

Supporting information for Polymeric ligands as homogeneous, reusable catalyst systems for copper assisted click chemistry

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Experimental part:

Materials.

Sodium azide (NaN_3), phenyl acetylene (98%, Aldrich), DMF, diethyl ether, LiBr (99,999%, Aldrich), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (98%, Aldrich), sodium ascorbate (> 99 %, Aldrich), sodium bicarbonate(> 99 %, Acros), ammonium chloride (> 99 %, Acros), tert-BuOH, EtOAc, THF, dioxane and diethoxypropane (**1**, Scheme 1) were used as received. Dibenzyltrithiocarbonate (DBTC) was provided by Arkema®. 4-Chloromethyl styrene (90 %, Aldrich) and styrene (99 %, Aldrich) were distilled under reduced pressure. Azobisisobutyronitrile (AIBN, 98%, Aldrich) was recrystallized from MeOH (2 times) and stored at -4 °C. Cu(I)Br (98%, Aldrich) was purified by stirring with acetic acid, washed with methanol, and finally dried under vacuum at 70 °C. Benzyl azide¹ and poly(ethylene oxide) containing two azide chain ends ($\text{N}_3\text{-PEO-N}_3$)¹, N,N-Bis[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]prop- 2-yn-1-amine (**2**, Scheme 1)² and benzyl trithiocarbonate propionic acid (BTTCPA)³ were synthesized according to literature reports.

Methods of Analysis:

^1H NMR spectra were recorded in CDCl_3 at room temperature on a Bruker AM500 spectrometer at 500 MHz or on a Bruker Avance 300 at 300 MHz.

Size Exclusion Chromatography (SEC) was performed on a Waters instrument, with a refractive-index (RI) detector (2410 Waters), equipped with Waters Styragel HR3, HR4 and HR5 serial columns (5 micron particle size) at 35 °C. Polystyrene standards were used for calibration and CHCl_3 was used as an eluent at a flow rate of 1.5 mL/min. Molecular weight and polydispersity index were determined using the Breeze Millennium software. Infrared spectra were obtained with ReactIR 4000 instrument (Mettler Toledo AutoChem React IRTM) using a silicone probe (SiComp, optical range 4400-650 cm^{-1}). For online measurements, the probe was introduced into a two-necked glass flask and spectra were recorded every 30 seconds for 3 hours. For the experiments using benzyl azide, this compound was added after 2 scans via a syringe to the reaction mixture while stirring. For the polymeric azide-compound , the PEO-azide was first added and phenyl acetylene was added when the azide signal had stabilized. Elemental analyses (EA) were performed by Warwick Analytical Services and all measurements were performed in duplicate. Atomic absorption

analyses (AAS) were performed with a VARIAN spextrAA-140. The samples were prepared as follows: samples were weighed into porcelain crucibles. They were pre-ashed in a muffle furnace at a temperature of 250°C and subsequently ashed during 3 hours at 450°C. The crucible was transferred to a hot plate, 5 ml of 6 M HNO₃ was added and the mixture was evaporated to a low volume. The residue was dissolved in 5 ml of 3 M HNO₃, filtered (S&S, blue ribbon, Schleicher & Schuell, Dassel, Germany) and diluted to 50 ml.

Synthesis of 4-azidomethylstyrene (**3**, Scheme 1)

4-(chloromethyl)styrene (5.0 g, 32.9 mmol) was dissolved in 40 ml DMF and stirred overnight with a 3 equiv. excess of NaN₃ (6.4 g, 98.7 mmol). Water (100 ml) was added and the product was extracted with diethylether (3 x 100 ml). The organic phase was washed with brine (3 x 100 ml) containing a small amount of LiBr to remove the DMF left in the organic phase. The organic phase was dried over MgSO₄ and was subsequently evaporated. The product **3** was isolated as a orange liquid in a 98 % yield.

Synthesis of TBTA-monomer (**4**, Scheme 1)

3 (1.2g, 7.6 mmol) and **2** (2.4 g, 6 mmol) were stirred in 2:1 t-BuOH/H₂O (30 mL). To this suspension, CuSO₄.5H₂O (7.5 mol %) was added, changing the color to deep blue. Finally, sodium ascorbate (30 mol%) was added, turning the solution clear. The reaction was stirred overnight at 40 °C. Ethyl acetate (60 mL) was added and the mixture was washed with NaHCO₃ (sat, 3 x 50 mL) containing a few NH₄Cl crystals, water (50 mL), and brine (2 x 50 mL). The organic layer was dried over MgSO₄ and the solvents removed *in vacuo*. The residue (0.62 g) was purified by column chromatography on silica, first eluting with ethyl acetate/n-hexane 80/20, then 5 % methanol in ethyl acetate/n-hexane mixture. The product was obtained as a off-white solid (0.43 g, 44% overall yield).

¹H NMR (500 MHz, CDCl₃): 7.69 (s, 3H, triazole-H), 7.39-7.19 (m, 14H, Ph-H), 6.68 (q, 1H, Ph-CH=CH₂), 5.75 (d, 1H, Ph-CH=CH₂), 5.49 (s, 4H, Ph-CH₂-triazole), 5.47 (s, 2H, styrene-CH₂-triazole), 5.26 (d, 1H, Ph-CH=CH₂), 3.72 (s, 6H, N-CH₂-triazole). ¹³C NMR (500 MHz, CDCl₃): 144.3 (**Cq**-N-triazole), 138 (**Cq**-N, triazole), 136 (CH-N, triazole), 134.8-134.1 (**Cq**, Ph or Styrene respectively), 129.4-126.9 (CH, Ph or styrene), 123.7 (CH, vinyl), 114.8 (CH₂, vinyl), 54.13 (Ph-CH₂-triazole), 53.8 (styrene-CH₂-triazole), 47.1 (N-CH₂-triazole). IR, ν (cm⁻¹): 3100-3000, 2965-2930, 1643, 1556, 1511, 1495, 1407, 1326, 1219, 1158, 1124, 1049, 1028, 989, 950, 915, 818, 797, 755, 696

Elemental analysis; theoretical %: C 69.04, H 5.79, N 25.16; experimental % C 69.13, H 5.74, N 25.14. ESI-MS: (m/z) 557.5 Da

Polymer catalyst system

A solution of styrene, **4**, RAFT agent, AIBN and solvent was prepared ([RAFT]₀/[AIBN] is (1:0.5) and placed in a 10 mL flask. After six freeze–pump–thaw cycles, the solution was heated under stirring to 85 °C. After 24 h, the reaction was quenched by placing the flask in an ice/water bath under air. The TBTA-containing polystyrene was isolated by a two-fold precipitation into cold methanol.

Cu (I) loading

In a 25 ml flame-dried two-necked round bottomed flask, TBTA-containing polystyrene was dissolved in degassed EtOAc, after which copper (I) bromide (1.05 equiv.) was added, under

a nitrogen flow. The mixture was stirred overnight and subsequently precipitated into degassed n-hexane. The greenish powder was dried under vacuum.

Typical CuAAC reaction

Phenyl acetylene (0.014 ml, 1.5 equiv. to benzyl azide) and Cu complexed TBTA-containing polystyrene (0.05 g, entry 5, Table 1) were dissolved in degassed solvent (2 ml). Addition of benzyl azide (0.01 ml) to the flask started the reaction. The progress of the reaction was monitored by online-FTIR following the decrease of the specific azide absorption at 2100 cm^{-1} .

Reuse of the TBTA-containing polystyrene

The TBTA-containing polystyrene was precipitated (4 times) in degassed n-hexane to remove the product of the click reaction (checked via ^1H NMR spectroscopy). The TBTA-containing polystyrene was washed through the filter with degassed THF. After evaporation of the solvent, the greenish powder was dried *in vacuo*. The polymeric catalyst was reused following the same procedure (same amounts) as described above.

Table S1: Results of the synthesis of linear polymer ligands using RAFT.

Entry	RAFT agent	Equiv. TBTA- monomer	Equiv. S	Equiv. AIBN	Solvent (66 v%)	Time (h)	$M_{n,\text{theo}}^{1)}$ (g/mol)	$M_{n,\text{SEC}}$	M_w/M_n	TBTA/S ²⁾
S1	BTTCPA	10	90	0.3	Benzyl alcohol	24	11300	4800	1.25	9/ 60
S2	BTTCPA	5	90	0.3	n-BuAc	35	6300	6300	1.20	2/50
S3	BTTCPA	5	90	0.3	THF/ DMF	35	6500	3200	1.27	1 to 2 /52

Reactions carried out at 85°C , ¹⁾ determined via a combination of elemental analysis and ^1H NMR analysis,²⁾ determined via elemental analysis.

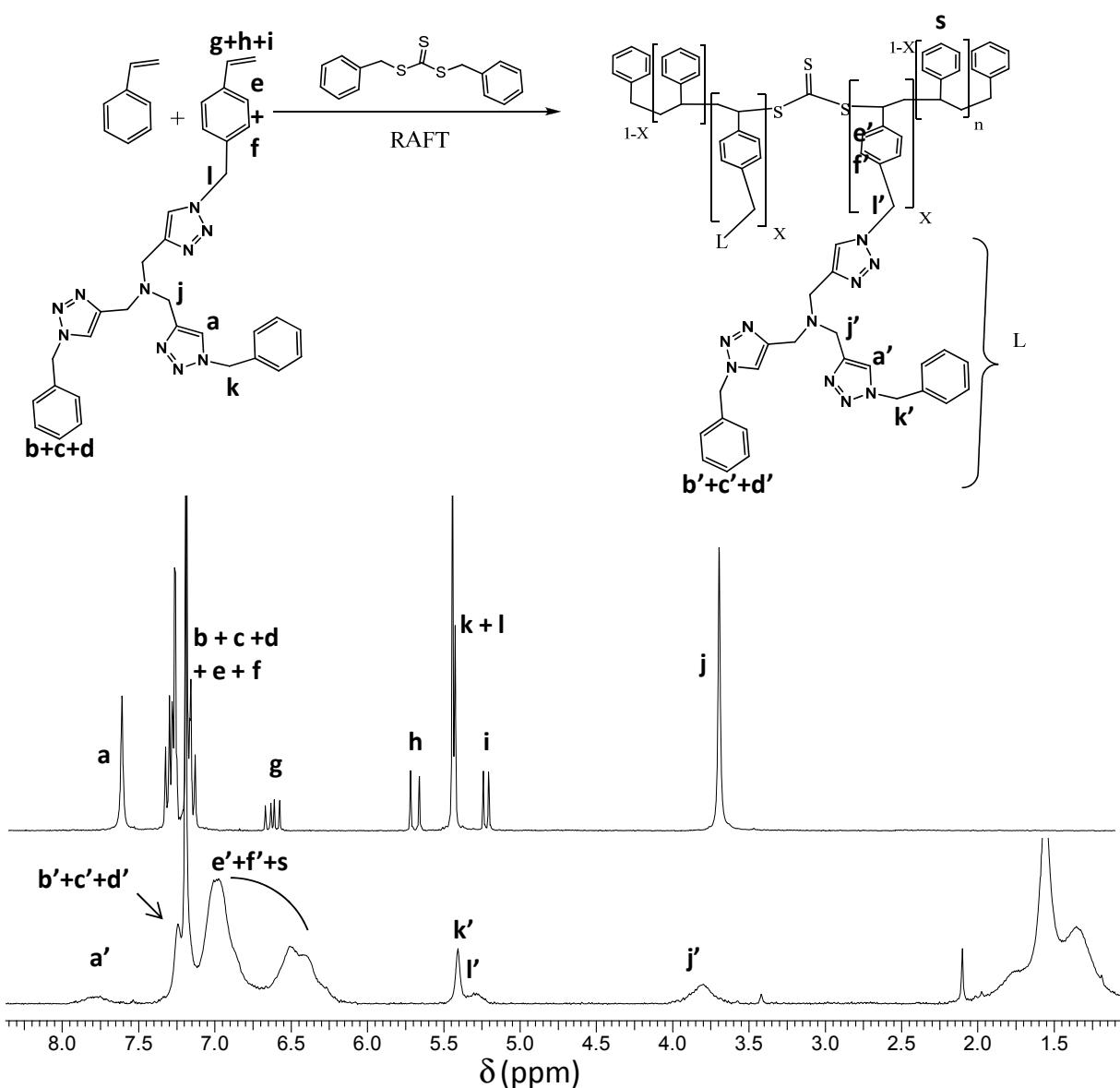


Figure S1. ¹H NMR spectrum of TBTA-monomer (upper) and copolymer based on styrene and TBTA-monomer (lower).

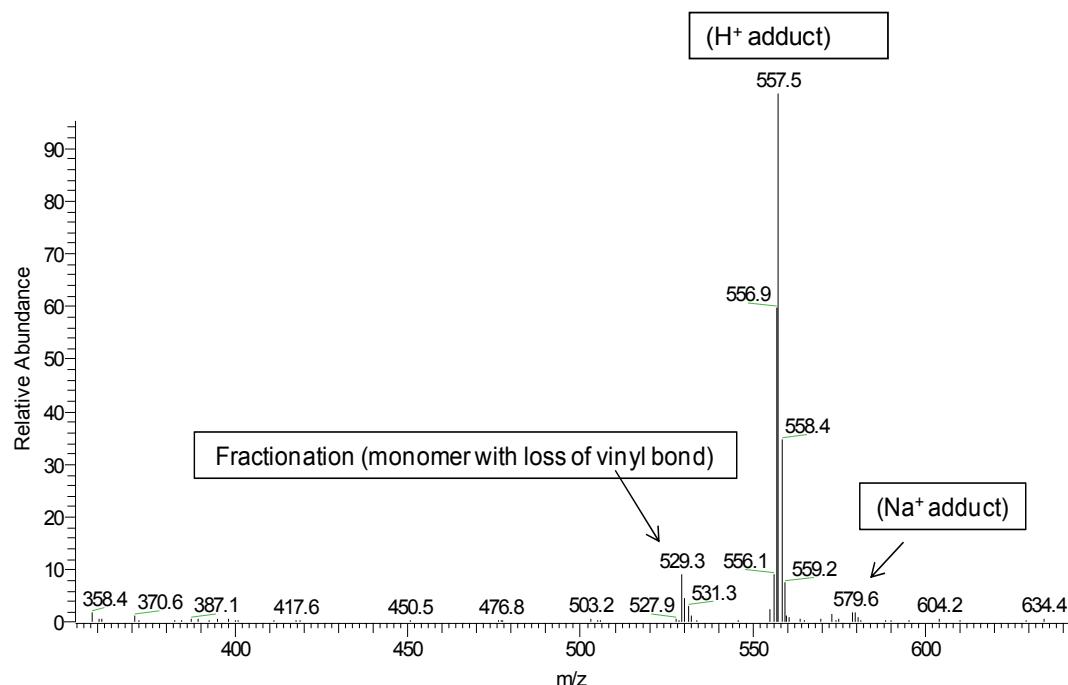


Figure S2. ESI spectrum of the TBTA monomer.

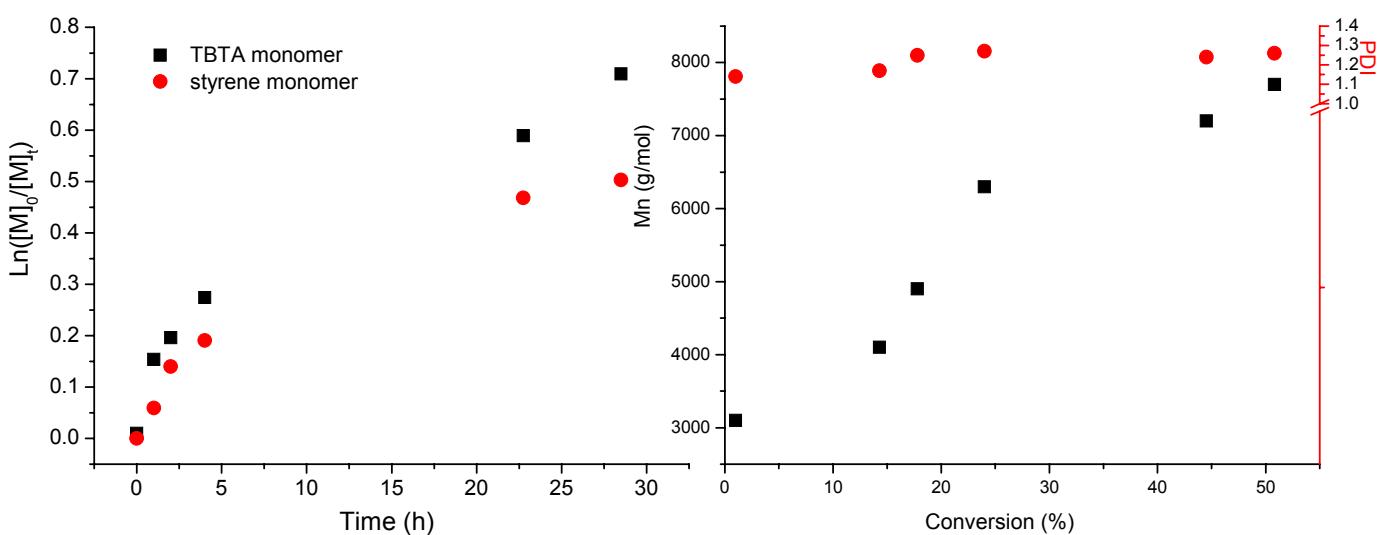


Figure S3. Kinetics of the synthesis of P(TBTA-co-S). First order kinetics (left) and evolution of $M_n(\square)$ and PDI (●) with conversion (right) (SEC DMA, calibrated with PMMA standards) (Entry 5, Table 1).

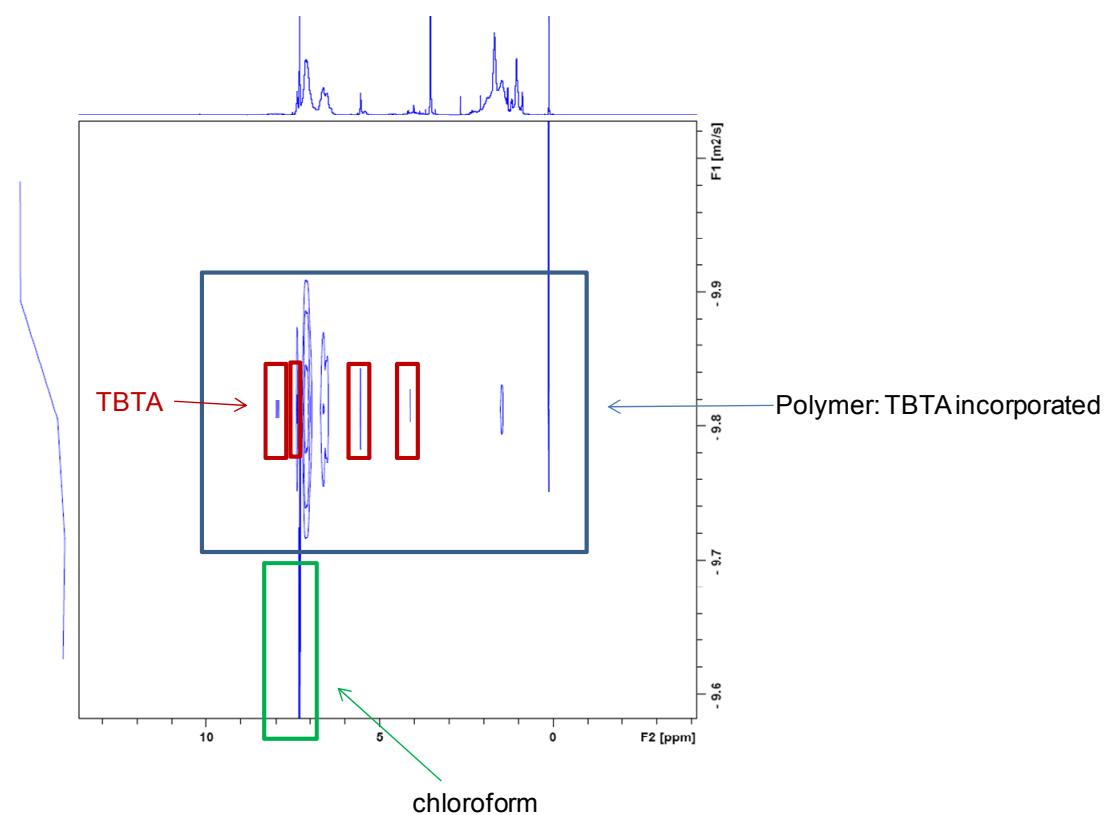


Figure S4. DOSY NMR spectrum of the polymeric ligand P(TBTA-co-S) (500 MHz, CDCl₃).

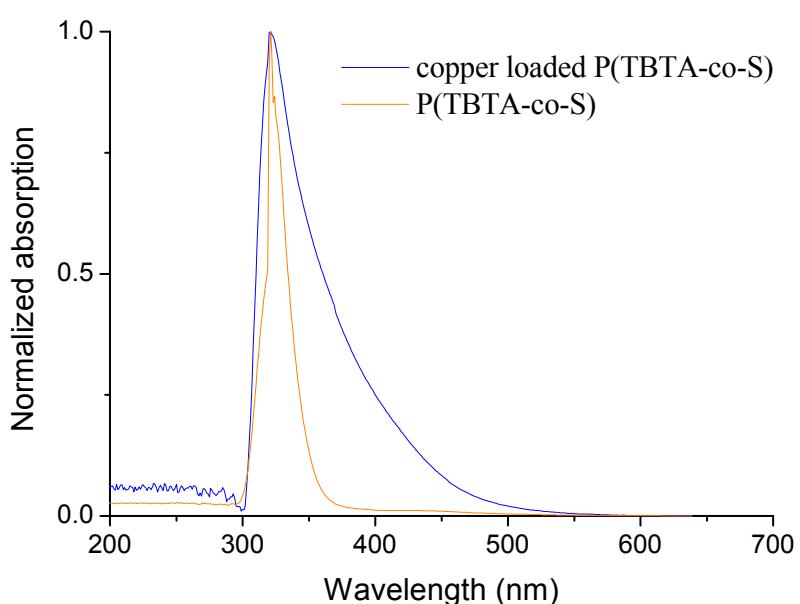


Figure S5. UV spectra of polymeric ligand P(TBTA-co-S) (orange) and copper loaded polymeric ligand P(TBTACu-co-S).

References

1. L. Bonami, W. Van Camp, D. Van Rijckegem and F. E. Du Prez, *Macromol. Rapid Commun.*, 2009, **30**, 34-38.
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