Pergamon

Tetrahedron Vol. 50, No. 11, pp. 3333-3348, 1994

0040-4020/94 $6.00+0.00

0040-4020(94)E0063-Y

FLUORIDE MEDIATED REACTIONS OF LACTONES WITH SILYL KETENE ACETALS

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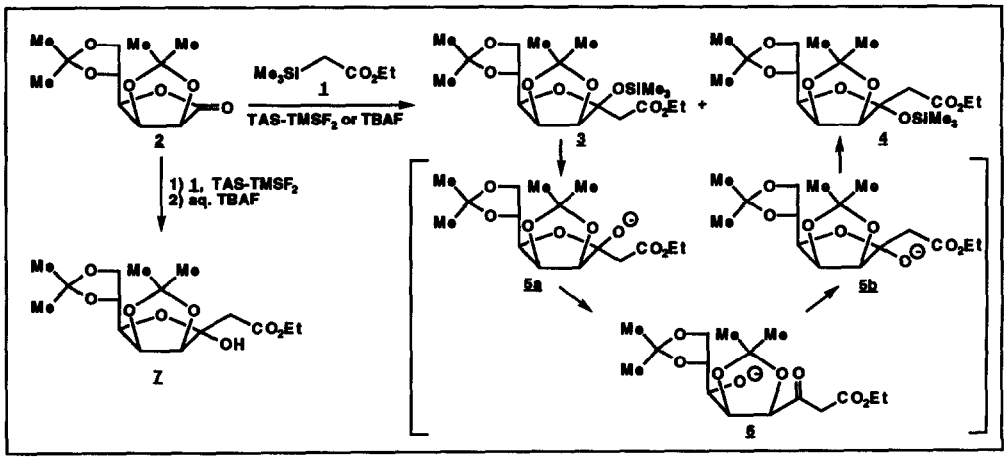
Key Words: aldolisation reactions; silyl ketene acetals; lactones; carbohydrates.

Abstract: *Aldolisation reactions of silyl ketene acetals with lactone carbonyls can be performed under very mild conditions in good yields in the presence of 5-10 mol-% of TAS-$TMSF_2$.*

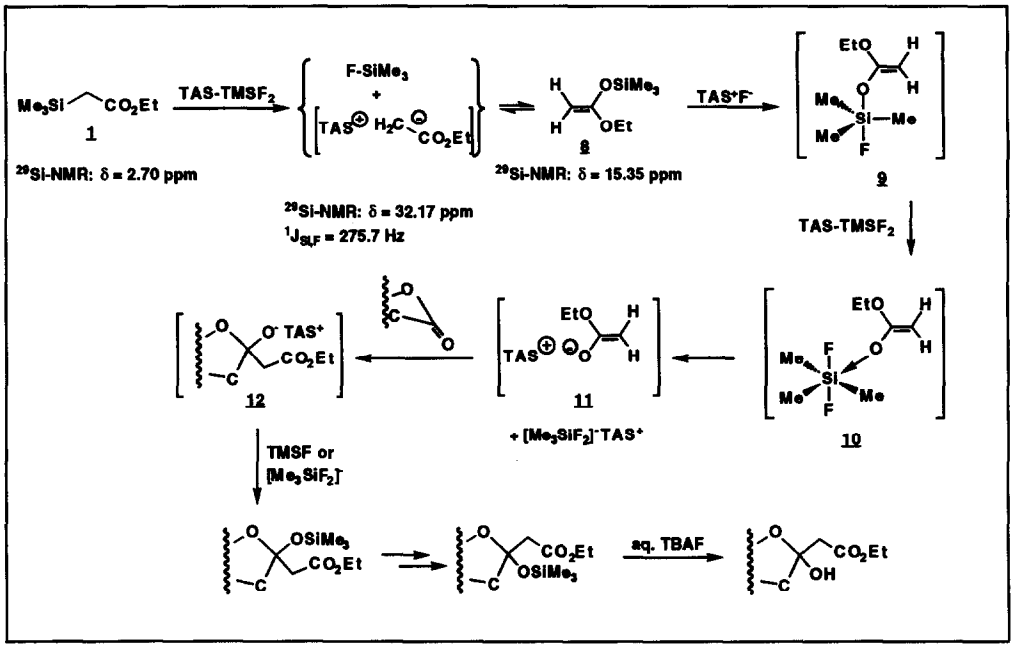
Introduction.- Numerous methods for C-C-bond formation with carbonyl compounds as starting materials have been established during the last two decades. Amongst these the reactions of carbanions with carbonyl groups have been in the focus of interest for several reasons. In this context it is well known that the reaction of non-enolizable carbonyl compounds with ethyl trimethylsilyl acetate (**1**) in the presence of tetra-*n*-butyl ammonium fluoride TBAF [1] and also with trimethylsilyl acetonitrile in the presence of tris(dimethylamido)sulfonium difluorotrimethylsilicate TAS-$TMSF_2$ [2] affords the corresponding β-trimethylsilyloxy esters or -nitriles in good to excellent yields. These procedures have been successfully extended to lactones [3] and even to intramolecular C-C-bond formation.[4] It is generally assumed for these reactions that silicon compounds with an anion stabilizing group in the α-position can be readily activated by nucleophiles to give reactions of the carbanion which results from C-Si cleavage.[5]

Results und Discussion.- Reaction of **1** with the aldonolactone 1,2;5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone (**2**) in the presence of a catalytic amount of dry tetra-*n*-butyl ammoninum fluoride TBAF [3] or TAS-$TMSF_2$ afforded a mixture of the β-silyloxyesters **3** and **4** in the ratio **3**:**4** = 33:57% . The ratio **3**:**4** strongly depends on the concentration of the reactants, the amount of catalyst and the reaction temperature. It was found that when the reaction time was prolonged **3** was transformed into **4**; this observation can be rationalized by assuming a rapid fluoride mediated desilylation of **3** to yield **5a** which is subsequently transformed *via* the acyclic ketone **6** into the α-configurated and thermodynamically favoured hemiacetal **5b** which is re-silylated by intermediary formed trimethylsilyl fluoride. Both **3** and **4** afford on TBAF assisted desilylation exclusively α-configurated **7**. [6, 7]



To gain further insights into the mechanism of this reaction and to verify our mechanistic assumptions, ^{29}Si-NMR spectroscopy was used as a mechanistic reporter. Thus, treatment of **1** with TBAF [3] or TAS-$TMSF_2$ in $CDCl_3$ revealed the formation of Me_3SiF and of small amounts of the trimethylsilyl ketene acetal, 1-ethoxy-1-trimethylsilyloxy-ethene (**8**). It seems most likely that an anionic activation of the Si-O bond of **8** proceeds *via* the formation of the pentacoordinate silyl intermediate **9**. Subsequent attack of fluoride anion on **9** should give a hexacoordinate difluoride complex **10** whose decomposition affords the formation of $[Me_3SiF_2]^-$ and "free enolate" **11** [5, 8] the latter of which is capable of reacting with the carbonyl

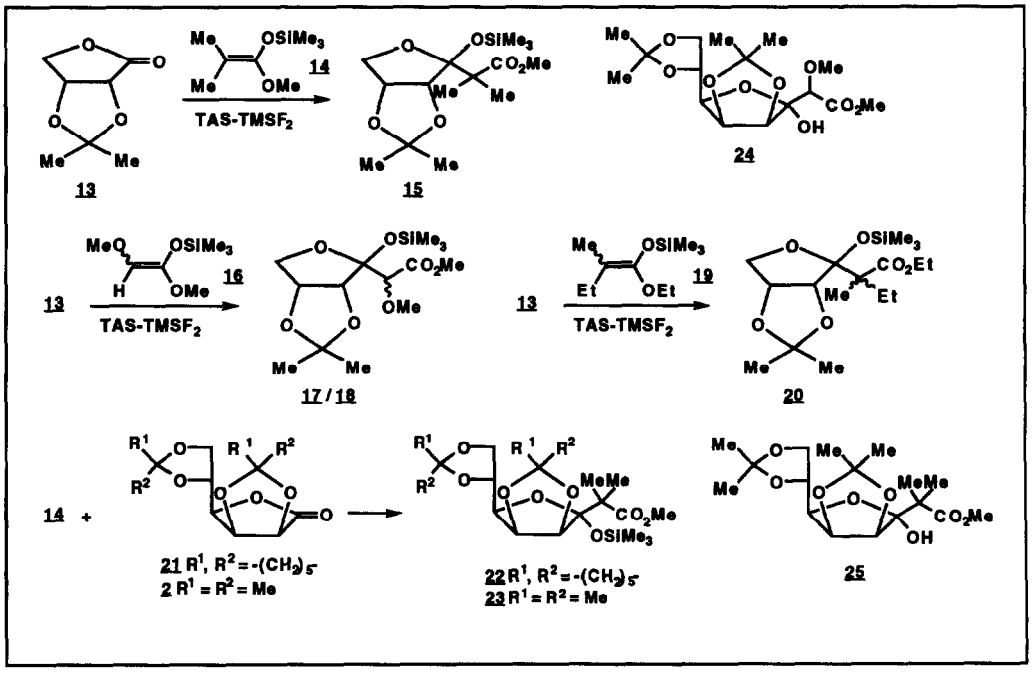
group of the lactone to yield **12**. Silylation of **12** by Me_3SiF or more likely by $[Me_3SiF_2]^-$ completes the sequence.[5, 8] Inspection of *Dreiding* models suggest that **11** should approach the carbonyl group from the less hindered face, *i.e.* opposite to the 2,3-*O*-isopropylidene group, thus resulting in the formation of **12** possessing the acetate group at the anomeric centre in a pseudoaxial configuration. This is in excellent agreement with experimental findings (^{1}H-NMR) of **3** being formed earlier than **4**. Anomerisation, however, can occur both with **12** as well as by a multistep desilylation/resilylation process (*vide supra*) starting from already formed **3**. These experimental data led to the hypothesis that silyl ketene acetals might be reactive intermediates in the reactions of α-C-trimethylsilylated esters with non enolisable carbonyl groups and should be regarded as valuable reagents in their own right.



Indeed, silyl ketene acetals are well known to react in the presence of fluoride or Lewis-acid catalysts with aldehydes and ketones, [9] Michael acceptors [10] or with organic halides [11] very easily but the reaction of trimethylsilyl ketene acetals with lactone carbonyls has been obtained only under forced conditions in the presence of triphenylium hexachloroantimonate or using a catalyst system consisting of antimony pentachloride, chlorotrimethylsilane, and

tin(II) chloride.[12] Very recently [13] we reported first successful examples of the very smooth reaction between silyl ketene acetals and lactone carbonyls using TAS-$TMSF_2$ as a catalyst.

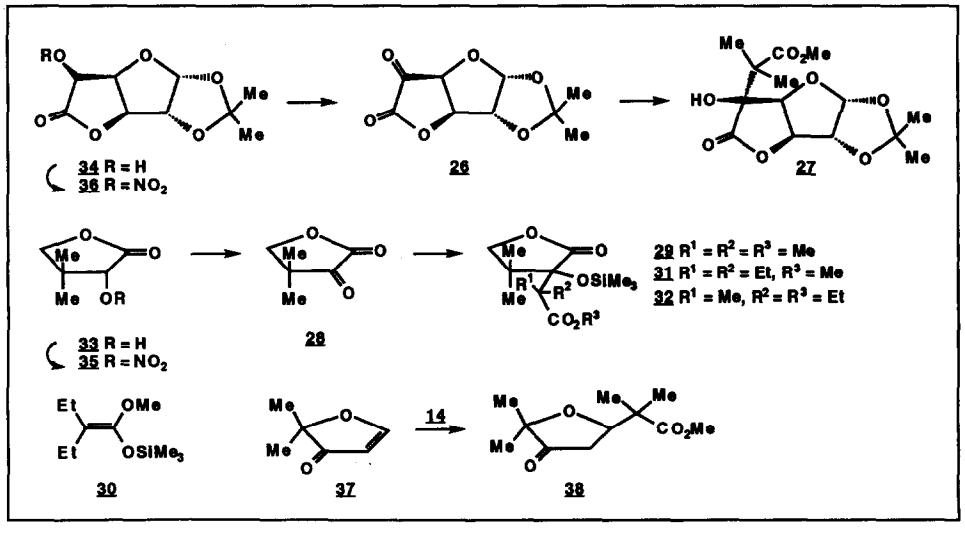
Thus, reaction of 2,3-*O*-isopropylidene-D-erythronolactone [14] (**13**) with 1-methoxy-2-methyl-1-trimethylsilyloxy-propene (**14**), *i.e.* the trimethylsilyl ketene acetal of methyl isobutyrate, in dry THF in the presence of catalytic amounts of TAS-$TMSF_2$ (5-10 mol-%) yielded chain elongated **15**;[15] reaction of **13** with 1-methoxy-2-methoxy-1-trimethylsilyloxy-ethene (**16**) gave a 31% yield of **17** and 19% of **18**. The analogous reaction with 1-ethoxy-2-methyl-1-trimethylsilyloxy-butene (**19**) afforded **20** in 71% yield as an inseparable 3:1 mixture of the corresponding diastereomers.



From 2,3;5,6-di-*O*-cyclohexylidene-D-mannono-1,4-lactone (**21**) and 1-methoxy-2-methyl-1-trimethylsilyloxy-propene (**14**) the octulosonate **22** was obtained in 74% yield. The isopropylidene analog of **21**, 2,3;5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone (**2**) allowed under the same conditions access to **23** (64% yield) whereas the reaction of this lactone with

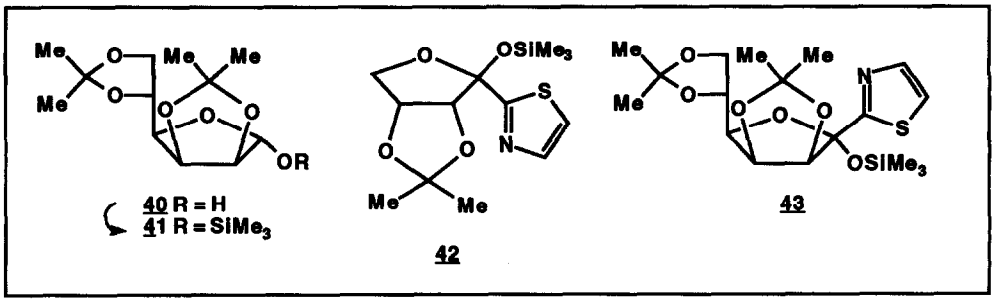
1-methoxy-2-methoxy-1-trimethylsilyloxy-ethene (**16**) gave 44% of **24**. Fluoride catalyzed desilylation of **23** afforded **25** in 83% yield.

Due to the increased reactivity of the carbonyl group of ketones as compared to the carbonyl moiety of lactones the mild conditions of our approach allows the selective transformation of α-ketolactones at their carbonyl group leaving the lactone moiety unaffected.[16] The very sensitive α-keto lactone **26**, 1,2-*O*-isopropylidene-α-D-xylo-5-hexulofuranurono-6,3-lactone[17] was transformed within a reaction time of 2 h at 0° in 44% yield stereoselectively into 1,2-*O*-isopropylidene-5-*C*-(1,1-dimethyl-methoxycarbonylmethyl)-α-D-glucofuranurono-6,3-lactone (**27**). Similarly, 4,4-dimethyl-tetrahydrofuran-2,3-dione (**28**) reacted with this silyl ketene acetal in the presence of TAS-$TMSF_2$ at 0° to **29** (91% yield). The reaction of **28** with 1-methoxy-2-ethyl-1-trimethylsilyloxy-butene (**30**) (10°, 2 h) afforded **31**; from the reaction of **28** with 1-ethoxy-2-methyl-1-trimethylsilyloxy-butene (**19**) a 92% yield of **32** as an inseparable 1:1 mixture of the corresponding stereoisomers was obtained. Both **26** and **28** were obtained from the corresponding α-hydroxy lactones **33** and **34** by their reaction with nitric acid/acetanhydride followed by subsequent treatment of the intermediary nitrates **35** or **36** with silica gel.[18, 19]



A very smooth reaction was observed for the vinylogous lactone 2,2-dimethyl-3(2H)furanone (**37**) which gave at 0° within 2 h 88% of the product of the conjugate addition, 2-(5,5-dimethyl-4-oxo-tetrahydrofuran-2-yl)-2-methyl propionic acid methyl ester (**38**).[20]

Concerning the synthesis of C_1 extended sugars from lactones a different synthetic scheme had to be applied. 2-(Trimethylsilyl)thiazole (**39**) is well known to react with reactive carbon electrophiles, *e.g.* aldehydes, [21] acyl chlorides [21] or heteroaryl cations [22] to give the corresponding 2-substituted thiazoles in good to excellent yields;[23] the reaction of ketenes afforded 2-thiazolyl silyl enol ethers; [24] unreactive carbonyl groups do not react under these conditions. The hemiacetal, 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranose (**40**) did not afford any chain extended product upon reaction with 2-(trimethylsilyl)thiazole even in the presence of TAS-$TMSF_2$ whereas **40** underwent a clean silylation at the hemiacetalic hydroxyl group and gave 2,3;5,6-di-*O*-isopropylidene-1-*O*-trimethylsilyl-α-D-mannofuranose (**41**) in 93% yield. Smooth chain elongation is observed, however, by the reaction of 2-(trimethylsilyl)thiazole/TAS-$TMSF_2$ with lactones. Thus, 2,3-*O*-isopropylidene-D-erythrono-lactone (**13**) afforded upon reaction with these reagents at 0° for 1 h 64% yield of **42**; 2,3;5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone (**2**) gave 40% of **43**.



Hence, these reactions extend the applicability of the classic thiazole-aldehyde approach [25-27] for the synthesis of chiral polyhydroxyalkyl natural products utilizing the synthetic potential of lactones.

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 distilled from sodium/benzophenone and all reactions were performed under dry argon.

Ethyl 2-deoxy-4,5;7,8-di-*O*-isopropylidene-3-*O*-trimethysilyl-β-D-*manno*-3-octulofuranosonate (3) and ethyl 2-deoxy-4,5;7,8-di-*O*-isopropylidene-3-*O*-trimethysilyl-α-D-*manno*-3-octulofuranosonate (4).- A catalytic amount of TAS-$TMSF_2$ was added at 0°C under argon to a THF solution (abs., 5 *ml*) of **2** (0.52 g, 2.0 mmol) and **1** (0.42 g, 2.6 mmol); this mixture was stirred (40 min at 25°C). After dilution with ethyl acetate (25 *ml*) the reaction mixture was washed with ice water and brine (2 *ml* each), dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was subjected to flash chromatography (silica gel, hexanes / ethyl acetate, 20:1 → 10:1) to afford **3** and **4**.

Data for **3**: (280 mg, 33%); oil; $[\alpha]_D^{25}$ = -7.5° (*c* = 1.8, $CHCl_3$); R_F 0.50 (hexanes / ethyl acetate 3:1); IR (film): 2990*s*, 2960*m*, 2940*m*, 2890*w*, 1730*s*, 1455*w*, 1385*s*, 1375*s*, 1320*m*, 1250*s*, 1165*s*, 1140*m*, 1070*s*, 1050*m*, 1025*s*, 850*s*; ^{1}H-NMR (400 MHz, $CDCl_3$): 0.10 (*s*, 9 H, 3 x Me); 1.10 (*t*, 3 H, *J* = 7.1, Me); 1.18 (*s*, 3 H, Me); 1.19 (*s*, 3 H, Me); 1.25 (*s*, 3 H, Me); 1.31 (*s*, 3 H, Me); 2.42 (*s*, 2 H, $H_{A,B}$-C(2)); 3.55 (*dd*, 1 H, *J* = 4.1, 7.7, H-C(6)); 3.89 (*dd*, 1 H, *J* = 4.6, 8.6, H_A-C(8)); 3.95 (*dd*, 1 H, *J* = 6.2, 8.6, H_B-C(8)); 4.00 (*q*, 2 H, *J* = 7.1, CH_2); 4.26 (*ddd*, 1 H, *J* = 4.6, 6.2, 7.7, H-C(7)); 4.64 (*dd*, 1 H, *J* = 4.1, 6.0, H-C(5)); 4.70 (*d*, 1 H, *J* = 6.0, H-C(4)); ^{13}C-NMR (62 MHz, $CDCl_3$): 1.78 (*q*, 3 x Me); 14.1 (*q*, Me); 24.3 (*q*, Me); 25.2 (*q*, Me); 25.6 (*q*, Me); 26.9 (*q*, Me); 44.1 (*t*); 60.7 (*t*); 66.9 (*t*); 73.2 (*d*); 78.3 (*d*); 79.4 (*d*); 82.1 (*d*); 104.8 (*s*); 109.3 (*s*); 112.9 (*s*); 169.2 (*s*); MS (ci, ammonia): 436 ($[M+NH_3+1]^+$); Anal. calcd. for $C_{19}H_{34}O_8Si$ (418.56): C, 54.52; H, 8.19; Si, 6.71; found: C, 54.30; H, 8.34; Si, 6.74.

Data for **4**: (480 mg, 57%): oil; $[\alpha]_D^{25}$ +23.4° (*c* = 2.2, $CHCl_3$); R_F 0.65; hexanes / ethyl acetate 3:1); IR (film): 2990*m*, 2960*m*, 2940*w*, 2900*w*, 1740*s*, 1480*w*, 1460*m*, 1385*s*, 1375*s*, 1340*m*, 1255*s*, 1190*s*, 1120*s*, 1080*s*, 1070*s*, 1040*s*, 900*s*; ^{1}H-NMR (400 MHz, $CDCl_3$): 0.13 (*s*, 9 H, 3 x Me); 1.35 (*t*, 3 H, *J* = 7.1, Me); 1.31 (*s*, 3 H, Me); 1.35 (*s*, 3 H, Me); 1.42 (*s*, 3 H, Me); 1.43 (*s*, 3 H, Me); 2.76 (*d*, 1 H, *J* = 16.1, H_A-C(2)); 3.03 (*d*, 1 H, *J* = 16.1, H_B-C(2)); 3.95 (*dd*, 1 H, *J* = 3.9, 7.4, H-C(6)); 3.98 (*dd*, 1 H, *J* = 4.6, 8.8, H_A-C(8)); 4.04 (*dd*, 1 H, *J* = 6.2, 8.8, H_B-C(8)); 4.13 (*q*, 2 H, *J* = 7.1, CH_2); 4.35 (*ddd*, 1 H, *J* = 4.6, 6.2, 7.4, H-C(7)); 4.68 (*d*, 1 H, *J* = 5.9, H-C(4)); 4.78 (*dd*, 1 H, *J* = 3.9, 5.9, H-C(5)); ^{13}C-NMR (62 MHz, $CDCl_3$): 1.38 (*q*, 3 x Me); 14.1 (*q*, Me); 24.4 (*q*, Me); 25.3 (*q*, Me); 25.8 (*q*, Me); 26.8 (*q*, Me); 40.2 (*t*); 60.2 (*t*); 66.4 (*t*); 73.2 (*d*); 78.9 (*d*); 79.5 (*d*); 86.4 (*d*); 106.2 (*s*); 108.9 (*s*); 112.2 (*s*); 168.9 (*s*); MS (ci, ammonia): 436 ($[M+NH_3+1]^+$);

Anal. calcd. for $C_{19}H_{34}O_8Si$ (418.56): C, 54.52; H, 8.19; Si, 6.71; found: C, 54.38; H, 8.28; Si, 6.72.

Ethyl 2-deoxy-4,5;7,8-di-*O*-isopropylidene-α-D-*manno*-3-octulofuranosonate (7).-

a) From **2** with **1**/TAS-$TMSF_2$: A solution of **2** (0.57 g, 2.2 mmol) and **1** (0.42 g, 2.6 mmol) in abs. THF (5 *ml*) was treated at 0° C under argon with a catalytic amount of TAS-$TMSF_2$. After stirring (120 min at 25° C) methanol/water (9:1, 1 *ml*) and a catalytic amount of TBAF trihydrate were added and stirring was continued for an additional 45 min, the reaction mixture was diluted with ethyl acetate (25 *ml*), washed with ice water and brine (2 *ml* each) and dried over sodium sulfate. The solvent was evaporated *in vacuo* and the residue subjected to chromatography (silica gel, hexanes / ethyl acetate 5:1) to afford **7** (0.64 g, 92%) as an oil; $[\alpha]_D^{25}$ = +5.7° (*c* = 1.3, $CHCl_3$).

b) By desilylation of **4**: To a solution of **4** (0.22 g, 0.53 mmol) in THF/methanol (9:1, 2 *ml*) TBAF-trihydrate (0.17 g, 0.55 mmol) was added at room temperature and the mixture was stirred for 20 min. Work up is performed as described under a) and **7** (165 mg, 91%) was obtained after chromatography; $[\alpha]_D^{25}$ = +5.4° (*c* = 0.2, $CHCl_3$).

c) By desilylation of **3**: Similar to the desilylation of **4** the reaction of **3** (0.22 g, 0.53 mmol) afforded **7** (0.16 g, 89%) as an oil; $[\alpha]_D^{25}$ = +5.7° (*c* = 0.1, $CHCl_3$); R_F 0.38 (hexanes / ethyl acetate 3:1); IR (film): 3460*bm*, 2990*s*, 2940*m*, 2810*w*, 1715*s*, 1405*m*, 1385*s*, 1375*s*, 1340*m*, 1245*m*, 1090*s*, 1065*s*, 1115*m*, 1060*s*, 1045*s*; ^{1}H-NMR (400 MHz, $CDCl_3$): 1.29 (*t*, 3 H, *J* = 7.2, Me), 1.37 (*s*, 3 H, Me), 1.42 (*s*, 3 H, Me), 1.46 (*s*, 3 H, Me), 2.72 (*d*, 1 H, *J* = 16.6, H_A-C(2), 2.82 (*d*, 1 H, *J* = 16.6, H_B-C(2)), 3.99 (*dd*, 1 H, *J* = 6.1, 8.7, H_A-C(8)), 4.06 (*dd*, 1 H, *J* = 4.5, 8.7, H_B-C(8)), 4.09 (*dd*, 1 H, *J* = 3.7, 8.0, H-C(6), 4.20 (*q*, 2 H, *J* = 7.2, CH_2), 4.35 (*ddd*, 1 H, *J* = 4.5, 6.1, 8.0, H-C(7)), 4.51 (*d*, 1 H, *J* = 5.8, H-C(4)), 4.84 (*dd*, 1 H, *J* = 3.7, 5.8, H-C(5)), 4.89 (*br. s*, 1 H, exch. with D_2O, HO-C(4)); ^{13}C-NMR (62 MHz, $CDCl_3$): 14.0 (*q*, Me); 24.4 (*q*, Me); 25.3 (*q*, Me); 25.9 (*q*, Me); 26.8 (*q*, Me); 38.3 (*t*, C(2)); 61.0 (*t*); 66.9 (*t*); 73.0 (*d*); 79.4 (*d*); 80.1 (*d*); 85.7 (*d*); 103.9 (*s*); 109.1 (*s*); 112.8 (*s*); 172.0 (CO); MS (ci, isobutane): 297 ([M-H_2O+1]$^+$); Anal. calcd. for $C_{16}H_{26}O_6$ (314.38): C, 61.13; H, 8.34; found: C, 61.24; H, 8.39.

Methyl 2-deoxy-4,5-*O*-isopropylidene-2,2-dimethyl-3-*O*-trimethylsilyl-α-D-erythro-3,6-furanoso-3-hexulosonate (15).- To a solution of **13** (0.32 g, 2.02 mmol) in dry THF (2 *ml*) and **14** (0.7 g, 4.02 mmol) a catalytic amount of TAS-$TMSF_2$ was added at 0° and the mixture was stirred under argon at 25°C for 3 h. Upon the addition of TAS-$TMSF_2$ the colour of the reaction mixture turned yellow/orange. The mixture was then diluted with ethyl acetate (25 *ml*) and washed with ice water and brine (2 *ml* each). The organic layer was dried over sodium sulfate, the solvent was removed *in vacuo* and the residue subjected to flash chromatography (silica gel, ethyl acetate / hexanes 1:10) to yield **15** (0.42 g, 63%) as an oil; $[\alpha]_D^{20}$ +24.4° (*c* 1.9, $CHCl_3$); R_F 0.47 (hexanes / ethyl acetate 3:1); IR (film): 2990*s*, 2960*s*, 2900*m*, 1735*s*, 1475*m*, 1460*w*, 1440*w*, 1385*m*, 1375*m*, 1275*m*, 1265*m*, 1350*s*, 1210*s*, 1170*m*, 1140*s*, 1105*s*, 1095*s*, 1050*m*, 1030*m*, 905*m*, 880*m*, 840*s*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.20 (*s*, 9 H, $OSiMe_3$), 1.21, 1.27, 1.38, 1.59 (each *s*, 3 H, Me), 3.66 (*s*, 3 H, OMe), 3.90 (*virt. d*, *J* = 9, 2 H, $H_{A,B}$-C(6)), 4.77 (*m*, 1 H, H-C(5)), 4.97 (*d*, *J* = 6, 1 H, H-C(4)); ^{13}C-NMR (75 MHz, $CDCl_3$):

176.054 (*s*, CO), 113.07 (*s*), 110.01, 81.16 (*d*), 80.27 (*d*), 72.28 (*t*, C(6)), 51.91 (*d*), 51.46 (*s*, C(2)), 26.12 (*q*, Me), 24.28 (*q*, Me), 22.09 (*q*, Me), 20.48 (*q*, Me), 2.25 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 12.94; MS (ei, 80 eV, 55°): 317 (18.3), 259 (14.3), 231 (73.1), 219 (49.1), 203 (13.3), 187 (10.3), 183 (32.1), 174 (11.0), 145 (14.6), 131 (40.9); Anal. calcd. for $C_{15}H_{28}O_6Si$ (332.47): C, 54.19; H, 8.49; found: C, 54.03; H, 8.55.

(2 *RS*)- and (2 *SR*) -Methyl 4,5-*O*-isopropylidene-3-*O*-trimethylsilyl-β-D-erythro-glycero-3,6-furanoso-3-hexulosonate (17) and (18).- From the reaction of **13** (0.32 g, 2.02 mmol) and **16** (0.71 g, 4.02 mmol) for 3 h at 25° **17** (0.13 g, 19%) and **18** (0.21 g, 31%) were obtained as oils.

Data for **17**: $[\alpha]_D^{20}$ 4.95° (*c* 1.0, $CHCl_3$); R_F 0.29 (hexanes / ethyl acetate 3:1); IR (film): 2960*s*, 2910*m*, 2840*w*, 1750*s*, 1460*m*, 1440*w*, 1385*m*, 1375*m*, 1360*m*, 1310*w*, 1255*s*, 1210*s*, 1170*m*, 1115*s*, 1100*s*, 1050*m*, 1020*s*, 980*w*, 905*m*, 880*s*, 845*s*, 760*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.19 (*s*, 9 H, $OSiMe_3$), 1.35 (*s*, 3 H, Me), 1.53 (*s*, 3 H, Me), 3.33 (*s*, 3 H, OMe), 3.77 (*s*, 3 H, COOMe), 3.85 (*s*, 1 H, H-C(2)), 3.96 and 4.05 (*AB of ABM*, *J* = 1.9, 5.1, 9.6, 2 H, $H_{A,B}$-C(6)), 4.78 (*M of ABM*, *J* = 1.9, 5.1, 6.2, 1 H, H-C(5)), 4.97 (*d*, *J* = 6.2, 1 H, H-C(4)); ^{13}C-NMR (62.89 MHz, $CDCl_3$): 170.18 (*s*, C(1)); 112.72 (*s*, C_q^i), 106.39 (*s*, C(3)), 87.05, 80.49, 79.30 (each *d*, C(2,4,5)), 72.50 (*t*, C(6)), 58.37 (*q*, OMe), 51.95 (*q*, OMe), 26.28 (*q*, Me^i), 24.80 (Me^i), 1.52 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 15.97; MS (ei, 80 eV, 65°): 319 (5.5), 287 (1.4), 276 (0.8), 259 (1.3), 231 (27.6), 221 (15.6), 161 (19.8), 145 (10.1), 131 (21.8); Anal. calcd. for $C_{14}H_{26}O_7Si$ (334.44): C, 50.28; H, 7.84; found: C, 50.38; H, 7.75.

Data for **18**: $[\alpha]_D^{20}$ -21.9° (*c* 1.4, $CHCl_3$); R_F 0.42 (hexanes / ethyl acetate 3:1); IR (film): 2960*s*, 2910*m*, 2840*w*, 1755*s*, 1460*w*, 1440*w*, 1385*w*, 1380*w*, 1360*w*, 1250*s*, 1210*s*, 1170*m*, 1140*s*, 1100*s*, 1050*m*, 1010*s*, 890*m*, 875*m*, 845*s*, 760*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.19 (*s*, 9 H, $OSiMe_3$), 1.35 (*s*, 3 H, Me), 1.57 (*s*, 3 H, Me), 3.38 (*s*, 3 H, OMe), 3.77 (*s*, 3 H, COOMe), 3.89 (*s*, 1 H, H-C(2)), 3.93 and 3.99 (*AB of ABX*, *J* = 1.9, 4.3, 9.9, 2 H, $H_{A,B}$-C(6)), 4.75 (*m*, 1 H, H-C(5)), 4.77 (*s*, 1 H, H-C(4)); ^{13}C-NMR (75.43 MHz, $CDCl_3$): 169.45 (*s*, C(1)), 113.07 (*s*, C_q^i), 106.01 (*s* C(3)), 86.57, 81.54, 79.91 (*d* each, C(2, 4, 5)), 71.95 (*t*, C(6)), 58.84 (*q*, OMe), 51.85 (*q*, OMe), 26.11 (*q*, Me), 24.71 (*q*, Me), 1.83 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 15.02; MS (ei, 80 eV, 72°): 319 (5.5), 287 (0.6), 275 (2.0), 261 (2.1), 231 (27.8), 221 (17.5), 185 (8.1), 176 (18.1), 161 (21.2), 145 (11.3), 131 (21.8), 114 (7.7), 103 (27.1); Anal. calcd. for $C_{14}H_{26}O_7Si$ (344.44): C, 50.28; H, 7.84; found: C, 50.48; H, 7.88.

(2 *RS*) Ethyl 2-deoxy-2-*C*-ethyl-4,5-*O*-isopropylidene-2-*C*-methyl-3-*O*-trimethylsilyl-3,6-furanoso-3-hexulosonate (20).- From the reaction of **13** (0.32 g, 2.02 mmol) and **19** (0.87 g, 4.02 mmol) for 2 h at 25° **20** (0.52 g, 71%) was obtained as a 3:1 mixture of diastereoisomers (+ major isomer, - minor isomer): oil; $[\alpha]_D^{20}$ 24.2° (*c* 2.7, $CHCl_3$); R_F 0.75 (hexanes / ethyl acetate); IR (film): 2980*s*, 2950*s*, 2890*w*, 1715*s*, 1460*m*, 1380*m*, 1305*w*, 1245*s*, 1205*m*, 1160*m*, 1140*m*, 1090*s*, 1060*m*, 1030*m*, 870*m*, 845*s*, 755*w*; ^{1}H-NMR (250 MHz, $CDCl_3$): 0.19 (*s*, $OSiMe_3$, -), 0.20 (*s*, $OSiMe_3$, +), 0.83 (*t*, *J* = 7.5, $CH_2\underline{Me}$), 1.21 (*s*, Me, +), 1.24 (*s*, Me, -), 1.26 (*t*, *J* = 7.1, $OCH_2\underline{Me}$, -), 1.27 (*t*, *J* = 7.1, $OCH_2\underline{Me}$, +), 1.36 (*s*, Me, -), 1.37 (*s*, Me, +), 1.58 (*s*, Me), 1.80-1.93 (*m*, $-CH_2-$, -), 1.94-2.03 (*m*, $-CH_2-$, +), 3.73-4.20 (*m*, OCH_2), 4.64-4.76 (*m*, OCH), 4.98 (*d*, *J* = 6.5, H-C(4), -), 5.14 (*d*, *J* = 6.7, H-C(4), +); ^{13}C-NMR (62 MHz, $CDCl_3$): 175.15 (*s*, +), 174.56 (*s*, -), 113.18 (*s*, -), 113.03 (*s*, +), 110.30 (*s*, -), 81.01 (*d*,

-), 80.77 (*d*, +), 80.19 (*d*, +), 79.56 (*t*, *t*, C(6), -), 72.45 (*t*, C(6), +), 60.61 (*t*, +), 60.51 (*t*, -), 56.31 (*s*, -), 55.92 (*s*, +), 28.12 (*t*, +), 26.38 (*q*, -), 26.33 (*t*, -), 25.98 (*q*, +), 24.51 (*q*, -), 24.14 (*q*, +), 16.70 (*q*, -), 16.01 (*q*, +), 14.19 (*q*, +), 9.23 (*q*, -), 8.99 (*q*, +), 2.28 (*q*, +), 2.16 (*q*, -), 1.33 (*q*, both isomers); ^{29}Si-NMR (40 MHz, $CDCl_3$): 12.80 (+), 12.72 (-); MS (ei, 80 eV, 75°): 345 (4.6), 315 (1.1), 287 (4.3), 247 (13.3), 231 (44.3), 202 (7.5), 197 (13.3), 157 (12.1), 131 (19.1), 129 (14.5); Anal. calcd. for $C_{17}H_{32}O_6Si$ (360.53): C, 56.64; H, 8.95; found: C, 56.57; H, 8.72.

Methyl 4,5;7,8-di-*O*-cyclohexylidene-2-deoxy-2,2-dimethyl-3-*O*-trimethylsilyl-β-D-manno-3,6-furanoso-3-octulosonate (22).- From the reaction of **21** (0.86 g, 2.01mmol) and **14** (0.7 g, 4.02 mmol) for 2 h at 25° **22** (0.76 g, 74%) was obtained as an oil; $[\alpha]_D^{20}$ -27.1° (*c* 1.6, $CHCl_3$); R_F 0.53 (hexanes /ethyl acetate 3:1); IR (film): 2940*s*, 2880*s*, 1725*s*, 1470*m*, 1450*s*, 1435*m*, 1370*m*, 1335*m*, 1300*s*, 1265*m*, 1240*s*, 1090*s*, 1050*s*, 1010*m*, 950*m*, 925*m*, 905*m*, 850*s*, 760*s*; ^{1}H-NMR (250 MHz, $CDCl_3$): 0.16 (*s*, 9 H, $OSiMe_3$); 1.23 (*s*, 3 H, Me); 1.31 (*s*, 3 H, Me); 1.47-1.80 (*m*, 20 H, cyclohex.); 3.40 (*s*, 3 H, OMe); 3.95-4.75 (*m*, 6 H); 4.82 (*d*, *J* = 6.2, H-C(4)); ^{13}C-NMR (75 MHz, $CDCl_3$): 173.78 (*s*, CO), 110.50 (*s*, C_q of acetal), 107.06 (*s*, C_q of acetal), 106.90 (*s*, C(3)), 77.94 (*d*), 77.46 (*d*), 77.06 (*d*), 70.60 (*d*), 64.26 (*t*, C(8)), 49.50 (*q*, OCH_3), 48.88 (*s*, C(2)), 34.11, 32.47, 32.27, 30.28, 22.82, 22.68, 21.60, 21.40, 21.05 (each *t* of cyclohexylidene), 19.85 (*q*, Me), 17.72 (*q*, Me), 3.10 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 13.78; MS (ei, 80 eV, 132°): 512 (22.5), 469 (3.5), 411 (24.9), 371 (9.7), 307 (7.9), 219 (14.9), 196 (53.7), 171 (21.2), 153 (30.3), 141 (59.6); Anal. calcd. for $C_{26}H_{44}O_8Si$ (512.72): C, 60.91; H, 8.65; found: 61.09; H, 8.67

Methyl 2-deoxy-4,5;7,8-5-di-*O*-isopropylidene-2,2-dimethyl-3-*O*-trimethylsilyl-β-D-manno-3,6-furanoso-3-octulosonate (23).- From the reaction of **2** (0.52 g, 2.01 mmol) and **14** (0.7 g, 4.02 mmol) for 2 h at 25° **23** (0.56 g, 64%) was obtained as an oil; $[\alpha]_D^{20}$ -45.16° (*c* 1.5, $CHCl_3$); R_F 0.48 (hexanes / ethyl acetate 3:1); IR (film): 2990*s*, 2960*s*, 2910*m*, 1740*s*, 1460*m*, 1440*m*, 1385*s*, 1375*s*, 1270*s*, 1250*s*, 1210*s*, 1140*s*, 1110*s*, 1050*s*, 1015*m*, 880*m*, 845*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.17 (*s*, 9 H, $OSiMe_3$), 1.24, 1.31, 1.38, 1.42, 1.62 (each *s*, 3 H, Me), 3.60-3.62 (*m*, 1 H), 3.67 (*s*, 3 H, OMe), 4.0-4.44 (*m*, 3 H), 4.73 (*dd*, *J* = 6, 8, 1 H), 5.13 (*d*, *J* = 6, 1 H, H-C(4)); ^{13}C-NMR (62 MHz, $CDCl_3$): 176.27 (*s*, CO), 112.39 (*s*), 109.69 (*s*), 109.56 (*s*), 80.99 (*d*), 80.13 (*d*), 79.75 (*d*), 73.47 (*d*), 67.21 (*t*, C(8)), 52.05 (*q*, Me), 51.37 (*s*, C(2)), 27.09 (*q*, Me), 25.37 (*q*, Me), 25.27 (*q*, Me), 23.48 (*q*, Me), 22.40 (*q*, Me), 20.16 (*q*, Me), 2.53 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 14.11; MS (ei, 80 eV, 92°): 417 (13.1), 359 (9.3), 331 (55.5), 301 (5.7), 273 (9.7), 241 (6.5), 219 (27.5), 215 (11.4), 187 (10.2), 171 (9.7), 156 (14.1), 141 (46.3), 126 (25.3), 101 (97.4); Anal. calcd. for $C_{20}H_{36}O_8Si$ (432.58): C, 55.53; H, 8.39; found: C, 55.47; H, 8.35.

(2 *RS*) Methyl 4,5;7,8-di-*O*-isopropylidene-2-*O*-methyl-3-*O*-trimethylsilyl-α-D-manno-glycero-3,6-furanoso-3-octulosonate (24).- From the reaction of **2** (0.52 g, 2.01 mmol) and **16** (0.71 g, 4.02 mmol) for 90 min at 25° **24** (0.38 g, 44%) was obtained as an oil; $[\alpha]_D^{20}$ -23.2° (*c* 1.1, $CHCl_3$); R_F 0.19 (hexanes / ethyl acetate 3:1); IR (film): 2990*m*, 2960*m*, 2940*m*, 1705*s*, 1385*m*, 1375*m*, 1250*s*, 1205*s*, 1170*s*, 1110*s*, 1070*s*, 1050*s*, 1015*m*, 975*m*, 905*m*, 850*s*; ^{1}H-NMR (250 MHz, $CDCl_3$): 0.16 (*s*, 9 H, $OSiMe_3$), 1.37 (*s*, 3 H, Me), 1.39 (*s*, 3 H, Me), 1.46 (*s*, 3 H, Me), 1.54 (*s*, 3 H, Me), 3.32 (*s*, 3 H, OMe), 3.77 (*s*, 3 H, COOMe), 3.90 (*s*, 1 H, H-C(2)), 4.01-4.15 (*m*, 2 H, $H_{A,B}$-C(8)), 4.30-4.79 (*m*, 3 H, H-C(5,6,7)), 5.03 (*d*, *J* = 6.2, 1 H, H-

C(4)); ^{13}C-NMR (62 MHz, $CDCl_3$): 169.86 (*s*, CO), 112.46 (*s*), 109.25 (*s*), 105.67 (*s*) (2 x C_q^i and C(3)), 87.78 (*d*), 80.35 (*d*) 80.19 (*d*), 79.66 (*d*), 73.72 (*d*), 66.85 (*t*, C(8)), 58.14 (*q*, OMe), 51.96 (*q*, OMe), 26.98, 25.54, 25.23, 24.08 (each *q*, Me^i), 1.63 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 16.85; MS (ei, 80 eV, 111°): 419 (14.5), 361 (5.5), 331 (44.1), 243 (3.7), 221 (21.5), 215 (10.4), 187 (5.9), 176 (23.7), 161 (10.8), 141 (25.0), 131 (21.8); Anal calcd. for $C_{19}H_{34}O_9Si$ (434.55): C, 52.53; H, 7.83; found: C, 52.50; H, 7.95.

Methyl 2-deoxy-4,5;7,8-di-*O*-isopropylidene-2,2-dimethyl-α-D-manno-3,6-furanoso-3-hexulosonate (25).- To a solution of **23** (0.4 g, 0.92 mmol) in methanol/water (2 *ml*, 9:1 *v/v*) a catalytic amount of TBAF-trihydrate was added. After stirring for 62 h the mixture was diluted with ethyl acetate (25 *ml*) and washed with cold water and brine (2 *ml* each). The organic layer was dried over sodium sulfate, the solvent was removed in vacuo and the residue subjected to flash chromatography (silica gel, hexanes / ethyl acetate 5:1) to afford **25** (0.28 g, 83%); mp 44°, $[\alpha]_D^{20}$ 13.4° (*c* 1.6, $CHCl_3$), R_F 0.17 (hexanes / ethyl acetate 3:1); IR (KBr): 3460*s*, 2990*s*, 2970*s*, 1720*s*, 1480*m*, 1460*m*, 1440*m*, 1380*s*, 1280*s*, 1210*s*, 1170*s*, 1120*s*, 1050*s*, 1010*m*, 975*m*, 925*w*, 910*w*, 885*m*, 850*m*; ^{1}H-NMR (250 MHz, $CDCl_3$): 1.29, 1.38. 1.43, 1.44, 1.46, 1.58 (each *s*, 3 H, Me), 3.72 (*s*, 3 H, OMe), 4.05 (*m*, $H_{A,B}$-C(8)), 4.14-4.17 (*m*, 1 H, H-C(6)), 4.34-4.39 (*m*, 1 H, H-C(7)), 4.61 (*d*, *J* = 6.1, 1 H, H-C(4)), 4.81-4.85 (*m*, 1 H, H-C(5)), 4.85 (*s*, 1 H, exch. with D_2O, HO-C(4)); ^{13}C-NMR (62 MHz, $CDCl_3$): 178.37 (*s*, CO), 112.61 (*s*), 108.07 (*s*), 106.29 (*s*), 86.38 (*d*), 79.72 (*d*), 78.66 (*d*), 73.53 (*d*), 66.62 (*t*, C(8)), 52.34 (*q*, OMe), 48.43 (*s*, C(2)), 26.70 (*q*, Me), 25.49 (*q*, Me), 25.29 (*q*, Me), 23.24 (*q*, Me), 22.00 (*q*, Me), 21.20 (*q*, Me); MS (80 eV, 104°): 345 (23.3), 287 (3.8), 259 (5.4), 227 (8.6), 201 (13.9), 195 (3.5), 167 (8.7), 147 (7.3), 141 (165), 129 (21.56); Anal. calcd. for $C_{17}H_{28}O_8$ (360.41): C, 56.66; H, 7.83; found: C, 56.56; H, 7.92.

1,2-*O*-Isopropylidene-α-D-xylo-5-hexulofuranurono-6,3-lactone (26).- According to the procedure given for the preparation of tetrahydrofuran-2,3-dione (*vide infra*) from 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (**34**) (25.0 g, 115.6 mmol) in acetanhydride (80 *ml*) and nitric acid/acetanhydride (78 *ml*/196 *ml*) **26** (17.4 g, 70%) was obtained; mp 152-154°, $[\alpha]_D^{20}$ 74.3° (*c* 1.5, H_2O); lit.: mp 153-154°, $[\alpha]_D^{20}$ 75.6° (H_2O) [18], $[\alpha]_D^{22}$ 73.0° (H_2O), [29]. An analytical sample of the intermediary 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone-5-nitrate (**36**) showed a mp 106-108° (twice from 2-propanol), $[\alpha]_D^{20}$ +70.9° (*c* 1.4, $CHCl_3$), lit.: mp 105-106°, $[\alpha]_D^{20}$ +72.0° ($CHCl_3$).[18] IR (KBr pellet): 2990*m*, 2950*m*, 1785*s*, 1650*s*, 1375*m*, 1280*m*, 1240*m*, 1175*m*, 1160*m*, 1120*m*, 1100*m*, 1035*m*, 1020*m*, 955*m*, 845*m*, 685*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 1.36 (*s*, 3 H, Me), 1.52 (*s*, 3 H, Me), 4.85 (*d*, *J* = 3.5, 1 H, H-C(2)), 4.98 (*d*, *J* = 3.0, 1 H, H-C(3)), 5.15 (*dd*, *J* = 3.0, 4.5, H-C(4)), 5.69 (*d*, *J* = 4.5, 1 H, H-C(5), 6.02 (*d*, *J* = 3.5, 1 H, H-C(6)); ^{13}C-NMR (62 MHz, $CDCl_3$): 26.48 (*q*, Me), 26.87 (*q*, Me), 76.14, 76.45, 82.44, 82.60 (each *d*, C(2,3,4,5)), 107.0 (*d*, C(1)), 113.93 (*s*, Cq^i), 166.87 (*s*, C(6)); MS (ei, 80 eV, 65°): 248 (0.1), 247 (0.5), 246 (6.1), 215 (0.7), 199 (4.3), 157 (6.7), 127 (5.8); Anal. calcd. for $C_9H_{11}NO_8$ (261.19): C, 41.39; H, 4.25; N, 5.36; found: C, 41.67; H, 4.29; N, 5.07.

1,2-*O*-Isopropylidene-5-*C*-(1,1-dimethylmethoxycarbonylmethyl)-α-D-glucofuranurono-6,3-lactone (27).- From the reaction of **26** (0.43 g, 2.02 mmol) and **14** (0.7 g, 4.02 mmmol) for 3h at 25° **27** (0.28 g, 44%) was obtained; mp 98-99°, $[\alpha]_D^{20}$ +12.86° (*c* 1.4, $CHCl_3$); R_F 0.2 (hexanes / ethyl acetate 3:1); IR (KBr): 3440*bs*, 2990*m*, 2960*m*, 1780*s*,

1720*s*, 1480*m*, 1455*m*, 1425*w*, 1385*m* , 1375*m*, 1325*m*, 1300*w*, 1270*m*, 1260*m*, 1215*m*, 1170*s*, 1160*s*, 1135*s*, 1085*m*, 1070*m*, 1020*s*, 990*m*, 980*m*, 940*w*, 920*w*, 895*w*, 850*w*, 840*w*, 820*w*; ^{1}H-NMR (300 MHz, $CDCl_3$): 1.37 (*s*, 6 H) 1.45 (*s*, 3 H), 1.53 (*s*, 3 H) 4 x Me, 3.66 (*bs*, 1 H, exch. with D_2O), 3.73 (*s*, 3 H, OMe), 4.82 (*d*, *J* = 4.3, 1 H, H-C(3)); 4.85 (*d*, *J* = 3.5, 1 H, H-C(2)); 4.92 (*d*, *J* = 4.3, 1 H, H-C(4)); 5.89 (*d*, *J* = 3.5, 1 H, H-C(1)); ^{13}C-NMR (75 MHz, $CDCl_3$): 175.22 (*s*, CO), 173.90 (*s*, CO), 113.81 (*s*, C_q^i), 106.14 (*s*, (C(1)), 83.72 (*d*), 81.96 (*d*), 80.44 (*d*), 77.96 (*s*, C(5)), 52.49 (*q*, OMe), 48.20 (*s*, CMe_2), 27.27 (*q*, Me), 27.25 (*q*, Me), 26.63 (*q*, Me), 20.67 (*q*, Me), 20.65 (*q*, Me), 20.30 (*q*, Me); MS (ei, 80 eV, 84°) 316 (10.2), 301 (13.2), 269 (14.9), 257 (3.9), 241 (12.0), 216 (1.5), 199 (6.5), 171 (5.5), 158 (6.3), 129 (32.6), 113 (47.9); Anal. calcd. for $C_{14}H_{20}O_8$ (316.31): C, 53.16; H, 6.37; found: C,53.30; H, 6.48.

4,4-Dimethyl-tetrahydrofuran-2,3-dione (28).- *DL*-2-Hydroxy-3,3-dimethyl-γ-butyrolactone **33** (*rac.* pantolactone, 3.25 g, 24.9 mmol) was dissolved in freshly distilled, dry, -10° cold acetanhydride (20 *ml*). A mixture of conc. nitric acid (17 *ml*) and acetanhydride (42 *ml*) at -20° (prepared by the slow and cautious addition of nitric acid to the acetanhydride at -20°; CAUTION: the temperature must not exceed -15° during this addition; efficient cooling is required) was added under vigorous stirring in two portions to this solution. Stirring was continued for 30 min, then the mixture was poured into ice water (350 *ml*), stirred for 30 min and extracted with ethyl acetate (5 x 50 *ml*). The combined organic layers were washed with water, sodium bicarbonate and brine. The solution was concentrated under diminished pressure to ca 100 *ml* and then pumped onto a chromatographic column (silica gel, 5 x 40 cm, preconditioned with ethyl acetate). After standing for 18 h the elution (ethyl acetate) afforded **28** (2.2 g, 68%), mp 67-69°, lit.: 68-70°.[28]

Methyl 2-(4,4-dimethyl-2-oxo-3-trimethylsilyloxy-tetrahydrofuran-3-yl)-2-methyl-propionate (29).- From the reaction of **28** (0.26 g, 2.02 mmol) and **14** (0.7 g, 4.02 mmol) for 1 h at 0° **29** (0.56 g, 91%) was obtained as an oil; R_F 0.52 (hexanes / ethyl acetate 3:1); IR (film): 2995*m*, 2960*s*, 2920*m*, 1790*s*, 1740*s*, 1480*m*, 1455*w*, 1440*w*, 1400*w*, 1390*w*, 1370*m*, 1255*s*, 1190*m*, 1140*s*, 1100*s*, 1035*s*, 885*s*, 850*s*, 760*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.20 (*s*, 9 H, $OSiMe_3$), 1.07, 1.18, 1.31, 1.47, (each *s*, 3 H, Me), 3.67 (*s*, 3 H, OMe), 3.81 and 3.72 (*AB*, *J* = 11.0, 2 H, CH_2-O); ^{13}C-NMR (62.89 MHz, $CDCl_3$): 176.09 (*s*, CO), 175.22 (*s*, CO), 82.77 (*s*, $\underline{C}OSiMe_3$), 76.89 (*t*, OCH_2), 51.88 (*q*, OMe), 48.97 (*q*), 45.08 (*q*), 24.44 (*q*, Me), 23.50 (*q*, Me), 22.74 (*q*, Me), 21.27 (*q*, Me), 1.87 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 15.14; MS (ei, 70 eV, 70°): 302 (19.7), 287 (17.3), 243 (7.1), 201 (12.4), 187 (8.4), 174 (14.8), 159 (5.2), 157 (4.5), 145 (5.0), 129 (6.2), 101 (11.0), 89 (20.7), 75 (24.7), 73 (100.0); Anal. calcd. for $C_{14}H_{26}O_5Si$ (302.45): C, 55.60, H, 8.67; found: C, 55.58; H, 8.67.

Methyl 2-ethyl-2-(4,4-diethyl-2-oxo-3-trimethylsilyloxy-tetrahydrofuran-3-yl)-butyrate (31).- From the reaction of **28** (0.26 g, 2.02 mmol) and **30** (0.81 g, 4.0 mmol) for 2h at 10° **31** (0.47g, 71%) was obtained as an oil; R_F 0.63 (hexanes / ethyl acetate 3:1); IR (film): 2960*s*, 2910*m*, 2890*m*, 1785*s*, 1730*s*, 1475*w*, 1460*w*, 1370*w*, 1300*w*, 1255*s*, 1230*s*, 1135*s*, 1095*s*, 1040*m*, 1030*m*, 925*w*, 905*w*, 870*s*, 840*s*, 755*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.16 (*s*, 9 H, $OSiMe_3$), 0.71 (*t*, *J* = 7.5, Me), 0.96 (*t*, *J* = 7.6, Me), 1.10 (*s*, 6 H, 2 x Me), 2.68 (*dq*, *J* = 1.2, 7.5, 1 H) and 1.73-2.09 (*m*, 3 H) (3 x CH_2), 3.61 (*s*, 3 H, OMe, 3.73 and 3.61 (*AB*, *J* = 8.7, 2 H, CH_2O); ^{13}C-NMR (75 MHz, $CDCl_3$): 174.93 (*s*, CO), 174.41 (*s*, CO), 84.79 (*s*, $\underline{C}OSiMe_3$), 76.

46 (*t*, OCH_2), 55.55 (*s*), 51.47 (*q*, OMe), 45.44 (*q*), 23.26 (*q*, Me), 23.08 (*t*, CH_2), 22.61 (*t*, CH_2), 22.40 (*q*, Me), 9.82 (*q*, Me), 8.44 (*q*, Me), 1.84 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz,): $CDCl_3$ 14.99; MS (ei, 70 eV, 86°): 330 (16.9), 315 (9.6), 271 (5.0), 202 (29.5), 201 (22.5), 187 (17.3); Anal. calcd. for $C_{16}H_{30}O_5Si$ (330.49): C, 58.15; H, 9.15; found: C, 58.23; H, 9.11.

Ethyl 2-(4,4-dimethyl-2-oxo-3-trimethylsilyloxy-tetrahydrofuran-3-yl)-2-methyl-butyrate (32).- From the reaction of **28** (0.26 g, 2.02 mmol) and **19** (0.87 g, 4.02 mmol) for 30 min at 10° **32** (0.61 g, 92%) was obtained as an oil; 1:1 mixture of diastereoisomers; R_F 0.72 (hexanes / ethyl acetate 3:1); IR (film): 2975*s*, 2920*w*, 1780*s*, 1730*s*, 1475*m*, 1460*m*, 1365*w*, 1315*w*, 1250*s*, 1235*s*, 1140*s*, 1100*s*, 1040*s*, 1025*s*, 1000*m*, 890*s*, 840*s*, 760*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.19 and 0.20 (*s*, 9 H, $OSiMe_3$), 0.76 and 0.83 (*t*, *J* = 7.5, 3 H, CH_2-Me) 1.03, 1.09, 1.14, 1.25 (each *s*, 3 H, Me), 1.26 and 1.28 (*t*, *J* = 7.2, 3 H, OCH_2-Me), 1.33 (*s*, 3 H, Me), 1.45-1.52 (*m*, 1 H, CH_2), 1.85-1.92 (*m*, 1 H, CH_2), 2.10-2.17 (*m*, 1 H, CH_2), 2.63-2.70 (*m*, 1 H, CH_2), 3.64-3.89 (*m*, 4 H, OCH_2), 4.05-4.20 (*m*, 4 H, OCH_2Me); ^{13}C-NMR (75 MHz, $CDCl_3$): 175.15 (*s*, CO), 174.75 (*s*, CO), 174.24 (*s*, CO), 174.19 (*s*, CO), 83.91 (*s*, COSiMe$_3$), 83.57 (*s*, COSiMe$_3$), 76.49 (*t*, CH_2 of ester), 76.33 (*t*, CH_2 of ester), 60.69 (*t*, C(5)), 60.49 (*t*, C(5)), 53.66 (*s*, C(4)), 51.72 (*s*, C(4)); 45.58 (*s*, C(2)), 45.45 (*s*, C(2)), 27.91 (*t*, C(3)), 26.82 (*t*, C(3)), 24.11 (*q*, Me), 23.06 (*q*, Me), 22.43 (*q*, 2 x Me), 17.64 (*q*, Me), 15.91 (*q*, Me), 13.92 (*q*, Me), 13.76 (*q*, Me), 8.79 (*q*, Me), 8.27 (*q*, Me), 1.97 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 14.28, 14.89; MS (ei, 80 eV, 70°): 330 (16.5), 315 (9.5), 285 (3.4), 257 (8.8), 202 (25.9), 187 (12.2), 157 (11.3); Anal. calcd. for $C_{16}H_{30}O_5Si$ (330.50): C, 58.15; H, 9.15; found: C, 57.91; H, 9.12.

Methyl 2-(5,5-dimethyl-4-oxo-tetrahydrofuran-2-yl)-2-methylpropionate (38): From the reaction of **37** (0.22g, 1.96 mmol) and **14** (0.7 g, 4.02 mmol) for 2 h at 0° **38** (0.39 g, 92%) was obtained as an oil; R_F 0.45 (hexanes / ethyl acetate 3:1); IR (film): 2980*s*, 2940*m*, 2880*m*, 1760*s*, 1735*s*, 1460*m*, 1435*w*, 1390*w*, 1375*w*, 1360*w*, 1030*w*, 1275*m*, 1250*w*, 1190*m*, 1175*s*, 1155*s*, 1110*s*, 1010*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 1.18, 1.22, 1.23, 1.24 (each *s*, 3 H, Me), 2.47 (*bd*, *J* = 9, 2 H, CH_2); 3.68 (*s*, 3 H, OMe); 4.36 (*t*, *J* = 9, CH-O); ^{13}C-NMR (62 MHz, $CDCl_3$): 217.13 (*s*, CO); 176.19 (*s*, COO), 81.05 (*s*, OCMe$_2$), 77.28 (*d*, OCH), 51.6 (*q*, OMe), 45.26 (*s*, CMe$_2$), 37.30 (*t*, CH2), 24.00 (*q*, Me), 21.90 (*q*, Me), 21.02 (*q*, Me), 20.69 (*q*, Me); MS (ei, 70 eV, 35°): 214 (3.3), 186 (4.3), 155 (10.0), 128 (52.9), 113 (47.4), 96 (12.5); Anal. calcd. for $C_{11}H_{18}O_4$ (214.26): C, 61.66; H, 8.46; found: C, 61.44; H, 8.37.

2,3;5,6-Di-*O*-isopropylidene-1-*O*-trimethylsilyl-α-D-mannofuranose (41).- From the reaction of **40** (0.52 g, 2.0 mmol) and **39** (0.63 g, 4.0 mmol) for 3 h at 25° **41** was obtained as an oil (0.63 g, 93%); $[\alpha]_D^{20}$ 31.9° (*c* 1.4, $CHCl_3$); R_F 0.54 (hexanes / ethyl acetate 3:1); IR (film): 2980*m*, 2940*m*, 2895*w*, 1370*m*, 1255*s*, 1210*m*, 1160*m*, 1120*m*, 1080*s*, 1040*m*, 1025*m*, 875*s*, 850*s*; ^{1}H-NMR (250 MHz, $CDCl_3$): 5.30 (*s*, 1 H, H-C(1)), 4.80 (*dd*, 1 H, *J* = 3.6, 5.8, H-C(3)), 4.54 (*d*, 1 H, *J* = 5.8, H-C(2)), 4.38 (*ddd*, 1 H, *J* = 4.8, 6.1, 7.6, H-C(5)), 3.97-4.12 (*m*, 3 H, H-C(4), $H_{A,B}$-C(6)), 1.46 (*s*, 3 H, Me^i), 1.44 (*s*, 3 H, Me^i), 1.38 (*s*, 3 H, Me^i), 1.31 (*s*, 3 H, Me^i), 0.16 (*s*, 9 H, $OSiMe_3$); ^{13}C-NMR (62 MHz, $CDCl_3$): 112.26 (*s*, C_q^i), 109.01 (*s*, C_q^i), 101.51 (*d*, C(1)), 86.84 (*d*), 80.20 (*d*), 79.62 (*d*), 73.17 (*d*), 66.74 (*t*, C(6)), 26.80 (*q*, Me^i), 25.79 (*q*, Me^i), 25.24 (*q*, Me^i), 24.42 (*q*, Me^i), -0.16 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 19.84; MS (ei, 80eV, 75°): 318 (5.7), 3.17 (28.6), 259 (3.4), 217 (3.3), 201 (6.3), 199 (5.8), 171 (3.9), 156 (8.2), 145 (9.9), 141 (35.1); Anal. calcd. for $C_{15}H_{28}O_6Si$ (332.47): C, 54.19; H, 8.49; found: C, 54.48; H, 8.75.

2,3-*O*-Isopropylidene-1-*C*-(thiazolyl-2-yl)-1-*O*-trimethylsilyl-β-D-erythrofuranose (42).- From the reaction of **13** (0.32 g, 2.02 mmol) and **39** (0.63 g, 4.0 mmol) for 1 h at 0° **42** (0.41 g, 64%) was obtained as an oil; $[\alpha]_D^{20}$ -94.7° (*c* 1.03, $CHCl_3$); R_F 0.36 (hexanes / ethyl acetate 3:1); IR (film): 2960*m*, 2890*w*, 1505*m*, 1460*w*, 1430*w*, 1385*m*, 1375*m*, 1325*w*, 1260*s*, 1210*s*, 1165*s*, 1140*s*, 1090*s*, 1045*s*, 1000*s*, 980*w*, 930*w*, 890*s*, 860*s*, 840*s*, 760*m*, 730*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.09 (*s*, 9 H, $OSiMe_3$), 1.26 (*s*, 3 H, Me), 1.35 (*s*, 3 H, Me), 4.15-4.17 (*m*, 2 H, OCH_2), 4.83 (*d*, *J* = 5.8, 1 H, H-C(2)), 5.01 (*m*, 1 H, H-C(3)), 7.37 (*d*, *J* = 3.2, 1 H, $H_{thiazole}$-C(5), 7.85 (*d*, *J* = 3.2, 1 H, $H_{thiazole}$-C(4)); ^{13}C-NMR (62 MHz, $CDCl_3$): 168.92 (*s*, SC=N), 142.69 (*d*, NC=C), 120.15 (*d*, SC=C), 112.69 (*s*, C_q^i), 107.06 (*s*, C(1)), 88.20 (*d*), 80.61 (*d*), 72.04 (*t*, OCH_2), 26.07 (*q*, Me), 24.80 (*q*, Me), 0.87 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 12.05; MS (ei, 80 eV, 98°): 315 (14.6), 300 (56.3), 257 (15.9), 240 (4.7), 228 (33.2), 202 (97.4), 198 (26.1), 186 (93.3), 143 (6.9), 112 (57.1); Anal. calcd. for $C_{13}H_{21}NO_4SSi$ (315.46): C, 49.50; H, 6.71; N, 4.44; S, 10.16; found: C, 49.74, H, 6.74; N, 4.55; S, 10.28.

2,3:5,6-Di-*O*-isopropylidene-1-*C*-(thiazol-2-yl)-1-*O*-trimethylsilyl-α-D-mannofuranose (43).- From the reaction of **2** (0.52 g, 2.01 mmol) and **39** (0.63 g, 4.0 mmol) for 3 h at 0° **43** (0.84 g, 40%) was obtained as an oil; R_F 0.27 (hexanes / ethyl acetate 3:1); IR (film): 2990*m*, 2960*m*, 2900*w*, 2880*w*, 1500*w*, 1460*w*, 1385*m*, 1375*m*, 1250*s*, 1210*s*, 1170*m*, 1105*m*, 1070*m*, 1045*m*, 980*m*, 900*m*, 850*s*, 760*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): 0.26 (*s*, 9 H, $OSiMe_3$), 1.40 (*s*, 3 H, Me), 1.43 (*s*, 3 H, Me), 1.44 (*s*, 3 H, Me), 1.64 (*s*, 3 H, Me), 3.93 (*dd*, *J* = 4.2, 8.1, H-C(4)), 4.02 and 4.12 (*AB of ABX*, *J* = 4.5, 6.2, 8.7, 2 H, $H_{A,B}$-C(6)), 4.48 (*X of ABX*, *J* = 4.5, 6.2, 8.2, 1 H, H-C(5)), 4.99 (*dd*, 1 H, *J* = 4.2, 6.0, H-C(3)), 5.07 (*d*, *J* = 6.0, H-C(2)), 7.37 (*d*, *J* = 3.2, 1 H, $H_{thiazole}$-C(4′), 7.73 (*d*, *J* = 3.2, 1 H, $H_{thiazole}$-C(5′); ^{13}C-NMR (75 MHz, $CDCl_3$): 172.99 (*s*, SC=N), 142.31 (*d*, NC=N), 119.82 (*d*, SC=C), 112.91 (*s*, C_q^i), 109.23 (*s*, C_q^i), 103.78 (*s*, C(1)), 83.00 (*d*), 79.99 (*d*), 78.27 (*d*), 73.14 (*d*), 66.96 (*t*, C(6)), 26.94 (*q*, Me), 25.69 (*q*, Me), 25.23 (*q*, Me), 24.46 (*q*, Me), 1.84 (*q*, $OSiMe_3$); ^{29}Si-NMR (40 MHz, $CDCl_3$): 18.49; MS (ei, 80 eV, 103°): 415 (11.2), 400 (12.3), 357 (3.3), 298 (5.9), 256 (6.8), 202 (100), 186 (14.4), 166 (16.6), 141 (39.6); Anal. calcd. for $C_{18}H_{29}NO_6SSi$ (415.58): C, 52.02; H, 7.03; N, 3.37; S, 7.71; found: C, 52.18; H, 7.18; N, 3.45; S, 7.84.

Acknowledgment.- Financial support by the European Communities (SC1*-CT92-0780) and the Fonds der Chemischen Industrie is gratefully acknowledged; we are indebted to *Prof. Dr. R. Neidlein*, Pharmazeutisch-Chemisches Institut, Universität Heidelberg, for his encouragement, to *Dr. P. Rosyk* for his help with the manuscript and to Perkin-Elmer for support.

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(*Received in Germany* 12 *November* 1993; *accepted* 13 *January* 1994)