

# Catalyst-controlled polycondensation of glycerol with diacyl chlorides: linear polyesters from a trifunctional monomer

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## Electronic Supplementary Information

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### General

Reactions were carried out in oven-dried glassware without effort to exclude air, unless otherwise indicated. Stainless steel syringes were used to transfer air- and moisture-sensitive liquids. Flash chromatography was carried out using neutral silica gel from Silicycle. Analytical TLC was carried out using aluminum-backed silica gel 60 F<sub>254</sub> plates (EMD).

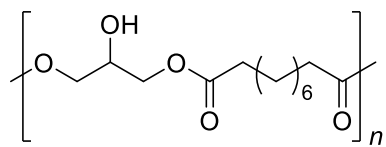
**Materials.** HPLC grade tetrahydrofuran (THF) and dichloromethane (DCM) were dried and purified using a solvent purification system equipped with columns of activated alumina, under nitrogen (Innovative Technology, Inc.). Dodecanedioyl chloride was synthesized as described below. All other reagents and solvents were purchased from Sigma Aldrich and used without further purification.

**Instrumentation.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded using an Agilent DD2-500 (500 MHz) spectrometer with XSENS cryogenic probe. The spectra were processed using MestreNova. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane with the solvent resonance resulting from incomplete deuteration as the internal standard. For  $^1\text{H}$  NMR:  $\text{CDCl}_3$  7.26 ppm;  $\text{DMSO-}d_6$  2.50 ppm, p; for  $^{13}\text{C}$  NMR:  $^{13}\text{CDCl}_3$  77.0 ppm, t;  $\text{DMSO-}d_6$  39.52 ppm, hept. Spectral features are tabulated in the following order: chemical shift ( $\delta$ , ppm); multiplicity (s-singlet, d-doublet, t-triplet, q-quartet, m-complex multiplet, app-apparent); coupling constants ( $J$ ); number of protons. For quantitative  $^{13}\text{C}$  NMR, samples were dissolved in  $\text{DMSO-}d_6$  containing 65 mM of relaxation agent  $\text{Cr}(\text{acac})_3$  with a concentration of 250 mg/mL. Acquisition parameters were set to a 10 second relaxation delay to allow for full relaxation of the  $^{13}\text{C}$  nuclei. Infrared (IR) spectra were obtained on a Perkin-Elmer Spectrum 100 instrument equipped with a single-bounce diamond / ZnSe ATR accessory either in the solid state or as neat liquids, as indicated. The spectra were processed using Spectrum Express. Spectral features are tabulated by wavenumber ( $\text{cm}^{-1}$ ). GPC was conducted at 85 °C using a 1.0 g/L solution of lithium chloride in *N*-methylpyrrolidone (NMP) as eluent, at a flow rate of 1.0 mL/min through two Agilent PLgel 5 $\mu\text{m}$  MIXED-C columns with refractive index detection. Poly(methyl methacrylate) (PMMA) standards were used for calibration.

## Polymer Synthesis

**General Procedure for Polymer Synthesis GP1.** Glycerol (1 equivalent) and **1c** (1–5 mol %) were weighed into a 100 mL round bottom flask equipped with a stir bar. THF (0.3 M) and *N,N*-diisopropylethylamine (3 equivalents, or 2.05 equivalents for PGA) were added *via* syringe and the resulting solution was stirred at 0 °C. Diacyl chloride (1 equivalent) was added dropwise (for isophthaloyl chloride, a solution in THF was made so that the final concentration of the reaction was 0.3 M; terephthaloyl chloride was added neat and allowed to dissolve slowly). A white precipitate appeared. The reaction was heated to 70 °C for 5 hours, cooled, and stopped by adding 5 mL methanol. The solution was concentrated by rotary evaporation, dissolved in a minimum amount of appropriate solvent, and precipitated by dropwise addition into a poor solvent or solvent mixture (see below for details).

**Poly(glycerol sebacate) (PGS).** Polymer was prepared from 1.128 g (12.3 mmol) glycerol and 2.642 mL (12.3 mmol) sebacoyl chloride using 1 mol % **1c** according to GP1. The resulting oil was dissolved in a minimum amount of THF and precipitated from 1 L of a 95:5 (v/v) mixture of methanol and water at 0 °C. Filtration followed by washing with methanol and drying under vacuum afforded the product as a beige powder (93%,  $M_n = 2.44$



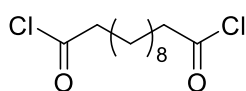
$\times 10^4$ ;  $\bar{D} = 1.40$ ). Ratio of 1,2 to 1,3 linkages was 7:93 as calculated from the ratio of  $^{13}\text{C}$  signals at 71.9 and 66.1 ppm, respectively.

*Signals corresponding to 1,3-linkages (major):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  5.24 (d,  $J = 5.2$  Hz, 1H), 4.00–3.93 (m, 4H), 3.89–3.80 (m, 1H), 2.28 (t,  $J = 7.4$  Hz, 4H), 1.72–1.40 (m, 4H), 1.31–1.13 (m, 8H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.7, 66.1, 64.8, 33.4, 28.6, 28.4, 24.4.

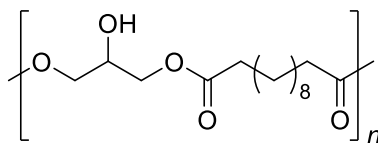
*Signals corresponding to 1,2-linkages (minor):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  5.00–4.88 (m, 2H), 4.25 (dd,  $J = 11.9, 3.3$  Hz, 1H), 4.09–4.04 (m, 1H), 3.48 (t,  $J = 5.8$  Hz, 2H), 2.28 (t,  $J = 7.4$  Hz, 4H), 1.72–1.40 (m, 4H), 1.31–1.13 (m, 8H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.8, 71.9, 62.3, 59.6, 33.4, 28.6, 28.4, 24.4.

IR (neat) 3464, 2924, 2851, 1732, 1716, 1217, 1167, 1136  $\text{cm}^{-1}$ .

**Dodecanedioyl chloride.** Dodecanedioic acid (2.303 g, 10 mmol) was added to a 100 mL round bottom flask equipped with a stir bar and dissolved in 20 mL anhydrous  $\text{CHCl}_3$ . One drop of *N,N*-dimethylformamide was then added by syringe at room temperature, followed by a dropwise addition of 1.8 mL (21 mmol) oxalyl chloride. The reaction was stirred at room temperature for 15 hours, then was heated to 60  $^\circ\text{C}$  for 1 hour, after which the solvent and excess oxalyl chloride were removed by rotary evaporation. The title compound was dried under vacuum and isolated as a clear oil (98%) and used without further purification. Spectral data matched those reported in the literature.<sup>1</sup>



**Poly(glycerol dodecanoate) (PGD).** Polymer was prepared from 594.8 mg (6.47 mmol) glycerol and 1.666 mL (6.47 mmol) dodecanedioyl chloride using 1 mol % **1c** according to GP1. The resulting oil was dissolved in a minimum amount of THF and precipitated from 800 mL of a 95:5 mixture of methanol and water at 0  $^\circ\text{C}$ . Filtration followed by washing with methanol and drying under vacuum afforded the product as a beige powder (87%,  $M_n = 1.96 \times 10^4$ ;  $\bar{D} = 1.10$ ). Ratio of 1,2 to 1,3 linkages was 5:95 as calculated from the ratio of  $^{13}\text{C}$  signals at 71.9 and 66.1 ppm, respectively.



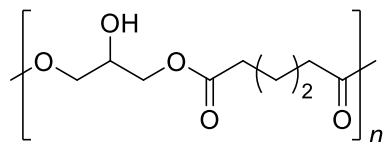
*Signals corresponding to 1,3-linkages (major):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  5.24 (m, 1H), 4.01–3.92 (m, 4H), 3.89–3.78 (m, 1H), 2.28 (t,  $J = 7.4$  Hz, 4H), 1.57–1.43 (m, 4H), 1.28–1.17 (m, 12H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.7, 66.1, 64.7, 33.4, 28.9, 28.7, 28.5, 24.4.

*Signals corresponding to 1,2-linkages (minor):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  4.97–4.87 (m, 1H), 4.79–4.61 (m, 1H), 4.23 (dd,  $J = 11.9, 3.2$  Hz, 1H), 4.06–4.01 (m, 1H), 3.48–3.44 (m, 2H), 2.26 (t,  $J = 7.4$  Hz, 4H), 1.56–1.39 (m, 4H), 1.26–0.99 (m, 12H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.7, 71.9, 62.3, 59.5, 33.4, 28.9, 28.7, 28.4, 24.4.

<sup>1</sup> K. Yamaguchi, Y. Tsuda, T. Shimakage and A. Kusumi, *Bull. Chem. Soc. Jpn*, 1998, **71**, 1923–1929.

IR (neat) 3425, 2915, 2851, 1731, 1209, 1169, 1105  $\text{cm}^{-1}$ .

**Poly(glycerol adipate) (PGA).** Polymer was prepared from 638.6 mg (6.94 mmol) glycerol and 1030  $\mu\text{L}$  (6.94 mmol) adipoyl chloride using 5 mol % **1c** according to GP1. The resulting oil was dissolved in a minimum amount of THF and precipitated from 900 mL diethyl ether. The resulting amber oil was decanted, redissolved in THF, and precipitated from 800 mL water. Filtration followed by washing with water and toluene and drying under vacuum afforded the product as an amber oil (94%,  $M_n = 3.00 \times 10^4$ ;  $\bar{D} = 1.42$ ). Ratio of 1,2 to 1,3 linkages was 3:97 as calculated from the ratio of  $^{13}\text{C}$  signals at 72.0 and 66.3 ppm, respectively.

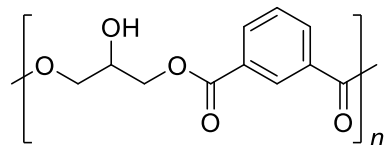


*Signals corresponding to 1,3-linkages (major):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  5.25 (d,  $J = 5.3$  Hz, 1H), 4.03–3.93 (m, 4H), 3.90–3.82 (m, 1H), 2.35–2.27 (m, 4H), 1.66–1.43 (m, 4H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.7, 66.2, 64.9, 33.1, 23.8.

*Signals corresponding to 1,2-linkages (minor):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  5.05–4.89 (m, 2H), 4.24 (dd,  $J = 11.9, 3.5$  Hz, 1H), 4.08 (dd,  $J = 5.6, 11.9$  Hz, 1H), 3.49 (t,  $J = 5.6$  Hz, 2H), 2.36–2.16 (m, 4H), 1.64–1.44 (m, 4H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.7, 72.0, 62.3, 59.5, 33.1, 23.8.

IR (neat) 3458, 2954, 1727, 1134, 1069  $\text{cm}^{-1}$ .

**Poly(glycerol isophthalate) (PGI).** Polymer was prepared from 582.1 mg (6.33 mmol) glycerol and 1.2844 g (6.33 mmol) isophthaloyl chloride using 2 mol % **1c** according to GP1. The resulting oil was dissolved in a minimum amount of THF and precipitated from 1 L isopropanol at 0  $^\circ\text{C}$ . Filtration followed by washing with isopropanol and drying under vacuum afforded the product as a brittle white solid (90%,  $M_n = 1.00 \times 10^4$ ;  $\bar{D} = 1.55$ ). Ratio of 1,2 to 1,3 linkages was 15:85 as calculated from the ratio of  $^{13}\text{C}$  signals at 73.4 and 66.2 ppm, respectively.

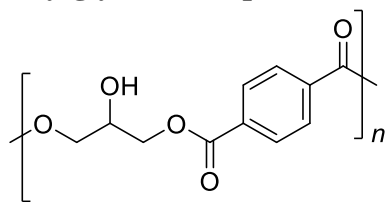


*Signals corresponding to 1,3-linkages (major):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.66–8.33 (m, 1H), 8.29–7.97 (m, 2H), 7.78–7.46 (m, 1H), 4.60–4.32 (m, 4H), 4.28–4.11 (m, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  164.9, 133.8, 130.2, 129.9, 129.4, 66.3, 66.2.

*Signals corresponding to 1,2-linkages (minor):*  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  164.9, 133.8, 130.2, 129.9, 129.4, 73.5, 63.7, 59.6.

IR (neat) 3449, 2960, 1713, 1608, 1223, 1074, 725  $\text{cm}^{-1}$ .

**Poly(glycerol terephthalate) (PGT).** Polymer was prepared from 849.0 mg (9.22 mmol)



glycerol and 1.8713 g terephthaloyl chloride (9.22 mmol) using 2 mol % **1c** according to GP1. The resulting oil was dissolved in a minimum amount of DCM and methanol and precipitated from 1 L isopropanol. Filtration followed by washing with isopropanol and drying under vacuum afforded the product as a white solid (92%,  $M_n = 1.00 \times 10^4$ ;  $D = 1.44$ ). Ratio of 1,2 to 1,3

linkages was 13:87 as calculated from the adjusted ratio of  $^{13}\text{C}$  signals at 73.4 and 66.1 ppm, respectively.

*Signals corresponding to 1,3-linkages (major):*  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.13–7.96 (m, 4H), 4.44–4.33 (m, 4H), 4.25–4.18 (m, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.2, 133.8, 129.8, 66.1.

*Signals corresponding to 1,2-linkages (minor):*  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  165.2, 133.8, 129.8, 73.8, 63.5, 59.8.

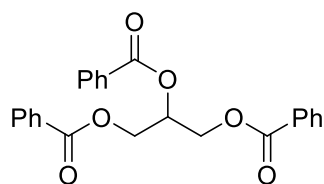
IR (neat) 3496, 2955, 1712, 1244, 1098, 873, 724  $\text{cm}^{-1}$ .

## Isolation of Unfractionated Polymers

**General Procedure.** Polymers were prepared according to GP1. After the reaction was stopped and concentrated, it was diluted with DCM and transferred to a 250 mL separatory funnel. The organic phase was washed twice with a saturated aqueous solution of ammonium chloride, dried over sodium sulfate, filtered, and concentrated by rotary evaporation. Crude samples were then dried under vacuum and analyzed by NMR and GPC as described above.

## Model Compounds

**Glycerol tribenzoate.** Glycerol (46.0 mg, 0.5 mmol) and 4-(dimethylamino)pyridine (DMAP)

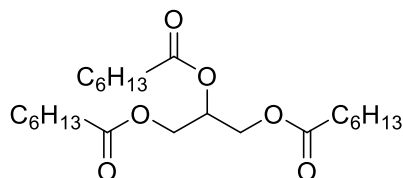


(18.0 mg, 0.15 mmol) were loaded into a scintillation vial equipped with a stir bar and dissolved in 2 mL DCM. Triethylamine (452  $\mu\text{L}$ , 3.3 mmol), was added by syringe and the solution was cooled to 0  $^\circ\text{C}$ . Benzoyl chloride (350  $\mu\text{L}$ , 3 mmol) was added dropwise and the solution was warmed to room temperature and stirred overnight.

Upon completion of the reaction, the organic layer was washed with water, dried over  $\text{MgSO}_4$ , and the product was purified by column chromatography to yield 205.4 mg of light yellow solid (99%).  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  7.99–7.91 (m, 6H), 7.68–7.61 (m, 3H), 7.51 (td,  $J =$

7.9, 1.9 Hz, 6H), 5.78 (m, 1H), 4.76 (dd,  $J = 12.0, 3.8$  Hz, 2H), 4.68 (dd,  $J = 12.0, 6.4$  Hz, 2H).  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  165.4, 133.5, 129.3, 128.8, 69.9, 63.0 ppm.

**Glycerol triheptanoate** (Model compound **2**). Glycerol (51.3 mg, 0.56 mmol) and DMAP (13.6 mg, 0.11 mmol) were loaded into a 25 mL round bottom flask equipped with a stir bar and dissolved in 3.5 mL DCM.



Triethylamine (467  $\mu\text{L}$ , 3.36 mmol), was added by syringe and the solution was cooled to 0  $^{\circ}\text{C}$ . Heptanoyl chloride (432  $\mu\text{L}$ , 2.79 mmol) was added dropwise and the solution was warmed

to room temperature and stirred overnight. Upon completion, the organic layer was washed with a solution of  $\text{NaHCO}_3$ , dried over  $\text{MgSO}_4$ , and the product was purified by column chromatography to yield 205.4 mg of light yellow solid (98%).  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  5.27–5.10 (m, 1H), 4.25 (dd,  $J = 12.0, 3.8$  Hz, 2H), 4.12 (dd,  $J = 12.0, 6.5$  Hz, 2H), 2.27 (q,  $J = 7.1$  Hz, 6H), 1.50 (m, 6H), 1.35–1.14 (m, 18H), 0.85 (t,  $J = 6.8$  Hz, 9H).  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  68.7, 61.8, 30.9, 24.3, 21.9, 13.8 ppm.

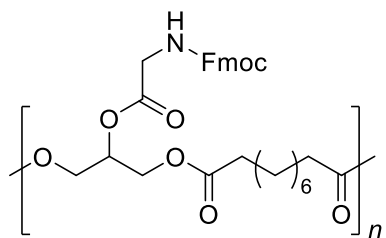
## Polymer Post-Modification

**General Procedure for Polymer Peracetylation GP2.** 0.3 mmol of polymer was placed in a 2-dram vial equipped with a stir bar and dissolved in 1 mL pyridine. 1 mL acetic anhydride was added dropwise. Then, the reaction was stirred for 20 hours. The solvent was removed by rotary evaporation, and the residue was dried under vacuum.

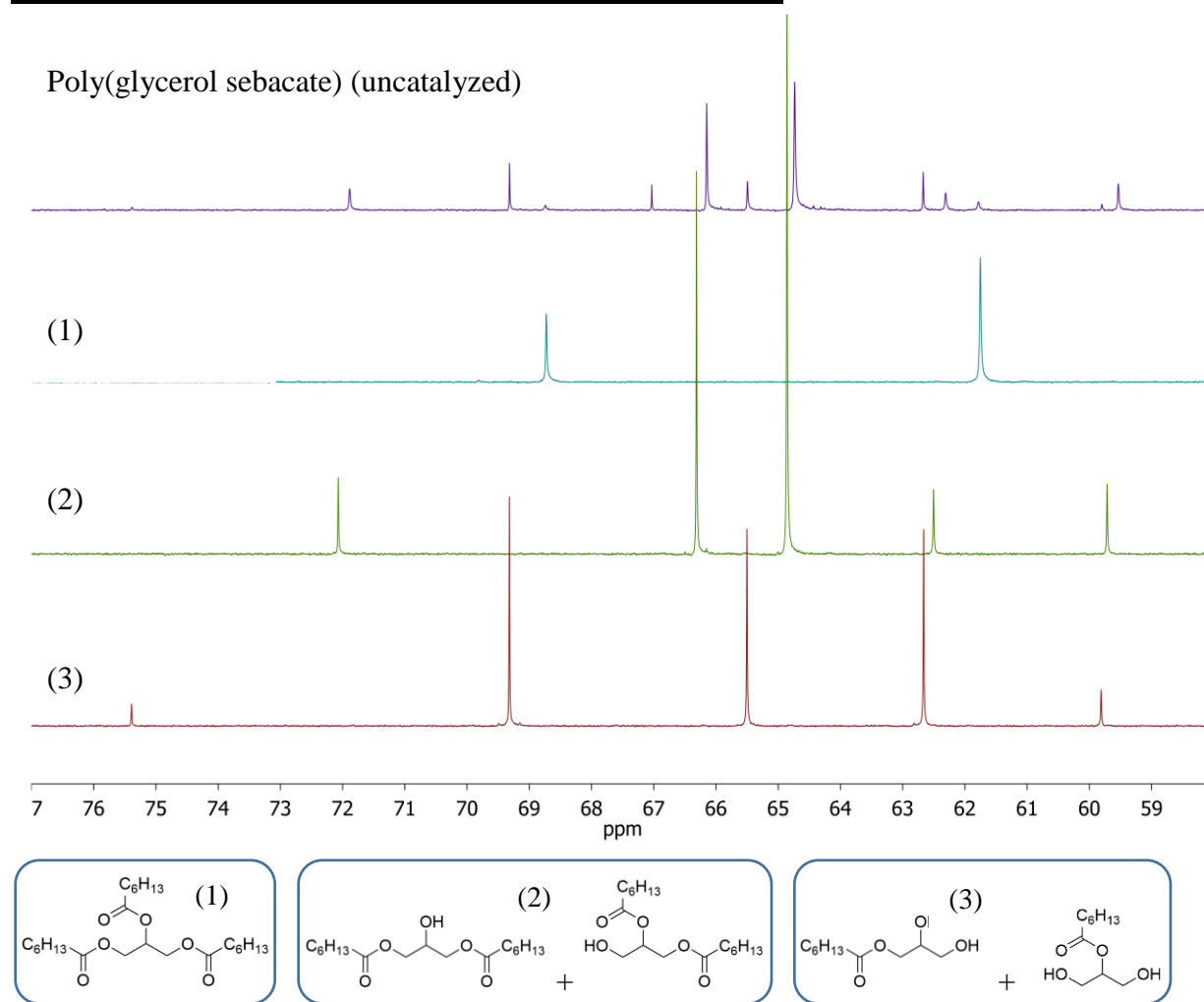
**General Procedure for Polymer Isomerization GP3.** 0.3 mmol of polymer was placed in a 2-dram vial equipped with a stir bar and dissolved in 1 mL THF. 3 equivalents of  $\text{Et}_3\text{N}$  were added *via* syringe and the solution was heated to 70  $^{\circ}\text{C}$  for 10 hours. The solvent was removed by rotary evaporation and the resulting polymer was dried under vacuum and analyzed by quantitative  $^{13}\text{C}$  NMR.

**General Procedure for Introduction of Cross-Links GP4.** 1.2 mmol of polymer was placed in a 2-dram vial equipped with a stir bar and dissolved in 2.5 mL THF. The solution was heated to 50  $^{\circ}\text{C}$  under argon and hexamethylene diisocyanate (0.5–20 mol %) was added dropwise *via* syringe. The reaction was allowed to stir overnight, stopped with 0.5 mL methanol, and the solvent was removed by rotary evaporation. The resulting cross-linked polymer was analyzed by FTIR.

**Poly(glycerol sebacate) glycinate.** PGS (50.7 mg, 0.2 mmol) and Fmoc-glycine (70.1 mg, 0.24 mmol) were placed in a 10 mL round bottom flask equipped with a stir bar and dissolved and sonicated in 3 mL DCM. The solution was cooled to 0 °C and *N,N'*-diisopropylcarbodiimide (46  $\mu$ L, 0.3 mmol) was added dropwise and one fleck of DMAP was added. The reaction was stirred for 22 hours at room temperature under argon, filtered and precipitated from methanol at 0 °C to yield an off-white, brittle solid (84%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.75 (d, *J* = 7.4 Hz, 2H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 5.43–5.18 (m, 2H), 4.39 (d, *J* = 7.1 Hz, 2H), 4.33 (dd, *J* = 12.1, 4.1 Hz, 2H), 4.22 (t, *J* = 7.1 Hz, 1H), 4.14 (dd, *J* = 12.1, 6.0 Hz, 2H), 4.00 (d, *J* = 5.7 Hz, 2H), 2.28 (t, *J* = 7.7 Hz, 4H), 1.58 (m, 4H), 1.33–1.12 (m, 8H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  173.4, 169.5, 156.4, 143.9, 141.4, 127.8, 127.2, 125.2, 120.1, 70.7, 67.4, 61.9, 47.2, 42.8, 34.0, 29.1, 24.8.



## Modelling of Isomer Linkages to Assign $^{13}\text{C}$ NMR Signals



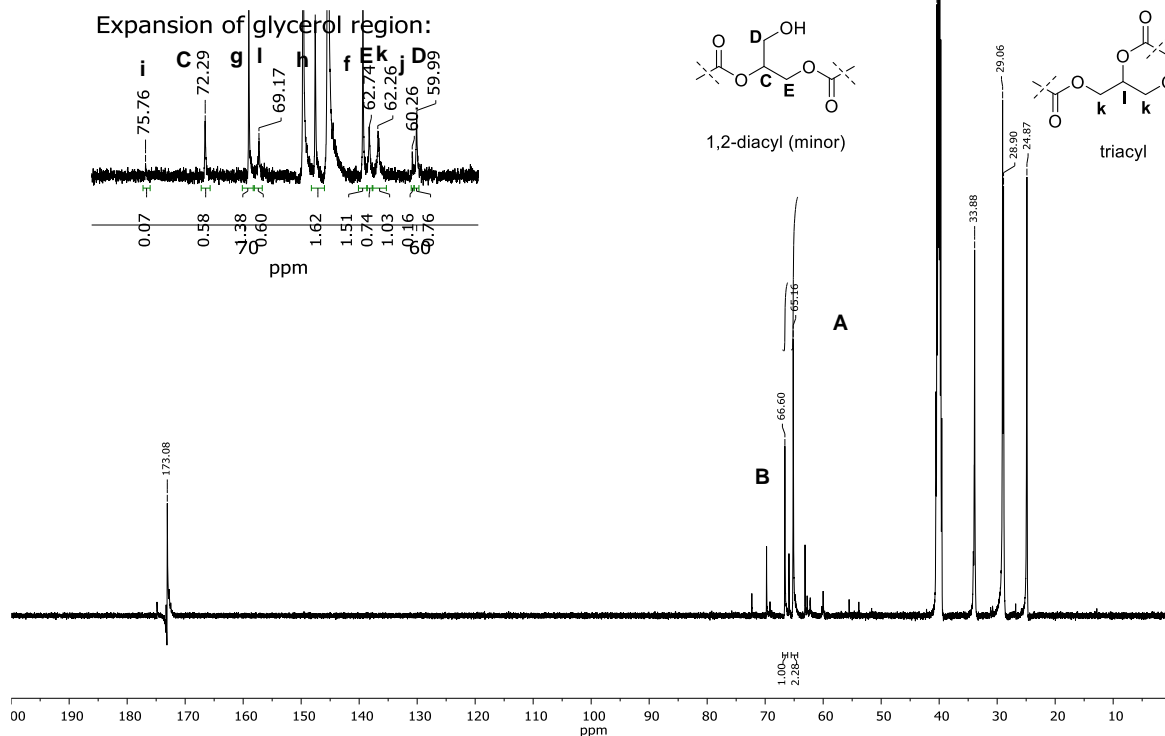
**Fig. S1**  $^{13}\text{C}$  NMR spectra of poly(glycerol sebacate), tri-, di-, and monoacyl glycerol model compounds (126 MHz,  $\text{DMSO-}d_6$ ). Model mono- and diacyl glycerides (2) and (3) were prepared as previously reported<sup>2</sup> without separating regioisomers.

<sup>2</sup> T. Fukuoka, S. Ikeda, H. Habe, S. Sato, H. Sakai, M. Abe, D. Kitamoto and K. Sakaki, *J. Oleo Sci.*, 2012, **61**, 343–348.

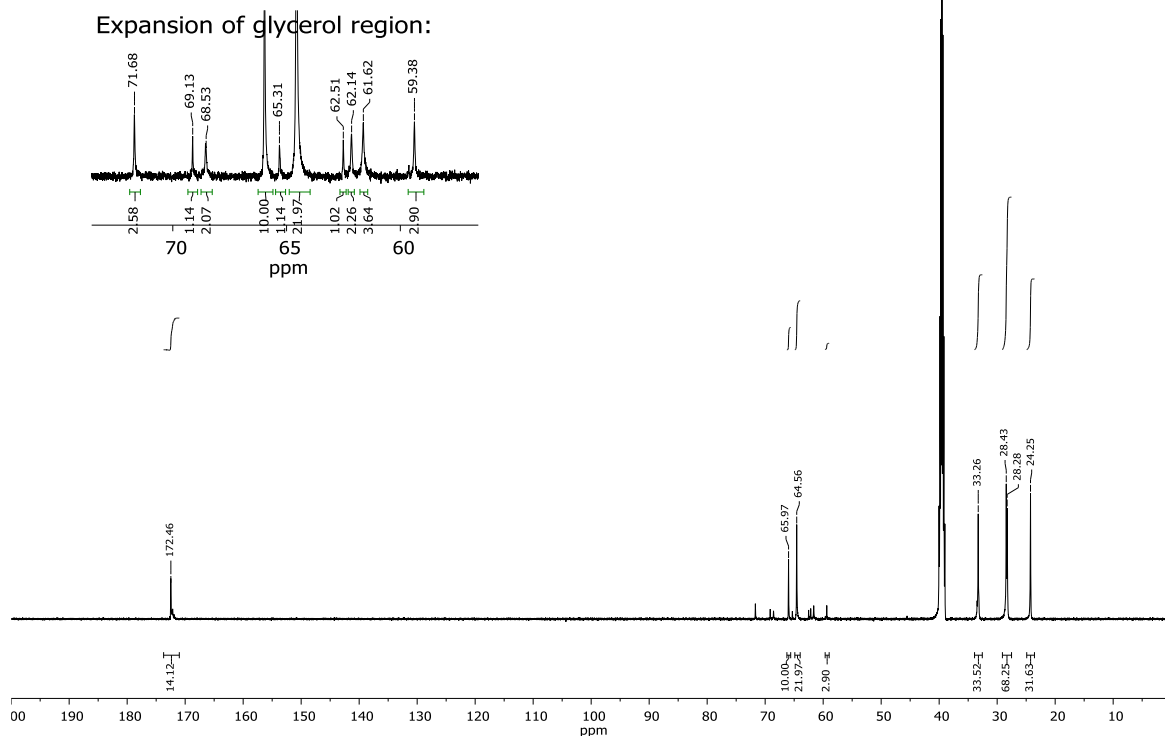


# Quantitative <sup>13</sup>C NMR Studies

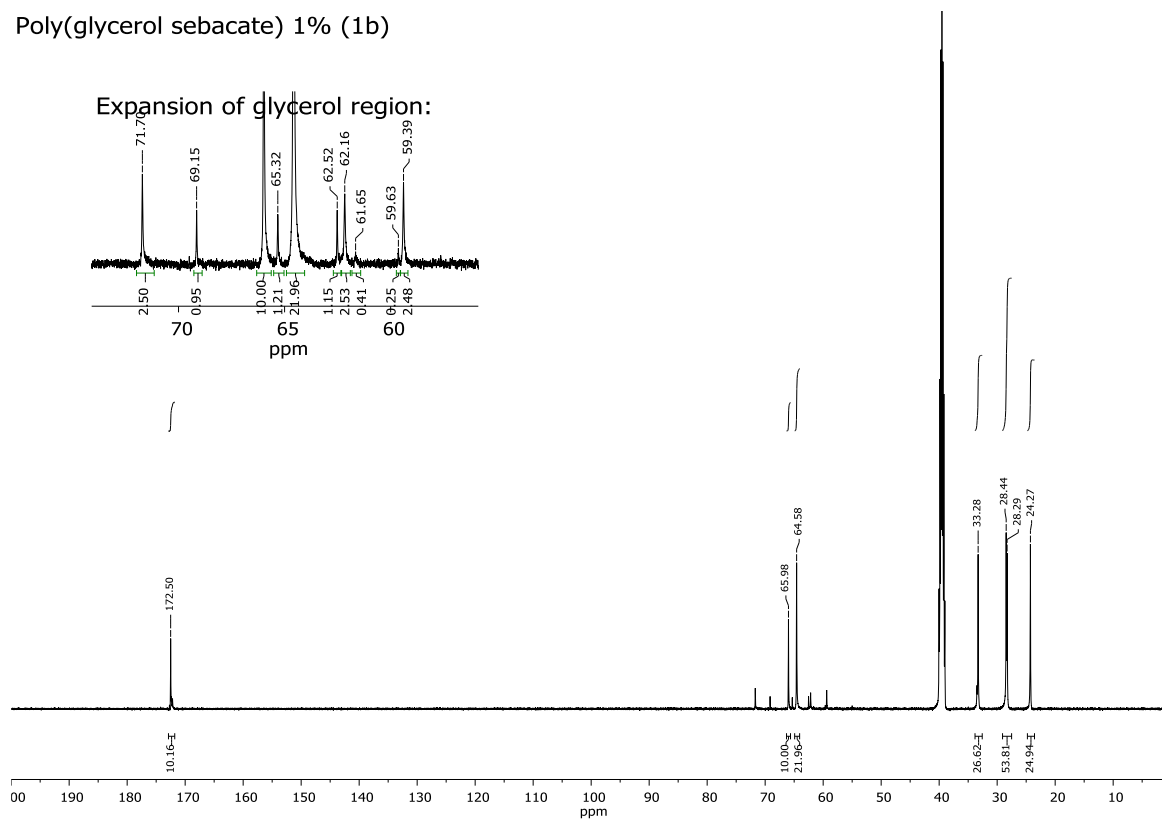
Poly(glycerol sebacate) uncatalyzed



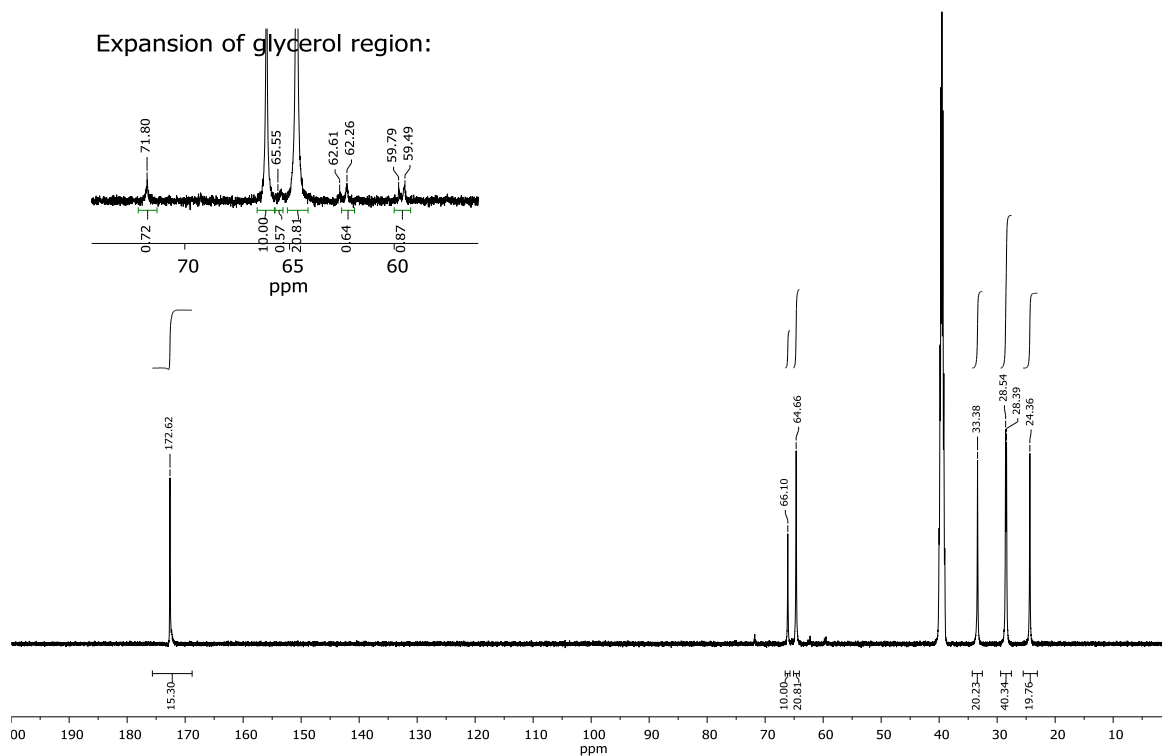
Poly(glycerol sebacate) 1% (1a)



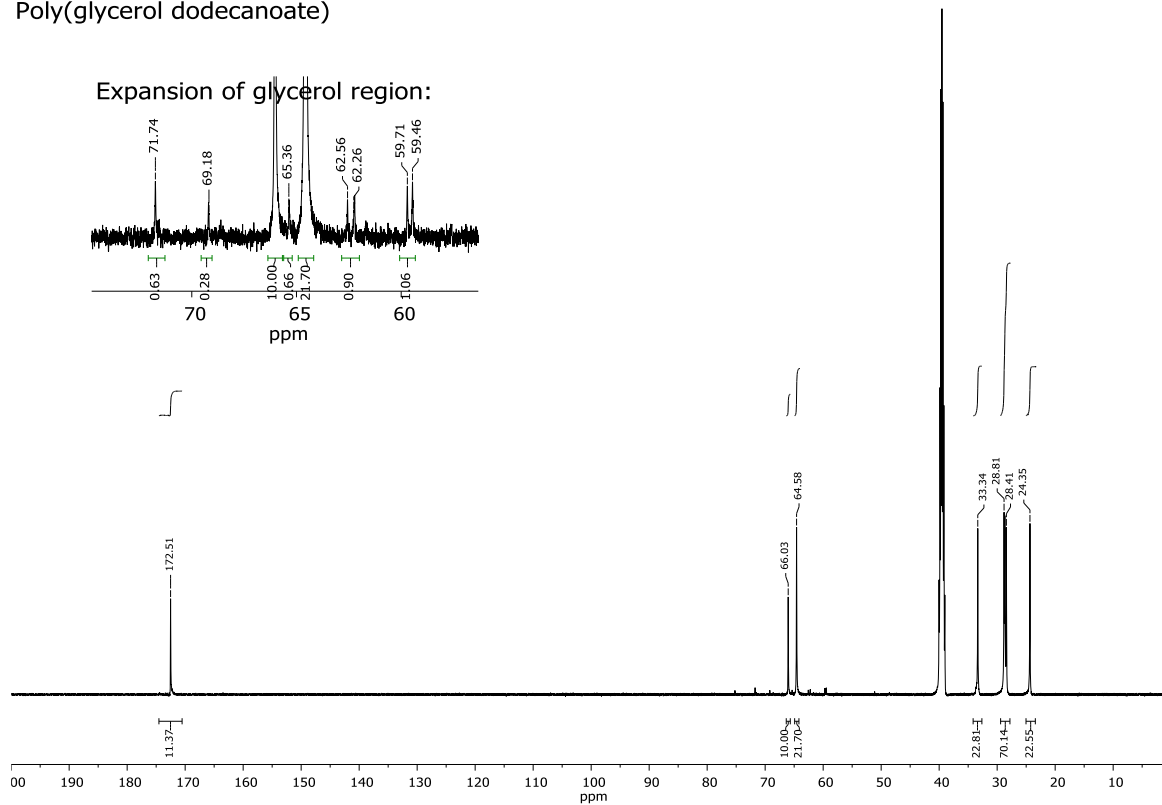
Poly(glycerol sebacate) 1% (1b)



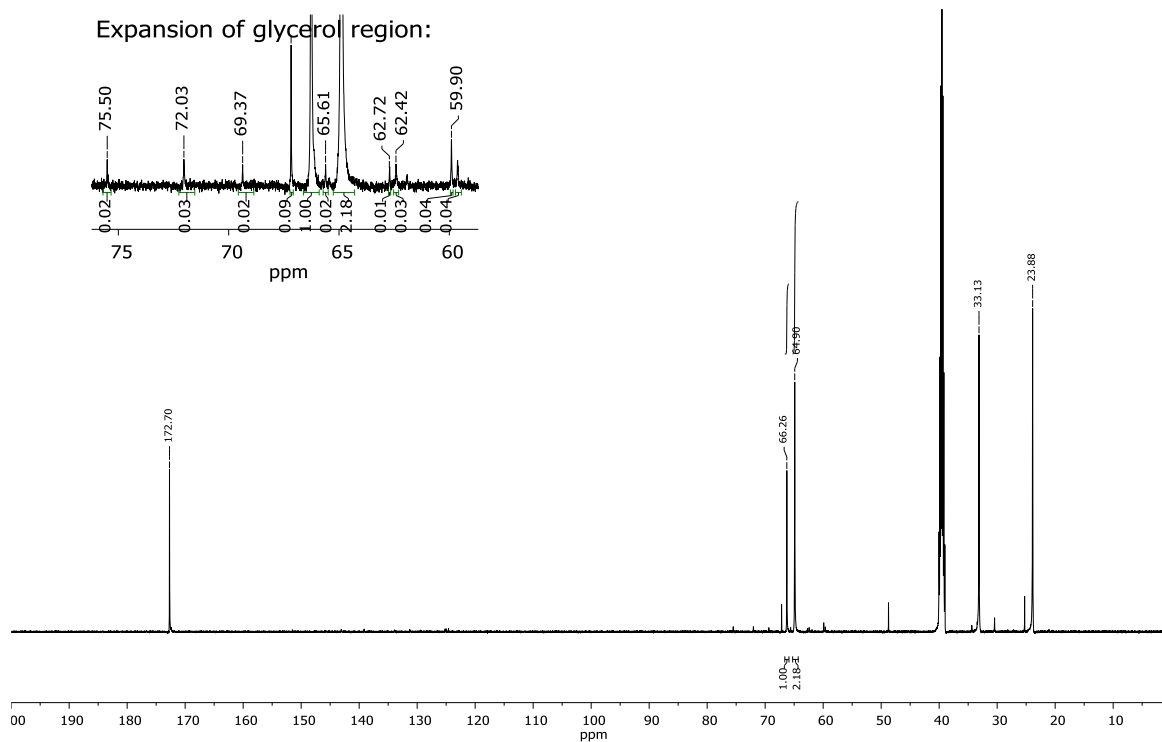
Poly(glycerol sebacate)



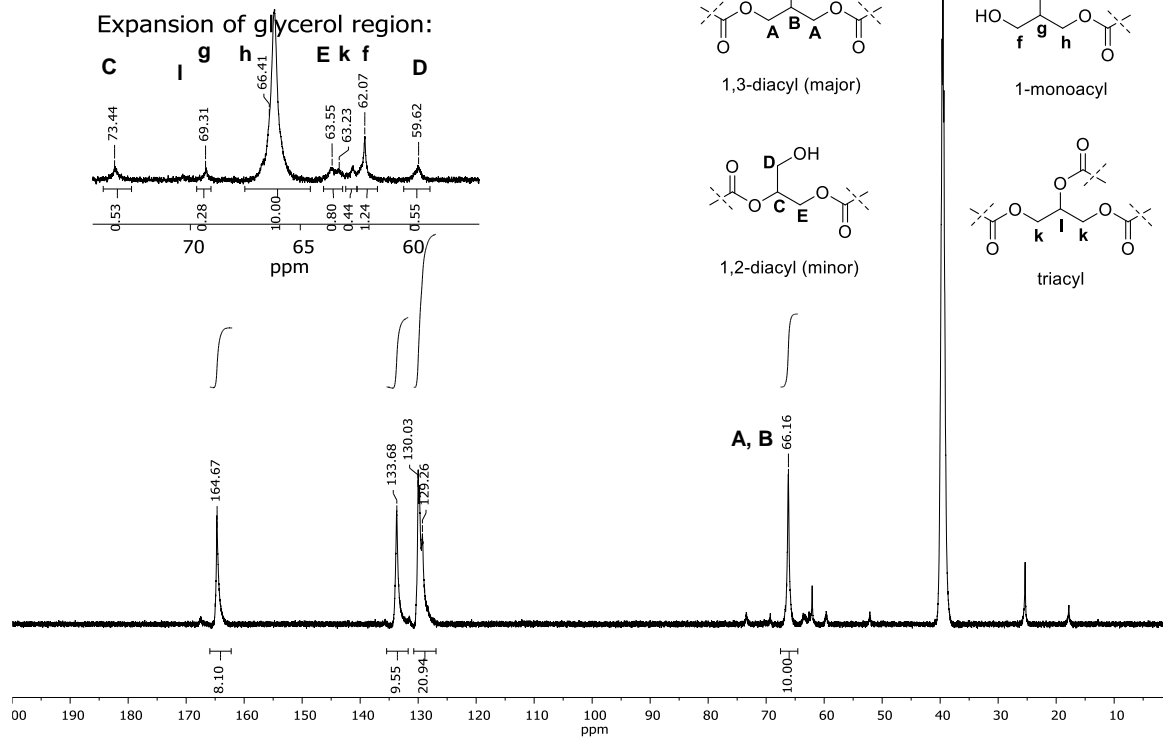
Poly(glycerol dodecanoate)



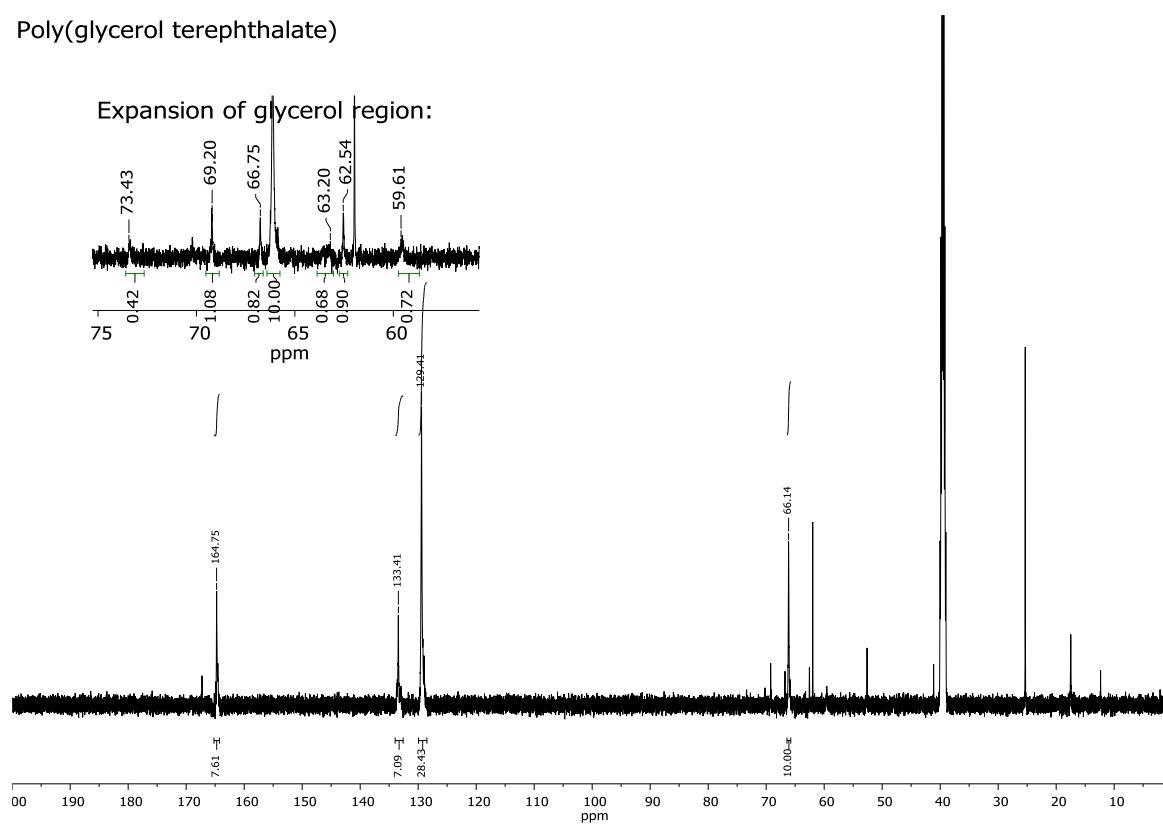
Poly(glycerol adipate)



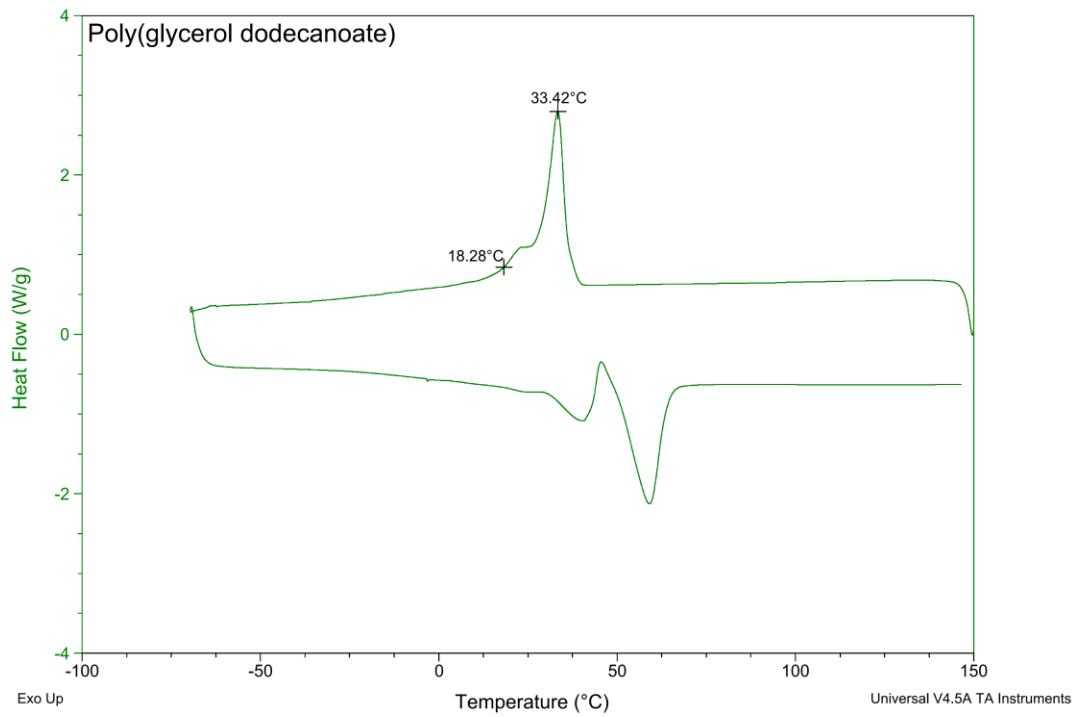
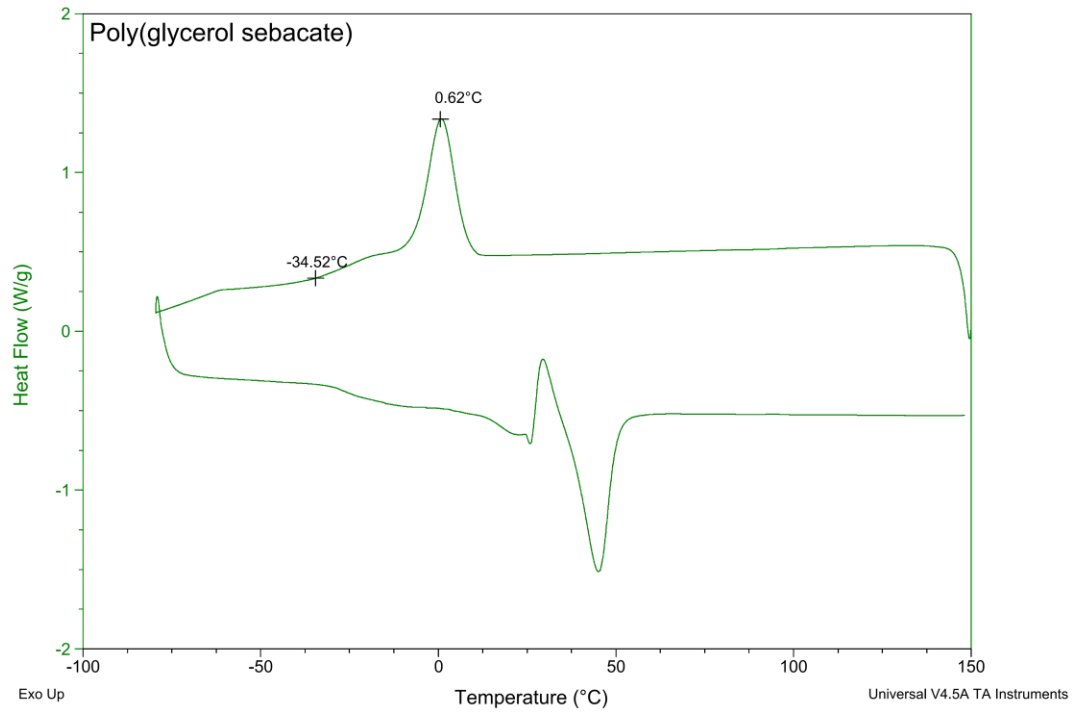
Poly(glycerol isophthalate)

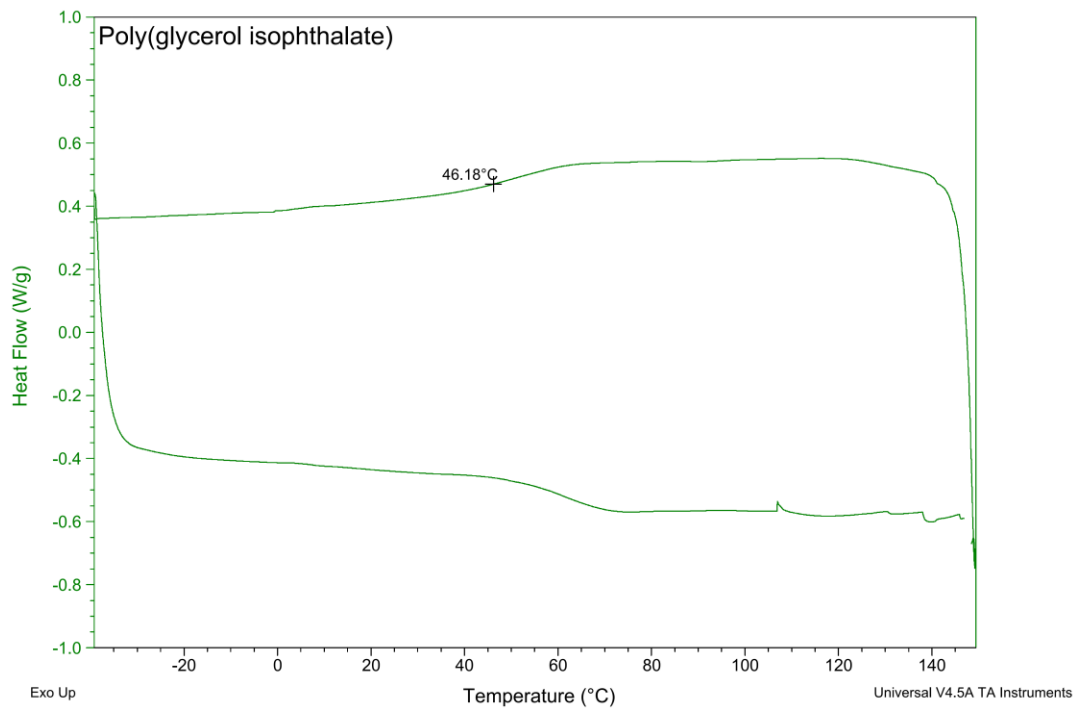
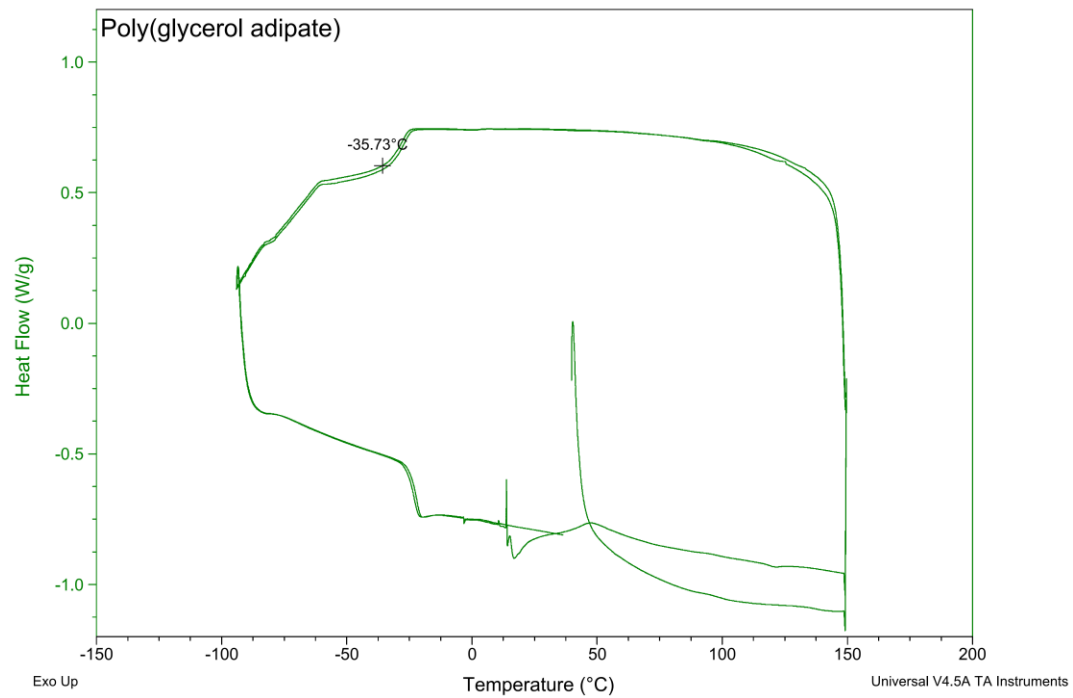


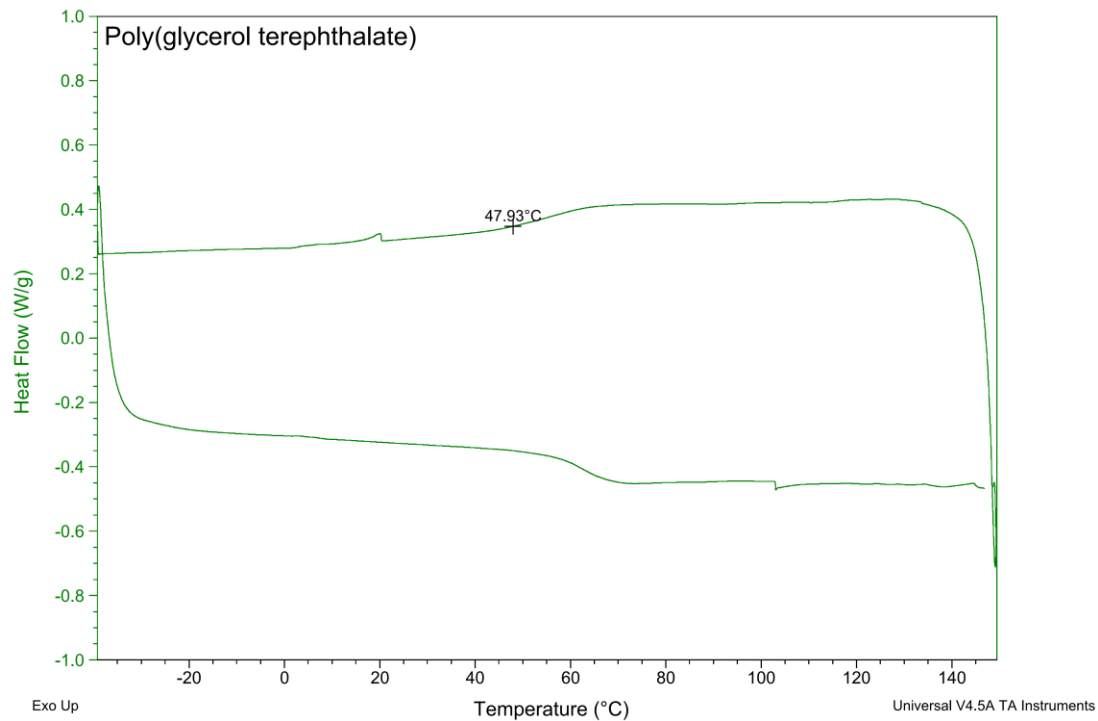
Poly(glycerol terephthalate)



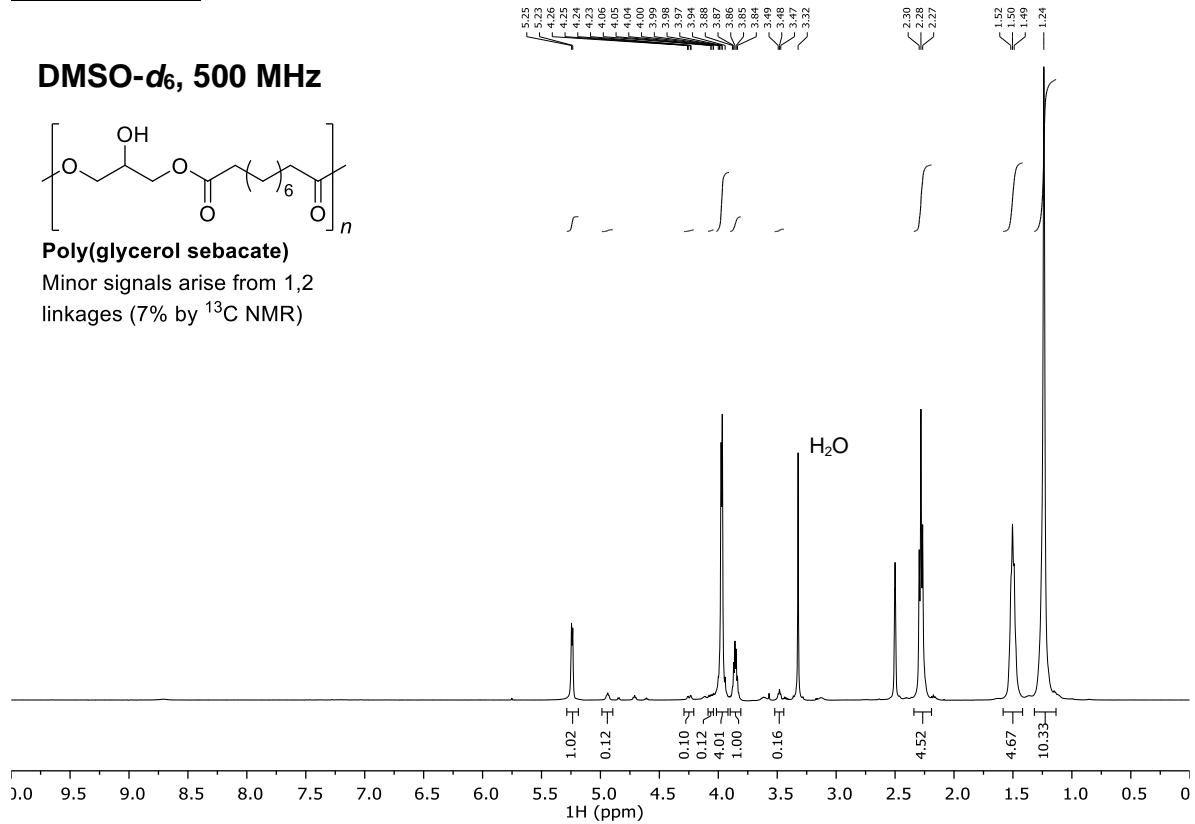
## Differential Scanning Calorimetry





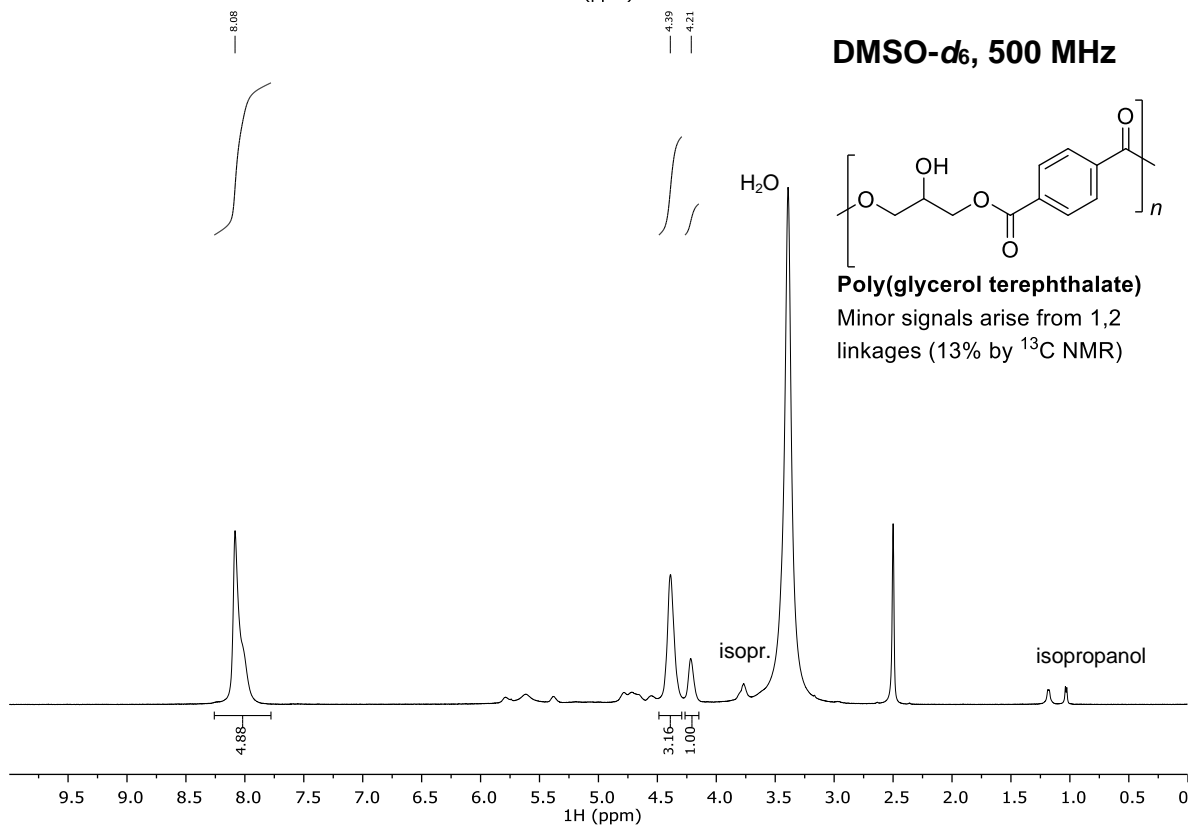
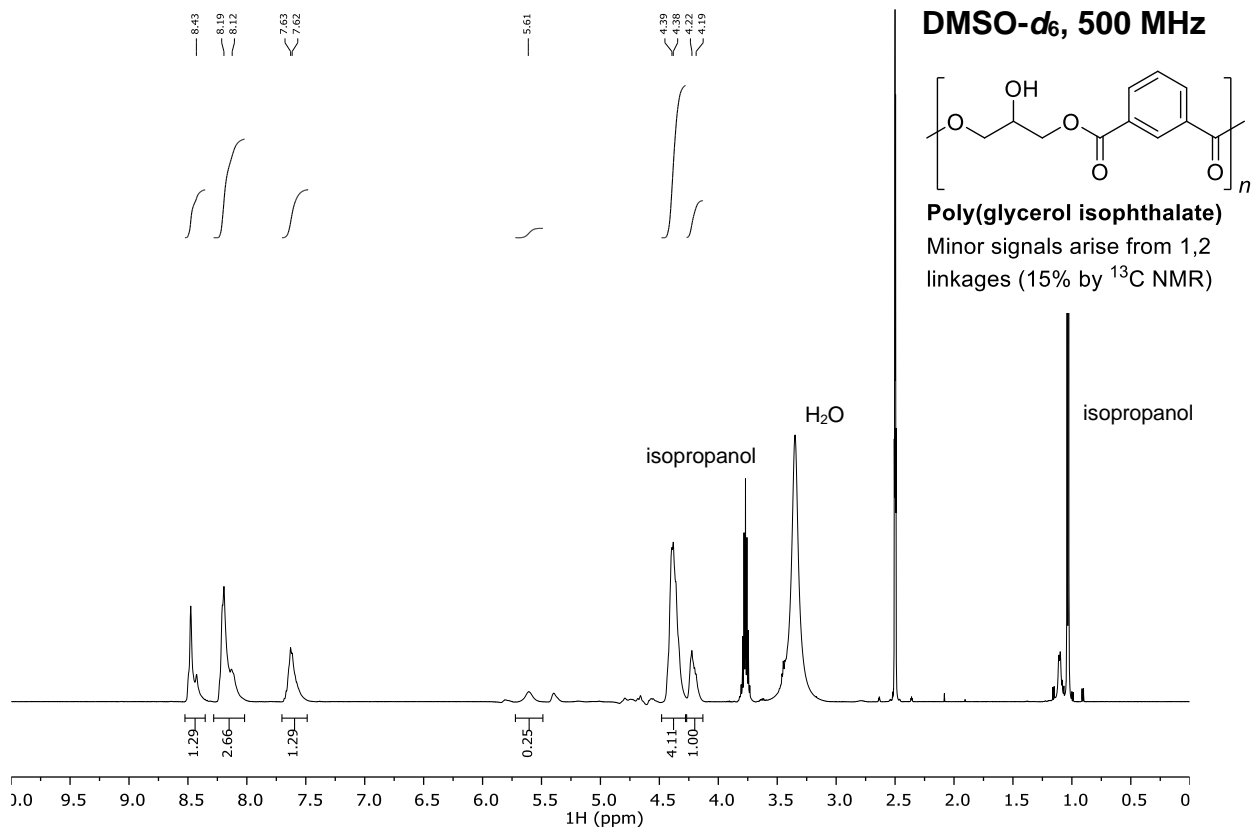


## NMR Spectra

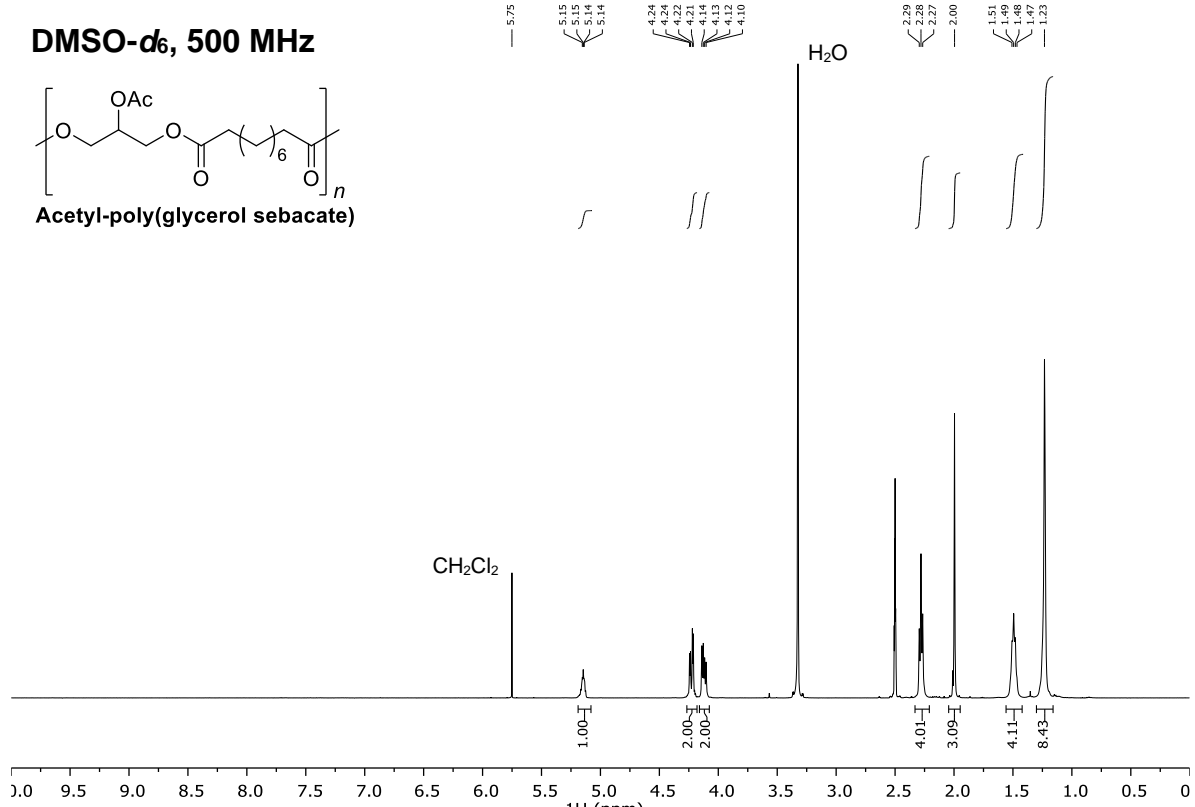
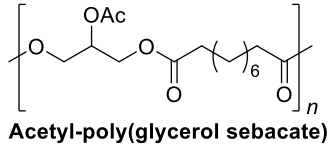




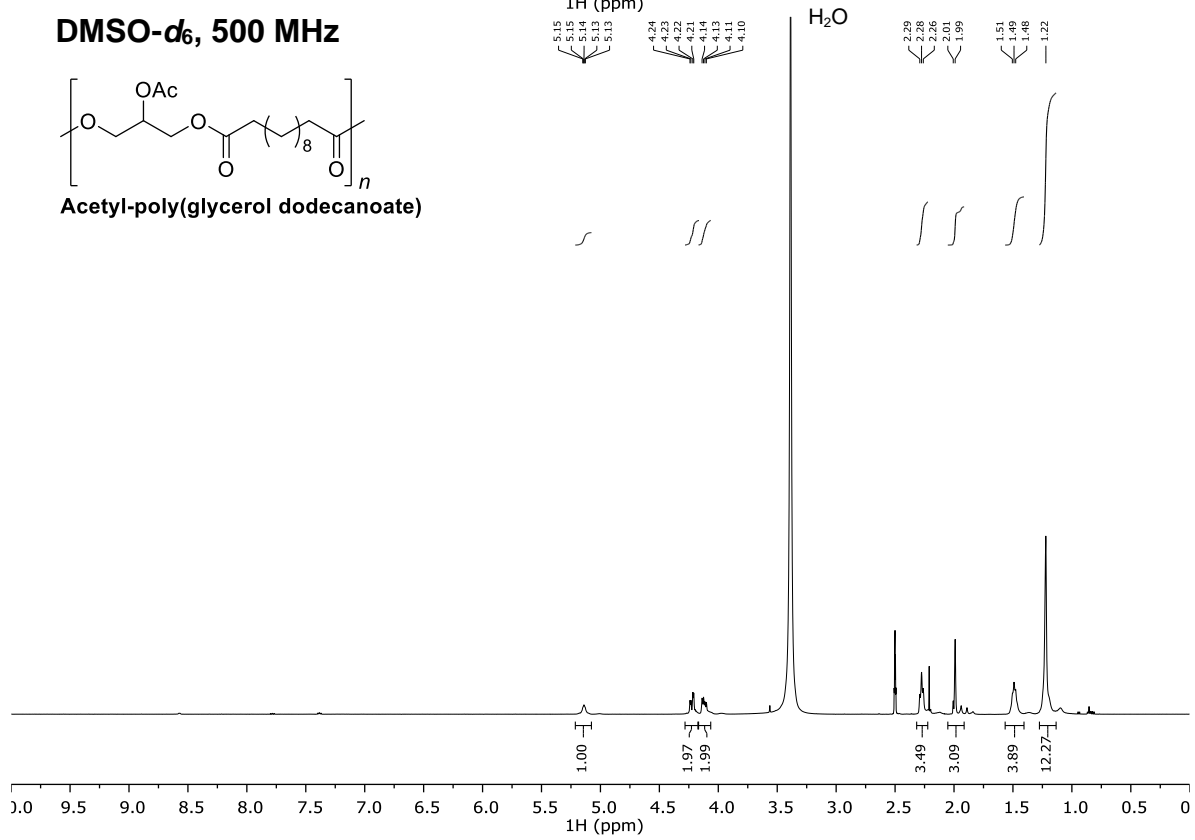
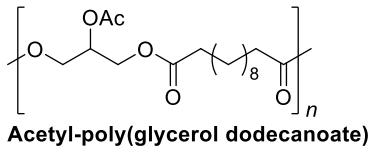




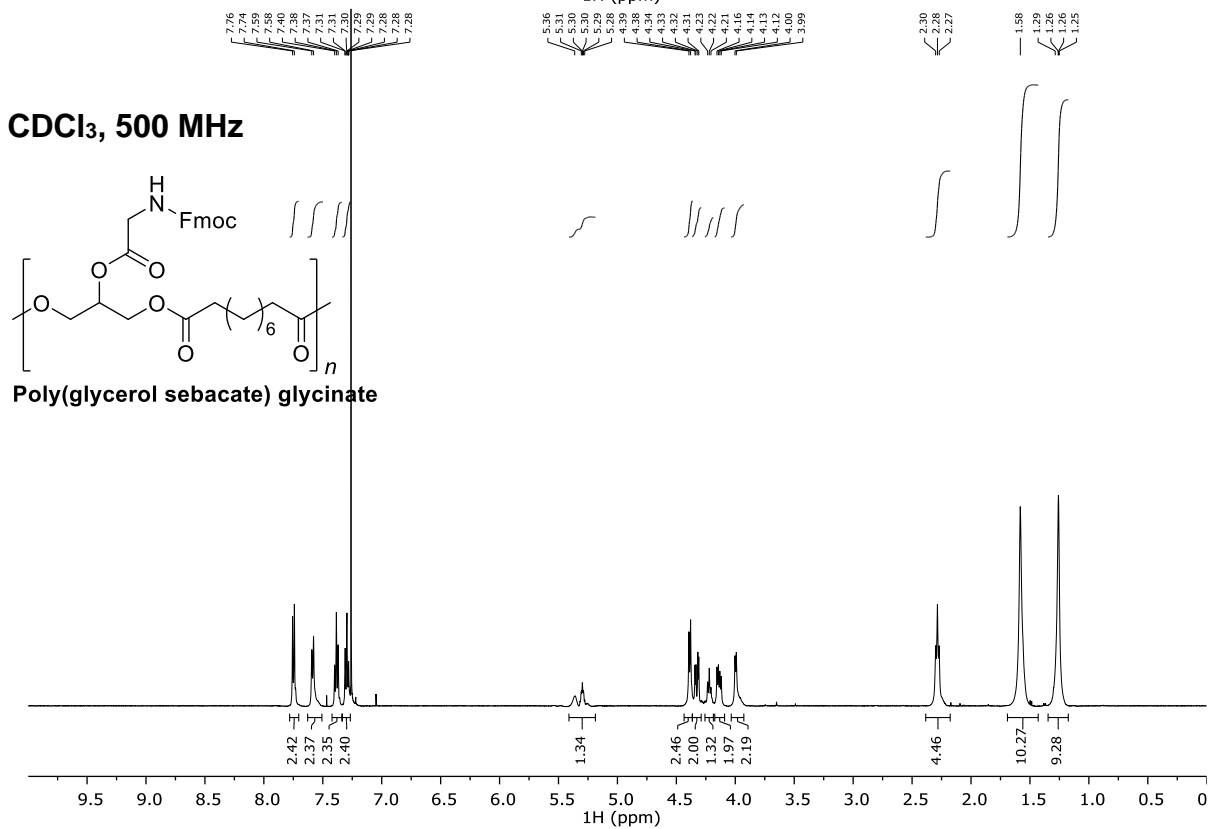
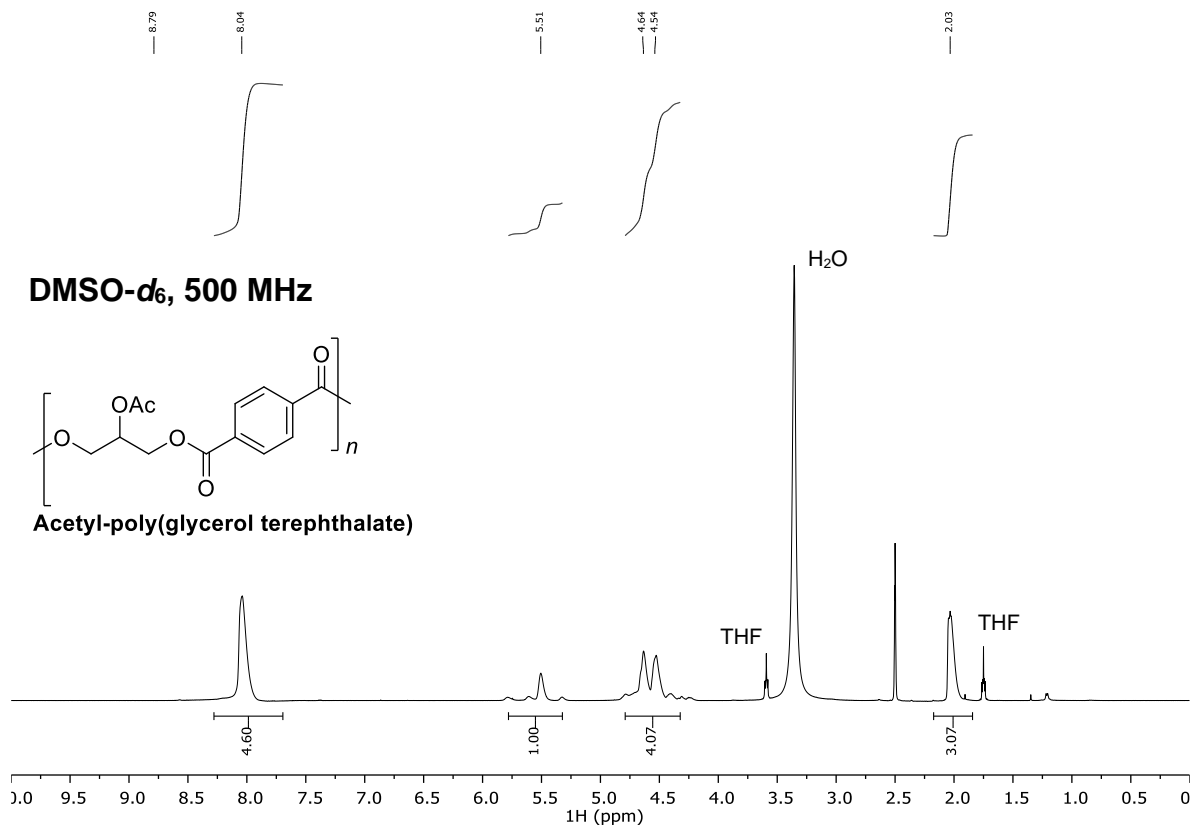
DMSO-*d*<sub>6</sub>, 500 MHz



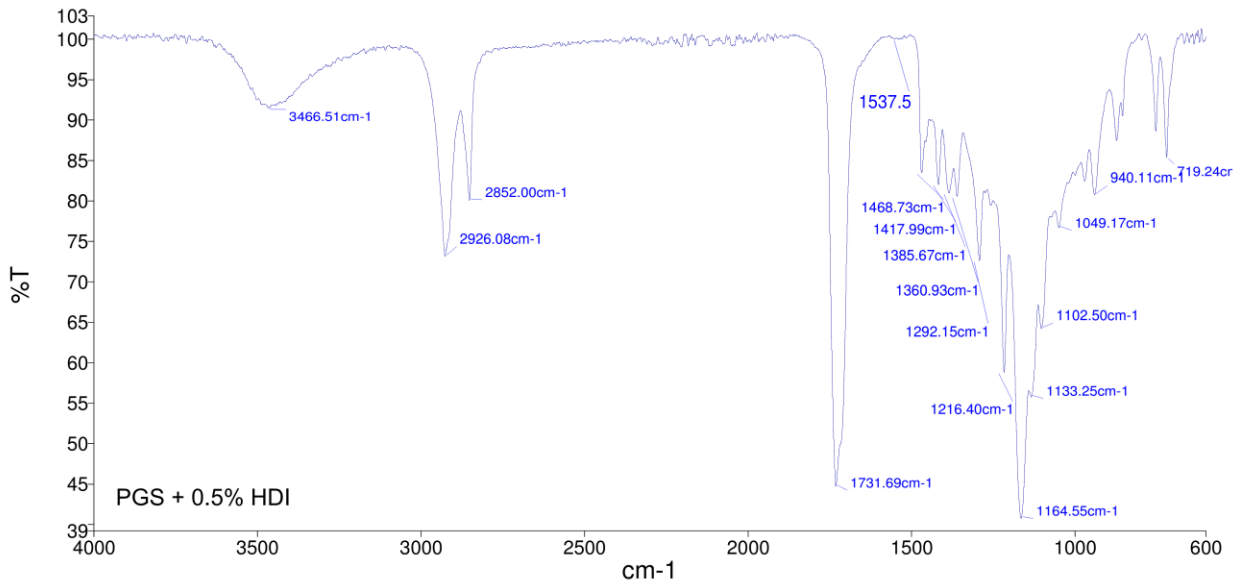
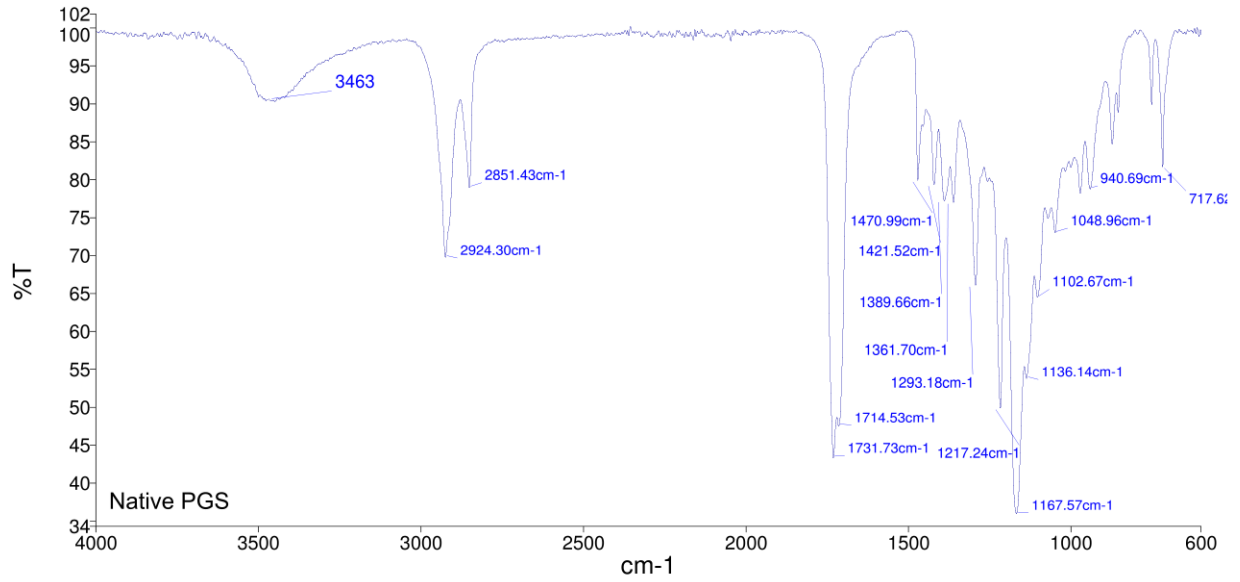
DMSO-*d*<sub>6</sub>, 500 MHz

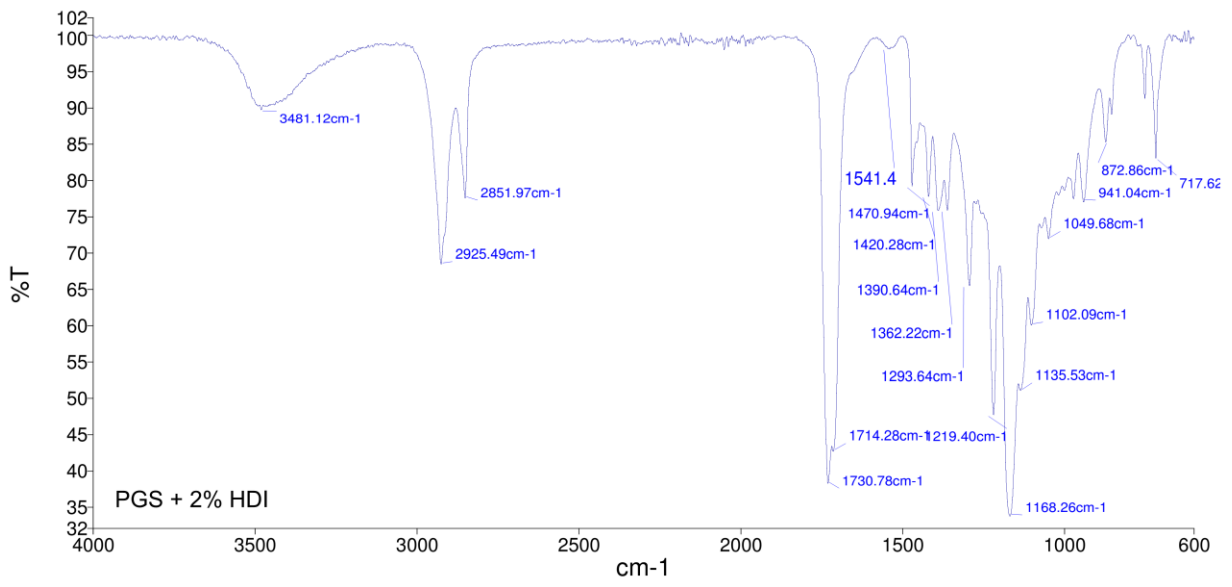
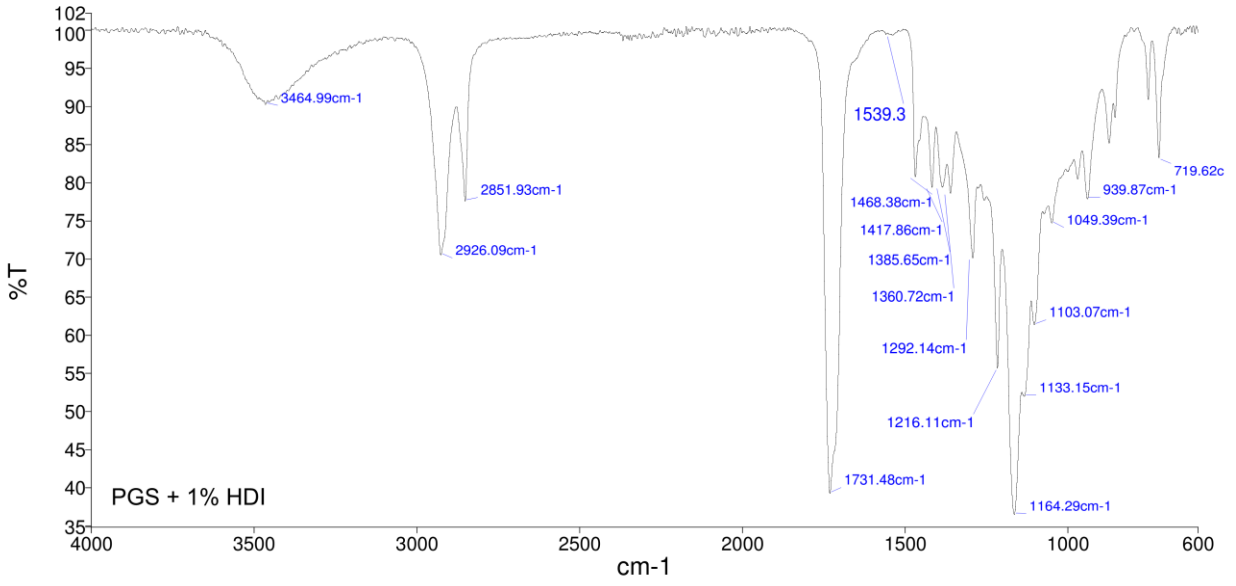


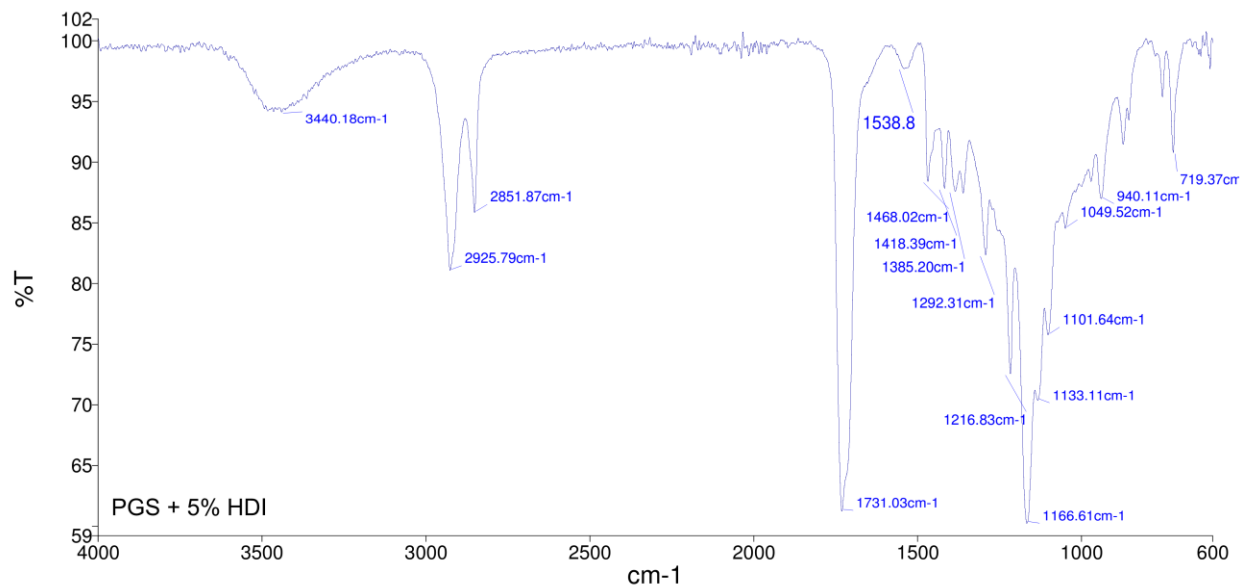
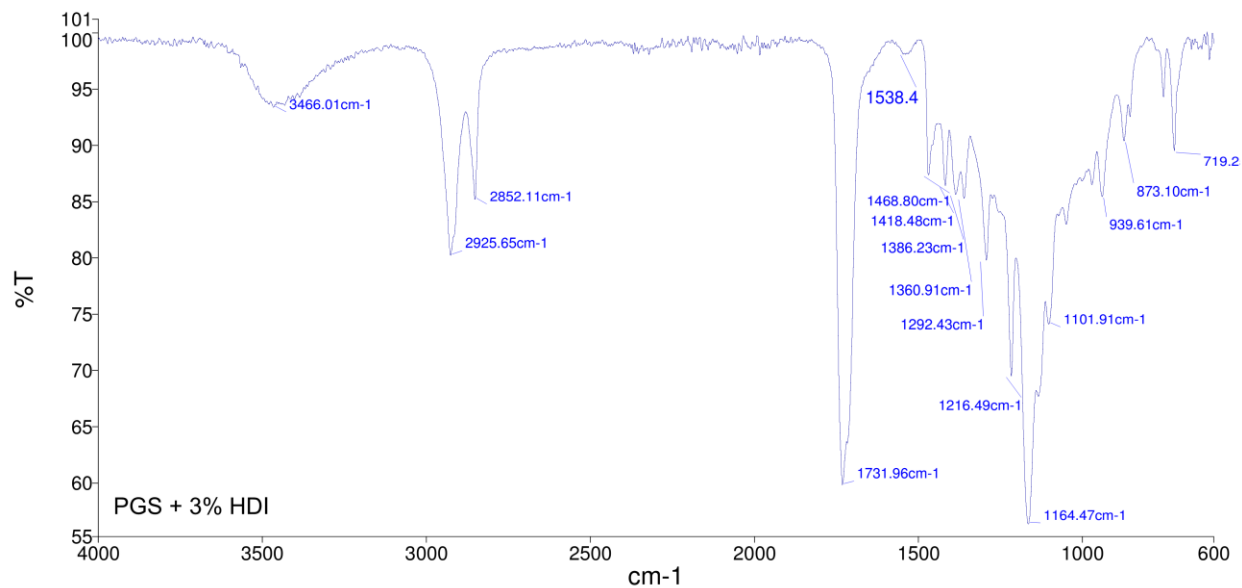


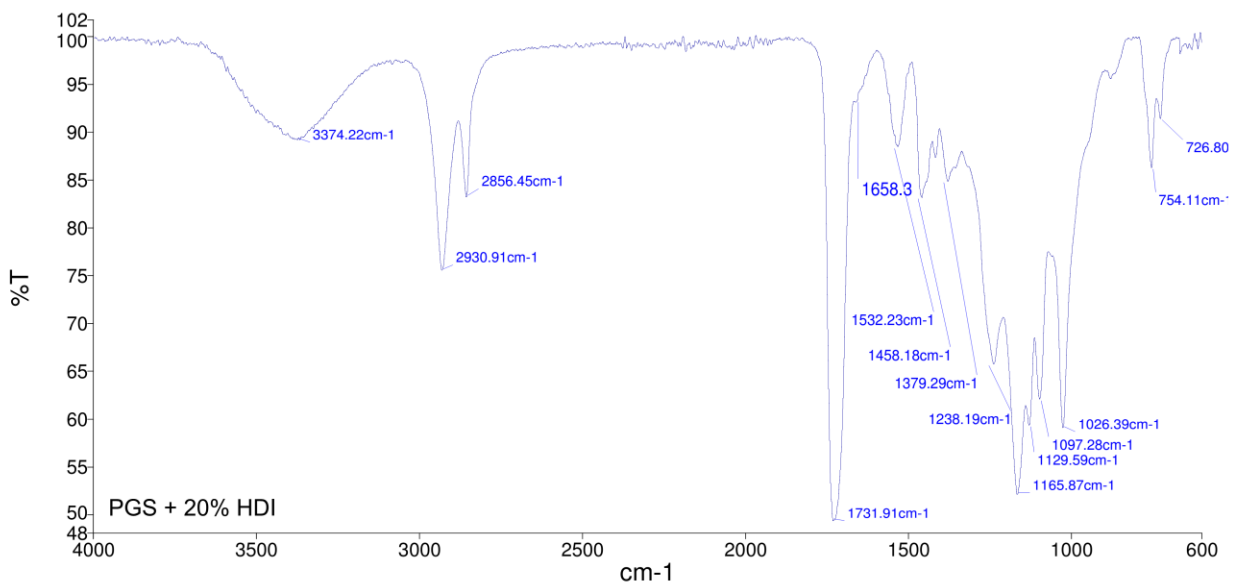
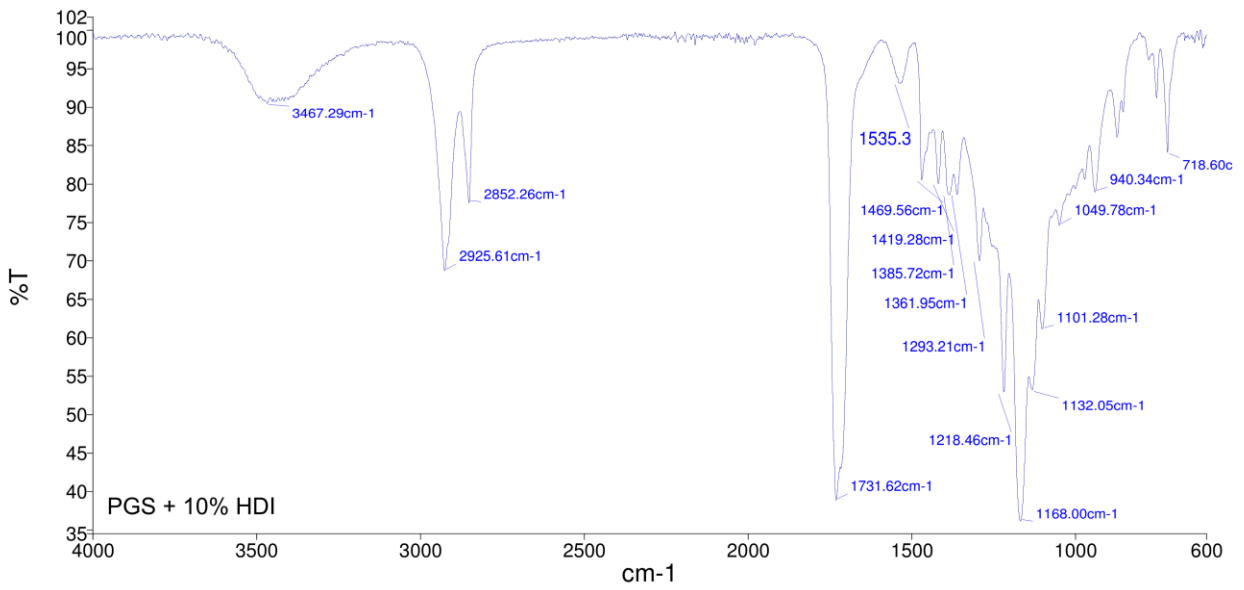


# IR Spectra

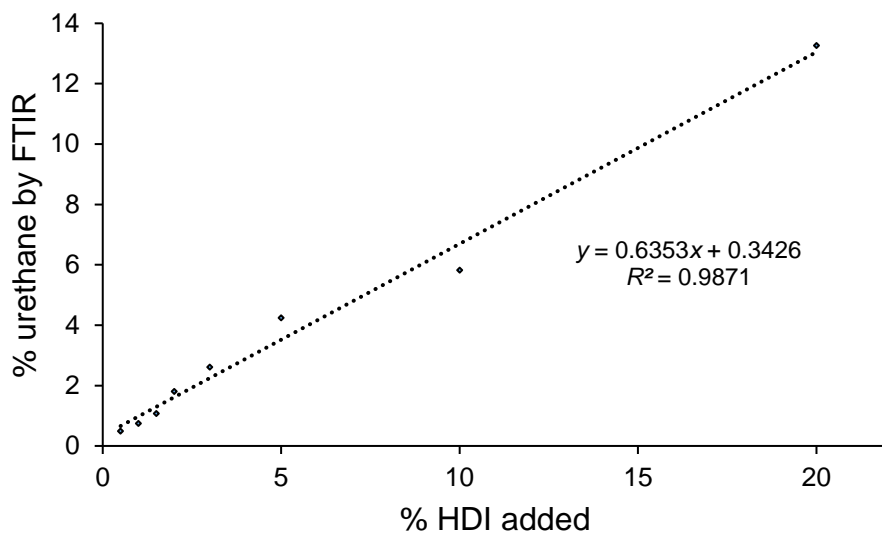












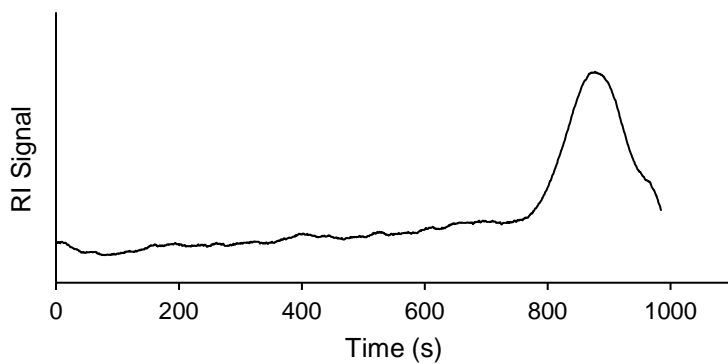
**Fig. S2** Percent peak height of urethane C=O stretch with respect to ester C=O stretch of modified PGS versus percent cross-linking agent used.

### GPC Data

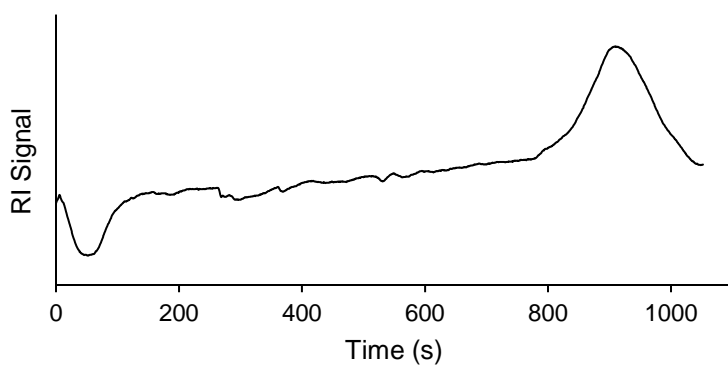
**Table S1** GPC data for linear and cross-linked PGS.

	Native PGS	1% HDI	2% HDI	3% HDI
$M_n$ (kDa)	24.4	28.4	29.7	33.7
$\bar{D}$	1.40	1.45	1.45	1.48

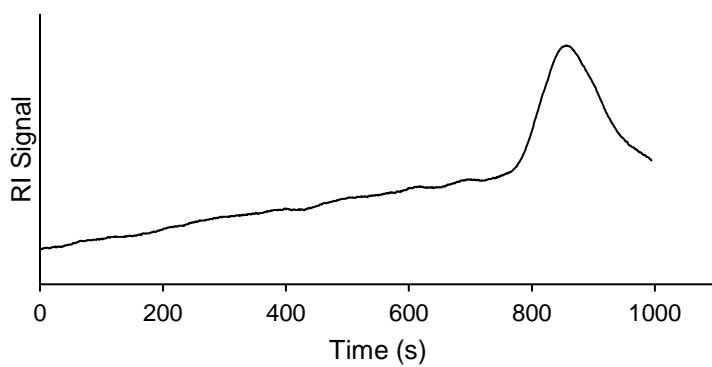
Poly(glycerol sebacate)



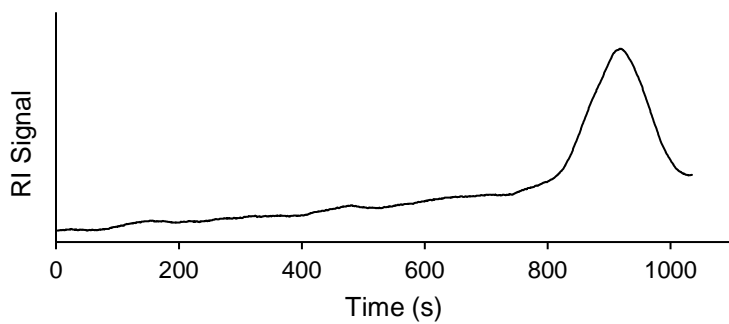
Poly(glycerol dodecanoate)



Poly(glycerol adipate)



### Poly(glycerol isophthalate)



### Poly(glycerol terephthalate)

