

Supplementary Information

An Atom-Efficient Conjugation Approach to Well-Defined Block Copolymers Using RAFT Chemistry and Hetero Diels-Alder Cycloaddition

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Experimental Section

1. Materials

Benzyl (diethoxyphosphoryl)dithioformate (**1a**)^[1,2] and benzyl pyridine-2-ylidithioformate (**1b**)^[3,4] were synthesized according to the literature. Styrene (Aldrich) was passed through a column of basic alumina (Ajax Finechem) and stored at -19 °C. 2,2'-Azobisisobutyronitrile (AIBN, DuPont) was recrystallized twice from methanol before use and stored at 4 °C. ϵ -Caprolactone (Aldrich) was distilled over calcium hydride and stored over molecular sieves (3 Å, BDH). *trans,trans*-2,4-Hexadien-1-ol (Aldrich) was used as received. Lipase acrylic resin from *Candida antarctica* (Sigma) was stored over phosphorus pentoxide (Fluka) at 4 °C. Toluene (anhydrous, water < 30 ppm, Sigma-Aldrich) and trifluoroacetic acid (Sigma-Aldrich) were used as received. Zinc chloride (Sigma) was stored over phosphorus pentoxide.

2. Measurements

The structures of the synthesized compounds were proven by ¹H- and ¹³C-NMR spectroscopy using a Bruker DPX 300 spectrometer at 300 MHz for hydrogen nuclei and 75 MHz for carbon nuclei. All samples were dissolved in CDCl₃. The δ -scale was calibrated to the according solvent signal at 7.258 ppm (¹H) and 76.98 ppm (¹³C).

GPC measurements were performed on a Shimadzu modular system, comprising an auto injector, a Polymer Laboratories 5.0 μ m bead-size guard column (50 x 7.5 mm), followed by three linear PL columns (10⁵, 10⁴ and 10³ Å) and a differential refractive index detector using THF as the eluent at 40 °C with a flow rate of 1 mL·min⁻¹. The GPC system was calibrated using poly(styrene) standards ranging from 540 to 2·10⁶ g·mol⁻¹. For poly(ϵ -caprolactone), the resulting molecular weight distribution has been corrected using the Mark-Houwink relationship with $K = 13.95 \cdot 10^{-5} \text{ dL} \cdot \text{g}^{-1}$, $\alpha = 0.786$, for poly(ϵ -caprolactone)^[5] and $K = 14.1 \cdot 10^{-5} \text{ dL} \cdot \text{g}^{-1}$ and $\alpha = 0.70$, for poly(styrene).^[6]

Electrospray ionization mass spectrometry (ESI-MS) measurements were performed on a Thermo Finnigan LCQ Deca quadrupole ion trap mass spectrometer (Thermo Finnigan, San Jose, CA) equipped with an atmospheric pressure ionization source operating in the nebulizer assisted electrospray mode which was used in positive ion mode. Polymer samples (0.2 - 0.25 mg·mL⁻¹) were dissolved in a tetrahydrofuran/methanol (3:2) mixture. Mass calibration was performed using caffeine, MRFA (Sigma-Aldrich)

and Ultramark 1621 (Sigma-Aldrich) in the m/z range 195–1822 Da. All spectra were acquired over the m/z range 150–2 000 Da with a spray voltage of 5 kV and a capillary temperature of 275 °C. Nitrogen was used as a sheath gas (flow: 45 % of maximum) and helium was used as the auxiliary gas (flow: 5 % of maximum). MS-MS investigations were performed with parent masses of $m/z=1680$ and 1735 and an isolation width of $m/z=1.0$ for **6** and **7**, respectively. A normalized collision energy of 25 % at an activation time of 30 ms was used.

3. Synthesis

3.1 Styrene polymerization: A solution of styrene (80 mL, 0.70 mol), RAFT agent **1a,b** ($1.62 \cdot 10^{-3}$ mol) and AIBN (0.043 g, $0.27 \cdot 10^{-3}$ mol) was prepared and placed in a 250 mL round bottom flask. The flask was subsequently purged with nitrogen for 30 minutes to remove any residual oxygen. The polymerization reaction was performed at 60 °C. After a certain reaction time (8.5 h for **1a** and 11 h for **1b**), the reaction was quenched by placing the flask in an ice/water mixture and a small amount of hydroquinone added to suspend the reaction. The polymers **3a,b** were isolated by two fold precipitation in cold methanol.

1a:

GPC (THF): $M_n=2820 \text{ g} \cdot \text{mol}^{-1}$, $PDI=1.11$

¹H-NMR (CDCl₃): $M_n=2340 \text{ g} \cdot \text{mol}^{-1}$

1b:

GPC (THF): $M_n=2230 \text{ g} \cdot \text{mol}^{-1}$, $PDI=1.14$

¹H-NMR (CDCl₃): $M_n=2460 \text{ g} \cdot \text{mol}^{-1}$

3.2 ϵ -Caprolactone polymerization: Under a nitrogen atmosphere, a mixture of *trans,trans*-2,4-hexadien-1-ol (430 mg, 4.4 mmol), ϵ -caprolactone (9.3 ml, 10 g, 88 mmol), toluene (10 mL) and lipase acrylic resin (250 mg) were placed in a dried schlenk flask. The solution was stirred at 70 °C for 1.5 h. After cooling down to room temperature, the lipase acrylic resin was removed by filtration. The polymer **4** was precipitated from the filtrate in a cold mixture of diethylether/n-hexane (1:1). Yield: 9.34 g, 90 %. GPC (THF): $M_n=2550 \text{ g} \cdot \text{mol}^{-1}$, $PDI=1.37$. ¹H-NMR (CDCl₃): $M_n=2520 \text{ g} \cdot \text{mol}^{-1}$ ¹H-NMR (300 MHz, CDCl₃, 25 °C): $\delta = 6.21$ (dd; CH^d), 6.01 (dd; CH^c), 5.71 (dq; CH^b), 5.58 (dt; CH^e), 4.53 (d; CH₂^f), 4.03 (t; CH₂^k), 3.60 (t; CH₂^{k'}), 2.7 (t; CH₂^g), 1.5-1.7 (m; CH₂^{h,j}), 1.25-1.45 ppm (m; CH₂ⁱ); ¹³C-NMR (75 MHz, CDCl₃, 25 °C): $\delta = 173.4$ (CH₂^g), 123.6, 130.3, 131.1, 134.7 (CH^{b-e}), 64.7 (CH₂^f), 64.0 (CH₂^l), 62.4 (CH₂^{l'}), 34.0 (CH₂^h), 32.1 (CH₂^k), 28.2 (CH₂^k), 25.4 (CH₂^j), 24.5 (CH₂ⁱ), 18.0 ppm (CH₃^a).

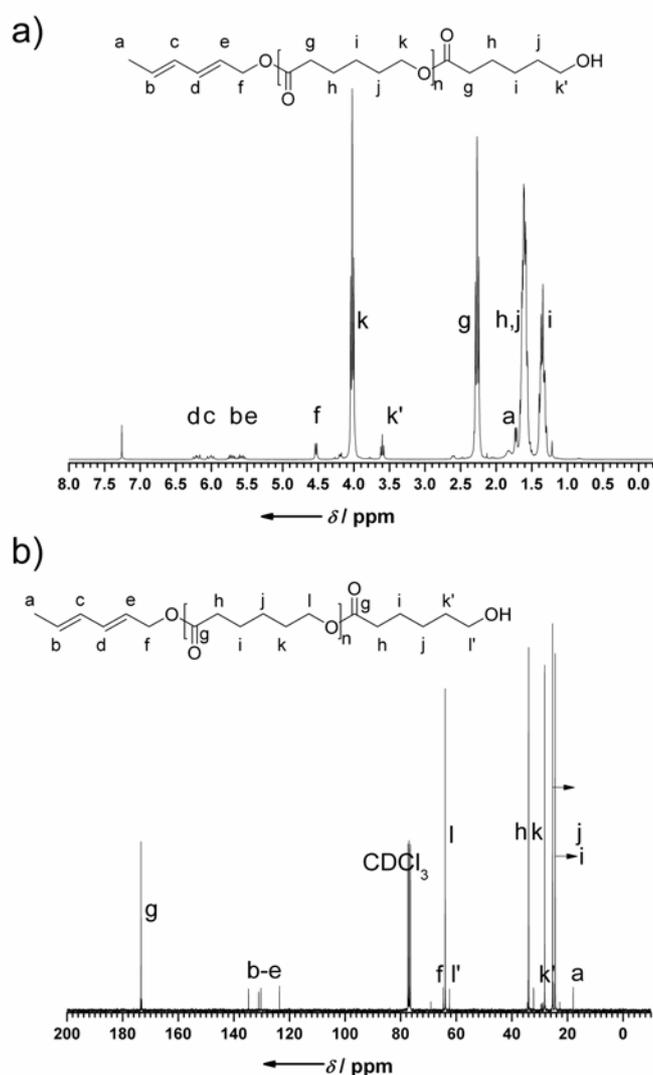


Figure SI-1. a) $^1\text{H-NMR}$ and b) $^{13}\text{C-NMR}$ of PCL 4.

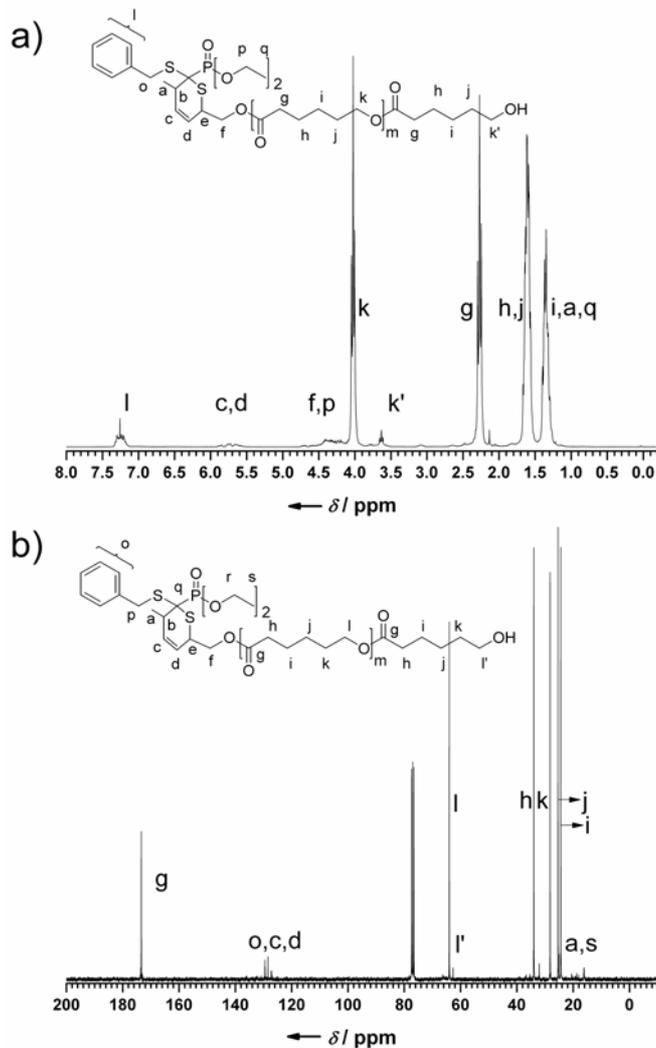


Figure SI-2. a) $^1\text{H-NMR}$ and b) $^{13}\text{C-NMR}$ of PCL 6.

3.3 Model reaction between poly(ϵ -caprolactone) 4 and benzyl (diethoxyphosphoryl)dithioformate 1a: A solution of PCL 4 (200 mg, 78 μmol), 2 eq. of 1a (48 mg, 158 μmol) and 1 eq. zinc chloride (10 mg, 78 μmol) in 1 mL chloroform was kept at 50 $^\circ\text{C}$ for 24 hours. The polymer 6 was precipitated in a cold mixture of diethylether/n-hexane (1:1). GPC (THF): $M_n=2800 \text{ g}\cdot\text{mol}^{-1}$, $PDI=1.27$; $^1\text{H-NMR}$ (300 MHz, CDCl_3 , 25 $^\circ\text{C}$): $\delta = 7.1\text{-}7.4$ (m, CH^l), 5.5-5.9 (m, CH^{c+d}), 4.0-4.8 (m, CH^{f+p}), 4.02 (t, CH_2^k), 3.63 (t, $\text{CH}_2^{k'}$), 2.71 (t, CH_2^g), 1.5-1.7 (CH_2^{h+j}), 1.25-1.45 ppm (CH_2^{i+a+q}); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , 25 $^\circ\text{C}$): $\delta = 173.4$ (CH_2^g), 127-130 (CH^{o+c+d}), 64.7 (CH_2^l), 62.4 ($\text{CH}_2^{l'}$), 34.0 (CH_2^h), 28.2 (CH_2^k), 25.4 (CH_2^j), 24.5 (CH_2^i), 16.2 ppm (CH_3^{a+s}).

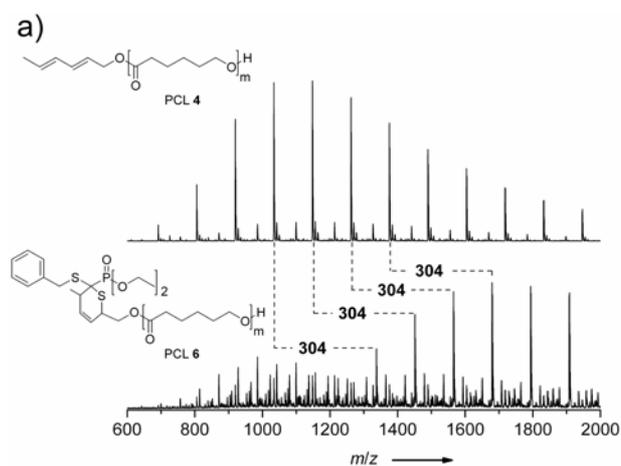


Table SI-2. Theoretical and experimental m/z values for the first peak in the isotopic distributions of PCL 6 in the m/z range between 1660 and 1780.

$m/z_{\text{exp.}}$	Ion Assignment	Formula	m/z_{theo}
1679.6	PCL 6 _(m=11) + Na ⁺	[C ₈₄ H ₁₃₇ O ₂₆ PS ₂ Na] ⁺	1679.9
1695.6	PCL 6 _(m=11) + K ⁺	[C ₈₄ H ₁₃₇ O ₂₆ PS ₂ K] ⁺	1695.8
1706.9	PCL 6 _(m=26) + 2 Na ⁺	[C ₁₇₄ H ₂₈₇ O ₅₆ PS ₂ Na ₂] ⁺⁺	1706.9
1717.9	PCL 4 _(m=14) + Na ⁺	[C ₉₀ H ₁₅₀ O ₂₉ Na] ⁺	1718.0
1729.5	-	-	-
1739.8	-	-	-
1745.5	-	-	-
1763.8	PCL 6 _(m=27) + 2 Na ⁺	[C ₁₈₀ H ₂₉₇ O ₅₈ PS ₂ Na ₂] ⁺⁺	1764.0

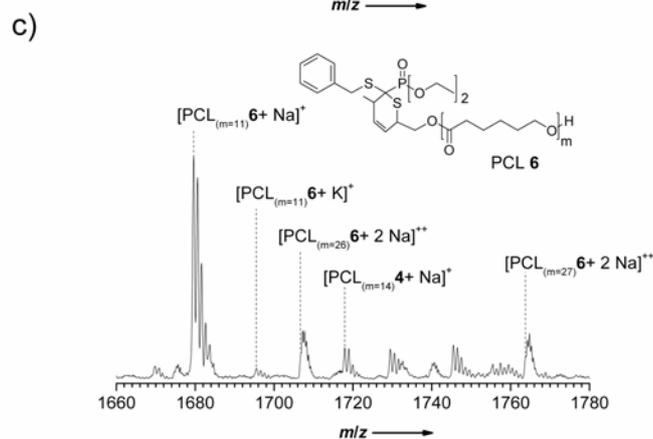
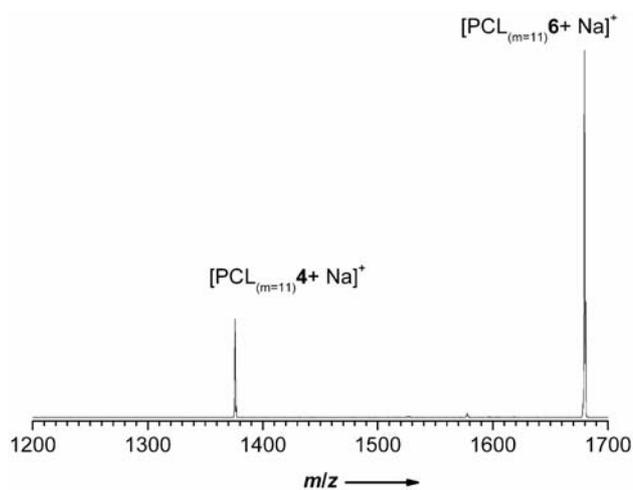
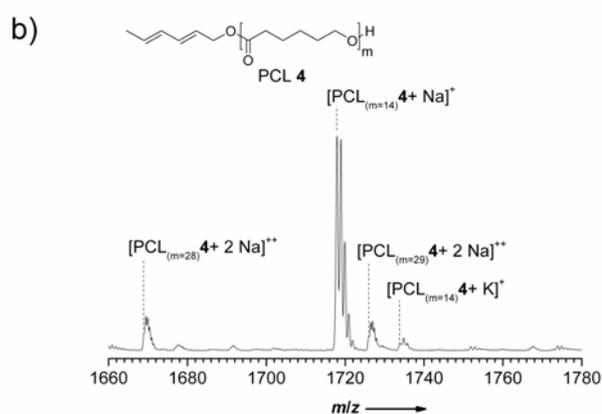


Figure SI-3. ESI-MS spectra of PCL 4 and 6; a) full spectra; b) PCL 4, 1660-1780 m/z region and c) PCL 6, 1660-1780 m/z region.

Figure SI-4. MS-MS spectrum of the parent mass $m/z=1680$ which corresponds to PCL 6.

Table SI-1. Theoretical and experimental m/z values for the first peak in the isotopic distributions of PCL 4 in the m/z range between 1660 and 1780.

$m/z_{\text{exp.}}$	Ion Assignment	Formula	m/z_{theo}
1668.9	PCL 4 _(m=28) + 2 Na ⁺	[C ₁₇₄ H ₂₉₀ O ₅₇ Na ₂] ⁺⁺	1669.0
1717.9	PCL 4 _(m=14) + Na ⁺	[C ₉₀ H ₁₅₀ O ₂₉ Na] ⁺	1718.0
1726.0	PCL 4 _(m=29) + 2 Na ⁺	[C ₁₈₀ H ₃₀₀ O ₅₉ Na ₂] ⁺⁺	1726.0
1733.9	PCL 4 _(m=14) + K ⁺	[C ₉₀ H ₁₅₀ O ₂₉ K] ⁺	1734.0

3.4 Model reaction between poly(ϵ -caprolactone) **4 and benzyl pyridine-2-ylidithioformate **1b**:** A solution of PCL **4** (200 mg, 78 μ mol), 2 eq. of **1b** (38 mg, 158 μ mol) and 1.1 eq. TFA (6.4 μ L, 86 μ mol) in 1 mL chloroform was kept at 50 $^{\circ}$ C for 2 hours. The polymer **7** was precipitated in a cold mixture of diethylether/n-hexane (1:1). GPC (THF): $M_n=2780$ g \cdot mol $^{-1}$, $PDI=1.26$. ; $^1\text{H-NMR}$ (300 MHz, CDCl_3 , 25 $^{\circ}$ C): $\delta = 8.54$ (d, CH^p), 7.79 (d, CH^s), 7.66 (dd, CH^q), 7.2-7.0 (m, CH^{r+l}), 5.5-5.9 (m, CH^{c+d}), 4.34 (s, CH_2^o), 4.07 (t, CH_2^k), 3.66 (t, $\text{CH}_2^{k'}$), 2.71 (t, CH_2^g), 1.5-1.7 (CH_2^{h+j}), 1.25-1.38 (CH_2^i), 0.78 ppm (s, CH_3^a); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , 25 $^{\circ}$ C): $\delta = 173.4$ (CH_2^o), 127-130 ($\text{CH}^{c+d+o+r}$), 64.0 (CH_2^l), 62.4 ($\text{CH}_2^{l'}$), 34.0 (CH_2^h), 28.2 (CH_2^k), 25.4 (CH_2^j), 24.5 ppm (CH_2^i).

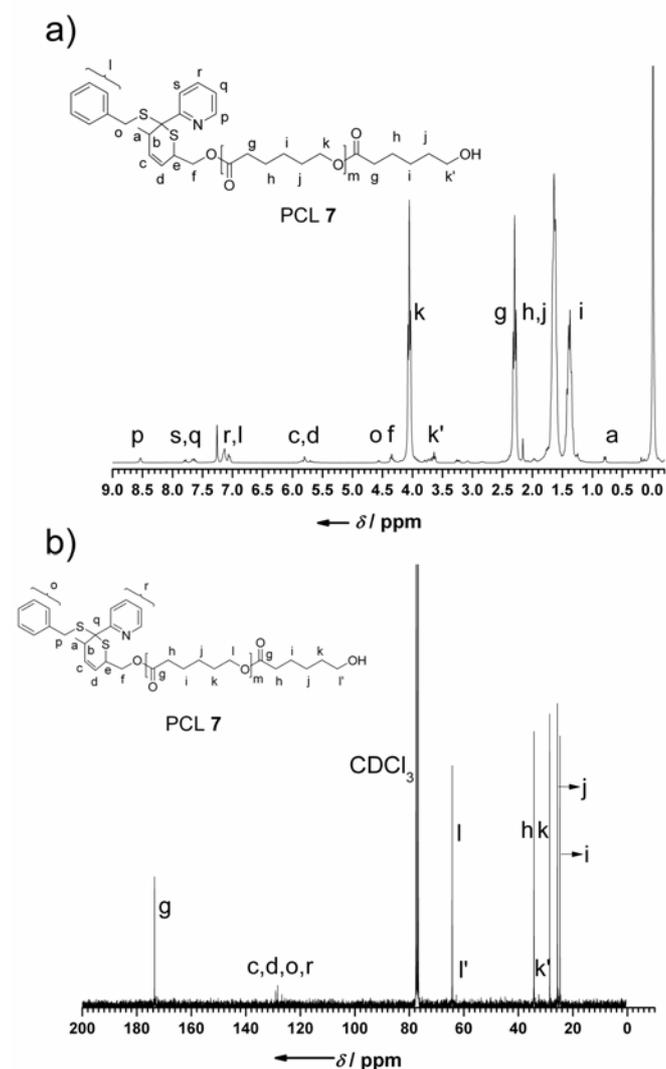


Figure SI-5. a) $^1\text{H-NMR}$ and b) $^{13}\text{C-NMR}$ of PCL **7**.

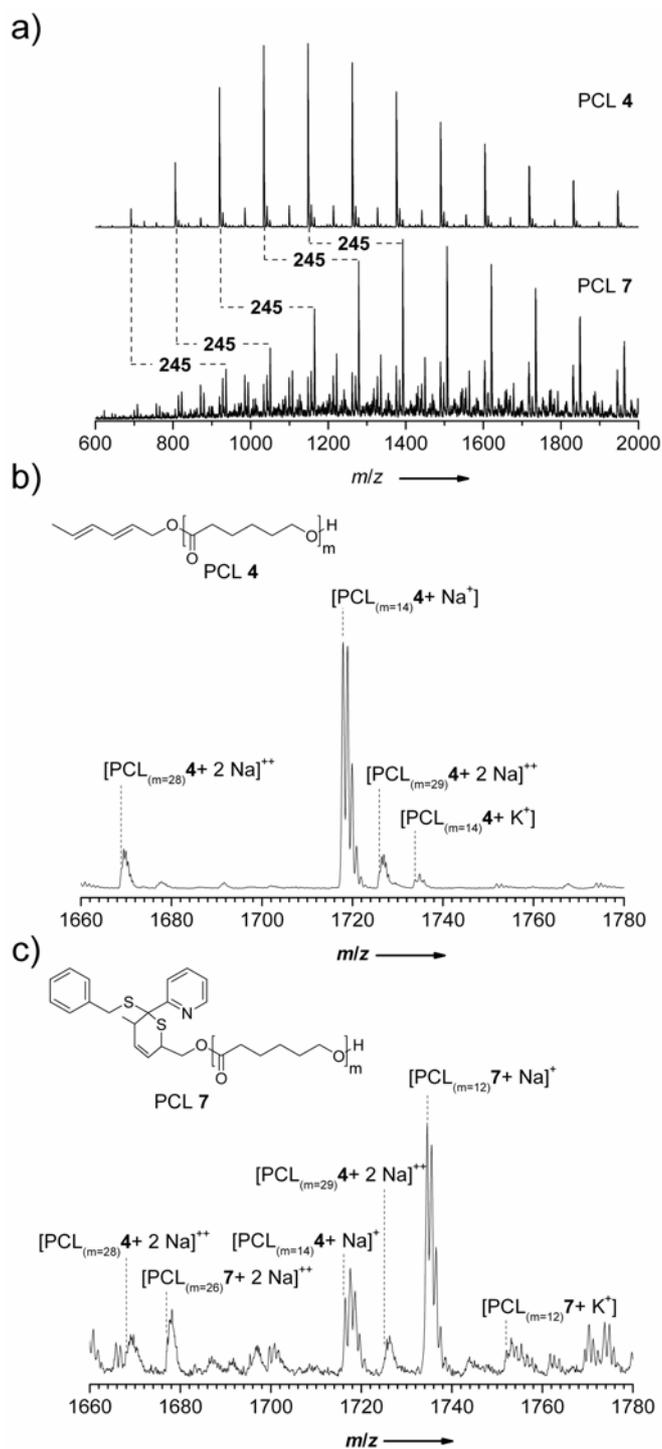


Figure SI-6. ESI-MS spectra of PCL **4** and **7**; a) full spectra; b) PCL **4**, 1660-1780 m/z region and c) PCL **7**, 1660-1780 m/z region.

Table SI-3. Theoretical and experimental m/z values for the first peak in the isotopic distributions of PCL **7** in the m/z range between 1660 and 1780.

$m/z_{\text{exp.}}$	Ion Assignment	Formula	m/z_{theo}
1667.9	PCL 4 _(m=28) + 2 Na ⁺	[C ₁₇₄ H ₂₉₀ O ₅₇ Na ₂] ⁺⁺	1669.0
1677.0	PCL 7 _(m=26) + 2 Na ⁺	[C ₁₇₅ H ₂₈₁ O ₅₃ NS ₂ Na ₂] ⁺⁺	1677.4
1695.4	-	-	-
1699.7	-	-	-
1716.5	-	-	-
1717.5	PCL 4 _(m=14) + Na ⁺	[C ₉₀ H ₁₅₀ O ₂₉ Na] ⁺	1718.0
1725.7	PCL 4 _(m=29) + 2 Na ⁺	[C ₁₈₀ H ₃₀₀ O ₅₉ Na ₂] ⁺⁺	1726.0
1734.6	PCL 7 _(m=12) + Na ⁺	[C ₉₁ H ₁₄₁ O ₂₅ NS ₂ Na] ⁺	1734.9
1750.5	PCL 7 _(m=12) + K ⁺	[C ₉₁ H ₁₄₁ O ₂₅ NS ₂ K] ⁺	1750.9
1761.7	-	-	-
1769.4	-	-	-
1773.6	-	-	-

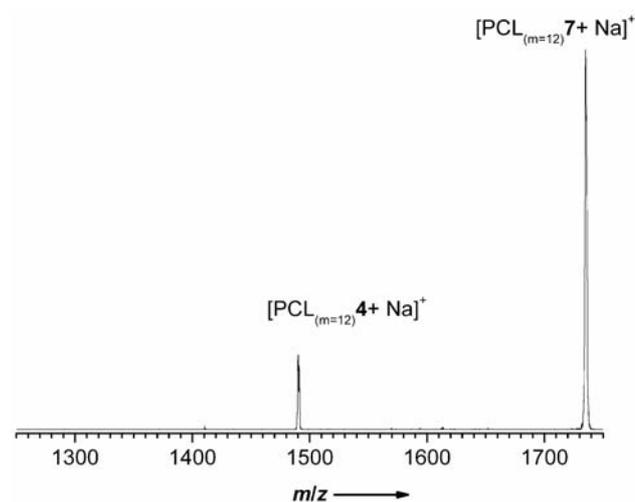


Figure SI-7. MS-MS spectrum of the parent mass $m/z=1735$ which corresponds to PCL **7**.

3.5 Hetero Diels-Alder cycloaddition between (diethoxyphosphoryl)dithioformate terminated poly(styrene) **3a and 2,4-hexadienoyl terminated poly(ϵ -caprolactone) **4**:** A solution of PS **3a** (141 mg, 50 μmol), PCL **4** (128 mg, 50 μmol) and 1 eq. zinc chloride (6.5 mg, 50 μmol) in 1.5 mL chloroform was kept at 50 $^{\circ}\text{C}$ for 24 hours. The polymer **5a** was isolated by removing the solvent *in vacuo*. GPC (THF): $M_n=5540 \text{ g}\cdot\text{mol}^{-1}$, $PDI=1.28$.

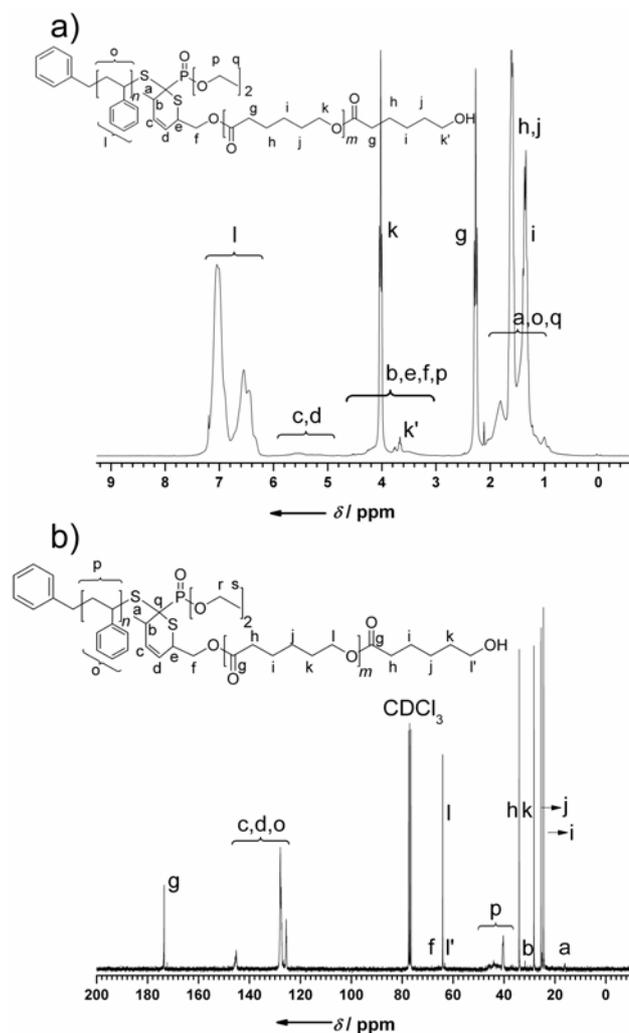


Figure SI-8. a) ¹H-NMR and b) ¹³C-NMR of PS-*b*-PCL **5a**.

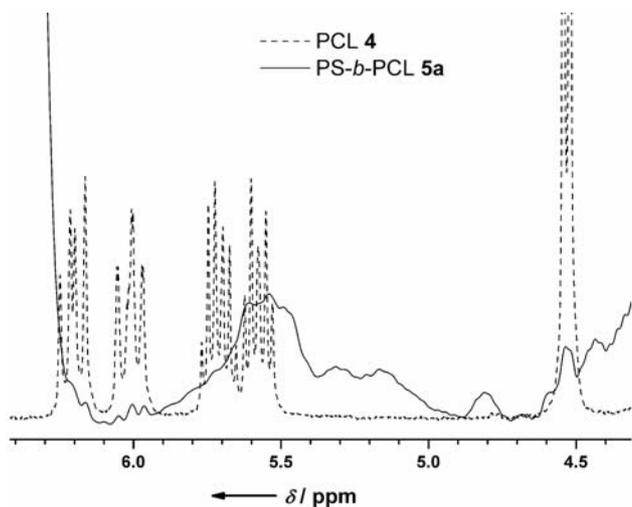


Figure SI-9. Overlay of the $^1\text{H-NMR}$ spectra (4.3-6.5 ppm region) of PCL **4** and PS-*b*-PCL **5a**.

3.6 Hetero Diels-Alder cycloaddition between pyridin-2-ylidithioformate terminated poly(styrene) **3b and 2,4-hexadienoyl terminated poly(ϵ -caprolactone) **4**:** A solution of PS **3b** (112 mg, 50 μmol), PCL **4** (128 mg, 50 μmol) and 1.1 eq. TFA (4 μL , 55 μmol) in 1.5 mL chloroform was kept at 50 $^\circ\text{C}$ for 2 hours. The polymer **5b** was isolated by removing the solvent *in vacuo*. GPC (THF): $M_n=4690 \text{ g}\cdot\text{mol}^{-1}$, $PDI=1.24$.

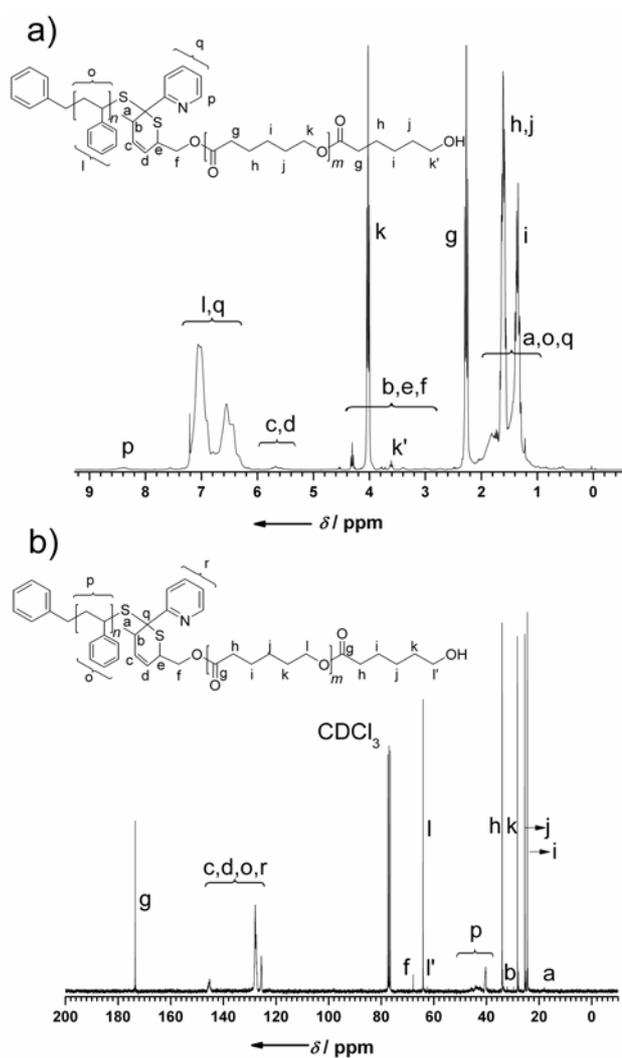


Figure SI-10. a) $^1\text{H-NMR}$ and b) $^{13}\text{C-NMR}$ of PS-*b*-PCL **5b**.

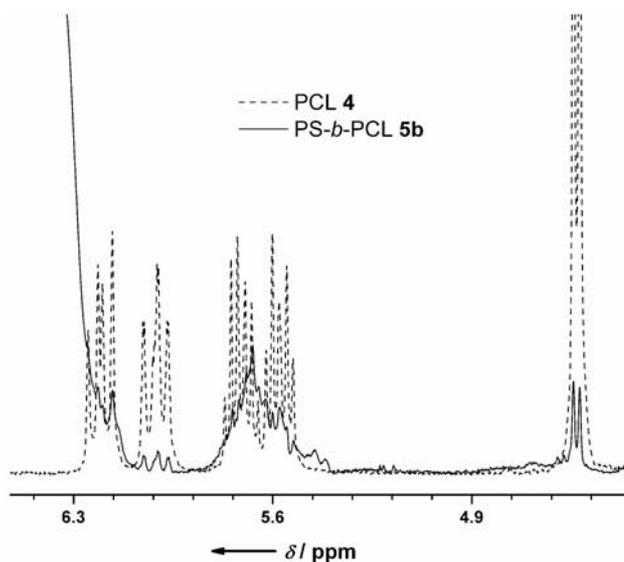


Figure SI-11. Overlay of the $^1\text{H-NMR}$ spectra (4.3-6.5 ppm region) of PCL **4** and PS-*b*-PCL **5a**.

3.7 Stability of PS-*b*-PCL 5b: 10 mg of polymer **5b** were dissolved in 100 μ L of chloroform and kept at 60 °C in a pressure resistant tube for 24 h. After removal of the solvent *in vacuo*, the residue was analyzed by GPC (Figure SI-6).

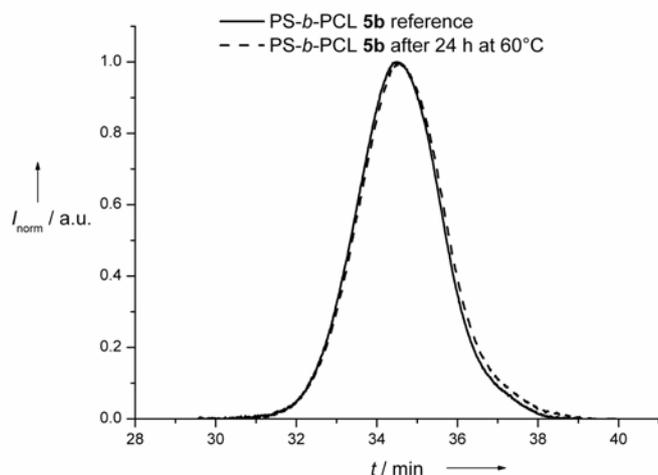


Figure SI-12. Overlay of GPC traces of PS-*b*-PCL **5b** before and after thermal treatment at 60 °C in chloroform solution.

- [1] M. Laus, R. Papa, K. Sparnacci, A. Alberti, M. Benaglia, D. Macciantelli, *Macromolecules* **2001**, *34*, 7269-7275.
- [2] ¹H-NMR (300 MHz, CDCl₃, 25 °C): δ = 7.28 (s, 5H; Ph), 4.44 (s, 2H; SCH₂Ph), 4.24 (m, 4H; CH₂CH₂O) 1.33 ppm (t, ³J(H,H) = 7.2 Hz, 6H; CH₂CH₂O); ¹³C-NMR (75 MHz, CDCl₃, 25 °C): δ = 228 (d, ¹J(C,P) = 175 Hz; PC(S)S), 134, 129, 129, 128 (s,s,s,s, Ph), 64.6 (d, ³J(C,P) = 6.79 Hz, CH₃CH₂O), 40.5 (d, ³J(C,P) = 2.79 Hz, SCH₂Ph), 16.2 ppm (d, ²J(C,P) = 6.19 Hz, CH₃CH₂O).
- [3] A. Alberti, M. Benaglia, M. Guerra M. Gulea, P. Hapiot, M. Laus, D. Macciantelli, S. Masson, A. Postma, K. Sparnacci, *Macromolecules* **2005**, *38*, 7610-7618
- [4] ¹H-NMR (300 MHz, CDCl₃, 25 °C): δ = 8.60 (ddd, ³J(H,H) = 4.7 Hz, ⁴J(H,H) = 1.8 Hz, ⁵J(H,H) = 0.9 Hz, 1H; Py), 8.33 (ddd, ³J(H,H) = 8.0 Hz, ⁴J(H,H) = 1.0 Hz, ⁵J(H,H) = 1.0 Hz, 1H; Py), 7.79 (ddd, ³J(H,H) = 7.8 Hz, ³J(H,H) = 7.7 Hz, ⁴J(H,H) = 1.8 Hz, 1H; Py), 7.46 (ddd, ³J(H,H) = 7.6 Hz, ³J(H,H) = 4.7 Hz, ⁴J(H,H) = 1.2 Hz, 1H; Py), 7.18 – 7.48 (m, 5H; C₆H₅), 4.54 ppm (s, 2H; SCH₂); ¹³C NMR (75 MHz, CDCl₃, 25 °C): δ = 226.0 (C=S), 122.1, 126.7, 127.5, 128.5, 129.4, 135.0, 136.8, 147.9, 156.4 (arom), 41.5 ppm (SCH₂).
- [5] A. Schindler, Y. M. Hibionada, C. G. Pitt, *J. Polym. Sci., Polym. Chem. Ed.* **1982**, *20*, 319–326.
- [6] C. Strazielle, H. Benoit, O. Vogl, *Eur. Polym. J.* **1978**, *14*, 331-334.