The Enantioselective α-Arylation of Aldehydes via Organo-SOMO Catalysis: An Explanation of Conflicting Results and Mechanistic Interpretations

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Supporting Information

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] All solvents were purified according to the method of Grubbs.[2] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using force-flow chromatography on Silicycle silica gel according to the method of Still.[3] Thin-layer chromatography (TLC) was performed on Silicycle 250 μm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching or anisaldehyde stain.

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(1) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.
(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics,* **1996**, *15*, 1518.
(3) Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova (400 MHz) or a Bruker Advance (500 MHz) and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced at δ 7.24 ppm for ^{1}H and δ 77.23 ppm for ^{13}C). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, ddd = doublet of doublet of doublets and m = multiplet), integration, coupling constant (Hz) and assignment. Structures with numbering are for NMR assignments and do not necessarily conform with the given chemical name. Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm). IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra were obtained from the Princeton University mass spectral facility. Supercritical fluid chromatography (SFC) was performed on a Berger Minigram equipped with a diode array UV detector (λ = 214–258 nm) using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. High pressure liquid chromatography (HPLC) was performed on a Hewlett-Packard 1100 Series chromatograph using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in 10^{-1} (deg cm^2 g^{-1}); concentration (c) is in g/100 mL. $[Fe(phen)_3]\cdot(PF_6)_3$ was prepared according to literature procedure.[4]

[4] Schmittel, M.; Levis, M. *Synlett*, **1996**, 315.

General Procedure A: $[Fe(phen)_3]\cdot(PF_6)_3$, $NaHCO_3$/HOPiv and MeCN:

To an oven dried 10 mL round bottom flask equipped with a Teflon septum and a magnetic stir bar was added (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (0.2 equiv), $[Fe(phen)_3]\cdot(PF_6)_3$ (2.5 equiv), and $NaHCO_3$ (5.0 equiv). The flask was sealed with a septum, degassed by pulling vacuum and then refilling with argon five times, then cooled to –78 ºC. Next degassed MeCN (to make 0.15 M in aldehyde), H_2O (1.0 equiv) and lastly aldehyde (1.0 equiv) were added. The reaction mixture was then carefully degassed through alternating vacuum evacuation and charging the vessel with argon (5×). The flask was then placed in a –20 °C cryocool and and stirred for 24 h. The reaction was then cooled to –78 °C and quickly diluted with cold ether and stirred for 5 minutes where precipitation of red solid was observed.

[1] *For isolation as aldehyde products*: the reaction mixture was filtered through a pad of silica gel and then concentrated *in vacuo*. The crude oil was then purified by column chromatography with the solvent mixture as noted to yield the desired aldehyde product.

[2] *For isolation as alcohol products*: the red solid was filtered through a glass frit funnel into a 100 mL round bottom flask having excess amount of $NaBH_4$ (10 equiv). 10 mL of EtOH was added to the reaction vessel at –40 °C. The reaction temperature was slowly increased to –10 °C, at which point complete consumption of the aldehyde product was observed by TLC analysis. A saturated aqueous solution of NH_4Cl was added to quench the excess $NaBH_4$. The mixture was then extracted with ether. The ether layer was washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude oil was then purified by column chromatography with the solvent mixture as noted to yield the desired alcohol product.

General Procedure B: $[Fe(phen)_3](PF_6)_3$, Na_2HPO_4 and Acetone:

To a Schlenk tube equipped with a magnetic stir bar was added (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (20 mol %). After cooling to –78 °C, an acetone solution containing the substrate (100 mol %) and H_2O (100 mol %) was added. The reaction mixture was then carefully degassed through alternating vacuum evacuation and charging the vessel with argon (5×). Next, against the flow of argon, $[Fe(phen)_3]\cdot(PF_6)_3$ (200 mol %) and Na_2HPO_4 (100 mol %) were added. After degassing of the reaction mixture (5×), the tube was moved to a –30 °C cryocool where it was stirred for 24 h. The reaction was then cooled to –78 °C and quenched with an excess amount of ether causing the precipitation of a red solid.

[1] *For isolation as aldehyde products*: the reaction mixture was filtered through a pad of silica gel and then concentrated *in vacuo*. The crude oil was then purified by column chromatography with the solvent mixture as noted to yield the desired aldehyde product.

[2] *For isolation as alcohol products*: the red solid was filtered through a glass frit funnel into a 100 mL round bottom flask having excess amount of $NaBH_4$ (10 equiv). 10 mL of EtOH was added to the reaction vessel at –40 °C. The reaction temperature was slowly increased to –10 °C, at which point complete consumption of the aldehyde product was observed by TLC analysis. A saturated aqueous solution of NH_4Cl was added to quench the excess $NaBH_4$. The mixture was then extracted with ether. The ether layer was washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude oil was then purified by column chromatography with the solvent mixture as noted to yield the desired alcohol product.

General Procedure C: CAN, $NaHCO_3$/NaO_2CCF_3 and Acetone:

To a Schlenk tube equipped with a magnetic stir bar was added (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (20 mol %). After cooling to –78 °C, an acetone solution containing the substrate (100 mol %) and H_2O (100 mol %) was added. The reaction mixture was then carefully degassed through alternating vacuum evacuation and charging the vessel with argon (5×). Next, against the flow of argon, ammonium cerium(IV) nitrate (CAN) (200 mol %), $NaHCO_3$ (200 mol %) and NaO_2CCF_3 (200 mol %) were added. After degassing of the reaction mixture (5×), the tube was moved to a –30 °C cryocool where it was stirred for 24 h. The reaction was then cooled to –78 °C and quenched with an excess amount of ether causing the precipitation of a white solid.

[1] *For isolation as aldehyde products*: the reaction mixture was filtered through a pad of silica gel and then concentrated *in vacuo*. The crude oil was then purified by column chromatography with the solvent mixture as noted to yield the desired aldehyde product.

[2] *For isolation as alcohol products*: the red solid was filtered through a glass frit funnel into a 100 mL round bottom flask having excess amount of $NaBH_4$ (10 equiv). 10 mL of EtOH was added to the reaction vessel at –40 °C. The reaction temperature was slowly increased to –10 °C, at which point complete consumption of the aldehyde product was observed by TLC analysis. A saturated aqueous solution of NH_4Cl was added to quench the excess $NaBH_4$. The mixture was then extracted with ether. The ether layer was washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude oil was then purified by column chromatography with the solvent mixture as noted to yield the desired alcohol product.

Note on the isolation of aldehyde products: The aldehyde products were generally unstable even for short-term storage at low temperature. The alcohol products could be stored safely for several months at –30 °C.

Automated Reaction Optimization

High-throughput optimization was performed using a Chemspeed Accelerator robotic platform. Reactions were carried out under an inert atmosphere in 2 mL double jacketed reactors at –20 °C or –30 °C. The reactions were done on 0.05 mmol aldehyde scale. The general reaction sequence used to optimize the reaction was programmed as follows:

1. $[Fe(phen)_3]\cdot(PF_6)_3$ was delivered via the solid dispensing unit.
2. $NaHCO_3$ was delivered via the solid dispensing unit.
3. The atmosphere within the accelerator enclosure was purged out with N_2 for 1 h. This was typically done while the solids were being added to the reactors.
4. The reactors were evacuated (5 mbar) and filled with N_2 five times.
5. The reactors were cooled to –20 °C and kept under N_2 atmosphere.
6. Degassed MeCN was dispensed by the liquid handling arm.
7. Stock solutions of catalyst, water, additive and substrate were added.
8. The reactors were degassed again by evacuating (5 mbar) and filling with N_2 five times.
9. Under an atmosphere of N_2 the reactors were vortexed at 800 rpm for 24 h.
10. Internal standard (methyl benzoate) was added as a stock solution to the reactions.
11. To precipitate out the solids 1.5 mL of ether was added and the reactions warmed to room temperature
12. To avoid any precipitate, the liquid handling robotic arm was then used to remove 100 μL of the reaction mixture 1 cm above bottom of the reactor and moved into a 96-well plate. The analysis sample was then diluted with 1 mL of toluene and analyzed by GC-FID. The yield was referenced to the response of the internal standard.

Lead reactions were then validated on bench scale to determine the isolated yield and enantiomeric excess.

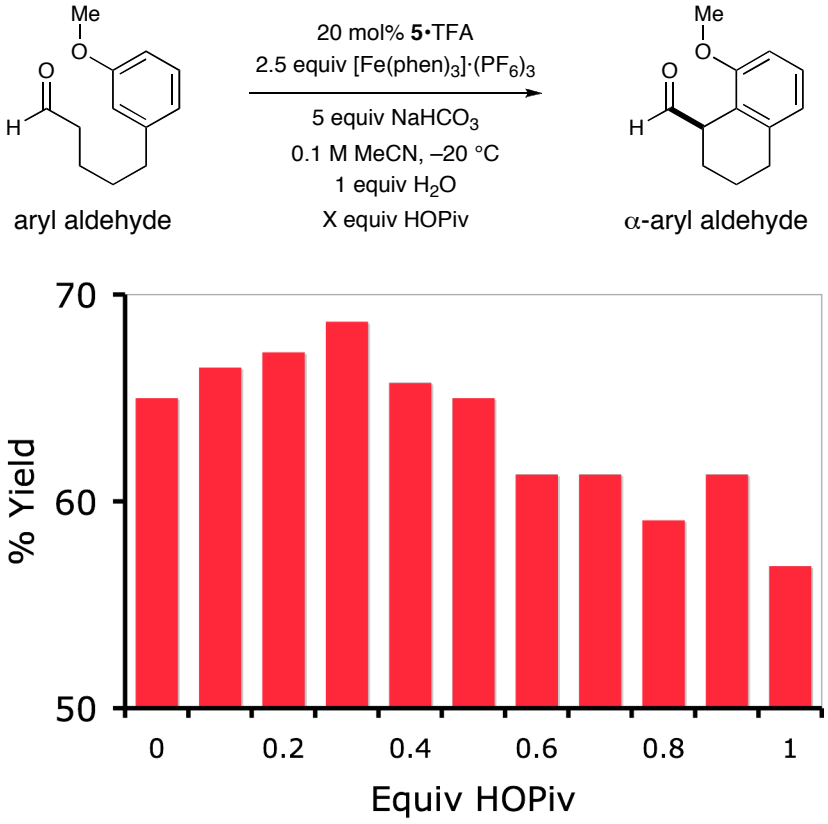


Figure S1. Optimization of the equivalents of pivalic acid additive for the α-arylation of aldehydes.

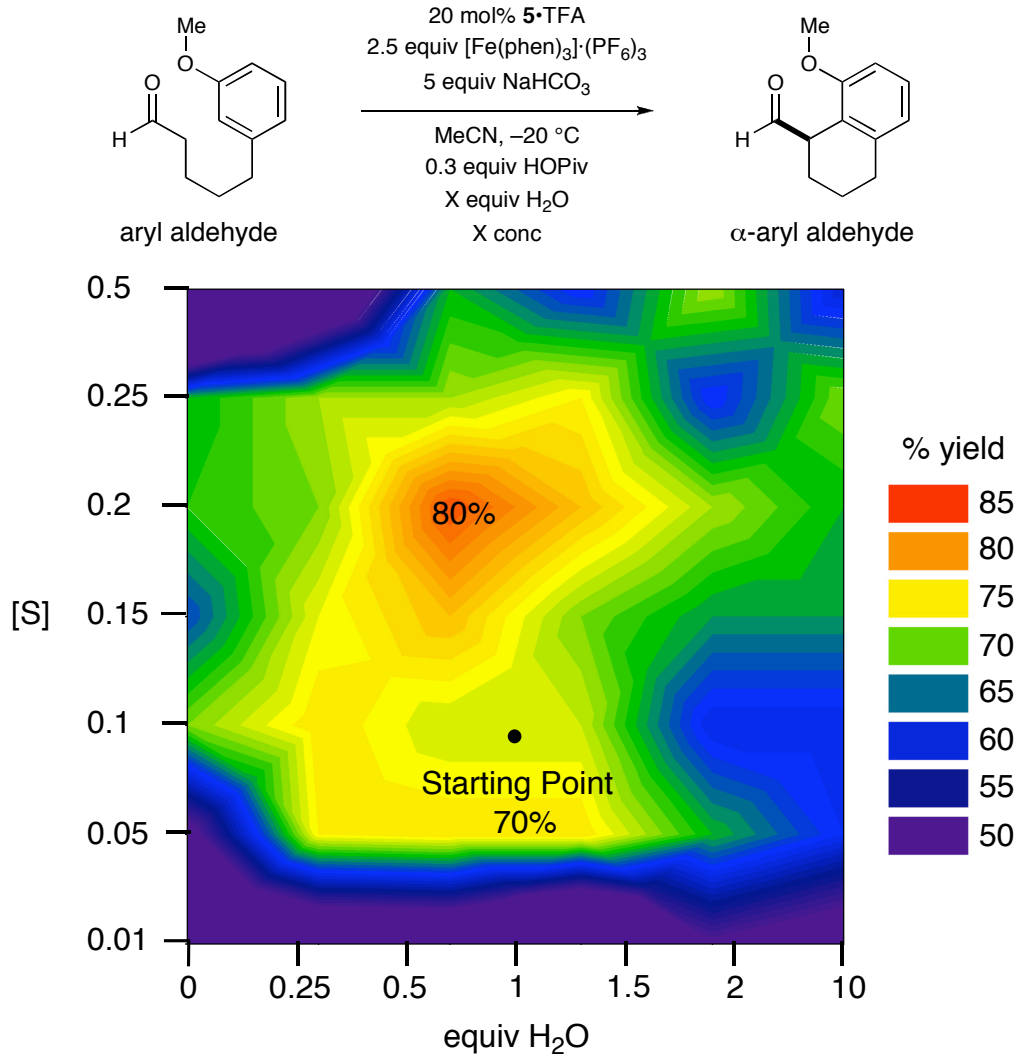
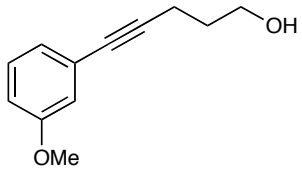
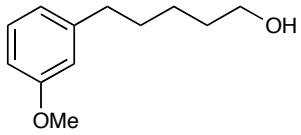


Figure S2. Fine-tuning of the α-arylation conditions from Table 1, entry 6. Optimal conditions: 0.3 equiv HOPiv, 0.5 equiv H_2O: 80% yield, 98% ee; starting point: Table 1, entry 5.



5-(3-Methoxyphenyl)pent-4-yn-1-ol

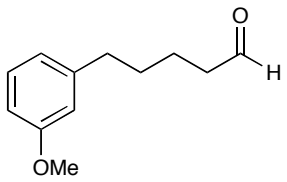
To an oven dried 500 mL 3-neck round bottom flask equipped with a stir bar was added 200 mL acetonitrile, 3-iodoanisole (10 g, 43.2 mmol) and 4-pentyn-1-ol (4 g, 47.6 mmol). The reagents were degassed by evacuating and back filling with argon three times. Against a positive pressure of argon solid CuI (1.6 g, 8.6 mmol) and $PdCl_2(PPh_3)_2$ (1.5 g, 2.15 mmol) were then added. The flask was cooled to 0 °C and 20 mL NEt_3 was added slowly. After 1 h the reaction was warmed to 21 °C and stirred for another 16 h. The reaction was then filtered through a plug of Florosil, washed with EtOAc, concentrated *in vacuo* and then purified by column chromatography (40% EtOAc/hexane) to provide the title compound as a clear oil (6.98 g, 85% yield). IR (film) ν (cm^{-1}) 3396, 2942, 2835, 1597, 1574, 1481, 1465, 1427, 1316, 1286, 1205, 1175, 1164, 1044, 908, 779, 730. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (t, 1H *J* = 8.0, Ar**H**), 6.98 – 6.94 (m, 1H, Ar**H**), 6.90 (t, 1H, *J* = 1.1, Ar**H**), 6.81 (ddd, 1H, *J* = 8.0, 2.7, 1.1, Ar**H**), 3.79 (q, 2H, *J* = 6.0, HOC**H$_2$**), 3.76 (s, 3H, OC**H$_3$**), 2.51 (t, 2H *J* = 6.9, CC**H$_2$**CH_2), 1.84 (p, 2H, *J* = 6.9, CH_2**CH_2**CH_2), 1.76 (m, 1H, O**H**). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 129.4, 124.9, 124.3, 116.6, 114.5, 89.4, 81.2, 61.9, 55.4, 31.5, 16.1. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{12}H_{15}O_2$) requires *m/z* 191.1072 found *m/z* 191.1066.



5-(3-Methoxyphenyl)pentan-1-ol

To an oven dried 500 mL 3-neck round bottom flask equipped with a stir bar was added 5-(3-methoxyphenyl)pent-4-yn-1-ol (6 g, 31.9 mmol) and 100 mL of MeOH. The solution was then degassed by evacuating and back filling the flask three times with argon. Against a positive flow of argon 10% palladium on carbon (700 mg, 0.66 mmol) was added. A balloon filled with H_2 was then fitted to the reaction and stirred for 24 h. After the reaction was judged complete by TLC, the Pd/C was removed by filtering

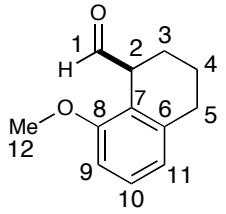
through a pad of Celite and the product was flushed through with 200 mL EtOAc. After concentrating *in vacuo* the product was purified by column chromatography (40% EtOAc/hexane) to provide the title compound as a colorless oil (5.12 g, 83% yield). IR (film) ν (cm^{-1}) 3344, 2933, 2858, 1601, 1584, 1487, 1454, 1258, 1151, 1044, 777, 736, 695. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (t, 1H, *J* = 7.7, Ar**H**), 6.75 (d, 1H, *J* = 7.5, Ar**H**), 6.73 – 6.69 (m, 2H, Ar**H**), 3.78 (s, 3H, OC**H**$_3$), 3.65 – 3.58 (m, 2H, C**H**$_2$OH), 2.58 (t, 2H, *J* = 7.6, ArC**H**$_2$), 1.64 – 1.54 (m, 4H, C**H**$_2$C**H**$_2$CH$_2$OH), 1.47 (s, 1H, O**H**), 1.38 (m, 2H, ArCH$_2$C**H**$_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 144.4, 129.4, 121.0, 114.3, 111.0, 62.9, 55.3, 36.1, 32.7, 31.3, 25.6. HRMS (ESI$^+$) exact mass calc'd for $[M+H]^+$ ($C_{12}H_{19}O_2$) requires *m/z* 195.1385, found *m/z* 195.1289.



5-(3-methoxyphenyl)pentanal

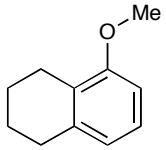
A 3-neck round bottom flask containing 5 g of 5 Å molecular sieves and a stir bar was dried in an oven overnight. After cooling under vacuum and refilling with argon MeCN (50 mL), 5-(3-methoxyphenyl)pentan-1-ol (5 g, 25.8 mmol), *N*-methyl-morpholine oxide (NMO, 3.9 g, 38.7 mmol) and tetrapropylammonium perruthenate (TPAP, 91 mg, 0.258 mmol) were added. The reaction was stirred for 12 h after which the solution was concentrated *in vacuo* then purified by column chromatography (40% Et_2O/pentane) to afford the title compound as a colorless oil (3.95g, 80%). IR (film) ν (cm^{-1}) 2940, 2861, 1722, 1601, 1584, 1488, 1455, 1264, 1152, 1043, 736, 698. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.73 (t, 1H, *J* = 1.7, C**H**O), 7.18 (d, 1H, *J* = 7.6, Ar**H**), 6.75 – 6.70 (m, 3H, Ar**H**), 3.78 (s, 3H, OC**H**$_3$), 2.59 (t, 2H, *J* = 7.1, ArC**H**$_2$), 2.45 – 2.41 (m, 2H, CHOC**H**$_2$), 1.68 – 1.59 (m, 4H, CH$_2$(C**H**$_2$)$_2$CH$_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 159.8, 143.7, 129.5, 121.0, 114.4, 111.2, 55.3, 43.9, 35.8, 30.9, 21.8. HRMS (ESI$^+$) exact mass calc'd for $[M+H]^+$ ($C_{12}H_{17}O_2$) requires *m/z* 193.1229, found *m/z* 193.1209.

Table 2, Entry 1:



8-Methoxy-1,2,3,4-tetrahydronaphthalene-1-carbaldehyde

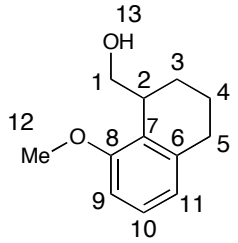
Prepared according to procedure A-1: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (82 mg, 0.3 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (2.58 g, 2.5 mmol), pivalic acid (30 mg, 0.3 mmol), $NaHCO_3$ (420 mg, 5 mmol), MeCN (5 mL), H_2O (9 μl, 0.5 mmol) and 5-(3-methoxyphenyl)pentanal (200 mg, 1.0 mmol). The title compound was isolated as a clear oil. (*Note: yield and % ee were determined with the corresponding alcohol*). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58 (s, 1H, H1), 7.18 (t, 1H, *J* = 7.9, H10), 6.76 (d, 1H, *J* = 7.65, H9), 6.72 (d, 1H, *J* = 8.15, H11), 3.79 (s, 3H, H12), 3.79 – 3.75 (m, 1H, H2), 2.78 – 2.70 (m, 2H, H5), 2.17 – 2.11 (m, 1H, H3a), 1.84 – 1.63 (m, 3H, H3b, H4). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2 (C1), 157.5 (C8), 139.7 (C6), 127.9 (C10), 122.0 (C11), 121.2 (C7), 107.6 (C9), 55.5 (C12), 46.7 (C2), 29.4 (C5), 23.4 (C3), 20.5 (C4).



Similar ^{1}H NMR spectra have been reported for 5-methoxy-dihydrotetralene:[5]

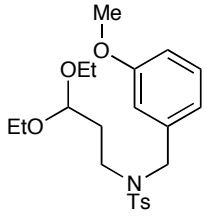
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (t, *J* = 7.93, 1H), 6.70 (d, *J* = 7.93, 1H), 6.65 (d, *J* = 7.93, 1H), 3.81(s, 3H), 2.75 (t, *J* = 6.10, 2H), 2.64 (t, *J* = 6.10, 2H), 1.79-1.73 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.34, 138.51, 125.93, 125.65, 121.39, 106.74, 55.22, 29.71, 29.64, 23.06, 22.83.

[5] Yoshimi, T.;, Ishise, A.; Oda, H.; Moriguchi, Y.; Kanezaki, H.; Nakaya, Y.; Katsuno, K.; Itou, T.; Inagaki, S.; Morita, T.; Hatanaka, M. *Tetrahedron Lett*. **2008**, *49*, 3400.



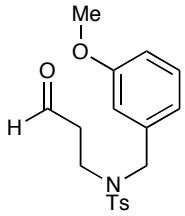
(8-Methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)methanol

Prepared according to procedure A-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (82 mg, 0.3 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (2.58 g, 2.5 mmol), pivalic acid (30 mg, 0.3 mmol), $NaHCO_3$ (420 mg, 5 mmol), MeCN (5 mL), H_2O (9 μl, 0.5 mmol) and 5-(3-methoxyphenyl)pentanal (200 mg, 1.0 mmol). The title compound was isolated as a white solid (156 mg, 80% yield, 98% ee). IR (film) ν (cm^{-1}) 3376, 2935, 2837, 1582, 1466, 1438, 1336, 1265, 1252, 1101, 1031, 771, 737. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (t, 1H, *J* = 8.0, H10), 6.71 (d, 1H, *J* = 8.0, H11), 6.67 (d, 1H, *J* = 8.0, H9), 3.83 – 3.80 (m, 4H, H12, H1a), 3.58 (dd, 1H, *J* = 8.3, 10.4, H1b), 3.27 – 3.21 (m, 1H, H2), 2.82 – 2.67 (m, 2H, H5), 2.13 – 2.06 (m, 1H, H3b), 1.99 – 1.88 (m, 1H, H13), 1.84 – 1.62 (m, 3H, H3a, H4). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6 (C8), 139.4 (C7), 126.8 (C10), 125.8 (C6), 122.0 (C11), 107.5 (C9), 65.8 (C1), 55.5 (C12), 35.4 (C2), 29.6 (C5), 24.6 (C3), 18.4 (C4). HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{12}H_{17}O_2$) requires *m/z* 193.1229, found *m/z* 193.1219. The enantiomeric excess was determined by HPLC using a Chiracel AS-H column (25 cm × 0.46 cm) with 5% ethanol in hexane as the mobile phase; t_r = 10.20 and 16.43 min. $[\alpha]_D^{23}$ = 92.2 (c = 0.9, $CHCl_3$, 92% ee). The regiochemistry is assigned on the basis of the aromatic ^{1}H NMR coupling pattern where a triplet δ 7.09 (H10) is coupled to two doublets 6.71 (H11) and 6.67 (H9) ppm. These correlations show up clearly in the ^{1}H-^{1}H COSY NMR experiment and the 8.0 Hz coupling constant is consistent with vicinal ^{1}H coupling (see provided NMR spectra). If the arylation occurred para to the methoxy group two doublets that couple to each other and a singlet would be expected. Further support is found in the 2-D HSQC and HMBC experiments. Key HMBC correlations show a cross-peak between H10 and C9/C11 establishing the aromatic substitution as having three adjacent proton bearing carbons.



_N_-(3,3-Diethoxy-propyl)-_N_-(3-methoxy-benzyl)-4-methyl-benzenesulfonamide

To an oven dried 250 mL round bottom flask equipped with a stir bar was added *N*-(3,3-diethoxypropyl)-4-methylbenzenesulfonamide (5.5g. 18.4 mmol), THF (60 mL, 0.3 M) and then solid NaH (808 mg, 20.2 mmol). After stirring for 30 min at 0 °C, 3-methoxybenzyl bromide (2.6 mL, 18.4 mmol) was added at room temperature and then stirred for 12 h at 80 °C. The reaction was quenched with 30 mL saturated aqueous NH_4Cl. The product was extracted with 100 mL ether and then the organic layer was washed with 100 mL brine, dried with $MgSO_4$, filtrated, and concentration *in vacuo*. The title compound was purified by column chromatography (20% EtOAc/hexane) and isolated as a clear oil (6.26 g, 81%). IR (film) ν (cm^{-1}) 2974, 2930, 2878, 1599, 1587, 1490, 1455, 1338, 1263, 1157, 1053, 931, 869, 814, 748, 736, 657. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.0, Ar**H**), 7.27 (d, 2H, *J* = 8.0, Ar**H**), 7.17 (t, 1H, *J* = 8.0, Ar**H**), 6.82 (d, 1H, *J* = 7.5, Ar**H**), 6.79 – 6.75 (m, 2H, Ar**H**), 4.23 (t, 1H, *J* = 5.5, $(OEt)_2$**CH**), 4.24 (s, 2H, TsN**CH_2**Ar), 3.71 (s, 3H, ArO**CH_3**), 3.46 – 3.41 (m, 2H, CH_3**CH_2**OCH), 3.31 – 3.25 (m, 2H, CH_3**CH_2**OCH), 3.14 (t, 2H, *J* = 7.5, CH_2**CH_2**NTs), 2.39 (s, 3H, Ar**CH_3**), 1.67- 1.63 (m, 2H, CH**CH_2**CH_2), 3.14 (t, 6H, *J* = 7.0, OCH_2**CH_3**). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 143.2, 137.9, 136.63, 129.7, 129.6, 129.5, 129.4, 120.5, 120.5, 113.4, 100.7, 100.8, 61.3, 55.1, 55.0, 53.2, 44.1, 32.3, 21.4, 21.3, 15.2, 15.1, 15.1, 15.0. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{22}H_{31}NNaO_5S$) requires *m*/*z* 421.1923 found *m*/*z* 421.1919.



***N*-(3-Methoxy-benzyl)-4-methyl-*N*-(3-oxo-propyl)-benzenesulfonamide**

To an oven dried 50 mL round bottom flask equipped with a stir bar was added *N*-(3,3-diethoxy-propyl)-*N*-(3-methoxy-benzyl)-4-methyl-benzenesulfonamide (1.79 g, 4.24 mmol), $CHCl_3$ (8.5 mL), H_2O (4.3 mL) and then TFA (4.3 mL). *(Note: $CHCl_3$:H_2O:TFA = 2:1:1, 17 mL, 0.25 M)*. The reaction was stirred for 2 h at 0 °C then stirred for 12 h at room temperature. The reaction was slowly quenched with 30 mL saturated aqueous $NaHCO_3$. The product was extracted with 100 mL ether and then the organic layer was washed with 100 mL brine. After drying with $MgSO_4$, filtration, concentration *in vacuo*, the title compound was purified by column chromatography (20% EtOAc/hexane) and isolated as a clear oil (1.29 g, 88%). IR (film) ν (cm^{-1}) 2922, 2837, 2734, 1720, 1598, 1586, 1489, 1454, 1437, 1381, 1334, 1305, 1262, 1154, 1114, 1088, 1039, 1014, 920, 848, 814, 774, 655. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.51 (d, 1H, *J* = 1.0, C**H**O), 7.70 (dt, 2H, *J* = 8.5, 2.0, Ar**H**), 7.31 (d, 2H, *J* = 8.0, Ar**H**), 7.19 (t, 1H, *J* = 7.7, Ar**H**), 6.82 – 6.77 (m, 3H, Ar**H**), 4.23 (s, 2H, TsNC**H₂**Ar), 3.73 (s, 3H, ArOC**H₃**), 3.36 (t, 2H, *J* = 7.2, CH_2**C**$\mathbf{H_2}$NTs), 2.53 (t, 2H, *J* = 7.2, CHO**C**$\mathbf{H_2}$$CH_2$), 2.41 (s, 3H, Ar**C**$\mathbf{H_3}$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.1, 200.0, 159.8, 143.6, 137.5, 135.9, 129.8, 129.7, 129.6, 127.2, 127.1, 120.5, 120.4, 113.7, 113.6, 113.5, 113.4, 55.1, 55.0, 43.5, 41.9, 21.4, 21.3. HRMS (ESI$^+$) exact mass calc'd for $[M+Na]^+$ ($C_{18}H_{21}NNaO_4S$) requires *m/z* 347.119 found *m/z* 347.1185.

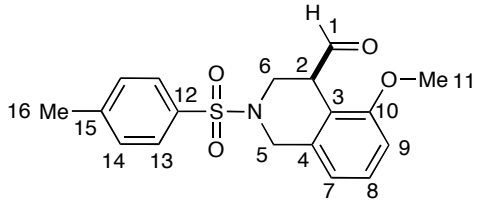


Table 2, Entry 2:

5-Methoxy-2-(toluene-4-sulfonyl)-1,2,3,4-tetrahydro-isoquinoline-4-carbaldehyde

Prepared according to general procedure A-1: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (515 mg, 0.5 mmol), and pivalic acid (6.13 mg, 0.06 mmol), CH_3CN (1 mL, 0.2 M), H_2O (1.8 μl, 0.1 mmol) and *N*-(3-methoxy-benzyl)-4-methyl-*N*-(3-oxo-propyl)-benzenesulfonamide (69.5 mg, 0.2 mmol). The title compound was isolated as a clear oil (*Note: yield and % ee were determined with the corresponding alcohol*). IR (film) ν (cm^{-1}) 2936, 2839, 1721, 1592, 1472, 1457, 1351, 1337, 1263, 1162, 1088, 1073, 1012, 950, 913, 815, 774, 732, 666. ^1H NMR (300 MHz, $CDCl_3$) δ 9.60 (d, 1H, *J* = 8.4, H1), 7.71 (d, 2H, *J* = 8.1, H13), 7.32 (d, 2H, *J* = 8.1, H14), 7.22 (t, 1H, *J* = 8.0, H8), 6.82 (d, 1H, *J* = 7.5, H9), 6.76 (d, 1H, *J* = 8.4, H7), 4.47 (d, 1H, *J* = 15.3, H5a), 4.21 (ddd, 1H, *J* = 12.0, 3.0, 1.2, H6a), 3.88 (d, 1H, *J* = 15.3, H5b), 3.77 – 3.42 (m, 4H, H11 and H2), 2.87 (dd, 1H, *J* = 12.2, 1.6, H6b), 2.41 (s, 3H, H16). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.7 (C1), 157.2 (C10), 143.9 (C15), 133.8 (C3), 132.5 (C12), 129.7 (C13), 128.7 (C8), 127.8 (C14), 118.7 (C7), 118.0 (C4), 108.5 (C9), 55.5 (C11), 47.3 (C5), 45.9 (C2), 43.3 (C6), 21.5 (C16). HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{18}H_{19}NO_4S$) requires *m/z* 345.1035, found *m/z* 345.1035. The regiochemistry is assigned on the basis of the aromatic ^1H NMR coupling pattern where a triplet δ 7.22 is coupled (8.0 Hz) to two doublets 6.82 and 6.76 ppm. These correlations show up clearly in the ^1H-^1H COSY NMR experiment and the coupling constant is consistent with vicinal ^1H coupling (see also provided NMR spectra). If the arylation occurred para to the methoxy group one would expect there to be two doublets that couple to each other and a singlet.

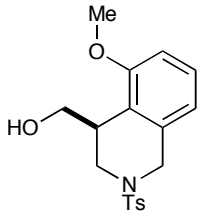
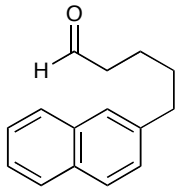


Table 2, Entry 2:

[5-Methoxy-2-(toluene-4-sulfonyl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-methanol

Prepared according to general procedure A-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (515 mg, 0.5 mmol), and pivalic acid (6.13 mg, 0.06 mmol), CH_3CN (1 mL, 0.2 M), H_2O (1.8 μl, 0.1 mmol) and *N*-(3-Methoxy-benzyl)-4-methyl-*N*-(3-oxo-propyl)-benzenesulfonamide (69.5 mg, 0.2 mmol). The title compound was isolated as a clear oil (59.5 mg, 86% yield, 95% ee). IR (film) ν (cm^{-1}) 3491, 2935, 2887, 2838, 1732, 1589, 1470, 1459, 1439, 1336, 1258, 1161, 1082, 1016, 947, 910, 815, 804, 773, 729, 708, 666. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, 2H, *J* = 8.4, Ar**H**), 7.32 (d, 2H, *J* = 8.4, Ar**H**), 7.12 (t, 1H, *J* = 8.0, Ar**H**), 6.67 (d, 1H, *J* = 8.1, Ar**H**), 6.62 (d, 1H, *J* = 7.8, Ar**H**), 4.66 (d, 1H, *J* = 15.0, NTs**CH$_2$**Ar), 4.22 (dt, 1H, *J* = 12.0, 1.7, NTs**CH$_2$**Ar), 3.86 – 3.69 (m, 3H, HOC**H**$_2$CH, NTsC**H**$_2$Ar), 3.78 (s, 3H, ArO**CH$_3$**), 3.27 – 3.21 (m, 1H, NTs**CH$_2$**Ar), 2.52 (brs, 1H, O**H**), 2.48 (dd, 1H, *J* = 3.1, 0.9, CH_2C**H**CH_2), 2.41 (s, 3H, ArC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 143.6, 133.3, 132.2, 129.7, 127.6, 127.5, 122.4, 118.4, 108.2, 62.3, 55.2, 47.3, 44.1, 36.3, 21.4. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{18}H_{22}NO_4S$) requires *m/z* 347.1191, found *m/z* 347.1191. The enantiomeric excess was determined by HPLC using an Chiracel OD-H column (25 cm × 0.46 cm) column with 10% isopropanol in hexane as the mobile phase; t_r = 18.29 and 21.80 min. $[\alpha]_D^{24}$ = 12.7 (c = 1.0, $CHCl_3$, 95% ee).



5-Naphthalen-2-yl-pentanal

To an oven dried 250 mL round bottom flask equipped with a stir bar was added 5-naphthalen-2-yl-pent-4-yn-1-ol[6] (1.23 g, 5.84 mmol) and EtOAc (89 mL, 0.066M). The solution was then degassed by evacuating and back filling the flask three times with argon. Against a positive flow of argon 10% palladium on carbon (123 mg, 10 wt%) was added. A balloon filled with H_2 was then fitted to the reaction and stirred for 12 h. After the reaction was judged complete by TLC, the Pd/C was removed by filtering through a pad of Celite and the product was flushed through with 200 mL EtOAc. After concentrating *in vacuo*, the crude product (5-naphthalen-2-yl-pentan-1-ol) was dissolved in CH_2Cl_2 (55 mL, 0.1 M) and pyridinium chlorochromate (1.99 g, 9.25 mmol) was added in one portion. After stirring for 4 h, Et_2O (20 mL) and hexane (5 mL) were added, and the suspension was filtered through silica gel and washed with Et_2O (100 mL). After concentration, the residue was purified by column chromatography (hexane:EtOAc = 8:1) to afford the title compound as a colorless oil (890 mg, 77% yield). IR (film) ν (cm^{-1}) 3051, 2933, 2857, 2719, 1720, 1632, 1599, 1507, 1459, 1389, 1365, 1270, 1144, 1124, 1076, 1016, 961, 893, 855, 815, 745. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.74 (t, 1H, *J* = 1.7, C**H**O), 7.81 – 7.76 (m, 3H, Ar**H**), 7.61 (s, 1H, Ar**H**), 7.41 – 7.40 (m, 2H, Ar**H**), 7.32 (dd, 1H, *J* = 7.3, 1.5, Ar**H**), 2.80 (t, 2H, *J* = 7.0, $CH_2C\mathbf{H}_2$Ar), 2.75 (dt, 2H, *J* = 7.5, 1.8, CHOC$\mathbf{H}_2$ CH_2), 1.78 – 1.66 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.3, 139.3, 133.5, 131.9, 127.8, 127.5, 127.3, 127.1, 126.3, 125.8, 125.0, 43.6, 35.6, 30.6, 21.5. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{15}H_{16}NaO$) requires *m/z* 212.1201, found *m/z* 212.1200.

(6) Brimble, M. A.; Pavia, G. S.; Stevenson, R. J. *Tetrahedron Lett.* **2002**, *43*, 1735.

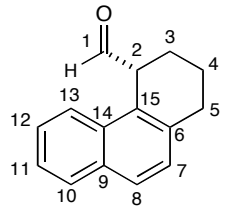


Table 2, Entry 3:

(R)-1,2,3,4-Tetrahydro-phenanthrene-4-carbaldehyde

Prepared according to general procedure B-1: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (430 mg, 0.42 mmol), and Na_2HPO_4 (28 mg, 0.4 mmol), acetone (0.5 mL, 0.4 M), H_2O (3.6 μl, 0.2 mmol) and 5-naphthalen-2-yl-pentanal (42.5 mg, 0.2 mmol). The title compound was isolated as a colorless oil (*Note: yield and % ee were determined with the corresponding alcohol*). IR (film) ν (cm^{-1}) 3050, 2935, 2866, 1719, 1600, 1510, 1448, 1430, 1390, 1259, 1188, 1031, 956, 861, 846, 808, 780, 743. ^1H NMR (400 MHz, $CDCl_3$) δ 9.76 (d, 1H, *J* = 2.0, H1), 7.83 (d, 1H *J* = 8, H13), 7.80 (d, 1H, *J* = 8.4, H10), 7.72 (d, 1H, *J* = 8.4, H8), 7.52 – 7.49 (m, 1H, H12), 7.46 – 7.43 (m, 1H, H11), 7.27 (d, 1H, *J* = 8.4, H7), 4.25 (t, 1H, *J* = 3.0, H2), 2.96 (dd, 2H, *J* = 7.4, 4.6, H5), 2.48 – 2.42 (m, 1H, H3a), 2.04 – 2.77 (m, 3H, H3b H4). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8 (C1), 136.2 (C9), 132.5 (C6), 132.4 (C14), 128.8 (C13), 128.2 (C7), 127.7 (C8), 126.6 (C12), 126.2 (C15), 125.1 (C11), 122.7 (C10), 47.9 (C2), 30.0 (C5), 24.0 (C3), 19.7 (C4). HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{15}H_{14}NaO$) requires *m/z* 210.1045, found *m/z* 210.1045. The regiochemistry is assigned on the basis of the aromatic ^1H NMR coupling pattern where on the functionalized portion of the naphthal system two doublets (δ 7.72 and 7.27 ppm) are seen to couple to each other (8.4 Hz). These correlations show up clearly in the ^1H-^1H COSY NMR experiment and the coupling constant is consistent with vicinal ^1H coupling (see provided NMR spectra). If the arylation occurred at the naphthal 3-position two singlets would be expected.

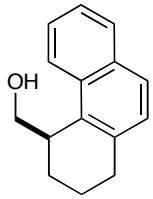
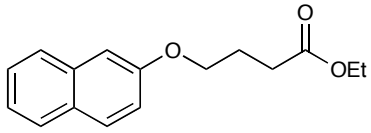


Table 2, Entry 3:

(R)-(1,2,3,4-Tetrahydro-phenanthren-4-yl)-methanol

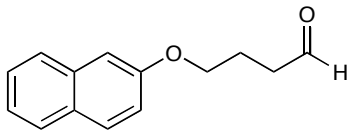
Prepared according to general procedure B-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (430 mg, 0.42 mmol), and Na_2HPO_4 (28 mg, 0.4 mmol), acetone (0.5 mL, 0.4 M), H_2O (3.6 μl, 0.2 mmol) and 5-naphthalen-2-yl-pentanal (42.5 mg, 0.2 mmol). The title compound was isolated as a colorless oil. (31 mg, 73% yield, 96% ee). IR (film) ν (cm^{-1}) 3307, 3048, 2930, 1624, 1600, 1509, 1455, 1429, 1389, 1266, 1183, 1093, 1028, 908, 844, 806, 780, 743. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, 1H, *J* = 8.5, Ar**H**), 7.78 (d, 1H, *J* = 8.0, Ar**H**), 8.61 (d, 1H, *J* = 8.5, Ar**H**), 7.49 (ddd, 1H, *J* = 7.0, 5.1, 1.5, Ar**H**), 7.42 (d, 1H, *J* = 7.5, Ar**H**), 7.18 (d, 1H, *J* = 8.0, Ar**H**), 3.97 (d, 1H, *J* = 10.5, HO**CH$_2$**CH), 3.76 (d, 1H, *J* = 10.5, HO**CH$_2$**CH), 3.72 – 3.69 (m, 1H, CH_2**CH**CH_2), 2.92 (dd, 2H, *J* = 8.5, 4.0, CH_2**CH$_2$**Ar), 2.36 – 2.31 (m, 1H, CH**CH$_2$**CH_2), 2.04 – 1.94 (m, 1H, CH**CH$_2$**CH_2), 1.90 – 1.81 (m, 2H, CH_2**CH$_2$**CH_2), 1.56 (brs, 1H, O**H**). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 132.4, 132.1, 131.1, 128.7, 128.1, 126.2, 126.0, 124.6, 122.8, 65.2, 36.6, 30.0, 24.0, 17.8. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{15}H_{16}NaO$) requires *m*/*z* 212.1201, found *m*/*z* 212.1201. The enantiomeric excess was determined by HPLC using a Chiracel OD-H column (25 cm × 0.46 cm) with 5% isopropanol in hexane as the mobile phase; t_r = 12.32 and 14.98 min. $[\alpha]_D^{24}$ = -20.9 (c = 1.0, $CHCl_3$, 96% ee).



Ethyl 4-(naphthalen-2-yloxy)butanoate

To a dry round bottom flask was added naphthalen-2-ol (2 g, 13.9 mmol), 50 mL DMF and NaH (367 mg, 15.3 mmol). After stirring for 30 min ethyl 4-bromobutanoate (4 mL, 27.7 mmol) was added and then the reaction was stirred for a further 12 h. The reaction

was quenched with 100 mL saturated aqueous NH_4Cl, the product extracted with 200 mL EtOAc then the organic layer was washed with 100 mL saturated aqueous $NaHCO_3$ and 100 mL brine. After concentration *in vacuo* the title compound was purified by column chromatography (20% EtOAc/hexane) and isolated as a clear oil 3.2 g (90%). IR (film) ν (cm^{-1}) 3058, 2980, 1731, 1629, 1601, 1511, 1466, 1443, 1390, 1375, 1258, 1216, 1179, 1120, 1034, 972, 838, 811, 748. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 3H, Ar**H**), 7.42 (t, 1H, *J* = 7.5, Ar**H**), 7.32 (t, 1H, *J* = 7.5, Ar**H**), 7.14 – 7.11 (m, 2H, Ar**H**), 4.15 (q, 2H, *J* = 9.1, $CO_2C\mathbf{H}_2CH_3$), 4.10 (t, 2H, *J* = 6.2, $OC\mathbf{H}_2CH_2$), 2.55 (t, 2H, *J* = 7.2, $O_2CC\mathbf{H}_2CH_2$), 2.16 (p, 2H, *J* = 6.2, $OCH_2C\mathbf{H}_2CH_2$), 1.26 (t, 3H, *J* = 7.2, $OCH_2C\mathbf{H}_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 156.9, 134.7, 129.5, 129.1, 127.8, 126.8, 126.5, 123.7, 119.0, 106.7, 66.8, 60.6, 31.0, 24.8, 14.4. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{16}H_{19}O_3$) requires *m/z* 259.1334, found *m/z* 259.1329.



4-(Naphthalen-2-yloxy)butanal

A dry flask containing ethyl 4-(naphthalen-2-yloxy)butanoate (4.8 g, 18.58 mmol) and 300 mL CH_2Cl_2 was cooled to –78 °C and 3.47 mL (19.5 mmol) of diisobutylaluminium hydride (DIBAL-H) was added. After 3 h the reaction was quenched at 0 °C with 0.8 mL H_2O, 0.8 mL 1M NaOH solution and then 2 mL H_2O. The mixture was then warmed to 21 °C and stirred for 15 min. $MgSO_4$ was then added and stirred for 15 min. The filtrate was then collected, concentrated *in vacuo* and purified by column chromatography yielding white solid (3.04 g, 76%). IR (film) ν (cm^{-1}) 3058, 2940, 2827, 2725, 1722, 1628, 1509, 1465, 1389, 1258, 1216, 1181, 1120, 1057, 1017, 994, 959, 839, 813, 749. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H, C**H**O), 7.77 – 7.16 (m, 3H, Ar**H**), 7.44 (t, 1H, *J* = 7.8, Ar**H**), 7.34 (t, 1H, *J* = 7.8, Ar**H**), 7.14 – 7.10 (m, 2H, Ar**H**), 4.08 (t, 2H, *J* = 6.0, $OC\mathbf{H}_2CH_2$), 2.67 (t, 2H, *J* = 7.1, $CH_2C\mathbf{H}_2CHO$), 2.18 – 2.13 (m, 2H, $CH_2C\mathbf{H}_2CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.0, 156.8, 134.6, 129.6, 129.1, 127.8, 126.9, 126.6, 123.8, 118.9, 106.8, 66.8, 40.8, 22.1. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{14}H_{15}O_2$) requires *m/z* 215.1072, found *m/z* 215.1068.

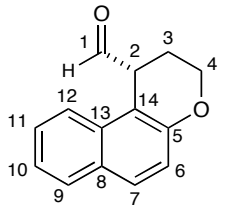


Table 2, Entry 4:

(R)-1,3,4-Trihydro-phenanthren-(1-ether)-4-carbaldehyde

Prepared according to procedure B-1: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (50 mg, 0.122 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (1318 mg, 1.28 mmol), and Na_2HPO_4 (87 mg, 0.609 mmol), acetone (6 mL), H_2O (11 μL, 0.609 mmol) and 4-(naphthalen-2-yloxy)butanal (131 mg, 0.609 mmol). (*Note: yield and % ee were determined with the corresponding alcohol*). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1H, H1), 7.80 (d, 1H, *J* = 8.1, H9), 7.76 (d, 1H, *J* = 8.5, H12), 7.71 (d, 1H, *J* = 9.0, H7), 7.51 (t, 1H, *J* = 8.1, H11), 7.37 (t, 1H, *J* = 7.7, H10), 7.08 (d, 1H, *J* = 9.0, H6), 4.36 – 4.33 (m, 1H, H4), 4.17 – 4.16 (m, 1H, H2), 4.06 (td, 1H, *J* = 11.5, 2.3, H4), 2.55 (ddd, 1H, *J* = 14.1, 5.6, 2.8, H3), 2.21 – 2.13 (m, 1H, H3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.2 (C1), 153.7 (C5), 133.0 (C13), 129.9 (C7), 129.4 (C8), 129.2 (C9), 127.4 (C11), 123.9 (C10), 121.7 (C12), 119.5 (C6), 108.5 (C14), 63.6 (C4), 43.8 (C2), 22.1 (C3).

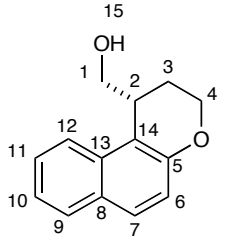
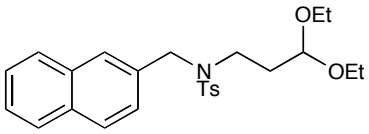


Table 2, Entry 4:

(R)-1,3,4-Trihydro-phenanthren-(1-ether)-4-methanol

Prepared according to procedure B-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (50 mg, 0.122 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (1318 mg, 1.28 mmol), and Na_2HPO_4 (87 mg, 0.609 mmol), acetone (6 mL), H_2O (11 μl, 0.609 mmol) and 4-(naphthalen-2-yloxy)butanal (131 mg, 0.609

mmol). The title compound was isolated as a white solid (92 mg, 70%, 95% ee). IR (film) ν (cm^{-1}) 3395, 2935, 2884, 1622, 1599, 1514, 1469, 1434, 1403, 1375, 1266, 1234, 1093, 1013, 814, 749. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, 1H, *J* = 8.5, H12), 7.74 (d, 1H, *J* = 8.1, H9), 7.61 (d, 1H, *J* = 8.9, H7), 7.50 – 7.45 (m, 1H, H11), 7.35 – 7.29 (m, 1H, H10), 7.02 (d, 1H, *J* = 8.9, H6), 4.34 – 4.29 (m, 2H, H4), 4.11 – 4.09 (m, 1H, H1), 3.82 – 3.77 (m, 1H, H1), 3.58 – 3.55 (m, 1H, H2), 2.34 – 2.31 (m, 1H, H3), 2.16 – 2.09 (m, 1H, H3), 1.67 (s, 1H, H15). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 133.0, 129.3, 129.0, 128.9, 126.8, 123.3, 121.9, 119.3, 113.0, 65.1, 62.2, 33.0, 23.2. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{14}H_{15}O_2$) requires *m/z* 215.1072, found *m/z* 215.1064. The enantiomeric excess was determined by HPLC using a Chiracel OD-H column (25 cm × 0.46 cm) with 5% isopropanol in hexane as the mobile phase; t_r = 21.43 and 25.77 min. $[\alpha]_D^{23}$ = -255 (c = 1, $CHCl_3$, 92% ee). The regiochemistry is assigned on the basis of the aromatic ^{1}H NMR coupling pattern where on the functionalized portion of the naphthal system two doublets (δ 7.61 and 7.02 ppm) are seen to couple to each other (8.9 Hz). These correlations show up clearly in the ^{1}H-^{1}H COSY NMR experiment and the coupling constant is consistent with vicinal ^{1}H coupling (see provided NMR spectra). If the arylation occurred at the naphthal 3-position two singlets would be expected.

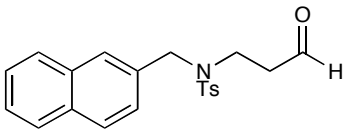


***N*-(3,3-diethoxypropyl)-*N*-(naphthalen-2-ylmethyl)-para-toluenesulfonamide**

To a dry round bottom flask charged with a stir bar was added 1 g (3.32 mmol) *N*-(3,3-diethoxypropyl)-para-toluenesulfonamide,[7] 10 mL DMF and then solid NaH (88 mg, 3.32 mmol) NaH. After stirring for 30 min 0.733 g (3.32 mmol) 2-(bromomethyl)naphthalene was added and stirred for 12 h. The reaction was quenched with 100 mL saturated aqueous NH_4Cl, the product extracted with 200 mL EtOAc then the organic layer was washed with 100 mL saturated aqueous $NaHCO_3$ and 100 mL brine. After concentration *in vacuo* the title compound was purified by column chromatography (20% EtOAc/hexane) and isolated as a clear oil (1.3 g, 89%). IR (film) ν (cm^{-1}) 2977, 1599,

(7) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54.

1339, 1266, 1160, 1123, 1060, 930, 816, 737, 659. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.70 (m, 5H, Ar**H**), 7.64 (s, 1H, Ar**H**), 7.47 – 7.42 (m, 3H, Ar**H**), 7.30 (d, 2H, *J* = 8.0, Ar**H**), 4.44 (s, 2H, NC**H**$_2$Ar), 4.26 (t, 1H, *J* = 5.5, EtO_2C**H**), 3.41 – 3.34 (m, 2H, NC**H**$_2$$CH_2$), 3.23 – 3.17 (m, 4H, OC**H**$_2$$CH_3$), 2.42 (s, 3H, ArC**H**$_3$), 1.69 – 1.63 (m, 2H, EtO_2CHC**H**$_2$), 1.00 (t, 6H, *J* = 7.1, OCH_2C**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 136.9, 134.1, 133.4, 133.2, 130.0, 128.7, 127.9, 127.9, 127.5, 127.4, 126.4, 126.4, 126.3, 100.9, 61.6, 52.8, 44.4, 32.7, 21.7, 15.3. HRMS (ESI$^+$) exact mass calc'd for $[M+Na]^+$ ($C_{25}H_{31}NNaO_4S$) requires *m/z* 464.1871, found *m/z* 464.1867.



***N*-(naphthalen-2-ylmethyl)-*N*-(3-oxopropyl)-para-toluenesulfonamide**

A solution of *N*-(3,3-diethoxypropyl)-*N*-(naphthalen-2-ylmethyl)-para-toluenesulfonamide (1 g, 2.26 mmol) in 8 mL $CHCl_3$ and 4 mL H_2O was treated with trifluoroacetic acid (5 g, 20 equiv) and stirred for 12 h. The reaction was quenched with 250 mL saturated aqueous $NaHCO_3$ and extracted with 250 mL EtOAc. After washing the organic phase with brine (250 mL) and concentration *in vacuo*, the title compound was purified by column chromatography and isolated as a white solid (520 mg, 63%). IR (film) ν (cm^{-1}) 3059, 2921, 2830, 1722, 1599, 1450, 1338, 1160, 1114, 1089, 1025, 936, 816, 748, 660. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.49 – 9.47 (m, 1H, C**H**O), 7.82 – 7.79 (m, 2H, Ar**H**), 7.75 – 7.74 (m, 3H, Ar**H**), 7.62 (s, 1H Ar**H**), 7.48 – 7.43 (m, 3H, Ar**H**), 7.33 (d, 2H, *J* = 8.4, Ar**H**), 4.43 (s, 2H, NC**H**$_2$Ar), 3.40 (t, 2H, *J* = 7.1, NC**H**$_2$$CH_2$), 2.53 (t, 2H, *J* = 7.1, CHOC**H**$_2$$CH_2$), 2.44 (s, 3H, ArC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 144.0, 136.2, 133.7, 133.4, 133.2, 130.2, 129.0, 128.0, 128.0, 127.5, 127.5, 126.7, 126.5, 126.3, 53.8, 44.1, 42.2, 21.8. HRMS (ESI$^+$) exact mass calc'd for $[M]^{+\bullet}$ ($C_{21}H_{21}NO_3S$) requires *m/z* 367.1242, found *m/z* 367.1242.

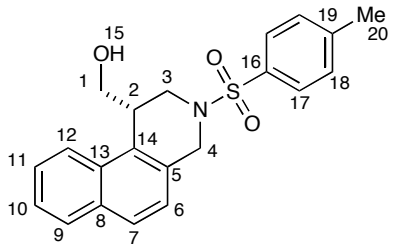
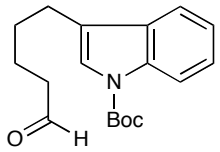


Table 2, Entry 5:

(*R*)-1,3,4-Trihydro-phenanthren-(3-*N*-para-toluenesulfonyl-amido)-4-methanol

Prepared according to procedure B-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (41 mg, 0.1 mmol), $[Fe(phen)_3]\cdot(PF_6)_3$ (1082 mg, 1.05 mmol), and Na_2HPO_4 (71 mg, 0.5 mmol), acetone (5 mL), H_2O (9 μl, 0.5 mmol) and *N*-(naphthalen-2-ylmethyl)-*N*-(3-oxopropyl)-para-toluenesulfonamide (184 mg, 0.5 mmol). The title compound was isolated as a white solid (130 mg, 71%, 96% ee). IR (film) ν (cm^{-1}) 3520, 3055, 2926, 2884, 1598, 1459, 1337, 1162, 1118, 1091, 1032, 951, 811, 781, 748, 706, 666. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, 1H, *J* = 8.5, H12), 7.81 – 7.55 (m, 3H, H9, H17), 7.66 (d, 1H, *J* = 8.5, H7), 7.52 (t, 1H, *J* = 8.1, H11), 7.44 (t, 1H, *J* = 7.8, H10), 7.35 (d, 2H, *J* = 8.2, H18), 7.09 (d, 1H, *J* = 8.5, H6), 4.86 (d, 1H, *J* = 15.4, H4), 4.43 (d, 1H, *J* = 15.4, H3), 3.97 – 3.65 (m, 3H, H1 H4), 3.67 (t, 1H, *J* = 6.9, H3), 2.77 (brs, 1H, H15), 2.67 (dd, 1H, *J* = 11.9, 2.7, H2), 2.41 (s, 3H, H20). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.1, 133.5, 132.7, 131.6, 130.1, 129.6, 129.0, 129.0, 127.9, 127.7, 127.0, 125.9, 125.9, 124.4, 122.9, 63.1, 48.0, 44.2, 38.4. HRMS (ESI^+) exact mass calc'd for $[M]^{+\bullet}$ ($C_{21}H_{21}NO_3S$) requires *m/z* 367.1242, found *m/z* 367.1243. The enantiomeric excess was determined by HPLC using a Chiracel OD-H column (25 cm × 0.46 cm) with 10% isopropanol in hexane as the mobile phase; t_r = 16.19 and 20.32 min. $[\alpha]_D^{23}$ = 51.0 (c = 1, $CHCl_3$, 96% ee). The regiochemistry is assigned on the basis of the aromatic ^{1}H NMR coupling pattern, where on the functionalized portion of the naphthal system two doublets (δ 7.66 and 7.09 ppm) are seen to couple to each other (8.5 Hz). These correlations show up clearly in the ^{1}H-^{1}H COSY NMR experiment and the coupling constant is consistent with vicinal ^{1}H coupling (see provided NMR spectra). If the arylation occurred at the naphthal 3-position two singlets would be expected.



3-(5-Oxo-pentyl)-indole-1-carboxylic acid *tert*-butyl ester

To a solution of 3-(4-ethoxycarbonyl-butyl)-indole-1-carboxylic acid *tert*-butyl ester[8] (1.85 g, 5.34 mmol) in CH_2Cl_2 (106 mL, 0.05 M), which was kept stirring under Ar at –78 °C, was added 6.4 mL of diisobutylaluminium hydride (DIBAL-H) solution (1.0 M in hexane) at such a rate that the temperature never rose above –70 °C. When the addition was complete, stirring was continued for an additional 30 min. Then the homogeneous and colorless mixture was transferred rapidly into 100 mL of ice-cold, vigorously stirred saturated aqueous solution of tartaric acid via a double-ended stainless steel needle. After removal of the organic layer, the aqueous phase was extracted with 2 × 100 mL CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and evaporated. Purification by column chromatography (hexane : ethyl acetate = 8:1) yielded the title compound as a colorless oil (1.61 g 83% yield). IR (film) ν (cm^{-1}) 2978, 2932, 2861, 2719, 1721, 1570, 1475, 1451, 1368, 1308, 1252, 1223, 1152, 1093, 1068, 1015, 856, 766, 743. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 – 9.76 (m, 1H, C**H**O), 8.14 (s, 1H, Ar**H**), 7.53 – 7.51 (m, 1H, Ar**H**), 7.37 (s, 1H, Ar**H**), 7.35 – 7.30 (m, 1H, Ar**H**), 7.27 – 7.22 (m, 1H, Ar**H**), 2.74 – 2.69 (m, 2H, $CH_2C\mathbf{H}_2Ar$), 1.81 – 1.74 (m, 2H, $CHOC\mathbf{H}_2CH_2$), 1.78 – 1.72 (m, 4H, $CH_2C\mathbf{H}_2CH_2$), 1.68 (s, 9H, $C(\mathbf{CH_3})_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 150.1, 135.8, 130.9, 124.5, 122.6, 122.5, 120.8, 119.2, 115.5, 83.6, 43.9, 28.9, 28.5, 24.9, 22.1. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{18}H_{24}NO_3$) requires *m/z* 301.1678, found *m/z* 301.1677.

(8) Beck, A. L.; Mascal, M.; Moody, C. J.; Slawin, A. M. Z.; Williams, D. J.; Coates, W. J. *J. Chem. Soc. Perkin Trans. I* **1992**, 813.

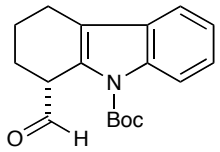


Table 2, Entry 6:

1-Formyl-1,2,3,4-tetrahydro-carbazole-9-carboxylic acid *tert*-butyl ester

Prepared according to general procedure C-1: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), CAN (230 mg, 0.21 mmol), and $NaHCO_3$ (33.6 mg, 0.4 mmol), NaO_2CCF_3 (55.6 mg, 0.4 mmol), acetone (2 mL, 0.1 M), H_2O (3.6 μl, 0.2 mmol) and 3-(5-oxo-pentyl)-indole-1-carboxylic acid *tert*-butyl ester (60.3 mg, 0.2 mmol). The title compound was isolated as a colorless oil (*Note: yield and % ee were determined with the corresponding alcohol*). IR (film) ν (cm^{-1}) 2977, 2933, 1719, 1612, 1477, 1456, 1362, 1317, 1257, 1220, 1153, 1138, 1116, 1086, 1044, 1030, 1018, 932, 841, 745. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (d, 1H, *J* = 1.2, C**H**O), 8.07 (d, 1H, *J* = 8.4, Ar**H**), 7.44 – 7.42 (m, 1H, Ar**H**), 7.28 (ddd, 1H, *J* = 8.4, 7.2, 1.2, Ar**H**), 7.24 – 7.20 (m, 1H, Ar**H**), 3.28 (m, 1H, CHO**C**HCH_2), 2.75 (dt, 1H, *J* = 16.8, 4.6, CH_2**C**$\mathbf{H_2}$Ar), 2.65 – 2.57 (m, 1H, CH_2**C**$\mathbf{H_2}$Ar), 2.29 – 2.23 (m, 1H, CH**C**$\mathbf{H_2}CH_2$), 2.01 – 1.94 (m, 1H, CH**C**$\mathbf{H_2}CH_2$), 1.93 – 1.85 (m, 1H, CH_2**C**$\mathbf{H_2}CH_2$), 1.73 – 1.65 (m, 1H, CH_2**C**$\mathbf{H_2}CH_2$), 1.63 (s, 9H, C(**C**$\mathbf{H_3})_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 150.5, 135.8, 130.7, 129.3, 124.5, 122.6, 119.6, 118.1, 115.7, 84.2, 47.5, 28.2, 24.5, 20.8, 19.5. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{18}H_{21}NNaO_3$) requires *m*/*z* 299.1521, found *m*/*z* 299.1525.

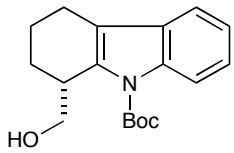
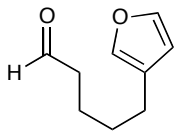


Table 2, Entry 6:

(*R*)-1-Hydroxymethyl-1,2,3,4-tetrahydro-carbazole-9-carboxylic acid *tert*-butyl ester

Prepared according to procedure C-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), CAN (230 mg, 0.21 mmol), and $NaHCO_3$ (33.6 mg, 0.4 mmol), NaO_2CCF_3 (55.6 mg, 0.4 mmol), acetone (2 mL, 0.1 M), H_2O (3.6 μl, 0.2 mmol) and 3-(5-oxo-pentyl)-indole-1-carboxylic

acid *tert*-butyl ester (60.3 mg, 0.2 mmol). The title compound was isolated as a colorless oil (49.5 mg, 84% yield, 96% ee). IR (film) ν (cm^{-1}) 3409, 2935, 1725, 1609, 1477, 1456, 1394, 1363, 1315, 1257, 1224, 1164, 1138, 1116, 1043, 988, 897, 844, 745. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, 1H, *J* = 8.2, 1.0, Ar**H**), 7.40 – 7.38 (m, 1H, Ar**H**), 7.24 (ddd, 1H, *J* = 8.0, 7.5, 1.5, Ar**H**), 7.19 (ddd, 1H, *J* = 7.5, 2.5, 1.0, Ar**H**), 3.96 (dd, 1H, *J* = 17.8, 8.5, HOC**H$_2$**CH), 3.68 (dd, 1H, *J* = 14.0, 8.5, HOC**H$_2$**CH), 3.67 (s, 1H, OH),), 2.76 (dd, 1H, *J* = 17.0, 4.5, CH_2C**H$_2$**Ar), 2.64 – 2.56 (m, 1H, CH_2**CH**CH_2), 2.18 – 2.17 (m, 1H, CH_2**CH$_2$**Ar), 21.12 (s, 1H, CH_2**CH$_2$**Ar), 1.90 – 1.78 (m, 3H, CHC**H$_2$**CH_2 and CH_2**CH$_2$**CH_2), 1.68 (s, 9H, $(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.8, 135.9, 135.3, 129.6, 123.7, 122.4, 118.1, 117.8, 115.7, 83.7, 65.2, 36.9, 28.2, 25.3, 20.8, 17.6. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{18}H_{24}NO_3$) requires *m/z* 301.1678, found *m/z* 301.1678. The enantiomeric excess was determined by HPLC using a Chiracel OJ-H column (25 cm × 0.46 cm) with 5% isopropanol in hexane as the mobile phase; t_r = 12.10 and 26.82 min. $[\alpha]_D^{23}$ = 18.0 (c = 1, $CHCl_3$, 96% ee).



5-Furan-3-yl-pentanal

To an oven dried 100 mL round bottom flask equipped with a stir bar was added 5-furan-3-yl-penta-2,4-dienoic acid methyl ester[9] (484 mg, 2.52 mmol) and THF (25 mL, 0.1 M). The solution was then degassed by evacuating and back filling the flask three times with argon. Against a positive flow of argon $RhCl(PPh_3)_3$ (Wilkinson's catalyst) (65 mg, 0.063 mmol) was added. A balloon filled with H_2 was then fitted to the reaction and stirred for 6 h at 40 °C. After the reaction was judged complete by TLC, excess amount of ether (~ 50 mL) was added to precipitate the $RhCl(PPh_3)_3$ catalyst. Then the precipitated dark brown solid was removed by filtering through a pad of silica gel and the product was flushed through with 100 mL ether. After concentrating *in vacuo*, the crude product (5-furan-3-yl-pentanoic acid methyl ester) was dissolved in CH_2Cl_2 (44 mL, 0.1 M). To the solution, which was kept stirring under Ar at –78 °C, was added 2.4 mL of

(9) Tufariello, J. J.; Dyszlewski, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1138.

diisobutylaluminium hydride (DIBAL-H) solution (1.0 M in hexane) at such a rate that the temperature stayed below –70 °C. When the addition was complete, stirring was continued for an additional 30 min. Then the homogeneous and colorless mixture was transferred rapidly into 100 mL of ice-cold, vigorously stirred saturated aqueous solution of tartaric acid via a double-ended stainless steel needle. After removal of the organic layer, the aqueous phase was extracted with 2 × 50 mL CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and evaporated. Purification by column chromatography (hexane : ethyl acetate = 10:1) yielded the title compound as a colorless oil (326 mg, 85% yield over two steps). IR (film) ν (cm^{-1}) 2934, 2860, 2720, 1721, 1501, 1460, 1410, 1390, 1163, 1064, 1023, 873, 779, 727. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (td, 1H, *J* = 9.8, 2.0, C**H**O), 7.32(dd, 1H, *J* = 2.0, 1.5, Ar**H**), 7.19 – 7.18 (m, 1H, Ar**H**), 6.22 (s, 1H, Ar**H**), 2.44 – 2.40 (m, 4H, CHO**C**$\mathbf{H_2}$$CH_2$ and CH_2**C**$\mathbf{H_2}$Ar), 1.67 – 1.61 (m, 2H, CH_2**C**$\mathbf{H_2}$$CH_2$), 1.60 – 1.53 (m, 2H, CH_2**C**$\mathbf{H_2}$$CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.4, 142.7, 138.8, 124.5, 110.8, 43.6, 29.4, 24.4, 21.5. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_9H_{13}O_2$) requires *m/z* 152.0837, found *m/z* 152.0835.

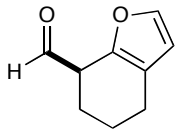


Table 2, Entry 7:

4,5,6,7-Tetrahydro-benzofuran-7-carbaldehyde

Prepared according to general procedure C-1: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), CAN (230 mg, 0.21 mmol), and $NaHCO_3$ (33.6 mg, 0.4 mmol), NaO_2CCF_3 (55.6 mg, 0.4 mmol), acetone (2 mL, 0.1 M), H_2O (3.6 μl, 0.2 mmol) and 5-furan-3-yl-pentanal (30.5 mg, 0.2 mmol). The title compound was isolated as a colorless oil (*Note: yield and % ee were determined with the corresponding alcohol*). IR (film) ν (cm^{-1}) 2934, 2853, 2716, 1723, 1631, 1502, 1442, 1388, 1349, 1298, 1235, 1214, 1156, 1132, 1104, 1036, 891, 732. ^{1}H NMR (400 MHz, C_6D_6) δ 9.42 (d, 1H, *J* = 2.0, C**H**O), 7.05 (dd, 1H, *J* = 2.0, 0.8, Ar**H**), 5.96 (d, 1H, *J* = 2.0, Ar**H**), 3.12 – 3.10 (m, 1H, CHO**C**$\mathbf{H}$$CH_2$), 2.11 – 2.02 (m, 2H, CH_2**C**$\mathbf{H_2}$Ar), 1.77 – 1.71 (m, 1H, CH**C**$\mathbf{H_2}$$CH_2$), 1.38 – 1.21 (m, 3H, CH**C**$\mathbf{H_2}$$CH_2$ and

$CH_2\mathbf{CH_2}CH_2$). ^{13}C NMR (125 MHz, C_6D_6) δ 198.5, 146.2, 142.6, 120.4, 111.1, 47.8, 23.6, 22.3, 21.4. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_9H_{11}O_2$) requires *m/z* 150.0681, found *m/z* 150.0680.

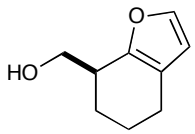
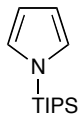


Table 2, Entry 7:

(4,5,6,7-Tetrahydro-benzofuran-7-yl)-methanol

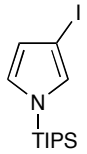
Prepared according to procedure C-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), CAN (230 mg, 0.21 mmol), and $NaHCO_3$ (33.6 mg, 0.4 mmol), NaO_2CCF_3 (55.6 mg, 0.4 mmol), acetone (2 mL, 0.1 M), H_2O (3.6 μl, 0.2 mmol) and 5-furan-3-yl-pentanal (30.5 mg, 0.2 mmol). The title compound was isolated as a colorless oil (29.4 mg, 96% yield, 90% ee). IR (film) ν (cm^{-1}) 3350, 2929, 2852, 1504, 1446, 1217, 1135, 1107, 1044, 891, 726. ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, 1H, *J* = 2.5, Ar**H**), 6.19 (d, 1H, *J* = 2.5, Ar**H**), 3.79 – 3.71 (m, 2H, HO$\mathbf{CH_2}$CH), 2.97 – 2.91 (m, 1H, $CH_2\mathbf{CH}CH_2$), 2.42 – 2.39 (m, 2H, $CH_2\mathbf{CH_2}$Ar), 1.94 – 1.79 (m, 2H, $CH_2\mathbf{CH_2}CH_2$), 1.69 – 1.56 (m, 3H, $CH_2\mathbf{CH_2}CH_2$ and O**H**). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 140.9, 118.3, 110.4, 65.5, 37.2, 26.1, 22.1, 21.7. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_9H_{13}O_2$) requires *m/z* 152.0837, found *m/z* 152.0835. The enantiomeric excess was determined by HPLC using a Chiracel OD-H column (25 cm × 0.46 cm) with 2% isopropanol in hexane as the mobile phase; t_r = 31.22 and 33.10 min. $[\alpha]_D^{23}$ = -1.14 (c = 1, $CHCl_3$, 90% ee).



1-(triisopropylsilyl)-pyrrole

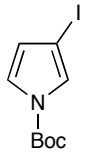
To a suspension of NaH (1.97 g, 49.2 mmol) in DMF (70 mL) at 0 °C was added a solution of pyrrole (3.10 mL, 44.7 mmol) in DMF (10 mL) in a dropwise manner. The reaction mixture was maintained at 0 °C for 1.5 h, and triisopropylsilyl chloride was

added dropwise. After stirring at 0 °C for 45 minutes, the reaction was quenched with H_2O (100 mL), and the aqueous phase extracted with Et_2O (2 × 200 mL). The combined organics were washed with H_2O (2 × 200 mL), and dried over Na_2SO_4. Evaporation of solvent yielded the product (9.06 g, 91%) as a colorless liquid. The ^1H NMR spectrum was identical to that reported in literature.[10]



3-iodo-1-(triisopropylsilyl)-pyrrole

To a solution of 1-(triisopropylsilyl)-1H-pyrrole (877 mg, 3.93 mmol) in acetone (30 mL) at –78 °C was added *N*-iodosuccinimide (1.06 g, 4.71 mmol) in one portion. The reaction mixture was stirred at –78 °C for 6 h, then warmed to room temperature over 3 h. After evaporation of the solvent, hexanes (6 mL) was added, and the suspension filtered through a plug of alumina. The filtrate was concentrated *in vacuo* and the residue purified by column chromatography (100% petroleum ether) to yield the title compound (1.07 g, 78%) as a pale yellow oil. ^1H spectrum was identical to that reported in literature.[8]

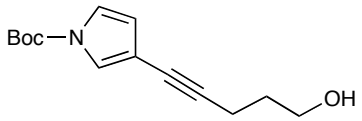


***tert*-butyl 3-iodo-pyrrole-1-carboxylate**

Tetrabutylammonium fluoride (5.66 g, 21.6 mmol) was added to a solution of 3-iodo-1-(triisopropylsilyl)-pyrrole (7.13 g, 20.4 mmol) in THF (60 mL) at room temperature. After stirring for 10 min Et_2O (225 mL) was added, and the opaque mixture was washed successively with H_2O (150 mL) and brine (150 mL), the organic layer was separated, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was dissolved in MeCN (45 mL), then 4-dimethylaminopyridine (295 mg, 2.42 mmol) was added followed by di-*tert*-

(10) Bray, B. L.; Mathies, P. H.; Naef, R.; Solas, D. R.; Tidwell, T. T.; Artis, D. R.; Muchowski, J. M. *J. Org. Chem.* **1990**, *55*, 6317.

butyl dicarbonate (5.35 g, 24.5 mmol). After stirring for 1.5 h Et_2O (240 mL) was added, followed by 1 M $KHSO_4$ (100 mL). The layers were separated, and the organic phase washed with 1 M $KHSO_4$ (5 × 50 mL), H_2O (80 mL), 1 M $NaHCO_3$ (50 mL), and brine (2 × 80 mL). After drying over $MgSO_4$ and evaporation of solvent, the residue was purified by column chromatography (100% petroleum ether) to afford the title compound as an orange oil in quantitative yield (3.49 g). ^1H and ^{13}C spectra were identical to those reported in literature.[11]

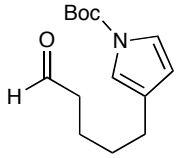


***tert*-butyl 3-(5-hydroxypent-1-ynyl)-pyrrole-1-carboxylate**

$Pd(PPh_3)_2Cl_2$ (165 mg, 0.24 mmol) and CuI (90 mg, 0.47 mmol) were dissolved in degassed triethylamine (30 mL), and the suspension was degassed by sparging with argon for a further 20 min. In a separate flask, *tert*-butyl 3-iodo-pyrrole-1-carboxylate (690 mg, 2.35 mmol) and 4-pentyn-1-ol (0.23 mL, 2.47 mmol) were dissolved in degassed triethylamine (12 mL), and then this solution was degassed for an additional 20 minutes. The substrate solution was then added to the flask containing catalyst via syringe at room temperature. The reaction mixture was heated to 50 °C and left to stir under an atmosphere of argon for 23 h. The solvent was removed *in vacuo* and the residue dissolved in hexane/EtOAc (1:1 v/v), filtered through a Florosil plug, washing with hexane/EtOAc (1:1 v/v), and concentrated *in vacuo*. Purification by column chromatography (petroleum ether : ether = 2:1) yielded the title compound as a brown oil (491 mg, 84%). IR (film) ν (cm^{-1}) 3377, 2980, 2937, 1746, 1490, 1385, 1343, 1271, 1258, 1219, 1158, 1137, 1074, 973, 849, 793, 771. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (s, 1H, Ar**H**), 7.13 (s, 1H, Ar**H**), 6.21(s, 1H, Ar**H**), 3.80 (t, 2H, J = 6.1, $CH_2CH_2\mathbf{CH_2}OH$), 2.50 (t, 2H, J = 6.9, $C\mathbf{H_2}CH_2CH_2OH$), 1.82 (m, 2H, $CH_2C\mathbf{H_2}CH_2OH$), 1.59 (s, 1H, O**H**) 1.58 (s, 9H, $O(C\mathbf{H_3})_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.2, 122.9, 119.9, 114.7, 108.4,

(11) Liu, J.-H.; Chan, H.-W.; Xue, F.; Wang, Q.-G.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **1999**, *64*, 1630.

89.1, 84.2, 74.8, 61.9, 31.4, 27.9, 16.1. HRMS (ESI$^+$) exact mass calc'd for $[M+H]^+$ ($C_{14}H_{20}NO_3$) requires *m/z* 250.1443, found *m/z* 250.1436.



***tert*-butyl 3-(5-oxopentyl)-1H-pyrrole-1-carboxylate**

A solution of *tert*-butyl 3-(5-hydroxypent-1-ynyl)-1H-pyrrole-1-carboxylate (485 mg, 1.95 mmol) in CH_2Cl_2 (20 mL) was degassed with H_2 for 15 min and Wilkinson's catalyst (90.0 mg, 97.3 mmol) added in one portion. The reaction mixture was stirred under an atmosphere of H_2 at room temperature for 7 h, the solvent evaporated, and Et_2O (25 mL) added. The suspension was filtered through Celite, flushing with Et_2O (100 mL), and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (17 mL) and pyridinium chlorochromate (713 mg, 3.31 mmol) was added in one portion. After stirring for 4 h, Et_2O (20 mL) and hexane (5 mL) were added, and the suspension was filtered through silica, washing with Et_2O (100 mL). After concentration, the residue was purified by column chromatography (petroleum ether : ether = 9:1) to afford 284 mg (60%) of the product as a colorless oil. IR (film) ν (cm^{-1}) 2981, 2935, 2862, 2719, 1737, 1486, 1459, 1403, 1370, 1348, 1319, 1245, 1160, 1122, 1067, 971, 853, 829, 772, 712. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (s, 1H, C**H**O), 7.15 (s, 1H , Ar**H**), 6.98 (s, 1H , Ar**H**), 6.07 (s, 1H, Ar**H**), 2.47 – 2.43 (m, 4H, ArC$\mathbf{H_2}$$CH_2CH_2C\mathbf{H_2}$CHO), 1.70 – 1.64 (m, 2H, $ArCH_2$$\mathbf{CH_2}$), 1.62 – 1.58 (m, 11H, $\mathbf{CH_2}CH_2CHO$, O(C$\mathbf{H_3}$)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.8, 148.9, 127.2, 120.1, 116.7, 112.7, 83.3, 43.8, 29.7, 28.0, 26.6, 21.7. HRMS (ESI$^+$) exact mass calc'd for $[M+H]^+$ ($C_{14}H_{22}NO_3$) requires *m/z* 252.1600, found *m/z* 252.1593.

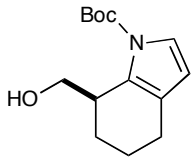
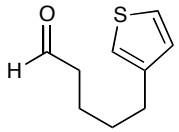


Table 2, Entry 8:

***tert*-butyl 7-(hydroxymethyl)-4,5,6,7-tetrahydro-indole-1-carboxylate**

The title compound was prepared according to general procedure C-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (14 mg, 0.04 mmol), cerric ammonium nitrate (218 mg, 0.40 mmol), $NaHCO_3$ (84 mg, 0.99 mmol), and sodium trifluoroacetate (54 mg, 0.40 mmol), acetone (2 mL), H_2O (3.6 μl, 0.20 mmol) and *tert*-butyl 3-(5-oxopentyl)-1H-pyrrole-1-carboxylate (50 mg, 0.20 mmol). The title compound was isolated in 42 mg as a colorless oil (82% yield, 96% ee). IR (film) ν (cm^{-1}) 3392, 2934, 1736, 1497, 1477, 1456, 1429, 1369, 1322, 1310, 1240, 1155, 1135, 1063, 1018, 927, 856, 773, 722. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, 1H, *J* = 3.4, Ar**H**), 5.95 (d, 1H, *J* = 3.4, Ar**H**), 3.85 – 3.81 (m, 1H, C$\mathbf{H_2}$OH), 3.61 – 3.56 (m, 1H, C$\mathbf{H_2}$OH), 3.41 – 3.34 (m, 1H, C**H**CH_2OH), 2.49 – 2.36 (m, 2H, ArC$\mathbf{H_2}CH_2CH_2$), 2.06 – 2.03 (m, 1H, $ArCH_2CH_2C\mathbf{H_2}$), 1.95 – 1.88 (m, 1H, $ArCH_2CH_2C\mathbf{H_2}$), 1.75 – 1.61 (m, 3H, $ArCH_2C\mathbf{H_2}CH_2$, O**H**), 1.56 (s, 9H, $O(C\mathbf{H_3})_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 129.4, 123.6, 120.6, 111.0, 83.4, 65.7, 36.3, 28.1, 25.2, 23.1, 18.2. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{14}H_{21}NNaO_3$) requires *m/z* 274.1419, found *m/z* 274.1413. The enantiomeric excess was determined by HPLC using a Chiracel OJ-H column (25 cm x 0.46 cm) with 2% isopropanol in hexane as the mobile phase; t_r = 15.92 and 18.18 min. $[\alpha]_D^{23}$ = –13.4 (*c* = 1.1, $CHCl_3$, 91% ee).



5-Thiophen-3-yl-pentanal

To an oven dried 100 mL round bottom flask equipped with a stir bar was added 5-thiophen-3-yl-pent-4-yn-1-ol[12] (851 mg, 5.0 mmol) and MeOH (89 mL, 0.2M). The

[12] Feuerstein, M.; Dpicet, H.; Santelli, M. *J. Mol. Catal. A: Chem.* **2006**, *256*, 75.

solution was then degassed by evacuating and back filling the flask three times with argon. Against a positive flow of argon 10% palladium on carbon (85.1 mg, 10 wt%) was added. A balloon filled with H_2 was then fitted to the reaction and stirred for 12 h. After the reaction was judged complete by TLC, the Pd/C was removed by filtering through a pad of Celite and the product was flushed through with 100 mL EtOAc. After concentrating *in vacuo*, the crude product (5-thiophen-3-yl-pentan-1-ol) was dissolved in CH_2Cl_2 (50 mL, 0.1 M) and pyridinium chlorochromate (1.62 g, 7.5 mmol) was added in one portion. After stirring for 4 h, Et_2O (30 mL) and hexane (10 mL) were added, and the suspension was filtered through silica, washing with Et_2O (100 mL). After concentration, the residue was purified by column chromatography (hexane:EtOAc = 10:1) to afford the title compound as a colorless oil (614 mg, 73% yield). IR (film) ν (cm^{-1}) 3103, 2933, 2859, 2721, 1720, 1536, 1459, 1409, 1389, 1232, 1153, 1079, 856, 833, 773, 685. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 – 9.76 (m, 1H, C**H**O), 7.26 – 7.24 (m, 1H, Ar**H**), 6.94 (s, 1H, Ar**H**), 6.94 – 6.93 (m, 1H, Ar**H**), 2.67 (t, 2H, *J* = 6.7, $CH_2C\mathbf{H}_2Ar$), 2.48 – 2.44 (m, 2H, CHOC$\mathbf{H}_2$ CH_2), 1.70 – 1.64 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 142.2, 128.0, 125.3, 120.1, 43.6, 29.9, 29.9, 21.6. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_9H_{13}OS$) requires *m/z* 168.0609, found *m/z* 168.0604.

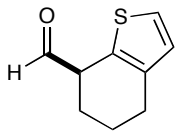


Table 2, Entry 9:

4,5,6,7-Tetrahydro-benzo[b]thiophene-7-carbaldehyde

Prepared according to procedure C-1: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), CAN (230 mg, 0.21 mmol), and $NaHCO_3$ (33.6 mg, 0.4 mmol), NaO_2CCF_3 (55.6 mg, 0.4 mmol), acetone (2 mL, 0.1 M), H_2O (3.6 μl, 0.2 mmol) and 5-thiophen-3-yl-pentanal (33.7 mg, 0.2 mmol). The title compound was isolated as a colorless oil (*Note: yield and % ee were determined with the corresponding alcohol*). IR (film) ν (cm^{-1}) 3106, 2933, 2841, 2722, 1721, 1553, 1440, 1390, 1320, 1286, 1199, 1138, 1092, 1064, 1022, 1005, 962, 875, 851, 822, 802, 705. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (d, 1H, *J* = 2.0, C**H**O), 7.20 (dd, 1H, *J*

= 5.2, 0.8, Ar**H**), 6.84 (d, 1H, *J* = 5.2, Ar**H**), 3.63 (dt, 1H, *J* = 12.0, 6.0, CHO**CH**CH_2), 2.64 (dt, 2H, *J* = 6.0, 1.6, CH_2**C**$\mathbf{H_2}$Ar), 2.20 – 2.13 (m, 1H, CH**C**$\mathbf{H_2}CH_2$), 2.06 – 1.98 (m, 1H, CH**C**$\mathbf{H_2}CH_2$), 1.84 – 1.78 (m, 2H, CH_2**C**$\mathbf{H_2}CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.4, 137.7, 129.0, 127.9, 124.4, 48.6, 25.3, 23.9, 20.7. HRMS (EI^+) exact mass calc'd for $[M+H]^+$ ($C_9H_{11}OS$) requires *m/z* 166.0451, found *m/z* 166.0451.

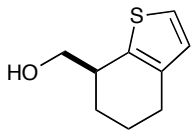
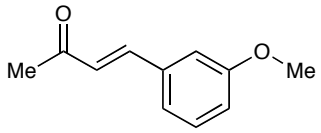


Table 2, Entry 9:

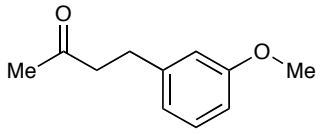
(4,5,6,7-Tetrahydro-benzo[b]thiophen-7-yl)-methanol

Prepared according to procedure C-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (16.4 mg, 0.04 mmol), CAN (230 mg, 0.21 mmol), and $NaHCO_3$ (33.6 mg, 0.4 mmol), NaO_2CCF_3 (55.6 mg, 0.4 mmol), acetone (2 mL, 0.1 M), H_2O (3.6 μl, 0.2 mmol) and 5-thiophen-3-yl-pentanal (33.7 mg, 0.2 mmol). The title compound was isolated as a colorless oil (32.5 mg, 96% yield, 94% ee). IR (film) ν (cm^{-1}) 3341, 2926, 2857, 1669, 1442, 1314, 1047, 877, 833, 705, 664. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, 1H, *J* = 5.0, Ar**H**), 6.80 (d, 1H, *J* = 5.0, Ar**H**), 3.77 (d, 2H, *J* = 6.0, HO**C**$\mathbf{H_2}$CH), 3.04 (p, 1H, *J* = 6.0, CH_2**CH**CH_2), 2.67 - 2.55 (m, 2H, CH_2**C**$\mathbf{H_2}$Ar), 2.01 – 1.96 (m, 1H, CH**C**$\mathbf{H_2}CH_2$), 1.95 – 1.89 (m, 1H, CH**C**$\mathbf{H_2}CH_2$), 1.75 – 1.63 (m, 3H, CH_2**C**$\mathbf{H_2}CH_2$ and **H**OCH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.9, 136.0, 127.7, 122.6, 67.5, 38.9, 26.6, 25.8, 21.4. HRMS (EI^+) exact mass calc'd for $[M+H]^+$ ($C_9H_{13}OS$) requires *m/z* 168.0609, found *m/z* 168.0612. The enantiomeric excess was determined by HPLC using a Chiracel OD-H column (25 cm × 0.46 cm) with 3% isopropanol in hexane as the mobile phase; t_r = 24.11 and 26.57 min. $[\alpha]_D^{23}$ = –40.65 (c = 1, $CHCl_3$, 94% ee).



(*E*)-4-(3-methoxyphenyl)but-3-en-2-one

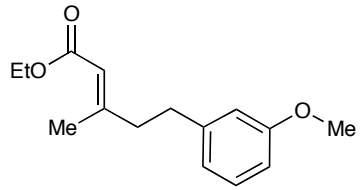
To a solution of 3-methoxybenzaldehyde (4.47 mL, 36.7 mmol) in acetone (27 mL, 367 mmol) was added 1 M NaOH (75 mL) via dropwise addition funnel over 40 min. After stirring for 1 h the reaction mixture was neutralized with 6 M HCl, and the aqueous phase extracted with EtOAc (2 × 75 mL). The combined organics were washed with brine (1 × 80 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Purification by flash chromatography (petroleum ether : ether = 5:1/v:v) yielded 5.40 g (83%) of the desired product. The ^{1}H NMR spectrum is in agreement to that reported in literature.[13]



4-(3-methoxyphenyl)butan-2-one

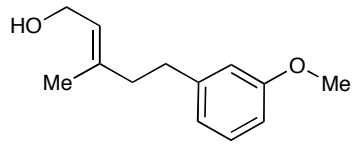
A solution of (*E*)-4-(3-methoxyphenyl)but-3-en-2-one (9.70 g, 55.0 mmol) and glacial acetic acid (94.5 μL, 1.65 mmol) in EtOH (85 mL) was degassed with Ar for 20 min, and then palladium on carbon (970 mg, 10 wt %) was added. After stirring for 2 days the reaction mixture was filtered through Celite, washing with EtOAc (100 mL), and the filtrate concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc = 5:1/v:v) to yield the product (9.01 g, 92%) as a pale yellow liquid. ^{1}H NMR and ^{13}C NMR data are identical to that reported in literature.[14]

(13) Evans, D. A.; Gauchet-Prunet, J. A.; Carreira, E. M.; Charette, A. B. *J. Org. Chem.* **1991**, *56*, 741.
(14) Ranu, B. C.; Dutta, J.; Guchhait, S. K. *Org. Lett.* **2001**, *3*, 2603.



(*E*)-ethyl 5-(3-methoxyphenyl)-3-methylpent-2-enoate

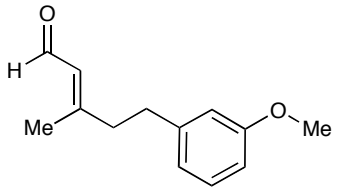
NaH (52 mg, 2.19 mmol) was added to a solution of triethylphosphonoacetate (0.42 mL, 2.08 mmol) in THF (1 mL) and the reaction mixture stirred for 30 min at room temperature. To the suspension was added a solution of 4-(3-methoxyphenyl)butan-2-one (371 mg, 2.08 mmol) in THF (1 mL), and the mixture stirred for 17 h. The solvent was removed *in vacuo*, the residue dissolved in CH_2Cl_2, and a saturated solution of $NaHCO_3$ was added. The aqueous layer was extracted with ether, dried over $MgSO_4$, and concentrated *in vacuo*. Purification by column chromatography (petroleum ether : ether = 16:1/v:v) yielded 255 mg (49%) of the title compound, as well as 28 mg (5%) of the corresponding (Z)-isomer. IR (film) ν (cm^{-1}) 2979, 2941, 2836, 1713, 1648, 1602, 1585, 1489, 1456, 1438, 1383, 1368, 1352, 1258, 1223, 1144, 1095, 1044, 868, 782, 695. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (t, 1H, *J* = 7.84, Ar**H**), 6.78-6.72 (m, 3H, Ar**H**), 5.69 (s, 1H, C=C**H**), 4.15 (q, 2H, *J* = 7.13, O**CH_2**CH_3), 3.80 (s, 3H, ArO**CH_3**), 2.76 (dd, 2H, *J* = 6.83, 9.41, Ar**CH_2**CH_2), 2.44 (m, 2H, $ArCH_2$**CH_2**), 2.21 (s, 3H, OCH_2**CH_3**), 1.28 (t, 3H, *J* = 7.13, C=CC**H_3**). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 159.8, 159.0, 142.8, 129.4, 120.7, 116.1, 114.2, 111.4, 59.6, 55.2, 42.7, 34.1, 19.0, 14.4. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_{15}H_{21}O_3$) requires *m/z* 249.1491, found *m/z* 249.1382.



(*E*)-5-(3-methoxyphenyl)-3-methylpent-2-en-1-ol

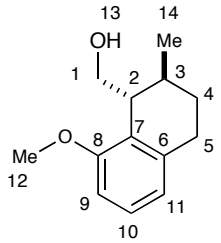
To a solution of (*E*)-ethyl 5-(3-methoxyphenyl)-3-methylpent-2-enoate (2.04 g, 8.22 mmol) in Et_2O (20 mL) at 0 °C was added a 1.0 M solution of diisobutylaluminium hydride (DIBAL-H) in hexanes (16.4 mL) in a dropwise manner, and the reaction warmed to room temperature over 3.5 h. The mixture was diluted with Et_2O (65 mL), cooled to 0 °C and quenched slowly with brine (50 mL). 4 M HCl (50 mL) was then

added drop-wise, and the aqueous layer extracted with Et_2O (3 × 60 mL) and the combined organics washed with brine (1 × 70 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane : EtOAc = 2:1/v:v) to afford 1.48 g (88%) of the desired product as a colorless oil. IR (film) ν (cm^{-1}) 3338, 2936, 1602, 1585, 1489, 1455, 1437, 1313, 1253, 1152, 1052, 996, 873, 780, 695. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (m, 1H, Ar**H**), 6.77 (d, 1H, *J* = 7.3, Ar**H**), 6.74 (m, 2H, Ar**H**), 5.43 (t, 2H, *J* = 6.3, C=C**H**), 4.15 (m, 2H, C**H**$_2$OH), 3.80 (s, 3H, OC**H**$_3$), 2.72 (m, 2H, ArC**H**$_2$CH$_2$), 2.32 (m, 2H, ArCH$_2$C**H**$_2$), 1.73 (s, 3H, C=CC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 143.6, 139.2, 129.3, 123.8, 120.8, 114.2, 111.1, 59.4, 55.2, 41.3, 34.4, 16.4. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{13}H_{18}NaO_2$) requires *m/z* 229.1204, found *m/z* 229.1051.



(*E*)-5-(3-methoxyphenyl)-3-methylpent-2-enal

To a solution of (*E*)-5-(3-methoxyphenyl)-3-methylpent-2-en-1-ol (483 mg, 2.34 mmol) in dry CH_2Cl_2 (12 mL) was added MnO_2 (1.02 g, 11.7 mmol). The reaction mixture was stirred for 2 days, filtered through a pad of Celite, and washed with CH_2Cl_2. The filtrate was concentrated *in vacuo* and the residue purified by column chromatography (petroleum ether : ether = 4:1/v:v) to obtain 252 mg (52%) of the title compound. IR (film) ν (cm^{-1}) 2945, 2836, 1671, 1602, 1585, 1490, 1455, 1438, 1382, 1259, 1195, 1152, 112, 1053, 869, 781, 696. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (d, 1H, J = 8.0, C**H**O), 7.21 (t, 1H, *J* = 7.9, Ar**H**), 6.80-6.70 (m, 3H, Ar**H**), 5.90 (d, 1H, *J* = 8.0), 3.80 (s, 3H, OC**H**$_3$), 2.80 (m, 2H, ArC**H**$_2$CH$_2$), 2.52 (m, 2H, ArCH$_2$C**H**$_2$), 2.20 (s, 3H, C=CC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.3, 162.9, 159.7, 142.2, 129.6, 127.6, 120.6, 114.2, 111.4, 55.2, 42.1, 33.6, 17.8. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_{13}H_{16}NaO_2$) requires *m/z* 227.1048, found *m/z* 227.0922.

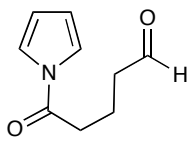


(1*R*, 2*S*)-((8-methoxy-2-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)methanol

A solution of (*E*)-5-(3-methoxyphenyl)-3-methylpent-2-enal (50.0 mg, 0.24 mmol) in $CHCl_3$ (1.2 mL) was degassed with argon (ca. 2 min), and the mixture cooled to –78 °C. The trichloroacetic acid salt of (*S*)-2-*tert*-butyl-3-methylimidazolidin-4-one (16 mg, 49 μmol) and Hanztsch *tert*-butyl ester (96 mg, 0.32 mmol) were then added and the reaction mixture warmed to –60 °C. After stirring for 12 h, the mixture was filtered through silica, washing with Et_2O, and the filtrate washed successively with 5 M HCl (6 × 2 mL), saturated aqueous $NaHCO_3$ (2 × 2 mL), and brine (1 × 2 mL). The organics were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was then dissolved in acetone (2.4 mL) and the solution degassed with argon (ca. 2 min) before being added to a Schlenk tube containing the trifluoro acetic acid salt of (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methylimidazolidin-4-one at –78 °C under an atmosphere of argon. The mixture was then placed under vacuum at –78 °C for 30 min and backfilled with argon before adding $[Fe(phen)_3]\cdot 3PF_6$ (505 mg, 0.49 mmol) and Na_2HPO_4 (34 mg, 0.24 mmol). The reaction mixture was warmed to –30 °C for 17 h, cooled to –78 °C, and Et_2O (12 mL) was added. The suspension was filtered through a fritted funnel into a solution of $NaBH_4$ (93 mg, 2.45 mmol) in EtOH (5 mL) at –78 °C and stirred for 45 min before being warmed to 0 °C for an additional 10 min. The reaction was quenched with saturated aqueous NH_4Cl (5 mL) and the organic phase extracted with Et_2O (3 × 15 mL). The combined organics were washed with brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane : EtOAc = 5:1/v:v) to yield the product as a white solid (35 mg, 70% yield). IR (film) ν (cm^{-1}) 3372, 2924, 1583, 1466, 1438, 1336, 1254, 1097, 1078, 1052, 1026, 780, 764. ^1H NMR (500 MHz, $CDCl_3$) δ 7.08 (t, 1H, *J* = 7.9, H10), 6.71 (d, 1H, *J* = 7.6, H9), 6.67 (d, 1H, *J* = 8.2, H11), 3.83 (s, 3H, H12), 3.78 – 3.74 (m, 1H, H1), 3.68 – 3.63 (m, 1H, H1), 2.96 – 2.93 (m, 1H, H2), 2.76 – 2.63 (m, 2H, H5), 2.22 – 2.17 (m, 1H, H3), 1.94 – 1.86 (m, 1H, H4), 1.82 – 1.79

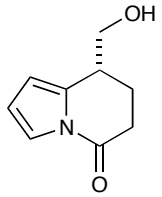
(m, 1H, H13), 1.47 – 1.42 (m, 1H, H4), 0.98 (d, 3H, J = 7.0, H14). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9 (C8), 139.0 (C6), 126.5 (C10), 124.6 (C7), 121.6 (C9), 107.4 (C11), 66.7 (C1), 55.3 (C12), 42.5 (C2), 28.3 (C3), 25.8 (C5), 25.3 (C4), 19.5 (C14). HRMS (ESI$^+$) exact mass calc'd for $[M+Na]^+$ ($C_{13}H_{18}NaO_2$) requires m/z 229.1204, found m/z 229.1198. The enantiomeric excess was determined by HPLC using a Chiracel OJ-H column (25 cm x 0.46 cm) with 2% isopropanol in hexane as the mobile phase; t_r = 17.93 and 19.59 min. $[\alpha]_D^{23}$ = –34.2 (c = 0.60, $CHCl_3$, 98% ee). The regiochemistry is assigned on the basis of the aromatic ^{1}H NMR coupling pattern where a triplet δ 7.08 is coupled to two doublets 6.71 and 6.67 ppm. These correlations show up clearly in the ^{1}H-^{1}H COSY NMR experiment and the average 7.9 Hz coupling constant is consistent with vicinal ^{1}H coupling (see provided NMR spectra). If the arylation occurred para to the methoxy group two doublets that couple to each other and a singlet would be expected.

(–)-Tashiromine Synthesis



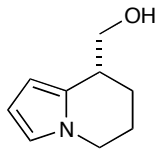
5-oxo-5-(1*H*-pyrrol-1-yl)pentanal

Methylmagnesium bromide (3 M in diethyl ether, 1.38 mL, 14.9 mmol) was added to toluene (45 mL) at 0 °C followed by freshly distilled pyrrole (1.00 g, 14.9 mmol) drop-wise, and the mixture heated to 55 °C for 1 h. A solution of δ-valerolactone (1.38 mL, 14.9 mmol) in toluene (7.5 mL) was then added drop-wise and the reaction stirred for 11 h. After cooling to room temperature, CH_2Cl_2 (150 mL) was added, followed by saturated aqueous NH_4Cl (75 mL), and the mixture adjusted to pH = 6 with 10% HCl. The aqueous layer was extracted with CH_2Cl_2 (3 x 35 mL) and the combined organics washed successively with H_2O (2 x 60 mL) and brine (60 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated to afford 2.12 g of a crude, purple oil. The residue was dissolved in dry CH_2Cl_2 (85 mL), pyridinium chlorochromate (4.65 g, 21.6 mmol) was added, and the reaction stirred under argon for 4 h at room temperature. Et_2O (100 mL) was added, followed by hexanes (50 mL), and the mixture filtered through a pad of silica, flushing with Et_2O. The filtrate was concentrated *in vacuo*, and the residue purified by flash chromatography (6:1 hexanes : EtOAc) to obtain 747 mg of a white solid (30% yield). IR (film) ν (cm^{-1}) 3144, 2916, 2830, 2729, 1714, 1469, 1407, 1375, 1331, 1269, 1123, 1071, 917, 743, 701. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (s, 1H, C**H**O), 7.31 (brs, 2H, Ar**H**), 6.30 (s, 2H, Ar**H**), 2.91 (t, 2H, *J* = 7.1, NC=OC**H$_2$**), 2.65 (t, 2H, *J* = 6.7, CH_2C**H$_2$**CHO), 2.11 (p, 2H, *J* = 7, C**H$_2$**CH_2CHO). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.6, 169.8, 119.0, 113.3, 42.7, 33.3, 16.8. HRMS (ESI^+) exact mass calc'd for $[M+Na]^+$ ($C_9H_{11}NNaO_2$) requires *m/z* 188.0682, found *m/z* 188.0677.



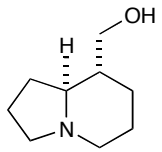
(*R*)-8-(hydroxymethyl)-7,8-dihydroindolizin-5(6*H*)-one

The title compound was prepared according to general procedure C-2: (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one trifluoroacetic acid salt (248 mg, 0.61 mmol), ceric ammonium nitrate (3.32 g, 6.05 mmol), $NaHCO_3$ (1.27 g, 15.1 mmol), and sodium trifluoroacetate (823 mg, 6.05 mmol), acetone (30 mL), H_2O (54.5 μL, 3.03 mmol), and 5-oxo-5-(1H-pyrrol-1-yl)pentanal (500 mg, 3.03 mmol). The crude product was chromatographed through silica gel (2:1 hex : EtOAc), and the inseparable product/catalyst mixture dissolved in Et_2O, with 4 M HCl in dioxane (0.13 mL, 0.53 mmol) added at 0 °C. The mixture was warmed to room temperature over 1.5 h, filtered, and concentrated to afford the title compound as a white solid (360 mg, 72% yield, 93% ee). IR (film) ν (cm^{-1}) 3424, 2937, 2881, 1717, 1574, 1489, 1404, 1361, 1304, 1210, 1149, 1103, 1075, 1052, 990, 874, 735, 687. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (brs, 1H, Ar**H**), 6.26 (brs, 1H, Ar**H**), 6.12 (brs, 1H, Ar**H**), 3.97 – 3.92 (m, 1H, C$\mathbf{H_2}$OH), 3.89 – 3.85 (m, 1H, C$\mathbf{H_2}$OH), 3.09 – 3.05 (m, 1H, ArC**H**), 2.87 – 2.82 (m, 1H, C=OC$\mathbf{H_2}$$CH_2$), 2.71 – 2.64 (m, 1H, C=OC$\mathbf{H_2}$$CH_2$), 2.25 – 2.19 (m, 1H, C=OCH_2C$\mathbf{H_2}$), 2.04 – 1.96 (m, 1H, C=OCH_2C$\mathbf{H_2}$), 1.58 (brs, 1H, O**H**). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 133.3, 116.8, 112.7, 108.8, 64.3, 36.3, 31.9, 24.6. HRMS (ESI^+) exact mass calc'd for $[M+H]^+$ ($C_9H_{12}NO_2$) requires *m/z* 166.0863, found *m/z* 166.0863. The enantiomeric excess was determined by SFC analysis using a Chiracel AS-H column (5% to 10% isopropanol, linear gradient, 100 bar, 35 °C oven, flow = 4.0 mL/min); (*R*)-enantiomer: t_r = 3.40 min, (*S*)-enantiomer: t_r = 3.59 min.



(*R*)-(5,6,7,8-tetrahydroindolizin-8-yl)methanol

To a flame-dried 2-dram vial charged with a suspension of $LiAlH_4$ (51 mg, 1.33 mmol) in dry THF (1 mL) at 0 °C was added $AlCl_3$ (178 mg, 1.33 mmol) in portions. The mixture was warmed to 35 °C with stirring for 30 min, and a solution of (*R*)-8-(hydroxymethyl)-7,8-dihydroindolizin-5(6*H*)-one in THF (0.25 mL) was added in a drop-wise manner. The reaction mixture was heated to 60 °C for 3 h, cooled to 0 °C, and H_2O (50 μL) added in a drop-wise fashion. After stirring for 10 min, 15% NaOH (aq, 50 μL) was added, the mixture stirred for an additional 10 min, and H_2O (0.15 mL) added. The solids were filtered through a pad of Celite, washing with EtOAc, and the filtrate concentrated *in vacuo*. The residue was purified by silica gel chromatography (2:1 hexanes : EtOAc) to afford the title compound as a colorless oil (15 mg, 83% yield). IR (film) ν (cm^{-1}) 3358, 2943, 2863, 1488, 1463, 1446, 1429, 1395, 1327, 1279, 1268, 1221, 1168, 1075, 1060, 1027, 976, 944, 776, 707. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (brs, 1H, Ar**H**), 6.15 (t, 1H, J = 3.1, Ar**H**), 5.98 (brs, 1H, Ar**H**), 4.00 – 3.96 (m, 1H, C$\mathbf{H_2}$OH), 3.90 – 3.77 (m, 3H, C$\mathbf{H_2}$OH, NC$\mathbf{H_2}$CH$_2$), 3.05 – 3.00 (m, 1H, C**H**CH$_2$OH), 2.09 – 1.99 (m, 2H, NCH$_2$C$\mathbf{H_2}$), 1.95 – 1.86 (m, 1H, C$\mathbf{H_2}$CHOH), 1.76 – 1.68 (m, 1H, C$\mathbf{H_2}$CHOH), 1.57 (brs, 1H, O**H**). ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.3, 119.7, 107.8, 103.8, 65.6, 45.4, 36.9, 24.3, 22.2. HRMS (ESI$^+$) exact mass calc'd for $[M+H]^+$ ($C_9H_{14}NO$) requires *m/z* 152.1070, found *m/z* 152.1069.



(–)-tashiromine

To an uncapped vial charged with MeOH (2 mL) and (*R*)-(5,6,7,8-tetrahydroindolizin-8-yl)methanol (46 mg, 0.30 mmol) was added 5% rhodium on alumina (14 mg, 30 w/w%) and the reaction vessel placed inside a sealed Parr autoclave. The autoclave was purged with hydrogen gas (4 x), then pressurized to 4 atm and the reaction mixture stirred at room temperature for 24 h, after which starting material was consumed as judged by TLC analysis. The suspension was filtered through a Celite pad, washing EtOAc, and concentrated *in vacuo*. The residue (98% NMR yield, 2:1 dr) was purified by silica gel chromatography (15% MeOH in CH_2Cl_2 with 1% aq. NH_4OH) to obtain 29 mg (62%) of the title compound. The spectral data was in agreement with those reported in literature.[15] $[\alpha]_D^{23} = -35$ (*c* 0.88, $CHCl_3$, 89% ee). (Note: % ee was determined, after conversion to the naphthoyl ester of the title compound, through HPLC analysis using a Chiracel OD-H column (25 cm x 0.46 cm) with 5% isopropanol in hexane as the mobile phase; t_r = 6.73 and 7.54 min).

Absolute Configuration of α-Aryl Products

Using the correlation with the natural product (–)-tashiomine's optical rotation we obtain (*R*)-configuration when using either the (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-(naphthalen-2-ylmethyl)imidazolidin-4-one (**5**) or (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-benzyl-imidazolidin-4-one (**2**) catalyst. This agrees with coincident report where the product crystal structure was obtained.[16]

(15) Kim, S.-H.; Kim, S.-I.; Lai, S.; Cha, J. K. *J. Org. Chem.* **1999**, *64*, 6771.
(16) Nicolaou, K. C.; Reingruber, R.; Sarlah, D.; Bräse, S. *J. Am. Chem. Soc.* **2009**, *131*, 2086.

The Enantioselective α-Arylation of Aldehydes via Organo-SOMO Catalysis: An Explanation of Conflicting Results and Mechanistic Interpretations

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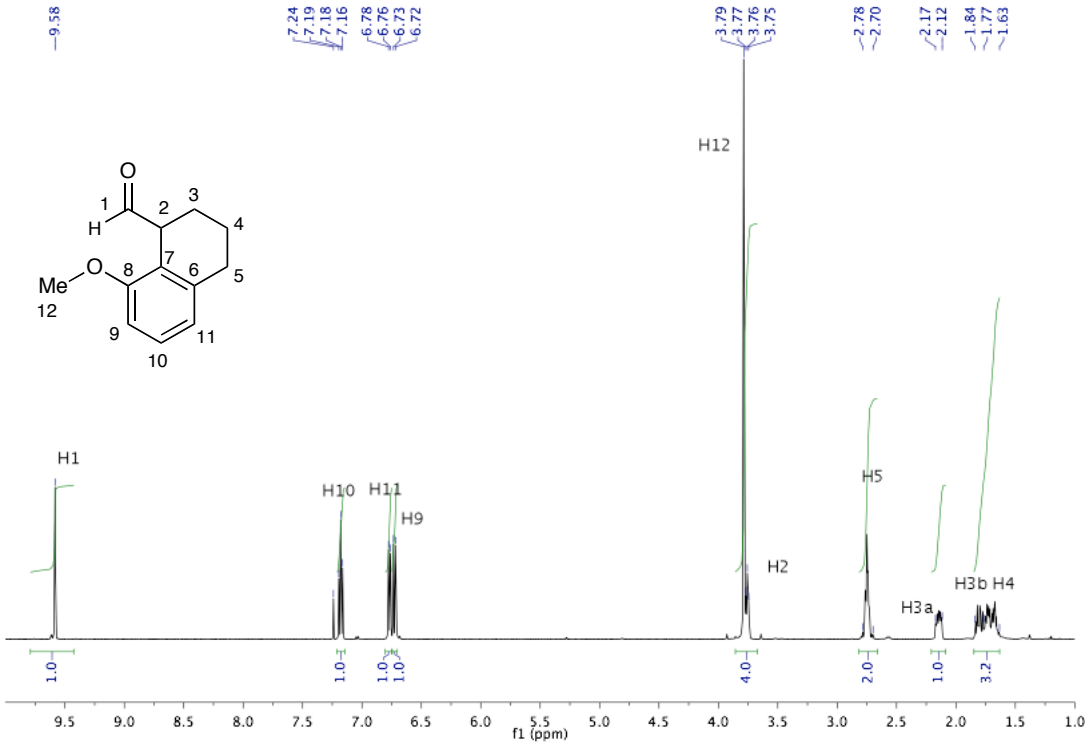
Supporting Information – NMR Spectra

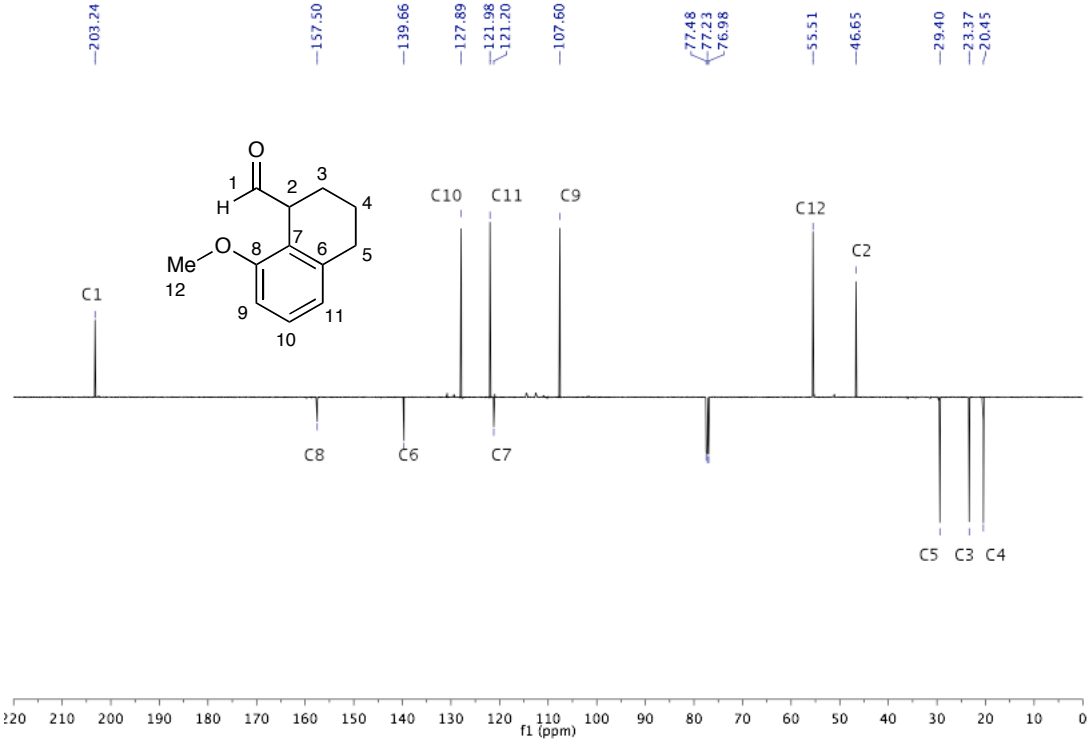
Table of Contents

Table 2, Entry 1:

^{1}H NMR $CDCl_3$ 500 MHz



^{13}C APT NMR $CDCl_3$ 125 MHz



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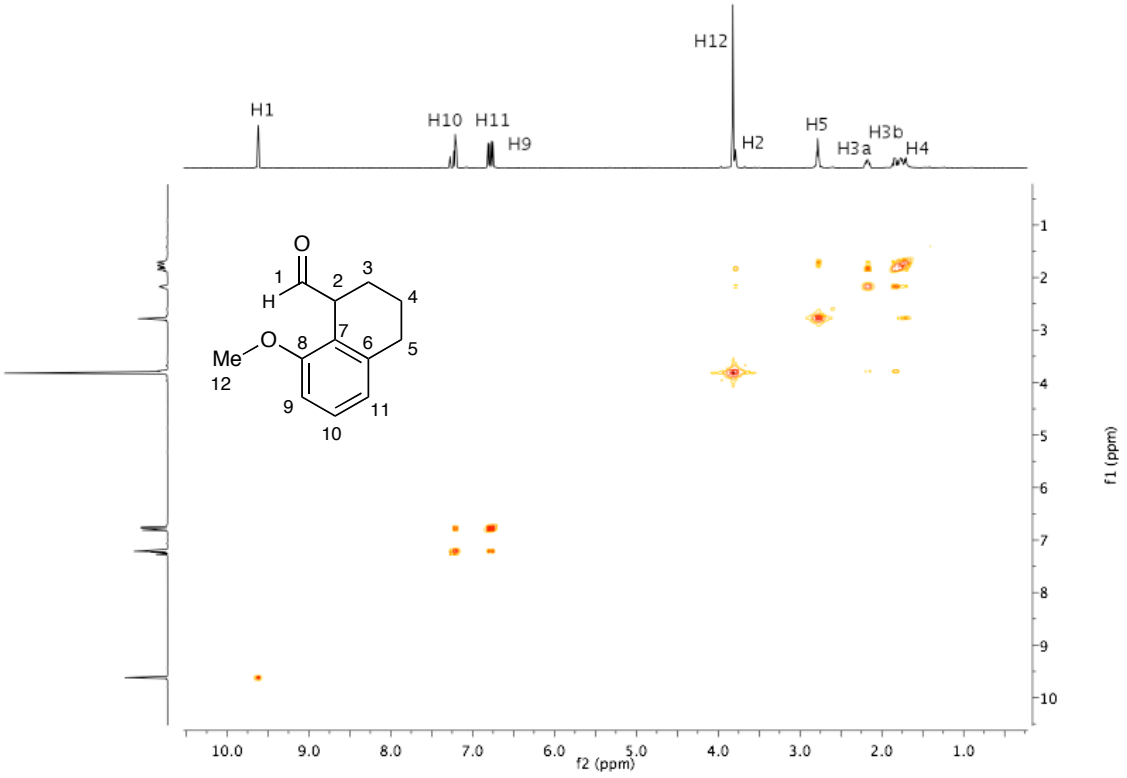
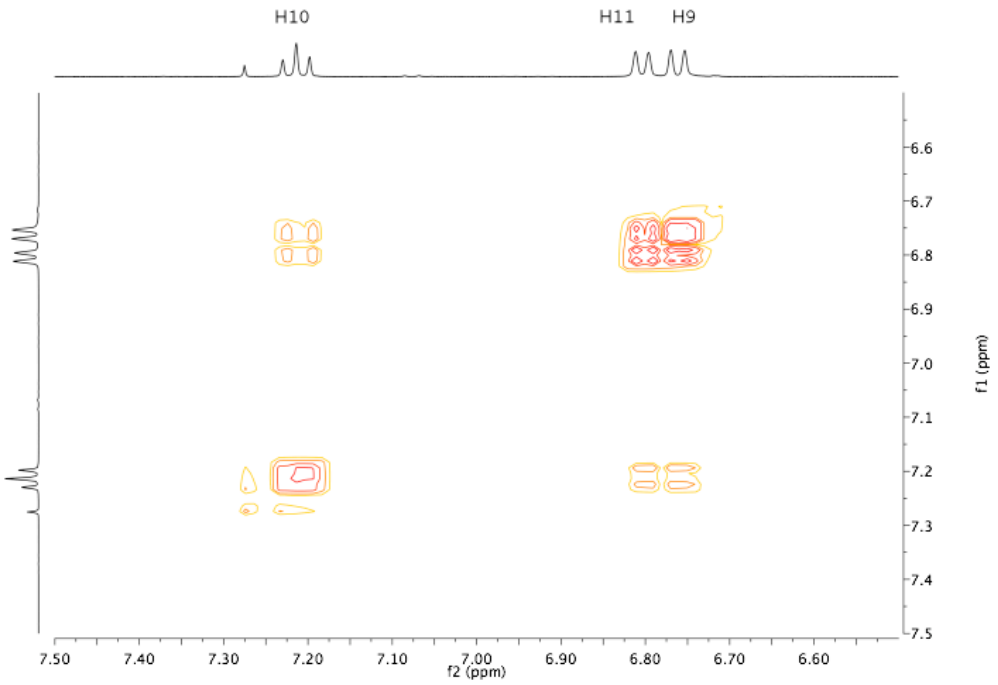
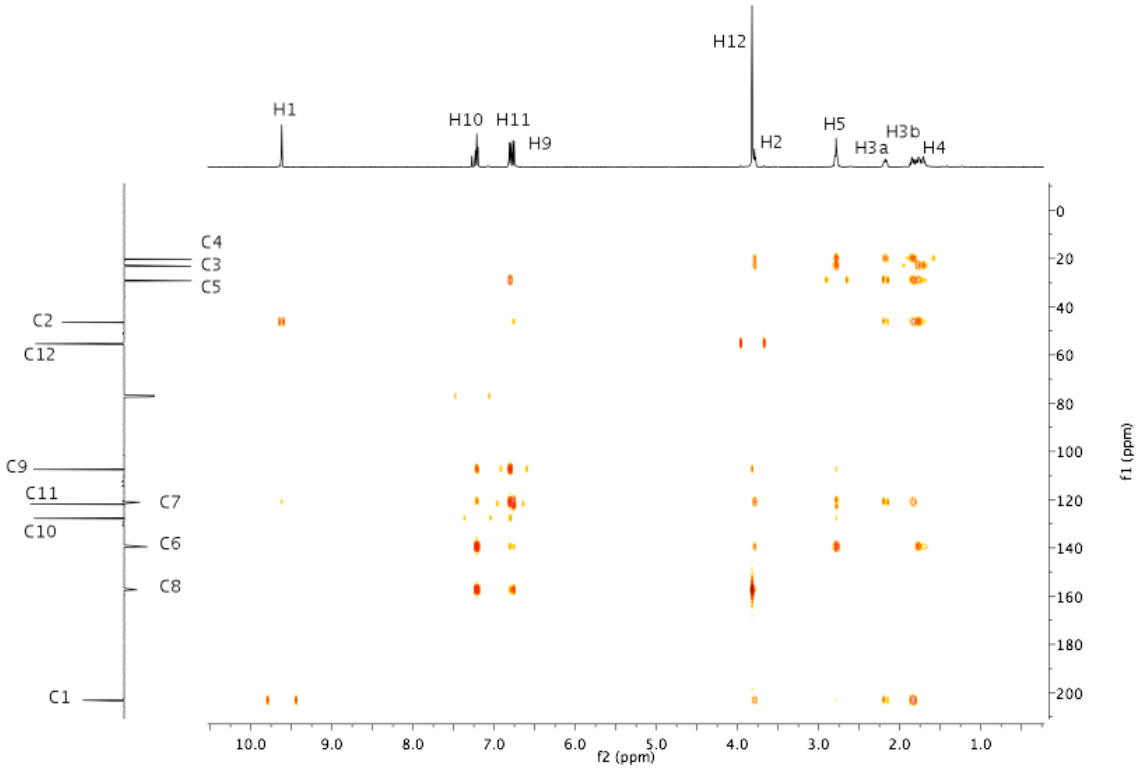
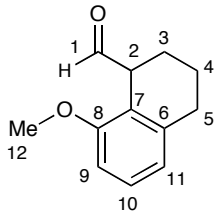




$^{1}H - {}^{13}C$ HMBC $CDCl_3$ 500 MHz





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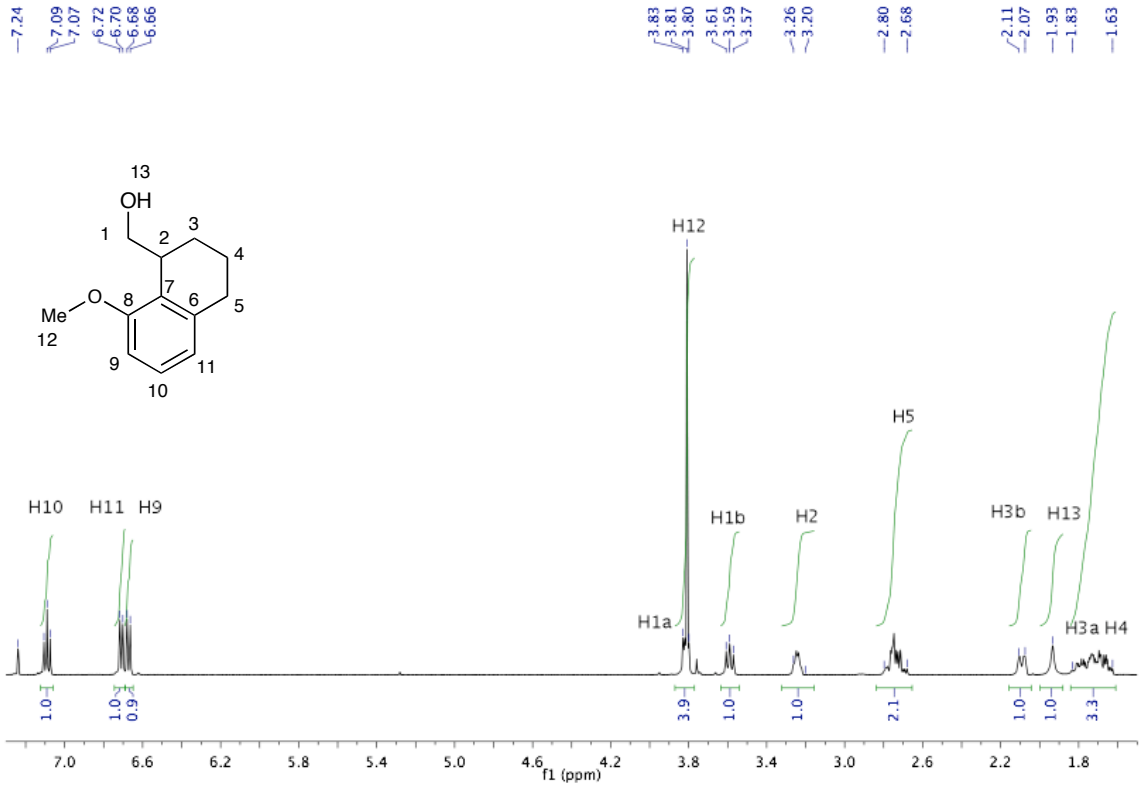
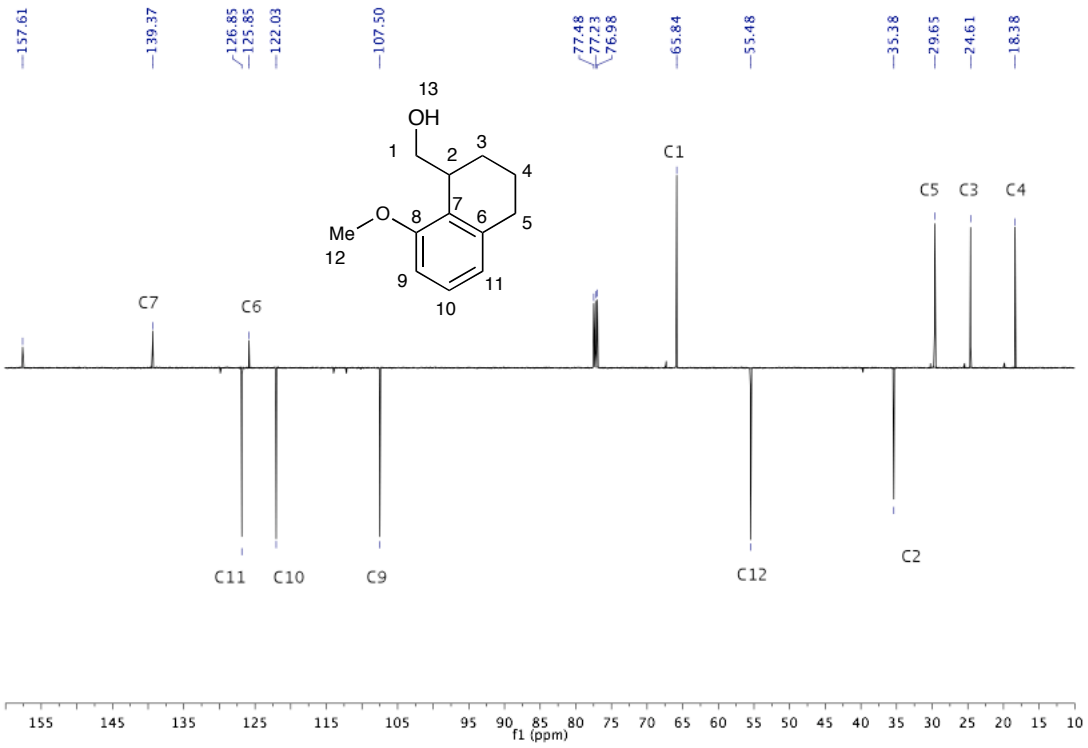


^{13}C APT NMR $CDCl_3$ 125 MHz



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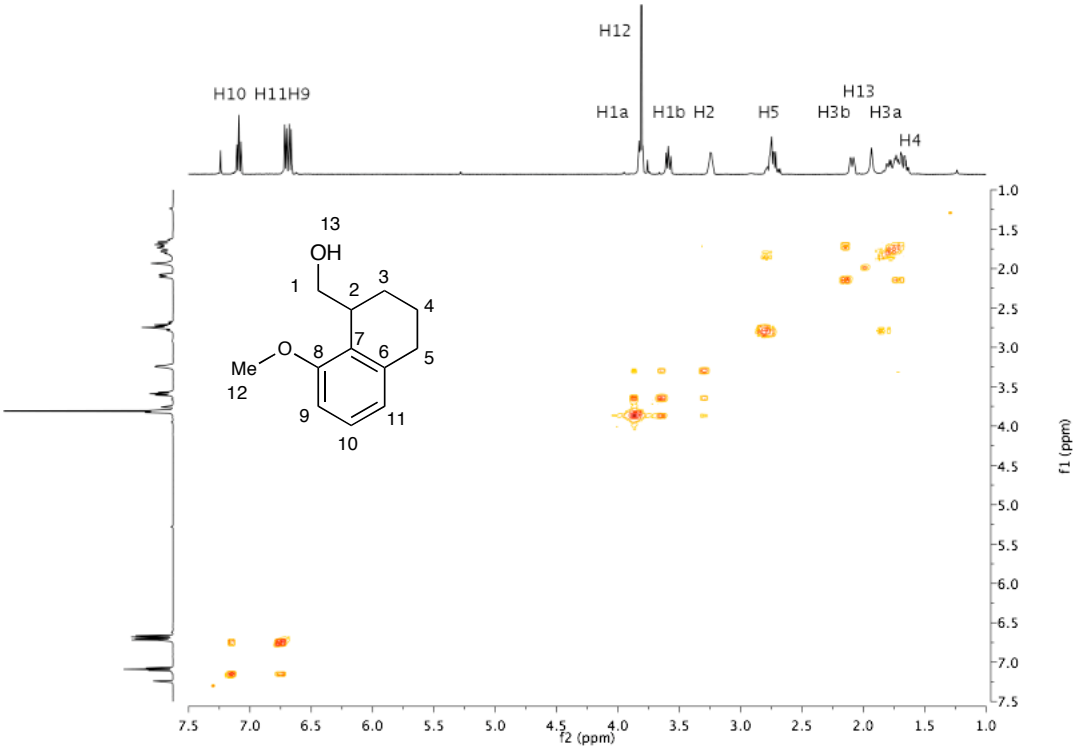
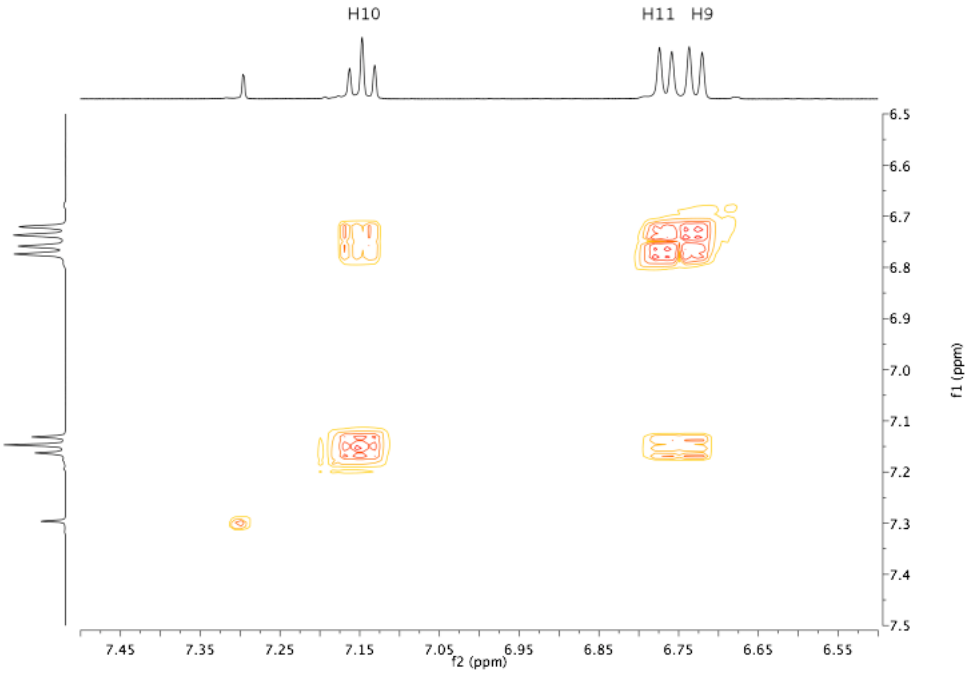
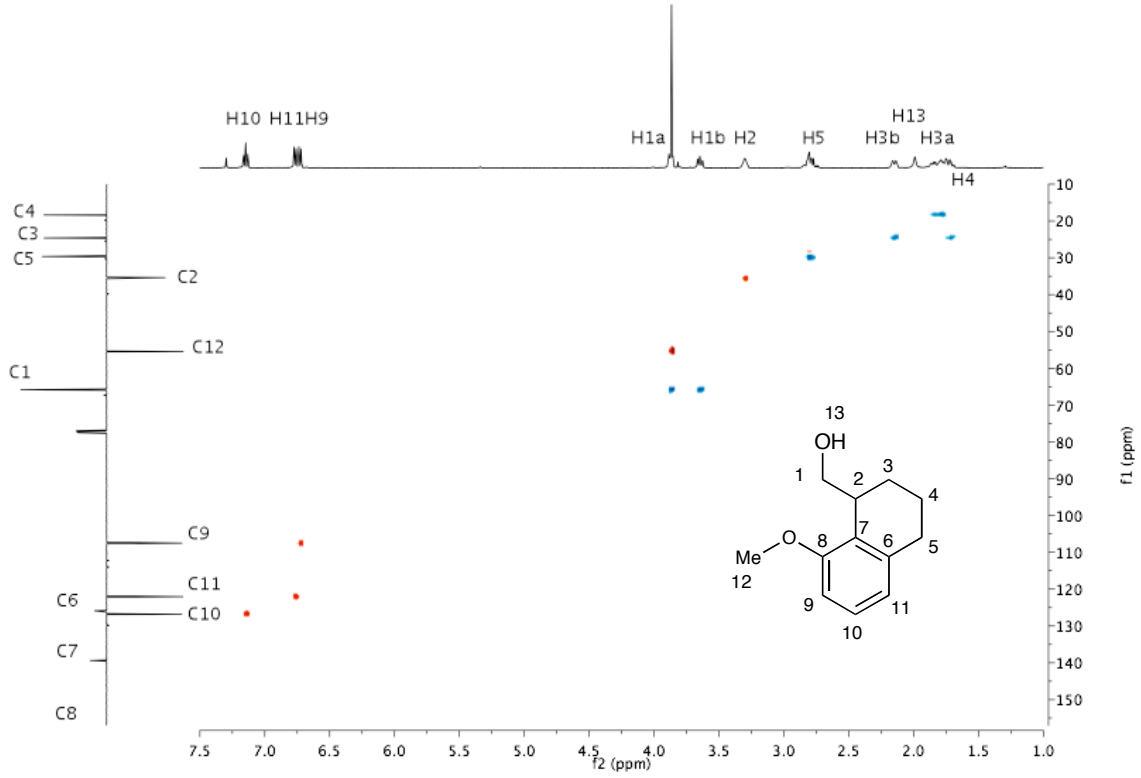




$^{1}H - ^{13}C$ HSQC $CDCl_3$ 500 MHz



$^{1}H - ^{13}C$ HMBC $CDCl_3$ 500 MHz

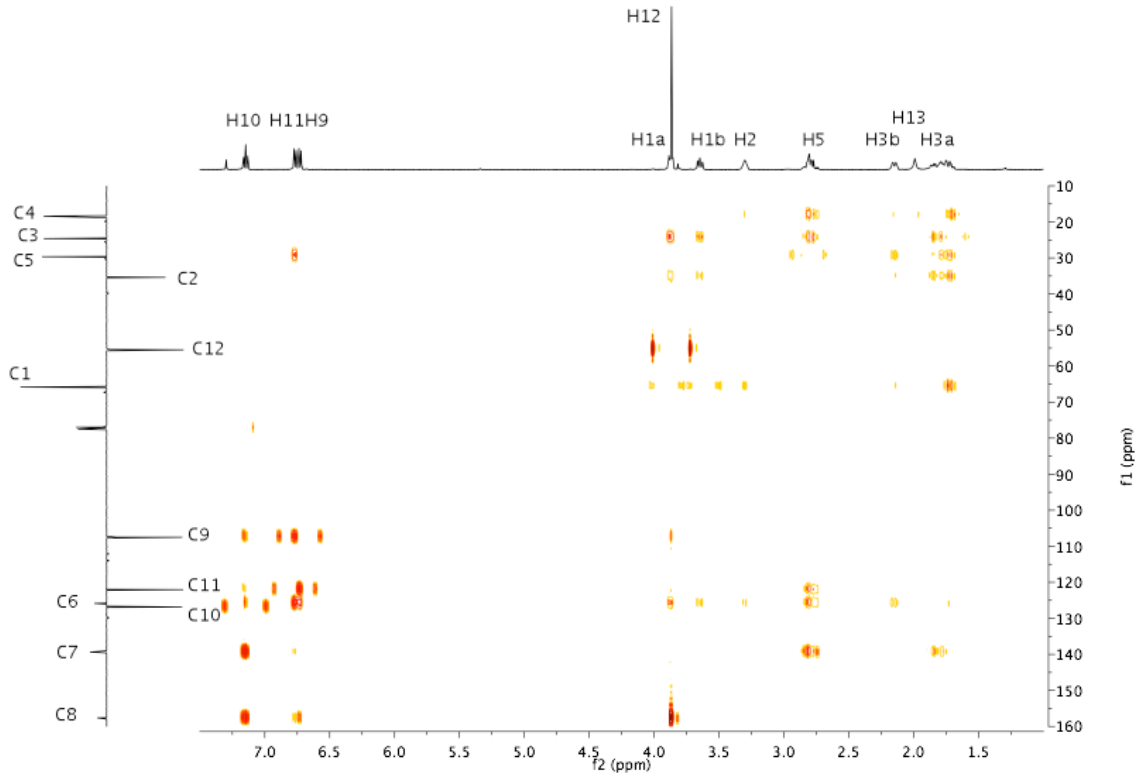


Table 2, Entry 2

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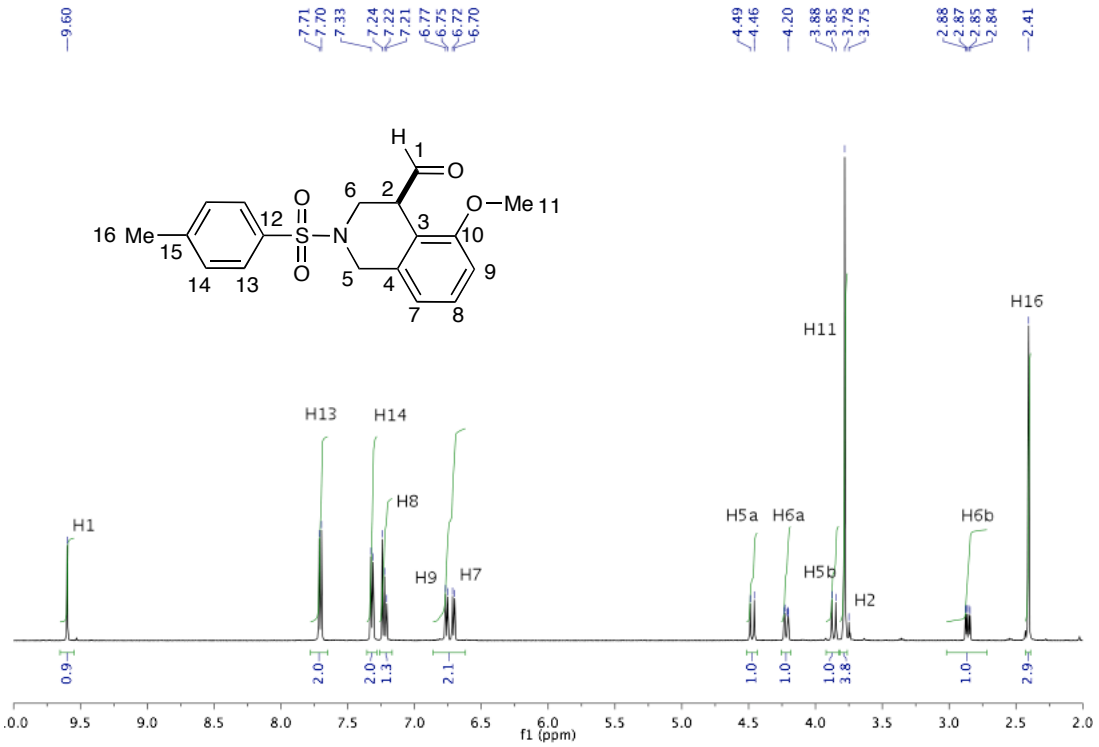
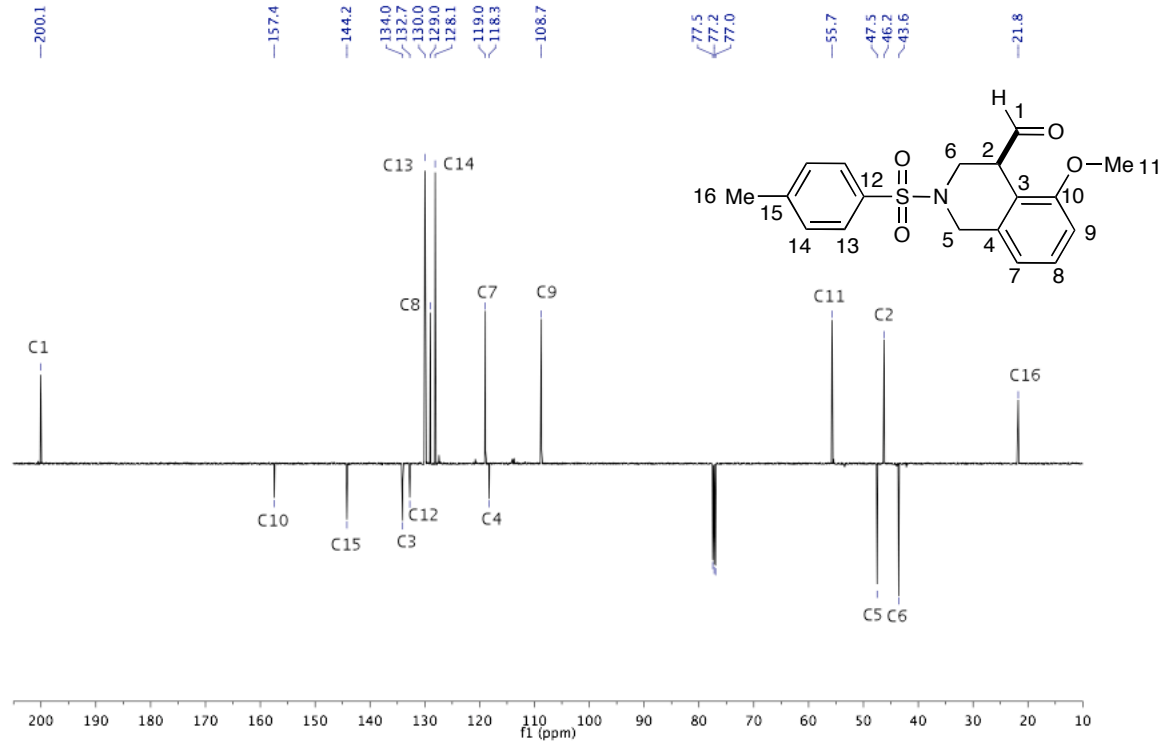
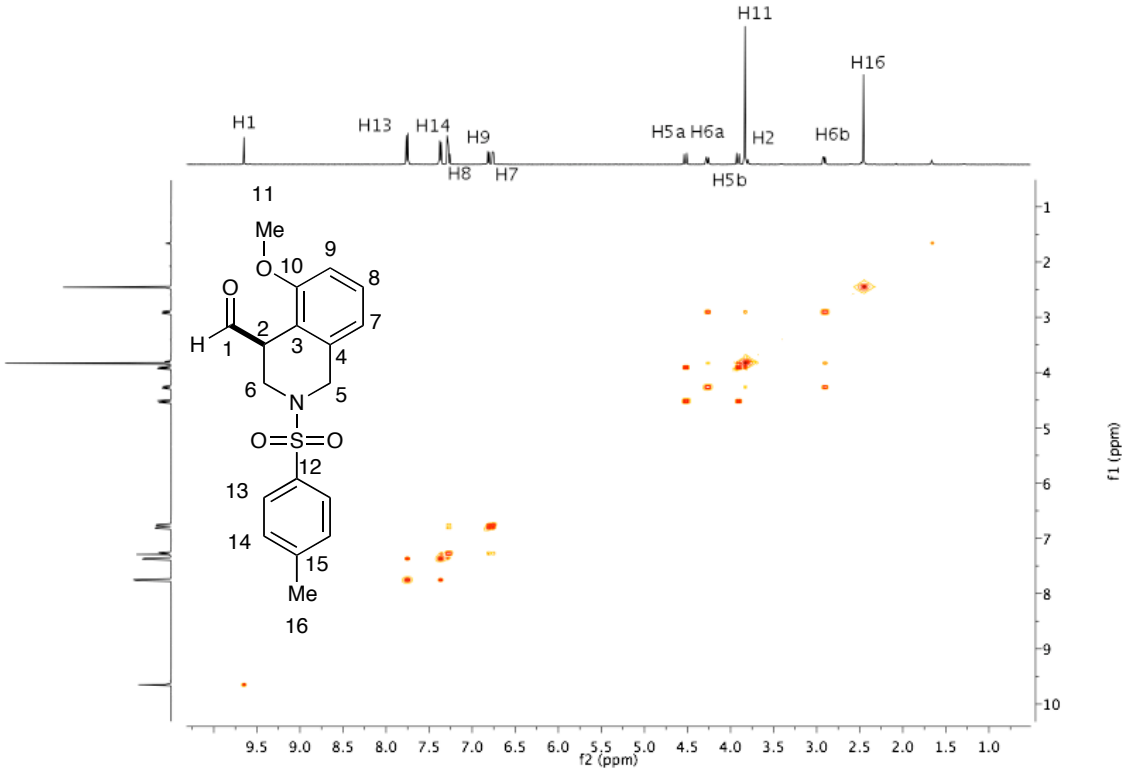
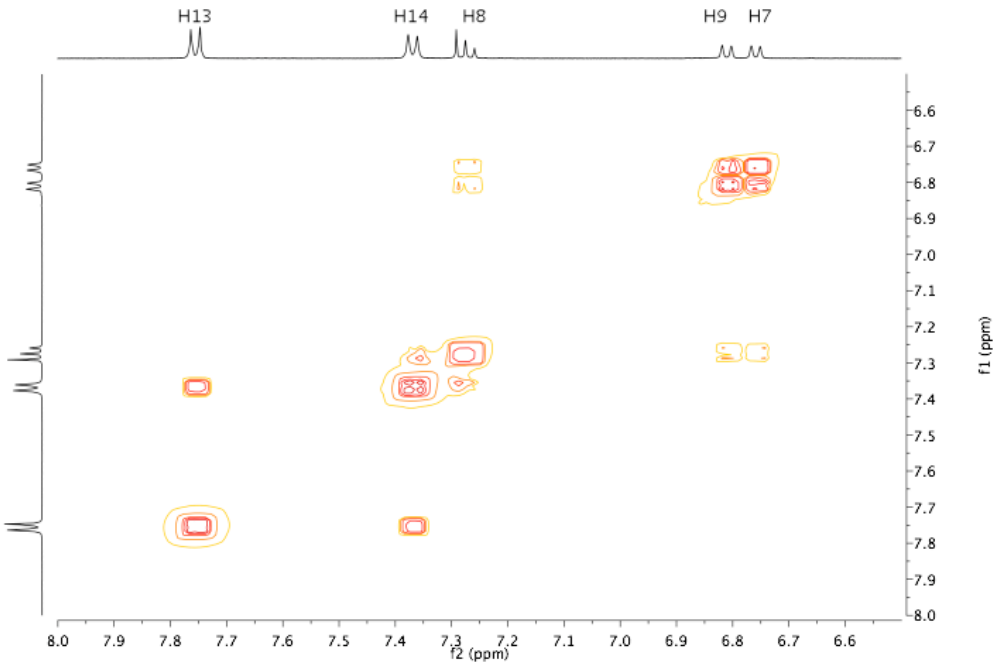


^{13}C NMR $CDCl_3$ 125 MHz

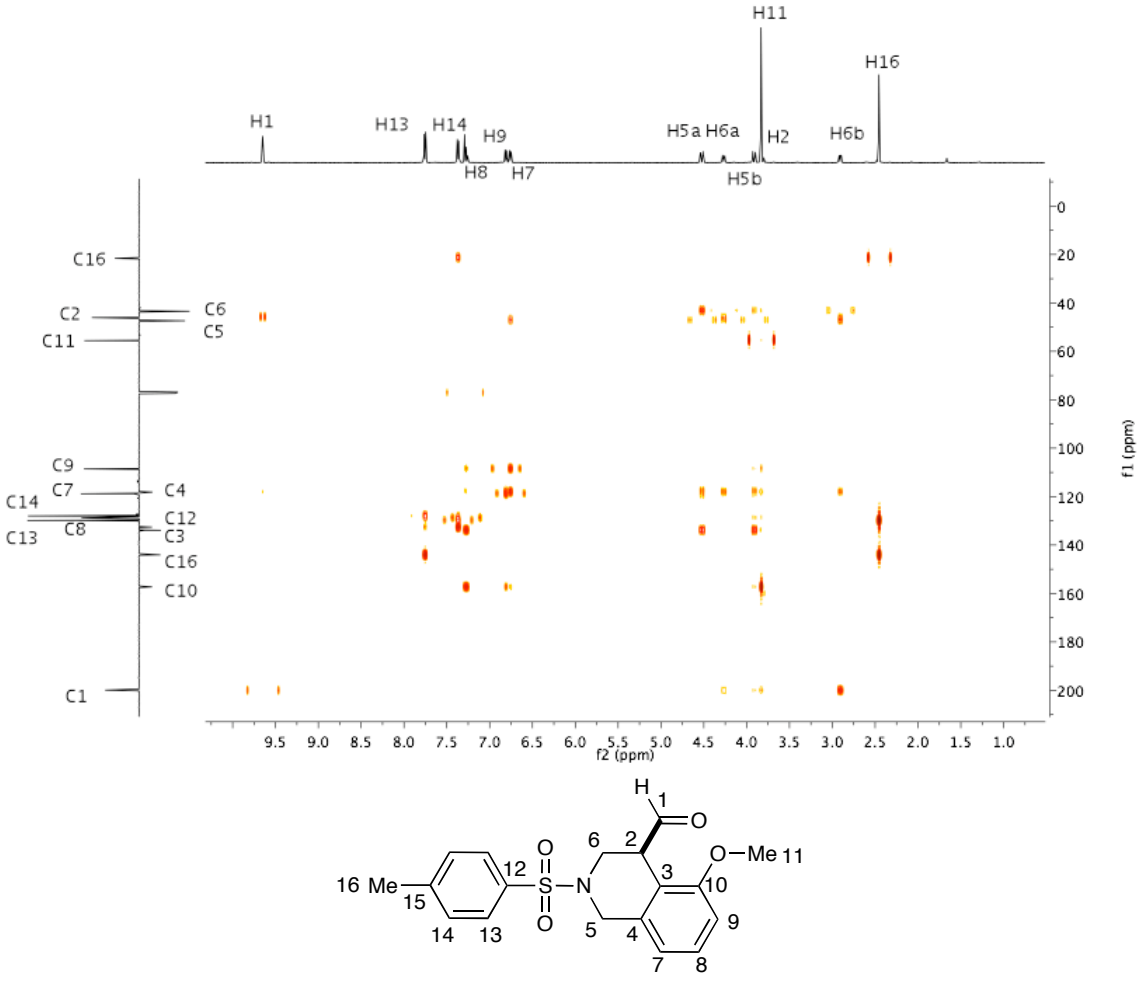


$^{1}H - {}^{1}H$ COSY 500 MHz $CDCl_3$





$^{1}H - {}^{13}C$ HMBC $CDCl_3$ 500 MHz



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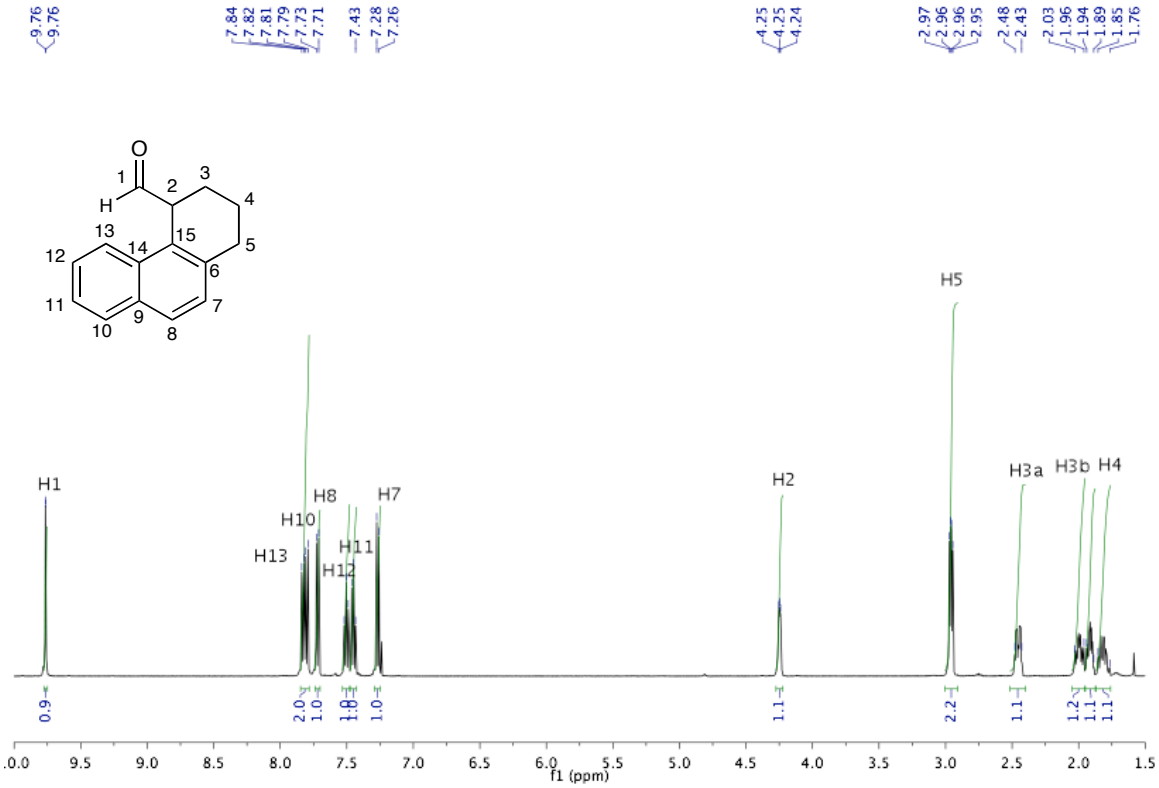
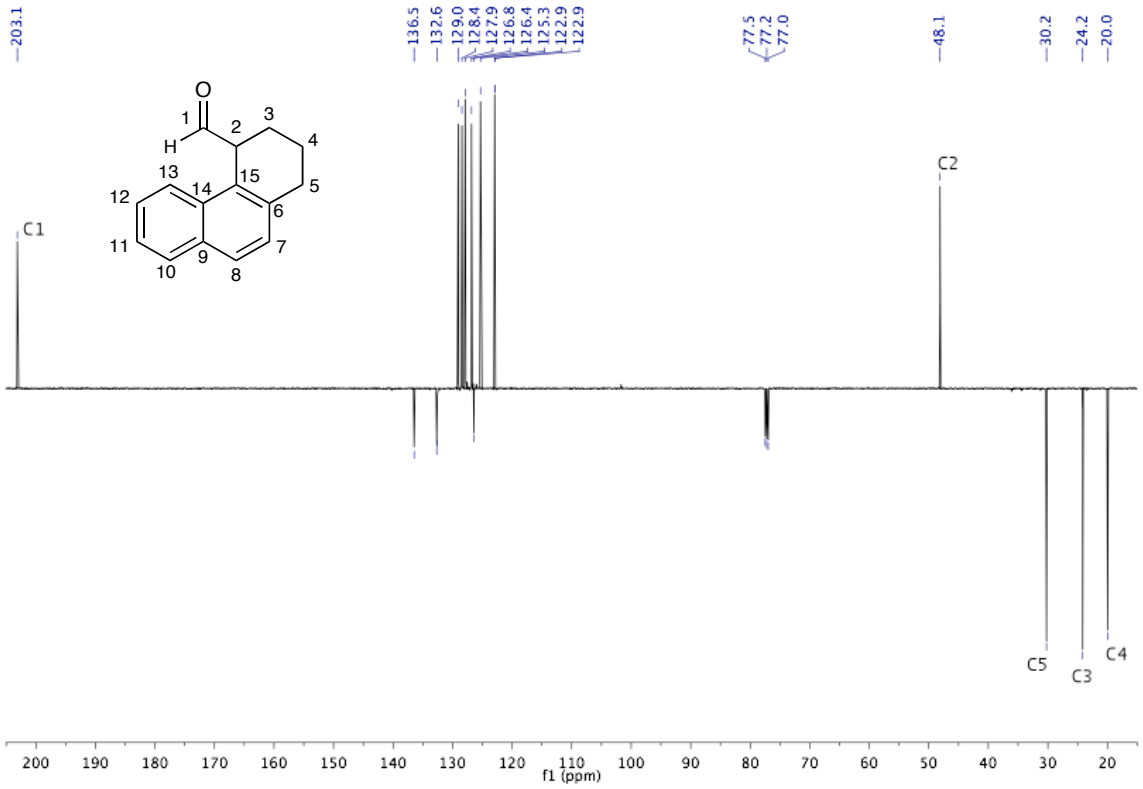
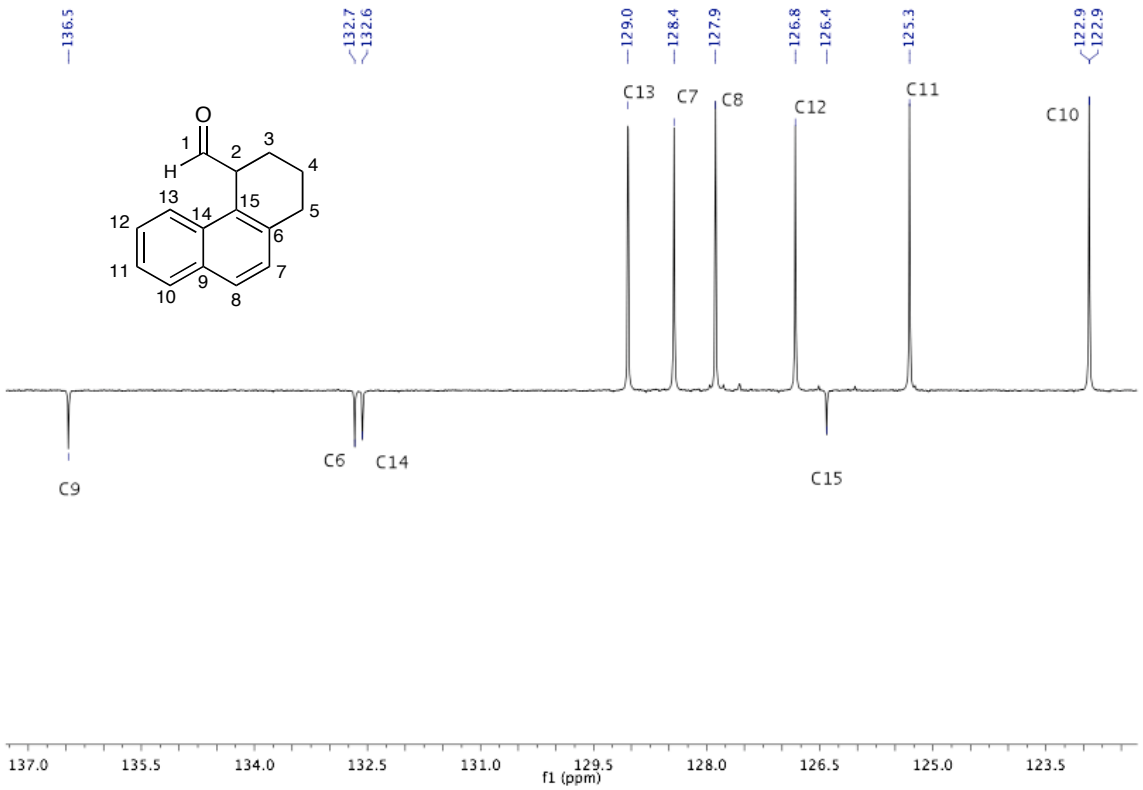
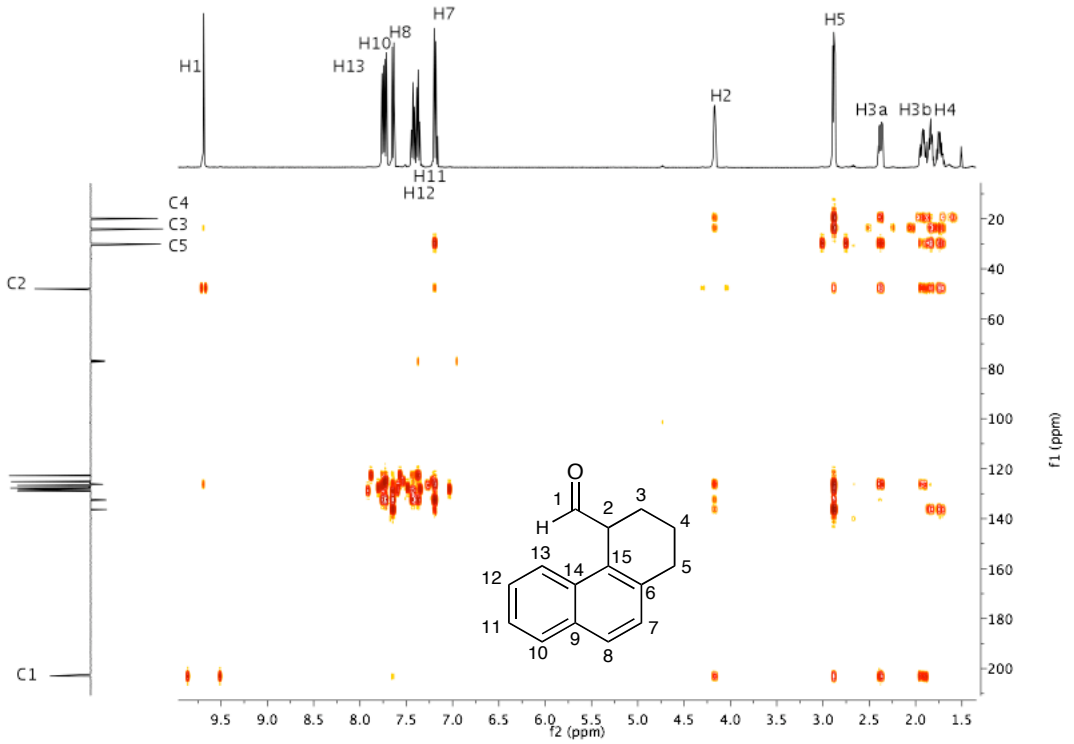


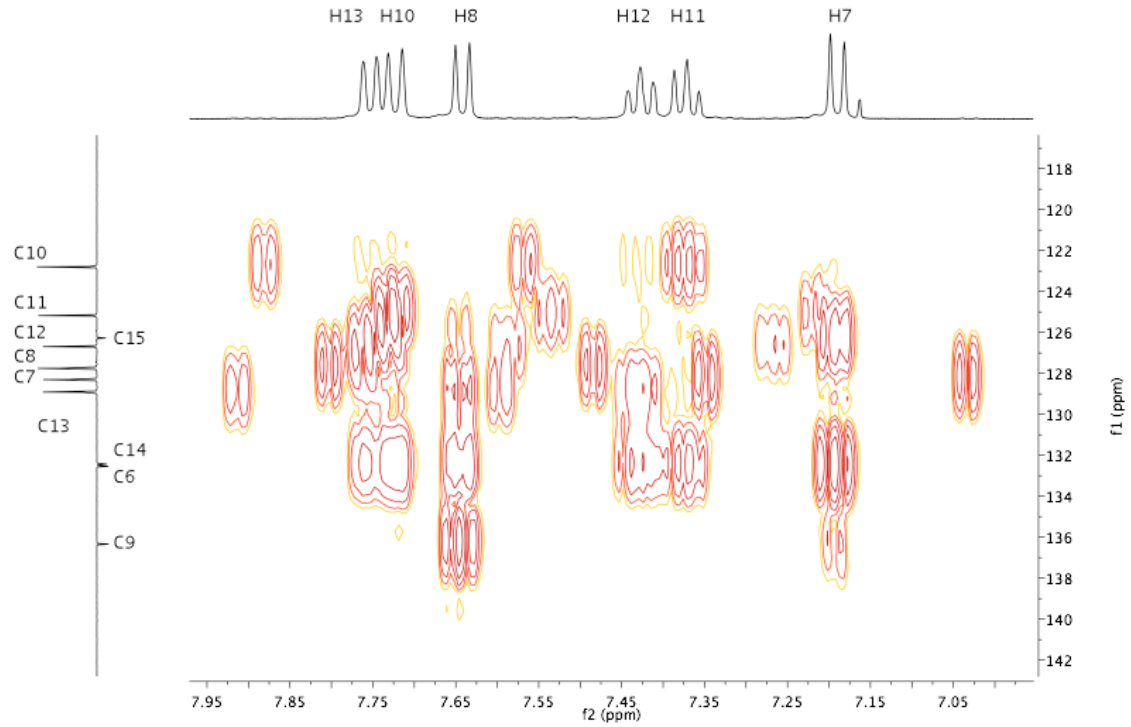
^{13}C APT NMR $CDCl_3$ 125 MHz



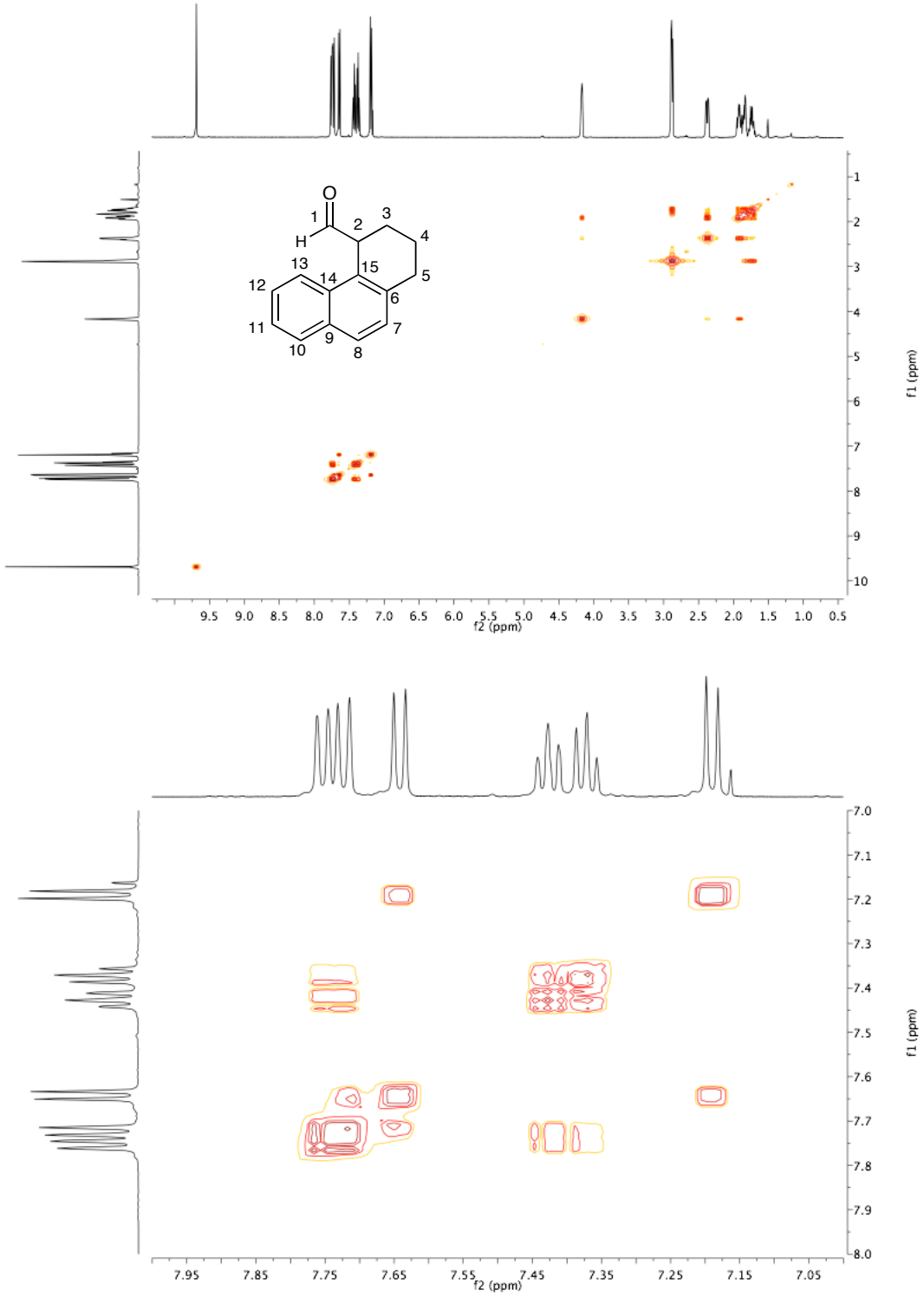


$^{1}H - ^{13}C$ HMBC $CDCl_3$ 500 MHz

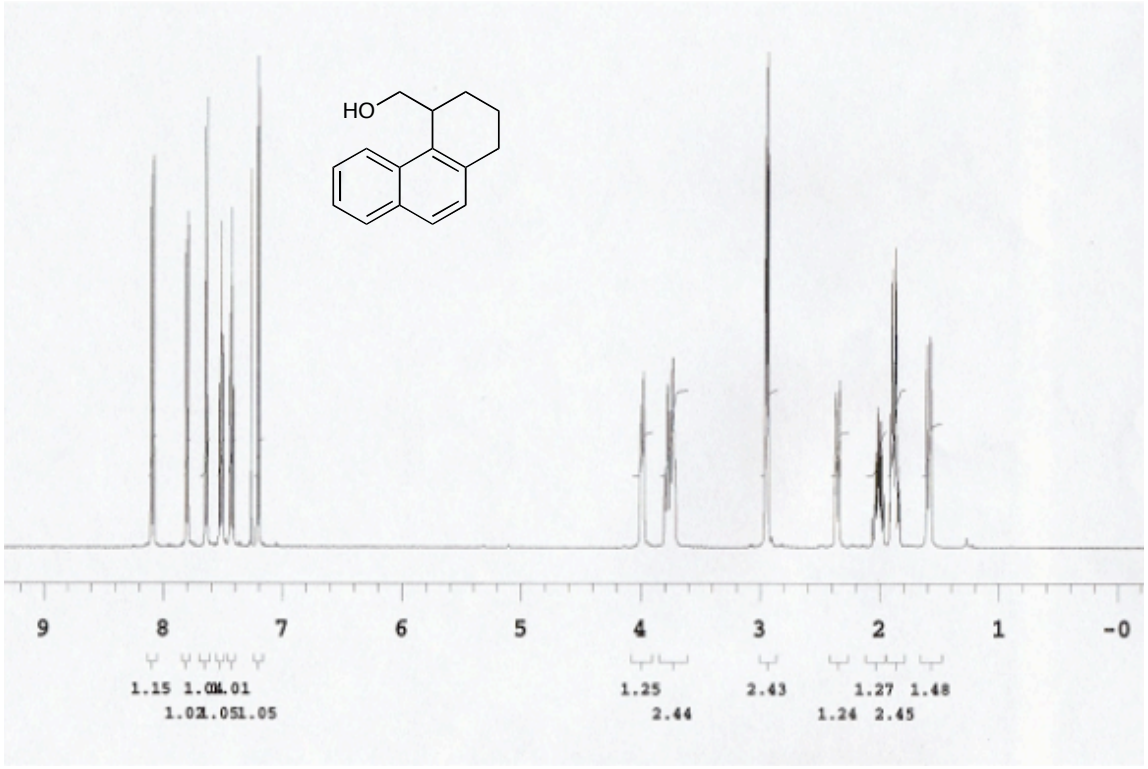




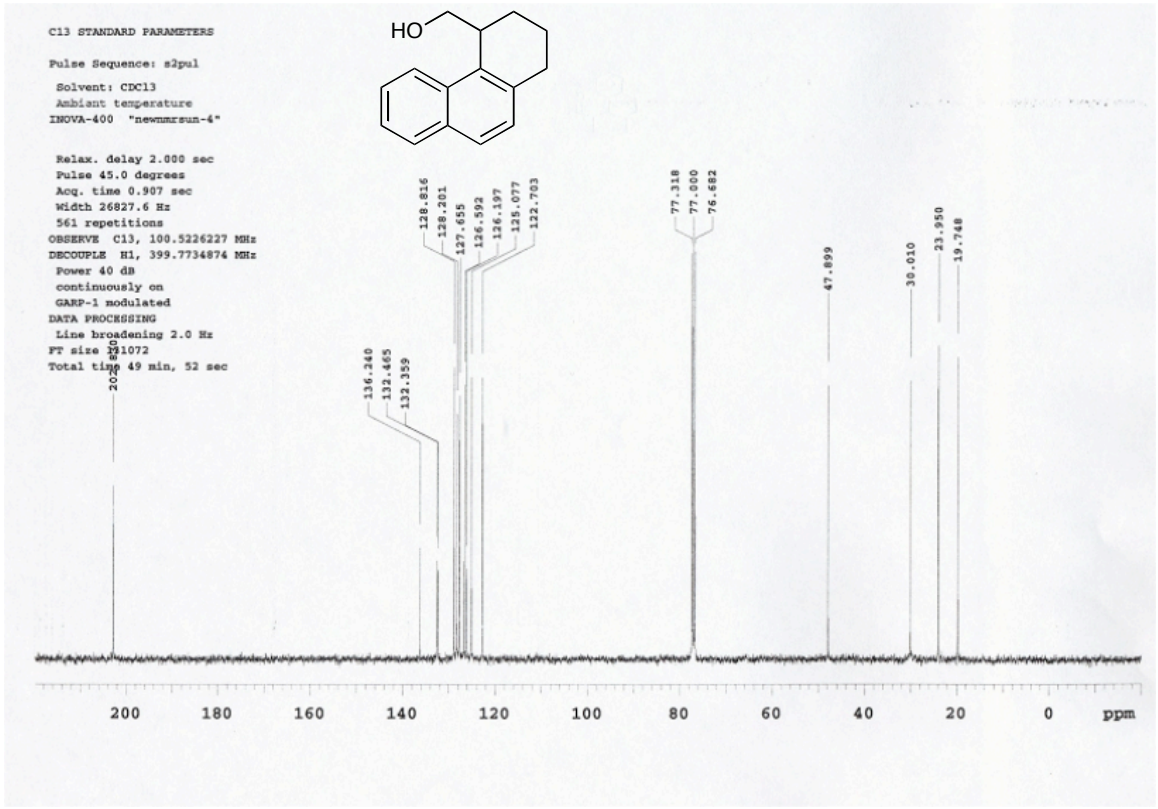
^{1}H-^{1}H COSY $CDCl_3$ 500 MHz



^{1}H NMR $CDCl_3$ 400 MHz



^{13}C NMR $CDCl_3$ 100 MHz



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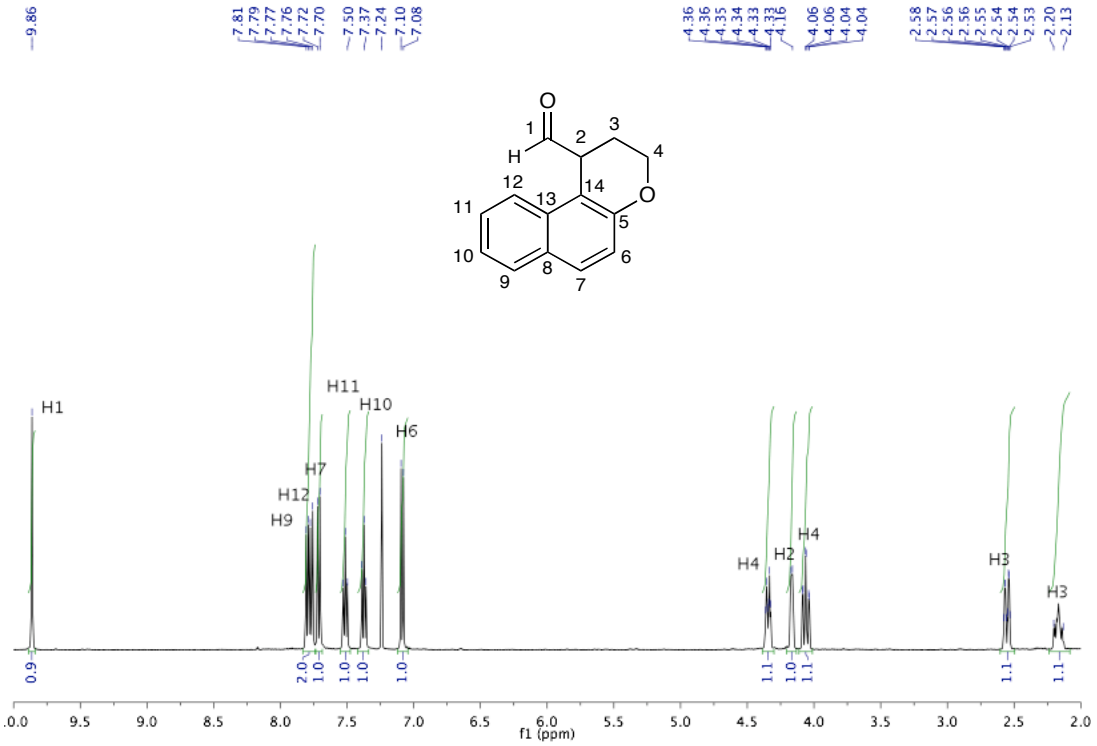
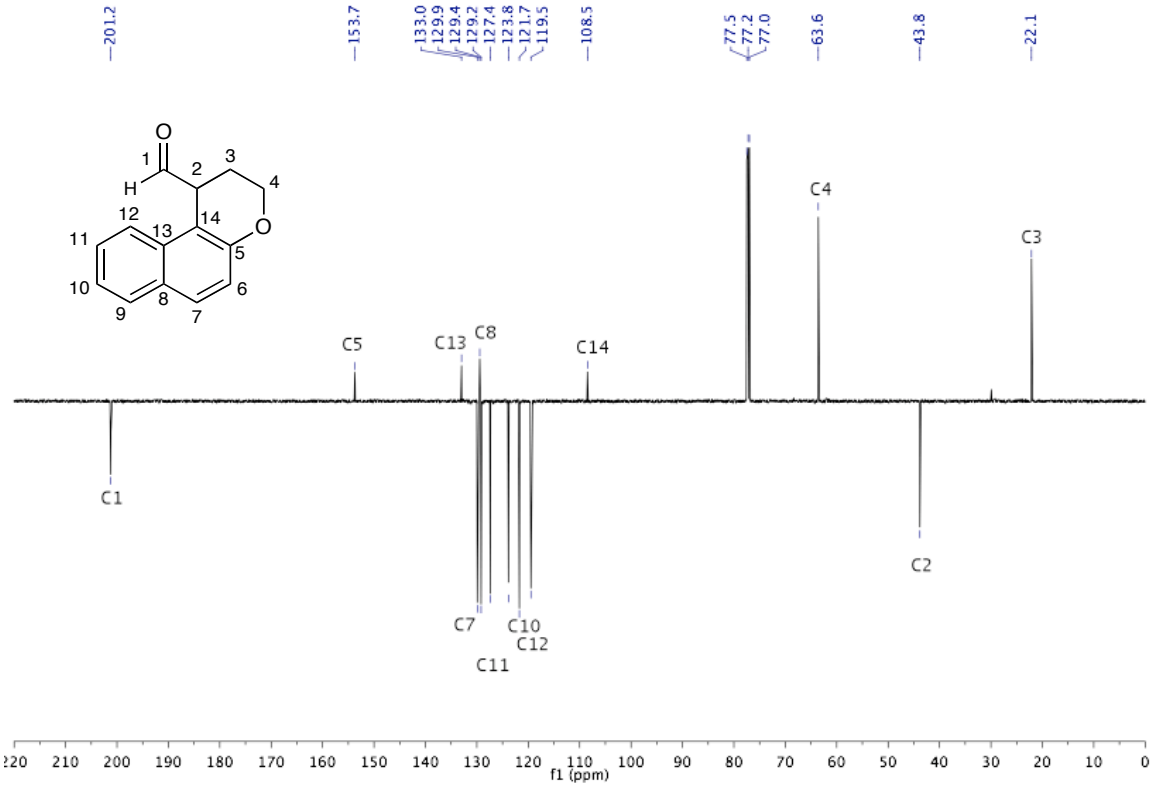
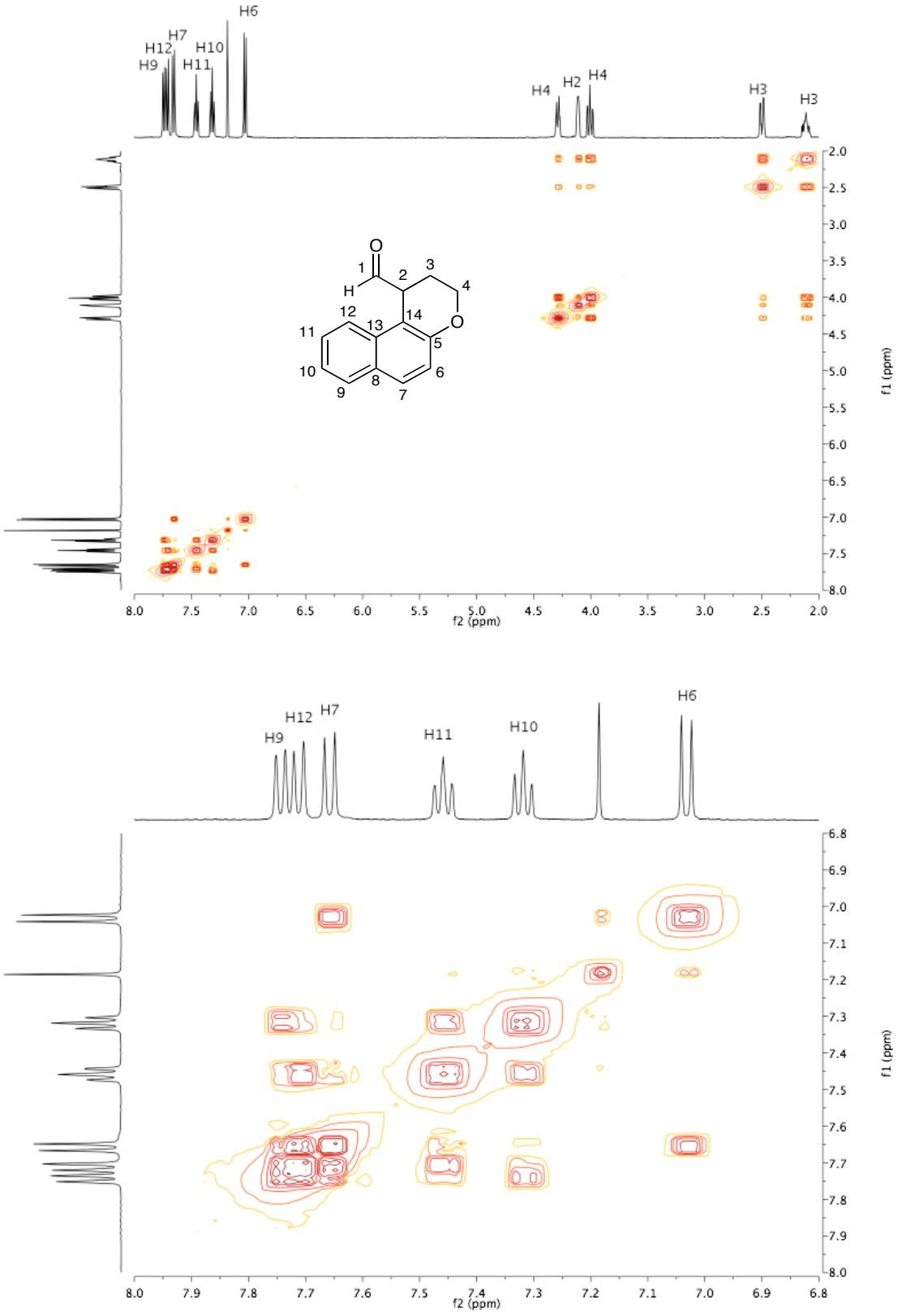
^{1}H NMR $CDCl_3$ 500 MHz



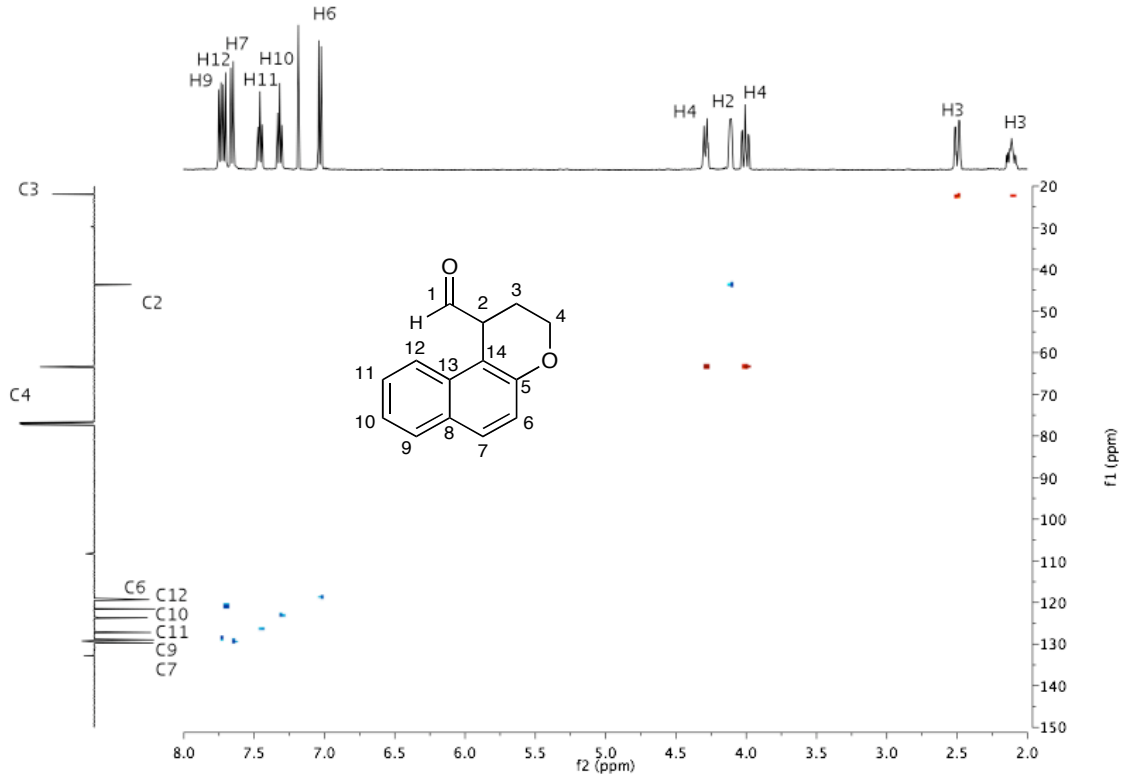
^{13}C APT NMR $CDCl_3$ 125 MHz



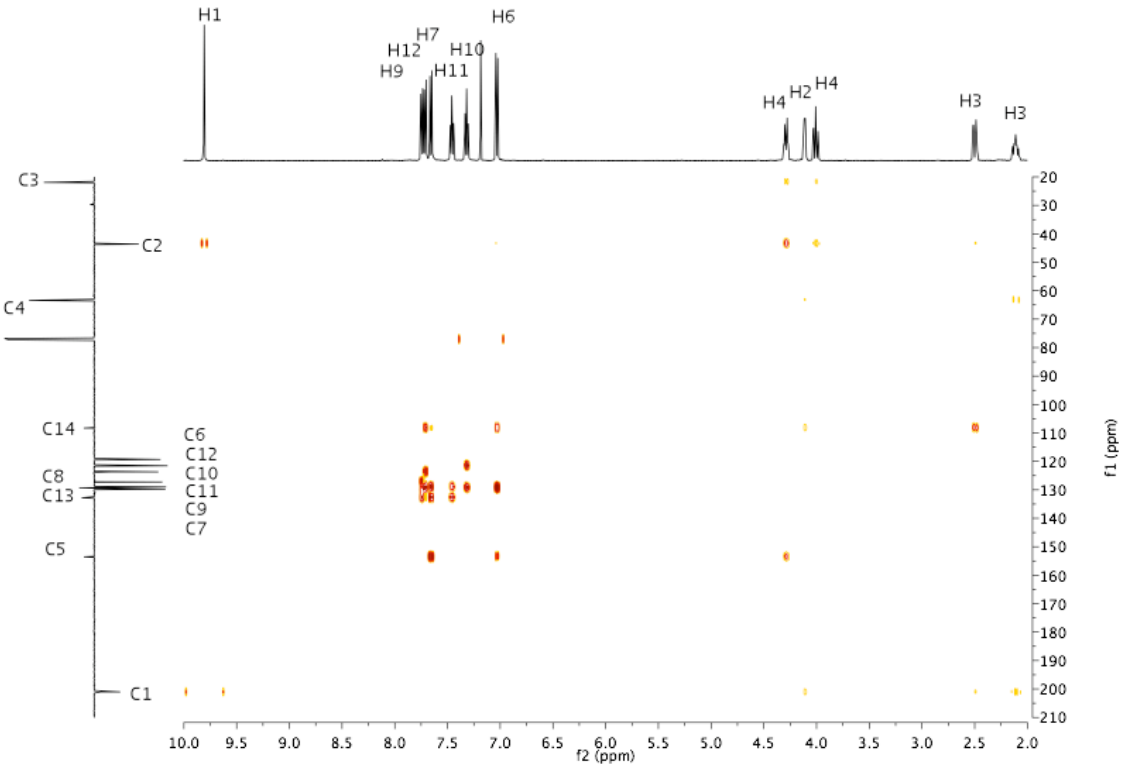
$^{1}H - {}^{1}H$ COSY $CDCl_3$ 500 MHz



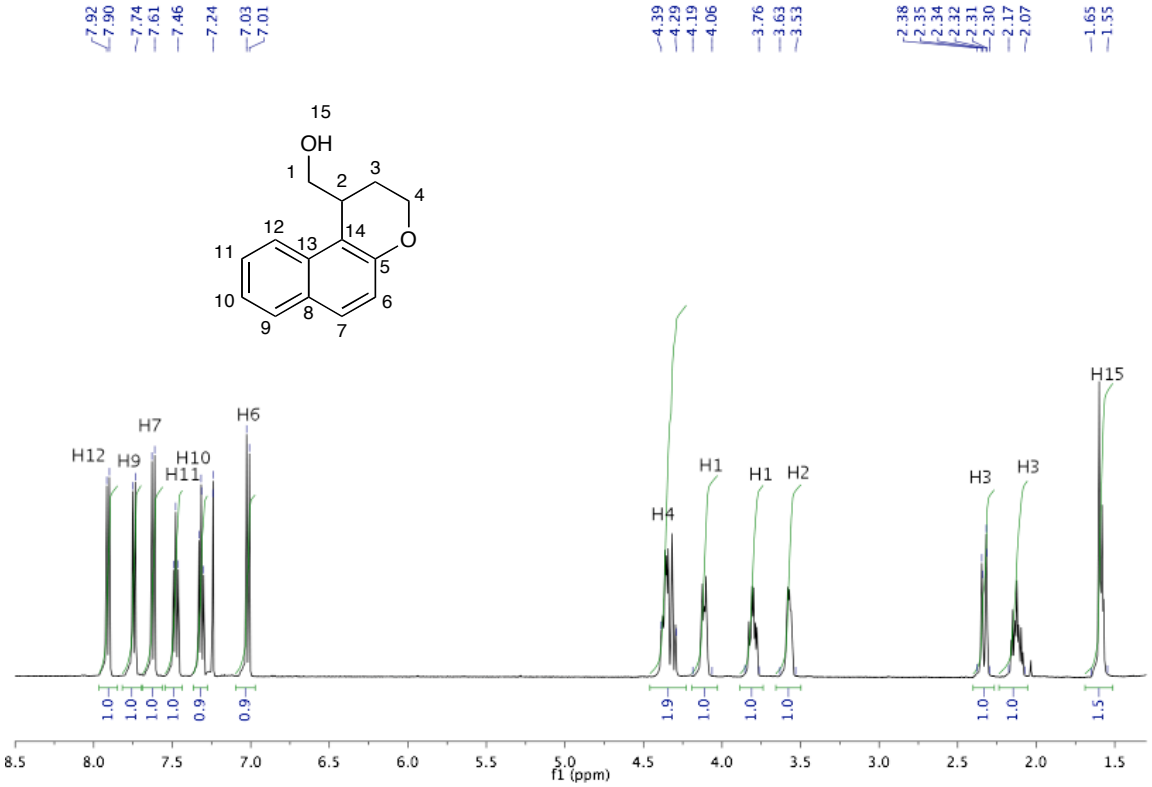
$^{1}H - {}^{13}C$ HSQC 500 MHz $CDCl_3$



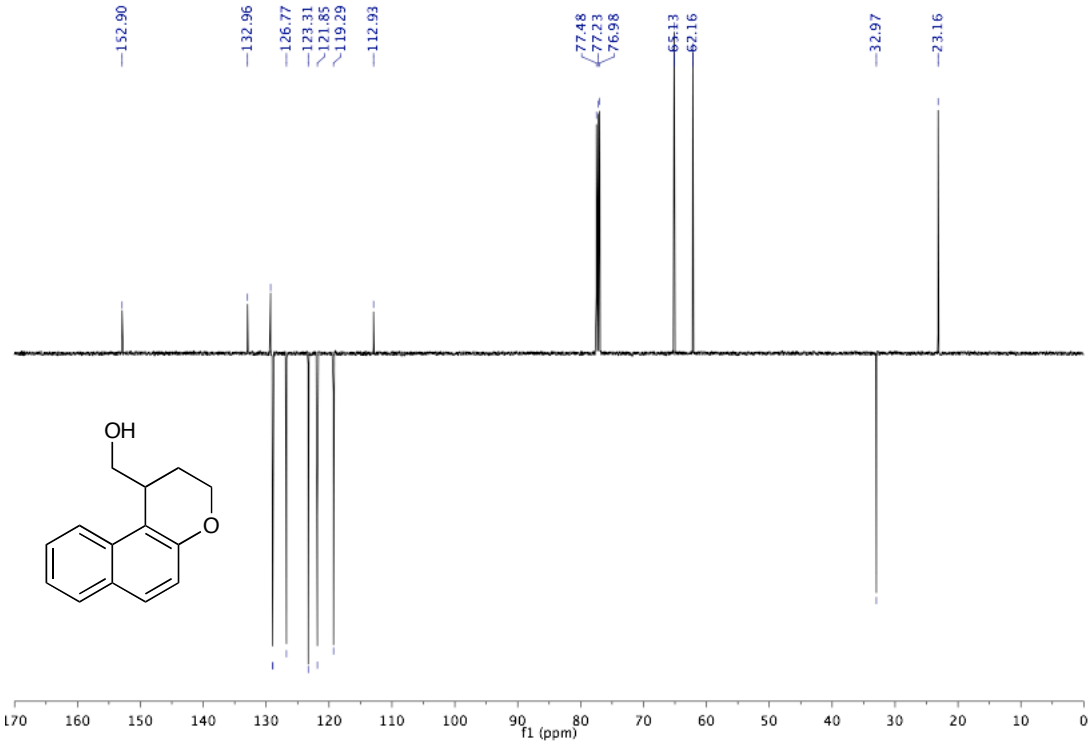
$^{1}H - {}^{13}C$ HMBC 500 MHz $CDCl_3$



^{1}H NMR $CDCl_3$ 500 MHz



^{13}C NMR $CDCl_3$ 125 MHz



$^{1}H - {}^{1}H$ COSY $CDCl_3$ 500 MHz

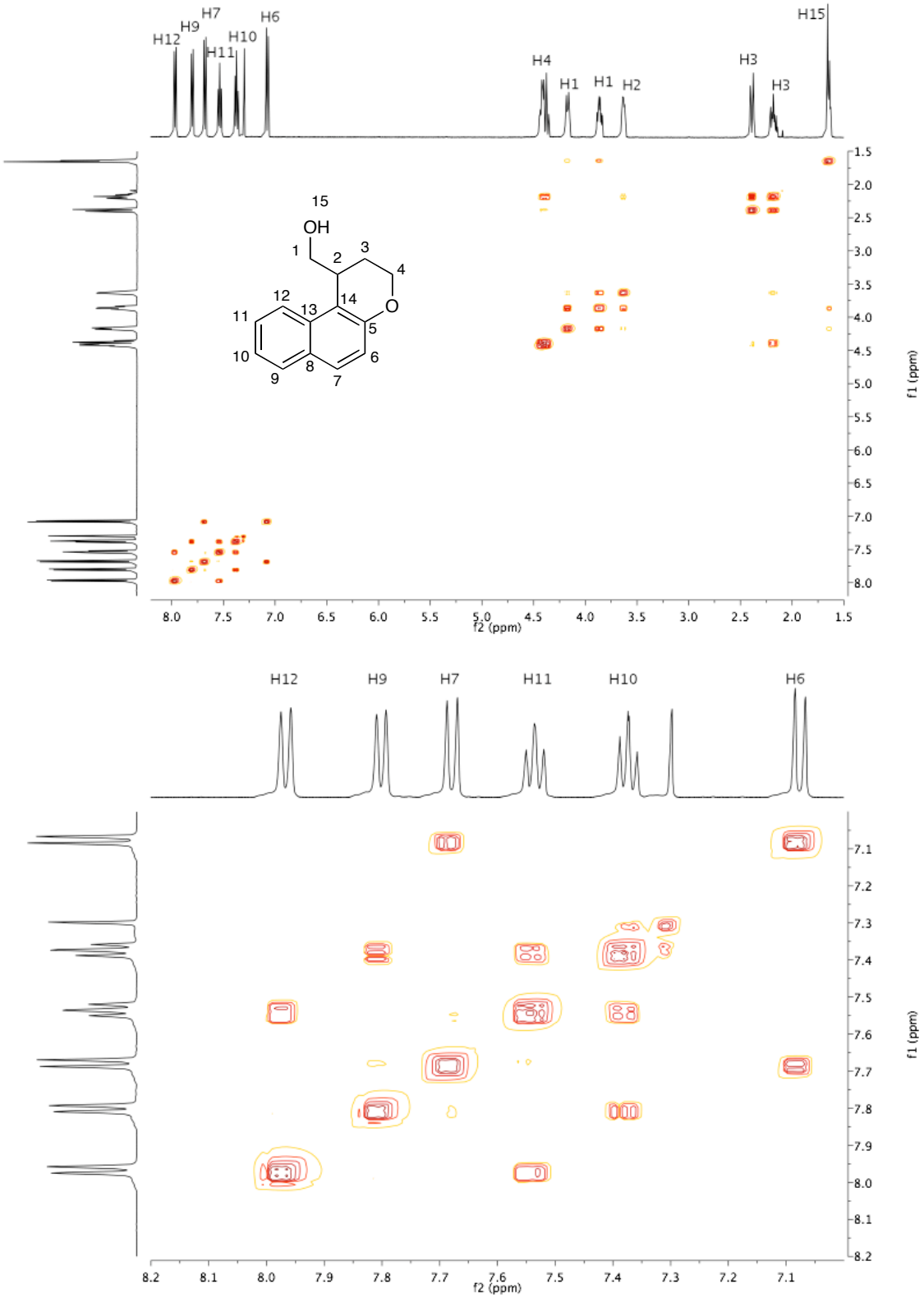
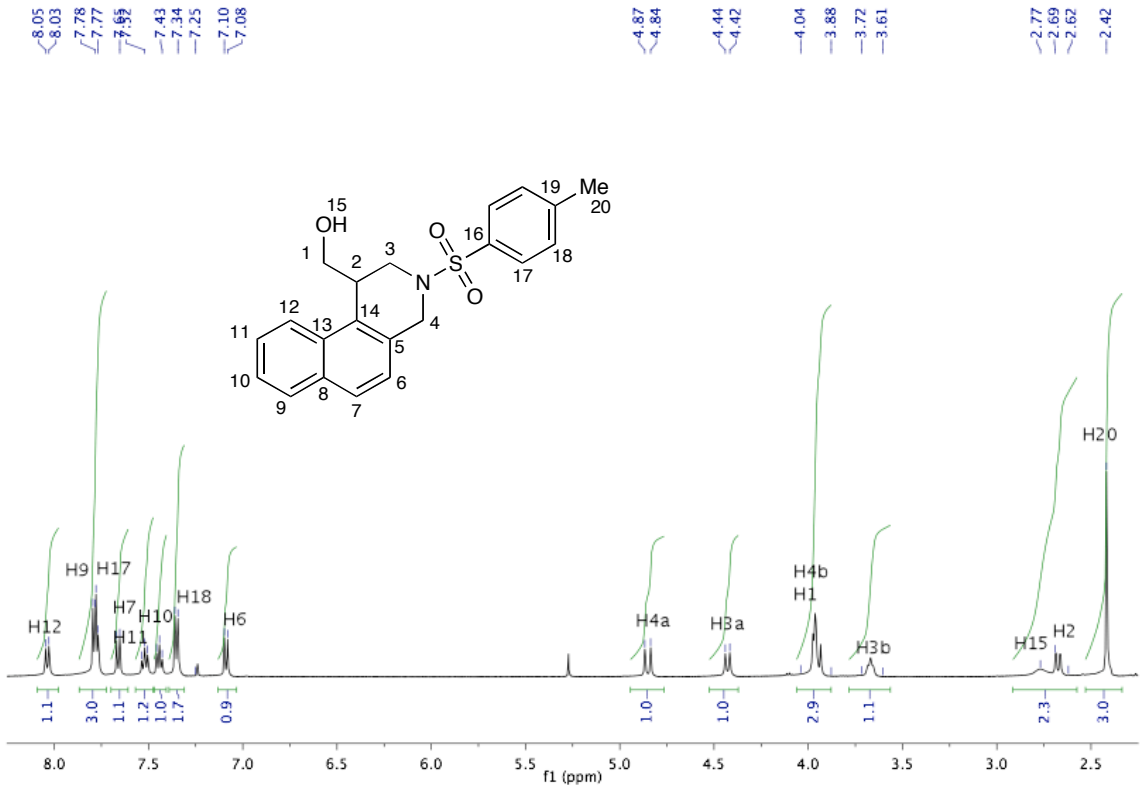
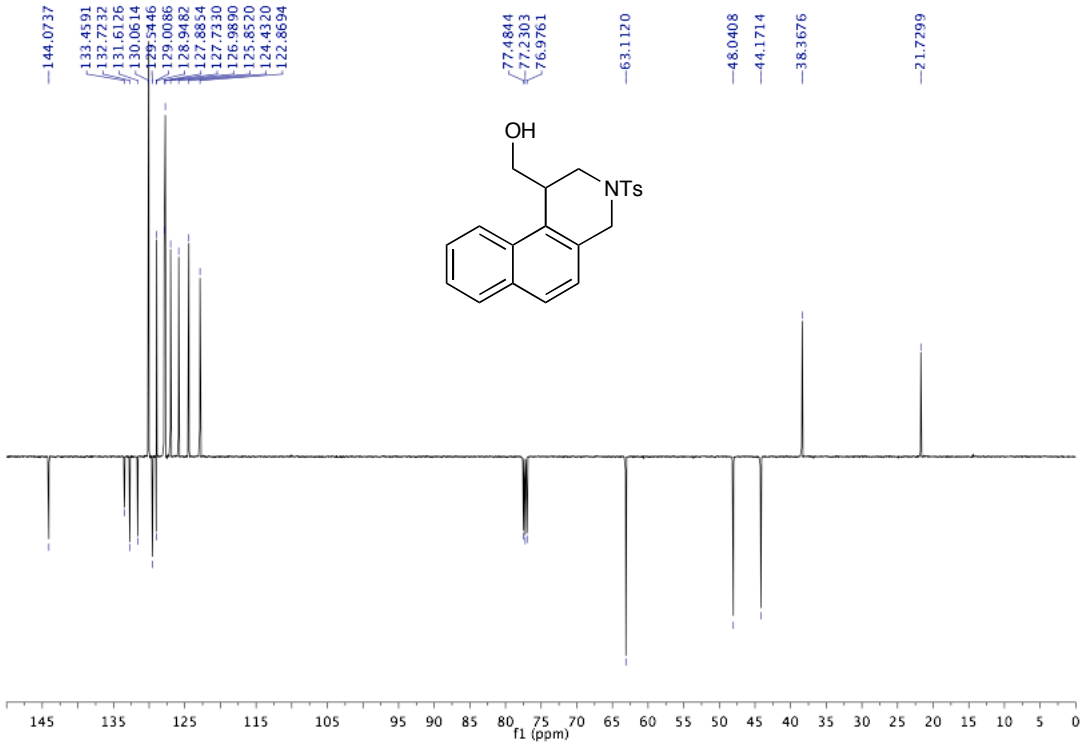


Table 2, Entry 5

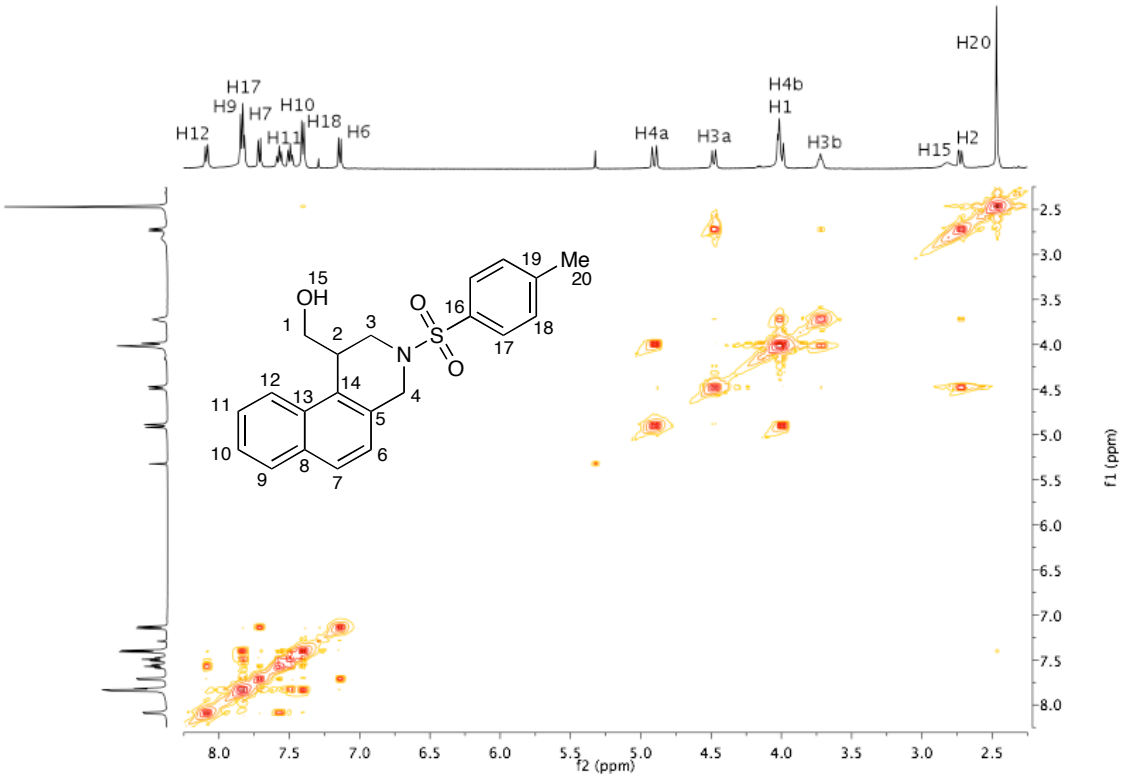
^{1}H NMR $CDCl_3$ 500 MHz

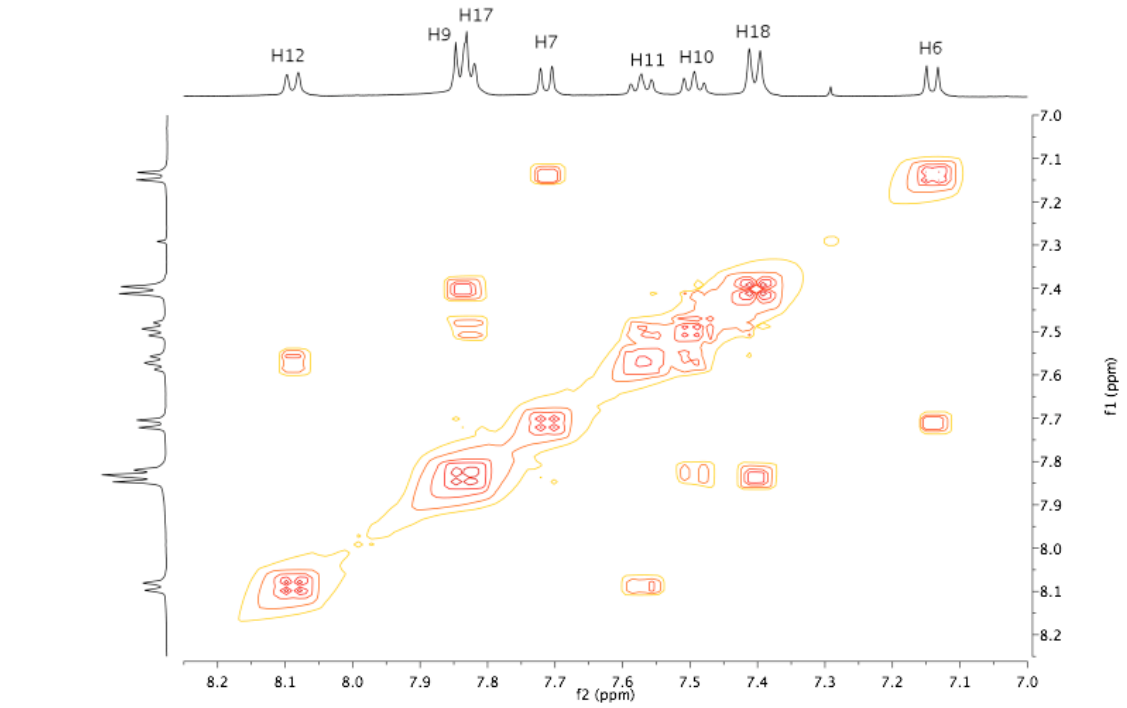


^{13}C APT NMR $CDCl_3$ 125 MHz



$^{1}H - {}^{1}H$ COSY $CDCl_3$ 500 MHz





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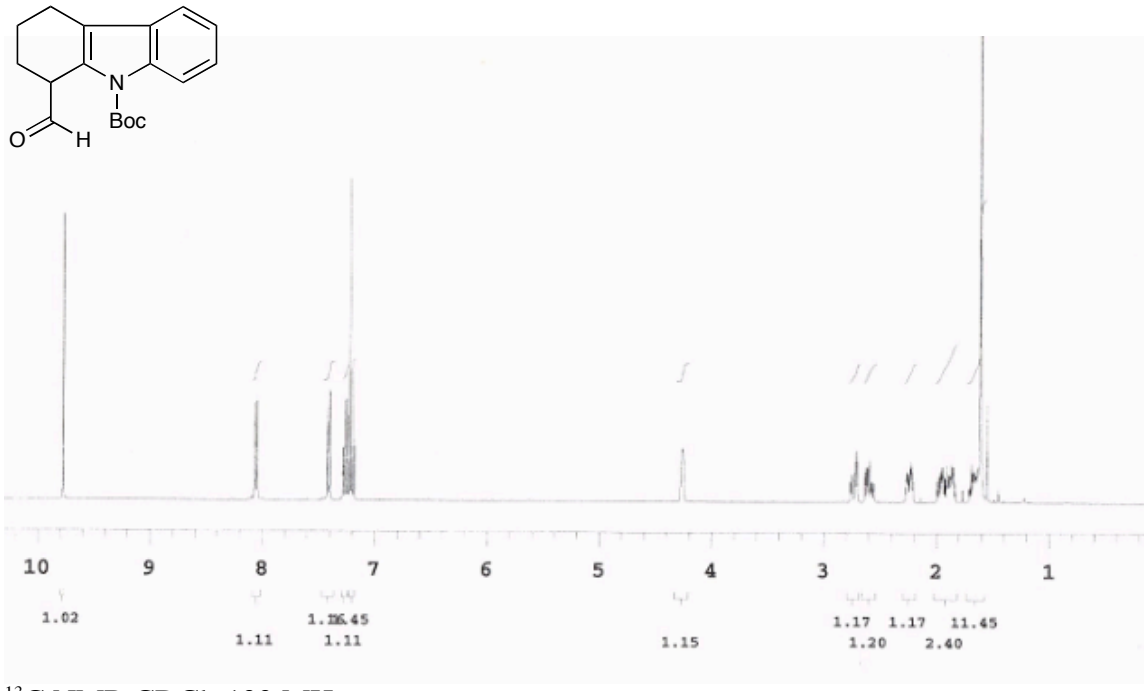
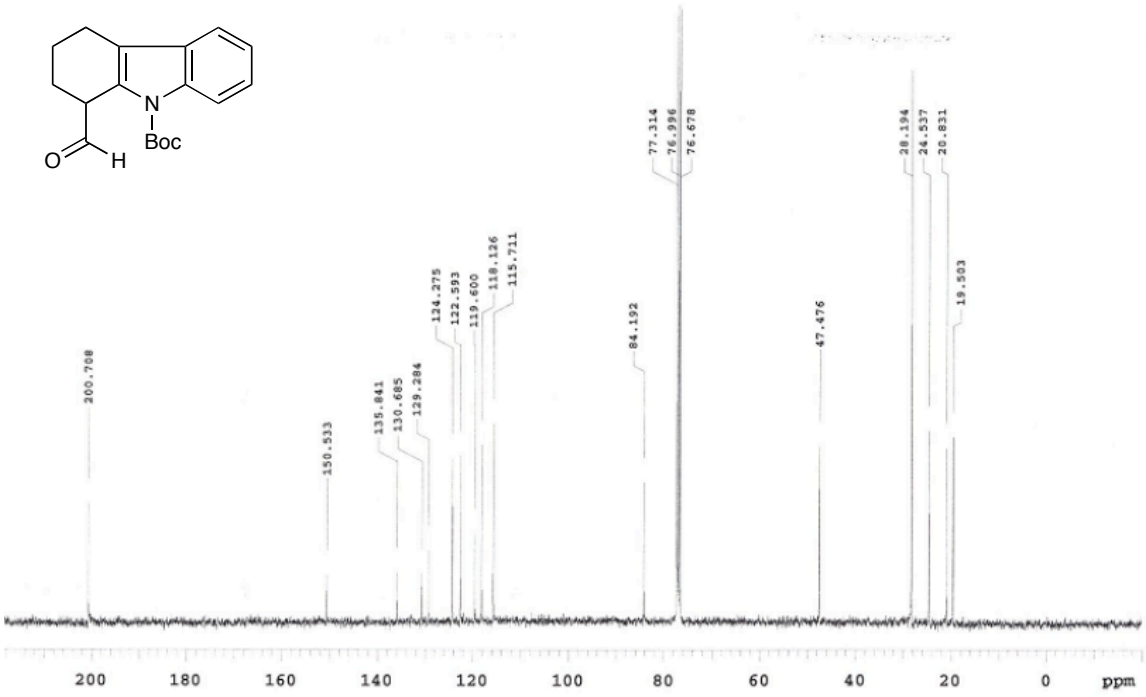
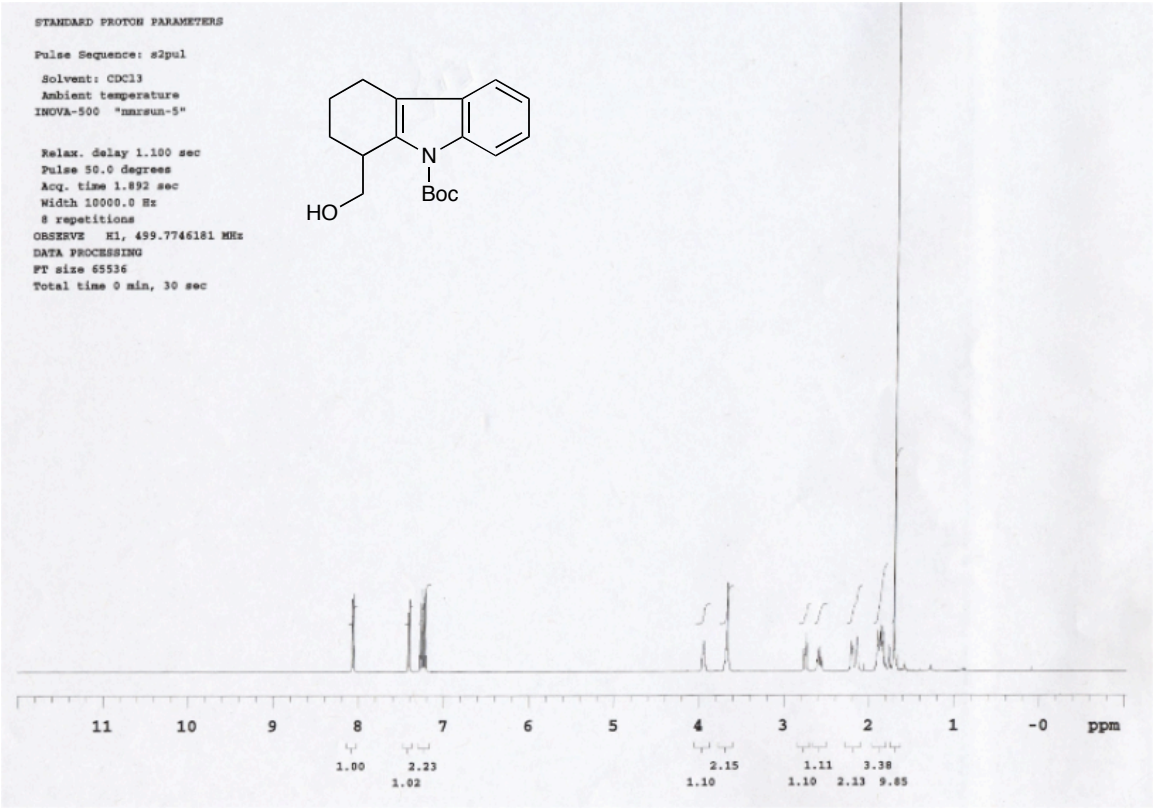


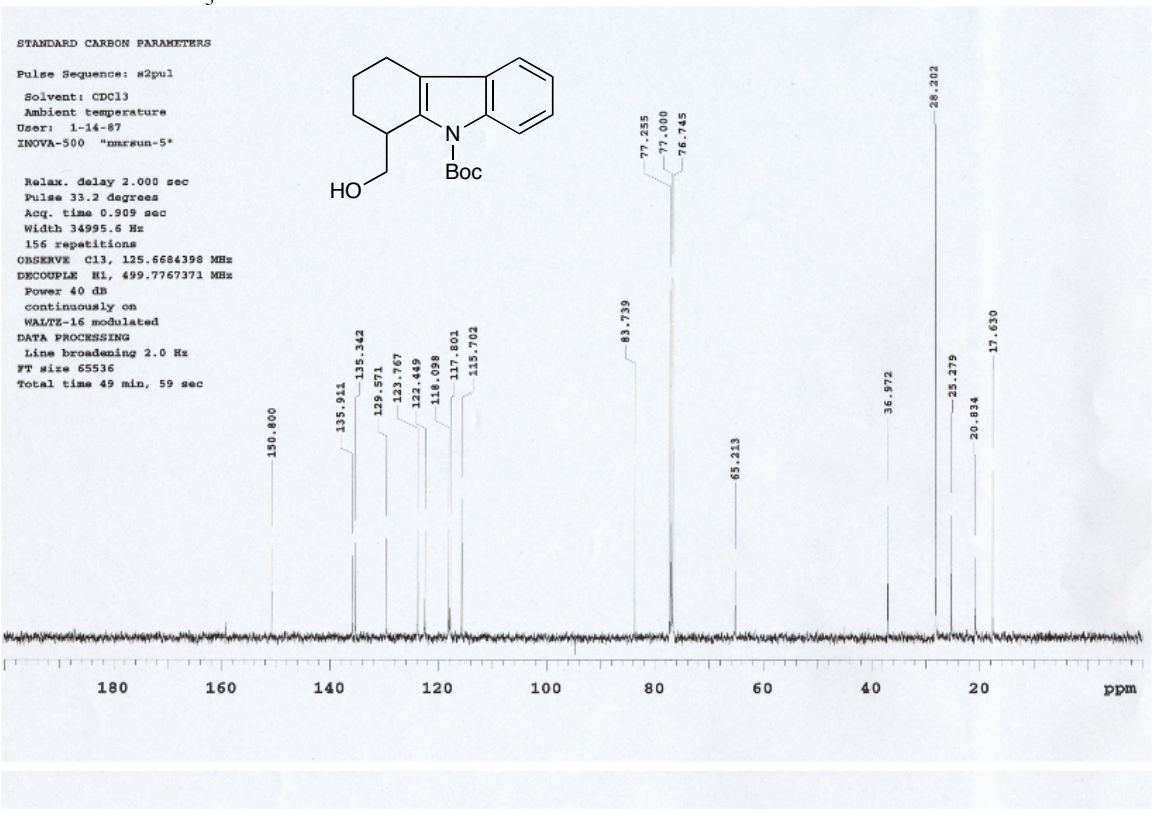
^{13}C NMR $CDCl_3$ 100 MHz



^{1}H NMR $CDCl_3$ 500 MHz



^{13}C NMR $CDCl_3$ 125 MHz



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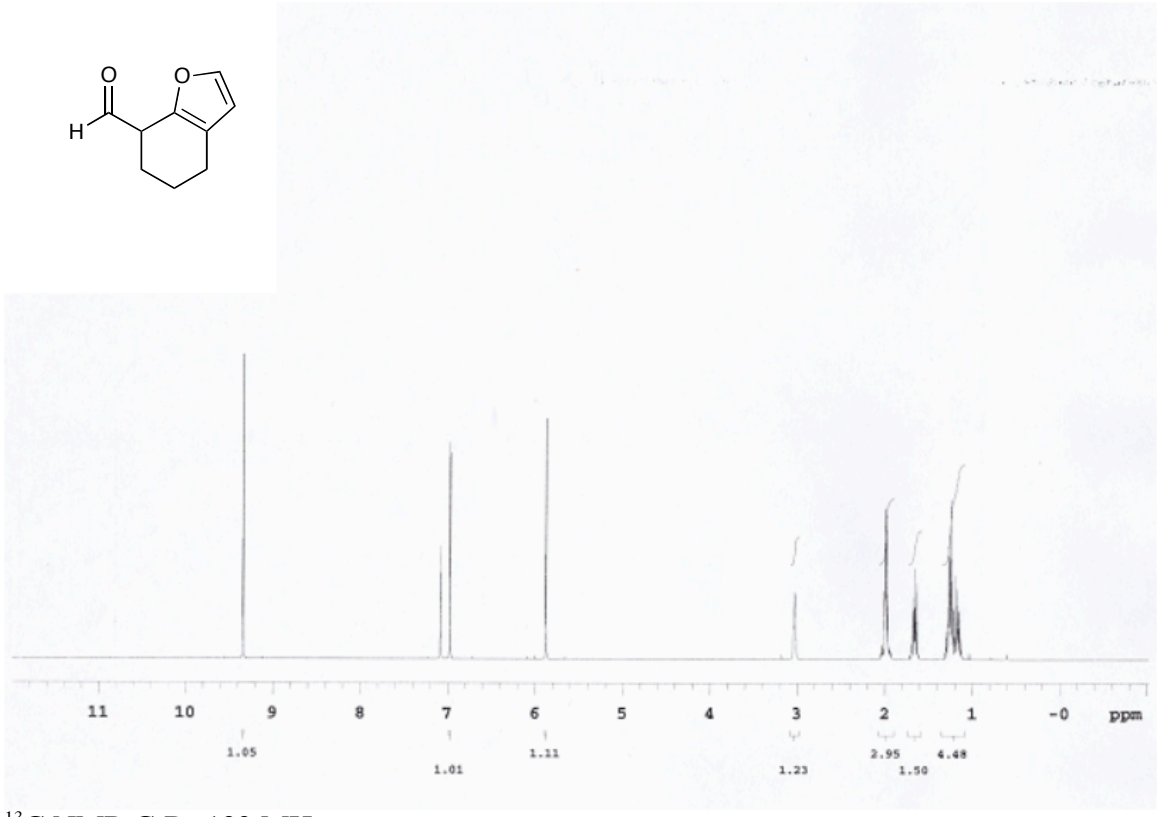
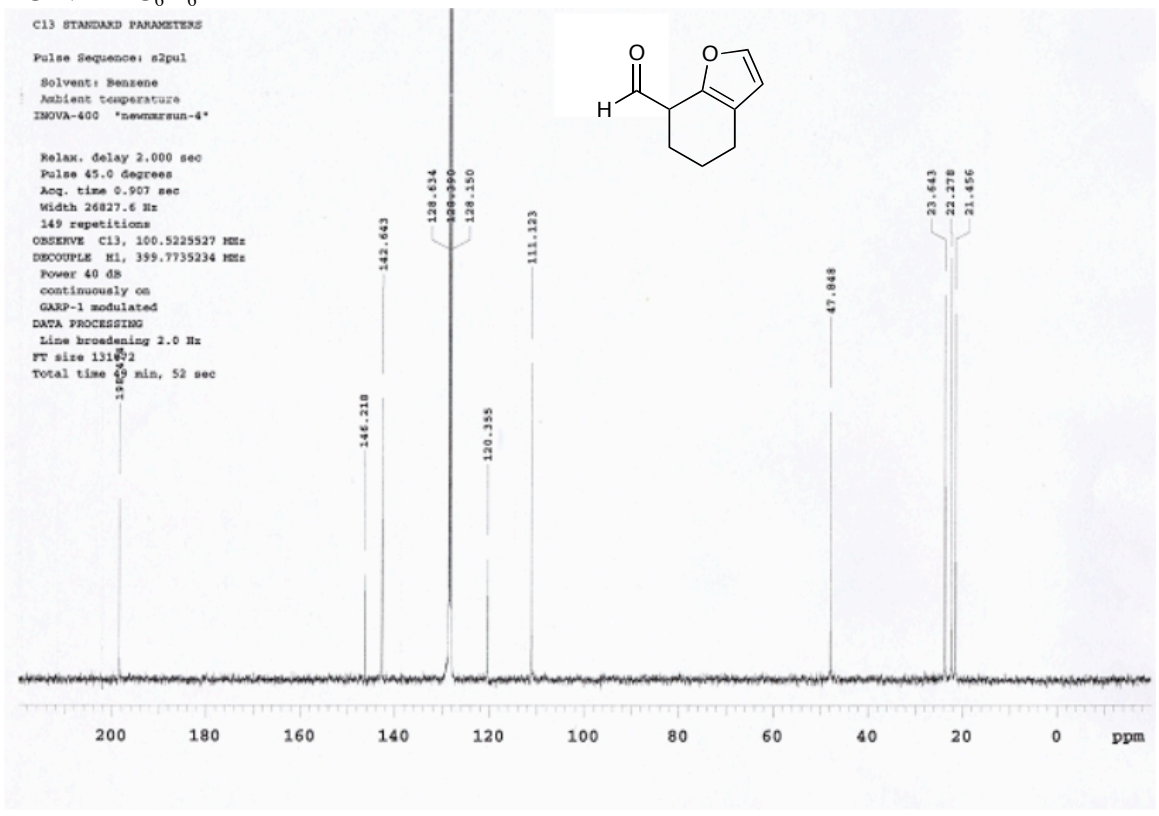
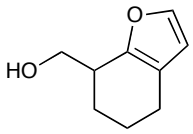


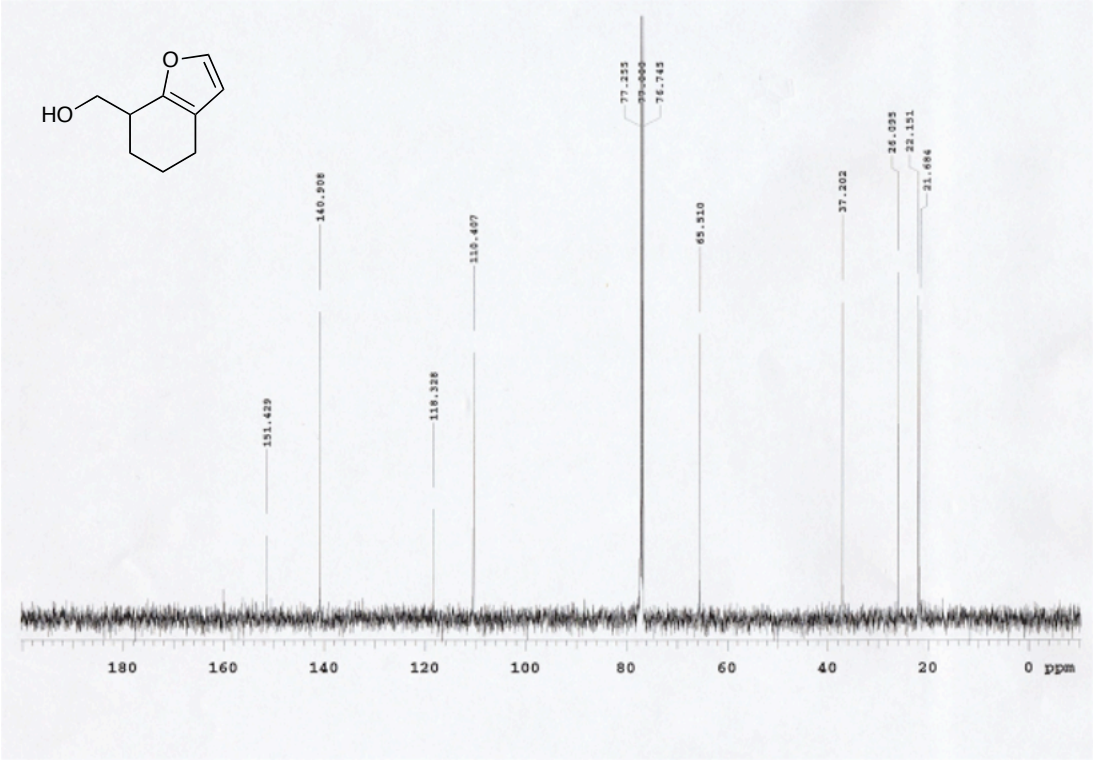
^{13}C NMR C_6D_6 100 MHz



^{1}H NMR $CDCl_3$ 400 MHz



^{13}C NMR $CDCl_3$ 100 MHz



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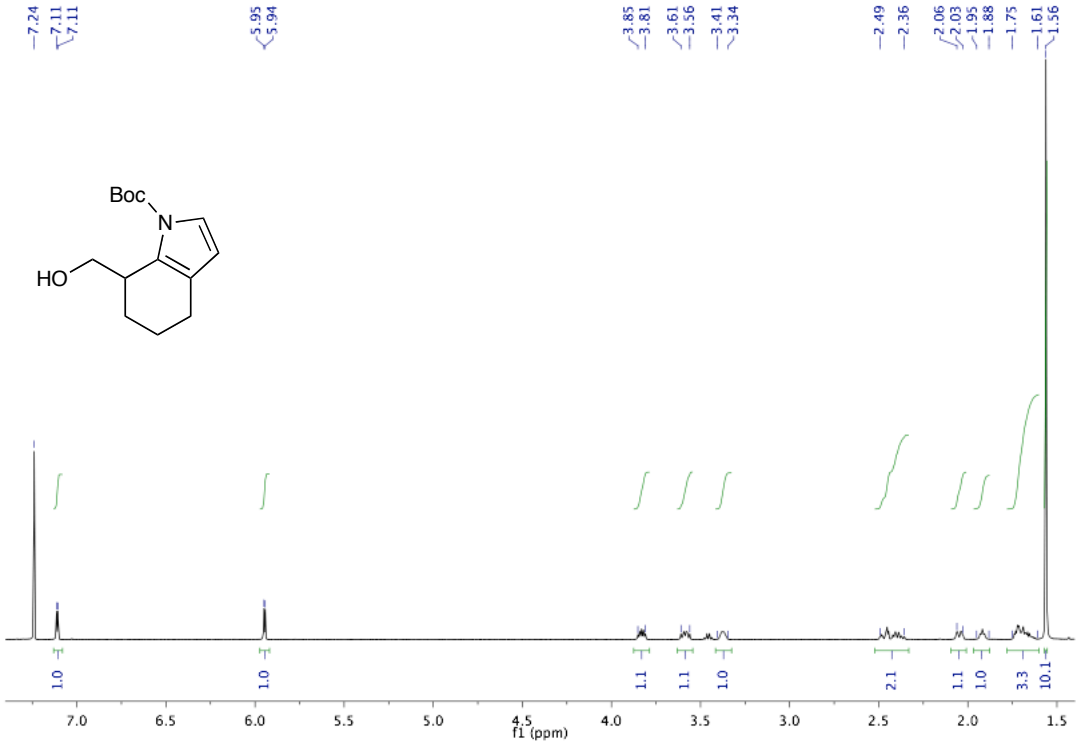
^{1}H NMR $CDCl_3$ 500 MHz



^{13}C NMR $CDCl_3$ 125 MHz

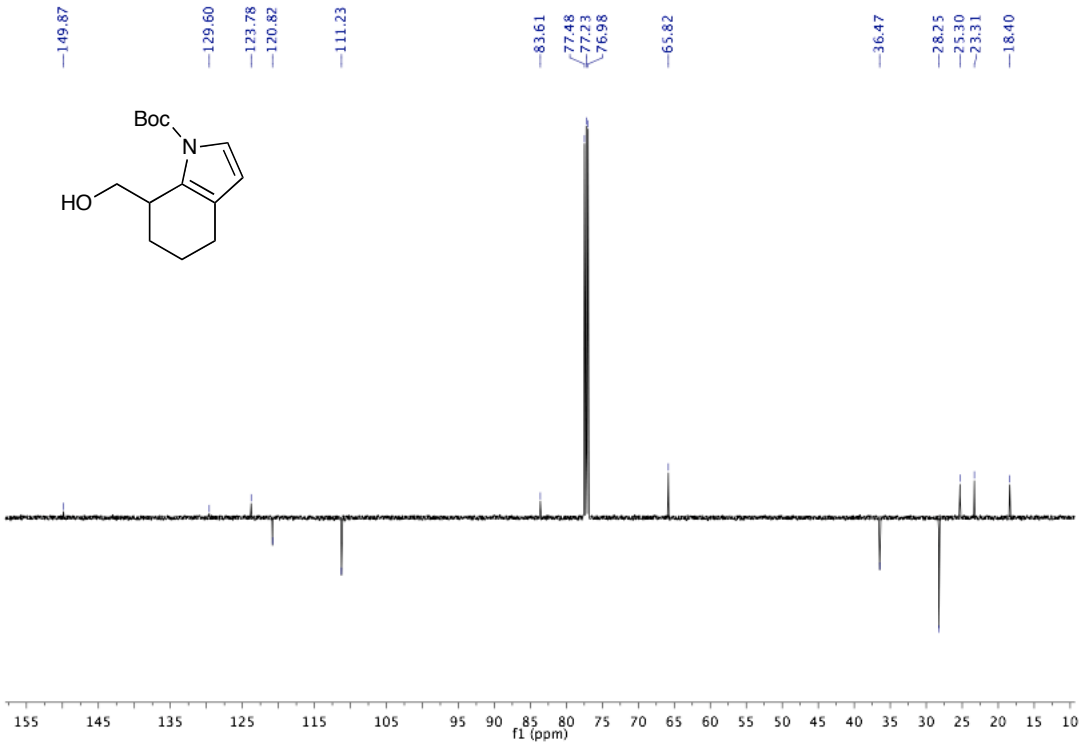
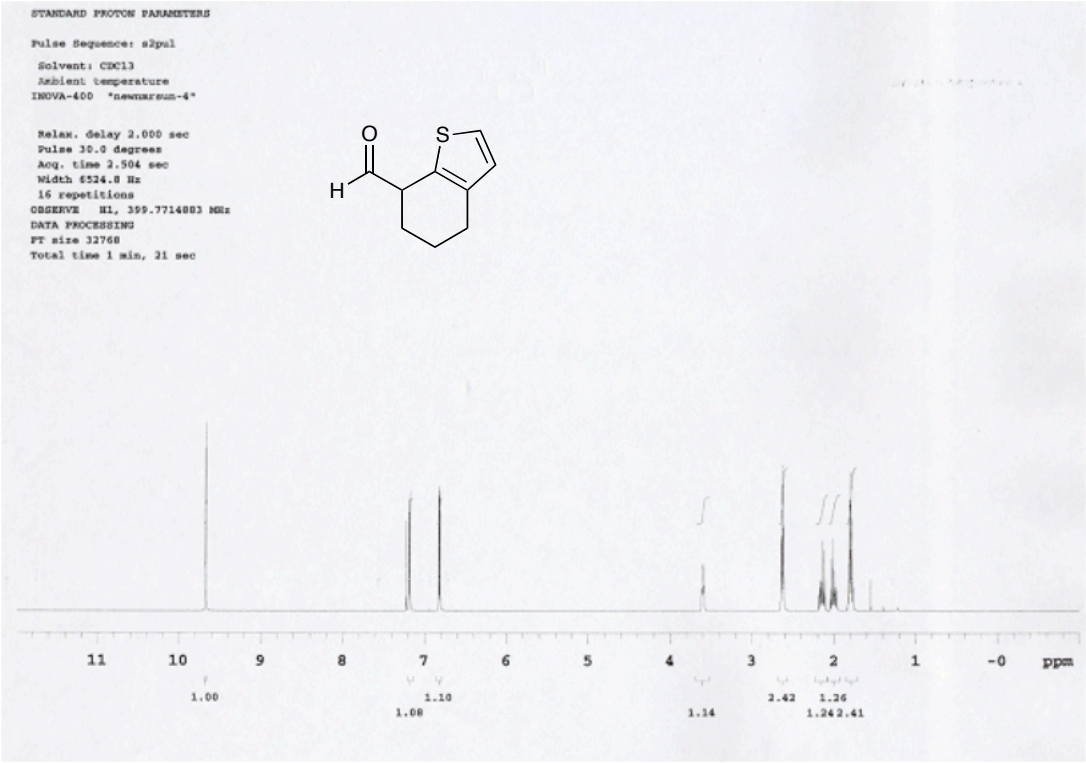
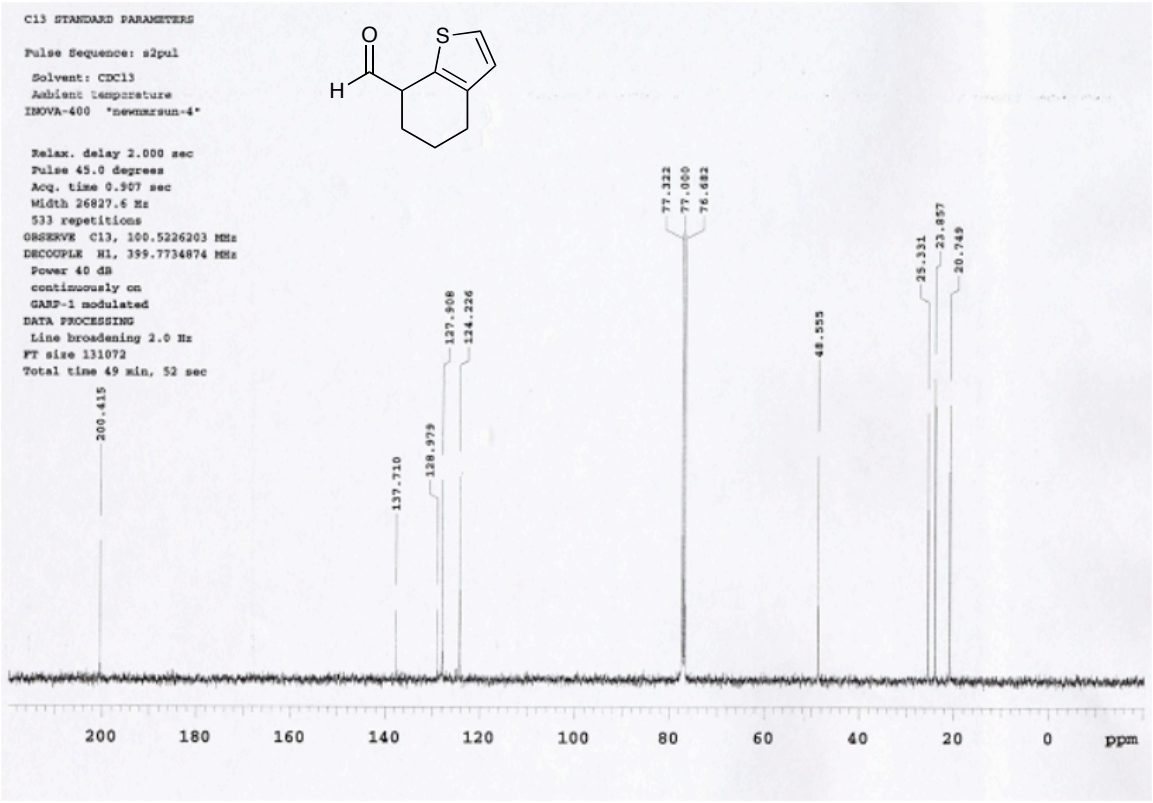


Table 2, Entry 9

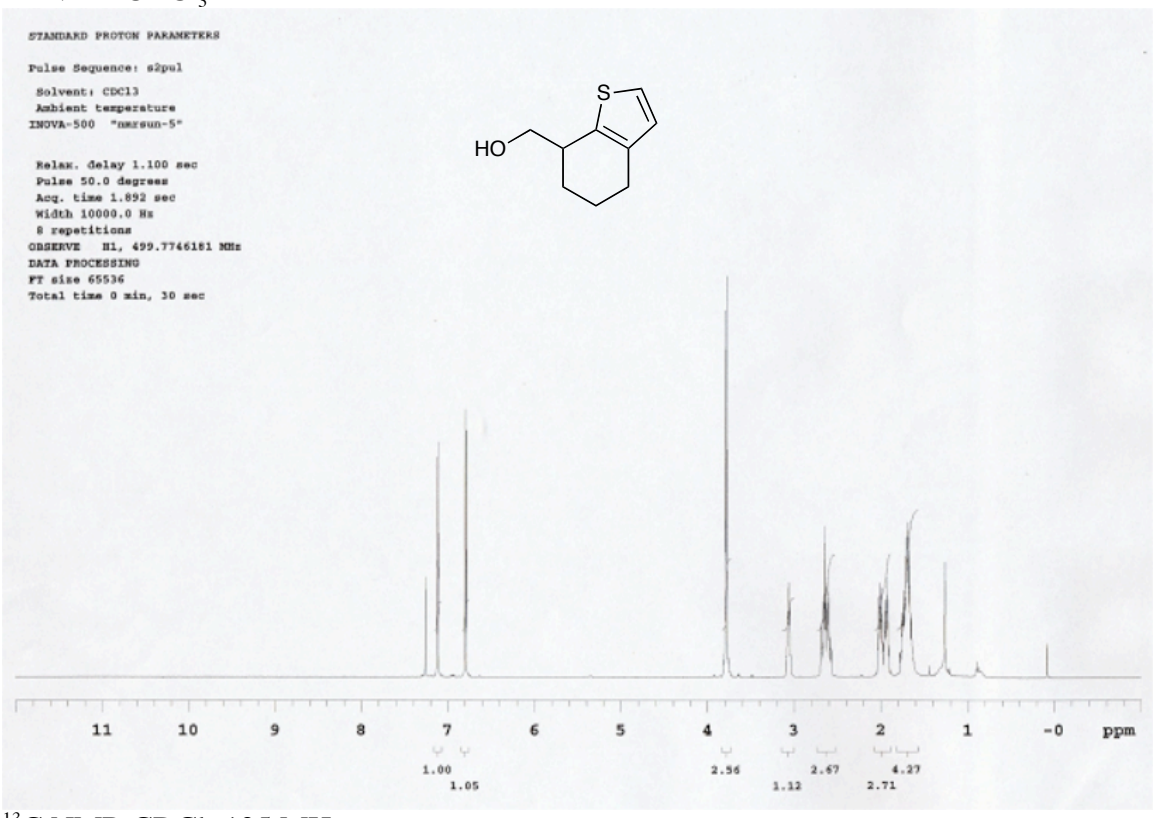
^{1}H NMR $CDCl_3$ 400 MHz



^{13}C NMR $CDCl_3$ 100 MHz



^{1}H NMR $CDCl_3$ 500 MHz



^{13}C NMR $CDCl_3$ 125 MHz

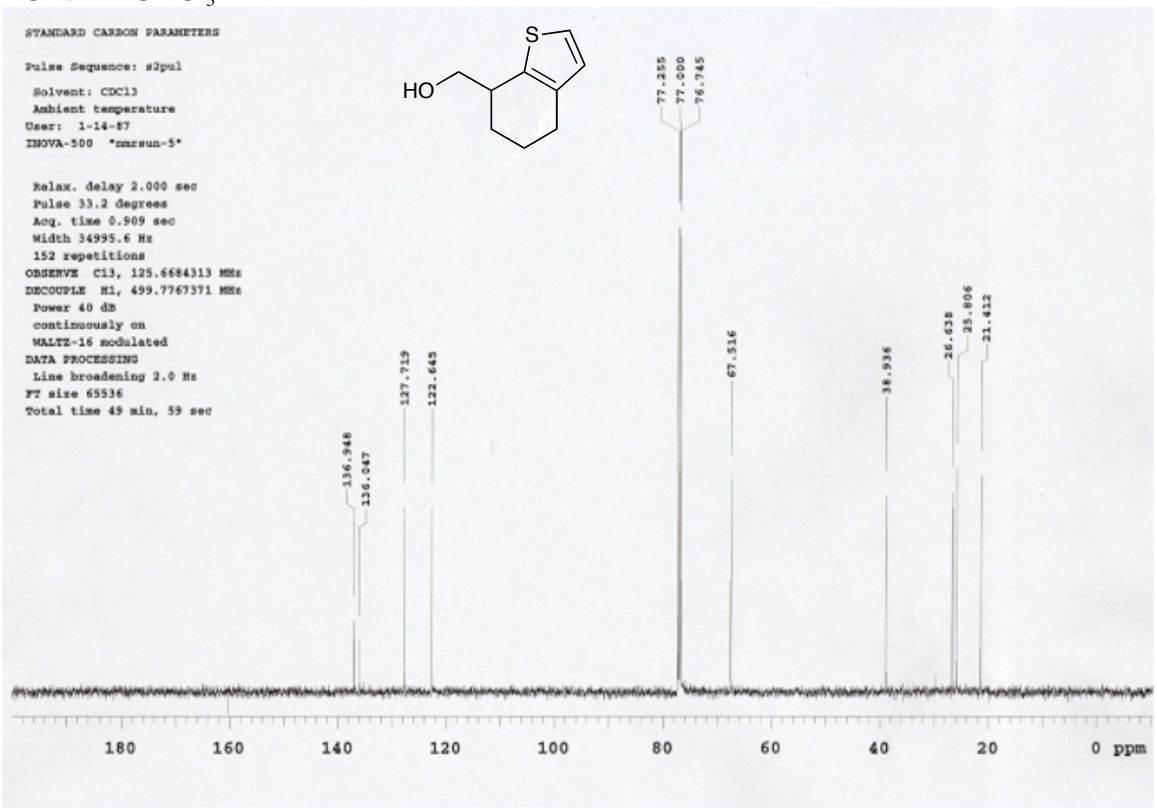
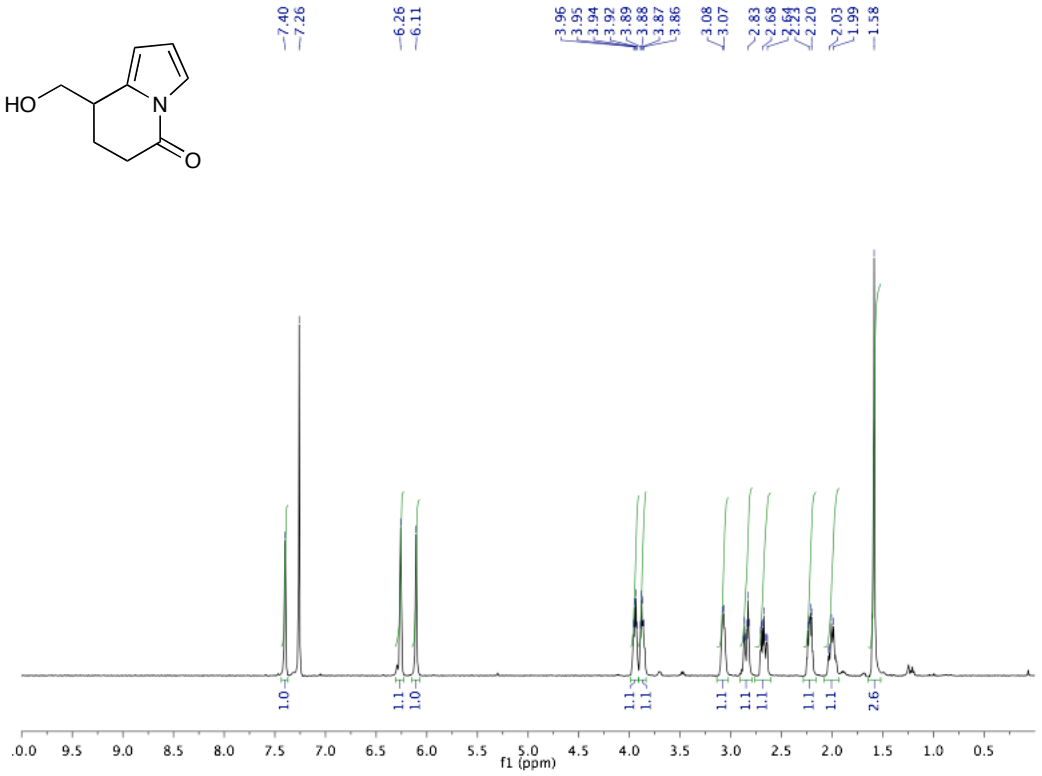
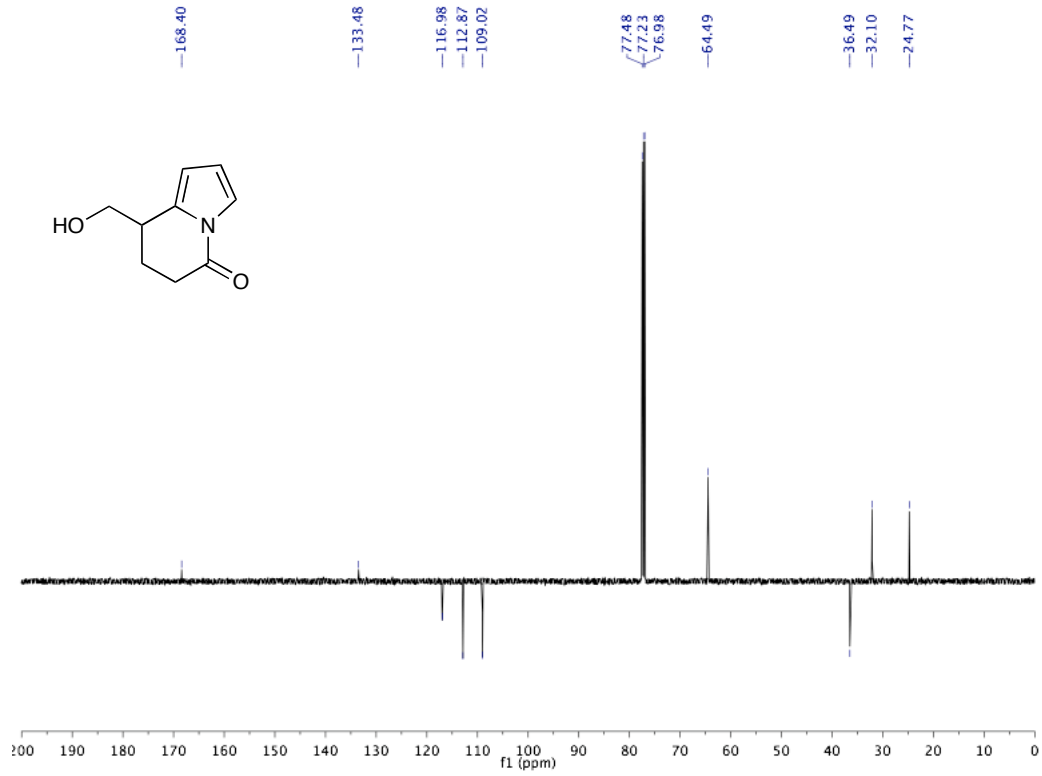


Table 2, Entry 10

^{1}H NMR $CDCl_3$ 500 MHz

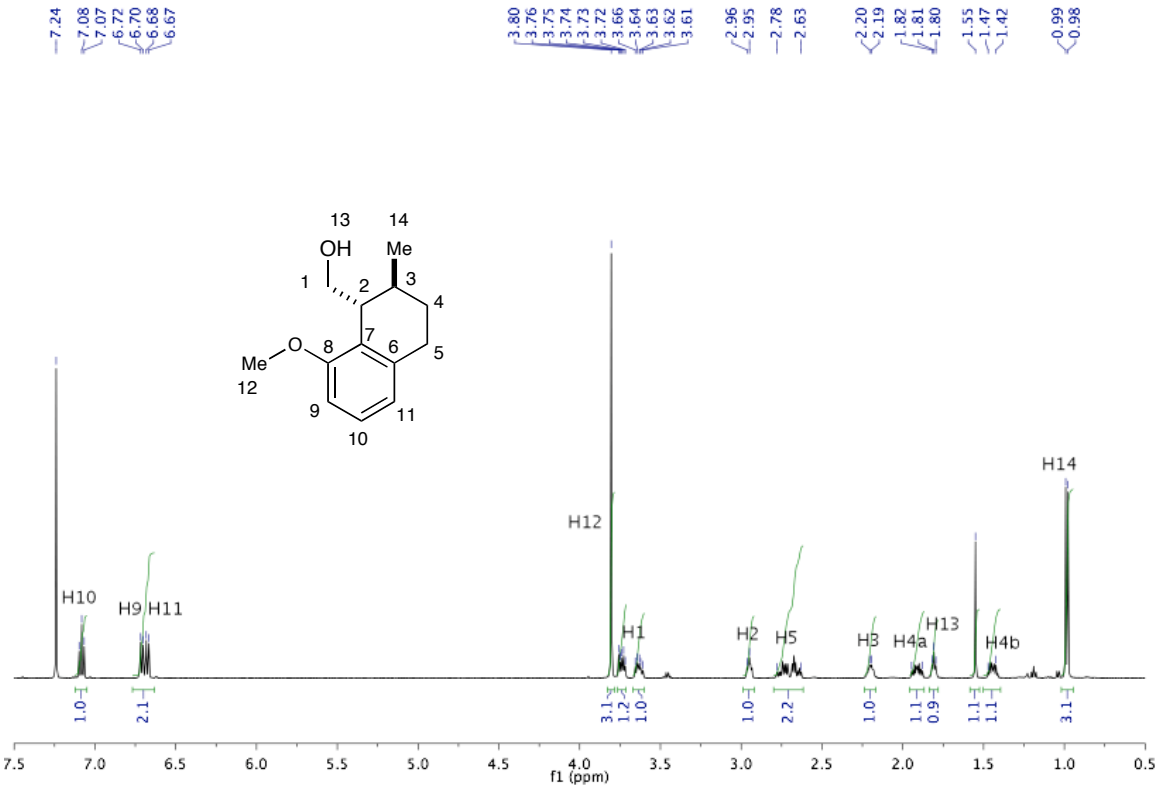


^{13}C NMR $CDCl_3$ 125 MHz

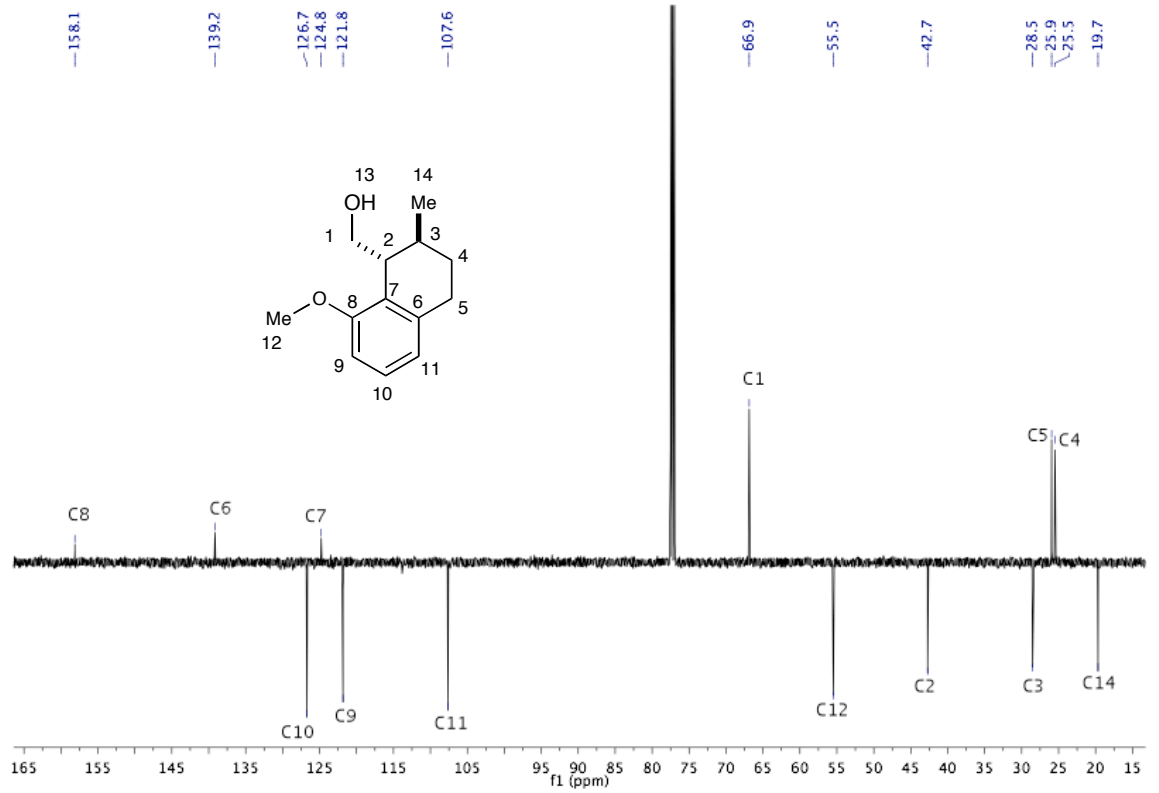


Equation 4 Product

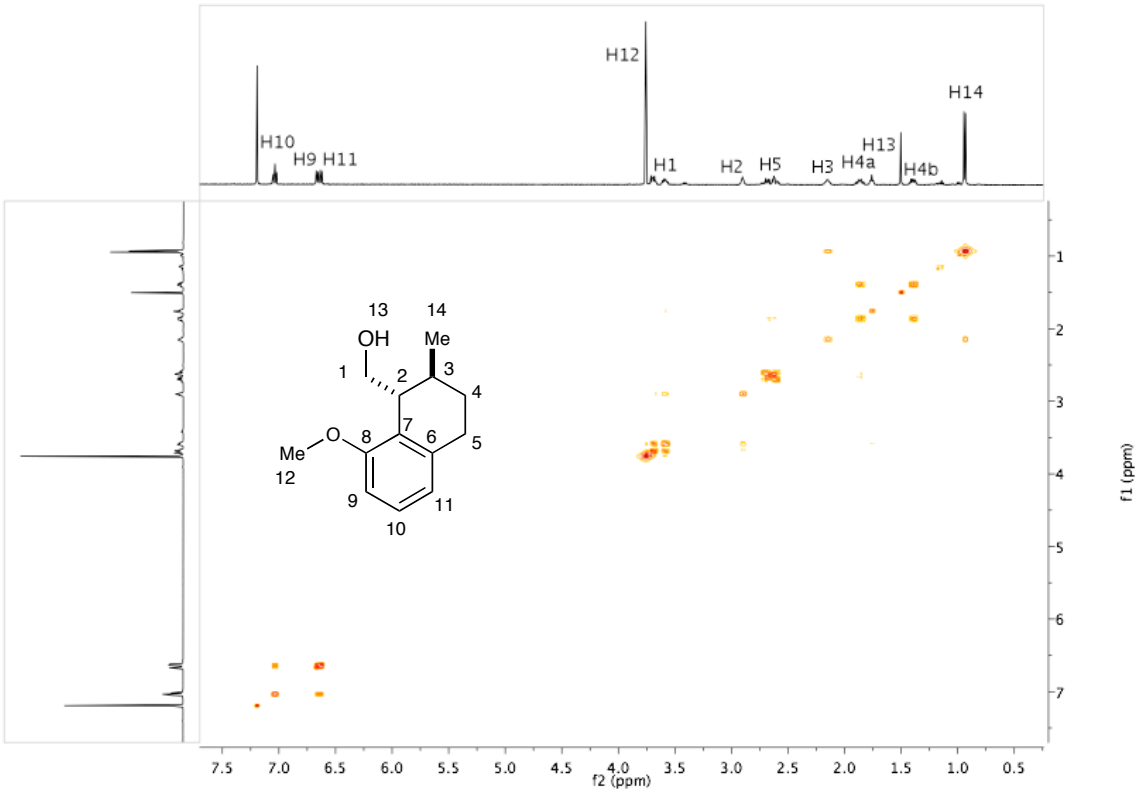
^{1}H NMR $CDCl_3$ 500 MHz



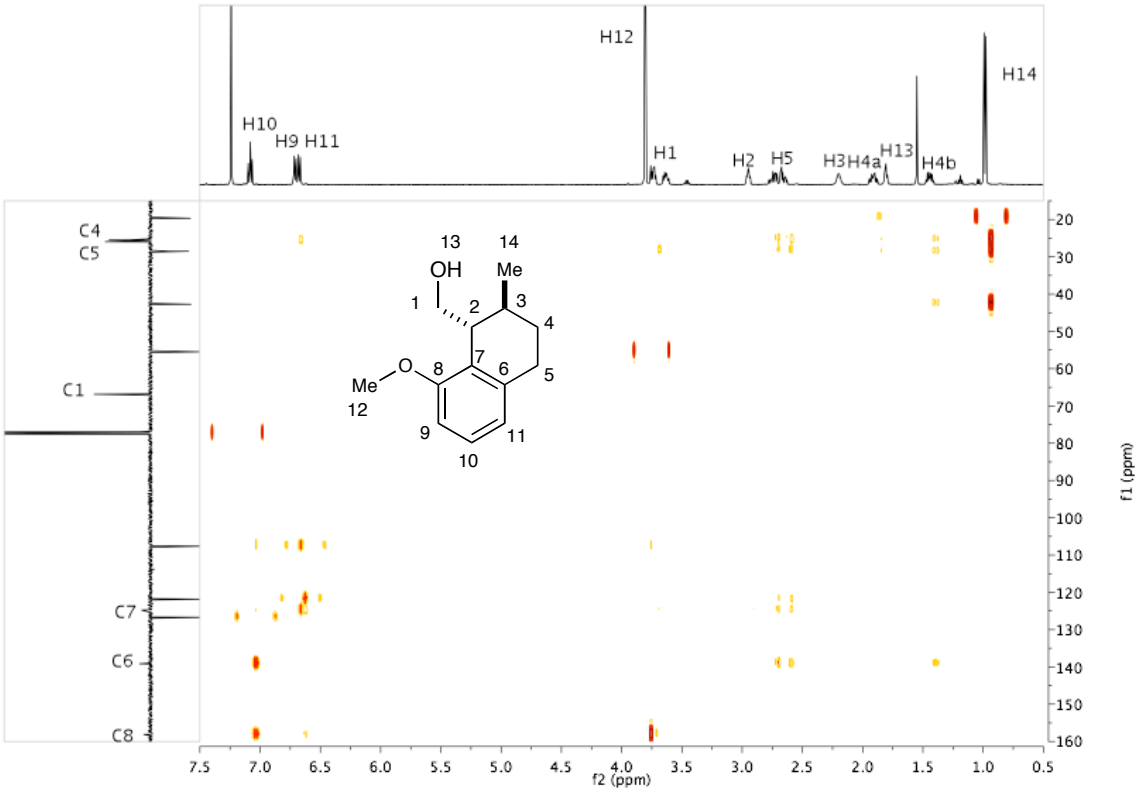
^{13}C NMR $CDCl_3$ 125 MHz



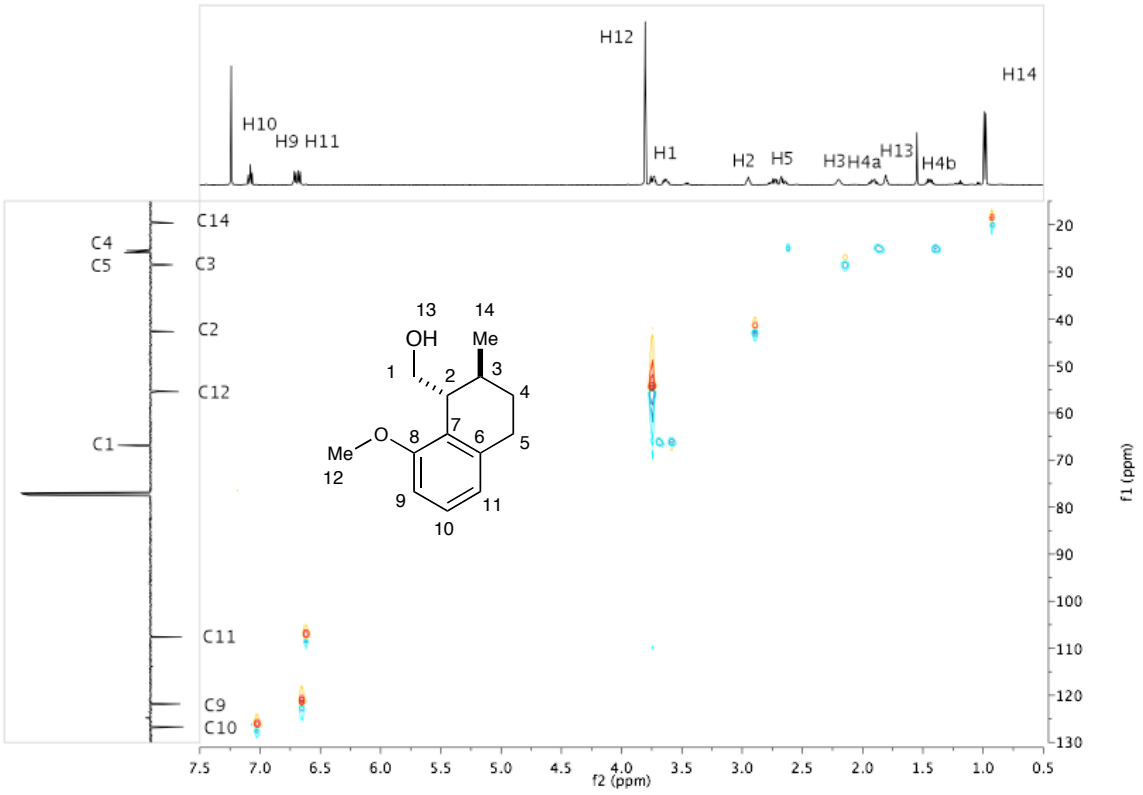
$^{1}H - {}^{1}H$ COSY $CDCl_3$ 500 MHz



$^{1}H - {}^{13}C$ HMBC $CDCl_3$ 500 MHz

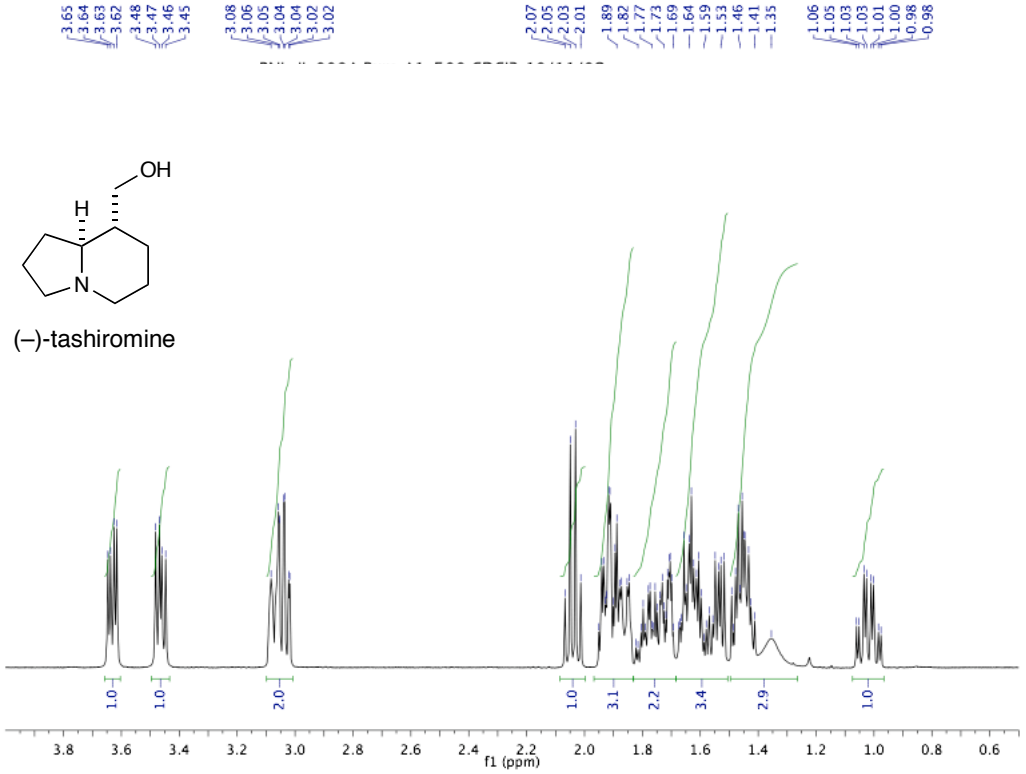


$^{1}H - ^{13}C$ HSQC $CDCl_3$ 500 MHz



(–)-tashiromine

^{1}H NMR $CDCl_3$ 500 MHz



^{13}C NMR $CDCl_3$ 125 MHz