Supporting information

Self-healing hydrogel based on multivalent H-bonding

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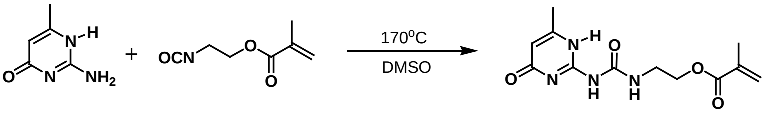
Experimental

Materials and methods.

2-Isocyanatoethyl methacrylate (98%, Aldrich), allyl isocyanate (98%, Aldrich), 2-nitrobenzyl chloride (99%, Aldrich), hexamethyldisilazane (HMDS, 99%, Aldrich), triethoxysilane (99%, Aldrich), $H_2PtCl_6.xH_2O$ (38% Pt basis, Sigma), and 6-methylisocytosine (MIS, 99%, Acros) were used as received. 2-(Dimethylamino)ethyl methacrylate (DMAEMA, 98%, Aldrich), 2-hydroxyethyl methacrylate (HEMA, 97%, Aldrich), 2-(2-methoxyethoxy)ethyl methacrylate (MEO2MA, 95%, Aldrich), N-isopropylacrylamide (NIPAm, 98%, Aldrich), N,N'-dimethylacrylamide (DMAA, 99%, Aldrich), and N,N'-methylene bisacrylamide (MBA, 99%, Aldrich) were passed through silica column to remove inhibitor before use. All other reagents and solvents were used as obtained unless otherwise specified.

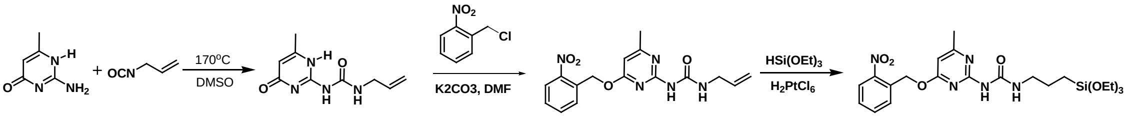
Solution ^1H and ^{13}C spectra were measured in $CDCl_3$ or DMSO-d_6 solution at 25 ºC on a Bruker Ultra Shield 250 MHz spectrometer. UV spectra were recorded on a Varian Cary 4000 UV-vis spectrometer (Varian Inc. Palo Alto, CA). Mass spectra were recorded on a Micromass Finnigan-MAT ZAB-HS mass spectrometer. Gel permeation chromatography (GPC) was performed with a polymer standard service (PSS) equipped with WinGPC. RI ERC 7512(ERMA Inc.) and UV–Visible S-3702(SOMA) were used as detectors. Tetrahydroforan (THF) was employed as eluent at a flow rate of 1.0 mL/min at 60 ºC and columns SDV from PSS (100, 103, 104, and 106 A° porosity; 10 mm bead size; dimensions of 0.8-30 cm). GPC curves were calibrated against polystyrene standards. Microscopy pictures were recorded on a Zeiss Axioskop polarizing light microscope equipped with a Linkam TMS 91/THMS 600 heating stage.

Synthesis



Scheme S1: Synthesis of SCMHBMA monomer

2-(3-(6-Methyl-4-oxo-1,4-dihydropyrimidin-2-yl)ureido)ethyl methacrylate (SCMHBMA).[1]
6-Methylisocytosine (MIS, 2.0 g, 16.0 mmol) was added to 50mL of DMSO and heated up to 170 °C for 10 min. Once the solid dissolved, the oil bath was removed. 2-Isocyanatoethyl methacrylate (2.75 g, 17.7 mmol) was added immediately to the flask under vigorous stirring. The mixture was quickly cooled using a water bath. A fine white solid precipitated upon cooling. The precipitate was collected and washed with excess acetone and dried under vacuum to obtain 4.03 g of a white solid (yield 90%). ^{1}H NMR (250 MHz, DMSO-d6, δ_{ppm}): 1.89 (s, 3H, CH_3), 2.11 (s, 3H, $ArCH_3$), 3.43-3.50 (m, 2H, $NHCH_2$), 4.15-4.20 (t, 2H, OCH_2), 5.70-5.72 (m, 1H, $C{=}CH_2$), 5.79 (s, 1H, aromatic ring), 6.07(s, 1H, $C{=}CH_2$), 7.60 (s, 1H, NH), 9.79 (s, 1H, NH), 11.43 (s, 1H, NH).



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Scheme S2: Synthesis of the UPy-based silane coupling agent

1-(3-(6-Methyl-4-oxo-1,4-dihydropyrimidin-2-yl)ureido)prop-2-ene (2)
6-Methylisocytosine (MIS, 1.0 g, 8.0 mmol) was added to 25mL of DMSO and heated up to 170 °C for 10 min. Once the solid dissolved, the oil bath was removed. Allyl isocyanate (0.66 g, 8.0 mmol) was added immediately to the flask under vigorous stirring. The mixture was quickly cooled using a water bath. A fine white needle crystal precipitated upon cooling. The precipitate was collected and washed with excess acetone and dried under vacuum to obtain 1.60 g of a white solid (yield 96%). ^{1}H NMR (250 MHz, DMSO-d$_6$, δ_{ppm}): 2.11 (s, 3H, $ArCH_3$), 3.77-3.82 (m, 2H, $NHCH_2$), 5.09-5.22 (m, 1H, $CH{=}CH_2$), 5.79 (s, 1H, aromatic ring), 5.80-5.93(m, 1H, $CH{=}CH_2$), 7.70 (s, 1H, NH). ^{13}C NMR (63 MHz, DMSO-d$_6$, δ_{ppm}): 23.24, 41.40,

64.24, 99.38, 114.48, 124.87, 129.25, 129.52, 131.76, 134.11 , 135.49, 147.31, 153.71, 157.51, 167.95, 169.00 (16C). EIMS *m/z*: 209 $[MH]^+$. Melt point: 248 °C (crystal from DMSO)

1-(3-(4-Methyl-6-((2-nitrobenzyl)oxy)pyrimidin-2-yl)ureido)prop-2-ene (3)

To a mixture of **2** (1.0g, 5 mmol) and K_2CO_3 (1.38g, 10 mmol) in 25 mL of dry DMF, 2-nitrobenzyl chloride (1.03g, 6 mmol) was added. The mixture was stirred at 90 °C for 12 h. The solution was poured into 200 mL water and then extracted with ethyl acetate. The organic layer was dried over with anhydrous $MgSO_4$. Afterwards the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel using dichloromethane/ethyl acetate (10/1, v/v) as eluent. 1.38g yellow solid was obtained (yield 80%). ^1H NMR (250 MHz, DMSO-d_6, δ_{ppm}): 2.31 (s, 3H, $ArCH_3$), 3.81-3.85 (m, 2H, $NHCH_2$), 5.04-5.19 (m, 2H, $CH{=}C\mathit{H}_2$), 5.72 (s, 2H, $ArCH_2$), 5.84-5.95 (d, 1H, $C\mathit{H}{=}CH_2$), 6.46 (s, 1H, Ar), 7.61-7.65 (m, 1H, Ar), 7.74-7.78 (m, 2H, Ar), 8.12-8.15 (d, 1H, Ar), 9.18-9.22 (t, 1H, NH), 9.61 (s, 1H, NH). ^{13}C NMR (63 MHz, DMSO-d_6, δ_{ppm}): 23.04, 41.24, 104.50, 115.17, 134.96 , 151.25, 157.78, 161.39, 164.62 (9C). EIMS *m/z*: 344 $[M\,H]^+$. Melt point: 128 °C.

3-(3-(4-Methyl-6-((2-nitrobenzyl)oxy)pyrimidin-2-yl)ureido)propyl-triethoxylsilane (1)

In a previously HMDS-passivated dry, round-bottomed flask, **3** (0.5 g, 1.46 mmol) and triethoxysilane (3.6 g, 21.6 mmol) were heated to 80 °C under an argon atmosphere. H_2PtCl_6 isopropanolic solution (100 μL, 0.03 mg/μL) was added and the mixture was stirred for 4 h at 80 °C. After the reaction, excess triethoxysilane was removed in vacuum, and the solid residue was taken up in dichloromethane and filtered through Celite500. The filtrate was concentrated under reduced pressure and determined to be **1** in a 45% mixture with the reduced compound. ^1H NMR (250 MHz, $CDCl_3$, δ_{ppm}): 0.59-0.65 (t, 2H, $SiCH_2$), 1.12-1.21 (m, 9H, CH_3), 1.59-1.62 (m, 2H, $SiCH_2C\mathit{H}_2$), 2.31 (s, 3H, $ArCH_3$), 3.20-3.31 (m, 2H, $NHCH_2$), 3.64-3.84 (m, 6H,

OCH_2), 5.68 (s, 2H, $ArCH_2$), 6. 21 (s, 1H, Ar), 6.97 (s, 1H, NH), 7.42-7.47 (m, 1H, Ar), 7.57 (m, 2H, Ar), 8.03-8.06 (d, 1H, Ar), 9.12 (s, 1H, NH). EIMS *m/z*: 508 $[M H]^+$

Copolymerization

DMAEMA (467 mg, 2.97 mmol) and SCMHBMA (72 mg, 0.26 mmol) were dissolved in 2 mL 1,4-dioxane. After purged with continuous N_2 for 10 min, AIBN (5 mg) was added and then the mixture was stirred at 70 ^oC for 10h. The solution was dilute with 15 mL 1,4-dioxane, following by precipitating in 400 mL hexane/chloroform (9/1, v/v). The precipitate was collected by filter and then dried under vacuum at 40 ^oC for 6 h. 485 mg white solid were obtained. Yield 90%.

Specify characterization, calculation of copolymer composition, indicate NMR spectra below.

Quartz crystal microbalance with dissipation monitoring (QCM-D)

The substrates (QCM-D crystal coated by silicon) were cleaned by plasma oxidation for 10 min using a gas mixture of oxygen and argon (1:9) and then immersed in siloxane derivative THF solution (1wt%) containing 0.01% 1 M NaOH aqueous solution for 2h. After washed with THF and water, the silicon substrates were baked at 90 ^oC for 1 h. Irradiation experiments were carried out using LED-UV light of 365 nm (PolychromeV lamp (TILL Photonics GmbH, Grafelfing, Germany), 4.7 μW cm^{-2}, irradiation time: 1.5h). QCM-D measurements (frequency change Δf and dissipation factor D) were carried out in a Q-Sense E1 system (Sweden). A silica-coated crystal was used (Q-Sense, Sweden). The crystal was excited at its fundamental frequency (5 MHz), and measurements were performed at the first, third, fifth, seventh, ninth, and thirteen overtones, corresponding to 5, 15, 25, 35, 45, and 55 MHz. Chloroform or 10 mM Tris·HCl aqueous solution (pH 8) without/with copolymer at concentrations of 2 mg/mL were used as flow mediums.

Preparation of covalent crosslinked hydrogel

To a mixture of SCMHBMA (180 mg), DMAEMA (1 g), and MBA (20 mg) in 4 mL 2 M HCl aqueous1 solution, 0.2 mL $Na_2S_2O_8$ solution (40 mg/mL) was added and then the mixture was heated up to 70 ^oC in a sealed tube for 20h, leading to a hydrogel. Resulting hydrogel was immersed in saturated $NaHCO_3$ aqueous solution (100 mL) for 48 h before further measurement.

An equivalent strategy was used for HEMA, NIPAm, MEO2MA, and DAMM

Figure S1. ^{1}H NMR spectra of SCMHBMA in DMSO-d_6 or $CDCl_3$

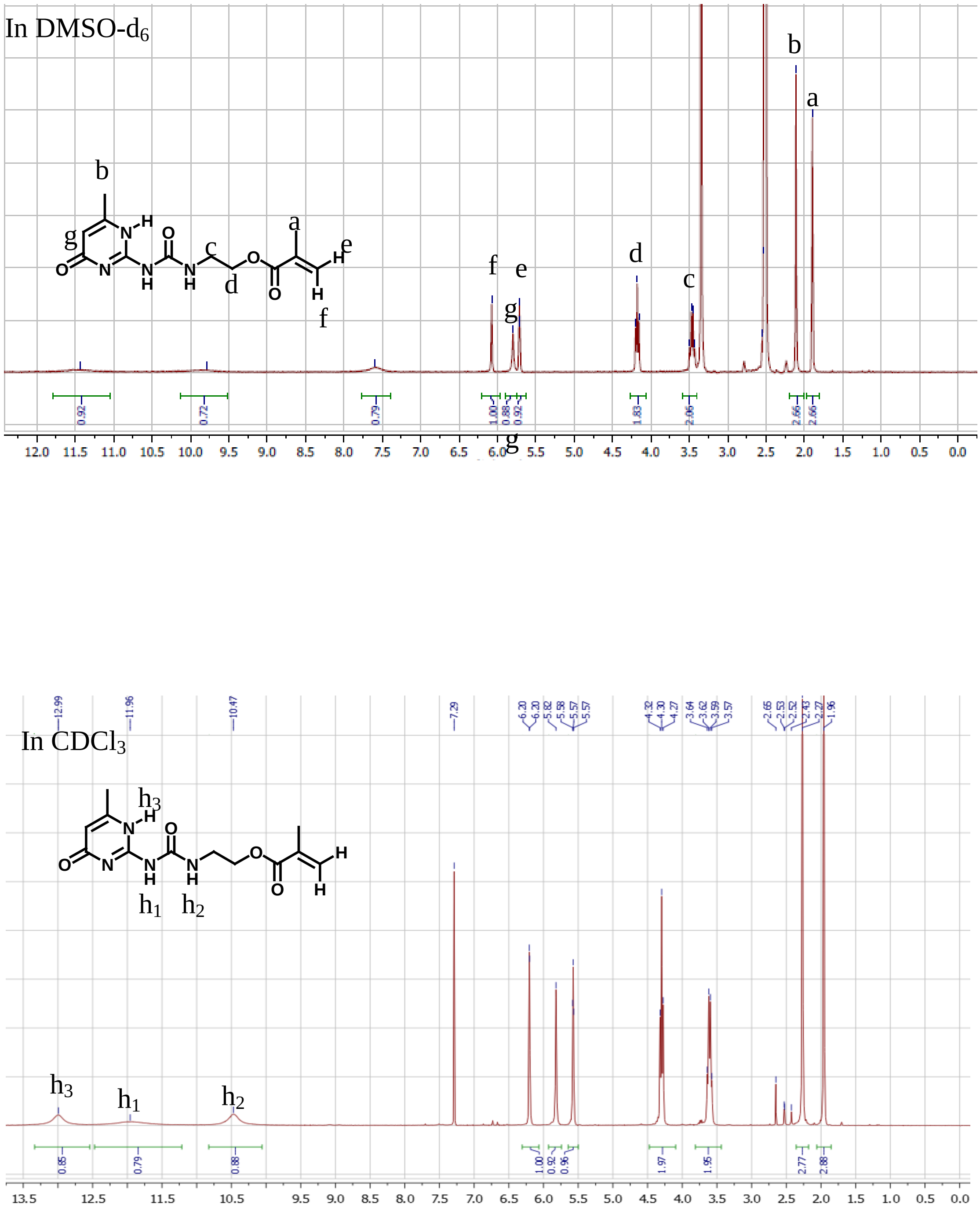


Figure S2. ^{1}H NMR spectrum of copolymer in $CDCl_3$. The compositions were calculated by proton-integrals of **g** (1), and **c** (19.2)

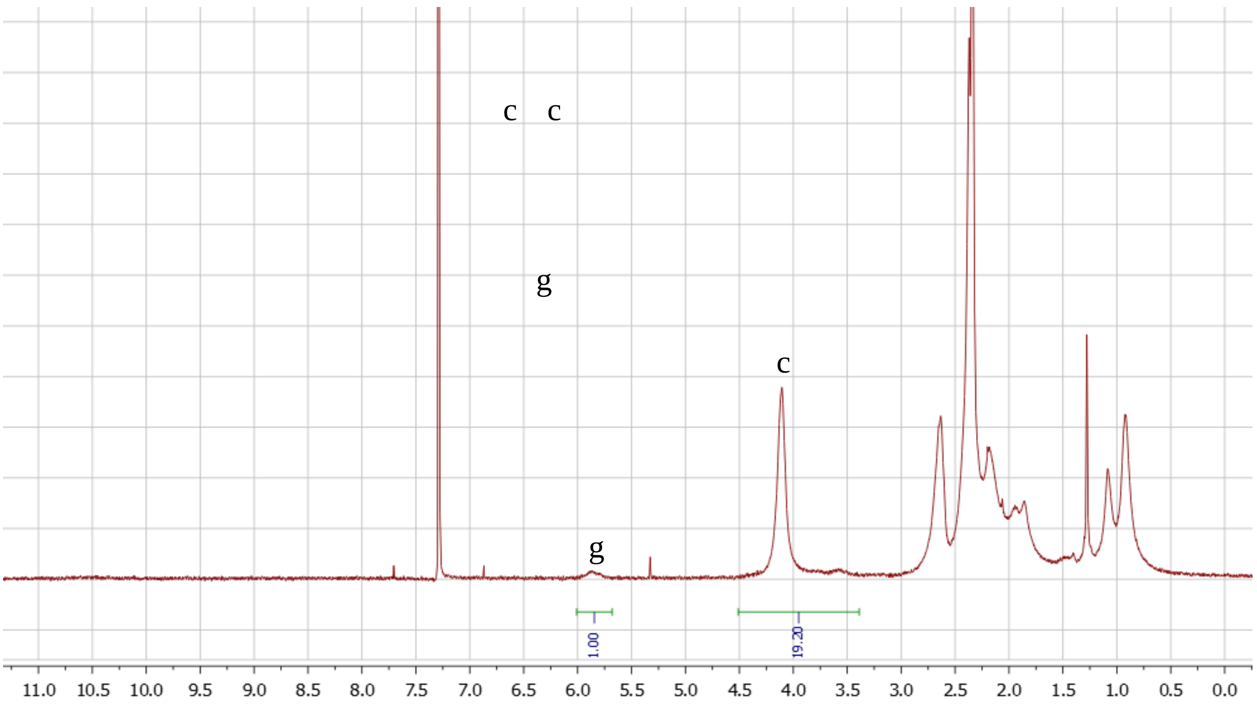


Figure S2. ^{1}H and ^{13}C NMR spectra of 2 in DMSO-d_6

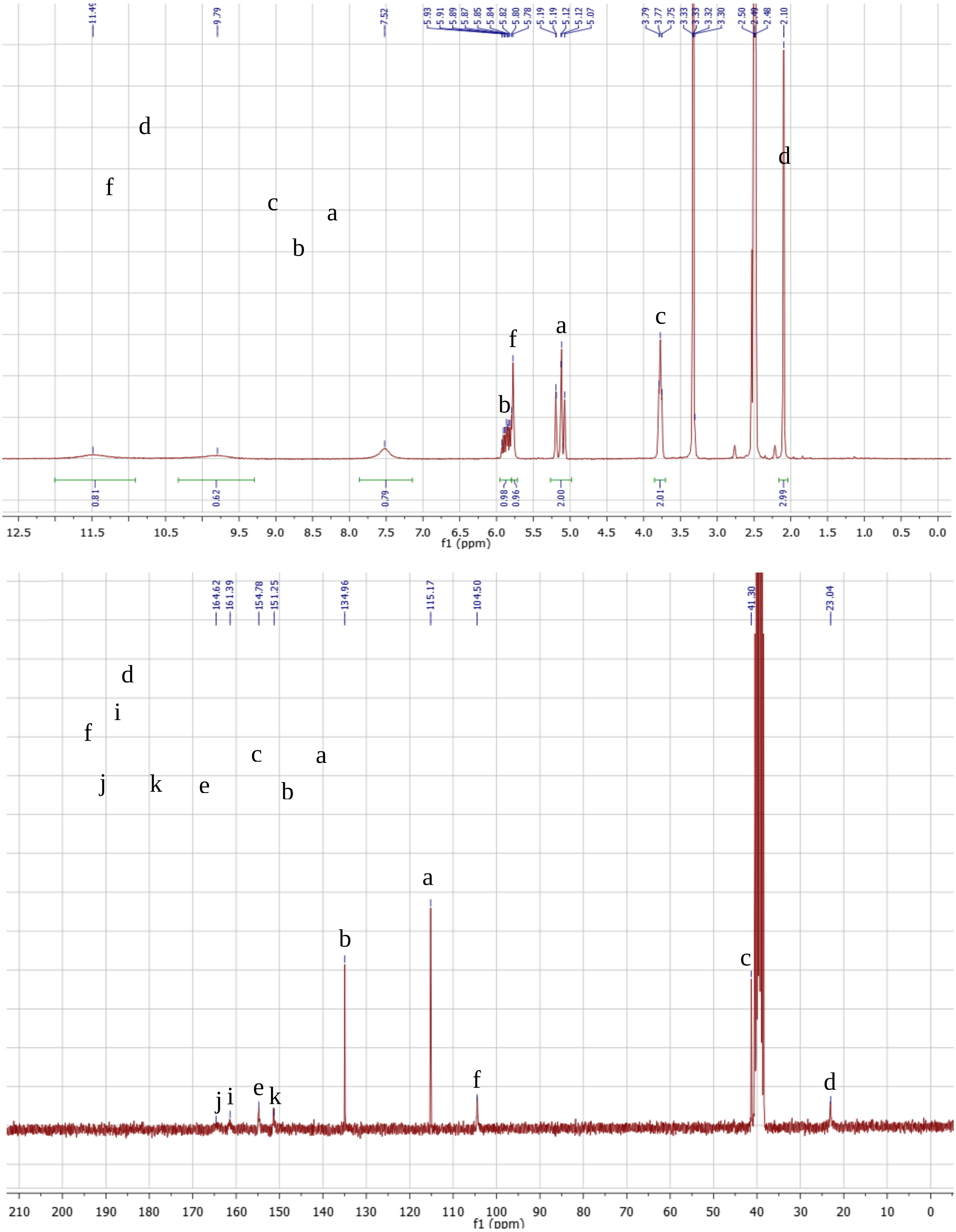


Figure S3. ^{1}H and ^{13}C NMR spectra of 3 in DMSO-d_6

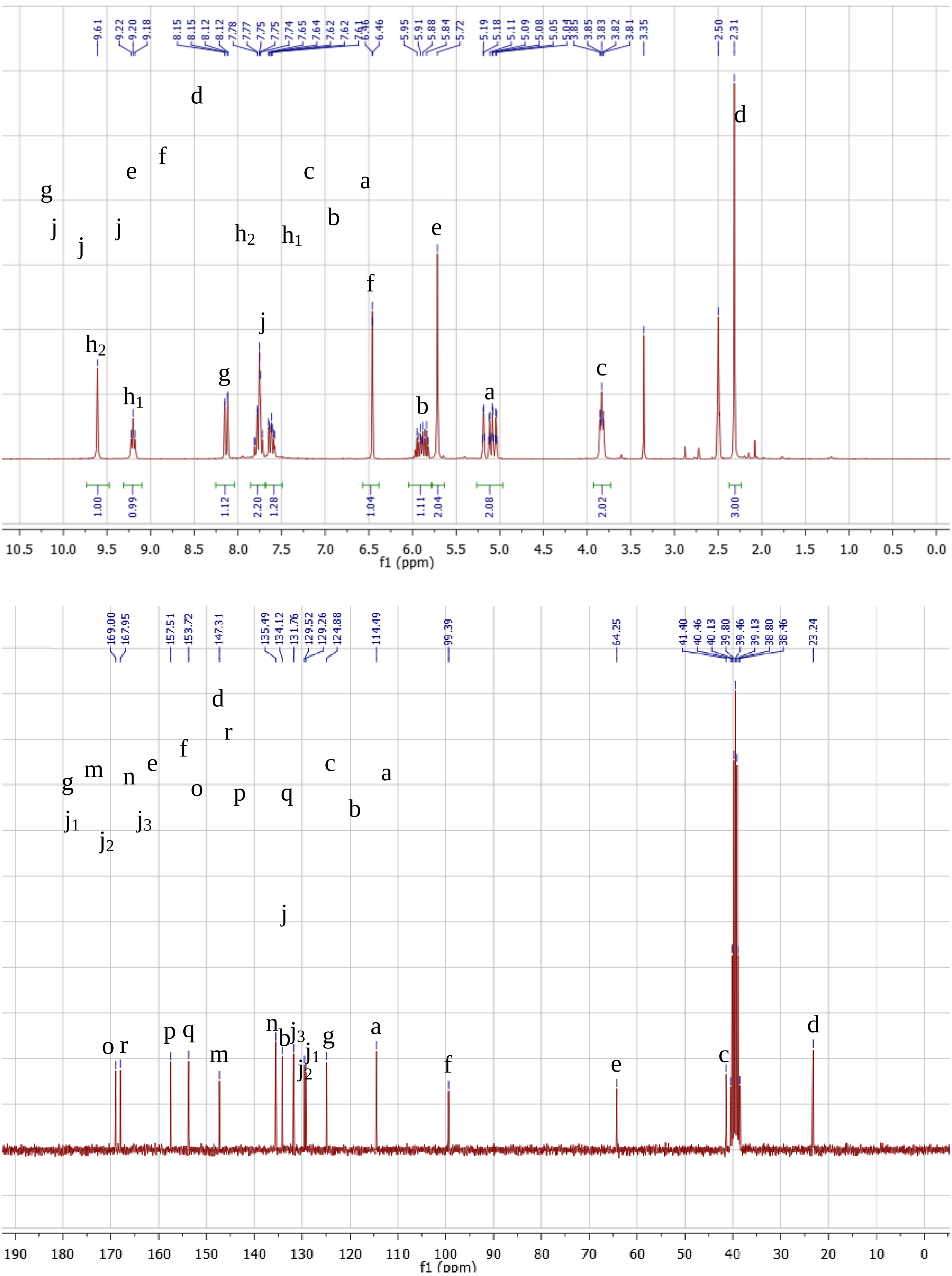
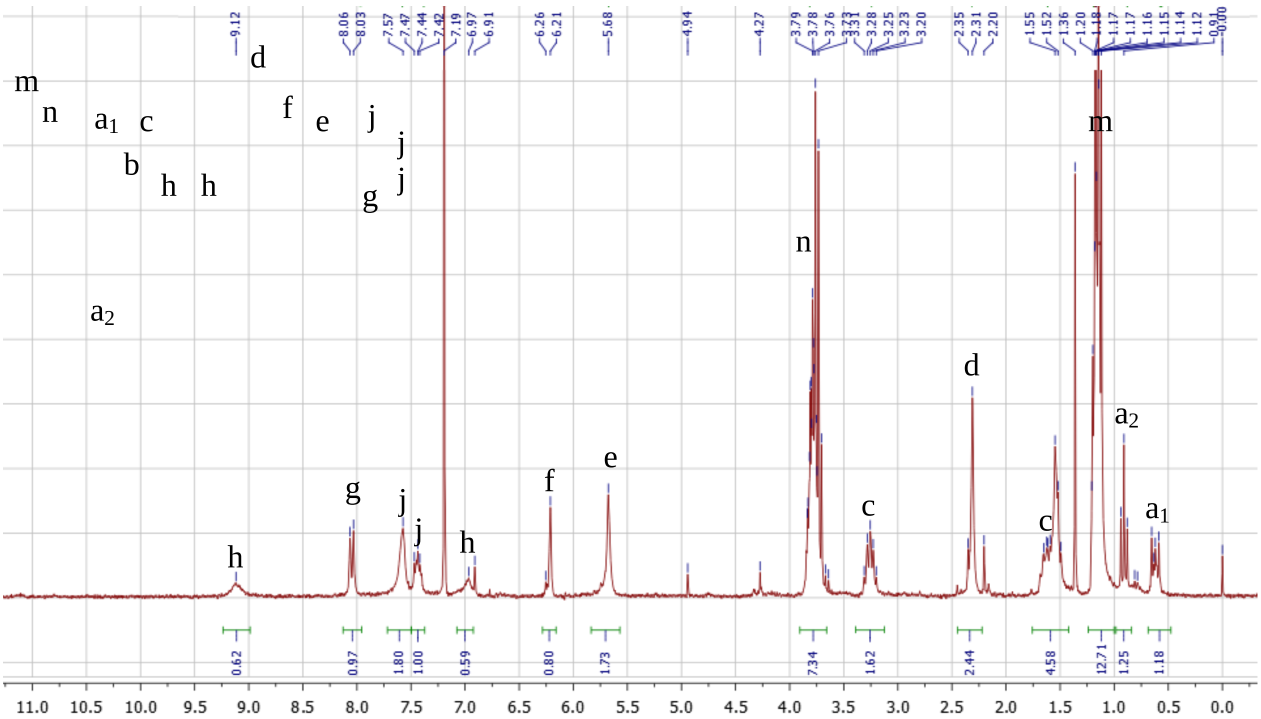


Figure S3. ^{1}H NMR spectrum of 1 in $CDCl_3$



(1) K. Yamauchi, J. R. Lizotte and T. E. Long, *Macromolecules* **2003**, *36*, 1083-1088