Electronic Supplementary Material (ESI) for ChemComm.

Hypervalent iodine-mediated alkene difunctionalization of vinylphenols: diastereoselective synthesis of substituted indoles and indolizines

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Supporting Information

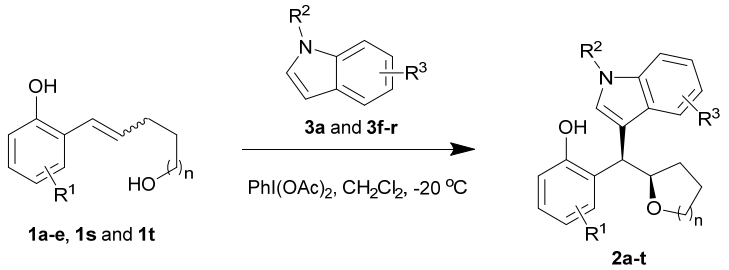
I) General Experimental Methods

All reactions were carried out under a nitrogen or argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), pentane, diethyl ether (Et_2O), 1,2-dimethoxyethane (DME), 1,4-dioxane, methylene chloride (CH_2Cl_2)，chloroform ($CHCl_3$) obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Ethyl acetate (EtOAc), diethyl ether (Et_2O), *N*,*N*-dimethylacetamide (DMA), methylene chloride (CH_2Cl_2), acetone and hexanes were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of ammonium molybdate, anisaldehyde, and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. NMR spectra were recorded on a Bruker AV-400 instrument and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad. IR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with diamond ATR accessory. Melting points (m.p.) are uncorrected, and recorded on a Buchi

B-540 melting point apparatus. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI TOF (time of flight) mass spectrometer at 3500 V emitter voltage.

Ⅱ) General Experimental Procedures and Characterization data

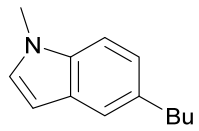
General procedure for the synthesis of 3-substituted indoles 2a–t through hypervalent iodine-mediated alkene difunctionalization of *o*-vinylphenols 1:



To a stirred solution of *o*-vinylphenols **1** (0.2 mmol) and indoles **3** (0.24 mmol) in CH_2Cl_2 (10 mL) at –20 °C was treated with $PhI(OAc)_2$ (0.24 mmol). The resulting mixture was stirred for 1 h before it was quenched with saturated $Na_2S_2O_3$ (sat. aq., 10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 20:1) afforded corresponding products **2a**–**t**.

Starting materials: *o*-Vinylphenols **1a**–**e**, **1s** and **1t**,[1] indoles **3a** and **3f**–**r**[2] were prepared according to the known literature procedures.

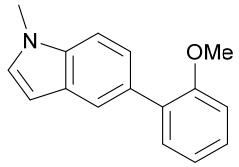
5-Butyl-1-methyl-1*H*-indole (3l): white solid; m.p. 40–42 °C; IR (film) ν_{max} 2919, 2594, 1560, 1110, 1006, 893, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.41 (s, 1 H), 7.21 (d, *J* = 8.3 Hz, 1 H), 7.05 (dd, *J* = 8.3, 1.2 Hz, 1 H), 6.97 (d, *J* = 3.0 Hz, 1 H), 6.40 (dd, *J* = 2.9, 0.6 Hz, 1 H), 3.72



3l

(s, 3 H), 2.76–2.61 (m, 2 H), 1.72–1.57 (m, 2 H), 1.37 (dq, *J* = 14.6, 7.3 Hz, 2 H), 0.92 ppm (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 135.3, 133.7, 128.7, 128.6, 122.6, 119.9, 108.8, 100.4, 35.7, 34.5, 32.7, 22.4, 14.0 ppm. HRMS (ESI): calcd for $C_{13}H_{18}N^+$ [M + H$^+$] 188.1434, found 188.1435.

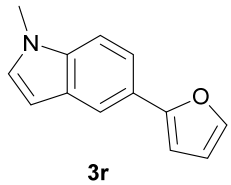
5-(2-Methoxyphenyl)-1-methyl-1*H*-indole (3q): white solid; m.p. 117–119 °C; IR



3q

(film) ν_{max} 2939, 2907, 1479, 1240, 1026, 886, 802, 748, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (s, 1 H), 7.53–7.44 (m, 2 H), 7.44–7.34 (m, 2 H), 7.16–7.09 (m, 2 H), 7.06 (d, *J* = 8.2 Hz, 1 H), 6.59 (s, 1 H), 3.87 (s, 3 H), 3.85 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.6, 135.9, 132.0, 131.3, 129.7, 129.0, 128.4, 127.9, 123.6, 121.7 120.7, 111.2, 108.5, 101.2, 55.5, 32.8 ppm. HRMS (ESI): calcd for $C_{16}H_{16}NO^+$ [M + H$^+$] 238.1226, found 238.1228.

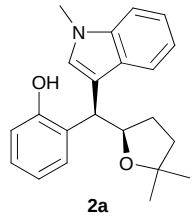
5-(Furan-2-yl)-1-methyl-1*H*-indole (3r): white solid; m.p. 70–72 °C; IR (film) ν_{max}



3r

2992, 2907, 1390, 1140, 1022, 986, 876, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.03 (s, 1 H), 7.62 (dd, *J* = 8.6, 1.3 Hz, 1 H), 7.51 (d, *J* = 0.9 Hz, 1 H), 7.35 (d, *J* = 8.6 Hz, 1 H), 7.08 (d, *J* = 3.0 Hz, 1 H), 6.64 (d, *J* = 3.2 Hz, 1 H), 6.56 (d, *J* = 3.0 Hz, 1 H), 6.53 (dd, *J* = 3.1, 1.8 Hz, 1 H), 3.79 ppm (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 141.0, 136.2, 129.5, 128.6, 122.8, 118.4, 116.3, 111.5, 109.4, 102.9, 101.4, 32.8 ppm. HRMS (ESI): calcd for $C_{13}H_{12}NO^+$ [M + H$^+$] 198.0913, found 198.0913.

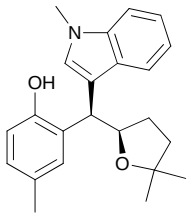
2-((5,5-Dimethyltetrahydrofuran-2-yl)(1-methyl-1*H*-indol-3-yl)methyl)phenol (2a): obtained in 84% yield and >20:1 dr as a white solid; m.p. 112–114 °C; IR (film)



2a

ν_{max} 3232, 3052, 2970, 1612, 1481, 1372, 1232, 1131, 1015, 884, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.84 (s, 1 H), 7.27 (d, *J* = 8.2 Hz, 1 H), 7.23 (d, *J* = 7.8 Hz, 1 H), 7.18 (t, *J* = 7.5 Hz, 1 H), 7.09 (t, *J* = 7.6 Hz, 1 H), 7.03 (s, 1 H), 6.97 (t, *J* = 7.5 Hz, 2 H), 6.84 (d, *J* = 7.6 Hz, 1 H), 6.67 (t, *J* = 7.4 Hz, 1 H), 4.93 (s, 1 H), 4.82 (td, *J* = 7.1, 2.3 Hz, 1 H), 3.78 (s, 3 H), 2.16 (dt, *J* = 13.8, 6.9 Hz, 1 H), 1.96–1.85 (m, 1 H), 1.74–1.63 (m, 1 H), 1.34–1.28 (m, 1 H), 1.27 (s, 3 H), 1.19 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 136.7, 130.9, 127.9(2C), 127.8, 127.0, 121.7, 119.8, 119.6, 118.9, 117.8, 113.2, 108.9, 82.2(2C), 41.4, 38.4, 32.7, 28.2, 27.6, 27.2 ppm; HRMS (ESI): calcd for $C_{22}H_{26}NO_2^+$ [M + H^+] 336.1958, found 336.1963.

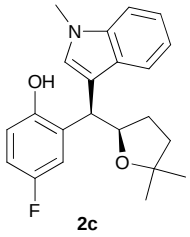
2-((5,5-Dimethyltetrahydrofuran-2-yl)(1-methyl-1*H*-indol-3-yl)methyl)-4-methyl-



2b

phenol (2b): obtained in 82% yield and >20:1 dr as a white solid; m.p. 110–112 °C; IR (film) ν_{max} 3235, 2969, 2925, 1614, 1492, 1371, 1229, 1130, 1016, 881, 819, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.69 (s, 1 H), 7.28 (d, *J* = 8.0 Hz, 1 H), 7.23 (d, *J* = 10.0 Hz, 1 H), 7.15 (t, *J* = 7.4 Hz, 1 H), 7.04 (s, 1 H), 6.97 (t, *J* = 7.4 Hz, 1 H), 6.85 (dt, *J* = 14.0, 4.9 Hz, 2 H), 6.65 (s, 1 H), 4.82 (d, *J* = 2.3 Hz, 1 H), 4.74 (td, *J* = 7.3, 2.6 Hz, 1 H), 3.76 (s, 3 H), 2.11 (dd, *J* = 13.7, 6.2 Hz, 1 H), 2.05 (s, 3 H), 1.87 (ddd, *J* = 16.1, 12.5, 7.5 Hz, 1 H), 1.66 (dt, *J* = 12.2, 7.8 Hz, 1 H), 1.37–1.27 (m, 1 H), 1.23 (s, 3 H), 1.14 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.1, 136.7, 131.3, 128.8, 128.5, 128.0, 127.8, 127.2, 121.7, 119.6, 118.9, 117.8, 113.2, 109.0, 82.4, 82.3, 41.8, 38.5, 32.8, 28.5, 27.8, 27.4, 20.6 ppm; HRMS (ESI): calcd for $C_{23}H_{28}NO_2^+$ [M + H^+] 350.2115, found 350.2112.

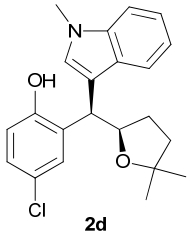
2-((5,5-Dimethyltetrahydrofuran-2-yl)(1-methyl-1*H*-indol-3-yl)methyl)-4-fluoro-



2c

phenol (2c): obtained in 83% yield and >20:1 dr as a colorless oil; IR (film) ν_{max} 3231, 2969, 2928, 1615, 1486, 1373, 1237, 1134, 1017, 879, 821, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.60 (s, 1 H), 7.33–7.28 (m, 1 H), 7.22 (d, *J* = 7.6 Hz, 2 H), 7.04–6.97 (m, 2 H), 6.91 (dd, *J* = 8.8, 5.0 Hz, 1 H), 6.78 (td, *J* = 8.3, 3.1 Hz, 1 H), 6.53 (dd, *J* = 9.9, 3.1 Hz, 1 H), 4.98 (d, *J* = 2.5 Hz, 1 H), 4.82 (td, *J* = 7.2, 2.8 Hz, 1 H), 3.82 (s, 3 H), 2.20 (dt, *J* = 14.7, 6.9 Hz, 1 H), 1.97–1.85 (m, 1 H), 1.78– 1.66(m, 1 H), 1.37–1.29 (m, 1 H), 1.27 (s, 3 H), 1.19 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.9, 155. 6, 151.6 (d, J_{C-F} = 2.0 Hz), 136.8, 129.5 (d, J_{C-F} = 6.5 Hz), 127.5, 126.8, 122.0, 119.3 (d, J_{C-F} = 38.5 Hz), 118.7 (d, J_{C-F} = 8.0 Hz), 116.9 (d, J_{C-F} = 23.6 Hz), 114.2 (d, J_{C-F} = 22.7 Hz), 112.6, 109.1, 82.3, 82.1, 40.7, 38.5, 32.8, 27.9, 27.6, 27.1 ppm; HRMS (ESI): calcd for $C_{22}H_{25}FNO_2^+$ [M + H^+] 354.1864, found 354.1868.

4-Chloro-2-((5,5-dimethyltetrahydrofuran-2-yl)(1-methyl-1*H*-indol-3-yl)methyl)-

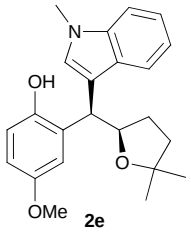


2d

phenol (2d): obtained in 86% yield and >20:1 dr as a white solid; m.p. 107–109 °C; IR (film) ν_{max} 3214, 2970, 2927, 1744, 1613, 1477, 1372, 1264, 1230, 1130, 1017, 881, 822, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.89 (s, 1 H), 7.30 (d, *J* = 8.2 Hz, 1 H), 7.24 (d, *J* = 5.1 Hz, 1 H), 7.20 (d, *J* = 7.5 Hz, 2 H), 7.04 (dt, *J* = 14.6, 5.6 Hz, 2 H), 6.90 (d, *J* = 8.5 Hz, 1 H), 6.81 (d, *J* = 2.5 Hz, 1 H), 4.92 (d, *J* = 2.4 Hz, 1 H), 4.78 (td, *J* = 7.3, 2.6 Hz, 1 H), 3.81 (s, 3 H), 2.19 (dd, *J* = 13.1, 6.8 Hz, 1 H), 1.96–1.82 (m, 1 H), 1.81–1.67 (m, 1 H), 1.42–1.31 (m, 1 H), 1.27 (s, 3 H), 1.19 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ =

154.3, 136.8, 130.3, 129.8, 127.8, 127.6, 127.0, 124.7, 122.0, 119.3(2C), 119.2, 112.3, 109.1, 82.3, 82.2, 41.0, 38.5, 32.8, 28.1, 27.6, 27.2 ppm; HRMS (ESI): calcd for $C_{22}H_{25}ClNO_2^+$ [M + H^+] 370.1568, found 370.1593.

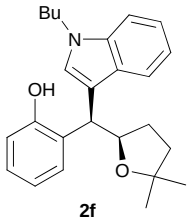
2-((5,5-Dimethyltetrahydrofuran-2-yl)(1-methyl-1*H*-indol-3-yl)methyl)-4-Metho-



2e

xyphenol (2e): obtained in 71% yield and >20:1 dr as a white solid; m.p. 96–98 °C; IR (film) ν_{max} 3229, 3033, 2970, 1612, 1481, 1370, 1132, 1031, 862, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.40 (s, 1 H), 7.28–7.25 (m, 2 H), 7.18 (t, *J* = 7.2 Hz, 1 H), 7.02 (s, 1 H), 6.99 (dd, *J* = 11.4, 4.4 Hz, 1 H), 6.90 (d, *J* = 8.7 Hz, 1 H), 6.65 (dd, *J* = 8.7, 3.1 Hz, 1 H), 6.43 (d, *J* = 3.1 Hz, 1 H), 4.93 (d, *J* = 2.6 Hz, 1 H), 4.80 (td, *J* = 7.2, 2.8 Hz, 1 H), 3.80 (s, 3 H), 3.58 (s, 3 H), 2.17 (dt, *J* = 14.6, 6.8 Hz, 1 H), 1.93 (ddd, *J* = 16.1, 10.6, 7.3 Hz, 1 H), 1.75–1.64 (m, 1 H), 1.36–1.28 (m, 1 H), 1.26 (s, 3 H), 1.18 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.0, 149.5, 136.8, 129.1, 127.8, 127.0, 121.8, 119.6, 119.0, 118.2, 117.2, 113.0, 112.0, 108.9, 82.4, 82.1, 55.5, 41.1, 38.5, 32.8, 28.2, 27.7, 27.2 ppm; HRMS (ESI): calcd for $C_{23}H_{28}NO_3^+$ [M + H^+] 366.2064, found 366.2067.

2-((1-Butyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)phenol (2f):

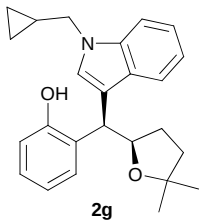


2f

obtained in 80% yield and >20:1 dr as a colorless oil; IR (film) ν_{max} 3256, 3049, 2965, 1738, 1612, 1465, 1369, 1272, 1234, 1134, 1016, 884, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.89 (s, 1 H), 7.30 (d, *J* = 8.2 Hz, 1 H), 7.24 (d, *J* = 8.8 Hz, 1 H), 7.15 (dd, *J* = 11.2, 4.0 Hz, 1 H), 7.11–7.08 (m, 2 H), 7.01–6.92 (m, 2 H), 6.83 (dd, *J* = 7.5, 1.3 Hz, 1 H), 6.73–6.60 (m, 1 H), 4.92 (d, *J* = 2.0 Hz, 1 H), 4.82 (td, *J* = 7.2, 2.5 Hz, 1 H), 4.11 (dd, *J* = 7.1, 5.6 Hz, 2 H),

2.17 (dt, *J* = 13.3, 7.3 Hz, 1 H), 1.98–1.88 (m, 1 H), 1.86–1.81 (m, 2 H), 1.74–1.63 (m, 1 H), 1.42–1.31 (m, 3 H), 1.27 (s, 3 H), 1.19 (s, 3 H), 0.96 ppm (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 136.0, 130.9, 128.0(2C), 127.9, 126.0, 121.5, 119.9, 119.7, 118.8, 117.9, 113.0, 109.2, 82.3, 82.2, 46.1, 41.4, 38.5, 32.4, 28.3, 27.7, 27.2, 20.2, 13.7 ppm; HRMS (ESI): calcd for $C_{25}H_{32}NO_2^+$ [M + H^+] 378.2428, found 378.2428.

2-((1-(Cyclopropylmethyl)-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)me-t

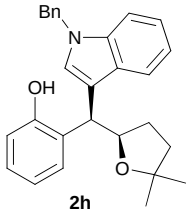


2g

hyl)phenol (2g): obtained in 78% yield and >20:1 dr as a white solid; m.p. 121–123 °C; IR (film) ν_{max} 3228, 3012, 2969, 1592, 1380, 1372, 1269, 1131, 1015, 854, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.89 (s, 1 H), 7.32 (d, *J* = 8.2 Hz, 1 H), 7.27–7.22 (m, 1 H), 7.16 (t, *J* = 7.6 Hz, 2 H), 7.13–7.06 (m, 1 H), 6.97 (t, *J* = 7.4 Hz, 2 H), 6.84 (t, *J* = 8.3 Hz, 1 H), 6.68 (t, *J* = 7.4 Hz, 1 H), 4.92 (d, *J* = 2.0 Hz, 1 H), 4.83 (td, *J* = 7.2, 2.5 Hz, 1 H), 3.98 (ddd, *J* = 32.0, 14.3, 6.7 Hz, 2 H), 2.16 (td, *J* = 13.7, 7.1 Hz, 1 H), 1.98–1.85 (m, 1 H), 1.70 (dt, *J* = 12.3, 7.4 Hz, 1 H), 1.38–1.28 (m, 2 H), 1.28 (s, 3 H), 1.19 (s, 3 H), 0.63 (d, *J* = 7.8 Hz, 2 H), 0.38 ppm (d, *J* = 4.7 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 136.2, 130.9, 128.0, 127.9(2C), 125.8, 121.6, 119.9, 119.6, 118.9, 117.9, 113.1, 109.2, 82.3, 82.2, 50.6, 41.6, 38.5, 28.3, 27.7, 27.3, 11.4, 4.1, 4.0 ppm; HRMS (ESI): calcd for $C_{25}H_{30}NO_2^+$ [M + H^+] 376.2271, found 376.2272.

2-((1-Benzyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)phenol

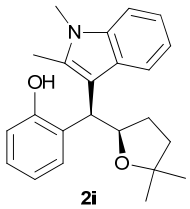
(2h): obtained in 75% yield and >20:1 dr as a white solid; m.p. 58–60 °C; IR (film) ν_{max} 3201, 2970, 1492, 1431, 1372, 1139, 998, 804, 741 cm^{-1}; ^{1}H NMR (400 MHz,



2h

$CDCl_3$) δ = 8.88 (s, 1 H), 7.38–7.26 (m, 3 H), 7.25 (d, *J* = 10.1 Hz, 2 H), 7.18–7.07 (m, 5 H), 6.99 (t, *J* = 7.5 Hz, 2 H), 6.85 (dd, *J* = 7.6, 1.5 Hz, 1 H), 6.69 (td, *J* = 7.5, 1.2 Hz, 1 H), 5.43–5.30 (m, 2 H), 4.95 (d, *J* = 2.3 Hz, 1 H), 4.82 (td, *J* = 7.2, 2.6 Hz, 1 H), 2.13 (dt, *J* = 14.6, 6.8 Hz, 1 H), 1.95–1.80 (m, 1 H), 1.73–1.62 (m, 1 H), 1.29 (dd, *J* = 7.3, 4.9 Hz, 1 H), 1.26 (s, 3 H), 1.15 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.6, 137.7, 136.4, 130.8, 128.8(2C), 128.1, 127.9, 127.8, 127.6, 126.6(2C), 126.4, 122.0, 119.9, 119.8, 119.2, 118.0, 114.0, 109.5, 82.2(2C), 50.0, 41.4, 38.4, 28.2, 27.6, 27.2 ppm; HRMS (ESI): calcd for $C_{28}H_{30}NO_2^+$ [M + H^+] 412.2271, found 412.2276.

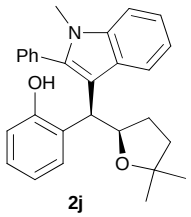
2-((1,2-Dimethyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)phenol



2i

(2i): obtained in 72% yield and >20:1 dr as a colorless oil; IR (film) ν_{max} 3232, 3052, 2970, 1612, 1481, 1372, 1232, 1131, 1015, 884, 741 cm^{-1}; IR (film) ν_{max} 3052, 2970, 2886, 1612, 1479, 1352, 1162, 1131, 1015, 894, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.69 (s, 1 H), 7.59 (d, *J* = 7.9 Hz, 1 H), 7.25 (t, *J* = 9.0 Hz, 1 H), 7.15 (dd, *J* = 9.0, 4.4 Hz, 2 H), 7.11–7.00 (m, 2 H), 6.89 (d, *J* = 7.5 Hz, 1 H), 6.70 (t, *J* = 7.2 Hz, 1 H), 4.79 (d, *J* = 1.9 Hz, 1 H), 4.76–4.69 (m, 1 H), 3.64 (s, 3 H), 2.30 (s, 3 H), 2.20 (dt, *J* = 12.4, 6.3 Hz, 1 H), 2.01–1.89 (m, 1 H), 1.71 (dt, *J* = 12.2, 7.8 Hz, 1 H), 1.60–1.46 (m, 1 H), 1.26 (s, 3 H), 1.16 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.0, 136.6, 134.9, 130.9, 127.8, 127.6(2C), 120.4, 119.7, 119.6, 118.9, 117.2, 110.1, 108.7, 82.4, 81.7, 42.1, 38.7, 29.9, 29.6, 27.9, 27.3, 11.1 ppm; HRMS (ESI): calcd for $C_{23}H_{28}NO_2^+$ [M + H^+] 350.2115, found 350.2113.

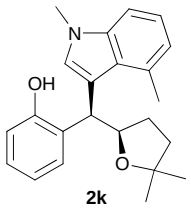
2-((5,5-Dimethyltetrahydrofuran-2-yl)(1-methyl-2-phenyl-1*H*-indol-3-yl)methyl)-



2j

phenol (2j): obtained in 68% yield and >20:1 dr as a white solid; m.p. 120–122 ^{o}C; IR (film) ν_{max} 3206, 3052, 2970, 1607, 1466, 1367, 1240, 1150, 1018, 885, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.74 (s, 1 H), 7.67 (d, *J* = 8.0 Hz, 1 H), 7.43 (s, 4 H), 7.35 (d, *J* = 8.2 Hz, 1 H), 7.23 (ddd, *J* = 9.6, 9.0, 4.1 Hz, 3 H), 7.16–7.01 (m, 2 H), 6.88 (dd, *J* = 8.0, 1.0 Hz, 1 H), 6.72–6.64 (m, 1 H), 4.78 (d, *J* = 2.1 Hz, 1 H), 4.67–4.46 (m, 1 H), 3.54 (s, 3 H), 1.88 (dt, *J* = 12.3, 5.4 Hz, 2 H), 1.68–1.57 (m, 1 H), 1.47 (ddd, *J* = 12.2, 8.9, 6.3 Hz, 1 H), 1.18 (s, 3 H), 1.15 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.1, 139.2, 137.3, 131.8, 131.0(2C), 130.8, 128.5, 128.4(2C), 127.7, 127.6, 127.2, 121.6, 121.2, 119.6, 119.4, 117.2, 112.4, 109.4, 83.0, 81.4, 42.2, 38.9, 30.9, 29.5, 27.7, 26.9 ppm; HRMS (ESI): calcd for $C_{28}H_{30}NO_2^+$ [M + H$^+$] 412.2271, found 412.2276.

2-((1,4-Dimethyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)phenol

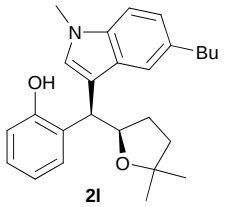


2k

(2k): obtained in 79% yield and >20:1 dr as a white solid; m.p. 120–125 ^{o}C; IR (film) ν_{max} 3212, 3022, 2890, 1609, 1521, 1286, 1097, 1015, 885, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.71 (s, 1 H), 7.12 (t, *J* = 6.4 Hz, 1 H), 7.07 (dd, *J* = 14.0, 7.7 Hz, 2 H), 6.97 (d, *J* = 8.0 Hz, 1 H), 6.88 (s, 1 H), 6.71 (d, *J* = 7.0 Hz, 1 H), 6.67 (d, *J* = 4.3 Hz, 2 H), 5.32 (s, 1 H), 4.89 (td, *J* = 7.0, 2.0 Hz, 1 H), 3.79 (s, 3 H), 2.25 (dd, *J* = 13.9, 6.3 Hz, 1 H), 2.20 (s, 3 H), 1.94 (ddt, *J* = 12.3, 8.9, 6.1 Hz, 1 H), 1.79–1.64 (m, 1 H), 1.29 (d, *J* = 16.7 Hz, 1 H), 1.27 (s, 3 H), 1.25 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.2, 137.4, 131.8, 131.0, 128.9, 127.7, 126.7, 126.0, 121.9, 121.0, 120.1, 117.7, 114.4, 106.8, 82.7, 81.6,

41.3, 38.5, 32.9, 28.0, 27.4, 26.6, 19.5 ppm; HRMS (ESI): calcd for $C_{23}H_{28}NO_2^+$ [M + H^+] 350.2115, found 350.2120.

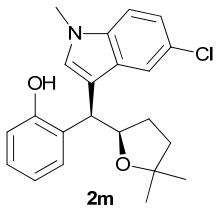
2-((5-Butyl-1-methyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)-p



2l

henol (2l): obtained in 81% yield and >20:1 dr as a white solid; m.p. 180–182 °C; IR (film) ν_{max} 3256, 2964, 2927, 1582, 1487, 1375, 1232, 1148, 1106, 873, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.88 (s, 1 H), 7.20 (d, *J* = 8.1 Hz, 1 H), 7.10 (t, *J* = 7.3 Hz, 1 H), 7.00 (dd, *J* = 17.3, 10.2 Hz, 4 H), 6.87 (d, *J* = 7.4 Hz, 1 H), 6.68 (t, *J* = 7.1 Hz, 1 H), 4.93 (s, 1 H), 4.81 (s, 1 H), 3.77 (s, 3 H), 2.59 (t, *J* = 7.4 Hz, 2 H), 2.17 (dd, *J* = 12.4, 6.6 Hz, 1 H), 2.01–1.82 (m, 1 H), 1.79–1.64 (m, 1 H), 1.54 (dd, *J* = 15.6, 8.2 Hz, 3 H), 1.33 (d, *J* = 15.1 Hz, 1 H), 1.28 (brs, 4 H), 1.20 (s, 3 H), 0.87 ppm (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 135.3, 133.5, 130.9, 127.9(2C), 127.8, 127.1, 122.8, 120.0, 118.8, 117.9, 112.7, 108.6, 82.4, 82.2, 41.2, 38.5, 35.7, 34.5, 32.8, 28.2, 27.7, 27.2, 22.3, 13.9 ppm; HRMS (ESI): calcd for $C_{26}H_{34}NO_2^+$ [M + H^+] 392.2584, found 392.2586.

2-((5-Chloro-1-methyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)-

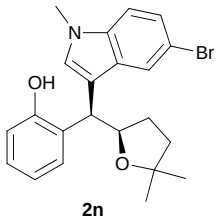


2m

phenol (2m): obtained in 76% yield and >20:1 dr as a white solid; m.p. 152–154 °C; IR (film) ν_{max} 3262, 2969, 2924, 1583, 1480, 1373, 1267, 1144, 1043, 865, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.84 (s, 1 H), 7.23 (s, 1 H), 7.18 (d, *J* = 8.6 Hz, 1 H), 7.15–7.07 (m, 3 H), 6.97 (d, *J* = 8.0 Hz, 1 H), 6.83 (d, *J* = 7.4 Hz, 1 H), 6.70 (t, *J* = 7.4 Hz, 1 H), 4.80 (s, 1 H), 4.77 (dd, *J* = 12.0, 4.9 Hz, 1 H), 3.78 (s, 3 H), 2.15 (dt, *J* = 12.9, 6.8 Hz, 1 H),

1.87 (dt, *J* = 15.8, 7.5 Hz, 1 H), 1.76–1.66 (m, 1 H), 1.37–1.29 (m, 1 H), 1.27 (s, 3 H), 1.18 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.4, 135.1, 130.7, 128.9, 128.4, 128.1, 127.7, 125.0, 122.1, 120.0, 118. 9, 118.1, 112.9, 110.1, 82.4, 82.1, 41.6, 38.4, 33.0, 28.4, 27.8, 27.3 ppm; HRMS (ESI): calcd for $C_{22}H_{25}ClNO_2^+$ [M + H^+] 370.1568, found 370.1566.

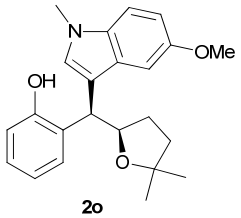
2-((5-Bromo-1-methyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)-



2n

phenol (2n): obtained in 73% yield and >20:1 dr as a white solid; m.p. 168–170 °C; IR (film) ν_{max} 3220, 2970, 1583, 1373, 1266, 1232, 1145, 1042, 887, 821, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.86 (s, 1 H), 7.40 (s, 1 H), 7.25 (d, *J* = 7.7 Hz, 1 H), 7.18–7.03 (m, 3 H), 6.97 (d, *J* = 7.9 Hz, 1 H), 6.84 (d, *J* = 7.5 Hz, 1 H), 6.70 (t, *J* = 7.4 Hz, 1 H), 4.80 (s, 1 H), 4.77 (t, *J* = 7.3 Hz, 1 H), 3.77 (s, 3 H), 2.15 (td, *J* = 13.4, 6.8 Hz, 1 H), 1.87 (dt, *J* = 15.8, 7.7 Hz, 1 H), 1.77–1.64 (m, 1 H), 1.40–1.29 (m, 1 H), 1.28 (s, 3 H), 1.19 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.4, 135.3, 130.7, 129.6, 128.3, 128.1, 127.7, 124.6, 121.9, 120.0, 118.1, 112.9, 112.5, 110.5, 82.4, 82.1, 41.6, 38.4, 33.0, 28.4, 27.8, 27.3 ppm; HRMS (ESI): calcd for $C_{22}H_{25}BrNO_2^+$ [M + H^+] 414.1063, found 414.1068.

2-((5,5-Dimethyltetrahydrofuran-2-yl)(5-methoxy-1-methyl-1*H*-indol-3-yl)meth-

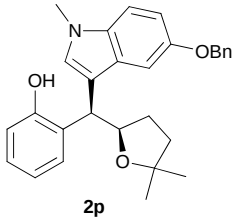


2o

yl)phenol (2o): obtained in 65% yield and 13:1 dr as a white solid; m.p. 125–127 °C; IR (film) ν_{max} 3256, 2968, 2925, 1580, 1489, 1372, 1271, 1224, 1038, 869, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.82 (s, 1 H), 7.16 (d, *J* = 8.8 Hz, 1 H), 7.09 (t, *J* = 7.5 Hz, 1 H),

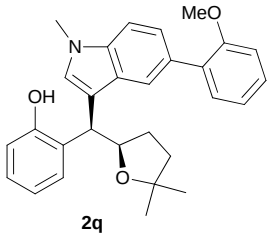
7.03–6.94 (m, 2 H), 6.84 (dd, *J* = 11.5, 4.8 Hz, 2 H), 6.69 (t, *J* = 7.2 Hz, 1 H), 6.63 (d, *J* = 1.9 Hz, 1 H), 4.87 (s, 1 H), 4.85–4.75 (m, 1 H), 3.77 (s, 3 H), 3.68 (s, 3 H), 2.16 (dt, *J* = 19.4, 7.0 Hz, 1 H), 2.00–1.86 (m, 1 H), 1.77–1.64 (m, 1 H), 1.38–1.28 (m, 1 H), 1.27 (s, 3 H), 1.19 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.6, 153.7, 132.2, 130.8, 128.1, 127.9, 127.7, 127.6, 119.90, 117.9, 112.7, 112.1, 109.7, 101.5, 82.3, 82.2, 55.9, 41.3, 38.5, 33.0, 28.2, 27.7, 27.2 ppm; HRMS (ESI): calcd for $C_{23}H_{28}NO_3^+$ [M + H$^+$] 366.2064, found 366.2060.

2-((5-(Benzyloxy)-1-methyl-1*H*-indol-3-yl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)phenol (2p): obtained in 63% yield and 15:1 dr as a white solid; m.p. 161–163 ^{o}C; IR (film) ν_{max} 3205, 3035, 2970, 1611, 1498, 1372, 1262, 1016, 883, 821, 735, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.03 (s, 1 H), 7.27–7.15 (m, 3 H), 7.12 (d, *J* = 6.5 Hz, 2 H), 7.02–6.90 (m, 3 H), 6.84–6.74 (m, 3 H), 6.60 (dd, *J* = 10.6, 4.2 Hz, 1 H), 6.34 (d, *J* = 7.7 Hz, 1 H), 5.37 (d, *J* = 2.0 Hz, 1 H), 4.99 (q, *J* = 12.4 Hz, 2 H), 4.62 (td, *J* = 7.6, 2.2 Hz, 1 H), 3.64 (s, 3 H), 1.97 (dt, *J* = 12.8, 6.4 Hz, 1 H), 1.90–1.78 (m, 1 H), 1.58 (dt, *J* = 12.2, 7.6 Hz, 1 H), 1.25 (ddd, *J* = 12.3, 8.9, 6.0 Hz, 1 H), 1.18 (s, 3 H), 1.10 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 153.7, 138.2, 137.4, 131.2, 130.0, 128.4(2C), 127.5, 127.4, 127.2(2C), 126.4, 122.2, 119.5, 117.8, 117.7, 113.5, 102.5, 100.8, 82.3, 82.1, 69.7, 42.8, 38.4, 33.0, 28.9, 27.9, 27.4 ppm; HRMS (ESI): calcd for $C_{29}H_{32}NO_3^+$ [M + H$^+$] 442.2377, found 442.2372.



2p

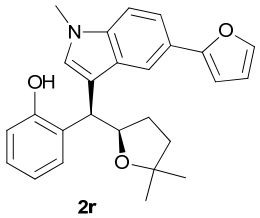
2-((5,5-Dimethyltetrahydrofuran-2-yl)(5-(2-methoxyphenyl)-1-methyl-1*H*-indol-3-yl)methyl)phenol (2q): obtained in 75% yield and >20:1 dr as a white solid; m.p.



2q

175–177 °C; IR (film) ν_{max} 3312, 3092, 2988, 1612, 1481, 1472, 1198, 1131, 1015, 834, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.89 (s, 1 H), 7.43–7.36 (m, 2 H), 7.30 (d, *J* = 9.0 Hz, 1 H), 7.28–7.20 (m, 2 H), 7.13–7.03 (m, 2 H), 7.01–6.84 (m, 4 H), 6.70 (dd, *J* = 10.6, 4.2 Hz, 1 H), 4.93 (d, *J* = 1.6 Hz, 1 H), 4.81 (td, *J* = 7.3, 2.5 Hz, 1 H), 3.80 (s, 3 H), 3.69 (s, 3 H), 2.17 (dq, *J* = 14.2, 6.9 Hz, 1 H), 2.03–1.88 (m, 1 H), 1.70 (dt, *J* = 12.3, 7.4 Hz, 1 H), 1.39–1.28 (m, 1 H), 1.27 (s, 3 H), 1.20 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.5, 155.5, 136.0, 131.8, 131.2, 131.0, 129.3, 128.0, 127.8, 127.8, 127.7, 127.4, 123.9, 120.7, 120.53, 119.9, 117.9, 113.5, 111.1, 108.4, 82.4, 82.2, 55.4, 41.5, 38.5, 32.8, 28.3, 27.7, 27.2 ppm; HRMS (ESI): calcd for $C_{29}H_{32}NO_3^+$ [M + H^+] 442.2377, found 442.2381.

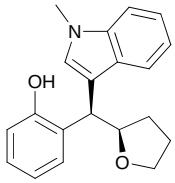
2-((5,5-Dimethyltetrahydrofuran-2-yl)(5-(furan-2-yl)-1-methyl-1*H*-indol-3-yl)methyl)phenol (2r): obtained in 70% yield and >20:1 dr as a white solid; m.p. 134–136 °C; IR (film) ν_{max} 3052, 2970, 2876, 1512, 1381, 1372, 1273, 1131, 1015, 984, 785, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.99 (s, 1 H), 7.59 (s, 1 H), 7.53 (d, *J* = 8.5 Hz, 1 H), 7.40 (s, 1 H), 7.28 (s, 1 H), 7.15–7.07 (m, 2 H), 6.98 (d, *J* = 7.9 Hz, 1 H), 6.91 (d, *J* = 7.5 Hz, 1 H), 6.69 (t, *J* = 7.3 Hz, 1 H), 6.47 (d, *J* = 3.1 Hz, 1 H), 6.44–6.39 (m, 1 H), 4.92 (s, 1 H), 4.79 (td, *J* = 7.4, 2.3 Hz, 1 H), 3.80 (s, 3 H), 2.17 (td, *J* = 13.0, 6.8 Hz, 1 H), 1.99–1.84 (m, 1 H), 1.70 (dt, *J* = 12.2, 7.5 Hz, 1 H), 1.39–1.31 (m, 1 H), 1.29 (s, 3 H), 1.20 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.5, 155.4, 141.1, 136.2, 130.9, 128.1, 128.0(2C), 127.9, 122.7, 119.9, 118.7, 118.1, 115.0, 113.7, 111.4, 109.3, 103.1,



2r

82.4, 82.3, 41.7, 38.5, 32.9, 28.5, 27.8, 27.3 ppm; HRMS (ESI): calcd for $C_{26}H_{28}NO_3^+$ [M + H^+] 402.2064, found 402.2070.

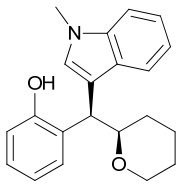
2-((1-Methyl-1*H*-indol-3-yl)(tetrahydrofuran-2-yl)methyl)phenol (2s): obtained in



2s

81% yield and >20:1 dr as a white solid; m.p. 139–141 °C; IR (film) ν_{max} 3205, 3035, 2970, 1611, 1498, 1262, 1016, 883, 735, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.77 (s, 1 H), 7.26 (dd, *J* = 13.6, 7.8 Hz, 2 H), 7.18 (t, *J* = 7.5 Hz, 1 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 7.03 (s, 1 H), 6.97 (dd, *J* = 17.1, 8.0 Hz, 2 H), 6.86 (d, *J* = 7.6 Hz, 1 H), 6.68 (t, *J* = 7.4 Hz, 1 H), 4.95 (d, *J* = 1.5 Hz, 1 H), 4.73 (td, *J* = 7.1, 2.8 Hz, 1 H), 3.85 (dd, *J* = 13.6, 7.5 Hz, 1 H), 3.78 (s, 3 H), 3.75 (d, *J* = 7.9 Hz, 1 H), 2.18–2.03 (m, 1 H), 1.83 (tt, *J* = 14.6, 7.2 Hz, 2 H), 1.58–1.46 ppm (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.4, 136.8, 130.9, 127.9, 127.7, 127.6, 127.0, 121.8, 119.9, 119.6, 119.0, 117.6, 113.1, 109.0, 83.2, 68.4, 41.7, 32.8, 28.0, 26.2 ppm; HRMS (ESI): calcd for $C_{20}H_{22}NO_2^+$ [M + H^+] 308.1645, found 308.1648.

2-((1-Methyl-1*H*-indol-3-yl)(tetrahydro-2H-pyran-2-yl)methyl)phenol (2t):

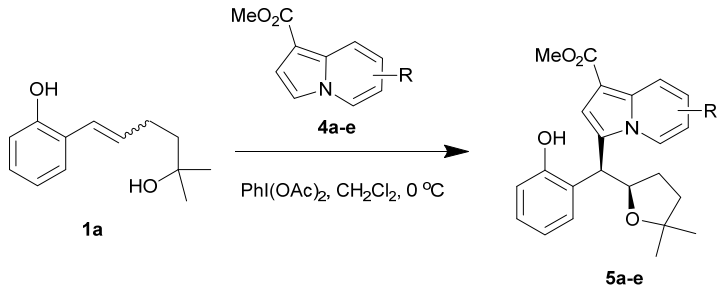


2t

obtained in 77% yield and >20:1 dr as a white solid; m.p. 124–126 °C; IR (film) ν_{max} 3232, 3052, 2970, 1612, 1481, 1332, 1231, 1115, 884, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.11 (s, 1 H), 7.36 (d, *J* = 7.9 Hz, 1 H), 7.24 (t, *J* = 10.9 Hz, 2 H), 7.16 (t, *J* = 7.5 Hz, 1 H), 7.08 (t, *J* = 7.4 Hz, 1 H), 7.01 (t, *J* = 7.5 Hz, 2 H), 6.89 (d, *J* = 7.8 Hz, 1 H), 6.71 (t, *J* = 7.3 Hz, 1 H), 4.47 (s, 1 H), 4.14 (dd, *J* = 31.5, 9.8 Hz, 2 H), 3.76 (s, 3 H), 3.66–3.54 (m, 1 H), 1.86–1.65 (m, 2 H), 1.54–1.46 ppm (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.2, 136.5,

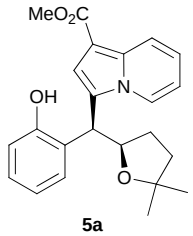
131.1, 129.2, 128.3, 128.1, 127.3, 121.5, 119.7, 119.2, 118.8, 117.9, 112.4, 109.0, 82.5, 69.2, 46.1, 32.8, 29.5, 25.4, 23.3 ppm; HRMS (ESI): calcd for $C_{21}H_{24}NO_2^+$ [M + H^+] 322.1802, found 322.1803.

General procedure for the synthesis of 2-substituted indolizines 5a–e through hypervalent iodine-mediated alkene difunctionalization of *o*-vinylphenol 1a:



To a stirred solution of *o*-vinylphenol **1a** (0.2 mmol) and indolizines **4a**–**e** (0.24 mmol) in CH_2Cl_2 (10 mL) at 0 °C was treated with $PhI(OAc)_2$ (0.24 mmol). The resulting mixture was stirred for 1 h before it was quenched with saturated $Na_2S_2O_3$ (sat. aq., 10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 20:1) afforded corresponding products **5a**–**e**.

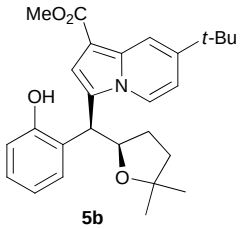
Starting materials：Indolizines **4a**–**e** were prepared according to the known literature procedures.[3]



Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(2-hydroxyphenyl)methyl) indolizine-1-carboxylate (5a): obtained in 87% yield and >20:1 dr as a white solid; m.p. 248–250 °C; IR (film) ν_{max} 3223, 2969, 2868, 1656, 1507, 1456, 1223, 1056, 879, 850, 766, 740 cm^{-1}; ^1H NMR (400

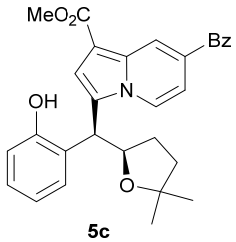
MHz, $CDCl_3$) δ = 8.42 (s, 1 H), 8.12 (d, *J* = 8.8 Hz, 1 H), 7.25 (d, *J* = 6.7 Hz, 1 H), 7.12 (s, 1 H), 7.07 (t, *J* = 7.2 Hz, 1 H), 7.02–6.89 (m, 2 H), 6.58 (t, *J* = 7.1 Hz, 1 H), 6.47 (t, *J* = 6.3 Hz, 1 H), 6.28 (d, *J* = 7.4 Hz, 1 H), 4.88 (s, 2 H), 3.85 (s, 3 H), 2.39–2.22 (m, 1 H), 1.88 (d, *J* = 4.9 Hz, 1 H), 1.74–1.62 (m, 1 H), 1.20 (s, 4 H), 1.14 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.3, 155.8, 136.0, 129.0, 128.8, 123.6(2C), 123.1, 122.3, 120.8, 119.6, 118.5, 115.3, 112.4, 102.7, 82.2, 81.5, 50.9, 40.6, 38.5, 27.7, 27.4, 26.8 ppm; HRMS (ESI): calcd for $C_{23}H_{26}NO_4^+$ [M + H^+] 380.1856, found 380.1852.

Methyl 7-(tert-butyl)-3-((5,5-dimethyltetrahydrofuran-2-yl)(2-hydroxyphenyl)-methyl)indolizine-1-carboxylate (5b): obtained in 82% yield and >20:1 dr as a white solid; m.p. 270–272 °C; IR (film) ν_{max} 3219, 2969, 2870, 1656, 1507, 1456, 1223, 1135, 860, 766, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.50 (s, 1 H), 8.15 (s, 1 H), 7.28 (s, 1 H), 7.18–7.09 (m, 2 H), 7.04 (d, *J* = 7.9 Hz, 1 H), 6.67 (t, *J* = 7.1 Hz, 1 H), 6.62 (dd, *J* = 7.4, 1.8 Hz, 1 H), 6.40 (d, *J* = 7.6 Hz, 1 H), 4.93 (s, 2 H), 3.92 (s, 3 H), 2.39 (td, *J* = 14.8, 7.3 Hz, 1 H), 2.03–1.88 (m, 1 H), 1.74 (ddd, *J* = 13.5, 7.9, 5.9 Hz, 1 H), 1.30 (s, 9 H), 1.27 (s, 4 H), 1.21 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.5, 155.9, 146.4, 136.6, 129.2, 128.8, 123.9, 123.1, 122.2, 120.8, 118.5, 115.1, 114.0, 111.9, 101.6, 82.2, 81.6, 50.8, 40.6, 38.5, 34.7, 30.5(3C), 27.7, 27.4, 26.8 ppm; HRMS (ESI): calcd for $C_{27}H_{34}NO_4^+$ [M + H^+] 436.2482, found 436.2483.



5b

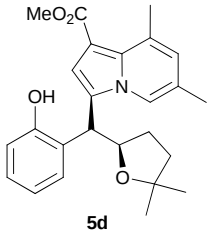
Methyl 7-benzoyl-3-((S)-((R)-5,5-dimethyltetrahydrofuran-2-yl)(2-hydroxyphen-yl)methyl)indolizine-1-carboxylate (5c): obtained in 78% yield and >20:1 dr as a



5c

white solid; m.p. 203–205 °C; IR (film) ν_{max} 3293, 2970, 2865, 1697, 1651, 1449, 1351, 1218, 1111, 1055, 879, 736, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.64 (s, 1 H), 8.41 (s, 1 H), 7.81 (d, *J* = 7.1 Hz, 2 H), 7.59 (t, *J* = 7.3 Hz, 1 H), 7.50 (t, *J* = 7.5 Hz, 2 H), 7.43 (d, *J* = 7.3 Hz, 1 H), 7.33 (s, 1 H), 7.21–7.09 (m, 2 H), 7.05 (d, *J* = 8.0 Hz, 1 H), 6.69 (t, *J* = 7.4 Hz, 1 H), 6.35 (d, *J* = 7.6 Hz, 1 H), 5.00 (d, *J* = 2.5 Hz, 1 H), 4.95 (td, *J* = 6.9, 3.0 Hz, 1 H), 3.89 (s, 3 H), 2.38 (td, *J* = 14.5, 7.3 Hz, 1 H), 1.96 (ddd, *J* = 15.1, 10.7, 6.6 Hz, 1 H), 1.82–1.70 (m, 1 H), 1.38–1.25 (m, 4 H), 1.22 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.5, 164.8, 155.7, 137.2, 133.7, 132.5, 130.0(2C), 129.7, 129.1, 128.8, 128.4(2C), 125.8, 124.0, 123.4, 123.2, 121.0, 118.6, 117.1, 111.9, 107.6, 82.4, 81.3, 51.2, 40.7, 38.4, 27.8, 27.5, 26.8 ppm; HRMS (ESI): calcd for $C_{30}H_{30}NO_5^+$ [M + H^+] 484.2118, found 484.2123.

Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(2-hydroxyphenyl)methyl)-6,8-dim

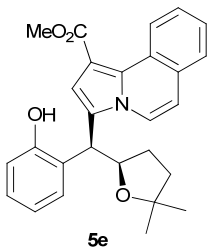


5d

ethylindolizine-1-carboxylate (5d): obtained in 80% yield and >20:1 dr as a white solid; m.p. 165–167 °C; IR (film) ν_{max} 2969, 2898, 1556, 1511, 1456, 1243, 1056, 880, 871, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.55 (s, 1 H), 7.13 (d, *J* = 11.6 Hz, 2 H), 7.03 (d, *J* = 7.8 Hz, 1 H), 6.97 (s, 1 H), 6.69–6.60 (m, 2 H), 6.37 (d, *J* = 7.3 Hz, 1 H), 5.02–4.76 (m, 2 H), 3.87 (s, 3 H), 2.75 (s, 3 H), 2.38 (dt, *J* = 14.8, 7.3 Hz, 1 H), 2.04 (s, 3 H), 1.94 (ddd, *J* = 12.8, 8.9, 6.6 Hz, 1 H), 1.82–1.63 (m, 1 H), 1.27 (s, 3 H), 1.22 ppm (s, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.1, 155.8, 134.1, 129.3, 129.1, 128.7, 126.9, 123.8, 122.1, 121.8, 120.7, 119.3, 118.4, 116.7, 103.7, 82.1, 81.7, 51.0, 40.7, 38.5, 27.8, 27.4,

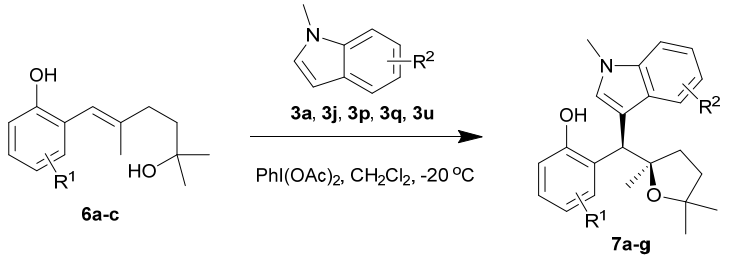
26.7, 22.0, 18.1 ppm; HRMS (ESI): calcd for $C_{25}H_{30}NO_4^+$ [M + H$^+$] 408.2169, found 408.2175.

Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(2-hydroxyphenyl)methyl)pyrrolo-[2,1-a]isoquinoline-1-carboxylate (5e): obtained in 72% yield and >20:1 dr as a white solid; m.p. 228–230 ^oC; IR (film) ν_{max} 3261, 2972, 1699, 1507, 1458, 1203, 1017, 789, 759 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.85 (d, *J* = 8.3 Hz, 1 H), 8.53 (s, 1 H), 7.59 (dd, *J* = 15.6, 7.5 Hz, 2 H), 7.52–7.45 (m, 1 H), 7.23–7.12 (m, 3 H), 7.05 (d, *J* = 7.8 Hz, 1 H), 6.78 (d, *J* = 7.3 Hz, 1 H), 6.66 (t, *J* = 7.3 Hz, 1 H), 6.40 (d, *J* = 7.5 Hz, 1 H), 5.00 (s, 2 H), 3.97 (s, 3 H), 2.42 (dd, *J* = 12.6, 7.1 Hz, 1 H), 2.15–1.90 (m, 1 H), 1.86–1.72 (m, 1 H), 1.30 (s, 4 H), 1.24 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.7, 155.7, 132.7, 129.4, 128.9, 128.7, 127.6, 127.5, 127.0, 126.6, 125.6, 124.6, 124.2, 121.5, 120.9, 118.5, 115.5, 113.5, 107.4, 82.2, 81.5, 51.4, 40.7, 38.5, 27.8, 27.4, 26.8 ppm; HRMS (ESI): calcd for $C_{27}H_{28}NO_4^+$ [M + H$^+$] 430.2013, found 430.2010.



5e

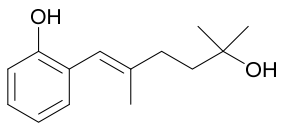
General procedure for the synthesis of 3-substituted indoles 7a–g through hypervalent iodine-mediated alkene difunctionalization of trisubstituted *o*-vinylphenols 6:



To a stirred solution of trisubstituted *o*-vinylphenols **6** (0.2 mmol) and indoles **3** (0.24 mmol) in CH_2Cl_2 (10 mL) at –20 °C was treated with $PhI(OAc)_2$ (0.24 mmol). The resulting mixture was stirred for 1 h before it was quenched with saturated $Na_2S_2O_3$ (sat. aq., 10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 20:1) afforded corresponding products **7a**–**g**.

Starting materials：Trisubstituted *o*-vinylphenols **6a**–**c** were prepared according to the known literature procedures.[4]

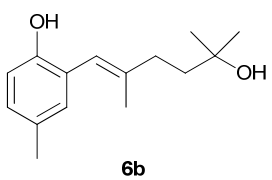
(*E*)-2-(5-Hydroxy-2,5-dimethylhex-1-en-1-yl)phenol (6a): white solid; m.p. 80–82



6a

°C; IR (film) ν_{max} 2981, 2886, 1581, 1268, 1150, 945, 816, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.13 (dd, *J* = 10.9, 4.3 Hz, 1 H), 7.03 (d, *J* = 7.1 Hz, 1 H), 6.86 (td, *J* = 8.4, 1.5 Hz, 2 H), 6.20 (s, 1 H), 5.90 (brs, 1 H), 2.44–2.27 (m, 2 H), 1.81–1.72 (m, 2 H), 1.69 (s, 3 H), 1.57 (brs, 1 H), 1.30 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.2, 143.9, 129.6, 128.1, 124.7, 119.9, 119.0, 115.0, 71.6, 41.0, 34.7, 29.5(2C), 17.6 ppm; HRMS (ESI): calcd for $C_{14}H_{21}O_2^+$ $[M + H^+]$ 221.1536, found 221.1534.

(*E*)-2-(5-Hydroxy-2,5-dimethylhex-1-en-1-yl)-4-methylphenol (6b): white solid;

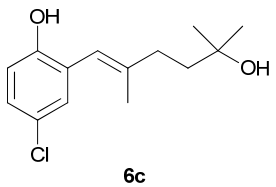


6b

m.p. 72–74 °C; IR (film) ν_{max} 2998, 2915, 1581, 1310, 1262, 1153, 898, 809, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 6.93 (d, *J* = 7.5 Hz, 1 H), 6.83 (s, 1 H), 6.77 (d, *J* = 8.0 Hz, 1 H), 6.17 (s, 1 H), 5.64 (brs, 1 H), 2.40–2.29 (m, 2 H), 2.25 (s, 3 H), 1.78–1.71 (m, 2

H), 1.69 (s, 3 H), 1.29 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9, 143.7, 129.9, 128.9, 128.6, 124.3, 119.1, 114.7, 71.6, 41.1, 34.7, 29.5(2C), 20.5, 17.6 ppm; HRMS (ESI): calcd for $C_{15}H_{23}O_2^+$ [M + H$^+$] 235.1693, found 235.1694.

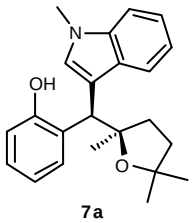
(*E*)-4-Chloro-2-(5-hydroxy-2,5-dimethylhex-1-en-1-yl)phenol (6c): white solid;



6c

m.p. 89–91 °C; IR (film) ν_{max} 2971, 2925, 1481, 1411, 1268, 1050, 905, 816, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (dd, *J* = 8.6, 2.2 Hz, 1 H), 7.00 (d, *J* = 2.1 Hz, 1 H), 6.80 (d, *J* = 8.6 Hz, 1 H), 6.11 (s, 1 H), 5.94 (brs, 1 H), 2.35 (t, *J* = 7.4 Hz, 2 H), 1.79–1.71 (m, 2 H), 1.67 (d, *J* = 0.9 Hz, 3 H), 1.30 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 145.4, 129.1, 128.0, 126.1, 124.4, 118.0, 116.3, 71.8, 40.6, 34.7, 29.6(2C), 17.6 ppm; HRMS (ESI): calcd for $C_{14}H_{20}ClO_2^+$ [M + H$^+$] 255.1146, found 255.1143.

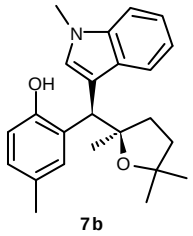
2-((1-Methyl-1*H*-indol-3-yl)(2,5,5-trimethyltetrahydrofuran-2-yl)methyl)phenol



7a

(7a): obtained in 76% yield and >20:1 dr as a white solid; m.p. 186–188 °C; IR (film) ν_{max} 2974, 2903, 1583, 1481, 1258, 1066, 880, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.40 (s, 1 H), 7.35 (d, *J* = 7.9 Hz, 1 H), 7.28 (s, 1 H), 7.21 (s, 1 H), 7.17 (t, *J* = 7.6 Hz, 1 H), 7.10–7.04 (m, 1 H), 7.00 (t, *J* = 7.5 Hz, 2 H), 6.90 (d, *J* = 7.9 Hz, 1 H), 6.69 (t, *J* = 7.4 Hz, 1 H), 4.64 (s, 1 H), 3.82 (s, 3 H), 2.24–2.08 (m, 1 H), 2.01–1.88 (m, 2 H), 1.83–1.70 (m, 1 H), 1.39 (s, 3 H), 1.38 (s, 3 H), 1.35 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 136.3, 131.4, 128.6, 128.4, 127.9, 127.2, 121.6, 119.6, 119.1, 118.9, 118.0, 113.2, 108.9, 89.3, 83.3, 50.4, 38.1, 38.0, 32.9, 30.4, 28.7, 25.1 ppm; HRMS (ESI): calcd for $C_{23}H_{28}NO_2^+$ [M + H$^+$] 350.2115, found 350.2121.

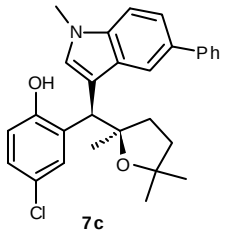
4-Methyl-2-((1-methyl-1*H*-indol-3-yl)(2,5,5-trimethyltetrahydrofuran-2-yl)methy



7b

l)phenol (7b): obtained in 73% yield and >20:1 dr as a white solid; m.p. 178–180 °C; IR (film) ν_{max} 2982, 2903, 1483, 1461, 1254, 1126, 786, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.16 (s, 1 H), 7.39 (d, *J* = 7.9 Hz, 1 H), 7.24 (dd, *J* = 7.7, 5.5 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H), 7.00 (t, *J* = 7.3 Hz, 1 H), 6.91–6.80 (m, 2 H), 6.76 (d, *J* = 7.9 Hz, 1 H), 4.55 (s, 1 H), 3.80 (s, 3 H), 2.24–2.04 (m, 4 H), 1.98–1.81 (m, 2 H), 1.81–1.66 (m, 1 H), 1.36 (s, 3 H), 1.33 ppm (d, *J* = 3.5 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.9, 136.2, 131.9, 128.7, 128.4(2C), 128.1, 127.3, 121.5, 119.0, 118.8, 117.8, 113.2, 108.9, 89.3, 83.3, 50.4, 38.0, 37.9, 32.9, 30.5, 28.7, 25.3, 20.7 ppm; HRMS (ESI): calcd for $C_{24}H_{30}NO_2^+$ [M + H^+] 364.2271, found 364.2274.

4-Chloro-2-((1-methyl-5-phenyl-1*H*-indol-3-yl)(2,5,5-trimethyltetrahydrofuran-2

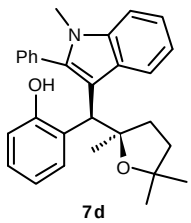


7c

-yl)methyl)phenol (7c): obtained in 80% yield and >20:1 dr as a white solid; m.p. 208–210 °C; IR (film) ν_{max} 2984, 2873, 1583, 1471, 1258, 1168, 1066, 870, 746, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.50 (s, 1 H), 7.61–7.52 (m, 3 H), 7.49–7.32 (m, 4 H), 7.30 (d, *J* = 7.2 Hz, 1 H), 7.23 (s, 1 H), 7.03 (d, *J* = 5.8 Hz, 2 H), 6.85 (d, *J* = 9.2 Hz, 1 H), 4.67 (s, 1 H), 3.86 (s, 3 H), 2.21–2.05 (m, 1 H), 2.05–1.86 (m, 2 H), 1.80 (d, *J* = 12.2 Hz, 1 H), 1.39 (s, 3 H), 1.38 (s, 3 H), 1.36 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.1, 142.4, 135.9, 132.8, 130.7, 130.2, 128.8, 128.6(2C), 127.9, 127.8, 127.4(2C), 126.3, 124.4, 121.8, 119.4, 117.2, 112.9, 109.4, 89.4, 83.7, 50.0, 38.2, 37.9, 33.1, 30.3, 28.7,

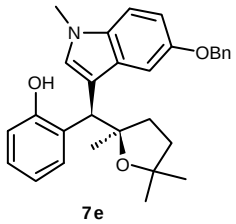
25.0 ppm; HRMS (ESI): calcd for $C_{29}H_{31}ClNO_2^+$ [M + H^+] 460.2038, found 460.2033.

2-((1-Methyl-2-phenyl-1*H*-indol-3-yl)(2,5,5-trimethyltetrahydrofuran-2-yl)methyl)phenol (7d): obtained in 64% yield and >20:1 dr as a white solid; m.p. 163–165 °C; IR (film) ν_{max} 2998, 2883, 1681, 1480, 1260, 1046, 780, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.65 (s, 1 H), 7.93 (d, *J* = 8.0 Hz, 1 H), 7.48 (brs, 1 H), 7.40 (d, *J* = 8.0 Hz, 3 H), 7.30–7.26 (m, 3 H), 7.23–7.17 (m, 1 H), 7.11 (dd, *J* = 10.9, 4.3 Hz, 1 H), 6.98–6.82 (m, 2 H), 6.67 (dd, *J* = 10.8, 4.1 Hz, 1 H), 4.54 (s, 1 H), 3.60 (s, 3 H), 1.90–1.73 (m, 1 H), 1.66 (ddd, *J* = 15.5, 10.7, 5.9 Hz, 1 H), 1.53–1.38 (m, 5 H), 1.23 (s, 3 H), 0.85 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 140.9, 137.7, 131.7, 131.1, 130.4, 128.9, 128.8, 128.4, 127.7, 127.0, 122.3(2C), 121.5, 119.6, 119.2, 117.5, 112.6(2C), 109.7, 89.5, 83.1, 51.4, 37.9, 37.5, 31.1, 30.0, 27.7, 26.8 ppm; HRMS (ESI): calcd for $C_{29}H_{32}NO_2^+$ [M + H^+] 426.2428, found 426.2423.



7d

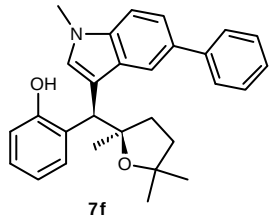
2-((5-(Benzyloxy)-1-methyl-1*H*-indol-3-yl)(2,5,5-trimethyltetrahydrofuran-2-yl)methyl)phenol (7e): obtained in 60% yield and 14:1 dr as a white solid; m.p. 134–136 °C; IR (film) ν_{max} 2971, 2925, 1580, 1497, 1377, 1258, 1065, 879, 753, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.55 (s, 1 H), 7.40–7.29 (m, 5 H), 7.22 (s, 1 H), 7.02 (dd, *J* = 15.7, 7.7 Hz, 2 H), 6.93–6.79 (m, 3 H), 6.63 (t, *J* = 7.0 Hz, 1 H), 6.44 (d, *J* = 7.7 Hz, 1 H), 5.37 (s, 1 H), 5.12 (q, *J* = 11.9 Hz, 2 H), 3.76 (s, 3 H), 2.20–2.01 (m, 1 H), 1.95–1.79 (m, 1 H), 1.77–1.62 (m, 2 H), 1.34 (s, 3 H), 1.29 (s, 3 H), 1.20 ppm (s, 3 H); ^{13}C NMR (100



7e

MHz, $CDCl_3$) δ = 155.5, 153.9, 137.9, 137.4, 132.3, 129.4, 128.4(2C), 127.7(3C), 127.5, 126.4, 121.9, 119.2, 117.9, 114.0, 102.5, 100.6, 89.5, 83.3, 69.9, 50.4, 37.9, 37.7, 33.1, 30.5, 29.7, 28.4, 25.7 ppm; HRMS (ESI): calcd for $C_{30}H_{34}NO_3^+$ [M + H^+] 456.2533, found 456.2539.

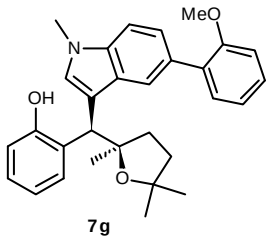
2-((1-Methyl-5-phenyl-1*H*-indol-3-yl)(2,5,5-trimethyltetrahydrofuran-2-yl)meth-



7f

yl)phenol (7f): obtained in 71% yield and >20:1 dr as a white solid; m.p. 70–72 °C; IR (film) ν_{max} 2981, 2934, 1569, 1476, 1277, 1253, 1061, 886, 753, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.43 (s, 1 H), 7.54 (d, *J* = 7.2 Hz, 3 H), 7.41 (dd, *J* = 15.4, 8.0 Hz, 3 H), 7.31 (dd, *J* = 17.6, 8.0 Hz, 2 H), 7.26 (s, 1 H), 7.07 (t, *J* = 6.9 Hz, 2 H), 6.90 (d, *J* = 7.5 Hz, 1 H), 6.72 (t, *J* = 7.0 Hz, 1 H), 4.67 (s, 1 H), 3.85 (s, 3 H), 2.24–2.11 (m, 1 H), 1.96 (ddd, *J* = 22.3, 14.7, 7.9 Hz, 2 H), 1.76 (dd, *J* = 15.1, 9.4 Hz, 1 H), 1.40 (s, 3 H), 1.38 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 142.6, 135.9, 132.6, 131.4, 129.6, 129.1, 128.6, 128.3, 128.0(2C), 127.4, 126.2, 121.6, 119.7, 118.1, 117.5, 115.3, 113.6, 109.2, 89.3, 83.4, 50.5, 38.0(2C), 33.0, 30.4, 28.8, 25.3 ppm; HRMS (ESI): calcd for $C_{29}H_{32}NO_2^+$ [M + H^+] 426.2428, found 426.2430.

2-((5-(2-Methoxyphenyl)-1-methyl-1*H*-indol-3-yl)(2,5,5-trimethyltetrahydrofur-a

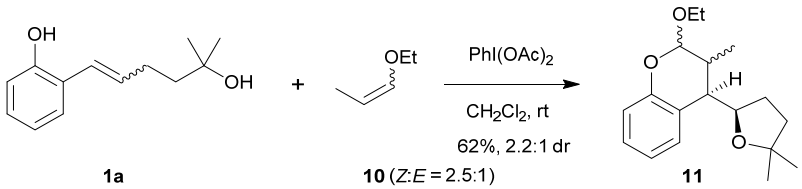


7g

n-2-yl)methyl)phenol (7g): obtained in 69% yield and >20:1 dr as a white solid; m.p. 154–156 °C; IR (film) ν_{max} 2972, 2900, 1582, 1482, 1378, 1252, 1059, 880, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.41 (s, 1 H), 7.50 (s, 1 H), 7.37 (d, *J* = 8.4 Hz, 1 H), 7.30–7.25 (m, 3 H), 7.22 (s, 1 H), 7.06 (t, *J* = 7.4 Hz, 2 H), 7.02–6.92 (m, 2 H), 6.88 (d, *J* = 7.9 Hz, 1

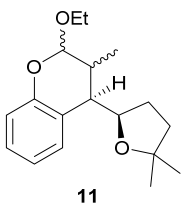
H), 6.71 (t, J = 7.4 Hz, 1 H), 4.64 (s, 1 H), 3.83 (s, 3 H), 3.72 (s, 3 H), 2.18 (dd, J = 20.7, 12.9 Hz, 1 H), 2.01–1.87 (m, 2 H), 1.82–1.74 (m, 1 H), 1.39 (s, 3 H), 1.36 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.5, 155.3, 135.6, 132.0, 131.5, 131.3, 129.3, 128.6, 128.4, 127.9, 127.7, 127.6, 123.8, 120.7, 120.0, 119.6, 118.0, 113.5, 111.2, 108.4, 89.4, 83.4, 55.5, 50.5, 38.1, 38.0, 32.9, 30.4, 28.7, 25.2 ppm; HRMS (ESI): calcd for $C_{30}H_{34}NO_3^+$ [M + H^+] 456.2533, found 456.2528.

Inverse-electron demand Diels–Alder reaction:



To a stirred solution of *o*-vinylphenol **1a** (41 mg, 0.20 mmol) and methyl-1-propenyl ether **10** (2.8 mL, 10 mmol, *Z*/*E* 2.5:1) in CH_2Cl_2 (10 mL) at room temperature was added $PhI(OAc)_2$ (77 mg, 0.24 mmol). The resulting mixture was stirred for 4 h before it was quenched with $NaHCO_3$ (sat. aq., 5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 80:1) afforded **11** (37.7 mg, 62%, dr = 2.2:1) as a colorless oil.

4-(5,5-Dimethyltetrahydrofuran-2-yl)-2-ethoxy-3-methylchromane (11): IR (film)

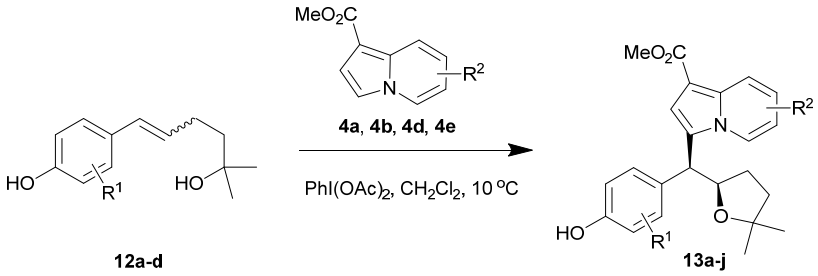


11

ν_{max} 2970, 2932, 1582,1486, 1241, 1146, 1110, 1044, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 (d, J = 7.5 Hz, 0.69 H), 7.29 (d, J = 7.6 Hz, 0.31 H), 7.12 (t, J = 7.0 Hz, 1 H), 6.85 (dd, J = 13.9, 7.7 Hz, 2

H), 5.14 (d, *J* = 2.2 Hz, 0.69 H), 5.05 (d, *J* = 2.1 Hz, 0.31 H), 4.35 (dd, *J* = 11.5, 6.6 Hz, 0.31 H), 4.17 (dd, *J* = 11.8, 6.0 Hz, 0.69 H), 4.03–3.88 (m, 1 H), 3.70–3.53 (m, 1 H), 3.09 (t, *J* = 4.8 Hz, 0.31 H), 2.74 (t, *J* = 4.6 Hz, 0.69 H), 2.49–2.37 (m, 0.31 H), 2.28–2.18 (m, 0.69 H), 2.16–2.06 (m, 0.31 H), 1.96–1.86 (m, 0.69 H), 1.65 (ddd, *J* = 15.2, 8.8, 3.1 Hz, 3 H), 1.31 (s, 1 H), 1.28 (s, 2 H), 1.26–1.19 (m, 6 H), 1.07 (d, *J* = 7.1 Hz, 1 H), 1.01 ppm (d, *J* = 6.9 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.0(2C), 130.3, 129.1, 127.6(2C), 123.0, 122.3, 120.3, 120.1, 116.7, 116.4, 101.4, 99.5, 81.20, 80.6, 79.40 77.6, 64.5, 64.4, 45.6, 43.2, 38.9, 38.5, 33.6, 33.0, 30.5, 29.4, 28.9, 28.8, 27.8, 27.1, 15.1(2C), 13.5, 10.3 ppm; HRMS (ESI): calcd for $C_{18}H_{27}O_3^+$ [M + H^+] 291.1955, found 291.1961.

General procedure for the synthesis of 2-substituted indolizines 13a–j through hypervalent iodine-mediated alkene difunctionalization of *p*-vinylphenols 12:

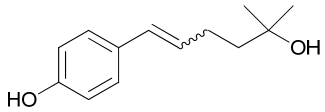


To a stirred solution of *p*-vinylphenol **12** (0.2 mmol) and indolizines **4** (0.24 mmol) in CH_2Cl_2 (10 mL) at 10 °C was treated with $PhI(OAc)_2$ (0.24 mmol). The resulting mixture was stirred for 1 h before it was quenched with saturated $Na_2S_2O_3$ (sat. aq., 10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in*

vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 20:1) afforded corresponding products **13a**–**j**.

Starting materials：*p*-Vinylphenols **12a**–**d** were synthesized according to the known literature procedures.[1]

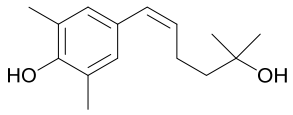
4-(5-Hydroxy-5-methylhex-1-en-1-yl)phenol (12a): ca. 6.7:1 inseparable mixture of



12a

Z/*E* isomers; white solid; m.p. 110–112 °C; IR (film) ν_{max} 2992, 2899, 1594, 1312, 1263, 1235, 1124, 1022, 882, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *Z* isomer) δ = 7.16 (d, *J* = 8.5 Hz, 2 H), 6.79 (d, *J* = 8.6 Hz, 2 H), 6.34 (d, *J* = 11.7 Hz, 1 H), 6.00 (s, 1 H), 5.55 (dt, *J* = 11.6, 7.2 Hz, 1 H), 2.42 (td, *J* = 8.7, 1.6 Hz, 2 H), 1.68–1.62 (m, 2 H), 1.60 (s, 1 H), 1.24 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$, *Z* isomer) δ = 154.6, 130.9, 130.1(2C), 128.6, 115.2(2C), 71.6, 43.7, 43.1, 29.2(2C), 23.6 ppm; HRMS (ESI): calcd for $C_{13}H_{19}O_2^+$ [M + H^+] 207.1380, found 207.1381.

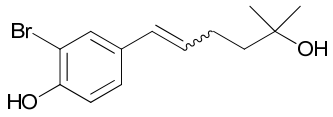
(*Z*)-4-(5-Hydroxy-5-methylhex-1-en-1-yl)-2,6-dimethylphenol (12b): white solid;



12b

m.p. 84–85 °C; IR (film) ν_{max} 3322, 2942, 2889, 1564, 1502, 1363, 1135, 1101, 896, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 6.93 (s, 2 H), 6.30 (d, *J* = 11.6 Hz, 1 H), 5.54 (dt, *J* = 11.6, 7.3 Hz, 1 H), 4.95 (s, 1 H), 2.42 (ddd, *J* = 8.7, 8.1, 1.5 Hz, 2 H), 2.24 (s, 6 H), 1.70–1.61 (m, 2 H), 1.24 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.0, 130.6(2C), 129.6, 129.0(2C), 128.7, 122.8, 71.2, 43.7, 29.1(2C), 23.7, 16.0(2C) ppm; HRMS (ESI): calcd for $C_{15}H_{23}O_2^+$ [M + H^+] 235.1693, found 235.1695.

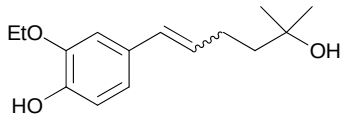
2-Bromo-4-(5-hydroxy-5-methylhex-1-en-1-yl)phenol (12c): ca. 4:1 mixture of *Z*/*E*



12c

isomers; white solid; m.p. 147–149 °C; IR (film) ν_{max} 3372, 2983, 2882, 1578, 1498, 1231, 1082, 1042, 856, 818, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 1.9 Hz, 0.2 H), 7.39 (d, *J* = 1.8 Hz, 0.8 H), 7.17 (dd, *J* = 8.6, 2.0 Hz, 0.2 H), 7.13 (dd, *J* = 8.4, 1.8 Hz, 0.8 H), 6.96 (d, *J* = 8.4 Hz, 0.8 H), 6.92 (d, *J* = 8.4 Hz, 0.2 H), 6.28 (d, *J* = 11.5 Hz, 1 H), 6.08 (dt, *J* = 15.7, 6.8 Hz, 0.2 H), 5.83 (s, 0.8 H), 5.76 (s, 0.2 H), 5.61 (dt, *J* = 11.5, 7.3 Hz, 0.8 H), 2.44–2.33 (m, 1.6 H), 2.33–2.23 (m, 0.4 H), 1.63 (dd, *J* = 9.7, 6.9 Hz, 2 H), 1.43 (s, 1 H), 1.26 (s, 1.2 H), 1.23 (s, 4.8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.3, 151.0, 132.4, 132.1, 131.6(2C), 130.1, 129.5, 129.3, 128.0, 127.2, 126.7, 116.1, 115.8, 110.4, 110.0, 71.2(2C), 43.6, 43.2, 29.3(2C), 29.2(2C), 27.9, 23.6 ppm; HRMS (ESI): calcd for $C_{13}H_{18}BrO_2^+$ [M + H^+] 285.0485, found 285.0489.

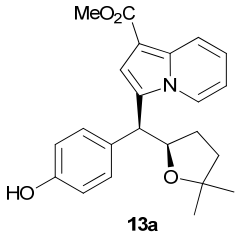
2-Ethoxy-4-(5-hydroxy-5-methylhex-1-en-1-yl)phenol (12d): ca. 7.7:1 mixture of



12d

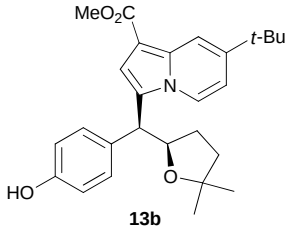
Z/*E* isomers; colorless oil; IR (film) ν_{max} 3392, 2972, 2929, 1594, 1512, 1263, 1235, 1122, 1042, 826, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *Z* isomer) δ = 6.88 (d, *J* = 8.0 Hz, 1 H), 6.82 (dd, *J* = 15.9, 8.1 Hz, 2 H), 6.32 (d, *J* = 11.5 Hz, 1 H), 5.54 (dt, *J* = 11.6, 7.2 Hz, 1 H), 4.08 (q, *J* = 6.9 Hz, 2 H), 2.41 (dd, J = 15.3, 7.2 Hz, 2 H), 1.63 (dd, *J* = 9.6, 6.8 Hz, 2 H), 1.42 (t, *J* = 7.0 Hz, 3 H), 1.21 ppm (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$, *Z* isomer) δ = 145.4, 144.5, 130.9, 129.8, 128.7, 121.8, 114.4, 112.3, 70.8, 64.3, 43.6, 29.1(2C), 23.6, 14.8 ppm; HRMS (ESI): calcd for $C_{15}H_{23}O_3^+$ [M + H^+] 251.1642, found 251.1643.

Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(4-hydroxyphenyl)methyl)indolizine-1-carboxylate (13a): obtained in 83% yield and >20:1 dr as a white solid; m.p. 216–218 °C; IR (film) ν_{max} 2971, 2925, 1692, 1663, 1510, 1259, 1227, 1058, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.16 (d, *J* = 9.0 Hz, 1 H), 7.62 (d, *J* = 7.1 Hz, 1 H), 7.30 (s, 1 H), 6.98 (t, *J* = 10.9 Hz, 3 H), 6.71 (d, *J* = 8.5 Hz, 2 H), 6.54 (t, *J* = 6.8 Hz, 1 H), 5.11 (brs, 1 H), 4.66 (dd, *J* = 13.7, 6.5 Hz, 1 H), 4.20 (d, *J* = 6.1 Hz, 1 H), 3.91 (s, 3 H), 1.94 (dt, *J* = 12.3, 6.9 Hz, 1 H), 1.80 (dt, *J* = 16.0, 7.7 Hz, 1 H), 1.65 (dd, *J* = 12.0, 7.7 Hz, 1 H), 1.44–1.31 (m, 1 H), 1.26 (s, 3 H), 1.15 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.7, 154.8, 136.1, 130.1, 129.9(2C), 125.7, 123.7, 121.8, 119.6, 115.3(2C), 115.0, 112.0, 102.6, 81.2, 80.0, 50.9, 47.7, 38.2, 30.0, 28.6, 27.8 ppm; HRMS (ESI): calcd for $C_{23}H_{26}NO_4^+$ [M + H^+] 380.1856, found 380.1860.



13a

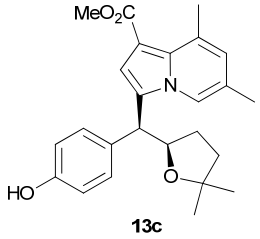
Methyl 7-(tert-butyl)-3-((5,5-dimethyltetrahydrofuran-2-yl)(4-hydroxyphenyl)methyl)indolizine-1-carboxylate (13b): obtained in 80% yield and >20:1 dr as a white solid; m.p. 221–223 °C; IR (film) ν_{max} 2981, 2919, 1691, 1563, 1510, 1351, 1219, 1158, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.09 (s, 1 H), 7.53 (d, *J* = 7.3 Hz, 1 H), 7.22 (s, 1 H), 6.97 (d, *J* = 8.1 Hz, 2 H), 6.71 (d, *J* = 8.1 Hz, 2 H), 6.60 (d, *J* = 6.1 Hz, 1 H), 5.74 (brs, 1 H), 4.64 (d, *J* = 6.4 Hz, 1 H), 4.18 (d, *J* = 5.7 Hz, 1 H), 3.91 (s, 3 H), 1.94 (dd, *J* = 12.4, 6.4 Hz, 1 H), 1.77 (dd, *J* = 19.9, 7.7 Hz, 1 H), 1.68–1.55 (m, 1 H), 1.42–1.25 (m, 13 H), 1.13 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.1, 155.0, 145.9, 136.7, 130.1, 129.7(2C), 124.9, 123.3, 115.3(2C), 114.7, 114.0, 111.4,



13b

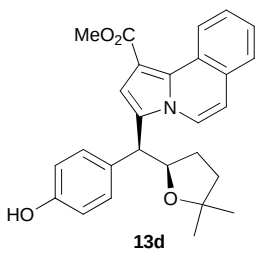
101.4, 81.1, 79.9, 50.8, 47.5, 38.2, 34.6, 30.4(3C), 29.7, 28.5, 27.8 ppm; HRMS (ESI): calcd for $C_{27}H_{34}NO_4^+$ [M + H$^+$] 436.2482, found 436.2487.

Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(4-hydroxyphenyl)methyl)-6,8-dimethylindolizine-1-carboxylate (13c): obtained in 77% yield and >20:1 dr as a white solid; m.p. 164–166 ^{o}C; IR (film) ν_{max} 2981, 2885, 1611, 1413, 1262, 1058, 789, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (s, 1 H), 7.25 (s, 1 H), 7.01 (d, *J* = 8.5 Hz, 2 H), 6.70 (d, *J* = 8.5 Hz, 2 H), 6.59 (s, 1 H), 4.94 (brs, 1 H), 4.65 (dd, *J* = 13.3, 6.7 Hz, 1 H), 4.16 (d, *J* = 6.1 Hz, 1 H), 3.85 (s, 3 H), 2.72 (s, 3 H), 2.08 (s, 3 H), 1.96 (td, *J* = 12.6, 6.5 Hz, 1 H), 1.86–1.74 (m, 1 H), 1.64 (dd, *J* = 12.1, 7.6 Hz, 1 H), 1.37–1.28 (m, 1 H), 1.25 (s, 3 H), 1.16 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.5, 154.7, 134.1, 130.2(2C), 129.4, 126.3, 124.7, 121.2, 119.4, 116.3, 115.2(2C), 103.8, 81.0, 80.1, 51.0, 47.7, 38.2, 29.9(2C), 28.6, 27.8, 22.0, 18.2 ppm; HRMS (ESI): calcd for $C_{25}H_{30}NO_4^+$ [M + H$^+$] 408.2169, found 408.2173.



13c

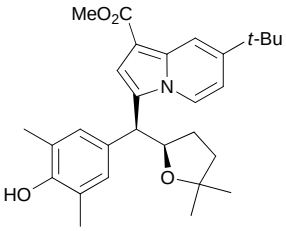
Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(4-hydroxyphenyl)methyl)pyrrolo[2,1-a]isoquinoline-1-carboxylate (13d): obtained in 70% yield and >20:1 dr as a white solid; m.p. 151–153 ^{o}C; IR (film) ν_{max} 3272, 2903, 1509, 1258, 1207, 1051, 887, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.82 (d, *J* = 8.3 Hz, 1 H), 7.54 (dd, *J* = 17.6, 9.7 Hz, 3 H), 7.48–7.40 (m, 1 H), 7.25 (d, *J* = 10.9 Hz, 1 H), 7.01 (d, *J* = 7.8 Hz, 2 H), 6.77 (d, *J* = 7.4 Hz, 1 H), 6.70 (d, *J* = 7.7 Hz, 2 H), 5.22 (brs, 1 H), 4.70 (dd, *J* = 12.7, 6.3 Hz, 1 H), 4.26 (d, *J* = 5.7 Hz, 1 H), 3.95 (s, 3 H), 2.06–1.93 (m, 1 H),



13d

1.82 (dd, *J* = 19.9, 7.5 Hz, 1 H), 1.65 (s, 1 H), 1.35 (dd, *J* = 12.3, 7.0 Hz, 1 H), 1.28 (s, 3 H), 1.18 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.1, 154.9, 132.6, 130.1(2C), 128.6, 127.3(2C), 127.0(3C), 126.5, 125.8, 121.8, 115.3, 115.2, 113.0(2C), 107.4, 81.2, 79.9, 51.4, 47.6, 38.2, 29.9, 28.6, 27.8 ppm; HRMS (ESI): calcd for $C_{27}H_{28}NO_4^+$ [M + H$^+$] 430.2013, found 430.2017.

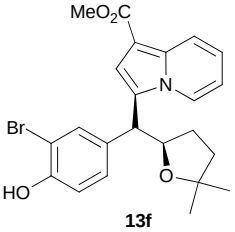
Methyl 7-(tert-butyl)-3-((5,5-dimethyltetrahydrofuran-2-yl) (4-hydroxy-3,5-dimethylphenyl)methyl)indolizine-1-carboxylate (13e):



13e

obtained in 76% yield and >20:1 dr as a white solid; m.p. 98–100 ^{o}C; IR (film) ν_{max} 2971, 2845, 1510, 1459, 1227, 1168, 887, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12 (s, 1 H), 7.60 (d, *J* = 7.3 Hz, 1 H), 7.23 (s, 1 H), 6.74 (s, 2 H), 6.62 (d, *J* = 6.9 Hz, 1 H), 4.73–4.55 (m, 2 H), 4.08 (d, *J* = 6.2 Hz, 1 H), 3.91 (s, 3 H), 2.16 (s, 6 H), 1.91 (dt, *J* = 12.6, 6.3 Hz, 1 H), 1.80 (dt, *J* = 14.8, 7.6 Hz, 1 H), 1.63 (dt, *J* = 15.0, 7.6 Hz, 1 H), 1.42–1.21 (m, 13 H), 1.14 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.9, 151.2, 145.7, 136.6, 129.5, 129.0(2C), 125.1, 123.3, 122.8(2C), 114.5, 114.0, 111.3, 101.5, 81.0, 80.1, 50.7, 47.8, 38.2, 34.6, 30.5(3C), 30.0, 28.6, 27.9, 15.9(2C) ppm; HRMS (ESI): calcd for $C_{29}H_{38}NO_4^+$ [M + H$^+$] 464.2795, found 464.2789.

Methyl 3-((3-bromo-4-hydroxyphenyl)(5,5-dimethyltetrahydrofuran-2-yl) methyl) indolizine-1-carboxylate (13f):

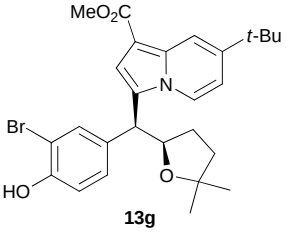


13f

obtained in 78% yield and >20:1 dr as a white solid; m.p. 155–157 ^{o}C; IR (film) ν_{max} 2988, 2875, 1563, 1310, 1126, 1058, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.18 (d, *J* = 9.0 Hz, 1 H), 7.60 (d, *J* = 7.0 Hz, 1 H), 7.29 (d, *J* = 3.5 Hz, 2 H), 7.05–

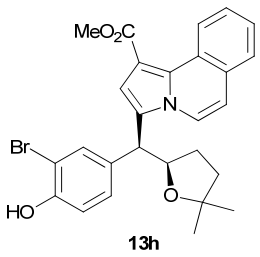
6.98 (m, 1 H), 6.94 (d, *J* = 8.3 Hz, 1 H), 6.88 (d, *J* = 8.3 Hz, 1 H), 6.58 (t, *J* = 6.7 Hz, 1 H), 5.67 (s, 1 H), 4.66 (dd, *J* = 13.0, 6.6 Hz, 1 H), 4.22 (d, *J* = 5.7 Hz, 1 H), 3.92 (s, 3 H), 2.02 (td, *J* = 13.0, 6.7 Hz, 1 H), 1.78 (td, *J* = 15.7, 7.7 Hz, 1 H), 1.66 (dd, *J* = 10.0, 5.3 Hz, 1 H), 1.36–1.28 (m, 1 H), 1.26 (s, 3 H), 1.15 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.6, 151.5, 136.2, 132.3, 131.4, 129.5, 124.7, 123.5, 122.0, 119.7, 115.9, 115.2, 112.2, 110.2, 102.8, 81.2, 79.7, 50.9, 47.1, 38.2, 29.7, 28.5, 27.7 ppm; HRMS (ESI): calcd for $C_{23}H_{25}BrNO_4^+$ [M + H^+] 458.0961, found 458.0964.

Methyl 3-((3-bromo-4-hydroxyphenyl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)-7-(tert-butyl)indolizine-1-carboxylate (13g): obtained in 75% yield and >20:1 dr as a white solid; m.p. 210–212 °C; IR (film) ν_{max} 3321, 2987, 2922, 1655, 1540, 1259, 1231, 1059, 866, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.14 (s, 1 H), 7.52 (d, *J* = 7.4 Hz, 1 H), 7.31 (d, *J* = 1.5 Hz, 1 H), 7.21 (s, 1 H), 6.94 (dd, *J* = 8.2, 1.7 Hz, 1 H), 6.88 (d, *J* = 8.3 Hz, 1 H), 6.65 (dd, *J* = 7.3, 1.7 Hz, 1 H), 5.70 (s, 1 H), 4.66 (dd, *J* = 12.6, 6.7 Hz, 1 H), 4.21 (d, *J* = 5.4 Hz, 1 H), 3.91 (s, 3 H), 2.04 (td, *J* = 13.2, 7.0 Hz, 1 H), 1.84–1.70 (m, 1 H), 1.70–1.58 (m, 1 H), 1.35–1.25 (m, 13 H), 1.14 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.7, 151.5, 146.1, 136.7, 132.4, 131.6, 129.6, 123.8, 123.0, 115.8, 114.9, 114.1, 111.7, 110.2, 101.7, 81.1, 79.6, 50.8, 46.9, 38.2, 34.6, 30.5(3C), 29.5, 28.4, 27.7 ppm; HRMS (ESI): calcd for $C_{27}H_{33}BrNO_4^+$ [M + H^+] 514.1587, found 514.1592.



13g

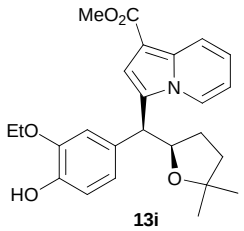
Methyl 3-((3-bromo-4-hydroxyphenyl)(5,5-dimethyltetrahydrofuran-2-yl)methyl)pyrrolo[2,1-a]isoquinoline-1-carboxylate (13h): obtained in 67% yield and >20:1 dr



13h

as a white solid; m.p. 144–146 °C; IR (film) ν_{max} 2988, 2925, 1695, 1633, 1410, 1259, 1227, 1058, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 10.27 (d, *J* = 8.3 Hz, 1 H), 8.05–7.98 (m, 2 H), 7.91 (t, *J* = 7.7 Hz, 2 H), 7.75 (d, *J* = 1.6 Hz, 1 H), 7.71 (s, 1 H), 7.44–7.38 (m, 1 H), 7.32 (d, *J* = 8.4 Hz, 1 H), 7.26 (d, *J* = 7.4 Hz, 1 H), 5.88 (s, 1 H), 5.14 (dd, *J* = 12.6, 6.7 Hz, 1 H), 4.73 (d, *J* = 5.3 Hz, 1 H), 4.39 (s, 3 H), 2.50 (td, *J* = 13.1, 6.7 Hz, 1 H), 2.24 (dt, *J* = 15.5, 7.4 Hz, 1 H), 2.17–2.05 (m, 1 H), 1.74 (d, *J* = 8.8 Hz, 1 H), 1.71 (s, 3 H), 1.61 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.9, 151.4, 132.7, 132.3, 131.8, 129.7, 128.6, 127.5, 127.4, 127.0, 126.6, 125.9, 125.8, 121.6, 115.9, 115.5, 113.3, 110.3, 107.6, 81.2, 79.6, 51.4, 47.0, 38.2, 29.6, 28.4, 27.7 ppm; HRMS (ESI): calcd for $C_{27}H_{27}BrNO_4^+$ [M + H^+] 508.1118, found 508.1125.

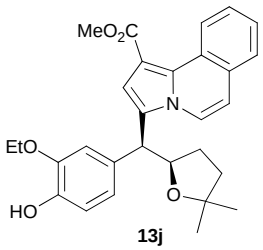
Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(3-ethoxy-4-hydroxyphenyl)methyl) indolizine-1-carboxylate (13i): obtained in 63% yield and >20:1 dr as a white solid; m.p. 176–178 °C; IR (film) ν_{max} 2971, 2925, 1692, 1663, 1510, 1259, 1227, 1128, 890, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.17 (d, *J* = 9.0 Hz, 1 H), 7.63 (d, *J* = 7.0 Hz, 1 H), 7.31 (s, 1 H), 7.03–6.93 (m, 1 H), 6.80 (d, *J* = 8.1 Hz, 1 H), 6.65 (d, *J* = 8.1 Hz, 1 H), 6.58 (s, 1 H), 6.54 (t, *J* = 6.8 Hz, 1 H), 5.61 (s, 1 H), 4.66 (dd, *J* = 13.4, 6.7 Hz, 1 H), 4.17 (d, *J* = 6.2 Hz, 1 H), 4.00 (dd, *J* = 16.0, 7.0 Hz, 2 H), 3.91 (s, 3 H), 1.95 (dt, *J* = 12.6, 6.6 Hz, 1 H), 1.88–1.75 (m, 1 H), 1.66 (dt, *J* = 12.3, 7.7 Hz, 1 H), 1.43–1.32 (m, 4 H), 1.27 (s, 3 H), 1.16 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.6, 145.8, 144.9, 136.1, 129.6, 125.6, 123.8, 121.7(2C), 119.6, 114.9, 114.1, 111.9(2C), 102.6, 81.1,



13i

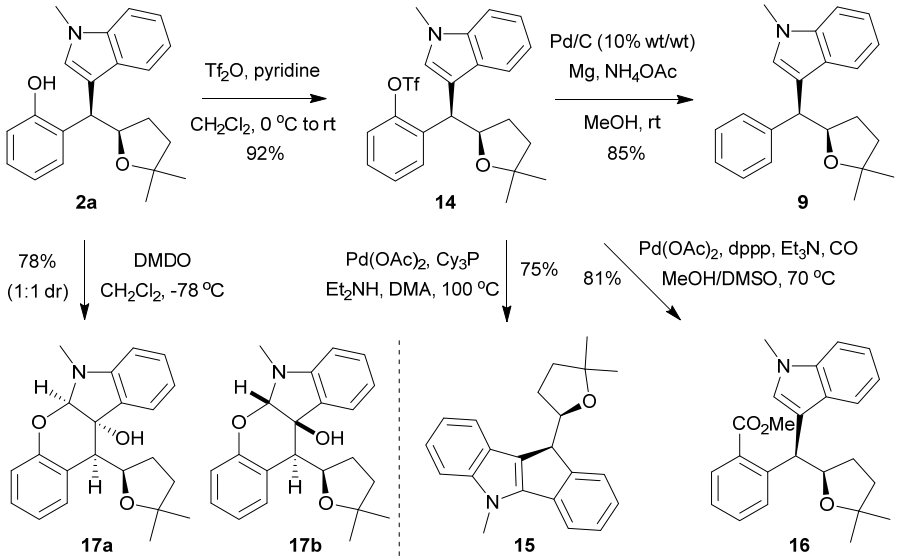
79.9, 64.4, 50.8, 48.2, 38.2, 30.0, 28.7, 27.9, 14.7 ppm; HRMS (ESI): calcd for $C_{25}H_{30}NO_5^+$ [M + H$^+$] 424.2118, found 424.2116.

Methyl 3-((5,5-dimethyltetrahydrofuran-2-yl)(3-ethoxy-4-hydroxyphenyl)methyl) pyrrolo[2,1-a]isoquinoline-1-carboxylate (13j): obtained in 55% yield and >20:1 dr as a white solid; m.p. 220–222 ^oC; IR (film) ν_{max} 2991, 2875, 1676, 1310, 1254, 1217, 1058, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.84 (d, *J* = 8.3 Hz, 1 H), 7.55 (dd, *J* = 15.0, 8.5 Hz, 3 H), 7.45 (t, *J* = 7.4 Hz, 1 H), 7.29 (s, 1 H), 6.79 (t, *J* = 8.3 Hz, 2 H), 6.72–6.58 (m, 2 H), 5.58 (s, 1 H), 4.70 (dd, *J* = 13.1, 6.5 Hz, 1 H), 4.25 (d, *J* = 5.8 Hz, 1 H), 4.09–3.82 (m, 5 H), 2.00 (td, *J* = 12.9, 6.5 Hz, 1 H), 1.85 (td, *J* = 15.7, 7.9 Hz, 1 H), 1.74–1.61 (m, 1 H), 1.36 (t, *J* = 6.9 Hz, 4 H), 1.29 (s, 3 H), 1.18 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.0, 145.7, 144.9, 132.5, 130.0, 128.6, 127.3(2C), 126.9(2C), 126.5, 125.8, 121.9, 121.8, 115.2, 114.1, 113.0, 112.1, 107.4, 81.0, 79.9, 64.4, 51.3, 48.1, 38.2, 30.0, 28.7, 27.8, 14.8 ppm; HRMS (ESI): calcd for $C_{29}H_{32}NO_5^+$ [M + H$^+$] 474.2275, found 474.2278.



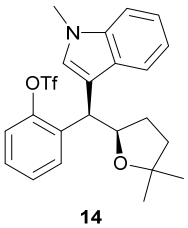
13j

Synthetic application of indole derivative 2a



Preparation of triflate 14: To a stirred solution of indole **2a** (335 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) at 0 °C were added pyridine (0.19 mL, 2.4 mmol) and Tf_2O (0.20 mL, 1.2 mmol). The resulting mixture was warmed to room temperature and stirred for further 1 h before it was quenched with NH_4Cl (sat. aq., 10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 10:1) afforded triflate **14** (430 mg, 92%) as a colorless oil.

2-((5,5-Dimethyltetrahydrofuran-2-yl)(1-methyl-1*H*-indol-3-yl)methyl)phenyl



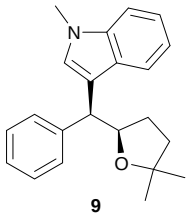
14

trifluoromethanesulfonate (14): IR (film) ν_{max} 2970, 2875, 1481, 1416, 1211, 1141, 1070, 891, 766, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.56 (dd, *J* = 6.4, 2.8 Hz, 1 H), 7.44 (d, *J* = 8.0 Hz, 1 H), 7.25–7.18 (m, 5 H), 7.15 (t, *J* = 7.5 Hz, 1 H), 7.00 (t, *J* = 7.5 Hz, 1 H), 4.70 (d, *J* = 6.3 Hz, 1 H), 4.61 (dd, *J* = 14.2, 6.4 Hz, 1 H), 3.76 (s, 3 H), 1.93–1.84 (m, 1 H), 1.84–

1.73 (m, 1 H), 1.72–1.56 (m, 2 H), 1.25 (s, 3 H), 1.20 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.4, 136.7, 136.5, 131.2, 128.2, 128.0, 127.9, 127.8, 121.4, 120.9, 119.5, 118.8, 118.6 ($J_{C\text{-}F}$ = 318 Hz), 113.6, 108.9, 81.5, 81.2, 40.9, 38.2, 32.8, 30.6, 28.9, 28.3 ppm; HRMS (ESI): calcd for $C_{23}H_{25}F_3NO_4S^+$ [M + H^+] 468.1451, found 468.1453.

Synthesis of indole 9:[5] To a stirred solution of triflate **14** (46.7 mg, 0.1 mmol) in MeOH (1 mL) at room temperature were added Pd/C (5 mg, 10% wt/wt), magnesium metal (3 mg, 0.12 mmol) and ammonium acetate (7.8 mg, 0.1 mmol). The resulting mixture was stirred for 5 h before it was filtered through a short pad of celite. The filtrate was concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded **9** (27 mg, 85%) as a white solid.

3-((5,5-Dimethyltetrahydrofuran-2-yl)(phenyl)methyl)-1-methyl-1*H*-indole (9):

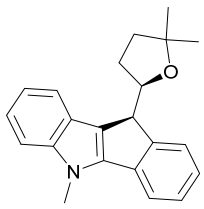


9

m.p. 108–110 °C; IR (film) ν_{max} 2967, 2929, 2863, 1467, 1366, 1143, 1052, 906, 739, 703 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (t, *J* = 6.3 Hz, 2 H), 7.26–7.18 (m, 4 H), 7.18–7.07 (m, 3 H), 6.92 (t, *J* = 7.4 Hz, 1 H), 4.61 (q, *J* = 7.1 Hz, 1 H), 4.28 (d, *J* = 7.1 Hz, 1 H), 3.77 (s, 3 H), 1.76 (dq, *J* = 12.4, 7.5 Hz, 2 H), 1.64 (dt, *J* = 12.0, 7.9 Hz, 1 H), 1.54–1.45 (m, 1 H), 1.27 (s, 3 H), 1.20 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.9, 136.9, 129.0(2C), 128.1, 128.0(2C), 126.9, 126.1, 121.2, 119.8, 118.4, 115.9, 108.8, 81.4, 81.0, 48.6, 38.3, 32.7, 30.7, 29.0, 28.2 ppm; HRMS (ESI): calcd for $C_{22}H_{26}NO^+$ [M + H^+] 320.2009, found 320.2012.

Synthesis of tetracycle 15:[6] To a stirred solution of triflate **14** (46.7 mg, 0.1 mmol) in *N*,*N*-dimethylacetamide (1 mL) were added $Pd(OAc)_2$ (2.0 mg, 0.01 mmol), Cy_3P (5.6 mg, 0.02 mmol) and Et_2NH (20.6 μL, 0.2 mmol). The resulting mixture was stirred at 100 °C for 5 h before it was cooled to room temperature and concentrated in *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 10:1) afforded tetracycle **15** (28 mg, 75%) as a white solid.

10-(5,5-Dimethyltetrahydrofuran-2-yl)-5-methyl-5,10-dihydroindeno[1,2-b]-indol

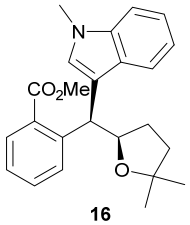


15

e (15): m.p. 120–122 °C; IR (film) ν_{max} 2961, 2926, 2856, 1462, 1261, 1134, 1049, 802, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 7.5 Hz, 1 H), 7.71 (d, *J* = 7.8 Hz, 1 H), 7.63 (d, *J* = 7.5 Hz, 1 H), 7.36 (t, *J* = 8.2 Hz, 2 H), 7.25–7.12 (m, 3 H), 4.76 (dt, *J* = 11.9, 6.0 Hz, 1 H), 4.21 (d, *J* = 5.3 Hz, 1 H), 4.06 (s, 3 H), 1.64–1.55 (m, 2 H), 1.51–1.42 (m, 1 H), 1.40 (s, 3 H), 1.30 (s, 3 H), 1.16–1.05 ppm (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.9, 144.1, 142.0, 136.1, 127.1(2C), 124.5, 124.1, 122.04, 121.2, 119.6(2C), 117.5, 109.7, 81.1, 79.8, 46.9, 38.5, 31.1, 28.7, 27.6, 27.5 ppm; HRMS (ESI): calcd for $C_{22}H_{24}NO^+$ [M + H^+] 318.1852, found 318.1853.

Synthesis of ester 16:[7] To a stirred solution of triflate **14** (46.7 mg, 0.1 mmol) in MeOH/DMSO (1.5 mL, 1:2) were added $Pd(OAc)_2$ (2.0 mg, 0.01 mmol), dppp (4.1 mg, 0.01 mmol) and Et_3N (27.7μL, 0.2 mmol). The resulting mixture was stirred under CO atmosphere at 70 °C for 12 h before it was cooled to room temperature and concentrated in *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 10:1) afforded ester **16** (31 mg, 81%) as a while solid.

Methyl 2-((5,5-dimethyltetrahydrofuran-2-yl)(1-methyl-1*H*-indol-3-yl)methyl)-

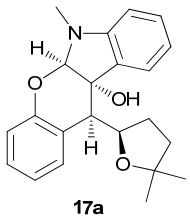


16

benzoate (16): m.p. 93–95 °C; IR (film) ν_{max} 2929, 2868, 1750, 1373, 1237, 1134, 879, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.74 (d, *J* = 7.6 Hz, 1 H), 7.36 (dd, *J* = 15.0, 7.8 Hz, 2 H), 7.22 (dq, *J* = 14.5, 7.5 Hz, 4 H), 7.12 (t, *J* = 7.5 Hz, 1 H), 6.93 (t, *J* = 7.4 Hz, 1 H), 5.48 (d, *J* = 6.7 Hz, 1 H), 4.59 (q, *J* = 6.9 Hz, 1 H), 3.92 (s, 3 H), 3.77 (s, 3 H), 1.85–1.70 (m, 2 H), 1.69–1.55 (m, 1 H), 1.55–1.45 (m, 1 H), 1.25 (s, 3 H), 1.17 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.3, 143.6, 136.8, 131.2(2C), 129.9, 129.5, 128.2, 127.3, 125.7, 121.2, 119.9, 118.5, 115.9, 108.7, 81.7, 81.1, 52.1, 42.4, 38.3, 32.8, 30.0, 28.8, 28.2 ppm; HRMS (ESI): calcd for $C_{24}H_{28}NO_3^+$ [M + H^+] 378.2064, found 378.2060.

Synthesis of tetracycles 17a and 17b:[8] To a stirred solution of indole **2a** (33.5 mg, 0.1 mmol) in CH_2Cl_2 (2 mL) at –78 °C was added a solution of DMDO in acetone (0.06 M, 3.3 mL, 0.2 mmol). The resulting mixture was stirred for 1 h before it was diluted with CH_2Cl_2 (5 mL) and quenched with H_2O (5 mL). The layers were separated, and the organic layer was washed with brine (10 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 80:1) afforded tetracycles **17a** and **17b** (78%, dr = 1:1) as colorless oils.

(5a,10b)-11-(5,5-Dimethyltetrahydrofuran-2-yl)-6-methyl-5a,6,10b,11-tetrahy-dr

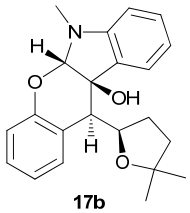


17a

ochromeno[2,3-*b*]indol-10b-ol (17a): IR (film) ν_{max} 2971, 2885, 1657, 1510, 1359, 1246, 1055, 890, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 7.3 Hz, 1 H), 7.10 (t, *J* = 7.4 Hz, 1 H), 6.98

(dd, *J* = 13.1, 7.7 Hz, 2 H), 6.86 (t, *J* = 7.5 Hz, 1 H), 6.78 (d, *J* = 7.5 Hz, 1 H), 6.57 (t, *J* = 7.4 Hz, 1 H), 6.15 (d, *J* = 7.8 Hz, 1 H), 5.88 (s, 1 H), 5.47 (s, 1 H), 4.99–4.82 (m, 1 H), 3.20 (d, *J* = 10.5 Hz, 1 H), 2.86 (s, 3 H), 2.61 (td, *J* = 11.5, 4.8 Hz, 1 H), 1.93 (s, 3 H), 1.48 (s, 3 H), 1.45 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.5, 151.3, 129.3, 128.8, 127.4, 127.2, 125.3, 125.1, 122.8, 118.7, 116.9, 104.7, 103.8, 85.8, 82.6, 77.3, 48.5, 38.0, 33.0, 30.3, 28.8, 27.3 ppm; HRMS (ESI): calcd for $C_{22}H_{26}NO_3^+$ [M + H^+] 352.1907, found 352.1912.

(5a,10b)-11-(5,5-Dimethyltetrahydrofuran-2-yl)-6-methyl-5a,6,10b,11-tetrahy-dr



17b

ochromeno[2,3-*b*]indol-10b-ol (17b): IR (film) ν_{max} 2979, 2897, 1657, 1599, 1501, 1344, 1242, 1151, 883, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.10 (d, *J* = 7.2 Hz, 1 H), 6.98 (dt, *J* = 12.6, 7.5 Hz, 2 H), 6.87 (d, *J* = 6.7 Hz, 1 H), 6.81 (d, *J* = 7.9 Hz, 1 H), 6.75 (t, *J* = 7.3 Hz, 1 H), 6.56 (t, *J* = 7.3 Hz, 1 H), 6.50 (s, 1 H), 6.23 (d, *J* = 7.8 Hz, 1 H), 5.57 (s, 1 H), 4.59 (dd, *J* = 14.3, 8.5 Hz, 1 H), 3.27 (d, *J* = 9.8 Hz, 1 H), 2.97 (s, 3 H), 1.89–1.61 (m, 4 H), 1.42 (s, 3 H), 1.33 ppm (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.9, 150.9, 131.3, 129.4, 129.2, 128.2, 126.7, 122.6, 122.3, 117.9, 117.6, 105.2, 101.2, 83.5, 83.2, 80.1, 51.2, 37.2, 32.6, 30.0, 29.3, 28.5 ppm; HRMS (ESI): calcd for $C_{22}H_{26}NO_3^+$ [M + H^+] 352.1907, found 352.1910.

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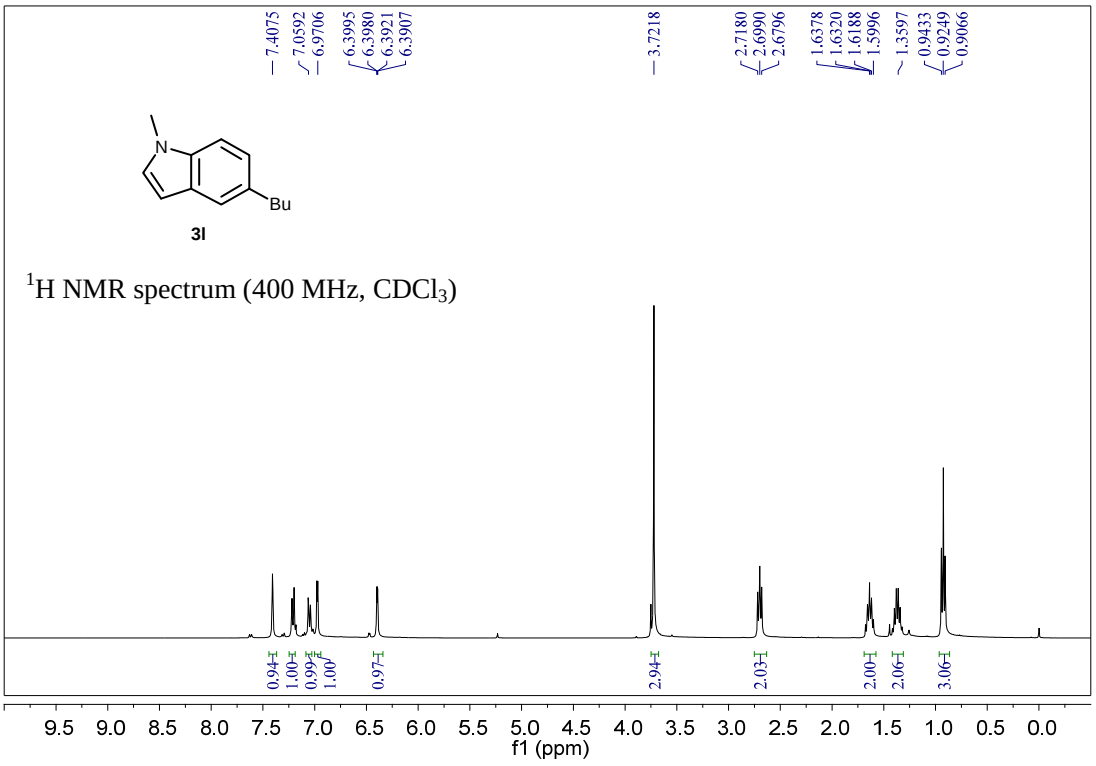
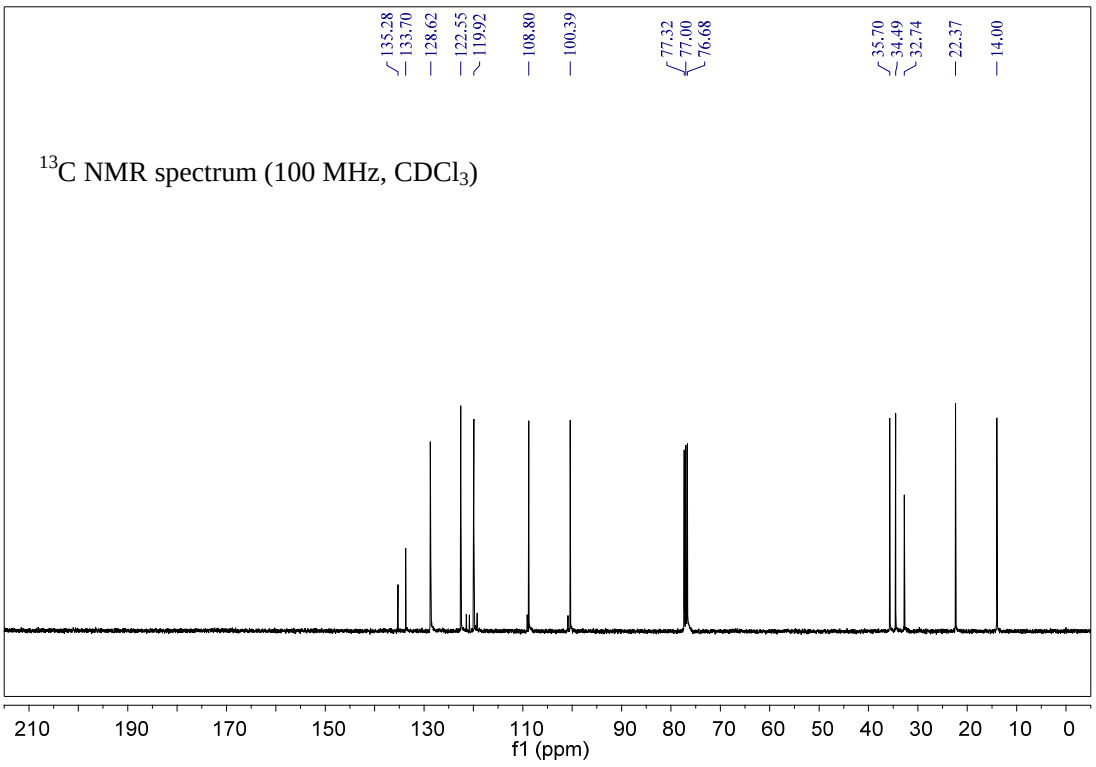
IV) ^{1}H and ^{13}C NMR Spectra of Compounds

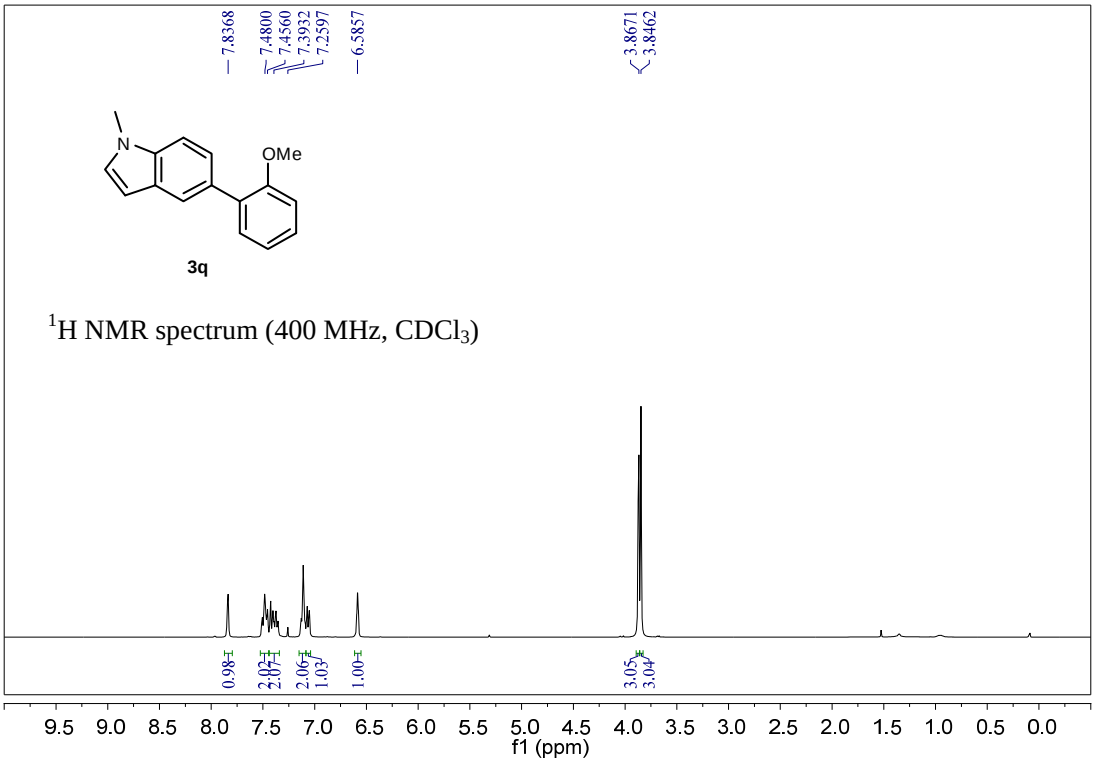


3l

^{1}H NMR spectrum (400 MHz, $CDCl_3$)

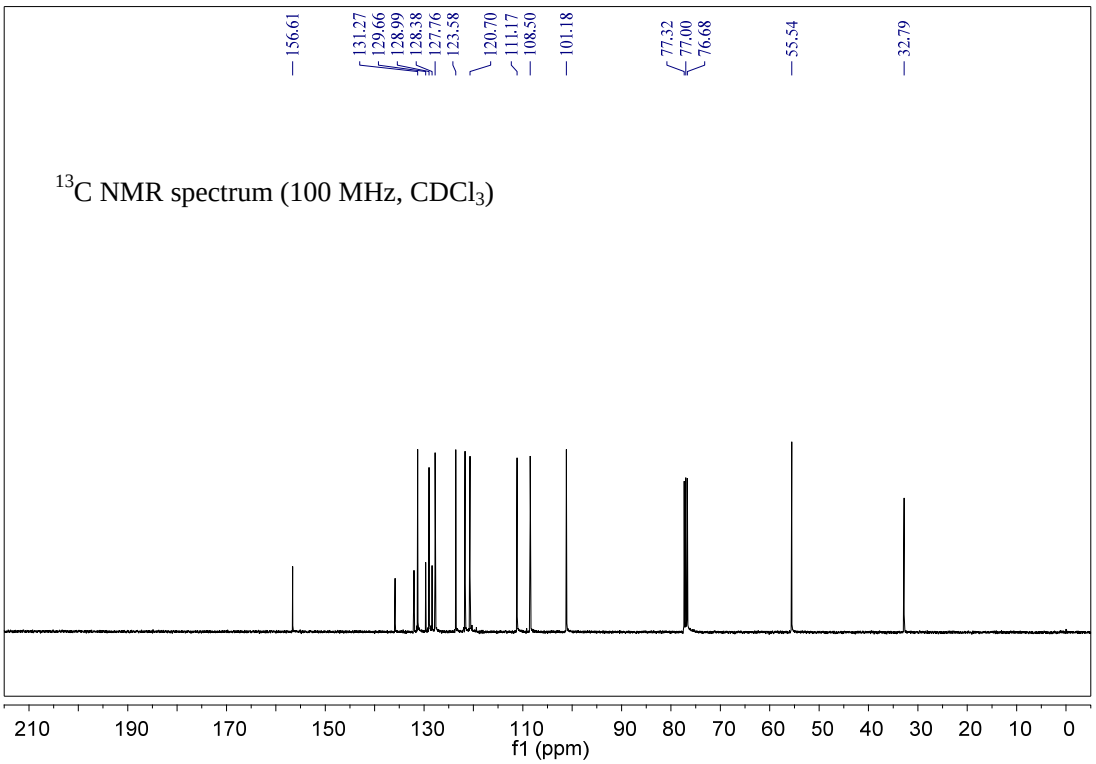


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

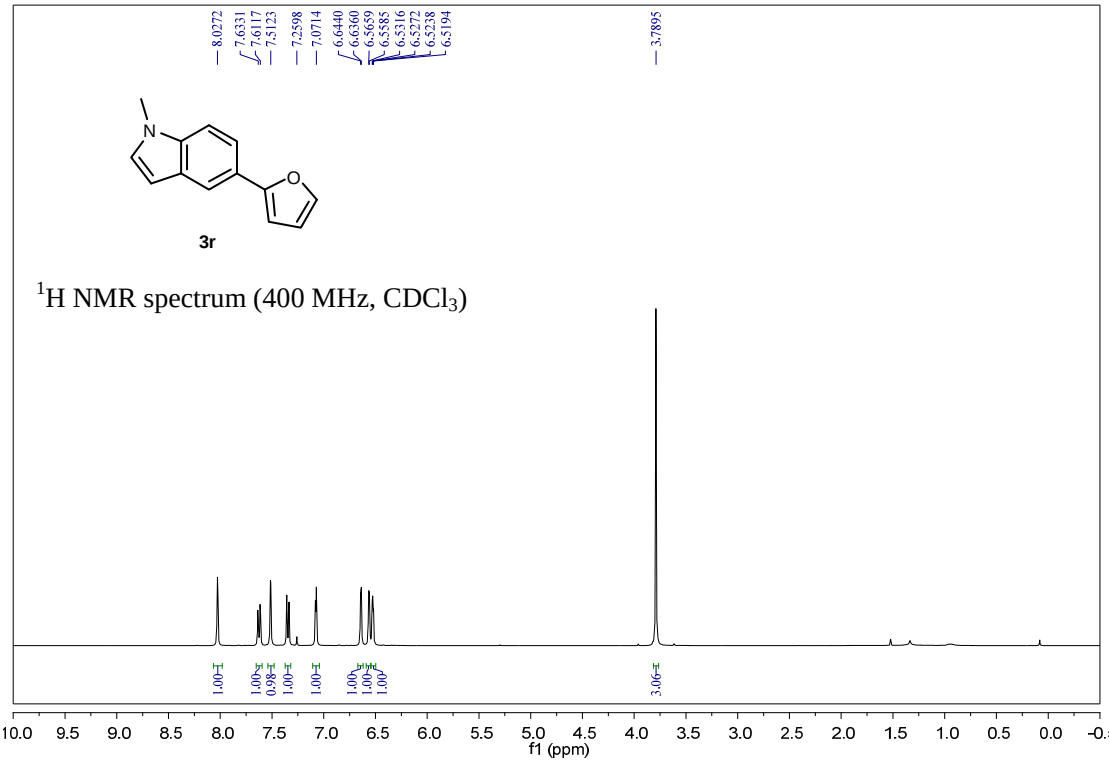


3q

^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)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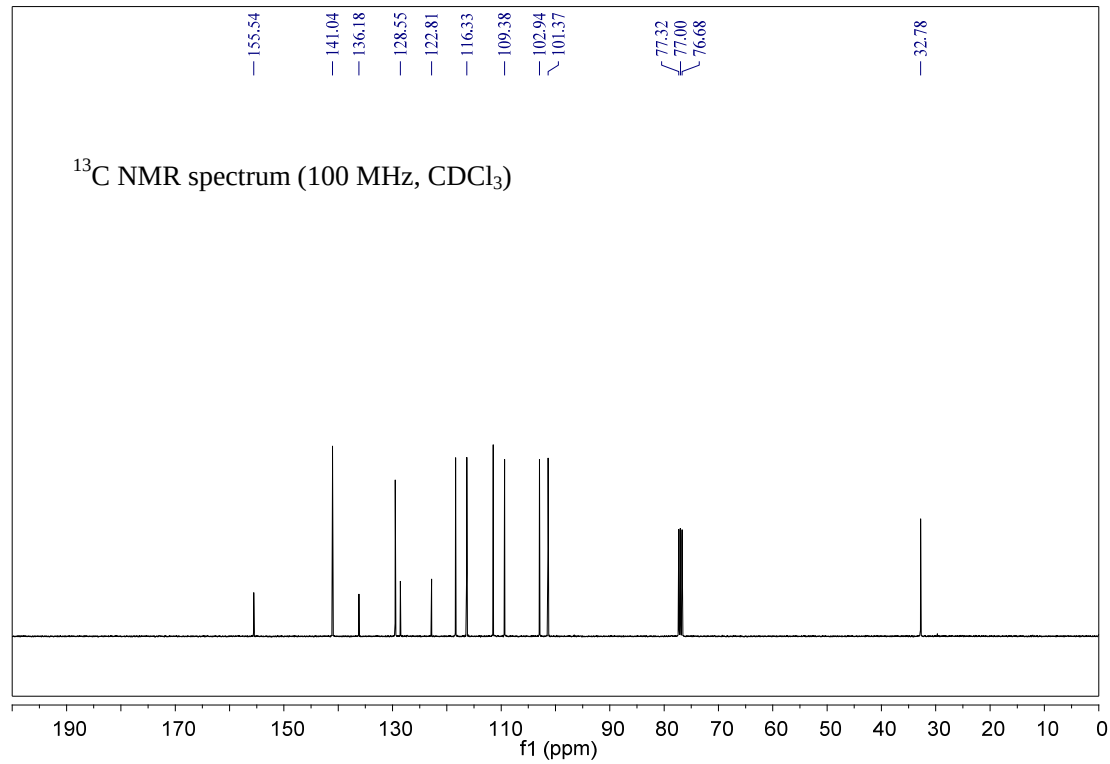
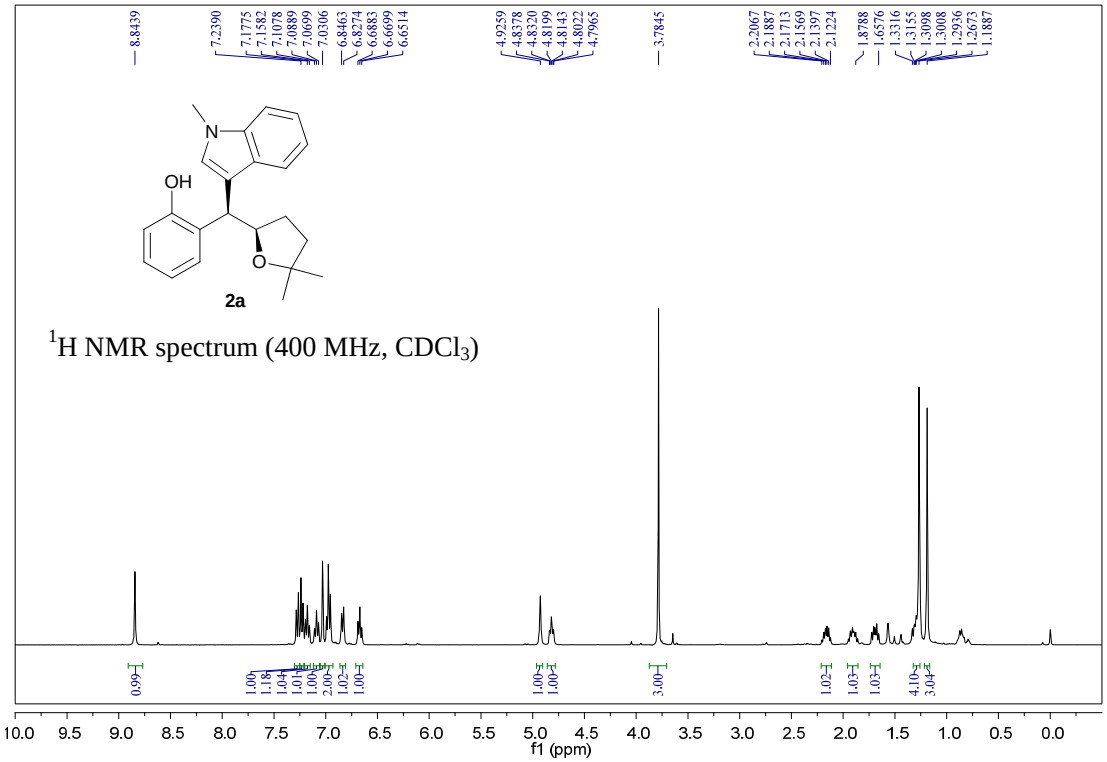
7.6331
7.6117
7.5123
7.2598
7.0714
6.6440
6.6360
6.5659
6.5585
6.5316
6.5272
6.5238
6.5194
3.7895
N
O
3r
1H NMR spectrum (400 MHz, CDCl3)
1.00
1.00
0.98
1.00
1.00
1.00
1.00
1.00
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


155.54
141.04
136.18
128.55
122.81
116.33
109.38
102.94
101.37
77.32
77.00
76.68
32.78
13C NMR spectrum (100 MHz, CDCl3)
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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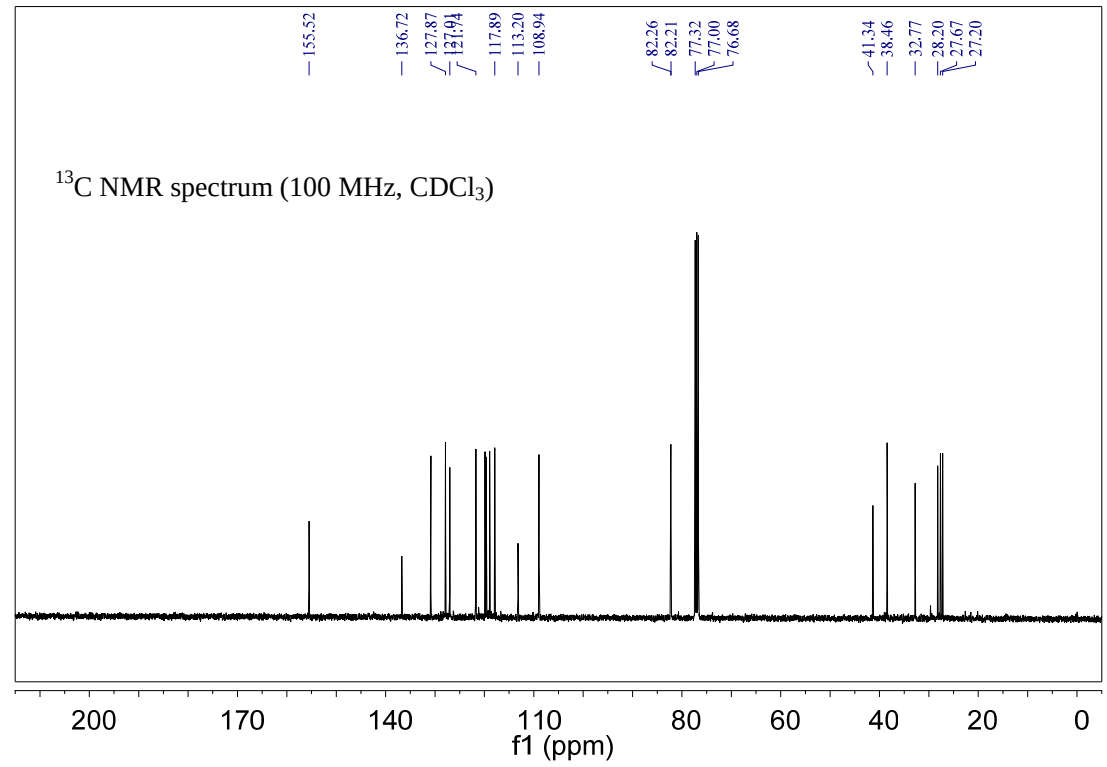
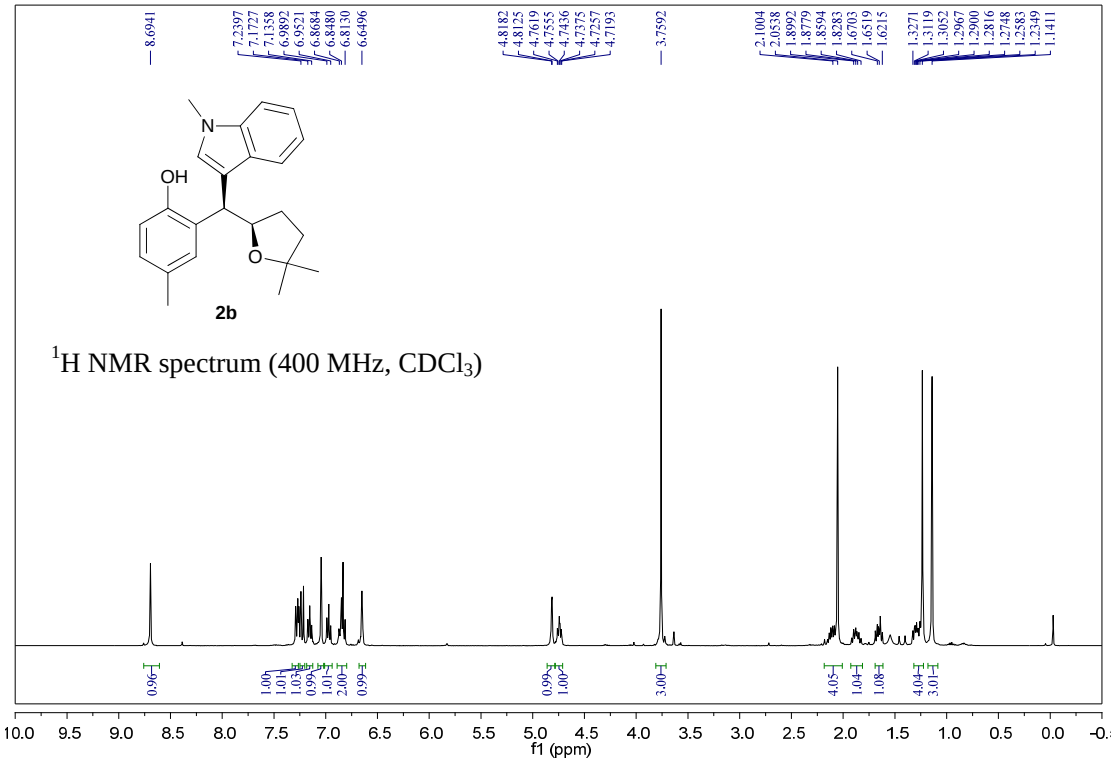
7.1775
7.1582
7.1078
7.0889
7.0699
7.0306
6.8463
6.8274
6.6883
6.6699
6.6514
4.9259
4.8378
4.8320
4.8199
4.8143
4.8022
4.7965
3.7845
2.2067
2.1887
2.1713
2.1569
2.1397
2.1224
1.8788
1.6576
1.3316
1.3155
1.3098
1.3008
1.2936
1.2673
1.1887
N
OH
O
2a
1H NMR spectrum (400 MHz, CDCl3)
0.99
1.00
1.18
1.04
1.01
1.00
2.00
1.02
1.00
1.00
1.00
3.00
1.02
1.03
1.03
4.10
3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


155.52
136.72
127.87
127.94
121.91
117.89
113.20
108.94
82.26
82.21
77.32
77.00
76.68
41.34
38.46
32.77
28.20
27.67
27.20
13C NMR spectrum (100 MHz, CDCl3)
200 170 140 110 80 60 40 20 0
f1 (ppm)


8.6941
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4.8182
4.8125
4.7619
4.7555
4.7436
4.7375
4.7257
4.7193
3.7592
2.1004
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1.8992
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1.8594
1.8283
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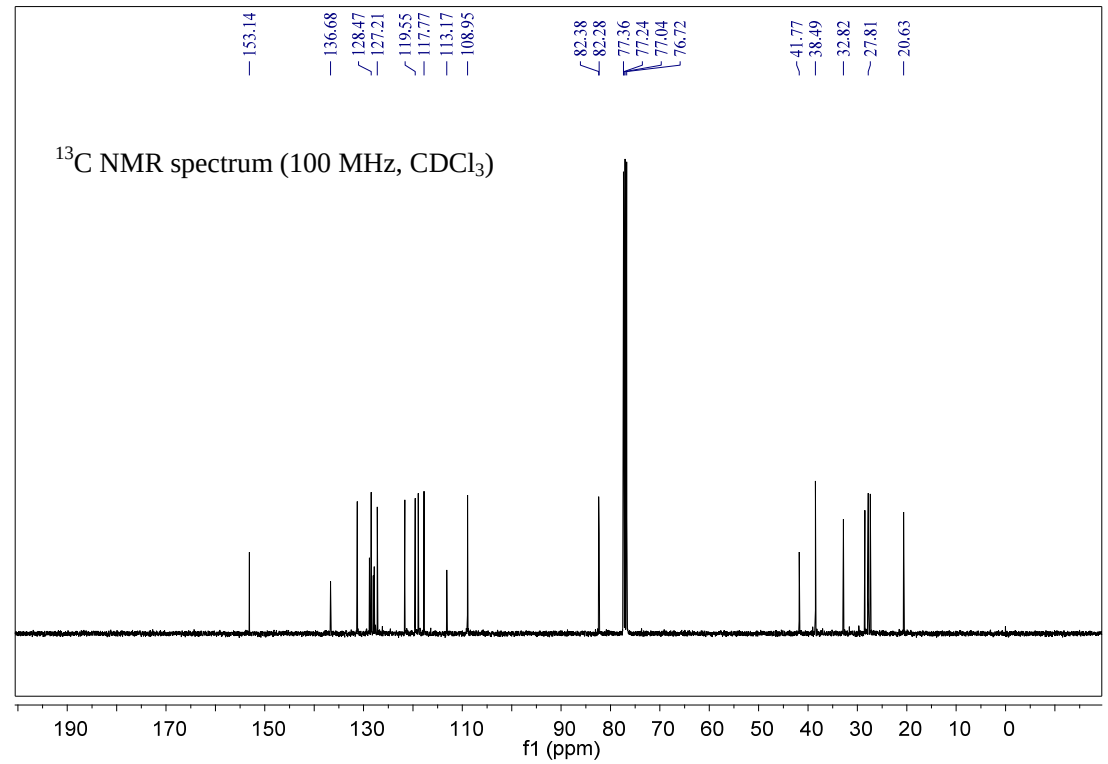
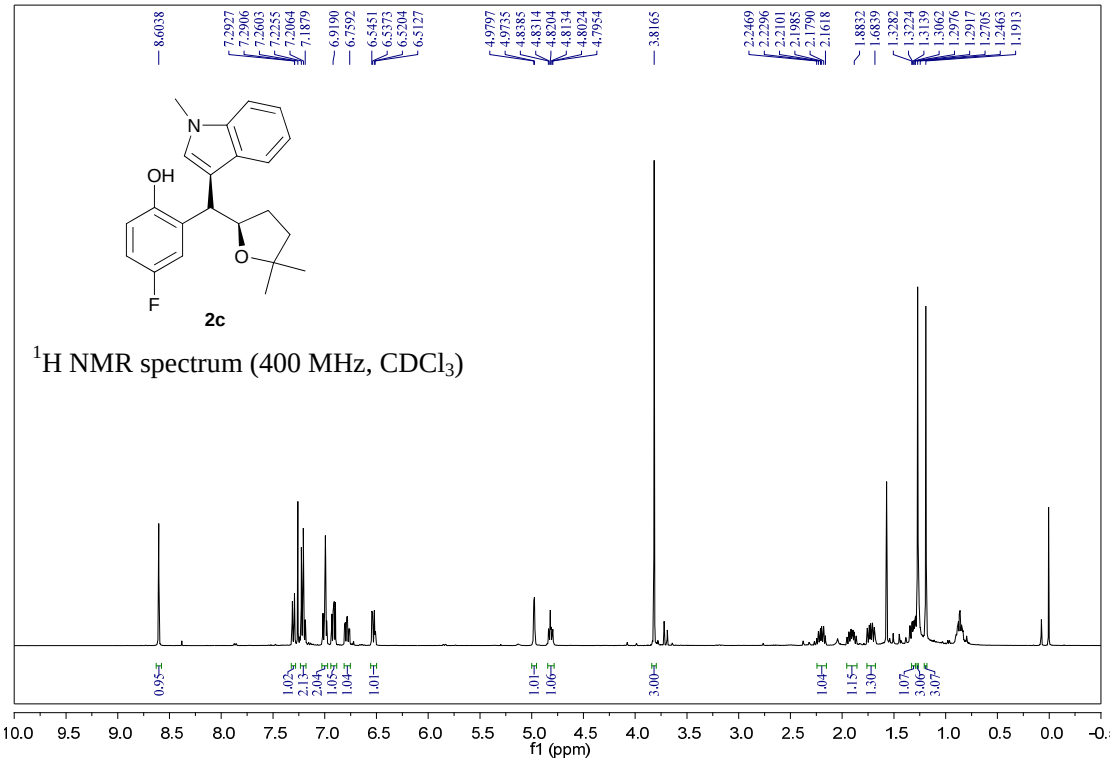
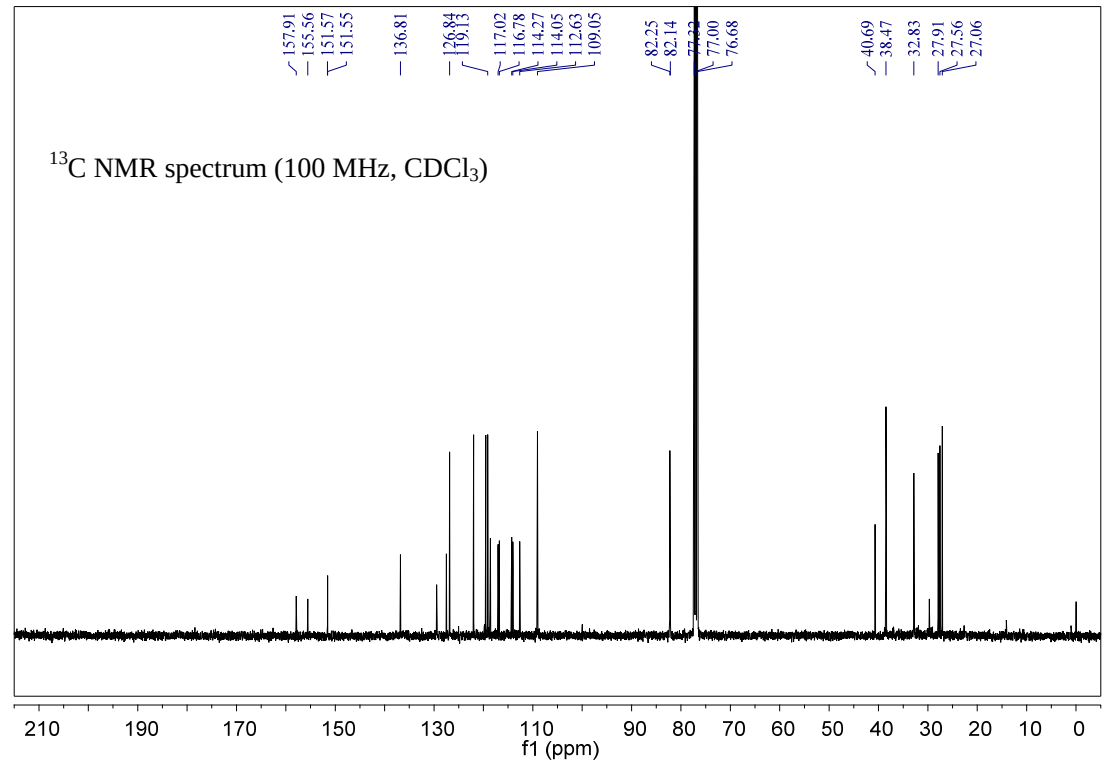
1.3052
1.2967
1.2900
1.2816
1.2748
1.2583
1.2349
1.1411
N
OH
O
2b
1H NMR spectrum (400 MHz, CDCl3)
0.96
1.00
1.01
1.03
0.99
1.01
2.00
0.99
0.99
1.00
3.00
4.05
1.04
1.08
4.04
3.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

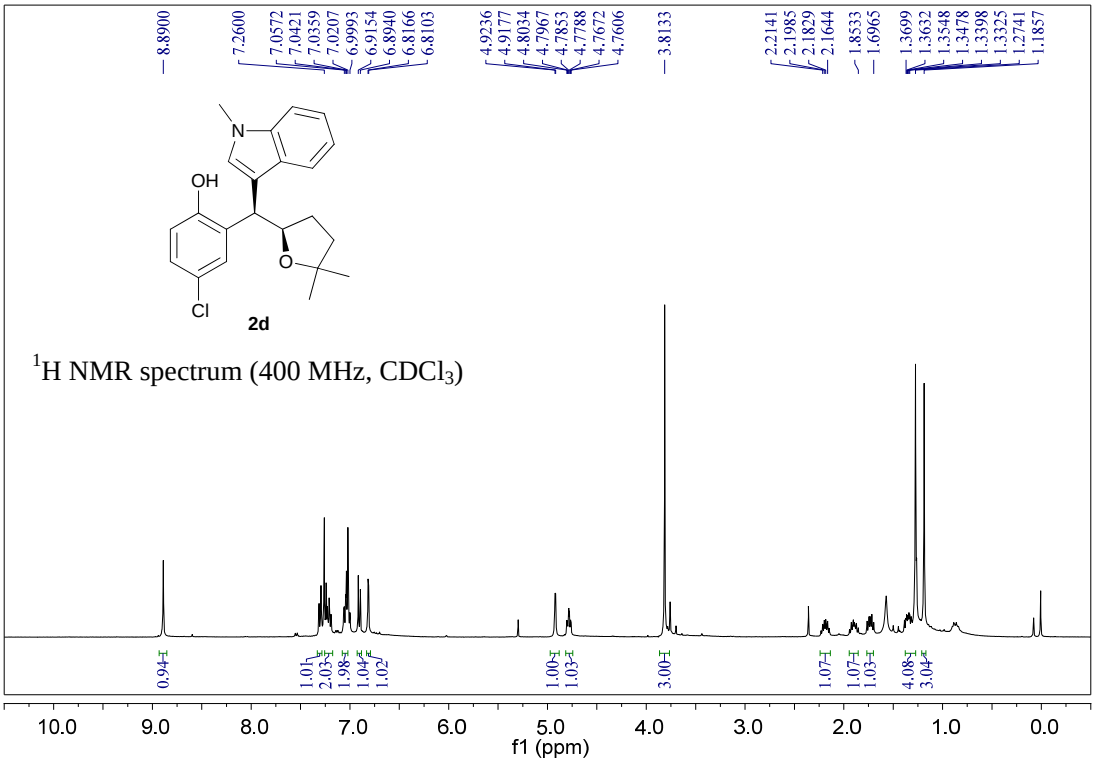

153.14
136.68
128.47
127.21
119.55
117.77
113.17
108.95
82.38
82.28
77.36
77.24
77.04
76.72
41.77
38.49
32.82
27.81
20.63
13C NMR spectrum (100 MHz, CDCl3)
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)



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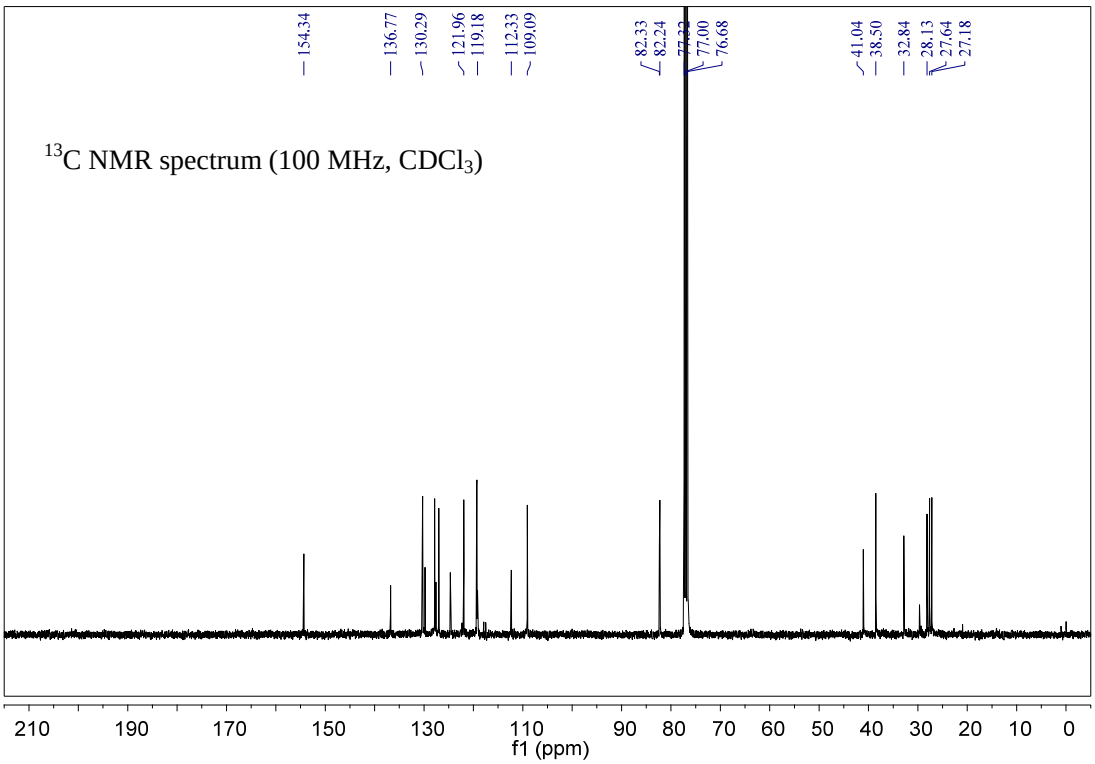

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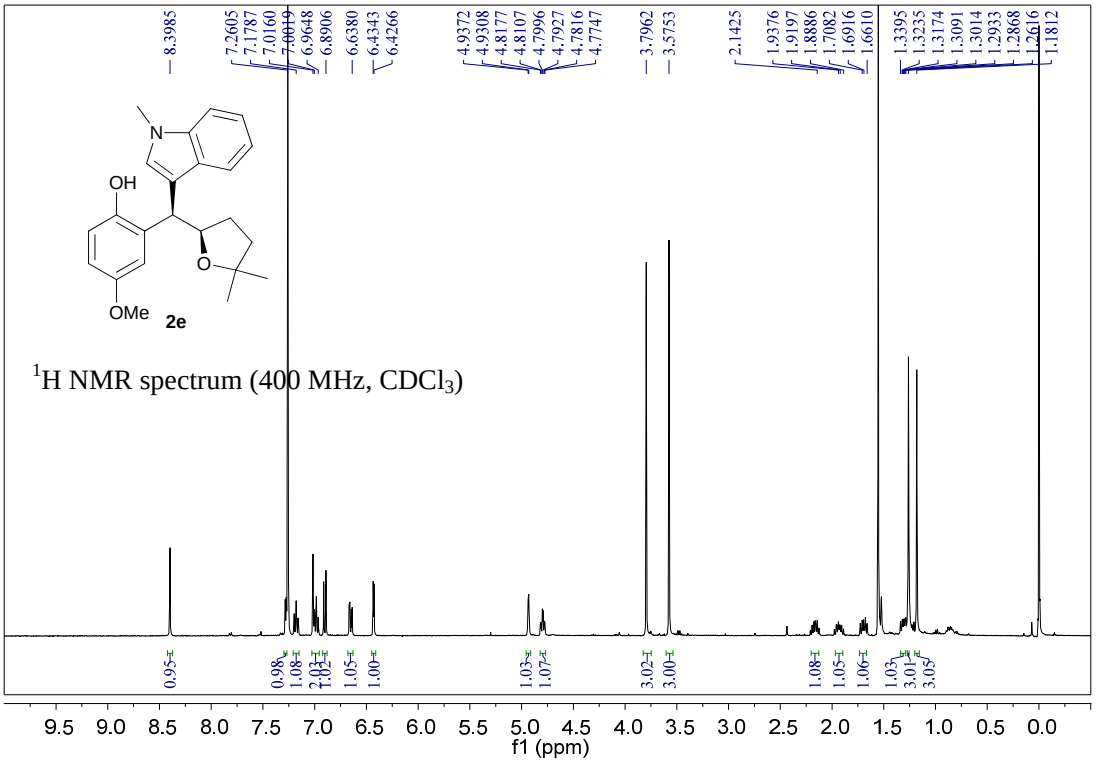
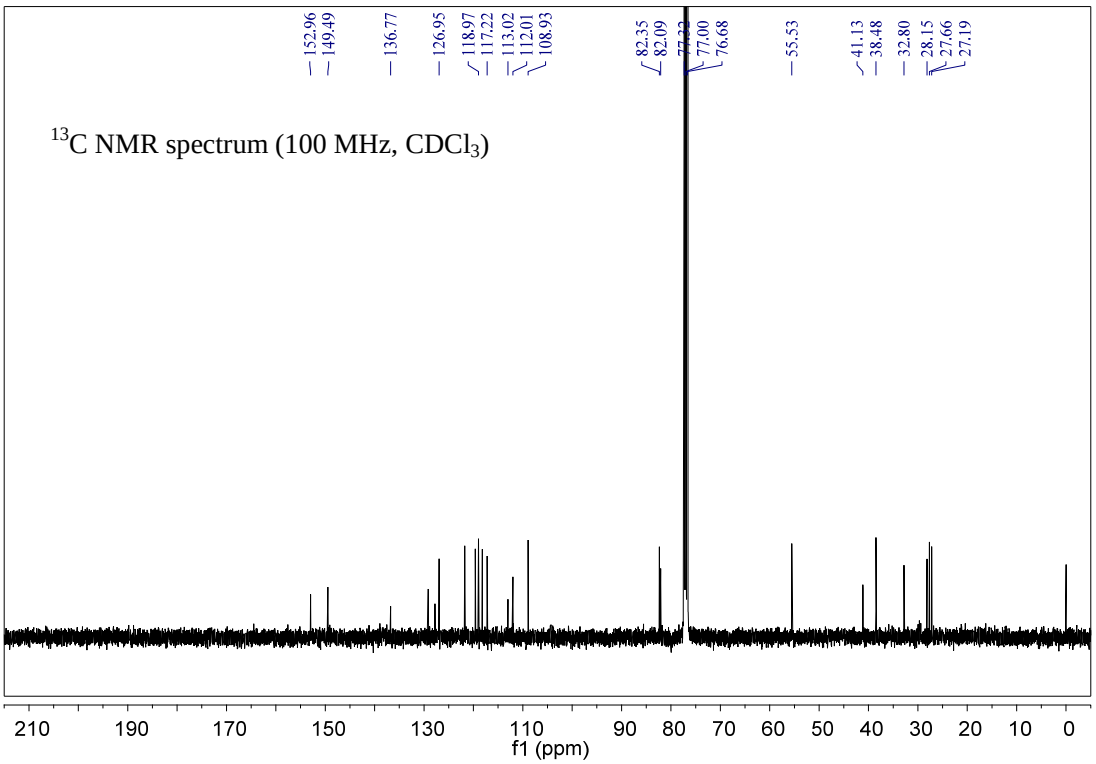
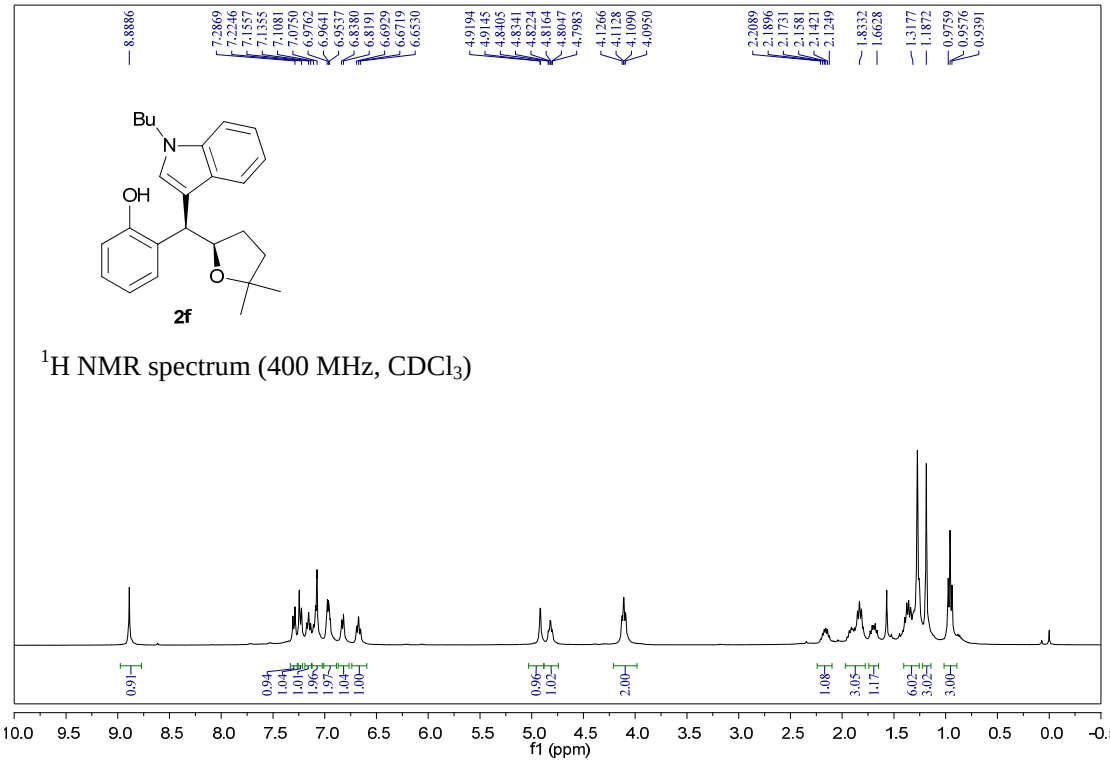


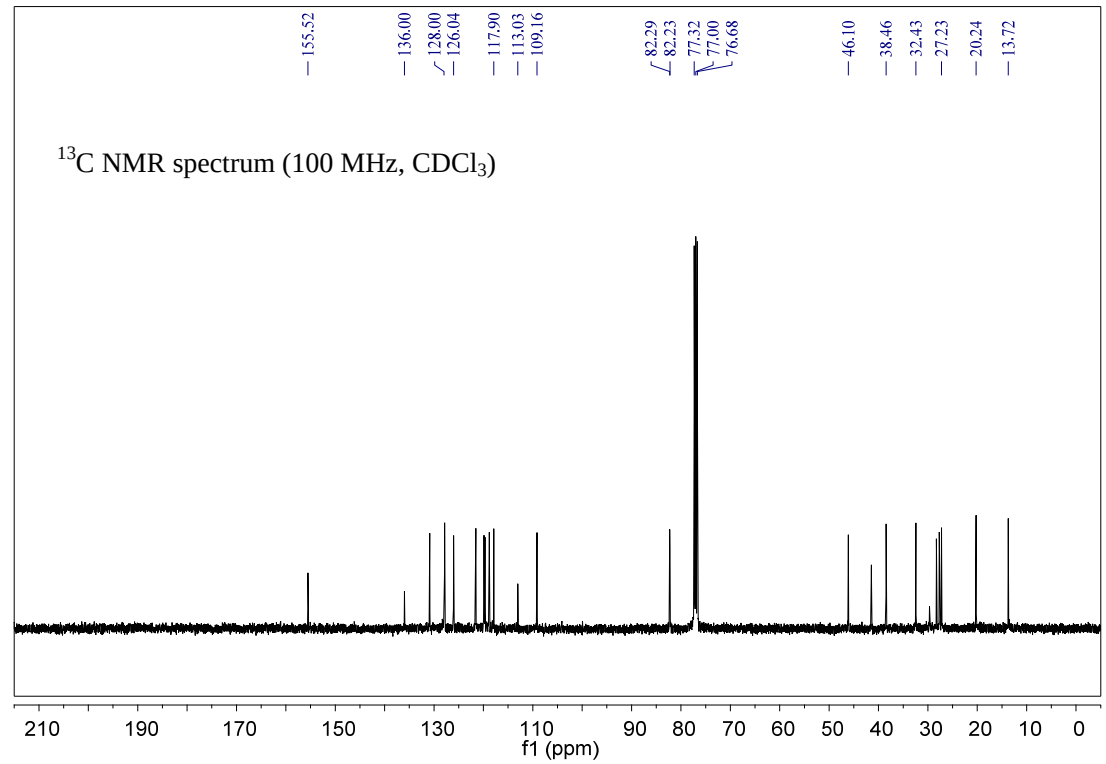
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



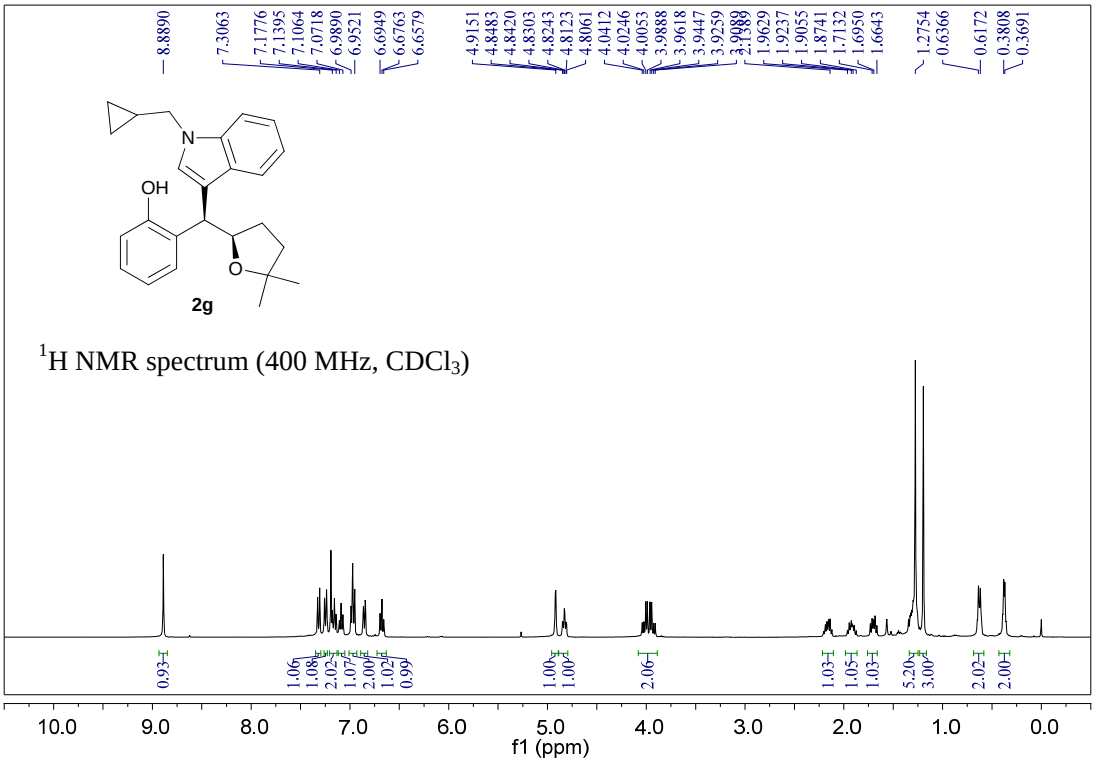
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



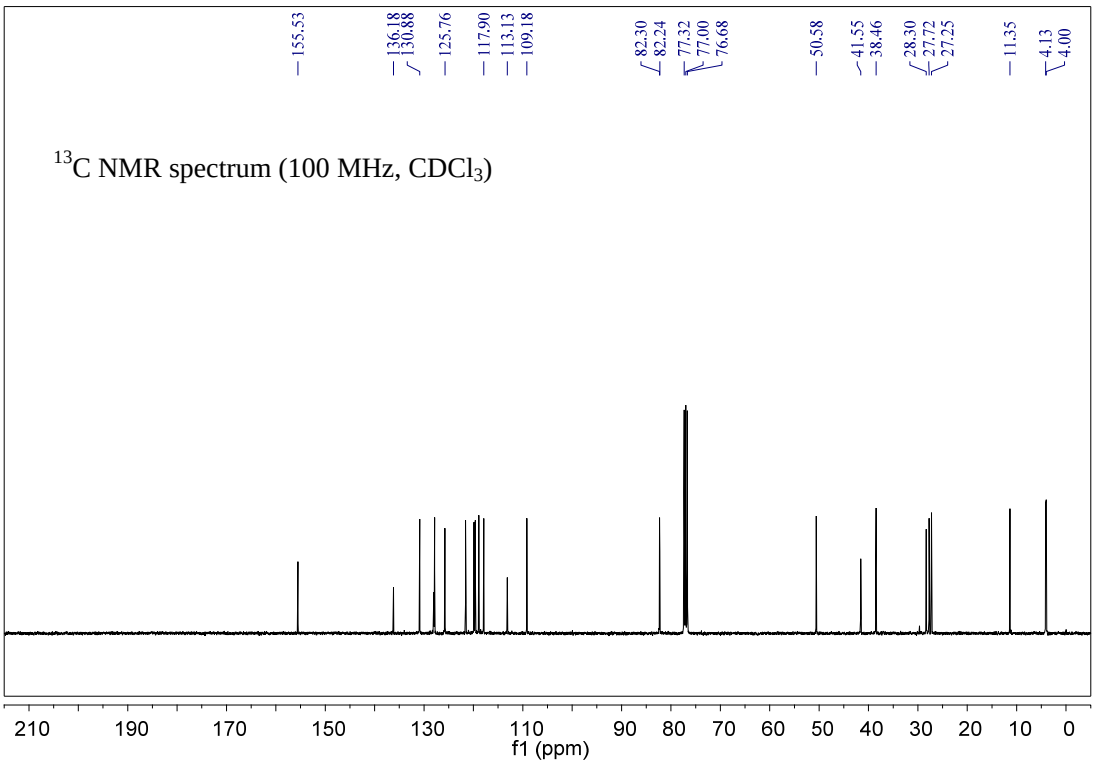
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



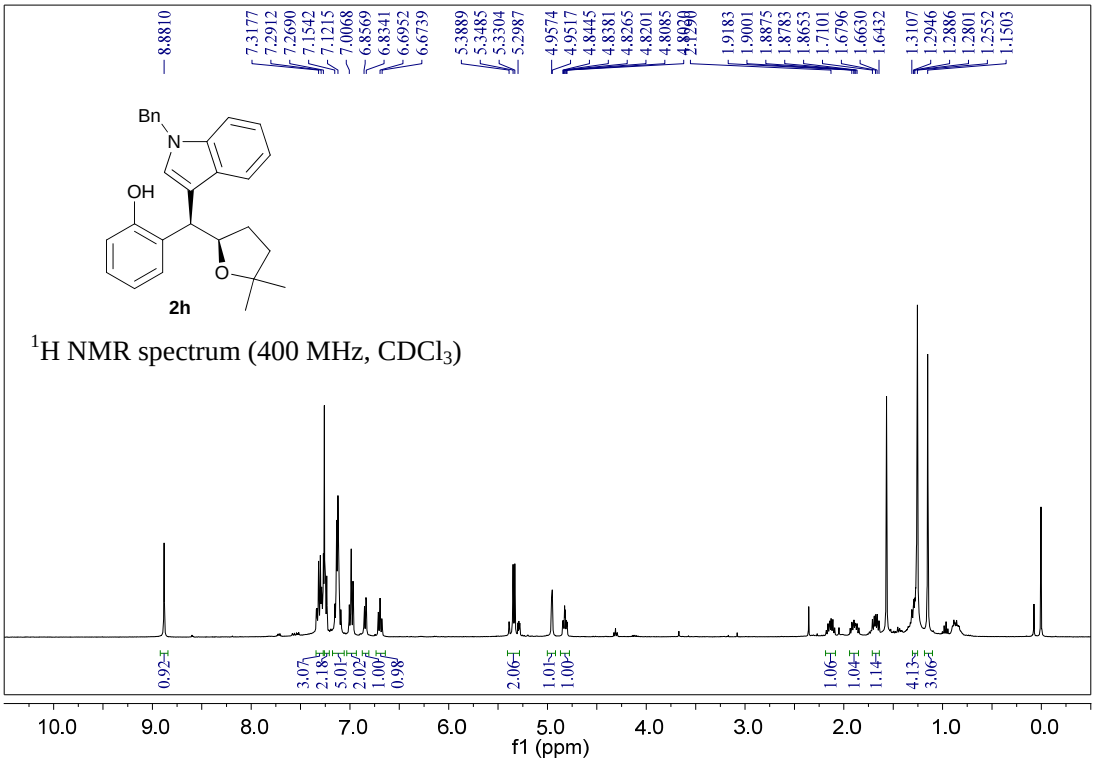
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



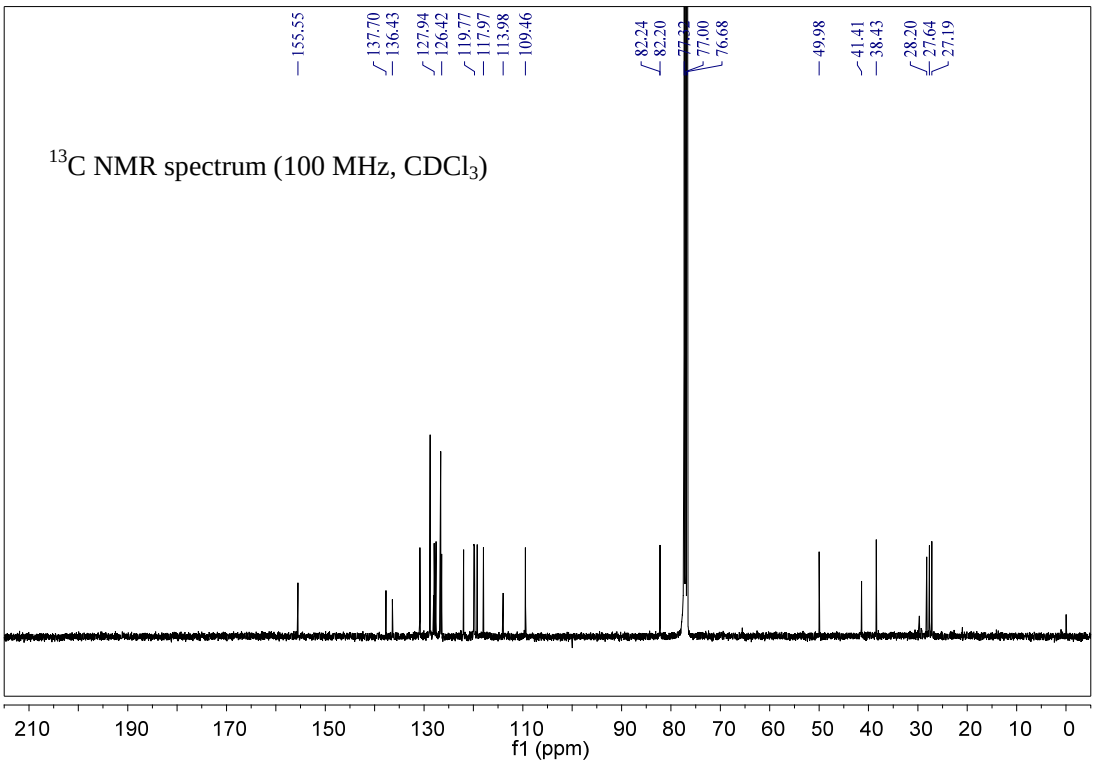
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



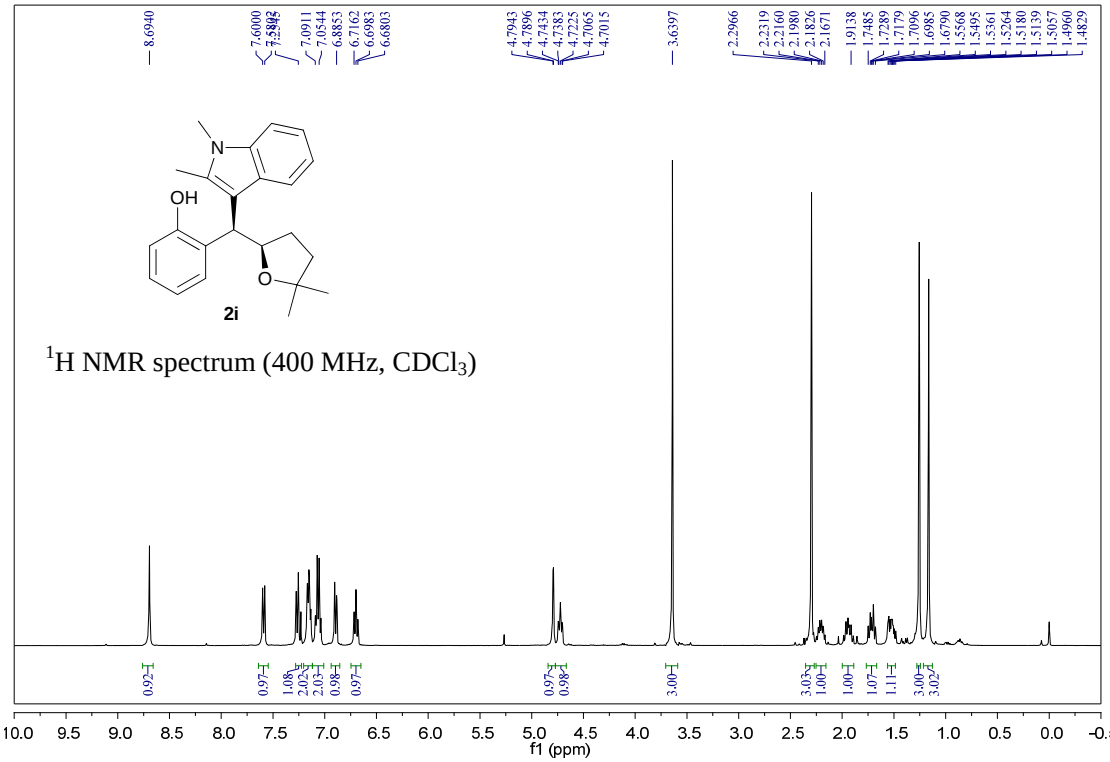
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



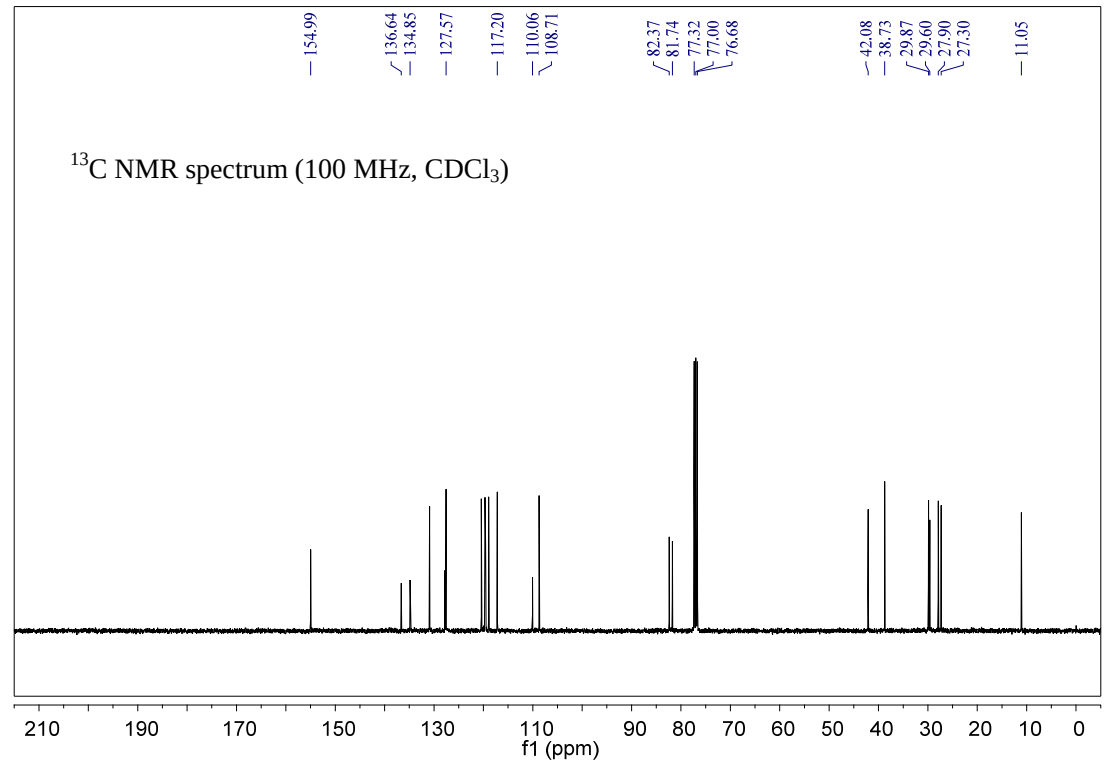
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



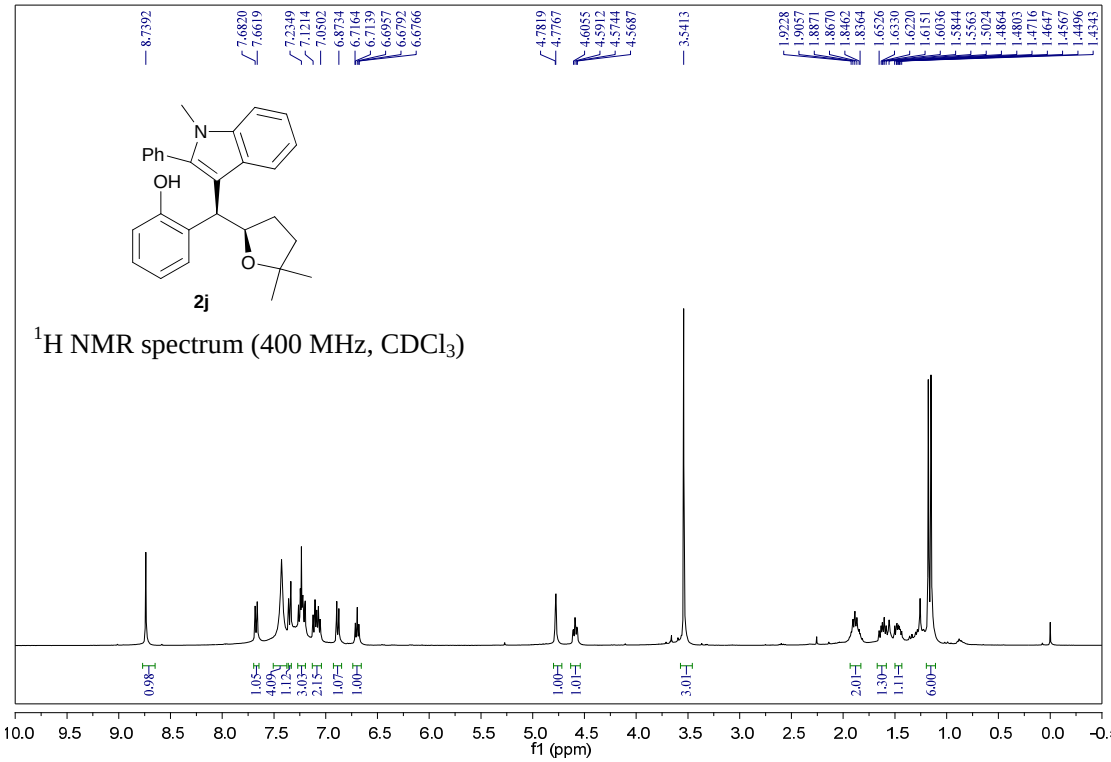
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



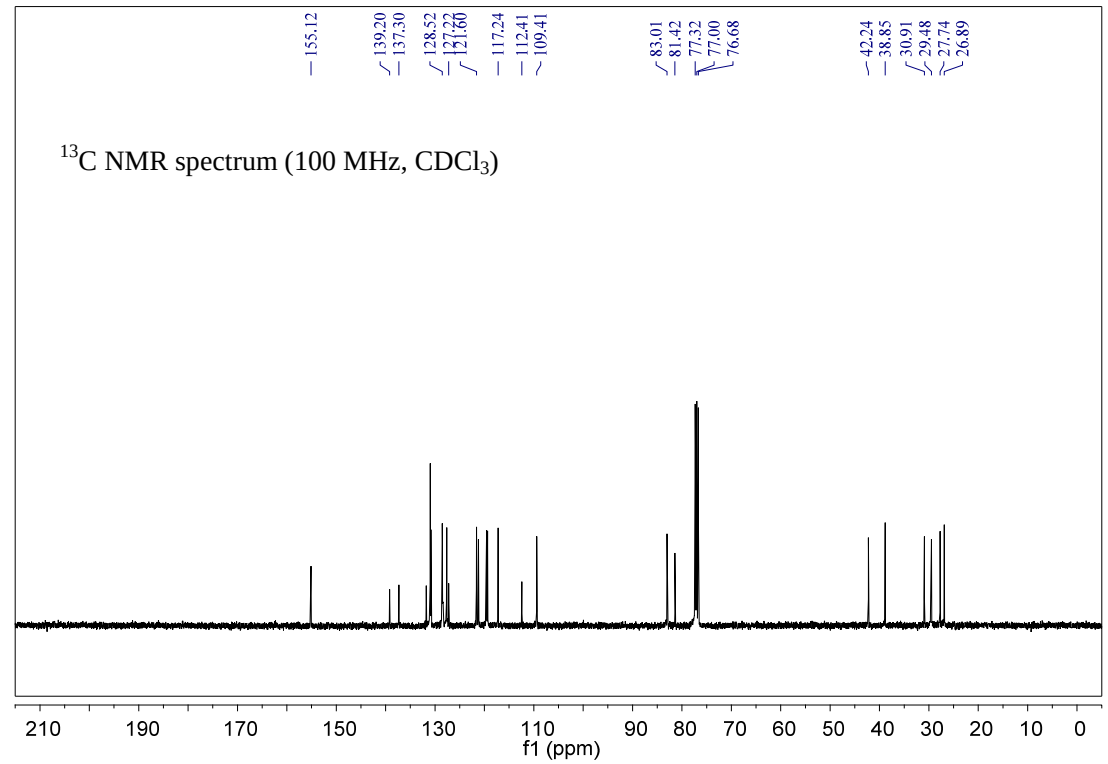
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



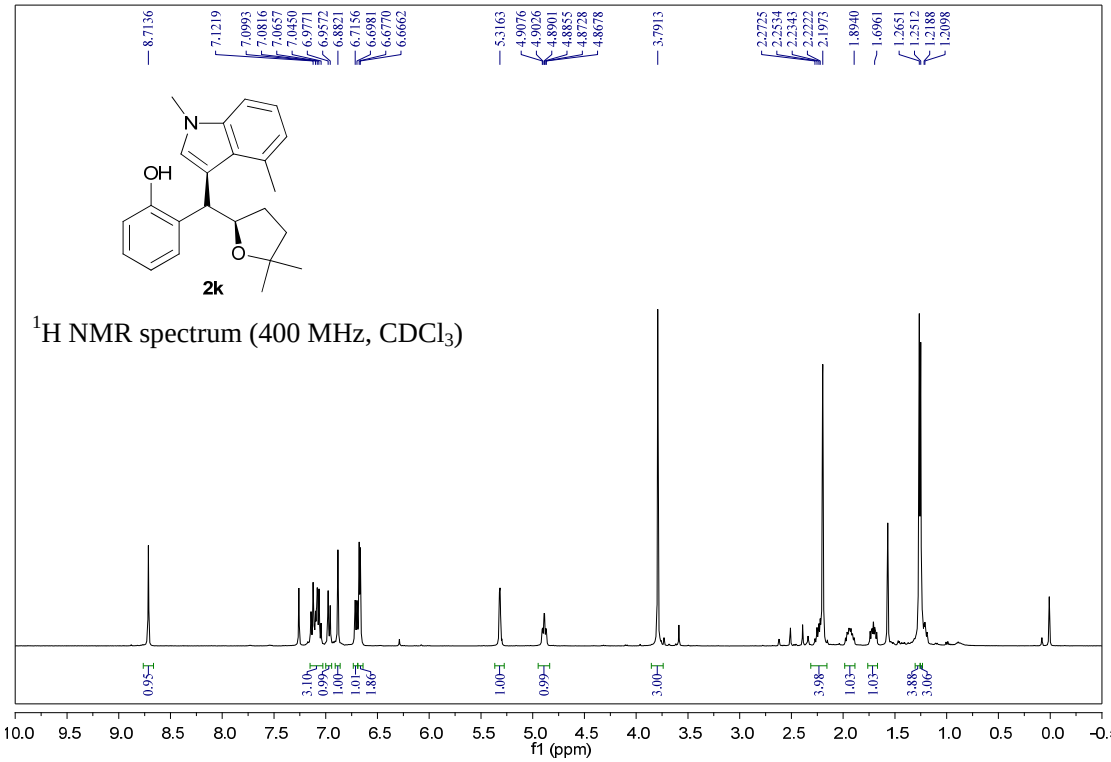
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



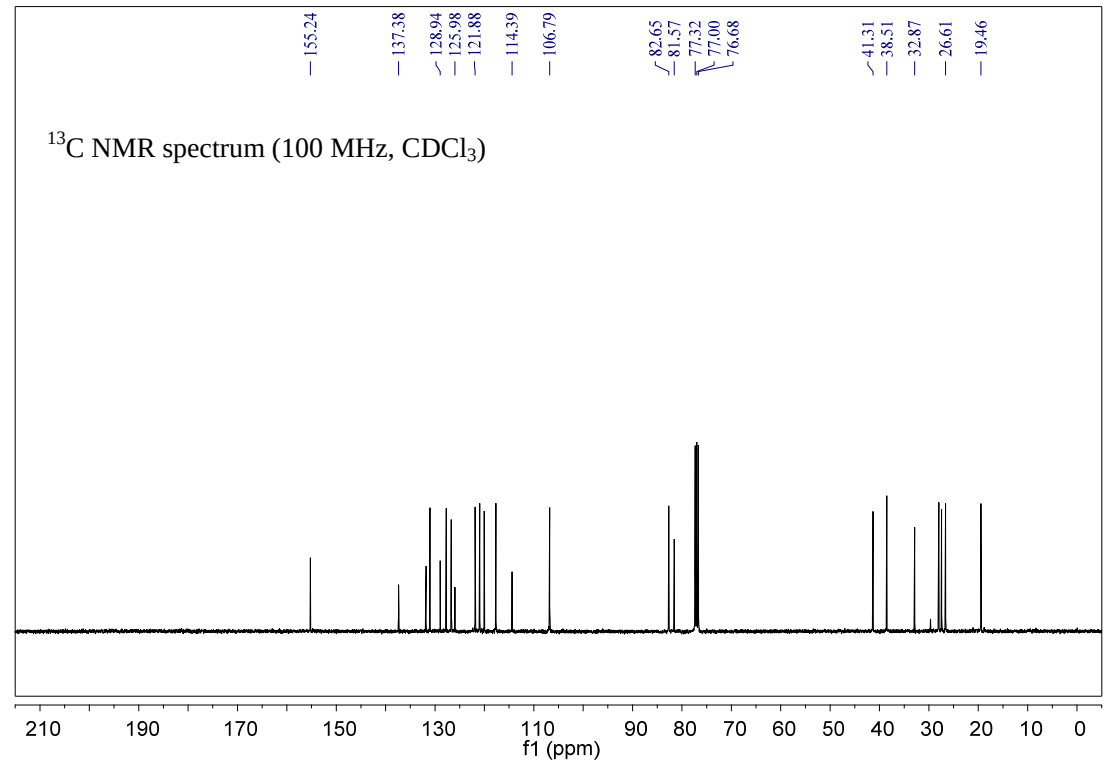
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



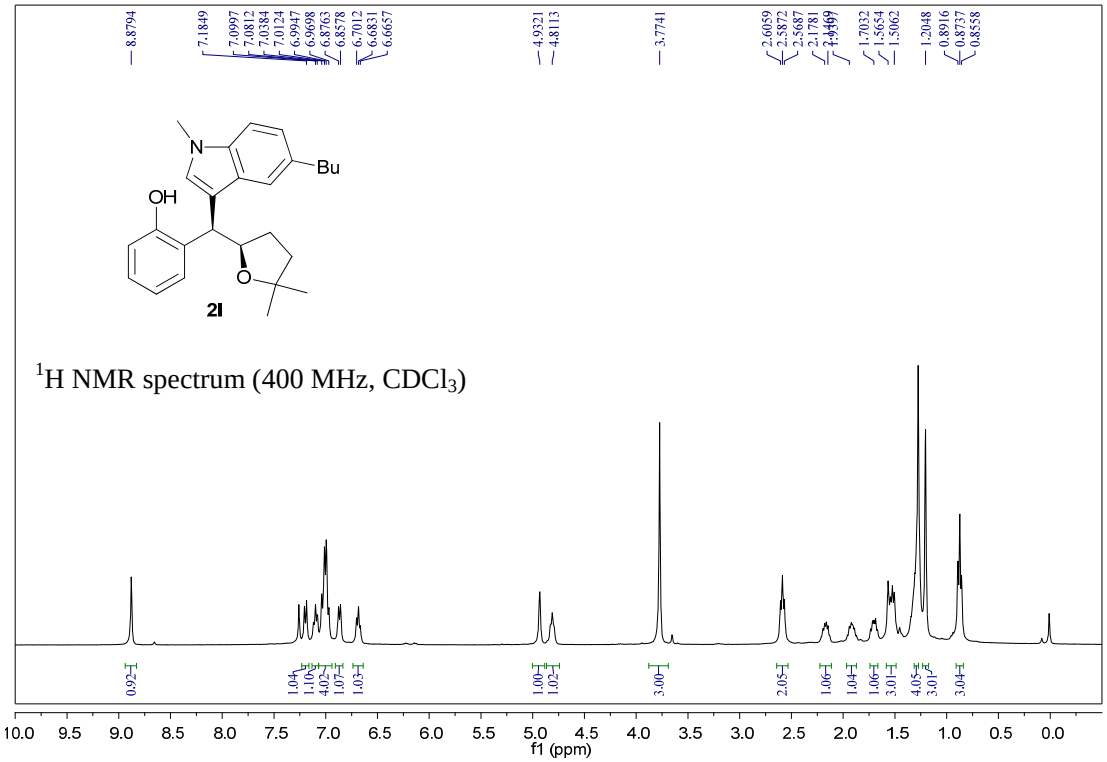
^{13}C NMR spectrum (100 MHz, $CDCl_3$)

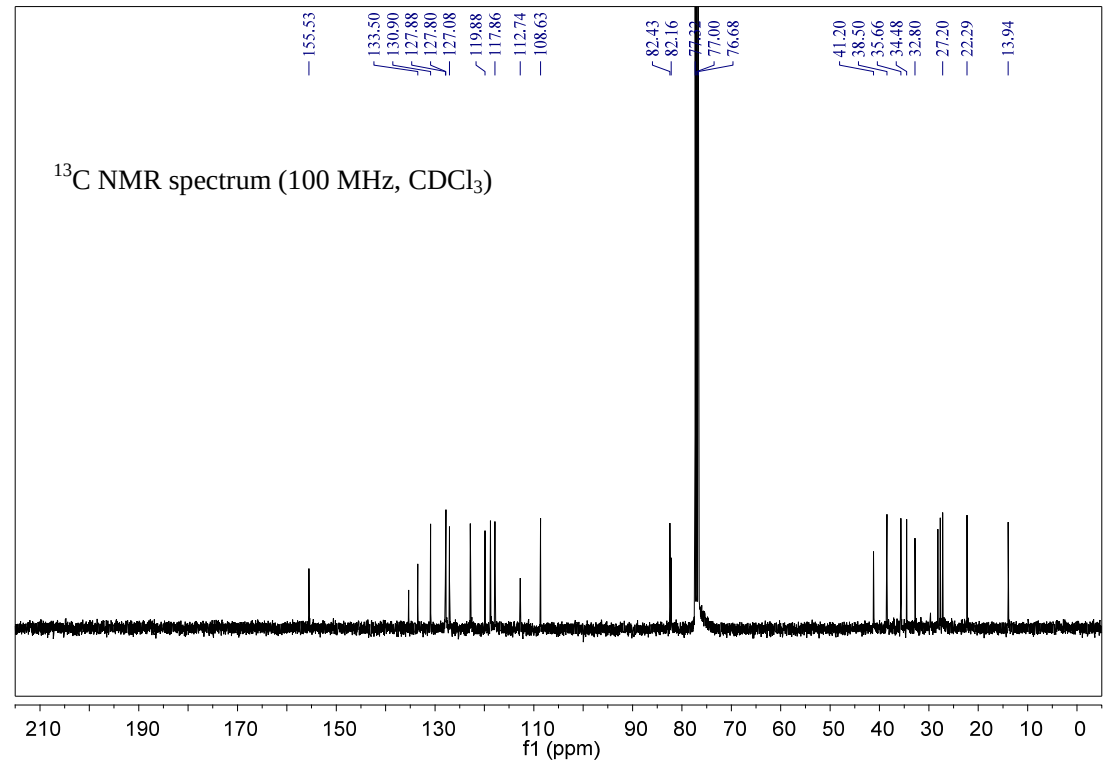


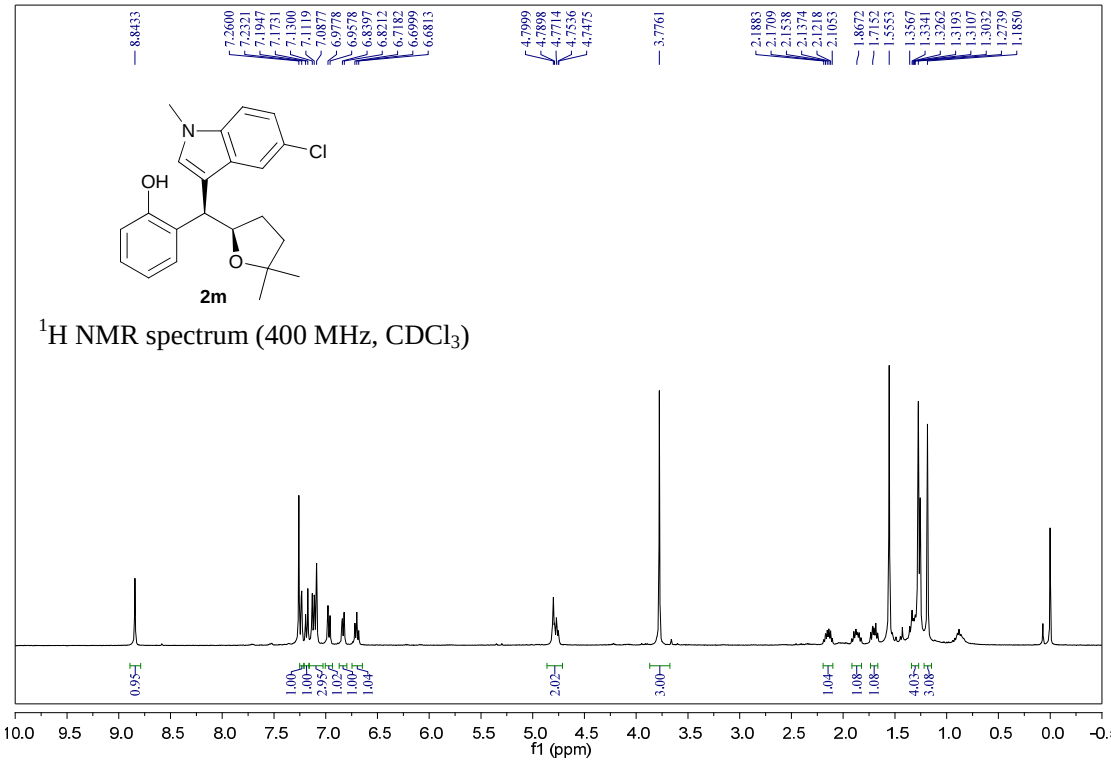
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



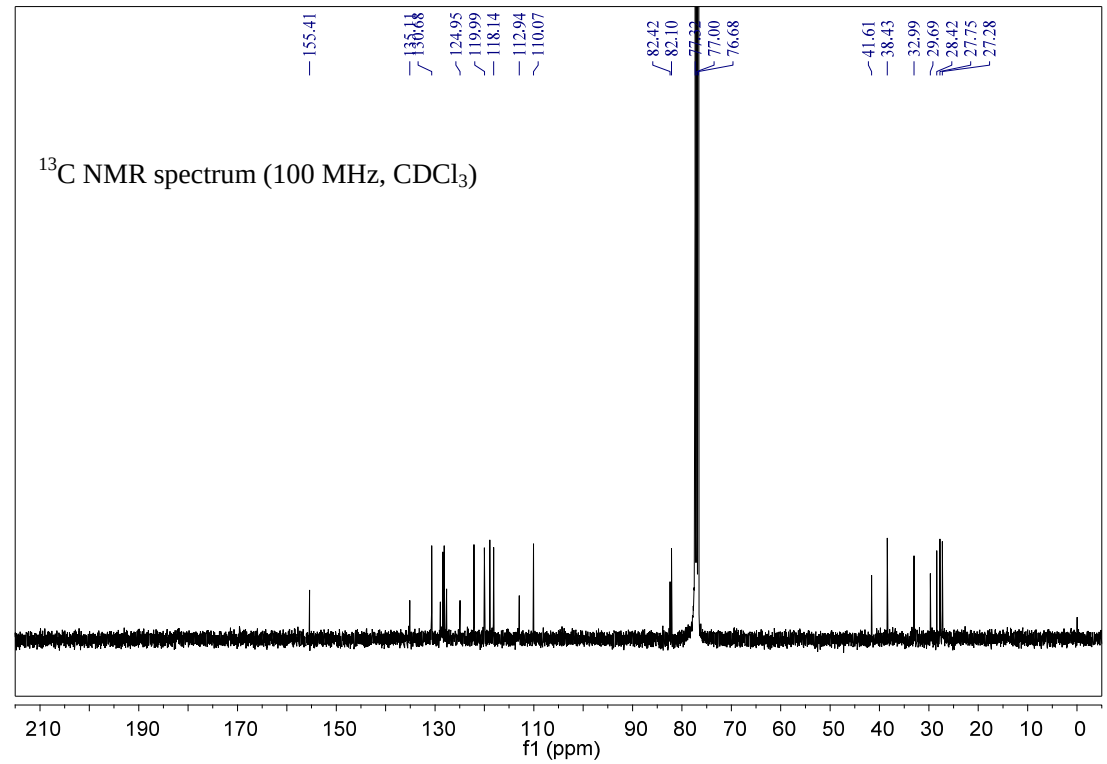
^{13}C NMR spectrum (100 MHz, $CDCl_3$)


8.8794
7.1849
7.0997
7.0812
7.0384
7.0124
6.9947
6.9698
6.8763
6.8578
6.7012
6.6831
6.6657
4.9321
4.8113
3.7741
2.6059
2.5872
2.5687
2.1781
1.7032
1.5654
1.5062
1.2048
0.8916
0.8737
0.8558
N
Bu
OH
O
2l
1H NMR spectrum (400 MHz, CDCl3)
0.92
1.04
1.10
4.02
1.07
1.03
1.00
1.02
3.00
2.05
1.06
1.04
1.06
3.01
4.05
3.01
3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

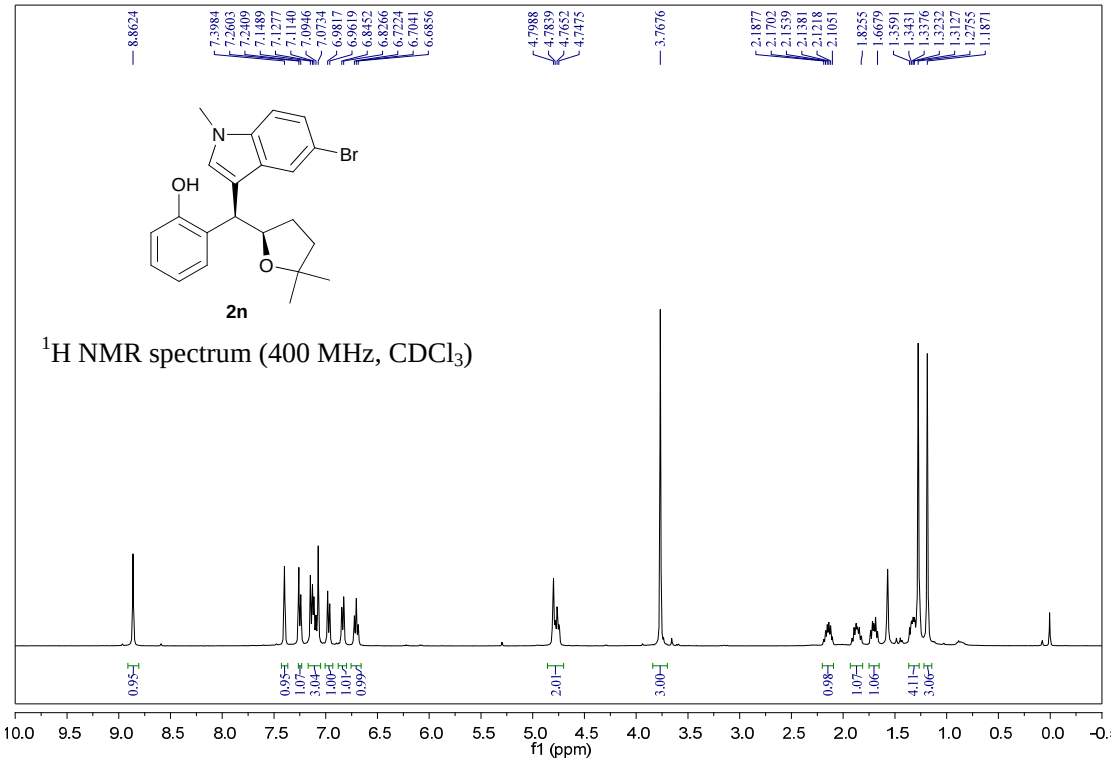

155.53
133.50
130.90
127.88
127.80
127.08
119.88
117.86
112.74
108.63
82.43
82.16
77.33
77.00
76.68
41.20
38.50
35.66
34.48
32.80
27.20
22.29
13.94
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



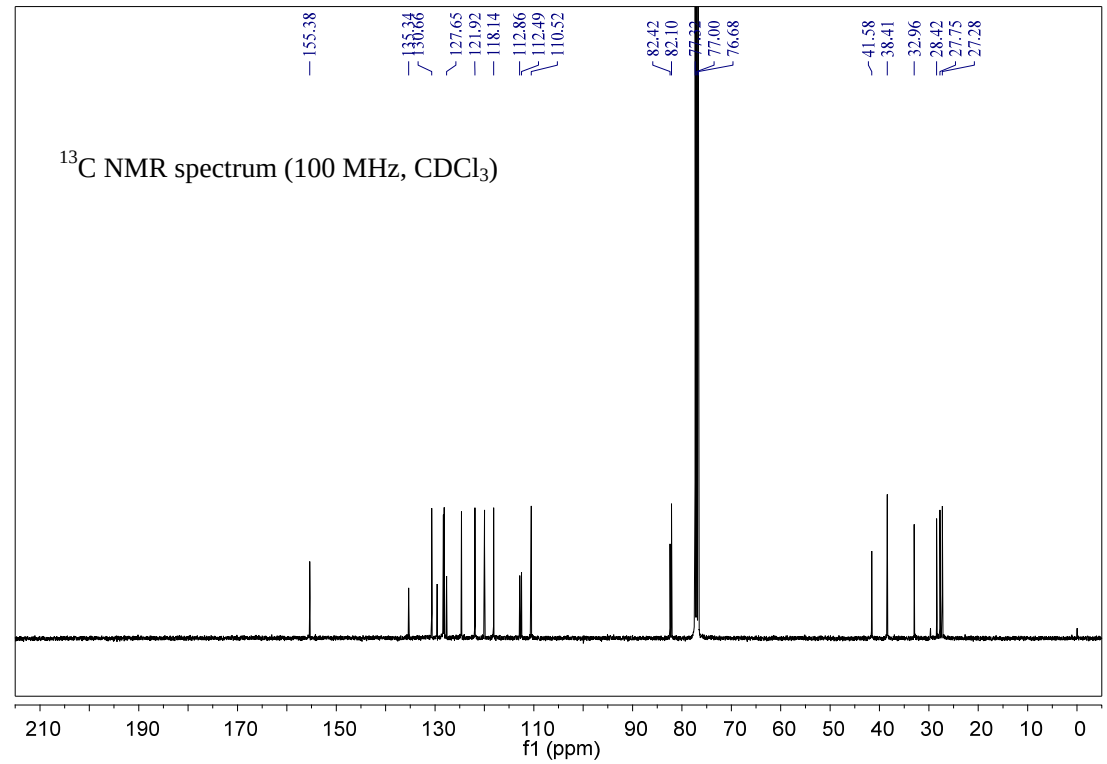
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



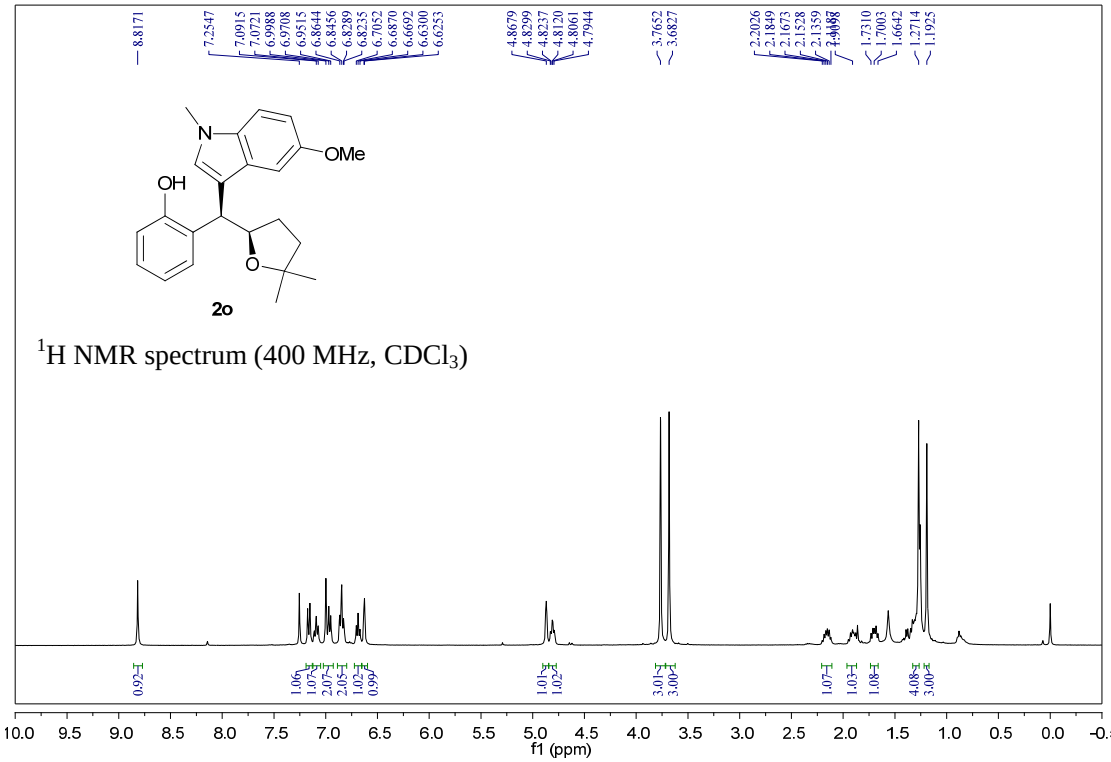
^{13}C NMR spectrum (100 MHz, $CDCl_3$)

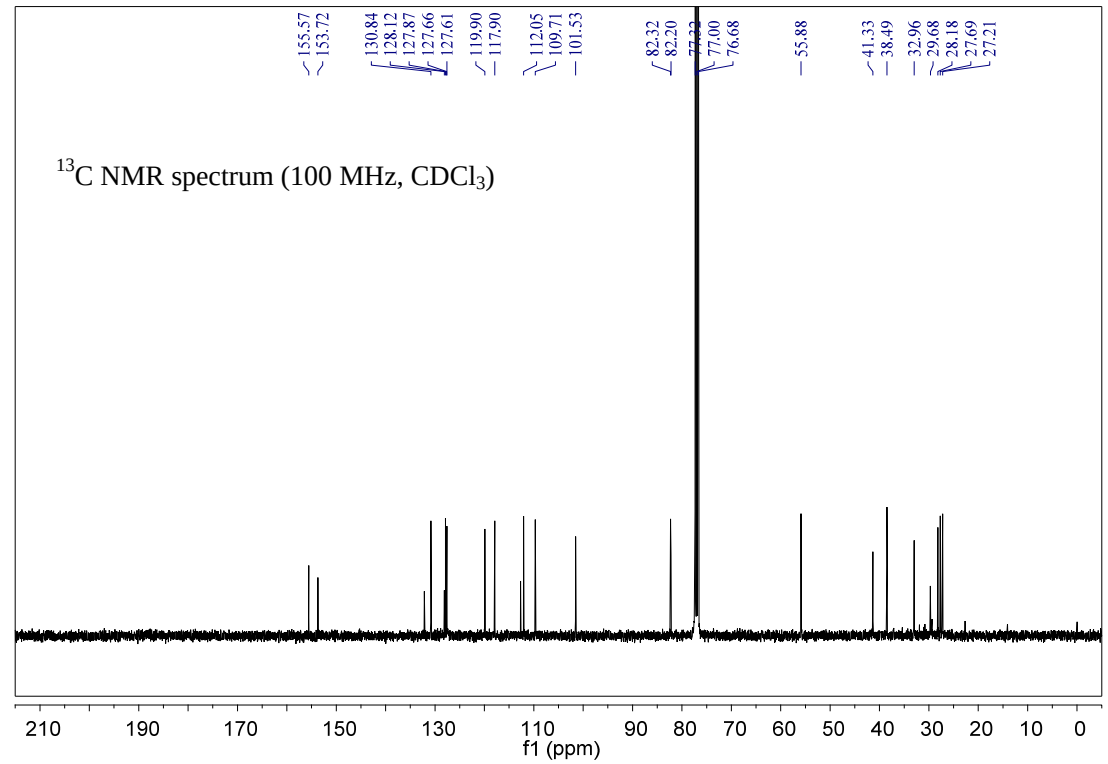


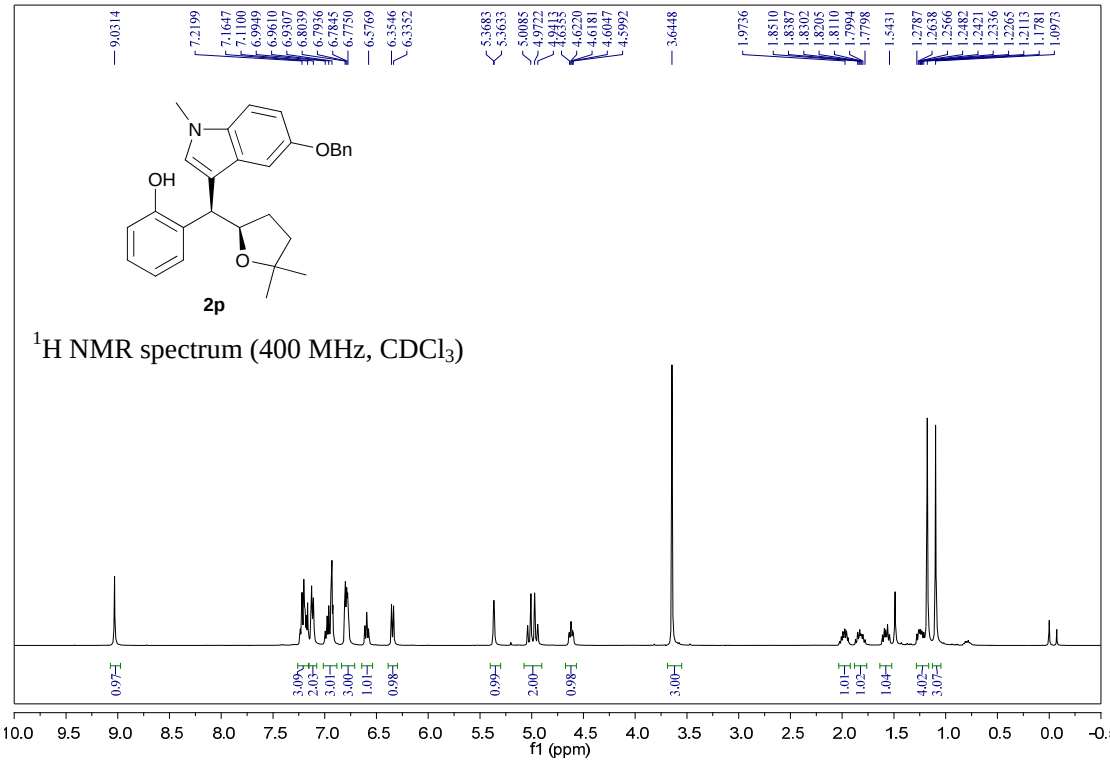
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



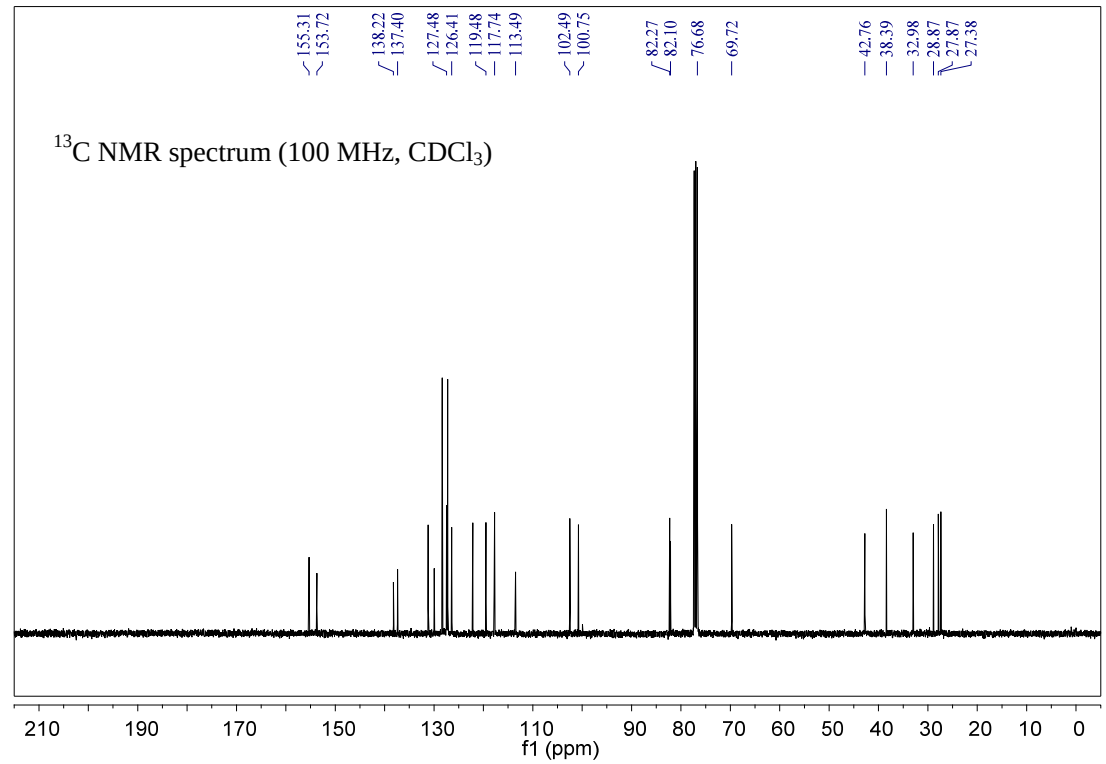
^{13}C NMR spectrum (100 MHz, $CDCl_3$)


8.8171
7.2547
7.0915
7.0721
6.9988
6.9708
6.9515
6.8644
6.8456
6.8289
6.8235
6.7052
6.6870
6.6692
6.6300
6.6253
4.8679
4.8299
4.8237
4.8120
4.8061
4.7944
3.7652
3.6827
2.2026
2.1849
2.1673
2.1528
2.1359
1.7310
1.7003
1.6642
1.2714
1.1925
N
OMe
OH
O
2o
1H NMR spectrum (400 MHz, CDCl3)
0.92
1.06
1.07
2.07
2.05
1.02
0.99
1.01
1.02
3.01
3.00
1.07
1.03
1.08
4.08
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

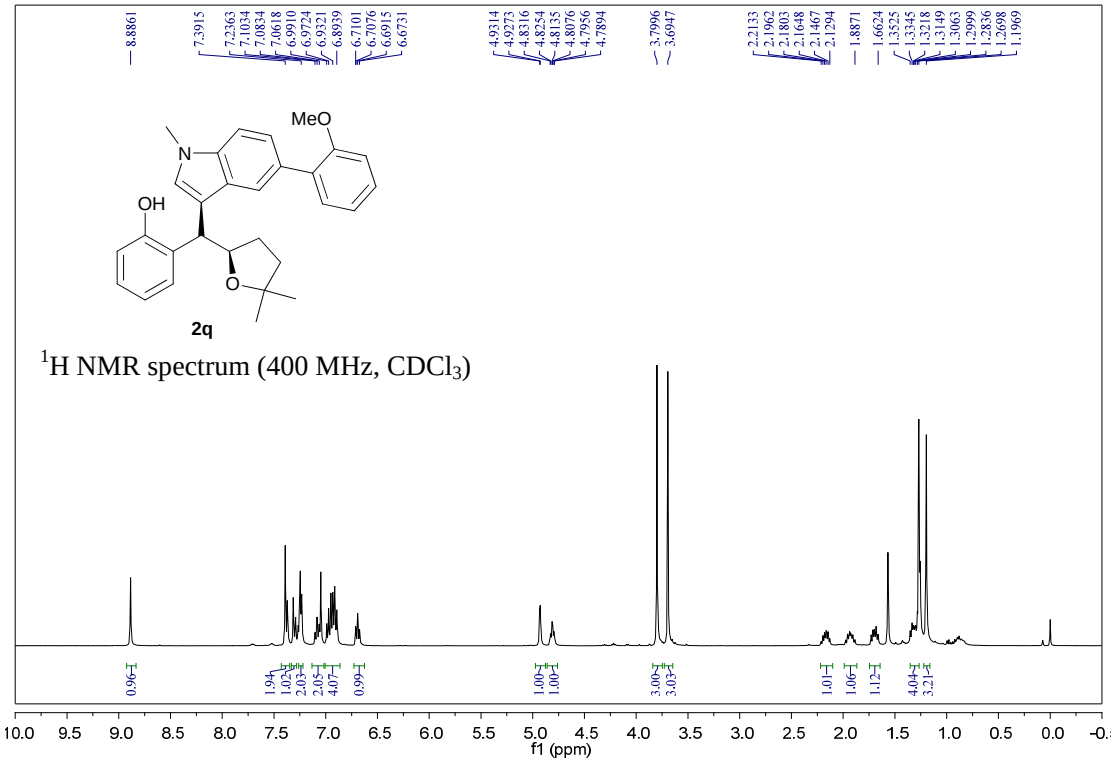

155.57
153.72
130.84
128.12
127.87
127.66
127.61
119.90
117.90
112.05
109.71
101.53
82.32
82.20
77.32
77.00
76.68
55.88
41.33
38.49
32.96
29.68
28.18
27.69
27.21
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



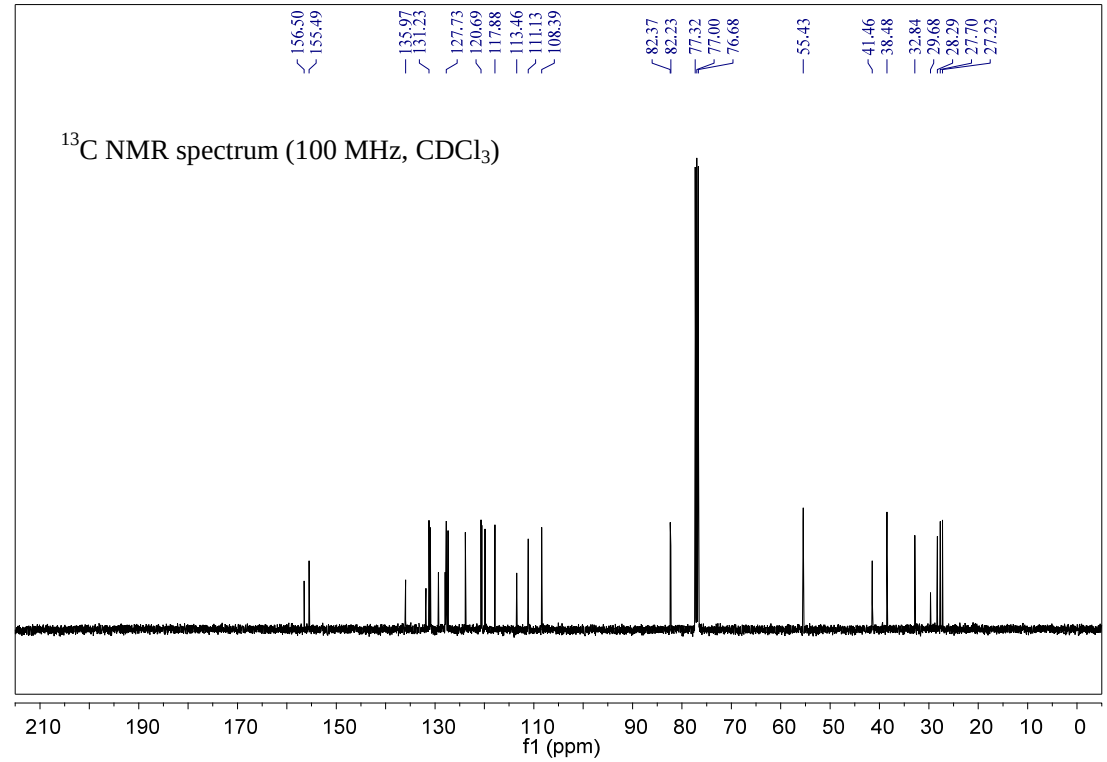
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



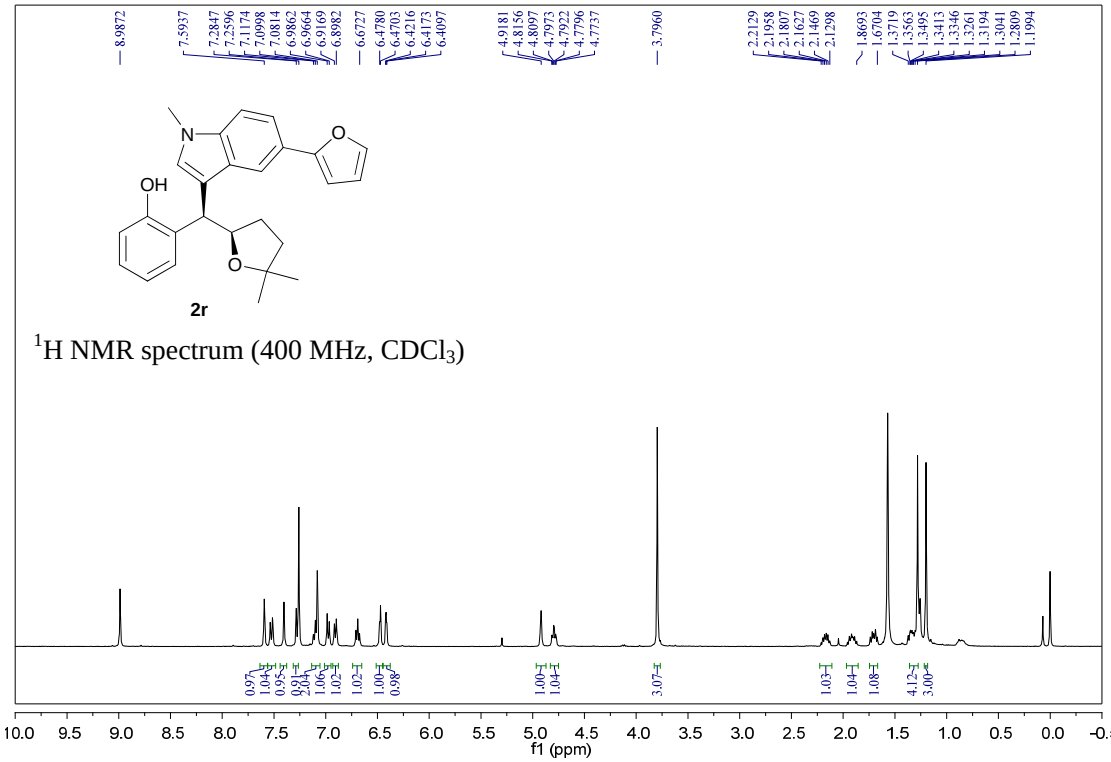
^{13}C NMR spectrum (100 MHz, $CDCl_3$)

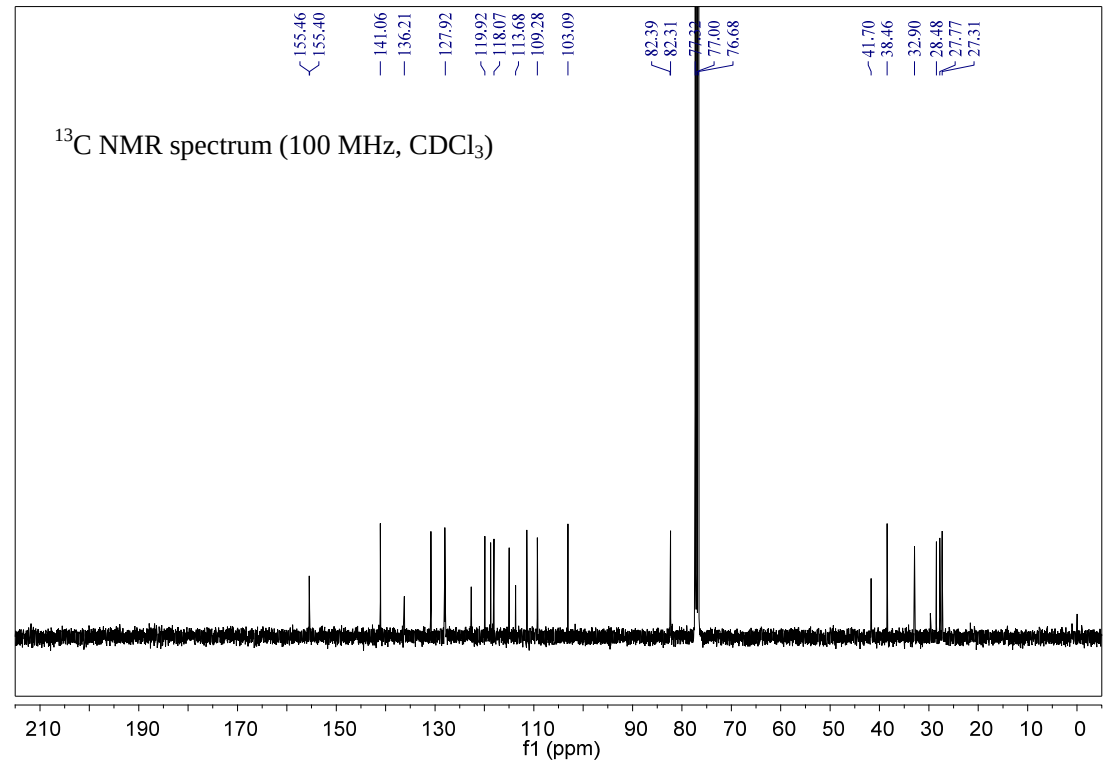


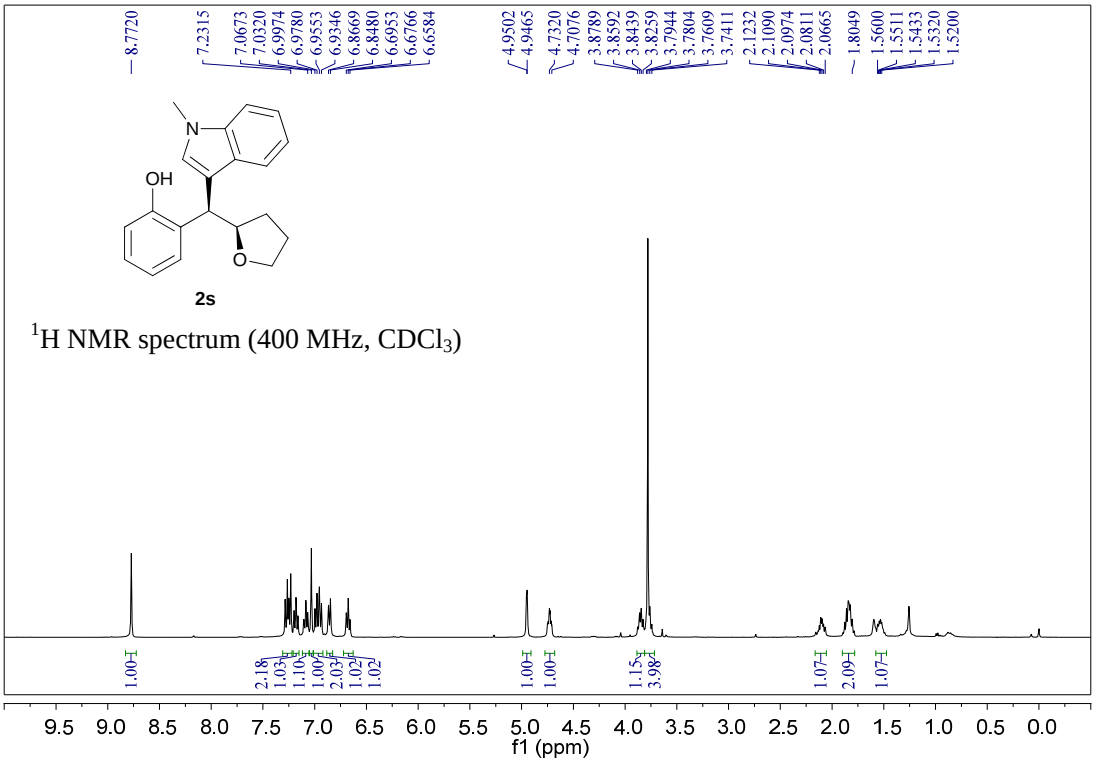
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)

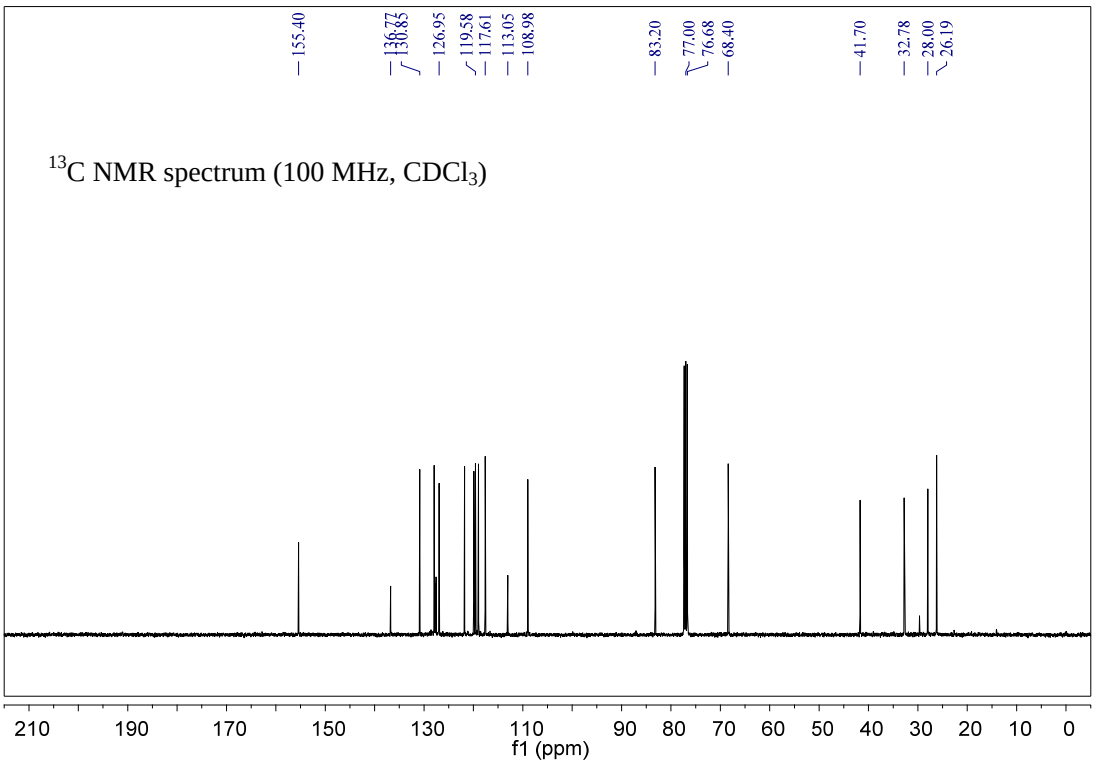

8.9872
7.5937
7.2847
7.2596
7.1174
7.0981
7.0814
6.9862
6.9664
6.9169
6.8982
6.6727
6.4780
6.4703
6.4216
6.4173
6.4097
4.9181
4.8156
4.8097
4.7973
4.7922
4.7796
4.7737
3.7960
2.2129
2.1958
2.1807
2.1627
2.1469
2.1298
1.8693
1.6704
1.3719
1.3563
1.3495
1.3413
1.3346
1.3261
1.3194
1.3041
1.2809
1.1994
N
O
OH
O
2r
1H NMR spectrum (400 MHz, CDCl3)
0.97
1.04
0.95
0.91
2.04
1.06
1.02
1.02
1.00
0.98
1.00
1.04
3.07
1.03
1.04
1.08
4.12
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


155.46
155.40
141.06
136.21
127.92
119.92
118.07
113.68
109.28
103.09
82.39
82.31
77.32
77.00
76.68
41.70
38.46
32.90
28.48
27.77
27.31
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

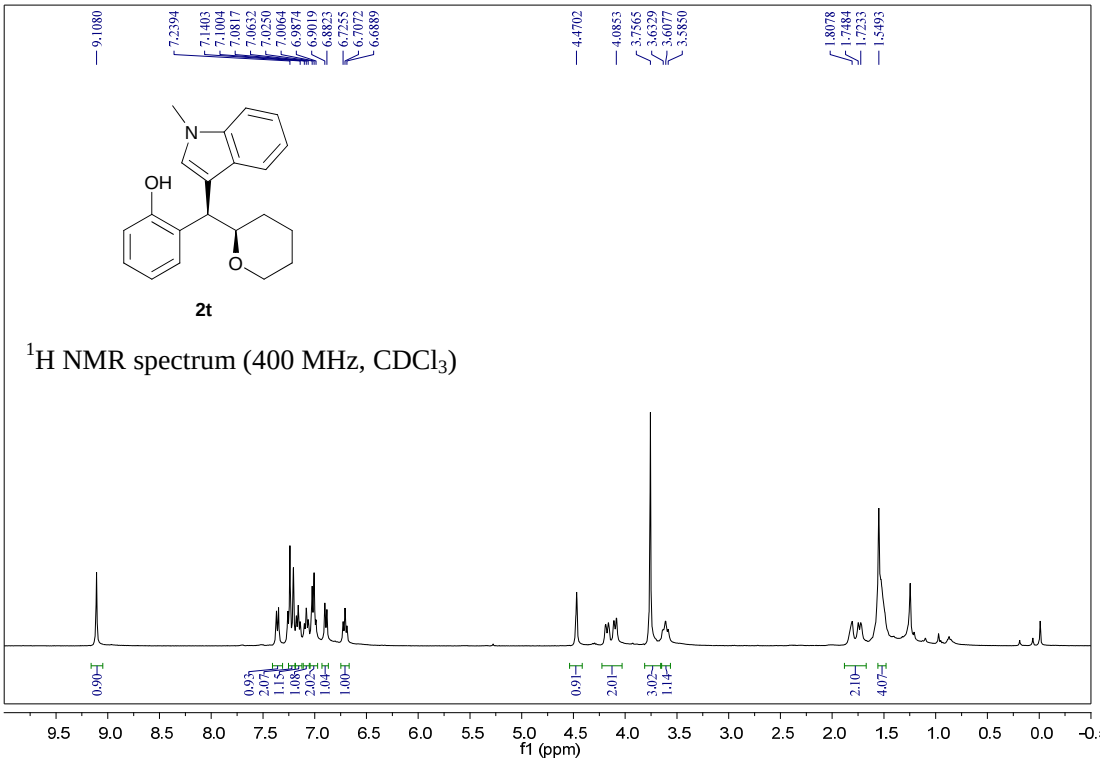


2s

^{1}H NMR spectrum (400 MHz, $CDCl_3$)

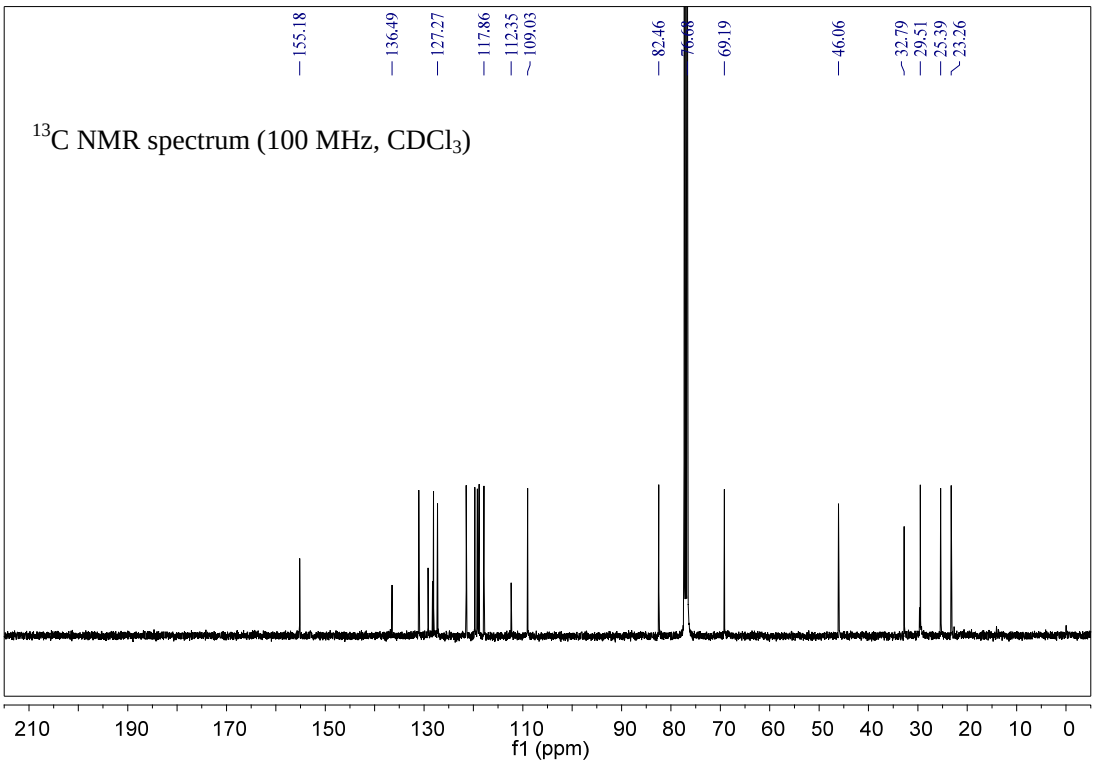


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

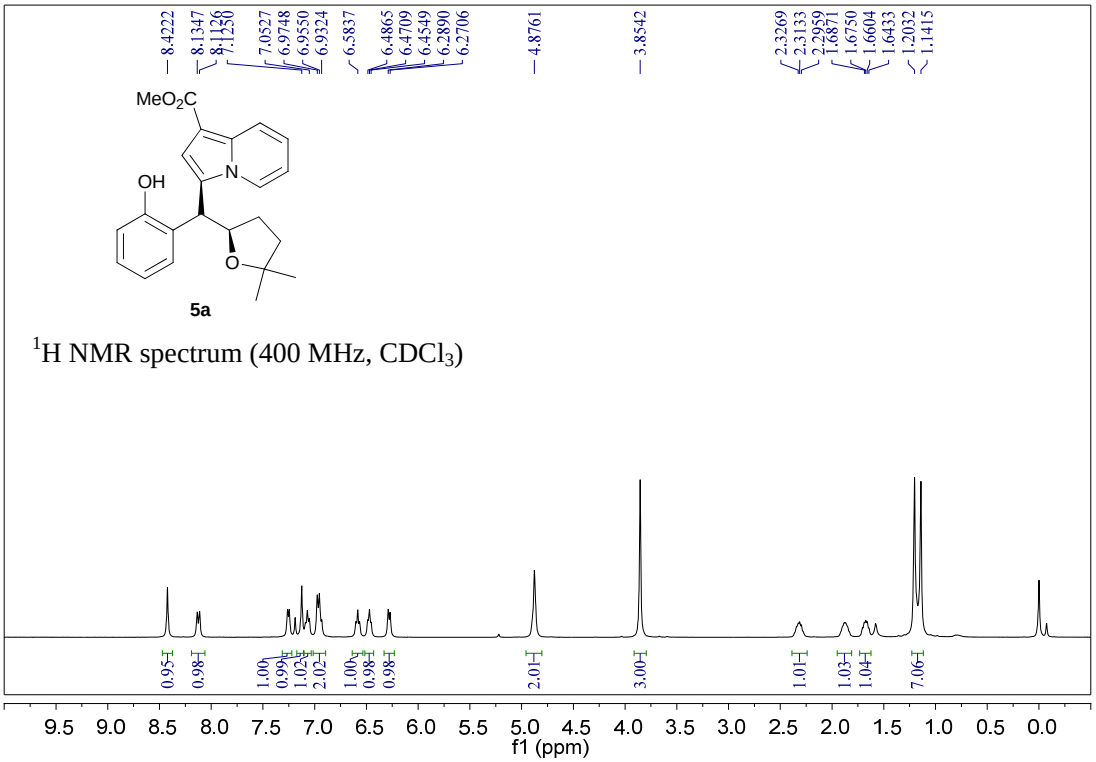


2t

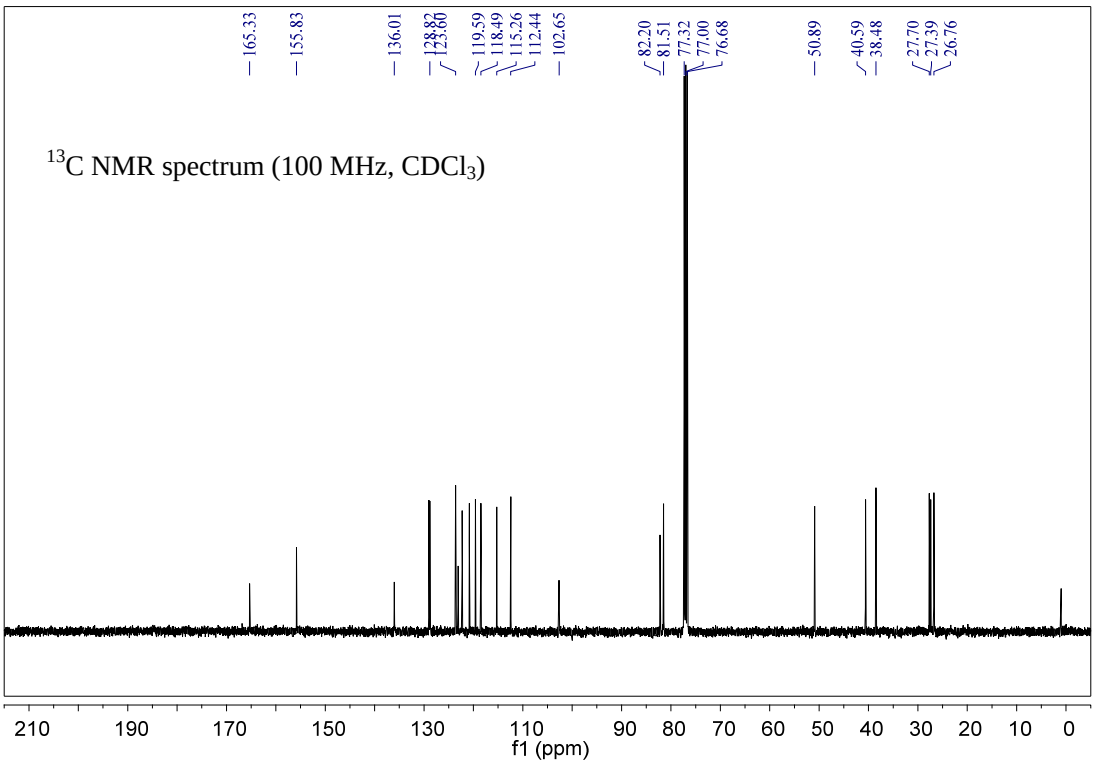
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



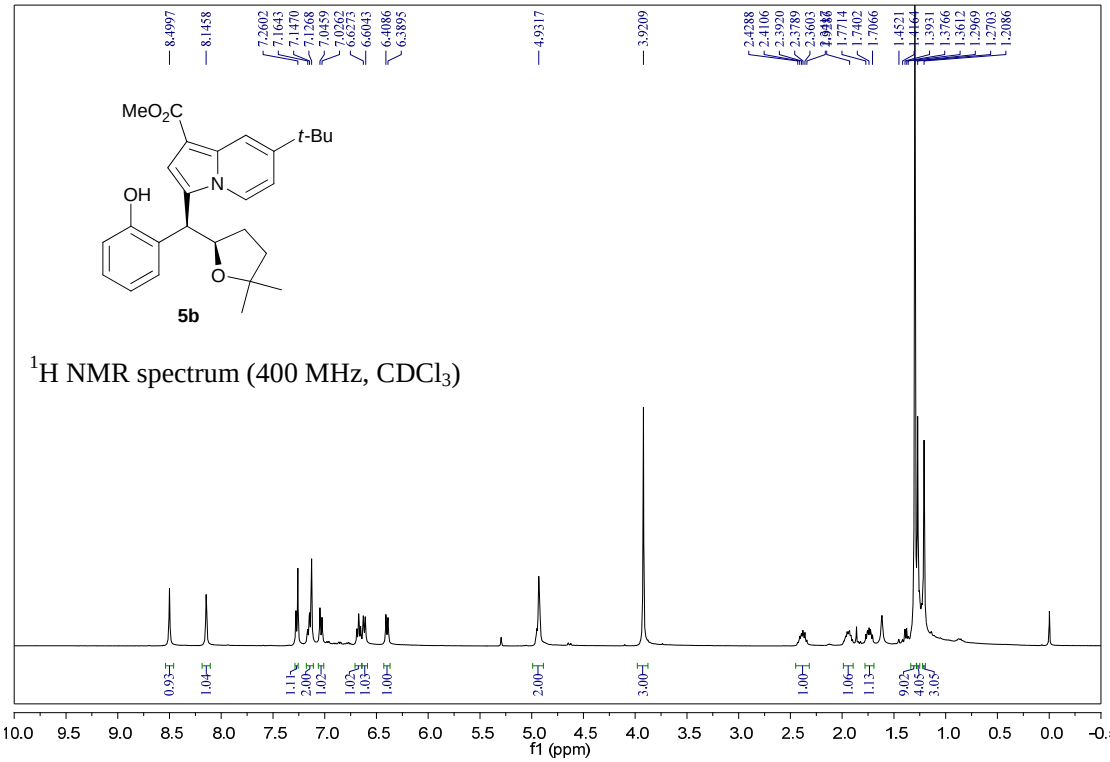
^{13}C NMR spectrum (100 MHz, $CDCl_3$)

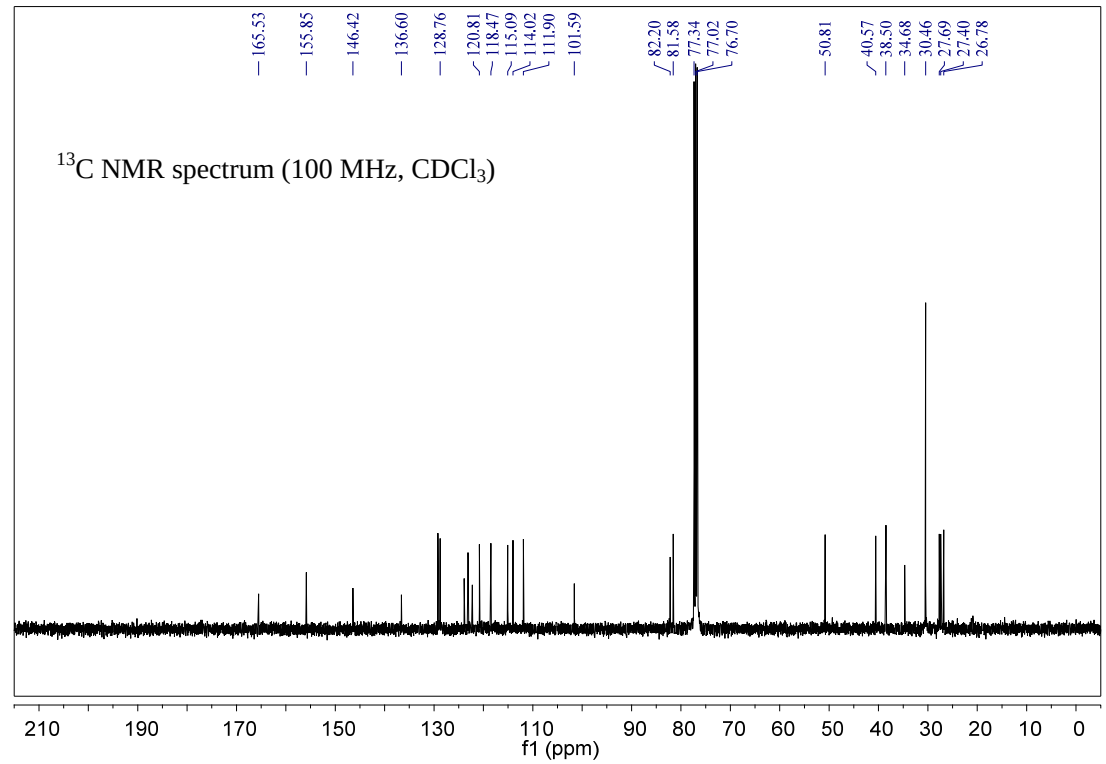


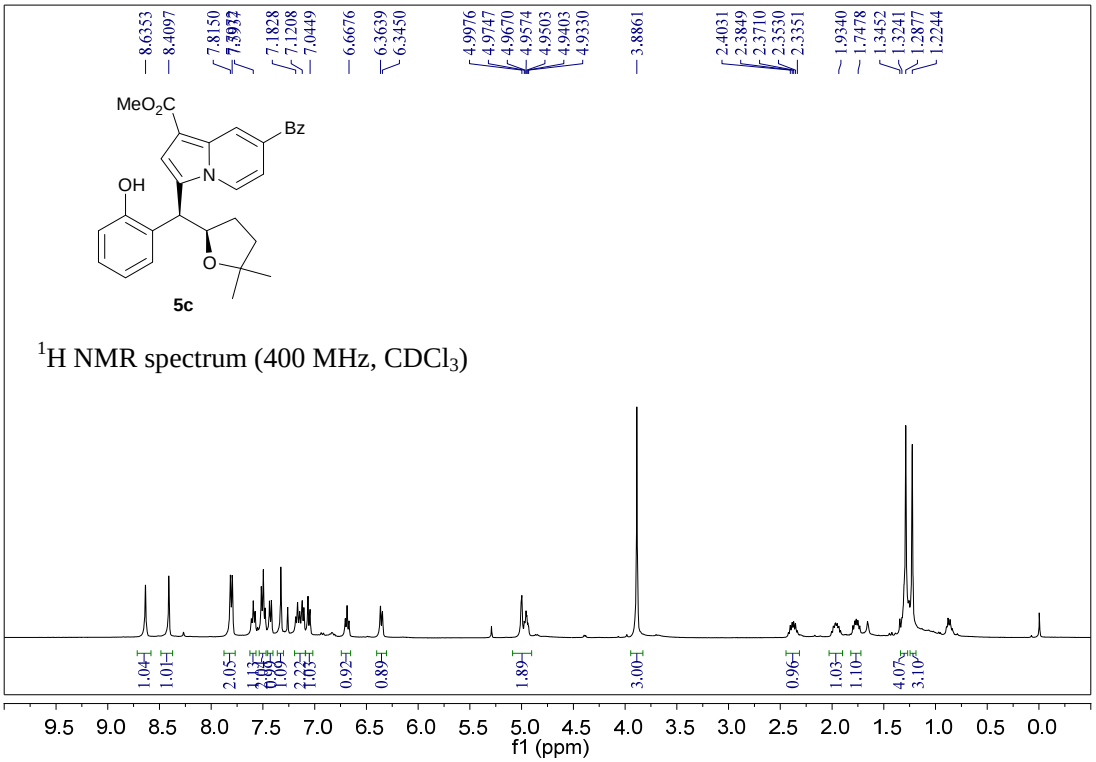
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

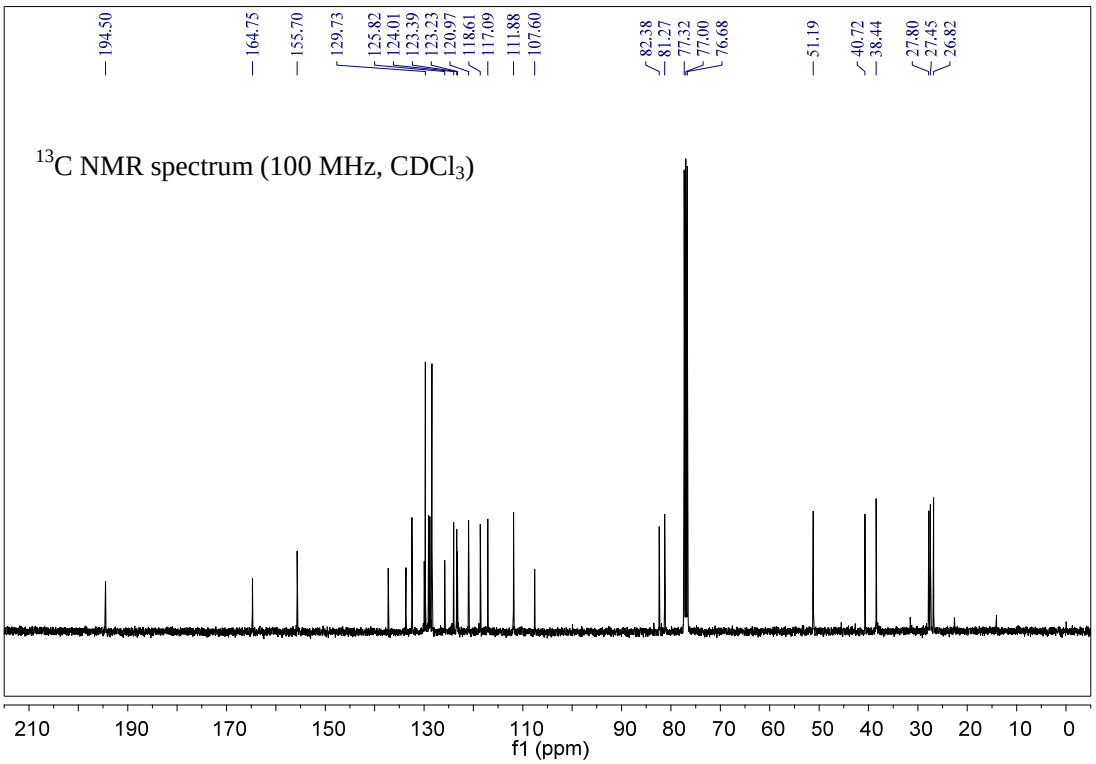


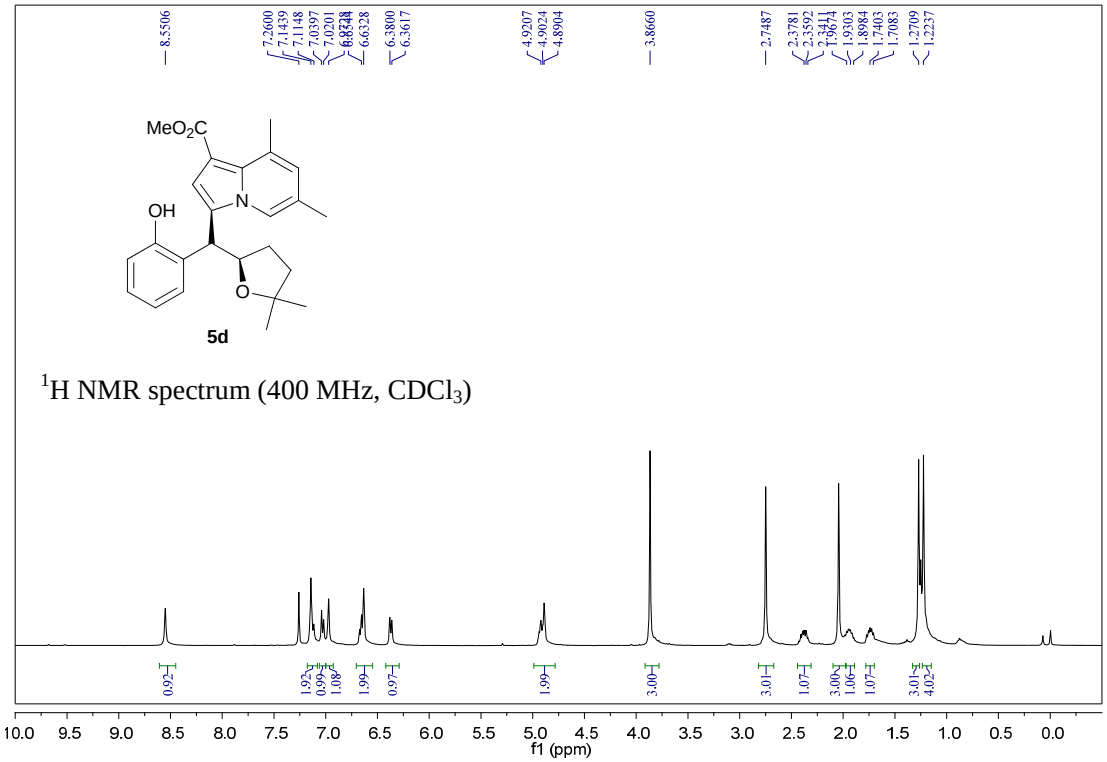
^{13}C NMR spectrum (100 MHz, $CDCl_3$)

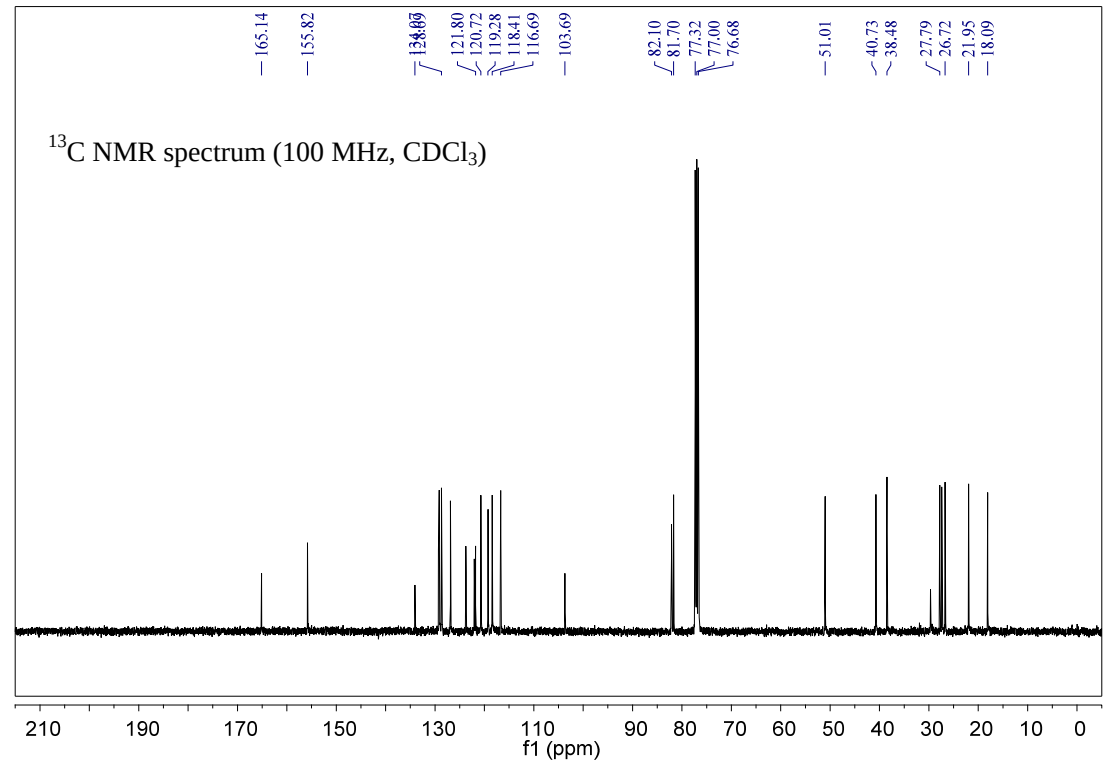

MeO2C
t-Bu
N
OH
O
5b
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

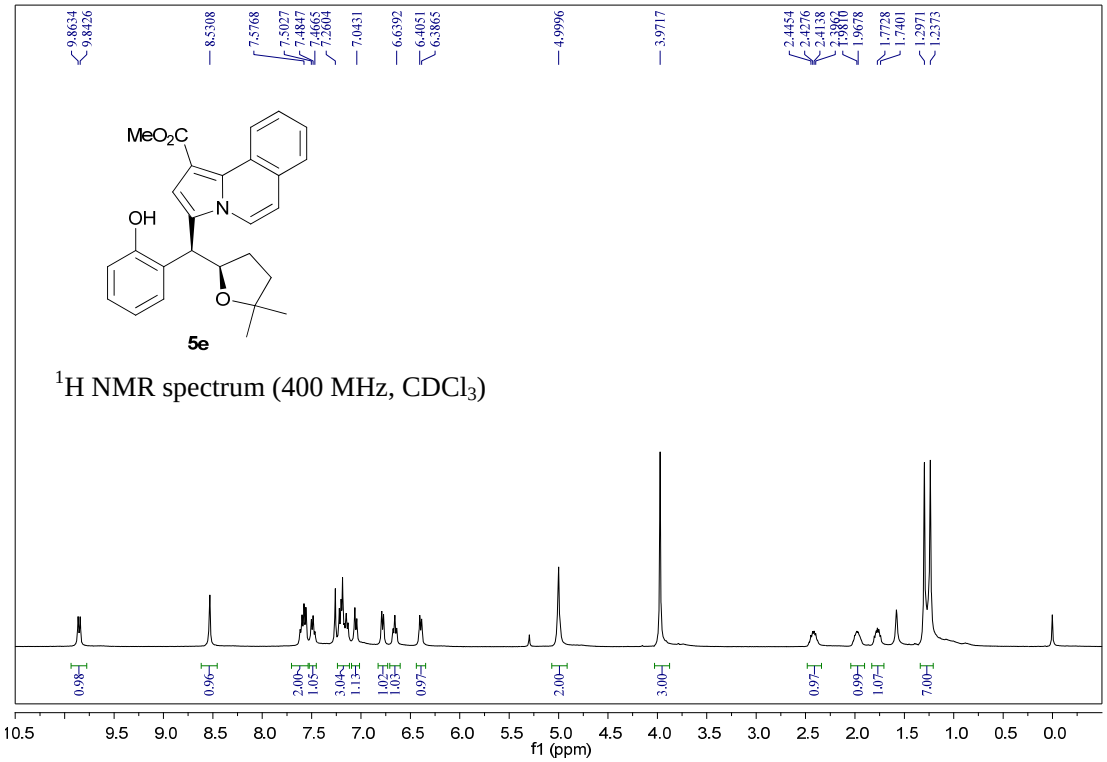

13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)


8.6353
8.4097
7.8150
7.7932
7.7737
7.1828
7.1208
7.0449
6.6676
6.3639
6.3450
4.9976
4.9747
4.9670
4.9574
4.9503
4.9403
4.9330
3.8861
2.4031
2.3849
2.3710
2.3530
2.3351
1.9340
1.7478
1.3452
1.3241
1.2877
1.2244
MeO2C
Bz
N
OH
O
5c
1H NMR spectrum (400 MHz, CDCl3)
1.04
1.01
2.05
0.92
0.89
1.89
3.00
0.96
1.03
1.10
4.07
3.10
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

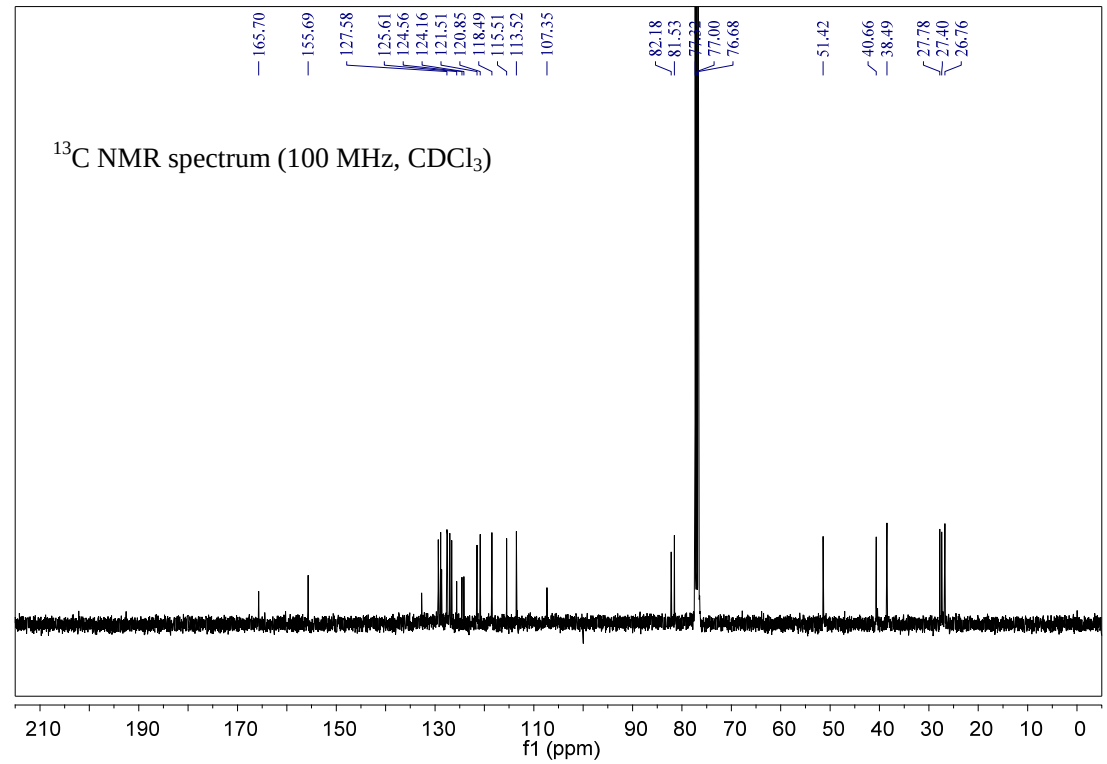

194.50
164.75
155.70
129.73
125.82
124.01
123.39
123.23
120.97
118.61
117.09
111.88
107.60
82.38
81.27
77.32
77.00
76.68
51.19
40.72
38.44
27.80
27.45
26.82
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.5506
7.2600
7.1439
7.1148
7.0397
7.0201
6.6328
6.3800
6.3617
4.9207
4.9024
4.8904
3.8660
2.7487
2.3781
2.3592
2.3411
1.9674
1.9303
1.8984
1.7403
1.7083
1.2709
1.2237
MeO2C
OH
N
O
5d
1H NMR spectrum (400 MHz, CDCl3)
0.92
1.93
0.99
1.08
1.99
0.97
1.99
3.00
3.01
1.07
3.00
1.06
1.07
3.01
4.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

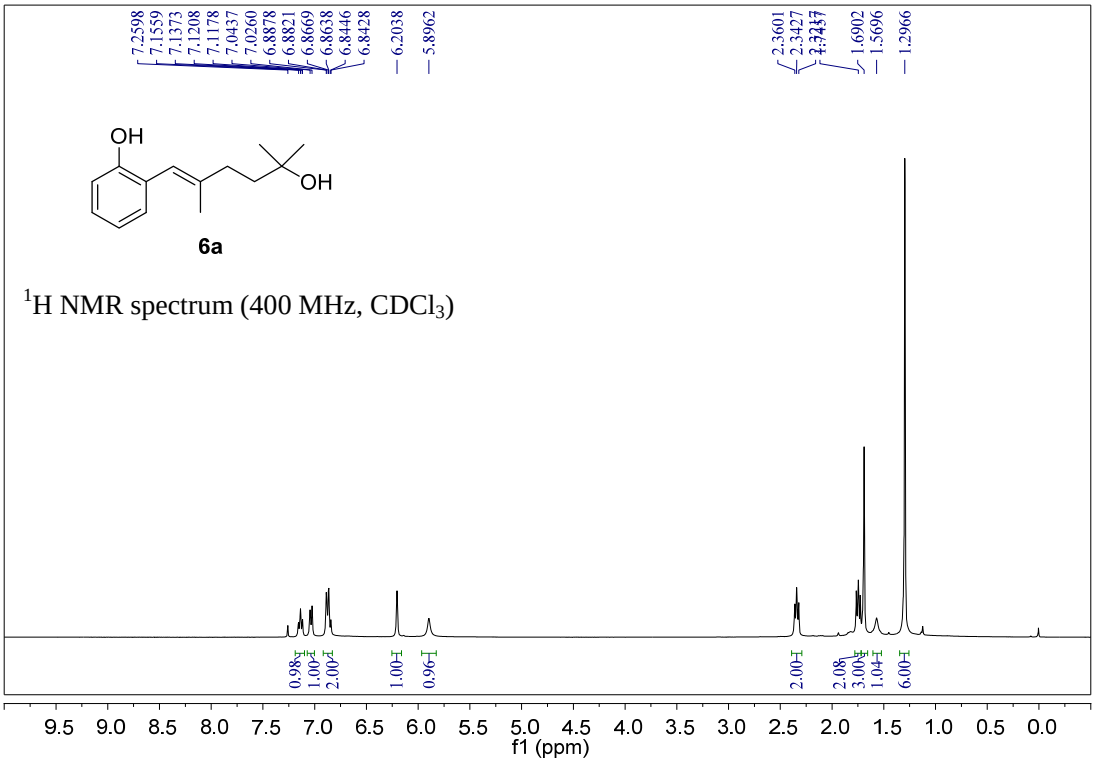

165.14
155.82
134.89
134.80
121.80
120.72
119.28
118.41
116.69
103.69
82.10
81.70
77.32
77.00
76.68
51.01
40.73
38.48
27.79
26.72
21.95
18.09
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



^{1}H NMR spectrum (400 MHz, $CDCl_3$)

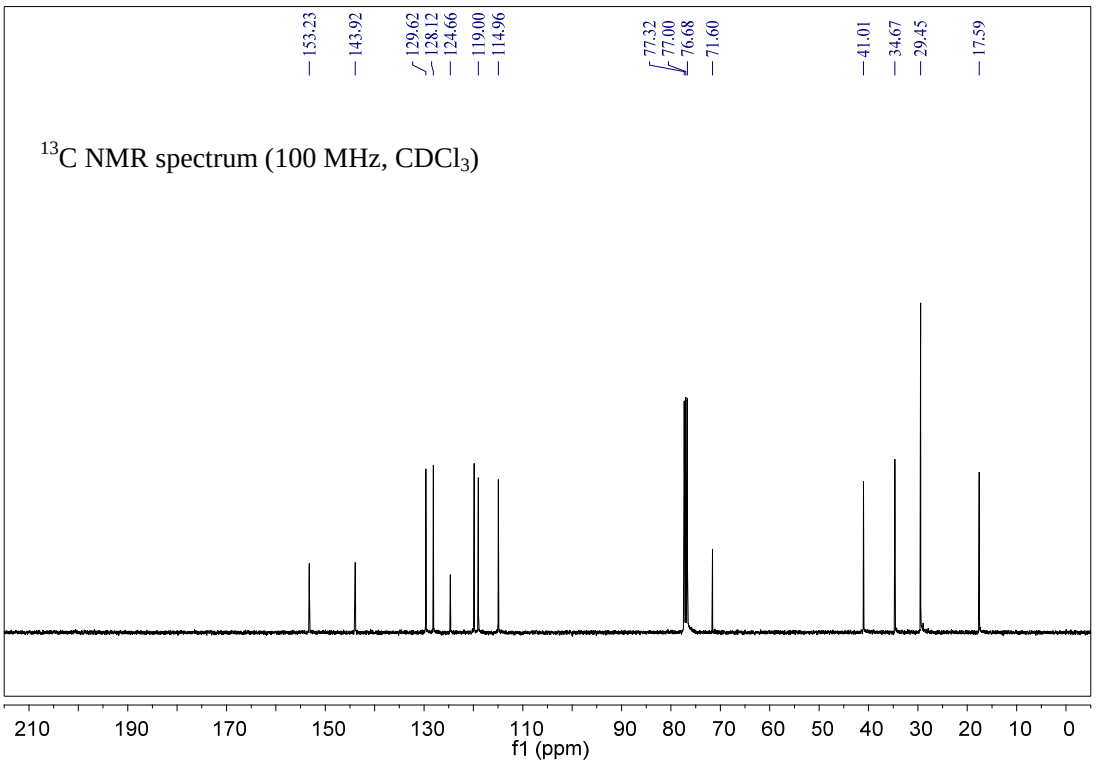


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

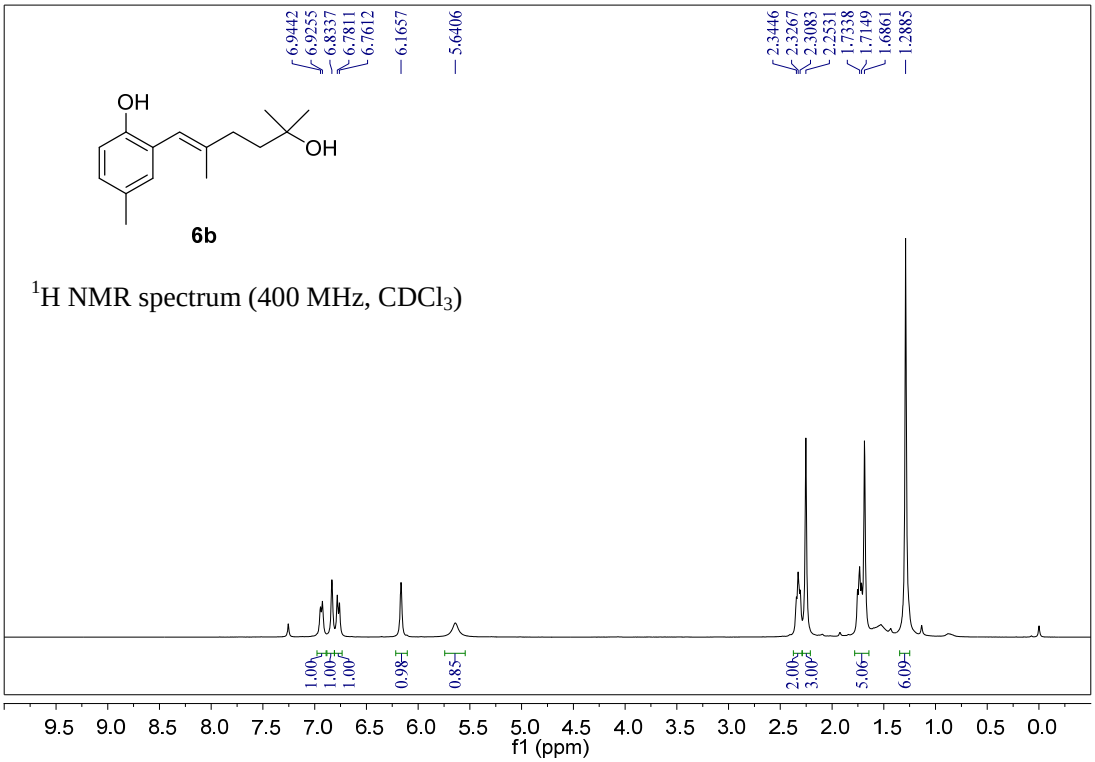


6a

^{1}H NMR spectrum (400 MHz, $CDCl_3$)

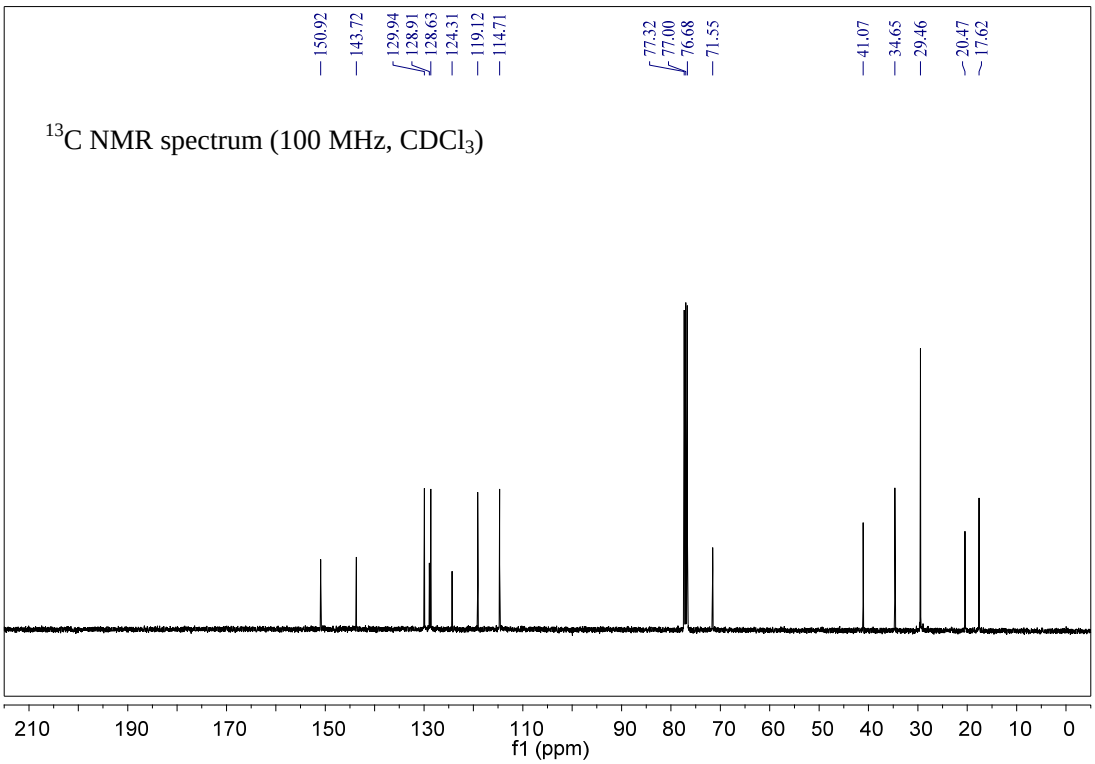


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

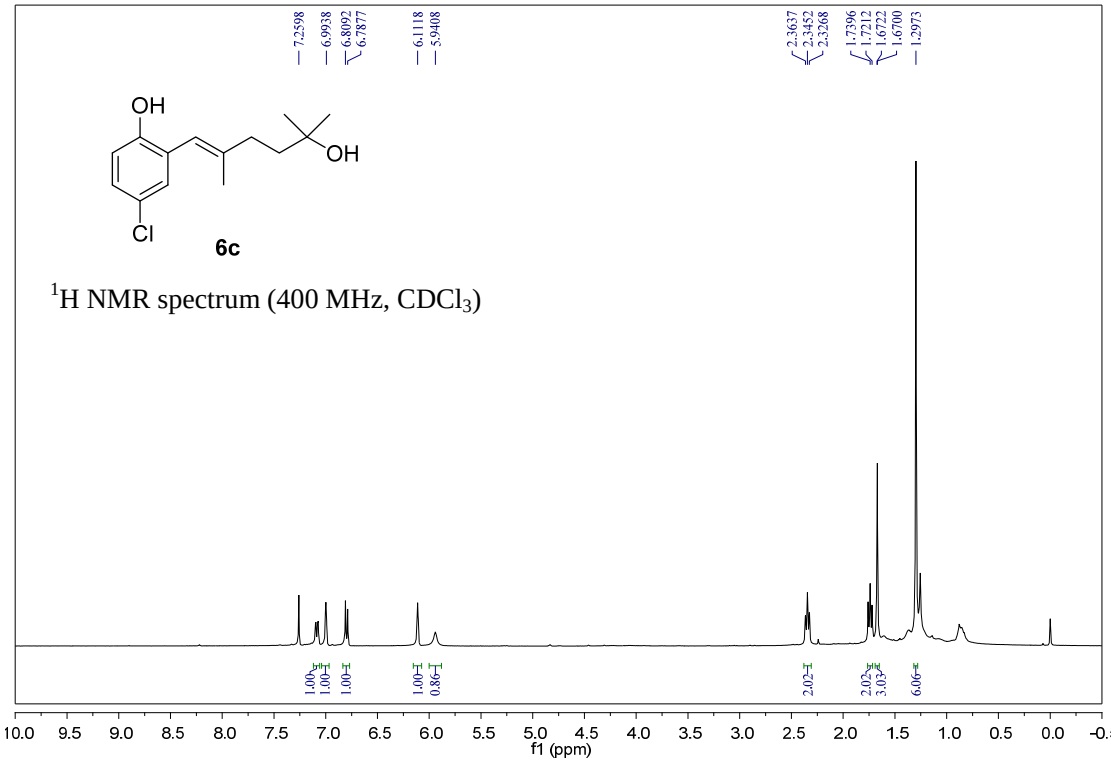


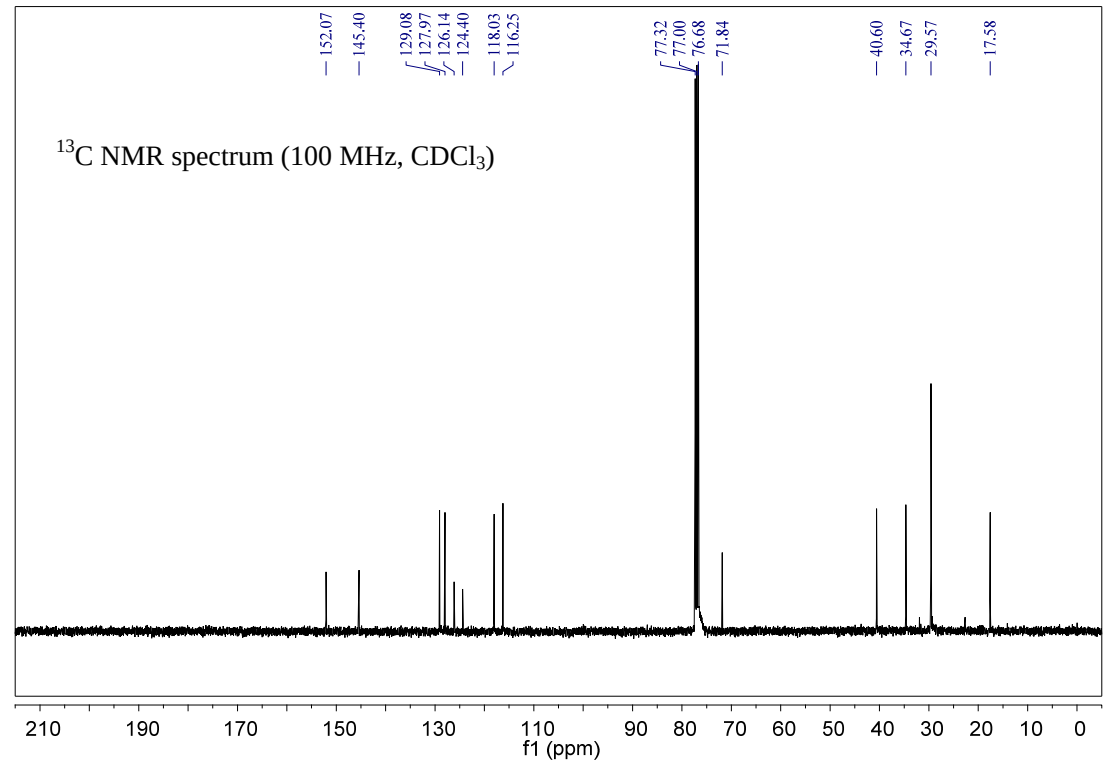
6b

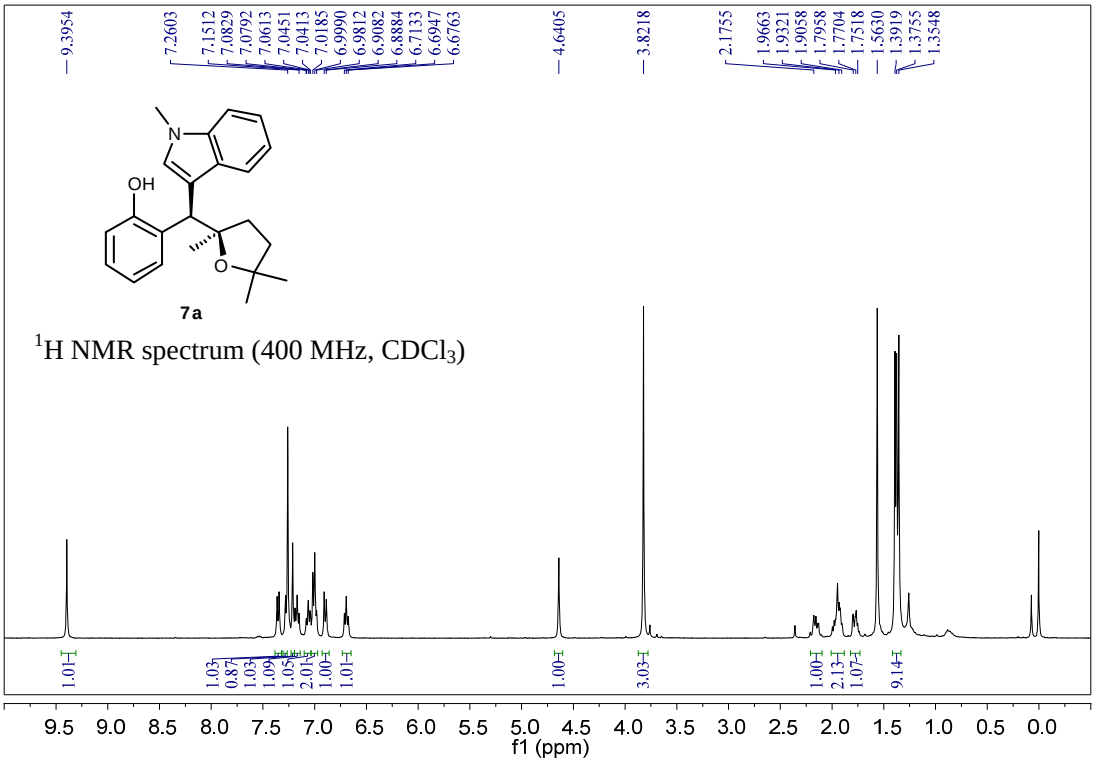
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



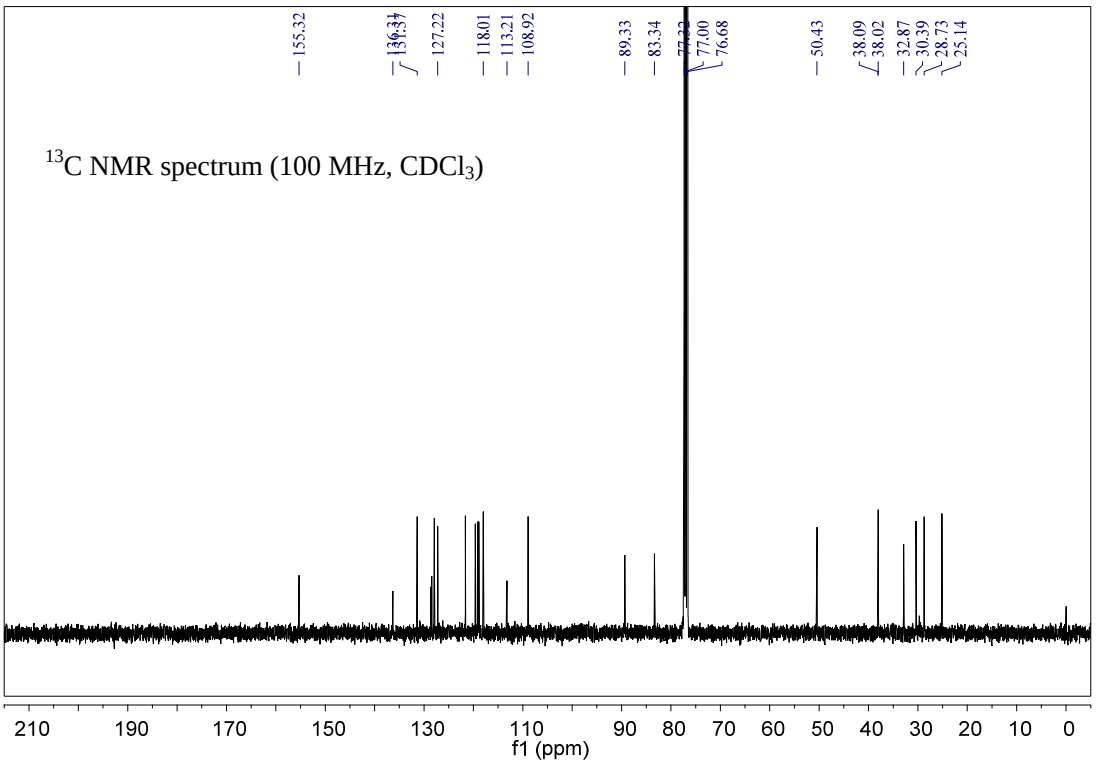
^{13}C NMR spectrum (100 MHz, $CDCl_3$)


7.2598
6.9938
6.8092
6.7877
6.1118
5.9408
2.3637
2.3452
2.3268
1.7396
1.7212
1.6722
1.6700
1.2973
OH
OH
Cl
6c
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

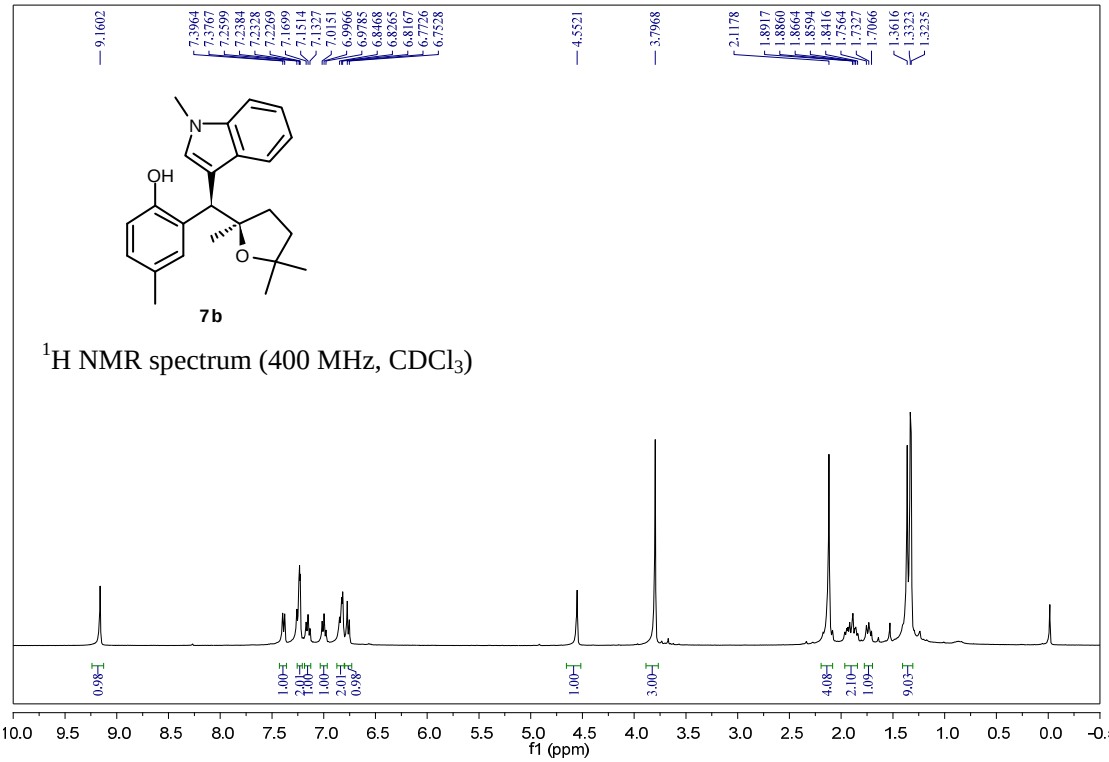

152.07
145.40
129.08
127.97
126.14
124.40
118.03
116.25
77.32
77.00
76.68
71.84
40.60
34.67
29.57
17.58
13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)



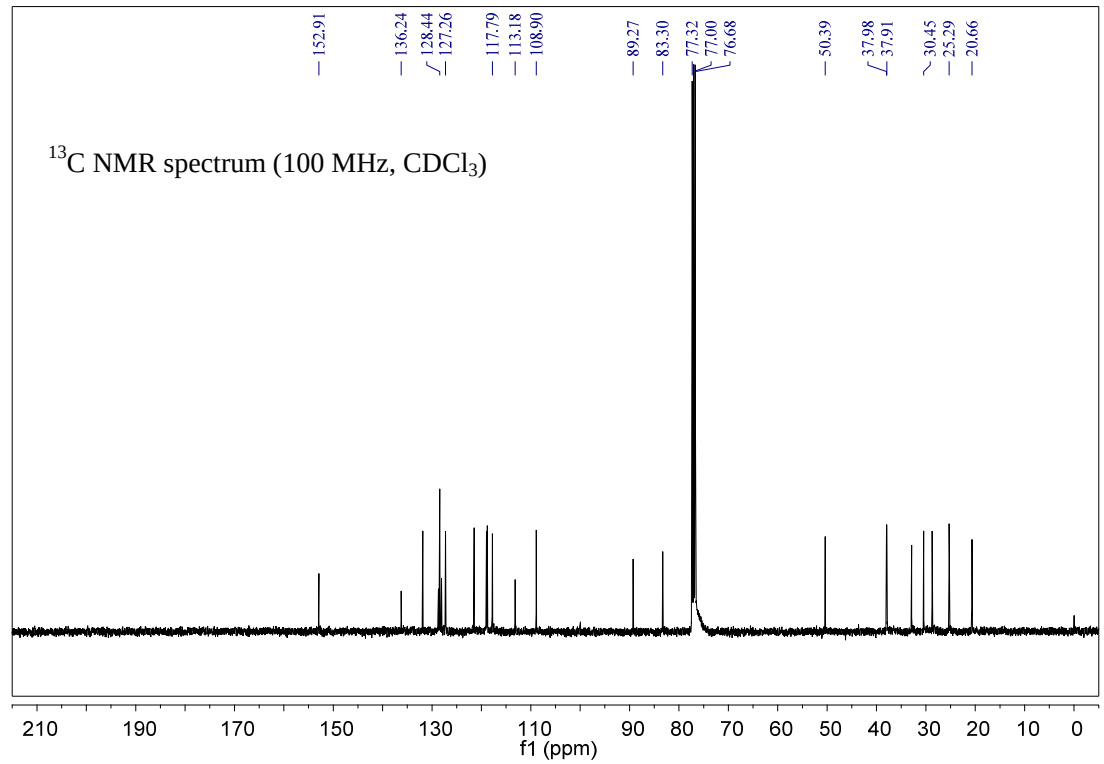
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



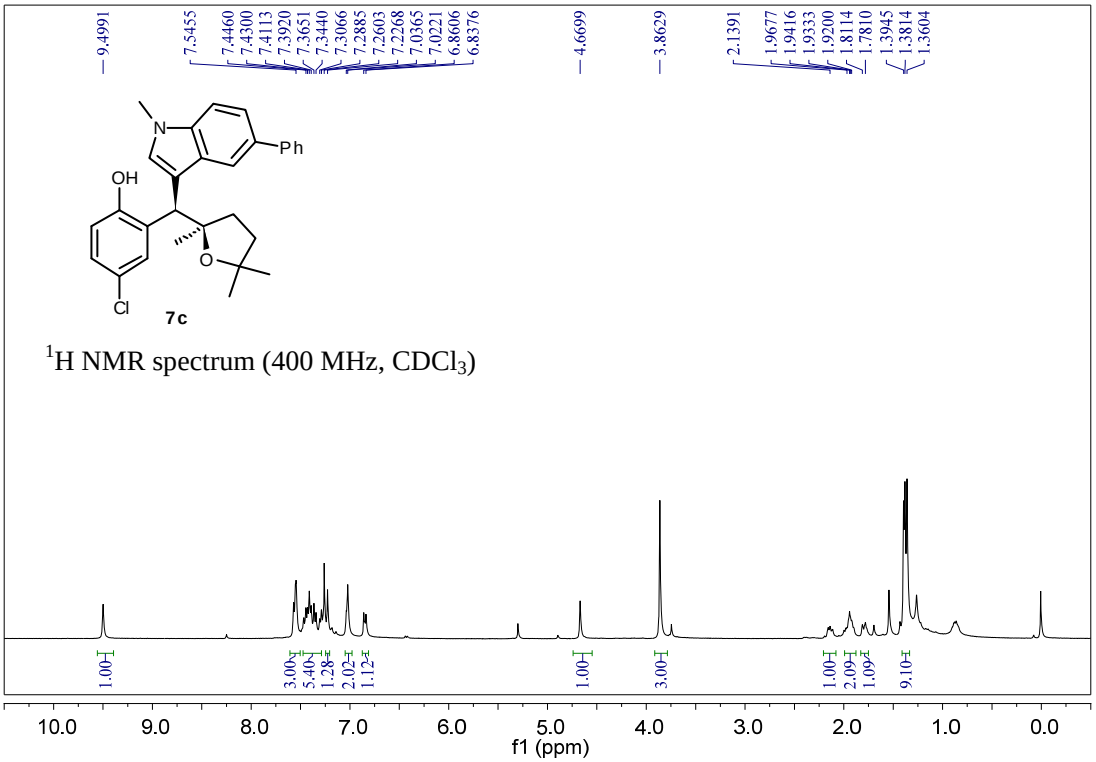
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



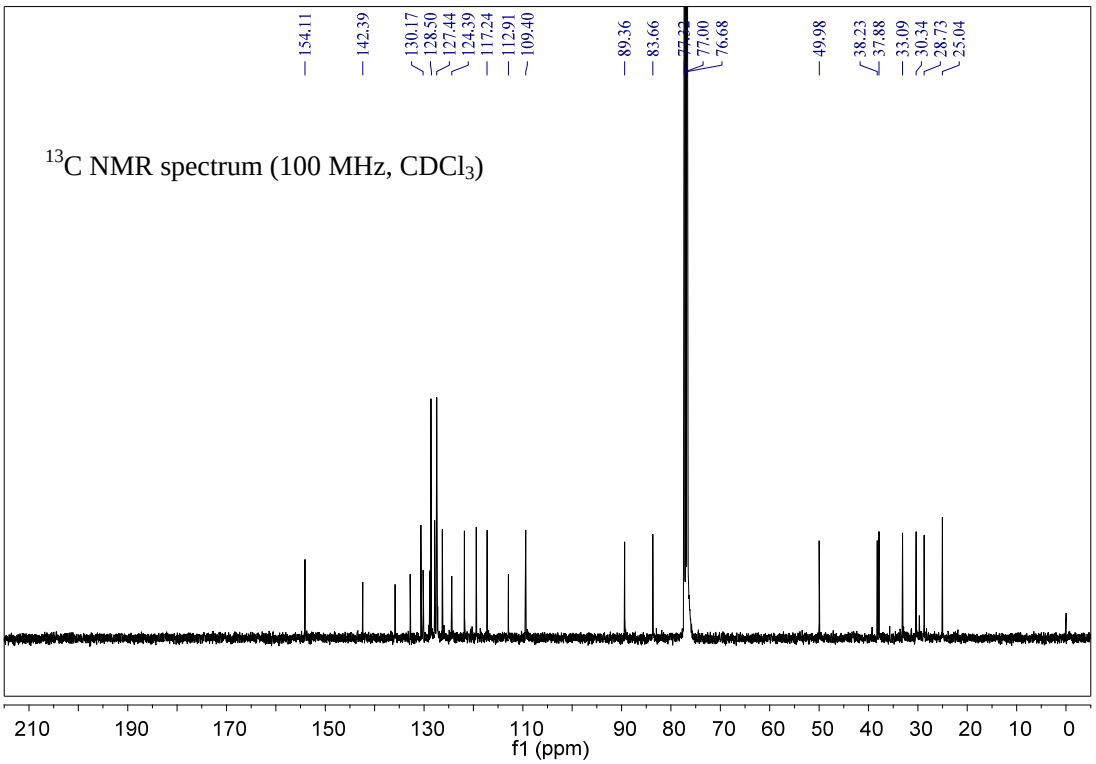
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



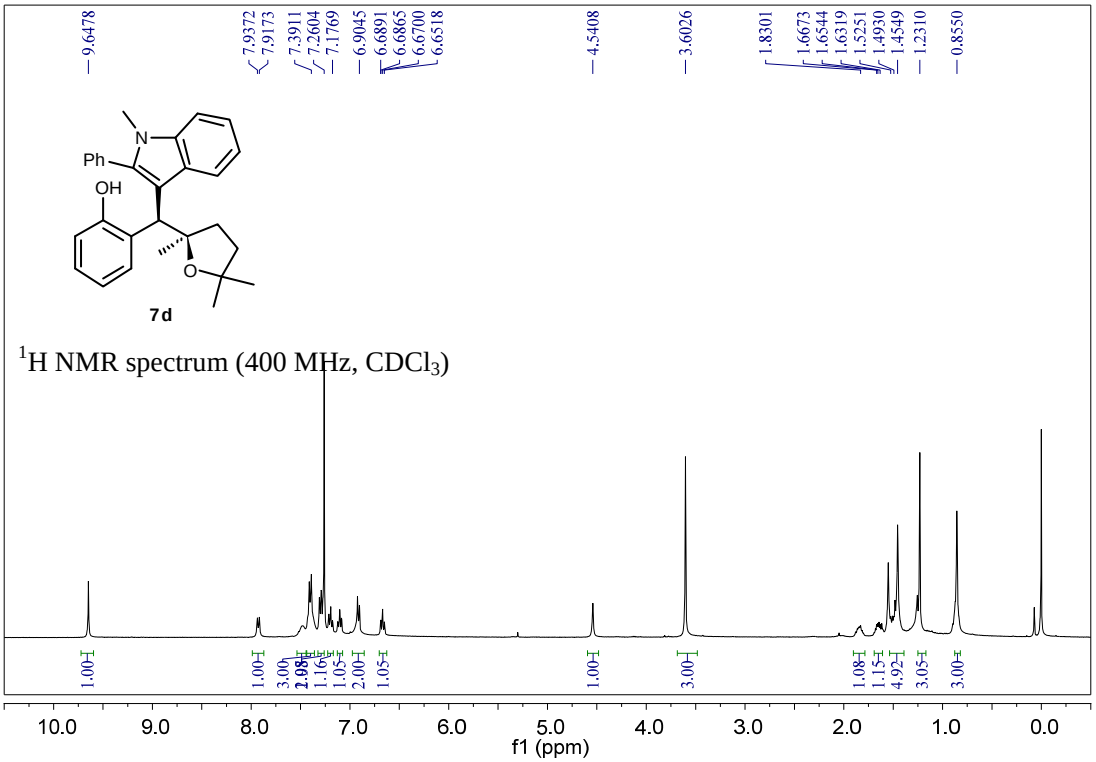
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)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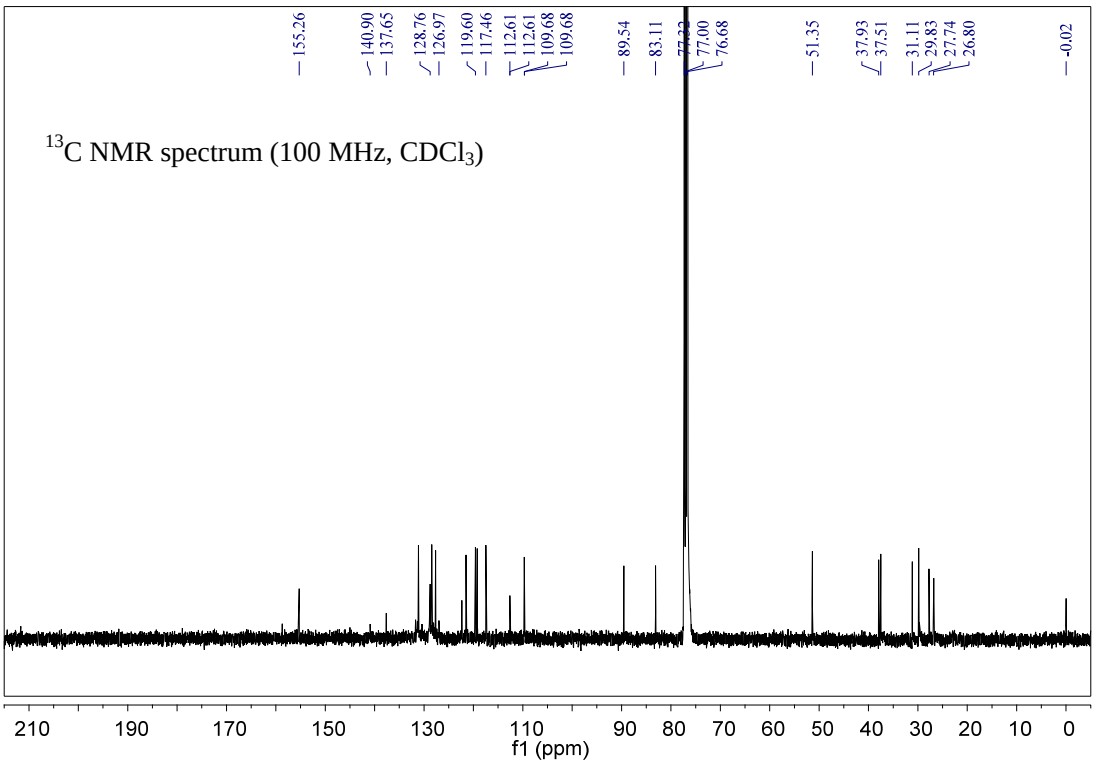
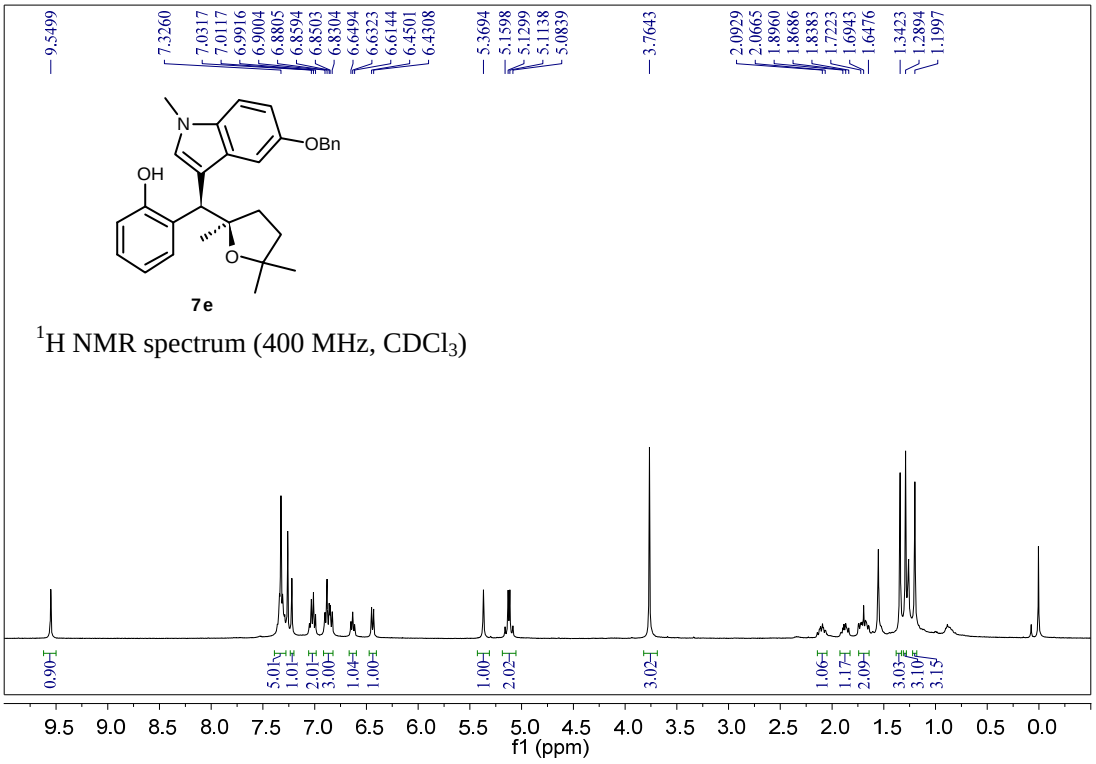
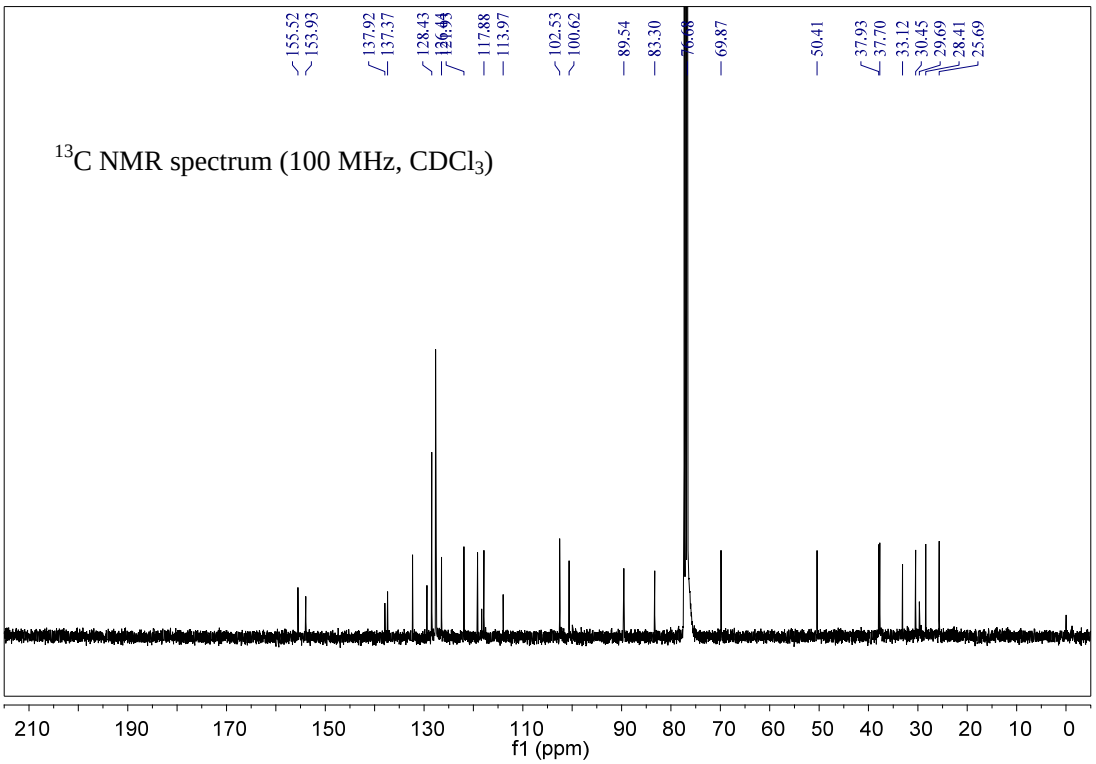
7.9372
7.9173
7.3911
7.2604
7.1769
6.9045
6.6891
6.6865
6.6700
6.6518
4.5408
3.6026
1.8301
1.6673
1.6544
1.6319
1.5251
1.4930
1.4549
1.2310
0.8550
N
Ph
OH
O
7d
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

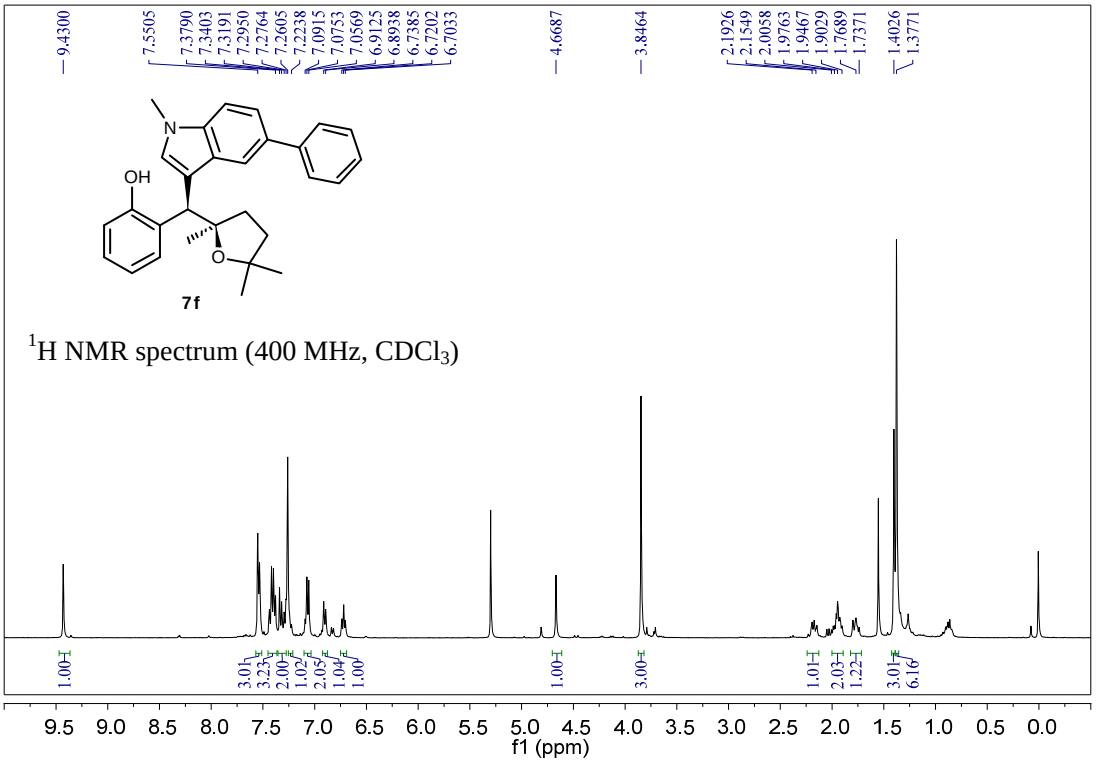

155.26
140.90
137.65
128.76
126.97
119.60
117.46
112.61
112.61
109.68
109.68
89.54
83.11
77.32
77.00
76.68
51.35
37.93
37.51
31.11
29.83
27.74
26.80
-0.02
13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)

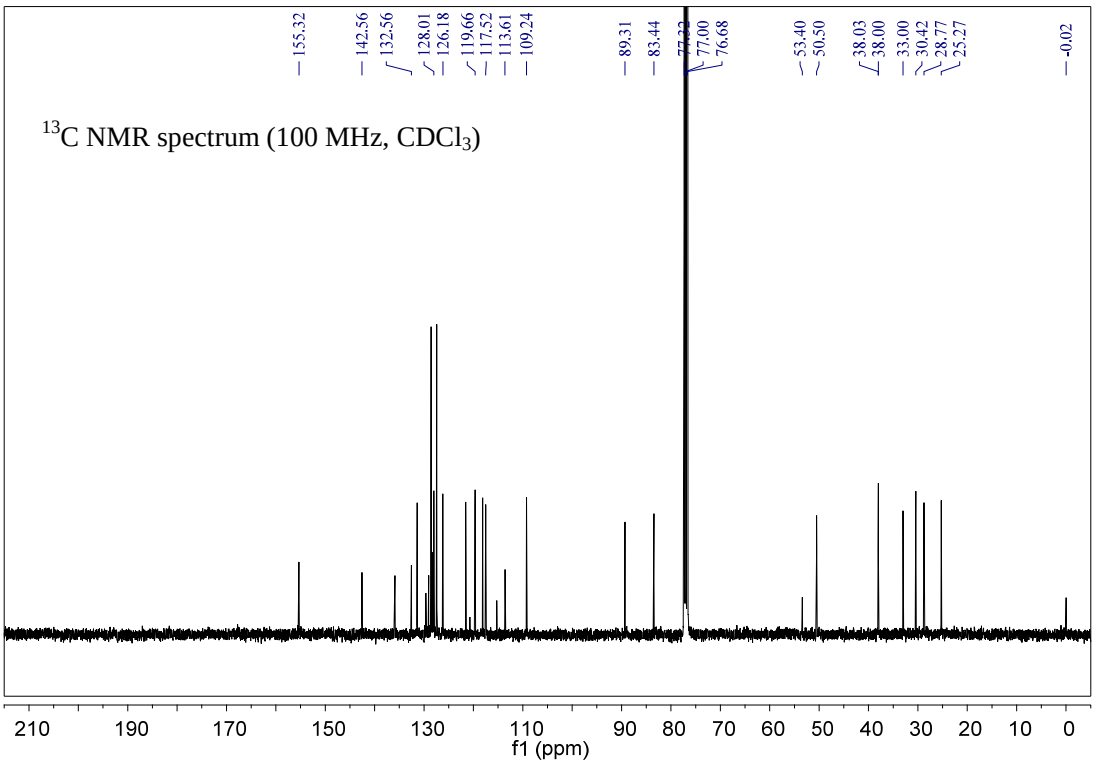


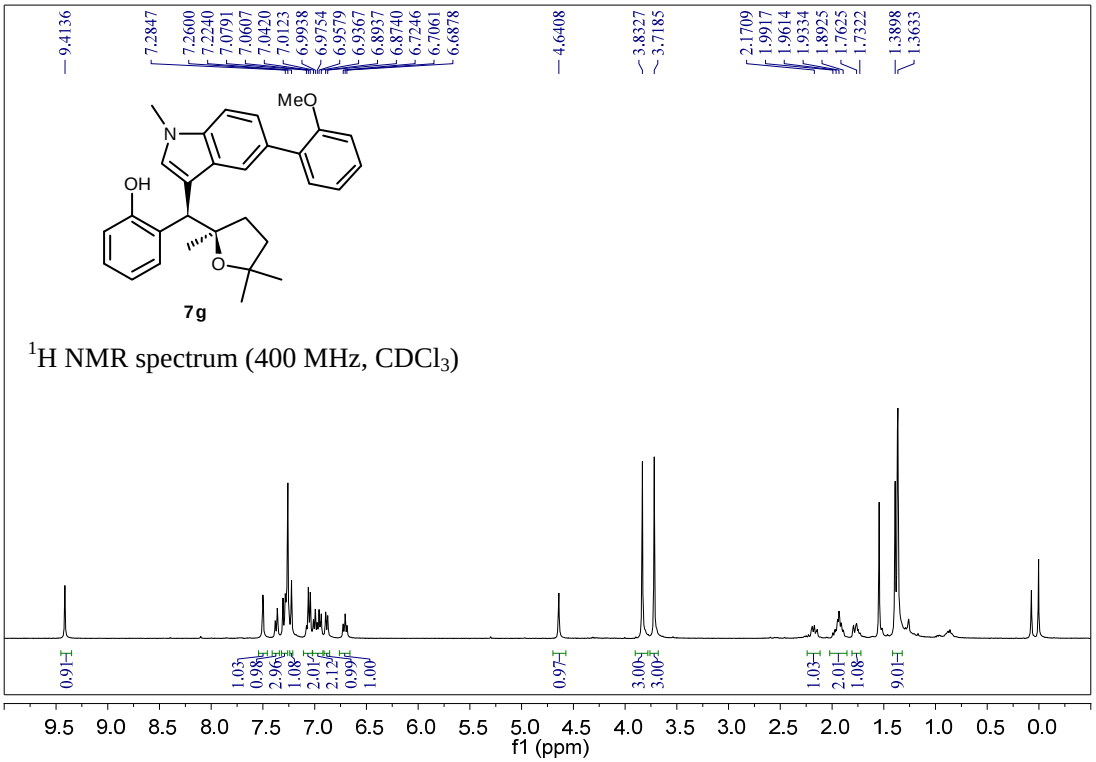
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



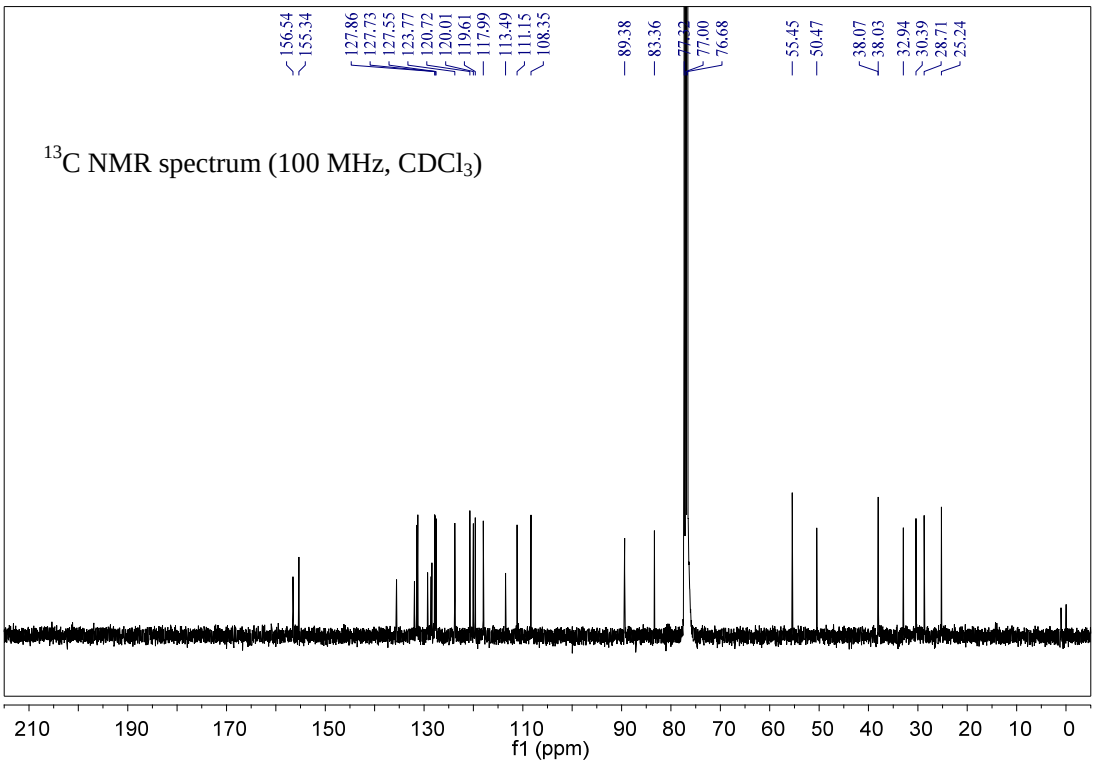
^{13}C NMR spectrum (100 MHz, $CDCl_3$)


9.4300
7.5505
7.3790
7.3403
7.3191
7.2950
7.2764
7.2605
7.2238
7.0915
7.0753
7.0569
6.9125
6.8938
6.7385
6.7202
6.7033
4.6687
3.8464
2.1926
2.1549
2.0058
1.9763
1.9467
1.9029
1.7689
1.7371
1.4026
1.3771
OH
N
O
7f
1H NMR spectrum (400 MHz, CDCl3)
1.00
3.01
3.23
2.00
1.02
2.05
1.04
1.00
1.00
3.00
1.01
2.03
1.22
3.01
6.16
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

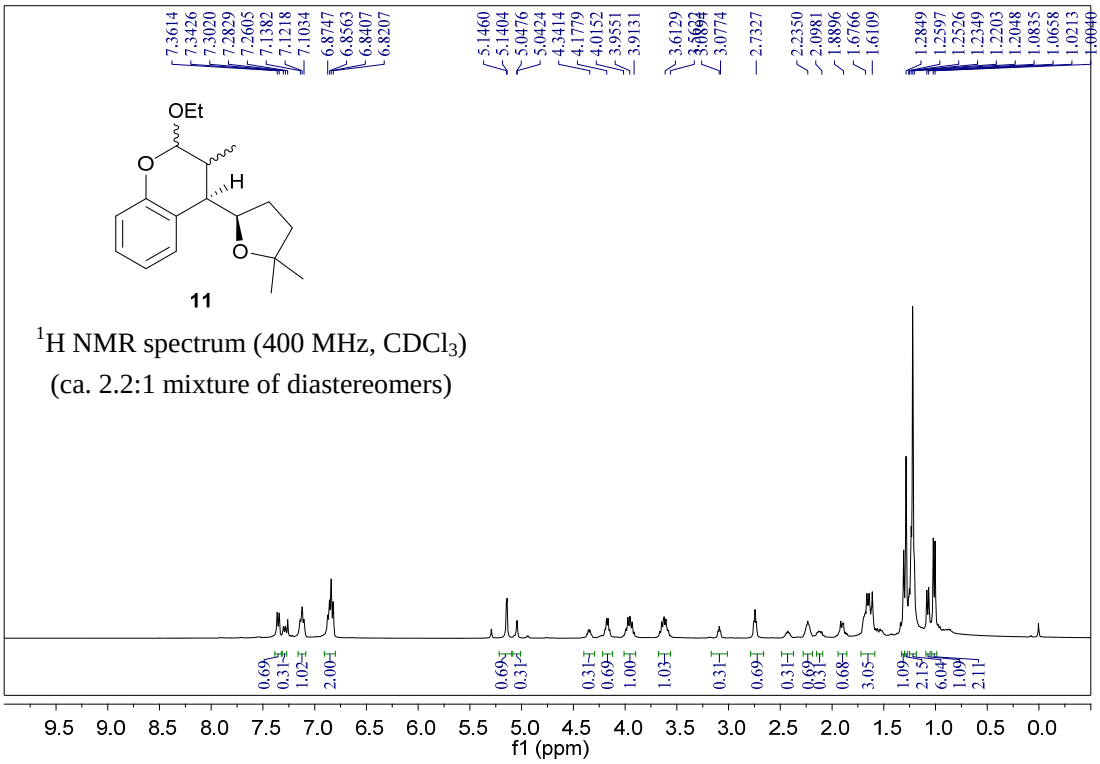

155.32
142.56
132.56
128.01
126.18
119.66
117.52
113.61
109.24
89.31
83.44
77.32
77.00
76.68
53.40
50.50
38.03
38.00
33.00
30.42
28.77
25.27
-0.02
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

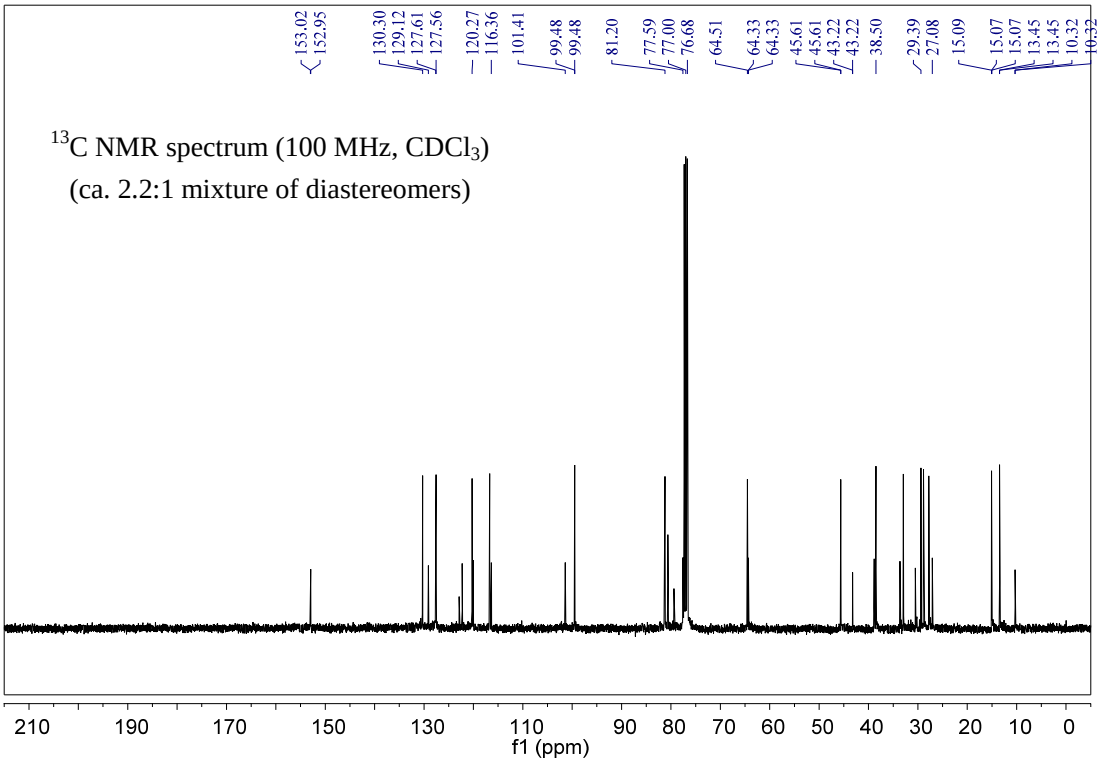


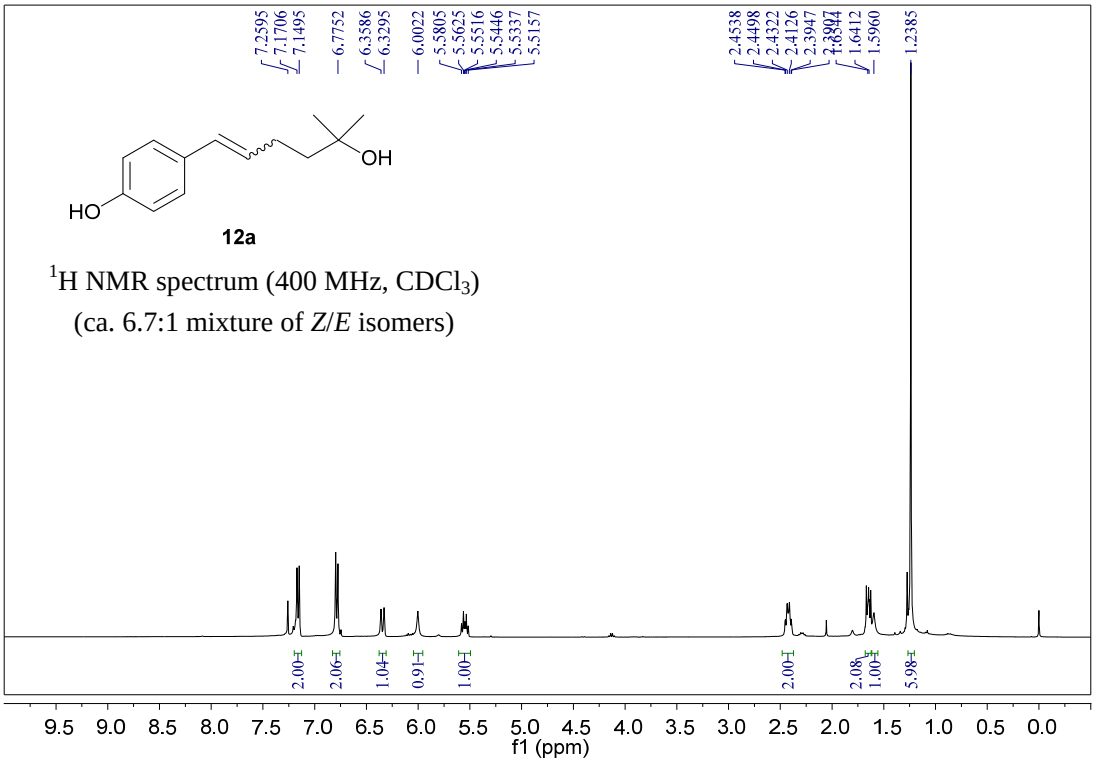
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)


OEt
O
H
O
11
^{1}H NMR spectrum (400 MHz, $CDCl_3$)
(ca. 2.2:1 mixture of diastereomers)
f1 (ppm)

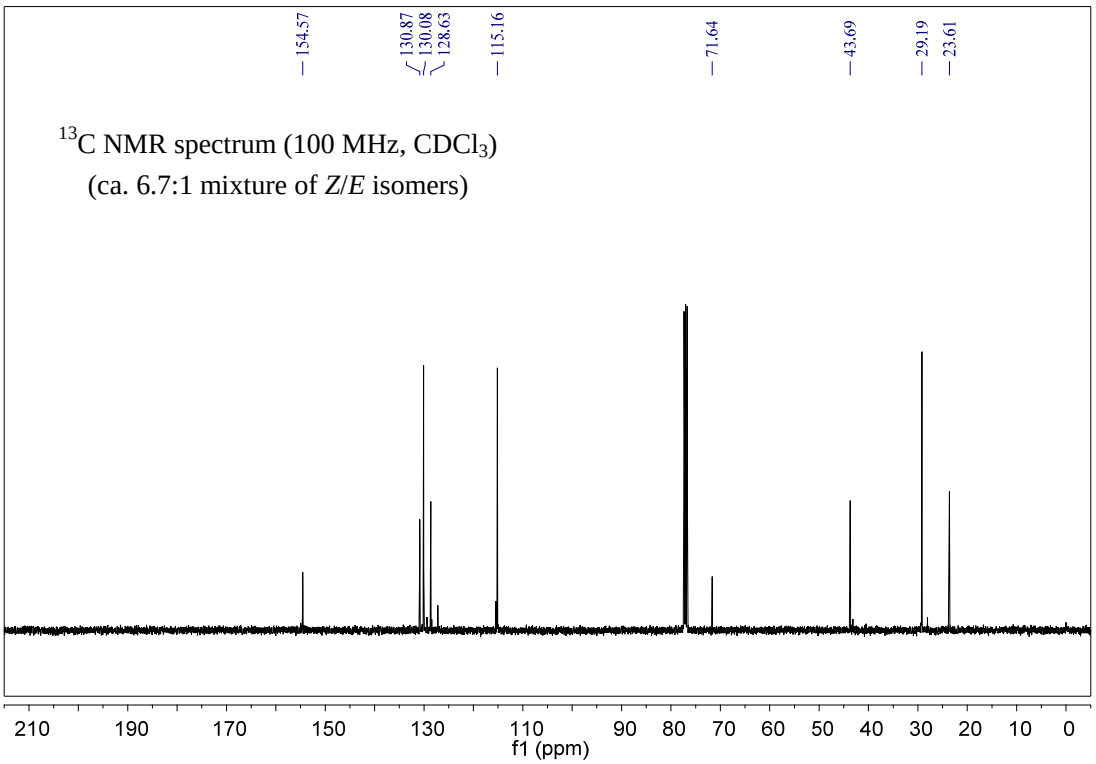

^{13}C NMR spectrum (100 MHz, $CDCl_3$)
(ca. 2.2:1 mixture of diastereomers)
f1 (ppm)



12a

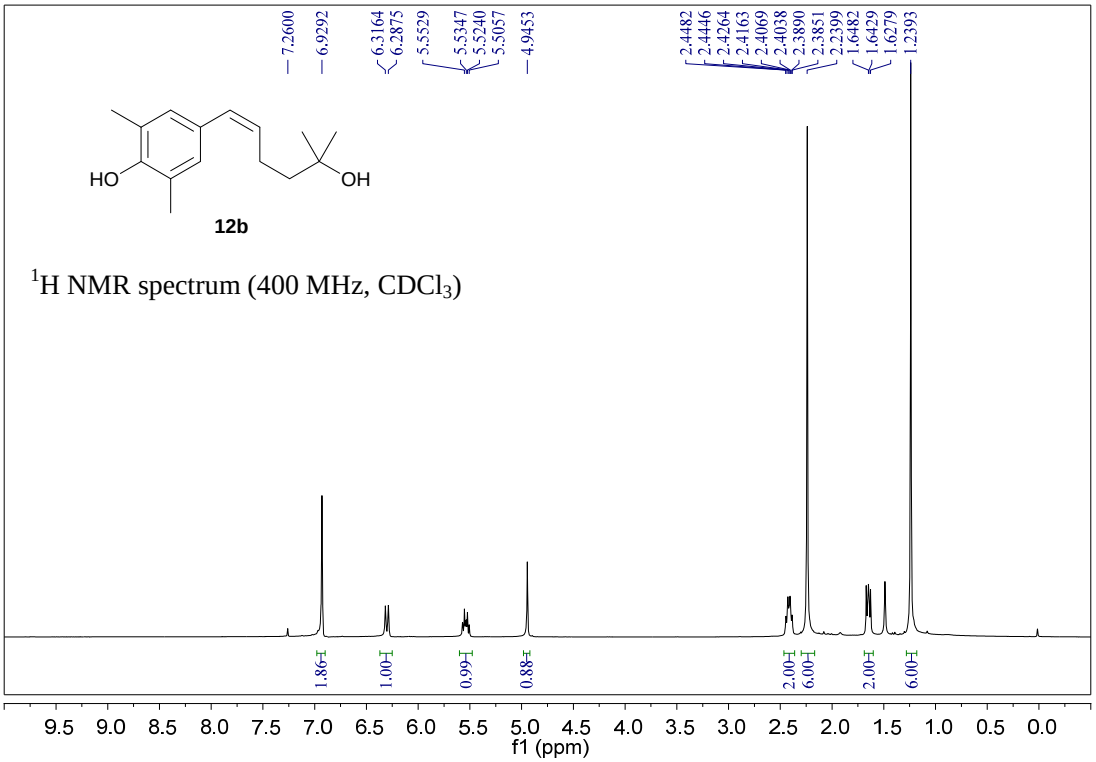
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

(ca. 6.7:1 mixture of *Z*/*E* isomers)

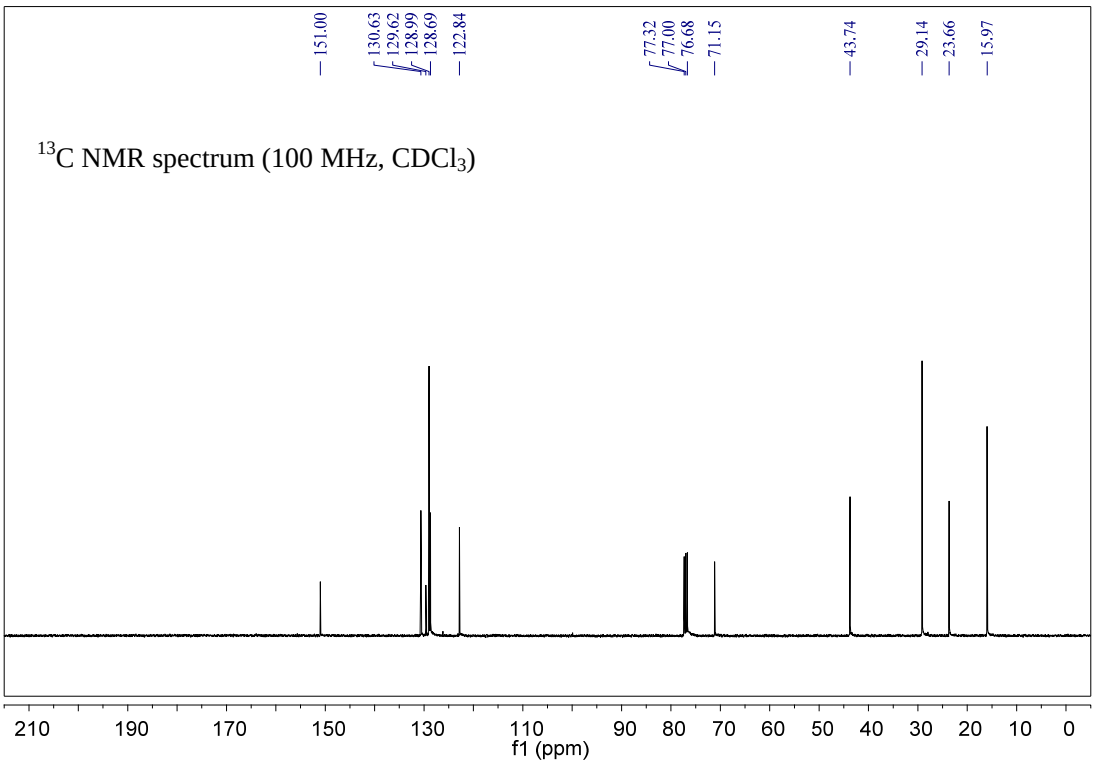


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

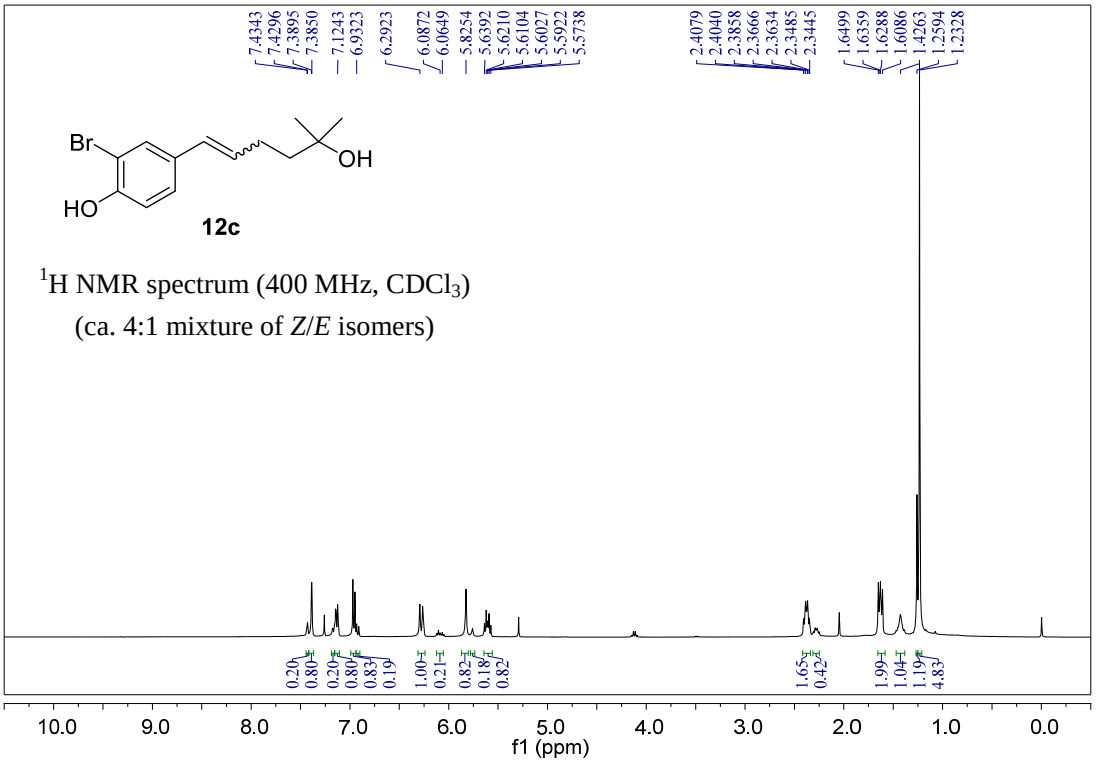
(ca. 6.7:1 mixture of *Z*/*E* isomers)



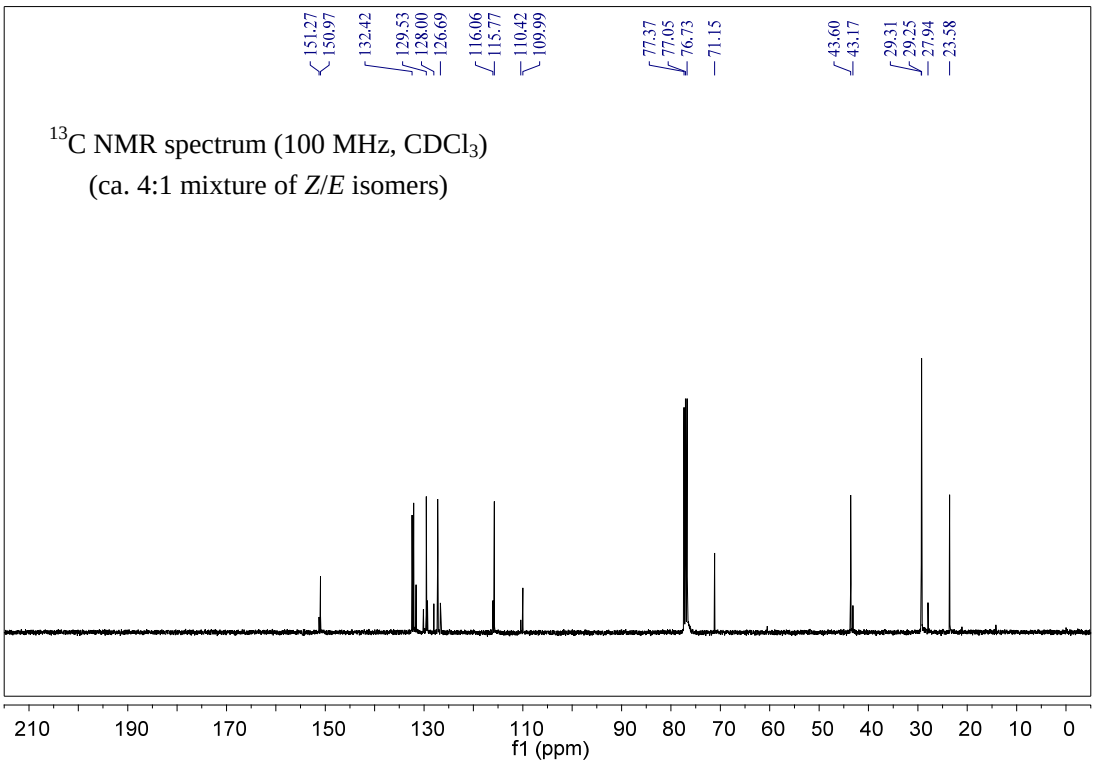
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



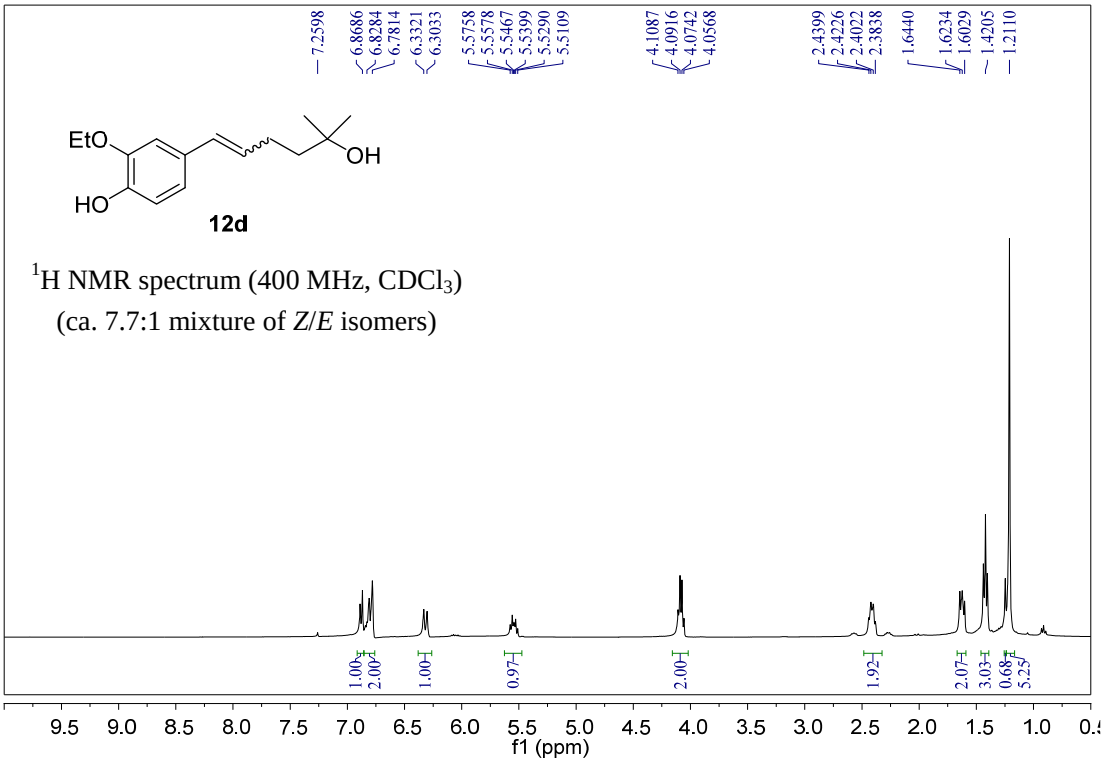
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



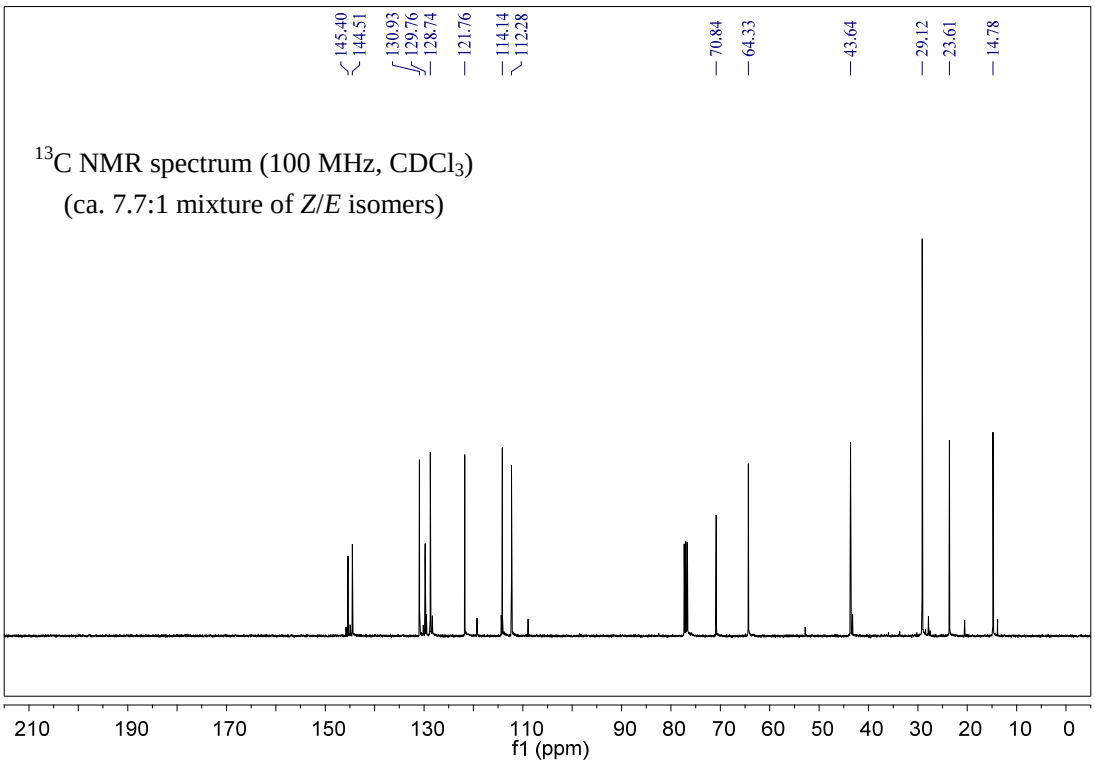
^{1}H NMR spectrum (400 MHz, $CDCl_3$)
(ca. 4:1 mixture of *Z*/*E* isomers)



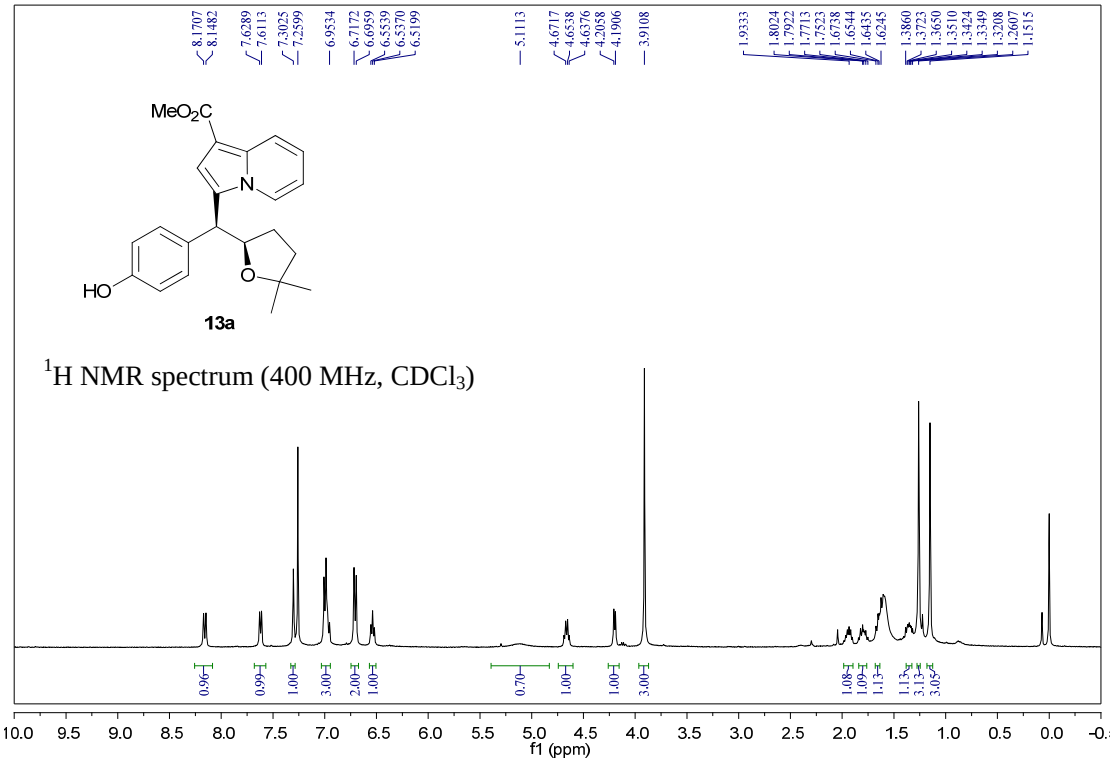
^{13}C NMR spectrum (100 MHz, $CDCl_3$)
(ca. 4:1 mixture of *Z*/*E* isomers)

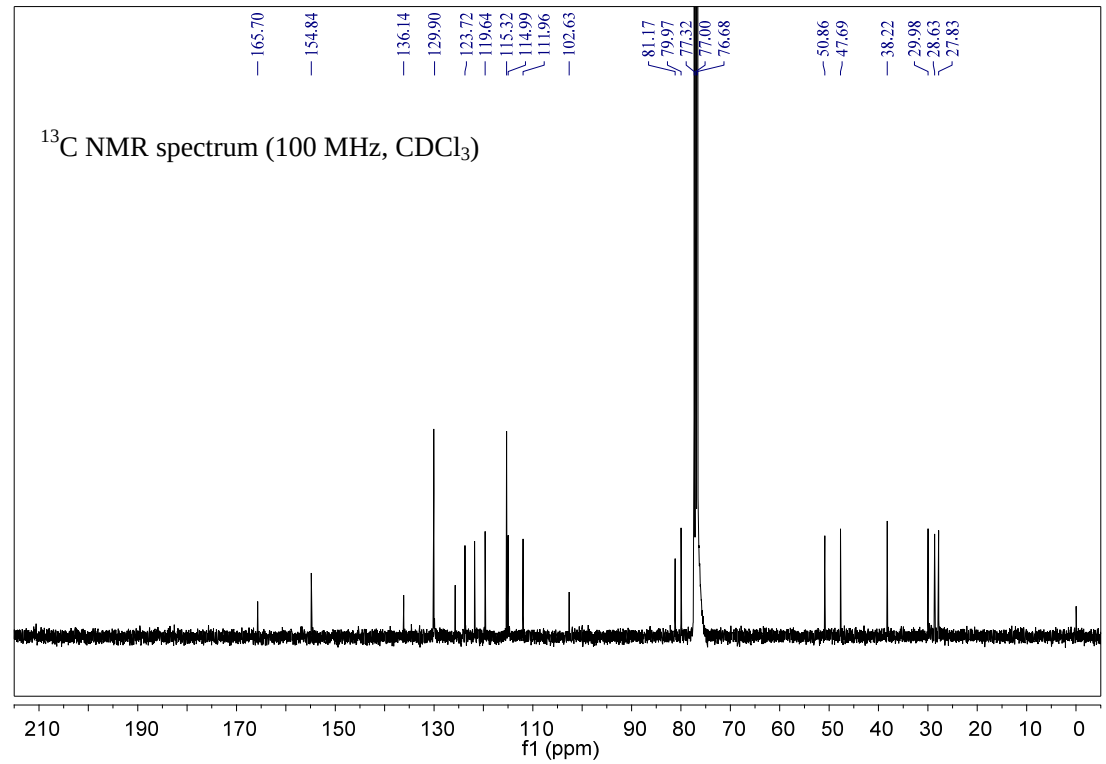


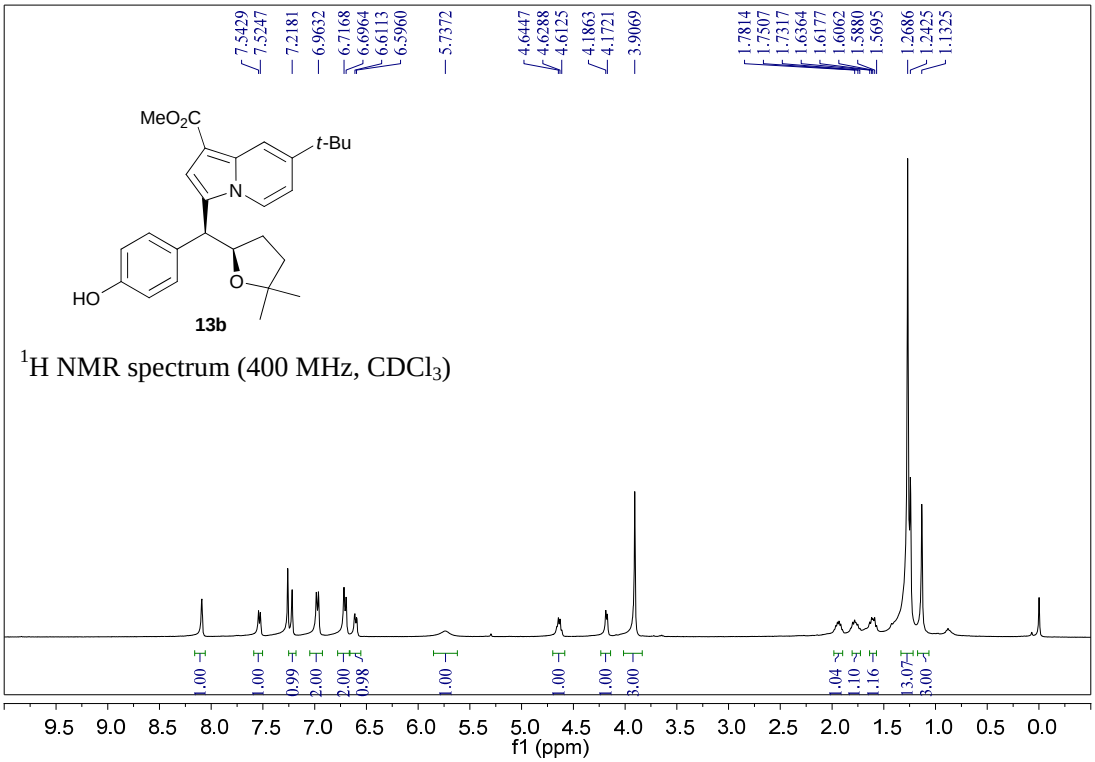
^{1}H NMR spectrum (400 MHz, $CDCl_3$)
(ca. 7.7:1 mixture of *Z*/*E* isomers)



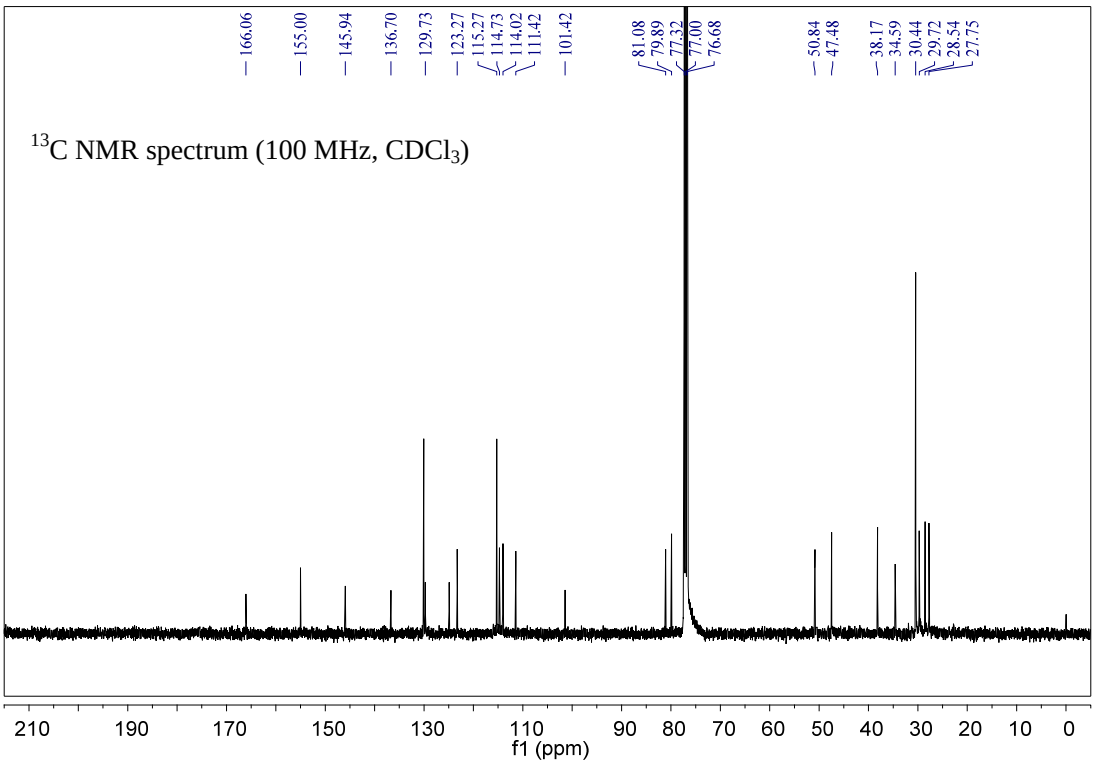
^{13}C NMR spectrum (100 MHz, $CDCl_3$)
(ca. 7.7:1 mixture of *Z*/*E* isomers)


MeO2C
N
HO
O
13a
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

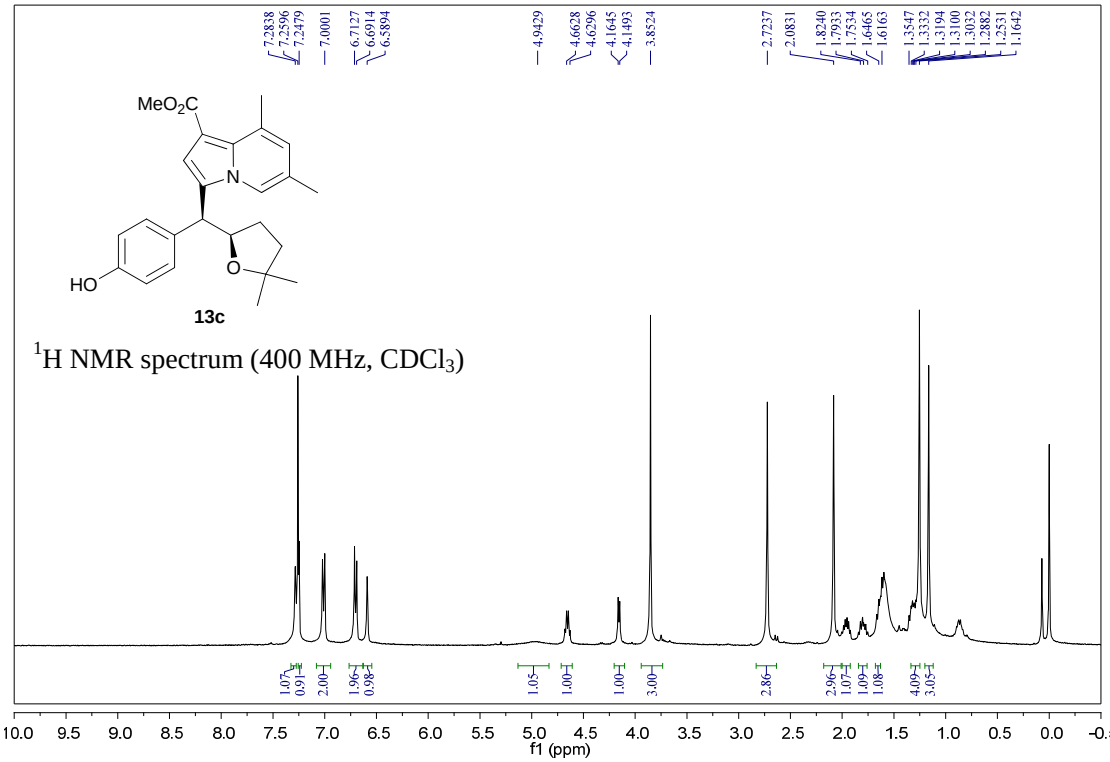

13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)

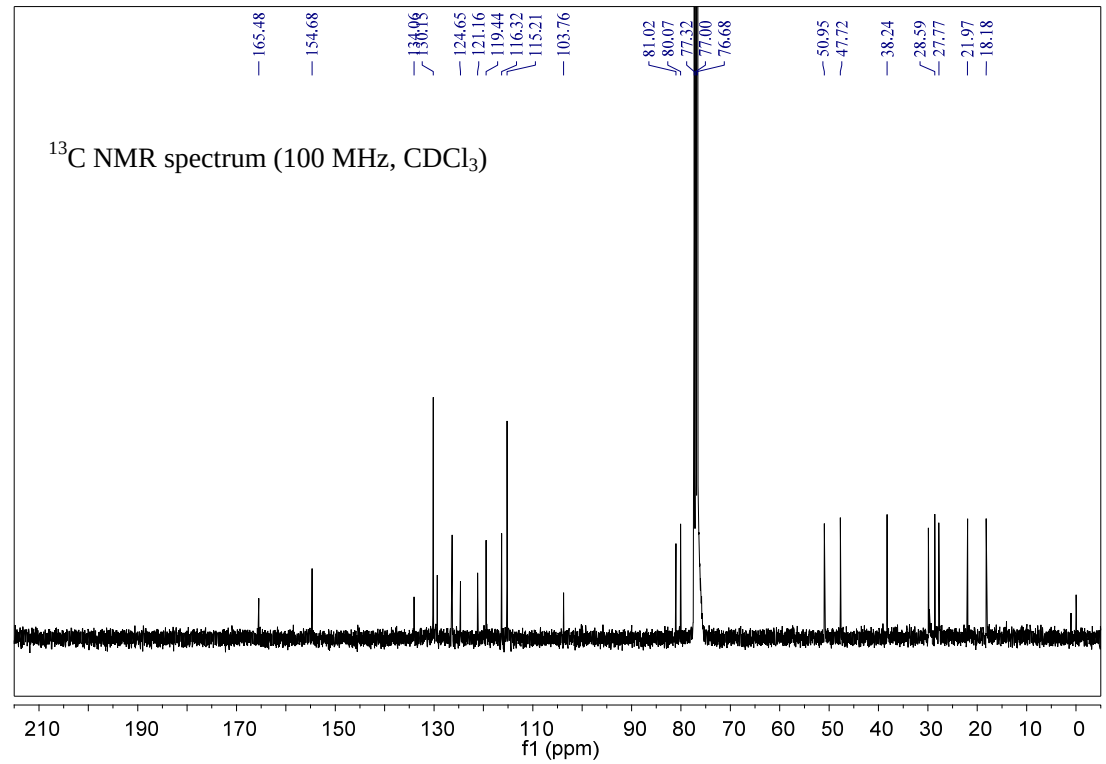


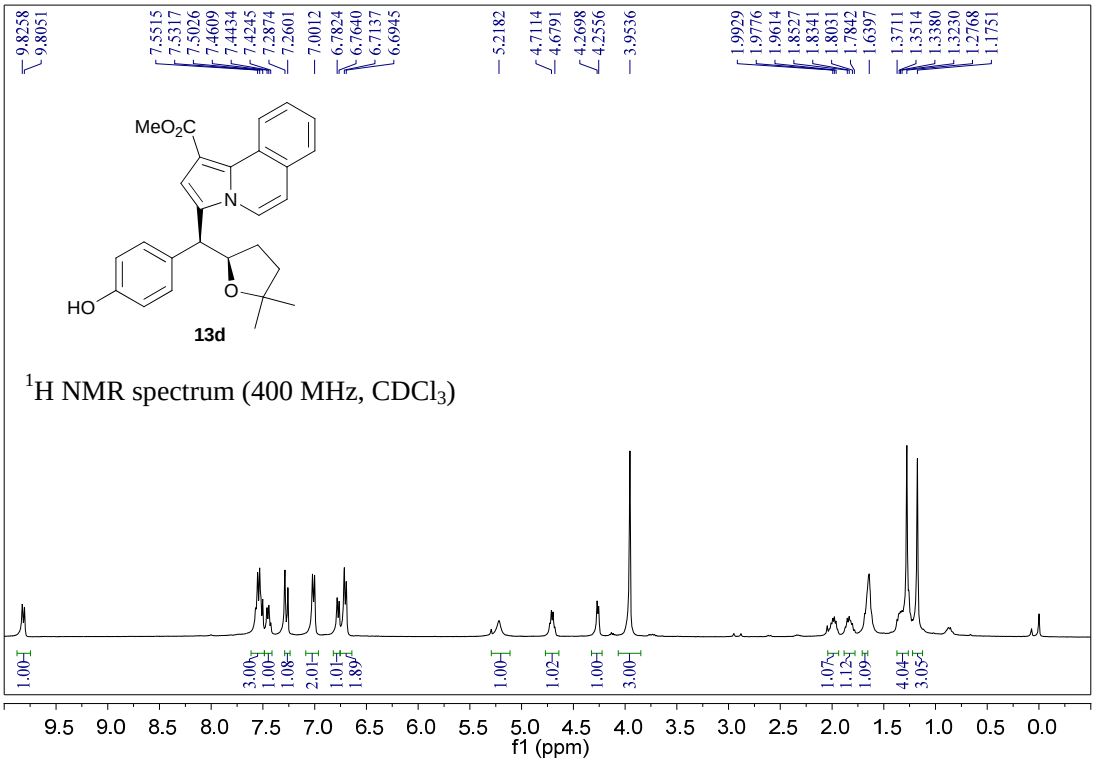
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)


MeO2C
N
HO
O
13c
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)


13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)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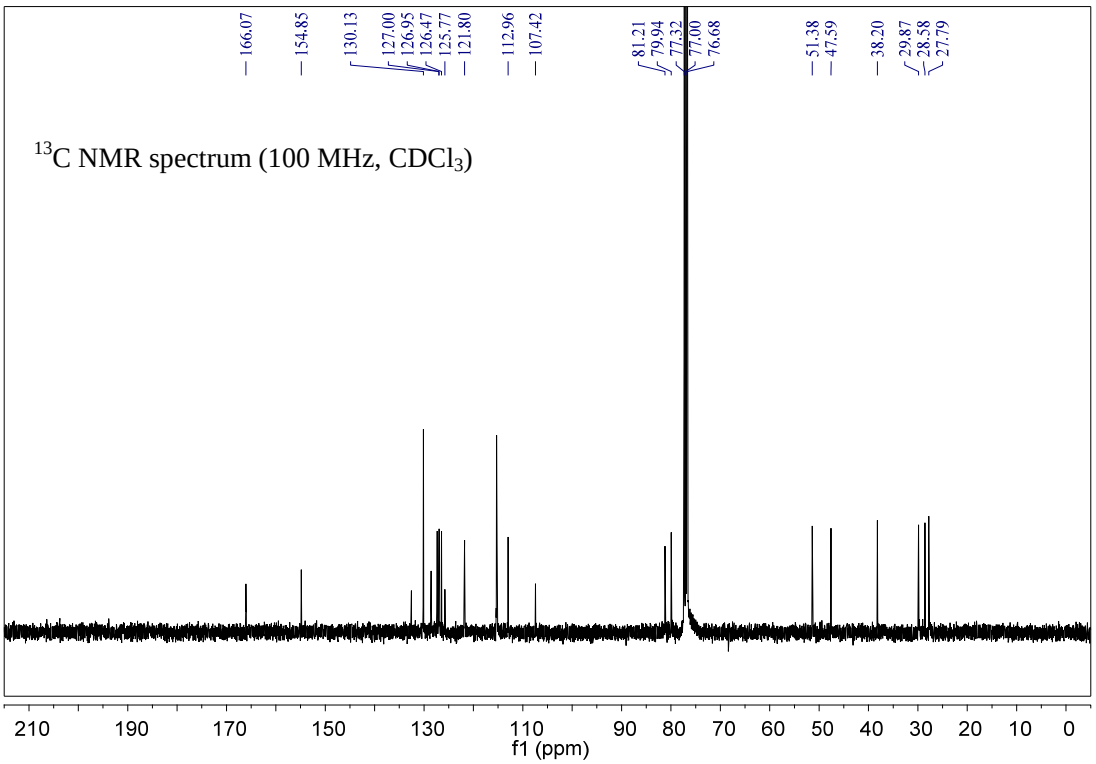
7.5317
7.5026
7.4609
7.4434
7.4245
7.2874
7.2601
7.0012
6.7824
6.7640
6.7137
6.6945
5.2182
4.7114
4.6791
4.2698
4.2556
3.9536
1.9929
1.9776
1.9614
1.8527
1.8341
1.8031
1.7842
1.6397
1.3711
1.3514
1.3380
1.3230
1.2768
1.1751
MeO2C
N
O
HO
13d
1H NMR spectrum (400 MHz, CDCl3)
1.00
3.00
1.00
1.08
2.01
1.01
1.89
1.00
1.02
1.00
3.00
1.07
1.12
1.09
4.04
3.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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154.85
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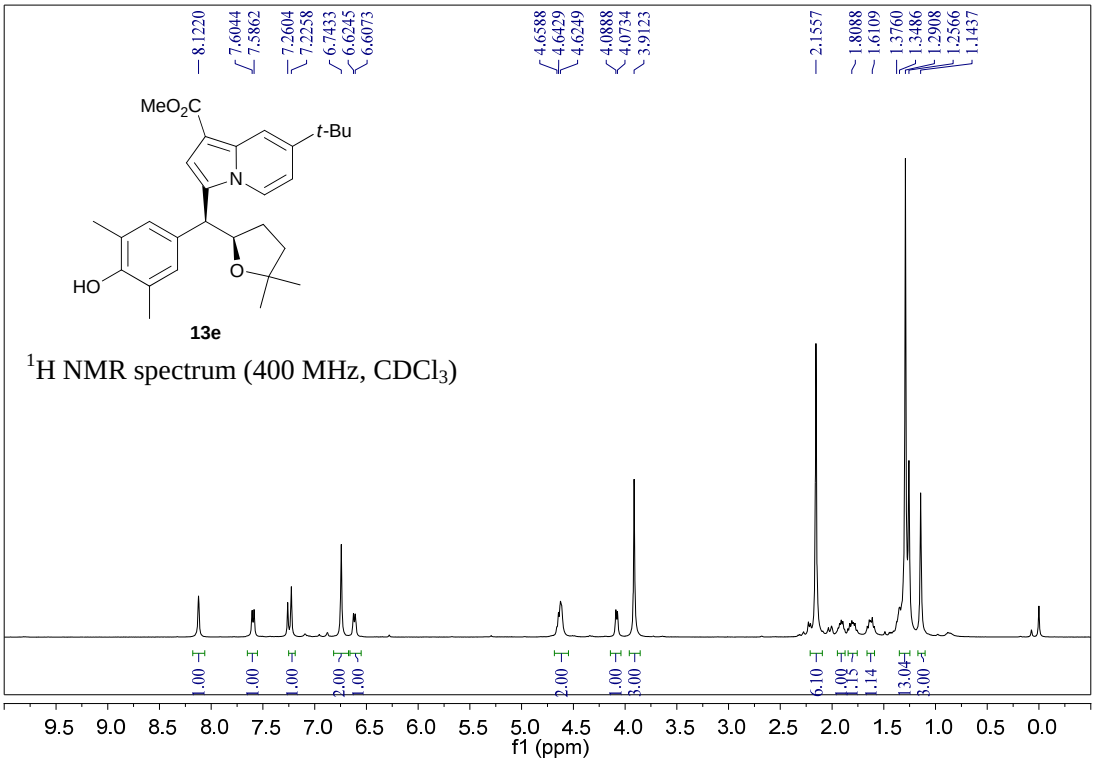
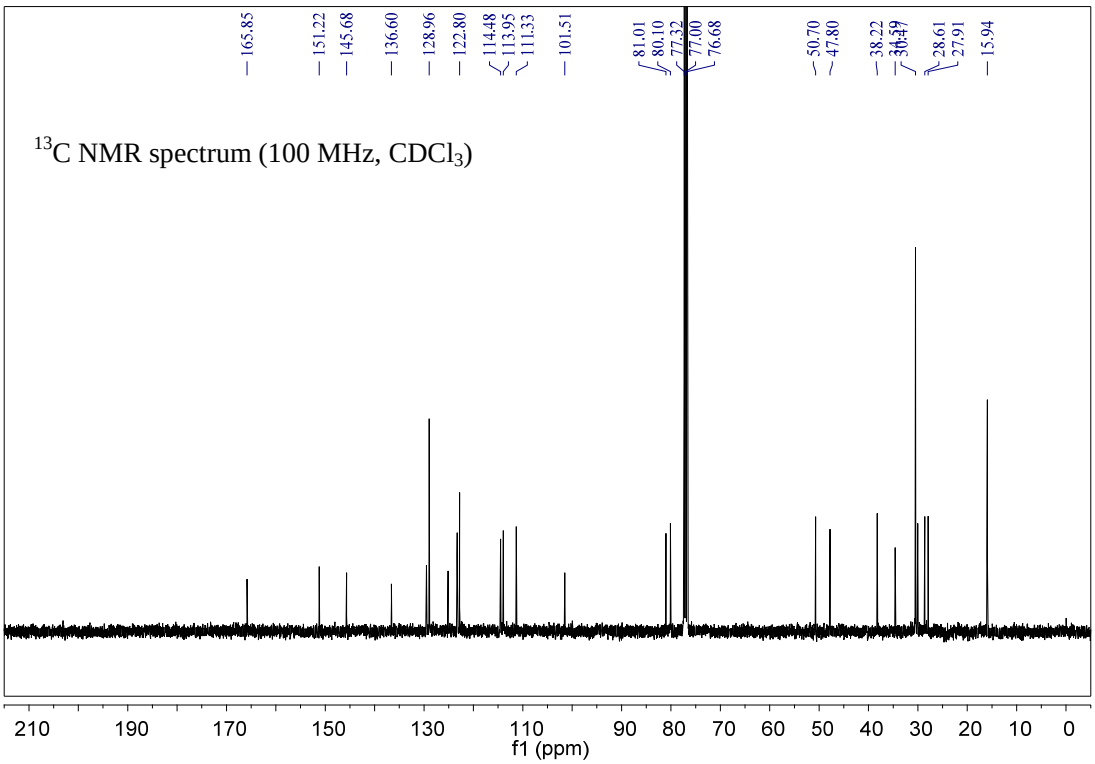
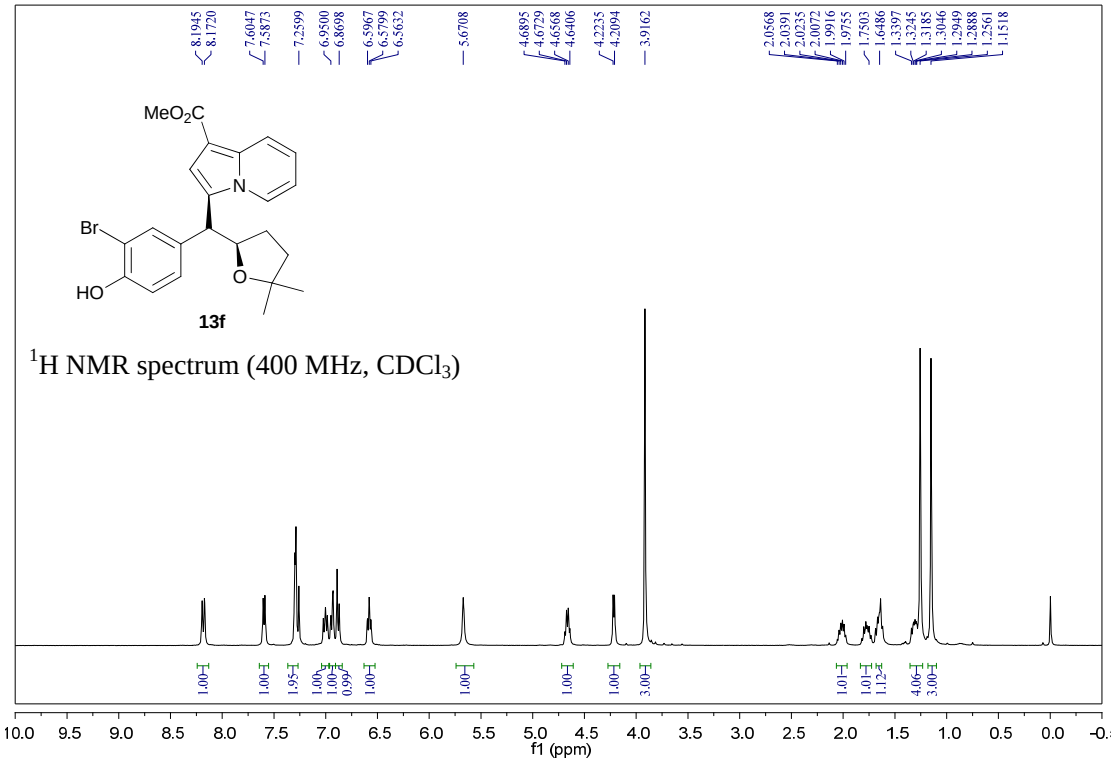
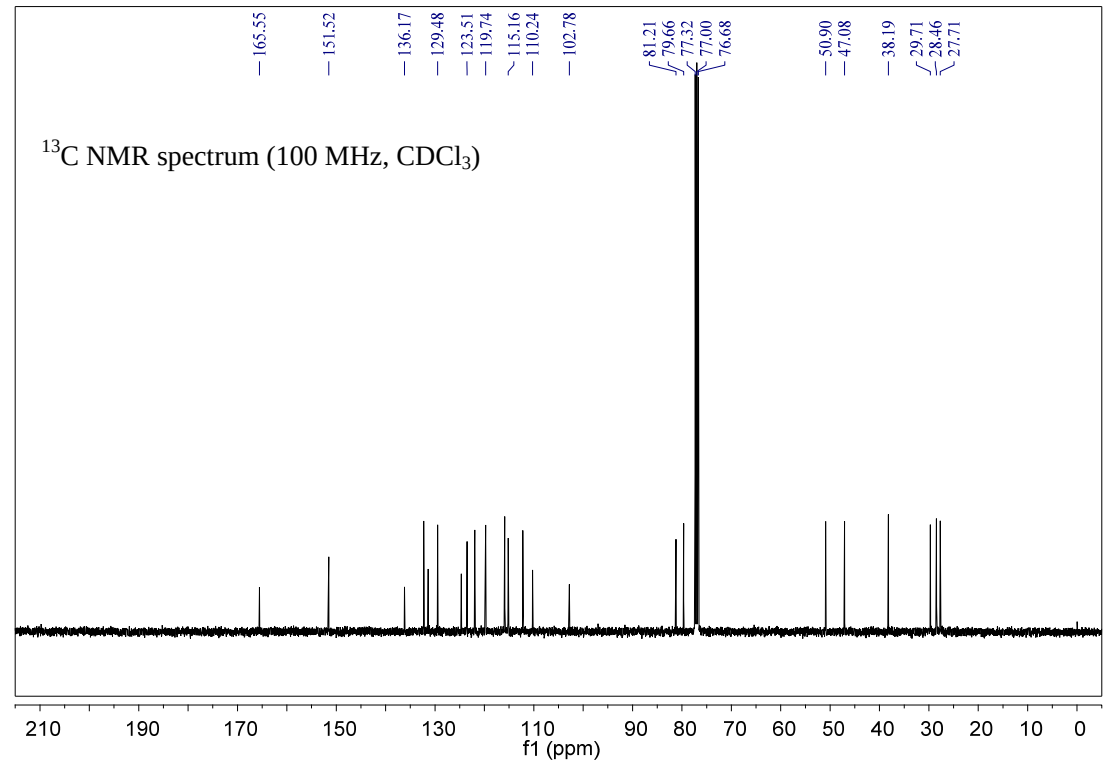
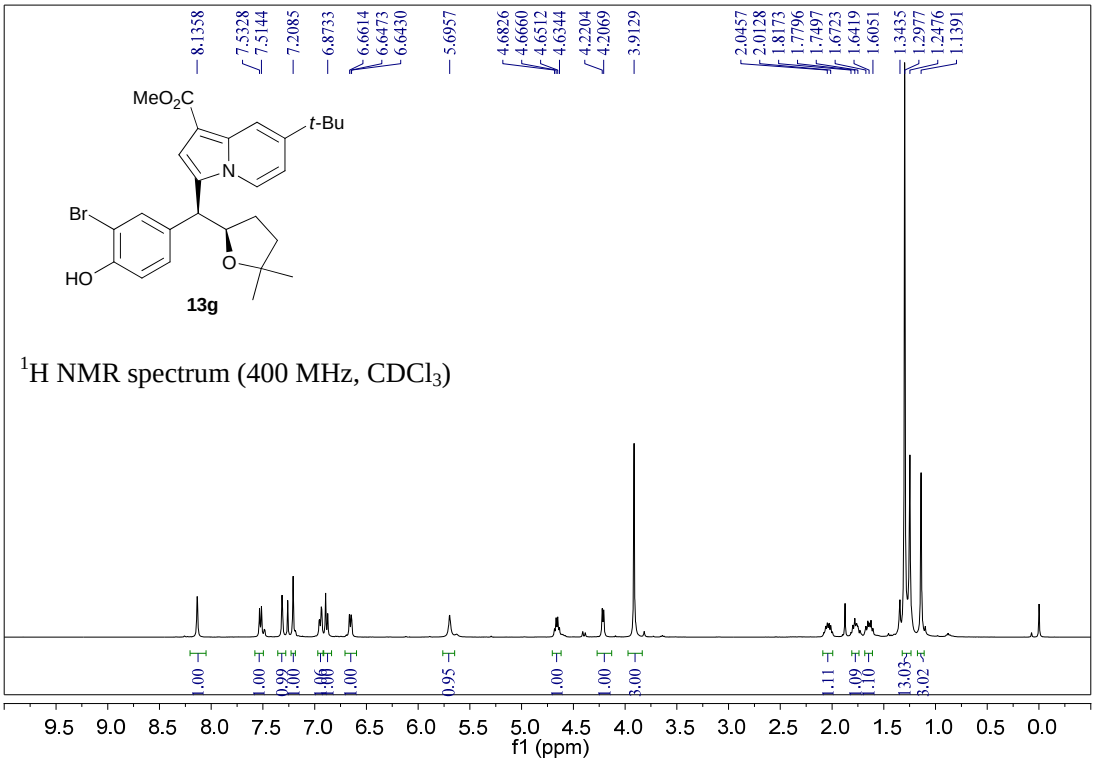
127.00
126.95
126.47
125.77
121.80
112.96
107.42
81.21
79.94
77.32
77.00
76.68
51.38
47.59
38.20
29.87
28.58
27.79
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

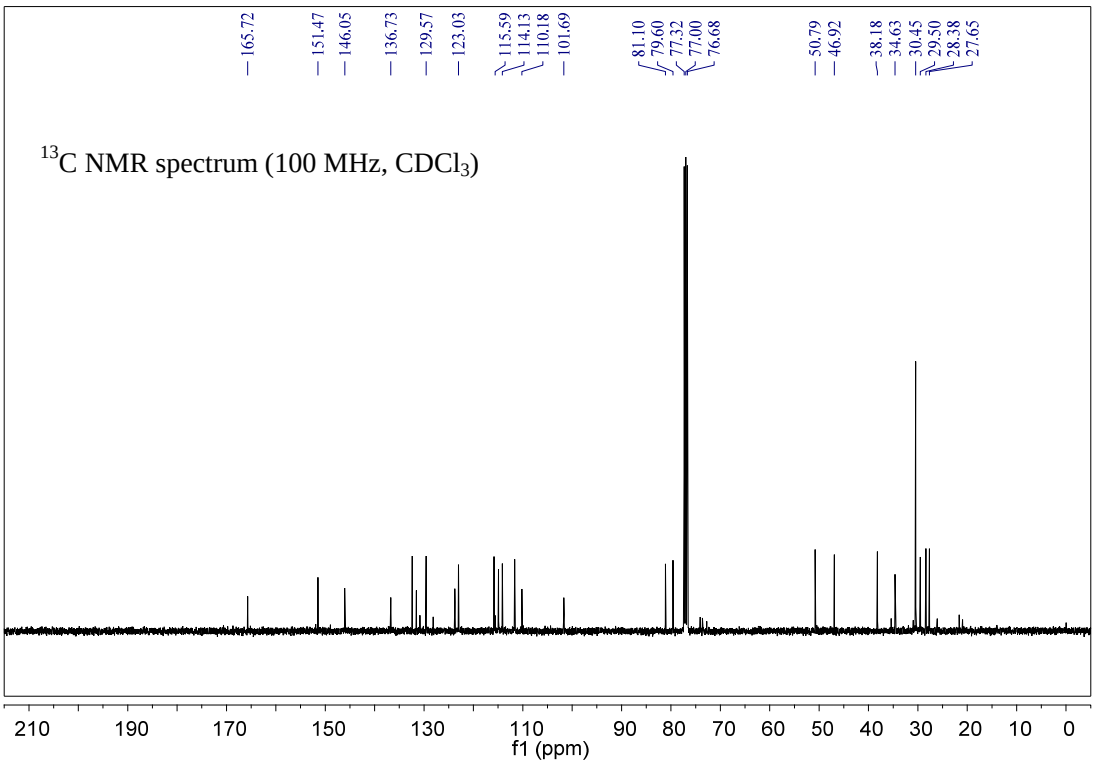

MeO2C
t-Bu
N
HO
O
13e
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

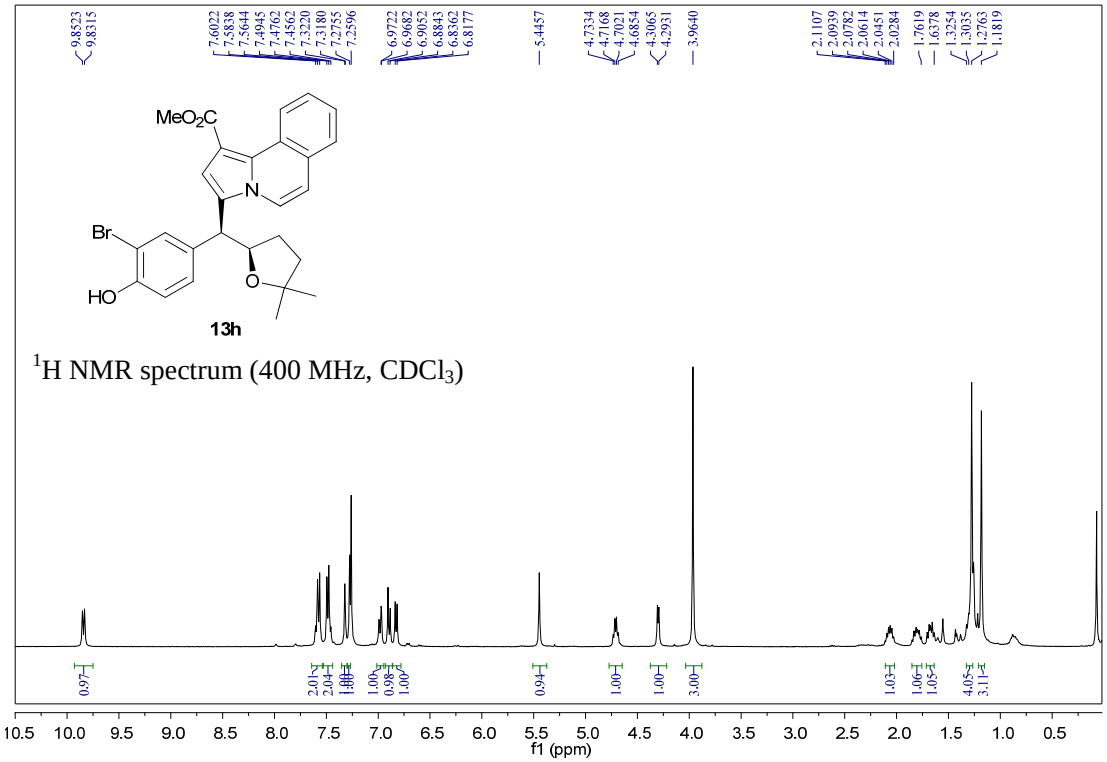

13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)

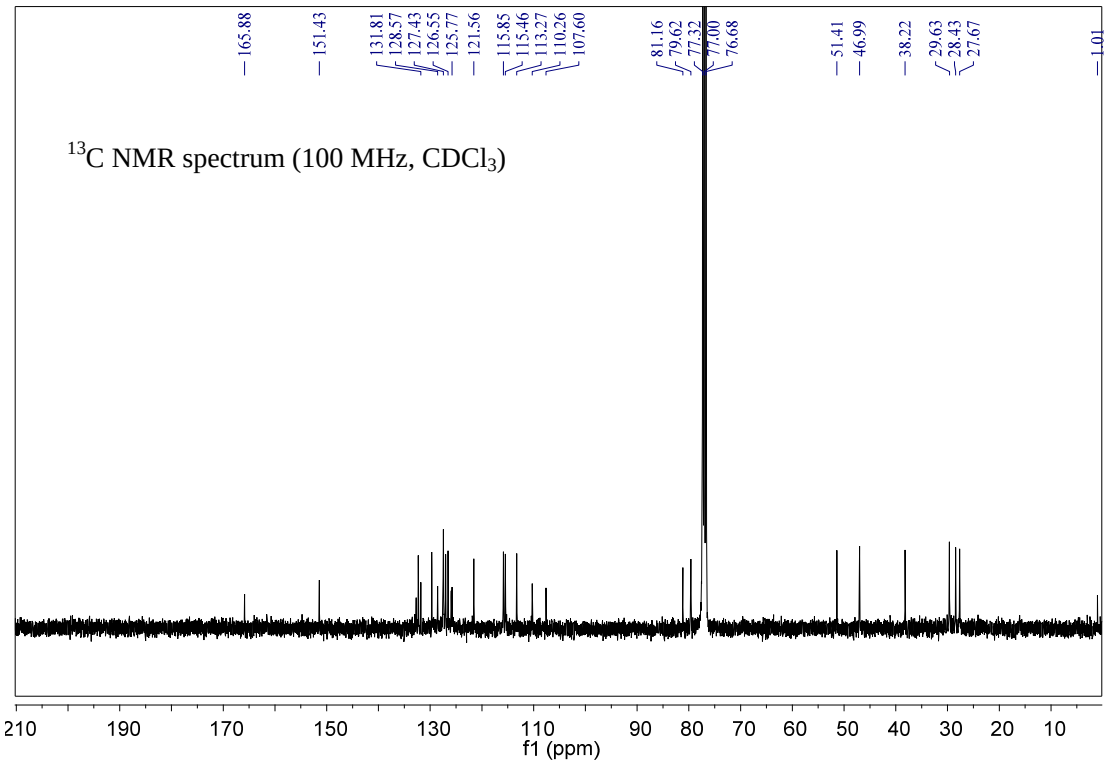

MeO2C
N
Br
HO
O
13f
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

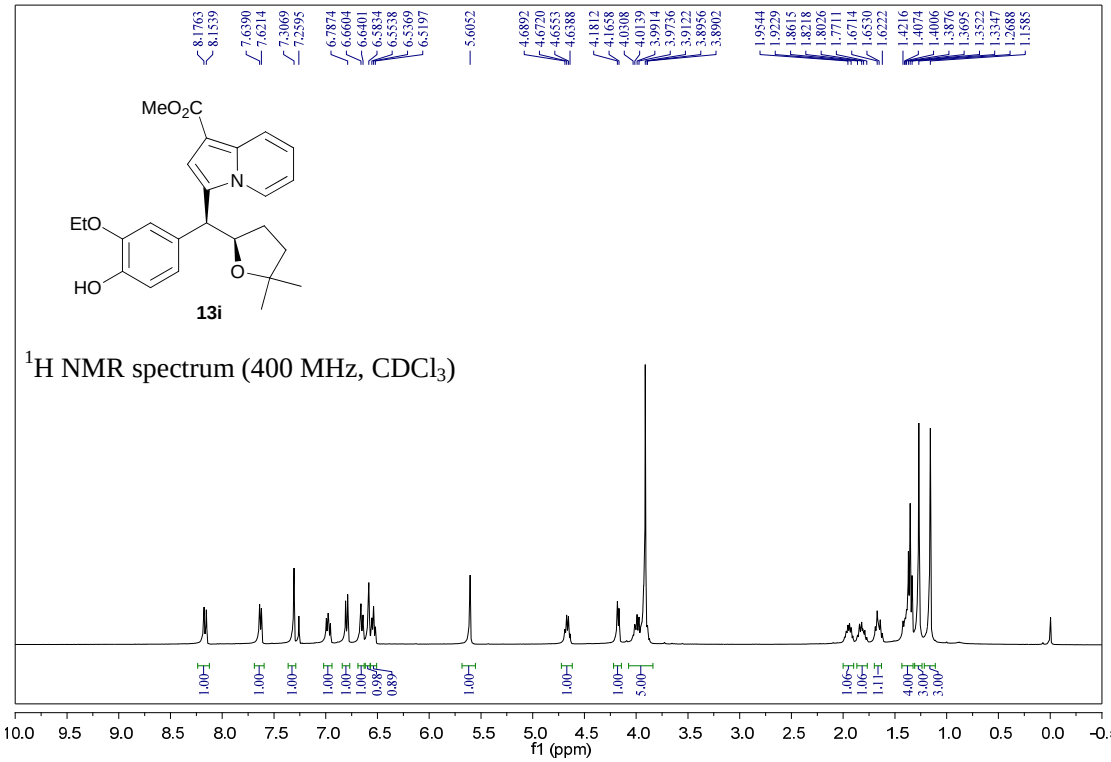

13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)

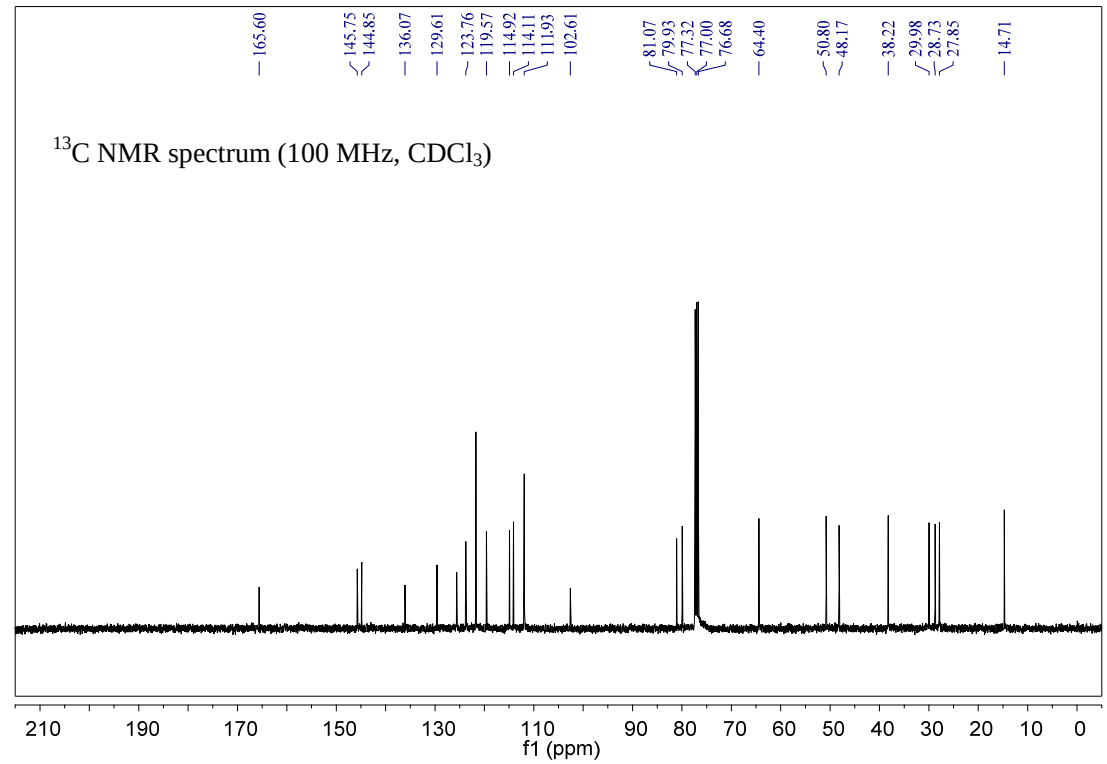

8.1358
7.5328
7.5144
7.2085
6.8733
6.6614
6.6473
6.6430
5.6957
4.6826
4.6660
4.6512
4.6344
4.2204
4.2069
3.9129
2.0457
2.0128
1.8173
1.7796
1.7497
1.6723
1.6419
1.6051
1.3435
1.2977
1.2476
1.1391
MeO2C
t-Bu
N
Br
HO
O
13g
1H NMR spectrum (400 MHz, CDCl3)
1.00
1.00
0.99
1.00
1.00
1.00
0.95
1.00
1.00
3.00
1.11
1.09
1.10
13.03
3.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

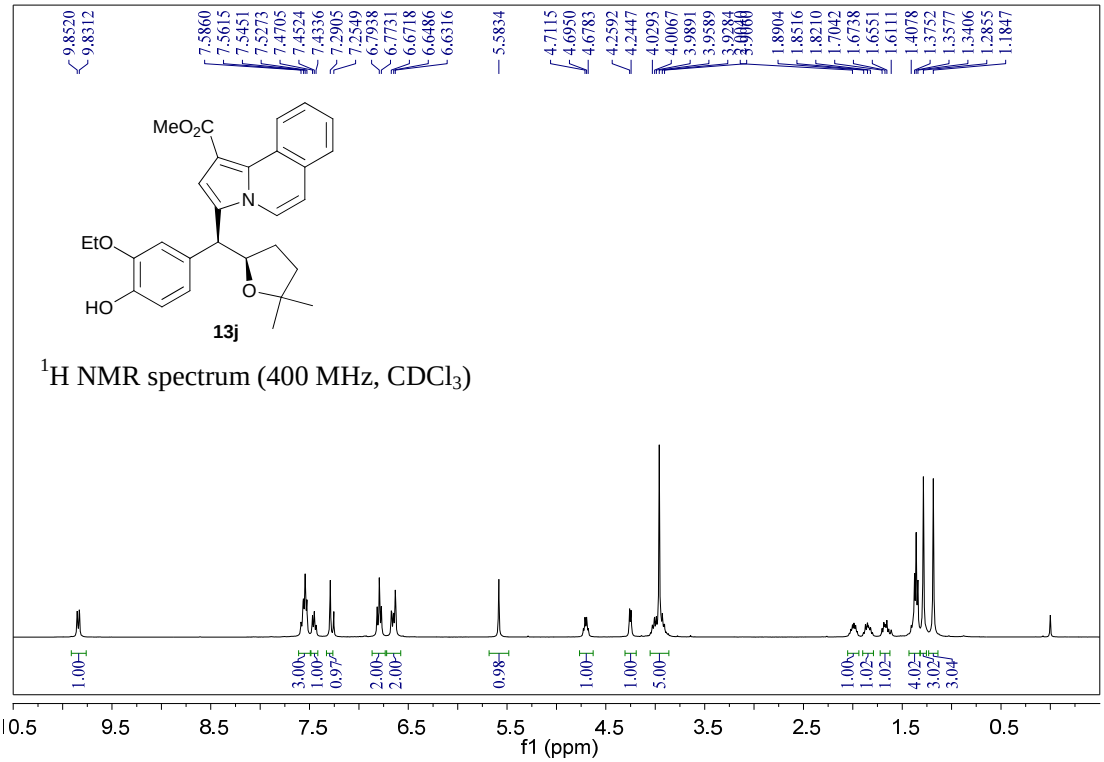

165.72
151.47
146.05
136.73
129.57
123.03
115.59
114.13
110.18
101.69
81.10
79.60
77.32
77.00
76.68
50.79
46.92
38.18
34.63
30.45
29.50
28.38
27.65
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


MeO2C
N
Br
HO
O
13h
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

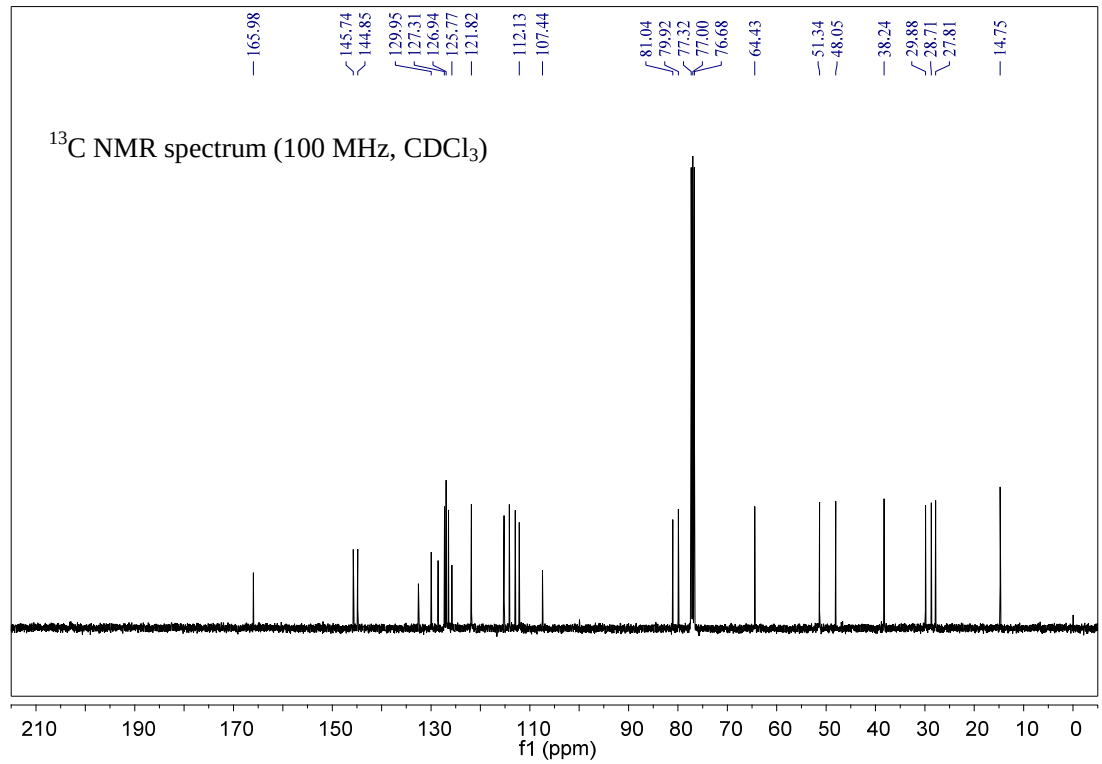

13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)


MeO2C
N
EtO
HO
O
13i
1H NMR spectrum (400 MHz, CDCl3)
f1 (ppm)

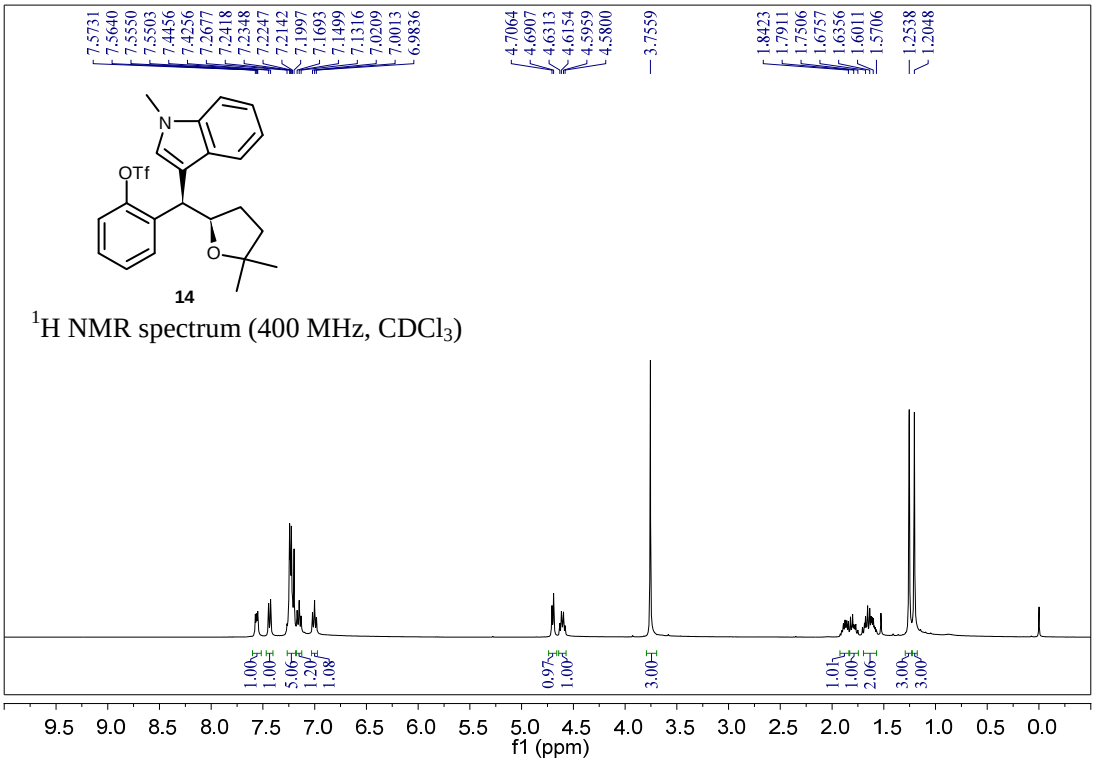

13C NMR spectrum (100 MHz, CDCl3)
f1 (ppm)



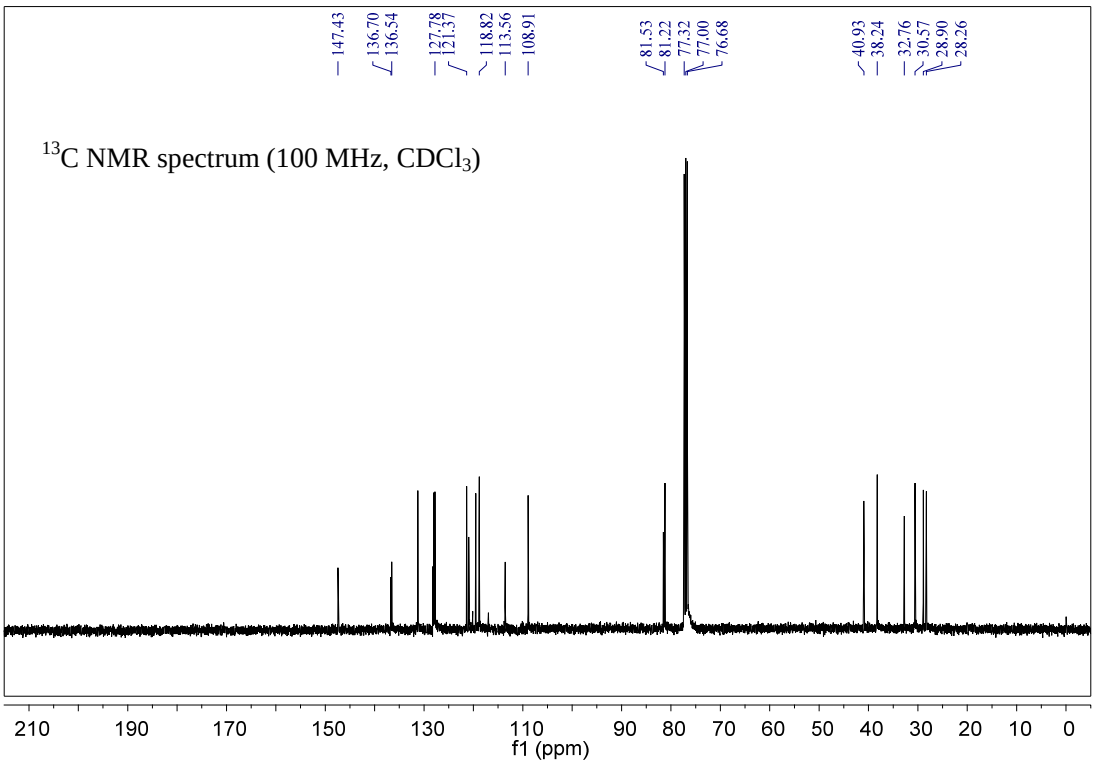
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



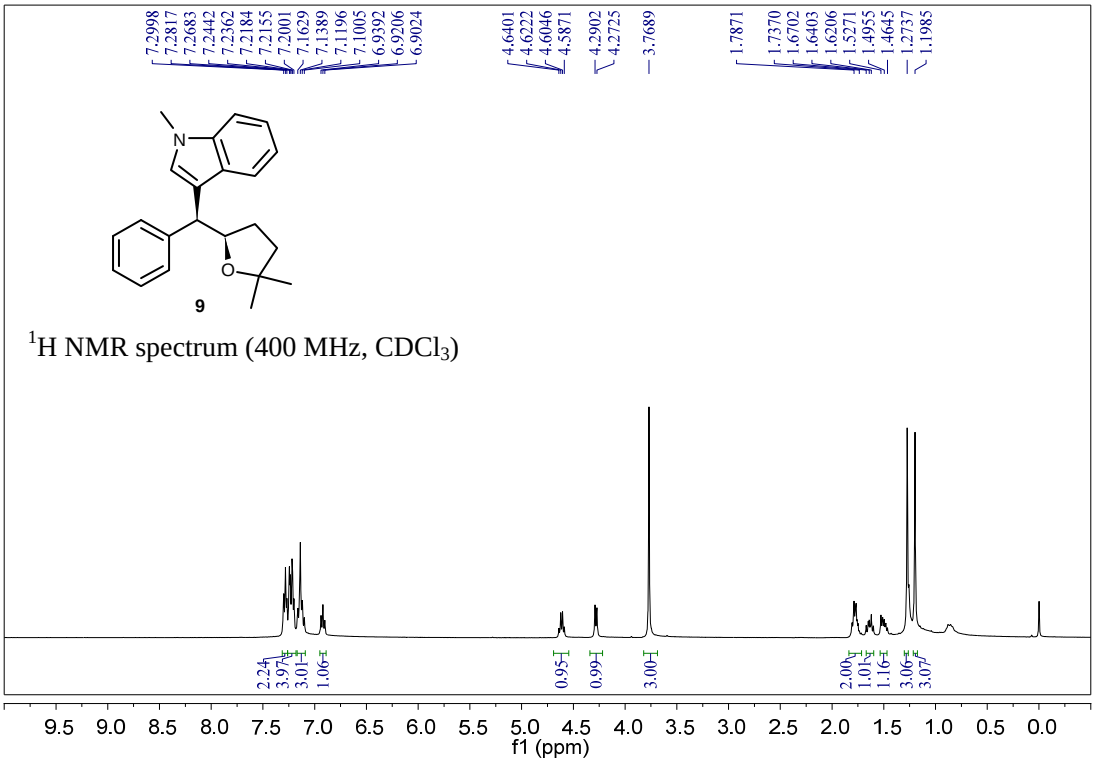
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



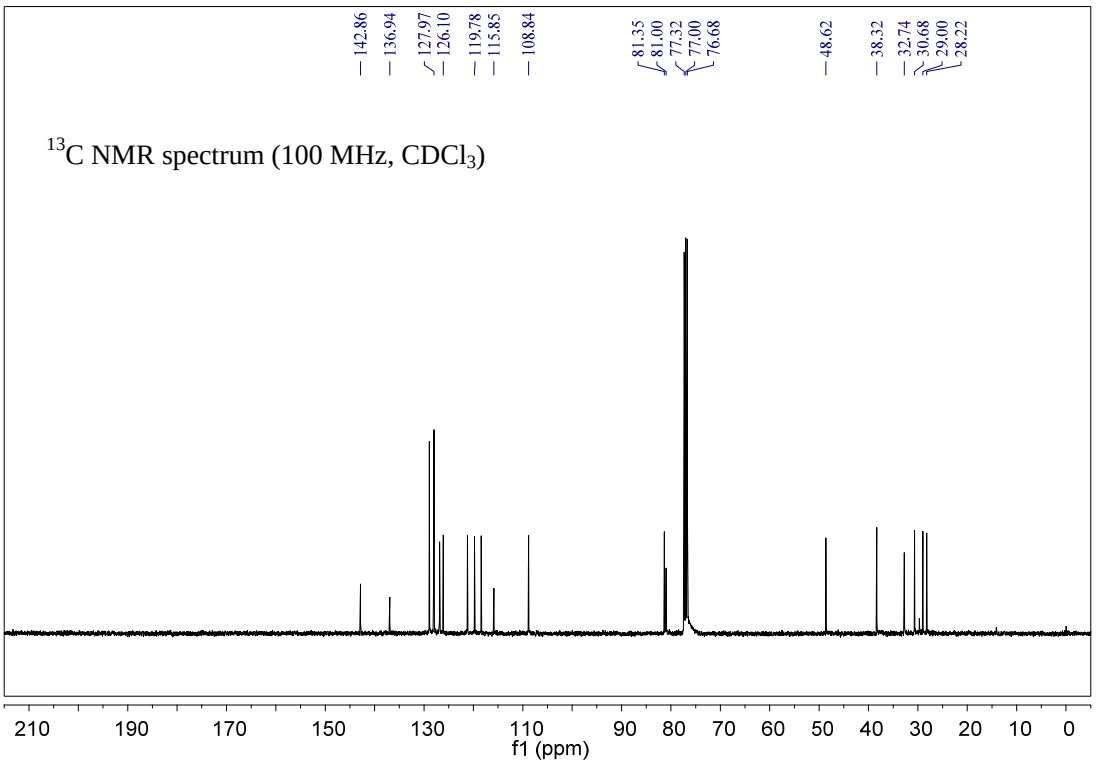
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



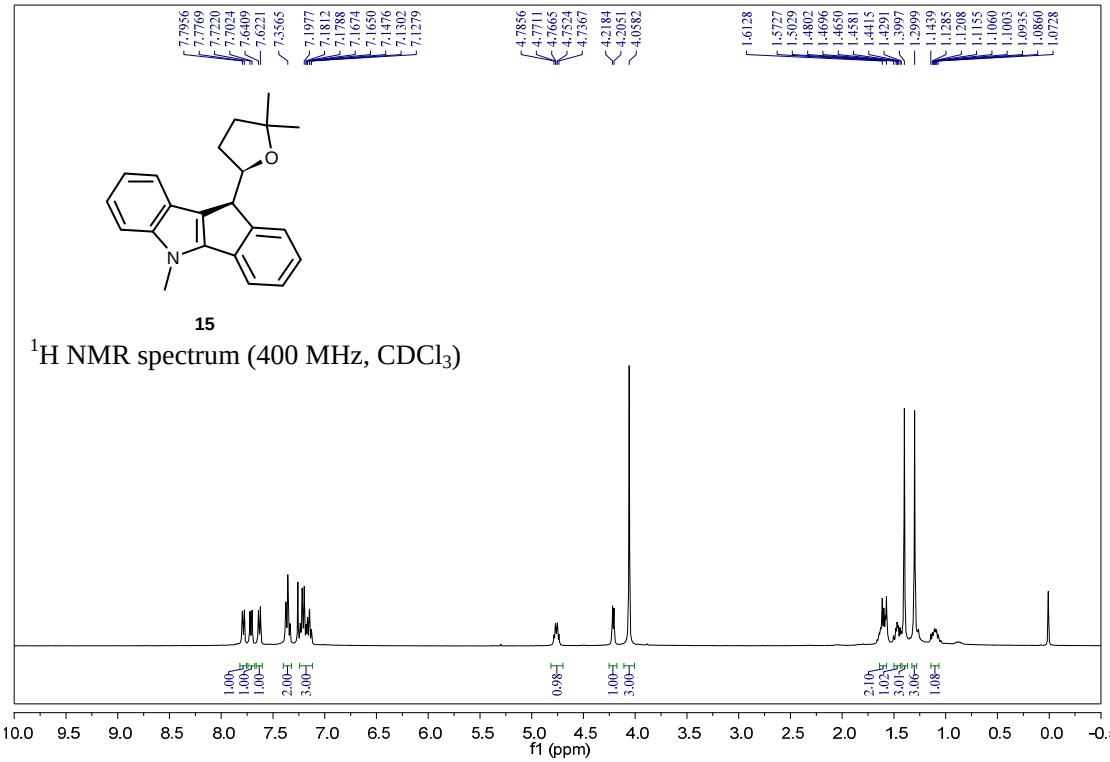
^{13}C NMR spectrum (100 MHz, $CDCl_3$)

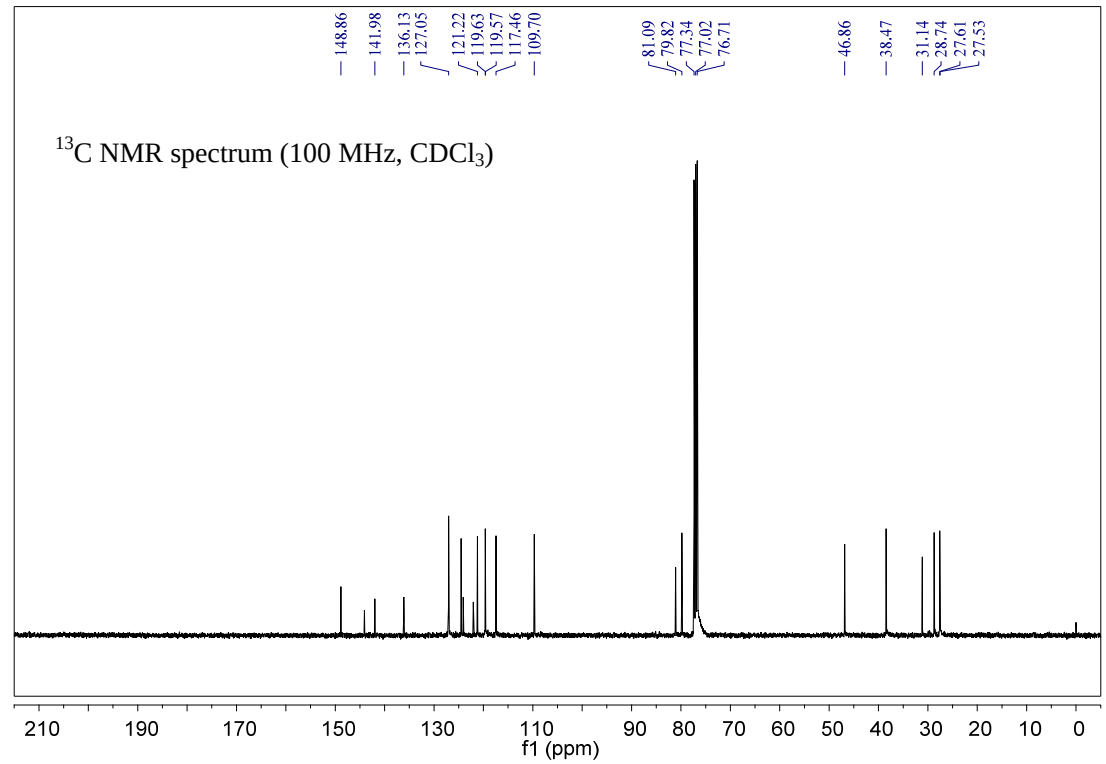


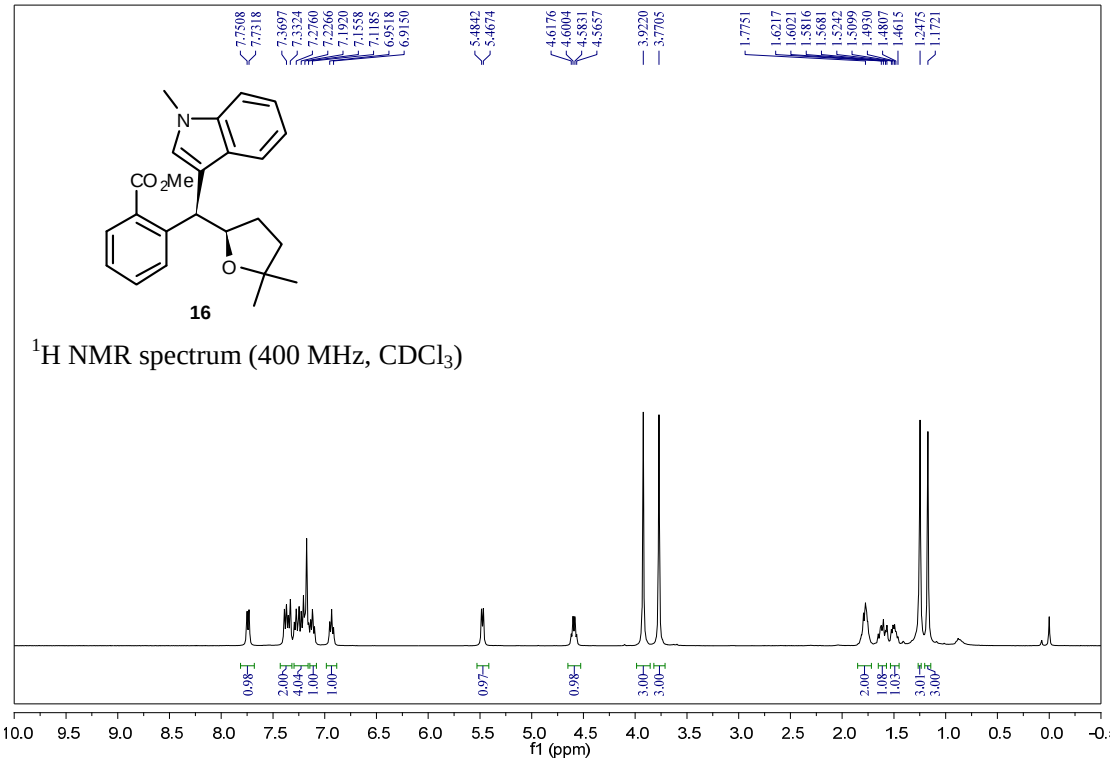
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

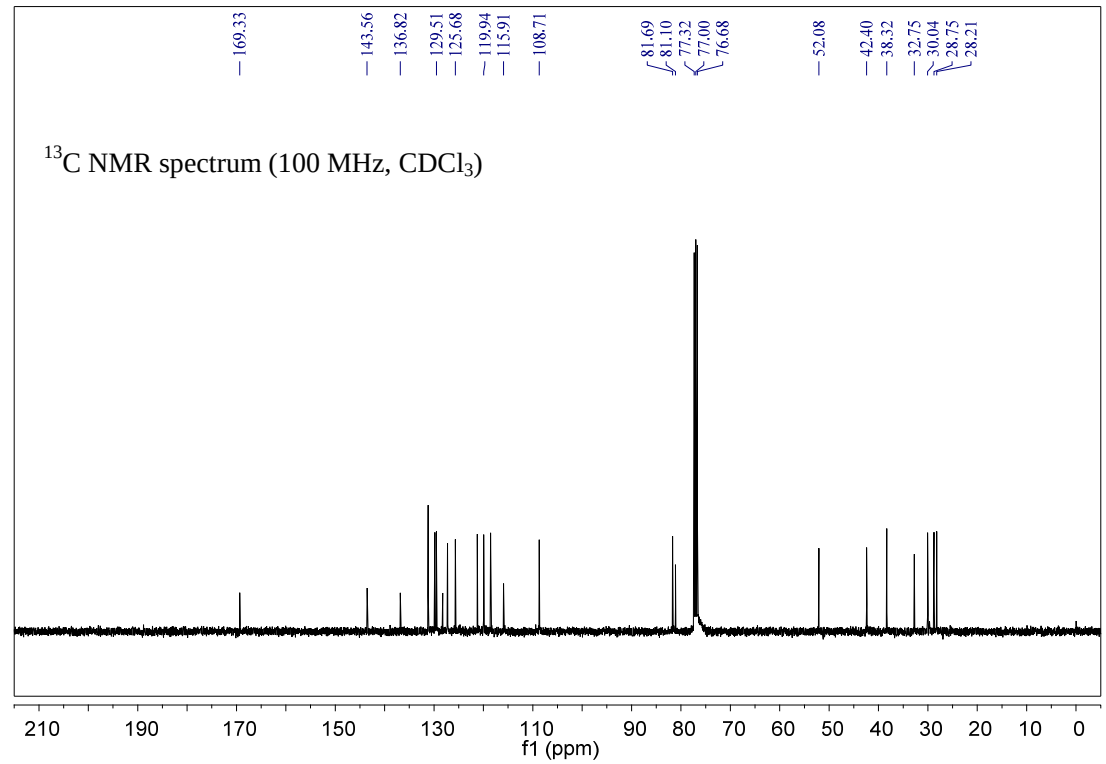


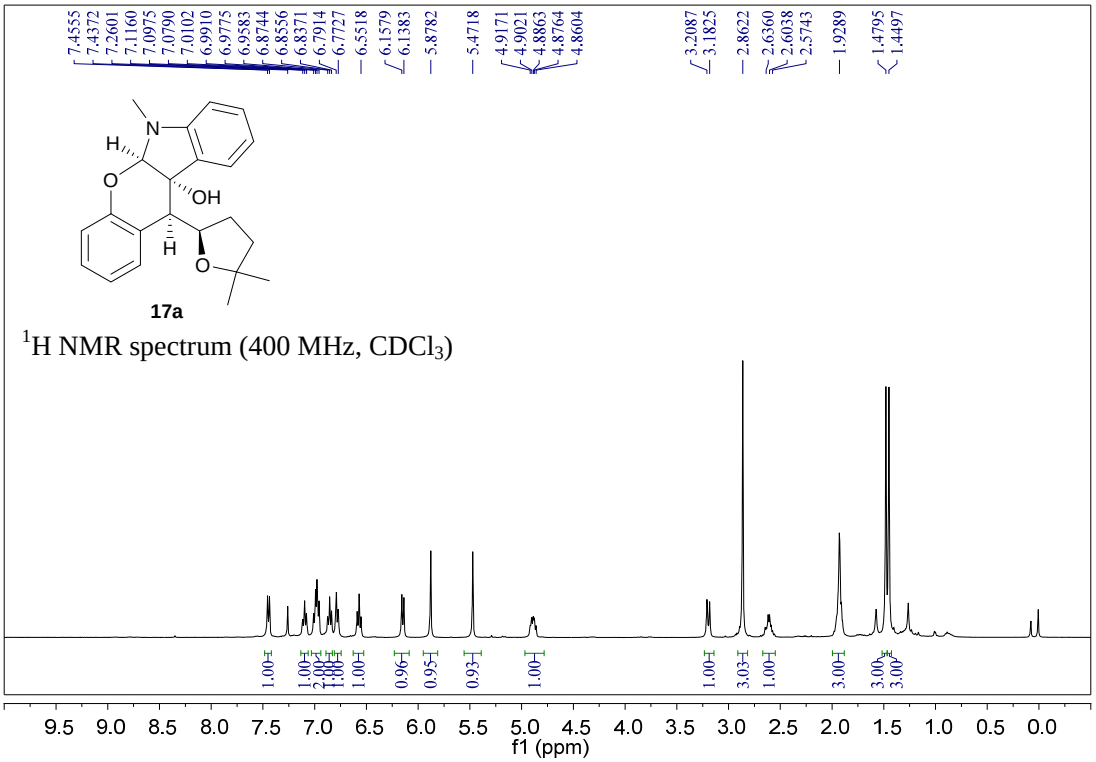
^{13}C NMR spectrum (100 MHz, $CDCl_3$)


7.7956
7.7769
7.7220
7.7024
7.6409
7.6221
7.3565
7.1977
7.1812
7.1788
7.1674
7.1650
7.1476
7.1302
7.1279
4.7856
4.7711
4.7665
4.7524
4.7367
4.2184
4.2051
4.0582
1.6128
1.5727
1.5029
1.4802
1.4696
1.4650
1.4581
1.4415
1.4291
1.3997
1.2999
1.1439
1.1285
1.1208
1.1155
1.1060
1.1003
1.0935
1.0860
1.0728
O
N
15
1H NMR spectrum (400 MHz, CDCl3)
1.00
1.00
1.00
2.00
3.00
0.98
1.00
3.00
2.10
1.02
3.01
3.06
1.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


148.86
141.98
136.13
127.05
121.22
119.63
119.57
117.46
109.70
81.09
79.82
77.34
77.02
76.71
46.86
38.47
31.14
28.74
27.61
27.53
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

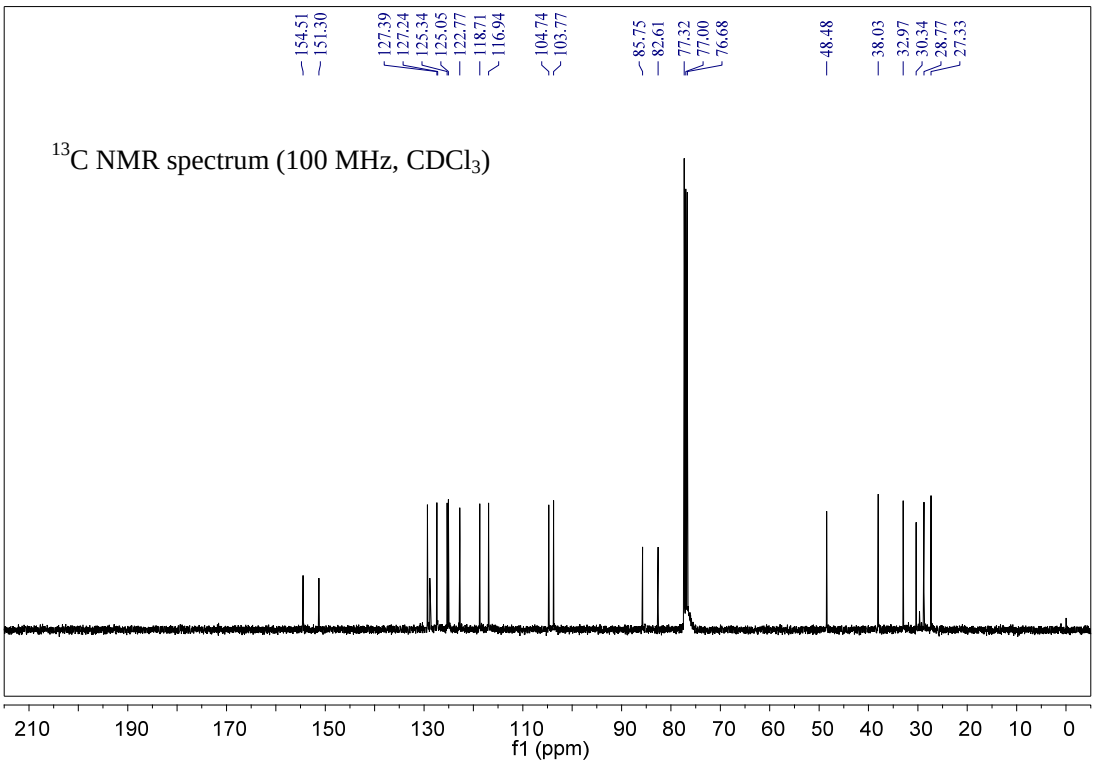

7.7508
7.7318
7.3697
7.3324
7.2760
7.2266
7.1920
7.1558
7.1185
6.9518
6.9150
5.4842
5.4674
4.6176
4.6004
4.5831
4.5657
3.9220
3.7705
1.7751
1.6217
1.6021
1.5816
1.5681
1.5242
1.5099
1.4930
1.4807
1.4615
1.2475
1.1721
N
CO2Me
O
16
1H NMR spectrum (400 MHz, CDCl3)
0.98
2.00
4.04
1.00
1.00
0.97
0.98
3.00
3.00
2.00
1.08
1.03
3.01
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


169.33
143.56
136.82
129.51
125.68
119.94
115.91
108.71
81.69
81.10
77.32
77.00
76.68
52.08
42.40
38.32
32.75
30.04
28.75
28.21
13C NMR spectrum (100 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

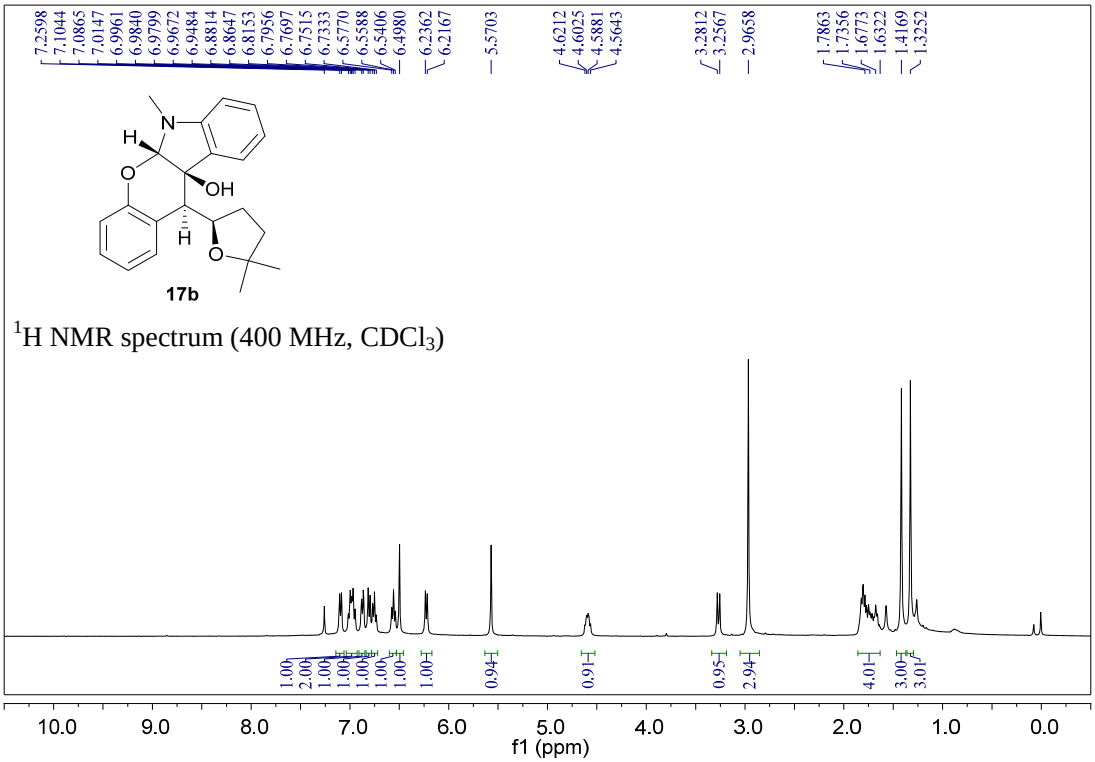


17a

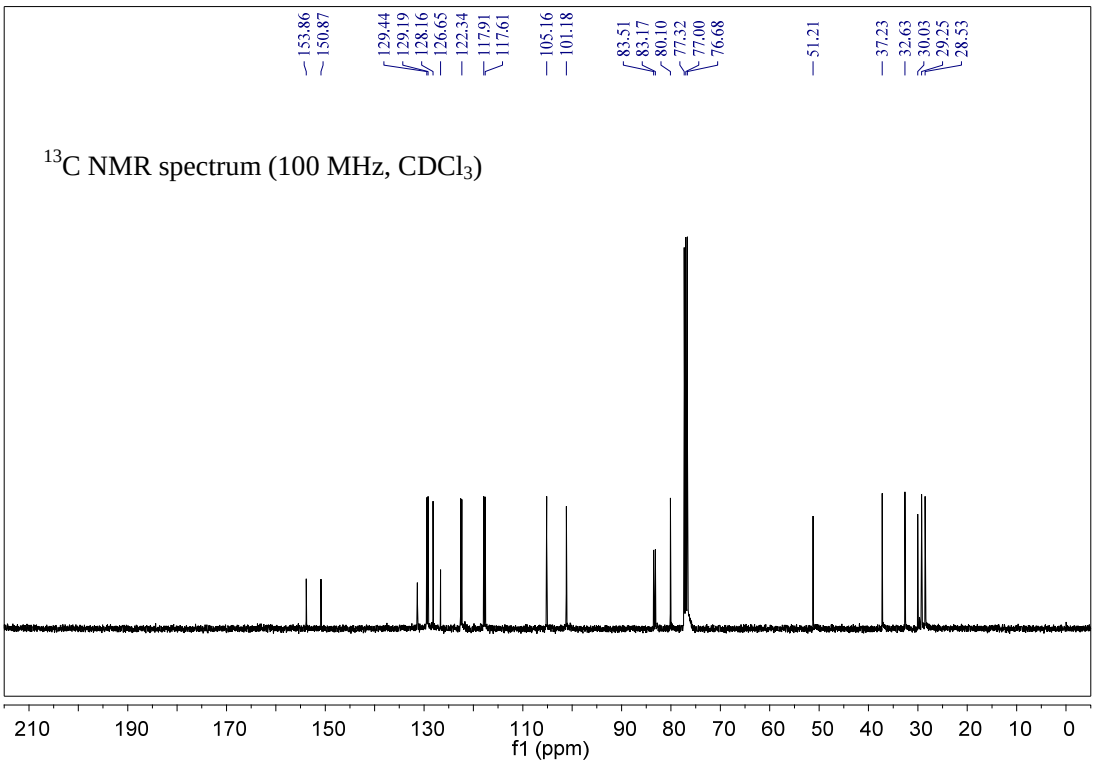
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)



^{1}H NMR spectrum (400 MHz, $CDCl_3$)



^{13}C NMR spectrum (100 MHz, $CDCl_3$)