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Chemoenzymatic synthesis of glycosyl-deoxyinositol derivatives. First example of a fagopyritol β-analogue containing an aminoinositol unit

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ABSTRACT

The first synthesis of two fagopyritol β-analogues (β-D-galactopyranosyl-(1′→1)-conduramine F-4 and β-D-galactopyranosyl-(1′→3)-4-aminodeoxy-L-*chiro*-inositol) has been accomplished by a chemoenzymatic route in satisfactory yields. The key step of the synthesis is the TMSOTf-promoted glycosylation reaction of a deoxyconduritol derivative. The methodology is amenable to scale-up and expandable to the preparation of other pseudofagopyritols.

1. Introduction

Over 40 years ago, Gibson et al. reported the controlled microbial oxidation of several benzene derivatives to cyclohexadienediols employing the blocked mutant *Pseudomonas putida* F39/D.[1,2] Despite the complete stereospecificity of the reaction, little use of this transformation had been made in organic synthesis until nearly twenty years after with the synthesis of (+)-pinitol from benzene by Ley et al.[3] After this, the growth in applications of the arene dioxygenase enzymes to enantioselective synthesis has been large and it has been the object of several reviews.[4,5]

To the best of our knowledge, there are no reports in the literature on the use of these bacterial metabolite derivatives as partners in a glycosylation reaction to generate fagopyritol analogues.

Fagopyritols are pseudo-oligosaccharides composed of a cyclitol unit and a sugar molecule. Particular importance is given to dimers formed by D- and L-*chiro*-inositol with hexoses since there is evidence that insulin resistance is related to a decreased D-*chiro*-inositol concentration in plasma in type II diabetes mellitus patients.[6]

Therefore, we have embraced the search for a short strategy to prepare fagopyritol β-analogues and we report herein the first synthesis of β-D-galactopyranosyl-(1′→1)-conduramine F-4 and β-D-galactopyranosyl-(1′→3)-4-aminodeoxy-L-*chiro*-inositol where the cyclitol moiety was prepared by a chemoenzymatic route and glycosylated using the trichloroacetimidate method.

2. Results and discussion

We first made use of the enzymatic catalysis by exposing bromobenzene to a culture of the mutant strain *P. putida* F39/D to incorporate chirality and prepared the *cis*-cyclohexadienediol **2** with complete regio- and stereoselectivity (Scheme 1). We have previously used this methodology for the preparation of inositols,[7] aminoconduritols,[8] and sulfur containing cyclitol analogues[9,10] introducing the required functionality in the cyclohexadiene nucleus in a stereospecific fashion. The known epoxide **3**[11] was available in two steps from the homochiral metabolite **2** which was subjected to radical dehalogenation using $SnBu_3H$ as the hydrogen donor and azobiscyclohexancarbonitrile (ABCC) as an initiator. Azidolysis of the debrominated compound gave hydroxyazide **4**,[12] which was envisioned to be a useful intermediate bearing a nucleophilic hydroxyl moiety that can operate in the glycosylation reaction.

Glycoside bond formation is often the key step in most carbohydrate synthesis.[13] The ability of *O*-glycosyl trichloroacetimidates (*O*-TCAs)[14] to act as glycosyl donors under mild acid catalysis, usually giving a high product yield and excellent stereoselectivity,[15] prompted us to choose **5** (Scheme 2) as a donor because of its accurate reactivity to furnish regio- and stereoselectively the β-isomer as the main product in the glycosylation reaction. Compound **5** was prepared according to the established literature procedures.[16]

The glycosylation of acceptor **4** with donor **5** in the presence of a catalytic amount of TMSOTf at −15 °C yielded glycoside **6** in excellent yield, and no additional products were detected in the reaction (Scheme 2). The structure of compound **6** was corroborated by means of 2D NMR spectroscopy (COSY, HSQC) which identified the anomeric proton (δ = 4.8 ppm, J = 8.0 Hz) and confirmed the downfield shift of the carbon bearing the glycosidic moiety. In this case, the stereochemical outcome of the glycosylation reaction is governed by neighboring group participation.[17–20] Zemplen's method was applied to the deacylation of **9** giving the desired compound **7** in 74% yield.

In order to obtain the desired pseudodisaccharide, two final steps were required: removal of the isopropylidene group and

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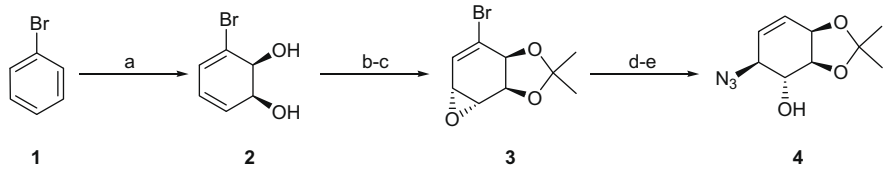
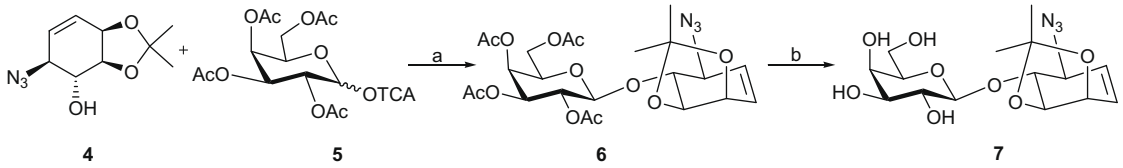


Scheme 1. Chemoenzymatic preparation of the azidoconduritol derivative **4**. Reagents and conditions: (a) *P. putida* F39/D, mineral broth, arginine, 28 °C, 48 h, 2 g/L; (b) DMP, *p*-TsOH, acetone, rt, 30 min, 98%; (c) *m*-CPBA, CH_2Cl_2, rt, overnight, 85%; (d) ABCC, HBu_3Sn, THF, reflux, 88%; (e) NaN_3, NH_4Cl, THF–EtOH–H_2O, reflux, 1 h, 95%.

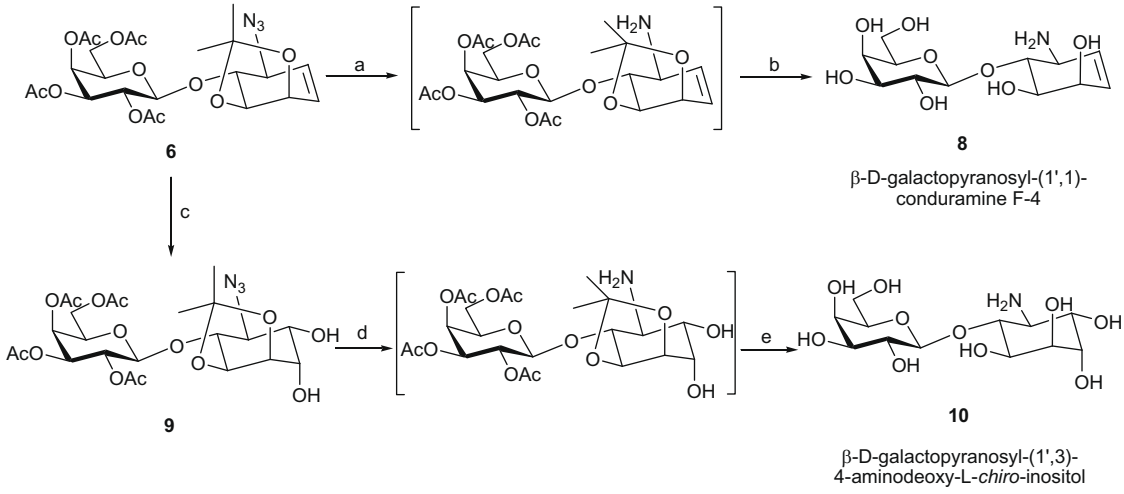


Scheme 2. Glycosylation reaction between hydroxyazide **4** and trichloroacetimidate **5** and deacylation of **6**. Reagents and conditions: (a) TMSOTf, CH_2Cl_2, −15 °C, 0.5 h, 92%; (b) MeONa, MeOH, rt, 1 h, 74%.

reduction of the azide group in dimer **7**. Therefore, the compound was subjected to Dowex resin acid-catalyzed hydrolysis at room temperature to remove the acetal, but the starting material was recovered unchanged. At this point, we decided to warm the reaction mixture initially to 40 °C and then to reflux. Unfortunately, mild warming of the reaction was ineffective and the products obtained by heating at reflux were derived from the cleavage of the glycosidic linkage.

In light of this, we reasoned out that the desired compound could be obtained by inverting the order of events so as to avoid the problems which arose during hydrolysis of the cyclic acetal. First, we exposed **6** to a Staüdinger type reduction of the azide group and then we subjected the crude mixture to Dowex resin catalyzed hydrolysis (Scheme 3). This last step was carried out inside a chromatography column loaded with Dowex resin in its acidic form. We had previously used this protocol with very good results in the synthesis of (−)-conduramine C-4,[8] hence we decided to test it in the one-pot synthesis of **8** from **9**. We were thrilled when this procedure gave enantiopure β-D-galactopyranosyl-(1′→1)-6-amino-cyclohex-4-ene-2,3-diol **8** (conduramine F-4 numbering) as the only product in 80% yield for the two consecutive operations (51% overall yield from **2**). Spectroscopic analysis showed that the compound was obtained free from any residue of the starting azide or aminoacetonide but along with variable amounts of ammonium acetate. The contaminant did not preclude the analysis but was observable as a sharp peak in the proton NMR.

In an attempt to synthesize a fagopyritol analogue bearing an inositol unit, glycoside **6** was oxidized using catalytic $RuCl_3$ and $NaIO_4$ as a co-oxidant. In particular, Hudlicky and Desjardins had described the dihydroxylation of a conduritol acetal with a $RuCl_3$–$NaIO_4$ mixture in their synthesis of *allo*-inositol.[21] RuO_4 is isoelectronic to OsO_4 and several reports in the literature describe its use as an effective and greener alternative for the dihydroxylation of unreactive alkenes.[22–24] It is known that RuO_4 can rapidly cleave C,C-double bonds.[25,26] However, the nucleophilic addition of water to the intermediate ruthenate is faster in a 3:3:1 mixture of ethyl acetate, acetonitrile and water. Any other solvent combination facilitated the scission reaction.[25] As a consequence we chose this ternary solvent mixture. Under these conditions, dihydroxylation of **6** furnished *syn*-diol **9** with the reaction completed within 2 h. With dihydroxylation under kinetic control being the less hindered L-*chiro*-like isomer was exclusively formed as we previously observed in our thiocyanodeoxy-L-*chiro*-inositol synthesis.[9] Analysis of the spectra of compound **9** showed that the key



Scheme 3. One-pot sequence for the synthesis of fagopyritol analogues **8** and **10**. Reagents and conditions: (a) PPh_3, THF, rt, 24 h, then H_2O, rt, 4 h; (b) Dowex-resin (H^+ form), MeOH and then NH_4OH 2 M, 80% (both steps); (c) $RuCl_3$–$NaIO_4$, AcOEt–CH_3CN–H_2O, 0 °C, 3 h, 91%; (d) PPh_3, THF, rt, 24 h, then H_2O, rt, 24 h; (e) Dowex-resin (H^+ form), MeOH and then NH_4OH 2 M, 51% (both steps).

proton H3 is a triplet coupled with a large diaxial coupling constant (J = 10.1 Hz) to the neighboring protons H2 and H4.

The same one-pot procedure applied to the synthesis of **8** was successfully employed here giving **10** in 51% overall yield for both steps (Scheme 3) and in 30% overall yield from metabolite **2**. As for compound **8**, glycoside **10** was obtained next to variables amounts of ammonium acetate.

3. Conclusions

In conclusion, we have completed the first synthesis of a fagopyritol analogue by a chemoenzymatic route. The analogue, β-D-galactopyranosyl-aminodeoxy-L-*chiro*-inositol **10** is the first example of an aminodeoxy-inositol glycoside, and in light of the known literature on fagopyritol bioactivity it might be a potential lead for new biomedical compounds. Furthermore, the one-pot sequence developed for the end game of the synthesis rendered the free glycoside in good yield and is probably amenable for process scale-up. Research on the biological activity of the dimers synthesized is currently in progress and will be disclosed in forthcoming reports.

4. Experimental

4.1. General

All non-hydrolytic reactions were carried out under either a nitrogen or argon atmosphere, with standard techniques for the exclusion of moisture. All solvents were purified and dried prior to use. The commercially available reagents were purchased from Aldrich or Acros and were used without further purification. Optical rotations were measured using a Zuzi 412 automatic polarimeter with a 7 mL cell, a Kruss Optronic GmbH P8000 polarimeter with a 0.5 mL cell or a Perkin–Elmer 341 polarimeter with a 1 mL cell (concentration c given as g/100 mL). Infrared spectra were recorded using a Matheson Excalibur spectrometer and a Vector 22 (Bruker) and peaks are reported in reciprocal centimeter along with relative signal intensities and characteristics: s (strong); m (medium); and w (with). Nuclear magnetic resonance spectra were recorded on a Bruker Avance DPX-400 instrument or a DPX-500 instrument. Chemical shifts (δ) are given in parts per million and coupling constants (J) are reported in hertz. Low-resolution mass spectra were performed on a Micromass Autospec instrument. High-resolution mass spectra were performed on a Bruker Daltonics model TOF_Q (ESI + mode). Analytical TLC was performed on Silica Gel 60F-254 plates and visualized with UV light (254 nm) and/or anisaldehyde–H_2SO_4–AcOH, ninhydrin, phosphomolybdic acid–Ce_2SO_4–H_2SO_4–H_2O as detecting agent. Flash column chromatography was performed in silica gel (Kieselgel 60, EM Reagents, 230–400 mesh or Merck 60 15–40 mesh.

4.2. (1*R*,2*S*,5*R*,6*R*)-2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′→1)-2-azido-5,6-*O*-isopropylidenedioxycyclohex-3-ene 6

A mixture of hydroxyazide **4**[12] (75.7 mg, 0.36 mmol) and galactopyranosyl-trichloroacetimidate **5** (270.8 mg, 0.55 mmol) in dry CH_2Cl_2 (6.0 mL) was cooled to −15 °C and treated with a solution of TMSOTf in CH_2Cl_2 (9 μL, 0.1 equiv). The reaction mixture was stirred for 30 min at −15 °C until consumption of the starting materials, as monitored by TLC. The suspension was quenched with Et_3N (0.5 mL) and the solvent was evaporated under vacuum to give a residue that was purified by flash chromatography (60/40: hexane/ethyl acetate) to obtain pseudodisaccharide **6** as a colorless oil in 92% yield. $[\alpha]_D^{20} = +20$ (c 0.84, $CHCl_3$); IR (film) ν_{max}/cm^{-1}: 2973 and 2942 (s, C═C), 2109 (s, N_3), 1756 (s, C═O (OAc)), 1097 (s, C–O–C: glycosidic linkage), 1069, 1051 and 1042 (s, C–O–C–O–C: isopropylidene); ESI-MS m/z: 564.0 ((M^++Na), 100), 536.0 ((M^++Na)−N_2, 21); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.96 (dt, 1H, $J_{4,3}$ 10.0 Hz, $J_{4,5}$ 2.4 Hz, H-4), 5.76 (dd, 1H, $J_{3,4}$ 10.0 Hz, $J_{3,2}$ 2.7 Hz, H-3), 5.38 (dd, 1H, $J_{4',3'}$ 3.4 Hz, $J_{4',5'}$ 0.8 Hz, H-4'), 5.26 (dd, 1H, $J_{2',1'}$ 8.1 Hz, $J_{2',3'}$ 10.4 Hz, H-2'), 5.04 (dd, 1H, $J_{3',4'}$ 3.5 Hz, $J_{3',2'}$ 10.4 Hz, H-3'), 4.83 (d, 1H, $J_{1',2'}$ 8.0 Hz, H-1'), 4.61 (m, 1H, H-5), 4.25 (dd, 1H, $J_{6,5}$ 6.4 Hz, $J_{6,1}$ 8.0 Hz, H-6), 4.15 (d, 2H, $J_{6',5'}$ 6.6 Hz, H-6'), 3.91 (d, 1H, $J_{5',6'}$ 6.8 Hz, H-5'), 3.88 (br d, 1H, $J_{2,1}$ 8.2 Hz, H-2), 3.69 (t, 1H, $J_{1,6}$ 8.0 Hz, $J_{1,2}$ 8.0 Hz, H-1), 2.14 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.49 (s, 3H, CH_3), 1.38 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.2 (C (OAc)), 170.0 (C (OAc)), 169.3 (2 C (OAc)), 127.9 (C 3), 126.7 (C 4), 110.3 (C, isopropylidene), 101.0 (C 1'), 79.7 (C 1), 75.5 (C 6), 72.0 (C 5), 71.0 (C 3'), 70.9 (C 5'), 69.0 (C 2'), 67.1 (C 4'), 61.3 (C 6'), 61.0 (C 2), 27.9 (CH_3, isopropylidene), 25.7 (CH_3, isopropylidene), 20.6 (CH_3 (OAc)), 20.5 (CH_3 (OAc)), 20.5 (CH_3 (OAc)), 20.4 (CH_3 (OAc)). HRMS (FAB^+) m/z calcd for $(C_{23}H_{31}N_3O_{12}Na)^+$: 564.1805; found: 564.1825.

4.3. (1*R*,2*S*,5*R*,6*R*)-β-D-Galactopyranosyl-(1'→1)-2-azido-5,6-*O*-isopropylidenedioxycyclohex-3-ene 7

To a solution of **6** (16.0 mg, 0.029 mmol) in anhydrous MeOH (3 mL), MeONa (10.0 mg, 0.185 mmol) was added under an argon atmosphere. The reaction mixture was stirred at rt for 1 h whereupon it was quenched with Amberlite IR-120 H^+ resin. The resin was filtered off and the solvent was removed under reduced pressure to give **7** in 74% yield as a colorless oil. $[\alpha]_D^{20} = +11$ (c 0.40, MeOH); IR (film) ν_{max}/cm^{-1}: 3458-3284 (w, OH), 2100 (s, N_3), 1065 (s, C–O–C: glycosidic linkage), 1042 (s, C–O–C–O–C: isopropylidene); ESI-MS (m/z): 396 (M^++Na, 100); ^{1}H NMR (MeOD, 500 MHz) δ: 5.97 (dt, 1H, $J_{4,3}$ 10.0 Hz, $J_{4,5}$ 2.0 Hz, H-4), 5.83 (dd, 1H, $J_{3,4}$ 10.0 Hz, $J_{3,2}$ 1.5 Hz, H-3), 4.69 (m, 1H, H-5), 4.58 (d, 1H, $J_{1',2'}$ 7.5 Hz, H-1'), 4.37 (t, 1H, $J_{6,1}$ 7.0 Hz, $J_{6,5}$ 7.0 Hz, H-6), 4.08 (br dd, 1H, $J_{2,3}$ 1.5 Hz, $J_{2,1}$ 7.5 Hz, H-2), 3.89 (t, 1H, $J_{1,2}$ 7.5 Hz, $J_{1,6}$ 7.5 Hz, H-1), 3.86 (m, 1H, H-4'), 3.77 (d, 2H, $J_{6',5'}$ 6.5 Hz, H-6'), 3.59–3.54 (m, 2H, H-3' and H-5'), 3.51 (dd, $J_{2',1'}$ 7.0 Hz, $J_{2',3'}$ 9.5 Hz, H-2'), 1.50 (s, 3H, CH_3), 1.39 (s, 3H, CH_3); ^{13}C NMR (MeOD, 125 MHz) δ: 128.8 (C 3), 128.1 (C 4), 111.4 (C, isopropylidene), 104.5 (C 1'), 79.2 (C 1), 76.9 (C 6), 76.6 (C 5'), 75.1 (C 2'), 73.4 (C 5), 72.7 (C 3'), 70.3 (C 4'), 62.2 (C 6'), 61.7 (C 2), 28.3 (CH_3, isopropylidene), 26.1 (CH_3, isopropylidene). HRMS (FAB^+) m/z calcd for $(C_{15}H_{23}N_3O_8Na)^+$: 396.1383; found: 396.1401.

4.4. β-D-Galactopyranosyl-(1'→1)-conduramine F-4 8

Pseudodisaccharide **6** (30.6 mg, 0.057 mmol) was dissolved in anhydrous THF (2 mL) after which PPh_3 was added (53.8 mg, 0.205 mmol) under N_2 atmosphere. After stirring for 24 h at rt, water (25 equiv) was added to the system and the reaction was stirred for other 4 h. The reaction mixture was concentrated under vacuum and the solid obtained was taken in CH_2Cl_2 and applied to a Dowex-50 (H^+ form, 100 mesh) column. It was first eluted with MeOH (to remove triphenylphosphine and triphenylphosphine oxide) and then NH_4OH 2 M (20 mL) was used. The alkaline eluate was evaporated under reduced pressure at 30 °C to give compound **8** as a syrup (80%). $[\alpha]_D^{20} = -12$ (c 0.26, H_2O)*; ^{1}H NMR (MeOD, 400 MHz) δ: 5.92 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{4,3}$ 4.7 Hz, H-4), 5.76 (dd, 1H, $J_{5,4}$ 10.1 Hz, $J_{5,6}$ 2.0 Hz, H-5), 4.48 (d, 1H, $J_{1',2'}$ 7.6 Hz, H-1'), 4.28 (t, 1H, $J_{3,4}$ 4.4 Hz, $J_{3,2}$ 4.4 Hz, H-3), 3.92 (t, 1H, $J_{1,6}$ 8.1 Hz, $J_{1,2}$ 8.1 Hz, H-1), 3.80–3.76 (m, 3H, H-2, H-6 and H-4'), 3.68–3.61 (m, 3H, H-6' (2H) and H-5'), 3.56 (dd, 1H, $J_{3',4'}$ 3.2 Hz, $J_{3',2'}$ 9.9 Hz, H-3'), 3.51 (dd, 1H, $J_{2',1'}$ 7.6 Hz, $J_{2',3'}$ 9.9 Hz, H-2'), 1.78 (s, 1H, NH_4OAc); ^{13}C NMR (D_2O, 100 MHz) δ: 130.4 (C 4), 125.3 (C 5), 103.0 (C 1'), 78.5 (C 1), 75.7 (C 5'), 72.6 (C 3'), 70.7 (C 2'), 69.3 (C

2), 68.6 (C 4'), 66.0 (C 3), 61.0 (C 6'), 52.4 (C 6); HRMS: calcd for $(C_{12}H_{21}NO_8H)^+$: 308.1326; found: 308.1340.

(*) Compound concentration was adjusted to account for the ammonium acetate present in the solution.

4.5. (1*S*,2*S*,3*S*,4*R*,5*S*,6*R*)-2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′→4)-3-azido-5,6-*O*-isopropylidenedioxycyclohexan-1,2-diol 9

A stirred solution of **6** (40.0 mg, 0.073 mmol) in a mixture of ethyl acetate (1.5 mL) and acetonitrile (1.5 mL) was cooled to 0 °C and treated with a mixture of $RuCl_3$ (2.6 mg, 6%)/$NaIO_4$ (24.4 mg, 0.114 mmol) in water (0.5 mL). After being left to stand at 0 °C for 2 hours, $Na_2S_2O_3$ (aq) 20% was added and the mixture was filtered using a pad of silica and washed several times with ethyl acetate. Concentration of the solution rendered a crude oily product, which was purified over silica flash using 40:60 hexane/ethyl acetate as the eluting solvents affording **9** as a colorless oil in 91% yield. $[\alpha]_D^{20} = -57$ (*c* 0.24, CH_2Cl_2); IR (film): 3500 (w, OH), 2116 (s, N_3), 1752 (s, C=O (OAc)), 1078 (s, C–O–C: glycosidic linkage); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.38 (br d, 1H, $J_{4',3'}$ 3.4 Hz, H-4'), 5.25 (dd, 1H, $J_{2',1'}$ 8.1 Hz, $J_{2',3'}$ 10.4 Hz, H-2'), 5.03 (dd, 1H, $J_{3',4'}$ 3.5 Hz, $J_{3',2'}$ 10.4 Hz, H-3'), 4.84 (d, 1H, $J_{1',2'}$ 8.1 Hz, H-1'), 4.28 (m, 3H, H-1, H-5 and H-6), 4.15 (d, 2H, $J_{6',5'}$ 6.6 Hz, H-6'), 3.91 (t, 1H, $J_{5',6'}$ 6.0 Hz, $J_{5',4'}$ 6.0 Hz, H-5'), 3.72 (br d, 1H, $J_{2,3}$ 9.2 Hz, H-2), 3.64 (t, 1H, $J_{3,2}$ 10.1 Hz, $J_{3,4}$ 10.1 Hz, H-3), 3.55 (dd, 1H, $J_{4,5}$ 10.2 Hz, $J_{4,3}$ 10.1 Hz, H-4), 2.99 and 2.92 (br s, 2H, OH), 2.15 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.46 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.5 (C (OAc)), 170.5 (C (OAc)), 170.3 (C (OAc)), 169.7 (C (OAc)), 109.4 (C, isopropylidene), 100.9 (C 1'), 81.9 (C 4), 76.7 (C 5), 76.5 (C 6), 71.1 (C 3'), 71.0 (C 5'), 70.5 (C 2), 69.1 (C 2'), 68.8 (C 1), 67.2 (C 4'), 64.1 (C 3), 61.4 (C 6'), 28.0 (CH_3, isopropylidene), 26.0 (CH_3, isopropylidene), 20.8 (CH_3 (OAc)), 20.7 (2 CH_3 (OAc)), 20.6 (CH_3 (OAc)).

4.6. β-D-Galactopyranosyl-(1′→3)-4-aminodeoxy-L-*chiro*-inositol 10

Pseudoglycoside **9** (24.0 mg, 0.041 mmol) was dissolved in dry THF (4 mL) and PPh_3 (39.0 mg, 0.149 mmol) was added under N_2. The reaction was stirred for 24 h at rt followed by addition of water (25 equiv) and stirred for further 24 h at rt. The reaction mixture was concentrated at reduced pressure and the white residue was dissolved in CH_2Cl_2 and applied to a Dowex-50 (H^+ form, 100 mesh) column, eluting first with MeOH (to remove triphenylphosphine and triphenylphosphine oxide) and then with 2 M NH_4OH (10 mL). The alkaline eluate was concentrated at 30 °C to afford the amino compound **10** as a syrup in 51% yield. $[\alpha]_D^{22} = +12$ (*c* 0.48, H_2O)*; ^{1}H NMR (D_2O, 400 MHz) δ: 4.46 (d, 1H, $J_{1',2'}$ 7.6 Hz, H-1'), 3.99 (m, 1H, H-5'), 3.93 (t, 1H, $J_{4',3'}$ 3.4 Hz, $J_{4',5'}$ 3.4 Hz, H-4'), 3.85–3.82 (m, 4H, H-1, H-3, H-5 and H-6), 3.69–3.63 (br s, 3H, H-6' (2H) and H-2), 3.59 (dd, 1H, $J_{3',2'}$ 9.9 Hz, $J_{3',4'}$ 3.2 Hz, H-3'), 3.56 (dd, 1H, $J_{2',1'}$ 7.5 Hz, $J_{2',3'}$ 9.9 Hz, H-2'), 3.28 (t, 1H, $J_{4,3}$ 9.0 Hz, $J_{4,5}$ 9.0, H-4), 1.80 (s, NH_4OAc); ^{13}C NMR (D_2O, 100 MHz) δ: 103.0 (C 1'), 80.0 (C 3), 75.7 (C 2), 72.5 (C 3'), 71.1 (C 5'), 71.0 (C 4'), 70.7 (C 2'), 69.0 (C 1), 68.5 (C 6), 67.7 (C 5), 60.9 (C 6'), 53.6 (C 4). HRMS: *m/z* calcd for $(C_{12}H_{23}NO_{10}H)^+$: 342.1395; found: 342.1378.

(*) Compound concentration was adjusted to account for the ammonium acetate present in the solution.

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