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UV initiated thiol-ene chemistry: A facile and modular synthetic methodology for the construction of functional 3D networks with tunable properties.

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Materials

1,3,5-Triallyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (TTT) **(1)**, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-Heneicosafluorododecyl acrylate **(10)**, Pentaerythritol tetrakis(3-mercaptopropionate) (PTM) **(4)**, acrylic acid **(8)**, acrylamide **(9)**, 2-allyloxyethanol, 4-(dimethylamino)pyridine (DMAP), disperse red 13, succinic anhydride, 5,5´-dithiobis-2-nitrobenzoic acid (DTNB) and phosphate buffer solution pH 7 were obtained from Aldrich. Polyethylene glycol (PEG_{3000}) (M=3000 g/mol) and Polyethylene glycol monomethyl ether (PEG_{2000}) (M=2000 g/mol) were purchased from Fluka. Tris[2-(3-mercaptopropionyloxy)ethyl]isocyanurate (TMI) **(2)** was purchased from Wako. 2,2-Dimethoxy-2-phenylacetophenone (DMPA) was obtained from Ciba. Silicone materials were all purchased from ABCR: vinyldimethylsiloxy terminated polydimethylsiloxane (VT-PDMS, AB109358) **(5)** and poly(Mercaptopropyl) methylsiloxane (99-100% Mercaptopropyl) methylsiloxane) (MP100-MS, AB113729) **(6)**. DCC, MgSO4 was purchased from Acros. Solvents were obtained from Merck.

Analysis and equipment

Nuclear Magnetic Resonance (NMR) ^{1}H and ^{13}C spectra were acquired from Bruker Avance 400 MHz instrument using $CDCl_3$ as a solvent.

Fourier Transformed Infrared Spectroscopy (FTIR) experiments were performed on a Perkin-Elmer Spectrum 2000 FT-IR equipped with a heat controlled single reflection attenuated total reflection (ATR) accessory from Specac Ltd. (Kent, England). Each spectrum was based on 32 scans averaged at 4.0 cm^{-1} resolution in the range of 600-4000 cm^{-1}.

FT-Raman Spectroscopy was performed using a Perkin-Elmer Spectrum 2000 NIR FT-Raman instrument. Each spectrum was based on 32 scans using 1500 mW laser power.

UV-visible-Spectrometry was achieved by a Hamamatsu L5662 equipped with a standard medium-pressure 200 W L6722-01 Hg-Xe lamp and provided with optical fibers was used as the UV-source for the photo-RTIR measurement.

Static contact angle measurements were performed on a KSV Instruments CAM 2000 equipped with a Basler A602f camera, using 5 and 10 μL droplets of MiliQ water under 50% relative humidity environment. Determination of the contact angles was performed using CAM software.

Tensile tests were performed with Instron5944 tensile mode. The samples were tested under conditioned atmosphere of 50% relative humidity and 23 °C in 3-6 identical replicas for statistical data.

Dynamical Mechanical Analysis (DMA) tests were performed on a TA instruments DMA, model Q800 in tensile mode temperature ramp program.

Field-Emission Scanning Electron Microscope (FE-SEM) images were recorded on a Hitashi S-4300 FE-SEM. The samples were coated with 7nm thickness of gold using an Agar High resolution Sputter Coater (model 208RH).

UV- induced cross-linking was performed using a Fusion UV Curing System Model F300, equipped with Fusion electrodeless bulbs standard type BF9. The intensity of the UV light was 184 mW/cm^2 measured in the wavelength interval 320-390 nm. Every sample was passed through the lamp with the speed of 6.52 m/min for 5 times resulting in the total irradiation time of 0.5 seconds.

For swelling and leaching tests, materials were swelled in acetone (rigid network), deionized water (hydrogel network) and chloroform (soft network). Each material was tested in three identical replicas. The degree of swelling was calculated according to:

$$\% \, swelling = \frac{m_{swollen} - m_{dry}}{m_{dry}} \times 100 \tag{1}$$

Were $m_{swollen}$ and m_{dry} are the weights in the swollen and dry state. Leaching of was performed using chloroform or water. The degree of leaching was calculated using

$$gel \, fraction = 1 - \left(\frac{m_{initial} - m_{leached}}{m_{initial}}\right) \tag{2}$$

Were $m_{initial}$ is the initial dry weight and $m_{leached}$ is the weight after leaching and drying. All swelling and leaching measurements were done in triplicates.

The completion of leaching test was confirmed by leaching in deuterium and $CDCl_3$ and analyzing by ^{1}H-NMR to confirm the absence of extractable components.

Network formation

Film formation of rigid networks

Table S1: Formulations of rigid networks with varying excess of allyl and thiol functionalities.

Sample Code	TTT	TMI	Molar ratio allyl : thiol
R1	47 wt%	53 wt%	1.9 : 1
R2	42 wt%	58 wt%	1.5 : 1
R3	32 wt%	68 wt%	1 : 1
R4	24 wt%	76 wt%	1 : 1.5
R5	20 wt%	80 wt%	1 : 1.9
R6	16 wt%	84 wt%	1 : 2.5

1,3,5-Triallyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (TTT) **(1)** and Tris[2-(3-mercaptopropionyloxy)ethyl] isocyanurate (TMI) **(2)** were thoroughly mixed in glass vials covered with aluminum foil preventing exposure to light. 2,2-Dimethoxy-2-phenylacetophenone (DMPA) was added as photo initiator with the amount of 0.58 % wt of the monomer mixture. The mixtures were heated by the hot gun to eliminate the bubbles trapped in the mixture. After that, the mixtures were poured into 1mm thick teflon mould and cured by passing through a fusion UV-belt with a dosage of 372 mJ/cm^2. The crosslinked networks were easily lifted off from the mould using tweezers. Six different network formulations were prepared with series of stoichiometric ratios. The library consists of systems with excess of allyl functional, thiol functional and a balanced ratio with no excess of any functional group.

Film formation of hydrogel network

Table S2: Formulations of hydrogel networks

Sample Code	PEG$_{(3000)}$ allyl	PTM	Molar ratio allyl : thiol
H1	94 wt%	6 wt%	1 : 1
H2	89 wt%	11 wt%	1 : 2

diallyl polyethylene glycol **(3)** (see Figure S1 for the synthesis steps) was used to produce the hydrogel network with pentaerythritol tetrakis(3-mercaptopropionate) (PTM) **(4)** as a crosslinker. 2,2-Dimethoxy-2-phenylacetophenone (DMPA) was added as photo initiator with the amount of 0.58 % wt of the monomer mixture. All reactants were dissolved in ethanol with 33% wt in glass vial covered with aluminium foil preventing exposure to light. The mixture was heated by the hot gun to obtain homogenous solution. After that, the mixtures were poured into 1mm thick teflon mould and cured by passing through a fusion UV-belt with a dosage of 372 mJ/cm^2. The crosslinked networks were easily lifted off from the mould using tweezers. The hydrogel networks were first dried overnight under the vacuum. Two different network formulations were prepared.

All the characterization of hydrogel networks except IR spectroscopy after post functionalization were performed in fully swollen state after immersion in water for 3 days.[1]

Film formation of soft network

Table S3: Formulations of soft networks with varying excess of thiol functionality.

Sample Code	Vinyl - PDMS	Thiol – PDMS	Molar ratio vinyl : thiol*
S1	98 wt%	2 wt%	1 : 2
S2	97 wt%	3 wt%	1 : 3
S3	95 wt%	5 wt%	1 : 6
S4	92 wt%	8 wt%	1 : 9

*Theoretical values calculated from thiol and vinyl content specified by supplier.

Vinyl-functional PDMS (VT-PDMS) **(5)** and thiol-functional PDMS (SH-PDMS) **(6)** were thoroughly mixed in glass vials covered with aluminum foil preventing exposure to light. The mixtures were heated by the hot gun to eliminate the bubbles trapped in the mixture. After that, the mixtures were poured into 1 mm thick teflon mould and cured by passing through a fusion UV-belt with a dosage of 372 mJ/cm^2. The crosslinked networks were easily lifted off from the mould using tweezers. Four different network formulations were prepared. The library consists of systems with only excess of thiol functional with varying amount.

Synthesis of precursor materials for post functionalization

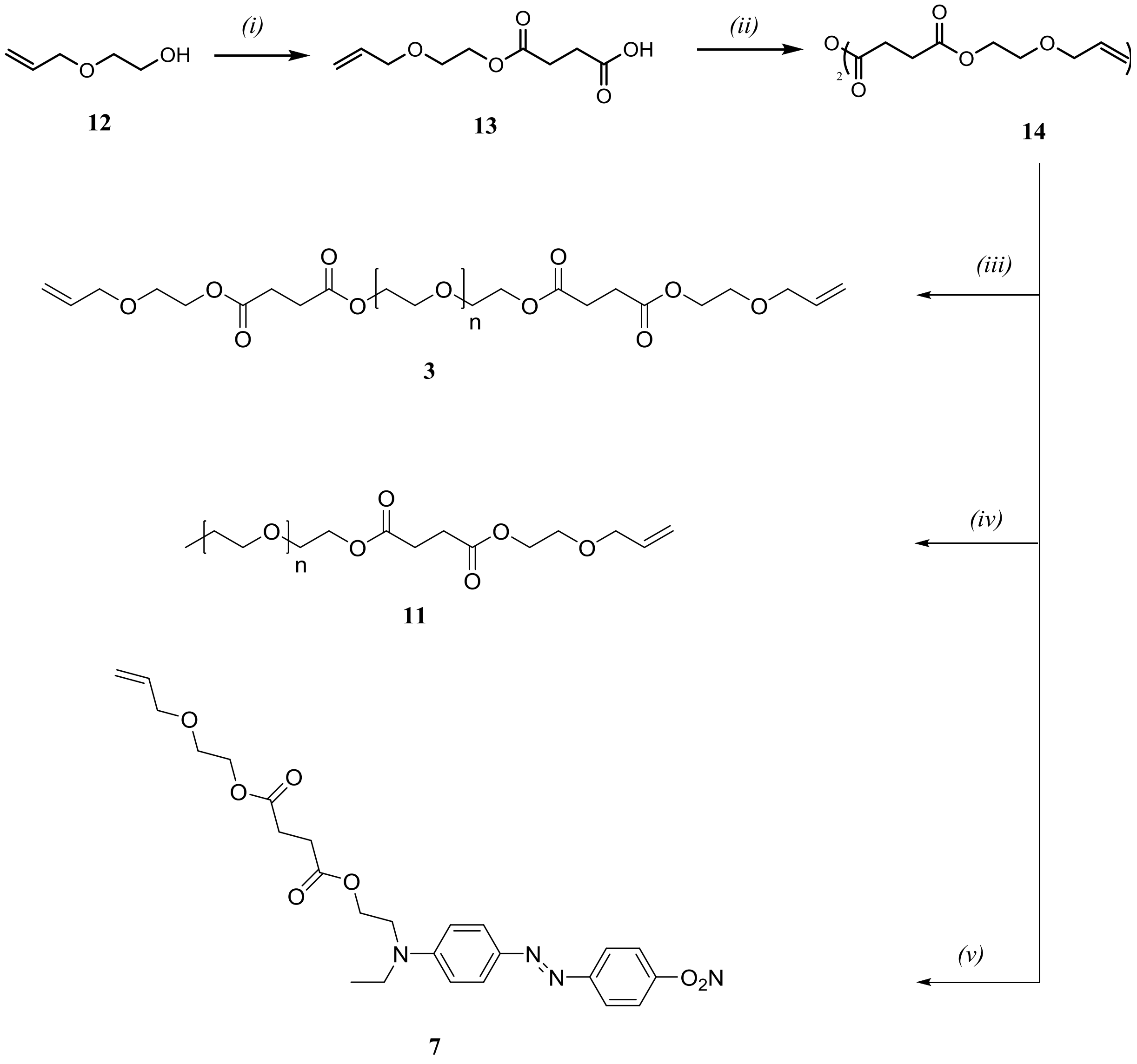


Figure S1: Synthesis of diallyl polyethylene glycol **(3)**, allyloxy polyethylene glycol **(11)** and allyloxy dispersed red 13 **(7)** ; (*i*) Succinic anhydride and DMAP in DCM, (*ii*) DCC in DCM at 0°C-RT, (*iii*) PEG_{2000} and DMAP in THF, (*iv*) Polyethylene glycol, DMAP and pyridine in DCM and (*v*) Disperse Red 13 and DMAP in THF

Synthesis of allyloxy acid (13), allyloxy anhydride (14) and diallyl polyethylene glycol (3)

The synthesis of allyloxy acid (**13**), allyloxy anhydride (**14**) and diallyl polyethylene glycol **(3)**, was done as published in previous work[1, 2].

Synthesis of allyloxy polyethylene glycol (11)

PEG_{2000} momomethyl ether (20 g, 0.01mol) was dissolved in CH_2Cl_2 together with DMAP (0.244g, 2.00mmol) and 10ml of pyridine. And excess of allyl anhydride (7.72g, 0.02mol) was added in portions to the solution and the reaction was allowed to proceed overnight. The reaction was followed by ^{13}C NMR. The solvent was evaporated and then the mixture was precipitated into 2L of diethyl ether followed by filtration. The product was obtained as a white powder after solvent evaporation (21g, 96% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ_{ppm} 5.82-5.87 (m, 1H, $CH_2{=}CH$-), 5.27-5.15 (m, 2H, $CH_2{=}CH$-), 4.22-4.19 (m, 4H, -OCH_2CH_2O-), 3.99-3.97 (m, 2H, $CH_2{=}CHCH_2O$-), 3.76-3.41 (m, PEG backbone), 3.33 (s, 3H, -OCH_3), 2.62 (s, 4H, -$COCH_2CH_2CO$-)

Synthesis of allyloxy dispersed red 13 (7)

Disperse red 13 (5g, 14.33 mmol) was dissolved in THF (50 ml) together with DMAP (350 mg, 2.87 mmol). Compound **14** (10.6 g, 27.4 mmol) was added stepwise and the reaction was allowed to proceed overnight. The excess anhydride was quenched with water (20 ml) and reaction was left overnight once again. The solvent was evaporated and the reaction mixture was dissolved in DCM (300 ml) and extracted with $NaHSO_4$ (10%) and $NaHCO_3$ (10%) followed by drying with $MgSO_4$. The product was concentrated to a dark red liquid. Yield: 72.3 % (5.52 g). **^{1}H NMR** (400 MHz, $CDCl_3$): δ_{ppm} 8.36 (d, 1H, J = 2.4, aromatic), 8.12 (d, 1H, J =11.6 Hz, aromatic), 7.92 (m, 2H ,aromatic), 7.75 (d, 1H, J=8.8 Hz, aromatic), 6.78 (m, 2H, aromatic), 5.88 (m, 1H, -CH_2CHCH_2), 5.22 (m, 2H, CH_2-CH-), 4.30 (t, 2H, J=12.4 Hz, -CH_2CH_2O-), 4.24 (t, 2H, J=9.6 Hz, -OCH_2CH_2-), 4.00 (m, 2H, -OCH_2CH-), 3.67 (t, 2H, J=12.8 Hz, -NCH_2CH_2-), 3.62 (t, 2H, J=9.6 Hz, -CH_2CH_2O-), 3.52 (m, 2H, -NCH_2CH_3), 2.64 (m, 4H, -$OOCCH_2CH_2COO$-), 1.24 (t, 3H, J=14.4 Hz, -CH_2CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$): δ_{ppm} 172.41, 172.38, 153.26, 151.86, 147.38, 144.64, 134.53, 134.19, 127.15, 126.21, 122.80, 118.22, 117.67, 111.71, 72.33, 67.96, 64.20, 61.69, 48.98, 45.99, 29.15, 29.09, 12.49

UV analysis/ Ellman's reagent

The evaluation of thiol surplus was done by utilizing Ellman's reagent. Ellman's Reagent (5,5'-dithio-bis-[2-nitrobenzoic acid]) (DTNB) reacts with thiol compound forming yellow chromophore, (5,-thio-2-nitrobenzoic acid (TNB)) which has high absorbance at 412 nm. The reaction between DTNB and thiol compounds is known as rapid and stoichiometric[3] enabling the back calculation for the amount of thiol. The 3.0 mM DTNB phosphate buffer solution, pH 7, was prepared and stored in the fridge. The linear calibration curve for comparison was obtained from the series of known amount reduced gluthathione (GSH)[4]. By extrapolating with the calibration curve, the amount of thiol can be obtained.

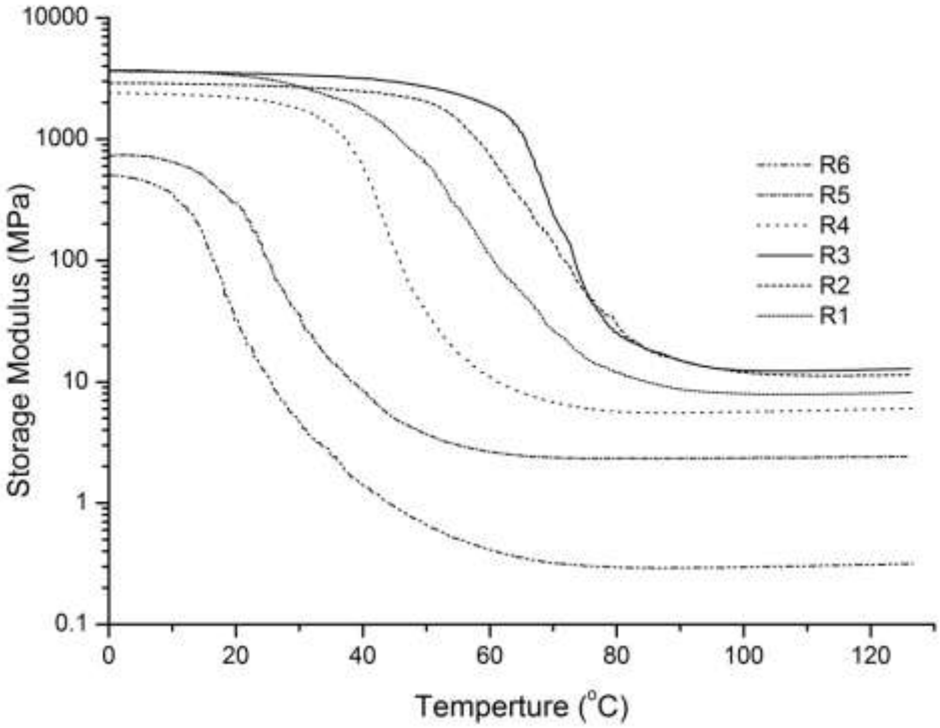
Hydrogel networks were prepared from the Teflon mould and leached out in deionized water for 3 days. The completion of leaching was confirmed by final leaching in $CDCl_3$ and D_2O and analyzing by 1H-NMR if all the extractable substances are all leached. The freeze dried hydrogel network was left in 30 ml of DTNB solution to fully swell for 3 days with the aluminum foil cover. Later on, the solution was analyzed by UV-vis to observe the absorption at 412 nm.

Table S2: The amount of thiol in rigid network assessing by Ellman's reagent

Sample Code	Allyl:thiol ratio	TNB Concentration (μM)	Amount of thiol (μmol/g)	Network density in dry state (g/ml)	Amount of thiol (molecule /nm^3)
H1	1:1	154.029	25 ±4	1.14	0.01715
H2	1:2	276.877	44 ±2	1.16	0.03107

Series of rigid and soft networks were evaluated with Ellman's reagent in the similar protocol. The rigid networks were leached in acetone and the soft networks were leached in Chloroform. The UV-vis detection at 412 nm reveals insignificant information due to the insufficient amount of thiol that can be reacted with the Ellman's reagent. The main difference from hydrogel network is the ability to swell in Ellman's solution. The rigid and soft network have a more hydrophobic nature which were tested for water absorption and showed very low swelling properties (less than 1% swelling after 24 hour soaking). This means that with the Ellman's experiment the thiol molecules that can be detected only locates on the surface and are too little to be interpreted using Ellman's reagent method.

DMA curves (Storage modulus vs Temperature) of rigid networks



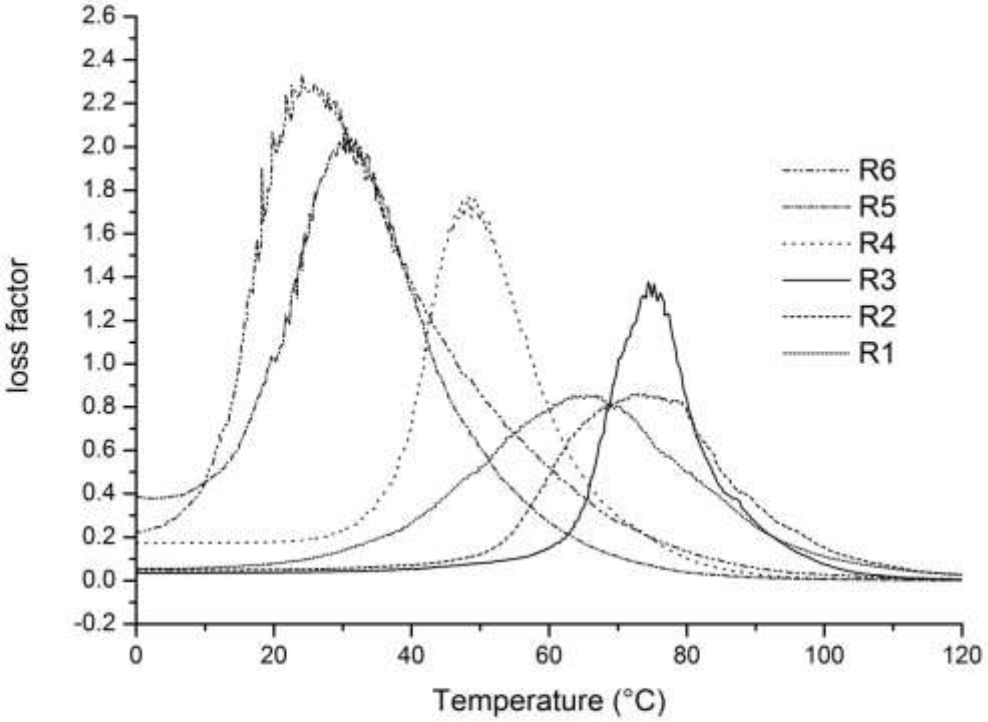


Figure S2: Storage modulus vs. temperature of rigid networks (upper) and loss factor (tanδ) of rigid network (lower)

Figure S2 shows the dynamic mechanical properties of the rigid networks. The samples were formed from a Teflon mould and cut into rectangular shape (10 mm length, 8 mm width and 1 mm thickness) for DMA measurement. The oscillation frequency was held at 1 Hz at constant amplitude of 10 µm. The test was performed from 0-120 °C with 5 °C temperature ramping. The storage modulus of the sample at the rubber plateau region was obtained at 110 °C. Glass transition temperature was obtained at the maximum value of loss factor ($\frac{E''}{E'} = \tan\delta$) shown in figure S3.

DMA curves (Storage modulus vs Temperature) of soft networks

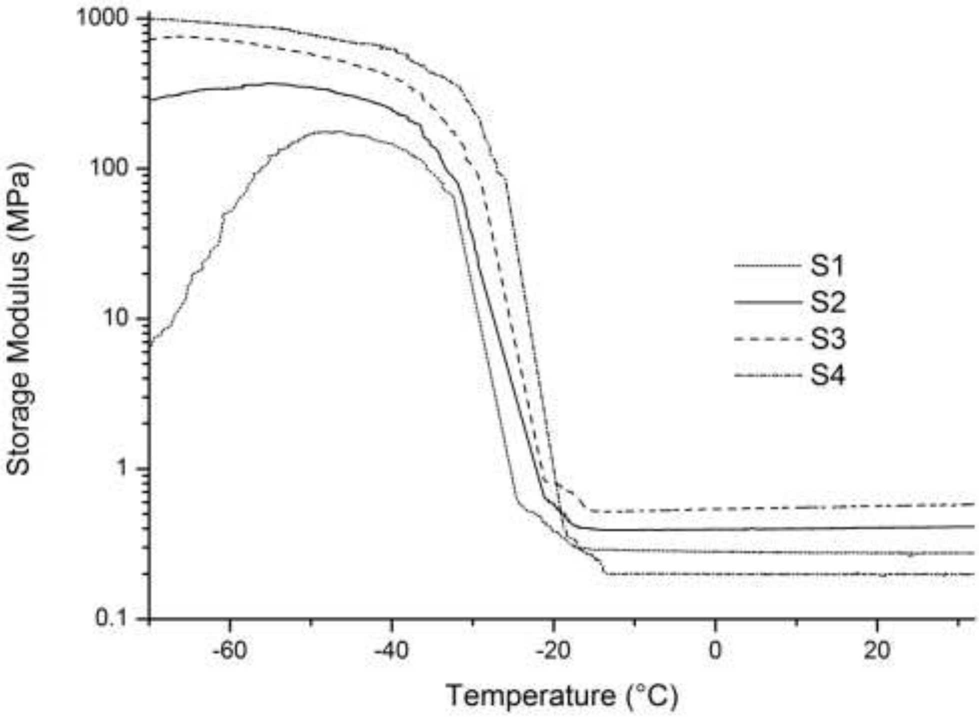


Figure S3: Storage modulus vs. temperature of soft networks

Figure S3 shows the dynamic mechanical properties of the soft networks. The samples were formed from a Teflon mould and cut into rectangular shape (10 mm length, 5 mm width and 1 mm thickness) for DMA measurement. The oscillation frequency was held at 10 Hz at constant amplitude of 15 µm. The test was performed from -70-30 °C with 5 °C temperature ramping. The storage modulus of the sample at the rubber plateau region was obtained at 20 °C.

Average molecular weight between crosslinks ($\bar{M}_c$)

For rigid and soft networks, average molecular weight between crosslinks ($\bar{M}_c$) was calculated as

$$\bar{M}_c = \frac{3\rho RT}{E'} \qquad (3)$$

Where ρ is the network density, R is the ideal gas constant, T is the temperature where the density measurement was performed and E′ is the storage modulus of the network at the rubber plateau region above the transition temperature.

Specific density measurements of the crosslinked materials were performed with a Mettler Toledo Precisa XR 20SSM-DR kit utilizing Archimedes principle. Each material was measured in three identical replicas using ethanol as auxiliary liquid at ambient temperature.

For hydrogel network, ($\bar{M}_{c,T}$) was calculated based on the stiffness properties of hydrogel[1] as

$$\frac{1}{\bar{M}_{c,T}} = \frac{GQ^{\frac{1}{3}}}{RTC_{z,r}} + \frac{2}{\bar{M}_n} \qquad (4)$$

Where $C_{z,r}$ is the mass concentration of polymer in solution before crosslinked (1.6 g/cm^3), R is the gas constant (8.314 cm^3.Pa.K^{-1}.mol^{-1}), T is the temperature when performing the tensile test, $\bar{M}_n$ is the average molecular mass of PEG allyl (3368 g/mol) and the shear modulus (G) is calculated from Young's modulus (E) obtained from tensile test from

$$G = \frac{E}{2(1+v)} \qquad (5)$$

Where v is the Poisson ratio assumed to be 0.5 for hydrogel[1], and Q is the water-induced volume swelling ratio of hydrogel calculated by the following formula

$$Q = \frac{\left[1+\frac{\left(\frac{m_s}{m_d}-1\right)\rho_p}{\rho_{water}}\right]}{\left[1+\frac{\left(\frac{m_c}{m_d}-1\right)\rho_p}{\rho_{sol}}\right]} \qquad (6)$$

Where m_s is the weight equilibrium swollen network, m_d is the weight of dry network, m_c is the weight of the network after cure, ρ_p is the density of PEG assumed to be 1.12 g/cm^3 and considered the allyl functional has no effect, ρ_{water} is the density of water 1 g/cm^3 and $\rho_{solvent}$is the density of solvent used in film formation (ethanol 0.79 g/cm^3).

Table S3: Calculation of average molecular weight between crosslinks ($\bar{M}_c$) of rigid network and soft networks

Sample Code	**Double bond : Thiol ratio**	ρ (g/cm^3)	E' (kPa)	$\bar{M}_c$ (g/mol)
R1	1.9:1	1.315	7 900	1 200
R2	1.5:1	1.329	11 400	900
R3	1:1	1.351	12 400	800
R4	1:1.5	1.332	5 700	1 700
R5	1:1.9	1.281	2 300	4 000
R6	1:2.5	1.263	300	31 000
S1	1:2	0.956	190	36 000
S2	1:3	0.955	570	12 000
S3	1:6	0.963	410	17 000
S4	1:9	0.966	270	26 000

Table S6: Calculation of average molecular weight between crosslinks ($\bar{M}_c$) of hydrogel network

Sample Code	**Allyl : Thiol ratio**	m_s (mg)	m_d (mg)	m_c (mg)	Q	E^* (kPa)	$\bar{M}_{c,T}$ (g/mol)
H1	1:1	1164	184	201	6.393	80	1623
H2	1:2	1602	236	264	6.373	133	1586

Network post functionalization

Surface postfunctionalization of rigid network

The postfunctionalization of rigid network was performed on the surface. Series of samples with different excess of thiol amount (R4, R5 and R6) were cleaned by ultrasonication with ethanol and acetone. Allyloxy Disperse Red 13 **(7)** (20 mg, 40.1 µmol) was dissolved in 10 ml of chloroform with the presence of catalytical amount of DMPA as the photo initiator. The mixture was later applied on the surface of the samples and exposed to UV initiation by a fusion UV-belt with a dosage of 372 mJ/cm^2. After that, the samples were washed by ultrasonication with acetone and ethanol alternately two times.

To introduce the tuneable wettability, acrylic acid **(8)**, allyloxy polyethylene glycol **(11)** and heneicosafluorododecyl acrylate **(10)** which possess different surface energy were chosen for surface post functionalization on sample R5. Acrylic acid **(8)** (100 µl, 1.46 mmol), mono allyloxy polyethylene glycol **(11)** (135 mg, 57 µmol) were each dissolved in 1 ml of chloroform and heneicosafluorododecyl acrylate **(10)** (20 µl, 42.7 µmol) were dissolved in 400 µl of heptane followed by the same procedure as the post functionalization of allyloxy disperse red 13.

It should be noted that FT-IR spectra of rigid network after postfunctionalization shows no trace of chemical modification because of the penetration depth of 1 micron which is far too deep in the sample.

Network incorporation of soft network and hydrogel network

The post functionalization of the soft and hydrogel network was performed throughout the whole network not only on the surface. Both soft and hydrogel network were swollen in the post functionalization solution 3 hours prior the reaction. Allyloxy Disperse Red 13 **(7)** (20 mg, 40.1 µmol), acrylic acid **(8)** (250 µl, 3.65 mm) and acrylamide **(9)** (100 mg, 1.41 mmol) were selected for the post functionalization and each dissolve in 2ml of solvent. The reactions were performed in chloroform in soft network while the reaction with hydrogel network was done in acetone. The swollen samples were exposed to UV initiation by a fusion UV-belt with a dosage of 372 mJ/cm^2. After that the samples were leached 3 hours each in chloroform, acetone, dichloromethane and water (only hydrogel network).

FT-IR spectra of post functionalized hydrogel network

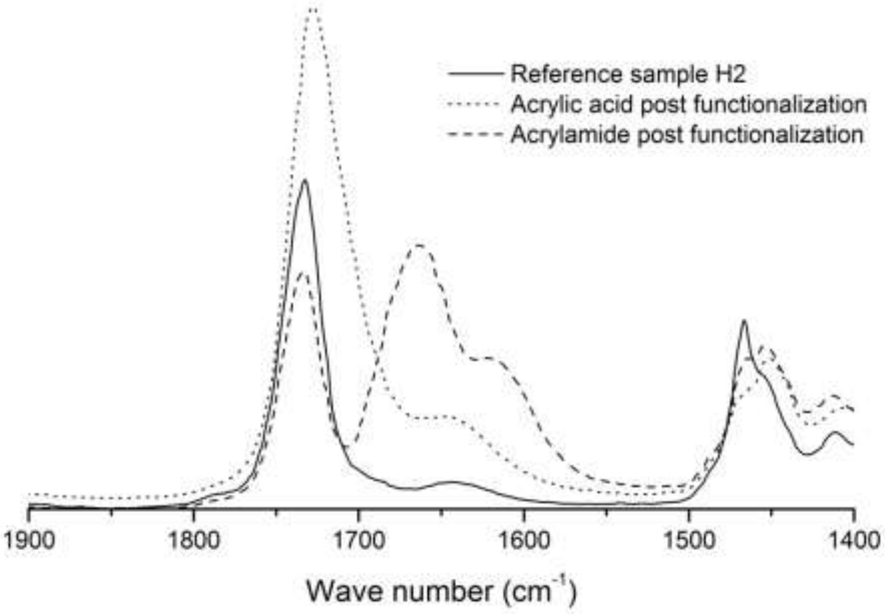


Figure S4: FTIR spectra of a) reference hydrogel network H2, b) after post functionalized with acrylic acid and c) after post functionalized with acrylamide

Figure S4 illustrates the FTIR spectra of hydrogel network prior and after post functionalization with acrylic acid and acrylamide. The acrylamide post functionalization was performed successfully with the presence of characteristic peaks at 1666 cm^{-1} and 1608 cm^{-1} representing C=O and N-H stretching respectively. The post functionalization with acrylic acid shifted the C-O stretching form reference sample H2 at 1733 cm^{-1} to 1727 cm^{-1} caused by the presence of carbonyl group from acrylic acid.

FT-IR spectra of post functionalized soft network

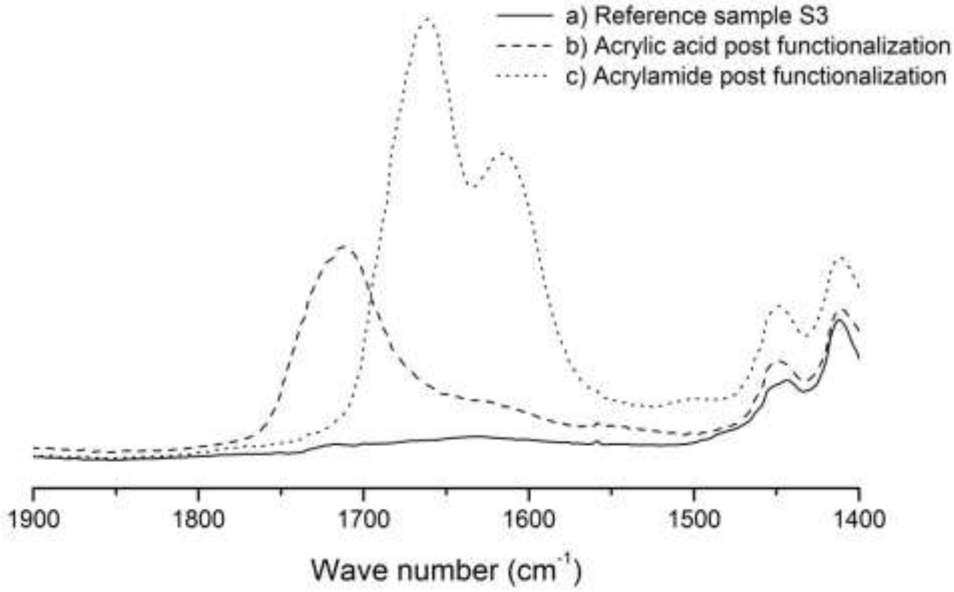


Figure S5: FTIR spectra of a) reference silicone network S4, b) after post functionalization with acrylic acid and c) after post functionalization with acrylamide

Figure S5 illustrates the FTIR spectra of soft network prior and after post functionalization with acrylic acid and acrylamide. The acrylamide post functionalization was performed successfully with the presence of characteristic peaks at 1666 cm^{-1} and 1608 cm^{-1} representing C=O and N-H stretching respectively. The post functionalization with acrylic acid is confirmed by the presence of carbonyl stretching at 1710 cm^{-1}.

Molding technique

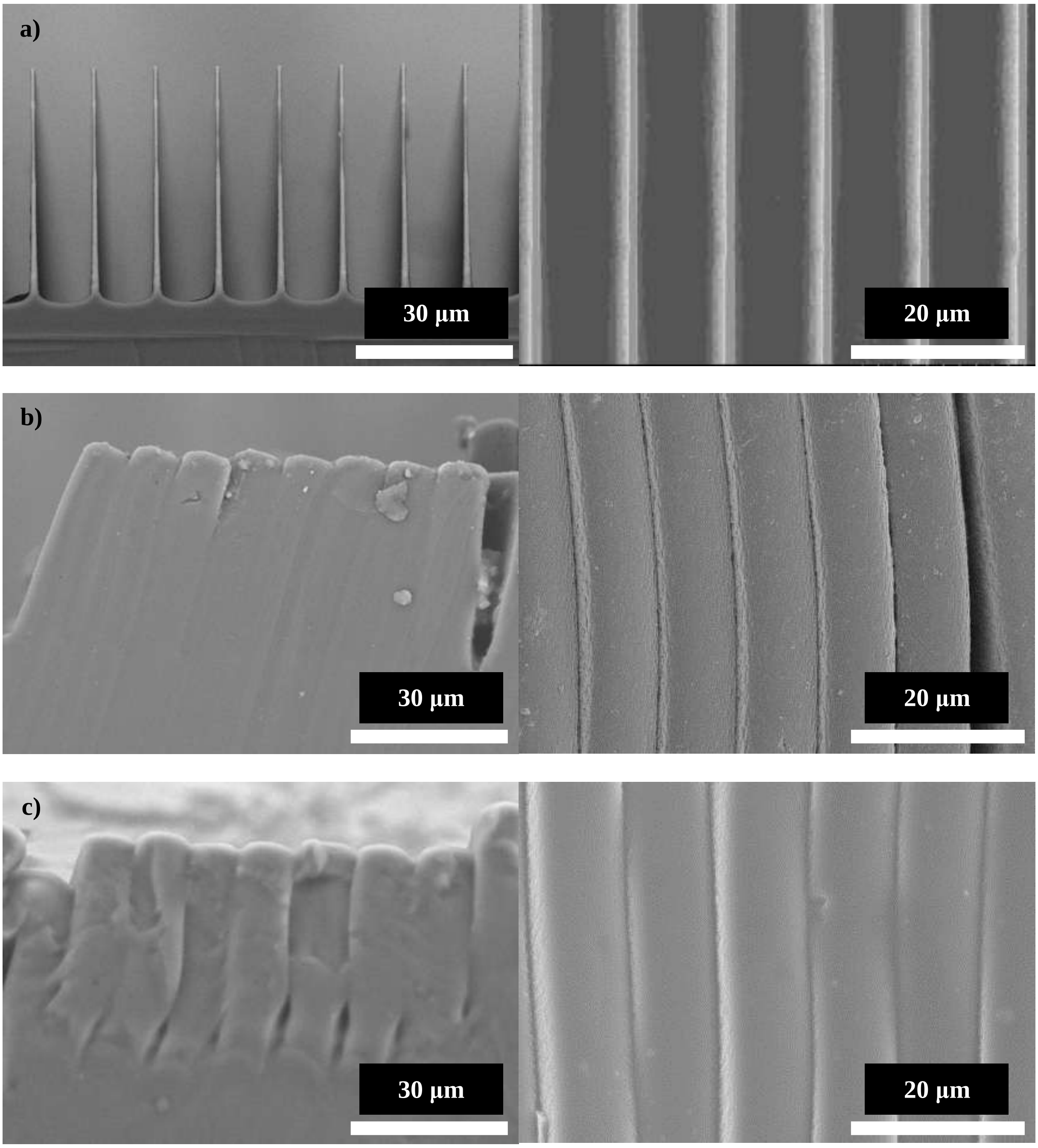


Figure S6: SEM image of a) silicon master: cross section on the left and top view on the right, b) rigid network (R5) replica, cross section on the left and top view on the right and c) soft network replica (S3), cross section on the left and top view on the right

Graphics software name and version

Fig. 1: Adobe Illustrator CS2, ChemBioDraw Ultra 13.0

Fig. 2: Origin 8

Fig. 3: Adobe Illustrator CS2, ChemBioDraw Ultra 13.0

Fig. 4: Microsoft PowerPoint 2010

Fig. 5: Microsoft PowerPoint 2010, ChemBioDraw Ultra 13.0

Fig. 6: Microsoft PowerPoint 2010, ChemBioDraw Ultra 13.0

Figure S1: ChemBioDraw Ultra 13.0

Figure S2: Origin 8

Figure S3: Origin 8

Figure S4: Origin 8

Figure S5: Origin 8

Figure S6: Microsoft Word 2010

Video S1: KSV Instruments CAM 2000 software

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