

Supporting Information for

Iron Complex Catalyzed Selective C-H Bond Oxidation with Broad Substrate Scope

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General Considerations

All reagents were obtained commercially unless otherwise stated. Unless mentioned separately, the reactions were performed at room temperature under air. Analytical thin layer chromatography (TLC) was performed on TLC Silica gel 60 F254. Visualization was accomplished with short wave UV light or with PMA, 2,4-DNP and KMnO₄ staining solutions followed by heating. Purification of desired products were performed by column chromatography which was performed on silica gel (230-400 mesh or 100-200 mesh) by standard techniques eluting with solvents as indicated. NMR solvents were dried using pre-activated 4 Å molecular sieves. All indicated solvents were purified prior to use as per standard literature protocols.

Materials

Fe-bTAML: (Et₄N)₂[Fe^{III}(Cl)(bTAML)] and NO₂-substituted Fe-bTAML (**1**) were synthesized by our previously reported methodology.^{1, 2} *meta*-Chloroperbenzoic acid (*m*CPBA, Aldrich 77%) was purified established methodology.³ Acetonitrile (LC-MS Chromasolv. grade, Aldrich) was passed through an activated neutral alumina column and used thereafter. All the substrates (Aldrich, 99.8% or TCI India) were used as received unless otherwise stated and purity was checked by GC.

General Instrumentation

UV-vis spectral studies were carried out using an Agilent diode array 8453 spectrophotometer with an attached electrically controlled thermostat. Gas chromatography (GC) was performed on a PerkinElmer Arnel Clarus 500 instrument equipped with a hydrogen flame ionization detector; HP5 columns (polar) (12 m×0.32 mm×1.0 μm) were used with helium as the carrier gas at a flow rate of 1 mL min⁻¹. GC-MS was performed on a Thermo Scientific ISQ QD Mass Spectrometer attached with Thermo Scientific TRACE 1300 gas chromatograph using an HP-5ms capillary column (30 m×0.25 mm×0.25 μm, J&W Scientific) with helium as the carrier gas. Chiral GC was performed with γ-DEX 225 column equipped with FID. HR-MS was performed in a Thermo Scientific Q-Exactive Orbitrap analyzer using an electrospray ionization source connected with a C18 column (150 m×4.6 mm×8.0 μm). ¹H and ¹³C NMR spectra were recorded on Bruker AV 400 or JEOL 400 instruments in solvents as indicated. Chemical shifts (δ) are given in ppm. The residual solvent signals (CDCl₃ or DMSO-d₆) were used as references and the chemical shifts converted to the TMS scale (CDCl₃: δH = 7.26 ppm, δC = 77.16 ppm, or DMSO-d₆: δH = 2.50 ppm, δC = 39.51 ppm). Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Bellingham Stanley ADP220 Polarimeter. This was obtained with a sodium lamp and was reported as follows: [α]_D²⁰ (c = g/100mL, solvent).

GC-MS method: Oven temperature program (20 min) for Papaverine (**21a**):

Initial temperature: 70 °C, hold for 1.00 min

Ramp1: 20.0 °C/min to 310 °C, hold for 7.00 min

Injector temperature: 320 °C; Detector temperature: 340 °C

GC-MS method: Oven temperature program (22 min) for **rest** of the substrates except Artemisinin (**18a**):

Initial temperature: 50 °C, hold for 1.00 min

Ramp1: 12.0 °C/min to 270 °C, hold for 2.67 min

Injector temperature: 280 °C; Detector temperature: 300 °C

Chiral GC method: Oven temperature program (42 min)

Initial temperature: 50 °C, hold for 2 min

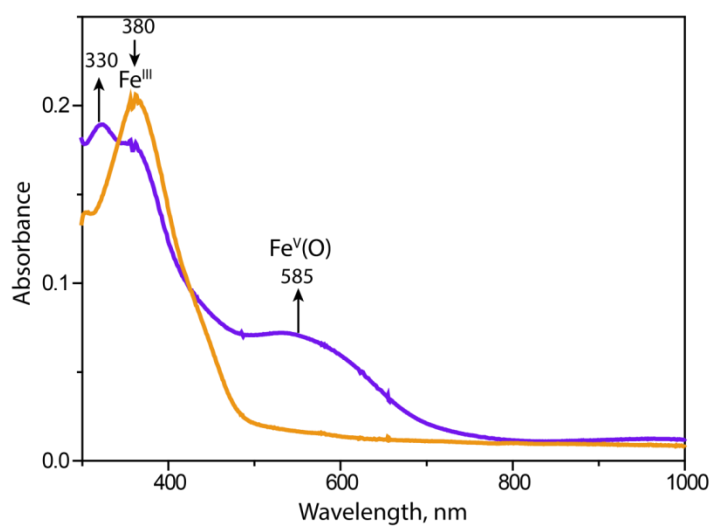
Ramp 1: 10.0 °C/min to 100 °C, no hold

Ramp 2: 2.0 °C/min to 160 °C, no hold

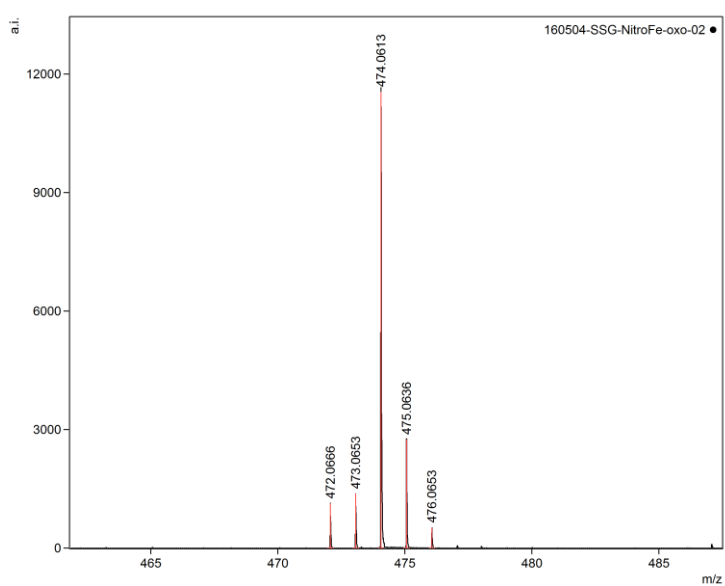
Ramp 3: 10.0 °C/min to 210 °C, no hold

Inlet temperature: 210 °C, FID temperature: 300 °C

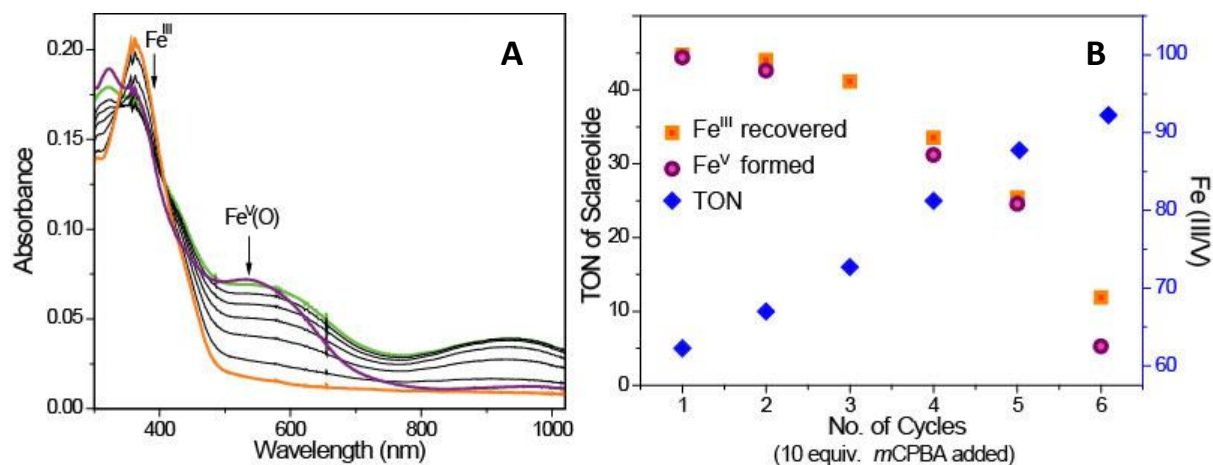
Characterization data of 2:



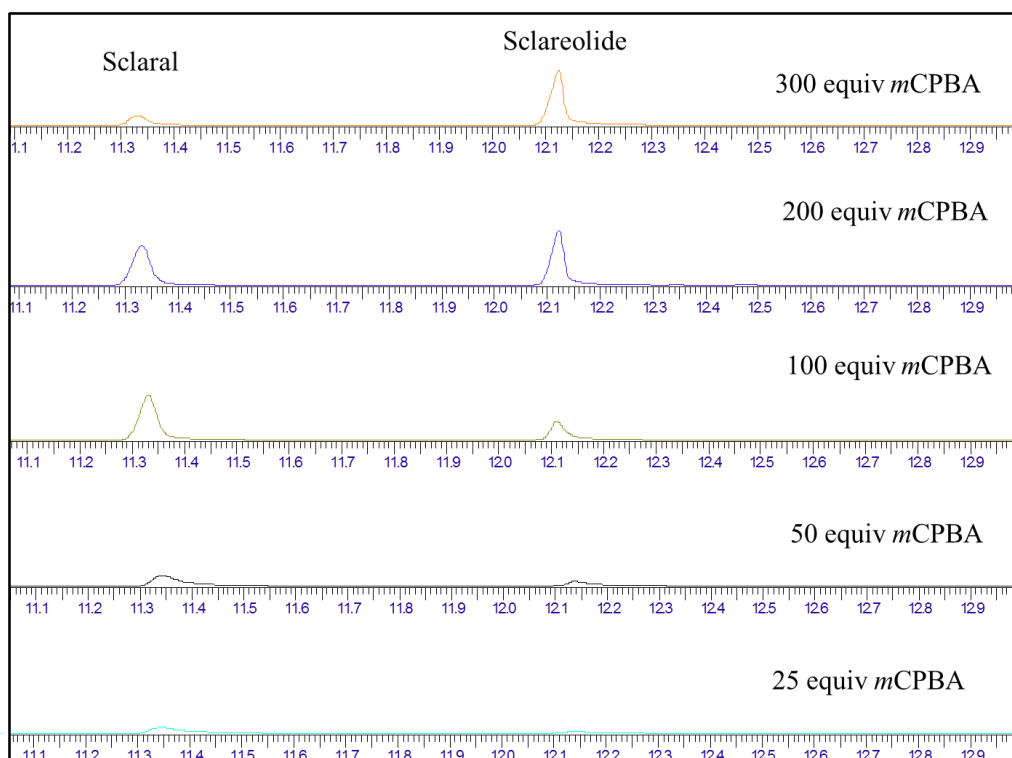
ESI S1: UV-vis plot showing characteristic peaks for Fe^{III} , **1** and $\text{Fe}^{\text{V}}(\text{O})$, **2**



ESI S2: ESI-MS data of **2** (m/z calc'd: 474.0586, found 474.0613)



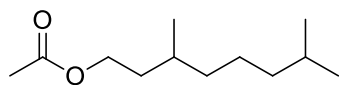
ESI S3: Oxidation of ambroxide with **1** in $\text{CH}_3\text{CN}/\text{H}_2\text{O}/\text{K}_2\text{HPO}_4$ using the iterative 0.02 equiv. of *mCPBA* addition protocol: **A.** UV-Vis plot during the course of the reaction; **B.** The correlation of product sclareolide formed (TON from GC) with Fe^{III} regenerated and $\text{Fe}^{\text{V}}(\text{O})$ formed in each cycle is presented.



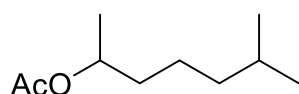
ESI S4: Increment of sclareolide formation in ambroxide/**1**/*mCPBA* reaction with increase of [*mCPBA*]; initially (at 25 equiv.), sclaral (11.34 min) and sclareolide (12.2 min) formed in 4:1 ratio. (GC method: 60°C to 250°C, ramp 12°C/min, hold for 2 mins).

Synthesis and Characterization of Substrates

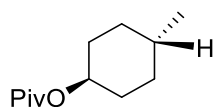
Synthesis of **5a**, **9a**, **10a** and **14a** were carried out as previously reported.



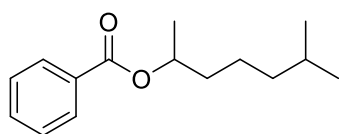
3,7-Dimethyloctyl acetate (Table 1, entry 6a): To a solution of 3,7-dimethyl-1-octanol (1.26 mmol, 241 μ L) in pyridine (10 mL), was added excess acetic anhydride (25.27 mmol, 2.4 mL) and the reaction mixture was stirred for 12h at room temperature. After completion of reaction, the reaction mixture was concentrated by rotary evaporator and dissolved in chloroform. The chloroform part was then washed with brine, followed by subsequent washings with 1(N) HCl and saturated sodium bicarbonate (aq.) solutions. The organic part was concentrated and purified by flash column chromatography (19:1 hexane:EtOAc) to get the desired product in 80% yield (202 mg) as a colourless liquid. ^1H NMR (200.13 MHz, CDCl_3) δ 4.13-4.06 (m, 2H), 2.04 (s, 3H), 1.68-1.62 (m, 1H), 1.56-1.49 (m, 2H), 1.47-1.40 (m, 1H), 1.33-1.21 (m, 3H), 1.18-1.09 (m, 3H), 0.91-0.89 (d, 3H, J = 6.36 Hz), 0.88-0.86 (d, 6H, J = 6.85 Hz) ppm; ^{13}C NMR (50.32 MHz, CDCl_3) δ 171.24, 63.07, 39.17, 37.10, 35.47, 29.81, 27.93, 24.57, 22.57, 21.02 and 19.48 ppm.



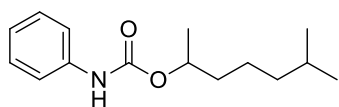
6-methylheptan-2-yl acetate (Table 1, entry 5a): Synthesis same as 6a



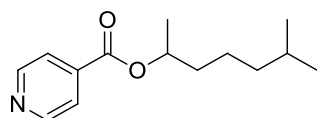
trans-4-methylcyclohexyl pivalate (Table 1, entry 9a): Literature⁴



6-methylheptan-2-yl benzoate (Table 2, entry 10a): Literature⁵

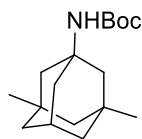


6-methylheptan-2-yl phenylcarbamate (Table 2, entry 11a): Phenyl isocyanate (0.84 mmol, 92 μ L) was slowly added to a stirred solution of 6-methylheptan-2-ol (0.76 mmol, 121 μ L) and triethylamine (1.68 mmol, 234 μ L) in dry dichloromethane (6 mL) at 0 $^{\circ}\text{C}$ under nitrogen, and then stirred at room temperature. After a period of up to 24 h, the mixture was quenched with water and extracted with ethyl acetate. The ethyl acetate layer was washed with brine, dried (Na_2SO_4) and evaporated in vacuum to give an oil which was purified by column chromatography (9:1 hexane: EtOAc) to give the product in 70% yield (133 mg). ^1H NMR (200.13 MHz, CDCl_3) δ 7.42-7.27 (m, 4H), 7.10-7.01 (m, 1H), 6.55 (s, 1H), 4.99-4.83 (m, 1H), 1.66-1.51 (m, 3H), 1.30-1.27 (d, 2H, J =6.19 Hz), 1.25-1.18 (m, 2H), 0.90-0.86 (d, 2H, J =6.57 Hz) ppm; ^{13}C NMR (50.32 MHz, CDCl_3) δ 152.74, 137.48, 128.35, 122.53, 117.89, 71.51, 38.10, 35.71, 27.2, 22.52, 21.9, 19.57 ppm.

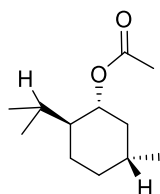


6-methylheptan-2-yl isonicotinate (Table 2, entry 12a): To a chilled solution of isonicotinoyl chloride (0.71 mmol, 100 mg) in dry dichloromethane (5 mL), was added a chilled solution of 6-methylheptan-2-ol (0.64 mmol, 102 μ L) and triethylamine (1.41 mmol, 197 μ L) in dry dichloromethane (5 mL) slowly at 0 $^{\circ}\text{C}$. After addition, the reaction was continued at room temperature. After 10h, the reaction mixture was concentrated and purified by

column chromatography (13:1 hexane: EtOAc) to give the product as an oil in 75% yield (113 mg). ^1H NMR (200.13 MHz, CDCl_3) δ 8.79-8.77 (d, 2H, $J = 5.94$ Hz), 7.86-7.83 (d, 2H, $J = 6.06$ Hz), 5.26-5.10 (m, 1H), 1.82-1.47 (m, 4H), 1.37-1.34 (d, 3H, $J = 6.32$ Hz), 1.99-1.25 (t, 2H, $J = 13.52$ Hz), 0.88-0.85 (d, 6H, $J = 6.57$ Hz) ppm; ^{13}C NMR (50.32 MHz, CDCl_3) δ 164.69, 150.51, 138.03, 122.80, 72.93, 38.62, 36.07, 27.77, 23.12, 22.47, 19.90 ppm.



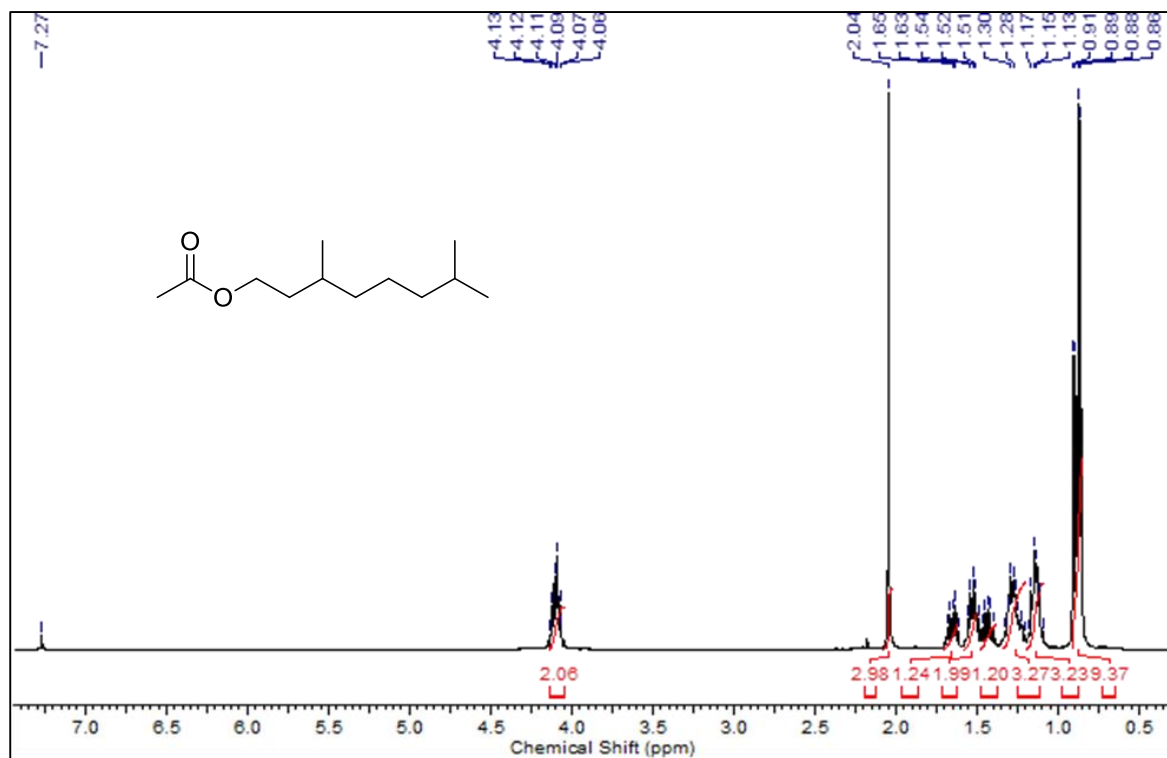
tert-butyl ((1r,3R,5S,7r)-3,5-dimethyladamantan-1-yl)carbamate (Table 2, entry 13a): To a solution of Boc anhydride (2.24 mmol, 390 mg) in dry THF, was added a chilled solution of 1,3-dimethyl-5-adamantanamine (1.12 mmol, 200 mg) and triethylamine (2.24 mmol, 311 μL) under nitrogen atmosphere at 0 $^\circ\text{C}$. The reaction mixture was allowed to stir at room temperature overnight. After completion of the reaction, the mixture was concentrated and purified by column chromatography (4:1 hexane: EtOAc) to give the product as a colourless liquid in 90% yield (280 mg). ^1H NMR (200.13 MHz, CDCl_3) δ 4.39 (s, 1H), 2.13-2.09 (m, 1H), 1.74-1.73 (d, 2H, $J = 2.91$ Hz), 1.52 (bs, 5H), 1.42 (s, 9H), 1.33-1.28 (d, 3H, $J = 8.97$ Hz), 1.13 (s, 2H), 0.84 (s, 6H) ppm; ^{13}C NMR (50.32 MHz, CDCl_3) δ 146.07, 84.48, 51.40, 49.94, 47.20, 42.03, 39.85, 31.70, 29.43, 27.81, 26.74 ppm.



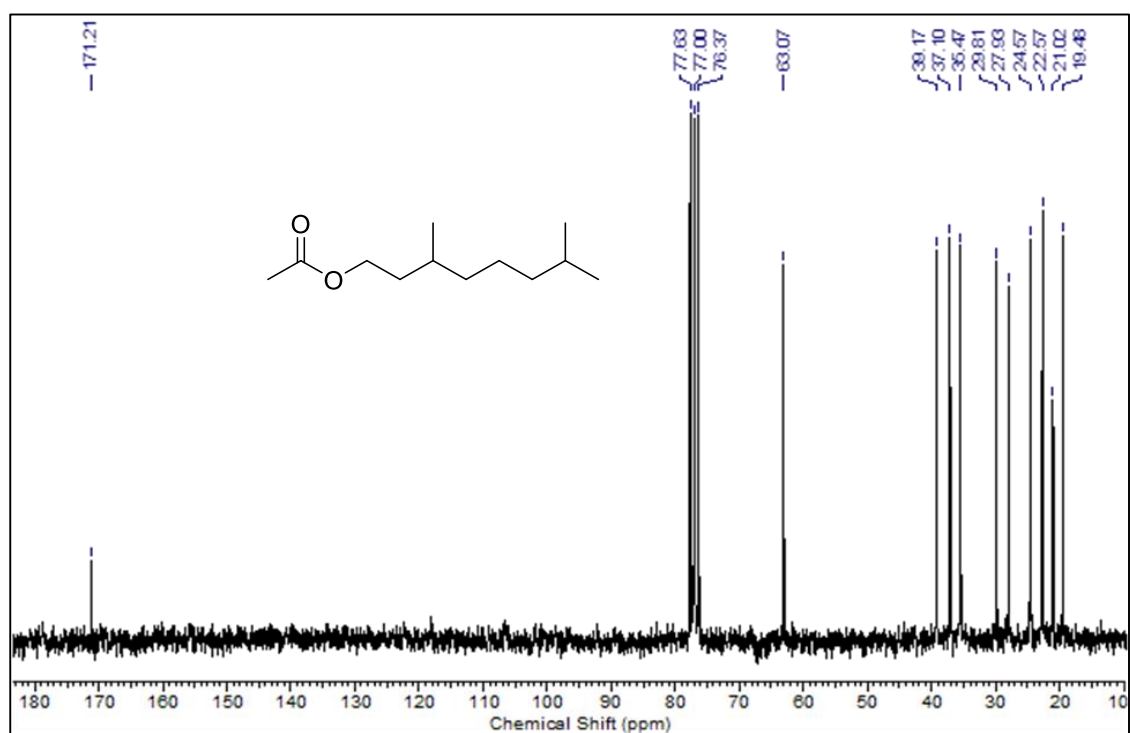
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl acetate (Table 3, entry 14a): Synthesis same as 6a.

NMR Data of Synthesized Starting Materials:

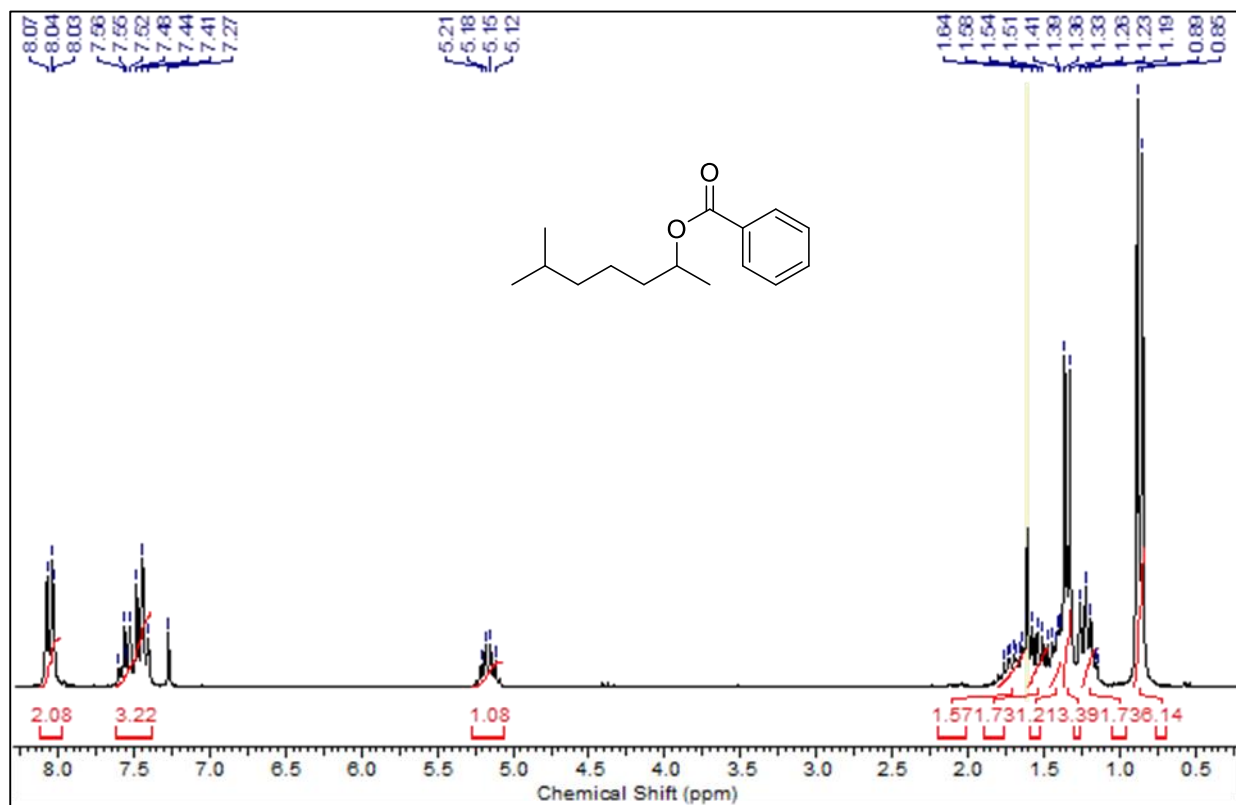
^1H NMR of 6a:



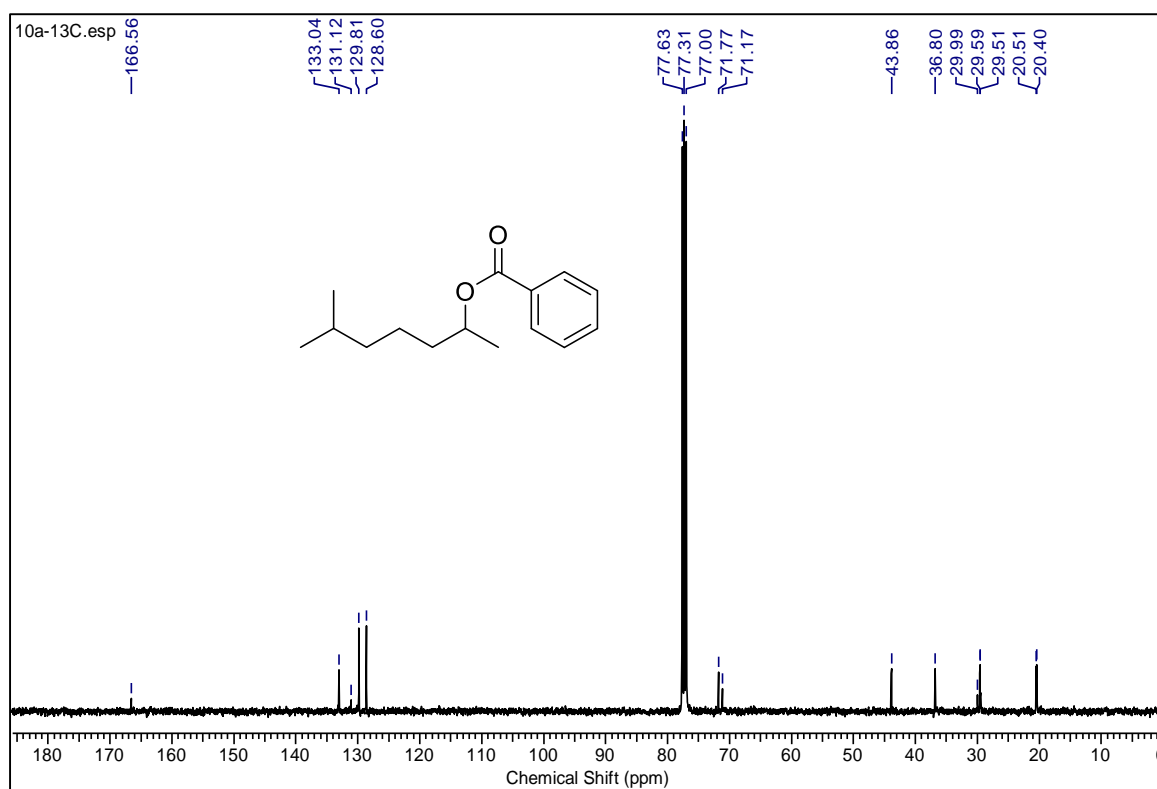
^{13}C NMR of 6a:



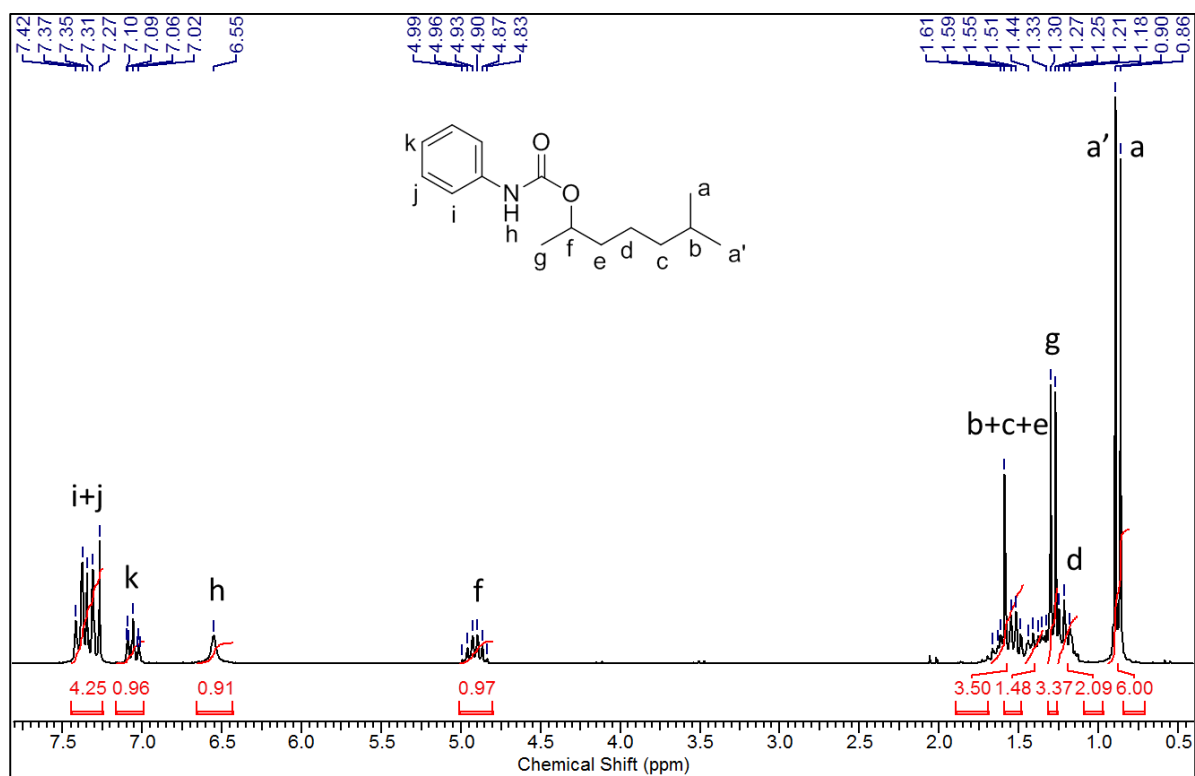
^1H NMR of 10a:



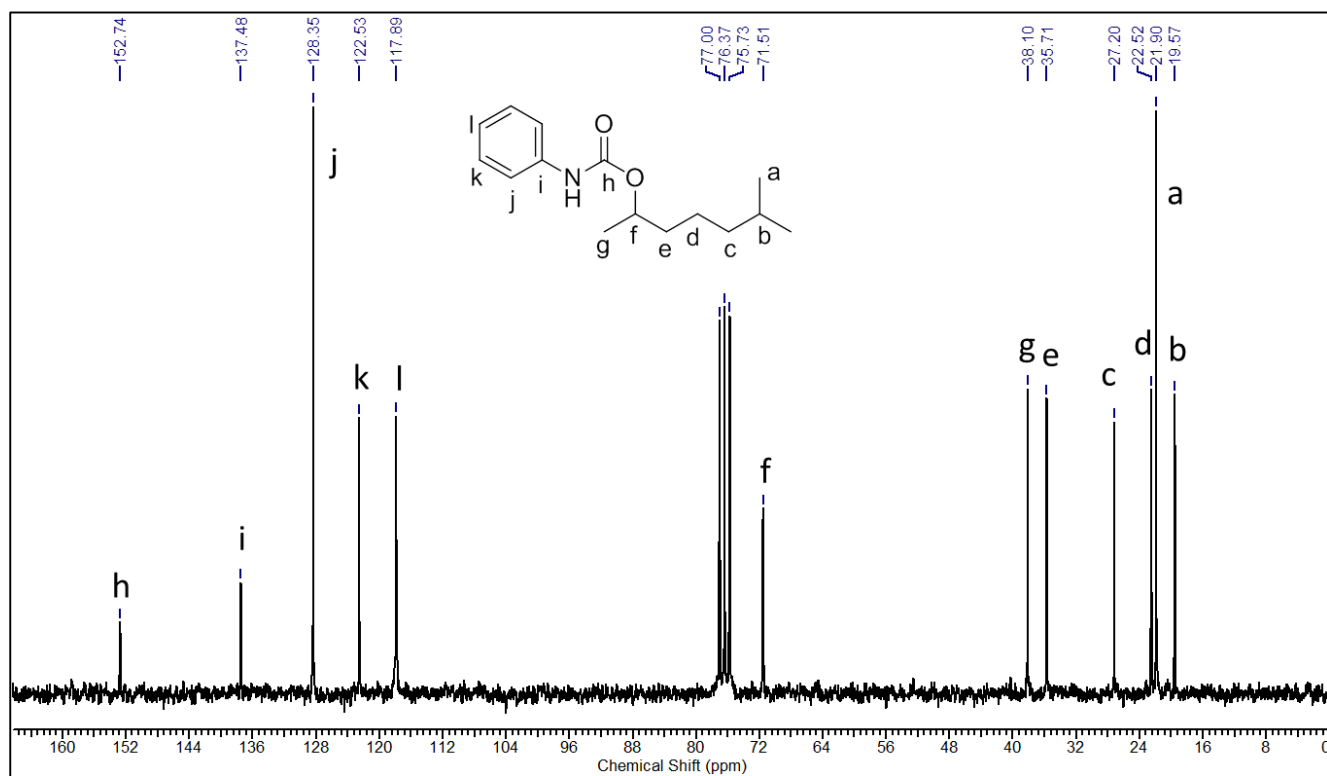
^{13}C NMR of 10a:



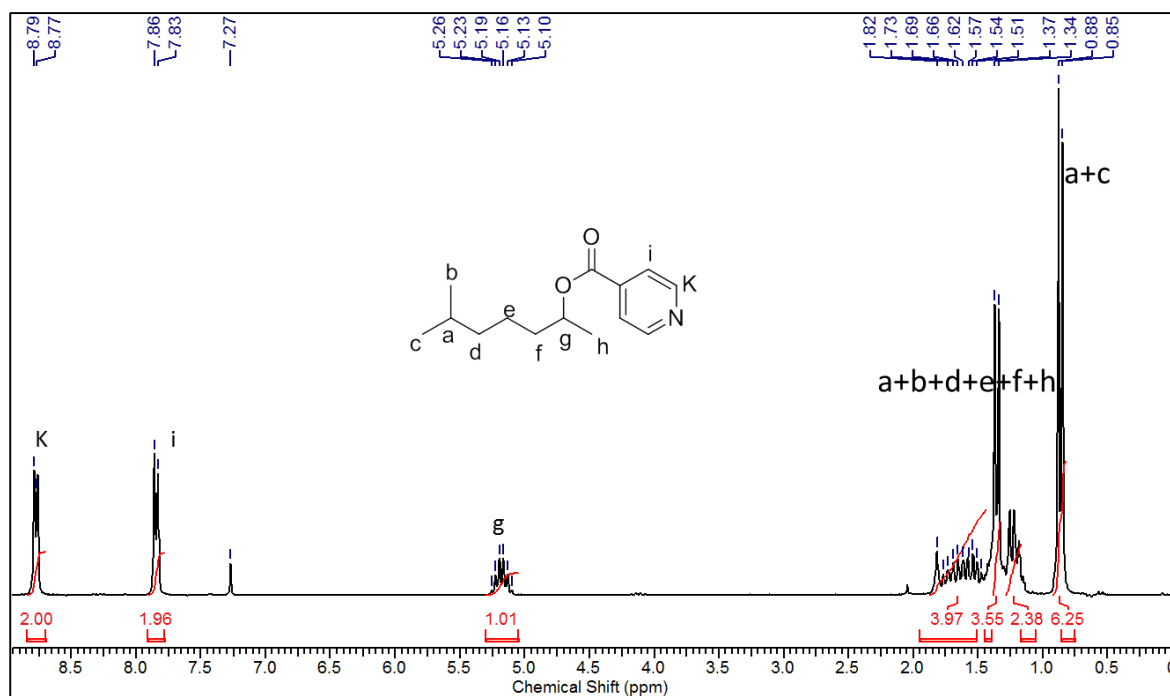
^1H NMR of 11a:



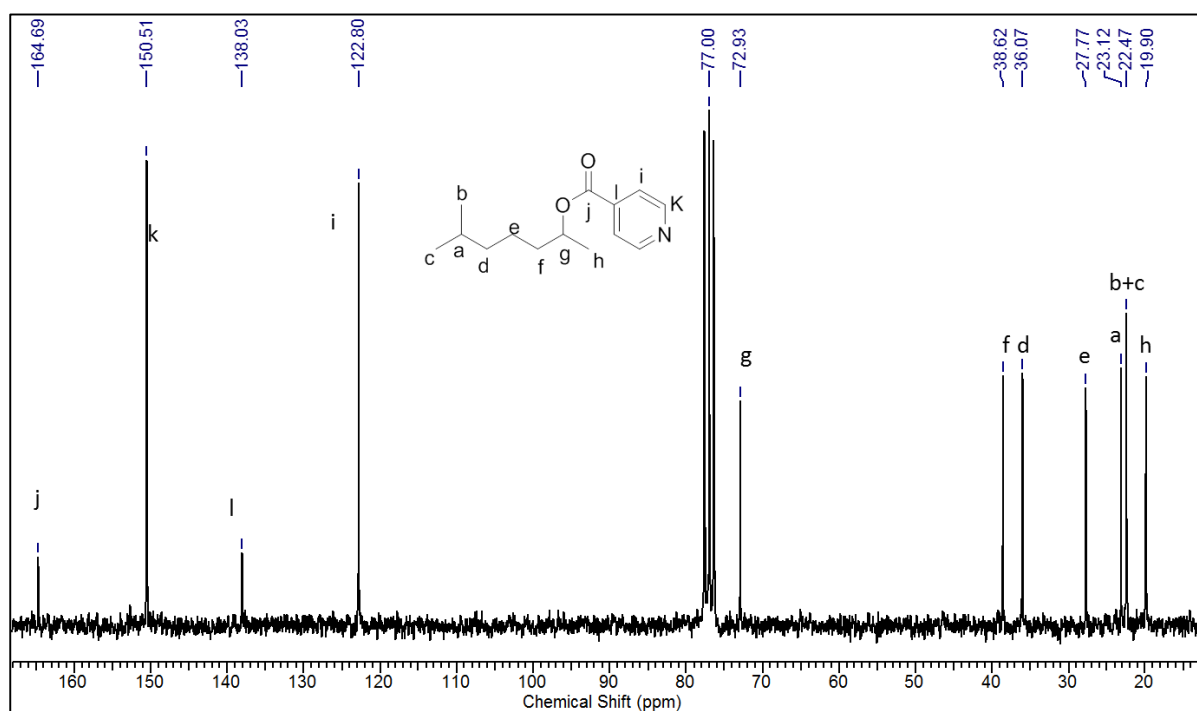
^{13}C NMR of 11a:



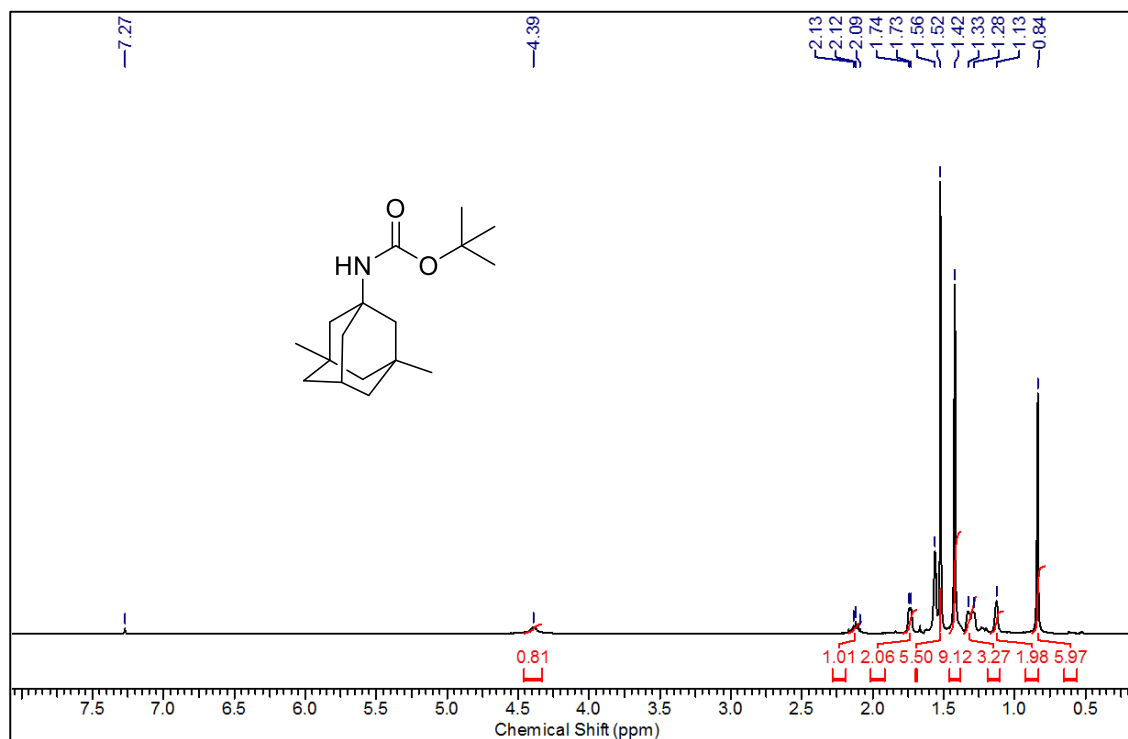
^1H NMR of 12a:



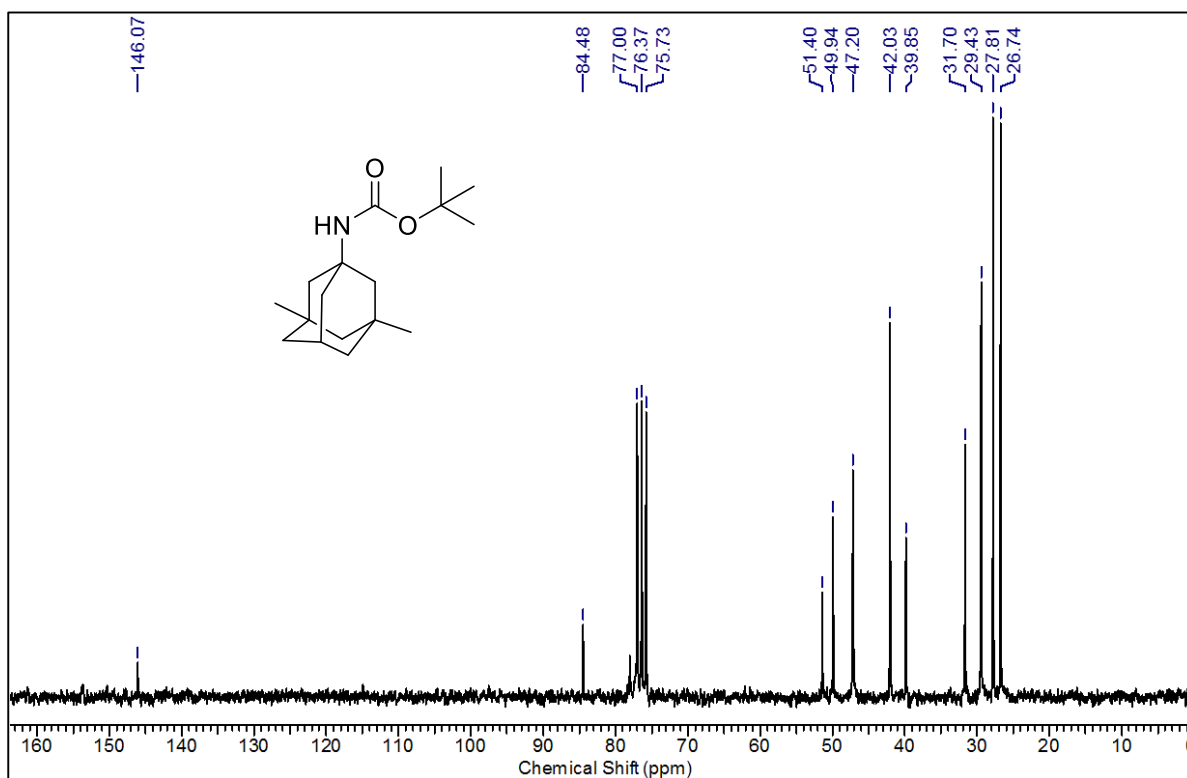
¹³C NMR of 12a:



¹H NMR of 13a:



¹³C NMR of 13a:

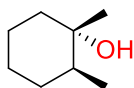


Hydroxylation Reaction Procedure:

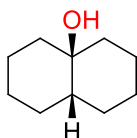
To a 25 mL round-bottom flask containing a magnetic stir bar, NO₂-substituted Fe-bTAML catalyst **1** (1-2 μmol, 1-2 mol %), substrate (0.1 mmol, 1.0 equiv.) and K₂HPO₄ (0.2 mmol, 2 equiv.) in 4 mL CH₃CN-1 mL H₂O were added. A solution of *m*CPBA (0.2-0.5 mmol, 2-5 equiv) in CH₃CN was added *via* syringe pump with continuous stirring over a period of 2-12h at room temperature. The reaction was monitored by TLC and/or GC. After completion of the reaction, the solvent (CH₃CN) was removed under reduced pressure (NB: for more volatile substrates slow and careful evaporation was performed at reduced temperatures). Saturated aq. solution of sodium bicarbonate was added to the residual portion and extracted with dichloromethane (2 times). The organic part was dried with anhydrous Na₂SO₄, analysed by GC to estimate substrate conversion and then further purified by column chromatography to obtain the desired product (silica gel, 100-200 or 230-400 mesh). The purity of the obtained product was determined by ¹H, ¹³C NMR, HRMS and GC.

The regioselectivity and diastereoselectivity in the products are in accordance with the NMR data of the reported products as referenced in the characterization data.

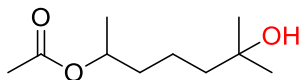
Product Characterization Data:



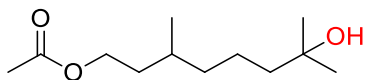
(1*S*,2*S*)+(1*R*,2*R*)-1,2-dimethylcyclohexanol ⁴(Table 1, entry 3*b*): Purified by column chromatography using 5.7:1 hexane:EtOAc. Isolated yield: 85%, 22 mg. TLC *R*_f = 0.6 (4:1 hexane:EtOAc). ¹H NMR (400.13 MHz, CDCl₃, δ, ppm) δ 1.73-1.63 (m, 4H), 1.53-1.47 (m, 1H), 1.41-1.29 (m, 2H), 1.28-1.25 (m, 2H), 1.10 (s, 3H), 0.93-0.91 (d, 3H, *J* = 6.85 Hz); ¹³C NMR (100.61 MHz, CDCl₃) δ 73.09, 42.35, 41.39, 32.08, 25.32, 24.16, 20.88, 15.23 ppm; GC-MS (EI) *m/z*: M⁺ peak: 128.20, base peak: 71.10, t_R: 6.04 min.



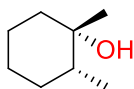
cis-9-Decalinol^{6,7,8} (Table 1, entry 4b): Purified by column chromatography using 6:1 hexane:EtOAc. Isolated yield: 77%, 24 mg. TLC R_f = 0.7 (7:3 hexane:EtOAc). ^1H NMR (200.13 MHz, CDCl_3 , δ , ppm) δ 1.90–1.15 (m, 18H); ^{13}C NMR (50.32 MHz, CDCl_3) δ 71.78, 42.75, 27.98 (br), 22.93 ppm; GC-MS (EI) m/z : M^+ peak: 154.09, base peak: 111.07, tR: 8.54 min.



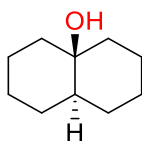
6-hydroxy-6-methylheptan-2-yl acetate (Table 1, entry 5b): Purified by column chromatography using 4:1 hexane:EtOAc. Isolated yield: 52%, 10 mg. TLC R_f = 0.6 (7:3 hexane:EtOAc). ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 4.97–4.89 (m, 1H), 2.05 (s, 3H), 1.64–1.60 (m, 1H), 1.51–1.36 (m, 5H), 1.24 (d, 3H), 1.22 (s, 6H); ^{13}C NMR (100.61 MHz, CDCl_3) δ 170.85, 70.82, 70.85, 43.52, 36.34, 29.29, 29.21, 21.40, 20.15, 19.98 ppm; HRMS (ESI) m/z calc'd $\text{C}_{10}\text{H}_{20}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 211.1305, found 211.1306.



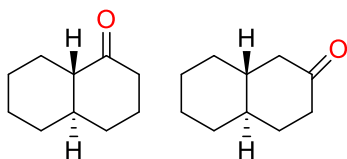
7-hydroxy-3,7-dimethyloctyl acetate (Table 1, entry 6b): Purified by column chromatography using 4:1 hexane:EtOAc. Isolated yield: 51%, 11 mg. TLC R_f = 0.5 (3:1 hexane:EtOAc). ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 4.15–4.05 (m, 2H), 2.05 (s, 3H), 1.71–1.63 (m, 2H), 1.57–1.56 (m, 1H), 1.43–1.42 (m, 3H), 1.35–1.32 (m, 2H), 1.22 (s, 6H), 0.93–0.91 (d, 3H, J = 6.85 Hz); ^{13}C NMR (100.61 MHz, CDCl_3) δ 171.26, 71.02, 63.00, 44.07, 37.34, 35.44, 29.81, 29.29, 29.22, 21.58, 21.04, 19.44 ppm; HRMS (ESI) m/z calc'd $\text{C}_{12}\text{H}_{24}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 239.1618, found 239.1619.



(1S,2R)+(1R,2S)-1,2-dimethylcyclohexanol⁹ (Table 1, entry 7b): Purified by column chromatography using 19:1 hexane:EtOAc. Isolated yield: 60%, 15 mg. TLC R_f = 0.5 (7:3 hexane:EtOAc); ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 1.89–1.34 (m, 10H), 1.19 (s, 3H), 0.92–0.91 (d, 3H, J = 6.10 Hz); GC-MS (EI) m/z : M^+ peak: 128.21, base peak: 71.10, tR: 5.78 min.

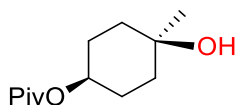


trans-9-Decalinol¹⁰ (Table 1, entry 8b): Purified by column chromatography using 19:1 hexane:EtOAc. Isolated yield: 27%, 8 mg. TLC R_f = 0.6 (3:1 hexane:EtOAc); GC-MS (EI) m/z : M^+ peak: 154.23, base peak: 111.15, tR: 9.24 min. ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 2.42–1.87 (m, 1H), 1.64–1.48 (m, 7H), 1.34–1.19 (m, 8H); ^{13}C NMR (50.32 MHz, CDCl_3) δ 71.33, 39.70, 28.63, 28.25, 21.63 ppm. GC-MS (EI) m/z : M^+ peak: 154.23, base peak: 111.15, tR: 9.24 min.

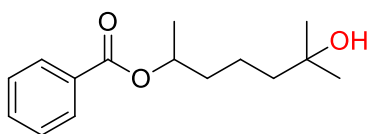


(4aR,8aR)-octahydronaphthalen-1-one (Table 1, entry 8c): Purified by column chromatography using 19:1 hexane:EtOAc. Isolated yield: 34%, 10 mg. TLC R_f = 0.6 (3:1 hexane:EtOAc); ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 2.44–2.29 (m, 2H), 2.10–1.93 (m, 2H), 1.79–1.66 (m, 4H), 1.43–1.29 (m, 4H), 1.22–0.95 (m, 3H); ^{13}C NMR

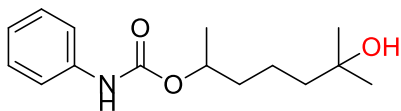
(50.32 MHz, CDCl₃) δ 211.30, 48.67, 43.37, 41.72, 41.64, 34.25, 33.68, 32.72, 29.69, 26.15, 25.63 ppm. GC-MS (EI) m/z : M^+ peak: 152.22, base peak: 108.15, t_R : 10.15 min. HRMS (ESI) m/z calc'd C₁₀H₁₇O [$M+H$]⁺: 153.1274, found 153.1279.



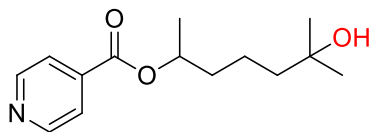
(1S,4S)+(1R,4R)-4-hydroxy-4-methylcyclohexyl pivalate ^{4,11}(Table 1, entry 9b): Purified by column chromatography using 3:1 hexane:EtOAc. Isolated yield: 85%, 18 mg. TLC R_f = 0.5 (1:1 hexane:EtOAc). ¹H NMR (400.13 MHz, CDCl₃, δ , ppm) δ 4.73-4.68 (m, 1H), 1.78-1.69 (m, 6H), 1.54-1.47 (m, 2H), 1.25 (s, 3H), 1.19 (s, 9H); ¹³C NMR (100.61 MHz, CDCl₃) δ 178.11, 71.22, 68.75, 38.69, 36.46, 29.57, 27.13 ppm; HRMS (ESI) m/z calc'd C₁₂H₂₂O₃Na [$M+Na$]⁺: 237.1461, found 237.1460.



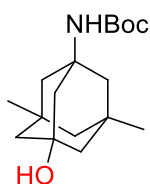
6-hydroxy-6-methylheptan-2-yl benzoate (Table 2, entry 10b): Purified by column chromatography using 3:1 hexane:EtOAc. Isolated yield: 51%, 13 mg. TLC R_f = 0.5 (7:3 hexane:EtOAc). ¹H NMR (400.13 MHz, CDCl₃, δ , ppm) δ 8.06-8.04 (d, 2H, J = 7.82), 7.58-7.54 (t, 1H, J = 14.67 Hz), 7.46-7.43 (2H, t, J = 15.16 Hz), 5.22-5.17 (m, 1H), 1.79-1.75 (m, 1H), 1.66-1.62 (m, 1H), 1.54-1.50 (m, 3H), 1.46-1.42 (m, 2H), 1.37-1.35 (d, 3H, J = 6.36 Hz), 1.21 (s, 6H); ¹³C NMR (100.61 MHz, CDCl₃) δ 166.56, 133.04, 131.12, 129.81, 128.60, 71.77, 71.17, 43.86, 36.80, 29.99, 29.59, 29.51, 20.51, 20.40 ppm; HRMS (ESI) m/z calc'd for C₁₅H₂₂O₃Na [$M+Na$]⁺: 273.1461, found 273.1459.



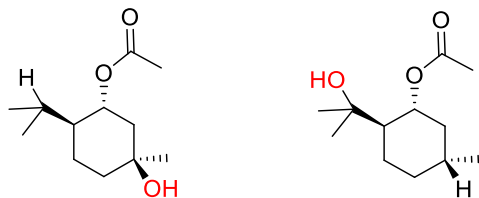
6-hydroxy-6-methylheptan-2-yl phenylcarbamate (Table 2, entry 11b): Purified by column chromatography using 7:3 hexane:EtOAc. Isolated yield: 65%, 17 mg. TLC R_f = 0.4 (7:3 hexane:EtOAc). ¹H NMR (400.13 MHz, CDCl₃, δ , ppm) δ 7.40-7.38 (d, 2H, J = 8.31 Hz), 7.33-7.27 (m, 2H), 7.08-7.04 (t, 1H, J = 14.64 Hz), 6.59 (s, 1H), 4.96-4.92 (m, 1H), 1.62 (bs, 2H), 1.51-1.45 (m, 4H), 1.30-1.29 (d, 2H, J = 6.36 Hz), 1.22 (s, 6H); ¹³C NMR (100.61 MHz, CDCl₃) δ 153.68, 138.36, 129.34, 123.58, 118.86, 72.19, 71.18, 43.86, 36.88, 29.64, 29.54, 20.57, 20.45 ppm; HRMS (ESI) m/z calc'd C₁₅H₂₃O₃NNa [$M+Na$]⁺: 288.1570, found 288.1568.



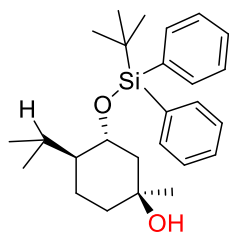
6-hydroxy-6-methylheptan-2-yl isonicotinate (Table 2, entry 12b): Purified by column chromatography using 1:1 hexane:EtOAc. Isolated yield: 74%, 19 mg. TLC R_f = 0.3 (1:1 hexane:EtOAc). ¹H NMR (400.13 MHz, CDCl₃, δ , ppm) δ 8.78-8.76 (d, 2H, J = 5.49 Hz), 7.85-7.84 (d, 2H, J = 6.10 Hz), 5.25-5.17 (1H, m), 1.83-1.74 (m, 1H), 1.67-1.62 (m, 1H), 1.51-1.49 (m, 3H), 1.38-1.36 (d, 3H, J = 6.10 Hz), 1.26 (bs, 2H), 1.21 (s, 6H); ¹³C NMR (100.61 MHz, CDCl₃) δ 165.02, 150.81, 138.27, 123.14, 73.03, 71.05, 43.75, 36.64, 29.98, 29.56, 20.44, 20.26 ppm; HRMS (ESI) m/z calc'd C₁₄H₂₂O₃N [$M+Na$]⁺: 252.1594, found 252.1595.



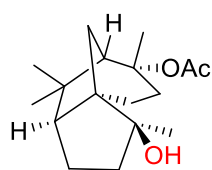
tert-butyl ((1*r*,3*s*,5*R*,7*S*)-3-hydroxy-5,7-dimethyladamantan-1-yl)carbamate (Table 2, entry 13b): Purified by column chromatography using 1:1 hexane:EtOAc. Isolated yield: 80%, 24 mg. TLC R_f = 0.3 (7:3 hexane:EtOAc). ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 4.47 (s, 1H), 1.79 (s, 2H), 1.59 (s, 4H), 1.473 (s, 9H), 1.38-1.36 (m, 4H), 1.10-1.09 (d, 2H, J = 4.48 Hz), 0.93 (s, 6H); ^{13}C NMR (100.61 MHz, CDCl_3) δ 153.87, 78.69, 70.08, 53.53, 50.11, 49.13, 47.70, 46.42, 33.82, 28.81, 28.11 ppm; HRMS (ESI) m/z calc'd $\text{C}_{17}\text{H}_{29}\text{O}_3\text{NNa}$ $[\text{M}+\text{Na}]^+$: 318.2040, found 318.2038.



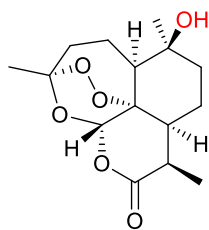
(1*R*,2*S*,5*S*)-5-hydroxy-2-isopropyl-5-methylcyclohexyl acetate ^{4,9,12}(Table 3, entry 14b): Purified by column chromatography using 6:1 hexane:EtOAc. Isolated yield (**14b** + **14c**): 55%, 24 mg. TLC R_f = 0.5 (4:1 hexane:EtOAc). HRMS (ESI) m/z calc'd $\text{C}_{12}\text{H}_{22}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 237.1461, found 237.1460. ^1H NMR (200.13 MHz, CDCl_3 , δ , ppm) δ 5.06-4.75 (m, 1H), 2.04 (s, 3H), 2.00-1.85 (m, 2H), 1.66-1.63 (m, 1H), 1.54-1.46 (m, 2H), 1.43-1.34 (m, 3H), 1.25 (s, 3H), 0.94-0.91 (d, 3H, J = 7.07 Hz), 0.83-0.79 (d, 3H, J = 6.95 Hz).



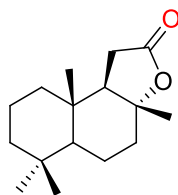
(1*S*,3*R*,4*S*)-3-((tert-butyldiphenylsilyl)oxy)-4-isopropyl-1-methylcyclohexanol ¹³(Table 3, entry 15b): Purified by column chromatography using 6:1 hexane:EtOAc. Isolated yield: 65%, 27 mg. TLC R_f = 0.6 (4:1 hexane:EtOAc). ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 7.74-7.68 (m, 4H), 7.46-7.37 (m, 6H), 3.81-3.75 (m, 1H), 2.41-2.34 (m, 1H), 1.70-1.66 (m, 1H), 1.59-1.59 (m, 2H), 1.45-1.35 (m, 3H), 1.27-1.24 (m, 4H), 1.06 (bs, 12H), 0.91-0.89 (d, 3H, J = 6.85 Hz), 0.58-0.57 (d, 3H, J = 6.85 Hz); ^{13}C NMR (100.53 MHz, CDCl_3) δ 135.99, 129.59, 129.34, 127.50, 127.29, 71.31, 70.75, 50.25, 48.32, 32.77, 31.41, 27.06, 25.07, 21.31, 19.44, 18.50, 15.85 ppm; HRMS (ESI) m/z calc'd $\text{C}_{26}\text{H}_{39}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$: 411.2719, found 411.2669.



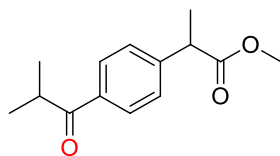
Cedryl acetate ^{14,15}(Table 4, entry 17b): Purified by column chromatography using 7:1 hexane:Et₂O. Isolated yield: 80%, 45 mg. TLC R_f = 0.7 (7:3 hexane:EtOAc). ^1H NMR (400.13 MHz, CDCl_3 , δ , ppm) δ 2.44-2.43 (d, 1H, J = 5.49 Hz), 2.10-2.05 (dd, 1H, J = 18.50 Hz), 1.95 (s, 3H), 1.92-1.89 (m, 2H), 1.86-1.81 (m, 2H), 1.62-1.58 (m, 2H), 1.55 (s, 3H), 1.52-1.48 (m, 2H), 1.44-1.36 (m, 1H), 1.30-1.25 (m, 2H), 1.17 (s, 3H), 1.15 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (100.61 MHz, CDCl_3) δ 170.36, 85.85, 79.37, 57.32, 54.85, 53.69, 44.81, 41.19, 35.67, 33.52, 29.56, 27.91, 26.69, 25.83, 24.16, 22.69, 21.44 ppm; HRMS (ESI) m/z calc'd $\text{C}_{17}\text{H}_{28}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 303.1931, found 303.1929.



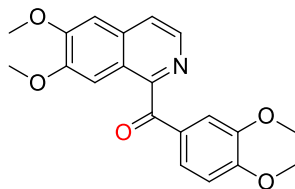
10β-Hydroxy-Artemisinin ¹⁶(Table 4, entry 18b): Purified by column chromatography using 1:1 hexane:EtOAc. Isolated yield: 38%, 23 mg. TLC R_f = 0.5 (3:2 hexane:EtOAc). ¹H NMR (400.13 MHz, CDCl₃, δ, ppm) δ 8.41-8.40 (d, 1H, J = 5.38 Hz), 7.87-7.85 (d, 1H, J = 5.38 Hz), 7.58 (s, 1H), 7.50 (s, 1H), 7.30 (s, 1H), 7.26-7.24 (d, 1H, J = 8.31 Hz), 7.04-7.02 (1H, d, J = 8.31 Hz), 3.96 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H) ppm; ¹³C NMR (125.76 MHz, CDCl₃) δ 172.37, 105.20, 94.34, 79.90, 72.21, 51.55, 45.31, 39.90, 35.54, 32.88, 29.693, 25.24, 19.55, 19.08, 12.59 ppm; HRMS (ESI) m/z calc'd C₁₅H₂₂O₆Na [M+Na]⁺: 321.1309, found 321.1302; $[\alpha]_D^{33}$ +75° (c 0.40 MeOH); literature $[\alpha]_D^{25}$ +60.3° (c 0.55 MeOH).



(3aR)-(+)-Sclareolide (Table 5, entry 19b): Purified by column chromatography using 19:1 hexane:EtOAc. Isolated yield: 90%, 23 mg. TLC R_f = 0.5 (9:1 hexane:EtOAc). ¹H NMR (200.13 MHz, CDCl₃, δ, ppm) δ 2.50-2.17 (m, 2H), 2.12-1.82 (m, 3H), 1.77-1.63 (m, 2H), 1.51-1.33 (m, 7H), 1.28-1.18 (m, 1H), 1.12-1.02 (m, 2H), 0.91 (s, 3H), 0.89 (s, 3H), 0.84 (s, 3H) ppm; ¹³C NMR (100.61 MHz, CDCl₃) δ 177.49, 86.98, 59.71, 57.24, 42.76, 40.09, 39.30, 36.64, 33.76, 29.31, 22.17, 21.52, 21.15, 18.68, 15.87 ppm; HRMS (ESI) m/z calc'd C₁₆H₂₆O₂Na [M+Na]⁺: 273.1825, found 273.1823.



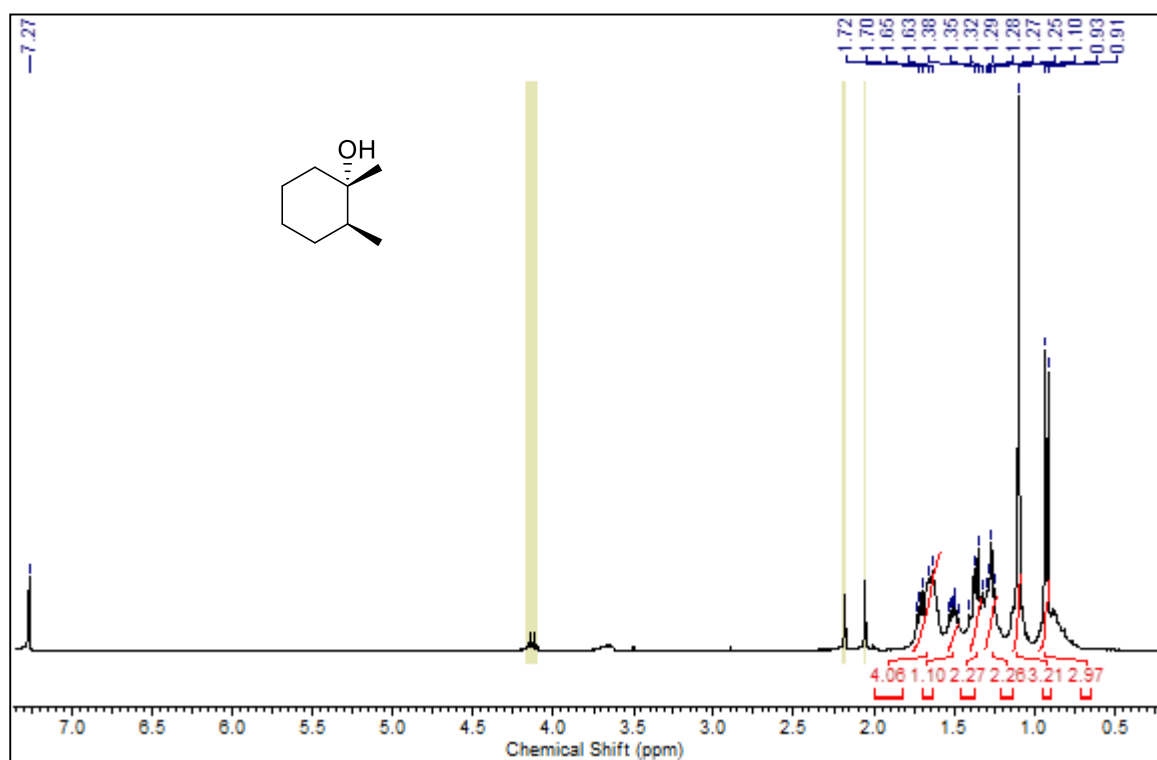
Methyl-2-(4-isobutyrylphenyl)propanoate (Table 5, entry 20b): Purified by column chromatography using 6:1 hexane:EtOAc. Isolated yield: 50%, 12 mg. TLC R_f = 0.6 (7:3 hexane:EtOAc). ¹H NMR (400.13 MHz, CDCl₃, δ, ppm) δ 7.94-7.92 (d, 2H, J = 8.31 Hz), 7.40-7.39 (d, 2H, J = 8.31 Hz), 3.82-3.73 (m, 1H), 3.68 (s, 3H), 3.58-3.58 (m, 1H), 1.54-1.52 (d, 3H, J = 6.85 Hz), 1.23-1.21 (d, 6H, J = 6.85 Hz); ¹³C NMR (100.61 MHz, CDCl₃) δ 203.97, 174.32, 144.94, 135.14, 128.77, 127.81, 52.22, 45.41, 35.34, 19.14, 18.14 ppm; HRMS (ESI) m/z calc'd C₁₄H₁₉O₃ [M+H]⁺: 235.1329, found 235.1330.



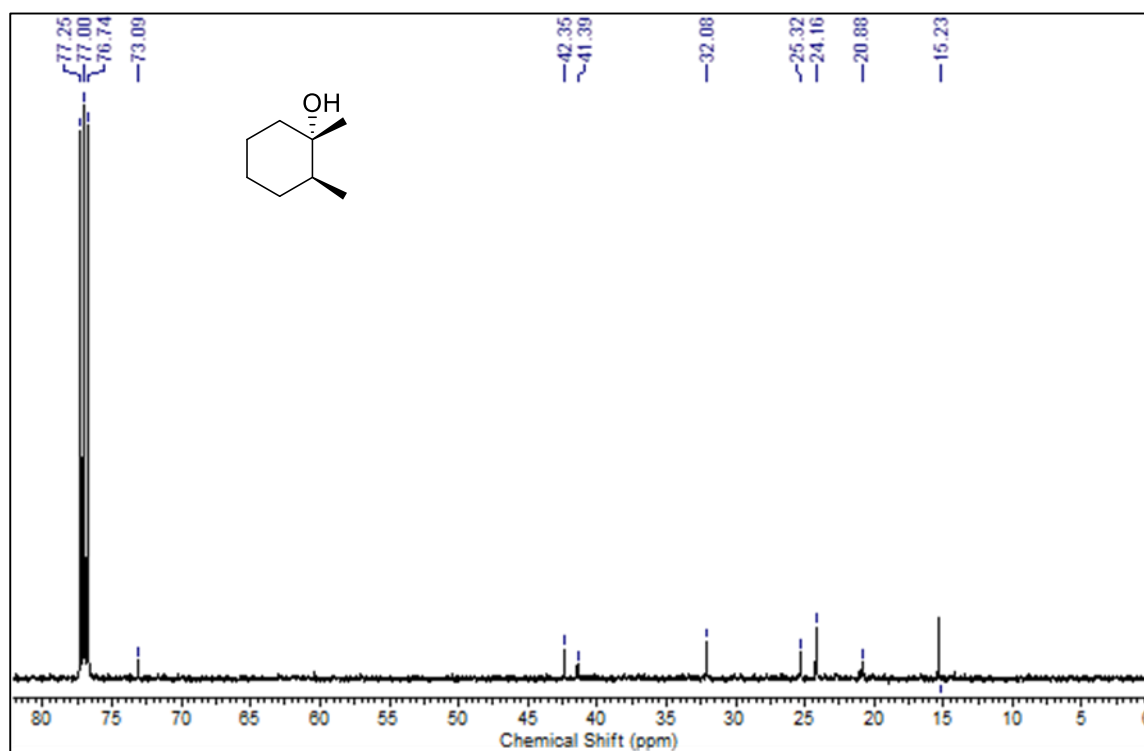
6,7-dimethoxyisoquinolin-1-yl(3,4-dimethoxyphenyl)methanone (Table 5, entry 21b): Purified by column chromatography using 1:1 hexane:EtOAc. Isolated yield: 68%, 24 mg. TLC R_f = 0.5 (3:2 hexane:EtOAc). ¹H NMR (400.13 MHz, DMSO-d₆, δ, ppm) δ 8.41-8.40 (d, 1H, J = 5.38 Hz), 7.87-7.85 (d, 1H, J = 5.38 Hz), 7.58 (s, 1H), 7.50 (s, 1H), 7.30 (s, 1H), 7.26-7.24 (d, 1H, J = 8.31 Hz), 7.04-7.02 (1H, d, J = 8.31 Hz), 3.96 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H) ppm; ¹³C NMR (100.61 MHz, DMSO d₆) δ 193.67, 154.05, 153.36, 151.16, 149.13, 140.27, 133.89, 129.58, 127.05, 122.16, 121.05, 111.81, 111.15, 106.02, 103.64, 56.35, 55.98, 55.61 ppm; HRMS (ESI) m/z calc'd C₂₀H₂₀O₅N [M+H]⁺: 354.1336, found 354.1334.

Product NMR Spectra:

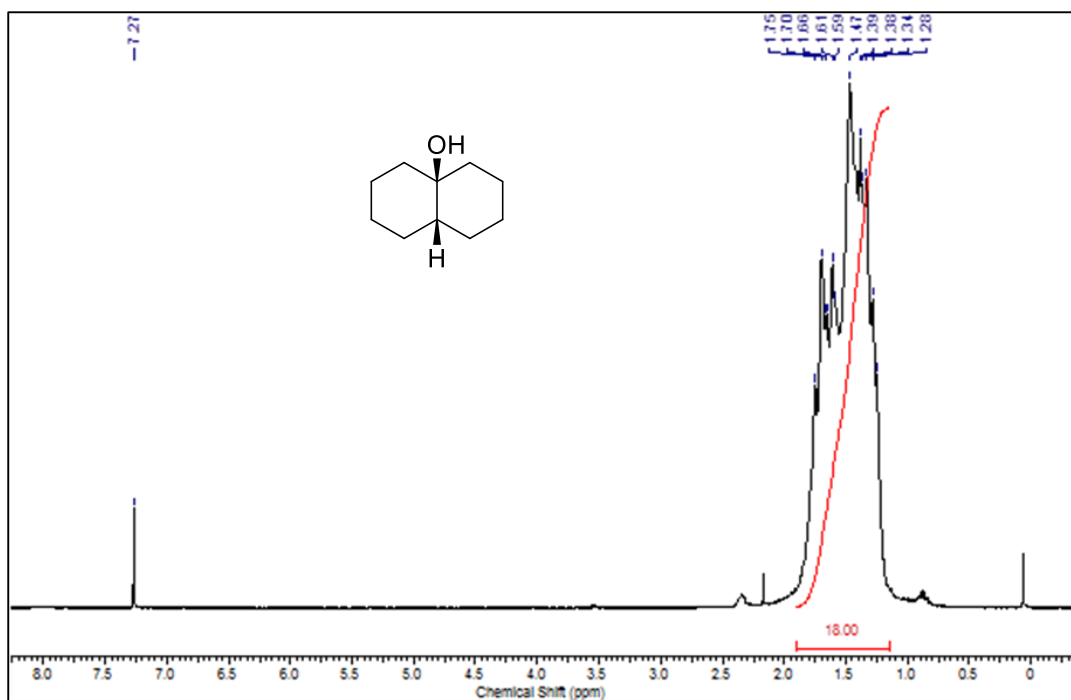
¹H NMR of 3b:



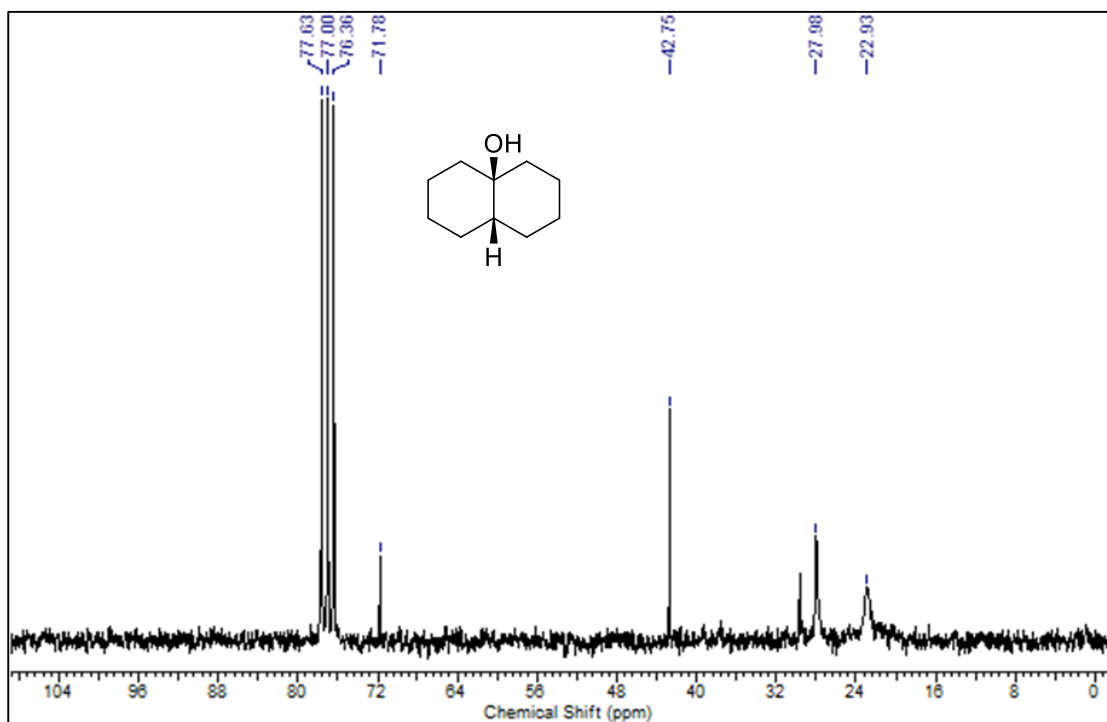
¹³C NMR of 3b:



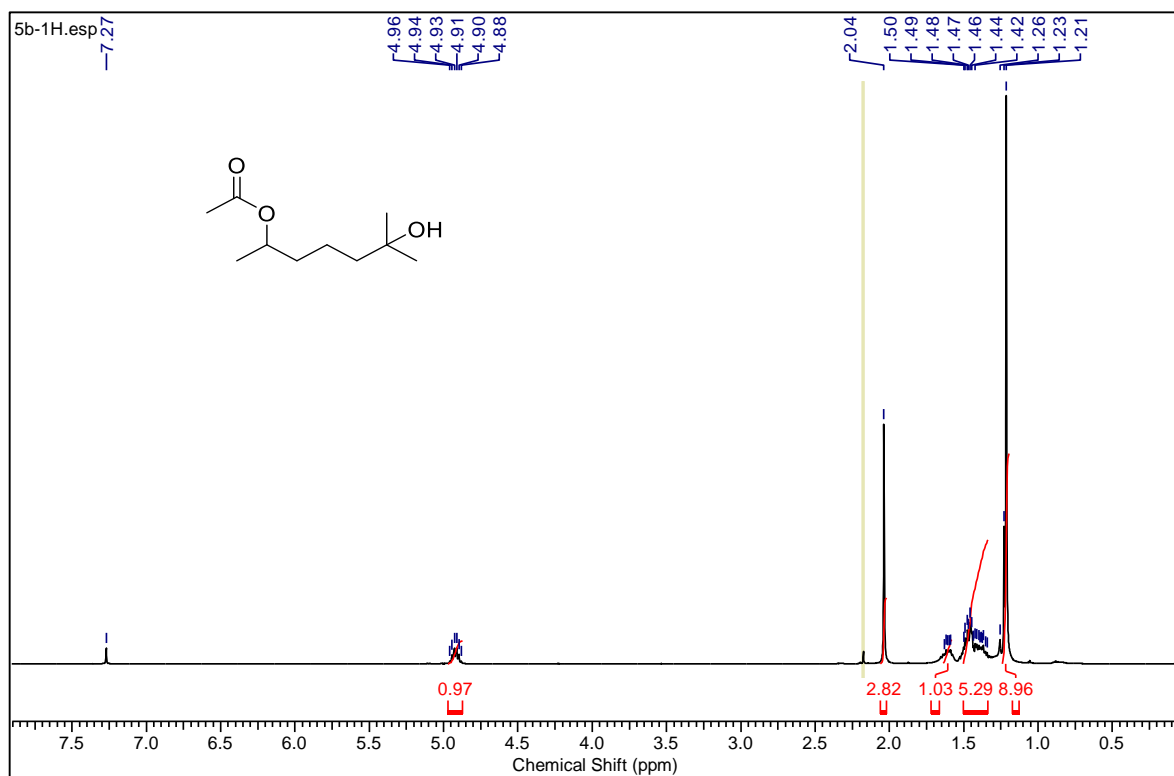
¹H NMR of 4b:



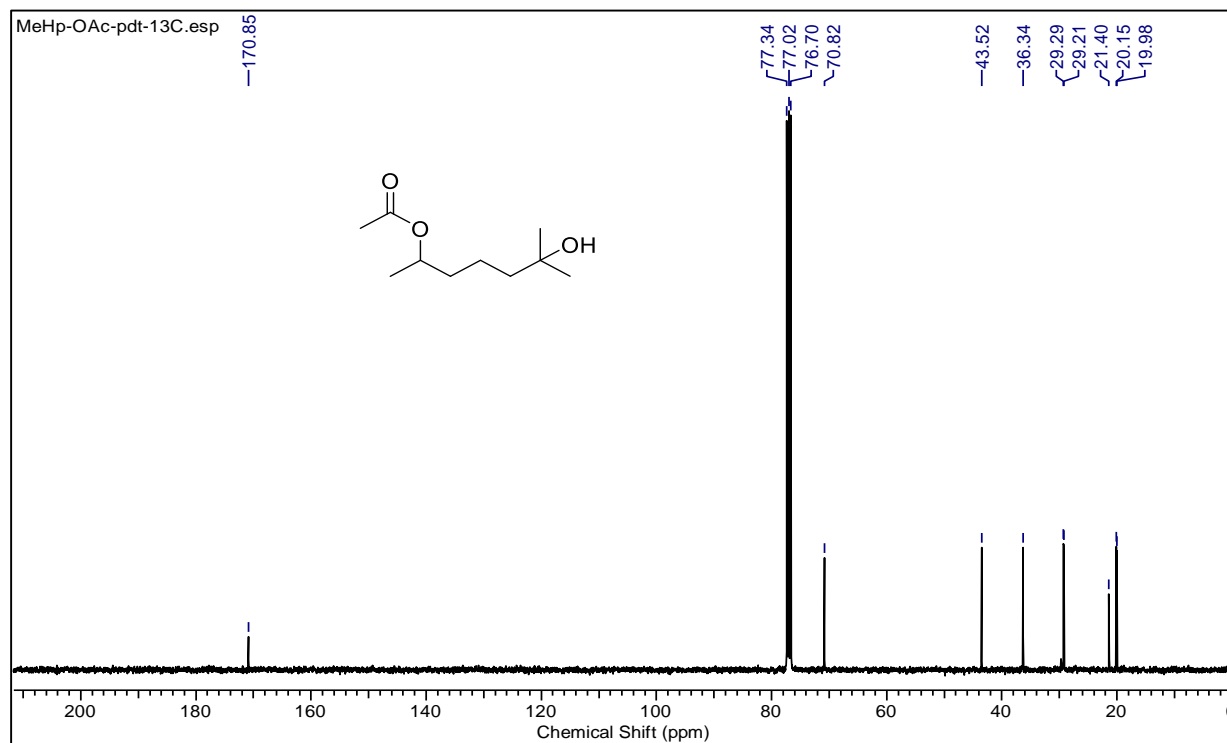
¹³C NMR of 4b:



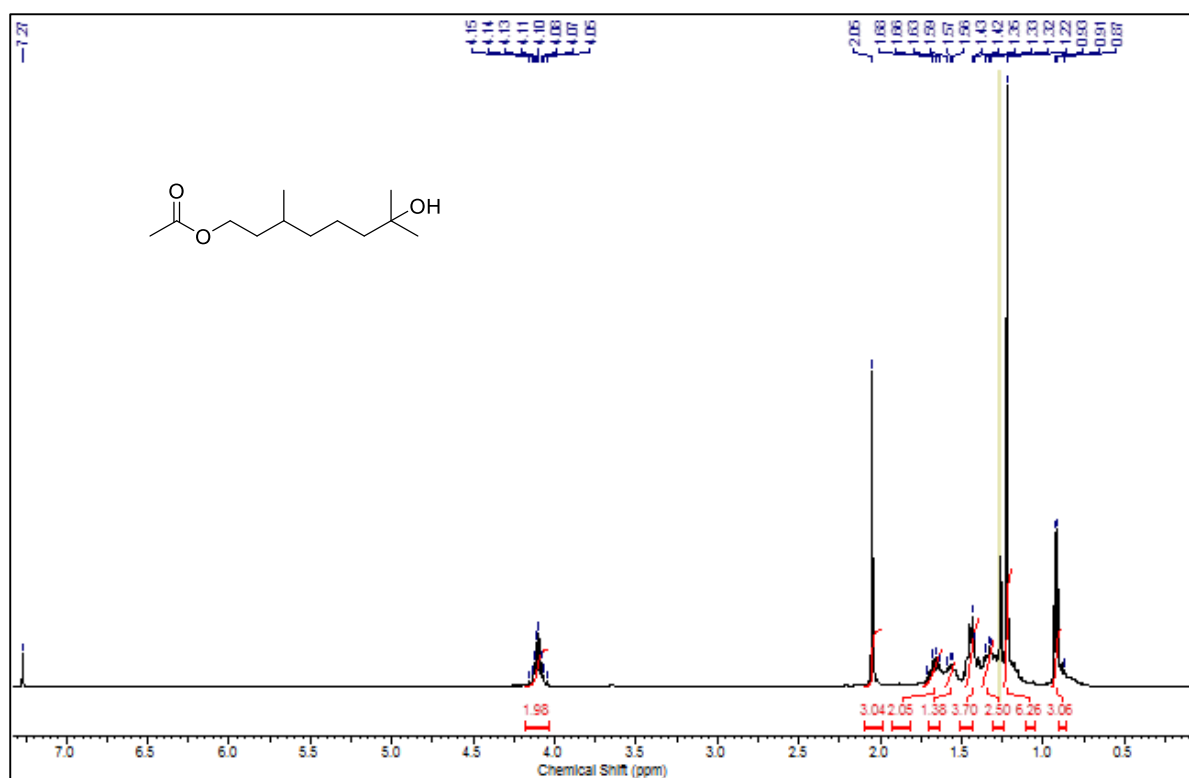
¹H NMR of 5b:



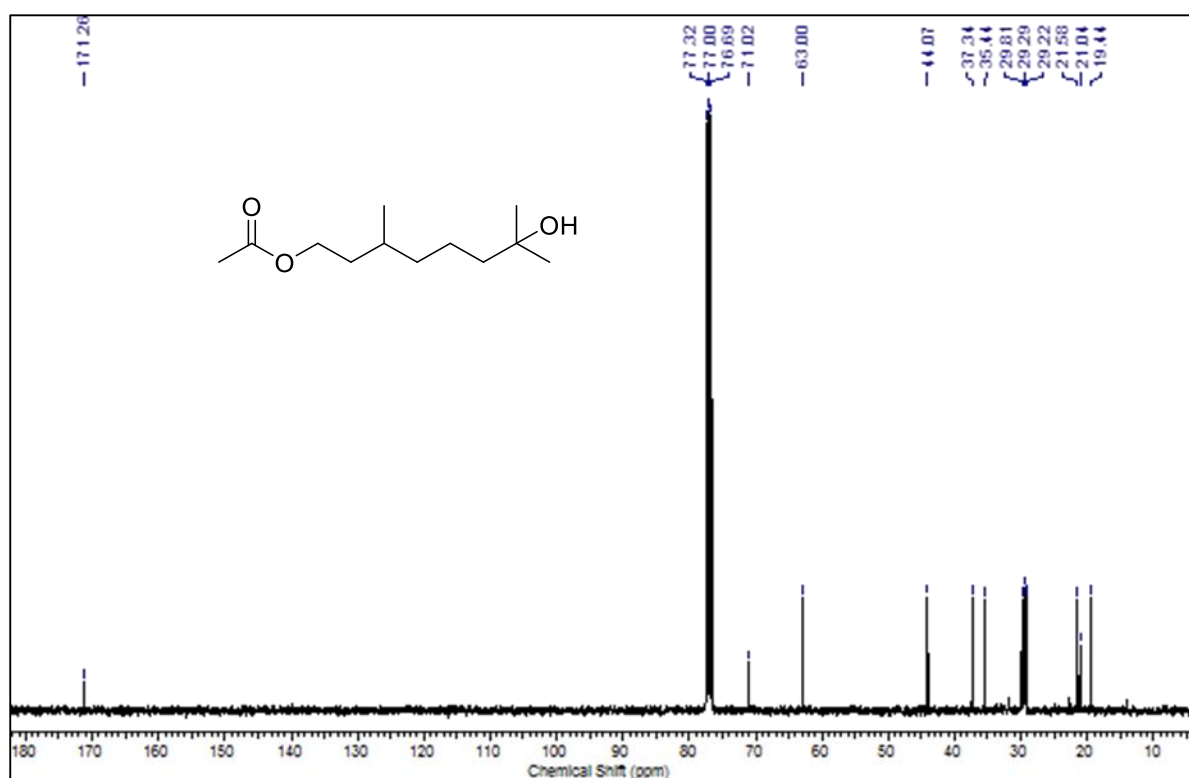
¹³C NMR of 5b:



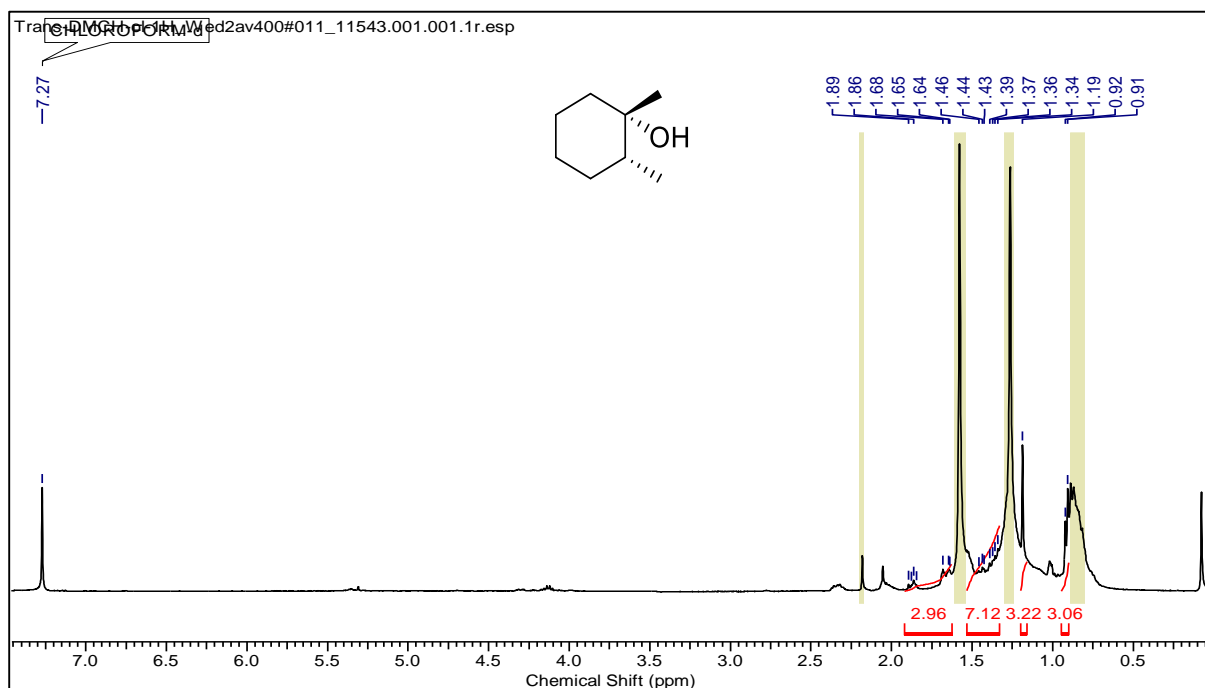
¹H NMR of 6b:



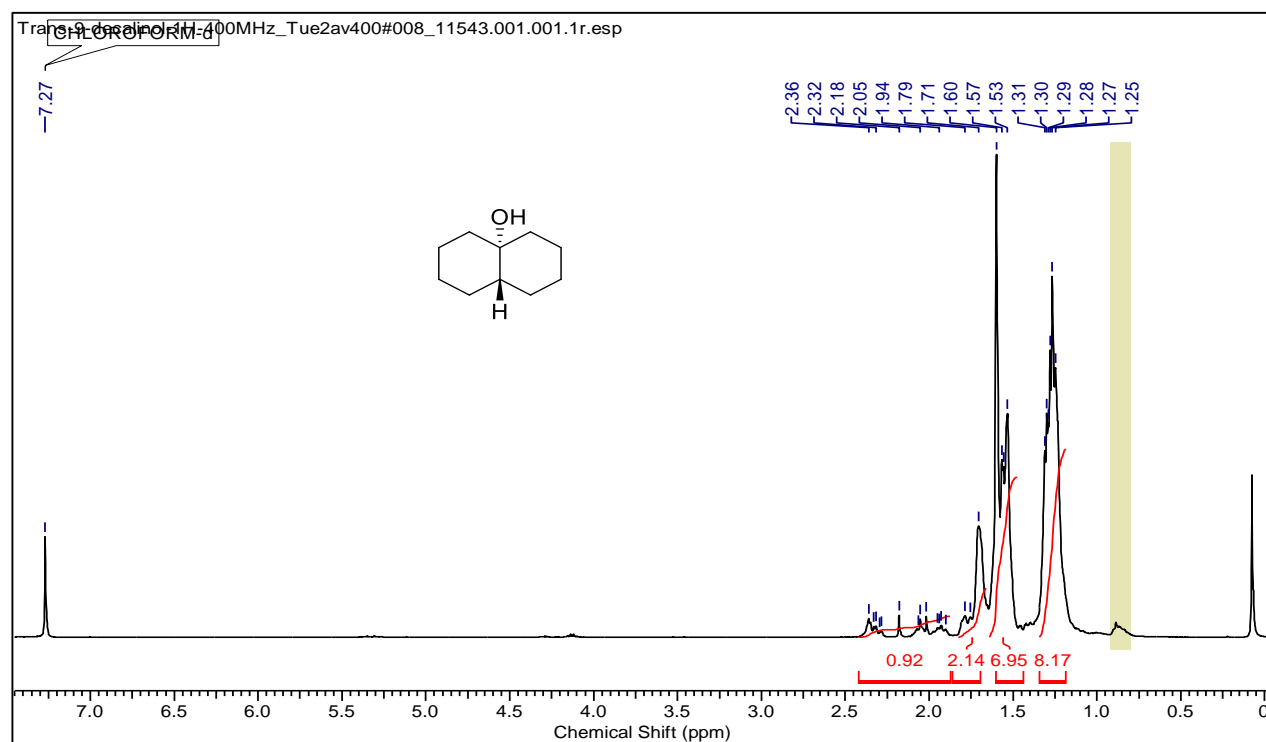
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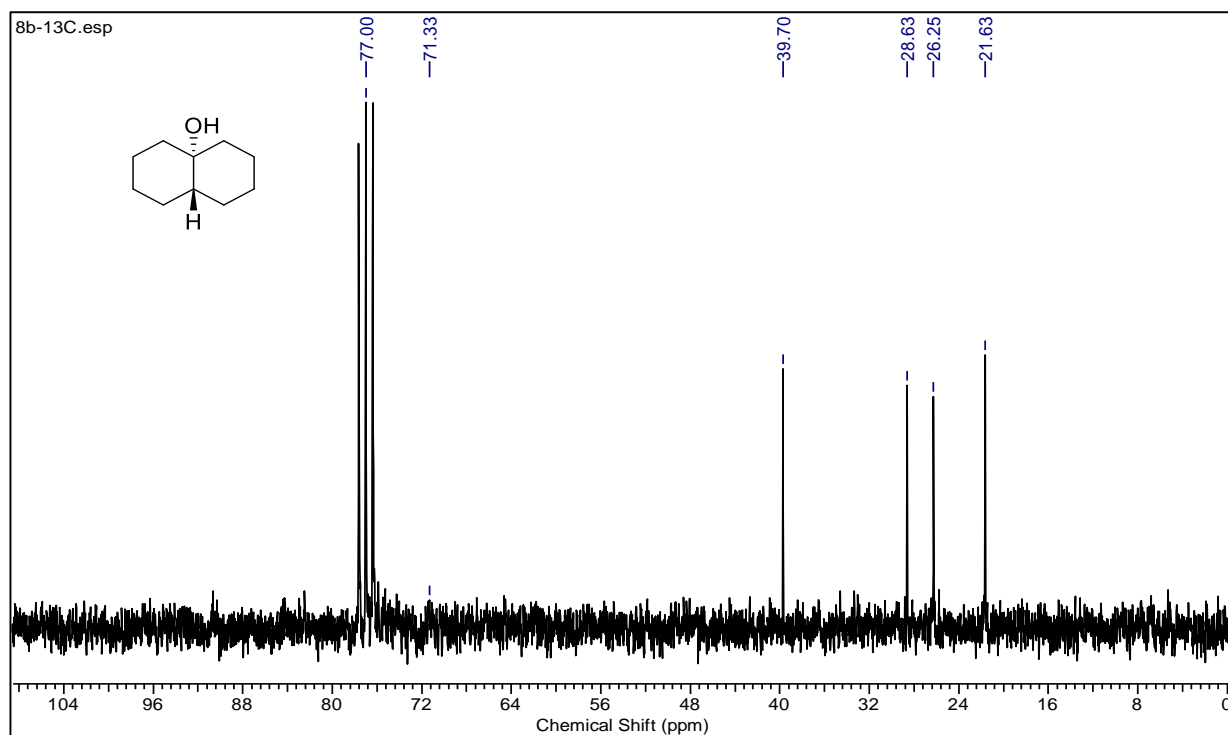
¹H NMR of 7b:



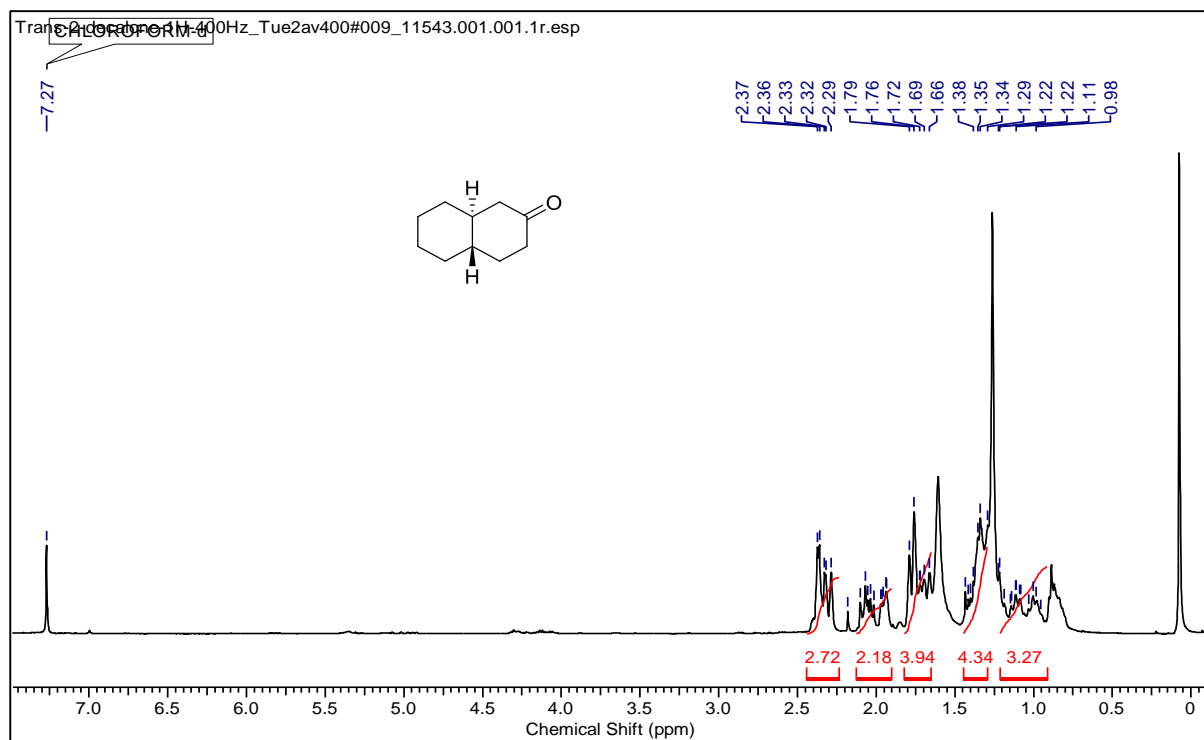
¹H NMR of 8b:



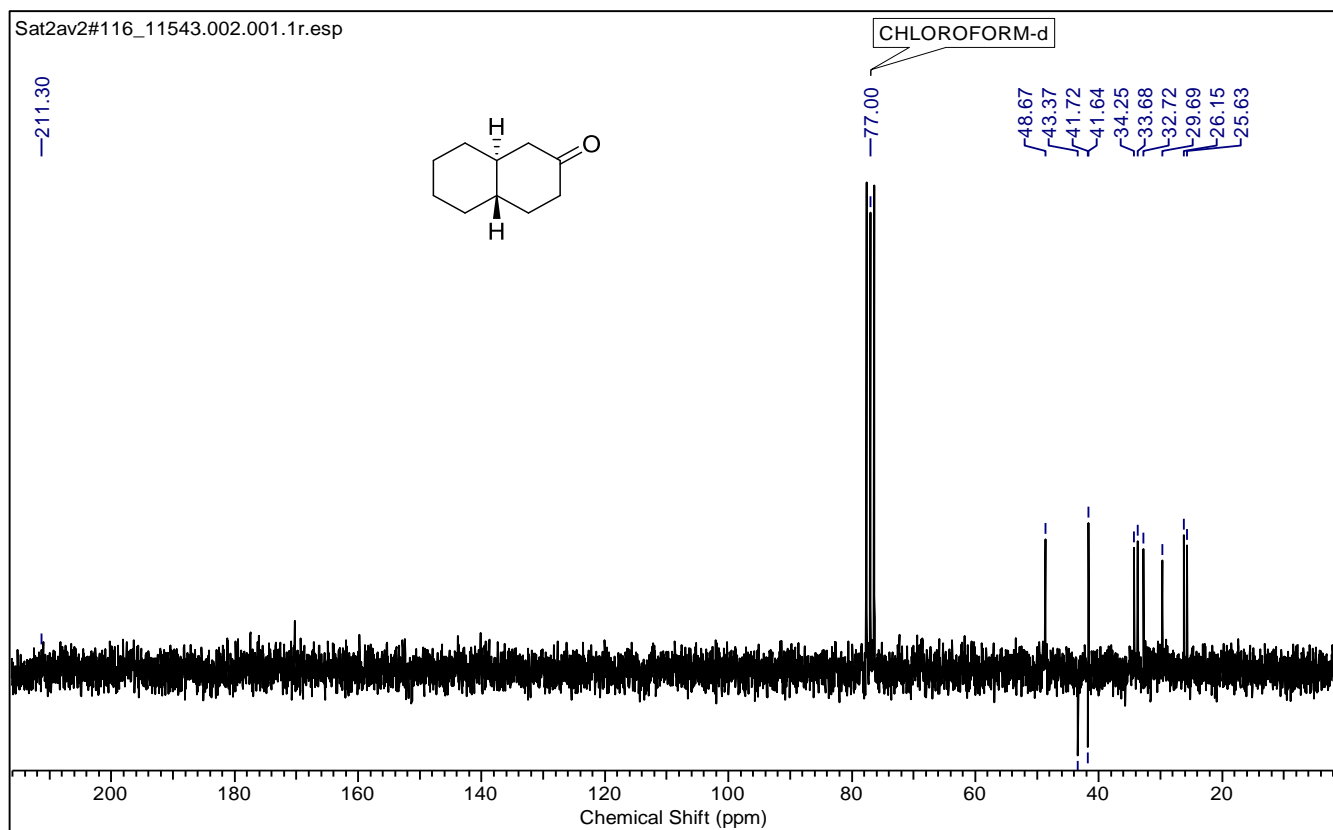
^{13}C NMR of 8b:



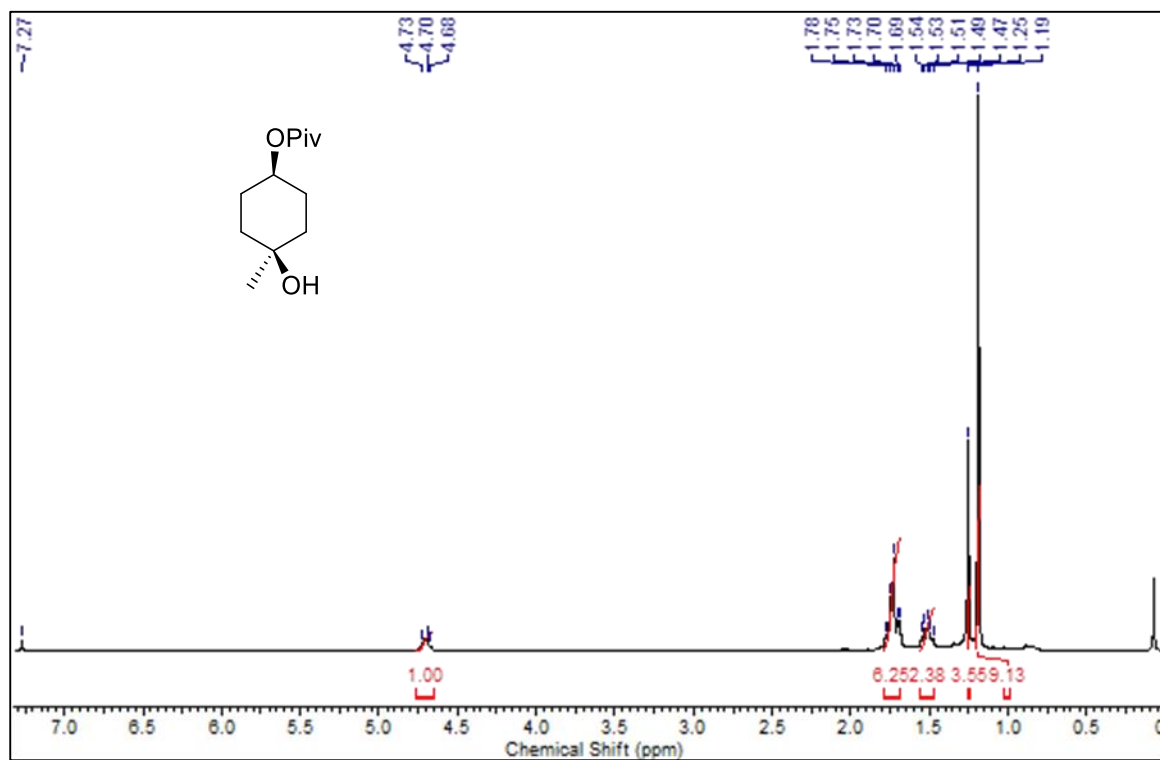
^1H NMR of 8c:



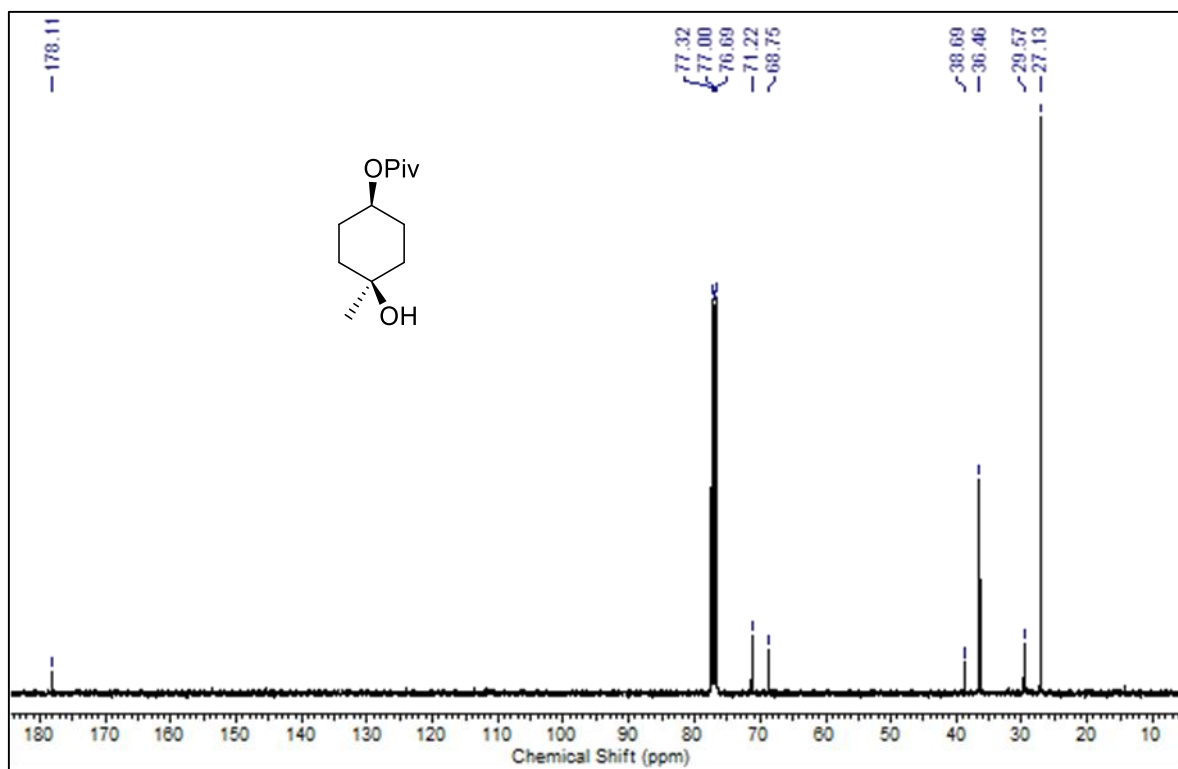
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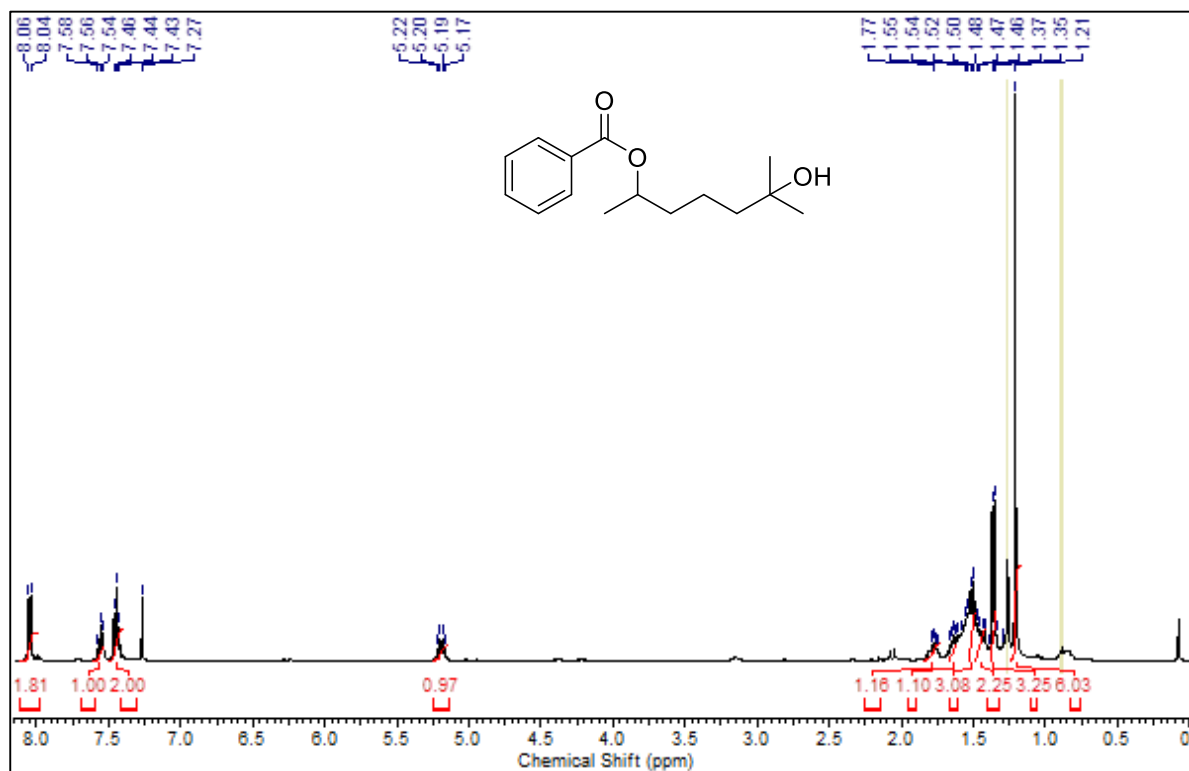
^1H NMR of 9b:



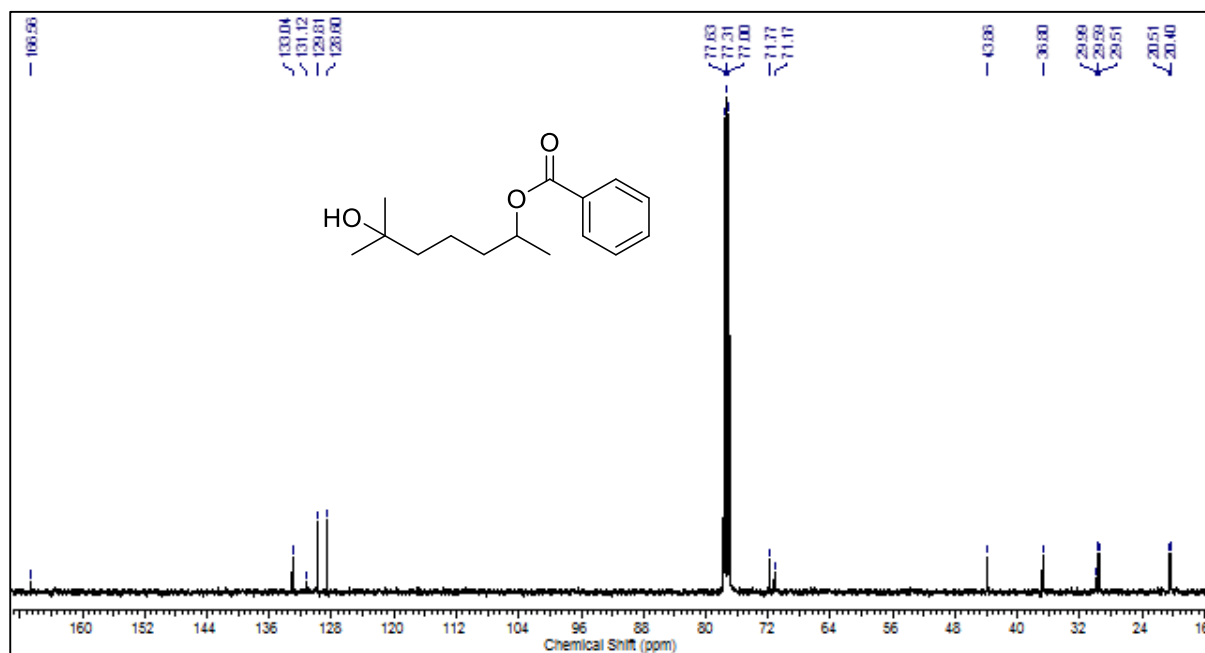
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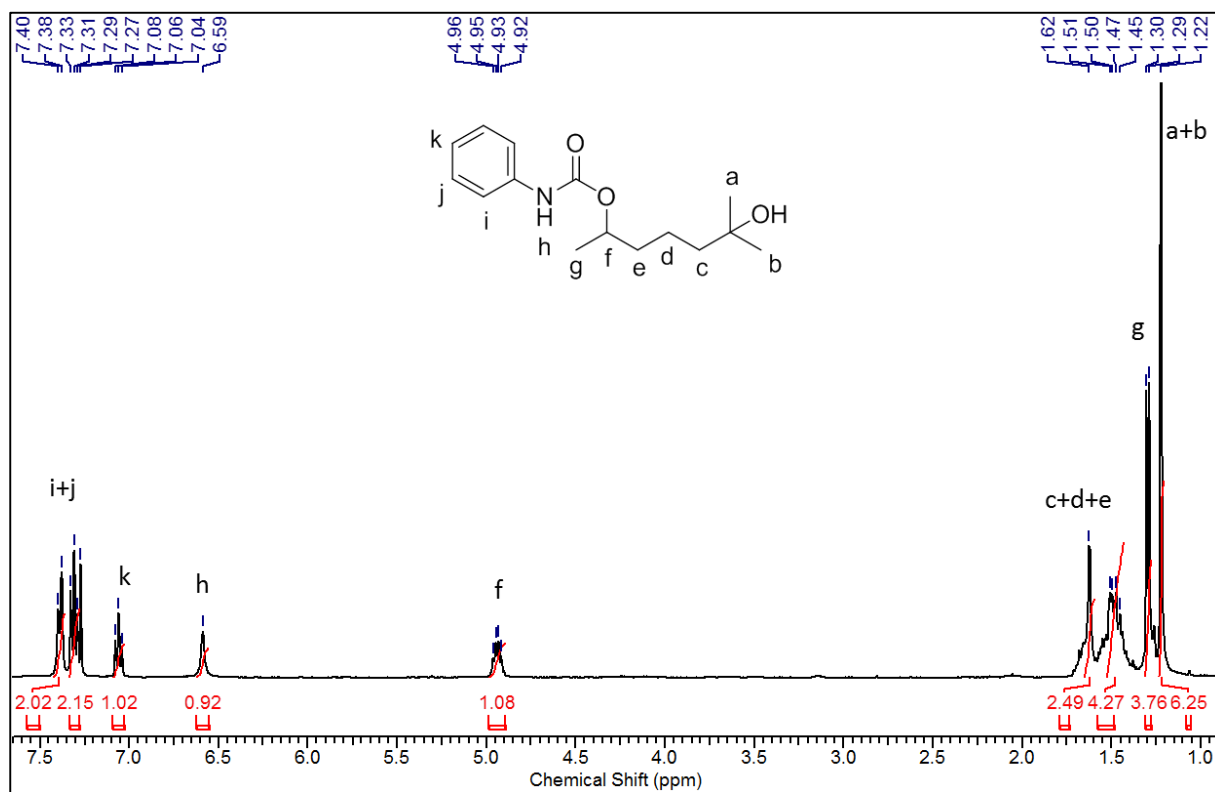
^1H NMR of 10b:



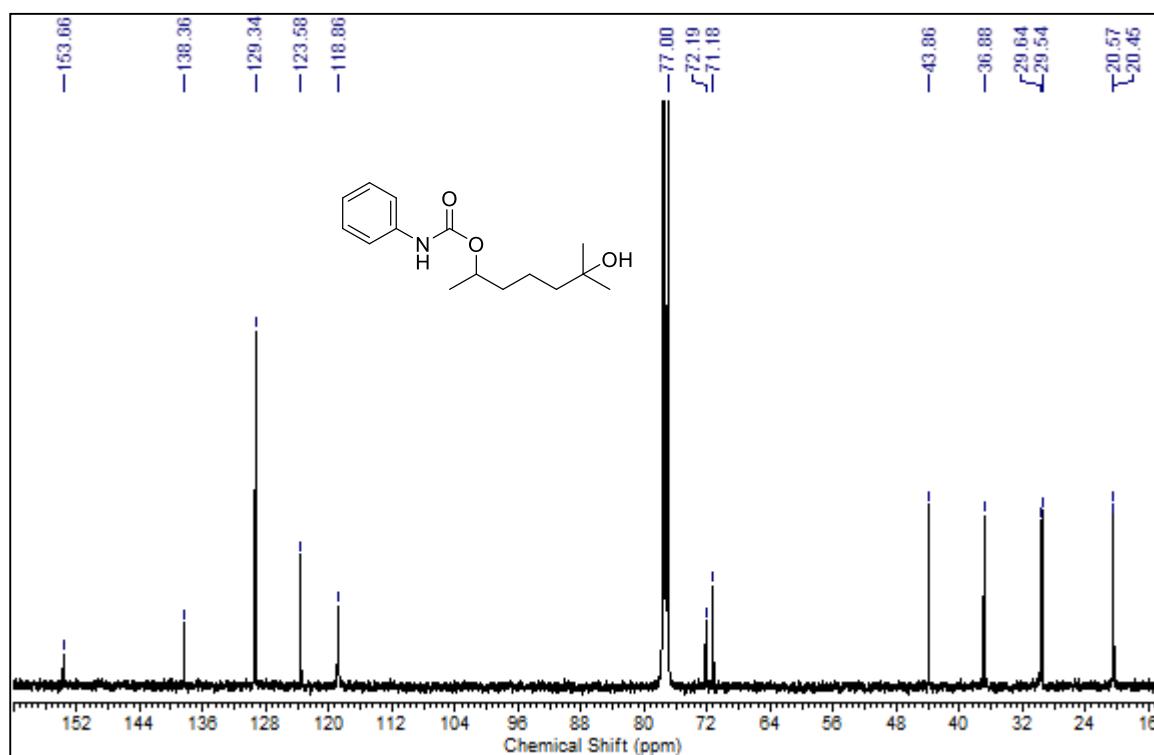
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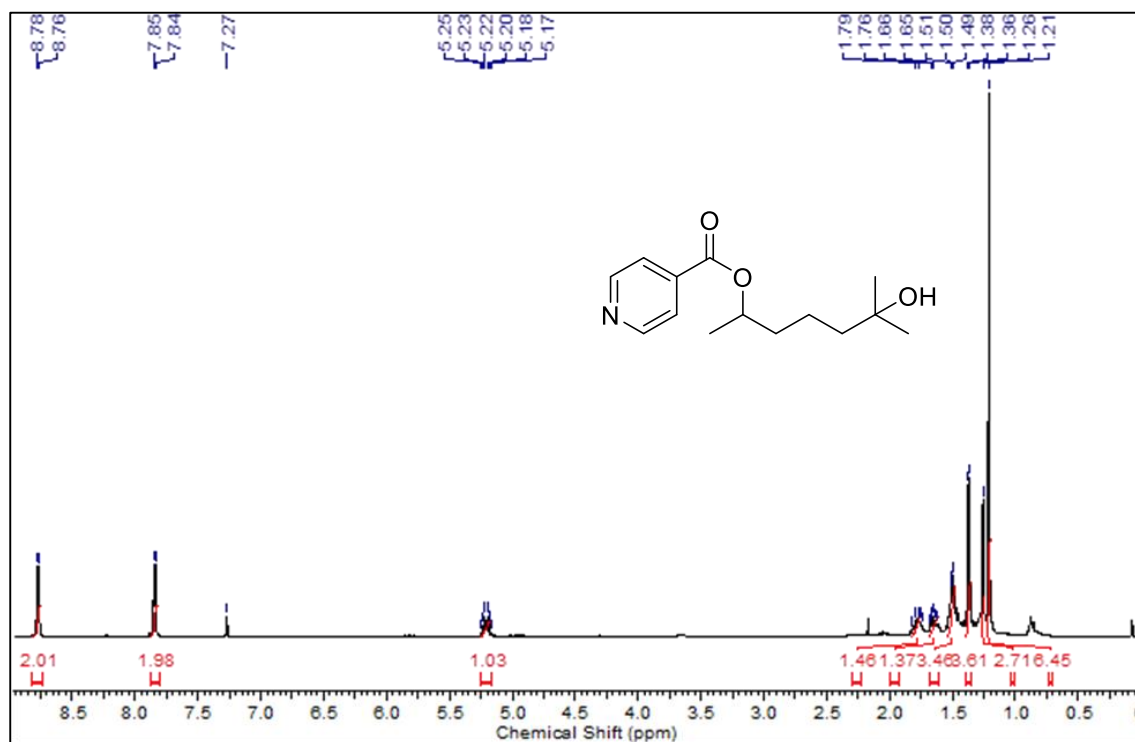
^1H NMR of 11b:



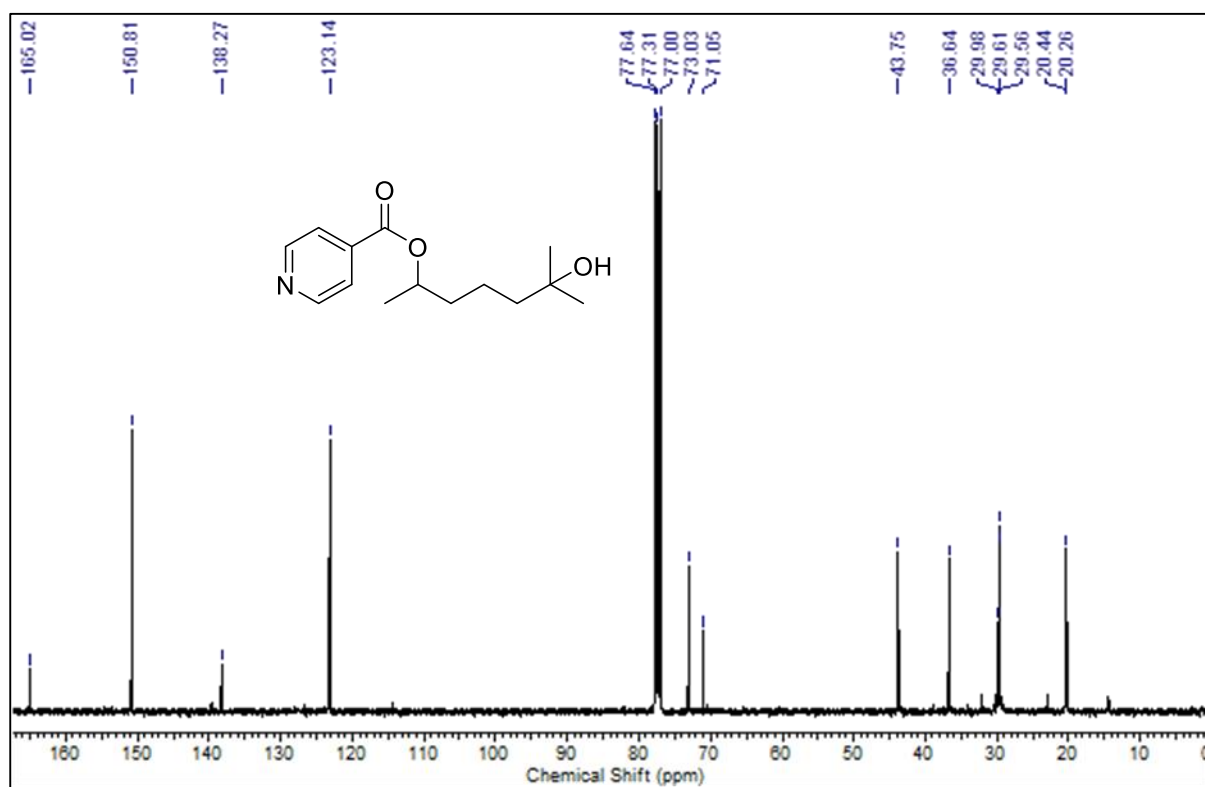
^{13}C NMR of 11b:



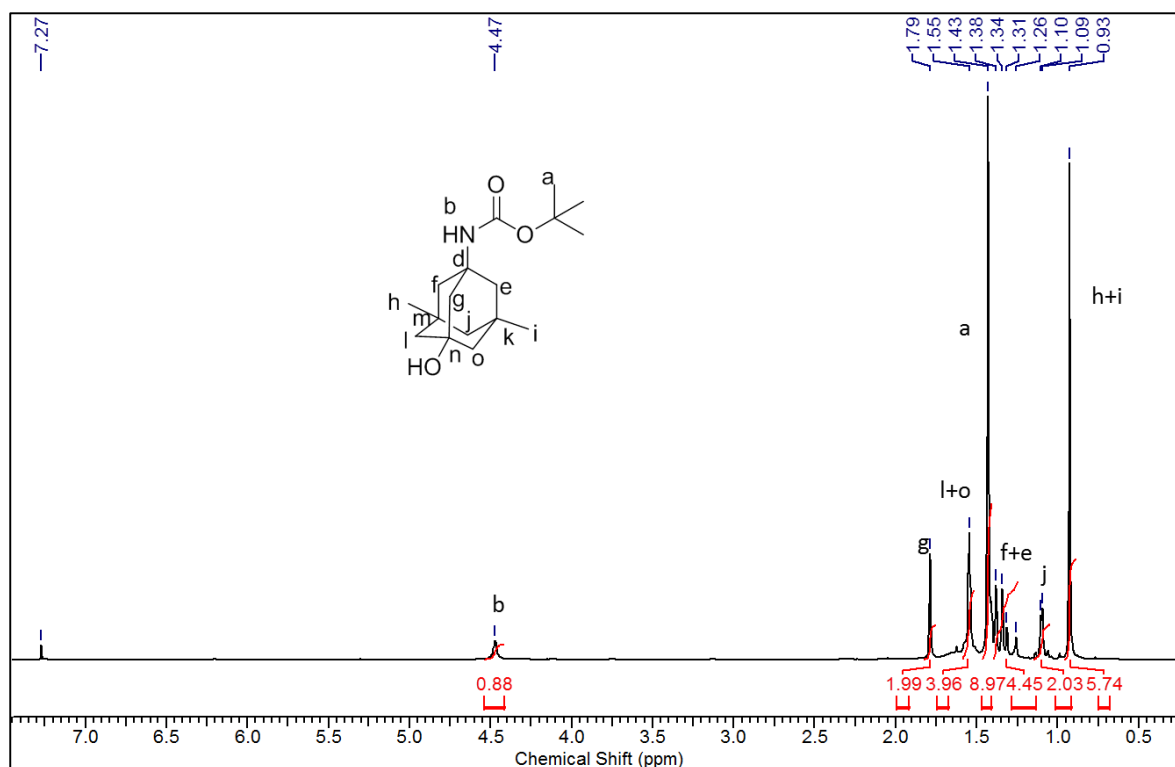
^1H NMR of 12b:



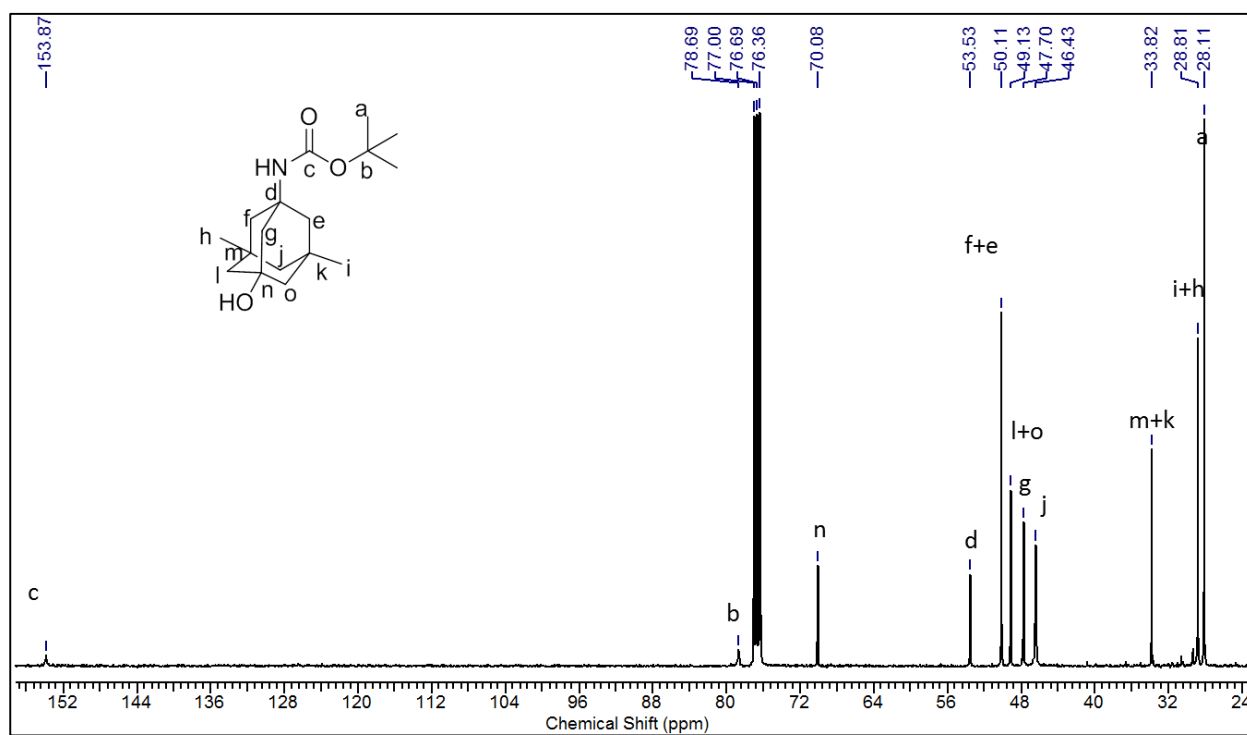
^{13}C NMR of 12b:



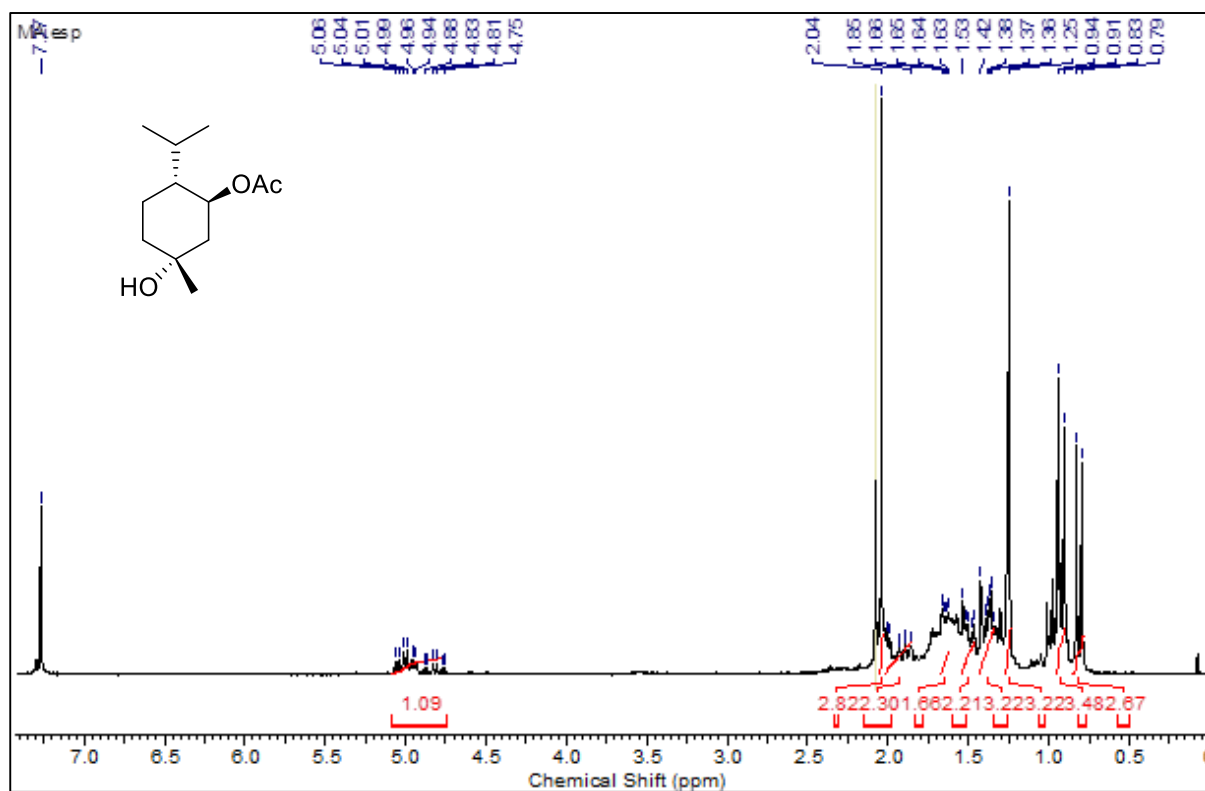
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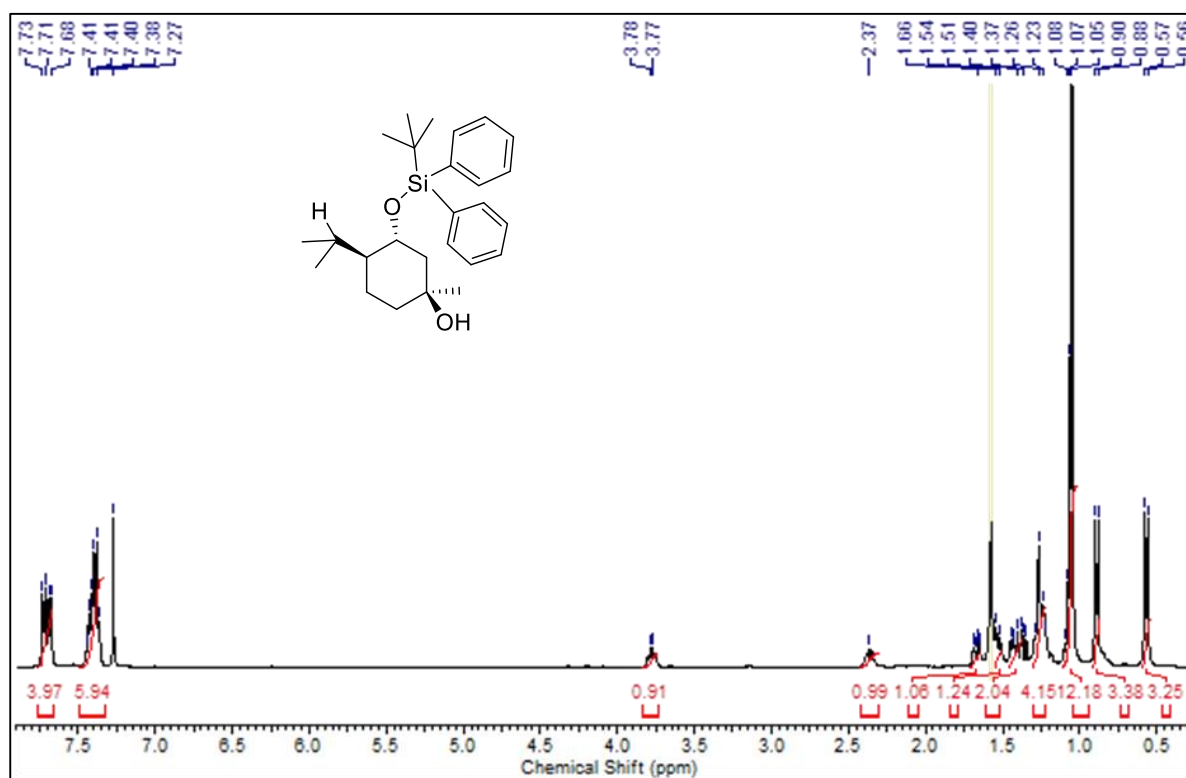
^{13}C NMR of 13b:



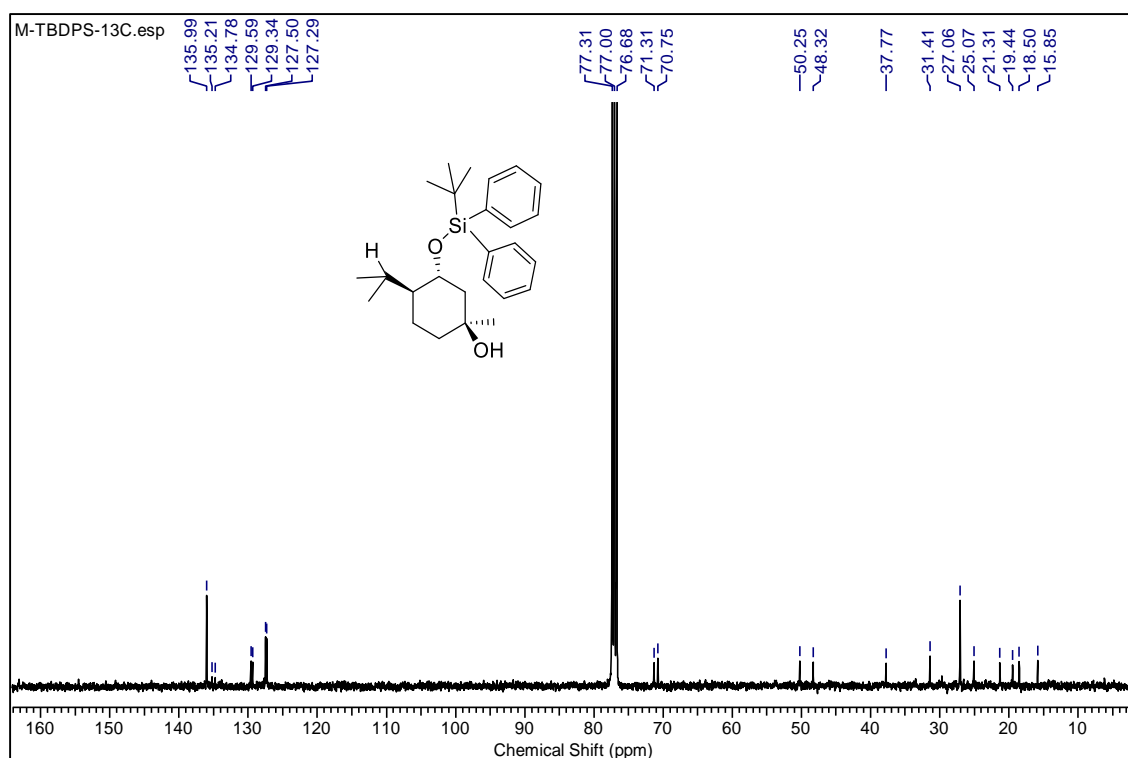
^1H NMR of 14b:



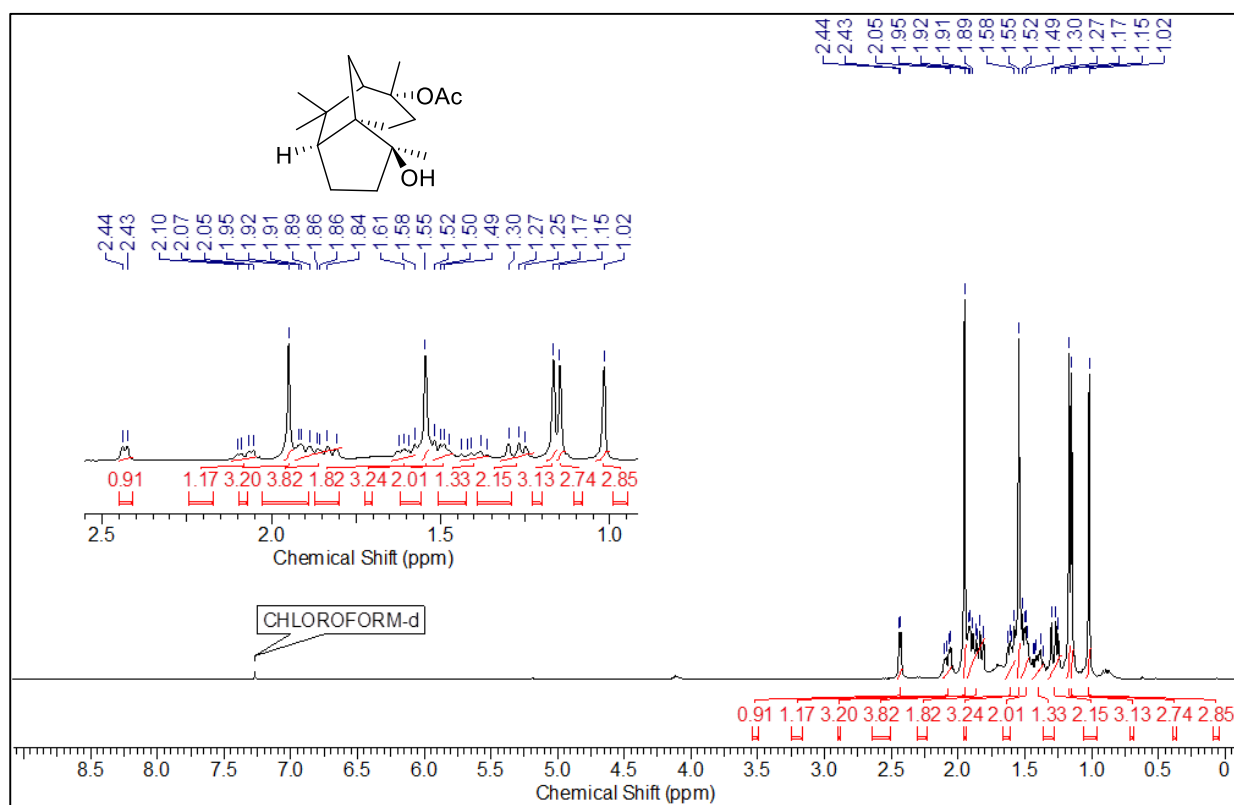
¹H NMR of 15b:



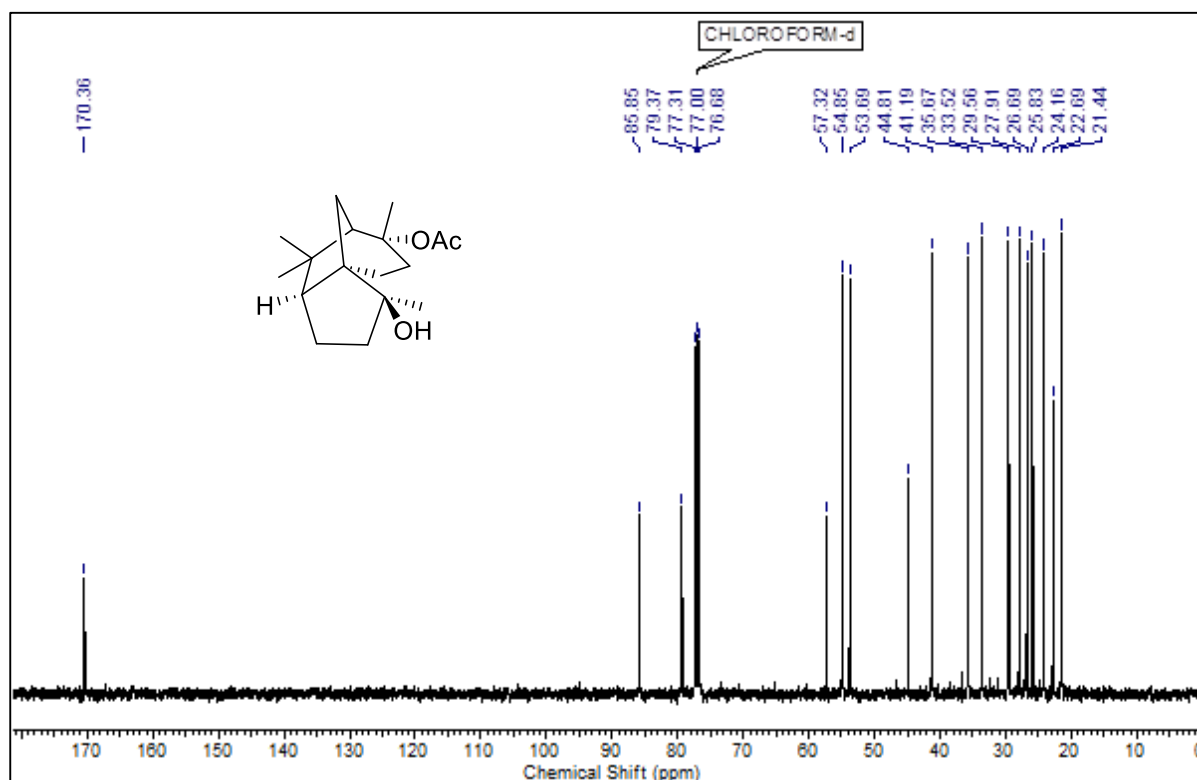
¹³C NMR of 15b:



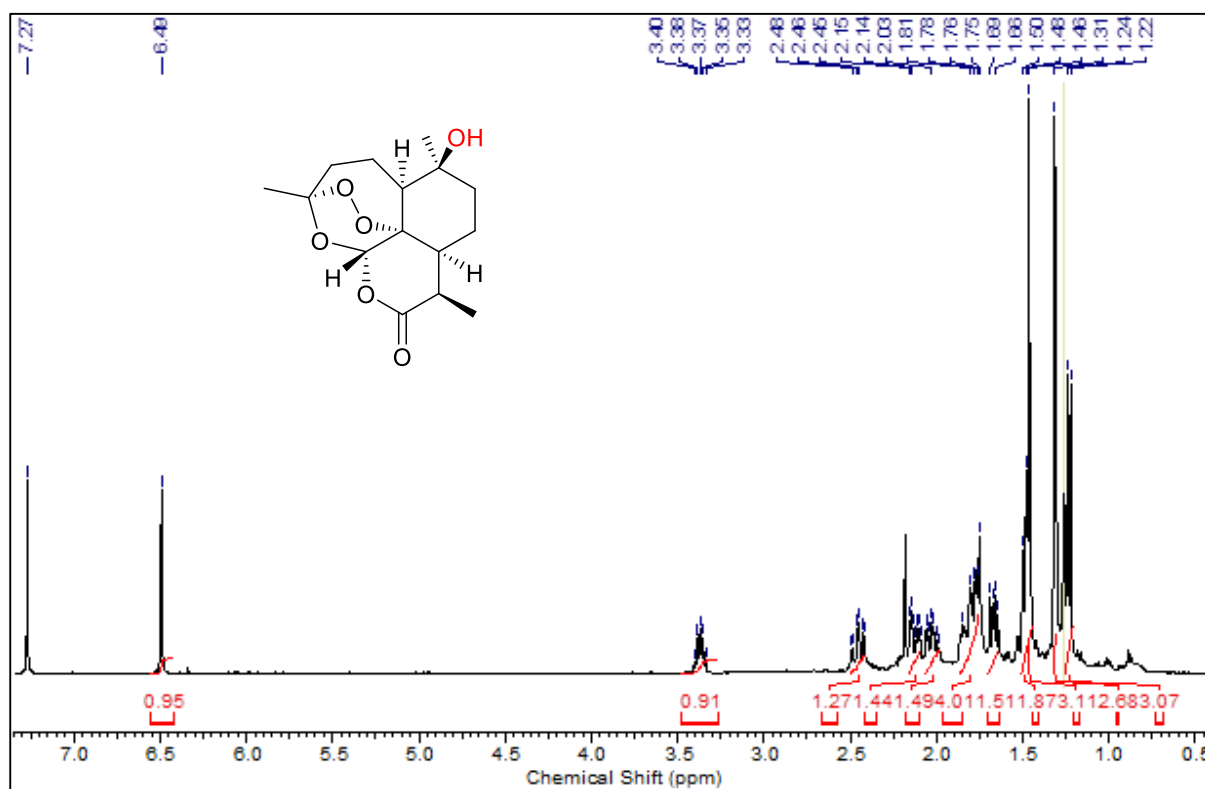
¹H NMR of 17b:



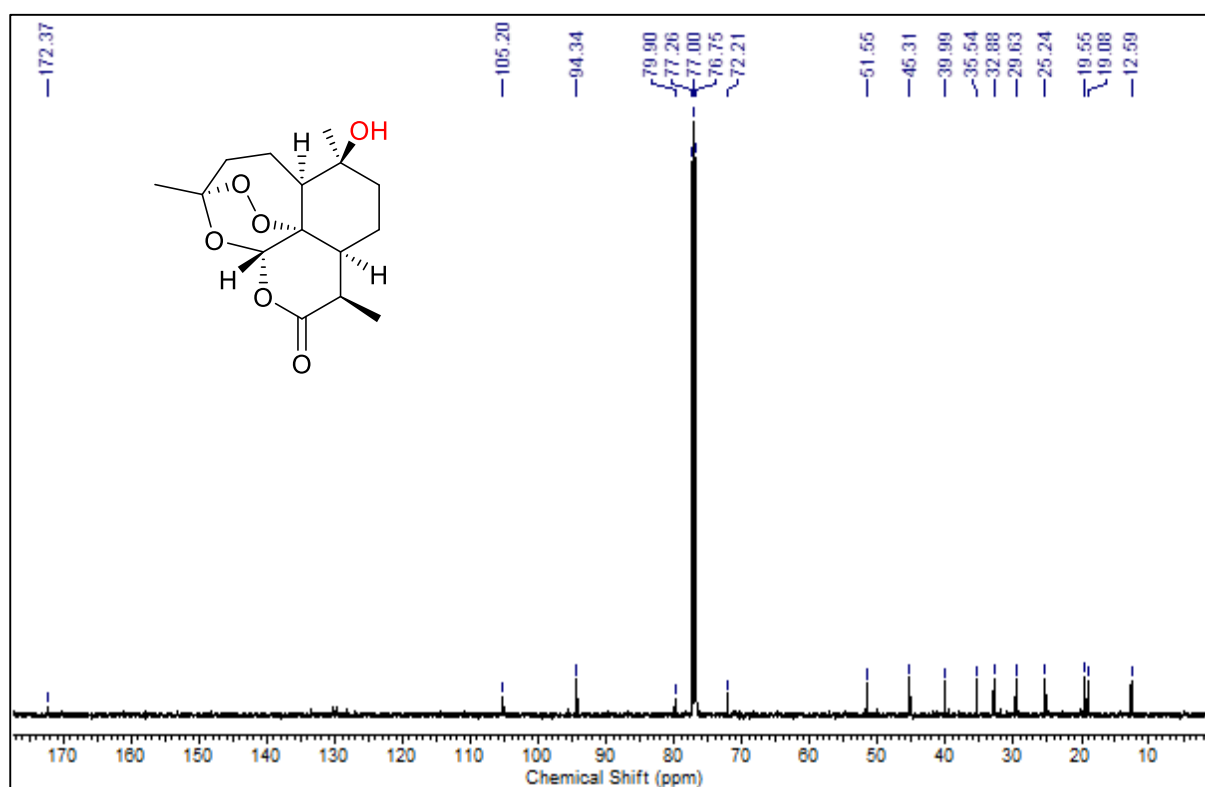
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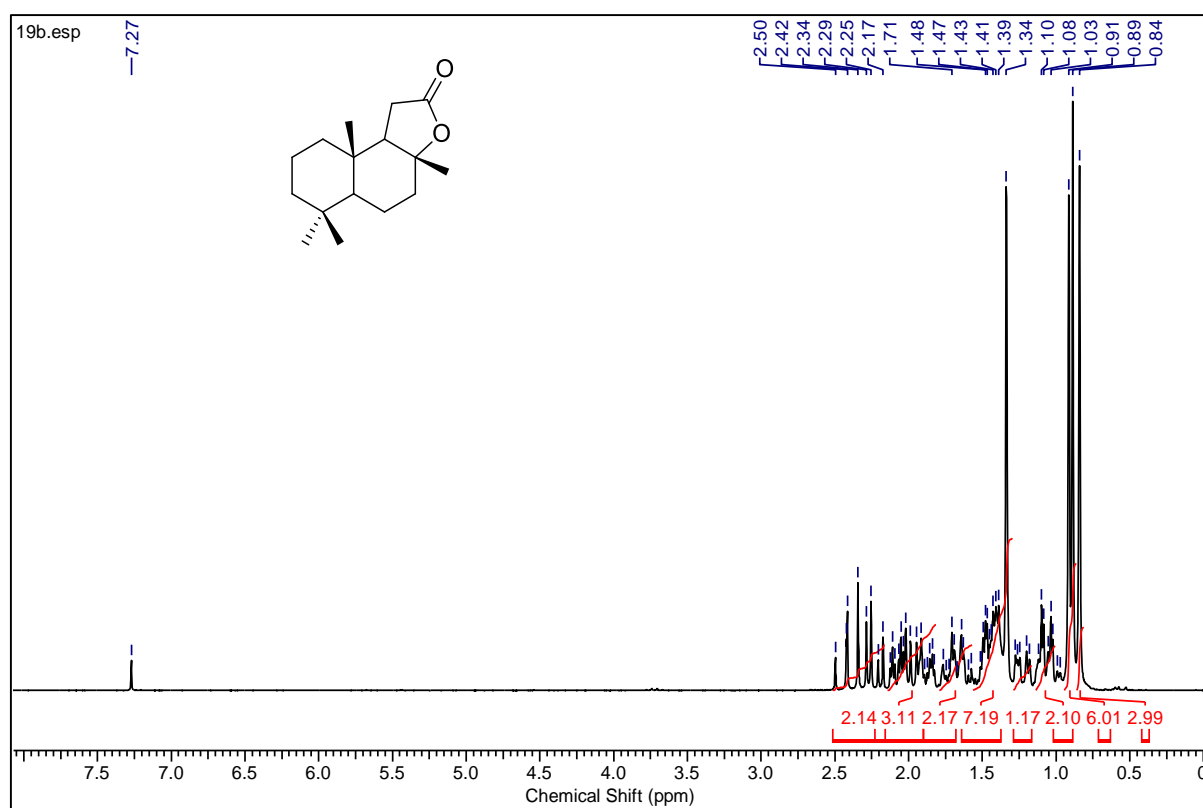
¹H NMR of 18b:



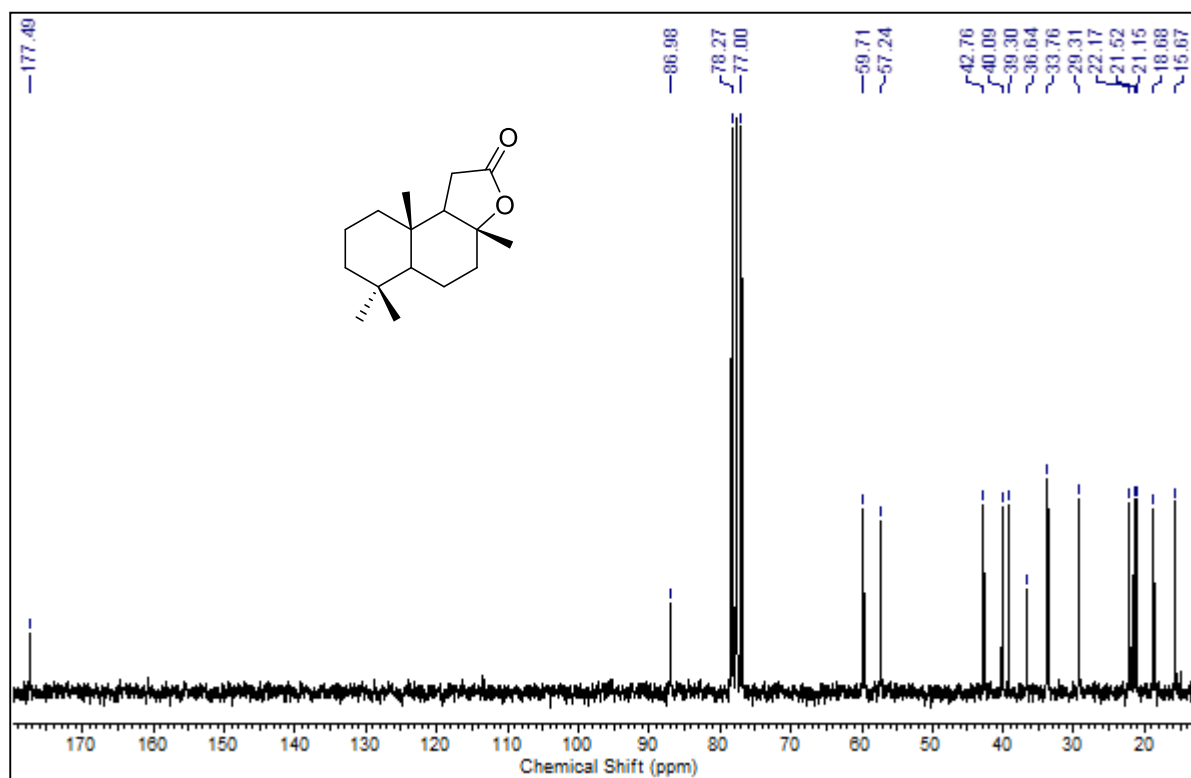
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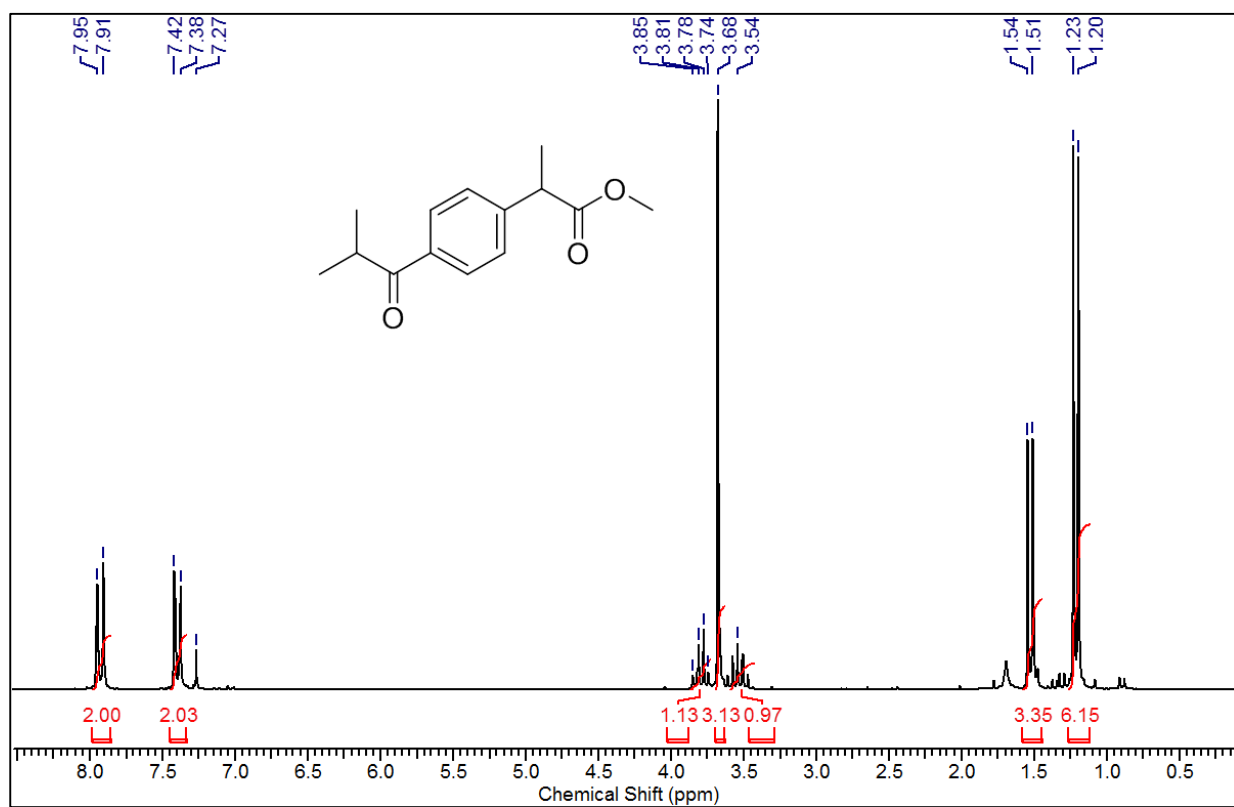
^1H NMR of 19b:



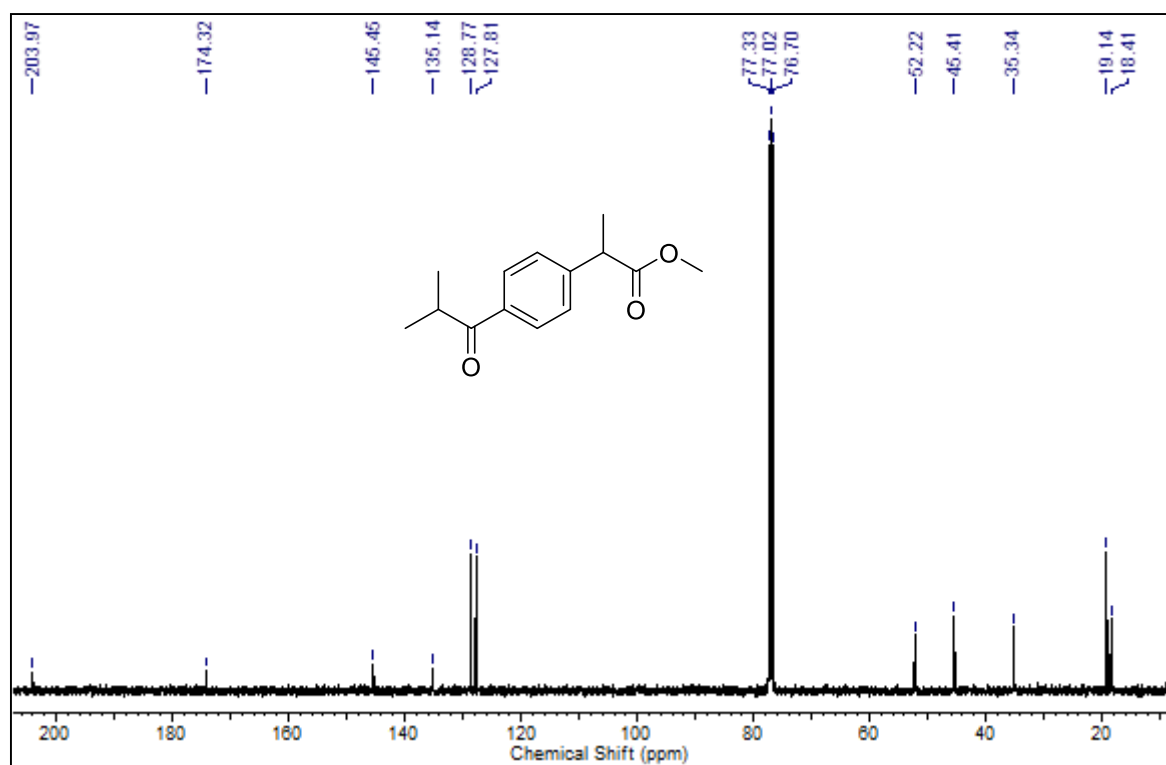
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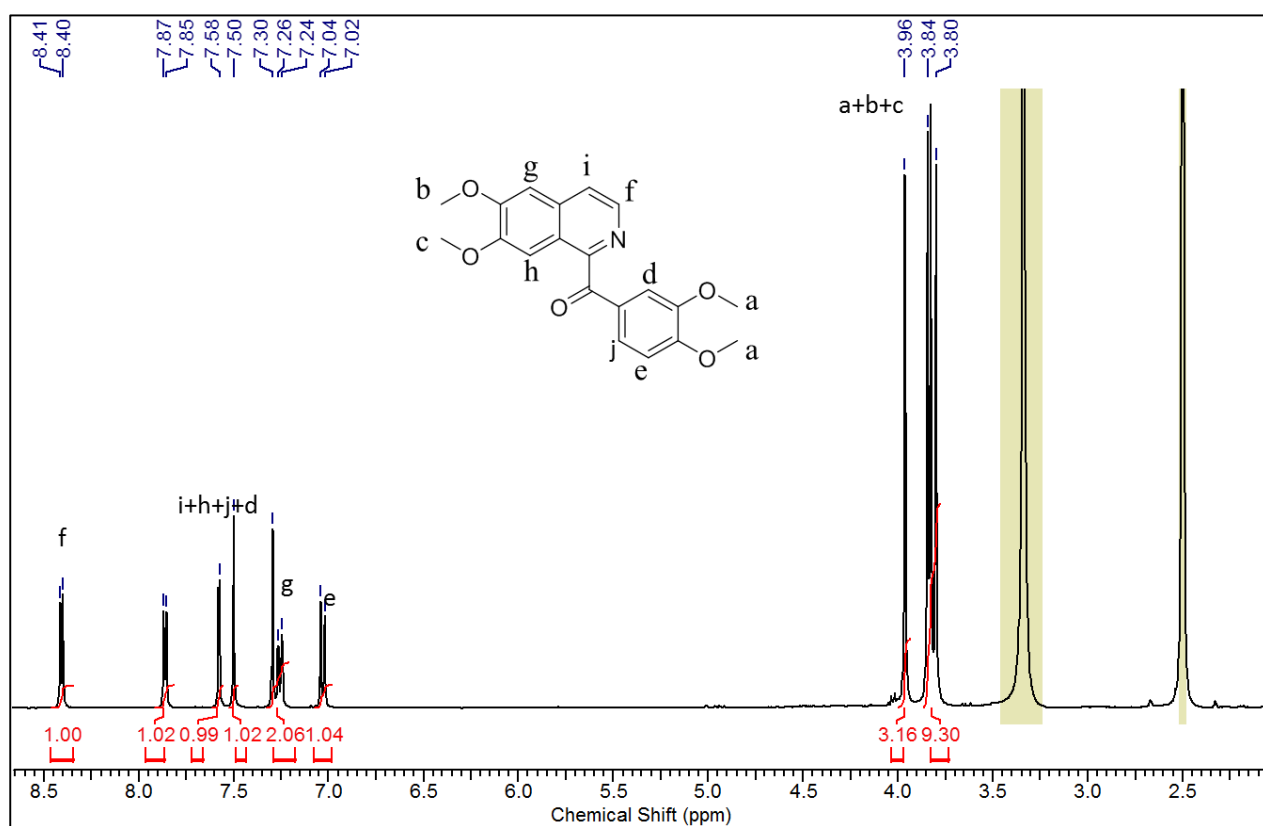
¹H NMR of 20b:



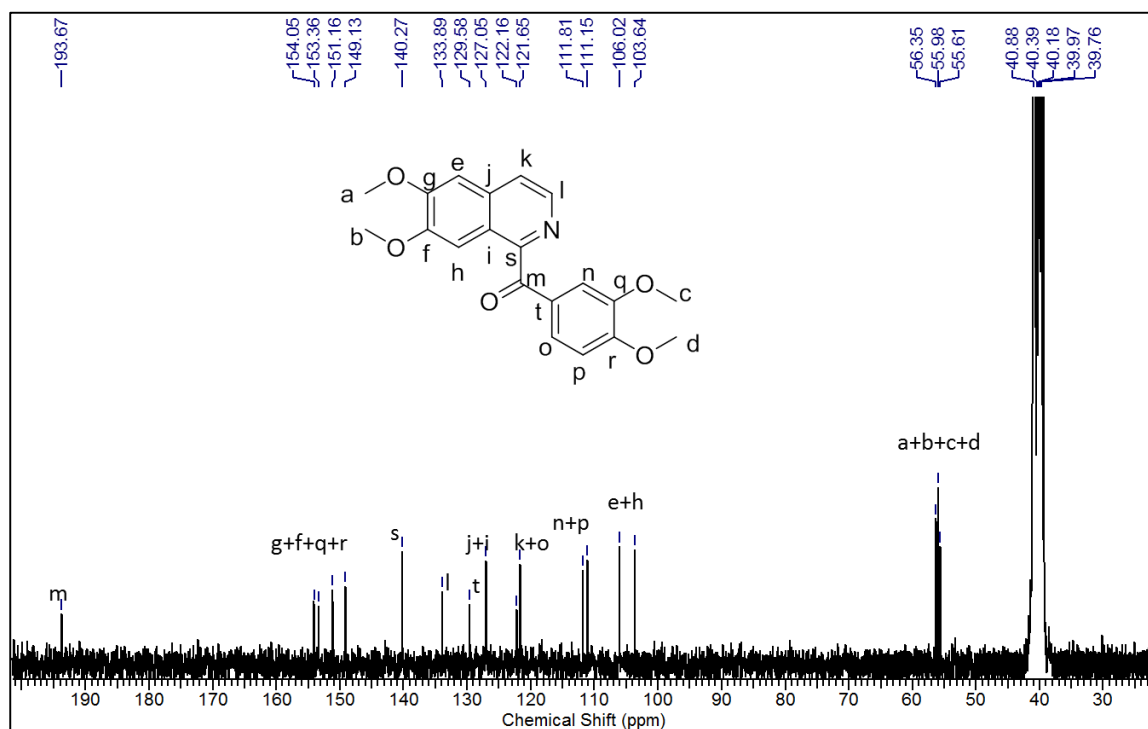
¹³C NMR of 20b:



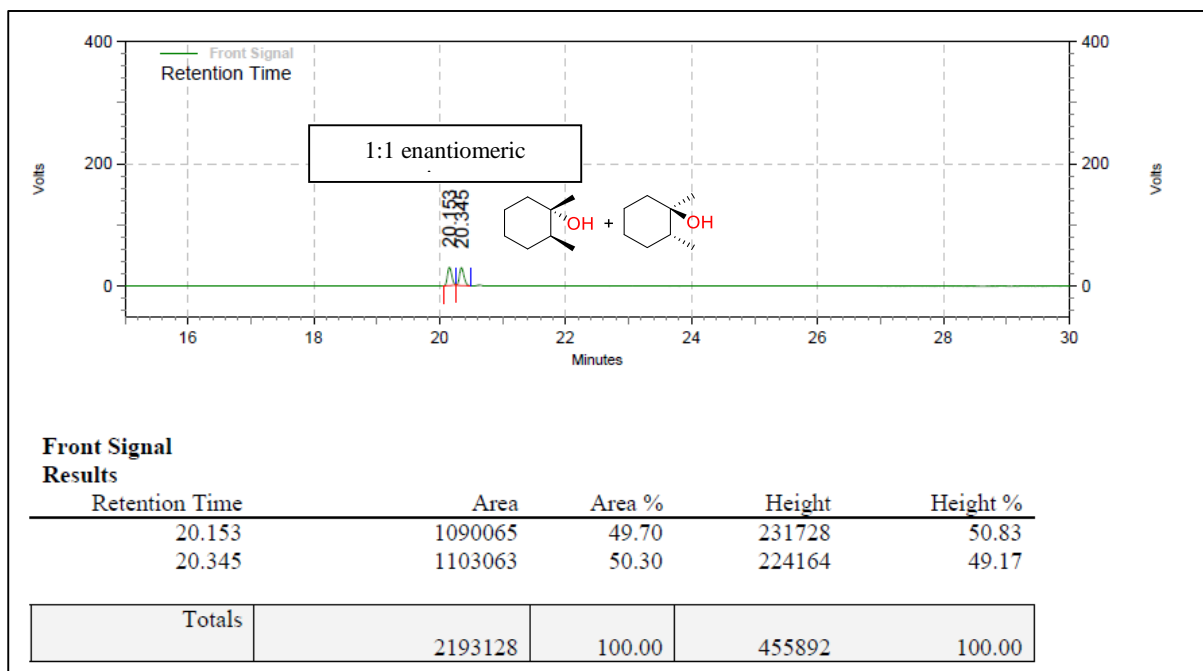
¹H NMR of 21b:



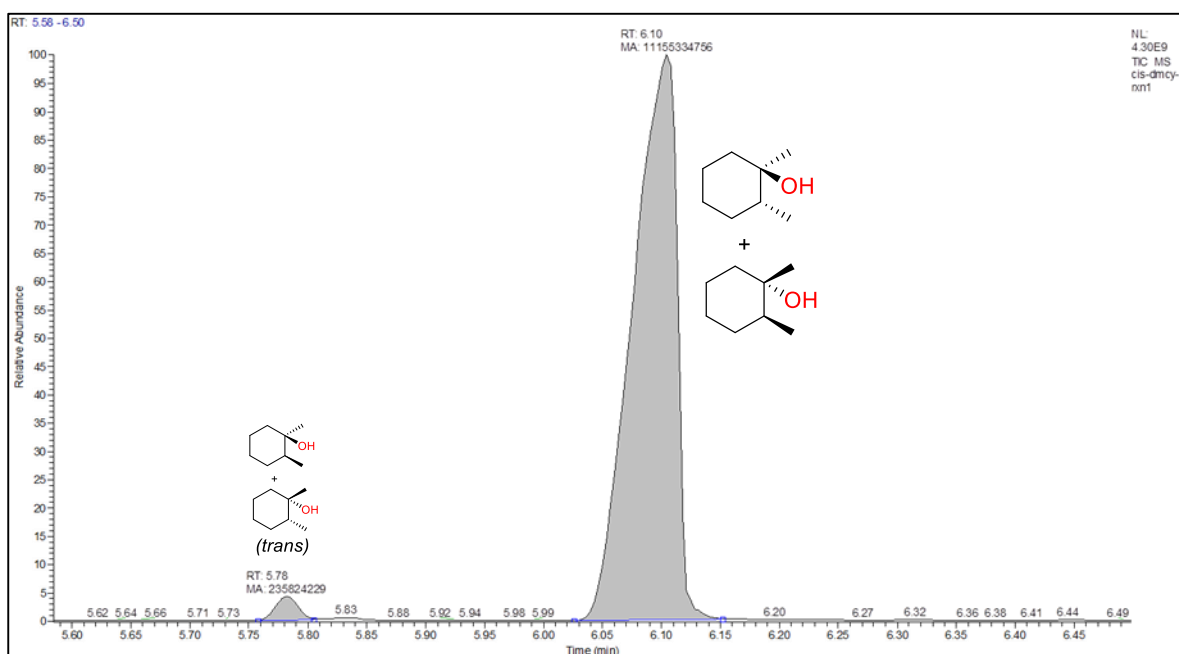
¹³C NMR of 21b:



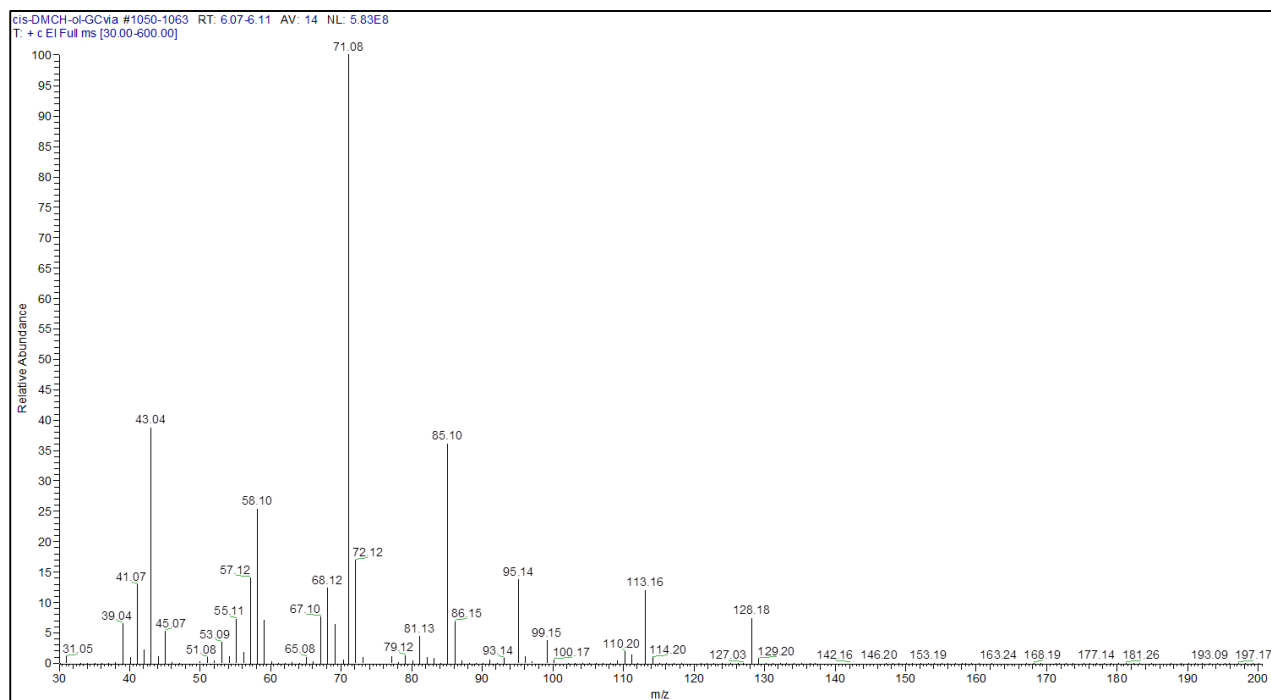
Chiral GC of 3b:



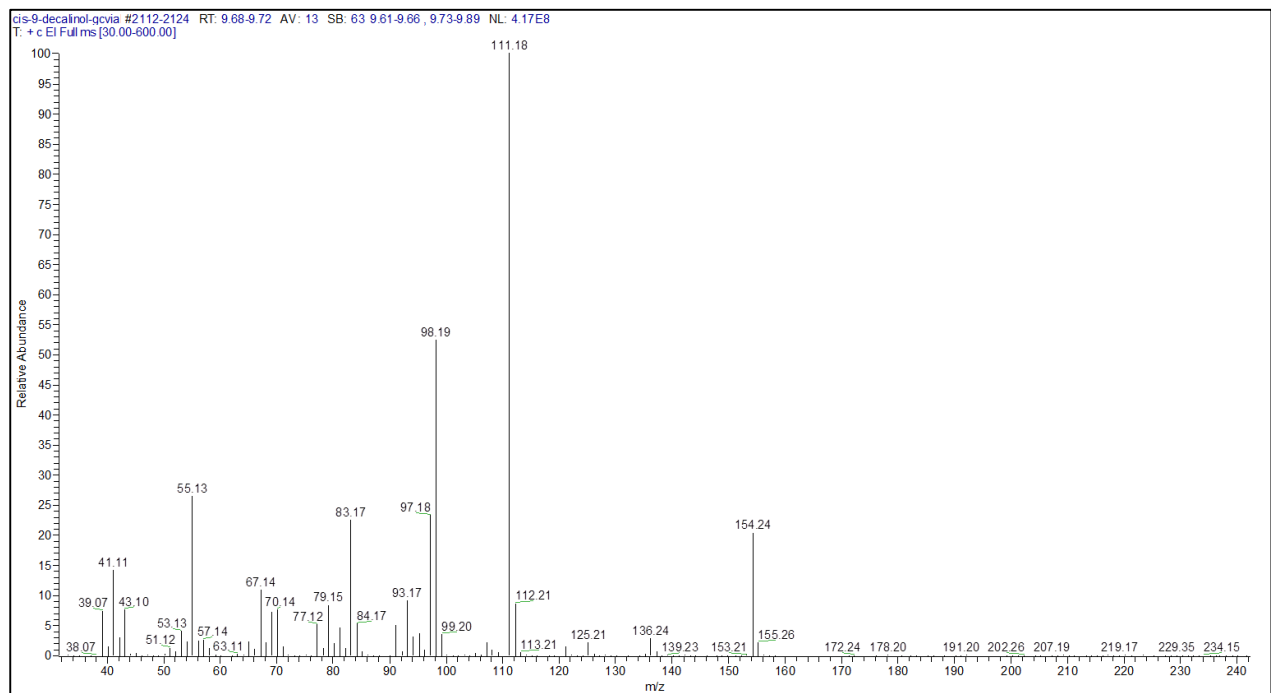
GC Quantification of 3b:



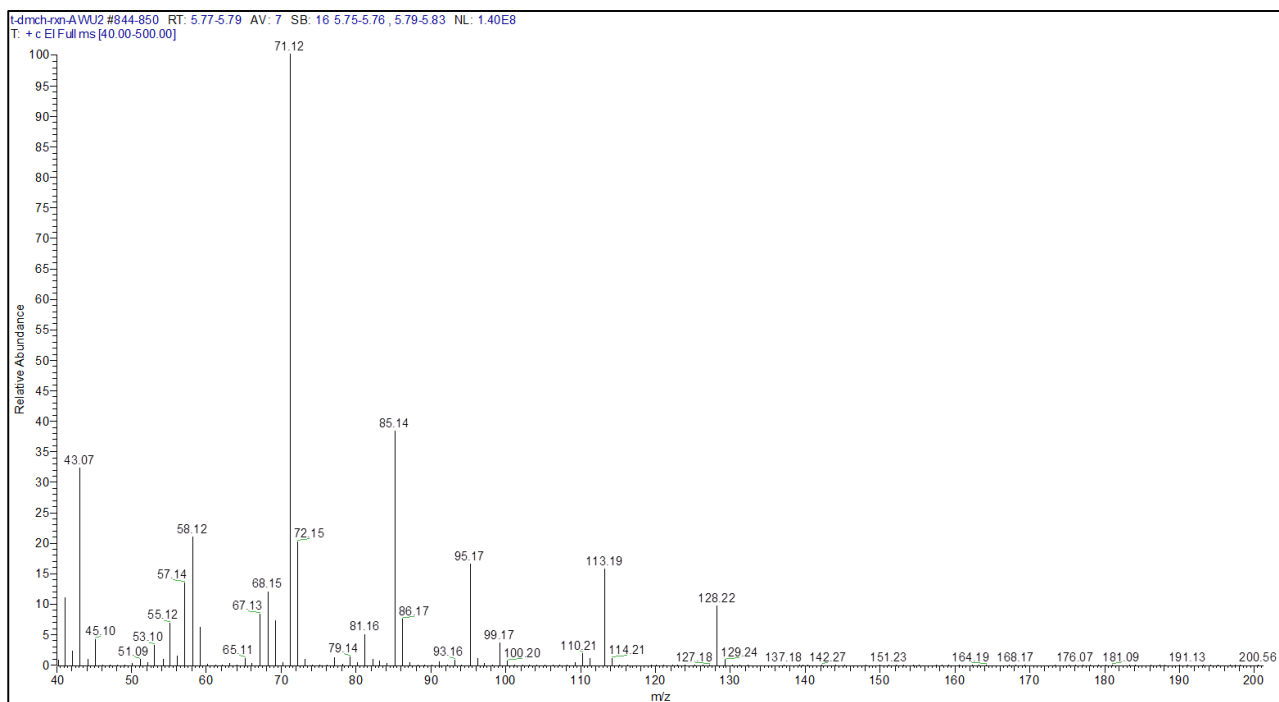
GC-MS of 3b:



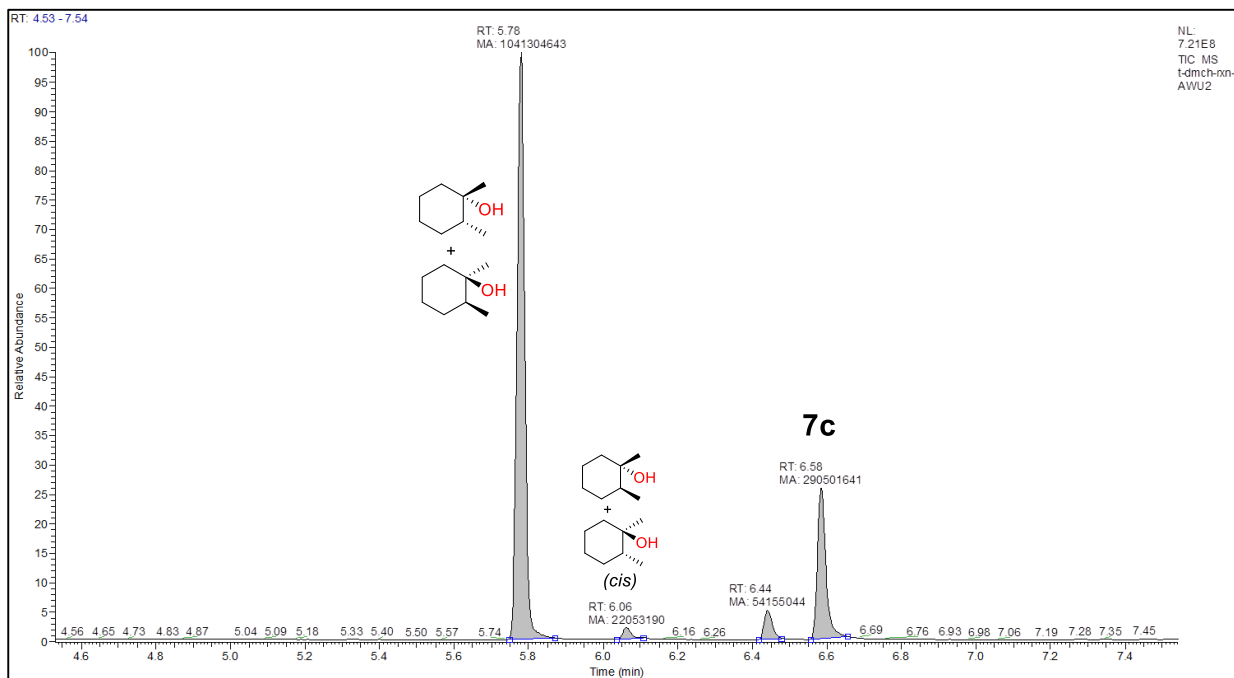
GC-MS of 4b:



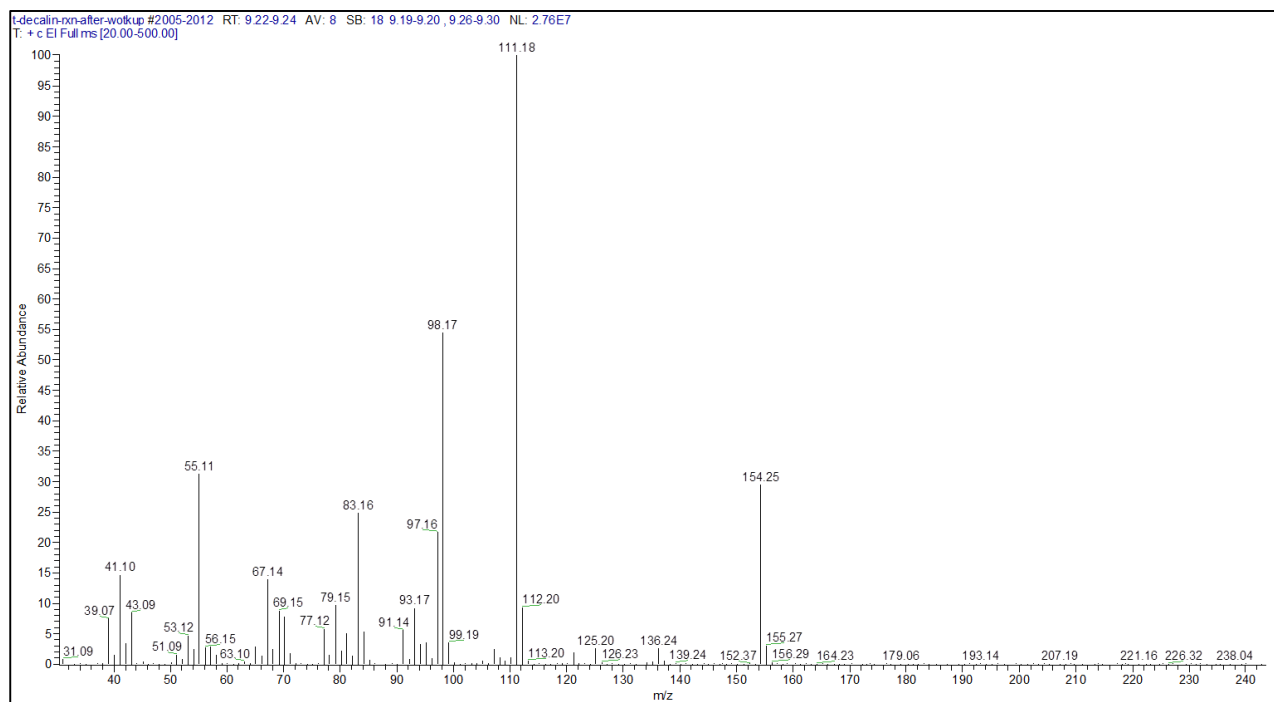
GC-MS of 7b:



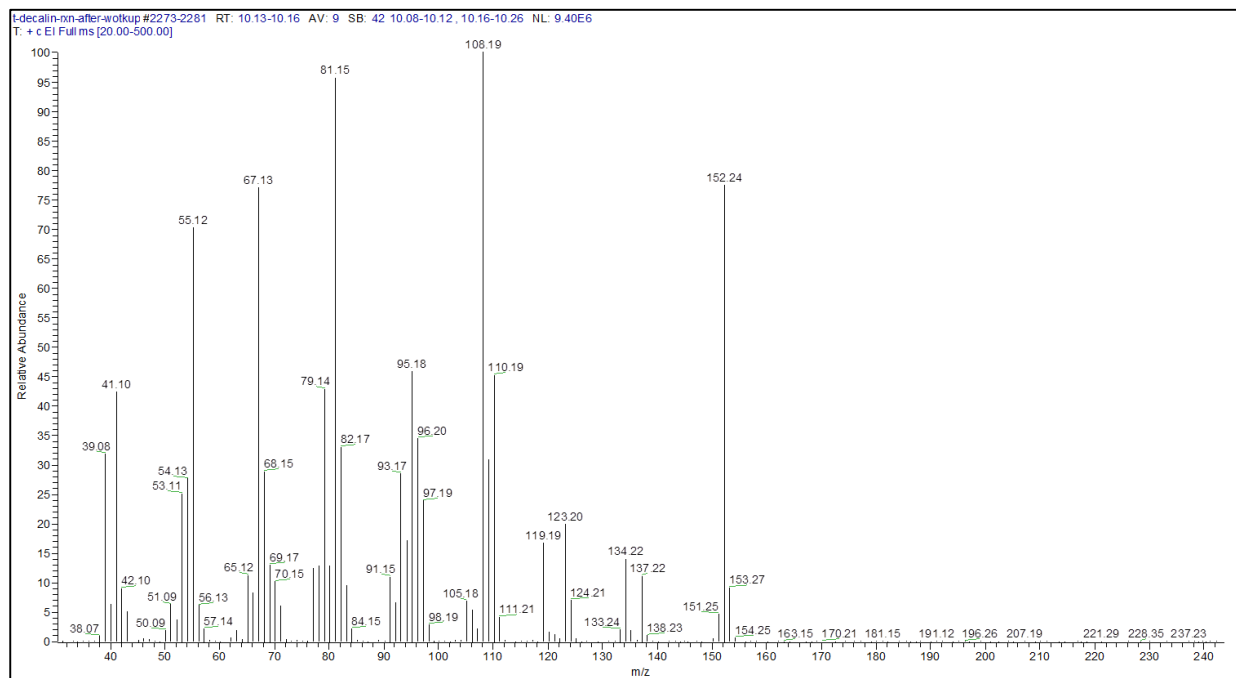
GC Quantification of 7b and 7c:



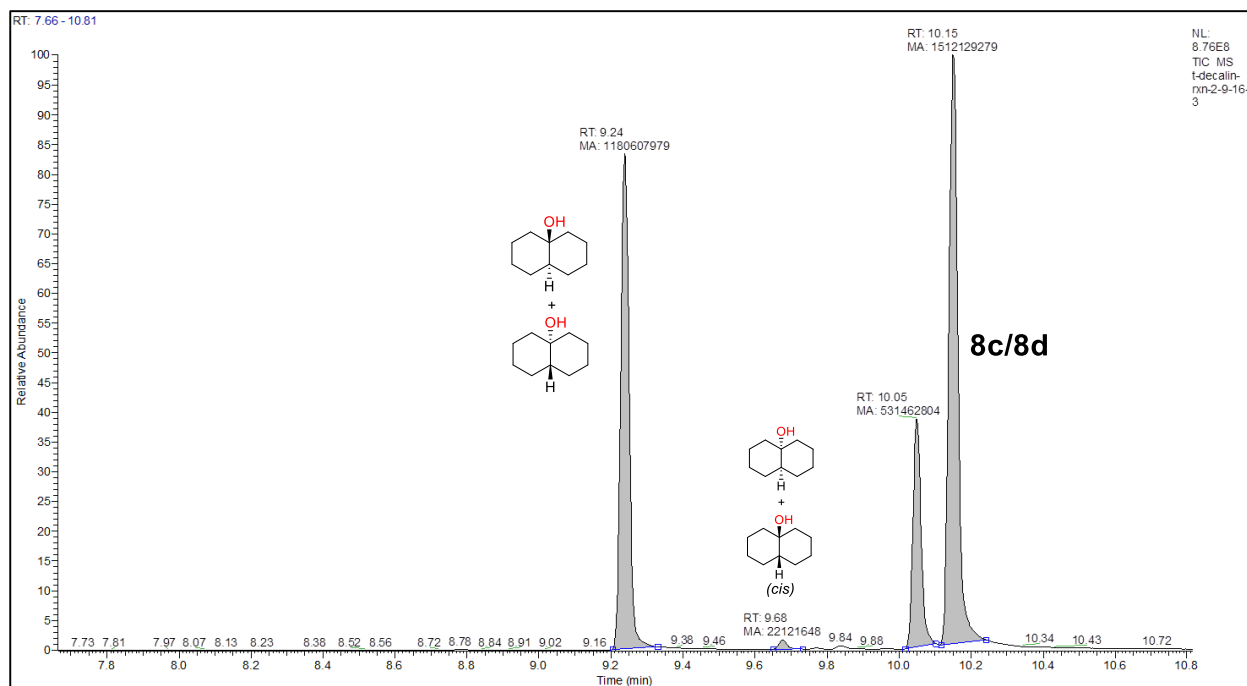
GC-MS of 8b:



GC-MS of 8c/8d:



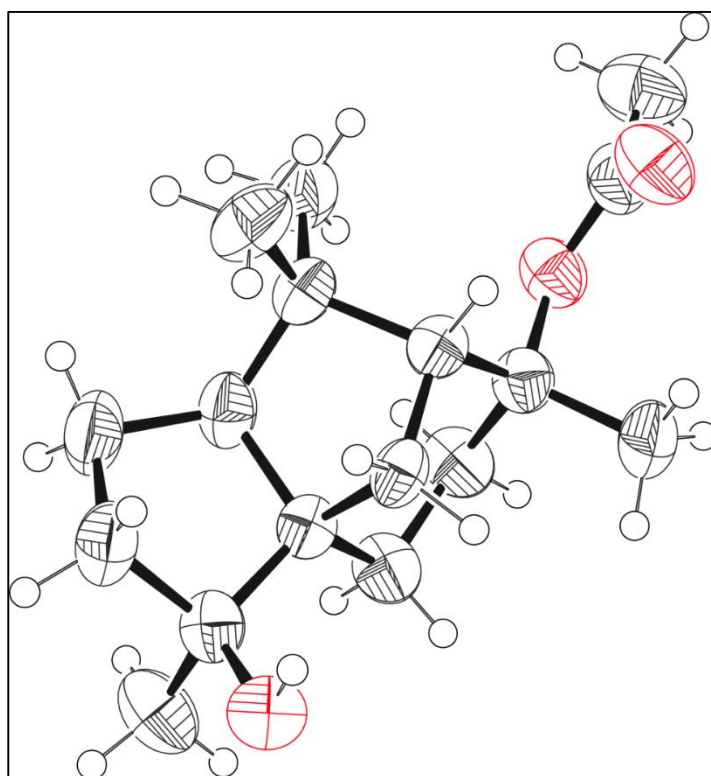
GC Quantification of 8b and 8c:



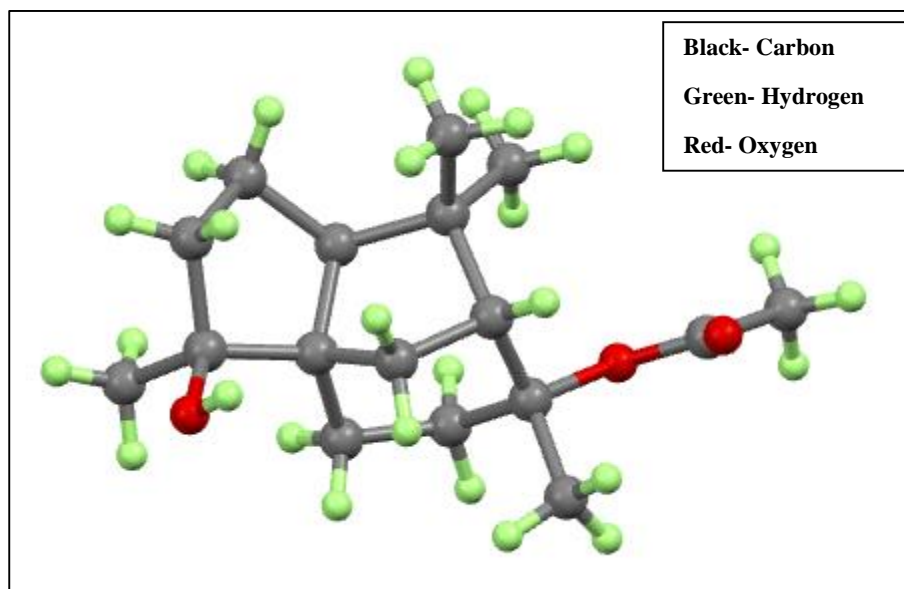
Procedure for the synthesis of 17b in 1 mmol scale using 1 and *m*CPBA

To a 50 mL round-bottom flask containing a magnetic stir bar, NO₂-substituted Fe-bTAML catalyst **1** (1 mM, 2 mol %), substrate (1 mmol, 270 mg) and K₂HPO₄ (2 mmol, 2 equiv.) in 16 mL CH₃CN-4 mL H₂O were added. A solution of *m*CPBA (2 mmol, 2 equiv) in CH₃CN was added *via* syringe pump with continuous stirring over a period of 8h at room temperature. The reaction was monitored by TLC and/or GC. After completion of the reaction, the solvent (CH₃CN) was removed under reduced pressure. Saturated aq. solution of sodium bicarbonate was added to the residual portion and extracted with dichloromethane (2 times). The organic part was dried with anhydrous Na₂SO₄, analysed by GC to estimate substrate conversion and then further purified by column chromatography to obtain the desired product (silica gel, 230-400 mesh). The purity of the obtained product was determined by ¹H, ¹³C NMR and GC, and crystallisation was done using EtOAc-hexane solvent system. The isolated yield was found to be 70 % as white solid.

Crystal Structure of 17b:



ESI S5: ORTEP Diagram of crystal structure for 17b (taken with 50% probability)



ESI S6: Crystal Structure of 17b (Ball and Stick model)

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