Polymer-immobilized Catalyst for Asymmetric Hydrogenation of Racemic α-(*N*-Benzoyl-*N*-Methylamino)Propiophenone

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Experimental section

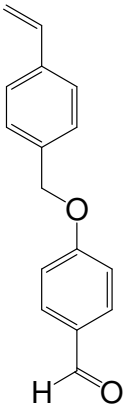
Divinylbenzene (96 %) was obtained from Nippon Steel Chemical Co., Ltd. DMF, ethylene glycol dimethacylate (EGDMA), methyl methacrylate (MMA) and *N*-isopropylacrylamide (NIPAM) were distilled over calcium hydride under reduced pressure prior to use. 2-hydroxyethyl methacrylate (HEMA) was vacuum distilled (71 °C, 2 mmHg) and washed with hexane twice. Styrene was washed with aqueous sodium hydroxide and aqueous sodium thiosulphate and then distilled under reduced pressure over calcium hydride. Radical initiator, 2,2'-Azobis(isobutyronitrile) (AIBN) was purified by recrystallization from anhydrous methanol at least three times. THF was distilled over sodium metal in the presence of benzophenone.

Optical rotations were measured with a 10 cm thermostat microcell. ^{1}H-NMR and ^{13}C-NMR spectra were taken at 300 MHz and 725 MHz, respectively. Chemical shift values are expressed in ppm relative to internal TMS and the *J* values were recorded in Hertz.

Preparation of 3d

1. **Synthesis of 4-(4-vinylbenzyloxy)benzaldehyde**

(4-4)-1

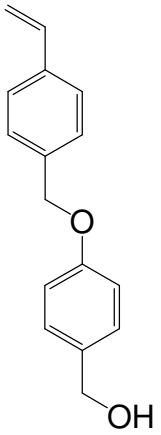


A 200 mL round bottomed flask was equipped with reflux condenser, magnetic stirrer and charged with 5 g (40.9 mmol) of *p*-hydroxybenzaldehyde, 5.66 g (40.9 mmol) of potassium carbonate, 6.4 mL (44.99 mmol) of *p*-vinylbenzylchloride and 100 mL of acetonitrile. A few milligrams of 1,1-diphenyl-2-picrylhydrazyl free radical was also added to the mixture. The mixture was stirred and

heated (50 ^{o}C) for 48 h. After cooling down to room temperature, the mixture was filtered to remove salts and washed with dichloromethane. The filtrate was evaporated under reduced pressure and the residue extracted with dichloromethane and water. Combined organic layers were dried over magnesium sulphate and evaporated under reduced pressure to give crude product. Desired product **(4-4)-1** was obtained by purification with column chromatography.
[hexane:ethylacetate; 3:1. R_f 4-(4-vinylbenzyloxybenzaldehyde) = 0.52] Yield (77 %).
^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 5.10 (s, 2H; OCH_2), 5.26 (d, *J* = 11.7 Hz, 1H; vinyl), 5.76 (d, *J* = 18.3 Hz, 1H; vinyl), 6.72 (dd, *J* = 10.8, 10.5 Hz, 1H; vinyl), 7.24 (d, *J* = 9.3 Hz, 2H; Ar-H), 7.3 – 7.5 (m, 6H; Ar-H), 9.96 (s, 1H; COH).

2. Synthesis of 4-(4-vinylbenzyloxy)benzylalcohol

(4-4)-2

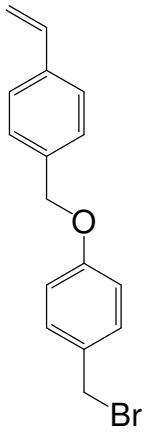


A 100 mL round-bottomed flask was charged with stirrer, 6.5 g (27.2 mmol) of **(4-4)-1**, dried and flushed with argon gas and then charged with 40 mL of ethanol, 20 mL of THF, 1.54 g (40.8 mmol) of sodium borohydride under inert conditions (nitrogen gas) at 0 ^{o}C. The mixture was stirred for 24 h. After the reaction was complete, drop-wise addition of 2N HCl was performed to decompose excess sodium borohydride while stirring. The solution was evaporated and the residue extracted with dichloromethane and washed with water. Combined organic phases were dried over magnesium sulphate and concentrated to give desired product **(4-4)-2**.
[hexane:ethylacetate; 3:1. R_f 4-(4-vinylbenzyloxybenzylalcohol) = 0.25] Yield (94 %).

^{1}HNMR (300 MHz, $CDCl_3$, TMS): δ = 4.65 (d, *J* = 5.1 Hz, 2H; CH_2OH), 5.10 (s, 2H; OCH_2), 5.26 (d, *J* = 11.7 Hz, 1H; vinyl), 5.76 (d, *J* = 18.3 Hz, 1H; vinyl), 6.72 (dd, *J* = 11.1, 10.8 Hz, 1H; vinyl), 7.24 (d, *J* = 9.3 Hz, 2H; Ar-H), 7.2 – 7.5 (m, 6H; Ar-H).

3. Synthesis of 4-(4-vinylbenzyloxy)benzyl bromide

(4-4)-3

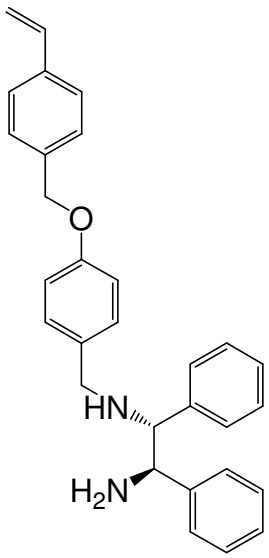


A 200 mL round-bottomed flask was charged with stirrer, 2 g (8.3 mmol) of **(4-4)-2**, dried and flushed with argon gas and then charged with 80 mL THF at O ^oC under inert conditions. Once the alcohol dissolved, 4.3 g (12.5 mmol) of carbon tetrabromide and 3.3 g (12.5 mmol) of triphenylphosphine were added. The mixture was stirred at O ^oC for 1 h, then at room temperature for 20 h. The solution was poured into water and extracted with ether. The organic phases were combined, dried over magnesium sulphate and concentrated. The residue was purified by column chromatography to give **(4-4)-3**.

[hexane:acetone; 3:1. R_f 4-(4-vinylbenzyloxybenzyl bromide) = 0.55] Yield (90%).

^{1}HNMR (300 MHz, $CDCl_3$, TMS): δ = 4.50 (s, 2H; CH_2Br), 5.10 (s, 2H; OCH_2), 5.26 (d, *J* = 11.7 Hz, 1H; vinyl), 5.76 (d, *J* = 18.3 Hz, 1H; vinyl), 6.72 (dd, *J* = 11.1, 10.8 Hz, 1H; vinyl), 6.93 (d, *J* = 8.7 Hz, 2H; Ar-H), 7.2 – 7.5 (m, 6H; Ar-H).

4. Synthesis of 4-(4-vinylbenzyloxy)benzyl diamine monomer

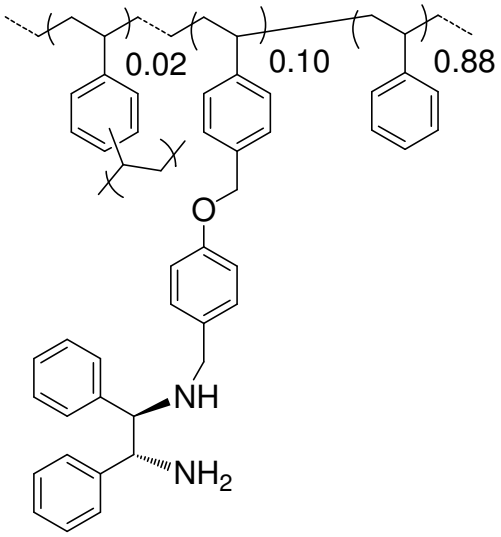


3d

A 100 mL round-bottomed flask equipped with stirrer, 0.5 g (1.65 mmol) of **(4-4)-3**, 0.88 g (4.13 mmol) of (*R,R*)-1,2-diphenylethylenediamine and a few milligrams of radical inhibitor was dried and flushed with argon. The flask was then charged with 5 mL of dried DMF under nitrogen atmosphere at 0 °C. The mixture was stirred for 2 h in the absence of light and then extracted with ether, washed with water and the aqueous phase further extracted twice. The combined organic phase was dried over magnesium sulphate, concentrated and purified by column chromatography. [chloroform:methanol = 8:1, R_f = 0.56]. Yield (71%).

^{1}HNMR (300 MHz, $CDCl_3$, TMS): δ = 1.96 (s, 3H; NH_2, NH), 3.39 (d, *J* = 9.9 Hz, 1H; CH_2NH), 3.60 (d, *J* = 9.9 Hz, 1H; CH_2NH), 3.73 (d, *J* = 5.4 Hz, 1H; $CHNH_2$), 3.98 (d, *J* = 5.4 Hz, 1H; CHNH), 5.02 (s, 2H; OCH_2), 5.25 (d, *J* = 8.1 Hz, 1H; vinyl), 5.75 (d, *J* = 13.2 Hz, 1H; vinyl), 6.72 (dd, *J* = 11.1, 10.8 Hz, 1H; vinyl), 6.87 (d, *J* = 6.3 Hz, 2H; Ar-H), 7.0 – 7.5 (m, 16H; Ar-H); IR (KBr): *v* = 3350, 3294 cm^{-1} (NH_2), 3160 cm^{-1} (NH), 3083, 3023 cm^{-1} ($CH=CH_2$), 2920 cm^{-1} (CH), 1612 cm^{-1} (NH bend), 1110 cm^{-1} (CO); Mp: 107 – 113 °C; Elem. Anal. Calcd. for $C_{30}H_{30}N_2O$: C, 82.91%; H, 6.96%; N, 6.45%. Found: C, 83.11%; H, 6.85%; N, 6.49%.

Preparation of 4a

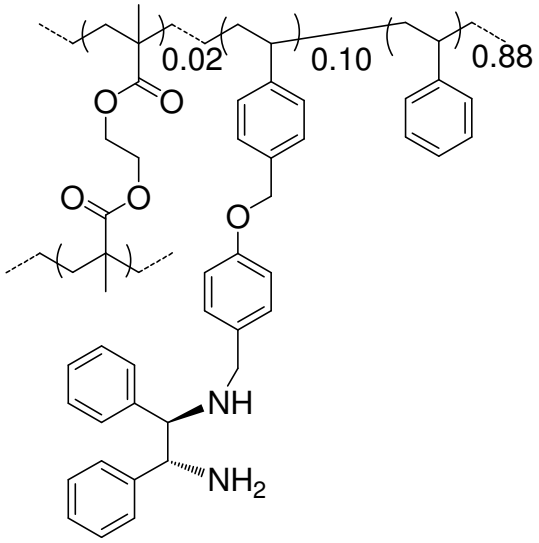


4a

An ampoule charged with stirrer, **3d** (0.2 g, 0.46 mmol), styrene (0.422 g, 0.47 mL), AIBN (0.019 g), Divinylbenzene (0.012 g, 0.013 mL) and 1.5 mL of dry DMF, was degassed under three vacuum freeze-thaw cycles and sealed. The mixture was then stirred and heated at 70 °C for 24 h after gel formation. The ampoule was opened and the yellow polymer formed was washed with methanol and THF over a glass filter and dried *in vacuo*.

Elem. Anal. Calcd. for $(C_8H_8)_{0.88}(C_{10}H_{10})_{0.02}(C_{30}H_{30}N_2O)_{0.10}$: C, 85.45%; H, 9.06%; N, 3.50%. Found: C, 87.18%; H, 9.96%; N, 3.92%.

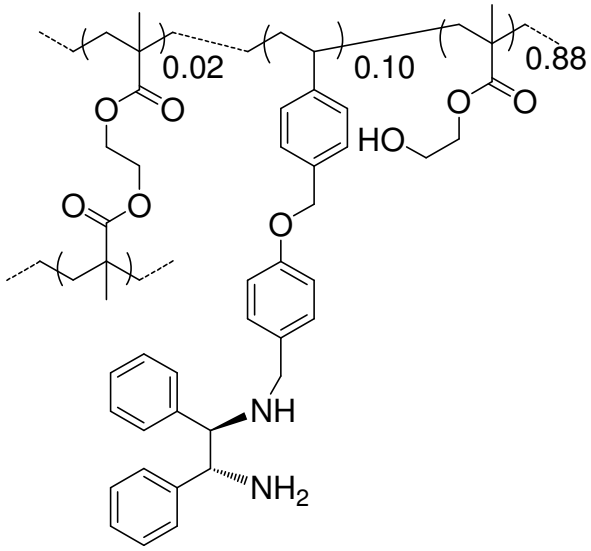
Preparation of 4b



4b

An ampoule charged with stirrer, **3d** (0.1 g, 0.23 mmol), styrene (0.21 g, 2.02 mmol), AIBN (0.016 g), EGDMA (0.0091 g, 0.046 mmol) and 1.5mL of dry DMF, was degassed under three vacuum freeze-thaw cycles and sealed. The mixture was then stirred and heated at 70 °C for 48 h. The ampoule was opened and the resulting mixture was poured into methanol. A pale yellow polymer was obtained by washing with methanol and THF over a glass filter and dried *in vacuo*.
^{1}HNMR (300MHz, $CDCl_3$, TMS): δ = 6.8-7.6 (br; Ar-H); Elem. Anal. Calcd. for $(C_{10}H_{14}O_4)_{0.02}$ $(C_{30}H_{30}N_2O)_{0.10}$ $(C_8H_8)_{0.88}$: C, 79.05%; H, 8.69%; N, 3.18%. Found: C, 77.95%; H, 9.77%; N, 4.00%.

Preparation of 4c

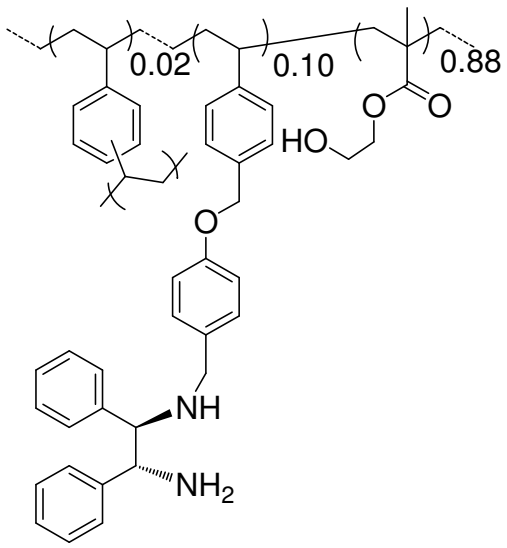


4c

An ampoule charged with stirrer, **3d** (0.1 g, 0.23 mmol), HEMA (0.264 g, 2.025 mmol), AIBN (0.018 g), EGDMA (0.0091 g, 0.046 mmol) and 1mL of dry DMF, was degassed under three vacuum freeze-thaw cycles and sealed. The mixture was then stirred and heated at 70 °C for 24 h after gel formation. The ampoule was opened and the yellow polymer formed was washed with methanol and THF over a glass filter and dried *in vacuo*.

^{1}HNMR (300MHz, $CDCl_3$, TMS): δ = 0.8-1.8 (br; CH_2, CH), 2.7-3.3 (br; N-CH_2), 3.3-4.3 (br; CH_2), 6.5-7.9 (br; Ar-H); IR (KBr): ν = 3448 cm^{-1} (OH of HEMA); Elem. Anal. Calcd. for $(C_{10}H_{14}O_4)_{0.02}$ $(C_{30}H_{30}N_2O)_{0.10}$ $(C_6H_{10}O_3)_{0.88}$: C, 74.14%; H, 8.67%; N, 3.09%. Found: C, 72.94%; H, 7.58%; N, 2.70%.

Preparation of 4d

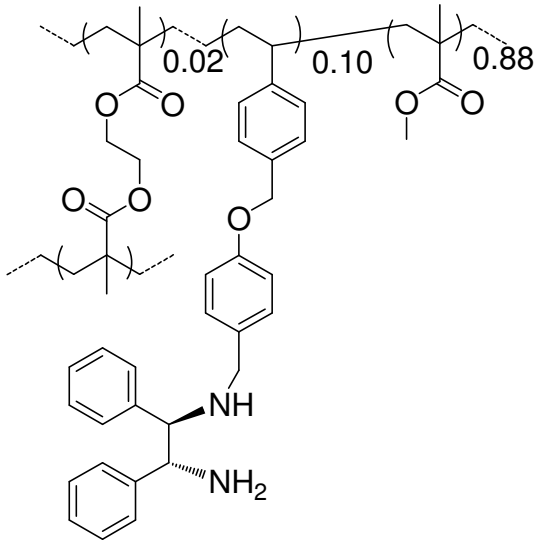


4d

An ampoule charged with stirrer, **3d** (0.15 g, 0.35 mmol), HEMA (0.4 g, 3.09 mmol), AIBN (0.028 g), DVB (0.0091 g, 0.07 mmol) and 1mL of dry DMF, was degassed under three vacuum freeze-thaw cycles and sealed. The mixture was then stirred and heated at 70 °C for 72 h. The ampoule was opened and the resulting mixture was poured into methanol. A pale yellow polymer was obtained by washing with methanol and THF over a glass filter and dried *in vacuo*.

Elem. Anal. Calcd. for $(C_{10}H_{10})_{0.02}$ $(C_{30}H_{30}N_2O)_{0.10}$ $(C_6H_{10}O_3)_{0.88}$: C, 79.86%; H, 9.02%; N, 3.39%. Found: C, 79.06%; H, 9.64%; N, 3.88%.

Preparation of 4e

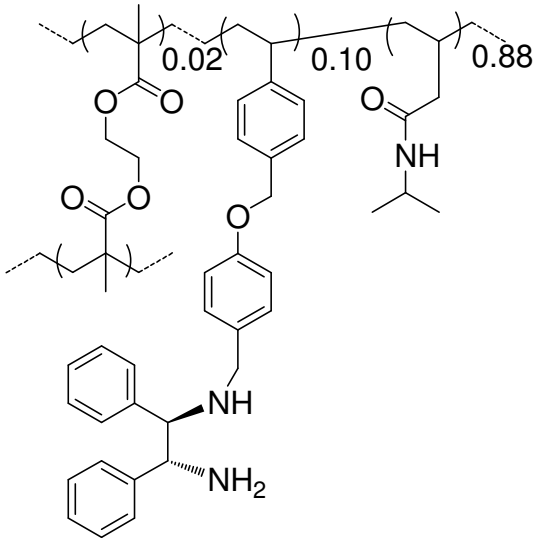


4e

An ampoule charged with stirrer, **3d** (0.12 g, 0.27 mmol), MMA (0.23 g, 2.33 mmol), AIBN (0.018 g), EGDMA (0.011 g, 0.053 mmol) and 1 mL of dry DMF, was degassed under three vacuum freeze-thaw cycles and sealed. The mixture was then stirred and heated at 70 °C for 24 h after gel formation. The ampoule was opened and the yellow polymer formed was washed with methanol and THF over a glass filter and dried *in vacuo*.

IR (KBr): ν = 1387 cm^{-1} (CH_3 of MMA); Elem. Anal. Calcd. for $(C_{10}H_{14}O_4)_{0.02}$ $(C_{30}H_{30}N_2O)_{0.10}$ $(C_5H_8O_2)_{0.88}$: C, 75.31%; H, 8.73%; N, 3.19%. Found: C, 66.95%; H, 7.72%; N, 2.21%.

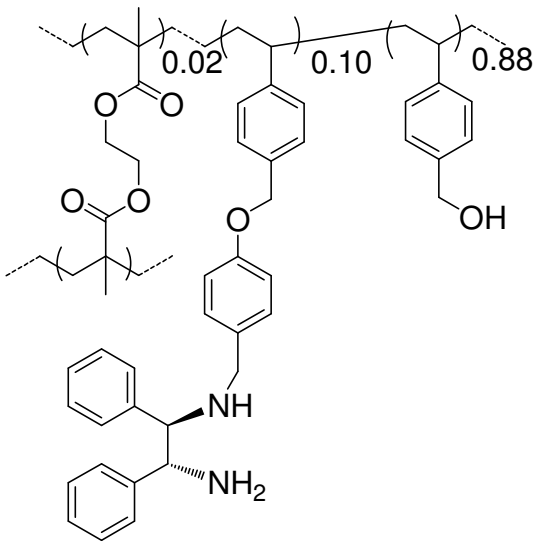
Preparation of 4f



4f

An ampoule charged with stirrer, **3d** (0.12 g, 0.27 mmol), NIPAM (0.26 g, 2.33 mmol), AIBN (0.02 g), EGDMA (0.015 g, 0.053 mmol) and 1.5 mL of dry DMF, was degassed under three vacuum freeze-thaw cycles and sealed. The mixture was then stirred and heated at 70 °C for 72 h. The ampoule was opened and the resulting mixture was poured into methanol. A yellow polymer was obtained by washing with methanol and THF over a glass filter and dried *in vacuo*.
^{1}H NMR (300MHz, $CDCl_3$, TMS): δ = 6.5-7.9 (br; Ar-H); IR (KBr): ν = 1387 cm^{-1} (CH_3 of NIPAM); Elem. Anal. Calcd. for $(C_{10}H_{14}O_4)_{0.02}$ $(C_{30}H_{30}N_2O)_{0.10}$ $(C_6H_{11}NO)_{0.88}$: C, 75.71%; H, 9.03%; N, 4.65%. Found: C, 69.85%; H, 8.36%; N, 5.41%.

Preparation of 4g



4g

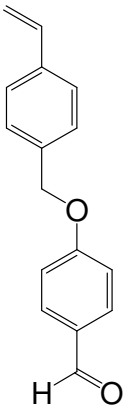
An ampoule charged with stirrer, **3d** (0.12 g, 0.27 mmol), 2-hydroxymethylstyrene (0.31 g, 2.33 mmol), AIBN (0.02 g), EGDMA (0.015 g, 0.053 mmol) and 1 mL of dry DMF, was degassed under three vacuum freeze-thaw cycles and sealed. The mixture was then stirred and heated at 70 °C for 72 h. The ampoule was opened and the resulting mixture was poured into methanol. A yellow polymer was obtained by washing with methanol and THF over a glass filter and dried *in vacuo*.

IR (KBr): ν = 3389 cm^{-1} (OH of 2-hydroxymethylstyrene); Elem. Anal. Calcd. for $(C_{10}H_{14}O_4)_{0.02}$ $(C_{30}H_{30}N_2O)_{0.10}$ $(C_9H_{10}O)_{0.88}$: C, 77.76%; H, 8.63%; N, 3.07%. Found: C, 76.79%; H, 9.54%; N, 3.37%.

Recycle of Polymer-supported catalyst

A 20 mL schlenk vessel equipped with magnetic stirrer was charged with chiral diamine ligand (0.015 mmol), $RuCl_2$/(*S*)-BINAP$(dmf)_n$ (0.007 g, 0.0075 mmol) and 1 mL of dry DMF. The mixture was degassed and heated at 80 °C for 2 h. DMF was removed under reduced pressure and the solid obtained transferred together with α-amide ketone (0.2 g, 0.75 mmol) to a 100 mL autoclave equipped with a pressure gauge and hydrogen gas inlet tube. The autoclave was flushed with argon to replace air after which a degassed solution of 1:1 mixture of 2-propanol (1 mL) / DMF (1 mL) and 1.0M *t*-BuOK solution in *t*-BuOH (0.075 mL) was added. Hydrogen was then introduced to the autoclave and pressurized to 1 MPa. The reaction mixture was stirred at room temperature until the reaction was complete. After carefully venting the hydrogen gas, alcohol product was easily separated from the catalyst by filtration for analysis. The same polymeric catalyst was then recharged into the autoclave for the next reaction, following the same procedure described above.

(4-4)-1



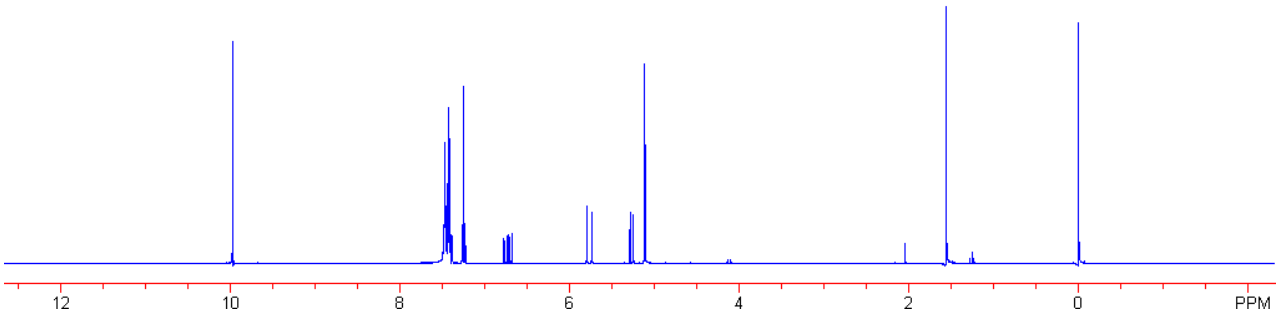


Figure S1. ^{1}H NMR spectrum of **(4-4)-1.**

(4-4)-2

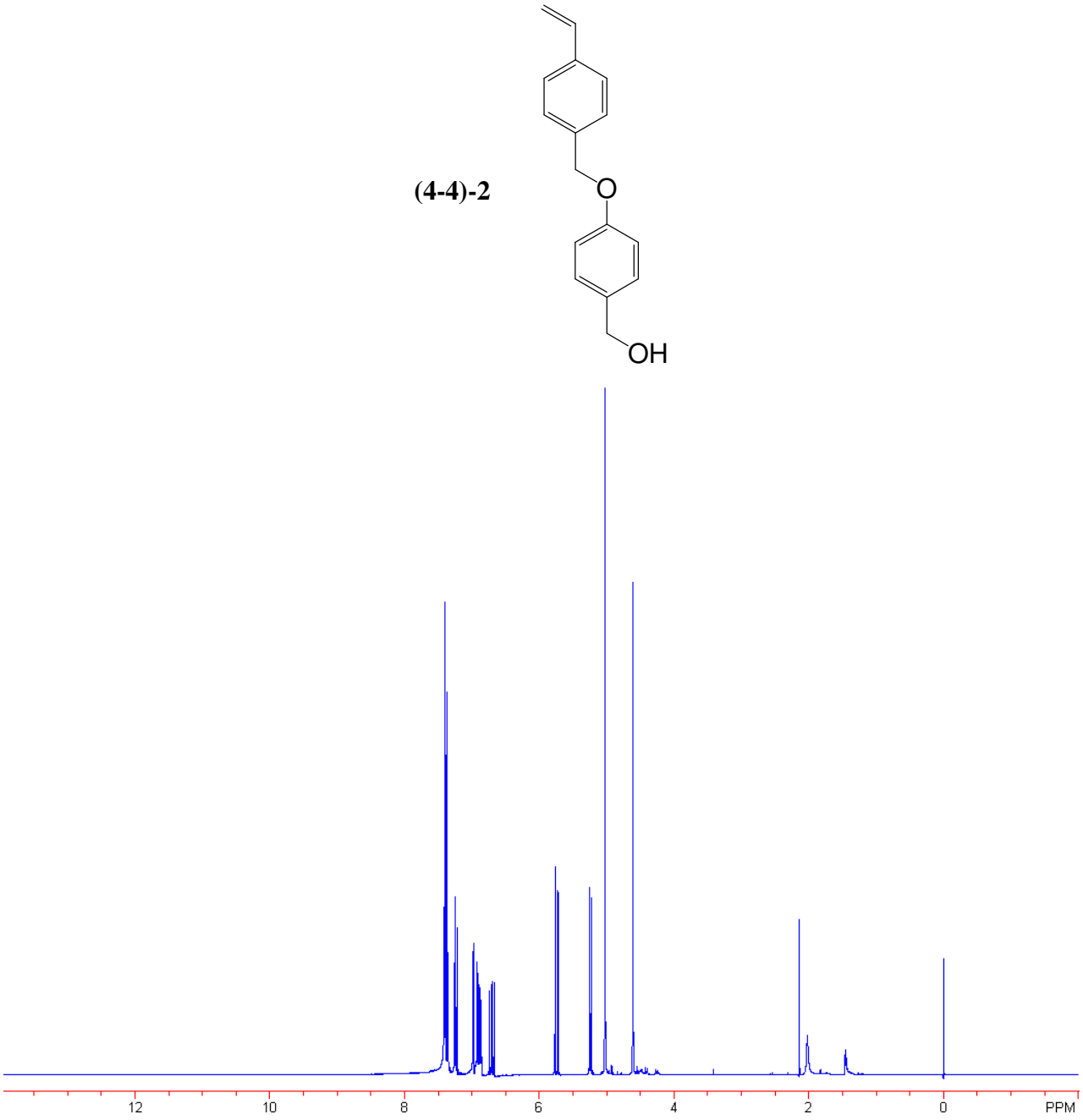


Figure S2. ^{1}H NMR spectrum of **(4-4)-2.**

(4-4)-3

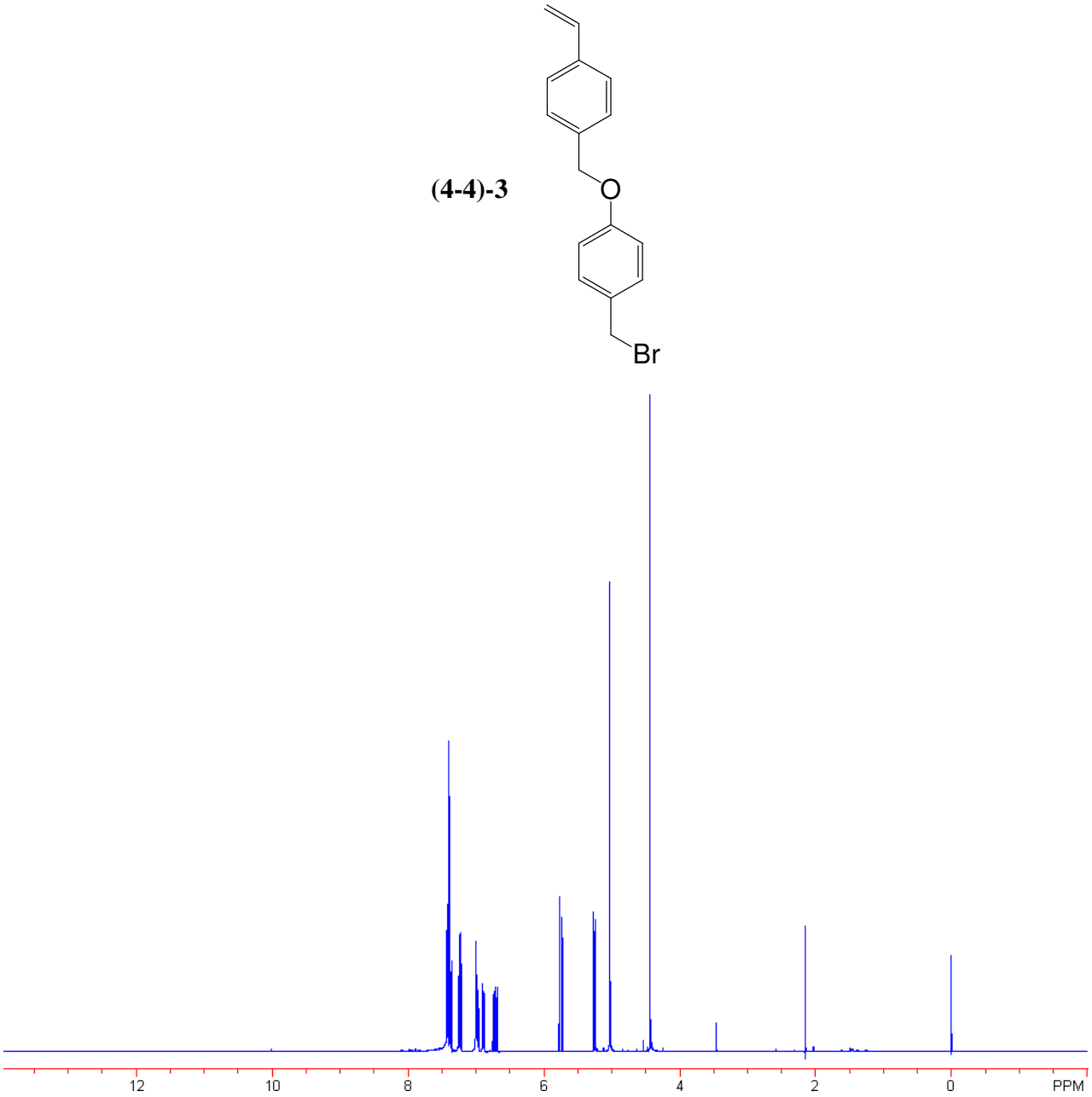


Figure S3. ^{1}H NMR spectrum of **(4-4)-3.**

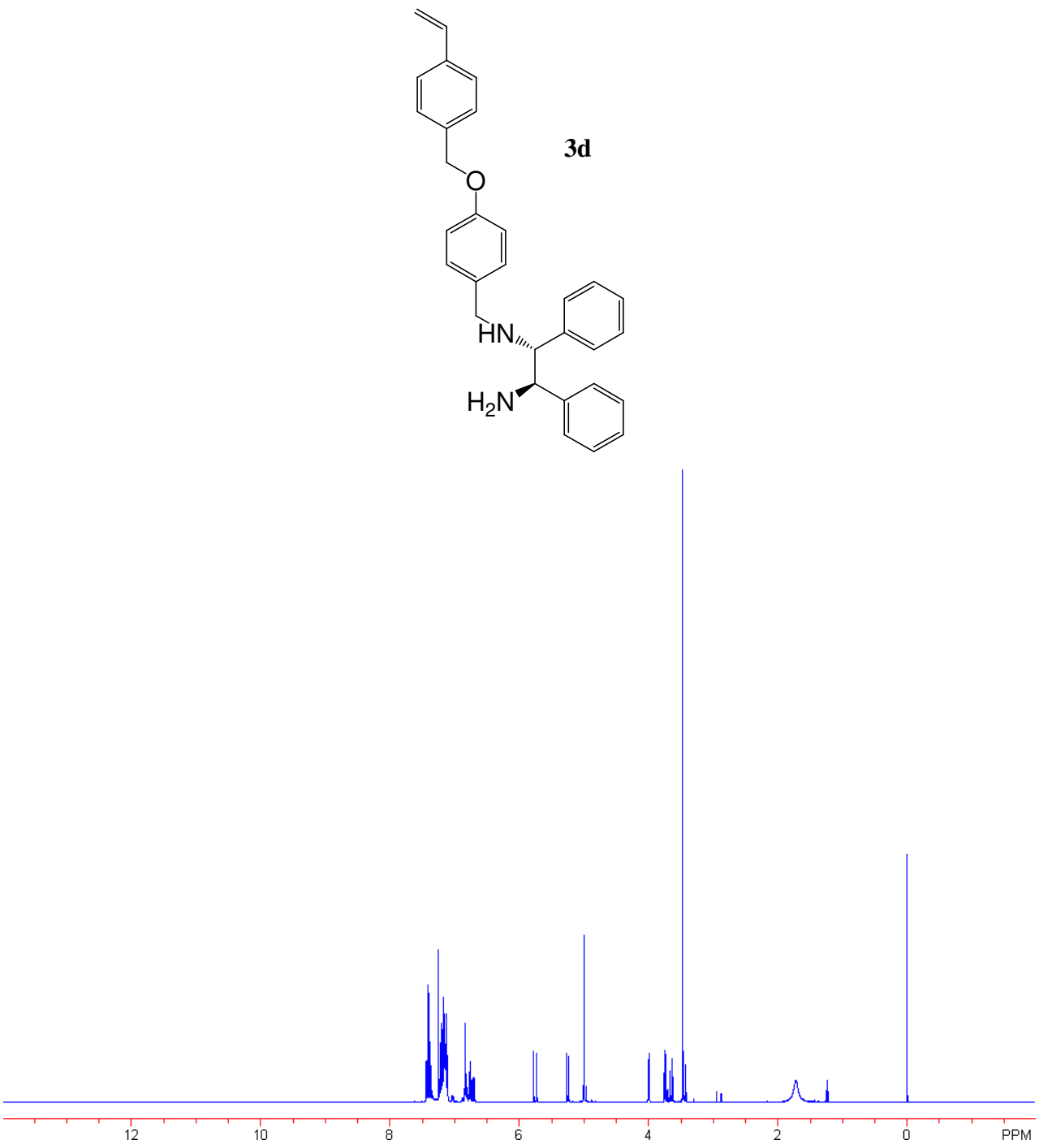
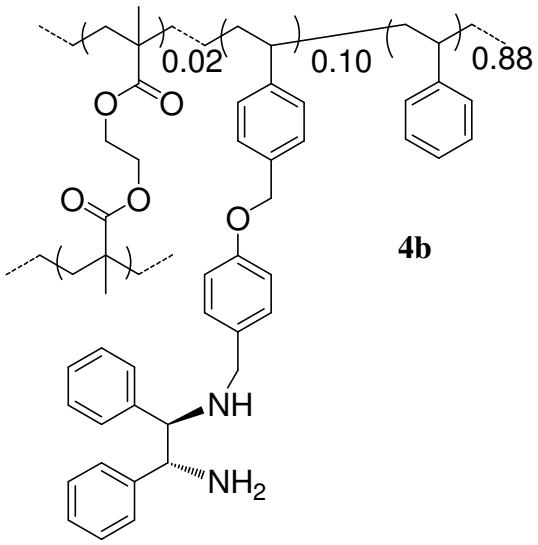


Figure S4. ^{1}H NMR spectrum of **3d.**



4b

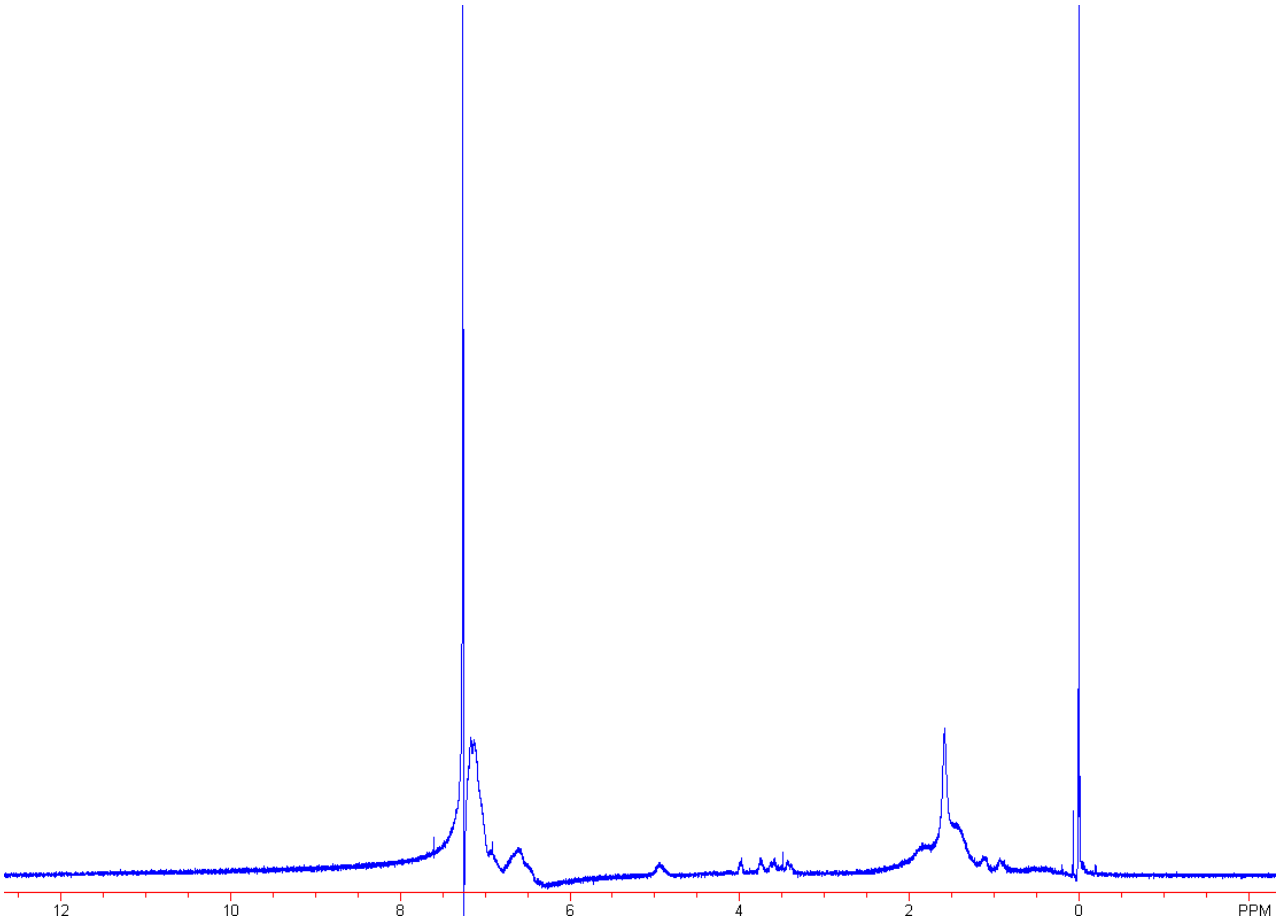
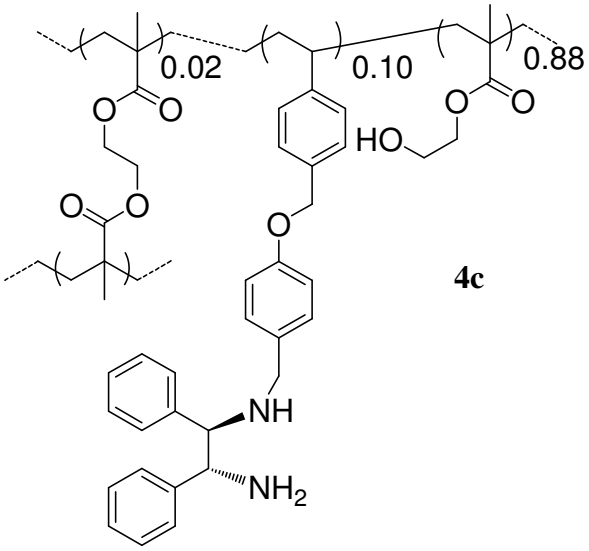


Figure S5. ^{1}H NMR spectrum of **4b.**



4c

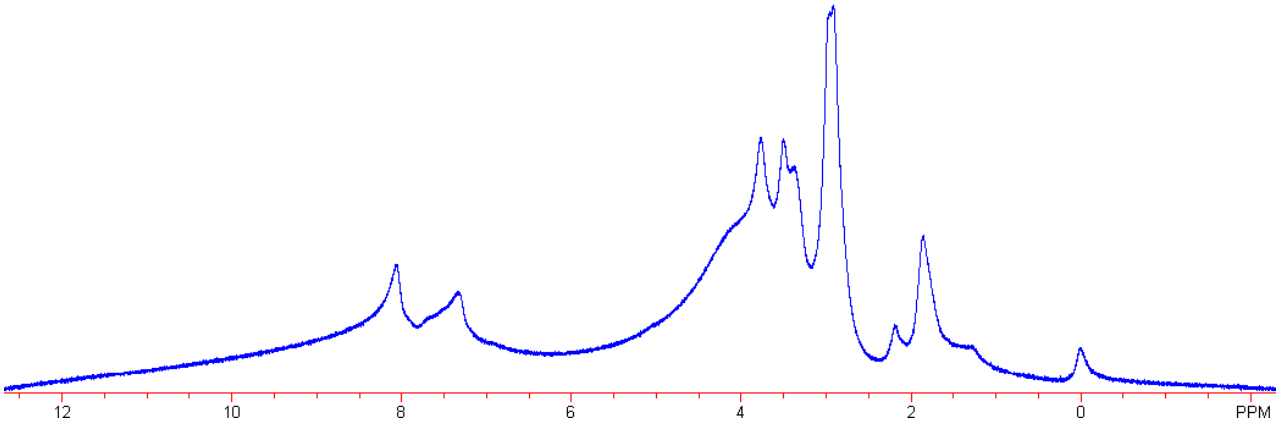
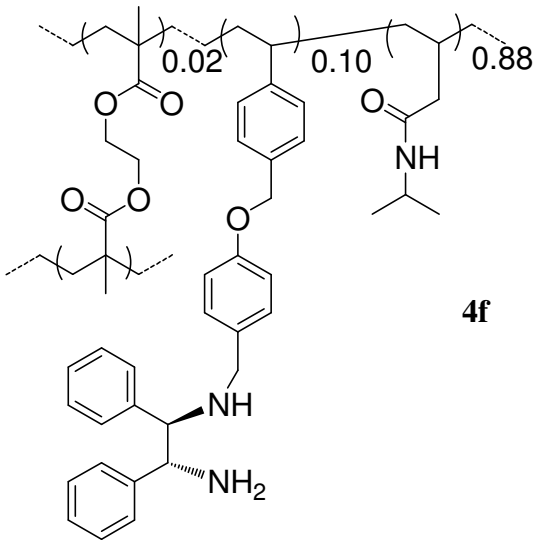


Figure S6. ^{1}H NMR spectrum of **4c.**



4f

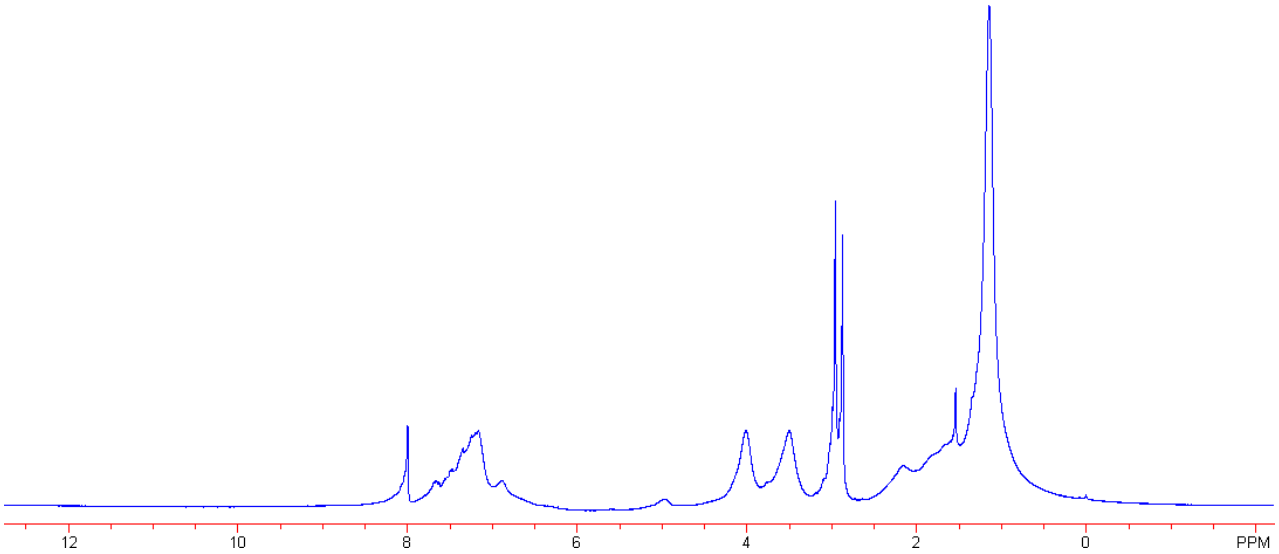
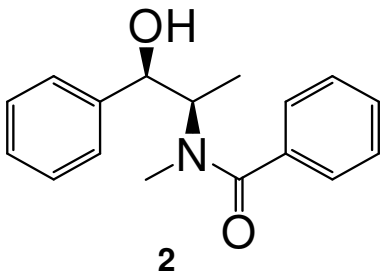


Figure S7. ^{1}H NMR spectrum of **4f.**



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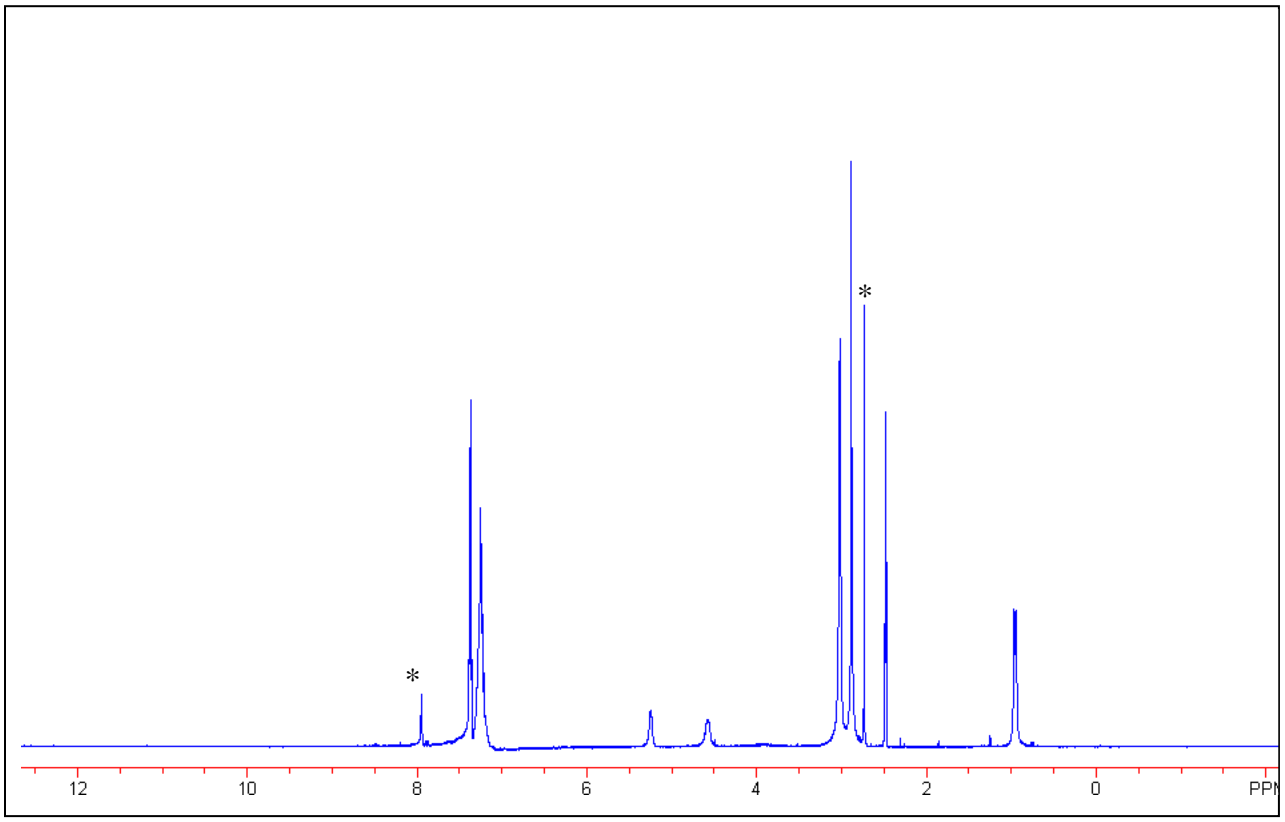

Figure S8. ^{1}H NMR spectrum of *syn*-β-amide alcohol **2** (in DMSO at 100 °C). Peaks marked with * are assigned to DMF.

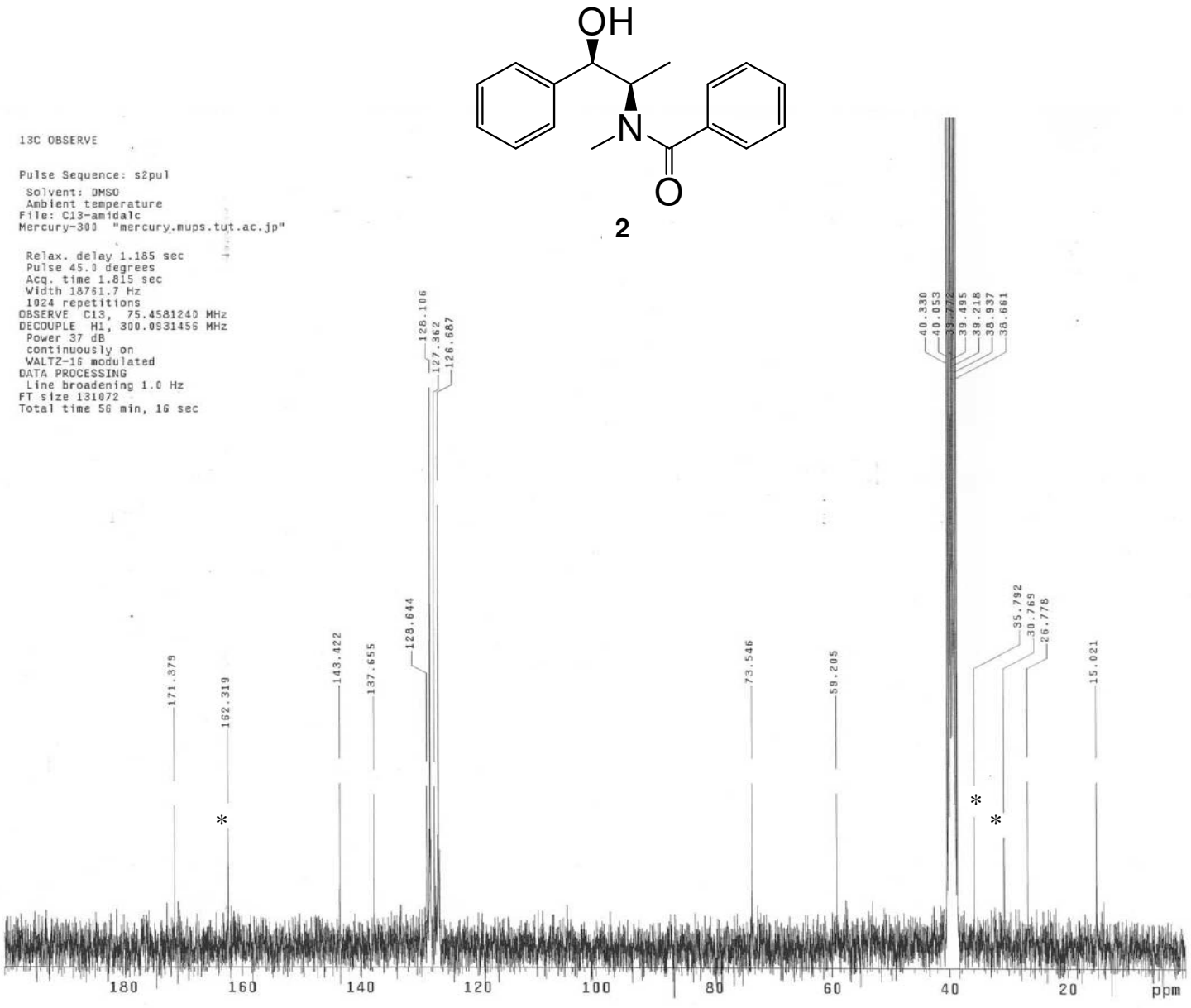

Figure S9. ^{13}C NMR spectrum of *syn*-β-amide alcohol **2** (in DMSO at 25 °C). Peaks marked with * are assigned to DMF.