Supplementary Material (ESI) for Chemical Communications

One-pot Tandem Living Radical Polymerisation/Huisgens Cycloaddition Process ("Click") Catalysed by N-alkyl-2-pyridylmethanimine/Cu(I)Br Complexes.

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1.0 General

1.1 Reagents

Copper(I) bromide (Aldrich, 98 %) was purified according to the method of Keller and Wycoff.[1] The *N*-(ethyl)-2-pyridylmethanimine and *N*-(*n*-propyl)-2-pyridylmethanimine ligands were prepared as described earlier[2] and stored at 0 ºC under a dinitrogen atmosphere. 1-Octyl azide was prepared following the procedure described by Alvarez and co-workers.[3] Triethylamine (Fischer, 99 %) was stored over sodium hydroxide pellets. A solution of Polyethylene glycol (M_n~400, PEG_{400}) in toluene was refluxed for 18 h in a round-bottom flask equipped with a Dean-Stark trap for azeotropic removal of water. Toluene was then evaporated under reduced pressure and the PEG_{400} was stored at room temperature under a dinitrogen atmosphere. All other reagents and solvents were obtained at the highest purity available from Aldrich Chemical Company and used without further purification unless stated.

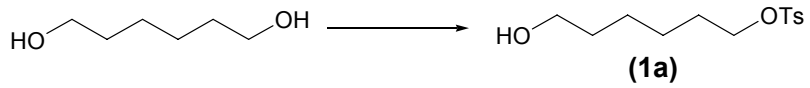
1.2 Analysis

All reactions were carried out using standard Schlenk techniques under an inert atmosphere of oxygen-free nitrogen, unless otherwise stated. R_f values refer to analytical TLC performed using pre-coated silica gel 60 F254 and developed in the solvent system indicated. Compounds were visualized by use of UV light (254 nm) or a basic solution (10 % w/w K_2CO_3 in water) of $KMnO_4$. Merck 60 (230-400 mesh) silica gel was used for column chromatography. Molar mass distributions were

measured using size exclusion chromatography (SEC), on a system equipped with two PL gel 5 mm mixed C-columns (300 x 7.5 mm) and one PL gel 5 mm guard column (50 x 7.5 mm) (Polymer Laboratories) with differential refractive index detection using THF/triethylamine 95:5 at 1.0 mL min^{-1} as the eluent. Poly(MMA) standards ($1.5 \cdot 10^6$-200 g mol^{-1}) were used to calibrate the SEC. The analyzed samples contained (0.2 % vol) toluene as the flow marker. The M_n reported in the M_n vs Conversion (%) plots are obtained from SEC data calibrated with PMMA standards. NMR spectra were obtained on a Bruker DPX300 and Bruker DPX400 spectrometer. All chemical shifts are reported in ppm (δ) relative to tetramethylsilane, referenced to the chemical shifts of residual solvent resonances (^1H and ^{13}C). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, bs = broad singlet, m = multiplet. The molecular weight of the polymers The conversions were calculated via ^1H NMR by following the decreasing of the integrals of the monomer vinyl signals (5.6 and 6.2 ppm), using the peak of mesitylene (6.9 ppm) as internal standard. Alternatively, the conversions can be calculated by comparison between the integrals of the OCH_3 peaks of the polymer and the monomer (ca. 3.8 and 3.9 respectively). Infrared absorption spectra were recorded on a Bruker VECTOR-22 FTIR spectrometer using a Golden Gate diamond attenuated total reflection cell. Mass spectra were recorded using a Micromass Autospec apparatus. The melting points were measured on a Büchi 510 apparatus using open glass capillaries, the data are uncorrected. The yields are not optimized.

2.0 Synthesis of initiators, intermediates and dyes

Toluene-4-sulfonic acid 6-hydroxy-hexyl ester (1a)

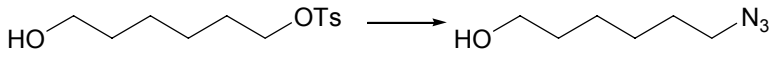


(1a)

1,6-hexanediol (59.0 g, 499 mmol) was dissolved in pyridine (250 mL) and the solution was cooled down to 0 ^{o}C. *p*-Toluene-sulfonyl chloride (19.1 g, 100 mmol) was then added in small portions and the mixture was stirred overnight at ambient temperature. The solvent was then removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (300 mL), washed with 0.1 M aqueous HCl (100 mL) and water (2 x 100 mL). The organic layer was dried over $MgSO_4$ and filtrated. The crude residue obtained after removal of the solvent was purified by flash chromatography (CC, SiO_2, Petroleum ether/Et_2O 2:1) to give **(1a)** (19.1 g, 70 %) as colourless oil.

IR (neat): $\tilde{\nu}$ = 3407 (broad, OH), 2934, 2861, 1598, 1461, 1355, 1188, 1175, 1096, 1056, 924, 814, 664, 552, 521 cm^{-1}; ^{1}H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 1.31-1.33 (m, 4H, CH_2), 1.49-1.53 (m, 2H, CH_2), 1.63-1.67 (m, 2H, CH_2), 2.44 (s, 3H, CH_3), 3.59 (t, *J* = 6.5 Hz, 2H, C*H*$_2$OH), 4.02 (t, *J* = 6.5 Hz, 2H, CH_2OTs), 7.33 (d, *J* = 8.2 Hz, 2H, CH), 7.77 (d, *J* = 8.2 Hz, 2H, CH); ^{13}C{^{1}H} NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 21.75 (1C, CH_3), 25.21 (1C, CH_2), 25.27 (1C, CH_2), 28.90 (1C, CH_2), 32.55 (1C, CH_2), 62.77 (1C, CH_2OH), 70.64 (1C, CH_2OTs); 127.99 (2C, CH), 129.95 (2C, CH), 133.30 (1C, C), 144.82 (1C, C). Anal. Calcd. for $C_{13}H_{20}O_4S$: C, 57.33; H, 7.40; Found C, 56.72; H, 7.70.

6-Azido-hexan-1-ol (2a)

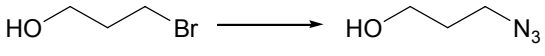


(1a) **(2a)**

(1a) (5.00 g, 18.4 mmol) and sodium azide (1.96 g, 30.1 mol) were dissolved in a mixture of acetone (60 mL) and water (10 mL) and the resulting solution was refluxed overnight. Most of the acetone was then removed under reduced pressure, 50 mL of water were added and the mixture was extracted with diethyl ether (3 x 50 mL). The organic layers, collected, were dried over $MgSO_4$ and, after removal of the solvent under reduced pressure, **(2a)** was isolated as colourless oil (2.40 g, 16.8 mmol, 89 %).

IR (neat): $\tilde{\nu}$ = 3325 (broad, OH), 2934, 2861, 2093, 1455, 1349, 1261, 1055, 799, 730, 549, 527, 508 cm^{-1}; ^1H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 1.39-1.41 (m, 4H, CH_2), 1.56 (m, 4H, CH_2), 3.26 (t, *J* = 6.9 Hz, 2H, CH_2N_3), 3.64 (t, *J* = 6.5 Hz, 2H, CH_2OH); $^{13}C\{^1H\}$ NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 25.46 (1C, CH_2), 26.65 (1C, CH_2), 28.94 (1C, CH_2), 32.68 (1C, CH_2), 51.51 (1C, CH_2N_3), 62.90 (1C, CH_2OH); Anal. Calcd. for $C_6H_{13}N_3O$: C, 50.33; H, 9.15; N, 29.35; Found C, 49.75; H, 9.08; N, 29.01.

3-Azido-propan-1-ol (2b)



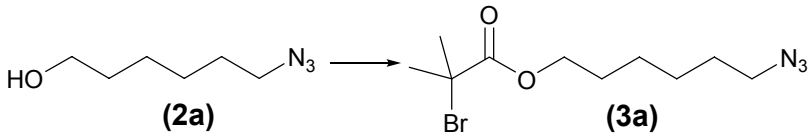
(2b)

The procedure was identical to the one used for the synthesis of **(2a)**. Yield 73 % (colourless oil).

IR (neat): $\tilde{\nu}$ = 3331 (broad, OH), 2954, 2882, 2094, 1455, 1344, 1260, 1048, 956, 901, 633, 543, 531, 508 cm^{-1}; ^1H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 1.77 (app.

quint., J = 6.3 Hz, 2H, $CH_2CH_2CH_2$), 3.39 (t, 2H, J = 6.6 Hz, CH_2N_3), 3.68 (t, J = 6.0 Hz, 2H, CH_2OH); $^{13}C\{^1H\}$ NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 31.43 (1C, $CH_2CH_2CH_2$), 48.39 (1C, CH_2N), 59.61 (1C, CH_2OH). Anal. Calcd. for $C_3H_7N_3O$: C, 35.64; H, 6.98; N, 41.56; Found C, 35.11; H, 7.04; N, 39.74.

2-Bromo-2-methyl-propionic acid 6-azido-hexyl ester (3a)



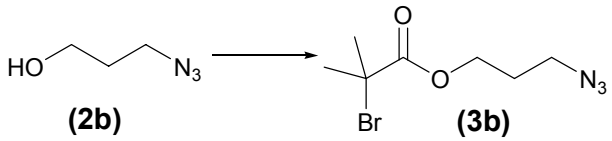
(2a) **(3a)**

A solution of **(2)** (2.40 g, 16.76 mmol) and triethylamine (2.60 mL, 18.4 mol) in Et_2O (50 mL) was cooled to 0 °C and 2-bromo-2-methyl propionyl bromide (2.28 mL, 18.4 mmol) was added slowly via syringe (in ca. 1 min). After stirring 1 h at 0 °C and overnight at room temperature the resulting white suspension was filtered and the pale yellow solution was washed with saturated $NaHCO_3$ aqueous solution (2 x 100 mL) and dried with $MgSO_4$. After filtration the solvent was removed under reduced pressure and the yellow oily residue was purified by flash chromatography (CC, SiO_2, Petroleum ether / Et_2O 20:1) to give **(3a)** (4.26 g, 14.6 mmol, yield: 87 %) as colourless oil.

IR (neat): $\tilde{\nu}$ = 2936, 2862, 2093, 1733, 1463, 1389, 1371, 1275, 1162, 1108, 1011 cm^{-1}; ^1H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 1.40-1.44 (m, 4H, CH_2), 1.60-1.63 (m, 4H, CH_2), 1.93 (s, 6H, CH_3); 3.27 (t, J = 6.9 Hz, 2H, CH_2N_3), 4.17 (t, J = 6.6 Hz, 2H, CH_2O); $^{13}C\{^1H\}$ NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 25.45 (1C, CH_2), 26.33 (1C, CH_2), 28.25 (1C, CH_2), 28.75 (1C, CH_2); 30.78 (2C, CH_3), 51.33 (1C, CH_2N_3),

56.00 (1C, Br*C*$(CH_3)_2$); 65.84 (1C, CH_2O); 171.67 (1C, CO_{ester}); Anal. Calcd. for $C_{10}H_{18}BrN_3O_2$: C, 41.11; H, 6.21; N, 14.38; Found C, 41.17; H, 6.28; N, 14.51.

2-Bromo-2-methyl-propionic acid 3-azido-propyl ester (3b)

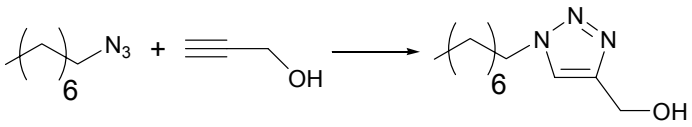


(2b) **(3b)**

The procedure was identical to the one used for the synthesis of **(3a)**. The yellow oily crude residue was purified by flash chromatography (CC, SiO_2, Petroleum ether / Et_2O 20:1 , R_f 0.15) to give **(3b)** as colourless oil in 70 % yield.

IR (neat): $\tilde{\nu}$ = 2972, 2932, 2098, 1735, 1462, 1273, 1162, 1108 cm^{-1}; ^1H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 1.93 (s, 6H, CH_3); 1.96 (app. quint., *J* = 6.4 Hz, 2H, $CH_2CH_2CH_2$), 3.44 (t, 2H, *J* = 6.6 Hz, CH_2N_3), 4.27 (t, *J* = 6.2 Hz, 2H, CH_2OH); $^{13}C\{^1H\}$ NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 28.08 (1C, $CH_2CH_2CH_2$), 30.81 (2C, CH_3); 48.14 (1C, CH_2N), 55.78 (1C, *C*Br$(CH_3)_2$); 62.84 (1C, CH_2O), 171.63 (1C, CO_{ester}).

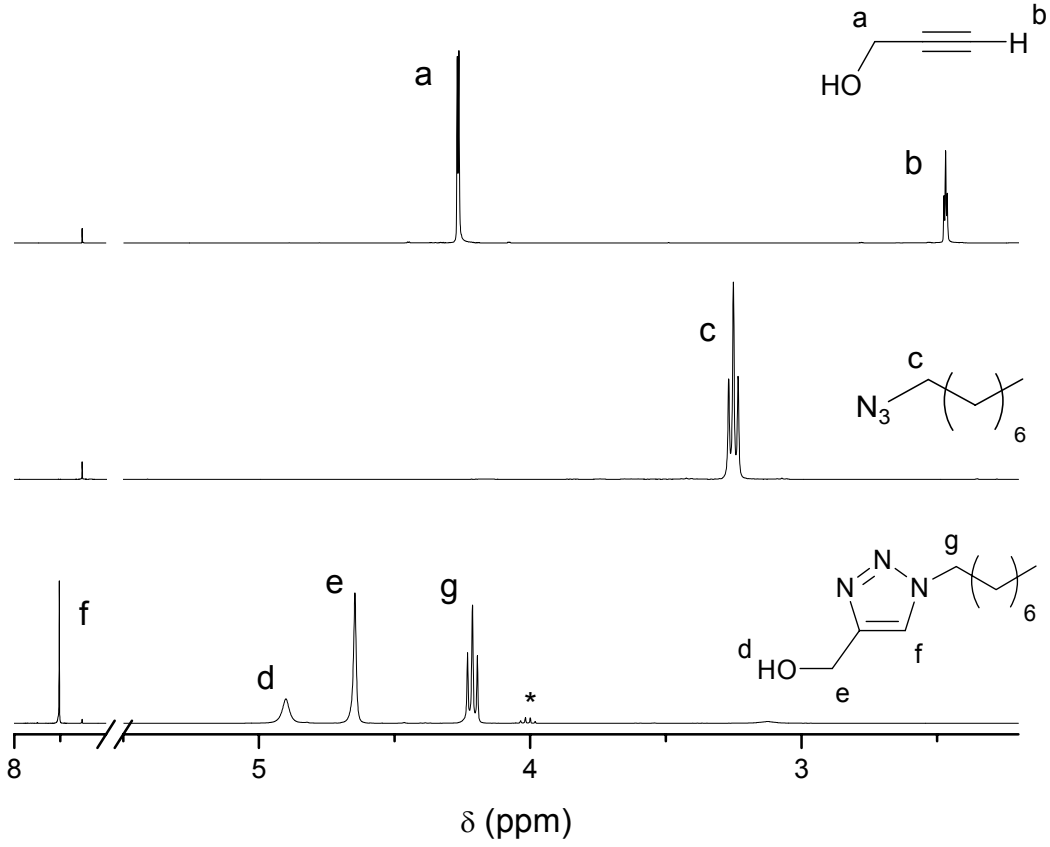
(1-Octyl-1H-[1,2,3]triazol-4-yl)-methanol



1-Octyl azide (0.848 g, 5.46 mmol), propargyl alcohol (0.280 mL, 5.46 mmol), *N*-(ethyl)-2-pyridylmethanimine ligand (0.150 mL, 1.09 mmol) and toluene (5 mL) were subjected to five freeze-thaw cycles and the resulting pale yellow solution was cannulated into a schlenk tube, previously evacuated and filled with nitrogen,

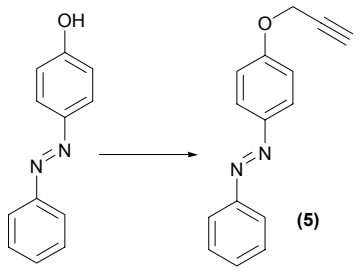
containing Cu(I)Br (0.074 g, 0.52 mmol) and Cu(II)Br_2 (0.006 g, 0.03 mmol). The resulting brown mixture was heated up to 70 ^{o}C and the reaction was monitored by ^{1}H NMR analysis on aliquots taken at regular intervals of time. After 50 min the reaction was found to be finished. An analytical sample was obtained by purification of the brown crude by flash chromatography (CC, SiO_2, 100 % ethyl acetate) to give the expected (1-Octyl-1H-[1,2,3]triazol-4-yl)-methanol product as off-white solid.

m.p. 53-53 °C. IR (neat): $\tilde{\nu}$ = 3310, 2956, 2920, 2848, 1462, 1378, 1336, 1211, 1146, 1039, 1015, 844, 784, 753, 727; cm^{-1}; ^{1}H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 0.77 (t, *J* = 6.8 Hz, 3H, CH_3), 1.15-1.21 (m, 10H, CH_2), 1.78 (app. quint., *J* = 7.2 Hz, 2H, C*H*$_2$$CH_2N$), 4.21 (t, *J* = 7.2 Hz, 2H, CH_2C*H*$_2$N), 4.65 (s, 2H, C*H*$_2$OH), 4.90 (s, 1H, CH_2O*H*), 7.51 (s, 1H, CH); ^{13}C{^{1}H} NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 13.92 (1C, CH_3), 22.45 (1C, CH_2), 26.34 (1C, CH_2), 28.83 (1C, CH_2), 28.91 (1C, CH_2), 30.13 (1C, CH_2), 31.57 (1C, CH_2), 50.24 (1C, CH_2N), 55.73 50.24 (1C, CH_2OH), 121.79 (1C, CH), 147.91 (1C, C).



S1. "Clicking" of 1-octyl azide and propargyl alcohol: partial ^{1}H NMR spectra of the reactants and the "clicked" triazole product. *: traces of ethyl acetate.

Phenyl-(4-prop-2-ynyloxy-phenyl)-diazene (6)

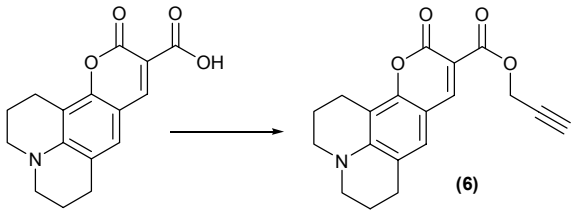


4-Phenylazophenol (3.00 g, 15.13 mmol) was dissolved in dry DMF (70 mL) and the resulting orange solution was cooled down to 0 ^{o}C. NaH (60 % w/w, 0.636 g, 15.9 mmol) was added in small portions, under nitrogen. After 30 min the formation of an

orange insoluble salts was observed and propargyl bromide (80 % w/w solution in toluene, 2.0 mL, 18 mmol) was added via syringe. The mixture was then allowed to reach room temperature and after 1 h a limpid dark-orange solution was observed. After 3 hours the solution was poured in 400 mL of water, the cloudy orange mixture was extracted with Et_2O/CH_2Cl_2 (4:1 v/v, 2 x 200 mL) and the organic layers, combined, were washed with brine (2 x 100 mL) and dried over $MgSO_4$. Removal of the solvent under reduced pressure gave 2.96 g (12.5 mmol, 83 %) of **(5)** as a dark-orange solid that could be used for the next step without further purifications. An analytical sample was obtained by crystallisation from CH_2Cl_2 / petroleum ether.

m.p. 91-92 °C; IR (neat): $\tilde{\nu}$ = 3266, 1601, 1583, 1498, 1454, 1415, 1374, 1299, 1234, 1143, 1070, 1015, 978, 909, 830, 766, 715 cm^{-1}; ^1H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 2.57 (t, *J* = 2.3 Hz, 1H, C≡CH), 4.78 (d, *J* = 2.3 Hz, 2H, CH_2O), 7.09-7.12 (m, 2H, CH); 7.43-7.53 (m, 3H, CH); 7.88-7.97 (m, 4H, CH); $^{13}C\{^1H\}$ NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 56.14 (1C, CH_2O), 76.13 (1C, CH, C≡*C*H), 78.18 (1C, C, *C*≡CH), 115.29 (2C, CH), 122.75 (2C, CH), 124.79 (2C, CH), 129.16 (2C, CH), 130.64 (1C, CH), 147.66 (1C, C), 152.85 (1C, C), 159.97 (1C, C); Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86; : C, 41.11; H, 6.21; N, 14.38; Found C, 76.05; H, 5.17; N, 11.87.

10-Oxo-2,3,5,6-tetrahydro-1H,4H,10H-11-oxa-3a-aza-benzo[de]anthracene-9-carboxylic acid prop-2-ynyl ester (Coumarin 343 propargyl ester) (7)



Coumarin 343 (0.150 g, 0.526 mmol), propargyl alcohol (0.150 mL, 2.63 mmol) and EDC·HCl (0.300 g, 1.58) were dissolved in CH_2Cl_2 (20 mL). DMAP (0.006 g, 0.05 mmol) was then added and the solution was stirred overnight at ambient temperature. The resulting orange solution was washed with 20 mL of saturated aqueous $NaHCO_3$ then with water (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The organic layers, combined, were dried over $MgSO_4$. After filtration the solvent was removed under reduced pressure to give an orange residue that was purified by flash chromatography (CC, SiO_2, 100 % Et_2O). **(6)** was isolated as a yellow solid (0.110 g, 65 %).

m.p. 143-145 °C; IR (neat): $\tilde{\nu}$ = 3262, 2924, 1711, 1682, 1621, 1582, 1561, 1517, 1440, 1363, 1308, 1238, 1205, 1175, 1113, 979, 927, 904, 789, 750 cm^{-1}; ^1H NMR (400.03 MHz, $CDCl_3$, 298 K) δ = 1.93-2.00 (m, 4H, 2 CH_2), 2.49 (t, *J* = 2.5 Hz, 1H, C≡CH), 2.75 (t, *J* = 6.5 Hz, 2H, CH_2), 2.86 (t, *J* = 6.4 Hz, 2H, CH_2), 3.31-3.35 (m, 4H, CH_2N); 4.88 (d, *J* = 2.5 Hz, 2H, OCH_2), 6.93 (s, 1H, CH_{vinyl}), 8.35 (s, 1H, CH_{aryl}); $^{13}C\{^1H\}$ NMR (100.59 MHz, $CDCl_3$, 298 K) δ = 20.20 (1C, CH_2), 20.27 (1C, CH_2), 21.24 (1C, CH_2), 27.55 (1C, CH_2), 50.07 (1C, CH_2), 50.45 (1C, CH_2), 52.39 (1C, CH_2), 74.94 (1C, CH, C≡*C*H), 78.20 (1C, C, *C*≡CH), 105.92 (1C, C), 106.29 (1C, C), 107.67 (1C, C), 119.45 (1C, C), 127.29 (1C, CH), 149.01 (1C, C), 149.86 (1C, CH), 153.79 (1C, C), 158.55 (1C, C), 163.69 (1C, C).

3.0 Polymerization: General Procedure

The methyl methacrylate monomer and the initiator were charged to a dry Schlenk tube along with the chosen solvent (66 % v/v) and mesitylene as internal ^{1}H NMR standard. The tube was sealed with a rubber septum and subjected to five freeze-pump-thaw cycles. Cu(I)Br and the *N*-(propyl)-2-pyridylmethanimine ligand were then added sequentially, under nitrogen. The brown solution was subsequently heated to the desired temperature with constant stirring (t = 0). Samples were removed periodically using a degassed syringe for molecular weight (SEC) and conversion analysis (^{1}H NMR).

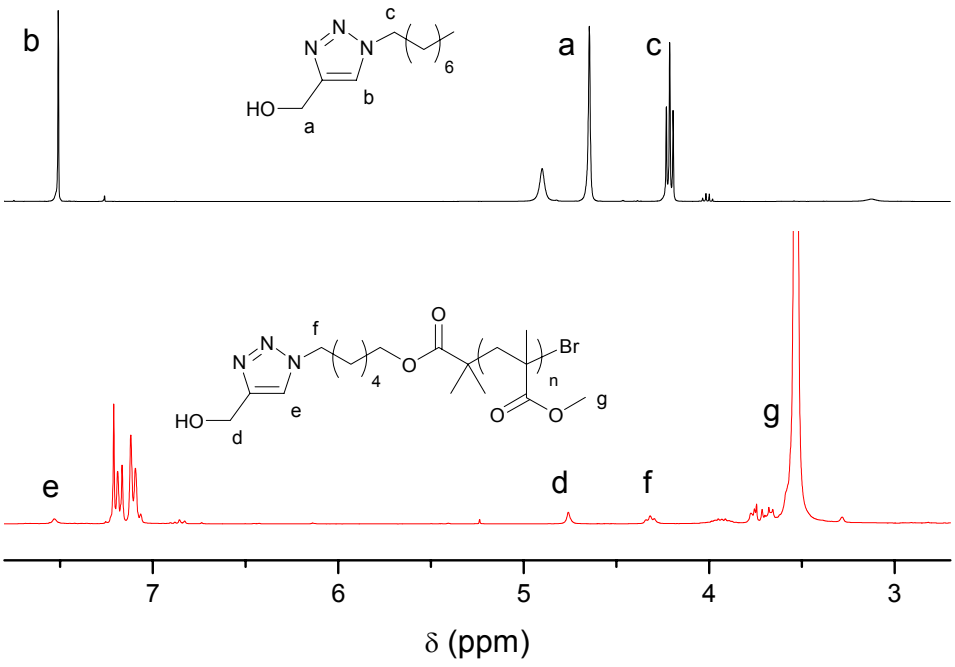
Once a conversion of 87-95 % was reached, half of the brown solution was removed via degassed syringe and precipitated into petroleum ether. The solid product obtained was dissolved in the minimum amount of toluene and passed through a short column of neutral alumina, eluting with the same solvent. After concentration and reprecipitation in petroleum ether a white powder was obtained and used for the characterization of the azido-terminated polymers .

An appropriate alkyne (propargyl alcohol, **(5)** or **(6)**; 1.2 equivalents with respect to the residue azide polymer still present) was then added under nitrogen to the reaction mixture and the dark brown solution allowed to stir overnight.

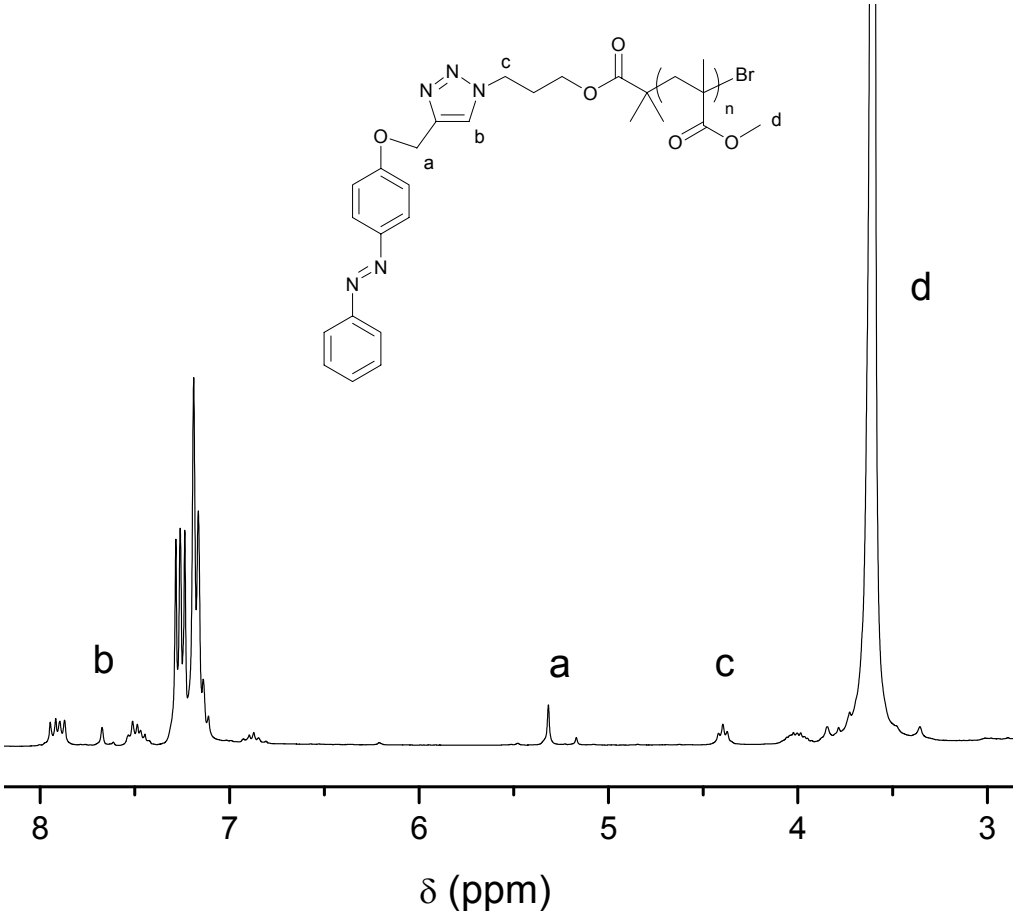
Purification of the "clicked" polymers: ^{1}H NMR of an aliquot taken from the reaction mixture allowed to identify the 1,2,3-triazole unit and confirmed that the azide moiety was no longer present. The reaction mixture was cooled to room temperature and an excess of 1,1,4,7,7-pentamethyldiethylenetriamine (ca. 10-fold molar excess with respect to the Cu(I)Br present) was added. Et_2O was then slowly added in order to precipitate the copper as insoluble complexes. After filtration the

solution was concentrated and the polymer was precipitated into petroleum ether in order to remove the residual monomer and the excess of polydentate amine (when PEG_{400} was used, after the filtration step the solution was washed 3 times with brine). The solid was then filtrated, washed with petroleum ether and dried under reduced pressure to give the expected polymers **(4)** as fine powders.

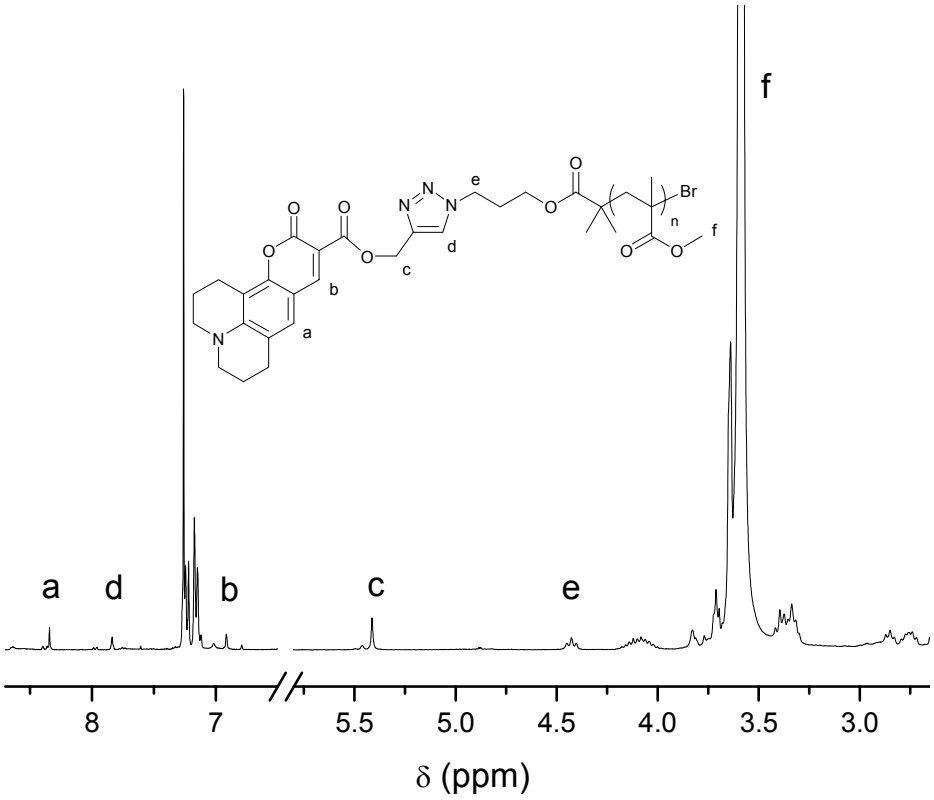
Polymer (Code)	**Conversion (%)**	**M_n**	**M_w / M_n**
(4a) - toluene	90	6000	1.28
(4b) – PEG_{400}	87	4900	1.23
(4b) - toluene	92	4000	1.27
(4b) - anisole	95	4200	1.21



S2. Partial ^{1}H NMR of **(4a)** "clicked" with propargyl alcohol (below) and a model 1,2,3-triazole (above). The two compounds showed an analogous pattern of signals relative to the triazole unit.



S3. Partial ^{1}H NMR of **(4b)** "clicked" with the diaza dye **(5)**.



S4. Partial ^{1}H NMR of **(4b)** "clicked" with the coumarin 343 dye **(6)**.

4.0 References

1 R. N. Keller and H. D. Wycoff, *Inorg. Chem.* 1946, 1.

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3 S. G. Alvarez and M. T. Alvarez, *Synthesis*, 1997, 413.