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The use of reduced copper metal-organic frameworks to facilitate CuAAC click chemistry

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Experimental section

Materials

1,3,5-Benzenetricarboxylic acid (BTC, 95%), copper(II) nitrate trihydrate $Cu(NO_3)_2{\cdot}3H_2O$, copper(I) bromide (CuBr, > 99.9%), copper(II) bromide (Cu_2Br, > 99.9%), *N*,*N*,*N*′,*N*′′,*N*′′-pentamethyldiethylenetriamine (PMDETA, 99%), 2,2′-bipyridyl (Bpy, 99%), propargyl alcohol (99%), hydroquinone (99%), sodium azide (NaN_3, > 99.5%), methanesulfonyl chloride (99.7%), *α*-bromoisobutyryl bromide (98%), 2-((2E)-3-(4-tert-Butylphenyl)-2-methylprop-2-enylidene) malononitrile (DCTB), trifluoroacetic acid (TFA) and poly(ethylene glycol) methyl ether (PEG, M_n = 1.0 kDa) were purchased from Aldrich and used as received. $RuCp^*Cl(PPh_3)_2$ was provided by Wako and used as received. Deuterated methanol (CD_3OD-d_4, 99.8 %) and deuterated chloroform ($CDCl_3$, 99.9 %) were purchased from Cambridge Isotope Laboratories, Inc. Chloroform and triethylamine (TEA) were distilled from calcium hydride under argon to obtain the anhydrous solvents. Tetrahydrofuran (THF) were distilled from benzophenone and sodium metal under argon. Thionyl chloride ($SOCl_2$), magnesium sulfate ($MgSO_4$), AR grade hexane, methanol, ethanol, dimethylformamide (DMF), dimethyl sulfoxide (DMSO), ethyl acetate (EtOAc) and other solvents were purchased from Chem-Supply Pty. Ltd. and used as received. The propan-2-yne 2-bromo-2-methylpropanoate (PgBr) was prepared using a previously published synthetic method.[1] The dimethyl 2-chloro-2,4,4-trimethylpentanedioate ($(MMA)_2$-Cl), was prepared using previously published synthetic methods.[2]

Preparation of Cu-BTC (HKUST-1)

A precursor solution was prepared by dissolving $Cu(NO_3)_2{\cdot}3H_2O$ (1.22 g, 5 mmol) and 1,3,5-benzenetricarboxylic acid (0.58 g, 2.7 mmol) in DMSO (5 g) and kept at 20 ^oC. MOF samples were then obtained by evaporating this solution at 100 ^oC. The resulting powder was washed with ethanol and dried *in vacuo* at 120 ^oC for 12 h to yield blue crystals.

Hydrothermal reduction of Cu-BTC to afford rCu-MOF

Preformed Cu-BTC (100 mg), DI H_2O (10.0 g) and hydroquinone (1.0 g) were mixed together in a small glass vessel. When the hydroquinone was completely dissolved, the mixture was heated in a sealed autoclave at 150 °C under autogenous pressure for 16 h. After the autoclave had cooled to R.T., the resulting material was collected and washed with methanol. The crystals were dried *in vacuo* at 120 ^oC for 12 h, resulting in dark colour products. The yields of the rCu-MOF were of ~ 50 %.

Preparation of propargyl 1-pyrenebutyrate (C1).

1-Pyrenebutyric acid (2.88 g, 10 mmol) was dissolved in anhydrous chloroform (50 mL) in a round bottomed flask under nitrogen and cooled to 0 °C. Oxalyl chloride (1.03 mL, 12 mmol, 1.2 equiv) was then added slowly into the flask. Two drops of dimethyl formamide (DMF) were added as a catalyst for the reaction. The reaction mixture was stirred at room temperature for 20 h with constant stirring. The solvent and any excess oxalyl chloride was removed by rotary evaporation to obtain the acid chloride. The acid chloride was directly used in the next step without further purification. The acid chloride (1.0 equiv.) was dissolved in anhydrous chloroform (20 mL) and added slowly to a solution of propargyl alcohol (0.87 mL, 15 mmol, 1.5 equiv) dissolved in anhydrous chloroform (50 mL) and under nitrogen. The mixture was then stirred for 3 h. The chloroform and excess propargyl alcohol were removed *in vacuo*. The crude product was purified by flash chromatography (elution:

hexane/DCM = 1/1 v/v to DCM/MeOH = 95/5 v/v) to yield the propargyl 1-pyrenebutyrate (**C1**). Rf (hexane/DCM = 1/1 v/v): 0.45; ^{1}H-NMR (400 MHz, $CDCl_3$, δ_H ppm): 8.31-7.85 (m, 9H, Ar***H***), 4.71 (d, 2H, -OC***H₂***C≡CH), 3.43-3.39 (m, 2H, -PyC***H₂***-), 2.54-2.48 (m, 3H, -C***H₂***C(O)- and -C≡C***H***), 2.26-2.17 (m, 2H, -C***H₂***-); ^{13}C NMR (400 MHz, $CDCl_3$, δ_C ppm): 172.7, 135.6, 131.6, 131.1, 130.2, 128.9, 127.6, 127.6, 127.5, 126.9, 126.0, 125.3, 125.1, 125.1, 125.0, 124.9, 123.4, 75.0, 52.0, 51.7, 33.7, 32.8, 26.8.

Preparation of 3-azidopropyl anthrancene-9-carboxylate (C3).

Anthrancene carboxylic acid (1.11 g, 5.0 mmol) and thionyl chloride ($SOCl_2$) (20 mL) were added to a dried flask under argon. The mixture was refluxed under argon for 1 h and then excess $SOCl_2$ was removed by rotary evaporation. The resulting residue was azeotroped with benzene (10 mL × 3), redissolved in anhydrous THF (20 mL) and cooled to 0 ^{o}C. Triethylamine (1.20 mL, 16.3 mmol) was added, followed by 3-azidopropanol (0.50 g, 4.9 mmol) in anhydrous THF (30 mL) dropwise. The reaction solution was stirred at 0 ^{o}C for 30 min, warmed to room temperature and stirred for another 48 h, and then filtered and concentrated. The crude product was redissolved in dichloromethane (50 mL), washed with 2M NaOH (30 mL × 2), 2M HCl (30 mL × 2) and DI water (30 mL × 2), dried ($MgSO_4$), filtered, and concentrated *in vacuo* as a light brown solid, 1.41 g (92.4 %). ^{1}H NMR (400 MHz, $CDCl_3$, δ_H ppm): 8.48 (s, 1H, Ar***H***), 7.95-8.14 (m, 4H, 4Ar***H***), 7.44-7.54 (m, 4H, 4Ar***H***), 4.67 (t, 2H, J = 5.2 Hz, -C***H₂***N_3), 3.45 (t, 2H, J = 5.2 Hz, -OC***H₂***-), 2.09 (2H, J = 6.4 Hz, -C***H₂***-). ^{13}C NMR (400 MHz, $CDCl_3$, δ_C ppm): 169.6, 131.0, 129.5, 128.7, 128.5, 127.7, 127.2, 125.6, 124.7, 62.5, 48.2, 8.3.

Synthesis of azido functionalized poly(ethylene glycol) (PEG-N₃, P1).

Poly(ethylene glycol) methyl ether (PEG, M_n = 1.0 kDa, 2.0 g, 2 mmol) was initially dried *via* azeotropic distillation with toluene (20 mL). Subsequently, anhydrous triethylamine (2.4 mmol) and dichloromethane (20 mL) were added and the mixture was cooled to 0 ^{o}C before methanesulfonyl chloride (3 mmol) was added dropwise. The reaction was kept at 0 ^{o}C for 30 min and then at room temperature for 12 h. The reaction was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in DMF (20 mL), and NaN_3 (20 mmol) was added. The reaction mixture was heated to 65 ^{o}C for 12 h, cooled to room temperature and concentrated *in vacuo*. The residue was dissolved in water (50 mL) and then washed with dichloromethane (25 mL × 2). The organic extracts were collected, washed with water (50 mL) and saturated NaCl (50 mL × 2), dried ($MgSO_4$), filtered, and concentrated in vacuo to afford the desired PEG-N_3 (**P1**). ^{1}H NMR (400 MHz, $CDCl_3$, δ_H ppm): 3.45-3.85 (m, 4H, -C***H₂***C***H₂***O-) ppm, 3.37-3.41 (s, 3H, -OC***H₃*** and t, 2H, -C***H₂***N_3). MALDI-ToF MS: M_n = 1.07 kDa, PDI = 1.02.

Synthesis of azido functionalized poly(methy methacrylate) (PMMA-N₃, P2).

The ATRP of MMA was performed according to the previously established procedure:[3] Ru catalyst ($RuCp^*Cl(PPh_3)_2$ 21.7 mg, 0.028 mmol) was added to a dry round bottom flask equipped with a three-way stopcock in a glove box, followed by addition (under dry N_2) of toluene (3.96 ml), MMA (3 ml, 0.028 mol), *n*-Bu_3N (0.28 mmol) and initiator $(MMA)_2$-Cl (0.28 mmol). The reaction vessel was then heated at 80 ^{o}C for 33 h. A sample was extracted for ^{1}H NMR analysis and the remaining polymeric product was precipitated twice in hexane followed by drying *in vacuo* to afford the product PMMA-Cl a white solid, 2.4 g (80%). The PMMA-Cl (6.8 g, M_n = 5.2 kDa, 1.31 mmol), NaN_3 (0.85 g, 13 mmol) and L-ascorbic acid (0.035 g, 0.20 mmol) were dissolved in CH_3CN/H_2O (9 : 1) in a round bottom flask, and the

mixture was degassed by bubbling N_2 for 10 min. A standard catalyst solution of $CuCl/CuCl_2$/Bpy (0.1/0.067/0.33 M in CH_3CN/H_2O (9 : 1), 7.85 mL) was then added and the reaction solution was stirred at 40 °C for 24 h. The crude product solution was extracted with EtOAc (50 mL x 3), and the organic layers were collected, combined and then washed with HCl (1 M, 50 mL x 3) and H_2O (50 mL x 3). The solution was then concentrated (to ~50 mL), and passed through a short neutral alumina column before dried *in vacuo* to afford PMMA-N_3 (**P2**) as a white crystal (6.8 g, > 99%). GPC: M_n = 5.2 kDa, M_w/M_n = 1.11. ^{1}H NMR (400 MHz, $CDCl_3$, δ_H ppm): 3.70-3.80 (s, 3H, ω-OC***H₃***), 3.50-3.65 (m, 3H, -OC***H₃***), 1.75-2.05 (m, 2H, -C***H₂***-), 0.78-1.20 (m, 3H, -CC***H₃***).

Synthesis of alkyne functionalized poly(methy methacrylate) (alkyne-PMMA, P3).

The alkyne-PMMA was synthesized according to a previous reported procedure:[1] CuBr (36.0 mg, 0.25 mmol) and $CuBr_2$ (5.6 mg, 0.025 mmol) were added to a dry round bottom flask equipped with a 3-way stopcock in a glove box, followed by addition (under dry N_2) MMA (2.7 mL, 25.2 mmol), bpy (495 mM in toluene, 1.0 mL) and PgBr (503 mM in toluene, 0.50 mL). The reaction was conducted at 0 °C with samples taken periodically under N_2. The polymerization was terminated after 11 h by cooling the reaction to -78 °C. A sample was extracted for ^{1}H NMR spectroscopic analysis, and the remaining product was diluted with EtOAc (200 mL), washed with 1 M HCl (100 mL × 2), then distilled water (150 mL × 2). The extracted product was collected, concentrated and then precipitated in hexane, followed by drying in vacuo to afford the alkyne-PMMA (**P3**) as a white solid, 0.28 g (85.1 %). GPC: M_n = 12.0 kDa, M_w/M_n = 1.27. ^{1}H NMR (400 MHz, $CDCl_3$, δ_H ppm): 4.63 (m, 2H, CH≡CC***H₂***O-), 3.50-3.65 (m, 3H, -OC***H₃***), 2.70 (m, 1H, C***H***≡CCH_2O-), 1.75-2.05 (m, 2H, -C***H₂***-), 0.78-1.20 (m, 3H, -CC***H₃***).

Copper-catalyzed azide-alkyne cycloaddition (CuAAC) chemistry.

(1) Coupling reaction of PEG (P1) and propargyl 1-pyrene butyrate (C1).

A 10 mL flask was charged with PEG-N_3 (P1, M_n = 1 kDa, 0.2 g, 0.2 mmol), propargyl 1-pyrene butyrate (C1, 6.56 mg, 0.2 mmol), rCu-MOF (0.2 mg) and DMSO (4 mL). This was degassed by bubbling N_2 for 20 min and placed in an oil bath at 60 °C. The reaction was stopped after 4 h and the rCu-MOF was removed by centrifugation. The crude product was precipitated into cold DEE/Acetone (95/5 v/v) mixture. After removal of the solvents, the coupling product PEG-PPy was dried *in vacuo* (1 mbar) at 30 °C prior to MALDI-ToF MS analysis. The ^{1}H NMR ($CDCl_3$) spectrum of the product is shown in Fig. S3a.

(2) Coupling reaction of PEG (P1) and propargyl alcohol (C2).

A 10 mL flask was charged with PEG-N_3 (M_n = 1 kDa, 0.2 g, 0.2 mmol), propargyl alcohol (C2, 11.2 mg, 0.2 mmol), rCu-MOF (0.2 mg) and DI H_2O (4 mL). The mixture was degassed by bubbling N_2 for 20 min and placed in an oil bath at 60 °C. The reaction was stopped after 4 h and the rCu-MOF was removed by centrifugation. The crude product was extracted with $CHCl_3$. After removal of $CHCl_3$ by evaporation, the coupling product was dried *in vacuo* (1 mbar) at 30 °C prior to MALDI-ToF MS analysis. The ^{1}H NMR (D_2O) spectrum of the product is shown in Fig. S3b.

(3) Preparation of pseudo-block copolymers PMMA-b-PMMA.

A 25 mL flask was charged with PMMA-N_3 (P2, M_n = 5.2 kDa, 0.26 g, 0.05 mmol), alkyne PMMA (P3, M_n = 12.0 kDa, 0.6 g, 0.05 mmol), rCu-MOF (0.2 mg) and THF/DMSO (4 mL, v/v = 1/1). The mixture was degassed by bubbling N_2 for 20 min and placed in an oil bath at 60 ^oC. The reaction was performed under argon positive pressure. The reaction was stopped after 12 h and the rCu-MOF was removed by centrifugation. The crude product was precipitated into cold hexane followed by drying *in vacuo* prior to GPC measurement. The ^1H NMR ($CDCl_3$) spectrum of the product is shown in Fig. S3c.

(4) Recyclability of the rCu-MOF catalyst.

A stock solution of propargyl alcohol (C2, 14.0 mg, 0.25 mmol) and 3-azidopropyl anthrancene-9-carboxylate (C3, 76.3 mg, 0.25 mmol) in CD_3OD (5 mL) was prepared. The mixture was degassed by bubbling N_2 for 20 min before each reaction. A NMR tube charged with 1 mL stock solution and 1.2 mg rCu-MOF was placed in an oil bath at 60 ^oC. The reactant conversion was monitored by ^1H NMR analysis at various time intervals. The rCu-MOF was collected and washed with methanol followed by drying *in vacuo* prior to next reaction. This reaction was repeated by another twice. The mass of recovered rCu-MOF is *ca.* 1.2 mg.

The control experiments by using Cu-BTC (1.0 mg, Entry C-1 in Table 1), CuBr (1.0 mg, Entry C-2 in Table 1) and CuBr/PMDETA (1.0 mg/1.2 mg, 1/1 mol/mol, Table S2) as catalysts were also conducted under the same condition.

Characterization

Gel-Permeation Chromatography (GPC).

GPC with THF as mobile phase was conducted using a Shimadzu system fitted with a Wyatt DAWN DSP multi-angle laser light scattering detector (690 nm, 30 mW) and a Wyatt OPTILAB EOS interferometric refractometer (690 nm). Three Agilent PLgel columns (MIXED-C; 5µm bead size) were employed, operating at 1 mL per minute at a column temperature of 45 °C. To process the GPC data, the program 'Astra' by Wyatt technologies was used. All samples were filtered through 0.45 µm nylon filters prior to injection.

Nuclear Magnetic Resonance (NMR) Spectroscopy.

^1H NMR spectroscopy and ^{13}C NMR spectroscopy were conducted on a Varian Unity 400 MHz spectrometer operating at 400 MHz, using the solvent deuterated chloroform ($CDCl_3$) (Cambridge Isotope Laboratories) as reference and sample concentrations of approximately 10 mg mL^{-1}.

Matrix-assisted laser desorption/ionization time of flight mass spectroscopy (MALDI-ToF MS).

MALDI-ToF MS was performed on a Bruker Autoflex III Mass Spectrometer operating in positive linear mode; the analyte, matrix (DCTB) and cationisation agent (NaTFA) were dissolved in THF at a concentration of 10 mg mL^{-1}, and then mixed in a volume ratio of 1:10:1. Then 0.3 µL of this solution was spotted onto a ground steel target plate and the solvent was allowed to evaporate prior to analysis. FlexAnalysis (Bruker) was used to analyse the data.

Dynamic Light Scattering (DLS).

DLS measurements were conducted on a Wyatt DynaPro NanoStar DLS/SLS instrument with a GaAs laser (658 nm) at an angle of 90º and a temperature of 25 ± 0.1 °C. Stable spectra were determined at sample concentrations of 1 mg mL^{-1}.

Scanning Electron Microscopy (SEM).

SEM measurements were conducted on a Quanta FEG 200 ESEM. Samples were coated with a gold using a Dynavac Mini Sputter Coated prior to imaging.

X-ray photoelectron spectroscopy (XPS).

XPS analysis was performed on a VG ESCALAB 220i-XL spectrometer under ultra-high vacuum (6×10^{-9} mbar) to reveal the surface composition of the polymer coating. A fixed photon energy (Al Kα 1486.6 eV) was used. A survey scan was performed between 0 and 1200 eV with a resolution of 1.0 eV and pass energy of 100 eV. High resolution scans for C1s (276 to 296 eV) and O1s (522 to 542 eV) were also conducted with a resolution of 0.05 eV and a pass energy of 20 eV.

X-ray diffraction (XRD).

XRD patterns of the samples were recorded on a Bruker D8 Advance instrument with Cu Kα radiation (40 kV, 40 mA) and a nickel filter, and the samples were exposed at a scanning rate of $2\theta = 0.020\ °\cdot s^{-1}$ in the range of 3-70°.

Thermogravimetric analysis (TGA).

TGA was performed on a PerkinElmer Pyris-1 thermogravimetric analyzer, and the samples were heated from 30 to 600 °C at a heating rate of 2 K min^{-1} under a N_2 flow (20 mL min^{-1}).

Gas adsorption.

The specific surface area of the Cu-BTC and rCu-MOF was measured by Micromeritics ASAP 2050 Xtended Pressure Sorption Analyzer with CO_2 as absorbate at 0 ^oC. Before the measurements, all the samples were degassed at 120 ^oC for 16 h. The specific surface area was obtained by the BET equation.

Inductively coupled plasma optical emission spectrophotometer (ICP-OES).

The ICP-OES was performed on a Perkin Elmer Optima 4300 DV using calibration curves generated from standard solutions (0.01 – 1 ppm).

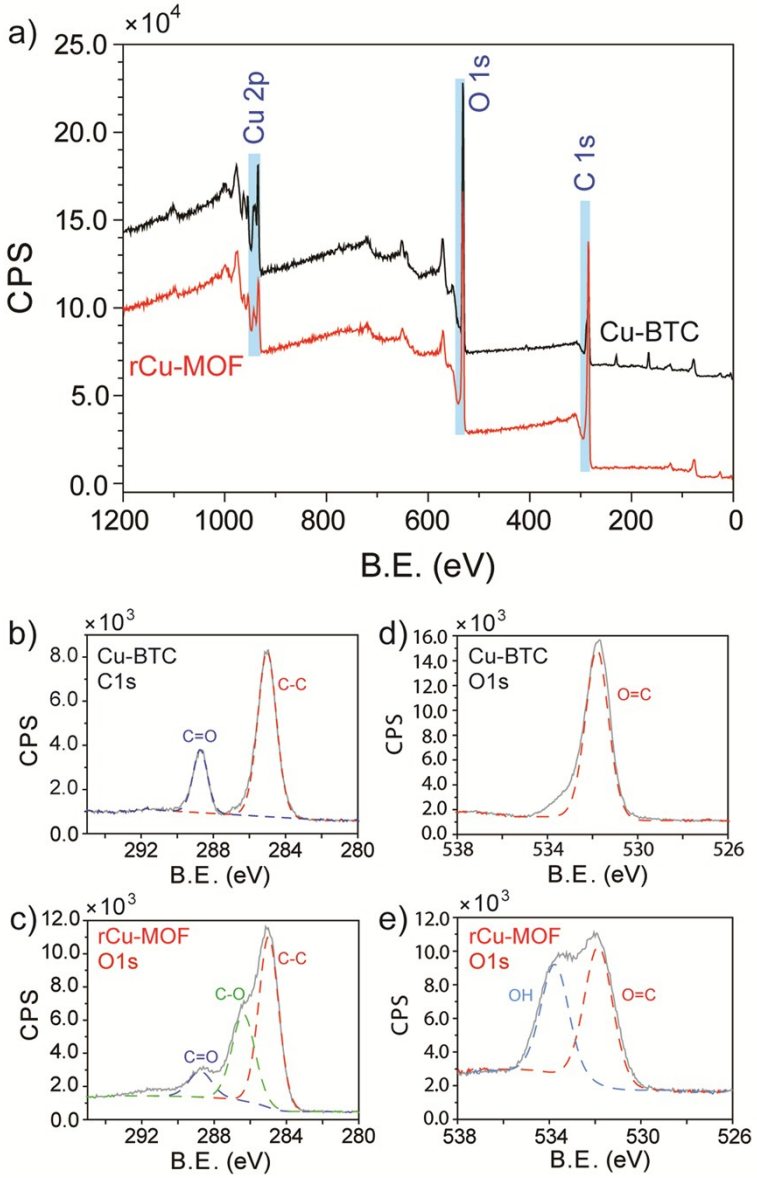

Fig. S1 (a) XPS spectra of Cu-BTC (top) and rCu-MOF (bottom). High resolution XPS spectra of (b) C 1s and (d) O 1s for Cu-BTC; and of (c) C 1s and (e) O 1s for rCu-MOF, respectively.

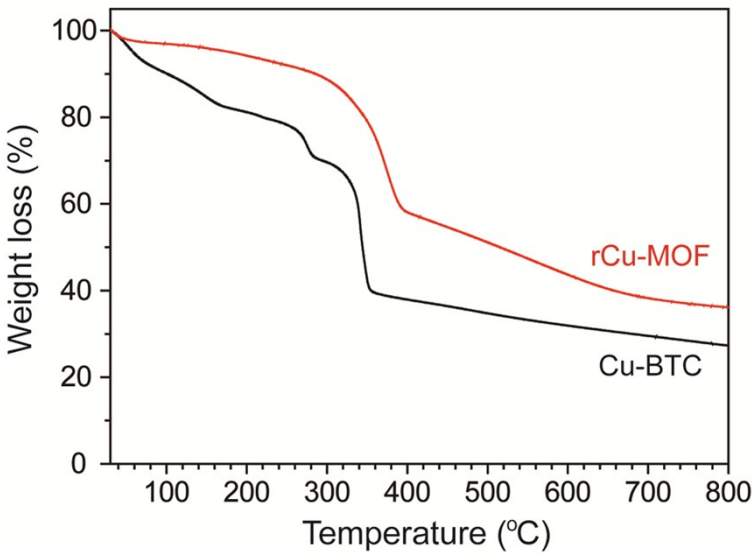

Fig. S2 The TGA profiles of the Cu-BTC and rCu-MOF. All the tests were performed in nitrogen with the heating rate of 2 K min^{-1}.

The typical weight loss curves are displayed in Fig. S2. The rCu-MOF started to lose weight at *ca.* 320 °C and the weight residual (Wr) at 800 °C is 36.1 % for Cu.

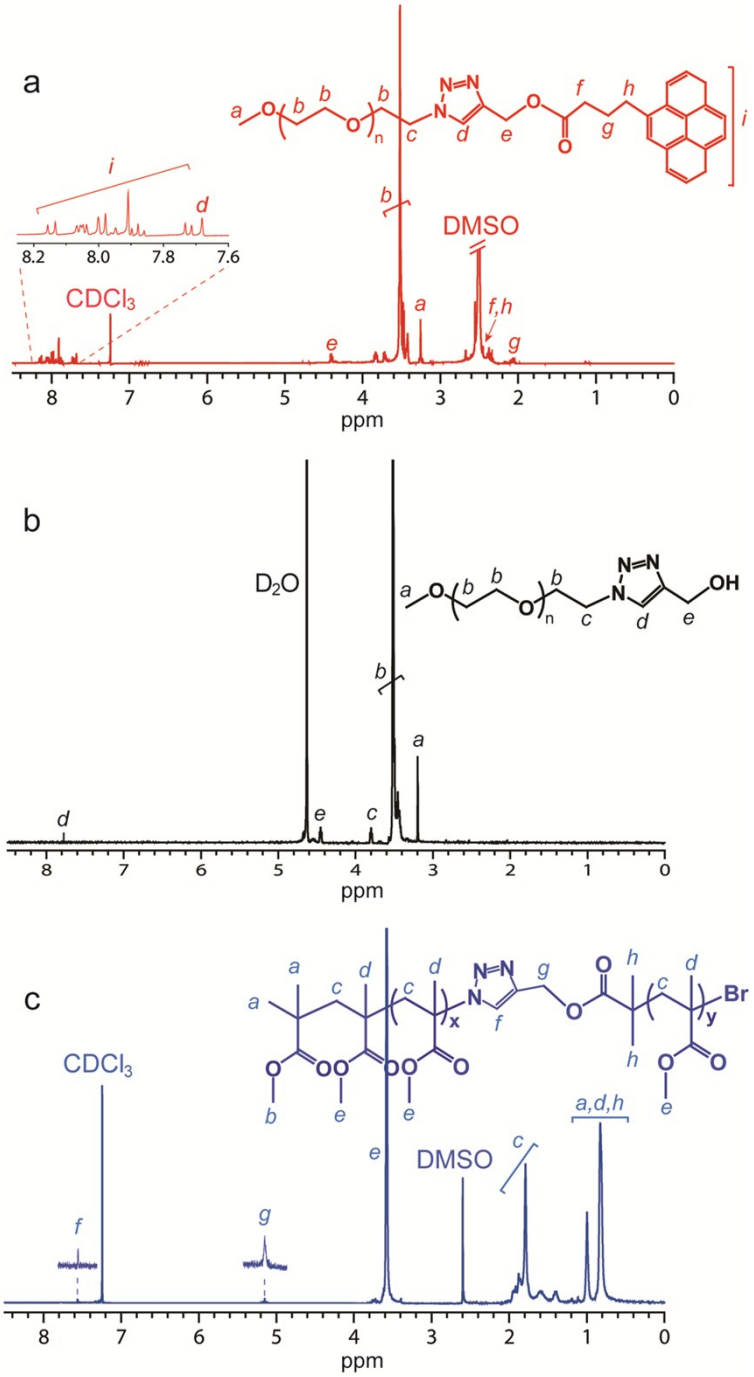

Fig. S3 ^{1}H NMR spectra of the resultant (a) *ω*-pyrene terminated PEG, (b) *ω*-OH terminated PEG and c) PMMA-*b*-PMMA *pseudo*-block copolymer.

Table S1. The calculated conversion of reactants via *in situ* ^{1}H NMR analysis.

Cycle-1		Cycle-2		Cycle-3		C2	
Time (min)	Conv. (%)	Time (min)	Conv. (%)	Time (min)	Conv. (%)	Time (min)	Conv. (%)
0	0	0	0	0	0	0	0
20	17.8	15	12.1	25	21.1	45	32.5
45	40.7	40	34.9	60	50.6	75	53.8
70	58.7	70	57.1	90	71.5	100	72.1
100	80.3	95	76.6	120	87.8	120	82.7
125	92.9	125	91.2				

Table S2. The calculated TOF of a homogeneous catalytic system.

CuBr/PMDETA system[a]		
Time (min)	Conv. (%)[b]	TOF (min^{-1})[c]
0	0	27.0
20	57.1	
35	98.9	

[a]The CuBr (1.0 mg) and PMDETA (1.2 mg) were fed as catalysts. [b]The conversion was calculated by ^{1}H NMR analysis. [c]TOF is calculated based on the total number of Cu^{I} ions.

Reference

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2. T. Ando, M. Kamigaito and M. Sawamoto, *Macromolecules*, 2000, **33**, 2819-2824.
3. T. K. Goh, S. Yamashita, K. Satoh, A. Blencowe, M. Kamigaito and G. G. Qiao, *Macromol. Rapid Commun.*, 2011, **32**, 456-461.