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Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 1349–1354

The direct synthesis of 6-amino-6-deoxyaldonic acids as monomers for the preparation of polyhydroxylated nylon 6

Ludovic Chaveriat, Imane Stasik,* Gilles Demailly and Daniel Beaupère

Laboratoire des Glucides, UMR 6219, Université de Picardie Jules Verne, 33 Rue Saint-Leu, 80039 Amiens, France

Received 3 March 2006; accepted 18 April 2006

Abstract—6-Azido-6-deoxy-D-galactitol and D-mannitol were obtained quantitatively via the reduction of the corresponding 6-azido-6-deoxy-D-hexono-1,4-lactones, and 6-azido-6-deoxy-D-glucitol was obtained by the reduction of 6-azido-6-deoxyglucose in good yields. The reduction of monoazidodeoxyhexitols by catalytic hydrogenation gave the monoaminohexitol analogues in 95–98% yields. Oxidation of these afforded the corresponding 6-amino-6-deoxy-D-aldonic acids in moderate yields. Alternatively, saponification of 6-azido-6-deoxy-D-hexonolactones gave 6-azido-6-deoxyaldonic acid salts which, after reduction followed by neutralization, led to the expected compounds in 82–88% overall yields.

1. Introduction

In recent years, efforts have been made to synthesize polymers that are more hydrophilic and degradable.[1] The majority of commercially available synthetic biodegradable polymers have been limited to polyesters.[2]

The synthesis of polyamides that are more hydrophilic and degradable than industrial nylons has attracted considerable attention.[3] This biodegradability of polyamides has found many applications, such as biomedical materials for temporary surgical use and in drug delivery.[4]

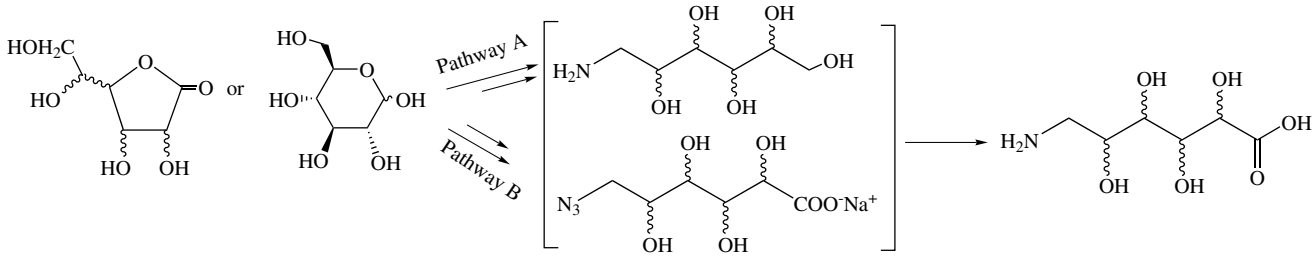
Apart from the work of Fleet[2,5] and Varela,[1b,6] there have been no reports on the synthesis of polymeric sugar analogues of polyhydroxylated nylon 6.

In contrast, polyhydroxylated nylon 6,6 has been extensively studied.[3,7] This is due, undoubtedly, to the difficulty in accessing polyhydroxylated 6-aminohexanoic acid monomers, which require longer synthetic sequences.[2]

2. Results and discussion

Herein, we report a direct and efficient synthesis of fully hydroxylated 6-amino-6-deoxyaldonic acids from unprotected D-hexonolactones and D-glucose as starting materials either via 6-amino-6-deoxy-D-hexitols (pathway A, Scheme 1) or via 6-amino-6-deoxy-D-aldonic acid salts (pathway B, Scheme 1).

The obtained 6-amino-6-deoxyaldonic acids should provide monomers for polymerization to afford fully



Scheme 1.

* Corresponding author. Tel.: +33 3 22 82 75 66; fax: +33 3 22 82 75 60; e-mail: imane.Stasik@sc.u-picardie.fr

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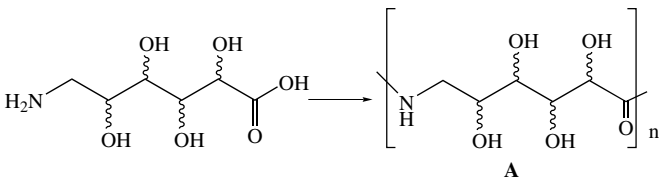
doi:10.1016/j.tetasy.2006.04.018



Scheme 2.

hydroxylated polymers of nylon 6, such as species **A** (Scheme 2).

The preceding paper described the synthesis of 5-amino-deoxypentitols from unprotected D-pentono-1,4-lactones in 84–92% overall yields.[8] In pathway A, we applied this strategy for the synthesis of 6-amino-6-deoxy-D-hexitols.

We have previously described the preparation of 6-bromo-6-deoxy-D-galactono-1,4-lactone **1** from the unprotected corresponding D-galactono-1,4-lactone in good yield (82%), by means of carbon tetrabromide–triphenylphosphine in pyridine.[9]

Thus treatment of **1** with lithium azide in *N*,*N*-dimethylformamide gave 6-azido-6-deoxy-D-galactono-1,4-lactone **2** in 91% yield. Compound **2** was then treated with sodium borohydride in EtOH (The pH was maintained below 7.) to give 6-azido-6-deoxy-D-galactitol **3** in 98% yield. Catalytic hydrogenation of **3** over palladium on charcoal (10%), at 50 °C in EtOH, produced the desired 6-amino-6-deoxy-D-galactitol **4** in 98% yield[9] (Scheme 3).

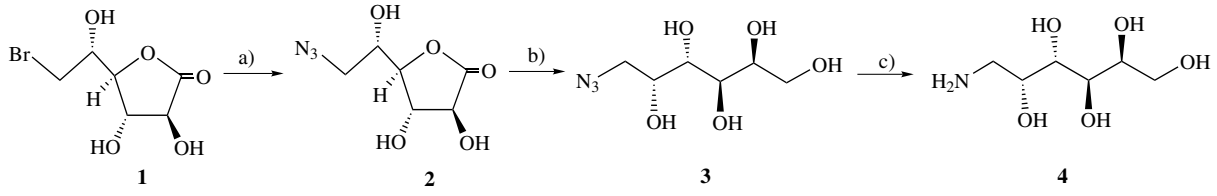
D-Mannono-1,4-lactone was used as the key starting material for the synthesis of 6-amino-6-deoxy-D-mannitol **8**. For the synthesis of D-mannono-1,4-lactone, which was not commercially available, we oxidized D-mannose, using a modified procedure, and obtained the title product, which was isolated in quantitative yield (bromine-water in the presence of sodium hydrogencarbonate).[9]

Bromination of D-mannono-1,4-lactone using a PPh_3/CBr_4 system in pyridine, followed by azidation (LiN_3/DMF), afforded 6-azido-6-deoxy-D-mannono-1,4-lactone **6** in 98% yield. Treatment of **6** with sodium borohydride produced 6-azido-6-deoxy-D-mannitol **7** in 98% isolated yield. Catalytic hydrogenation of **7** gave 6-amino-6-deoxy-D-mannitol **8** in 98% isolated yield[9] (Scheme 4).

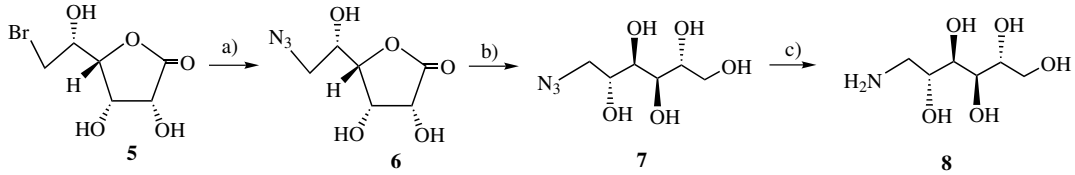
For the synthesis of 6-amino-6-deoxy-D-glucitol **12**, we first selected D-gluconolactone as a starting material. D-Glucono-1,5-lactone was subjected to bromination, for the preparation of 6-bromo-6-deoxy-D-glucono-1,4-lactone, by using carbon tetrabromide–triphenylphosphine system. However, in all instances and under different reaction conditions, the bromination was unsuccessful. The NMR spectra of the resulting product showed the formation of 3,6-anhydro-D-glucono-1,4-lactone. This cyclization suggested the attack of the alkoxyphosphonium group at C-3–C-6, with nucleophilic displacement of the bromide atom. Tosylation of D-glucono-1,5-lactone afforded the same compound.

The $SOBr_2$/DMF system which, with the pentonolactones, regioselectively gives, the 5-bromo derivatives[10] led in this case to a complex mixture. In a second reaction time, bromination of D-gluconolactone using 32% HBr in acetic acid,[11] afforded a mixture of 6-bromo-6-deoxy-D-glucono-1,4-lactone and 2,6-dibromo derivative.

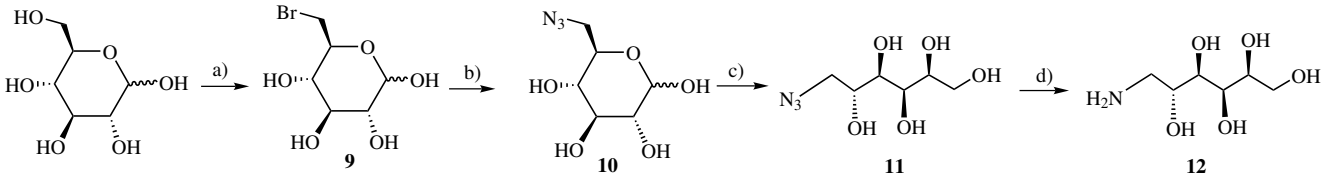
Due to the difficulties in obtaining 6-bromo-6-deoxy-D-glucono-1,4-lactone, we tried an alternative synthetic pathway for the preparation of 6-amino-6-deoxy-D-glucitol **12** starting from D-glucose (Scheme 5). Treatment of D-glucose with carbon tetrabromide–triphenylphosphine in DMF gave 6-bromo-6-deoxy-D-glucose **9** in 56% yield (**9** should be employed crudely for the next step). The nucleophilic substitution of the bromide in compound **9** with lithium azide readily took place and gave the expected azide derivative **10** in 70% yield. Product **10** was accompanied, under different reaction conditions, by the presence of a by-product, which was identified as 3,6-anhydro-D-glucose. When **10** was treated by sodium borohydride in ethanol, 6-azido-6-deoxy-D-glucitol **11** was isolated in 96% yield. Catalytic hydrogenation of **11** gave 6-amino-6-deoxy-D-glucitol **12** in 95% yield.



Scheme 3. Reagents and conditions: (a) LiN_3–DMF, 91%; (b) $NaBH_4$–EtOH, 98%; (c) H_2–Pd/C, 98%.



Scheme 4. Reagents and conditions: (a) LiN_3–DMF, 98%; (b) $NaBH_4$–EtOH, 98%; (c) H_2–Pd/C, 98%.



Scheme 5. Reagents and conditions: (a) PPh_3–CBr_4, DMF, 56%; (b) LiN_3–DMF, 70%; (c) $NaBH_4$–EtOH, 96%; (d) H_2–Pd/C, 95%.

For the oxidation of 6-amino-6-deoxy-D-hexitols to 6-amino-6-deoxy-D-glyconic acids, we proceeded using the same method with compound **4**. Thus, an aqueous solution of 6-amino-6-deoxy-D-galactitol **4** was treated with TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) in the presence of sodium hypochlorite and potassium bromide.[12] After 4 days, as evolution was no longer noted, and the reaction was stopped. NMR spectra of the crude material showed the presence of the starting material **4** and the formation of a second product. This later presents, in particular, in addition to the signal at 43 ppm (corresponding to the aminomethylene group) a signal at 178 ppm corresponding to a carbonyl group. The mass spectrum showed a diagnostic peak at m/z 218 $(M+Na)^+$, which confirms the formation of the 6-amino-6-deoxy-D-galactonic acid. In the non-resoluble mixture (by liquid chromatography and HPLC) of 6-amino-6-deoxy-D-galactonic acid **14** and compound **4**, the ratio was **4**:**14** = 3:2.

To avoid this difficult step of separation, we investigated a second route (pathway B). Treatment of 6-azido-6-deoxy-D-galactono-1,4-lactone **2** with NaOH (2 equiv), in EtOH/water at room temperature for 1 h, allowed us to obtain 6-azido-6-deoxy-D-galactonic acid salt **13** in 95% yield (Scheme 6). Catalytic hydrogenation (Pd/C 10%) of **13**, in water at room temperature for 1 h, followed by treatment with acidic resin (Amberlite IR-120^+) afforded, after filtration, 6-amino-6-deoxy-D-galactonic acid **14** in 93% yield (Scheme 6).

Using this strategy, 6-azido-6-deoxy-D-mannono-1,4-lactone **6** and 6-azido-6-deoxy-D-glucono-1,5-lactone **17** were treated using the same conditions to give 6-amino-6-deoxy-D-mannonic acid **16** and 6-amino-6-deoxy-D-gluconic acid (**19**) in 88% and 85% yields, respectively.

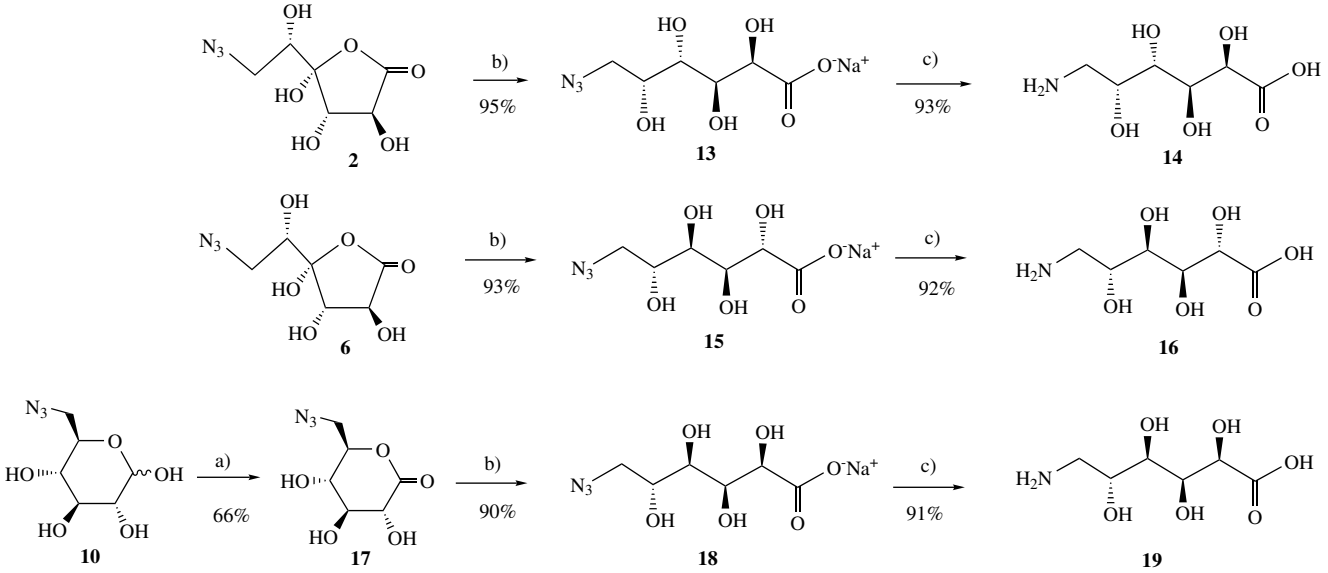
3. Conclusion

In summary, we have reported a new procedure for the synthesis of 6-amino-6-deoxy-D-galactitol (**4**), D-mannitol (**8**) and D-glucitol (**12**) in good yields. We have also developed a direct synthesis of 6-amino-6-deoxy-D-galactonic acid (**14**), 6-amino-6-deoxy-D-mannonic acid (**16**) and 6-amino-6-deoxy-D-gluconic acid (**19**), which may be suitable monomers for the preparation of new polymers as polyhydroxylated nylon 6.

4. Experimental

4.1. General

Melting points were determined on a Buchi 535 apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter, using a sodium lamp ($\lambda = 589$ nm) at 24 °C. ^1H and ^{13}C NMR spectra were recorded in D_2O, in MeOD or in DMSO-d_6. Me_4Si was used as an internal standard on a Bruker 300 MHz



Scheme 6. Reagents and conditions: (a) Br_2, $NaHCO_3$, H_2O; (b) NaOH, EtOH–H_2O, rt; (c) H_2, Pd/C, H_2O; Amberlite IR-120^+.

spectrometer. Thin-layer chromatography (TLC) was performed on E. Merck glass plates coated with silica gel sheets (Silica Gel F_{254}) and stained with phosphomolybdic acid–aqueous H_2SO_4 solution. Column chromatography was carried out on silica gel (E. Merck 230–400 mesh). All solvents were distilled before use.

4.1.1. 6-Bromo-6-deoxy-D-glucose 9. A solution of D-glucose (1 g, 5.55 mM) in DMF (50 mL) was treated with triphenylphosphine (2.91 g, 2 equiv) and carbon tetrabromide (3.68 g, 2 equiv) at 20 min intervals. The mixture was stirred, under an inert atmosphere, at 50 °C, for 1.5 h. The solution was concentrated in vacuo, the residue was diluted with water and washed with CH_2Cl_2. The water extracts were concentrated in vacuo and the obtained residue chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (9:1) gave **9** (0.75 g, 56%) as a white solid; ($\alpha/\beta = 1$); R_f 0.4 (EtOAc–MeOH 9:1; ^{13}C NMR (75 MHz, MeOD): δ 99.2, 96.3, 76.2, 75.2, 75.0, 73.4, 72.3, 70.6, 34.0, 33.2; LC–MS (*m*/*z*): 266 $(M+Na)^+$. Anal. Calcd for $C_6H_{11}BrO_5$: C, 29.65; H, 4.56; Br, 32.88. Found: C, 29.60; H, 4.59; Br, 32.83.

4.1.2. 6-Azido-6-deoxy-D-glucose 10. A stirred solution of 6-bromo-6-deoxy-D-glucose **9** (0.4 g, 1.65 mM) in DMF (5 mL) was treated with lithium azide (20% in H_2O) (6 mL, 1.3 equiv) and set aside at 80 °C for 1 h. The mixture was poured into ice-water (7 mL) and the product extracted with ethyl acetate. The organic layer was concentrated in vacuo and the obtained residue was chromatographed on silica gel. Elution with EtOAc–hexanes (7:3) gave **10** (0.243 g, 70%) as a yellow oil: R_f 0.4 (EtOAc–MeOH 9:1; ^{13}C NMR (75 MHz, MeOD): δ 97.0, 92.9, 76.7, 75.4, 75.1, 73.6, 72.6, 71.5, 71.2, 71.0, 51.6; LC–MS (*m*/*z*): 228 $(M+Na)^+$. Anal. Calcd for $C_6H_{11}N_3O_5$: C, 35.12; H, 5.40; N, 20.48. Found: C, 35.08; H, 5.43; N, 20.45.

4.1.3. General procedure for the reduction of 6-azido-6-deoxy derivatives. To a solution of 6-azido-6-deoxy-D-hexono-1,4-lactones **2**, **6** (0.56–0.46 g) or 6-azido-6-deoxy-D-glucose **10** (0.29 g) in EtOH (20 mL) was added $NaBH_4$ (8 mM) at such a rate that the pH was maintained below 7. Then a further amount of $NaBH_4$ (9.5 mM) was added to increase the pH to 9. Stirring was continued at room temperature, for 1 h, before adding more ion exchange resin (Dowex 50×8–100 ion) to decrease the pH to 3. The resin was then removed by filtration. The filtrate was concentrated and co-concentrated with MeOH (3×18 mL) to give the crude mixture, which was chromatographed on silica gel; elution was done with EtOAc–MeOH (1:1).

4.1.3.1. 6-Azido-6-deoxy-D-galactitol 3. White solid (0.56 g, 98%): R_f 0.65 (EtOAc–MeOH 7:3); $[\alpha]_D = -15.4$ (*c* 0.50, DMSO); mp 141–142 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.87 (m, 1H), 3.69 (dd, 1H, $J = 4.6$, 12.3 Hz), 3.40 (m, 4H), 3.17 (dd, 1H, $J = 4.6$, 12.3 Hz). ^{13}C NMR (75 MHz, DMSO-d_6): δ 70.9, 70.7, 70.0, 63.9, 54.9; LC–MS (*m*/*z*): 230 $(M+Na)^+$. Anal. Calcd for $C_6H_{13}N_3O_5$: C, 34.78; H, 6.32; N, 20.28. Found: C, 34.75; H, 6.36; N, 20.33.

4.1.3.2. 6-Azido-6-deoxy-D-mannitol 7. White solid (0.46 g, 98%): R_f 0.61 (EtOAc–MeOH 7:3); $[\alpha]_D = +27$ (*c* 1.00, H_2O); mp 119–120 °C; ^{1}H NMR (300 MHz, MeOD): δ 3.85 (m, 4H), 3.70 (m, 2H), 3.57 (dd, 1H, $J = 6.4$, 12.9 Hz), 3.41 (dd, 1H, $J = 2.6$ Hz). ^{13}C NMR (75 MHz, MeOD): δ 71.7, 70.6, 70.2, 69.5, 63.8, 54.7; LC–MS (*m*/*z*): 230 $(M+Na)^+$. Anal. Calcd for $C_6H_{13}N_3O_5$: C, 34.78; H, 6.32; N, 20.28. Found: C, 34.81; H, 6.35; N, 20.25.

4.1.3.3. 6-Azido-6-deoxy-D-glucitol 11. White solid (0.282 g, 96%): R_f 0.56 (EtOAc–MeOH 7:3); mp 187–188 °C; $[\alpha]_D = +12.2$ (*c* 0.50, H_2O); ^{1}H NMR (300 MHz, D_2O): δ 4.06 (m, 1H), 3.76 (dd, 1H, $J = 4.5$, 8.2 Hz), 3.42 (m, 3H), 3.27 (dd, 1H, $J = 7.0$, 12.6 Hz), 3.21 (dd, 1H, $J = 4.4$ Hz); ^{13}C NMR (75 MHz, D_2O): δ 73.0, 71.9, 71.2, 69.7, 63.4, 54.5; LC–MS (*m*/*z*): 230 $(M+Na)^+$. Anal. Calcd for $C_6H_{13}N_3O_5$: C, 34.78; H, 6.32; N, 20.28. Found: C, 34.73; H, 6.29; N, 20.32.

4.1.4. General procedure for the reduction of 6-azido-6-deoxy-D-galactitol, D-mannitol and D-glucitol by catalytic hydrogenation. A solution of 6-azido-6-deoxy-D-galactitol **3**, D-mannitol **7**, or D-glucitol **11** (0.2 g, 0.97 mM) in EtOH (8 mL) was treated with palladium on charcoal (10%, 0.035 g) and then hydrogenated, for 2 h, at 50 °C. The mixture was filtered through a layer of Celite and the filtrate was concentrated in vacuo to give the desired monoaminoalditol.

4.1.4.1. 6-Amino-6-deoxy-D-galactitol 4. White solid (0.171 g, 98%): R_f 0.31 (EtOAc–MeOH 5:5); $[\alpha]_D = +22$ (*c* 0.80, H_2O); mp 157–158 °C; ^{1}H NMR (300 MHz, D_2O): δ 3.92 (m, 3H), 3.31 (m, 2H), 2.63 (d, 2H); ^{13}C NMR (75 MHz, D_2O): δ 71.9, 71.1, 63.8, 63.6, 43.9; LC–MS (*m*/*z*): 204 $(M+Na)^+$. Anal. Calcd for $C_6H_{15}O_5N$: C, 39.77; H, 8.34; N, 7.73. Found: C, 39.73; H, 8.30; N, 7.69.

4.1.4.2. 6-Amino-6-deoxy-D-mannitol 8. White solid (0.168 g, 98%): R_f 0.25 (EtOAc–MeOH 5:5); $[\alpha]_D = +28.4$ (*c* 1, H_2O); mp 149–151 °C; ^{1}H NMR (300 MHz, D_2O): δ 3.79 (dd, 1H, $J = 2.3$, 11.5 Hz), 3.65 (m, 4H), 3.57 (dd,1H, $J = 7.1$ Hz). 2.94 (dd, 1H, $J = 2.8$, 14.8 Hz), 2.63 (dd, 1H, $J = 7.6$ Hz); ^{13}C NMR (75 MHz, D_2O): δ 71.2, 71.0, 69.6, 63.6, 43.7; LC–MS (*m*/*z*): 204 $(M+Na)^+$. Anal. Calcd for $C_6H_{15}O_5N$: C, 39.77; H, 8.34; N, 7.73. Found: C, 39.70; H, 8.37; N, 7.69.

4.1.4.3. 6-Amino-6-deoxy-D-glucitol 12. White solid (0.166 g, 95%): R_f 0.32 (EtOAc–MeOH 5:5); $[\alpha]_D = +4.2$ (*c* 1, H_2O); mp 179–180 °C; ^{1}H NMR (300 MHz, D_2O): δ 3.90 (m, 1H), 3.63 (m, 5H), 3.02 (dd, 1H, $J = 6.7$, 12.2 Hz) , 2.28 (dd, 1H); ^{13}C NMR (75 MHz, D_2O): δ 71.3, 70.6, 69.9, 67.2, 64.1, 44.9; LC–MS (*m*/*z*): 204 $(M+Na)^+$. Anal. Calcd for $C_6H_{15}O_5N$: C, 39.77; H, 8.34; N, 7.73. Found: C, 39.73; H, 8.30; N, 7.68.

4.1.5. 6-Azido-6-deoxy-D-glucono-1,5-lactone 17. To a solution of 6-azido-6-deoxy-D-glucose **10** (0.77 g, 3.76 mM) and sodium hydrogencarbonate (1.12 g, 1.5 equiv) in distilled water (10 mL) cooled at 0 °C, bromine (3×0.07 mL, 1.5 equiv) was added at 20 min intervals.

The reaction mixture was stirred at this temperature for 1 h and then for 3 h at room temperature. Sodium thiosulfate was added to destroy the excess of bromine, and the solvent was removed in vacuo to give a white solid. The solid obtained was extracted with acetone at 50 °C. The mixture was filtered through a layer of Celite and the filtrate concentrated in vacuo to give **17** (0.5 g, 66%) as a yellow oil: R_f 6 (EtOAc–MeOH 6:1); $[\alpha]_D = +79$ (*c* 0.5, MeOH); ^{1}H NMR (300 MHz, MeOD): δ 4.08 (d, 1H), 4.0 (d, 1H, $J = 9.3$ Hz), 3.82 (dd, 1H, $J = 7.5$ Hz), 3.72 (t, 1H, $J = 9.1$ Hz), 3.15 (dd, 1H, $J = 2.6$, 14.4 Hz), 2.97 (dd, 1H, $J = 4.0$ Hz); ^{13}C NMR (75 MHz, MeOD): δ 173.2, 78.1, 74.5,72.8, 71.6, 53.4; LC–MS (*m*/*z*): 226 $(M+Na)^+$. Anal. Calcd for $C_6H_9N_3O_5$: C, 35.47; H, 4.47. N, 20.68. Found: C, 35.40; H, 4.42; N, 20.71.

4.1.6. General procedure for preparation of 6-azido-6-deoxy-D-aldonic acid sodium salts. To a solution of 6-azido-6-deoxy-D-hexonolactone **2**, **6** or **17** (1 g, 4.92 mM) in EtOH/water (3:1, 10 mL) was added NaOH (2 equiv). The reaction mixture was stirred at room temperature for 1 h 30 min and EtOH (10 mL) was added. The suspension was then filtered, and the white solid obtained was washed with EtOH/water (3:1, 10 mL) to give the desired 6-azido-6-deoxy-D-glyconic acid salt.

4.1.6.1. 6-Azido-6-deoxy-D-galactonic acid sodium salt (13). White solid (1.13 g, 95%): $[\alpha]_D = +64.7$ (*c* 0.4, H_2O); mp 203–204 °C; ^{1}H NMR (300 MHz, D_2O): δ 4.13 (d, 1H, $J = 1.8$ Hz), 3.95 (m, 1H), 3.84 (dd, 1H, $J = 9.9$ Hz), 3.46 (dd, 1H, $J = 2.0$ Hz), 3.39 (dd, 1H, $J = 6.3$, 11.8 Hz), 3.29 (dd, 1H, $J = 3.3$ Hz); ^{13}C NMR (75 MHz, D_2O): δ 179.8, 71.8, 71.7, 70.6, 69.2, 54.1; LC–MS (*m*/*z*): 266 $(M+Na)^+$. Anal. Calcd for $C_6H_{10}N_3NaO_6$: C, 29.64; H, 4.15; N, 17.28. Found: C, 29.60; H, 4.10; N, 17.32.

4.1.6.2. 6-Azido-6-deoxy-D-mannonic acid sodium salt 15. White solid (1.11 g, 93%): $[\alpha]_D = +5.1$ (*c* 0.6, H_2O); mp 191–192 °C; ^{1}H NMR (300 MHz, D_2O): δ 3.95 (d, 1H, $J = 5.7$ Hz), 3.80 (dd, 1H, $J = 2.0$ Hz), 3.66 (m, 1H), 3.52 (dd, 1H, $J = 9.5$ Hz), 3.42 (dd, 1H, $J = 2.6$, 13.2 Hz), 3.27 (dd, 1H, $J = 6.6$ Hz); ^{13}C NMR (75 MHz, D_2O): δ 180.0, 74.7, 71.8, 70.9, 70.5, 54.4; LC–MS (*m*/*z*): 266 $(M+Na)^+$. Anal. Calcd for $C_6H_{10}N_3NaO_6$: C, 29.64; H, 4.15; N, 17.28. Found: C, 29.69; H, 4.12; N, 17.23.

4.1.6.3. 6-Azido-6-deoxy-D-gluconic acid sodium salt 18. Yellow oil (1.08 g, 90%): $[\alpha]_D = +7.0$ (*c* 0.3, H_2O); ^{1}H NMR (300 MHz, D_2O): δ 4.26 (d, 1H, $J = 2.2$ Hz), 4.17 (dd, 1H, $J = 4.4$ Hz), 3.88 (m, 1H), 3.69 (dd, 1H, $J = 3.9$, 14.5 Hz), 3.62 (dd, 1H, $J = 4.2$ Hz); ^{13}C NMR (75 MHz, D_2O): δ 171.7, 74.6, 73.1, 71.8, 70.5, 54.3; LC–MS (*m*/*z*): 266 $(M+Na)^+$. Anal. Calcd for $C_6H_{10}N_3NaO_6$: C, 29.64; H, 4.15; N, 17.28. Found: C, 29.61; H, 4.18; N, 17.24.

4.1.7. General procedure for the preparation of 6-amino-6-deoxy-D-glyconic acids. A solution of 6-azido-6-deoxy-D-glyconic acid salt **13**, **15** or **18** (0.5 g, 2.06 mM) in water (10 mL) was treated with palladium on charcoal 10% (0.05 g), hydrogenated for 1 h at room temperature and the mixture filtered through a layer of Celite. The acidic resin (Amberlite IR-120+) was added and the suspension stirred for 30 min. The resin was then removed by filtration. The filtrate was concentrated in vacuo to give the desired 6-amino-6-deoxy-D-glyconic acid.

4.1.7.1. 6-Amino-6-deoxy-D-galactonic acid 14. White solid (0.375 g, 93%): $[\alpha]_D = +83.2$ (*c* 0.4, H_2O); mp 202–203 °C; ^{1}H NMR (300 MHz, D_2O): δ 4.27 (d, 1H, $J = 1.5$ Hz), 4.04 (m, 1H), 3.88 (dd, 1H, $J = 9.5$ Hz), 3.49 (dd, 1H, $J = 1.6$ Hz), 3.06 (d, 2H, $J = 6.2$ Hz); ^{13}C NMR (75 MHz, D_2O): δ 178.4, 71.4, 71.1, 70.8, 66.5, 43.0; LC–MS (*m*/*z*): 218 $(M+Na)^+$. Anal. Calcd for $C_6H_{13}NO_6$: C, 36.92; H, 6.72; N, 7.18. Found: C, 36.88; H, 6.76; N, 7.21.

4.1.7.2. 6-Amino-6-deoxy-D-mannonic acid 16. White solid (0.371 g, 92%): $[\alpha]_D = +4.3$ (*c* 0.6, H_2O); mp 199–201 °C; ^{1}H NMR (300 MHz, D_2O): δ 4.04 (d, 1H, $J = 5.7$ Hz), 3.89 (dd, 1H, $J = 1.6$ Hz), 3.84 (m, 1H,), 3.66 (dd, 1H, $J = 8.1$ Hz), 3.29 (dd, 1H, $J = 3.3$, 13.2 Hz), 2.97 (dd, 1H, $J = 8.6$ Hz); ^{13}C NMR (75 MHz, D_2O): δ 179.4, 74.0, 72.5, 70.7, 67.6, 42.7; LC–MS (*m*/*z*): 218 $(M+Na)^+$. Anal. Calcd for $C_6H_{13}NO_6$: C, 36.92; H, 6.72; N, 7.18. Found: C, 36.95; H, 6.69; N, 7.13.

4.1.7.3. 6-Amino-6-deoxy-D-gluconic acid 19. White solid (0.367 g, 91%): $[\alpha]_D = +18.7$ (*c* 0.5, H_2O); mp 199–201 °C; ^{1}H NMR (300 MHz, D_2O): δ 3.61 (d, 1H, $J = 5.1$ Hz), 3.43 (dd, 1H, $J = 2.0$ Hz), 3.29 (m, 2H,), 2.81 (dd, 1H, $J = 3.9$, 14.1 Hz), 2.70 (dd, 1H, $J = 3.6$ Hz; ^{13}C NMR (75 MHz, D_2O): δ 177.0, 77.1, 75.9, 72.6, 69.9, 43.0; LC–MS (*m*/*z*): 218 $(M+Na)^+$. Anal. Calcd for $C_6H_{13}NO_6$: C, 36.92; H, 6.72; N, 7.18. Found: C, 36.91; H, 6.77; N, 7.24.

Acknowledgements

We thank the Ministère de la Recherche and the Conseil Régional de Picardie for financial support.

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