Supporting Information

to accompany

Synthesis of (+)-Madindoline A and (+)-Madindoline B

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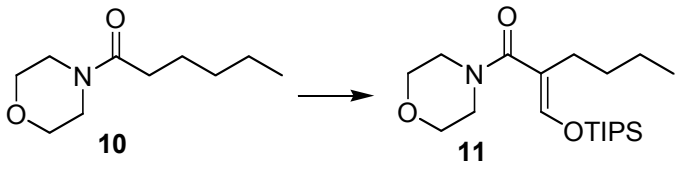
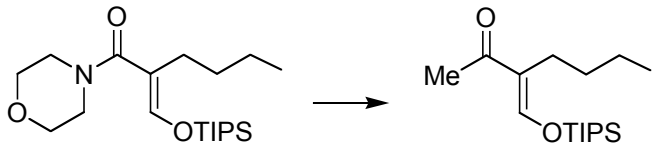
General: ^{1}H NMR and ^{13}C NMR spectra were recorded on either a Varian Mercury Plus 300 operating at 300 MHz (^{1}H) or 75 MHz (^{13}C), on a Varian Unity Inova 500 operating at either 500 MHz (^{1}H) or 125 MHz (^{13}C). Chemical shifts are reported in parts per million (δ) and are referenced to the solvent, *i.e* 7.26/77.0 for $CDCl_3$, 7.15/128.0 for C_6D_6. Multiplicities are indicated as br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), or m (multiplet). Coupling constants (*J*) are reported in Hertz (Hz). Infrared spectra were recorded on a Perkin Elmer IR 1430 spectrometer. Electron impact mass spectra were recorded on a VG-70SE mass spectrometer. Thin layer chromatography (TLC) was performed on Sigma-Aldrich TLC plates, 250 μm, particle size 5-17 μm, pore size 60 Å. Flash column chromatography was performed on silica gel, 200-400 mesh and on premium R_f, 60 Å, 40-75 μm. Purity and homogeneity of all materials was determined from TLC, ^{1}H NMR, and ^{13}C NMR. Anhydrous THF, DCM, DMF and Et_2O were taken from a solvent purification system. All moisture sensitive reactions were performed under a static atmosphere of nitrogen or argon atmosphere in oven dried or flame dried glassware.

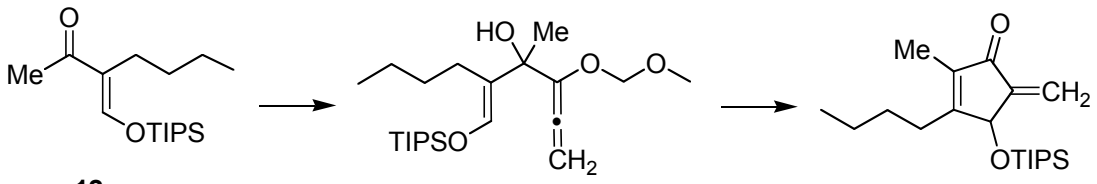


To a solution of *n*-BuLi (480 µL, 2.5 M in hexanes, 1.2 mmol) in 2 mL THF at - 40 ºC was added diisopropylamine (210 µL, 1.5 mmol) dropwise. After 15 min, the mixture was cooled to -78 ºC and amide **10** (185 mg, 1 mmol) in 2 mL THF was added. After 1 h, methyl formate (96 mg, 1.6 mmol) in 4 mL THF was added via cannula. The mixture was stirred for an additional 30 min, quenched with saturated $NaHCO_3$ and extracted with EtOAc. The combined organic layers were washed with brine and dried over Na_2SO_4. After concentration, the crude residue and a catalytic amount of DMAP were dissolved in 2 mL DCM. Hünig's base (437 µL, 2.5 mmol) and TIPSCl (356 µL, 1.7 mmol) were added into the solution dropwise. After stirring at room temperature overnight, the mixture was quenched with ice-cold saturated $NaHCO_3$ and extracted with EtOAc. The combined organic layer was washed with brine and dried over Na_2SO_4. The crude residue was purified by flash column chromatography on silica gel (20% EtOAc in hexanes) to yield **11** as a yellowish oil (168 mg, 50% yield). ^{1}H NMR (300 MHz, C_6D_6): δ 6.64 (s, 1 H), 3.40-3.37 (m, 4 H), 3.33-3.30 (m, 4 H), 2.53 (t, *J* = 7.5 Hz, 2 H), 1.57-1.48 (m, 2 H), 1.42-1.30 (m, 2 H), 0.98 (s, 21 H), 0.90 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6): δ 170.5, 142.5, 118.3, 67.0, 45.7, 30.8, 26.0, 23.0, 17.7, 14.1, 12.0; IR (film) 2955, 2866, 1642, 1456 cm^{-1}; EIMS: *m/z* (%) 369 (M^+, 0.1), 326 (38), 283 (8), 85 (13), 84 (100), 82 (16); HREIMS calcd for $C_{20}H_{39}NO_3Si$ 369.2699, found 369.2707.



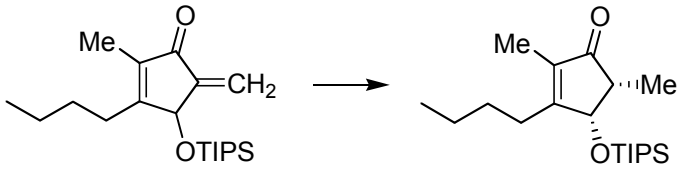
11 **12**

To a solution of compound **11** (185 mg, 0.5 mmol) in 1 mL THF at -78 ºC was added MeLi (375 µL, 1.6 M in diethyl ether, 0.6 mmol). After stirring at -78 ºC for 5 h, the reaction was quenched by ice-cold saturated $NaHCO_3$ and extracted with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. Purification by flash column chromatography on silica gel (5% EtOAc in hexanes) gave **12** as a clear oil (104 mg, 70% yield). ^{1}H NMR (300 MHz, C_6D_6): δ 7.44 (s, 1 H), 2.57 (t, *J* = 7.5 Hz, 2 H), 2.00 (s, 3 H), 1.65-1.52 (m, 2 H), 1.47-1.34 (m, 2 H), 0.97 (m, 21 H), 0.94 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6): δ 195.7, 153.0, 126.9, 31.4, 25.3, 23.3, 23.1, 17.6, 14.3, 11.9; IR (film) 2955, 2943, 2862, 1712, 1619, 1464 cm^{-1}; EIMS *m/z* (*%*) 298 (M^+, 0.2), 257 (6), 256 (25), 255 (100), 77 (3), 69 (8); HREIMS calcd for $C_{17}H_{34}O_2Si$ 298.2328, found 298.2313.



12 **13** **14**

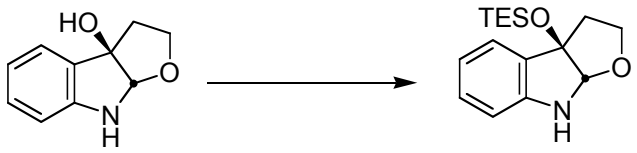
A solution of 1-lithio-1-(methoxy)methoxyallene was prepared in 2 mL THF at -78 ºC from 140 mg (1.4 mmol) of (methoxy)methoxyallene and 480 µL *n*-BuLi (2.50 M in hexanes, 1.2 mmol). After 20 min, a solution of compound **12** (298 mg, 1 mmol) in 2mL THF was added at -78 ºC *via* cannula. After 30 min, the reaction mixture was quenched by water and extracted with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. To a solution of crude tertiary alcohol **13** and 2,6-lutidine (349 µL, 3 mmol) in 2 mL DCM at -20 ºC was added trifluoroacetic anhydride (284 µL, 2 mmol) dropwise over a period of 15 min. After 1 h, the reaction mixture was quenched with ice-cold saturated $NaHCO_3$. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. Purification by flash column chromatography on silica gel (5% EtOAc in hexanes) gave **14** as a yellow oil (296 mg, 88% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.08 (s, 1 H), 5.52 (s, 1 H), 5.24 (s, 1 H), 2.57-2.00 (m, 2 H), 1.78 (s, 3 H), 1.63-1.27 (m, 4 H), 1.19-1.01 (m, 21 H), 0.92 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.4, 168.8, 145.4, 139.1, 116.3, 71.5, 29.6, 26.9, 23.0, 18.2, 13.8, 13.2, 8.2; IR (film) 2959, 2866, 1771, 1701, 1635, 1464 cm^{-1}; EIMS: *m/z* (%) 336 (M^+, 0.1), 294 (17), 293 (100), 75 (13); HREIMS calcd for $C_{20}H_{36}O_2Si$ 336.2485, found 336.2478.



14 **15**

To a solution of compound **14** (134 mg, 0.4 mmol) in 2 mL ethanol was added 5% Pd/C (8 mg, 1 mol%) at room temperature. The reaction flask was degassed by vacuum and filled with H_2. After 10 min, the reaction mixture was filtered through a column of Celite and concentrated. Purification by flash column chromatography on silica gel (5% EtOAc in hexanes) gave **15** as a clear oil (135 mg, 100% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.96 (d, J = 5.1 Hz, 1 H), 2.61-2.51 (m, 1 H), 2.49-2.29 (m, 2 H), 1.68 (s, 1 H), 1.48-1.32 (m, 4 H), 1.12-1.03 (m, 24 H), 0.92 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.3, 172.6, 135.0, 73.4, 46.5, 30.1, 27.3, 23.0, 18.2, 13.9, 13.5, 13.3, 13.0, 7.9; IR (film) 2963, 2943, 2866, 1704, 1654, 1464 cm^{-1}; EIMS: *m/z* (*%*) 297 (16), 295 (100), 165(42), 131 (42); HREIMS calcd for ($C_{20}H_{38}O_2Si$ – C_3H_7) 295.2093, found 295.2110.

(-)-3a-Hydroxyfuroindoline **25** was obtained in 30% yield and 100% *ee* through Sharpless epoxidation of tryptophol after two recrystallizations from hexanes/DCM.[1] The *ee* was determined by integration of the trifluoromethyl signals in the ^{19}F NMR spectrum of the derived diastereomeric Mosher amides.

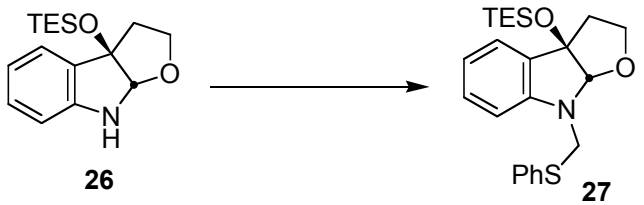


25 **26**

To a solution of **25** (531 mg, 3 mmol) and K_2CO_3 (1.242 g, 9 mmol) in 12 mL MeCN at 0 ºC was added benzyl chloroformate (856 µL, 6 mmol). The reaction mixture was stirred at 0 ºC for 30 min and warmed up to room temperature for an additional 30 min. The reaction was quenched with water and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. To a solution of the crude residue and Et_3N (842 µL, 6 mmol) in 12 mL DCM at 0 ºC was added TESOTf (813 µL, 3.6 mmol). The reaction mixture was kept at 0 ºC for 1 h and warmed up to room temperature for 1 h. The reaction was quenched by ice-cold saturated $NaHCO_3$ and extracted with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. The organic residue was dissolved in 18 mL ethanol and 5% Pd/C (319 mg, 5 mol%) was added. The mixture was stirred under a H_2 atmosphere at room temperature for 3 h, followed by filtration through Celite. The filtrate was concentrated and purified by flash column chromatography on silica gel (6% EtOAc in hexanes) to yield **26** as a colorless oil (717 mg, 82% yield). ^1H NMR (300

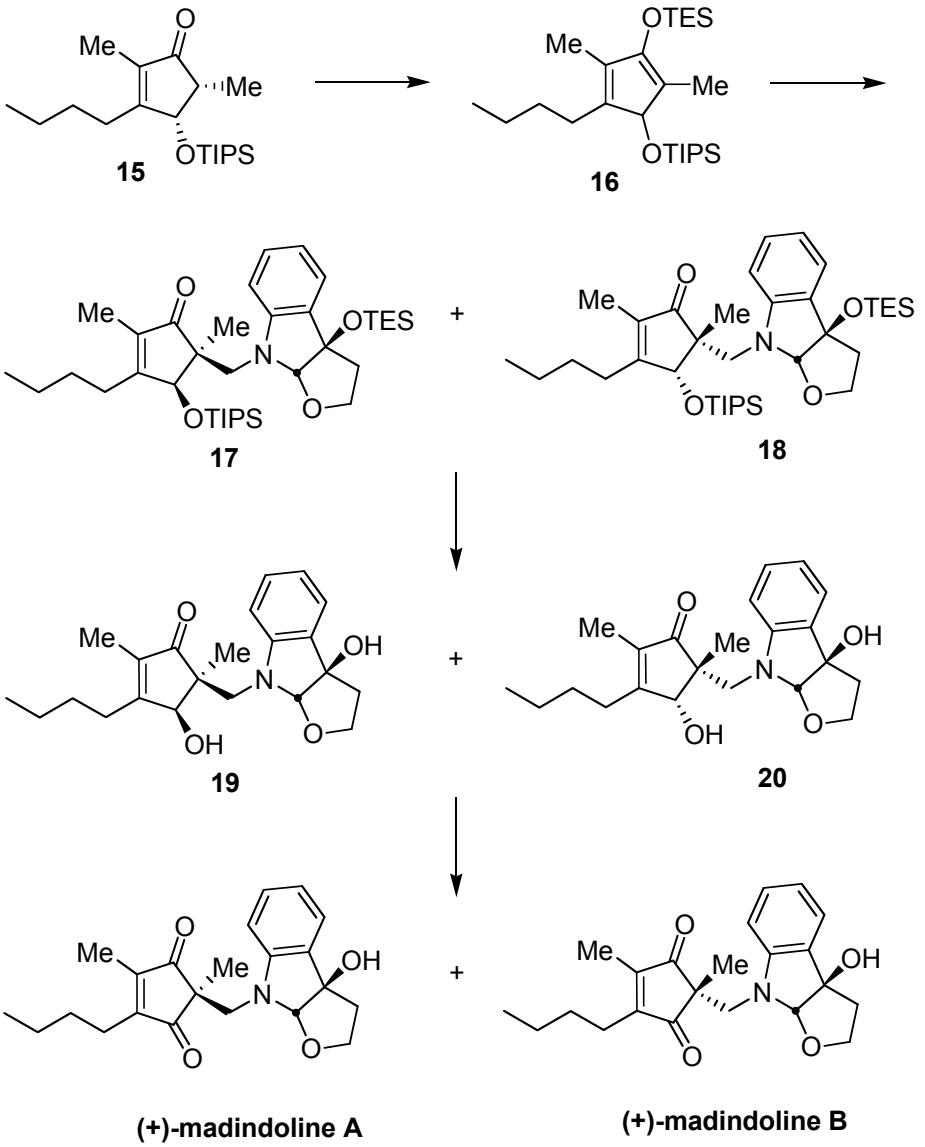
[1] (a) Sunazuka, T.; Tomoyasu, H.; Shirahata, T.; Harigaya, Y.; Hayashi, M.; Komiyama, K.; Ōmura, S.; Smith, A. B., III. *J. Am. Chem. Soc.* **2000**, *122*, 2122. (b) Hirose, T.; Sunazuka, T.; Yamamoto, D.; Kojima, N.; Shirahata, T.; Harigaya, Y.; Kuwajima, I.; Ōmura, S. *Tetrahedron* **2005**, *61*, 6015.

MHz, C_6D_6): δ 7.21 (d, *J* = 7.5 Hz, 1 H), 7.00 (t, *J* = 7.5 Hz, 1 H), 6.68 (t, *J* = 7.5 Hz, 1 H), 6.29 (d, *J* = 7.5 Hz, 1 H), 5.38 (s, 1 H), 4.09 (s, 1 H), 3.78 (t, *J* = 7.8 Hz, 1 H), 3.47-3.39 (m, 1H), 2.45-2.35 (m, 1 H), 2.10 (dd, *J* = 11.4, 4.5 Hz, 1 H), 0.91 (t, *J* = 7.8 Hz, 9 H), 0.50 (q, *J* = 7.8 Hz, 6 H); ^{13}C NMR (75 MHz, C_6D_6): δ 150.5, 130.6, 130.1, 124.9, 118.8, 109.0, 99.0, 91.2, 67.1, 43.5, 7.1, 6.1; IR (film) 3355, 2955, 2875, 1614, 1471 cm^{-1}; EIMS: *m/z* (%) 291 (M^+, 100), 262 (90), 244 (15); HREIMS calcd for $C_{16}H_{25}NO_2Si$ 291.1780, found 291.1781.



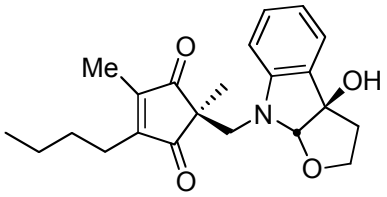
26 **27**

To a solution of **26** (81 mg, 0.28 mmol) in 3 mL 95% ethanol was added thiophenol (34 mg, 0.30 mmol) and 37% aqueous formaldehyde (25 mg, 0.30 mmol). The mixture was refluxed at 80 ºC overnight. After cooling to room temperature, the solvent was removed in vacuo. The residue was dissolved in Et_2O, washed with brine, dried over Na_2SO_4 and concentrated. Purification by flash column chromatography on silica gel (5% EtOAc in hexanes) gave **27** as a colorless oil (107 mg, 93% yield). ^{1}H NMR (300 MHz, C_6D_6): δ 7.41 (d, *J* = 7.5 Hz, 2 H), 7.22 (d, *J* = 7.5 Hz, 1 H), 7.03-6.89 (m, 4 H), 6.69 (t, *J* = 7.5 Hz, 1 H), 6.31 (d, *J* = 7.5 Hz, 1 H), 5.61 (s, 1 H), 4.86 (d, *J* = 13.8 Hz, 1 H), 4.71 (d, *J* = 13.8 Hz, 1 H), 3.76 (t, *J* = 8.1 Hz, 1 H), 3.38-3.30 (m, 1 H), 2.40-2.30 (m, 1 H), 2.30 (dd, *J* = 12.0, 4.5 Hz, 1 H), 0.90 (t, *J* = 8.1 Hz, 9 H), 0.50 (q, *J* = 8.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.8, 135.6, 131.9, 131.2, 129.7, 128.9, 127.0, 124.3, 118.7, 107.0, 101.6, 89.5, 67.1, 51.4, 43.8, 6.8, 5.8; IR (film) 3054, 2953, 2874, 1609, 1487 cm^{-1}; EIMS: *m/z* (%) 304 (100), 218 (25), 144 (45), 109 (16); HREIMS calcd for $C_{23}H_{31}NO_2SSi$ 413.1845, found 413.1838.



To a solution of *n*-BuLi (236 µL, 2.5 M in hexanes, 0.59 mmol) in 2 mL THF at -40 ºC diisopropylamine (120 µL, 0.85 mmol) was added dropwise. After 15 min, the mixture was cooled to -78 ºC and a solution of compound **15** (160 mg, 0.47 mmol) in 2 mL THF was added. After 1 h at -78 ºC, TESCl (105 µL, 0.62 mmol) was added. The reaction mixture was stirred at -78 ºC for 1 h, warmed to –50 ºC over 15 min and stirred further for 2 h at -50 ºC. The reaction was quenched by ice-cold saturated $NaHCO_3$ and extracted with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. The crude residue of **16** was used in the next step without

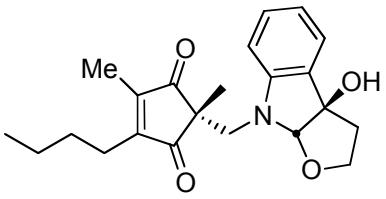
purification. To a solution of **27** (235 mg, 0.57 mmol) with $ZnBr_2$ (117 mg, 0.52 mmol) in 2 mL DCM at -30 °C was added a solution of **16** in 2 mL DCM. The reaction mixture was stirred at -30 °C for additional 6 h. The reaction was quenched by addition of water and extracted with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated to yield a crude mixture of **17** and **18**. To a solution of the crude mixture of **17** and **18** in 4 mL THF at room temperature was added TBAF (1.17 mL, 1 M in THF, 1.17 mmol). After stirring at room temperature for 30 min, the reaction mixture was quenched with water and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated to afford the crude residue of **19** and **20**. To a solution of the crude residue of **19** and **20** in 2 mL DMF at room temperature was added PDC (444 mg, 1.18 mmol). After 2 h, the reaction mixture was quenched with water and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. Purification by flash column chromatography on silica gel (30% EtOAc in hexanes) gave yellowish solids: (+)-madindoline A (26 mg, 15% yield) and (+)-madindoline B (26 mg, 15% yield).



(+)-madindoline A

mp 108-110 °C; $[\alpha]^{20}_D$ +126° (c 0.30, MeOH), $[\alpha]^{21}_D$ +110° (c 0.35, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.19 (m, 2 H), 6.75 (dt, *J* = 7.5, 0.5 Hz, 1 H), 6.64 (d, *J* = 8.0 Hz, 1 H), 4.93 (s, 1 H), 3.84 (ddd, *J* = 9.0, 7.5, 1.5 Hz, 1 H), 3.71 (d, *J* = 14.5 Hz, 1 H), 3.48 (d, *J* = 14.5 Hz, 1 H), 3.16 (ddd, *J* = 11.5, 9.0, 5.0 Hz, 1 H), 2.40-2.30 (m, 3 H), 2.18 (ddd, *J* = 12.0, 5.0, 1.5 Hz, 1 H), 2.00 (s, 3 H), 1.99 (s, 1 H), 1.34-1.28 (m, 2 H), 1.23-

1.17 (m, 2 H), 1.13 (s, 3 H), 0.77 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.4, 206.3, 157.7, 156.6, 150.5, 130.5, 129.5, 123.5, 119.1, 108.0, 106.2, 88.0, 66.6, 53.6, 50.6, 41.1, 29.9, 23.5, 22.7, 17.3, 13.6, 9.4; IR (film) 3416, 3052, 2932, 1740, 1694, 1610, 1487 cm^{-1}; EIMS: *m/z* (*%*) 369 (M^+, 10), 190 (100), 172 (17), 144 (17); HREIMS calcd for $C_{22}H_{27}NO_4$ 369.1940, found 369.1943.



(+)-madindoline B

mp 114-115 °C; $[\alpha]^{20}_D$ +87.3° (c 0.45, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (m, 2 H), 6.74 (dt, J = 7.5, 1 Hz, 1 H), 6.63 (d, J = 8.0 Hz, 1 H), 4.91 (s, 1 H), 3.84 (ddd, J = 9.0, 7.5, 1.5 Hz, 1 H), 3.70 (d, J = 14.5 Hz, 1 H), 3.50 (d, J = 14.5 Hz, 1 H), 3.17 (ddd, J = 11.5, 9.0, 5.0 Hz, 1 H), 2.49-2.43 (m, 1 H), 2.40-2.34 (m, 1 H), 2.33 (ddd, J = 12.0, 11.5, 7.5 Hz, 1 H), 2.19 (ddd, J = 12.0, 5.0, 1.0 Hz, 1 H), 2.00 (s, 1H), 1.94 (s, 3 H), 1.41-1.35 (m, 2 H), 1.32-1.24 (m, 2 H), 1.13 (s, 3 H), 0.86 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.6, 205.9, 160.3, 153.7, 150.4, 130.5, 129.4, 123.5, 118.9, 107.8, 105.0, 87.9, 66.7, 52.1, 50.5, 41.2, 29.5, 24.0, 22.9, 17.4, 13.7, 9.1; IR (film) 3418, 3052, 2930, 1741, 1696, 1610, 1488 cm^{-1}; EIMS: *m/z* (*%*) 369 (M^+, 9), 190 (100), 172 (16), 149 (44), 144 (18), 97 (24), 83 (24), 71 (28), 69 (31); HREIMS calcd for $C_{22}H_{27}NO_4$ 369.1940, found 369.1946.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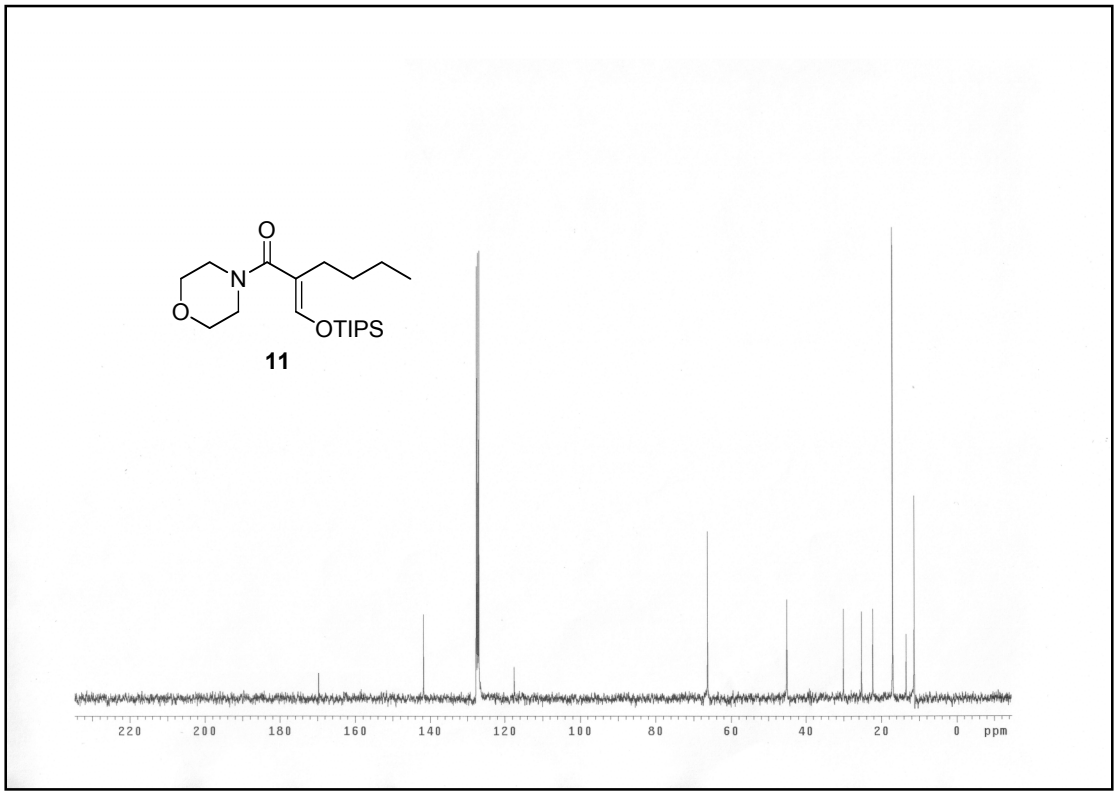
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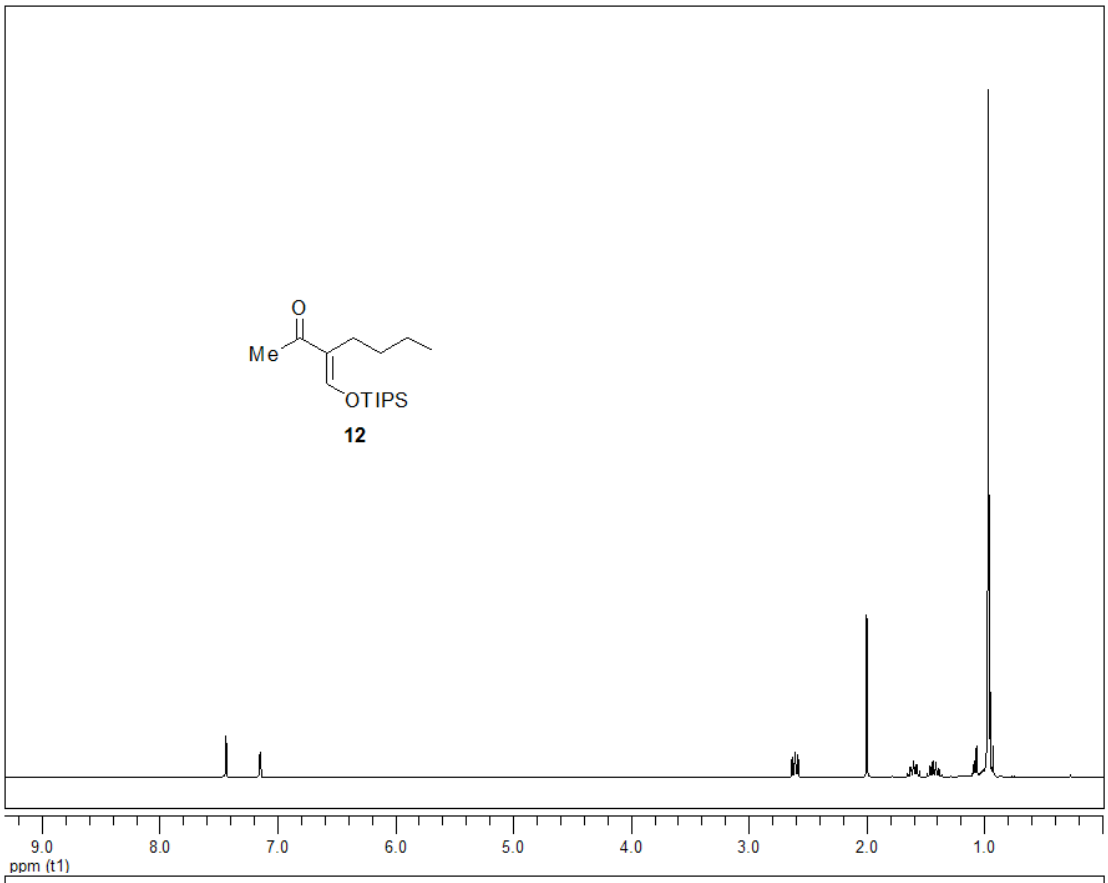
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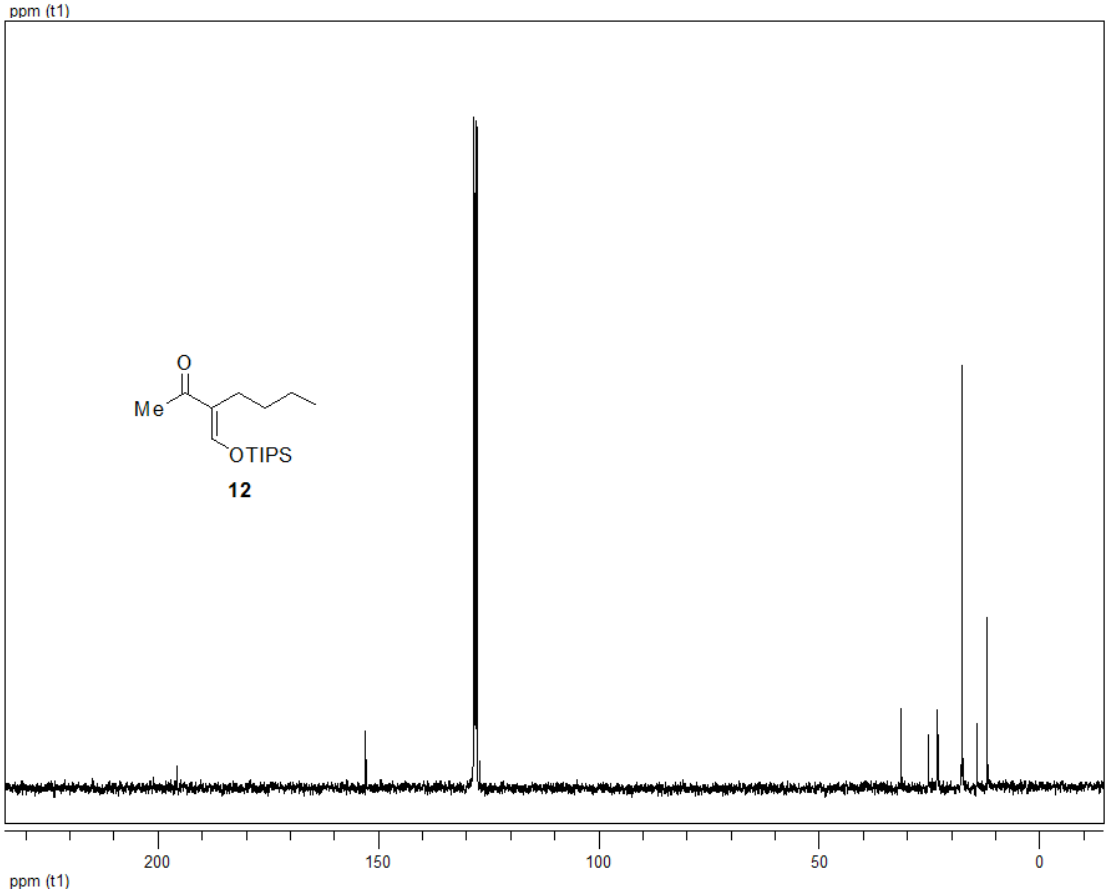
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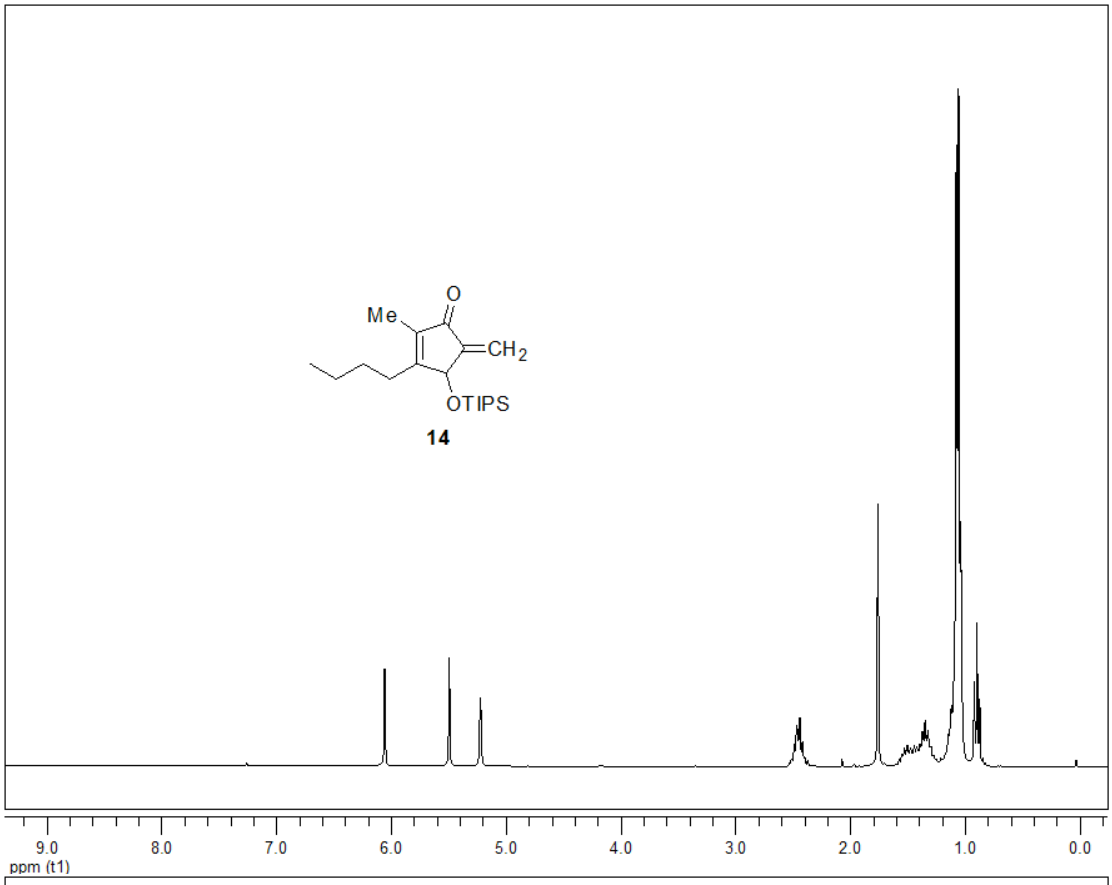
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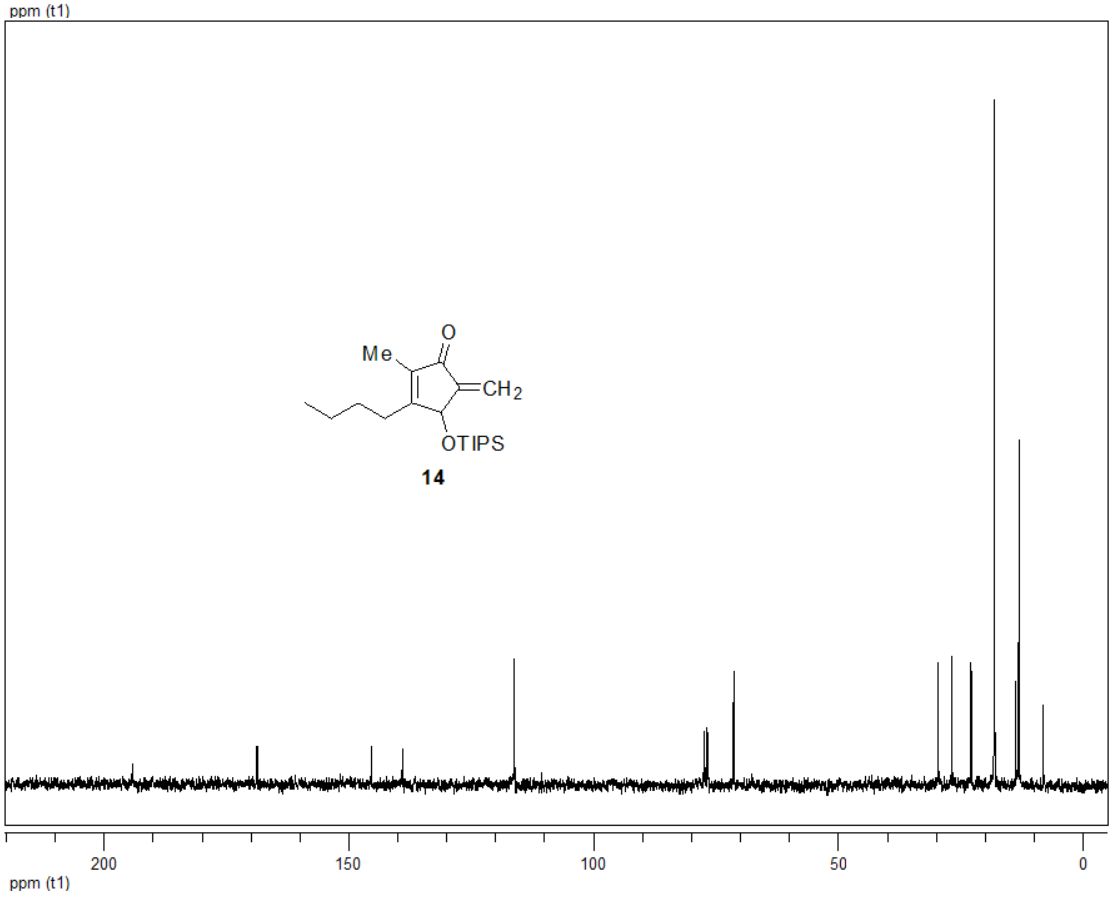
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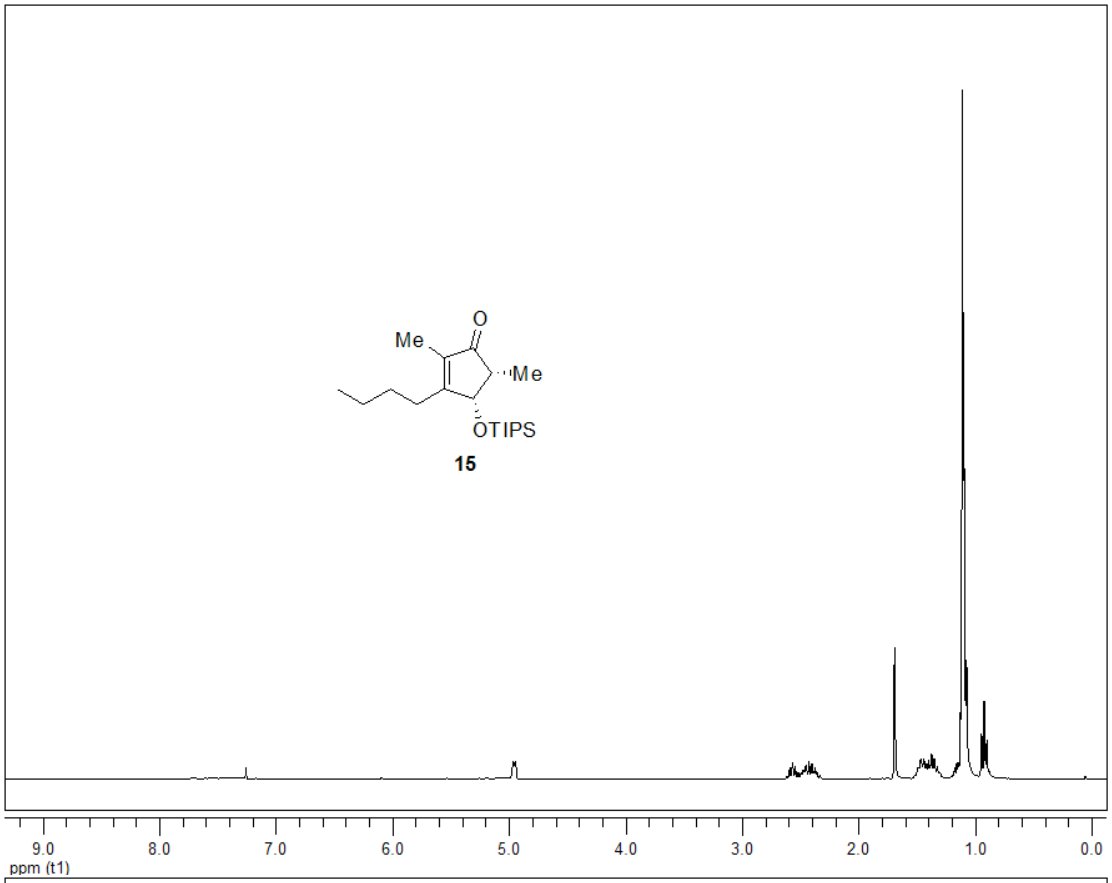
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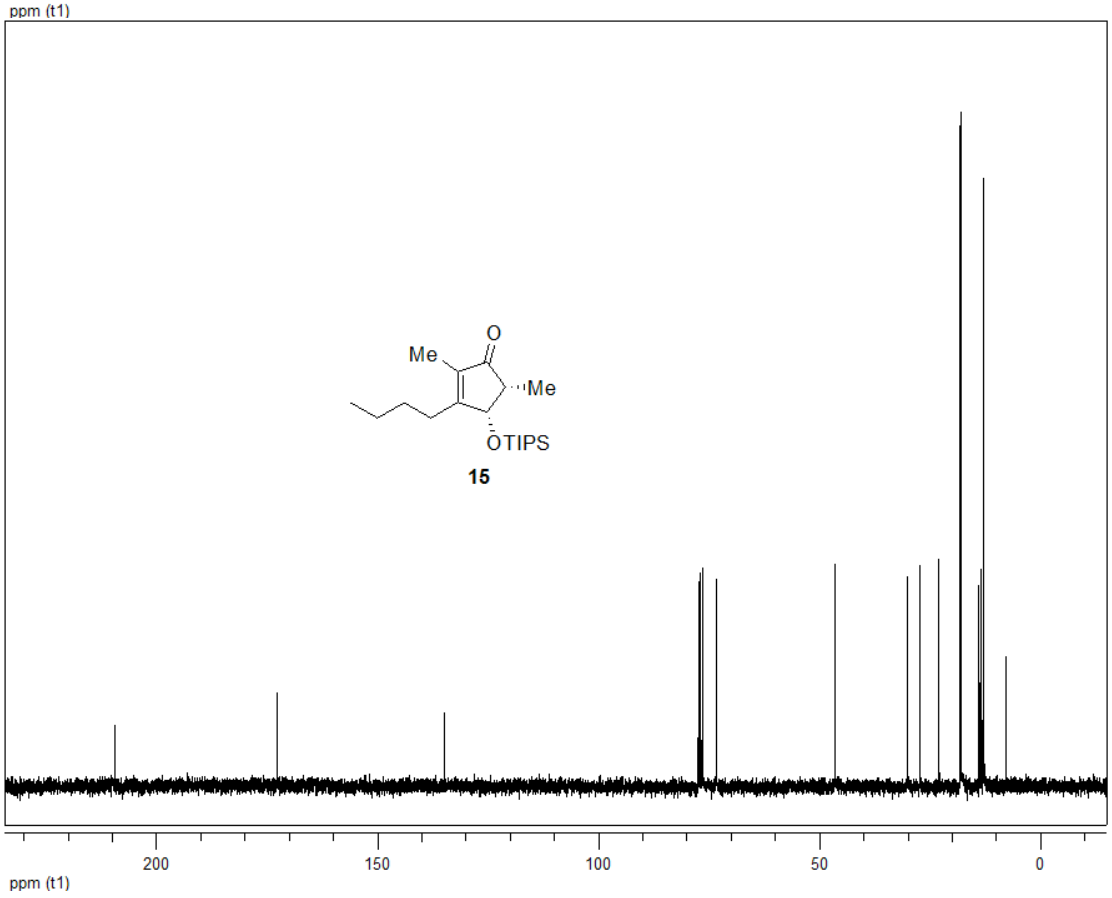
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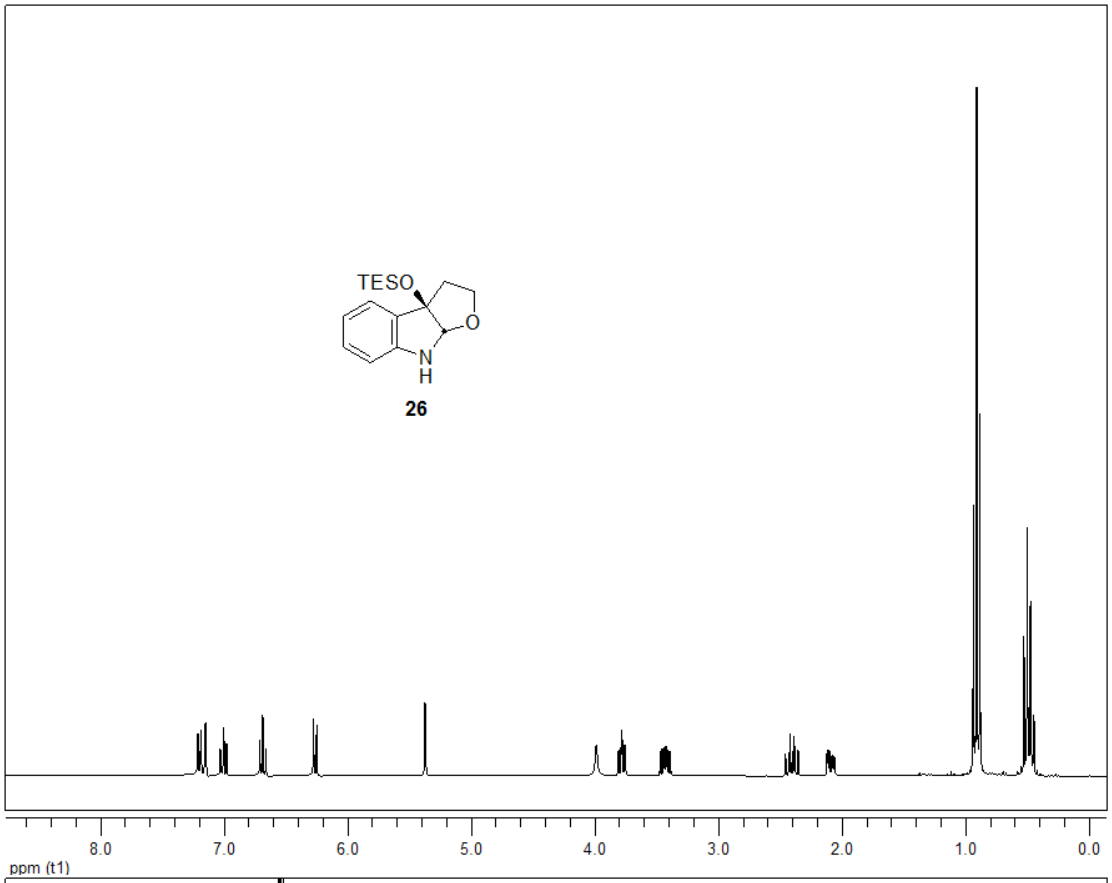
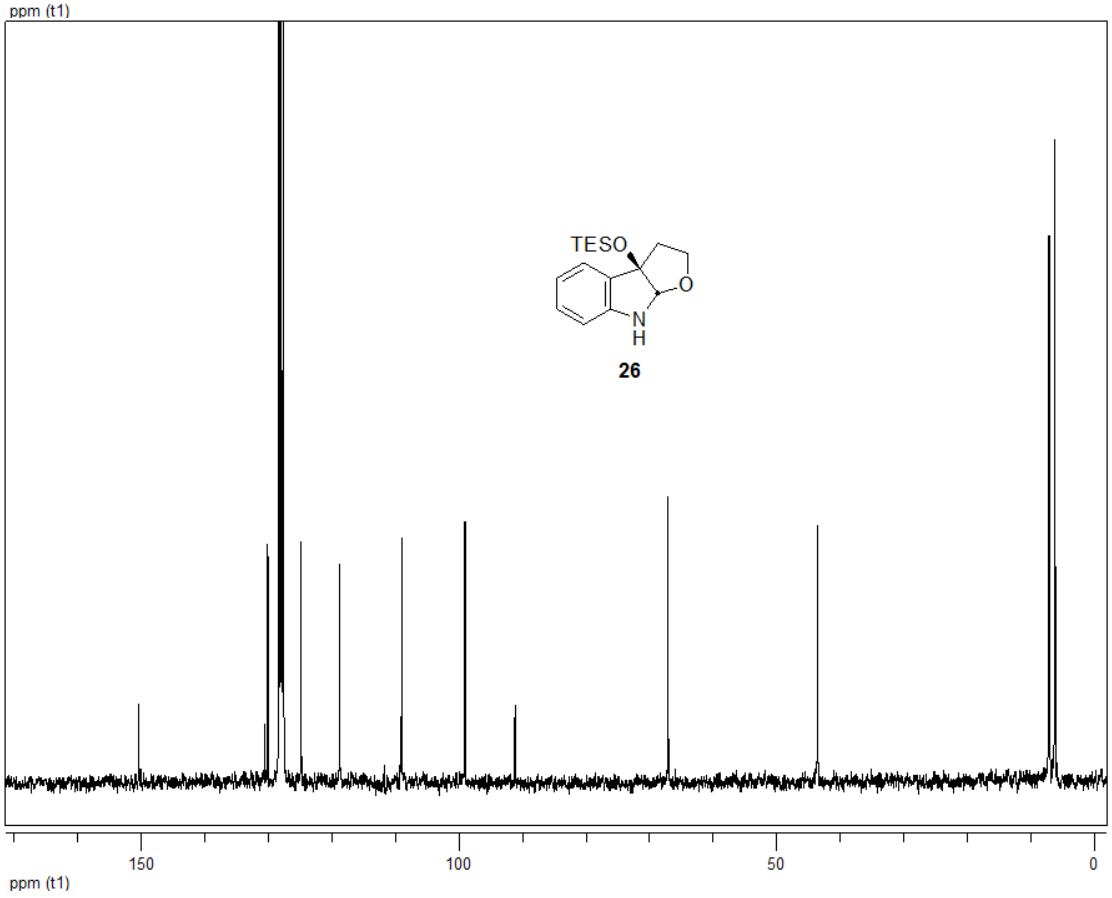
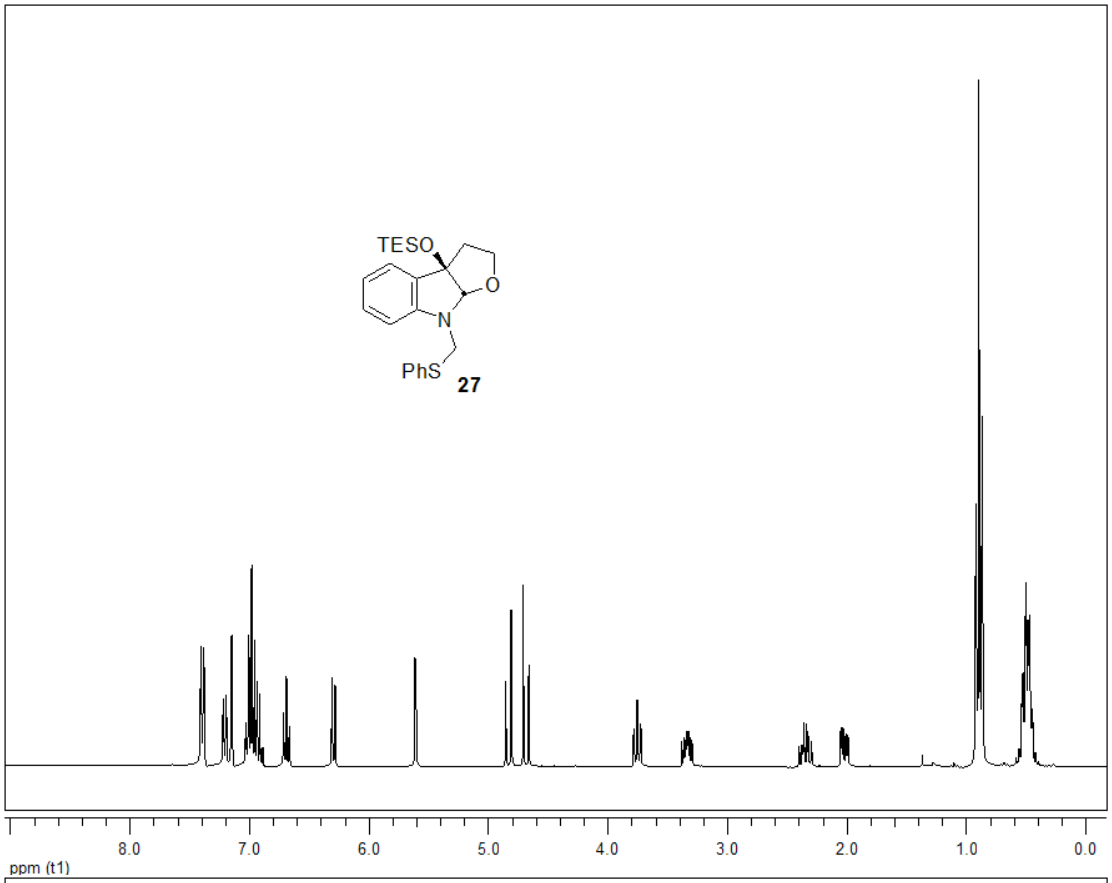
ppm (t1)

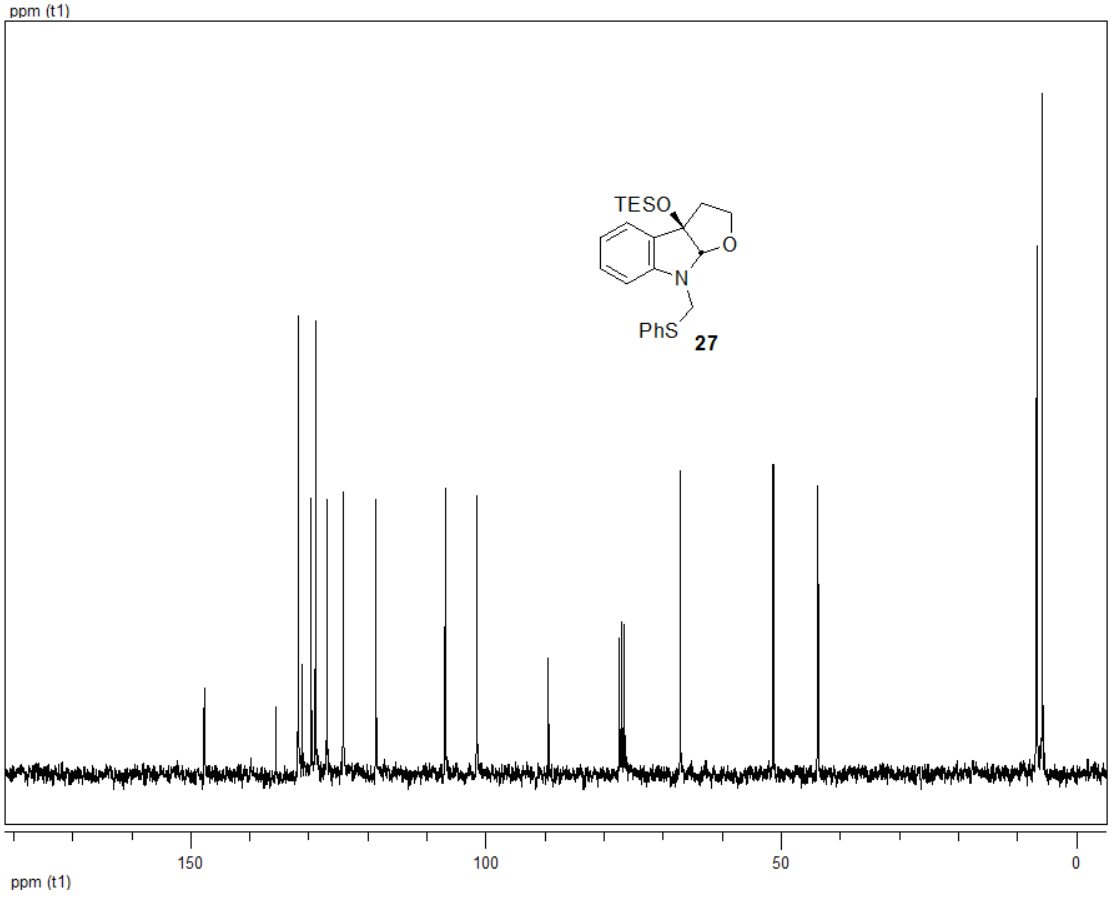

TESO
O
N
H
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

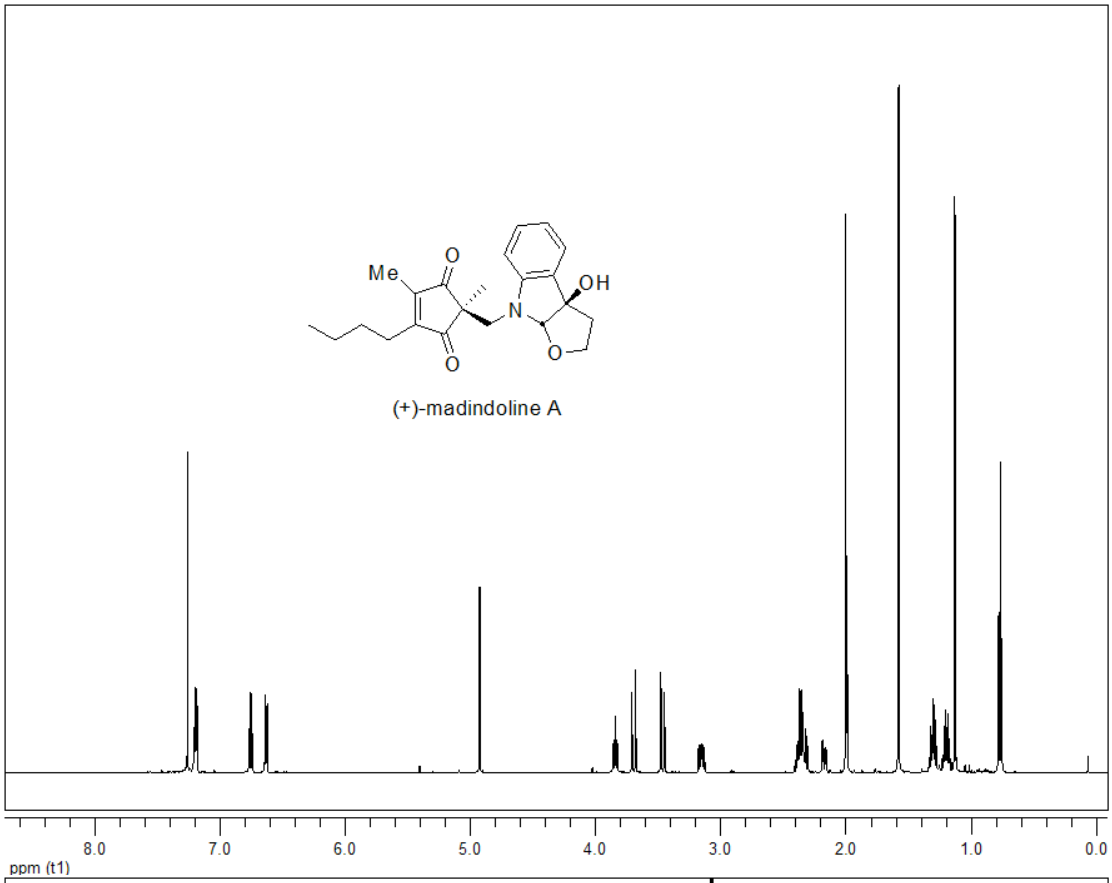
26

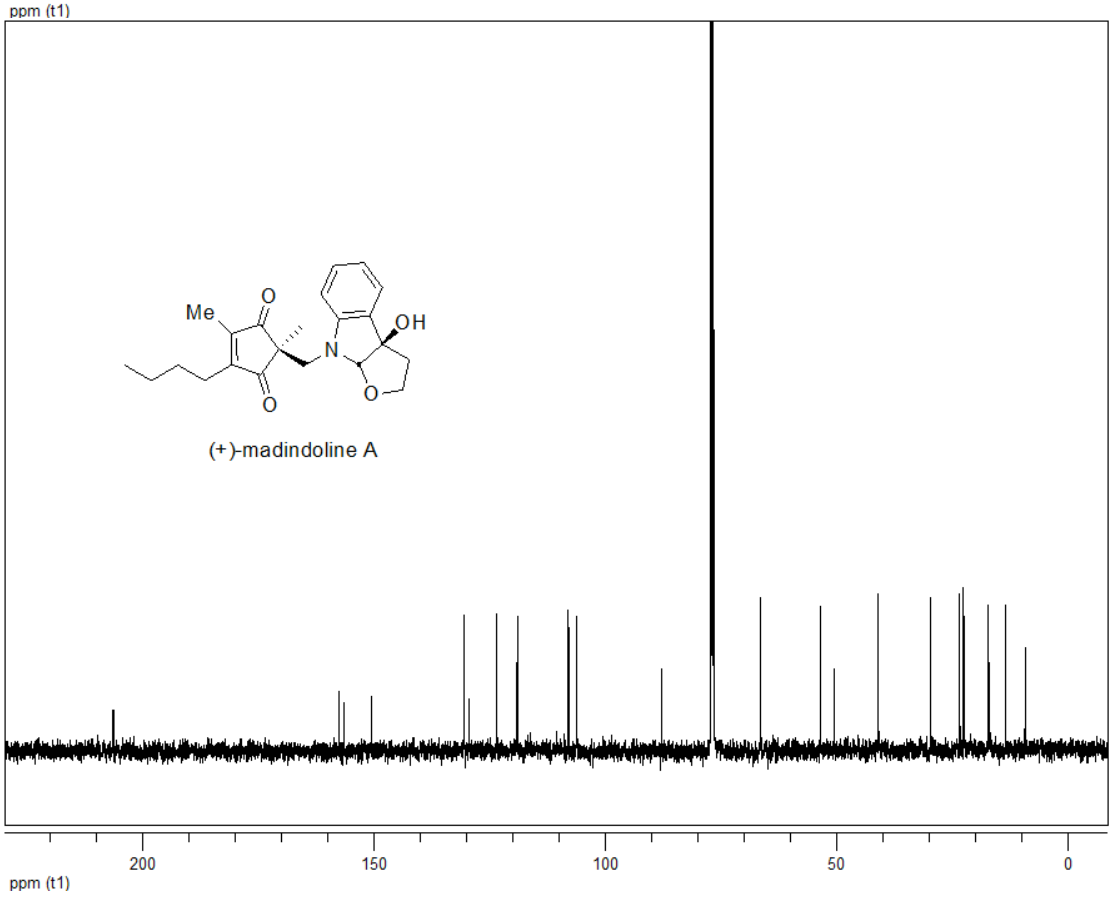

TESO
O
N
H
150
100
50
0
ppm (t1)

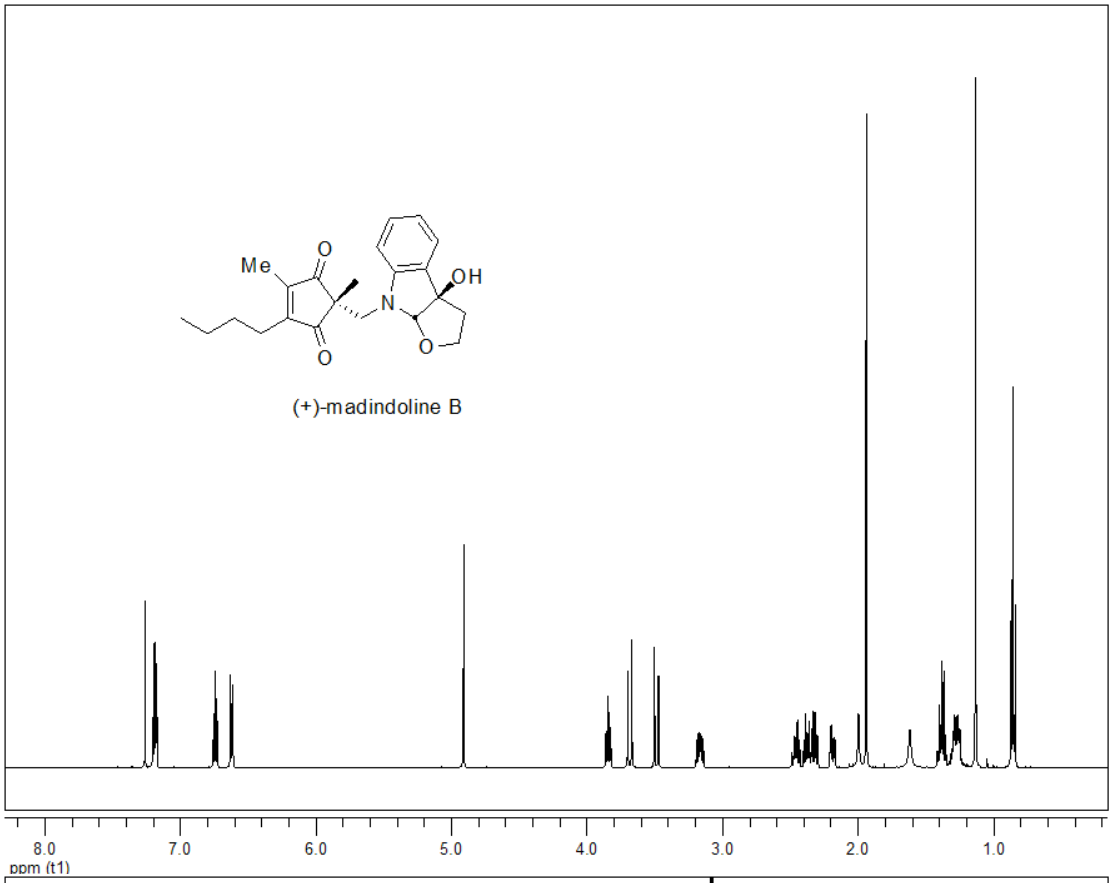
26

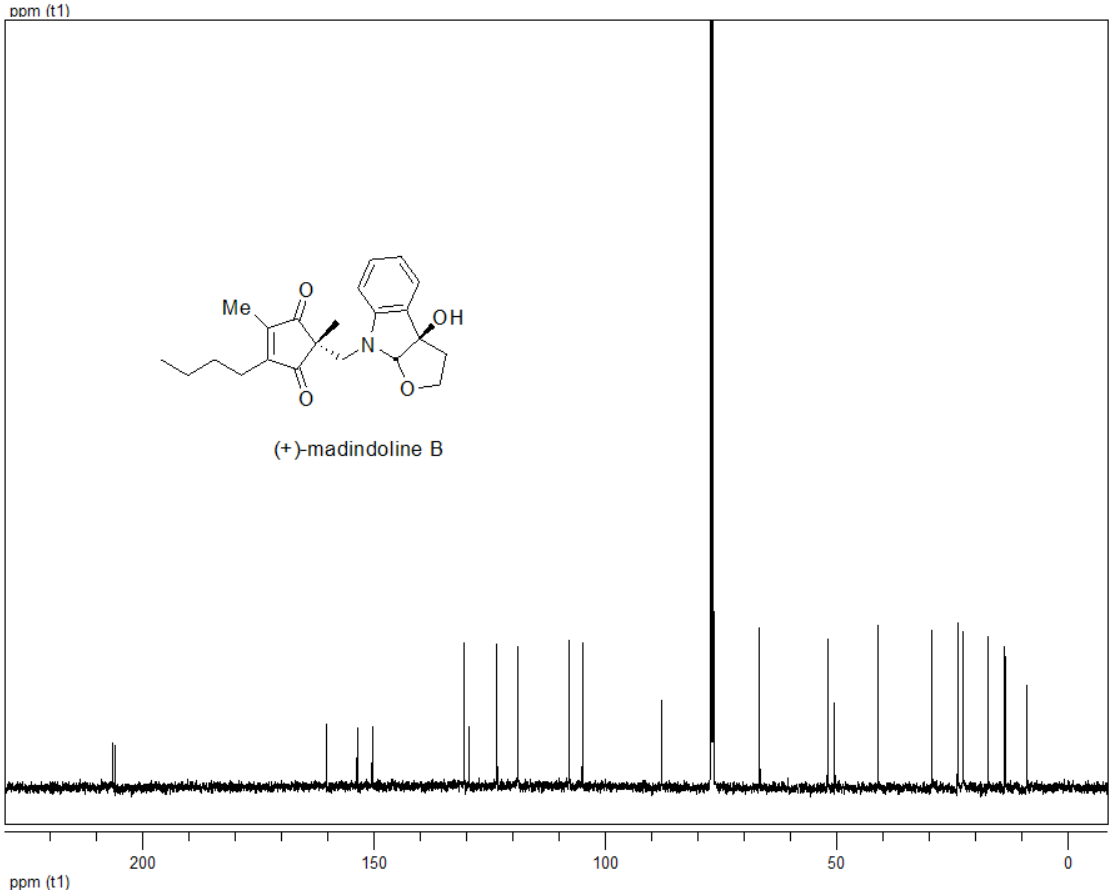

TESO
O
N
PhS
27
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


TESO
O
N
PhS
27
150
100
50
0
ppm (t1)


Me
O
O
N
OH
O
(+)-madindoline A
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


Me
O
O
N
OH
O
(+)-madindoline A
200
150
100
50
0
ppm (t1)


Me
O
O
N
OH
O
(+)-madindoline B
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


Me
O
O
N
OH
O
(+)-madindoline B
200
150
100
50
0
ppm (t1)