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ORIGINAL RESEARCH

Synthesis of an enantiomer of cellulose via cationic ring-opening polymerization

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Abstract The enantiomer of natural "D-cellulose" (= "L-cellulose"), which consists of L-glucose, was synthesized from L-glucose via cationic ring-opening polymerization. L-Glucose (**1L**) was converted to 3-*O*-benzyl-2,6-di-*O*-pivaloyl-β-L-glucose 1,2,4-orthopivalate (**6L**) by five reaction steps. L-Glucose and its derivatives showed almost the same reactivity as D-glucose and its derivatives during the synthesis of compound **6L**. Cationic ring-opening polymerization of compound **6L** under atmospheric pressure proceeded smoothly to give 3-*O*-benzyl-2,6-di-*O*-pivaloyl-β-L-glucopyranan (**7L**) with a degree of polymerization (*DPn*) of 32.8 (*Mw/Mn* = 2.19). Removal of the benzyl and pivaloyl groups of compound **7L** and subsequent acetylation gave acetylated β-L-glucopyranan. ^{1}H and ^{13}C NMR spectra of the acetylated β-L-glucopyranan had the same profiles as those of commercial cellulose triacetate prepared from natural cellulose, while its specific rotation was opposite, indicating the successful synthesis of L-cellulose. The synthesized L-cellulose had a cellulose II crystal structure. This is the first reported synthesis of L-cellulose, an L-polysaccharide that consists of an L-monosaccharide.

Keywords Chirality · Enantiomer · L-Cellulose · L-Sugar · Stereoisomer

Introduction

In nature, D-sugars are generally found in natural products because of the low abundance of L-sugars. Cellulose, which is the main constituent of the plant cell wall and the most abundant polymer in nature, is a linear homopolymer consisting of D-anhydroglucose units (hereafter "D-cellulose"). Much attention has been paid to high-value added D-cellulose utilization although D-cellulose is widely used in our daily life. One important property of D-cellulose for such utilization is chirality. Indeed, D-cellulose derivatives for chiral separation (Francotte 1994, Okamoto and Yashima 1998, Yamamoto and Okamoto 2004, D'Orazio et al. 2018, Chankvetadze 2020), chiral nematic D-cellulose liquid crystalline (Nishio et al. 2016), and D-cellulose-based organocatalysts for asymmetric synthesis (Yasukawa et al. 2015; Ranaivoarimanana et al. 2019) have been proposed and put to partial practical use. However, the effect of

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the chirality of D-cellulose on the applications was not well understood.

L-Glucose, an enantiomer of D-glucose, can be obtained by chemical synthesis (Sowa 1969; Weymouth-Wilson et al. 2009; Martínez et al. 2014; Xia et al. 2014). Therefore, there is theoretically an enantiomer of D-cellulose, that is, a homopolymer consisting of L-glucose (hereafter "L-cellulose") (Fig. 1).

To the best of our knowledge, L-cellulose is not found in nature, and has not been synthesized, although it is essential for basic research of the chirality of D-cellulose and its derivatives. There are currently two synthetic methods for D-cellulose, that is, enzymatic polymerization (Kobayashi et al. 1991; Egusa et al. 2007) and cationic ring-opening polymerization (Nakatsubo et al. 1996; Kamitakahara et al. 1996; Adelwöhrer et al. 2009). However, the former might not be suitable for the synthesis of L-cellulose because of the substrate specificity of the enzyme used for the preparation. Therefore, the latter method was applied to the synthesis of L-cellulose (Scheme 1). This paper describes the first synthesis of L-cellulose using cationic ring-opening polymerization.

Experimental

Materials

L-Glucose (**1L**) was purchased from Tokyo Kasei Industry Co. (Tokyo, Japan) and dried in a vacuum desiccator under high vacuum (less than 1 hPa) at 70 °C for 16 h before use. Commercial D-cellulose triacetate (D-CTA) (*DPn* = 366, *Mw/Mn* = 1.21) was kindly supplied by Daicel Co. (Osaka, Japan). Powdered molecular sieves 4 Å was activated in a Shibata glass tube oven GTO-2000 (Shibata Scientific Technology Ltd, Tokyo, Japan) under high vacuum (less than 1 hPa) at 300 °C for 3 h and kept at 105 °C in an Masuda drying oven SA46 (Masuda Co., Osaka, Japan) before use. All other chemicals were purchased from Nacalai Tesque (Kyoto, Japan) and FUJIFILM Wako Pure Chemical Co. (Osaka, Japan) and used without further purification. Compound purifications were performed by silica gel chromatography using Wakogel® C-200 (FUJIFILM Wako Pure Chemical Co.).

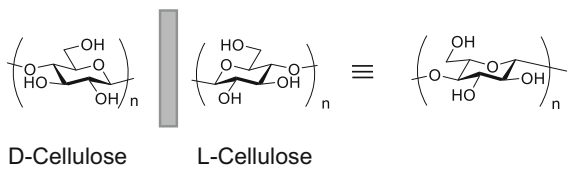


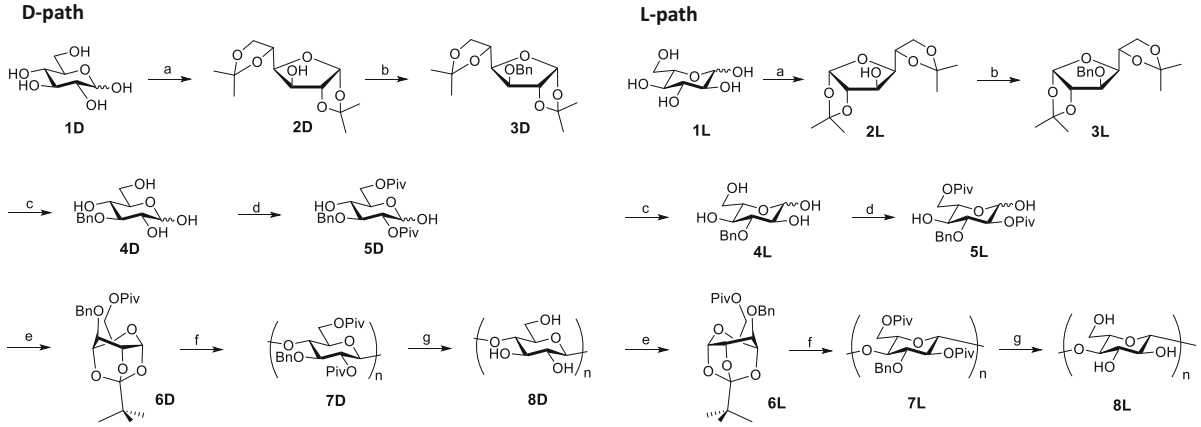
Fig. 1 Chemical structure of D-Cellulose and L-Cellulose

Measurements

Melting points were measured using a micro melting point apparatus (Yanagimoto Seisakusho, Kyoto, Japan). Specific rotations were recorded on a JASCO P-2200 polarimeter (JASCO, Hachioji, Japan), and were determined as the average values of five measurements. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 500 NMR spectrometer (500 MHz, Agilent Technologies, Santa Clara, CA,USA) using tetramethylsilane (TMS) as an internal reference standard in $CDCl_3$ as the solvent if not otherwise stated. Chemical shifts (δ) and coupling constants (J) are reported in ppm (parts per million) and Hz, respectively. Matrix-assisted laser desorption/ionization time-of-flight mass (MALDI-TOF MS) spectra were recorded on a Bruker MALDI-TOF MS REFLEX III (Bruker, Billerica, MA, USA) in the positive and linear ion modes. A nitrogen laser was used for the ionization of the samples. All spectra were measured with 2,5-dihydroxybenzoic acid as the matrix. Fourier-transform infrared (FT-IR) spectra were recorded in KBr pellets with a Shimadzu IRPrestige-21 spectrophotometer (Shimadzu, Kyoto, Japan). Gel permeation chromatography (GPC) was performed on a Shimadzu LC-10 system (Shimadzu) equipped with a Shimadzu UV–vis detector (SPD-10AVp) and a Shimadzu RI detector (RID-10A) under the following conditions: columns: Shodex K-802, K-802.5, and K-805 (Showa Denko K.K., Tokyo, Japan) in series; eluent: $CHCl_3$; temperature: 40 °C; flow rate: 1.0 mL/min; standards: polystyrene standards (Showa Denko K.K.). X-ray diffractograms were recorded on a Rigaku RINT-Ultima IV (Rigaku, Tokyo, Japan).

1,2;5,6-Di-*O*-isopropylidene-α-L-glucofuranose (**2L**)

L-Glucose (**1L**, 2.00 g, 11.1 mmol) was stirred in dry acetone (100 mL) with anhydrous $FeCl_3$ (600 mg,



Scheme 1 Synthetic routes for the preparation of D-cellulose (**8D**) and L-cellulose (**8L**) [Reaction conditions; **a** Acetone/H_2SO_4. **b** Benzyl bromide/NaH/DMF. **c** DoweX 50-W/H_2O–EtOH (3:1, v/v). **d** Pivaloyl chloride/Bu_2SnO/pyridine/toluene. *e*: Benzenesulfonyl chloride/Et_3N/CH_2Cl_2 **f** $BF_3 \cdot Et_2O$/CH_2Cl_2. **g** (i) H_2/Pd–C/THF-AcOH (1:1, v/v) and (ii) NaOMe/THF–MeOH (10:1, v/v)]

3.67 mmol) at 60 °C for 3 h. The reaction mixture was cooled down to room temperature (r.t.), neutralized with a saturated aqueous $NaHCO_3$ solution and filtered and washed with ethyl acetate (EtOAc). The filtrate was concentrated in vacuo to remove acetone, and extracted with CH_2Cl_2 five times. The extracts were combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The product was recrystallized from *n*-hexane to give compound **2L** (2.44 g, 85% yield) as a colorless crystal.

Compound **2L**: melting point: 109–110 °C; $[\alpha]_D^{25}$ = + 9.9° (c = 0.1 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.95 (d, 1H, *J* = 3.9, H-1), 4.54 (d, 1H, *J* = 3.6, H-2), 4.38–4.31 (m, 2H, H-5, H-3), 4.17 (dd, 1H, *J* = 8.7, 6.0, H-6a), 4.07 (dd, 1H, *J* = 7.8, 2.7, H-4), 3.99 (dd, 1H, *J* = 8.7, 5.4, H-6b), 2.62 (d, 1H, *J* = 3.6, OH-3),1.50, 1.49, 1.37, 1.32 (s, 3H, –C(C$\underline{H}_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ 111.8, 109.7 (–$\underline{C}$(CH$_3$)$_2$), 105.2 (C-1), 85.0 (C-2), 81.0 (C-4), 75.2 (C-5), 73.5 (C-3), 67.6 (C-6), 26.8, 26.7, 26.2, 25.1 (–C($\underline{C}$H$_3$)$_2$); MALDI-TOF/MS: *m/z* calcd. for $C_{12}H_{20}O_6Na$ $[M+Na]^+$ 283.13, found 283.06.

3-*O*-Benzyl-1,2;5,6-di-*O*-isopropylidene-α-L-glucofuranose (**3L**)

Compound **2L** (2.00 g, 7.69 mmol) was dissolved in DMF (35 mL). NaH (60% oil suspension, 370 mg, 9.25 mmol) was added to the solution at 0 °C. After stirring at 0 °C for 30 min, the solution of benzyl bromide (1.1 mL, 9.25 mmol) in dry DMF (10 mL) was added dropwise over a period of 30 min. The reaction mixture was stirred at r.t. for 3 h. A small amount of MeOH was carefully added dropwise to the mixture at 0 °C until the foaming stopped, and then more water (105 mL) was added. The reaction mixture was twice extracted with EtOAc/*n*-hexane (1/4, v/v). The extracts were combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by silica gel column chromatography eluted with EtOAc/*n*-hexane (1/5, v/v) (Rf = 0.39) to afford compound **3L** (2.71 g, 98% yield) as a colorless oil.

Compound **3L**: $[\alpha]_D^{25}$ = + 22.5° (c = 0.4 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.36–7.26 (m, 5H, -C$\underline{H}_2$Ph), 5.90 (d, 1H, *J* = 3.6, H-1), 4.69 (d, 1H, *J* = 12.0, –C$\underline{H}_2$Ph), 4.63 (d, 1H, *J* = 12.0, –C$\underline{H}_2$Ph), 4.59 (d, 1H, *J* = 3.6, H-2), 4.37 (dt, 1H, *J* = 8.7, 6.0, H-5), 4.15 (dd, 1H, *J* = 7.8, 3.0, H-4), 4.12 (dd, 1H, *J* = 8.7, 6.0, H-6a), 4.02 (t, 1H, *J* = 2.7, H-3), 4.01 (dd, 1H, *J* = 8.7, 5.4, H-6b), 1.49, 1.43, 1.38, 1.31 (s, 3H, –C(C$\underline{H}_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ 137.7, 128.5, 127.9, 127.7 (–$\underline{C}$H$_2$Ph), 111.8, 109.0 (–$\underline{C}$(CH$_3$)$_2$), 105.3 (C-1), 82.7 (C-2), 81.7 (C-3), 81.3 (C-5), 72.5 (C-4), 72.4 (–$\underline{C}$H$_2$Ph), 67.4 (C-6), 26.9, 26.8, 26.3, 25.5 (–C($\underline{C}$H$_3$)$_2$); MALDI-TOF/MS: *m/z* calcd. for $C_{19}H_{26}O_8Na$ $[M+Na]^+$ 373.17, found 373.04.

3-*O*-Benzyl-L-glucopyranose (**4L**)

Compound **3L** (3.00 g, 8.57 mmol) was dissolved in EtOH/H_2O (1/3, v/v, 12 mL), and Dowex-50WX8 (Sigma-Aldrich, St. Louis, MO, USA) (1.20 g) was added to the solution. The reaction mixture was stirred under reflux for 5 h, neutralized with 28% NaOMe in MeOH, and filtered with EtOH. The filtrate was concentrated in vacuo to remove EtOH, and then lyophilized. The residue was purified by silica gel column chromatography eluted with MeOH/CH_2Cl_2 (15/85, v/v) (Rf = 0.27), and recrystallized from EtOAc to give compound **4L** (1.92 g, 83% yield) as a colorless crystal.

Compound **4L**: melting point: 124–126 °C;$[\alpha]_D^{25}$ = − 33.5° (c = 0.1 in H_2O); ^{1}H NMR (D_2O): δ 7.49–7.36 (m, 5H, –CH_2Ph), 5.20 (d, 1H, J = 3.6, H-1α), 4.82 (d, 2H, J = 18.0, –CH_2Ph), 4.63 (d, 1H, J = 7.8, H-1β), 3.84 (dd, 1H, J = 12.0, 2.1, H-6a), 3.74–3.68 (m, 1H, H-4), 3.64 (dd, 1H, J = 12.0, 5.4, H-6b), 3.53–3.40 (m, 2H, H-3, H-5), 3.31 (m, 1H, H-2); ^{13}C NMR (D_2O): δ 140.1 × 2, 131.5, 131.3, 131.0 (–CH_2Ph), 98.6 (C-1β), 94.9 (C-1α), 86.6, 84.0 (C-3), 78.6, 77.8 (C-5), 77.6 (–CH_2Ph), 76.6, 74.2 (C-2), 74.0, 72.0 (C-4), 63.3, 63.1 (C-6); MALDI-TOF/MS: *m/z* calcd. for $C_{13}H_{18}O_6Na$ $[M+Na]^+$ 293.11, found 293.02.

3-*O*-Benzyl-2,6-di-*O*-pivaloyl-L-glucopyranose (**5L**)

Compound **4L** (2.03 g, 7.51 mmol), Bu_2SnO (4.06 g, 16.3 mmol) and powdered molecular sieves 4 Å (3.00 g) were combined and dried in vacuo overnight. After the addition of anhydrous toluene (60 mL), the reaction mixture was stirred at 105 °C for 20 min and cooled down to r.t. Anhydrous pyridine (1.6 mL, 19.8 mmol) was added to the mixture at r.t. The reaction mixture was further cooled to − 15 °C. Pivaloyl chloride (2.02 mL, 16.3 mmol) in anhydrous toluene (20 mL) was added dropwise to the mixture over 30 min. The reaction mixture was kept at − 15 °C for 2.5 h. MeOH (5 mL) was added at this temperature. The reaction mixture was filtered and washed with EtOAc. The filtrate was concentrated azeotropically with EtOH to give a yellow oil. The oil was purified by column chromatography using 10% K_2CO_3/silica gel (w/w) (Harrowven et al 2010) eluted with EtOAc/*n*-hexane (1/2, v/v) (Rf = 0.50 on silica gel) to afford compound **5L** (2.11 g, 65% yield) as a colorless oil.

Compound **5L**: $[\alpha]_D^{25}$ = − 27.8° (c = 0.4 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.37–7.25 (m, 5H, –CH_2Ph), 5.38 (t, 1H, J = 3.3, H-1), 4.84 (d, 1H, J = 11.4, –CH_2Ph), 4.80–4.67 (m, 1H, H-2), 4.77 (d, 1H, J = 11.4, –CH_2Ph), 4.38–4.28 (m, 2H, H-6a and H-6b), 4.03–3.90 (m, 1H, H-5), 3.98–3.87 (m, 1H, H-3), 3.58–3.40 (m, 1H, H-4), 3.14 (d, 1H, J = 3.3, OH-1), 2.95 (d, 1H, J = 3.3, OH-4), 1.25–1.19 (m, 18H, –C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$): δ 179.4, 179.3, 178.8, 178.0 (C=O), 138.1, 137.8, 128.5, 128.4, 128.2, 127.9, 127.7, 127.6 (–CH_2Ph), 95.9, 90.1 (C-1), 81.7, 78.9 (C-3), 77.4, 77.0 (–CH_2Ph), 76.6, 75.2 (C-2), 74.9, 74.2 (C-5), 70.0, 69.5 (C-4), 62.9, 62.6 (C-6), 38.9, 38.8, 38.7 (× 2) (–C(CH_3)$_3$), 27.1, 27.0, 26.9 (-C(CH_3)$_3$); MALDI-TOF/MS: *m/z* calcd. for $C_{23}H_{34}O_6Na$ $[M+Na]^+$ 461.23, found 461.10.

3-*O*-Benzyl-2,6-di-*O*-pivaloyl-α-L-glucopyranose-1,2,4-orthopivalate (**6L**)

Compound **5L** (1.48 g, 3.37 mmol) dried in a vacuum desiccator under high vacuum (less than 1 hPa) at r.t. for 16 h was dissolved in anhydrous CH_2Cl_2 (30 mL), and Et_3N (0.94 mL, 6.74 mmol) and benzenesulfonyl chloride (0.46 mL, 3.59 mmol) were added. The reaction mixture was stirred at r.t. overnight, and concentrated to give a yellow oil. The oil was purified by silica gel column chromatography with CH_2Cl_2/*n*-hexane (1/2, v/v) (Rf = 0.22) and then CH_2Cl_2 to give white solid, which was recrystallized from *n*-hexane to afford compound **6L** (1.15 g, 81% yield) as a colorless crystal.

Compound **6L**: melting point: 73–74 °C; $[\alpha]_D^{25}$ = − 30.6° (c = 0.1 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.40–7.30 (m, 5H, –CH_2Ph), 5.77 (d, 1H, J = 5.1, H-1), 4.63 (s, 2H, –CH_2Ph), 4.50 (broad t, 1H, J = 6.6, H-5), 4.42 (dd, 1H, J = 11.1, 6.0, H-6a), 4.41 (dd, 1H, J = 5.1, 2.1, H-2), 4.34 (dd, 1H, J = 11.1, 6.0, H-6b), 4.16 (dd, 1H, J = 4.8, 2.1, H-3), 3.95 (broad dd, 1H, J = 4.8, 1.2, H-4),1.23 (s, 9H, –C(CH_3)$_3$), 1.03 (s, 9H, –C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$): δ 178.2 (C=O), 137.4, 128.6, 128.1, 127.6, (–CH_2Ph), 123.0 ((–O_3)C(CH_3)$_3$), 97.5 (C-1), 75.3 (–CH_2Ph), 72.2 (C-3), 72.0 (C-5), 71.4 (C-4), 71.2 (C-2), 64.4 (C-6), 38.8 (pivaloyl–C(CH_3)$_3$), 35.7 (orthopivalate–C(CH_3)$_3$), 27.2

(pivaloyl–C(CH$_3$)$_3$), 24.9 (orthopivalate–C(CH$_3$)$_3$); MALDI-TOF/MS: *m/z* calcd. for $C_{23}H_{33}O_7$ $[M+H]^+$ 421.21 and $C_{23}H_{32}O_7Na$ $[M+Na]^+$ 443.21, found 421.08 and 443.11.

3-*O*-Benzyl-2,6-di-*O*-pivaloyl-(1→4)-β-L-glucopyranan (**7L**)

(Typical method 1) Compound **6L** (50 mg, 0.12 mmol) was placed in a glass ampoule under high vacuum overnight on a vacuum line. CH_2Cl_2 (100 μL) was distilled from CaH_2, degassed by three freeze/thaw cycles and transferred to a polymerization ampule on the vacuum line. BF_3–Et_2O (0.73 μL, 5 mol%) was added via a syringe through the sealed cap of the glass ampule. The reaction mixture was stirred under high vacuum at r.t. for 24 h, after which time it was partly solidified. After the reaction, the mixture was dissolved in $CHCl_3$ (10 mL). The organic layer was washed with water, a saturated aqueous $NaHCO_3$ solution, and brine, dried over anhydrous Na_2SO_4, and concentrated to afford compound **7L** as a colorless solid in quantitative yield.

(Typical method 2) Compound **6L** (200 mg, 0.48 mmol) was placed in a glass ampoule in a vacuum desiccator under high vacuum (less than 1 hPa) at r.t. for 16 h. Anhydrous CH_2Cl_2 (200 μL), which was distilled from CaH_2, and BF_3–Et_2O (2.90 μL, 5 mol%) was added via a syringe through the sealed cap of a glass ampoule. The reaction mixture was stirred under atmospheric pressure at 40 °C for 24 h, after which time it was partly solidified. The work-up method was carried out by the same method described in Typical method 1 to give compound **7L** as a colorless solid in quantitative yield.

Compound **7L**: $[\alpha]_D^{26} = +7.3°$ (c = 0.5 in $CHCl_3$); *DPn* = 32.8 (*Mw/ Mn* = 1.97); ^{1}H NMR ($CDCl_3$): δ 7.34–7.10 (m, 5H, –CH$_2$Ph), 4.95 (broad d, 1H, *J* = 10.8, –CH$_2$Ph), 4.83 (broad s, 1H, H-2), 4.41 (broad d, 1H, *J* = 10.8, –CH$_2$Ph), 4.28 (broad s, 1H, H-1), 4.09 (broad s, 1H, H-6a), 3.83 (broad s, 1H, H-6b), 3.64 (broad s, 1H, H-5), 3.46 (broad s, 1H, H-4), 3.33 (broad s, 1H, H-3), 1.05–0.85 (m, 18H, –C(CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$): δ 177.5, 176.3 (C=O), 138.6, 128.4, 128.0, 127.1, 126.7 (–CH$_2$Ph), 100.1 (C-1), 80.7 (C-3), 74.7 (C-5), 73.2 (–CH$_2$Ph), 72.2 (C-2), 62.3 (C-6), 35.8 (× 2) (–C(CH$_3$)$_3$), 27.1, 27.0, 26.9 ((–C(CH$_3$)$_3$).

(1→4)-β-L-Glucopyranan (L-Cellulose, **8L**),

Compound **7L** (200 mg, 0.48 mmol) was dissolved in THF/AcOH (1/1, v/v) (5 mL). $Pd(OH)_2$ on charcoal (200 mg) was added. The reaction mixture was hydrogenated with vigorous stirring under H_2 at atmospheric pressure and r.t. for 24 h, filtered through Celite® 535RVS (Nacalai Tesque) with THF/AcOH (1/1, v/v), washed with THF/AcOH (1/1, v/v) and concentrated azeotropically with EtOH to give a partially debenzylated product as a colorless solid. The product was subjected to debenzylation under the same conditions again to give a fully debenzylated product as a colorless solid. The product was dissolved in THF/MeOH (10/1, v/v) (60 mL) and 28% MeONa in MeOH solution (0.8 mL) was added. The reaction mixture was stirred at 50 °C overnight, and neutralized with 1 M HCl aqueous solution. The resulting precipitation was collected by centrifugation (5538×*g*), washed several times with water and MeOH, and dried in vacuo to afford compound **8L** (49 mg, 64% yield) as a brownish solid.

Compound **8L**: FT-IR (KBr): *v* 3402, 2891, 1602, 1375, 1159, 1065, 1026, 895 cm^{-1}.

Compound **8L** was acetylated with Ac_2O/pyridine at 110 °C for 24 h, and subjected to ^{1}H and ^{13}C NMR measurements.

Acetylated compound **8L**:$[\alpha]_D^{25} = +8.3°$ (c = 0.02 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.07 (H-3), 4.79 (H-2), 4.41(H-1), 4.38 (H-6a), 4.06 (H-6b), 3.71 (H-4), 3.54 (H-5), 2.12, 2.00, 1.94 (–COCH$_3$); ^{13}C NMR ($CDCl_3$): δ 170.2, 169.7, 169.3 (C=O), 100.5 (C-1), 76.0 (C-4), 72.8, 72.5, 71.8 (C-2, C-3, C-5), 62.0 (C-6).

(1→4)-β-D-Glucopyranan (D-Cellulose, **8D**)

D-Cellulose (**8D**) was also prepared from D-glucose (**1D**) according to previously reported methods (Nakatsubo et al. 1996; Kamitakahara et al. 1996; Adelwöhrer et al. 2009).

Compound **2D**: melting point: 110–112 °C; $[\alpha]_D^{25} = -9.6°$ (c = 0.1 in $CHCl_3$); MALDI-TOF/MS: *m/z* calcd. for $C_{12}H_{20}O_6Na$ $[M+Na]^+$ 283.13, found 283.07.

Compound **3D**: $[\alpha]_D^{25}$ = − 23.7° (c = 0.4 in $CHCl_3$); MALDI-TOF/MS: *m/z* calcd. for $C_{19}H_{26}O_8$-Na $[M+Na]^+$ 373.17, found 372.93.

Compound **4D**: melting point: 124–125 °C;$[\alpha]_D^{25}$ = + 33.8° (c = 0.1 in H_2O); MALDI-TOF/MS: *m/z* calcd. for $C_{13}H_{18}O_6Na$ $[M+Na]^+$ 293.11, found 293.04.

Compound **5D**: $[\alpha]_D^{25}$ = + 26.8° (c = 0.3 in $CHCl_3$); MALDI-TOF/MS: *m/z* calcd. for $C_{23}H_{34}O_6$-Na $[M+Na]^+$ 461.23, found 461.25.

Compound **6D**: melting point: 73–74 °C; $[\alpha]_D^{25}$ = + 30.6° (c = 0.1 in $CHCl_3$); MALDI-TOF/MS: *m/z* calcd. for $C_{23}H_{33}O_7$ $[M + H]^+$ 421.21 and $C_{23}H_{32}$-O_7Na $[M+Na]^+$ 443.21, found 421.12 and 443.11.

Compound **7D**: *DPn* of 11.9 (*Mw/Mn* = 1.86); $[\alpha]_D^{26}$ = − 3.7° (c = 0.1 in $CHCl_3$).

Acetylated compound **8D**:$[\alpha]_D^{25}$ = − 4.8° (c = 0.07 in $CHCl_3$).

Results and discussion

Synthesis of glucose orthoester derivative 6L

Compound **6L** was synthesized from L-glucose (**1L**) by five reaction steps using a modified method for compound **6D** as previously reported (Scheme 1) (Nakatsubo et al. 1996; Kamitakahara et al. 1996; Karakawa and Nakatsubo 2002; Adelwöhrer et al. 2009). All the reaction steps proceeded smoothly to afford the final compound **6L**. Indeed, the reactivity of L-glucose and its derivatives (compounds **1L** to **5L**) was found to be almost the same as those of the corresponding D-glucose and its derivatives (compounds **1D** to **5D**). Similar reactivities among L-glucose and D-glucose derivatives have been reported in the syntheses of digitoxigenin glucoside (Rathore et al. 1985) and coniferin (coniferyl alcohol glucoside) (Maeda et al 2019).

The main points of our modification are as follows. (1) Compound **2D** has been reported to be prepared by the reactions of D-glucose (**1D**) with a dry acetone/H_2SO_4 system and with a dry acetone/$CuSO_4$/H_2SO_4 system. Compound **2L** has also been prepared from the reaction of 1-deoxy-1-nitroglucitol with a dry acetone/H_2SO_4 system (Hoeltgebaum Thiesen et al. 2017) and from 1,2-*O*-isopropylidene-α-L-glucose with a dry acetone/H_2SO_4 system (Weymouth-Wilson et al. 2009). Therefore, the dry acetone/H_2SO_4 system was applied to the synthesis of compound **2L**. However, the reaction time was long, and the yield of compound **2L** was not very high. After investigation of other acid catalysts, compound **2L** was obtained in 85% yield from the reaction of compound **1L** with dry acetone/anhydrous $FeCl_3$ at 60 °C for 3 h. (2) Compound **4D** was prepared in high yield by benzylation and the subsequent removal of isopropylidene groups (Adelwöhrer et al. 2009). In the latter reaction, the purification of compound **4D** by five or six rounds of recrystallization was reported to be required to ensure the high yield of compound **5D** in the next reaction step. This was laborious work and sometimes caused the yield of compound **4D** to decrease. The reaction product resulting from the removal of the isopropylidene groups was purified by silica gel column chromatography eluted with 15% MeOH/CH_2Cl_2 followed by one recrystallization from EtOAc to afford compound **4L** in 83% yield. (3) In the selective pivaloylation, compound **5D** was reported to be purified by two different rounds of silica gel column chromatography because the organotin impurities negatively influenced the yield of compound **6D** in the next reaction step (Karakawa and Nakatsubo 2002; Adelwöhrer et al. 2009). This was also laborious work. Harrowven et al. reported that a stationary phase composed of 10% powdered anhydrous K_2CO_3 and silica gel was effective for the removal of organotin impurities from reaction products (Harrowven et al 2010). Selective pivaloylation of compound **4L** using Bn_2SnO was conducted in anhydrous conditions according to the synthesis of compound **5D**, and the product was purified using 10% anhydrous K_2CO_3/silica gel column chromatography to afford compound **5L** in 65% yield. (4) In the synthesis of compound **6D**, the reaction mixture had to be quickly transferred to a silica gel column after the reaction because compound **6D** was highly sensitive to traces of acid. However, the volume of the reaction mixture applied to the column was sometimes too large to efficiently separate compound **6D**. For the synthesis of compound **6L**, the reaction mixture was concentrated before applying it to the silica gel column. Compound **6L** was stable during the concentration process. In this way, compound **6L** was obtained in 81% yield.

All products were characterized by their ^1H and ^{13}C NMR and MALDI-TOF MS spectra, and their specific

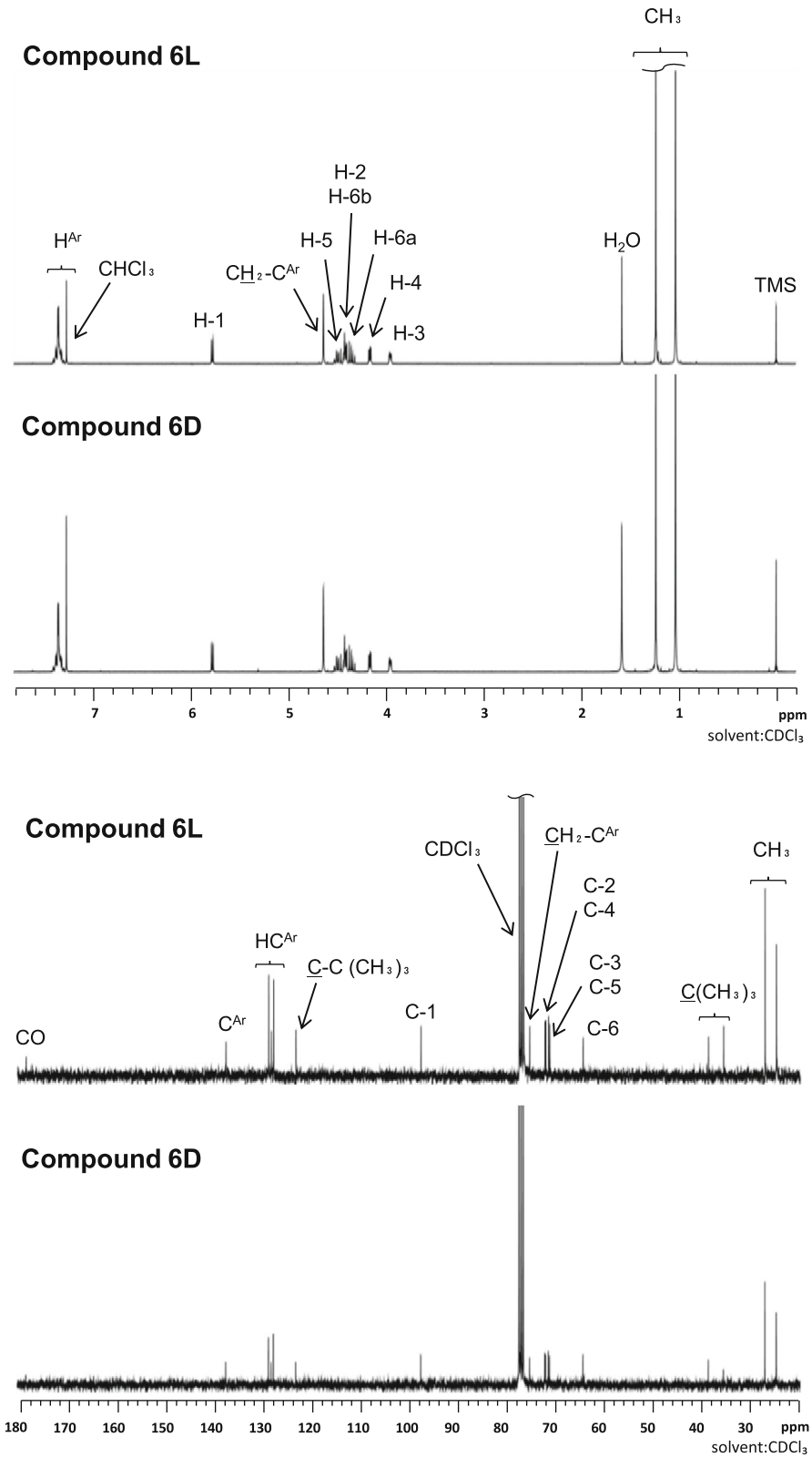


Fig. 2 ^{1}H and ^{13}C NMR spectra of compounds **6L** and **6D**

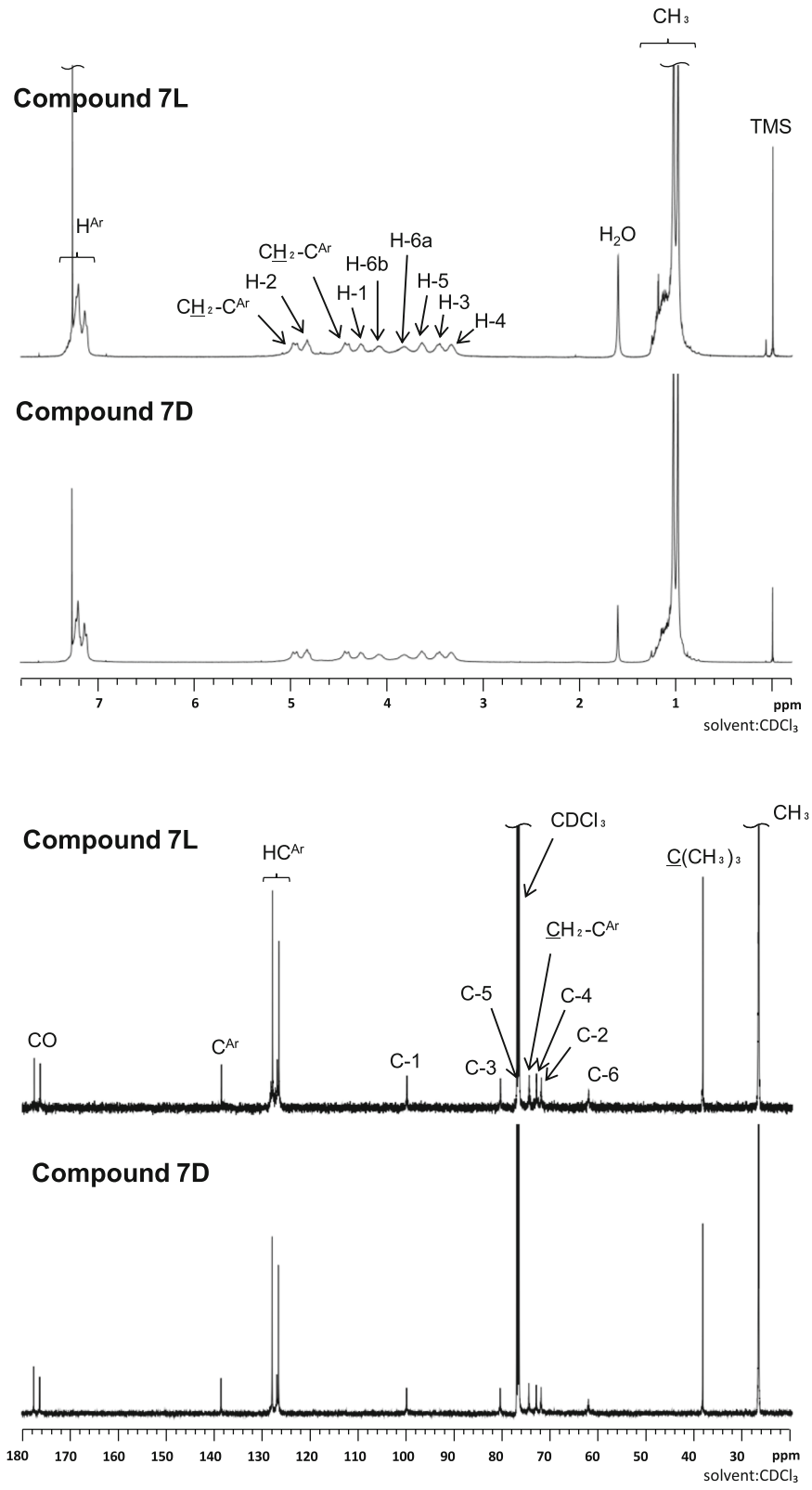


Fig. 3 ^{1}H and ^{13}C NMR spectra of compounds **7L** and **7D**

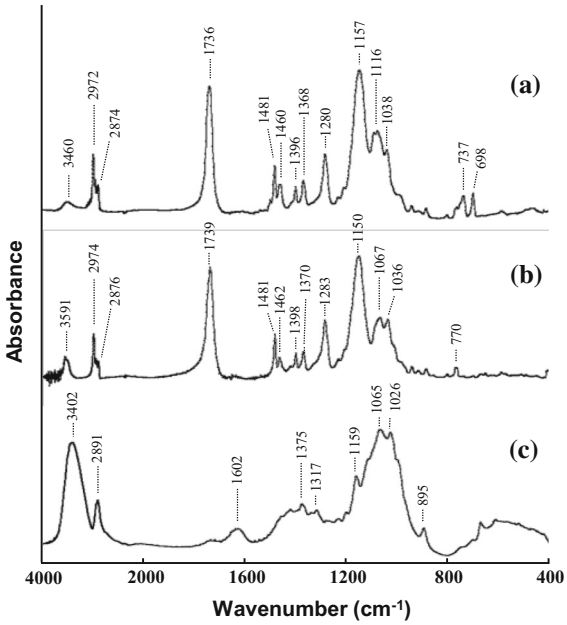


Fig. 4 FT-IR spectra of compound **7L** (**a**); debenzylated **7L** (**b**); compound **8L** (**c**)

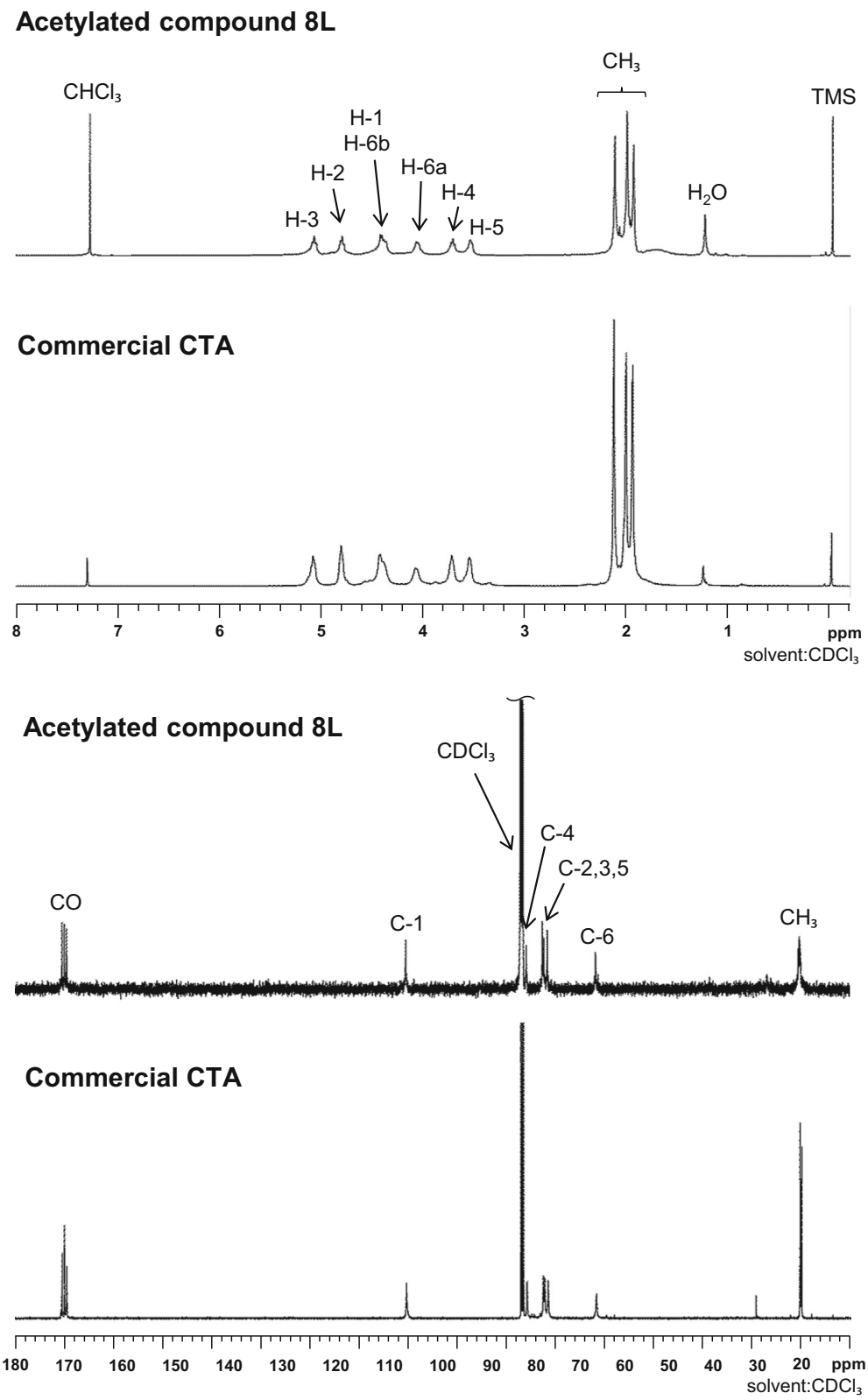
rotation. The ^{1}H and ^{13}C NMR spectra of all the L-glucose derivatives had the same peak pattern as those of the corresponding D-glucose derivatives (Figures S1 and S2), but the sign of the specific rotation of the L-glucose derivatives was opposite to that of the specific rotation of the corresponding D-glucose derivatives. For example, the ^{1}H and ^{13}C NMR spectra of compounds **6L** and **6D** are shown in Fig. 2. The spectra of compound **6L** were the same as those of compound **6D**. The measurement *m/z* values of $[M+H]^+$ and $[M+Na]^+$ for compound **6L** from the MALDI-TOF–MS spectrum also corresponded to its calculated values. The specific rotations of compounds **6L** and **6D** were − 30.6° and + 30.6°, respectively. These results clearly indicate that compound **6L** was an enantiomer of compound **6D**.

Cationic ring-opening polymerization of glucose orthoester derivative 6L

First, cationic ring-opening polymerization under vacuum of compound **6L** was performed according to the polymerization method of compound **6D** to afford compound **7L** in quantitative yield. However, the polymerization under vacuum required a special reaction apparatus (vacuum line) and complicated operations. By comparison, the ring-opening polymerization of compound **6L** under atmospheric pressure was carried out to give compound **7L** in quantitative yield. Compound **7D** was also prepared by the ring-opening polymerization of compound **6D** as a control. Figure 3 shows the ^{1}H and ^{13}C NMR spectra of compounds **7L** and **7D**. Both spectra of compound **7L** had the same profile as those of compound **7D**. In particular, the signal derived from C-1 at 100.1 ppm was only found in the ^{13}C NMR spectrum of compound **7L**, suggesting that only β-bonds were formed in the polymerization of compound **6L**. The *DPn* of compound **7L** was 32.8 (*Mw/Mn* = 1.97). It has been reported that the positive sign of the specific rotation of compound **6D** changed to a negative sign for compound **7D** after the ring-opening polymerization of compound **6D** in two previous papers (Kamitakahara et al.1996; Adelwöhrer et al. 2009). During the ring-opening polymerization of compound **6L**, the negative specific rotation sign of compound **6L** (− 30.6°) changed to a positive sign for compound **7L** (+ 7.3°), and that of compound **7D** with a *DPn* of 11.9 (*Mw/Mn* = 1.86), which was synthesized in this study, was negative (− 3.7°). Please note that the specific rotation seemed to be influenced by the *DPn*. These results indicated that compound **7L** was the expected β-1,4-L-glucopyranan derivative.

Conversion of polymer 7L into (1→4)-β-L-glucopyranan (8L)

Debenzylation of compound **7D** has been reportedly performed under high pressure with H_2 for 24 h (Adelwöhrer et al. 2009). In an effort to simplify the operation, debenzylation of compound **7L** was done under atmospheric pressure with H_2 for 24 h. However, the debenzylation did not proceed completely. Then, the partially debenzylated product was further debenzylated under atmospheric pressure with H_2 for 24 h to give a fully debenzylated product. By comparison, the debenzylation of compound **7L** under atmospheric pressure with H_2 for 48 h did not proceed completely. The repetition of the benzylation was effective for the full removal of the benzyl groups of compound **7L**. The fully debenzylated product was treated with 28% NaOMe–MeOH at 50 °C overnight to give compound **8L** in 64% yield (based on compound **7L**).


Acetylated compound 8L
CHCl3
CH3
TMS
H-1
H-6b
H-2
H-6a
H-4
H-3
H-5
H2O
Commercial CTA
8
7
6
5
4
3
2
1
ppm
solvent:CDCl3
Acetylated compound 8L
CDCl3
C-4
C-2,3,5
CO
C-1
C-6
CH3
Commercial CTA
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
solvent:CDCl3

◀**Fig. 5** ^{1}H and ^{13}C NMR spectra of acetylated compound **8L** and commercial CTA (D-CTA)

Figure 4 shows the FT-IR spectra of compound **7L**, the debenzylated product and compound **8L**. The bands from the benzyl groups around 698 cm^{-1} and the pivaloyl groups around 1736 cm^{-1} disappeared in the FT-IR spectrum of compound **8L**, suggesting that the protective groups were completely removed from compound **7L**. Furthermore, compound **8L** was treated with Ac_2O/pyridine at 110 °C for 24 h to fully afford acetylated compound **8L** for characterization.

Figure 5 shows the ^{1}H and ^{13}C NMR spectra of acetylated compound **8L** and commercial cellulose triacetate (D-CTA from natural cellulose). The ^{1}H and ^{13}C NMR spectra of acetylated compound **8L** were completely identical with those of authentic D-CTA. The specific rotation of acetylated compound **8L** was positive (+ 8.3°), whereas that of authentic D-CTA was negative (− 23.4°). These results suggested that acetylated compound **8L** was an enantiomer of D-CTA (L-CTA), and thus compound **8L** was the expected L-cellulose.

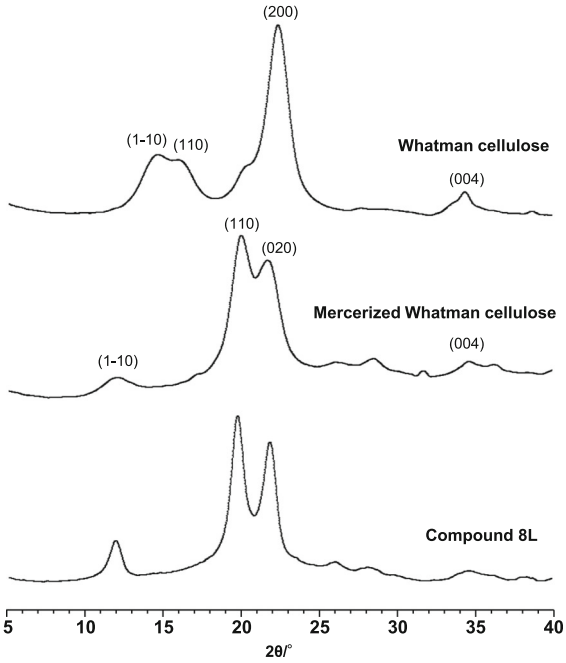


Fig. 6 X-ray diffractograms of Whatman cellulose CF11, mercerized Whatman cellulose CF11 and compound **8L**

X-ray diffractograms of Whatman cellulose CF-11, mercerized Whatman cellulose CF-11, and compound **8L** are shown in Fig. 6. The representative diffractions at 12°, 20°, and 22° derived from cellulose II were observed for compound **8L** as well as for mercerized Whatman cellulose. These results indicated that compound **8L** had a cellulose II crystal structure similar to that previously reported for compound **8D** (Nakatsubo et al.1996).

Conclusion

L-Cellulose (**8L**) was synthesized from L-glucose (**1L**) by a modified synthetic method for D-cellulose (**8D**) using cationic ring-opening polymerization (Scheme 1). L-Sugars showed almost the same reactivities as D-sugars during the synthesis. The availability of L-cellulose (**8L**) is largely expected to pave the way for new research concerning the chirality of cellulose in the future. This is also the first synthesis of a polysaccharide that consists of an L-monosaccharide (L-polysaccharide).

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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