SUPPORTING INFORMATION

A Hybrid Au/Ru Catalyst for Sequential Alkyne Hydration/Asymmetric Transfer Hydrogenation Reactions

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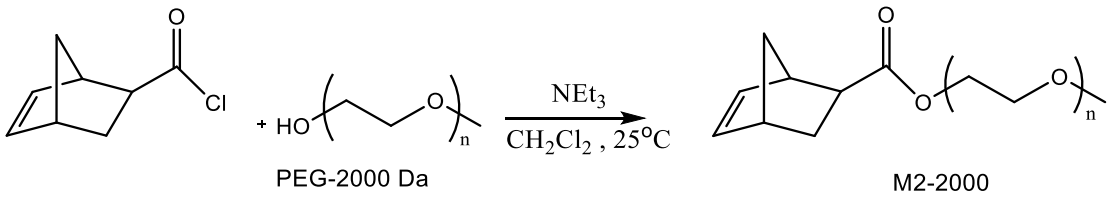
CONTENT

Experimental Section

Otherwise noted all chemicals were purchased from Sigma-Aldrich and used as received. $[RuCl_2(p\text{-cymene})]_2$ complex was purchased from Strem and used as received. 1S,2S)-1,2bis(4hydroxyphenyl)ethylenediamine was purchased from Sigma-Aldrich. Dimethylformamide was dried over molecular sieves 4A overnight and drying agent was removed through decantation, followed by vacuum distillation. THF was pre-dried over CaH_2 and distilled over Na-wire/benzophenone under a nitrogen atmosphere. N_2 physical adsorption tests were performed on a Quantachrome Corporation, Autosorb-6 adsorption analyzer (samples were degassed at 160 °C for 8 h before the measurements). The BET surface areas were evaluated from data in the relative pressure range from 0.05 to 0.25. The total pore volume was estimated from the amount adsorbed at the highest P/P_0 (above 0.99). The surface chemistry of the functionalized particles was analyzed with X-ray photoelectron spectroscopy (XPS) (K-Alpha XPS, ThermoFisher Scientific, U.S.A) in order to characterize the content. Environmental Scanning Electron Microscope (SEM) images were recorded using FEI Quanta 200 FEG ESEM device. Gas chromatography-mass spectrometry (GC-MS) analyses were performed with a Shimadzu GC-MS 2010Plus using a Restek Rxi-5Sil column (30 m × 0.25 mm × 0.25 µm) and a temperature range of 50-320 °C with a constant helium flow rate of 1 mL/min. Enantioselectivity of chiral alcohols was determined by GC-MS analysis using TrajanTM SGE-Cydex-B column (25m x 0.22 mm x 0.25 µm) with a constant helium flow rate of 1 ml/min. Dynamic light scattering (DLS) analysis was carried out using a Malvern Seta-Sizer Nano-ZS90 with a fixed scattering angle 90°. High contrast transmission electron microscopy (TEM) images were recorded at METU Central Lab (Ankara) with FEI Tecnai G2 Spirit Bio(TWIN) 600 TEM at 120 kV using carbon filmed coated copper grids via dropping 1 µL of samples into the grids from EtOH diluted samples.

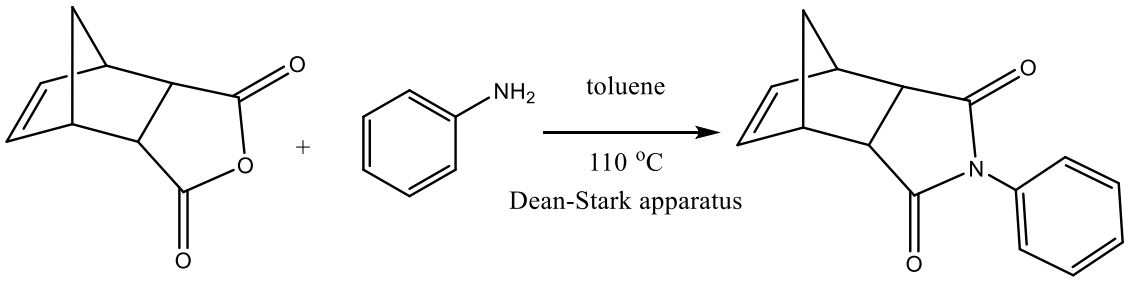
Synthesis of M1



Scheme S1. Synthesis of hydrophilic monomer (M2)

Polyetilenglikol monomethyl ether (PEG_{2000}, 22.0 g, 11.0 mmol) was taken to a 100 mL glass balloon and dry dichloromethane (50 mL) and molecular sieve 4Å was added to the reactor and stirred overnight to dry the PEG. Molecular sieves were separated from the reaction mixture through filtration and the organic solution was taken to a glass balloon. Bicyclo[2.2.1]hept-5-ene-2-carbonyl chloride (1.0 g, 6.39 mmol) and triethylamine (0.71 g, 7.0 mmol) were added to the reactor and the reaction mixture was stirred for 24 h at room temperature under nitrogen atmosphere. After 24 h, the polymer was precipitated in cold diethyl ether and stored at -24 °C overnight. The precipitated white solid was separated from the mixture through filtration. The compound was characterized by means of SEC, MALDI-ToF-MS, ^{1}H and ^{13}C NMR spectroscopy.

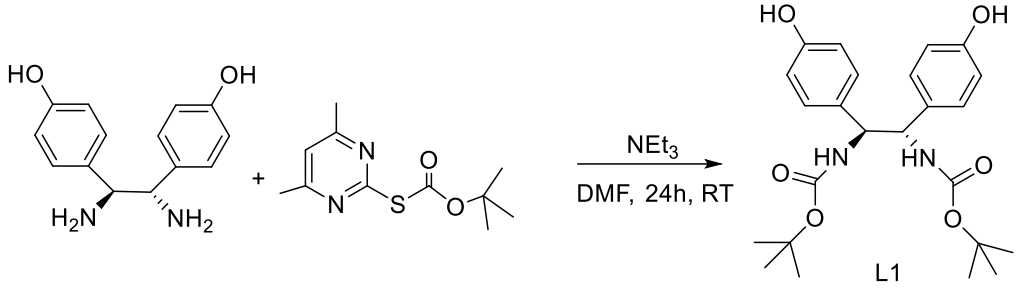
Synthesis of M2



Scheme S2. Synthesis of hydrophobic monomer (M2)

5-norbornene-2,3-dicarboxylic anhydride (10 g, 61.0 mmol) and dry toluene (20 mL) was taken to a glass flask equipped with a Stark apparatus. Aniline (6.8 g, 73.0 mmol) was added to the reaction vessel and the reaction mixture was heated to 110 °C in a pre-heated oil bath. After 48 h, the reaction mixture was cooled to room temperature and the monomer was precipitated in cold diethyl ether. The white solid was separated through vacuum filtration and dried under vacuum at 40 °C, overnight. The monomer (exo&endo mixture) was characterized by means of ^{1}H and ^{13}C NMR and GC-MS analysis.

Synthesis of L1

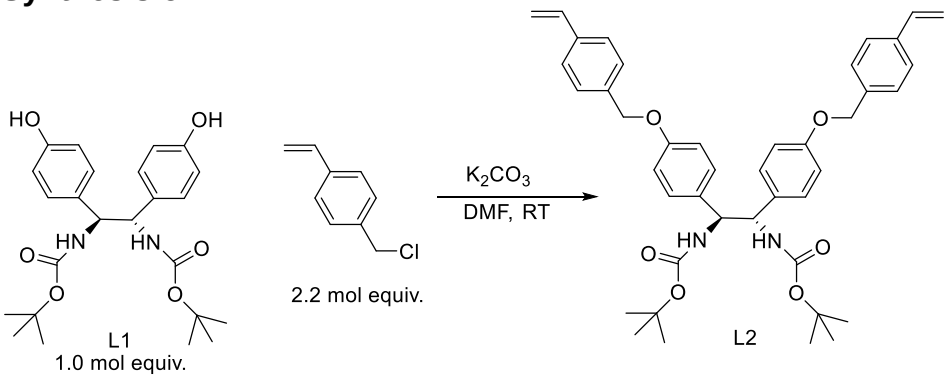


Scheme S3. Synthesis of L1

A 100 mL two-necked glass flask (100 mL) was charged with (1S, 2S)-1,2-bis(4-hydroxyphenyl)ethylenediamine (1.0 g, 4.1 mmol) and S-Boc-2-mercapto-4,6-dimethylpyrimidine (3.97 g, 16.5 mmol) in 10 mL of dry DMF. The reaction mixture was stirred at room temperature for 24 h under a nitrogen atmosphere. The solvent was evaporated under a vacuum resulting in a dark yellow solid. The flask was charged with dichloromethane (20 mL) to dissolve the unreacted starting materials and side products. The resulting suspension was filtrated and the remaining solid was washed with hexane (10 mL x2) and dried under high vacuum, resulting in a light yellow/off-white solid (yield %: 60 %). ESI-MS: 443.2188; 443.2201

^{1}H NMR (400 MHz, DMSO) δ 9.54 (s, 2H), 7.04 (d, *J* = 21.1 Hz, 2H), 6.64 (d, *J* = 45.7 Hz, 2H), 5.38 (s, 2H), 1.29 (s, 18H). ^{13}C NMR (100 MHz, DMSO) δ 155.99, 154.06, 129.24, 127.76, 119.04, 114.44, 77.79, 28.60

Synthesis of L2



Scheme S4. Synthesis of L2

L1 (0.30 g, 0.7 mmol) was dissolved in 5 mL of dry DMF at room temperature in a 50 mL glass flask. K_2CO_3 (0.6 g, 4.34 mmol) was added to the reaction flask in small portions over a period of one hour. p-vinylbenzyl chloride (0.45 g, 2.95 mmol) was added to the reaction flask and

stirred at room temperature for 24 h. The reaction mixture was filtrated over a small pad of silica gel and solvent and excess p-vinylbenzyl chloride was removed by a rotary evaporator under vacuum. The resulting yellow solid was washed with diethtyl ether (10 mL x 2) and dried under a high vacuum. (Yield %: 46 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.05 (m, 12H), 6.91-6.79 (m, 6H), 5.83 (d, *J* = 17.8 Hz, 4H), 5.68 (d, J=2.4 Hz, 2H), 5.29 (d, *J* = 11.3 Hz, 2H), 4.96 (s, 4H), 1.29 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.22, 136.60, 128.88, 128.27, 127.47, 126.62, 126.40, 120.49, 113.87, 111.79, 78.80, 69.64, 56.63, 46.14, 28.49

Synthesis of Amph

A Schlenk reactor was charged with M1 monomer (0.64 g, 0.15 mmol) in 10 mL of dry toluene. Hoveyda-Grubbs 2nd generation catalyst (HG2, 0.010 g, 0.015 mmol) was added to the reactor and stirred at 80 °C under a nitrogen atmosphere. After 30 minutes, M1 monomer (0.36 g, 1.50 mmol) and L2 (0.02g, 0.03 mmol) as chain-transfer agent was added to the reactor and stirred at 80 °C for 12 h. After 12h, the reaction mixture was cooloed down to room temperature and poured into cold diethyl ether and the precipitated polymer was isolated by simple filtration. The off-white polymer was redissolved in THF and precipitated in cold diethyl ether to remove the unreacted monomers and residual catalysts. The amphiphilic polymer was characterized by means of ^{1}H NMR, SEC, DLS and high contrast TEM analysis.

Synthesis of Ru@Amph (Ru-L3)

Amphiphilic polymer (Amph was dissolved in dry THF (5 mL) at room temperature. Following this protocol, aqueous 4 M HCl (400 µL) was added to the solution to remove the protecting t-Boc groups to obtain free amine groups on the polymer backbone. The reaction mixture was washed with saturated $NaHCO_3$ solution to remove the excess acid and then extracted with deionized water. The organic phase was separated and the polymer was precipitated in cold diethyl ether. The polymer was dried under a high vacuum overnight. The polymer (L3) was taken to a Schlenk reactor and the polymer was dissolved in dry dichloromethane (10 mL). After dissolution of L3, triethylamine (1.6 mol equivalent) and p-toluenesulfonyl chloride (1.2 mol equivalent relative to amine group) was added to the reactor and stirred at room temperature for 4 h under a nitrogen atmosphere. Following this protocol, $[RuCl_2(p\text{-cymene})]_2$ was added to the reactor and stirred for 12 h at room temperature. After 12 h, the reaction mixture was filtrated over a pad of silica gel and precipitated in cold diethyl ether.

0.20 g of Ru@amph (L3) was dispersed in 10 mL of pure water and diluted with 90 mL of ethanol using mechanical stirrer. 0.10 g Synperonic®F108 and 0.10 g centrimonium bromide (CTAB) were added to the reaction mixture and stirred for one hour to ensure the complete dissolution of the added surfactants. After one hour, concentrated ammonia (1 mL) was added to the reaction mixture and stirred for five minutes. Tetraethylorthosilicate (TEOS) (1.50 g) was added dropwise to the solution under mechanical stirring at 280 rpm. Following the addition of TEOS, the reaction mixture was stirred for 24 h at room temperature. Silica coated particles were isolated by centrifugation of the reaction mixture at 6000 rpm. The isolated silica particles were washed with ethanol (10 mL x 2) and dried under a high vacuum overnight.

Immobilization of Au on SiO_2@Ru-amph (Au@SiO_2@Ru-amph)

SiO_2@Ru@amph (0.50 g) was taken to a Schlenk reactor and dispersed in 10 mL of dichloromethane. IPrAuCl (0.025 g) in dichloromethane (1 mL) was added to the reaction medium and stirred magnetically at 800 rpm. After 24 h, dichloromethane was removed under a high vacuum. The resulting solid was washed with ethanol (2 mL x 2). 90 % wt. of added gold complex was immobilized on the support material. The Au content was found to be 0.077 mmol Au/g as confirmed by ICP-MS.

Post-pore size reduction of Au@SiO_2@Ru@L3 through silylation reactions

A 100 mL three necked Schlenk flask was charged with SiO_2@Ru-Amph (1.0 g, 0.118 mmol Ru/g) and dispersed in dry dichloromethane through ultrasound for five minutes. After that, IPrAuCl (10 mg, 0.0161 mmol) were added to the reaction medium and stirred for 12 h at room temperature under nitrogen atmosphere. To reduce the pore-size, dichlorodiphenylsilane ($SiCl_2Ph_2$, 20 µL, 0.096 mmol) and 2-methylpyridine (0.20 mmol, 20 µL) was added to the reaction media and stirred for 12 h at room temperature. Solvent was evaporated under high vacuum. The resulting orange/yellow solid was washed with dichloromethane (2 mL x 2) and dried under vacuum at 30 °C.

Alkyne Hydration Reactions in the presence of Au@SiO_2@Amph or en-Au@SiO_2@Ru-Amph catalysts

A Schlenk reactor was charged with Au@SiO_2@L3 or en-Au@SiO_2@L3 (encapsulated) (100 mg, 0.077 mmol Au/g or 100 mg, 0.012 mmol Au/g) and dispersed within MeOH/H_2O (1 mL/ 1 mL) using sonication. Phenylacetylene (0.77 mmol, 85 µL or 0.12 mmol, 13 µL) were added to the reactor and silver (I) salts (1 mol % equivalent, AgOTf or $AgSbF_6$) were added. When the conversion of substrate has reached a plateau the reaction was cooled to room temperature and the product was extracted with diethyl ether.

Asymmetric Transfer Hydrogenation Reactions in the presence of Au@SiO_2@Amph or Ru@Amph

A Schlenk reactor was charged with Ru@amph (0.016 mmol Ru/g) or en-Au@SiO_2@Ru-amph and dispersed in methanol/H_2O (1 mL/1 mL) mixture at room temperature under nitrogen atmosphere. Acetophenone (1.6 mmol, 190 µL) and sodium formate (HCOONa, 3.2 mmol, 0.22 g) was added to the reaction media to initiate the reaction. The reaction was monitored by taking aliquots (10 µL) from the reaction mixture and analysed by GC-MS. Once the conversion of acetophenone has reached a plateau, the reaction mixture was cooled down to room temperature and extracted with diethyl ether.

Sequential Alkyne Hydration/Asymmetric Transfer Hydrogenation Reactions in the Presence of en-Au@SiO_2@Ru-amph

A Schlenk reactor was charged with en-Au@SiO_2@Ru-amph (100 mg, 0.0120 mmol Au/g, 0.118 mmol Ru/g) and dispersed in MeOH/H_2O (2 mL). Phenylacetylene (1000 mol equivalent to Au and 100 mol equivalent to ruthenium) was added to the reaction media and alkyne hydration reaction was initiated by addition of AgOTf (1 mol %, 0.0120 mmol, 3.0 mg) and the reaction mixture was stirred at 80 °C under nitrogen atmosphere. Once all the phenylacetylene was converted to the desired hydration product; acetophenone, sodium formate (2.4 mmol, 0.163 g) was added to the reaction media to initiate the asymmetric transfer hydrogenation reactions. After the conversion of acetophenone has reached a plateau, the catalyst was separated by centrifugation at 5000 rpm for 2 minutes and the solution phase was taken to a separation funnel and extracted with diethyl ether.

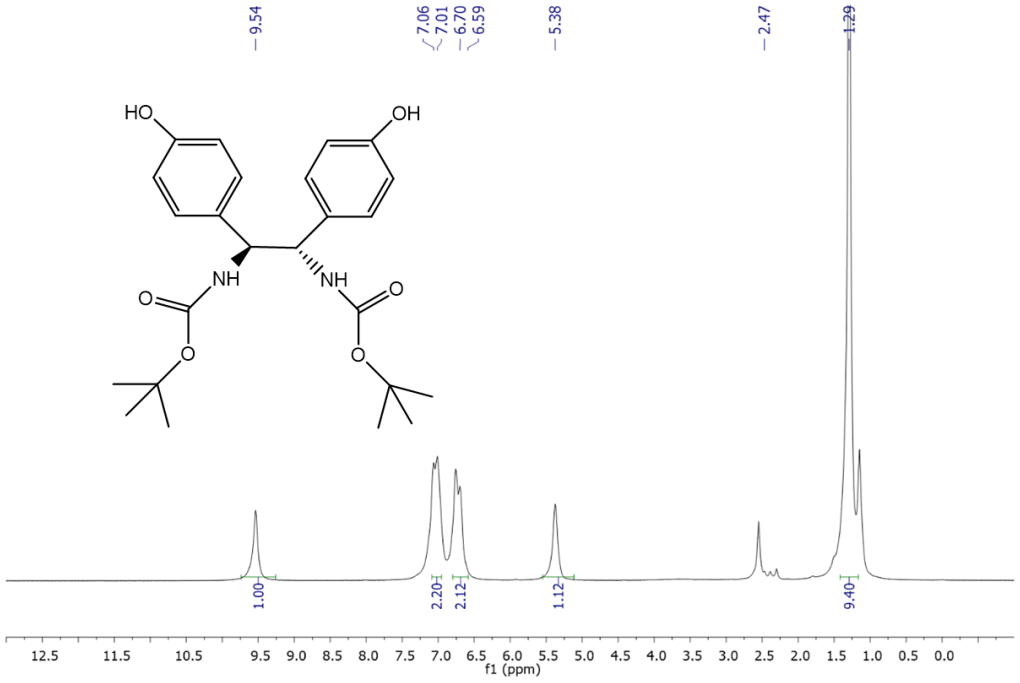


Figure S1. ^{1}H NMR spectrum of L1 (400 MHz, d_6-DMSO)

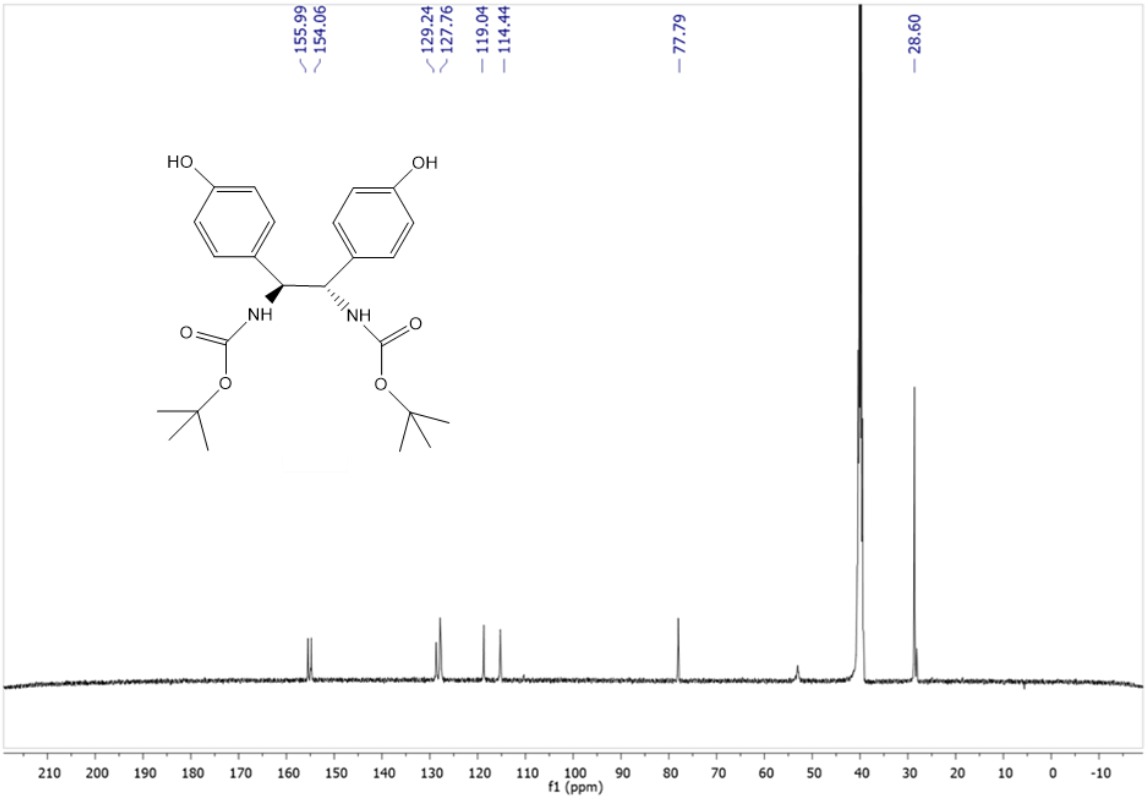


Figure S2. ^{13}C NMR spectrum of L1 (100 MHz, d_6-DMSO)

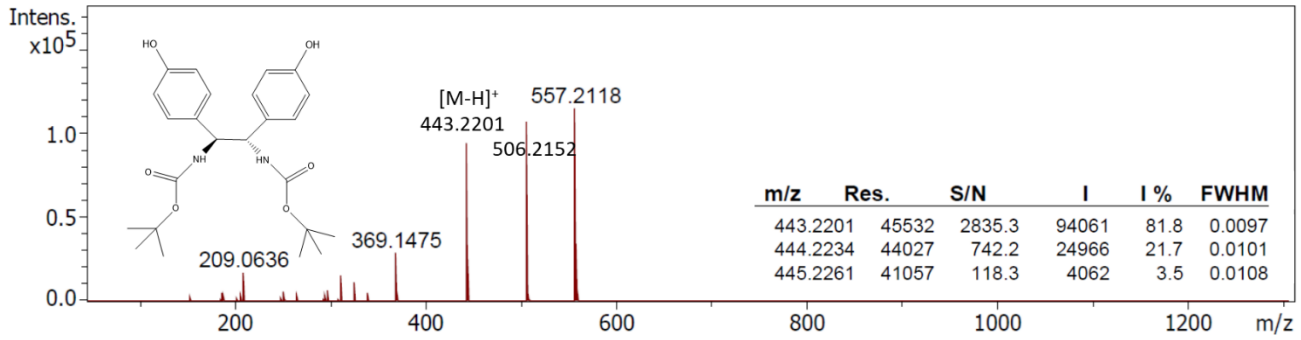


Figure S3. ESI-MS spectrum of L1 (Negative mod)

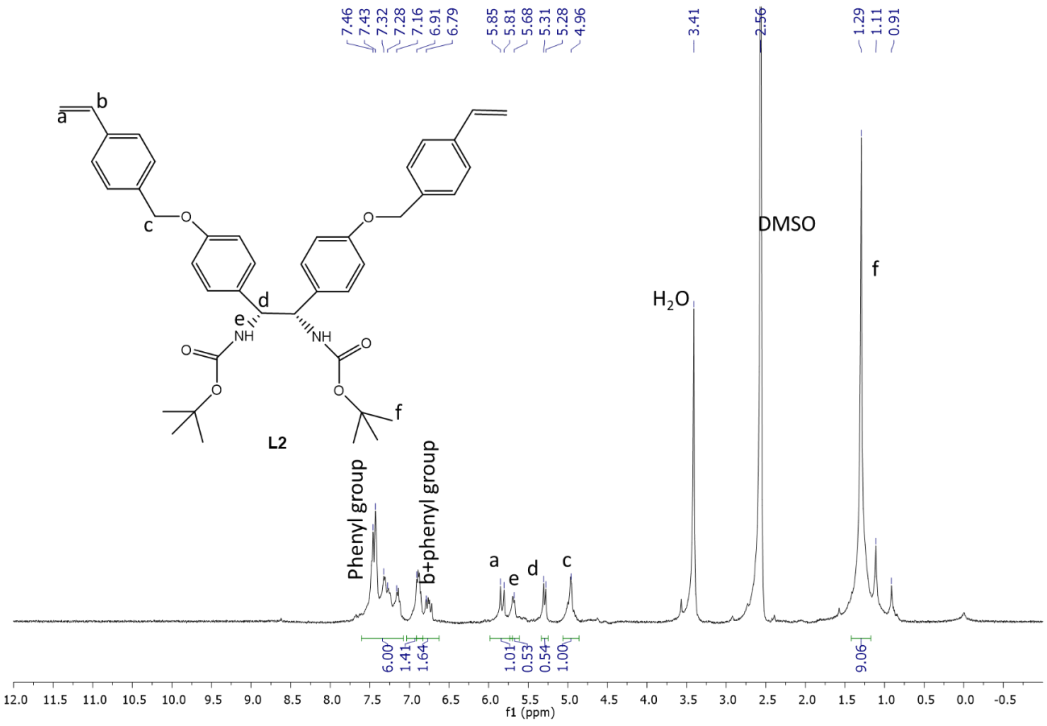


Figure S4. ^{1}H NMR spectrum of L2 (400 MHz, d_6-DMSO)

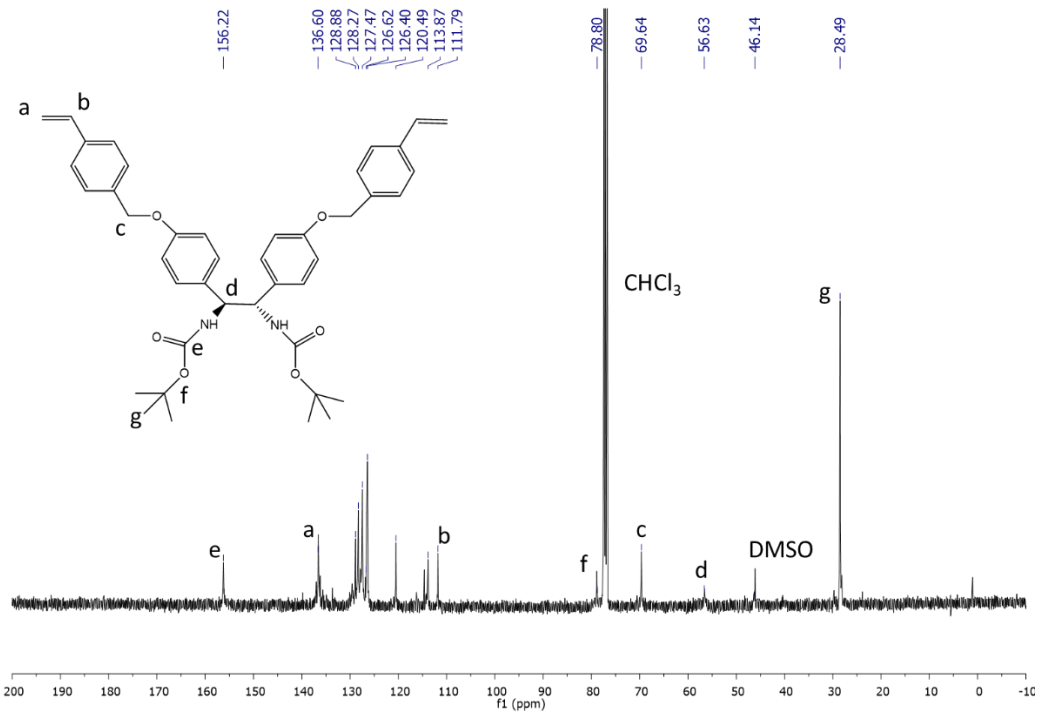


Figure S5. ^{13}C NMR spectrum of L2 (100 MHz, $CDCl_3$)

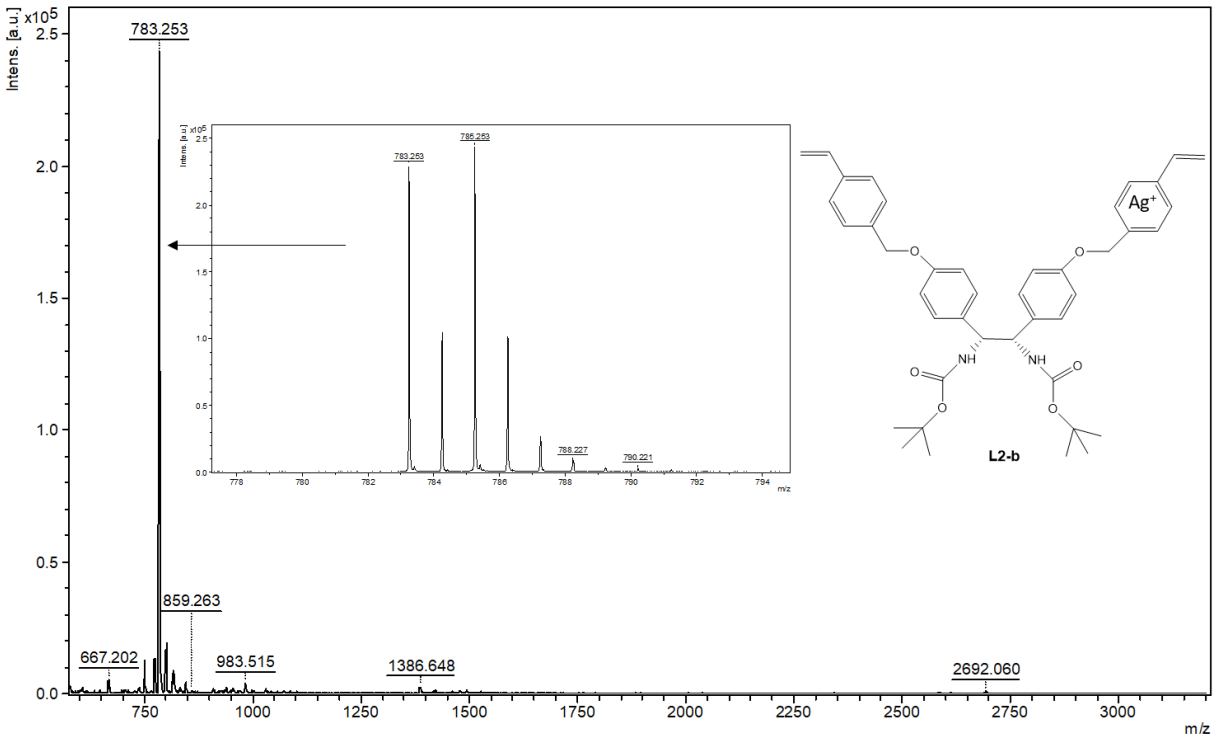


Figure S6. MALDI ToF-MS spectrum of L2

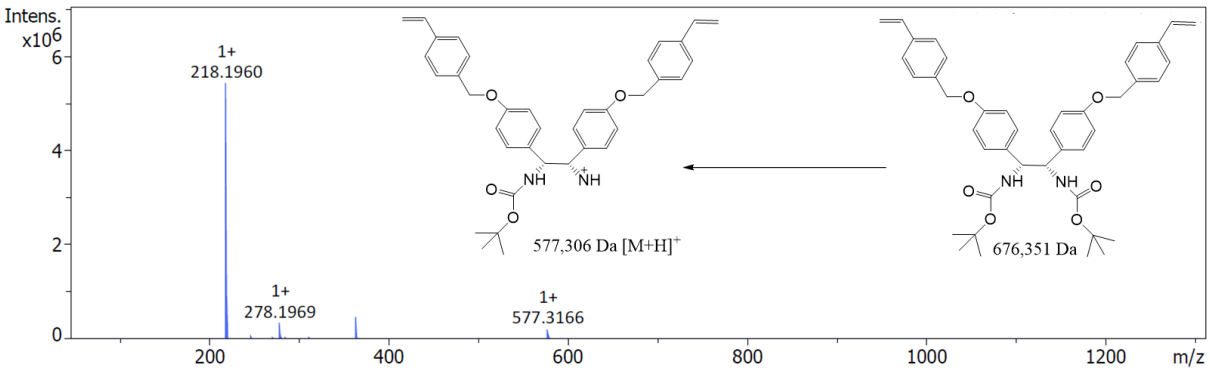


Figure S7. ESI-MS spectrum of L2 (positive mode)

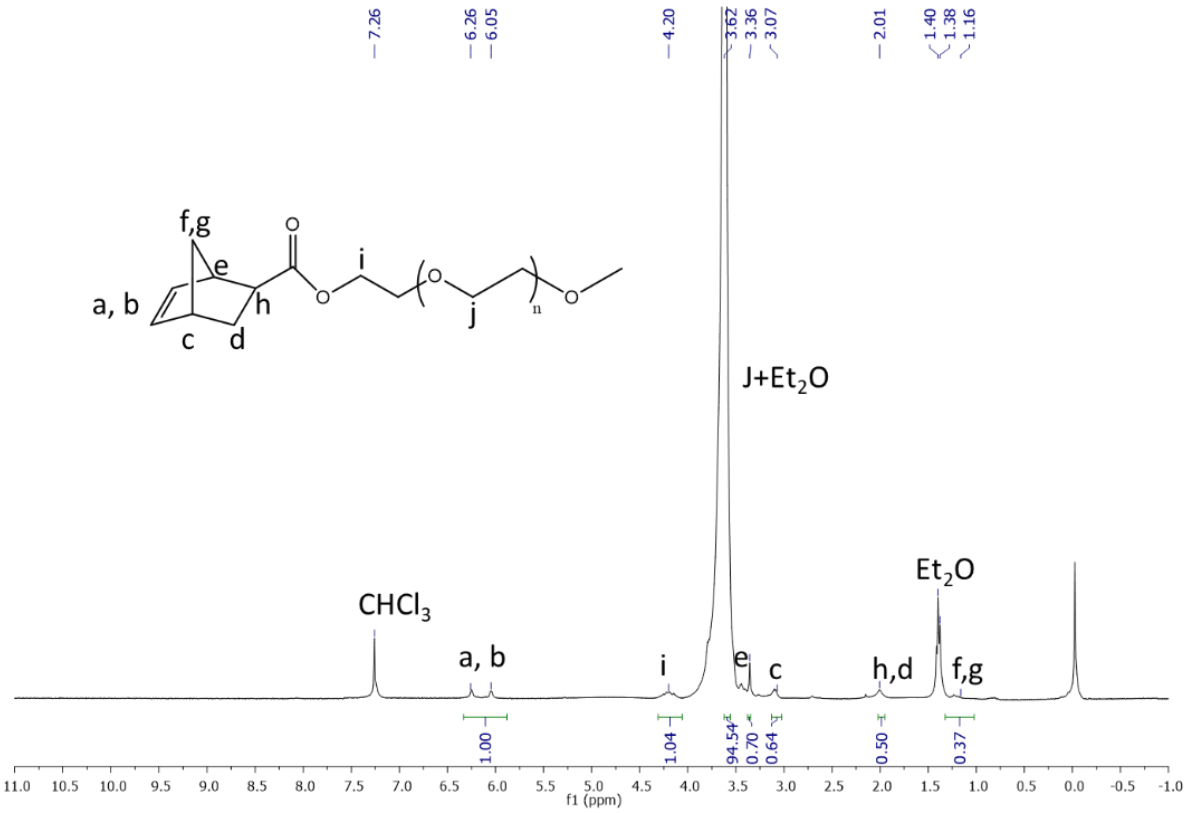


Figure S8. ^{1}H NMR spectrum of hydrophilic monomer (M1) (400 MHz, $CDCl_3$)

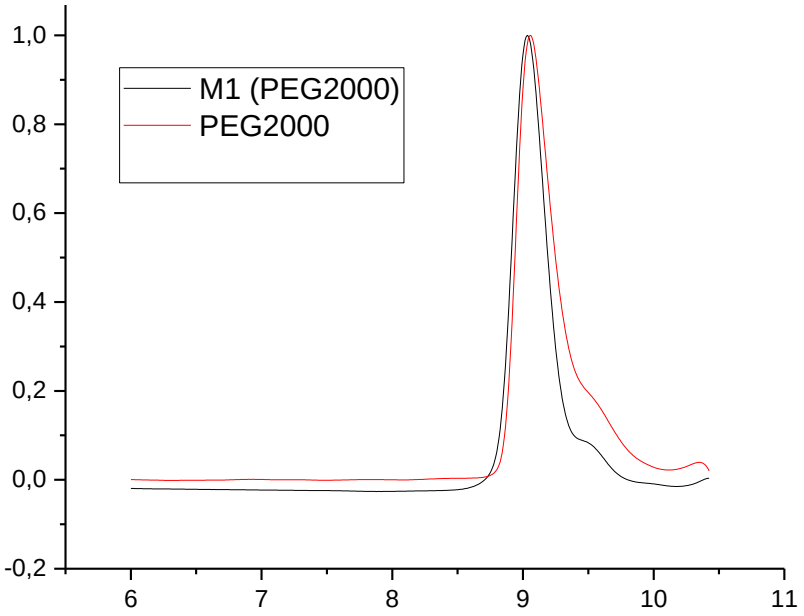


Figure S9. Size-exclusion chromatography of hydrophilic monomer M1 in THF (1mL/min.)

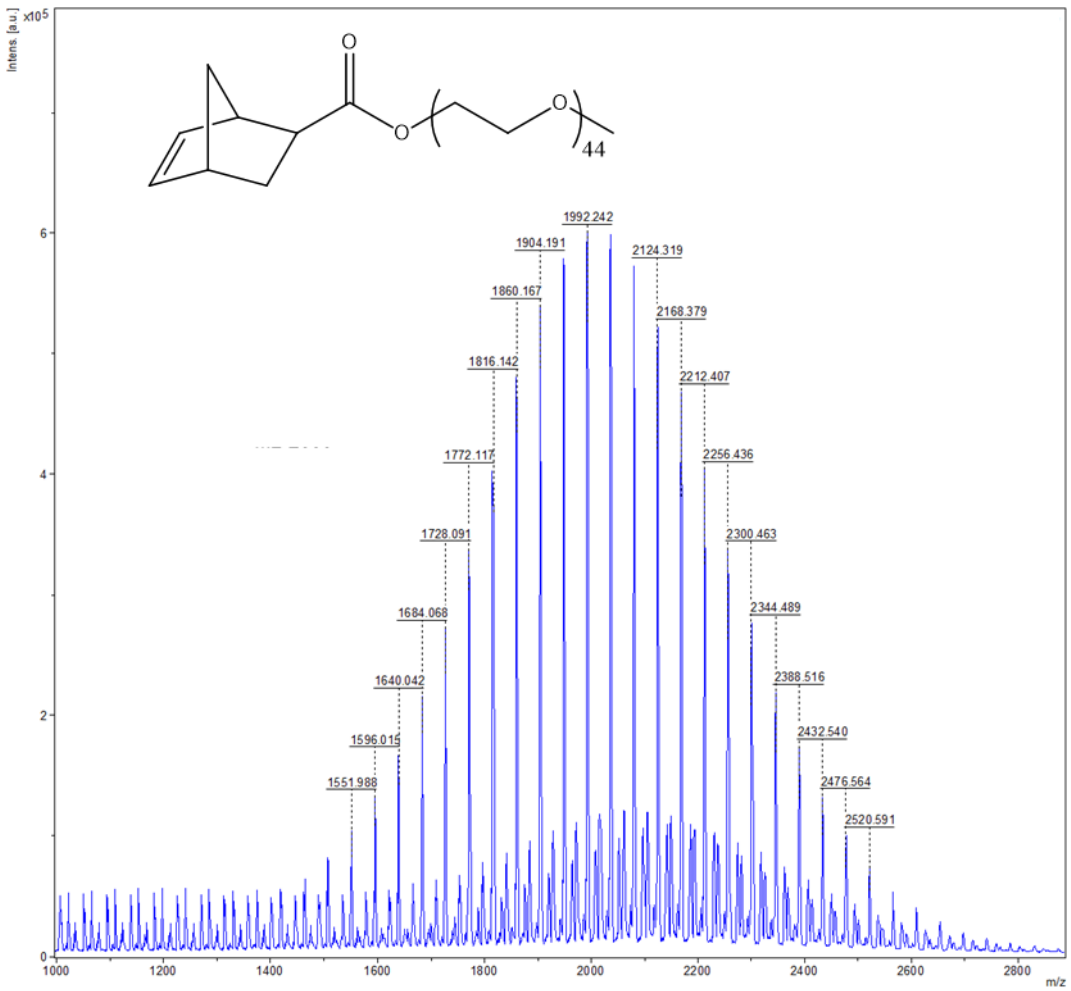


Figure S10.MALDI ToF-MS spectrum of hydrophilic monomer M1

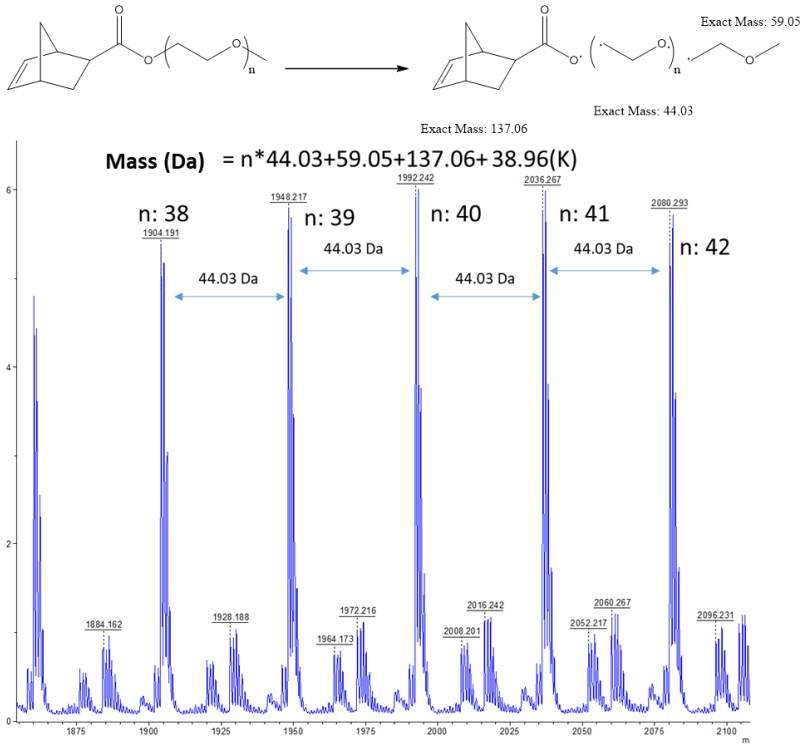


Figure S11. The detailed MALDI ToF-MS spectrum of hydrophilic monomer M1

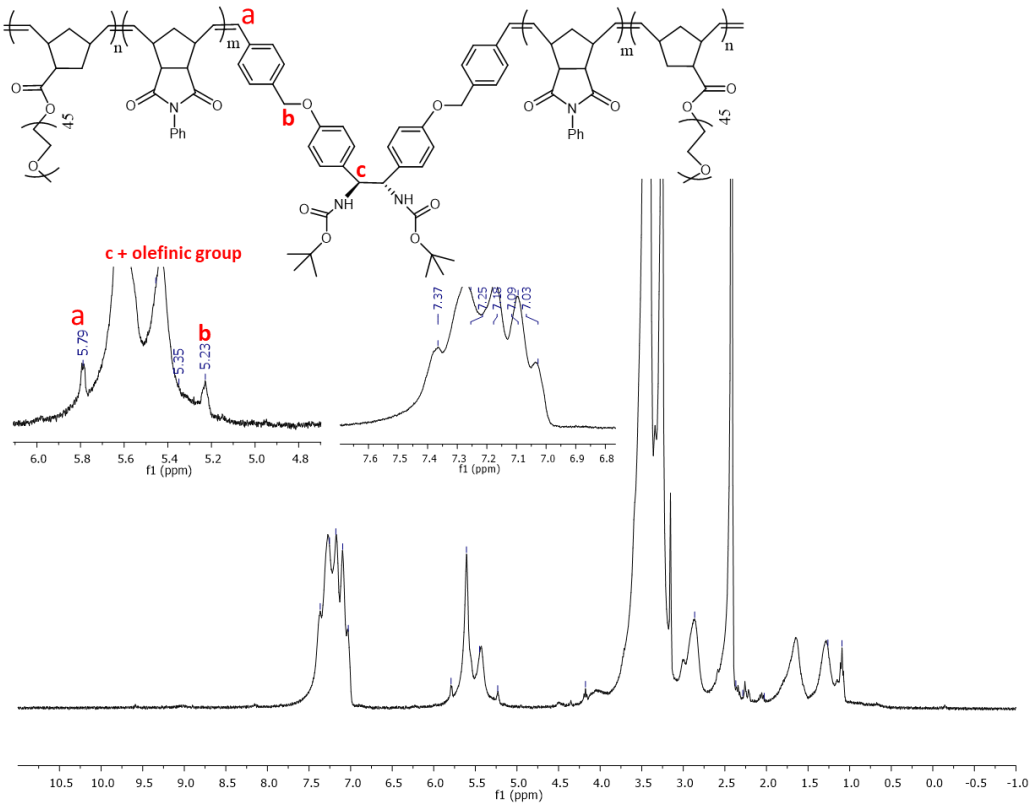


Figure S 12. ^{1}H NMR spectrum of Amph (400 MHz, $CDCl_3$)

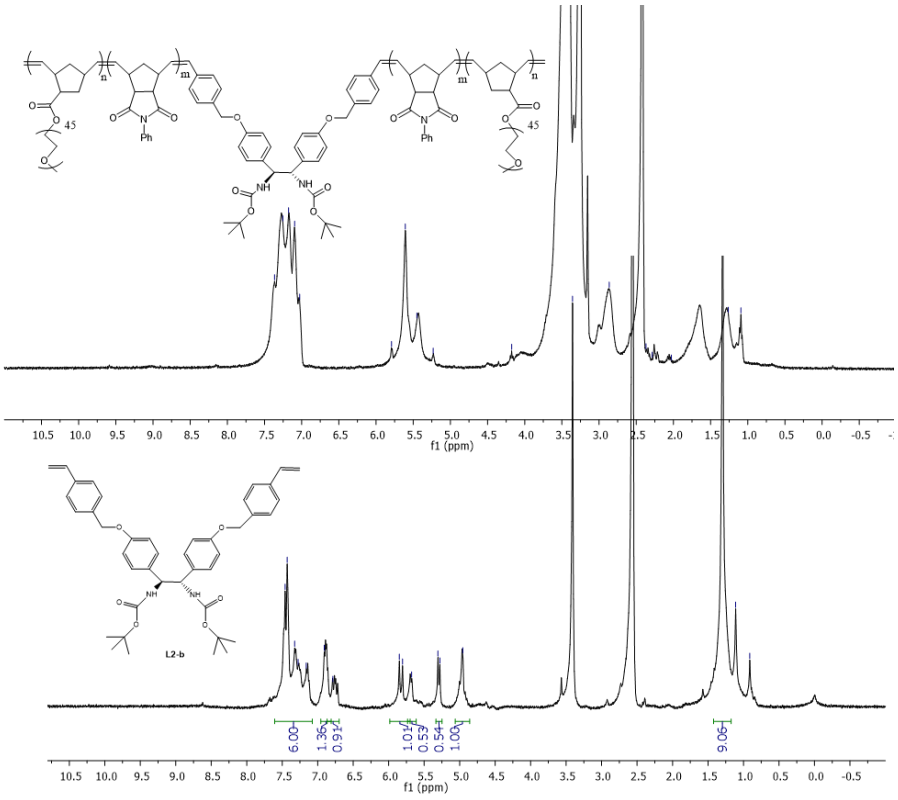


Figure S 13. ^{1}H NMR spectrum comparison of Amph(L3) and L2

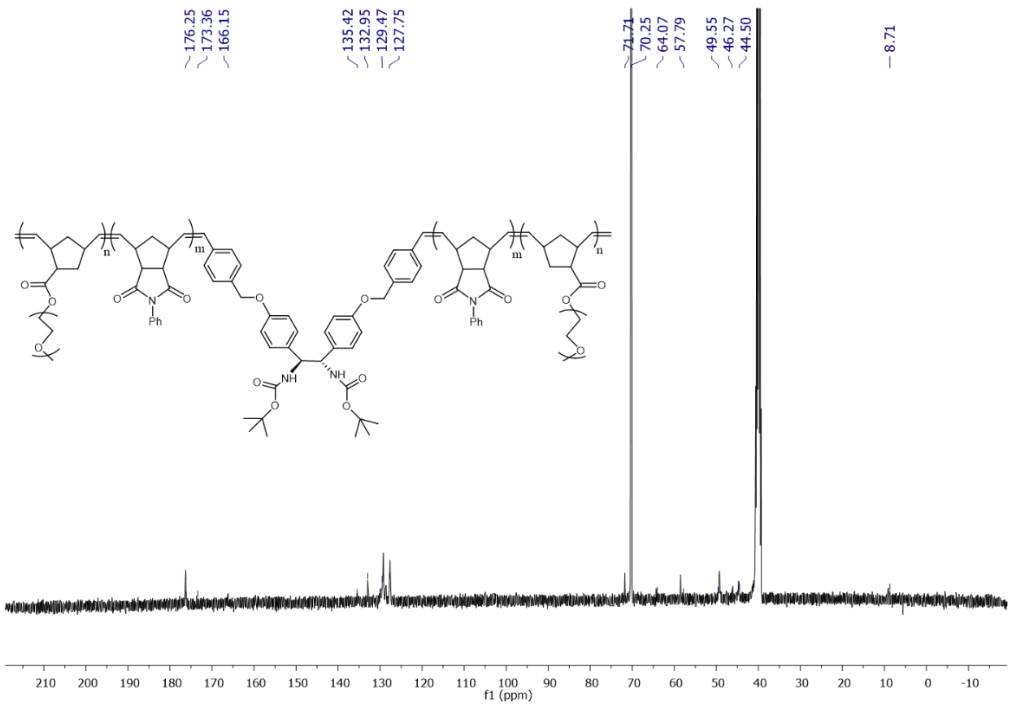


Figure S 14. ^{13}C NMR spectrum of Amph (L3) (100 MHz, $CDCl_3$)

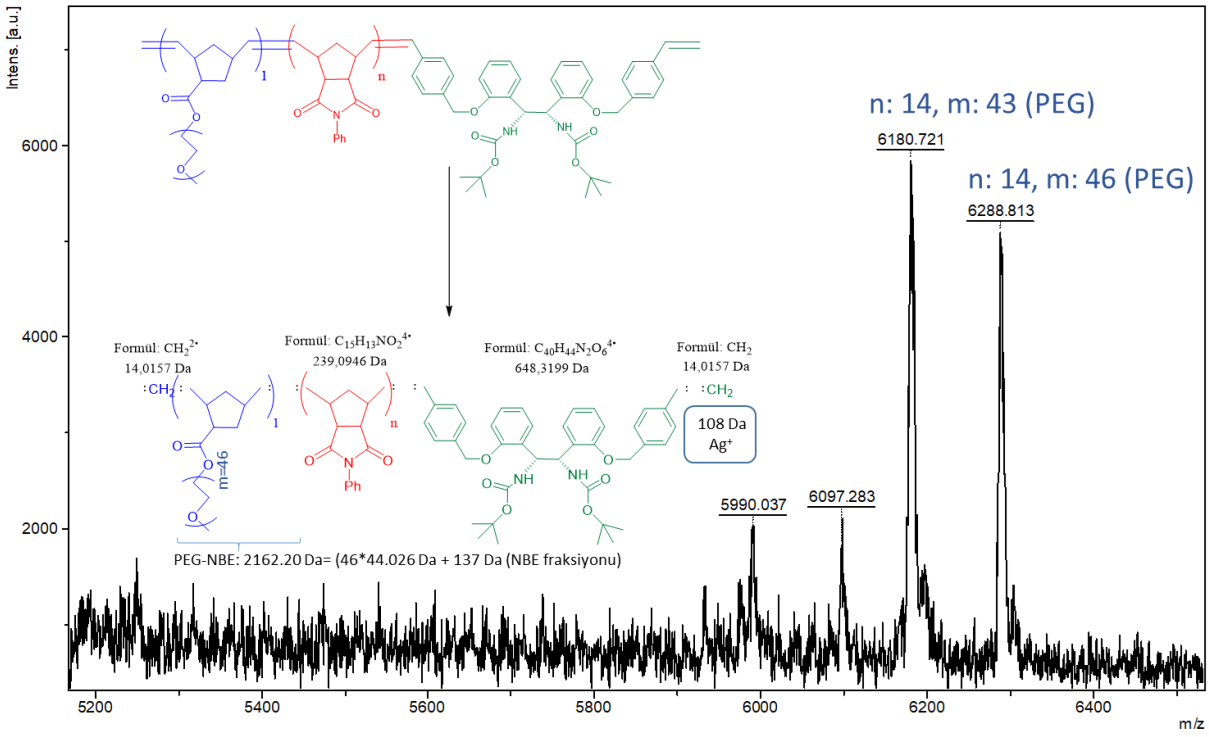


Figure S 15. MALDI ToF-MS spectrum of Amph (For clarity polymer was showed as mono-substituted on CTA)

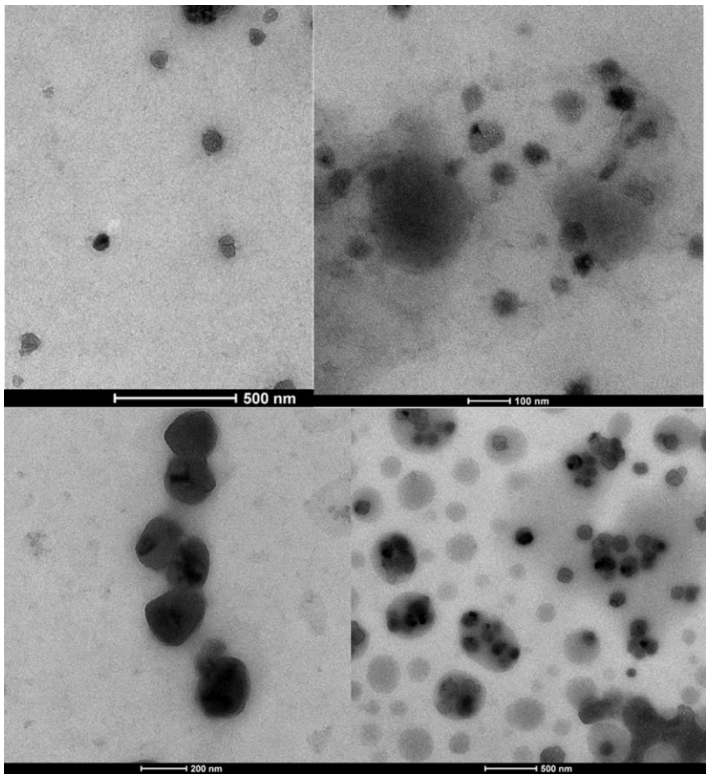


Figure S 16. High contrast TEM images of Amph

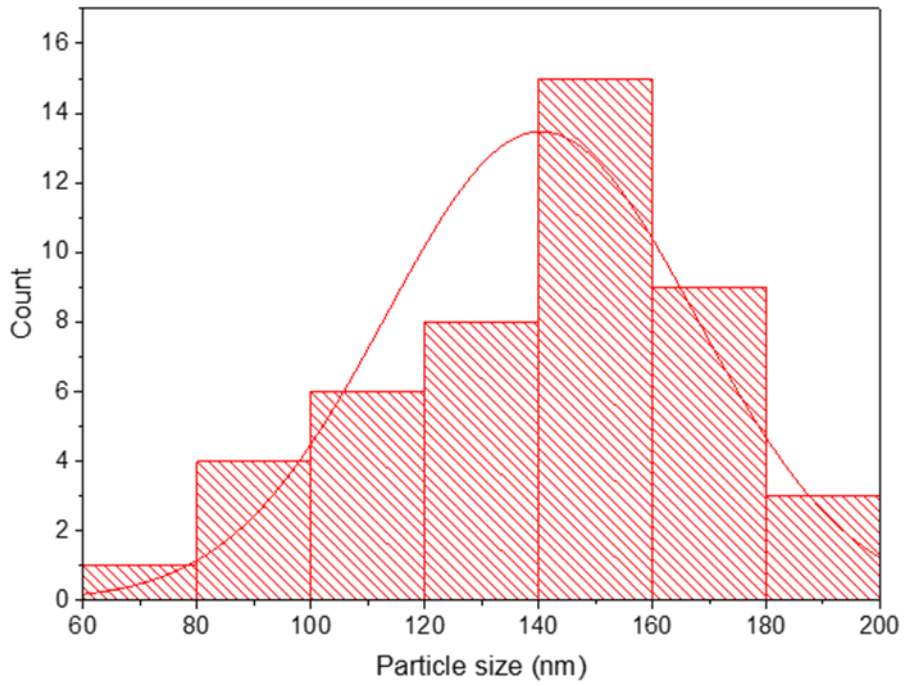


Figure S 17. Average particle size of Amph obtained from TEM analysis (140 nm (± 30 nm))

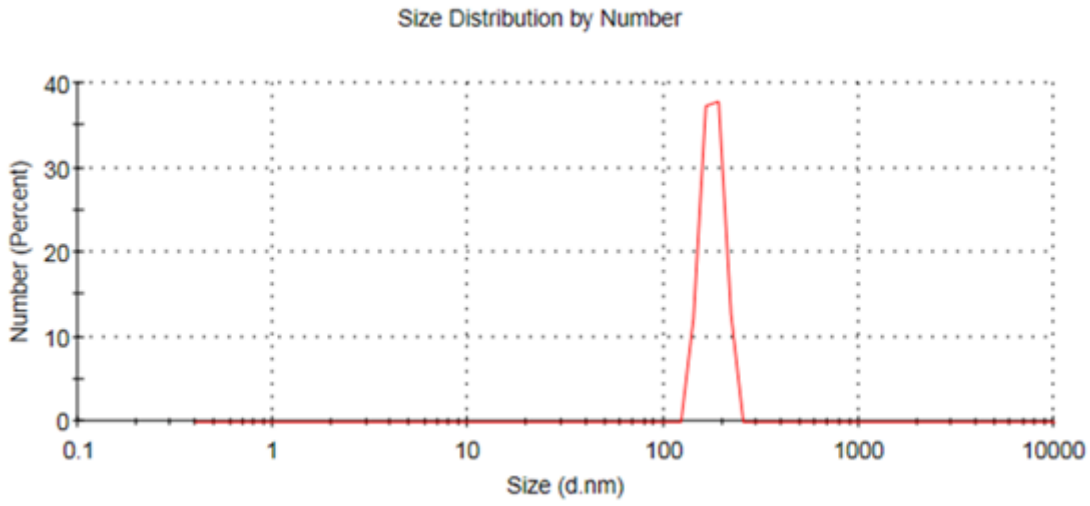


Figure S 18. DLS analysis of Amph in water (170 nm (± 23 nm))

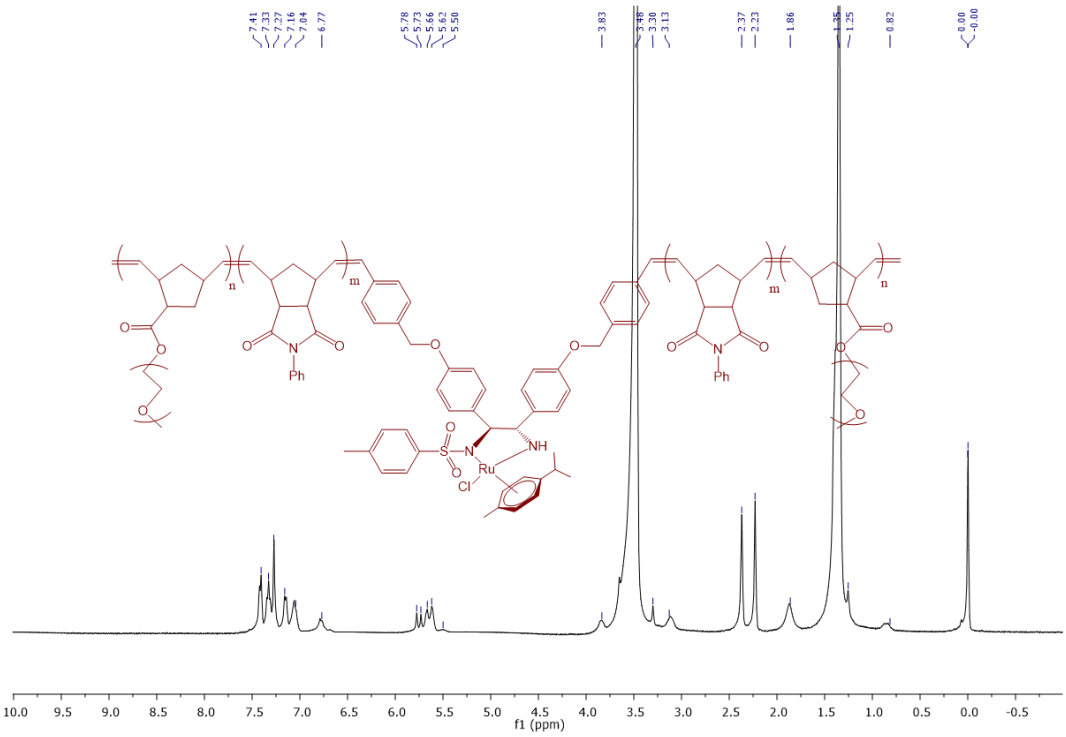


Figure S 19. ^{1}H NMR spectrum of Ru@amph (400 MHz, d_6-DMSO)

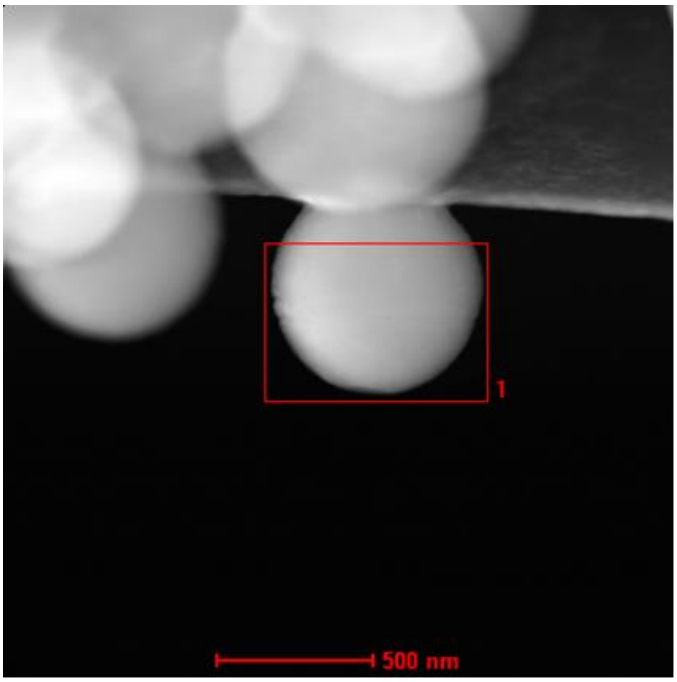


Figure S 20. HR-TEM images of SiO_2@Ru@Amph (Please note that relatively larger particles are specifically chosen to obtain a more detailed EDX-line analysis)

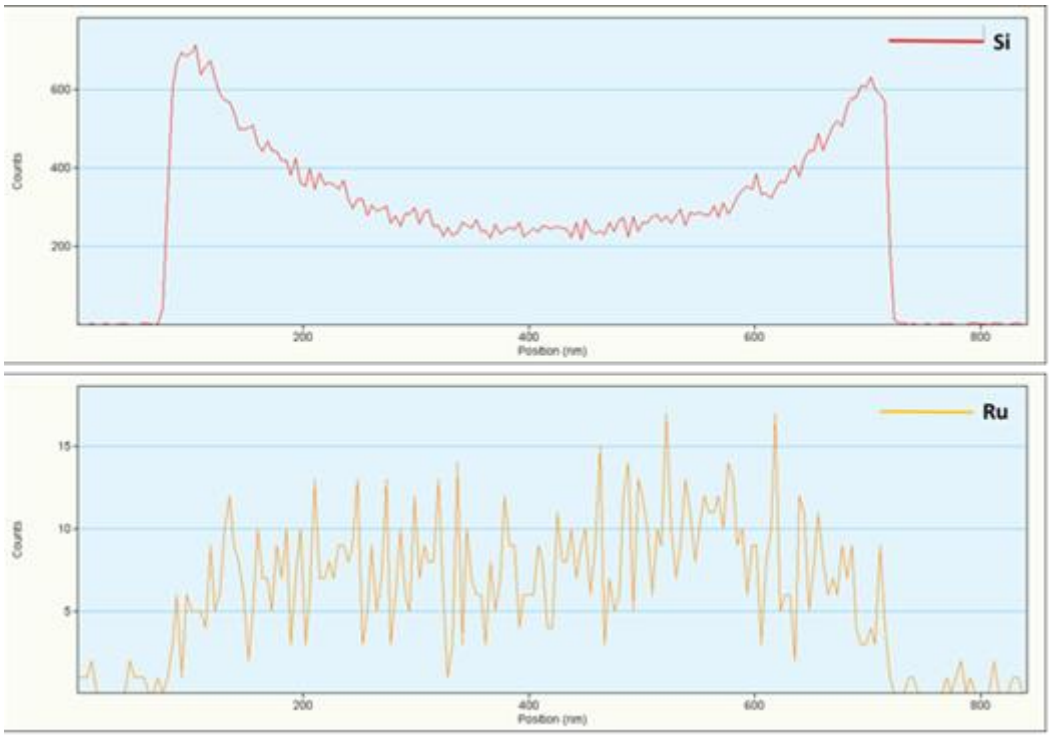


Figure S 21. EDX line analysis for SiO_2@Ru@Amph (Ru and Si)

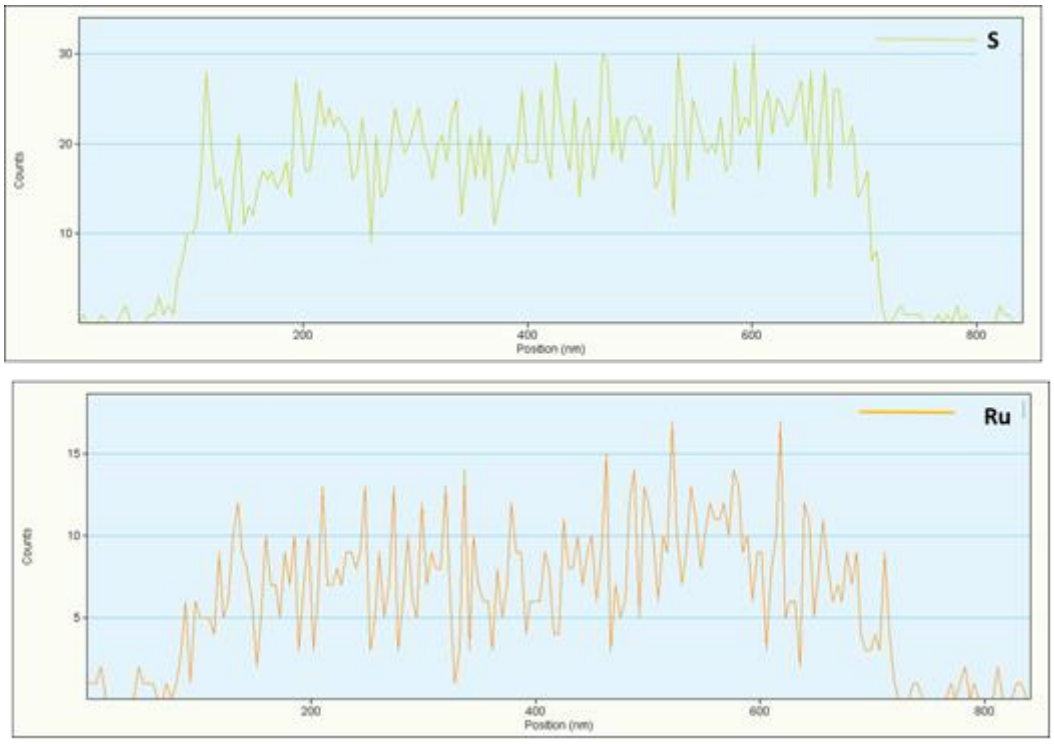


Figure S 22. EDX line analysis for SiO_2@Ru@Amph (Ru and S)

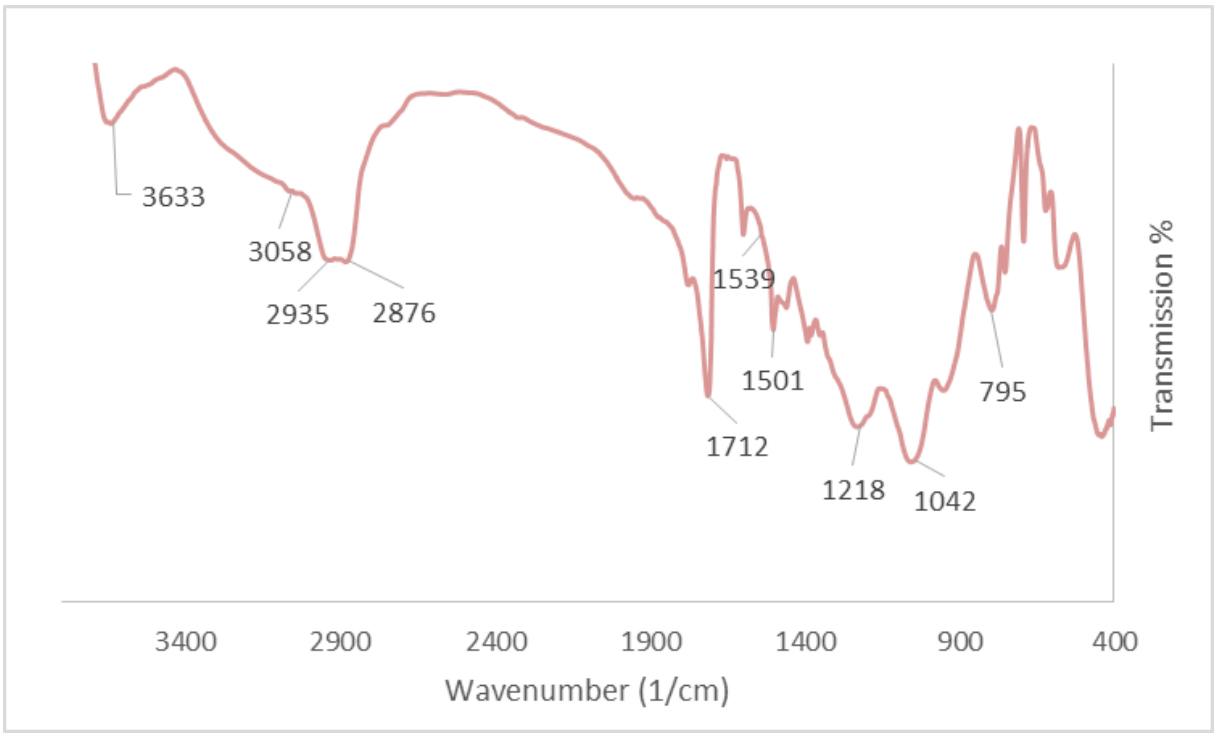


Figure S 23. FTIR spectrum of SiO_2@Amph

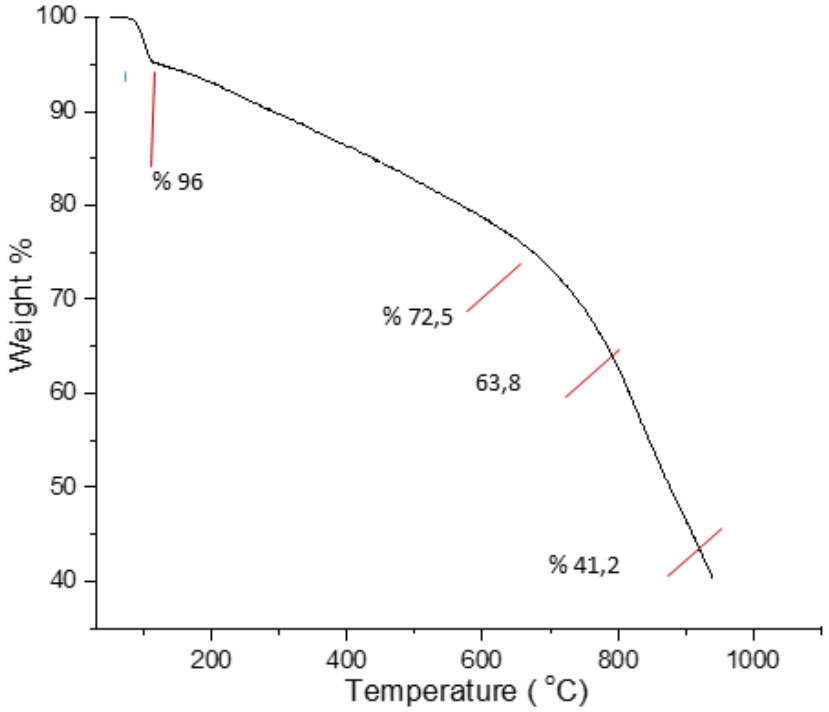


Figure S 24. TGA analysis of SiO_2@Amph

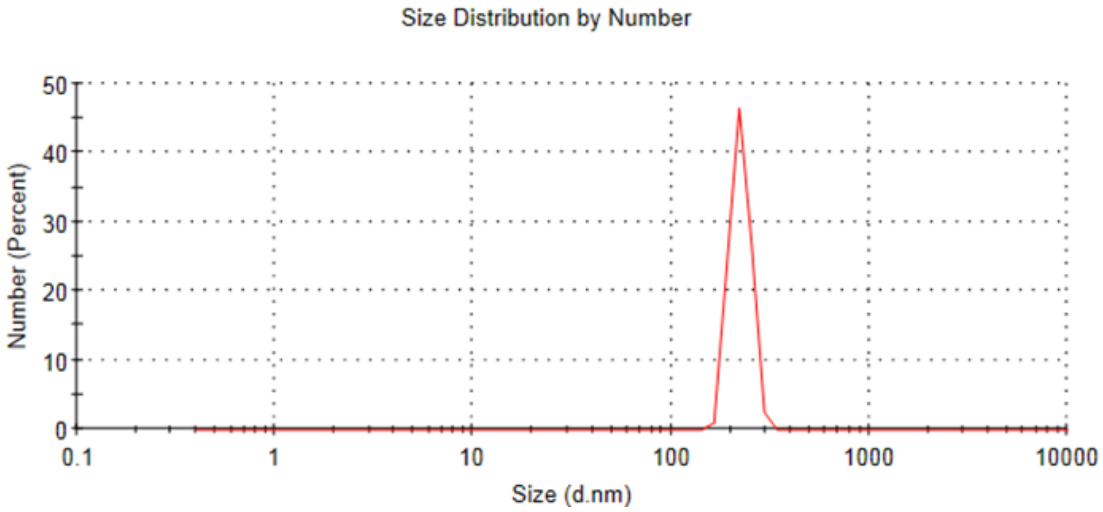


Figure S 25. DLS analysis of SiO_2@Amph in water (200.10 nm ±26.41 nm)

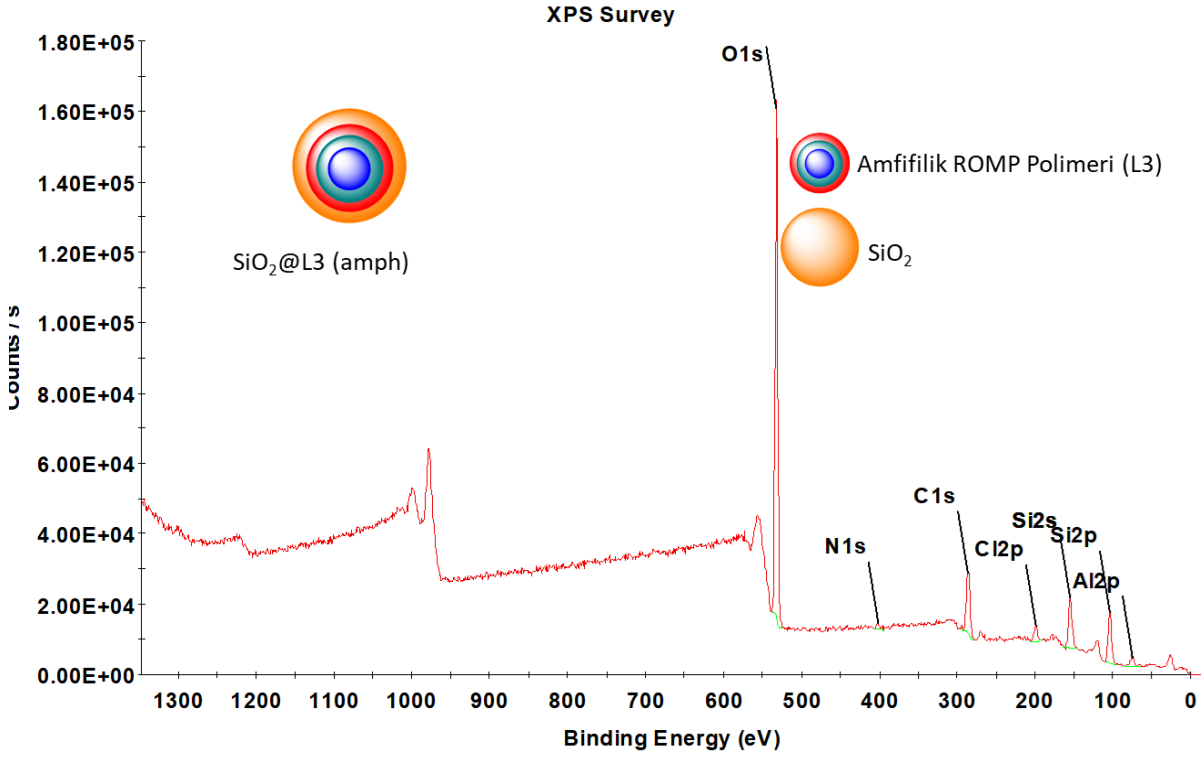


Figure S 26. XPS scan survey of SiO_2@Amph

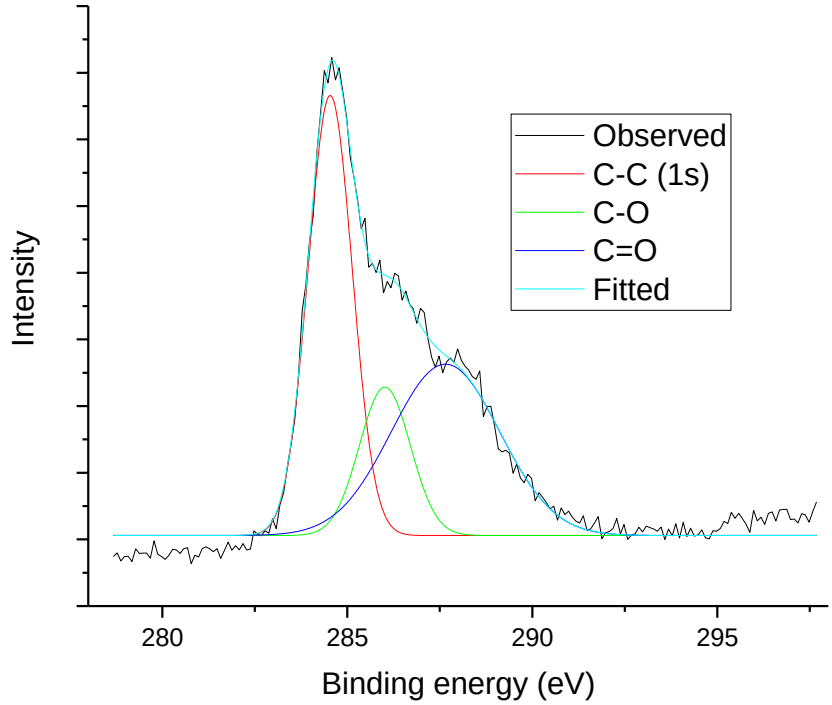


Figure S 27. C(1s) XPS spectrum of SiO_2@Amph

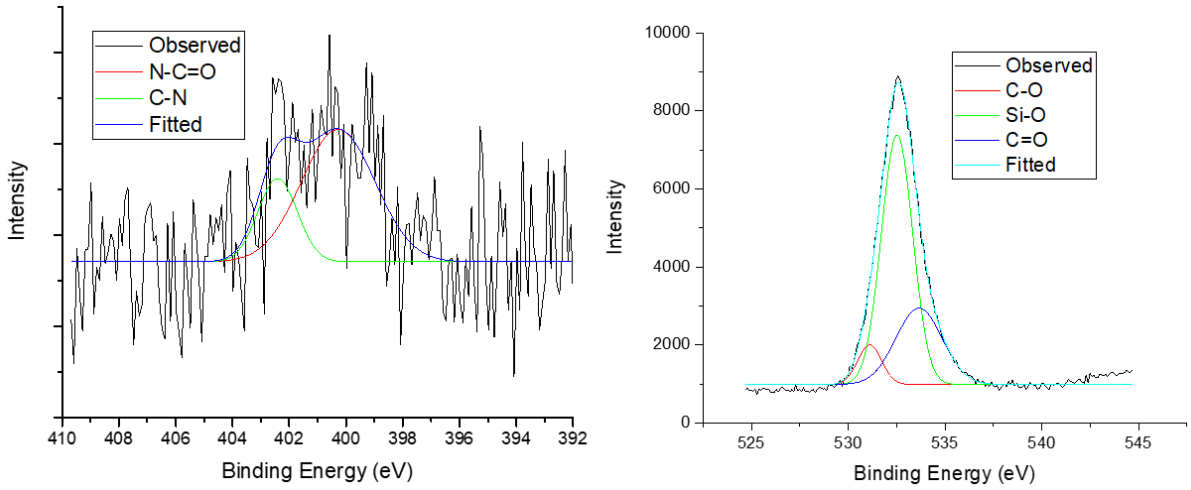


Figure S 28. a) N(1s) and b) C(1s) XPS spectrum of SiO_2@Amph

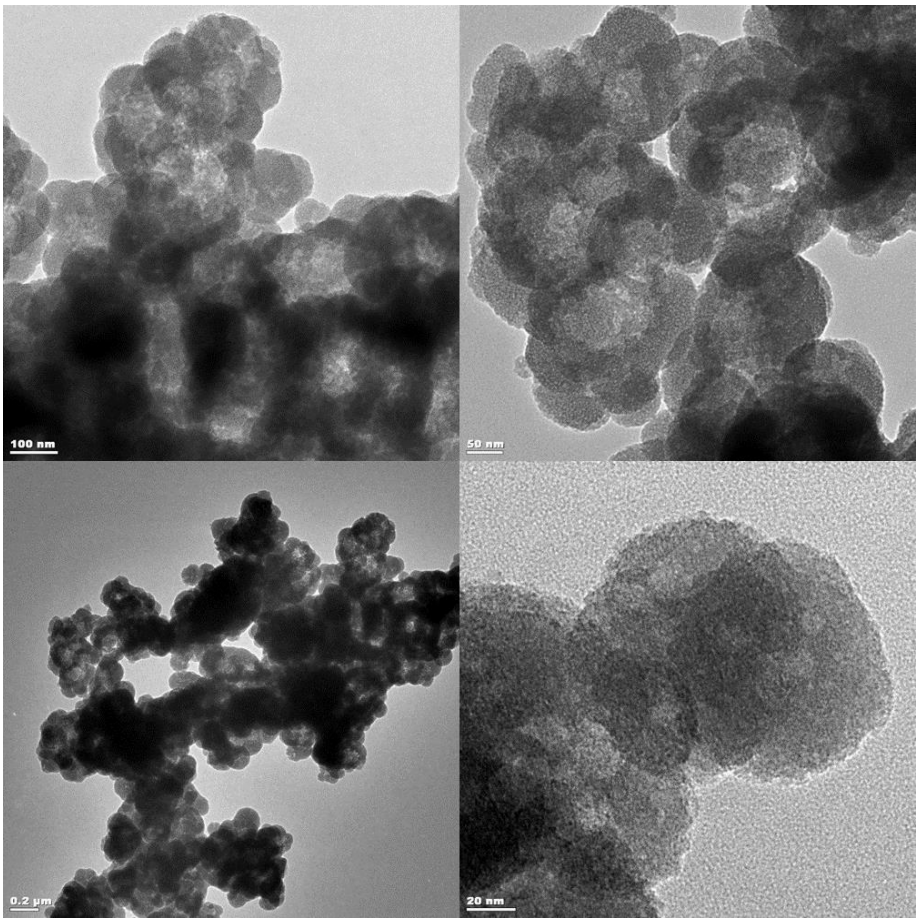


Figure S 29. High resolution (HR) TEM images of SiO_2@Amph

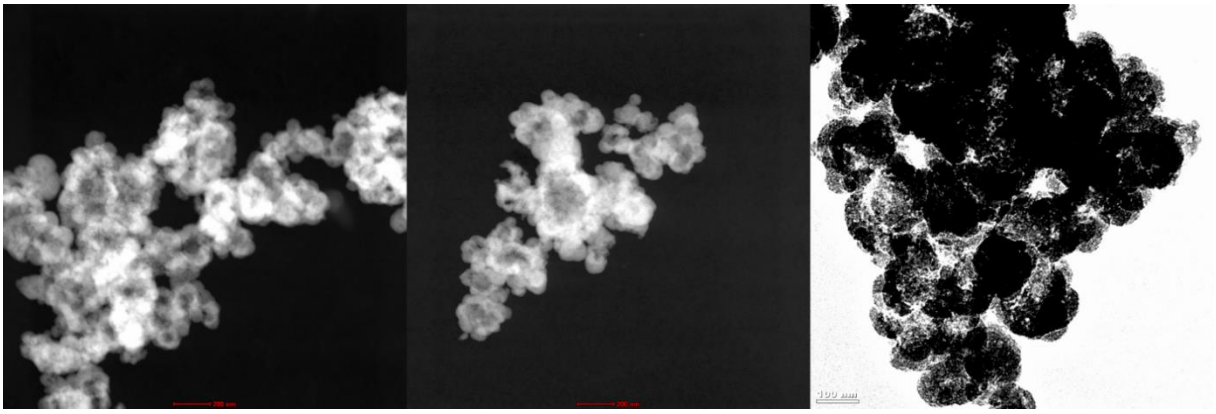


Figure S 30. HR-TEM images of SiO_2@Amph

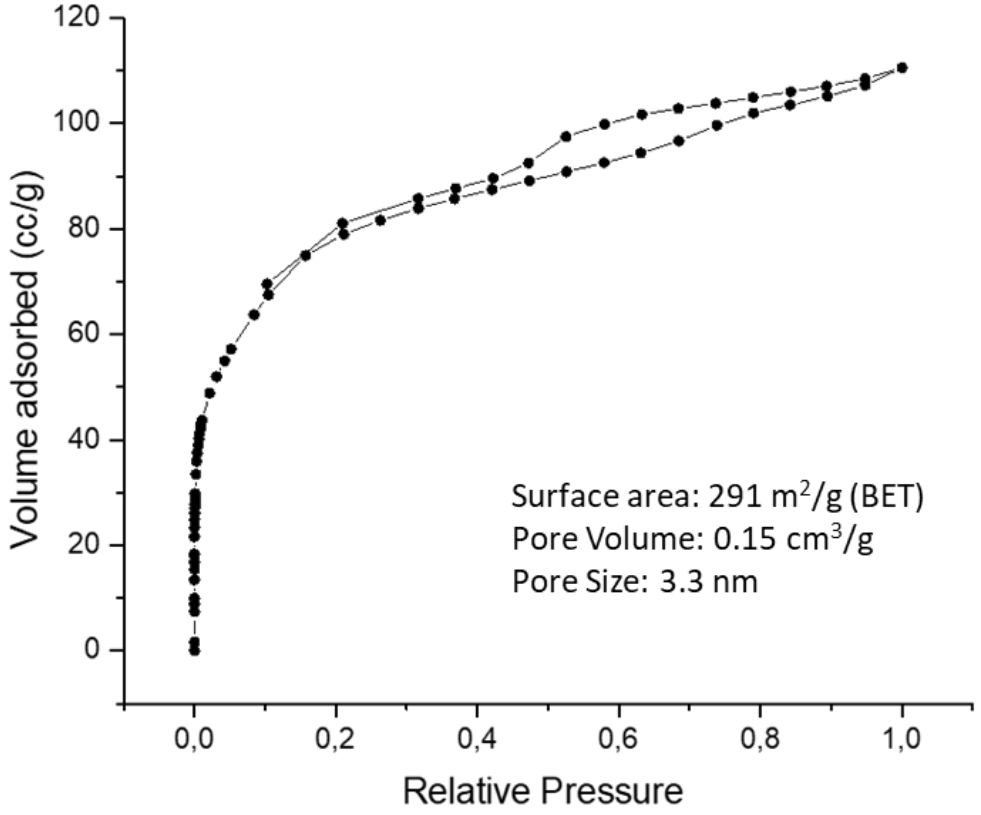


Figure S 31. N_2 adsorption/desorption isotherm of SiO_2@Amph (Ruthenium free silica gel)

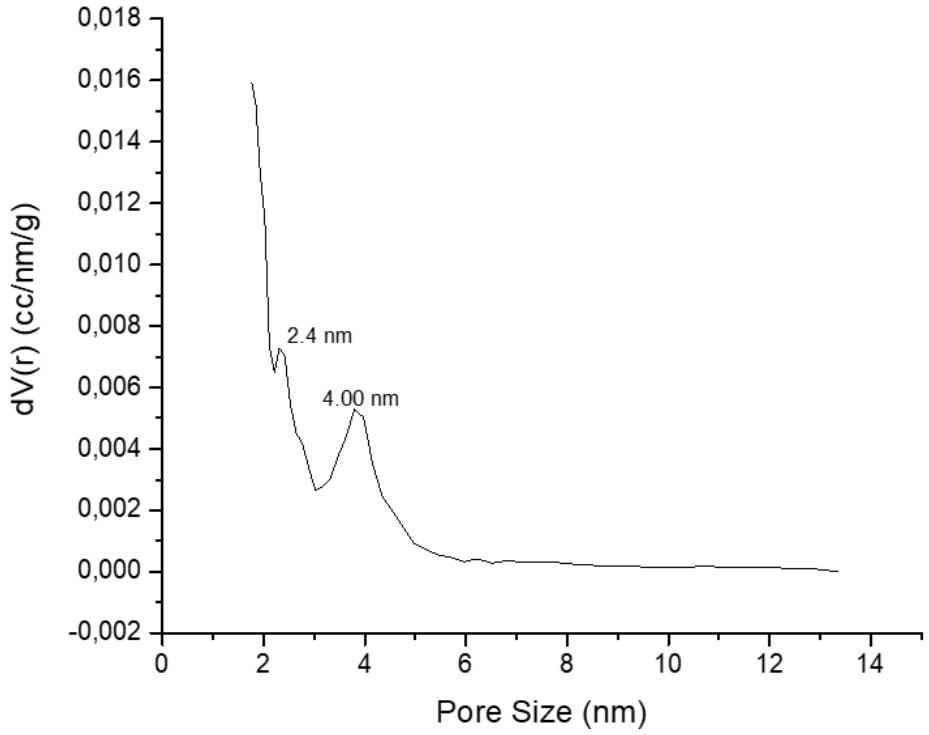


Figure S 32. Pore size distribution of SiO_2@Amph (Ruthenium free)

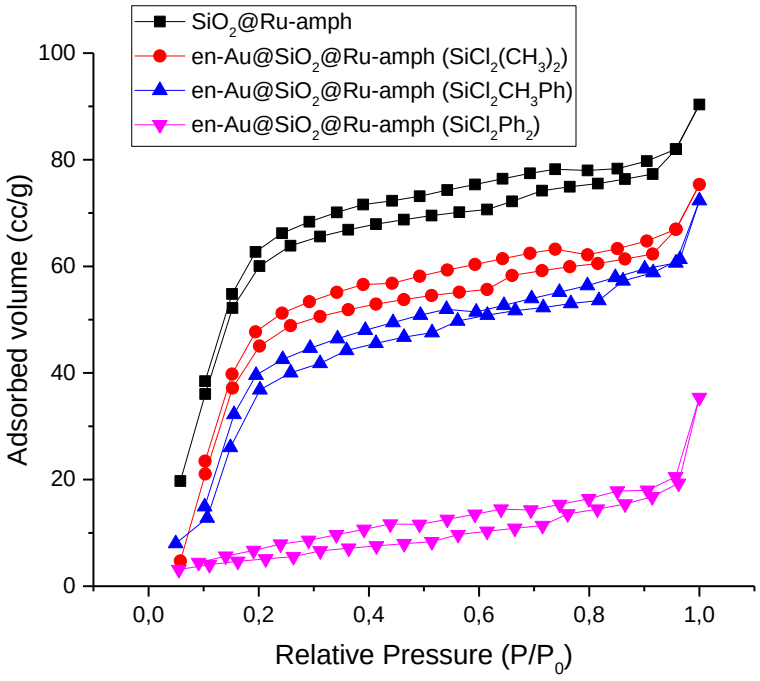


Figure S 33. N_2 adsorption/desorption isotherms of encapsulated catalysts

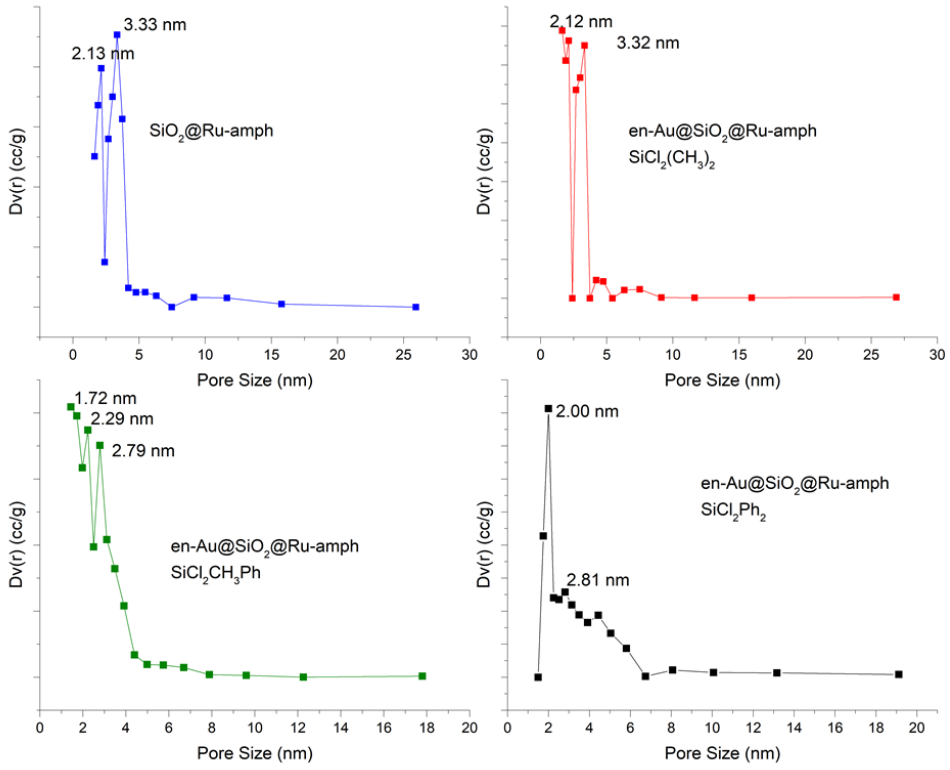


Figure S 34. Pore size distribution of encapsulated catalysts using different silylation agents

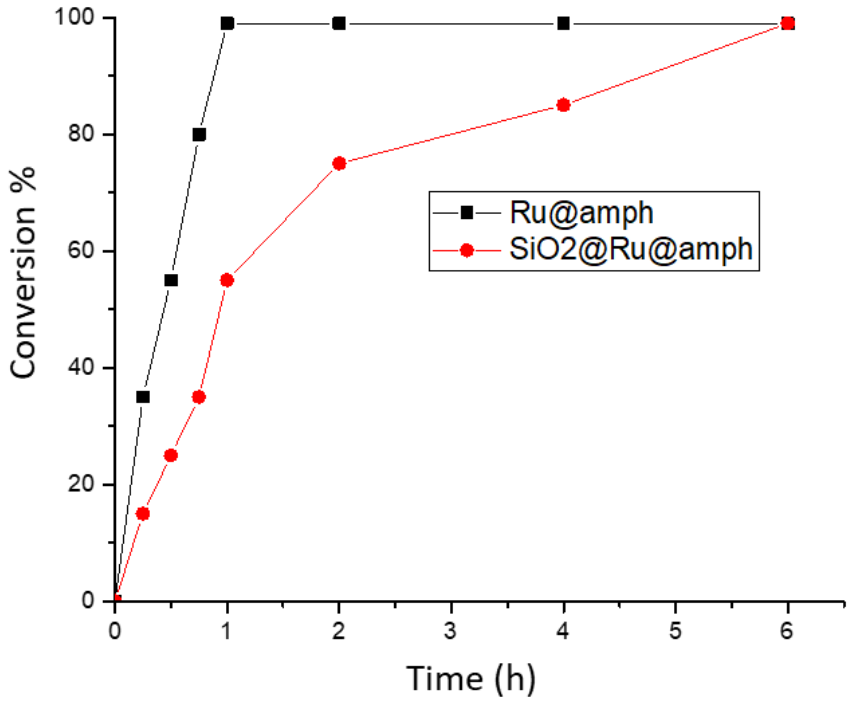


Figure S 35. Comparison of ATH reactions of acetophenone using different catalysts

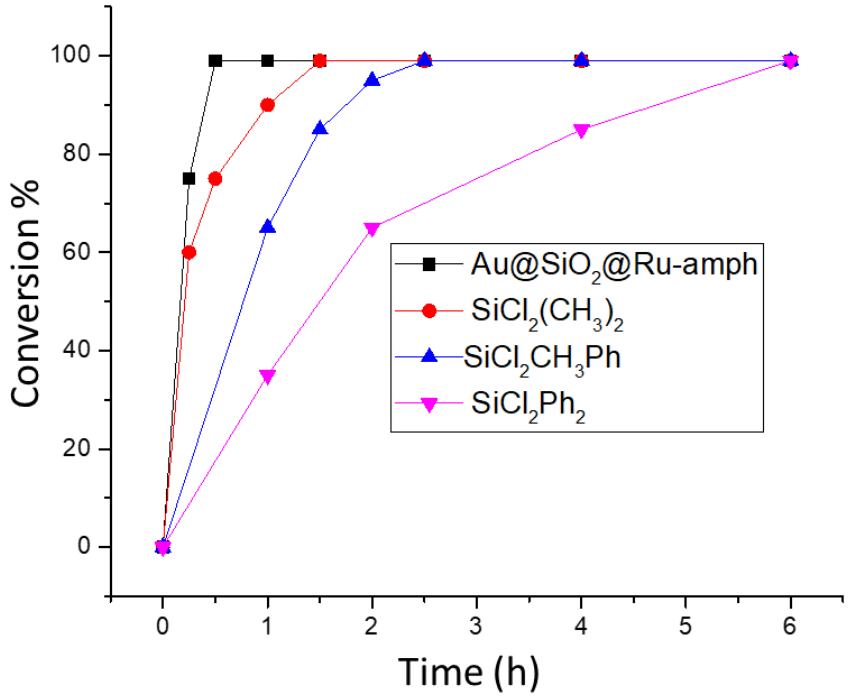


Figure S 36. Comparison of AH reactions of phenylacetylene using encapsulated catalysts

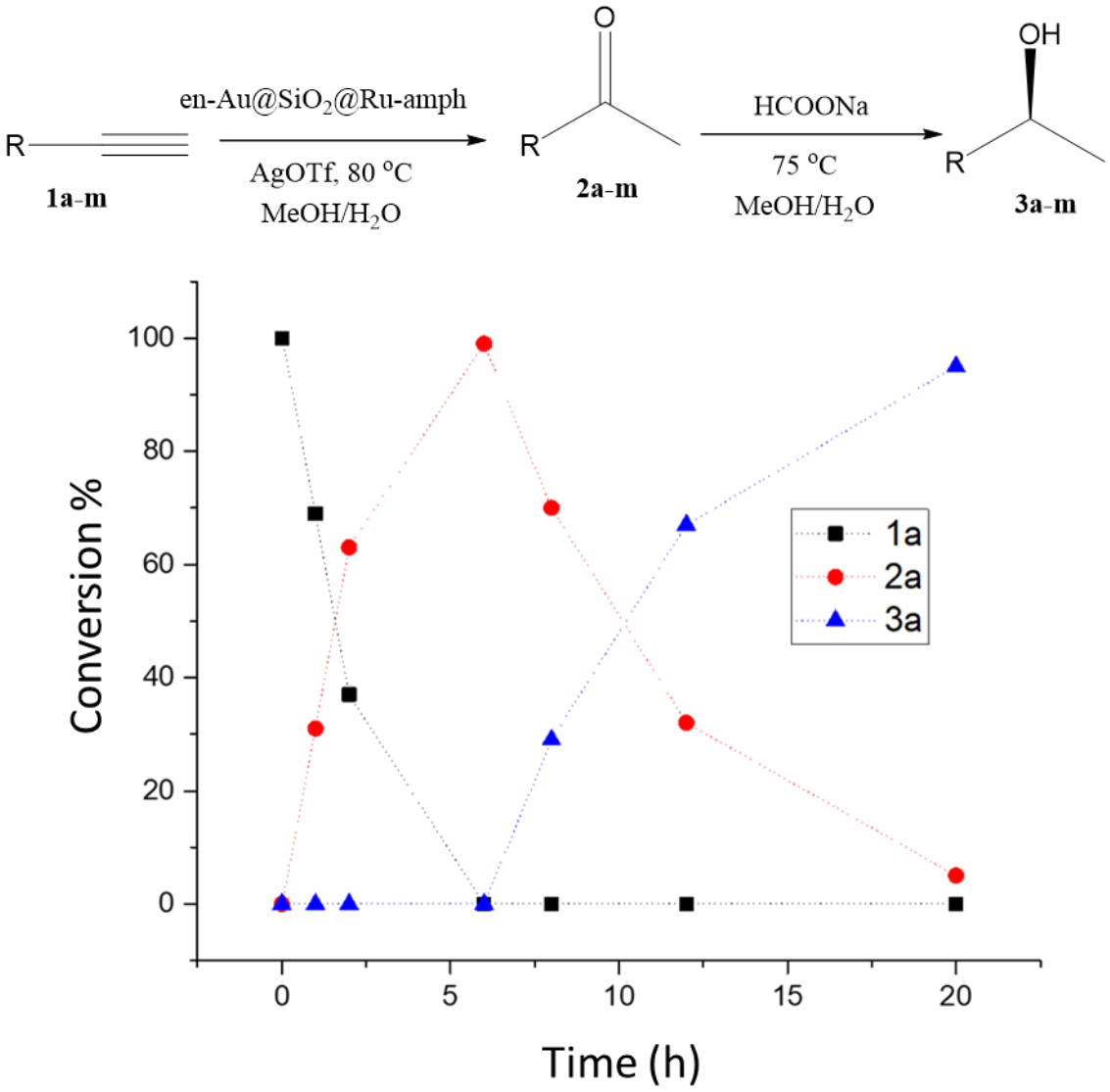


Figure S 37. Sequential AH/ATH reactions using en-Au@SiO_2@Ru-amph (-$SiCl_2Ph_2$)

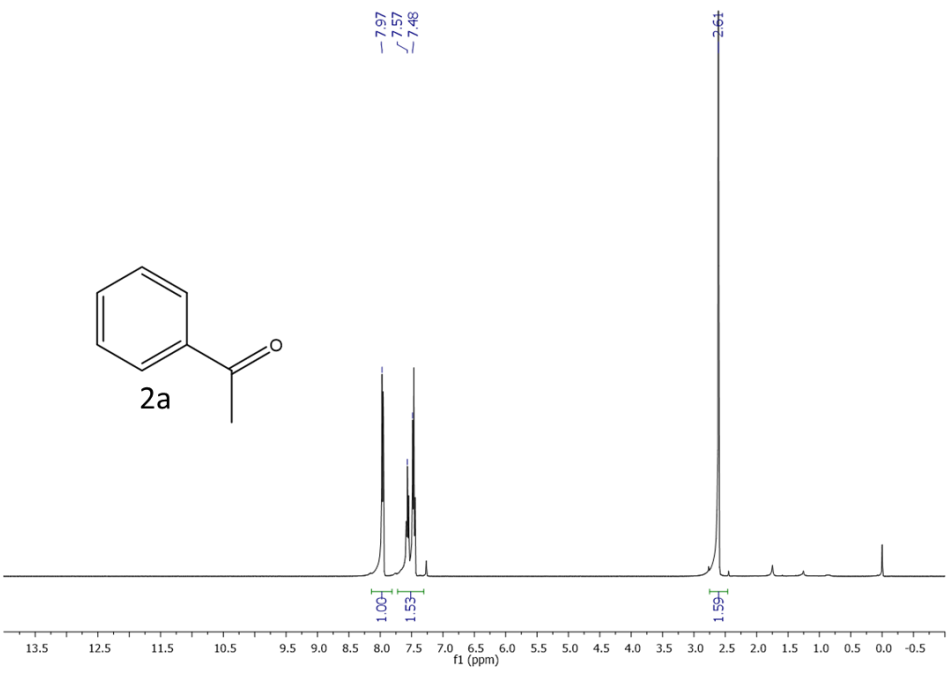
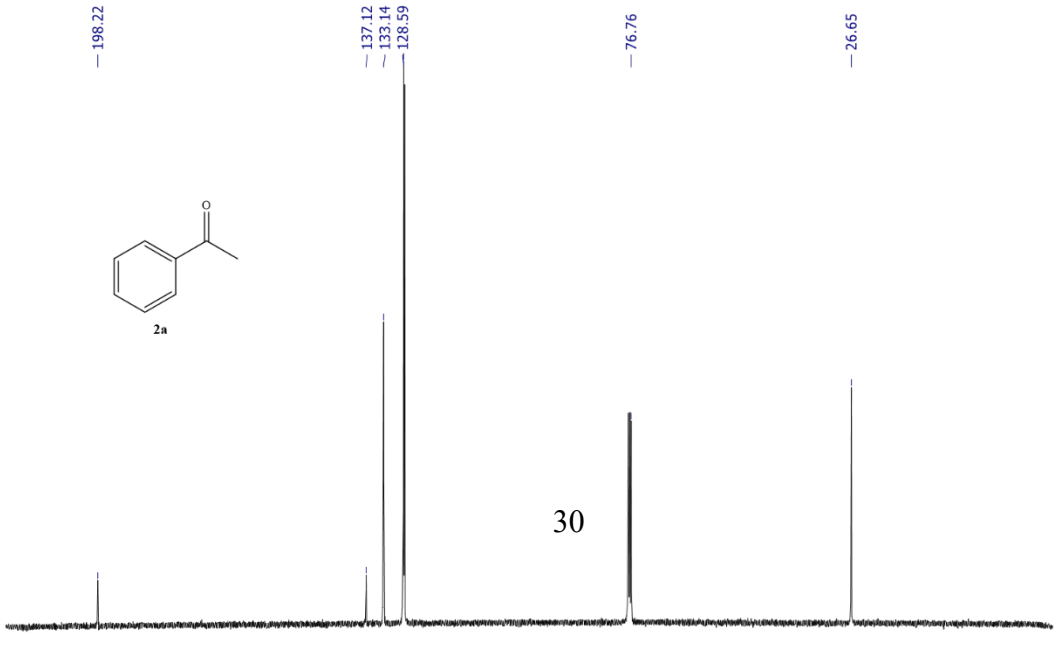


Figure S 38. ^{1}H NMR spectrum of 2a (400 MHz, $CDCl_3$)



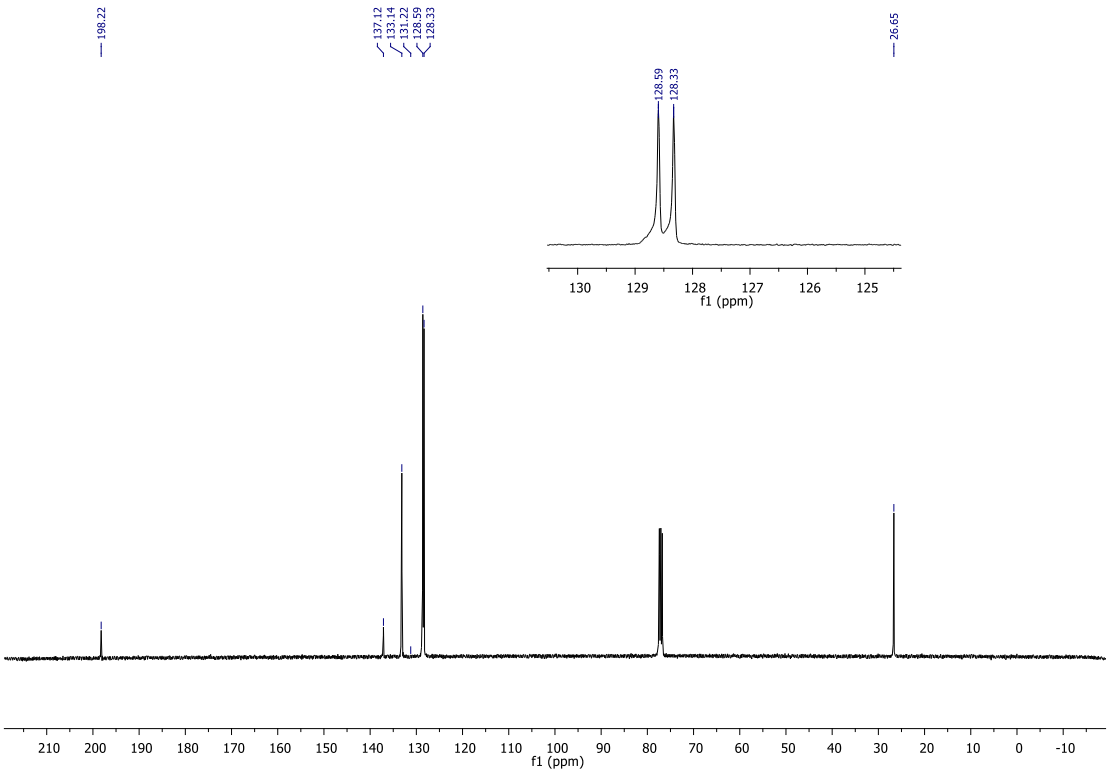
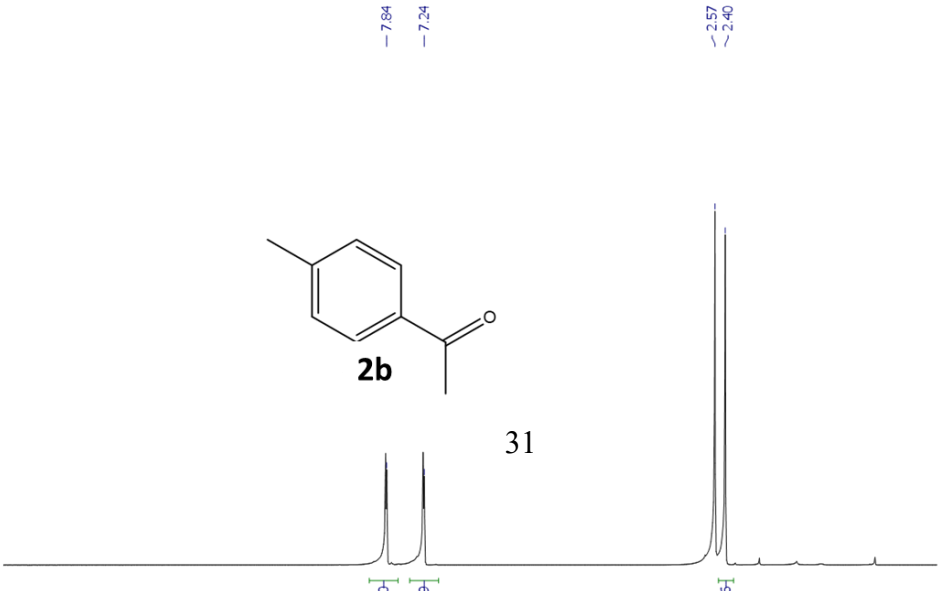


Figure S 40. ^{13}C NMR spectrum of 2a with expanded region (100 MHz, $CDCl_3$)



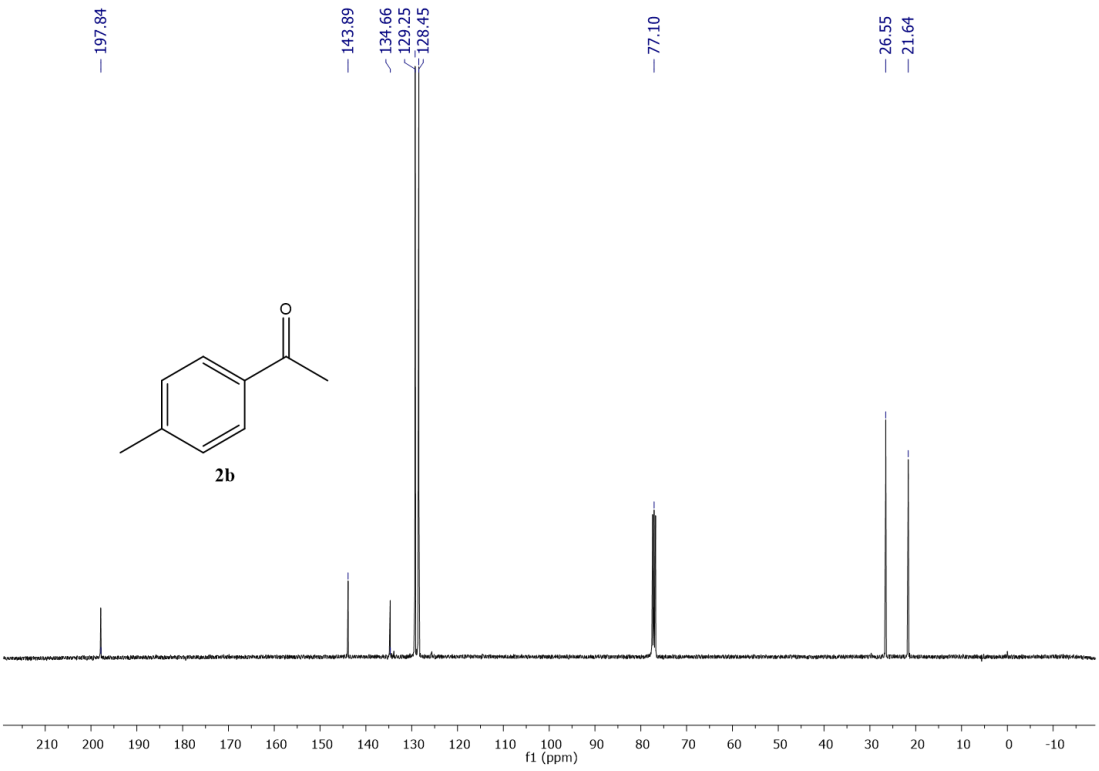
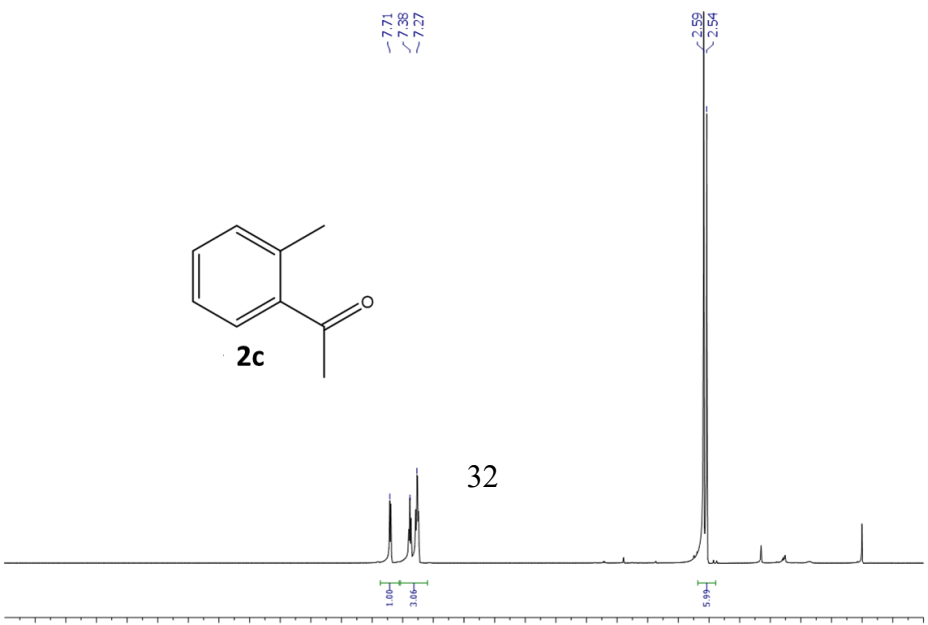


Figure S 42.^{13}C NMR spectrum of 2b (100 MHz, $CDCl_3$)



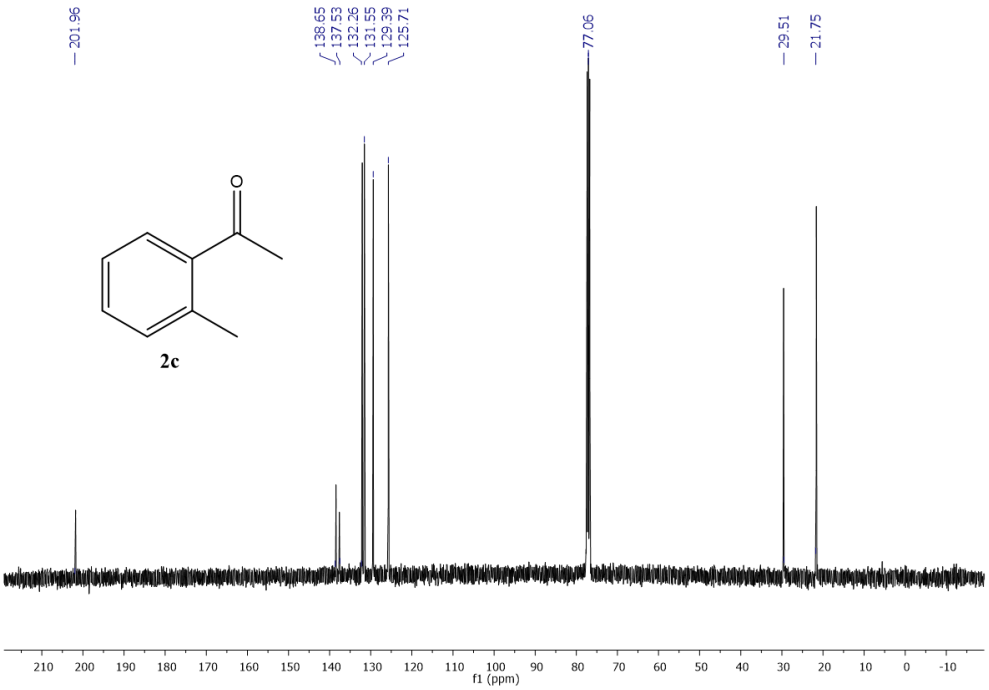
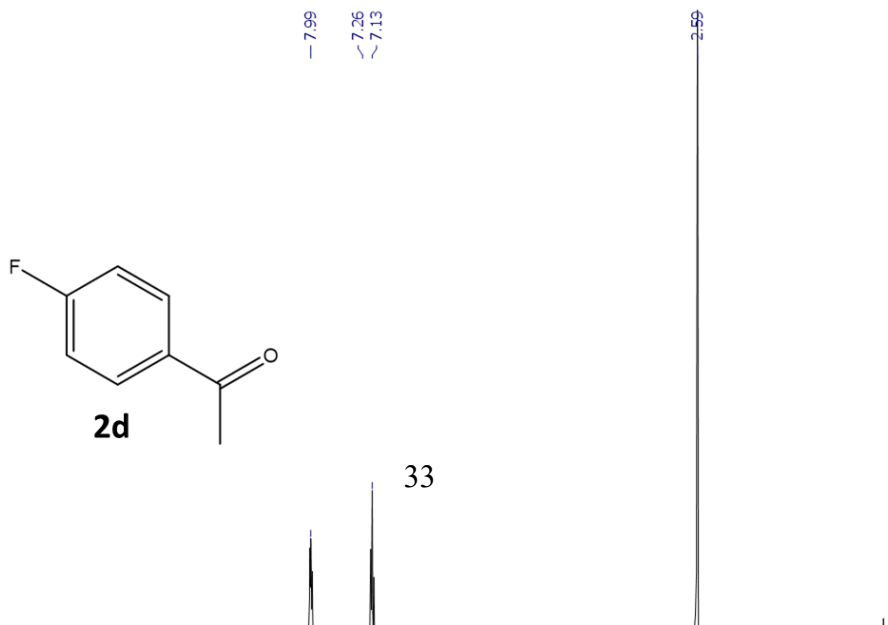


Figure S 44. ^{13}C NMR spectrum of 2c (100 MHz, $CDCl_3$)



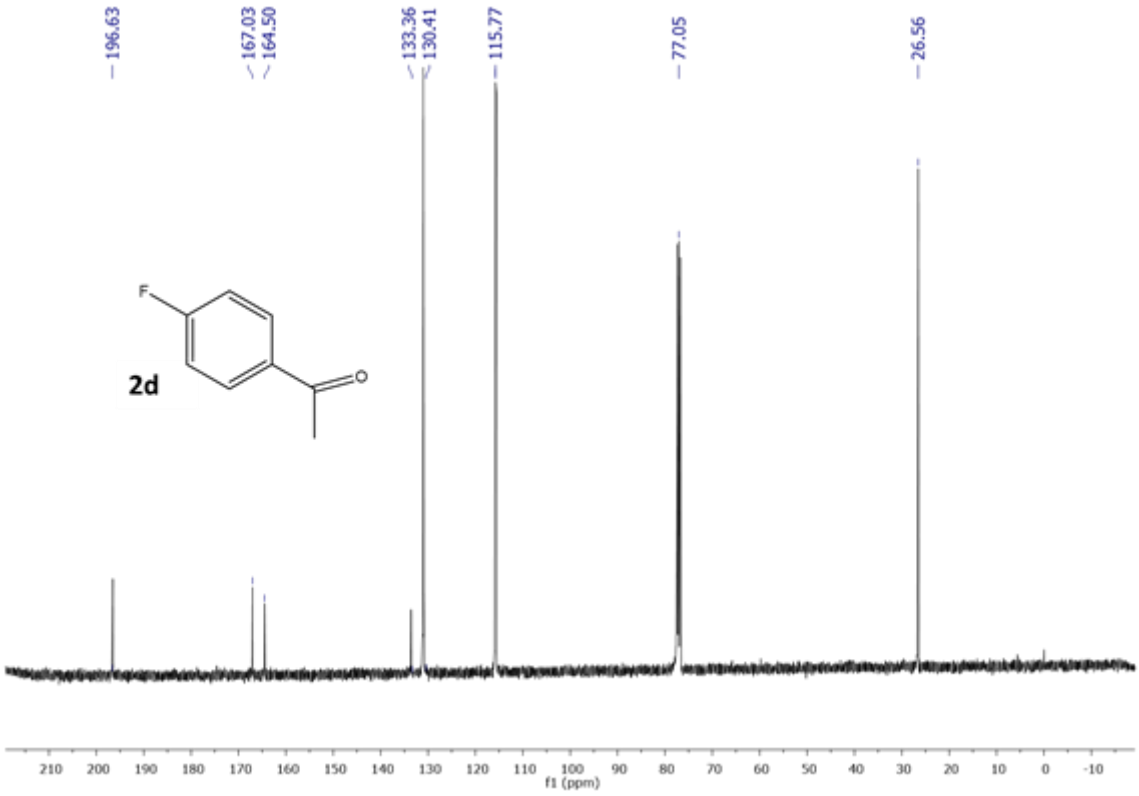
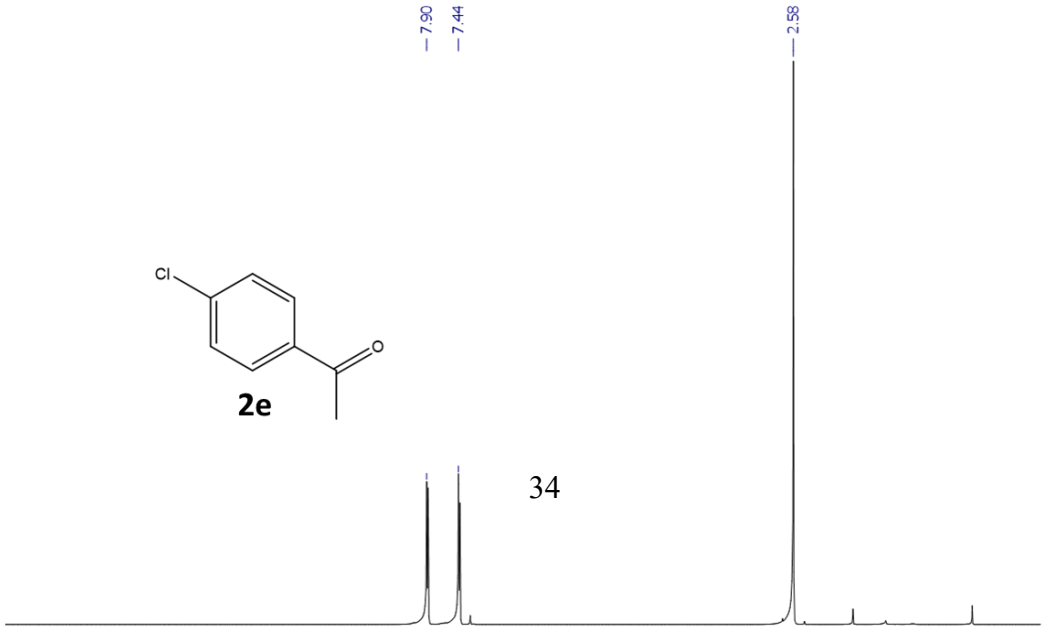


Figure S 46. ^{13}C NMR spectrum of 2d (100 MHz, $CDCl_3$)



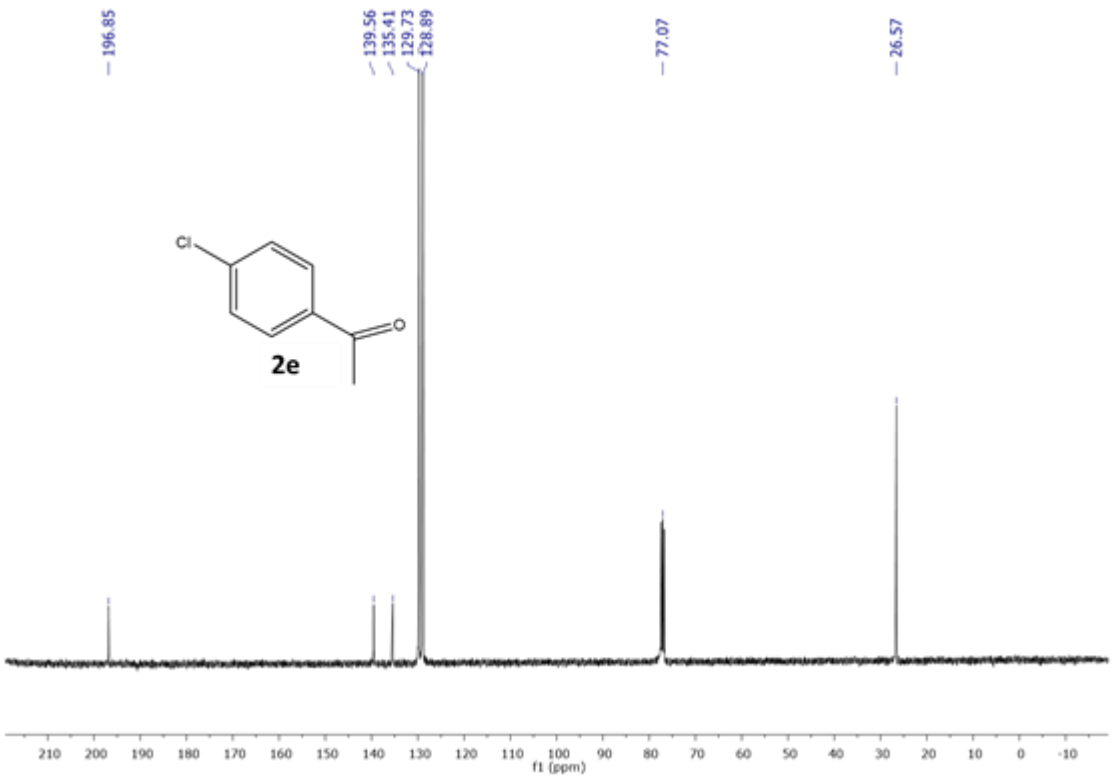


Figure S 48.^{13}C NMR spectrum of 2e (100 MHzi $CDCl_3$)

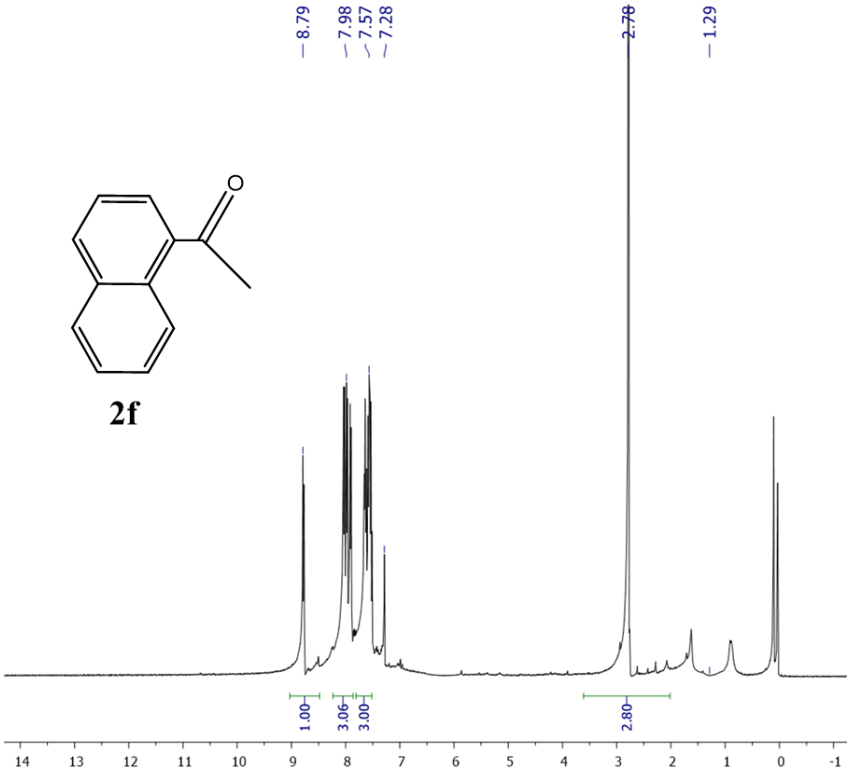


Figure S 49.^{1}H NMR spectrum of 2f (400 MHz, $CDCl_3$)

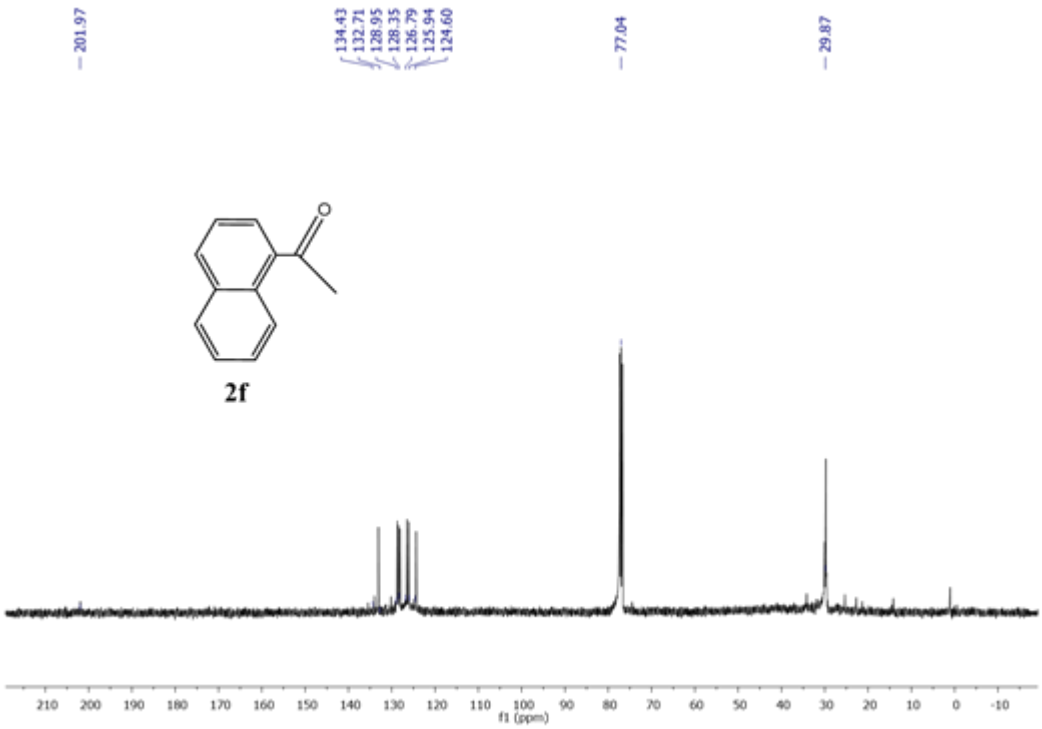


Figure S 50.^{13}C NMR spectrum of 2f (100 MHz, $CDCl_3$)

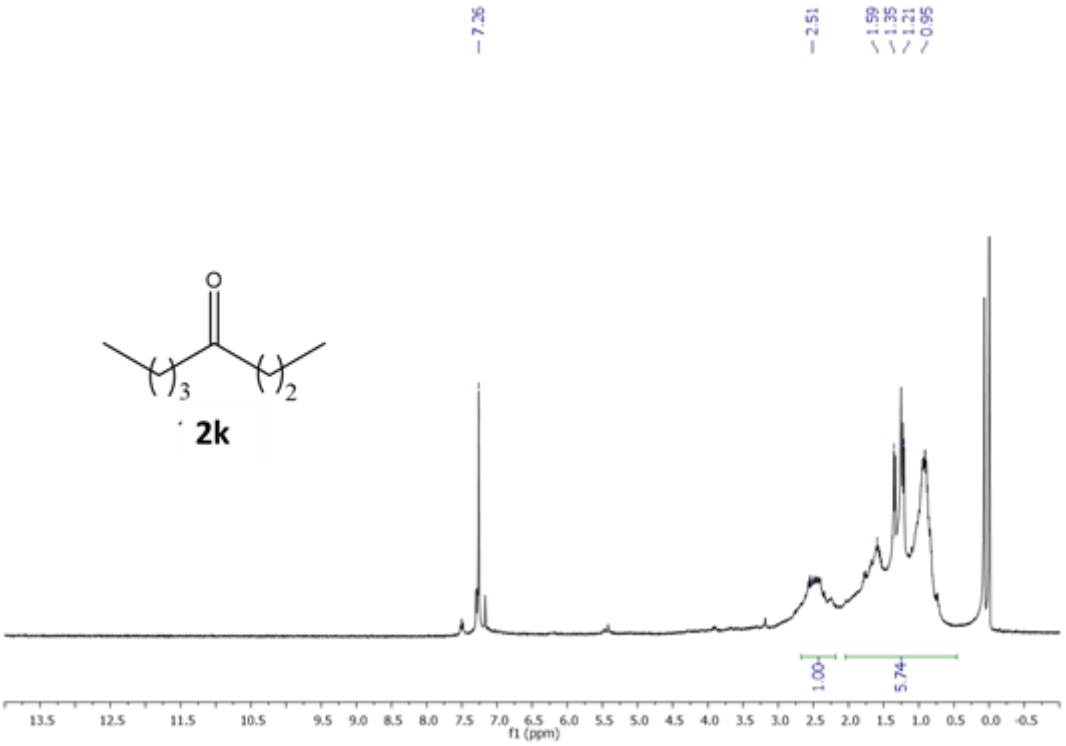


Figure S 51. ^{1}H NMR spectrum of 2k (400 MHz, $CDCl_3$)

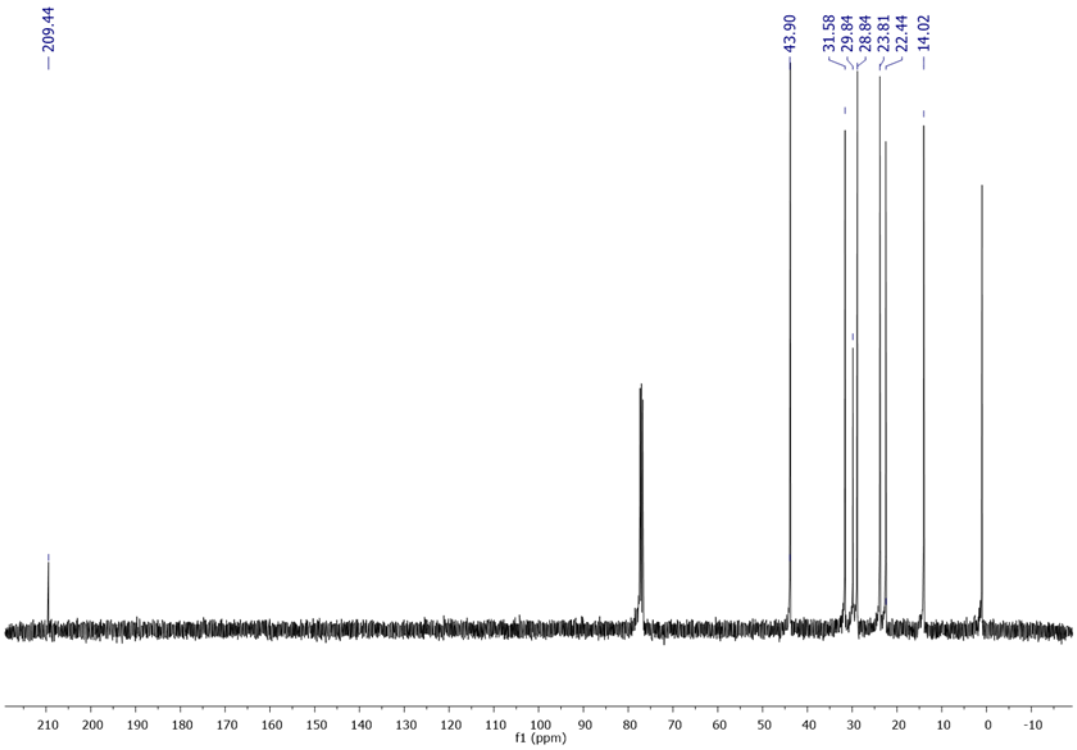


Figure S 52. ^{13}C NMR spectrum of 2k (100 MHz, $CDCl_3$)

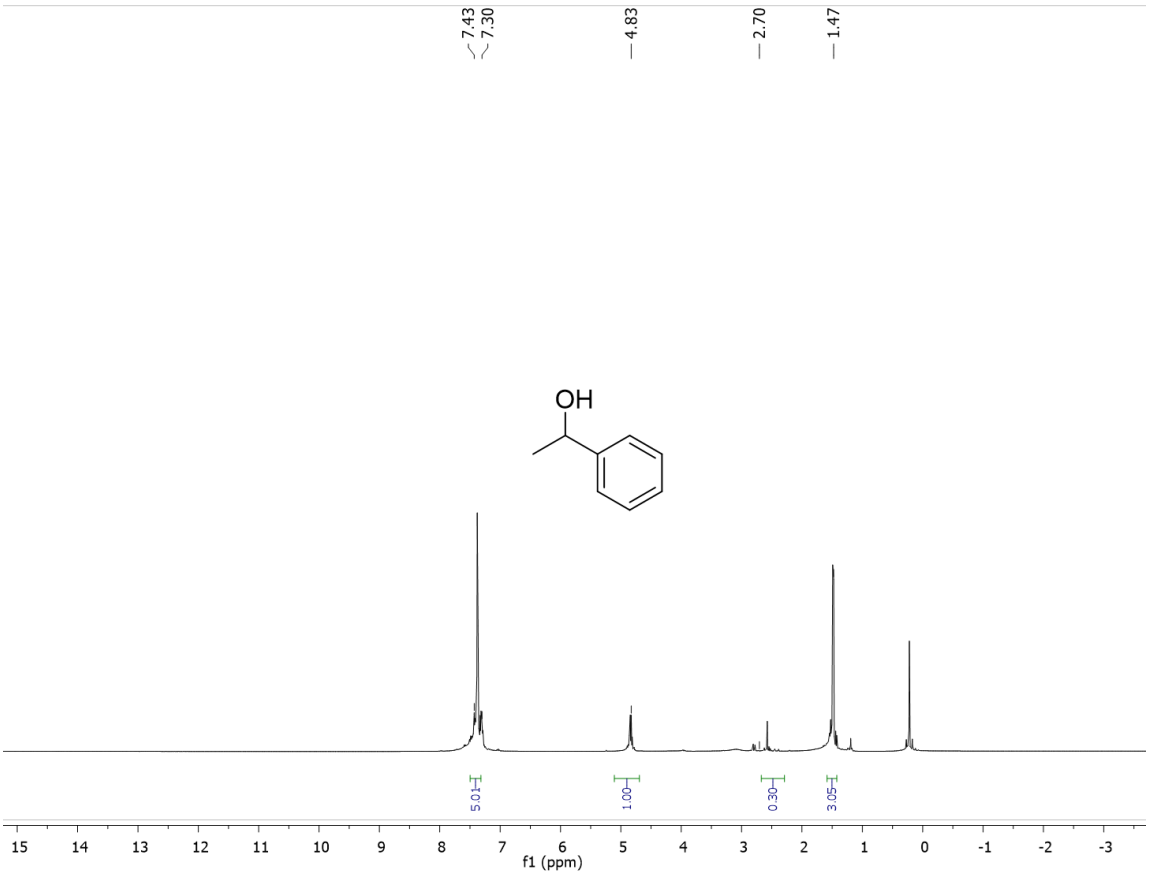


Figure S 53. ^{1}H NMR spectrum of 3a (400 MHz, $CDCl_3$)

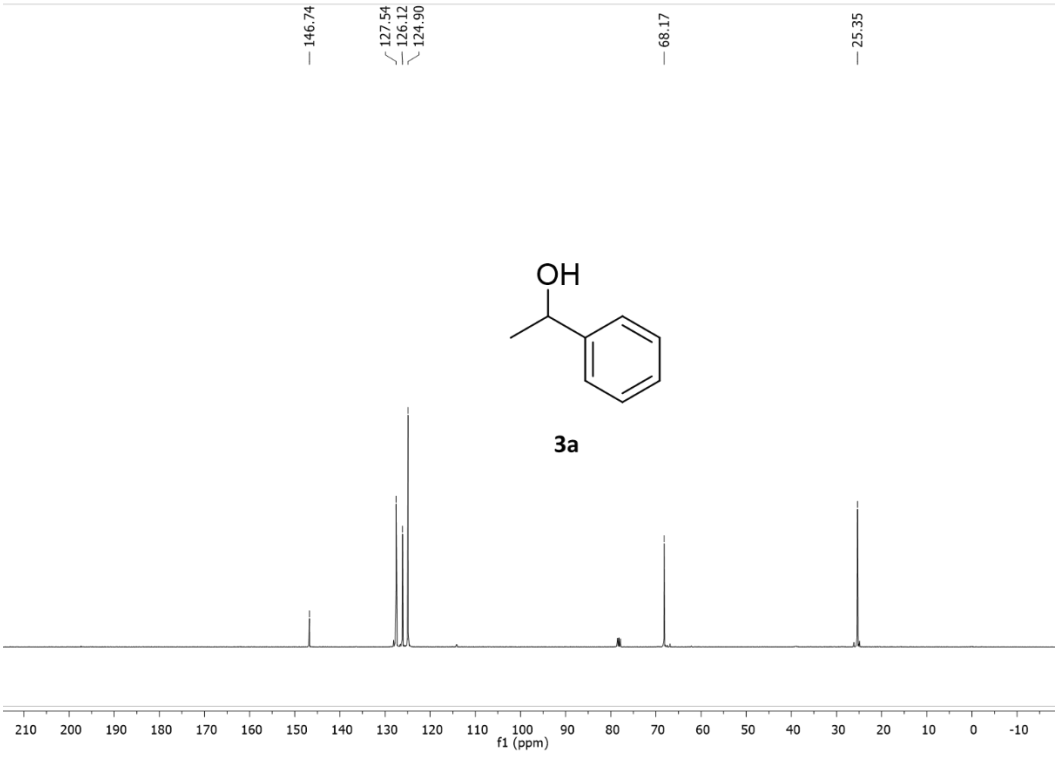


Figure S 54. ^{13}C NMR spectrum of 3a (100 MHz, $CDCl_3$)

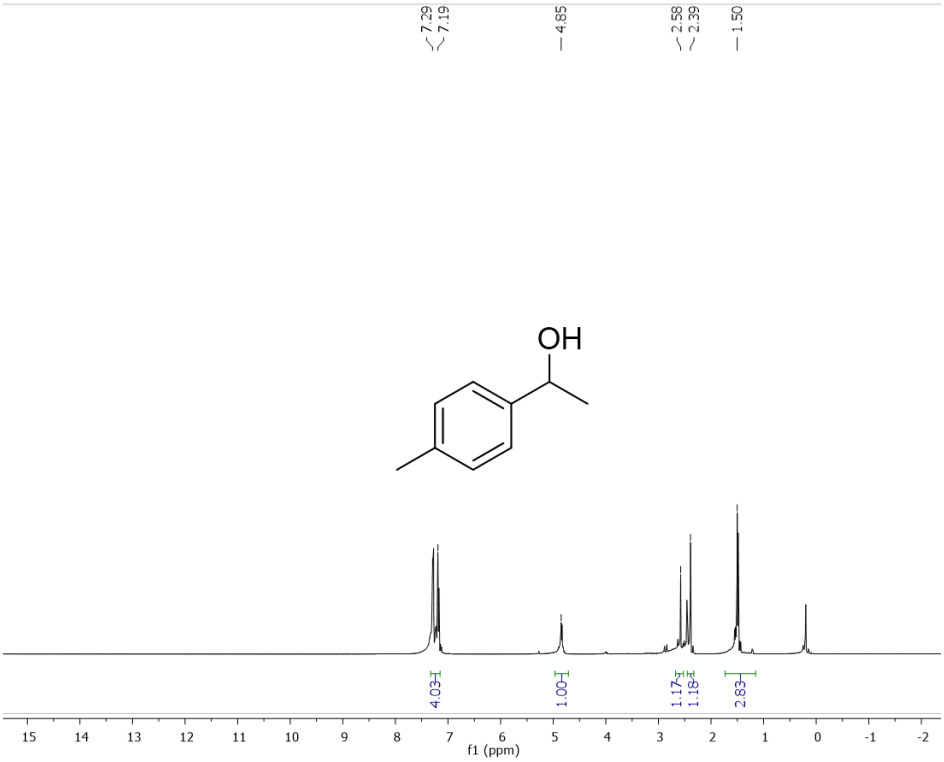


Figure S 55. ^{1}H NMR spectrum of 3b (400 MHz, $CDCl_3$)

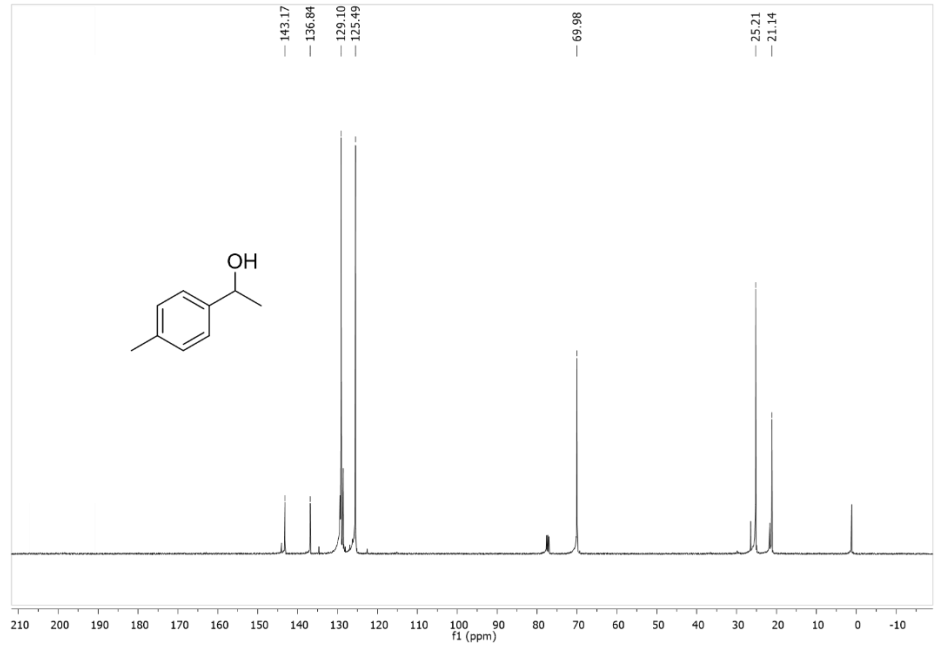


Figure S 56. ^{13}C NMR spectrum of 3b (100 MHz, $CDCl_3$)

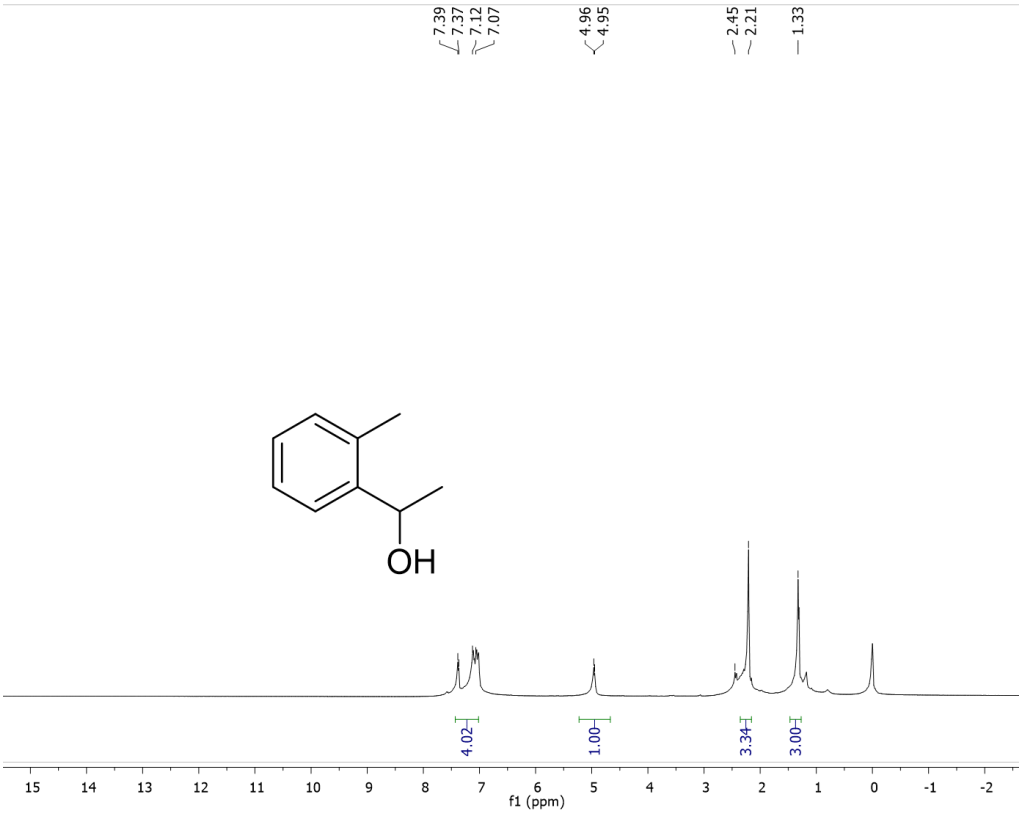


Figure S 57. ^{1}H NMR spectrum of 3c (400 MHz, $CDCl_3$)

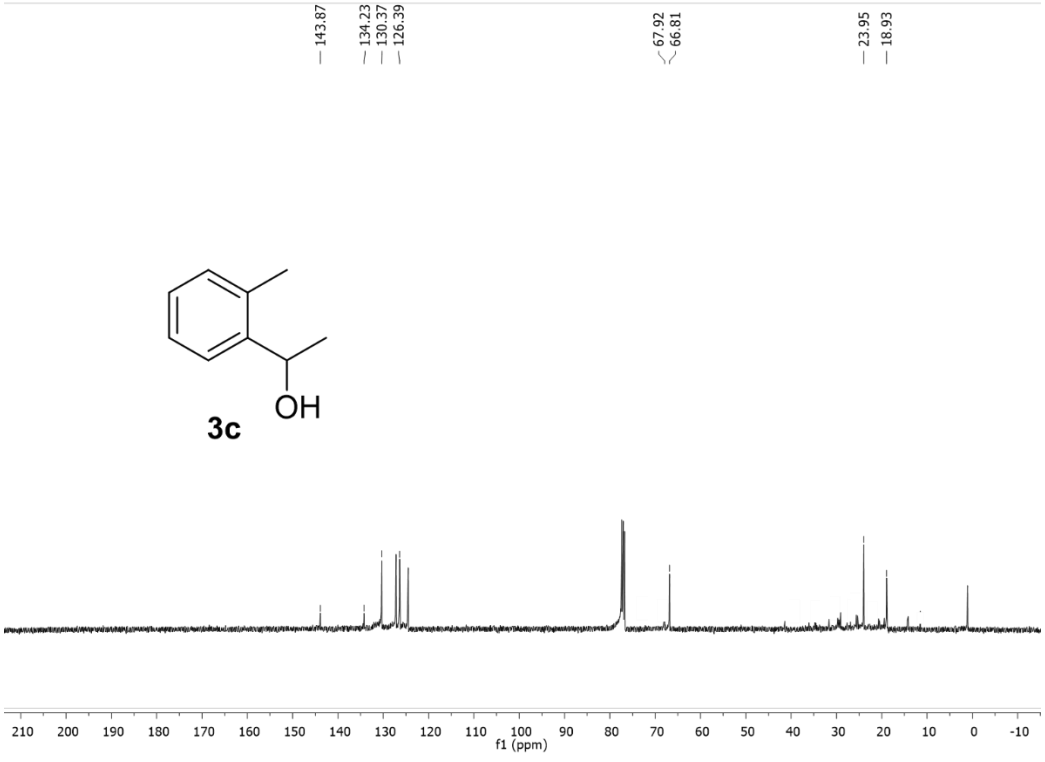


Figure S 58.^{13}C NMR spectrum of 3c (100 MHz, $CDCl_3$)

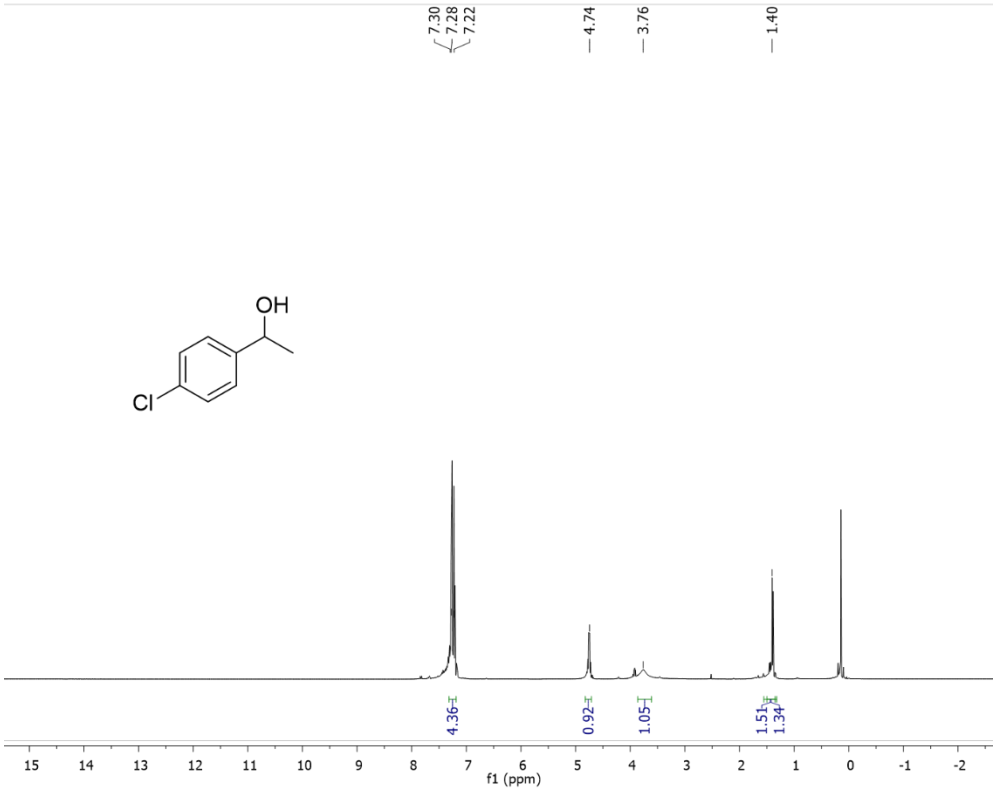


Figure S 59. ^{1}H NMR spectrum of 3e (400 Mhz, $CDCl_3$)

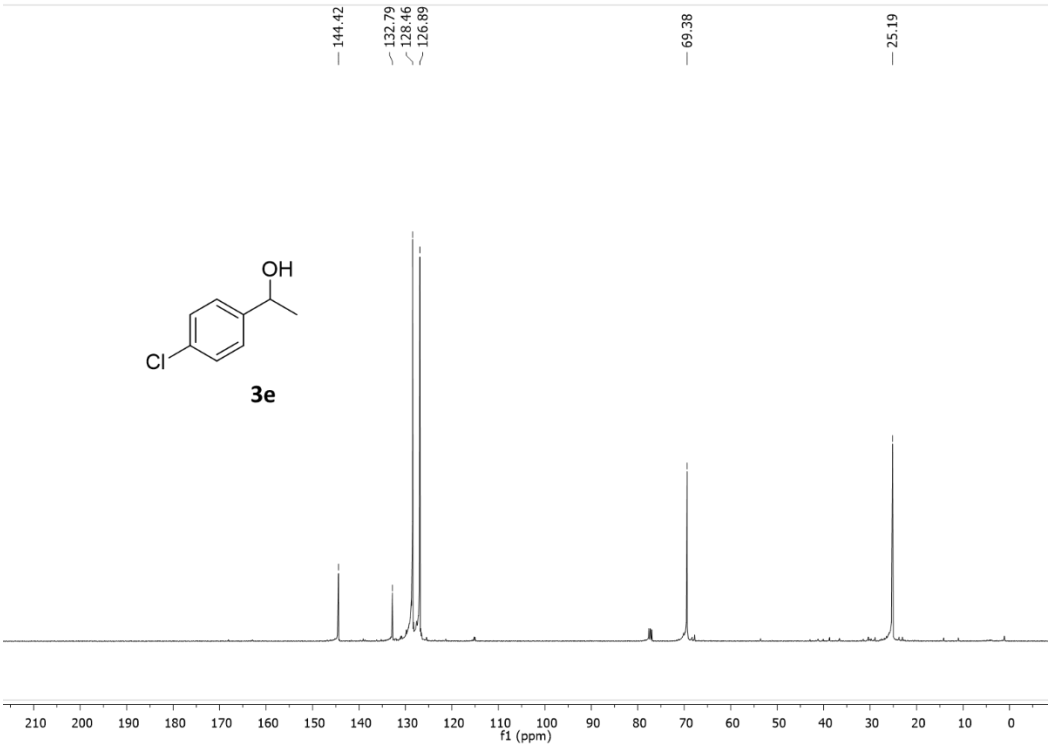


Figure S 60. ^{13}C NMR spectrum of 3e (100 MHz, $CDCl_3$)

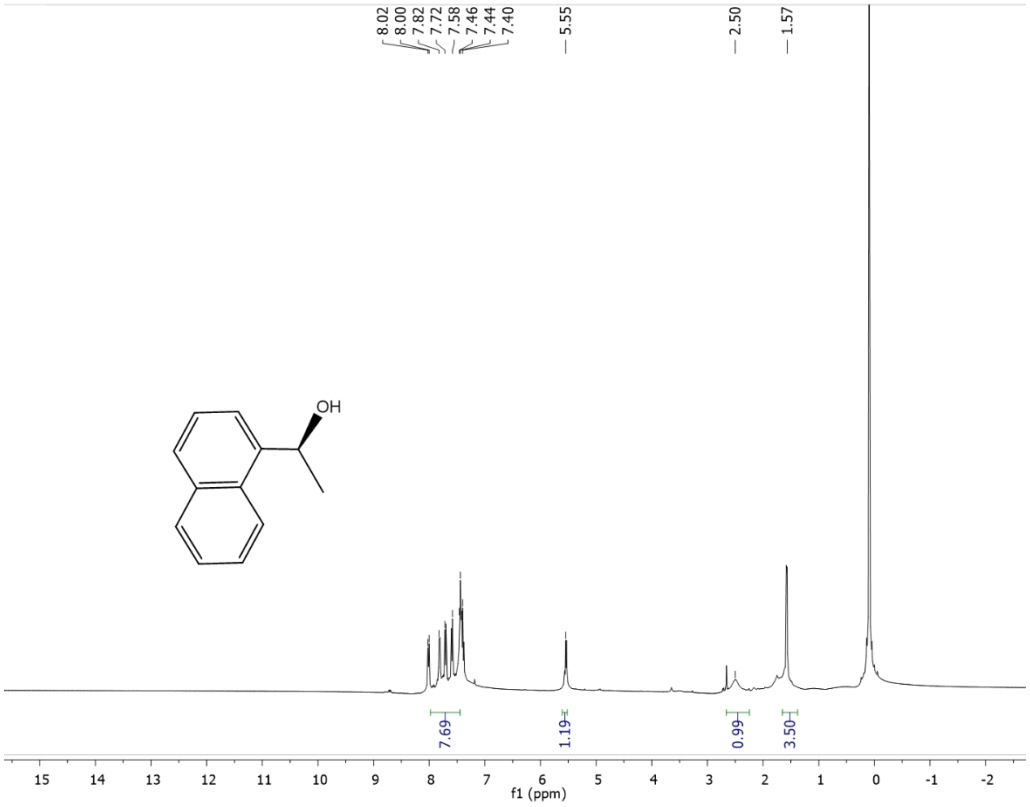


Figure S 61. ^{1}H NMR spectrum of 1f (400 MHz, $CDCl_3$)

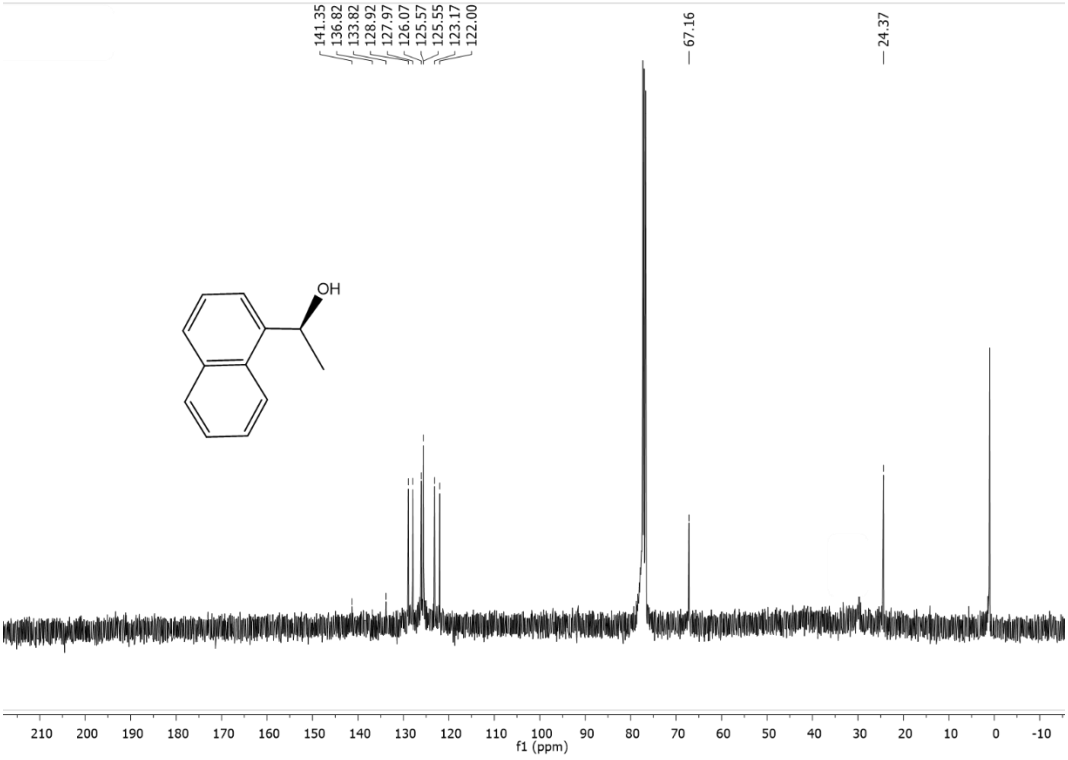


Figure S 62. ^{13}C NMR spectrum of 1f (100 MHz, $CDCl_3$)

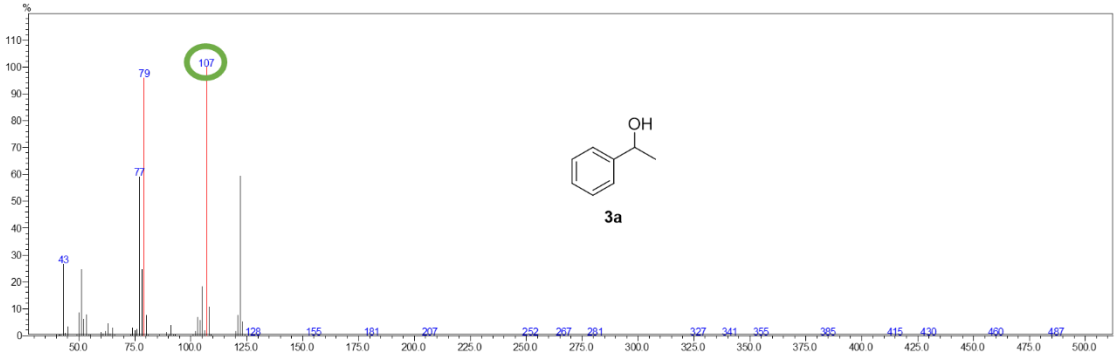


Figure S 63. MS (EI) spectrum of 3a

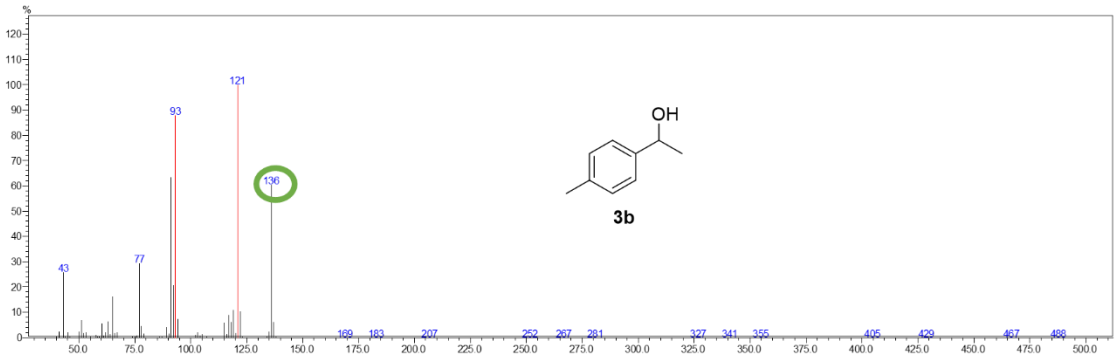


Figure S 64. MS (EI) spectrum of 3b

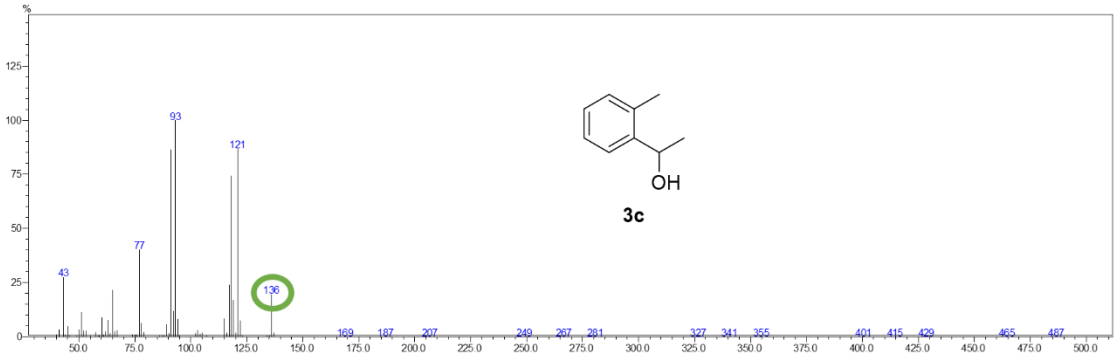


Figure S 65. MS (EI) spectrum of 3c

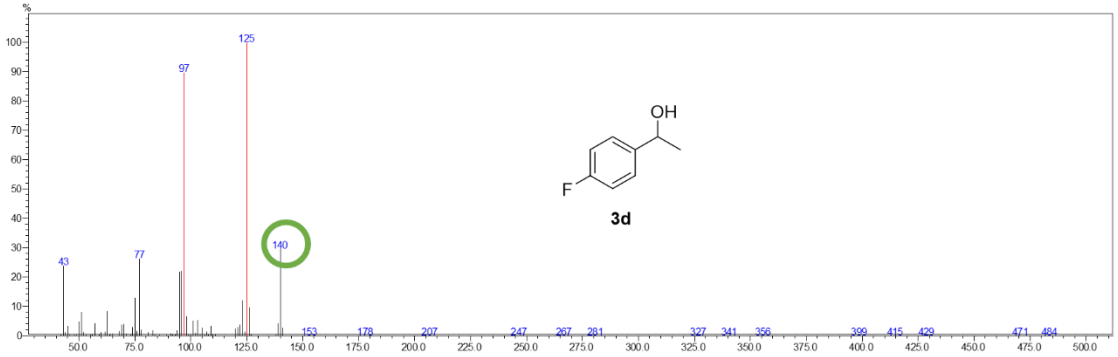


Figure S 66. MS (EI) spectrum of 3d

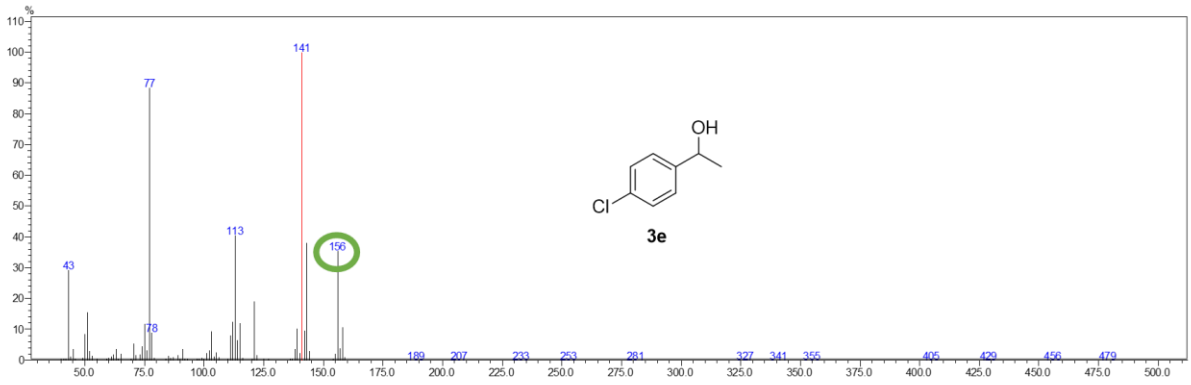


Figure S 67. MS (EI) spectrum of 3e

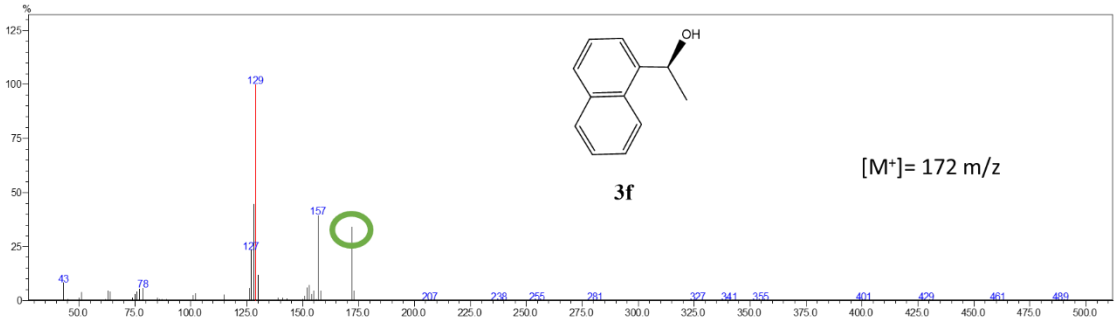
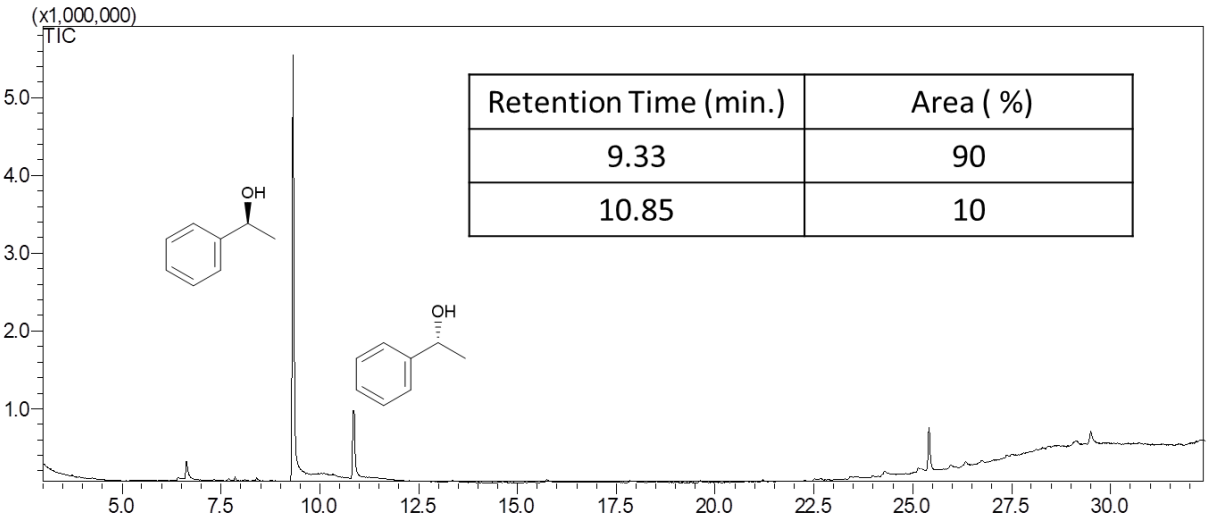
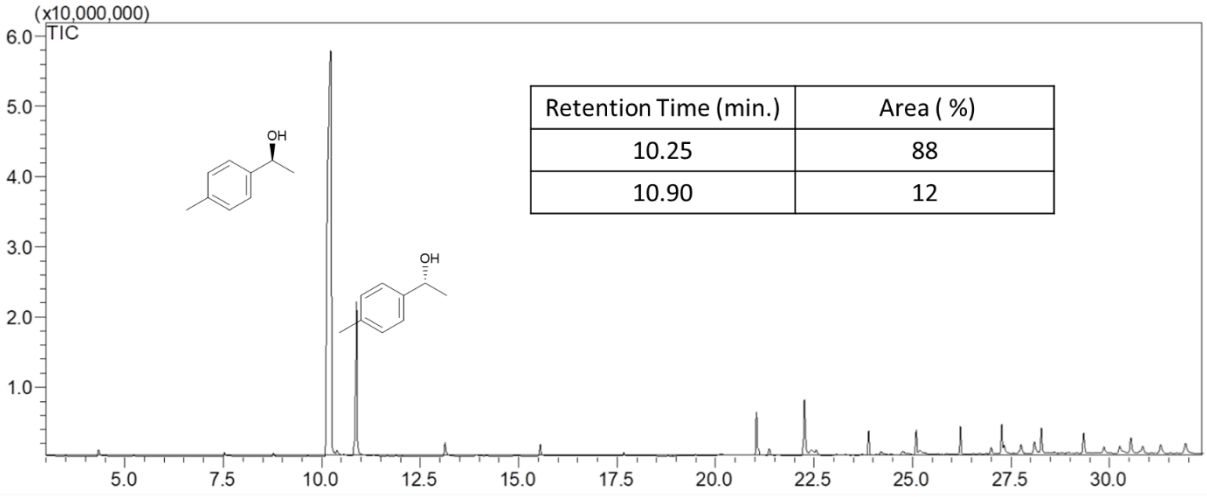


Figure S 68. MS (EI) spectrum of 3f



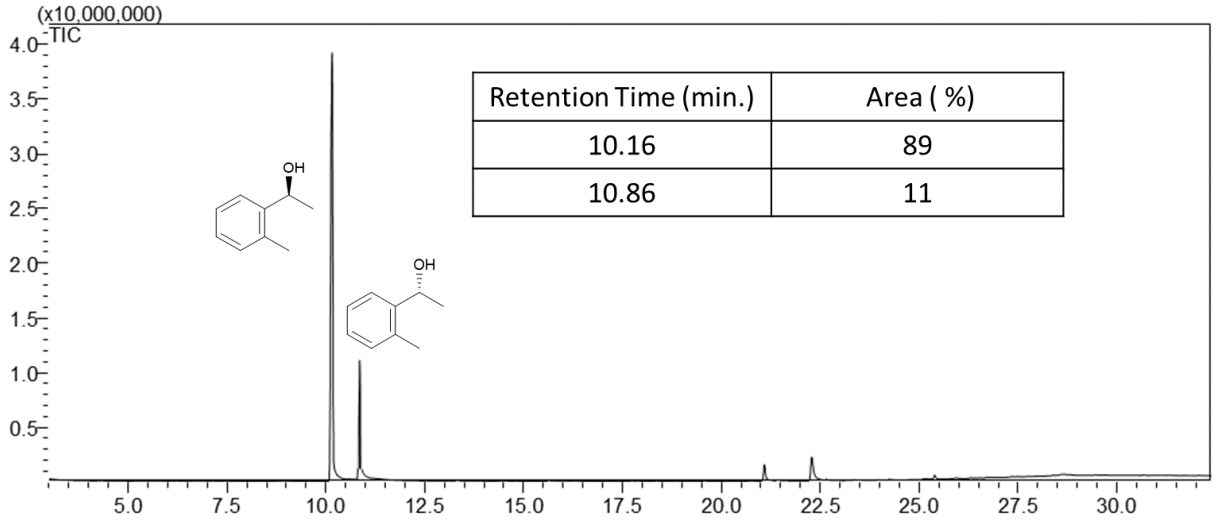
Retention Time (min.)	Area (%)
9.33	90
10.85	10

Figure S 69. Chiral GC chromatogram of 3a



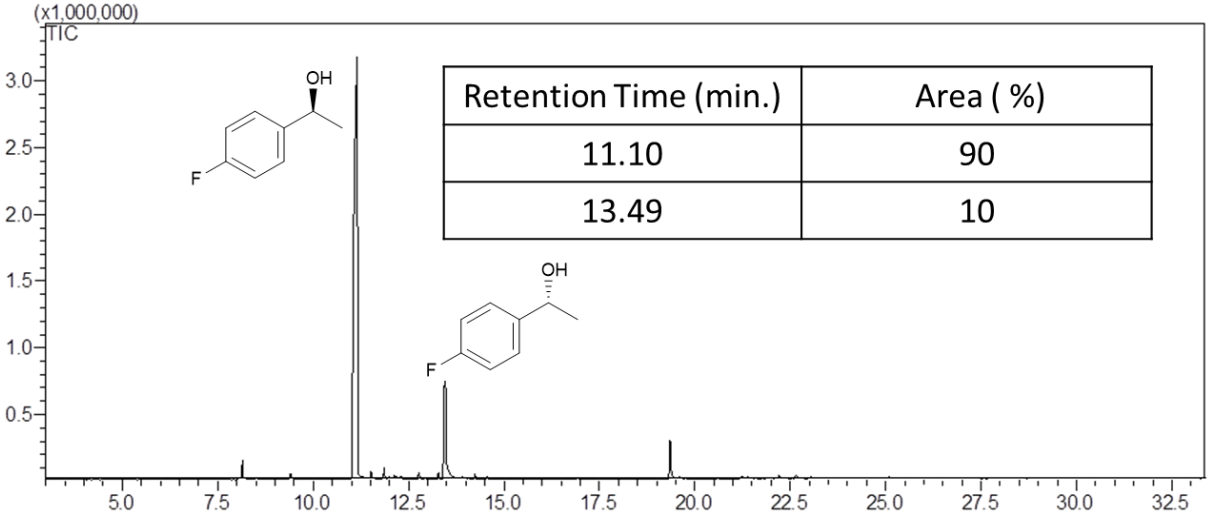
Retention Time (min.)	Area (%)
10.25	88
10.90	12

Figure S 70. Chiral GC chromatogram of 3b



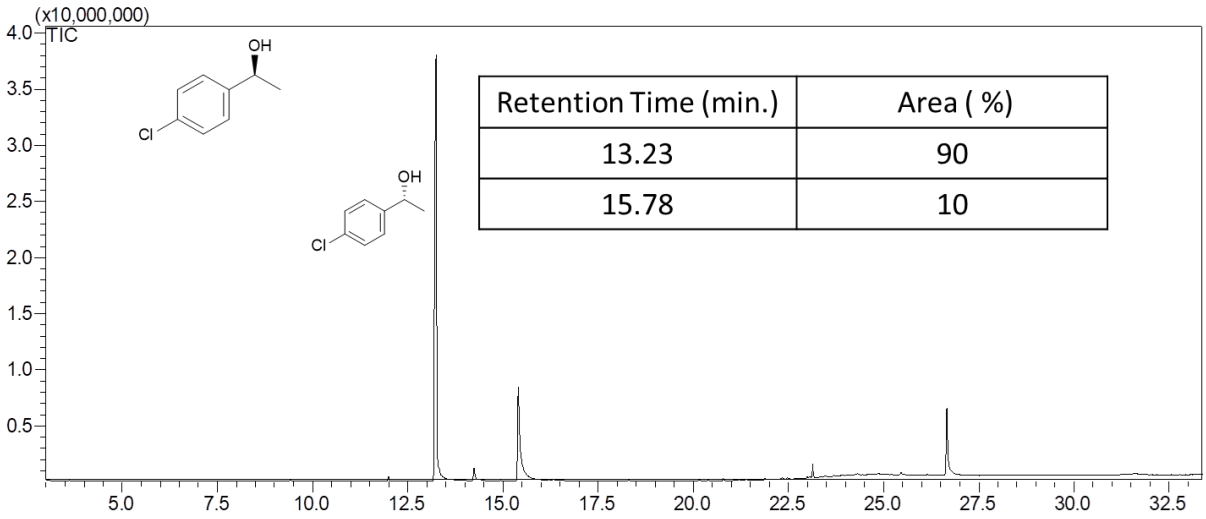
Retention Time (min.)	Area (%)
10.16	89
10.86	11

Figure S 71. Chiral GC chromatogram of 3c



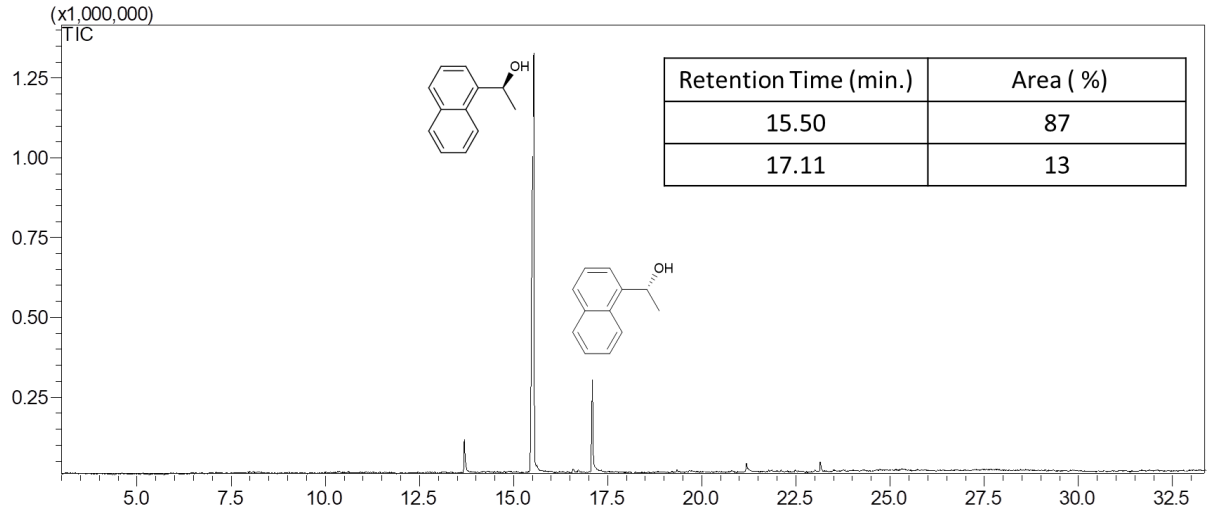
Retention Time (min.)	Area (%)
11.10	90
13.49	10

Figure S 72. Chiral GC chromatogram of 3d



Retention Time (min.)	Area (%)
13.23	90
15.78	10

Figure S 73. Chiral GC chromatogram of 3e



Retention Time (min.)	Area (%)
15.50	87
17.11	13

Figure S 74. Chiral GC chromatogram of 3f