Supporting Information

Stereodivergent Access to Polyhydroxylated 10-Azabicyclo[4.3.1]decanes as New Calystegine Analogs

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1. General information

Reactions in anhydrous solvents, prepared by standard procedures, were performed under an argon atmosphere. All reactions were monitored by thin layer chromatography (TLC) on precoated silica gel plates; spots were visualized by UV light (254 nm) or by staining with aqueous KMnO₄ solution or Hanessian’s stain. The peak assignments in the 1H and 13C NMR data were made on basis of 2D NMR methods (COSY, HMQC, HMBC).

2. Synthesis of compounds 3 from Diacetone-d-glucose.

![Diagram of the synthesis reaction]

**Procedure:**

Diacetone-D-glucofuranose (12 g, 46.1 mmol) was dissolved in 60% aqueous acetic acid (180 mL, 1.89 mol) and the reaction mixture was stirred at room temperature overnight (21 h). The liquids were evaporated in vacuo and the residual AcOH was removed by co-evaporation with H₂O to give desired 1,2-O-isopropylidene-D-glucofuranose as white crystals.


![Diagram of the oxidation reaction]

**Procedure:**

Sodium periodate (11.07 g, 51.8 mmol) was added portionwise over 10 min. to a solution of the previous crude 1,2-O-isopropylidene-α-D-glucofuranose (10.15 g, 46.1 mmol) in water (180 mL). After stirring overnight (16h) the precipitated white solid was filtered off and the product was extracted with EtOAc. The organic phases were dried (MgSO₄) and concentrated to provide the crude aldehydo-sugar.

![Diagram of the Dowex® reaction]

**Procedure:**

Sodium periodate (11.07 g, 51.8 mmol) was added portionwise over 10 min. to a solution of the previous crude 1,2-O-isopropylidene-α-D-glucofuranose (10.15 g, 46.1 mmol) in water (180 mL). After stirring overnight (16h) the precipitated white solid was filtered off and the product was extracted with EtOAc. The organic phases were dried (MgSO₄) and concentrated to provide the crude aldehydo-sugar.
The crude aldehyde (8.67 g, 46.1 mmol) was redissolved in water (115 mL) and treated with cation exchange resin (Dowex® 50W100, H⁺ form) (14.75 g) at 70°C overnight (16 h). The resin was removed by filtration and the filtrate was used directly in the next step.

Procedure:

The previous dialdehydo-sugar (6.82 g, 46.0 mmol) was added to a vigorously stirred solution of benzotriazole (10.97 g, 92 mmol) and benzylamine (5 mL, 46.0 mmol) in water (360 mL). The reaction mixture immediately turned cloudy followed by formation of a gummy solid after 6 h. The product was extracted into EtOAc (5x200 mL) and the organic phases were dried (MgSO₄) and concentrated under vacuum. Reduction of the volume to 200 mL under reduced pressure resulted in crystallization of 3. The product was collected by filtration as a white solid; additional product crystallized from the mother liquor upon standing overnight. The combined yield was 9.4 g (45%). Another attempt of crystallization led to impurities (BtH).

3. Synthesis of compounds 4 by alkylation of compounds 3

Procedure:

A three-neck reactor containing Zinc dust (5.15 g, 79 mmol) and a magnetic stirring bar was dried in an oven (120°C) for 12 h. Then a condenser was attached and 1,2-dibromoethane (0.34 mL, 3.93 mmol) in anhydrous THF (60 mL) was added under Ar. The reaction mixture was vigorously stirred and heated to 65°C for 15 min. The mixture was allowed to cool down to room temperature and chlorotrimethylsilane (0.1 mL, 0.787 mmol) was added. The mixture was vigorously stirred for 15 min. Allyl bromide (2.8 mL, 32.8 mmol) in anhydrous THF (30 mL) was then added slowly and the reaction was stirred for another 15-30 min. Compounds 3 (3 g, 6.56 mmol) in anhydrous THF (450 mL) were added slowly at r.t. and the reaction mixture was stirred overnight (20 h). Water was then added and the solids were removed by filtration over celite. Satd. aq. Na₂CO₃ (100 mL) were added and another
filtration over celite was carried out. The filtrate was extracted with AcOEt (3x) and the organic phases were dried and concentrated under vacuum. The filtrate was extracted with AcOEt (3x) and the organic phases were dried and concentrated under vacuum.

DMAP (0.401 g, 3.28 mmol) was added to a solution of this crude mixture (1.99 g, 6.56 mmol) in dry CH$_2$Cl$_2$ (100 mL). Then acetic anhydride (6.19 mL, 65.6 mmol) was added dropwise and the reaction mixture was stirred overnight at r.t. Water (20 mL) was added while keeping stirring for 30 min and Na$_2$CO$_3$ was added until a basic pH was reached.

The aqueous phase was extracted using CH$_2$Cl$_2$ (3x) and the organic phases were combined and concentrated under vacuum. The desired products were obtained by purification over silica gel chromatography using EtOAc/PE (20/80), which afforded compounds 4 (1.611 g, 3.75 mmol, 57 % yield) (mixture of stereoisomers).

**4. Synthesis of compounds 5. Deprotection of compounds 4**

![Chemical structure of compounds](image)

**Procedure:**

To the mixture 4 (1.446 g, 3.37 mmol), dissolved in a 5:1 mixture of THF (190 mL) and water (37 mL), CAN (7.38 g, 13.47 mmol) was added in portions. When the reaction was complete (5 h), the mixture was treated with sat aq NaHCO$_3$ until a basic pH was reached and extracted with EtOAc. The organic phase was dried (MgSO$_4$), filtered and concentrated. The different products were isolated by flash chromatography using EtOAc/PE (20/80):

- 5a (29%; 331 mg)
- 5b (13%; 149 mg)

**5a:**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 5.71 (tdd, $J = 6.0, 8.4, 14.5$, 2H, H-8, H-11), 5.15 – 5.08 (m, 4H, H-9, H-12), 5.04 (t, $J = 9.4$, 1H, H-4), 4.78 (t, $J = 9.6$, 2H, H-3, H-5), 2.71 (td, $J = 3.4$, 9.2, 2H, H-2, H-6), 2.32 (dd, $J = 5.2$, 10.0, 2H, H-10, H-7), 2.07 – 2.00 (m, 2H, H-10, H-7), 2.02 (s, 6H, CH$_3$CO), 1.99 (s, 3H, CH$_3$CO), 1.68 (s, NH).

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 170.7 (CO), 170.1 (CO), 134.0 (C-11, C-8), 119.0 (C-12, C-9), 75.7 (C-4), 74.0 (C-3, C-5), 56.5 (C-2, C-6), 36.3 (C-10, C-7), 21.0 (2xCH$_3$CO), 20.9 (CH$_3$CO).

IR (cm$^{-1}$) (NaCl ; FTIR) : 1749.0 ; 1247.6 ; 1225.7 ; 1030.0.

HRMS: [M+H]$^+$ = 340.1753 (calculated for C$_{17}$H$_{26}$NO$_6$ = 340.1760)

**5b:**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 5.77 (ddt, $J = 7.1, 10.2, 17.3$, 2H, H-11, H-8), 5.20 – 5.05 (m, 4H, H-9, H-12), 4.99 (t, $J = 2.6$, 1H, H-4), 4.82 – 4.71 (m, 2H, H-3, H-5), 3.04 (t, $J = 7.1$, 2H, H-7), 2.93 (t, $J = 7.1$, 2H, H-6), 2.80 (m, 2H, H-10, H-2), 2.26 (s, 6H, CH$_3$CO), 1.98 (s, 3H, CH$_3$CO), 1.68 (s, NH).

IR (cm$^{-1}$) (NaCl ; FTIR) : 1749.0 ; 1247.6 ; 1225.7 ; 1030.0.
2H, H-2, H-6), 2.21 (t, J = 6.9, 4H, H-7, H-10), 2.12 (s, 6H, CH₃COO), 2.11 (s, 3H, CH₃COO).

**1³C NMR (101 MHz, CDCl₃):** δ 169.7 (CO), 168.3 (CO), 134.2 (C-8, C-11), 118.1 (C-9, C-12), 68.1 (C-3, C-5), 67.5 (C-4), 54.2 (C-2, C-6), 35.9 (C-7, C-10), 20.9 (CH₃CO).

**IR (cm⁻¹) (NaCl; FTIR):** 1741.0 ; 1370.2 ; 1246.0 ; 1218.8 ; 1036.9

**HRMS:** [M+H]⁺ = 340.1765 (calculated for C₁₇H₂₆NO₆ = 340.1760)

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**5c:**

**1³H NMR (400 MHz, CDCl₃):** δ 5.75 – 5.59 (m, 2H, H-8, H-11), 5.24 (t, J = 8.0, 1H, H-4), 5.17 – 5.06 (m, 4H, H-9, H-12), 5.03 (dd, J = 5.7, 10.0, 1H, H-5), 4.73 (t, J = 9.4, 1H, H-3), 3.34 (ddd, J = 4.2, 5.5, 10.0, 1H, H-6), 2.90 (td, J = 3.4, 9.2, 1H, H-2), 2.40 (ddd, J = 8.6, 11.3, 14.2, 1H, H-7), 2.35 – 2.21 (m, 2H, H-10, H-7), 2.07 – 1.96 (m, 11H, CH₃CO, H-10).

**1³C NMR (101 MHz, CDCl₃):** δ 170.3, 170.0 and 169.9 (COO), 134.6 and 133.9 (C-8, C-11), 118.7 and 118.1 (C-9, C-12), 74.3 (C-4), 72.5 (C-5), 71.6 (C-3), 52.6 (C-6), 50.1 (C-2), 36.4 (C-10), 30.3 (C-7), 20.9, 20.8 and 20.8 (CH₃CO).

**IR (cm⁻¹) (NaCl; FTIR):** 1746.5 ; 1225.2 ; 1030.3

**HRMS:** [M+Na]⁺ = 340.1747 (calculated for C₁₇H₂₆NO₆NaCl₃ : 340.1760)

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### 5. Synthesis of compound 6a from 5a.

![Synthesis Scheme](image)

**Procedure:**

2,2,2-trichloroethyl chloroformate (0.608 mL, 4.42 mmol) was slowly added to a solution of 5a (300 mg, 0.884 mmol) in dry pyridine (19 mL). The reaction was stirred for 48 h and the pyridine was then evaporated. The crude product was redissolved in CH₂Cl₂ and the organic phase was washed using HCl 1N (a sufficient amount to remove pyridine and the unreacted starting material (same Rf)). The desired product 6a was purified by flash chromatography using EtOAc/PE (20/80) (400 mg; 88%)

**1³H NMR (400 MHz, CDCl₃) δ 5.78 (ddt, J = 7.0, 10.3, 17.2, 2H, H-8, H-11), 5.19 – 4.99 (m, 7H, H-9, H-12, H-3, H-5, H-4), 4.80 (s, 2H, H-13), 4.43 (dt, J = 7.4, 3.2 Hz, 2H, H-2, H-6), 2.68 – 2.46 (m, 4H, H-3, H-7), 2.09 (s, 3H, CH₃CO), 2.03 (s, 6H, CH₃CO).

**1³C NMR (101 MHz, CDCl₃) δ 169.6 (CO), 169.0 (CO), 154.1 (NCO), 133.6 (C-8, C-11), 118.3 (C-9, C-12), 95.4 (CCl₃), 75.2 (C-13), 70.2 (C-3, C-5), 69.9 (C-4), 55.5 (C-2, C-6), 39.0 (C-7, C-10), 20.9 (CH₃CO), 20.7 (CH₃CO).

**IR (cm⁻¹) (NaCl; FTIR):** 2951.2 ; 1750.3 ; 1714.8 ; 1223.0

**HRMS:** [M+Na]⁺ 536.0617 (calculated for C₂₀H₂₆NO₈NaCl₃ : 536.0622)
6. Synthesis of compound 6b from 5b

![Chemical structure of 5b and 6b]

Procedure:

2,2,2-trichloroethyl chloroformate (0.312 mL, 2.269 mmol) was slowly added to a solution of 5b (154 mg, 0.454 mmol) in dry pyridine (10 mL). The reaction was vigorously stirred for 48 h and the pyridine was evaporated. The crude product was then redissolved in CH₂Cl₂ and the organic phase was washed using HCl 1N (a sufficient amount to remove pyridine and the unreacted starting material (same Rf)). The desired product 6b was purified by flash chromatography using EtOAc/PE (20/80) (159 mg; 73%).

¹H NMR (400 MHz, CDCl₃) δ 5.90 – 5.68 (m, 2H, H-8, H-11), 5.56 (t, J = 10.5, 1H, H-4), 5.13-5.06 (2 d, J = 11.3, 13.7, 4H, H-9, H-12), 5.02 – 4.97 (m, 2H, H-3, H-5), 4.95 (d, J ~ 12.0 1H, H-13B), 4.93 – 4.83 (m, 2H, H-2, H-6), 4.61 (d, J ~ 12.0, 1H, H-13A), 2.77 – 2.57 (m, 2H, H-7, H-10), 2.55 – 2.32 (m, 2H, H-7, H-10), 2.13 – 1.90 (m, 10H, OAc).

¹³C NMR (101 MHz, CDCl₃) δ 170.0 (CO), 169.6-169.4 (CO), 153.8 (NCOO), 135.2-134.9 (C-8, C-11), 117.5-117.2 (C-9, C-12), 95.1 (CCl₃), 75.5 (C-13), 70.9-70.3 (C-3, C-5), 66.8 (C-4), 53.0-52.7 (C-2, C-6), 35.7-35.0 (C-7, C-10), 20.7 (CH₃CO), 20.7 (CH₃CO).

IR (cm⁻¹) (NaCl; FTIR) : 3078.2 ; 2951.8 ; 1751.2 ; 1715.9 ; 1224.5

HRMS: [M+Na]^+ = 536.0609 (calculated for C₂₀H₂₆NO₈NaCl₃ : 536.0622)

7. Synthesis of compound 7a from 6a. RCM

![Chemical structure of 6a and 7a]

Procedure:

To a solution of 6a (0.400 g, 0.777 mmol) in anhydrous CH₂Cl₂ (16 mL) under Ar, was added Grubbs’ catalyst I (0.064 g, 0.078 mmol), the mixture was degassed and then heated under reflux. After 4 h the reaction was cooled down. DMSO (0.27 mL, 3.89 mmol) was added and
the reaction mixture was stirred overnight. The desired product 7a (371 mg; 98%) was purified by column chromatography using EtOAc/PE (20/80).

$^1$H NMR (400 MHz, CDCl$_3$) δ 5.91 (br s, 2H, H-8, H-9), 5.28 (m, 1H, H-4), 5.03 – 4.90 (m, 3H, H-3, H-5, H-11B), 4.68 (m, 1H, H-11A), 4.48 (2 m, 2H, H-2, H-6), 2.71 – 2.42 (m, 4H, H-7, H-10), 2.06 (2s, 6H, CH$_3$CO), 2.02 (s, 3H, CH$_3$CO).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.8-170.2 (CO), 153.0 (NCO), 129.6-129.1 (C-8, C-9), 75.2 (C-11), 72.7-72.6 (C-3, C-5), 70.3 (C-4), 56.4-56.3 (C-2, C-6), 33.6-33.1 (C-3, C-7), 20.8-20.7 (CH$_3$COO).

IR (cm$^{-1}$) (NaCl ; FTIR) : 2957.5 ; 1746.5 ; 1712.3 ; 1215.5

HRMS: [M+Na]$^+$ = 508.0296 (calculated for C$_{18}$H$_{22}$NO$_8$NaCl$_3$ = 508.0309)

8. Synthesis of compound 7b from 6b. RCM

![Diagram showing the reaction](image)

Procedure:

To a solution of 6b (117 mg, 0.227 mmol) in anhydrous CH$_2$Cl$_2$ (5 mL) under Ar, was added Grubbs' catalyst I (18 mg, 0.023 mmol) and the mixture was degassed and then heated under reflux. After 3 h the reaction was cooled down. Then DMSO (0.081 mL, 1.136 mmol) was added and the reaction mixture was stirred overnight. The desired product 7b (106 mg; 96%) was purified by column chromatography using EtOAc/PE (20/80).

$^1$H NMR (400 MHz, CDCl$_3$) δ 6.07 (t, J = 10.0, 1H, H-4), 5.95 (bs, 2H, H-8, H-9), 5.16 – 5.02 (m, 2H, H-3, H-5), 4.99 (d, J = 11.9, 1H, H-11B), 4.83 (bs, 2H, H-2, H-6), 4.64 (d, J = 11.9, 1H, H-11A), 2.56 – 2.39 (m, 4H, H-7, H-10), 2.09-2.07 (s, 6H, CH$_3$COO), 2.00 (s, 3H, CH$_3$COO).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.8 (CO), 169.6 (CO), 153.3 (NCO), 130.6 (C-8, C-9), 130.2 (C-8, C-9), 95.2 (CCl$_3$), 75.3 (C-11), 71.9 (C-3, C-5), 71.4 (C-3, C-5), 69.4 (C-4), 50.4 (C-2, C-6), 29.4 (CH$_3$COO), 28.9 (CH$_3$COO).

IR (cm$^{-1}$) (NaCl ; FTIR) : 1751.3 ; 1717.8 ; 1215.5

HRMS: [M+Na]$^+$ = 508.0323 (calculated for C$_{18}$H$_{22}$NO$_8$NaCl$_3$ = 508.0309)

9. Deprotection of the Troc protecting groups.

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Procedure:

To a solution of 7a (100 mg, 0.205 mmol) in EtOAc (4 mL)/acetic acid (0.4 mL) (10/1, v/v) was added Zinc dust (1 g, 15.41 mmol). After having been stirred at r.t. for 12 h, the reaction mixture was diluted with CH$_2$Cl$_2$ and filtered through a short pad of celite. The filtrate was washed with sat aq NaHCO$_3$, dried over MgSO$_4$ and concentrated under reduced pressure. The product 8a was purified by silica gel chromatography using EtOAc as the eluant (52 mg, 0.167 mmol, 81 % yield).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.02 – 5.87 (m, 2H, H-8, H-9), 5.46 (t, $J$ = 9.5, 1H, H-4), 4.83 (dd, $J$ = 3.4, 9.5, 2H, H-3, H-5), 4.64 (bs, NH), 3.54 (m, $J$ = 3.7, 7.4, 2H, H-2, H-6), 2.73 – 2.50 and 2.38 – 2.32 (m, 4H, H-7, H-10), 2.06 (s, 6H, CH$_3$COO), 2.03 (s, 3H, CH$_3$CO).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.2 (COO), 169.9 (COO), 129.9 (C-8, C-9), 73.0 (C-3, C-5), 70.4 (C-4), 55.9 (C-2, C-6), 34.1 (C-7, C-10), 20.9 (CH$_3$CO), 20.7 (CH$_3$CO).

IR (cm$^{-1}$) (NaCl ; FTIR) : 2934.0 ; 1738.0 ; 1225.1 ; 1031.1

HRMS: [M+H]$^+$= 312.1454 (Calculated for C$_{15}$H$_{22}$NO$_6$ = 312.1447).

Procedure:

To a solution of 7b (0.106 g, 0.218 mmol) in EtOAc (4.4 mL)/acetic Acid (0.44 mL) (10/1, v/v) was added Zinc dust (1g, 16.33 mmol). After having been stirred at r.t. for 12 h, the reaction mixture was diluted with CH$_2$Cl$_2$ and filtered through a short pad of celite. The filtrate was washed with sat aq NaHCO$_3$, dried over MgSO$_4$ and concentrated under reduced pressure. The product 8b was purified by silica gel chromatography using EtOAc as solvent (56 mg, 0.180 mmol, 83 % yield).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.02 (t, $J$ = 9.9, 1H, H-4), 5.97 – 5.87 (m, 2H, H-8, H-9), 4.96 (dd, $J$ = 6.7, 9.9, 2H, H-3, H-5), 3.57 – 3.44 (m, 2H, H-2, H-6), 2.48 – 2.30 (m, 4H, H-7, H-10), 2.05 (s, 6H, CH$_3$CO), 1.99 (s, 3H, CH$_3$CO).
$^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.3 (s, COO), 170.3 (s, COO), 131.1 (s, C-8, C-9), 75.1 (s, C-3, C-5), 69.9 (s, C-4), 50.5 (s, C-2, C-6), 31.8 (s, C-7, C-10), 20.9 (s, CH$_3$CO), IR (cm$^{-1}$) (NaCl ; FTIR) : 2936.6 ; 1743.4 ; 1228.5
HRMS: [M+H]$^+$ = 312.1448 (calculated for C$_{15}$H$_{22}$NO$_6$ = 312.1447)

10. Synthesis of compound 9a from 8a

![Chemical structure of 8a and 9a]

Procedure:

To a solution of 8a (56 mg, 0.180 mmol) in dry THF (12 mL) was added 1M allylmagnesium bromide in Et$_2$O (1.26 mL, 1.26 mmol). The reaction mixture was stirred for 12 h under Ar. The crude mixture was hydrolyzed with water and the two phases were filtered over celite. The aqueous phase was evaporated and the desired product 9a purified over Dowex® (50W100, H$^+$ form) (30 mg, 0.162 mmol, 90 % yield)

$^1$H NMR (400 MHz, CD$_3$OD) δ 5.81 – 5.70 (m, 2H, H-8, H-9), 3.50 (t, J = 9.7, 1H, H-4), 3.24 (dd, J = 4.2, 9.6, 2H, H-3, H-5), 3.12 (m, 2H, H-2, H-6), 2.58 – 2.33 (m, 4H, H-7, H-10). $^{13}$C NMR (101 MHz, CD$_3$OD) δ 130.7 (C-8, C-9), 75.9 (C-4), 75.7 (C-3, C-5), 60.3 (C-2, C-6), 36.5 (C-7, C-10). IR (cm$^{-1}$) (NaCl ; FTIR) : 3295.1 ; 2916.8 ; 1428.3 ; 1016.2
HRMS: [M+H]$^+$ = 186.1123 (Calculated for C$_9$H$_{16}$NO$_3$ = 186.1130).

11. Synthesis of compound 9b from 8b

![Chemical structure of 8b and 9b]

Procedure:

To a solution of 8b (56 mg, 0.180 mmol) in dry THF (12 mL) was added 1M allylmagnesium bromide in Et$_2$O (1.26 mL, 1.26 mmol). The reaction mixture was stirred for 12 h under Ar. The crude product was hydrolyzed with water and the two phases were filtered over celite.
The aqueous phase was evaporated and the desired product 9b purified over Dowex® (50W100, H+ form) (33 mg, 0.180 mmol, 100 % yield).

\(^1\)H NMR (400 MHz, D\(_2\)O) δ 5.93 – 5.81 (m, 2H, H-8, H-9), 4.29 (t, \(J = 9.6\), 1H, H-4), 3.77 (dd, \(J = 6.5, 9.6\), 2H, H-3, H-5), 3.53 (m, 2H, H-2, H-6), 2.67 (ddd, \(J = 3.7, 8.1, 16.4\), 2H, H-7, H-10), 2.43 (dd, \(J = 3.4, 16.1\), 2H, H-7, H-10).

\(^13\)C NMR (101 MHz, D\(_2\)O) δ 133.3 (C-8, C-9), 76.0 (C-3, C-5), 74.2 (C-4), 55.2 (C-2, C-6), 30.8 (C-7, C-10).

IR (cm\(^{-1}\)) (NaCl ; FTIR) : 3329.1 ; 2925.4 ; 1599.2 ; 1032.4

HRMS: [M+H]\(^+\) = 186.1125 (Calculated for C\(_9\)H\(_{16}\)NO\(_3\) = 186.1130).


Procedure:

To a solution of 7a (0.189 g, 0.388 mmol) in THF (1.8 mL)/t-BuOH (5.4 mL)/Water (0.9 mL) was added NMO (N-methyl morpholine N-oxide) (55 mg, 0.466 mmol), and the solution was stirred for 5 min. at ambient temperature. A 2.5% solution of osmium tetroxide in t-BuOH (0.32 mL, 0.026 mmol) was added, and stirring was maintained at r.t. for 18h. The resulting solution was diluted with sat aq Na\(_2\)S\(_2\)O\(_5\) (1 mL), stirred for 30 min and the solids removed by filtration. The filtrate was diluted with water and CH\(_2\)Cl\(_2\) and the aqueous phase was separated and extracted with CH\(_2\)Cl\(_2\). The organic phases were dried and concentrated under vacuum. The crude was engaged in the next step without any purification.

To a solution of this crude mixture (185 mg, 0.355 mmol) in EtOAc (7.6 mL)/acetic acid (770 µL) (10/1, v/v) was added Zinc dust (1.7 g, 26.6 mmol). After having been stirred at r.t. for 16 h, the reaction mixture was diluted with EtOAc and filtered through a short pad of celite. The filtrate was dried over MgSO\(_4\) and concentrated under reduced pressure. Purification over silica gel chromatography using EtOAc/Acetone (80/20) yielded 2 products:

13a (22 mg, 0.064 mmol, 18 % yield) Rf: 0.34

\(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 5.24 (t, \(J = 8.5\), 1H, H-4), 4.96 (dd, \(J = 4.4, 8.4\), 2H, H-3, H-5), 4.00 (bd, \(J = 9.7\), 2H, H-8, H-9), 3.28 (dt, \(J = 5.8, 7.1\), 2H, H-2, H-6), 2.28 – 2.12 (m, 2H, H-10, H-7), 2.06 (s, 6H, CH\(_3\)COO), 2.04 (s, 3H, CH\(_3\)COO), 1.79 (ddd, \(J = 3.5, 5.8, 15.0\), 2H, H-10, H-7).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) δ 170.1 (COO), 170.0 (COO), 73.6 (C-8, C-9), 73.4 (C-3, C-5), 73.2 (C-4), 53.2 (C-2, C-6), 34.3 (C-10, C-7), 20.9 (CH\(_3\)COO), 20.8 (CH\(_3\)COO).

IR (cm\(^{-1}\)) (NaCl ; FTIR) : 3339.0 ; 2923.9 ; 1747.2 ; 1234.6
HRMS:  \([\text{M+H}^+]= 346.1490\) (Calculated for \(C_{15}H_{24}NO_8 = 346.1502\)).

12a (45 mg, 0.290 mmol, 37 % yield) Rf: 0.25.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.28 – 5.13 (m, 3H, H-3, H-4, H-5), 4.17 (dd, \(J = 3.0, 5.5, 2H, H-8, H-9\)), 3.19 (td, \(J = 3.9, 6.9, 2H, H-2, H-6\)), 2.15 – 2.07 (m, 2H, H-10, H-7), 2.06 (s, 6H, CH\(_3\)COO), 2.04 (s, 3H, CH\(_3\)COO), 1.97 (ddd, \(J = 3.4, 7.5, 15.0, 2H, H-10, H-7\)).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 171.0 (COO), 170.5 (COO), 75.8 (C-3, C-5), 73.6 (C-4), 72.3 (C-8, C-9), 53.9 (C-2, C-6), 35.3 (C-10, C-7), 21.2 (CH\(_3\)COO), 21.1 (CH\(_3\)COO).

IR (cm\(^{-1}\)) (NaCl; FTIR) : 3439.1; 2925.3; 1734.0; 1232.4

HRMS:  \([\text{M+H}^+]= 346.1489\) (Calculated for \(C_{15}H_{24}NO_8 = 346.1502\)).

Deprotection of acetates, compound 15a:

A catalytic amount of sodium was added to dry methanol (5.79 mL) and this mixture was added dropwise to 12a (26 mg, 0.075 mmol). The reaction mixture was stirred for 2 h and then water (1 mL) was added. The aqueous phase was then loaded onto Dowex\(^8\) (50W100, H\(^+\) form) and the desired product purified to give compound 15a as a white solid (10 mg, 0.046 mmol, 61 % yield).

\(^1\)H NMR (400 MHz, CD\(_3\)OD) \(\delta\) 4.10 – 4.05 (m, 2H, H-8, H-9), 3.79 (dd, \(J = 4.2, 8.3, 2H, H-3, H-5\)), 3.00 – 2.88 (m, 2H, H-2, H-6), 2.06 (dt, \(J = 6.4, 14.5, 2H, H-7, H-10\)), 1.80 (ddd, \(J = 3.6, 7.7, 14.8, 2H, H-7, H-10\)).

\(^13\)C NMR (101 MHz, CD\(_3\)OD) \(\delta\) 79.33 (C-4), 76.70 (C-3, C-5), 73.43 (C-8, C-9), 57.95 (C-2, C-6), 36.12 (C-7, C-10).

IR (cm\(^{-1}\)) (NaCl; FTIR): 3314.1; 2921.3; 1082.4

HRMS:  \([\text{M+H}^+]= 220.1192\) (calculated for \(C_9H_{18}NO_5 = 220.1185\))

13. Synthesis of compounds 10b and 11b from 7b

![Diagram](image)

Procedure:

To a solution of 7b (134 mg, 0.275 mmol) in THF (2.7 mL)/t-BuOH (8 mL)/water (1.3 mL) was added NMO (N-methyl morpholine N-oxide) (39 mg, 0.330 mmol), and the solution was stirred for 5 min. at ambient temperature. A 2.5% solution of osmium tetroxide in t-BuOH (228 µL, 0.018 mmol) was added and stirring was maintained at r.t. for 18 h. The resulting solution was diluted with satd aq Na\(_2\)S\(_2\)O\(_5\) (1 mL), stirred for 30 min. and filtered. The filtrate was diluted with water and CH\(_2\)Cl\(_2\) and the aqueous phase was extracted with CH\(_2\)Cl\(_2\). The organic phases were dried and concentrated under vacuum. The crude product was engaged in the next step without any purification.
To a solution of this crude mixture (143 mg, 0.275 mmol) in EtOAc (5.5 mL) /acetic acid (555 µL) (10/1, v/v) was added Zinc dust (1.35 mg, 20.60 mmol). After being stirred at room temperature for 16 h, the reaction mixture was diluted with EtOAc and filtered through a short pad of celite. The filtrate was dried over MgSO₄ and concentrated under reduced pressure. Purification by flash chromatography was carried out using CH₂Cl₂/MeOH/NH₃ (97/2/1).

**11b** (41 mg, 0.119 mmol, 43 % yield)

**¹H NMR (400 MHz, CDCl₃)** δ 5.35 (t, J = 10.4, 1H, H-4), 4.82 (dd, J = 6.6, 10.4, 2H, H-3, H-5), 4.02 (dd, J = 2.5, 6.2, 2H, H-8, H-9), 3.70 (ddd, J = 4.2, 6.6, 9.3, 2H, H-2, H-6), 2.10 – 1.98 (m, 11H, CH₃COO, H-7, H-10), 1.97 – 1.83 (m, 2H, H-7, H-10).  

**¹³C NMR (101 MHz, CDCl₃)** δ 170.1 (COO), 170.0 (COO), 73.7 (C-8, C-9), 73.6 (C-3, C-5), 68.2 (C-4), 49.0 (C-2, C-6), 30.0 (C-7, C-10), 20.7 (CH₃COO), 20.7 (CH₃COO).  

**IR (cm⁻¹) (NaCl ; FTIR)** : 3337.5 ; 2936.5 ; 1745.3 ; 1227.2  

**HRMS:** [M+H]^+ = 346.1489 (Calculated for C₁₅H₂₄NO₈ = 346.1502)

**10b** (14 mg, 0.041 mmol, 15 % yield)

**¹H NMR (400 MHz, CDCl₃)** δ 5.98 (t, J = 10.0, 1H, H-4), 4.77 (dd, J = 6.4, 10.0, 2H, H-3, H-5), 4.31 – 4.18 (m, 2H, H-8, H-9), 3.58 (dt, J = 6.5, 9.5, 2H, H-2, H-6), 2.10 – 1.98 (m, 11H, CH₃COO, H-7, H-10), 1.92 – 1.82 (m, 2H, H-7, H-10).  

**¹³C NMR (101 MHz, CDCl₃)** δ 170.4 (COO), 170.3 (COO), 74.7 (C-3, C-5), 70.1 (C-8, C-9), 68.6 (C-4), 48.8 (C-2, C-6), 31.5 (C-7, C-10), 20.8 (CH₃COO).  

**IR (cm⁻¹) (NaCl ; FTIR)** : 3347.7 ; 2929.1 ; 1796.0 ; 1739.9 ; 1068.6  

**HRMS:** [M+H]^+ = 346.1486 (Calculated for C₁₅H₂₄NO₈ = 346.1502).

Crystal Data for compound 11b : formula C₁₅H₂₃NO₈, triclinic, space group P - T; a = 7.1040(3), b = 10.6930(5), c = 11.4430(4) Å, α = 88.492(2)°, β = 78.420(3)°, γ = 76.727(2)°, V = 828.63(6) Å³, Z = 2 ; M = 345.34 g ; Dₑ = 1.384 g.cm⁻³ ; F(000) = 368. Diffraction data were collected on a Nonius KappaCCD diffractometer with graphite monochromatized Mo Kα radiation (λ = 0.71073 Å) at 100(1) K and processed using DENZO/SCALEPACK program package [1]. The structure was solved by direct methods using SIR 97 [2] and subsequent analysis of difference Fourier maps. Refinement, based on F², was carried out by full matrix least squares with SHELXL-97 software [3] with anisotropic displacement parameters for all non-hydrogen atoms. The amine hydrogen was located on a difference Fourier map and refined with free displacement parameter. Other hydrogens were included at calculated positions and refined as riding with Uiso(H) values equal to 1.2 Ueq and 1.5 Ueq of carrier atom for sugar and methyl H atoms respectively. The refinement converged at R = 0.0441 for 2708 reflections (I > 2 σ(I)) and R = 0.0719, wR2 = 0.1022 for all 3785 reflections and S = 1.029. The highest residual electron density in the final difference Fourier map was 0.243 e.Å⁻³, the lowest was −0.236 e.Å⁻³.

14. ORTEP view of compound 11b

15. Synthesis of compound 14a, reduction of compound 8a

Procedure:

Crude 8a, obtained from 7a (71 mg, 0.146 mmol), was dissolved in methanol (10 mL) and palladium on carbon (10%) (10 mg, 0.094 mmol) was added. Then an aqueous solution of HCl 1M (0.19 mL) was added and the reaction mixture was degassed and stirred under a hydrogen atmosphere for 2 h. The product was purified over Dowex® (50W100, H⁺ form).

A catalytic amount of sodium was added to dry methanol (7.36 mL) and this mixture was added dropwise to the previous crude mixture (30 mg, 0.096 mmol). The reaction mixture was stirred for 2 h and water (1 mL) was added. The crude was then purified over Dowex® (50W100, H⁺ form). Desired product 14a was obtained in 66% over 3 steps.

$^1$H NMR (400 MHz, CD$_3$OD): $\delta$ 3.69 (t, $J = 9.4$, 1H, H-4), 3.60 (dd, $J = 6.3$, 9.2, 2H, H-3, H-5), 3.35 (m, 2H, H-2, H-6), 1.97 – 1.84 (m, 2H, H-7, H-10), 1.83 – 1.70 (m, 2H, H-8, H-9), 1.69 – 1.58 (m, 4H, H-7, H-9, H-8, H-10).
$^{13}$C NMR (101 MHz, CD$_3$OD): δ 75.0 (C-3, C-5), 73.4 (C-4), 56.7 (C-2, C-6), 27.5 (C-7, C-10), 24.7 (C-8, C-9).

IR (cm$^{-1}$) (NaCl; FTIR): 3314.8; 2932.8; 1074.1

HRMS: [M+H]$^+$ = 188.1285 (calculated for C$_9$H$_{18}$NO$_3$ = 188.1287).