Supplementary Information (SI) for Polymer Chemistry.
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Supporting Information

for

On-Demand Degradable Thiol-Maleimide PEG Hydrogels as Abrasion-Free Adhesives

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1. Material and methods

1.1. Purchased materials

Poly(ethylene glycol) (PEG) (M_w = 1.5 kDa, 3.5 kDa and 7.5 kDa), potassium carbonate (K_2CO_3), sodium acetate (NaOAc), and methacrylic acid (MAA) were used as received from SHOWA. Sodium azide (NaN_3) (**DANGER, Highly toxic; exposure could be fatal**), 4-toluenesulfonyl chloride (TsCl) (**DANGER, corrosive**), 4-dimethylamino-pyridine (DMAP), and dimethylformamide (DMF) were used as received from Acros Organics. 2,3-dibromomaleimide (DBM), L-cysteine methyl ester hydrochloride (CME), and 2-hydroxy-4'-(2-hydroxyethoxy)-2-methylpropiophenone (Irgacure-2959) were used as received from Tokyo Chemical Industry. Triethylamine, propargyl bromide (**DANGER, Highly toxic; exposure could be fatal**), 2-mercaptoethanol, 1-(3-dimethylaminopropyl)-3-ethylcarbo-diimide hydrochloride (EDC·HCl), and thiophenol were used as received from Alfa Aesar. Copper(I) bromide (CuBr), *N,N,N',N'',N''*-penta-methyldiethylenetriamine (PMDETA), Poly(vinyl alcohol) (PVA, 85~98 kDa, 99% hydrolyzed), and gelatin (from porcine skin, 50 ~100 kDa, gel strength ~300 g Bloom) were used as received from Sigma Aldrich. Dichloromethane (DCM) was used as received from Seedchem. Acetone was used as received from Cecho. Phosphate-buffered saline (PBS) was prepared by dissolving Dulbecco's Phosphate-Buffered Saline powder from Thermal Fisher Scientific with water without further purification. Milli-Q water (18.2 MΩ cm) was used for all aqueous solutions in the experiments.

1.2. Analytical methods

^1H NMR spectra was recorded on Varian-500 spectrometer operated 500 MHz at 298 K. Chemical shifts are expressed in parts per million (ppm), and splitting patterns are designated as s (singlet), d (doublet), t (triplet), m (multiplet), b (broad), and combinations thereof. Scalar coupling constants J are reported in Hertz (Hz). ^1H and ^{13}C NMR spectra were referenced to residual monoproteo-solvent peaks as reported in literature.[1] The ultraviolet-visible (UV-vis) spectra was collected using a SHIMADZU UV-1800. The fluorescent spectra was recording using a JASCO FP-6500.

The *m/z* of organic compound was reported by using electrospray ionization mass spectrometry (ESI-MS) with VARIAN 901-MS (FT-ICR Mass) spectrometer. The mass number of polymeric products was conducted by using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) with Bruker Daltonics Autoflex III Smartbeam LRF 200-CID MALDI-TOF mass spectrometer (matrix: α-cyano-4-hydroxycinnamic acid, HCCA). Infrared spectra were recorded on a Bruker Vertex 80v FT-IR

Spectrometer.

2. Experimental procedures

2.1. Synthesis

Tosylated short chain length PEG (SC-PEG-OTs): A mixture of PEG (OH-PEG$_{28}$-OH, 2.00 g, 2.0 mmol) and 4-toluenesulfonyl chloride (2.00 g, 10.0 mmol) was dissolved in 50 mL of DCM. Triethylamine (1.40 mL, 10.0 mmol) was then slowly added to the mixture. The reaction was continuously stirred at room temperature under a nitrogen atmosphere for 24 hours. The reaction was quenched by adding 0.1 M hydrochloric acid (10 mL) and extracted with dichloromethane (3 × 25 mL). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The excess solvent was concentrated, and the crude product was precipitated by precipitation in cold diethyl ether, yielding a white product of **SC-PEG-OTs** with 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ2.42 ppm (s, 6H), 3.58-3.70 ppm (m, 124H), 7.31 ppm (d, J = 7.7 Hz, 4H), 7.76 ppm (d, J = 7.7 Hz, 4H).

Tosylated middle chain length PEG (MC-PEG-OTs): A mixture of di-hydroxyl terminated PEG (OH-PEG$_{68}$-OH, 5.00 g, 0.5 mmol) and 4-toluenesulfonyl chloride (1.57 g, 3.3 mmol) was dissolved in 25 mL of dichloromethane (DCM). Triethylamine (1.15 mL, 3.3 mmol) was then slowly added to the mixture. The reaction was continuously stirred at room temperature under a nitrogen atmosphere for 24 hours. The reaction was quenched by adding 0.1 M hydrochloric acid (10 mL) and extracted with dichloromethane (3 × 25 mL). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The excess solvent was concentrated, and the crude product was precipitated by precipitation in cold diethyl ether, yielding a white product of **MC-PEG-OTs** with 92% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ2.42 ppm (s, 6H), 3.58-3.70 ppm (m, 278H), 7.31 ppm (d, J = 7.7 Hz, 4H), 7.76 ppm (d, J = 7.7 Hz, 4H).

Tosylated long chain length PEG (LC-PEG-OTs): A mixture of di-hydroxyl terminated PEG (OH-PEG$_{170}$-OH, 2.00 g, 0.3 mmol) and 4-toluenesulfonyl chloride (1.02 g, 5.3 mmol) was dissolved in 10 mL of dichloromethane (DCM). Triethylamine (0.75 mL, 5.3 mmol) was then slowly added to the mixture. The reaction was continuously stirred at room temperature under a nitrogen atmosphere for 24 hours. The reaction was quenched by adding 0.1M hydrochloric acid (5 mL) and extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The excess solvent was concentrated, and the crude product was precipitated by precipitation in cold diethyl ether, yielding a white product of **LC-PEG-OTs** with 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ2.42 ppm (s, 6H), 3.58-3.70 ppm (m, 890H), 7.31 ppm (d, *J* = 7.7 Hz, 4H), 7.76 ppm (d, *J* = 7.7 Hz, 4H).

Diazido short chain length PEG (SC-PEG-N_3): A mixture of sodium azide (0.51 g, 8.7 mmol) and **SC-PEG-OTs** (1.28 g, 0.9 mmol) was dissolved in 85 mL of DMF. The solution was heated at 70 °C for 24 hours under a nitrogen atmosphere. The reaction mixture was then cooled to room temperature, and the excess DMF was removed. The crude product was dissolved in DCM, and the white solid was filtered out. The DCM solution was concentrated, and the crude product was further purified by precipitation with cold diethyl ether, yielding the white powder of **SC-PEG-N_3** with a 67% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 ppm (t, *J* = 3.4 Hz, 4H,), 3.58-3.70 ppm (m, 116H).

Diazido middle chain length PEG (MC-PEG-N_3): A mixture of sodium azide (7.8 mg, 0.12 mmol) and **MC-PEG-OTs** (50.0 mg, 0.012 mmol) was dissolved in 10 mL of DMF. The solution was heated at 70 °C for 24 hours under a nitrogen atmosphere. The reaction mixture was then cooled to room temperature, and the excess DMF was removed. The crude product was dissolved in DCM, and the white solid was filtered out. The DCM solution was concentrated, and the crude product was further purified by precipitation with cold diethyl ether, yielding the white powder of **MC-PEG-N_3** with a 41% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 ppm (t, *J* = 3.4 Hz, 4H,), 3.58-3.70 ppm (m, 278H).

Diazido long chain length PEG (LC-PEG-N_3): A mixture of sodium azide (65.0 mg, 1.0 mmol) and **LC-PEG-OTs** (295.0 mg, 0.05 mmol) was dissolved in 50 mL of DMF. The solution was heated at 70 °C for 24 hours under a nitrogen atmosphere. The reaction mixture was then cooled to room temperature, and the excess DMF was removed. The crude product was dissolved in DCM, and the white solid was filtered out. The DCM solution was concentrated, and the crude product was further purified by precipitation with cold diethyl ether, yielding the white powder of **LC-PEG-N_3** with a 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 ppm (t, *J* = 3.4 Hz, 4H,), 3.58-3.70 ppm (m, 278H).

***N*-propargyl-2,3-dithiomaleimide (*N*-propargyl-DBM):** A mixture of 2,3-dibromomaleimide (300.0 mg, 1.18 mmol) and anhydrous potassium carbonate (660.0 mg, 4.78 mmol) was dissolved in 20 mL of acetone. The solution was stirred at 0 °C for 30 minutes, then 3-bromopropyne (propargyl bromide, 0.26 mL, 2.91 mmol) was slowly added dropwise to the mixture. The reaction was continuously stirred at room temperature for 24 hours. The resulting brown solid was filtered, and the collected solution was concentrated. The crude product was purified by column chromatography using a 20% ethyl acetate/*n*-hexane eluent, yielding a white powder with a 58% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.24 ppm (t, J = 2.5 Hz, 1H), 4.35 ppm (d, J = 2.5 Hz, 2H).

***N*-propargyl-2,3- dithiomaleimide (DTM):** A mixture of ***N*-propargyl-DBM** (1130.0 mg, 3.85 mmol) and anhydrous sodium acetate (790.0 mg, 9.62 mmol) was dissolved in 20 mL of methanol. Then, 2-mercaptoethanol (0.68 mL, 9.62 mmol) was added dropwise to the mixture. The reaction was continuously stirred at room temperature for 4 hours. The completed reaction (TLC monitoring) was quenched by adding water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The excess solvent was concentrated, and the crude product was further purified by column chromatography using 30% ethyl acetate/n-hexane with 2% methanol, yielding a yellow liquid with a 63% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.24 ppm (t, J = 2.5 Hz, 1H), 3.48 ppm (t, J = 3.5 Hz, 4H), 3.83 ppm (t, J = 3.5 Hz, 4H), 4.35 ppm (d, J = 2.5 Hz, 2H).

***N*-propargyl-2,3-dithiomaleimide dimethacrylate (DTMDM):** A mixture of **DTM** and EDC·HCl (290.0 mg, 1.56 mmol) was dissolved in anhydrous DCM (8.00 mL) and stirred at 0 °C for 5 minutes. A solution of methacrylic acid (MAA, 0.63 mL, 7.45 mmol) and DMAP (6.0 mg, 0.05 mmol) in anhydrous DCM (2.00 mL) was then added to the mixture. The reaction was continuously stirred at 0 °C for 10 minutes, after which it was refluxed for 72 hours. The completed reaction (TLC monitoring) was allowed to cool to room temperature. The reaction was quenched by adding 5 mL of dichloromethane and 10 mL of water. The aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The crude product was purified by column chromatography using 10% ethyl acetate/n-hexane with 2% methanol, yielding a yellow liquid with 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ1.91 ppm (s, 6H), 2.24 ppm (t, J = 2.5 Hz, 1H), 3.48 ppm (t, J = 3.5 Hz, 4H), 3.83 ppm (t, J = 3.5 Hz, 4H), 4.35 ppm (d, J = 2.5 Hz, 2H), 5.57 ppm (*s*, 2H), 6.08 ppm (*s*, 2H). HRMS: *m/z* calc. for $C_{19}H_{21}NO_6S_2$+Na^+ 446.0539, found 446.0542.

Middle chain length thiol-maleimide-modified PEG (MC-TMPEG): The oxygen in a solution of **DTMDM** (135.0 mg, 0.32 mmol) and pentamethyldiethylenetriamine (PMDETA, 32 μL, 0.154 mmol) in 20 mL of DMF was removed by three freeze-pump-thaw cycles. Simultaneously, the oxygen in a mixture of CuBr (18.0 mg, 0.128 mmol) and **MC-PEG-N$_3$** (390 mg, 0.128 mmol) was removed by three vacuum/N_2 gas cycles. The solution was then added to the solid flask *via* a degassed syringe. The reaction was carried out at 60 °C for 72 hours. After cooling to room temperature, the residual copper complex was removed by passing through a neutral alumina oxide column. The solution was further purified using a dialysis bag with a molecular weight cutoff of 3,500, changing methanol six times over 48 hours. Deionized water was then used to remove the methanol through changing water four times over 24 hours, yielding a yellow powder with a 53% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ1.91 ppm (s, 12H), 3.58-3.70 ppm (m, 278H), 3.83 ppm (t, J = 3.5 Hz, 4H), 4.35 ppm (t, J = 3.5 Hz, 8H), 4.48 ppm (t, J = 3.5 Hz, 8H), 4.76 ppm (s, 4H), 5.54 ppm (*s*, 4H), 6.06 ppm (*s*, 4H), 7.72 (s, 2H).

Short chain length thiol-maleimide-modified PEG (SC-TMPEG): The oxygen in a solution of **DTMDM** (155.0 mg, 0.362 mmol) and pentamethyldiethylenetriamine (PMDETA, 90 μL, 0.434 mmol) in 30 mL of DMF was removed by three freeze-pump-thaw cycles. Simultaneously, the oxygen in a mixture of CuBr (31.0 mg, 0.220 mmol) and **SC-PEG-N$_3$** (207 mg, 0.144 mmol) was removed by three vacuum/N_2 gas cycles. The solution was then added to the solid flask *via* a degassed syringe. The reaction was carried out at 60 °C for 72 hours. After cooling to room temperature, the residual copper complex was removed by passing through a neutral alumina oxide column. The solution was further purified using precipitation with cold diethyl ether (2 times), yielding a yellow powder with a 62% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ1.91 ppm (s, 12H), 3.58-3.70 ppm (m, 112H), 3.83 ppm (t, J = 3.5 Hz, 4H), 4.35 ppm (t, J = 3.5 Hz, 8H), 4.48 ppm (t, J = 3.5 Hz, 8H), 4.76 ppm (s, 4H), 5.54 ppm (*s*, 4H), 6.06 ppm (*s*, 4H), 7.72 (s, 2H).

Long chain length thiol-maleimide-modified PEG (LC-TMPEG): The oxygen in a solution of **DTMDM** (125.0 mg, 0.288 mmol) and pentamethyldiethylenetriamine (PMDETA, 73 μL, 0.346 mmol) in 25 mL of DMF was removed by three freeze-pump-thaw cycles. Simultaneously, the oxygen in a mixture of CuBr (25.0 mg, 0.173 mmol) and **LC-PEG-N$_3$** (864.0 mg, 0.115 mmol) was removed by three vacuum/N_2 gas cycles. The solution was then added to the solid flask *via* a degassed syringe. The reaction was carried out at 60 °C for 72 hours. After cooling to room temperature, the residual copper complex was removed by passing through a neutral alumina oxide column. The solution was further purified using a dialysis bag with a molecular weight cutoff of 3,500, changing methanol six times over 48 hours. Deionized water was then used to remove the methanol through changing water four times over 24 hours, yielding a yellow powder with a 52% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ1.91 ppm (s, 12H), 3.58-3.70 ppm (m, 888H), 3.83 ppm (t, J = 3.5 Hz, 4H), 4.35 ppm (t, J = 3.5 Hz, 8H), 4.48 ppm (t, J = 3.5 Hz, 8H), 4.76 ppm (s, 4H), 5.54 ppm (*s*, 4H), 6.06 ppm (*s*, 4H), 7.72 (s, 2H).

2.2. The kinetics of the thiol exchange reaction

The thiol exchange reaction of **TMPEG** and thiol agent was kinetically investigated by the change of fluorescence emission in DI water and PBS with excitation 406 nm wavelength light source. Excess thiophenol and CME were added to a solution of **MC-TMPEG**, and aliquots of the mixture were periodically extracted for fluorescence spectroscopic analysis. The product was purified by a dialysis (molecular weight cutoff of was 3.5 kDa) again PBS three times before subjecting to a ^{1}H NMR characterization.

2.3. Preparation of the hydrogels

The hydrogels were prepared with an overall 20% w/v solid content by dissolving the mixture in PBS solution at room temperature. Subsequently, 1% w/v Irgacure-2959, a photo initiator, was added to the mixture. The solution was heated at 70 °C for 5 minutes and then cured under a 365 nm UV/Vis lamp with a light intensity of 6 W/cm² for gelation. The resulting gels were purified by pouring deionized water over them. The purified hydrogels were freeze-dried for 24 hours and then immersed in deionized water.

2.4. Swelling ratio test

The hydrogel was prepared and purified. Then, it was freeze-dried for 24 h. The lyophilized hydrogel was first weighed (W_I), followed by soaking in PBS solution for 24 h and weight again (W_S). The swelling ratio (%) of hydrogel was calculated using equation 1.

$$\text{Swelling capacity (\%)} = (W_S - W_I)/W_I \times 100 \qquad (1)$$

All measurements were performed in triplicates and the standard deviation is reported.

2.5. Degradation test

To evaluate the degradation rate of the hydrogels, 200 μL of each sample was prepared in 2.00 mL vials. Following complete gelation, the hydrogels were removed, purified, and freeze-dried for 24 hours. The initial dry weight of each sample was recorded as (W_0). Subsequently, the samples were immersed in 3 mL of 0.3 M CME in PBS and incubated at 100 rpm. On days 1, 2, 3, 4, and 5, post-immersion, the hydrogels were collected, freeze-dried for 24 hours, and their weights (W_i) were recorded. The degradation rate was determined using Equation 2.

$$\text{Remaining weight (\%)} = (W_i)/(W_0) \text{ x } 100 \qquad (2)$$

All measurements were performed in triplicates and the standard deviation is reported

2.6. Cell cytotoxicity test

Cytotoxicity of the hydrogels was estimated using an antiproliferation assay using the Cell Counting Kit-8 (CCK-8; Dojindo, Japan). The CCK-8 employs a highly water-soluble WST-8 salt, which is reduced to a water-soluble formazan dye in the presence of the electron mediator, 1-methoxy PMS. This reduction process, facilitated by cellular dehydrogenases, results in the formation of an orange-colored formazan dye. The quantity of formazan dye produced is directly proportional to the number of viable cells. The cell line used here was the human peripheral blood mononuclear cell line THP-1 was cultured in Roswell Park Memorial Institute 1640 medium (RPMI; Gibco) supplemented with 10% fetal bovine serum (Gibco, Lafayette, U.S.A.). The cells were cultured in T75 cell culture flasks at 37°C with 5% CO_2. To conduct the viability test, cells were first seeded into 12-well flat-bottom clear plates (Greiner Bio-One, Austria) at a density of 10^5 cells per well with RPMI medium supplemented with 10% heat-inactivated FBS. The cells were then incubated at 37°C in a 5% CO_2 environment for 24 hr. Subsequently, 2 mg of the hydrogel samples were prepared by first rinsing them with 75% ethanol and then washing them twice with PBS. The prepared hydrogel was then placed in each well for an additional 24 h incubation period. To prevent bacterial growth interference, all cells were treated with 50 µg/mL Gentamicin (Bio Basic, Markham, ON, Canada). Following this, 10 µL of CCK-8 solution was added to the cell culture medium, and the cells were further incubated under a 5% CO_2 atmosphere at 37°C for 2 hr. Finally, the absorbance at 460 nm for each well was quantified using a VersaMax microplate reader (Molecular Devices, USA).

3. Supplementary figures referenced in the main text

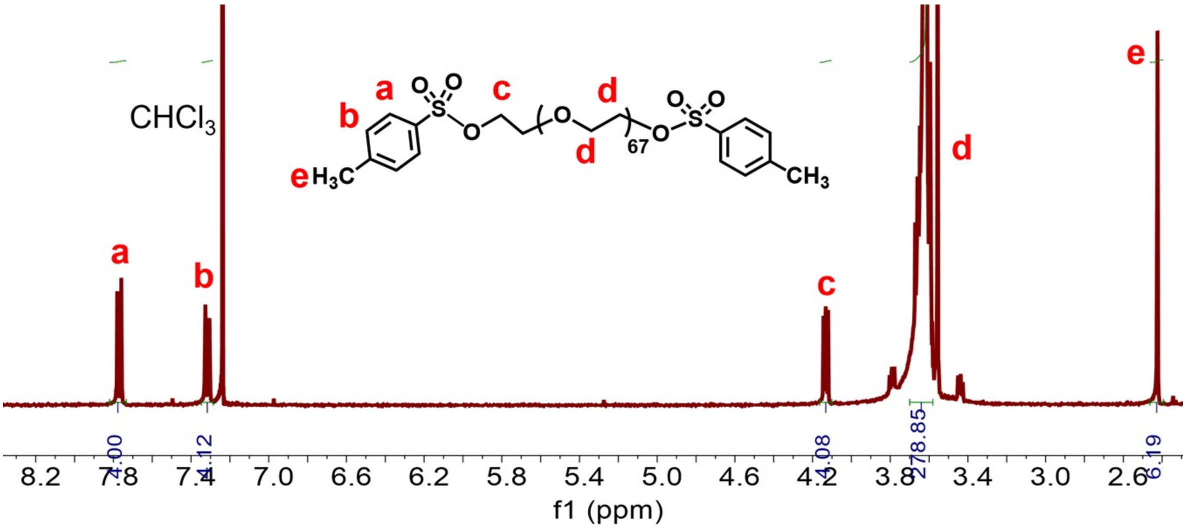

Figure S1. ^{1}H NMR specrtrum of **MC-PEG-OTs** in $CDCl_3$.

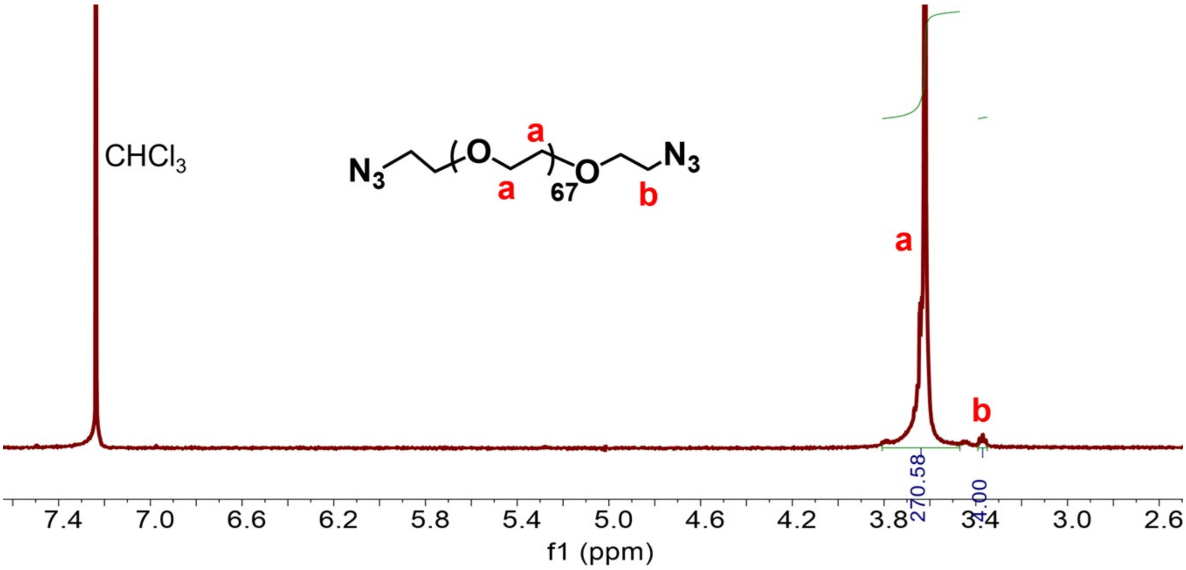

Figure S2. ^{1}H NMR specrtrum of **MC-PEG-N_3** in $CDCl_3$.

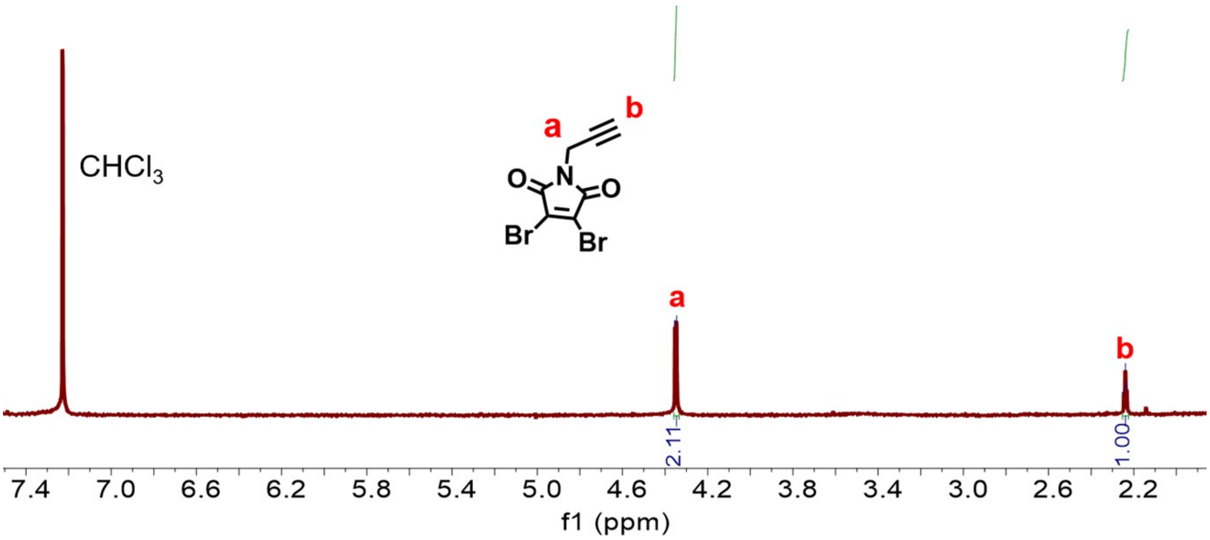

Figure S3. ^{1}H NMR specrtrum of **alkynyl DBM** in CDCl$_3$.

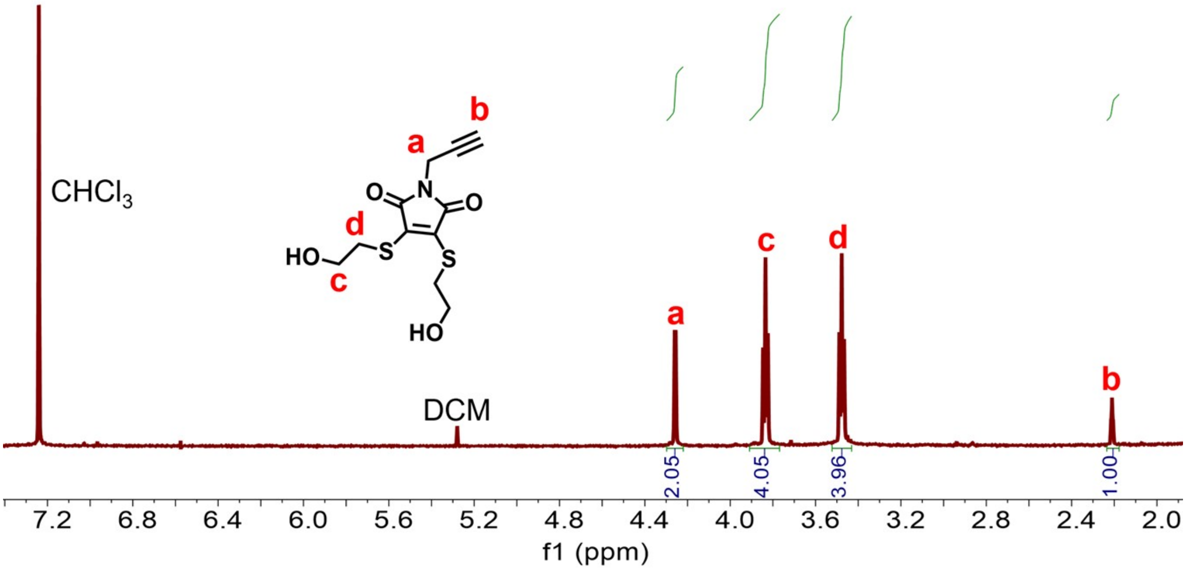

Figure S4. ^{1}H NMR spectrum of **DTM** in CDCl$_3$.

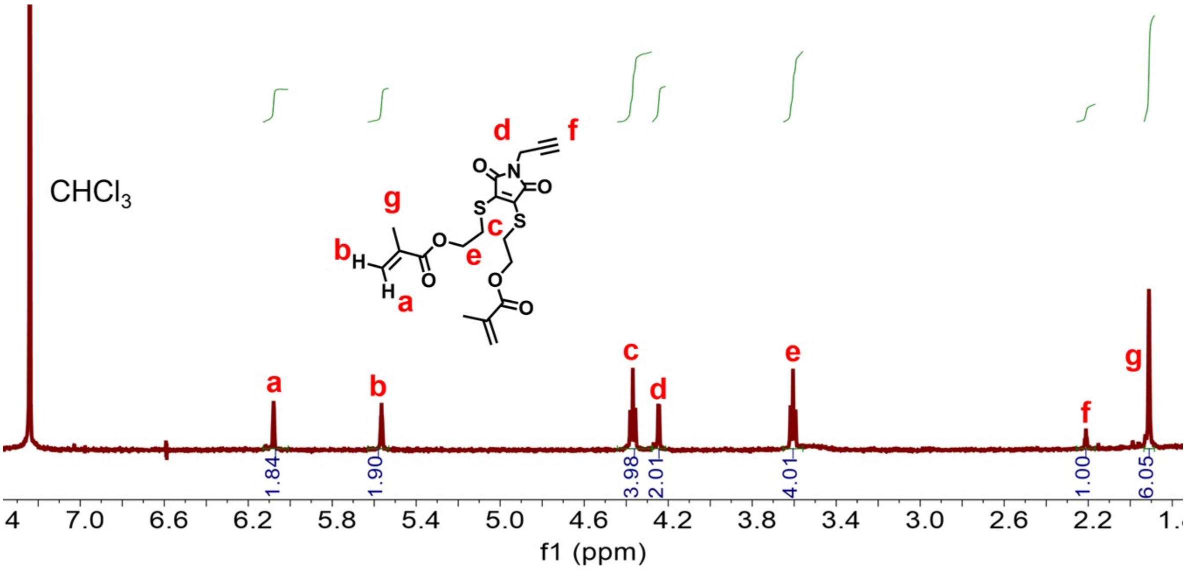

Figure S5. ^{1}H NMR spectrum of **DTMDM** in $CDCl_3$.

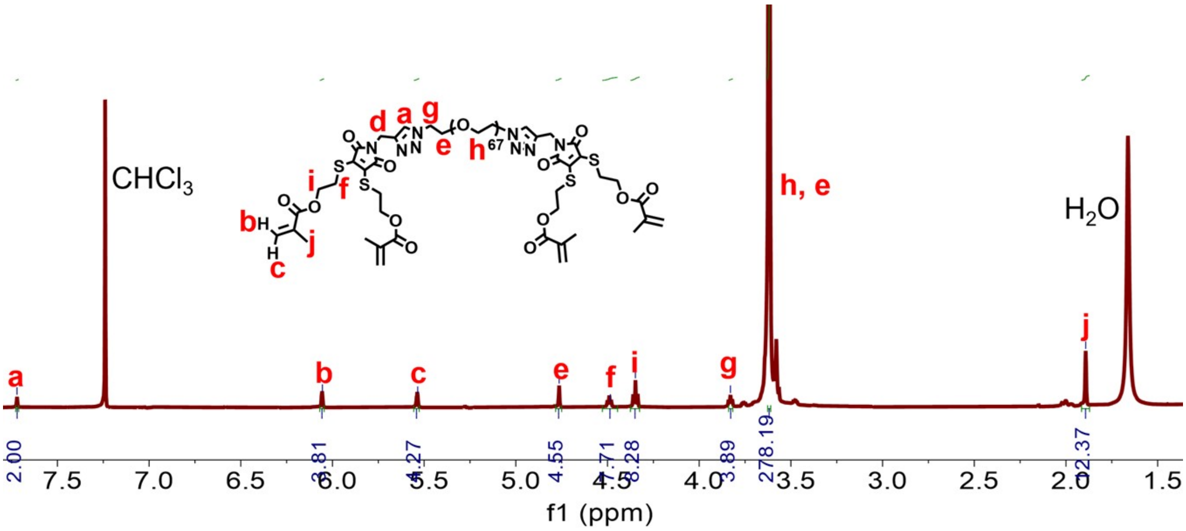

Figure S6. ^{1}H NMR spectrum of **MC-TMPEG** in $CDCl_3$.

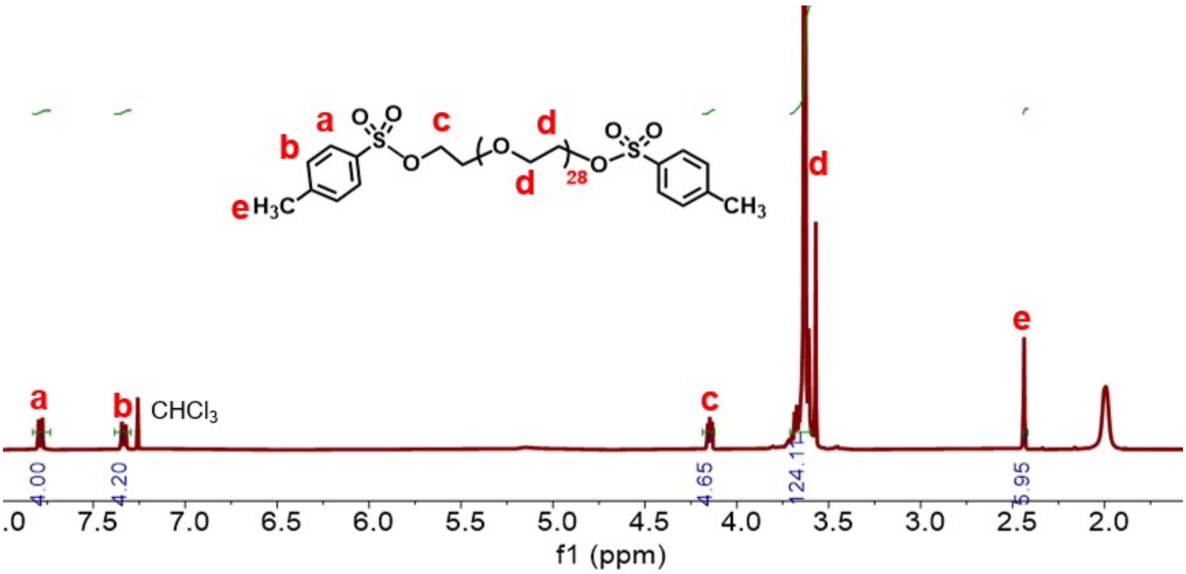

Figure S7. ^{1}H NMR specrtrum of **SC-PEG-OTs** in $CDCl_3$.

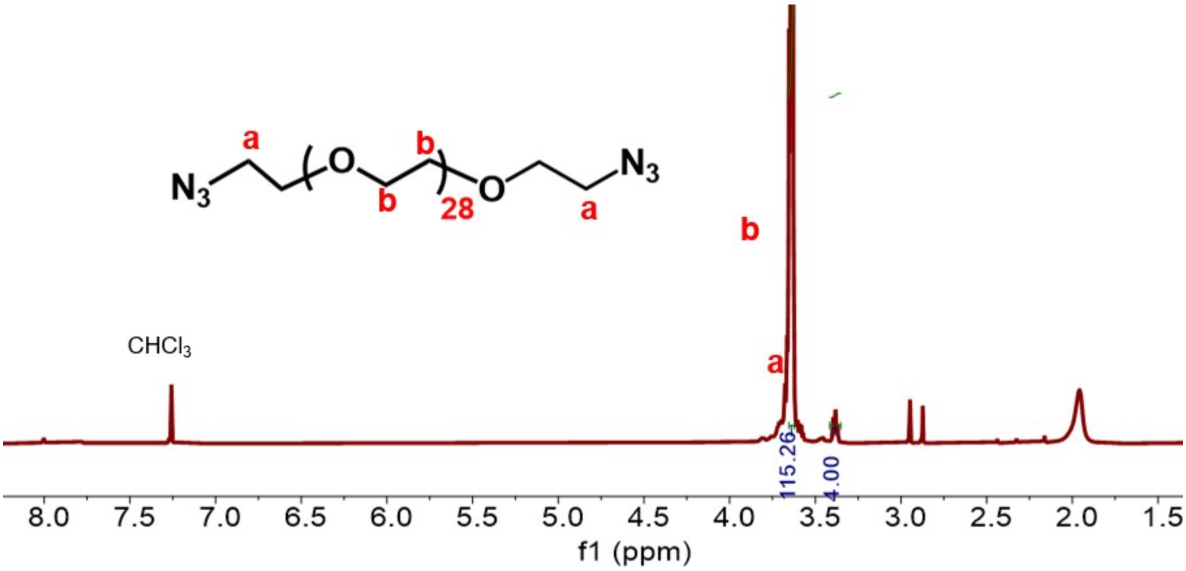

Figure S8. ^{1}H NMR specrtrum of **SC-PEG-N_3** in $CDCl_3$.

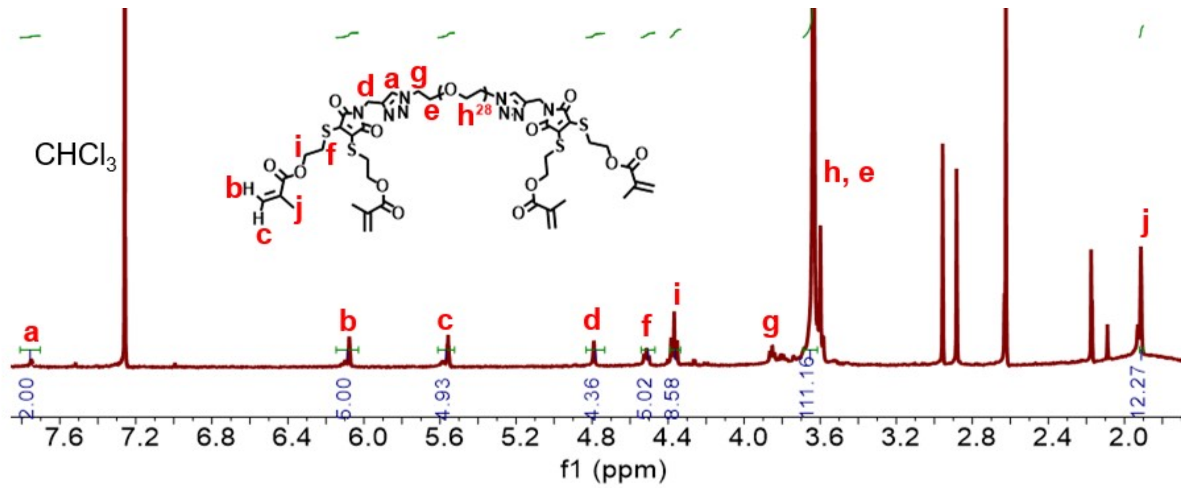

Figure S9. ^{1}H NMR spectrum of **SC-TMPEG** in $CDCl_3$.

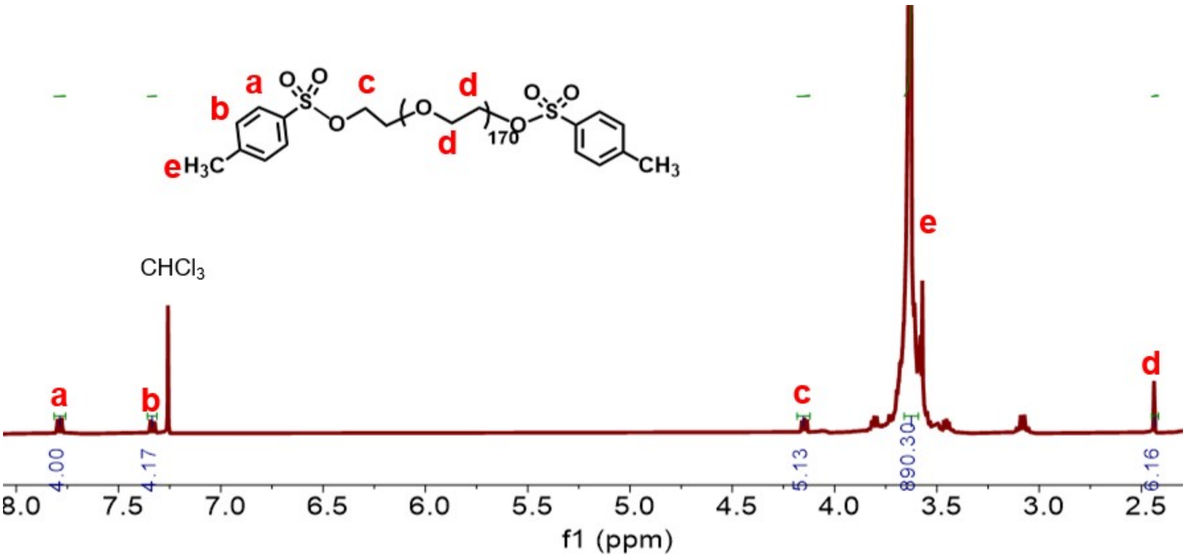

Figure S10. ^{1}H NMR specrtrum of **LC-PEG-OTs** in $CDCl_3$.

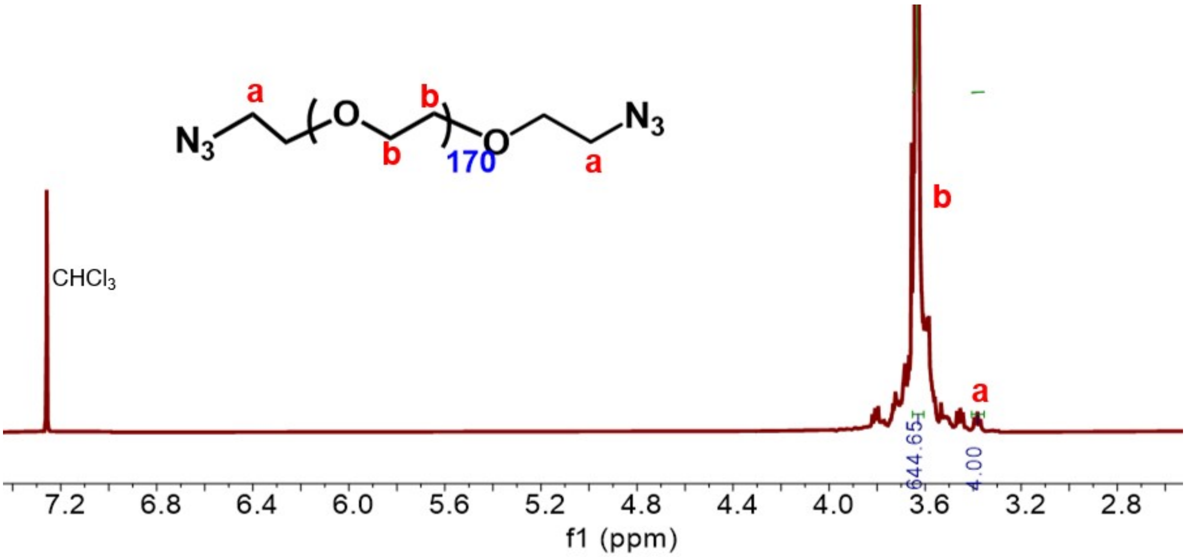

Figure S11. ^{1}H NMR specrtrum of **LC-PEG-N$_3$** in CDCl$_3$.

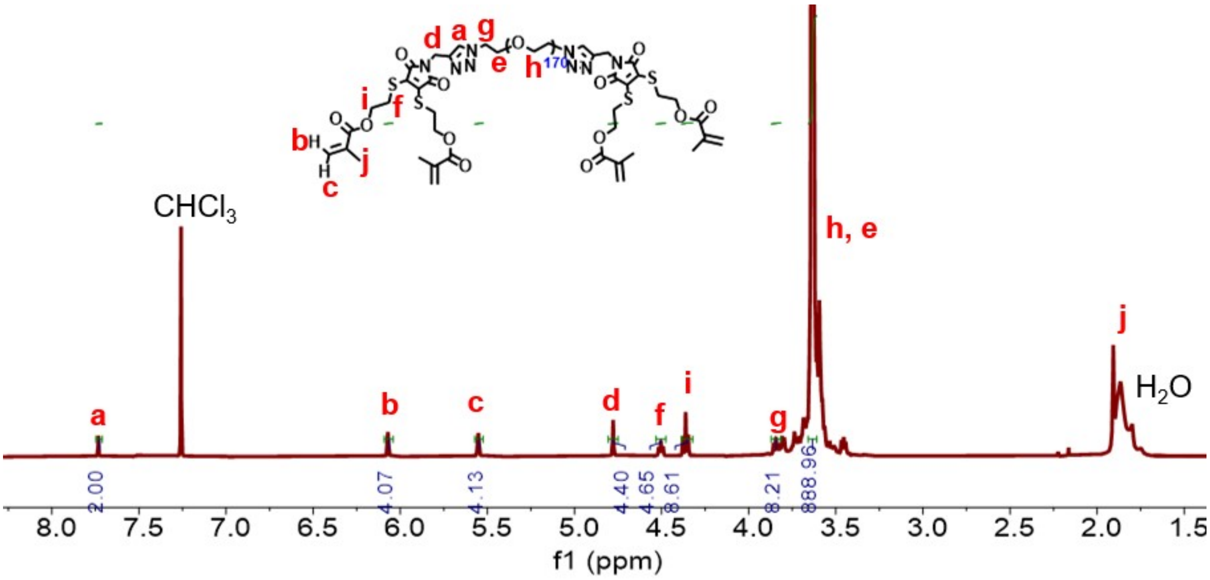

Figure S12. ^{1}H NMR spectrum of **LC-TMPEG** in CDCl$_3$.

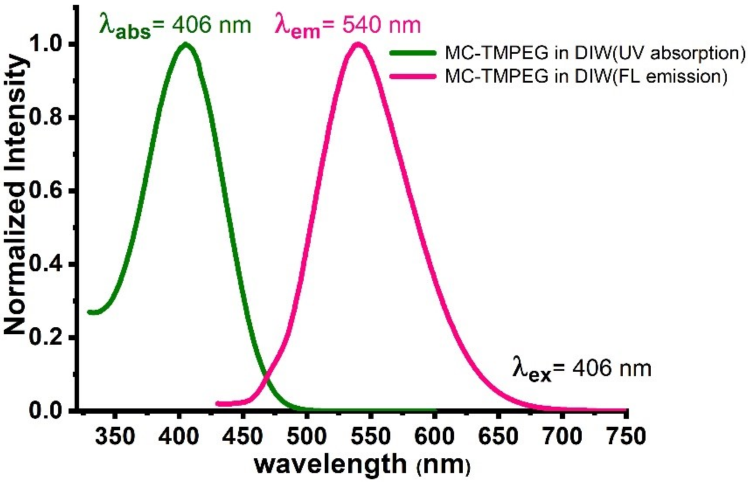

Figure S13. UV/vis absorption and emission spectreum of **MC-TMPEG** in DI-water.

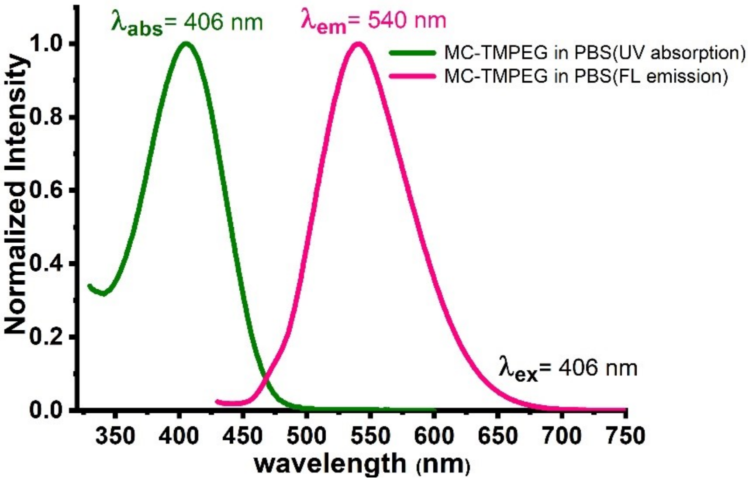

Figure S14. UV/vis absorption and emission spectreum of **MC-TMPEG** in PBS.

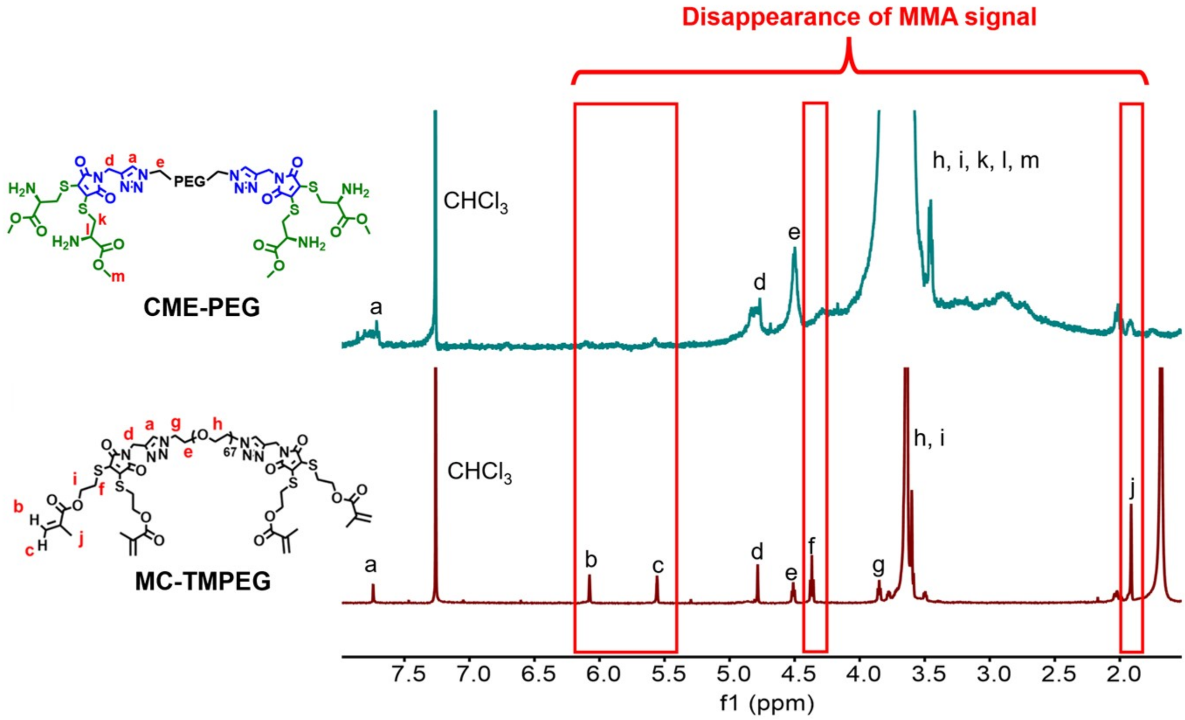

Figure S15. ^{1}H NMR specrtra of **CME-PEG** (up) and **MC-TMPEG** (down) in $CDCl_3$.

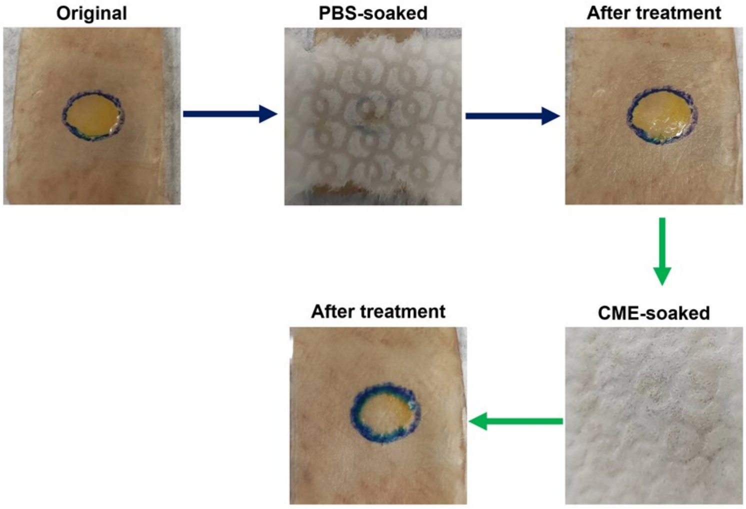

Figure S16. representative images of **LC-TMPEG** hydrogel after a treatment of PBS-impregnated fabric and then CME-impregnated fabric

4. References

(1) Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. NMR Chemical Shifts of Trace Impurities: Common

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