Efficient Synthesis of 1,2,3,4,6-Penta-*O*-acetyl-L-idopyranose

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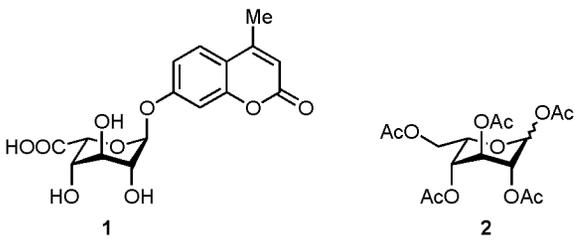
An efficient synthesis of 1,2,3,4,6-penta-*O*-acetyl-L-idopyranose **2** from 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose in five steps in 45% overall yield via hydroboration of enol ether, hydrolysis of L-idofuranosyl sugar and acetolysis of 1,6-anhydro-β-L-idopyranose as key steps is described here.

INTRODUCTION

The mucopolysaccharidoses ( ) are a group of heritable lysosomal storage disorders caused by lack of enzymes catalyzing the stepwise degradation of glycosaminoglycans.[1] α-L-Iduronidase (EC 3.2.1.76),[2] a lysosomal hydrolase that is deficient in Hurler and Scheie syndromes, hydrolyzes terminal α-L-idopyranosiduronic acid residues of heparan sulfate and dermantan sulfate. 4-Methylcoumarin-7-yl α-L-idopyranosiduronic acid **1**[3] is a known fluorogenic substrate for assay of α-L-iduronidase activity (Scheme I). Due to the fact that the 4-methylcoumarin-7-yl group is hydrophobic, the solubility of **1** in water becomes poor and a wide range of substrate concentrations is desirable in the determination of enzyme kinetics.[4] As part of our interest in developing new and highly soluble fluorogenic material, we need the rare 1,2,3,4,6-penta-*O*-acetyl-L-idopyranose **2** as a key intermediate for their synthesis.

Scheme I



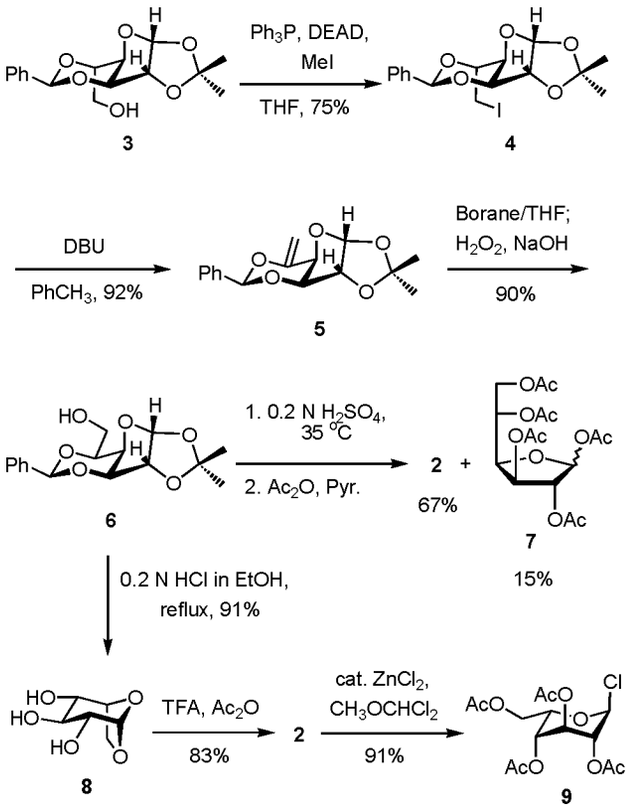
1 **2**

L-Idose is not available from a natural source. Numerous approaches for the synthesis of L-*ido* sugars has been reported and most strategies involve the selective inversion at the C5 position of D-glucose.[5] Neeser et al.[6] described that hydroboration-iodination of 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-6-deoxy-α-D-*xylo*-hex-5-enofuranose **5** could afford 3,5-*O*-benzylidene-6-iodo-6-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose. Theoretically, oxidative workup of the borane intermediate may lead to 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-β-L-idofuranose **6**. We have explored herein its preparation, its hydrolysis in acidic media, and its application in the synthesis of target molecule **2**.

RESULTS AND DISCUSSION

The transformation of α-D-glucofuranosyl sugar into β-L-idofuranosyl sugar via chiral center inversion at C5 and the preparation of L-idopyranosyl pentaacetate **2** are summarized in Scheme II. The enol ether **5** was generated from 3,5-

Scheme II



3 **4** **5** **6** **7** **8** **9**

O-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose **3**[7] by an improved method in two steps. Mitsunobu-type iodination (Ph_3P, DEAD and MeI)[8] of **3** furnished the 6-iodo compound **4**[9] (75%) which was subjected to β-elimination with DBU in toluene at 80 °C to provide **5**[10] in 92% yield. Treatment of **5** with a 1 M solution of borane in tetrahydrofuran followed by oxidative workup gave the L-idofuranose **6**[11] as a single diastereoisomer (90%). The NOESY spectrum illustrates that H5 has NOE effect with H3 and the benzylidene proton, respectively, which indicates the CH_2OH is at the equatorial position. Due to the *cis*-fused ring junction, the high selectivity is presumably induced by the steric effect.

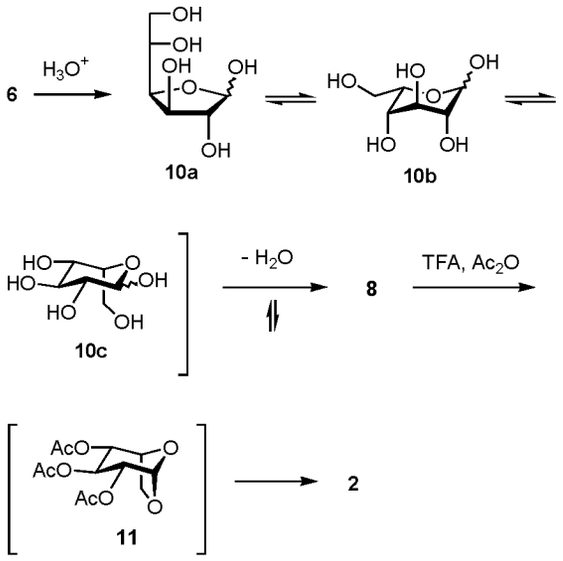
Hydrolysis of compound **6** in various acidic media at different temperatures was studied. Reaction of **6** with 0.2 N $H_2SO_{4(aq)}$ at 40, 50, 60 or 80 °C often afforded a mixture of L-idose **10** and 1,6-anhydro-β-L-idopyranose **8**. The results are different from the hydrolysis of 1,2-*O*-isopropylidene-β-L-idofuranose under similar conditions.[12] When **6** was hydrolyzed at 33-35 °C for two days, only L-idose was formed. Peracetylation of the crude L-idose led to the desired adduct **2** (α/β = 2.3/1)[13] and L-idofuranosyl pentaacetate **7** (α/β = 1/1) in 67% and 15% yields, respectively. An alternative method for avoiding the formation of side product **7** was executed. Reflux of **6** in 0.2 N $H_2SO_{4(aq)}$ obtained **8** in 72% yield. Due to the low solubility of **6** in sulfuric acid aqueous solution, some tar occurred and the yield was perhaps decreased. This phenomenon could be improved by carrying out the hydrolysis in a solution of 0.2 N hydrochloric acid in ethanol and **8** was isolated in 91% yield. Acetolysis of the triol **8** with acetic anhydride in the presence of trifluoroacetic acid (TFA) provided the pentaacetate **2** (83%, α/β = 1/1). The absolute L-idopyranosyl configuration was determined by the X-ray single crystal structural analysis of 2,3,4,6-tetra-*O*-acetyl-α-L-idopyranosyl chloride **9** which was derived from **2** in 91% yield via anomeric transformation with dichloromethyl methyl ether (DCMME) and zinc chloride.[14] The bond distances and bond angles of **9** are shown in Table 1. The ORTEP drawing is outlined in Fig. 1 and it indicates that only the CH_2OAc group is at the equatorial position of C5 and the other substituted groups are all at the axial positions.

The possible hydrolysis pathway of **6** in acidic condition is described in Scheme III. The kinetic adduct **10** was initially formed at low temperature, which had an equilibrium between the L-idofuranose **10a** and L-idopyranose **10b** as well as **10c**. When the temperature of the oil bath was raised to 100 °C (reflux), the thermodynamically stable 1,6-anhydro-β-L-idopyranose **8** was afforded via elimination of a water molecule from **10c**. With acetolysis of **8** with TFA and acetic anhydride in a short period, the triacetate **11**[15] was isolated as a major compound. When the reaction was carried out for a longer pe-

Table 1. Bond Distances and Bond Angles of **9**

Bond lengths (Å)			
Cl1-C1	1.802(4)	C4-H4	1.000
O1-C1	1.388(4)	C5-C6	1.507(5)
O1-C5	1.443(4)	C5-H5	1.000
O2-C2	1.448(4)	C6-H6a	1.000
O2-C21	1.336(4)	C6 -H6b	1.000
O3-C3	1.441(4)	C21-C22	1.480(6)
O3-C31	1.360(4)	C22-H22a	1.000
O4-C4	1.440(4)	C22-H22b	1.000
O4-C41	1.353(5)	C22-H22c	1.000
O6-C6	1.426(5)	C31-C32	1.476(6)
O6-C61	1.355(4)	C32-H32a	1.000
O21-C21	1.169(5)	C32-H32b	1.000
O31-C31	1.189(5)	C32-H32c	1.000
O41-C41	1.194(5)	C41-C42	1.479(6)
O61-C61	1.192(5)	C42-H42a	1.000
C1-C2	1.516(5)	C42-H42b	1.000
C1-H1	1.000	C42-H42c	1.000
C2-C3	1.511(5)	C61-C62	1.479(6)
C2-H2	1.000	C62-H62a	1.000
C3-C4	1.528(5)	C62-H62b	1.000
C3-H3	1.000	C62-H62c	1.000
C4-C5	1.504(5)		
Bond angles (deg)			
C1-O1-C5	114.4(3)	C1-C2-H2	109.8(3)
C2-O2-C21	117.0(3)	C3-C2-H2	109.5(3)
C3-O3-C31	116.0(3)	O3-C3-C2	109.7(3)
C4-O4-C41	116.2(3)	O3-C3-C4	105.5(3)
C6-O6-C61	115.7(3)	O3-C3-H3	110.3(3)
Cl1-C1-O1	111.38(25)	C2-C3-C4	112.8(3)
Cl1-C1-C2	109.7(3)	C2-C3-H3	109.1(3)
O1-C1-C2	113.0(3)	C4-C3-H3	109.3(3)
O2-C2-C1	105.5(3)	O4-C4-C3	107.5(3)
O2-C2-C3	106.8(3)	O4-C4-C5	108.9(3)
O2-C2-H2	110.0(3)	O4-C4-H4	109.6(3)
C1-C2-C3	115.0(3)	C3-C4-C5	112.3(3)
C3-C4-H4	108.7(3)	O31-C31-C32	127.0(3)
C5-C4-H4	109.8(3)	C31-C32-H32a	109.9(4)
O1-C5-C4	111.1(3)	C31-C32-H32b	109.9(3)
O1-C5-C6	104.2(3)	C31-C32-H32c	111.6(4)
O1-C5-H5	109.1(3)	H32a-C32-H32b	107.1(4)
C4-C5-C6	115.5(3)	H32a-C32-H32c	109.3(4)
C4-C5-H5	109.0(3)	H32b-C32-H32c	108.9(4)
C6-C5-H5	107.6(3)	O4-C41-O41	122.2(4)
O6-C6-C5	106.2(3)	O4-C41-C42	111.3(3)
O6-C6-H6a	113.0(3)	O41-C41-C42	126.4(4)
O6-C6-H6b	110.3(4)	C41-C42-H42a	110.6(4)
C5-C6-H6a	112.9(4)	C41-C42-H42b	110.1(3)
C5-C6-H6b	108.6(3)	C41-C42-H42c	112.5(4)
H6a-C6-H6b	105.9(4)	H42a-C42-H42b	106.5(4)
O2-C21-O21	122.6(3)	H42a-C42-H42c	108.7(4)
O2-C21-C22	111.6(3)	H42b-C42-H42c	108.3(5)
O21-C21-C22	125.8(3)	O6-C61-O61	121.6(3)
C21-C22-H22a	110.9(4)	O6-C61-C62	111.8(3)
C21-C22-H22b	111.4(4)	O61-C61-C62	126.6(3)
C21-C22-H22c	109.7(4)	C61-C62-H62a	109.9(4)
H22a-C22-H22b	108.8(4)	C61-C62-H62b	110.3(4)
H22a-C22-H22c	107.4(4)	C61-C62-H62c	109.9(4)
H22b-C22-H22c	108.6(4)	H62a-C62-H62b	109.1(4)
O3-C31-O31	121.8(3)	H62a-C62-H62c	108.8(4)
O3-C31-C32	111.2(3)	H62b-C62-H62c	108.9(4)

Scheme III



riod, only the product **2** was generated. It indicates that the acetylation of three hydroxyls is faster than the opening of a 1,6-anhydro ring.

In conclusion, an efficient synthesis of rare 1,2,3,4,6-penta-*O*-acetyl-L-idopyranose **2** from 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose in five steps in 45% overall yield is successfully developed here. Application of **2** in the synthesis of fluorogenic substrates for the detection of α-L-iduronidase activity is under investigation.

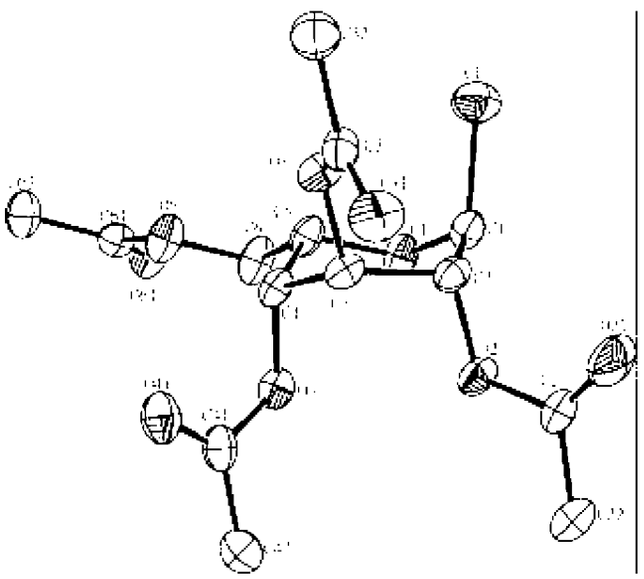


Fig. 1. The ORTEP drawing of **9**.

EXPERIMENTAL SECTION

Solvents were purified and dried from a safe purification system.[16] Anhydrous pyridine and DMF were purchased from Aldrich company. Flash chromatography[17] was carried out as recommended with Silica Gel 60 (230-400 mesh, E. Merk). TLC was performed on pre-coated glass plates of Silica Gel 60 F254 (0.25 mm, E. Merck); detection was executed by spraying with a solution of $Ce(NH_4)_2(NO_3)_6$, $(NH_4)_6Mo_7O_{24}$, as well as H_2SO_4 in water and subsequent heating on a hot plate. Melting points were determined with a Büchi B-540 apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-370 polarimeter at ~25 °C. ^1H and ^{13}C NMR spectra were recorded with Bruker AC300 and AMX400 MHz instruments. Chemical shifts are in ppm from Me_4Si, generated from the $CHCl_3$ lock signal at δ 7.26. Mass spectra were obtained with a VG 70-250S mass spectrometer in the EI and FAB modes. IR spectra were taken with a Perkin-Elmer Paragon 1000 FT-IR spectrometer. Elemental analyses were measured with a Perkin-Elmer 2400CHN instrument.

6-Iodo-6-deoxy-3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose (4)

A mixture of **3**[7] (1.35 g, 4.37 mmol) and Ph_3P (1.72 g, 6.55 mmol) was dissolved in THF (14 mL) under nitrogen and the solution was cooled to 0 °C. Diethyl azodicarboxylate (1.1 mL, 6.12 mmol) and methyl iodide (0.5 mL, 6.33 mmol) were consecutively added and the ice bath was removed. After 19 h, the reaction was quenched with saturated $NaHCO_3$, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/Hex = 1/10) to afford **4**[9] (1.37 g) in 75% yield. mp 135-136 °C; $[\alpha]_D^{25}$ +23 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2996, 1435, 1215, 1173, 1008, 885, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.37-7.33 (m, 3H), 6.03 (d, *J* = 3.5 Hz, 1H), 5.65 (s, 1H), 4.66 (d, *J* = 3.5 Hz, 1H), 4.43-4.39 (m, 2H), 4.27-4.26 (m, 1H), 3.51, 3.48 (dABq, *J* = 7.9, 10.6 Hz, 2H), 1.52 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.88 (C), 128.89 (CH), 128.01 (CH), 125.89 (CH), 111.78 (C), 104.90 (CH), 92.28 (CH), 83.23 (CH), 76.48 (CH), 73.23 (CH), 73.12 (CH), 29.44 (CH_2), 26.58 (CH_3), 26.01 (CH_3); HRMS (EI, M^+) calcd for $C_{16}H_{19}O_5I$ 418.0269, found 418.0261. Anal. Calcd for $C_{16}H_{19}O_5I$: C, 45.95; H, 4.58. Found: C, 46.08; H, 4.62.

3,5-*O*-Benzylidene-1,2-*O*-isopropylidene-6-deoxy-α-D-*xylo*-hex-5-enofuranose (5)

To a solution of **4** (2.45 g, 5.85 mmol) in toluene (18

mL) was added DBU (1.8 mL, 11.71 mmol) at room temperature under nitrogen. The mixture was warmed at 80 °C for 12 h, then cooled to room temperature. The solution was diluted with hexane (20 mL) and the mixture was sequentially washed with 1 M H_2SO_4, saturated $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/Hex = 1/8) to afford **5**[10] (1.57 g) in 92% yield. mp 126-127 °C; $[\alpha]_D^{25}$ +61 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3066, 2992, 1663, 1080, 885, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2H), 7.40-7.36 (m, 3H), 6.04 (d, *J* = 3.7 Hz, 1H), 5.55 (s, 1H), 4.94 (d, *J* = 1.2 Hz, 1H), 4.79 (d, *J* = 1.2 Hz, 1H), 4.68 (d, *J* = 3.7 Hz, 1H), 4.51 (d, *J* = 2.3 Hz, 1H), 4.43 (d, *J* = 2.3 Hz, 1H), 1.54 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.58 (C), 136.43 (C), 129.48 (CH), 128.32 (CH) 126.20 (CH), 112.00 (C), 105.42 (CH), 101.50 (CH_2), 100.22 (CH), 83.54 (CH), 80.18 (CH), 73.05 (CH), 26.66 (CH_3), 26.05 (CH_3); HRMS (FAB, M^+) calcd for $C_{16}H_{18}O_5$ 290.1154, found 290.1160. Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.20; H, 6.25. Found: C, 66.23; H, 6.22.

3,5-*O*-Benzylidene-1,2-*O*-isopropylidene-β-L-idofuranose (6)

To a solution of **5** (0.50 g, 1.73 mmol) in THF (8.5 mL) was added a 1 M solution of borane/THF complex in THF (1.0 mL, 1.0 mmol) at room temperature under nitrogen. After 3 h, the mixture was cooled in an ice-bath and a solution of 30% H_2O_2 (1 mL) and 3 M NaOH (1 mL) was added. The mixture was extracted with EtOAc (3 × 5 mL) and the organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/Hex = 1/2) to afford **6**[11] (0.48 g) in 90% yield. mp 115-116 °C; $[\alpha]_D^{25}$ +4 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3290, 2913, 1457, 1146, 1100, 1014, 885, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.39-7.36 (m, 3H), 6.04 (d, *J* = 3.6 Hz, 1H), 5.53 (s, 1H), 4.63 (d, *J* = 3.6 Hz, 1H), 4.43 (d, *J* = 1.7 Hz, 1H), 4.20-4.16 (m, 2H), 3.99 (dd, *J* = 11.9, 7.1 Hz, 1H), 3.86 (dd, *J* = 11.9, 4.1 Hz, 1H), 2.22 (bs, 1H), 1.52 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.18 (C), 129.18 (CH), 128.24 (CH), 126.15 (CH), 111.96 (C), 105.66 (CH), 99.37 (CH), 82.94 (CH), 79.46 (CH), 76.52 (CH), 72.32 (CH), 62.61 (CH_2), 26.60 (CH_3), 26.05 (CH_3); HRMS (FAB, M^+) calcd for $C_{16}H_{20}O_6$ 308.1258, found 308.1256. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.28; H, 6.60.

1,2,3,4,6-Penta-*O*-acetyl-L-idopyranose (2α & 2β)

(a) Via L-idose **10**: A mixture of **6** (100 mg, 0.32 mmol) in 0.1 M H_2SO_4 aqueous solution (2 mL) was warmed at 35 °C for 48 h. After cooling to room temperature, the reaction was neutralized with $NaHCO_3$ solid (200 mg) and the mixture was filtered. The filtrate was co-evaporated with ethanol and toluene at reduced pressure to afford a pale yellow residue. This crude L-idose was dissolved in pyridine (1 mL) under nitrogen and the mixture was cooled to 0 °C. Acetic anhydride (0.5 mL) was slowly added to the solution and the ice bath was removed. After 12 h, the reaction was quenched by slow addition of methanol (0.5 mL) at 0 °C and the mixture was kept stirring for half hour. The resulting solution was evaporated at reduced pressure and the residue was diluted with ethyl acetate (15 mL). The mixture was sequentially washed with 1 N HCl, saturated $NaHCO_3$, water and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/Hex = 2/3) to afford **2α**[13] (58 mg, 47%) and **2β**[13] (25 mg, 20%). **2α**: IR ($CHCl_3$) 2990, 2938, 1374, 1204, 1164, 1090, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.03 (d, *J* = 1.8 Hz, 1H, H-1), 5.05 (dt, *J* = 3.9, 0.8 Hz, 1H, H-3), 4.92 (dd, *J* = 3.9, 2.4 Hz, 1H, H-4), 4.86 (ddd, *J* = 3.9, 1.8, 0.8 Hz, 1H, H-2), 4.45 (dt, *J* = 2.4, 6.3 Hz, 1H, H-5), 4.20, 4.14 (dABq, *J* = 6.3, 9.9 Hz, 2H, H-6a,6b), 2.094 (s, 3H, Ac), 2.090 (s, 3H, Ac), 2.088 (s, 3H, Ac), 2.078 (s, 3H, Ac), 2.04 (s, 3H, Ac); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.34 (C), 169.55 (C), 168.90 (C), 168.68 (C), 168.30 (C), 90.53 (CH), 66.64 (CH), 66.23 (CH), 66.17 (CH), 66.06 (CH), 61.64 (CH_2), 20.70 (CH_3), 20.57 (CH_3), 20.49 (CH_3). Anal. Calcd for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68. Found: C, 49.44; H, 5.80. **2β** : ^1H NMR (400 MHz, $CDCl_3$) δ 6.06 (d, *J* = 2.2 Hz, 1H, H-1), 5.24 (t, *J* = 4.8 Hz, 1H, H-3), 4.99 (dd, *J* = 4.8, 2.2 Hz, 1H, H-2), 4.89 (dd, *J* = 4.8, 2.4 Hz, 1H, H-4), 4.44 (ddd, *J* = 8.8, 6.3, 2.4 Hz, 1H, H-5), 4.20-4.14 (m, 2H, H-6a,b), 2.14 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.120 (s, 3H, Ac), 2.117 (s, 3H, Ac), 2.065 (s, 3H, Ac); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.33 (C), 169.35 (C), 169.30 (C), 168.53 (C), 168.46 (C), 89.75 (CH), 71.84 (CH), 67.04 (CH), 66.26 (CH), 66.11 (CH), 62.05 (CH_2), 20.71 (CH_3), 20.58 (CH_3), 20.54 (CH_3), 20.48 (CH_3), 20.44 (CH_3).

(b) Via 1,6-anhydro-β-L-idopyranose **8**: Compound **6** (503 mg, 1.93 mmol) dissolved in a 0.2 N solution of HCl in ethanol (15 mL) and the mixture was refluxed for 18 h. After cooling to room temperature, the reaction was neutralized with $Ag_2CO_{3(s)}$ (400 mg) and the $AgCl_{(s)}$ was filtered, then washed by ethanol. The filtrate was concentrated *in vacuo* and the residuce was purified by flash column chromatography (EtOAc) to afford **8** (275 mg) in 88% yield. $[\alpha]_D^{30}$ +93.3 (*c* 0.58, MeOH); ^1H NMR (400 MHz, CD_3COCD_3) δ 5.15 (d, *J* = 1.5 Hz, 1H, H-1), 4.42 (d, *J* = 4.2 Hz, 1H, O*H*-4), 4.32 (t, *J* = 4.6 Hz, 1H, H-5), 4.19 (d, *J* = 4.6 Hz, 1H, O*H*-3), 4.00 (d, *J* = 6.6 Hz, 1H, O*H*-2), 3.96 (d, *J* = 7.4 Hz, 1H, H-6a), 3.66-3.62 (m, 1H. H-4), 3.58 (dd, *J* = 7.4, 4.6 Hz, 1H, H-6b), 3.48-3.45 (m, 1H, H-3), 3.33 (td, *J* = 6.6, 1.5 Hz, 1H, H-2); ^{13}C NMR (75

MHz, $CDCl_3$) δ 102.93 (CH), 76.39 (CH), 76.09 (CH), 72.41 (CH), 65.35 (CH_2). Anal. Calcd for $C_6H_{10}O_5$: C, 44.45; H, 6.22, Found: C, 44.05; H, 6.16.

To a solution of **8** (75 mg, 0.4 mmol) in acetic anhydride (4 mL, 40 mmol) was added trifluoroacetic acid (1.6 mL, 14 mol) at 0 °C under nitrogen. After the ice-bath was removed, the mixture was kept stirring at room temperature for 24 h. The reaction was quenched by slow addition of methanol (4 mL) at 0 °C and the mixture was co-evaporated with toluene and ethanol *in vacuo*. The residue was purified by flash column chromatography (EtOAc/Hex = 1/1) to afford **2** (137 mg, 83%, α/β = 1/1 determined by NMR).

2,3,4,6-tetra-*O*-acetyl-α-L-idopyranosyl chloride (9)

A mixture of **2** (520 mg, 1.33 mmol) and freshly fused $ZnCl_2$ (19 mg, 0.14 mmol) was dissolved in CH_2Cl_2 (2.2 mL) at room temperature under nitrogen and dichloromethyl methyl ether (2.2 mL) was added. The solution was refluxed for 0.5 h, then cooled in an ice-bath. The mixture was diluted with CH_2Cl_2 (3 mL) followed by neutralisation with saturated $NaHCO_{3(aq)}$. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/Hex/Et_3N = 8/12/1) to afford **9** (441 mg) in 91% yield. mp 115-116 °C; $[\alpha]_D^{31}$ -114.3 (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) 2973, 1747, 1372, 1218, 1047 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.02 (s, 1H, H-1), 5.03-4.99 (m, 2H, H-2,3), 4.93-4.92 (m, 1H, H-4), 4.68 (td, *J* = 6.2, 1.7 Hz, 1H, H-5), 4.25, 4.21 (dABq, *J* = 5.6, 11.7 Hz, 2H, H-6a,b), 2.16 (s, 3H, Ac), 2.14 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.10 (s, 3H, Ac); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.47 (C), 169.54 (C), 168.89 (C), 168.80 (C), 88.23 (CH), 68.46 (CH), 66.35 (CH), 65.87 (CH), 65.60 (CH), 61.74 (CH_2), 20.79 (CH_3), 20.68 (CH_3), 20.59 (CH_3); LRMS (FAB, *m/z* %) 367 (MH^+, 88), 331 (96), 307 (100), 289 (90), 219 (49). Anal. Calcd for $C_{14}H_{19}ClO_9$: C, 45.84; H, 5.22. Found: C, 45.85; H, 5.26.

X-ray Structural Determination of 9

Crystallographic details: colorless crystals from chloroform/hexane, $C_{14}H_{19}ClO_9$, fw = 366.75, M*r* = 414.46, crystal dimensions: 0.50 × 0.44 × 0.25 mm^3, crystal system: orthorhombic, space group: P21, unit-cell dimensions: *a* = 8.295(3), *b* = 12.902(4), *c* = 8.895 (3) Å, *V* = 855.0(5) $Å^3$, *Z* = 2, ρ_{calcd} = 1.425 gcm^{-3}, wavelength = 0.7107 Å, F(000) = 383.97, mu = 0.27 mm^{-1}, 2θ(max) = 50.0.

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Key Words

L-Idopyranoses; 1,6-Anhydro-L-idopyranoses; Acetolysis.

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