Supporting Information

Synthesis and [2 + 2]-photodimerisation of monothiomaleimide functionalised linear and brush-like polymers

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Experimental

1. Materials

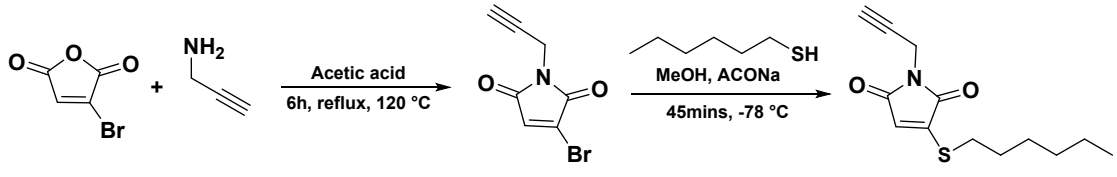
All reagents were used as received from suppliers without any further purification unless stated. Bromomaleic anhydride 97% was purchased from Fisher Scientific. Propargylamine, hexane-1-thiol, methoxy poly(ethylene glycol) azide M_n = 2000 g.mol^{-1}, 2,2'-bipyridine, copper sulphate pentahydrate, L-ascorbic acid, oligo (ethylene glycol) methyl ether acrylate M_n = 480 g.mol^{-1} containing 100 ppm BHT and 100 ppm MEHQ as inhibitors, copper (II) bromide, sodium azide, 3-bromopropan-1-ol, 2-bromoisobutyryl bromide 98%, were purchased from Aldrich. Acetic acid and triethylamine were purchased from Merck. Copper (I) bromide was purchased from ALFA and washed with acetic acid and rinsed with ethanol three times. Tris-(2-(dimethylamino) ethyl) amine (Me_6Tren) was synthesised according to the literature.[1] 3-azidopropyl-2-bromoisobutyrate was synthesised according to previous literature and was spectroscopically pure.[2] Deuterated solvents (D_2O, CD_3CN $CDCl_3$, and d_6-DMSO) were purchased from Aldrich.

2. Instruments

The instruments used for all experiments were Infrared Bruker vector 22 FT-IR spectrometer provided by a golden gate diamond attenuated reflection cell, and the samples were run from 550 – 4000 cm^{-1} wavenumber. ^{1}H and ^{13}C NMR spectrums were obtained using Bruker AV-300,

HD-300, and HD-400 spectrometers utilising deuterated solvents provided from Sigma-Aldrich. Chemical shifts are given in ppm downfield from the internal standard tetramethylsilane. UV-Vis spectra were recorded on an Agilent Technologies Cary 60 UV-Vis in the range of 200-800 nm using a cuvette with a 10 mm optical path length. MALDI-ToF-MSwas carried out using a Bruker Daltonics Ultraflex II. MALDI-ToF mass spectrometer, equipped with a nitrogen laser delivering 2 ns laser pulses at 337 nm. Positive ion ToF detection was conducted using an accelerating voltage of 25 KV. Samples for MALDI were mixed into a water/THF 50:50 mix at concentrations of 10 mg/ml, with 15 mg/ml of DCTB and 0.1 mg/ml of NaI. Mass spectrometry was conducted using Agilent 6130B ESI-Quad. It is provided by autosampler and isocratic pump from an Agilent 1100 to deliver the samples and the solvent used. In this system the solvent was 80:20 methanol: water (HPLC grade). Size exclusion chromatography was performed using Agilent Infinity II MDS instruments equipped with differential refractive index (DRI), viscometry (VS), dual angle light scatter (LS) and multiple wavelength UV detectors. The system was equipped with 2 x PLgel Mixed C columns (300 x 7.5 mm) and a PLgel 5 µm guard column. The eluent is THF with 2 % TEA (triethylamine) and 0.01 % BHT (butylated hydroxytoluene) additives. Samples were run at 1 ml /min at 30 °C. Poly(methyl methacrylate) and polystyrene standards (Agilent EasiVials) were used for calibration, and the calibration range was 500 – 1,500.000 g.mol^{-1}. Analyte samples were filtered through a GVHP membrane with 0.22 µm pore size before injection. Respectively, experimental number average molecular weights (Mn, SEC) and dispersity (Đ) values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software. For [2 + 2]-photocycloaddition reactions following light sources were employed; a UV nail gel curing lamp (commercially available from a range of suppliers) (λ_{max} ~ 365 nm) equipped with four 9W bulbs and an Omnicure S2000 linked to an optical probe and fitted with Lumen Dynamics 200W Mercury lamp and bandpass filter (320 – 390 nm).

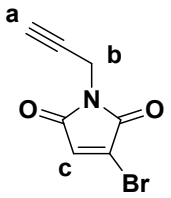
3. Synthetic procedures



(**1**)

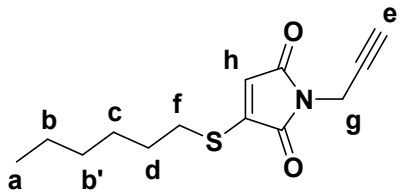
Scheme S1. Reaction scheme for the synthesis of *N*-propargyl-3-monothiohexylmaleimide **(1)**

***N*-Propargyl-3-bromomaleimide**



The reaction was adapted from previous literature.[3] Maleic anhydride (8.0 g, 45.0 mmol) was dissolved in acetic acid (100 mL) and propargylamine (3.0 mL, 45.0 mmol) was added dropwise. The reaction mixture was stirred and heated at 130 °C for 6 hours. Toluene was added several times to remove acetic acid by azeotropic distillation. The crude product was purified by flash chromatography using (80 % petroleum ether and 20 % ethyl acetate) to obtain *N*-propargyl-3-bromomaleimide as a brown solid in 75 % yield (9.6 g, 45 mmol). Melting point 103-104 ° C; IR υ/cm^{-1} 3268, 3100, 2950, 2125, 1692, 1400, 550-600; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.25 (s, *J* = 1.74 Hz, $1H_a$), 4.35 (d, $2H_b$), 6.94 (s,$1H_c$); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 27, 72, 76, 131, 132, 163, and 166); (MS) *m/z* 267.96 $([C_8H_8Br^{79}NNaO_3]^+)_{th}$ 268.22 $([C_8H_8Br^{79}NNaO_3]^+)_{exp}$, 269.96 $([C_8H_8Br^{81}NNaO_3]^+)_{th}$, 270.21 $([C_8H_8Br^{81}NNaO_3]^+)_{exp}$ (M^+: M^{2+} = 1 :1).

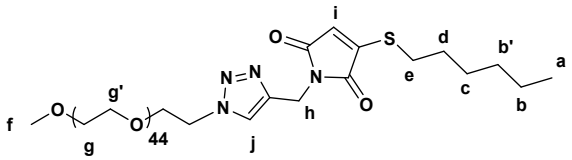
***N*-Propargyl-3-thiohexylmaleimide (1)**



The reaction was adapted from previous literature with temperature and time changes.[4] To a solution of *N*-propargyl-3-bromomaleimide (3.0 g, 14.0 mmol) in methanol (50 mL), sodium acetate (1.1 g, 14.0 mmol) was added, and the solution was cooled down to -78 °C. Then while the solution was stirred, hexane-1-thiol (2.3 ml, 14.0 mmol) was dropped slowly. The reaction mixture was monitored by TLC and the reaction was completed after 45 minutes. The crude was then purified by dry flash chromatography using (95% petroleum ether and 5% ethyl acetate) to obtain *N*-propargyl-3-thiohexylmaleimide as a pale green solid in 75% yield (2.64 g, 10.5 mmol). IR solid υ/cm^{-1} 3300, 3110, 2960, 1707, 1550; ^{1}H NMR (300MHz, $CDCl_3$) δ (ppm) 0.83 (t, *J* = 6.40 Hz, $3H_a$) 1.26 (m, $4H_b$), 1.38 (qui, $2H_c$) 1.68 (quin, *J* = 7.35 Hz, $2H_d$) 2.14 (s, *J* =

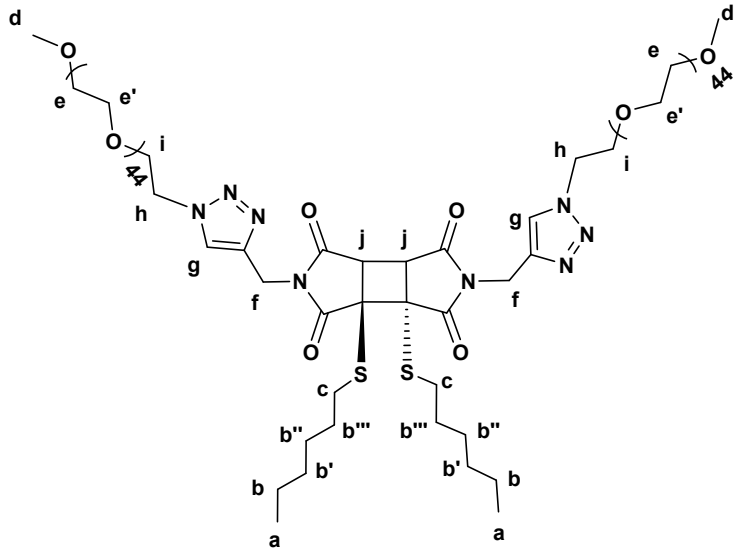
2.45 Hz, 1H_e) 2.85 (t, *J* = 7.35 Hz, 2H_f) 4.21 (d, *J* = 2.45 Hz, 2H_g) 6.10 (s, 1H_h); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 14, 22.5, 27, 27.5, 28.5, 31, 32, 71.5, 117, 152, 166.5, 168); (MS) *m/z* 274.09 $([M+Na]^+)_{th}$, 274.30 $([M+Na]^+)_{exp}$; UV; λ_{max} = 350 nm.

Poly (ethylene glycol)-3-thiohexyl-1-(prop-2-yn-1-yl)-1H-pyrrole-2, 5-dione (MTM-PEG)



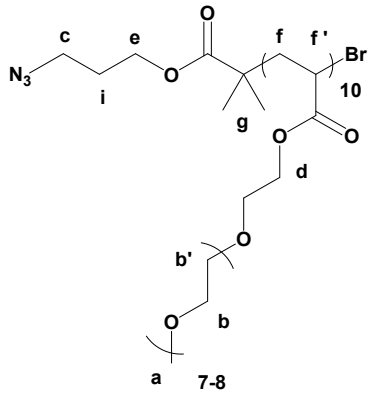
Huisgen's alkyne-azide click reaction protocol was adapted from previous literature.[2] α-Methoxy-ω-azido poly(ethylene glycol) M_n =2000 g.mol^{-1} (200 mg, 100 µmol) and *N*-propargyl-3-thiohexylmaleimide (27.6 mg, 110 µmol) were dissolved in methanol (8 mL). Separately, copper sulphate (27.4 mg, 110 µmol) and L-ascorbic acid (19.4 mg, 110 µmol) were dissolved in water (2 mL) and then transferred to the organic mixture. The reaction was conducted with the exclusion of the light and left stirring at room temperature overnight. The solution was purified by aqueous dialysis whilst excluded light before the water was removed using lyophilisation to obtain MTM-PEG in 94 % yield (212 mg, 94.2 µmol). IR solid υ/cm^{-1} 2950, 1700, 1460, 1090; ^{1}H NMR (300MHz, D_2O: CD3CN 95:5 %) δ (ppm) 0.86 (t, H_a) 1.2 (m, $H_{b,\ b',c}$) 1.7 (qui, H_d) 3.04 (s, H_e) 3.36 (t, H_f) 3.67 (s, $H_{g,\ g'}$) 4.57 (d, H_h) 6.45 (s, H_i) 8.0 (s, H_j); SEC M_n = 4100 g mol^{-1}, $Đ$ = 1.20.

[2 + 2]-Photocycloaddition of MTM-PEG



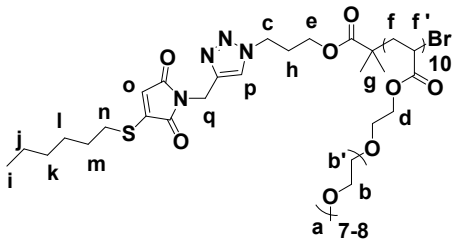
For all the different sources of light experiments, MTM-PEG (20.0 mg, 9.90 µmol) was dissolved in deuterated acetonitrile and deuterium oxide (5: 95). The polymer solution was transferred to NMR tube and exposed to the light source. IR solid υ/cm^{-1} 2950, 1700, 1460, 1090; ^{1}H NMR (300MHz, D_2O: CD3CN 95: 5 %) δ (ppm) 0.86 (t, H_a), 1.2 (m, $H_{b, b', b'', b'''}$), 2.56-2.91 (m, $H_{c,c'}$), 3.36 (s, H_d), 3.60 (s, H_j), 3.67 (s, $H_{e,e'}$), 3.99 (m, H_i), 4.67 (m, H_h), 5.00 ppm (br, H_f), 8.19 (s, H_g); SEC M_n = 7900 g mol^{-1}, $Đ$ = 1.20.

Cu(0)-mediated polymerisation of oligo(ethyl glycol) methyl ether acrylate (M_n = 480 g.mol^{-1}) (N_3-POEGA$_{480}$)



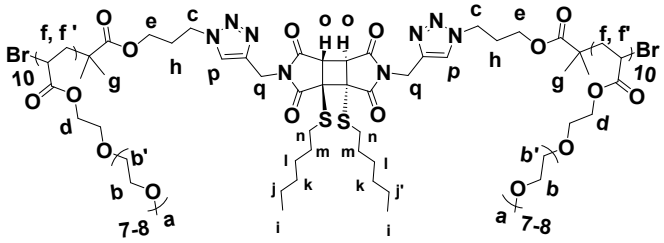
The reaction was adapted from previous reports.[5] Copper (II) bromide (10.3 mg, 0.045 mmol), Me_6Tren (42.6 µL, 0.16 mmol), 3-azidopropyl-2-bromo-2-methylpropanoate (230 mg, 0.9 mmol) and oligo(ethylene glycol) methyl ether acrylate (4.36 g, 9.08 mmol) were dissolved in DMSO (4 mL) and deoxygenated by bubbling with N_2 for 20 minutes. Copper (0) wire (5 cm) was wrapped around a magnetic stirrer bar and activated by submersion in hydrochloric acid 37% for 20 minutes before addition to the reaction mixture. The polymerization reaction was carried out for 3 hours at room temperature. Conversion (94%) was determined by ^{1}H NMR and purification to remove unreacted monomer and soluble copper species was achieved by aqueous dialysis (1K MWCO) for 3 days. The final polymer was isolated by lyophilisation to yield a colourless oil. ^{1}H NMR (300MHz, DMSO) δ (ppm) 1-2 (b, $H_{f, f', i, g}$) 3.22 (s, H_a) 3.51 (s, $H_{b, b'}$) 3.73 (s, 2H_c) 4.1 (s, H_d) 4.22 (t, H_e); SEC M_n = 5400 g mol^{-1}, $Đ$ = 1.26.

MTM-Poly(oligo[ethylene glycol] methyl ether acrylate), MTM-POEGA$_{480}$



The reaction was adapted from previous reports.[6] N_3-POEGA$_{480}$ (0.2 g, 37 µmol) and *N*-propargyl-3-thiohexylmaleimide (10.2 mg, 40.7 µmol) were dissolved in DMSO (2 mL) and deoxygenated by bubbling with N_2 for 20 minutes. In a separate vial, copper (I) bromide (5.3 mg, 37 µmol) and bipyridine (5.8 mg, 37 µmol) were dissolved in DMSO (2 mL) and deoxygenated by bubbling with N_2 for 20 minutes. The catalyst solution was transferred to the reagent solution and stirred at room temperature for 2 days under N_2. The mixture was purified aqueous dialysis (1K MWCO) for 3 days. The final polymer was isolated by lyophilisation to yield a pale green oil (194 mg, 93%). ^{1}H NMR (300MHz, D_2O) δ (ppm) 0.8-3 (m, $H_{f, f', g, h, i, j, k, l, m, n, o}$) 3.33 (s, H_a) 3.62 (s, H_b, $_{b'}$) 3.85 (s, H_C) 4.21 (s, H_d) 4.51 (s, H_e) 4.87 (s, H_q) 6.40 (s, 1H_o) 8.00 (s, 1H_p); SEC M_n = 6000 g mol^{-1}, $Đ$ = 1.36.

[2 + 2]-Photocycloaddition of MTM-POEGA



MTM-PEG (56 mg, 9.90 µmol) was dissolved in deuterated acetonitrile and deuterium oxide (5:95). The polymer solution was transferred to NMR tube and exposed to the light source. ^{1}H NMR (300MHz, D_2O: CD_3CN 95:5 %) δ (ppm) 0.8-3 (m, $H_{f, f', g, h, i, j, k, l, m, n}$) 3.33 (s, H_a) 3.62 (s, H_b, $_{b'}$) 3.85 (s, H_C) 4.21 (s, H_d) 4.51 (s, H_e) 4.87 (s, H_q) 6.40 (s, 1H_o) 8.00 (s, 1H_p); SEC M_n = 6400 g mol^{-1}, $Đ$ = 1.67.

Supporting Figures

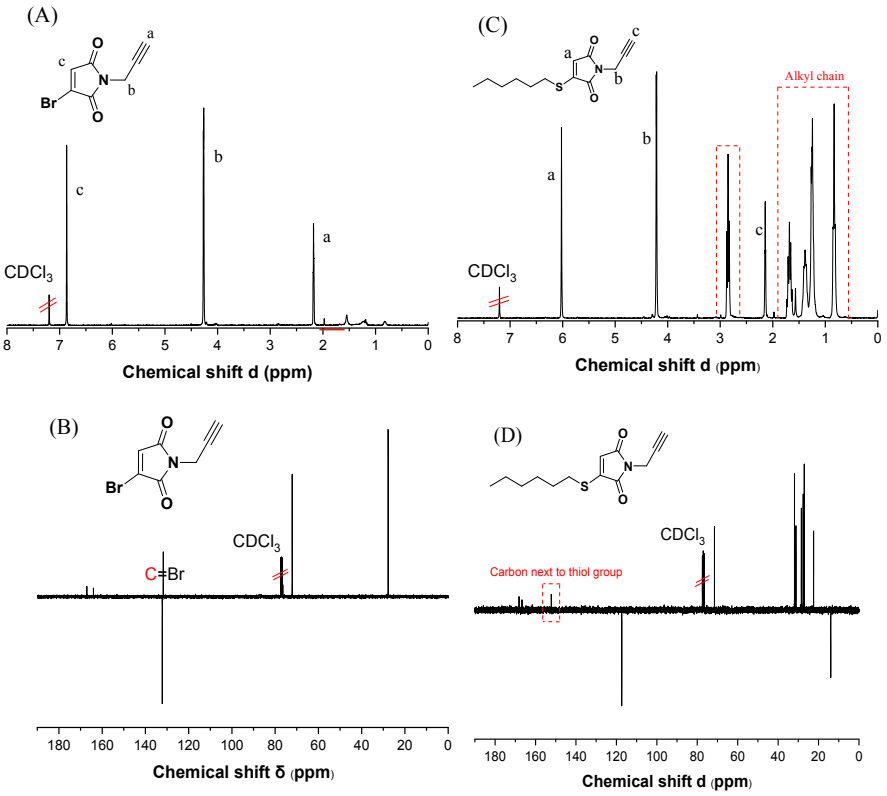


Fig S1. ^{1}H NMR of *N*-propargyl-3-monobromomaleimide (MBM) and *N*-propargyl-3-monothiohexylmaleimide (**1**) in $CDCl_3$ solvent. A) ^{1}H NMR of MBM, B) ^{13}C NMR of MBM, C) ^{1}H NMR of MTM, and D) ^{13}C NMR of MTM.

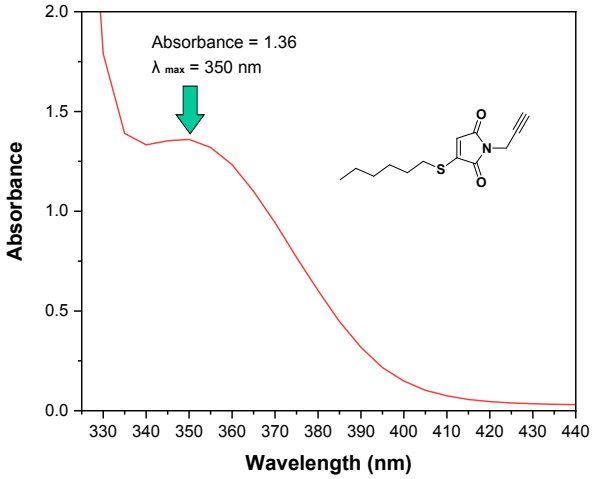


Fig S2. UV-Vis spectrum of **1** in CH_3CN.

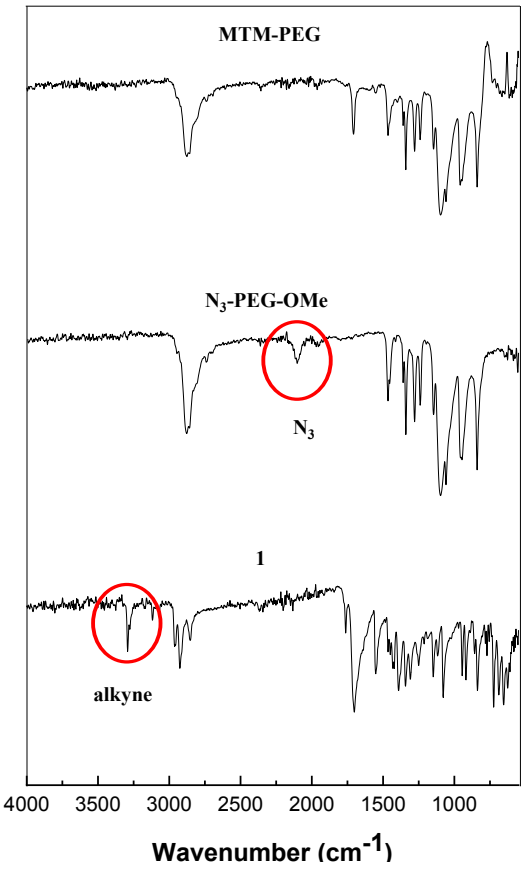


Fig S3. FTIR of **1**, **N_3-PEG-OMe** and **MTM-PEG**.

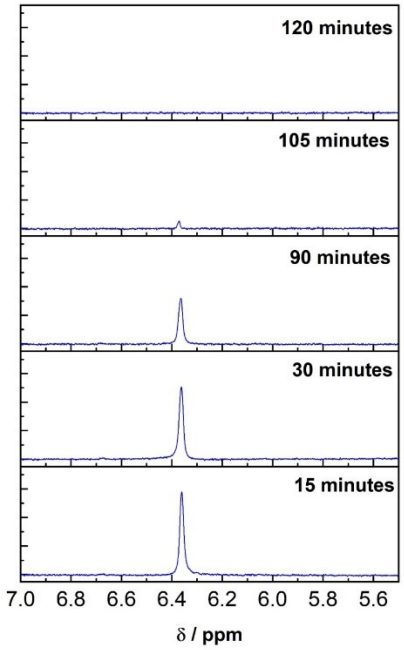


Fig S4. ^{1}H NMR (D_2O/CD_3CN) data following disappearance of the olefinic proton in **MTM-PEG** at 6.35 ppm using a commercially available UV nail gel curing lamp containing four 9 W bulbs (λ max ~ 365 nm) for irradiation.

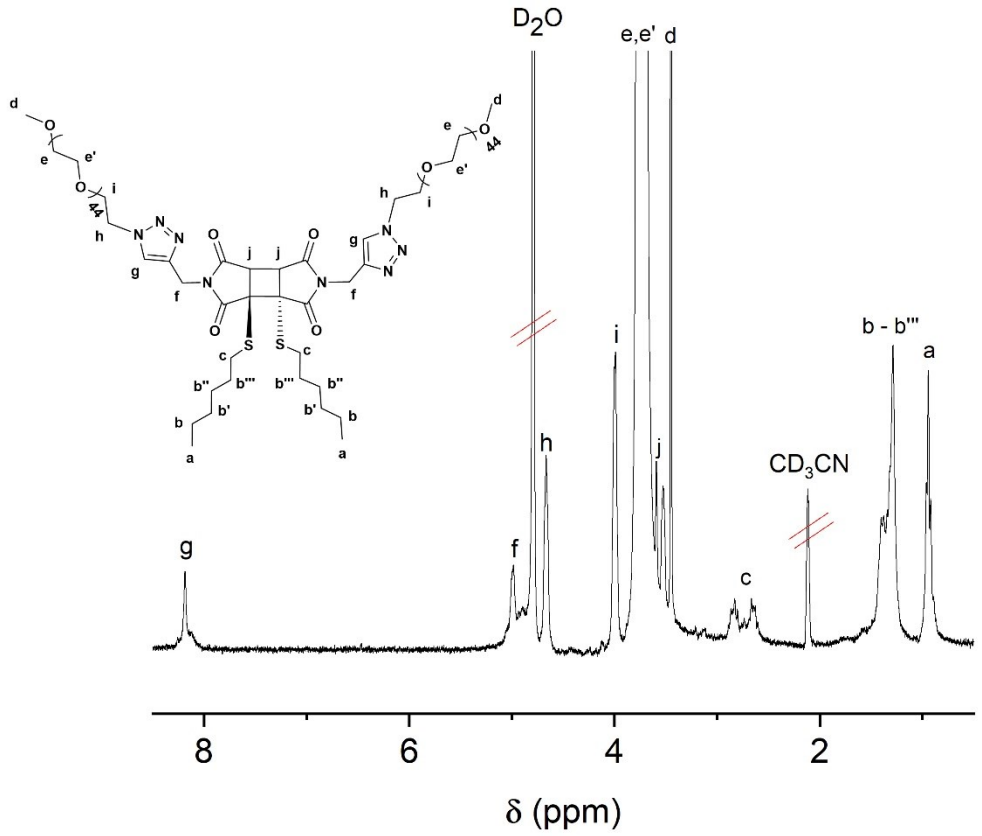


Fig S5. ^{1}H NMR (D_2O/CD_3CN) data of the **MTM-PEG** dimer after irradiation using a commercially available UV nail gel curing lamp containing four 9 W bulbs (λ max ~ 365 nm) for 120 mins.

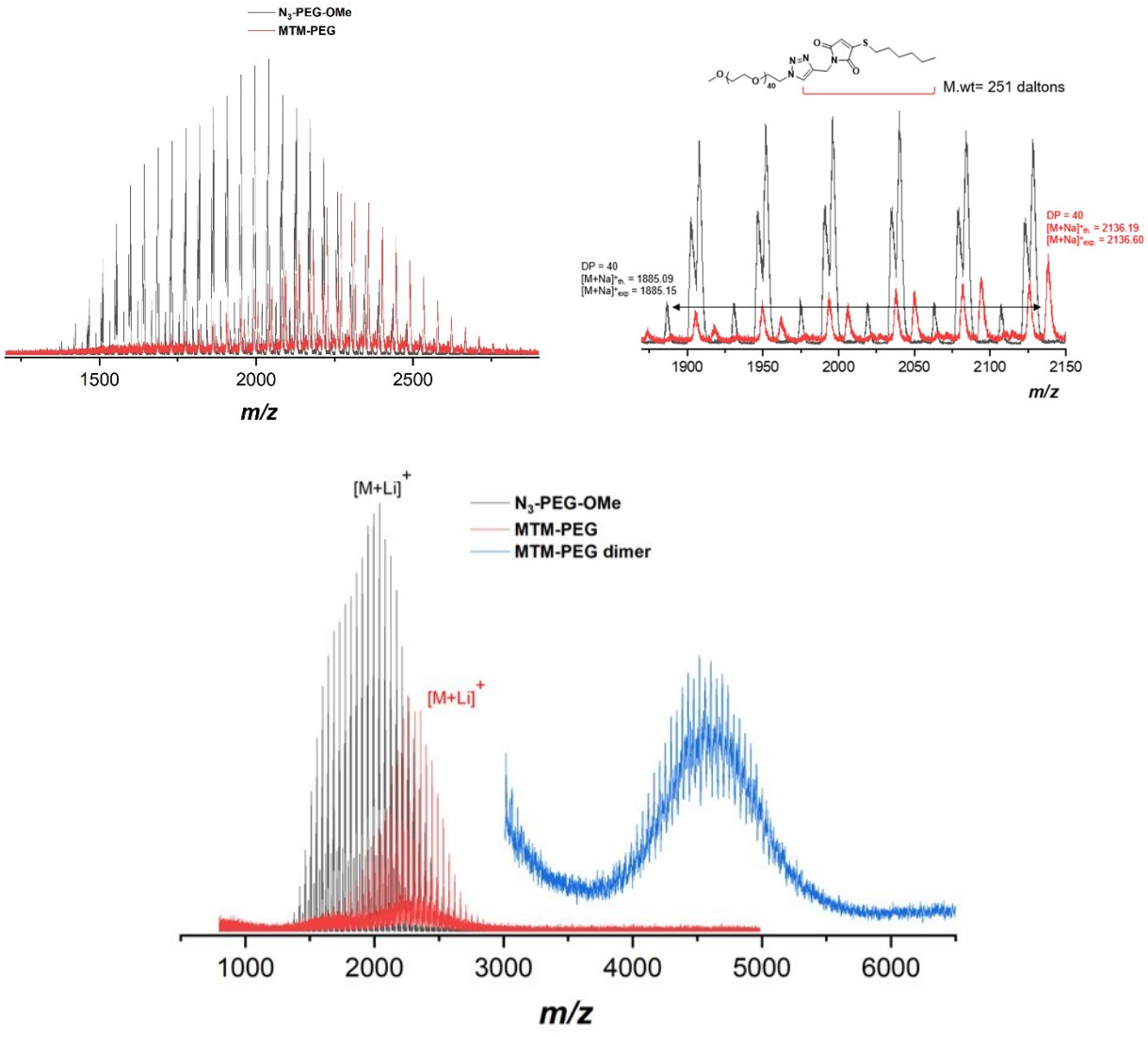


Fig S6. MALDI spectrum shows the differences in molecular weight distribution between **N_3-PEG-OMe** (black), **MTM-PEG** (red) and the resulting dimer (blue)

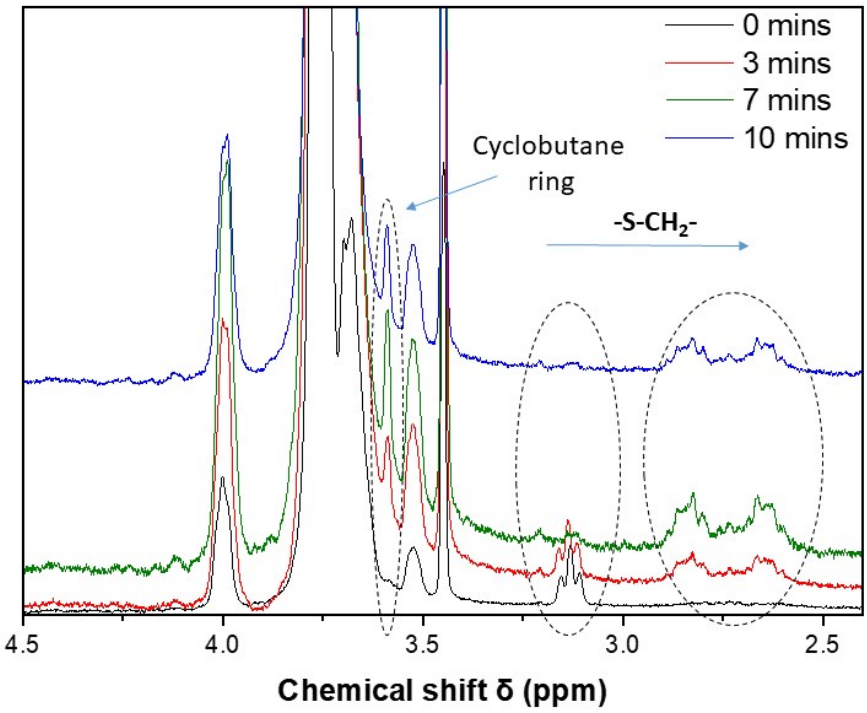


Fig S7. ^{1}H NMR (D_2O/CD_3CN) following the emergence of the signals associated with the cyclobutane motif and the methylene adjacent to the thio-group during the [2 + 2]-photodimerisation of **MTM-PEG** using Omnicure s2000, 200 W, λ = 320-390 nm.

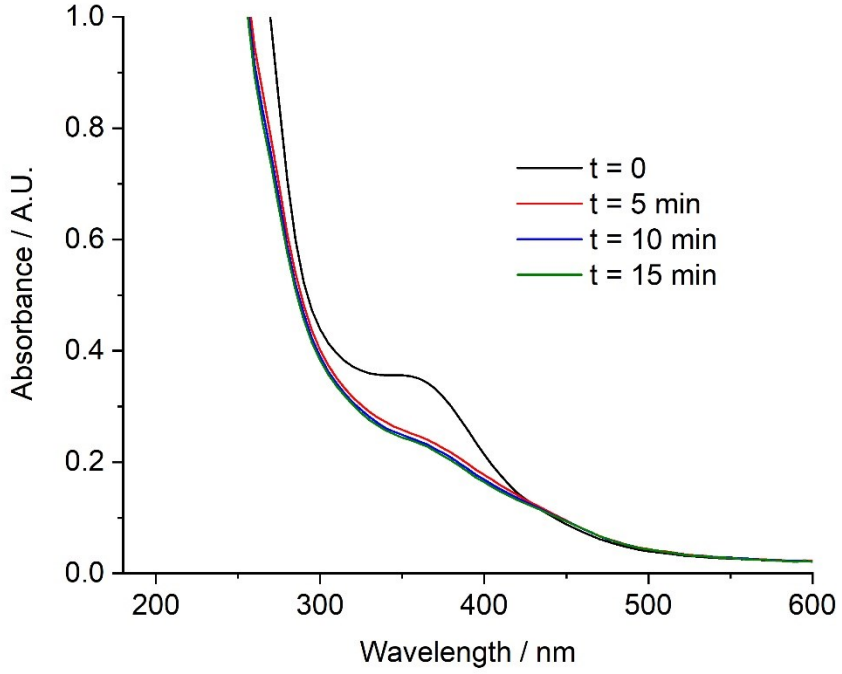


Fig S8. UV-vis spectroscopy following the consumption of the thiomaleimide group (λ ≈ 350 nm) during the [2 + 2]-photodimerisation of **MTM-PEG** using Omnicure s2000, 200 W, λ = 320-390 nm.

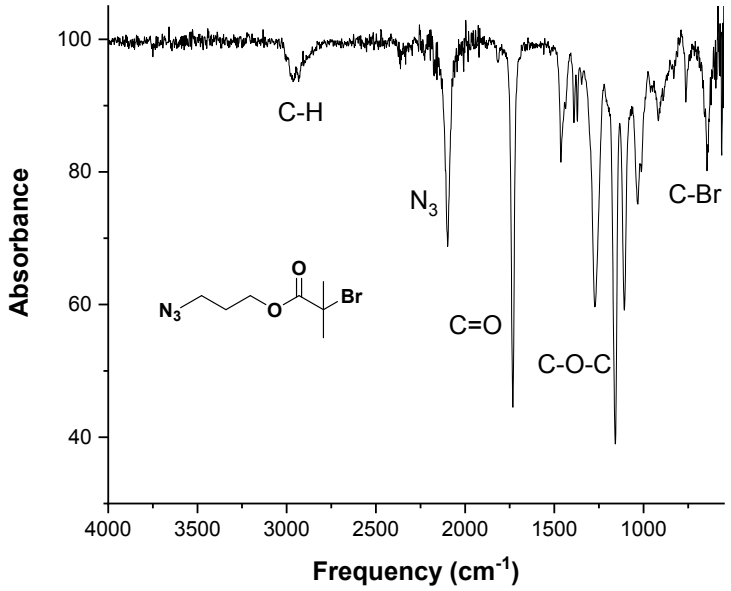


Fig S9: FTIR spectrum of 3-azidopropyl-2-bromoisobutyrate initiator.

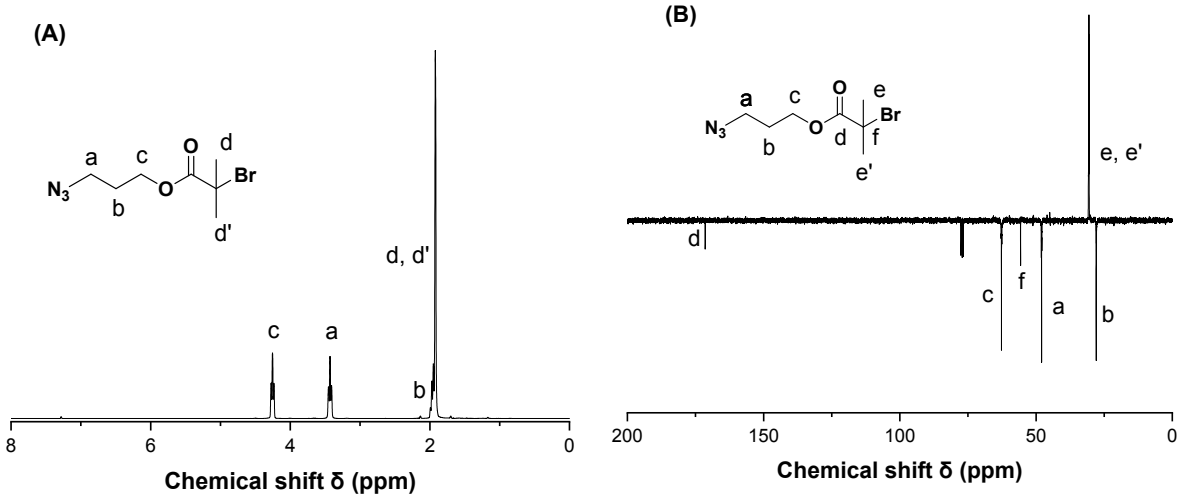


Fig S10: A) ^{1}H NMR and B) ^{13}C NMR of 3-azidopropyl-2-bromoisobutyrate initiator.

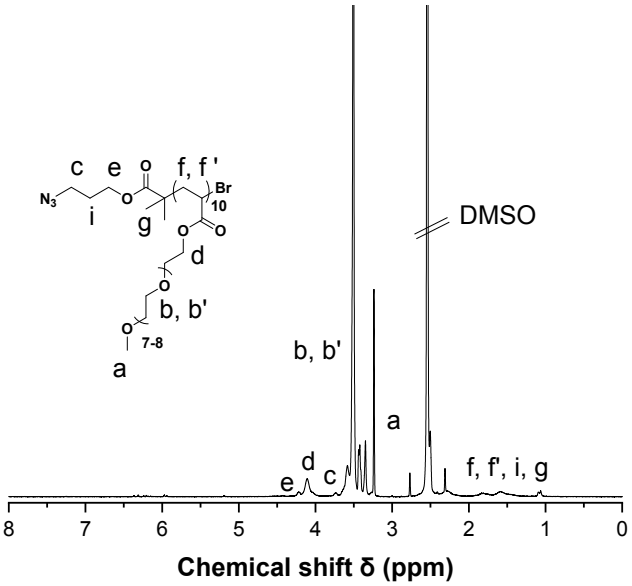


Fig S11: ^{1}H NMR (d_6-DMSO) of **N_3-POEGA$_{480}$** polymerised using 3-azidopropyl-2-bromoisobutyrate initiator.

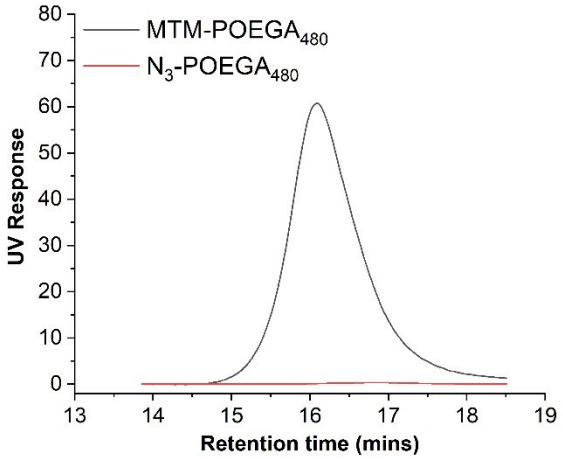


Fig S12. B) SEC UV traces of **N_3-POEGA$_{480}$** and **MTM-POEGA$_{480}$** (λ = 320 nm)

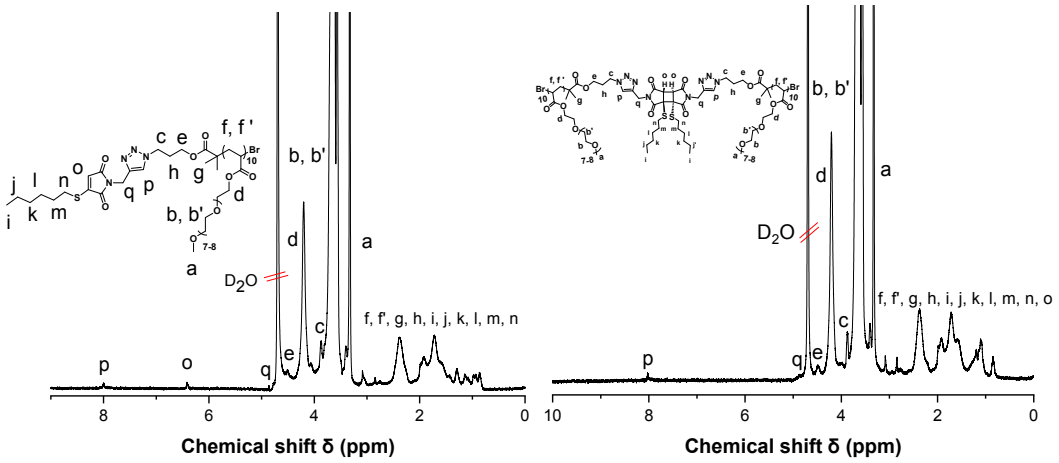


Fig S13: ^{1}H NMR (D_2O/CD_3CN) of **MTM-POEGA$_{480}$** and its dimer.

References

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