Electronic supplementary information (ESI)

for

Rapid alcoholysis of cyclic esters using metal alkoxides: access to linear lactyllactate-grafted polyglycidol

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Experimental section

Materials

All syntheses and manipulations were carried out under nitrogen atmosphere using standard Schlenk techniques, or in a nitrogen-filled glovebox (MBRAUN, MB 200G, equipped with a purification system). Dichloromethane and toluene were dried using a solvent purification system (PURE SOLV MD-5, Innovative Technology). Al(O^{i}Pr)$_3$ was purchased from Acros Organics and used as received. *L*-Lactide was recrystallized in dry toluene, followed by sublimation three times prior to use. ε-Caprolactone (ε-CL), δ-valerolactone (δ-VL), β-butyrolactone *(β-BL)*, γ-butyrolactone (γ-BL), methanol, ethanol, benzyl alcohol, isopropanol, propargyl alcohol, and glycidol were distilled twice over calcium hydride. 2-Hydroxyethyl methacrylate (HEMA) was dried over activated 4-Å-molecular sieves and stored in the glovebox at -30°C.

Measurements

^{1}H, ^{13}C, and 2D-DOSY NMR spectra were recorded on a Bruker AVANCE III HD-600 MHz spectrometer at 30°C in chloroform-*d* (CDCl$_3$) and deuterium oxide (D$_2$O) referenced to a protic residual solvent peak at 7.26 and 4.79 ppm, respectively as an internal standard. High-resolution mass spectra were obtained by compact QTOF Bruker mass spectrometer, using QtofControl analysis, atmospheric pressure compressed interface (APCI) mode. GPC analysis for poly(glycidyl lactyllactate) was performed on a Malvern Viscotek TDAmax double detector device with a refractive index detector and a viscometer with two 300 mm x 8.0 mm ID columns packed with a porous styrene divinylbenzene copolymer. GPC columns were eluted using tetrahydrofuran with a flow rate of 1.0 mL/min at 35°C. The universal calibration curve was calibrated with polystyrene standards ranging from 1,200 to 4,200,000 amu. Molecular weight and polydispersity were calculated by the conventional method using refractive index.[1, 2] GPC analysis of polyglycidol was carried out on Shimadzu HPLC 10Avp equipped with a refractive index detector. GPC column, Shodex SB-804 HQ, was eluted by DI water with a flow rate of 0.5 mL/min at 30°C. The water solution of polymer was filtered and injected into the GPC column (20 μL) with a run time of 30 min. Molecular weight and polydispersity were determined by the conventional method using refractive index calibrated with Pullulan standards ranging from 500-800,000 Da.

Thermogravimetric Analysis (TGA) was determined by Rigaku STA8122 Thermogravimetric Analyzer over a temperature range from 40°C to 500°C at a heating rate of 10°C/min under a nitrogen atmosphere with a gas flow rate of 200 mL/min. Differential Scanning Calorimetry (DSC) measurement was performed on a PerkinElmer DSC-8500 to analyze the glass-transition temperature (T_g) of polymers over a temperature range from -60°C to 100°C at a heating rate of 10°C/min and a gas flow rate of 20 mL/min under nitrogen atmosphere.

**General procedure for the alcoholysis of cyclic esters using metal alkoxides**

A solution of Al(O^{i}Pr)$_3$ (35.5 mg, 174 µmol, 5 mol%) and dry alcohol (17.4 mmol, 5 equiv.) in 2 mL of toluene was prepared and added to a solution of cyclic esters (3.5 mmol, 1 equiv.) in 2 mL of toluene. The reaction mixture was then heated at 70°C with stirring. After completion or at the desire time, the reaction was quenched with a few drops of acetic acid. All volatile components were subsequently removed under reduced pressure and further purified by vacuum distillation and/or silica gel column chromatography with stepwise gradient polarity using ethyl acetate:hexane (10:90, 20:80, 30:70, 40:60, and 50:50), giving colorless liquid as a product. The products were then analysed by ^{1}H- and ^{13}C-NMR spectroscopy and APCI mass spectrometry. The amounts of other catalysts, alcohols, and cyclic esters in other alcoholysis were modified accordingly. Alcoholysis was performed in triplicate.

Methyl (*S*,*S*)-lactyllactate
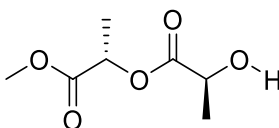
Colorless liquid, 90% isolated yield, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.20 (q, *J* = 7.1 Hz, 1H), 4.36 (p, *J* = 6.6 Hz, 1H), 3.76 (s, 3H), 2.68 (d, *J* = 5.9 Hz, 1H), 1.54 (d, *J* = 7.1 Hz, 3H), 1.50 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 175.29, 170.76, 69.49, 66.89, 52.64, 20.64, 17.02. APCI MS (*m/z*) calc. for C$_7$H$_{12}$O$_5$ [M-H]$^+$ = 177.0757, found 177.0772.

Methyl 3-hydroxybutyrate
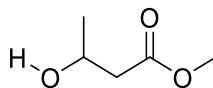
Colorless liquid, 90% isolated yield, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.19 (ddt, *J* = 12.5, 9.5, 4.8 Hz, 1H), 3.71 (s, 3H), 2.95 (s, 1H), 2.49 (dd, *J* = 16.5, 3.4 Hz, 1H), 2.43 (dd, *J* = 16.5, 8.8 Hz, 1H), 1.23 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 173.46, 64.39, 51.86, 42.69, 22.58. APCI MS (*m/z*) calc. for C$_5$H$_{10}$O$_3$ [M-H]$^+$ = 119.0703, found 119.0719.

**Methyl 4-hydroxybutanoate**
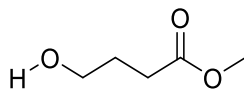
    Colorless liquid, 35% isolated yield, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 3.71-3.69 (m, 5H), 2.45 (t, *J* = 7.1 Hz, 2H), 1.89 (t, *J* = 6.6 Hz, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.53, 62.28, 51.85, 30.95, 27.82. APCI MS (*m/z*) calc. for $C_5H_{10}O_3$ [M-H]$^+$ = 119.0703, found 119.0580.

Methyl 5-hydroxypentanoate
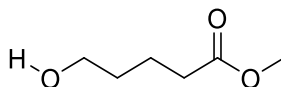
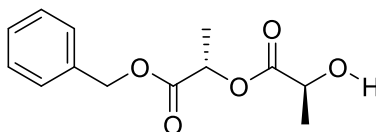   Colorless liquid, 82% isolated yield, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 3.66 (s, 3H), 3.64 (t, *J* = 6.4 Hz, 2H), 2.35 (t, *J* = 7.3 Hz, 2H), 1.71 (p, *J* = 7.4 Hz, 2H), 1.59 (p, *J* = 6.5 Hz, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.32, 62.37, 51.68, 33.78, 32.17, 21.21. APCI MS (*m/z*) calc. for $C_6H_{12}O_3$ [M-H]$^+$ = 133.0859, found 133.0931.

Methyl 6-hydroxyhexanoate
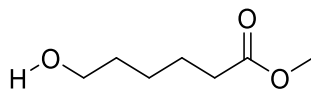
    Colorless liquid, 90% isolated yield, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 3.66 (s, 3H), 3.64 (t, *J* = 6.5 Hz, 2H), 2.32 (t, *J* = 7.5 Hz, 2H), 1.74 (s, 1H), 1.65 (p, *J* = 7.5 Hz, 2H), 1.57 (p, *J* = 6.7 Hz, 2H), 1.39 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.32, 62.77, 51.63, 34.12, 32.44, 25.42, 24.76. APCI MS (*m/z*) calc. for $C_7H_{14}O_3$ [M-H]$^+$ = 147.1016, found 147.1074.

Ethyl (*S,S*)-lactyllactate
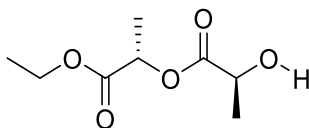
    Colorless liquid, 5% isolated yield, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.17 (q, *J* = 7.1 Hz, 1H), 4.35 (p, *J* = 6.9 Hz, 1H), 4.21 (qd, *J* = 7.2, 2.6 Hz, 2H), 2.70 (d, *J* = 5.9 Hz, 1H), 1.53 (d,

J = 7.1 Hz, 3H), 1.50 (d, J = 7.0 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 175.32, 170.30, 69.62, 66.87, 61.74, 20.68, 17.00, 14.21. APCI MS (m/z) calc. for $C_8H_{14}O_5$ [M-H]$^+$ = 191.0914, found 191.0784.

Benzyl (*S,S*)-lactyllactate

Colorless liquid, 17% isolated yield, ^{1}H NMR (600 MHz, Chloroform-d) δ 7.35 (dt, J = 21.7, 7.1 Hz, 5H), 5.26–5.13 (m, 3H), 4.34 (p, J = 6.6 Hz, 1H), 2.67 (d, J = 5.9 Hz, 1H), 1.54 (d, J = 7.2 Hz, 3H), 1.44 (d, J = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 175.29, 170.13, 135.22, 128.80, 128.71, 128.41, 69.57, 67.42, 66.86, 20.60, 16.98. APCI MS (m/z) calc. for $C_{13}H_{16}O_5$ [M-H]$^+$ = 253.1071, found 253.1074.

Isopropyl (*S,S*)-lactyllactate
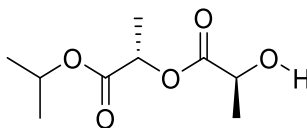
Colorless liquid, 13% isolated yield, ^{1}H NMR (600 MHz, Chloroform-d) δ 5.13 (q, J = 7.1 Hz, 1H), 5.06 (p, J = 6.3 Hz, 1H), 4.35 (p, J = 6.9 Hz, 1H), 2.69 (d, J = 5.6 Hz, 1H), 1.51 (dd, J = 9.2, 7.0 Hz, 6H), 1.26 (dd, J = 15.3, 6.2 Hz, 6H). ^{13}C NMR (151 MHz, Chloroform-d) δ 175.30, 169.83, 69.75 (d, J = 2.7 Hz), 69.47 (d, J = 2.3 Hz), 66.83, 21.79 (d, J = 4.6 Hz), 20.69, 16.93. APCI MS (m/z) calc. for $C_9H_{16}O_5$ [M-H]$^+$ = 205.1071, found 205.1103.

2-(methacryloyl)ethyl-(*S,S*)-lactyllactate
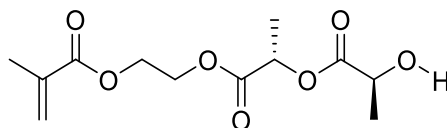
Colorless liquid, 55% isolated yield, ^{1}H NMR (600 MHz, Chloroform-d) δ 6.12 (s, 1H), 5.60 (s, 1H), 5.20 (q, J = 7.1 Hz, 1H), 4.50 – 4.41 (m, 1H), 4.39-4.33 (m, 4H), 1.94 (s, 3H), 1.53 (d, J = 7.1 Hz, 3H), 1.48 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 175.17, 170.10,

167.17, 135.95, 126.38, 69.37, 66.87, 63.27, 62.16, 20.56, 18.34, 16.96. APCI MS (*m/z*) calc. for C$_{12}$H$_{18}$O$_7$ [M-H]$^+$ = 275.1125, found 275.1173.

Propargyl-(*S,S*)-lactyllactate
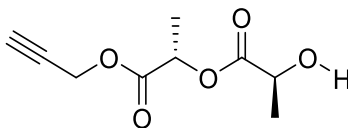
Colorless liquid, 34% isolated yield, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.22 (q, *J* = 7.0 Hz, 1H), 4.74 (qd, *J* = 15.5, 2.5 Hz, 2H), 4.36 (p, *J* = 6.8 Hz, 1H), 2.67 (d, *J* = 5.9 Hz, 1H), 2.50 (t, *J* = 2.5 Hz, 1H), 1.56 (d, *J* = 7.1 Hz, 3H), 1.51 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 175.25, 169.54, 76.87, 75.75, 69.29, 66.88, 53.09, 20.67, 16.86. APCI MS (*m/z*) calc. for C$_9$H$_{12}$O$_5$ [M-H]$^+$ = 201.0757, found 201.0883.

Glycidyl-(*S,S*)-lactyllactate
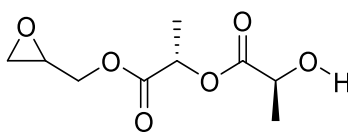
Colorless liquid, 85% isolated yield. Product existed as a pair of diastereomers. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.20 (p, *J* = 6.9 Hz, 1H), 4.48 (td, *J* = 12.2, 2.8 Hz, 1H), 4.35 (p, *J* = 6.3 Hz, 1H), 4.00 (ddd, *J* = 17.9, 12.2, 6.3 Hz, 1H), 3.19 (ddd, *J* = 13.2, 5.9, 3.0 Hz, 1H), 2.84 (q, *J* = 4.3 Hz, 1H), 2.77 (d, *J* = 4.6 Hz, 1H), 2.64 (ddd, *J* = 15.5, 4.4, 2.5 Hz, 1H), 1.55 (d, *J* = 7.1 Hz, 3H), 1.50 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 175.26 (d, *J* = 2.3 Hz), 170.06, 69.42 (d, *J* = 1.1 Hz), 66.88 (d, *J* = 1.2 Hz), 66.16, 65.72, 49.14 (d, *J* = 1.2 Hz), 44.66, 44.61, 20.61 (d, *J* = 2.1 Hz), 16.98 (d, *J* = 1.9 Hz). APCI MS (*m/z*) calc. for C$_9$H$_{14}$O$_6$ [M-H]$^+$ = 219.0863, found 219.0931.
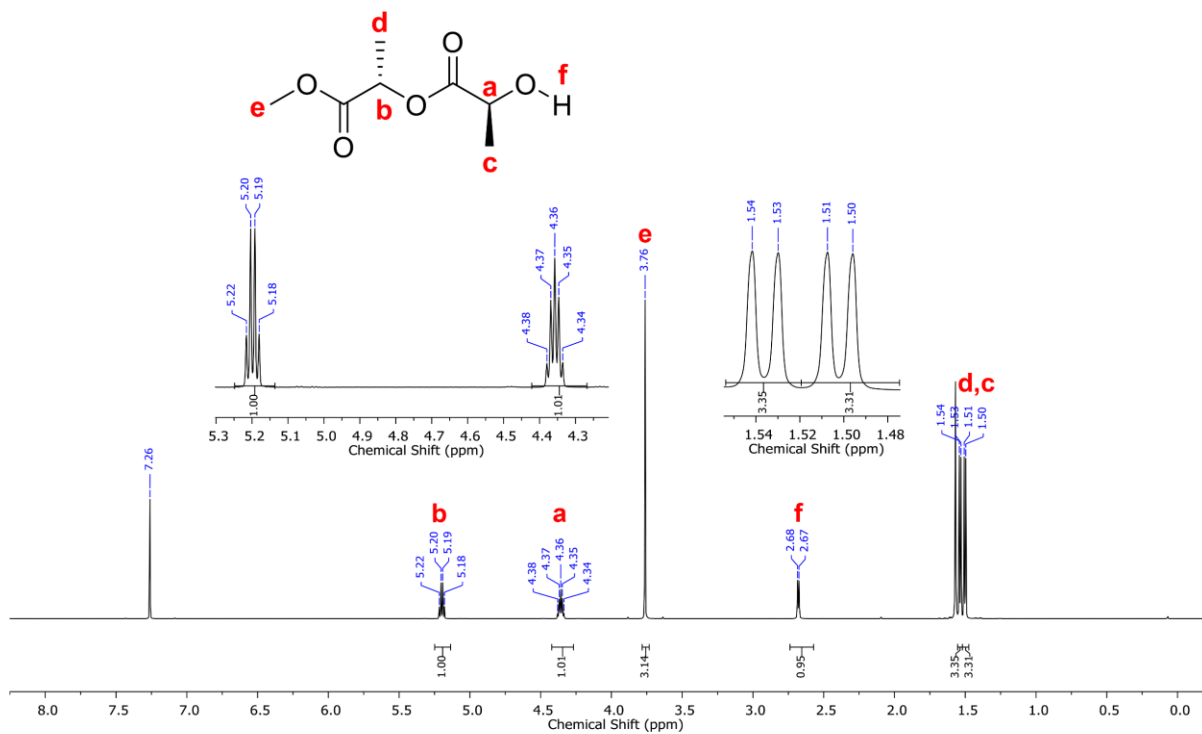
Figure S1 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified methyl (*S,S*)-lactyllactate.
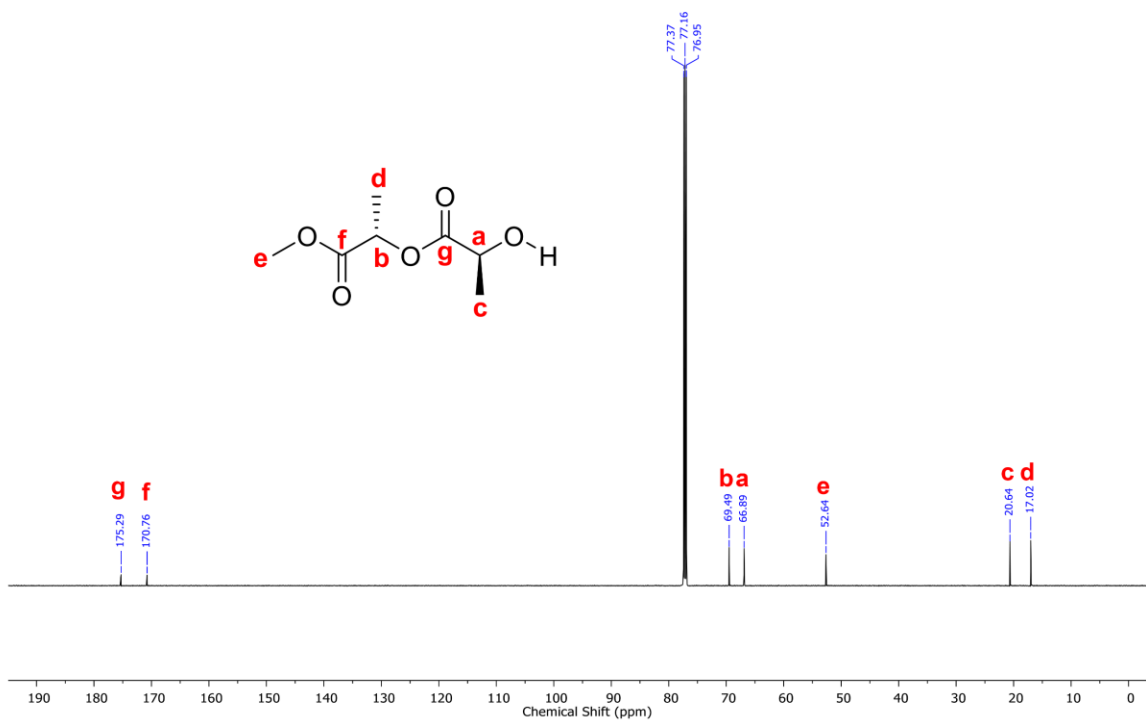
Figure S2 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified methyl (*S,S*)-lactyllactate.
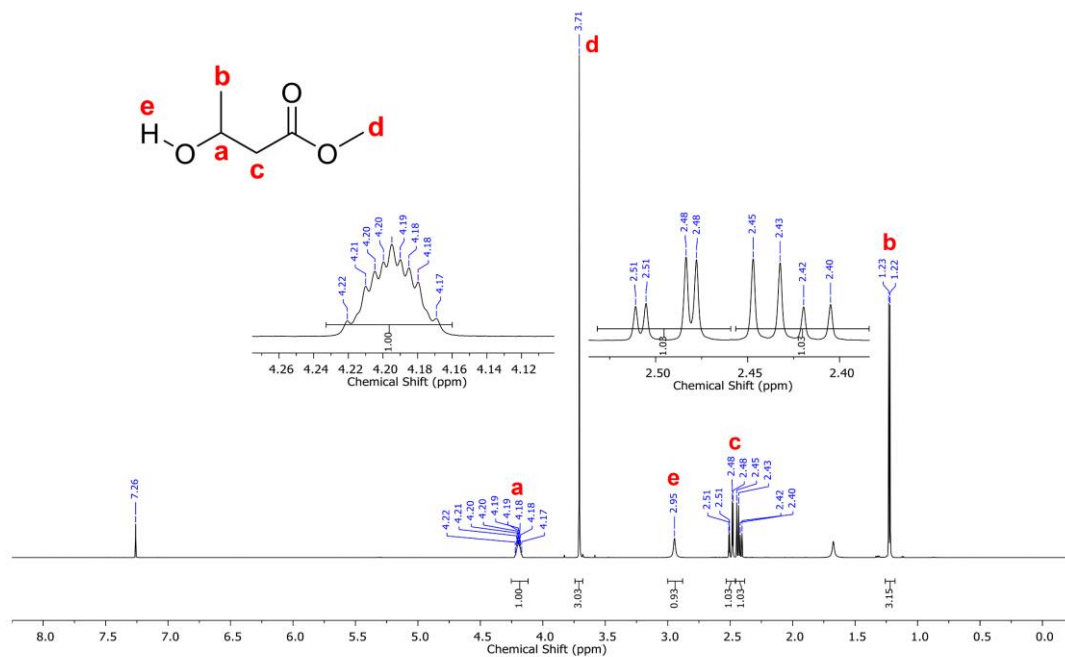
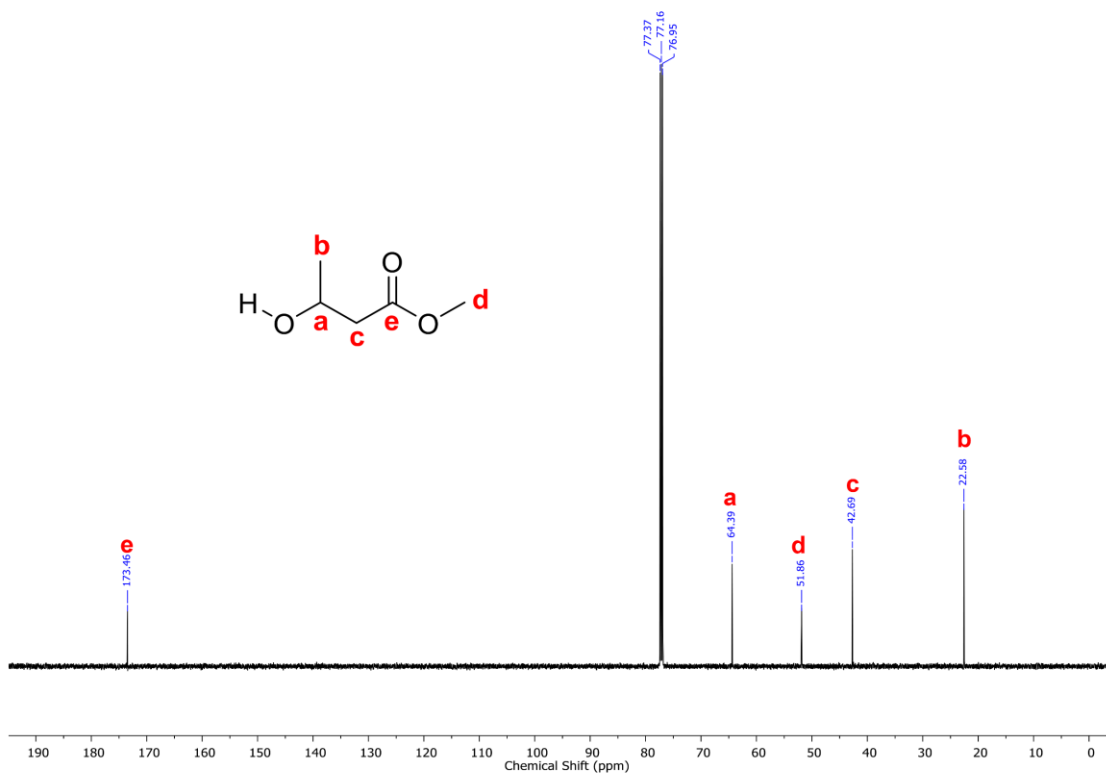**Figure S3** ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified methyl 3-hydroxybutyrate.

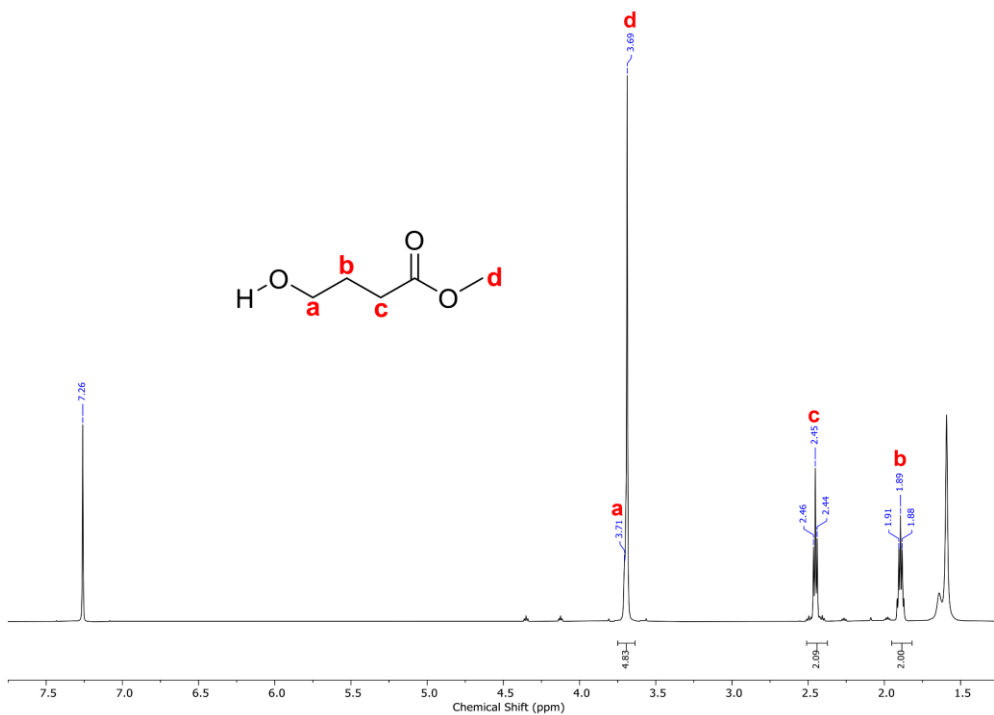**Figure S4** ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified methyl 3-hydroxybutyrate.
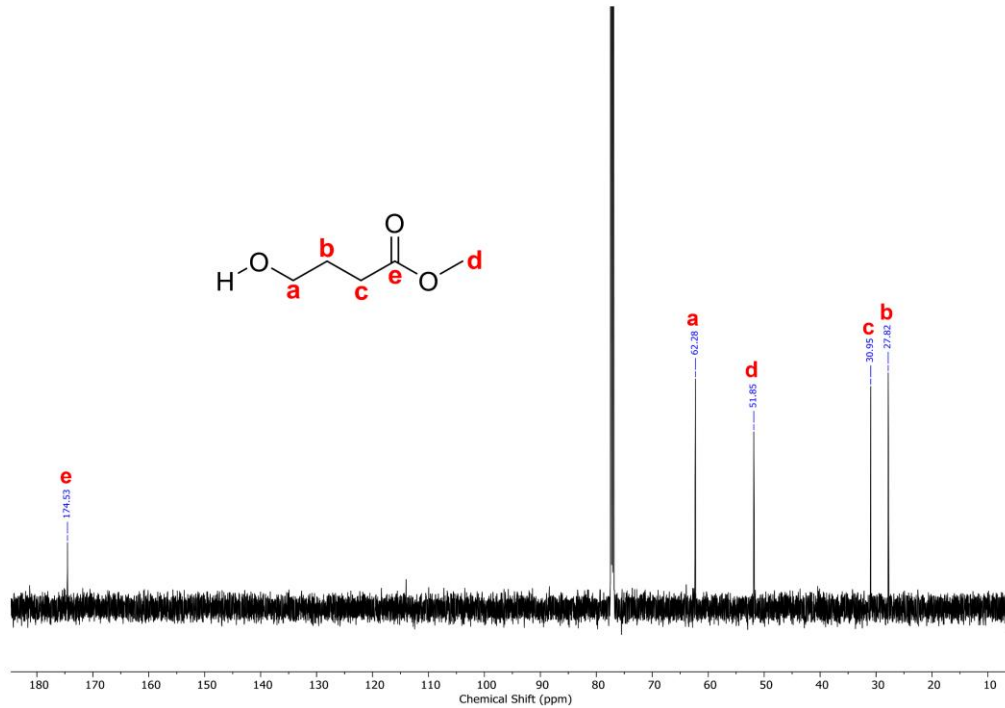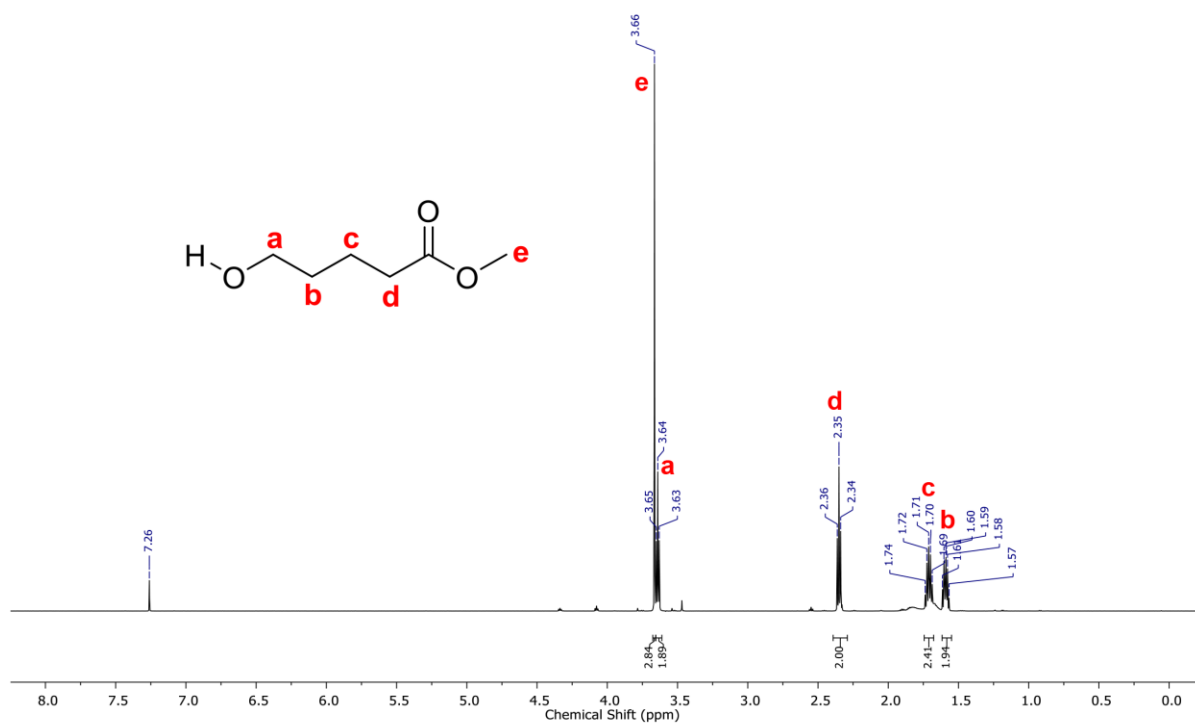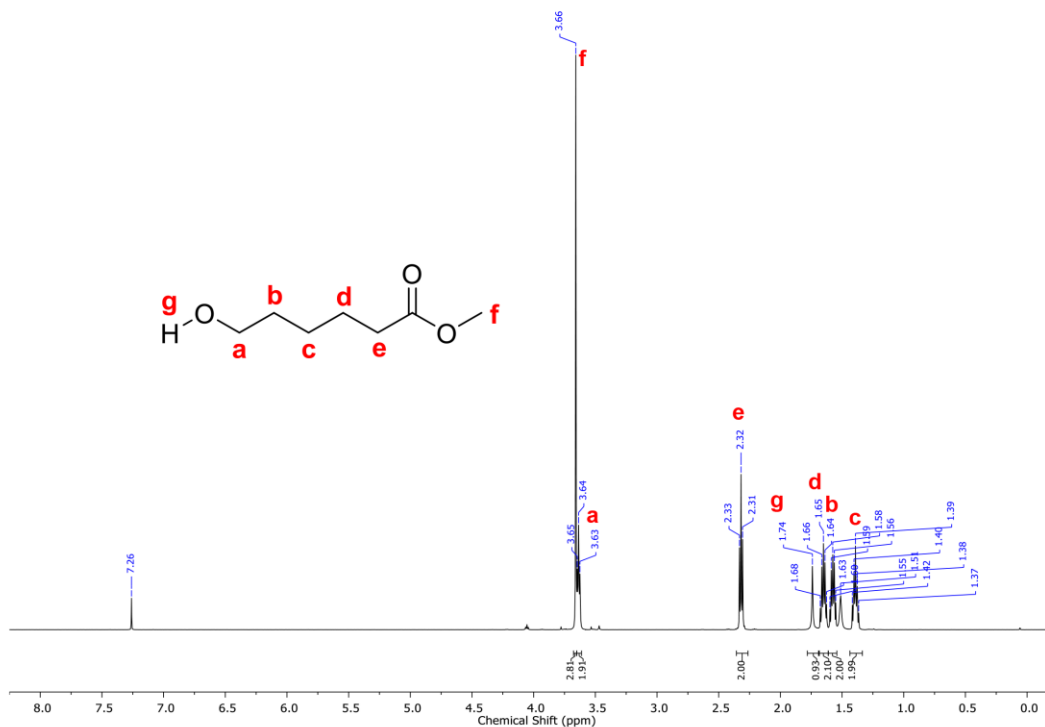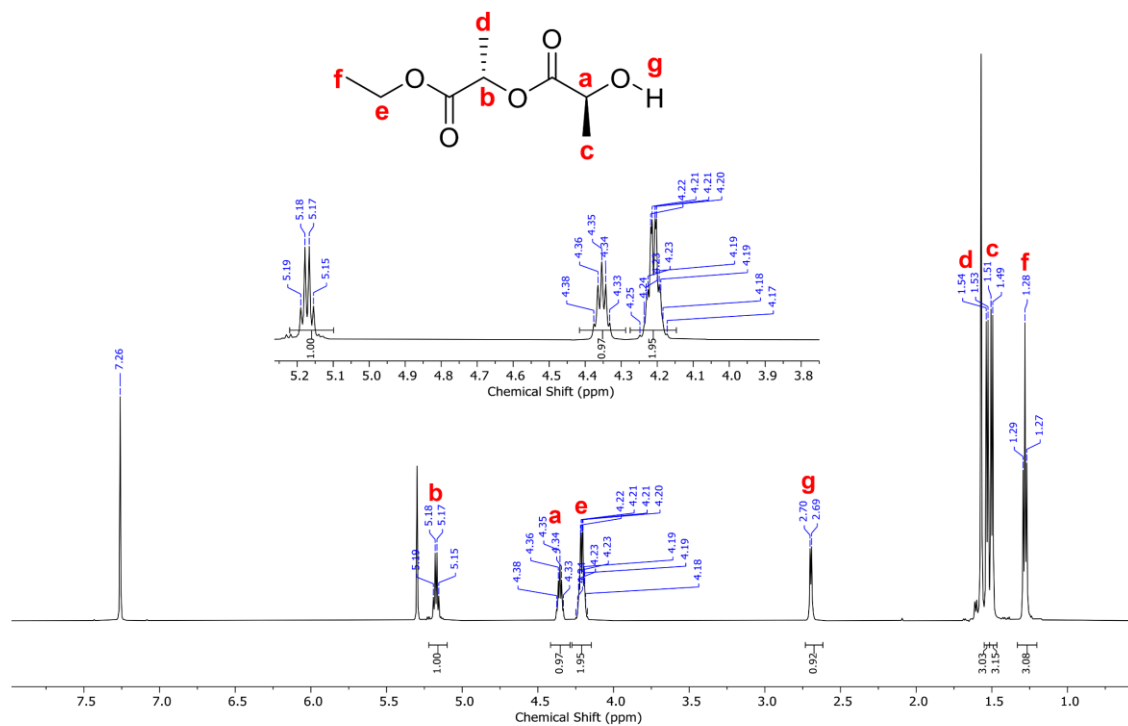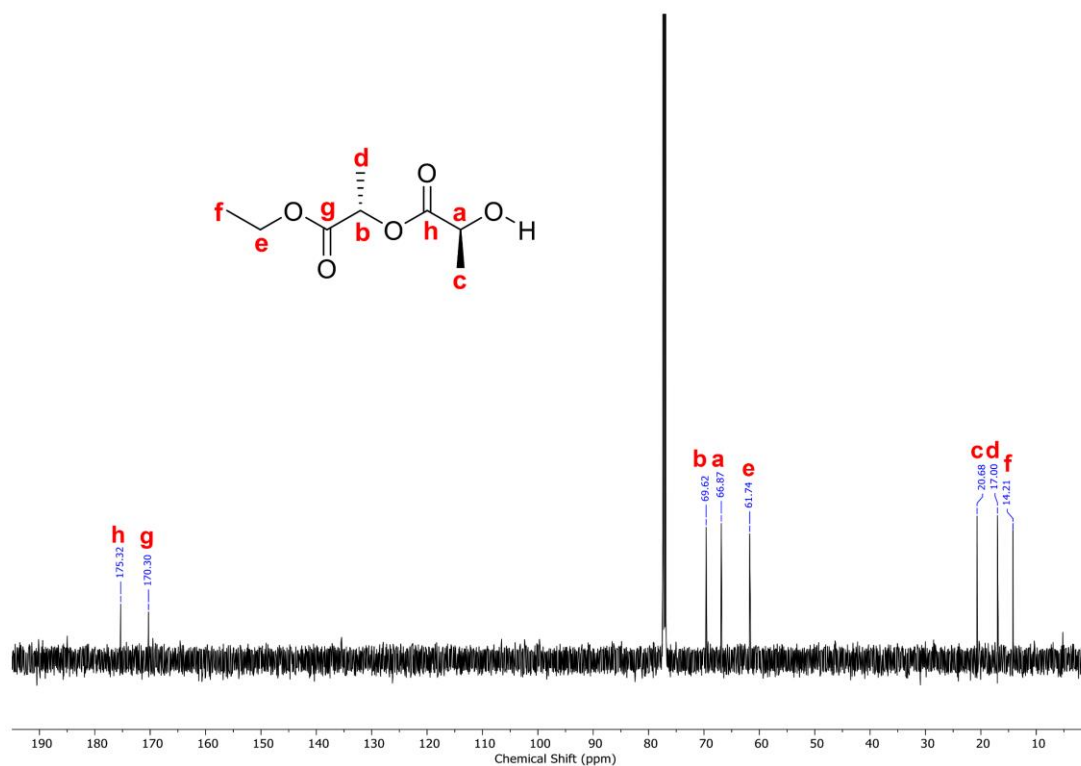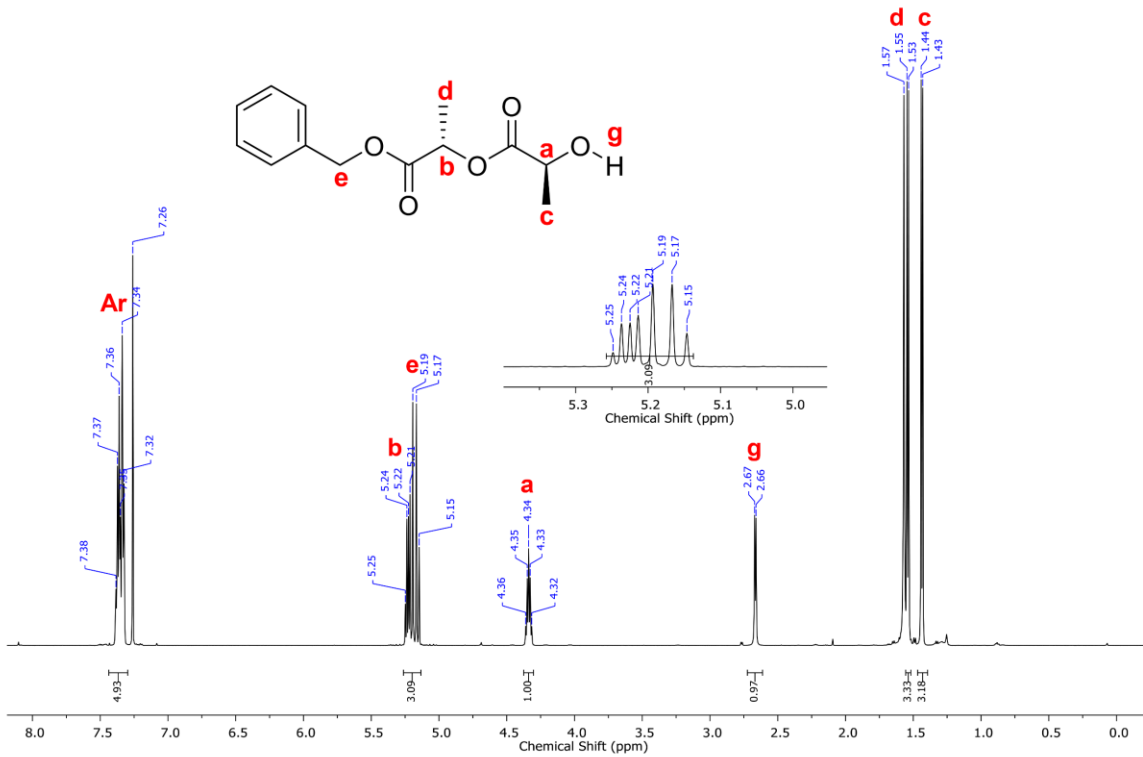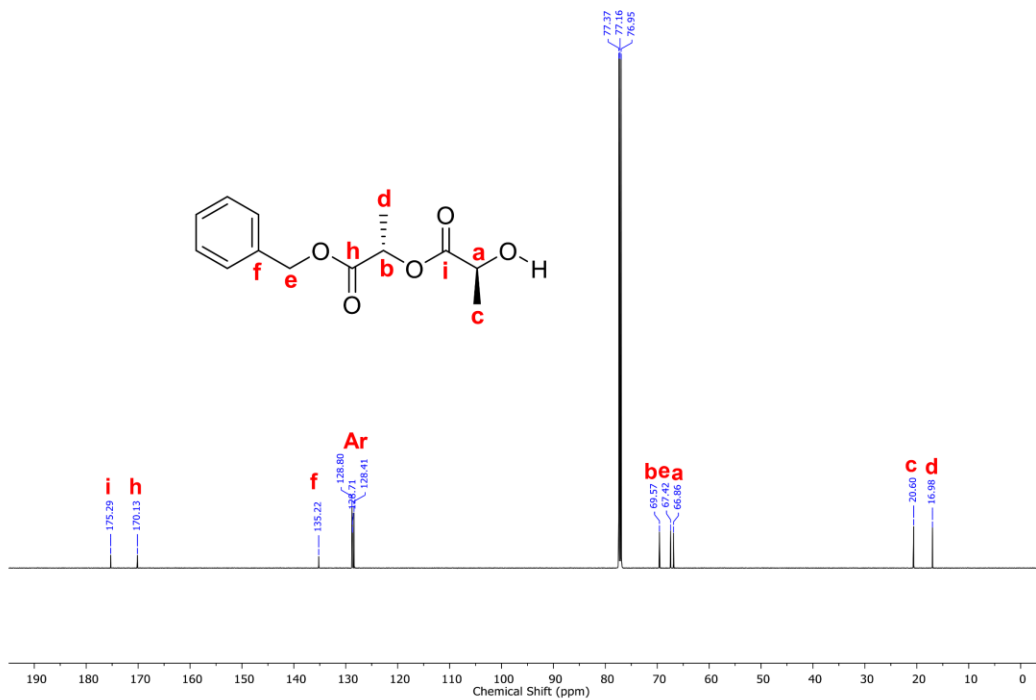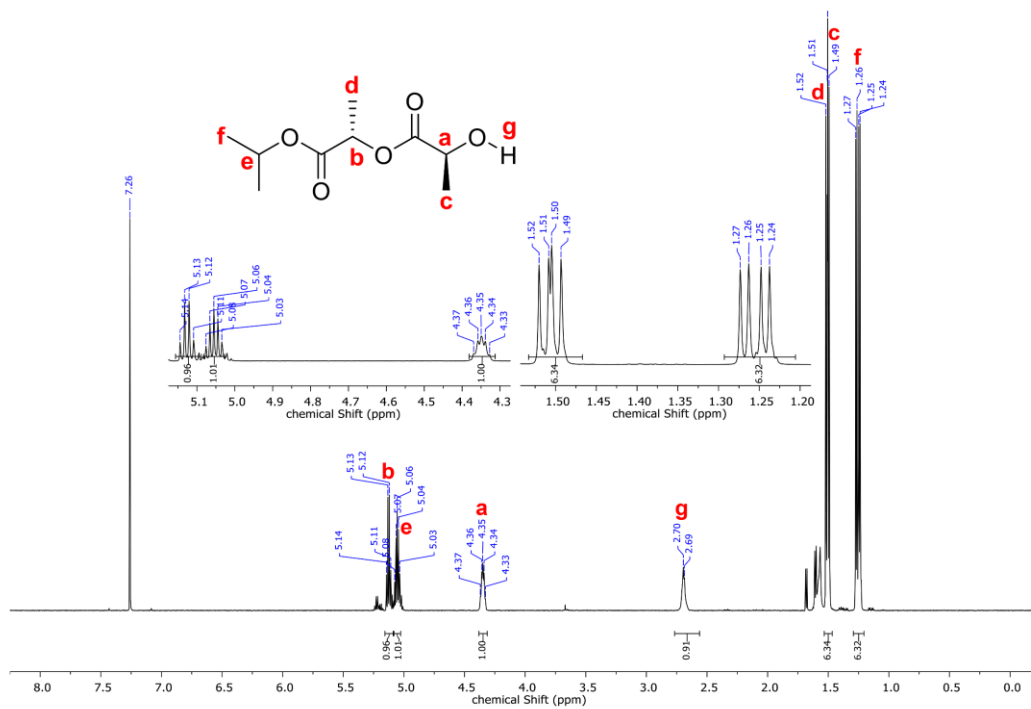
Figure S5 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified methyl 4-hydroxybutanoate.

Figure S6 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified methyl 4-hydroxybutanoate.

Figure S7 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified methyl 5-hydroxypentanoate.
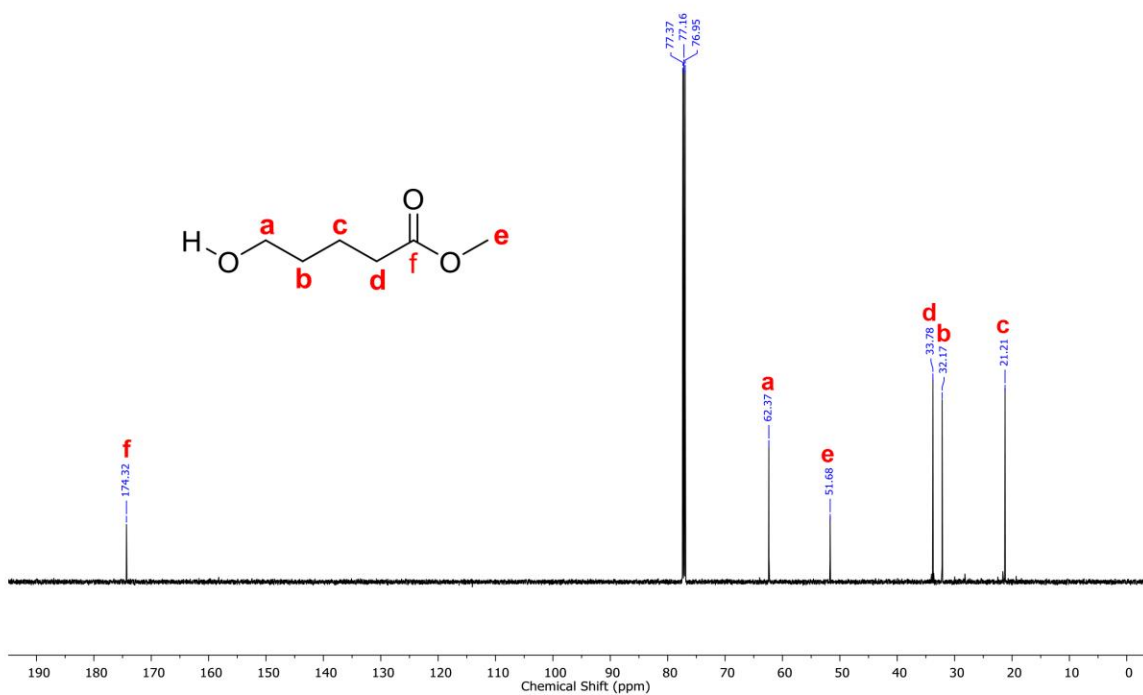
Figure S8 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified methyl 5-hydroxypentanoate.

Figure S9 ¹H-NMR spectrum (CDCl₃, 600 MHz, 30°C) of the purified methyl 6-hydroxyhexanoate.
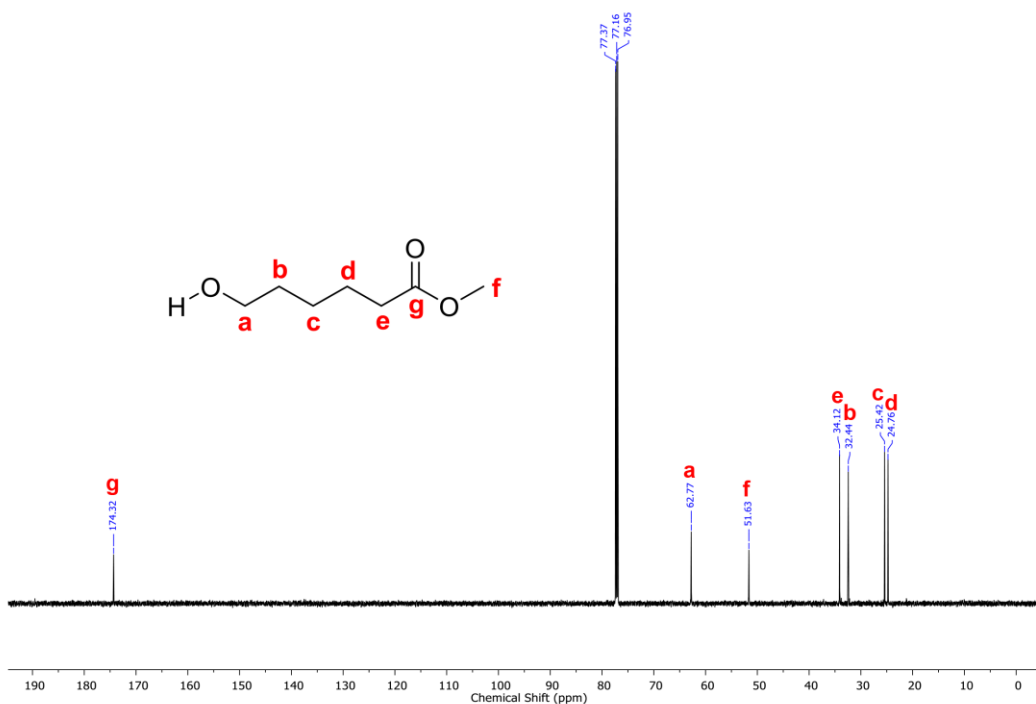
Figure S10 ¹³C-NMR spectrum (CDCl₃, 151 MHz, 30°C) of the purified methyl 6-hydroxyhexanoate.

Figure S11 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified ethyl (*S*,*S*)-lactyllactate.

Figure S12 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified ethyl (*S*,*S*)-lactyllactate.
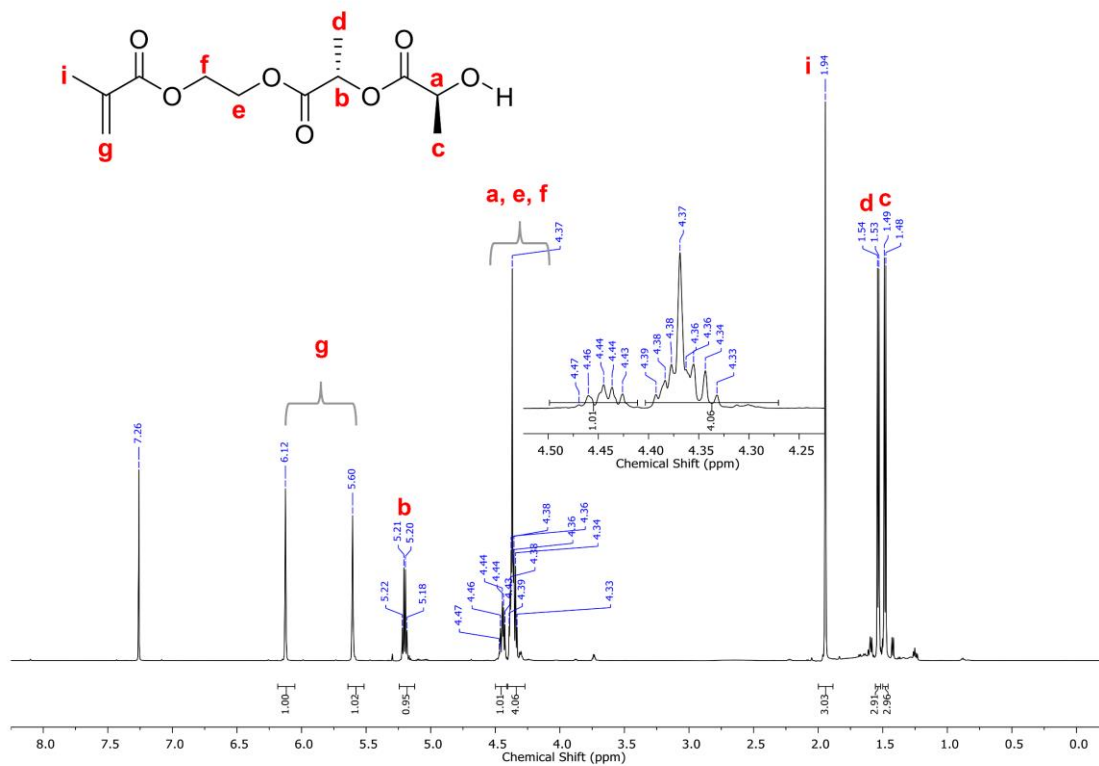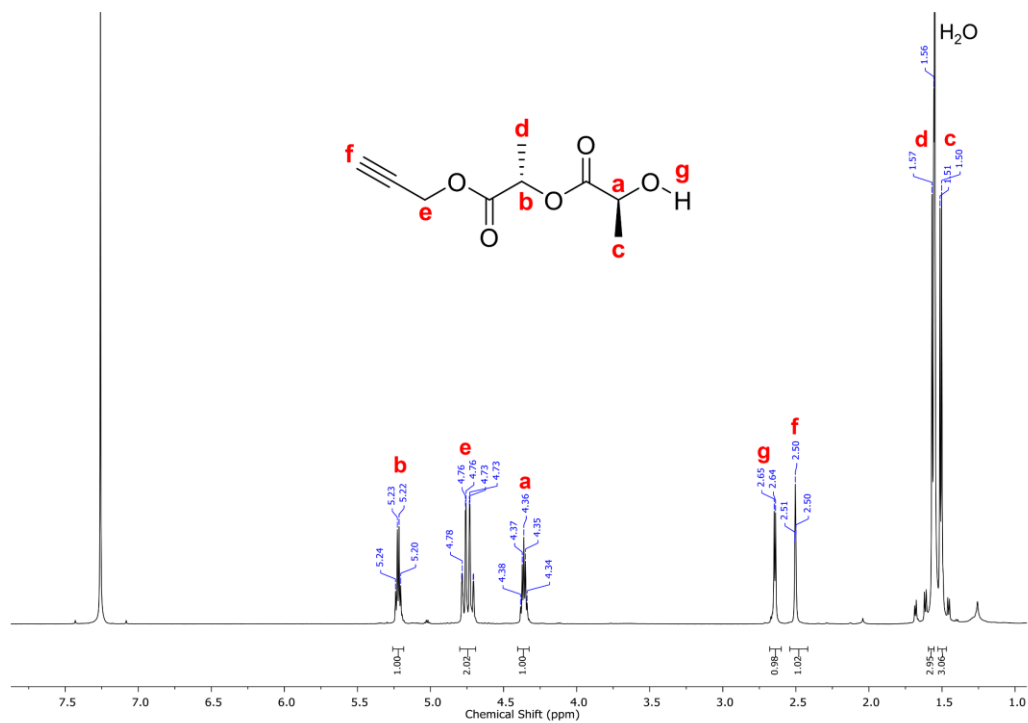
Figure S13 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified benzyl (*S*,*S*)-lactyllactate.

Figure S14 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified benzyl (*S*,*S*)-lactyllactate.

S13

Figure S15 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified isopropyl (*S*,*S*)-lactyllactate.
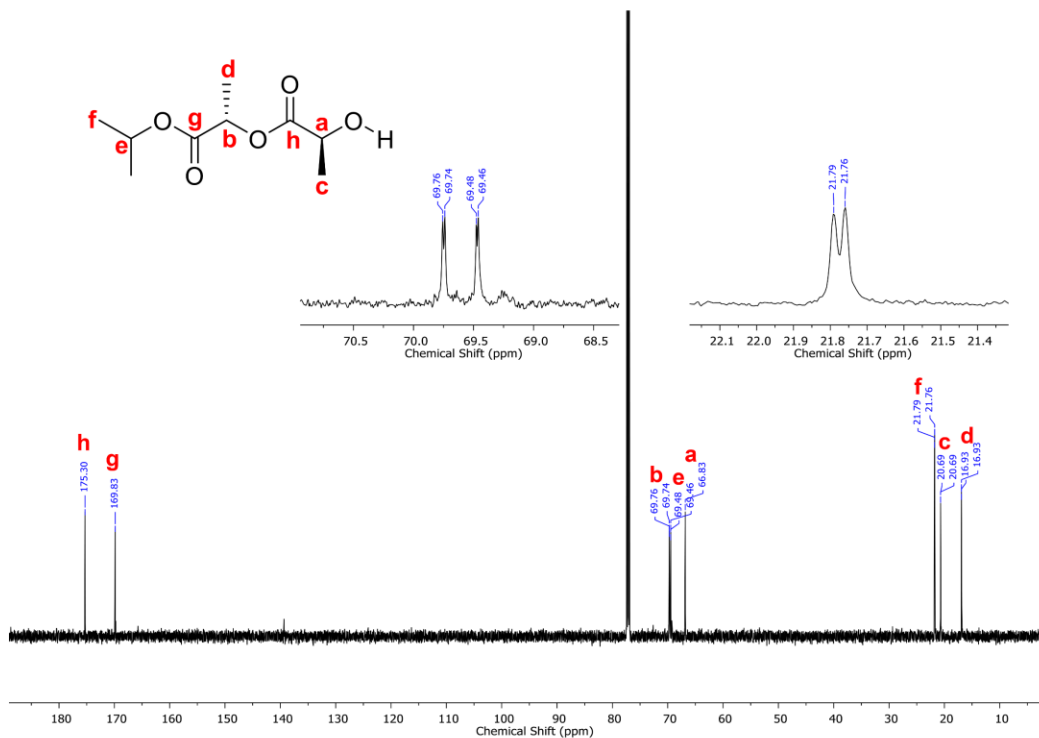
Figure S16 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified isopropyl (*S*,*S*)-lactyllactate.

S14

Figure S17 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified 2-(methacryloyl)ethyl (*S*,*S*)-lactyllactate.
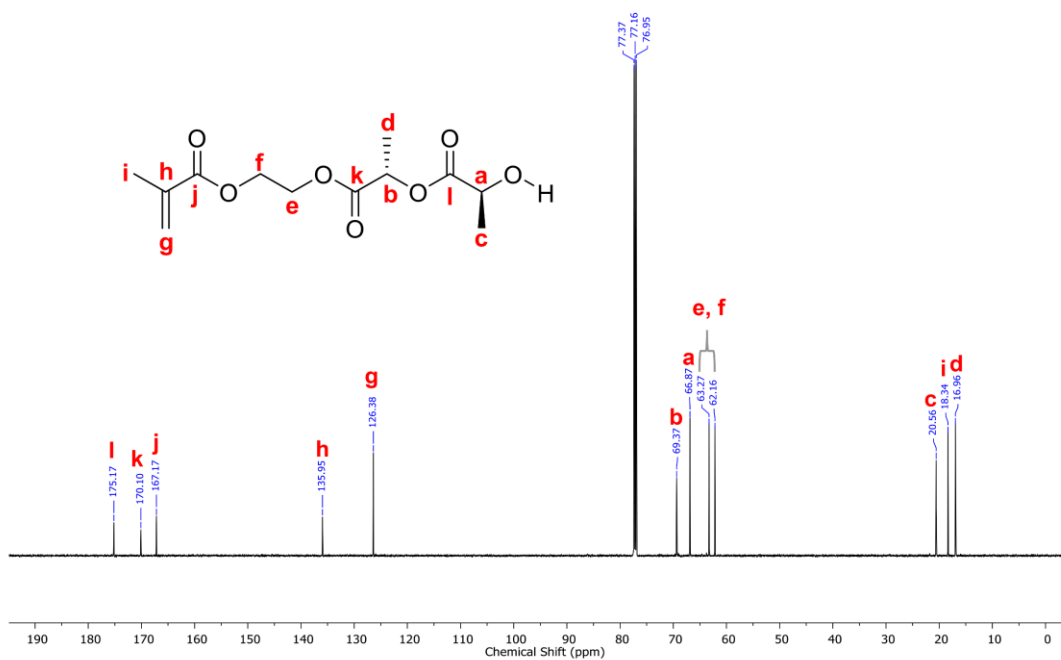
Figure S18 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified 2-(methacryloyl)ethyl (*S*,*S*)-lactyllactate.

S15

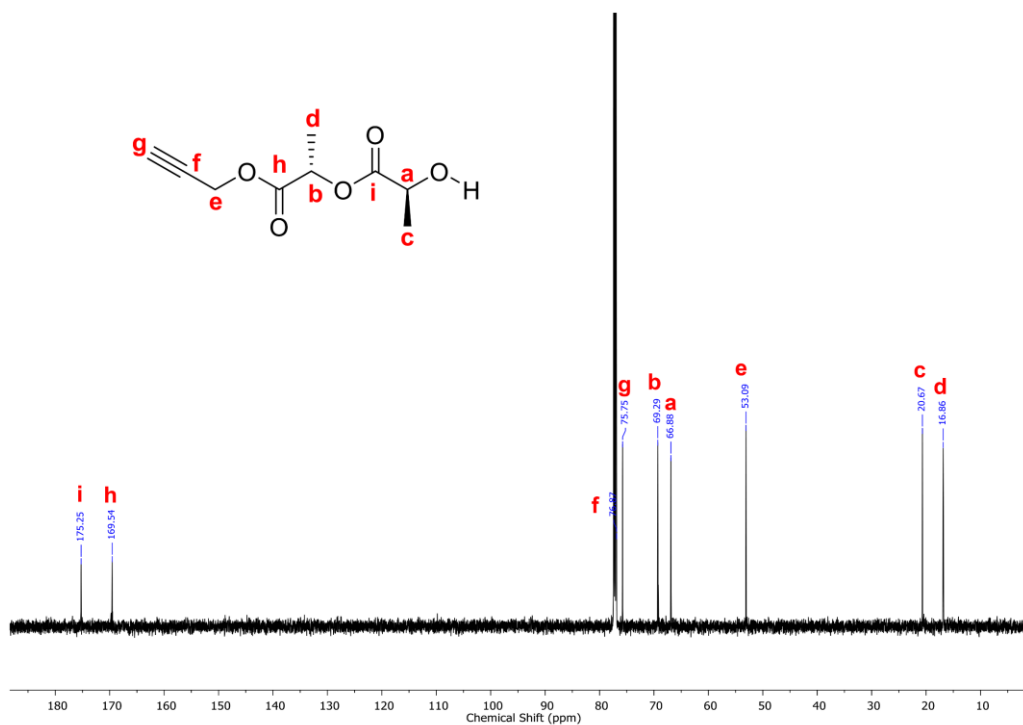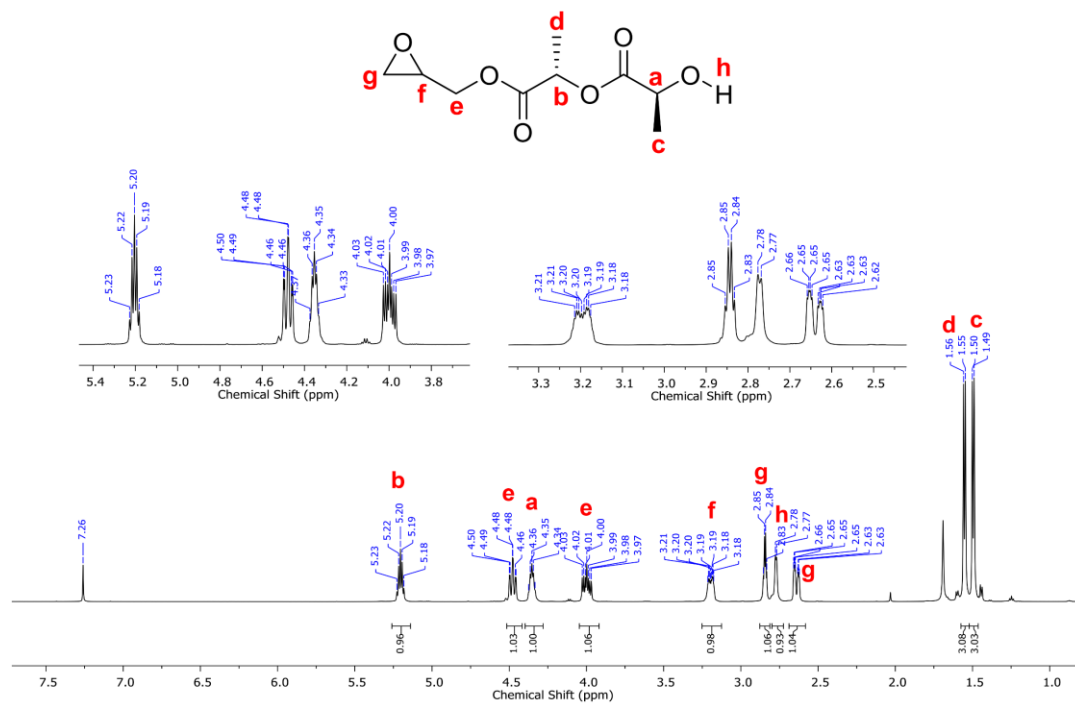**Figure S19** ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified propargyl (*S,S*)-lactyllactate.

Figure S20 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified propargyl (*S,S*)-lactyllactate.

S16

Figure S21 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the purified glycidyl (*S,S*)-lactyllactate (mixtures of diastereomers).
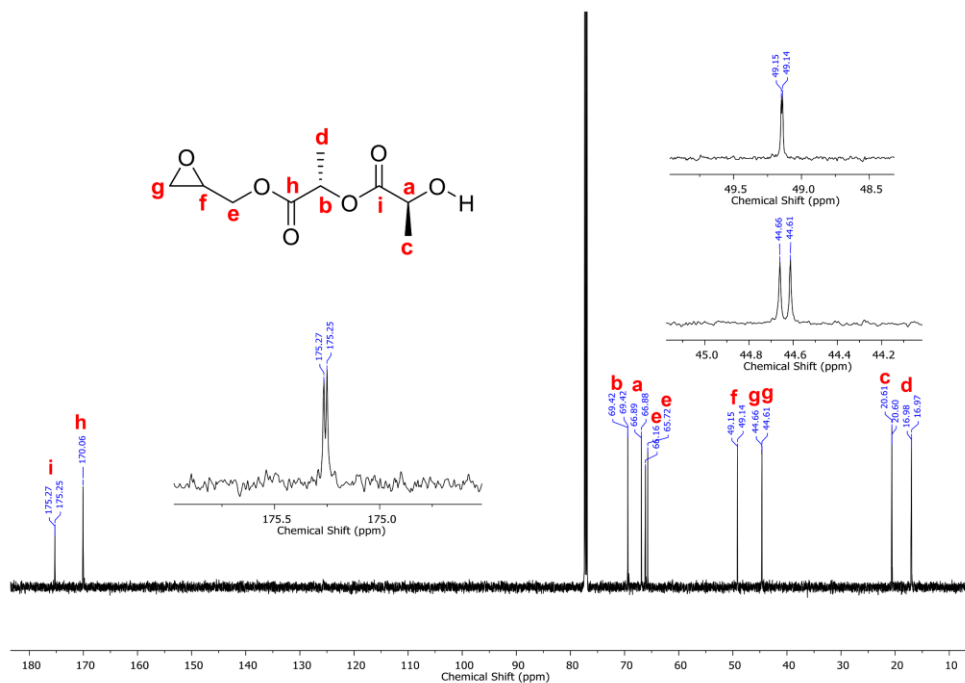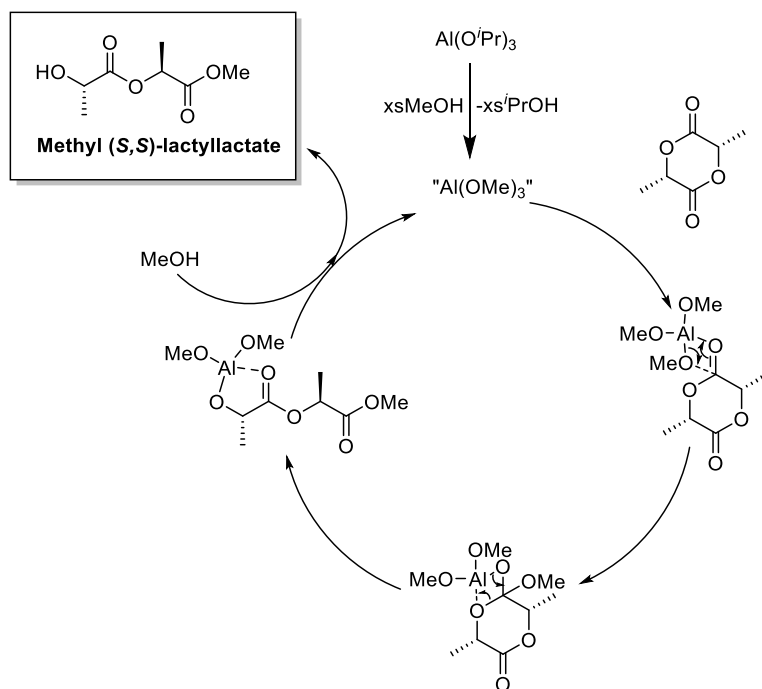

Figure S22 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the purified glycidyl (*S,S*)-lactyllactate (mixtures of diastereomers).

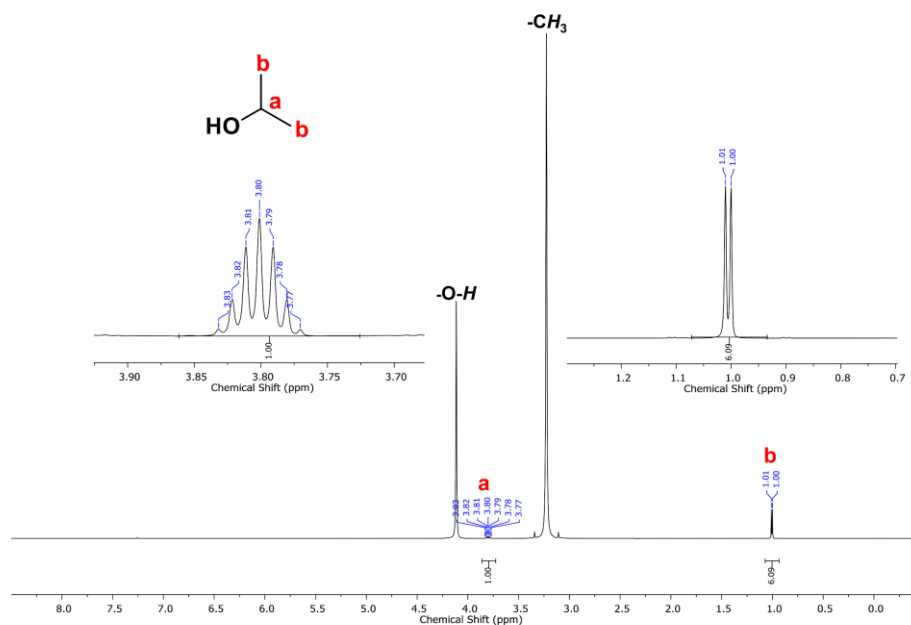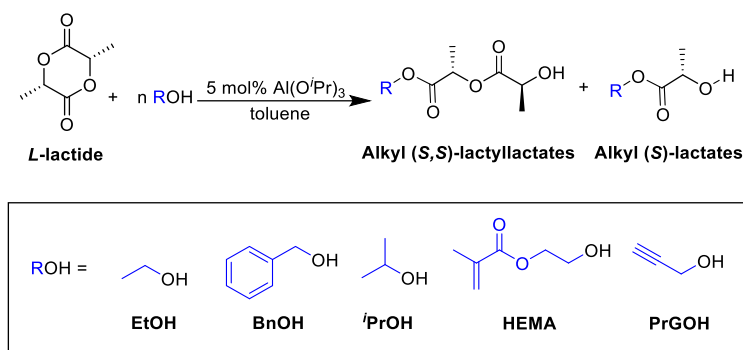**Scheme S1** Proposed mechanism of the methanolysis of *L*-lactide.

Figure S23 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the free isopropanol generated instantaneously from the fast proton exchange between Al(O*^{i}*Pr)$_3$ and excess methanol.

Table S1 Alcoholysis of *L*-lactide with different alcohols

| Entry	ROH	[ROH]/ [LA]	T (°C)	Time (min)	%Conv^a	Product Distribution	
						%ALL^a	%AL^a
1	EtOH	5	70	10	98	18	82
2	BnOH	5	70	15	99	34	66
3	^{i}PrOH	5	70	2 h	94	30	70
4	HEMA	1.5	90	30	94	75	25
5	PrGOH	1.5	90	10	97	35	65

Reaction conditions: *L*-lactide (3.47 mmol), alcohol, catalyst (5 mol%, 174 µmol), toluene (4 mL), performed at least in duplicate. ^{a}Determined by ^{1}H-NMR analysis.

Table S2 Methanolysis of lactones catalyzed by Al(O^{i}Pr)$_3$ catalyst
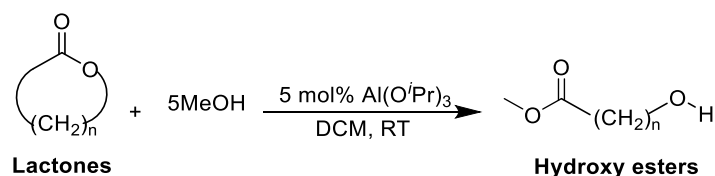
Entry	Monomer	Time (h)	%Conv^a
1	*β*-BL	8	94
2	*γ*-BL	2	92
3	*δ*-VL	1.5	94
4	*ε*-CL	4	93

Reaction conditions: lactone (3.47 mmol), methanol (0.7 mL, 17.4 mmol), Al(O^{i}Pr)$_3$ (5 mol%, 174 µmol), DCM (4 mL), RT. ^{a}Determined by ^{1}H-NMR analysis.

General procedure for the synthesis of poly(glycidyl lactyllactate) (PGDLA)
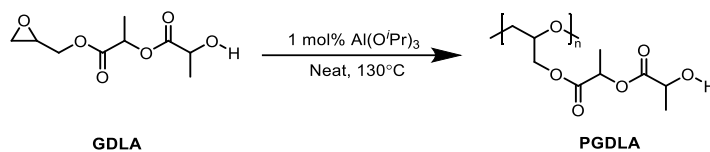
The reaction mixture of GDLA (1.83 mmol, 0.4 g) in the presence of Al(O^{i}Pr)$_3$ catalyst (3.74 mg, 18.3 µmol, 1 mol%) was prepared and then heated at 130°C with stirring for 72 h yielding viscous PGDLA polymer (93% conversion of GDLA). The crude polymer was dissolved in dichloromethane and then filtered to remove all solid components. The resulting polymers were subsequently purified by precipitating in cold hexane and dry under vacuum. The product was analysed by ^{1}H- and ^{13}C-NMR spectroscopy, GPC, TGA, and DSC measurements.
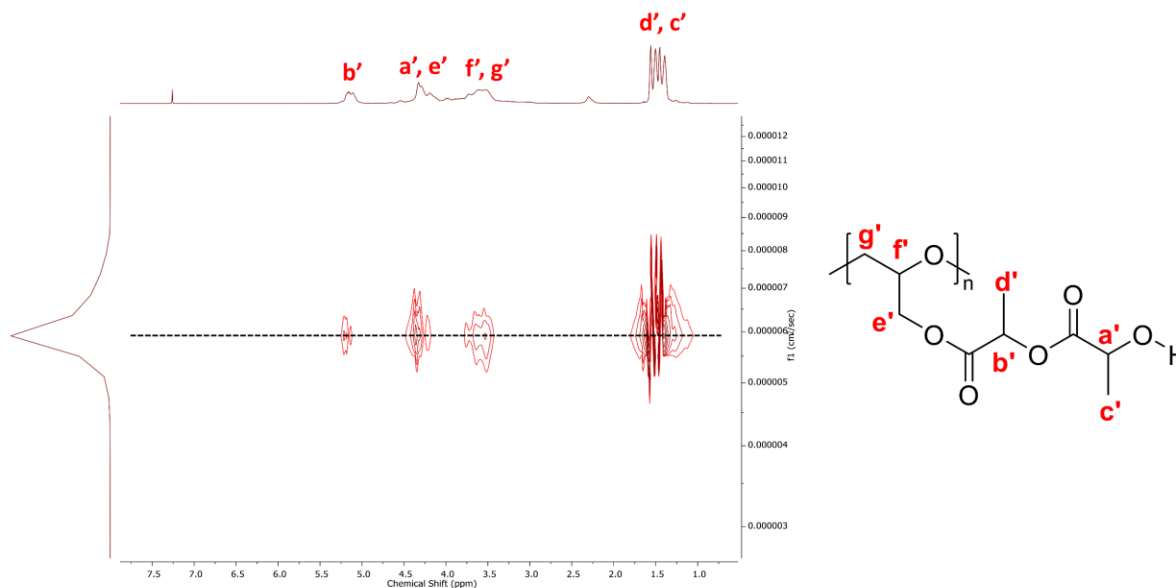

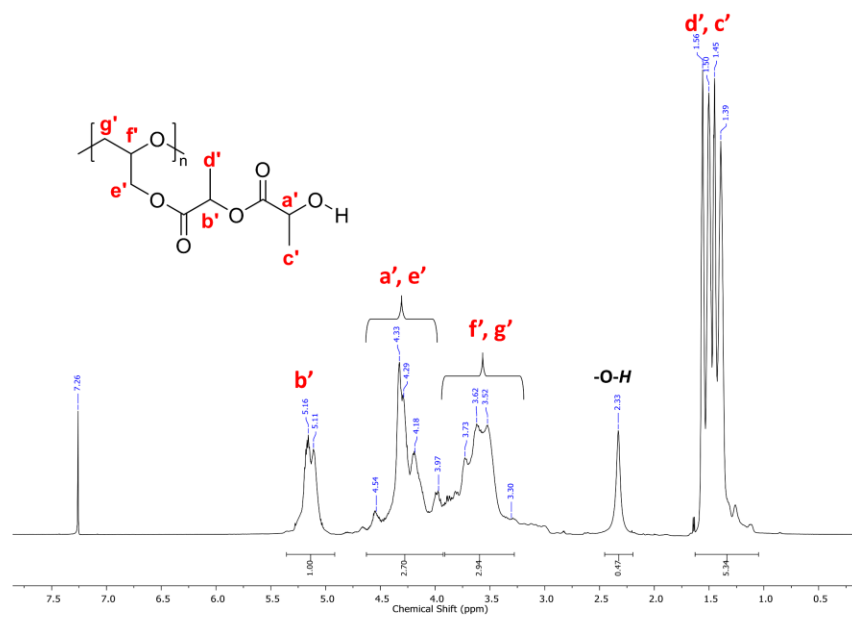**Figure S24** ^{1}H-DOSY-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the resulting poly(glycidyl lactyllactate).

Figure S25 ^{1}H-NMR spectrum (CDCl$_3$, 600 MHz, 30°C) of the resulting poly(glycidyl lactyllactate).
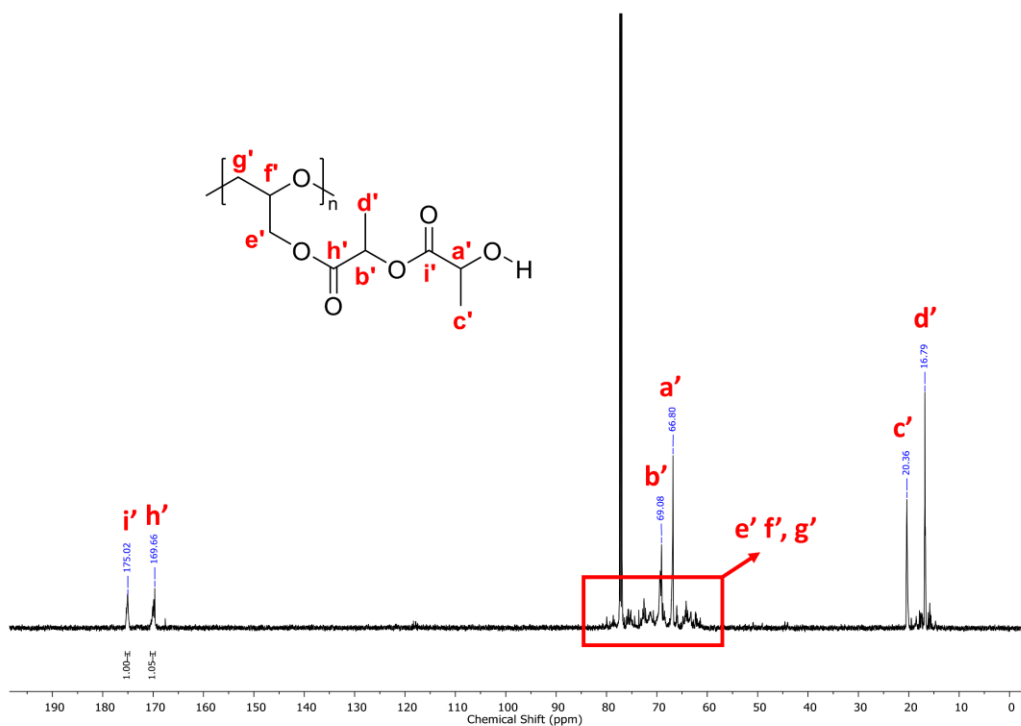

Figure S26 ^{13}C-NMR spectrum (CDCl$_3$, 151 MHz, 30°C) of the resulting poly(glycidyl lactyllactate).
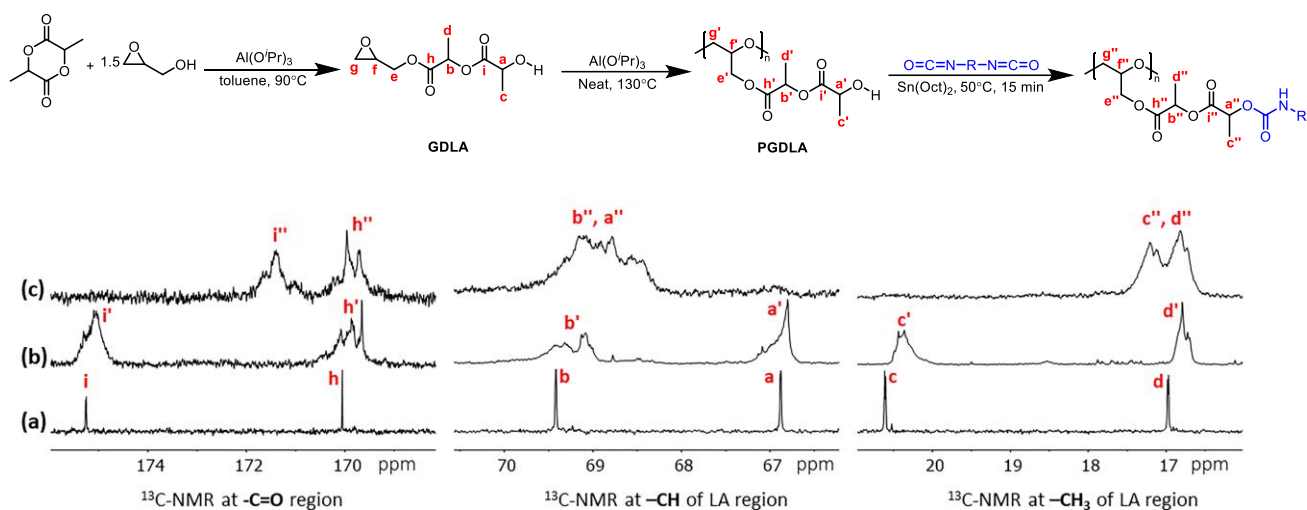
S21

Figure S27 ^{13}C-NMR spectra (CDCl$_3$, 30°C) at carbonyl, methine, and methyl carbon regions of (a) glycidyl (*S*,*S*)-lactyllactate (GDLA), (b) poly(glycidyl lactyllactate) (PGDLA), and (c) PGDLA reacted with excess HDI.
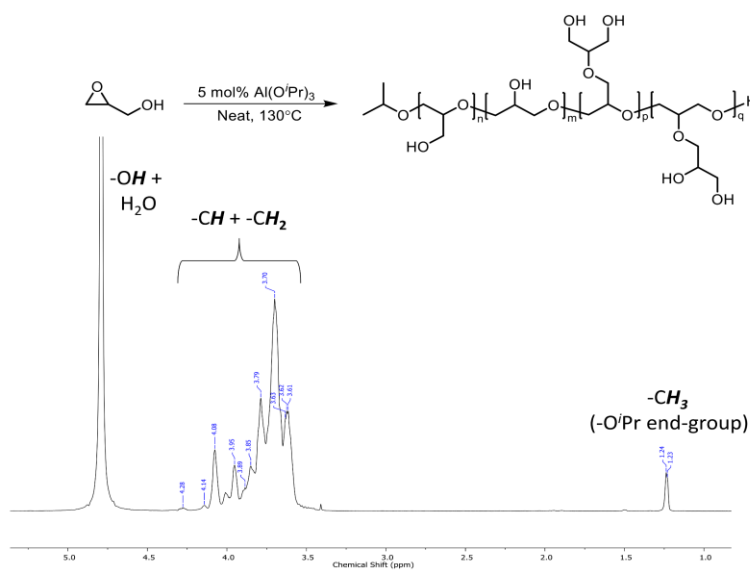

Figure S28 ^{1}H-NMR spectrum (D$_2$O, 600 MHz, 30°C) of the obtained polyglycidol (PGD) from the ring-opening polymerization of glycidol at 130°C under neat condition using 5 mol% Al(O^{i}Pr)$_3$ as a catalyst.
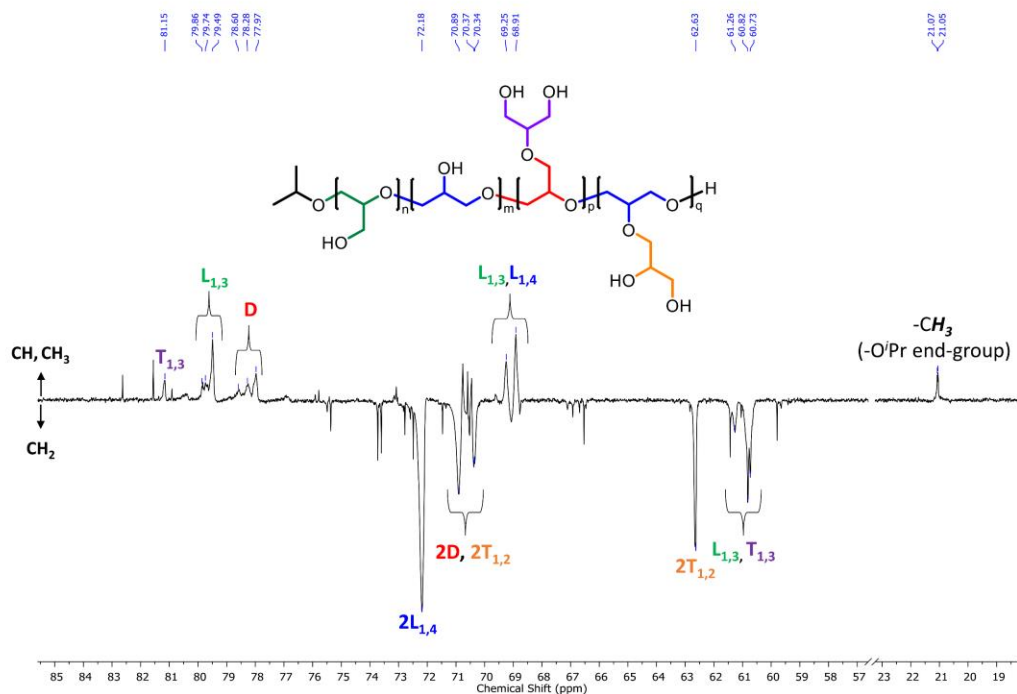
Figure S29 DEPT-135 ^{13}C-NMR spectrum (D$_2$O, 151 MHz, 30°C) of the obtained polyglycidol (PGD) from the ring-opening polymerization of glycidol at 130°C under neat condition using 5 mol% Al(O^{i}Pr)$_3$ as a catalyst.[3, 4] D: Dendritic units; L$_{1,3}$: Linear 1,3 units; L$_{1,4}$: Linear 1,4 units; T$_{1,2}$: Terminal 1,2 units; T$_{1,3}$: Terminal 1,3 units.

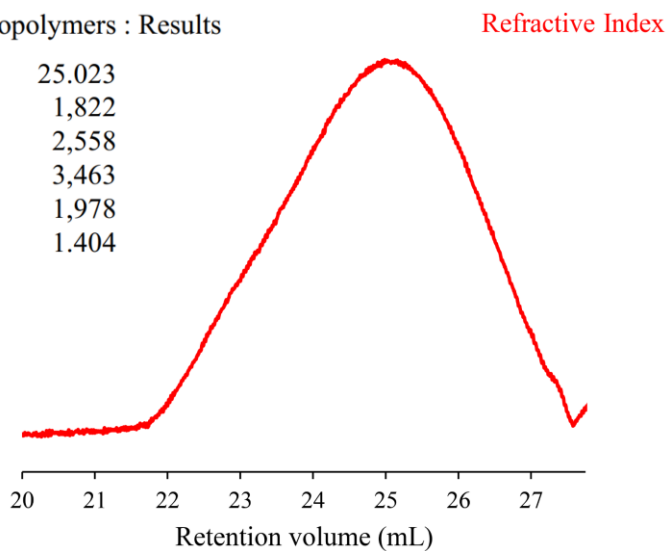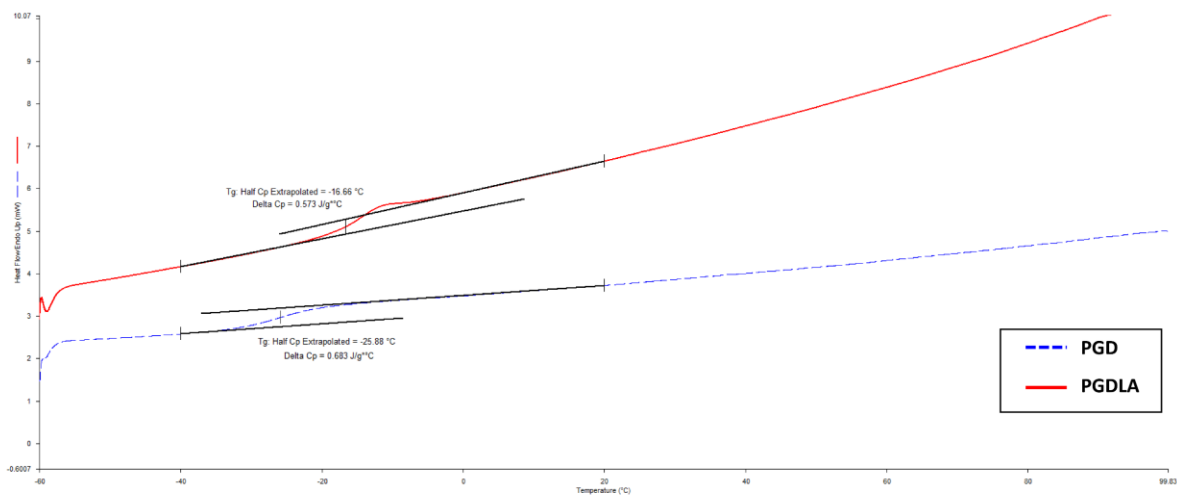**Figure S30** GPC profile of the resultant poly(glycidyl lactyllactate) (PGDLA) obtained using 1 mol% Al(O^{i}Pr)$_3$ as a catalyst.

Figure S31 DSC curves of the polymers obtained by using Al(O^{i}Pr)$_3$ as a catalyst. PGD: Polyglycidol. PGDLA: Poly(glycidyl lactyllactate).
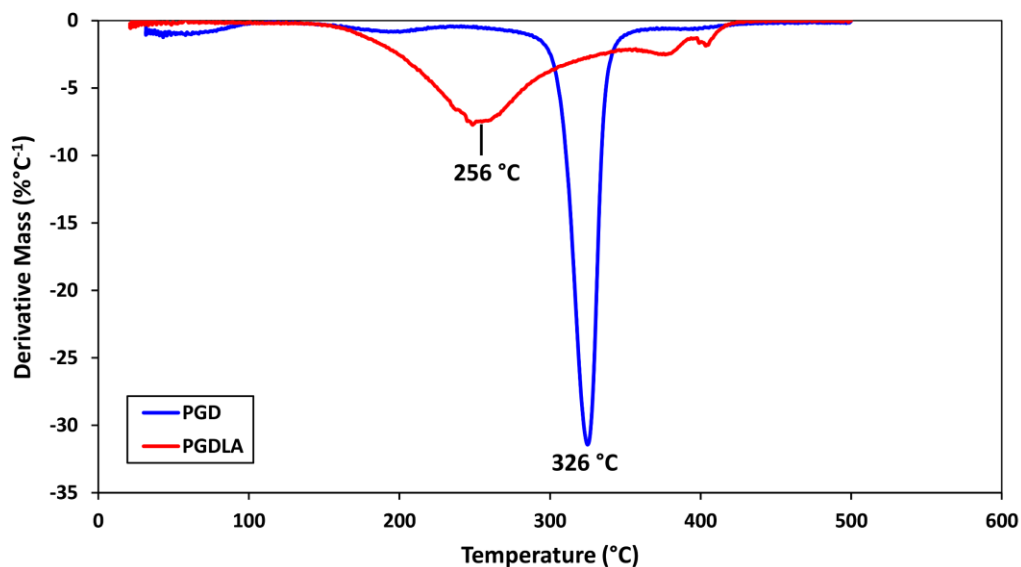

Figure S32 Derivative mass curves for the polymers heated at a heating rate of 10°C/min. The numbers represent the temperatures of maximum mass loss rate (T_{max}). PGD: Polyglycidol. PGDLA: Poly(glycidyl lactyllactate).
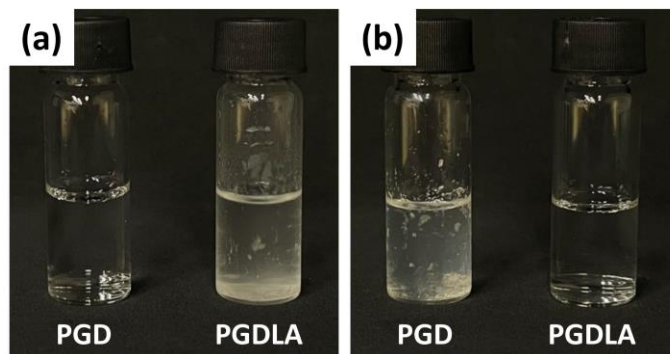
Figure S33 The solubility of PGD and PGDLA in (a) water and (b) DCM.

References

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