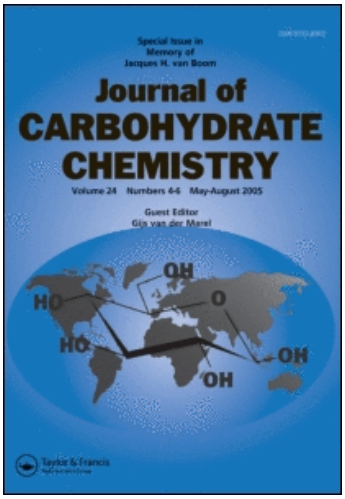

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A Convenient Synthesis of 3-Deoxy-D-*gluco*-2-octulosonate (D-*gluco*-KDO)

Dominique Lafont[ab]; Monika Hoch[a]; Richard R. Schmidt[a]
[a] Fakultät Chemie, Universität Konstanz, Konstanz, Germany [b] Laboratoire de Chimie Organique 2, Université Claude-Bernard Lyon 1, Villeurbanne Cedex, France

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A CONVENIENT SYNTHESIS OF 3-DEOXY-D-GLUCO-2-OCTULOSONATE (D-GLUCO-KDO)[1]

Dominique Lafont,[2] Monika Hoch, and Richard R. Schmidt*
Fakultät Chemie, Universität Konstanz
Postfach 5560, D-7750 Konstanz, Germany

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ABSTRACT

ß-Lithiated acrylates have proven to be versatile pyruvate ß-carbanion equivalents which are also useful in D-manno-KDO synthesis. The secondary amine adducts of acetylenedicarboxylate 4 display the same versatility, as demonstrated in this paper. However, on reaction with 2,3:4,5-di-O-isopropylidene-D-arabinose 6, the diastereofacial selectivity is in favor of the gluco-isomer, thus leading with lithiated compounds 4A, preferentially to α-amino-butenolides 7-(g). The best results were obtained with the morpholine adduct of di-tert.-butyl acetylenedicarboxylate 4d which afforded the gluco-isomer 7d-(g) as an easily separable crystalline material. Its deamination and concomitant deisopropylidenation with trifluoroacetic acid provided the known α-hydroxy-butenolide 8b-(g), which was transformed via decarboxylation product 9-(g) to D-gluco-KDO 10-(g) thus concluding a convenient four step synthesis of this compound via crystalline intermediates.

INTRODUCTION

3-Deoxy-D-manno-2-octulosonate (D-manno-KDO) is an integral part of the lipopolysaccharide of Gram-negative bacteria.[3] Several in vitro-syntheses of this compound have been described, us-

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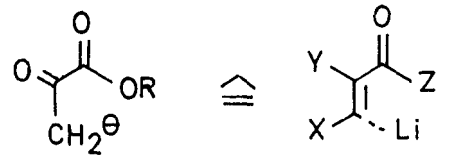
ing either D-mannose or D-arabinose derivatives and C_2- or C_3-units, respectively, as starting materials.[3-8] Biosynthetic studies have shown D-arabinose-5-phosphate and phosphoenol pyruvate as the precursors.[3] Therefore, in analogy to the biosynthesis we sought pyruvate equivalent C_3-synthons corresponding to intermediate 1A (Scheme 1), to react diastereoselectively with O-protected D-arabinose derivatives. We found that ß-lithiated functionally substituted acrylates provide such synthetic equivalents quite readily.[9] For instance, the dilithiated species 2A and 3A, obtained via direct lithiation of the corresponding hydrogen systems, provided, via manno-selective reactions with di-O-isopropylidene-D-arabinose, a straightforward entry into D-manno-KDO.[4,10,11] In species 3A the phenylthio group is a H-atom equivalent which supports ß-lithiation, reactivity, and diastereoselectivity of the carbonyl addition reaction.



1A ≙ 2A–4A

2A: X = H, Y = Ot-Bu, Z = NMeLi

3A: X = SPh, Y = OBzl, Z = NMELi

4A: X = COOR, Y = NR_2, Z = OR

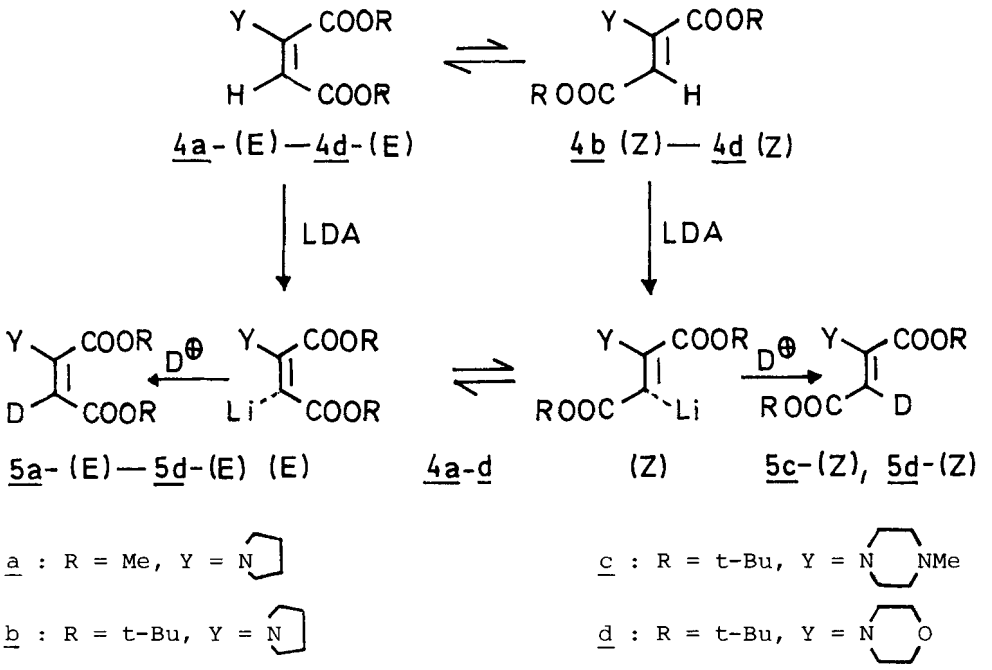
Scheme 1

Recently we observed that lithiated systems of type 4A can be readily generated via direct lithiation of the adducts formed from secondary amines and acetylenedicarboxylate.[12,13] Reaction with electrophiles affords products with a carboxylate group, easily replaced by hydrogen, next to the C-lithiated position. Therefore it seemed reasonable to apply these species in a similar fashion to syntheses of KDO derivatives.

RESULTS AND DISCUSSION

Pyrrolidine addition to dimethyl acetylenedicarboxylate gave, as described earlier, exclusively the (E)-adduct 4a-(E).[12,14] Li-

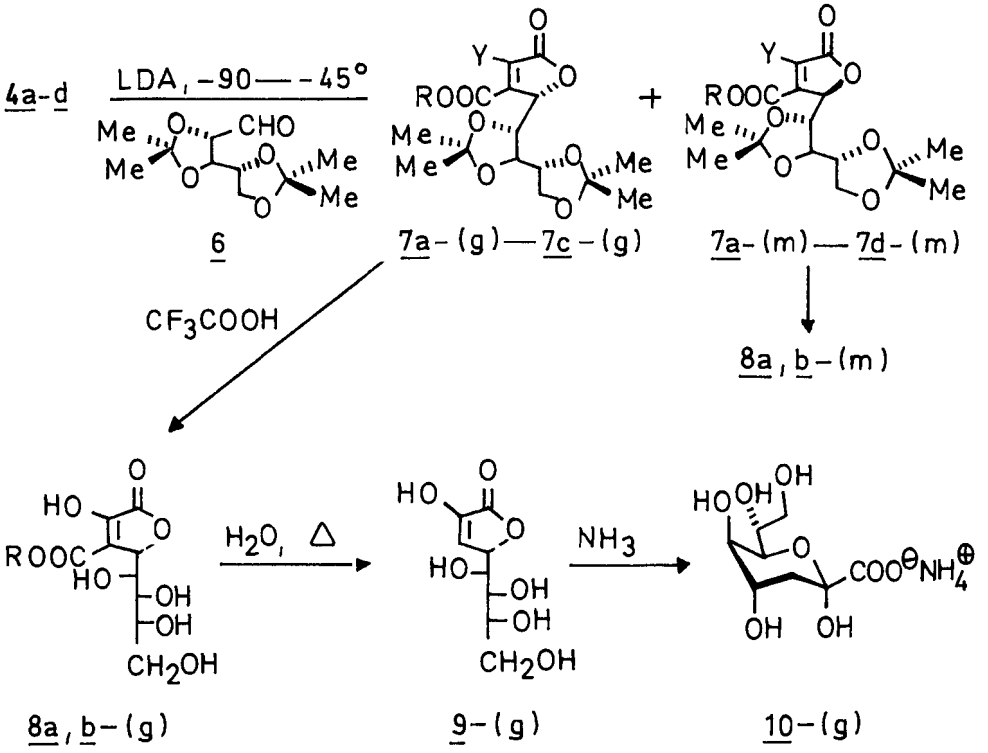
thiation with lithium diisopropylamide (LDA) and quenching with methanol-O-d gave via species 4Aa-(E) exclusively the (E)-product 5a-(E) (deuteration~90 %).[12] However, on reaction with aldehydes,



Scheme 2

butenolides were obtained, indicating equilibration under the reaction conditions into the (Z)-species 4Aa-(Z) which evidently is more nucleophilic than the (E)-species 4Aa-(E).[12,13,15] Reaction of 4a-(E) with LDA and subsequent addition of 2,3:4,5-di-O-isopropylidene-D-arabinose (6) afforded the expected α-amino-butenolides 7a-(m,g) in reasonable yields; however, no diastereofacial selectivity was observed (74 % yield, manno:gluco~1:1). Both compounds were easily separated by medium pressure chromatography on silica gel. The structures were assigned by comparison of the ^{1}H NMR data. Previously we had found[4,16] that the manno-isomer exhibits a downfield shift and a larger $J_{4,5}$ coupling than the gluco-isomer. Treatment of α-amino-butenolides 7a-(g) and 7a-(m)

with trifluoroacetic acid in a water/methanol mixture resulted in clean deamination and concomitant deisopropylidenation affording α-hydroxy-butenolides 8a-(g) and 8a-(m), respectively. However, attempts to dealkoxycarbonylate and introduce the required ß-hydrogen atom resulted mainly in decomposition.



Scheme 3

To facilitate the dealkoxycarbonylation step, tert.-butyl esters were needed. Therefore the pyrrolidine adduct to di-tert.-butyl acetylenedicarboxylate 4b was synthesized. Reaction in ether gave a 2:1 mixture of the (E)- and (Z)-isomers. Heating this mixture in cyclohexane afforded exclusively the (E)-isomer 4b-(E). The structural assignments are based on the comparison of the ^{1}H NMR data with those of compounds 4a-(E,Z). Direct lithiation of the (E)-isomer 4b-(E) with LDA under the reaction conditions described

for compound 4a-(E) furnished, according to quenching experiments with methanol-O-d 60 % deuterated (E)-isomer 5b-(E) [(E)/(Z) > 10:1]. This finding was confirmed by the reaction with arabinose derivative 6: a diastereomeric mixture of α-pyrrolidino-butenolides 7b-(g,m) was obtained in only 55 % yield, by contrast to the reactions with dilithiated species 2A and 3A, the gluco-isomer 7b-(g) preponderated (gluco/manno = 4:1). The isomers were easily separated by medium pressure chromatography on silica gel. Addition of HMPT or TMEDA to the reaction mixture or changing the reaction time and temperature did not lead to preferential formation of the manno-isomer 7b-(m) in acceptable yield; mostly, lower yields with gluco/manno-ratios ranging from 2:1 to 1:1 were observed. Treatment of these compounds with trifluoroacetic acid afforded deaminated and deisopropylidenated α-hydroxy-butenolides 8b-(g) and 8b-(m), respectively, which had identical physical data with materials synthesized from D-arabinose and di-tert.-butyl oxalacetate; however, the yields were unsatisfactory.[7,8] As described previously[7] the gluco-isomer 8b-(g) was readily converted into the dealkoxycarbonylation product 9-(g) by simply heating in water and treating the product with ammonia, to afford D-gluco-KDO 10-(g)[7,17] thus concluding a short stereocontrolled approach to this compound.

To improve the chemical yield in the CC-bond forming step, other amine adducts of di-tert.-butyl acetylenedicarboxylate were investigated. Addition of N-methyl-piperazine afforded a 4:1 mixture of compounds 4c-(E) and 4c-(Z). Heating of this mixture in cyclohexane afforded exclusively the (E)-isomer 4c-(E). The structural assignments are again based on the chemical shifts of the vinylic protons which are generally more downfield for the (Z)-isomer. Direct lithiation with LDA and subsequent deuteration experiments demonstrated convenient and practically quantitative hydrogen/lithium exchange. However, for product 5c the (E):(Z)-ratio was reversed to 1:4 which is not in accordance with the results for compounds 5a,b. Reaction of the lithiated species with

the arabinose derivative 6 gave a 79 % yield of α-amino-butenolides 7c-(g,m), however, the gluco/manno-ratio was reduced to 2:1. For structural proof, compound 7c-(g) was converted into the deaminated and deisopropylidenated product, identical with α-hydroxy-butenolide 8b-(g).

Better results were obtained with morpholine addition yielding in ethyl ether a 1:1-mixture of the isomers 4d-(E) and 4d-(Z) (isolated yields 5:4) which had the expected vinylic ^{1}H NMR signals. Both compounds could easily be separated. Heating the mixture in cyclohexane afforded only the (E)-isomer, 4d-(E). When the (E)-isomer was treated with LDA and subsequently quenched with methanol-O-d, a ca. 1:3-ratio of compounds 5d-(E) and 5d-(Z) was obtained with almost complete deuteration. This demonstrates that the (E):(Z)-ratio in the lithiated species 4Aa-d is very sensitive to subtle differences in the inductive effect of the amine substituent: with pyrrolidine the (E)-isomer is preferred and with N-methylpiperazine and morpholine a 1:4- and 1:3-(E):(Z)-ratio, respectively, is found. Reaction of the lithiated species 4Ad with the arabinose derivative 6 gave, in 72 % yield, a 4:1-mixture of compounds 7d-(g) and 7d-(m). The gluco-isomer 7d-(g) was easily separated from the reaction mixture by crystallisation, making this compound readily available. Treatment with trifluoroacetic acid provided, via deamination and deisopropylidenation, the known α-hydroxy-butenolide 8b-(g) thus concluding a convenient approach to D-gluco-KDO 10-(g) via compounds 7d-(g), 8b-(g), and 9-(g), all purified by direct crystallisation.

EXPERIMENTAL

General Procedures. Melting points are uncorrected. ^{1}H NMR spectra were recorded in the solvents noted (Me_4Si, 0.00 ppm) with a Bruker CP 80 CW and a Bruker WM 250 Cryospec. R_F values refer to TLC performed on silica gel (Merck) with the solvent systems noted. Column chromatography was performed under normal pressure with si-

lica gel (Merck, 70-230 mesh), under medium pressure with silica gel (Merck, "LiChroprep" Si60, 40-60 µm) and by flash chromatography with silica gel (Merck, 230-400 mesh). Optical rotation was determined with a Perkin-Elmer 241 MC. IR-spectra were recorded with a Perkin-Elmer Model 621.

Synthesis of amine adducts to acetylenedicarboxylate. As described for the synthesis of compound 4a[12]; compounds 4b-4d were also obtained; see below.

Di-tert.-butyl(E)- and (Z)-2-(1-pyrrolidinyl)-butenediolate [4b-(E) and 4b-(Z)]. From di-tert.-butyl acetylenedicarboxylate (50 g, 22.1 mmol) and pyrrolidine (5.1 g, 72 mmol) in dry ether (165 mL) after 16 h at room temperature quantitative reaction was observed. The solvent and excess pyrrolidine was removed by evaporation. According to ^{1}H NMR the reaction mixture consisted of two parts (E)-isomer and one part (Z)-isomer. ^{1}H NMR ($CDCl_3$), (E)-isomer: δ 4.35 (s, 1H, -CH=), 3.40-3.10 (m, 4H, $-CH_2-N-CH_2$), 2.10-1.75 (m, 4H, CH_2-CH_2), 1.60 (s, 9H, $-C(CH_3)_3$), 1.45 (s, 9H, $C(CH_3)_3$); (Z)-isomer: δ 4.75 (s, 1H, -CH=), 3.60-3.35 (m, 4H, CH_2-N-CH_2), 2.10-1.75 (m, 4H, $-CH_2-CH_2$), 1.60 (s, 9H, $C(CH_3)_3$), 1.45 (s, 9H, $C(CH_3)_3$).

Refluxing the reaction mixture in cyclohexane (40 mL) for 20 min gave exclusively the (E)-isomer. The solvent was removed by evaporation and the residue flashed through silica gel (petroleum ether/ethyl acetate = 4:1). The product obtained crystallized from petroleum ether; yield 5.6 g (85 %) colorless crystals of 4b-(E); mp. 101-102°C, TLC R_F = 0.55 (petroleum ether/ethyl acetate = 4:1).

Anal.Calcd. for $C_{16}H_{27}NO_4$ (297.4): C, 64.62; H, 9.16; N, 4.74. Found 4b-(E): C, 64.88; H, 9.16; N, 4.72.

Di-tert.-butyl(E)- and (Z)-2-(4-methyl-1-piperazinyl)-butendioate [4c-(E) and 4c-(Z)]. From di-tert.-butyl acetylenedicarboxylate (1 g, 4.42 mmol) and N-methyl-piperazine (1.47 mL, 13.26 mmol) in dry ether (30 mL) after 1 h at 0°C quantitative reaction

was observed. The solvent and excess N-methylpiperazine was evaporated under vacuum (0.01 torr) and the residue filtered through silica gel (ethyl acetate/petroleum ether = 3:1); yield 1.27 g (88 %) slightly yellowish oil which according to ^{1}H NMR consisted of a 4:1 mixture of 4c-(E) and 4c-(Z), which was used for the subsequent lithiation experiments. ^{1}H NMR ($CDCl_3$), (E)-isomer: δ 4.70 (s, 1H, -CH=), 3.21-3.12 (m, 4H, CH_2-N-CH_2), 2.51-2.42 (m, 4H, CH_2-NCH_3-CH_2), 2.32 (s, 3H, NCH_3), 1.59 (s, 9H, $C(CH_3)_3$), 1.47 (s, 9H, $C(CH_3)_3$; (Z)-isomer: δ 5.06 (s, 1H, -CH=), 3.33-3.24 (m, 4H, CH_2-N-CH_2), 2.55-2.44 (m, 4H, CH_2-NCH_3-CH_2), 2.33 (s, 3H, NCH_3), 1.53 (s, 9H, $C(CH_3)_3$), 1.47 (s, 9H, $C(CH_3)_3$).

Refluxing the reaction mixture in cyclohexane (40 mL) for 20 min gave exclusively the (E)-isomer 4c-(E) as indicated by ^{1}H NMR after removal of the solvent.

Di-tert.-butyl(E)- and (Z)-2-(4-morpholinyl)-butendioate [4d-(E) and 4d-(Z)]. From di-tert.-butyl acetylenedicarboxylate (1 g, 4.42 mmol) and morpholine (1.16 mL, 13.26 mmol) in dry ether (30 mL) after 75 min at room temperature quantitative reaction was observed. The solvent and excess morpholine was evaporated under reduced pressure (10 torr) and the residue treated with petroleum ether at 0°C, which led to crystallisation of the (E)-isomer; yield 659 mg (48 %), colorless crystals; mp. 128-129°C. The (Z)-isomer is obtained from the mother liquor as yellow oil; yield 527 mg (38 %); TLC R_F = 0.37 (petroleum ether/ethyl acetate = 3:1). Refluxing the (Z)-isomer or a mixture of both isomers in cyclohexane for 1.5 h afforded exclusively the (E)-isomer. ^{1}H NMR ($CDCl_3$), (E)-isomer: δ 4.75 (s, 1H, -CH=), 3.90-3.70 (m, 4H, CH_2-O-CH_2), 3.25-3.08 (CH_2-N-CH_2), 1.56-1.44 (2s, 18H, 2 $C(CH_3)_3$; (Z)-isomer: δ 5.20 (br s, 1H, -CH=), 3.90-3.65 (m, 4H, CH_2-O-CH_2), 3.38-3.18 (m, 4H, CH_2-N-CH_2), 1.51, 1.46 (2s, 18H, 2 $C(CH_3)_3$).

Lithiation of Compounds 4a-d and Subsequent Deuteration to Compounds 5a-d. General Procedure.[12] A solution of 4 (1 mmol) in dry THF (5 mL) is added at -90°C to a solution of LDA (1.2 mmol)

in dry THF (50 mL). After the time t_1 methanol-O-d (0.15 mL) is added to the reaction mixture which after the time t_2 is poured on a saturated solution of ammonium chloride (100 mL). The organic phase is extracted with ether (2 x 50 mL), the ether phase dried over $MgSO_4$, the solvent evaporated, and the residue filtered through silica gel as described for 4a-d. The (E)/(Z)-ratio and the percentage of deuteration at the vinylic position was determined by recording ^1H NMR spectra. 4a-(E): t_1 = 30 min; t_2 = 30 min quantitative yield of compound 5a-(E), deuteration: > 90 %[12] 4b-(E): t_1 = 2.5 h, t_2 = 2 h; yield 90 % of compound 5b-(E) deuteration 60 %. 4c [(E)/(Z)-ratio = 4:1]; t_1 = 2 h, t_2 = 1 h; yield 84 % of a 1:4-mixture of compounds 5c-(E) and 5c-(Z). 4d-(E), 4d-(Z), and a 1:1 mixture of both isomers: t_1 = 2 h, t_2 = 1 h; yield 90 % of a 1:3 mixture of compounds 5d-(E) and 5d-(Z).

2,3:4,5-Di-O-isopropylidene-D-arabinose (6). This compound was prepared as described by Zinner et al.[18]

Reaction of Compounds 4a-d with Arabinose Derivative 6 to Compounds 7a-d. General Procedure: A solution of 4 (1 mmol) in dry THF (5 mL) is added at -90°C to a solution of LDA (1.2 mmol) in dry THF (10 mL). After the time t_1 compound 6 (1.5 mmol) dissolved in dry THF (5 mL) is added. The reaction temperature is raised to -80°C and after the time t_2 it is kept for 12 h at -45°C. The reaction mixture is then poured on a saturated solution of ammonium chloride (100 mL). The organic phase is extracted with ether (3 x 50 mL), the ether phase dried over $MgSO_4$, the solvent evaporated, and the residue worked up as described below.

2,3-Dideoxy-5,6:7,8-di-O-isopropylidene-3-methoxycarbonyl-2-pyrrolidinyl)-D-gluco- and D-manno-2-octeno-1,4-lactone [7a-(g) and 7a-(m)]. From compound 4a-(E) (t_1 = 2 h, t_2 = 2 h) an oily residue was obtained, which was filtered through silica gel (ethyl ether) and for separation chromatographed on silica gel (medium pressure; ethyl acetate/petroleum ether = 3:7). 7a-(g): Yield 37 %, colorless crystals, mp. 94°C from petroleum ether;

$[\alpha]_D^{20}$ = +78.4°C (c = 1.40, $CHCl_3$); TLC R_F = 0.68 (ethyl acetate/petroleum ether = 1:1); ^{1}H NMR ($CDCl_3$) δ 5.20 (s, 1H, H-4), 4.38 (d, 1H, H-5), 4.16-3.98 (m, 4H, H-6, H-7, H-8, H-8'), 3.90-3.71 (m, 4H, CH_2-N-CH_2), 3.76 (s, 3H, OCH_3), 2.00-1.85 (m, 4H, CH_2-CH_2), 1.44, 1.36, 1.35, 1.32 (4s, 12H, 4 CH_3).

Anal.Calcd. for $C_{20}H_{29}NO_8$ (411.5): C, 58.38; H, 7.10; N, 3.50. Found: C, 58.49; H, 7.34; N, 3.56.

7a-(m): Yield 37 %, colorless crystals, mp. 99°C from petroleum ether; $[\alpha]_D^{20}$ = -56.3° (c = 1.86, $CHCl_3$); TLC R_F = 0.73 (ethyl acetate/petroleum ether = 1:1); ^{1}H NMR ($CDCl_3$) δ 5.35 (d, 1H, H-4; $J_{4,5}$ = 2.4 Hz), 4.56 (dd, 1H, H-5, $J_{4,5}$ = 2.4 Hz, $J_{5,6}$ = 6.1 Hz), 4.09 (dd, 1H, H-6, $J_{5,6}$ = 6.1 Hz, $J_{6,7}$ = 7.40 Hz), 3.98 (m, 1H, H-7), 3.85 (dd, 1H, H-8), 3.83-3.75 (m, 4H, CH_2-N-CH_2), 3.73 (s, 3H, OCH_3), 3.69 (dd, 1H, H-8'), 1.98-1.82 (m, 4H, CH_2-CH_2), 1.47, 1.40, 1.31, 1.30 (4s, 12H, 4 CH_3).

Anal.Calcd. for $C_{20}H_{29}NO_8$ (411.5): C, 58.38; H, 7.10; N, 3.40. Found: C, 58.40; H, 7.11; N, 3.58.

3-tert.-Butoxycarbonyl-2,3-dideoxy-5,6:7,8-di-O-isopropylidene-2-(1-pyrrolidinyl)-D-gluco- and -D-manno-2-octeno-1,4-lactone [7b-(g) and 7b-(m)]. From compound 4b-(E) (t_1 = 2 h, t_2 = 3 h) an oily residue was obtained, which was filtered through silica gel (petroleum ether/ethyl acetate = 6:1) and for separation chromatographed on silica gel (medium pressure; toluene/ethyl acetate = 15:1). - 7b-(g): Yield 44 %, colorless crystals, mp. 101°C from petroleum ether; $[\alpha]_D^{20}$ = +70.3° (c = 1, $CHCl_3$); TLC R_F = 0.45 (petroleum ether/ethyl acetate = 6:1); ^{1}H NMR ($CDCl_3$) δ 5.17 (s, 1H, H-4), 4.42 (d, 1H, H-5), 4.22-3.90 (m, 4H, H-6, H-7, H-8, H-8'), 3.90-3.65 (m, 4H, CH_2-N-CH_2), 1.95-1.80 (m, 4H, CH_2-CH_2), 1.51 (s, 9H, $C(CH_3)_3$, 1.42-1.31 (4s, 12H, 4 CH_3).

Anal.Calcd. for $C_{23}H_{35}NO_8$ (453.5): C, 60.90; H, 7.78; N, 3.09. Found: C, 61.18; H, 7.77; N, 2.97.

7b-(m): Yield 11 %, colorless crystals, mp. 92-93°C from petroleum ether; $[\alpha]_D^{20}$ = -41.3° (c = 1, $CHCl_3$); TLC R_F = 0.45 (petroleum ether/ethyl acetate = 6:1); ^{1}H NMR ($CDCl_3$) δ 5.29 (d, 1H,

H-4; $J_{4,5}$ = 2.2 Hz), 4.60 (dd, 1H, H-5; $J_{4,5}$ = 2.2 Hz, $J_{5,6}$ = 6.0 Hz), 4.10, 4.00, 3.88, 3.67 (4 dd, 4H, H-6, H-7, H-8, H-8'), 3.82-3.70 (m, 4H, CH_2-N-CH_2), 1.95-1.80 (m, 4H, CH_2-N-CH_2), 1.51 (s, 9H, $C(CH_3)_3$), 1.52-1.34 (4s, 12H, 4 CH_3). For structural proof this material was converted into compound 8b-(m).

3-tert.-Butoxycarbonyl-1,2-dideoxy-5,6:7,8-di-O-isopropylidene-2-(4-methylpiperazinyl)-D-gluco- and -D-manno-2-octeno-1,4-lactone [7c-(g) and 7c-(m)]. From a 1:4-mixture of compounds 4c-(E) and 4c-(Z) (t_1 = 2 h, t_2 = 1 h) an oily residue was obtained which was filtered through silica gel (petroleum ether/ethyl acetate = 1:3); yield 79 % of a 2:1-mixture of compounds 7c-(g) and 7c-(m) as indicated by ^{1}H NMR. Separation of these isomers was achieved by medium pressure chromatography on silica gel (acetone). - ^{1}H NMR ($CDCl_3$), 7c-(g) δ 5.15 (s, 1H, H-4), 4.40 (d, 1H, H-5), 4.23-3.94 (m, 4H, H-6, H-7, H-8, H-8'), 3.89-3.57 (m, 4H, CH_2-N-CH_2), 2.60-2.40 (m, 4H, CH_2-NCH_3-CH_2), 2.30 (s, 3H, N-CH_3), 1.52 (s, 9H, $C(CH_3)_3$), 1.44, 1.37, 1.35, 1.34 (4s, 12H, 4 CH_3).

7c-(m) δ 5.25 (d, 1H, H-4; $J_{4,5}$ = 2.4 Hz), 4.62 (dd, 1H, H-5; $J_{4,5}$ = 2.4 Hz, $J_{5,6}$ = 5.8 Hz), 4.10, 3.98, 3.83, 3.61 (4 dd, 4H, H-6, H-7, H-8, H-8'), 3.72-3.63 (m, 4H, CH_2-N-CH_2), 2.57-2.42 (m, 4H, CH_2-NCH_3-CH_2), 2.30 (s, 3H, NCH_3), 1.52 (s, 9H, $C(CH_3)_3$, 1.50, 1.40, 1.33, 1.31 (4s, 12H, 4 CH_3).

For structural proof compound 7c-(g) was transformed into compound 8b-(g).

3-tert.-Butoxycarbonyl-2,3-dideoxy-5,6:7,8-di-O-isopropylidene-2-(4-morpholinyl)-D-gluco- and -D-manno-2-octeno-1,4-lactone [7d-(g) and 7d-(m)]. From compound 4d-(E) or 4d-(Z) (t_1 = 2 h, t_2 = 3 h) an oily residue was obtained which was flash chromatographed through silica gel (petroleum ether/ethyl acetate = 3:1); yield 72 % of a 4:1-mixture of compounds 7d-(g) and 7d-(m) as indicated by ^{1}H NMR. Treatment of this mixture with petroleum ether afforded crystals of compound 7d-(g), yield 52 %, mp. 116-118°C; $[\alpha]_D^{20}$ = +46.6° (c = 1, $CHCl_3$); TLC R_F = 0.40 (petroleum ether/

ethyl acetate = 3:1); ^{1}H NMR ($CDCl_3$) δ 5.16 (s, 1H, H-4), 4.40 (d, 1H, H-5), 4.21-3.55 (m, 12H, H-6, H-7, H-8, H-8', CH_2-N-CH_2, CH_2-O-CH_2), 1.52 (s, 9H, $C(CH_3)_3$, 1.45, 1.36, 1.32, 1.31 (4s, 12H, 4 CH_3).

Anal.Calcd. for $C_{23}H_{35}NO_9$ (469.5): C, 58.84; H, 7.51; N, 2.98. Found: C, 59.28; H, 7.78; N, 3.02.

A complete purification of compound 7d-(m) as present in the mother liquor after crystallisation of compound 7d-(g) by chromatography on silica gel (medium pressure: toluene/ethyl acetate = 5:1) was not achieved. However, the material obtained had typical ^{1}H NMR data ($CDCl_3$): δ 5.26 (d, 1H, H-4; $J_{4,5}$ = 2.4 Hz), 4.62 (dd, 1H, H-5; $J_{4,5}$ = 2.4 Hz, $J_{5,6}$ = 5.8 Hz).

3-Deoxy-3-methoxycarbonyl-D-gluco-2-octeno-1,4-lactone [8a-(g)]. A solution of lactone 7a-(g) (1.0 g, 2.4 mmol) in methanol/water (72 mL + 16 mL) is treated with trifluoroacetic acid (8 mL) for 72 h. The reaction mixture is evaporated under reduced pressure (10 torr), the residue dissolved in water (10 mL), and the solution again evaporated. After washing with ethyl acetate the crystalline product was recrystallized from methanol/ethyl acetate. Yield 570 mg (85 %), colorless crystals, mp. 158°C (decomp.); $[\alpha]_D^{20}$ = +71.5° (c = 1.2 MeOH); ^{1}H NMR (DMSO-d_6) δ 5.30 (d, 1H, H-4; $J_{4,5}$ = 1 Hz), 5.20-4.30 (m, 5 OH), 4.09 (m, 1H, H-5), 3.70 (s, 3H, OCH_3), 3.65-3.40 (m, 4H, H-6, H-7, H-8, H-8').

Anal.Calcd. for $C_{10}H_{14}O_9$ (278.2): C, 43.17; H, 5.07. Found: C, 43.09; H, 4.97.

3-Deoxy-3-methoxycarbonyl-D-manno-2-octeno-1,4-lactone [8a-(m)]. As described above from lactone 7a-(m) (1.0 g, 2.4 mmol) a crystalline product was obtained, which was recrystallized from methanol/water. Yield 500 mg (75 %), colorless crystals, mp. 190°C (decomp.); $[\alpha]_D^{20}$ = -7.7° (c = 0.8, MeOH); ^{1}H NMR (DMSO-d_6) δ 5.22 (d, 1H, H-4; $J_{4,5}$ = 5.2 Hz), 5.20-4.30 (m, 5 OH), 4.10-3.10 (m, 5H, H-5, H-6, H-7, H-8, H-8'), 3.70 (s, 3H, OCH_3).

Anal.Calcd. for $C_{10}H_{14}O_9$ (278.2): C, 43.17; H, 5.07. Found: C, 43.36; H, 4.83.

3-tert.-Butoxycarbonyl-3-deoxy-D-gluco-2-octeno-1,4-lactone [8b-(g)]. As described above, a crystalline product was obtained from lactone 7b-(g) (768 mg, 1.69 mmol). This was recrystallized from ethyl acetate to afford colorless crystals; yield 325 mg (60 %); mp. 139-140°C (lit.[7] mp. 138.5-140°C); $[\alpha]_D^{20}$ = +60.7° (c = 1.45, MeOH) (lit.[7] $[\alpha]_D^{24}$ = 61.4° (c = 1.6, MeOH); ^{1}H NMR (DMSO-d_6) δ 5.22 (s, 1H, H-4), 4.77, 4.68, 4.55, 4.38 (4 OH), 4.05 (m, 1H, H-5), 3.65-3.40 (m, 5H, OH, H-6, H-7, H-8, H-8'), 1.46 (s, 9H, $C(CH_3)_3$).

Anal.Calcd. for $C_{13}H_{20}O_9$ (320.3): C, 48.75; H, 6.29. Found: C, 48.75; H, 6.08.

Using the same procedure, compound 8b-(g) was obtained from compounds 7c-(g) and 7d-(g) in 55 % and 61 % yields, respectively.

3-tert.-Butoxycarbonyl-3-deoxy-D-manno-2-octeno-1,4-lactone [8b-(m)]. As described above a crystalline product was obtained from lactone 7b-(m) (384 mg, 0.85 mmol) which was recrystallized from yield 163 mg (60 %); mp. 154°C (from ethyl acetate) (lit.[7] mp. 152-154°C); $[\alpha]_D^{20}$ = -8.5° (c = 1.0, MeOH) (lit.[7] $[\alpha]_D^{24}$ = -5.2° (c = 3.0, MeOH); ^{1}H NMR (DMSO-d_6) δ 5.12 (d, 1H, H-4; $J_{4,5}$ = 5.2 Hz), 4.75, 4.58, 4.97, 4.28 (4 OH), 4.01 (m, 1H, H-5), 3.62-3.20 (m, 5H, OH, H-6, H-7, H-8, H-8'), 1.46 (s, 9H, $C(CH_3)_3$).

3-Deoxy-D-gluco-2-octeno-1,4-lactone [9-(g)] and Ammonium 3-Deoxy-D-gluco-2-octulosonate [10-(g)]. Lactone 8b-(g) (104 mg, 0.325 mmol) was transformed into compound 9-(g) as described in the literature[7]. Yield 53 mg (74 %), colorless powder which had IR-data and optical rotation in agreement with published values; ^{1}H NMR (DMSO-d_6) δ 6.21 (s, 1H, -CH=). - This compound was subsequently transformed into D-gluco-KDO 10-(g) as described.[7] Thus, the published procedure was confirmed.

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