations. To estimate this transient equilibrium AM1 calculations [27] were performed and the calculated values for the heat of formation of the respective anomers were compared. These calculations revealed for the anomers of **11** a difference in the heat of formation of 2.55 kcal/mol and for **13/14** of 0.64 kcal/mol - both in favour of the respective β-anomer although it should be considered that calculated energy differences between anomers are often overestimated.[28] In addition, these calculations predict an influence of the size of the β-substituent of the butyrolactone-ring onto the equilibrium since a unsubstituted compound possesses a $\Delta\Delta H$=2.25 kcal/mol; for a methyl substitution a $\Delta\Delta H$=0.64 in favour of the corresponding β-anomer is calculated, whereas for an ethyl substituent a $\Delta\Delta H$= 0.35 kcal/mol in favour of the α-anomer is obtained. A verification of these calculations is found experimentally since the α:β ratio decreases from **13**:**14**=1:3 to **15**:**16**=1:2 (*vide infra*).

Similiar to the reaction of the uloside **1**, the reaction of **2** with ethyl (*Z*)-2-bromomethyl-2-pentenoate (**8**) [22] and zinc-silver/graphite afforded a more complex reaction mixture. Besides small amounts of 2,5-dipropylidene-hexanedioic-acid diethyl ester which again results from an *Wurtz* type coupling of the intermediary organozinc compound and unchanged starting material (25%), three carbohydrate derived products **15** (9%), **16** (19%) and **17** (15%) could be isolated by chromatography of the crude reaction mixture.[29]

The spectroscopic data of **15** and **16** are very similar to each other and also to **13/14**. From these data the structures of spiroanellated compounds, *i.e.* of substituted 1,6-dioxaspiro [4.4]

nonane-2-ones were again deduced; **15** and **16** differ only in the absolute configuration at the anellation point. The formation of **15/16** results from an attack of the *si*-face of the organometallic intermediate **18** onto the less hindered *si*-face of the lactone-carbonyl group followed either by an anomerisation reaction and cyclisation- resulting in the formation of **16**, or by a spontaneous cyclisation without prior anomerisation thus yielding **15**. **17**, however, is formed by a *si-si*-attack of the organozinc species **19** which results from **18** by allylic rearrangement; the (*E*)-configuration of the final double bond was deduced from ^{1}H and ^{13}C-NMR spectroscopic data.

EXPERIMENTAL

The melting points are uncorrected (*Reichert* hot stage microscope), optical rotations were obtained using a Perkin-Elmer 243B polarimeter (1 cm micro cell), NMR spectra (internal Me_4Si) were recorded using either a Bruker AM250 or a Varian XL300 instrument (δ given in ppm, J in Hz), IR spectra (film or KBr-pellet) on a Perkin-Elmer 298 instrument, MS spectra were taken either on a MAT311A or a Varian-112S instrument; for elemental analysis a Foss-Heraeus Vario EL instrument was used. TLC was performed on silica gel (Merck 5554, detection by dipping in a solution containing 10% sulfuric acid (400 *ml*), ammonium molybdate (20 g) and cerium(IV) sulfate (20 mg) followed by heating to 150° C. The THF used throughout for all reactions was freshly distiled from sodium/benzophenone and all reactions were performed under dry argon.

General procedure for the Dreiding-Schmidt *reactions.*- Degassed graphite (Fluka, 1.56 g, 130 mmol, 150°, 30 min) and clean, freshly cut potassium (0.66 g, 16.88 mmol) were stirred at 150° C under argon as previously described.[15] To the resulting bronze-coloured C_8K suspended in THF (100 *ml*) a mixture of anhydrous zinc chloride (1.1 g, 8.2 mmol) and silver acetate (0.12 g, 0.72 mmol) was added in several portions at room temperature with vigorous stirring. The addition of these salts caused the solvent to boil; heating and reflux was continued for an additional 25 min, the suspension was cooled to -78° C and a solution of the carbonyl compound and of the halo ester (for quantities *vide infra*) in abs. THF (15 *ml*) was added slowly. After stirring for the period and temperature given (*vide infra*) the mixture was filtered over a pad of Celite, diluted with ethyl acetate (150 *ml*) and extracted with ice water (10 *ml*) and brine (10 *ml*). The organic layer was dried over sodium sulfate, the solution was evaporated below 35° C and the remaining residue subjected to column chromatography (ethyl acetate/hexanes 10:1 → 5:1 (*v/v*)) to afford the corresponding products.

Crystal structure analysis of **9**.- Diffraction data were collected at room temperature on a Siemens P4 diffractometer using graphite monochromated MoK_α radiation (λ = 0.71069 Å); crystal size: 0.27 * 0.11 * 0.08 mm. Unit cell parameters were obtained by least square refinement of the setting angles of 50 reflections with $15° \leq 2\Theta \leq 22°$; d_{calc}= 1.248 g/cm^3, μ=

0.09 mm^{-1}. Data (Wyckoff-scan, $\Delta\omega$=0.8°) were collected ($3° \leq 2\Theta \leq 45°$) yielding 2569 unique and 1627 observed ($F_o \geq 4\ \sigma(F)$) intensities; R = 0.0526, R_ω= 0.060, $\omega^{-1} = \sigma^2(F_o)+0.00615 \times F_o^2$ for 232 parameters. Hydrogen atoms were treated as riding groups with isotropic displacement parameters.Computer-program: SHELXTL-PLUS; a final difference electron density map showed a maximum of 0.38 e/Å^3 and a minimum of -0.27 e/Å^3. The absolute structure could not be unambiguously defined.

Methyl 4,6-O-benzylidene-2-deoxy-3-C-(2-ethoxycarbonyl-2-propenyl)-α-D-ribo-hexopyranoside (**3**).- From **1** (1.90 g, 7.2 mmol) and **4** (1.58 g, 8.2 mmol) at -78° C for 30 min **1** (2.58 g, 95%) was obtained as an oil; $[\alpha]_D^{25}$ = +64.9°(*c* 1.0, $CHCl_3$); Lit.:[16] $[\alpha]_D^{25}$ = +63.2° (*c* 1.5, $CHCl_3$).

Methyl 4,6-O-benzylidene-2-deoxy-3-C-[(1S)-2-carboxy-1-methyl-2-propenyl)-α-D-ribo-hexopyranoside-γ-lactone (**6**).- From **1** (1.90 g, 7.2 mmol) and **5** (1.70 g, 8.2 mmol) at -30° C for 7 h **6** (1.84 g, 74%) was obtained as an oil; unchanged starting material (**3**, 0.40 g, 21%) was recovered. $[\alpha]_D^{25}$ = +59.1°(*c* 1, $CHCl_3$); IR (film): 2990*m*, 2940*m*, 2880*m*, 1770*s*, 1715*m*, 1455*m*, 1410*m*, 1380*m*, 1340*w*, 1270*m*, 1230*w*, 1210*w*, 1180*m*, 1130*s*, 1095*s*, 1060*s*, 1050*s*, 1000*m*; ^{1}H-NMR (250 MHz, $CDCl_3$): 1.15 (*d*, *J* = 7.2, 3 H, H_3C-C(3')); 2.02 (*bd*, *J* = 3.8, 1 H, H_A-C(2)); 2.35 (*bs*, 1 H, H_B-C(2)); 3.26 (*bq*, *J* = 7.2, 1 H, H-C(3')); 3.39 (*s*, 3 H, OCH_3); 3.53 (*d*, *J* = 9.9, 1 H, H_A-C(6)); 3.70 (*virt. t*, *J* = 9.9, 1 H, H_B-C(6)); 4.27-4.42 (*m*, 2 H, $H_{A,B}$-C(4), H-C(5)); 4.83 (*bd*, *J* = 3.8, 1 H, H-C(1)); 5.45 (*d*, *J* = 2.6, 1 H, H_A-C(3'")); 5.55 (*s*, 1 H, Ph-CH); 6.17 (*d*, *J* = 2.6, 1 H H_B-C(3'")); 7.15-7.39 (*m*, 5 H, aromat); ^{13}C-NMR (50 MHz, $CDCl_3$): 14.77 (*q*, CH_3); 35.25 (*t*, C(2)); 38.38 (*d*, C(3')); 55.59 (*d*, C(5)); 69.15 (*t*, C(6)); 79.73 (*d*, C(4)); 81.60 (*s*, C(3)); 97.59 (*d*, C(1)); 101.89 (*d*, CH-Ph); 119.86 (*t*, C(3'")); 126.16 (*d*), 128.14 (*d*), 129.00 (*d*) each of aromat; 137.16 (*s*, aromat); 141.16 (*s*, 3")); 169.31 (*s*, CO); MS (ei, 75 eV, 159°): 346 (M, 5.5%), 303 (14.7%). Anal. calcd. for $C_{19}H_{22}O_6$ (346.38): C, 65.88; H, 6.40. Found: C, 65.81; H, 6.29.

Methyl 4,6-O-benzylidene-2-deoxy-3-C-[(1S)-2-carboxy-1-ethyl-2-propenyl]-α-D-ribo-hexopyranoside-γ-lactone (**9**) and *methyl 4,6-O-benzylidene-3-C-[(2E)-2-carboxy-2-pentenyl]-α-D-ribo-hexopyranoside-γ-lactone* (**10**).- From **1** (1.90 g, 7.2 mmol) and **8** (3.32 g, 15.0 mmol) at 25° C for 1 h **9** (2.14 g, 83%), **10** (0.25 g, 10%) and 2,5-dipropylidene-hexanedioic acid diethylester (0.57 g) were isolated.

Data for **9**: mp.: 129.5-131°; $[\alpha]_D^{25}$ = +32.1° (*c* 1, $CHCl_3$); IR (KBr): 2980*m*, 2950*m*, 2920*m*, 2900*m*, 2870*w*, 2840*w*, 1770*s*, 1460*w*, 1415*m*, 1390*m*, 1370*m*, 1340*m*, 1320*w*, 1270*s*, 1230*m*, 1210*m*, 1170*m*, 1140*s*, 1120*m*, 1100*s*, 1075*m*, 1060*s*, 1040*s*, 1015*s*; ^{1}H-NMR (250 MHz, C_6D_6): 1.01 (*t*, *J* = 7.3, 3 H, H_3C of ethyl); 1.41 and 1.65 (*dqxAB*, *J* = 7.0, 7.3, 14.2 and 5.5, 7.3, 14.2, 2 H, H_2C of ethyl); 2.05 (*dxAB (A-part)*, *J* = 3.6, 14.0, 1 H, H_A-C(2)); 2.16 (*AB (B-part)*, *J* = 14.0, 1 H, H_B-C(2)); 2.93 (*dddd*, *J* = 1.4, 2.2, 5.5, 7.0, 1 H, H-C(3')); 3.39 (*s*, 3 H, OCH_3); 3.52-3.74 (*m*, 2 H, $H_{A,B}$-C(6); 4.25-4.38 (*m*, 2 H, $H_{A,B}$-C(4), H-C(5)); 4.84 (*d*, *J* = 3.6, 1 H, H-C(1)); 5.45 (*d*, *J* = 1.4, 1 H, H_A-C(3'")); 5.54 (*s* 1 H, CH-Ph); 6.17 (*d*, *J* = 2.2, 1 H, H_B-C(3'")); 7.29-7.38 (*m*, 5 H, aromat); ^{13}C-NMR (50 MHz, $CDCl_3$): 11.06 (*q*, CH3); 21.52 (*t*, H_2C of ethyl); 35.45 (*t*, C(2)); 45.95 (*d*, C(3')); 55.44 (*q*, OCH_3); 59.48 (*d*, C(5)); 69.19 (*t*, C(6)); 81.33 (*s*, C(3)); 81.45 (*d*, C(4)); 97.63 (*d*, C(1)); 101.91 (*d*, CH-Ph); 120.22 (*t*, C(3'")); 126.12 (*d*), 128.18 (*d*), 129.03 (*d*), 137.08 (*s*) each of aromat; 139.17 (*s*, C(3")); 169.62 (*s*, CO); MS (ei, 75 eV, 113°): 361 (M+1, 1%), 360 (M, 7.9%); 317 (11.9%); 223 (20.6%); 211 (65.8%). Anal. calcd. for $C_{20}H_{24}O_6$ (360.41): C, 66.65; H, 6.71. Found: C, 66.72; H, 6.60.

Data for **10**: mp: 149-149.5°; $[\alpha]_D^{25}$ = +5.0°(*c* 1, $CHCl_3$); IR (KBr):2970*m*, 2940*m*, 2900*m*, 2890*m*, 1760*s*, 1695*m*, 1455*m*, 1440*m*, 1405*m*, 1390*m*, 1370*m*, 1345*m*, 1310*m*, 1240*s*, 1225*m*, 1210*m*, 1150*m*, 1130*s*, 1105*s*, 1075*m*, 1050*s*, 1030*s*, 1010s; ^{1}H-NMR (250 MHz, $CDCl_3$): 1.01 (*t*, *J* = 7.6, 3 H, CH_3); 2.05-2.21 (*m*, 4 H, $H_{A,B}$-C(3''''), $H_{A,B}$-C(2)); 3.0 (*m*, 1 H, H_A-C(3'); 3.07 (*m*, 1 H, H_B-C(3')); 3.39 (*s*, 3 H, OCH_3); 3.51-3.75 (*m*, 2 H, $H_{A,B}$-C(6)); 4.12-4.40 (*m*, 2 H, H-C(4), H-C(5)); 4.78 (*d*, *J* = 4.3, 1 H, H-C(1)); 5.55 (*s*, 1 H, CH-Ph); 6.61-6.68 (*m*, 1 H, H-C(3'')); 7.26-7.42 (*m*, 5 H, aromat); ^{13}C-NMR (50 MHz, $CDCl_3$): 12.54 (*q*, CH_3); 23.51 (*t*, C(3'')); 34.55 (*t*, C(2)); 41.09 (*t*, C(3')); 55.39 (*q*, OCH_3); 59.44 (*d*, C(5)); 69.22 (*t*, C(6)); 78.39 (*s*, C(3)); 81.79 (*d*, C(4)); 97. 56 (*d*, C(1)); 101.88 (*d*, CH-Ph); 125.66 (*s*, C(3")); 126.14 (*d*), 128.20 (*d*), 129.03 (*d*), 137.16 (*s*) each of aromat; 140.69 (*d*, C(3'')); 170.19 (*s*, CO); MS (ei, 75 eV, 120°): 361 (M+1, 2.9%); 360 (M, 15.1%); 317 (7.2%); 223 (21.9%); 211 (78.3%). Anal. calcd. for $C_{20}H_{24}O_6$ (360.41): C, 66.65; H, 6.71. Found: C, 66.81; H, 6.53.

*Ethyl 2,3-dideoxy-5,6-*O*-isopropylidene-2-C-methylene-β-D-erythro-4-heptulofuranosonate* (**11**).- From **2** (1.14 g, 7.2 mmol) and **4** (1.58 g, 8.2 mmol) at 0° C and 1 h **11** (1.81 92%) was obtained as an oil; $[\alpha]_D^{25}$ =-42.4° (Lit.: $[\alpha]_D^{25}$ -41.8° [17]); IR (film): 3440 *bs*, 2995*s*, 2940*s*, 2880*m*, 1710*s*, 1680*m*, 1460*w*, 1405*w*, 1370*s*, 1335*m*, 1305*s*, 1270*s*, 1210*s*, 1180*s*, 1160*s*, 1100*s*, 1060*m*, 1040*s*, 1000*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 1.27 (*t*, *J* = 7.0, 3 H, CH_3); 1.28 (*s*, 3 H, CH_3^i); 1.45 (*s*, 3 H, CH_3^i); 2.77 (*d*, *J* = 14.2, 1 H, H_A-C(3)); 2.94 (*d*, *J* = 14.2, 1 H, H_B-C(3)); 3.82 (*d*, *J* = 10.2, 1 H, H_A-C(7)); 3.95 (*dd*, *J* = 4.0, 10.2, 1 H, H_B-C(7)); 4.20 (*q*, *J* = 7.0, 2 H, CH_2); 4.33 (*d*, *J* = 5.9, 1 H, H-C(5)); 4.80 (*dd*, *J* = 4.0, 5.9, 1 H, H-C(6)); 5.83 (*bs*, exchangeable with D_2O, 1 H, HO-C(4)); 5.84 (*d*, *J* = 1.3, 1 H, H_A-C(2')); 6.28 (*d*, *J* = 1.3, 1 H, H_B-C(2')); ^{13}C-NMR (50 MHz): 13.91 (*q*, CH_3 of ester); 25.00 (*q*, CH_3^i); 26.29 (*q*, CH_3^i); 36.58 (*t*, C(3)); 61.32 (*t*, CH_2 of ester); 70.84 (*t*, C(7)); 80.5 (*d*), 84.5 (*d*) (C-(5), C(6)); 105.70 (*s*, C-(4)); 112.17 (*s*, C_q^i); 129.73 (*t*, C-(2')); 135.14 (*s*, C(2)); 169.20 (*s*, CO); MS (ci, isobutane): 255 (M-H_2O+1). Anal. calcd. for $C_{13}H_{20}O_6$ (272.30): C, 57.34; H, 7.40. Found: C, 57.29; H, 7.44.

*(3R) 2,3-Dideoxy-5,6-*O*-isopropylidene-3-C-methyl-2-C-methylene-α-*D*-erythro-4-heptulo-furanosono-1,4-lactone* (**13**) and (3R) *2,3-dideoxy-5,6-*O*-isopropylidene-3-C-methyl-2-C-methylene-β-*D*-erythro-4-heptulofuranosono-1,4-lactone* (**14**).- From **2** (1.14 g, 7.2 mmol) and **5** (2.07 g, 10 mmol) at 25° C for 3 h **13** (0.52 g, 30%) and **14** (0.15 g, 9%) were obtained; unchanged starting material **2** (0.59 g, 52%) was recovered.

Data for **13**: obtained as an oil; $[\alpha]_D^{25}$ = -126.0° (*c* 1.0, $CHCl_3$); IR (film): 3000*m*, 2950*m*, 2890*w*, 1776*s*, 1720*m*, 1670*w*, 1460*m*, 1400*m*, 1385*s*, 1380*s*, 1335*m*, 1310*m*, 1255*s*, 1210*s*, 1170*s*, 1165*s*, 1145*s*, 1100*s*, 1080*s*, 1065*s*, 1045*s*, 1020*s*; ^{1}H-NMR (250 MHz, $CDCl_3$): 1.15 (*d*, *J* = 7.0, 3 H, H_3C-C(3)); 1.17 (*s*, 3 H, CH_3^i); 1.33 (*s*, 3 H, CH_3^i); 3.18 (*ddq*, *J* = 3.0, 3.4, 7.0 H-C(3)); 3.84 (*dd*, *J* = 3.5, 10.4, 1 H, H_A-C(7)); 3.92 (*d*, *J* = 10.4, 1 H, H_B-C(7)); 4.55 (*d*, *J* = 5.8, 1 H, H-C(5)); 4.77 (*dd*, *J* = 3.5, 5.8, H-C(6)); 5.44 (*d*, *J* = 3.0, H_A-C(2')); 6.08 (*d*, *J* = 3.4, 1 H, H_B-C(2')); ^{13}C-NMR (50 MHz, $CDCl_3$): 12.73 (*q*, C(3')); 23.84 (*q*, CH_3^i); 25.42 (q, CH_3^i); 37.59 (*d*, C(3)); 72.00 (*t*, C(7)); 78.99 (*d*, C(5)); 84.44 (*d*, C(6)); 112.33(*s*, C_q^i); 113.47 (*s*, C(4)); 120.89 (*t*, C(2')); 139.09 (*s*, C(2)); 167.81 (*s*, C(1)); MS (ci, isobutane): 241 (M+1); MS (ei, 75 eV, 48°): 225 (16.1%); 196 (5.7%); 185 (7.0%); 165 (12.6%); 127 (16.1%); 114 (30.5%). Anal. calcd. for $C_{12}H_{16}O_5$ (240.26): C, 59.99; H, 6.71. Found: C, 59.83; H, 6.84.

Data for **14**: mp: 52-52.5°; $[\alpha]_D^{25}$ = -62.4° (*c* 1.0, $CHCl_3$); IR (KBr): 3000*m*, 2940*m*, 2890*w*, 1785*s*, 1720*m*, 1670*w*, 1460*m*, 1385*m*, 1375*m*, 1305*w*, 1270*s*, 1230*m*, 1210*s*, 1160*s*, 1115*m*,

1100*m*, 1080*m*, 1055*w*, 1020*s*; ^{1}H-NMR (250 MHz, $CDCl_3$): 1.34 (*s*, 3 H, CH_3^i); 1.35 (*d*, *J* = 7.3, 3 H, H_3C-C(3')); 1.48 (*s*, 3 H, CH_3^i); 3.17 (*ddq*, *J* = 1.4, 1.6, 7.3, 1 H, H-C(3)); 3.98 (*s*, 1 H, H_A-C(7)); 4.00 (*d*, *J* = 1.8, H_B-C(7)); 4.69 (*d*, *J* = 5.8, H-C(5)); 4.93 (*dd*, *J* = 1.8, 5.8, H-C(6));5.65 (*bd*, *J* = 1.4, 1 H, H_A-C(2')); 6.21 (*bd*, *J* = 1.6, 1 H, H_B-C(2')); ^{13}C-NMR (50 MHz, $CDCl_3$): 17.32 (*q*, CH_3); 25.07 (*q*, CH_3^i); 26.35 (*q*, CH_3^i); 41.19 (*d*, C(3)); 72.67 (*t*, C(7)); 79.87 (*d*), 82.35 (*d*) (C(5) and C(6)); 112.92 (*s*, C_q^i); 115.15 (*s*, C(4)); 121.55 (*t*, C(2')); 140.82 (*s*, C(2)); 170.05 (*s*, C(1)); MS (ei, 75 eV, 65°): 241 (M+1, 0.4%); 225 (20.5%); 196 (7.8%); 185 (5.7%); 165 (16.8%). Anal. calcd. for $C_{12}H_{16}O_5$ (240.26): C, 59.99; H, 6.71. Found: C, 60.06; H, 6.65.

(3 R) *2,3-Dideoxy-3-C-ethyl-5,6-O-isopropylidene-2-C-methylene-α-D-erythro-4-heptulofuranosono-1,4-lactone* (**15**), (3R) *2,3-dideoxy-3-C-ethyl-5,6-O-isopropylidene-2-C-methylene-β-D-erythro-4-heptulofuranosono-1,4-lactone* (**16**) and (Z) *2,3-dideoxy-5,6-O-isopropylidene-2-C-propylidene-β-D-erythro-4-heptulofuranosono-1.4-lactone* (**17**).- From **2** (1.19 g, 7.5 mmol) and **20** (3.31 g, 15 mmol) after 3 h at 25° C **15** (0.18 g, 9%), **16** (0.37 g, 19%) and **17** (0.276 g, 14.5%) were obtained. In addition, 2,5-dipropylidene-hexanedioic acid diethylester (0.38 g), and unchanged starting material **2** (0.29 g, 25%) were isolated by chromatography.

Data for **15**: obtained as an oil; $[\alpha]_D^{25}$ = -84.5° (*c* 1.1, $CHCl_3$); IR (film): 2990*m*, 2980*m*, 2950*m*, 2890*w*, 1785*s*, 1720*w*, 1670*w*, 1465*w*, 1385*m*, 1380*m*, 1310*m*, 1275*s*, 1220*s*, 1155*s*, 1120*s*, 1100*s*, 1070*w*, 1040*w*, 1000*s*; ^{1}H-NMR (250 MHz, $CDCl_3$): 0.93 (*t*, *J* = 7.4, 3 H, H-C-(3")); 1.35 (*s*, 3 H, CH_3^i); 1.48 (*s* 3 H, CH_3^i); 2.25 (*m*, 2 H, $H_{A,B}$-C(3')); 2.94 (*m*, H-C(3)); 3.97 (*virt. d*, *J* = 2.3, 2 H, $H_{A,B}$-C(7)); 4.72 (*d*, *J* = 5.7, 1 H, H-C(5)); 4.93 (*m*, 1 H, H-C(6)); 5.62 (*d*, *J* = 1.1, 1 H, H_A-C(2')); 6.25 (*d*, *J* = 1.3, 1 H, H_B-C(2')); ^{13}C-NMR (50 MHz, $CDCl_3$): 9.96 (*q*, C(3")); 21.24 (*t*, C(3')); 24.92 (*q*, CH_3^i); 26.21 (*q*, CH_3^i); 47.45 (*d*, C(3)); 72.25 (*t*, C(7)); 79.72 (*d*), 81.97 (*d*) C(5) and C(6)); 112.71 (*s*, C_q^i); 114.78 (*s*, C(4)); 122.27 (*t*, C(2')); 137.78 (*s*, C(2)); 168.59 (*s*, C(1)); MS (ci, isobutane): 255 (M+1); MS (ei, 75eV, 90°): 239 (15.7%); 210 (1.7%); 199 (5.7%); 179 (10.2%); 141 (18.1%); 114 (26.6%). Anal. calcd. for $C_{13}H_{18}O_5$ (254.28): C, 61.41; H, 7.13. Found C, 61.61; H, 7.02.

Data for **16**: obtained as an oil; $[\alpha]_D^{25}$ = -105.3° (*c* 1.0, $CHCl_3$); IR (film): 2990*m*, 2950*m*, 2890*w*, 1780*s*, 1720*m*, 1690*w*, 1460*w*, 1405*w*, 1390*m*, 1380*m*, 1310*w*, 1280*s*, 1260*m*, 1210*s*, 1170*m*, 1135*m*, 1100*s*, 1050*m*, 1000*m*; ^{1}H-NMR(250 MHz, $CDCl_3$): 1.07 (*t*, *J* = 7.4, 3 H, H-C(3")); 1.33 (*s*, 3 H, CH_3^i); 1.49 (*s*, 3 H, CH_3^i); 2.10 (*m*, 2 H, $H_{A,B}$-C(3')); 3.23 (*m*, 1 H, H-C(3)); 4.11 (*m*, 2 H, $H_{A,B}$-C(7)); 4.58 (*d*, *J* = 5.8, 1 H, H-C(5)); 4.93 (*m*, 1 H, H-C(6)); 5.68 (*d*, *J* = 2.4, 1 H, H_A-C(2')); 6.29 (*d*, *J* = 2.9, 1 H, H_B-C(2')); ^{13}C-NMR (50 MHz, $CDCl_3$): 11.81 (*q*, H_3C-C(3")); 22.61 (*t*, CH_2-C(3')); 23.99 (*q*, CH_3^i); 25.44 (*q*, CH_3^i); 43.03 (*d*, C(3)); 72.57 (*t*, C(7)); 79.09 (*d*), 84.53 (*d*) (C(5) and C(6)); 112.50 (*s*, C_q^i); 114.15 (*s*, C(4)); 121.98 (*t*, C(2')); 138.68 (*s*, C(2)); 167.72 (*s*, C(1)); MS (ei, 75 eV, 91°): 239 (8.9%); 210 (2.2%); 199 (4.3%); 179 (5.5%), 141 (18.5%); 114 (16.3%). Anal. calcd. for $C_{13}H_{18}O_5$ (254.28): C, 64.41; H, 7.14. Found: C, 64.47; H, 7.38.

Data for **17**: obtained as an oil; $[\alpha]_D^{25}$ = -127.7° (*c* 1.1, $CHCl_3$); IR (film): 2980*m*, 2950*m*, 2890*w*, 1780*s*, 1715*w*, 1690*m*, 1465*w*, 1435*w*, 1385*m*, 1375*m*, 1315*m*, 1305*w*, 1275*s*, 1250*m*, 1215*s*, 1165*m*, 1140*m*, 1100*s*, 1090*w*, 1045*m*, 1000*s*; ^{1}H-NMR (250 MHz, $CDCl_3$): 1.10 (*t*, *J* = 7.5, 3 H, H_3C (C2"')); 1.35 (*s*, 3 H, CH_3^i); 1.49 (*s*, 3 H, CH_3^i); 2.23 (*m*, 2 H, $H_{A,B}$-C(2")); 2.85 (*dd*, *J* = 1.1, 18.0, 1 H, H_A-C(3)); 3.23 (*dd*, *J* = 1.8, 18.0, 1 H, H_B-C(3)); 4.04 (*m*, 2 H, $H_{A,B}$-C(7)); 4.62 (*d*, *J* = 4.6, H-C(5)); 4.93 (*dd*, *J* = 4.6, 5.4, 1 H, H-C(6)); 6.77 (*m*, 1 H, H-C(2')); ^{13}C-NMR (50 MHz, $CDCl_3$): 12.46 (*q*, C(2"')); 23.55 (*t*, H_2C-C(2")); 24.96 (*q*, CH_3^i); 26.22 (*q*, CH_3^i); 30.93 (*t*, C(3));

72.68 (*t*, C(7)); 80.01 (*d*), 84.18 (*d*) (C(5) and C(6)); 112.93 (*s*, C_q^i); 113.02 (*s*, C(4)); 124.44 (*s*, C(2)); 143.29 (*d*, C(2')); 172.88 (*s*, C(1)); MS (ei, 75 eV, 90°): 239 (10.8%); 199 (5.8%); 179 (10.6%); 153 (3.6%); 141 (44.0%); 114 (31.8%). Anal. calcd. for $C_{13}H_{18}O_5$ (254.29): C, 61.41; H, 7.14. Found: C, 61.32; H, 7.29.

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29 The reactions of 2,3;5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone with various alkyl 3-alkyl-2-(bromomethyl)-propenoates gave access to alkyl-2,3-dideoxy-2-*C*-alkylidene-5,6;8,9-di-*O*-isopropylidene-α-D-manno-4-nonulo-furanosonates in high yields but, unfortunately, from these reactions no spiro-anellated products were obtained. Cyclisation experiments failed due to the pronounced tendency of these compounds to undergo polymerisation reactions.

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