

Supplementary Materials for

## **One-Pot Synthesis of Alternating Peptides Exploiting a New Polymerization Technique based on Ugi's 4CC Reaction**

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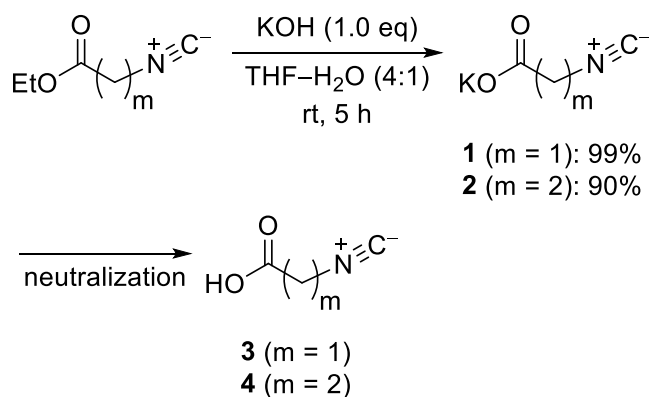
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## General methods:

**Materials.** Ethylisocynoacetate (Sigma-Aldrich), ethylisocyanopropionate (Sigma-Aldrich), trifluoromethanesulfonic acid (TfOH, Kanto chemicals), *N*-(4-methoxybenzylidene)aniline (**9**, TCI), and 6,7-dimethoxy-3,4-dihydroisoquinoline (**11**, Ark Pharm, Inc.) were used as obtained. Molecular sieves 3 Å (MS 3A) as a dehydrator was activated by careful heating by a heat gun under vacuum. The other chemicals and solvents were used without purification.

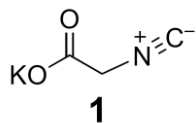
**Measurements.**  $^1\text{H}$ NMR (400 MHz) and  $^{13}\text{C}$  NMR (100 MHz) spectra were recorded on JEOL JNM-ESC400 and Bruker AVANCE II 400 spectrometers using  $\text{CDCl}_3$ ,  $\text{CD}_3\text{OD}$ , and  $\text{DMSO}-d_6$  as the solvent, calibrated using residual undeuterated solvent and tetramethylsilane as the internal standard. DOSY spectra were recorded on a Bruker AVANCE II 400 spectrometer. All experiments were run without spinning to avoid convection. The standard Bruker pulse program, ledbpgp2s, employing simulated echo and longitudinal eddy delay with bipolar gradients and two spoil gradients, was utilized. The obtained DOSY spectra were processed by Topspin 3.2 software. Diffusion dimension was generated using the inversion of Laplace transform driven by the CONTIN method.<sup>1</sup> Diffusion coefficients of a chosen narrow chemical shift in the spectra of the polymers were extracted from T1/T2 analysis module of Topspin 3.2. FT-IR spectra were measured using a Thermo Fischer Scientific Nexus 870 spectrometer. MALDI-TOF MS spectra for small molecules were recorded on a Shimadzu AXIMA-CFR plus mass spectrometer (matrix:  $\text{CHC}\alpha$ ). Hydrodynamic diameters of the polymers were estimated by dynamic light scattering (DLS) measurements (Malvern, Zetasizer nanoZSP) using 1.0 mg/mL polymer solutions in THF at 25 °C.

## Synthesis of ambident molecules<sup>2</sup>



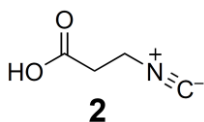
**Scheme S1.** Preparation of ambident molecules.

### Synthesis of **1**<sup>2</sup>



To a solution of ethylisocynoacetate (4.0 g, 35 mmol) in THF (20 mL) was added a solution of KOH (85%, 2.0 g, 30 mmol) in H<sub>2</sub>O (5.0 mL) at room temperature. The mixture was stirred for 5 h and concentrated in vacuo to give a crude. The crude was pulverized in a mortar, washed with Et<sub>2</sub>O (50 mL), and dried in vacuo to give **1** (4.31 g, 99%) as pale yellow solids: mp 160–162 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K) δ 4.03 (s, 2H, CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>, 298 K) δ 165.0 (C=O), 160.7 (N≡C), 46.2 (t, <sup>1</sup>J<sub>CN</sub> = 6.6 Hz, CH<sub>2</sub>) ppm; IR (KBr) ν 3437, 2173, 1626, 1387, 1304, 699 cm<sup>-1</sup>; MALDI-TOF MS (matrix CHCα) calc'd for C<sub>3</sub>H<sub>2</sub>KNO<sub>2</sub> [M<sup>+</sup>] 122.97; found 122.41.

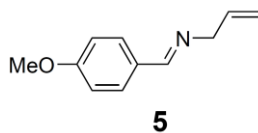
### Synthesis of **2**



To a solution of ethylisocyanopropionate (2.5 g, 20 mmol) in THF (13 mL) was added a solution of KOH (85%, 1.3 g, 20 mmol) in H<sub>2</sub>O (3.0 mL) at room temperature. The mixture was stirred for 14.5 h and concentrated in vacuo to give a crude. The crude was pulverized in a mortar, washed with Et<sub>2</sub>O and CHCl<sub>3</sub>, and dried in vacuo to give **2** (2.42 g, 90%) as brown solids. The neutralization of **2** gave **4**: mp 166–168 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K) δ 3.64 (brd, 2H, CH<sub>2</sub>-N), 2.50 (brd, 2H, CO-CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>, 298 K) δ 171.3 (C=O), 154.4 (N≡C), 38.1 (C-N), 29.0 (CO-C) ppm; IR (KBr) ν 3372, 2167, 1632, 1574, 1406, 1351, 1315, 644 cm<sup>-1</sup>; MALDI-TOF MS (matrix CHCα) calc'd for C<sub>4</sub>H<sub>4</sub>KNO<sub>2</sub> [M<sup>+</sup>] 136.99; found 136.47.

### Synthesis of imines

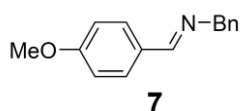
#### Synthesis of **5**



Allylamine (616 μL, 8.23 mmol) was added to a solution of anisaldehyde (1.00 mL, 8.15 mmol) in CHCl<sub>3</sub> (8.2 mL) at room temperature. After stirring for 2 h, the mixture was concentrated in vacuo. The crude was diluted with CHCl<sub>3</sub> (4.1 mL) again and the additional allylamine (616 μL, 8.23 mmol) was added to the solution. After stirring for 1 d, the mixture was concentrated in vacuo to give **5** (1.32 g, 92%) as a yellow oil: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K) δ 8.21 (brd, 1H, HC=N), 7.68 (d, *J* = 8.8 Hz, 2H, Ar), 6.91 (d, *J* = 8.8 Hz, 2H, Ar), 6.05 (ddt, *J* = 16.8, 10.0, 6.0 Hz, 1H, CH=CH<sub>2</sub>), 5.22 (dq, *J*

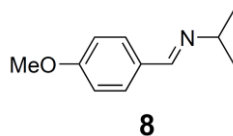
= 16.8, 1.6 Hz, 1H, CH=CH<sub>2</sub>), 5.13 (dq, *J* = 10.0, 1.6 Hz, 1H, CH=CH<sub>2</sub>), 4.21 (dq, *J* = 6.0, 1.6 Hz, 2H, CH<sub>2</sub>), 3.83 (s, 3H, OCH<sub>3</sub>) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K) δ 161.7 (Ar; C-OCH<sub>3</sub>), 161.4 (HC=N), 136.3 (CH=CH<sub>2</sub>), 129.8 (Ar), 129.2 (Ar), 116.0 (Ar), 114.0 (CH=CH<sub>2</sub>), 63.6 (CH<sub>2</sub>), 55.4 (OCH<sub>3</sub>) ppm; IR (NaCl) ν 2837, 1646, 1606, 1511, 1252, 1167, 1031, 832 cm<sup>-1</sup>; MALDI-TOF MS (matrix CHCα) calc'd for C<sub>11</sub>H<sub>14</sub>NO<sup>+</sup> [M+H<sup>+</sup>] 176.11; found 176.05.

#### Synthesis of **7**



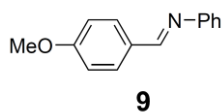
Benzylamine (899 μL, 8.23 mmol) was added to a solution of anisaldehyde (1.00 mL, 8.23 mmol) in CHCl<sub>3</sub> (8.0 mL) at room temperature. The mixture was stirred for 1 h and concentrated in vacuo to give **7** (1.79 g, 96.8%) as a yellow oil: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K) δ 8.33 (s, 1H, HC=N), 7.73 (d, *J* = 8.8 Hz, 2H, Ar), 7.34–7.33 (m, 5H, Ar), 6.93 (d, *J* = 8.8 Hz, 2H, Ar), 4.79 (s, 2H, CH<sub>2</sub>), 3.84 (s, 3H, OCH<sub>3</sub>) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K) δ 161.5 (Ar; C-OCH<sub>3</sub>), 161.3 (HC=N), 129.8 (Ar), 129.7 (Ar), 128.5 (Ar), 128.0 (Ar), 126.9 (Ar), 114.0 (Ar), 65.0 (CH<sub>2</sub>), 55.4 (OCH<sub>3</sub>) ppm; IR (NaCl) ν 3028, 2837, 1647, 1606, 1578, 1512, 1453, 1441, 1378, 1343, 1307, 1252, 1166, 1108, 1030, 834 cm<sup>-1</sup>; MALDI-TOF MS (matrix CHCα) calc'd for C<sub>15</sub>H<sub>16</sub>NO<sup>+</sup> [M+H<sup>+</sup>] 226.12; found 226.73.

#### Synthesis of **8**



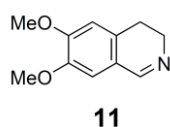
*i*-Propylamine (1.06 mL, 12.3 mmol) was added to a solution of anisaldehyde (1.00 mL, 8.23 mmol) in CHCl<sub>3</sub> (8.0 mL) at room temperature. The mixture was stirred for 1 d and concentrated in vacuo to give **8** (1.49 g, quant.) as a yellow oil: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K) δ 8.23 (s, 1H, HC=N), 7.66 (d, *J* = 8.8 Hz, 2H, Ar), 6.91 (d, *J* = 8.8 Hz, 2H, Ar), 3.83 (s, 3H, OCH<sub>3</sub>), 3.50 (sext, *J* = 6.4 Hz, 1H, CH), 1.25 (d, *J* = 6.4 Hz, 6H, CH<sub>3</sub>) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K) δ 161.4 (Ar; C-OCH<sub>3</sub>), 157.6 (HC=N), 129.6 (Ar), 129.5 (Ar), 113.9 (Ar), 61.5 (CH), 55.3 (OCH<sub>3</sub>), 24.2 (CH<sub>3</sub>) ppm; IR (NaCl) ν 2997, 2837, 1640, 1608, 1579, 1513, 1465, 1303, 1250, 1163, 1143, 1034, 832 cm<sup>-1</sup>; MALDI-TOF MS (matrix CHCα) calc'd for C<sub>11</sub>H<sub>16</sub>NO<sup>+</sup> [M+H<sup>+</sup>] 178.12; found 178.14.

**9**



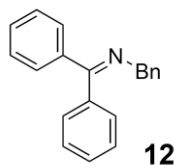
Commercially available **9** was directly used without purification; IR (NaCl)  $\nu$  3048, 2963, 2937, 2909, 2881, 2838, 1623, 1604, 1587, 1576, 1509, 1421, 1302, 1250, 1182, 1172, 1108, 1074, 1031, 979, 967, 881, 837, 760, 721, 693  $\text{cm}^{-1}$ .

**11**



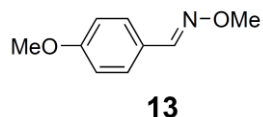
Commercially available **11** was directly used without purification; IR (NaCl)  $\nu$  2940, 2837, 1630, 1605, 1574, 1518, 1465, 1352, 1326, 1281, 1240, 1224, 1192, 1121, 1016, 819, 778  $\text{cm}^{-1}$ .

#### Synthesis of **12**



Benzylamine (900  $\mu\text{L}$ , 8.23 mmol) was added to a solution of benzophenone (1.37 mL, 8.23 mmol) in  $\text{CHCl}_3$  (8.0 mL) at room temperature. The mixture was stirred for 12 d and concentrated in vacuo to give **12** (2.37 g, quant.) as colorless needles: mp 54–56  $^{\circ}\text{C}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  7.69–7.20 (m, 15H, Ar), 4.61 (s, 2H,  $\text{CH}_2$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  168.8 (C=N), 140.6 (Ar), 140.0 (Ar), 136.7 (Ar), 130.0 (Ar), 128.6 (Ar), 128.53 (Ar), 128.49 (Ar), 128.3 (Ar), 128.0 (Ar), 127.8 (Ar), 127.6 (Ar), 126.5 (Ar), 57.4 ( $\text{CH}_2$ ) ppm; IR (NaCl)  $\nu$  3060, 3027, 2895, 1957, 1660, 1623, 1577, 1493, 1446, 1349, 1287, 1179, 1154, 1074, 1028, 940, 696, 645  $\text{cm}^{-1}$ ; MALDI-TOF MS (matrix  $\text{CHC}\alpha$ ) calc'd for  $\text{C}_{20}\text{H}_{18}\text{N}^+$   $[\text{M}+\text{H}^+]$  272.14; found 272.69.

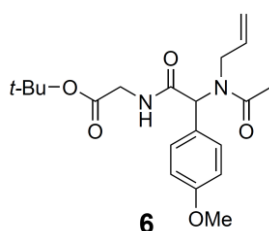
#### Synthesis of **13**



Sodium hydroxide (2.26 g, 56.5 mmol) was dissolved in MeOH (40 mL). To the solution was added anisaldehyde (5.72 mL, 47.1 mmol) and a solution of  $\text{MeONH}_2\cdot\text{HCl}$  (4.72 g, 56.5 mmol) in  $\text{H}_2\text{O}$  (8.0 mL) at 0  $^{\circ}\text{C}$ . The mixture was warmed to room temperature, stirred for 1 h, and quenched by the

addition of water (40 mL). The products were extracted with  $\text{CHCl}_3$ . The combined organic layer was dried over  $\text{MgSO}_4$ , filtered, and concentrated in vacuo to give **13** (7.85 g, quant.) as a yellow oil:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  8.01 (s, 1H,  $\text{HC}=\text{N}$ ), 7.50 (d,  $J = 8.8$  Hz, 2H, Ar), 6.88 (d,  $J = 8.8$  Hz, 2H, Ar), 3.94 (s, 3H,  $\text{OCH}_3$ ), 3.80 (s, 3H,  $\text{OCH}_3$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  161.0 (Ar;  $\text{C}-\text{OCH}_3$ ), 148.3 ( $\text{HC}=\text{N}$ ), 128.6 (Ar), 124.9 (Ar), 114.2 (Ar), 61.9 ( $\text{OCH}_3$ ), 55.4 ( $\text{OCH}_3$ ) ppm; IR (NaCl)  $\nu$  2937, 2900, 2837, 1607, 1513, 1464, 1365, 1306, 1252, 1171, 1057, 1033, 953, 918, 856, 831  $\text{cm}^{-1}$ ; MALDI-TOF MS (matrix  $\text{CHC}\alpha$ ) calc'd for  $\text{C}_9\text{H}_{12}\text{NO}_2^+$   $[\text{M}+\text{H}^+]$  166.09; found 166.82.

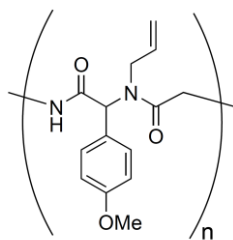
#### Synthesis of unit model **6**



Acetic acid (59.0  $\mu\text{L}$ , 1.03 mmol) was added to a mixture of anisaldehyde (126  $\mu\text{L}$ , 1.03 mmol) and allylamine (77.1  $\mu\text{L}$ , 1.03 mmol) in MeOH (1.0 mL) at room temperature. After stirring for 10 min, *tert*-butylisocynoacetate (150  $\mu\text{L}$ , 1.03 mmol) was added to the mixture. The resulting mixture was warmed to 60  $^\circ\text{C}$ , stirred for 1 d, cooled to room temperature, and concentrated in vacuo. The crude was purified by a silica gel column chromatography (eluent: hexane-ethylacetate 2:1  $\rightarrow$  1:1  $\rightarrow$  ethylacetate) to give **6** (237 mg, 62.9%) as pale yellow solids: mp 97–99  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  7.23 (d,  $J = 7.2$  Hz, 2H, Ar), 6.77 (d,  $J = 7.2$  Hz, 2H, Ar), 6.61 (brd, 1H, NH), 6.04 (s, 1H, CH), 5.29 (ddt,  $J = 18.0, 12.0, 5.6$  Hz, 1H,  $\text{CH}=\text{CH}_2$ ), 4.88 (d,  $J = 12.0$  Hz, 1H,  $\text{CH}=\text{CH}_2$ ), 4.87 (d,  $J = 18.0$  Hz, 1H,  $\text{CH}=\text{CH}_2$ ), 3.89–3.69 (m, 4H,  $\text{CH}_2$ ), 3.69 (s, 3H,  $\text{OCH}_3$ ), 2.02 (s, 3H,  $\text{CH}_3$ ), 1.35 (s, 9H, *tert*-Bu) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  172.1 ( $\text{C}=\text{O}$ , ester), 170.1 ( $\text{C}=\text{O}$ , amide), 168.7 ( $\text{C}=\text{O}$ , amide), 159.7 (Ar;  $\text{C}-\text{OCH}_3$ ), 134.2 ( $\text{CH}=\text{CH}_2$ ), 131.2 (Ar), 127.1 (Ar), 116.4 ( $\text{CH}=\text{CH}_2$ ), 114.1 (Ar), 82.0 (quaternary C of *tert*-Bu), 60.7 (CH), 55.3 ( $\text{OCH}_3$ ), 49.3 ( $\text{CH}_2$ ), 42.2 ( $\text{CH}_2$ ), 28.1 ( $\text{CH}_3$ ), 22.1 ( $\text{CH}_3$ ) ppm; IR (KBr)  $\nu$  3242, 2069, 2979, 1741, 1726, 1652, 1613, 1541, 1518, 1458, 1404, 1368, 1251, 1157, 1034, 834  $\text{cm}^{-1}$ ; MALDI-TOF MS (matrix  $\text{CHC}\alpha$ ) calc'd for  $\text{C}_{20}\text{H}_{28}\text{N}_2\text{NaO}_5^+$   $[\text{M}+\text{Na}^+]$  399.19; found 399.30.

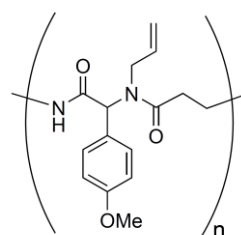
Typical procedure for the polymerization to give alternating peptides

#### Synthesis of **Poly-5a**



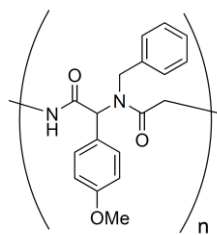
**Poly-5a**

To a suspension of **5** (175 mg, 1.00 mmol) and **1** (123 mg, 1.00 mmol) in *i*-PrOH (0.5 mL) was added TfOH (88.5  $\mu$ L, 1.00 mmol) at 0 °C. The mixture was warmed to room temperature, stirred for 2 d, and concentrated in vacuo. The resulting crude was further stirred for 1 d at room temperature and diluted with CHCl<sub>3</sub>. The reaction was quenched by the addition of water. The products were extracted with CHCl<sub>3</sub>. The combined organic layer was dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. The crude was diluted with a small amount of CHCl<sub>3</sub> and the solution was reprecipitated in hexane to give hexane-insoluble part (**Poly-5a**, 246 mg, 94%) as a brown solid and hexane-soluble part (18.0 mg, 6%) as a yellow oil:  $M_w$  8,600 Da (estimated by DOSY); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  7.5–6.5 (m, Ar, NH, CH), 6.0–5.7 (m, CH=CH<sub>2</sub>), 5.3–4.8 (m, CH=CH<sub>2</sub>), 4.1–3.7 (m, CH<sub>2</sub>, OCH<sub>3</sub>) ppm; D:  $5.79\text{--}6.76 \times 10^{-10}$  m<sup>2</sup>/S; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  165.3 (C=O, amide), 160.8 (C=O, amide), 160.0 (Ar; C-OCH<sub>3</sub>), 134.0, 132.0, 131.2, 130.3, 128.6, 125.4, 124.5, 122.9, 118.8, 116.0, 114.9, 114.6, 114.1, 63.0 (CH), 55.3 (OCH<sub>3</sub>), 55.0 (OCH<sub>3</sub>), 48.1 (CH<sub>2</sub>), 42.4 (CH<sub>2</sub>) ppm; IR (KBr)  $\nu$  2839, 1659, 1607, 1513, 1462, 1371, 1253, 1177, 1114, 1031, 933, 832, 639, 540 cm<sup>-1</sup>.



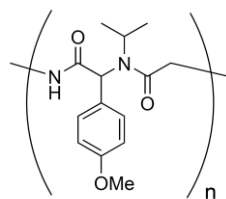
**Poly-5b**

**Poly-5b**: a brown oil;  $M_w$  2,200 Da (estimated by DOSY); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  7.63 (t,  $J$  = 6.0 Hz, NH), 7.28 (d,  $J$  = 8.6 Hz, Ar), 6.86 (d,  $J$  = 8.6 Hz, Ar), 6.02 (brd, CH), 5.92–5.72 (m, CH=CH<sub>2</sub>), 5.21–5.10 (m, CH=CH<sub>2</sub>), 4.24 (s, NH), 3.90–3.78 (m, CH<sub>2</sub>), 3.80 (s, OCH<sub>3</sub>), 3.64–3.45 (m, CH<sub>2</sub>), 3.22 (d,  $J$  = 6.0 Hz, CH<sub>2</sub>), 2.42 (t,  $J$  = 6.0 Hz, CH<sub>2</sub>) ppm; D:  $8.42\text{--}9.21 \times 10^{-10}$  m<sup>2</sup>/S; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  172.1 (C=O, amide), 171.1 (C=O, amide), 159.7 (Ar; C-OCH<sub>3</sub>), 134.2 (CH=CH<sub>2</sub>), 134.0 (CH=CH<sub>2</sub>), 128.8 (Ar), 118.1 (Ar), 116.5 (CH=CH<sub>2</sub>), 114.3 (Ar), 65.2 (CH), 55.3 (OCH<sub>3</sub>), 50.1 (CH<sub>2</sub>), 42.0 (CH<sub>2</sub>), 35.7 (CO-CH<sub>2</sub>), 35.6 (CO-CH<sub>2</sub>) ppm; IR (NaCl)  $\nu$  3305, 3078, 1655, 1611, 1513, 1252, 1180, 1031, 756 cm<sup>-1</sup>.



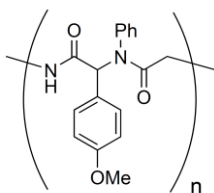
**Poly-7**

**Poly-7:** a yellow solid;  $M_w$  4,400 Da (estimated by DOSY);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  7.5–6.6 (m, Ar, CH), 4.4–4.3 (m,  $\text{CH}_2$ ), 3.9–3.6 (m,  $\text{OCH}_3$ ,  $\text{CH}_2$ ) ppm; D:  $7.10\text{--}7.61 \times 10^{-10} \text{ m}^2/\text{S}$ ;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  165.5 (C=O, amide), 160.3 (C=O, amide), 160.0 (Ar; C- $\text{OCH}_3$ ), 138.3, 131.4, 131.0, 130.4, 129.4, 129.1, 128.7, 128.5, 128.4, 128.3, 127.6, 127.1, 125.7, 114.7, 114.5, 113.8, 64.4 (CH), 55.3 ( $\text{OCH}_3$ ), 55.1 ( $\text{OCH}_3$ ), 50.7 ( $\text{CH}_2$ ), 43.8 ( $\text{CH}_2$ ), 43.3 ( $\text{CH}_2$ ) ppm; IR (NaCl)  $\nu$  3296, 2842, 1655, 1605, 1512, 1455, 1255, 1176, 1030, 752  $\text{cm}^{-1}$ .



**Poly-8**

**Poly-8:** a yellow solid;  $M_w$  6,100 Da (estimated by DOSY);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  8.4–8.3 (m, Ar), 7.6–6.6 (m, Ar, CH), 3.9–3.7 (m, CH,  $\text{CH}_2$ ,  $\text{OCH}_3$ ), 1.3–0.9 (m,  $\text{CH}_3$ ) ppm; D:  $6.90\text{--}7.87 \times 10^{-10} \text{ m}^2/\text{S}$ ;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  164.6 (C=O, amide), 164.4 (C=O, amide), 160.0 (C=O, amide), 159.7 (Ar; C- $\text{OCH}_3$ ), 133.9, 131.3, 130.9, 130.3, 129.6, 129.3, 129.1, 128.6, 126.1, 114.6, 114.3, 114.0, 113.7, 113.4, 61.7 (CH), 55.5 ( $\text{OCH}_3$ ), 55.3 ( $\text{OCH}_3$ ), 55.1 ( $\text{OCH}_3$ ), 48.1 (CH), 41.8 ( $\text{CH}_2$ ), 22.6 ( $\text{CH}_3$ ), 22.3 ( $\text{CH}_3$ ), 22.2 ( $\text{CH}_3$ ), 21.6 ( $\text{CH}_3$ ), 21.0 ( $\text{CH}_3$ ), 19.9 ( $\text{CH}_3$ ) ppm; IR (NaCl)  $\nu$  2972, 2838, 1659, 1605, 1513, 1463, 1304, 1254, 1176, 1031, 831, 755  $\text{cm}^{-1}$ .

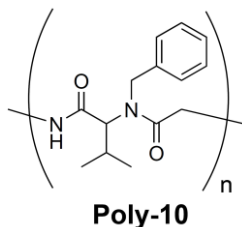


**Poly-9**

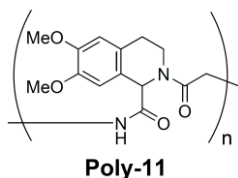
**Poly-9:** a yellow solid;  $M_w$  4,400 Da (estimated by DOSY);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  8.3–8.2 (m, Ar), 7.8–6.5 (m, Ar), 4.8–4.7 (m, CH), 4.2–3.7 (m,  $\text{CH}_2$ ,  $\text{OCH}_3$ ) ppm; D:  $6.70\text{--}8.70 \times 10^{-10} \text{ m}^2/\text{S}$ ;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  173.1 (C=O, amide), 172.5 (C=O, amide), 172.0 (C=O, amide), 166.9 (C=O, amide), 162.6 (C=O, amide), 159.8 (Ar; C- $\text{OCH}_3$ ), 159.7 (Ar; C- $\text{OCH}_3$ ),



146.5 (Ar; C-N), 146.3 (Ar; C-N), 137.4, 135.5, 133.3, 132.0, 130.4, 130.1, 129.6, 129.4, 129.3, 129.2, 128.9, 128.7, 128.5, 128.1, 126.0, 124.4, 120.0, 119.2, 119.0, 114.6, 114.5, 114.3, 114.0, 113.8, 113.7, 69.3 (CH), 63.1 (CH), 55.6 (OCH<sub>3</sub>), 55.3 (OCH<sub>3</sub>), 43.9 (CH<sub>2</sub>), 41.5 (CH<sub>2</sub>) ppm; IR (NaCl)  $\nu$  2839, 1661, 1601, 1510, 1252, 1178, 1031, 753 cm<sup>-1</sup>.

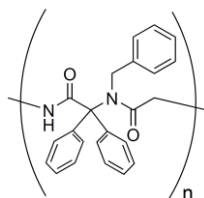


**Poly-10:** Since the typical procedure gave a complex mixture by the degradation of **10**, the modified procedure involving the preparation of **10** *in situ* was performed to give **Poly-10**. To a suspension of benzylamine (109  $\mu$ L, 1.00 mmol) and **1** (123 mg, 1.00 mmol) in *i*-PrOH (0.5 mL) was added TfOH (88.5  $\mu$ L, 1.00 mmol) and isobutylaldehyde (91.3  $\mu$ L, 1.00 mmol) at 0 °C. The mixture was warmed to room temperature, stirred for 2 d, and concentrated in vacuo. The resulting crude was further stirred for 1 d at room temperature and diluted with CHCl<sub>3</sub>. The reaction was quenched by the addition of water. The products were extracted with CHCl<sub>3</sub>. The combined organic layer was dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. The crude was diluted with a small amount of CHCl<sub>3</sub> and the solution was reprecipitated in hexane to give hexane-insoluble part (**Poly-10**, 201 mg, 82%) as a white solid and hexane-soluble part (45.9 mg, 18%) as a yellow oil:  $M_w$  8,600 Da (estimated by DOSY); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  7.5–6.8 (m, Ar), 6.4–6.3 (m, NH), 4.6–3.4 (m, CH, CH<sub>2</sub>), 2.7–2.2 (m, CH), 1.2–0.7 (m, CH<sub>3</sub>) ppm; D:  $6.46\text{--}8.27 \times 10^{-10}$  m<sup>2</sup>/S; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  170.2 (C=O, amide), 168.7 (C=O, amide), 165.3 (C=O, amide), 141.0, 138.2, 137.9, 135.1, 130.3, 130.0, 129.5, 129.3, 129.1, 128.9, 128.8, 128.5, 128.0, 127.7, 127.4, 127.3, 127.2, 126.9, 66.5 (CH), 65.9 (CH), 51.9 (CH<sub>2</sub>), 51.8 (CH<sub>2</sub>), 43.7 (CH<sub>2</sub>), 43.4 (CH<sub>2</sub>), 43.2 (CH<sub>2</sub>), 30.2 (CH), 30.0 (CH), 27.3 (CH), 21.9 (CH<sub>3</sub>), 21.8 (CH<sub>3</sub>), 21.5 (CH<sub>3</sub>), 21.1 (CH<sub>3</sub>), 20.0 (CH<sub>3</sub>), 19.4 (CH<sub>3</sub>), 18.7 (CH<sub>3</sub>), 18.3 (CH<sub>3</sub>), 18.1 (CH<sub>3</sub>) ppm; IR (NaCl)  $\nu$  2965, 1655, 1535, 1455, 1247, 1165, 1030, 753 cm<sup>-1</sup>.



**Poly-11:** a yellow solid;  $M_w$  12,200 Da (estimated by DOSY); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  7.2–6.4 (m, Ar, CH), 4.2–2.5 (m, CH<sub>2</sub>, OCH<sub>3</sub>) ppm; D:  $4.30\text{--}5.12 \times 10^{-10}$  m<sup>2</sup>/S; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  171.0 (C=O, amide), 168.7 (C=O, amide), 153.9 (Ar; C-OCH<sub>3</sub>), 149.3 (Ar; C-OCH<sub>3</sub>), 148.0 (Ar; C-OCH<sub>3</sub>), 126.9, 124.5, 121.8, 118.6, 113.5, 112.3, 111.4, 109.5, 57.2 (CH), 55.8 (OCH<sub>3</sub>),

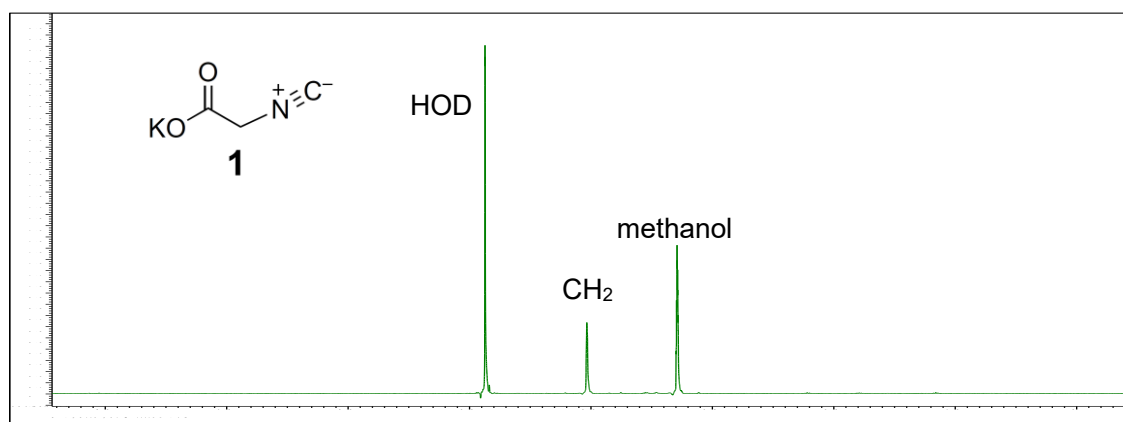
43.2 (CH<sub>2</sub>), 41.5 (CH<sub>2</sub>), 40.5 (CH<sub>2</sub>), 27.8 (CH<sub>2</sub>), 25.1 (CH<sub>2</sub>) ppm; IR (NaCl)  $\nu$  3333, 2939, 1657, 1518, 1465, 1362, 1258, 1120, 1030, 753 cm<sup>-1</sup>.



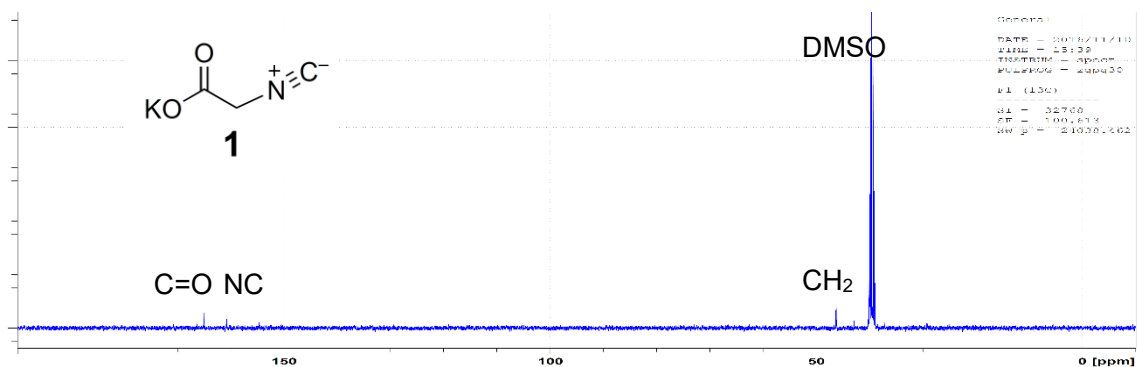
**Poly-12**

**Poly-12:** a yellow solid;  $M_w$  4,400 Da (estimated by DOSY); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  8.3–8.2 (m, Ar), 7.5–7.0 (m, Ar), 6.1 (brd, NH), 4.6–3.9 (m, CH<sub>2</sub>), 3.4–3.3 (m, CH<sub>2</sub>) ppm; D:  $7.64\text{--}8.20 \times 10^{-10}$  m<sup>2</sup>/S; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 298 K)  $\delta$  173.0 (C=O, amide), 172.7 (C=O, amide), 172.3 (C=O, amide), 168.9 (C=O, amide), 141.7, 137.8, 128.66, 128.60, 128.58, 128.55, 128.27, 128.21, 128.1, 127.64, 127.52, 127.43, 127.39, 127.33, 72.89 (quaternary C), 72.75 (quaternary C), 48.6 (CH<sub>2</sub>), 43.41 (CH<sub>2</sub>), 43.37 (CH<sub>2</sub>), 41.7 (CH<sub>2</sub>) ppm; IR (NaCl)  $\nu$  3316, 3062, 3029, 2931, 2864, 1659, 1495, 1452, 1218, 1079, 1030, 754, 699 cm<sup>-1</sup>.

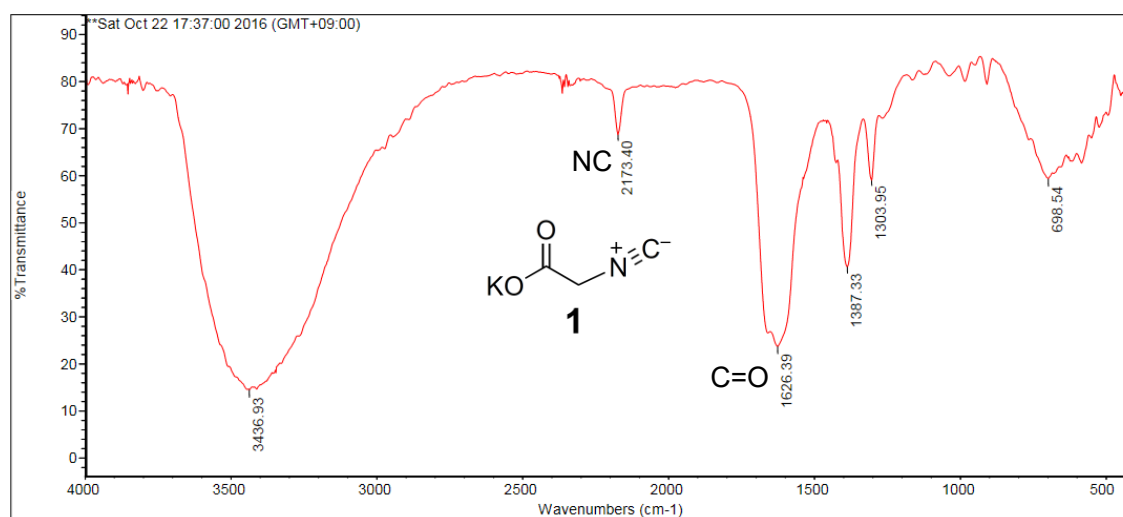
**$^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, DOSY, and IR spectra**



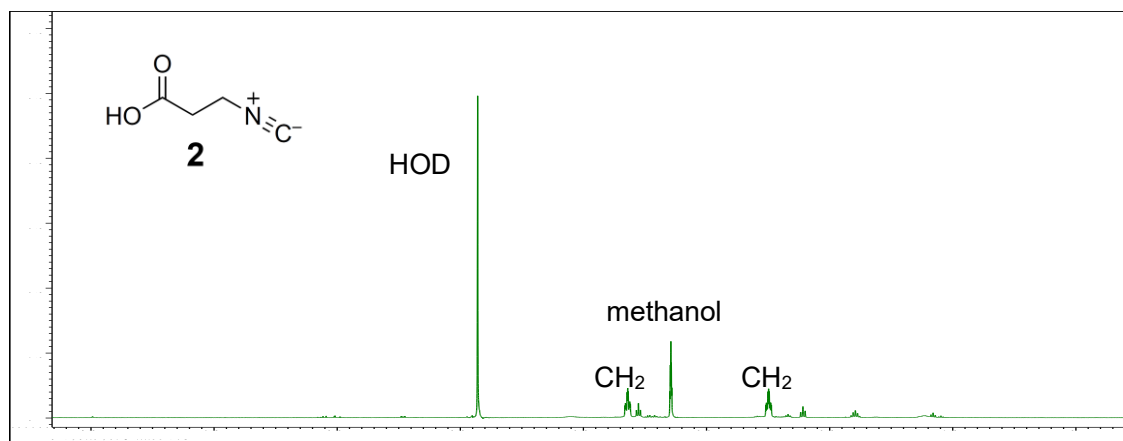
**Figure S1.**  $^1\text{H}$  NMR spectrum of **1** (400 MHz,  $\text{CD}_3\text{OD}$ , 298 K).



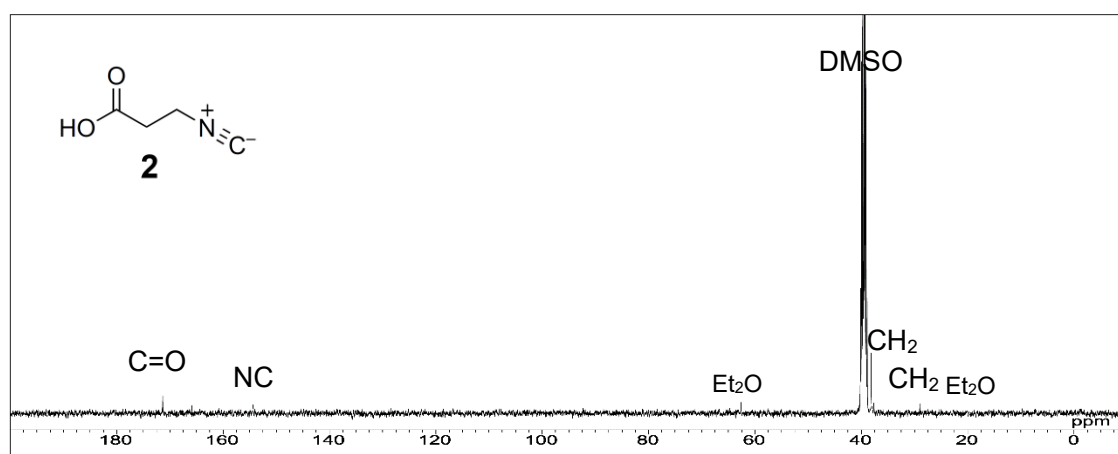
**Figure S2.**  $^{13}\text{C}$  NMR spectrum of **1** (100 MHz,  $\text{DMSO}-d_6$ , 298 K).



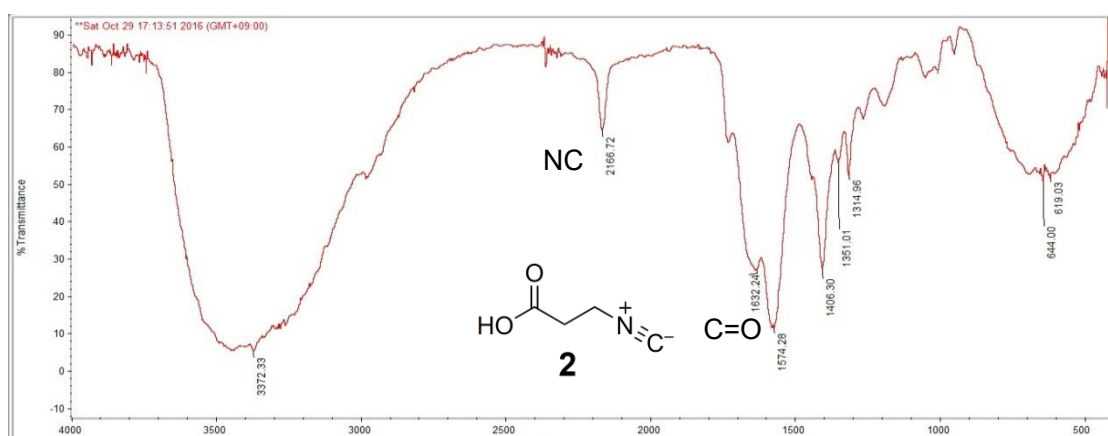
**Figure S3.** IR spectrum of **1** (KBr).



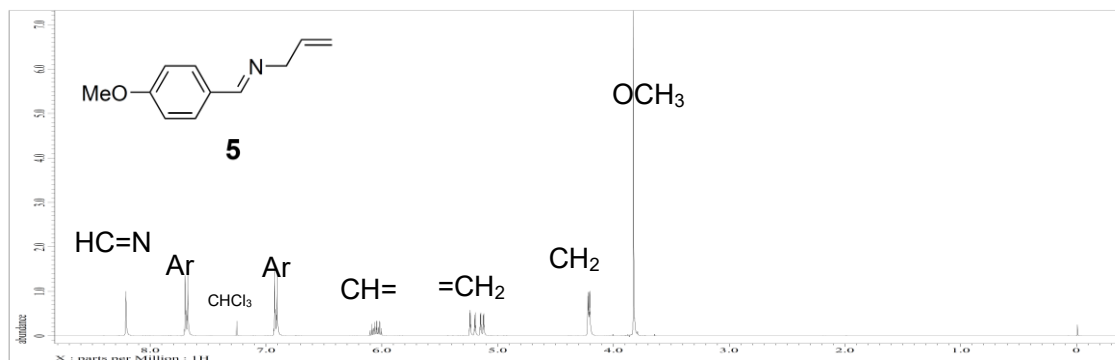
**Figure S4.** <sup>1</sup>H NMR spectrum of **2** (400 MHz, CD<sub>3</sub>OD, 298 K).



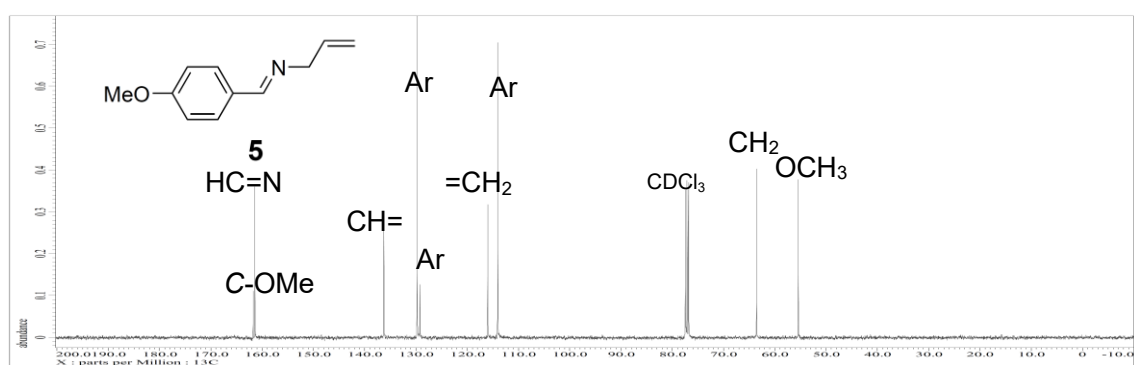
**Figure S5.** <sup>13</sup>C NMR spectrum of **2** (100 MHz, DMSO-*d*<sub>6</sub>, 298 K).



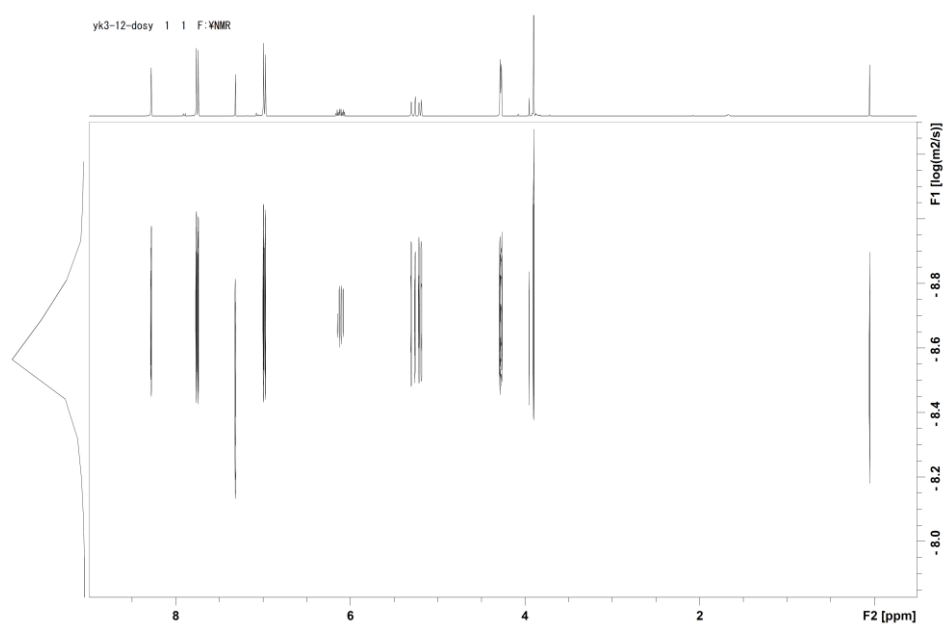
**Figure S6.** IR spectrum of **2** (KBr).



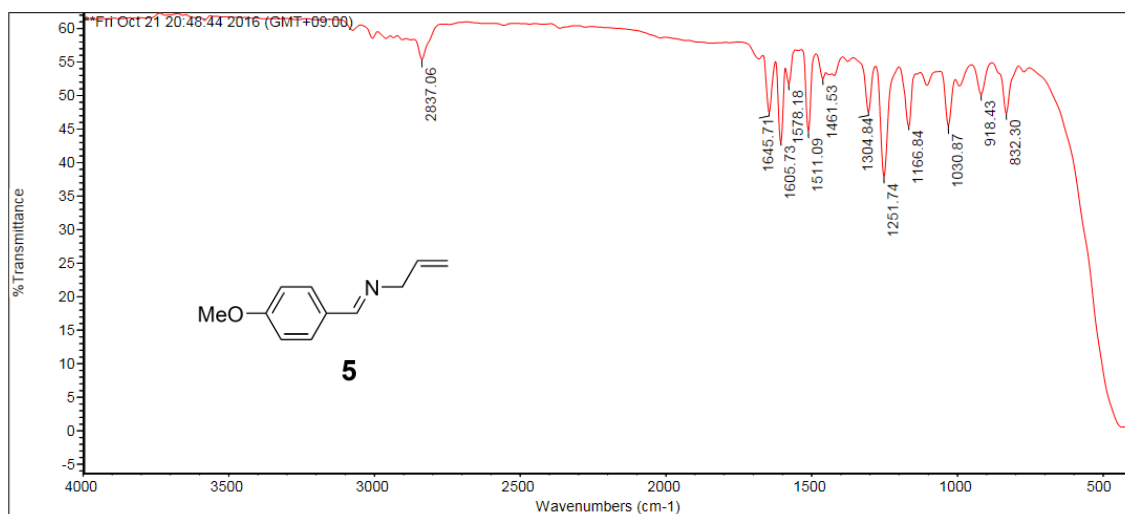
**Figure S7.**  $^1\text{H}$  NMR spectrum of **5** (400 MHz,  $\text{CDCl}_3$ , 298 K).



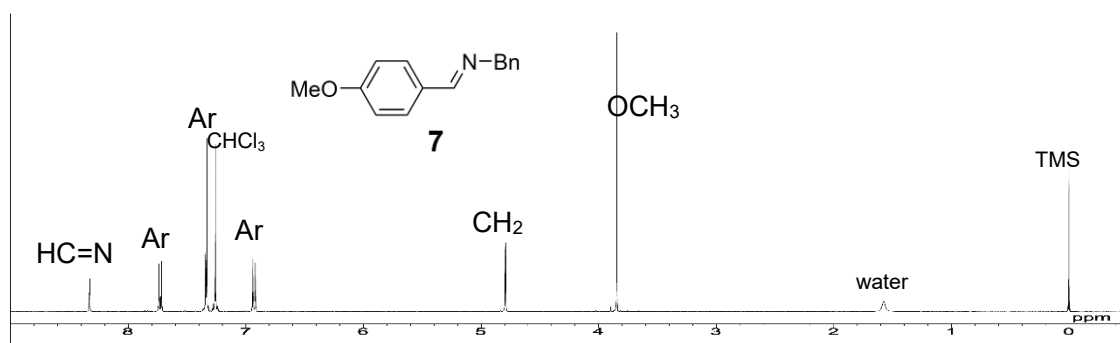
**Figure S8.**  $^{13}\text{C}$  NMR spectrum of **5** (100 MHz,  $\text{CDCl}_3$ , 298 K).



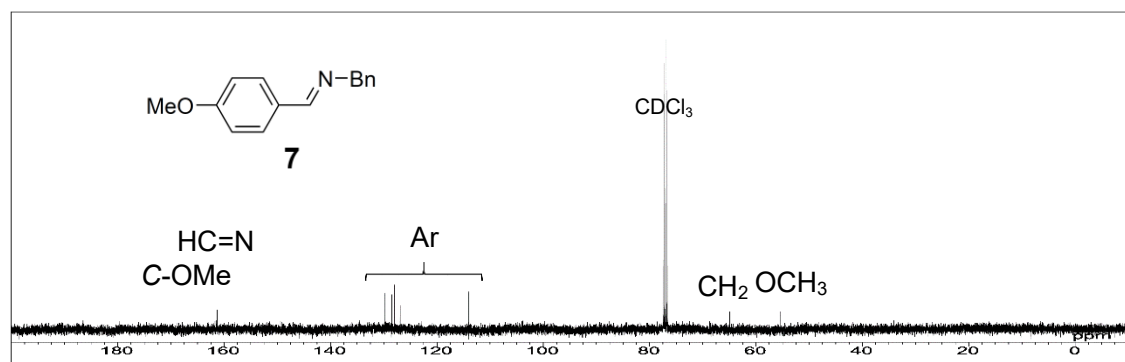
**Figure S9.** DOSY correlations of **5** (400 MHz,  $\text{CDCl}_3$ , 298 K).



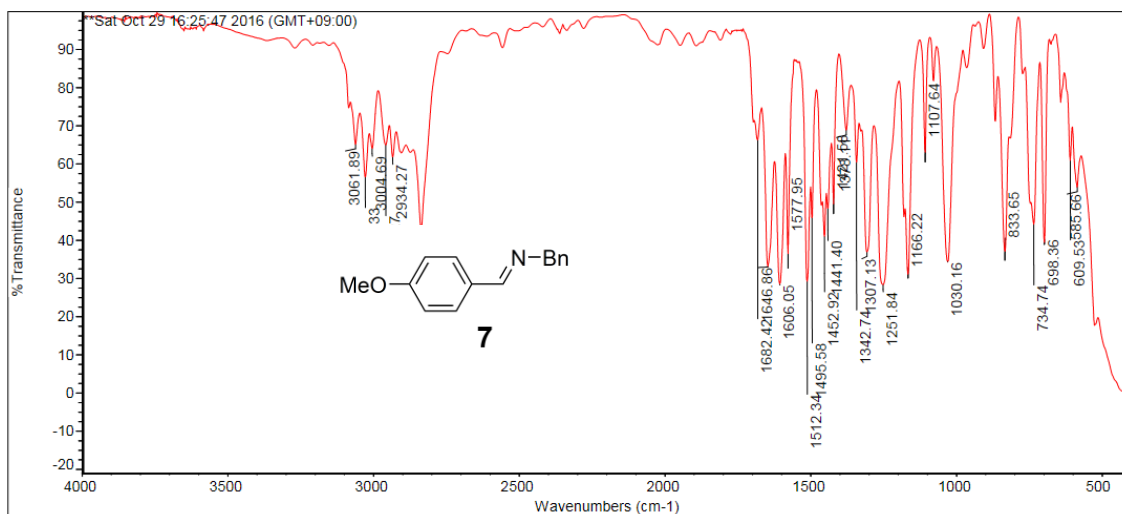
**Figure S10.** IR spectrum of **5** (NaCl).



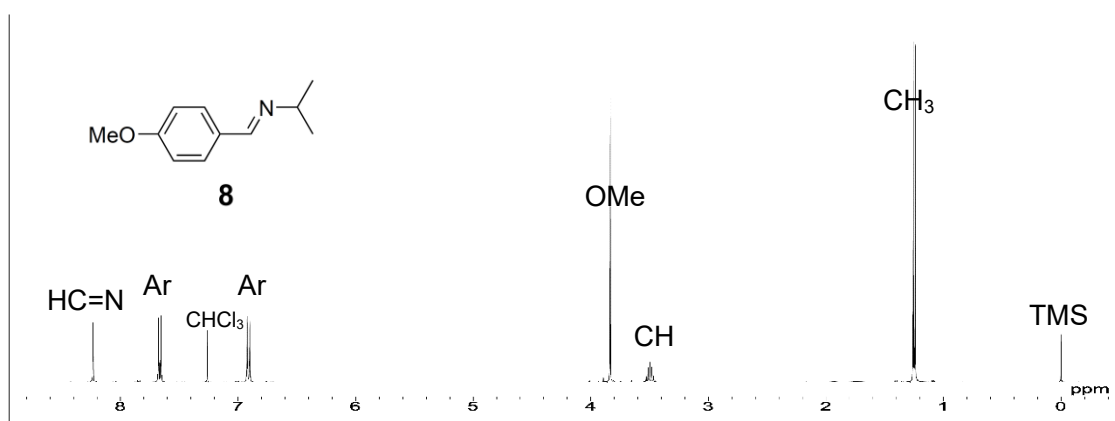
**Figure S11.** <sup>1</sup>H NMR spectrum of **7** (400 MHz, CDCl<sub>3</sub>, 298 K).



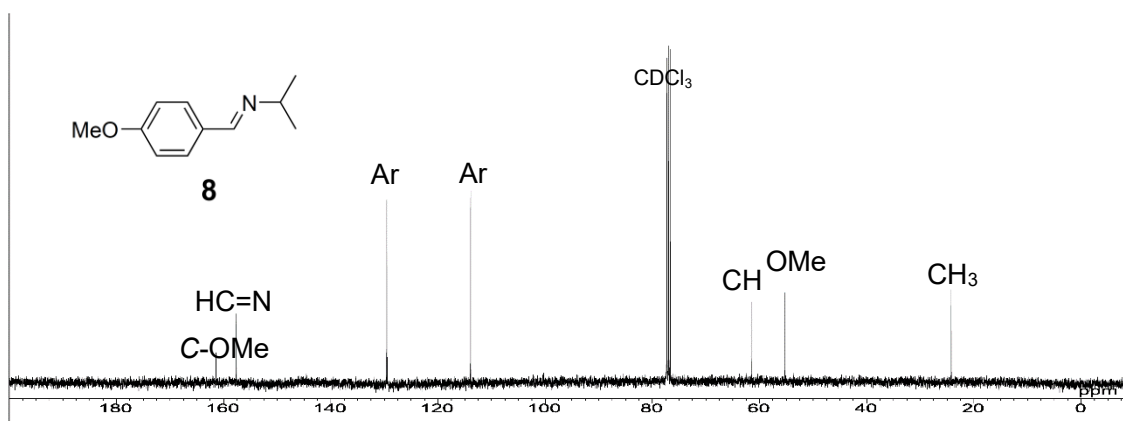
**Figure S12.** <sup>13</sup>C NMR spectrum of **7** (100 MHz, CDCl<sub>3</sub>, 298 K).



**Figure S13.** IR spectrum of **7** (NaCl).



**Figure S14.** <sup>1</sup>H NMR spectrum of **8** (400 MHz, CDCl<sub>3</sub>, 298 K).



**Figure S15.** <sup>13</sup>C NMR spectrum of **8** (100 MHz, CDCl<sub>3</sub>, 298 K).

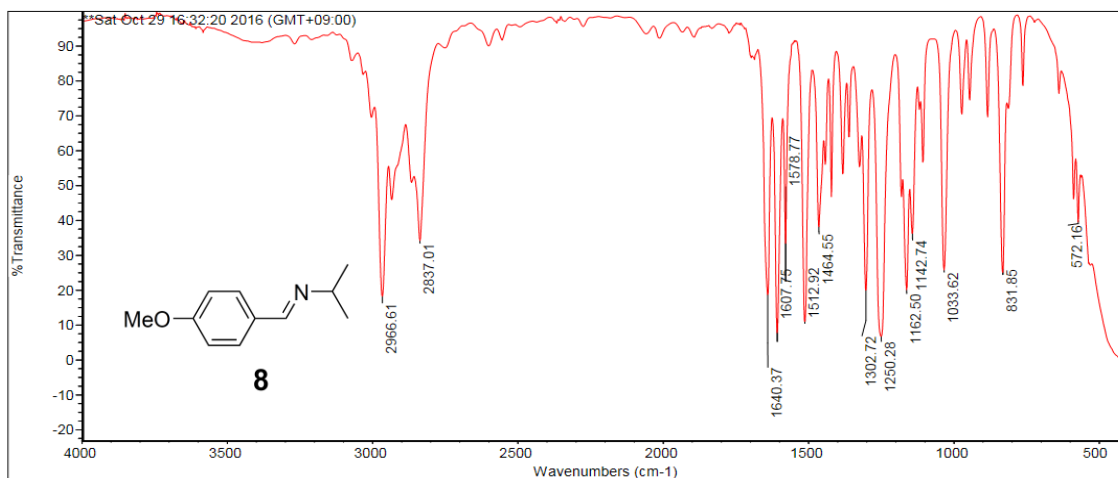


Figure S16. IR spectrum of **8** (NaCl).

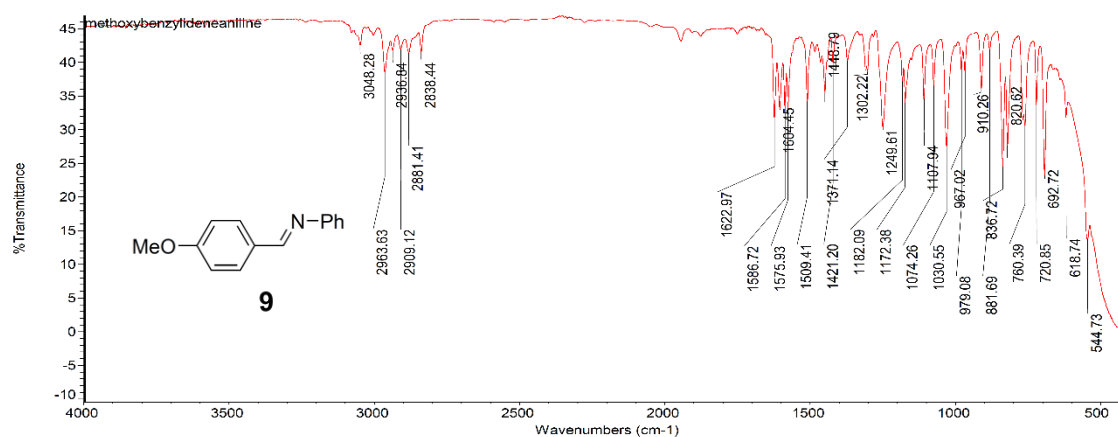


Figure S17. IR spectrum of **9** (NaCl).

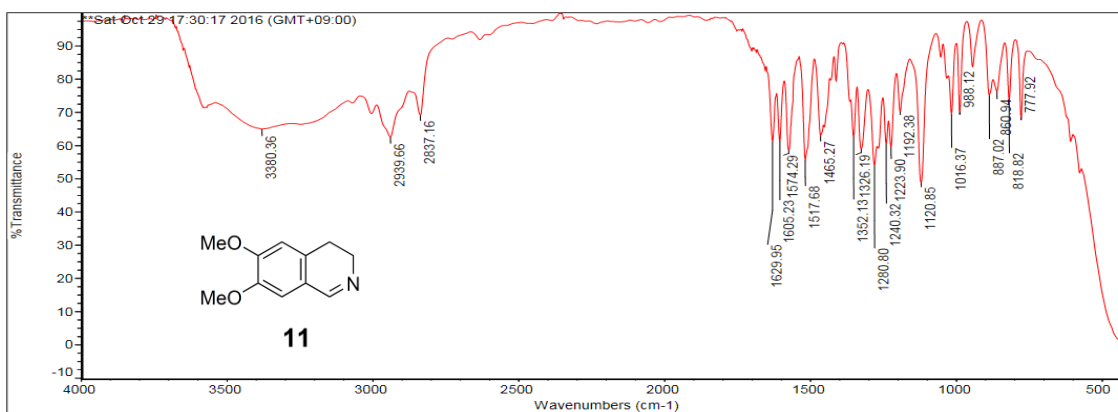
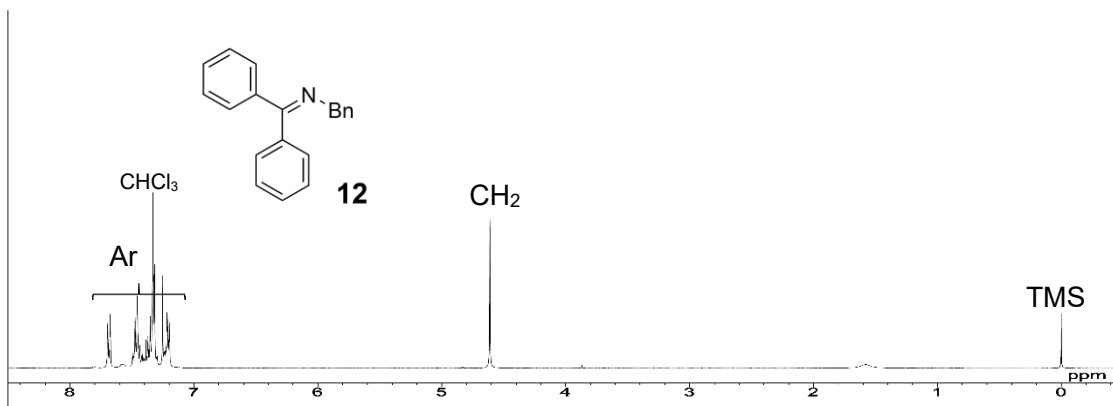
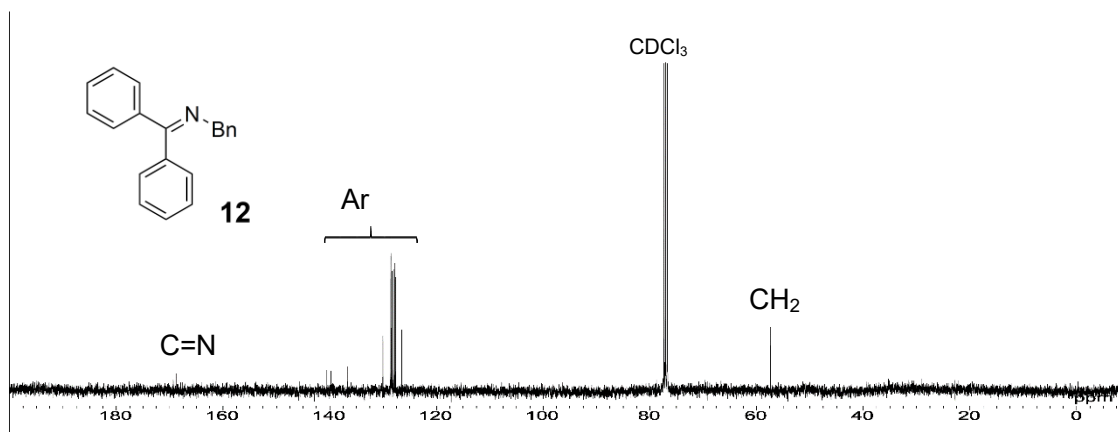


Figure S18. IR spectrum of **11** (NaCl).

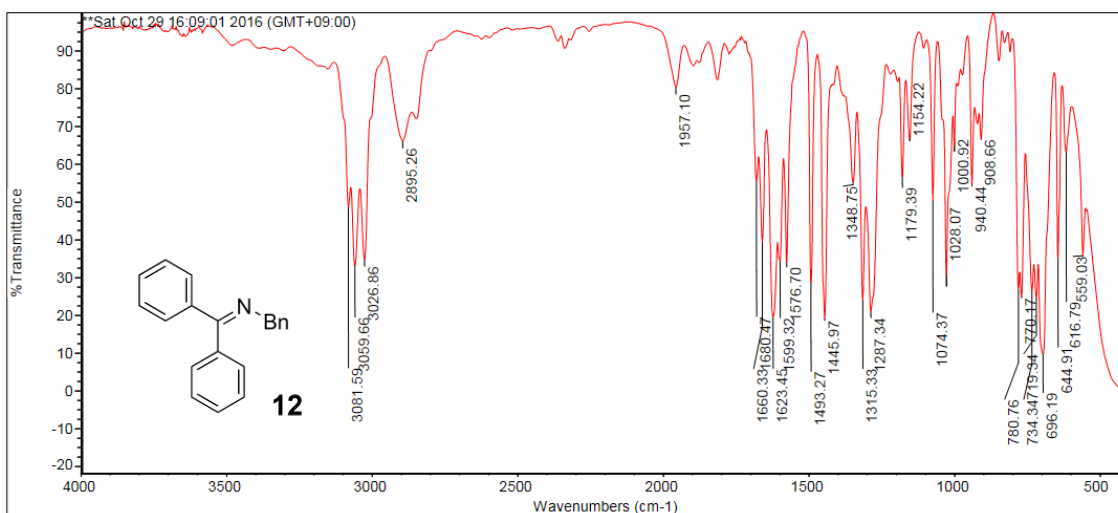




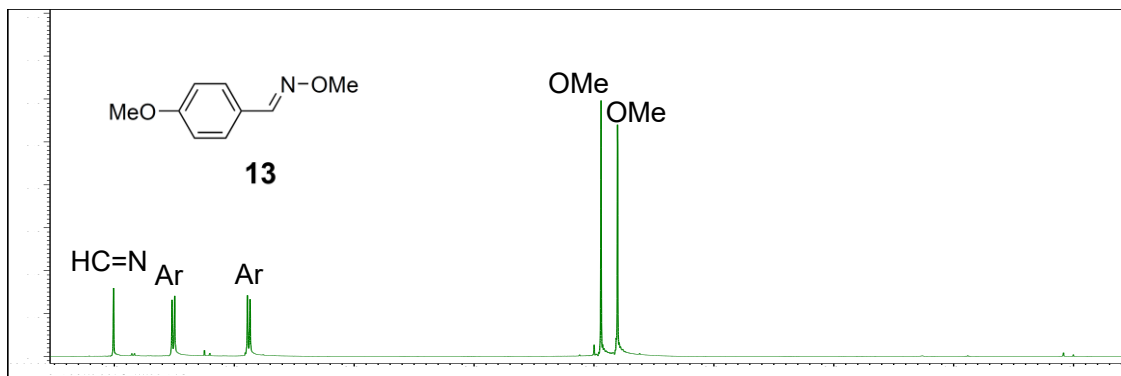
**Figure S19.** <sup>1</sup>H NMR spectrum of **12** (400 MHz, CDCl<sub>3</sub>, 298 K).



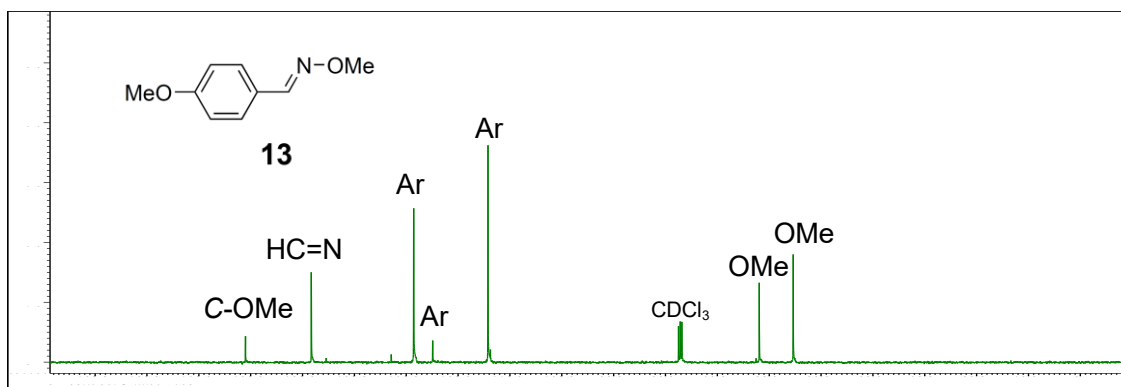
**Figure S20.** <sup>13</sup>C NMR spectrum of **12** (100 MHz, CDCl<sub>3</sub>, 298 K).



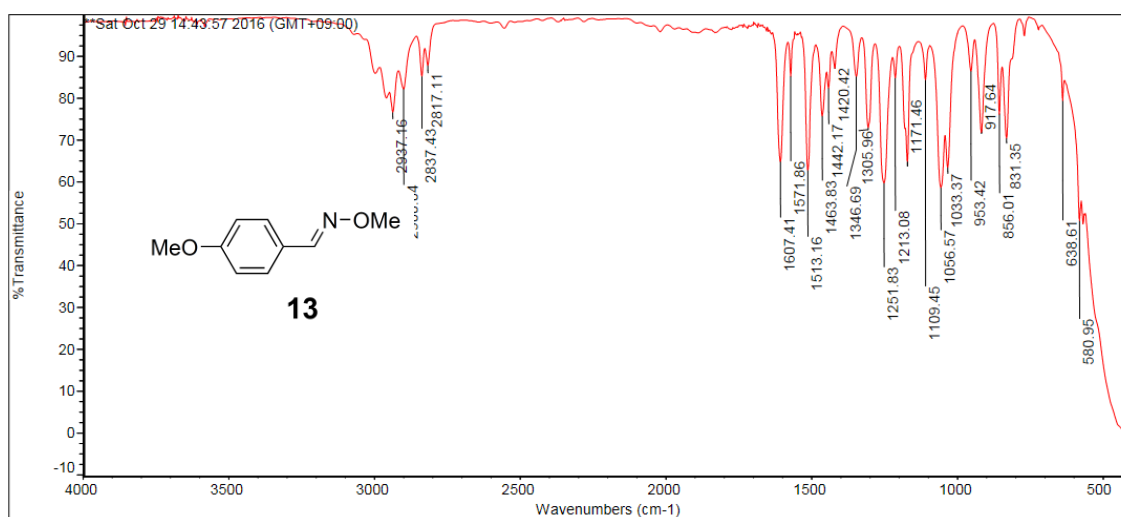
**Figure S21.** IR spectrum of **12** (NaCl).



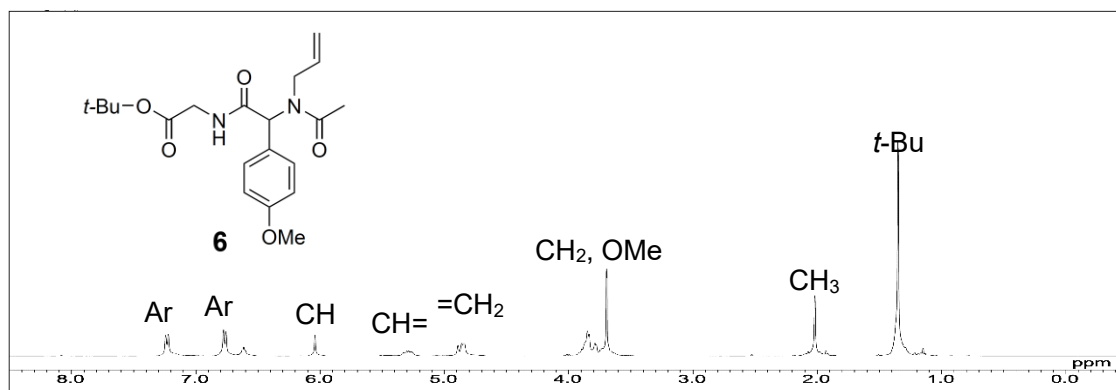
**Figure S22.** <sup>1</sup>H NMR spectrum of **13** (400 MHz, CDCl<sub>3</sub>, 298 K).



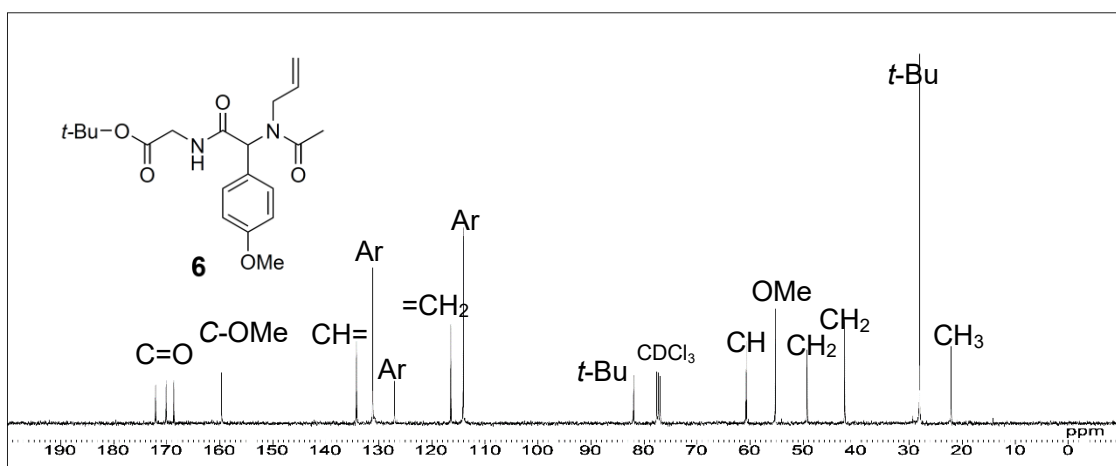
**Figure S23.** <sup>13</sup>C NMR spectrum of **13** (100 MHz, CDCl<sub>3</sub>, 298 K).



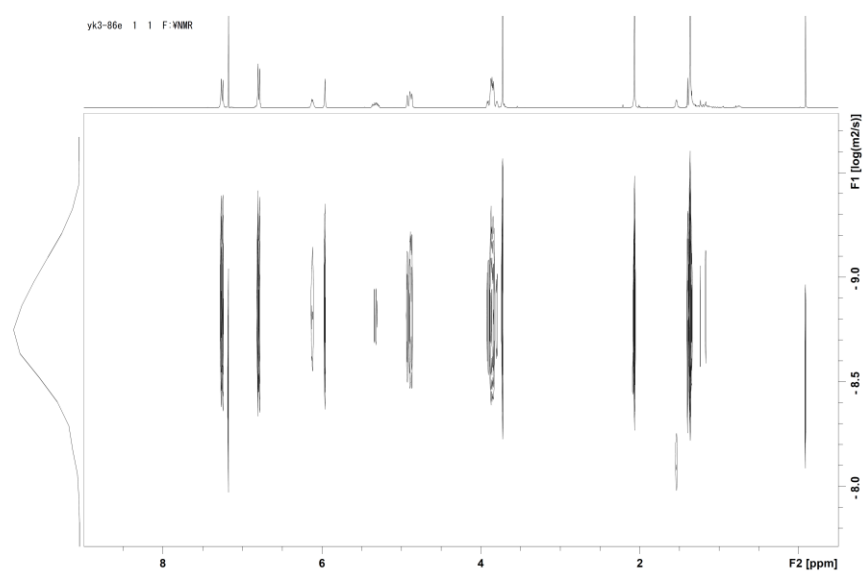
**Figure S24.** IR spectrum of **13** (NaCl).



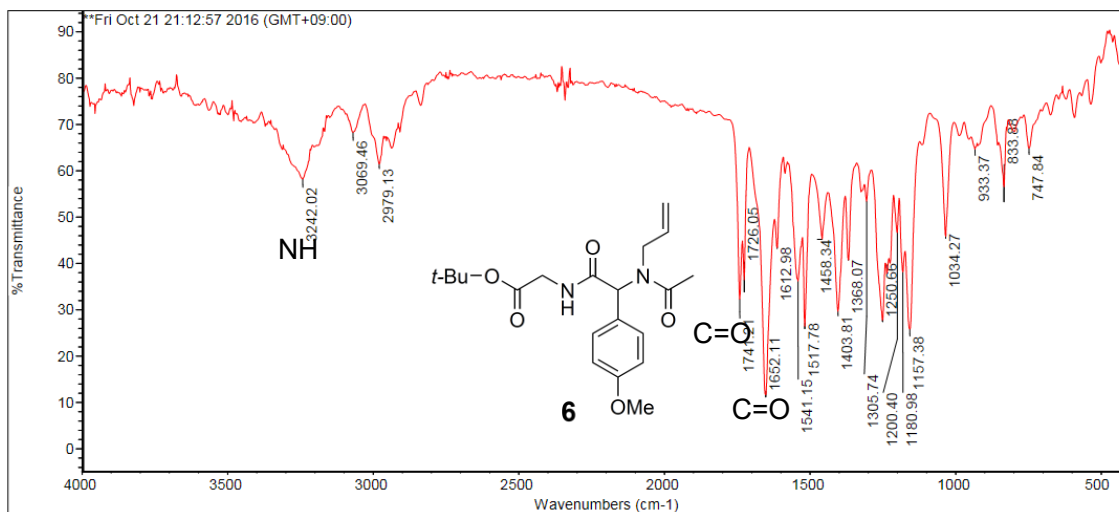
**Figure S25.**  $^1\text{H}$  NMR spectrum of **6** (400 MHz,  $\text{CDCl}_3$ , 298 K).



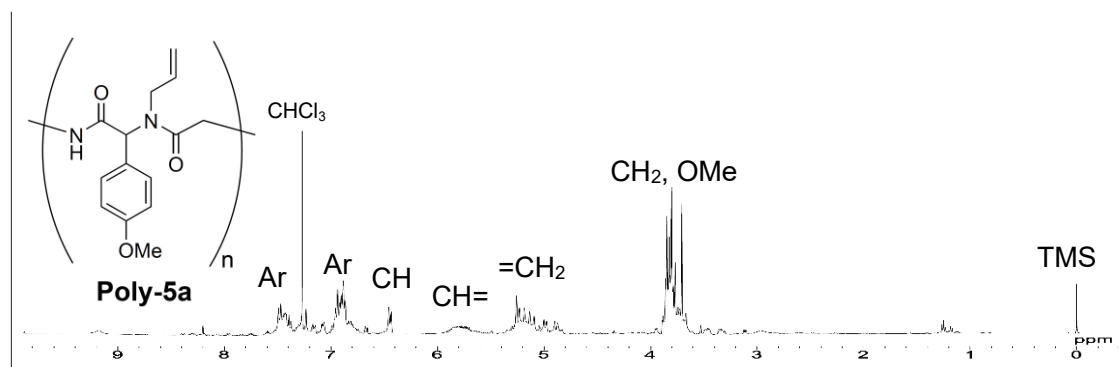
**Figure S26.**  $^{13}\text{C}$  NMR spectrum of **6** (100 MHz,  $\text{CDCl}_3$ , 298 K).



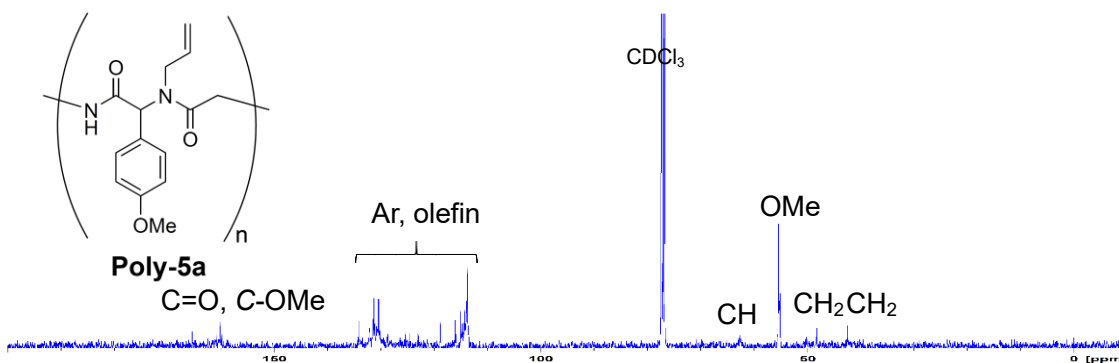
**Figure S27.** DOSY correlations of **6** (400 MHz,  $\text{CDCl}_3$ , 298 K).



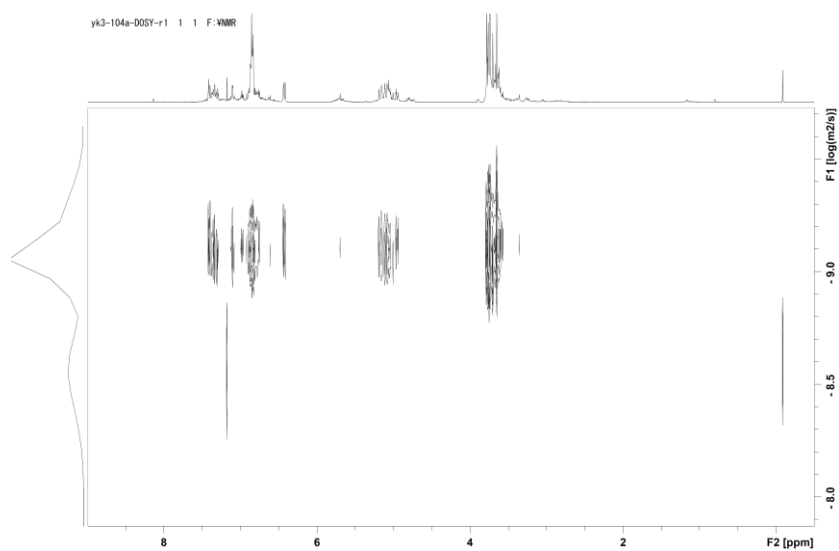
**Figure S28.** IR spectrum of **6** (KBr).



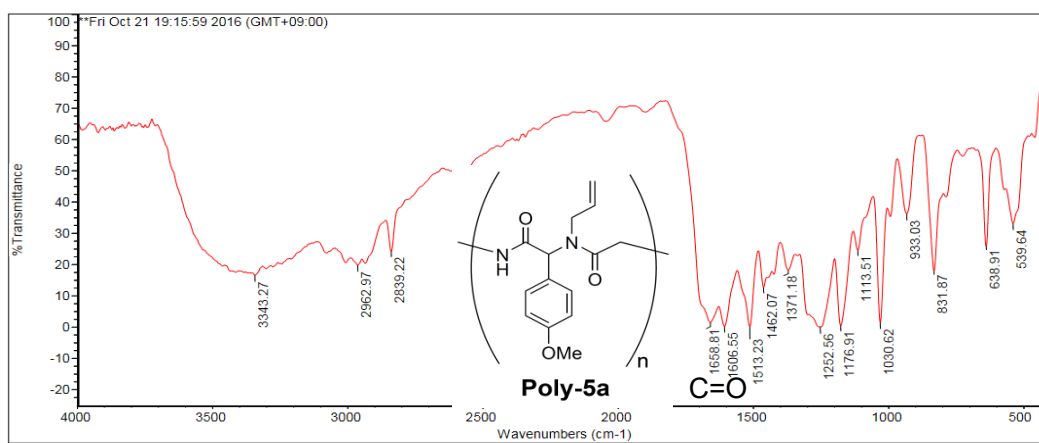
**Figure S29.**  $^1\text{H}$  NMR spectrum of **Poly-5a** (400 MHz,  $\text{CDCl}_3$ , 298 K).



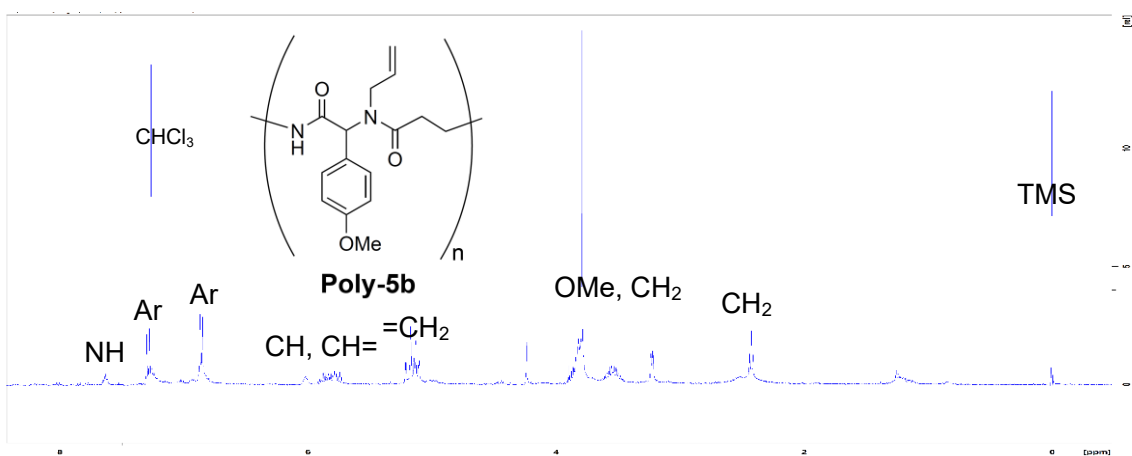
**Figure S30.**  $^{13}\text{C}$  NMR spectrum of **Poly-5a** (100 MHz,  $\text{CDCl}_3$ , 298 K).



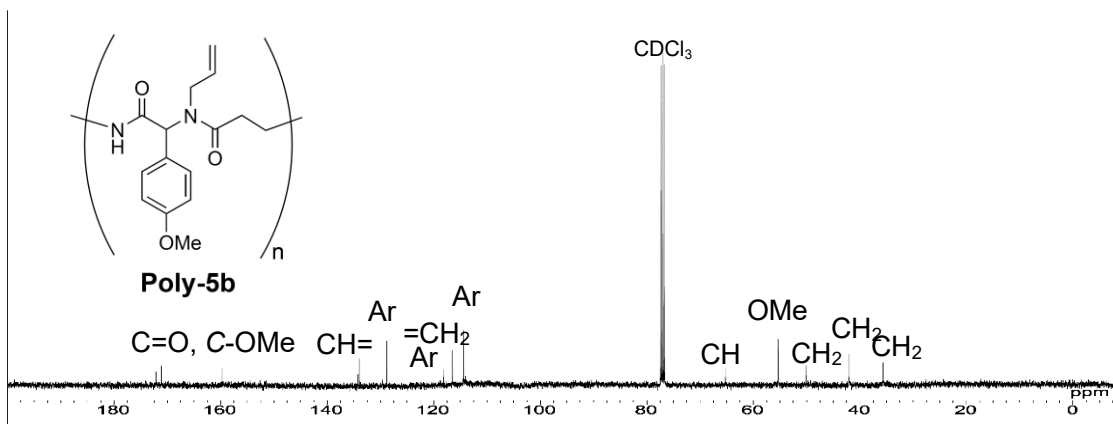
**Figure S31.** DOSY correlations of **Poly-5a** (400 MHz,  $\text{CDCl}_3$ , 298 K).



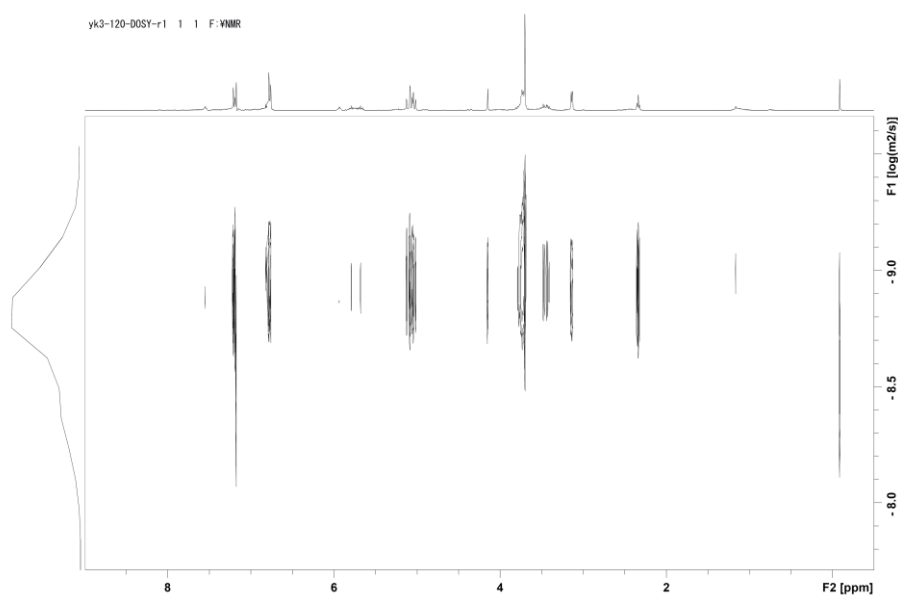
**Figure S32.** IR spectrum of **Poly-5a** (KBr).



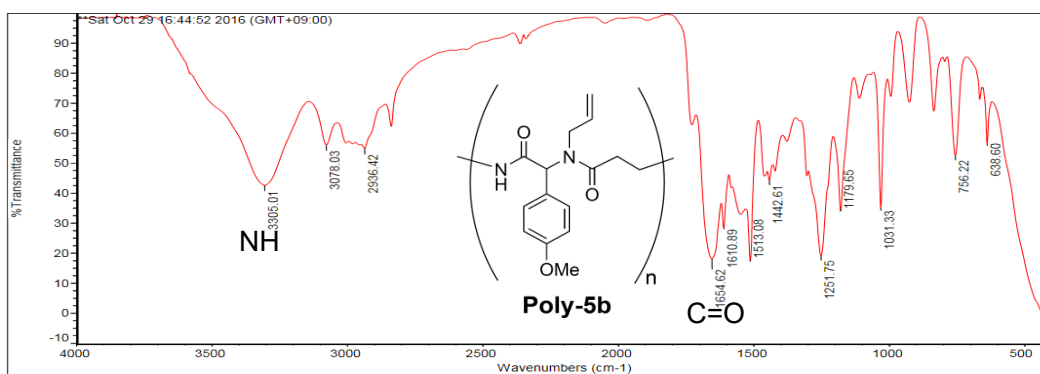
**Figure S33.**  $^1\text{H}$  NMR spectrum of **Poly-5b** (400 MHz,  $\text{CDCl}_3$ , 298 K).



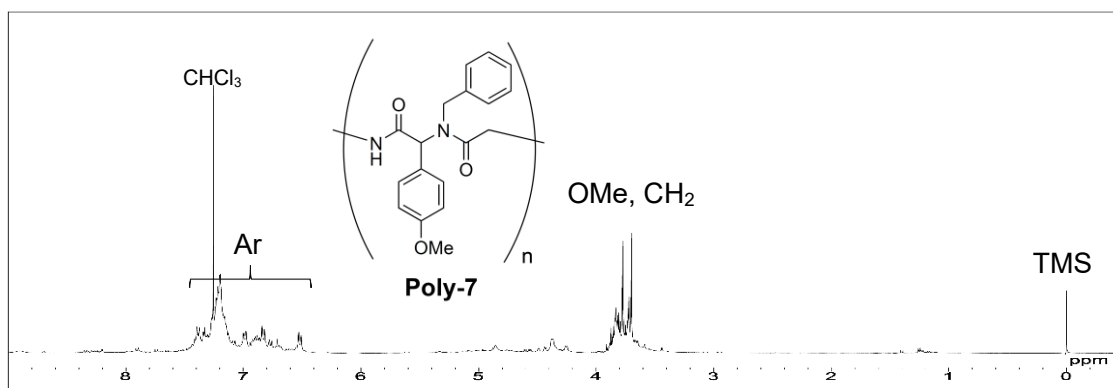
**Figure S34.**  $^{13}\text{C}$  NMR spectrum of **Poly-5b** (100 MHz,  $\text{CDCl}_3$ , 298 K).



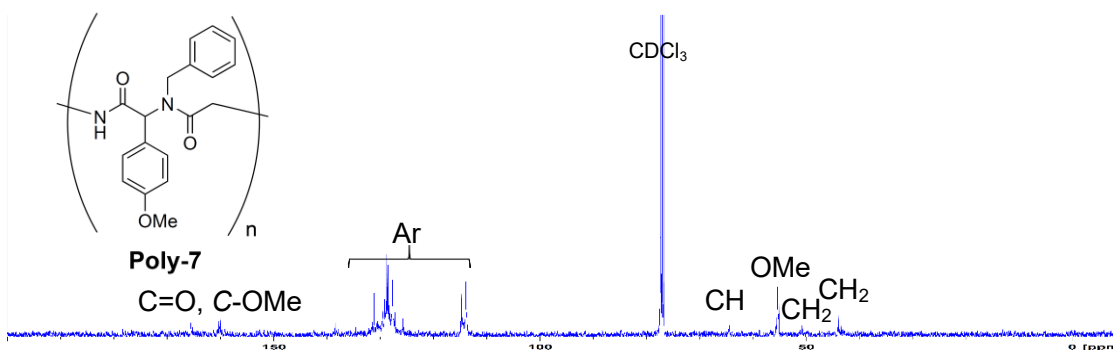
**Figure S35.** DOSY correlations of **Poly-5b** (400 MHz,  $\text{CDCl}_3$ , 298 K).



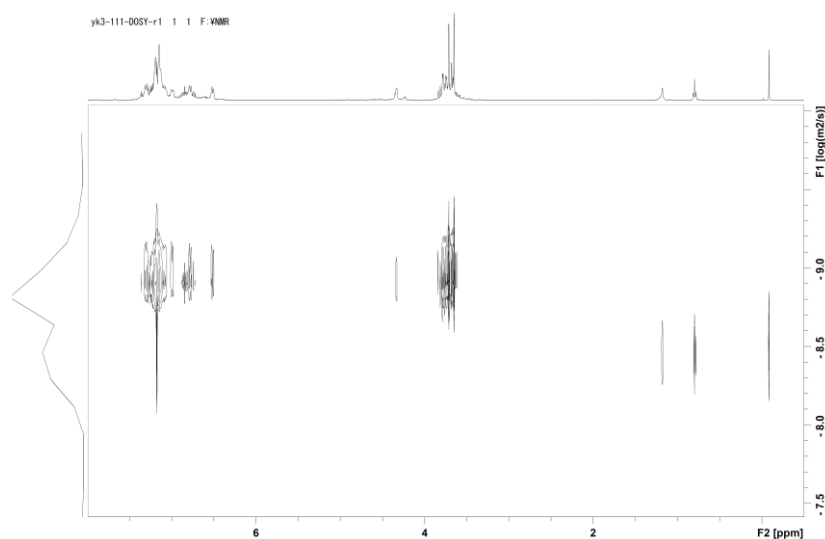
**Figure S36.** IR spectrum of **Poly-5b** (NaCl).



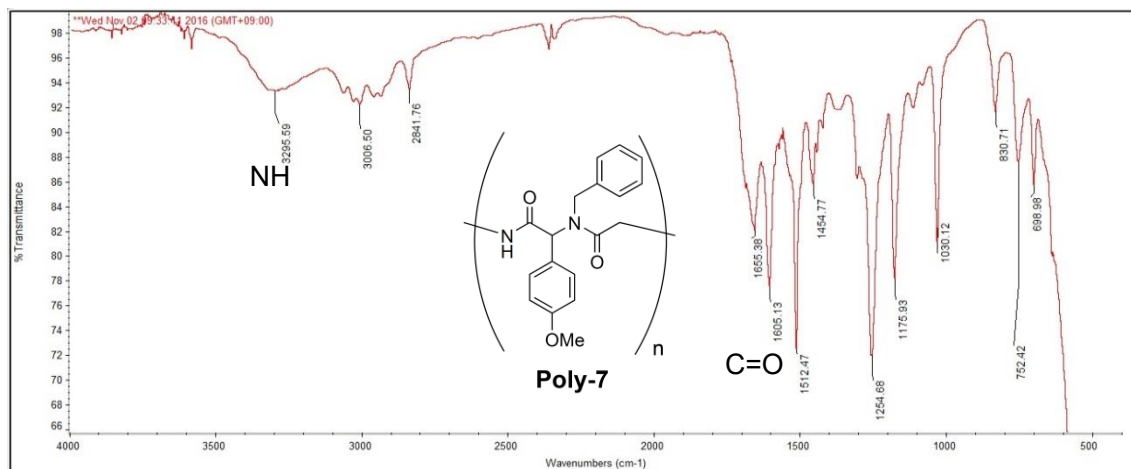
**Figure S37.**  $^1\text{H}$  NMR spectrum of **Poly-7** (400 MHz,  $\text{CDCl}_3$ , 298 K).



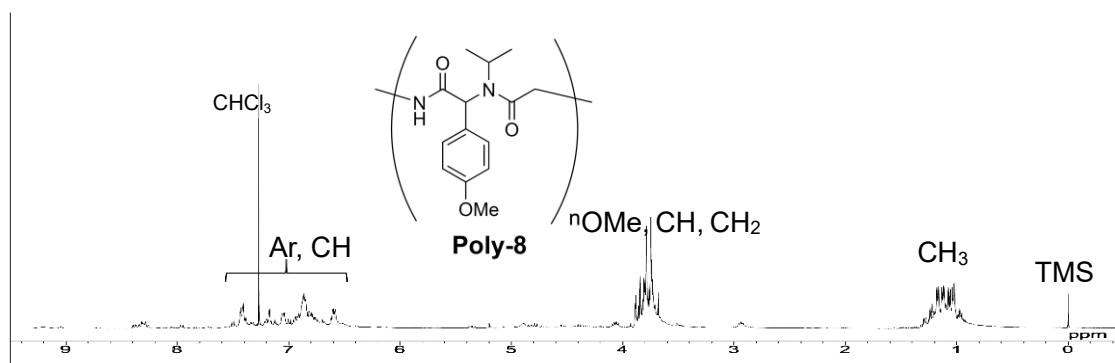
**Figure S38.**  $^{13}\text{C}$  NMR spectrum of **Poly-7** (100 MHz,  $\text{CDCl}_3$ , 298 K).



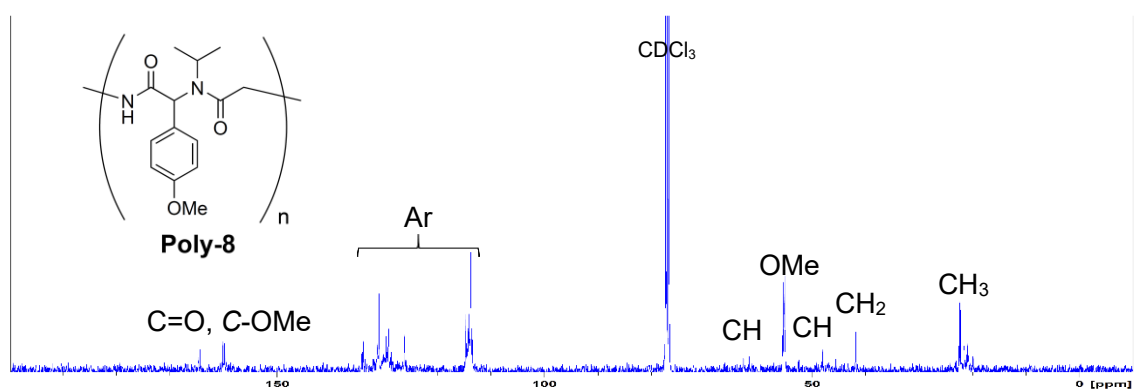
**Figure S39.** DOSY correlations of **Poly-7** (400 MHz,  $\text{CDCl}_3$ , 298 K).



**Figure S40.** IR spectrum of **Poly-7** (NaCl).

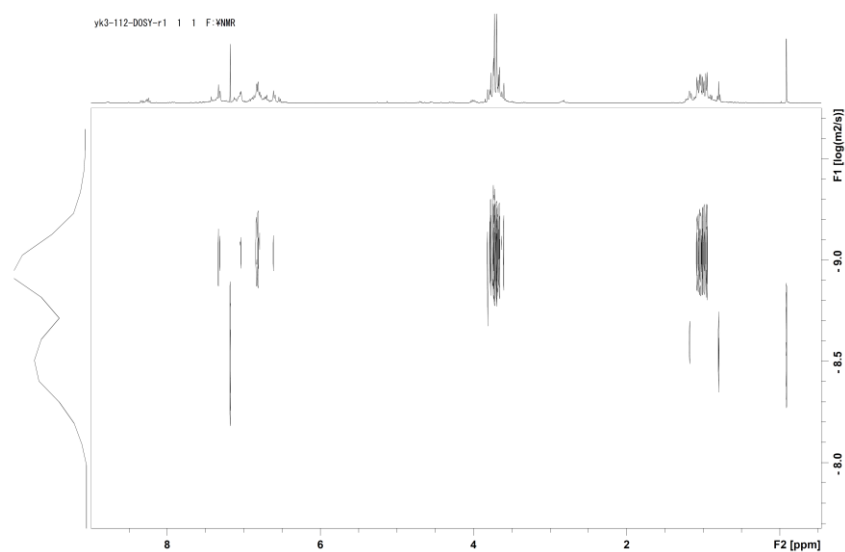


**Figure S41.**  $^1\text{H}$  NMR spectrum of **Poly-8** (400 MHz,  $\text{CDCl}_3$ , 298 K).

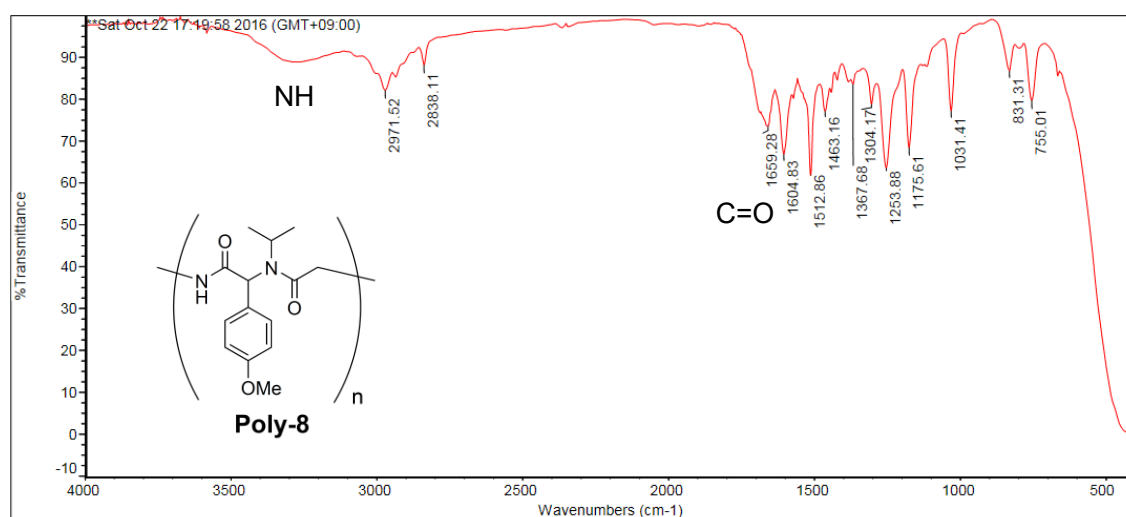


**Figure S42.**  $^{13}\text{C}$  NMR spectrum of **Poly-8** (100 MHz,  $\text{CDCl}_3$ , 298 K).

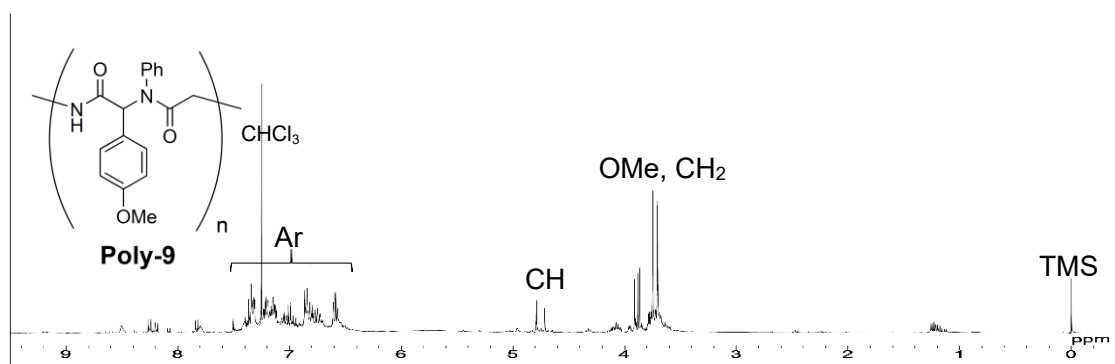




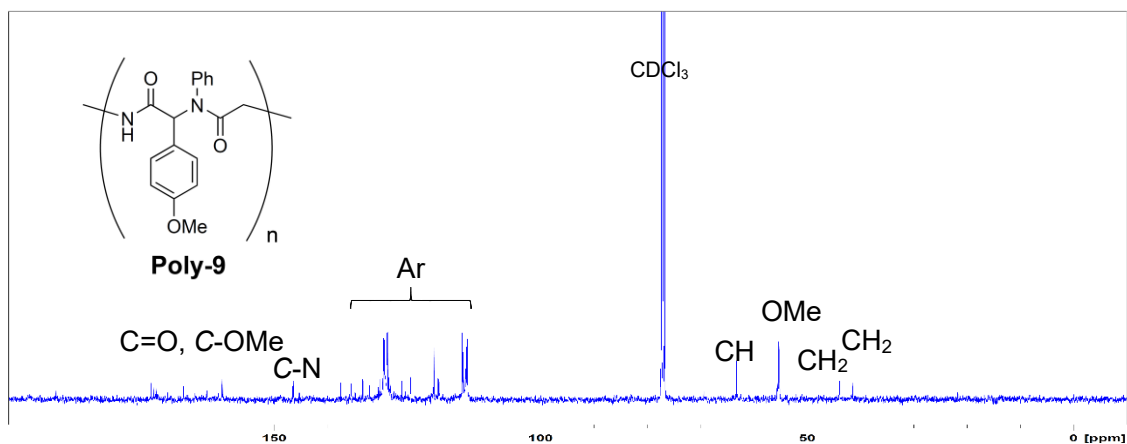
**Figure S43.** DOSY correlations of **Poly-8** (400 MHz,  $\text{CDCl}_3$ , 298 K).



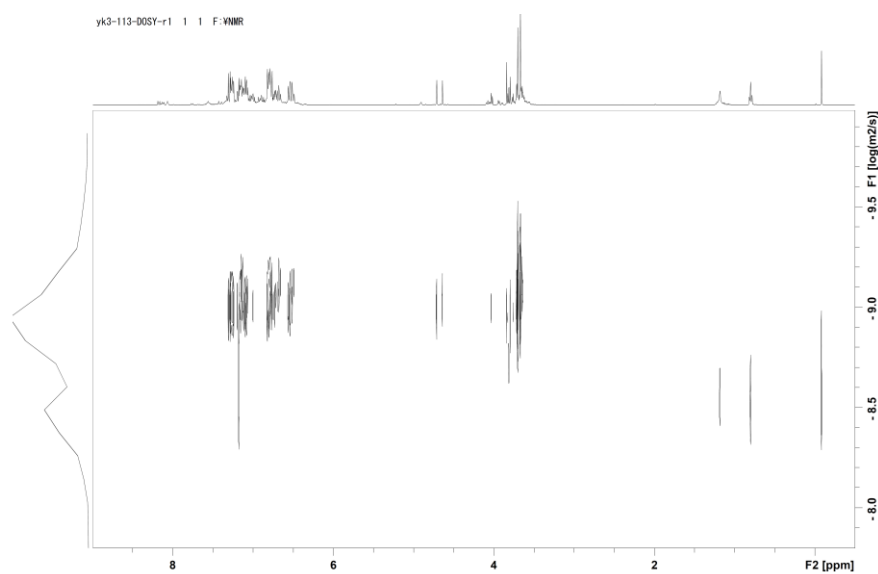
**Figure S44.** IR spectrum of **Poly-8** (NaCl).



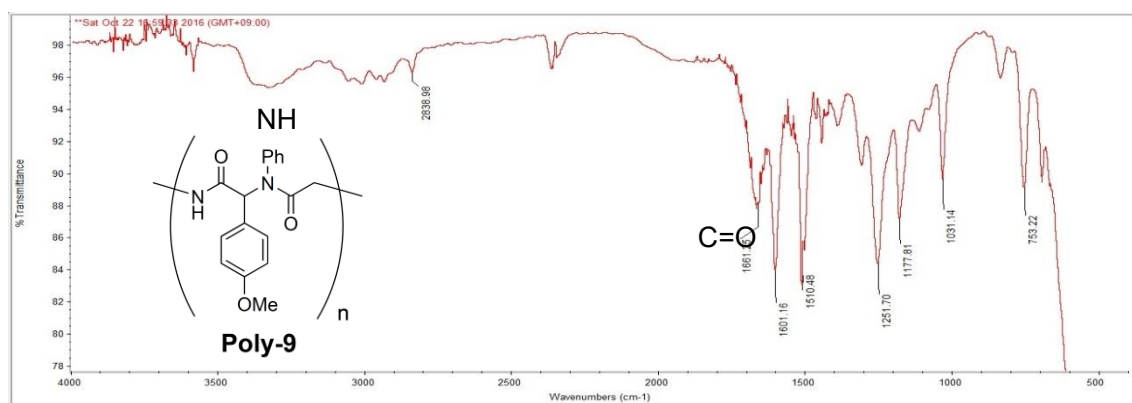
**Figure S45.**  $^1\text{H}$  NMR spectrum of **Poly-9** (400 MHz,  $\text{CDCl}_3$ , 298 K).



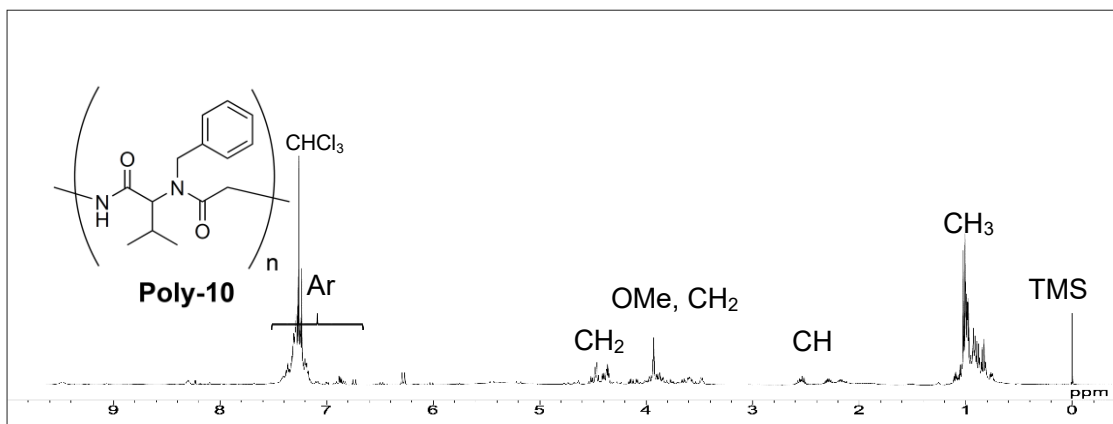
**Figure S46.**  $^{13}\text{C}$  NMR spectrum of **Poly-9** (100 MHz,  $\text{CDCl}_3$ , 298 K).



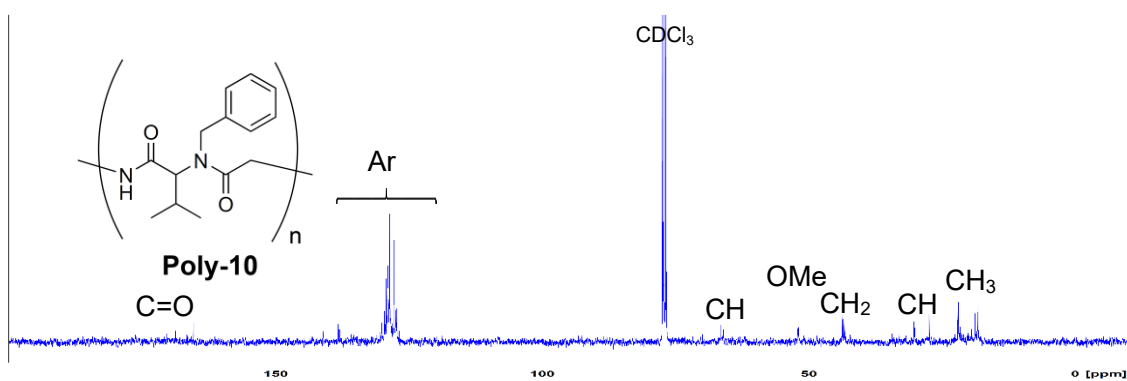
**Figure S47.** DOSY correlations of **Poly-9** (400 MHz,  $\text{CDCl}_3$ , 298 K).



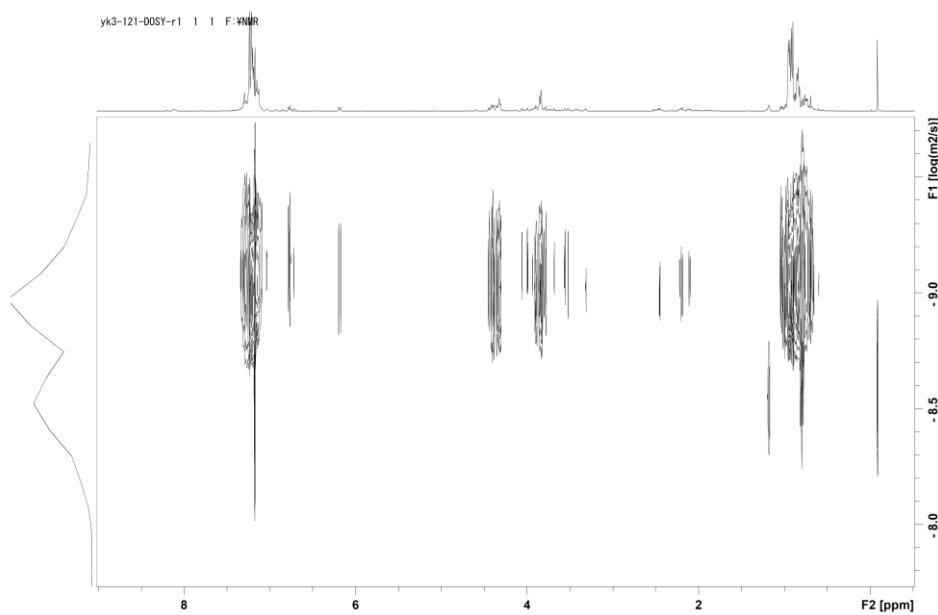
**Figure S48.** IR spectrum of **Poly-9** (NaCl).



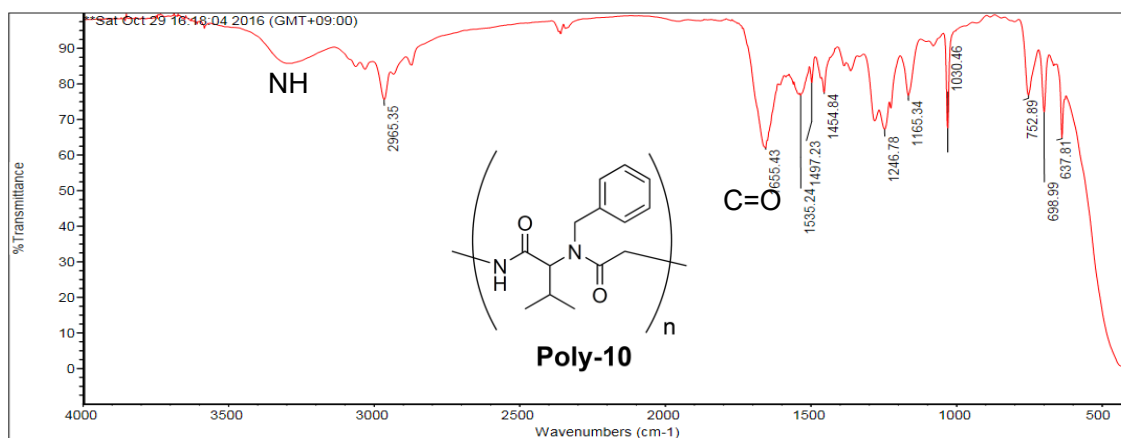
**Figure S49.**  $^1\text{H}$  NMR spectrum of **Poly-10** (400 MHz,  $\text{CDCl}_3$ , 298 K).



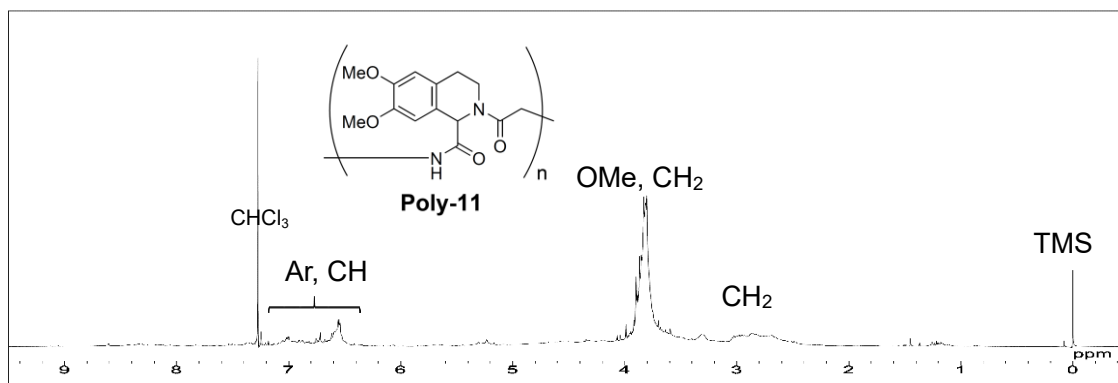
**Figure S50.**  $^{13}\text{C}$  NMR spectrum of **Poly-10** (100 MHz,  $\text{CDCl}_3$ , 298 K).



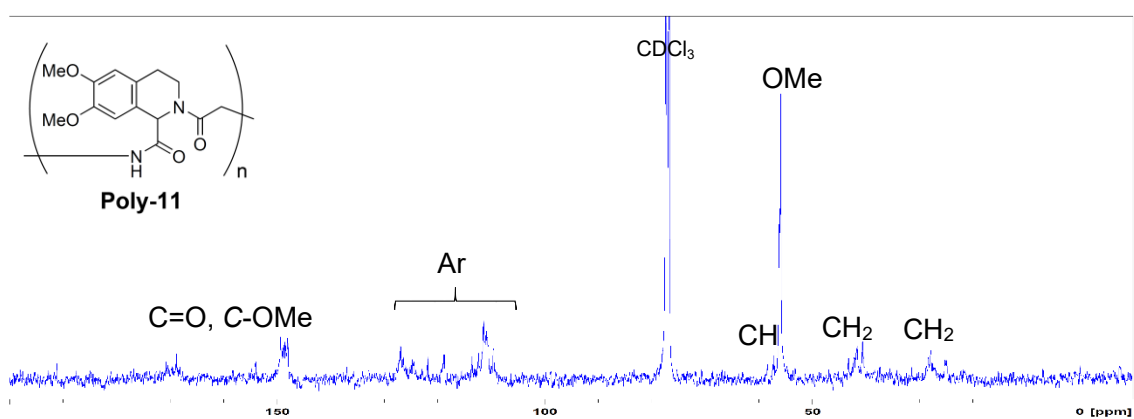
**Figure S51.** DOSY correlations of **Poly-10** (400 MHz,  $\text{CDCl}_3$ , 298 K).



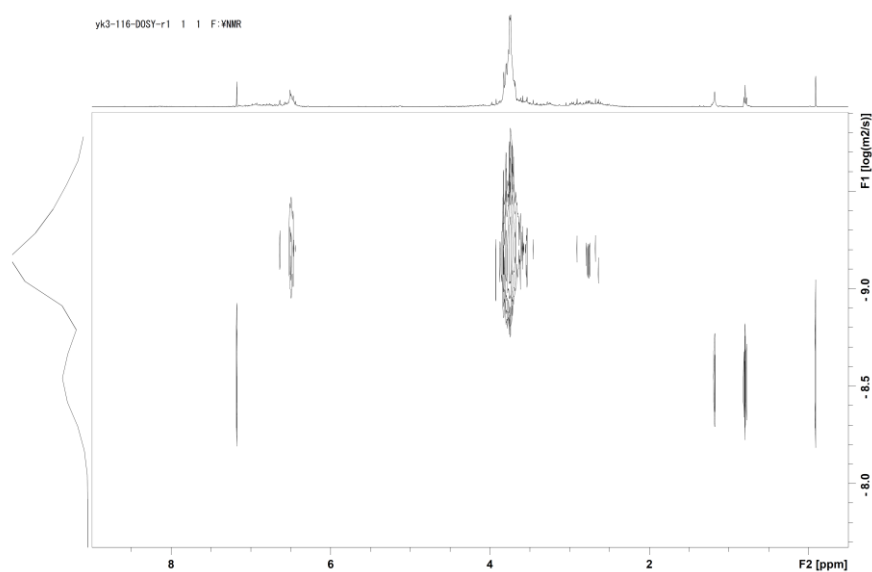
**Figure S52.** IR spectrum of Poly-10 (NaCl).



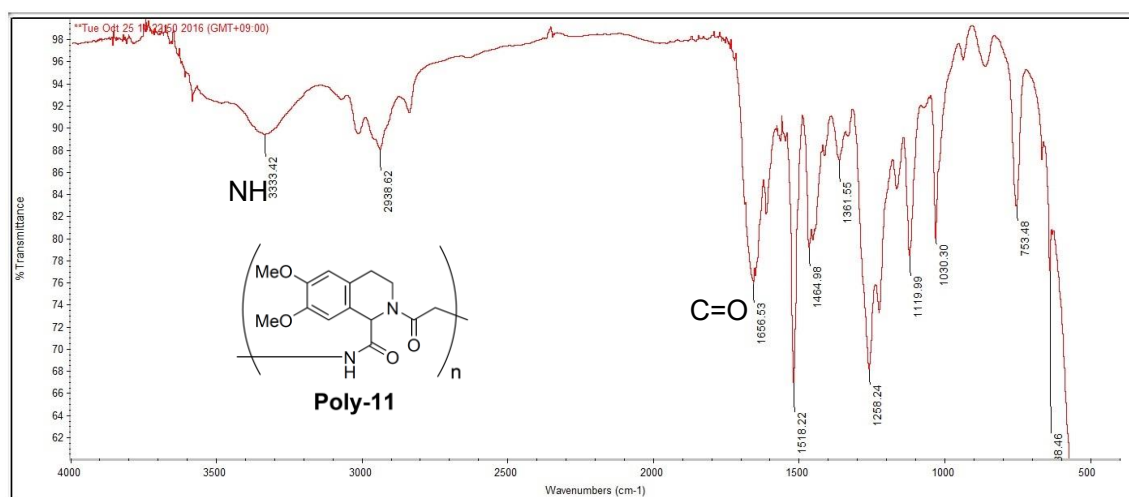
**Figure S53.** <sup>1</sup>H NMR spectrum of Poly-11 (400 MHz, CDCl<sub>3</sub>, 298 K).



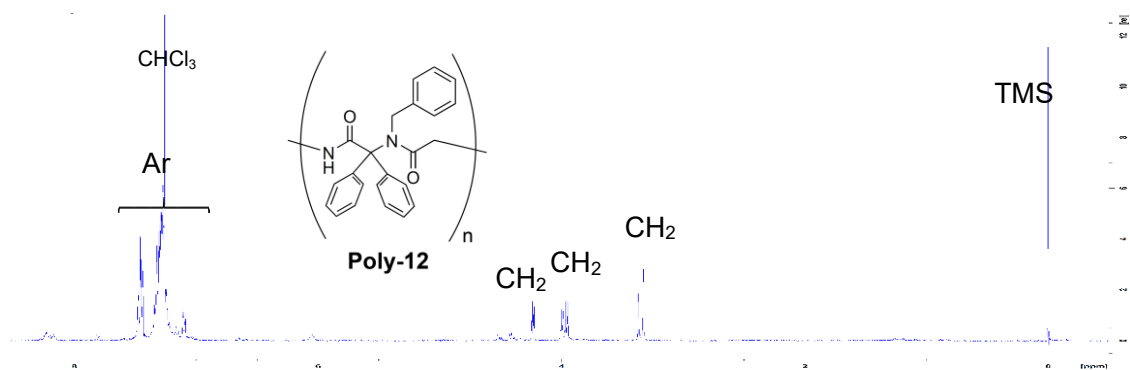
**Figure S54.** <sup>13</sup>C NMR spectrum of Poly-11 (100 MHz, CDCl<sub>3</sub>, 298 K).



**Figure S55.** DOSY correlations of **Poly-11** (400 MHz,  $\text{CDCl}_3$ , 298 K).



**Figure S56.** IR spectrum of **Poly-11** (NaCl).



**Figure S57.**  $^1\text{H}$  NMR spectrum of **Poly-12** (400 MHz,  $\text{CDCl}_3$ , 298 K).

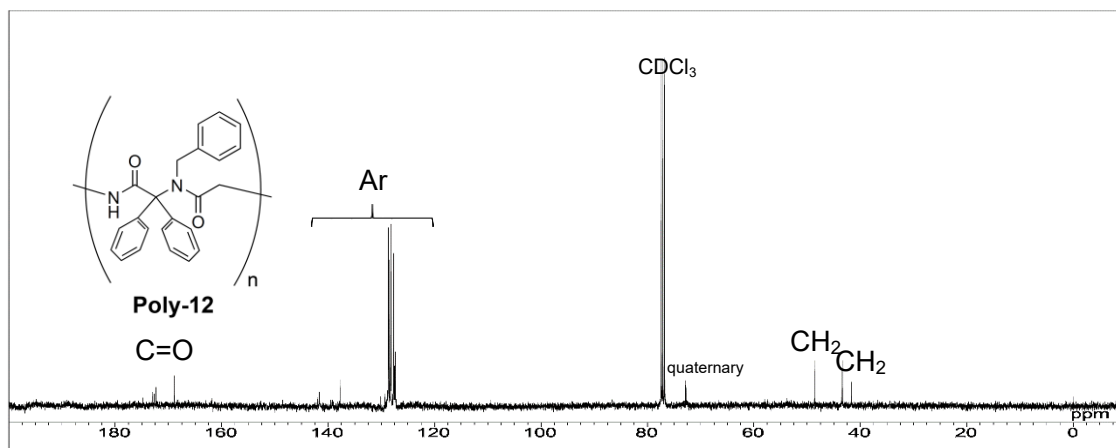


Figure S58. <sup>13</sup>C NMR spectrum of **Poly-12** (100 MHz, CDCl<sub>3</sub>, 298 K).

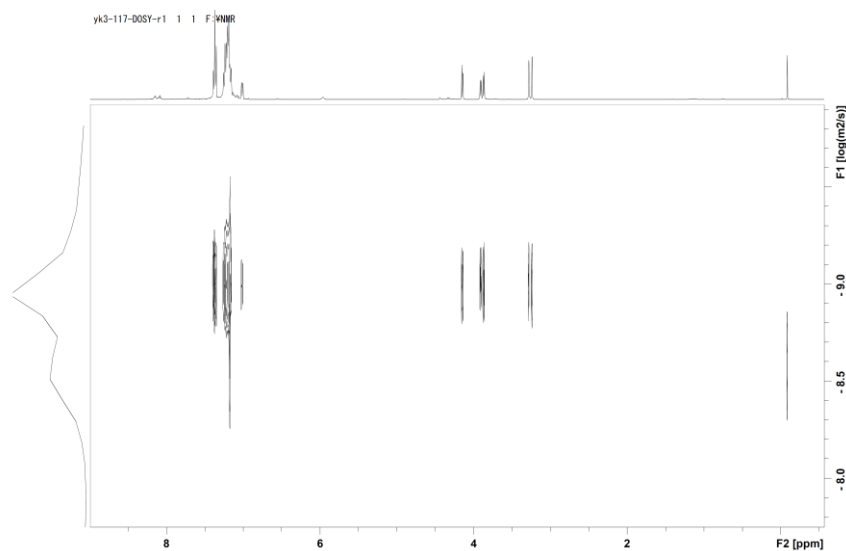


Figure S59. DOSY correlations of **Poly-12** (400 MHz, CDCl<sub>3</sub>, 298 K).

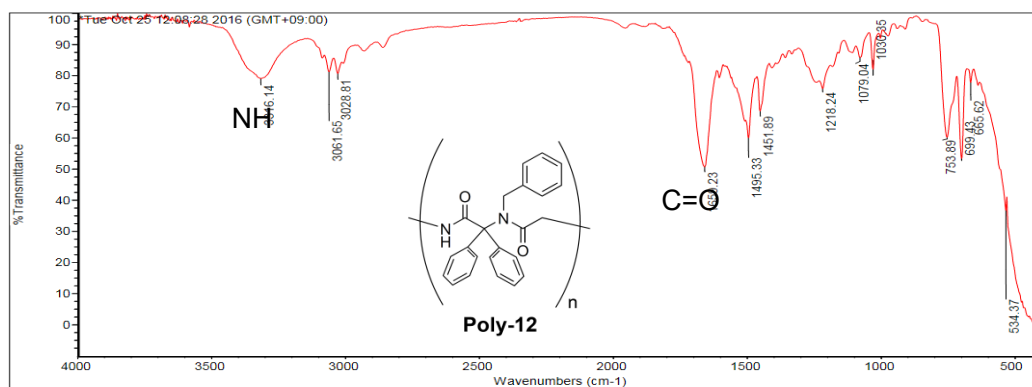
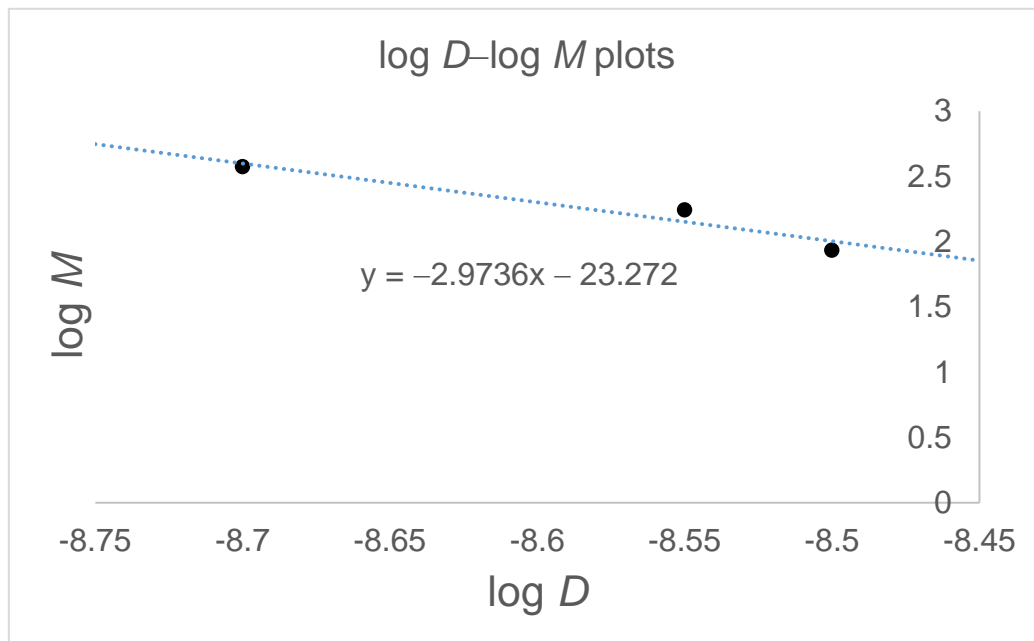


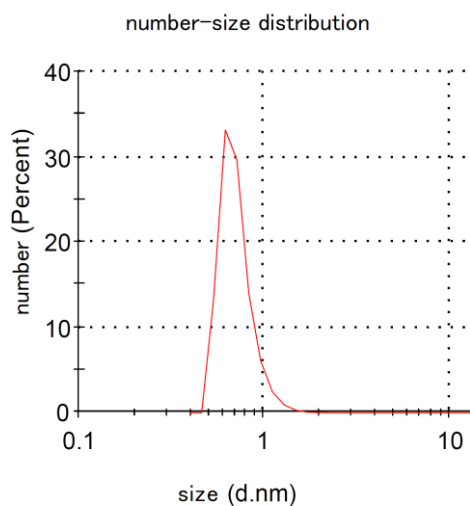
Figure S60. IR spectrum of **Poly-12** (NaCl).

**Calibration curve in  $\text{CDCl}_3$  for  $M_w$  prediction**

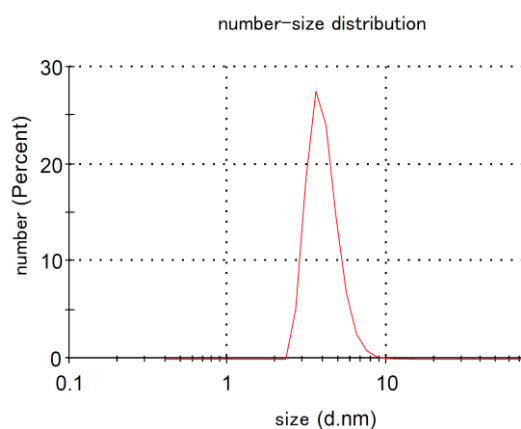


**Figure S61.** Calibration curve in  $\text{CDCl}_3$  for  $M_w$  prediction using **6** (MW: 376.45, log D: -8.70), **5** (MW: 175.23, log D: -8.55), and hexane (MW: 86.18, log D: -8.50) as standards.

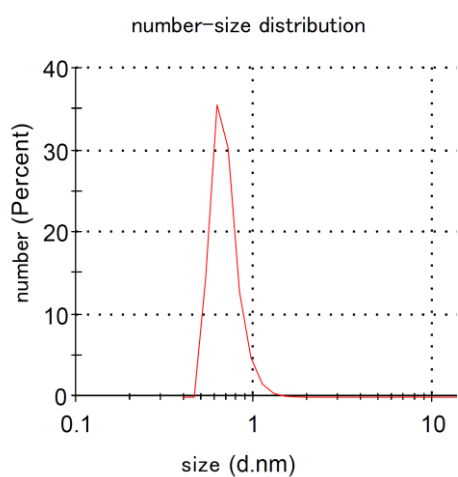
**Hydrodynamic diameters of polymers obtained by DLS measurements.**



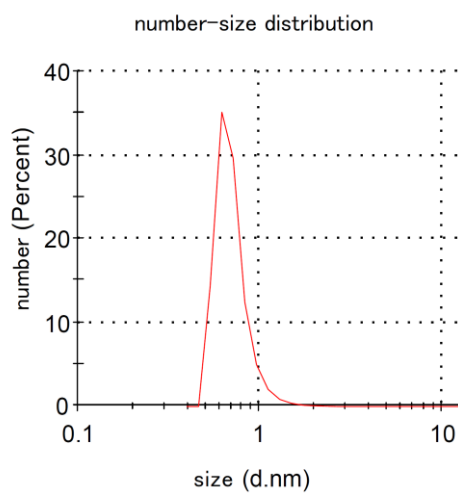
**Figure S62.** DLS profile of **Poly-5a**.



**Figure S63.** DLS profile of **Poly-5b**.

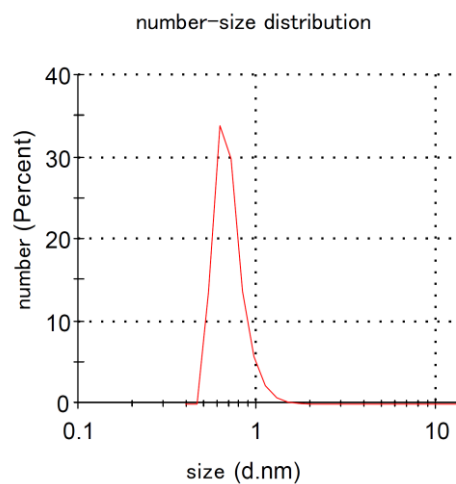


**Figure S64.** DLS profile of **Poly-7**.

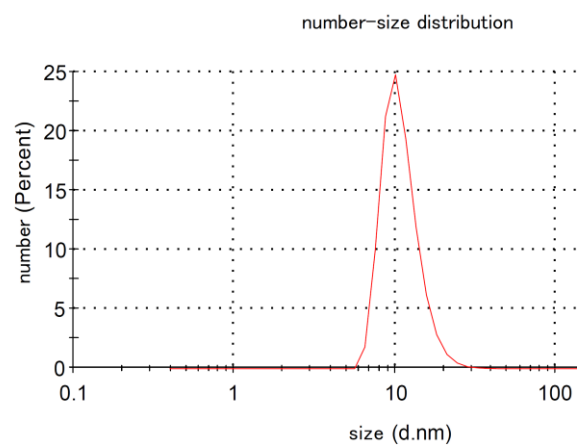


**Figure S65.** DLS profile of **Poly-8**.

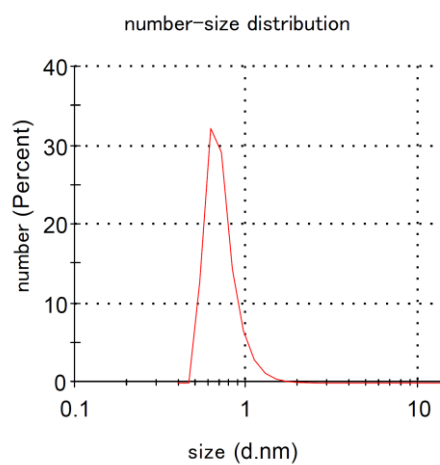




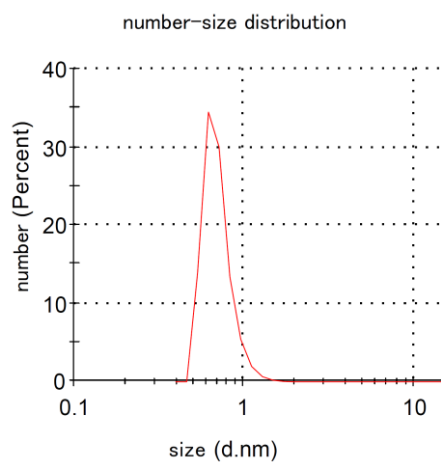
**Figure S66.** DLS profile of **Poly-9**.



**Figure S67.** DLS profile of **Poly-10**.



**Figure S68.** DLS profile of **Poly-11**.



**Figure S69.** DLS profile of **Poly-12**.

#### References

1. (a) S. W. Provencher, *Comp. Phys. Commun.* **1982**, *27*, 213. (b) S. W. Provencher, *Comp. Phys. Commun.* **1982**, *27*, 229.
2. (a) R. J. Spandl, H. Rudyk, D. R. Spring, *Chem. Commun.* **2008**, *44*, 3001. (b) B. R. Galan, K. P. Kalbarczyk, S. Szczepankiewicz, J. B. Keister, S. T. Diver, *Org. Lett.* **2007**, *9*, 1203. (c) D. Bonne, M. Dekhane, J. Zhu, *Org. Lett.* **2004**, *6*, 4771.