

Note

A concise synthesis of 5-amino-5-deoxyaldonic acids as monomers for the preparation of nylon 5

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Abstract—Saponification of 5-azido-5-deoxy-D-pentonolactones (*ribo*-, *arabino*-, *xylo*-) with NaOH gave the corresponding 5-azido-5-deoxyaldonic acids sodium salts which, after regeneration of the acid form followed by catalytic reduction, led to the target compounds in 98% overall yields.

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Efforts have been developed in the last few years towards the synthesis of hydrophilic and biodegradable polymers.¹

The majority of the commercially available synthetic biodegradable polymers are polyesters.² Polyhydroxylated polyamides are of interest being more hydrophilic and biodegradable as compared to commercial nylons.³ These have found applications, such as biomedical materials for temporary surgical use and in drug delivery.⁴ Hydroxylated polyamides might then be of interest as substitutes.

Except for our work,⁵ and the results of Fleet and co-workers,^{2,6} Varela and co-workers,^{1b,7} there is no other report on the synthesis of polymeric sugar analogues of polyhydroxylated nylons 5 and 6. On the other hand, polyhydroxylated nylon 5,5; 5,6 and 6,6 has been extensively studied.^{3,8} This is due, undoubtedly, to the difficulty of accessing to polyhydroxylated 5 and 6-amino-deoxyaldonic acid monomers, which require longer synthetic sequences.²

Herein we describe a concise synthesis of fully hydroxylated 5-amino-5-deoxyaldonic acids from unprotected D-pentonolactones as starting materials via 5-azido-5-

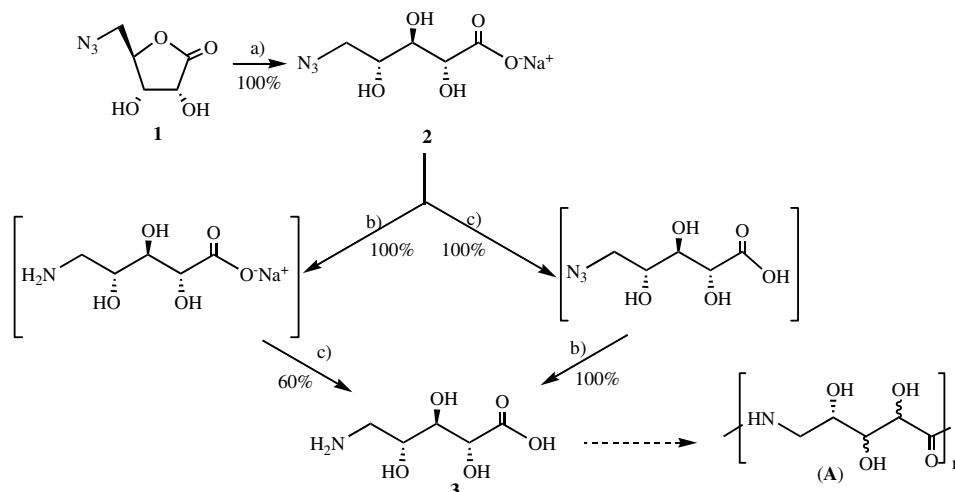
deoxy-D-aldonic acid salts. The obtained 5-amino-5-deoxyaldonic acids should provide a convenient source of monomers for polymerisation to afford more hydrophilic analogues of nylon 5, such as polyamide A (Scheme 1).

Reaction of 5-azido-5-deoxy-D-ribo-1,4-lactone⁹ (**1**) with NaOH (2 equiv) in EtOH–water at room temperature for 1 h led to 5-azido-5-deoxy-D-ribonic acid sodium salt (**2**) in 98% yield (Scheme 1). Catalytic hydrogenation (Pd/C 10%) of **2**, in water at room temperature for 1 h, followed by treatment with Amberlite IR-120 H⁺ afforded, after filtration, 5-amino-5-deoxy-D-ribonic acid (**3**) in only 60% yield (Scheme 1). This moderate yield can be explained by some retention of the amino derivative on the resin.

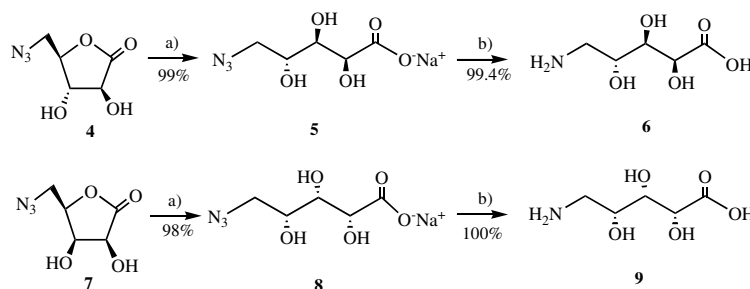
To avoid this difficulty and to improve the yield, we have reversed the order of the last two steps. Indeed, treatment of the 5-azido-5-deoxy-D-ribonic acid salt (**2**) with the acidic resin followed by catalytic hydrogenation (Pd/C 10%) afforded 5-amino-5-deoxy-D-ribonic acid (**3**) in quantitative yield. This second approach presents the advantage of improving the overall yield of the synthesis and allows an easy follow up of the advancement of the hydrogenation step by TLC.

Using this strategy, 5-azido-5-deoxy-D-arabinono-(**4**) and D-xylo-1,4-lactones⁹ (**7**) were treated in the same conditions to give 5-amino-5-deoxy-D-arabinonic acid

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Scheme 1. Reagents and conditions: (a) NaOH, EtOH–H₂O, rt; (b) H₂, Pd/C, H₂O; (c) Amberlite IR-120⁺.



Scheme 2. Reagents and conditions: (a) NaOH, EtOH–H₂O, rt; (b) Amberlite IR-120⁺; H₂, Pd/C, H₂O.

(6) and 5-amino-5-deoxy-D-xylonic acid (9) in 98% overall yields (Scheme 2).

In summary, we have developed a concise synthesis of 5-amino-5-deoxy-D-ribonic acid (3), 5-amino-5-deoxy-D-arabinonic acid (6) and 5-amino-5-deoxy-D-xylonic acid (9), which are suitable monomers for the preparation of new hydrophilic polymers such as polyhydroxylated nylon 5.

1. Experimental

1.1. General methods

Melting points were determined on a Büchi 535 apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter, using a sodium lamp (λ 589 nm) at 24 °C. ¹H and ¹³C NMR spectra were recorded in D₂O on a Bruker 300 MHz spectrometer; Me₄Si was used as an internal standard. Mass spectra were recorded on a Q-TOF Global mass spectrometer in ESI mode. Thin-layer chromatography (TLC) was performed on E. Merck glass plates silica gel sheets (Silica Gel F₂₅₄) and stained with phosphomolybdic acid–aq H₂SO₄ soln. Column

chromatography was carried out on silica gel (E. Merck 230–400 mesh). All solvents were purified in a conventional manner.

1.2. General procedure for the preparation of 5-azido-5-deoxy-D-aldonic acid sodium salts (2, 5 and 8)

To a soln of 5-azido-5-deoxy-D-pentono-1,4-lactones⁹ (1, 4 or 7) (0.25 g, 1.45 mM) in 3:1 EtOH–water (5 mL) was added NaOH (2 equiv). The reaction mixture was stirred at room temperature for 1 h and EtOH (5 mL) was added. The suspension was then filtered and the obtained white solid was washed with 3:1 EtOH–water (5 mL) to give the desired 5-azido-5-deoxy-D-aldonic acid sodium salt.

1.2.1. 5-Azido-5-deoxy-D-ribonic acid sodium salt (2). (0.303 g, 98.5%); white solid: $[\alpha]_D^{20} +8.0$ (*c* 0.25, water); mp 204–205 °C; ¹H NMR (300 MHz, D₂O): δ 4.07 (d, 1H, *J* 3.3 Hz, H-2), 3.86 (dd, 1H, *J* 7.5 Hz, H-3), 3.79 (m, 1H, *J* 2.8 Hz, H-4), 3.49 (dd, 1H, *J* 6.9 Hz, H-5a), 3.37 (dd, 1H, *J* 13.1 Hz, H-5b); ¹³C NMR (75 MHz, D₂O): δ 178.2, 73.6, 73.5, 70.4, 53.7; ESIMS: *m/z* 236 (M+Na)⁺. Anal. Calcd for C₅H₈N₃NaO₅: C, 28.18; H, 3.78; N, 19.72. Found: C, 28.30; H, 3.72; N, 19.52.

1.2.2. 5-Azido-5-deoxy-D-arabinonic acid sodium salt (5). (0.305 g, 99%); white solid: $[\alpha]_{\text{D}}^{20} +3$ (c 0.23, water); mp >280 °C; ^1H NMR (300 MHz, D_2O): δ 4.14 (d, 1H, J 3.8 Hz, H-2), 3.94 (m, 1H, J 2.9 Hz, H-4), 3.83 (dd, 1H, J 7.5 Hz, H-3), 3.57 (dd, 1H, J 6.9 Hz, H-5a); 3.44 (dd, 1H, J 13.0 Hz, H-5b); ^{13}C NMR (75 MHz, D_2O): δ 178.5, 73.9, 73.5, 70.8, 53.8; ESIMS: m/z 236 ($\text{M}+\text{Na}$) $^+$. Anal. Calcd for $\text{C}_5\text{H}_8\text{N}_3\text{NaO}_5$: C, 28.18; H, 3.78; N, 19.72. Found: C, 28.27; H, 3.68; N, 19.61.

1.2.3. 5-Azido-5-deoxy-D-xyloonic acid sodium salt (8). (0.302 g, 98%); white solid: $[\alpha]_{\text{D}}^{20} +18$ (c 0.23, water); mp 205 °C; ^1H NMR (300 MHz, D_2O): δ 4.04 (d, 1H, J 2.5 Hz, H-2), 3.89 (m, 1H, J 3.6 Hz, H-4), 3.82 (dd, 1H, J 6.1 Hz, H-3), 3.50 (dd, 1H, J 6.9 Hz, H-5a), 3.41 (dd, 1H, J 13 Hz, H-5b); ^{13}C NMR (75 MHz, D_2O): δ 178.7, 72.9, 72.8, 71.6, 53.3; ESIMS: m/z 236 ($\text{M}+\text{Na}$) $^+$. Anal. Calcd for $\text{C}_5\text{H}_8\text{N}_3\text{NaO}_5$: C, 28.18; H, 3.78; N, 19.72. Found: C, 28.11; H, 3.81; N, 19.80.

1.3. General procedure for the preparation of 5-amino-5-deoxy-D-aldonic acids (3, 6 and 9)

A soln of 5-azido-5-deoxy-D-aldonic acid sodium salt (2, 5 or 8) (0.20 g, 0.94 mM) in water (5 mL) was treated with Amberlite IR-120 H^+ . The suspension was stirred for 30 min at room temperature. The resin was filtered off and the filtrate was concentrated under diminished pressure. To a soln of the obtained residue in water was added palladium on charcoal 10% (50 mg) and the suspension was hydrogenated for 1 h at room temperature. The suspension was filtered through a layer of Celite to give the desired 5-amino-5-deoxy-D-aldonic acid.

1.3.1. 5-Amino-5-deoxy-D-ribonic acid (3). (0.155 g, 100%); white solid: $[\alpha]_{\text{D}}^{20} +20$ (c 0.21, water); mp 200 °C; ^1H NMR (300 MHz, D_2O): δ 4.08 (d, 1H, J 3.5 Hz, H-2), 3.90 (m, 1H, J 3.2 Hz, H-4), 3.86 (dd, 1H, J 6.0 Hz, H-3), 3.26 (dd, 1H, J 8.2 Hz, H-5a), 3.00 (dd, 1H, J 13.1 Hz, H-5b); ^{13}C NMR (75 MHz, D_2O): δ 178.3, 73.1, 72.7, 68.6, 41.6; ESIMS: m/z 188 ($\text{M}+\text{Na}$) $^+$. Anal. Calcd for $\text{C}_5\text{H}_{11}\text{NO}_5$: C, 36.36; H, 6.71; N, 8.48. Found: C, 36.38; H, 6.80; N, 8.37.

1.3.2. 5-Amino-5-deoxy-D-arabinonic acid (6). (0.154 g, 98.4%); white solid: $[\alpha]_{\text{D}}^{20} +4$ (c 0.24, water); mp 220 °C; ^1H NMR (300 MHz, D_2O): δ 4.14 (d, 1H, J 1.7 Hz, H-2), 3.86 (m, 1H, J 8.4 Hz, H-4), 3.76 (dd, 1H, J 3.1 Hz, H-3), 3.32 (dd, 1H, J 8.9 Hz, H-5a), 2.98 (dd, 1H, J 13.1 Hz, H-5b); ^{13}C NMR (75 MHz, D_2O): δ 178.7, 73.7, 71.3, 67.5, 42.3; ESIMS: m/z 188

($\text{M}+\text{Na}$) $^+$. Anal. Calcd for $\text{C}_5\text{H}_{11}\text{NO}_5$: C, 36.36; H, 6.71; N, 8.48. Found: C, 36.28; H, 6.90; N, 8.59.

1.3.3. 5-Amino-5-deoxy-D-xyloonic acid (9). (0.155 g, 98%); white solid: $[\alpha]_{\text{D}}^{20} +23$ (c 0.25, water); mp 200 °C; ^1H NMR (300 MHz, D_2O): δ 3.96 (d, 1H, J 2.9 Hz, H-2), 3.91 (m, 1H, J 3.0 Hz, H-4), 3.73 (dd, 1H, J 5.2 Hz, H-3), 3.13 (dd, 1H, J 9.3 Hz, H-5a), 2.99 (dd, 1H, J 13.1 Hz, H-5b); ^{13}C NMR (75 MHz, D_2O): δ 177.8, 73.1, 72.7, 68.6, 41.8; ESIMS: m/z 188 ($\text{M}+\text{Na}$) $^+$. Anal. Calcd for $\text{C}_5\text{H}_{11}\text{NO}_5$: C, 36.36; H, 6.71; N, 8.48. Found: C, 36.42; H, 6.68; N, 8.53.

Acknowledgements

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