Electronic Supplementary Material (ESI) for Polymer Chemistry.

Electronic Supplementary Information

Poly(sulfur ylides): A new class of zwitterionic polymers with distinct thermal and solution behavior

Georgia Poulladofonou[a], dr. Kevin Neumann[a*]

[a]Systems Chemistry Department, Institute for Molecules and Materials

Radboud University Nijmegen, The Netherlands

Contents

1. Experimental

1.1 Materials

Reagents were obtained from Sigma Aldrich/Merck (Zwijndrecht, The Netherlands), Fluorochem BV (Amsterdam, The Netherlands) and TCI Europe (Zwijndrecht, Belgium). The reagents were used without purification unless otherwise stated. Vinyl benzoic acid was obtained from Carbosynth. Solvents were obtained from VWR, Fisher, Acros Organic and Sigma Aldrich/Merck. Solvents were dried by passing over activated alumina columns in a MBraun MB SPS800 under a nitrogen atmosphere and stored under argon. Reactions were carried under air unless stated otherwise. Typically, such air-sensitive reactions were carried out under atmosphere of nitrogen using Schlenk technique. Styrene given on alumina and stirred for 10 min to remove the inhibitor 4-tert-butylcatechol. Ultrapure Milli-Q water was obtained from QPOD Milli-Q system.

Reactions and fractions from flash column chromatography were monitored by thin layer chromatography using glass TLC plates (Merck, TLC Silica gel 60 F_{254}) and if necessary visualized by staining with $KMnO_4$ solution. Column chromatography was performed on VWR SiO_2 Type (40-63 mesh) using a forced flow of air at 0.5-1.0 bar.

1.2 Instrumentation

Nuclear Magnetic resonance (NMR) characterization was carried out on a Bruker AVANCE HD nanobay console with a 9.4 T Ascend magnet (400 MHz) and a Bruker AVANCE III console with a 11.7 T UltraShield Plus magnet (500 MHz) equipped with a Bruker Prodigy cryoprobe, in chloroform ($CDCl_3$) or DMSO-d_6. NMR spectra were recorded at 298 K unless otherwise specified. Chemical shifts are given in parts per million (ppm) with respect to tetramethylsilane (TMS, δ 0.00 ppm) as internal standard for ^1H NMR. Coupling constants are reported as J values in Hz. Peak assignment is based on 2D COSY, $^1H-^{13}C$ HSQC, and $^1H-^{13}C$ HMBC spectra. The splitting patterns are indicated as follows: s, singlet; br. s, broad singlet; d, doublet; t, triplet; m, multiplet. Gel permeation chromatography (GPC) equipped with PL gel 5 µm mixed D column calibrated for polystyrene (580− 377400 g/mol) was carried out on a Shimadzu instrument with THF as eluent using differential refractive index and UV absorbance (254 nm).

2. Supporting Figures

2.1 Solubility

Solubility of poly(sulfur ylides) was determined by dissolving 10 mg of polymer in 3 ml of solvent (Table S1) at room temperature. The solution was stirred for one hour to guarantee full solubility. Solubility was determined by visual appearance.

Table S1. Solubility of PS-*co*-P(SY) with varying lengths and weight content of ylide functionality. Green = fully soluble, red = insoluble, yellow = partly soluble.

Polymer (X_n, w_{SY})	Water	THF	Toluene	AcOH	Water/THF (1:1, v:v)
PS-*co*-P(SY) **5** (49, 0.36)	🟥	🟩	🟨	🟩	🟥
PS-*co*-P(SY) **7** (104, 0.69)	🟥	🟨	🟥	🟩	🟩

2.2 Self-assemblies

Samples were prepared by dissolving PS-*b*-P(SY) **9** in DMF (8 mg/mL). The solution was diluted with water until the water content reached 33 v%. An aliquot (200 µL) was rapidly diluted in water (5 mL) and filtered through syringe filters (0.22 µM). The obtained samples were stored at room temperature.

Dynamic light scattering was conducted on *block*-copolymer PS-*b*-P(SY) **9** (0.24 mg/mL) using a Malvern DLS-Zetasizer. Samples for transmission electron microscopy (TEM) were prepared by air-drying of a solution of sample (5 µL) on a carbon-coated Cu TEM grid (200 mesh). JEOL TEM 1400 microscope with an acceleration voltage of 120 kV was utilized for analyzing the samples.

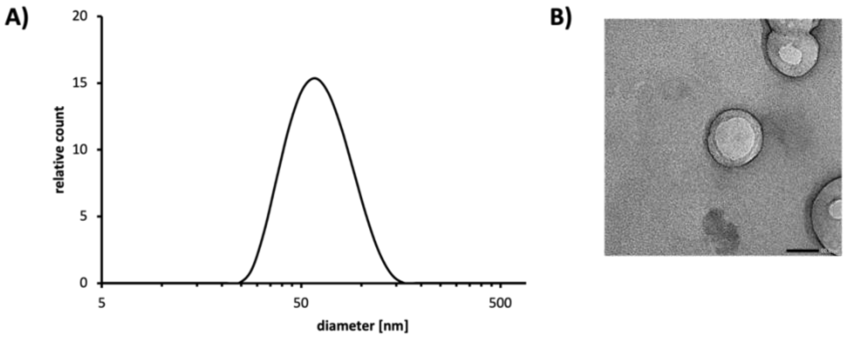


Figure S1 **A)** Dynamic light scattering on PS-*co*-P(SY) **9** (0.24 mg/mL) displays a size distribution of ~67 nm. **B)** TEM image of the obtained self-assemblies (scalebar = 50 nm).

2.3 Stability

Stability of poly(sulfur ylides) was determined by incubating PS-*co*-P(SY) **5** (50 mg) under conditions 1-3 at room temperature. For solubility reasons, aqueous solutions were mixed with THF. After purification by precipitation in cold MeOH (x2) for conditions 1 and 2 and precipitation in Et_2O (x1) and cold MeOH (x1) for condition 3, the stability was determined by ^{1}H-NMR (Figure S2).

Conditions:

1. Acidic aqueous solution: PS-*co*-P(SY) **5** was dissolved in aqu. HCl/THF (2M HCl, v:v, 1:2) and it was incubated overnight.
2. Basic aqueous solution: PS-*co*-P(SY) **5** was dissolved in aqu. NaOH/THF (2M NaOH, v:v, 1:2) and it was incubated overnight.
3. Organic acid: PS-*co*-P(SY) **5** was dissolved in TFA (2 ml) and it was incubated for 4 hours.

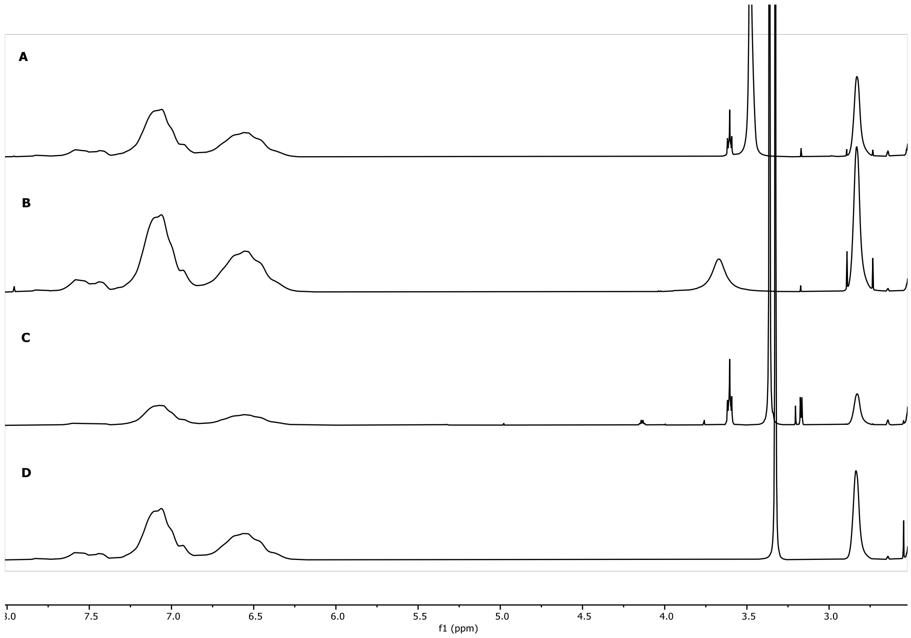
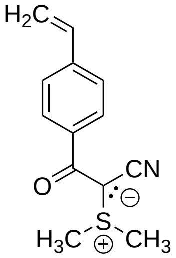


Figure S2 ^{1}H-NMR of PS-*co*-P(SY) **5** in DMSO-d$_6$ **A.** After treatment with HCl, **B.** After treatment with TFA, **C.** After treatment with NaOH and **D.** Purified polymer prior incubation. The ratio of methyl signals to aromatic signals does not chance indicating that the polymer is not degrading under the given conditions.

3. Experimental Protocols

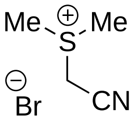
3.1 Small Molecule Synthesis

Sulfur-Ylide Monomer **1**



4-vinyl benzoic acid (1 g, 6.76 mmol) was dissolved in 41 mL DCM and the mixture was stirred. Et_3N (3.4 mL, 20.2 mmol) was added followed by T_3P (5.3 mL, 8.73 mol). The mixture was stirred for a while and then (cyanomethyl)dimethylsulfonium bromide (1.48 g, 8.03 mmol) was added. The reaction mixture was stirred at room temperature overnight. It was then diluted with DCM and it was washed with sat. $NaHCO_3$ (x1), H_2O (x1) and brine (x1). The crude product was dried over Na_2SO_4 and purified via column chromatography on silica gel eluting with DCM/MeOH mixtures (gradient from 98:2 to 90:10 by volume) to obtain the product as brown solid (675 mg, 43% yield). ^1H NMR (400 MHz, DMSO) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 6.77 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.92 (d, *J* = 17.6 Hz, 1H), 5.34 (d, *J* = 11.8 Hz, 1H), 2.86 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 183.32, 139.13, 138.24, 136.03, 127.74, 125.71, 119.61, 115.85, 57.10, 27.42. HRMS (ESI): calculated for $[C_{13}H_{14}NOS]^+$: m/z 232.07961 , found : m/z 232.07854.

Sulfonium Salt **2**



Sulfonium salt **2** was synthesized according to a literature protocol.[1] In brief, bromoacetonitrile (10 mL, 144 mmol) was placed in a Schlenk-flask under N_2 and dimethylsulfide (10.6 mL, 144 mmol) was added slowly. The solution was stirred for 24 h. The obtained solid was washed several times with diethylether and dried under reduced pressure. The product was obtained as a white solid (23180.3 mg, 88 % yield).

^1H NMR (400 MHz, DMSO) δ (ppm): 4.93 (s, 2H), 3.05 (s, 6H).

3.2 Polymer Synthesis

General remarks

The obtained polymers were analyzed by ^{1}H-NMR and SEC. For determination of M_n by NMR, the C-H signal adjacent to the RAFT agent was used (4.95–4.55 ppm, Figure S3). SEC analysis was done by using a polystyrene calibration. Please note that THF is not considered as a good solvent for poly(sulfur ylide); for that reason, the determined M_n by SEC differs significantly for PS-*co*-P(SY), which display a high fraction of ylide. For PS-*co*-P(SY) with a minor fraction of ylide, M_n determined by SEC is in good agreement with M_n as determined by NMR.

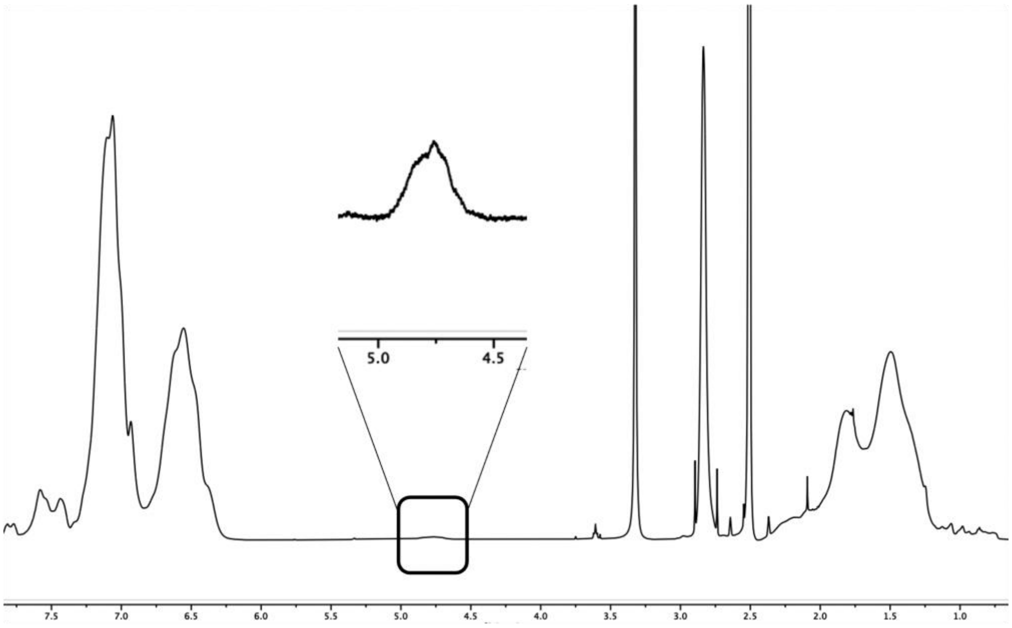


Figure S3. Zoom-in of proton signal adjacent to dithioester, which was used for integration.

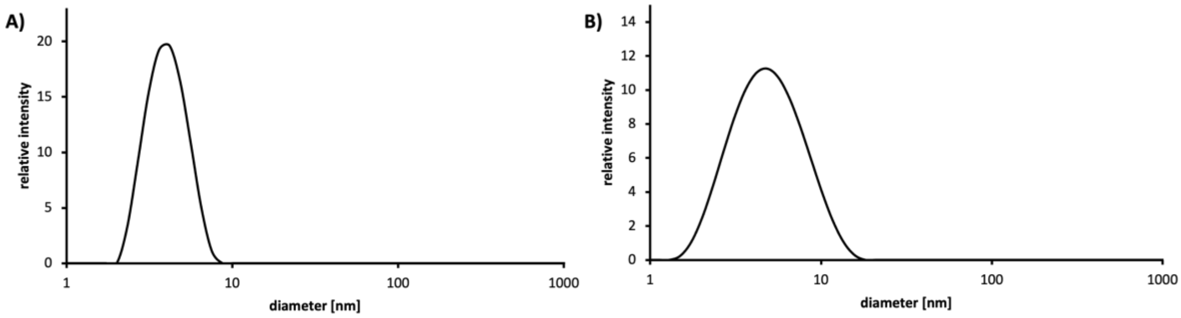
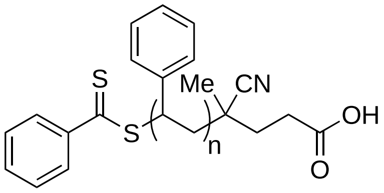


Figure S4. Dynamic light scattering on **A)** PS-*co*-P(SY) **4** and B) **B)** PS-*co*-P(SY) **5** to confirm the absence of polymer aggregates in THF.

Protocol for Synthesis of Polystyrene

PS **8**

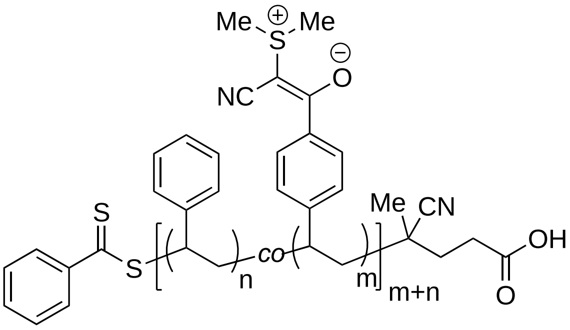


A flame dried Schlenk tube was purged with N_2 and charged with 4-Cyano-4-(phenylcarbonothioylthio)pentanoic acid (61.5 mg, 2.2 mmol) and AIBN (12 mg, 0.0733 mmol). The solids were dissolved in anisole (35 mL). Styrene (6 mL, 52.3 mmol) was added under N_2. The solution was degassed for 15 min and a sample for NMR analysis was taken (*t* = 0 h). The solution was heated to 70°C and the reaction was monitored by NMR. After the desired conversion was indicated, the reaction solution was allowed to reach to room temperature and exposed to air. The product was precipitated dropwise in cold MeOH, re-dissolved in CH_2Cl_2 and subsequently precipitated dropwise in cold MeOH again. The product was dried under vacuum overnight. The product was obtained as a pink solid (1296 mg).

SEC (THF, polystyrene calibration): M_n=6.9 × 10^3 g/mol, M_w/M_n=1.08. The polymer was characterized by ^{1}H-NMR in $CDCl_3$. M_n (NMR) =7.7 × 10^3 g/mol

^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm): 7.40–6.30 (br. m, arom. C-H), 2.45–1.25 (br. m, backbone).

General Protocol for Polymer PS-co-P(SY) Synthesis



A flame dried Schlenk tube was purged with N_2 and charged with 4-Cyano-4-(phenylcarbonothioylthio)pentanoic acid (1.0 eq.), AIBN (0.35 eq.) and Sulfur-Ylide Monomer **1**. The solids were dissolved in DMSO (1.5 M) and styrene was added under N_2 flow. Anisole was added as internal standard. The solution was degassed for 15 min and a sample for NMR analysis was taken (*t* = 0 h). The solution was heated to 80°C – 90°C and the reaction was monitored by NMR. After the desired conversion was indicated, the reaction solution was allowed to reach to room temperature and exposed to air. The product was precipitated dropwise in cold MeOH, re-dissolved in CH_2Cl_2 and subsequently precipitated dropwise in cold MeOH again. The product was dried under vacuum overnight.

PS-*co*-P(SY) **4**

The general protocol for polymer synthesis was followed with RAFT-agent (21.1 mg, 0.076 mmol), AIBN (4.8 mg, 0.029 mmol), Sulfur-Ylide Monomer **1** (200 mg, 0.866 mmol), styrene (0.89 mL, 7.77 mmol) in DMSO (6 mL). The product was obtained as a pink solid (144 mg).

SEC (THF, polystyrene calibration): M_n=3.4 × 10^3 g/mol, M_w/M_n = 1.10.

^{1}H-NMR (500 MHz, DMSO-d_6) δ(ppm): 7.90–6.20 (br. m, arom. C-H of PS and P(SY)), 2.90–2.73 (br. s, $S(CH_3)_2$), 2.40–0.70 (br. m, backbone). M_n (NMR) =4.6 × 10^3 g/mol. F_{SY} = 0.12

PS-*co*-P(SY) **5**

The general protocol for polymer synthesis was followed with RAFT-agent (40.23 mg, 0.144 mmol), AIBN (7.1 mg, 0.0432 mmol), Sulfur-Ylide Monomer **1** (650 mg, 2.81 mmol), styrene (2.38 mL, 25.27 mmol) in DMSO (18.7 mL). The product was obtained as a pink solid (688 mg).

SEC (THF, polystyrene calibration): M_n=3.2 × 10^3 g/mol, M_w/M_n=1.10.

^{1}H-NMR (500 MHz, DMSO-d_6) δ(ppm): 7.90–6.15 (br. m, arom. C-H of PS and P(SY)), 2.90–2.73 (br. s, $S(CH_3)_2$), 2.43–0.70 (br. m, backbone). M_n (NMR) = 6.2 × 10^3 g/mol. F_{SY} = 0.18

PS-*co*-P(SY) **6**

The general protocol for polymer synthesis was followed with RAFT-agent (20.25 mg, 0.073 mmol), AIBN (4.17 mg, 0.0254 mmol), Sulfur-Ylide Monomer **1** (301.5 mg, 1.305 mmol), styrene (0.35 mL, 3.045 mmol) in DMSO (2.8 mL). The product was obtained as a pink solid (211 mg).

SEC (THF, polystyrene calibration): M_n= 1.4 × 10^3 g/mol, M_w/M_n=1.08.

^{1}H-NMR (500 MHz, DMSO-d_6) δ(ppm): 7.90–6.20 (br. m, arom. C-H of PS and P(SY)), 2.90–2.76 (br. s, $S(CH_3)_2$), 2.43–0.70 (br. m, backbone). M_n (NMR) = 5.8 × 10^3 g/mol. F_{SY} = 0.30

PS-*co*-P(SY) **7**

The general protocol for polymer synthesis was followed with RAFT-agent (21.1 mg, 0.076 mmol), AIBN (4.8 mg, 0.029 mmol), Sulfur-Ylide Monomer **1** (1000 mg, 4.32 mmol), styrene (0.5 mL, 4.32 mmol) in DMSO (6 mL). The product was obtained as a pink solid (607 mg).

^{1}H-NMR (500 MHz, DMSO-d_6) δ(ppm): 7.90–6.15 (br. m, arom. C-H of PS and P(SY)), 2.90–2.73 (br. s, $S(CH_3)_2$), 2.40–0.70 (br. m, backbone). M_n (NMR) = 17.7 × 10^3 g/mol. F_{SY} = 0.52

PS-*b*-P(SY) **9**

A flame dried Schlenk tube was purged with N_2 and charged with PS **8** polymer (macro-initiator, 350 mg, 0.047 mmol), AIBN (1.94 mg, 0.0118 mmol) and Sulfur-Ylide Monomer **1** (255 mg, 1.10 mmol). The solids were dissolved in DMSO (0.75 M). Anisole was added as internal standard. The solution was degassed for 15 min and a sample for NMR analysis was taken (*t* = 0 h). The solution was heated to 90°C and the reaction was monitored by NMR. After the desired conversion was indicated, the reaction solution was allowed to reach to room temperature and exposed to air. The product was precipitated dropwise in cold MeOH, re-dissolved in CH_2Cl_2 and subsequently precipitated dropwise in cold MeOH again. The product was dried under vacuum overnight. The product was obtained as a pink solid (470 mg).

SEC (THF, polystyrene calibration): M_n = 6.9 × 10^3 g/mol, M_w/M_n = 1.04.

^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm): 8.15–6.15 (br. m, arom. C-H of PS and P(SY)), 3.05–2.60 (br. s, $S(CH_3)_2$), 2.15–1.25 (br. m, backbone). M_n (NMR) = 10.3 × 10^3 g/mol. F_{SY} = 0.14

4. Differential scanning calorimetry

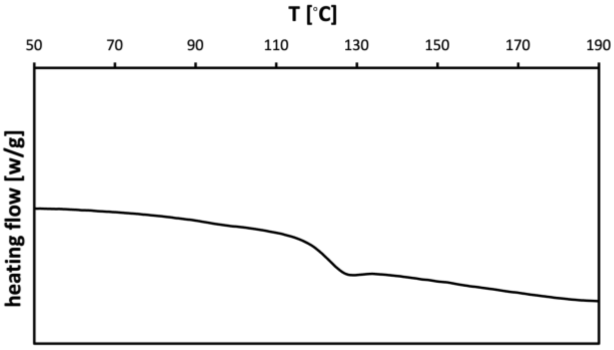


Figure S5. *DSC trace of* PS-*co*-P(SY) **4** with a heating rate of 10 K min^{-1} (T_g = 117.4°C).

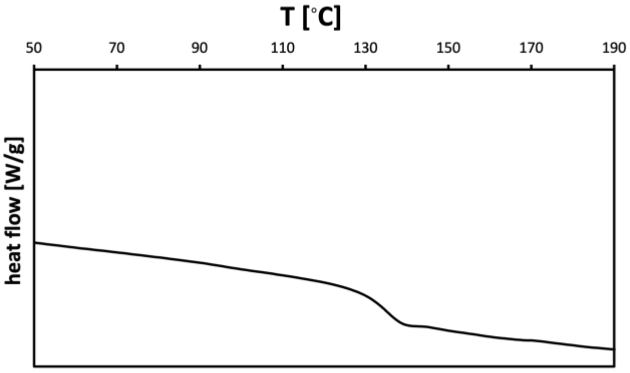


Figure S6. *DSC trace of* PS-*co*-P(SY) **5** with a heating rate of 10 K min^{-1} (T_g = 129.1°C).

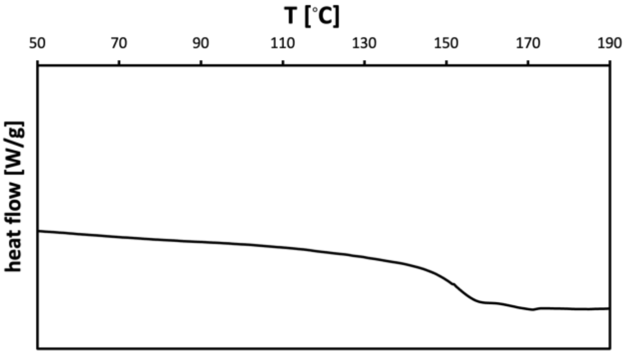


Figure S7. *DSC trace of* PS-*co*-P(SY) **6** with a heating rate of 10 K min^{-1} (T_g = 149.2°C).

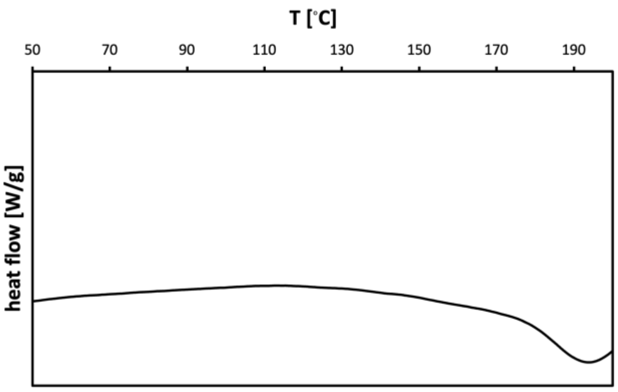


Figure S8. DSC trace of PS-*co*-P(SY) **7** with a heating rate of 10 K min^{-1} (T_g = 180.0°C). Please, note that above 210°C, sulfur ylide bearing copolymers show signs of thermal degradation.

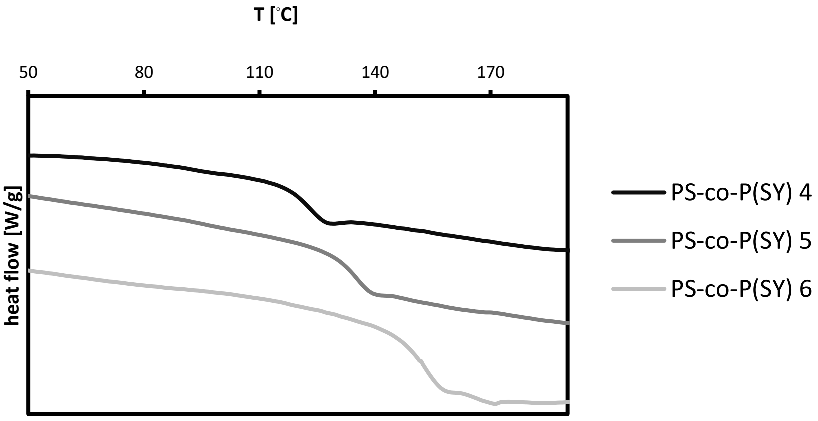


Figure S9. Comparison of DSC trace of PS-*co*-P(SY) **4, 5** and **6** with a heating rate of 10 K min^{-1}.

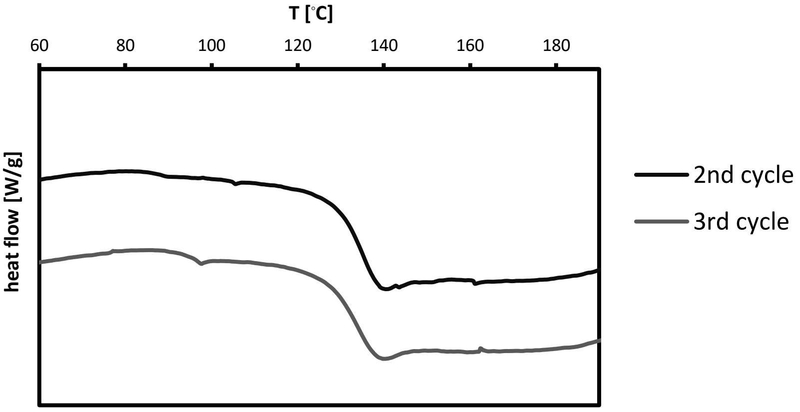


Figure S10. Comparison of DSC trace of PS-*co*-P(SY) **5** after three cycles with a heating rate of 10 K min^{-1}.

5. Gel Permeations Chromatograms

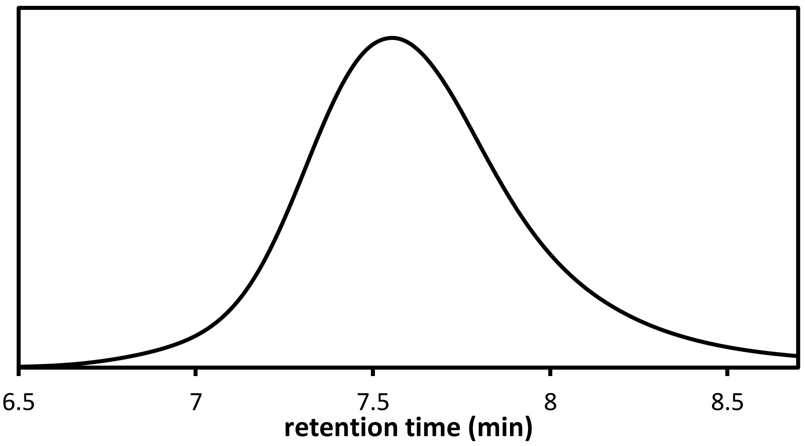


Figure S11. *SEC trace of* PS-*co*-P(SY) **4**.

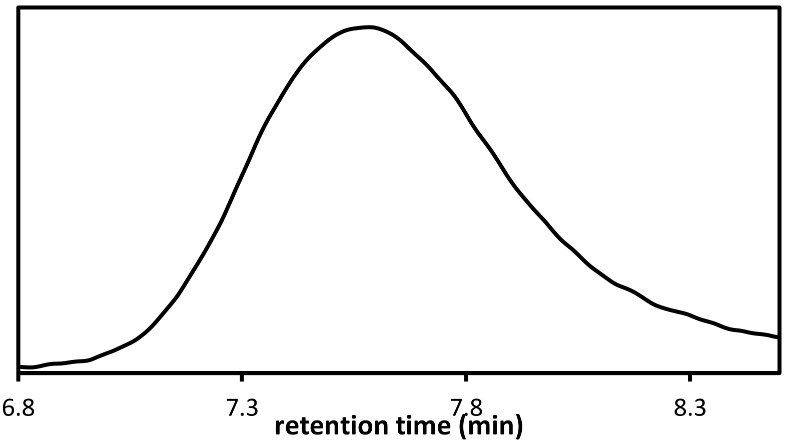


Figure S12. *SEC trace of* PS-*co*-P(SY) **5**.

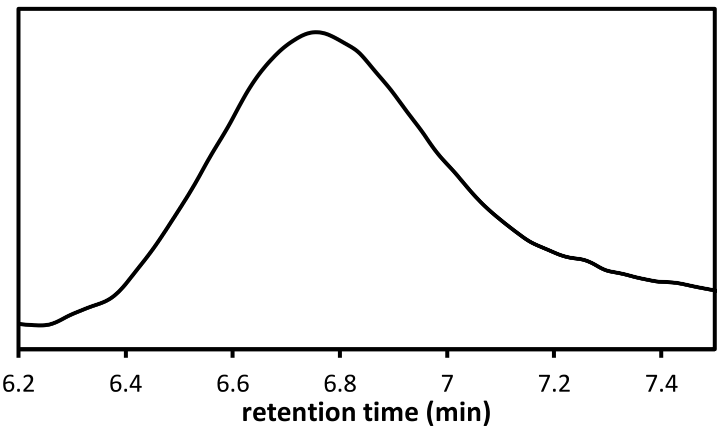


Figure S13. *SEC trace of* PS **8**.

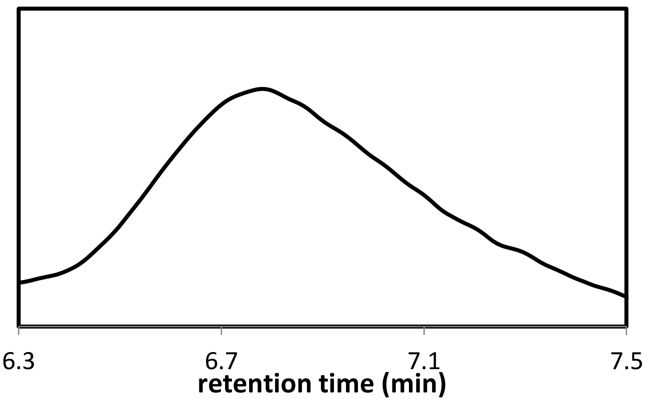


Figure S14. *SEC trace of* PS-*b*-P(SY) **9**.

6. NMR-Spectra

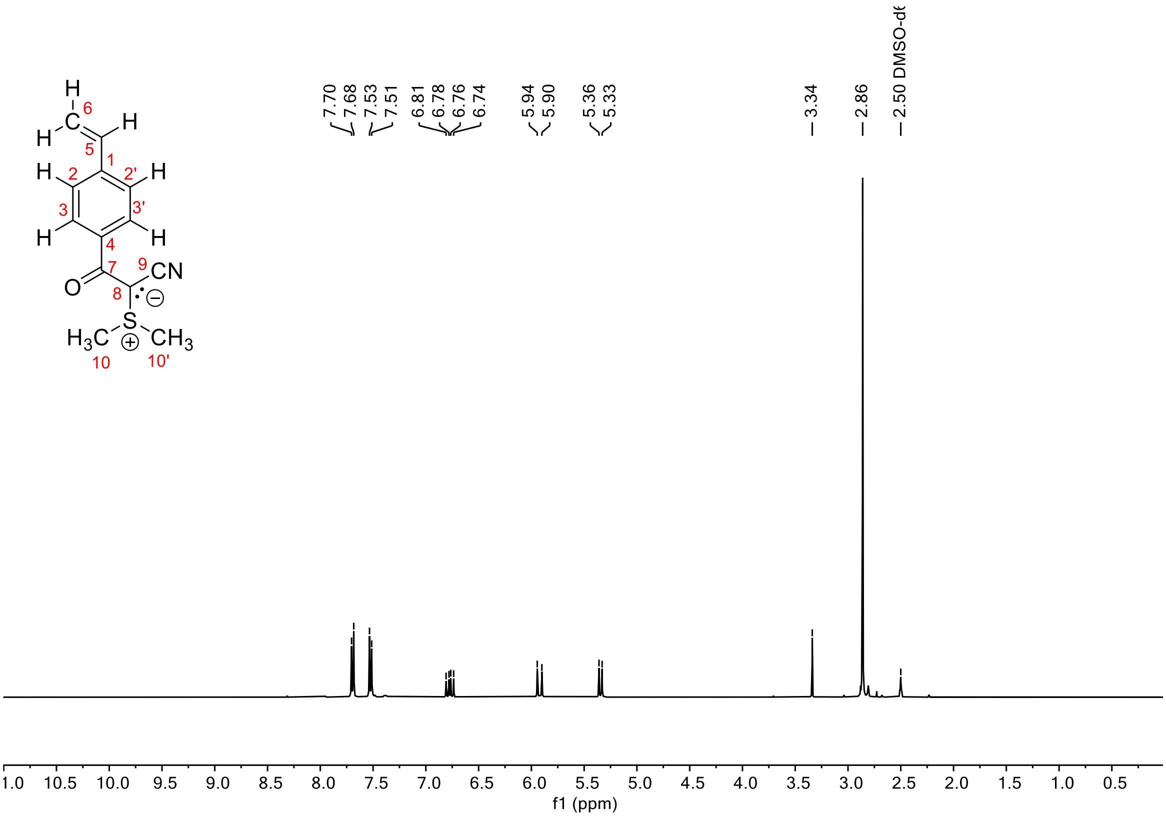


Figure S15. ^{1}H-NMR of compound **1**.

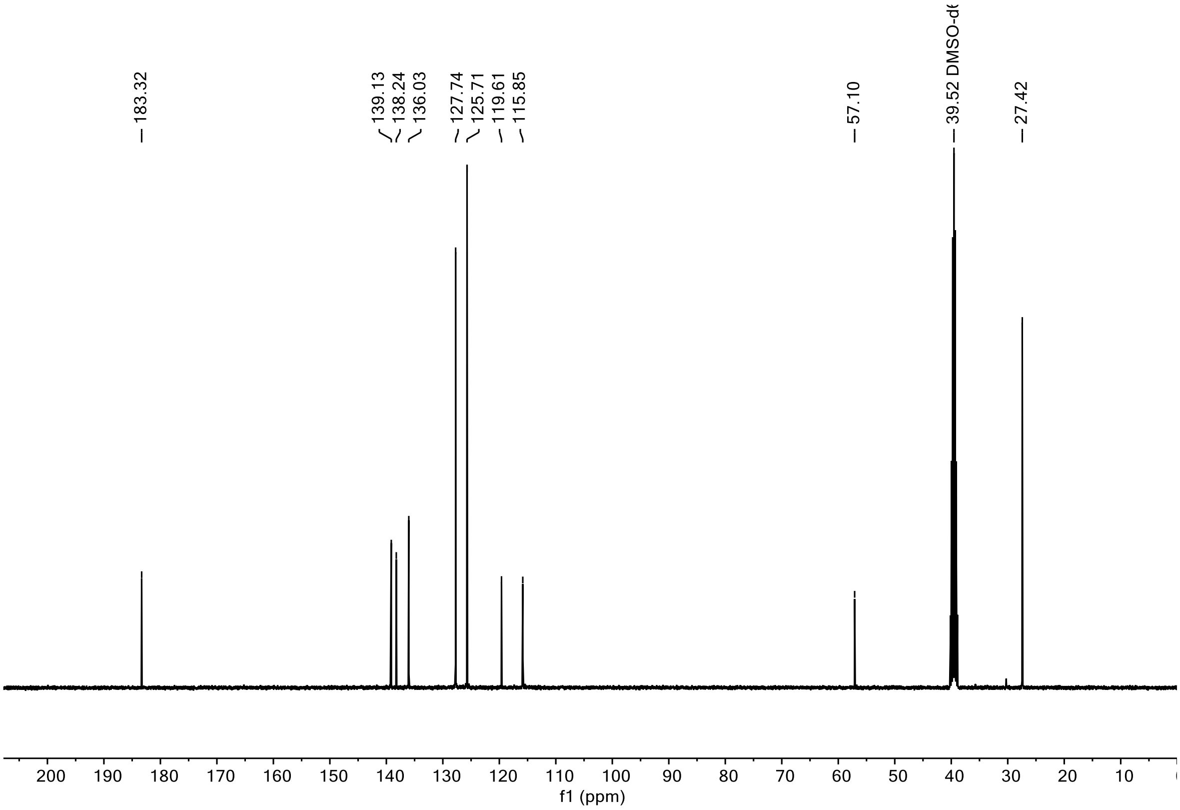


Figure S16. ^{13}C-NMR of compound **1.**

Table S2. Full assignment of compound **1** NMR signals

	^{1}H	^{13}C
1	-	139.13
2	7.52	125.71
3	7.69	127.74
4	-	138.24
5	6.77	136.03
6-trans	5.92	115.85
6-cis	5.34	
7	-	183.32
8	-	57.10
9	-	119.61
10	2.86	27.42

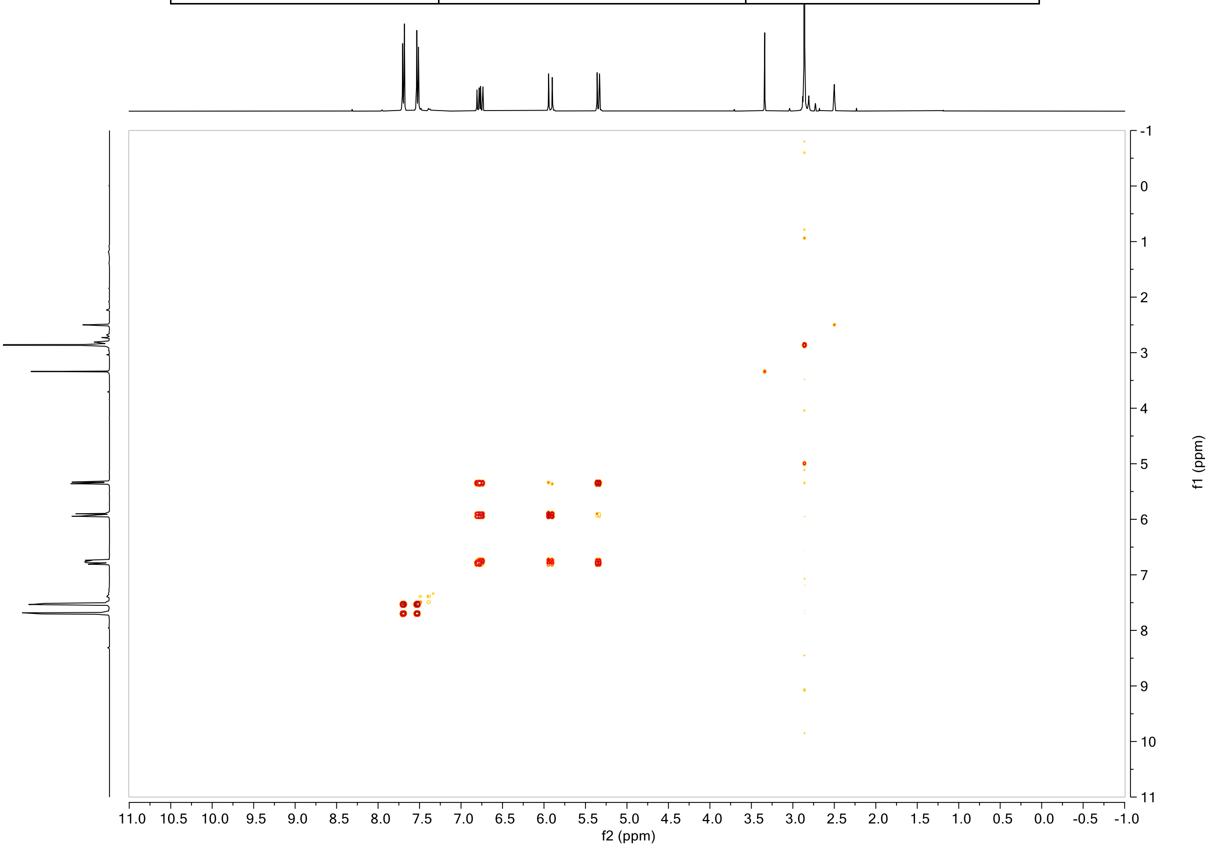


Figure S17. COSY-NMR of compound **1.**

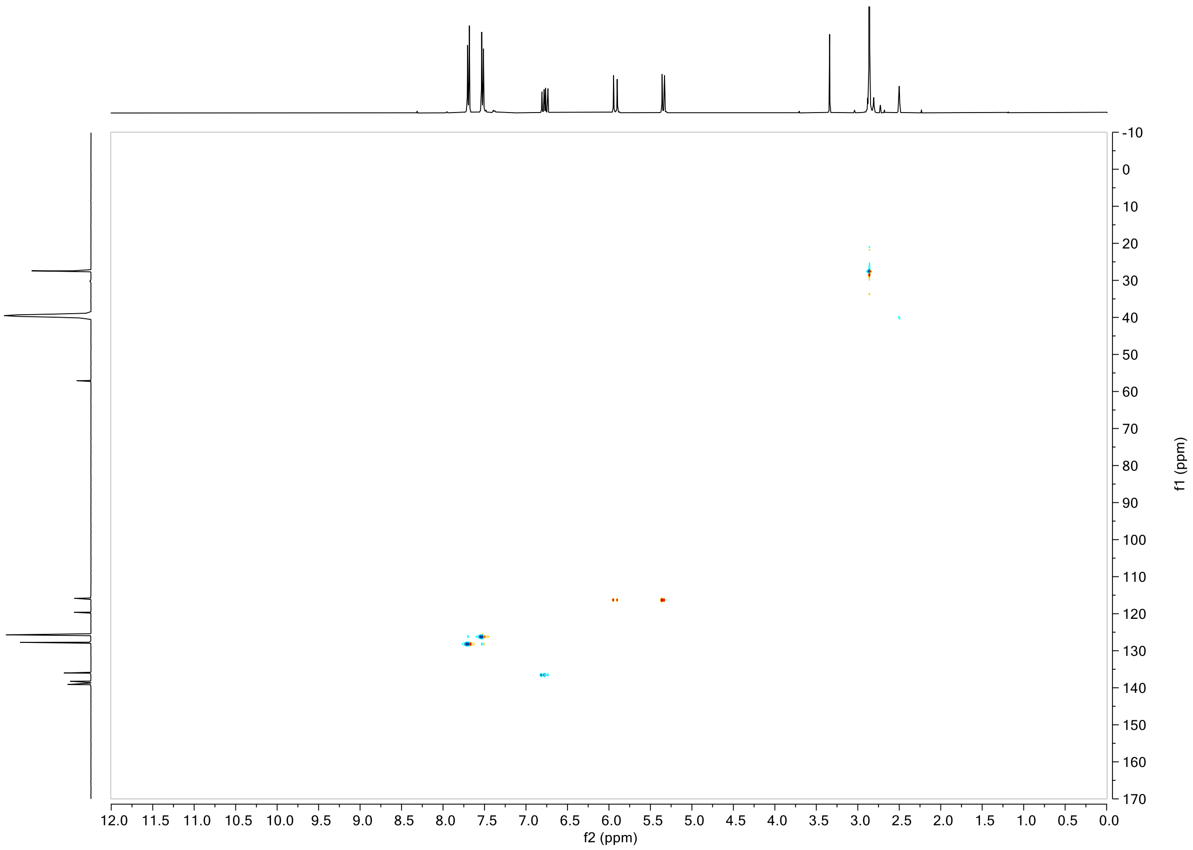


Figure S18. HSQC-NMR of compound **1.**

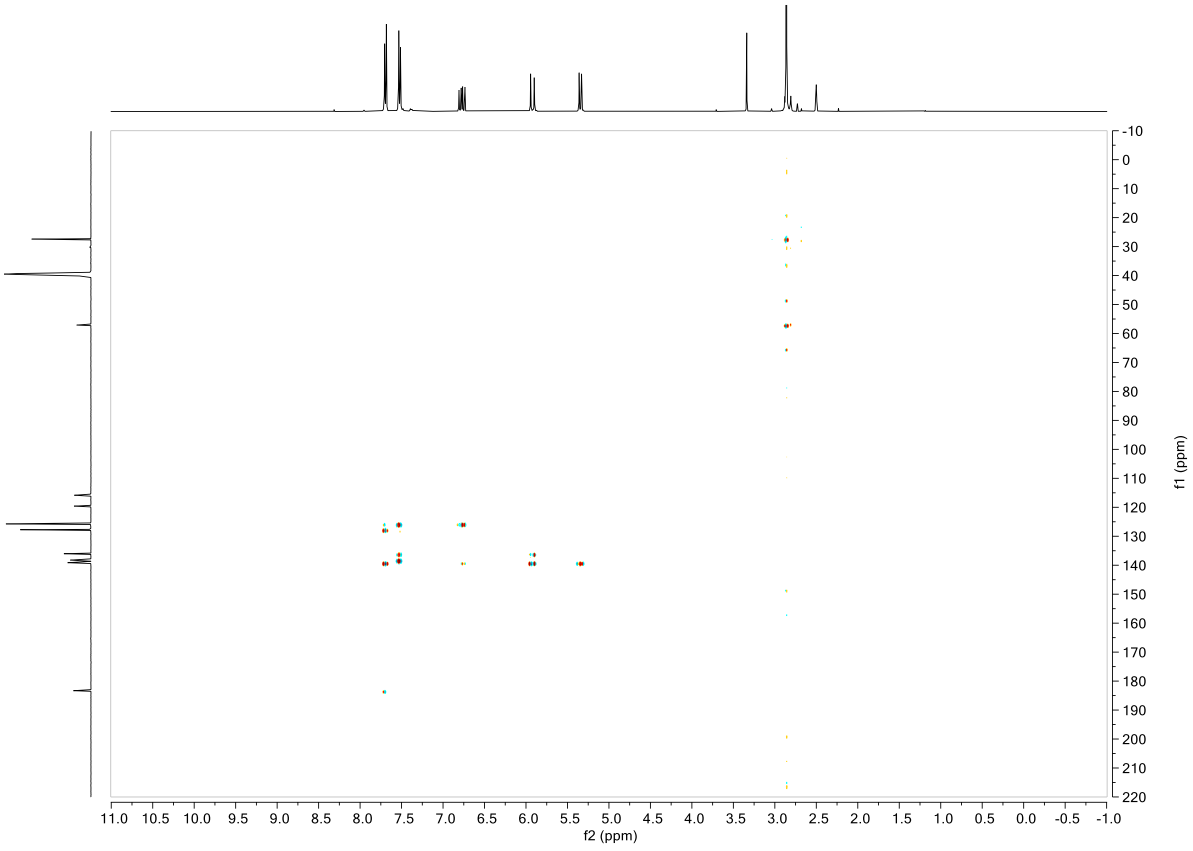


Figure S19. HMBC-NMR of compound **1.**

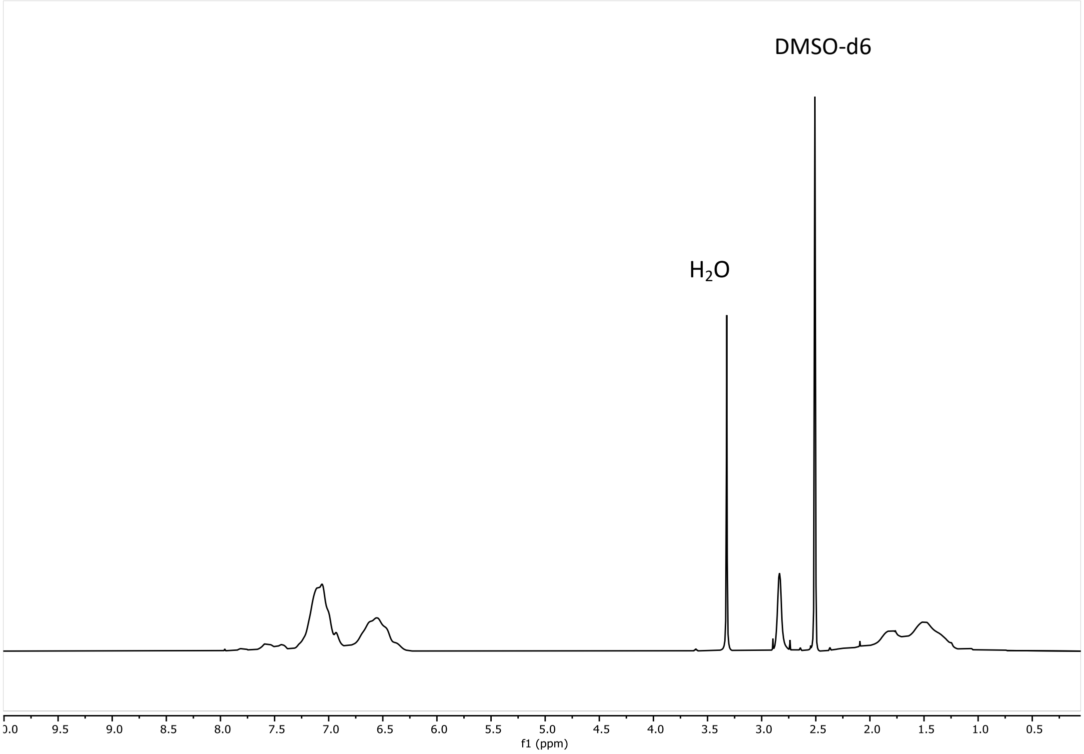


Figure S20. ^{1}H-NMR of compound PS-co-P(SY) **4**.

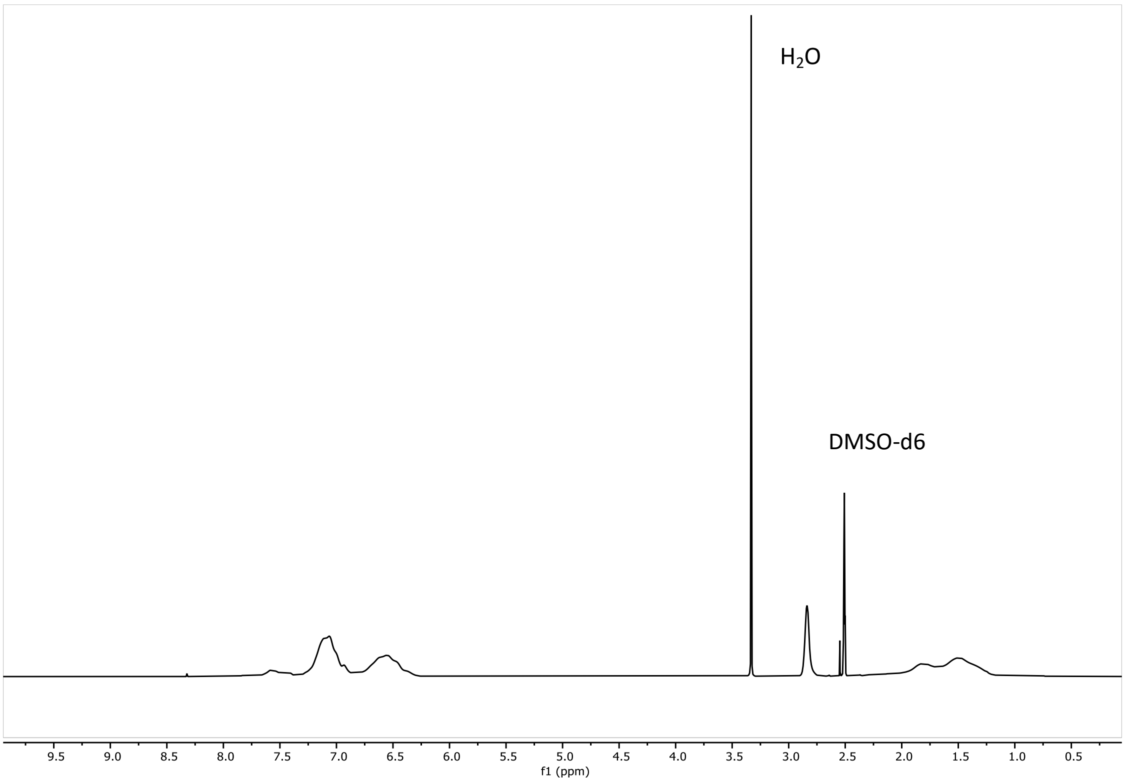


Figure S21. ^{1}H-NMR of compound PS-co-P(SY) **5**.

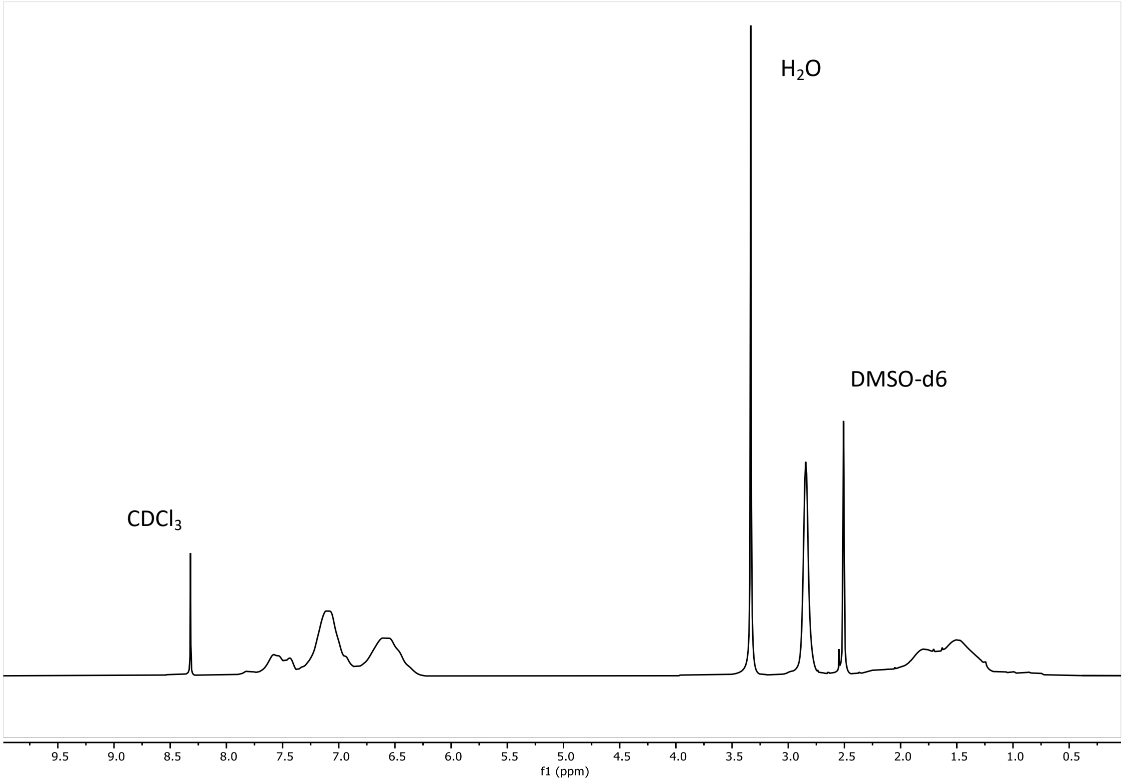


Figure S22. ^{1}H-NMR of compound PS-co-P(SY) **6**.

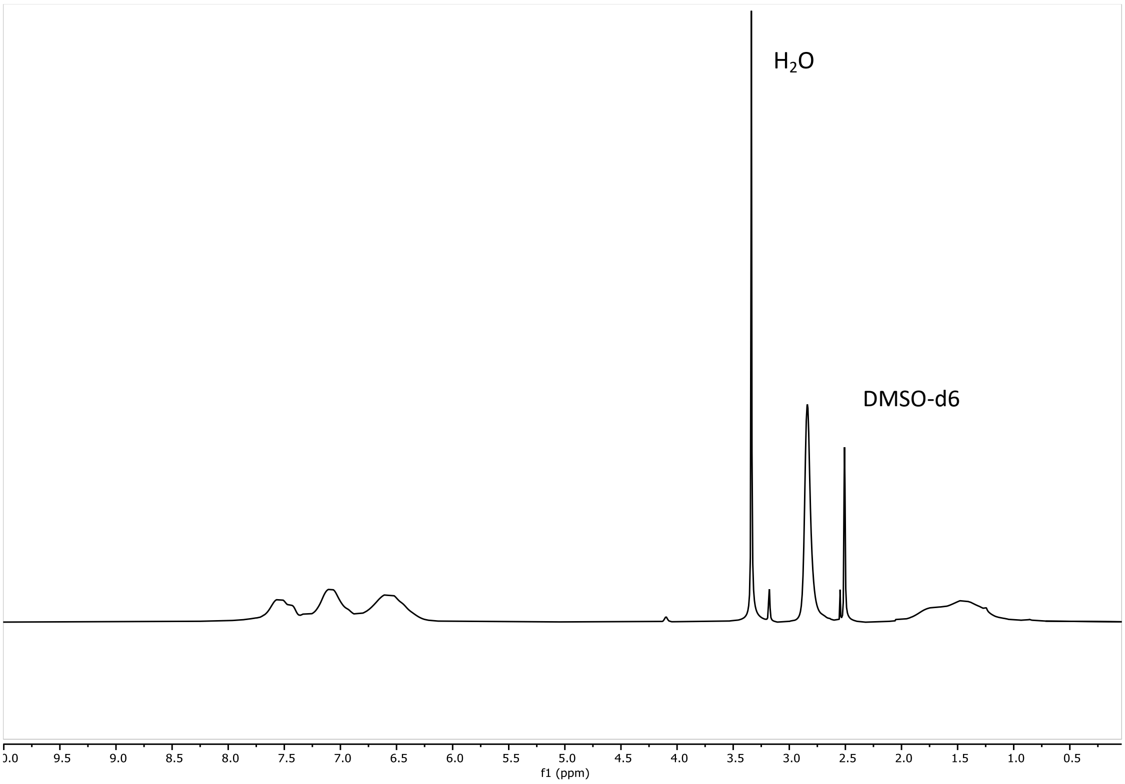


Figure S23. ^{1}H-NMR of compound PS-co-P(SY) **7**.

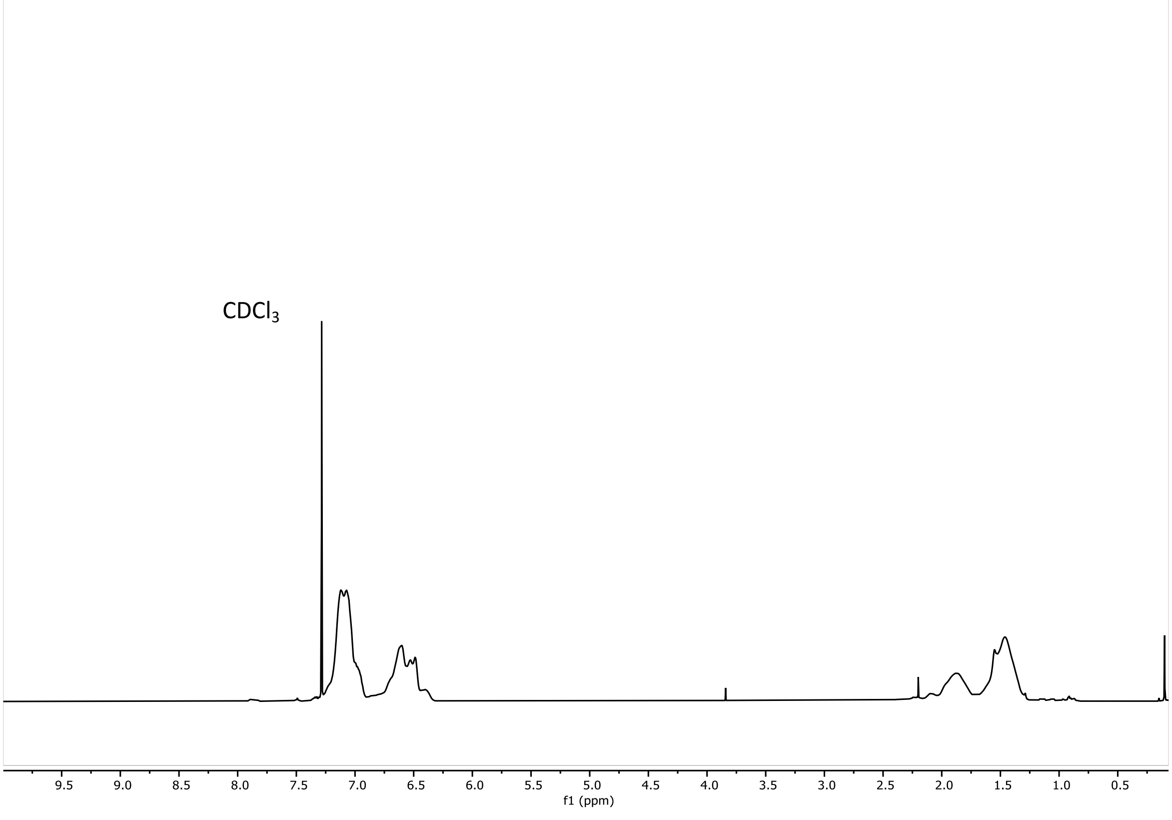


Figure S24. ^{1}H-NMR of compound PS **8**.

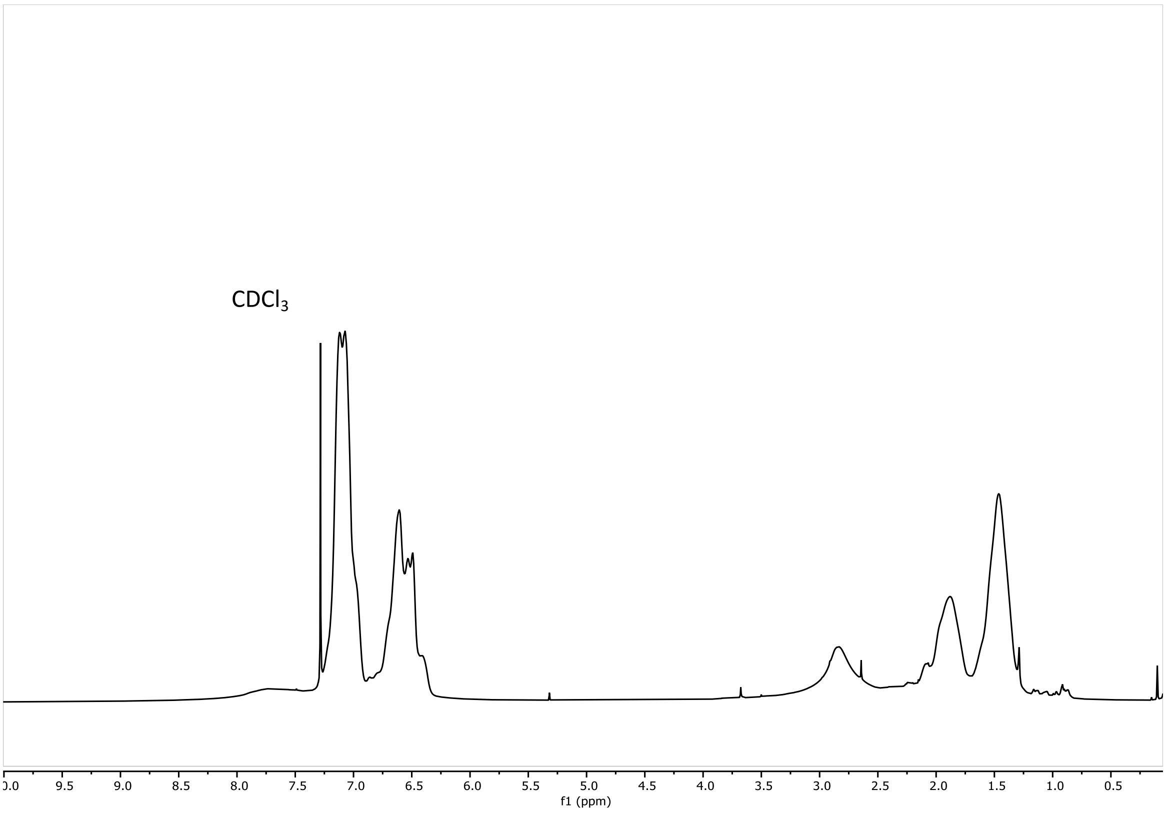


Figure S25. ^{1}H-NMR of compound PS-b-P(SY) **9**.

7. References

1. C. T. Lollar, K. M. Krenek, K. J. Bruemmer, A. R. Lippert, *Org. Biomol. Chem*., **2014**, 12, 406-409.