

# Poly(lactic acid) polymer stars built from early generation dendritic polyols

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Abstract: A family of polymer stars has been prepared from early generation dendritic cores with four, six, and eight arms. Four dendritic cores were prepared from the sequential reaction of a multifunctional alcohol with a protected anhydride, followed by deprotection to afford two or three new alcohol functionalities per reactive site. These cores were used as initiators for the tin-catalyzed ring-opening polymerization of L-lactide and rac-lactide to afford isotactic and atactic degradable stars, respectively. Two series of stars were prepared for each monomer, either maintaining total molecular weight or number of monomer units per arm. The polymers were characterized by NMR spectroscopy, light-scattering gel-permeation chromatography, differential scanning calorimetry, and thermogravimetric analysis. Our results support previous work that suggests that the length of the arms dictates thermal properties rather than the total molecular weight of the star. Little effect was noted between aromatic and aliphatic cores, presumably due to the flexibility of the rest of the core molecule. We have shown that early generation dendrimers can serve as excellent core structures for building core-first polymer stars via the ring-opening of cyclic esters.

Key words: poly(lactic acid), dendrimer, biodegradable polymer, synthesis, star polymer, thermal properties, DSC, TGA.

Résumé : On a préparé une famille de polymères en étoile à partir de cœurs dendritiques de premières générations possédant quatre, six ou huit branches. On a produit quatre cœurs dendritiques en partant de la réaction séquentielle d'un alcool multifonctionnel avec un anhydride protégé, suivie d'une déprotection de manière à donner deux ou trois nouvelles fonctions alcool par site de réaction. Ces cœurs ont servi d'initiateurs de polymérisation par ouverture de cycle, catalysée par l'étain, du L-lactide et du rac-lactide pour obtenir des étoiles dégradables de formes isotactique et atactique, respectivement. Pour chaque monomère, on a préparé deux séries d'étoiles, en maintenant le même poids moléculaire total ou le même nombre d'unités monomériques par branche. On a caractérisé les polymères par spectrométrie RMN, par chromatographie par perméation de gel associée à un détecteur à diffusion de lumière, par calorimétrie différentielle à balayage (DSC) et par analyse thermogravimétrique (ATG). Nos résultats corroborent ceux de travaux antérieurs donnant à penser que la longueur des branches dicte les propriétés thermiques plutôt que le poids moléculaire total de l'étoile. Nous n'avons constaté que peu de différence entre les cœurs aromatiques et aliphatiques, probablement en raison de la flexibilité du reste de la molécule centrale. Nous avons montré que les dendrimères de premières générations peuvent constituer d'excellentes structures de base pour la construction de polymères en étoile à partir du cœur par ouverture d'esters cycliques. [Traduit par la Rédaction]

Mots-clés : acide polylactique, dendrimère, polymère biodégradable, synthèse, polymère en étoile, propriétés thermiques, DSC, ATG.

# Introduction

Control over polymer macrostructure, especially over polymer topology, is an increasingly important method to modify polymer properties. These branched structures include graft, comb, brush, cross-linked, dendritic, and star polymer topologies.1-3 Of particular interest, star polymers possess multiple arms connecting at a central core to form a globular core-shell macrostructure with increased chain-end density and short linear segments.<sup>4</sup> The stars can be synthesized through two methods. The arm-first approach uses pre-synthesized linear polymers that are attached onto a central core through either a coupling strategy or the addition of a bifunctional comonomer terminator.<sup>5</sup> The core-first approach is complementary, and arguably offers a more systematic variation of core composition and control over the number of arms.<sup>6</sup> This route exploits a multifunctional initiator from which polymer arms are grown.

Our particular interest in this field is in the preparation of polymer stars of aliphatic polyesters such as poly(lactic acid). The

increased number of chain-end functionalities and the improved control over degradation have promoted these structures as alternatives to linear poly(lactic acid) in biomedical and nanotechnology applications.<sup>7-10</sup> Thermal properties are also affected, with lower glass transition, melting, and crystallization temperatures observed when compared with linear polymers of the same molecular weight.<sup>11</sup> The effect of tacticity on these systems is also profound, with significant changes in thermal properties and degradation observed in concert with their more extensively explored linear counterparts.<sup>6,7</sup> The nature of the core in polymer stars has also been previously studied; in particular, examining the number of arms and molecule rigidity.12

In parallel with the development of star polymer topologies, dendritic systems have seen explosive growth in research and applications. These repetitively branched molecules can offer even higher numbers of end-group functionalities and modified properties.<sup>13</sup> They are traditionally difficult to synthesize to high molecular weights and generations, but have found important

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applications from drug and gene delivery to sensor technology.<sup>13,14</sup> We were interested in merging these two fields and examining early-generation dendritic cores as potential initiators for poly(lactic acid) polymer stars. This work presents the use of four dendritic polyols as novel nontoxic cores for the synthesis of stars with 4, 6, and 8 arms with both 1- and *rac*-lactide as feedstocks to generate isotactic and atactic arms (Scheme 1). Two tetraols differentiated by the presence of aromatic or aliphatic backbones at the dendrimer cores were targeted. Two families are examined, investigating stars of similar molecular weights and similar arm lengths, respectively.

## **Results and discussion**

The desired early generation polyester dendrimers were synthesized using standard techniques.<sup>15</sup> The aryl-substituted tetraol **4**, was prepared by reaction of 1,4-bis-(2-hydroyethoxy)benzene **1**,<sup>16</sup> with 2.4 equiv of anhydride **2**,<sup>17</sup> followed by deprotection, as shown in Scheme 2. Repetition of the reaction sequence extended compound **4** to the second generation polyester dendrimer: the octaol **6** as shown in Scheme 3. The same anhydride reaction and deprotection steps were also used to convert 1,8-octanediol **7** into the first generation tetraol **9**, as shown in Scheme 4. The final core, hexaol **11**, was prepared according to procedures found in the literature (Scheme 5).<sup>16</sup>

Polymer stars with each of the four cores were synthesized using  $Sn(Oct)_2$  as a catalyst for the ring-opening polymerization of cyclic esters. Using *rac*- or 1-lactide as the feedstock produced atactic or isotactic polymer stars, respectively. While ring-opening polymerizations catalyzed by  $Sn(Oct)_2$  are usually conducted in solution at 70 °C to minimize transesterification reactions, the low solubility of initiators **4**, **6**, **9**, and **11** led to inefficient initiation and broad polydispersities (PDIs) under these conditions. Lower PDIs were obtained by performing the polymerizations under an inert atmosphere in neat, molten lactide at 120 °C for 30 min or less. Longer reaction times led to lowered molecular weights and increased PDIs, while shorter times led to variability in molecular weights. Reaction times were tuned by multiple

Scheme 2. Formation of tetraol 4.



screening reactions, which also confirmed that the differences observed were a result of changes to core structure rather than slight deviations in molecular weights. The polymerization data for these experiments, producing four series of polymer stars, are shown in Table 1, with further details provided in the Supplementary data (supporting information). Molecular weights were determined by GPC, and the number of monomer units per PLA arm was calculated from the  $M_n$  value, correcting for the nature of the core initiator.

Series 1 and 2 stars were prepared from isopure L-lactide with high levels of control. Series 1 represents a family of stars with similar overall molecular weights (29.5–32.4 kDa), while Series 2 attempted to produce a family of stars with similar arm lengths (49–54 lactic acid units per arm). Although PDIs of 1.07 or less were maintained, in all instances a small amount of low molecular weight homopolymer was observed in the GPC traces (<2% of the total sample mass), characteristic of some self-initiation reactions. Purification of the material by reprecipitation removed the low molecular weight impurities.

Similarly, Series 3 and 4 were prepared from *rac*-lactide, equivalent to Series 1 and 2, respectively, with similar overall molecular weights and arm lengths. The equimolar mixture of D- and

Scheme 3. Elaboration of tetraol 4 into octaol 6.



Scheme 4. Formation of first generation dendrimer 9 from 1,8-octanediol.



Scheme 5. Preparation of hexaol 11.16



**Table 1.** Polymerization data for poly(lactic acid) polymer stars using four dendritic initiators.

Series	Monomer	Initiator	$M_{ m n}{}^a$	PDI	Monomer units/arm
1	l-LA	<b>4</b> (4-arm)	32400	1.17	54
	l-LA	<b>11</b> (6-arm)	29500	1.01	34
	L-LA	6 (8-arm)	32100	1.01	27
	l-LA	<b>9</b> (4-arm)	29600	1.02	50
2	L-LA	4	32400	1.07	54
	l-LA	11	43100	1.02	49
	L-LA	6	61200	1.03	52
	L-LA	9	29600	1.02	50
3	rac-LA	4	30800	1.39	53
	rac-LA	11	30600	1.18	36
	rac-LA	6	29200	1.09	22
	rac-LA	9	29300	1.31	50
4	rac-LA	4	30800	1.39	53
	rac-LA	11	47000	1.25	53
	rac-LA	6	58500	1.29	50
	rac-LA	9	29300	1.31	50

**Note:** Polymerizations conducted at 120 °C in neat molten lactide for 15, 20, or 30 min to high conversion with variable feedstock ratios of core:catalyst:lactide (see also supplementary data, Table S1).

<sup>a</sup>Molecular weights determined using GPC with a light-scattering detector using a dn/dc value for poly(lactic acid) of 0.051.

I-lactide produces an atactic chain, as Sn(Oct)<sub>2</sub> offers no tacticity control over the reaction. Increased polydispersities (up to 1.39) were noted for these amorphous materials relative to the semicrystalline stereoregular material in Series 1 and 2, although only monomodal traces were observed, and no transesterification reaction products found by MALDI–TOF MS. The oligomeric material observed in Series 1 and 2 was not observed, and is assumed to be too low to be quantified by GPC (Supplementary data, Figs. S1 and S2). In all instances for Series 1–4, characterization of the polymer stars by <sup>1</sup>H NMR spectroscopy indicated complete initiation of all alcohol sites, as supported by the disappearance of CH<sub>2</sub>–OH resonances.

Our premise in starting this work was that the early-generation dendritic cores could capably function as foundation pieces for polymer star synthesis. We also wished to explore the relationship between star molecular weight, arm length, and thermal properties in these systems. Differential scanning calorimetry and thermogravimetric analysis accessed glass ( $T_g$ ), crystallization ( $T_c$ ), melting ( $T_m$ ), and decomposition ( $T_d$ ) temperatures for these systems. The data for the L-lactide stars are provided in Table 2.

As is characteristic for these semi-crystalline materials,  $T_{o}$ ,  $T_{c}$ , and  $T_{\rm m}$  temperatures are all observed. Matching what is often observed in linear poly(lactic acid)s, two melting peaks are present (see Fig. 1), although only the largest of these two peaks is tabulated below, owing to inadequate resolution of the smaller peak. For the stars of similar total mass (Table 2, Series 1), an increase in arm number resulted in lowered melting temperatures for stars of similar total molecular weight: a trend that supports previous reports from the literature.<sup>18</sup> Melting temperatures for stars with arms of similar lengths (Table 2, Series 2) were noticeably consistent, with the exception of 2-4, suggesting that arm length is an important factor in determining the  $T_{\rm m}$ . With stars of similar total mass, enhancement of  $T_c$  with increasing number of arms was observed, indicating that a decrease in molecular weight of the individual PLA arms corresponds to a higher  $T_c$ . The opposite trend was seen for stars of similar arm length, with crystallization occurring at a lower temperature for the stars with a greater number of arms. Hence, the lower total molecular weight stars had a higher  $T_c$ , demonstrating that  $T_c$ s are dependent on both the total star molecular weight and the molecular weight of each individual arm. No discernable trends were observed in  $T_{o}$ s, except for a remarkable consistency in the data for the stars of similar arm length. This is consistent with the  $T_{\rm m}$  data,

**Table 2.** Thermal properties of isotactic polymer stars of similar total molecular weight and similar arm molecular weight.

Series	Core	$T_{\rm g}(^{\circ}{ m C})$	$T_{\rm c}$ (°C)	$T_{\rm m}(^{\circ}{\rm C})$	$T_{d}$ (°C)
1	4	52.3	94.2	160.1	240.0
1	11	53.5	95.7	152.6	250.0
1	6	52.1	96.5	147.2	249.2
1	9	52.3	88.7	158.8	247.9
2	4	52.3	94.2	160.1	240.0
2	11	52.2	85.0	158.4	239.0
2	6	52.4	84.5	158.4	240.5
2	9	52.3	88.7	158.8	247.9

**Note:** DSC conditions: 50 mL min<sup>-1</sup> N<sub>2</sub> purge flow, heating/ cooling rate of 5 °C min<sup>-1</sup>, heat/cool/heat cycle. TGA conditions: 60 mL min<sup>-1</sup> N<sub>2</sub> sample purge flow, heating rate of 10 °C min<sup>-1</sup>, decomposition temperature measured at point of fastest weight loss.

Fig. 1. Example from differential scanning calorimetry (1-11).



which suggests that arm length is crucial in controlling phase transition temperatures.

The nature of the core, the length of the arms, and the number of arms had little correlation with the decomposition properties of the PLA star polymers.  $T_{\rm d}s$  are reported at the point of fastest weight loss, which was also when the material had lost approximately 50% of its total weight. For isotactic stars,  $T_{\rm d}$  values ranged from 239–250 °C, with complete degradation occurring by 397 °C in all instances. Significant differences in these thermal transitions were noted, however, for the atactic stars. These data are shown in Table 3.

As expected, atactic poly(lactic acid) stars lacked crystallization and melting peaks. The amorphous polymers had  $T_{\rm g}$ s that were significantly lower than for the isotactic stars, in agreement with previous studies on tacticity-controlled star polymers and linear PLA. While no apparent trends were evident for stars of similar arm length (Table 3, Series 4), Series 3 again showed that an increase in the number of arms corresponded to a slight lowering of  $T_{\rm g}$  values, which may be attributable to modest differences in polymer dispersity. Previous studies have demonstrated the association of PDI with  $T_{\rm g}$ , with increased polymerization control corresponding to lower  $T_{\rm g}$  values.<sup>2</sup>  $T_{\rm d}$ s were higher than for the isotactic samples, although onset and maximum decomposition temperatures were similar.

Finally, the comparison of aromatic and aliphatic backbones is possible by comparing samples from core **9** and core **4**. The nature of the backbone appeared to have little effect on the thermal properties of the polymer stars studied. The differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) data collected for the atactic and isotactic stars with cores **9** and **4** were

**Table 3.** Thermal properties of atactic polymer

 stars of similar total molecular weight and similar

 arm molecular weight.

Series	Core	$T_{\rm g}$ (°C)	$T_{\rm d}$ (°C)
3	4	43.8	273.4
3	11	40.8	279.7
3	6	37.4	279.2
3	9	39.8	277.3
4	4	43.8	258.3
4	11	33.8	279.2
4	6	42.9	295.4
4	9	39.8	277.2

**Note:** DSC conditions: 50 mL min<sup>-1</sup> N<sub>2</sub> purge flow, heating/cooling rate of 5 °C min<sup>-1</sup>, heat/cool/heat cycle. TGA conditions: 60 mL min<sup>-1</sup> N<sub>2</sub> sample purge flow, heating rate of 10 °C min<sup>-1</sup>, decomposition temperature measured at point of fastest weight loss.

generally very similar, with the phase transition temperature for the flexible core slightly lower.

## Conclusions

The effects of core structure and polymer arm tacticity on poly-(lactic acid) star polymer properties were investigated via the synthesis and characterization of four series of polymer stars. Tacticity was shown to have important implications on the phase transition and degradation temperatures of these stars, as has been observed in previous studies involving both linear and starshaped polymers. To fully discern the consequences of changing the number of arms in such polymers, stars of similar total molecular weight as well as stars of similar arm molecular weight were synthesized with each of the four dendritic polyol initiators. The isotactic stars in particular showed some interesting trends in the phase transition temperatures. These  $T_{\rm m}s$  and  $T_{\rm g}s$  showed reliance on individual arm length. The crystallization temperatures, however, showed dependence on both arm molecular weight and total molecular weight, with lower weights corresponding to a higher transition temperature. The nature of the core backbone was also explored as a possible factor in the determination of star properties, and little difference between aliphatic and aromatic cores was observed. This study supported the utility of dendritic polyol cores in polymer star synthesis, suggesting that star size, and thus bioactive loading, can be easily altered with higher dendrimer generations without affecting overall polymer properties. In addition, it provided clear lessons in catalyst choice, suggesting that robust aluminum catalysts can offer better control in macromolecular synthesis. We will continue to develop our interest in dendritic cores as frameworks for building aliphatic stars in the future, further investigating the relationship between chemical composition and star arms on polymer properties.

# Experimental

#### Materials and general methods

HPLC-grade THF was purchased from Caledon Laboratory Chemicals and deuterated solvents were purchased from Cambridge Isotopes. Tin(II) ethylhexanoate was purchased from Sigma–Aldrich and distilled under reduced pressure prior to use. Purasorb *rac*-lactide and L-lactide purchased form PURAC Biomaterials were purified by sublimation under vacuum three times prior to use. Dichloromethane was refluxed over calcium hydride and distilled onto molecular sieves. MeOH was also dried over calcium oxide and distilled over molecular sieves. Pyridine was dried over potassium hydroxide and was stored over molecular sieves. Unless otherwise noted, non-aqueous reactions were carried out under a nitrogen atmosphere. Compounds were visualized/ located by spraying the TLC plate with a solution of 2% ceric ammonium sulfate in  $0.5 \text{ mol/L H}_2\text{SO}_4$ , followed by heating on a hot plate until color developed.

<sup>1</sup>H NMR spectra of polymeric materials were collected using a 300 MHz Bruker Avance Spectrometer. <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR spectra of core molecules were recorded on a 500 MHz NMR spectrometer operating at 500.13 and 125.7 MHz respectively using the solvent resonances as secondary standards. Coupling constant (J) values are reported in Hz. High-resolution mass spectra were recorded using electrospray ionization with a time of flight mass analyzer. Melting points are uncorrected. All syntheses involving air-sensitive compounds were performed under an inert nitrogen atmosphere in an MBraun LABmaster sp glovebox. GPC analyses were performed with a Polymer Laboratories PL-GPC 50 plus system equipped with 2 × 7.8 mm DVB Jordi gel columns and a Wyatt MiniDawn light scattering detector. HPLC-grade THF was used to dissolve and elute the samples (flow rate: 1 mL min<sup>-1</sup>) at 50 °C. Thermogravimetric analyses were either performed on a TA Instruments TGA Q500 under nitrogen with balance and purge flow rates of 40 mL min<sup>-1</sup> and 60 mL min<sup>-1</sup> and a heating rate of 10 °C min-1 or on a Thermo-Microbalance TG 209 F3 Tarsus instrument under an argon atmosphere, using a flow rate of 60 mL min<sup>-1</sup> and a heating rate of 10 °C min<sup>-1</sup>. Differential scanning calorimetry was carried out using a TA Instruments DSC Q100 with hermetically sealed aluminum pans. A flow rate of 50 mL min<sup>-1</sup> was used and a heat (200 °C)/cool (-50 °C)/heat (200 °C) cycle was employed with heating and cooling rates of 5 °C min-1.

#### General procedure for formation of dendritic esters

The acetonide-protected anhydride of 2,2-bis(hydroxymethyl)propanoic acid, the hydroxyl-terminated dendrimer or core, and N,N-dimethyl-4-aminopyridine (DMAP) were dissolved in a 3:1 mixture of  $CH_2Cl_2$ /pyridine (v/v) under a nitrogen atmosphere in an oven-dried round-bottomed flask equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 4-6 h, and then diluted with water (3 mL) in pyridine (3 mL). Stirring was continued overnight to quench the excess anhydride. The mixture was diluted further using CH<sub>2</sub>Cl<sub>2</sub> (60 mL), then washed with NaHCO<sub>3</sub> (1 mol/L,  $3 \times 15$  mL), 10% Na<sub>2</sub>CO<sub>3</sub> ( $3 \times 15$  mL), brine (2  $\times$  15 mL), water (15 mL), dried (MgSO<sub>4</sub>), filtered, and concentrated. The crude product was then purified using precipitation out of hexanes/EtOAc or column chromatography to give the desired product (>94% yield). The NaHCO<sub>3</sub> layers were combined, acidified (pH = 5-6), and the precipitated carboxylic acid byproduct was recovered.

# General procedure for the removal of isopropylidene acetals

An acetonide-protected dendrimer was dissolved in  $CH_2Cl_2$  (5 mL) and the mixture was diluted using methanol (15 mL). A teaspoon of DOWEX, H<sup>+</sup> resin was added and the mixture was stirred for 3 h at room temperature until TLC confirmed complete removal of the protective groups. The resin was filtered off and carefully washed with methanol. Methanol was removed under vacuum to give hydroxyl-terminated products as colorless crystal-line products (>96% yield).

# 1,4-Bis-(2-((2,2,5-trimethyl-1,3-dioxan-5-yl) methanoyloxy)ethoxy)benzene (3)

1,4-Bis-(2-hydroxyethoxy)benzene **1** (0.750 g, 3.78 mmol), dry pyridine (11 mL),  $CH_2CI_2$  (33 mL), DMAP (0.203 g, 1.66 mmol) and 2,2,5-trimethyl-1,3-dioxane-5-carboxylic anhydride **2** (3.00 g, 9.08 mmol) were stirred at room temperature for 4 h under nitrogen. After work up and purification as described above, the product was obtained as a colourless crystalline solid (1.85 g, 96% yield):  $R_F$  0.50 (hexanes/EtOAc; 1:1); mp 75–77 °C; <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>)  $\delta$  1.17 (s, 6H, CH<sub>3</sub>), 1.35 (s, 6H, CH<sub>3ax</sub>), 1.40 (s, 6H, CH<sub>3eq</sub>), 3.62 (d, *J* = 12 Hz, 4H, H-4<sub>ax</sub>, H-6<sub>ax</sub>), 4.12 (t, *J* = 5 Hz, 4H, PhOCH<sub>2</sub>), 4.17 (d, *J* = 11.5 Hz, 4H, H-4<sub>eq</sub>, H-6<sub>eq</sub>), 4.44 (t, *J* = 4.5 Hz, 4H, CH<sub>2</sub>OC=O), 6.82

(s, 4H, PhH); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CDCl<sub>3</sub>)  $\delta$  174.2 (2 C=O), 153.1, 115.9 (PhC), 98.1 (C-2), 66.7 (PhOCH<sub>2</sub>), 66.0 (C-4, C-6), 63.2 (CH<sub>2</sub>OC=O), 41.9 (C<sub>quat</sub>), 24.6 (CH<sub>3eq</sub>), 22.8 (CH<sub>3ax</sub>), 18.7 (CH<sub>3</sub>). HR EI MS: *m*/*z* calculated for C<sub>26</sub>H<sub>38</sub>NaO<sub>10</sub>: 533.2357. Found 533.2371.

**1,4-Bis-(2-(2,2-bis(hydroxymethyl)propanoyloxy)ethoxy)benzene (4)** Compound **3** (1.50 g, 2.94 mmol) was deprotected as described above in the general procedure for the removal of isopropylidene acetals to give the title compound **4** as colourless crystals (1.24 g, 98% yield). <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR data match previously reported data.<sup>16</sup>

# 1,4-Bis-(2-(2,2-bis((2,2,5-trimethyl-1,3-dioxan-5-yl) methanoyloxymethyl)propanoyloxy)-ethoxy)benzene (5)

Compound 4 (0.650 g, 1.51 mmol), dry pyridine (10 mL), CH<sub>2</sub>Cl<sub>2</sub> (30 mL), DMAP (0.162 g, 1.33 mmol) and anhydride **2** (2.40 g, 7.26 mmol) were stirred at room temperature for 5 h under nitrogen. After work up and purification as described above, the product was obtained as a colourless crystalline solid (1.50 g, 94% yield); mp 110–112 °C; <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>)  $\delta$  1.12 (s, 12H, 4 CH<sub>3</sub>), 1.30 (s, 6H, 2 CH<sub>3</sub>), 1.34 (s, 12H, 4 CH<sub>3ax</sub>), 1.40 (s, 12H, 4 CH<sub>3eq</sub>), 3.60 (d, *J* = 13 Hz, 8H, H-4<sub>ax</sub>, H-6<sub>ax</sub>), 4.11–4.15 [(m, 8H (H-4<sub>eq</sub> + H-6<sub>eq</sub>) & 4H (PhOCH<sub>2</sub>)], 4.33 (s, 8H, 4 CH<sub>2</sub>), 4.43 (t, *J* = 5 Hz, 4H, CH<sub>2</sub>OC=O), 6.81 (s, 4H, PhH); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CDCl<sub>3</sub>)  $\delta$  173.7 (4 C=O), 172.7 (2 C=O), 153.1, 115.9 (PhC), 98.2 (C-2), 66.4 (PhOCH<sub>2</sub>), 66.10, 66.06 (C-4, C-6), 65.4 (4 CH<sub>2</sub>), 63.8 (OCH<sub>2</sub>CH<sub>2</sub>OC=O), 46.9 (2 C<sub>quat</sub>), 42.2 (4 C<sub>quat</sub>), 25.3 (4 CH<sub>3eq</sub>). 22.2 (4 CH<sub>3ax</sub>), 18.6 (4 CH<sub>3</sub>), 17.8 (2 CH<sub>3</sub>). HR EI MS: *m/z* calculated for C<sub>52</sub>H<sub>78</sub>NaO<sub>22</sub>: 1077.4877. Found 1077.4873.

## 1,4-Bis-(2-(2,2-bis(2,2-bis(hydroxymethyl)propanoyloxymethyl) propanoyloxy)ethoxy)benzene (6)

Compound 5 (1.49 g, 1.41 mmol) was deprotected as described above in the general procedure for the removal of isopropylidene acetals to give the product as colourless crystals (1.24 g, 98% yield). <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR data matched previously reported data.<sup>16</sup>

### 1,8-Bis-((2,2,5-trimethyl-1,3-dioxan-5-yl)propanoyloxy)octane (8)

1,8-Octanediol 7 (1.00 g, 6.84 mmol), dry pyridine (12 mL), CH<sub>2</sub>Cl<sub>2</sub> (36 mL), DMAP (0.360 g, 2.95 mmol) and anhydride **2** (5.50 g, 16.6 mmol) were stirred at room temperature for 4 h under nitrogen. After work up and purification as described above, the product was obtained as colourless oil (2.98 g, 95% yield):  $R_F 0.49$ (hexanes/EtOAc; 2: 1); <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>)  $\delta$  0.92 (s, 6H, 2 CH<sub>3</sub>), 1.10–1.15 (m, 20H, 2 CH<sub>3ax</sub>, 2 CH<sub>3eq</sub>, 8 octyl H), 1.38 (quint, *J* = 6.5 Hz, 4H, octyl OCH<sub>2</sub>CH<sub>2</sub>), 3.36 (d, *J* = 11.5 Hz, 4H, H-4<sub>ax</sub>, H-6<sub>ax</sub>), 3.87 (t, *J* = 6.5 Hz, 4H, octyl OCH<sub>2</sub>), 3.90 (d, *J* = 11.5 Hz, 4H, H-4<sub>eq</sub>, H-6<sub>eq</sub>); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CDCl<sub>3</sub>)  $\delta$  173.5 (2 C=0), 97.3 (C-2), 65.4 (C-4, C-6), 64.1 (octyl OCH<sub>2</sub>CH<sub>2</sub>), 41.2 (C<sub>quar</sub>), 28.6 (octyl OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 28.1 (octyl OCH<sub>2</sub>CH<sub>2</sub>), 25.2 (CH<sub>3eq</sub>), 23.9 (CH<sub>3ax</sub>), 22.5 (octyl OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 18.2 (2 CH<sub>3</sub>). HR EI MS: *m/z* calculated for C<sub>24</sub>H<sub>42</sub>NaO<sub>8</sub>: 481.2772. Found 481.2768.

#### 1,8-Bis-(2,2-bis(hydroxymethyl)propanoyloxy)octane (9)

Compound **8** (2. 00 g, 4.36 mmol) was deprotected as described above in the general procedure for the removal of isopropylidene acetals to give the title compound (**9**) as a colourless crystalline solid (1.58 g, 96% yield):  $R_F$  0.30 (EtOAc); mp 65–67 °C; <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>)  $\delta$  1.15 (s, 6H, 2 CH<sub>3</sub>), 1.36–1.43 (m, 8H, 8 octyl H), 1.64 (quint, *J* = 6.5 Hz, octyl OCH<sub>2</sub>CH<sub>2</sub>), 3.65 (AB q,  $\Delta \nu_{AB}$  = 24.5 Hz,  $J_{AB}$  = 11 Hz, 8H, CH<sub>2</sub>OH), 4.10 (t, *J* = 6.5 Hz, 4H, octyl OCH<sub>2</sub>); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CDCl<sub>3</sub>)  $\delta$  176.5 (2 C=O), 65.7 (CH<sub>2</sub>OH), 65.6 (octyl OCH<sub>2</sub>), 51.3 (C<sub>quar</sub>), 30.0 (octyl OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 29.4 (octyl OCH<sub>2</sub>CH<sub>2</sub>), 26.8 (octyl OCH<sub>2</sub>CH<sub>2</sub>), 17.3 (CH<sub>3</sub>). HR EI MS: *m/z* calculated for C<sub>18</sub>H<sub>34</sub>NaO<sub>8</sub>: 401.2146. Found 401.2161.

### **Polymerization experiments**

Polymerization reactions were performed at 120 °C in sealed ampoules under an inert atmosphere. A molar ratio of catalyst/ alcohol functionality of 1:1 and a variety of monomer/initiator ratios were employed to obtain polymers of desirable molecular weights. Sn(Oct)<sub>2</sub> was used as a catalyst with rac-lactide and L-lactide monomers and complex polyol initiators. The reaction proceeded for 30 min and was followed by quenching with 10:1 (v/v) CHCl<sub>2</sub>/MeOH for 30 min. The polymer was precipitated by dropwise addition to cold methanol followed by filtration and drying in vacuo before performing analysis.

For example, rac-lactide (1.02 g, 7.09 mmol), 1 (0.0079 g, 0.018 mmol), Sn(Oct)<sub>2</sub> (0.0291 g, 0.0781 mmol) and a magnetic stir bar were added to an ampoule in the glovebox. The sealed ampoule was removed from the glovebox and placed in a preheated oil bath at 120 °C for 30 min. The ampoule was removed from the oil bath, cooled to room temperature, opened to the atmosphere, and the contents were dissolved in an 11 mL solution of  $10:1 (v/v) CH_2 Cl_2/v$ MeOH. The solution was stirred for 30 min and then added dropwise to 100 mL of stirring, cold methanol. The white polymer precipitate was collected by filtration and dried in vacuo for a minimum of 12 h. Monomer conversion was determined to be 95% by <sup>1</sup>H NMR spectroscopy of the crude mixture in chloroform.

## Supplementary data

<sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} spectra for novel compounds, detailed polymerization data and GPC traces. Supplementary data are available with the article through the journal Web site at http:// nrcresearchpress.com/doi/suppl/10.1139/cjc-2012-0471.

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