catalysts

MDPI

Supplementary Materials

Ionic, Core-Corona Polymer Microsphere-Immobilized MacMillan Catalyst for Asymmetric Diels-Alder Reaction

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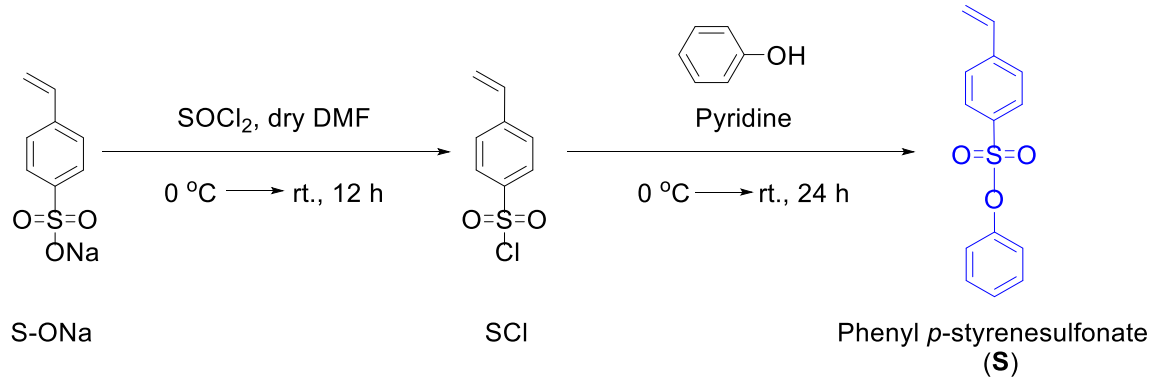
Synthesis of phenyl *p*-styrenesulfonate (S)



Synthesis of SCl

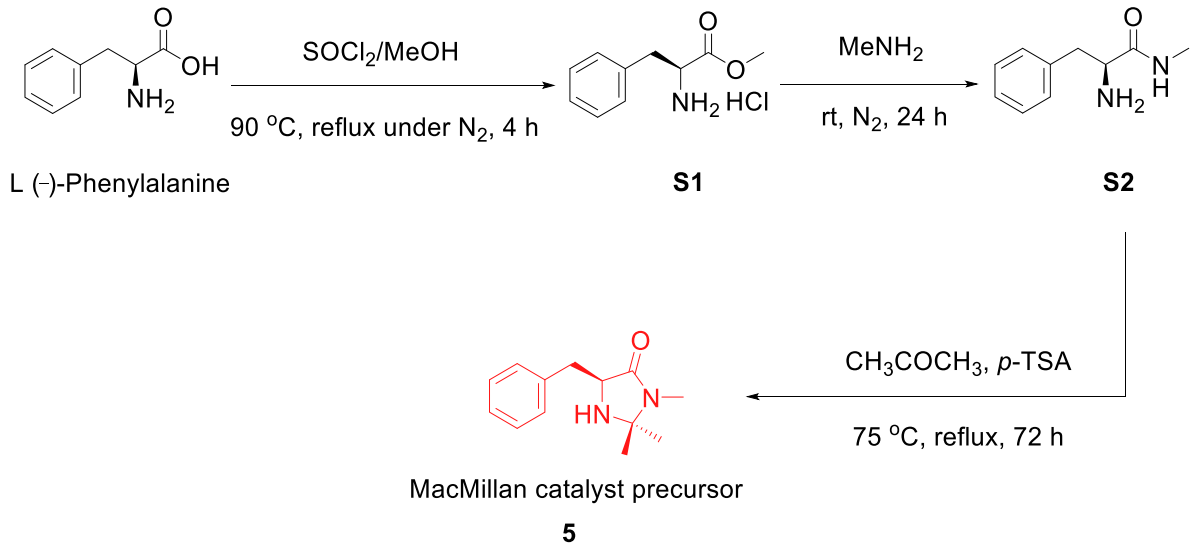
A 100-mL round-bottomed flask with a magnetic stirring bar was slowly charged with thionyl chloride (12.4 mL, 171 mmol) under N_2 gas at room temperature and then *p*-styrenesulfonic acid sodium salt, **S-ONa** (5.081 g, 24.64 mmol) was added to the solution. Immediately, the flask was transferred in an ice bath and 7.5 mL of dry DMF was added via a syringe in very slowly at 0 °C. The ice bath was removed after adding DMF. The flask was covered by aluminium foil, and the reaction was continued for 12 h at room temperature under N_2 gas. The crude product was extracted with Et_2O (50 mL × 3). Diethyl ether was removed by rotary evaporator and pumped up for 10 mins. The purified compound, *p*-styrenesulfonyl chloride, **SCl** is light yellow liquid. 5.03 g, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.26 ($CDCl_3$, TMS): δ = 5.54 (d, *J* = 11.0 Hz, 1H), 5.97 (d, *J* = 17.7 Hz, 1H), 6.71 (dd, *J* = 11.0, 17.7 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.99 (d, *J* = 8.5 Hz, 2H).

Synthesis of S

Phenol (2.346 g, 24.93 mmol) was taken in 100-mL round bottomed flask with a magnetic stirring bar inside, and pyridine (9.95 mL, 124 mmol) was added at room temperature. Immediately, the flask was transferred in an ice bath and *p*-styrenesulfonyl chloride, **SCl** (5.030 g, 24.82 mmol) added by pipette. After adding **SCl**, the ice bath was removed. The flask was covered by aluminium foil, and the reaction was continued for 24 h at room temperature. The crude product was extracted with 60 mL 1 M HCl and 100 mL $CHCl_3$. The organic phase was washed 60 mL 1M HCl and 5% K_2CO_3 (50 mL × 2), respectively. The extracted solvent ($CHCl_3$) was removed by rotary evaporator. The crude product was purified by column chromatography on silica gel with hexane/DCM = 1.5:1 as eluents to afford the compound, phenyl *p*-styrenesulfonate, **S** as yellowish liquid. 4.13 g, 82% yield; R_f = 0.51.

^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.26 ($CDCl_3$),TMS): δ = 5.48 (d, J = 10.7 Hz, 1H), 5.92 (d, J = 17.6 Hz, 1H), 6.75 (dd, J = 10.7, 17.6 Hz, 1H), 6.99 (d, J = 8.0 Hz, 2H), 7.23–7.31 (m, 3H), 7.52 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77.18 ($CDCl_3$), TMS): δ = 118.50, 122.47, 126.78, 127.29, 128.96, 129.77, 134.07, 136.19, 143.38, 149.69. HRMS (ESI, m/z): $[M + Na]^+$ calcd. for $C_{14}H_{12}NaO_3S$: 283.0399, found: 283.0422.

Synthesis of MacMillan catalyst precursor 5



Synthesis of S1

A 100-mL round-bottomed flask with a magnetic stirring bar was charged with MeOH (40.0 mL, 90.0 mmol) and $SOCl_2$ (6.40 mL, 88.0 mmol) was added slowly under N_2 gas at 0 °C. The ice bath was removed after adding $SOCl_2$ and then L (–) - phenylalanine (3.03 g, 18.34 mmol) was added. The reaction was continued for 4 h at 90 °C under N_2 gas. The solvent used was evaporated and pumped up. The obtained crude product **S1** is a white solid (3.93 g, >99% yield). ^{1}H NMR (400 MHz, δ = 4.66 (D_2O): δ = 3.09–3.14 (m, 1H), 3.21–3.26 (m, 1H), 3.71 (s, 3H), 4.32 (dd, J = 1.8, 5.8 Hz, 1H), 7.16–7.32 (m, 5H).

Synthesis of S2

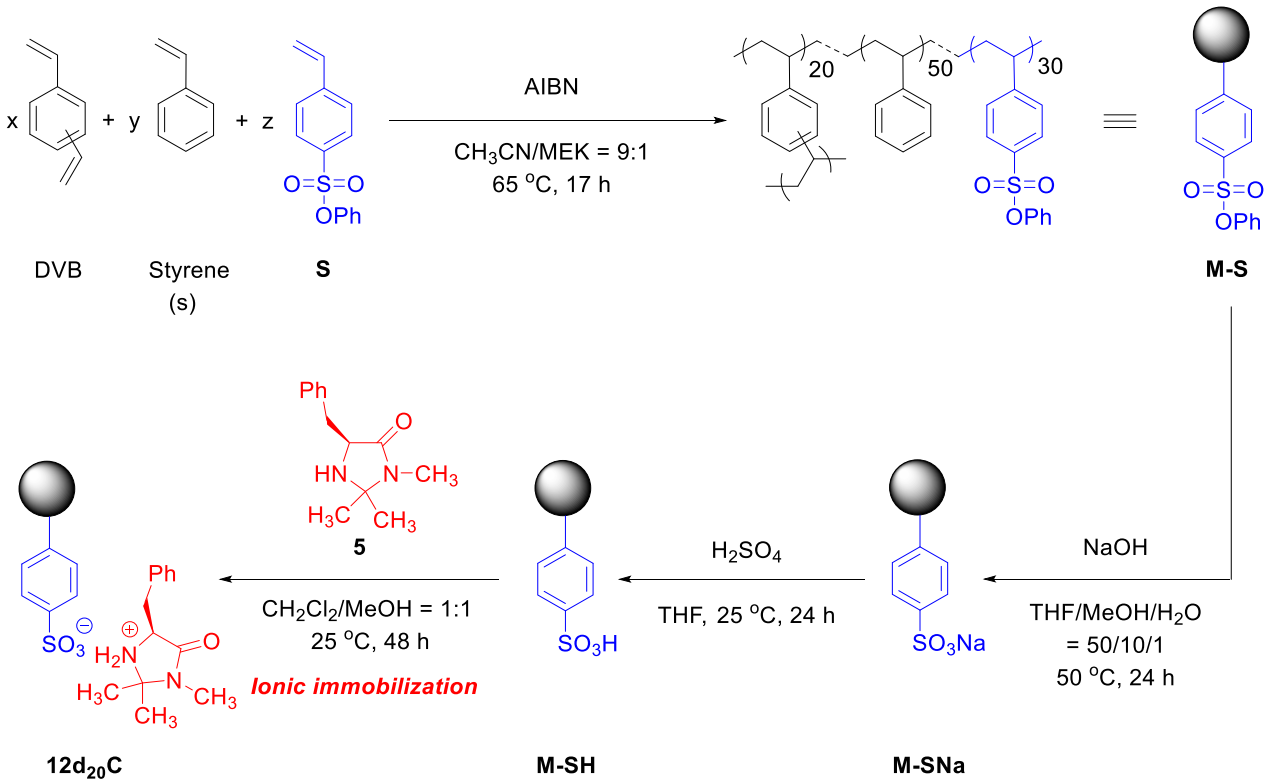
A 100-mL round-bottomed flask with a magnetic stirring bar was charged with **S1** (3.43 g, 15.90 mmol) and $MeNH_2$ (17.0 mL, 204 mmol). The reaction was carried out for 24 h at room temperature under N_2 gas. The reaction mixture was pumped up and extracted with Et_2O (40 mL × 2). The bottom phase was evaporated by rotary evaporator and then added saturated $NaHCO_3$ to make basic medium (pH >7). The solution was transferred into separatory funnel and extracted with $CHCl_3$ (40 mL × 3). The organic phase was dried over $MgSO_4$. After removing $MgSO_4$ by filtration, the solvent ($CHCl_3$) was removed by rotary evaporator and pumped up. The obtained product **S2** is a white solid (1.74 g, 9.76 mmol, 51% yield). ^{1}H NMR (400 MHz, δ = 4.66 (D_2O): δ = 2.59 (m, 3H), 2.87 (d, J = 7.0 Hz, 2H), 3.55 (t, J = 6.7 Hz, 1H), 7.18–7.34 (m, 5H).

Synthesis of MacMillan catalyst precursor 5

A 100-mL round-bottomed flask with a magnetic stirring bar was charged with **S2** (1.74 g, 9.76 mmol), p-TSA (7.0 mg, 0.037 mmol) and acetone (26.7 mL). The reaction was continued for 72 h at 75 °C. The reaction mixture was evaporated by rotary evaporator and pumped up. The crude product was purified by column chromatography on silica gel with EtOAc/Hexane = 4:1 as eluents to afford the compound, **5** as a reddish liquid (1.36 g, 78 % yield, R_f = 0.14). ^{1}H NMR (400 MHz, δ = 4.66 (D_2O): δ = 1.14 (s, 3H), 1.24 (s, 3H), 2.73 (s, 3H), 2.97–3.01 (m, 1H), 3.11–3.14 (m, 1H), 3.77 (dd, J = 1.9, 4.6 Hz,

1H), 7.20–7.29 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77.17 ($CDCl_3$), TMS): δ = 25.32, 25.39, 27.30, 37.32, 59.36, 75.65, 126.88, 128.68, 129.60, 137.24, 173.49. HRMS (ESI, *m*/*z*): $[M + Na]^+$ calcd. for $C_{13}H_{18}N_2NaO$: 241.1311, found: 283.0422.

Synthesis of uniform polymer microsphere-supported MacMillan catalyst 12d$_{20}$C



Synthesis of M-S

A 30 mL HDPE narrow-mouth bottle was charged with DVB (169 mg, 1.30 mmol) St (334 mg, 3.21 mmol), **S** (507 mg, 1.95 mmol), AIBN (20 mg), and 27 mL of acetonitrile and 3 mL of MEK under N_2 gas. Polymerization was carried out in an incubator at a constant temperature of 65 °C for 17 h with rolling the bottle horizontally at 9 rpm. The reaction mixture was cooled to room temperature, and the insoluble fraction was collected by centrifugation and washed with THF, methanol, and acetone. The solid product was dried under vacuum at 40 °C for 24 h. 0.378 g, 37% yield; phenyl *p*-styrenesulfonate moiety content: 1.90 mmol g^{-1}; FTIR (KBr): ν = 1376, 1176 (S=O), 1596, 1488, 1454 (C=C in aromatic ring), 3060, 3025 (C–H in aromatic ring), and 2924, 2853 (C–H in alkyl) cm^{-1}. The number-average diameter, (D_n) and polydispersity index (D_w/D_n) measured from SEM image was found 1.26 μm and 1.01, respectively.

Synthesis of M-SNa

M-S (299 mg, 0.568 mmol of phenyl *p*-styrenesulfonate moiety) and NaOH (70 mg, 1.6 mmol) were taken in a flask with a magnetic stir bar inside and a mixed solvents 50:10:1 THF:MeOH:H_2O (= 9.54/1.91/0.19 (mL)) was added. The reaction was carried out in an oil bath at 50 °C for 24 h. The reaction mixture was cooled to room temperature, and the particles were collected by centrifugation and washed with methanol, water and acetone. The solid product was dried at 40 °C under vacuum for 24 h. 0.282 g, >99% yield; sodium sulfonate moiety content: 2.12 mmol g^{-1}; FTIR (KBr): ν = 1190 (S=O stretching in SO_3Na), 1601, 1507, 1452 (C=C in aromatic ring), 3024 (C–H in aromatic ring), and 2924, 2854 (C–H in alkyl) cm^{-1}.

Synthesis of M-SH

M-SNa (165 mg, 0.350 mmol of sodium sulfonate moiety) was taken in a flask with a magnetic stir bar inside and then THF (18 mL) added. The diluted solution of H_2SO4 (0.37 mL) was added slowly into the mixture. The reaction was carried out at room temperature for 24 h. The reaction mixture was cooled to room temperature, and the particles were collected by centrifugation and washed with water, methanol and acetone. The solid product was dried at 40 °C under vacuum for 12 h. 150 mg, 96% yield; sulfonic acid moiety content: 2.23 mmol g^{-1}; FTIR (KBr): ν = 1217, 1175 (S=O stretching in SO_3H), 1601, 1558, 1456 (C=C in aromatic ring), 3025 (C–H in aromatic ring), and 2924, 2854 (C–H in alkyl) cm^{-1}.

Synthesis of 12d$_{20}$C

M-SH (142 mg, 0.317 mmol of sulfonic acid moiety) was taken in a Schlenk tube with a magnetic stir bar inside and **5** (141 mg, 0.646 mmol) was dissolved in 1.0 mL of MeOH. The solution of **5** was added into the tube and then 1.0 mL of CH_2Cl_2 was added. The reaction was continued at room temperature for 48 h. The resulting polymer particles were isolated by centrifugation and redispersed in MeOH, and acetone. The catalyst immobilized core-corona polymer particles were dried at 40 °C under vacuum. The unreacted catalysts were recovered from the collected supernatant by removing solvent mixtures through vacuum evaporator, followed by pumped up. The degree of immobilization and catalyst content were 66 % and 1.12 mmol g^{-1}, respectively.

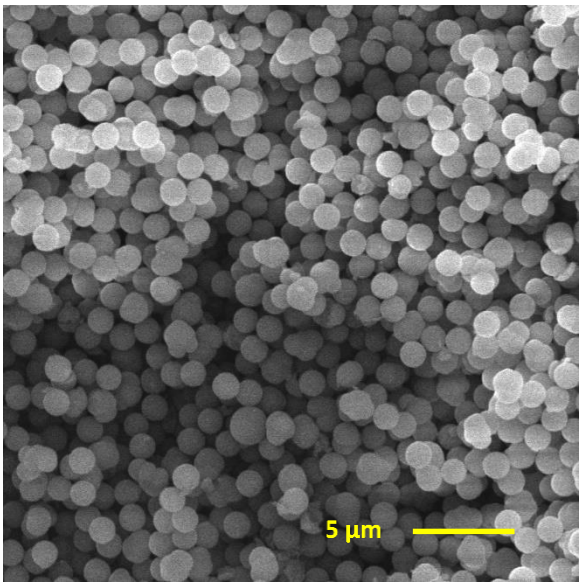


Figure S1. SEM image of 12d$_{20}$C.

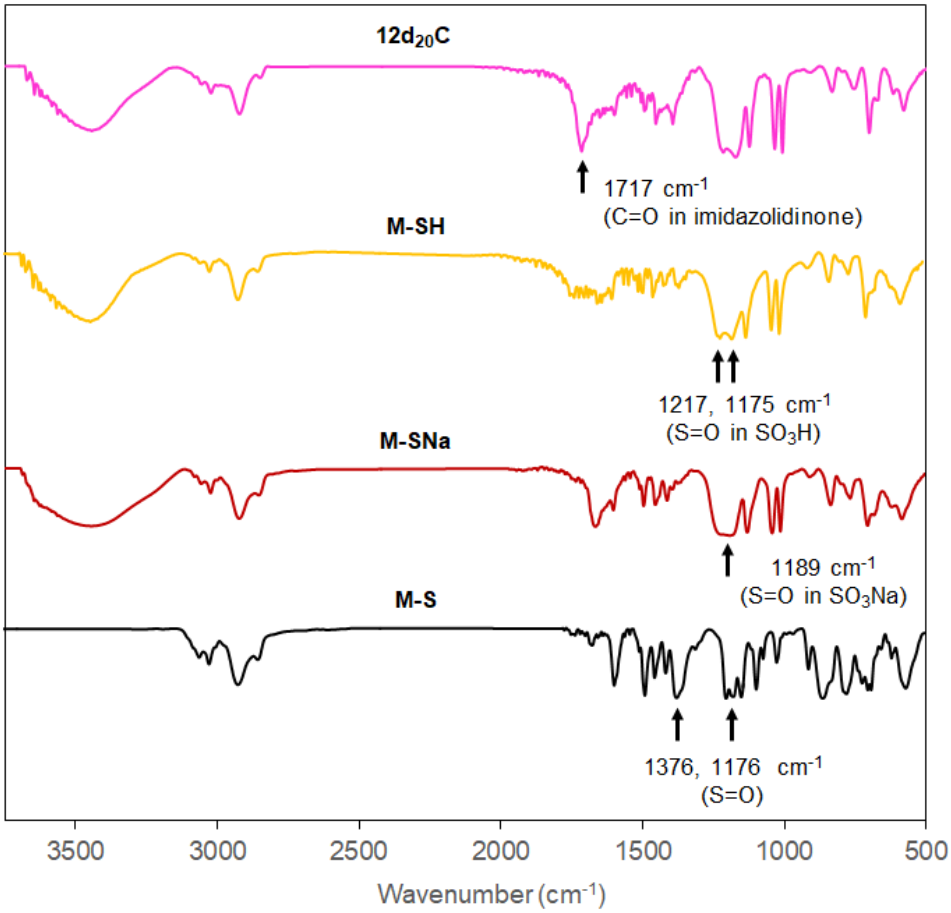
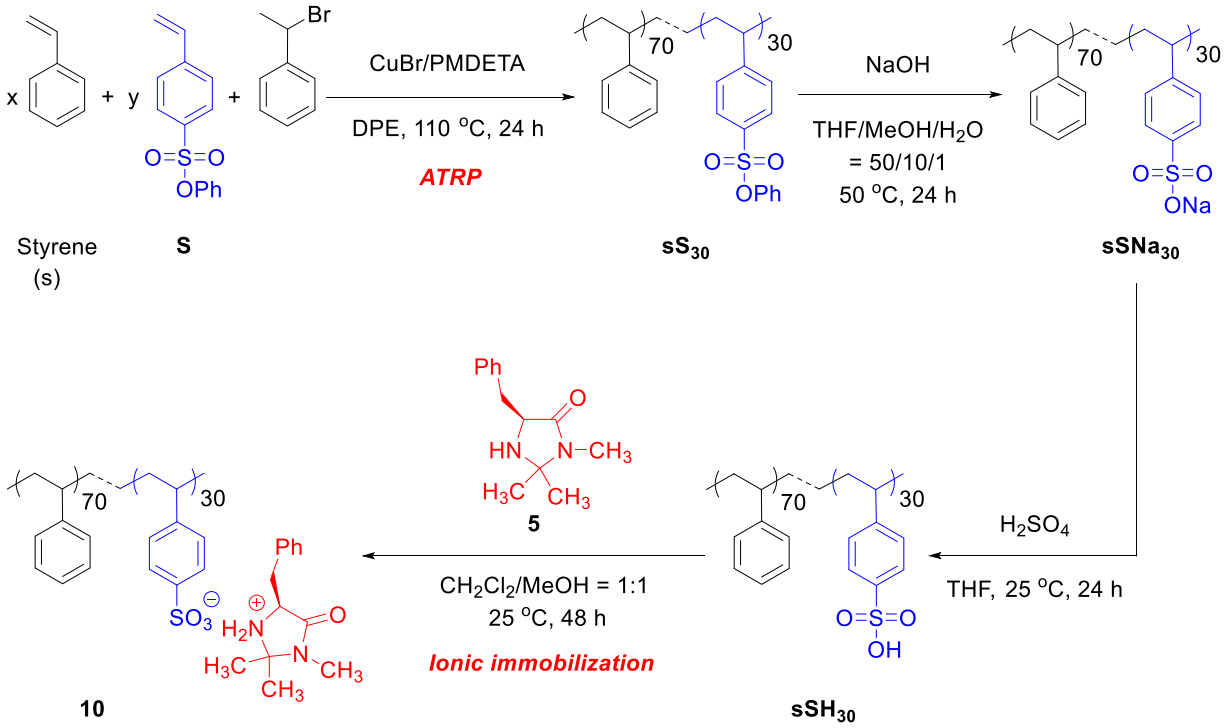


Figure S2. FT-IR spectra of **M-S**, **M-SNa**, **M-SH**, and **12d$_{20}$C**.

Synthesis of 10



Synthesis of sS_{30}

CuBr (14 mg, 0.098 mmol), St (365 mg, 3.50 mmol), S (392 mg, 1.51 mmol), and diphenyl ether (1.25 mL) were added to 6 mL vial successively. The reaction mixture was purged with argon for 5 min and then PMDETA (52 mg, 0.30 mmol) was added. After another 5 min of argon bubbling, initiator, 1-PEBr (20 mg, 0.11 mmol) was added into the system. The reaction was carried out for 24 h at a stirring rate of 400 rpm in an oil bath at 110 °C temperature. The resulting polymers were collected by drop wise adding in MeOH (100–125 mL). The polymers were collected by filtration which then dried at 40 °C temperature to provide a white powder. 347 mg, 45% yield. $M_{n,\,NMR}$ = 9,200 g mol^{-1}, $M_{n,\,SEC}$ = 19,000, M_n/M_w = 1.53; FT-IR (KBr): ν = 1376, 1175 (S=O stretching), 1597, 1489, 1453 (C=C in aromatic ring), 3060, 3025 (C–H in aromatic ring), and 2924, 2850 (C–H in alkyl) cm^{-1}.

Synthesis of $sSNa_{30}$

The reaction conditions are similar to that of **M-SNa**. The resulting polymers were collected by drop wise adding in ether. The insoluble fraction was collected by centrifugation and washed with small amount of methanol, and acetone. The solid product was dried under vacuum at 40 °C for 24 h. 94% yield; sodium sulfonate moiety content: 2.23 mmol g^{-1}; FT-IR (KBr): ν = 1189 (S=O stretching in SO_3Na), 1601, 1493, 1452 (C=C in aromatic ring), 3059, 3025 (C–H in aromatic ring), and 2923, 2848 (C–H in alkyl) cm^{-1}.

Synthesis of sSH_{30}

The reaction conditions are similar to that of **M-SH**. The resulting polymers were collected by drop wise adding in ether. The insoluble fraction was collected by centrifugation and washed with small amount of methanol, and acetone. The solid product was dried under vacuum at 40 °C for 24 h. 95% yield; sulfonic acid moiety content: 2.35 mmol g^{-1}; FT-IR (KBr): ν = 1217 (S=O stretching in SO_3H), 1601, 1494, 1454 (C=C in aromatic ring), 3059, 3025 (C–H in aromatic ring), and 2923, 2850 (C–H in alkyl).

Synthesis of 10

The synthesis procedure is similar to that of **12d$_{20}$C**. The resulting polymers were extracted with CH_2Cl_2 (two times). The extracted solvent was evaporated and pumped up. Finally, the polymers were washed with hexane. The solid product was pumped up and dried under vacuum at 40 °C for 24 h. The degree of immobilization and catalyst content were 100% and 1.61 mmol g^{-1}, respectively.

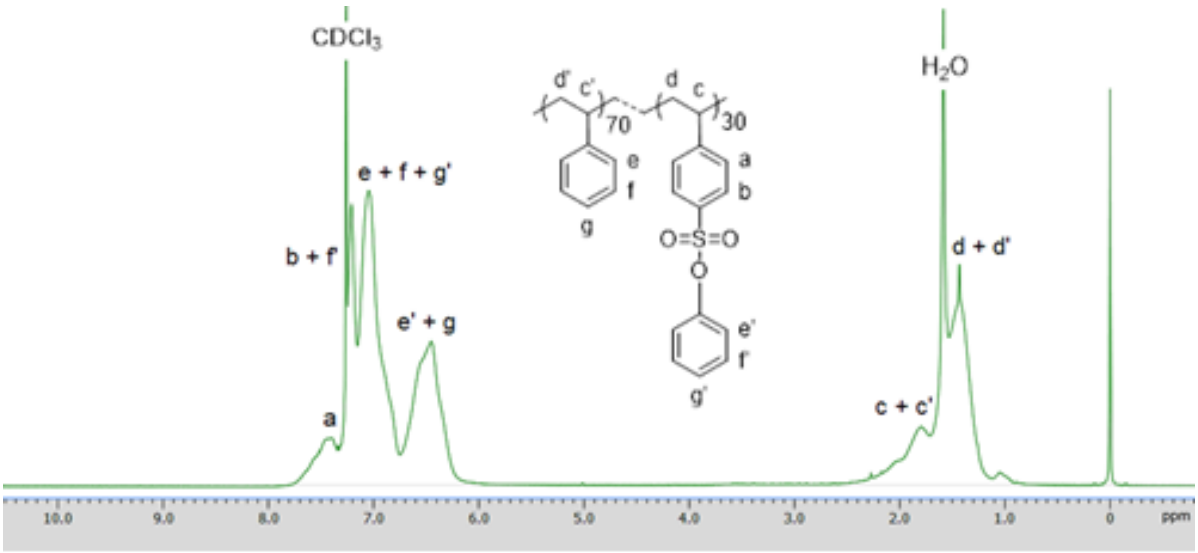


Figure S3. ^{1}H NMR of **sS$_{30}$** in $CDCl_3$.

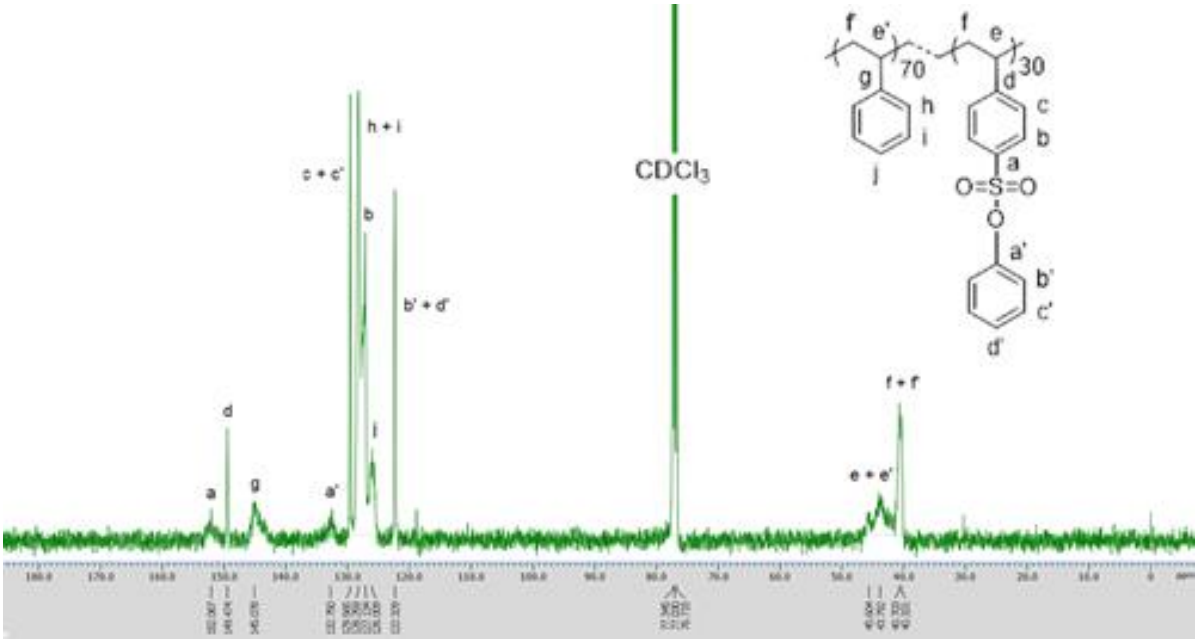


Figure S4. ^{13}C NMR of **sS$_{30}$** in $CDCl_3$.

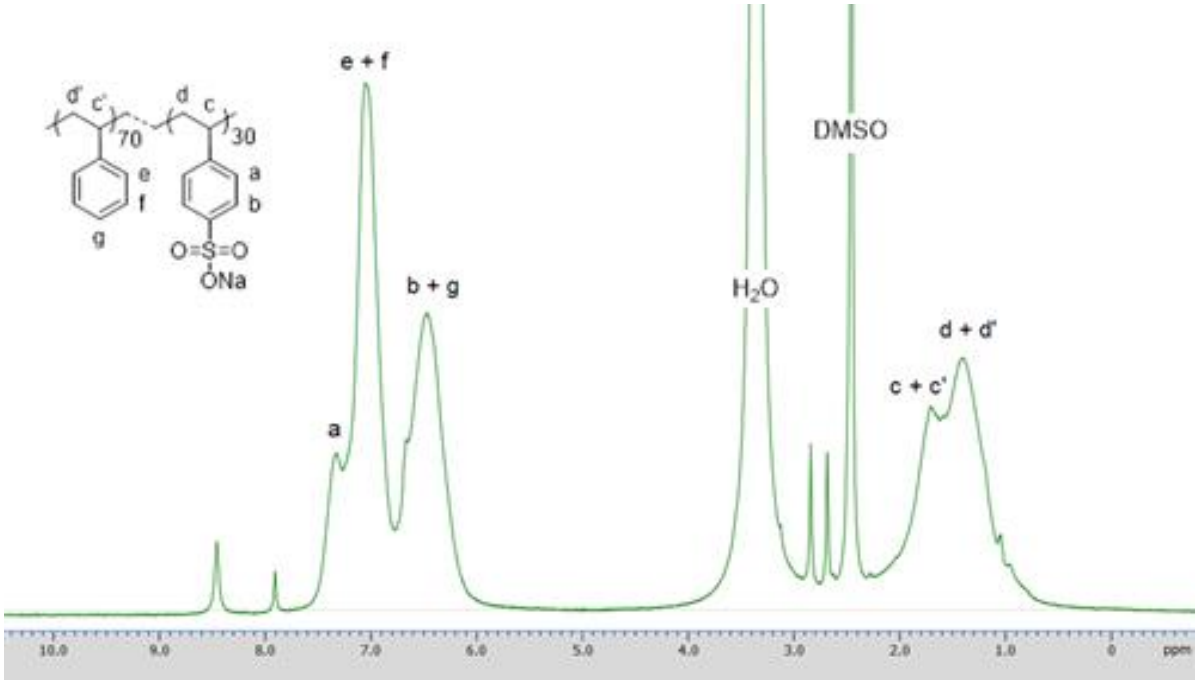


Figure S5. ^{1}H NMR of **sSNa$_{30}$** in $CDCl_3$.

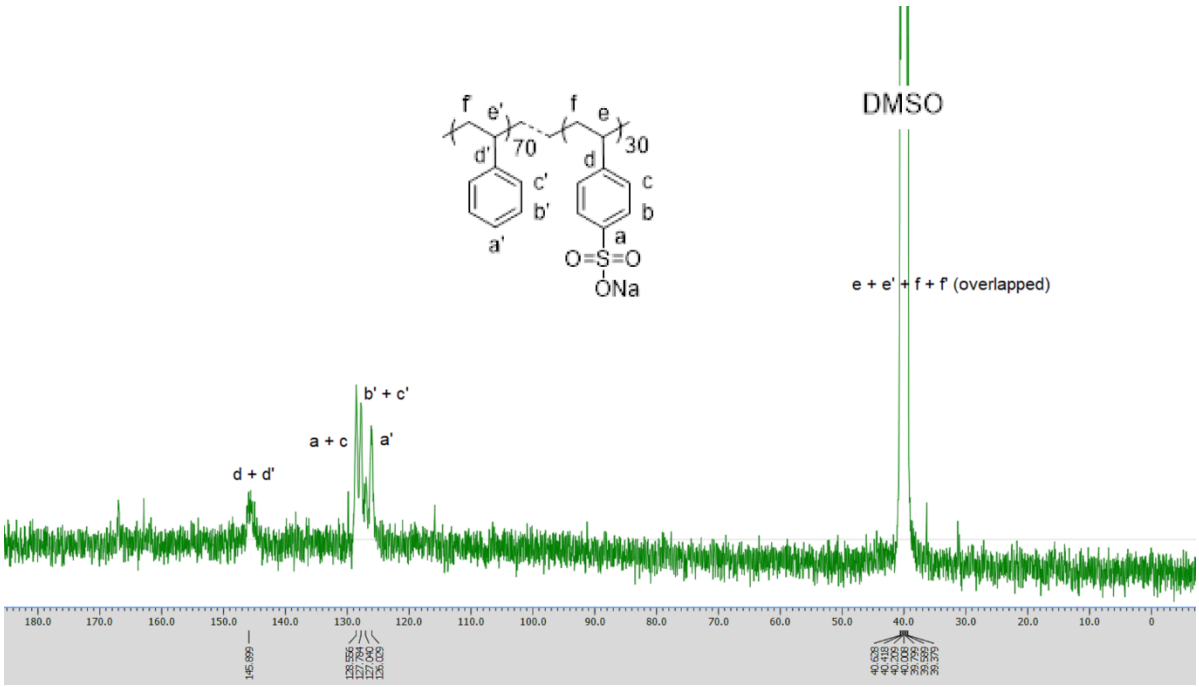


Figure S6. ^{13}C NMR of **sSNa$_{30}$** in $CDCl_3$.

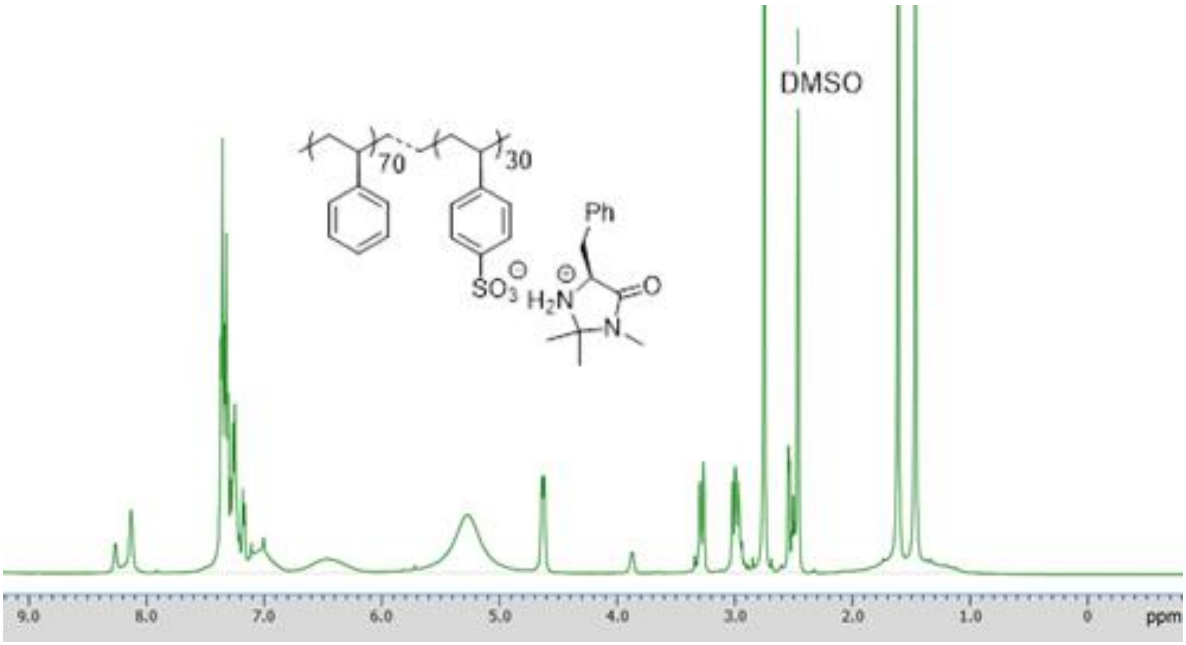


Figure S7. ^{1}H NMR of **10** in DMSO-d_6.

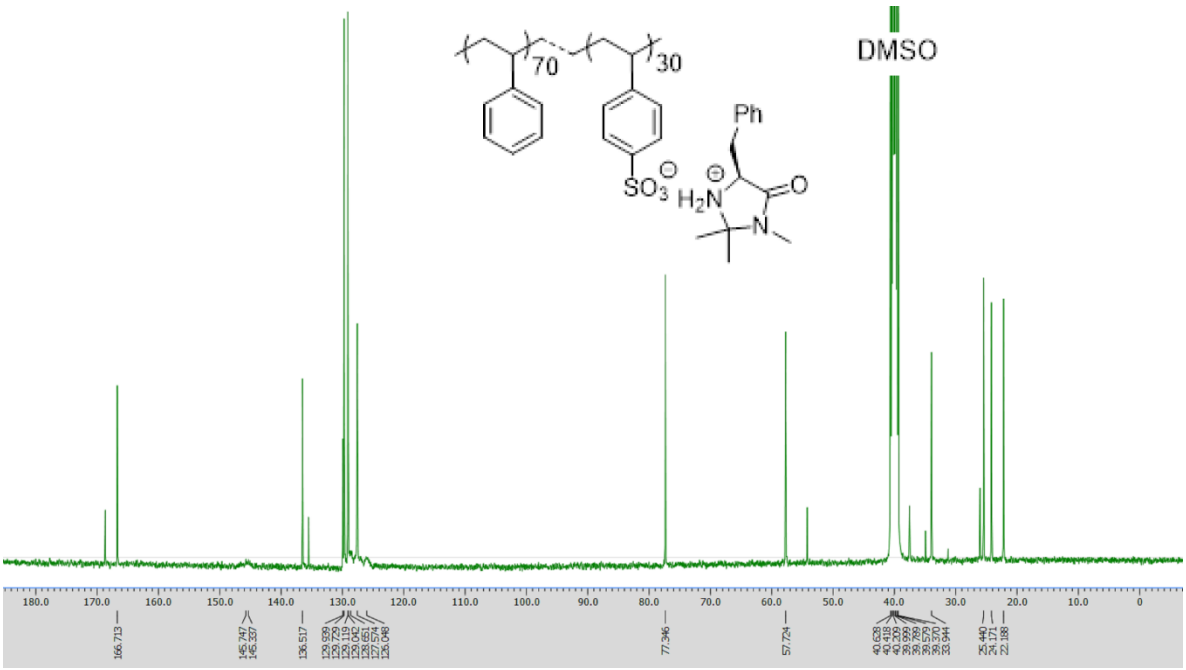


Figure S8. ^{13}C NMR of **10** in DMSO-d_6.

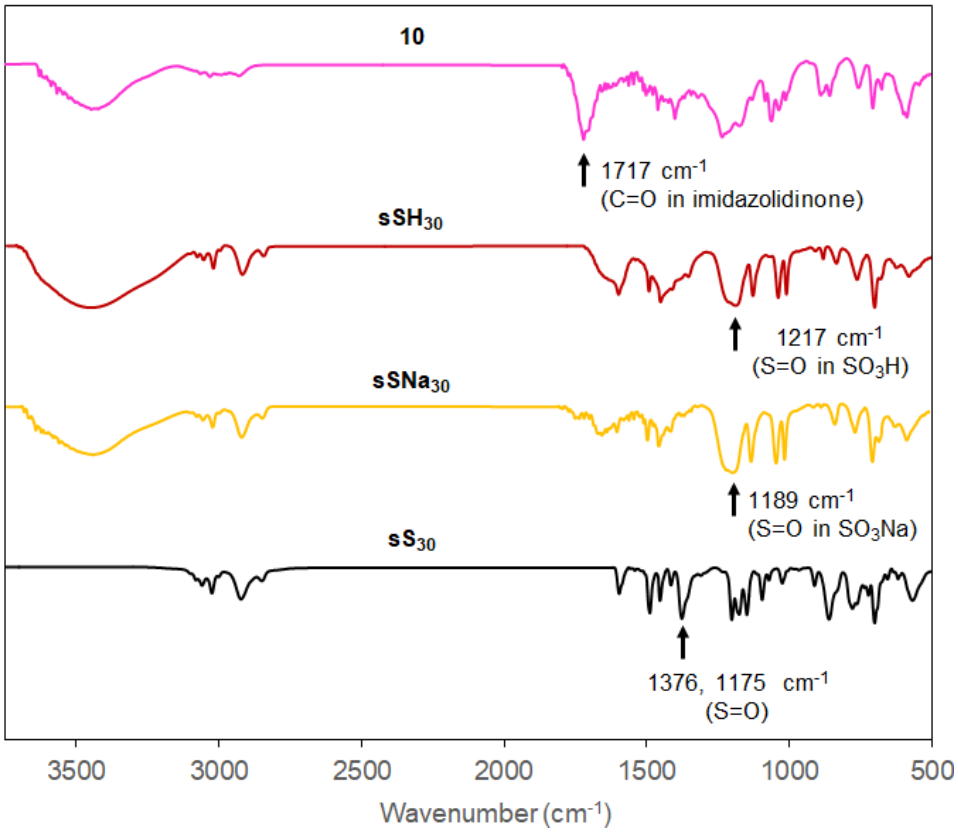
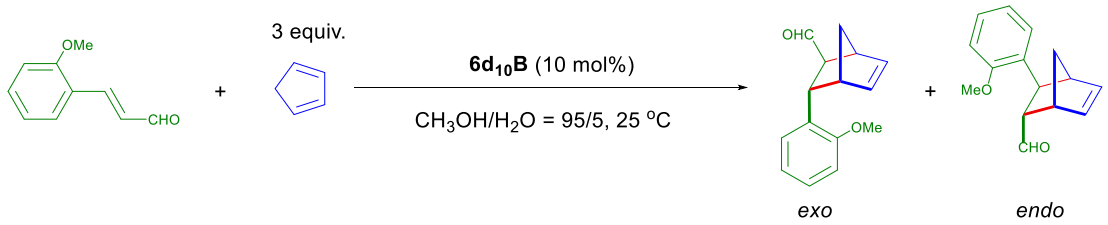


Figure S9. FT-IR spectra of **sS**$_{30}$, **sSNa**$_{30}$, **sSH**$_{30}$ and **10**.

Check for MacMillan catalyst leaching

After the reaction, the polymeric catalyst was isolated by centrifugation. Firstly, the leaching of McMillan catalyst was checked by TLC by using the solution of product. The solution was then concentrated by rotary evaporator until the solution being 1mL. The deprotection of the acetal was carried out by adding 2/2/1 CH_2Cl_2/H_2O/TFA to the concentrated solution, and stirred at room temperature for 2 h. The mixture was then added to saturated $NaHCO_3$ aqueous solution. After the extraction with Et_2O, the combined organic layer was washed with saturated NaCl aqueous solution and dried with anhydrous $MgSO_4$. The removal of $MgSO_4$ by filtration and the concentration by rotary evaporator and vacuum gave the crude. The leaching of MacMillan catalyst was again checked by TLC of crude product, and the elemental analysis for nitrogen content.

Asymmetric Diels-Alder reaction of (*E*)-2-methoxycinnamaldehyde with 1,3-cyclopentadiene 8



exo *endo*

8 **14**

The reaction conditions are similar to that of **7** and **8**. The yield and e*xo*/*endo* ratio were determined using ^{1}H NMR through the comparison of the proton signals of the aldehyde. The reduction of **14** was performed by adding $NaBH_4$ (0.15 g, 4.0 mmol) in methanol (2 mL) at 0 °C for 2 h. Resulting chiral alcohols were purified using silica gel column chromatography (hexane:ethyl acetate = 3:1 as an eluent). The enantiomeric excess was determined using HPLC through comparison

of the peak area ratio (Chiralcel OJ-H, hexane:2-propanol = 95:5, 0.6 mL/min, 210 nm; retention time: 17.6 min (*endo*-minor), 20.8 min (*exo*-minor), 22.1 min (*endo*-major), and 31.9 min (*exo*-major). The assignment of each peak in HPLC was carried out with the ESI of the following reference: Li, N.; Liang, X.; Su, W. **RSC Adv.** 2015, **5**, 106234-106238.

14: ^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.26 ($CDCl_3$)): δ = 9.93 (d, J = 2.8 Hz, 1H), 9.50 (d, J = 4.0 Hz, 1H), 7.23–7.15 (m, 3H), 7.03 (d, J = 7.4 Hz, 1H), 6.96–6.92 (m, 1H), 6.87–6.80 (m, 3H), 6.42 (dd, J = 5.5, 2.4 Hz, 1H), 6.26 (dd, J = 5.8, 2.4 Hz, 1H), 6.18 (dd, J = 5.5, 2.4 Hz, 1H), 3.88 (dd, J = 5.2, 2.1 Hz, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 3.30–3.16 (m, 3H), 3.16 (d, J = 4.3 Hz, 1H), 3.08 (d, J = 1.20, 1H), 2.56–2.53 (m, 1H), 2.36–2.33 (m, 1H), 1.74–1.67 (m, 2H), 1.62–1.54 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77.1 ($CDCl_3$)): δ = 206.3, 204.2, 157.5, 157.4, 138.5, 136.8, 136.3, 134.2, 132.3, 131.0, 127.3, 127.2, 127.2, 125.5, 120.4, 119.9, 109.9, 109.9, 59.7, 57.9, 56.0, 54.8, 47.8, 47.3, 47.0, 46.2, 46.1, 45.5, 40.7, 40.2.

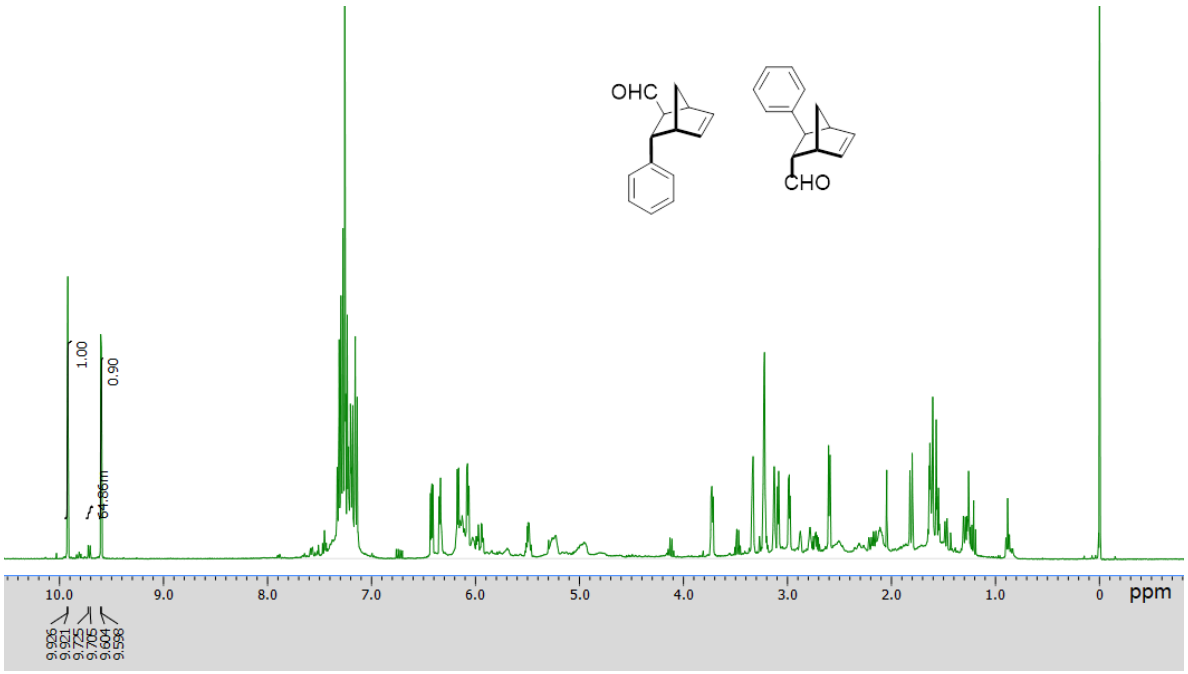


Figure S10. ^{1}H NMR of crude **9** in $CDCl_3$.

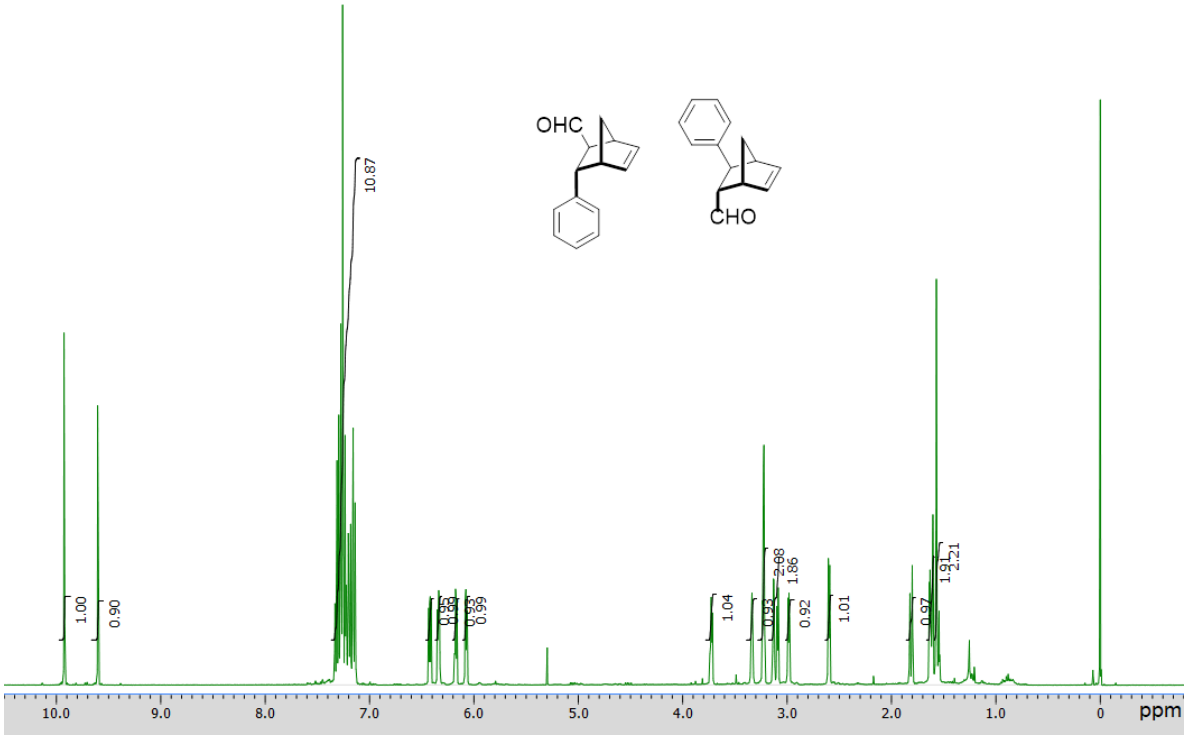


Figure S11. ^{1}H NMR of **9** after purification in $CDCl_3$.

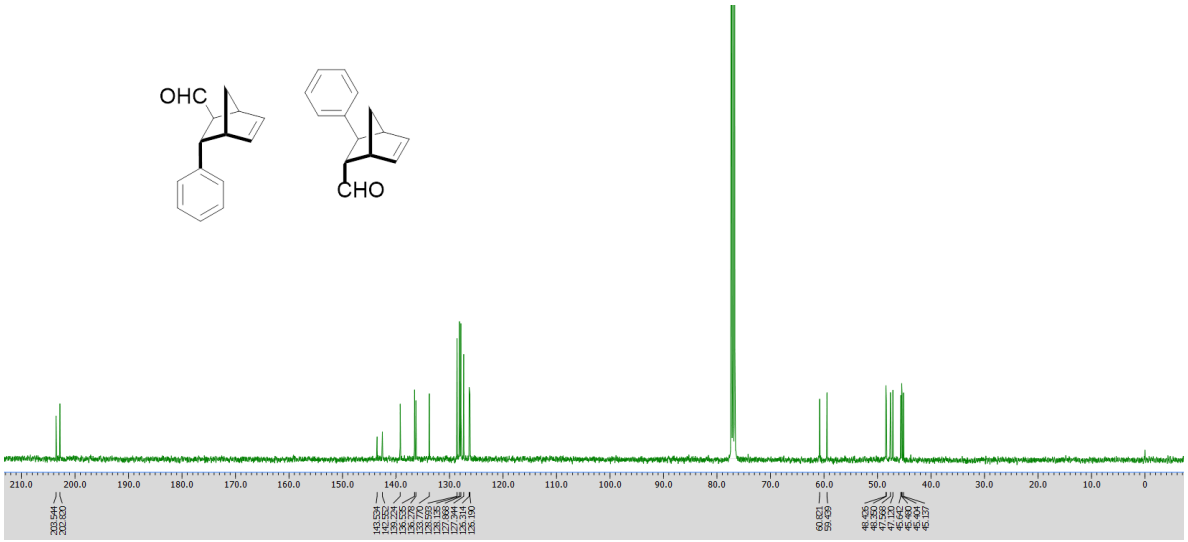


Figure S12. ^{13}C NMR of **9** after purification in $CDCl_3$.

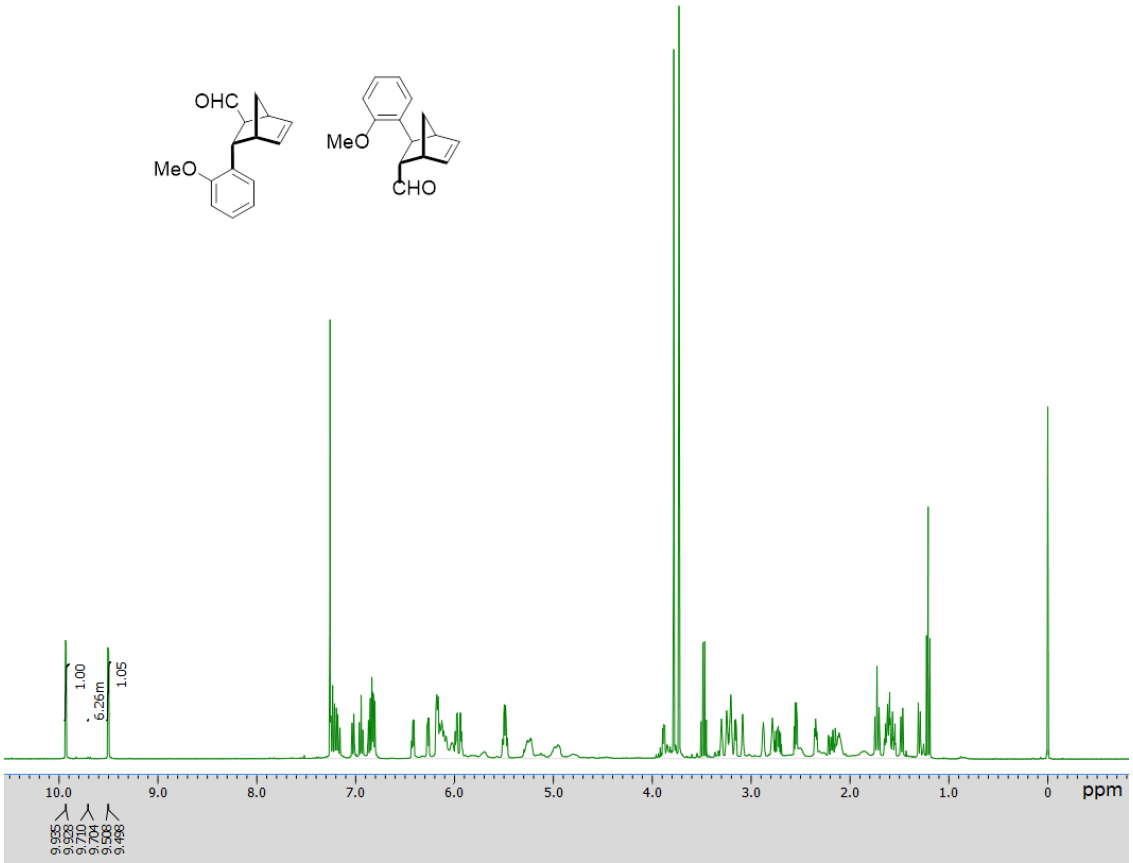


Figure S13. ^{1}H NMR of crude **14** in $CDCl_3$.

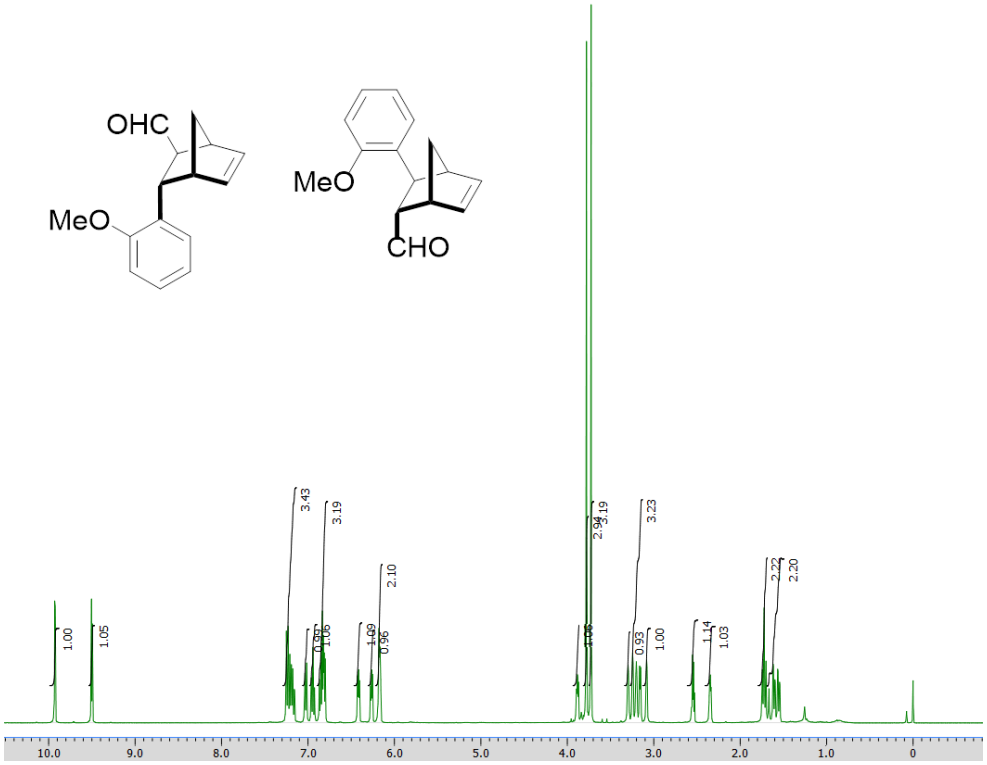


Figure S14. ^{1}H NMR of **14** after purification in $CDCl_3$.

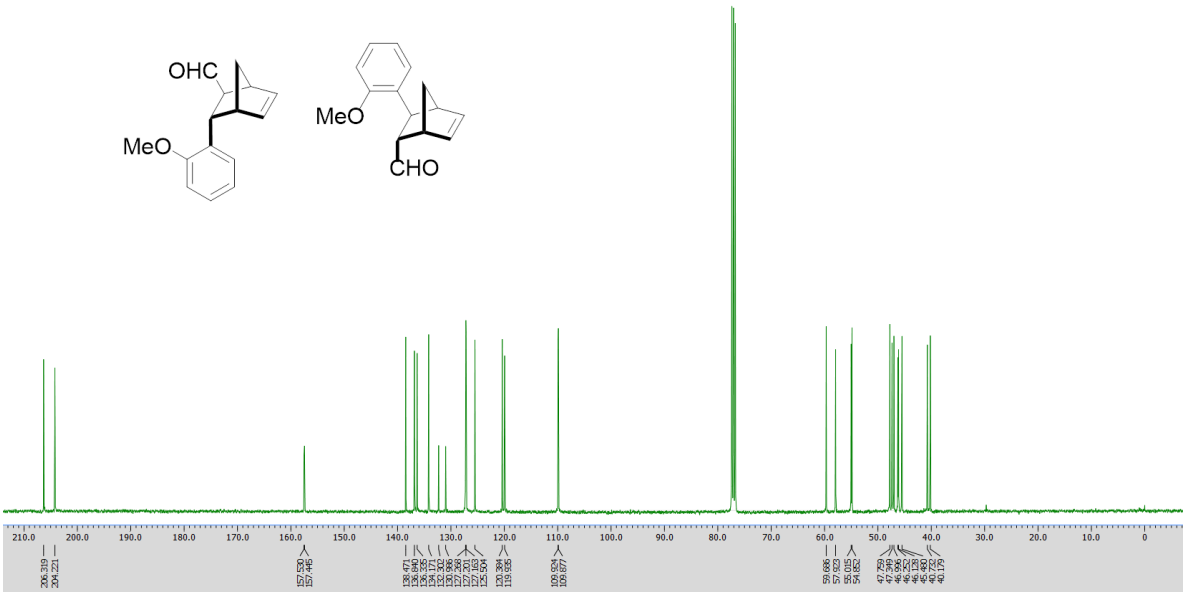


Figure S15. ^{13}C NMR of **14** after purification in $CDCl_3$.

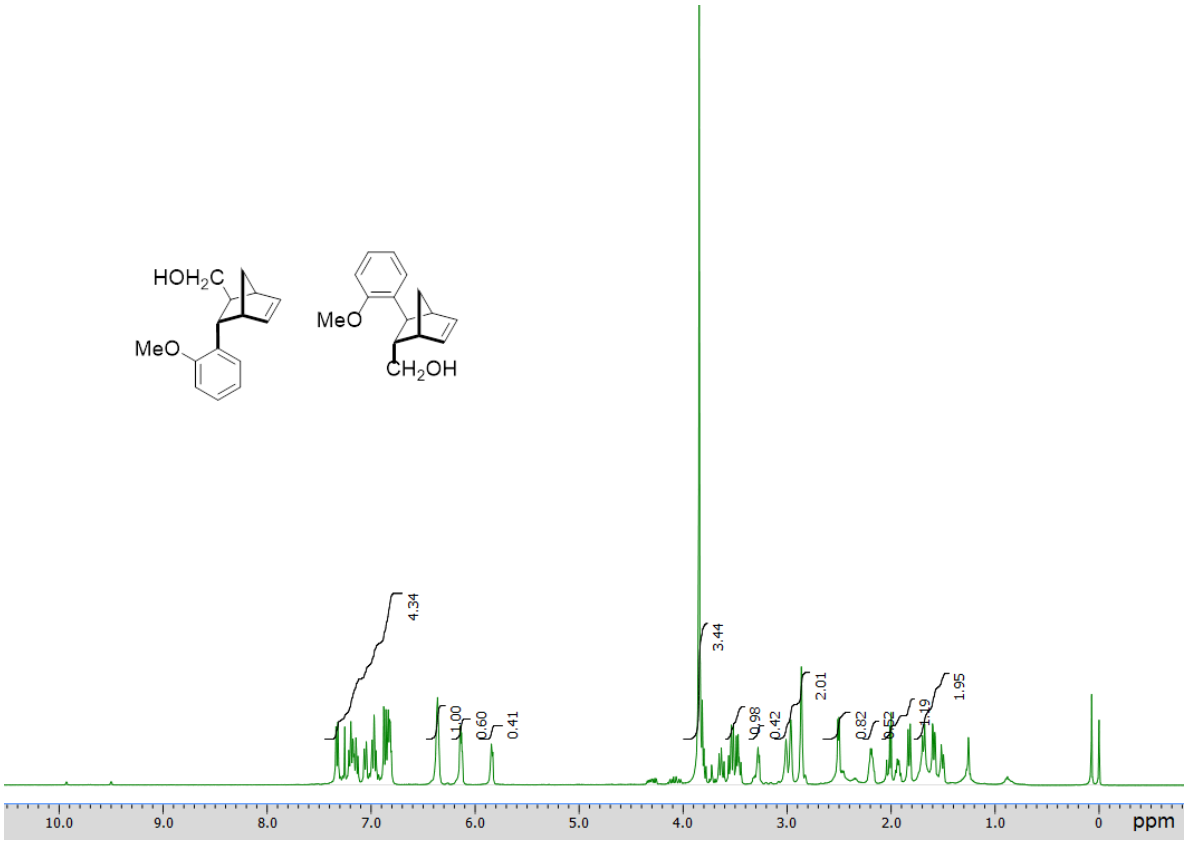


Figure S16. ^{1}H NMR of **14** after reduction in $CDCl_3$.

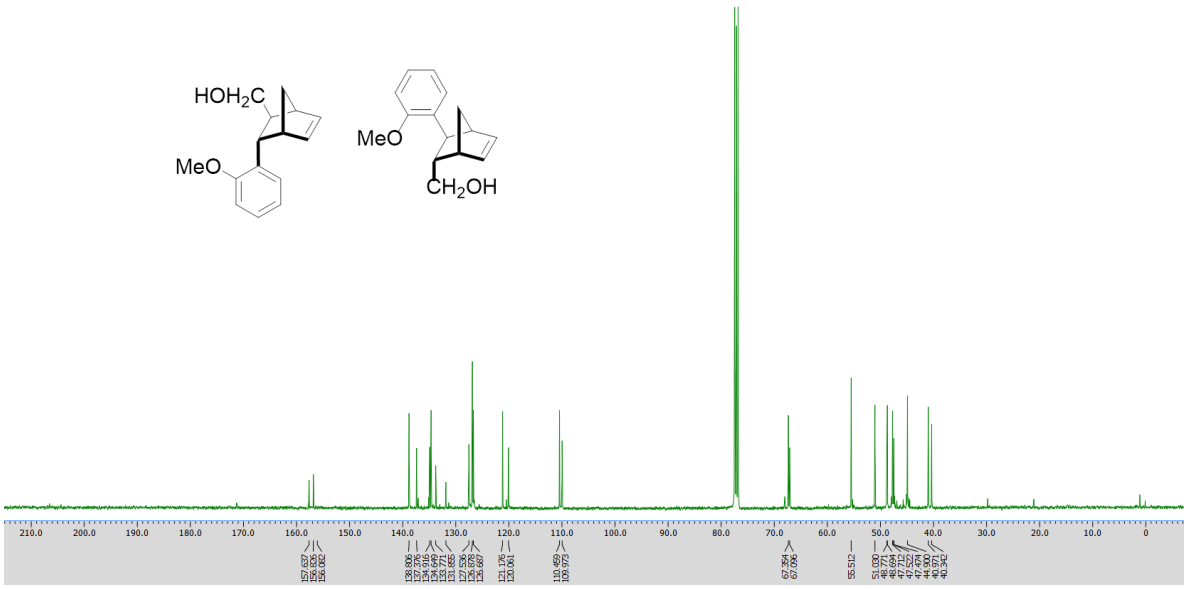
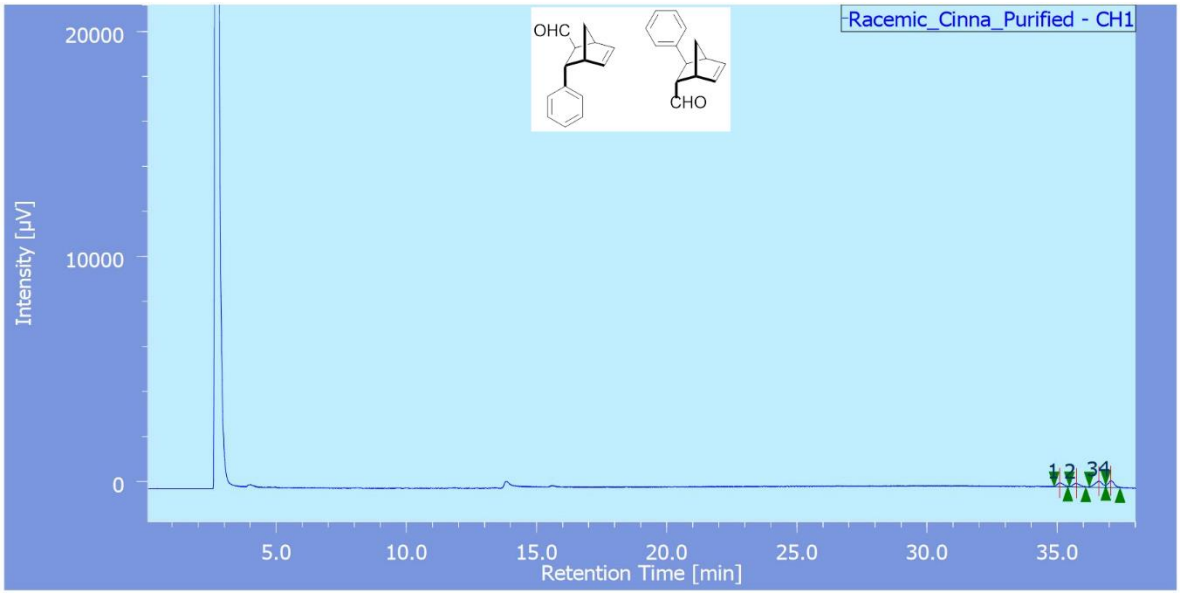


Figure S17. ^{13}C NMR of **14** after reduction in $CDCl_3$.

(a)



(b)

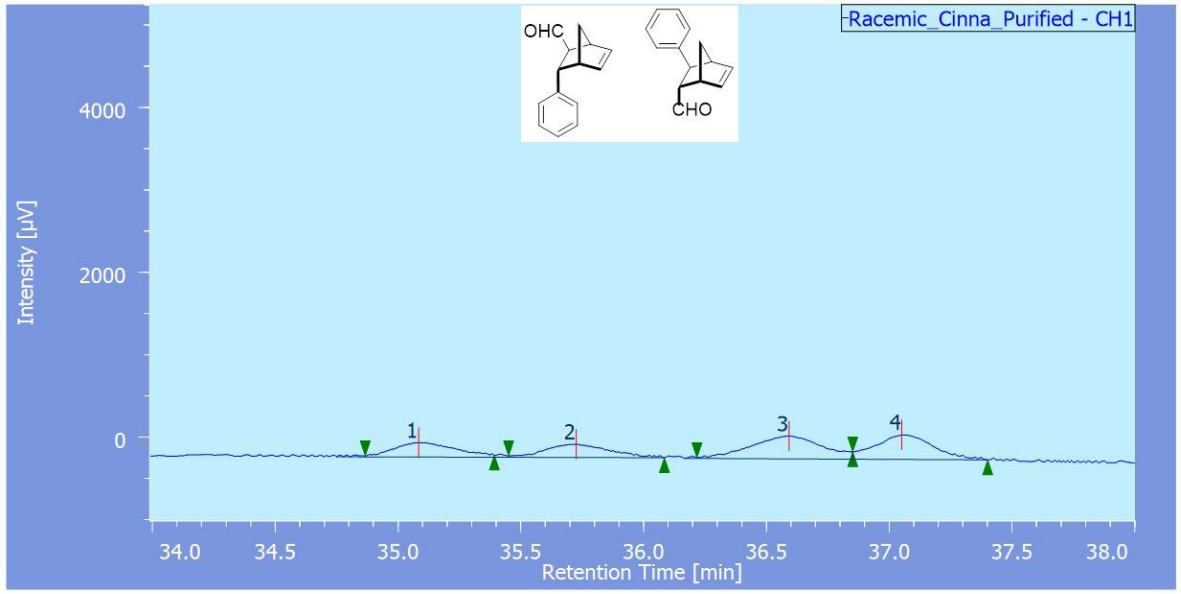
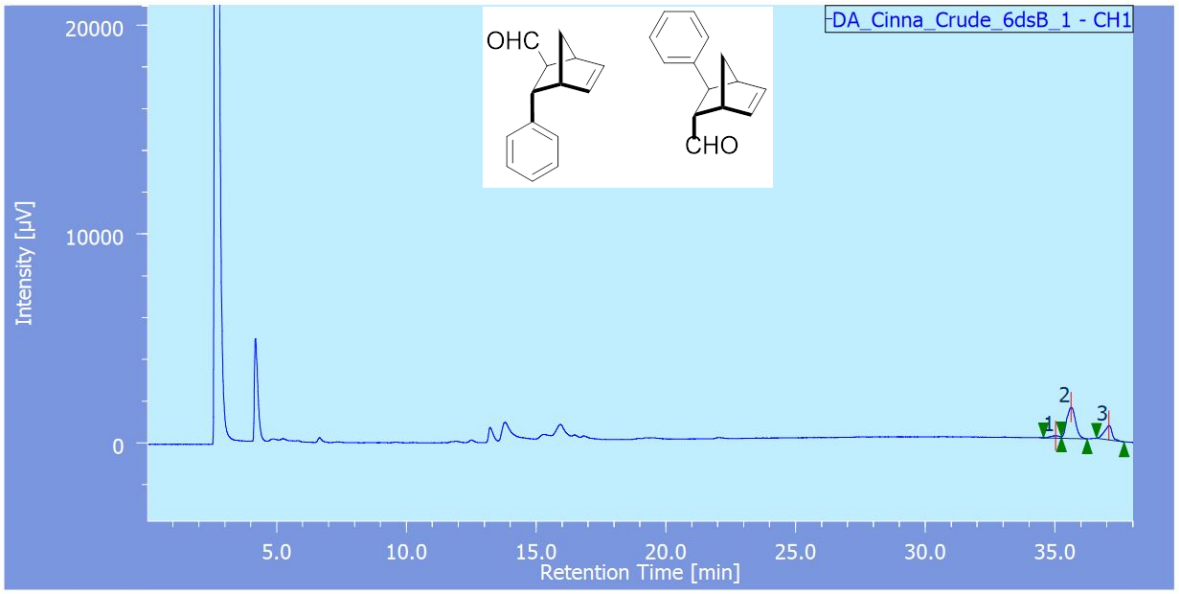


Figure S18. GC chromatogram of racemic **9**. (a) Full chromatogram. (b) Expanded chromatogram.

(a)



(b)

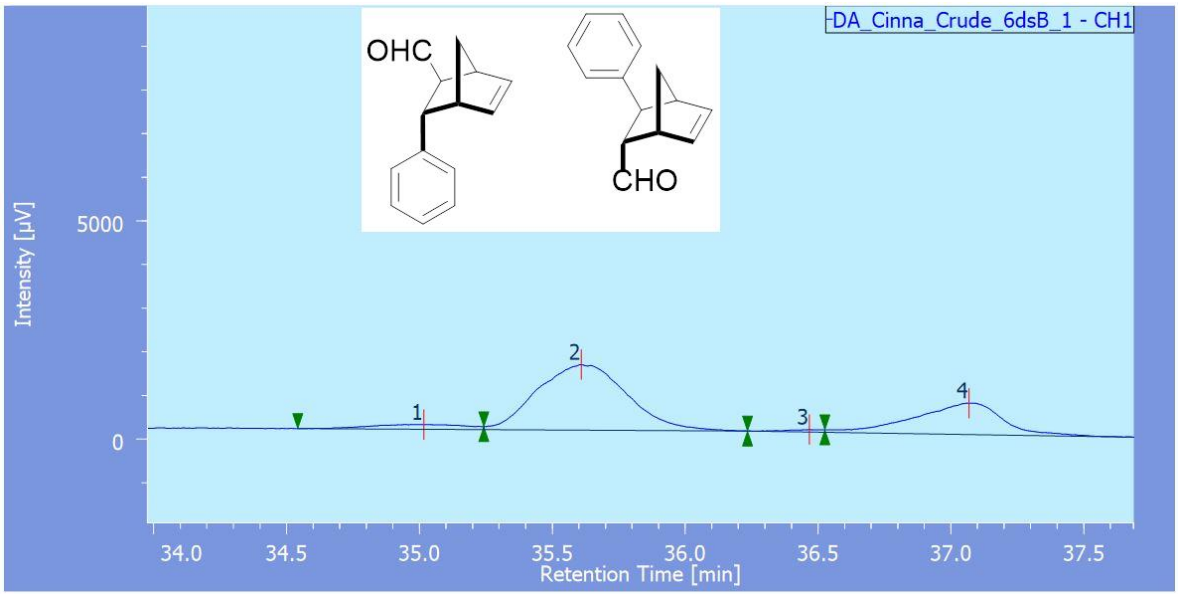
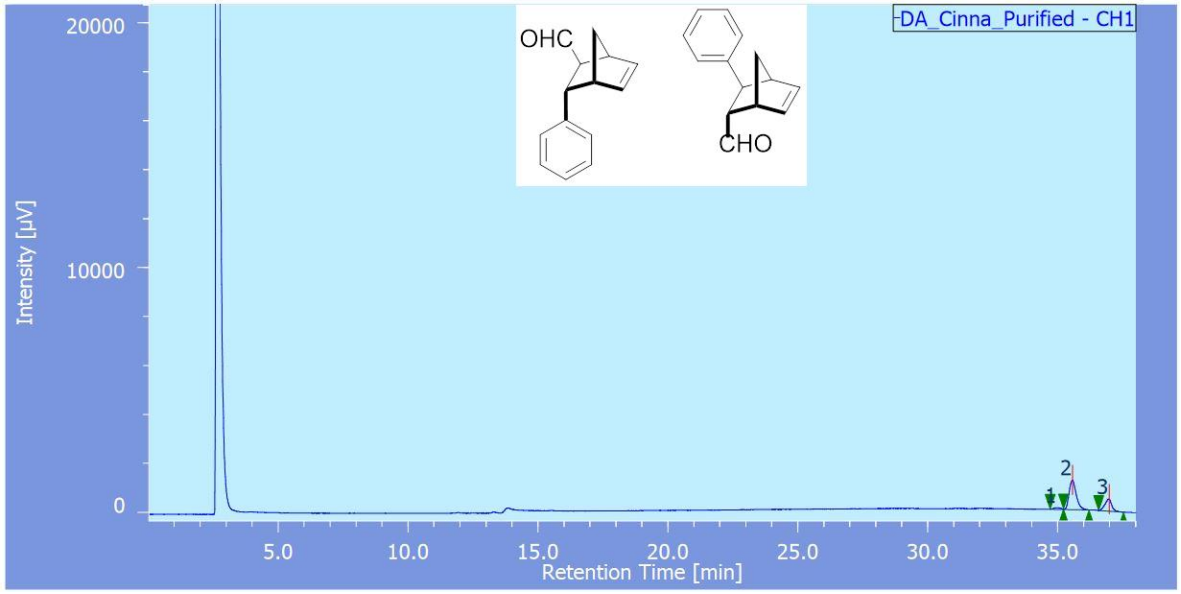


Figure S19. GC chromatogram of crude **9** (entry 7 in Table 4). (a) Full chromatogram. (b) Expanded chromatogram.

(a)



(b)

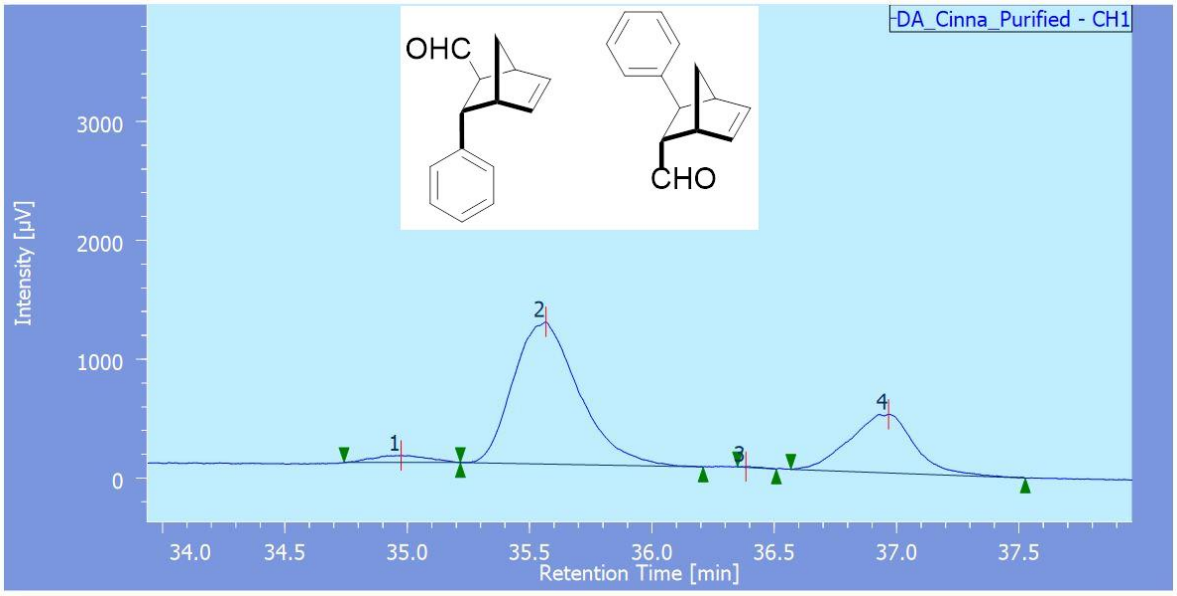


Figure S20. GC chromatogram of **9** after purification (entry 7 in Table 4). (a) Full chromatogram. (b) Expanded chromatogram.

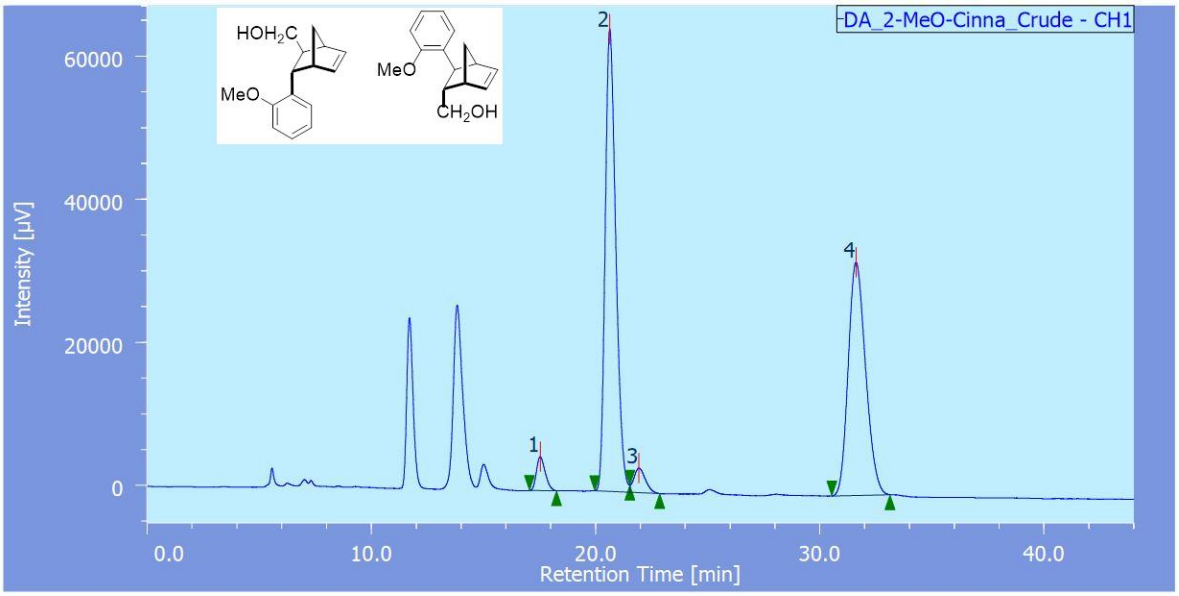


Figure S21. HPLC chromatogram of crude **14** after reduction.

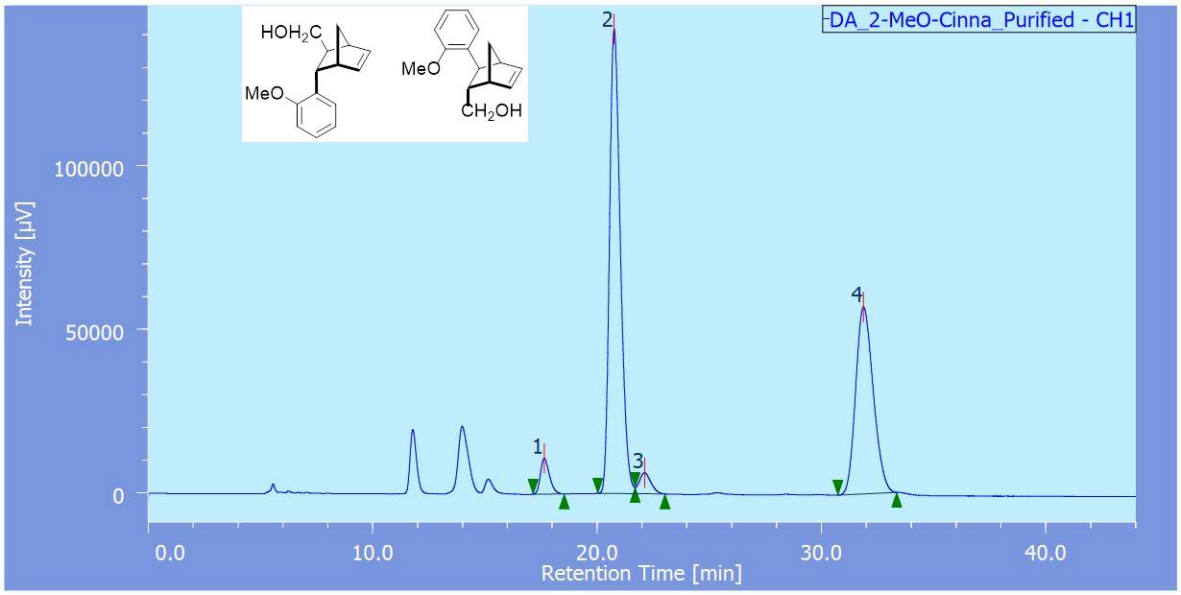


Figure S22. HPLC chromatogram of **14** after reduction.