

Electronic Supplementary Information (ESI)

Synthesis and characterization of sulfated-lactose polyurethane hydrogels

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1 Experimental

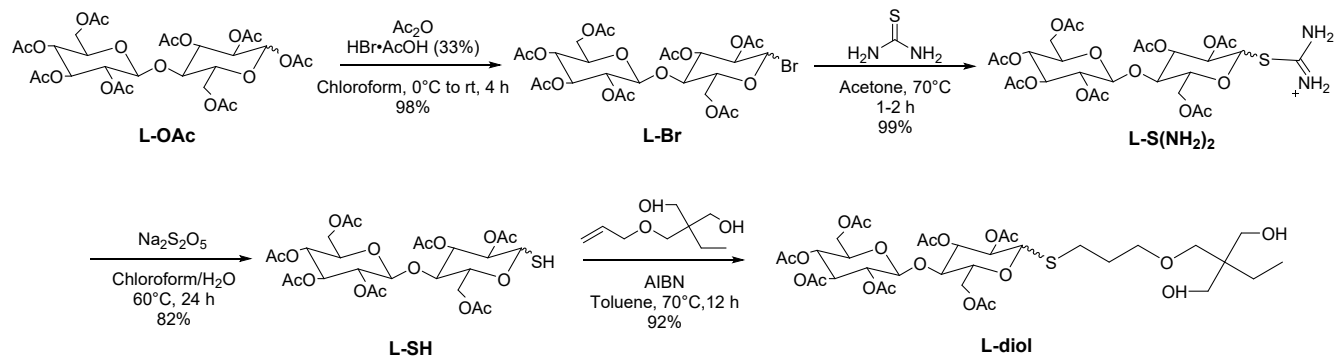
1.1 Materials

All starting materials were obtained from Sigma-Aldrich, except polyethylene glycol-400, which was purchased from Oakwood Chemical and Hydrogen bromide, 33 wt% solution in glacial acetic acid, which was purchased from Fisher Scientific. The chemicals were used as received without further purification.

1.2 Methods

^1H and ^{13}C NMR spectroscopy was performed using a Bruker Ultrashield 400 MHz (100 MHz for ^{13}C NMR) instrument. The data were processed using MestReNova software (version 6.1.0). Chemical shifts (δ) are listed in ppm. Splitting patterns were described as either s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; or m, multiplet; or br, broad. Fourier transform infrared spectra (FTIR) were collected using a Nicolet 6700 spectrometer and analyzed with OMNIC32 software. Mass spectrometry was performed using a Micromass Q-TOF-2TM spectrometer. Galbraith Laboratories Inc. performed elemental analyses. Analytical thin layer chromatography (TLC) was performed on silica gel (layer thickness, 0.25 mm). For detection of intermediates, TLC plates were dipped in ceric ammonium molybdate stain followed by brief heating. Molecular weight averages of polymers were determined using gel permeation chromatography (GPC) with an Agilent 1100 Series HPLC equipped with a PSS SDV Lux column (5 μm) guard column and two PSS SDV Linear XL Lux Columns (5 μm), and Optilab rEX differential refractometer (light source =658 nm; Wyatt Technology Corporation). The mobile phase was DMF + 0.1 M LiBr at a flow rate of 0.5 mL/min at 60 $^\circ\text{C}$. The polymers were dissolved in eluent DMF and filtered through 0.2 μm membrane filters before injection. ASTRA software version 5.4.14 was used to determine the molecular weight averages and polydispersity.

2 Supplementary analysis of lactose diol monomer



Scheme S1. Synthesis of lactose diol monomer

2.1 Spectral data for L-OAc

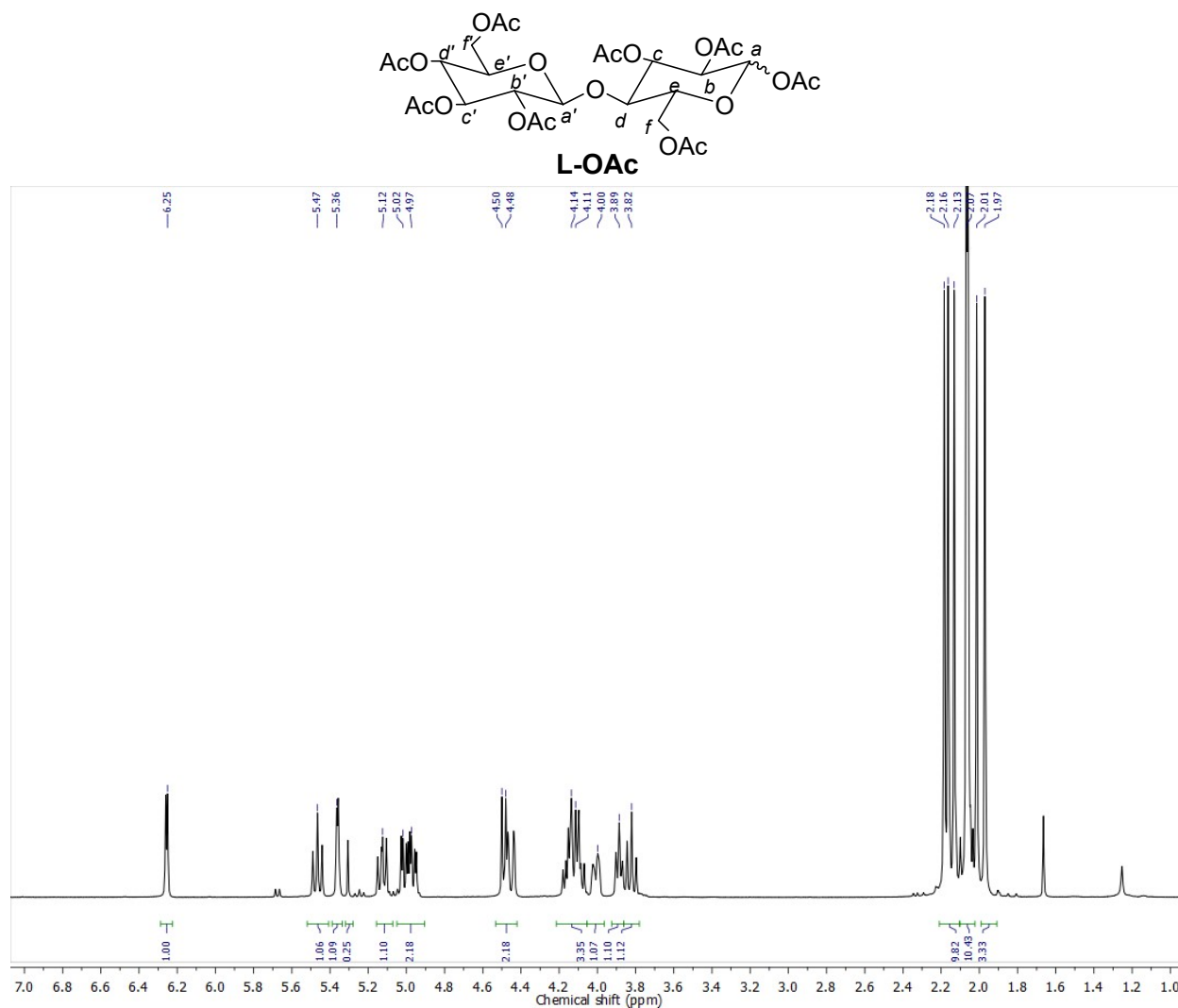


Figure S1. ^1H NMR spectrum for compound L-OAc

The peak assignments are reported using the following format: ppm value (splitting pattern, number of protons, proton assignment)

^1H NMR (400 MHz, CDCl_3): δ (ppm) 6.25 (d, 1H, H-a), 5.47 (dd, 1H, H-d'), 5.36 (dd, 1H, H-c'), 5.12 (dd, 1H, H-b), 5.01-4.90 (m, 2H, H-c, H-b'), 4.50 (d, 1H, H-a'), 4.44 (m, 1H, H-f), 4.15 (m, 1H, H-f), 4.14 (m, 1H, H-f), 4.11 (m, 1H, H-f), 4.00 (m, 1H, H-f), 3.99 (dd, 1H, H-e'), 3.89 (d, 1H, H-d), 3.82 (d, 1H, H-e), 2.16-1.97 (s, 21H, 7 x OAc).

FT-IR (cm^{-1}): 1739 (C=O), 1371 (C-H), 1047 (C-O)

2.2 Spectral data for L-Br

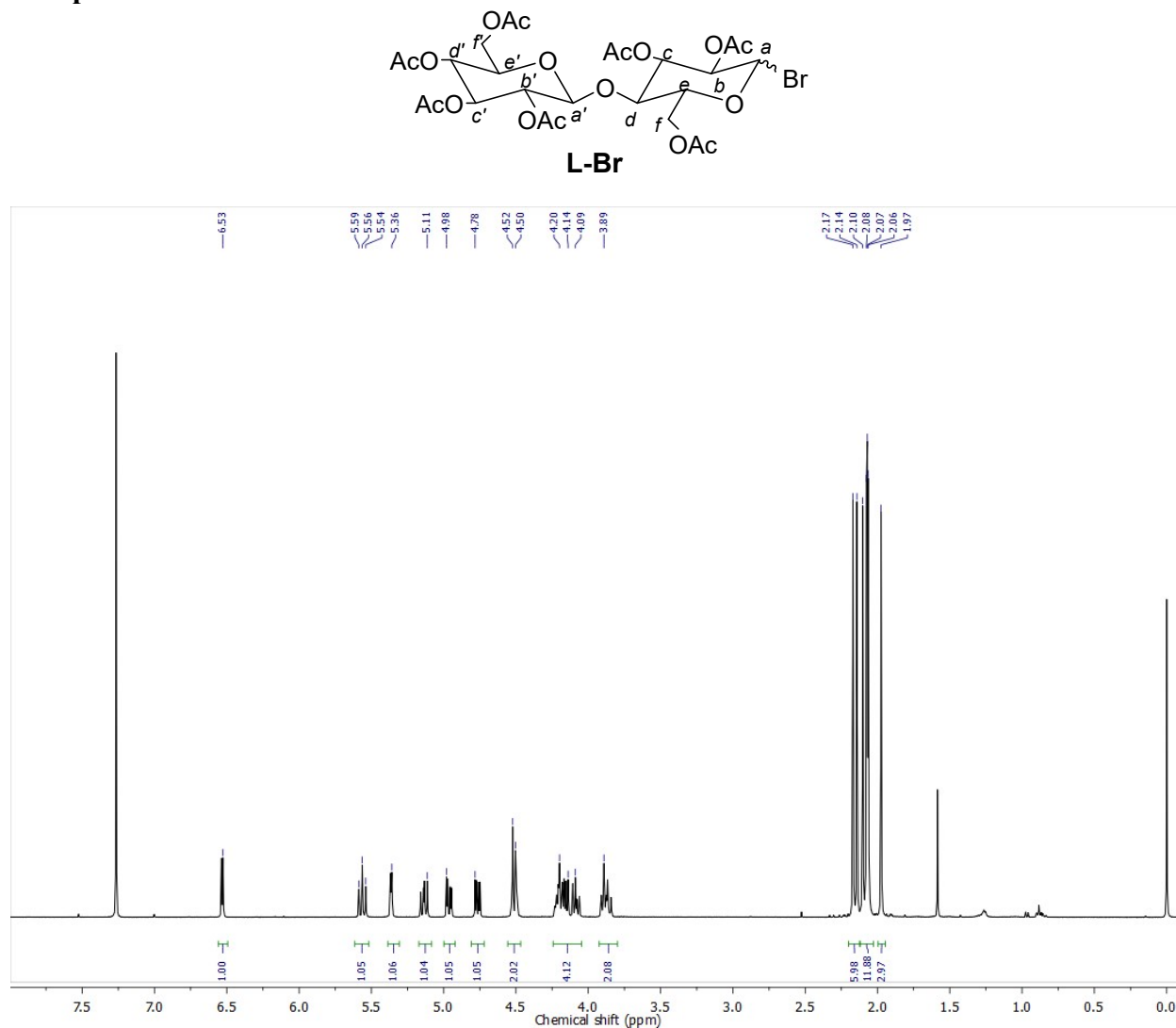


Figure S2. ¹H NMR spectrum for compound L-Br

The peak assignments are reported using the following format: ppm value (splitting pattern, number of protons, proton assignment)

¹H NMR (400 MHz, CDCl₃): δ 6.56 (d, 1H, H-*a*), 5.56 (t, 1H, H-*c'*) 5.36 (dd, 1H, H-*d'*), 5.13 (dd, 1H, H-*d*), 4.98 (dd, 1H, H-*c*), 4.78 (dd, 1H, H-*b*) 4.52 (d, 1H, H-*a'*), 4.20-4.06 (m, 4H, H-*f* and H-*f'*), 4.15 (m, 1H, H-*f*; 2H, H-*f'*), 3.99 (dd, 1H, H-*e'*), 3.89 (d, 1H, H-*d*), 3.91-3.82 (m, 2H, H-*e* and H-*e'*), 2.16-1.97 (s, 21H, 7 x OAc)

FT-IR (cm⁻¹): 1739 (C=O), 1371 (C-H), 1047 (C-O), 645 (C-Br)

2.3 Spectral data for L-SH

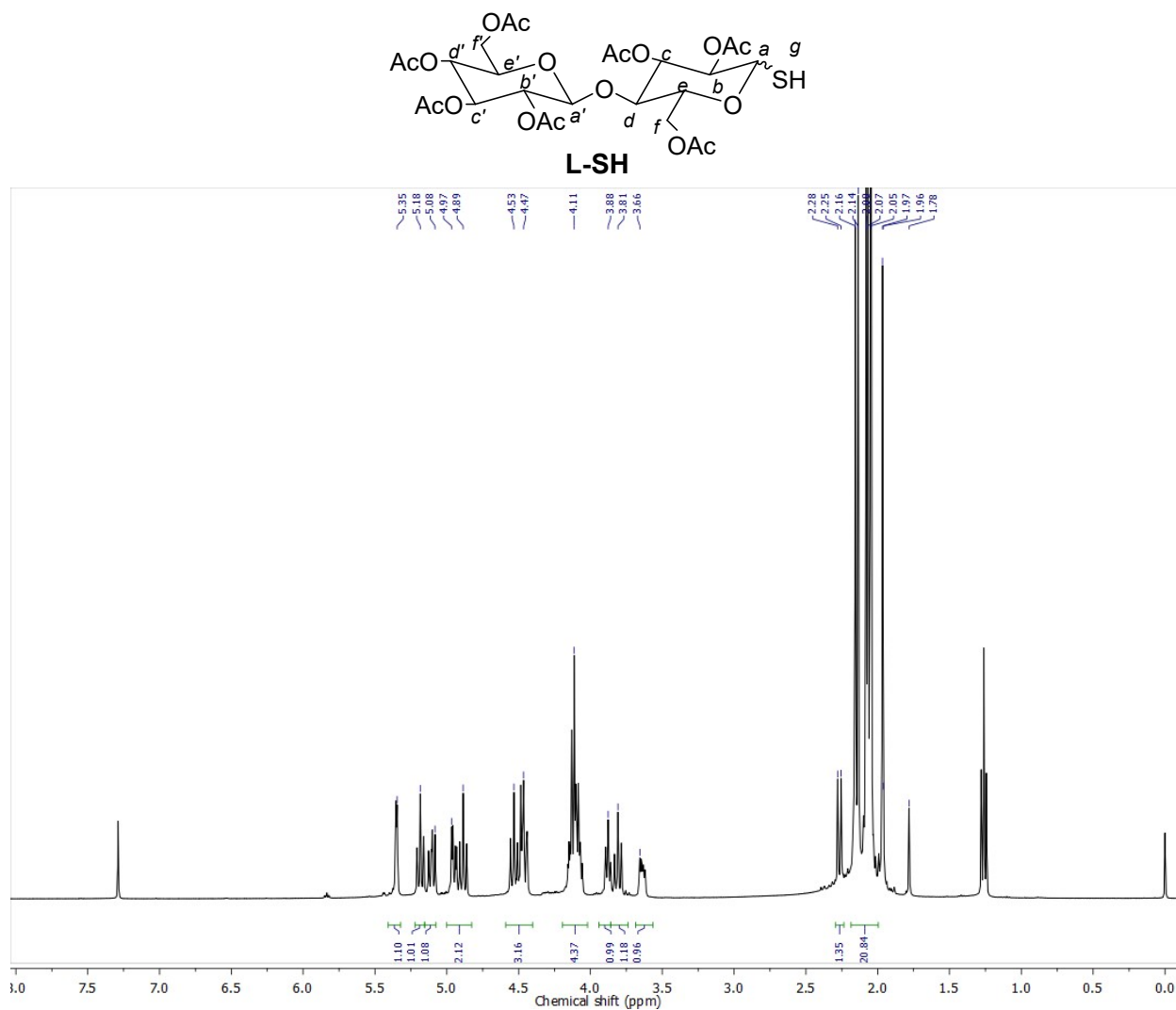


Figure S3. ¹H NMR spectrum for compound L-SH

The peak assignments are reported using the following format: ppm value (splitting pattern, number of protons, proton assignment)

¹H NMR (400 MHz, CDCl₃): δ 5.34 (d, 1H, H-d') 5.15 (1H, dd, H-c'), 5.10 (dd, 1H, H-b), 4.96 (dd, 1H, H-c), 4.89 (dd, 1H, H-b'), 4.53 (dd, 1H, H-a), 4.46 (dd, 1H, H-a'), 4.43 (dd, 1H, H-f), 4.13–4.08 (m, 4H, H-f, H-f'), 3.88 (m, 1H, H-e'), 3.81 (dd, 1H, H-d), 3.64 (m, 1H, H-e), 2.21 (d, 1H, SH), 2.12–1.93 (21H, 7 × OAc)

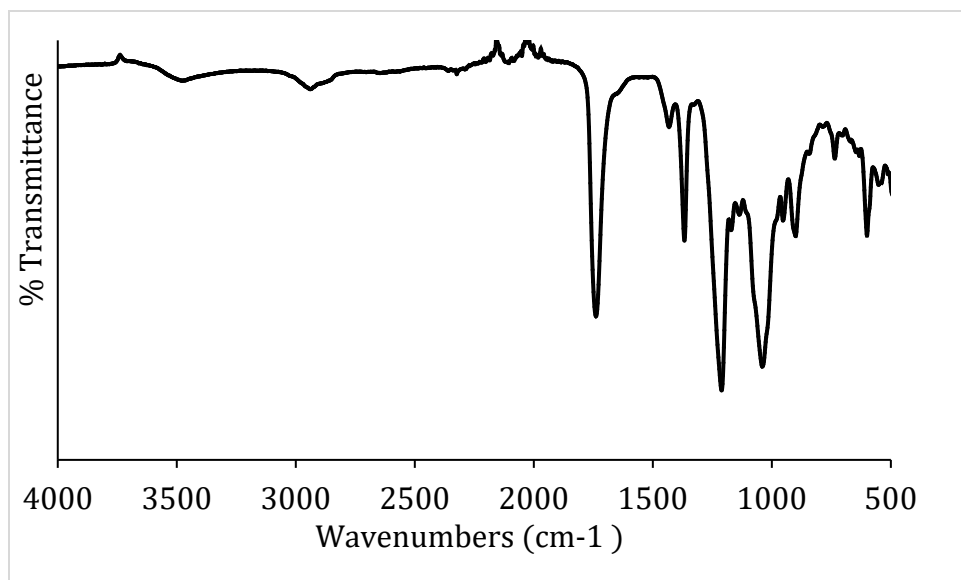


Figure S4. FTIR spectrum of **L-SH**

FT-IR (cm⁻¹): 1739 (C=O), 1371 (C-H), 1047 (C-O)

MS (TOF MS ESI): 675.15 M+Na⁺ (Calculated: 675.15 M+Na⁺)

2.4 Spectral data for L-diol

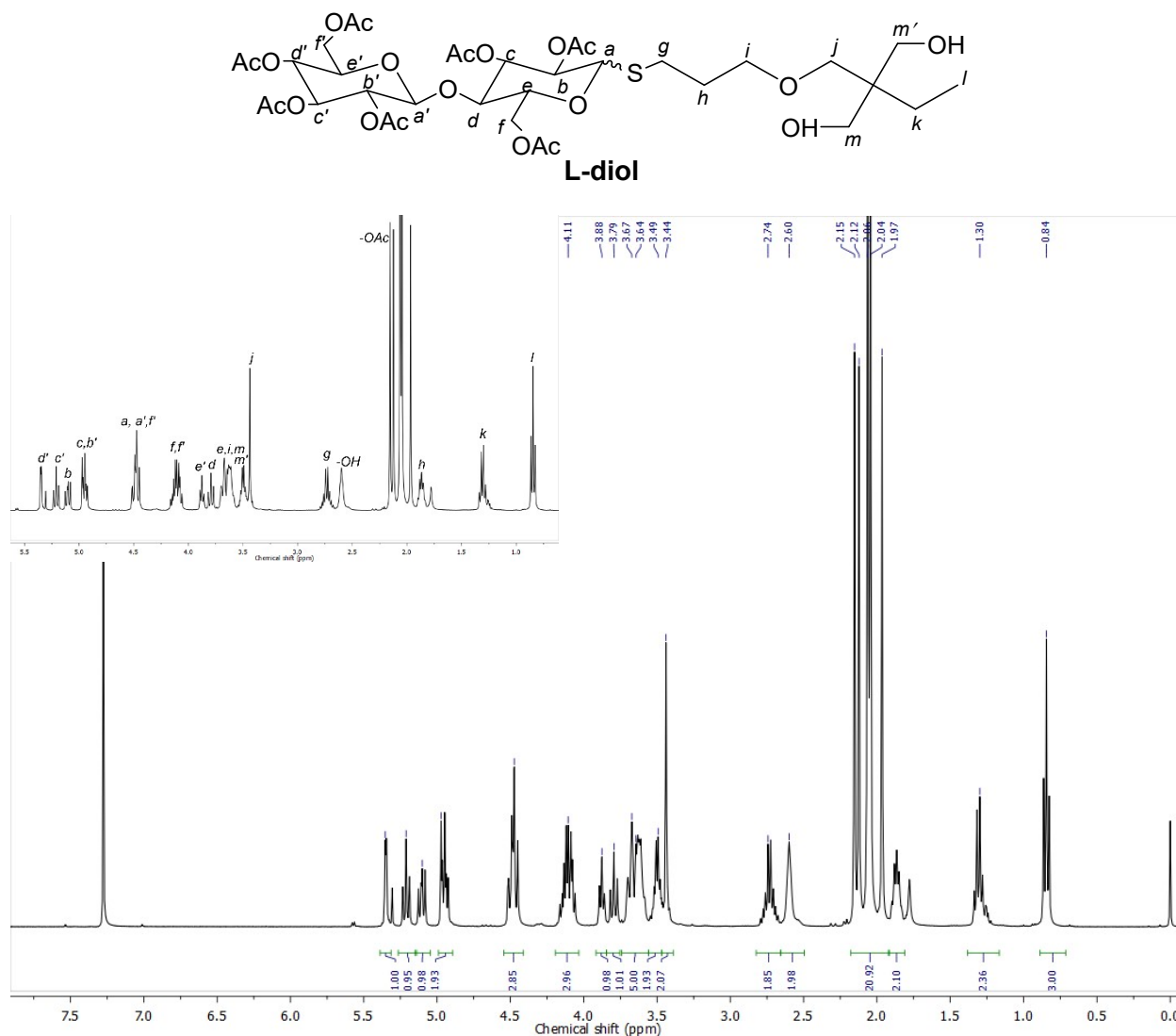


Figure S5. ¹H NMR spectrum for compound **L-diol** with inset showing peak assignments.

The peak assignments are reported using the following format: ppm value (splitting pattern, number of protons, proton assignment)

¹H NMR (400 MHz, CDCl₃): δ 5.35 (d, 1H, H-*d'*) 5.21 (1H, dd, H-*c'*), 5.10 (dd, 1H, H-*b*), 4.97 (dd, 2H, H-*c*, dd, 1H, H-*b'*), 4.48 (m, 3H, H-*a*, H-*a'*, H-*f'*), 4.12–4.05 (m, 3H, H-*f*, H-*f'*), 3.88 (m, 1H, H-*e'*), 3.79 (dd, 1H, H-*d*), 3.67 (m, 5H, H-*e*, H-*i*, H-*m*), 3.49 (dd, 2H, *m'*), 3.44 (s, 2H, *j*), 2.74 (m, 2H, H-*g*), 2.60 (br, 2H, OH), 2.12–1.93 (21H, 7 × OAc), 1.85 (q, 2H, H-*h*), 1.32 (m, 2H, H-*k*), 0.86 (t, 3H, H-*l*)

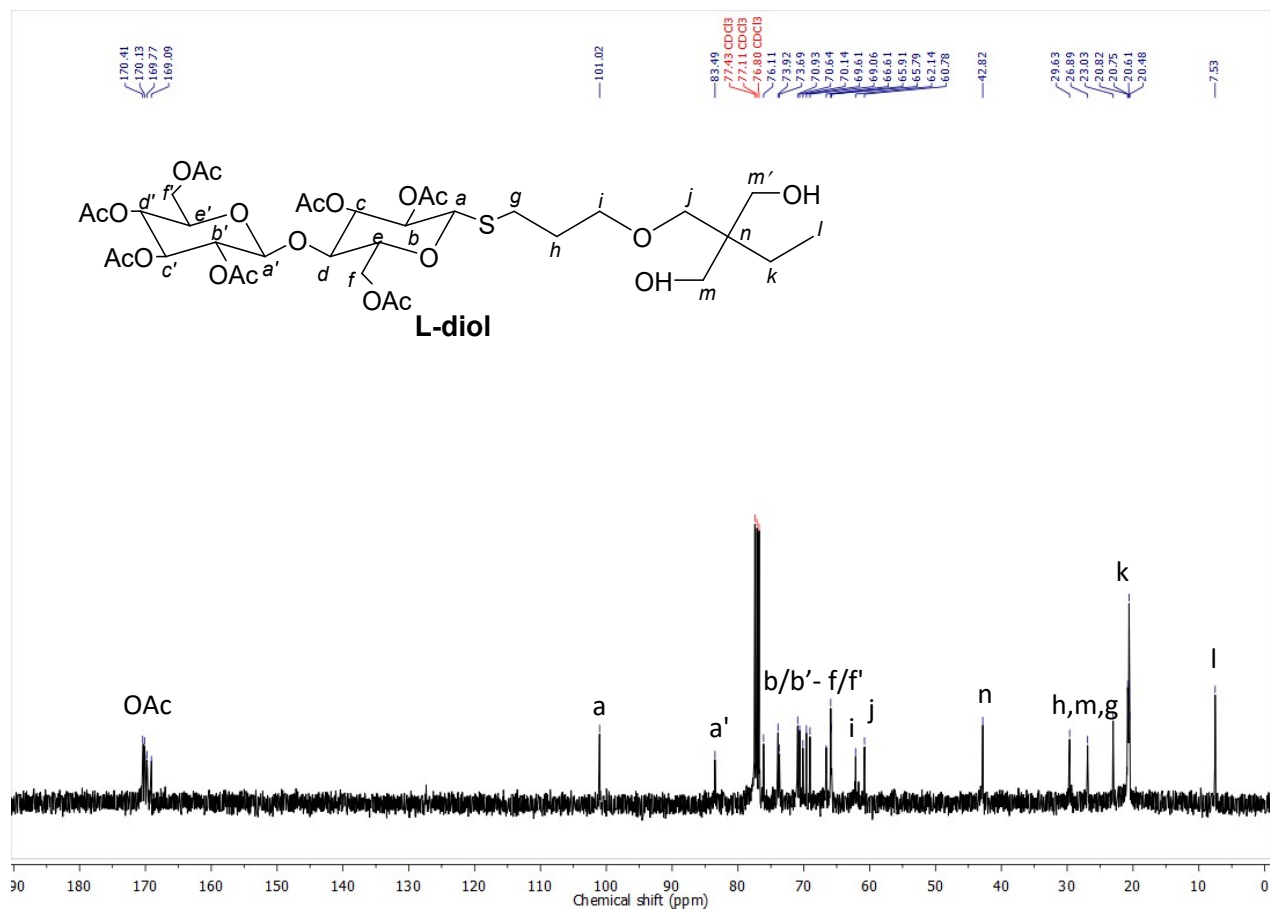


Figure S6. ¹³C NMR spectrum for compound **L-diol**

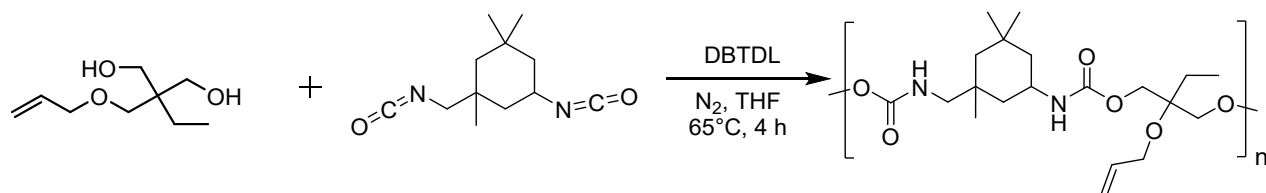
¹³C NMR (400 MHz, CDCl₃): δ 170.41 (C=O), 170.13 (C=O), 169.77 (C=O), 101.07 (C-a), 83.49 (C-a'), 76.11 (C-d), 73.92 (C-b), 73.69 (C-c'), 70.93 (C-c), 70.64 (C-b'), 70.14 (C-e'), 69.61 (C-e), 69.06 (C-d'), 65.91 (C-f), 65.91 (C-f'), 65.79 (C-i), 60.78 (C-j), 42.82 (C-n), 29.63 (C-h), 26.89 (C-m), 23.03 (C-g), 20.82 (C-k), 20.76 (CH₃), 20.61 (CH₃), 20.48 (CH₃), 7.53 (C-l)

FT-IR (cm⁻¹): 3300 (O-H), 1739 (C=O), 1371 (C-H), 1047 (C-O)

MS (TOF MS ESI): 849.28 M+Na⁺ (Calculated: 849.28 M+Na⁺)

3 Supplemental synthesis and analysis of model polymers

3.1 Synthesis and characterization of PU-ene



Scheme S2. Synthesis of PU-ene

PU-ene was prepared through step growth polymerization of IPDI and TMPAE. Briefly, IPDI (26.7 g, 24.4 mL, 0.12 mol) and TMPAE (17.4 g, 17.3 mL, 0.100 mol) were added to a flame dried round bottom flask equipped with a stir bir. The flask was purged with N₂ for 15 minutes before adding 110 mL of anhydrous THF. Under nitrogen protection, ~ 20 mg of DBTDL was added to the solution using a needle tipped syringe. The solution was then stirred at 65°C until it became too viscous to stir, approximately 4 hours. The polymer solution was then diluted with 100 mL of THF and precipitated into 1L cold hexane. The precipitation was performed twice to ensure polymer purity. The pure polymer, PU-ene (collected 41 g), was characterized with NMR, FT-IR, and GPC.

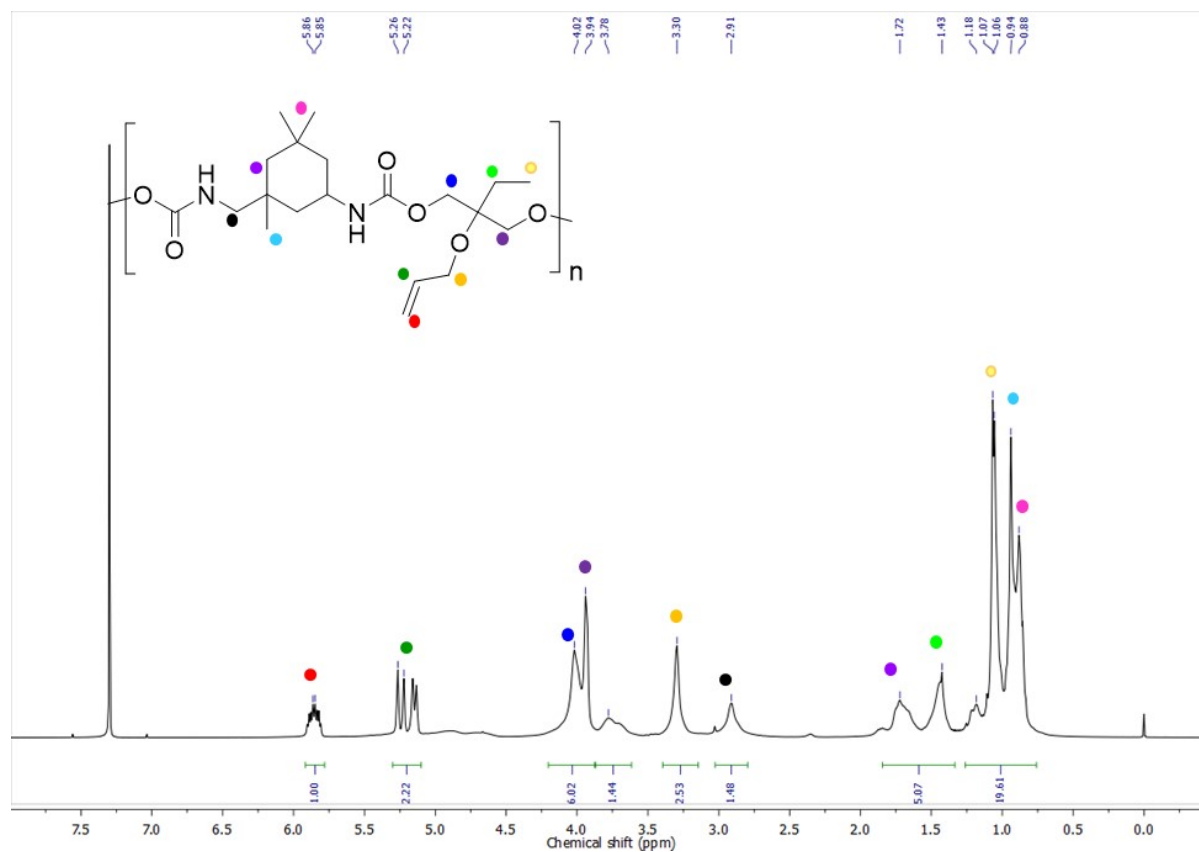


Figure S7. ^1H NMR of PU-ene

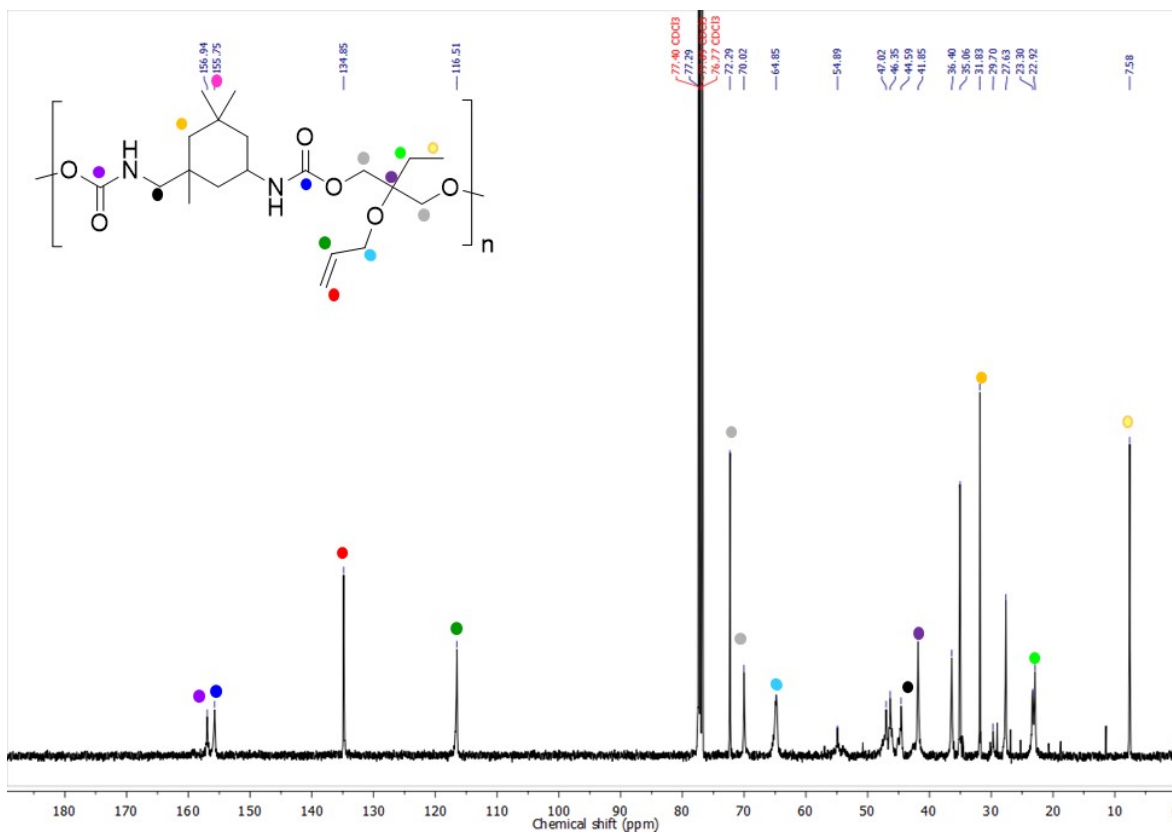


Figure S8. ^{13}C NMR of PU-ene

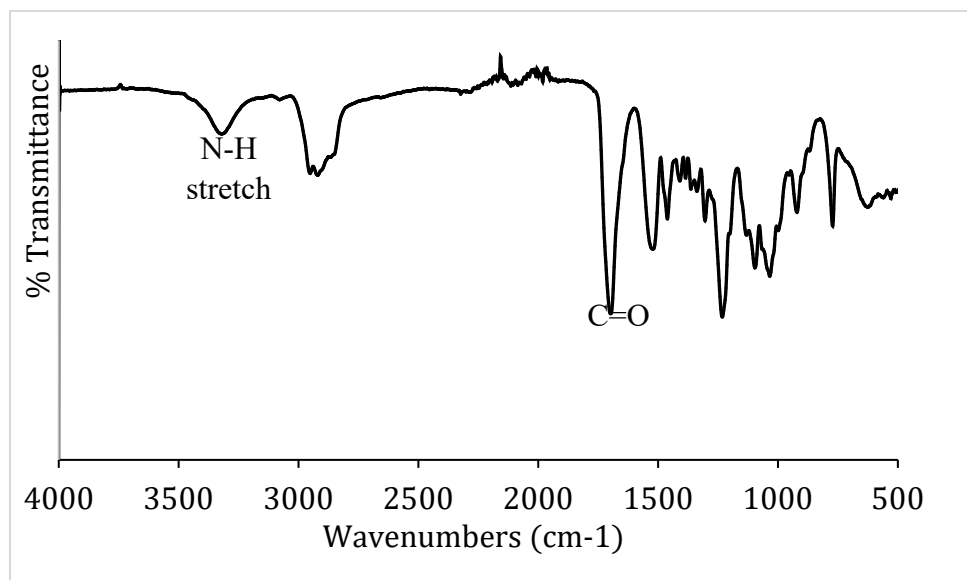
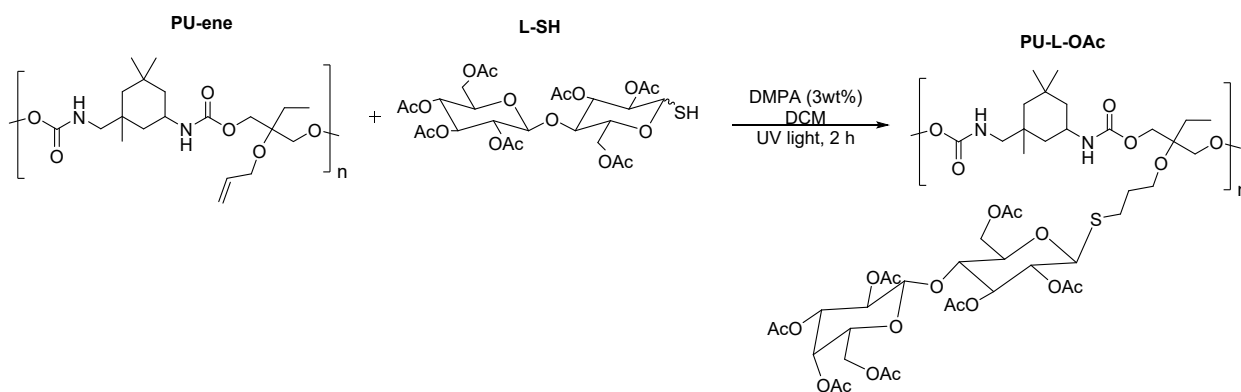


Figure S9. FTIR spectrum of PU-ene

3.2 Synthesis and characterization of PU-L-OAc



Scheme S3. Synthesis of PU-L-OAc

PU-L-OAc was prepared through a photoinitiated thiol-ene reaction between PU-ene and L-SH. PU-ene (10 g, 1.0 equiv) and L-SH (29.8 g, 1.5 equiv) were dissolved in 100 mL of DCM in a flat-bottomed flask equipped with a stir bar. Excess thiol was used to enable full conversion of vinyl groups. DMPA (3 wt % relative to the thiol, 0.896 g) was added to the solution. The solution was then exposed to UV light, with stirring, for 2 h. The crude mixture was precipitated into cold diethyl ether twice to give polymer. The polymer, PU-L-OAc, (9.6 g, 37 % yield) was

characterized by NMR, FT-IR, and GPC. The NMR indicated unreacted lactose which was carried forward to the next reaction.

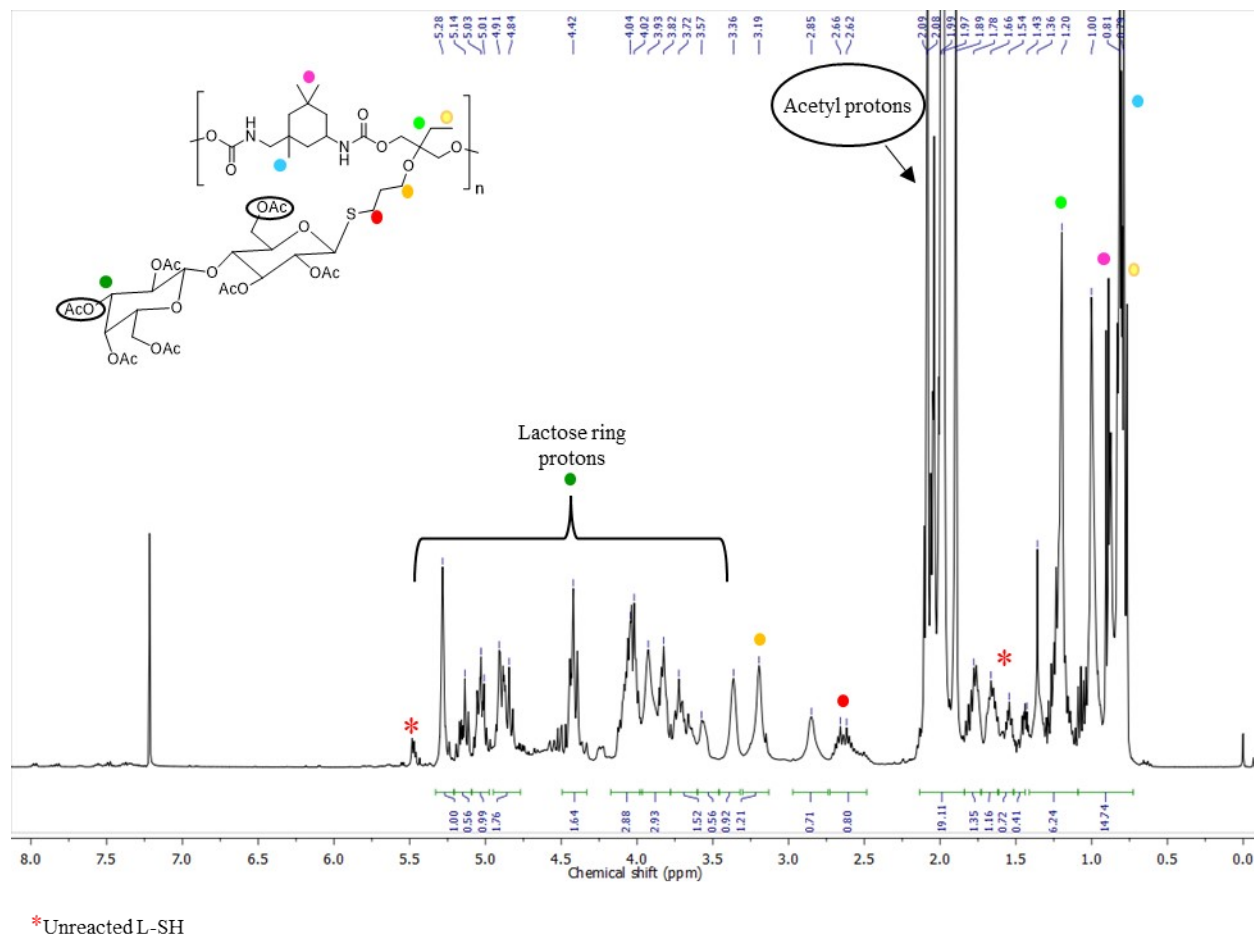


Figure S10. ¹H NMR of PU-L-OAc

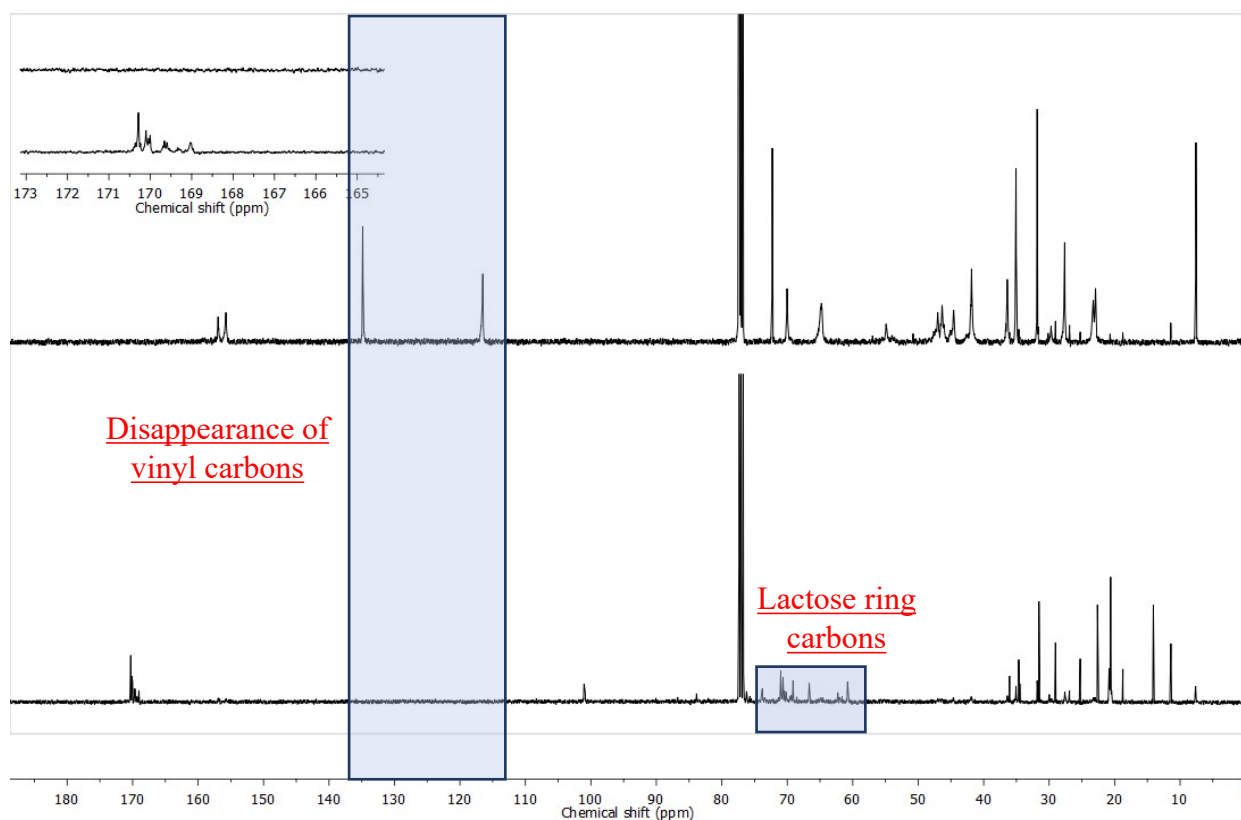


Figure S11. Stacked ^{13}C NMR PU-ene (top) and PU-L-OAc (bottom)

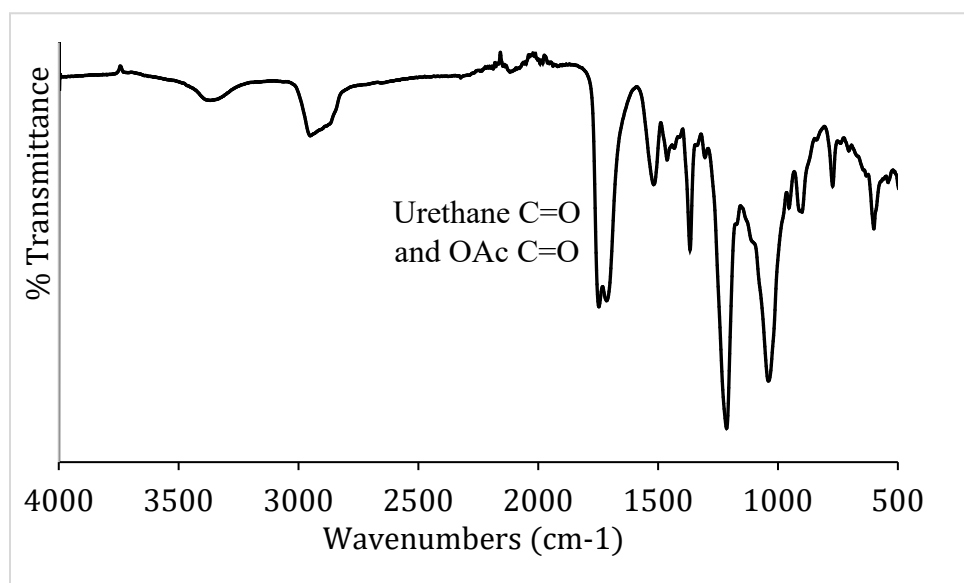
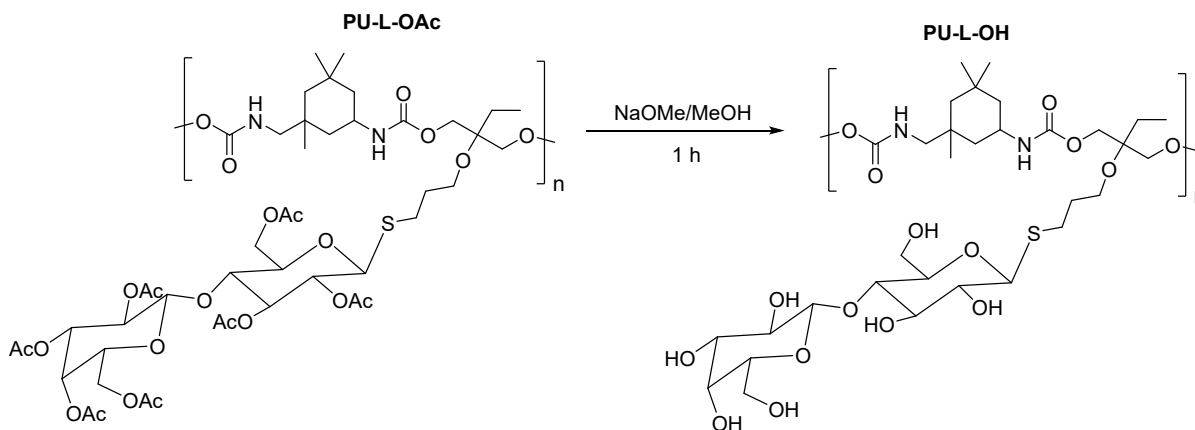


Figure S12. FTIR spectrum of PU-L-OAc

3.3 Synthesis and characterization of PU-L-OH



Scheme S4. Synthesis of PU-L-OH

Deacetylation of PU-L-OAc was carried out following previously published protocols.¹⁻³ Briefly, PU-L-OAc (2.0 g) was dissolved in 40 mL of methanol before adding a catalytic amount of NaOMe (~1 drop) to the solution. The solution was allowed to stir for 1 hour before a precipitate formed. The precipitate was filtered and washed several times with water before filtering to collect the solids (1.4 g, 97 % yield). The pure polymer, PU-L-OH, was characterized by NMR, FT-IR, and GPC.

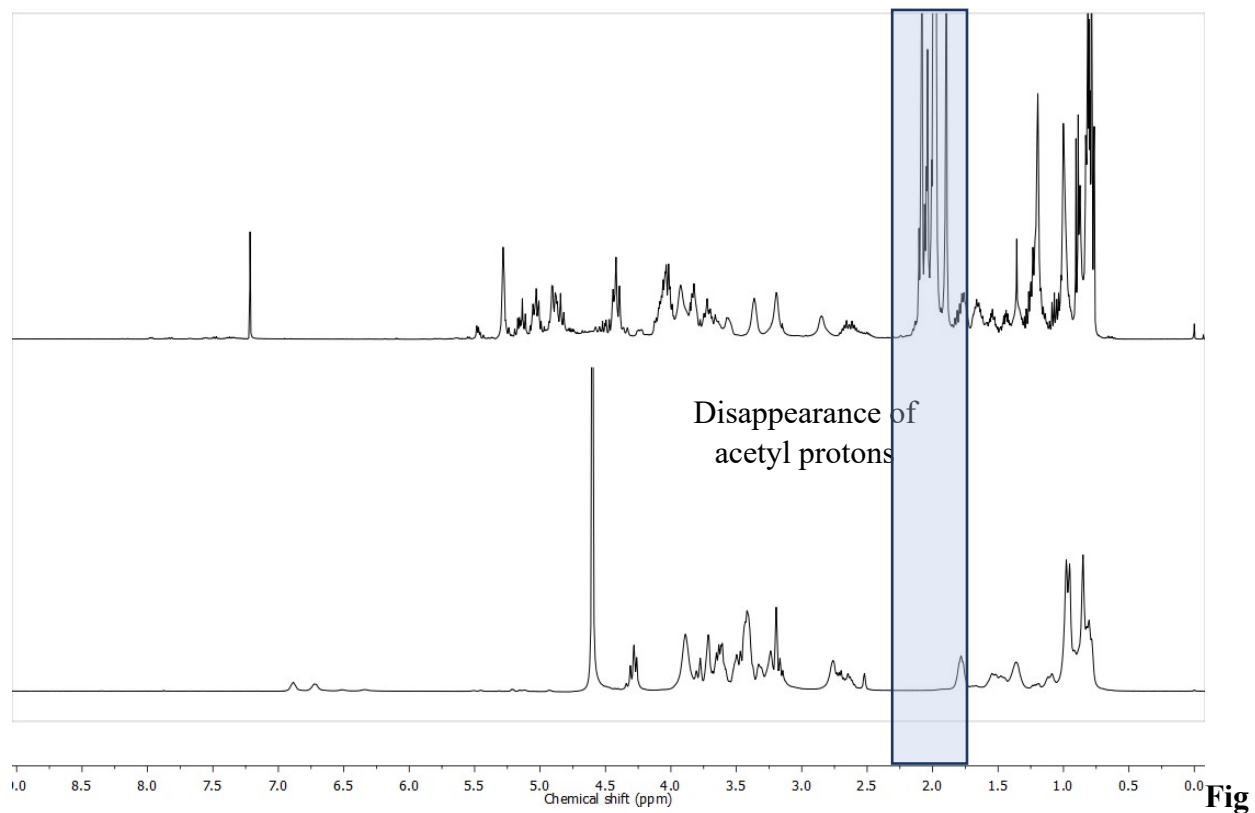


Figure S13. Stacked ^1H NMR of PU-L-OAc (top) and PU-L-OH (bottom)

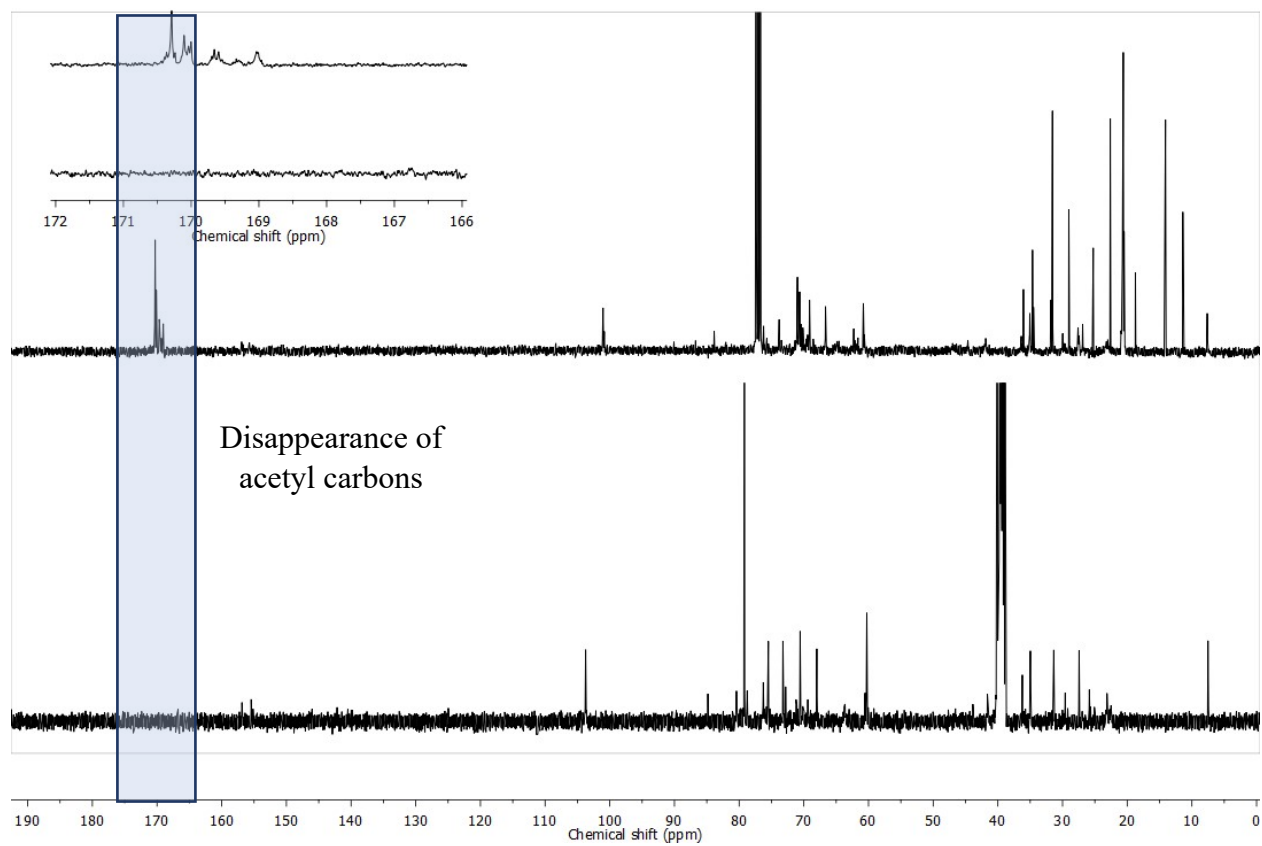


Figure S14. ^{13}C NMR of PU-L-OAc (top) and PU-L-OH (bottom)

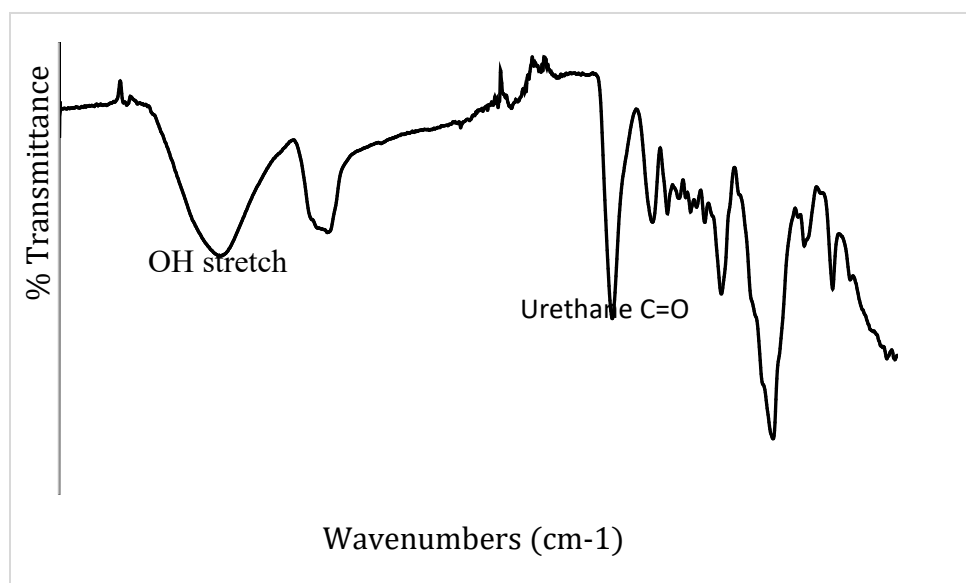


Figure S15. FTIR spectrum of PU-L-OH

3.4 GPC data of model polymers

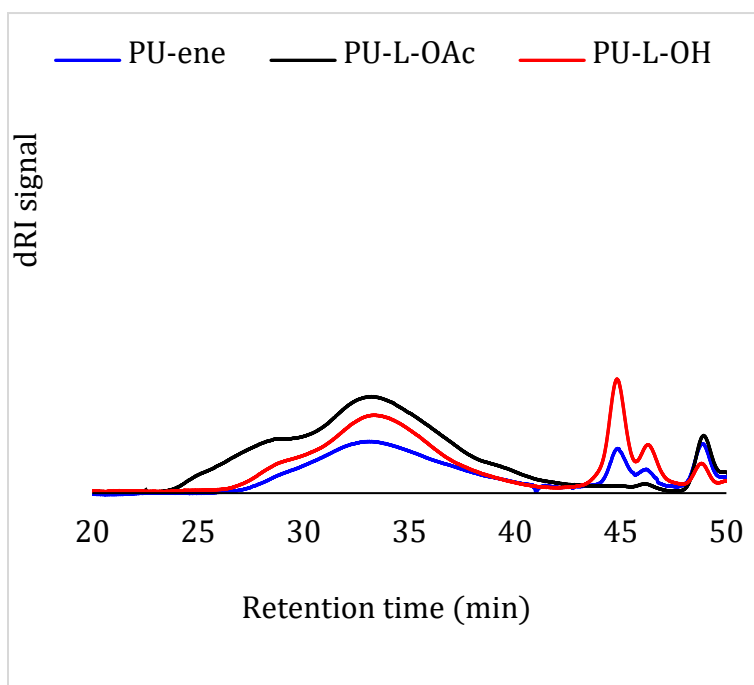


Figure S16. Overlaid GPC traces of PU-ene (blue, PU-L-OAc (black), and PU-L-OH (red).

Table 1. M_n and Dispersity of model polymers

Polymer	M_n (kDa)	\mathbf{D}
PU-ene	29.7	2.51
PU-L-OAc	40.7	3.6
PU-L-OH	35.3	2.3