Synthesis of Oligo(spiroketal)s by Polycondensation of Silyl Ethers Derived from Naturally Occurring *myo*-Inositol with 1,4-Cyclohexanedione

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ABSTRACT: Oligo(spiroketal)s (OSKs) were synthesized from *myo*-inositol, a naturally occurring cyclic compound bearing six hydroxyl groups. The successful synthesis of OSKs was achieved using silyl ethers **2** derived from 1,4-di-*O*-alkylated *myo*-inositol **1** as monomers, which underwent polycondensation with 1,4-cyclohexanedione (CHD) at 0 °C in the presence of trimethylsilyl triflate as a catalyst. Because of the irreversible nature of the condensation reaction of silyl ethers with ketones, the resulting OSKs **7** had higher molecular weights than previously reported OSKs that were obtained by polycondensation of tetraols **1** with CHD, where backward hydrolysis of the ketal functions occurred. In addition, another series of OSKs, **8,** were synthesized using silyl ethers **3** derived from 2,5-di-*O*-alkylated *myo*-inositol **6**, which are more symmetric monomers than silyl ethers **2**. Silyl ethers **3** underwent efficient polycondensation with CHD, whereas tetraol **6** did not, demonstrating that the derivation of such tetraols into the corresponding silyl ethers is a powerful strategy to access OSKs. © 2019 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2019**

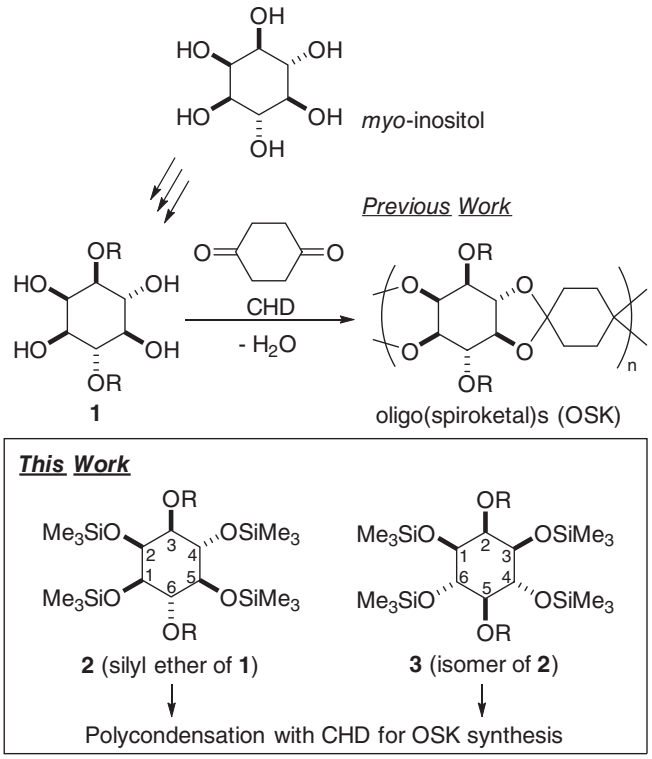
KEYWORDS: high performance polymers; *myo*-inositol; oligo (spiroketal); renewable resources; silyl ether; step-growth polymerization

INTRODUCTION Spiropolymers and spirooligomers have attracted considerable attention because of their double-stranded and thus rigid structures, permitting them to exhibit high mechanical and thermal stability.[1–6] Their rigid rod-like structures enable the spiropolymers to undergo spontaneous alignment into bundle-like packing, which enhances their heat resistance and mechanical strength. For example, Yaghi and coworkers reported the dense packing of rigid nanorods of an oligo(spiroorthocarbonate) (OSOC) synthesized by the polycondensation of pentaerythritol and tetraethylorthocarbonate.[7] Endo and coworkers reported the successful synthesis of a series of OSOCs bearing alkyl or aryl side chains that enhance their solubility.[8] They demonstrated crosslinking reactions of the OSOCs based on the ability of the spiroorthocarbonate moieties in the main chain to undergo cationic ring-opening homopolymerization and copolymerization with epoxide.[9,10]

Poly(spiroketal)s are also an attractive family of rigid rod-like polymers, which can be synthesized easily by polycondensation of tetraols with diketones.[1–3] Previously, we reported the polycondensation of tetraols **1** with 1,4-cyclohexanedione (CHD) giving oligo(spiroketal)s (OSKs) (Scheme 1).[11] The tetraols were derived from naturally occurring *myo*-inositol, a cyclic hexaol that can be produced from its phosphorylated derivative, phytic acid, found in rice bran.[12,13] The well-established protocol for the regioselective dialkylation of hydroxyl groups of *myo*-inositol at the 1- and 4-positions enables us to synthesize a variety of tetraols **1**.[14,15] The substituent R can be chosen from methyl, benzyl, and allyl. When allyl was chosen, the resulting OSK was applicable as a precursor for functionalized OSKs based on the thiol–ene reaction of the allyl groups. This structural diversity of OSKs demonstrated a distinct advantage of their synthesis from *myo*-inositol-derived tetraols. However, the number-average molecular weights of OSKs ranged from 1400 to 2100, prompting us to develop a more efficient method to synthesize OSKs with higher molecular weights.

Herein, we report an improved synthesis of OSKs by polycondensation of silyl ethers **2** with CHD, yielding the corresponding OSKs with higher molecular weights than the OSKs obtained from the polycondensation of tetraol **1** with CHD (Scheme 1). The use of silyl ether for ketalization was developed by Noyori and coworkers.[16] It allows synthesis of cyclic ketals from silyl ethers of 1,2-diols and ketones under mild conditions (such as 0 °C) catalyzed by trimethylsilyl trifluoromethanesulfonate (TMSOTf). The byproduct of this reaction is TMS_2O, which does not react with the product

Additional supporting information may be found in the online version of this article.



SCHEME 1 Outline of this work.

ketals, leading to the efficient suppression of the backward reaction from ketals to the starting materials. This method was used by Wessig and Mollnitz for a stepwise synthesis of well-defined rigid rod-like oligomers.[4]

Another highlight of this study is the use of silyl ether **3**, a stereoisomer of **2**, as a monomer for synthesizing OSKs with different stereochemistry from that of OSKs obtained by the polycondensation of silyl ether **2**. Silyl ether **3** was synthesized from *myo*-inositol via *O*-alkylation of two hydroxyl groups at the 2- and 5-positions.[15]

EXPERIMENTAL

Chemicals

Sodium hydride (60 wt % in mineral oil) and triethylamine (TEA, >99.0%) were purchased from Kishida Chemical Co., Ltd., Osaka and used as received. (4-*tert*-Butyl)phenylmethyl bromide (>97%), *N*,*N*-dimethylformamide (DMF; >99.5%), and 1,2-dichloroethane (>99.7%) were purchased from Wako Pure Chemical Industries Co., Ltd., Osaka and distilled over calcium hydride prior to use. Chlorotrimethylsilane (TMSCl) and TMSOTf were purchased from Shin-Etsu Chemical Osaka and used as received. CHD (>98%) was purchased from Tokyo Chemical Industry Co., Ltd., Tokyo and was used as received. 2,5-Dihydroxybenzoic acid (DHB; >98.0%) and sodium trifluoromethanesulfonate (TfONa; >95%) were purchased from Wako Pure Chemical Industries Co., Ltd., and used as received. Other reagents and solvents were purchased from Wako Pure Chemical Industries Co., Ltd., and used as received.

1,4-Di-*O*-methyl-*myo*-inositol (**1a**) and 1,4-di-*O*-phenylmethyl-*myo*-inositol (**1b**) were synthesized and purified according to the reported procedures.[15] 1,6:3,4-Bis-[*O*-(2,3-dimethoxybutane-2,3-diyl)]-*myo*-inositol (**4**), 1,6:3,4-bis-[*O*-(2,3-dimethoxybutane-2,3-diyl)]-2,5-di-*O*-methyl-*myo*-inositol (**5a**), 1,6:3,4-bis-[*O*-(2,3-dimethoxybutane-2,3-diyl)]-2,5-di-*O*-phenylmethyl-*myo*-inositol (**5b**), 2,5-di-*O*-methyl-*myo*-inositol (**6a**), and 2,5-di-*O*-phenylmethyl-*myo*-inositol (**6b**) were synthesized and purified according to the reported procedures.[15]

Instruments

Nuclear magnetic resonance (NMR) spectra (400 MHz for ^{1}H; 100.6 MHz for ^{13}C) were recorded on a JEOL JNM-AL400 NMR spectrometer. Chemical shifts, δ, and coupling constants, *J*, are reported in ppm and Hz, respectively. Solid-state ^{13}C-NMR spectra (100.6 MHz) were recorded on a Bruker Biospin NMR AVANCE HD400WB spectrometer.

The number-average molecular weight (M_n) and weight-average molecular weight (M_w) were estimated by size exclusion chromatography (SEC), performed on a Tosoh HLC-8120GPC chromatograph equipped with Tosoh TSK gel-Super HM-H styrogel columns (6.0 mm ϕ × 15 cm). DMF containing 1 wt % lithium bromide was used as an eluent at a flow rate of 0.6 mL min^{-1} after calibration with polystyrene standards.

Thermogravimetric (TG) analyses were carried out using a SHIMADZU DTG-60 TG/DTA simultaneous measuring system under nitrogen flow. Each sample was heated from 50 to 500 °C, at a rate of 10 °C min^{-1}. Differential scanning calorimetry (DSC) was carried out using a SHIMADZU DSC (model DSC-60 Plus) under nitrogen flow. Each sample was heated from 30 °C to 250–300 °C depending on the thermal degradation behavior of the polymer and then cooled to 0 °C at a rate of 20 °C min^{-1}. Then, the sample was heated from 0 °C at a rate of 10 °C min^{-1} for the acquisition of the DSC data. The sample was cooled again to 0 °C and then heated at a rate of 10 °C min^{-1} to confirm the reproducibility.

Matrix-assisted laser desorption ionization-time-of-flight (MALDI-TOF) spectra were recorded on a SHIMADZU AXIMA Confidence Mass Spectrometer. DHB and TfONa were used as the matrix and ionization reagents, respectively. Samples were prepared by mixing OSKs (3 mg) with DHB (10 mg) and TfONa (10 mg) in tetrahydrofuran (1 mL). The resulting solution was dropped on a sample plate and dried under air.

Monomer Synthesis

*1,4-Di-*O*-Methyl-2,3,5,6-Tetra-*O*-Trimethylsilyl-*myo*-Inositol (2a)*

To a solution of tetraol **1a** (2.08 g, 10.00 mmol) in DMF (100 mL), TEA (16.0 mL), and TMSCl (7.0 mL, 55 mmol) were added successively and the resulting solution was stirred at 25 °C for 24 h. To the solution, hexane (300 mL) and water (500 mL) were added and separated. The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting solid was recrystallized from methanol (30 mL) to obtain **2a** (4.62 g, 9.30 mmol, 93%) as a

colorless solid: mp 79.5–80.0 °C; ^{1}H NMR ($CDCl_3$, δ): 3.93 (br t, 1H), 3.77 (t, *J* = 10.7), 3.45 (s, 3H), 3.30–3.20 (m, 3H), 2.70 (dd, *J* = 9.3, 2.0, 1H), 0.16 (s, 9H), 0.14 (s, 9H), 0.12 (s, 9H), 0.10 (s, 9H); ^{13}C NMR ($CDCl_3$, δ): 83.48, 82.45, 77.18, 76.86, 74.35, 74.11, 71.18, 61.49, 57.08, 1.12, 1.05, 0.60, 0.43; high-resolution mass spectrometry (HRMS) (electrospray ionization [ESI] *m*/*z*): $[M + H]^+$ calcd for $C_{20}H_{49}O_6Si_4$, 497.2606; found, 497.2611.

1,4-Di-O-*Phenylmethyl-2,3,5,6-Tetra*-O-*Trimethylsilyl*-myo-*Inositol (2b)*

According to the procedure for the silylation of tetraol **1a** into **2a**, tetraol **1b** (3.60 g, 10.0 mmol) was silylated. The resulting crude **2b** was distilled under vacuum using a Kugelrohr apparatus to obtain purified **2b** (4.88 g, 7.52 mmol, 75%) as a white solid: mp 73.5–74.0 °C; ^{1}H NMR ($CDCl_3$, δ): 7.54–7.33 (m, 10H), 5.01 (d, *J* = 12.2, 1H), 4.89 (d, *J* = 12.2, 1H), 4.73 (s, 2H), 4.12 (t, *J* = 8.8, 1H), 4.06 (t, *J* = 1.0, 1H), 3.78 (t, *J* = 9.3, 1H), 3.53 (t, *J* = 8.8, 1H),3.52 (dd, *J* = 9.3, 2.5, 1H), 3.20 (dd, *J* = 9.3, 2.5, 1H), 0.28 (s, 9H), 0.27 (s, 9H), 0.24 (s, 9H), 0.15 (s, 9H); ^{13}C NMR ($CDCl_3$, δ): 139.75, 138.68, 128.36, 127.87, 127.59, 126.97, 126.76, 81.85, 80.45, 75.02, 74.27, 74.11, 72.81, 72.24, 1.29, 1.22, 0.84, 0.32; HRMS (ESI, *m*/*z*): $[M + H]^+$ calcd for $C_{32}H_{57}O_6Si_4$, 649.3232; found, 649.3219.

2,5-Di-O-*(4*-tert-*butyl)Phenylmethyl*-myo-*Inositol (6c)*

Sodium hydride (60% dispersion in mineral oil; 2.00 g, 50.0 mmol) was placed in a flask and washed with anhydrous hexane (10 mL) three times under argon. Then, DMF (120 mL) and **4** (4.08 g, 10.0 mmol) were added successively. The reaction mixture was stirred at 25 °C for 1 h, and then cooled to 0 °C. To the mixture, (4-*tert*-butyl)phenylmethyl bromide (7.50 g, 33.0 mmol) was added in drops. The mixture was allowed to warm to 25 °C and stirred for 24 h. Water (10 mL) was added slowly, and the mixture was then diluted with ethyl acetate (200 mL), transferred into a separation funnel, and washed with water (50 mL) three times. The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure to obtain crude 1,6:3,4-Bis-[*O*-(2,3-dimethoxybutane-2,3-diyl)]-2,5-di-*O*-(4-*tert*-butylphenyl) methyl-*myo*-inositol (**5c**): mp 138.0–138.5 °C; ^{1}H NMR ($CDCl_3$, δ): 7.44 (d, *J* = 8.3, 2H), 7.33 (s, 4H), 7.32 (d, *J* = 8.3, 2H), 4.83 (s, 2H), 4.81 (s, 2H), 4.18 (dd, *J* = 9.3, 9.8, 2H), 3.80 (t, *J* = 2.4, 1H), 3.57 (dd, *J* = 2.4, 9.8, 2H), 3.53 (t, *J* = 9.3, 1H), 3.27 (s, 6H), 3.25 (s, 6H), 1.33 (s, 6H), 1.32 (s, 9H), 1.31 (s, 6H), 1.30 (s, 9H).

Crude **5c** was dissolved in 1,4-dioxane (100 mL). To this solution, 35% hydrochloric acid (10 mL) was added, and the resulting mixture was stirred at 25 °C for 24 h. The volatiles were removed under reduced pressure to obtain a solid. This solid was recrystallized from a mixture of methanol (40 mL) and ethyl acetate (8 mL) to obtain **6c** (3.51 g, 7.44 mmol, 74% from **4**) as a white powder: mp 218.5–219.0 °C; ^{1}H NMR ($CDCl_3$, δ): 7.38–7.24 (br m, 8H), 4.78 (d, *J* = 4.9, 2H), 4.73 (d, *J* = 2.9, 4H), 4.71 (d, *J* = 4.9, 2H), 3.71 (br t, 1H), 3.60–3.52 (m, 2H), 3.34–3.28 (br m, 2H), 3.01 (t, *J* = 9.0, 1H), 1.26 (s, 18H).

2,5-Di-O-*Methyl-1,3,4,6-Tetra*-O-*Trimethylsilyl*-myo-*Inositol (3a)*

To a solution of tetraol **6a** (1.04 g, 5.00 mmol) in DMF (50 mL), trimethylamine (8.0 mL) and trimethylsilylchloride (4.0 mL, 32 mmol) were successively added and the resulting solution was stirred at 25 °C for 24 h. To the solution, hexane (300 mL) and water (500 mL) were added and separated. The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting solid was recrystallized from methanol (15 mL) to obtain **3a** (2.26 g, 4.55 mmol, 91%) as a colorless solid: mp 82.0–83.0 °C; ^{1}H NMR ($CDCl_3$, δ): 3.72 (t, *J* = 9.3, 2H), 3.55 (s, 3H), 3.47 (s, 3H), 3.37 (t, *J* = 2.4, 1H), 3.32 (dd, *J* = 9.3, 2.4 Hz), 2.71 (t, *J* = 9.3, 1H), 0.14 (s, 36H); ^{13}C NMR ($CDCl_3$, δ): 86.46, 83.80, 74.20, 73.81, 61.88, 61.40, 0.81, 0.30; HRMS (ESI, *m*/*z*): $[M + H]^+$ calcd for $C_{20}H_{49}O_6Si_4$, 497.2606; found, 497.2598.

2,5-Di-O-*Phenylmethyl-1,3,4,6-tetra*-O-*Trimethylsilyl*-myo-*Inositol (3b)*

According to the procedure given for the silylation of tetraol **6a** into **3a**, tetraol **6b** (1.80 g, 5.00 mmol) was silylated. The resulting crude **3b** was distilled under reduced pressure using a Kugelrohr apparatus to obtain purified **6b** (4.84 g, 7.47 mmol, 75%) as a colorless oil, which solidified upon cooling: mp 79.5–80.0 °C; ^{1}H NMR ($CDCl_3$, δ): 7.50–7.10 (m, 10H), 4.80 (s, 2H), 4.77 (s, 2H), 3.94 (t, *J* = 9.3, 2H), 3.62 (t, *J* = 2.2, 1H), 3.37 (dd, *J* = 9.3, 2.2, 2H), 3.04 (t, *J* = 9.3, 1H), 0.08 (s, 18H), 0.01 (s, 18H); ^{13}C NMR ($CDCl_3$, δ): 139.93, 139.65, 128.23, 127.92, 127.53, 127.31, 126.60, 126.47, 84.90, 82.59, 75.32, 74.97, 74.50, 74.00, 1.05, 0.46; HRMS (ESI, *m*/*z*): $[M + H]^+$ calcd for $C_{32}H_{57}O_6Si_4$, 649.3232; found, 649.3219.

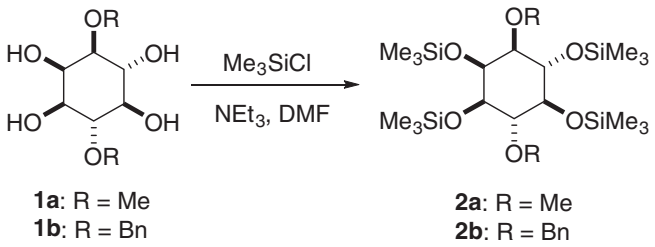
2,5-Di-O-*(4*-tert-*butyl)Phenylmethyl-1,3,4,6-Tetra*-O-*Trimethylsilyl*-myo-*Inositol (3c)*

According to the procedure given for the silylation of tetraol **6a** into **3a**, tetraol **6b** (0.94 g, 2.00 mmol) was silylated. The resulting crude **3c** was recrystallized from a mixture of methanol (60 mL) and ethyl acetate (10 mL) to obtain purified **3c** (0.86 g, 1.56 mmol) as a white powder: mp 136.5–137.0 °C; ^{1}H NMR ($CDCl_3$, δ): 7.42 (br s, 4H), 7.34 (d, *J* = 8.4, 2H), 7.28 (d, *J* = 8.4, 2H), 4.83 (s, 4H), 4.01 (t, *J* = 9.1, 2H), 3.69 (br s, 1H), 3.43 (dd, *J* = 2.2, 9.1, 2H), 3.11 (t, *J* = 9.1, 1H), 1.37 (s, 9H), 1.34 (s, 9H), 0.16 (s, 18H), 0.09 (s, 18H); ^{13}C NMR ($CDCl_3$, δ): 150.22, 149.47, 127.52, 126.64, 125.15, 124.78, 85.06, 82.21, 75.53, 74.73, 74.47, 74.03, 34.65, 34.55, 31.57, 1.13, 0.47; HRMS (ESI, *m*/*z*): $[M + H]^+$ calcd for $C_{40}H_{73}O_6Si_4$, 761.4484; found, 761.4457.

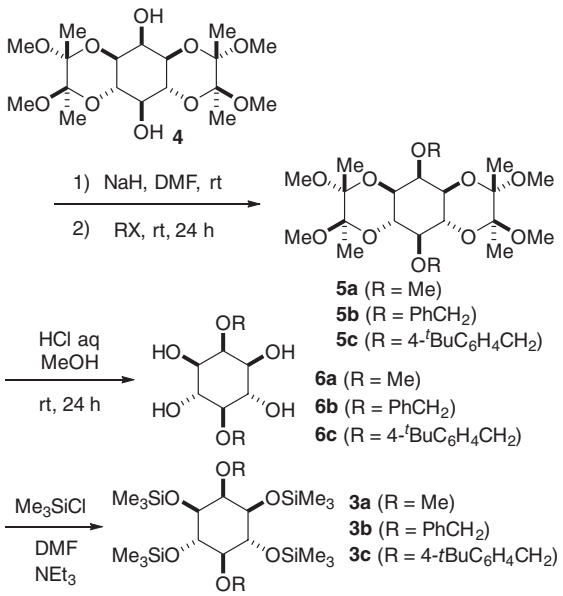
Polycondensations

Typical Procedure (Polycondensation of 2a with CHD)

To a solution of **2a** (0.498 g, 1.00 mmol) and CHD (0.112 g, 1.00 mmol) in 1,2-dichloroethane (1.0 mL) cooled to 0 °C, TMSOTf (9.0 μL, 11 mg, 0.050 mmol) was added. The mixture was stirred at 0 °C for 24 h. To the resulting gel, a solution of sodium hydroxide (1.0 g) in methanol (50 mL) was added and the mixture was stirred vigorously. The resulting precipitate was collected by filtration with suction and dried under vacuum to obtain $\mathbf{7a_3}$ (0.264 g, 93%) as a white powder.



SCHEME 2 Silylation of tetraols **1**.



SCHEME 3 Synthesis of silyl ethers **3**.

Polycondensation of 2b with CHD

According to the typical procedure, polycondensation of **2a** (0.650 g, 1.00 mmol) with CHD (0.112 g, 1.00 mmol) was conducted to obtain $\mathbf{7b_2}$ (0.415 g, 95%) as a white powder.

Polycondensation of 3a with CHD

According to the typical procedure, polycondensation of **3a** (0.498 g, 1.00 mmol) with CHD (0.112 g, 1.00 mmol) was conducted to obtain **8a** (0.281 g, 99%) as a white powder.

Polycondensation of 3b with CHD

According to the typical procedure, polycondensation of **3b** (0.650 g, 1.00 mmol) with CHD (0.112 g, 1.00 mmol) was conducted to obtain **8b** (0.431 g, 99%) as a white powder.

Polycondensation of 3c with CHD

According to the typical procedure, polycondensation of **3c** (0.762 g, 1.00 mmol) with CHD (0.112 g, 1.00 mmol) was conducted to obtain **8c** (0.427 g, 78%) as a white solid.

RESULTS AND DISCUSSION

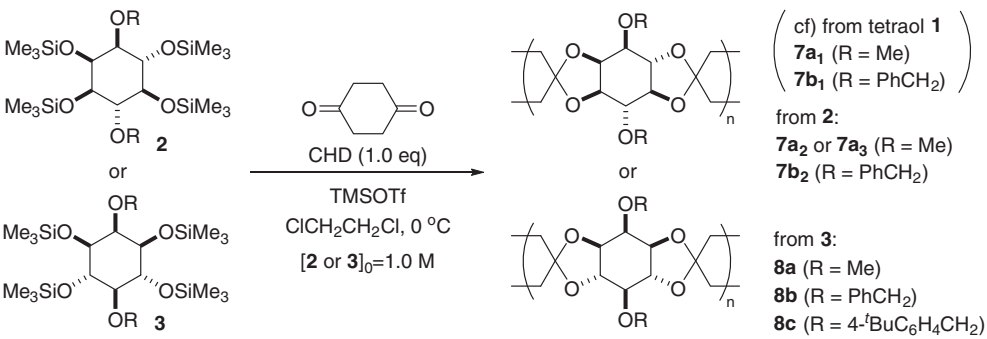
Monomer Synthesis

The tetraols **1a** and **1b** were converted into **2a** and **2b** (Scheme 2) by following a standard *O*-silylation protocol. Silyl ethers **3**, which are isomers of **2**, were synthesized from diol **4** (Scheme 3).[15] The two hydroxyl groups of **4** were alkylated to obtain diethers **5**, and then their 1,2-diacetal protections were removed under acidic conditions to obtain the corresponding tetraols **6**. Finally, **6** were silylated to obtain **3**.

Polycondensation of 2 with CHD

Polycondensation of **2a** with CHD was performed (Scheme 4). The conditions and the results are summarized in Table 1, along with the results of the polycondensations of tetraols **1** with CHD and the properties of the resulting OSKs $\mathbf{7a_1}$ and $\mathbf{7b_1}$, which have been reported in our previous paper,[11] and shown for comparison (Entries 1 and 2). For the polycondensation of **1** with CHD, dimethylsulfoxide (DMSO) was used because tetraols **1** were soluble only in such highly polar solvents. Due to the high miscibility of DMSO with water, complete removal of water formed by the polycondensation from DMSO was difficult. In addition, the high temperature also prompted the backward reaction, that is, hydrolysis of the ketal functions, leading to the low molecular weights of **1** ranging from 1400 to 2100 (estimated by SEC).

In contrast, the polycondensation of silyl ethers **2** with CHD occurred efficiently at 0 °C. 1,2-Dichloroethane, a much less polar solvent than DMSO could be employed because it dissolved both the monomers and the resulting OSKs **7**. In entry 3, the polycondensation of **2a** and CHD was conducted using 1 mol % of TMSOTf. The initial concentrations of **2a** and CHD were set to be 1.0 M. The resulting OSK $\mathbf{7a_2}$ was isolated as a



SCHEME 4 Polycondensation of silyl ethers **2** and **3** with CHD.

TABLE 1 Synthesis of OSKs and their Properties

Entry	Monomer	Amount of TMSOTf (mol %)	Time (h)	OSK	Yield (%)[a]	M_n (M_w/M_n) by MALDI-TOF MS[b]	M_n (M_w/M_n) by SEC[c]	T_{d5} (°C)[d]	T_{d10} (°C)[d]
1	**1a**	–	48	**7a$_1$**	–	2720 (1.4)	2100 (1.9)	328	341
2	**1b**	–	48	**7b$_1$**	–	1710 (1.5)	1400 (1.7)	307	324
3	**2a**	1	24	**7a$_2$**	36	3630 (1.3)	–[e]	–[e]	–[e]
4	**2a**	5	24	**7a$_3$**	93	3750 (1.3)	5600 (2.9)	347	364
5	**2b**	5	24	**7b$_2$**	95	2680 (1.6)	4500 (1.5)	338	350
6	**3a**	5	24	**8a**	99	–[f]	–[g]	277	295
7	**3b**	5	24	**8b**	99	–[f]	–[g]	271	293
8	**3c**	5	24	**8c**	78	–[f]	4100 (2.3)	302	328

[a] Methanol-insoluble parts.
[b] Measured in the *m/z* region 1000–10,000.
[c] Eluent: DMF containing 1 wt % LiBr; calibrated with polystyrene standards.
[d] Determined by thermogravimetric analysis.
[e] Not measured.
[f] Suitable conditions for efficient ionization were not found.
[g] Not measurable due to the poor solubility.

methanol-insoluble fraction in 36%. To evaluate the efficiency of chain growth in the polycondensation, **7a$_2$** was analyzed by MALDI.

TOF mass spectrometry (MS) (Fig. 1; the peak list is shown in Table S1). Compared to **7a$_1$** obtained by the polycondensation of tetraol **1a** with CHD, **7a$_2$** exhibited much higher molecular weights, confirming that the use of the silylated monomer **2a** improved the efficiency of the chain growth.

The MALDI-TOF technique allowed detailed study of the terminal structures of **7a$_2$**. In Figure 2, the spectrum of **7a$_2$** focusing on the region from *m/z* 4000–6000 is shown. There are three series of signals, confirming the presence of polymer chains with different combinations of terminal structures. The signals in Series A, B, and C were attributed to (a) OSKs bearing a diol and ketone moiety on each of the chain ends, (b) OSKs bearing ketone moieties on both chain ends, and (c) OSKs bearing diol moieties on both chain ends, respectively. The signals within

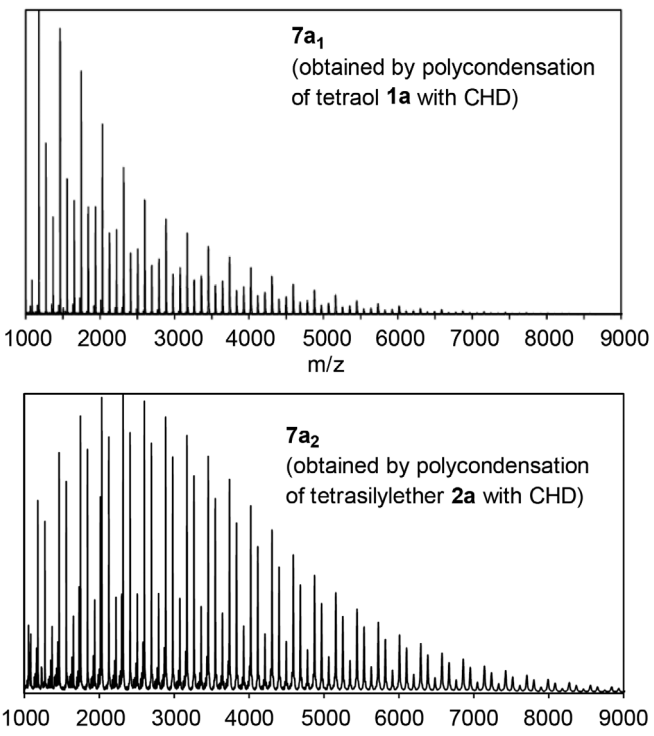


FIGURE 1 MALDI-TOF mass spectra of **7a$_1$** and **7a$_2$**.

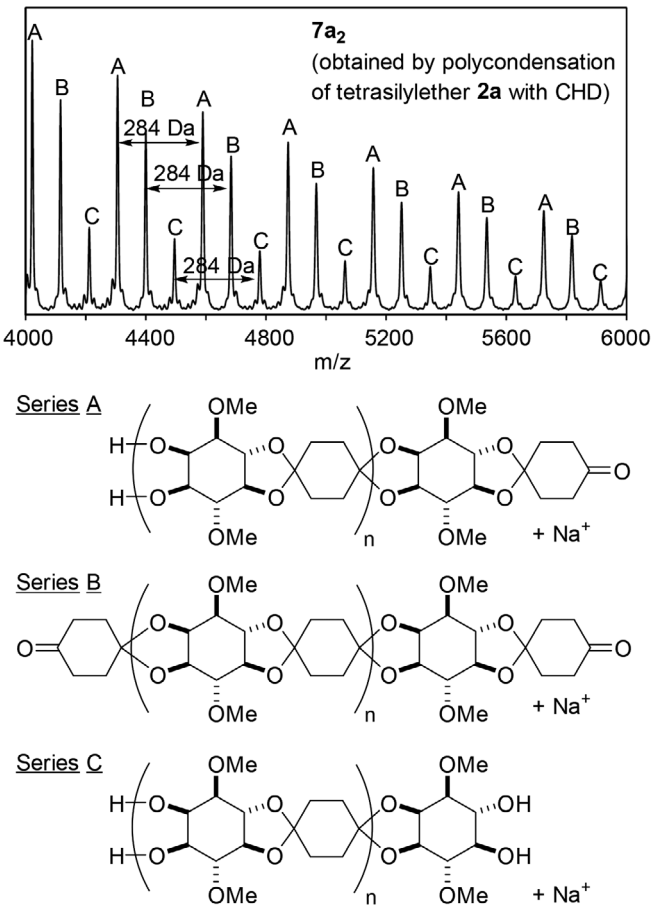


FIGURE 2 Expanded MALDI-TOF MA of **7a$_2$** and peak assignments.

each series differed by 284 Da, which corresponded to the molecular weight of the repeating unit of **7a$_2$**.

For the ^{13}C-NMR analysis of **7a$_2$**, solid-state spectroscopy with cross-polarization magic angle spinning (CPMAS) was used, because the spectra measured in solution were rather complicated, presumably due to the restricted conformational changes of the main chain. Figure 3 shows the spectrum, where signals attributable to the quaternary carbons α and β in the spirocyclic structures were clearly observed.

Upon confirming the successful formation of OSK by the polycondensation of silyl ether **2a** with CHD, the polycondensation was carried out after increasing the amount of TMSOTf to 5 mol % (Entry 4). As a result, OSK **7a$_3$** was obtained in 94% yield. Its MALDI-TOF mass and solid-state ^{13}C-NMR spectra were virtually the same as those of **7a$_2$** (Figs. S1 and S2). SEC analysis of **7a$_3$** revealed that the M_n and M_w values were larger than those of OSK **7a$_1$** by a factor >2.

Under the conditions given in Entry 4, the polycondensation of silylether **2b** with CHD was performed (Entry 5). As a result, the corresponding OSK **7b$_2$** was obtained in 95% yield. SEC analysis revealed that its M_n and M_w were larger than those of OSK **7b$_1$** obtained by the polycondensation of tetraol **1b** and CHD, confirming that the use of silylated monomer improved the efficiency of OSK synthesis.

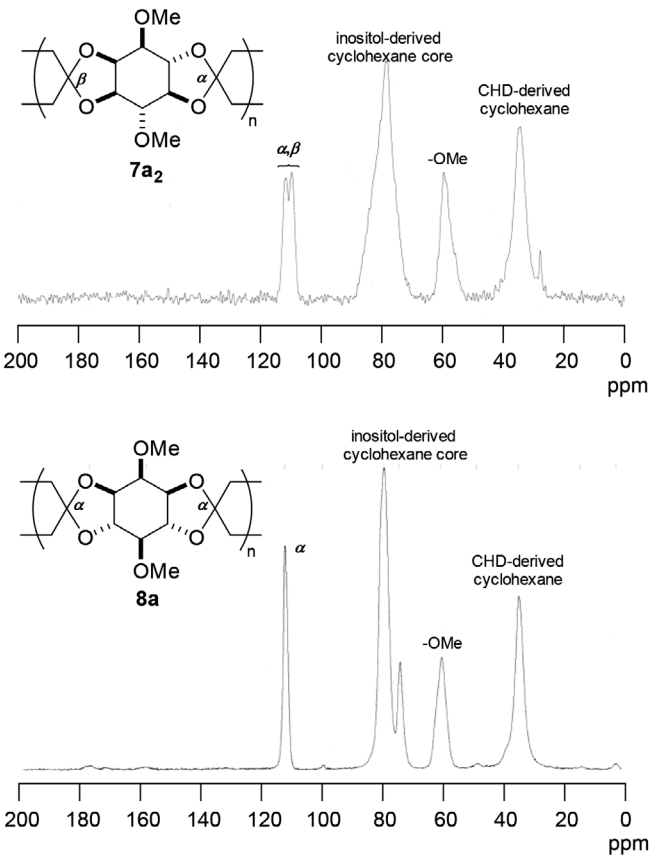


FIGURE 3 Solid-state ^{13}C-NMR spectra (CPMAS) of **7a$_2$** and **8a**.

MALDI-TOF mass analysis of **7b$_2$** confirmed the successful formation of the OSK structures (Figs. S3 and S4, Table S2). The spectrum showed three major series of peaks (Series A, B, and C), confirming the presence of polymer chains with different combinations of terminal structures.

The signals within each series differ by 436 Da, which corresponded to the molecular weight of the repeating unit of **7b$_2$**. In addition, there was a minor series of peaks (Series C′), whose m/z values were smaller than those of Series C by 91 Da, corresponding to the replacement of one benzyl group by one proton in one polymer chain during the ionization process in MALDI. Solid-state ^{13}C-NMR (CPMAS) analysis of **7b$_2$** confirmed its structure. Figure S5 shows the spectrum, where signals attributable to the aromatic carbons in the benzyl groups and quaternary carbons α and β in the spirocyclic structures were clearly observed.

Polycondensation of 3 **with CHD**

We then investigated the polycondensation of tetraol **6a** with CHD under the same conditions as those for the polycondensation of tetraol **1a** with CHD to obtain OSK **7a$_1$**, expecting that the resulting OSK **8a** would have higher stereoregularity than OSK **7a**. However, the target OSK **8a** was not obtained, suggesting that bisketals of **6a** are less stable than the bisketals of **1a**. The former has 1,6-*trans* and 3,4-*trans* configuration, which is intrinsically less stable than the latter having 1,2-*cis* and 4,5-*trans* configuration, leading to greater extent of hydrolysis under the conditions. This indicated that the use of silylether **3** would enable its polycondensation with CHD under much milder conditions, suitable for the formation of less stable bisketals in the main chain of **8a**.

The polycondensation of silylether **3a** with CHD was performed under the same conditions used for the polycondensation of **2a** (Scheme 4). The resulting OSK **8a** was insoluble in various organic solvents. Similarly, the polycondensation of **3b** was carried out to obtain OSK **8b**, which was also insoluble in various organic solvents.

NMR analysis of **8a** and **8b** in solution phase was not possible due to their insolubility. Their MALDI-TOF MS analysis was not successful due to the difficulty in ionization of these OSKs. Thus, these OSKs were analyzed by solid-state ^{13}C-NMR (CPMAS) (Figs. 3 and S5). As can be expected from the higher symmetry of the inositol-derived component in **8a** than that in **7a**, a sharp signal attributable to the two equivalent quaternary carbons, α, knotting the cyclic moieties in a spirocyclic manner was observed at 112 ppm, suggesting the successful formation of spiroketal structure in the main chain. Similarly, the spectrum of **8b** showed a sharp signal at 112 ppm, confirming the main chain structure of **8b**.

The major reason for the insolubility of **8a** and **8b** is likely their tendency to form densely packed states allowed by their highly rigid rod-like structures with higher symmetry than **7**. Figure S6 shows three-dimensional molecular structures of model Compounds **9** and **10** (corresponding to the repeating

units of **7** and **8**, respectively) that were optimized by molecular mechanics calculation. In comparison to **9** with a rather bended conformation, **10** had more laterally extended conformation, suggesting that **8** would be more rod-like than **7**. However, another possibility, that is, the formation of crosslinked structures by intermolecular ketalization could not be excluded completely. In the solid-state ^{13}C-NMR spectra of **8a** and **8b**, a weak signal was detected at 100 ppm, which could be attributed to the quaternary carbon in the acyclic ketal moiety linking oligomer chains.

In contrast to **8a** and **8b**, OSK **8c** obtained by the polycondensation of **3c** with CHD was soluble in chloroform and DMF, presumably due to the presence of bulky and hydrophobic tertiary butyl groups that hindered aggregation of the chains. The solubility of **8c** enabled its SEC analysis to estimate its molecular weight, yielding M_n and M_w/M_n of 4100 and 2.3, respectively, suggesting efficient chain growth in the polycondensation. It was possible to measure ^{1}H-NMR spectrum in $CDCl_3$ solution (Fig. S7). Although the signals were quite broad, the ratio of the integrated signal intensities ([aromatic protons]: [inositol-derived cyclohexane ring + methylene of benzyl group]: [*t*-butyl group]) agreed with the theoretical value. The solid-state ^{13}C-NMR spectrum (CPMAS) provided more detailed information about the structure of **8c** (Fig. S8). Similar to the spectra of **8a** and **8b**, that of **8c** indicated a signal at 112 ppm that could be attributed to the quaternary carbons α. Although there was a weak signal at 100 ppm to suggest the presence of acyclic ketal, its amount would be too small to render **8c** insoluble. The ratio in signal intensity between these two signals was virtually same as those in **8a** and **8b**, suggesting that the probability of intermolecular ketalization resulting in a spirocyclic structure in the main chain and intermolecular ketalization leading to a crosslinking structure was not influenced by the bulkiness of the alkyl substituent (Me or Bn or 4-*t*-Bu-benzyl). This observation indicates that the insoluble nature of **8a** and **8b** is likely caused by their packing ability.

Thermal Properties of OSKs

The obtained OSKs, $\mathbf{7a_3}$, $\mathbf{7b_2}$, **8a**, **8b**, and **8c** were subjected to TG analyses. The resulting thermograms are shown in Figure S9. The temperatures for 5% weight loss (T_{d5}s) and 10% weight loss (T_{d10}s) are summarized in Table 1.

The T_{d5} and T_{d10} values of $\mathbf{7a_3}$, the product of the polycondensation of silylether **3a** with CHD, were much higher than those of $\mathbf{7a_1}$, the product of the polycondensation of tetraol **2a** with CHD, confirming the enhancement of the thermal stability due to the increase of molecular weight of **7a**. Similarly, $\mathbf{7b_2}$, having higher molecular weight than $\mathbf{7b_1}$, was more thermally stable.

The T_{d5}s of OSKs **8a** and **8b** were lower than 300 °C confirming that they are more thermally degradable than **7a** and **7b**. The higher degradability of **8** suggested that the 5–6-5 fused ring system in **8** combined through *cis* and *trans* configurations would be more distorted than that that in **7**, which is combined through *trans* and *trans* configurations. This consideration is in good agreement with the fact that the polycondensation of tetraol **3** with CHD was not successful.

OSK **8c** was more thermally stable than **8a** and **8b**. The difference in the thermal stability could be correlated with the difference in their molecular weights: OSK **8c**, whose main chain was allowed to grow efficiently in the polymerization solution, would have higher molecular weight than **8a** and **8b**, which were less soluble and thus precipitated out from the polymerization solutions before sufficient propagation.

The OSKs were also subjected to DSC analyses. OSKs $\mathbf{7a_3}$, $\mathbf{7b_2}$, **8a**, and **8b** did not exhibit glass transition, while **8c** revealed a glass transition temperature of 113 °C (Fig. S10).

CONCLUSIONS

Derivation of *myo*-inositol into its silyl ethers and their polycondensation with CHD gave an efficient and versatile route for the synthesis of OSKs with higher molecular weights than those obtained by the conventional polycondensation of tetraols with CHD. The use of the silyl ethers **2** and **3**, possessing different configurations, allowed us to synthesize two series of OSKs, **7** and **8**, exhibiting different properties. OSKs **7** were soluble in organic solvents, while OSKs **8** (except **8c**) were insoluble, presumably because of the efficient packing of the more symmetric and thus more rigid rod-like chains. The difference in stereochemistry between **7** and **8** also influenced their thermal stabilities; the OSKs **7** formed by the ketalization of silyl ether **2** bearing 1,2-*cis* and 4,5-*trans* configuration were more stable than OSKs **8** formed by the ketalization of silyl ether **3** bearing 1,6-*trans* and 3,4-*trans* configuration.

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