Electronic Supplementary Material (ESI) for Polymer Chemistry.

Blood compatibility of heparin-inspired, lactose containing, polyureas depends on the chemistry of the polymer backbone

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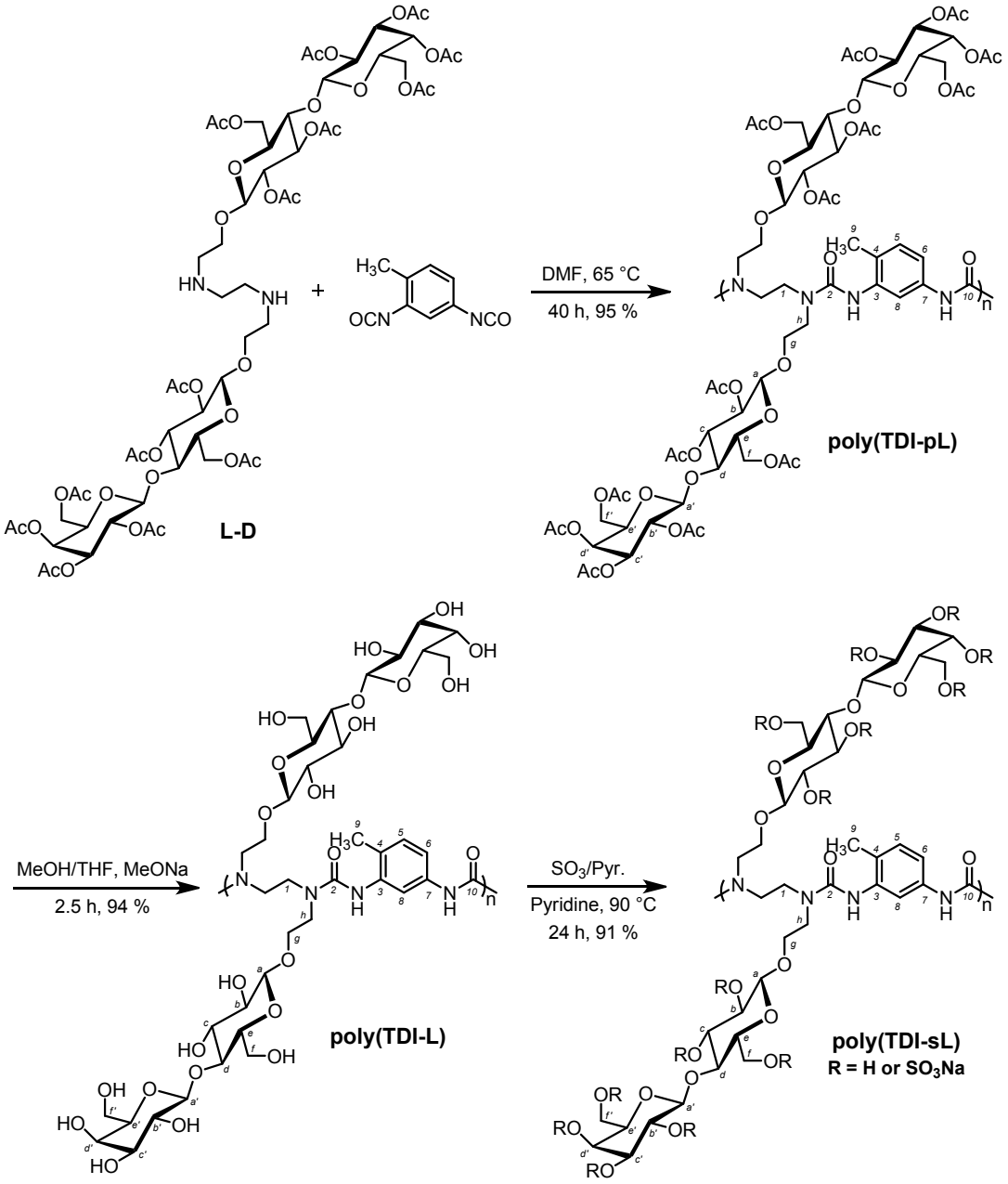
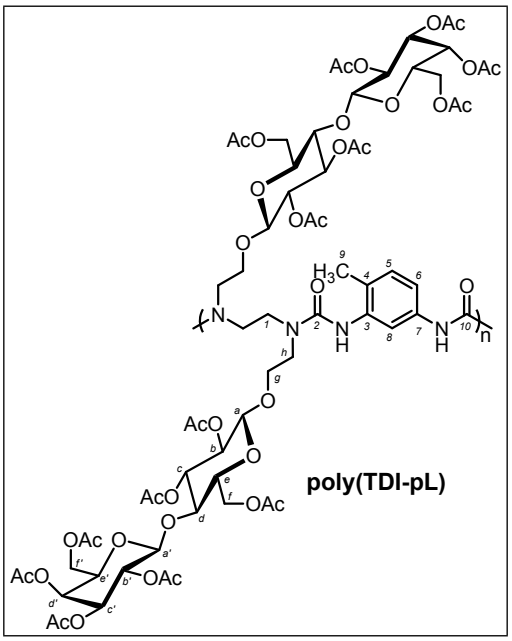
Table of Contents

Part S1: Synthesis and spectra of poly(TDI-sL) from L-D and TDI



The detailed synthesis procedures are listed in the manuscript.



Synthesis of **poly(TDI-pL)**:

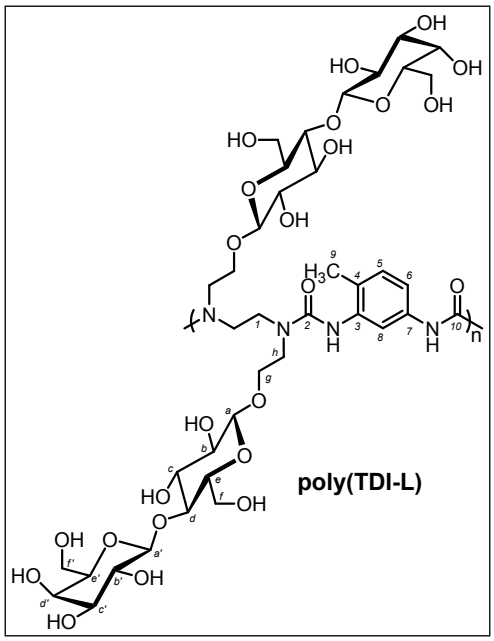
^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.03 (m, 3 H, =C*H*), 5.34 (s, 2 H, *d*-H), 5.17 (m, 2 H, *c'*-H), 5.09 (t, J = 8.0 Hz, 2 H, *b*-H), 4.98 (m, 2 H, *c*-H), 4.89 (m, 2 H, *b'*-H), 4.51 (m, 6 H, *a*-H, *a'*-H, *f'*-H_a), 4.12–4.07 (m, 6 H, *f*-H, *g*-H_a), 3.90–3.45 (m, 18 H, *e*-H, *g*-H_b, *d'*-H, *e'*-H, *f'*-H_b, *h*-H, *1*-H), 2.15, 2.04, 1.96 (3 × s, 45 H, 15 × CH_3)

^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 170.19 (CH_3C=O), 170.02 (CH_3C=O), 169.90 (CH_3C=O), 169.56 (CH_3C=O), 168.98 (CH_3C=O), 156.41 (C-*2*, C-*10*), 137.37 (C-*3*, C-*4*, C-*7*), 130.10 (C-*5*), 117.04, 116.40 (C-*6*, C-*8*), 100.89 (C-*a*, C-*a'*), 76.11 (C-*d*), 72.76 (C-*b*), 71.30 (C-*c'*), 70.84 (C-*c*), 70.45 (C-*b'*), 69.01 (C-*e'*), 66.55 (C-*e*), 65.69 (C-*d'*), 61.92 (C-*f*), 60.64 (C-*f'*), 53.55 (C-*g*), 48.66 (C-*1*, C-*h*), 20.67,20.52 (CH$_3$C=O), 17.47 (C-*9*)

FT-IR: (cm^{-1}) 2940, 1743, 1661, 1531, 1427, 1367, 1213, 1040, 900

GPC data: number average molecular weight (Mn): 10.8 kDa; weight average molecular weight (Mw): 27.1 kDa; polydispersity ($Đ$): 2.51

Contact Angle: Static: 47°; Advancing: 53°; Receding: 35°



Synthesis of **poly(TDI-L)**:

^{1}H NMR (D_2O, 400 MHz): δ (ppm) 7.03 (m, 3 H, =C*H*), 4.39–3.32 (m, 4 H, *d*-H, *c'*-H), 3.82–3.47 (m, 36 H, *a*-H, *b*-H, *c*-H, *e*-H, *f*-H, *g*-H, *h*-H, *a'*-H, *b'*-H, *d'*-H, *e'*-H, *f'*-H, *1*-H), 2.07 (s, 3 H, *9*-H)

DEPT–135 (D_2O, 100 MHz): δ (ppm) 130.58 (C-*5*), 102.84 (C-*a*), 102.37 (C-*a'*), 78.28 (C-*d*), 75.20 (C-*b*), 74.59 (C-*c'*), 74.37 (C-*c*), 72.70 (C-*b'*), 72.48 (C-*e'*), 70.77 (C-*e*), 68.42 (C-*d'*), 60.86 (C-*f*), 60.01 (C-*f'*), 16.73 (C-*9*)

^{13}C NMR (D_2O, 100 MHz): δ (ppm) 158.84 (C-*2*, C-*10*), 136.27 (C-*3*, C-*4*, C-*7*), 130.55 (C-*5*), 119.70,119.07 (C-*6*, C-*8*), 102.87 (C-*a*), 102.37 (C-*a'*), 78.34 (C-*d*), 75.22 (C-*b*), 74.61 (C-*c'*), 74.40 (C-*c*), 72.71 (C-*b'*), 72.51 (C-*e'*), 70.79 (C-*e*), 68.45 (C-*d'*), 60.88 (C-*f*), 60.04 (C-*f'*), 47.43,45.78 (C-*1*, C-*h*), 16.75 (C-*9*)

FT-IR: (cm^{-1}) 3311, 2881, 1639, 1526, 1494, 1372, 1236, 1020

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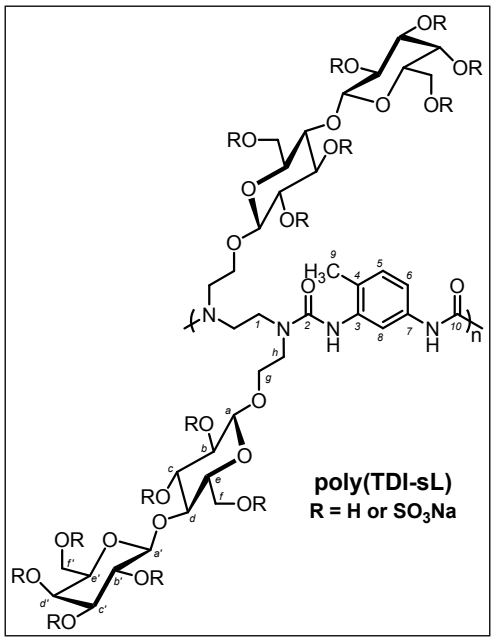


Synthesis of **poly(TDI-sL)**:

^{1}H NMR (D_2O, 400 MHz): δ (ppm) 8.82–7.12 (m, 3 H, =C*H*), 5.19 (s, 2 H, *d*-H), 5.05–5.00 (m, 2 H, *c'*-H), 4.89 (m, 2 H, *b*-H), 4.49–3.46 (m, 34 H, *a*-H, *c*-H, *e*-H, *f*-H, *g*-H, *h*-H, *a'*-H, *b'*-H, *d'*-H, *e'*-H, *f'*-H, *1*-H), 2.33 (s, 3 H, *9*-H)

^{13}C NMR (D_2O, 100 MHz): δ (ppm) 157.21 (C-*2*, C-*10*), 145.21 (C-*3*, C-*4*, C-*7*), 128.19 (C-*5*), 101.09, 100.83 (C-*a*), 100.28 (C-*a'*), 78.02, 77.84, 77.66 (C-*d*), 77.25 (C-*b*), 75.88, 75.70 (C-*c'*), 75.27 (C-*c*), 74.97 (C-*b'*), 73.27 (C-*e'*), 73.09 (C-*e*), 72.00 (C-*d'*), 69.12 (C-*g*), 66.89, 66.66, 66.16 (C-*f*), 65.08 (C-*f'*), 47.33, 46.50, 46.24 (C-*h*, C-*1*), 16.72 (C-*9*)

FT-IR: (cm^{-1}) 3481, 1634, 1220, 999, 931, 799

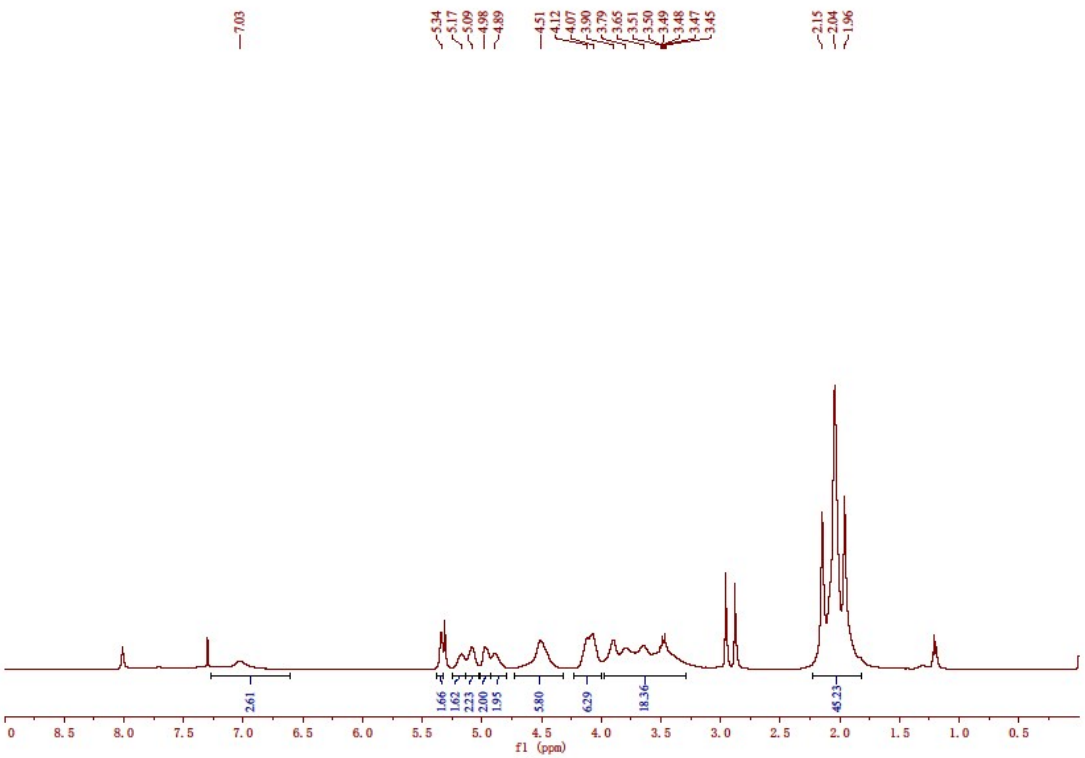


Figure S01. [1]H NMR spectrum for **poly(TDI-pL)**

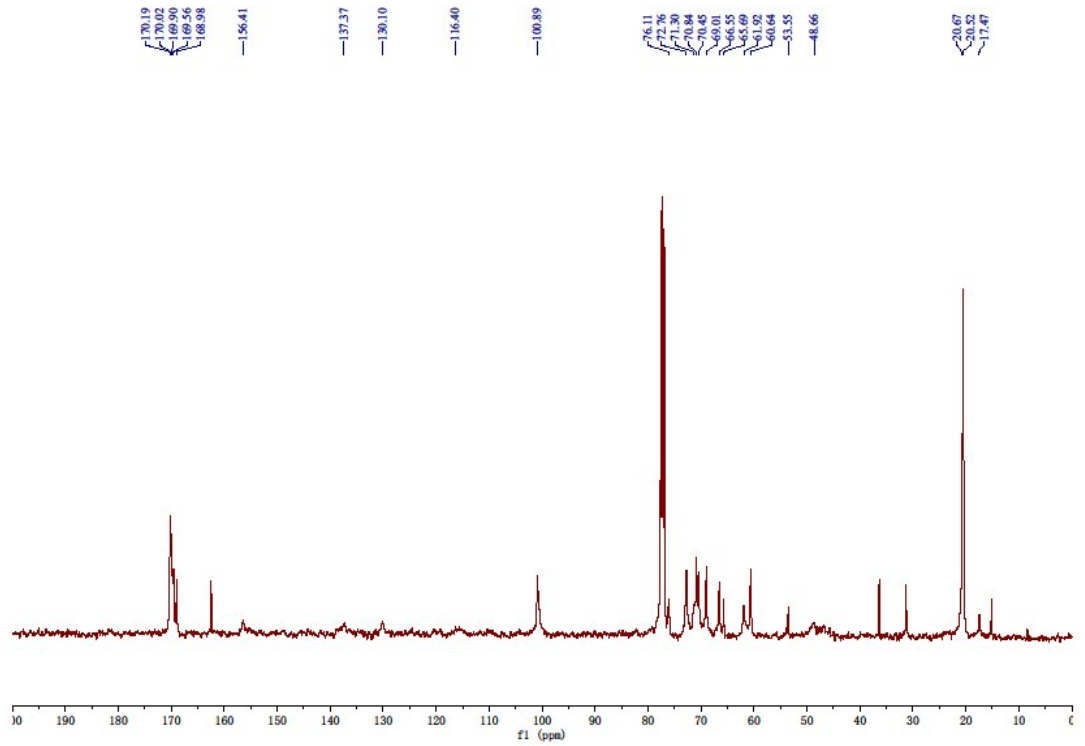


Figure S02. [13]C NMR spectrum for **poly(TDI-pL)**

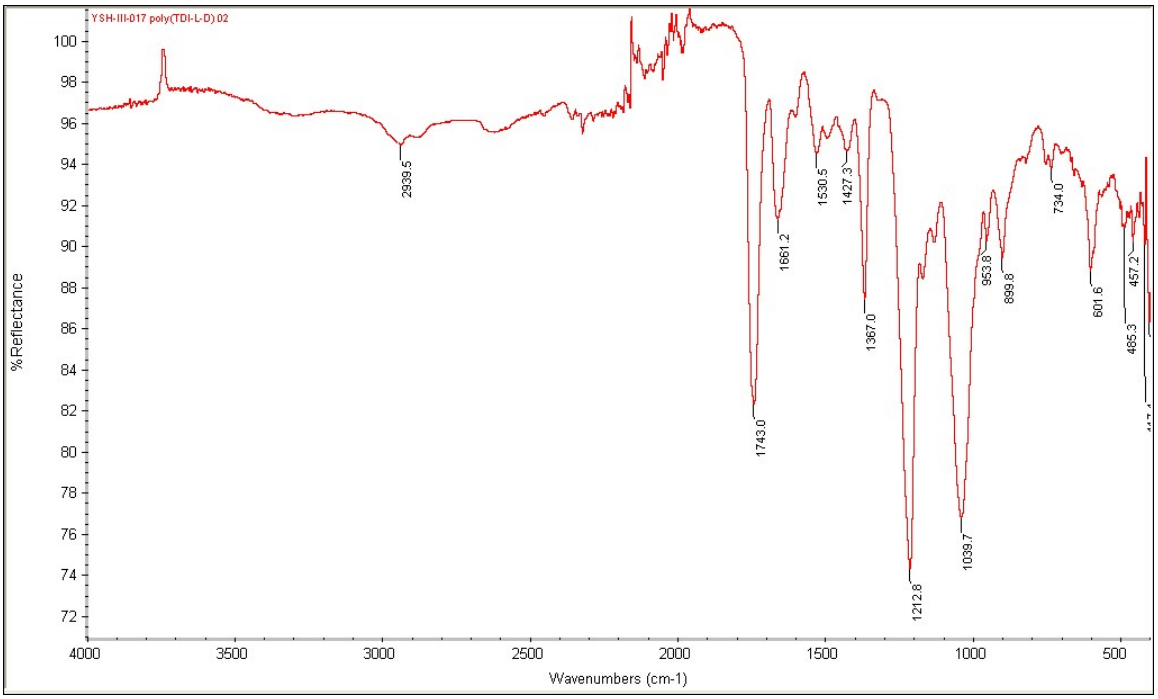


Figure S03. FT-IR spectrum for **poly(TDI-pL)**

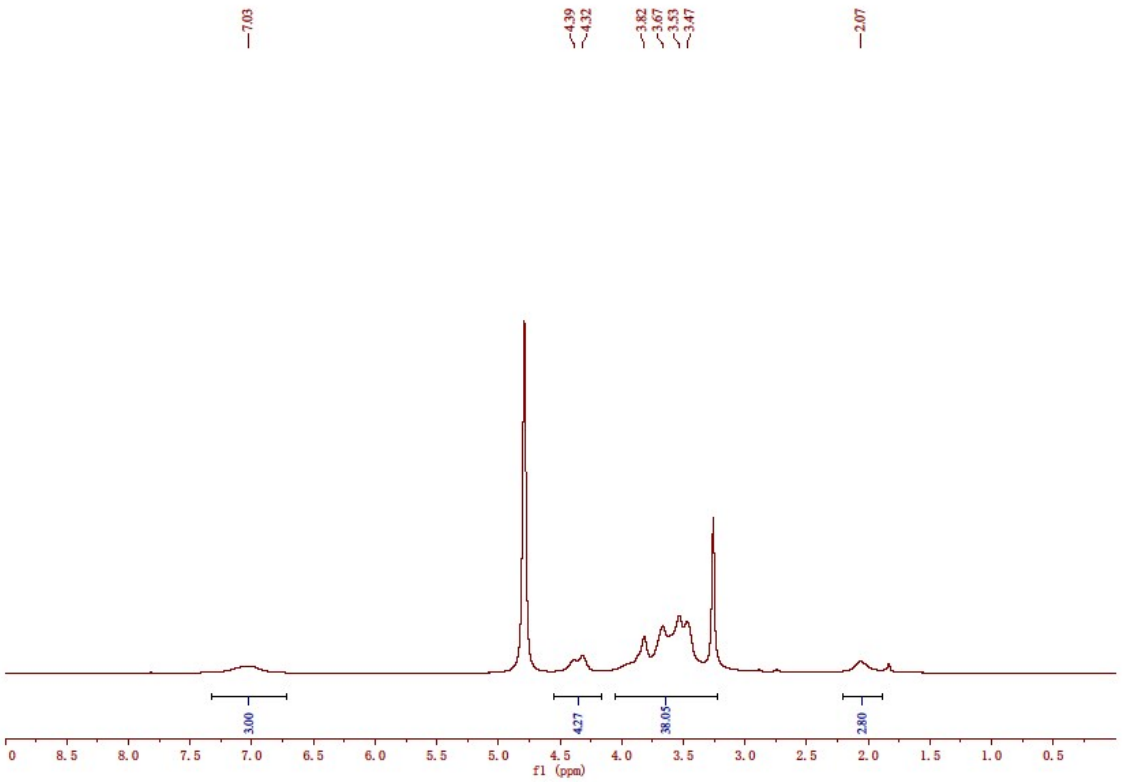


Figure S04. ^{1}H NMR spectrum for **poly(TDI-L)**

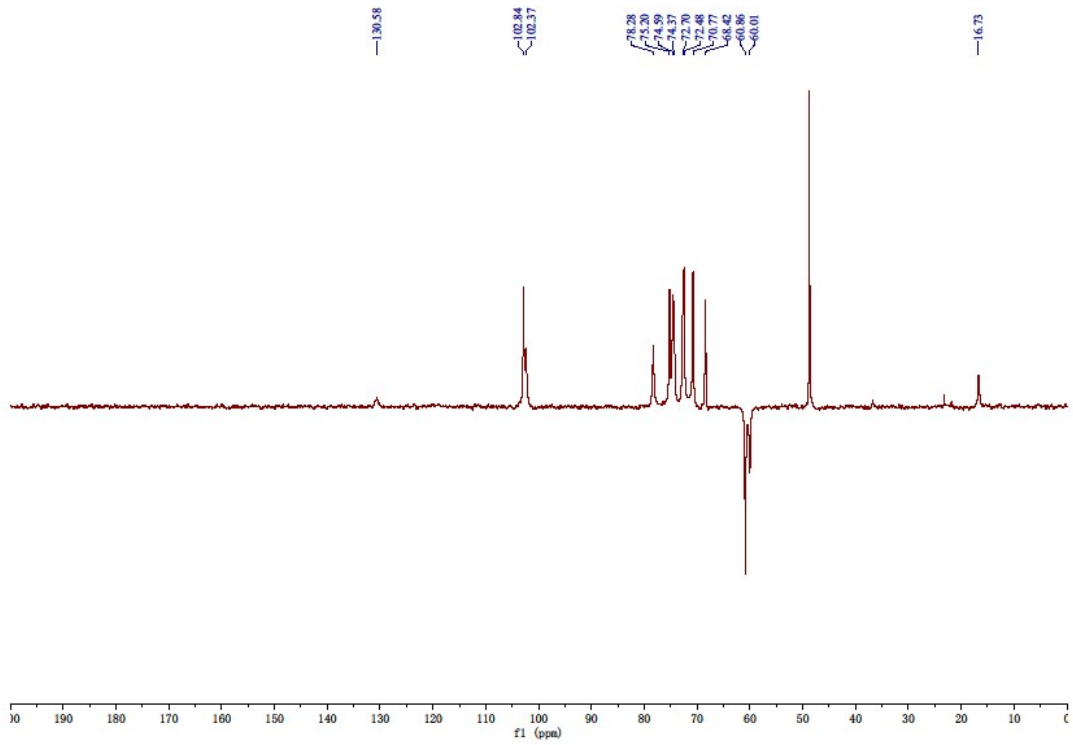


Figure S05. DEPT-135 spectrum for **poly(TDI-L)**

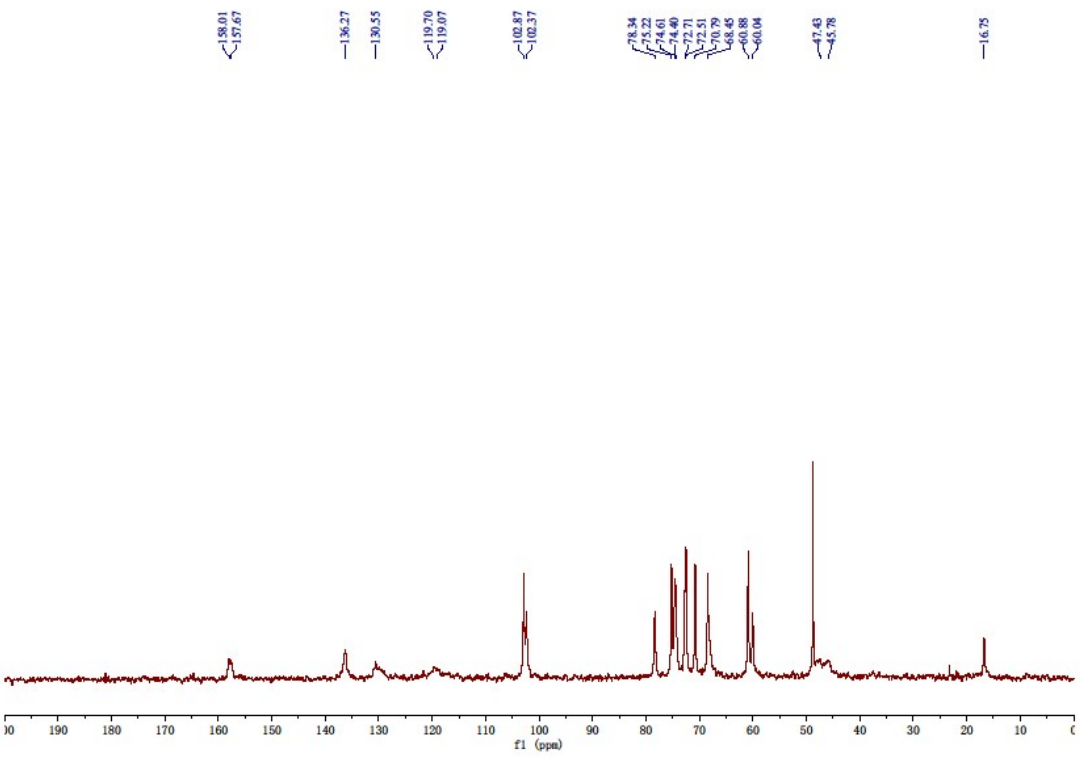


Figure S06. ^{13}C NMR spectrum for **poly(TDI-L)**

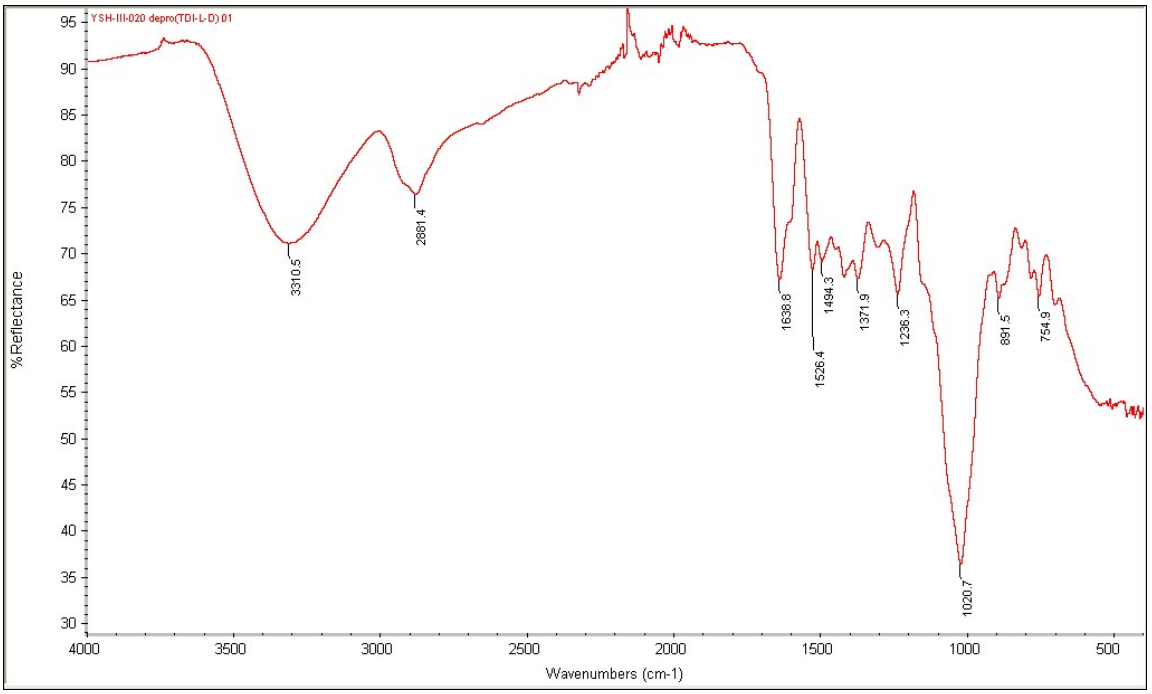


Figure S07. FT-IR spectrum for **poly(TDI-L)**

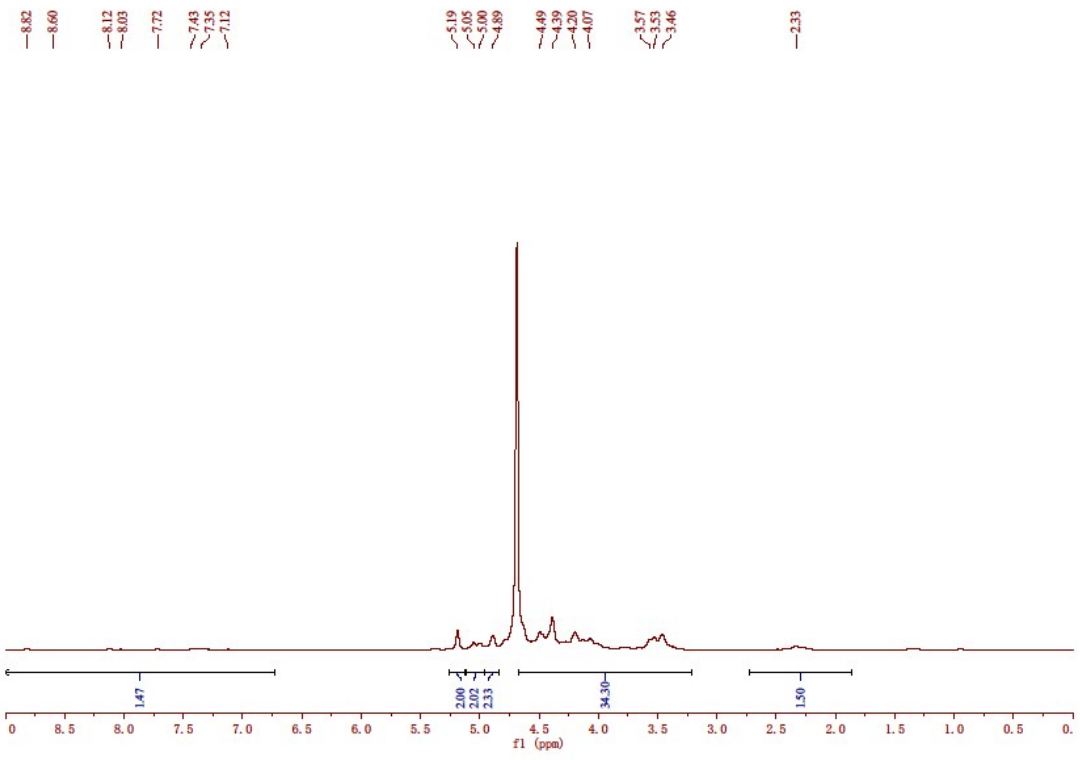


Figure S08. ^{1}H NMR spectrum for **poly(TDI-sL)**

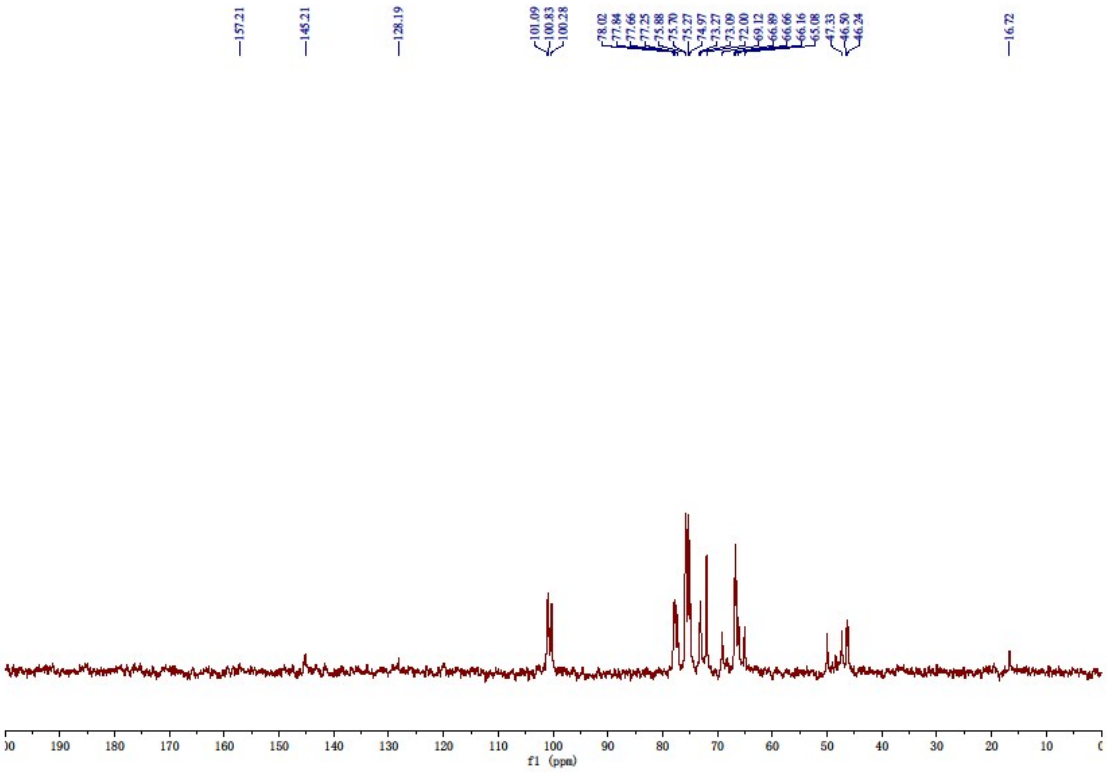


Figure S09. ^{13}C NMR spectrum for **poly(TDI-sL)**

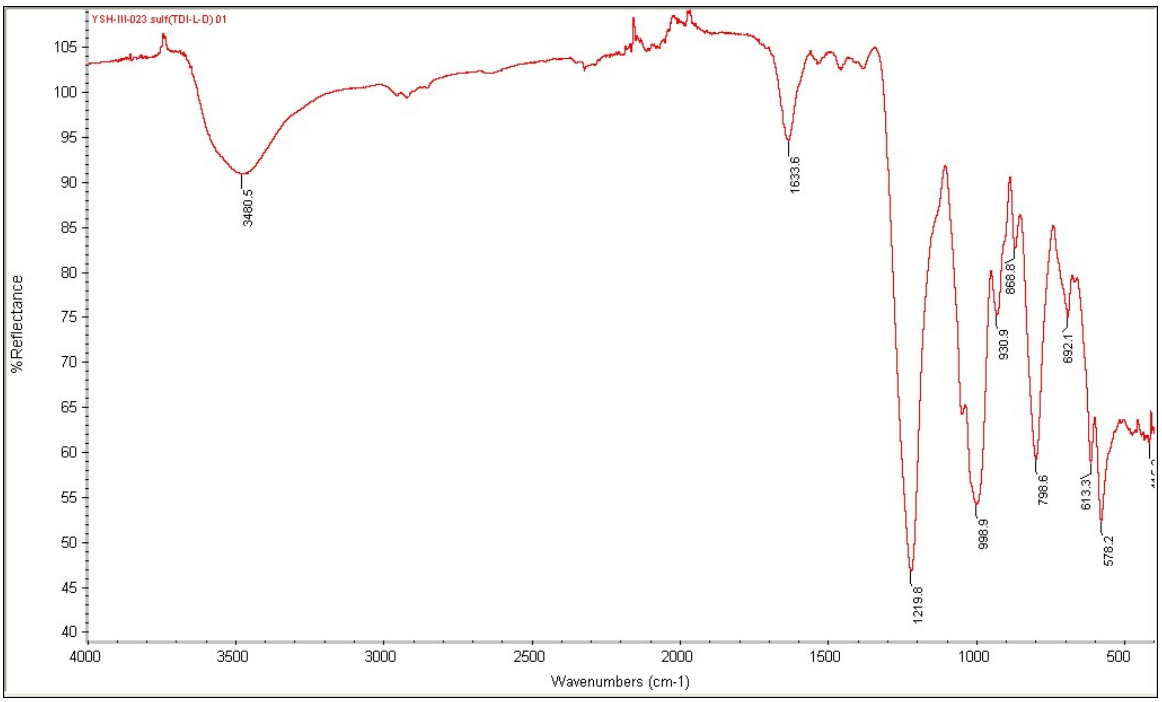
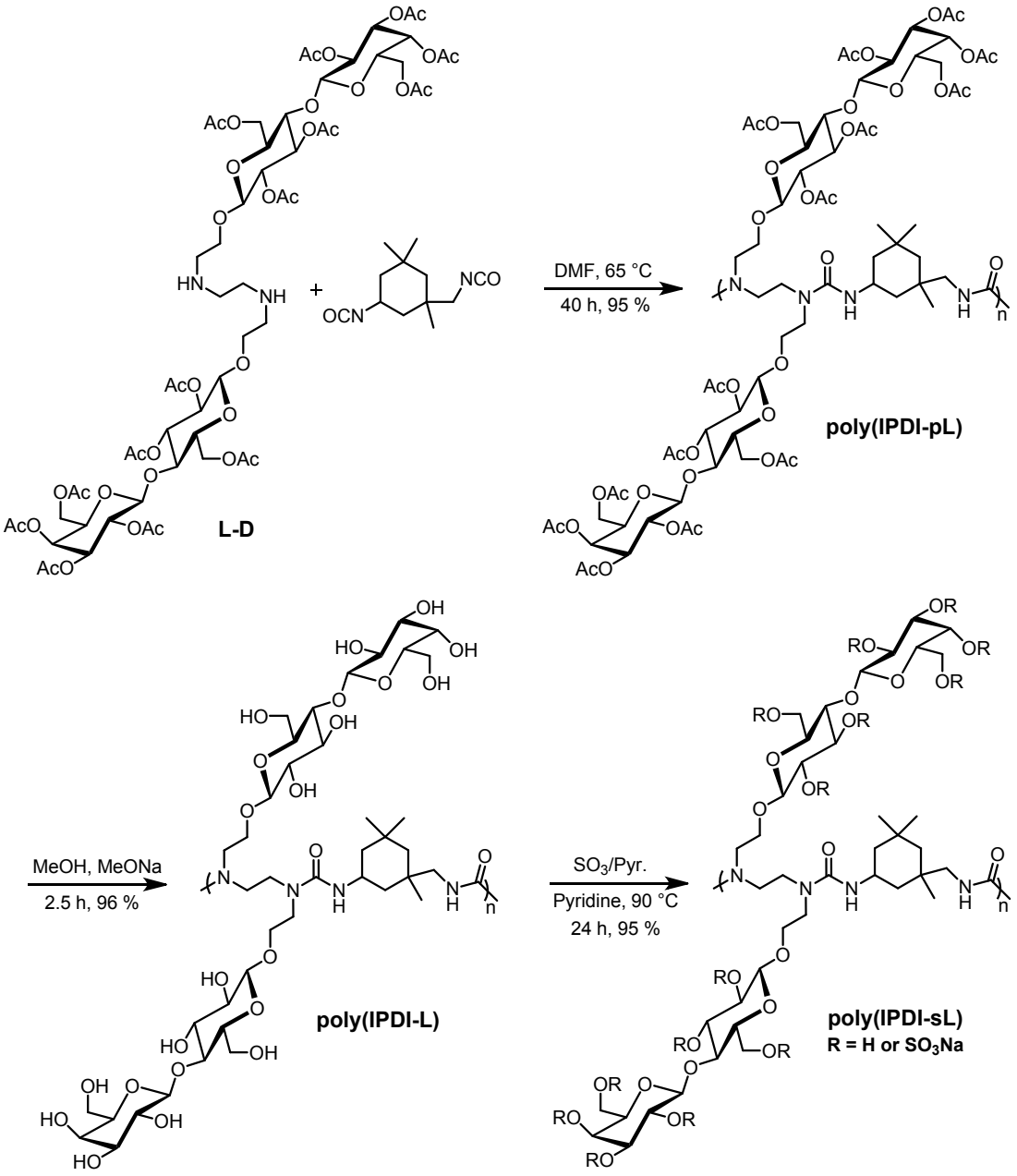
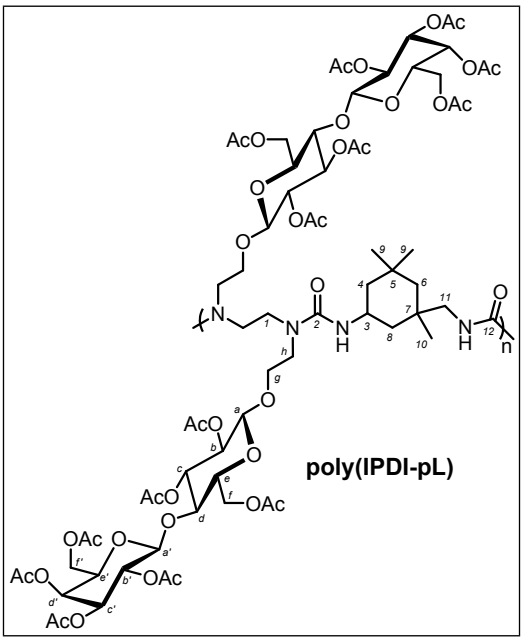


Figure S10. FT-IR spectrum for **poly(TDI-sL)**

Part S2: Synthesis and spectra of poly(IPDI-sL) from L-D and IPDI





Synthesis of **poly(IPDI-pL)**:

L-D (2.90 g, 1.0 equiv.) was added into a flame-dried flask. After evacuating and refilling with nitrogen three times, 10 mL of anhydrous DMF was injected under nitrogen protection followed by isophorone diisocyanate (**IPDI**) (0.489 g, 1.05 equiv.). This solution was stirred at 65 °C for 40 h before removing the DMF. The residue was dissolved in a minimum amount of DCM and precipitated out from cold ether three times. The solvent was removed under vacuum to yield 3.26 g product as a white powder in 95 % yield

^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 5.35 (s, 2 H, *d*-H), 5.18 (m, 2 H, *c'*-H), 5.10 (t, J = 8.0 Hz, 2 H, *b*-H), 4.98–4.96 (m, 2 H, *c*-H), 4.86 (m, 2 H, *b'*-H), 4.51 (m, 6 H, *a*-H, *a'*-H, *f'*-H_a), 4.12–4.09 (m, 6 H, *f*-H, *g*-H_a), 3.90 (m, 4 H, *e*-H, *f'*-H_b), 3.80 (m, 2 H, *d'*-H), 3.64 (m, 4 H, *g*-H_b, *e'*-H), 3.40–3.11 (m, 11 H, *h*-H, *1*-H, *3*-H, *11*-H), 2.15, 2.12, 2.05, 2.01, 1.97 (6 × s, 42 H, 14 × CH_3), 1.69 (m, 2 H, *8*-H), 1.06–0.93 (m, 13 H, *4*-H, *6*-H, *9*-H, *10*-H)

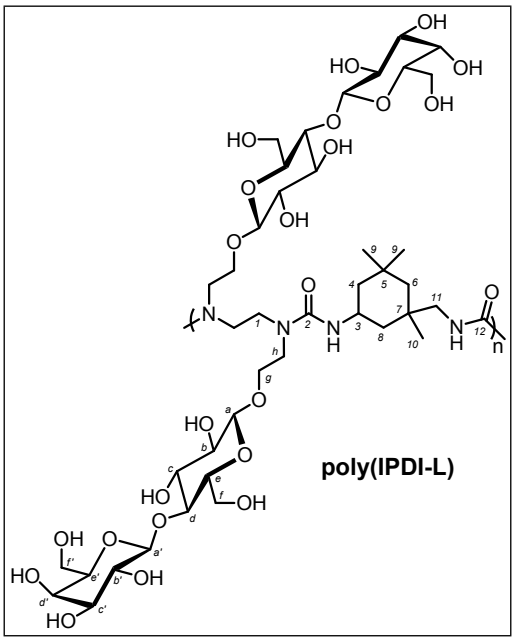
^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 170.00 (CH_3C=O), 169.85 (CH_3C=O), 169.72 (CH_3C=O), 169.37 (CH_3C=O), 168.79 (CH_3C=O), 158.60, 157.82 (C-*2*, C-*12*), 100.71 (C-*a*, C-*a'*), 75.99 (C-*d*), 72.55 (C-*b*), 71.23 (C-*c'*), 70.68 (C-*c*), 70.32 (C-*b'*), 68.85 (C-

e'), 66.40 (C-*e*), 65.51 (C-*d'*), 61.70 (C-*f*), 60.53 (C-*f'*), 48.24, 48.02, 47.40, 46.85, 45.72, 43.93 (C-*1*, C-*3*, C-*11*, C-*h*), 35.04, 31.62 (C-*4*, C-*5*, C-*6*, C-*7*, C-*8*), 27.51 (C-*9*), 22.99 (C-*10*), 20.36 (*C*H_3C=O)

FT-IR: (cm^{-1}) 1743, 1634, 1531, 1366, 1212, 1039, 900

GPC data: Mn: 12.3 kDa; Mw: 15.2 kDa; *Đ*: 1.24

Contact Angle: Static: 57°; Advancing: 64°; Receding: 43°



Synthesis of **poly(IPDI-L)**:

In a flame-dried flask, **poly(IPDI-pL)** (3.00 g) was dissolved in 40 mL anhydrous methanol, followed by adding catalytic amount of MeONa/MeOH solution. This solution was stirred at room temperature (r.t.) for 2.5 h with the formation of precipitation. The solvent was poured into a beaker. MeOH was used to wash the precipitate and combined with the original solvent. Dowex 50WX8 hydrogen form resin was added into the solvent to adjust pH around 6.0. After filtration to remove the Dowex 50WX8 resin, the solvent was removed to yield the product. This product is combined with the precipitate to obtain 1.85 g product in 96 % yield

^{1}H NMR (D_2O, 400 MHz): δ (ppm) 4.40 (m, 4 H, *d*-H, *c'*-H), 3.88–3.52 (m, 39 H, *a*-H,

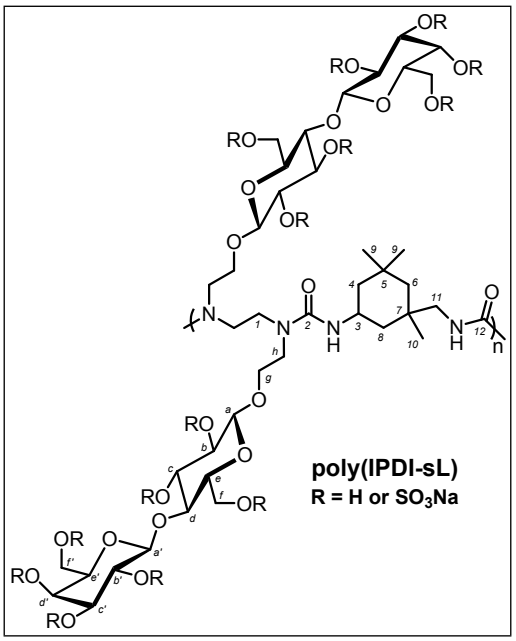
b-H, *c*-H, *e*-H, *f*-H, *g*-H, *h*-H, *a'*-H, *b'*-H, *d'*-H, *e'*-H, *f'*-H, *1*-H, *3*-H, *11*-H), 1.58 (m, 2 H, *8*-H), 1.01–0.91 (m, 13 H, *4*-H, *6*-H, *9*-H, *10*-H)

DEPT–135 (D_2O, 100 MHz): δ (ppm) 102.91 (C-*a*), 102.33 (C-*a'*), 78.40 (C-*d*), 75.27 (C-*b*), 74.70 (C-*c'*), 74.44 (C-*c*), 72.78 (C-*b'*), 72.51 (C-*e'*), 70.85 (C-*e*), 68.47 (C-*d'*), 60.92 (C-*f*), 60.10 (C-*f'*)

^{13}C NMR (D_2O, 100 MHz): δ (ppm) 159.80, 159.03 (C-*2*, C-*12*), 102.95 (C-*a*), 102.36 (C-*a'*), 78.46 (C-*d*), 75.30 (C-*b*), 74.73 (C-*c'*), 74.48 (C-*c*), 72.81 (C-*b'*), 72.55 (C-*e'*), 70.89 (C-*e*), 68.50 (C-*d'*), 60.95 (C-*f*), 60.14 (C-*f'*), 47.49, 46.81, 46.36 (C-*h*, C-*1*, C-*11*), 44.27 (C-*3*), 36.50, 35.30, 31.59 (C-*4*, C-*5*, C-*6*, C-*7*, C-*8*), 27.77 (C-*9*), 23.26 (C-*10*)

FT-IR: (cm^{-1}) 3328, 2890, 1622, 1532, 1365, 1245, 1021

Contact Angle: Static: 41°; Advancing: 51°; Receding: 25°



Synthesis of **poly(IPDI-sL)**:

Poly(IPDI-L) (0.82 g, 1.0 equiv.) and SO_3/pyridine complex (5.22 g, 42.0 equiv.) was added into a flame-dried flask. After evacuating and refilling with nitrogen for three times, 15 mL anhydrous pyridine was injected. It was heated at 90 °C for 24 h. After the solvent was removed, saturated $NaHCO_3$ solution was added to adjust the pH to 8.0 and the

polymer was isolated through dialysis and lyophilization to give white foam product. Yield = 1.84 g, 95 %

^{1}H NMR (D_2O, 400 MHz): δ (ppm) 5.23 (s, 2 H, *d*-H), 4.99–4.93 (m, 4 H, *c'*-H, *b*-H), 4.67–3.62 (m, 37 H, *a*-H, *c*-H, *e*-H, *f*-H, *g*-H, *h*-H, *a'*-H, *b'*-H, *d'*-H, *e'*-H, *f'*-H, *1*-H, *3*-H, *11*-H), 1.76 (m, 2 H, *8*-H), 1.19–1.10 (m, 13 H, *4*-H, *6*-H, *9*-H, *10*-H)

^{13}C NMR (D_2O, 100 MHz): δ (ppm) 160.04, 159.03 (C-*2*, C-*12*), 101.00 (C-*a*), 100.77 (C-*a'*), 77.77 (C-*b*, C-*d*), 77.30 (C-*c'*), 75.84 (C-*c*), 75.60 (C-*b'*), 75.23 (C-*e*, C-*e'*), 73.19 (C-*d'*), 71.89 (C-*g*), 68.29 (C-*f*), 66.60 (C-*f'*), 46.91, 45.99 (C-*h*, C-*1*, C-*11*), 44.54 (C-*3*), 36.64, 34.79, 31.48 (C-*4*, C-*5*, C-*6*, C-*7*, C-*8*), 27.20 (C-*9*), 22.91 (C-*10*)

FT-IR: (cm^{-1}) 3480, 2953, 1630, 1538, 1221, 999

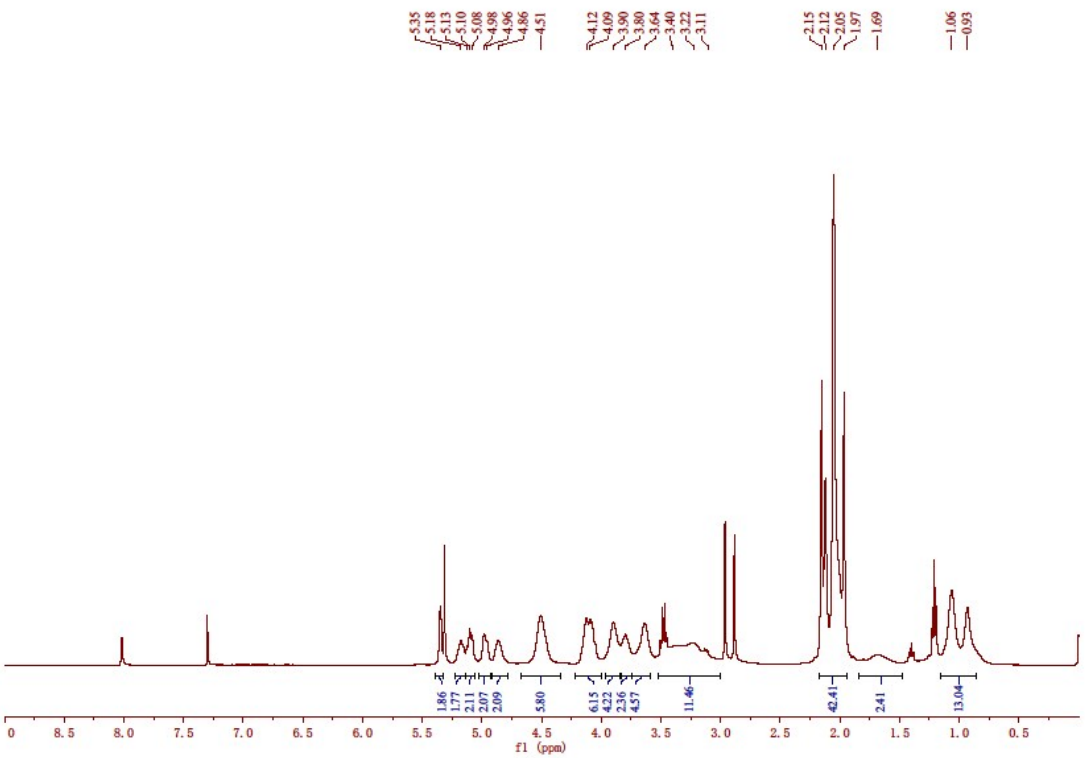


Figure S11. ^{1}H NMR spectrum for **poly(IPDI-pL)**

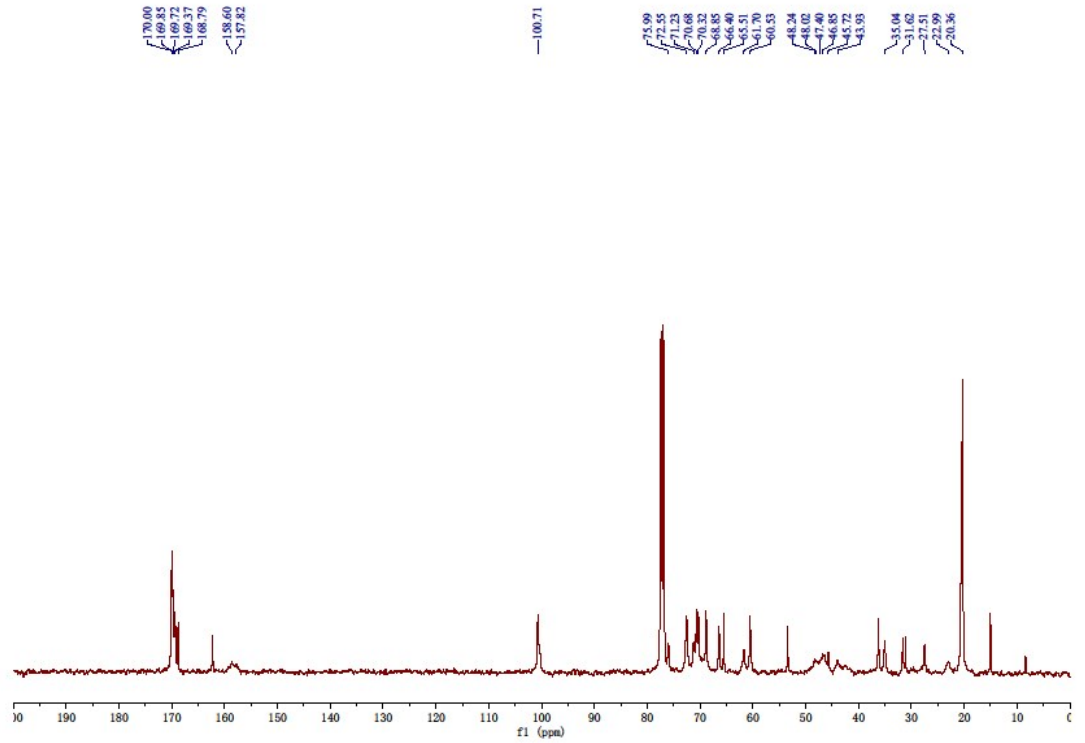


Figure S12. ^{13}C NMR spectrum for **poly(IPDI-pL)**

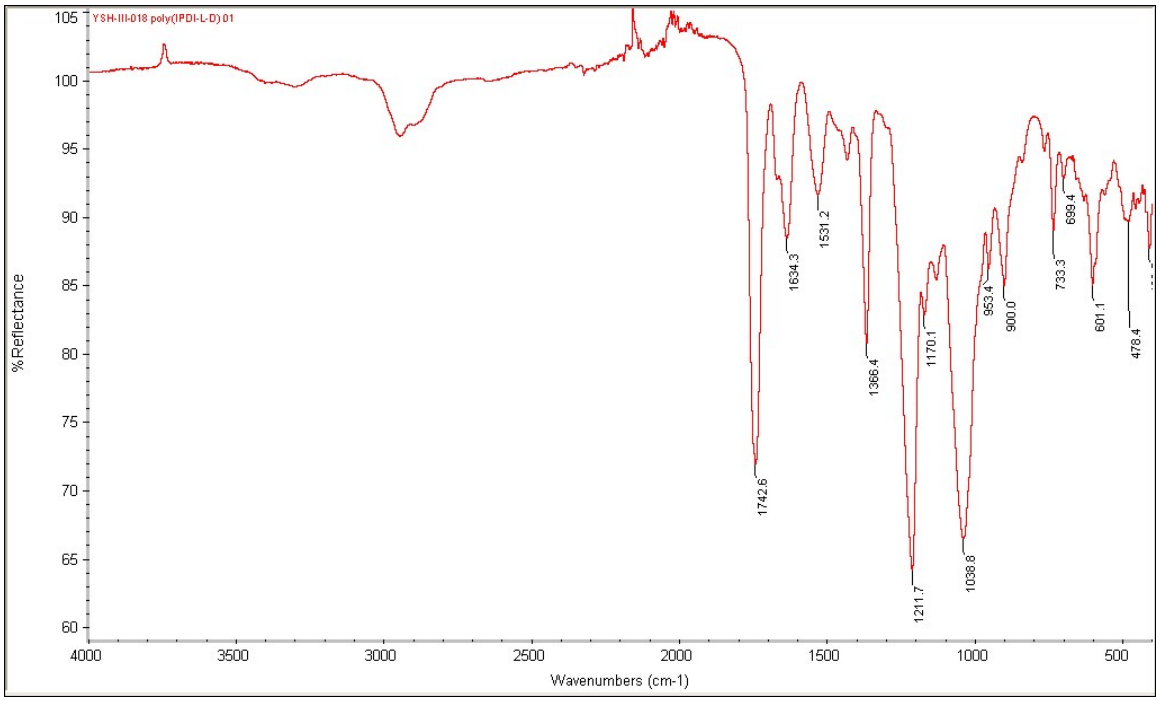


Figure S13. FT-IR spectrum for **poly(IPDI-pL)**

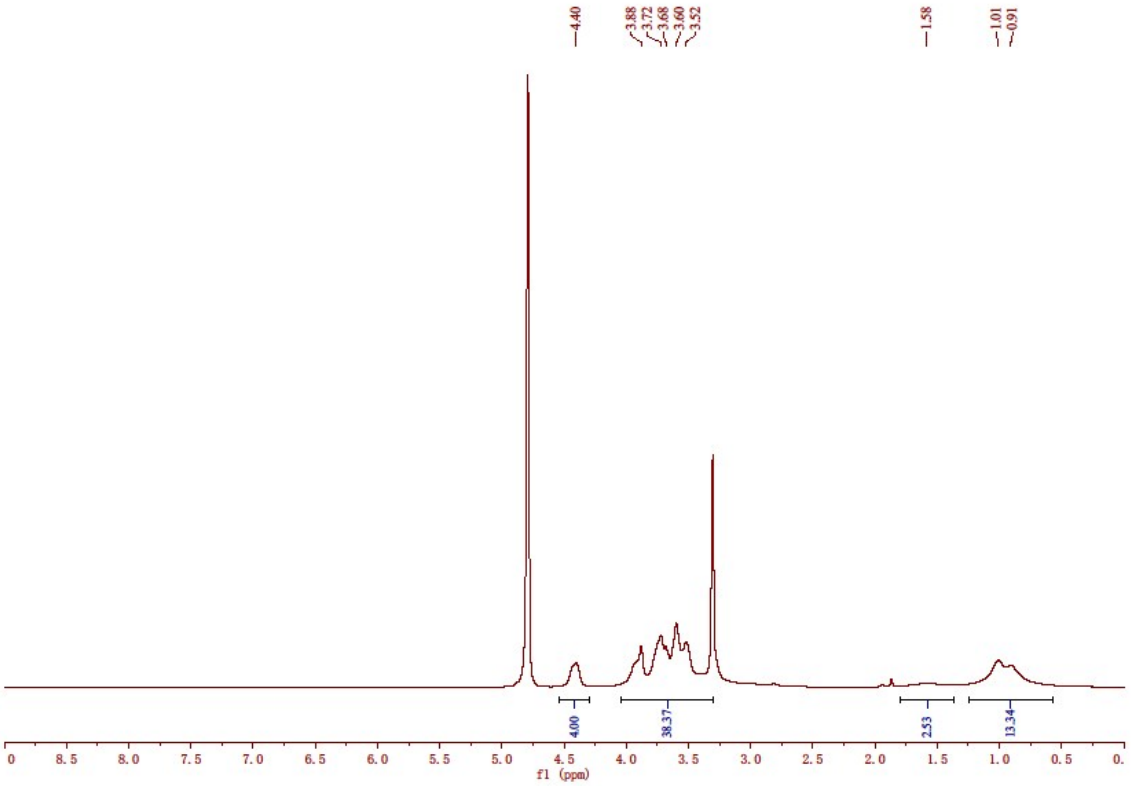


Figure S14. ^{1}H NMR spectrum for **poly(IPDI-L)**

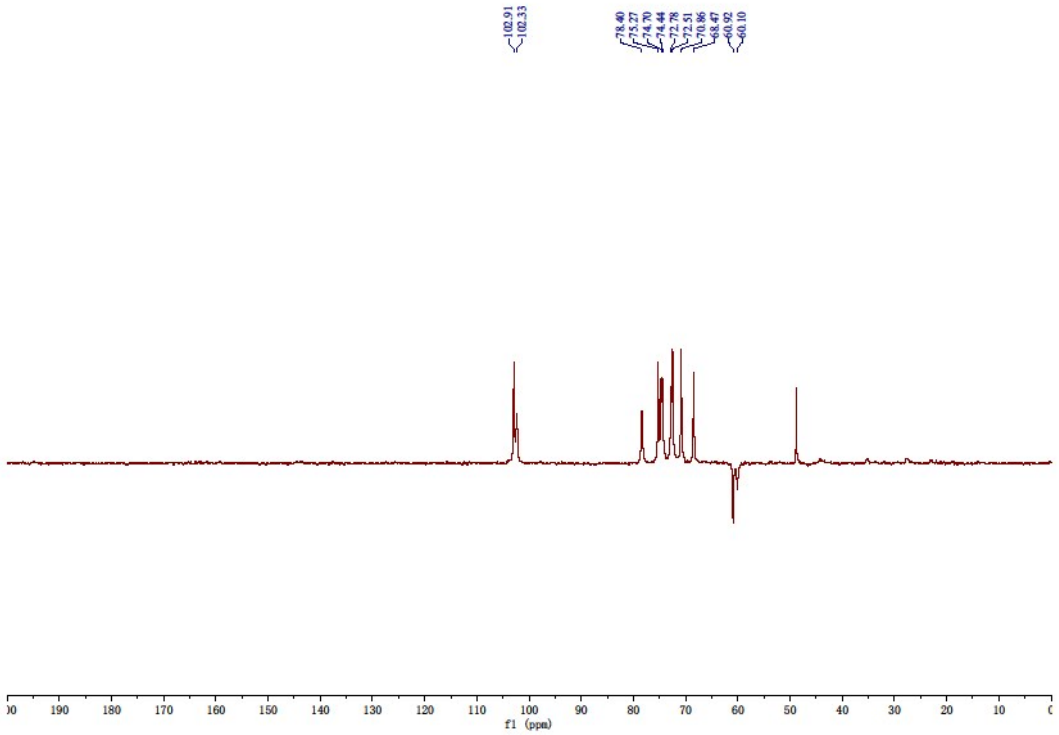


Figure S15. DEPT-135 spectrum for **poly(IPDI-L)**

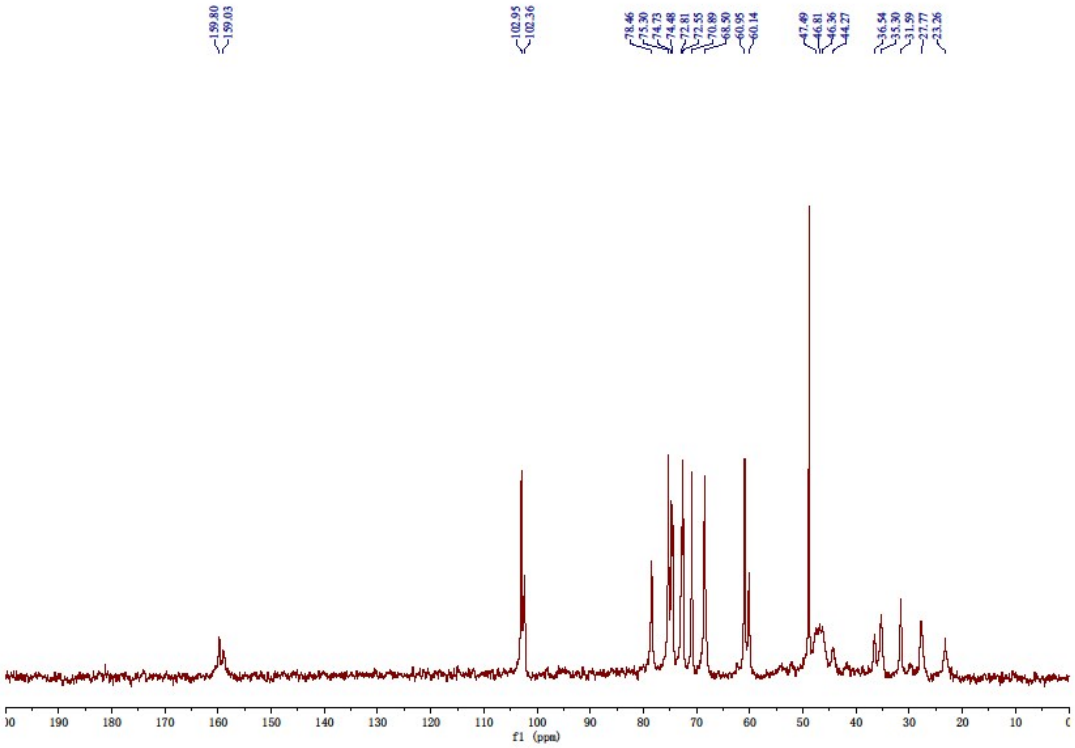


Figure S16. ^{13}C NMR spectrum for **poly(IPDI-L)**

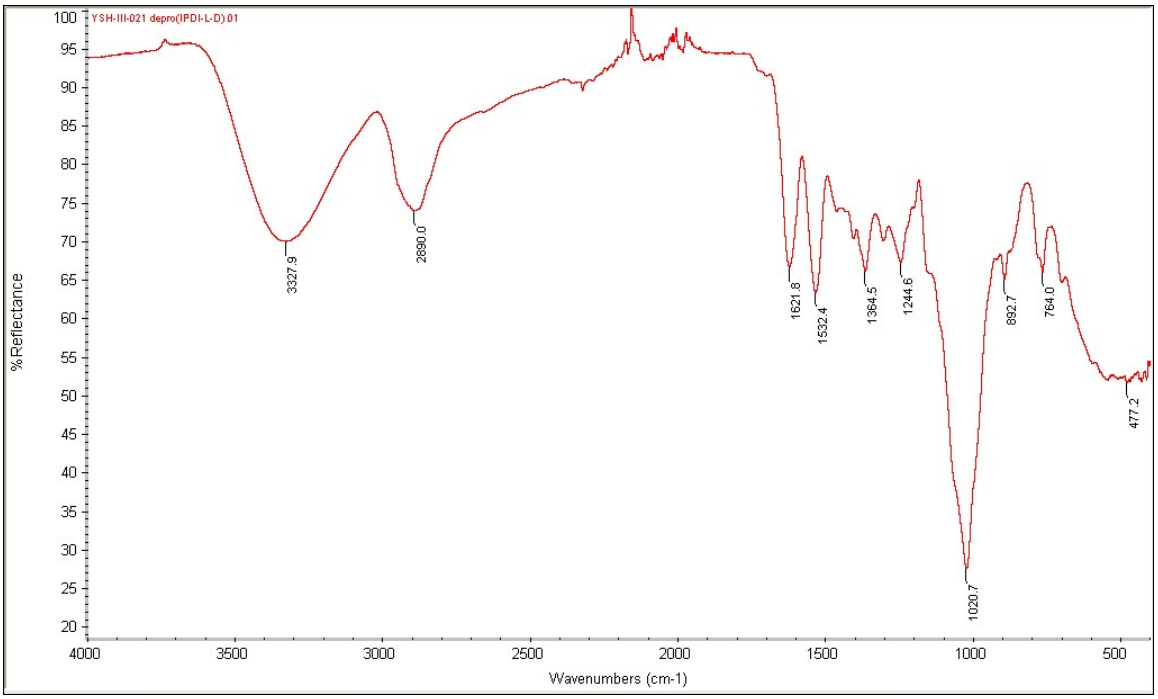


Figure S17. FT-IR spectrum for **poly(IPDI-L)**

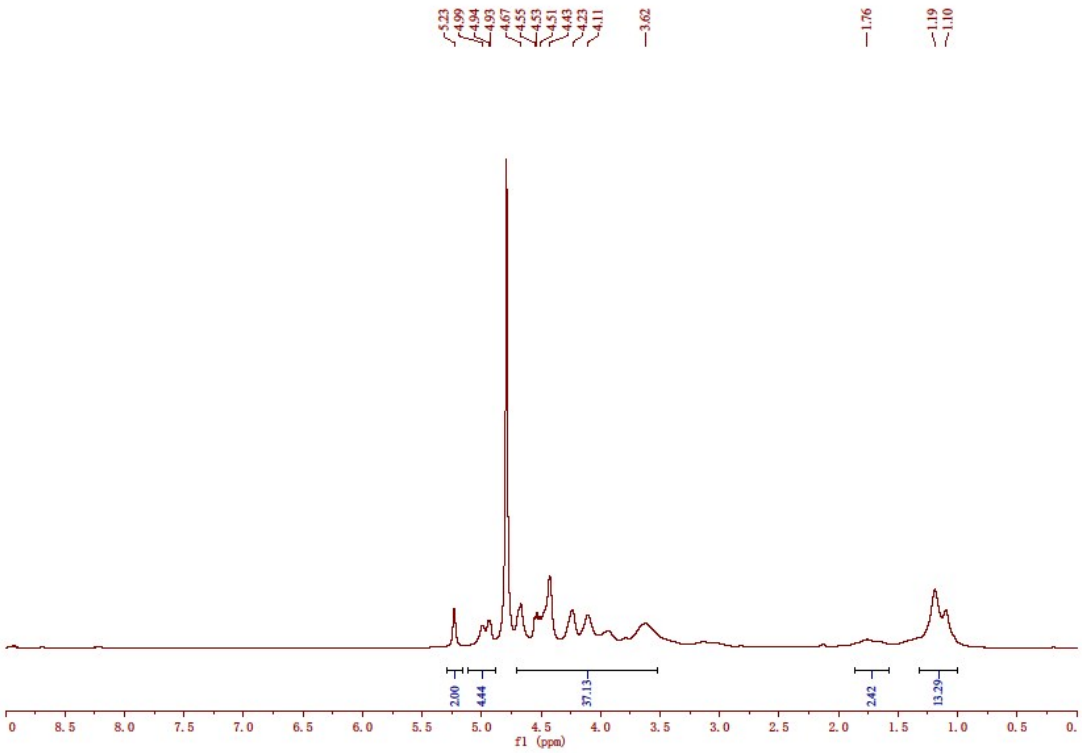


Figure S18. ^{1}H NMR spectrum for **poly(IPDI-sL)**

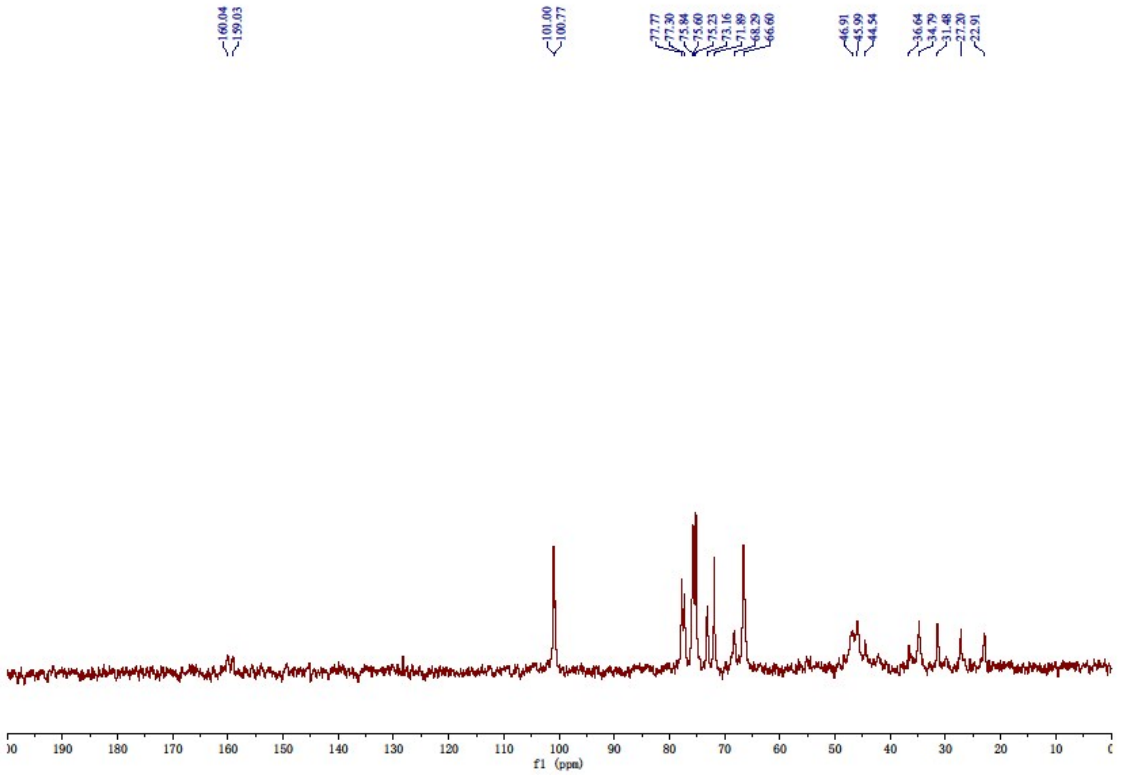


Figure S19. ^{13}C NMR spectrum for **poly(IPDI-sL)**

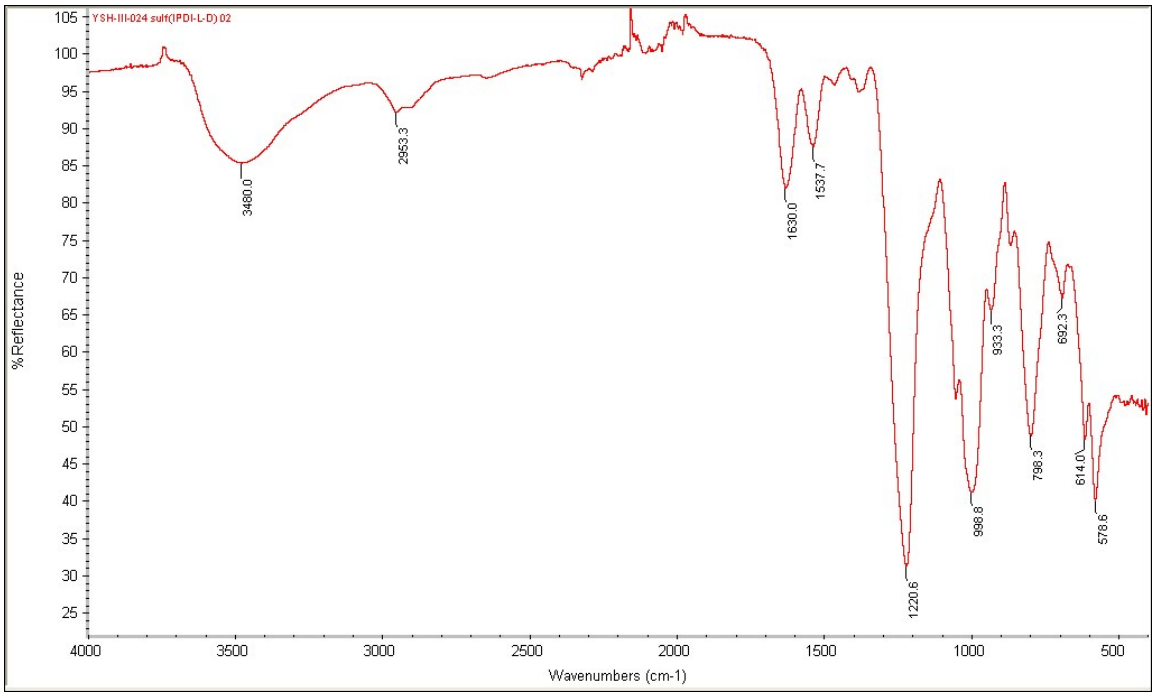
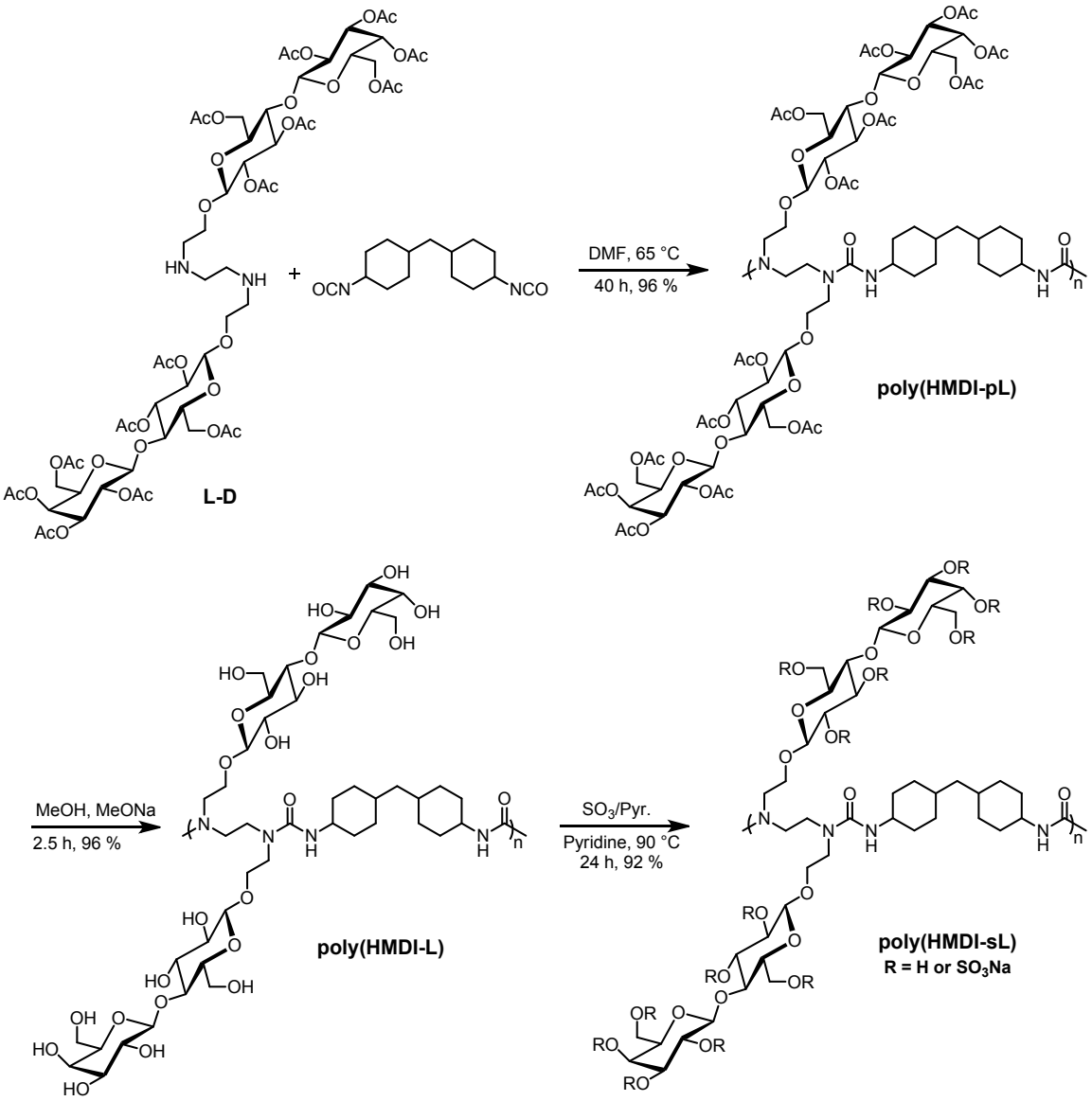
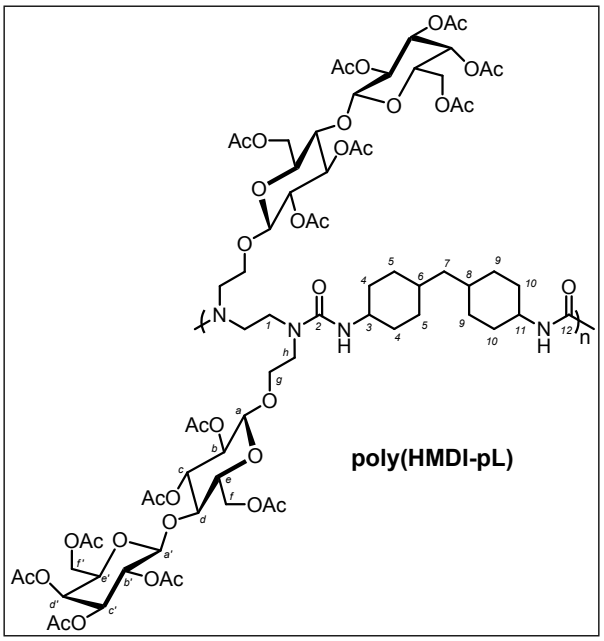


Figure S20. FT-IR spectrum for **poly(IPDI-sL)**

Part S3: Synthesis and spectra of poly(HMDI-sL) from L-D and HMDI





Synthesis of **poly(HMDI-pL)**:

L-D (2.870 g, 1.0 equiv.) was added into a flame-dried flask. After evacuating and refilling with nitrogen for three times, 10 mL anhydrous DMF was injected under nitrogen protection, followed by 4,4'-methylenebis(cyclohexyl isocyanate) (**HMDI**) (0.634 g, 1.05 equiv., 90 % purity). This solution was stirred at 65 °C for 40 h before removing the DMF. The residue was dissolved in a minimum amount of DCM, and precipitated out from cold ether three times. The solvent was removed under vacuum to yield 3.320 g product as a white powder in 96 % yield

^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 5.35 (s, 2 H, *d*-H), 5.18 (m, 2 H, *c'*-H), 5.10 (t, J = 8.0 Hz, 2 H, *b*-H), 4.98–4.95 (m, 2 H, *c*-H), 4.86 (m, 2 H, *b'*-H), 4.50 (m, 6 H, *a*-H, *a'*-H, *f'*-H_a), 4.13–4.04 (m, 6 H, *f*-H, *g*-H_a), 3.89 (m, 4 H, *e*-H, *f'*-H_b), 3.81–3.77 (m, 2 H, *d'*-H), 3.64 (m, 4 H, *g*-H_b, *e'*-H), 3.44–3.11 (m, 10 H, *h*-H, *1*-H, *3*-H, *11*-H), 2.15, 2.12, 2.06, 2.05, 2.01, 1.97 (6 × s, 42 H, 14 × CH_3), 1.73–1.54, 1.27–0.97 (m, 20 H, *4*-H, *5*-H, *6*-H, *7*-H, *8*-H, *9*-H, *10*-H)

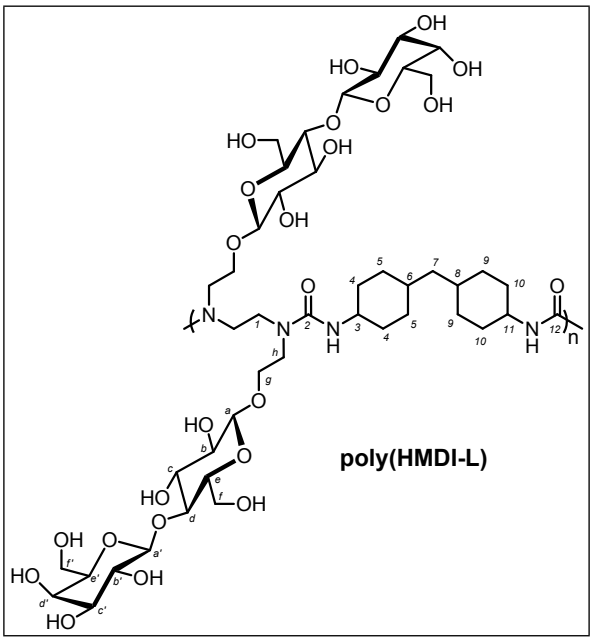
^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 170.08 (CH_3C=O), 169.91 (CH_3C=O), 169.80 (CH_3C=O), 169.44 (CH_3C=O), 168.84 (CH_3C=O), 157.76 (C-*2*, C-*12*), 100.77 (C-*a*), 100.49 (C-*a'*), 75.97 (C-*d*), 72.66 (C-*b*), 71.20 (C-*c'*), 70.71 (C-*c*), 70.38 (C-*b'*), 68.90

(C-*e'*), 66.42 (C-*e*), 65.58 (C-*d'*), 61.77 (C-*f*), 60.56 (C-*f'*), 50.02 (C-*g*), 48.18, 46.90, 46.64, 45.77 (C-*1*, C-*3*, C-*11*, C-*h*), 33.61, 33.17, 32.15, 31.94, 29.54, 27.93, 27.33 (C-*4*, C-*5*, C-*6*, C-*7*, C-*8*, C-*9*, C-*10*), 20.59, 20.42 (*C*H_3C=O)

FT-IR: (cm^{-1}) 2927, 1742, 1634, 1526, 1366, 1212, 1038, 890

GPC data: Mn: 11.0 kDa; Mw: 15.6 kDa; PDI: 1.42

Contact Angle: Static: 56°; Advancing: 60°; Receding: 45°



Synthesis of **poly(HMDI-L)**:

In a flame-dried flask, **poly(HMDI-pL)** (3.10 g) was dissolved in 40 mL anhydrous methanol, followed by adding catalytic amount of MeONa/MeOH solution. This solution was stirred at r.t. for 2.5 h with the formation of precipitation. The solvent was poured into a beaker. MeOH was used to wash the precipitate and combined with the original solvent. Dowex 50WX8 hydrogen form resin was added into the solvent to adjust pH around 6.0. After filtration to remove the Dowex 50WX8 resin, the solvent was removed to yield the product. This product was combined with the precipitate to get 1.93 g product in 96 % yield

^{1}H NMR (D_2O, 400 MHz): δ (ppm) 4.42 (m, 4 H, *d*-H, *c'*-H), 3.90–3.54 (m, 38 H, *a*-H,

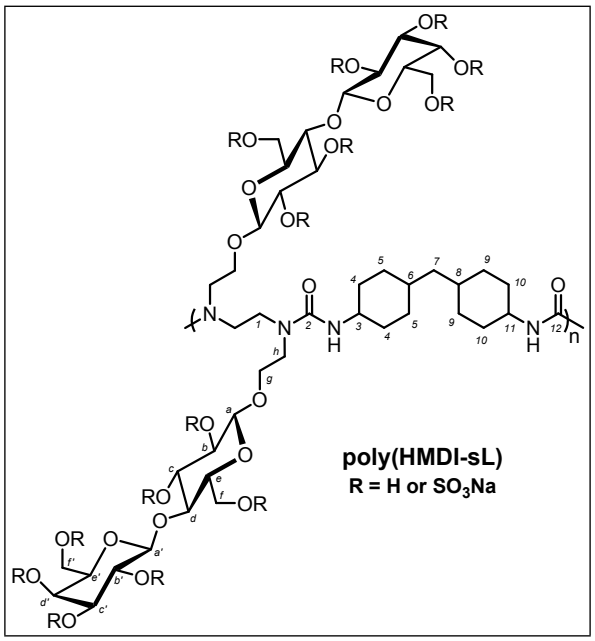
b-H, *c*-H, *e*-H, *f*-H, *g*-H, *h*-H, *a'*-H, *b'*-H, *d'*-H, *e'*-H, *f'*-H, *1*-H, *3*-H, *11*-H), 1.83–0.90 (br, 20 H, *4*-H, *5*-H, *6*-H, *7*-H, *8*-H, *9*-H, *10*-H)

DEPT–135 (D_2O, 100 MHz): δ (ppm) 102.96 (C-*a*), 102.39 (C-*a'*), 78.52 (C-*d*), 75.30 (C-*b*), 74.74 (C-*c'*), 74.48 (C-*c*), 72.80 (C-*b'*), 72.53 (C-*e'*), 70.87 (C-*e*), 68.47 (C-*d'*), 60.93 (C-*f*), 60.16 (C-*f'*)

^{13}C NMR (D_2O, 100 MHz): δ (ppm) 158.84 (C-*2*, C-*12*), 102.99 (C-*a*), 102.43 (C-*a'*), 78.57 (C-*d*), 75.33 (C-*b*), 74.76 (C-*c'*), 74.53 (C-*c*), 72.85 (C-*b'*), 72.56 (C-*e'*), 70.90 (C-*e*), 68.50 (C-*d'*), 60.96 (C-*f*), 60.22 (C-*f'*), 47.61, 46.68 (C-*1*, C-*3*, C-*11*, C-*h*), 33.78, 33.40, 32.21, 31.70, 29.84, 29.14, 28.71 (C-*4*, C-*5*, C-*6*, C-*7*, C-*8*, C-*9*, C-*10*)

FT-IR: (cm^{-1}) 3330, 2918, 1615, 1530, 1447, 1406, 1367, 1249, 1023

Contact Angle: Static: 47°; Advancing: 53°; Receding: 32°



Synthesis of **poly(HMDI-sL)**:

Poly(HMDI-L) (0.80 g, 1.0 equiv.) and SO_3/pyridine complex (4.91 g, 42.0 equiv.) was added into a flame-dried flask. After evacuating and refilling with nitrogen for three times, 15 mL anhydrous pyridine was injected. It was heated at 90 °C for 24 h. After the solvent was removed, saturated $NaHCO_3$ solution was added to adjust the pH to 8.0 and the

polymer was isolated through dialysis and lyophilization to give white foam product. Yield = 1.71 g, 92 %

^{1}H NMR (D_2O, 400 MHz): δ (ppm) 5.19 (s, 2 H, *d*-H), 4.96–4.88 (m, 4 H, *c'*-H, *b*-H), 4.62–3.55 (m, 36 H, *a*-H, *c*-H, *e*-H, *f*-H, *g*-H, *h*-H, *a'*-H, *b'*-H, *d'*-H, *e'*-H, *f'*-H, *1*-H, *3*-H, *11*-H), 1.97–1.02 (m, 20 H, *4*-H, *5*-H, *6*-H, *7*-H, *8*-H, *9*-H, *10*-H)

^{13}C NMR (D_2O, 100 MHz): δ (ppm) 159.08 (C-*2*, C-*12*), 101.03 (C-*a*), 100.71, 99.91 (C-*a'*), 77.66 (C-*b*, C-*d*), 77.25 (C-*c'*), 75.82 (C-*c*), 75.54 (C-*b'*), 75.21 (C-*e*, C-*e'*), 73.31 (C-*d'*), 71.89 (C-*g*), 68.14 (C-*f*), 66.55 (C-*f'*), 50.77, 47.27, 46.76, 46.12 (C-*h*, C-*1*, C-*3*, C-*11*), 33.02, 32.16, 29.92, 29.58, 29.09, 28.19 (C-*4*, C-*5*, C-*6*, C-*7*, C-*8*, C-*9*, C-*10*)

FT-IR: (cm^{-1}) 3486, 2925, 1630, 1537, 1225, 1053, 1006

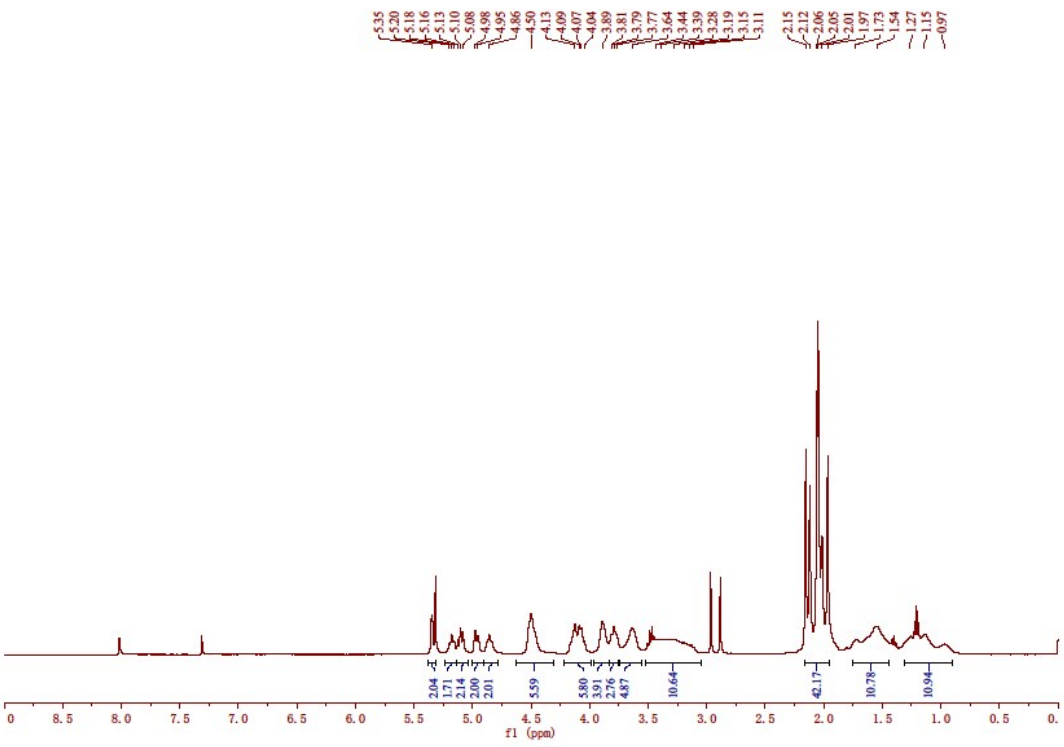


Figure S21. ^{1}H NMR spectrum for **poly(HMDI-pL)**

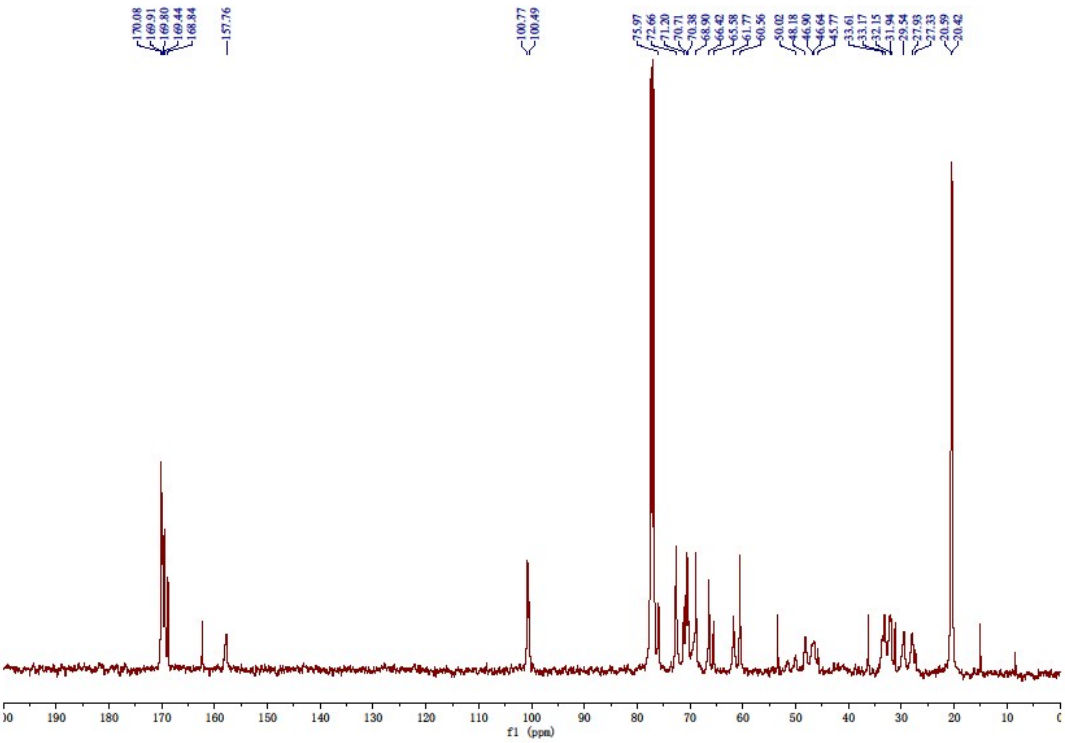


Figure S22. ^{13}C NMR spectrum for **poly(HMDI-pL)**

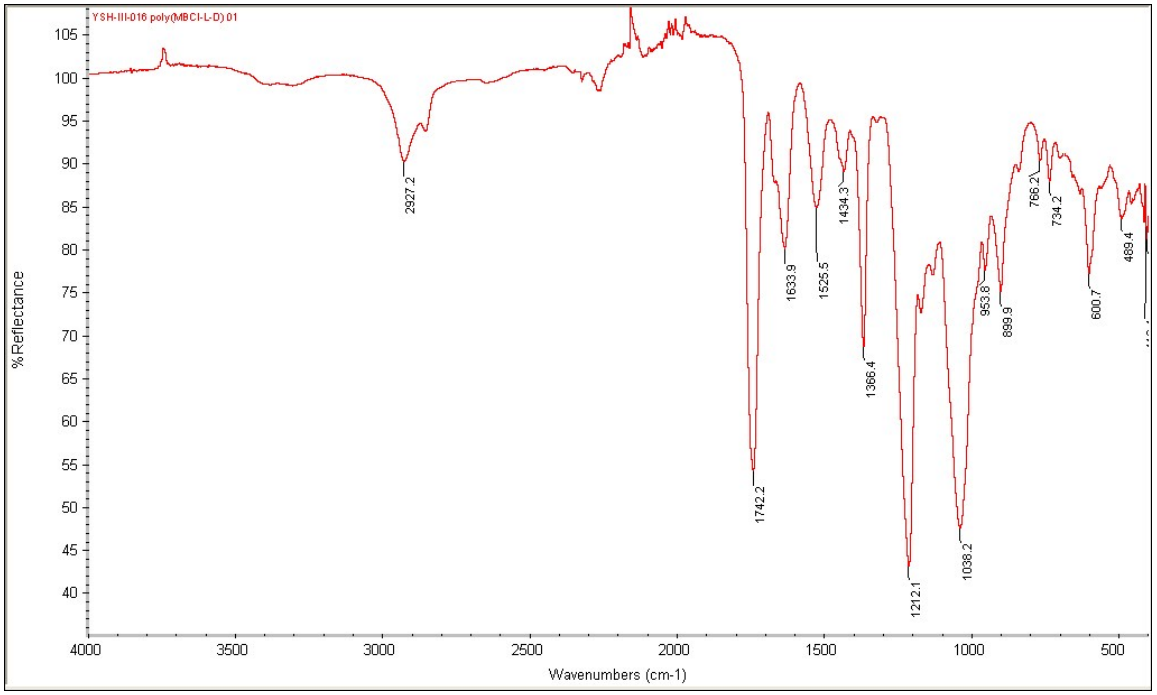


Figure S23. FT-IR spectrum for **poly(HMDI-pL)**

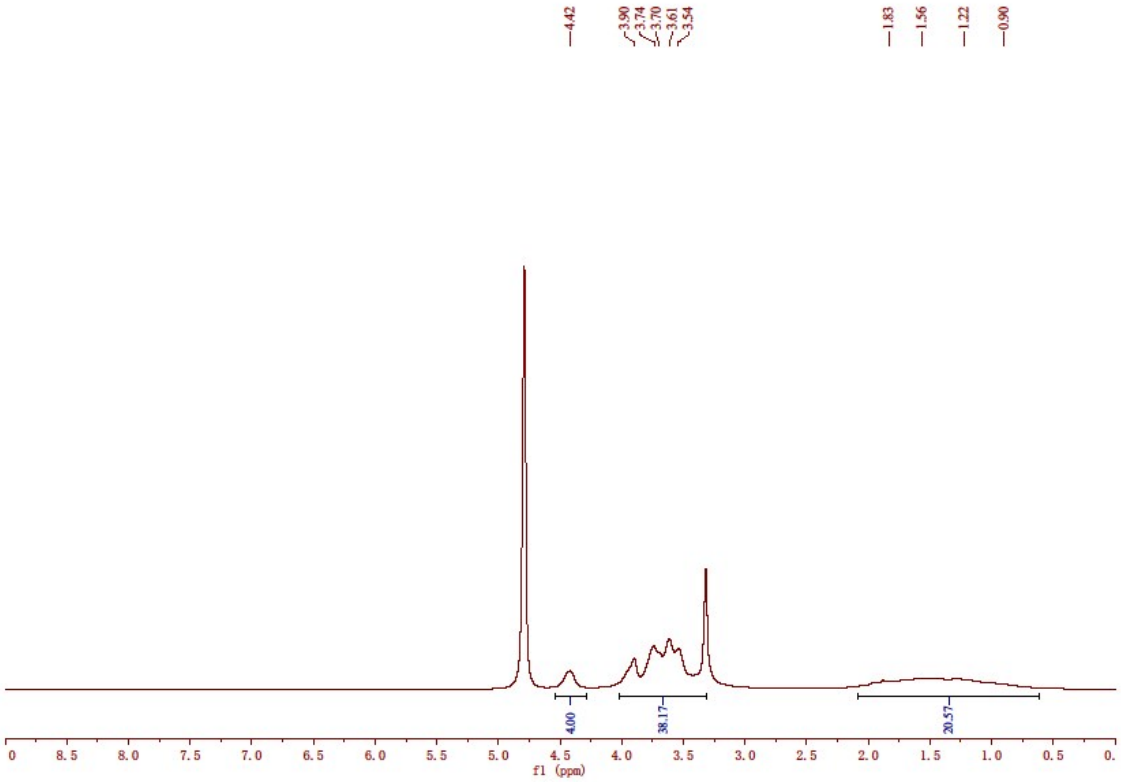


Figure S24. ^{1}H NMR spectrum for **poly(HMDI-L)**

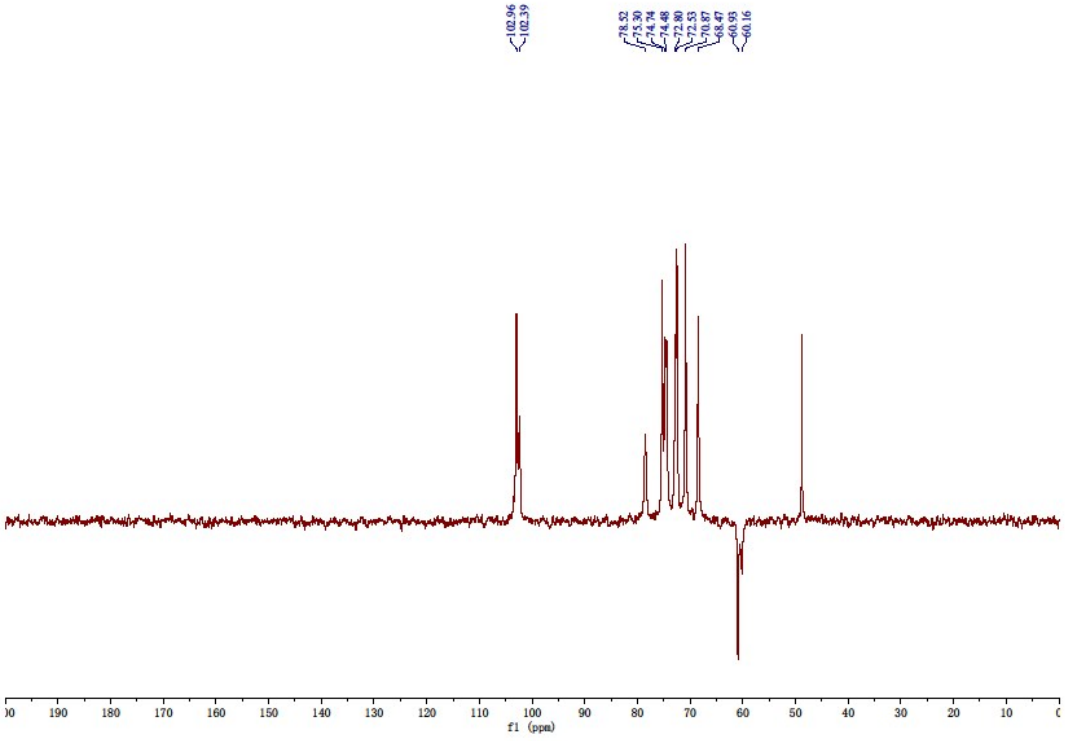


Figure S25. DEPT-135 spectrum for **poly(HMDI-L)**

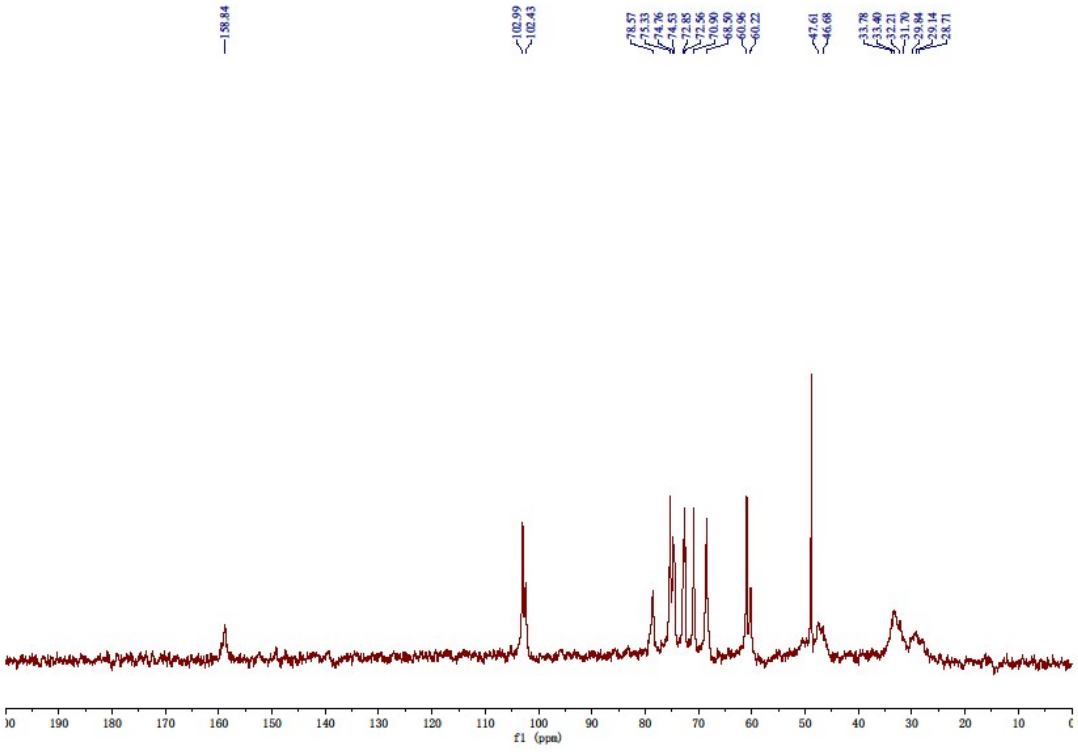


Figure S26. ^{13}C NMR spectrum for **poly(HMDI-L)**

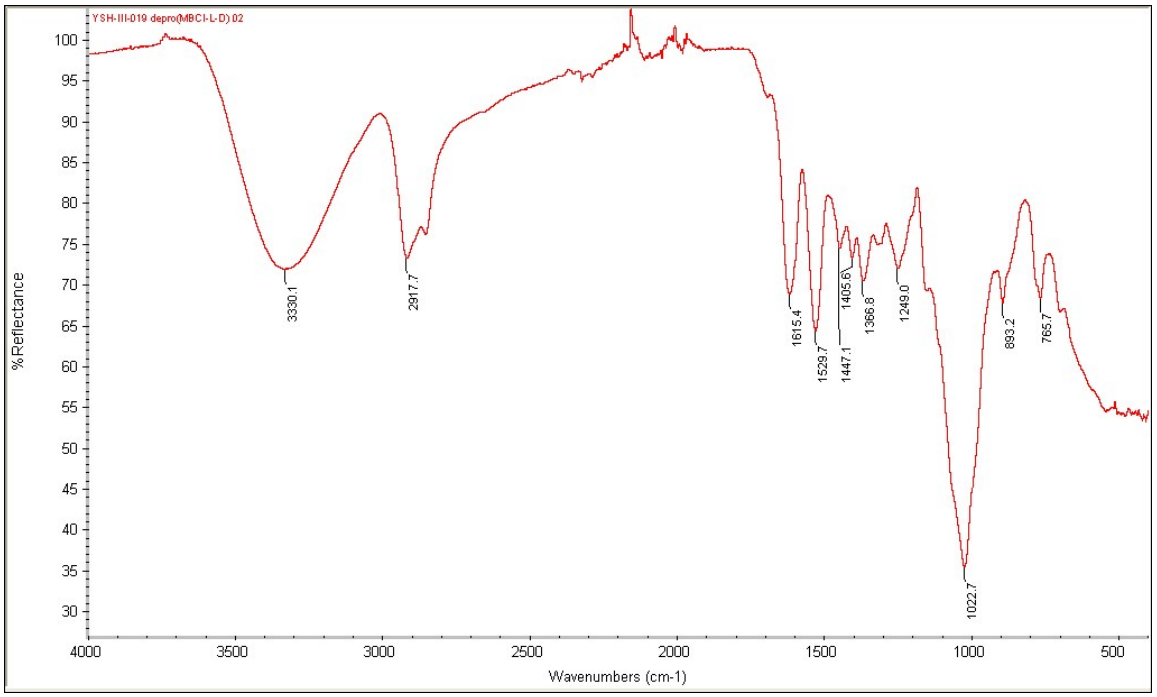


Figure S27. FT-IR spectrum for **poly(HMDI-L)**

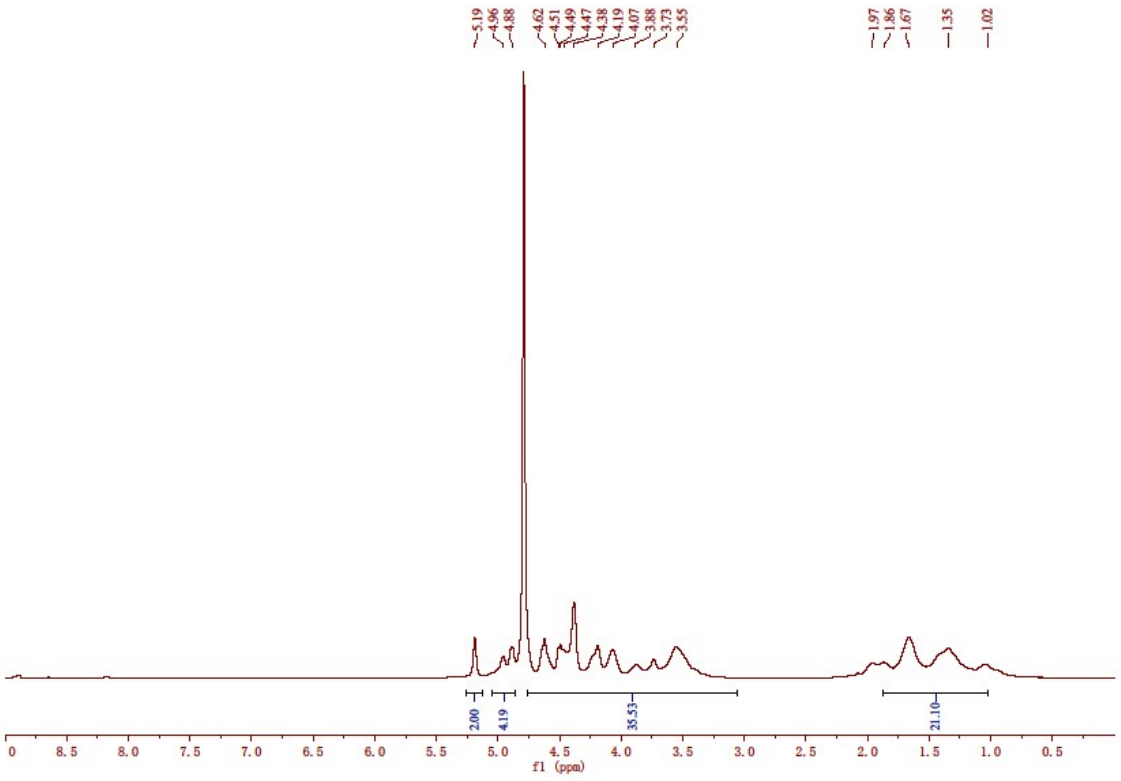


Figure S28. ^{1}H NMR spectrum for **poly(HMDI-sL)**

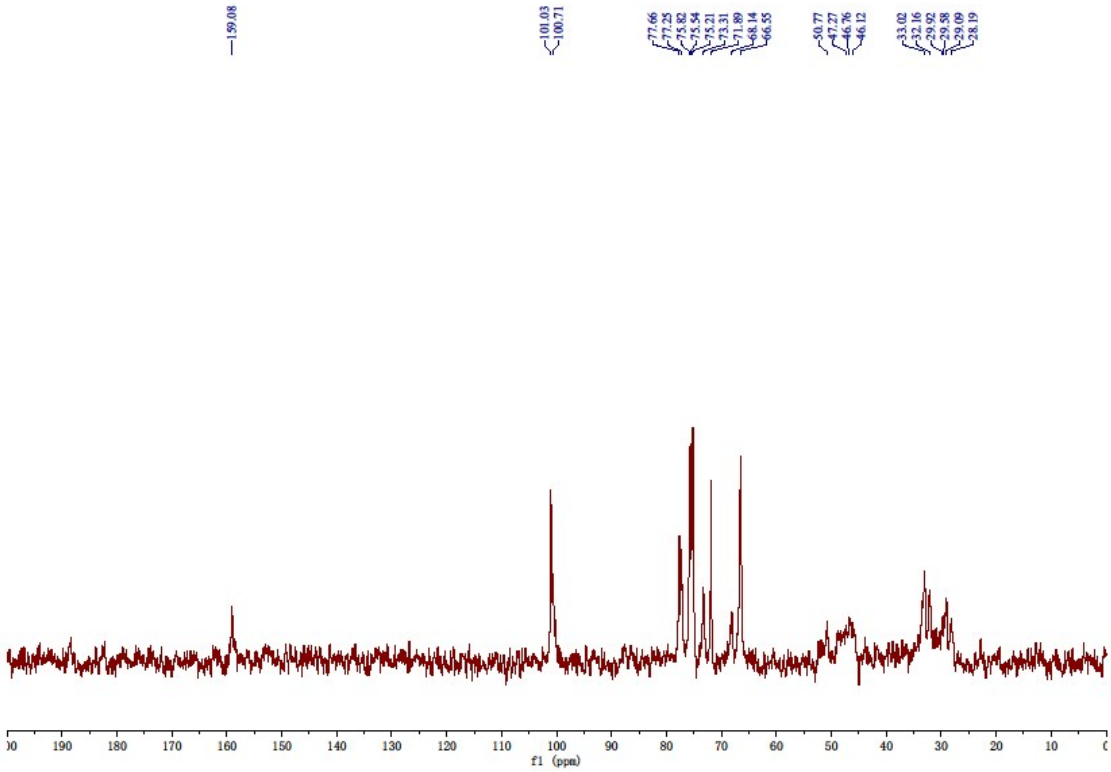


Figure S29. ^{13}C NMR spectrum for **poly(HMDI-sL)**

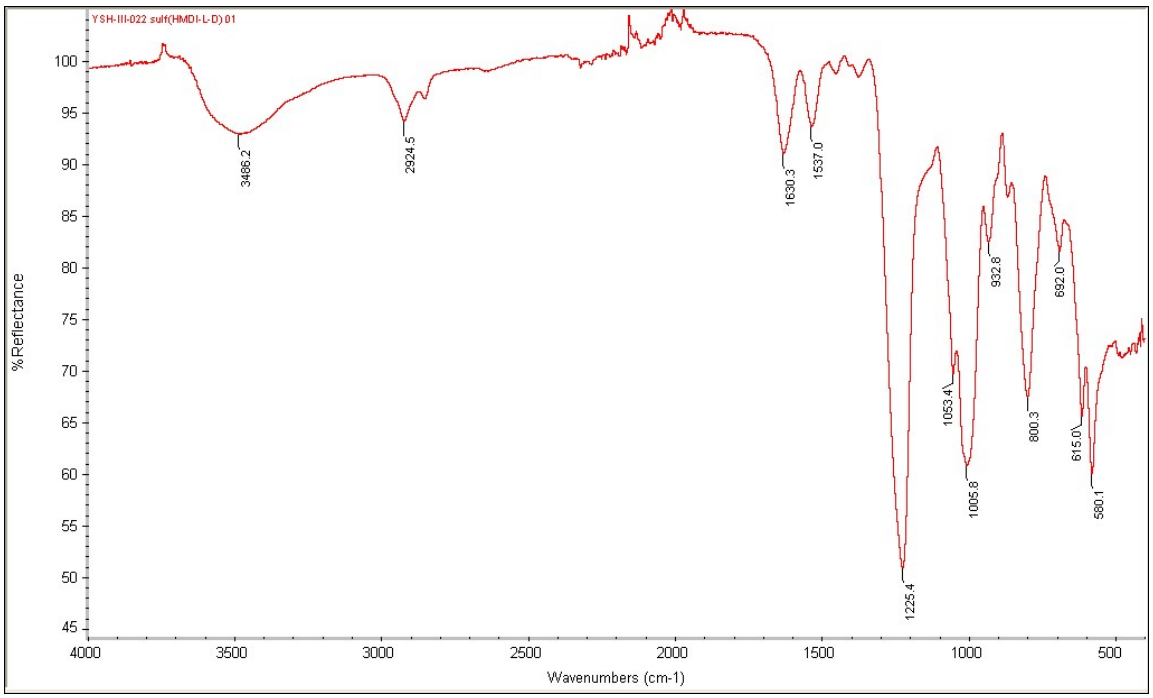
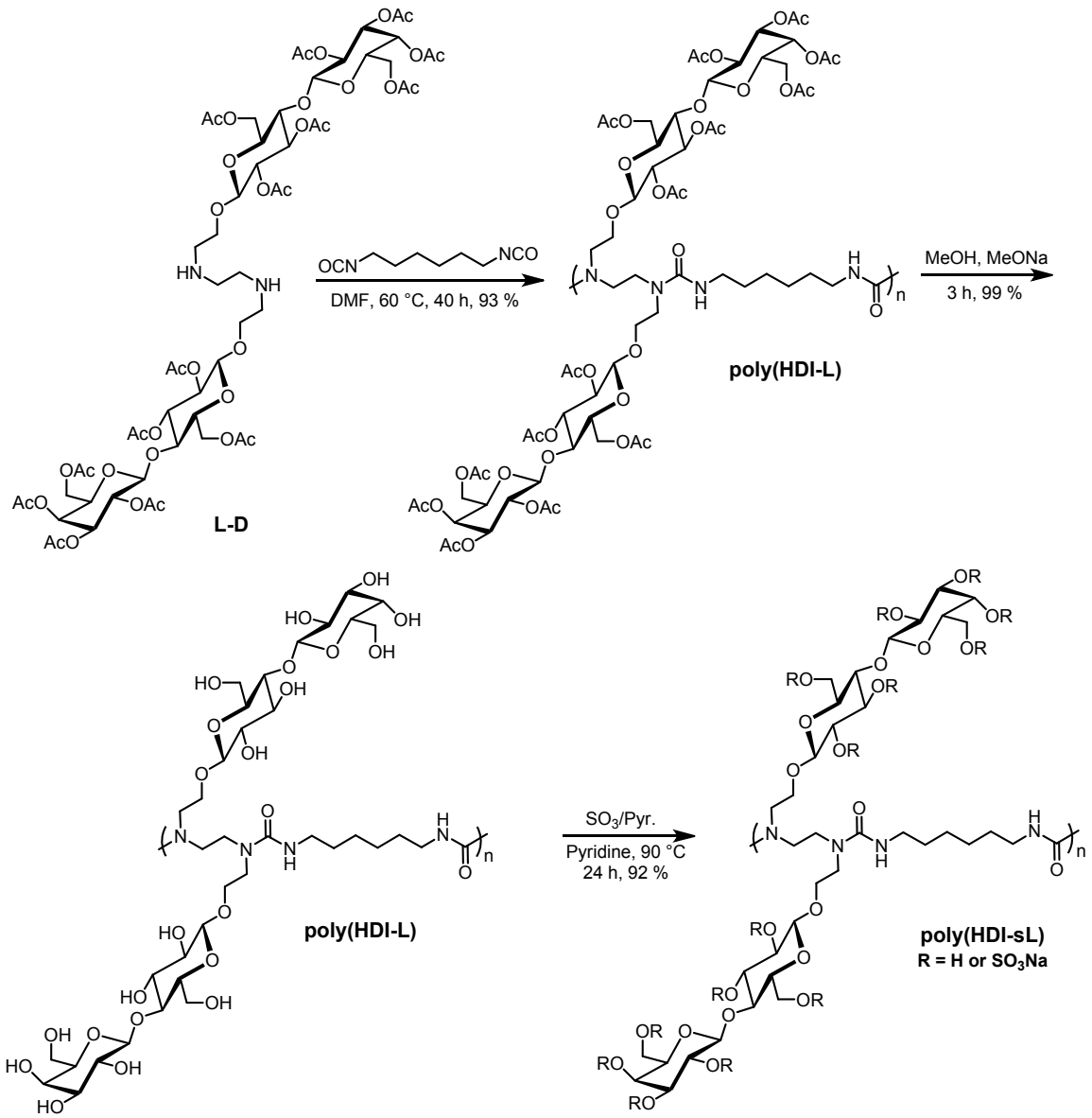


Figure S30. FT-IR spectrum for **poly(HMDI-sL)**

Part S4: Synthesis and spectra of poly(HDI-sL) from L-D and HDI



The detailed synthesis procedures, as well as the spectra, can be found from our previous reported publication.[1]

Part S5: Differential scanning calorimetry of the synthesized polymers

A NETZSCH DSC 200 F3 Maia® was utilized to measure the thermal phase transitions of the deprotected and sulfated polymers by subjecting to two heating and cooling cycles with a cooling rate of 5 °C/min and a heating rate of 10 °C/min under N_2 atmosphere. The polymers were first cooled to -20 °C and heated to 100 °C. Then, it was cooled back to 25 °C and heated to 200 °C. The second heating/cooling cycle was used to identify the glass transition temperature (T_g), which was taken as the midpoint of the stepwise change in the heat flow signal.

The glass transition temperatures (T_g) of the deprotected and sulfated polymers were measured using differential scanning calorimetry (DSC). The data from the second heating cycle were used to obtain glass transition temperatures to avoid artifacts due to initial thermal treatment.[2] The measured glass transition temperatures are summarized in Table S1. As expected, the deprotected polymers containing HDI has the lowest T_g with a value of 68 °C for poly(HDI-L). The lower T_g values can be attributed to the flexible molecular structure of HDI segment.[3, 4] The more rigid HMDI, TDI and IPDI containing polymers have higher T_g values at 84, 87, and 93 °C, for poly(HMDI-pL), poly(TDI-pL), and poly(IPDI-pL), respectively. Interestingly, only HDI-containing poly(HDI-sL) was found with an observable T_g value of 97 °C; values far above those used in the blood compatibility assays. No T_g values were recorded for the other sulfated polymers before the onset of decomposition.

Table S1. Glass transition temperature (T_g) of the deprotected and sulfated polymers. The absence of a value (-) reflects that no T_g was observed in the measurement.

Polymer	T_g (°C)	Polymer	T_g (°C)
poly(TDI-L)	87	poly(TDI-sL)	-
poly(IPDI-L)	93	poly(IPDI-sL)	-

poly(HMDI-L)	84	poly(HMDI-sL)	-
poly(HDI-L)	68	poly(HDI-sL)	97

Part S6: Contact angle of the synthesized polymers

Contact angles were determined with a Ramé-hart contact angle goniometer (Model 200-F1). DCM or methanol solutions of the synthesized polymers were cast onto a polished Si wafer and dried overnight to produce solvent-cast thin films. Ten microliters of distilled water was placed onto the polymer surface using a micropipette. Contact angles were calculated with a tangent method using the software supplied with the goniometer. Each sample was measured at least three times with different drops of water and the averaged data are reported. The advancing and receding contact angles were recorded by tilting the base to 35°.

Table S2. Contact angle measurements of the synthesized polymers.

Polymer	$\theta^{o}_{(static)}$	$\theta^{o}_{(Receding)}$	$\theta^{o}_{(Advancing)}$
poly(TDI-pL)	47	35	53
poly(TDI-L)	42	24	51
poly(IPDI-pL)	57	43	64
poly(IPDI-L)	41	25	51
poly(HMDI-pL)	56	45	60
poly(HMDI-L)	47	32	53
poly(HDI-pL)	43	31	49
poly(HDI-L)	30	20	45

Part S7: Elemental analysis of the sulfated polymers

Table S3. Elemental analysis of the sulfated polymers with different diisocyanates.

Polymer	Carbon	Hydrogen	Nitrogen	Sodium	Sulfur	DS[a]
poly(TDI-sL)	15.80%	2.89%	1.59%	11.57%	17.13%	7.92
poly(IPDI-sL)	18.97%	3.54%	2.22%	10.85%	14.51%	6.02
poly(HMDI-sL)	21.86%	3.71%	2.35%	10.46%	15.44%	5.97
poly(HDI-sL)	18.08%	3.44%	2.36%	10.27%	15.42%	6.88

[a]: DS = average degree of sulfation per disaccharide unit.

Table S4. Sulfation of poly(HMDI-L) with different equivalents of the sulfation reagent and the measured degree of sulfation by elemental analysis. (The numbers after the polymer name, i.e. 0.57, 1.60, 3.20, 4.44 and 5.97, represent the degree of sulfation of these sulfated polymers).

Polymer	SO_3·pyr.[a]	Carbon	Hydrogen	Nitrogen	Sulfur	DS[c]
poly(HMDI-sL)-0.57	2.0	43.82%	6.80%	5.04%	2.95%	0.57
poly(HMDI-sL)-1.60	6.0	28.75%	4.77%	3.22%	5.44%	1.60
poly(HMDI-sL)-3.20	8.0	22.99%	4.01%	2.59%	8.72%	3.20
poly(HMDI-sL)-4.44	10.0	21.00%	3.69%	2.34%	11.04%	4.44
poly(HMDI-sL)-5.97	3.0[b]	21.86%	3.71%	2.35%	15.44%	5.97

[a]: equivalents of sulfation reagent per lactose unit in DMF solution used in the reaction for 24 hours at room temperature;

[b]: equivalents of sulfation reagent per hydroxyl group in pyridine solution used in the reaction for 24 hours at 90 °C;

[c]: average degree of sulfation per lactose unit.

Part S8: Original data of activated Partial Thromboplastin Time of the sulfated glycopolymers

Table S5. aPTT (s) results of glycopolymers from L-D and different diisocyanates

Concentration	**Poly(HDI-sL)**		***Average***	**Poly(HMDI-sL)**		***Average***
0.5 mg/mL	>300	>300	*>300*	>300	>300	*>300*
50 μg/mL	153.0	136.0	*144.5*	>300	>300	*>300*
5.0 μg/mL	40.0	39.0	*39.5*	49.0	48.0	*48.5*
0.5 μg/mL	27.0	27.0	*27.0*	31.0	31.0	*31.0*
Concentration	**Poly(TDI-sL)**		***Average***	**Poly(IPDI-sL)**		***Average***
0.5 mg/mL	>300	>300	*>300*	>300	>300	*>300*
50 μg/mL	104.0	104.0	*104.0*	145.0	195.0	*170.0*
5.0 μg/mL	46.0	46.0	*46.0*	48.0	48.0	*48.0*
0.5 μg/mL	33.0	33.0	*33.0*	31.0	31.0	*31.0*

Table S6. aPTT (s) results of poly(HMDI-sL) with different degrees of sulfate

Concentration	**Poly(HMDI-sL)-0.57**		***Average***	**Poly(HMDI-sL)-1.60**		***Average***
0.5 mg/mL	34.0	33.0	*33.5*	>300	>300	*>300*
50 μg/mL	28.0	28.0	*28.0*	42.0	42.0	*42.0*
5.0 μg/mL	30.0	29.0	*29.5*	28.0	28.0	*28.0*
0.5 μg/mL	29.0	29.0	*29.0*	29.0	29.0	*29.0*
Concentration	**Poly(HMDI-sL)-3.20**		***Average***	**Poly(HMDI-sL)-4.44**		***Average***
0.5 mg/mL	>300	>300	*>300*	>300	>300	*>300*
50 μg/mL	77.0	78.0	*77.5*	152.0	139.0	*145.5*
5.0 μg/mL	35.0	35.0	*35.0*	41.0	41.0	*41.0*
0.5 μg/mL	29.0	29.0	*29.0*	30.0	30.0	*30.0*

Table S7. aPTT (s) results of deprotected glycopolymers from L-D with different diisocyanates and HEPES only

Polymer	**Concentration (6.67 mg/mL)**		***Average***
poly(HMDI-L)	32.0	30.0	*31.0*
poly(TDI-L)	28.0	28.0	*28.0*
poly(IPDI-L)	29.0	29.0	*29.0*
HEPES only	28.4	28.2	*28.2*

Part S9: Original data of Prothrombin Time of the sulfated glycopolymers

Table S8. PT (s) results of glycopolymers from L-D and different diisocyanates

Concentration	**Poly(HDI-sL)**		***Average***	**Poly(HMDI-sL)**		***Average***
0.5 mg/mL	> 60	> 60	*> 60*	> 60	> 60	*> 60*
50 μg/mL	> 60	> 60	*> 60*	> 60	> 60	*> 60*
5.0 μg/mL	13.0	13.0	*13.0*	14.0	14.0	*14.0*
0.5 μg/mL	15.0	14.0	*14.5*	14.0	13.5	*13.8*
Concentration	**Poly(TDI-sL)**		***Average***	**Poly(IPDI-sL)**		***Average***
0.5 mg/mL	> 60	> 60	*> 60*	> 60	> 60	*> 60*
50 μg/mL	14.0	14.0	*14.0*	> 60	> 60	*> 60*
5.0 μg/mL	14.5	14.0	*14.3*	14.0	14.0	*14.0*
0.5 μg/mL	14.0	14.0	*14.0*	14.0	15.0	*14.5*
Concentration	**Poly(HDI-L)**		***Average***	**Poly(HMDI-L)**		***Average***
0.5 mg/mL	15.5	14.0	*15.0*	14.0	14.0	*14.0*
Concentration	**Poly(TDI-L)**		***Average***	**Poly(IPDI-L)**		***Average***
0.5 mg/mL	14.0	14.0	*14.0*	14.0	15.0	*14.5*
Concentration	**HEPES only**		***Average***	**Heparin (0.7 U/mL)**		***Average***
N.A.	14.5	14.5	*14.5*	> 60	> 60	*> 60*

Table S9. PT (s) results of poly(HMDI-sL) with different degrees of sulfate

Concentration	**Poly(HMDI-sL)-0.57**		***Average***	**Poly(HMDI-sL)-1.60**		***Average***
0.5 mg/mL	15.0	15.0	*15.0*	20.0	20.5	*20.3*
50 μg/mL	14.0	15.0	*14.5*	16.0	15.0	*15.5*
5.0 μg/mL	15.0	15.0	*15.0*	14.0	13.0	*13.5*
0.5 μg/mL	14.5	15.0	*14.8*	14.5	15.0	*14.8*
Concentration	**Poly(HMDI-sL)-3.20**		***Average***	**Poly(HMDI-sL)-4.44**		***Average***
0.5 mg/mL	>60	>60	>60	>60	>60	>60
50 μg/mL	20.0	17.5	*18.8*	18.0	17.0	*17.5*
5.0 μg/mL	15.0	15.0	*15.0*	14.0	15.0	*14.5*
0.5 μg/mL	14.0	13.5	*13.8*	14.0	14.0	*14.0*

Part S9: Original data of Thrombin Time of the sulfated glycopolymers

Table S10. PT (s) results of glycopolymers from L-D and different diisocyanates

Concentration	**Poly(HDI-sL)**		***Average***	**Poly(HMDI-sL)**		***Average***
0.5 mg/mL	> 75	> 75	*> 75*	> 75	> 75	*> 75*
50 μg/mL	> 75	> 75	*> 75*	> 75	> 75	*> 75*
5.0 μg/mL	> 75	> 75	*> 75*	> 75	> 75	*> 75*
0.5 μg/mL	24.5	25.0	*24.8*	23.0	29.0	*26.0*
Concentration	**Poly(TDI-sL)**		***Average***	**Poly(IPDI-sL)**		***Average***
0.5 mg/mL	> 75	> 75	*> 75*	> 75	> 75	*> 75*
50 μg/mL	> 75	> 75	*> 75*	> 75	> 75	*> 75*
5.0 μg/mL	> 75	> 75	*> 75*	> 75	> 75	*> 75*
0.5 μg/mL	24.0	24.5	*24.3*	23.5	24.0	*23.8*
Concentration	**Poly(HDI-L)**		***Average***	**Poly(HMDI-L)**		***Average***
0.5 mg/mL	23.0	24.5	*23.8*	24.0	25.0	*24.5*
Concentration	**Poly(TDI-L)**		***Average***	**Poly(IPDI-L)**		***Average***
0.5 mg/mL	24.0	28.0	*26.0*	26.0	23.0	*24.5*
Concentration	**HEPES only**		***Average***	**Heparin (0.1 U/mL)**		***Average***
N.A.	21.0	22.5	*21.8*	> 75	> 75	*> 75*

Table S11. PT (s) results of poly(HMDI-sL) with different degrees of sulfate

Concentration	**Poly(HMDI-sL)-0.57**		***Average***	**Poly(HMDI-sL)-1.60**		***Average***
0.5 mg/mL	36.5	38.0	*37.3*	> 60	> 60	*> 60*
50 μg/mL	25.0	24.0	*24.5*	32.0	31.5	*31.8*
5.0 μg/mL	25.0	24.0	*24.5*	22.0	22.0	*22.0*
0.5 μg/mL	22.5	21.5	*22.0*	20.0	19.5	*19.8*
Concentration	**Poly(HMDI-sL)-3.20**		***Average***	**Poly(HMDI-sL)-4.44**		***Average***
0.5 mg/mL	> 60	> 60	*> 60*	> 60	> 60	*> 60*
50 μg/mL	> 60	> 60	*> 60*	> 60	> 60	*> 60*
5.0 μg/mL	25.0	24.0	*24.5*	25.0	26.5	*25.8*
0.5 μg/mL	24.0	27.5	*25.8*	18.5	24.0	*21.3*

Part S11: IC_{50} values of the sulfated polymers

Table S12: IC_{50} values of the sulfated polymers

Polymer	IC_{50} (µg/mL), with antithrombin	IC_{50} (µg/mL), without antithrombin
Heparin	0.0011 ± 0.0004	>100.0
Poly(HMDI-sL)	0.059 ± 0.002	1.09 ± 0.02
Poly(IPDI-sL)	0.0221 ± 0.0012	4.56 ± 1.29
Poly(HDI-sL)	>0.1000	0.30 ± 0.02
Poly(TDI-sL)	>0.1000	>100.0

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