Supplementary material

Functionalized polyesters from organocatalyzed ROP of gluOCA, the *O*–carboxyanhydride derived from glutamic acid

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Synthetic procedures and Spectroscopic data

Materials. All reactions were performed under inert atmosphere of argon, using standard Schlenk techniques. Solvents were dried and distilled prior to use: toluene (>99.9%), THF (>99.9%) and diethyl ether (>99.9%) over sodium, pentane (>99%) over calcium dihydride and dichloromethane (>99.95%) over phosphorous pentoxide. *L*–lacOCA was prepared according to literature procedure,[1] purified by two recrystallisations in diethyl ether and stored under argon at –20°C. Dimethylaminopyridine (DMAP) (99%, ALDRICH) was purified by recrystallization in toluene and stored under argon. Diisopropylethylamine was distilled over KOH and stored under argon. *n*–Pentanol (99+%) and *neo*–Pentanol (99%) were dried over sodium and distilled before use. PS–Diisopropylethylamine, (+)–α–methylbenzylamine (99%), diphosgene, Pd/C and acetic anhydride were used as received. γ–Benzyl 2–hydroxy glutaric acid was prepared following a literature procedure.[2]

Characterizations. NMR Spectra were recorded in $CDCl_3$ on BRUKER Avance 300, 400 and 500 MHz spectrometers at room temperature. Chemical shifts are reported in ppm relative to Me_4Si as an external standard. ^1H NMR measurements were used to determine the monomer conversion and the chain end groups. The degree of polymerization DP was determined from the relative integration of the signals for the lactate units and chain ends.

[1] O. Thillaye du Boullay, E. Marchal, B. Martin-Vaca, F. Cossío and D. Bourissou, *J. Am. Chem. Soc.,* 2006, **128**, 16442.
[2] S. Deechongkit, S.-L. You and J. W. Kelly, *Org. Lett*., 2004, **6**, 497.

IR spectra were recoded on a Perkin Elmer 1600 FTIR spectrometer.

The number–average and weight–average molar masses (M_n and M_w, respectively) and polydispersity indexes (M_w/M_n) of the polyester samples were determined by size exclusion chromatography (SEC) at 35°C with a Waters 600 liquid chromatograph equipped with a Waters 2410 Refractive Index Detector. Tetrahydrofuran (THF) was used as the eluent and the flow rate was set up at 1.0 mL/min. A Waters pre–column and a Waters STYRAGEL column (HR 4E, 50–100,000 g/mol) were used. Calibrations were performed using polystyrene standards (400–100,000 g/mol).

Maldi-ToF-MS analysis was performed on a Voyager System DE–STR from Applied Biosystems equipped with a 337 nm nitrogen laser. An accelerating voltage of 20 kV was applied. Mass spectra of 1000 shots were accumulated. The polymer sample was dissolved in CH_2Cl_2 at a concentration of 1 mg.ml^{-1}. The cationization agent used was NaI dissolved in MeOH at a concentration of 10 mg.ml^{-1}. The matrix used was dithranol and was dissolved in CH_2Cl_2 at a concentration of 10 mg.ml^{-1}. Solutions of matrix, salt, and polymer were mixed in a volume ratio of 3:1:1 respectively. The mixed solution was hand-spotted on a stainless steel MALDI target and left to dry. The spectrum was recorded in the reflectron mode. Baseline corrections and data analyses were performed using Data Explorer version 4.0 from Applied Biosystems.

Synthesis of γ-benzyl-2-hydroxyglutaric acid synthesis:

A 2M solution of a $NaNO_2$ in water (20.0 mmol) was added dropwise in 30 min, at 0°C, to a suspension of L-BnOGIu (2.37 g; 10.0 mmol) in 100 mL of a mixture H_2O/AcOH 8/2. The reaction mixture was stirred at this temperature for an additional 4 h, and became homogeneous. Water (100 mL) was added and the title compound was extracted by ethyl acetate (3 x 50 mL). The organic layer was washed with water, brine and dried over sodium sulphate. The solvent was removed by evaporation to give 2.70 g of a viscous oil. The crude hydroxyacid was purified by flash chromatography (100 g of silica, eluent: DCM 95 / MeOH 4,5 / AcOH 0,5) to give a light yellow viscous oil (1.38 g, 58%) that slowly crystallizes upon standing.

^{1}H NMR ($CDCl_3$ - 300 MHz): δ_{ppm} 7.35 (m, 5H, Ph); 5.13 (s, 2H, C*H*$_2$Ph); 4.31 (dd, IH, J^{HH} = 7,6 et 3,9 Hz, C*H*OH); 2.6 (m, 2H, $CH_2CH_2CO_2$); 2.23-2.30 (m, 1H, CH*H*CH_2CO_2); 2.01-2.07 (m, 1H, CH*H*CH_2CO_2).

^{13}C NMR ($CDCl_3$ -75 MHz) : δ_{ppm} 171.2; 166.6; 147.9; 135.2; 128.7-128.2; 78.0; 67.1; 28.4; 26.0.

Mp: 59-60 °C

Synthesis of the dicyclohexylamine salt of the α-hydroxy acid:

Dicyclohexyamine (1.0 mmol, 200µL) was added to a cooled solution of crude hydroxyacid (1.0 mmol, 240 mg) in 6.0 mL of diethyl ether. The mixture was stirred 30 min at this temperature. The salt was filtered, washed with diethyl ether, dried under vacuum to give a white powder (320 mg, 76%).

^{1}H NMR ($CDCl_3$, 300 MHz): δ_{ppm} 7.33 (m, 5H, Ph); 5.11 (s, 2H, C*H*$_2$Ph); 3.90 (dd, IH, J^{HH} = 7,6 and 3,9 Hz, C*H*OH); 2.96 (m, 2H, NC*H*(cyclohexyl)); 2.6 (m, 2H, $CH_2CH_2CO_2$); 2.18 (m, 1H, CH*H*CH_2CO_2); 2.00-1.10 (m, 22H, CH*H*CH_2CO_2, C*H*$_2$Cyclohexyl, O*H*).

Mp: 125-126°C

Synthesis of L–GluOCA

Diphosgene (0.36 mL, 3.0 mmol) was added to a suspension of the hydroxyacid dicyclohexylamine salt (1.26 g, 3.0 mmol) and polystyrene supported diisopropylethylamine (1.0 g, 3.0 mmol) in diethylether (20 mL). The reaction mixture was stirred 4 h at room temperature and then the PS–supported ammonium salts were filtered off and washed with diethylether. The solvent was evaporated under vacuum and the oil residue was washed with pentane in order to eliminate diphosgene residues. The oil residue became solid in the fridge (0.53 g, 67 %).

****Caution*. Diphosgene is highly toxic. All reactions with diphosgene were carried out in a well-ventilated hood under a slight stream of inert gas (argon). The gas outlet was bubbled through a mixed solution of aq. NH_3 (20% in weight), aq. NaOH (10% in weight) and ethanol (1/1/1 in volume).***

^{1}H NMR ($CDCl_3$, 300 MHz): δ_{ppm} 7.36 (m, 5H, Ph); 5.21 (dd, 1H, J_{HH} = 5.4 and 7.8 Hz, C*H*); 5.14 (s, 2H, CH_2Ph); 2.63 (t, 2H, J_{HH} = 6.7 Hz, CH_2CO_2); 2.44–2.22 (m, 2H, C$H_2CH_2CO_2$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_{ppm} 171.2 (s, CO_2); 166.6 (s, CO_2Bn); 147.9 (s, CO_3); 135.2 (s, C_{ipso} Ph); 128.7–128.2 (s, Ph); 78.0 (s, CH); 67.1 (s, *C*H_2Ph); 28.3 (s, $CH_2CH_2CO_2$); 26.0 (s, *C*$H_2CH_2CO_2$). IR (KBr, cm^{-1}): 1891; 1805; 1740. MS (IE) (M = 264.23): 264 [M^+]; 236 [M^+–CO]; 174 [M^+–Bn]. M.p. : 59–60°C. Anal. Calcd for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 59.23; H, 4.18.

Optical purity determination of L–gluOCA.

(+)–α–methylbenzylamine (70 μL, 0.54 mmol) was added to a solution of *L*–gluOCA (94 mg, 0.36 mmol) in dichloromethane (2 mL) at room temperature. The reaction mixture was then stirred until CO_2 no longer evolved (around 5 min.). The reaction mixture was diluted with DCM (5 mL), washed with cold 2N HCl (2 x 5 mL), brine (5 mL) and dried over Na_2SO_4. The solvent was removed by evaporation to give the amide adduct as a white solid (105 mg, 85 %). HPLC eluent H_2O/CH_3CN (gradient 90/10 to 20/80 over 13 min.): diastereomer mixture 95/5.

^{1}H NMR ($CDCl_3$, 300 MHz): δ_{ppm} 7.35–7.11 (m, 10H, Ph); 7.07 (br d, 1H, J_{HH} = 8.1 Hz, NH); 5.05 (s, 2H, CH_2Ph); 5.04 (m overlapped, 1H, C*H*CH_3); 4.11 (dd, 1H, J_{HH} = 3.6 and 7.5 Hz, C*H*); 2.52–2.38 (m, 2H, $CH_2CH_2CO_2$); 2.19–2.082 (m, 1H, CH'*H*CH_2CO_2); 1.99–1.88(m, 1H, C*H*'HCH_2CO_2); 1.43 (d, 3H, J_{HH} = 6.9 Hz, CH_3).

General procedure for the polymerization of L–gluOCA .

L–gluOCA was recristallized twice from an *i*–Pr_2O/Et_2O mixture (2/1) before polymerisation reactions. *L*–gluOCA (370 mg, 1.58 mmol, 20 equiv.) was dissolved in dichloromethane (5 mL). *n*–Pentanol (9 µL, 0.079 mmol, 1 equiv) and DMAP (10 mg, 0.079 mmol, 1 equiv) were added. The reaction mixture was stirred at room temperature until CO_2 no longer evolved (less than 5 min.). The complete monomer consumption was confirmed by ^{1}H NMR spectroscopy. The reaction mixture was diluted with DCM (5 mL), washed with cold 2N HCl (2 x 5 mL), brine (5 mL) and dried over Na_2SO_4. The solvent was removed by evaporation to give the polymer as a white solid (120 mg, 75 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ_{ppm} 7.30 (m, 100 H, Ph); 5.10 (m, 59 H, C*H*$_2$Ph and C*H*OCO); 4.29 (dd, 1H, $^3J_{HH}$ = 4.2 Hz, $^3J_{HH}$ = 7.8 Hz, C*H*OH); 4.04 (t, 2H, $^3J_{HH}$ = 6.8 Hz, OC*H*$_2$CH$_2$); 2.60–2.30 (m, 40 H, CH$_2$C*H*$_2$CO$_2$Bn); 2.30–1.90 (m, 40 H, C*H*$_2$CH$_2$CO$_2$Bn); 1.50 (m, 2H, OCH$_2$C*H*$_2$CH$_2$); 1.23 (m, 4H , C*H*$_2$C*H*$_2$CH$_3$); 0.83 (t, 3H, $^3J_{HH}$ = 6.8Hz, CH$_2$CH$_2$C*H*$_3$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_{ppm} 172.1 (CO); 168.2 (COBn); 135.9 (C_{ipso} Ph); 128.6 and 127.9 (C_{ortho}, C_{meta}, C_{para} Ph, overlapped); 71.6 (CH), 66.5 (*C*H$_2$Ph); 28.9 (*C*H$_2$CO); 25.9 (CH$_2$). SEC (THF): M_n = 2060, M_w/M_n = 1.24.

General procedure for the polymer acetylation.

Acetic anhydride (2 equiv.) was added at room temperature to the reaction mixture at the end of the polymerization and the solution was stirred during 1h. ^{1}H NMR spectroscopy indicated the complete disappearance of the terminal C*H*OH signal. The reaction mixture was then diluted with DCM (5 mL), washed with cold 2N HCl (2 x 5 mL), brine (5 mL) and dried over Na_2SO_4. Evaporation of the dichloromethane under vacuum yielded the acetylated polymer.

General procedure for the polymer deprotection.

The acetylated polymer was dissolved in ethyl acetate and Pd/C 10 % was added. The reaction mixture was stirred during 1 h under an H_2 atmosphere (1 atm), filtered on celite and concentrated under vacuum. The residue was dissolved in THF, concentrated again and finally precipitated by addition of chloroform. The deprotected polymer was obtained as a white solid.

General Procedure for the block copolymerization of L–lacOCA and L–gluOCA.

L–lacOCA (205 mg, 1.77 mmol, 20 equiv.) was dissolved in dichloromethane (3 mL). *n*–Pentanol (10 μL, 0.88 mmol) and DMAP (10 mg, 0.88 mmol) were successively added. The reaction mixture was stirred at room temperature until CO_2 no longer evolved (less than 5 min.). The complete monomer consumption was confirmed by ^{1}H NMR spectroscopy.

^{1}H NMR ($CDCl_3$, 300 MHz): δ_{ppm} 5.15 (m, 19H, C*H*OCO); 4.30 (q, 1H, $^3J_{HH}$ = 6.9 Hz, C*H*OH); 4.10 (m, 2H, OC*H*$_2$CH$_2$); 1.50 (m, 60H, C*H*$_3$CH and OCH$_2$C*H*$_2$CH$_2$); 1.30 (m, 4H, C*H*$_2$C*H*$_2$CH$_3$); 0.90 (t, 3H, CH$_2$CH$_2$C*H*$_3$). SEC (THF): M_n = 1140; M_w/M_n = 1.24

To the precedent solution was added *L*–gluOCA (230 mg, 0.88 mmol, 10 equiv.) in solution in dichloromethane (2 mL). After stirring for 5 min. at room temperature, ^{1}H NMR spectroscopy showed total consumption of the *L*–gluOCA monomer. The reaction mixture was diluted with DCM (5 mL), washed with cold 2N HCl (2 x 5 mL), brine (5 mL) and dried over Na_2SO_4. The solvent was removed by evaporation to give the polymer as a white solid (330 mg, 88 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ_{ppm} 7.30 (m, 50H, Ph); 5.10 (m, 50H, CH$_2$Ph and C*H*OCO); 4.30 (dd, 1H, $^3J_{HH}$ = 4.2 and 7.8 Hz, C*H*OH); 4.10 (m, 2H, OC*H*$_2$CH$_2$); 2.50–2.10 (m, 40H, C*H*$_2$C*H*$_2$CO$_2$Bn); 1.50 (m, 62H, C*H*$_3$CH and OCH$_2$C*H*$_2$CH$_2$); 1.30 (m, 4H, C*H*$_2$C*H*$_2$CH$_3$); 0.90 (t, 3H, CH$_2$CH$_2$C*H*$_3$). SEC (THF): M_n = 2540; M_w/M_n = 1.23.

General procedure for the random copolymerization of L–lacOCA and L–gluOCA.

poly(Lac)$_{10}$poly(BnGlu)$_{10}$

L–gluOCA (250 mg, 0.95 mmol) and LacOCA (110 mg, 0.95 mmol) were dissolved in dichloromethane (5 mL). *n*–Pentanol (10 μL, 0.095 mmol) and DMAP (12 mg, 0.095 mmol) were added. The reaction mixture was stirred at room temperature until CO_2 no longer evolved (5 min.). The complete monomer consumption was confirmed by ^{1}H NMR spectroscopy. The reaction mixture was diluted with DCM (5 mL), washed with cold 2N HCl (2 x 5 mL), brine (5 mL) and dried over Na_2SO_4. The solvent was removed by evaporation to give the polymer as a white solid (250 mg, 87 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ_{ppm} 7.30 (m, 50H, Ph); 5.07 (m, 40H, C*H*$_2$Ph and C*H*OCO); 4.30 (m, 1H, C*H*OH); 4.05 (m, 2H, OC*H*$_2$CH$_2$); 2.50–2.10 (m, 40H, C*H*$_2$C*H*$_2$CO$_2$Bn); 1.53 (m, 32H, C*H*$_3$CH and OCH$_2$C*H*$_2$CH$_2$); 1.23 (m, 4H, C*H*$_2$C*H*$_2$CH$_3$); 0.80 (t, 3H, CH$_2$CH$_2$C*H*$_3$). SEC (THF): M_n = 2800; M_w/M_n = 1.38

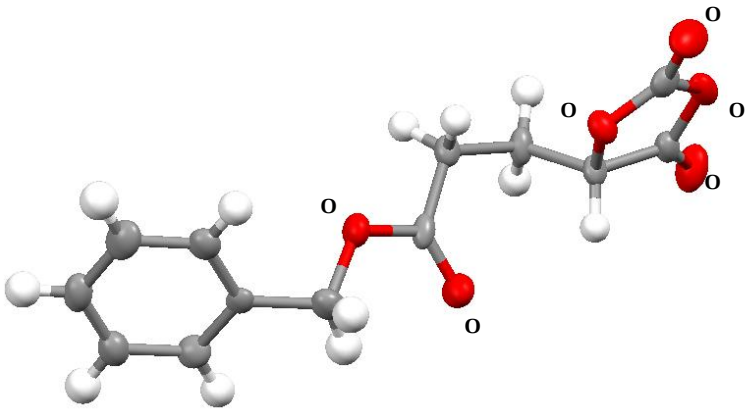

Figure S1. Molecular view of *L*–gluOCA in the solid state.

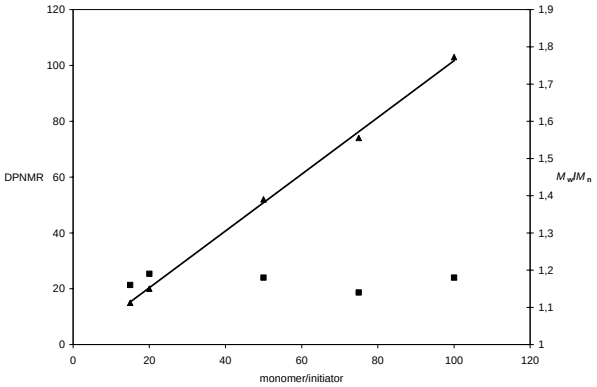

Figure S2. DP_{NMR} (▲) and M_w/M_n (■) versus $[L\text{–gluOCA}]_0/[neo\text{–pentOH}]_0$ ratio (CH_2Cl_2, 25°C, $[I]_0/[Cat]_0 = 1$).

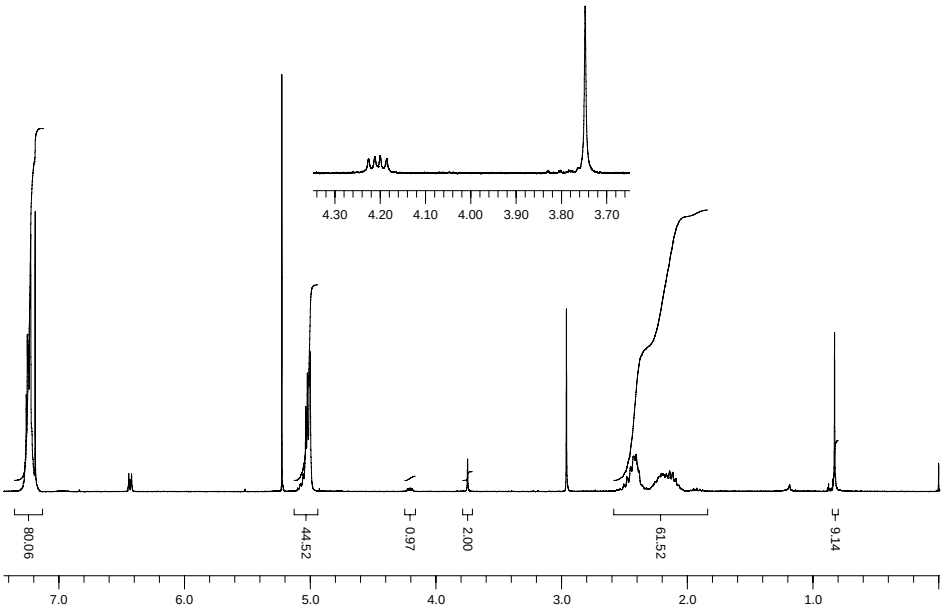

Figure S3. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) of a polyester obtained by polymerization of *L*–gluOCA with *neo*–pentOH as initiator (CH_2Cl_2, 25°C, [*L*–gluOCA]$_0$/[*neo*–pentOH]$_0$/[DMAP]$_0$ 15/1/1).

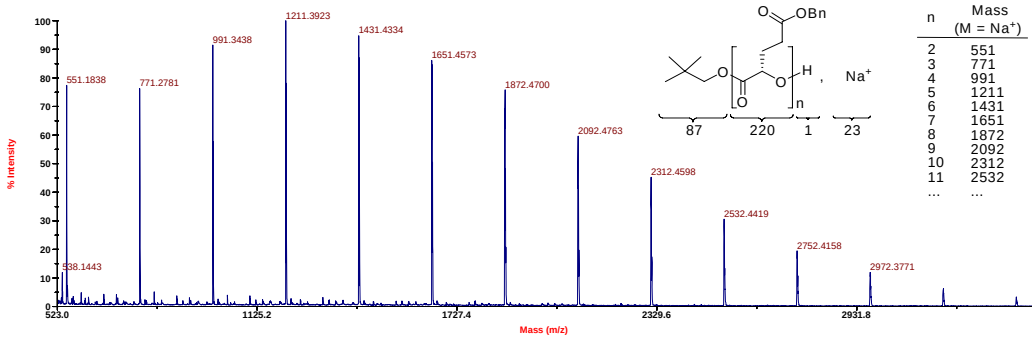

Figure S4. MALDI–TOF mass spectra (Region *m/z* 520 to 3000) of a polyester prepared by polymerization of *L*–gluOCA with *neo*–pentanol as initiator (CH_2Cl_2, 25°C, [*L*–gluOCA]$_0$/[*neo*–pentOH]$_0$/[DMAP]$_0$ 15/1/1)

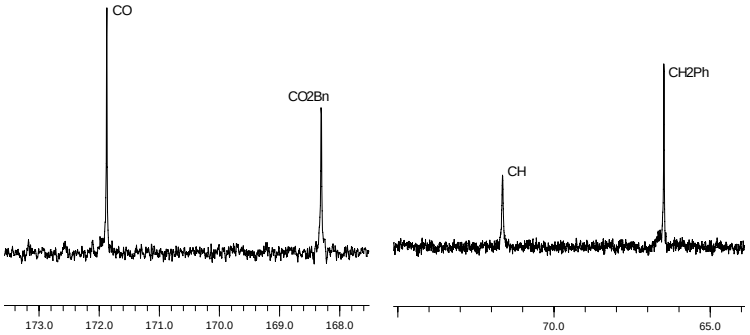

Figure S5. ^{13}C NMR spectra ($CDCl_3$, 300 MHz, CO and C*H*OH regions) of a polyester obtained by polymerization of *L*–gluOCA with *neo*–pentanol as initiator (CH_2Cl_2, 25°C, $[L\text{–gluOCA}]_0/[neo\text{–pentOH}]_0/[DMAP]_0$ 100/1/1). In the region of carbonyl groups, only two singlet signals are observed: one (at δ 168.3 ppm) corresponding to the pendant benzyl ester moieties and the other one (at δ 171.9 ppm) attributed to the ester functions of the polymer backbone, confirming that there is only one stereochemical environment.

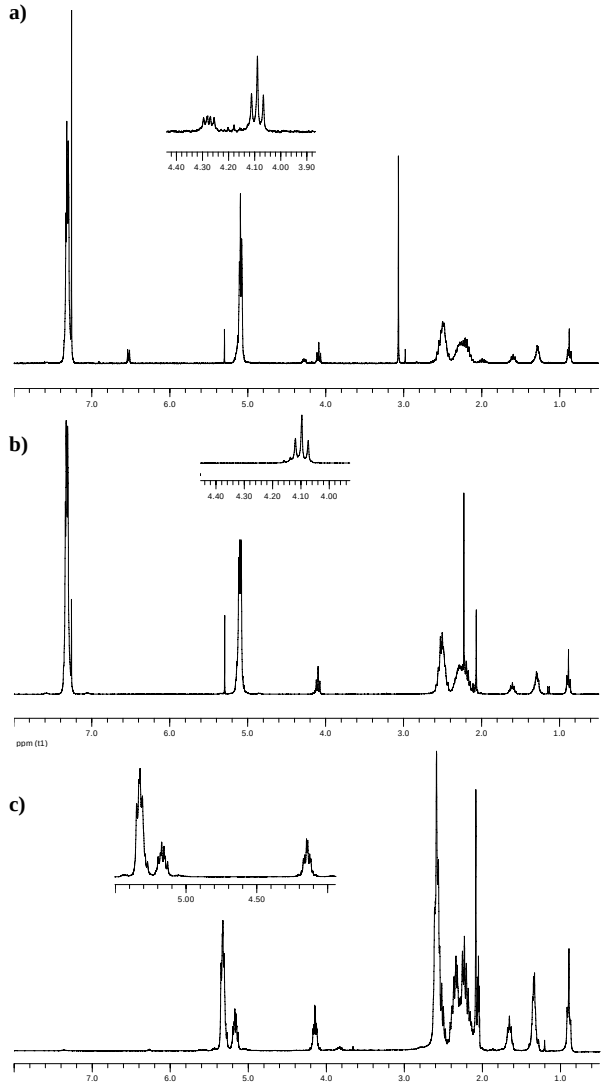

Figure S6. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) of a poly(*L*–glu) sample obtained by **a)** polymerization of *L*–gluOCA with *n*–pentOH as initiator, **b)** acetylation of the terminal hydroxyl group and **c)** deprotection of the pendant carboxyl groups.

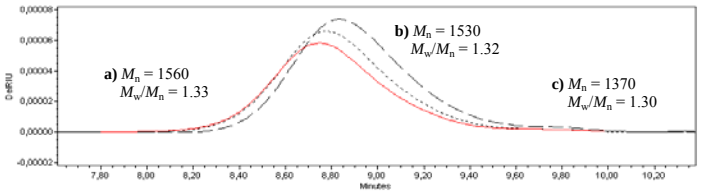

Figure S7. SEC traces of a **a)** poly(*L*–glu) DP = 20 (full line), **b)** acetylated poly(*L*–glu) (dotted line) and **c)** deprotected poly(*L*–glu) (dashed line).

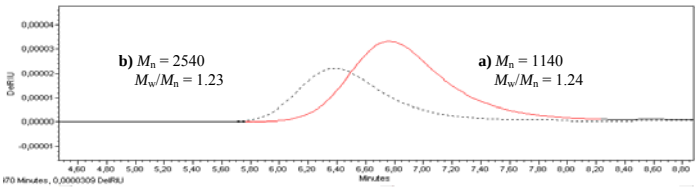

Figure S8. SEC traces of **a)** poly(*L*–lac) DP = 20 (full line) and **b)** co–poly(*L*–lac–*b*–*L*–glu) (20/10) (dotted line).

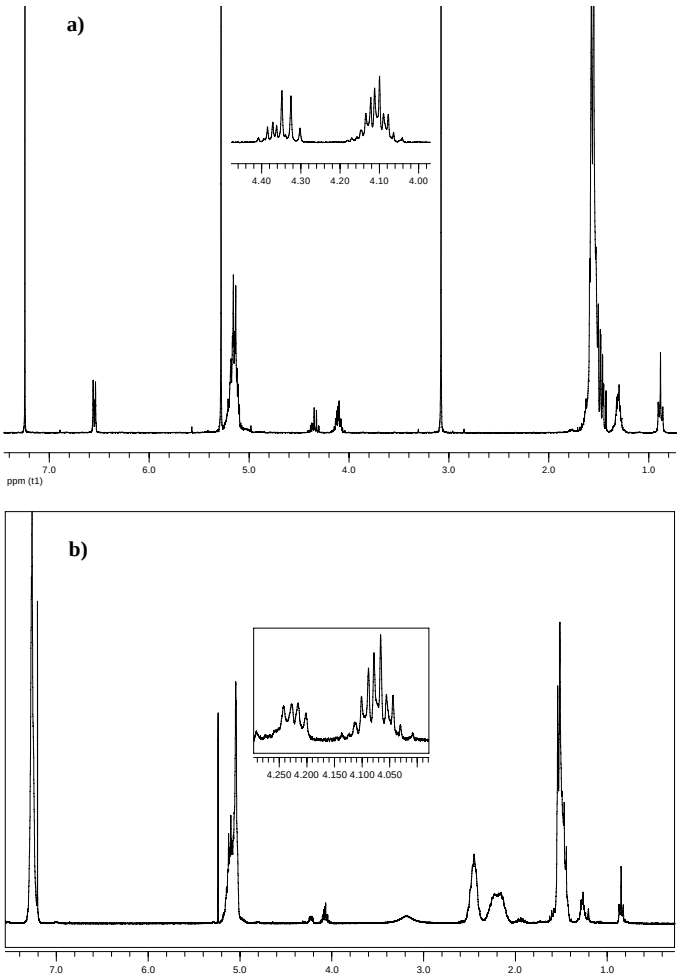

Figure S9. ^{1}H NMR spectra ($CDCl_3$, 300 MHz) of a co–poly(*L*–lac–*b*–*L*–glu) sample obtained by block copolymerization of *L*–lacOCA and *L*–gluOCA with *n*–pentanol as initiator (CH_2Cl_2, 25°C, [*L*–lacOCA]$_0$/[*n*–pentOH]$_0$/[DMAP]$_0$ 20/1/1): **a)** First poly(*L*–lac) block and **b)** co–poly(*L*–lac–*b*–*L*–glu) sample obtained alter addition of 10 equivalents of *L*–gluOCA.

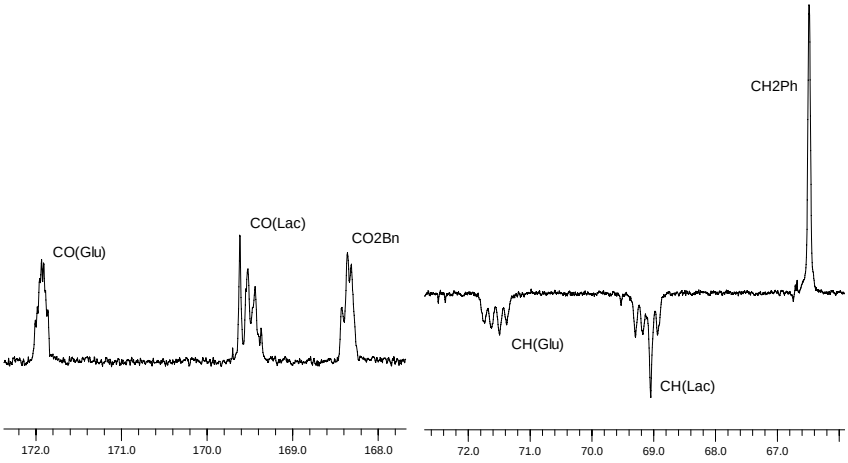

Figure S10. ^{13}C NMR spectra ($CDCl_3$, 300 MHz, JMOD, CO and C*H*OH regions) of a co–poly(*L*–glu–*r*–*L*–lac) sample obtained by random copolymerization of *L*–gluOCA and *L*–lacOCA with *neo*–pentanol as initiator (CH_2Cl_2, 25°C, [*L*–lacOCA]/[*L*–gluOCA]$_0$/[*neo*–pentOH]$_0$/[DMAP]$_0$ 55/45/1/1). The splitting of the ^{13}C signals is typical for random copolymers and results from the different monomer sequences.

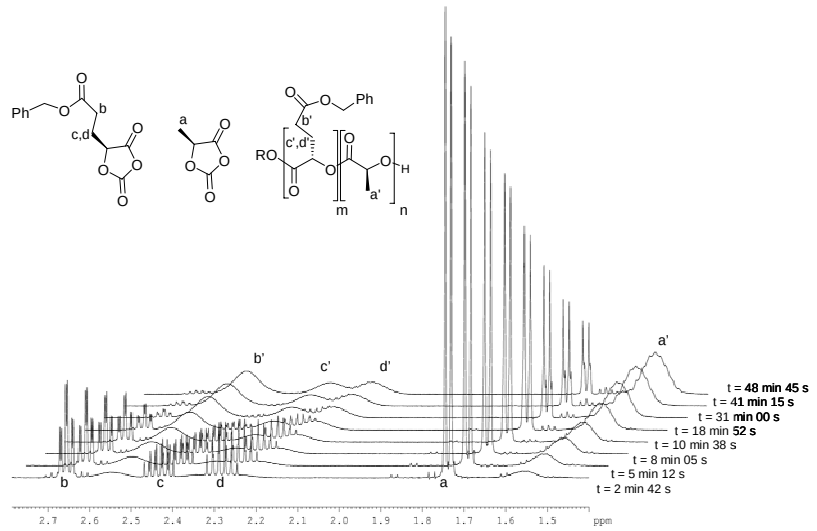

Figure S11. *L*–lacOCA and *L*–gluOCA conversions monitored *in situ* by ^1H NMR spectroscopy for a random copolymerisation with *neo*–pentanol as initiator (CH_2Cl_2, 25°C, [*L*–lacOCA]/[*L*–gluOCA]$_0$/[*neo*–pentOH]$_0$/[DMAP]$_0$ 55/45/1/1).