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Stereoselective Synthesis of α-Substituted Ulosonic Acids by Magnesio-Reformatsky Reactions

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Abstract: A new method of homologation of aldonolactones allowing the incorporation of propionate units with excellent chemo- and stereoselectivity is performed by the magnesium-graphite mediated reaction between Oppolzer sultam derived α-halogenated amides and an aldonolactone.

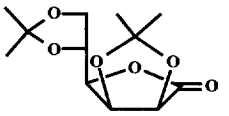
INTRODUCTION

Recognition of the importance of ulosonic acid derivatives for the regulation of a great variety of biological phenomenas has fueled the pronounced interest in these compounds over the last years.[1] Amongst the most essential members of this class of carbohydrate constituents of cellular and bacterial membranes are KDO (3-deoxy-D-manno-2-octulosonic acid),[2] Neu5Ac (5-acetamido-3,5-dideoxy-D-glycero-D-galacto-2-nonulosonic acid)[3] and KDN (3-deoxy-D-glycero-D-galacto-nonulosonic acid).[4] In addition, the 2-(2-hydroxy-tetrahydropyran-2-yl)-propionic acid moiety has been found in various natural products including the fungicidal and cytotoxic macrolide soraphen A, [5] the toxin pederin [6] and ionophore antibiotics. As a part of our studies on the synthetic utility of the highly active metal-graphite surface compounds [7] we reported the application of a Reformatsky reaction to aldonolactones.[8, 9] Only scarcely informations are available, however, for the reactions of α-halo-alkanoates with carbonyl groups,[10] in the presence of metallic magnesium, the so-called „magnesio-Reformatsky reaction".

RESULTS AND DISCUSSION

It seems well established that α-halo-alkanoates afford upon reaction with carbonyls in presence of magnesium only sluggish mixtures of several products among them the products of self condensations and Wurtz-type couplings most dominating. Interestingly enough, *tert.* butyl bromo-acetate (**1**) gave upon reaction with the protected aldonolactone 2,3:5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone (**2**) in the presence of the magnesium/ graphite surface compound [11] the chain elongated product **3** in a smooth reaction in 88% isolated yield.[12-14] Similarly, from **2** and *tert.* butyl 3-bromopropionate (**4**)[15] the non-4-ulosonate **5** was

obtained.[13] Reaction of **2** with racemic *tert.* butyl 2-bromo-propionate (**6**)[16, 17] and magnesium/graphite afforded a 91% yield of a 48:52 mixture of the diastereomers **7** and **8**, that was easily separated by column chromatography.[18]



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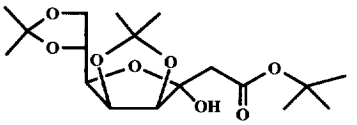

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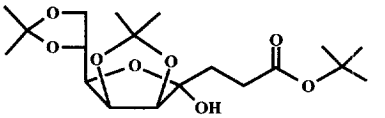

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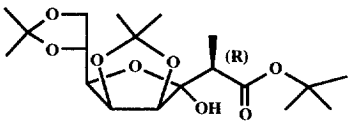

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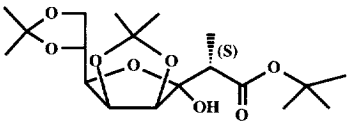

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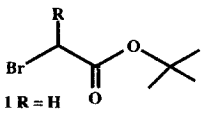
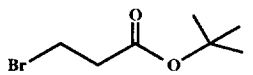


1 R = H
6 R = CH_3



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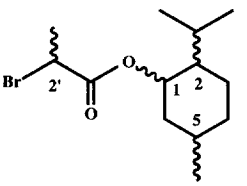
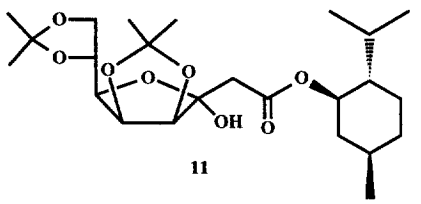


	1	2	5	2'	
(–)-9	R	S	R	R	[(–)-menthyl]
(+)-9	S	R	S	S	[(+)-menthyl]
(–)-10	R	S	R	S	[(–)-menthyl]
(+)-10	S	R	S	R	[(+)-menthyl]

In order to obtain products possessing a methyl substituent at C(2) in a more stereospecific manner, the menthyl esters (–)-**9**, (+)-**9**, (–)-**10** and (+)-**10** were prepared from the enantiomerically pure 2-bromo-propionic acids [19] by their treatment with thionyl chloride leading to the corresponding acyl chlorides that were allowed to react with (+)- or (–)-menthol in the presence of *N,N*-dimethyl-aniline to afford the stereomerically pure menthyl 2-bromo-propionates (–)- and (+)-**9** and (–)- and (+)-**10**, respectively.[20, 21] To facilitate the interpretation of the spectroscopic data of the products, compounds **11**–**14** were prepared.[22]



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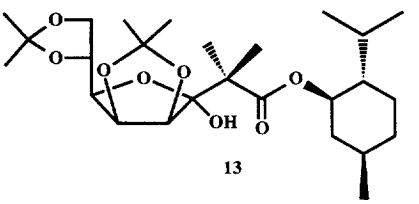

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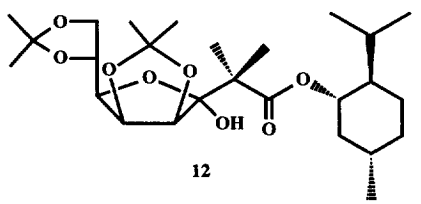

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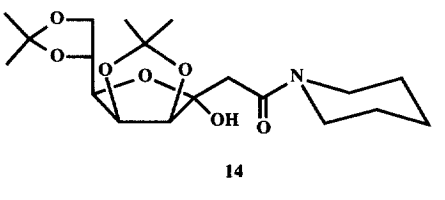

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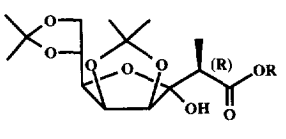
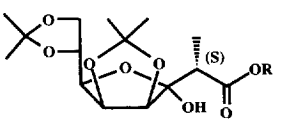
The results from the reactions of **2** with these esters in the presence of Mg-graphite or Zn/Ag-graphite as compiled in Table 1 clearly show that the absolute configuration at C(2) of the acid part of the ester has no influence onto the final product distribution hence suggesting the reaction to proceed *via* an enolate rather than *via* a *C*-metallated species. Worthwhile to mention in this context that for the zinc/silver-graphite mediated reaction of **2** with the ester **6** a predominance in the formation of a (*S*)-configurated product is observed whereas for all reactions of the menthyl esters a predominant formation of the (*R*) configurated products is found.

Table 1: Metal-graphite mediated reactions of **2** with (-)- **9**, (+)-**9**, (−)-**10** and (+)-**10**

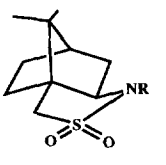
Metal	Ester	Abs. Config. at C(2) of Ester	R	Yield [%]	Diastereomers
Mg	(−)-**15**	*R, S*	(−)-menthyl	67	**16**:**17** = 60:40
Mg	(−)-**15a**	*R*	(−)-menthyl	86	**16**:**17** = 59:41
Mg	(−)-**15b**	*S*	(−)-menthyl	70	**16**:**17** = 57:43
Zn/Ag	(−)-**15**	*R, S*	(−)-menthyl	59	**16**:**17** = 69:31
Zn/Ag	(−)-**15a**	*R*	(−)-menthyl	59	**16**:**17** = 70:30
Zn/Ag	(−)-**15b**	*S*	(−)-menthyl	61	**16**:**17** = 68:32
Mg	(+)-**15**	*R, S*	(+)-menthyl	70	**18**:**19** = 56:44
Mg	(+)-**15a**	*R*	(+)-menthyl	76	**18**:**19** = 53:47
Mg	(+)-**15b**	*S*	(+)-menthyl	77	**18**:**19** = 54:46
Zn/Ag	(+)-**15**	*R, S*	(+)-menthyl	62	**18**:**19** = 90:10
Zn/Ag	(+)-**15a**	*R*	(+)-menthyl	61	**18**:**19** = 90:10
Zn/Ag	(+)-**15b**	*S*	(+)-menthyl	62	**18**:**19** = 89:11



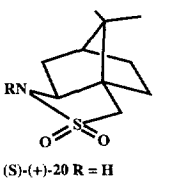
16 R = (−)-(1R, 2S, 5R)-menthyl
18 R = (+)-(1S, 2R, 5S)-menthyl



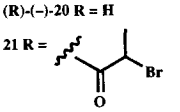
17 R = (−)-(1R, 2S, 5R)-menthyl
19 R = (+)-(1S, 2R, 5S)-menthyl



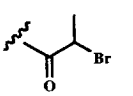
(R)-(−)-**20** R = H



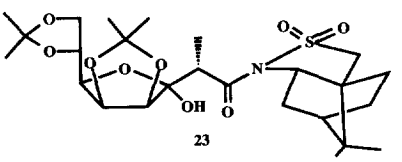
(S)-(+)-**20** R = H



21 R =



22 R =



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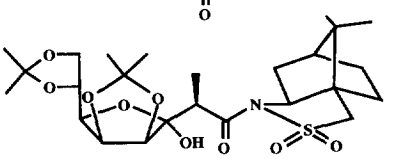

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To find a more suitable auxiliar the enantiomeric Oppolzer sultams (–)-**20** and (+)-**20** were transformed into the corresponding bromo-propionyl derivatives **21** and **22**.[23, 24] Thus, reaction of **2** with **21** in the presence of Mg-graphite afforded **23** in 83% yield as a single stereoisomer whereas for the reaction of **2** with **22** the C(2)-epimer **24** was obtained. To establish the absolute configuration at the two newly created stereogenic centers single crystals of **23** were grown and subjected to a X-ray analysis whose results are depicted in Fig.1 and Tables 3-5. From these data a (2 *S*)-configuration as well as a pseudo-axially orientation of the anomeric hydroxy group can be established.

Fig. 1: X-ray analysis of **23**: MoK_α, ω-2Θ scan, ortho-rhombic, space group $P2_12_12_1$, a = 10.211(2) Å, b = 12.388(3) Å, c = 21.622(4) Å, V = 2725(2) Å^3, Z = 4, R = 0.036 for 1911 observed reflections (I > 3σ(I); 2727 independent reflections measured.[25]

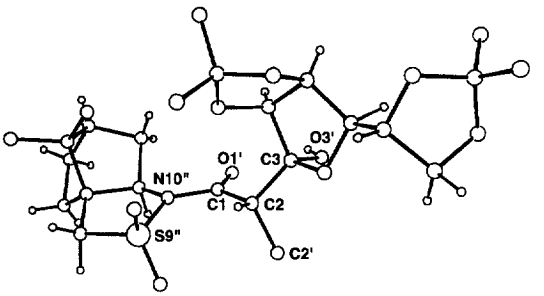

Table 2: Selected bond lengths (Å) of **23**:

C1-C2	1.484(6)	C2-C3	1.525(6)	S9"-N10"	1.682(3)
C1-O1'	1.215(5)	C2-C2'	1.532(6)	C2-H2	0.83(3)
C1-N10"	1.407(5)	C3-O3'	1.411(5)	O3'-HO3'	0.67(3)

Table 3: Selected bond angles (°) of **23**:

C2-C1-O1'	122.3(4)	C1-C2-C2'	110.0(3)	C1-N10"-C2"	120.1(3)
C2-C1-N10"	120.2(3)	C3-C2-C2'	111.9(3)	C1-N10"-S9"	124.1(3)
O1'-C1-N10"	117.5(4)	C2-C3-O3'	112.8(3)	C2"-N10"-S9"	113.7(3)
C1-C2-C3	109.3(3)				

Table 4: Selected torsion angles (°) of **23**:

O1'-C1-C2-C3	44.8(5)	N10"-C1-C2-C2'	100.5(4)	C1-C2-C3-O3'	-68.9(4)
O1'-C1-C2-C2'	-78.4(4)	C2-C1-N10"-S9"	-13.6(5)	C2'-C2-C3-O3'	53.2(4)
N10"-C1-C2-C3	-136.2(3)	O1'-C1-N10"-C2"	3.0(5)		

The formation of **23** as a single stereoisomer can be explained by an attack of the organometallic compound onto the *re*-face of the lactone carbonyl moiety; the *si*-face of the lactone carbonyl group is less

accessible due to the presence of the isopropylidene acetals. Inspection of *Dreiding* models revealed that the transition state from a *si*-face attack of the magnesium enolate from **21** would result most probably in the formation of an unfavourable boat like transition state whereas for the *re*-face attack of the enolate a chair like transition state **A** (Fig. 2) can be formed additionally stabilized by a coordination of the magnesium to one of the oxygens of the sultam moiety. From this chair-like transition state **A** followed by a magnesio [3.3]sigmatropic rearrangement a product possessing a (*S*)-configuration at C(2) is deduced; this is in excellent aggreement with the results from the X-ray analysis. In a similar way (*via* a *re-re* attack and transition state **B**) the formation of a product possessing a (*R*)-configuration at C(2) can be rationalized for the reaction of **22** with **2**.

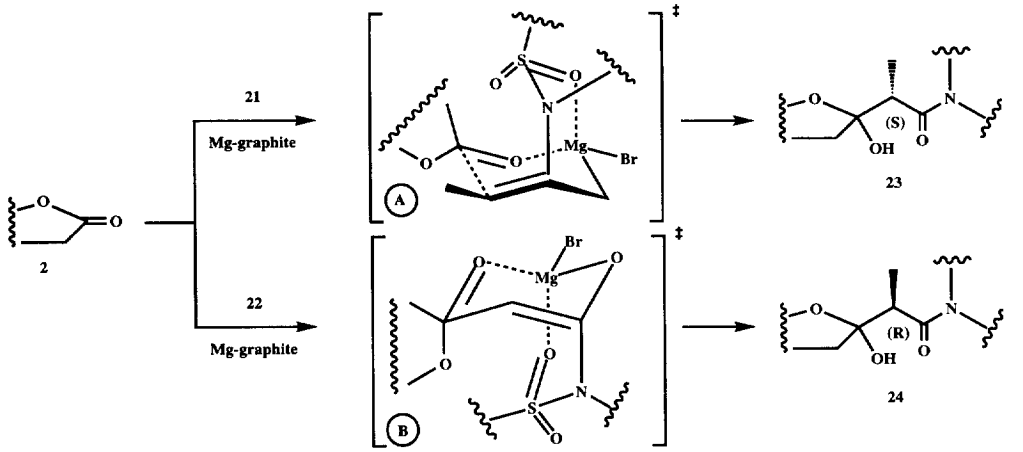

Fig. 2: Transition states for the reaction of **2** with **21** and **22**, respectively

In conclusion, we have described a new method of homologation of aldonolactones allowing the incorporation of propionate units with excellent chemo- and stereoselectivity.

EXPERIMENTAL

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, internal Me_4Si), IR spectra (film or KBr pellet) on a Perkin–Elmer 298 instrument or on a Perkin–Elmer 1605 FT–IR, 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 tetrahydrofuran used throughout for all reactions was freshly distilled from sodium/benzophenone; all reactions were performed under dry argon.

General procedure for the synthesis of magnesium/graphite. From graphite (0.9 g, 75 mmol) and potassium (0.36 g, 9.2 mmol) potassium graphite was prepared [11] and suspended in dry THF (40 *ml*). Dry magnesium chloride (0.44 g, 4.6 mmol) was added in one portion at 25 °C and the mixture was then heated under reflux for an additional 30 min. This suspension was used throughout all reactions.

General procedure for the reaction of 2 with menthyl 2-bromopropionates in the presence of zinc/silver-graphite. To a freshy prepared suspension of Zn/Ag-graphite (4.6 mmol) in THF (40 *ml*) at 0 °C a solution of **2** (0.3 g, 1.16 mmol) and the corresponding menthyl 2-bromopropionate (1.34 g, 4.6 mmol) in dry THF (10 *ml*) was slowly added and stirred at 0°C until the reaction came to completion (as checked by t.l.c). The the mixture was filtered through Celite, the filter cake was rinsed with ethyl acetate (100 *ml*), the combined filtrates were washed with cold aqueous hydrochloric acid (1 N) and brine (10 *ml* each), dried ($MgSO_4$), filtered, the solvent was removed under reduced pressure and the residue subjected to column chromatography (hexane / ethyl acetate 10:1 → 5:1) to afford the products.

General procedure for the reaction of 2 with menthyl 2-bromopropionates in the presence of magnesium/graphite To a suspension of magnesium-graphite (4.6 mmol) in THF (40 *ml*) a solution of **2** (0.3 g, 1.16 mmol) in THF (5 *ml*) was added at 0°C. At this temperature a solution of the corresponding menthyl 2-bromopropionate (1.34 g, 4.6 mmol) in dry THF (10 *ml*) was added within 15 min, the reaction was stirred for another 15 min and worked up as described above.

General procedure for the reaction of aldonolactones with 2-bromo-alkanoyl-sultamamides in the presence of zinc/silver-graphite. To a suspension of zinc/silver-graphite (3.1 mmol) in dry THF (40 *ml*) a solution of the lactone (1.16 mmol) and 2-bromo-alkanoyl-sultamamide (3.10 mmol) in dry THF (10 *ml*) was added and stirring was continued until tlc revealed the completion of the reaction or at least no further progress. The mixture was filtered through a short path of Celite, the filter cake was washed with ethyl acetate (3 x 30 *ml*) and the combined organic phases were washed with cold aqueous hydrochloric acid (1 N) and brine (10 *ml*) each, dried ($MgSO_4$), the solvent was removed under reduced pressure and the remaining residue subjected to chromatography (hexane / ethyl acetate 5:1 → 3:1) to afford the product.

General procedure for the reaction of aldonolactones with 2-bromo-alkanoyl-sultamamides in the presence of magnesium-graphite. To a suspension of magnesium graphite (3. 10 mmol) in THF (40 *ml*) at -5°C a solutio of the lactone (1.16 mml) in THF (5 *ml*) is added followed by the slow addition (15 min) of a solution of the 2-bromo-alkanoyl-sultamamide (3.10 mmol) in THF (10 ml). Stirring is continued for another 15 min and the mixture is worked up accordingly.

tert. **Butyl 2-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-4-ulofuranosonate (3).** To the suspension of magnesium/graphite (4.6 mmol) a solution of **2** (0.3 g, 1.2 mmol) in dry THF (5 *ml*) was added at 0 °C followed by the dropwise addition of a solution of *tert.* butyl-2-bromoacetate **1** (0.90 g, 4. 6 mmol) in dry THF (10 *ml*). After completion of the addition (15 min) the mixture was stirred for another 15 min at 0°C, then filtered through Celite, the filter cake was washed with ethyl acetate (3 x 30 *ml*) and the combined filtrates were washed with cold 1 N aqueous hydrochloric acid and brine (10 *ml* each), dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The residue was subjected to column chromatography [silica gel, hexane/ethyl acetate 5:1 (*v/v*)] to afford **3** (0.4 g, 88%) as a colorless solid; mp 105-107°C (lit.: 107 °C [9]); $[\alpha]_D^{20}$ = +9.9° (*c* = 1.3, $CHCl_3$) (lit.: +10.6° (*c* = 1.0 CHCl3)[9]), R_F 0.32 (hexane/ethyl acetate 3:1); IR (KBr): ν = 3440*s*, 2989*m*, 2943*w*, 1718*s*, 1381*m*, 1371*s*, 1257*m*, 1212*s*, 1162*s*, 1066*s*, 863*w*, 852*w*; ^{1}H NMR (300 MHz, $CDCl_3$): δ =1.08, 1.14, 1.20 (each *s*, 3 H, CH_3 (isopropyl)), 1.24 (*s*, 12 H, CH_3 (isopropyl) and CH_3 (*tert.* butyl)), 2.40, 2.49 and 2.54 (AB-system, *J* = 16.3, 2 H, $H_{A,B}$-C(2)), 3.76 (*dd*, *J* = 4.7, 8.7, 1 H, H_A-C(8)), 3.82 (*dd*, *J* = 6.1, 8.7, 1 H, H_BC(8)), 3.86 (*dd*, *J* = 3.7, 7.8, 1 H, H-C(6)), 4.13 (*ddd*, *J* = 4.7, 6.1, 7.8, 1 H, H-C(7)), 4.25 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.60 (*dd*, *J* = 3.7, 5.9, 1 H, H-C(5)), 4.86 (*s*, 1 H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.44, 25.39, 25.87, 26.85 (each *q*, CH_3 (isopropyl)), 28.02 (*q*, CH_3 (*tert.* butyl)), 39.18 (*t*, C(2)), 66.78 (*t*, C(8)), 73.02, 79.18, 80.08, 85.65 (each *d*, C(4,5,6,7)), 82.05 (*s*, C_q (*tert.* butyl)), 103.90 (*s*, C(3)), 109.00, 112.64 (each *s*, C_q (isopropyl)), 171.23 (*s*, C(1)); MS (ei, 80 eV, 59 °C): 359(29.9), 303(15.0), 301(16.0), 260(9.3), 243(11.6), 217(19.3), 201(9.3), 185(8.6), 141(24.8), 126(16.1), 101(88.8), 98(34.6); Anal. calcd. for $C_{18}H_{30}O_8$ (374.43): C, 57.62, H, 8.06; found: C, 57.71, H, 7.89.

***tert.* Butyl 2,3-dideoxy-5,6:8,9-di-*O*-isopropylidene-α-D-manno-non-4-ulofuranosonate (5).** To the suspenion of magnesium/graphite (4.6 mmol) a solution of **2** (0.3 g, 1.2 mml) in dry THF (5 *ml*) was added at 0 °C followed by the dropwise addition of a solution of *tert.* butyl-3-bromopropionate **4** (0.96 g, 4. 6 mmol) in dry THF (10 *ml*). After completion of the addition (15 min) the mixture was stirred for another 15 min at 0°C, then filtered through Celite, the filter cake was washed with ethyl acetate (3 x 30 *ml*) and the combined filtrates were washed with cold 1 N aqueous hydrochloric acid and brine (10 *ml* each), dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The residue was subjected to column chromatography [silica gel, hexane/ethyl acetate 5:1 (*v/v*)] to afford besides some unreacted **2** (0.13 g, 43%) **5** (0.10 g, 15%) as a colorless oil; $[\alpha]_D^{20}$ = +5.2° (*c* = 1.0, $CHCl_3$), R_F 0.40 (hexane/ethyl acetate 3:1); IR (film): ν = 3420*m*, 2983*s*, 2938*s*, 1733*s*, 1456*m*, 1373*s*, 1307*m*, 1256*m*, 1151*m*, 1114*s*, 1064*s*, 973*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32, 1.38, 1.44 (each *s*, 3 H, CH_3 (isopropyl)), 1.45 (*s*, 12 H, CH_3 (isopropyl) and CH_3 (*tert.*-butyl)), 1.92-2.17, 2.39-2.62 (each *m*, 2 H, H_A- and H_B-C(2,3), 4.00 (*d*, *J* = 8.6, 4.8, 1 H, H_A-C(9)), 4.04-4.10 (*m*, 2 H, H_B-C(9) and H-C(8)), 4.32-4.39 (*m*, 2 H, H-C(7) and OH), 4.45 (*d*, *J* = 5.9, 1 H, H-C(5)), 4.84 (*dd*, *J* = 5.9, 3.9, 1 H, H-C(6)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.48, 25.32, 25.89, 26.86 (each *q*, CH_3 (isopropyl)), 28.02 (q, CH_3(*tert. butyl*)), 29.24, 30.26 (each *t*, C(2,3)), 66.74 (*t*, C(9)), 73.19, 78.59, 80.25, 84.90 (each *d*, C(5,6,7,8)), 105.57 (*s*, C_q(*tert. butyl*)), 108.90, 112.43 (each *s*, C_q(isopropyl)), 174.54 (*s*, C(1)); MS (ei, 80 eV, 126 °C): 388(0.02), 373(15.0, 315(8.1), 259(8.3), 231(11.5), 199(9.8), 173(10.9), 156(7.6), 144(25.1), 141(19.1), 126(14.6), 101(100.0), 98(34.8), 85(16.0), 73(23.1), 59(61.4), 57(95.7), 42(88.5); Anal. calcd. for $C_{19}H_{32}O_8$ (388.46): C, 58.75; H, 8.30; found: C, 58.70; H, 8.38.

***tert.* Butyl (2 *R*)-2-deoxy-4,5:7,8-di-*O*-isopropylidene-2-methyl-α-D-manno-oct-4-ulofuranosonate (7) and *tert.* butyl (2 *S*)-2-deoxy-4,5:7,8-di-*O*-isopropylidene-2-methyl-α-D-manno-oct-4-ulofuranosonate (8).** As described for **3** from **2** (0.3 g, 1.2 mmol), **6** (0.96 g, 4.6 mmol) and magnesium graphite (4.6 mmol) **7** (0.2 g, 44%) and **8** (0.21 g, 46.5%) were obtained after chromatographic work up (hexane/ethyl acetate 10:1 → 5:1).

Data for **7**: colorless solid, mp 81-83 °C (lit. 82-84 °C [9]); $[\alpha]_D^{20}$ = +2.3° (*c* = 1.0, $CHCl_3$), (lit +2.9 (*c* = 1.0, $CHCl_3$ [9]), R_F 0.47 (hexane/ethyl acetate 3:1); IR (KBr): ν = 3485*bm*, 2981*m*, 2935*m*, 2874*w*, 1701*s*, 1460*w*, 1381*s*, 1371*s*, 1348*w*, 1329*w*, 1257*m*, 1220*s*, 1157*s*, 1115*m*, 1083*s*, 1070*s*, 1040*m*, 987*m*, 899*w*, 867*w*, 849*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (*d*, *J* = 7.2, 3 H, H-C(2')), 1.31, 1.37, 1.42, 1.47 (each *s*, 3 H, CH_3 (isopropyl)), 1.46 (*s*, 9 H, CH_3 (*tert.* butyl)), 2.78 (*q*, *J* = 7.2, 1 H, H-C(2)), 3.96 (*dd*, *J* = 4.7, 8.6, 1 H, H_A-C(8)), 4.04 (*dd*, *J* = 6.2, 8.6, 1 H, H_B-C(8)), 4.09 (*dd*, *J* = 3.8, 7.7, 1 H, H-C(6)), 4.36-4.39 (*m*, 1 H, H-C(7)), 4.45 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.82 (*dd*, *J* = 3.8, 5.9, 1 H, H-C(4)), 4.89 (*s*, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.65 (*q*, C(2')), 24.37, 25.43, 25.84, 26.84 (each *q*, CH_3 (isopropyl)), 27.94 (*q*, CH_3 (*tert.* butyl)), 42.77 (*d*, C(2)), 66.66 (*t*, C(8)), 73.06, 79.02, 79.90, 84.14 (each *d*, C(4,5,6,7)), 81.59 (*s*, C_q(*tert.* butyl)), 106.39 (*s*, C(3)), 108.92, 112.44 (each *s*, C_q (isopropyl)), 175.59 (*s*, C(1)); MS (ei, 80 eV, 65 °C): 388(0.05), 373(29.1), 317(19.5), 315(18.8), 274(17.5), 259(13.9), 239(5.6), 231(11.4), 215(12.3), 199(10.2), 181(6.0), 173(8.5), 156(15.4), 141(37.8), 126(24.5), 101(100.0); Anal. calcd. for $C_{19}H_{32}O_8$ (388.46): C, 58.75, H, 8.13; found: C, 57.38; H, 8.43.

Data for **8**: colorless solid, mp 76-78 °C (lit. 75-77 °C [9]); $[\alpha]_D^{20}$ = +4.5° (*c* = 1.1, $CHCl_3$) (lit. +4.5 (*c* = 0.8, $CHCl_3$ [9]), R_F 0.67 (hexane/ethyl acetate 3:1); IR (KBr): ν = 3400*s*, 2992*s*, 2943*s*, 2906*w*, 2874*m*, 2694*s*, 1484*m*, 1461*s*, 1428*m*, 1377*s*, 1354*s*, 1333*m*, 1319*w*, 1297*w*, 1277*s*, 1253*s*, 1216*s*, 1153*s*, 1111*s*, 1067*s*, 1041*s*, 1004*m*, 984*s*, 970*m*, 962*w*, 890*s*, 861*s*, 841*s*; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.26 (*d*, *J* = 7.4, 3 H, H-C(2')), 1.29, 1.36, 1.42, 1.44 (each *s*, 3 H, CH_3 (isopropyl)), 1.46 (*s*, 9 H, CH_3 (*tert.*-butyl)), 2.88 (*q*, *J* = 7.4, 1 H, H-C(2)), 3.87 (*s*, 1 H, OH), 4.02-4.07 (*m*, 2 H, H-C(8)), 4.11 (*dd*, *J* = 3.8, 7.8, 1 H, H-C(6)), 4.30-4.36 (*m*, *J* = 7.8, 1 H, H-C(7)), 4.55 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.84 (*dd*, *J* = 3.8, 5.9, 1 H, H-C(5)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.30 (*q*, C(2')), 24.49, 25.41, 25.87, 26.83 (each *q*, CH_3 (isopropyl)), 27.92 (*q*, CH_3(*tert.*-

butyl)), 43.41 (*d*, C(2)), 66.72 (*t*, C(8)), 73.10, 79.56, 79.88, 86.64 (each *d*, C(4,5,6,7)), 81.26 (*s*, C_q(*tert.*-butyl)), 104.96 (*s*, C(3)), 108.96, 112.44 (each *s*, C_q(isopropyl), 175.11 (*s*, C(1)); MS (ei, 80 eV, 60 °C): 373(29.9), 317(8.2), 315(13.6), 274(9.0), 259(11.2), 231(20.1), 200(8.6), 144(11.6), 141(23.9), 126(18.4), 101(82.9), 98(35.5), 71(20.1), 59(78.6), 57(100.0); Anal. calcd. for $C_{19}H_{32}O_8$ (388.46): C, 58.75, H, 8.30, found: C, 58.73, H, 7.95.

[(1 *R*, 2 *S*, 5 *R*) 2-(Methylethyl)-5-methyl-cyclohex-1-yl] (2 *R*)-bromo–propionate [(–)-9] / [(1 *S*, 2 *R*, 5 *S*) 2-(methylethyl)-5-methyl-cyclohex-1-yl] (2 *S*)-bromopropionate [(+)-9] and [(1 *R*, 2 *S*, 5 *R*) 2-(methylethyl)-5-methyl-cyclohex-1-yl] (2 *S*)-2-bromopropionate [(–)-10] / [(1 *S*, 2 *R*, 5 *S*) 2-(methylethyl)-5-methyl-cyclohex-1-yl] (2 *R*)-2-bromopropionate [(+)-10]. (2 *R*) or (2 *S*) 2-bromopropionic acid (10 g, 65.4 mmol) was heated under reflux with thionyl chloride (7.15 *ml*, 11.7 g, 98 mmol) for 6 h and the reaction mixture was subjected to a distillation to afford (2 *R*) or (2 *S*) 2-bromopropionyl chloride (bp 28-30°C, 13 torr, 8.9 g, 80%) that was immedeately used. A solution of (–)- or (+)-menthol (4.0 g, 25.6 mmol) in dry dichloromethane (20 *ml*) containing dimethyl-aniline (3.2 *ml*, 3.1 g, 25.6 mmol) was cooled to 0°C and a solution of the 2-bromopropionyl chloride (4.0 g, 23 mmol) was slowly added at this temperature. After the addition was completed the mixture was allowed to warm to 25°C and stirred for another 60 min. Then the mixture was poured under vigorous stirring in cold aqueous hydrochloric acid (10%, 20 *ml*), the phases were separated, the aqueous layer was washed with dichloromethane (3 x 20 *ml*) and the combined organic phases were washed with an aqueous saturated solution of $NaHCO_3$ (2 x 10 *ml*) and brine (10 *ml*), dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure to afford an oily residue that was subjected to column chromatography to yield **(–)-9** (5.36 g, 79%), **(+)-9** (5.92 g, 89%), **(–)-10** (5.47 g, 81%) and **(+)-10** (6.1 g, 89%), respectively.

Data for **(–)-9**: $[\alpha]_D^{20}$ = –45.9° (*c* = 3.0, $CHCl_3$); for **(+)-9** $[\alpha]_D^{20}$ = +45.7° (*c* = 2.7, $CHCl_3$); R_F 0.69 (hexane/ethyl acetate 10:1); IR (film): ν = 2956*s*, 2870*m*, 1736*s*, 1448*m*, 1369*m*, 1335*m*, 1271*m*, 1225*s*, 1165*s*, 1150*m*, 1053*m*, 990*m*, 958*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (*d*, *J* = 6.9, 3 H), 0.90 (*d*, *J* = 7.0, 3 H), 0.92 (*d*, J = 6.5, 3H) (H_3-C(2_M´´A, 2_M´´B, 5_M´), 0.80-1-14 (*m*, 3 H), 1.39-1.54 (*m*, 2 H), 1.66-1.74 (*m*, 2 H), 1.86-1.95 (*m*, 1 H), 1.98-2.08 (*m*, 1 H) (H-C(2_M, 2_M´, 5_M), H_2-C(3_M, 4_M, 6_M)), 1.82 (*d*, *J* = 6.9, 3 H, H3-C(3)), 4.34 (*q*, *J* = 6.9, 1 H, H-C(2)), 4.72 (*dt*, *J* = 10.9, 4.4, 1 H, H-C(1_M)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.22, 20.69, 21.67, 21.96 (each *q*, C(2_M´´A, 2_M´´B, 5_M´), 23.37 (*t*, C(3_M or 4_M)), 26.17, 31.31 (each *d*, C(2_M´, 5_M)), 34.14 (*t*, C(3_M or 4_M)), 40.08 (*t*, C(6_M)), 40.71 (*d*, C(2)), 46.84 (*d*, C(2_M)), 75.83 (*d*, C(1_M)), 169.48 (*s*, C(1)); MS (ei, 80 eV, 50 °C): 291(0.02), 275(0.05), 277(0.05), 211(1.8), 155(1.0), 153(0.7), 138(100.0), 123(35.2), 95(83.8), 83(67.6), 81(65.0), 69(29.2), 55(32.1), 43(14.3); Anal. calcd. for $C_{12}H_{23}BrO_2$ (291.23): C, 53.62; H, 7.96; found: C, 53.67; H, 7.96.

Data for **(–)-10** $[\alpha]_D^{20}$ = –72.0° (*c* = 1.7, $CHCl_3$); data for **(+)-10**: $[\alpha]_D^{20}$ = +71.2° (*c* = 1.6, $CHCl_3$), R_F 0.69 (hexane/ethyl acetate 10:1); IR (film): ν = 2956*s*, 2870*m*, 1735*s*, 1449*m*, 1370*m*, 1337*m*, 1268*m*, 1225*s*, 1165*s*, 1150*m*, 1099*m*, 1053*m*, 990*m*, 958*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (*d*, *J* = 6.9, 3 H), 0.91 (*d*, *J* = 7.1, 3H), 0.92 (*d*, J = 6.5, 3 H) (H_3-C(2_M´´A, 2_M´´B, 5_M´), 0.82-1-13 (*m*, 3 H), 1.40-1.53 (*m*, 2 H), 1.66-1.74 (*m*, 2 H), 1.95-2.04 (*m*, 2 H) (H-C(2_M, 2_M´, 5_M), H_2-C(3_M, 4_M, 6_M)), 1.81 (*d*, *J* = 6.9, 3 H, H_3-C(3)), 4.34 (*q*, *J* = 6.9, 1 H, H-C(2)), 4.71 (*dt*, *J* = 11.0, 4.4, 1 H, H-C(1_M)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.07, 20.72, 21.57, 21.95 (each *q*, C(2_M´´A, 2_M´´B, 5_M´), 23.25 (*t*, C(3_M or 4_M)), 25.97, 31.34 (each *d*, C(2_M´, 5_M)), 34.13 (*t*, C(3_M or 4_M)), 40.43 (*t*, C(6_M)), 40.52 (*d*, C(2)), 47.02 (*d*, C(2_M)), 75.86 (*d*, C(1_M)), 169.54 (*s*, C(1)); MS (ei, 80 eV, 50 °C): 291(0.02), 275(0.05), 277(0.05), 211(1.8), 207(0.3), 205(0.3), 155(0.9), 138(100.0), 123(40.4), 95(90.9), 83(67.6), 81(69.8), 69(21.6), 57(27.5), 55(32.7), 43(15.8); Anal. calcd. for $C_{12}H_{23}BrO_2$ (291.23): C, 53.62; H, 7.96; found: C, 53.79; H, 7.99.

[(1 *R*, 2 *S*, 5 *R*) 2-(Methylethyl)-5-methyl-cyclohex-1-yl] 2-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofuranosonate (11). According to the procedure given for the preparation of **5** from

magnesium graphite (4.6 mmol), **2** (0.5 g, 1.9 mmol) and (–)-menthyl 2-bromo-acetate [22] (1.28 g, 4.6 mmol) **11** (0.52 g, 59%) was obtained after chromatography (hexane/ethyl acetate 5:1) as a colorless oil. $[\alpha]_D^{20}$ = –35.2° (*c* = 0.9, $CHCl_3$), R_F 0.55 (hexane/ethyl acetate 5:1); IR (film): ν = 3446*m*, 2956*s*, 2872*m*, 1713*s*, 1455*m*, 1372*s*, 1338*m*, 1323*m*, 2111*s*, 1113*m*, 1043*s*, 1010*m*, 985*m*, 895*m*, 847*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 (*d*, *J* = 6.9, 3 H), 0.90 (*d*, *J* = 7.0, 3 H), 0.92 (*d*, *J* = 6.4, 3 H) (H_3-C(2_M´´A, 2_M´´B, 5_M´)), 1.33, 1.37, 1.43, 1.48 (each *s*, 3 H, CH_3 (isopropyl)), 0.80-1.13 (*m*, 3 H), 1.22-1.54 (*m*, 2 H), 1.63 (*m*, 2 H), 1.81-1.88 (*m*, 1 H), 1.94-1.99 (*m*, 1 H) (H-C(2_M, 2_M´, 5_M, H_2-C(3_M, 4_M, 6_M)), 2.69 (*d*, *J* = 16.1, 1 H, H_A-C(2)), 2.80 (*d*, *J* = 16.1, 1 H, H_B-C(2)), 3.96 (*dd*, *J* = 8.6, 4.6, 1 H, H_A-C(8)), 4.04 (*dd*, *J* = 8.6, 6.1, 1 H, H_B-C(8)), 4.06 (*dd*, *J* = 8.2, 3.7, 1 H, H-C(6)), 4.35 (*ddd*, *J* = 8.2, 6.1, 4.6, 1 H, H-C(7)), 4.51 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.80 (*dt*, *J* = 10.8, 4.4, 1 H, H-C(1_M)), 4.85 (*dd*, *J* = 5.9, 3.7, 1 H, H-C(5)), 5.01 (*bs*, 1 H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.47, 20.56, 21.93 (each *q*, C(2_M´´A, 2_M´´B, 5_M´)), 23.63 (*t*, C(3_M or 4_M)), 24.70, 25.33, 25.85, 26.36 (each *q*, CH_3 (isopropyl)), 26.88 (*d*, C(2_M´)), 31.55 (*d*, C(5_M)), 34.11 (*t*, C(3_M or 4_M)), 38.65 (*t*, C(2)), 40.72 (*t*, C(6_M)), 46.83 (*d*, C(2_M)), 66.83 (*t*, C(6)), 72.91, 74.96, 79.30, 80.13, 85.60 (each *d*, C(1_M, 4,5,6,7)), 103.85 (*s*, C(3)), 109.06, 112.69 (each *s*, C_q(isopropyl)), 171.44 (*s*, C(1)); MS (ei, 80 eV, 96 °C): 456(0.1), 441(44.1), 423(5.2), 383(4.1), 355(2.4), 301(11.9), 283(28.5), 245(16.0), 225(22.0), 217(22.5), 201(10.3), 185(12.1), 167(14.9), 139(56.1), 101(100.0), 83(81.5), 69(42.2), 59(49.3), 43(65.1); Anal. calcd. for $C_{24}H_{40}O_8$ (456.58): C, 63.14; H, 8.83; found: C, 63.27; H 8.93.

[(1 *S*, 2 *R*, 5 *S*)-2-(Methylethyl)-5-methyl-cyclohex-1-yl] 2-deoxy-2,2-dimethyl-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofuranosonate (12). According to the general procedure **2** (0.3 g, 1.19 mmol) and (+)-menthyl 2-bromo-2-methyl-propionate (1.42 g, 4.6 mmol) were allowed to react in the presence of zinc/silver-graphite for 30 min at 0 °C. Workup afforded **12** (0.45 g, 80%) that contained 30% of the corresponding β-anomer (^{1}H NMR). This material was recrystallized from ethyl acetate/hexane and after standing at -25°C for 48 h **12** was isolated as colorless crystals, mp 101–103°C, $[\alpha]_D^{20}$ = +54.9° (*c* = 1.0, $CHCl_3$), R_F 0.54 (hexane/ethyl acetate 3:1); IR (KBr): ν = 3472*m*, 2985*s*, 2955*s*, 2872*m*, 1705*s*, 1456*m*, 1371*s*, 1270*s*, 1242*s*, 1210*s*, 1164*s*, 1120*m*, 1048*s*, 848*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75 (*d*, *J* = 6.9, 3 H), 0.90 (*d*, *J* = 7.1, 3 H), 0.91 (*d*, *J* = 6.4, 3H) (H_3-C(2_M´´A, 2_M´´B, 5_M´), 1.28, 1.38, 1.40, 1.42, 1.43, 1.46 (each *s*, 3 H, H_3-C(2´A, 2´B, CH_3 (isopropyl)), 0.85-1.08 (*m*, 3 H), 1.32-1.49 (*m*, 2 H), 1.67-1.72 (*m*, 2 H), 1.88-1.98 (*m*, 2 H) (H-C(2_M, 2_M´, 5_M), H_2-C(3_M, 4_M, 6_M)), 4.02 (*dd*, *J* = 8.5, 5.3, 1 H, H_A-C(8)), 4.04 (*m*, 1 H, H-C(7)), 4.07 (*dd*, *J* = 8.5, 6.1, 1 H, H_B-C(8)), 4.15 (*dd*, *J* = 7.1, 4.2, 1 H, H-C(6)), 4.61 (*d*, *J* = 6.1, 1 H, H-C(4)), 4.71 (*dt*, *J* = 11.0, 4.4, 1 H, H-C(1_M)), 4.83 (*dd*, *J* = 6.1, 4.2, 1 H, H-C(5)), 5.05 (*s*, 1 H, OH); ^{13}C NMR (65.4 MHz, $CDCl_3$): δ = 16.20, 20.83, 21.56, 21.86, 22.04 (each *q*, C(2´A, 2´B), H_3-C(2_M´´A, 2_M´´B, 5_M´)), 23.37 (*t*, C(3_M or 4_M)), 23.84, 23.36, 25.60, 26.85 (each *q*, CH_3 (isopropyl)), 26.19, 31.42 (each *d*, C(2_M, 5_M)), 34.26 (*t*, C(3_M or 4_M)), 40.55 (*t*, C(6_M)), 46.99 (*d*, C(2_M)), 48.47 (*s*, C(2)), 66.71 (*t*, C(8)), 73.47, 75.08, 78.70, 79.73, 86.76 (each *d*, C(4,5,6,7,1_M)), 106.28 (*s*, C(3)), 108.90, 112.58 (each *s*, C_q(isopropyl)), 177.74 (*s*, C(1)); MS (ei, 80 eV, 99 °C): 469(17.4), 411(2.3), 383(1.4), 351(1.6, 331(3.6), 325(2.7), 273(7.6), 721(5.6), 245(19.2), 227(4.5), 213(5.6, 187(6.9), 183(3.6), 139(44.1), 101(100.0), 83(80.8), 69(47.6), 59(51.7), 55(45.1), 42(73.8); Anal. calcd. for $C_{26}H_{44}O_8$ (484.63): C, 64.44; H, 9.15; found: C, 64.23; H, 9.03.

2-Deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofuranosono-piperidide (14). Following the general procedure from **2** (0.30 g, 1.16 mmol) and bromo-acetyl-piperidide (2-bromo-1-piperidino-1-ethanone, 0.96 g, 4.65 mmol) in the presence of magnesium-graphite (4.65 mmol) **14** (0.31 g, 71%) was obtained as colorless crystals; mp 99-101 °C; $[\alpha]_D^{20}$ = +12.6° (*c* = 1.4, $CHCl_3$), R_F 0.58 (hexane/ethyl acetate 1:1); IR (Film): ν = 3295*m*, 2986*s*, 2937*s*, 2860*m*, 1621*s*, 1446*s*, 1371*s*, 1211*s*, 1162s, 1114*m*, 1062s, 849*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33, 1.37, 1.43, 1.47 (each *s*, 3 H, CH_3 (isopropyl), 1.53-1.68 (*m*, 6 H, H_2-C(3_{Pip}, 4_{Pip}, 5_{Pip})), 2.69 (*d*, *J* = 15.8, 1 H, H_A-C(2)), 2.83 (*m*, *J* = 15.8, 1 H H_B-C(2)), 3.24, 3.57 (each *m*, 2 H, H_2-C(2_{Pip}, 6_{Pip})), 4.02 (*dd*, *J* = 8.6, 5.0, 1 H, H_A-C(8)), 4.06 (*dd*, *J* = 8.6, 5.8, 1 H, H_B-C(8)), 4.11 (*dd*, *J* = 8.1, 5.8, 1 H, H-C(6)), 4.35 (*ddd*, *J* = 8.1, 5.8, 5.0, 1 H H-C(7)), 4.53 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.86 (*dd*, *J* =

5.9, 3.8, 1 H, H-C(5)), 6.50 (*s*, 1 H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.40, 25.32, 26.26 (each *t*, $C(3_{Pip}, 4_{Pip}, 5_{Pip})$), 24.47, 25.32, 26.00, 26.88 (each *q*, CH_3 (isopropyl)), 35.20 (*t*, C(2)), 42.70, 46.84 (each *t*, $C(2_{Pip}, 6_{Pip})$), 66.98 (*t*, C(6)), 73.06, 79.20, 80.09, 86.00 (each *d*, C(4,5,6,7)), 104.42 (*s*, C(3)), 109.00, 112.39 (each *s*, C_q(isopropyl)), 169.29 (*s*, C(1)); MS (ei, 80 eV, 75 °C): 385(4.5), 370(14.9), 352(4.2), 327(4.5), 292(10.6), 284(20.2), 255(9.5), 226(14.3), 210(10.2), 197(16.1), 172(66.0), 154(21.5), 141(20.3), 127(42.7), 112(65.9), 84(57.2), 69(42.9), 59(27.4), 43(100.0); Anal. calcd. for $C_{19}H_{31}NO_7$ (385.46): C, 59.20; H, 8.11; N, 3.63; found: C, 59.21; H, 8.31; N, 3.37.

[(1 *R*, 2 *S*, 5 *R*)-2-(methylethyl)-5-methyl-cyclohex-1-yl] (2 *R*)-2-deoxy-2-methyl-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofuranosonate (16) and **[(1 *R*, 2 *S*, 5 *R*)-2-(methylethyl)-5-methyl-cyclohex-1-yl]-(2 *S*)-2-deoxy-2-methyl-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofurano–sonate (17).** According to the general procedure from **2** with a 1:1 mixture of **(–)-9** and **(–)-10** in the presence of zinc/silver-graphite **16** (0.22 g, 41%) and **17** (0.1 g, 18%) were obtained. Similiarly, from **2** and **(–)-9** in the presence of zinc/silver-graphite **16** (0.23 g, 41%) and **17** (0.1 g, 18%) were obtained. The reaction of **2** with **(–)-10** and zinc/silver-graphite gave **16** (0.23 g, 42%) and **17** (0.11 g, 20%). Accordingly from the magnesium-graphite mediated reaction of **2** with a 1:1 mixture of **(–)-9** and **(–)-10 16** (0.22 g, 40%) and **17** (0.15 g, 27%) were obtained whereas the reaction of **2** with **(–)-9** yielded **16** (0.28 g, 50%) and **17** (0.19 g, 36%) and the reaction of **2** with **(–)-10** in the presence of magnesium-graphite gave **16** (0.22 g, 40%) and **17** (0.17 g, 30%), respectively.

Data for **16**: colorless crystals, mp 119-121 °C, $[\alpha]_D^{20}$ = –30.8° (*c* = 1.6, $CHCl_3$), R_F 0.75 (hexane/ethyl acetate 3:1); IR (KBr): ν = 3454*m*, 2988*m*, 2960*m*, 1705*s*, 1457*w*, 1376*m*, 1194*s*, 1066*s*, 1043*m*, 986*w*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 (*d*, *J* = 7.0, 3 H), 0.89 (*d*, *J* = 6.9, 3 H), 0.91 (*d*, *J* = 6.5, 3 H) (H_3-C(2_M´´A, 2_M´´B, 5_M´)), 1.28 (*d*, *J* = 7.2, 3 H, H_3-C(2´)), 1.33, 1.37, 1.43, 1.48 (each *s*, 3 H, CH_3 (isopropyl)), 0.82-1.10 (*m*, 3 H), 1.26-1.54 (*m*, 2 H), 1.65-1.72 (*m*, 2 H), 1.82-1.94 (*m*, 2 H) (H-C(2_M, 2_M´, 5_M), H_2-C(3_M, 4_M, 6_M)), 2.87 (*q*, *J* = 7.2, 1 H, H-C(2)), 3.91 (*dd*, *J* = 8.6, 4.5, 1 H, H_A-C(8)), 4.01 (*dd*, J = 8.6, 6.1, 1 H, H_B-C(8)), 4.04 (*dd*, *J* = 8.5, 3.8, 1 H, H-C(6)), 4.33 (*ddd*, *J* = 8.5, 6.1, 4.5, 1 H, H-C(7)), 4.47 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.76 (*dt*, *J* = 10.8,4.4, 1 H, H-C(1_M)), 4.82 (s, 1 H, OH), 4.84 (*dd*, *J* = 5.9, 3.8, 1 H, H-C(5)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.70 (*q*, C(2´)), 16.67, 20.46, 21.96 (each *q*, C(2_M´´A, 2_M´´B, 5_M´)), 23.87 (*t*, C(3_M or 4_M)), 24.54, 25.36, 25.94, 26.50 (each *q*, CH_3 (isopropyl)), 26.95 (*d*, C(2_M´)), 31.33 (*d*, C(5_M)), 34.15 (*t*, C(3_M or 4_M)), 40.62 (*t*, C(6_M)), 42.38 (*d*, C(2)), 46.81 (*d*, C(2_M)), 66.92 (*t*, C(8)), 72.94, 74.52, 79.27, 80.04, 84.19 (each *d*, C(1_M, 4,5,6,7)), 106.32 (*s*, C(3)), 109.10, 112.54 (each *s*, C_q(isopropyl)), 175.76 (*s*, C(1)); MS (ei, 80 eV, 107 °C): 470(0.1), 455(31.6), 412(1.0), 397(4.1), 369(2.2), 317(3.6), 282(5.7), 259(9.7), 231(21.0), 215(6.6), 156(12.1), 145(15.5), 141(26.3), 139(47.9), 101(100.0), 98(38.6), 83(79.4), 69(36.6), 59(49.2), 55(43.5), 42(67.7); Anal. calcd. for $C_{25}H_{42}O_8$ (470.60): C, 63.81; H, 9.00; found: C, 63.72; H, 9.09.

Data for **17**: colorless crystals, mp 86-88 °C, $[\alpha]_D^{20}$ = –22.6° (*c* = 1.3, $CHCl_3$), R_F 0.54 (hexane/ethyl acetate 3:1); IR (Film): ν = 3468*m*, 2980*m*, 1699*s*, 1457*m*, 1384*m*, 1373*s*, 1265*m*, 1203*s*, 1176*m*, 1071*s*, 1043*m*, 997*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (*d*, *J* = 7.0, 3 H), 0.91 (*d*, *J* = 7.0, 3 H), 0.92 (*d*, *J* = 6.6, 3H) (H_3-C(2_M´´A, 2_M´´B, 5_M´)), 1.31 (*d*, *J* = 7.4, 3 H, H_3-C(2´)), 1.29, 1.38, 1.43, 1.44 (each *s*, 3 H, CH_3 (isopropyl)), 0.85-1.08 (*m*, 3 H), 1.40-1.50 (*m*, 2 H), 1.66-1.77 (*m*, 2 H), 1.87-2.02 (*m*, 2 H) (H-C(2_M, 2_M´, 5_M), H_2-C(3_M, 4_M, 6_M)), 2.96 (*q*, *J* = 7.4, 1 H, H-C(2)), 3.77 (s, 1 H, OH), 4.04 (*dd*, *J* = 8.7, 5.1, 1 H, H_A-C(8)), 4.08 (*dd*, J = 8.7, 5.8, 1 H, H_B-C(8)), 4.14 (*dd*, *J* = 7.8, 3.7, 1 H, H-C(6)), 4.35 (*ddd*, *J* = 7.8, 5.8, 5.1, 1 H, H-C(7)), 4.58 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.71 (*dt*, *J* = 10.9, 4.4, 1 H, H-C(1_M)), 4.85 (*dd*, *J* = 5.9, 3.7, 1 H, H-C(5)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.30 (*q*, C(2´)), 15.99, 20.78, 21.97 (each *q*, C(2_M´´A, 2_M´´B, 5_M´)), 23.21 (*t*, C(3_M or 4_M)), 24.51, 25.41, 25.89, 26.84 (each *q*, CH_3 (isopropyl)), 26.04 (*d*, C(2_M´)), 31.34 (*d*, C(5_M)), 34.18 (*t*, C(3_M or 4_M)), 40.52 (*t*, C(6_M)), 43.18 (*d*, C(2)), 46.90 (*d*, C(2_M)), 66.73 (*t*, C(8)), 73.09, 74.76, 79.68, 79.95, 86.78 (each *d*, C(1_M, 4,5,6,7)), 105.05 (*s*, C(3)), 108.00, 112.53 (each *s*, C_q(isopropyl)),

175.41 (*s*, C(1)); MS (ei, 80 eV, 109 °C): 470(0.05), 455(15.8), 397(1.7), 317(4.8), 315(4.2), 259(8.1), 231(10.0), 215(7.5), 141(24.3), 139(31.6), 126(16.4), 101(100.0), 98(34.7), 83(61.0), 69(27.9), 59(33.8), 55(32.2), 42(48.3); Anal. calcd. for $C_{25}H_{42}O_8$ (470.60): C, 63.81; H, 9.00; found: C, 63.59; H, 8.91.

[(1 *S*, 2 *R*, 5 *S*)-2-(Methylethyl-5-methyl-cyclo-hex-1-yl] (2 *R*)-2-deoxy-2-methyl-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulo-furanosonate (18) and [(1 *S*, 2 *R*, 5 *S*)-2-(methylethyl)-5-methyl-cyclohex-1-yl] (2 *S*)-2-deoxy-2-methyl-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofurano–sonate (19). From the reaction of **2** with a 1:1 mixture of **(+)-9** and **(+)-10** in the presence of zinc/silver-graphite **18** (0.3 g, 55%) and **19** (0.03 g, 6%) were obtained. The reaction of **2** with **(+)-9** and zinc/silver-graphite gave **18** (0.3 g, 55%) and **19** (0.03 g, 6%) whereas for the reaction of **2** with **(+)-10** in the presence of zinc/silver-graphite **18** (0.31 g, 56%) and **19** (0.04 g, 7%) were obtained. The magnesium-graphite mediated reaction of **2** with a 1:1 mixture of **(+)-9** and **(+)-10** gave **18** (0.21 g, 39%) and **19** (0.17 g, 31%). Accordingly from **2** and **(+)-9** and magnesium-graphite **18** (0.22 g, 40%) and **19** (0.2 g, 37%) were obtained whereas the reaction of **2** with **(+)-10** in the presence of magnesium-graphite gave **18** (0.22 g, 41%) and **19** (0.19 g, 35%), respectively.

Data for **18**: colorless crystals, mp 61-62 °C; $[\alpha]_D^{20}$ = +33.0° (*c* = 1.3, $CHCl_3$), R_F 0.75 (hexane/ethyl acetate 3:1); IR (film): ν = 3453*m*, 2956*s*, 2827*m*, 1703*s*, 1455*m*, 1372*s*, 1338*m*, 1194*s*, 1069*s*, 985*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (*d*, *J* = 7.0, 3 H), 0.91 (*d*, *J* = 6.8, 6 H) (H_3-C(2_M´´A, 2_M´´B, 5_M´)), 1.29 (*d*, *J* = 7.2, 3 H, H_3-C(2´)), 1.32, 1.37, 1.42, 1.48 (each *s*, 3 H, CH_3 (isopropyl)), 0.80-1.08 (*m*, 3 H), 1.24-1.51 (*m*, 2 H), 1.65-1.74 (*m*, 2 H), 1.86-2.05 (*m*, 2 H) (H-C(2_M, 2_M´, 5_M), H_2-C(3_M, 4_M, 6_M)), 2.89 (*q*, *J* = 7.2, 1 H, H-C(2)), 3.94 (*dd*, *J* = 8.6, 5.1, 1 H, H_A-C(8)), 4.03 (*dd*, J = 8.6, 6.2, 1 H, H_B-C(8)), 4.10 (*dd*, *J* = 7.6, 3.8, 1 H, H-C(6)), 4.35 (*ddd*, *J* = 7.6, 6.2, 5.1, 1 H, H-C(7)), 4.70 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.71 (*dt*, *J* = 10.9, 4.4, 1 H, H-C(1_M)), 4.79 (s, 1 H, OH), 4.83 (*dd*, *J* = 5.9, 3.8, 1 H, H-C(5)); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.78 (*q*, C(2´)), 16.18, 20.72, 22.00 (each *q*, C(2_M´´A, 2_M´´B, 5_M´)), 23.42 (*t*, C(3_M or 4_M)), 24.43, 25.52, 25.91, 26.91 (each *q*, CH_3 (isopropyl)), 26.28 (*d*, C(2_M´)), 31.39 (*d*, C(5_M)), 34.23 (*t*, C(3_M or 4_M)), 40.75 (*t*, C(6_M)), 42.81 (*d*, C(2)), 46.85 (*d*, C(2_M)), 66.82 (*t*, C(8)), 73.20, 75.02, 79.34, 80.10, 84.29 (each *d*, C(1_M, 4,5,6,7)), 106.58 (*s*, C(3)), 109.11, 112.70 (each *s*, C_q(isopropyl)), 176.17 (*s*, C(1)); MS (ei, 80 eV, 100 °C): 470(0.3), 455(34.3), 397(4.9), 315(4.4), 282(6.1), 259(9.9), 231(22.2), 139(50.0), 101(100.0), 83(84.1), 69(40.2), 59(42.4), 55(43.3), 42(64.8); Anal. calcd. for $C_{25}H_{42}O_8$ (470.60): C, 63.81; H, 9.00; found: C, 63.98; H, 8.97.

Data for **19**: colorless crystals, mp 128-130 °C, $[\alpha]_D^{20}$ = +42.3° (*c* = 1.1, $CHCl_3$), R_F 0.54 (hexane/ethyl acetate 3:1); IR (KBr): ν = 3481*m*, 2985*m*, 2948m, 2873w, 1700*s*, 1457*m*, 1381*s*, 1269*m*, 1202*s*, 1162*m*, 1076*s*, 1039*m*, 854*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (*d*, *J* = 6.9, 3 H), 0.90 (*d*, *J* = 7.1, 3H), 0.92 (*d*, *J* = 7.8, 3H) (H_3-C(2_M´´A, 2_M´´B, 5_M´)), 1.31 (*d*, *J* = 7.5, 3 H, H_3-C(2´)), 1.28, 1.38, 1.43, 1.44 (each *s*, 3 H, CH_3 (isopropyl)), 0.81-1.14 (*m*, 3 H), 1.23-1.52 (*m*, 2 H), 1.66-1.72 (*m*, 2 H), 1.92-2.05 (*m*, 2 H) (H-C(2_M, 2_M´, 5_M), H_2-C(3_M, 4_M, 6_M)), 2.96 (*q*, *J* = 7.5, 1 H, H-C(2)), 3.97 (s, 1 H, OH), 4.05 (*dd*, *J* = 8.6, 5.2, 1 H, H_A-C(8)), 4.09 (*dd*, J = 8.6, 5.9, 1 H, H_B-C(8)), 4.15 (*dd*, *J* = 7.8, 3.7, 1 H, H-C(6)), 4.35 (*ddd*, *J* = 7.8, 5.9, 5.2, 1 H, H-C(7)), 4.54 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.73 (*dt*, *J* = 10.9, 4.4, 1 H, H-C(1_M)), 4.86 (*dd*, *J* = 5.9, 3.7, 1 H, H-C(5)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.32 (*q*, C(2´)), 16.49, 20.51, 21.97 (each *q*, C(2_M´´A, 2_M´´B, 5_M´)), 23.58 (*t*, C(3_M or 4_M)), 24.35, 25.42, 25.82, 26.84 (each *q*, CH_3 (isopropyl)), 26.01 (*d*, C(2_M´)), 31.37 (*d*, C(5_M)), 34.19 (*t*, C(3_M or 4_M)), 40.47 (*t*, C(6_M)), 42.74 (*d*, C(2)), 46.92 (*d*, C(2_M)), 66.75 (*t*, C(8)), 73.05, 74.60, 79.88, 79.92, 86.73 (each *d*, C(1_M, 4,5,6,7)), 104.88 (*s*, C(3)), 109.01, 112.50 (each *s*, C_q(isopropyl)), 175.86 (*s*, C(1)); MS (ei, 80 eV, 115 °C): 479(0.01), 455(16.9), 412(1.1), 397(2.7), 317(3.6), 315(3.6), 259(7.3), 239(6.9), 231(7.6), 215(6.4), 199(5.4), 173(6.2), 156(10.8), 141(25.6), 139(32.9), 126(16.4), 101(100.0), 83(58.1), 69(31.9), 59(33.1), 55(35.3), 42(52.0); Anal. calcd. for $C_{25}H_{42}O_8$ (470.60): C, 63.81; H, 9.00; found: C, 63.71; H, 8.93.

***N*-[(5 *R*)-10,10-Dimethyl-3,3-dioxo-3λ^6-thia-4-aza-tricyclo[5.2.1.01,5]dec-4-yl]-(2 *RS*)-2-bromo-propionamide (21)** and ***N*-[(5 *S*)-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-aza-tricyclo[5.2.1.01,5]dec-4-yl]-(2 *RS*)-2-bromo-propionamide (22).** A mixture of (±)-2-bromo-propionic acid (5.0 *ml*, 8.5 g, 55.5 mmol) and oxalylic chloride (7.3 *ml*, 10.6 g, 83.3 mmol) was heated under reflux until the evolution of gases had ceased (approx. 6 h) and the mixture was subjected to a distillation (bp 28-30 °C, 13 torr) to afford (±)-2-bromopropionic chloride (7.43 g, 78%). To a suspension of sodium hydride (0.53 g, 14.7 mmol as its 80% dispersion in mineral oil, used as received) in abs. toluene (30 *ml*) a solution of **(–)-20** (2.10 g, 9.8 mmol) in toluene (60 ml) was slowly added. After stirring for 1 h at 25 °C a solution of the (±)-2-bromopropionic chloride (2.0 *ml*, 3.35 g, 19.5 mmol) in toluene (30 *ml*) was added and the stirring was continued for another 3 h. After completion of the reaction cold water (30 *ml*) was carefully added (temperature must not exceed 5 °C), the layers were separated and the aqueous layer was extracted with toluene (2 x 50 *ml*); the combined organic phases were washed with brine (2 x 30 *ml*), dried ($MgSO_4$) and the solvents were removed under reduced pressure. The residue was subjected to column chromatography (hexane / ethyl acetate 3:1) to afford **21** (3.20 g, 94%) as in inseparable mixture of the corresponding C(2)-epimers. Similiarly, from the reaction with **(+)-20** the product **22** (2.70 g, 79%) was obtained as an inseparable mixture of the two C(2)-epimers.

Data for **21** and **22**: amorphous solids, R_F 0.48 (hexane/ethyl acetate 3:1); IR (KBr): ν = 2952*m*, 1696*s*, 1378*m*, 1330*s*, 1283*m*, 1242*m*, 1138*m*, 1057*m*; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.99 (*s*, 3 H), 1.13 (*s*, 1.5 H), 1.20 (*s*, 1.5 H) (H_3-C(8_C, 9_C)), 1.82 (*d*, *J* = 6.6, 1.5 H), 1.87 (*d*, *J* = 6.8, 1.5 H) (H_3-C(3)), 1.36-1.44 (*m*, 2 H), 1.84-1.95 (*m*, 3 H), 2.06-2.12 (*m*, 2 H) (H-C(4_C), H_2-C(3_C, 5_C, 6_C)), 3.46 (*d*, *J* = 13.7, 1 H, H_A-C(10_C)), 3.54 (*d*, *J* = 13.7, 1 H, H_B-C(10_C)), 3.93 (*dd*, *J* = 6.8, 5.8, 1 H, H-C(2_C)), 4.98 (*q*, *J* = 6.6, 0.5 H), 5.04 (*q*, *J* = 6.8, 0.5 H) (H-C(2)); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.88, 20.46, 20.66, 20.79, 22.69, 23.00 (each *q*, C(3, 8_C, 9_C)), 26.35, 26.48, 32.75, 32.82, 37.58, 38.14 (each *t*, C(3_C, 5_C, 6_C)), 39.45, 41.08, 44.52, 44.57 (each *d*, C(2, 4_C)), 47.85, 48.79 (each *s*, C(1_C, 7)), 52.78, 52.98 (*t*, C(10_C)), 64.95, 65.58 (*d*, C(2_C)), 168.36, 168.75 (*s*, C(1)); MS (ei, 80 eV, 93 °C): 351(3.3), 349(3.4), 270(5.2), 242(3.9), 206(52.3), 134(100.0), 108(35.6), 93(34.6), 79(24.8), 67(26.7), 56(37.9), 55(38.7), 42(24.7); Anal. calcd. for $C_{13}H_{20}BrNO_3S$ (350.27): C, 44.58; H, 5.74; N, 4.00; S, 9.15; found: C, 44.61; H, 5.83; N, 3.89; S, 8.92.

***N*-[(5 *R*)-10,10-Dimethyl-3,3-dioxo-3λ^6-thia-4-aza-tricyclo[5.2.1.0^{1,5}]dec-4-yl] (2 *S*)-2-deoxy-2-methyl-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofuranosonamide (23).** Following the general procedure from **2** (0.3 g, 1.16 mmol) and **21** (1.09 g, 3.1 mmol) in the presence of magnesium-graphite **23** (0.27 g, 43%) was obtained as colorless crystals; mp 179-180 °C; $[\alpha]_D^{20}$ = –33.6° (*c* = 1.0, $CHCl_3$); R_F 0.56(hexane/ethyl acetate 3:1); IR (KBr): ν = 3453*m*, 2978*m*, 2942*m*, 1663*s*, 1457*m*, 1394m, 1383*s*, 1373*m*, 1337*m*, 1268*s*, 1241*s*, 1222s, 1169*m*, 1142*s*, 1121*m*, 1086*s*, 1070*s*, 974*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96, 1.19 (each *s*, 3 H, H_3-C(8_C, 9_C)), 1.21, 1.35, 1.41, 1.42 (each *s*, 3 H, CH_3 (isopropyl)), 1.39 (*d*, *J* = 7.1, 3 H, H_3-C(2′)), 1.30-1.56 (*m*, 2 H), 1.84-1.94 (*m*, 3 H), 2.00-2.04 (*m*, 1 H), 2.10-2.15 (*m*, 1 H) (H-C(4_C), H2-(3_C, 5_C, 6_C), 3.41 (*d*, *J* = 13.7, 1 H, H_A-C(10_C)), 3.48 (*d*, *J* = 13.7, 1 H, H_B-C(10_C)), 3.52 (*q*, *J* = 7.1, 1 H, H-C(2)), 3.86 (*dd*, *J* = 7.3, 5.1, 1 H, H-C(2_C)), 4.01-4.07 (*m*, 2 H, H_A-C(8), H_B-C(8)), 4.10 (*dd*, *J* = 8.1, 3.7, 1 H, H-C(6)), 4.14 (*bs*, 1 H, OH), 4.32 (*m*, 1 H, H-C(7)), 4.39 (*d*, *J* = 6.1, 1 H, H-C(4)), 4.82 (*dd*, *J* = 6.1, 3.7, 1 H, H-C(5)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.31 (*q*, C(2′)), 19.95, 20.57 (each *q*, C(8_C, 9_C)), 24.66, 25.40, 25.80, 26.87 (each *q*, CH_3 (isopropyl)), 26.40, 32.87, 38.31 (each *t*, C(3_C, 5_C, 6_C)), 42.71, 44.57 (each *d*, C(2, 4_C)), 44.69, 48.44 (each *s*, C(1_C, 7_C)), 52.95 (*t*, C(10_C)), 65.00 (*d*, C(2_C)), 66.83 (*t*, C(8)), 72.94, 79.91, 80.18, 86.69 (each *d*, C(4, 5, 6, 7)), 105.72 (*s*, C(3)), 109.05, 113.16 (each *s*, C_q(isopropyl)), 175.51 (*s*, C(1)); MS (ei, 80 eV, 145 °C): 529(0.1), 514(21.1), 471(5.1), 456(8.3), 371(6.5), 370(5.6), 316(18.9), 298(28.2), 271(11.6), 243(22.7), 216(32.4), 141(34.9), 135(43.6), 134(21.5), 126(18.7), 101(100.0), 98(28.7), 93(22.5), 81(25.5), 68(25.0), 59(42.0), 57(64.1), 43(100.0); Anal. calcd. for $C_{25}H_{39}NO_9S$ (529.64): C, 56.69; H, 7.42; N, 2.64; S, 6.05; found: C, 56.50; H, 7.42; N, 2.55; S, 5.75.

***N*-[(5 *S*)-10,10-Dimethyl-3,3-dioxo-3λ^6-thia-4-aza-tricyclo[5.2.1.01,5]dec-4-yl] (2 *R*)-2-deoxy-2-methyl-4,5:7,8-di-*O*-isopropylidene-α-D-manno-oct-3-ulofuranosonamide (24).** Following the general procedure from **2** (0.3 g, 1.16 mmol) and **22** (1.09 g, 3.1 mmol) in the presence of magnesium-graphite **24** (0.45 g, 72%) was obtained as colorless crystals; mp 154-155 °C, $[\alpha]_D^{20}$ = +29.7° (*c* = 1.3, $CHCl_3$); R_F 0.20 (hexane/ethyl acetate 3:1); IR (KBr): ν = 3452*m*, 2984*s*, 1667*s*, 1456*m*, 1372*s*, 1337*s*, 1269*s*, 1239*s*, 1166*s*, 1137*s*, 1068*s*, 1045*s*, 991*m*, 973*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97, 1.17 (each *s*, 3 H, H_3-C(8_C, 9_C)), 1.29 (*d*, *J* = 6.9, 3 H, H_3-C(2′)), 1.32, 1.35, 1.42, 1.51 (each *s*, 3 H, CH_3 (isopropyl)), 1.29-1.40 (*m*, 2 H), 1.85-1.93 (*m*, 3 H), 2.04-2.08 (*m*, 2 H) (H-C(4_C), H2-(3_C, 5_C, 6_C), 3.42 (*d*, *J* = 13.7, 1 H, H_A-C(10_C)), 3.51 (*d*, *J* = 13.7, 1 H, H_B-C(10_C)), 3.73 (*q*, *J* = 6.9, 1 H, H-C(2)), 3.87 (*m*, 1 H, H-C(2_C)), 3.89 (*dd*, *J* = 8.5, 4.3, 1 H, H_A-C(8)), 3.95 (dd, J = 8.5, 6.1, 1 H, H_B-C(8)), 4.02 (*dd*, *J* = 8.2, 3.6, 1 H, H-C(6)), 4.34 (*ddd*, *J* = 8.2, 6.1, 4.3, 1 H, H-C(7)), 4.49 (*d*, *J* = 5.9, 1 H, H-C(4)), 4.57 (*s*, 1 H, OH), 4.84 (*dd*, *J* = 5.9, 3.6, 1 H, H-C(5)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.12 (*q*, C(2′)), 19.83, 20.83 (each *q*, C(8_C, 9_C)), 24.96, 25.17, 25.87, 27.04 (each *q*, CH_3 (isopropyl)), 26.28, 32.81, 38.26 (each *t*, C(3_C, 5_C, 6_C)), 41.66, 44.78 (each *d*, C(2, 4_C)), 47.67, 48.32 (each *s*, C(1_C, 7_C)), 52.97 (*t*, C(10_C)), 64.83 (*d*, C(2_C)), 66.77 (*t*, C(8)), 72.92, 79.26, 80.13, 84.31 (each *d*, C(4, 5, 6, 7)), 107.84 (*s*, C(3)), 109.01, 113.17 (each *s*, C_q(isopropyl)), 175.62 (*s*, C(1)); MS (ei, 80 eV, 145 °C): 514(17.3), 472(2.4), 456(7.2), 428(5.4), 370(3.4), 316(16.5), 298(18.1), 271(5.9), 216(25.7), 141(24.4), 135(31.9), 126(13.7), 107(13.7), 101(56.6), 98(24.2), 93(20.3), 81(20.6), 59(32.2), 43(100.0); HRMS calcd. for $C_{25}H_{39}NO_9S$ (529.64): 529.2343; found: 529.2340.

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Dedicated to Professor Dr. Peter Welzel, Leipzig, on the occassion of his 60th birthday. Ad multos annos!

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12 Addition of **1** to freshly prepared magnesium/graphite followed by the addition of **2** only resulted in the formation of di-*tert.* butyl succinate in almost quantitative yield; **2** was recovered unchanged.

13 No useful reaction was obtained, however, with the corresponding ethyl ester. No product formation at all was observed for the reaction of **2** with **4** in the presence of zinc/silver-graphite.

14 Contrary to previously reported reactions of organolithium compounds with aldonolactones, no bis-addition reactions took place even in the presence of a 4 fold molar excess of the organomagnesium compound; *cf* Glänzer, B. I.; Csuk, R. *Carbohydr. Res.* **1991**, *220*, 79-92.

15 Prepared according to Ohta, S.; Shimabayashi, A., Makino, N.; Okamoto, *Yakugaku Zasshi* **1983**, *103*, 991-993. Thus, from 3-bromo-propionic acid (20.0 g), *tert.* butanol (130 *ml*), *tert.* butyl acetate (130 *ml*) and conc. sulfuric acid (13.2 *ml*), **4** (10.3 g, 38%) was obtained after distillation (63-65°C/1 torr), n_D^{20} = 1.4456, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (*s*, 9H, 3 x CH_3); 2.80 (*t*, *J* = 7 Hz, H_2-C(2)); 3.53 (*t*, *J* = 7 Hz, 2H, H_2-C(3)).

16 For the corresponding Sm-mediated reaction (*cf* 9) a ratio of 6:1 has been reported.

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18 The corresponding reaction using zinc/silver-graphite gave 84% of **7** and **8** in a 43:57 ratio.

19 Commercially obtained from Sigma Ltd. and used as received.

20 Reaction of (*R*)- or (*S*)-2-bromopropionyl chloride with (+)- or (–)-menthol in the presence of triethylamine, however, afforded mixtures of diastereomeric esters.

21 Previously known as a mixture of diastereomers: Yang, T.-K.; Teng, T.-F.; Lee, D.-S. *J. Chin. Chem. Soc.* **1991**, *38*, 375-378; Jin, C.; Xiong, L.; Chen, Z.; Yu, L. *Beijing Shifan Daxue Xuebao, Ziran Kexueban* **1993**, *29*, 224-227 (*Chem. Abs.* **1994**, *121*, 231284); Su, G.; Yu, L. *Guanxi Shifan Daxue Xuebao, Ziran Kexueban* **1993**, *11*, 54-57 (*Chem. Abs.* **1994**, *121*, 107954); Su, G.; Yu, L. *Huaxue Shiji* **1993**, *15*, 242-243 (*Chem. Abs.* **1994**, *120*, 134826); Raikova, T. S.; Andreeva, E. I.; Valimae, T.; Rozhkova, N. G.; Vakhrameeva, A. A.; Izotova, L. V. *Ves. Akad. Navuk BSSR, Ser. Chim. Navuk* **1988**, 74-78 (*Chem. Abs.* **1989**, *111*, 7619).

22 Palmer, M. H.; Reid J. A. *J. Chem. Soc.* **1960**, 931-938.

23 For a very recent use of Oppolzer sultam derived reagents in a zinc mediated *Dreiding-Schmidt* reaction for the stereoselective formation of α-methylene-γ-butyrolactones, *cf* Csuk, R.; C. Schröder, C.; Hutter, S.; Mohr, K.*Tetrahedron: Asymmetry*, **1997**, *8*, 1411-1429.

24 Compounds **21** and **22** were each obtained as an inseparable 1:1 mixture of the corresponding C(2')-epimers.

25 The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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