Supporting Information

Functional Diversification of Polymethacrylates by Dynamicβ-Ketoester Modification

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EXPERIMENTAL

MATERIALS

2-(Acetoacetoxy)ethyl methacrylate (AAEMA, Sigma-Aldrich) was inhibited with BHT upon receipt due to high tendency towards autopolymerization, then deinhibited by percolation over basic alumina immediately prior to use. Methyl methacrylate (MMA), poly(ethylene glycol) monomethyl ether methacrylate (PEGMA, M_n = 500 g/mol, Sigma-Aldrich), and dioxane (Millipore) were percolated over basic alumina prior to use. Chain transfer agents 4-cyano-4-(dodecylsulfanylthiocarbonylsulfanyl) pentanoic acid[1] (CDP) and 4-cyano-4-dithiobenzoyl pentanoic acid[2] (CTP) were synthesized according to literature procedures. Anhydrous *p*-toluenesulfonic acid (pTsOH) was prepared by drying the monohydrate (Fisher) *in vacuo* at 100 °C overnight then recrystallizing from chloroform overnight. Benzylamine ($BnNH_2$, Sigma-Aldrich) was distilled under vacuum prior to use. *p*-Anisidine (Sigma-Aldrich) was recrystallized from boiling 50% aqueous ethanol. *p*-Nitroaniline was recrystallized from boiling water. 4,4'-Azobis(4-cyanovaleric acid) (V-501, Wako) was dried *in vacuo* overnight prior to use. Azobisisobutyronitrile (AIBN, Sigma, 98%) was recrystallized from ethanol and dried *in vacuo* prior to use. All other materials were used as received.

INSTRUMENTATION

Nuclear magnetic resonance (NMR) spectroscopy. ^{1}H NMR spectra were recorded on a Varian Mercury 300 MHz or a Varian Inova2 500 MHz NMR spectrometer. Deuterated dimethyl sufoxide (DMSO-d_6) and deuterated chloroform ($CDCl_3$) were used as solvents, and the residual solvent signal served as a reference.

Gel permeation chromatography – multi-angle laser light scattering detection (GPC-MALLS). Molecular weights and molecular weight distributions were determined via multi-angle laser light scattering size exclusion chromatography in *N,N*-dimethylacetamide (DMAc) with 50 mM LiCl at 50 °C and a flow rate of 1.0 mL/min (Agilent isocratic pump, degasser, and autosampler; ViscoGel I-series 10 μ m guard column and two ViscoGel I-series G3078 mixed bed

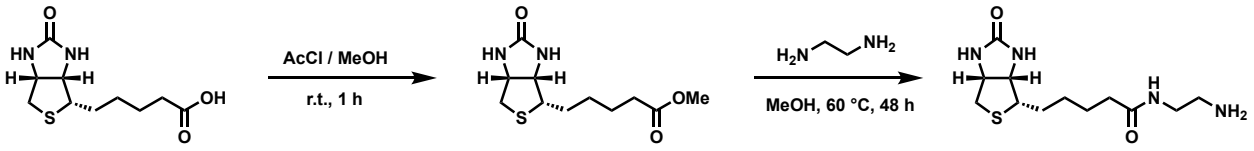
columns, with molecular weight ranges 0−20×10^3 and 0−10×10^6 g/mol, respectively). Detection consisted of a Viscotek VE 3210 UV/vis detector, a Wyatt Optilab T-rEX refractive index detector operating at 658 nm, and a Wyatt miniDAWN Treos light scattering detector operating at 659 nm. Absolute molecular weights and dispersities were calculated using Wyatt ASTRA software.

Infrared (IR) spectroscopy. Infrared spectra were acquired on a PerkinElmer Spectrum One FT-IR spectrometer equipped with a PIKE MIRacle single reflection ATR accessory containing a diamond crystal sample plate. Spectra were processed using PerkinElmer Spectrum 10 software.

Ultraviolet/visible (UV/vis) spectroscopy. Solution UV-vis measurements were performed using a Molecular Devices SpectraMax M2 Multimode Microplate Reader at 25 °C. Absorbance measurements were conducted with 200 μL of sample on clear 96-well polypropylene microplates (Greiner Bio-One).

PROCEDURES

Synthesis of amine-functional biotin (biotin-NH_2)



Biotin-OMe.[3] A solution of hydrogen chloride in methanol was first prepared by the dropwise addition of acetyl chloride (2.4 mL) to ice cold methanol (16 mL) over 15 min. This was then added to a stirred suspension of D-Biotin (2.03 g, 8.20 mmol) in methanol (16 mL) followed by an additional hour of stirring at room temp, over which time the suspension became homogeneous. The resultant solution was evaporated to a residue and partitioned between saturated aq. $NaHCO_3$ and 5% MeOH in CH_2Cl_2. The organic layer was isolated, dried over $MgSO_4$, and evaporated under vacuum to yield product as a white solid (1.74 g, 82% yield).

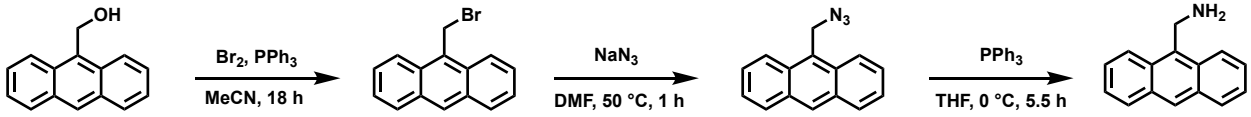
^{1}H NMR (500 MHz, DMSO-d_6) δ 6.44 (s, 1H), 6.36 (s, 1H), 4.31 (dd, J = 8.2, 4.6 Hz, 1H), 4.14 (ddt, J = 7.2, 4.4, 2.3 Hz, 1H), 3.59 (s, 0H), 3.10 (dp, J = 7.7, 2.9 Hz, 1H), 2.87 – 2.77 (m, 1H), 2.58 (d, J = 12.5 Hz, 1H), 2.30 (t, J = 7.1 Hz, 1H), 1.71 – 1.25 (m, 6H).

Biotin-NH_2.[4] Biotin-OMe (1.74 g, 6.74 mmol) was dissolved in methanol (60 mL), ethylene diamine (25 mL) was added, then the solution was then stirred at 60 °C for 48 h. After this, the solution was rotavapped to a residue followed by trituration with excess ethyl acetate. Drying *in vacuo* yielded product as a light solid (1.79 g, 93% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.74 (t, J = 5.7 Hz, 1H), 6.52 – 6.27 (m, 2H), 4.31 (ddt, J = 7.7, 5.2, 1.1 Hz, 1H), 4.13 (ddd, J = 7.7, 4.4, 1.9 Hz, 1H), 3.10 (ddd, J = 8.6, 6.2, 4.4 Hz, 1H), 3.03 (q, J = 6.2 Hz, 2H), 2.83 (dd, J = 12.4, 5.1 Hz, 1H), 2.60 – 2.52 (m, 3H), 2.06 (t, J = 7.4 Hz, 2H), 1.70 – 1.20 (m, 6H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 172.50 , 163.17 , 61.50 , 59.66 , 55.88 , 42.65 , 41.86 , 35.68 , 28.68 , 28.50 , 25.76

Synthesis of amine-functional anthracene[5]



9-Bromomethyl anthracene. Triphenylphosphine (1.09 g, 4.17 mmol, 1.00 equiv) was dissolved in dry acetonitrile (10 mL) and purged with Ar for 20 min followed by dropwise addition of bromine (0.21 mL, 4.17 mmol, 1.00 equiv). Next, 9-anthracenemethanol (1.00 g, 4.80 mmol, 1.15 equiv) was added in a single portion under a blanket of Ar and allowed to react for 1 h (note: 9-anthracenemethanol is not fully soluble under these conditions). The mixture was then transferred to the refrigerator overnight. The next day, the mixture was cooled to 0 °C for 30 min followed by vacuum filtration and washing with excess cold acetonitrile. Drying in vacuo yielded product as a light yellow solid (0.96 g, 85% yield)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.50 (s, 1H), 8.30 (d, J = 9.0 Hz, 2H), 8.04 (d, J = 8.5 Hz, 2H), 7.65 (dd, J = 8.9, 6.6 Hz, 2H), 7.50 (dd, J = 8.5, 6.6 Hz, 2H), 5.55 (s, 2H).

9-Azidomethyl anthracene. In a 100-mL round bottom flask, 9-bromomethylanthracene (0.96 g, 3.55 mmol, 1.00 equiv) was dissolved in degassed DMF (25 mL) followed by addition of sodium

azide (0.92 g, 14.2 mmol, 4.00 equiv) in a single portion. The reaction was then heated to 50 °C and stirred for 1 h. After this, the reaction was cooled to rt then partitioned between diethyl ether (50 mL) and DI water (50 mL). The organic layer was isolated then washed with deionized (DI) water (4 × 50 mL) and brine (50 mL) before drying over $MgSO_4$. Filtration, evaporation, and drying in vacuo yielded product as a yellow solid (0.76 g, 91% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 1.1 Hz, 1H), 8.30 (dq, *J* = 8.9, 1.0 Hz, 2H), 8.06 (ddt, *J* = 8.3, 1.4, 0.7 Hz, 2H), 7.66 – 7.45 (m, 2H), 5.34 (s, 2H), 1.66 (s, 2H).

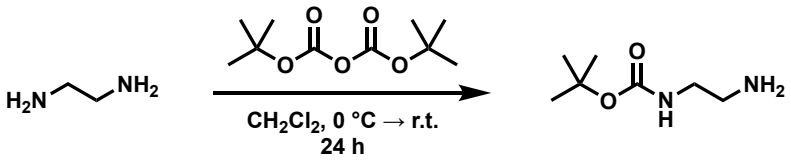
Note: As azides are potentially explosive, this reaction should be conducted behind a blast shield to ensure safety. Additionally, this reaction produces extremely hazardous aqueous sodium azide waste that should be destroyed by treatment with freshly prepared nitrous acid prior to disposal (refer to the following resource for information on safe destruction of azides: https://www.drs.illinois.edu/SafetyLibrary/SodiumAzide).

9-Aminomethyl anthracene. Under an Ar atmosphere, triphenylphosphine (0.93 g, 3.6 mmol, 1.10 equiv) was added to a 0 °C solution of 9-azidomethyl anthracene (0.76 g, 3.2 mmol, 1.00 equiv) in THF (6 mL). The reaction was stirred for 4.5 h while being allowed to warm to room temp, then 0.4 mL DI water was added followed by an additional hour of stirring. Next, diethyl ether (30 mL) was added and the solution cooled to 0 °C. Slow addition of 10% aq. HCl (4 mL) resulted in precipitation of the amine hydrochloride salt that was then filtered and washed with minimal cold 50/50 acetone/H_2O. Solids were transferred to an Erlenmeyer flask, taken up in ethyl acetate (50 mL), then neutralized with excess ammonium hydroxide. The resultant solution was washed with DI water (25 mL), the aqueous layer extracted with ethyl acetate (2 x 30 mL), then the combined organic fractions washed a final time with DI water (60 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated. Drying overnight in vacuo yielded the product as a yellow solid (0.40 g, 60% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.43 (s, 1H), 8.37 (dq, *J* = 8.9, 1.0 Hz, 2H), 8.05 (ddt, *J* = 8.4, 1.5, 0.7 Hz, 2H), 7.58 (ddd, *J* = 8.9, 6.5, 1.4 Hz, 2H), 7.51 (ddd, *J* = 8.5, 6.5, 1.1 Hz, 2H), 4.86 (s, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 134.67, 131.72, 129.35, 129.31, 126.92, 126.16, 124.99, 123.75, 38.30.

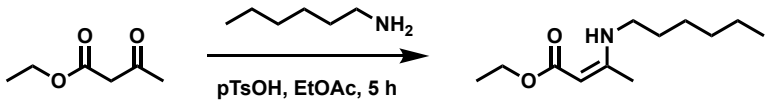
Synthesis of *N*-Boc-ethylenediamine



Ethylenediamine (76.5 mL, 1.15 mol, 10.0 equiv) was dissolved in dichloromethane (500 mL) and cooled to 0 °C with an ice bath. A solution of di-*tert*-butyl dicarbonate (25.0 g, 0.115 mol, 1.00 equiv) in dichloromethane (250 mL) was then added dropwise over 3 h followed by stirring overnight at room temp. The organic phase was isolated and washed with brine (4 × 500 mL) then collected and dried over $MgSO_4$ followed by filtration and evaporation to a viscous yellow oil. The crude was purified by vacuum distillation to yield the product as a clear oil (12.2 g, 66% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 4.91 (s, 1H), 3.15 (q, *J* = 6.0 Hz, 2H), 2.78 (t, *J* = 6.0 Hz, 2H), 1.43 (d, *J* = 1.5 Hz, 9H), 1.18 (s, 2H).

Synthesis of ethyl 3-(hexylamino)-2-butenoate



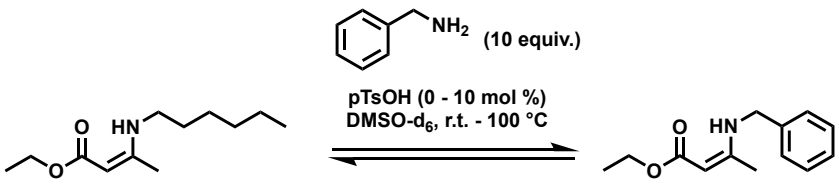
Ethyl acetoacetate (4.9 mL, 38 mmol, 1.0 equiv) and *p*-toluenesulfonic acid monohydrate (0.73 g, 3.8 mmol, 0.10 equiv) were dissolved in ethyl acetate (100 mL) followed by addition of hexylamine (25.2 mL, 192 mmol, 5.00 equiv). After stirring at room temp for 5 h, glacial acetic acid (12 mL) was slowly added to protonate the remaining hexylamine, then the organic layer was transferred to a separatory funnel and washed with DI water (4 × 100 mL) and brine (100 mL). The organic phase was then dried over $MgSO_4$, filtered, and evaporated to a light-yellow oil. Purification by vacuum distillation afforded product as a clear oil (6.56 g, 80% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (s, 1H), 4.34 (s, 1H), 3.95 (tt, *J* = 7.0, 3.5 Hz, 2H), 3.19 (d, *J* = 6.7 Hz, 2H), 1.89 (d, *J* = 2.4 Hz, 3H), 1.48 (dd, *J* = 9.9, 4.7 Hz, 2H), 1.35 – 1.22 (m, 7H), 1.14 (td, *J* = 7.1, 2.3 Hz, 3H), 0.88 (dt, *J* = 8.1, 4.4 Hz, 3H).

Reaction kinetics of enamine formation from ethyl acetoacetate

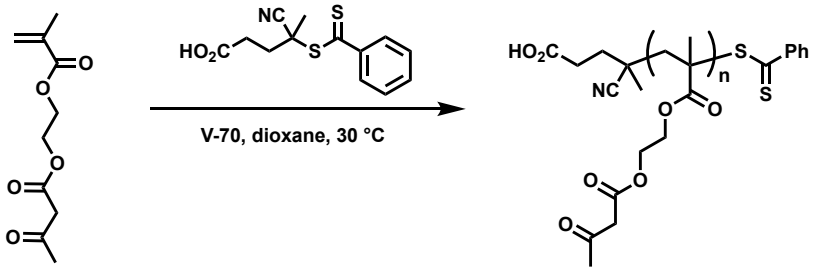
A solution of ethyl acetoacetate (30 □L, 0.23 mmol, 1.0 equiv) and pTsOH (2.2 mg, 0.012 mmol, 0.050 equiv) in 0.5 mL DMSO-d_6 were transferred to an NMR tube, then amine (1.2 mmol, 5.0 equiv) was added to initiate reaction. Scans were taken every 5 min for 75 min, and conversion was determined by integration of either the □ wa_3 or the *O*-CH_2 resonance of ethyl acetoacetate.

Reaction kinetics of enamine exchange



A solution of ethyl 3-(hexylamino)-2-butenoate (50 mg, 0.23 mmol enamine) and pTsOH (0 mmol – 2.34 mmol) in 0.5 mL DMSO-d_6 was transferred to a quartz NMR tube, then benzylamine (0.20 mL, 1.17 mmol) was added. ^{1}H NMR spectra were continuously acquired every 1 min for 30 min while maintaining the instrument at either 25, 60, 80, or 100 °C. Conversion was determined by integration of the □ NM_3 resonance of the initial *N*-hexyl enamine.

RAFT polymerization of AAEMA



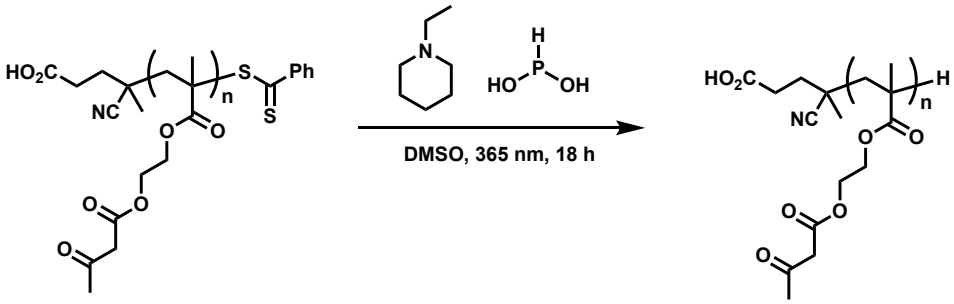
AAEMA (4.0 mL, 20 mmol, 75 equiv), CTP (74.9 mg, 0.268 mmol, 1.0 equiv.), V-70 (16.5 mg, 0.0536 mmol, 0.2 equiv), and a small amount of trioxane internal standard were combined in a

graduated cylinder and diluted to a volume of 10 mL with dioxane. The solution was transferred to a 25-mL Schlenk flask that was sealed and purged for 40 min with Ar over ice. After purging, the flask was transferred to an oil bath heated to 30 °C and allowed to react for 8 h. Polymer was purified by 3x precipitation into diethyl ether followed by drying *in vacuo* to yield PAAEMA-DTB as a sticky red solid (conversion = 66 %, M_n = 12,700 g/mol, Đ = 1.02).

Note: PAAEMA should be kept cold to improve handling.

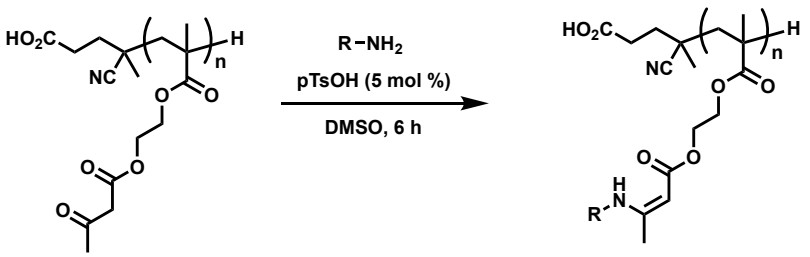
Kinetics of AAEMA polymerization. The polymerization was performed as above, except aliquots were withdrawn every hour under an Ar atmosphere for analysis. Conversion of AAEMA was determined by ^{1}H NMR spectroscopy, and molecular weights and dispersities were determined by GPC-MALLS.

Photoinduced end-group removal



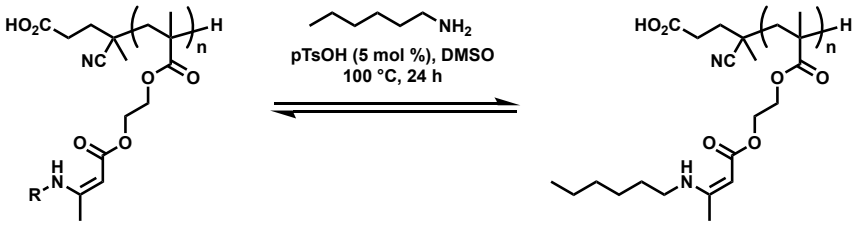
In a 25-mL Schlenk flask, PAAEMA-DTB (2.00 g, 0.158 mmol end-groups) and ethylpiperidine hyposphosphite (0.28 g, 1.58 mmol) were dissolved in DMSO (20 mL) and purged with Ar for 40 min. The solution was then irradiated for 18 h with 365 nm UV light at a luminous intensity of 7.0 mW/cm^2 in a USpicy® nail dryer. Polymer was purified by dialysis against THF for 48 h, then precipitation into ether. Drying *in vacuo* yielded PAAEMA-H as a light yellow solid (M_n = 12,600 g/mol, Đ = 1.04).

Amine functionalization of PAAEMA-H



PAAEMA-H (50 mg, 0.23 mmol mketoester) and pTsOH were dissolved in DMSO (0.5 mL), then amine (1.15 mmol) was added in a single portion. The solution was stirred at room temp for 6 h, then the functional polymer was purified by dialysis for 48 h against THF followed by precipitation into diethyl ether.

Amine exchange of PAAEMA-R



PAAEMA-R (20 mg), pTsOH (5 mol% relative to enamine groups), and either hexylamine or benzylamine (various equivalents) were dissolved in 0.5 mL DMSO and heated to 80 °C with stirring overnight. Polymer was purified by dialysis against THF for 48 h followed by precipitation into ether.

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SUPPLEMENTARY FIGURES

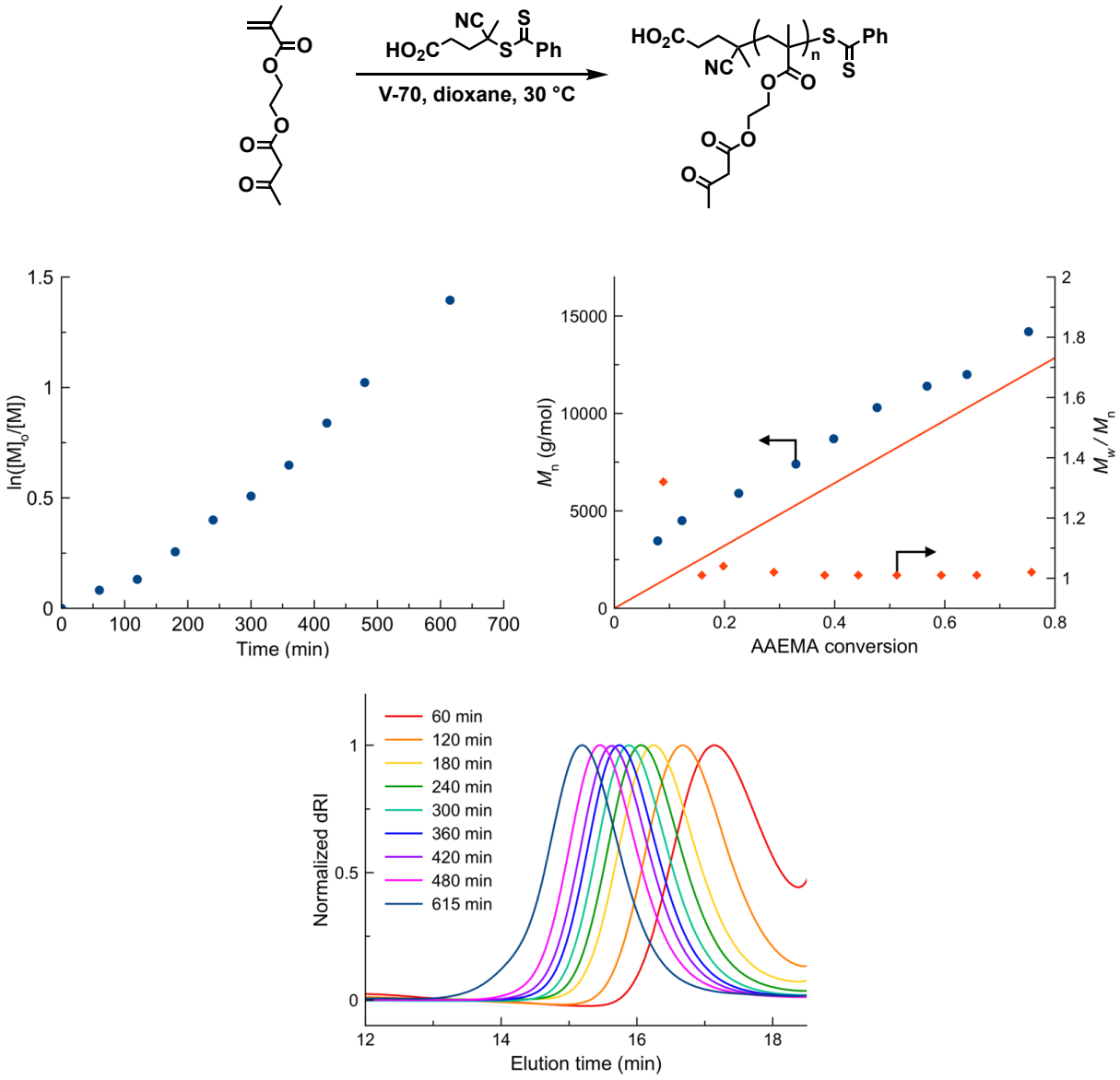


Figure S1. (A) Kinetic plot depicting pseudo-1st order conversion of AAEMA; (B) plot of linear PAAEMA molecular weight growth with monomer conversion (blue markers) with overlaid theoretical molecular weights (orange line), and plot of constant low dispersities throughout polymerization (orange markers); (C) overlaid GPC traces depicting growth of a symmetric, unimodal molecular weight distribution with time.

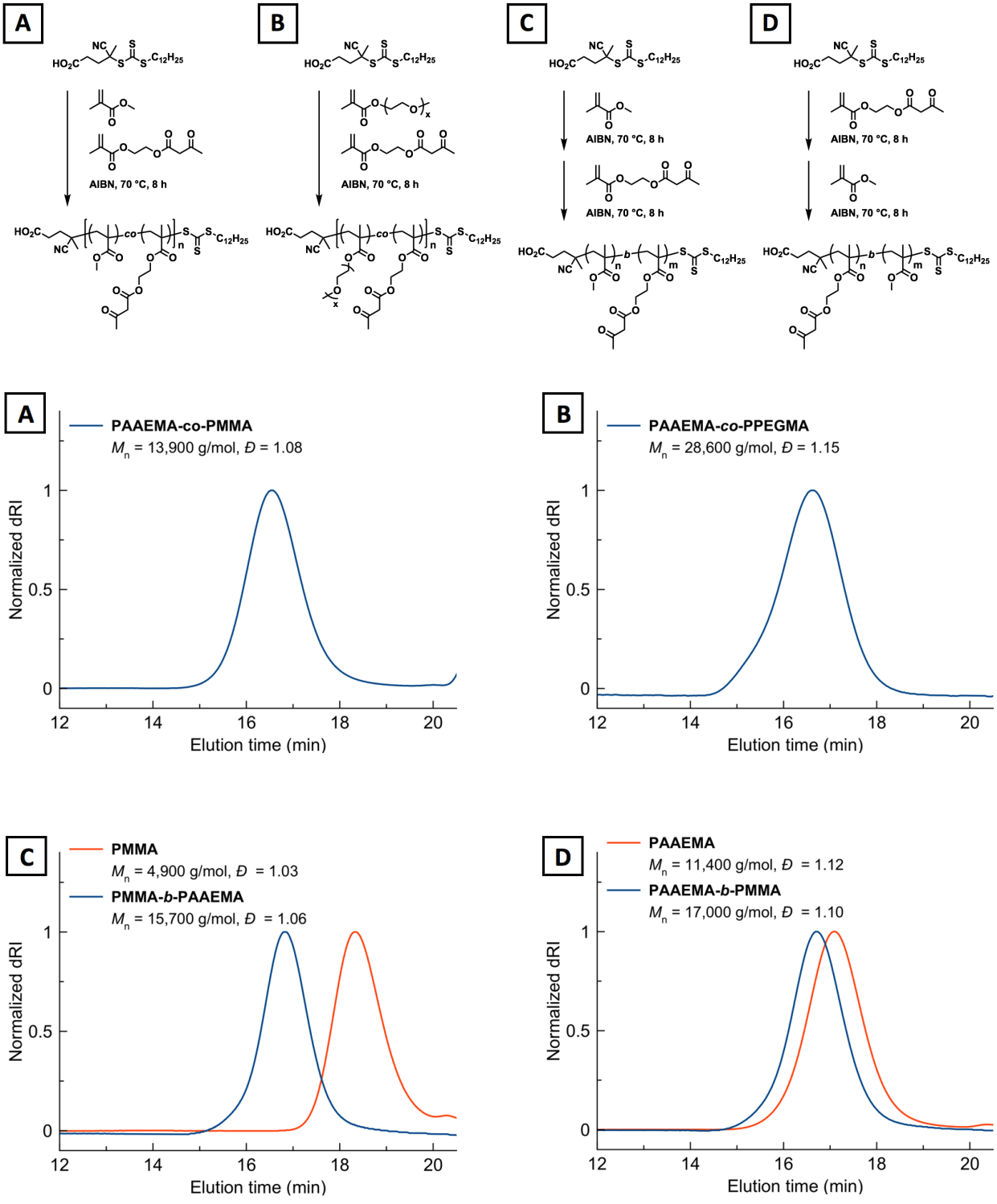


Figure S2. Synthesis of AAEMA-containing copolymers by RAFT polymerization with corresponding GPC traces depicting well-defined copolymers.

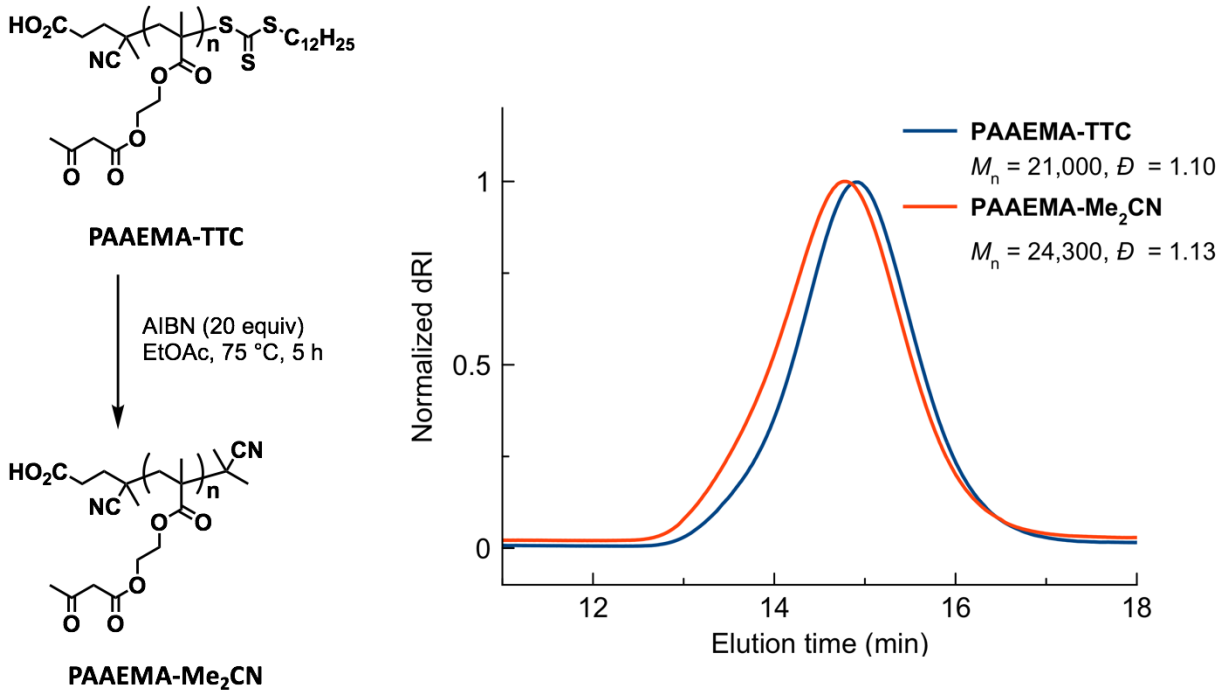


Figure S3. Trithiocarbonate end-group removal by treatment with excess initiator at elevated temperatures. Overlaid GPC traces of the polymer before (blue trace) and after (orange trace) reaction indicate a broadening of the molecular weight distribution, possibly due to chain transfer to the PAAEMA possibly

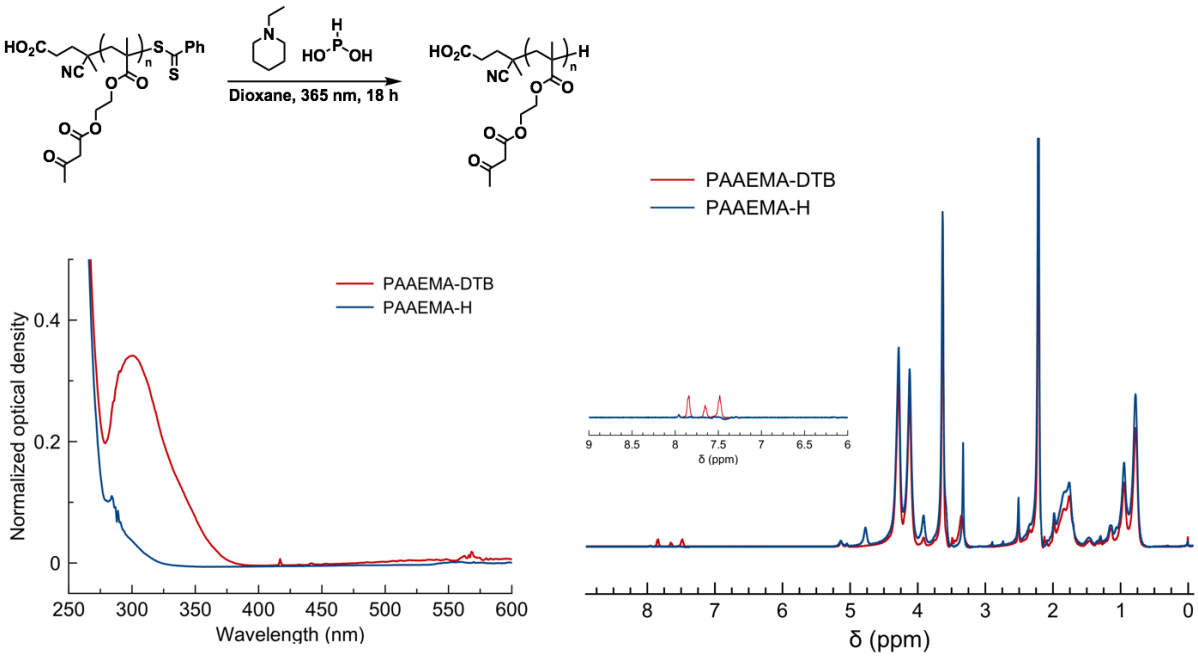


Figure S4. Spectroscopic characterization of photoinduced end-group removal of dithiobenozyl-terminated PAAEMA; (A) offline UV-Vis spectrum before (red trace) and after (blue trace) end-group removal depicting disappearance of the dithiobenzoate □→□is spectrum before (red trace) an^{1}H NMR spectrum before (red trace) and after (blue trace) end-group removal with inset depicting the disappearance of dithiobenzoate aromatic proton resonances.

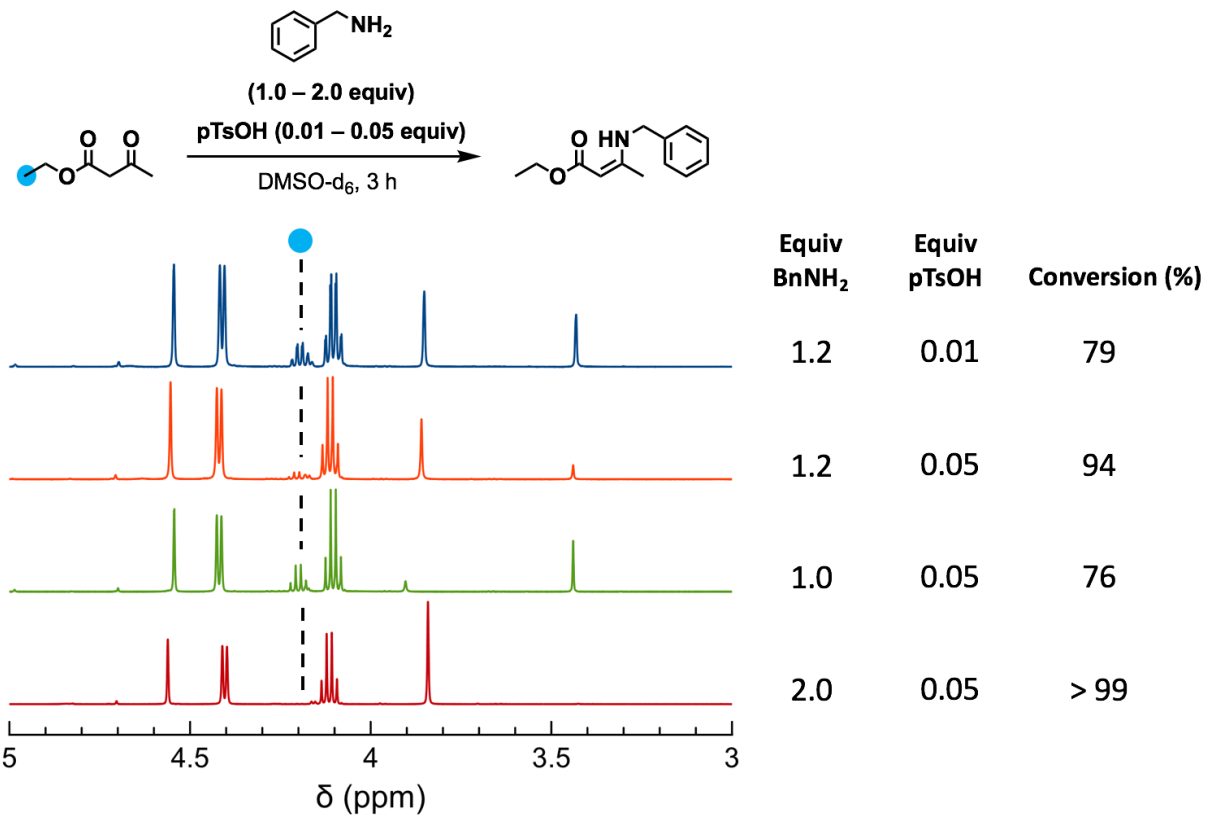


Figure S5. Optimization of the reaction between ethyl acetoacetate and benzylamine by *in situ* NMR analysis. Conversion of ethyl acetoacetate was determined by monitoring the disappearance of the depicted peak relative to an internal trioxane standard.

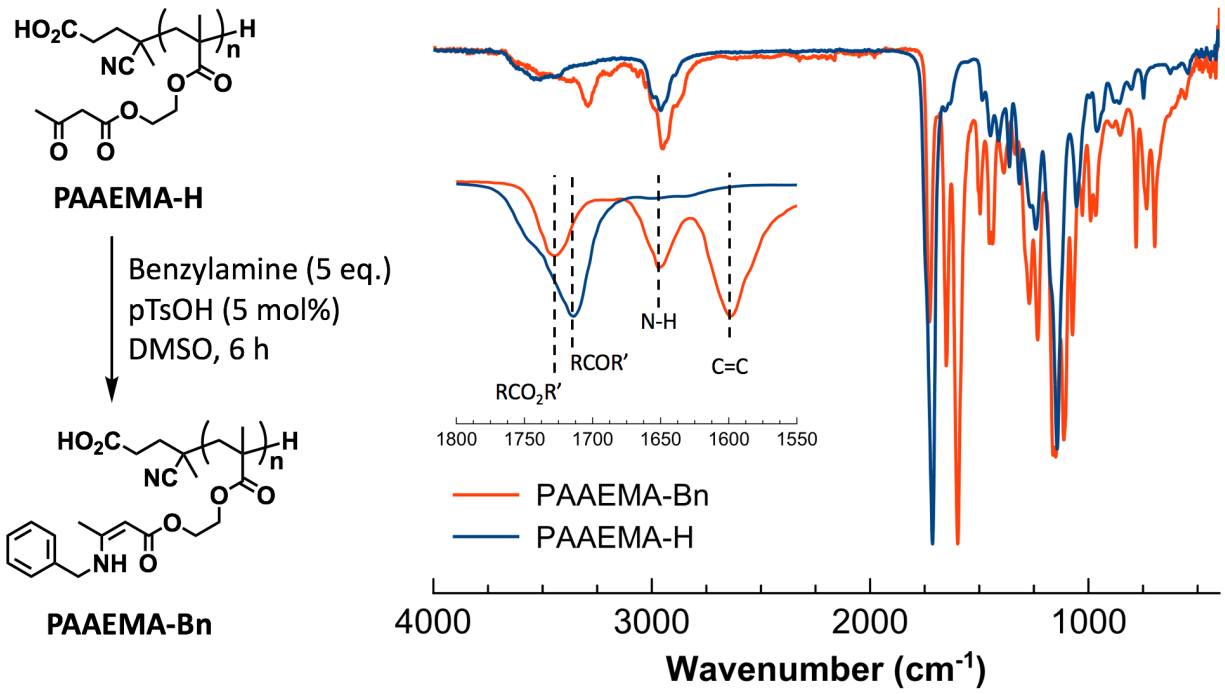


Figure S6. Overlaid IR spectrum of PAAEMA-H (blue trace) and PAAEMA-Bn (blue trace) with diagnostic changes in the spectrum depicted in the inset. A significant reduction in the carbonyl absorbance region is observed corresponding to consumption of pendent ketones, and new absorbances corresponding to N-H bending and C=C stretching modes of newly formed enamines are observed.

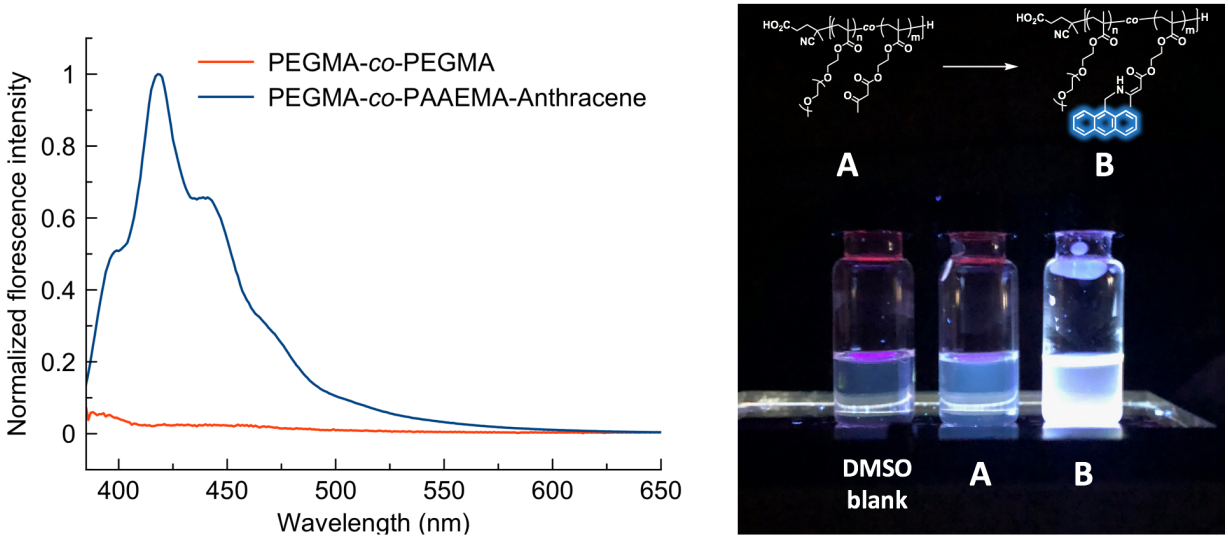


Figure S7. Fluorescence spectrum of PEGMA-PAAEMA before and after functionalization with 9-(aminomethyl)anthracene (left) and image of fluorescence under long-wave UV irradiation (right).

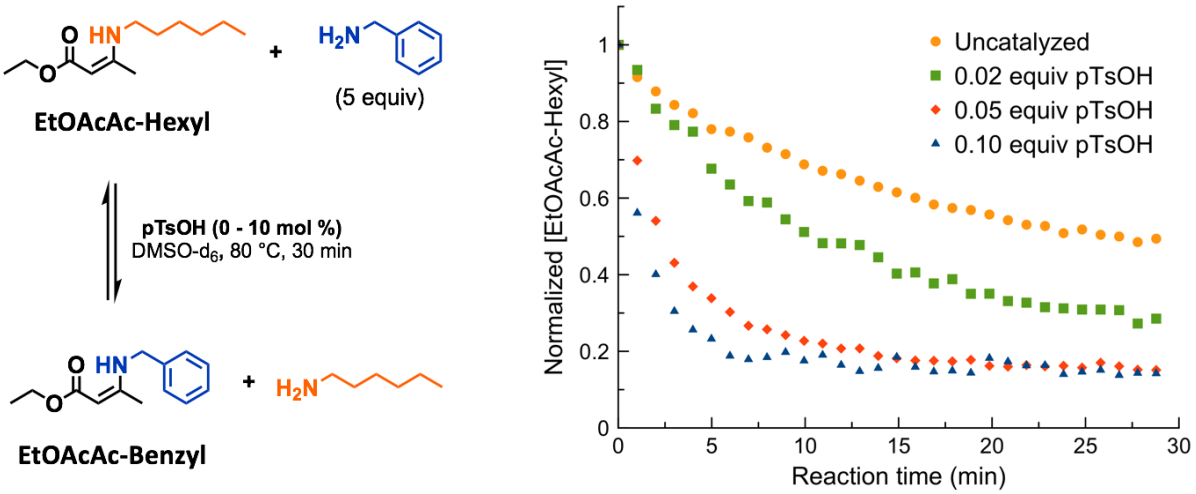


Figure S8. Kinetics of *N*-substituent exchange at 80 °C with varying equivalents of pTsOH catalyst. The reaction proceeds at an appreciable rate with no added catalyst (orange markers), but is accelerated with addition of increasing concentrations of catalyst.

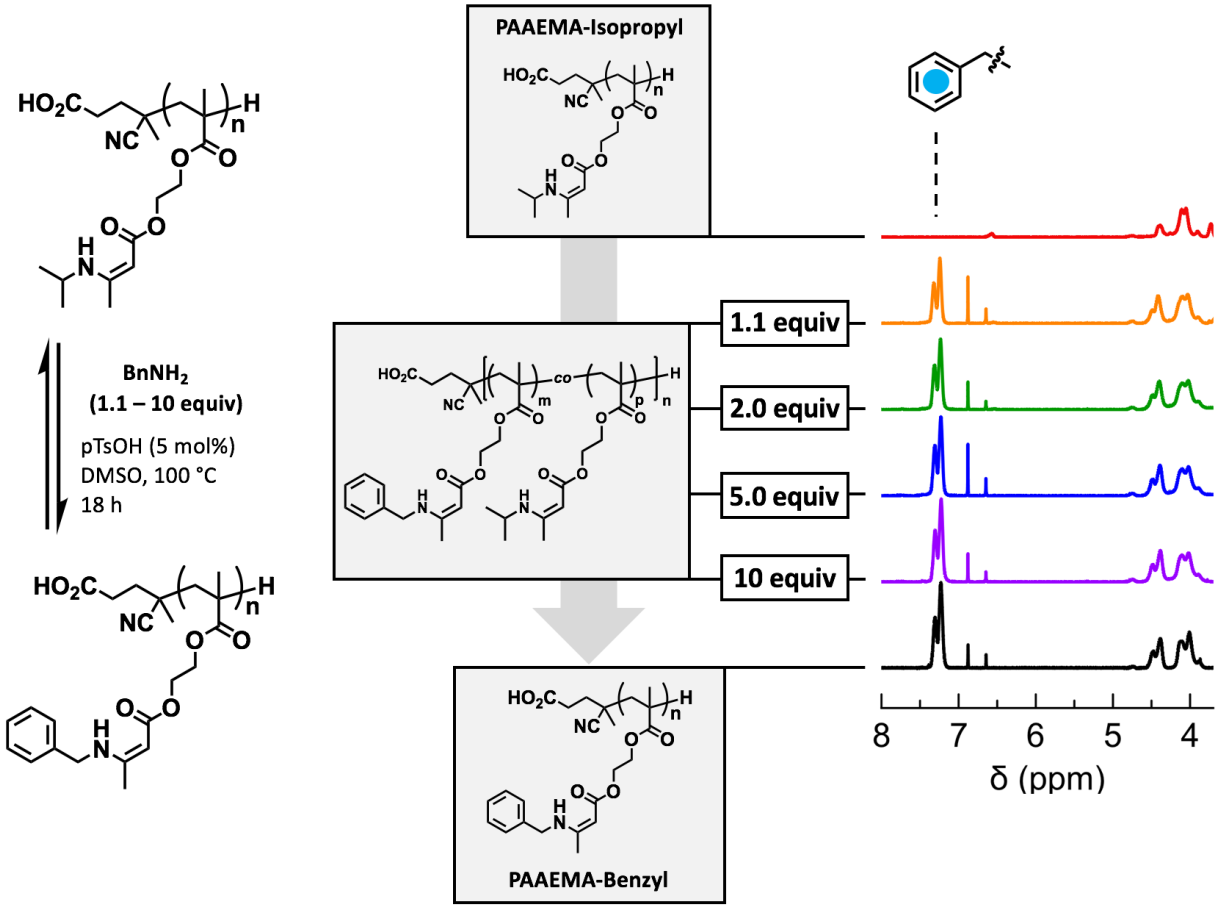


Figure S9. Exchange of pendent *N*-isopropyl substituents for *N*-benzyl substituents through dynamic enaminone exchange. Quantitative conversion of isopropyl substituents was observed presumably due to suppression of the reverse reaction of isopropylamine due to its steric bulk.

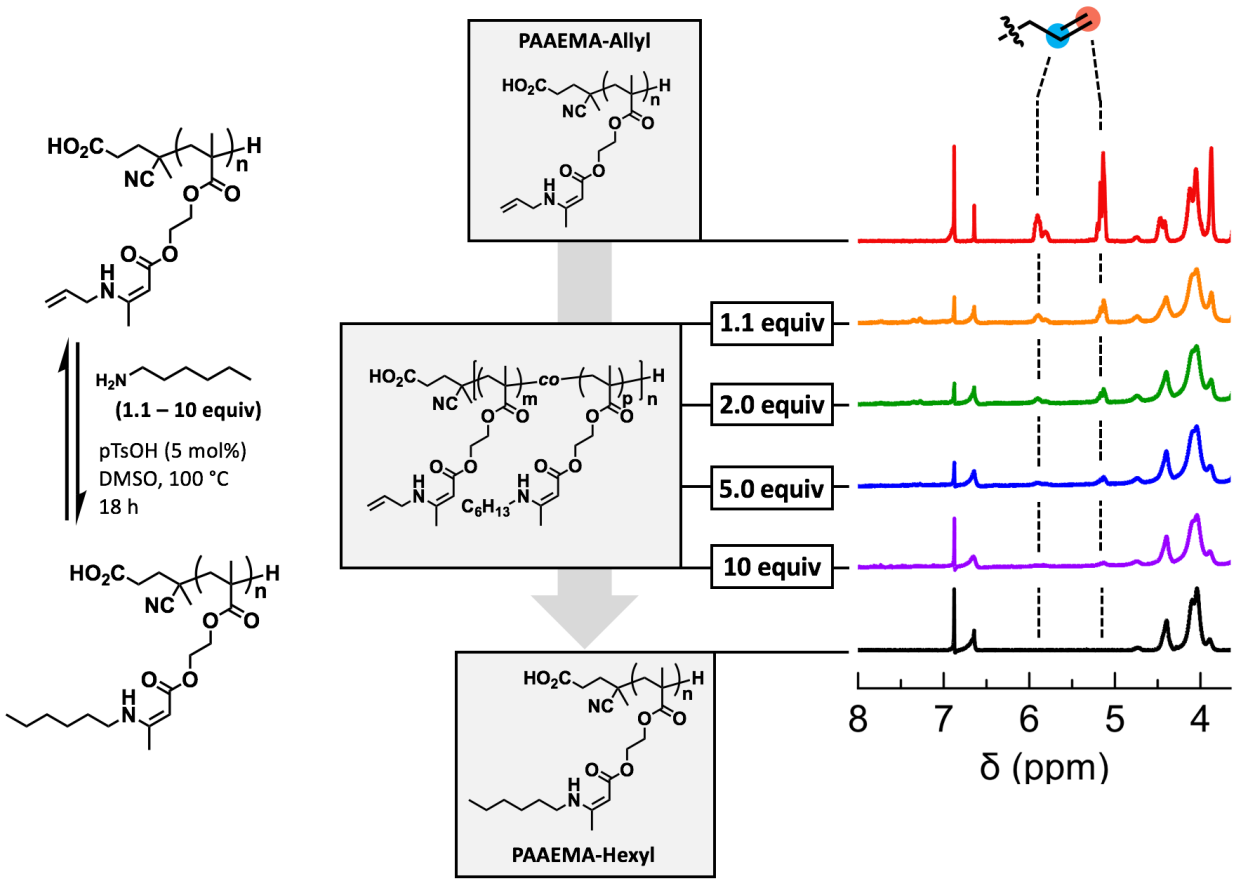
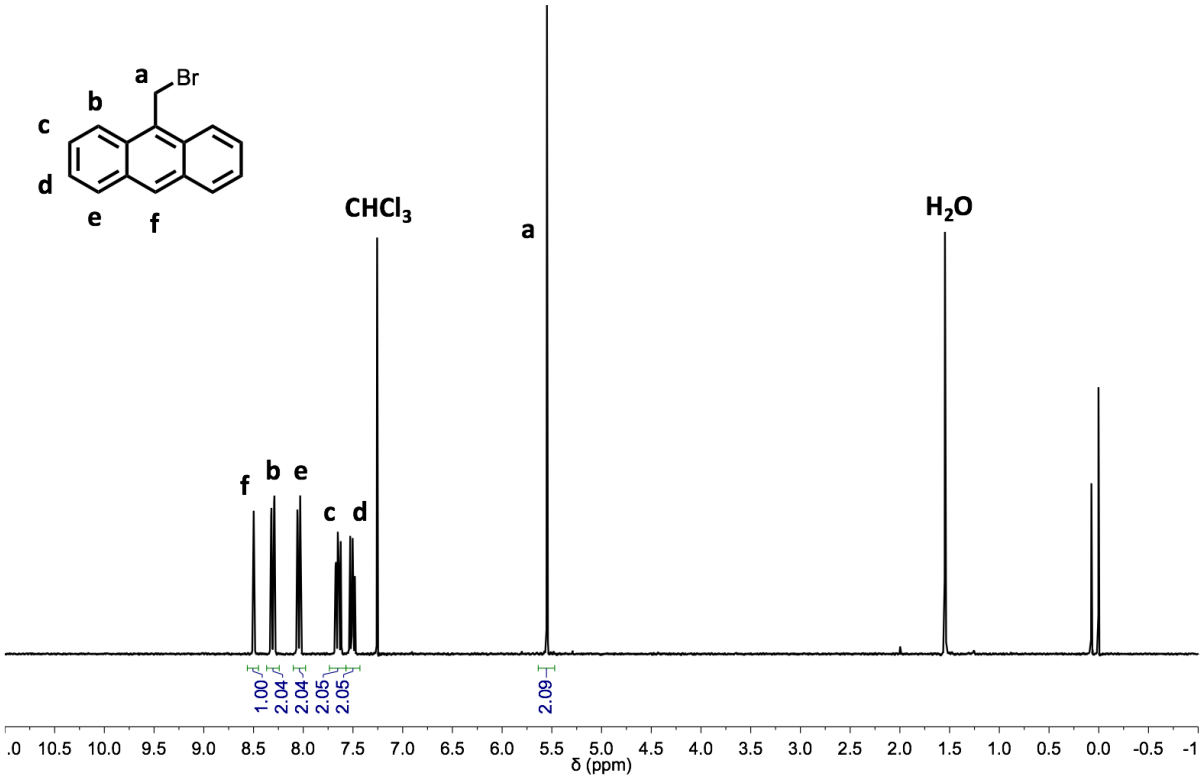


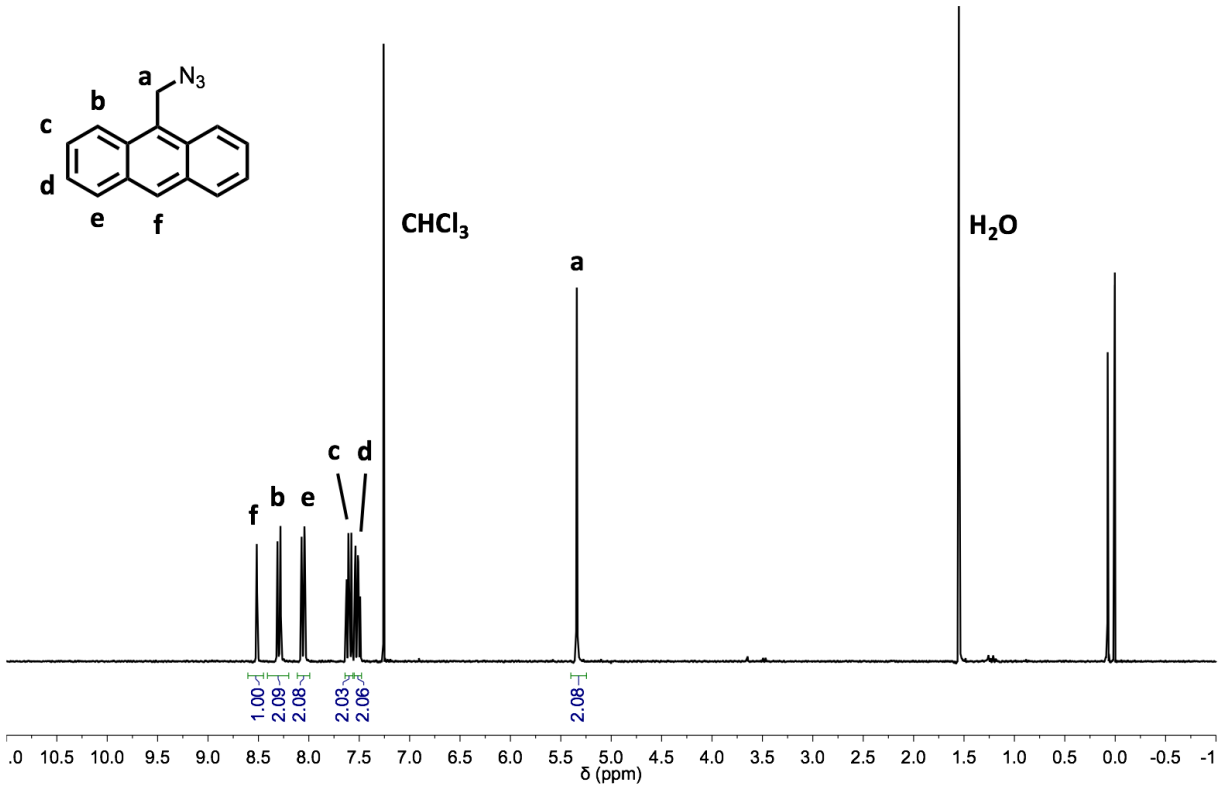
Figure S10. Exchange of pendent *N*-allyl substituents for *N*-hexyl substituents through dynamic enaminone exchange. Reactions were conducted open to air to promote volatilization of liberated allylamine and drive exchange to the hexyl product.

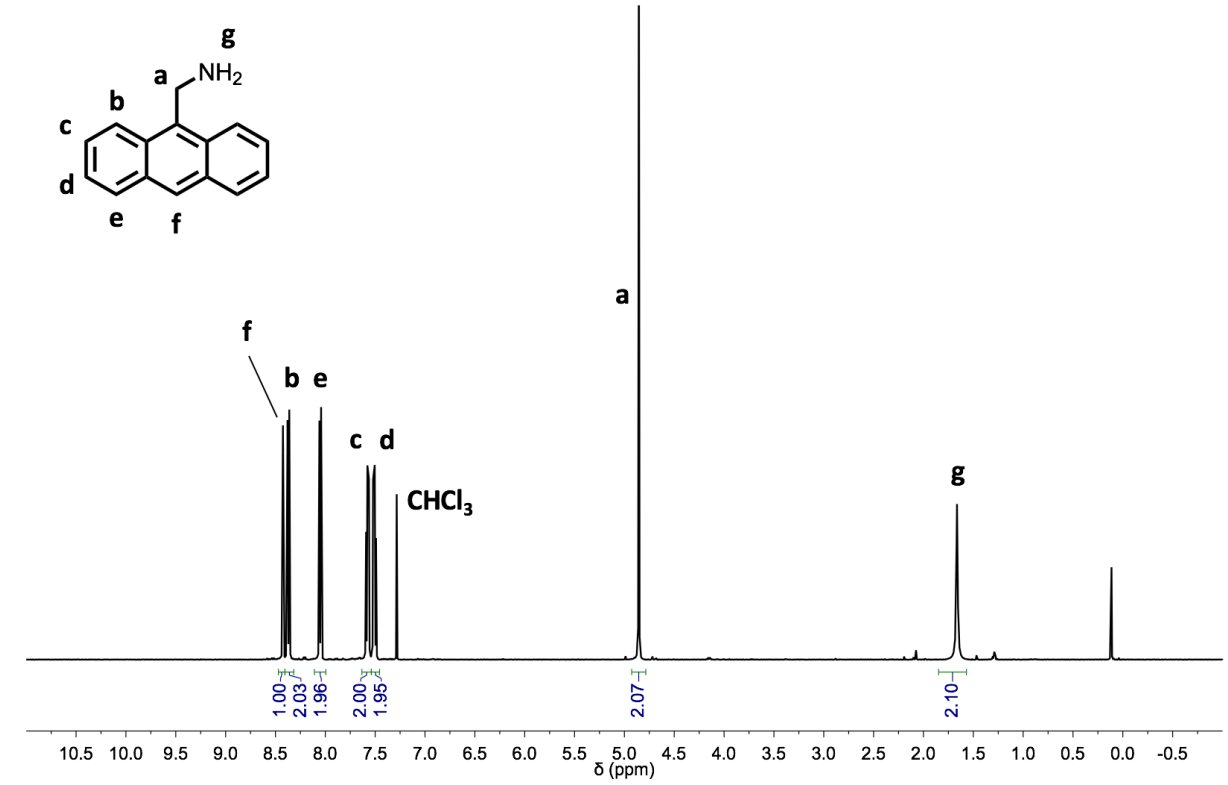
Table S1. Efficiency of functional exchange on PAAEMA-R as a function of initial *N*-substituent

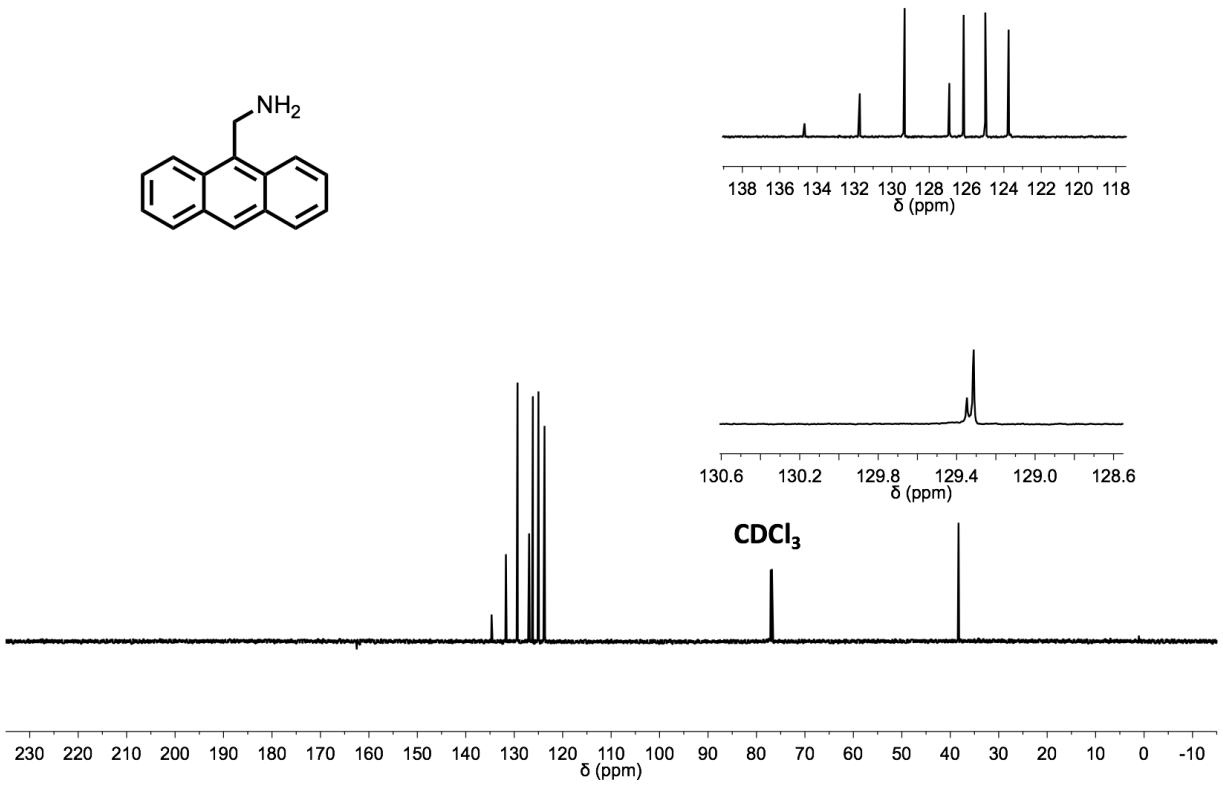
			Conversion of initial R-group (%)			
Entry	**Equiv hexyl-NH_2**	**Theo. Conversion (%)**	**R = Bn**	**R = Ph**	**R = Allyl**	**R = Isopropyl**
1	1.1	52	65	97	71	83
2	2.0	67	78	99	83	97
3	5.0	83	91	> 99	91	> 99
4	10	91	95	> 99	95	> 99

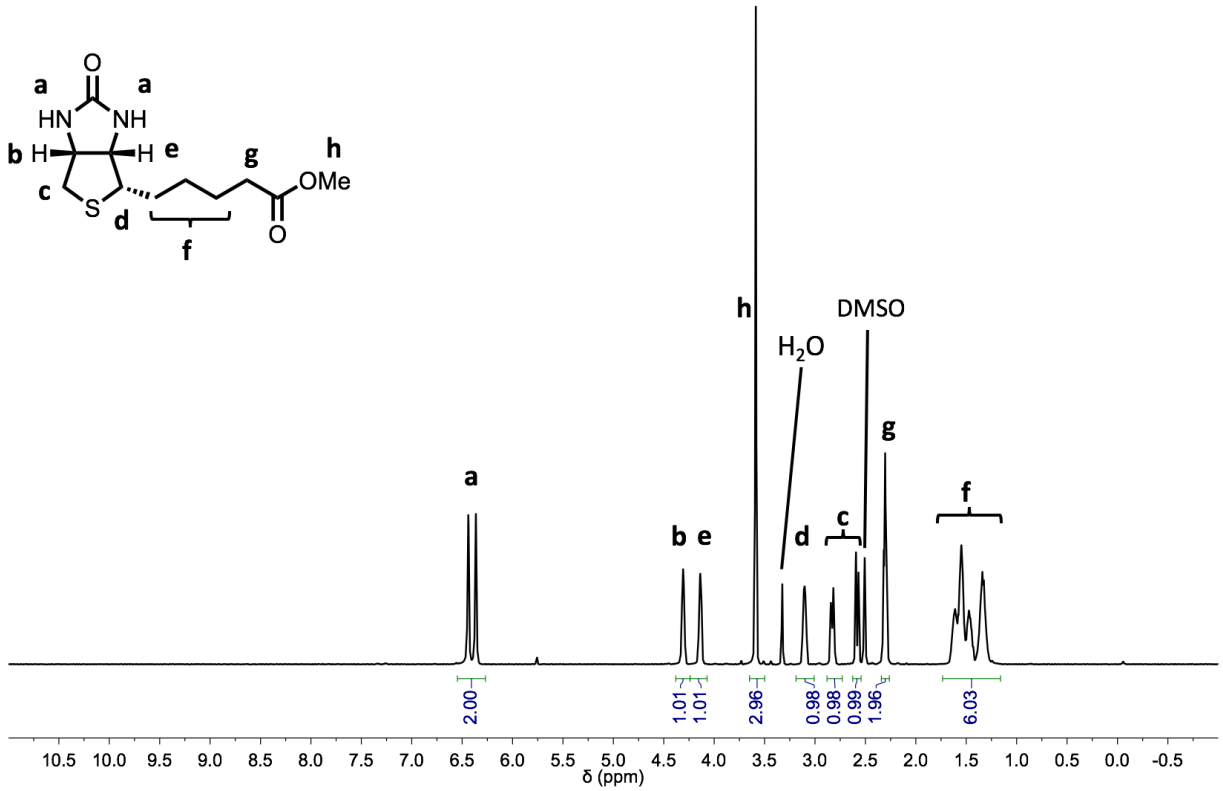
SPECTROSCOPIC CHARACTERIZATION

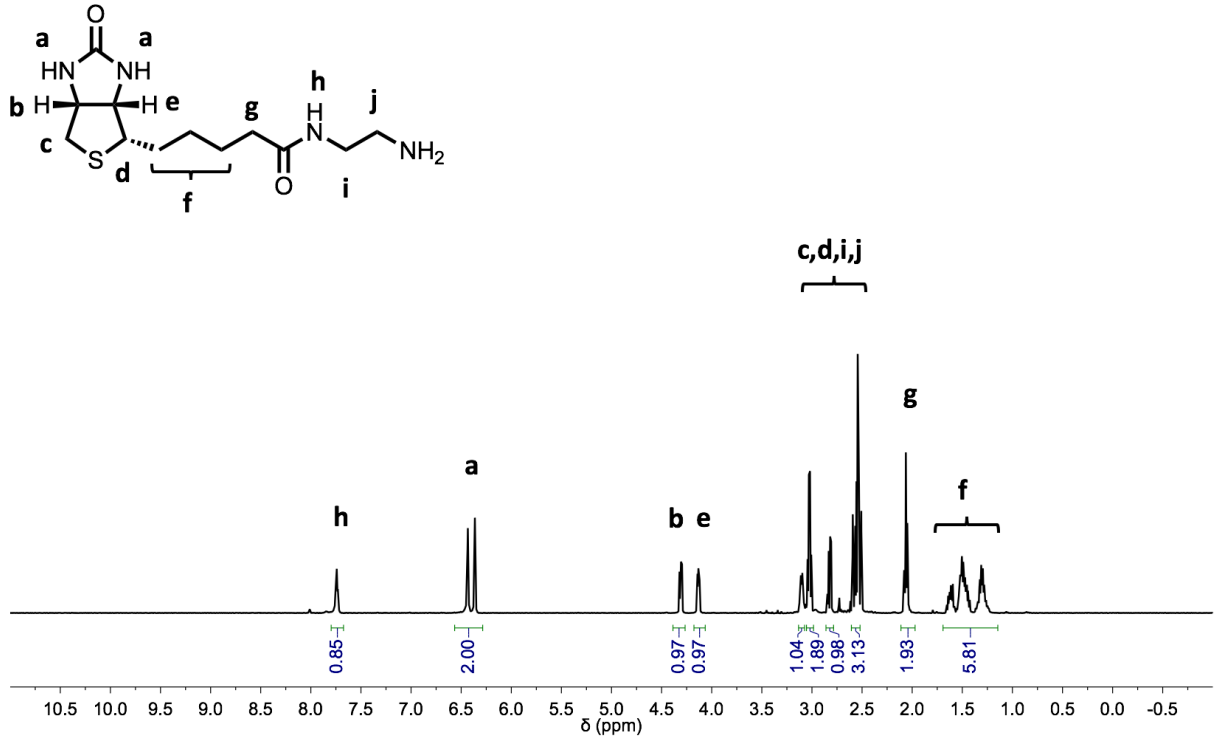


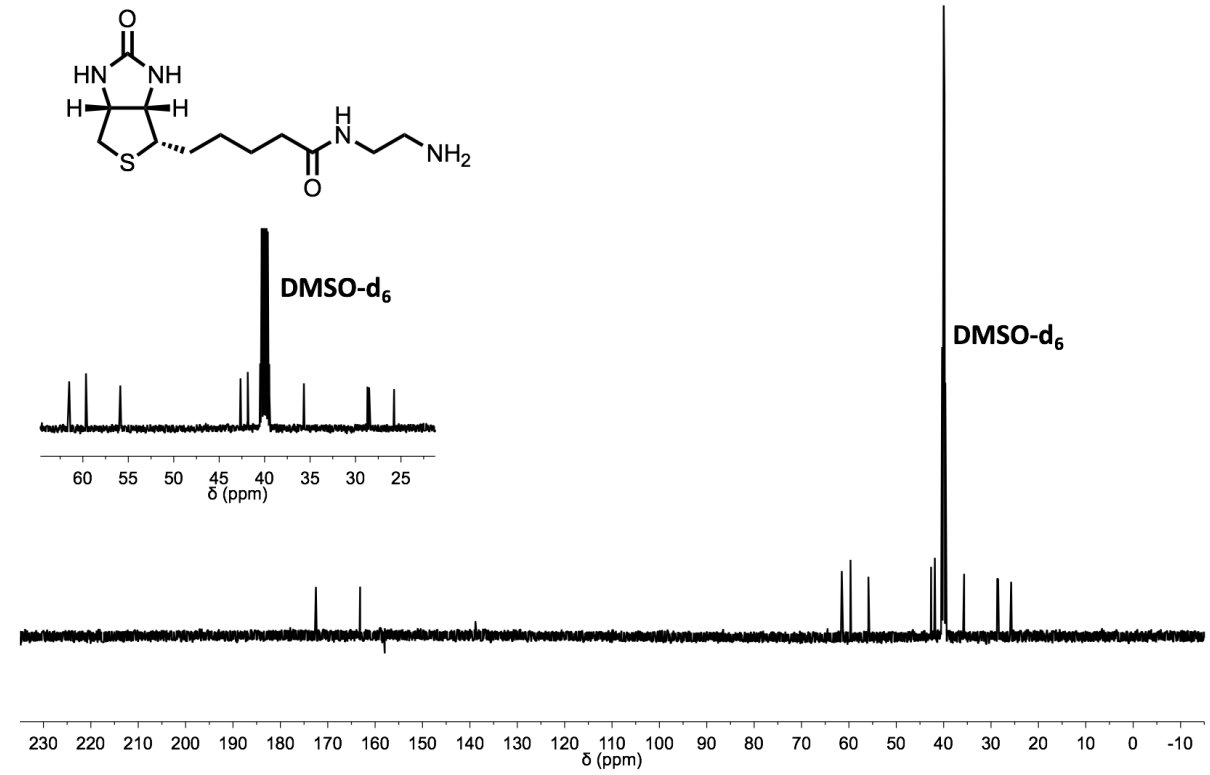


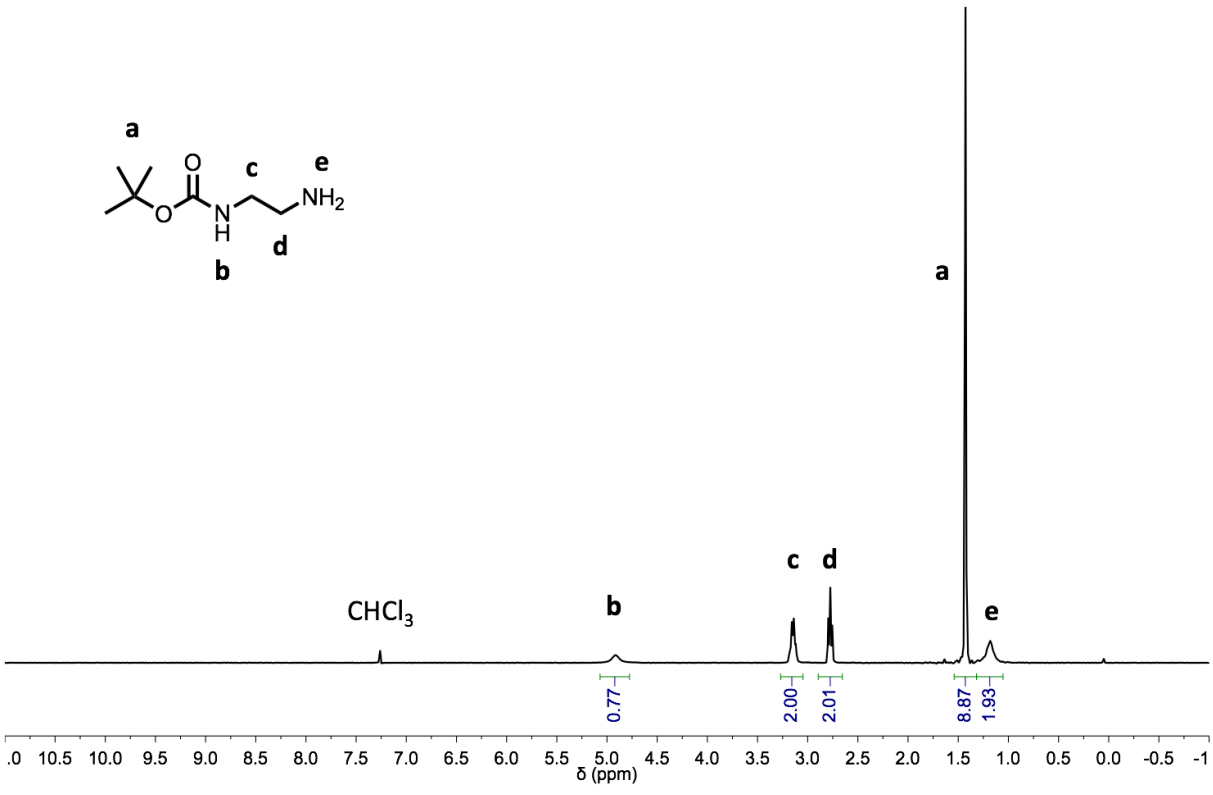

g
a
NH2
b
c
d
e
f
f
b e
c d
CHCl3
a
g
1.00
2.03
1.96
2.00
1.95
2.07
2.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

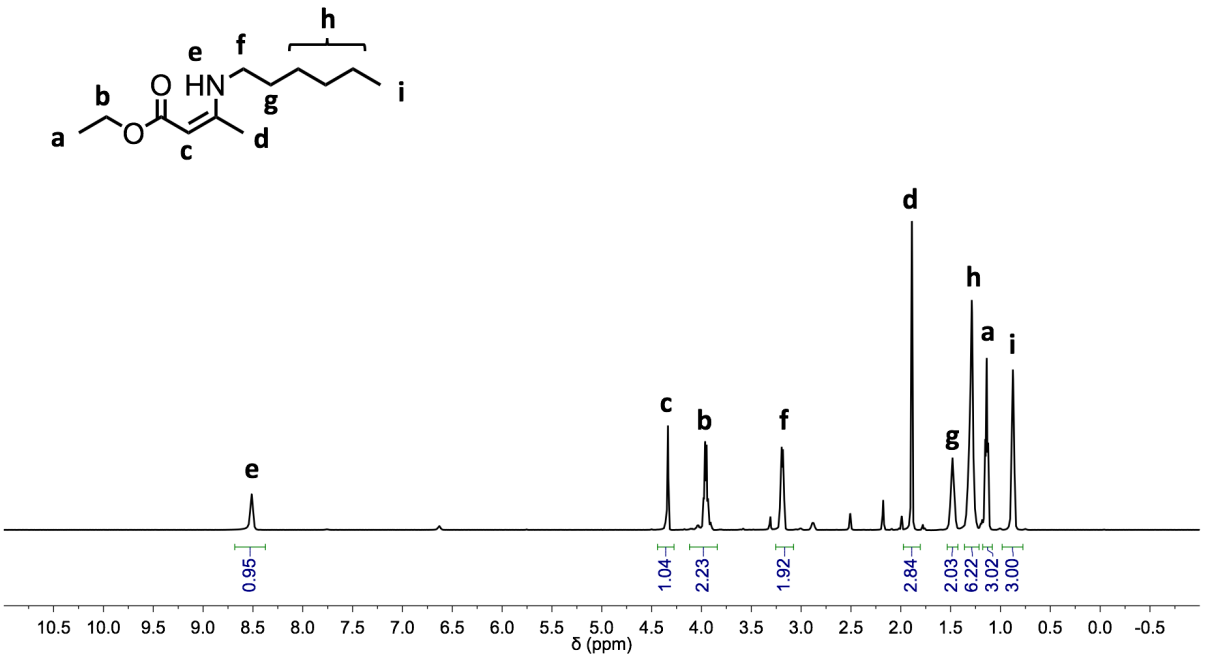

NH2
138 136 134 132 130 128 126 124 122 120 118
δ (ppm)
130.6 130.2 129.8 129.4 129.0 128.6
δ (ppm)
CDCl3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

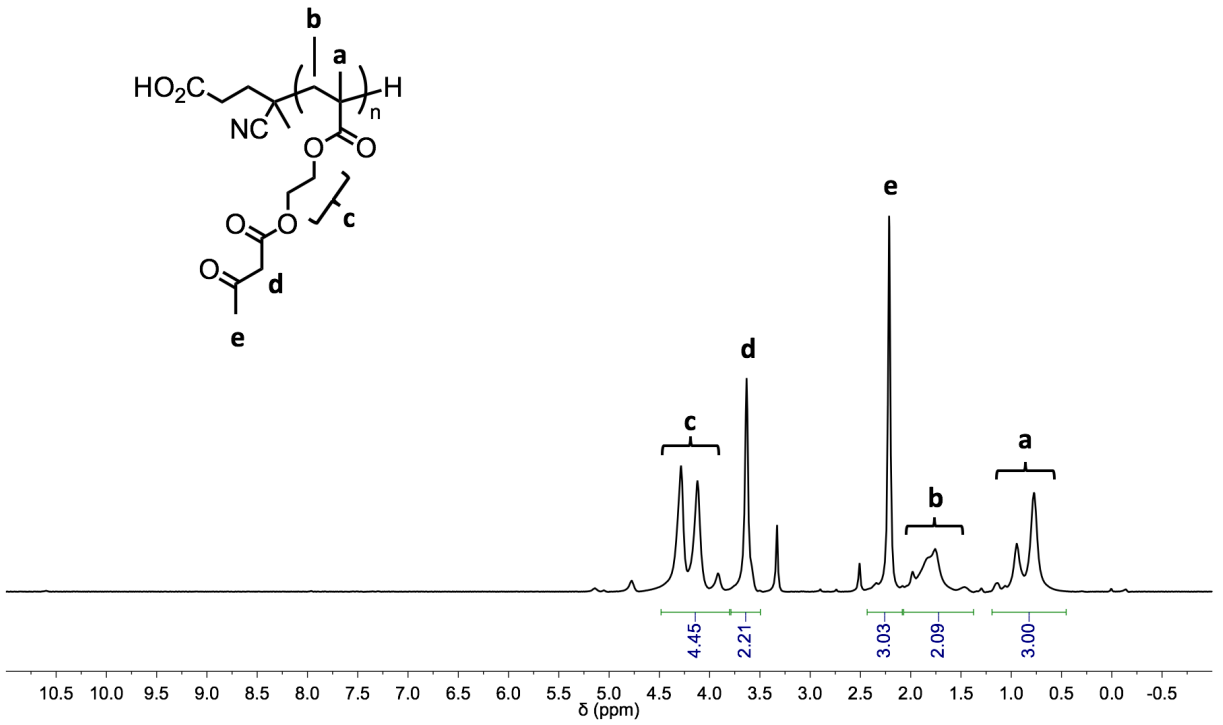

a
a
HN
NH
b H
H e
g
h
c
OMe
S
d
O
f
h
DMSO
H2O
g
a
f
b e
d
c
2.00
1.01
1.01
2.96
0.98
0.98
0.99
1.96
6.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

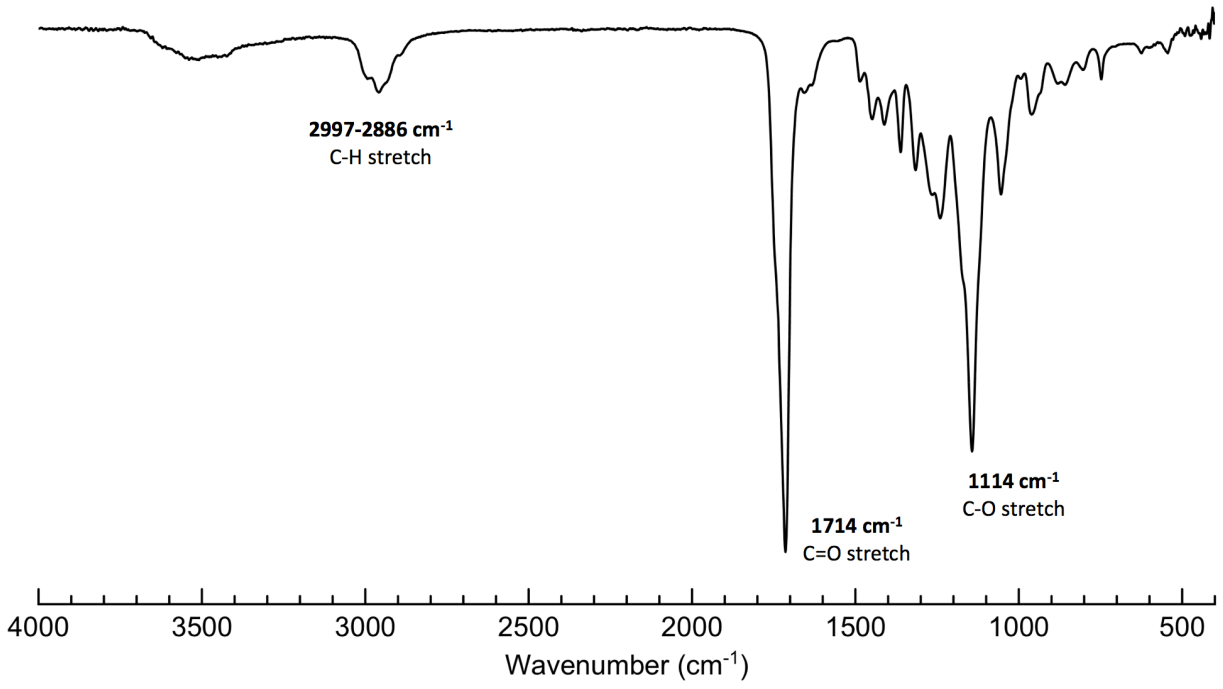

a
a
HN
NH
b H
H e
g
h
H
N
j
c
NH2
S
d
O
i
f
c,d,i,j
g
a
f
h
b e
0.85
2.00
0.97
0.97
1.04
1.89
0.98
3.13
1.93
5.81
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

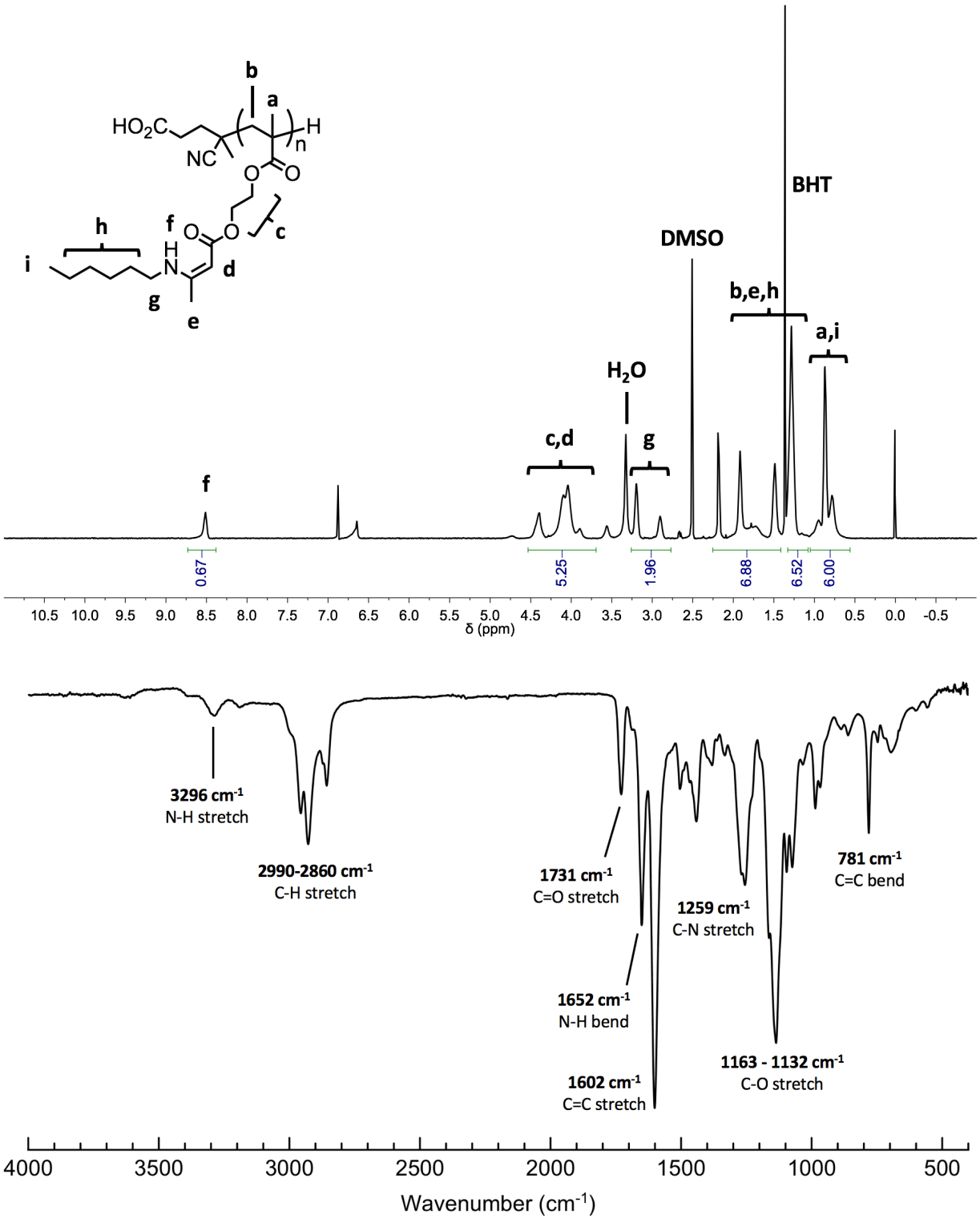

DMSO-d6
DMSO-d6
δ (ppm)
δ (ppm)

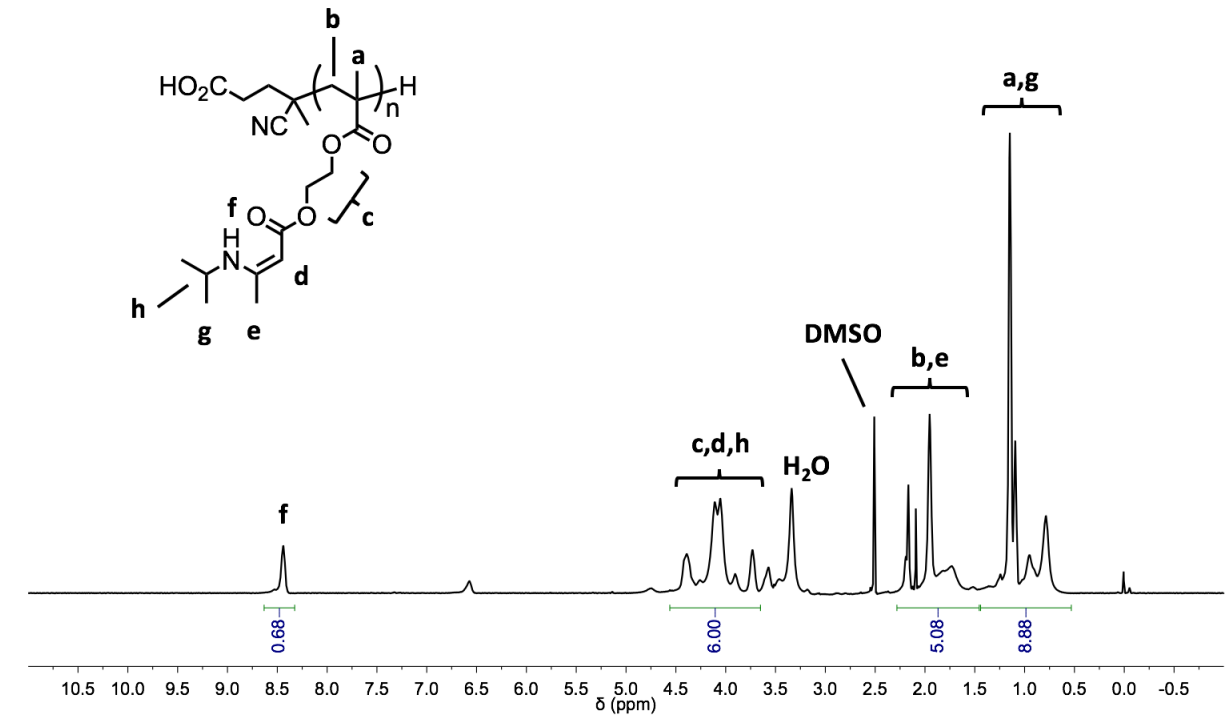

a
b
c
d
e
CHCl3
0.77
2.00
2.01
8.87
1.93
δ (ppm)

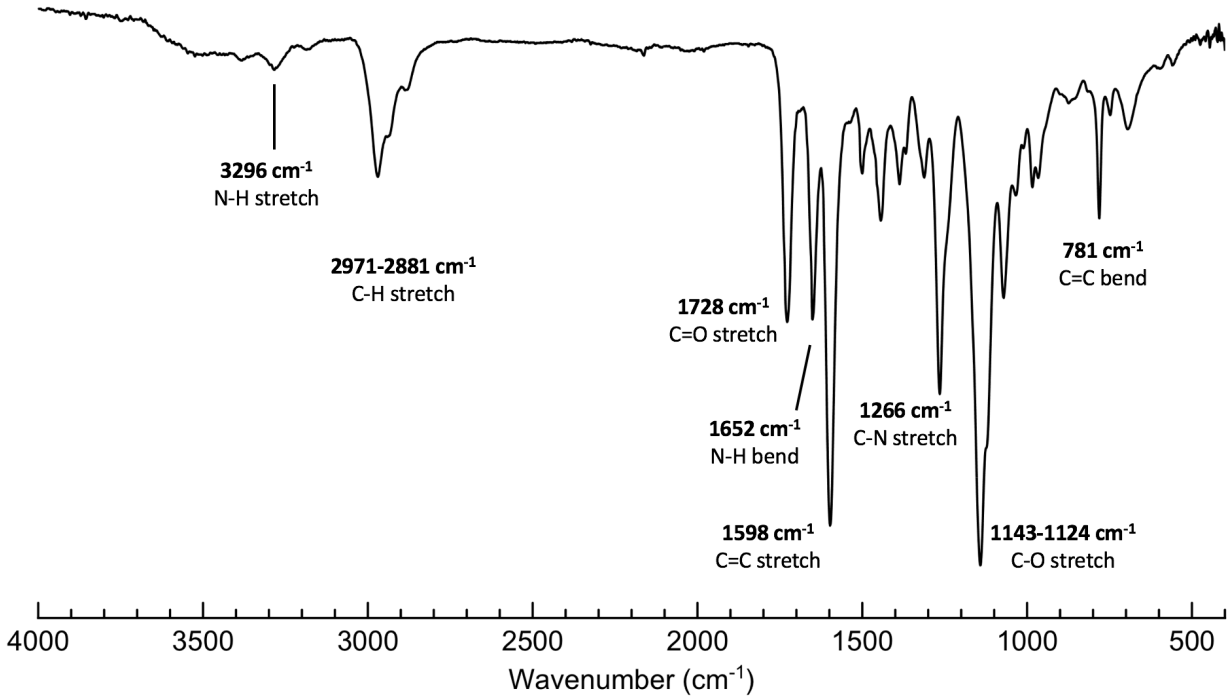

h
e
f
b
O
HN
g
i
a
O
c
d
d
h
a
i
c
b
f
g
e
0.95
1.04
2.23
1.92
2.84
2.03
6.22
3.02
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

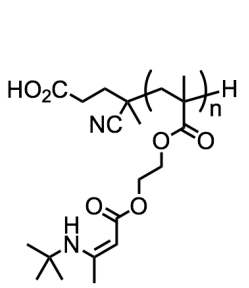

b
a
HO2C
H
n
NC
O
O
O
O
c
O
d
e
e
d
c
a
b
4.45
2.21
3.03
2.09
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)


2997-2886 cm-1
C-H stretch
1714 cm-1
C=O stretch
1114 cm-1
C-O stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

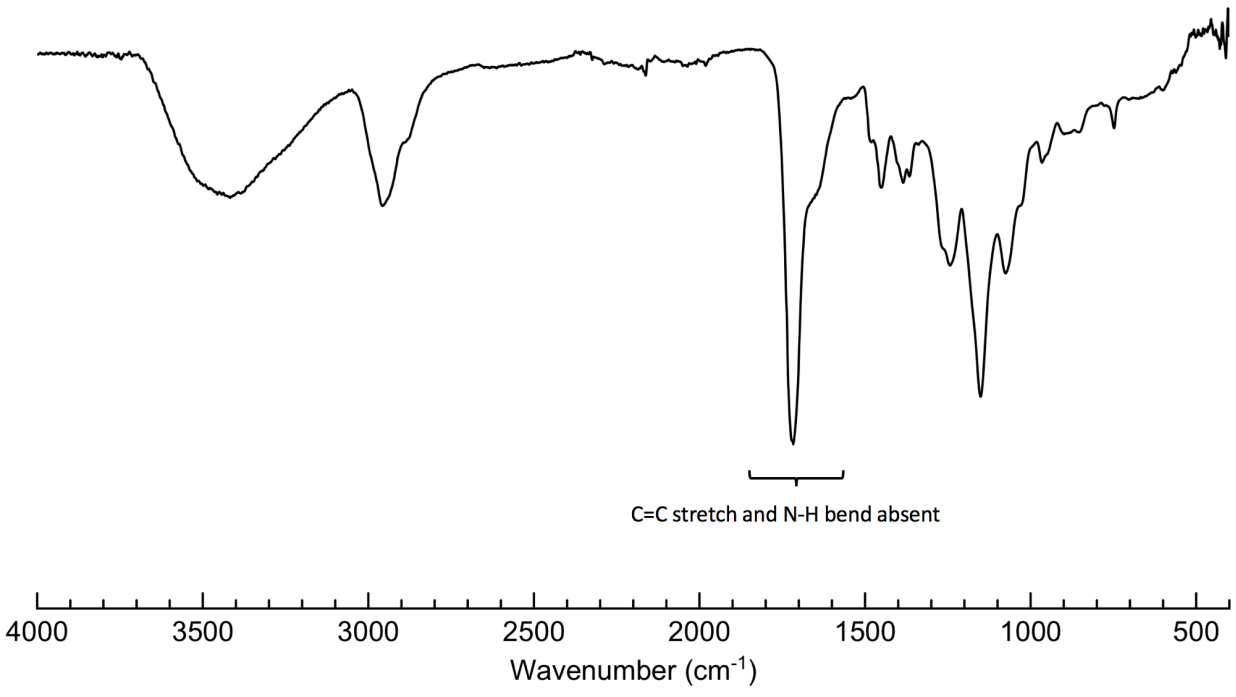

b
a
HO2C
H
n
NC
O
O
h
f
O
O
c
i
H
N
d
g
e
BHT
DMSO
b,e,h
a,i
H2O
c,d
g
f
0.67
5.25
1.96
6.88
6.52
6.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)
3296 cm-1
N-H stretch
2990-2860 cm-1
C-H stretch
1731 cm-1
C=O stretch
1652 cm-1
N-H bend
1602 cm-1
C=C stretch
1259 cm-1
C-N stretch
1163 - 1132 cm-1
C-O stretch
781 cm-1
C=C bend
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

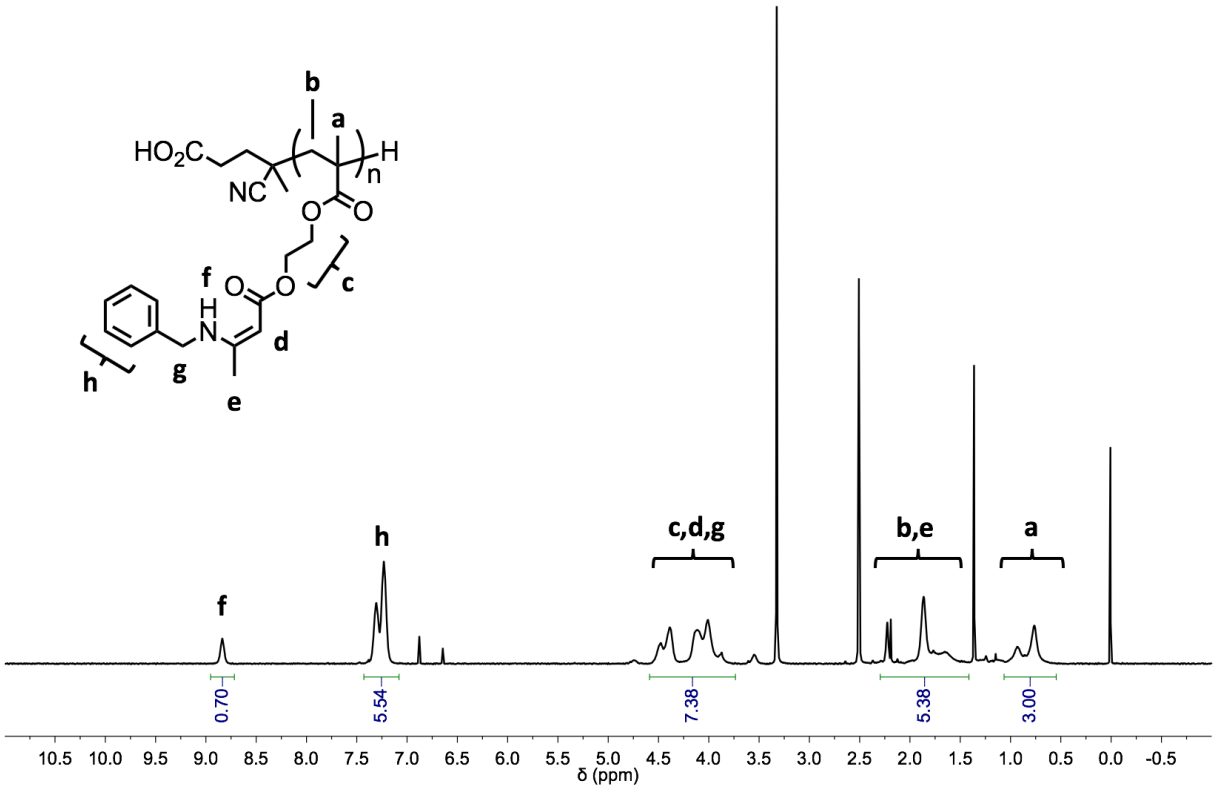

b
a
HO2C
H
n
NC
O
O
f
O
O
c
H
N
d
h
g
e
a,g
DMSO
b,e
c,d,h
H2O
f
0.68
6.00
5.08
8.88
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

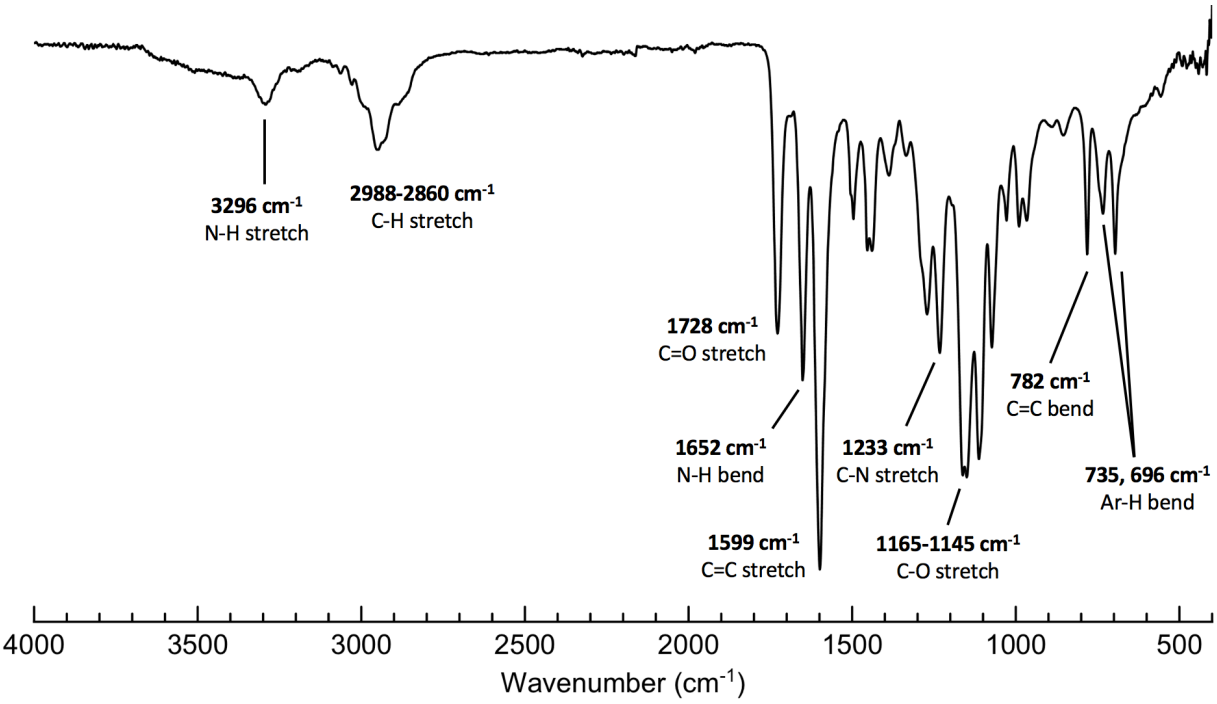

3296 cm-1
N-H stretch
2971-2881 cm-1
C-H stretch
1728 cm-1
C=O stretch
1652 cm-1
N-H bend
1598 cm-1
C=C stretch
1266 cm-1
C-N stretch
1143-1124 cm-1
C-O stretch
781 cm-1
C=C bend
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

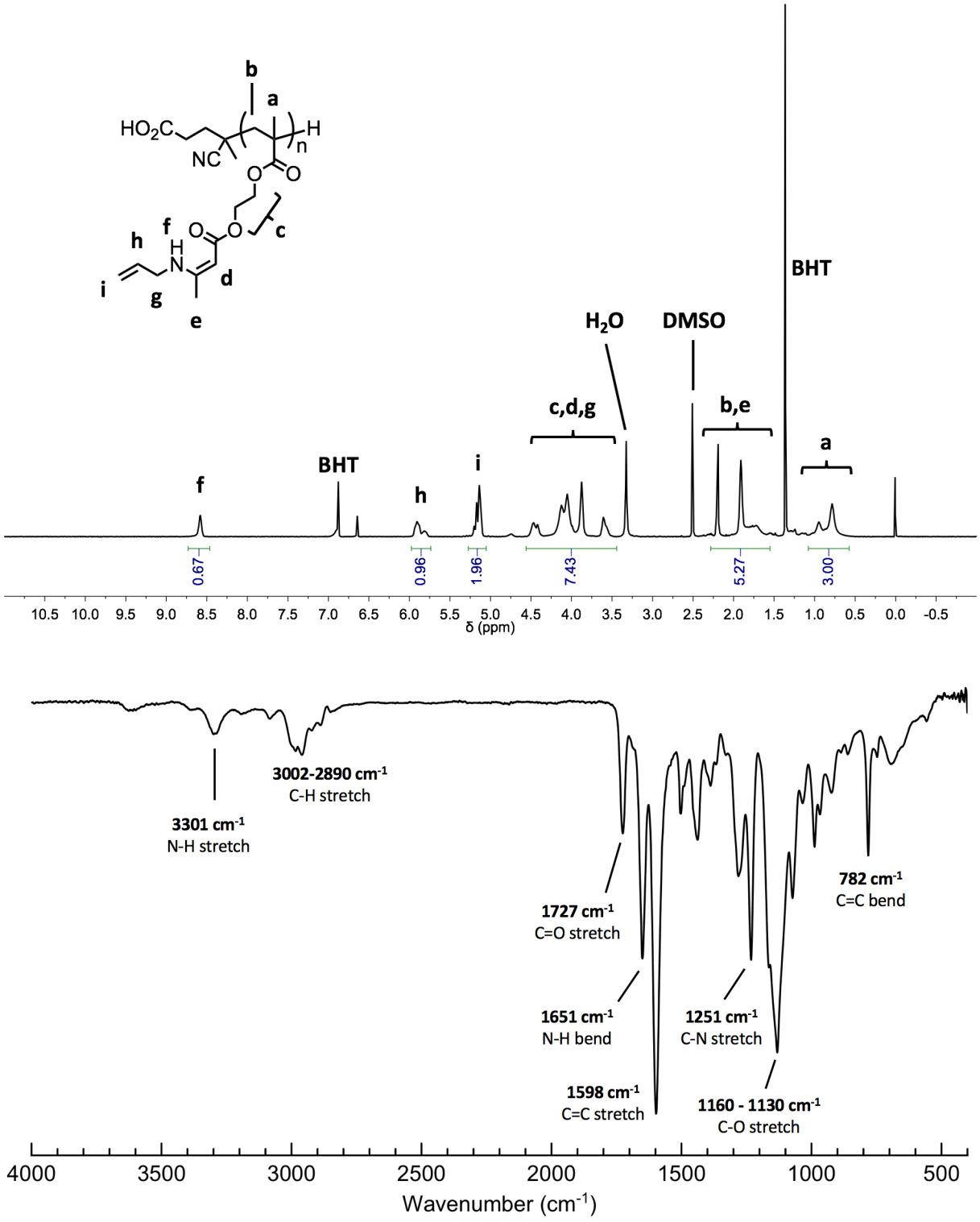


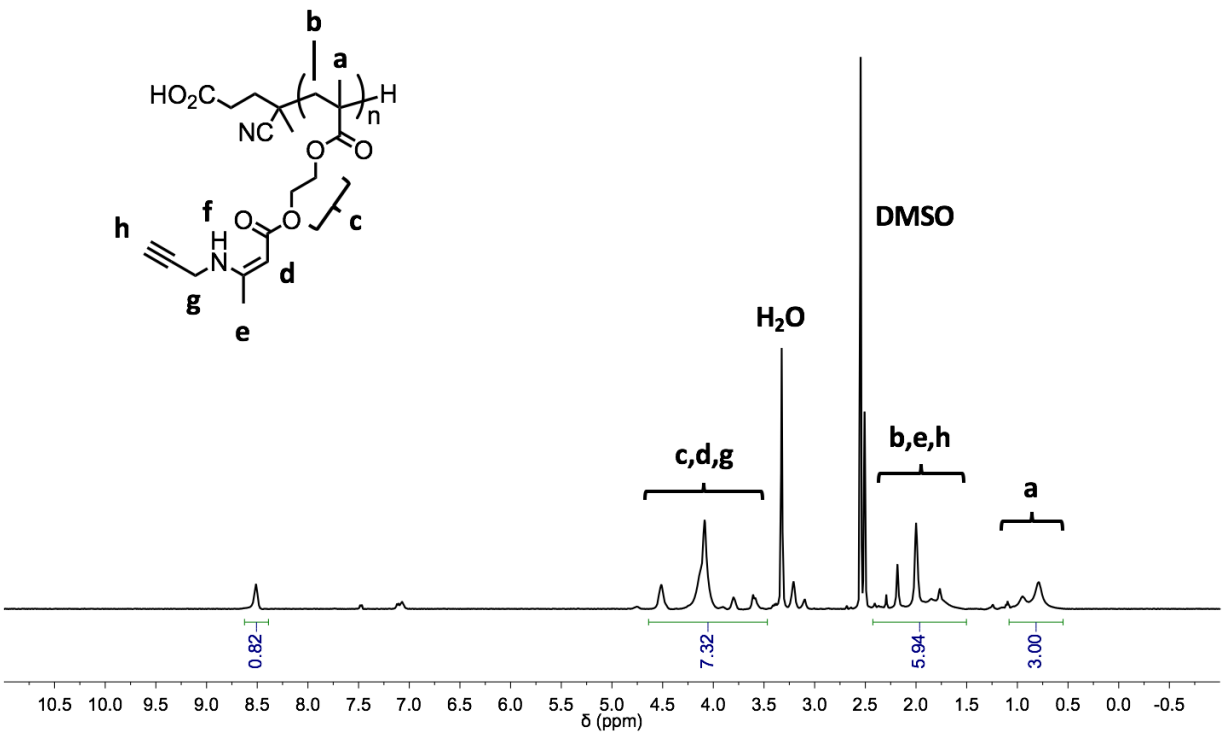
not detected

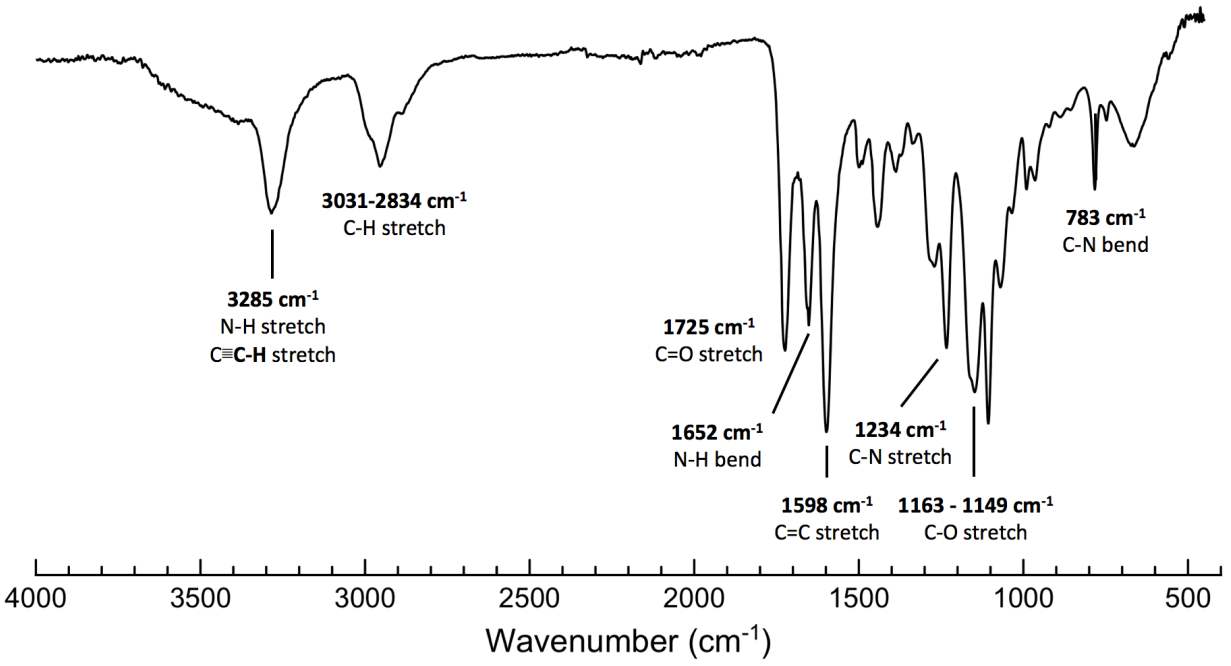


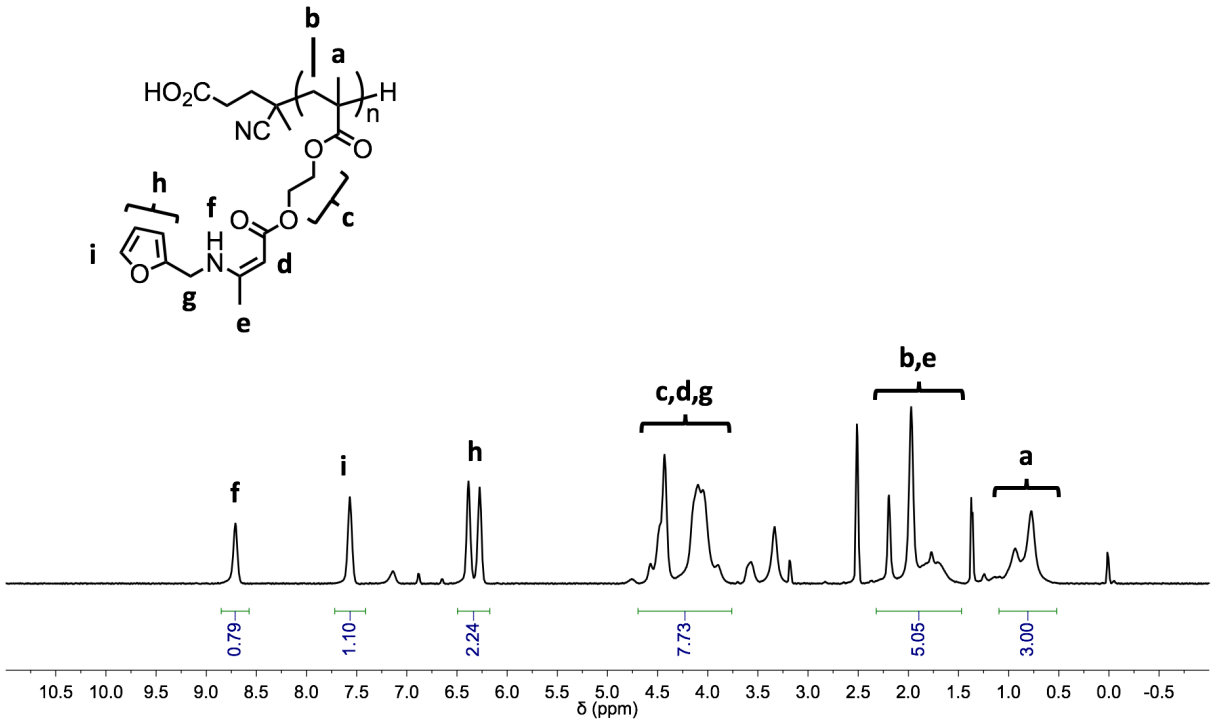

b
a
HO2C
H
n
NC
O
O
f
O
O
c
H
N
d
g
h
e
f
h
c,d,g
b,e
a
0.70
5.54
7.38
5.38
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

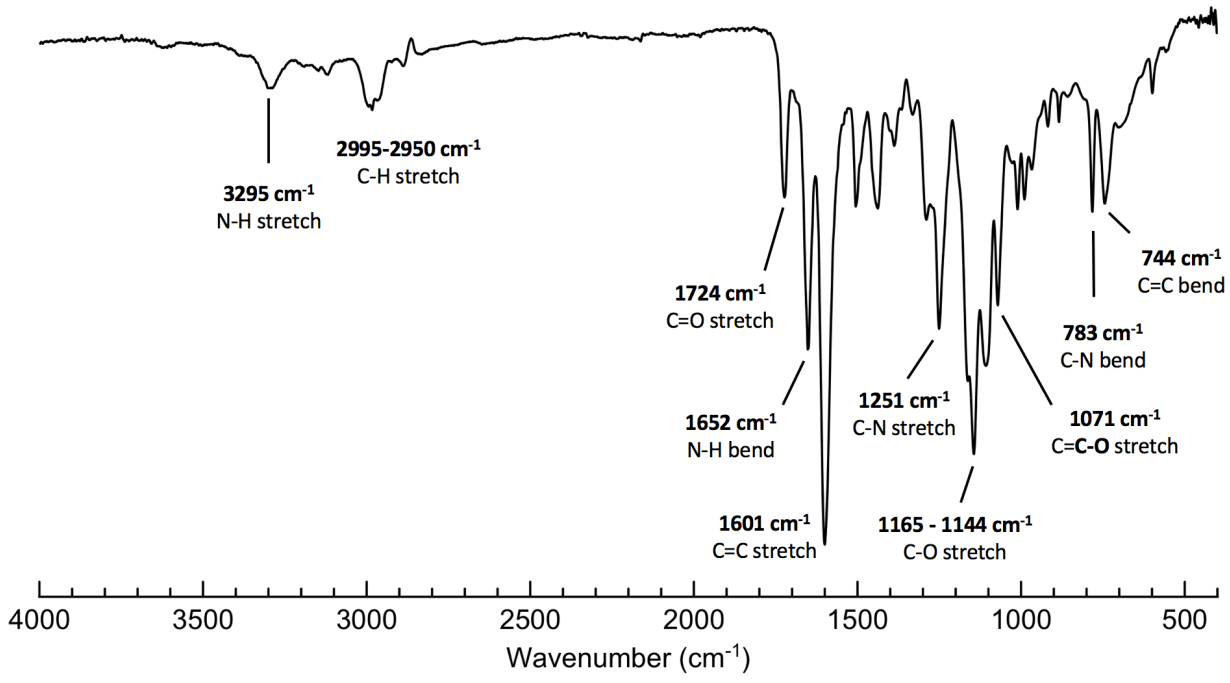

3296 cm-1
N-H stretch
2988-2860 cm-1
C-H stretch
1728 cm-1
C=O stretch
1652 cm-1
N-H bend
1599 cm-1
C=C stretch
1233 cm-1
C-N stretch
1165-1145 cm-1
C-O stretch
782 cm-1
C=C bend
735, 696 cm-1
Ar-H bend
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

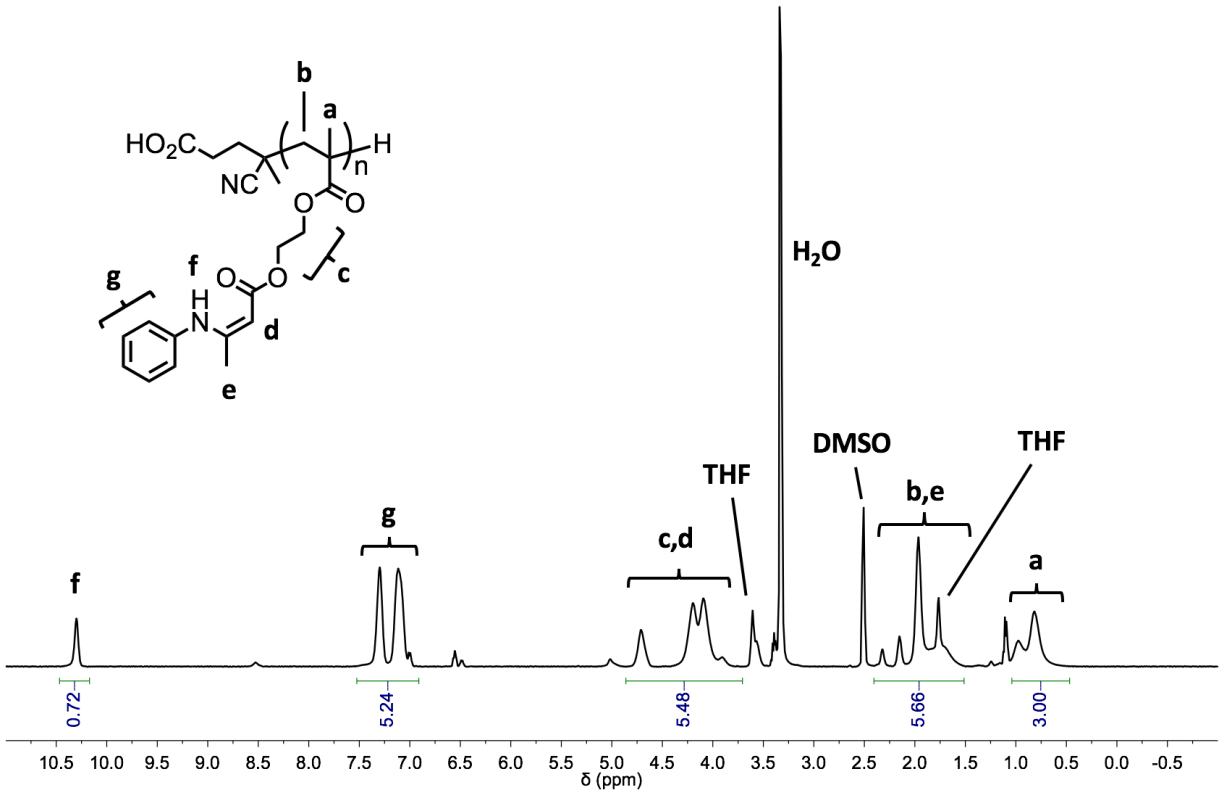

b
a
HO2C
NC
H
n
O
O
h
f
O
O
c
H
N
i
g
d
e
BHT
H2O
DMSO
c,d,g
b,e
a
f
BHT
h
i
0.67
0.96
1.96
7.43
5.27
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)
3301 cm-1
N-H stretch
3002-2890 cm-1
C-H stretch
1727 cm-1
C=O stretch
1651 cm-1
N-H bend
1598 cm-1
C=C stretch
1251 cm-1
C-N stretch
1160 - 1130 cm-1
C-O stretch
782 cm-1
C=C bend
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

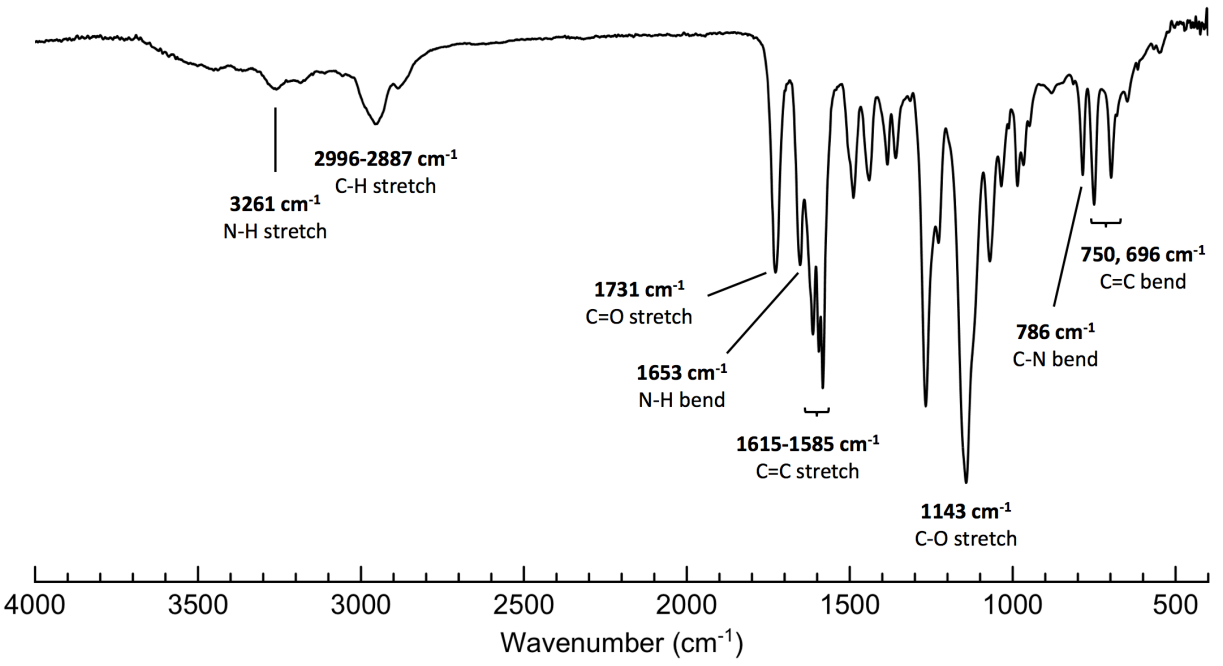

b
a
HO2C
NC
H
n
O
O
f
O
O
c
h
H
N
d
g
e
DMSO
H2O
c,d,g
b,e,h
a
0.82
7.32
5.94
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

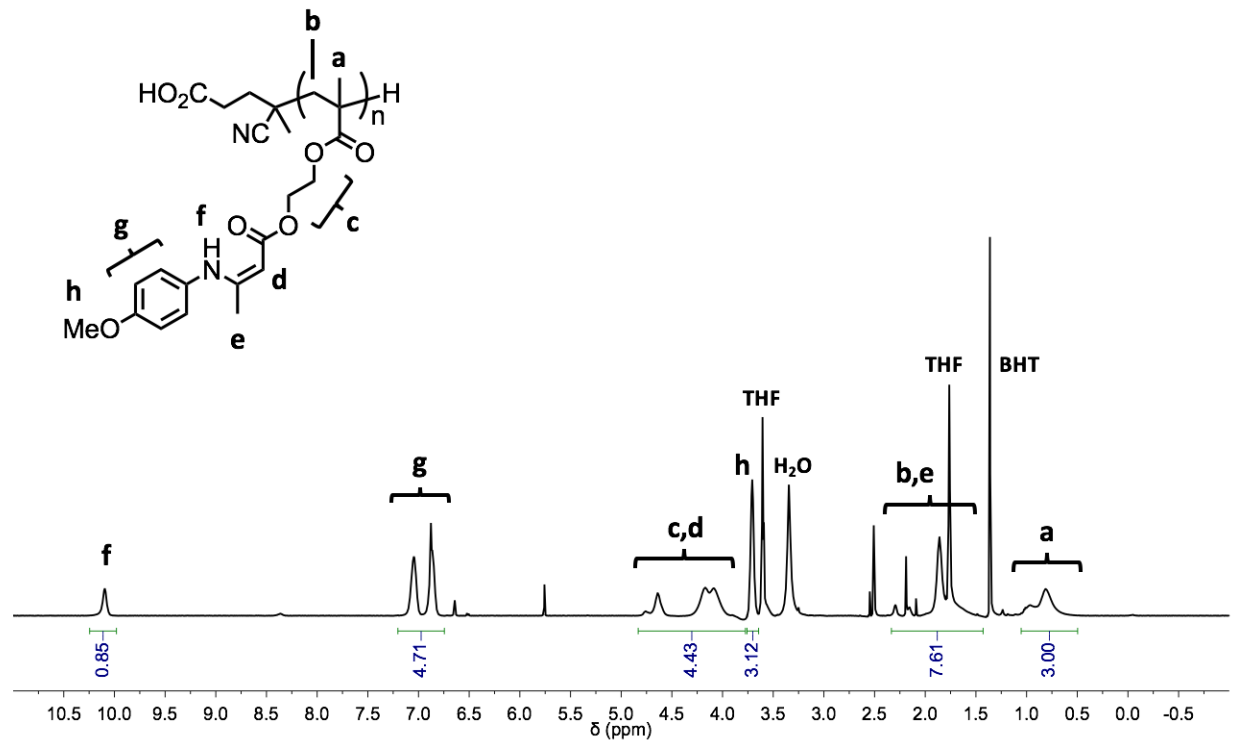

3031-2834 cm-1
C-H stretch
3285 cm-1
N-H stretch
C≡C-H stretch
1725 cm-1
C=O stretch
783 cm-1
C-N bend
1652 cm-1
N-H bend
1234 cm-1
C-N stretch
1598 cm-1
C=C stretch
1163 - 1149 cm-1
C-O stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

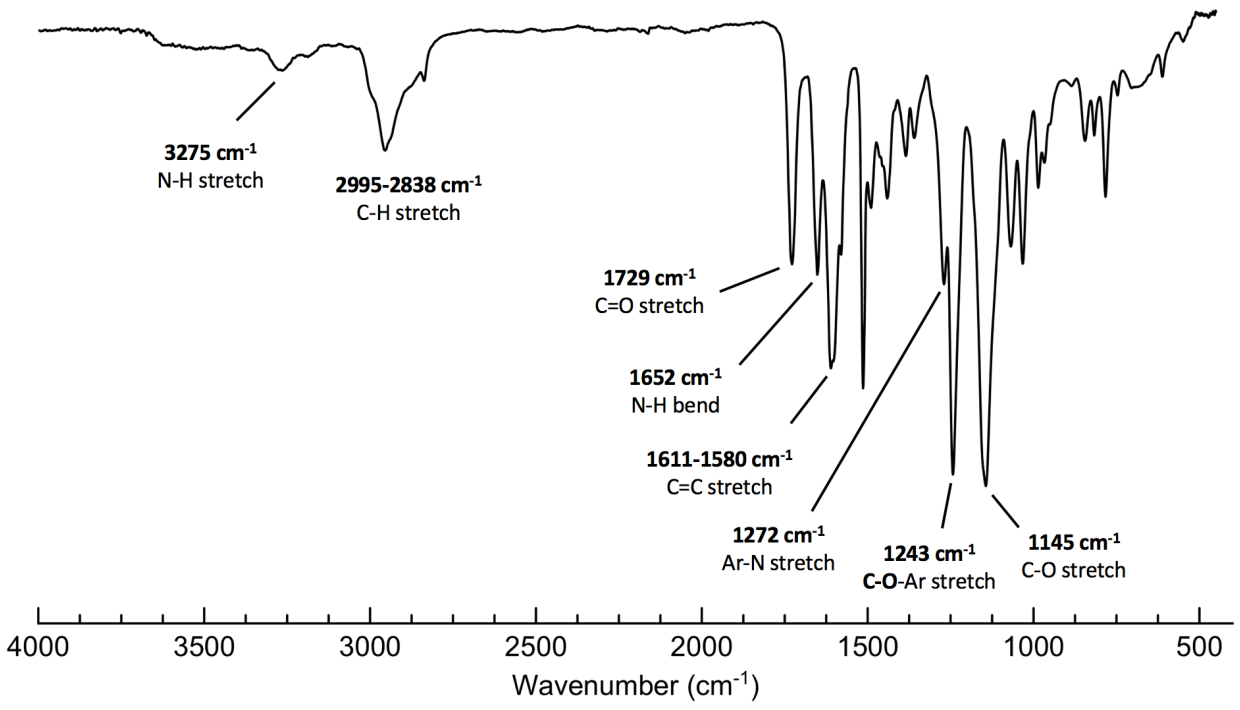

b
a
HO2C
H
n
NC
O
O
h
f
O
O
c
i
H
N
d
O
g
e
b,e
c,d,g
a
f
i
h
0.79
1.10
2.24
7.73
5.05
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

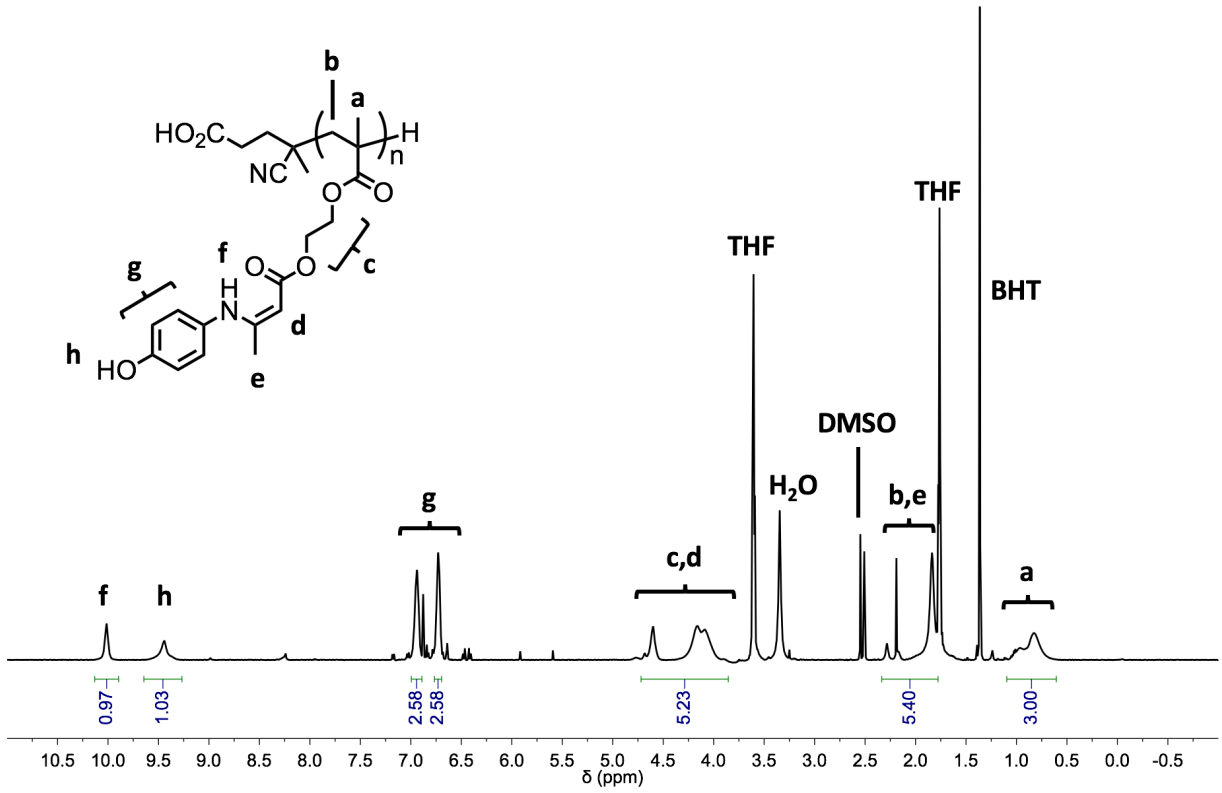

3295 cm-1
N-H stretch
2995-2950 cm-1
C-H stretch
1724 cm-1
C=O stretch
1652 cm-1
N-H bend
1601 cm-1
C=C stretch
1251 cm-1
C-N stretch
1165 - 1144 cm-1
C-O stretch
783 cm-1
C-N bend
744 cm-1
C=C bend
1071 cm-1
C=C-O stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

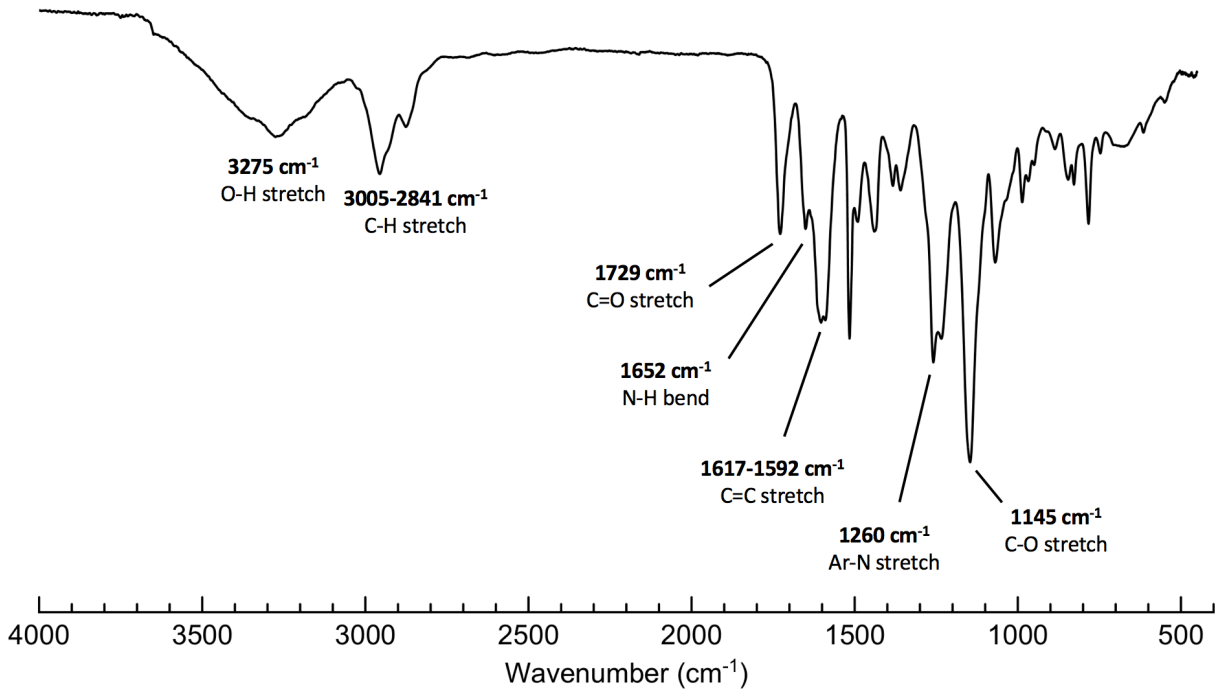

b
a
HO2C
NC
n
H
O
O
g
f
O
O
c
H
N
d
e
H2O
DMSO
THF
THF
b,e
g
c,d
a
f
0.72
5.24
5.48
5.66
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

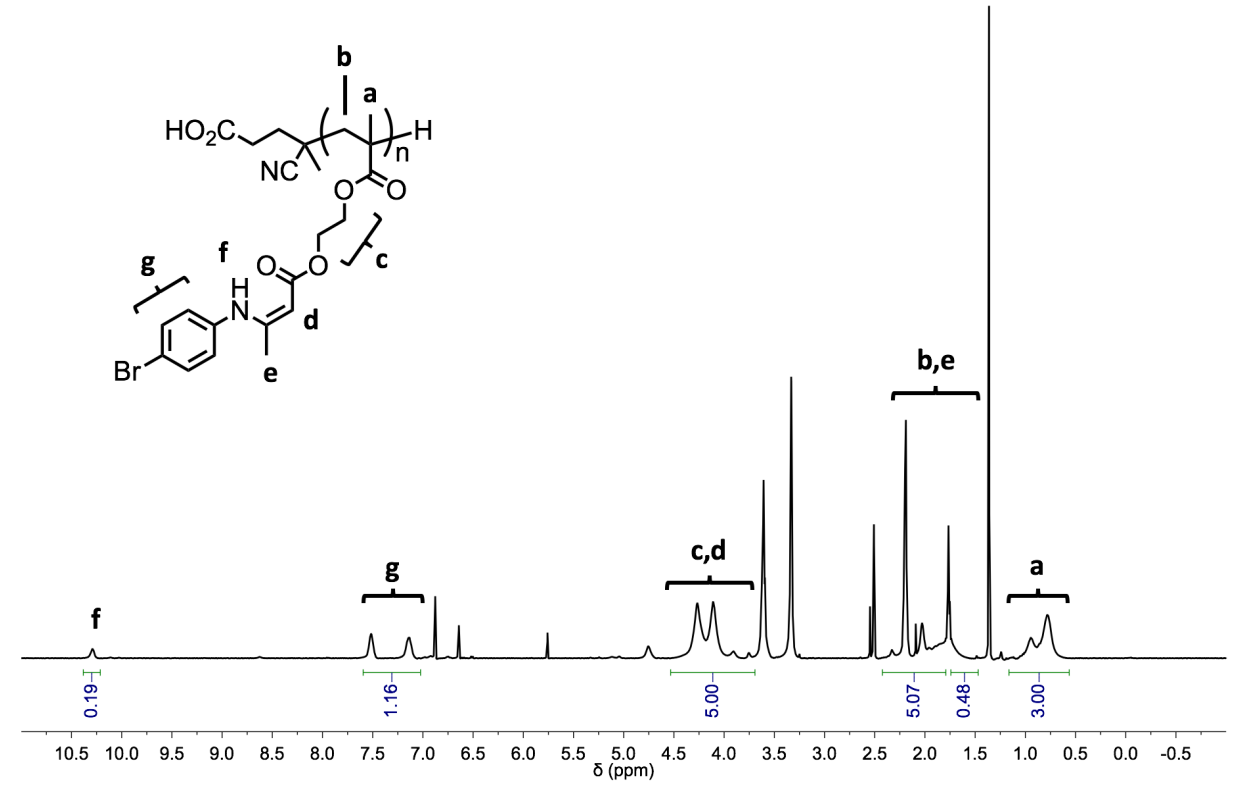

2996-2887 cm-1
C-H stretch
3261 cm-1
N-H stretch
1731 cm-1
C=O stretch
1653 cm-1
N-H bend
1615-1585 cm-1
C=C stretch
1143 cm-1
C-O stretch
786 cm-1
C-N bend
750, 696 cm-1
C=C bend
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

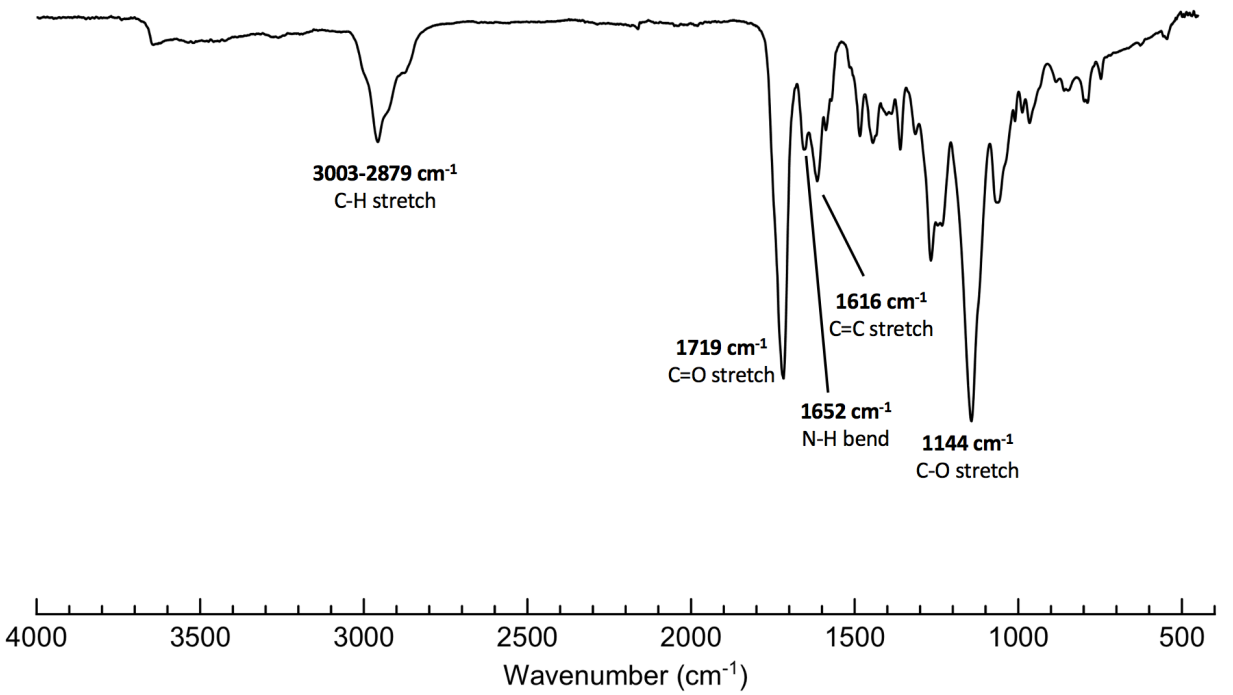

b
a
HO2C
NC
n
H
O
O
g
f
O
O
c
H
N
d
h
MeO
e
THF
BHT
THF
g
h
H2O
b,e
c,d
a
f
0.85
4.71
4.43
3.12
7.61
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

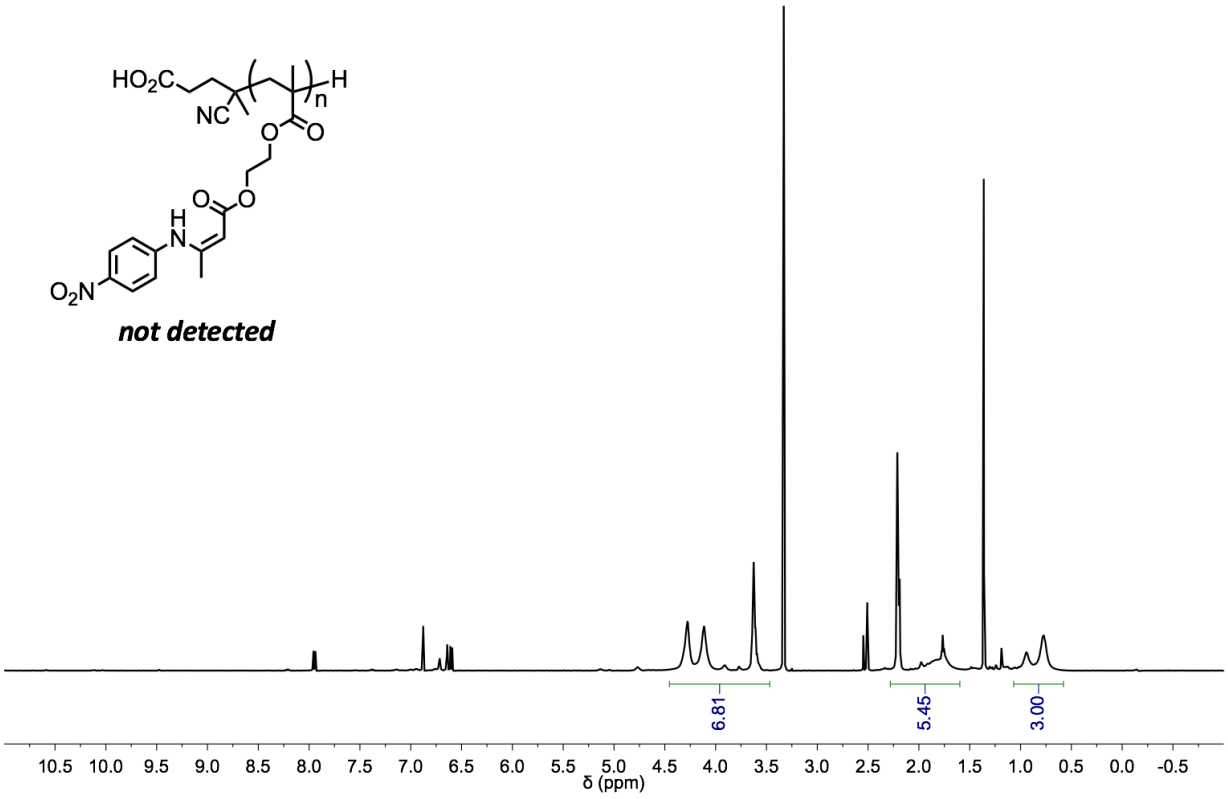

3275 cm-1
N-H stretch
2995-2838 cm-1
C-H stretch
1729 cm-1
C=O stretch
1652 cm-1
N-H bend
1611-1580 cm-1
C=C stretch
1272 cm-1
Ar-N stretch
1243 cm-1
C-O-Ar stretch
1145 cm-1
C-O stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

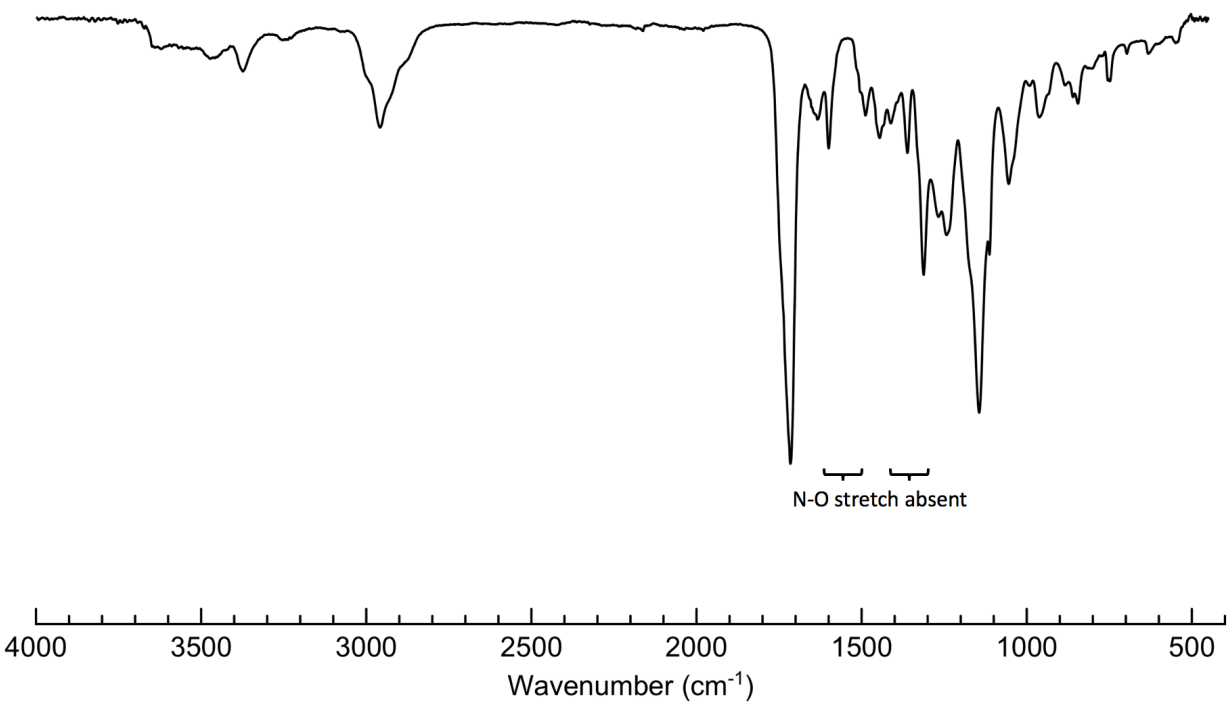

b
a
HO2C
NC
n
H
O
O
f
O
O
c
g
H
N
d
h
HO
e
THF
THF
BHT
DMSO
H2O
b,e
g
c,d
a
f
h
0.97
1.03
2.58
2.58
5.23
5.40
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

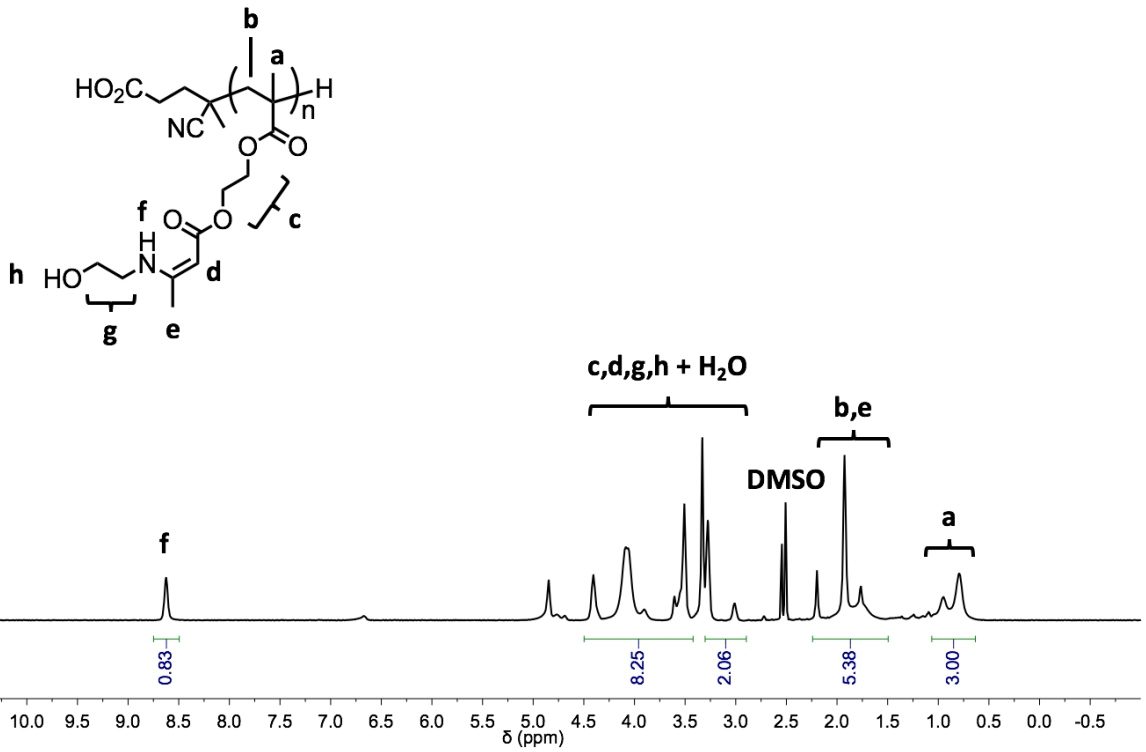

3275 cm-1
O-H stretch
3005-2841 cm-1
C-H stretch
1729 cm-1
C=O stretch
1652 cm-1
N-H bend
1617-1592 cm-1
C=C stretch
1260 cm-1
Ar-N stretch
1145 cm-1
C-O stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

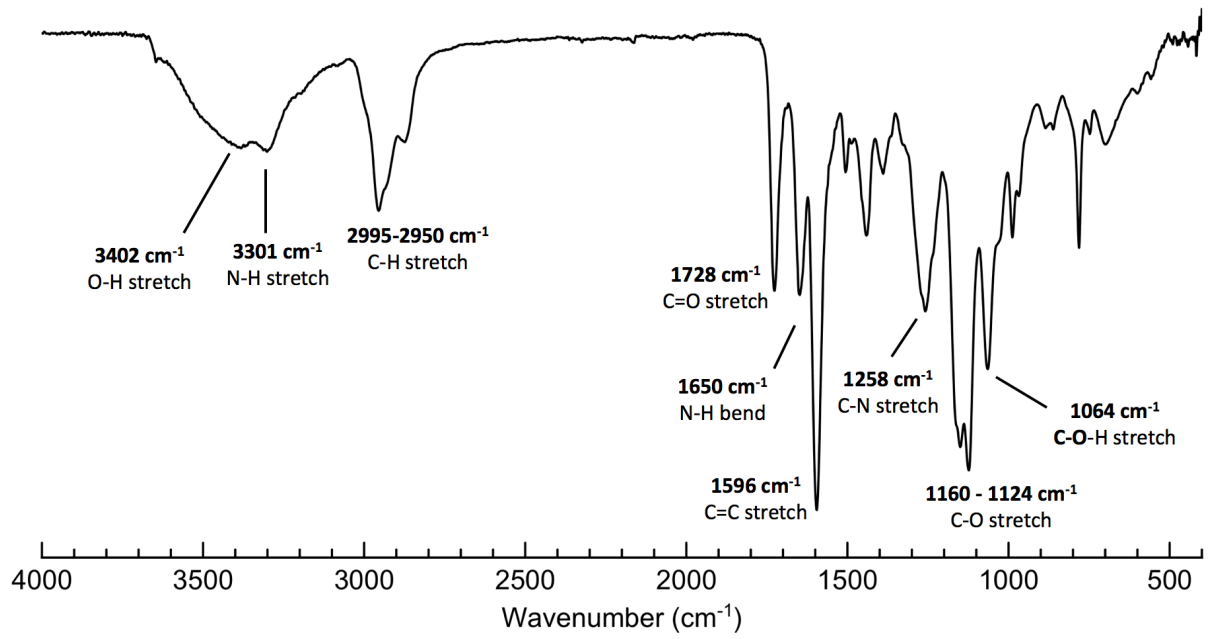

b
a
HO2C
H
n
NC
O
O
g
f
O
O
c
H
N
d
Br
e
b,e
c,d
g
a
f
0.19
1.16
5.00
5.07
0.48
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

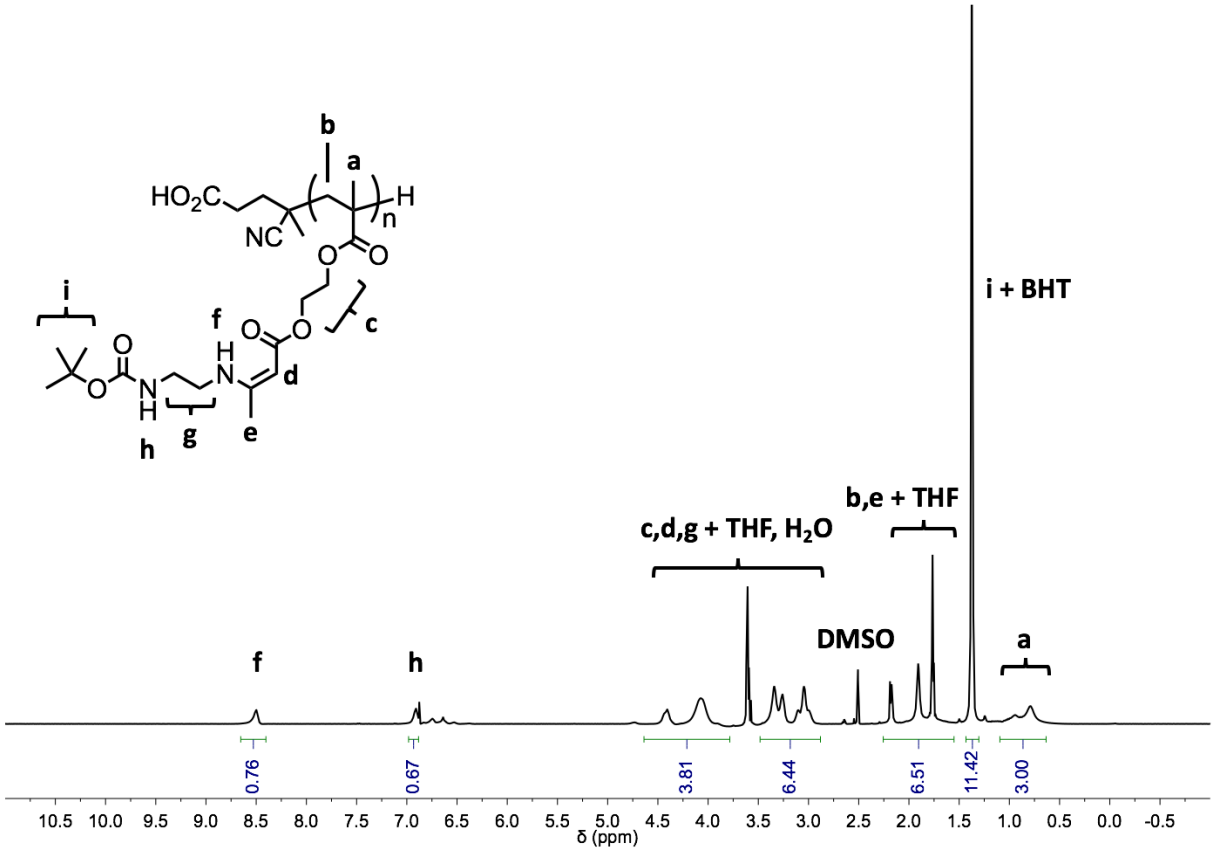

3003-2879 cm-1
C-H stretch
1719 cm-1
C=O stretch
1652 cm-1
N-H bend
1616 cm-1
C=C stretch
1144 cm-1
C-O stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

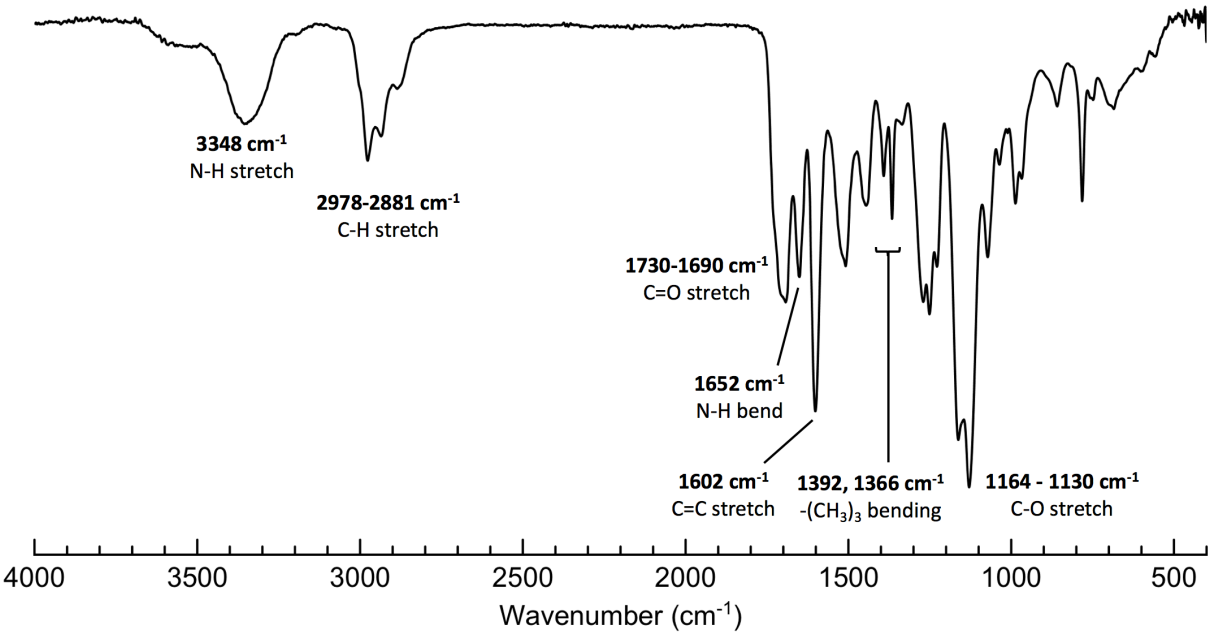

HO2C
NC
n
H
O
O
O
O
H
N
O2N
not detected
6.81
5.45
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

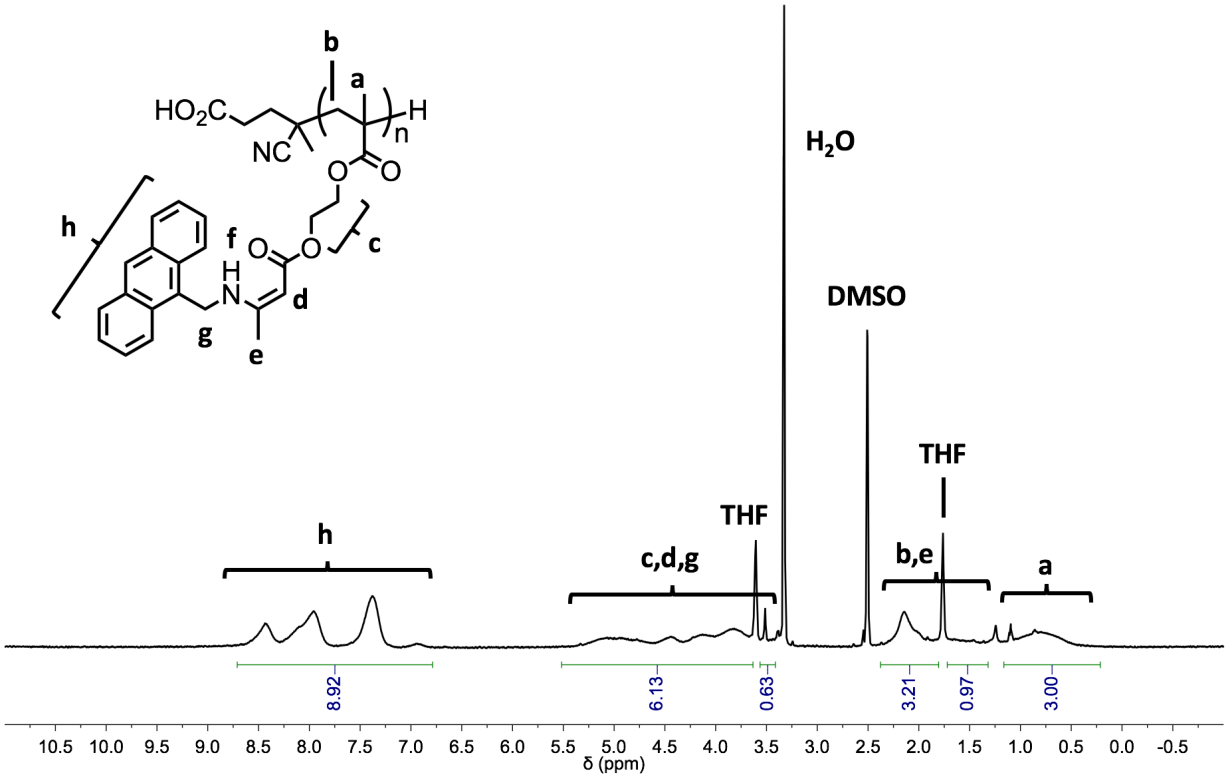

N-O stretch absent
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)

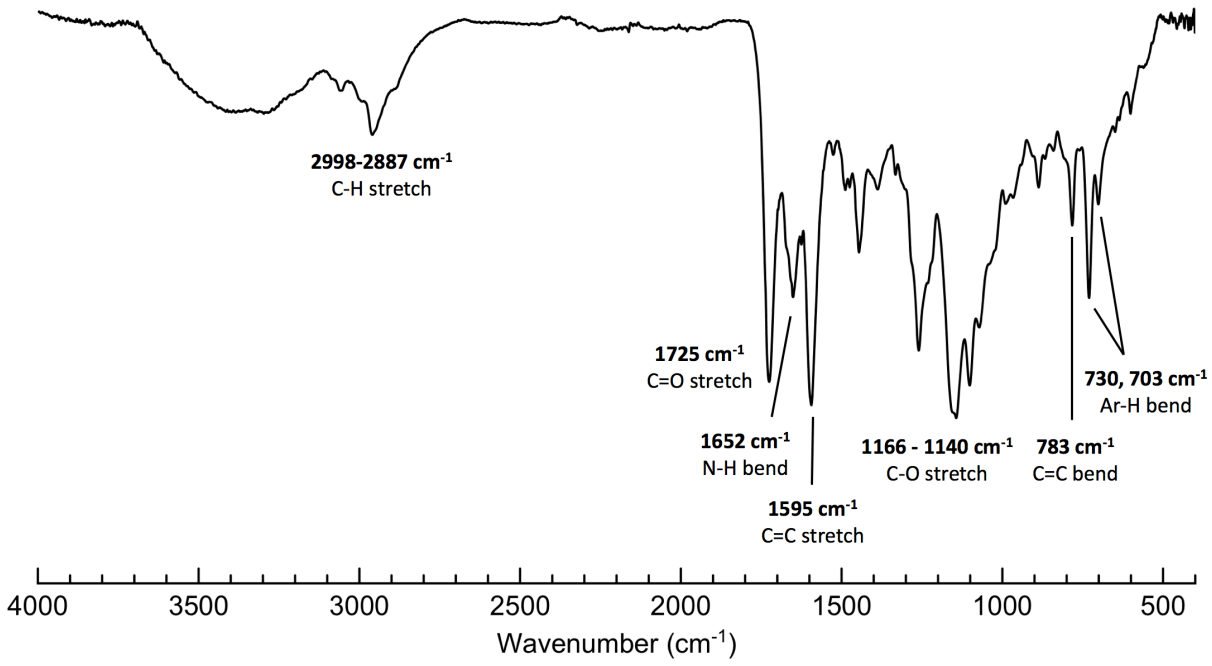

b
a
HO2C
NC
H
n
O
O
f
O
O
c
H
N
h
HO
d
g
e
c,d,g,h + H2O
b,e
DMSO
a
f
0.83
8.25
2.06
5.38
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)

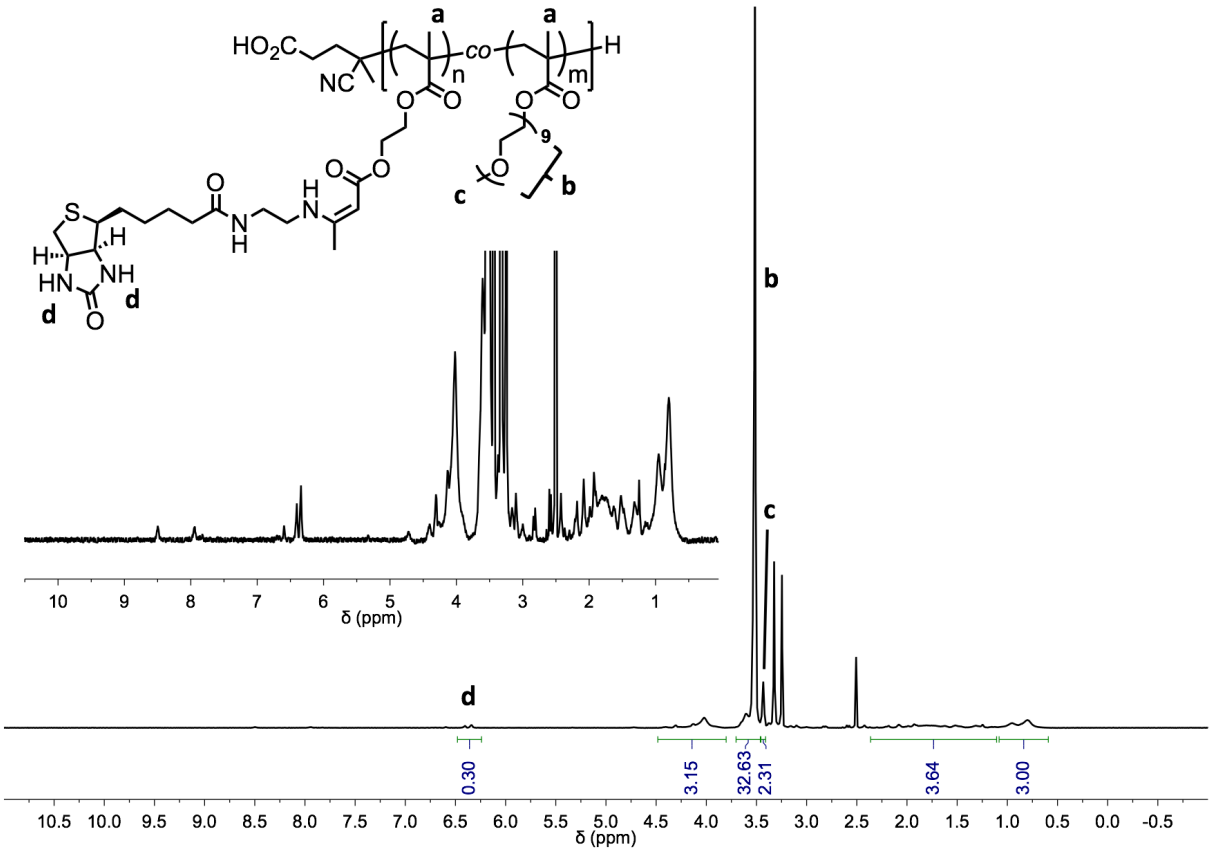

3402 cm-1
O-H stretch
3301 cm-1
N-H stretch
2995-2950 cm-1
C-H stretch
1728 cm-1
C=O stretch
1650 cm-1
N-H bend
1596 cm-1
C=C stretch
1258 cm-1
C-N stretch
1160 - 1124 cm-1
C-O stretch
1064 cm-1
C-O-H stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)


b
a
HO2C
NC
n
H
O
O
i
f
O
O
c
H
N
d
O
N
H
h
g
e
i + BHT
b,e + THF
c,d,g + THF, H2O
DMSO
a
f
h
0.76
0.67
3.81
6.44
6.51
11.42
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)


3348 cm-1
N-H stretch
2978-2881 cm-1
C-H stretch
1730-1690 cm-1
C=O stretch
1652 cm-1
N-H bend
1602 cm-1
C=C stretch
1392, 1366 cm-1
-(CH3)3 bending
1164 - 1130 cm-1
C-O stretch
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)


b
a
HO2C
H
n
NC
O
O
h
f
O
O
c
H
N
d
g
e
H2O
DMSO
THF
THF
h
c,d,g
b,e
a
8.92
6.13
0.63
3.21
0.97
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
δ (ppm)


2998-2887 cm-1
C-H stretch
1725 cm-1
C=O stretch
1652 cm-1
N-H bend
1595 cm-1
C=C stretch
1166 - 1140 cm-1
C-O stretch
783 cm-1
C=C bend
730, 703 cm-1
Ar-H bend
4000 3500 3000 2500 2000 1500 1000 500
Wavenumber (cm-1)


HO2C
NC
a
a
co
n
m
H
O
O
O
O
9
c
b
S
H
HN
NH
d
d
N
H
N
H
O
O
O
δ (ppm)
b
c
d
0.30
3.15
32.63
2.31
3.64
3.00
δ (ppm)