Supplementary Material (ESI) for Chemical Communications

Supporting information

Highly active and stereoselective zirconium and hafnium alkoxide initiators for solvent-free ring-opening polymerization of *rac*-lactide

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1 General Experimental Details

The ligand (L**H**$_3$, 2,2’,2’’-[Nitrilotris(methylene)]tris[4,6-di-tert-butylphenol] was prepared by the method of Kol and co-workers.[1] Complexes **1**[1] and **2**[2] were prepared as described in the literature. Ti(O^{i}Pr)$_4$ (97 %, Aldrich) was purified by vacuum distillation prior to use, Zr(O^{i}Pr)$_4$^{i}PrOH (99.9 %, Aldrich) and Hf(O^{i}Pr)$_4$^{i}PrOH (99%, Strem) were used without further purification. *rac*- Lactide (Purac), D-lactide (Purac) and L-lactide (Aldrich) were recrystallized from dry toluene and sublimed twice prior to use in polymerization reactions.

For the preparation and characterization of all metal complexes and for the ROP of LA, reactions and manipulations were performed under an inert atmosphere of argon using standard Schlenk or glove-box techniques. All solvents were freshly distilled from suitable drying agents and degassed prior to use (toluene over sodium/benzophenone and dichloromethane over calcium hydride, hexane was eluted over activated alumina columns and stored under argon).

^{1}H/^{13}C NMR spectra were recorded on a Bruker 300 MHz or 400 MHz spectrometer and referenced to residual protio and ^{13}C solvent peaks. Chloroform-*d*$_1$ (Aldrich) was distilled from calcium hydride prior to use. Coupling constants are given in Hertz. Elemental analysis was performed by Mr. A. K. Carver at the Department of Chemistry, University of Bath, on an Exeter Analytical CE440 Elemental Analyzer. Gel Permeation Chromatography (GPC) analyses were performed on a Polymer Laboratories PL-GPC 50 integrated system using a PLgel 5 µm MIXED-D 300×7.5 mm column at 35 °C, THF solvent (flow rate, 1.0ml/min). The polydispersity index (PDI) was determined from M_w/M_n, where M_n is the number average molecular weight and M_w the weight average molecular weight. The polymers were referenced to 11 narrow molecular weight polystyrene standards with a range of M_w 615 – 5680000 Da. MALDI-TOF Mass Spectra were recorded at the EPSRC National Mass Spectrometry Service Centre, Swansea, UK on an Applied Biosystems Voyager DE-STR instrument in the positive linear mode using a dithranol matrix and NaI or KI as the additive.

2 Preparation and Characterization of Complex 3

2.1 Preparation of 3

Hf(O^{i}Pr)$_4$^{i}PrOH (0.71 g, 1.5 mmol) was dissolved in toluene (20 ml) to which the ligand (1.0 g, 1.5 mmol) was added. The solution was stirred for 2 hrs, after which time the solvent was removed in vacuo and product recrystallized from hexane. at -20 °C, collected on a frit and dried in vacuo.

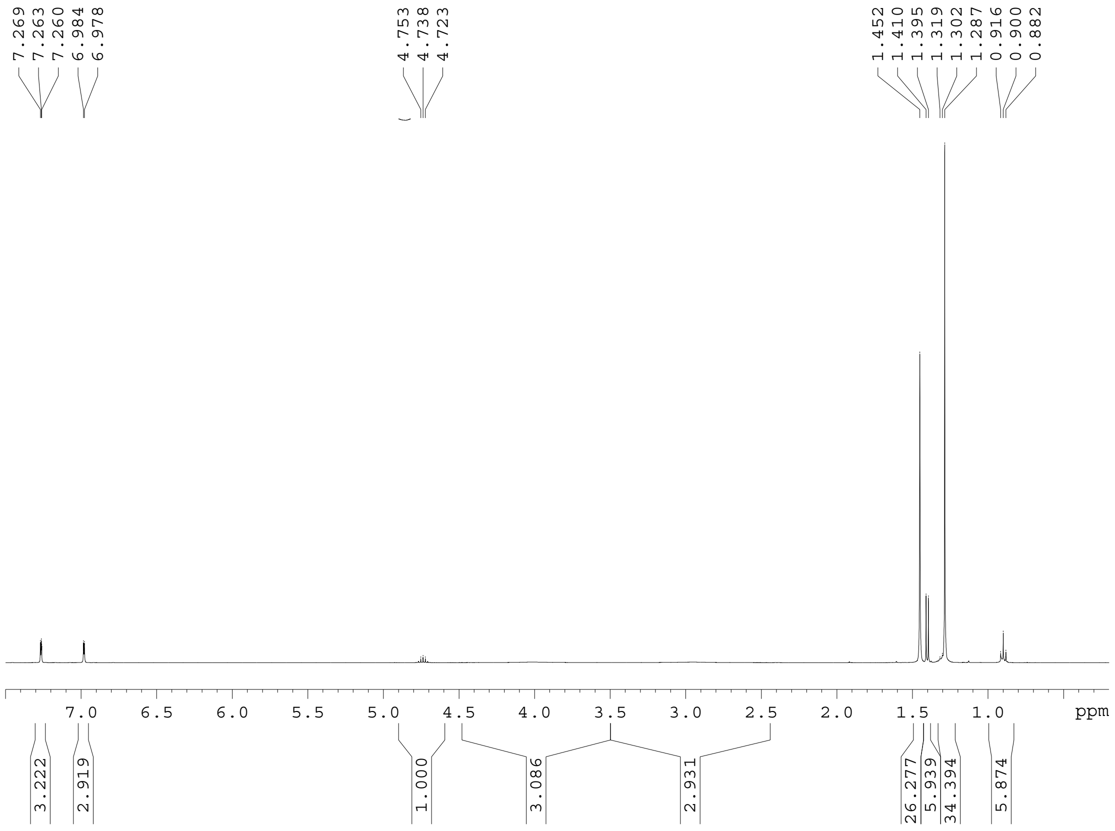
2.2 Spectroscopic data for 3:

Anal: Calc for $C_{54}H_{87}N_1O_4Hf$ C, 65.3; H, 8.83; N, 1.41. Found: C, 64.9; H, 8.79; N 1.18. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 ºC) 0.9 (m, 6H, CH_3 hexane), 1.29 (s, 35H ^{t}Bu and CH_2 hexane), 1.40 (d J = 6.0 Hz, 6H, $CH(C\mathit{H}_3)_2$), 1.45 (s, 27H, ^{t}Bu), 2.96 (br s, 3H, CH_2), 4.01 (br s, 3H, CH_2), 4.73 (sept J = 6.0 Hz, 1H $C\mathit{H}(CH_3)_2$), 6.98 (d J = 2.3 Hz, 3H Ar-H), 7.27 (d J = 2.3 Hz, 3H Ar-H). $^{13}C\{^1H\}$ NMR 14.1 (CH_3 hexane), 22.7 (CH_2 hexane) 27.4 ($CH(\underline{C}H_3)_2$), 27.7 ($C(\underline{C}H_3)_3$ tBu), 31.6 ($C(\underline{C}H_3)_3$ tBu), 31.6 (CH_2 hexane), 34.2 ($\underline{C}(CH_3)_3$ tBu), 34.9 ($\underline{C}(CH_3)_3$ tBu), 59.5 (NCH_2), 72.3 ($\underline{C}H(CH_3)_2$), 123.6 (Ar-C), 123.7 (Ar-H), 124.6 (Ar-H), 136.7 (Ar-C), 141.5 (Ar-C), 157.2 (Ar-O). ^{1}H and ^{13}C NMR spectra are shown in Figures S1 and S2. Variable-temperature ^{1}H NMR spectra are shown in Figure S3.

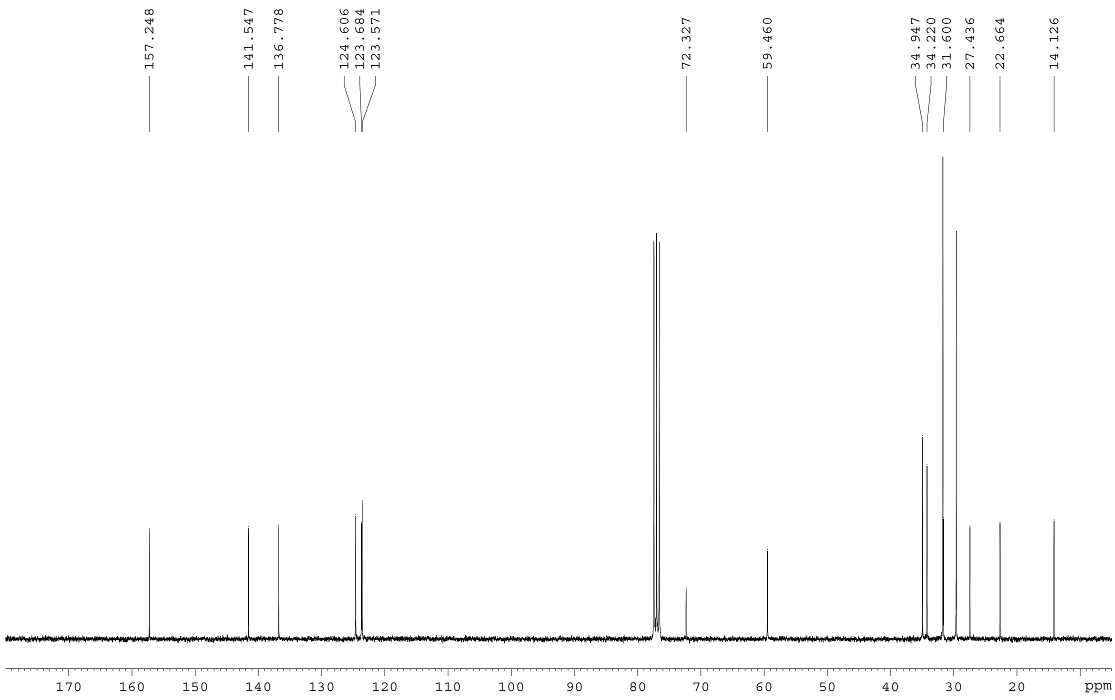
2.3 Crystallographic data for 3

Data were collected at 150 K on a Nonius KappaCCD area detector diffractometer using Mo-Kα radiation (λ = 0.71073 Å), and all structures were solved by direct methods and refined on all F^2 data using SHELXL-97 suite of programs, with hydrogen atoms either included in idealized positions and refined using the riding model or located in difference maps and refined freely.[3]

*X-ray data for **3**:* $C_{54}H_{87}HfNO_4$, M = 992.74, colourless prism, 0.50 × 0.40 × 0.35 mm^3, tetragonal, space group $P4_3$ (No. 78), $a = b$ = 14.57000(10), c = 25.4100(2) Å, V = 5394.16(7) Å^3, Z = 4, D_c = 1.222 g/cm^3, F_{000} = 2088, MoKα radiation, λ = 0.71073 Å, T = 150(2)K, $2\theta_{max}$ = 55.0º, 81147 reflections collected, 12310 unique (R_{int} = 0.0362). Final *GooF* = 1.064, *R1* = 0.0228, *wR2* = 0.0504, *R* indices based on 11451 reflections with I >2sigma(I) (refinement on F^2), 762 parameters, 1 restraint. Lp and absorption corrections applied, μ = 1.974 mm^{-1}. Absolute structure parameter = 0.432(6)[4]: structure refined as a racemic twin. The asymmetric unit consists of one disordered molecule of **3** and one molecule of lattice hexane (Figure S4). The ligand backbone (i.e. excluding t-butyl groups) exhibits disorder over two sites in approximately a 3:1 ratio. The methyl groups of the hafnium-bound isopropoxide ligand is also disordered and was modelled over three positions, each with ⅓ occupancy.



(a)



(b)

Figure S1: (a) ^{1}H NMR (CDCl$_3$, 400 MHz) spectrum of **3**; (b) ^{13}C{^{1}H} NMR (CDCl$_3$, 400 MHz) of **3**.

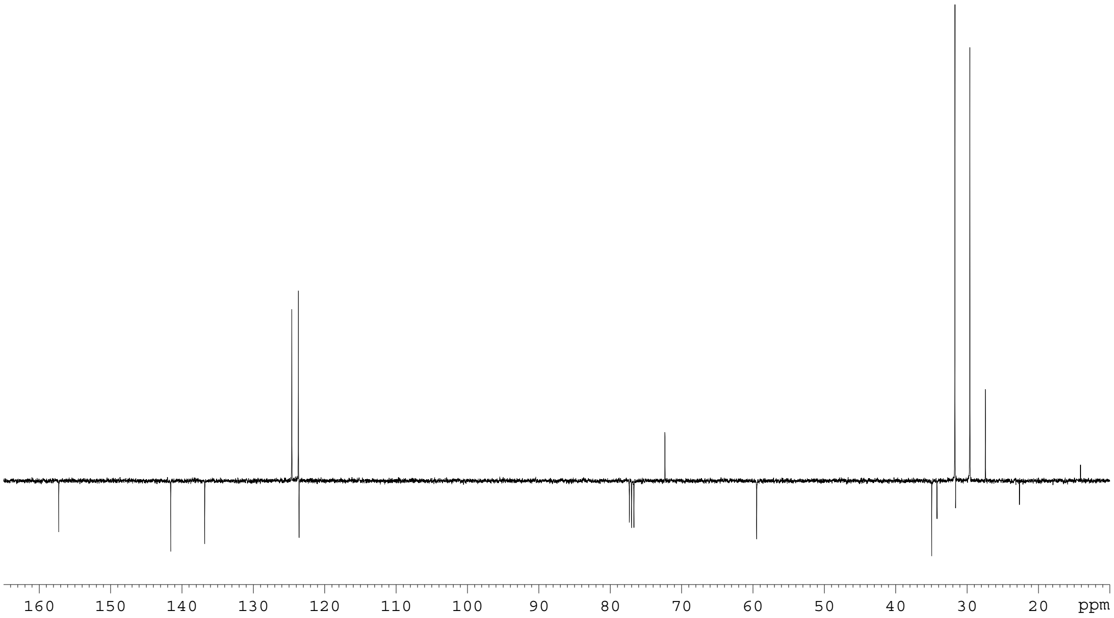


Figure S2:$^{13}C\{^{1}H\}$ pendant NMR ($CDCl_3$, 400 MHz) of **3**.

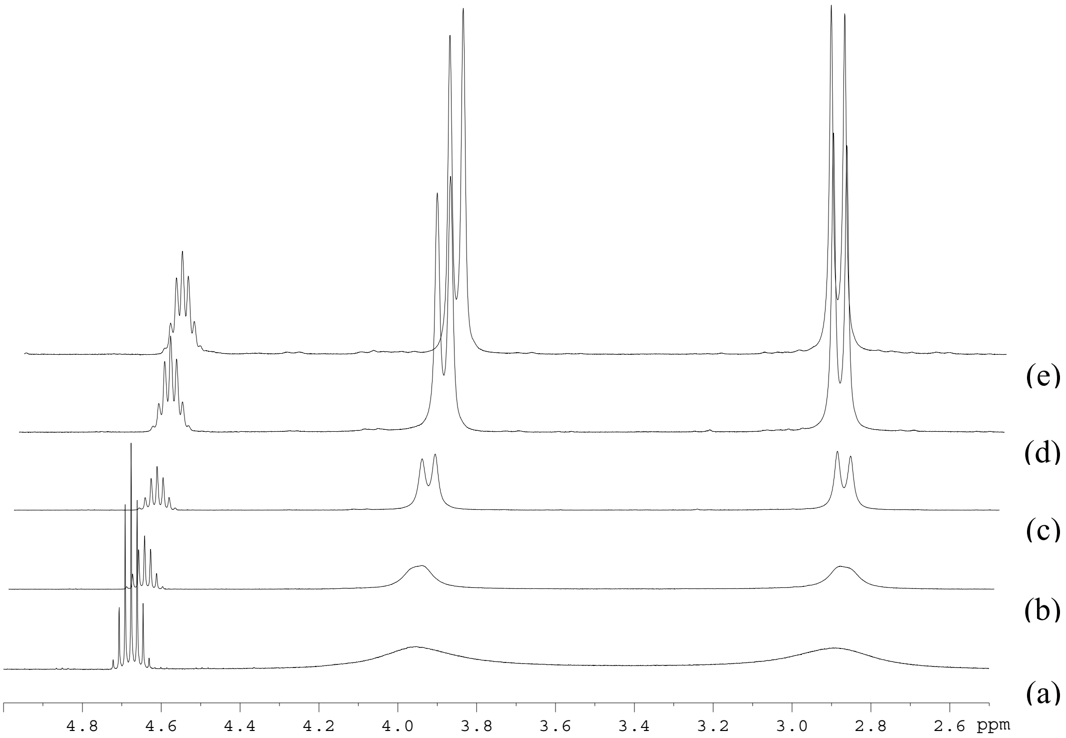
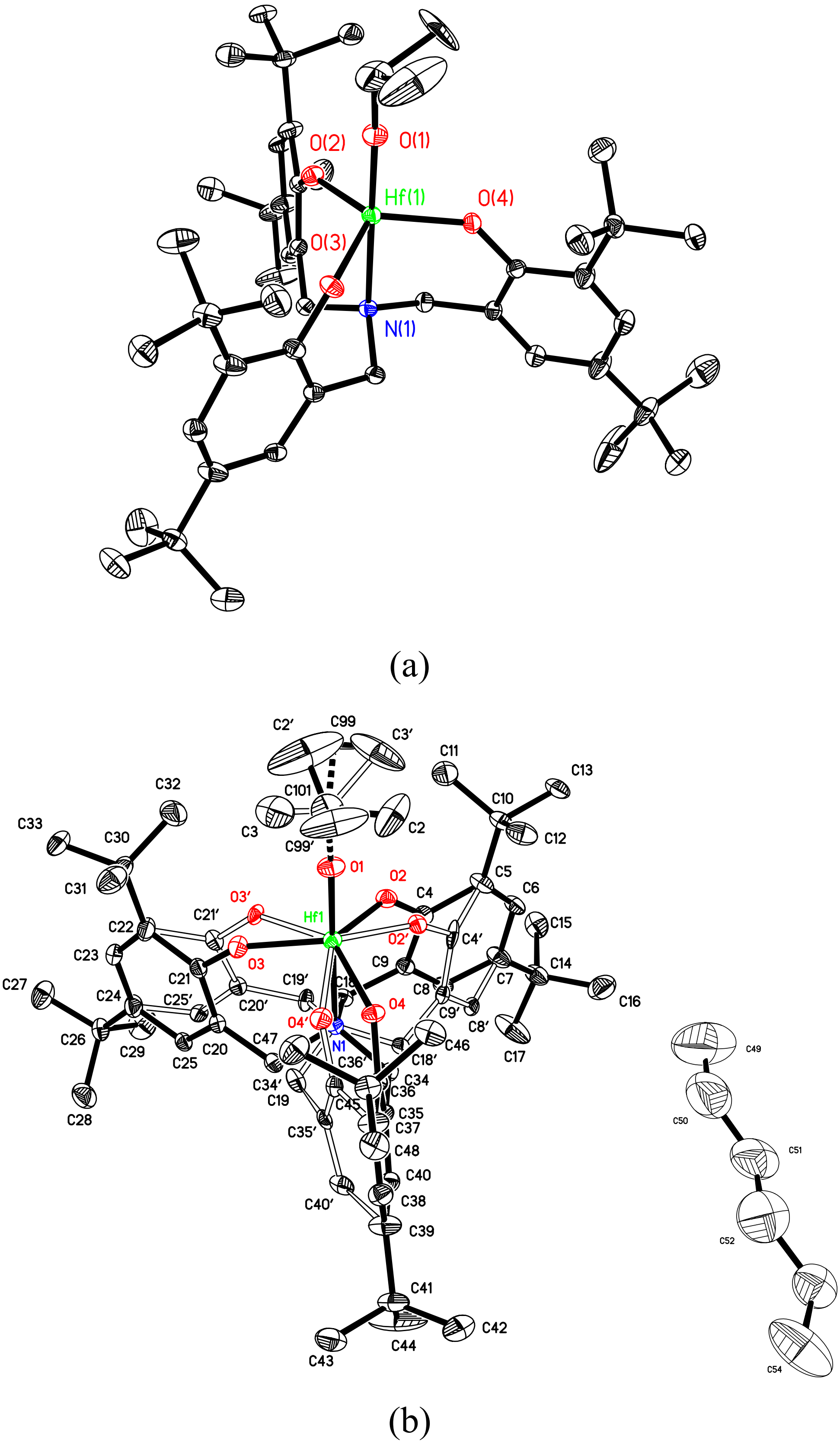


Figure S3: Variable temperature ^{1}H NMR spectra of **3** ($CDCl_3$, 400 MHz): (a) 298 K; (b) 273 K; (c) 253 K; (d) 233 K; (e) 213 K.



(a)

(b)

Figure S4: (a) molecular structure of **3** showing thermal ellipsoids at the 30% probability level, (b) asymmetric unit of **3** showing lattice solvent, disorder and numbering scheme.

3 Solvent-free Polymerization of *rac*-Lactide.

For solvent-free polymerizations the monomer:initiator ratio employed was 300:1 at a temperature of 130 °C, in all cases 2 g of *rac*-lactide were used. After the reaction time (up to 30 minutes) methanol (20 ml) was added to quench the reaction and the resulting solid was dissolved in dichloromethane. The solvents were removed in vacuo and the resulting solid was washed with copious amounts of methanol to remove any unreacted monomer. ^{1}H NMR spectroscopy ($CDCl_3$) and GPC (THF) were used to determine tacticity and molecular weights (M_n and M_w) of the polymers produced; P_r (the probability of heterotactic linkages) were determined by analysis of the methine region of the homonuclear decoupled ^{1}H NMR spectra, the equations used to calculate P_r and P_m are given by Coates *et al.*[5] ^{1}H and ^{13}C NMR spectra of polymers listed in Table 1 are given in Figures S8 to S14.

4 Solution Polymerization of *rac*-Lactide

In a typical run the initiator (0.05 mmol) was dissolved in toluene (10 ml) to which *rac*-lactide (5.0 mmol, 0.72 g) was added and the vessel left to stir at room temperature for 48 hours. The vessel was then exposed to air to terminate the polymerization. The solvent was removed and the resulting solid washed with methanol to remove any excess monomer and dried in vacuo. Polymers were characterized by MALDI-TOF mass spectrometry (Figures S5 and S6) which confirm the well-controlled nature of the polymerization process. ^{1}H NMR spectroscopy ($CDCl_3$) and GPC (THF) were used to determine tacticity and molecular weights (M_n and M_w) of the polymers produced; P_r (the probability of heterotactic linkages) were determined by analysis of the methine region of the homonuclear decoupled ^{1}H NMR spectra, the equations used to calculate P_r and P_m are given by Coates *et al.*[5] ^{1}H and ^{13}C NMR spectra of polymers listed in Table 1 are given in Figures S8 to S14.

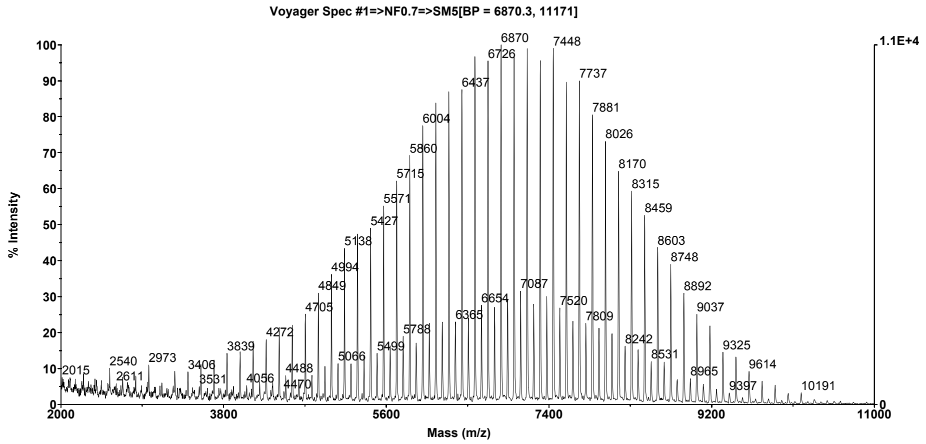


Figure S5: MALDI-TOF mass spectrum of the polymer produced with **2** under solution conditions (Table 1, entry 4). Major series corresponds to a repeat unit of 144, [C(O)CH(Me)C(O)CH(Me)]. Minor Series corresponds to a repeat unit of 72, [C(O)CH(Me)] and is indicative of a low degree of transesterification.

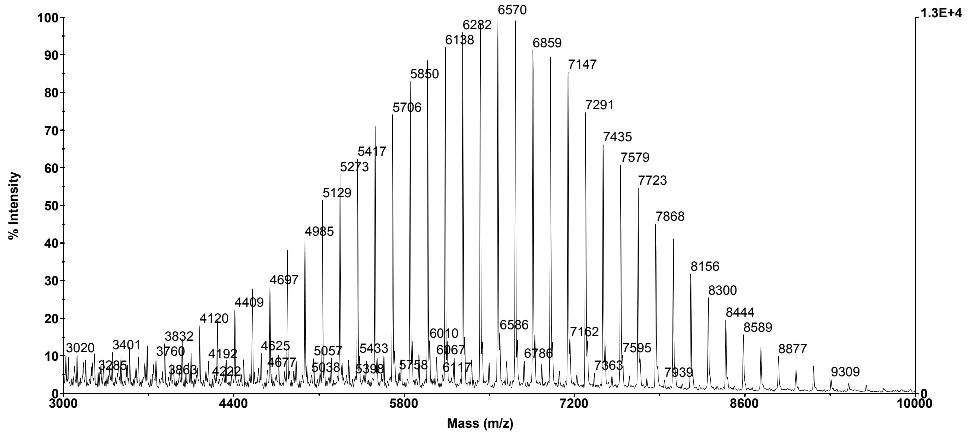


Figure S6: MALDI-TOF mass spectrum of the polymer produced with **3** under solution conditions (Table 1, entry 5). The repeat unit corresponds to 144, [C(O)CH(Me)C(O)CH(Me)] and indicates no detectable transesterification or back biting occurs.

4 Kinetic Studies on Polymerization of *rac*- (*R,R*)- and (*S,S*)-Lactide

For kinetic studies, polymerizations were carried out in $CDCl_3$ solution in an inert-atmosphere glovebox and aliquots of the reaction mixture removed periodically for ^1H NMR analysis during the course of polymerization.

In a typical experiment, 1.918 g *rac*-LA was stirred at room temperature in 20 ml $CDCl_3$. Aliquots of 0.1 ml were removed at intervals of 120 min and made up to 0.5 ml with $CDCl_3$ in an NMR tube, together with a drop of D_2O to quench the reaction. The degree of conversion was calculated from the relative integrals of the resonances due to polymer (5.16 to 5.31 ppm) and monomer (5.01 to 5.12 ppm) in the ^1H NMR spectrum. Semi-logarithmic first order plots of conversion vs. time were thus constructed (Figure S7, below) from which first order rate constants (k_{app}) were obtained.

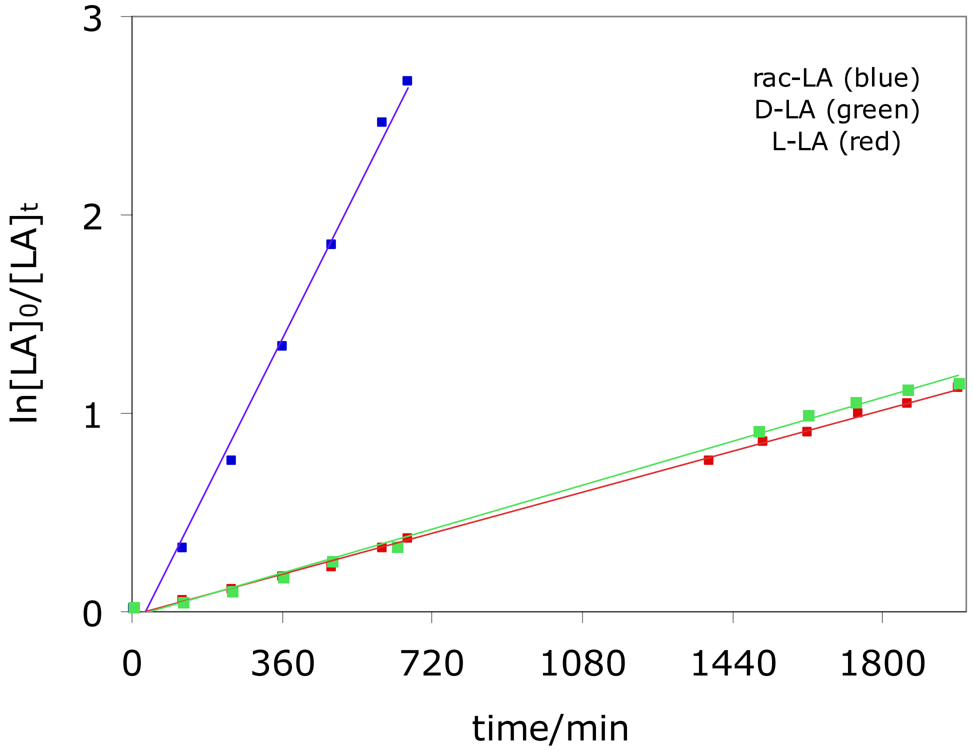


Figure S7: Plot of $\ln[LA]_0/[LA]_t$ vs time for the room temperature polymerization of (*R,R*)-lactide (red), (*S,S*)-lactide (green) and *rac*-lactide (blue) with **2** as the initiator. Equations of lines: *rac*-LA $y = 0.0042x - 0.1381$ ($r^2 = 0.9933$); (*R,R*)-LA $y = 0.0006x - 0.0226$ ($r^2 = 0.9992$), (*S,S*)-LA $y = 0.0006x - 0.0283$ ($r^2 = 0.9983$)

On completion of reactions (> 97% conversion by NMR), polymers were isolated and purified as in Section 4 above. ^1H NMR spectroscopy ($CDCl_3$) and GPC (THF) were used to determine tacticity and molecular weights (M_n and M_w) of the polymers produced; P_r (the probability of heterotactic linkages) were determined by analysis of the methine region of the homonuclear decoupled ^{1}H NMR spectra, the equations used to calculate P_r and P_m are given by Coates *et al.*[5] Results are shown in Table S1 below.

Table S1: Polymerization data for LA with initiator **2** ([M]/[I] = 100, room temperature, $CDCl_3$)

Monomer	NMR Conversion (%)	Isolated yield (%)	k_{app} (min^{-1})	M_n[a]	M_w/M_n[a]	P_r[b]
rac-LA	98	71	4.2×10^{-3}	13400	1.16	0.96
(*S,S*)-LA	98	77	0.6×10^{-3}	13400	1.06	-
(*R,R*)-LA	97	75	0.6×10^{-3}	13500	1.08	-

[a] Determined by gel permeation chromatography (GPC) in THF, relative to polystyrene standards. [b] P_r is the probability of heterotactic enchainment from ^{1}H homonuclear decoupled NMR spectra.

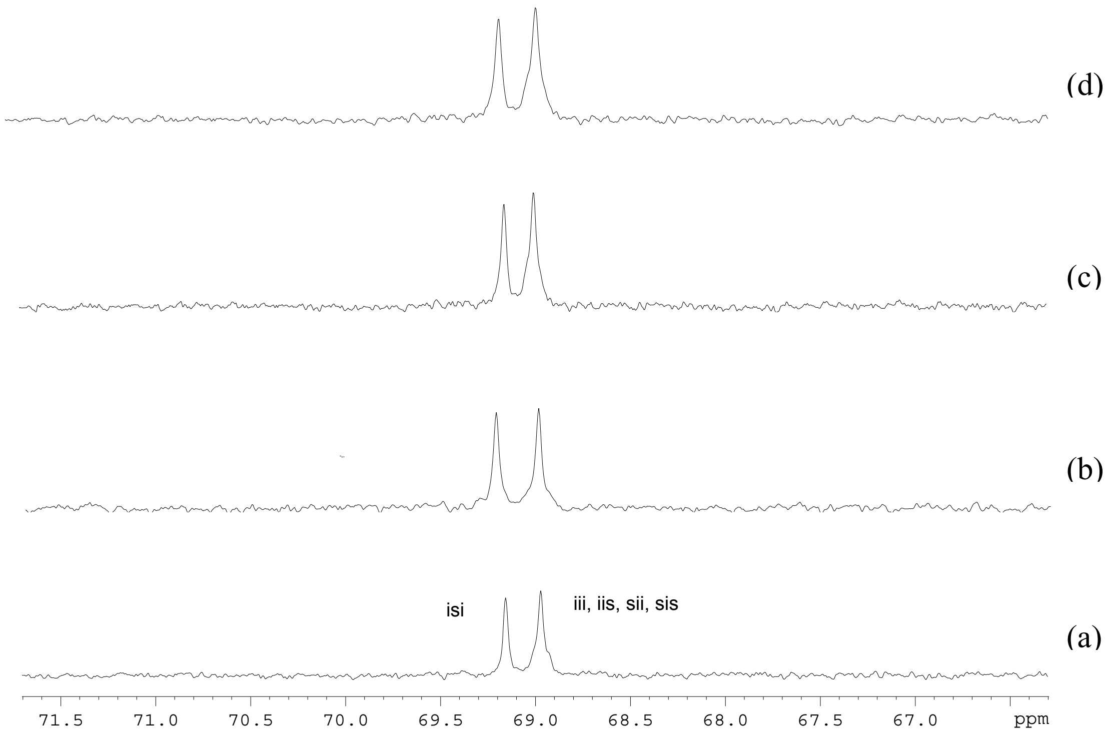


Figure S8: $^{13}C\{^{1}H\}$ NMR spectra ($CDCl_3$, 100 MHz) of PLA (methine region only): *(a)* **2** under melt condition (Table 1, entry 2); *(b)* **2** under solution condition (Table 1, entry 4); *(c)* **3** under melt condition (Table 1, entry 3); *(d)* **3** under solution condition (Table 1, entry 5). The observed enhancement of the *isi* tetrad is indicative of heterotactic PLA)

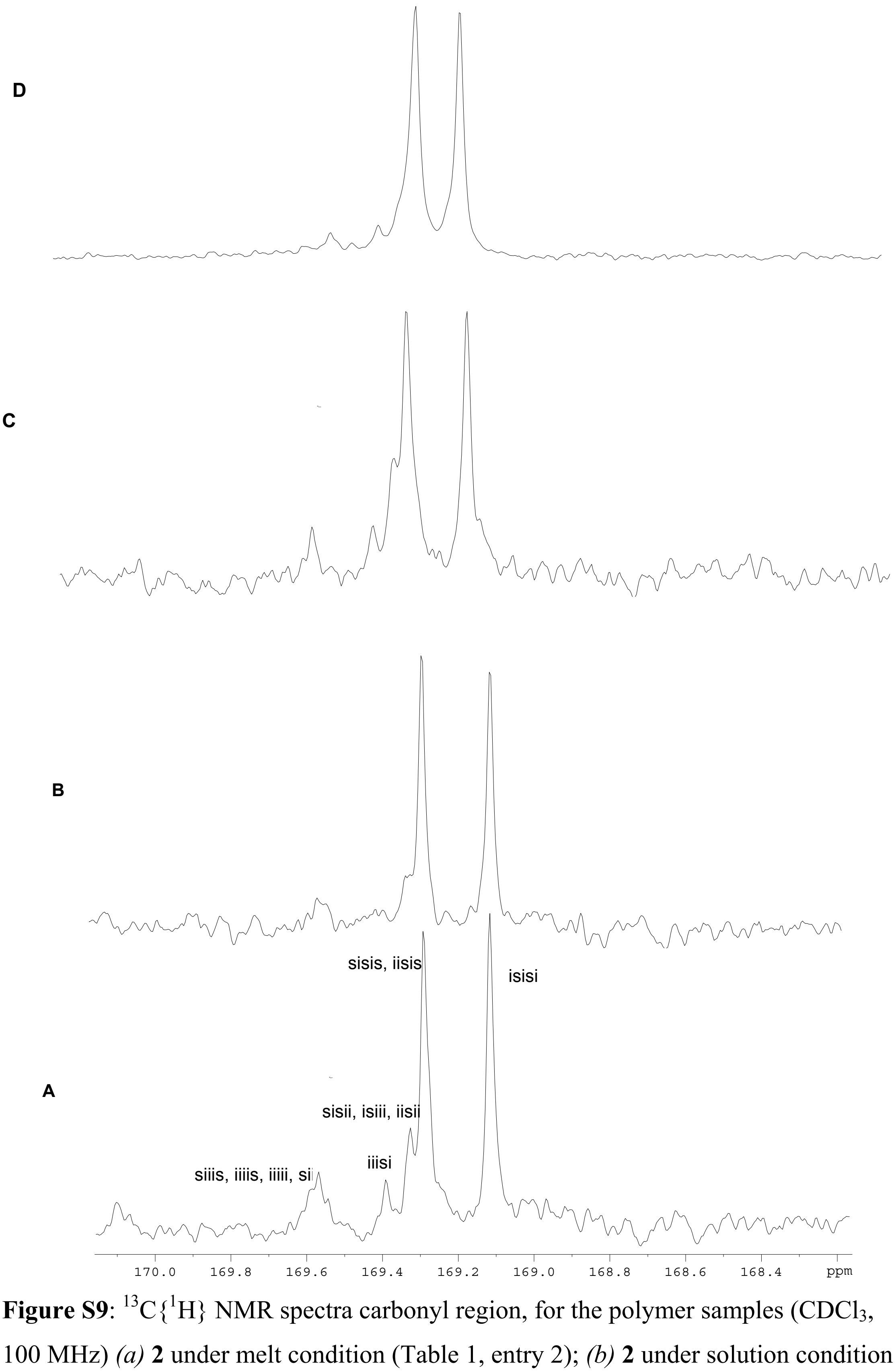


Figure S9: $^{13}C\{^{1}H\}$ NMR spectra carbonyl region, for the polymer samples ($CDCl_3$, 100 MHz) *(a)* **2** under melt condition (Table 1, entry 2); *(b)* **2** under solution condition (Table 1, entry 4); *(c)* **3** under melt condition (Table 1, entry 3) ; *(d)* **3** under solution condition (Table 1, entry 5). Hexads were identified using Kasperczyk's assignments.[6] Their relative intensities are indicative of highly heterotactic PLA.

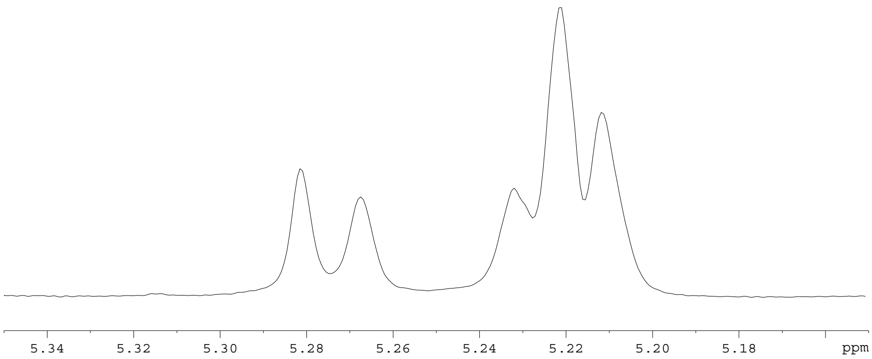


Figure S10: ^{1}H homonuclear decoupled NMR (methine region, $CDCl_3$, 400 MHz) for PLA formed in the melt using **1,** typical of atactic PLA. (Table 1, entry 1).

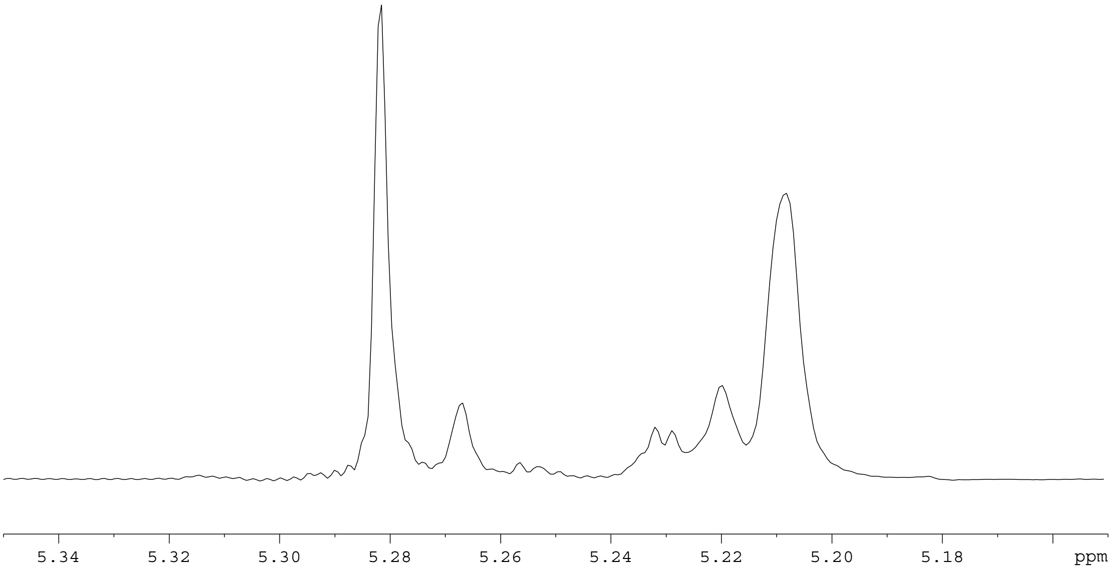


Figure S11: ^{1}H homonuclear decoupled NMR (methine region, $CDCl_3$, 400 MHz) for PLA formed in the melt using **2** (Table 1, entry 2).

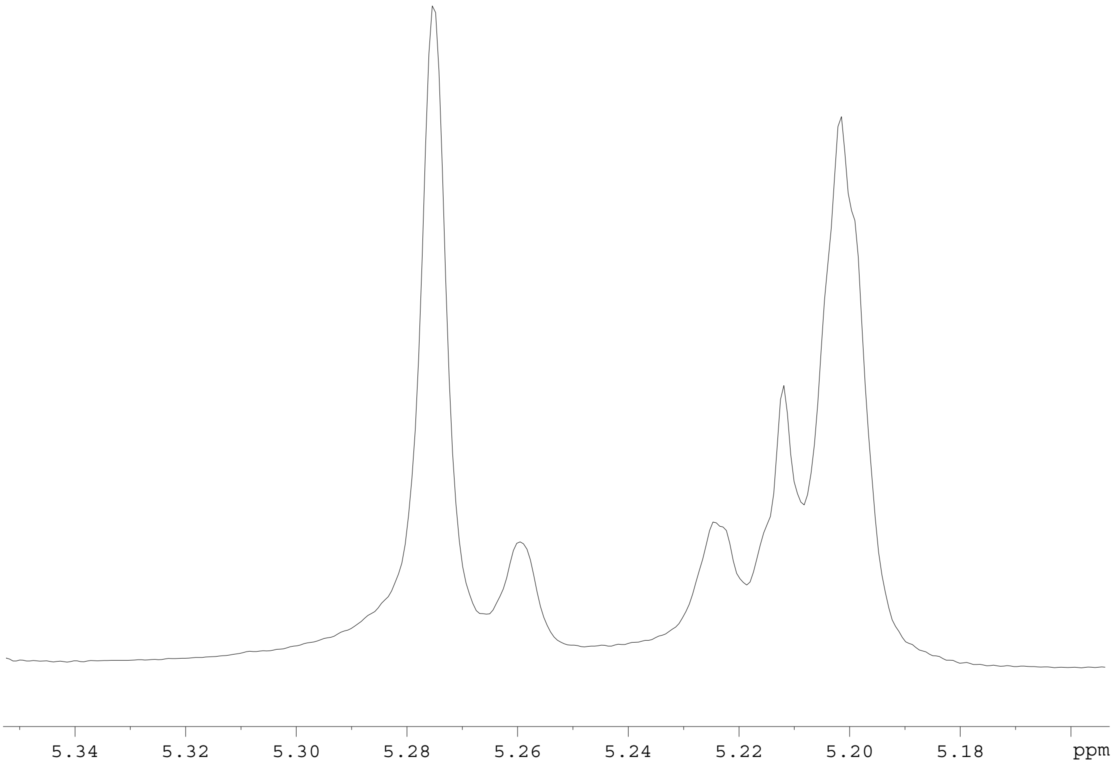


Figure S12: ^{1}H homonuclear decoupled NMR (methine region, $CDCl_3$, 400 MHz) for PLA formed in the melt using **3** (Table 1, entry 3)

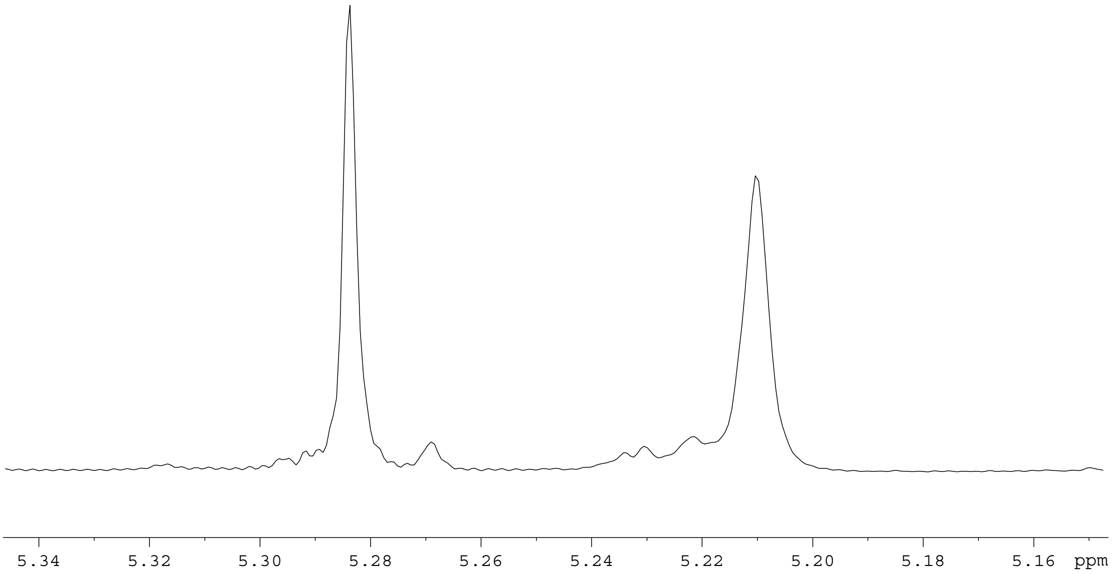


Figure S13: ^{1}H homonuclear decoupled NMR (methine region, $CDCl_3$, 400 MHz) for PLA formed in solution using **2** (Table 1, entry 4)

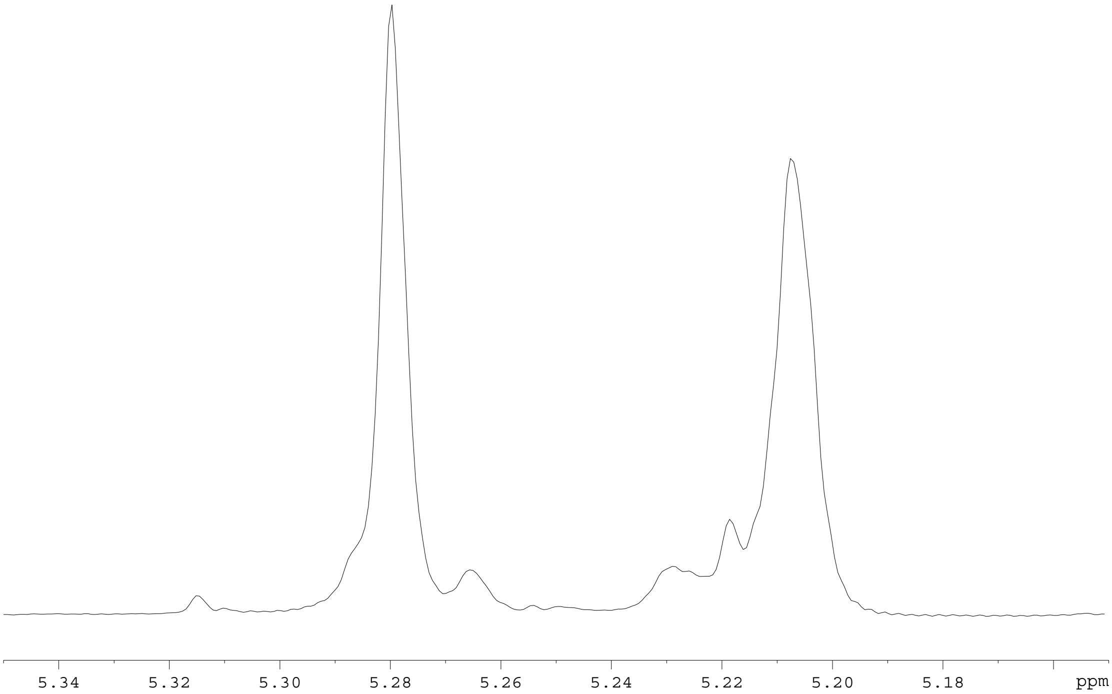


Figure S14: ^{1}H homonuclear decoupled NMR (methine region, $CDCl_3$, 400 MHz) for PLA formed in solution using **3** (Table 1, entry 5)

References:

(1) Kol, M.; Shamis, M.; Goldberg, I.; Goldschmidt, Z.; Alfi, S.; Hayut-Salant, E. *Inorg. Chem. Commun.* **2001**, *4*, 177-179.

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(6) J.E. Kasperczyk, *Macromolecules*, **1995**, *28*, 3937