

Low-Temperature and Purification-free Stereocontrolled Ring-Opening Polymerisation of Lactide in Supercritical Carbon Dioxide

Supporting Information

Simon P. Bassett,^{a†} Andrew D. Russell,^{b†} Paul McKeown,^b Isabel Robinson,^b Thomas R. Forder,^b Vincenzo Taresco,^a Matthew G. Davidson,^b and Steven M. Howdle^a

^aSchool of Chemistry, University of Nottingham, Nottingham, NG7 2RD, UK. Email: steve.howdle@nottingham.ac.uk

^bDepartment of Chemistry, University of Bath, Claverton Down, Bath, BA2 7AY, UK. Email: m.g.davidson@bath.ac.uk

Experimental

Materials

Catalyst/initiator [(ⁱPrO)Zr(OPh(^tBu)₂-CH₂)₃N] (**1**) was prepared *via* a literature procedure,¹ and purified through recrystallisation from hot toluene, subsequently cooled to -20 °C. Anhydrous toluene was obtained using a Grubbs' type solvent-purification system (SPS). *rac*-LA was purchased from Sigma Aldrich, recrystallised from hot toluene (dry), isolated and dried *in vacuo* for 16 h and stored under Ar. *Materials characterisation* (¹H NMR, MALDI-TOF) *facilities were provided through the Material and Chemical Characterisation Facility (MC²) at the University of Bath (<http://www.bath.ac.uk/research-facilities/material-and-chemical-characterisation-facility-mc2/>).*

Polymerisations in the melt

The procedure for a typical melt polymerisation was as follows: In a glove box, a J Young's tube was charged with *rac*-lactide (1 g, 6.9 mmol) and **1** in the associated stoichiometry for the experiment. The tube was sealed, removed from the glovebox and placed in an oil bath, pre-heated to the relevant temperature (180 °C). The monomer quickly liquefied and the reaction mixture gradually solidified over the course of the experiment. Upon complete solidification, the tube was removed, allowed to cool and CH₂Cl₂ (5 mL) was added to dissolve the solid residue. The resulting solution was precipitated into a vortex of MeOH (25 mL) to afford a white solid, which was isolated and dried *in vacuo* (40 °C) for 16 h.

Polymerisations in scCO₂

Polymerisation reactions were conducted in an in-house fabricated autoclave (University of Nottingham) which was leak tested prior to use using 60 bar of CO₂ at ambient temperature.²⁻³ A typical reaction involved charging the autoclave with *rac*-lactide (1 g) and **1** (57 mg), before purging with CO₂ at 2 bar for 10 min. The vessel was sealed, and the pressure increased to 55 bar at ambient temperature (typically 18 °C) through addition of CO₂. The temperature was then increased to the experimental temperature (60 – 130 °C), with agitation, before the pressure was raised to that required for the experiment (60 – 240 bar) for the set reaction time (0.1 – 24 h). Upon completion of the experiment, the autoclave was cooled over the period of 30 min to around 25 °C, then the pressure released by venting any remaining CO₂. The autoclave was then opened and the product removed. The unreacted LA was not removed and the samples were analysed without further purification.

Characterisation

NMR

CDCl₃ was purchased from Sigma Aldrich and used as received. ¹H NMR experiments were performed on a Bruker 300 MHz, 400 MHz or 500 MHz spectrometers. ¹H NMR spectra were referenced to the residual protons of the deuterated solvent (CDCl₃: δ = 7.27 ppm). Homonuclear decoupled (HND) ¹H NMR spectra were recorded on either a Bruker 400 MHz or 500 MHz spectrometer.

SEC

Molecular weight and dispersity ($D=M_w/M_n$) of all polymers were obtained by Size Exclusion Chromatography (SEC) which was performed at the University of Bath, using an Agilent 1260 Infinity Gel Permeation Chromatograph equipped with autosampler, pump, injector, in-line degasser, column oven (35 °C), 2 HFIPgel 300 x 7.5 mm columns, a HFIPgel 50 x 7.5 mm guard column, a refractive index detector (658 nm), a

viscometer detector and dual angle LS detectors. A flow rate of 1.0 mL min⁻¹ was used with THF as the eluent. Samples were dissolved in THF (1 mg mL⁻¹) and filtered (0.45 μM PTFE membrane).

MALDI

MALDI-TOF was conducted at the University of Bath using a Bruker Autoflex Speed MALDI mass spectrometer equipped with a 2 kHz Smartbeam-II laser. THF solutions of each polymer (5 mg mL⁻¹) were combined with sodium trifluoroacetate (0.1 M) and the matrix trans-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (10 mg mL⁻¹) in a 25:1:5 ratio, and the samples centrifuged for 5 minutes. A micropipette was used to spot ca. 2 μL of the solution onto a polished steel MALDI plate and the solvent allowed to evaporate in air. Once loaded, positive ion detection MALDI spectra were obtained in both linear and reflector modes. Laser intensity was varied. The data were analysed using the Flex Analysis software, version 3.4 (build 76).

Table S1. PLA synthesis in scCO₂

Entry	p / bar	T / °C	M/l	t / h	Monomer		P _r ^b	M _{n(theor)} ^c	M _n ^d	Đ ^d
					amount	Conv. / % ^a				
					(g)					
8*	60	80	100	1	1	31	n.d.	4500	n.d.	n.d.
9	120	80	100	1	1	83	0.82	12000	16,500	1.49
10	240	80	100	1	0.1	0	n.d.	n.d.	n.d.	n.d.
11	240	80	150	1	1	61	0.82	13200	14,100	1.32
12	240	80	300	1	3	47	0.83	20,300	15,650	1.15
13	240	80	300	16	3	87	0.76	37,600	10,000	1.23
14	240	80	300	24	3	84	0.74	36,300	12,850	1.18
15	240	100	300	1	3	71	0.80	30,700	15,950	1.48

[a] Determined by ¹H NMR spectroscopy. [b] P_r is the probability of heterotactic enchainment calculated through analysis of the homonuclear decoupled ¹H NMR spectra. [c] Theoretical M_n (Da) calculated using the formula $(\frac{[rac-LA]_0}{[1]_0}) \times M_{rac-LA} \times \text{conversion}/100 + M_{OIPr}$. [d] Molecular weight (Da) determined by triple detection SEC in THF.

*low conversion, P_r and GPC data could not be assessed.

SEC Traces

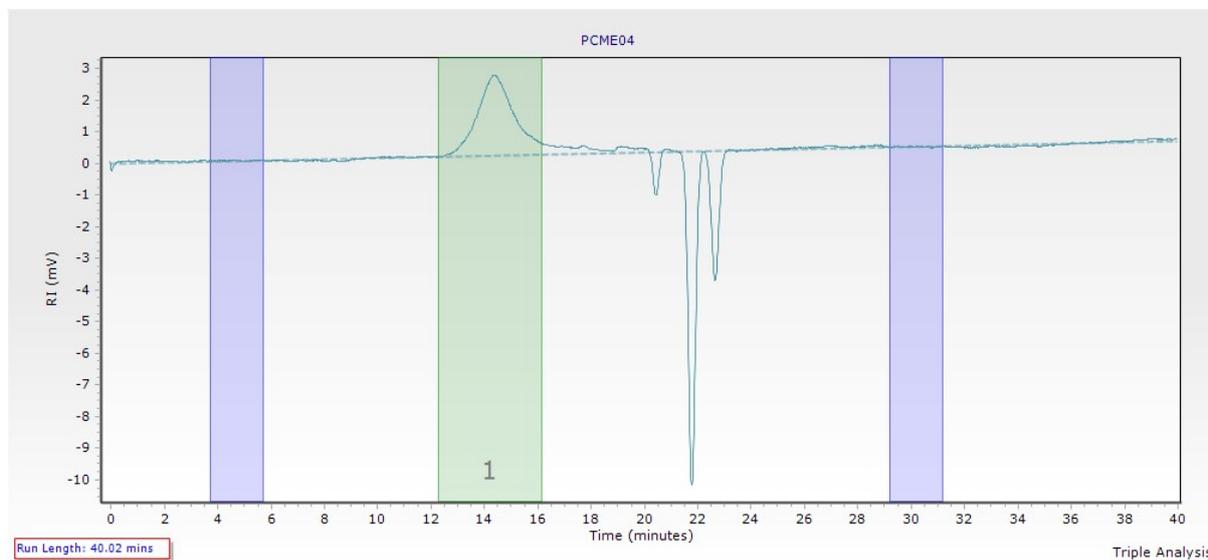


Figure S1. GPC trace for Table 1, Entry 2 (PLA furnished from a reaction at 240 bar CO₂, 80 °C, 100:1 [*rac*-LA]:[**1**] and 1 h reaction time).

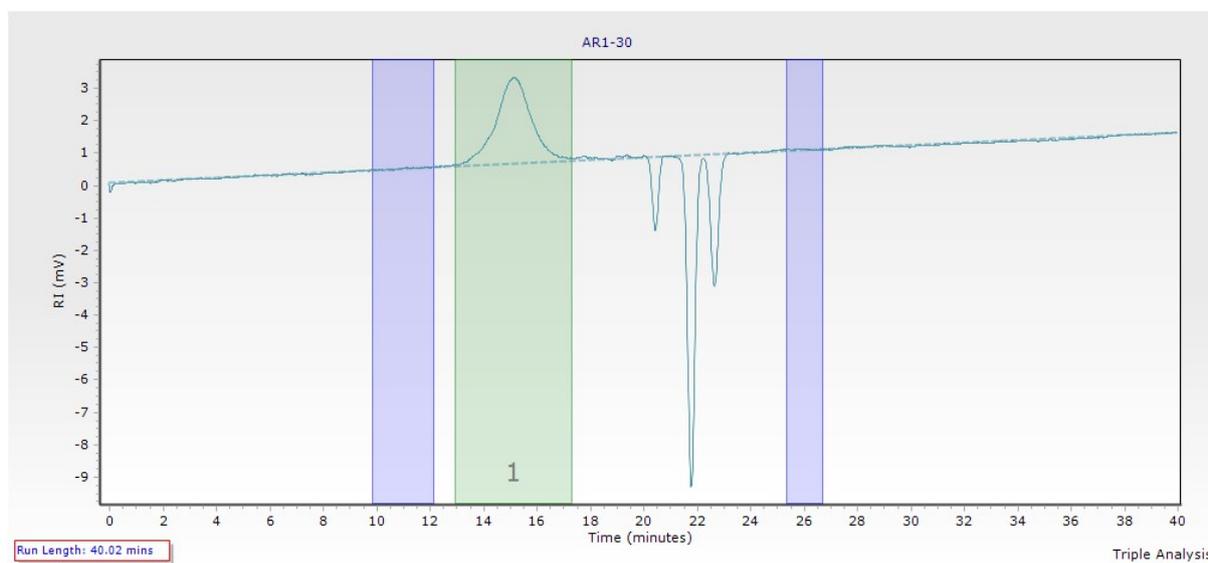


Figure S2. GPC trace for Table 1, Entry 3 (PLA furnished from a reaction at 240 bar CO₂, 100 °C, 100:1 [*rac*-LA]:[**1**] and 1 h reaction time).

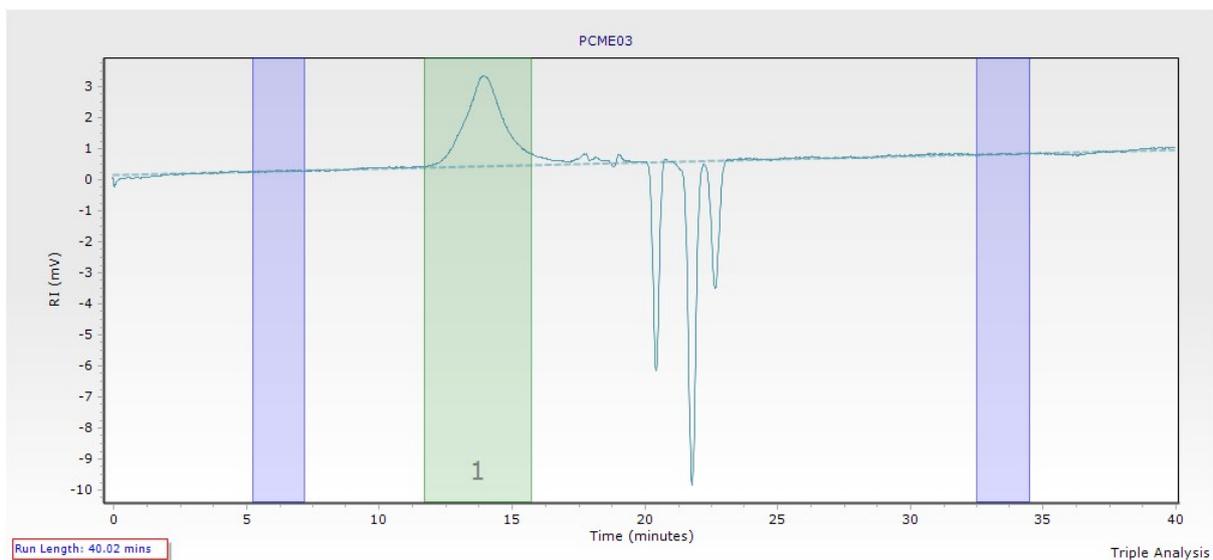


Figure S3. GPC trace for Table 1, Entry 4 (PLA furnished from a reaction at 240 bar CO₂, 130 °C, 100:1 [*rac*-LA]:[**1**] and 1 h reaction time).

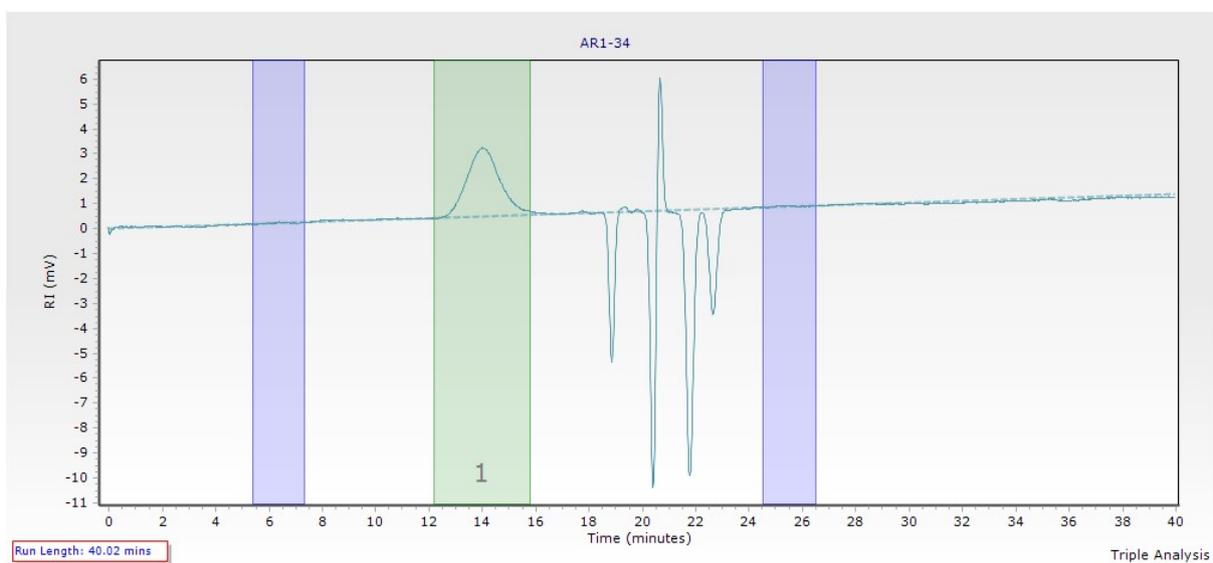


Figure S4. GPC trace for Table 1, Entry 5 (PLA furnished from a reaction at 240 bar CO₂, 80 °C, 100:1 [*rac*-LA]:[**1**] and 0.1 h reaction time).

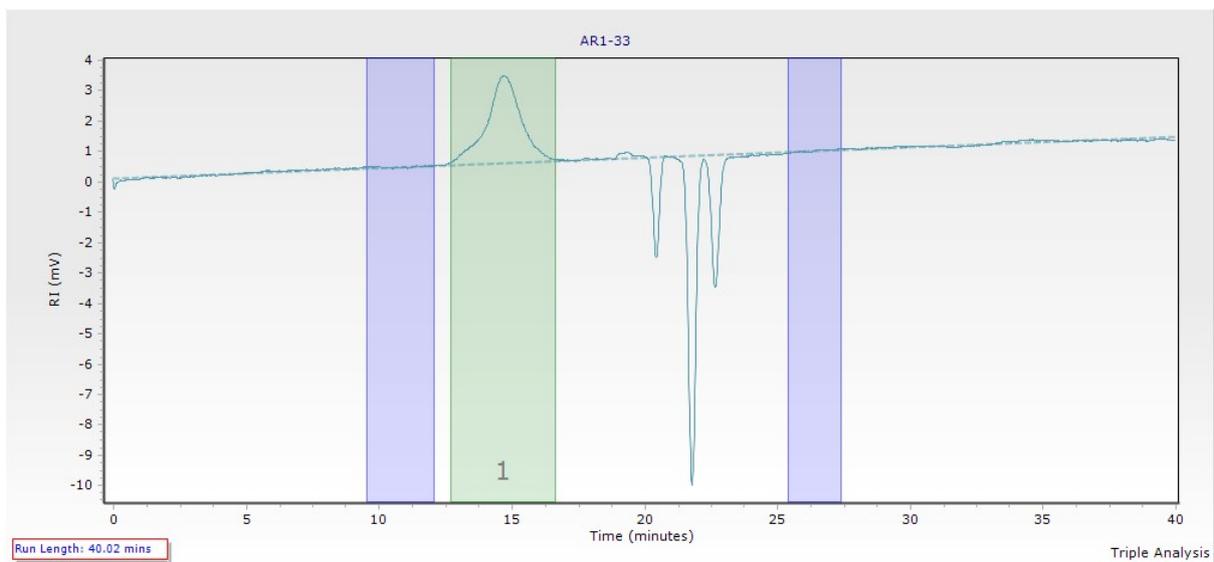


Figure S5. GPC trace for Table 1, Entry 6 (PLA furnished from a reaction at 240 bar CO₂, 100 °C, 100:1 [*rac*-LA]:[**1**] and 0.1 h reaction time).

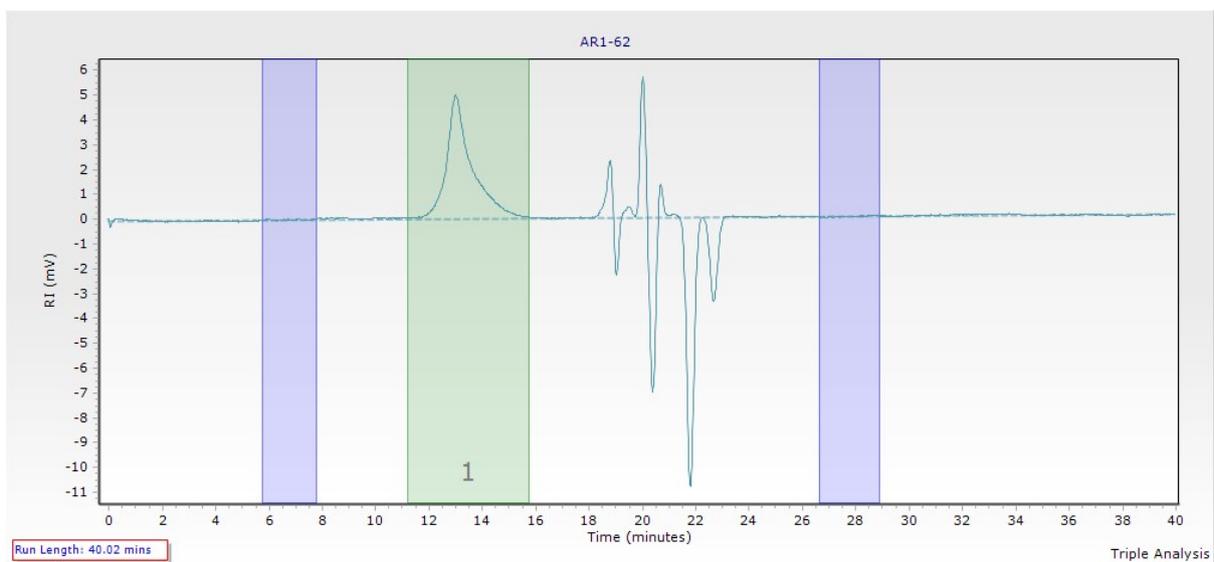


Figure S6. GPC trace for Table 1, Entry 7 (PLA furnished from a reaction in the melt, 180 °C, 100:1 [*rac*-LA]:[**1**] and 1 h reaction time).

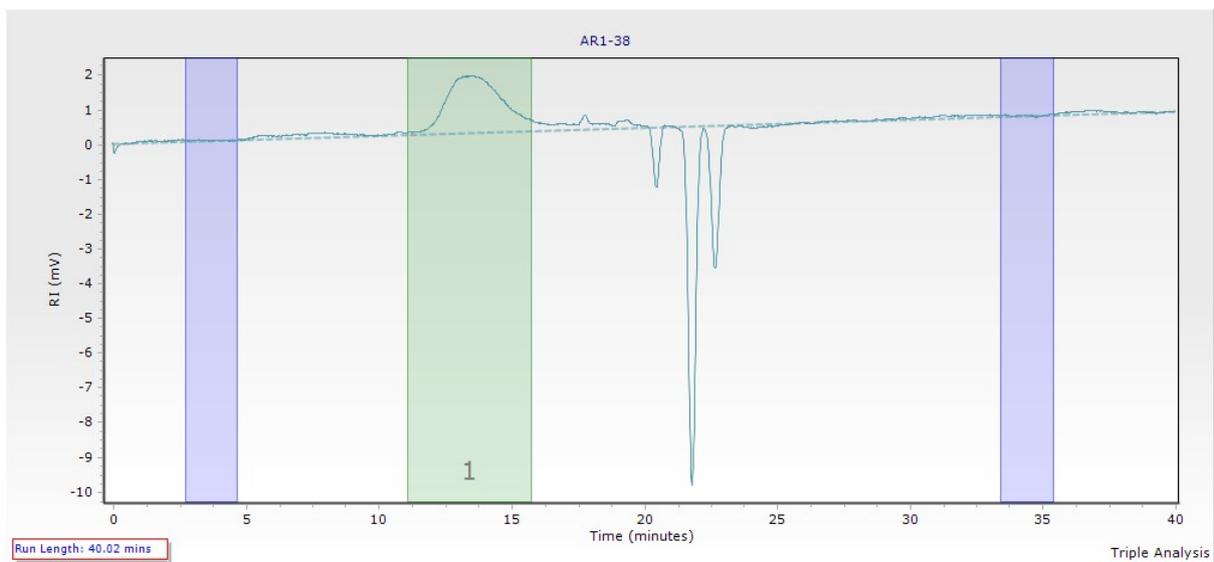


Figure S7. GPC trace for Table S1, Entry 9 (PLA furnished from a reaction at 120 bar CO₂, 80 °C, 100:1 [*rac*-LA]:[**1**] and 1 h reaction time).

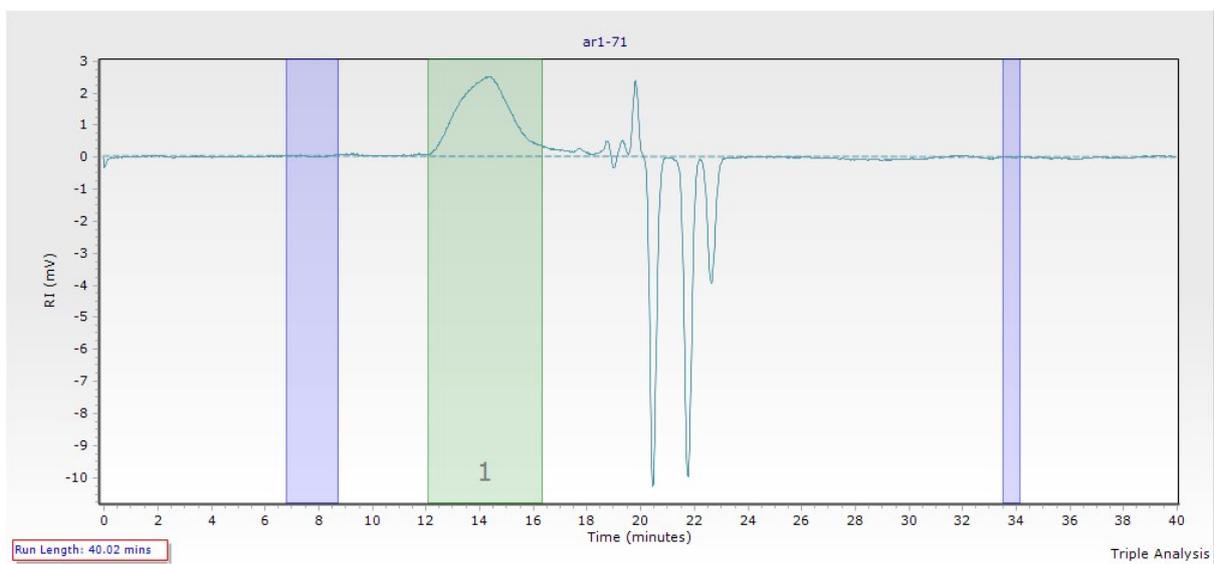


Figure S8. GPC trace for Table S1, Entry 11 (PLA furnished from a reaction at 240 bar CO₂, 80 °C, 150:1 [*rac*-LA]:[**1**] and 1 h reaction time).

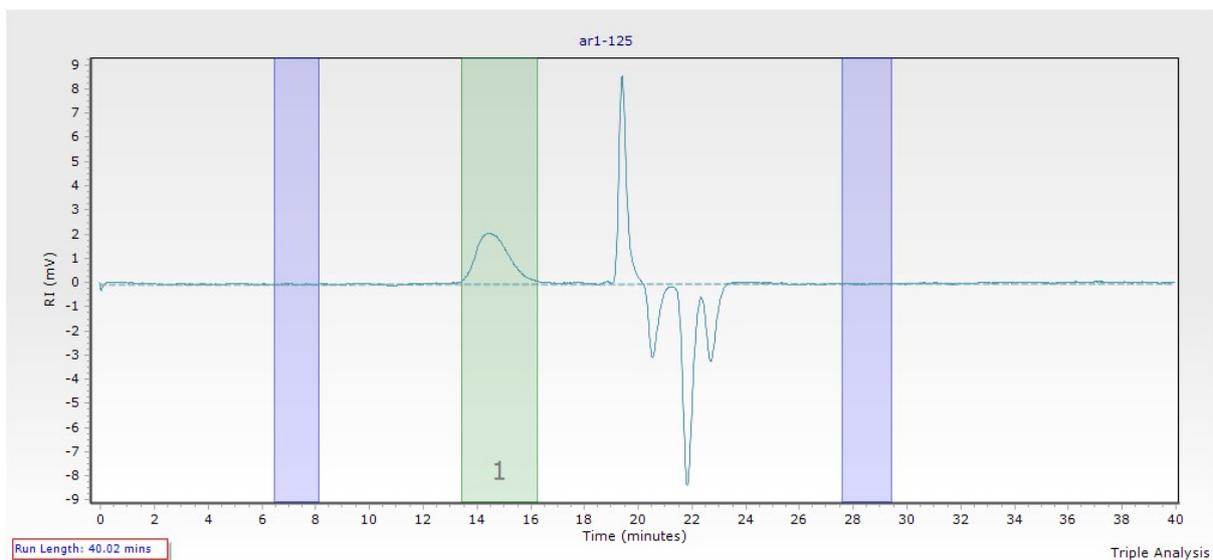


Figure S9. GPC trace for Table S1, Entry 12 (PLA furnished from a reaction at 240 bar CO₂, 80 °C, 300:1 [*rac*-LA]:[**1**] and 1 h reaction time).

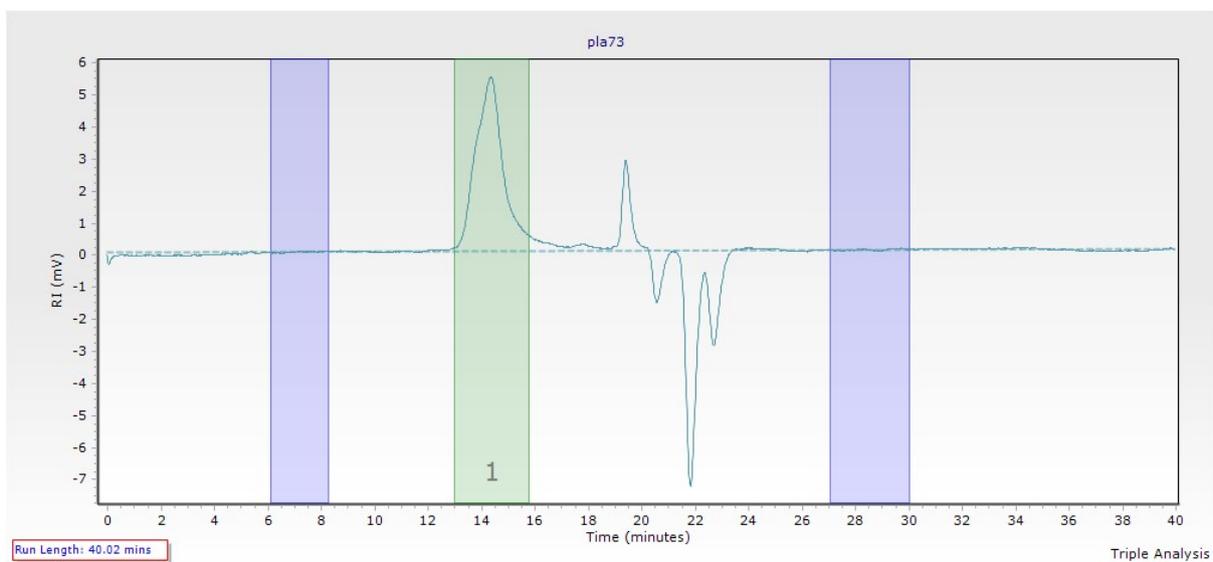


Figure S10. GPC trace for Table S1, Entry 13 (PLA furnished from a reaction at 240 bar CO₂, 80 °C, 300:1 [*rac*-LA]:[**1**] and 16 h reaction time).

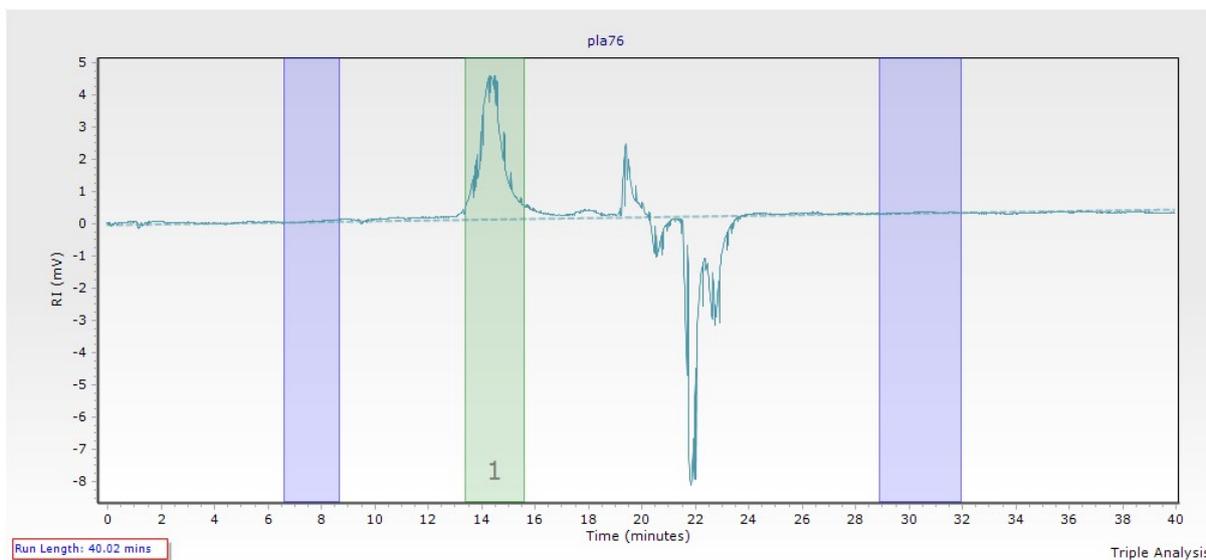


Figure S11. GPC trace for Table S1, Entry 14 (PLA furnished from a reaction at 240 bar CO₂, 80 °C, 300:1 [*rac*-LA]:[**1**] and 24 h reaction time).

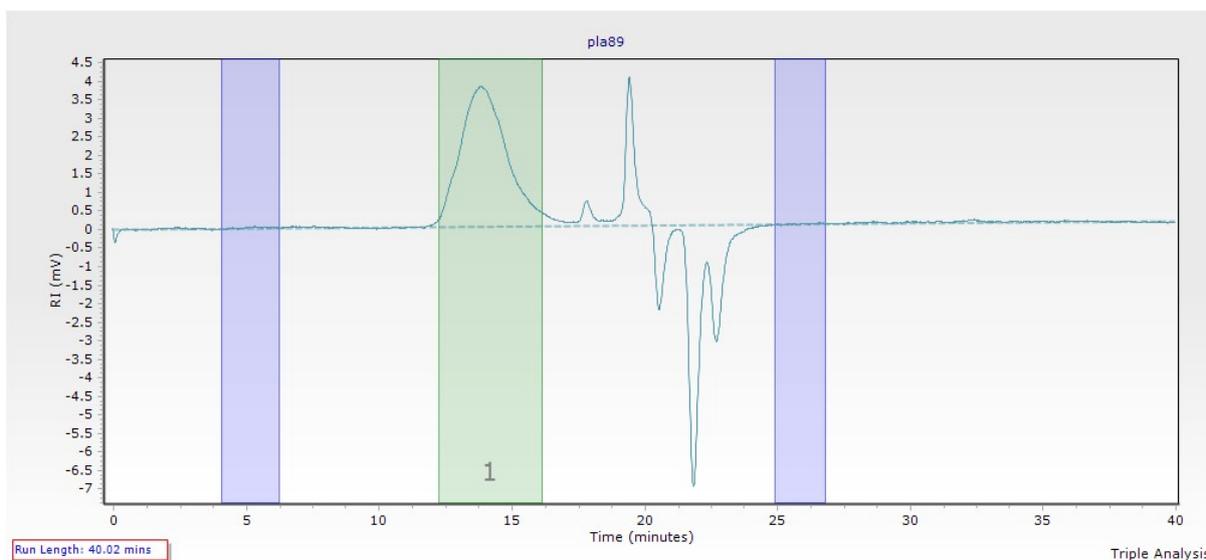


Figure S12. GPC trace for Table S1, Entry 15 (PLA furnished from a reaction at 240 bar CO₂, 100 °C, 300:1 [*rac*-LA]:[**1**] and 1.5 h reaction time).

MALDI-ToF spectrum

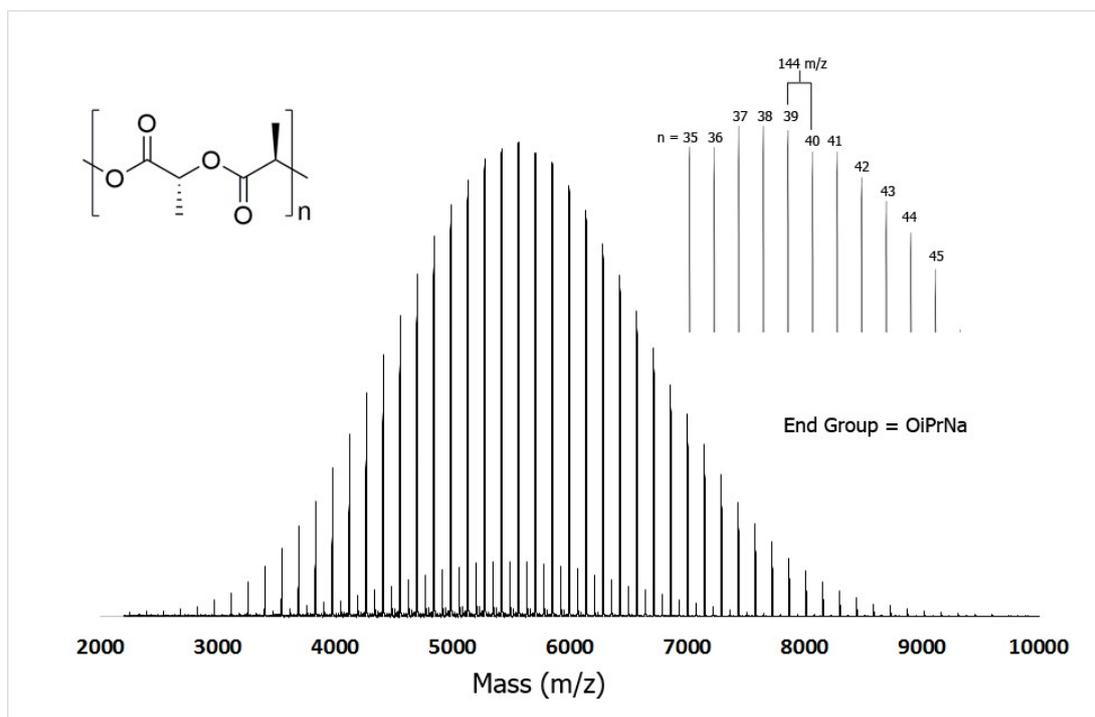


Figure S13. MALDI-TOF spectrum (reflector positive) for Table 1, Entry 3 (PLA furnished from a reaction at 240 bar CO₂, 100 °C, 100:1 [*rac*-LA]:[**1**] and 1 h reaction time). Inset: Enlarged portion of the spectrum showing the mass difference between polymeric species = 144 *m/z*. A low level of transesterification can be observed by the second smaller series with mass separation 72 *m/z*.

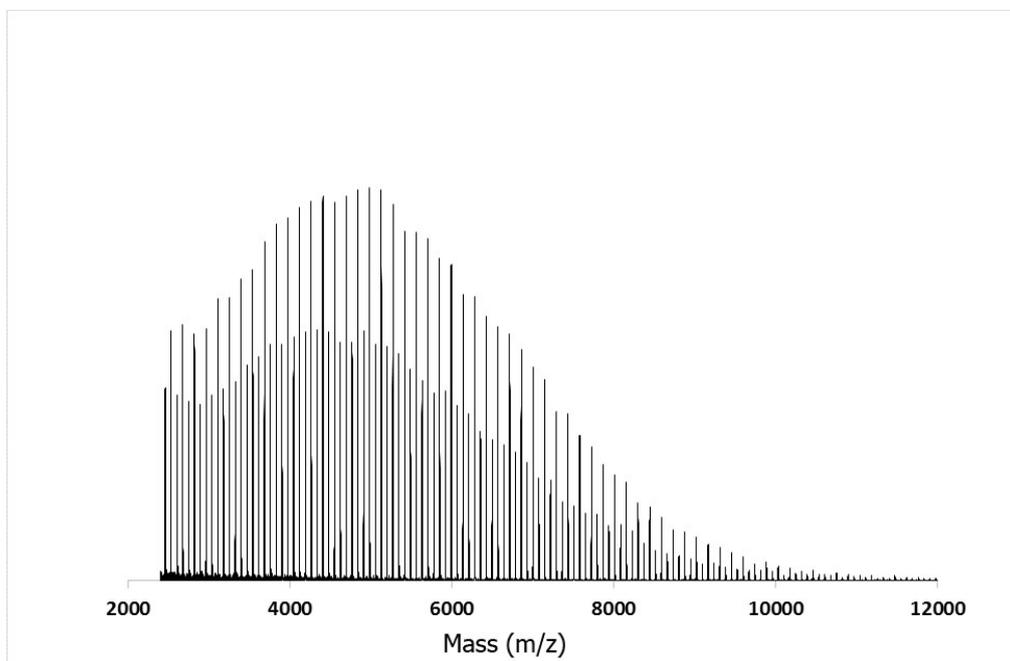


Figure S14. MALDI-TOF spectrum (reflector positive) for Table 1, Entry 4 (PLA furnished from a reaction at 240 bar CO₂, 130 °C, 100:1 [*rac*-LA]:[**1**] and 1 h reaction time). The much higher intensity of the second series with peak separation *ca.* 72 *m/z*, clearly suggests that significant transesterification has occurred.

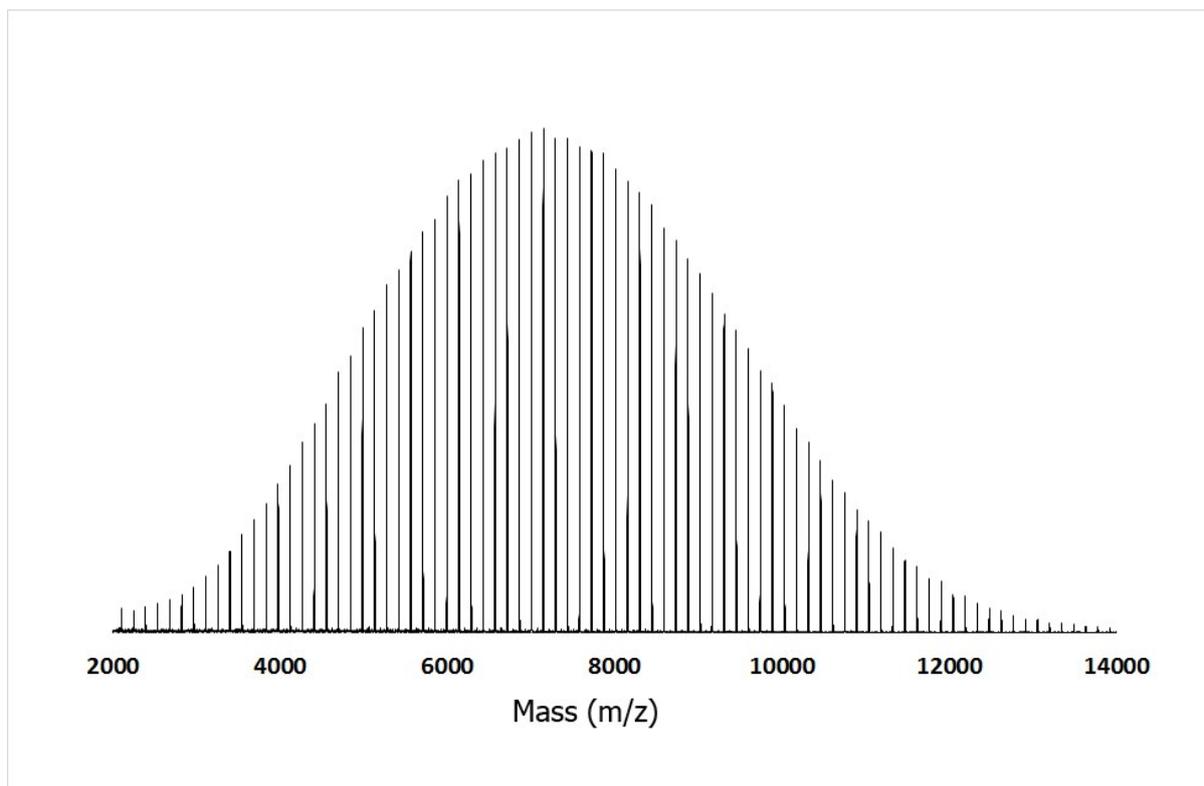


Figure S15. MALDI-TOF spectrum (reflector positive) for Table 1, Entry 5 (PLA from a reaction at 240 bar CO₂, 80 °C, 100:1 [*rac*-LA]:[**1**] and 0.1 h reaction time).

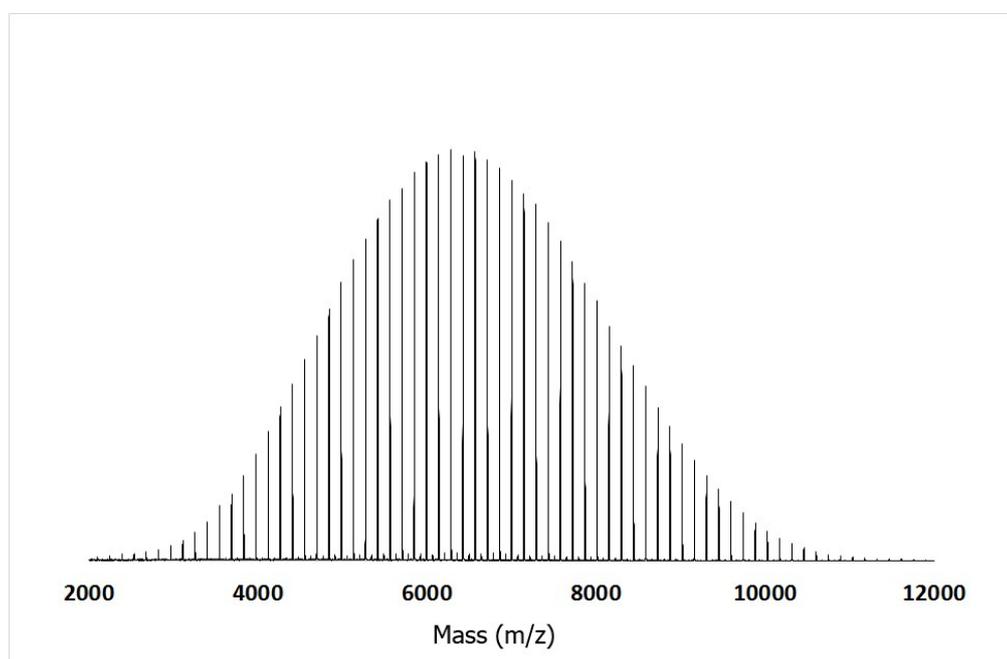
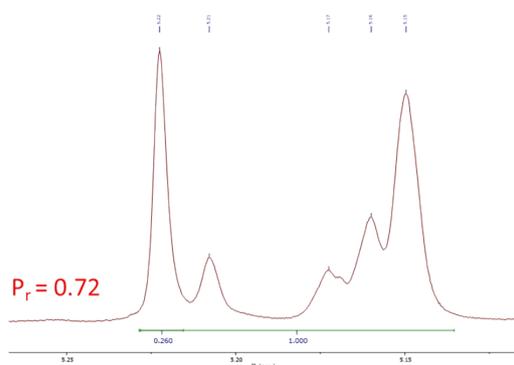


Figure S16. MALDI-TOF spectrum (reflector positive) for Table 1, Entry 6 (PLA from a reaction at 240 bar CO₂, 100 °C, 100:1 [*rac*-LA]:[**1**] and 0.1 h reaction time).

Homonuclear NMR Spectra

Melt polymerisation at 180 °C



Polymerisation in scCO₂ at 80 °C

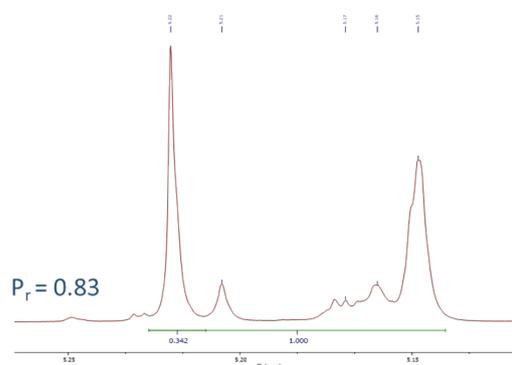


Figure S17. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in the melt at 180 °C (left) and in scCO₂ at 80 °C (right), (Table 1, entries 7 and 2 respectively).

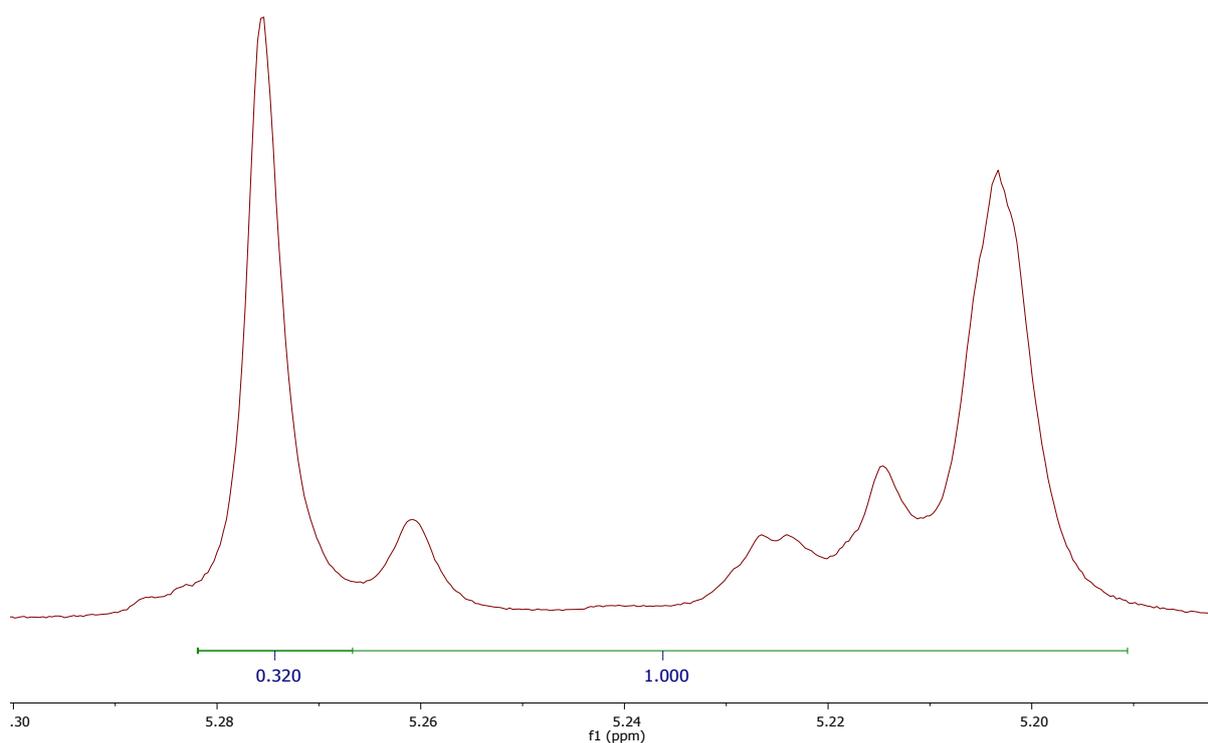


Figure S18. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 100 °C (Table 1, entry 3).

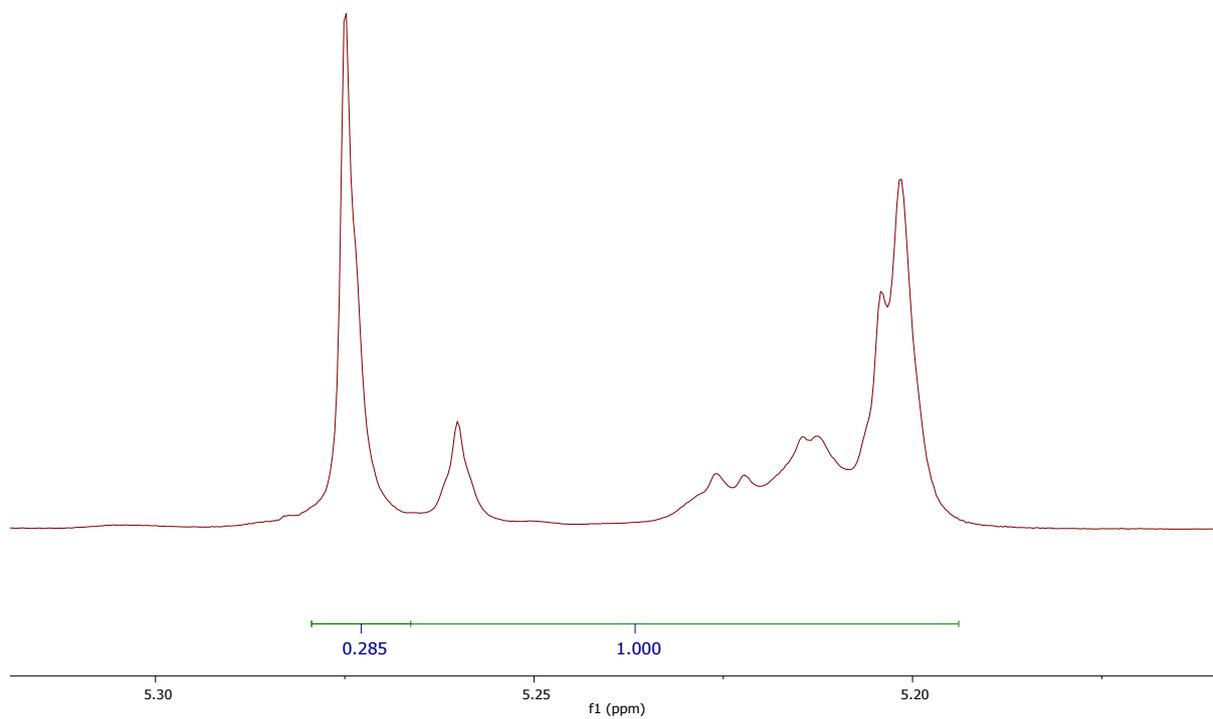


Figure S19. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 130 °C (Table 1, entry 4).

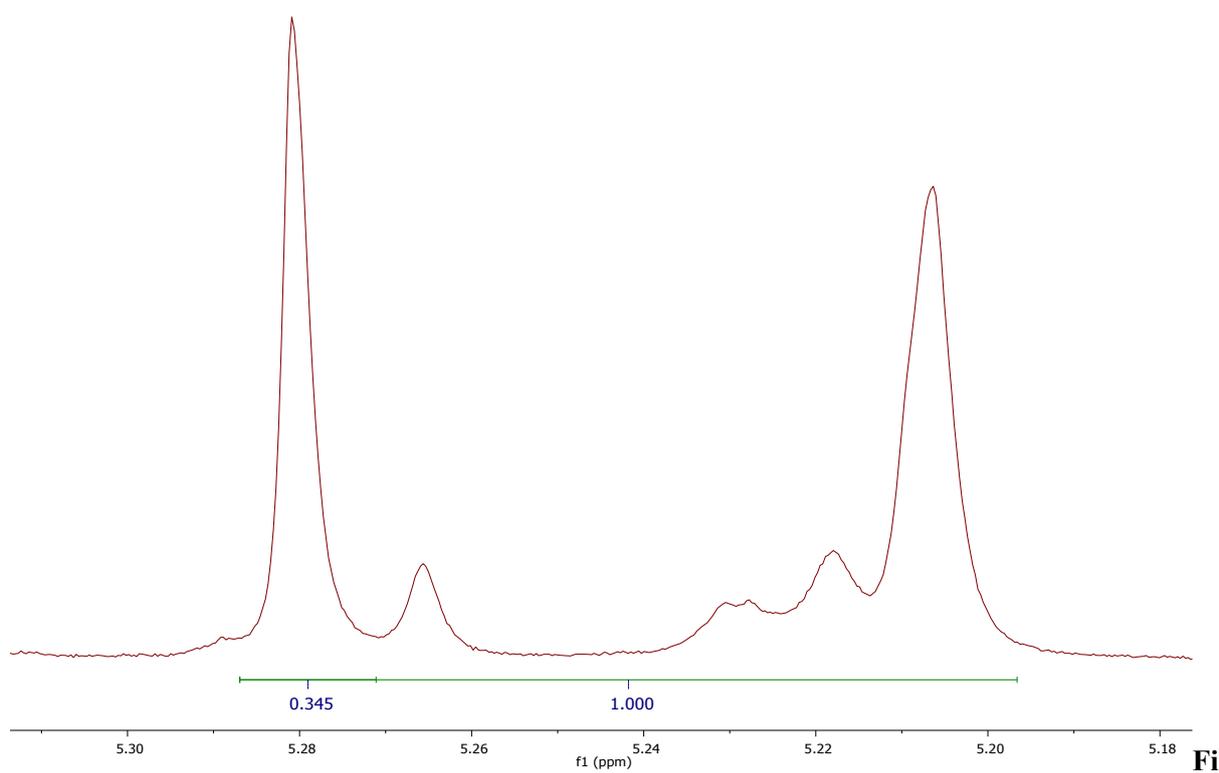


Figure S20. ^1H homonuclear decoupled NMR (methine region, CDCl_3) for PLA formed in scCO_2 at 80 $^\circ\text{C}$ (Table 1, entry 5).

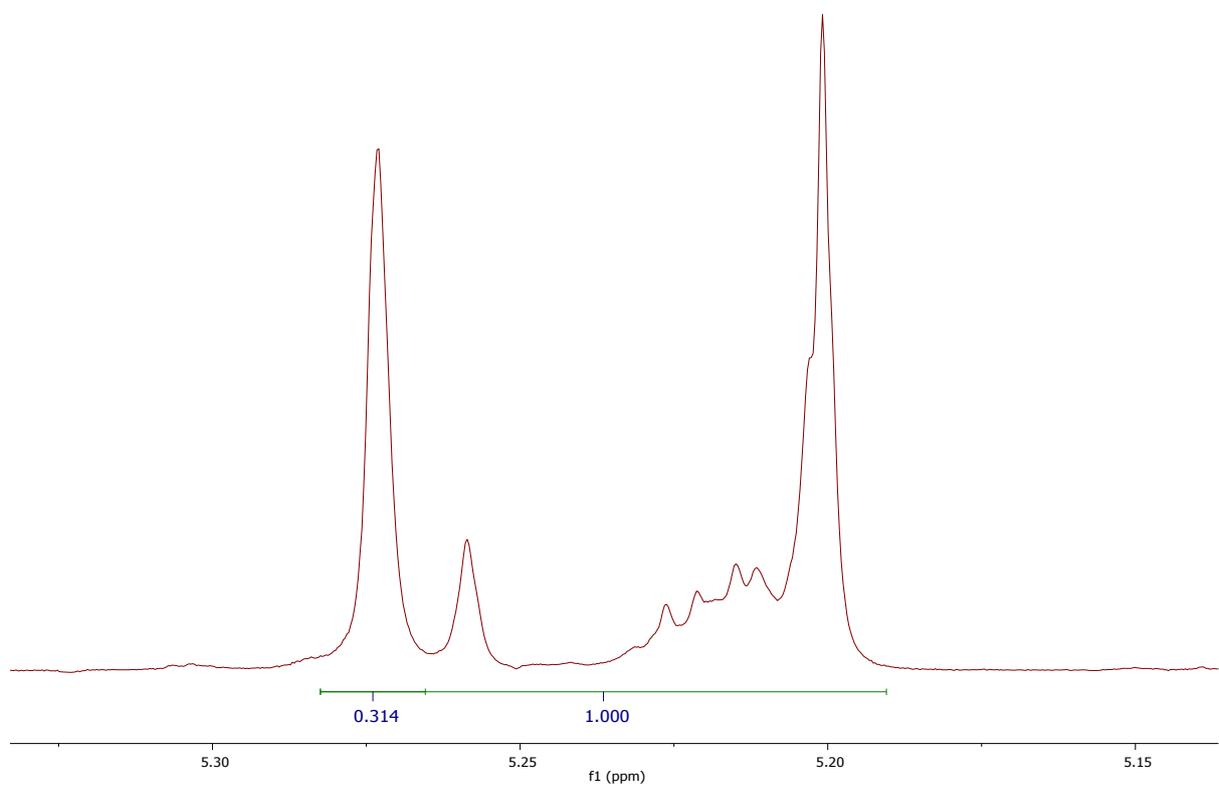


Figure S21. ^1H homonuclear decoupled NMR (methine region, CDCl_3) for PLA formed in scCO_2 at 100 $^\circ\text{C}$ (Table 1, entry 6).

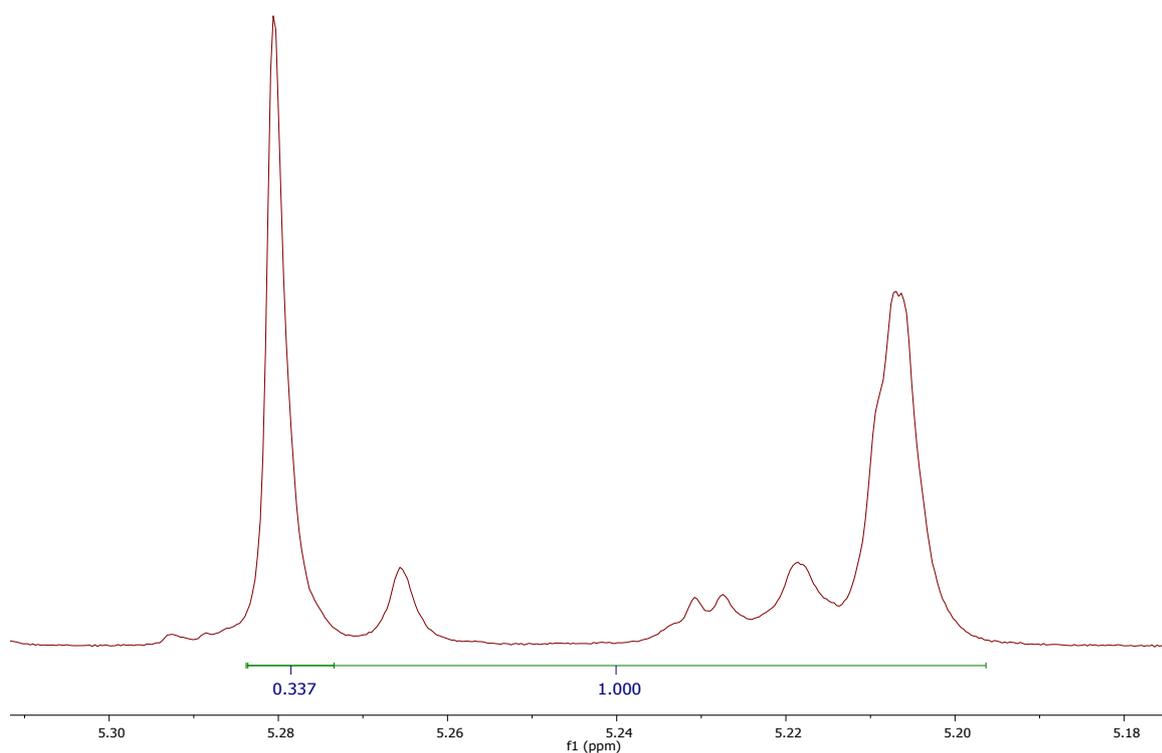


Figure S22. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 120 bar (Table S1, entry 9).

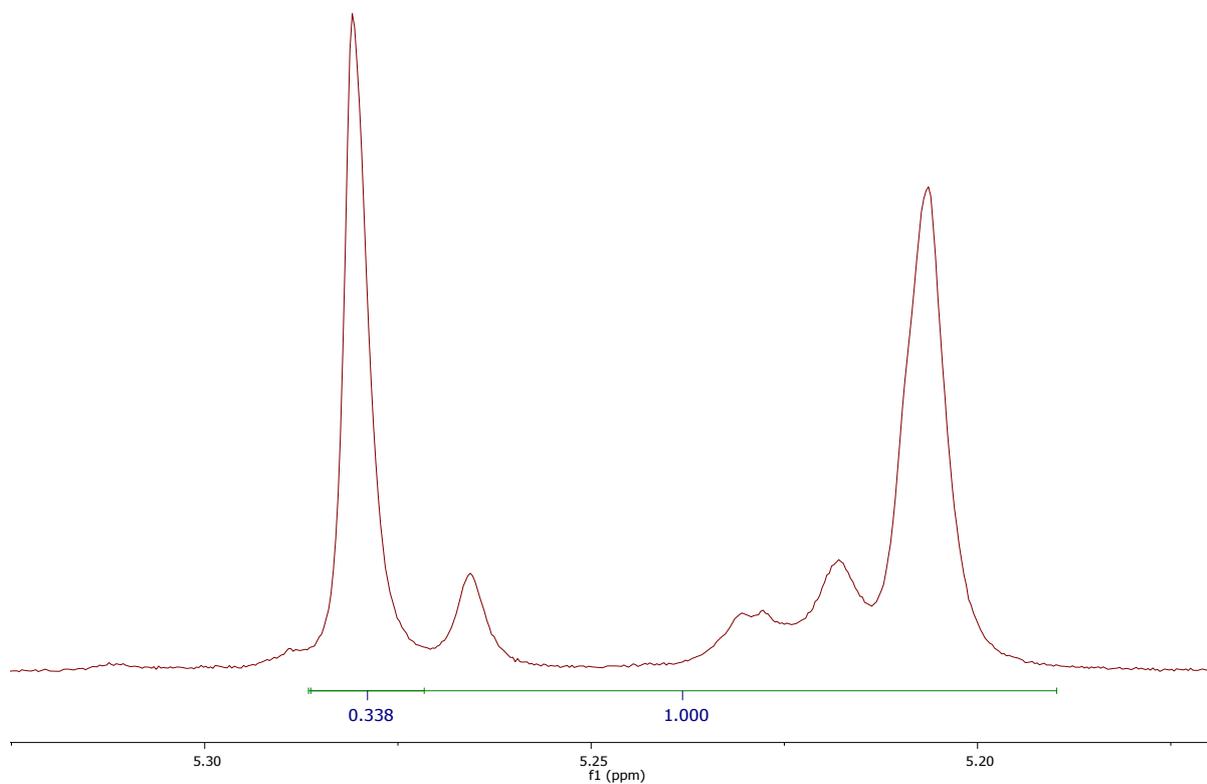


Figure S23. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 150:1 loading (Table S1, entry 11).

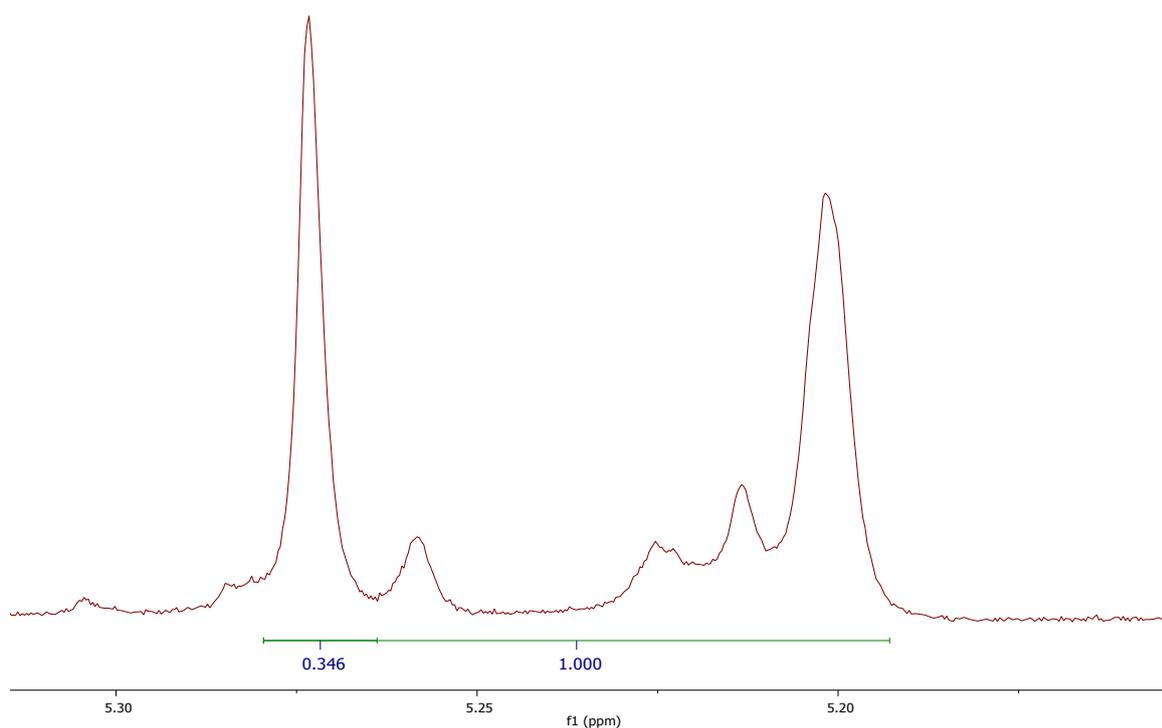


Figure S24. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 300:1 loading (Table S1, entry 12).

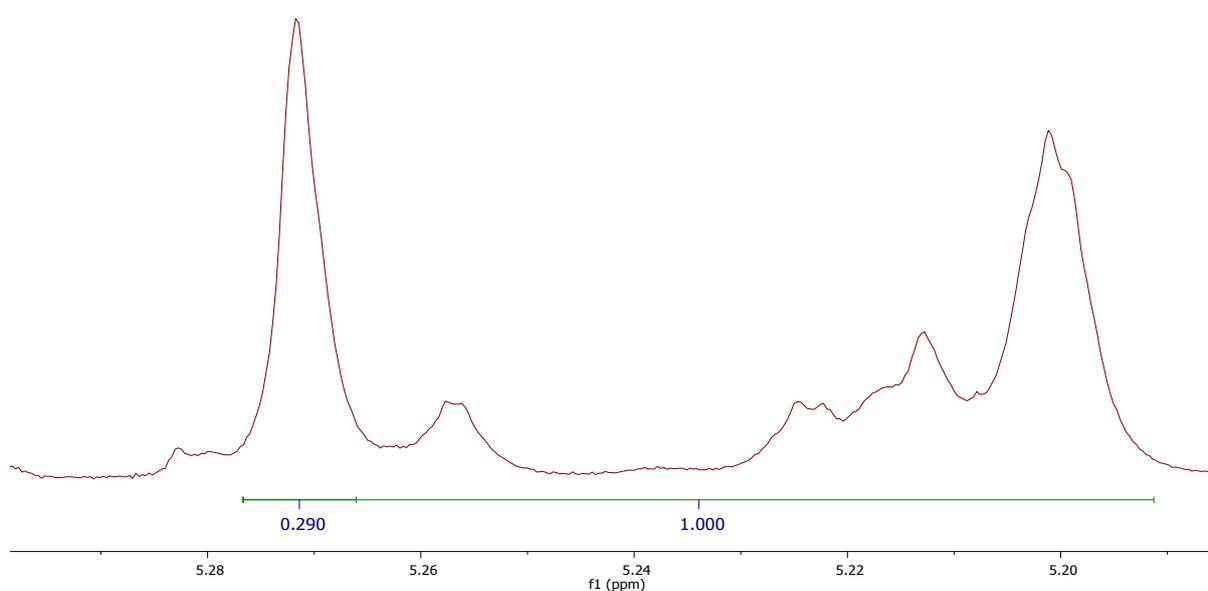


Figure S25. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 300:1 loading (Table S1, entry 13).

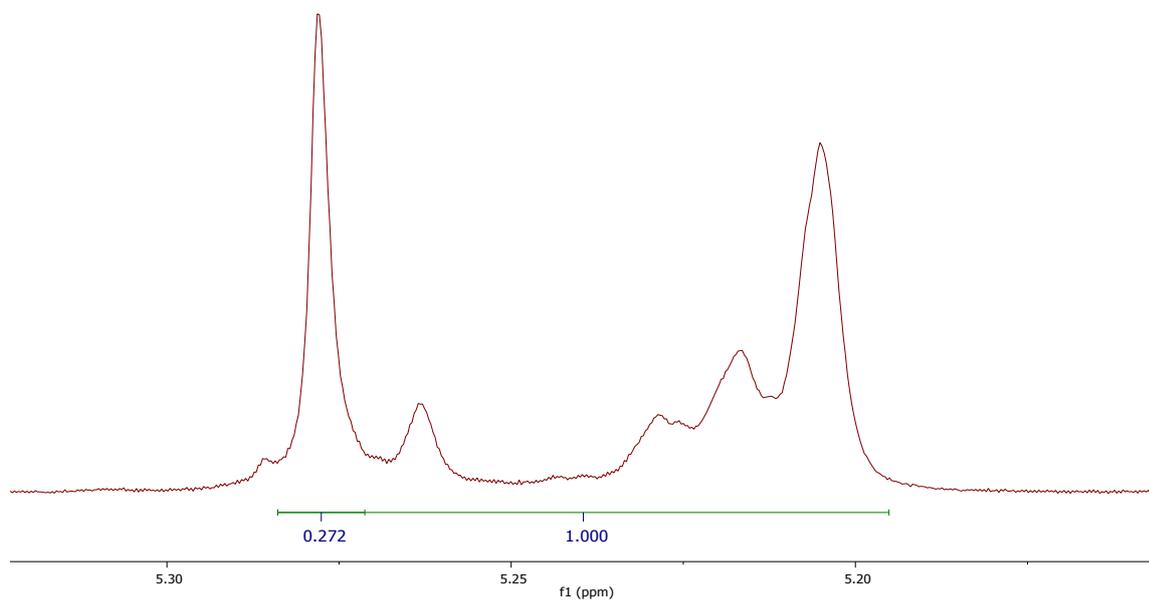


Figure S26. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 300:1 loading (Table S1, entry 14).

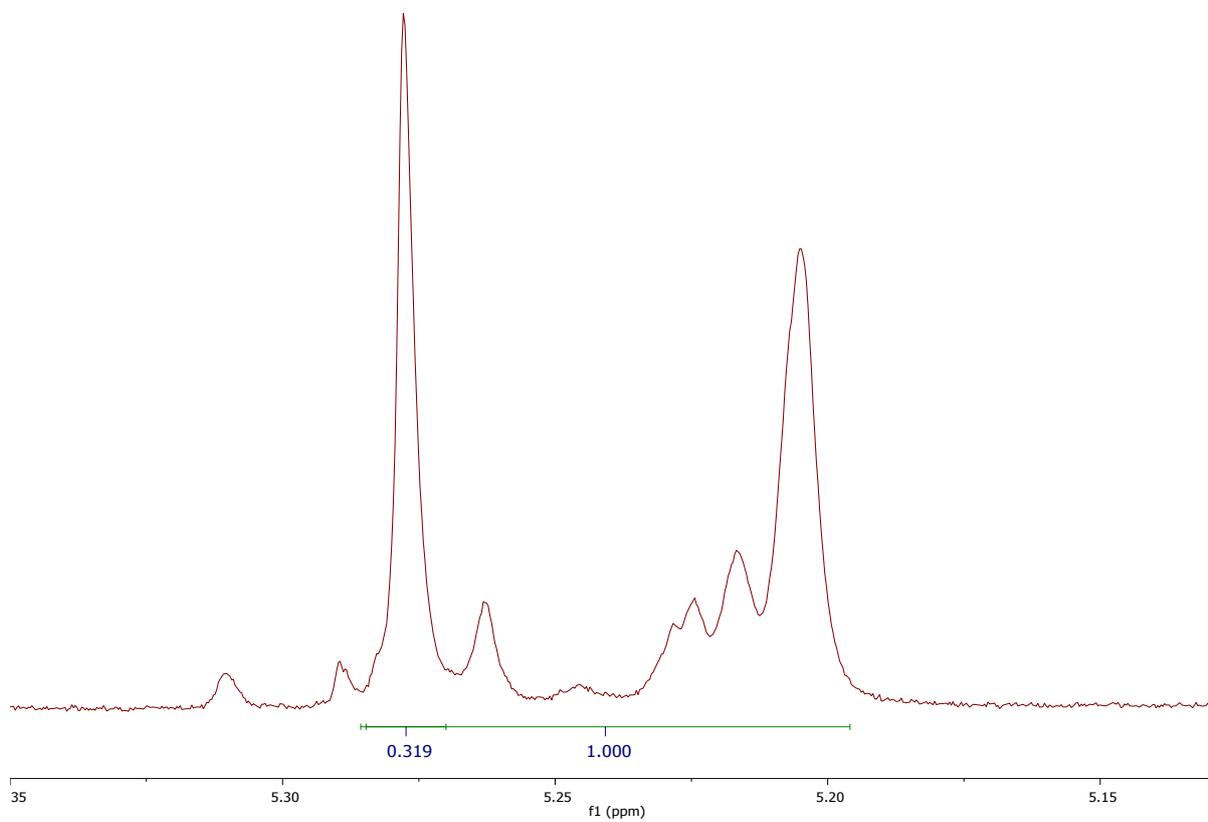


Figure S27. ¹H homonuclear decoupled NMR (methine region, CDCl₃) for PLA formed in scCO₂ at 300:1 loading and 100 °C (Table S1, entry 15).

References

1. Davidson, M. G.; Doherty, C. L.; Johnson, A. L.; Mahon, M. F., Isolation and characterisation of transition and main group metal complexes supported by hydrogen-bonded zwitterionic polyphenolic ligands. *Chem. Commun.* **2003**, (15), 1832-1833.
2. Thurecht, K. J.; Heise, A.; deGeus, M.; Villarroya, S.; Zhou, J.; Wyatt, M. F.; Howdle, S. M., Kinetics of Enzymatic Ring-Opening Polymerization of ϵ -Caprolactone in Supercritical Carbon Dioxide. *Macromolecules* **2006**, *39* (23), 7967-7972.
3. Blakey, I.; Yu, A.; Howdle, S. M.; Whittaker, A. K.; Thurecht, K. J., Controlled polymerisation of lactide using an organo-catalyst in supercritical carbon dioxide. *Green Chemistry* **2011**, *13* (8), 2032-2037.

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