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A facile synthesis of a novel polyacetal containing trehalose residue in the main chain

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Abstract

A novel polyacetal containing α,α-D-trehalose residue in the main chain was successfully synthesized by the reaction of α,α-D-trehalose with terephthalaldehyde bis(dimethyl acetal) in the presence of p-toluenesulfonic acid. As a result of examination of reaction condition, weight-average molecular weight (M_w) of the polyacetal ranged from 2000 to 8500 when measured by GPC. The polyacetal was soluble in dipolar aprotic solvents such as DMSO and DMF. The ^{1}H-NMR and MALDI-TOF MS spectra revealed that the polyacetal is composed of the molecules terminated by glucopyranosyloxy group, dimethylacetal group, and aldehyde group generated by the hydrolysis of dimethyl acetal group. The polyacetal with M_w 8500 showed no glass transition temperature up to the decomposition temperature (325 °C).
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1. Introduction

Environment-friendly polymers derived from renewable resources have attracted much attention in recent years (Kaplan, 1998). Starch, which is mainly obtained from corn or potato, is one of the least expensive biodegradable renewable resources. There have been already some starch-based plastics such as starch/modified poly(vinyl alcohol) blends with the trade name of Mater-Bi (Bastioli, 1998), esterified starches (Fringant, Desbrières, & Rinaudo, 1996; Wolff, Olds, & Hilbert, 1951), and alkyl-etherified starches (Teramoto, Motoyama, Yosomiya, & Shibata, 2002). Compared to common thermoplastics, however, starch-based thermoplastics still reveal many disadvantages, which are mainly attributed to the brittleness, poor processability, and highly hydrophilic character (Mohanty, Misra, & Hinrichsen, 2000). Conversion of starch to a biodegradable monomer by environment-friendly method and subsequent polymerization or co-polymerization with another monomer, which can give necessary properties would be

a solution to the drawbacks of starch-based plastics while retaining the biodegradability. The most representative example is poly(L-lactic acid) (PLLA), which is derived from starch via fermentation and chemical polymerization (Grijpma & Pennings, 1994). These kind of green polymers having various properties besides PLLA are strongly desired in view of effective utilization and bio-recycling of renewable natural resources. Recently, Hayashibara Co. Ltd developed an inexpensive and environment-friendly manufacturing process of α,α-D-trehalose (**1**) by the fermentation of starch (Shiosaka, 1997). The trehalose is a symmetric α-(1-1) linked non-reducing disaccharide of glucose, and very attractive resources of biodegradable polymer, because of the stability and the symmetrical structure. Kurita et al. (1994) reported the synthesis of polyurethane by the reaction of diisocyanate and 6,6′-diamino-6,6′-dideoxy-α,α-D-trehalose which is prepared by multi-step reactions containing protection and deprotection of hydroxyl groups of trehalose **1**. The present paper describes a facile synthesis of a novel polyacetal [poly(trehalose-*co*-terephtalaldehyde)] (**4**) by the regioselective acetalization of unprotected trehalose **1** with terephthalaldehyde (**2**) or terephthalaldehyde bis(dimethyl acetal) (**3**) (Scheme 1).

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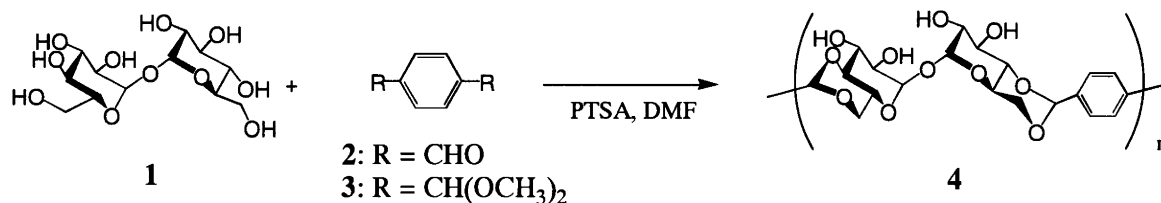
Scheme 1. Synthesis of polyacetal **4**.

2. Experimental

2.1. Materials

α,α-D-Trehalose dihydrate supplied by Hayashibara Co., Ltd (Japan) was dehydrated at 130 °C for 24 h before use. Trimethyl orthoformate and *N,N*-dimethylformamide (DMF; anhydrous) were used as received from Aldrich Chemical Company. Terephthalaldehyde (**2**), anhydrous methanol, *p*-toluenesulfonic acid monohydrate (PTSA), ammonium chloride, and sodium hydrogencarbonate were used as received from Kanto Chemical Company (Japan).

2.2. Measurements

IR and ^{1}H NMR spectra were recorded on a Shimadzu FT-IR 8100 and a Brucker AMX-400, respectively. GPC analysis was performed at 80 °C using a Shimadzu LC9A equipped with two linear PLgel 5 μm MIXED-D columns (Polymer Laboratories Ltd), using DMSO as the eluent, the elution rate was 0.5 ml/min and the detector was the refractive index type. Pullulan standards were used to generate a calibration curve for the molecular weight determination. Differential scanning calorimetry (DSC) measurement and thermogravimetric analysis (TGA) were performed using a Perkin Elmer Pyris 1 and TGA-7, respectively, with a heating rate of 20 °C/min in a nitrogen atmosphere. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) was performed on a Shimadzu KOMPACT Probe, using α-cyano-4-hydroxycinnamic acid as a matrix and dioxane/water (1/1) as a solvent.

2.3. Methods

2.3.1. Preparation of bis(dimethyl acetal) 3

To a solution of terephthalaldehyde **2** (8.05 g, 60.0 mmol) in 265 ml of methanol, was added ammonium chloride (1.05 g, 19.6 mmol). Trimethyl orthoformate (20 ml, 0.18 mol) was dropwise added to the mixture, and refluxed for 3 h in a nitrogen atmosphere. After evaporation of the solvent, 0.5% aqueous sodium hydrogen-carbonate solution was added to the residue, and the mixture was extracted with diethyl ether. The extract was washed twice with deionized water, dried over magnesium sulfate. After filtration, the filtrate was concentrated in

vacuo to give **3** as white powder (12.2 g, 90.0% yield). IR(KBr):3040, 3000(aromatic CH), 2961, 2903, 2836 (aliphatic CH), 1509, 1458, 1443(aromatic C=C), 1215, 1200, 1098, 1057 cm^{-1}(acetal); ^{1}H NMR (DMSO-d_6, 400 MHz,) $\delta = 7.39$ (s, 4H, aromatic), 5.39 (s, 2H, >C*H*Ph), 3.23 (s, 12H, OC*H*$_3$).

2.3.2. Preparation of polyacetal 4 by the reaction of 1 and 3

Before polycondensation reaction, a toluene–water azeotrope was distilled away under reduced pressure (120 Torr) from a solution of PTSA (0.951 g, 5.00 mmol) in DMF (100 ml) and toluene (20 ml), and then dried trehalose **1** (3.42 g, 10.0 mmol) and bis(dimethyl acetal) **3** (2.26 g, 10.0 mmol) were added. The resulting mixture was stirred at 100 °C for 8 h under reflux (~ 100 Torr). Methanol generated during the polycondensation reaction was succes-sively removed and condensed in an ice trap. After the mixture was concentrated to ca. 5 ml under reduced pressure, 0.5% aqueous sodium hydrogencarbonate solution was added. The resulting precipitate was gathered by filtration, washed with water, and dried at room temperature in vacuo for 24 h to give a crude product (4.4 g, 100% yield). The crude product was dissolved in DMF, repreci-pitated with methanol, filtered, and dried in vacuo for 24 h to give polyacetal **4** as a white solid (3.37 g, 76.6% yield).

IR (KBr): 3419(OH stretching), 2937, 2876(CH), 1698(C=O), 1509, 1475, 1420(aromatic C=C), 1375(OH bending), 1211, 1152, 1127, 1075 cm^{-1} (acetal).
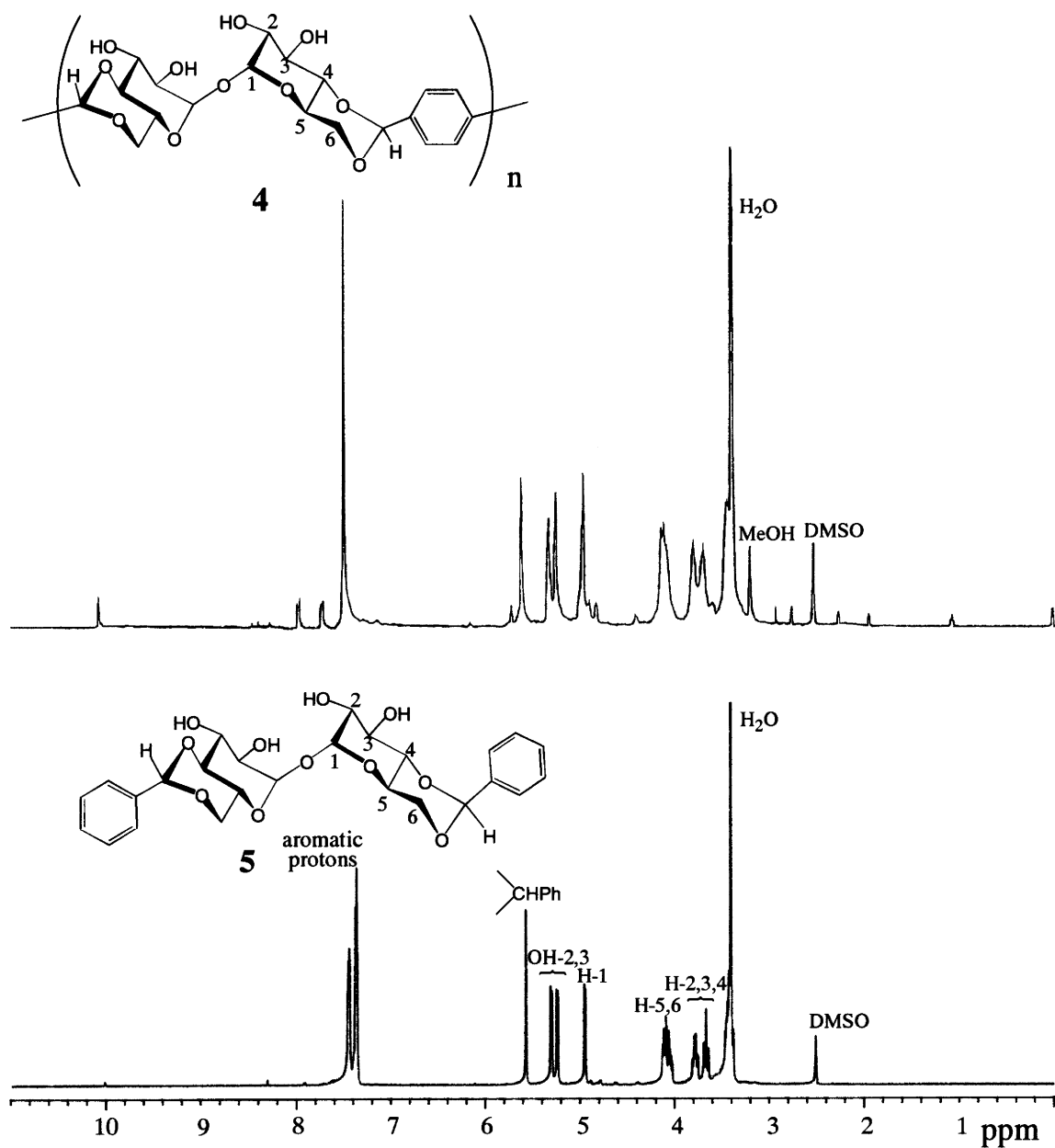
2.3.3. Preparation of polyacetal 4 by the reaction of 1 and 2

Before polycondensation reaction, the hydrated water of PTSA was removed under reduced pressure (120 Torr) via Dean-Stark apparatus by azeotropic distillation from a solution of PTSA (0.951 g, 5.00 mmol) in DMF (100 ml) and toluene (30 ml). After addition of dried trehalose **1** (3.42 g, 10.0 mmol) and bis(dimethyl acetal) **3** (2.26 g, 10.0 mmol), the mixture was refluxed at 100 °C for 8 h under reduced pressure (~ 180 Torr). The water generated during the polycondensation reaction was continuously removed via a Dean-Stark apparatus by azeotropic distilla-tion with toluene. After the mixture was concentrated to ca. 5 ml under reduced pressure, 0.5% aqueous sodium hydrogencarbonate solution was added. The resulting precipitate was gathered by filtration, washed with water, and dried at room temperature in vacuo for 24 h to give a crude product of polyacetal **4** (3.3 g, 74% yield).

Table 1
Synthetic conditions and molecular weight of polyacetal **4**

Exp. No.	Reactant with **1**	PTSA (mmol)	Temperature (°C)	Pressure (Torr)	Time (h)	Crude yield (%)	M_w	M_n
1	**3**	1.0	70	50	24	95	3600	2900
2[a]	**2**	1.0	70	80	24	–	1700	1500
3	**3**	5.0	70	50	24	92	4200	3100
4	**3**	5.0	70	50	4	100	6200	3800
5	**3**	5.0	100	100	8	100	8500	3800
6	**3**	5.0	100	100	3	53	4300	2600
7[a]	**2**	5.0	100	180	8	74	3700	1800
8	**3**	5.0	120	200	8	69	2000	1600
9	**3**	5.0	120	200	3	56	4000	2200

DMF 100 ml, **1** 10.0 mmol, and **3** (or **2**) 10.0 mmol were used in all the experiments.

[a] The water formed during the polycondensation reaction of **1** and **2** in DMF(100 ml)/toluene(30 ml) was azeotropically distilled by use of Dean-Stark trap.

Fig. 1. ^{1}H NMR spectra of **4** and **5** in DMSO-d_6.

(a)

(b)
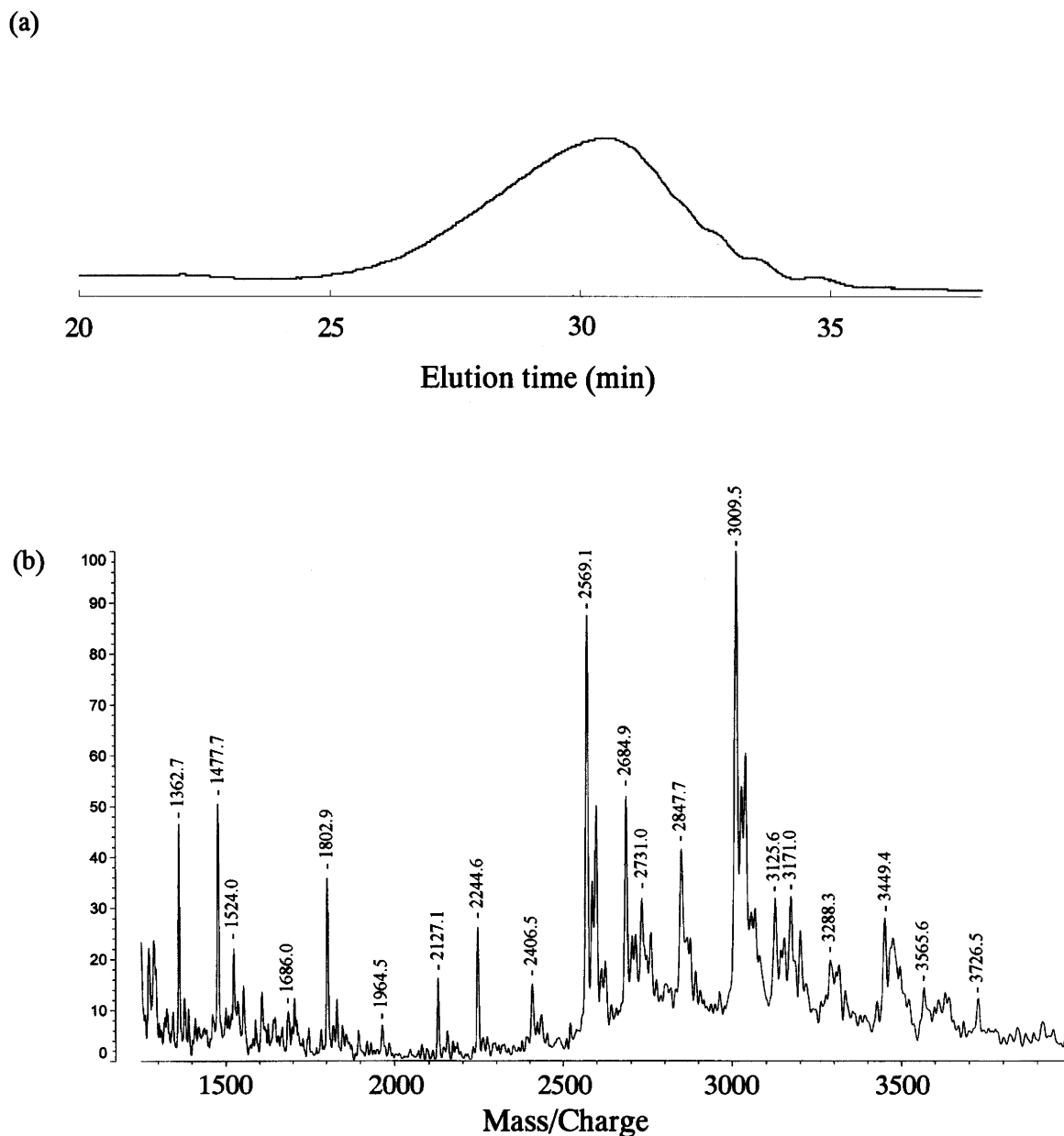

Fig. 2. GPC trace and MALDI-TOF mass spectrum of polyacetal **4**.

3. Results and discussion

The transformation of trehalose **1** to 4,6:4′,6′-di-*O*-benzylidene-α,α-trehalose (**5**) by the reaction with benzaldehyde or its dimethyl acetal is known as a protection method of the hydroxyl groups. Hough, Munroe and Richardson (1971) reported that the reaction of **1** and benzaldehyde gives **5** in 78% yield after recrystallization. Baer and Radatus (1984) reported that the reaction of **1** and benzaldehyde dimethyl acetal in DMF in the presence of PTSA gives **5** in 94% yield after recrystallization. As an application of this reaction to the polymer synthesis, trehalose **1** was reacted with terephthalaldehyde **2** or its bis(dimethylacetal) **3** in DMF in the presence of PTSA. In case of the reaction of **1** and **2**, the water generated during the reaction was continuously removed via a Dean-Stark apparatus by azeotropic distillation with toluene. Table 1 summarizes the synthetic conditions and the results of the polycondensation reactions. The polyacetal prepared from **3** had a higher molecular weight than that from **2** (Exp. 1 vs. 2, or Exp. 5 vs. 7). The equimolar reaction of **1** and **3** at 100 °C for 8 h (Exp. 5) afforded maximum weight-average (M_{w}) and number-average molecular weight (M_{n}) of 8500 and 3800 (GPC, pullulan standard), respectively. In this case, the higher boundary of the elution peak

reached ~98000. The reaction at a higher temperature (120 °C, Exp. 8 and 9) resulted in the decrease in molecular weight and yield. Polyacetal **4** was dissolved in DMSO, DMF, dioxane/water(1:1) and acetone/water (1:1), while it was insoluble in water, methanol, ethanol, diethyl ether, chloroform, THF, and ethyl acetate.

The ^{1}H NMR spectrum of **4** (Exp. 5) in DMSO-d_6 is shown as compared with that of **5** in Fig. 1. The protons of **4** were assigned based on the proton assignment for **5** shown in Fig. 1. Regarding polyacetal **4**, a peak observed at 7.5 ppm was assigned to aromatic protons and that at 5.6 ppm assigned to methine groups adjacent to the benzene unit. Two peaks around 5.3 ppm were assigned to 2,2′,3,3′-hydroxyl groups on the trehalose unit, and several peaks at 4.2–3.6 ppm were assigned to protons (H-2–6) bound to carbon atoms on the trehalose unit. The ^{1}H signals at 10.3 ppm(s) and 8.0 ppm(d), 7.7 ppm(d) were assigned to the aldehyde proton and aromatic protons on the terminal benzaldehyde group. The presence of aldehyde proton indicates that terminal dimethylacetal group is considerably hydrolyzed with the contaminated water. The proton signals related to dimethylacetal groups ($\delta \sim 3.5$) were not identified by overlapping of the signal of water ($\delta \sim 3.4$). When we assume that the presence of acetal-terminated molecule is negligible and that the number of terminal benzaldehyde group is the same as that of terminal glucopyranosyloxy group, number-average degree of polymerization is estimated to be ca. 7.5 ($M_n = 3300$) from the ratio of integration values between the benzene ring protons (28.357) in the repeating unit and terminal benzene ring protons (3.794). The M_n value evaluated roughly by NMR was in fairly good agreement with the M_n (3800) by GPC analysis (Fig. 2a).

Fig. 2b shows MALDI-TOF MS spectrum of polyacetal **4** (Exp.5). All the molecular ions were observed as the adducts of sodium ion. The number of the repeating unit where two molecules of water dehydrated from one trehalose and one terephthalaldehyde molecules ranged from 2 to 8 as is shown in Table 2. The values of mass/charge (*m/e*) indicated that the polyacetal **4** contains the molecules terminated by benzaldehyde, benzaldehyde dimethyl acetal, and glucopyranosyloxy groups, and that the polymer hardly contains cyclic molecule. The molecular ion peak related to telechelic acetal-terminated molecule was not observed. The presence of benzaldehyde-terminated molecules is consistent with the result of ^{1}H NMR. The highest peak of the polyacetal molecules was *m/e* obs. 3009.5 (calcd *m/e* 3007.8 = M_6 + TH + Na, telechelic trehalose unit-terminated hexamer), which valued was a little lower than the $M_n = 3800$ by GPC analysis.

The decomposition temperature of polyacetal **4** (Exp. 5) measured by TGA under nitrogen were 325 °C, which was higher than that of trehalose **1** (300 °C). No glass transition temperature was detected until the decomposition temperature in the DSC thermogram of poyacetal **4** (Exp.5).

Table 2
MALDI-TOF MS data of polyacetal **4** (Exp. 5)

Signal (*m/e*)	Relative intensity (%)	Assignment[a]	Calcd. (*m/e*)	Deviation[b]
1362.7	46	M_2 + TH + TA-H$_2$O + Na	1362.2	+0.5
1477.7	51	M_3 + TA + Na	1478.4	−0.7
1524.0	22	M_3 + TM + Na	1524.4	−0.4
1686.0	10	M_3 + TH + Na	1686.5	−0.5
1802.9	36	M_3 + TH + TA-H$_2$O + Na	1802.7	+0.2
1964.5	7	M_4 + TM + Na	1964.8	−0.3
2127.1	16	M_4 + TH + Na	2126.9	+0.2
2244.6	26	M_4 + TH + TA-H$_2$O + Na	2243.1	+1.5
2406.5	15	M_5 + TM + Na	2405.3	+1.2
2569.1	88	M_5 + TH + Na	2567.4	+1.7
2684.9	52	M_5 + TH + TA-H$_2$O + Na	2683.5	+1.4
2731.0	32	M_5 + TH + TM-H$_2$O + Na	2729.5	+1.5
2847.7	42	M_6 + TM + Na	2845.7	+2.0
3009.5	100	M_6 + TH + Na	3007.8	+1.7
3125.6	32	M_6 + TH + TA-H$_2$O + Na	3123.9	+1.7
3171.0	32	M_6 + TH + TM-H$_2$O + Na	3170.0	+1.0
3288.3	20	M_7 + TM + Na	3286.1	+2.2
3449.4	28	M_7 + TH + Na	3448.2	+1.2
3565.6	14	M_7 + TH + TA-H$_2$O + Na	3564.3	+1.3
3726.5	12	M_8 + TM + Na	3726.5	+0.0

[a] TH represents the molecular weight of trehalose ($C_{12}H_{22}O_{11}$:342.3), TA represents the molecular weight of terephthalaldehyde ($C_8H_6O_2$:134.1), TM represents the molecular weight of terephthalaldehyde mono(dimethyl acetal) ($C_{10}H_{12}O_3$:180.2). M_x represents the molecular weight of the segment having *x* repeating unit [(TH + TA-2H$_2$O) *x* = 440.4 *x*].
[b] Deviation = (Experimental value) − (Calculated value).

4. Conclusions

A novel polyacetal containing α,α-D-trehalose residue in the main chain was successfully synthesized by the polycondensation reaction of terephthalaldehyde bis(dimethyl acetal) and α,α-D-trehalose which can be derived from starch via fermentation. The synthesis can be carried out in a one-pot process, and proceeds in essentially quantitative yield. As a result of examination of reaction condition, the M_w of the polyacetal went up to 8500 and the higher boundary of the elution peak reached ~98000. The use of terephthalaldehyde instead of its bis(dimethyl acetal) resulted in the decrease in molecular weight and yield. The synthesis of this polyacetal analogues using various kinds of dialdehydes or its acetal derivatives are under current investigation.

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