Supporting Information

ROMP copolymers for orthogonal click functionalizations

*Mark Schäfer, Nils Hanik, Andreas F.M. Kilbinger**

University of Fribourg, Department of Chemistry, Chemin du Musée 9, CH-1700 Fribourg, Switzerland

(3-Bromoprop-1-yn-1-yl)trimethylsilane **(SI1)**: To a mixture of propargyl bromide (20.01 g, 168.2 mmol, 1.25 eq.) in dry THF (350 mL), ^{n}butyllithium (135 mmol) was dropped slowly at -80°C. The mixture was then stirred for 10 minutes and chlorotrimethylsilane (14.64 g, 134.7 mmol, 1 eq.) was added dropwise. Upon removal of the cooling bath the mixture was stirred for 5h at room temperature and quenched by adding saturated ammonium chloride solution (50 mL). Extraction of the aqueous phase with dichloromethane and column chromatography with petroleum ether as eluent led to 80% pure product which was used without further purification in an excess during the next reaction step. Yield: **SI1a** 15.79 g, 82.6 mmol, 61%, ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 3.92 (s, 2H, Br-C**H**$_2$); 0.19 (s, 9H, C**H**$_3$). **SI1b** 10.94 g from 10.02 g propargyl bromide, 39.74 mmol, 59%, ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 3.96 (s, 2H, Br-C**H**$_2$); 1.08 (s, 18H, C**H**$_3$); 1.06 (s, 3H, C**H**).

exo-N-[3-(Trimethylsilyl)prop-2-yn-1-yl]-5-norbornene-2,3-dicarboximide **(SI2)**: Anhydrous potassium carbonate (1.63 g, 11.83 mmol, 1.35 eq.), compound **3** (1.43 g, 8.76 mmol, 1 eq.) and dry acetone (20 mL) were combined in a Schlenk-flask and stirred for 10 minutes at 55°C before compound **4** (3.35 g, 17.53 mmol, 2.00 eq.) was added dropwise via a syringe. After 48h at 55°C the mixture was filtered and the organic solvent removed. The crude product was purified via column chromatography with dichloromethane as eluent. Yield: **SI2a** 2.02 g, 7.39 mmol, 84%, ^{1}H NMR (300 MHz, CDCl3), δ (ppm): 6.30 (s, 2H, C=C**H**); 4.23 (s, 2H, N-C**H**$_2$); 3.32 (s, 2H, CO-C**H**); 2.72 (s, 2H, =CH-C**H**); 1.52-1.49 (d, 1H, ^{2}J=9.99 Hz, C**H**$_2$-bridge); 1.29-1.26 (d, 1H, ^{2}J=9.99 Hz, C**H**$_2$-bridge); 0.12 (s, 9H, C**H**$_3$), ^{13}C NMR (75 MHz, CDCl3), δ (ppm): 176.60 (**C**O); 137.98 (**C**=**C**); 97.82 (CH$_2$-**C**≡); 88.09 (Si-**C**≡); 47.75 (CO-**C**H); 45.58 (=CH-**C**H); 42.55 (**C**H$_2$-bridge); 28.58 (N-**C**H$_2$); 0.31 (**C**H$_3$), ESI-MS: 296.0, 297.1 m/z (273.1 calc. + sodium). **SI2b** 6.53 g from 4.07 g compound **3**, 18.26 mmol, 75%, ^{1}H NMR (300 MHz, CDCl3), δ (ppm): 6.29 (s, 2H, C=C**H**); 4.25 (s, 2H, N-C**H**$_2$); 3.30 (s, 2H, CO-C**H**); 2.69 (s, 2H, =CH-C**H**); 1.49-1.45 (d, 1H, ^{2}J=9.82 Hz, C**H**$_2$-bridge); 1.33-1.30 (d, 1H, ^{2}J=9.82 Hz, C**H**$_2$-bridge); 1.01 (s, 21, C**H**(C**H**$_3$)$_2$), ^{13}C NMR (75 MHz, CDCl3), δ (ppm): 176.45 (**C**O); 137.96 (**C**=**C**); 99.70 (CH$_2$-**C**≡); 84.48 (Si-**C**≡); 47.65 (CO-**C**H); 45.62 (=CH-**C**H); 42.58 (**C**H$_2$-bridge); 28.70 (N-**C**H$_2$); 18.42(**C**H$_3$); 10.99 (**C**H), ESI-MS: 358.2, 359.2, 360.2, 361.2 m/z (357.2 calc. + proton).

Piperonyl bromide **(8)**: Piperonyl alcohol (1.5 g, 9.86 mmol, 1 eq.) and tetrabromomethane (3.8 g, 11.46 mmol, 1.16 eq.) were dissolved in dichloromethane (30 mL) and cooled to 0°C before triphenylphosphine (3.0 g, 11.45 mmol, 1.16 eq.) was added in small portions over 15 minutes. After stirring the mixture for 2h at room temperature, the solvent was removed and the product purified via column chromatography with petroleum ether : ethyl acetate (9:1) as eluent.

While diluting the crude product with eluent, a colorless precipitate occurred, that was removed by filtration before chromatographic purification. Yield: 1.89 g, 8.79 mmol, 89%, ^{1}H NMR (360 MHz, $CDCl_3$), δ (ppm): 6.89-6.75 (m, 3H, **Ar**); 5.98 (s, 2H, O-C**H**$_2$-O); 4.47, (s, 2H, Br-C**H**$_2$), ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 147.85 (**C**^{3}); 147.76 (**C**^{2}); 131.45 (**C**^{5}); 122.69 (**C**^{6}); 109.41 (**C**^{4}); 108.26 (**C**^{1}); 101.28 (O-**C**H$_2$); 34.17 (Br-**C**H$_2$).

Piperonyl azide **(9)**: Compound **8** (1.54 g, 7.16 mmol, 1 eq.) and sodium azide (0.69 g, 10.61 mmol, 1.5 eq.) dissolved in a mixture of DMF (20 mL) and water (4.5 mL) were stirred over night at 40°C under argon atmosphere. The aqueous phase was extracted with diethyl ether (3x50 mL) and the combined organic phases washed with brine (2x50 mL) before the solvent was evaporated under reduced pressure. Residual DMF was removed under high vacuo before the product was purified via column chromatography with ethyl acetate : petroleum ether (9:1) as eluent. Yield: 1.12 g, 6.33 mmol, 88%, ^{1}H NMR (360 MHz, $CDCl_3$), δ (ppm): 6.83-6.77 (m, 3H, **Ar**); 5.99 (s, 2H, O-C**H**$_2$-O); 4.24, (s, 2H, N_3-C**H**$_2$), ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 140.02 (**C**^{3}); 147.65 (**C**^{2}); 129.00 (**C**^{5}); 121.91 (**C**^{6}); 108.71 (**C**^{4}); 108.33 (**C**^{1}); 101.21 (O-**C**H$_2$); 54.68 (N_3-**C**H$_2$).

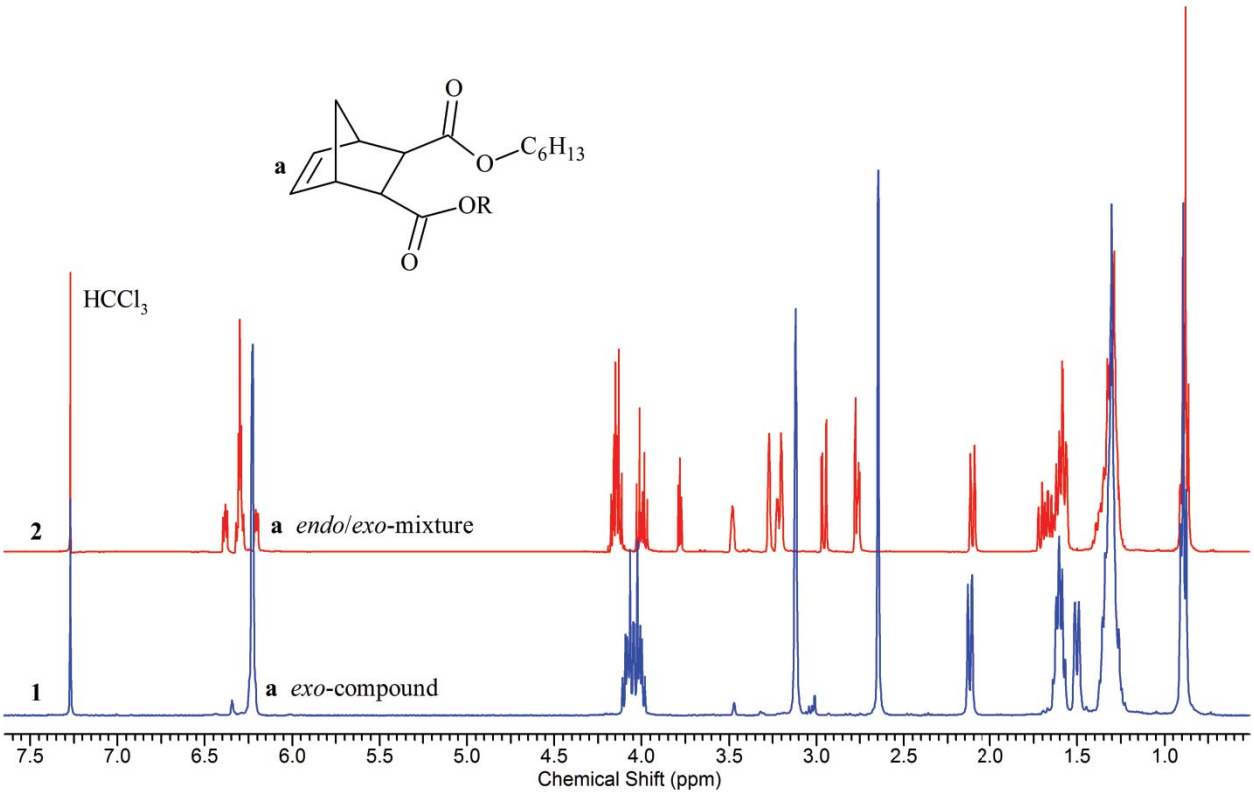


Figure SI1. Conversion of pure *exo*-compound **1** into an *endo*/*exo*-mixture of **2** via an intermediate ketene.

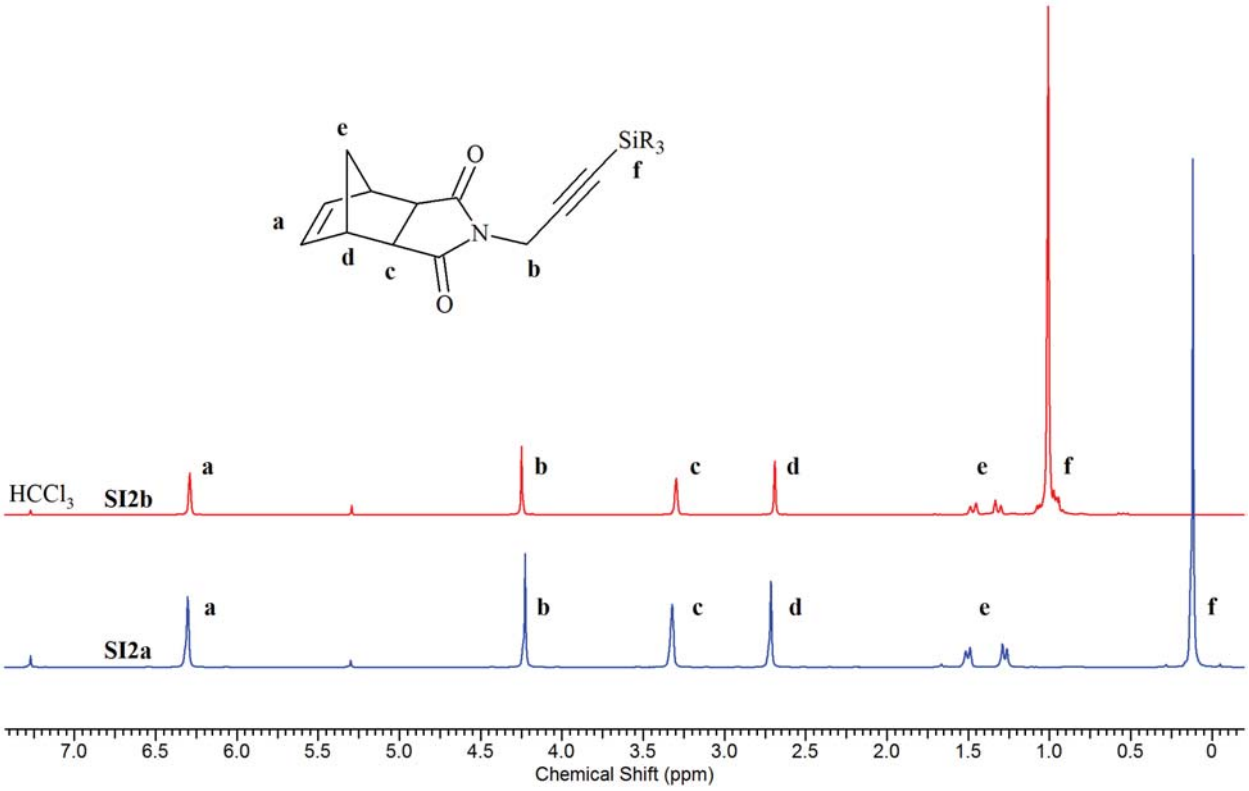


Figure SI2. ^{1}H NMR spectra of the trialkylsilyl-protected alkyne monomers.

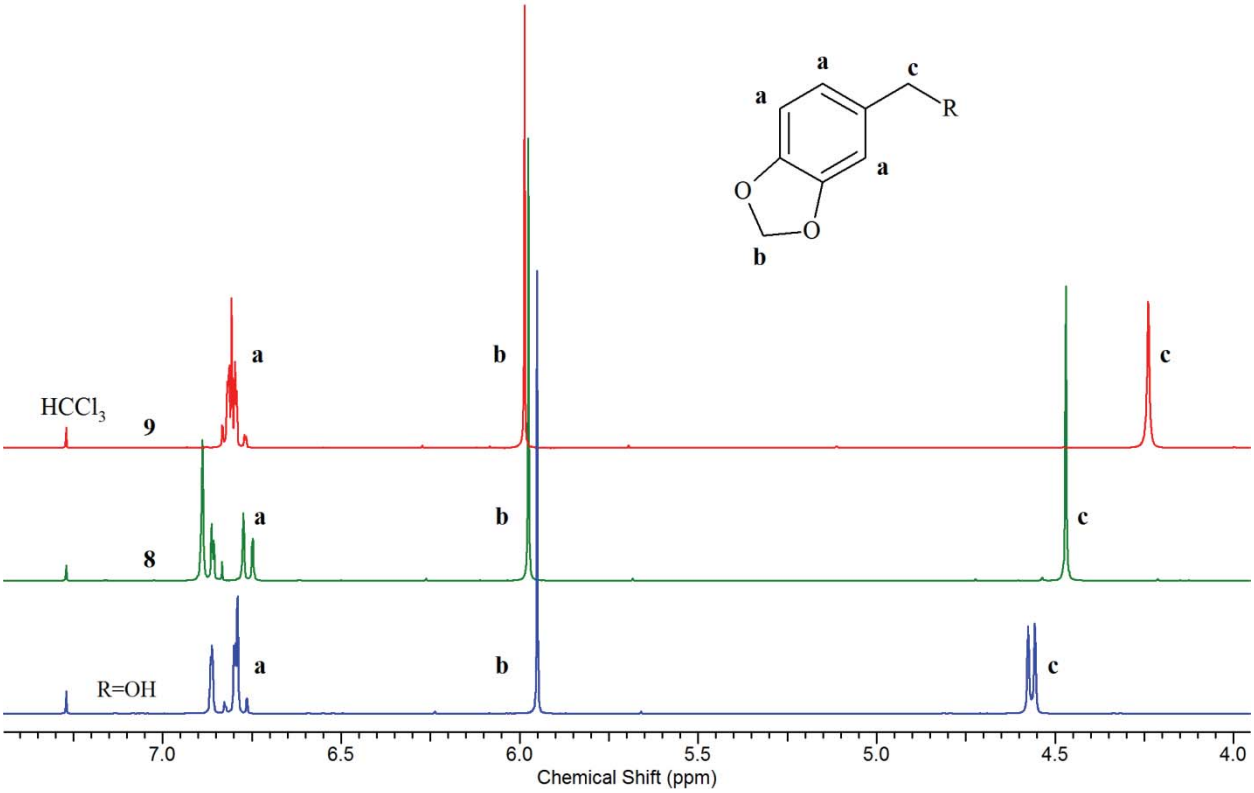
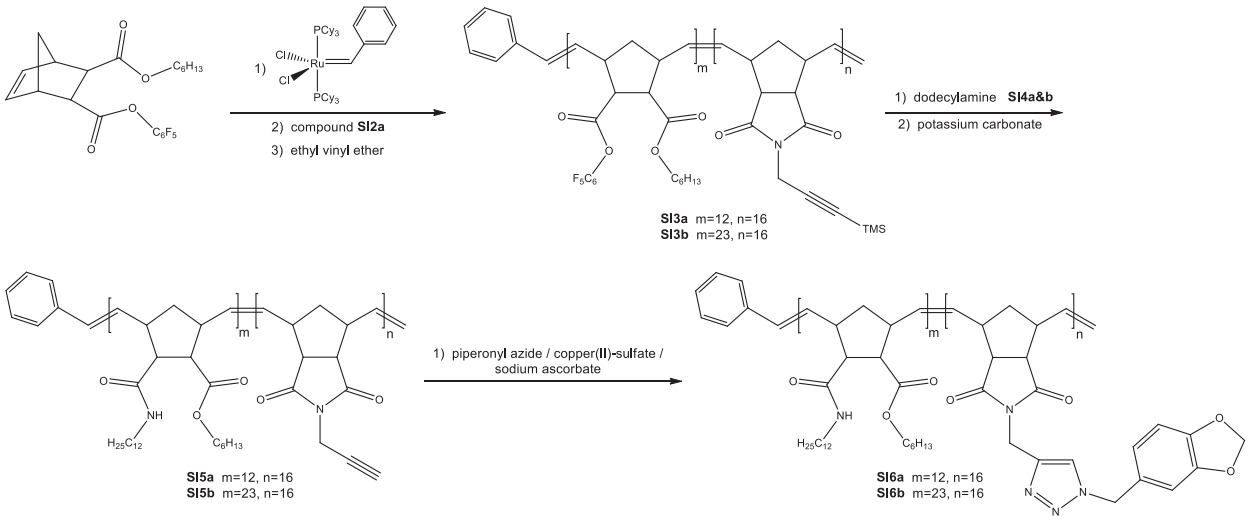


Figure SI3. Synthesis of piperonyl azide from piperonyl alcohol to the corresponding bromide to the azide clearly visualized by the change in chemical shift of the benzylic CH_2 protons **e**.



Scheme SI1. Synthetic scheme visualizing block copolymerization leading to bifunctional precursor polymers and their orthogonal "double-click" reaction.

With monomers **2**, **SI2a&b** in hand, we carried out block copolymer syntheses using Grubbs' first generation ruthenium carbene initiator (benzylidene-bis(tricyclohexylphosphine) dichlororuthenium) according to Scheme SI1.

Polymer samples were taken after the polymerization of each block in order to confirm successful block transfer. The synthesis of block copolymers gave well defined block lengths according to the chosen monomer/catalyst ratio based on the living character of this polymerization technique. Two polymers, **SI3a** and **SI3b** with the intended compositions, *m:n=12:16* and *m:n=23:16* respectively (see Scheme SI1), were synthesized and analyzed by ^{1}H NMR spectroscopy (Figure SI4) as well as gel permeation chromatography (Table SI1). Comparing the integral of the terminal methyl group at 0.86 ppm versus the integral of the protecting group at 0.15 ppm allowed us to calculate the content of the two functional monomers (**2** vs. **SI2a**). For polymer **SI3a** a ratio of *m:n=13.5:16* and for polymer **SI3b** a ratio of

m:n=24.5:16 was found, which agreed well with the aimed at values. Furthermore, it could be shown that introducing a covalently bound protecting group renders the alkyne sterically hindered, prevents enyne metathesis and the formation of previously proposed resting states that slow down propagation. Indicators for the absence of such side reactions are the narrow molecular weight distributions (lack of crosslinking) and the formation of the target molecular weights as shown in Table SI1.

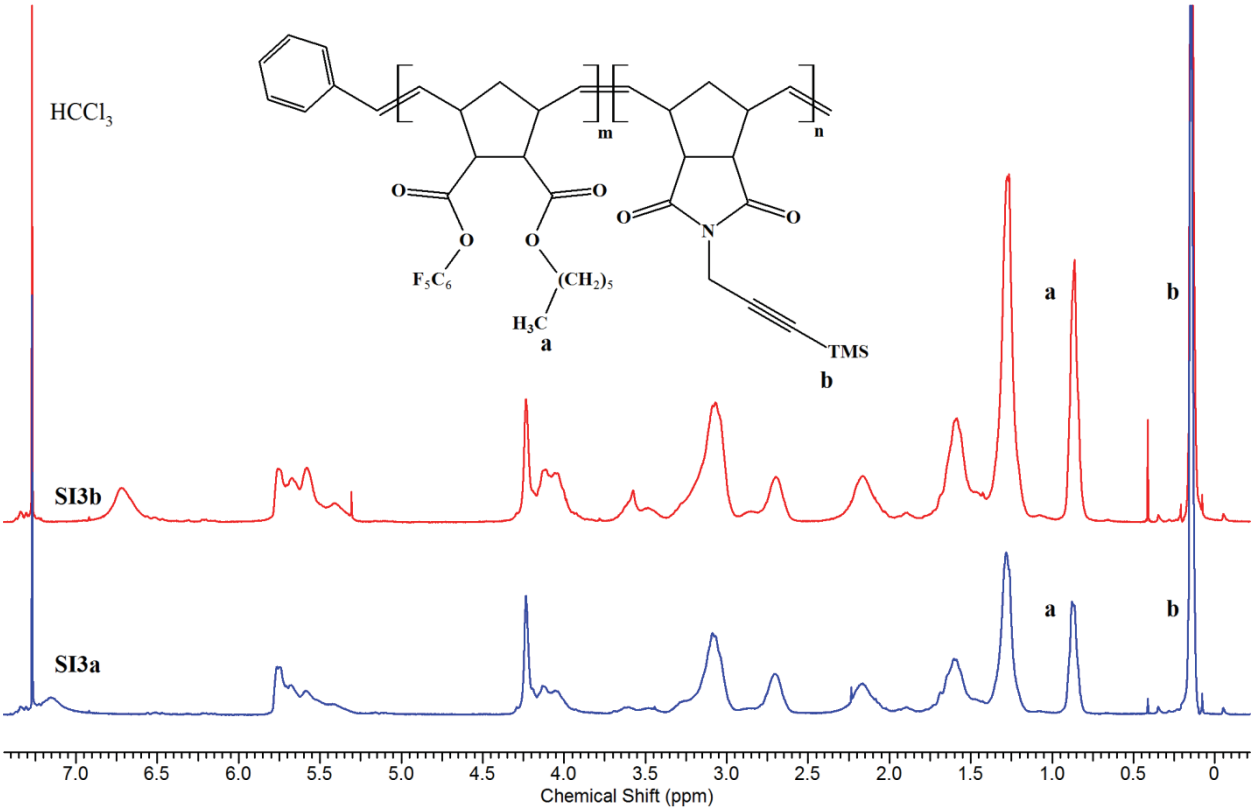


Figure SI4. ^{1}H NMR spectra of precursor polymers **SI3a** and **SI3b**. No signals for potential enyne-metathesis products can be observed.

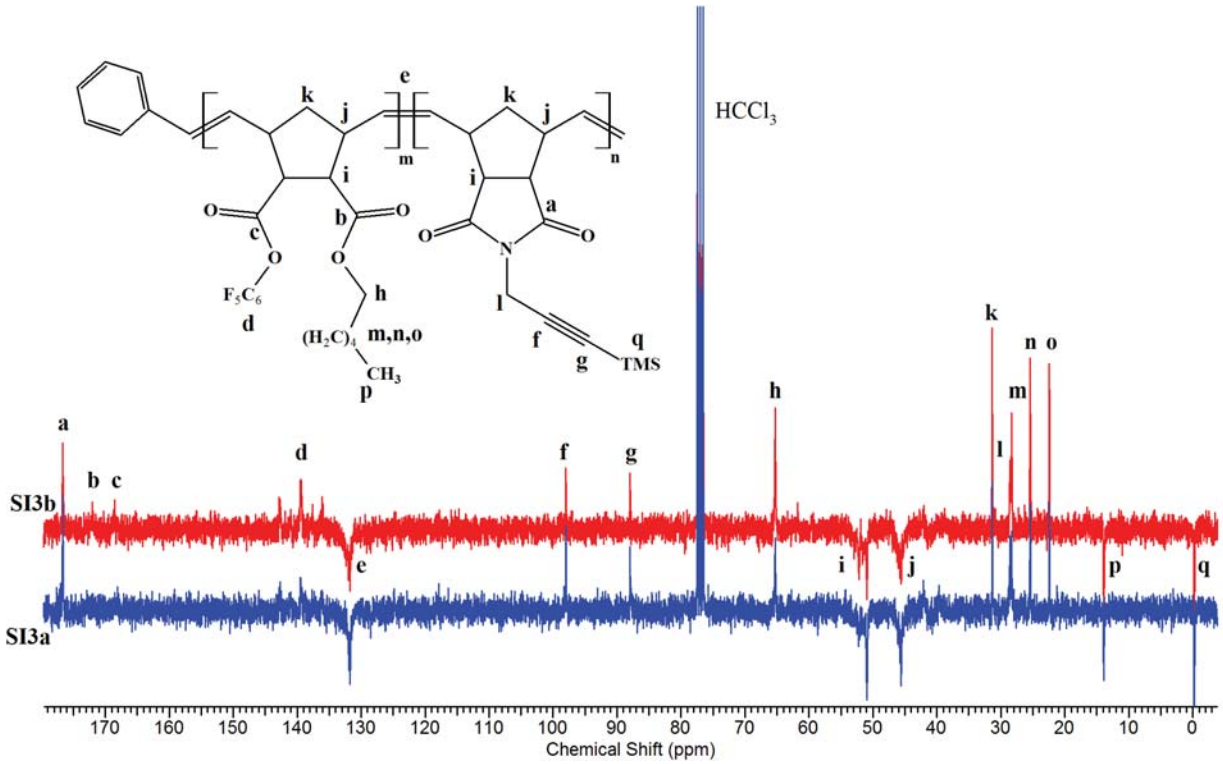


Figure SI5. Attached proton test (APT) NMR spectra of the precursor polymers **SI3a** and **SI3b** to indicate that no enyne metathesis occurred during the polymerization step.

Sample	calculated	RI detector		
	M_n [g/mol]	M_n [g/mol]	M_w [g/mol]	PDI
SI3a	9,300	15,300	19,400	1.26
SI3b	14,300	18,700	25,800	1.38
SI4a	9,300	16,100	19,600	1.21
SI4b	14,300	24,600	29,800	1.21
SI5a	8,200	15,500	18,200	1.17
SI5b	13,200	21,600	26,000	1.20
SI6a	11,000	12,700	13,800	1.09
SI6b	16,000	18,600	21,500	1.15

Table SI1. Results of GPC traces for precursor polymers **SI3**, intermediates **SI4** and **SI5** as well as "double-clicked" polymers **SI6**.

The functionalization of the amine selective esters in the first blocks of polymers **SI3a** and **SI3b** was performed with dodecylamine which served as a model reagent. This resulted in the formation of polymers **SI4a** and **SI4b** (not shown in Scheme SI1). In future investigations this model-amine could be substituted for functional groups bearing amines. The advantage of this primary n-alkyl amine is the fact that the terminal methyl groups can be easily integrated with respect to the alkyne-protecting group in order to calculate the degree of functionalization. The composition of polymer **SI4a** was found to be *m:n=13.4:16* and *m:n=24.2:16* for polymer **SI4b**, which suggested complete conversion of the reactive ester. Complete conversion could also be proven by the complete disappearance of the corresponding signals in the ^{19}F NMR spectra (Figure SI6).

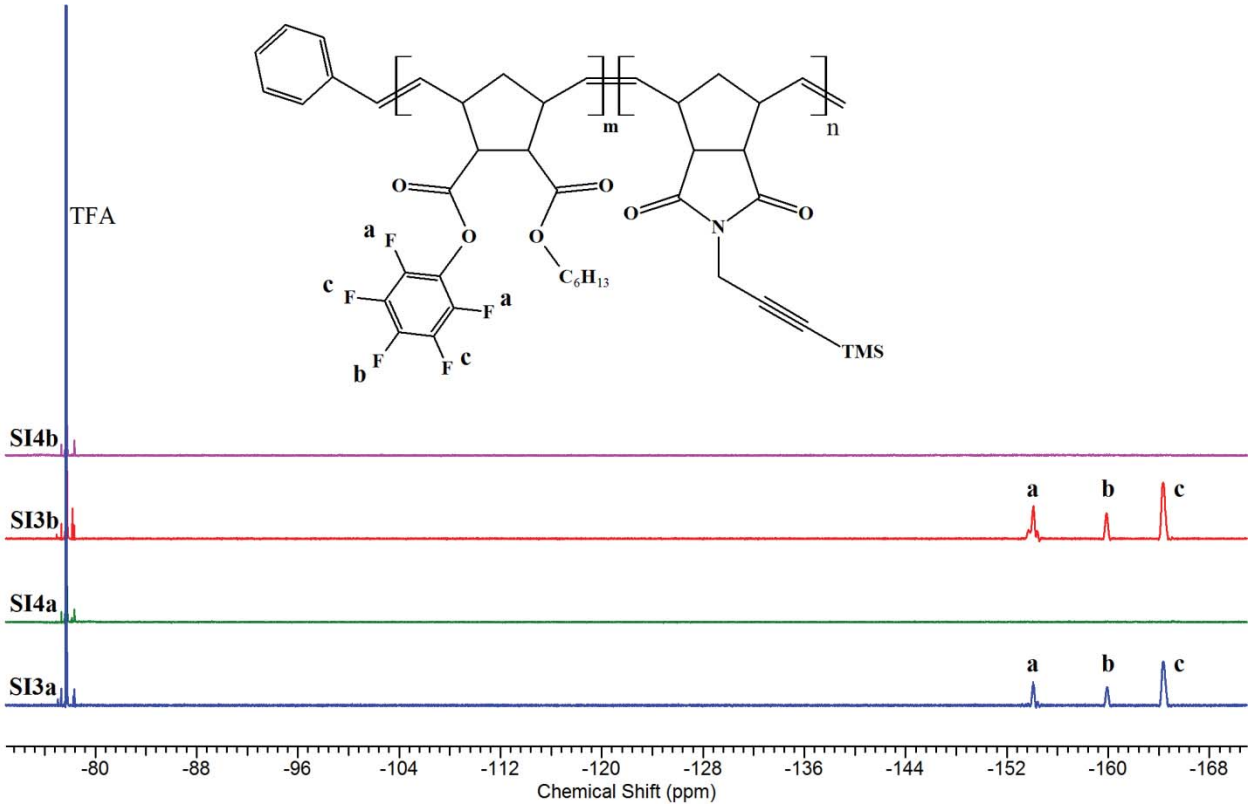


Figure SI6. ^{19}F NMR spectra of non-functionalized polymers **SI3** and functionalized polymers **SI4**. Quantitative conversion of the first click reaction is indicated by the disappearance of signals corresponding to the pentafluorophenyl ester.

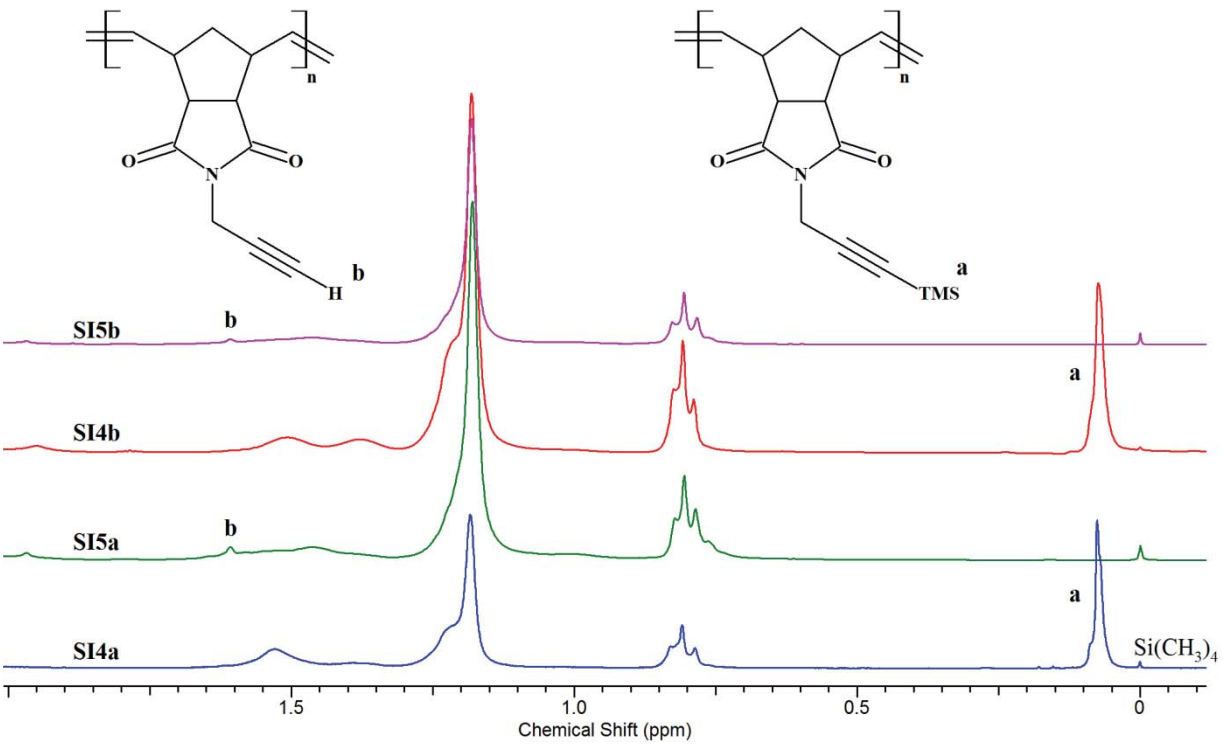


Figure SI7. ^{1}H NMR spectra showing complete liberation of the terminal alkyne by vanishing signals of the protecting group **a** as well as appearing of the terminal methyne **b**.

For the alkyne to be suitable for CuAAC (copper catalyzed azide-alkyne cycloaddition), the silyl protective groups had to be cleaved quantitatively. Standard deprotection conditions using a tetrabutylammonium fluoride (TBAF) solution in THF did not result in quantitative removal of the TMS and TIPS protective groups. Exposure of **SI4a** and **SI4b** to potassium carbonate for 72h at 50°C, however, lead to quantitative silyl-cleavage and the formation of polymers **SI5a** and **SI5b** as shown in Figure SI7. Due to the peak overlap of the terminal methyne proton at 1.67 ppm with signals of the polymer backbone, attached proton test (APT) NMR experiments (Figure SI8) were employed to visualize its formation.

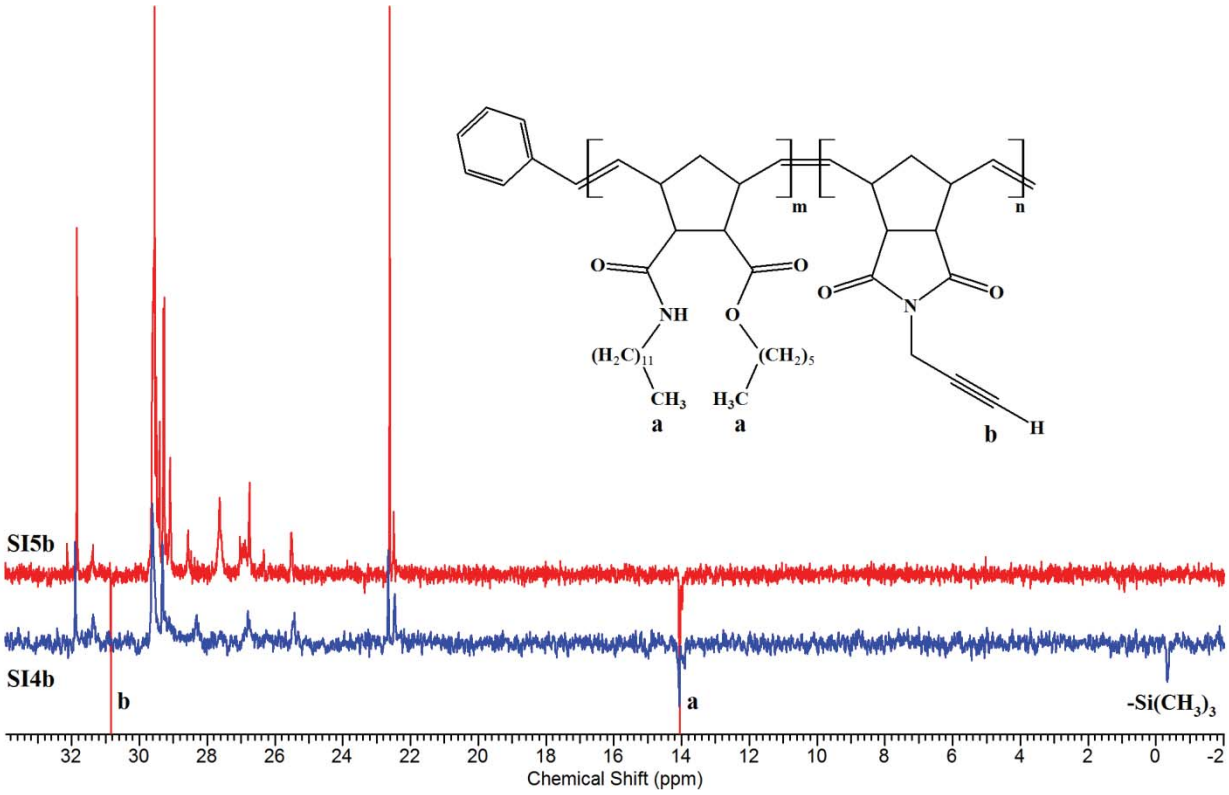


Figure SI8. Attached proton test (APT) NMR spectra showing complete deprotection of the terminal alkyne according to the disappearance of the TMS-signal and appearance of the terminal CH-signal **b**.

Cu-catalyzed reaction of the terminal alkynes in polymers **SI5a** and **SI5b** with compound **9** (Scheme 2) yielded the corresponding 1,2,3-triazoles. The copper(I) species were synthesized in situ by reduction of catalytic amounts of copper(II)sulfate with an excess of sodium L-ascorbate. The formation of the triazole can clearly be shown by investigating the ^{1}H NMR spectra of compounds **SI6a** and **SI6b** (Figure SI9) due to the occurrence of the aromatic and benzylic protons as well as the protons corresponding to the acetal. Two dimensional HMQC (heteronuclear multiple quantum coherence) NMR-spectra were recorded (see Supporting Information, Figure SI10) to show that quantitative conversion of the alkyne to the triazole had

taken place. According to the corresponding GPC traces (Figures SI11a and SI11b, data in Table 1) and contrary to our expectations, the molecular weights of polymers **SI6a** and **SI6b**, appeared to be smaller after the functionalization. This is believed to be caused by the collapse of the triazole-containing blocks due to poorer solvation of the aromatic catechol groups leading to a decrease in hydrodynamic volume.

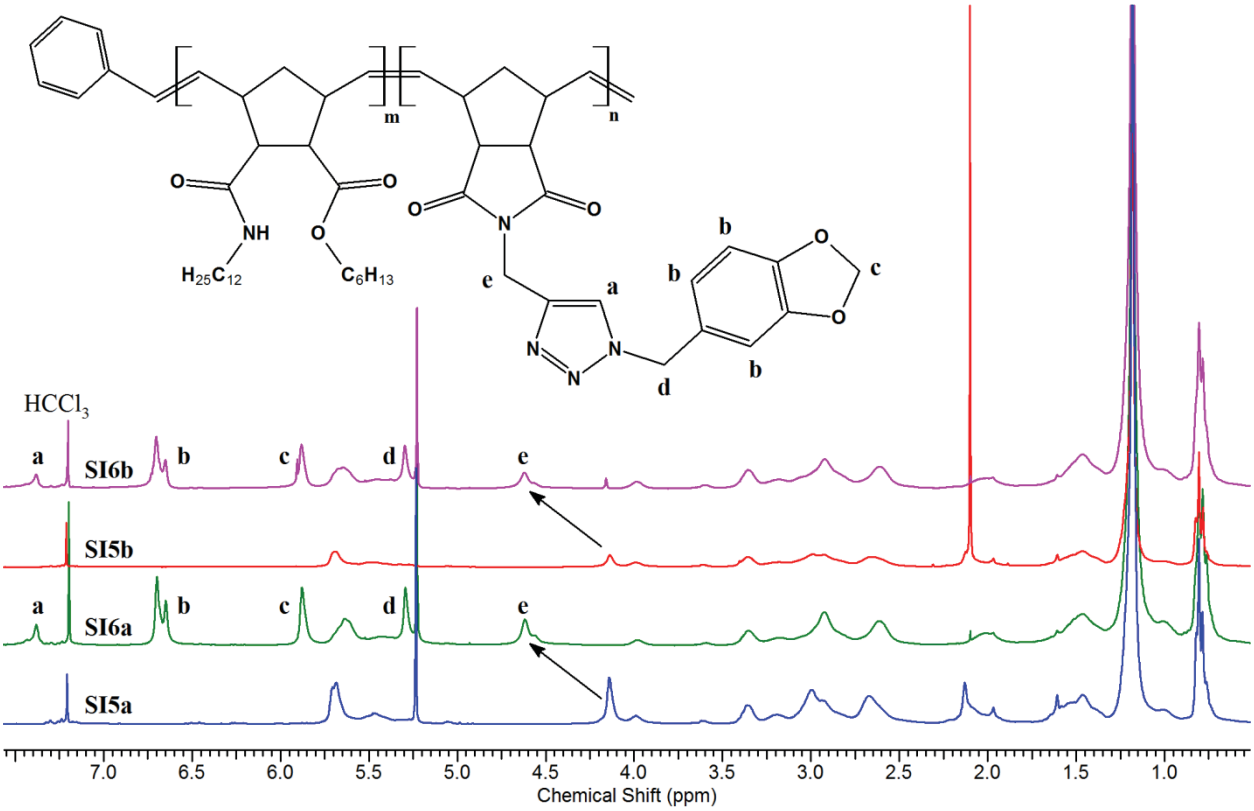


Figure SI9. ^{1}H NMR spectra before and after the second click reaction (CuAAC). Occurrence of signals corresponding to the triazole and catechol as well as a shift of the methylene protons **e** to 4.69 ppm can be observed. Polymer **SI6b** was not quantitatively functionalized indicated by a small residual peak at 4.23 ppm.

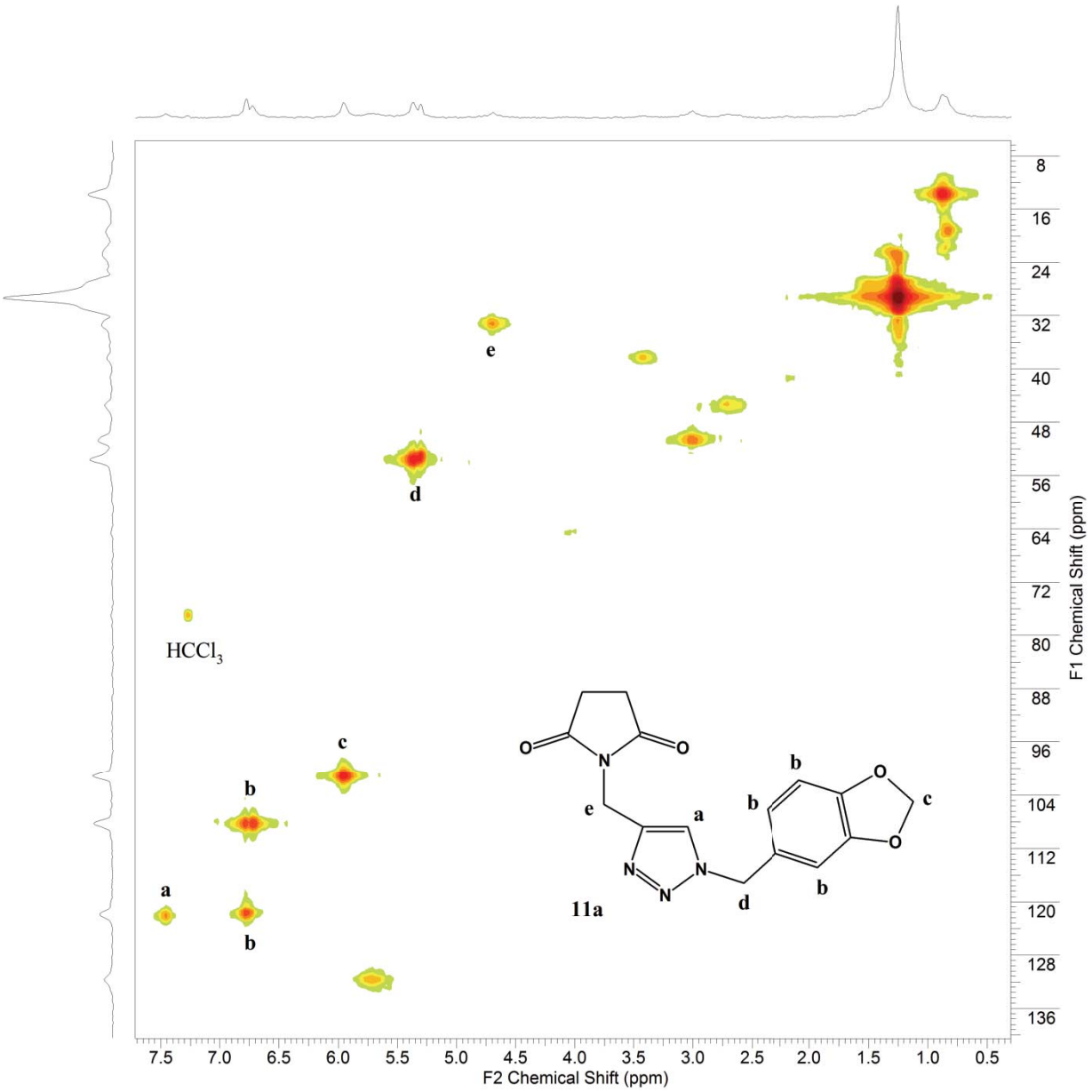


Figure SI10. Heteronuclear multiple quantum coherence (HMQC) NMR spectrum of compound **SI6a** shows formation of the triazole and no residual peak corresponding to the alkyne at 1.67 ppm (F2) and 30.85 ppm (F1).

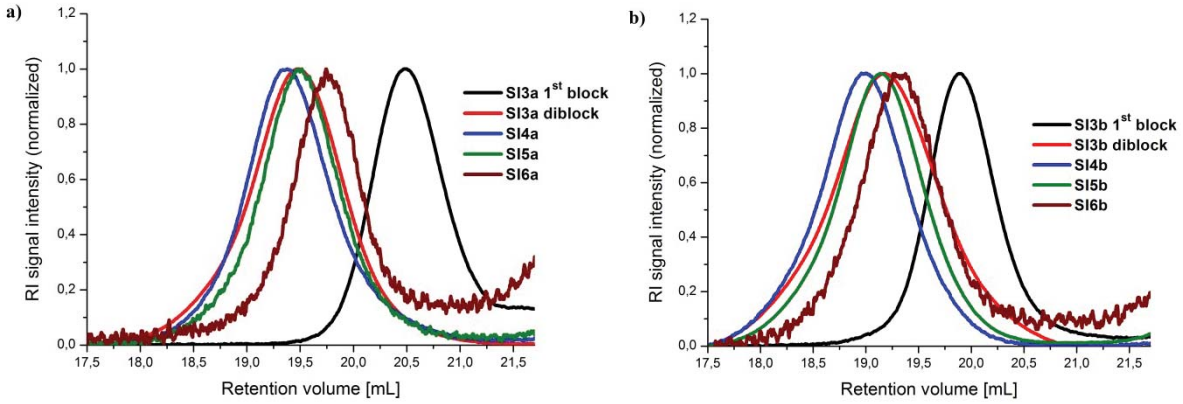


Figure SI11. Gel permeation chromatography (GPC, THF) traces of both polymers (**a** and **b**) throughout the whole reaction sequence. An increase in molecular weight from homoblock to diblock and first click reaction can be seen.

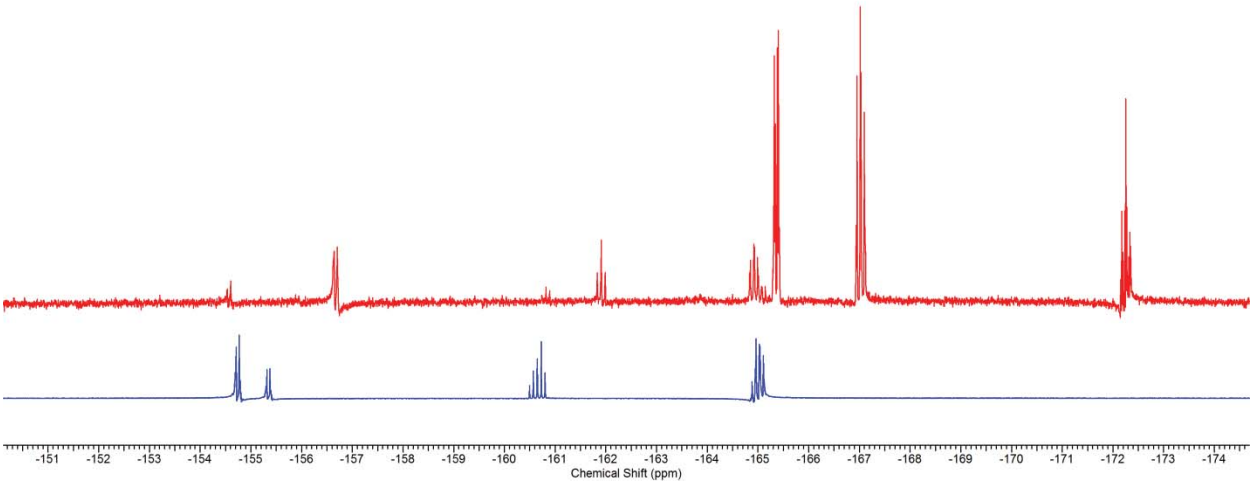


Figure SI12. ^{19}F NMR spectra of a mixture of compounds **2**, **5** and **7** before (blue) and 14h after addition of potassium carbonate (red). Spectra without offset in x-direction.