Supporting Information

One-Pot Multifunctional Polyesters by Continuous Flow Organocatalysed Ring-Opening Polymerisation for Targeted and Tunable Materials Design

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1. Materials

ε-Caprolactone was purchased from Sigma Aldrich (97%) dried over calcium hydride, cryo-distilled under vacuum and stored over molecular sieves. L-Lactide was purchased from Sigma Aldrich (98%), recrystallized thrice from dry toluene, dried under vaccum, and stored in the glovebox. Allylic alcohol (Sigma Aldrich, 95%) and trielthylamine (Acros, ≥99%) were dried over calcium hydride, cryo-distilled under vacuum and stored over molecular sieves. TBD and DBU were purchased from Sigma Aldrich, stored in the glovebox and used without any purifications. 1,2 Dichloroethane (DCE, Sigma Aldrich, ≥99%), terephtaloyl chloride (Sigma Aldrich, ≥ 99%) and 1,3,5-benzenetricarbonyl trichloride (Sigma, 99%), trimethylolpropane tris*(*3-mercaptopropionate) (Sigma Aldrich, ≥ 95%), the photoinitiator which is blend between diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide and 2-hydroxy-2 methylpropiophenone, the surfactant Hypermer B246, (Croda, triblock copolymer of polyhydroxystearic acid and polyethylene glycol), were used as received without any purification. Toluene and DCM (water and oxygen free) were used from a solvent purification system.

2. Instrumentation

NMR spectra were recorded on a Bruker DRX400 NMR spectrometer. Monomer conversions, end-group fidelity and detailed investigations of the chemical structure were established by Nuclear Magnetic Resonance (NMR) spectra. These spectra are generally recorded in $CDCl_3$ at room temperature on a 400 Megahertz (MHz; 9.4 Tesla) spectrometer. Residual $CHCl_3$ and DMSO were used as the internal standard for ^1H NMR spectra (7.26 ppm for $CHCl_3$ and 2.50 ppm for DMSO) with NMR data recorded as follows: chemical shift (δ) [multiplicity, coupling constant(s) *J* (Hz), relative integral], where multiplicity is defined: s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, m= multiplet or combinations thereof and prefixed br = broad.

SEC samples were measured on a custom-designed PSS system, operated by PSS WinGPC software, equipped with a PSS SDV analytical 3.0 µm guard column (50 x 8 mm), followed by one PSS SDV analytical column with 3.0 µm particles of porosity of 1000 Å (300 x 8 mm) and an evaporative light scattering detector (ELSD) ELS1300 using THF as eluent at 40 °C with a flow rate of 1 mL·min^{-1} using an isocratic PSS SECcurity pump. Both SEC systems were calibrated using linear narrow polystyrene standards ranging from 474 – 7.5 x 10^6 g·mol^{-1}.

ESI-MS analysis was carried out at the Monash Analytical Platform, Australia (School of Chemistry, Monash University). From each sample 1 mg was dissolved in 1 mL dichloromethane (DCM, HPLC grade). The DCM solution was diluted (±100 times) by adding 1 drop to a 1 mL mixture of DCM:methanol (MeOH) (DCM:MeOH = 3:2 v/v). This mixture was infused via a Kd Scientific infusion pump at a static flow rate of 300 mL/h and mixed via a T-piece with a solution consisting of 0.1% of formic acid in acetonitrile (0.1 mL/min) before infusion into the MS. The MS setup was as follows: Agilent 6220 time- of-flight mass spectrometry (Q-TOF MS) system (Santa Clara, CA, USA). The MS was operated in positive mode using the following conditions: nebulizer pressure 35 psi, gas flow-rate 8 L·min-1, gas temperature 300 °C, vaporizer temperature 250 °C, capillary voltage 250 V, fragmentor 150 V and skimmer 65 V. Instrument was operated in the extended dynamic range mode with data collected in m/z range 200–3000. Spectra were recorded over a 1 min. time period with 1 scan/s and subsequently averaged out before analysis. Spectra were analyzed with Agilent Masshunter Qualitative Analysis B.07.00.

SEM analysis was performed at the Monash Centre for Electron Microscopy (MCEM). Samples were prepared by slow drying from ethanol at – 4 °C and slicing thin sections, followed by conductive coating in a thin metal layer (~ 2 nm). Secondary electron SEM images were recorded on a FEI Nova NanoSEM 450 FEGSEM at 5 kV with a working distance of approximately 5 mm. Pore size analysis was performed using ImageJ software and counting 100 pores.

3. General protocols

CL and LA continuous flow polymerisation. In a typical polymerisation, 10 mL of monomer solution (2M in toluene for CL and 1.6M for LA in DCM) and catalyst solution ([TBD]=0.1M [ROH]=0.2M ; [DBU]=0.016M and [ROH]=0.16M) are prepared freshly in the glovebox, transferred into a flame-dried schlenk and then connected to an argon line. The flow reactor which consists of fluorinated gastight PFA tubing with a total internal reactor volume of 1.0 mL (ID = 0.50mm, L = 2.54m) attached to Y-shaped reactor. The flow rate of the reaction mixture is controlled using a Fusion 100 classic syringe pump and 2×10 mL SGE gastight syringes are used (Trajan Scientific Australia, Pty Ltd.). The total flow rate corresponds to twice the flow displayed by syringe pump (*e.g.* for a residence time of 20 min, the selected flow rate is 25µL•min^{-1} which corresponds a total flow rate of 50µL•min^{-1}). The polymerisation is then quenched by the addition of a solution of benzoic acid in toluene or DCM (10.0 mg•mL^{-1}) and the polymer is purified by precipitation in cold methanol.

CL and LA continuous flow polymerisation and post-modification. Same procedure as above-mentioned but instead of the addition of benzoic acid (quench), the flow reactor is connected to a collection flask (See Fig. S3) containing a solution of terephthaloyl chloride (2-Cl) or 1,3,5-benzenetricarbonyl trichloride (3-Cl) in equimolar proportion relative to hydroxyl function ([Cl]=[ROH]), and 2 eq. of NEt_3 in toluene or DCM. The coupling reaction was stopped 10 min after the last drop of crude polymer solution is added to the collection flask. The crude product is analysed by ^{1}H NMR spectroscopy to determine both conversion and coupling efficiency. The crude product is then purified by two successive precipitation in cold methanol and the resulting white powder is subsequently dried under high vacuum for 12h (for LA a previous precipitation in cold cyclohexane has been sometimes employed to increase the yield).

Linear PCL: ^{1}H NMR (298K, 400MHz, $CDCl_3$) δ(ppm): 8.02 (s, CH(Ar), 4H), 5.85 (m, =CH(allyl), 3H) ; 5.27-5.15 (m, $=CH_2$(allyl), 4H) ; 4.48 (d, CH_2(allyl), 4H, J = 6.0Hz); 4.27 (t, 6H, CH_2CO(Ar), J = 6.8Hz) ; 3.99 (t, 22H, J = 6.8Hz); 2.24 (t, $COCH_2$(backbone), 26H, J = 7.6Hz); 1.90-1.35 (br, CH_2(backbone) 84H)

^{13}C NMR (298K, 100MHz, $CDCl_3$) δ(ppm): 173.92; 132.08; 119.33; 65.76; 33.60; 29.54; 26.01.

Linear PLA: ^{1}H NMR (298K, 400MHz, $CDCl_3$) δ(ppm): 8.04 (s, CH(Ar), 4H), 5.82 (m, =CH(allyl), 2H) ; 5.33-5.20 (m, $=CH_2$(allyl), 4H) ; 5.12 (q, CH(lactide), 24H) 4.56 (m, CH_2(allyl), 4H); 1.68-1.35 (m, CH_3(lactide), 78H).

3-arms star PCL: ^{1}H NMR (298K, 400MHz, $CDCl_3$) δ(ppm) : 8.75 (s, CH(Ar), 3H), 5.85 (m, =CH(allyl), 3H) ; 5.20 (m, $=CH_2$(allyl), 6H) ; 4.50 (d, CH_2(allyl), 6H, J = 6.0Hz); 4.30 (t, 6H, CH_2CO(Ar), J = 6.8Hz) ; 4.02 (t, 54H, J = 6.8Hz); 2.23 (t, $COCH_2$(backbone), 60H, J = 7.6Hz); 1.90-1.35 (br, CH_2(backbone) 120H)

3-arms star PLA: ^{1}H NMR (298K, 400MHz, $CDCl_3$) δ(ppm): 8.86 (s, CH(Ar), 3H), 5.82 (m, =CH(allyl), 3H) ; 5.33-5.20 (m, $=CH_2$(allyl), 6H) ; 5.12 (q, CH(lactide), 24H) 4.56 (m, CH_2(allyl), 6H); 1.68-1.35 (m, CH_3(lactide), 81H).

^{13}C NMR (298K, 100MHz, $CDCl_3$) δ(ppm): 169.6; 131.34; 118.97; 69.25; 69.01; 66.02; 16.80; 16.65.

Crosslinking test via thermal initiated thiol-ene click reactions. In a typical reaction, equimolar amounts of polymer (100 mg, 3PCL-DP10, Entry 4, Table 1) and trimethylolpropane tris*(*3-mercaptopropionate) and AIBN (1 mol.%) were dissolved in 2mL of toluene in a septum capped vial. The solution was degassed by bubbling argon for 10 minutes and then heated at 80°C for an hour resulting in gel formation (See Fig. S8).

PolyHIPE preparation. The procedure was based on the earlier work.[1] Solution of polymer in 1,2 dichloroethane, surfactant Hypermer B246 and the photoinitiator were combined to form an oil phase in a two necked round bottom flask wrapped in aluminium foil to exclude light. The oil phase was stirred continuously with a rectangular (25 mm × 30 mm) polytetrafluoroethylene stirrer attached to an overhead stirrer. An aqueous phase of deionised water was added drop wise to form a HIPE at 20.0 $mL.min^{-1}$. Once the aqueous phase was added the HIPE was allowed to stir for a further minute. The formulations are detailed in Table 2. The HIPE was then transferred to glass mould. The mould is then passed under a UV irradiator (Fusion UV Systems Inc. Light Hammer® 6 variable power UV curing system with LC6E bench top conveyor) three times on each side of the emulsion. The resulting monolith was then carefully removed and immersed in an acetone bath for 48 h (with four changes), then in chloroform 24 h, then in ethanol 24 h, before transferring and storing in acetone.

Swellability tests: Approximately 5 – 10 mg of dried sample was immersed in solvent and left for 2 h. Subsequently, the sample was briefly touched to a paper towel to remove excess solvent and transferred to a pre-weighed vial. The swellability was calculated using the following equation:

$$Swellability\ (w/w\%) = \frac{W_f - W_i}{W_i} \times 100$$

Where W_i is the initial weight of the dry sample and W_f is the final weight of the swollen sample.

4. Optimisation of the Continuous flow OROP synthesis PCL and PLLA

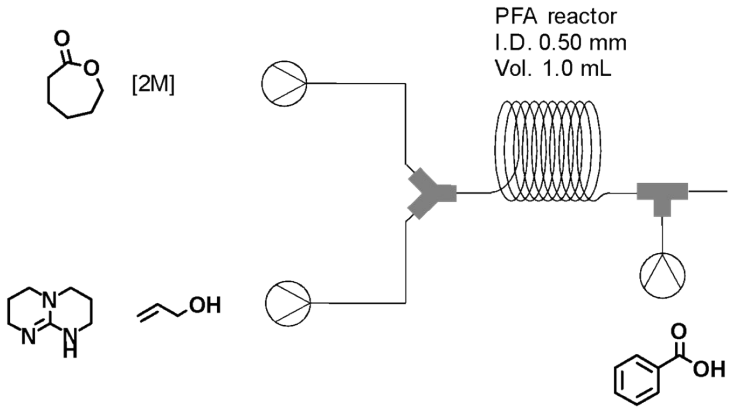


Figure S1. Optimisation of the conditions for the continuous flow ROP of ε-CL catalysed by TBD.

Table S1. Polymerisation conditions for the ROP of CL catalysed by TBD; [CL] = 2M, $DP_{(targeted)}$=10, Y mixer, PFA tubing (ID = 0.50mm ; 1.0 mL) at 25°C.

Entry	Solvent	[ROH]:[TBD]	Residence time / min	% Conv. / ^{1}H NMR [a]	M_n / g mol^{-1} [b]	$Đ$ [b]
1	Toluene	1 : 0.20	1	11	-	-
2	Toluene	1 : 0.20	5	24	-	-
3	Toluene	1 : 0.20	10	38	-	-
4	Toluene	1 : 0.20	20	66	800	1.26
5	Toluene	1 : 0.50	1	15	-	-
6	Toluene	1 : 0.50	5	40	-	-
7	Toluene	1 : 0.50	10	72	800	1.19
8	Toluene	1 : 0.50	20	91	1050	1.21
9	Toluene	1 : 0.75	1	60*	800	1.18
10	Toluene	1 : 0.75	5	88*	950	1.20
11	Toluene	1 : 1.00	1	85*	950	1.21
12	Toluene	1 : 1.00	5	98*	1080	1.19
13	DCM	1 : 0.50	20	43	-	-
14	DCM	1 : 0.50	45	81	800	1.22

a) Conversions measured by ^{1}H NMR spectroscopy b) M_n and dispersity of the crude product of polymerisation were measured by SEC vs. PS stantards * not reproducible due to the precipitation of TBD at [TBD] > 0.1M in dry toluene.

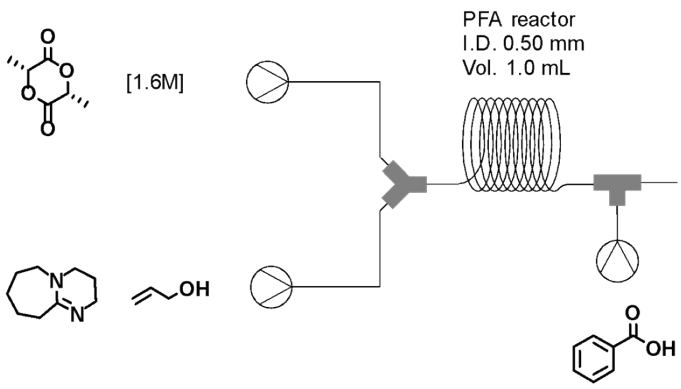


Figure S2. Optimisation of the conditions for the continuous flow ROP of L-LA catalysed by DBU.

Table S2. Polymerisation conditions for the ROP of L-LA catalysed by DBU; [LLA] = 1.6 M, $DP_{(targeted)}$=20, Y mixer, PFA tubing (ID = 0.50mm ; 1.0 mL) at 25°C.

Entry	Solvent	[ROH]:[DBU]	Residence time / s	% Conv. / ^{1}H NMR [a]	M_n / g•mol^{-1} [b]	$Đ$ [b]
1	DCM	1 : 0.10	6	61	660	1.38
2	DCM	1 : 0.10	12	80	850	1.32
3	DCM	1 : 0.10	30	98	1050	1.27
4	DCM	1 : 0.10	60	≥ 99	1080	1.29

a) Conversions measured by ^{1}H NMR spectroscopy b) M_n and dispersity of the crude product of polymerisation were measured by SEC vs. PS stantards.

Figure S3. Picture of the setup for the continuous flow organocatalysed polymerisation and post-modification reactions.

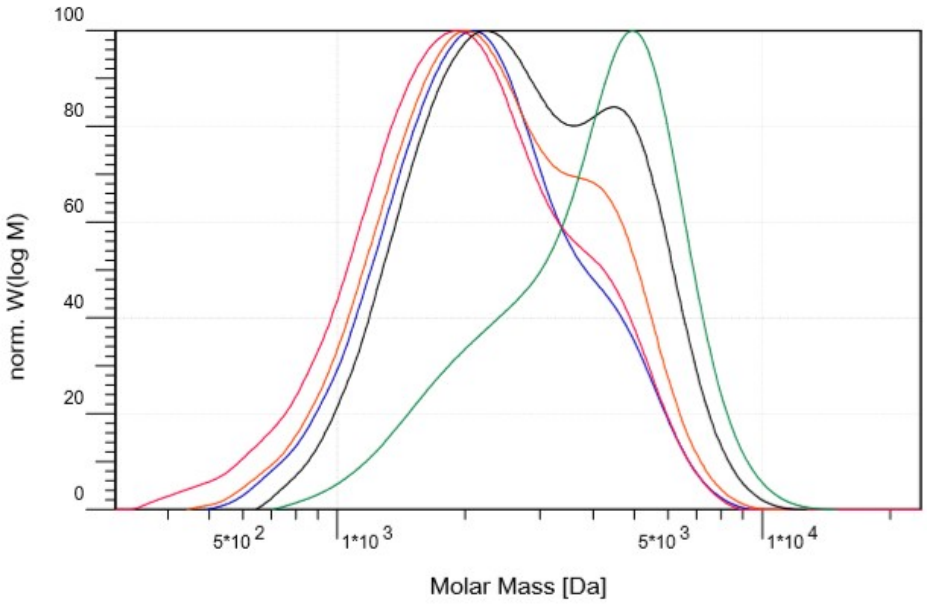


Figure S4. SEC traces (without purification) of the coupling evolution overtime for continuous flow ROP of CL (2M, [CL]:[ROH]:[TBD] = 10 : 1 : 0.5 in toluene) using the bifunctional acyl chloride coupling agent (2-Cl).

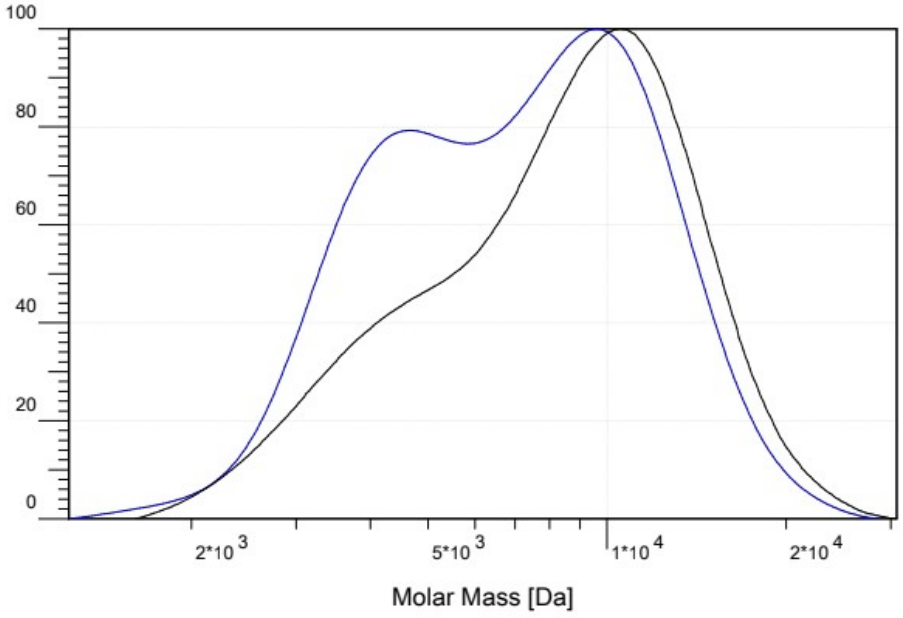


Figure S5. SEC traces of PLA obtained by flow ROP (1,6M, [LA]:[DBU]:[TBD] = 20 : 1 : 0.1 in DCM) and post-modification using 3-Cl coupling agent a) before purification (blue curve) b) after purification (black curve) by several precipitation in cold methanol.

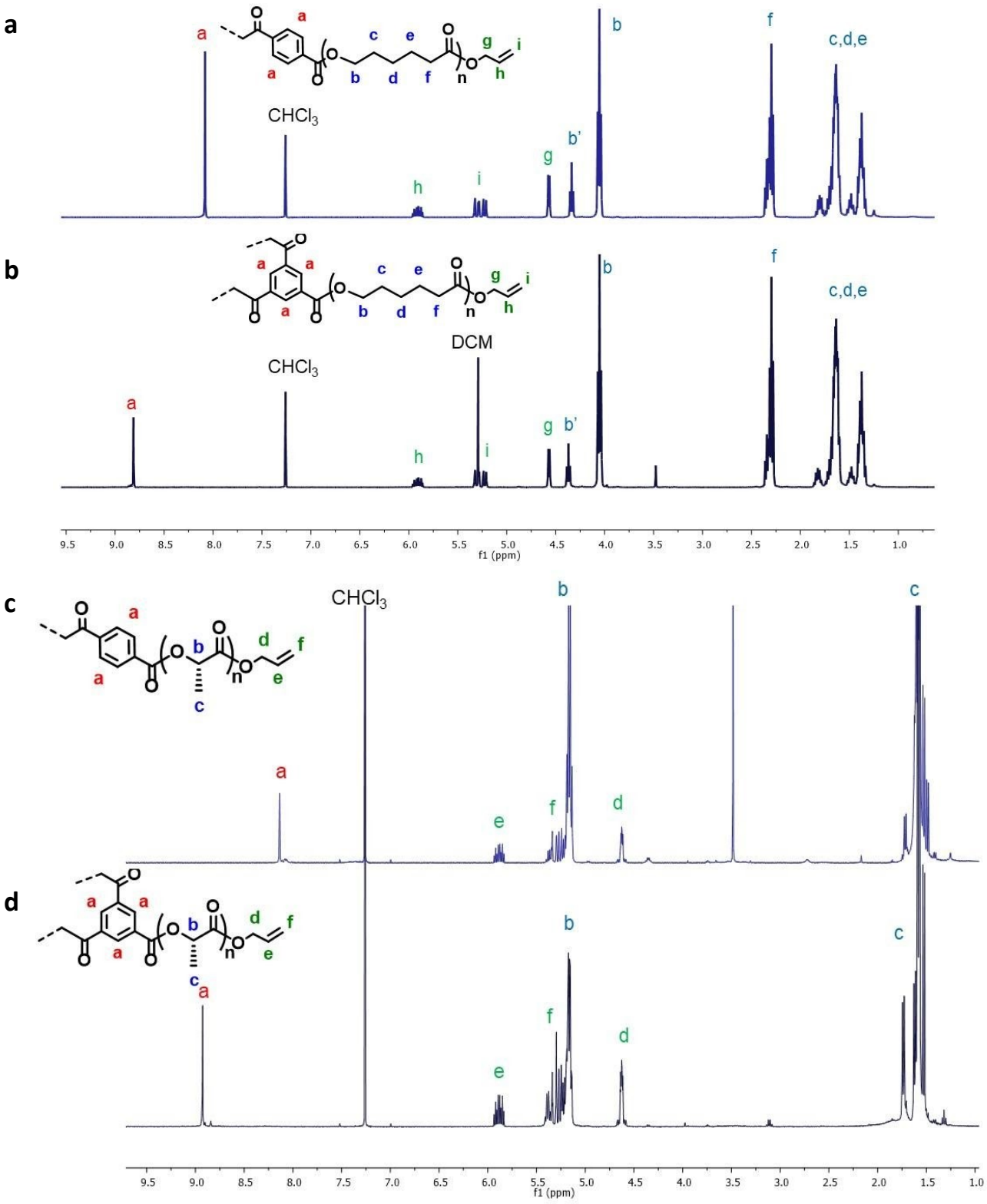


Figure S6. ^{1}H NMR (in CDCl3, 400 MHz) spectra of a purified a) linear and b) 3-arm star poly(caprolactone); c) linear and d) 3-arms star poly L-Lactide.

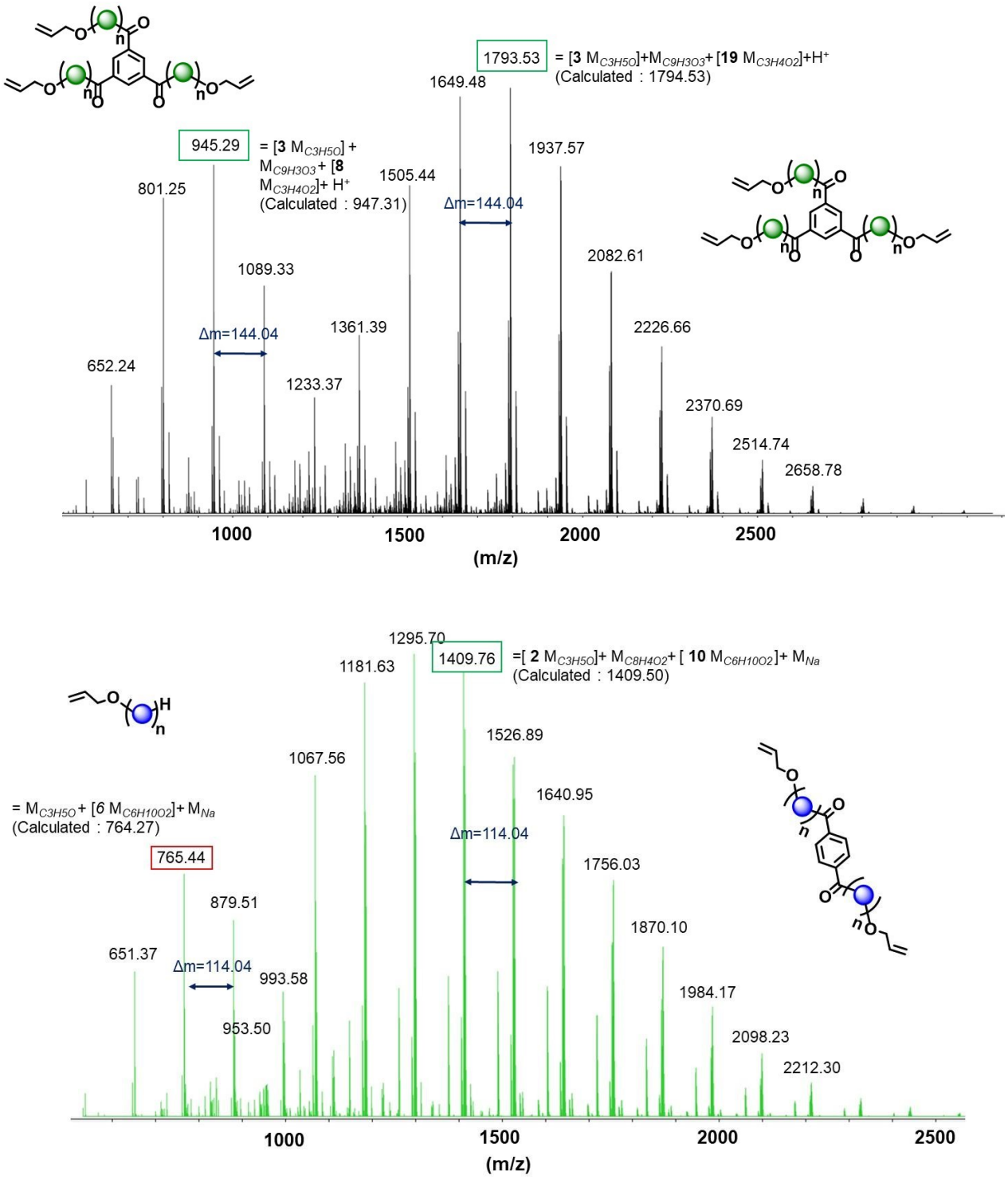
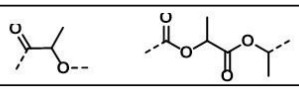
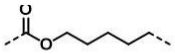
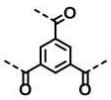
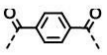


Figure S7. ESI spectrum of star-PLA (top, Entry 5, Table 1) and linear PCL (bottom, Entry 1, Table 1).

Table S3. Fragment identification and molar masses for ESI analysis.

Fragment	Formula	Exact mass (g.mol-1)
	$C_3H_4O_2$ $C_6H_8O_4$	77.02 144.04
	$C_6H_{10}O_2$	114.04
	C_3H_5O	57.04
	$C_9H_3O_3$	160.03
	$C_8H_4O_2$	132,04

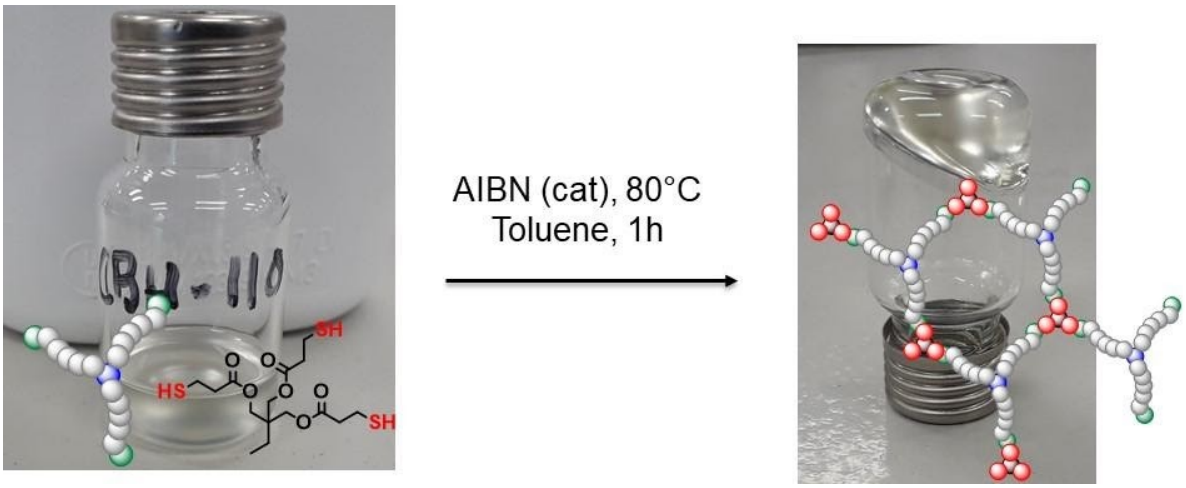


Figure S8. Thermally initiated thiol-ene click reaction by AIBN in toluene at 80°C for 1 h exemplified for 3-arm PCL (Entry 4, Table 1).

5. Optimisation of the polyHIPE preparation

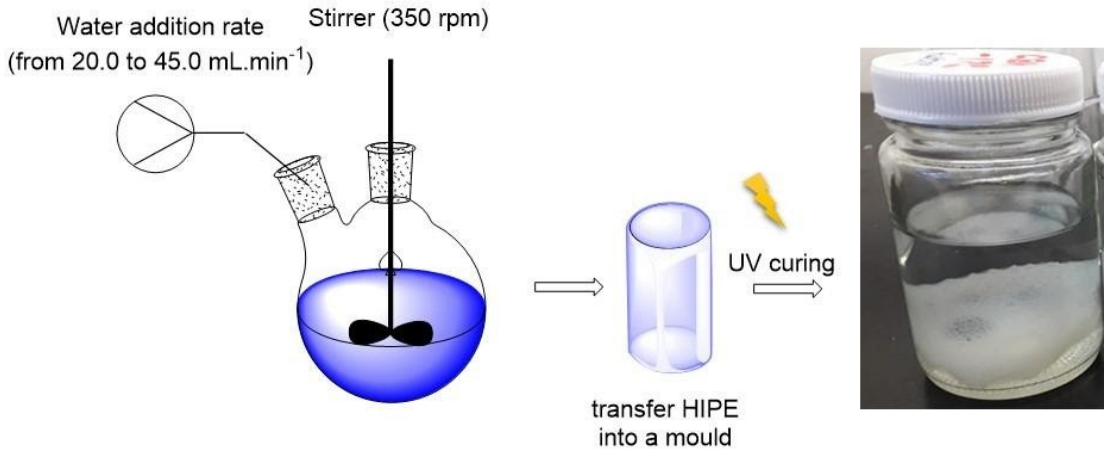


Figure S9. Graphic illustrating setup used to study the polyHIPE formation.

Table S4. Formulation tested for the preparation of HIPE with photo-curable PCL (fixed concentration of 200 mg•mL^{-1} in DCE).

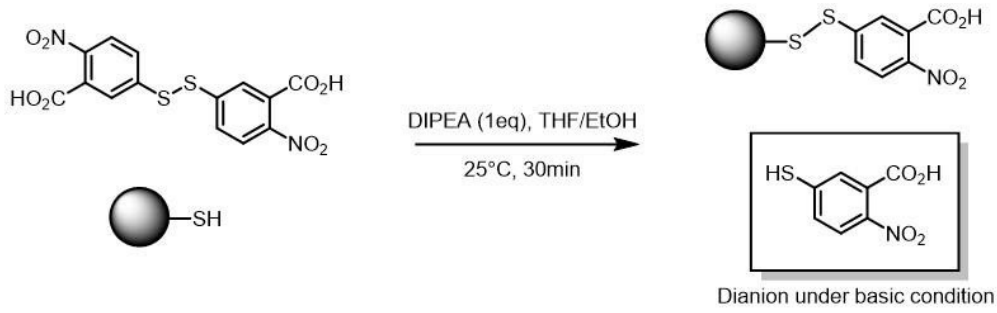
Polymer sample[a]	Surfactant / wt% [b]	Water addition / mL min^{-1}	Stirring time / h	HIPE stability / Y/N
1	5.0	20.0	1	N
1	7.5	20.0	1	N
1	10	20.0	1	N
1	10	45.0	1	N
1	10	20.0	4	N
1	10	20.0	12	Y
2	10	20.0	12	Y
3	10	20.0	12	Y
4	10	20.0	12	Y

a) Polymer samples as referred to in Table 1. b) wt%. surfactant is determined taking the mass of all the organic phases (DCE+polymer+photoinitiator+thiol).

6. Measurement of unreactive thiol group by Ellman's reaction

Measurement of unreacted thiols in the final polyHIPEs was performed based on a literature procedure:

J.P. Badyal et al., *Tet. Lett.*, 2001, **42**(48), 8531.



Sample	**m** / mg	**A** @ 412 nm	**[SH]** / µmol mg^{-1} [a]
2-PCL-DP5	8	0.021	1.36
3-PCL-DP5	5	0.018	1.87
3-PCL-DP10	10	0.032	1.66

a) Calculated using ε (ʎ = 412 nm) = 14150 M^{-1} cm^{-1}

Figure S10. Results for residual thiol concentrations using Ellman's reagent.

7. Pore size analysis of polyHIPE samples

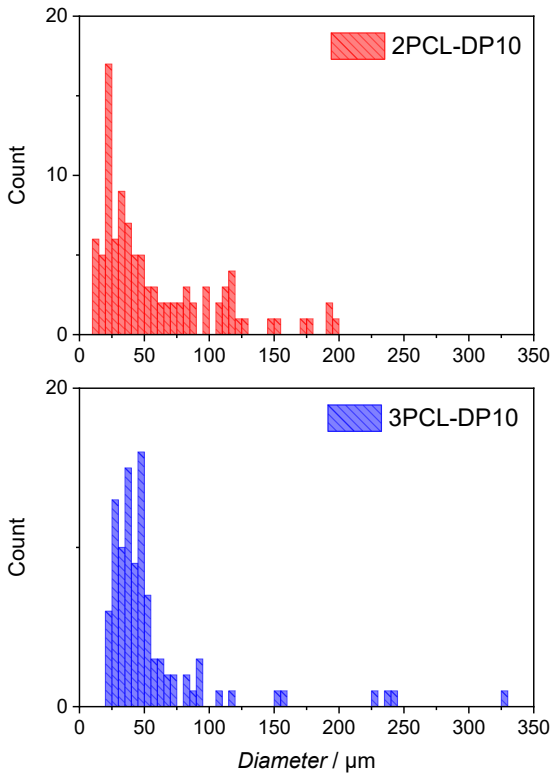


Figure S11. Pore size distributions for 2PCL-DP10 and 3PCL-DP10 (n = 100).

8. PolyHIPE swellability testing

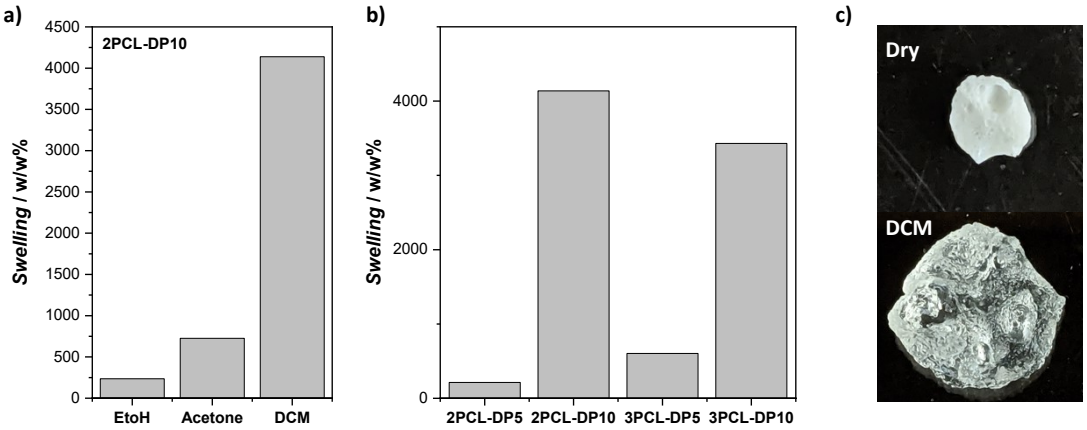


Figure S12. Swellability of porous polyester polyHIPEs a) between the four different samples; b) swelling of 2PCL-DP10 (Entry 2, Table 1) in various solvents; c) photograph of visual change of polyHIPE during swelling.

9. References

1 E. Lovelady, S. D. Kimmins, J. Wu and N. R. Cameron, *Polym. Chem.*, 2011, **2**, 559-562.