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TETRAHEDRON: *ASYMMETRY*

Convenient access to both enantiomers of new azido- and aminoinositols via a chemoenzymatic route

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Abstract

1,2-diacetylconduritol E, (±)-**1**, through complementary use of *Mucor miehei* (Lipozyme® IM) and *Candida cylindracea* lipases, affords (1*S*)-1,2-diacetylconduritol E, (+)-**1**, (1*R*)-1,2-diacetylconduritol E, (−)-**1**, (1*S*)-1,2,4-triacetylconduritol E, (+)-**2**, (1*R*)-1,2,4-triacetylconduritol E, (−)-**2**, with high enantiomeric excesses and chemical yields. Following two different methods, diester (+)-**1** has been transformed into azidoinositol (−)-**4** to give 1L-4-amino-4-deoxy-*chiro*-inositol, whereas triester (−)-**2** furnished the azidoinositol (+)-**13**, easily converted into 1L-4-amino-4-deoxy-*myo*-inositol. © 1998 Published by Elsevier Science Ltd. All rights reserved.

1. Introduction

The recent discovery that D-*myo*-inositol 1,4,5-tris(phosphate) is involved in signal transduction in animal cells has caused an increasing interest in inositol analogues. In particular, azido- and amino derivatives have great potential as bioactive molecules, since the direct antiproliferative activity on tumoral cells (fibroblasts) of azido *myo*-inositols has been well-recognised,[1] while the enzyme inhibitory activity of glycosidases reported for free and conjugated aminoinositols plays a central role in antibiotic action.[2]

The presence in the framework of these cyclitols of six stereogenic carbons makes their synthesis in enantiopure form very demanding and only a few examples have been reported as yet. *myo*-Inositol derivatives have been prepared starting from chiral L-quebrachitol[3] or D-glucose,[4] and aminoinositols with the *allo*-configuration have been obtained by stereoselective addition of chiral nitroso-dienophiles to *cis*-1,2-diacetoxycyclohexa-3,5-diene.[5]

Chiral conduritols are promising starting materials for the synthesis of azido- and aminoinositols, since they contain four stereogenic centres of defined configuration and a double bond suitable to introduce two

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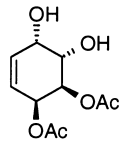
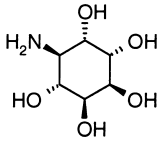
additional ones. Moreover, selective protection of all but one of the hydroxyl groups can be used for the conversion of the free OH group into a nitrogenous substituent or the generation of discriminatory effects at vinylic positions.

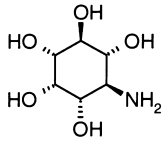
In this paper we wish to describe the preparation of the previously unreported enantiomers of both 4-amino-4-deoxy-*chiro*-inositol and 4-amino-4-deoxy-*myo*-inositol, starting from conduritol E diacetate, (±)-**1** and using biocatalytic procedures paired with stereospecific reactions.



(±)-**1**



4-amino-4-deoxy-*chiro*-inositol

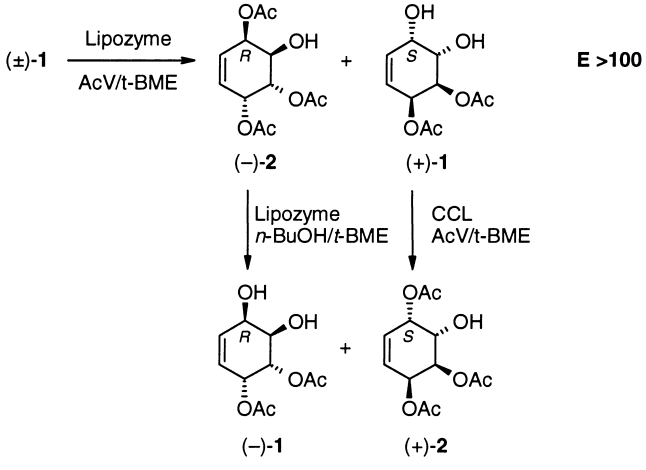


4-amino-4-deoxy-*myo*-inositol

2. Results and discussion

2.1. Preparation of enantiopure (−)-*1* and (+)-*2*

Resolution of (±)-**1** by esterification with vinyl acetate in *tert*-butyl methyl ether promoted by immobilised lipase from *Mucor miehei* (Lipozyme® IM) has been described in a previous paper.[6] This reaction led to the preparation of triacetate (−)-**2** and unreacted diacetate (+)-**1** with high chemical yields and enantiomeric excesses. At the onset of the present work aimed at the synthesis of new aminocyclitols we intended to prepare both enantioforms of these partial esters and therefore we screened several lipases in search of one possessing the opposite stereopreference to that of *M. miehei*. Among the lipases used, only *Candida cylindracea* lipase had the desired (*S*)-stereopreference, but unfortunately its enantioselectivity was low (E=20) and a preparative run afforded (+)-**2** and (−)-**1** with unsatisfactory e.e.[7] Therefore, we resorted to a different approach exploiting the opposite stereopreferences of *M. miehei* and *C. cylindracea* lipases in complementary transesterification reactions (Scheme 1).



Scheme 1.

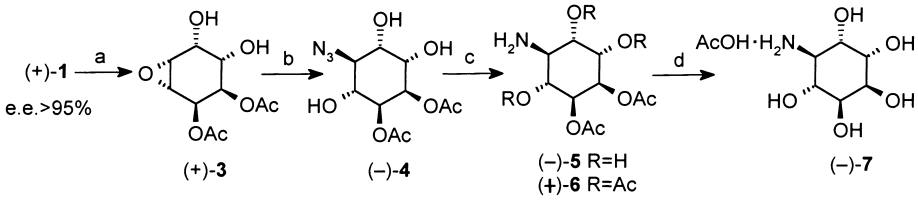
In a first step, racemic (±)-**1** was subjected to kinetic resolution by esterification catalysed by *M. miehei* lipase. Following chromatographic separation, triester (−)-**2** was subjected to regioselective alcoholysis by reaction with *n*-butanol in the presence of Lipozyme® IM to afford after 4 h (−)-**1** in 55% yield and

e.e.>95%. The amount of (−)-**1** did not increase by prolonging the reaction time and products of further deacylation began to form.[8]

Conversely, (+)-**2** with e.e.>95% was obtained by treatment of (+)-**1** with vinyl acetate in the presence of *C. cylindracea*. The hydroxyl group at C-2 did not suffer esterification even after prolonged reaction times, possibly due to steric hindrance, so that the desired triester was in any case the only product.

2.2. Synthesis of new aminoinositols

Enantiopure (+)-**1** and (−)-**2** have been transformed into three new aminoinositols following two different methodologies. In the first one, diester (+)-**1** was converted into amino-*chiro*-inositol (−)-**7** through stereoselective epoxidation followed by regioselective nucleophilic ring opening (Scheme 2).



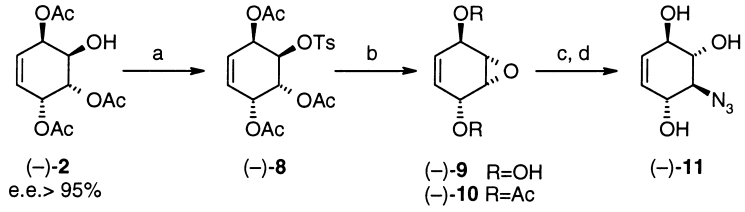
Scheme 2.

Since diester (+)-**1** lacks the C_2-symmetry of the parent tetrol, two diastereoisomeric epoxides could be expected by epoxidation from the double bond. As a matter of fact, reaction of (+)-**1** with *m*-CPBA afforded a single product, (+)-**3**, whose structure, anticipated by taking into consideration the reported *syn*-orientation effect of hydroxyl groups,[9] was subsequently confirmed by the stereochemical outcome of the following ring opening reaction. Treatment of (+)-**3** with NaN_3 yielded the partially protected azidoinositol (−)-**4** as a single product, whose catalytic hydrogenation (Pd/C) gave the corresponding aminoderivative (−)-**5**. In the ^{1}H NMR spectrum of the latter, a distinct resonance at δ 3.42 was present, assigned by heteronuclear correlation to the proton at C-4. Selective decoupling of H-4 showed that the amino group is not adjacent to the ester groups, thus indicating a regioselective attack of the N_3^- on the less hindered position of epoxyderivative (+)-**3**. The stereoselectivity observed in the nucleophilic ring opening of (+)-**3**, higher than that reported for the underivatised conduritol E epoxide,[10] is probably due to loss of C_2-symmetry following the introduction of acetoxy groups. Definite assignment of structure (−)-**5** was possible by its transformation into peracetate (+)-**6**, whose ^{1}H NMR spectrum showed distinct resonances for each methine proton. Complete analysis of all the observed coupling constants and in particular the large values of J_{H3-H4} and J_{H4-H5}, indicating the *trans–trans* diaxial orientation of the three protons in question, allowed compound (+)-**6** to be assigned the same stereochemistry as L-*chiro*-inositol.

Reaction of (−)-**5** with aqueous NH_4OH furnished quantitatively 1L-4-amino-4-deoxy-*chiro*-inositol, isolated as the salt with acetic acid, (−)-**7**. Following the same procedure, 1D-4-amino-4-deoxy-*chiro*-inositol can be prepared starting from (−)-**1**.

In the second method, triester (−)-**2** was profitably used in the preparation of other aminoinositol derivatives. By conventional tosylation it gave (−)-**8**, which has a *trans* relationship between the tosyloxy and a vicinal acetyloxy group, the appropriate requirement to give an intramolecular displacement.[11] Thus, treatment of (−)-**8** with KOH in MeOH (Scheme 3) afforded quantitatively epoxide (−)-**9**, in turn converted into acetate (−)-**10** to avoid possible epoxide migration, a reaction reported for α,β-epoxy alcohols.[12] Treatment of (−)-**10** with NaN_3 in the presence of NH_4Cl and subsequent hydrolysis with

aqueous NH_4OH gave two diastereoisomeric azides in a 9:1 ratio, as shown by ^1H NMR analysis of the crude product.[13]

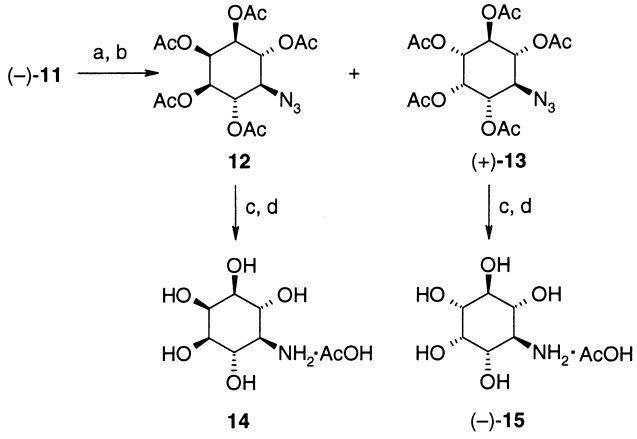


a: TsCl/Py, b: KOH/MeOH, c: NaN_3,NH_4Cl/DMF, d:NH_4OH/MeOH

Scheme 3.

After purification by column chromatography, the major azide, (−)-**11**, was assigned the structure of 2-azidoconduritol B from its magnetic resonance properties. Its ^1H NMR spectrum contains a broad singlet due to the olefinic protons, typical of the conduritol B series,[14] and in addition two partially superimposed double doublets for H-2 and H-3, whose coupling constants confirmed the all-*trans* orientation of H-1–H-4.

Azidoconduritol (−)-**11** by reaction with *N*-methylmorpholine oxide (NMMO) in the presence of catalytic amounts of OsO_4 in 48 h yielded two products of *cis*-dihydroxylation, which were isolated by column chromatography and further purified as the acetates **12** and (+)-**13**, obtained in a ratio of 4:6. Lack of optical activity and simplification of the ^1H NMR spectrum of **12** revealed its *meso*-nature and allowed the structure of 5-azido-5-deoxy-*myo*-inositol pentaacetate to be assigned. Conversely, the presence of five distinct singlets for CH_3CO groups in the ^1H NMR spectrum of (+)-**13** confirmed its structure of 1L-4-azido-4-deoxy-*myo*-inositol. Each azido inositol was then reduced with Pd/C and hydrolysed to give respectively amino derivatives **14** and (−)-**15**, isolated as salts with acetic acid (Scheme 4). Following the same procedure, the amino derivative (+)-**15** can be synthesised starting from triester (+)-**2**.



a: OsO_4/NMMO; b: Ac_2O/Py; c: Pd/C,H_2; d: NH_4OH/MeOH

Scheme 4.

3. Conclusion

The data obtained show that the complementary use of *Mucor miehei* and *Candida cylindracea* lipases, possessing opposite stereoreferences, allows access to both enantiomers of 1,2-diacetyl- and 1,2,4-triacetylconduritol E with high optical and chemical yield. Due to their structural features, these esters can be utilised as key intermediates in the synthesis of compounds of a more complex structure. In our laboratory, 1,2-diacetylconduritol E, (+)-**1**, has been transformed into 1L-4-amino-4-deoxy-*chiro*-inositol, (−)-**7** and 1,2,4-triacetylconduritol E, (−)-**2** has furnished 1L-4-amino-4-deoxy-*myo*-inositol, (−)-**15**, all in good overall yield. Furthermore, the described syntheses also allow chiral epoxy- or azido-derivatives to be obtained which could themselves be bioactive molecules and starting materials for the preparation of other enantiopure cyclitols.

4. Experimental section

^{1}H and ^{13}C NMR spectra were recorded at 250.13 and 62.9 MHz respectively. Chemical shifts (δ) are reported in ppm relative to TMS in the solvent specified; all coupling constants (J) are in hertz. Optical rotations were measured on a DIP 135 JASCO instrument. GC analyses were performed on HP-5 (5% phenylmethylsilicone) or Chiraldex G-DA (dialkyl γ-cyclodextrin) capillary column on a Perkin–Elmer 8500 instrument. Melting points were determined on a MELT-TEMP II, Lab. device and are uncorrected.

All chemicals were purchased from Aldrich or Fluka. Lipases from *Candida cylindracea* and *Pseudomonas cepacia* were obtained from Amano International Enzyme Co. Porcine pancreas lipase was from Sigma. Lipozyme® IM (immobilised lipase from *Mucor miehei*) and Novozym® 435 (immobilised lipase from *Candida antarctica*) are registered marks from Novo Nordisk. Conduritols (+)-**1** and (−)-**2** were available from previous work.[6] Column chromatography was performed on silica gel or LiChroprep® DIOL 40–63 μm (Merck); analytical TLC was carried out on Merck silica gel 60-F_{254} precoated glass plates and compounds were visualised by spraying with molybdophosphoric acid.

*4.1. General procedure for small-scale esterification of 1,2-dihydroxy-3,5-diacetyloxycyclohex-5-ene (±)-**1***

Lipase (20 mg/ml) was added to a solution of (±)-**1** (10 mg/ml) in *t*-BME containing vinyl acetate (30 μl/ml) and the suspension was shaken at 40°C. The progress of the reaction was monitored by GC analysis of aliquots, injected after acylation with propionic anhydride/pyridine. The reaction was then stopped, the enzyme filtered off and the filtrate taken to dryness. After work-up of the reaction mixture on the Si-DIOL column, the enantiomeric excess of triester **2** was determined by chiral GC after conventional acetylation. The stereochemistry of **2** was assessed from its known optical properties.[6]

*4.2. Kinetic resolution of (±)-**1** with* Candida cylindracea *lipase*

Lipase from *C. cylindracea* (600 mg) and vinyl acetate (0.3 ml, 3.2 mmol) were added to a solution of (±)-**1** (300 mg, 1.3 mmol) in *t*-BME (30 ml). The suspension was maintained at 45°C under continuous stirring until conversion of the substrate reached 49% (30 h). The reaction mixture was then filtered and the solution taken to dryness. The residue was then subjected to column chromatography on Si-DIOL (hexane:EtOAc=7:3) to give (+)-**2** with 80% e.e. and unreacted (−)-**1** with 77% e.e.

4.3. (1R,2R,3S,4R)-1,2-Dihydroxy-3,4-diacetyloxycyclohex-5-ene (−)-**1**

Lipozyme (200 mg) and *n*-BuOH (0.033 ml, 0.36 mmol) were added to a solution of (−)-**2** (100 mg, 0.36 mmol, e.e.>95%) in *t*-BME (10 ml). The reaction was monitored by GC analysis and after 4 h (−)-**1** was isolated by column chromatography (hexane:EtOAc=1:1), yield 55%, $[\alpha]_D$ −213.2 (*c* 1.2, $CHCl_3$).

4.4. (1S,2S,3R,4S)-2-Hydroxy-1,3,4-triacetyloxycyclohex-5-ene (+)-**2**

Lipase from *C. cylindracea* (140 mg) and vinyl acetate (0.033 ml, 0.36 mmol) were added to a solution of (+)-**1** (70 mg, 0.30 mmol, e.e.>95%) in *t*-BME (7 ml). After 24 h, conversion was complete (TLC) and (+)-**2** was crystallised from EtOAc:hexane (73 mg, 89% yield); $[\alpha]_D$ +275.8 (*c* 1.2, $CHCl_3$).

4.5. (1R,2S,3R,4S,5R,6R)-1,2-Dihydroxy-3,4-diacetyloxy-5,6-epoxycyclohexane (+)-**3**

3-Chloroperoxybenzoic acid (650 mg, 3.76 mmol) was added to a solution of (+)-**1** (420 mg, 1.82 mmol, e.e.>95%) in CH_2Cl_2 (20 ml) and the mixture kept at room temperature for 48 h. After evaporation of the solvent, the residue was subjected to column chromatography (EtOAc:hexane=1:1) to give (+)-**3** (385 mg, 86% yield); $[\alpha]_D$ +104.6 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.06 (3H, s), 2.11 (3H, s), 3.38 (1H, dd, *J*=3.3 and 2.2), 3.52 (1H, dd, *J*=3.6 and 3.3), 3.90 (1H, dd, *J*=9.3 and 5.2), 4.32 (1H, dd, *J*=5.2 and 3.6), 5.13 (1H, dd, *J*=9.3 and 3.5), 5.65 (1H, dd, *J*=3.5 and 2.2); ^{13}C NMR ($CDCl_3$) δ 20.6, 20.7, 54.1, 54.7, 65.4, 66.6, 66.7, 68.3, 169.7, 170.5.

4.6. 1L-1,2-Diacetoxy-4-azido-4-deoxy-chiro-inositol (−)-**4**

NaN_3 (154 mg, 2.36 mmol) and NH_4Cl (126 mg, 2.35 mmol) were added to a solution of epoxide (+)-**3** (345 mg, 1.40 mmol) in DMF (8 ml). The suspension was stirred for 36 h at 50°C and then filtered. The filtrate was taken to dryness and the residue purified on Si gel (EtOAc:hexane=3:2) to give azidoinositol (−)-**4** (323 mg, 79% yield); $[\alpha]_D$ −37.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (CD_3OD) δ 2.04 (3H, s), 2.09 (3H, s), 3.64 (3H, m), 3.89 (1H, m), 5.18 (1H, m), 5.31 (1H, m); ^{13}C NMR (CD_3OD) δ 20.7, 20.9, 67.9, 70.8, 71.0, 71.2, 71.8, 73.0, 171.3, 172.0. Anal. calcd for $C_{10}H_{15}N_3O_7$: C, 41.52; H, 5.23; N, 14.53. Found: C, 41.58; H, 5.29; N, 14.47.

4.7. 1L-1,2-Diacetoxy-4-amino-4-deoxy-chiro-inositol (−)-**5**

Azido compound (−)-**4** (300 mg, 1.02 mmol) in EtOH (8 ml) was hydrogenated in the presence of Pd/C (20 mg) at barometric pressure and room temperature. After 24 h, the reaction mixture was centrifuged and filtered and the supernatant taken to dryness to give (−)-**5** (263 mg, 98% yield); $[\alpha]_D$ −20.8 (*c* 0.4, EtOH); ^{1}H NMR (D_2O): δ 2.10 (3H, s), 2.15 (3H, s), 3.42 (1H, t, *J*=10.6), 4.06 (3H, m), 5.11 (1H, dd, *J*=10.0 and 3.1), 5.36 (1H, t, *J*=3.1); ^{13}C NMR (CD_3OD) δ 20.6, 20.7, 56.4, 68.5, 68.9, 70.6, 71.7, 73.4, 171.1, 171.9.

4.8. 1L-4-Amino-4-deoxy-chiro-inositole-hexaacetate (+)-**6**

An aliquot of (−)-**5** was subjected to conventional acetylation (Ac_2O/py) to give (+)-**6**; $[\alpha]_D$ +13.7 (*c* 0.3, C_6H_6); ^{1}H NMR (C_6D_6) δ 1.46 (3H, s), 1.59 (3H, s), 1.65 (3H, s), 1.72 (3H, s), 1.75 (6H, s), 4.71 (1H, d, *J*=9.9), 5.06 (1H, ddd, *J*=11.2, 10.3 and 9.9), 5.32 (1H, dd, *J*=11.2 and 2.8), 5.50 (1H, t, *J*=10.3),

5.68 (1H, dd, *J*=4.0 and 2.8), 5.73 (2H, m); ^{13}C NMR (C_6D_6) δ 20.4, 20.6, 20.9, 23.5, 50.8, 68.4, 68.7, 70.2, 70.6, 71.3, 169.3, 169.7, 170.1, 170.8, 171.1.

4.9. 1L-4-Ammonium-4-deoxy-chiro-*inositole acetate (−)-**7***

Deacetylation of (−)-**5** with MeOH:NH_4OH (9:1) gave (−)-**7**, $[\alpha]_D$ −28.7 (*c* 0.7, MeOH); ^{1}H NMR (CD_3OD) δ 2.04 (3H, s), 3.58 (1H, t, *J*=10.0), 3.77 (2H, m), 3.96 (2H, m), 4.05 (1H, t, *J*=10.0); ^{13}C NMR (CD_3OD) δ 22.9, 55.4, 71.2, 72.7, 72.9, 73.3, 73.5, 174.7.

*4.10. (1*R,*2*R,*3*R,*4*R*)-1,3,4-Triacetyloxy-2-tosyloxycyclohex-5-ene (−)-**8***

Pyridine (0.4 ml, 4.97 mmol) and *p*-toluensulfonyl chloride (900 mg, 4.72 mmol) were added to a solution of (−)-**2** (600 mg, 2.20 mmol, e.e.>95%) in CH_2Cl_2 (25 ml) and the mixture was stirred at 35°C overnight. After washing with H_2O, the organic layer was dried over Na_2SO_3 and the solvent removed under reduced pressure. The residue was purified by column chromatography over Si gel (hexane:EtOAc=8:2) and finally recrystallised from MeOH to give (−)-**8** (883 mg, 94%): mp 99–100°C; $[\alpha]_D$ −183.2 (*c* 2.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.91 (3H, s), 2.00 (3H, s), 2.04 (3H, s), 2.46 (3H, s) 5.06 (1H, dd, *J*=9.7 and 4.3), 5.35 (1H, dd, *J*=9.7 and 4.0), 5.58 (1H, dd, *J*=4.3 and 4.0), 5.64 (1H, dd, *J*=4.0 and 4.3), 5.86 (1H, dd, *J*=10.0 and 4.0), 5.94 (1H, dd, *J*=10.0 and 4.3), 7.36 (2H, d, *J*=8.3), 7.82 (2H, d, *J*=8.3); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.6, 21.6, 66.0, 66.3, 66.5, 73.5, 127.9, 129.8, 133.5, 145.2, 169.6, 169.8.

*4.11. (1*R,*2*R,*3*S,*4*R*)-1,4-Diacetyloxy-2,3-epoxycyclohex-5-ene (−)-**10***

Aqueous KOH was added dropwise to an icy solution of compound (−)-**8** (700 mg, 1.64 mmol) in MeOH (35 ml). After 30 min, the reaction was kept under stirring for 2 h at room temperature. After addition of ethyl acetate, the precipitate of potassium tosylate was filtered off and the filtrate was evaporated under reduced pressure to leave a residue that was subjected to conventional acetylation (Ac_2O/py) to afford (−)-**10**. Recrystallised from EtOAc:hexane (291 mg, 84% yield) it had mp 86–87°C, $[\alpha]_D$ −157.3 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.11 (3H, s), 2.19 (3H, s), 3.44 (1H, m), 3.62 (1H, m), 5.56 (1H, m), 5.72 (2H, m), 5.84 (1H, m); ^{13}C NMR ($CDCl_3$) δ 20.7, 20.9, 50.9, 51.8, 63.9, 66.8, 124.0, 127.0, 169.9, 170.4.

*4.12. (1*R,*2*R,*3*S,*4*R*)-1,2,4-Trihydroxy-3-azido-cyclohex-5-ene (−)-**11***

NaN_3 (273 mg, 4.20 mmol) and NH_4Cl (225 mg, 4.20 mmol) were added to a solution of (−)-**10** (290 mg, 1.37 mmol) in DMF (12 ml). After washing with H_2O, the organic layer was dried over Na_2SO_4 and evaporated to dryness to give a residue that was hydrolysed with MeOH:NH_4OH (9:1). Recrystallisation from EtOAc gave the desired azide (−)-**11** (225 mg, 78% yield): mp (dec.) 135–136°C; $[\alpha]_D$ −184.9 (*c* 0.8, EtOH); ^{1}H NMR (D_2O) δ 3.37 (1H, dd, *J*=11.0 and 8.0), 3.45 (1H, dd, *J*=11.0 and 7.5), 4.08 (2H, m), 5.54 (2H, m); ^{13}C NMR (D_2O) δ 69.7, 70.7, 71.9, 75.2, 129.3, 129.5.

4.13. 5-Azido-5-deoxy-myo-inositole-pentaacetate meso-**12** and 1L-4-azido-4-deoxy-myo-inositole-pentaacetate (+)-**13**

N-Methylmorpholine-*N*-oxide (140 mg, 1.19 mmol) and OsO_4 (15 mg, 0.06 mmol) were added to a solution of (−)-**11** (225 mg, 1.07 mmol) in 10 ml of H_2O:acetone (1:4) and the mixture was kept at room temperature for 4 days. The reaction course was monitored by TLC (EtOAc:MeOH=8:2) and when the substrate had disappeared (96 h) the solvent was evaporated to give a residue which was acetylated under standard conditions (Ac_2O/py). The crude product was chromatographed on Si gel ($CHCl_3$ as the eluent) to give **12** (149 mg, 34% yield) and (+)-**13** (174 mg, 42% yield).

12: ^{1}H NMR ($CDCl_3$) δ 2.03 (6H, s) 2.14 (6H, s), 2.23 (3H, s), 3.64 (1H, t, *J*=10.3), 5.07 (2H, dd, *J*=10.3 and 2.8), 5.41 (2H, t, *J*=10.3), 5.60 (1H, t, *J*=2.8); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.6, 20.7, 62.7, 68.1, 68.9, 69.4, 169.4, 169.6, 169.8. Anal. calcd for $C_{16}H_{21}N_3O_{10}$: C, 46.27; H, 5.10; N, 10.12. Found: C, 46.35; H, 5.08; N, 10.16.

(+)-**13**: $[\alpha]_D$ +14.3 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.01 (3H, s) 2.05 (3H, s), 2.11 (3H, s), 2.14 (3H, s), 2.23 (3H, s), 4.01 (1H, t, *J*=10.5), 4.95 (1H, dd, *J*=10.5 and 2.8), 5.06 (2H, m), 5.45 (1H, dd, *J*=10.5 and 10.4), 5.61 (1H, t, *J*=2.8); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.5, 20.7, 60.8, 68.2, 68.3, 69.1, 69.6, 71.0, 169.2, 169.3, 169.4, 169.6, 170.0. Anal. calcd for $C_{16}H_{21}N_3O_{10}$: C, 46.27; H, 5.10; N, 10.12. Found: C, 46.22; H, 5.12; N, 10.18.

4.14. 5-Ammonium-5-deoxy-myo-inositole acetate **14**

Compound **12** (140 mg, 0.34 mmol) was dissolved in 5 ml EtOH and hydrogenated in the presence of Pd/C (10 mg) at barometric pressure and room temperature. After 24 h, the catalyst was filtered off and the filtrate evaporated to dryness to leave a residue that was hydrolysed with MeOH:NH_4OH (9:1) to give **14** (75 mg, yield 98%); ^{1}H NMR (D_2O): δ 2.08 (3H, s), 3.66 (5H, m), 4.11 (1H, m); ^{13}C NMR (CD_3OD) δ 23.4, 56.9, 71.9, 73.1, 176.0.

4.15. 1L-4-Ammonium-4-deoxy-myo-inositole acetate (−)-**15**

(−)-**15** was prepared from (+)-**13** by hydrogenation and subsequent hydrolysis following the same procedure described above for the preparation of **14**: $[\alpha]_D$ −11.2 (*c* 0.1, MeOH); ^{1}H NMR (D_2O): δ 1.96 (3H, s), 3.61 (4H, m), 4.11 (2H, m); ^{13}C NMR (CD_3OD) δ 23.2, 61.5, 69.1, 70.1, 72.3, 76.1, 175.4.

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