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Efficient synthesis of L-altrose and L-mannose

Shang-Cheng Hung,* Cheng-Chung Wang and Shankar R. Thopate

Institute of Chemistry, Academia Sinica, Nankang, Taipei 11529, Taiwan

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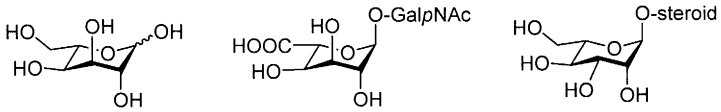
Abstract

Two convenient routes for the synthesis of L-altrose and L-mannose from 1,2:3,5-di-*O*-isopropylidene-β-L-idofuranose in four and six steps via the stereoselective hydroboration and hydrogenation of olefins as key steps are described here, respectively.

Keywords: carbohydrates; glycosides; L-altrose; L-mannose.

L-Altropyranosyl and L-mannopyranosyl units are structural elements of several naturally occurring products, as outlined in Scheme 1. L-Altrose is a component of the extracellular polysaccharide from *Butyrivibrio fibrisolvens* strain CF3.[1] The O-specific polysaccharide of the bacterium *Proteus mirabilis*, a human opportunistic pathogen causing urinary tract infections, contain L-altropyranouronic acid as a new component of O-antigens.[2] L-Mannopyranosides had been found in the sugar units of steroid glycosides[3] and their phenol derivatives are potent substrates for determining the α-L-mannosidase activity of commercial naringinase.[4]



Scheme 1.

Approaches for the synthesis of L-altrose have been reported including the asymmetric Sharpless epoxidation of olefins followed by ring opening,[5] intramolecular Tishchenko reactions of protected hexos-5-uloses[6] and bromination of Δ^4-uronate followed by a three-step conversion.[7] Some efforts had also been made toward the L-mannose comprising the asymmetric hetero Diels–Alder reaction followed by stereoselective hydroboration[8] and the applications of enantioselective Sharpless epoxidation[5] as well as dihydroxylation[9] of olefins. In association with our interest in the synthesis of biologically important L-hexoses, we have explored herein two short routes for the synthesis of L-altrose and L-mannose, respectively.

* Corresponding author.

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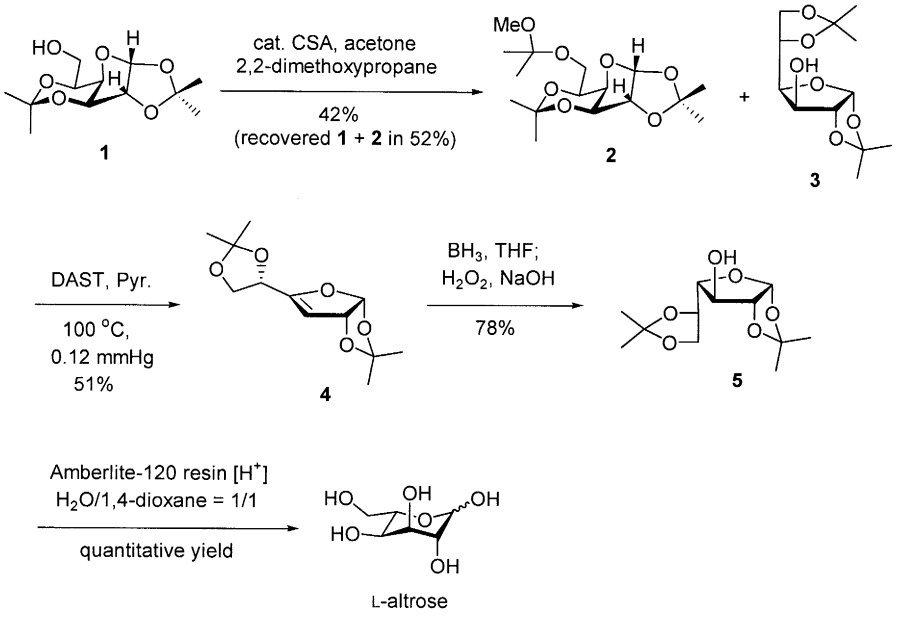
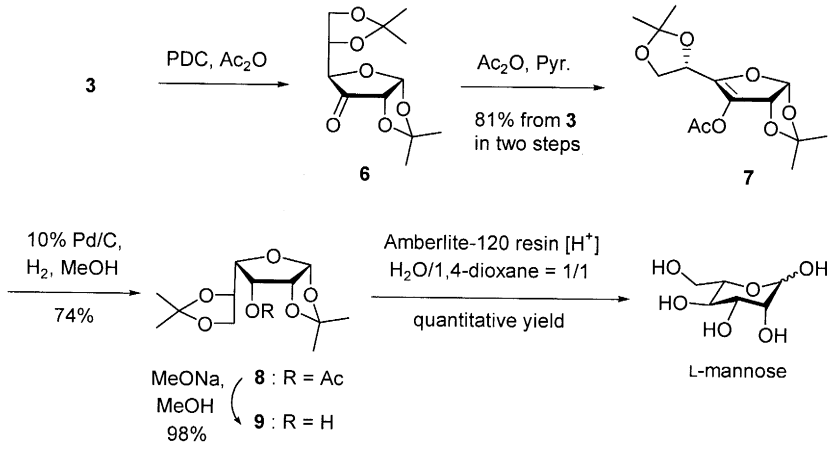
Scheme 2 illustrates an efficient synthesis of L-altrose from 1,2:3,5-di-*O*-isopropylidene-β-L-idofuranose **1** in four steps. The starting material **1**, generated from diacetone α-D-glucose in three steps,[10] underwent orthogonal isopropylidene rearrangement with a solution of 2,2-dimethoxypropane and acetone in the presence of catalytic amount of (±)-camphorsulfonic acid at room temperature to provide 1,2:5,6-di-*O*-isopropylidene-β-L-idofuranose **3** as a white solid (42% after recrystallization from hexane) and a mixture of **2** and unreacted **1** in ca. 52% yield. This mixture can be re-utilized under the same conditions and similar results are obtained. Epimerisation of **3** at C-4 into 1,2:5,6-di-*O*-isopropylidene-β-L-altrofuranose **5** could be carried out by sequential elimination of H_2O and stereoselective hydroboration via the olefin **4** as an intermediate. Diethylaminosulfur trifluoride (DAST)[11] and pyridine were consecutively added to a solution of **3** in dichloromethane at 0°C under nitrogen. The mixture was subjected to distillation by the Kugelhror apparatus at 100°C under 0.12 mmHg to give the olefin **4**[12] (51%) which was treated with borane reagent followed by oxidative work-up to provide **5**[12] as a single isomer in 78% yield. The high stereoselectivity is perhaps due to the steric hindrance of a 5,5-*cis*-fused ring configuration, forming the 3-hydroxy group toward up-face. Acidic hydrolysis of **5** in the presence of Amberlite-120 resin (H^+ form) afforded the desired L-altrose in quantitative yield. Comparison of our data with the literature report[13] revealed identity with respect to ^1H and ^{13}C NMR spectra.



Scheme 2.

The preparation of L-mannose from **3** in five steps is summarized in Scheme 3. The key step involving the inversion of chiral centers in **3** at C-3 and C-4 positions could be achieved by *syn*-reduction of the enol acetate **7**. Oxidation of **3** with PDC and acetic anhydride[14] led to the ketone **6** which underwent enolization in pyridine and acetic anhydride to furnish the enol acetate **7**[12] (81% from **3** in two steps). Stereoselective hydrogenation in the presence of 10% Pd/C as the catalyst provided 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-β-L-mannofuranose **8**[12] in 74% yield. The highly stereoselective *syn*-addition of hydrogen molecule with 3-*endo* double bond occurring from less-hindered side is perhaps induced by the *cis*-fused ring junction. Similar transformation of 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-endofuranose into 1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose via the $NaBH_4$ reduction had

been reported in 34% yield.[15] The yield can be improved by the hydrogenation reaction. Deacetylation of **8** with sodium methoxide in methanol obtained **9** (98%) which was hydrolyzed in acidic media to afford the target L-mannose in quantitative yield. The ^{1}H and ^{13}C NMR spectra are identical with the literature report.[16]



Scheme 3.

In conclusion, two convenient routes for the synthesis of L-altrose, L-mannose and their furanosyl derivatives are successfully developed here, respectively. The application of these carbohydrates for the synthesis of biologically important oligosaccharides is currently under investigation.

Acknowledgements

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12. The selected physical data of key compounds is listed. Compound **4**: IR ($CHCl_3$) ν 1669 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 (d, *J*=5.1 Hz, 1H, H-1), 4.27 (dd, *J*=5.1, 2.2 Hz, 1H, H-2), 5.23 (d, *J*=2.2 Hz, 1H, H-3), 4.57 (t, *J*=6.8 Hz, 1H, H-5), 4.12 (dd, *J*=8.3, 6.8 Hz, 1H, H-6), 3.91 (dd, *J*=8.3, 6.8 Hz, 1H, H-6), 1.43 (s, 3H, C-CH_3), 1.41 (s, 3H, C-CH_3), 1.39 (s, 3H, C-CH_3), 1.37 (s, 3H, C-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.76 (C), 112.26 (C), 110.29 (C), 106.50 (CH), 99.42 (CH), 83.33 (CH), 71.44 (CH), 67.21 (CH_2), 28.12 (CH_3), 27.81, (CH_3), 26.09 (CH_3), 25.48 (CH_3). Compound **5**: $[\alpha]_D^{25}=-17.7$ (*c* 1.0, $CHCl_3$); mp=87–88°C; IR ($CHCl_3$) ν 3390 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (d, *J*=3.9

Hz, 1H, H-1), 4.54 (d, *J*=3.9 Hz, 1H, H-2), 4.40 (t, *J*=2.5 1H, H-3), 4.23 (ddd, *J*=9.4, 6.1, 5.0 Hz, 1H, H-5), 4.09 (dd, *J*=8.7, 6.1 Hz, 1H, H-6), 3.92 (dd, *J*=8.7, 5.0 Hz, 1H, H-6), 3.77 (dd, *J*=9.4, 2.5 Hz, 1H, H-4), 2.96 (d, *J*=3.9 Hz, 1H, OH), 1.49 (s, 3H, C-CH_3), 1.41 (s, 3H, C-CH_3), 1.33 (s, 3H, C-CH_3), 1.30 (s, 3H, C-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.76 (C), 109.71 (C), 105.59 (CH), 88.27 (CH), 87.05 (CH), 76.68 (CH), 75.56 (CH), 67.62 (CH_2), 27.04 (CH_3), 26.90 (CH_3), 26.10 (CH_3), 25.31 (CH_3). Anal. calcd for $C_{12}H_{20}O_6$: C,55.37;H,7.74, found: C,55.68; H,7.79. Compound **7**: $[\alpha]_D^{28}=-41.5$ (*c* 1.0, $CHCl_3$); IR (neat) ν 1751 (s), 1623 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.02 (d, *J*=5.4 Hz, 1H, H-1), 5.38 (d, *J*=5.4 Hz, 1H, H-2), 4.67 (t, *J*=7.0 Hz, 1H, H-5), 4.10 (dd, *J*=8.3, 7.0 Hz, 1H, H-6), 3.99 (dd, *J*=8.3, 7.0 Hz, 1H, H-6), 2.19 (s, 3 H), 1.46 (s, 3 H), 1.43(s, 3 H), 1.43(s, 3 H), 1.37(s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.42 (C), 144.85 (C), 128.94 (C), 113.27 (C), 110.39 (C), 103.86 (CH), 81.03 (CH), 68.92 (CH), 65.73 (CH_2), 27.88 (CH_3), 27.80 (CH_3), 25.68 (CH_3), 20.48 (CH_3). Compound **8**: $[\alpha]_D^{30}=+26.6$ (*c* 1.0, $CHCl_3$); IR (neat) ν 1750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.70 (d, *J*=4.1 Hz, 1H, H-1), 5.16 (t, *J*=5.8 Hz, 1H, H-3), 4.74 (dd, *J*=5.8, 4.1 Hz, 1H, H-2), 4.50 (dt, *J*=8.7, 6.0 Hz, 1H, H-5), 4.07 (dd, *J*=8.7, 6.0 Hz, 1H, H-6), 4.01 (dd, *J*=8.7, 6.0 Hz, 1H, H-4), 3.97 (dd, *J*=8.7, 6.0 Hz, 1H, H-6), 2.12 (s, 3H), 1.54 (s, 3H), 1.34 (s, 3H), 1.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.15 (C), 114.63 (C), 109.57 (C), 104.68 (CH), 79.44 (CH), 73.49 (CH), 71.11 (CH), 67.18 (CH_2), 26.90 (CH_3), 26.73 (CH_3), 25.56 (CH_3), 20.74 (CH_3). Compound **9**: $[\alpha]_D^{30}=+3.4$ (*c* 1.1, $CHCl_3$); IR (neat) ν 3502 (br) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.68 (d, *J*=4.2 Hz, 1H, H-1), 4.65 (dd, *J*=5.8, 4.2 Hz, 1H, H-2), 4.55 (dt, *J*=8.7, 6.0, 1H, H-5), 4.28 (t, *J*=5.8, 1H, H-3), 4.11 (dd, *J*=8.7, 6.0 Hz, 1H, H-6), 3.96 (dd, *J*=8.7, 6.0 Hz, 1H, H-6), 3.83 (dd, *J*=8.7, 5.8 Hz, 1H, H-4), 3.00–2.80 (bs, 1H, OH) 1.57 (s, 3H), 1.41 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 114.77 (C), 109.67 (C), 105.06 (CH), 81.87 (CH), 80.13 (CH), 73.56 (CH), 70.06 (CH), 67.38 (CH_2), 26.99 (CH_3), 26.79 (CH_3), 25.37 (CH_3).

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