Supporting information to

Pushing the Limits for Thiol-Ene and CuAAc Reactions: Synthesis of a 6th Generation Dendrimer in a Single Day.

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Instrumentation

^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded using either a Bruker 200, 300 or 500 MHz or Varian 400 or 500 MHz spectrometer with the solvent signal as internal reference. Deuterated solvents were obtained from Cambridge Isotope Laboratories, Inc. CDCl3 was used unless otherwise noted. Column chromatography was performed on a Biotage SP1 Flash Purification System using FLASH 40+M cartridges. Gel permeation chromatography (GPC) was performed in N,N-dimethylformamide (DMF) on a Waters 2690 Separation Module equipped with a Waters 2414 Refractive Index Detector. Molecular weights were calculated relative to linear PS standards. Differential Scanning Calorimetry (DSC) was performed on a TA Instruments DSC Q2000 fitted with a RCS90 refrigerated cooling system at a sampling rate of 10 °C/min in the temperature range of -90 °C to 70 °C. Thermogravimetric analysis (TGA) was performed on a TA Instruments Q50 thermogravimetric analyzer under a nitrogen atmosphere at a heating rate of 10 °C/min. Infrared spectra were recorded on a Perkin Elmer Spectrum 100 with a Universal ATR sampling accessory. The MALDI-TOF mass spectra were collected on a Bruker UltraFlex MALDI-TOF MS with SCOUT-MTP Ion Source (Bruker Daltonics, Bremen) equipped with a N_2-laser (337nm), a gridless ion source and reflector design. Spectra of the 1st and 2nd generation dendrimers were acquired using a reflector-positive method with an acceleration voltage of 25 kV and a reflector voltage of 26,3 kV. Higher generation (3rd generation and higher) dendrimers were monitored using a linear mode. The detector mass range was set to 500-20000Da in order to exclude high intensity peaks from the lower mass range. The laser intensity was set to the lowest value possible to acquire high resolution spectra. Spectra were analyzed with FlexAnalysis Bruker Daltonics, Bremen, version 2.2. A Hamamatsu L5662-01 equipped with a 200W Hg-Xe lamp (230-436nm), λ_{max}=365, was used as a UV-light source. ESI mass spectrometry was performed on a Micromass QTOF2 Quadrupole/Time-of-Flight tandem mass spectrometer with the cone voltage set to 45V and the source temperature at 80°C.

Materials

Chemicals were purchased from Sigma-Aldrich (St. Louis, MO, USA) and used without further purification unless otherwise noted.

Abreviations

Bis-MPA = 2,2-bis(hydroxymethyl)propanoic acid

HED = 2-Hydroxyethyl disulfide

DMAP = 4-(Dimethylamino)pyridine

DCC = *N*,*N*′-Dicyclohexylcarbodiimide

Dowex = Acidic polymeric resin

DMPA = 2,2-Dimethoxy-2-phenylacetophenone

NaN_3 = Sodium azide

NaOH = Sodium hydroxide

DTT = DL-Dithiothreitol

TEA = Triethylamine

DCM = Dichloromethane

MeOH = Methanol

THF = Tetrahydrofuran

TAT = 2,4,6-tris(allyloxy)-1,3,5-triazine

G = Generation number

$[]_x$ = X is number of end-groups

Acet = Acetylene

Ene = Alkene

SH = Thiol

N_3 = Azide

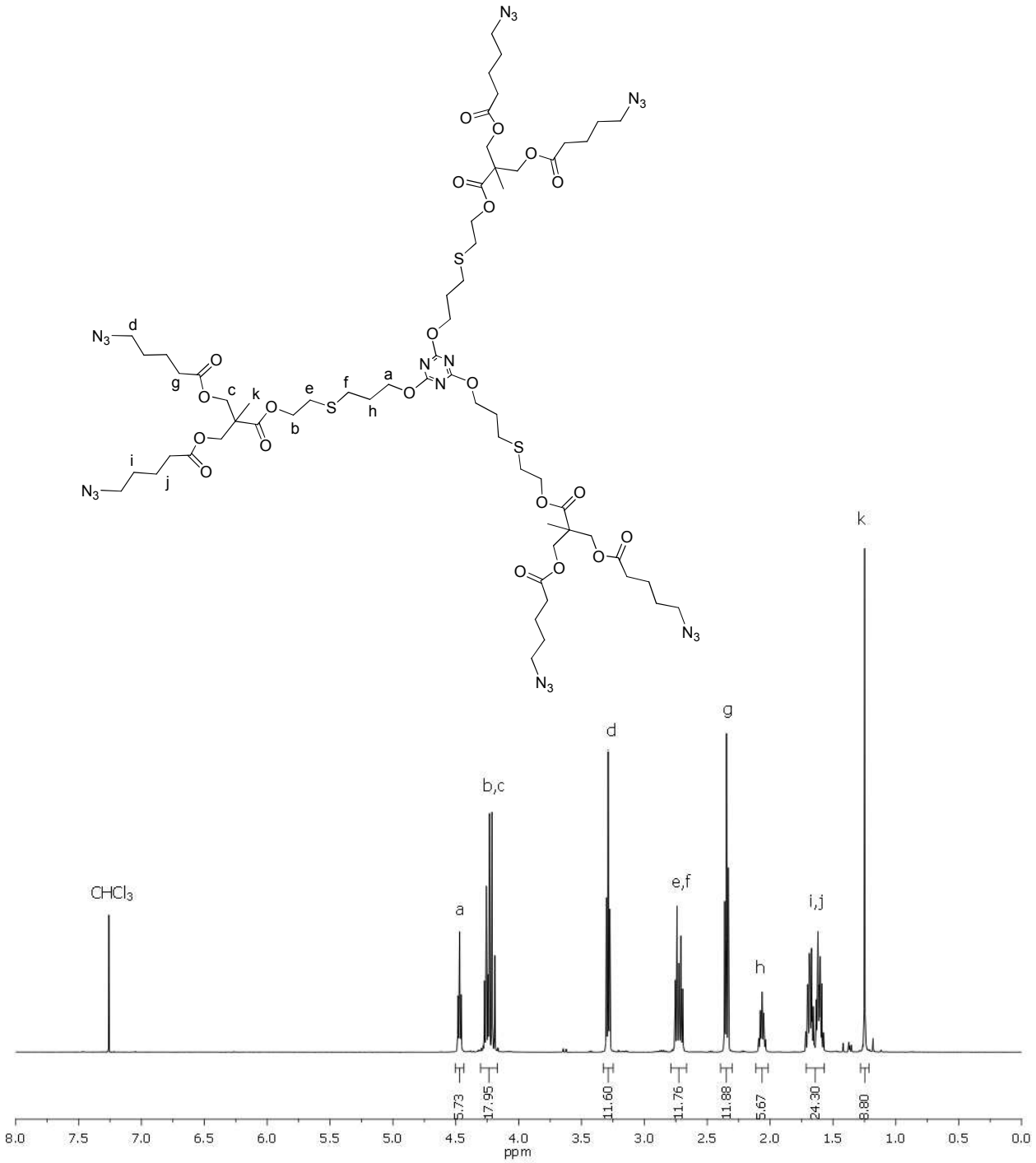


Figure S1. Structure and ^{1}H NMR spectrum of the 1st generation azide functional dendrimer (**7**).

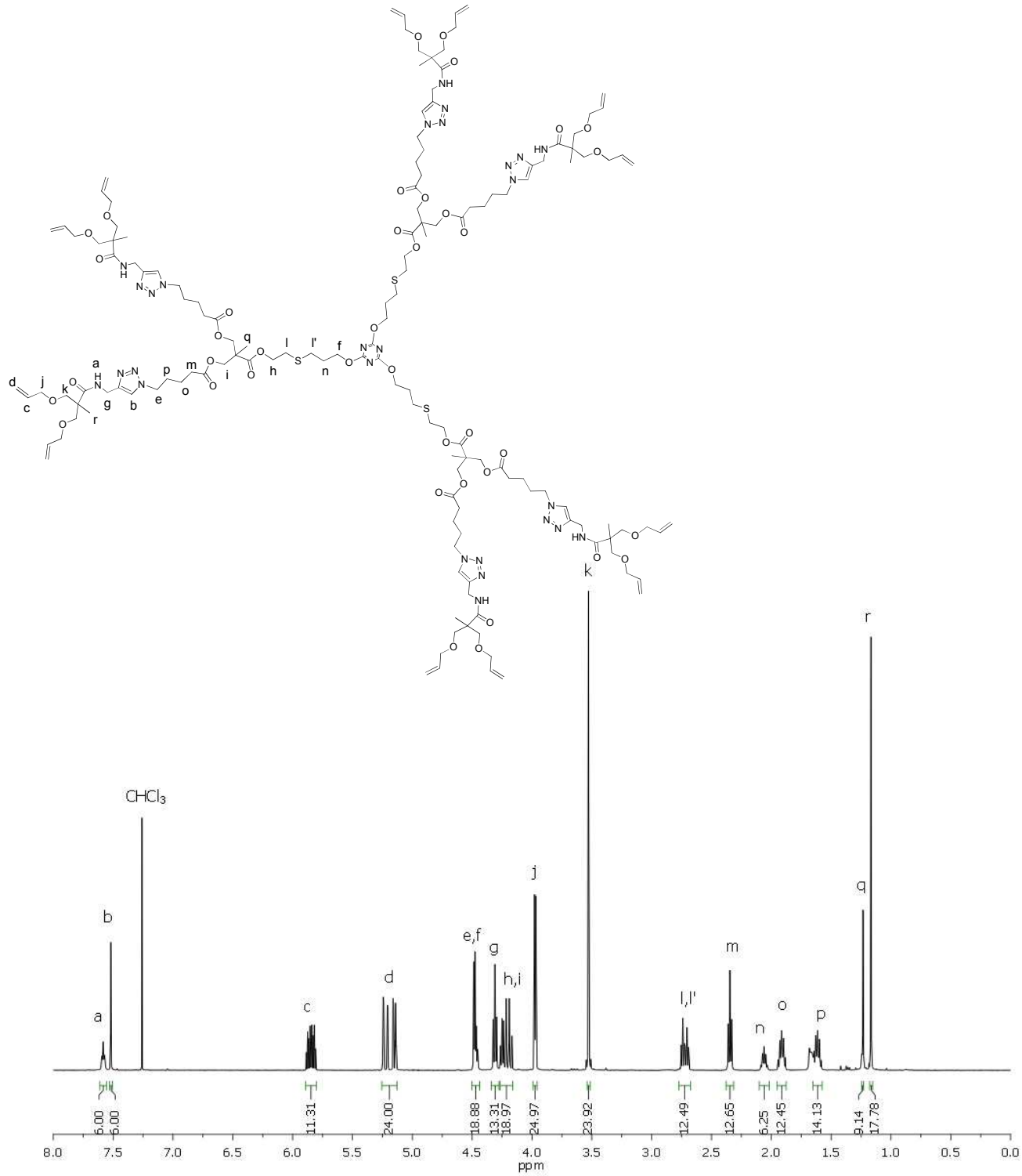


Figure S2. Structure and ^{1}H NMR spectrum of the 2nd generation alkene functional dendrimer (**8**).

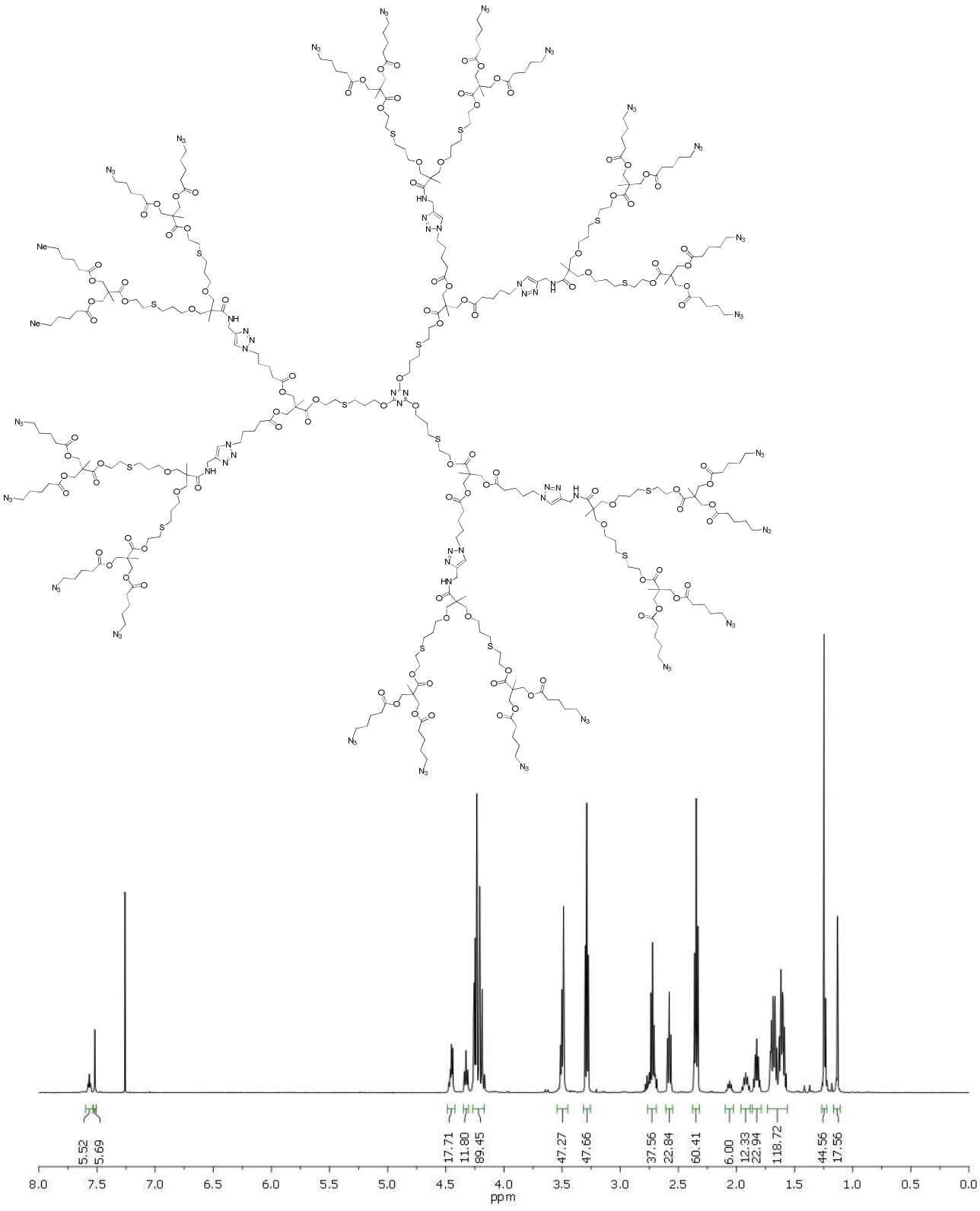


Figure S3. Structure and ^{1}H NMR spectrum of the 3rd generation azide functional dendrimer (**9**).

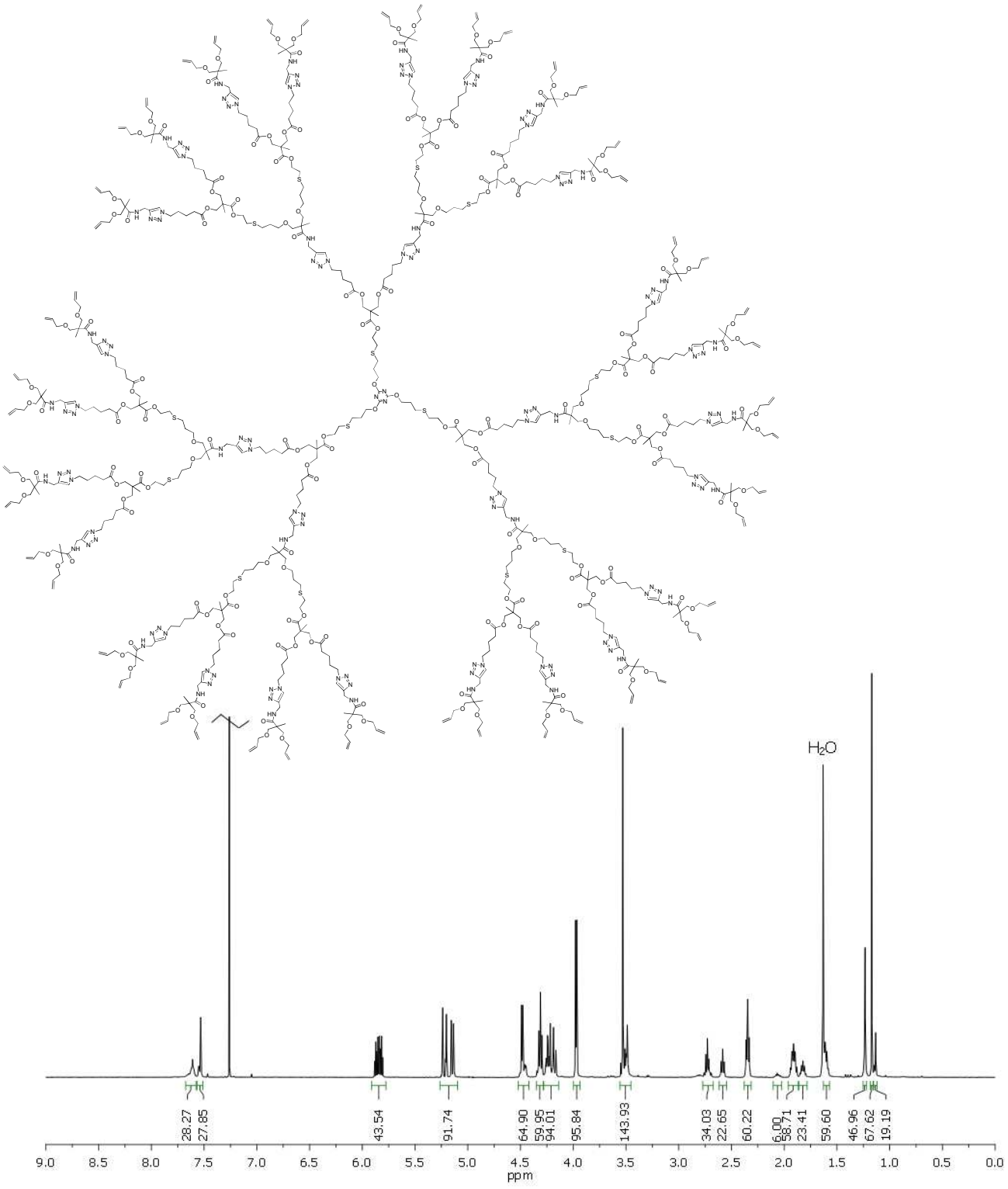


Figure S4. Structure and ^{1}H NMR spectrum of the 4th generation alkene functional dendrimer (**10**).

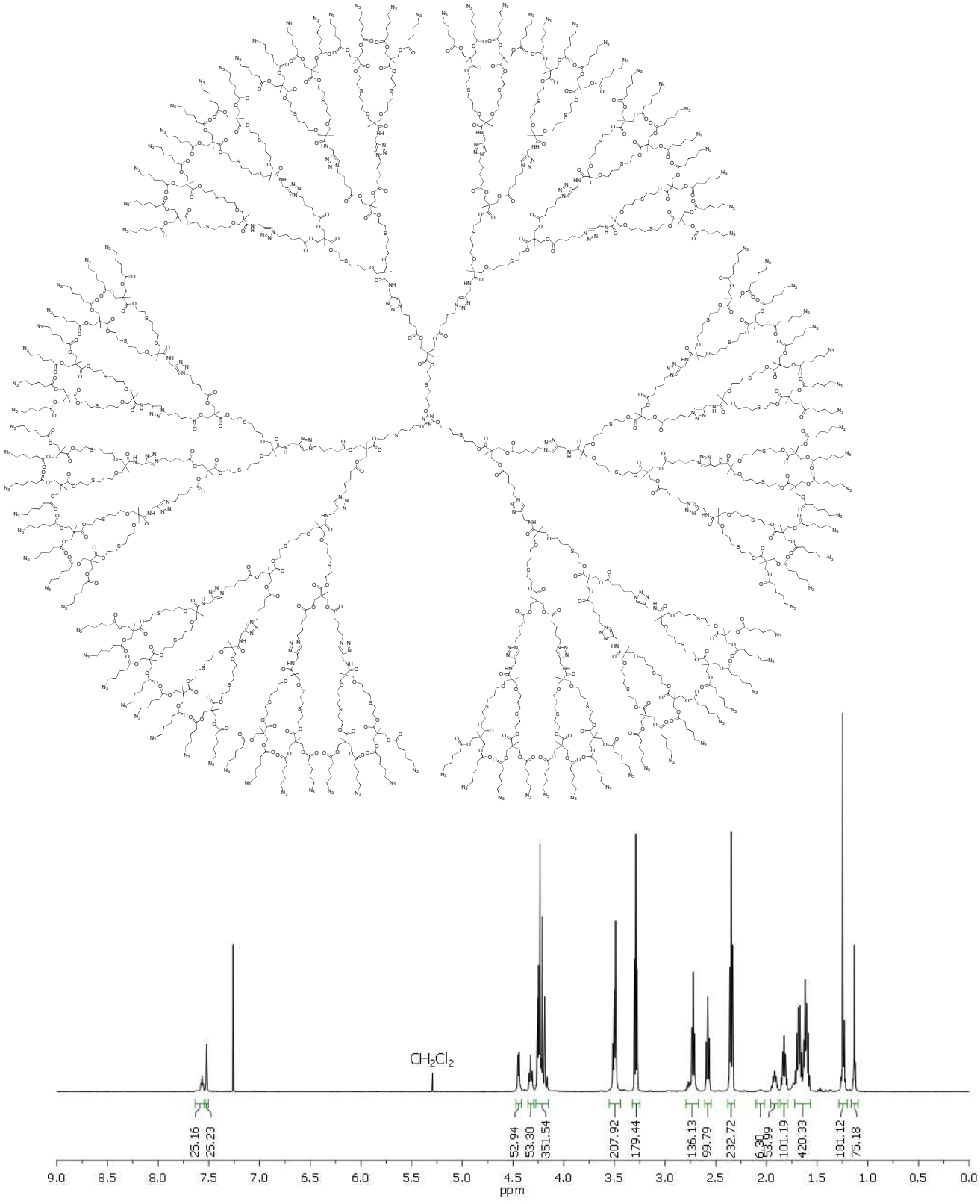


Figure S5. Structure and ^{1}H NMR spectrum of the 5th generation azide functional dendrimer (**11**).

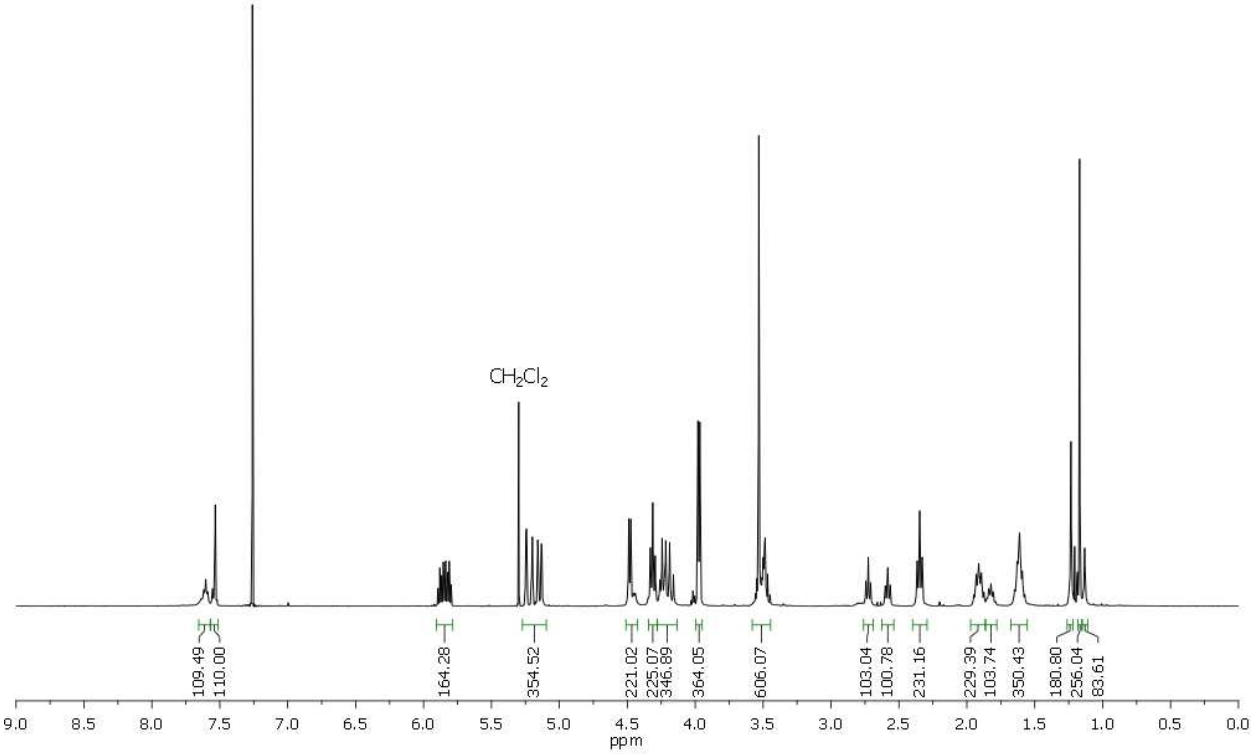
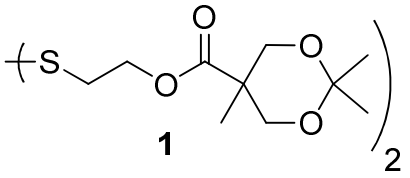


Figure S6. ^{1}H NMR spectrum of the 6th generation alkene functional dendrimer (**12**).

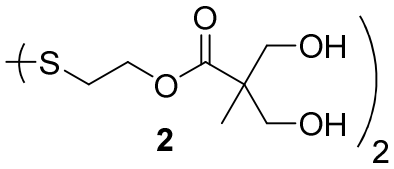
Monomer Synthesis



1

Synthesis of 2,2'-disulfanediylbis(ethane-2,1-diyl) bis(2,2,5-trimethyl-1,3-dioxane-5-carboxylate), HED-bis-MPA-Ac, (1).

Acetonide protected bis-MPA (42.6 g, 0.2448 mol, 2.4 eq.) was dissolved in 150 mL DCM together with HED (15.75g, 0.102 mol. 1 eq.) and DMAP (4.98 g, 0.0408 mol, 0.4 eq.). The solution was kept at 0°C upon addition of DCC (50.50 g, 0.2448 mol, 2.4 eq.). The reaction was left over night to reach RT. The slurry was filtered and the crude solution was concentrated and purified flash by chromatography eluting the product in 20:80 EtOAc:Hexanes as a viscous oil. Yield: 40.5 g (85%). ^{1}H-NMR: δ= 1.19 (s, 6H, -CH_3), 1.38 (s, 6H, -CH_3), 1.42 (s, 6H, -CH_3), 2.93 (t, 4H, -SCH_2CH$_2$O-), 3.63 (d, 4H, J=12 Hz, -CH_2O-), 4.18 (d, 4H, J=12 Hz, -CH_2O-) and 4.40 (t, 4H, -SCH$_2$CH_2O-) ppm. ^{13}C-NMR: δ= 18.6, 22.5, 24.7, 37.0, 41.9, 62.4, 65.9, 98.0 and 174.0 ppm, MS (ESI) m/z [M+Na]$^+$ calcd for [$C_{20}H_{34}O_8S_2$+Na]$^+$ 489.16, found [M+Na]$^+$ 489.16.

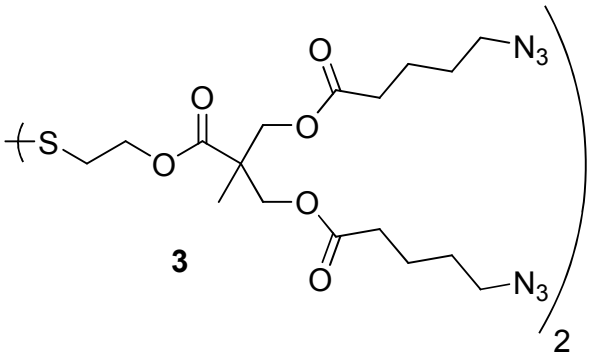


2

Synthesis of 2,2'-disulfanediylbis(ethane-2,1-diyl) bis(3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate)*, HED-bis-MPA-OH, (2).

1 (30 g) was dissolved in 300 mL MeOH and stirred over night vigoursly with 30 g of pre-washed acidic Dowex. The full deprotection of the end-groups was monitored by TLC. The polymer resin was filtered off and the solution was concentrated and used without any further purification. Yield: 24.6 g (99%). ^{1}H-NMR (d_6-acetone): δ= 1.11 (s, 6H, -CH_3), 2.98 (t, 4H, -SCH_2CH$_2$O-), 3.64 (d, 4H, J=10 Hz, -CH_2O-), 3.67 (d, 4H, J=10 Hz, -CH_2O-), 3.80 (bs, 4H, -O*H*), and 4.31 (t, 4H, -SCH$_2$CH_2O-) ppm. ^{13}C-NMR: δ= 17.2, 37.2, 49.4, 62.4, 68.0 and 175.6 ppm. MS (ESI) m/z [M+Na]$^+$ calcd for [$C_{14}H_{26}O_8S_2$+Na]$^+$ 409.08, found [M+Na]$^+$ 409.08.

*Oestmark, E.; Macakova, L.; Auletta, T.; Malkoch, M.; Malmstroem, E.; Blomberg, E. *Langmuir* **2005**, *21*, 4512-4519.

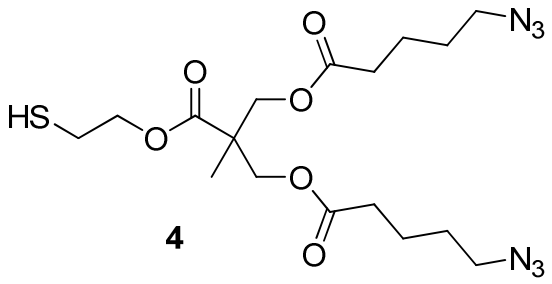


3

Synthesis of 2,2'-(2,2'-disulfanediylbis(ethane-2,1-diyl)bis(oxy))bis(oxomethylene)bis(2-methylpropane-3,2,1-triyl) tetrakis(5-azidopentanoate), HED-bis-MPA-N_3, (3).

2 (10 g, 0.026 mol, 1 eq.), 5-azidopentanoic acid** (17.80 g, 0.124 mol, 4.8 eq.), and DMAP (2.50 g, 0.022 mol, 0.8 eq.) were dissolved in 300 mL DCM and cooled in an ice bath. DCC (25.59 g, 0.124 mol, 4.8 eq.) was dissolved in 50 mL DCM and added drop wise to the 0°C solution. The reaction was left over night and the white precipitate was filtered off the following morning. The crude solution was washed with 3x50 mL 10 wt% $NaHSO_4$ (aq) and 3x50 mL 10 wt% $NaHCO_3$ (aq). The organic phase was washed once more with brine, dried using $MgSO_4$, concentrated, and purified by flash chromatography eluting the product in 30:70 EtOAc:Hexanes as a colorless oil. Yield: 20.6 g (91%). ^{1}H-NMR: δ= 1.24 (s, 6H, -CH_3), 1.56-1.71 (m, 16H, -CH_2CH_2-), 2.34 (t, 8H, -C=OCH_2-), 2.90 (t, 4H, -SCH_2CH$_2$O-), 3.28 (t, 8H, -CH_2N$_3$), 4.19 (d, 4H, J=12 Hz, -CH_2O-), 4.23 (d, 4H, J=12 Hz, -CH_2O-), and 4.37 (t, 4H, -SCH$_2$CH_2O-) ppm. ^{13}C-NMR: δ= 17.8, 22.0, 28.3, 33.4, 36.9, 46.3, 51.0, 62.6, 65.2, 172.4 and 172.5 ppm. MS (ESI) m/z [M+Na]$^+$ calcd for [$C_{34}H_{54}N_{12}O_{12}S_2$+Na]$^+$ 909.31, found [M+Na]$^+$ 909.36.

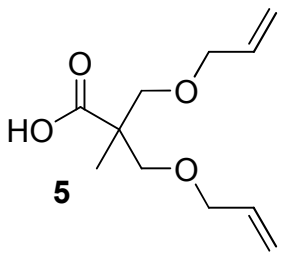
** Antoni, P.; Hed, Y.; Nordberg, A.; Nystrom, D.; von Holst, H.; Hult, A.; Malkoch, M. *Angewandte Chemie, International Edition* **2009**, *48*, 2126-2130.



4

Synthesis of 2-((2-mercaptoethoxy)carbonyl)-2-methylpropane-1,3-diyl bis(5-azidopentanoate), HED-bis-MPA-N_3, (4).

3 (14.0 g, 15.8 mmol, 1 eq.), DTT (4.87 g, 31.6 mmol, 2 eq.), and TEA (6.38 g, 63.2 mmol, 4 eq.) were dissolved in 100 mL DCM and flushed with argon for 15 min. The reaction was left to stir over night and then concentrated. The crude product was purified by flash chromatography eluting the product in 30:70 EtOAc:Hexanes as a colorless viscous oil. Yield: 11.2 g (80%). ^{1}H-NMR: δ= 1.24 (s, 3H, -CH_3), 1.46 (t, 1H, -S*H*), 1.56-1.72 (m, 8H, -CH_2CH_2-), 2.33 (t, 4H, -OC=OCH_2-), 2.73 (q, 2H, -SCH_2CH$_2$O-), 3.27 (t, 4H, -CH_2N$_3$), 4.20 (d, 2H, -CH_2O-), 4.22 (t, 2H, -SCH$_2$CH_2O-), and 4.23 (d, 2H, -CH_2O-) ppm. ^{13}C-NMR: δ= 17.8, 21.9, 23.1, 28.2, 33.4, 46.3, 50.9, 65.2, 65.3, 172.3 and 172.5 ppm. MS (ESI) m/z [M+Na]$^+$ calcd for [$C_{17}H_{28}N_6O_6S$+Na]$^+$ 467.15, found [M+Na]$^+$ 467.17.

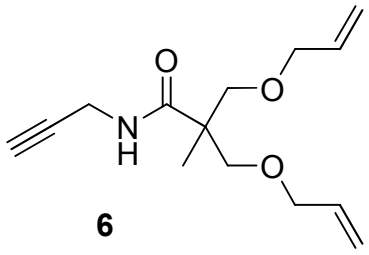


5

Synthesis of 3-(allyloxy)-2-(allyloxymethyl)-2-methylpropanoic acid, BAPA, (5).

Bis-MPA (20.0 g, 0.1491 mol, 1 eq.), NaOH (59.64 g, 1.491 mol, 10 eq.), and allyl bromide (125.27 g, 1.044 mol, 7 eq.) were added to 300 mL of toluene and left to reflux over night under vigorous stirring. The reaction was

removed from heat and 100 mL of H_20 was added to the crude solution followed by drop wise addition of conc. HCl until pH=1 was established. The reaction was washed with H_2O (2x 50 mL), dried over $MgSO_4$, and concentrated. The pure product was isolated as a yellow viscous oil. Yield: 25.6 g (80%). ^{1}H-NMR: δ= 1.22 (s, 3H, -CH_3), 3.54 (d, 2H, -CH_2O-), 3.57 (ABq, 2H, -CH_2O-), 3.98 (dt, 4H, J=6Hz, -OCH_2CHCH$_2$), 5.10-5.30 (m, 4H, -CHCH_2), 5.75-5.96 (m, 2H, -CHCH$_2$), and 9.68 (bs, 1H, -OH) ppm. ^{13}C-NMR: δ= 17.9, 48.1, 71.8, 72.3, 116.9, 1345 and 180.4 ppm. MS (ESI) m/z $[M+Na]^+$ calcd for $[C_{11}H_{18}O_4+Na]^+$ 237.09, found $[M+Na]^+$ 237.12.



6

Synthesis of 3-(allyloxy)-2-(allyloxymethyl)-2-methyl-N-(prop-2-ynyl)propanamide, BAP-Acet, (6).

5 (14.0 g, 0.0653 mol, 1 eq.), DMAP (1.59 g, 0.01306 mol, 0.2 eq.), and propargylamine (3.59 g, 0.0653 mol, 1 eq.) were dissolved in 100 mL DCM and cooled down to 0°C. DCC (13.47 g, 0.0653 mol, 1 eq.) was dissolved in 20 mL of DCM and added to the cold solution where after the reaction was left to stir over night. The white precipitate was filtered off and the crude solution was concentrated and purified by flash chromatography eluting the colorless, slightly viscous oil in 30:70 EtOAc:Hexanes. Yield: 12.6 g (77%). ^{1}H-NMR: δ= 1.17 (s, 3H, -CH_3), 2.18 (t, 1H, -CCH), 3.50 (d, 2H, -CH_2O), 3.52 (ABq, 2H, -CH_2O), 3.98 (m, 6H, -OCH_2CH- and -NCH_2CCH), 5.13-5.28 (m, 4H, -CHCH_2), 5.80-5.91 (m, 2H, -CHCH$_2$), and 7.28 (bs, 1H, -NHC=O-) ppm. ^{13}C-NMR: δ= 18.3, 29.0, 47.2, 71.2, 72.4, 73.0, 79.8, 117.1, 134.2 and 174.6 ppm. MS (ESI) m/z $[M+Na]^+$ calcd for $[C_{14}H_{21}NO_3+Na]^+$ 274.12, found $[M+Na]^+$ 274.15.

Dendrimer Synthesis

General procedure for synthesizing azide-functional dendrimers.

The alkene-functional dendrimer, AB_2-monomer (2 eq./alkene for G1, 4 eq./alkene for G3 and 7 eq./alkene for G5,), and DMPA (0.2 eq./alkene) were dissolved in inhibitor free THF. The vessel was sealed using a rubber septum and the solution was sparged with argon for 15 min before exposure to 365nm UV-light for 45 minutes with stirring. The 1st and 3rd generation dendrimers were purified by filtration through a silica plug while the 5th generation dendrimer was purified by precipitating two times into diethyl ether.

General procedure for synthesizing alkene-functional dendrimers.

The azide-functional dendrimer, CD_2-monomer (1.1 eq./azide for G2 and G4, 1.6 eq./azide for G6), and NaAsc (0.3 eq./azide) were dissolved in an inhibitor free THF/H_2O mixture. The vessel was sealed using a rubber septum and purged with argon for 10 minutes. $CuSO_4$ (0.1 eq./azide) was dissolved in H_2O and added to the solution. The reaction was kept under stirring for 1 hr where after the two phases were left to separate followed by removal of the water phase. The 2nd and 4th generation dendrimers were purified by filtration through a silica plug. For the 6th generation dendrimer, the organic phase was first diluted with DCM, extracted with H_2O (2x 2mL), Brine (1x 2mL), dried over $MgSO_4$, and partially concentrated. The dendrimer solution was precipitated two times into diethyl ether.

Synthesis of G1-$[N_3]_6$ (7).

TAT (0.6518 g, 2.615 mmol, 1 eq.), **4** (6.967 g, 15.67 mmol, 6 eq.), and DMPA (0.4052 g, 1.581 mmol, 0.6 eq.) were dissolved in 4 mL inhibitor free THF in a 50 mL round bottom flask (RBF) equipped with a stir bar and rubber septum. The solution was sparged with argon for 15 min before exposure to 365 nm UV-light. ^{1}H-NMR: δ= 1.25 (s, 9H), 1.57-1.72 (m, 24H), 2.06 (quintet, 6H), 2.35 (t, 12H), 2.69-2.75 (m, 12H), 3.29 (t, 12H), 4.19-4.27 (m, 18), and 4.47 (t, 6H) ppm. ^{13}C-NMR: δ= 18.0, 22.2, 28.4, 28.7, 28.8, 30.5, 33.6, 46.5, 51.2, 63.9, 65.4, 66.8, 172.6, 172.7, and 173.1 ppm. MS (MALDI-TOF) m/z $[M+Na]^+$ calcd for $[C_{63}H_{99}N_{21}O_{21}S_3+Na]^+$ 1,604.64, found $[M+Na]^+$ 1,605.23. T_g: -72 °C. PDI: 1.02.

Synthesis of G2-$[Ene]_{12}$ (8).

7 (1.460 g, 0.9227 mmol, 1 eq.), **6** (1.539 g, 6.123 mmol, 6.6 eq.), and NaAsc (0.3465 g, 1.749 mmol, 1.8 eq.) were added to a 50 mL RBF along with 20 mL inhibitor free THF and 4 mL H_2O. The flask was sealed with a rubber septum and purged with argon for 10 min. $CuSO_4$ (0.0965 g, 0.605 mmol, 0.6 eq.) was dissolved in 1 mL of H_2O and added to the reaction mixture. The reaction was kept under stirring for 1 hr at which point ^{1}H NMR showed complete conversion of terminal azides. ^{1}H-NMR: δ= 1.17 (s, 18H), 1.23 (s, 9H), 1.61 (quintet, 14H), 1.91 (quintet, 12H), 2.05 (quintet, 6H), 2.35 (t, 13H), 2.69-2.75 (m, 12H), 3.53 (s, 24H), 3.97 (dt, 25H), 4.17-4.26 (m, 19H), 4.31 (t, 13H), 4.45-4.49 (m, 19H), 5.13-5.25 (m, 24H), 5.81-5.89 (m, 11H), 7.52 (s, 6H) and 7.58 (t, 6H) ppm. ^{13}C-NMR: δ= 18.0, 18.5, 21.8, 28.7, 28.8, 29.7, 30.5, 33.3, 35.2, 46.5, 47.6, 49.9, 63.9, 65.3, 66.9, 72.5, 73.4, 117.1, 122.3, 134.5, 145.5, 172.4, 172.6, 173.1, and 175.3 ppm. MS (MALDI-TOF) m/z $[M+Na]^+$ calcd for $[C_{147}H_{225}N_{27}O_{39}S_3+Na]^+$ 3,111.55, found $[M+Na]^+$ 3,112.94. T_g: -34 °C. PDI: 1.02.

Synthesis of G3-$[N_3]_{24}$ (9).

8 (1.0515 g, 0.3402 mmol, 1 eq.), **4** (7.250 g, 16.31 mmol, 48 eq.), and DMPA (0.2215 g, 0.8642 mmol, 2.4 eq.) were dissolved in 4.5 mL inhibitor free THF in a 25 mL RBF equipped with a stir bar and rubber septum. The solution was sparged with argon for 15 min before exposure to 365 nm UV-light. ^{1}H-NMR: δ= 1.13 (s, 18H), 1.22-1.26 (m, 45H), 1.57-1.71 (m, 119H), 1.82 (quintet, 23H), 1.92 (quintet, 12H), 2.06 (quintet, 6H), 2.35 (t, 60H), 2.59 (t, 23H), 2.69-2.77 (m, 38H), 3.29 (t, 48H), 3.49-3.51 (m, 47H), 4.17-4.26 (m, 89H), 4.33 (t, 12H), 4.44-4.47 (m, 18H), 7.52 (s, 6H), and 7.57 (t, 6H) ppm. ^{13}C-NMR: δ= 18.0, 18.4, 21.8, 22.1, 28.4, 29.0, 29.6, 29.7, 30.4, 33.3, 33.6, 46.5, 47.5 50.0, 51.1, 64.0, 65.4, 70.0, 73.9, 122.2, 145.1, 172.4, 172.6, 172.7, 172.7, 173.1, and 175.2 ppm. MS (MALDI-TOF) m/z $[M+Na]^+$ calcd for $[C_{351}H_{561}N_{99}O_{111}S_{15}+Na]^+$ 8,418.71, found $[M+Na]^+$ 8,557.54. T_g: -54 °C. PDI: 1.03.

Synthesis of G4-$[Ene]_{48}$ (10).

9 (1.518 g, 0.1801 mmol, 1 eq.), **6** (1.197 g, 4.761 mmol, 26.4 eq.), and NaAsc (0.2622 g, 1.324 mmol, 7.2 eq.) were added to a 50 mL RBF along with 18 mL inhibitor free THF and 3.5 mL H_2O. The flask was sealed with a rubber septum and purged with argon for 10 min. $CuSO_4$ (0.0668 g, 0.419 mmol, 2.4 eq.) was dissolved in 1 mL of H_2O and added to the reaction mixture. The reaction was kept under stirring for 1 hr at which point ^{1}H NMR showed complete conversion of terminal azides. ^{1}H-NMR: δ= 1.12-1.15 (m, 19H), 1.17 (s, 68H), 1.22-1.25 (m,

47H), 1.59-1.65 (m, 60H), 1.82 (quintet, 23H), 1.91 (quintet, 59H), 2.07 (quintet, 6H), 2.35 (t, 60H), 2.58 (t, 23H), 2.69-2.76 (m, 34H), 3.48-3.55 (m, 144H), 3.97 (dt, 96H), 4.16-4.27 (m, 94H), 4.31 (t, 60H), 4.44-4.51 (m, 65H), 5.12-5.25 (m, 92H), 5.80-5.89 (m, 44H), 7.52-7.56 (m, 28H), and 7.58-7.66 (m, 28H) ppm. ^{13}C-NMR: δ= 18.0, 18.4, 21.8, 29.1, 29.6, 30.5, 33.2, 35.2, 46.4, 47.6, 50.0, 65.2, 69.9, 72.5, 73.4, 73.9, 117.0, 134.4, 172.4, 172.4, 172.4, 172.5, 172.6, and 175.2 ppm. MS (MALDI-TOF) Linear m/z $[M+Na]^+$ calcd for $[C_{687}H_{1065}N_{123}O_{183}S_{15}+Na]^+$ 14,469.35, found $[M+Na]^+$ 14,984.71. T_g: -23 °C. PDI: 1.03.

Synthesis of G5-$[N_3]_{96}$ (11).

10 (0.3931 g, 0.02719 mmol, 1 eq.), **4** (4.0883 g, 9.197 mmol, 338 eq.), and DMPA (0.0768 g, 0.300 mmol, 11 eq.) were dissolved in 2 mL inhibitor free THF in a scintillation vial equipped with a stir bar and rubber septum. The solution was sparged with argon for 15 min before exposure to 365 nm UV-light. ^{1}H-NMR: δ= 1.11-1.15 (m, 75H), 1.21-1.27 (m, 181H), 1.57-1.72 (m, 420H), 1.83 (quintet, 101H), 1.92 (quintet, 54H), 2.06 (quintet, 6H), 2.35 (t, 233H), 2.58 (t, 100H), 2.68-2.79 (m, 136H), 3.29 (t, 180H) 3.47-3.52 (m, 208H), 4.16-4.27 (m, 352H), 4.33 (t, 53H), 4.42-4.47 (m, 53H), 7.52 (s, 25H), and 7.56-7.63 (t, 25H) ppm. ^{13}C-NMR: δ= 18.0, 18.5, 21.9, 22.2, 28.4, 29.1, 29.7, 29.8, 30.5, 33.3, 33.6, 35.2, 46.5, 51.2, 64.0, 65.4, 70.0, 74.0, 122.3, 145.2, 172.5, 172.7, 172.7, and 175.2 ppm. T_g: -51 °C. PDI: 1.21.

Synthesis of G6-$[Ene]_{192}$ (12).

11 (0.1975 g, 0.005518 mmol, 1 eq.), **6** (0.2165 g, 0.8615 mmol, 154 eq.), and NaAsc (0.0354 g, 0.179 mmol, 29 eq.) were added to a vial along with 2.3 mL inhibitor free THF and 0.5 mL H_2O. The vial was sealed with a rubber septum and purged with argon for 10 min. $CuSO_4$ (0.0122 g, 0.0764 mmol, 14 eq.) was dissolved in 0.4 mL of H_2O and added to the reaction mixture. The reaction was kept under stirring for 2 hr at which point ^{1}H NMR showed complete conversion of terminal azides. ^{1}H-NMR: δ= 1.12-115 (m, 84H), 1.17 (s, 256H), 1.22-126 (m, 181H), 1.56-1.68 (m, 350H), 1.84 (quintet, 104H), 1.91 (quintet, 229H), 2.35 (t, 231H), 2.58 (t, 101H), 2.70-2.75 (m, 103H), 3.45-3.56 (m, 606H), 3.97 (dt, 364H), 4.15-4.26 (m, 347H), 4.33 (t, 225H), 4.44-4.50 (m, 221H), 5.12-5.26 (m, 355H), 5.80-5.90 (m, 164H), 7.52-7.55 (m, 110H), and 7.59-7.64 (m, 109H) ppm. ^{13}C-NMR: δ= 18.0, 18.4, 18.4, 21.8, 29.0, 29.2, 29.6, 29.6, 29.6, 30.4, 33.2, 35.2, 36.9, 37.0, 46.4, 47.4, 47.5, 49.9, 63.9, 65.2, 69.9, 71.3, 72.5, 73.2, 73.4, 73.8, 80.0, 117.0, 122.3, 134.4, 145.5, 172.4, 172.4, 172.5, 174.7, 175.1, and 175.1 ppm. T_g: -13 °C. PDI: 1.29.

Post Functionalizations

General remark about ^{13}C NMR and MALDI-TOF of post functionalized dendrimers.

Due to the high molecular weight (>15,000 g/mol) and many unique carbon atoms within the dendritic structure, a complete mapping of the ^{13}C shift was very difficult to obtain. This can be correlated to the same difficulties in finding the end groups in ^{13}C NMR of a high molecular weight linear polymer. Further, MALDI-TOF analysis of the functionalized dendrimers proved to be very difficult due to the complexicity of the end groups and high molecular weight.

Synthesis of G3-TEG (13).

9 (20 mg, 2.37 μmol), **18** (31 mg, 113 μmol), and NaAsc (28 mg, 142 μmol) were dissolved in 6 mL of THF. $CuSO_4$ (4.5 mg, 28.4 μmol) was dissolved in 1 mL of H_20 and added to the THF solution. The reaction was stirred for 45 min after which point ^{1}H-NMR confirmed the full conversion of the azide end-groups. The crude solution was purified by dialysis (MWCO=3,500) over night using a 6:1 ratio of THF:H_2O. Yield: 29 mg (72%). $Mw_{theoretic}$=14,960.88 g/mol. ^{1}H-NMR: δ= 1.13-1.25 (m, 144H), 1.62 (quintet, 60H), 1.80-1.99 (m, 160H), 2.06 (quintet, 6H), 2.33-2.42 (m, 108H), 2.57 (t, 24H), 2.68-2.77 (m, 80H), 3.50-3.69 (m, 312H), 4.16-4.46 (m, 222H), 7.48 (s, 30H), and 7.58 (t, 6H) ppm.

Synthesis of G3-Disperese-red-13 (14).

9 (20 mg, 2.37 μmol), **19** (30.5 mg, 62.7 μmol), and NaAsc (4.5 mg, 22.7 μmol) were dissolved in 6 mL of THF. $CuSO_4$ (1.8 mg, 11.4 μmol) was dissolved in 1 mL of H_20 and added to the THF solution. The reaction was stirred for 45 min after which point ^{1}H-NMR confirmed the full conversion of the azide end-groups. The crude product was purified by flash chromatography eluting the red solid dendrimer in 10:90 MeOH:EtOAc. Yield: 31 mg (65%). $Mw_{theoretic}$=20,110.50 g/mol. ^{1}H-NMR: δ= 1.14-1.26 (m, 18H), 1.57-1.75 (m, 84H), 1.89-2.17 (m, 78H), 2.33 (m, 24H), 2.48-2.77 (m, 132H), 3.41 (m, 24H), 3.53 (q, 48H), 3.64 (m, 24H), 3.70 (t, 48H), 4.12-4.28 (m, 102H), 4.33 (t, 48H), 6.78 (t, 6H), 6.79 (d, 48H), 7.48-7.58 (m, 30H) and 7.77 (d, 24H), 7.90 (d, 48H), 8.15 (dd, 24H), and 8.39 (d, 24H) ppm.

Synthesis of G3-Penicillin-G (15).

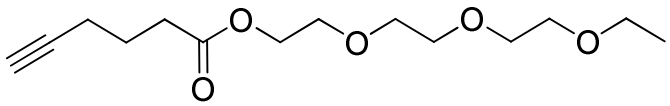
9 (20 mg, 2.37 μmol), **20** (44.4 mg, 113 μmol), and NaAsc (28 mg, 142 μmol) were dissolved in 6 mL of THF. $CuSO_4$ (4.5 mg, 28.4 μmol) was dissolved in 1 mL of H_20 and added to the THF solution. The reaction was stirred for 45 min after which point ^{1}H-NMR confirmed the full conversion of the azide end-groups. The crude solution was purified by dialysis (MWCO=3,500) over night using a 6:1 ratio of THF:H_2O. Yield: 32 mg (80%). $MW_{theoretical}$=16,824.34 g/mol. ^{1}H-NMR: δ= 1.19-1.25 (m, 135 H), 1.52-2.08 (m, 234H), 2.50-3.20 (m, 120H), 3.70-3.89 (m, 120H), 4.20-4.47 (m, 48H), 4.17-4.27 (m, 156H), 4.57 (m, 42H), 5.07 (b, 24H), 7.43-7.31 (m, 120H) 7.65 (s, 30H), and 7.72 (t, 6H) ppm.

Synthesis of G4-Thioglycerol (16).

10 (31.8 mg, 2.20 μmol, 1 eq.), 1-thioglycerol (80 mg, 740 μmol, 336 eq.), and DMPA (8.5 mg, 33.2 μmol, 15 eq.) were combined in a scintillation vial equipped with rubber septum. The vial was purged with N_2 for 5 min before exposure to 365 nm UV-light for 1 hr. The reaction mixture diluted with a small amount of DMF and precipitated three times into diethyl ether. Yield: 33.8 mg (78%) of an orange viscous liquid. ^{1}H-NMR (DMSO-d_6): δ= 1.04-1.07 (m, 86H), 1.16 (bs, 43H), 1.46 (quintet, 60H), 1.70 (quintet, 109H), 1.78 (quintet, 60H), 2.34 (t, 60H), 2.39-2.45 (m, 47H), 2.51 (t, 130H), 2.57-2.62 (m, 48H), 2.66-2.73 (m, 34H), 3.32-3.44 (m, 490H), 3.54 (quintet, 49H), 4.10-4.20 (m, 94H), 4.27-4.34 (m, 128H), 4.58 (bs, 48H), 4.76 (bs, 48H), 7.23-7.77 (m, 30H), and 7.96 (t, 30H) ppm. T_g: -41 °C. PDI: 1.17.

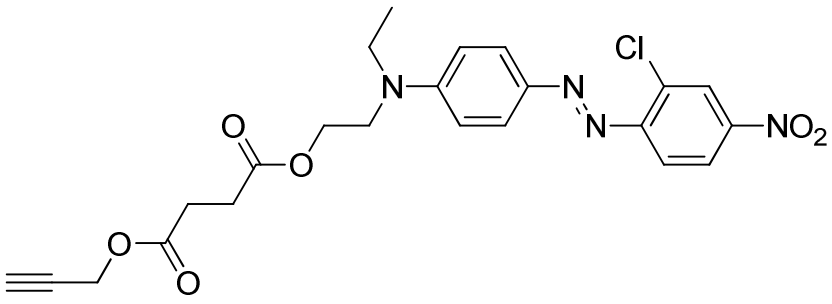
Synthesis of G5-Octane (17).

11 (0.2689 g, 7.513 μmol, 1 eq.), 1-decyne (0.16 g, 1.157 mmol, 154 eq.), and NaAsc (47.4 mg, 0.239 mmol, 32 eq.) were added to a vial along with 2.4 mL inhibitor free THF and 0.5 mL H_2O. The vial was sealed with a rubber septum and purged with argon for 10 min. $CuSO_4$ (16.7 mg, 0.105 mmol, 14 eq.) was dissolved in 0.4 mL of H_2O and added to the reaction mixture. The reaction was kept under stirring for 3 hr. The reaction mixture was diluted with 5 mL DCM, extracted with H_2O (3x 2 mL), brine (1x 50 mL), and dried over $MgSO_4$. The dendrimer solution was partially concentrated and precipitated two times into hexane. Yield: 0.2883 g (78%) of a yellow viscous liquid. ^{1}H-NMR: δ= 0.86 (t, 266H), 1.12-1.16 (m, 91H), 1.19-1.40 (m, 1094H), 1.56-1.69 (m, 56H), 1.82 (quintet, 102H), 1.92 (quintet, 228H), 2.35 (t, 233H), 2.58 (t, 100H), 2.65-2.75 (m, 280H), 3.47-3.52 (m, 207H), 4.14-4.27 (m, 352H), 4.32 (t, 235H), 4.41-4.51 (m, 56H), 7.30-7.34 (m, 78H), 7.53-7.59 (m, 26H), and 7.63-7.71 (m, 25H) ppm. T_g: -24 °C. PDI: 1.21.



Synthesis of 2-(2-(2-ethoxyethoxy)ethoxy)ethyl pent-4-ynoate, TEG-acetylene (18).

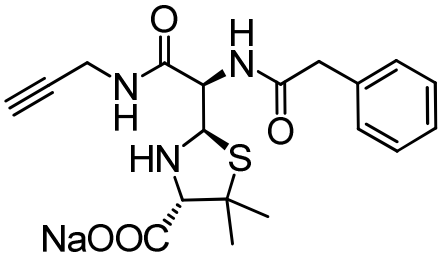
2-(2-(2-ethoxyethoxy)ethoxy)ethanol (722 mg, 4.05 mmol) was dissolved in 5 mL DCM together with hex-5-ynoic acid (0.5 g, 4.46 mmol), DPTS (239 mg, 0.81 mmol, and DMAP (99 mg, 0.81 mmol). The solution was kept at 0°C upon addition of DCC (920 mg, 4.46 mmol). The reaction was left over night to reach RT. The slurry was filtered and the crude solution was concentrated and purified by filtration. Yield: 1.0 g (92%) of a viscous oil.. ^{1}H-NMR: δ= 1.18 (t, 3H, -C*H*$_3$), 1.82 (quintet, 2H, -CH$_2$C*H*$_2$CH$_2$-), 1.93 (t, 12.24 (td, 2H, J=2.6 Hz, HCC*H*$_2$CH$_2$-), 2.42 (t. 2H, -C*H*$_2$C=OO-), 3.50 (q, 2H, -OC*H*$_2$CH$_3$), 3.56 (m, 2H, -OC*H*$_2$-), 3.62 (m, 6H, -OC*H*$_2$-), 3.67 (m, 2H, -OC*H*$_2$-) and 4.21 (t, 2H, -OC=OC*H*$_2$-) ppm. ^{13}C-NMR: δ= 15.1, 17.7, 23.5, 32.7, 63.5, 66.6, 69.0, 69.1, 69.7, 70.5, 70.6, 83.2 and 173.0 ppm.



Synthesis of 2-((4-((2-chloro-4-nitrophenyl)diazenyl)phenyl)(ethyl)amino)ethyl prop-2-ynyl succinate, Disperse-red-13-acetylene (19).

A solution of disperse red 13 (5g, 14.3 mmol), DMAP (350 mg, 3mmol), and pyridine (6 mL, 72 mmol) in 50 mL DCM was prepared in a round bottom flask and placed in an ice bath. 4-oxo-4-(prop-2-yn-1-yloxy)butanoic anhydride (5.6g, 18.6 mmol) dissolved in 20 mL DCM was added dropwise to the solution. The reaction was stirred overnight at room temperature and monitor by TLC (Hep/EtOAc) until complete disappearance of the starting material was observed. The reaction was quenched with water and the mixture was diluted with DCM

and extracted 5 times with 10 wt% $NaHSO_4$ (aq), 5 times with 10 wt% $NaHCO_3$ (aq), and brine. The organic phase was dried over $MgSO_4$, filtered, and evaporated to dryness to yield the pure product as a red solid. Yield: 6.4g (92%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ= 1.26 (t, 3H, 7.1 Hz, -CH_3), 2.47 (t, 1H, *J* = 2.4 Hz, -CC*H*), 2.67 (m, 4H, -COCH_2-), 3.54 (q, *J* = 7.1 Hz, 2H, -CH_2CH$_3$), 3.70 (t, *J* = 6.3 Hz, 2H, -NCH_2CH$_2$-), 4.33 (t, *J* = 6.3 Hz, 2H, -NCH$_2$CH_2-), 4.70 (d, *J* = 2,4 Hz, 2H, -CH_2CCH), 6.80 (d, *J*= 9.3 Hz, 2H, Ar), 7.77 (d, *J* = 9.1 Hz, 1H, Ar), 7.94 (d, *J* = 9.3 Hz, 2H, Ar), 8.15 (dd, *J*= 2.3 Hz, *J*= 9.1 Hz, 1H, Ar) and 8.38 (d, *J*= 2.3 Hz, 1H, Ar) ppm. ^{13}C-NMR (100 MHz, $CDCl_3$): δ= 12.2, 28.7, 28.8, 45.7, 48.7, 52.2, 61.5, 75.0, 77.1, 111.5, 117.4, 122.6, 126.0, 126.9, 133.9, 144.4, 147.2, 151.6, 153.0, 171.3 and 171.9 ppm.



Sodium(2R,4S)-5,5-dimethyl-2-((R)-2-oxo-1-(2-phenylacetamido)-2-(prop-2-ynylamino)ethyl) thiazolidine-4-carboxylate, Penicillin-G-acetylene (20).

Penicillin G sodium (1.068 g, 3 mmol) was dissolved in 3 mL water and propargylamine (247 μL, 3.6 mmol) was added to the solution. The mixture was stirred over night, dried under vacuum, and then freeze-dried to obtain the pure product as an orange solid. Yield: 1.16 g (94%). ^{1}H-NMR (400 MHz, D_2O): δ= 1.24 (s, 3H, -CH_3), 1.58 (s, 3H, -CH_3), 2.55 (t, *J* = 2.4 Hz, 1H, -CC*H*), 3.48 (s, 1H,C*H*COONa), 3.68 (bs, 2H, -CH_2 CCH), 3.93 (d, 2H, *J* = 4.3, -CH_2-Ph), 4.34 (d, 1H, *J* = 8.8 Hz, -C*H*-NHCO-), 4.95 (d, 1H, *J* = 8.8 Hz, -C*H*-S-) and 7.43-7.31 (m, 5H, Ph) ppm. ^{13}C-NMR (100 MHz, D_2O+CD_3OD): δ= 27.7, 27.8, 29.7, 43.0, 59.8, 60.4, 65.8, 72.9, 75.6, 79.96, 128.3, 129.9, 130.