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Note

Synthesis of 2-deoxy-2-(4-nitroimidazol-1-yl)-D-alditols

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Abstract—Small molecules possessing defined configuration at centres of chirality provide a valuable chiral pool. Among different strategies applied for modification of chiral compounds, the most common is to begin with a single stereoisomer and use a synthesis that does not affect the chiral centres. The ANRORC type reaction has been applied for conversion of unprotected 2-amino-2-deoxy-D-hexopyranoses into 2-deoxy-2-(4-nitroimidazol-1-yl)-D-hexopyranoses in a reaction of some 2-aminosugars with 1,4-dinitroimidazoles. The reaction occurs with retention of configuration at C-2 of sugar ring. The products of the reaction were obtained as anomeric mixtures and separated into anomers after acetylation followed by column chromatography. 2-Deoxy-2-(4-nitroimidazol-1-yl)-D-hexopyranoses treated with sodium borohydride in methanolic solution gave the corresponding 2-deoxy-2-(4-nitroimidazol-1-yl)-D-hexitols, characterised as per-*O*-acetylated derivatives.

Keywords: Alditols; 1,4-Dinitroimidazoles; Aminosugars; ANRORC reaction; Reduction; Stereoselectivity

Sugar alditols are of interest as synthetic intermediates,[1,2] as enzyme inhibitors,[3] alkylating agents used in chemotherapy[4] or as sweeteners.[5] These readily available building blocks have also been used for the synthesis of several macrocyclic compounds.[6,7] The ANRORC reaction (addition of nucleophile, ring opening, ring closure) is a well known versatile method for the transformation of heterocyclic systems.[8,9] The 1,4-dinitroimidazole and its 2-alkyl derivatives in reaction with compounds possessing primary amino group undergo transformation into appropriate 1-substituted derivatives according to this mechanism.[10,11] In the case of chiral amino compounds, complete stereoselectivity is observed.[12] Most *N*-alkyl-*C*-nitroimidazoles have been reported as agents for sensitising hypoxic cells to the effect of radiation.[13] They are also useful substrates in the synthesis of purine derivatives.[14] In order to determine the scope and limitations of the ANRORC type reaction in a series of 1,4-dinitroimidazoles, we investigated the reaction of these compounds with appropriate 2-amino-2-deoxy-monosaccharides. Here, we report the synthesis of hitherto unknown 2-deoxy-2-(4-nitroimidazol-1-yl)-D-alditols.

1,4-Dinitroimidazole **1a** and its 2-methyl-derivative **1b** were treated with hydrochlorides of unprotected 2-amino-2-deoxy-D-hexopyranoses **2a**–**c** in methanol–water solution in the presence of an equimolar amount of sodium bicarbonate necessary for releasing the free amine (Scheme 1). The crude products **3a**–**f** were isolated by column chromatography giving mixtures of anomers. Synthesis on a larger scale (14 mmol of starting sugar derivative) bypassed the use of column chromatography, as crystallisation from methanol gave a pure anomeric mixture in over 50% yield. For analytical purposes, products **3a**–**f** were subjected to a full acetylation using acetic anhydride in the presence of pyridine. Separation by column chromatography gave pure anomers **4**, **5a**–**f** with structures fully supported by ^{1}H and ^{13}C NMR and elemental analysis.

For the reduction of carbonyl groups, gaseous hydrogen in the presence of Raney's nickel is the most common agent.[15,16] Sodium borohydride in aqueous solution has also been used.[17,18] In preliminary experiments, we

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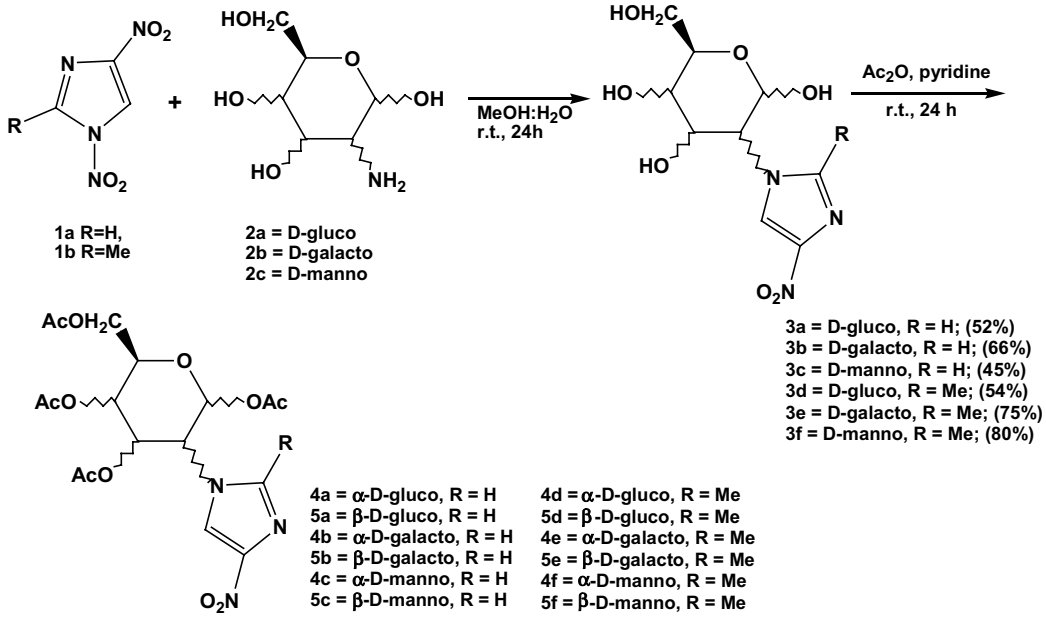
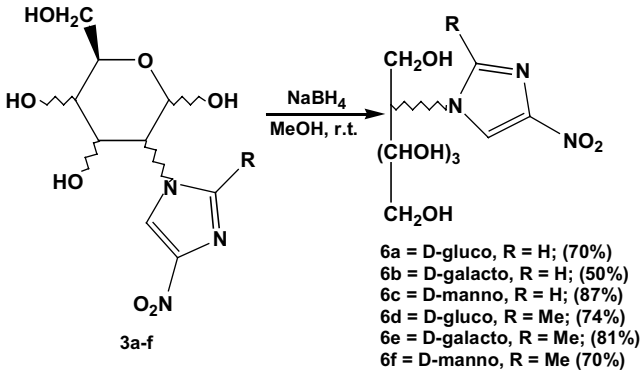
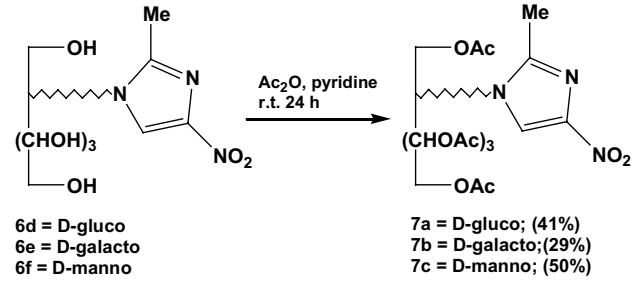


Scheme 1.



Scheme 2.

established that sodium borohydride used in molar excess sufficiently reduced carbonyl group of **3a**, when the reaction was carried out in methanol at room temperature. Under these conditions, the nitro group present in the imidazole molecule was resistant to reduction. The imidazole derivatives **3a**–**f** were treated with 3–4 equiv of sodium borohydride to give D-alditols **6a**–**f** (Scheme 2). Because their NMR spectra gave weakly resolved signals, several of the D-alditols (**6d**–**f**) were subjected to full acetylation using conditions mentioned above (Scheme 3). The structures of the acetyl derivatives **7a**,**b** and **c** were confirmed by ^{1}H COSY NMR spectroscopy and elemental analysis.



Scheme 3.

1. Experimental

1.1. General methods

Melting points are uncorrected. Elemental analyses were performed on Perkin–Elmer 240C apparatus and were correct within acceptable errors. ^{1}H and ^{13}C spectra were recorded on a Varian (300 and 75.5 MHz) spectrometer in DMSO-d_6 and $CDCl_3$ solutions with TMS as an internal standard.

Dinitroimidazoles **1a**,**b** were prepared according to reported procedures.[19] Other starting reagents and solvents were purchased from Aldrich. Column chromatography was performed using silica gel (Merck, 230–400 mesh).

1.2. 1-(2-Deoxy-2-D-hexopyranosyl)-4-nitroimidazole (3a–f) (general procedure)

2-Amino-2-deoxy-D-aldohexose hydrochloride **2a**–**c** (0.86 g, 4 mmol) was dissolved in aqueous methanol (1:1, v/v, 20 mL), cooled to 0 °C and solid $NaHCO_3$ (0.34 g, 4 mmol) was added with intensive stirring. After a few minutes, thoroughly powdered 1,4-dinitroimidazole (0.63 g **1a** or 0.69 g **1b**, 4 mmol) was added, the cooling bath was removed and stirring was continued at

25 °C. After the disappearance of starting material (TLC, MeOH–$CHCl_3$, 1:4, about 24 h), the solvent was evaporated to dryness below 40 °C. Water traces were removed by co-evaporation with toluene (2 × 25 mL). The residue was purified on a silica gel column using the mixture MeOH–$CHCl_3$ (1:4) as an eluent.

1.3. Peracetylated derivatives of 1-(2-deoxy-2-D-hexopyranosyl)-4-nitroimidazole (4a–f) and (5a–f)

The crude **3a**–**f** (approx. 4 mmol) was dissolved in anhydrous pyridine (6.4 mL, 20 mmol), acetic anhydride (16.3 mL, 160 mmol) was added and the mixture was stirred for 24 h at room temperature. The solvents were evaporated under reduced pressure and pyridine traces were removed by co-evaporation with toluene (2 × 25 mL). The remaining residue was separated on a chromatographic column, using the mixture of benzene–ethyl acetate (3:2) as eluent.

1.3.1. 1-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-α-2-D-glucopyranosyl)-4-nitroimidazole (4a) and 1-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-2-D-glucopyranosyl)-4-nitroimidazole (5a). Yield: 67%; α:β = 1:1.5.

Compound **4a**: Mp = 187–189 °C; $[\alpha]_D$ +140 (*c* 1.8, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (ppm) = 7.83 (d, 1H, $J_{2,5}$ = 1.6 Hz, H-5), 7.52 (d, 1H, $J_{2,5}$ = 1.6 Hz, H-2), 6.31 (d, 1H, $J_{1'2'}$ = 3.7 Hz, H-1′), 5.8 (dd, 1H, $J_{3',4'}$ = 9.1 Hz, $J_{2',3'}$ = 11.3 Hz, H-3′), 5.3 (dd, 1H, $J_{3',4',5'}$ = 9.1 Hz, H-4′), 4.59 (dd, 1H, $J_{1',2'}$ = 3.7 Hz, $J_{2',3'}$ = 11.3 Hz, H-2′), 4.36 (dd, 1H, $J_{5',6'a}$ = 3.8 Hz, $J_{6'a,6'b}$ = 12.4 Hz, H-6′$_a$), 4.24–4.05 (m, 2H, H-5′, H-6′$_b$), 2.21, 2.11, 2.08, 1.92 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.40, 169.65, 169.25, 167.60 (4 × CO), 148.57 (C-4), 135.75 (C-2), 118.48 (C-5), 89.83 (C-1′), 69.98 (C-5′), 69.78 (C-4′), 67.92 (C-3′), 61.12 (C-6′), 59.48 (C-2′), 20.76, 20.64, 20.46, 20.23 (4 × CH_3CO). Anal. Calcd for $C_{17}H_{21}N_3O_{11}$ (443.37): C, 46.05; H, 4.77; N, 9.48. Found: C, 46.24; H, 4.91; N, 9.31. EIMS: *m*/*z* 384 $(M-CH_3COO)^+$ (54%).

Compound **5a**: Mp = 148–150 °C; $[\alpha]_D$ +85 (*c* 1.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (ppm) = 7.84 (d, 1H, $J_{2,5}$ = 1.7 Hz, H-5), 7.49 (d, 1H, $J_{2,5}$ = 1.7 Hz, H-2), 5.97 (d, 1H, $J_{1'2}$ = 8.7 Hz, H-1′), 5.61 (dd, 1H, $J_{3',4'}$ = 9.2 Hz, $J_{2',3'}$ = 10.0 Hz, H-3′), 5.21 (dd, 1H, $J_{3',4',5'}$ = 9.2 Hz, H-4′), 4.41–4.25 (m, 2H, H-2′, H-6′$_a$), 4.17 (dd, 1H, $J_{5',6'b}$ = 2.3 Hz, $J_{6'a,6'b}$ = 12.7 Hz, H-6′$_b$), 4.03 (m, 1H, H-5′), 2.16, 2.10, 1.99, 1.95 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.43, 169.38, 169.20, 168.10 (4 × CO), 148.80 (C-4), 135.88 (C-2), 117.23 (C-5), 91.24 (C-1′), 75.18 (C-5′), 71.15 (C-4′), 67.86 (C-3′), 61.21 (C-6′), 61.06 (C-2′), 20.66, 20.48, 20.30, 20.18 (4 × CH_3CO). Anal. Calcd for $C_{17}H_{21}N_3O_{11}$ (443.37): C, 46.05; H, 4.77; N, 9.48. Found: C, 45.94; H, 4.90; N, 9.19. EIMS: *m*/*z* 384 $(M-CH_3COO)^+$ (52%).

1.3.2. 1-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-α-2-D-galactopyranosyl)-4-nitroimidazole (4b) and 1-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-2-D-galactopyranosyl)-4-nitroimidazole (5b). Yield: 45%; α:β = 1:1.

Compound **4b**: Mp = 154–156 °C; [α] +106.9 (*c* 0.452, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (ppm) = 7.85 (d, 1H, $J_{2,5}$ = 1.5 Hz, H-5), 7.53 (d, 1H, $J_{2,5}$ = 1.5 Hz, H-2), 6.36 (d, 1H, $J_{1',2'}$ = 3.6 Hz, H-1′), 5.75 (dd, 1H, $J_{3',4'}$ = 3.6 Hz, $J_{2',3'}$ = 11.7 Hz, H-3′), 5.75 (d, 1H, $J_{3',4'}$ = 3.6 Hz, H-4′), 4.82 (dd, 1H, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 11.7 Hz, H-2′), 4.23 (t, 1H, $J_{5',6'}$ = 7.0 Hz, H-5′), 4.13 (d, 2H, $J_{6'a,6'b}$ = 7.0 Hz, H-6′$_a$, H-6′$_b$), 2.21, 2.17, 2.05, 1.91 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.09, 169.59, 169.42, 167.72 (4 × CO), 148.35 (C-4), 135.58 (C-2), 118.14 (C-5), 90.28 (C-1′), 68.73 (C-5′), 66.32 (C-3′), 66.21 (C-4′), 60.65 (C-6′), 55.68 (C-2′), 20.56, 20.34, 20.26, 20.13 (4 × CH_3CO). Anal. Calcd for $C_{17}H_{21}N_3O_{11}$ (443.37): C, 46.05; H, 4.77; N, 9.48. Found: C, 46.34; H, 5.02; N, 9.31.

Compound **5b**: Mp = 84–86 °C; $[\alpha]_D$ +56.2 (*c* 0.420, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (ppm) = 7.93 (d, 1H, $J_{2,5}$ = 1.4 Hz, H-5), 7.54 (d, 1H, $J_{2,5}$ = 1.4 Hz, H-2), 6.05 (d, 1H, $J_{1',2'}$ = 8.7 Hz, H-1′), 5.58 (dd, 1H, $J_{3',4'}$ = 3.4 Hz, $J_{2',3'}$ = 11.2 Hz, H-3′), 5.54 (d, 1H, $J_{3',4'}$ = 3.4 Hz, H-4′), 4.17 (dd, 1H, $J_{1',2'}$ = 8.7 Hz, $J_{2',3'}$ = 11.2 Hz, H-2′), 4.34–4.20 (m, 3H, H-5, H-6′$_a$, H-6′$_b$), 2.22, 2.07, 2.06, 1.92 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.32, 169.62, 169.21, 168.02 (4 × CO), 148.58 (C-4), 135.98 (C-2), 117.30 (C-5), 91.40 (C-1′), 71.85 (C-5′), 69.32 (C-4′), 65.90 (C-3′), 60.78 (C-6′), 57.86 (C-2′), 20.56, 20.38, 20.20, 20.08 (4 × CH_3CO). Anal. Calcd for $C_{17}H_{21}N_3O_{11}$ (443.37): C, 46.05; H, 4.77; N, 9.48. Found: C, 46.24; H, 4.92; N, 9.37.

1.3.3. 1-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-α-2-D-mannopyranosyl)-4-nitroimidazole (4c) and 1-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-2-D-mannopyranosyl)-4-nitroimidazole (5c). Yield: 70%; α:β = 3:1.

Compound **4c**: Mp = 82–86 °C. ^{1}H NMR ($CDCl_3$): δ (ppm) = 8.29 (d, 1H, $J_{2,5}$ = 1.5 Hz, H-5), 7.57 (d, 1H, $J_{2,5}$ = 1.5 Hz, H-2), 6.41 (s, 1H, H-1′), 5.52 (dd, 1H, $J_{2',3'}$ = 4.9 Hz, $J_{3',4'}$ = 10.2 Hz, H-3′), 5.40–5.20 (m, 1H, H-4′), 4.88 (d, 1H, $J_{2',3'}$ = 4.9 Hz, H-2′), 4.40–4.10 (m, 3H, H-5′, H-6′$_a$, H − 6′$_b$), 2.26, 2.23, 2.05, 2.03 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.44, 169.79, 168.92, 167.76 (4 × CO), 148.59 (C-4), 137.09 (C-2), 119.23 (C-5), 90.40 (C-1′), 70.55 (C-5′), 68.06 (C-4′), 63.58 (C-3′), 60.86 (C-6′),

57.69 (C-2′), 20.66, 20.45, 20.43, 20.33 (4 × CH_3CO). Anal. Calcd for $C_{17}H_{21}N_3O_{11}$ (443.37): C, 46.05; H, 4.77; N, 9.48. Found: C, 46.34; H, 4.93; N, 9.27. CIMS (isobutane): *m*/*z* 444 $(M+1)^+$ (100%); requires: 443 $(M)^+$.

Compound **5c**: Syrup, ^1H NMR ($CDCl_3$): δ (ppm) = 8.13 (d, 1H, $J_{2,5}$ = 1.5 Hz, H-5), 7.57 (d, 1H, $J_{2,5}$ = 1.5 Hz, H-2), 6.65–6.57 (m, 1H, H-3′), 6.40–6.20 (m, 1H, H-4′), 6.18 (d, 1H, $J_{1',2'}$ = 2.0 Hz, H-1′), 5.00–4.95 (m, 1H, H-2′), 4.40–4.10 (m, 3H, H-5′, H-$6'_a$, H-$6'_b$), 2.24, 2.06, 2.05, 2.02 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.44, 169.76, 168.92, 167.76 (4 × CO), 148.57 (C-4), 137.66 (C-2), 120.26 (C-5), 89.65 (C-1′), 73.06 (C-5′), 70.45 (C-4′), 63.52 (C-3′), 60.80 (C-6′), 58.19 (C-2′), 20.66, 20.45, 20.43, 20.36 (4 × CH_3CO). Anal. Calcd for $C_{17}H_{21}N_3O_{11}$ (443.37): C, 46.05; H, 4.77; N, 9.48. Found: C, 46.24; H, 4.91; N, 9.37.

1.3.4. 1-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-α-2-D-glucopyranosyl)-2-methyl-4-nitroimidazole (4d) and 1-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-2-D-glucopyranosyl)-2-methyl-4-nitroimidazole (5d).

Yield: 52%; α:β = 1:1.

Compound **4d**: Mp = 278–280 °C; $[\alpha]_D$ +153 (*c* 1.8, $CHCl_3$).

^1H NMR ($CDCl_3$): δ (ppm) = 7.78 (s, 1H, H-5), 6.27 (d, 1H, $J_{1',2'}$ = 3.5 Hz, H-1′), 5.75 (dd, 1H, $J_{3',4'}$ = 9.2 Hz, $J_{2',3'}$ = 11.2 Hz, H-3′), 5.27 (dd, 1H, $J_{3',4',5'}$ = 9.2 Hz, H-4′), 4.45 (dd, 1H, $J_{1',2'}$ = 3.5 Hz, $J_{2',3'}$ = 11.2 Hz, H-2′), 4.43 (dd, 1H, $J_{5',6'a}$ = 4.4 Hz, $J_{6'a,6'b}$ = 12.7 Hz, H-$6'_a$), 4.22 (m, 1H, H-5′), 4.11 (dd, 1H, $J_{5',6'b}$ = 2.3 Hz, $J_{6'a,6'b}$ = 12.7 Hz, H-$6'_b$), 2.51 (s, 3H, CH_3), 2.21, 2.12, 2.07, 1.91 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.40, 169.51, 169.36, 167.70 (4 × CO), 147.40 (C-4), 145.18 (C-2), 117.03 (C-5), 89.25 (C-1′), 70.02 (C-5′), 69.22 (C-4′), 67.99 (C-3′), 61.09 (C-6′), 57.38 (C-2′), 20.75, 20.66, 20.48, 20.30 (4 × CH_3CO), 13.37 (CH_3). Anal. Calcd for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; N, 9.19. Found: C, 47.10; H, 5.12; N, 9.06. EIMS: *m*/*z*: 457 $(M)^+$ (17%).

Compound **5d**: Mp = 224–225 °C; $[\alpha]_D$ +98 (*c* 1.7, $CHCl_3$).

^1H NMR ($CDCl_3$): δ (ppm) = 7.78 (s, 1H, H-5), 5.93 (d, 1H, $J_{1',2'}$ = 8.7 Hz, H-1′), 5.53 (dd, 1H, $J_{3',4'}$ = 9.2 Hz, $J_{2',3'}$ = 11.0 Hz, H-3′), 5.23 (dd, 1H, $J_{3',4',5'}$ = 9.2 Hz, H-4′), 4.42 (dd, 1H, $J_{1',2'}$ = 8.7 Hz, $J_{2',3'}$ = 11.0 Hz, H-2′), 4.35 (dd, 1H, $J_{5',6'a}$ = 2.2 Hz, $J_{6'a,6'b}$ = 12.6 Hz, H-$6'_a$), 4.16 (dd, 1H, $J_{5',6'b}$ = 2.2 Hz, $J_{6'a,6'b}$ = 12.6 Hz, H-$6'_b$), 4.00 (m, 1H, H-5′), 2.51 (s, 3H, CH_3), 2.12, 2.06, 2.04, 1.92 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.42, 169.45, 169.12, 167.92 (4 × CO), 147.20 (C-4), 146.17 (C-2), 115.84 (C-5), 91.82 (C-1′), 73.21 (C-5′), 71.83 (C-4′), 67.90 (C-3′), 61.18 (C-6′), 59.15 (C-2′), 20.67, 20.52, 20.48, 20.20 (4 × CH_3CO), 13.34 (CH_3). Anal. Calcd for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; N, 9.19. Found: C, 47.11; H, 5.00; N, 9.10. EIMS: *m*/*z*: 457 $(M)^+$ (10%).

1.3.5. 1-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-α-2-D-galactopyranosyl)-2-methyl-4-nitroimidazole (4e) and 1-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-2-D-galactopyranosyl)-2-methyl-4-nitroimidazole (5e).

Yield: 90%; α:β = 3.5:1.

Compound **4e**: Mp = 186–188 °C, $[\alpha]_D$ +110.4 (*c* 0.608, $CHCl_3$).

^1H NMR ($CDCl_3$): δ (ppm) = 7.70 (s, 1H, H-5), 6.31 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1′), 5.78 (dd, 1H, $J_{3',4'}$ = 3.2 Hz, $J_{2',3'}$ = 11.5 Hz, H-3′), 5.59–5.58 (m, 1H, H-4′), 4.72 (dd, 1H, $J_{1',2'}$ = 3.4 Hz, $J_{2',3'}$ = 11.5 Hz, H-2′), 4.42 (t, 1H, $J_{5',6'}$ = 7.0 Hz, H-5′), 4.15 (d, 2H, $J_{5',6'}$ = 7.0 Hz, H-$6'_a$, H-$6'_b$), 2.52 (s, 3H, CH_3), 2.22, 2.17, 2.06, 1.92 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.1, 169.5, 169.3, 167.8 (4 × CO), 147.2 (C-4), 145.6 (C-2), 116.5 (C-5), 89.6 (C-1′), 68.8 (C-5′), 66.6 (C-4′), 66.4 (C-3′), 60.6 (C-6′), 53.6 (C-2′), 20.5, 20.4, 20.3, 20.2 (4 × CH_3CO), 13.2 (CH_3). Anal. Calcd for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; N, 9.19. Found: C, 47.18; H, 5.12; N, 9.18. CIMS (isobutane): *m*/*z* 457 $(M)^+$ (20%); requires: 457 $(M)^+$.

Compound **5e**: Mp = 100–102 °C; $[\alpha]_D$ +59.0 (*c* 0.564, $CHCl_3$).

^1H NMR ($CDCl_3$): δ (ppm) = 7.86 (s, 1H, H-5), 6.01 (d, 1H, $J_{1',2'}$ = 8.7 Hz, H-1′), 5.53–5.47 (m, 2H, H-3′, H-4′), 4.47 (dd, 1H, $J_{1',2'}$ = 8.7 Hz, $J_{2',3'}$ = 10.6 Hz, H-2′), 4.32–4.20 (m, 3H, H-5, H-$6'_a$, H − $6'_b$), 2.51 (s, 3H, CH_3), 2.23, 2.08, 2.04, 1.91 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.4, 169.6, 169.1, 167.9 (4 × CO), 147.4 (C-4), 146.3 (C-2), 115.6 (C-5), 91.9 (C-1′), 71.9 (C-5′), 70.0 (C-4′), 66.0 (C-3′), 60.8 (C-6′), 55.8 (C-2′), 22.1, 20.5, 20.4, 20.1 (4 × CH_3CO), 13.2 (CH_3). Anal. Calcd for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; N, 9.19. Found: C, 47.11; H, 5.14; N, 8.98. CIMS (isobutane): *m*/*z* 457 $(M)^+$ (35%); requires: 457 $(M)^+$.

1.3.6. 1-(1,3,4,6-Tetra-*O*-acetyl-2-deoxy-α-2-D-mannopyranosyl)-2-methyl-4-nitroimidazole (4f) and 1-(1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-2-D-mannopyranosyl)-2-methyl-4-nitroimidazole (5f).

Yield: 49%; α:β = 1:2.

Compound **4f**: Mp = 166–170 °C; $[\alpha]_D$ −64.9 (*c* 0.528, $CHCl_3$).

^1H NMR ($CDCl_3$): δ (ppm) = 8.41 (s, 1H, H-5), 6.29 (d, 1H, $J_{1',2'}$ = 1.1 Hz, H-1′), 5.60 (dd, 1H, $J_{2',3'}$ = 5.4 Hz, $J_{3',4'}$ = 10.2 Hz, H-3′), 5.42 (dd, 1H, $J_{3',4',5'}$ = 10.2 Hz, H-4′), 4.76 (dd, 1H, $J_{1',2'}$ = 1.1 Hz, $J_{2',3'}$ = 5.4 Hz, H-2′), 4.40–4.15 (m, 3H, H-5, H-$6'_a$, H − $6'_b$), 2.38 (s, 3H, CH_3), 2.26, 2.25, 2.05, 2.02 (4s, 4 × 3H, 4CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.76, 169.90, 169.13, 168.08 (4 × CO), 147.37 (C-4), 146.58 (C-2), 118.86 (C-5), 91.22 (C-1′), 70.73 (C-5′), 68.06 (C-4′), 63.67 (C-3′), 60.96 (C-6′),

56.11 (C-2′), 20.83, 20.57, 20.45, 18.10 (4 × CH_3CO), 13.33 (CH_3). Anal. Calcd for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; N, 9.19. Found: C, 47.12; H, 5.15; N, 8.99.

Compound **5f**: Mp = 145–147 °C; $[\alpha]_D$ −95.6 (*c* 0.404, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (ppm) = 8.44 (s, 1H, H-5), 6.1 (d, 1H, $J_{1',2'}$ = 2.0 Hz, H-1′), 5.47 (dd, 1H, $J_{4',5'}$ = 9.3 Hz, $J_{3',4'}$ = 10.2 Hz, H-4′), 5.37 (dd, 1H, $J_{2',3'}$ = 4.8 Hz, $J_{3',4'}$ = 10.2 Hz, H-3′), 4.89 (dd, 1H, $J_{1',2'}$ = 2.0 Hz, $J_{2',3'}$ = 4.8 Hz, H-2′), 4.33 (dd, 1H, $J_{5',6'}$ = 2.0 Hz, $J_{6'a,6'b'}$ = 12.7 Hz, H-6′$_a$), 4.24 (dd, 1H, $J_{5',6'}$ = 2.0 Hz, $J_{6'a,6'b'}$ = 12.7 Hz, H-6′$_b$), 3.99 (dt, 1H, $J_{5',6'}$ = 2.0 Hz, $J_{4',5'}$ = 9.3 Hz, H-5′), 2.34 (s, 3H, CH_3), 2.29 (s, 3H, CH_3CO), 2.06 (2s, 2 × 3H, 2CH_3CO), 2.01 (s, 3H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.75, 170.04, 169.15, 168.19 (4 × CO), 147.52 (C-4), 146.76 (C-2), 120.07 (C-5), 90.09 (C-1′), 73.29 (C-5′), 70.64 (C-4′), 63.53 (C-3′), 60.92 (C-6′), 56.28 (C-2′), 20.69, 20.66, 20.57, 18.19 (4 × CH_3CO), 13.41 (CH_3). Anal. Calcd for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; N, 9.19. Found: C, 47.11; H, 5.16; N, 8.98.

1.4. Reduction of carbonyl group in 1-(2-deoxy-2-D-hexopyranosyl)-4-nitroimidazoles (6a–f)

4-Nitroimidazole derivative **3a**–**f** (1 mmol) was dissolved in methanol (10 mL) and sodium borohydride (3 mmol) was added in portions while stirring. When the TLC (MeOH–$CHCl_3$, 1:4) indicated the consumption of the starting material, reaction mixture was carefully neutralized by addition of few drops of aqueous hydrochloride solution (5%). The solvent was evaporated under reduced pressure until dryness. The traces of water were removed by co-evaporation with toluene (2 × 10 mL). The residue was extracted with hot methanol (3 × 5 mL) and after evaporation was purified on a chromatographic column using a mixture of MeOH–$CHCl_3$ (1:4) as eluent.

1.4.1. 2-Deoxy-2-(4-nitroimidazol-1-yl)-D-glucitol (6a). Yield 70%; mp = 103–104 °C; $[\alpha]_D$ +6.7 (*c* 0.200, MeOH).

^{1}H NMR (DMSO-d_6): δ (ppm) = 8.33 (d, 1H, $J_{2',5'}$ = 1.2 Hz, H-5′), 7.88 (d, 1H, $J_{2',5'}$ = 1.2 Hz, H-2′), 5.20–4.30 (m, 6H), 4.20–4.00 (m, 1H), 3.90–3.30 (m, 6H). ^{13}C NMR (DMSO-d_6): δ (ppm) = 145.03 (C-4′), 135.10 (C-2′), 120.13 (C-5′), 69.62 (C-5), 68.88 (C-4), 66.96 (C-3), 62.36 (C-6), 61.33 (C-1), 58.79 (C-2). Anal. Calcd for $C_9H_{15}N_3O_7$ (277.23): C, 38.99; H, 5.45; N, 15.16. Found: C, 39.11; H, 5.26; N, 14.98. ESIMS (MeOH–H_2O 1:1, 1% AcOH): *m*/*z*: 278 $(M+1)^+$ (100); requires: 277 $(M)^+$.

1.4.2. 2-Deoxy-2-(4-nitroimidazol-1-yl)-D-galactitol (6b). Yield 50%; mp = 82–83 °C; $[\alpha]_D$ +23.7 (*c* 0.428, MeOH).

^{1}H NMR (DMSO-d_6): δ (ppm) = 8.18 (d, 1H, $J_{2',5'}$ = 1.2 Hz, H-5′), 7.73 (d, 1H, $J_{2',5'}$ = 1.2 Hz, H-2′), 5.60 (d, 1H, *J* = 5.7 Hz, OH), 5.13 (s, 1H, OH), 4.74–4.40 (m, 4H), 3.94–3.25 (m, 6H), 2.85–2.71 (m, 1H). ^{13}C NMR (DMSO-d_6): δ (ppm) = 146.79 (C-4′), 138.36 (C-2′), 122.22 (C-5), 69.57 (C-5), 69.32 (C-4), 67.90 (C-3), 62.74 (C-6), 62.09 (C-1), 61.97 (C-2). Anal. Calcd for $C_9H_{15}N_3O_7$ (277.23): C, 38.99; H, 5.45; N, 15.16. Found: C, 39.16; H, 5.16; N, 14.88.

1.4.3. 2-Deoxy-2-(4-nitroimidazol-1-yl)-D-mannitol (6c). Yield 87%; mp = 98–100 °C; $[\alpha]_D$ −1.6 (*c* 0.428, MeOH).

^{1}H NMR (DMSO-d_6): δ (ppm) = 8.35 (d, 1H, $J_{2',5'}$ = 1.5 Hz, H-5′), 7.80 (d, 1H, $J_{2',5'}$ = 1.5 Hz, H-2′), 5.14–5.05 (m, 2H), 4.80 (d, 1H, *J* = 7.8 Hz), 4.80 (d, 1H, *J* = 5.9 Hz), 4.43–4.32 (m, 2H), 4.80 (t, 1H, *J* = 8.3 Hz), 4.00–3.84 (m, 2H), 3.60–3.28 (m, 3H), 2.74 (t, 1H, *J* = 7.8 Hz). ^{13}C NMR (DMSO-d_6): δ (ppm) = 146.71 (C-4′), 137.48 (C-2′), 120.97 (C-5′), 70.49 (C-5), 69.29 (C-4), 68.24 (C-3), 63.18 (C-6), 61.93 (C-1), 60.53 (C-2). Anal. Calcd for $C_9H_{15}N_3O_7$ (277.23): C, 38.99; H, 5.45; N, 15.16. Found: C, 39.17; H, 5.19; N, 15.08.

1.4.4. 2-Deoxy-2-(2-methyl-4-nitroimidazol-1-yl)-D-glucitol (6d). Yield 74%; mp = 122–123 °C; $[\alpha]_D$ +14.9 (*c* 0.867, MeOH).

^{1}H NMR (DMSO-d_6): δ (ppm) = 8.33 (s, 1H, H-5′), 4.97 (t, 1H, *J* = 4.8 Hz, OH), 4.74 (d, 1H, *J* = 6.6 Hz, OH), 4.64 (d, 1H, *J* = 7.5 Hz, OH), 4.46 (d, 1H, *J* = 5.1 Hz, OH), 4.40–4.24 (m, 2H), 4.08–3.98 (m, 2H), 3.80–3.70 (m, 2H), 3.64–3.38 (m, 3H), 2.35 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ (ppm) = 147.06 (C-4′), 145.95 (C-2′), 121.17 (C-5′), 71.68 (C-5), 70.06 (C-4), 69.68 (C-3), 63.88 (C-6), 62.54 (C-1), 60.92 (C-2), 13.80 (CH_3). Anal. Calcd for $C_{10}H_{17}N_3O_7$ (291.26): C, 41.24; H, 5.88; N, 14.43. Found: C, 41.01; H, 5.66; N, 14.68.

1.4.5. 2-Deoxy-2-(2-methyl-4-nitroimidazol-1-yl)-D-galactitol (6e). Yield 81%; mp = 120–123 °C; $[\alpha]_D$ +0.9 (*c* 0.540, MeOH).

^{1}H NMR (DMSO-d_6): δ (ppm) = 8.13 (s, 1H, H-5′), 5.72 (d, 1H, *J* = 6.0 Hz, OH), 5.20–5.10 (m, 1H, OH), 4.60–4.48 (m, 4H, H-2, 3 × OH), 4.02–3.92 (m, 1H, H-3), 3.80–3.72 (m, 2H, H-6$_a$, H-6$_b$), 3.68–3.60 (m, 1H, H-4), 3.38–3.28 (m, 2H, H-1$_a$, H-1$_b$), 2.78 (t, 1H, *J* = 8.7 Hz, H-5′), 2.39 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ (ppm) = 146.70 (C-4′), 145.20 (C-2′), 120.72 (C-5′), 69.17 (C-5), 68.92 (C-4), 67.71 (C-3), 62.73 (C-6), 62.12 (C-1), 59.42 (C-2), 12.95 (CH_3). Anal. Calcd for $C_{10}H_{17}N_3O_7$ (291.26): C, 41.24; H, 5.88; N, 14.43. Found: C, 41.31; H, 5.66; N, 14.58.

1.4.6. 2-Deoxy-2-(2-methyl-4-nitroimidazol-1-yl)-D-mannitol (6f). Yield 70%; mp = 138–140 °C; $[\alpha]_D$ −10.68 (*c* 0.412, MeOH).

^{1}H NMR (CD_3OD): δ (ppm) = 8.17 (s, 1H, H-5′), 4.61 (s, 5H, 5 × OH), 4.45 (ddd, 1H, J = 7.0, 9.5, 3.2 Hz, H-2′), 4.27 (dd, 1H, J = 9.3, 1.0 Hz, CH), 4.09 (dd, 1H, J = 3.4, 12.2 Hz, H-1_a), 4.01 (dd, 1H, J = 7.3, 11.7 Hz, H-6_a), 3.76–3.52 (m, 4H, H-1_b, H-6_b, 2 × CH), 2.48 (s, 3H, CH_3). ^{13}C NMR (CD_3OD): δ (ppm) = 148.65 (C-4′), 148.00 (C-2′), 120.14 (C-5′), 72.28 (C-5), 70.82 (C-4), 69.98 (C-3), 64.61 (C-6), 62.87 (C-1), 61.44 (C-2), 13.17 (CH_3). Anal. Calcd for $C_{10}H_{17}N_3O_7$ (291.26): C, 41.24; H, 5.88; N, 14.43. Found: C, 41.33; H, 5.65; N, 14.55.

1.5. Peracetylated derivatives (7a–c)

Compound **6d**,**e** or **6f** (1 mmol) was dissolved in anhydrous pyridine (6.4 mL, 20 mmol), acetic anhydride (16.3 mL, 160 mmol) was added and the mixture was stirred for 24 h at room temperature. The solvents were evaporated under reduced pressure, pyridine traces were removed by co-evaporation with toluene (2 × 25 mL). The remaining residue was purified on a chromatographic column, using the mixture of MeOH–$CHCl_3$ (1:4) as eluent.

1.5.1. 1,3,4,5,6-Penta-*O*-acetyl-2-deoxy-(2-methyl-4-nitroimidazol-1-yl)-D-glucitol (7a). Yield 41%; mp = 146–148 °C; $[\alpha]_D$ +14.66 (*c* 0.440, $CHCl_3$).

^{1}H NMR (acetone-d_6): δ (ppm) = 8.24 (s, 1H, H-5′), 5.81 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{4,5}$ = 7.5 Hz, H-4), 5.52 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{2,3}$ = 8.1 Hz, H-3), 5.09 (ddd, 1H, $J_{1b,2}$ = 3.0 Hz, $J_{1a,2}$ = 5.4 Hz, $J_{2,3}$ = 8.1 Hz, H-2), 4.91 (dt, 1H, $J_{5,6b}$ = 4.6 Hz, $J_{4,5,6a}$ = 7.5 Hz, H-5), 4.57 (dd, 1H, $J_{5,6a}$ = 7.5 Hz, $J_{6a,6b}$ = 12.3 Hz, H-6_a), 4.50 (dd, 1H, $J_{5,6b}$ = 4.6 Hz, $J_{6a,6b}$ = 12.3 Hz, H-6_b), 4.26 (dd, 1H, $J_{1a,2}$ = 5.4 Hz, $J_{1a,1b}$ = 12.3 Hz, H-1_a), 4.08 (dd, 1H, $J_{1b,2}$ = 3.0 Hz, $J_{1a,1b}$ = 12.3 Hz, H-1_b), 2.40 (s, 3H, CH_3), 2.03, 2.028, 2.02, 2.01, 1.99 (5s, 5 × 3H, 5CH_3CO). ^{13}C NMR (acetone-d_6): δ (ppm) = 170.67, 170.55, 170.39, 170.16, 169.93 (5 × CO), 147.53 (C-4′), 146.88 (C-2′), 120.21 (C-5′), 69.47 (C-5), 69.33 (C-4), 69.29 (C-3), 63.50 (C-6), 62.27 (C-1), 57.41 (C-2), 20.82, 20.55, 20.51, 20.46, 20.36 (5 × CH_3CO), 13.19 (CH_3). Anal. Calcd For $C_{20}H_{27}N_3O_{12}$ (501.45): C, 47.91; H, 5.43; N, 8.38. Found: C, 47.75; H, 5.21; N, 8.14.

1.5.2. 1,3,4,5,6-Penta-*O*-acetyl-2-deoxy-(2-methyl-4-nitroimidazol-1-yl)-D-galactitol (7b). Yield 29%; Syrup, $[\alpha]_D$ +45.1 (*c* 0.440, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (ppm) = 7.92 (s, 1H, H-5′), 5.54 (dd, 1H, $J_{4,5}$ = 4.4 Hz, $J_{3,4}$ = 6.8 Hz, H-4), 5.38 (ddd, 1H, $J_{2,3}$ = 2.4 Hz, $J_{1a,2}$ = 5.4 Hz, $J_{1b,2}$ = 6.8 Hz, H-2), 5.17 (dd, 1H, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 6.8 Hz, H-3), 4.72 (ddd, 1H, $J_{4,5}$ = 4.4 Hz, $J_{5,6a}$ = 4.9 Hz, $J_{5,6b}$ = 7.3 Hz, H-5), 4.38–4.25 (m, 2H, H-6_a, H-6_b), 4.21 (dd, 1H, $J_{1a,2}$ = 5.4 Hz, $J_{1a,1b}$ = 11.7 Hz, H-1_a), 3.91 (dd, 1H, $J_{1b,2}$ = 6.8 Hz, $J_{1a,1b}$ = 11.7 Hz, H-1_b), 2.24 (s, 3H, CH_3), 2.14, 2.11 (2s, 2 × 3H, 2CH_3CO), 2.06 (s, 6H, 2CH_3CO), 2.03, (1s, 3H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.36, 170.02, 169.22, 169.08 (5 × CO), 147.21 (C-4′), 146.10 (C-2′), 117.79 (C-5′), 68.65 (C-5), 68.33 (C-4), 67.79 (C-3), 63.12 (C-6), 61.59 (C-1), 55.01 (C-2), 20.70, 20.60, 20.55, 20.46, 20.37 (5 × CH_3CO), 13.12 (CH_3). Anal. Calcd for $C_{20}H_{27}N_3O_{12}$ (501.45): C, 47.91; H, 5.43; N, 8.38. Found: C, 47.69; H, 5.28; N, 8.24.

1.5.3. 1,3,4,5,6-Penta-*O*-acetyl-2-deoxy-(2-methyl-4-nitroimidazol-1-yl)-D-mannitol (7c). Yield 50%; Syrup, $[\alpha]_D$ −9.2 (*c* 0.440, $CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (ppm) = 7.85 (s, 1H, H-5′), 5.62 (d, 1H, $J_{4,5}$ = 7.3 Hz, H-4), 5.12–4.99 (m, 2H, H-2, H-3), 4.62–4.52 (m, 1H, H-5), 4.37–4.27 (m, 2H, H-6_a, H-6_b), 4.23 (dd, 1H, $J_{1a,2}$ = 2.4 Hz, $J_{1a,1b}$ = 12.7 Hz, H-1_a), 3.91 (dd, 1H, $J_{1b,2}$ = 4.4 Hz, $J_{1a,1b}$ = 12.7 Hz, H-1_b), 2.43 (s, 3H, CH_3), 2.18, 2.11 (2s, 2 × 3H, 2CH_3CO), 2.03 (s, 6H, 2CH_3CO), 2.00, (s, 3H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.62, 170.03, 169.84, 169.74, 169.64 (5 × CO), 146.51 (C-4′), 145.83, (C-2′), 117.79 (C-5′), 68.65 (C-5), 68.33 (C-4), 67.79 (C-3), 63.12 (C-6), 61.59 (C-1), 55.01 (C-2), 20.70, 20.60, 20.55, 20.46, 20.37 (5 × CH_3CO), 13.12 (CH_3). Anal. Calcd for $C_{20}H_{27}N_3O_{12}$ (501.45): C, 47.91; H, 5.43; N, 8.38. Found: C, 47.72; H, 5.29; N, 8.19. CIMS (isobutane): *m/z* 502 $(M+1)^+$ (100%); requires: 501 $(M)^+$.

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