

## Supplementary Information

# RAFT copolymerization of itaconic anhydride and 2-methoxyethyl acrylate: a multifunctional scaffold for preparation of “clickable” gold nanoparticles

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### Materials

<sup>10</sup> 2-Methoxyethyl acrylate (MEA; Aldrich, 98 %) was passed through a short aluminum oxide column (Sigma-Aldrich, activated, basic, Brockmann I, standard grade, ~ 150 mesh, 58 Å) before use. Tetrahydrofuran (THF; Sigma-Aldrich, 99.9 %) and 1,4-dioxane (Sigma-Aldrich, ≥ 99.0 %) were dried over CaH<sub>2</sub>, and distilled under nitrogen flow. Copper (II) sulphate anhydrous (Fluka, ≥ 99.0 %), 2-cyano-2-propyl benzodithioate (CPBdT; Aldrich, > 97 %), gold (III) chloride trihydrate (Sigma-Aldrich, 99.9+ %), itaconic anhydride (IA; Aldrich, 95 %), lithium borohydride (2.0 M solution in THF; Aldrich), propargylamine (Aldrich, 98 %), sodium L-ascorbate (NaAsc; Aldrich, 99+ %), diethyl ether (Sigma-Aldrich, ≥ 99.8 %), *N,N*-dimethylformamide (DMF; Sigma-Aldrich, ≥ 99.9 %), heptane (Sigma-Aldrich, 99 %), methanol (Sigma-Aldrich, 99.9 %), CDCl<sub>3</sub> (Aldrich, 99.8 atom % D), D<sub>2</sub>O (Aldrich, 99.9 atom % D), and MeOH-*d*<sub>4</sub> (Aldrich, 100.0 atom % D) were used as received. 2,2'-Azobis(2-methylpropionitrile) (AIBN; from Ventron) was recrystallized from MeOH. The second generation *N*<sub>α</sub>,*N*<sub>ε</sub>-di-Boc-L-lysine dendron with the azide functional group at the focal point – (di-Boc-L-lys)<sub>G2</sub> – was synthesized according to the previously published three-step synthetic sequence.<sup>1</sup>

### <sup>20</sup> Analytical Techniques

NMR spectroscopy experiments were carried out on a Bruker Avance 300 MHz spectrometer. Chemical shifts are reported in ppm. Number average molecular weights and compositions of the copolymers as well as monomer conversion were determined by <sup>1</sup>H NMR experiments.

<sup>25</sup> Molecular weights and polydispersity indices were estimated by size exclusion chromatography (SEC) employing Viscotek GPCmax VE-2001 equipped with Viscotek TriSEC Model 302 triple detector array (refractive index detector, viscometer detector, and laser light scattering detector with the light wavelength of 670 nm, and measuring angles of 90° and 7°) and a Knauer K-2501 UV detector using two PLgel mixed-D columns from Polymer Laboratories (PL). The samples were run in THF at 30 °C (1 mL·min<sup>-1</sup>). Molecular weights were calculated using polystyrene standards from PL.

<sup>30</sup> ATR FT IR spectra in the range of 4000-350 cm<sup>-1</sup> were recorded on a Nicolet iS50 ATR spectrometer with a diamond crystal from Thermo Scientific.

UV-visible spectra in the range of 800-350 nm were acquired on a PerkinElmer Lambda 25 spectrometer. The samples were prepared by agitating solutions of the gold nanoparticles in deionised water or MeOH (~1.7 mg·mL<sup>-1</sup>) on a digital vortex mixer from VWR.

Thermogravimetric analysis was performed on a TGA Q500 apparatus from TA Instruments. Samples were heated from 20 °C to 800 °C with the heating rate of 20 °C·min<sup>-1</sup> under nitrogen flow.

<sup>35</sup> Transmission electron microscopy images were obtained on an FEI Tecnai T20 microscope operated at 200 kV. The samples were prepared by depositing and evaporating a few drops of the solutions of the gold nanoparticles in deionised water or MeOH (~5 mg·mL<sup>-1</sup>) on copper grids.

### Synthetic Procedures

*All reactions were carried out under nitrogen atmosphere. The glass equipment was dried in the oven at 140 °C before use.*

<sup>40</sup> **I**: A Schlenk tube was charged with MEA (4.0 mL, 31.1 mmol), IA (0.88 g, 7.85 mmol), CPBdT (0.15 g, 0.70 mmol), and AIBN (0.032 g, 0.19 mmol), and three freeze-pump-thaw cycles were performed. Then the tube was immersed in an oil bath at 70 °C, and the reaction was carried out for 6 h and 55 min. During the polymerization, aliquots were withdrawn with a nitrogen-flushed syringe, and analyzed by SEC and NMR spectroscopy. The reaction was quenched by immersing the tube in liquid nitrogen. The product was precipitated twice from THF in Et<sub>2</sub>O-heptane (1:1) mixture. It was then rinsed with heptane, and dried in the vacuum oven at room temperature. Yield: 41 %.

<sup>45</sup> *M*<sub>n</sub>(<sup>1</sup>H NMR) = 6050 Da, DP of IA was 16, DP of MEA was 31; *M*<sub>n</sub>(SEC) = 4100 Da, *M*<sub>w</sub>(SEC) = 5500 Da, *M*<sub>w</sub>/*M*<sub>n</sub> = 1.34. δ<sub>H</sub> (300 MHz; CDCl<sub>3</sub>) 7.90-8.00 (2H, b, *m*, -Ar), 7.48-7.60 (1H, b, *p*, -Ar), 7.33-7.45 (2H, b, *o*, -Ar), 3.95-4.45 (62H, b, CHC(O)OCH<sub>2</sub>), 3.45-3.75 (62H, b, CH<sub>3</sub>OCH<sub>2</sub>), 3.23-3.45 (93H, b, CH<sub>3</sub>O), 2.69-3.21 (32H, b, CCH<sub>2</sub>C(O)O), 2.05-2.69 (b, CH<sub>2</sub>CHC(O)O) and

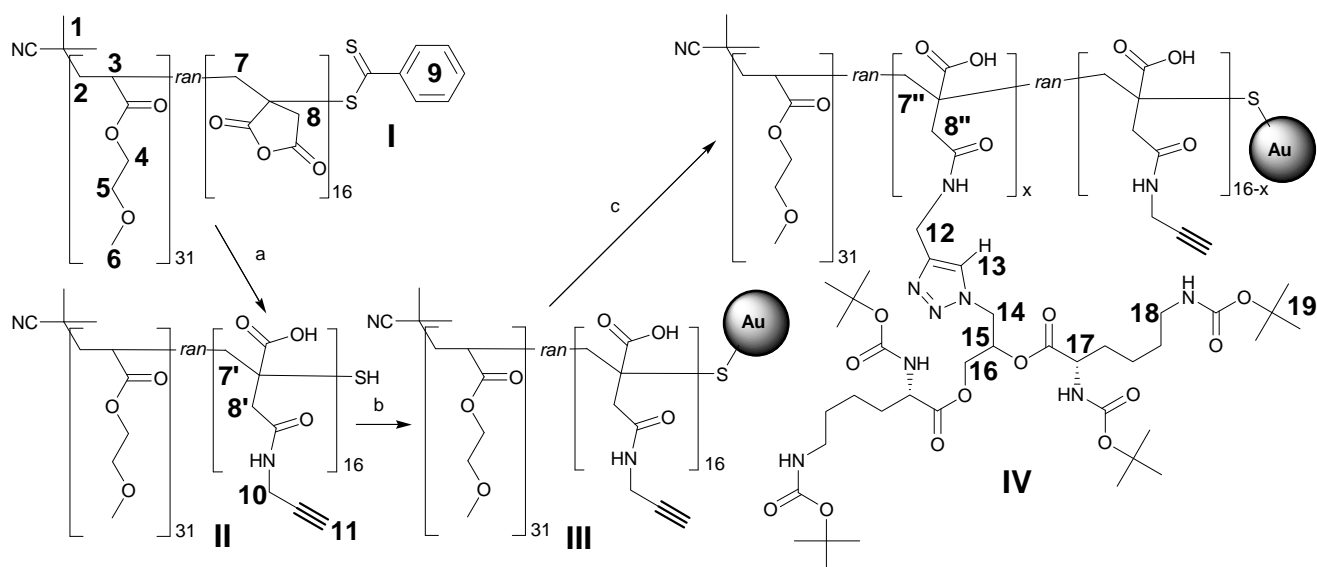
<sup>1</sup> I. Javakhishvili, W. H. Binder, S. Tanner and S. Hvilsted, *Polym. Chem.*, 2010, **1**, 506.

$CH_2CC(O)O$ , 1.20-2.05 (b,  $CH_2CHC(O)O$  and  $(CH_3)_2CCN$ ) (1.20-2.69 corresponds to 131 H).

**II:** A 50 mL round-bottom flask equipped with a stirring bar and a reflux condenser was charged with **I** (1.2 g, 3.2 mmol of the anhydride functional groups), THF (25 mL), and propargylamine (0.22 mL, 3.4 mmol). The reaction was carried out at 75 °C for 24 h. The product was isolated by precipitation in heptane. It was then precipitated from 1,4-dioxane-MeOH mixture in Et<sub>2</sub>O-heptane (1:5) mixture twice, and dried in the vacuum oven at room temperature. Yield: 76 %.  $M_n(^1H\ NMR) = 6930\ Da$ ,  $M_n(SEC) = 4100\ Da$ ,  $M_w(SEC) = 5700\ Da$ ,  $M_w/M_n = 1.40$ .  $\delta_H$  (300 MHz; CDCl<sub>3</sub>) 3.77-4.60 (94H, b,  $CHC(O)OCH_2$  and  $CH\equiv CCH_2NHC(O)$ ), 3.47-3.75 (62H, b,  $CH_3OCH_2$ ), 3.21-3.47 (93H, b,  $CH_3O$ ), 1.10-3.00 (b,  $CCH_2C(O)NH$ ,  $CH_2CHC(O)O$ ,  $CH\equiv CCH_2NHC(O)$ ,  $CH_2CHC(O)O$ ,  $CH_2CCOOH$ , and  $(CH_3)_2CCN$ ) (1.10-3.00 corresponds to 179 H).

**III:** A 50 mL two-neck round-bottom flask was charged with **II** (0.29 g, 0.04 mmol), gold (III) chloride trihydrate (0.037 g, 0.09 mmol), THF (10 mL) and DMF (5 mL). The resulting clear yellow solution was stirred at room temperature in the dark overnight. Afterward, freshly prepared 0.25 M solution of LiBH<sub>4</sub> in THF (5.5 mL, 1.4 mmol) was added in small aliquots. Vigorous gas evolution was observed. The reaction then proceeded in the dark for 2.5 h. The polymer protected gold nanoparticles were isolated by precipitation in Et<sub>2</sub>O-heptane (1:1) mixture, washed with heptane, and dried in the vacuum oven at room temperature.

**IV:** A 25 mL two-neck round-bottom flask was charged with gold nanoparticles (0.121 g, 0.20 mmol alkyne functional groups (residual solvent and gold content has been taken into consideration)), (di-Boc-L-lys)<sub>G2</sub> (0.081 g, 0.10 mmol), THF (6 mL), and deionised water (5 mL). The flask was cooled on ice/water bath, and the solutions of CuSO<sub>4</sub> (0.026 g, 0.16 mmol) in deionised water (0.2 mL) and of NaAsc (0.118 g, 0.60 mmol) in deionised water (0.7 mL) were injected. The reaction mixture was stirred in the ice/water bath for 30 min, and then at 30 °C for 44 h. Afterward, the solvent mixture was decanted, and the solid was precipitated from THF-MeOH (2:1) mixture in Et<sub>2</sub>O-heptane (1:2) mixture twice. It was dried in the vacuum oven at room temperature.



**Scheme S1** Synthetic layout for preparation of the AuNPs protected with dendronized linear copolymers. *Reagents and conditions:* (a) propargylamine, 75 °C, THF; (b) H<sub>2</sub>AuCl<sub>4</sub>·3H<sub>2</sub>O, LiBH<sub>4</sub>, THF-DMF; (c) (di-Boc-L-lys)<sub>G2</sub>, CuSO<sub>4</sub>, NaAsc, 30 °C, THF-H<sub>2</sub>O

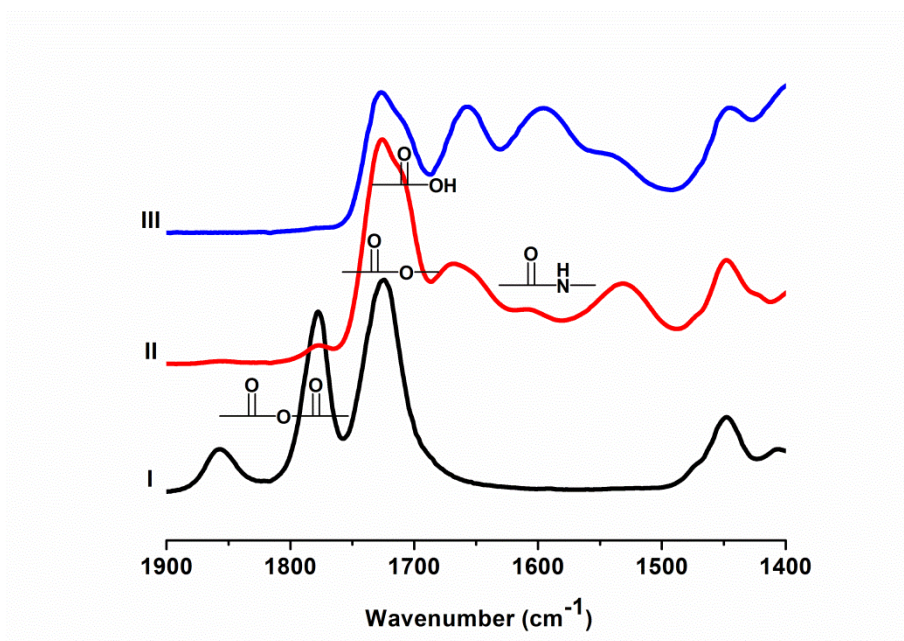


Fig. S1 Overlay of the FT IR spectra of the copolymers I and II, and the AuNPs III

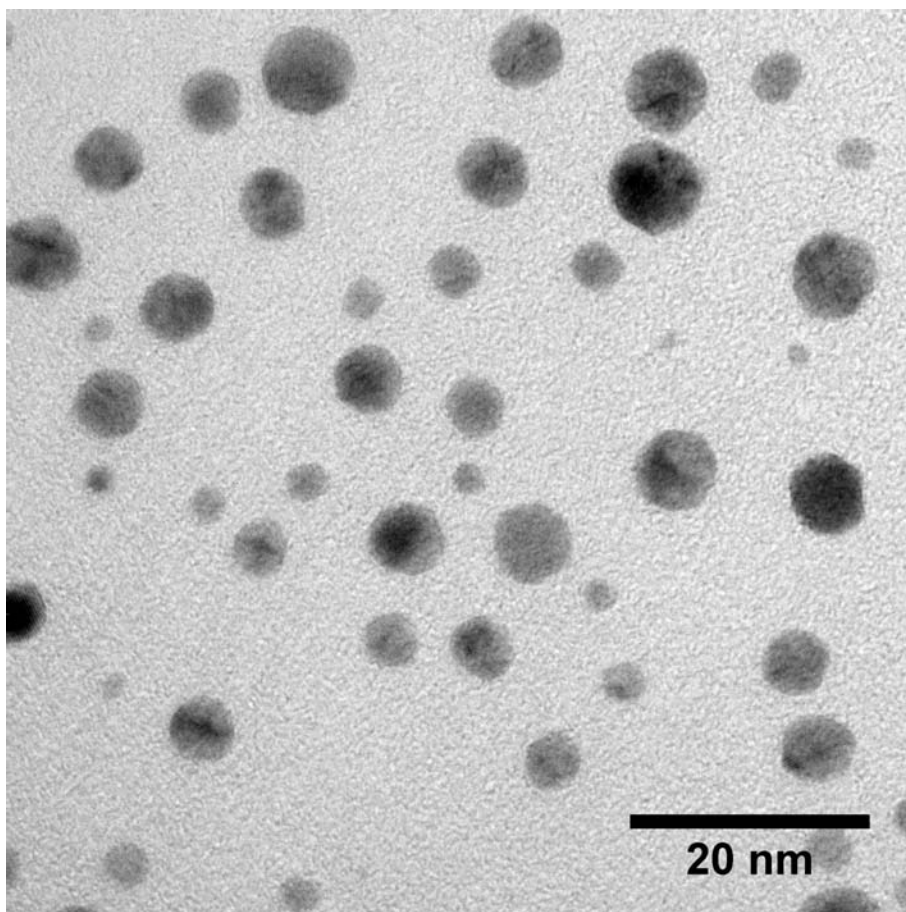


Fig. S2 TEM micrograph of the AuNPs prepared in THF-MeOH mixture

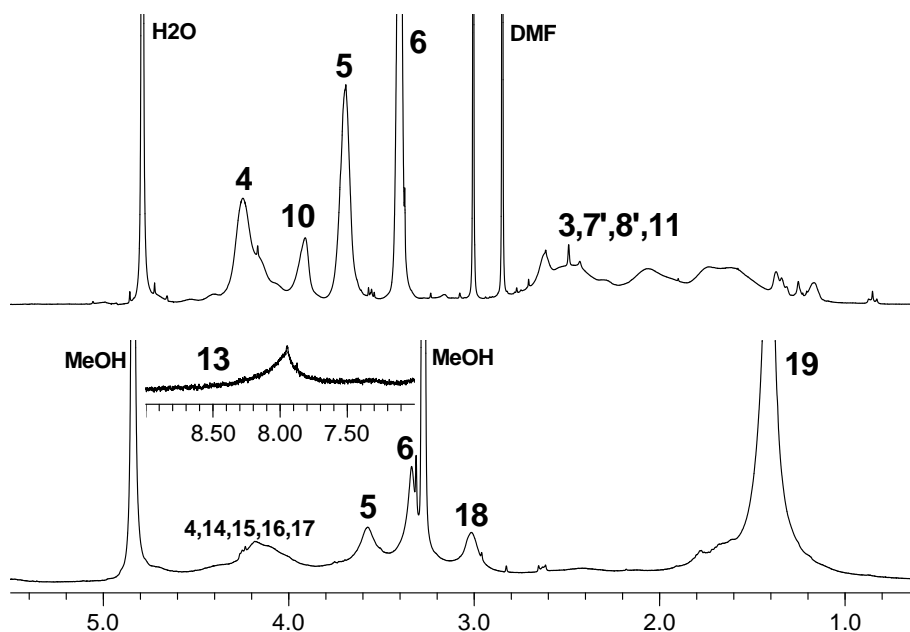


Fig. S3 Overlay of the <sup>1</sup>H NMR spectra of the AuNPs III (top, D<sub>2</sub>O) and IV (bottom, MeOH-*d*<sub>4</sub>)

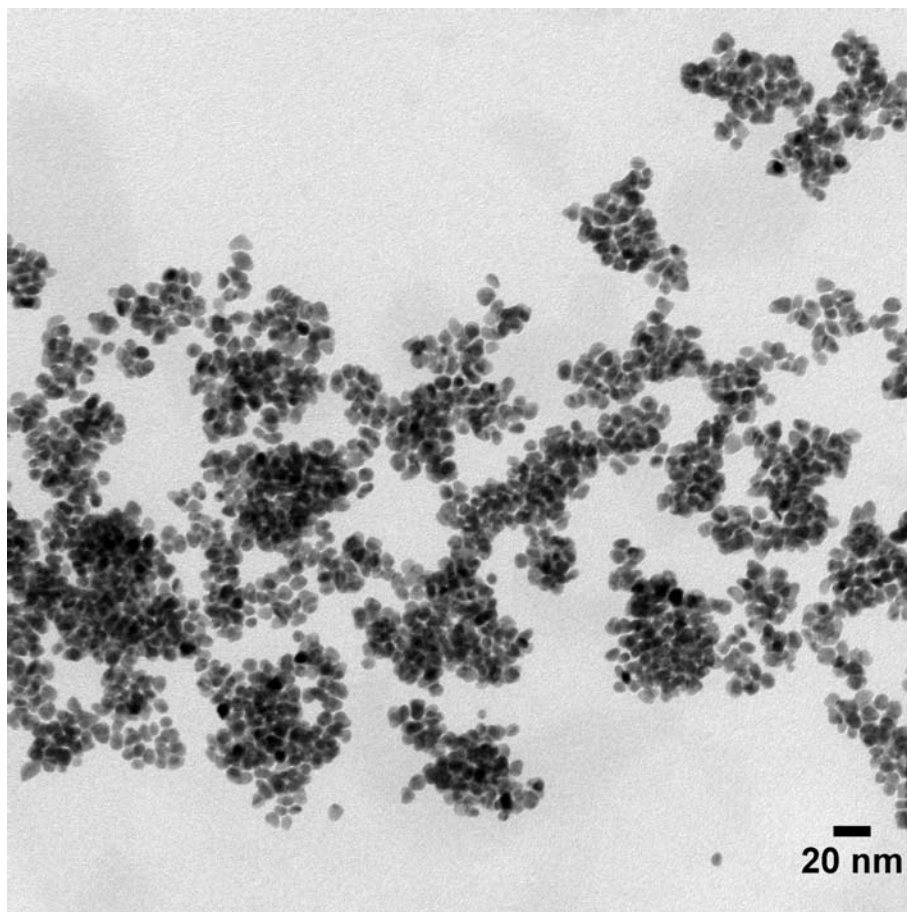


Fig. S4 TEM micrograph of the AuNPs III

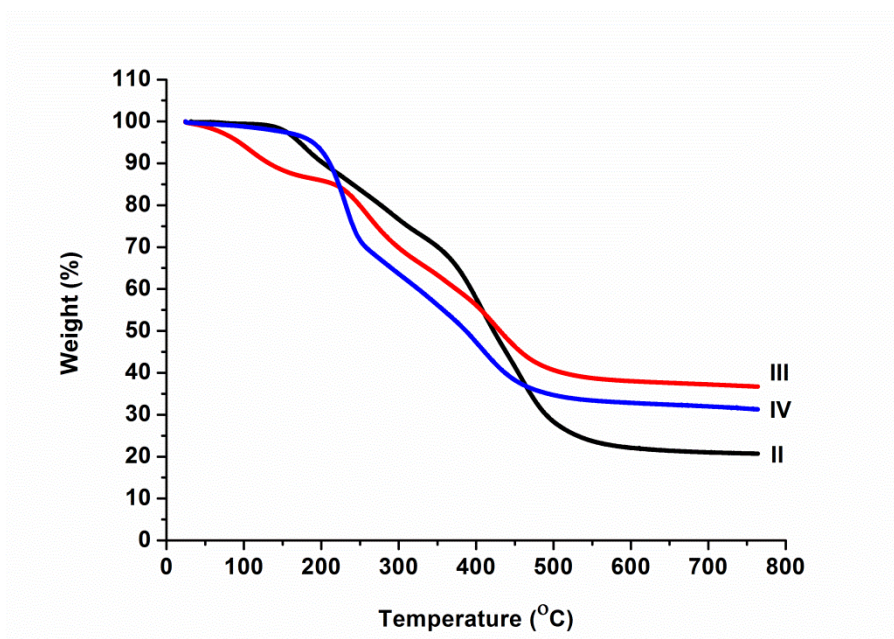


Fig. S5 Overlay of the TGA thermograms of the copolymer **II**, and the AuNPs **III** and **IV**

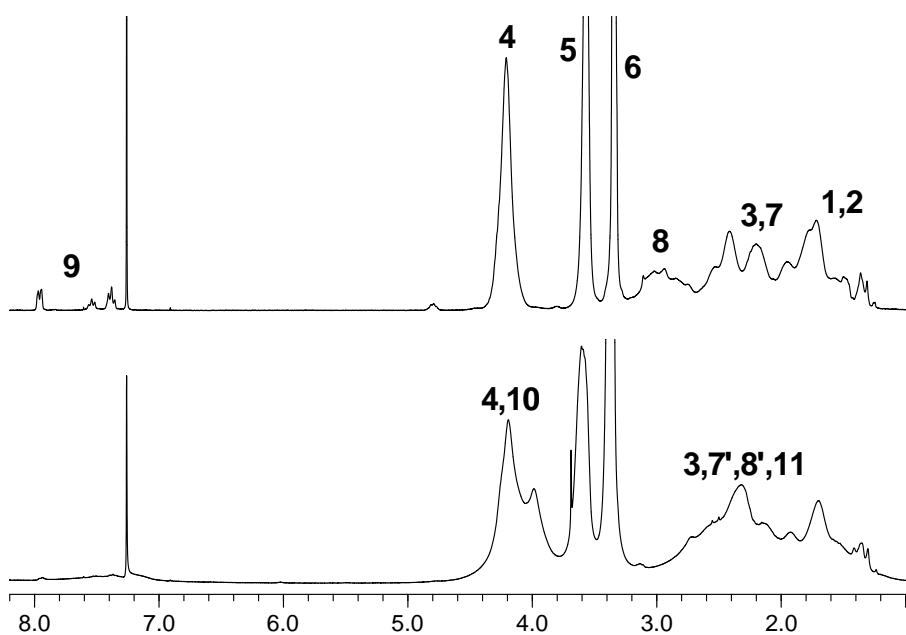


Fig. S6 Overlay of the  $^1\text{H}$  NMR spectra of the copolymers **I** (top) and **II** (bottom) acquired in  $\text{CDCl}_3$

Table S1 Surface coverage parameters of the AuNPs **III**<sup>2</sup>

Entry	Particle Surface Area <sup>a</sup> (nm <sup>2</sup> )	Particle Volume <sup>a</sup> (nm <sup>3</sup> )	Number of Gold Atoms <sup>b</sup>	Number of Chains per Particle	Chain Density (chains/nm <sup>2</sup> )	Chain Footprint (nm <sup>2</sup> /chains)
AuNPs <b>III</b>	238	345	20400	3000	13	0.08

<sup>a</sup> Assuming spherical clusters; <sup>b</sup> face centered cubic lattice verified by the diffraction pattern.

After the “click” reaction, number of dendrons per particle in AuNPs **IV** is approximately 2200.

<sup>2</sup> T. Azzam and A. Eisenberg, *Langmuir*, 2007, **23**, 2126.