

SUPPORTING INFORMATION

Tricyclic alkaloid core structures assembled by a cyclotrimerization-coupled intramolecular nucleophilic substitution reaction

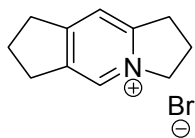
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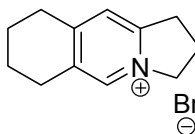
SYNTHETIC PROTOCOLS

General. All reagents used were commercial reagents without purification, unless otherwise stated. Dry solvents were distilled from Na and benzophenone. The ^1H NMR and ^{13}C NMR spectra were recorded on a 300 MHz or 400 MHz Varian NMR spectrometer, using CDCl_3 or CD_3OD as solvent. The IR data was recorded on a Jasco FT/IR-4100. The microwave reactions were carried out in a CEM Discover microwave synthesizer at 300 W in power mode using closed vessel conditions and an IR sensor to monitor the temperature.

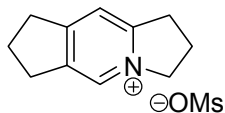
Representative procedure for compounds 15-18: 1,7-Octadiyne (10.7 mg, 0.1 mmol) and the corresponding nitrile (10 eq.) were added to a flame dried microwave vial and dissolved in dry toluene (2.5 mL). $\text{CpCo}(\text{CO})_2$ (2.3 μL , 20 mol %) was added and the vial was irradiated at 300 W for 40 minutes to 170 $^\circ\text{C}$ in a CEM Discover microwave synthesizer. The reaction was concentrated and the products were purified by silica gel flash chromatography, eluting with 20% MeOH/DCM.



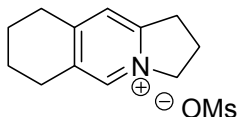
(15): 1,2,3,6,7,8-Hexahydrocyclopenta[f]indolizinium bromide (15): 7.9 mg, 33% yield, pale yellow oil; ^1H NMR (300 MHz, CD_3OD) δ 8.49 (s, 1H), 7.69 (s, 1H), 4.62 (t, $J = 7.6$ Hz, 2H), 3.31 (t, $J = 7.5$ Hz, 2H), 3.10 – 2.89 (m, 4H), 2.46 – 2.26 (m, 2H), 2.15 (p, $J = 7.7$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.4, 156.0, 143.9, 137.3, 119.7, 58.6, 33.6, 31.9, 30.3, 25.4, 22.2; HRMS (ESI^+) calcd for $\text{C}_{11}\text{H}_{14}\text{N}^+$ 160.1121, found 160.1123.



2,3,6,7,8,9-Hexahydro-1H-Pyrrolo[1,2-b]isoquinolinium bromide (16): 11.3 mg, 45% yield, pale yellow oil; ^1H NMR (300 MHz, CD_3OD) δ 8.48 (s, 1H), 7.59 (s, 1H), 4.64 (t, $J = 7.6$ Hz, 2H), 3.33 (t, $J = 7.8$ Hz, 2H), 2.92 (bs, 2H), 2.81 (bs, 2H), 2.49 – 2.29 (m, 2H), 1.86 – 1.73 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.6, 153.5, 141.3, 136.6, 123.8, 58.4, 31.7, 29.8, 26.1, 21.90, 21.2, 21.2; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{16}\text{N}^+$ 174.1277, found 174.1278.

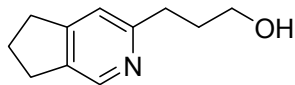


1,2,3,6,7,8-Hexahydrocyclopenta[f]indolizinium methanesulfonate (17): 5.5 mg, 22% yield, pale yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 9.04 (s, 1H), 7.65 (s, 1H), 4.93 (t, $J = 7.6$ Hz, 2H), 3.40 (t, $J = 7.6$ Hz, 2H), 3.04 (t, $J = 7.5$ Hz, 4H), 2.56 (s, 3H), 2.45 (p, $J = 7.6$ Hz, 2H), 2.17 (p, $J = 7.6$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 165.4, 156.0, 143.9, 137.3, 119.7, 58.6, 39.5, 33.6, 31.9, 30.3, 25.4, 22.2; HRMS (ESI^+) calcd for $\text{C}_{11}\text{H}_{14}\text{N}^+$ 160.1121, found 160.1123.

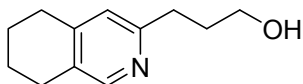


2,3,6,7,8,9-Hexahydro-1H-pyrrolo[1,2-b]isoquinolinium methanesulfonate (18): 9.6 mg, 36% yield, pale yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 9.05 (s, 1H), 7.50 (s, 1H), 4.94 (t, $J = 7.5$ Hz, 2H), 3.38 (t, $J = 7.6$ Hz, 2H), 2.88 (s, 4H), 2.61 (s, 3H), 2.54 – 2.28 (m, 2H), 1.96 – 1.56 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.6, 153.5, 141.3, 136.6, 123.8, 58.4, 39.5, 31.7, 29.8, 26.1, 21.9, 21.2, 21.2; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{16}\text{N}^+$ 174.1277, found 174.1278.

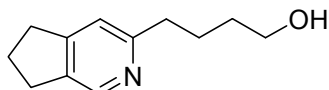
Representative procedure for compounds 21-24, 34-35: 1,7-Octadiyne (10.4 mg, 0.0983 mmol) and the corresponding nitrile (10 eq.) were added to a flame dried microwave vial and dissolved in dry toluene (2.4 mL). $\text{CpCo}(\text{CO})_2$ (2.25 μL , 20 mol%) was added and the vial was irradiated at 300 W for 40 minutes in a CEM Discover microwave synthesizer (final temperature of 150 $^\circ\text{C}$). The reaction was concentrated and the products were purified by silica gel flash chromatography, eluting with 5% MeOH/EtOAc.



3-(6,7-Dihydro-5H-cyclopenta[c]pyridin-3-yl)propan-1-ol (21): 17 mg, 89% yield, light yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.14 (s, 1H), 6.84 (s, 1H), 4.62 (s, 1H), 3.67 (s, 2H), 2.83 (t, $J = 6.8$ Hz, 2H), 2.67 (s, 4H), 2.01 – 1.86 (m, 2H), 1.83 – 1.64 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.9, 149.1, 147.1, 130.6, 123.3, 62.3, 34.9, 32.07, 28.8, 26.0, 22.8, 22.5; HRMS (ESI^+) calcd for $\text{C}_{11}\text{H}_{16}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 178.1232, found 178.1227.

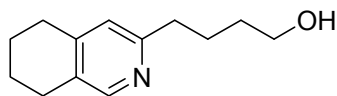


3-(5,6,7,8-Tetrahydroisoquinolin-3-yl)propan-1-ol (22): 18.6 mg, 90% yield, light yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.14 (s, 1H), 6.84 (s, 1H), 4.62 (s, 1H), 3.78 – 3.52 (m, 2H), 2.83 (t, $J = 6.8$ Hz, 2H), 2.76 – 2.55 (m, 4H), 2.06 – 1.83 (m, 2H), 1.83 – 1.62 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.9, 149.1, 147.1, 130.6, 123.3, 62.3, 34.9, 32.1, 28.8, 26.0, 22.8, 22.5; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{18}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 192.1388, found 192.1385.

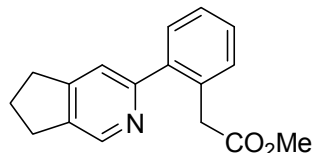


4-(6,7-Dihydro-5H-cyclopenta[c]pyridin-3-yl)butan-1-ol (23): 18 mg, 94% yield, light yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.34 (s, 1H), 7.03 (s, 1H), 3.67 (t, $J = 6.3$ Hz, 1H), 2.88 (dd, $J = 12.6, 7.3$ Hz, 2H), 2.79 (t, $J = 7.4$ Hz, 1H), 2.53 (s, 1H), 2.18 – 1.99 (m, 1H), 1.88 – 1.74 (m, 1H), 1.63 (dt, $J = 12.9, 6.4$ Hz, 1H);

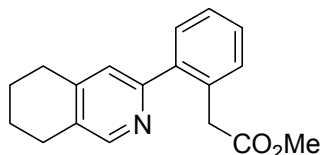
^{13}C NMR (75 MHz, CDCl_3) δ 159.5, 154.7, 144.8, 137.6, 119.2, 62.6, 37.4, 32.8, 32.3, 30.1, 26.3, 25.3; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{18}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 192.1388, found 192.1385.



4-(5,6,7,8-Tetrahydroisoquinolin-3-yl)butan-1-ol (24): 19.1 mg, 95% yield, light yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.16 (s, 1H), 6.82 (s, 1H), 3.66 (t, $J = 6.3$ Hz, 2H), 3.11 (s, 1H), 2.80 – 2.63 (m, 6H), 1.88 – 1.69 (m, 6H), 1.69 – 1.52 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.5, 149.6, 146.8, 130.4, 123.0, 62.4, 37.0, 32.3, 28.9, 26.2, 26.1, 22.9, 22.6; HRMS (ESI^+) calcd for $\text{C}_{13}\text{H}_{20}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 206.1545, found 206.1544.

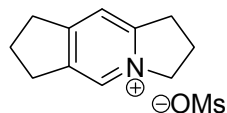


Methyl 2-(2-(6,7-dihydro-5H-cyclopenta[c]pyridin-3-yl)phenyl)acetate (34): 24.7 mg, 93% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.48 (s, 1H), 7.49 – 7.40 (m, 1H), 7.34 (dd, $J = 3.6, 2.3$ Hz, 4H), 3.81 (s, 2H), 3.61 (s, 3H), 2.96 (td, $J = 7.5, 3.7$ Hz, 4H), 2.14 (p, $J = 7.5$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.6, 157.1, 154.4, 144.8, 141.2, 138.5, 132.6, 131.3, 130.0, 128.3, 127.4, 120.2, 52.0, 39.3, 32.9, 30.2, 25.2; HRMS (ESI^+) calcd for $\text{C}_{17}\text{H}_{18}\text{NO}_2$ ($\text{M}+\text{H}$) $^+$ 268.1338, found 268.1334.

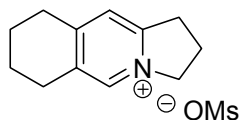


Methyl 2-(2-(5,6,7,8-tetrahydroisoquinolin-3-yl)phenyl)acetate (35): 24.2 mg, 86% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.32 (s, 1H), 7.41 (dt, $J = 5.5, 2.3$ Hz, 1H), 7.34 (d, $J = 2.7$ Hz, 3H), 7.13 (s, 1H), 3.81 (s, 2H), 3.62 (s, 3H), 2.88 – 2.67 (m, 4H), 1.94 – 1.74 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.6, 156.2, 149.7, 146.6, 140.8, 132.5, 131.4, 131.3, 129.9, 128.3, 127.4, 124.1, 52.0, 39.3, 29.0, 26.2, 22.8, 22.6; HRMS (ESI^+) calcd for $\text{C}_{18}\text{H}_{20}\text{NO}_2$ ($\text{M}+\text{H}$) $^+$ 282.1494, found 282.1493.

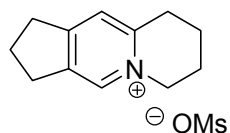
Representative procedure for compounds 25-28, 38-39: Piperidine polymer bound (Sigma-Aldrich, 3 mmol/g, 64 mg, 2 eq.) was added to compound **21** (17 mg) dissolved in dry DCM (2.4 mL) in a flame dried vial. This mixture was shaken for 5 min and then cooled to 0 °C. Methane sulfonyl chloride (1.5 eq.) was added dropwise at 0 °C, and the resulting mixture was shaken at room temperature for 1 h. The resin was filtered through a cotton plug and rinsed with DCM (2 mL) and MeOH (2 mL). The filtrate was concentrated and the residue was dissolved in H_2O (2 mL) and extracted with EtOAc (3×2 mL). The aqueous layer was concentrated to dryness to give the pure pyridinium compound.



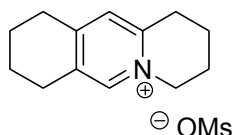
1,2,3,6,7,8-Hexahydrocyclopenta[fl]indolizinium methanesulfonate (25): 23 mg, 94% yield, pale yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 9.04 (s, 1H), 7.65 (s, 1H), 4.93 (t, $J = 7.6$ Hz, 2H), 3.40 (t, $J = 7.6$ Hz, 2H), 3.04 (t, $J = 7.5$ Hz, 4H), 2.56 (s, 3H), 2.45 (p, $J = 7.6$ Hz, 2H), 2.17 (p, $J = 7.6$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 165.4, 156.0, 143.9, 137.3, 119.7, 58.6, 39.5, 33.6, 31.9, 30.3, 25.4, 22.2; HRMS (ESI^+) calcd for $\text{C}_{11}\text{H}_{14}\text{N}^+$ 160.1121, found 160.1123.



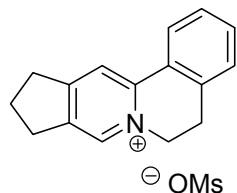
2,3,6,7,8,9-Hexahydro-1H-pyrrolo[1,2-*b*]isoquinolinium methanesulfonate (26): 25 mg, 100% yield, pale yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 9.05 (s, 1H), 7.50 (s, 1H), 4.94 (t, $J = 7.5$ Hz, 2H), 3.38 (t, $J = 7.6$ Hz, 2H), 2.88 (s, 4H), 2.61 (s, 3H), 2.54 – 2.28 (m, 2H), 1.96 – 1.56 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.6, 153.5, 141.3, 136.6, 123.8, 58.4, 39.5, 31.7, 29.8, 26.1, 21.9, 21.2, 21.2; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{16}\text{N}^+$ 174.1277, found 174.1278.



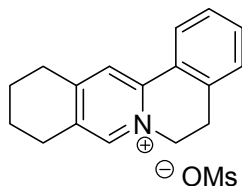
2,3,6,7,8,9-Hexahydro-1H-cyclopenta[*b*]quinolizinium methanesulfonate (27): 21.3 mg, 98% yield, pale yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 9.20 (s, 1H), 7.52 (s, 1H), 4.83 (t, $J = 6.0$ Hz, 2H), 3.17 (t, $J = 7.1$ Hz, 4H), 3.09 (t, $J = 7.6$ Hz, 2H), 2.71 (s, 3H), 2.32 – 2.10 (m, 4H), 2.00 (p, $J = 6.6$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 164.4, 153.0, 143.4, 141.5, 123.5, 55.7, 39.7, 33.7, 30.6, 28.8, 25.2, 21.5, 18.0; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{16}\text{N}^+$ 174.1277, found 174.1276.



1,2,3,4,7,8,9,10-Octahydropyrido[1,2-*b*]isoquinolinium methanesulfonate (28): 22.8 mg, 93% yield, pale yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 9.14 – 8.96 (m, 1H), 7.38 (s, 1H), 4.72 (t, $J = 6.1$ Hz, 2H), 3.10 (t, $J = 6.7$ Hz, 2H), 2.89 (d, $J = 15.0$ Hz, 4H), 2.68 (s, 3H), 2.17 – 2.02 (m, 2H), 2.02 – 1.88 (m, 2H), 1.86 – 1.72 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.0, 150.6, 145.1, 136.3, 127.7, 54.9, 39.6, 29.3, 27.8, 25.8, 21.4, 21.3, 21.2, 17.9; HRMS (ESI^+) calcd for $\text{C}_{13}\text{H}_{18}\text{N}^+$ 188.1434, found 188.1434.



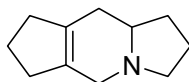
6,9,10,11-Tetrahydro-5H-cyclopenta[4,5]pyrido[2,1-*a*]isoquinolinium methanesulfonate (38): 9.4 mg, 93% yield, white solid; ^1H NMR (300 MHz, CDCl_3) δ 9.62 (s, 1H), 8.06 (s, 1H), 7.89 (d, $J = 7.2$ Hz, 1H), 7.61 – 7.43 (m, 2H), 7.39 (d, $J = 7.7$ Hz, 1H), 5.05 (t, $J = 6.6$ Hz, 2H), 3.36 – 3.12 (m, 6H), 2.77 (s, 3H), 2.28 (p, $J = 7.7$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.5, 146.7, 144.0, 142.5, 136.0, 133.4, 128.9, 128.8, 126.4, 126.4, 119.0, 54.8, 39.7, 34.1, 30.8, 27.4, 25.2; HRMS (ESI^+) calcd for $\text{C}_{16}\text{H}_{16}\text{N}^+$ 222.1277, found 222.1277.



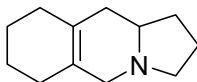
5,6,9,10,11,12-Hexahydroisoquino[3,2-*a*]isoquinolinium methanesulfonate (39): 9.3 mg, 100% yield, white solid; ^1H NMR (300 MHz, CDCl_3) δ 9.45 (s, 1H), 7.95 – 7.85 (m, 2H), 7.56 – 7.39 (m, 2H), 7.34 (d, $J = 7.4$ Hz, 1H), 4.95 (t, $J = 6.5$ Hz, 2H), 3.30 – 3.15 (m, 2H), 3.09 – 2.91 (m, 4H), 2.73 (s, 3H), 1.96 – 1.73 (m,

4H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.2, 146.1, 144.6, 137.1, 135.5, 133.0, 128.8, 128.8, 126.3, 125.9, 123.2, 54.0, 39.6, 29.9, 27.2, 26.0, 21.3; HRMS (ESI^+) calcd for $\text{C}_{17}\text{H}_{18}\text{N}^+$ 236.1434, found 236.1435.

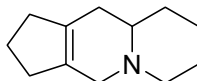
Representative procedure for compounds 29-32 and 40-41: NaBH_4 (8.5 mg, 0.225 mmol, 2.5 eq.) was added to a solution of **25** (23 mg, 0.09 mmol) in 2.2 mL $\text{H}_2\text{O}/\text{MeOH}$ (1:1). When the bubbling subsided, the reaction mixture was refluxed for 20 min. The reaction mixture was cooled to rt, sat. NH_4Cl (4 mL) was added, and the mixture was extracted with DCM (4×3 mL). The organic layers were dried over Na_2SO_4 , filtered and concentrated to dryness. The residue was purified by flash silica gel chromatography, eluting with 10% MeOH/DCM to deliver the amine **29**.



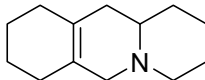
2,3,5,6,7,8,9,9a-octahydro-1H-cyclopenta[f]indolizine (29): 12.6 mg, 86% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 3.67 (d, $J = 15.5$ Hz, 1H), 3.59 – 3.41 (m, 1H), 3.12 (d, $J = 13.8$ Hz, 1H), 2.83 (bs, 1H), 2.60 (bs, 1H), 2.45 – 2.05 (m, 8H), 2.05 – 1.72 (m, 4H); ^{13}C NMR* (75 MHz, CDCl_3) δ 53.0, 51.7, 35.3, 33.5, 30.5, 29.9, 29.3, 22.8, 21.5; IR (DCM) 2927, 2703, 1640, 1457 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{11}\text{H}_{18}\text{N}$ ($\text{M}+\text{H}$) $^+$ 164.1439, found 164.1434. *Not all quarternary carbon centers were visible in the spectrum.



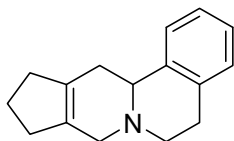
1,2,3,5,6,7,8,9,10,10a-decahydropyrrolo[1,2-b]isoquinoline (30): 6.5 mg, 100% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 3.46 (d, $J = 14.5$ Hz, 2H), 3.02 (d, $J = 13.5$ Hz, 1H), 2.76 (bs, 1H), 2.59 (bs, 1H), 2.35 – 2.00 (m, 4H), 2.00 – 1.76 (m, 6H), 1.76 – 1.61 (m, 2H), 1.59 – 1.38 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 127.9, 61.2, 53.9, 53.2, 34.0, 29.9, 29.5, 27.3, 22.6, 22.4, 20.9; IR (DCM) 2927, 2708, 1650, 1447 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{20}\text{N}$ ($\text{M}+\text{H}$) $^+$ 178.1596, found 178.1593.



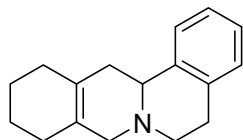
1,2,3,4,6,7,8,9,9a,10-decahydrocyclopenta[b]quinolizine (31): 10.5 mg, 70% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 3.39 (d, $J = 16.4$ Hz, 1H), 3.15 (d, $J = 11.6$ Hz, 1H), 2.89 (d, $J = 15.2$ Hz, 1H), 2.48 – 2.17 (m, 6H), 2.11 (bs, 2H), 1.96 – 1.66 (m, 6H), 1.62 – 1.43 (m, 1H), 1.44 – 1.30 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 133.3, 58.4, 55.9, 55.1, 35.4, 33.9, 33.1, 32.6, 29.9, 25.1, 23.8, 22.2; IR (DCM) 2926, 2734, 1635, 1453 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{12}\text{H}_{20}\text{N}$ ($\text{M}+\text{H}$) $^+$ 178.1596, found 178.1591.



2,3,4,6,7,8,9,10,11,11a-decahydro-1H-pyrido[1,2-b]isoquinoline (32): 8 mg, 100% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 3.07 – 2.89 (m, 2H), 2.62 (d, $J = 15.1$ Hz, 1H), 2.20 – 1.96 (m, 2H), 1.94 – 1.78 (m, 6H), 1.78 – 1.60 (m, 6H), 1.57 – 1.41 (m, 2H), 1.38 – 1.25 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 126.7, 58.4, 57.9, 55.4, 37.1, 32.3, 29.2, 27.2, 24.9, 23.7, 22.8, 22.7; IR (DCM) 2921, 2734, 1661, 1442 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{13}\text{H}_{22}\text{N}$ ($\text{M}+\text{H}$) $^+$ 192.1747, found 192.1749.

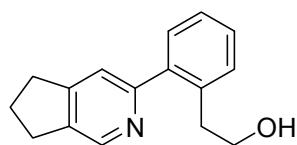


5,6,8,9,10,11,12,12a-Octahydrocyclopenta[4,5]pyrido[2,1-*a*]isoquinoline (40): 5 mg, 100% yield, light yellow solid; ^1H NMR (300 MHz, CDCl_3) δ 7.25 – 7.05 (m, 4H), 3.53 (dd, J = 10.5, 4.0 Hz, 1H), 3.37 (d, J = 15.1 Hz, 1H), 3.29 – 2.95 (m, 3H), 2.81 – 2.53 (m, 3H), 2.45 – 2.25 (m, 4H), 2.22 – 2.07 (m, 1H), 1.98 – 1.83 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 134.8, 134.2, 128.9, 126.1, 125.6, 59.8, 56.3, 51.6, 35.6, 34.5, 34.0, 30.0, 22.6; IR (DCM) 3020, 2921, 2734, 1495, 733 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{16}\text{H}_{20}\text{N}$ ($\text{M}+\text{H}$) $^+$ 226.1596, found 226.1594.

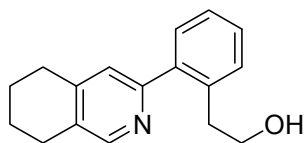


5,8,9,10,11,12,13,13a-Octahydro-6*H*-isoquino[3,2-*a*]isoquinoline (41): 6.5 mg, 100% yield, light yellow solid; ^1H NMR (300 MHz, CDCl_3) δ 7.23 – 7.05 (m, 4H), 3.57 – 3.40 (m, 1H), 3.29 – 3.11 (m, 2H), 3.11 – 3.00 (m, 1H), 2.92 (d, J = 15.9 Hz, 1H), 2.70 (d, J = 15.8 Hz, 1H), 2.60 – 2.43 (m, 2H), 2.21 – 2.05 (m, 1H), 1.93 (bs, 4H), 1.81 – 1.66 (m, 2H), 1.61 – 1.44 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.6, 134.6, 128.9, 127.3, 126.9, 126.1, 125.5, 59.8, 59.7, 51.2, 38.3, 29.7, 29.6, 27.5, 23.0, 22.9; IR (DCM) 3050, 2921, 2734, 1494, 739 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{17}\text{H}_{22}\text{N}$ ($\text{M}+\text{H}$) $^+$ 240.1752, found 240.1750.

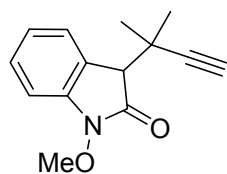
Representative procedure for compounds 36–37: LiAlH_4 (6.5 mg, 0.171 mmol, 2 eq.) was added to a solution of **34** (24 mg, 0.085 mmol) in 1.7 mL THF at 0 $^\circ\text{C}$ and stirred for 30 min. Ether (1.9 mL) was added followed by the addition of H_2O (7.9 μL), 4 M NaOH (7.9 μL), and H_2O again (15.8 μL) and the mixture was stirred for 30 min at rt. The mixture was filtered through celite, and the filtrate was dried over MgSO_4 and concentrated to give the pure alcohol **38**.



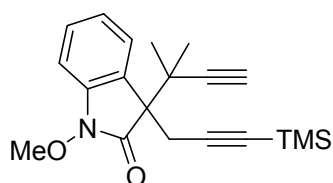
2-(2-(6,7-Dihydro-5H-cyclopenta[c]pyridin-3-yl)phenyl)ethanol (37): 20 mg, 91% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.44 (s, 1H), 7.42 – 7.37 (m, 3H), 7.35 (s, 1H), 7.33 – 7.25 (m, 1H), 3.99 (t, J = 5.7 Hz, 2H), 2.99 (t, J = 7.5 Hz, 4H), 2.94 – 2.83 (m, 2H), 2.17 (p, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 156.5, 156.0, 143.2, 140.3, 138.9, 138.9, 130.7, 130.0, 129.0, 126.5, 120.9, 64.4, 35.5, 33.0, 30.2, 25.3; HRMS (ESI^+) calcd for $\text{C}_{16}\text{H}_{18}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 240.1388, found 240.1384.



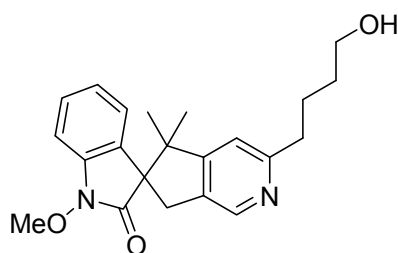
2-(2-(5,6,7,8-Tetrahydroisoquinolin-3-yl)phenyl)ethanol (38): 21 mg, 98% yield, yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 8.29 (s, 1H), 7.42 – 7.35 (m, 2H), 7.34 (s, 1H), 7.33 – 7.24 (m, 1H), 7.22 (s, 1H), 4.04 – 3.92 (m, 2H), 2.93 – 2.85 (m, 2H), 2.86 – 2.72 (m, 4H), 1.93 – 1.76 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 155.5, 148.2, 148.0, 140.0, 138.9, 131.8, 130.8, 129.9, 129.0, 126.4, 124.8, 64.4, 35.5, 29.1, 26.1, 22.7, 22.5; HRMS (ESI^+) calcd for $\text{C}_{17}\text{H}_{20}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 254.1545, found 254.1542.



1-Methoxy-3-(2-methylbut-3-yn-2-yl)indolin-2-one (43): A solution of NH_4Cl (1.01 g, 18.88 mmol in 9 mL H_2O) was added to a solution of **42** (1.16 g, 4.45 mmol) in MeOH (38 mL) followed by Zn dust (3.08 g, 47.4 mmol). The mixture was stirred at room temperature for 2 h, and filtered through a plug of celite which was subsequently washed with hot MeOH (40 mL). The MeOH was evaporated, brine (20 mL) was added, extracted with DCM (20 mL), and the DCM layer was dried over Na_2SO_4 , filtered and concentrated to dryness. The crude mixture was dissolved in dry DCM (28 mL) and PPh_3 (1.48 g, 5.66 mmol) and MeOH (229 μL , 5.66 mmol) were added. The solution was cooled to 0 $^\circ\text{C}$, DIAD (1.12 mL, 5.66 mmol) was added slowly and the reaction mixture was stirred at 0 $^\circ\text{C}$ until the reaction was complete as indicated by TLC (hexanes/EtOAc, 2:1). The solution was concentrated and the product was purified by flash silica gel chromatography, eluting with hexanes/EtOAc (4:1) to give **43** (613 mg, 60%) as a yellow solid. The analytical data was identical with literature reports.¹

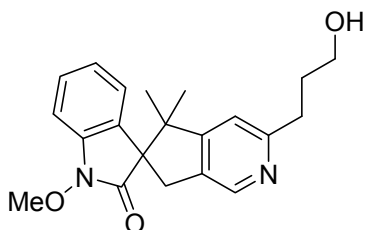


1-Methoxy-3-(2-methylbut-3-yn-2-yl)-3-(3-(trimethylsilyl)prop-2-ynyl)indolin-2-one (44): A solution of compound **43** (67 mg, 0.292 mmol) in DMF (1.5 mL) was added dropwise to a suspension of NaH (60%, 17.5 mg, 0.438 mmol) in DMF (1.5 mL) at 0 $^\circ\text{C}$. The mixture was stirred for 10 min at 0 $^\circ\text{C}$, 3-bromo-1-trimethylsilyl-1-propyne (71 μL , 0.438 mmol) was added dropwise, and stirring was continued for 15 min at 0 $^\circ\text{C}$. Sat. NH_4Cl (4 mL) was added and the aqueous layer was extracted with EtOAc (4 mL). The organic layer was washed with H_2O (2 \times 2 mL) and brine (2 mL), dried over MgSO_4 , filtered and concentrated to dryness. The residue was purified by flash silica gel chromatography, eluting with 10% EtOAc/hexanes to give **44** (64 mg, 65%) as a light yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.69 (d, J = 7.6 Hz, 1H), 7.37 – 7.28 (m, 1H), 7.13 – 7.06 (m, 1H), 6.96 (d, J = 7.7 Hz, 1H), 4.00 (s, 3H), 3.10 (d, J = 1.2 Hz, 2H), 2.34 (s, 1H), 1.52 (s, 3H), 1.06 (s, 3H), -0.15 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.1, 140.7, 128.6, 126.8, 125.7, 123.0, 106.6, 101.7, 88.5, 86.9, 71.7, 63.3, 54.8, 37.4, 25.4, 24.8, 24.3, -0.2; HRMS (ESI $^+$) calcd for $\text{C}_{20}\text{H}_{26}\text{NO}_2\text{Si}$ ($\text{M}+\text{H}$) $^+$ 340.1733, found 340.1732.

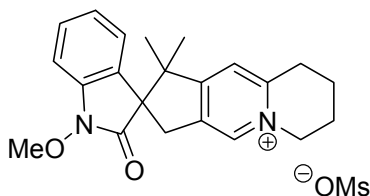


3-(4-Hydroxybutyl)-1'-methoxy-5,5-dimethyl-5,7-dihydrospiro[cyclopenta[c]pyridine-6,3'-indol]-2'(1'H)-one (45): The diyne **44** (20 mg, 0.059 mmol) and 5-hydroxypentanenitrile (58 mg, 0.589 mmol) were added to a flame dried microwave vial and dissolved in xylenes (1.5 mL). $\text{CpCo}(\text{CO})_2$ (1.36 μL , 0.012 mmol, 20 mol %) was added and the vial was irradiated at 300 W for 90 min to 200 $^\circ\text{C}$ in a CEM Discover microwave synthesizer. The mixture was evaporated to dryness and a mixture of the silylated and non-silylated cyclotrimerization product was isolated by flash silica gel chromatography, eluting with 4:1 hexanes/EtOAc to 10% MeOH/EtOAc. The remaining TMS groups were removed through a desilylation in THF (2 mL)/ H_2O (200

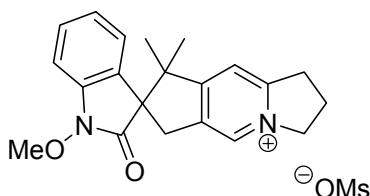
μL) with KF (8 mg) under microwave irradiation at 300 W for 2 min in a CEM Discover synthesizer. The solution was dried over MgSO_4 , filtered and concentrated to dryness. The residue was purified by flash silica gel chromatography, eluting with 10% MeOH/EtOAc to give **45** (10.7 mg, 42%) as a yellow oil that solidified over time. ^1H NMR (300 MHz, CDCl_3) δ 8.40 (s, 1H), 7.28 (td, $J = 7.7, 1.0$ Hz, 1H), 7.02 – 6.87 (m, 3H), 6.78 – 6.70 (m, 1H), 4.01 (s, 3H), 3.69 (t, $J = 6.3$ Hz, 2H), 3.50 (d, $J = 15.9$ Hz, 1H), 3.13 (d, $J = 15.9$ Hz, 1H), 2.86 (t, $J = 7.6$ Hz, 2H), 1.93 – 1.78 (m, 2H), 1.75 – 1.59 (m, 2H), 1.33 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.4, 161.4, 160.5, 144.8, 140.1, 133.3, 128.7, 127.9, 124.1, 123.0, 117.0, 107.5, 63.7, 62.4, 60.2, 51.2, 37.8, 37.5, 32.4, 26.2, 24.8, 24.6; HRMS (ESI^+) calcd for $\text{C}_{22}\text{H}_{27}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 367.2022, found 367.2022.



3-(3-Hydroxypropyl)-1'-methoxy-5,5-dimethyl-5,7-dihydrospiro [cyclopenta[c]pyridine-6,3'-indol]-2'(1'H)-one (46): The diyne **44** (30 mg, 0.088 mmol) and 4-hydroxybutanenitrile (75 mg, 0.881 mmol) were reacted following the same procedure to give **46** (12.7 mg, 41%) as an orange oil that solidified over time. ^1H NMR (300 MHz, CDCl_3) δ 8.42 (s, 1H), 7.30 (t, $J = 7.8$ Hz, 1H), 7.07 – 6.89 (m, 3H), 6.78 (d, $J = 7.4$ Hz, 1H), 5.37 (s, 1H), 4.02 (s, 3H), 3.84 – 3.64 (m, 2H), 3.50 (d, $J = 15.9$ Hz, 1H), 3.17 (d, $J = 16.0$ Hz, 1H), 3.01 (t, $J = 6.7$ Hz, 2H), 2.08 – 1.95 (m, 2H), 1.33 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.3, 161.5, 160.6, 144.0, 140.2, 128.8, 127.5, 124.2, 123.1, 117.6, 107.6, 63.7, 62.5, 60.2, 51.3, 37.5, 35.3, 31.9, 29.9, 24.9, 24.8, 24.6; HRMS (ESI^+) calcd for $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 353.1865, found 353.1863.

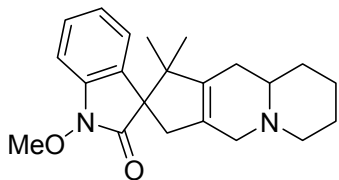


1'-Methoxy-1,1-dimethyl-2'-oxo-1',2',3,6,7,8,9-octahydrospiro[cyclopenta[b]quinolizinium-2,3'-indole] methanesulfonate (47): Compound **45** (19.5 mg, 0.532 mmol) was used following the procedure for **25-28** and **38-39** to give **47** (24 mg, 100%) as a pale yellow oil that solidified over time. ^1H NMR (300 MHz, CD_3OD) δ 8.60 (s, 1H), 7.81 (s, 1H), 7.50 – 7.37 (m, 2H), 7.23 – 7.10 (m, 2H), 4.61 (t, $J = 6.0$ Hz, 2H), 3.98 (s, 3H), 3.67 (d, $J = 17.1$ Hz, 1H), 3.43 (d, $J = 17.0$ Hz, 1H), 3.34 – 3.26 (m, 4H), 2.69 (s, 3H), 2.26 – 2.14 (m, 2H), 2.12 – 1.97 (m, 2H), 1.38 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.0, 170.8, 157.9, 141.9, 140.9, 140.3, 130.8, 127.1, 125.2, 124.8, 123.5, 109.1, 64.4, 61.5, 57.0, 52.8, 39.6, 37.5, 29.8, 26.9, 22.5, 21.7, 18.9; HRMS (ESI^+) calcd for $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_2^+$ 349.1911, found 349.1911.

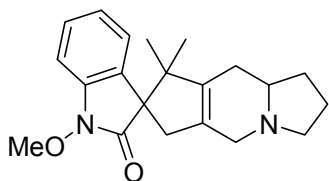


1'-Methoxy-8,8-dimethyl-2'-oxo-1',2,2',3,6,8-hexahydro-1H-spiro[cyclopenta[f]indolizinium-7,3'-indole] methanesulfonate (48): Compound **46** (12.5 mg, 0.035 mmol) was used following the procedure for **25-28** and **38-39** to give **48** (12.5 mg, 82%) as a light green oil that solidified over time. ^1H NMR (300 MHz, CDCl_3) δ 9.02 (s, 1H), 7.52 (s, 1H), 7.37 (t, $J = 7.6$ Hz, 1H), 7.33 – 7.28 (m, 1H), 7.12 (t, $J = 6.5$ Hz, 1H), 7.02

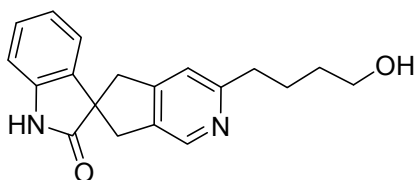
(d, $J = 7.7$ Hz, 1H), 5.29 (s, 1H), 4.74 (s, 1H), 4.33 (s, 1H), 3.97 (s, 3H), 3.82 – 3.52 (m, 2H), 3.52 – 3.31 (m, 2H), 2.74 (s, 3H), 2.60 – 2.39 (m, 1H), 1.36 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.2, 170.6, 157.9, 140.5, 140.2, 137.2, 129.6, 126.4, 123.7, 123.5, 117.8, 107.8, 63.7, 60.3, 59.3, 51.6, 39.7, 37.3, 32.7, 27.1, 22.3, 21.5; HRMS (ESI^+) calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_2^+$ 335.1760, found 335.1758.



1'-Hydroxy-1,1-dimethyl-1,4,6,7,8,9,9a,10-octahydro-3H-spiro[cyclopenta[b]quinolizine-2,3'-indol]-2'(1'H)-one (49): Compound **47** (24 mg, 0.054 mmol) was used following the procedure for **29-32**, and **40-41** to give **49** (13.6 mg, 72%) as a pale yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 7.26 – 7.21 (m, 1H), 7.16 (d, $J = 7.2$ Hz, 1H), 7.01 – 6.91 (m, 2H), 3.99 (s, 3H), 3.33 (d, $J = 16.4$ Hz, 1H), 3.12 – 2.95 (m, 2H), 2.87 (bs, 1H), 2.34 (d, $J = 15.5$ Hz, 1H), 2.18 (bs, 2H), 1.99 (bs, 2H), 1.81 (bs, 2H), 1.70 (bs, 2H), 1.37 (bs, 2H), 1.19 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.6, 139.9, 139.0, 128.0, 123.5, 122.7, 107.3, 63.7, 58.8, 57.7, 56.2, 55.2, 52.8, 41.2, 33.8, 30.2, 29.9, 26.0, 24.6, 23.8, 22.1; IR (DCM) 3057, 2931, 2853, 1723, 1614, 1463, 1322, 754 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{22}\text{H}_{29}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 353.2229, found 353.2228.



1'-Hydroxy-8,8-dimethyl-2,3,6,8,9,9a-hexahydro-1H,5H-spiro[cyclopenta[f]indolizine-7,3'-indol]-2'(1'H)-one (50): Compound **48** (12 mg, 0.028 mmol) was used following the procedure for **29-32**, and **40-41** to give **50** (7.7 mg, 82%) pale yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 7.39 (d, $J = 7.5$ Hz, 0.5H), 7.30 – 7.22 (m, 1H), 7.19 (d, $J = 7.4$ Hz, 1H), 7.08 – 6.91 (m, 2H), 4.00 (s, 3H), 3.99 (s, 1.5H), 3.54 (d, $J = 15.4$ Hz, 1H), 3.28 (t, $J = 7.4$ Hz, 1H), 2.89 (dd, $J = 28.8, 15.8$ Hz, 2H), 2.48 (dd, $J = 31.9, 16.1$ Hz, 3H), 2.31 – 2.09 (m, 2H), 2.02 (bs, 4H), 1.61 (bs, 2H), 1.17 (s, 3H), 1.10 (s, 1.5H), 0.86 (s, 1.5H), 0.77 (s, 3H); ^{13}C NMR* (101 MHz, CDCl_3) δ 128.2, 128.1, 125.3, 123.9, 123.1, 122.8, 107.4, 107.2, 63.7, 63.6, 60.6, 59.3, 53.5, 52.3, 52.2, 40.9, 30.2, 29.9, 23.6, 22.6, 22.4, 21.8; IR (DCM) 3062, 2927, 2854, 1723, 1614, 1463, 1322, 733 cm^{-1} ; HRMS (ESI^+) calcd for $\text{C}_{21}\text{H}_{27}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 339.2073, found 339.2070. *Not all quarternary carbon centers were visible in the spectrum.

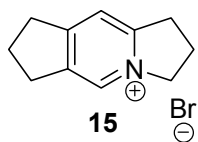


3-(4-Hydroxybutyl)-5,7-dihydrospiro[cyclopenta[c]pyridine-6,3'-indol]-2'(1'H)-one (52): The diyne **51**² (15.2 mg, 0.0726 mmol) and 5-hydroxypentanenitrile (72 mg, 0.726 mmol) were added to a flame dried microwave vial and dissolved in toluene (1.8 mL). $\text{CpCo}(\text{CO})_2$ (1.7 μL , 0.0145 mmol, 20 mol %) was added and the vial was irradiated at 300 W for 60 min in a CEM Discover microwave synthesizer (final temperature of 180 $^\circ\text{C}$). The mixture was evaporated to dryness and the product was isolated by flash silica gel chromatography, eluting with 10% MeOH/EtOAc to give **52** (18.7 mg, 83%) as a white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.88 (s, 1H), 8.42 (s, 1H), 7.20 (t, $J = 7.7$ Hz, 3H), 7.12 (s, 1H), 6.91 (t, $J = 7.4$ Hz, 2H), 6.82 (d, $J = 7.4$ Hz, 1H), 3.71 (t, $J = 6.2$ Hz, 2H), 3.58 (d, $J = 15.9$ Hz, 2H), 3.15 (d, $J = 12.1$ Hz, 1H), 3.10 (d, $J =$

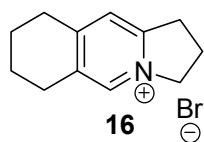
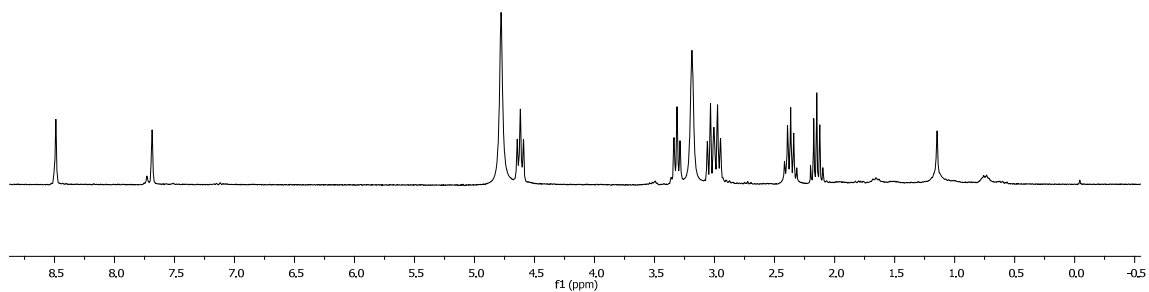
12.1 Hz, 1H), 2.87 (t, $J = 7.5$ Hz, 2H), 1.87 (p, $J = 7.5$ Hz, 2H), 1.72-1.63 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 182.2, 160.8, 152.0, 144.8, 140.0, 135.9, 135.0, 128.6, 123.1, 122.1, 119.4, 110.2, 62.6, 54.4, 43.9, 41.7, 37.6, 32.4, 26.3; HRMS (ESI^+) calcd for $\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 309.1598, found 309.1594.

¹H NMR Spectra for Compounds 15-18, 21-32, 34-41, and 44-50

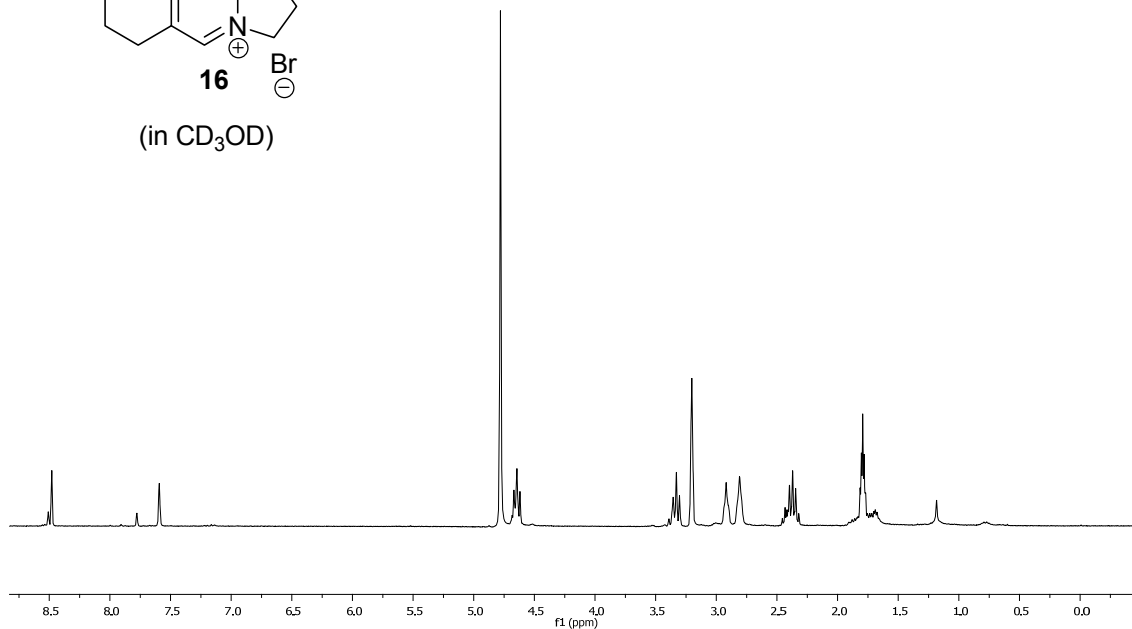
All spectra were recorded at 300 MHz in CDCl₃ unless noted otherwise.

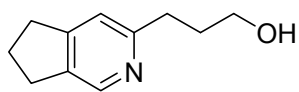


(in CD₃OD)

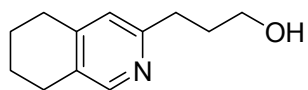
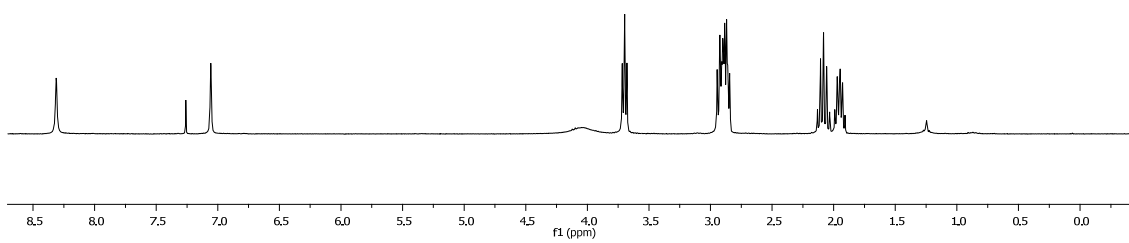


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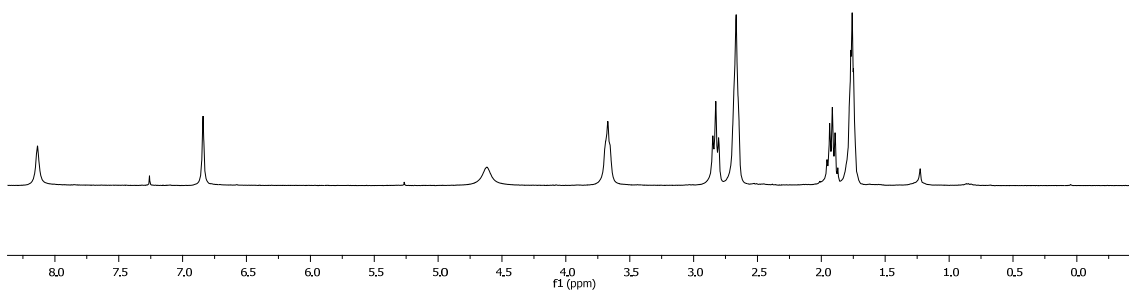


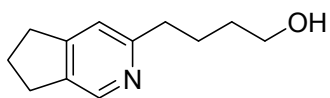


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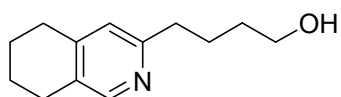
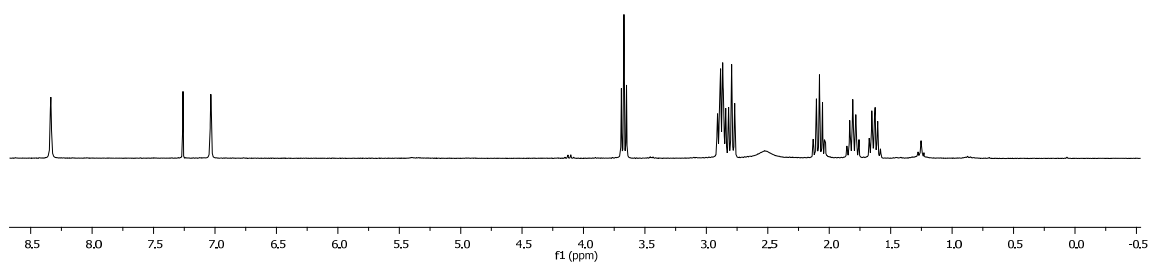


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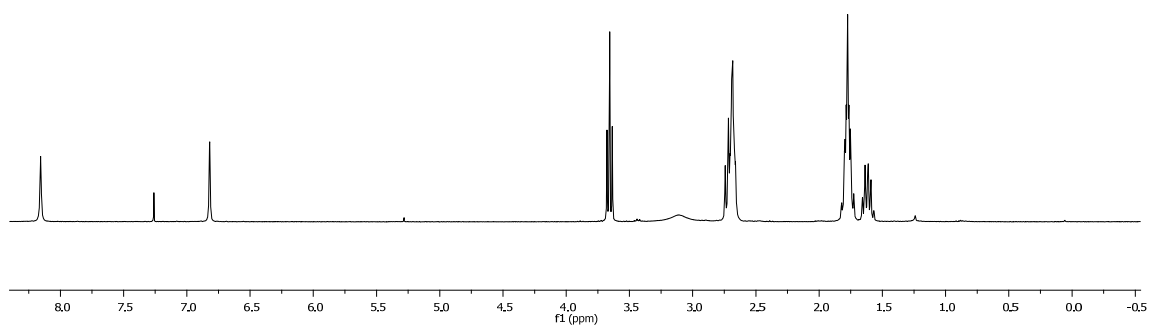


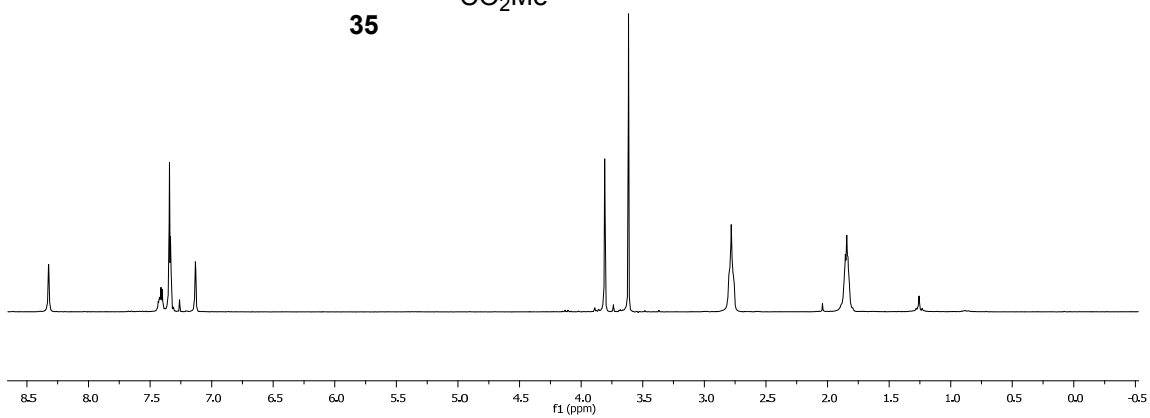
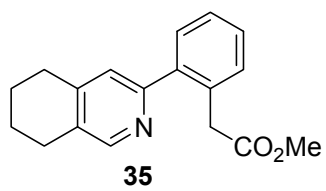
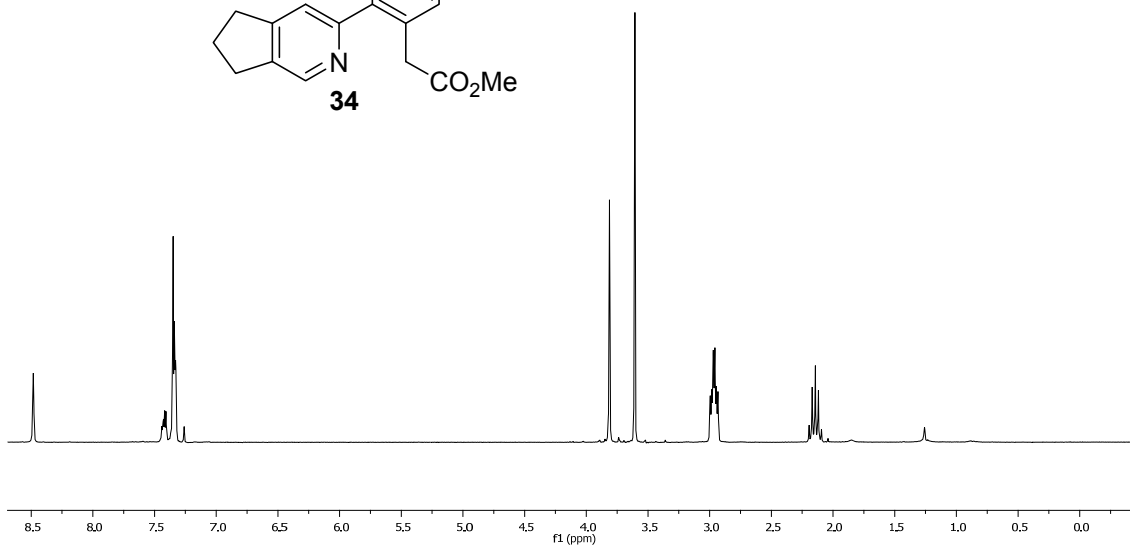
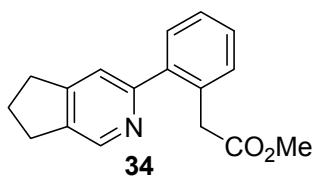


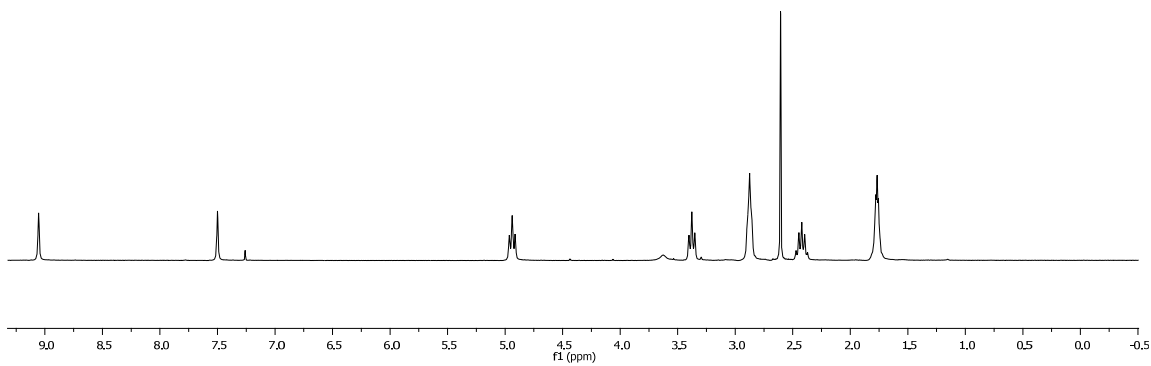
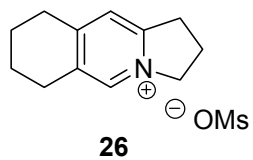
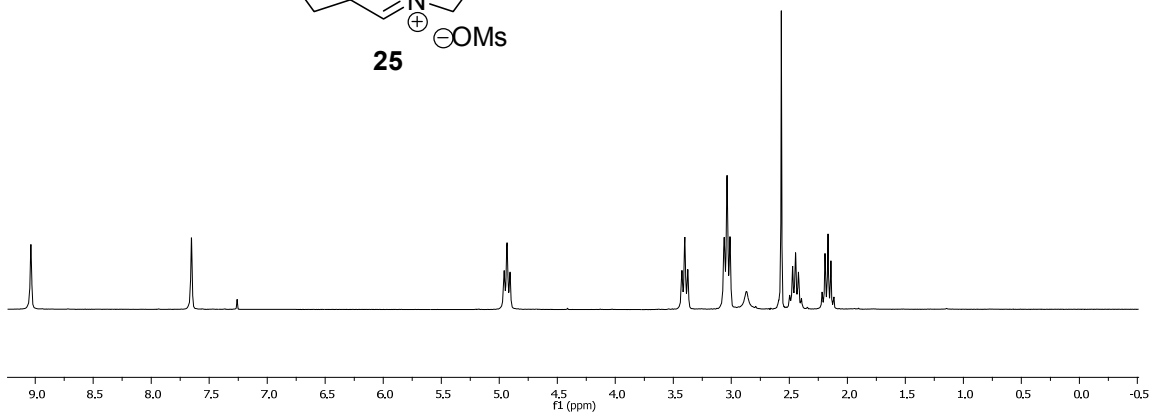
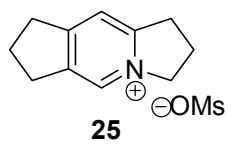
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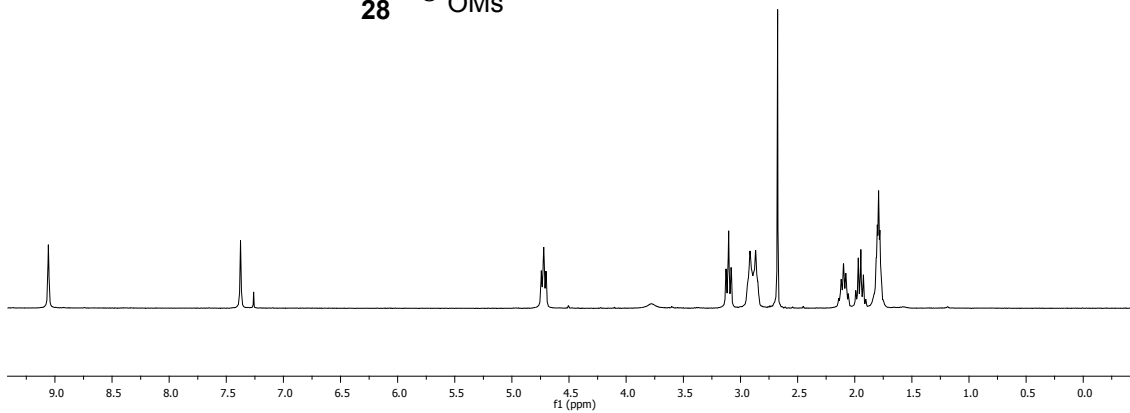
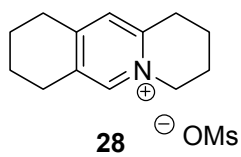
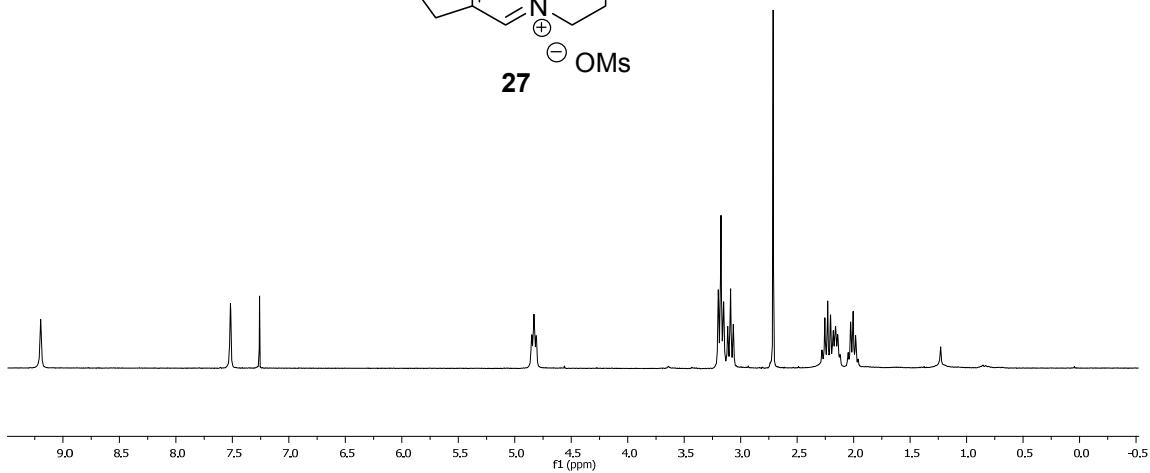
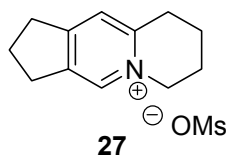


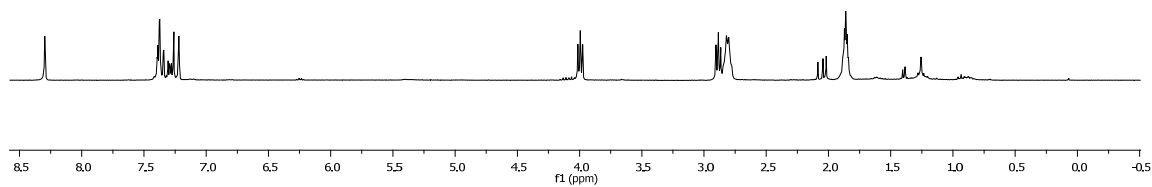
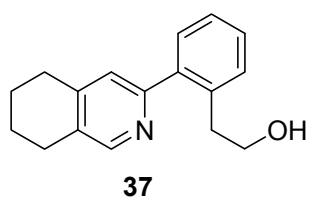
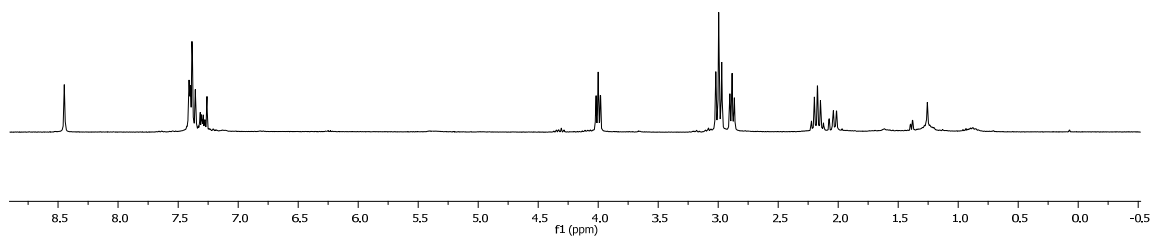
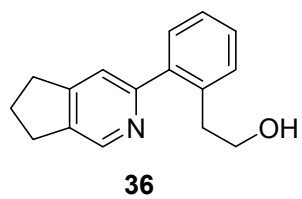
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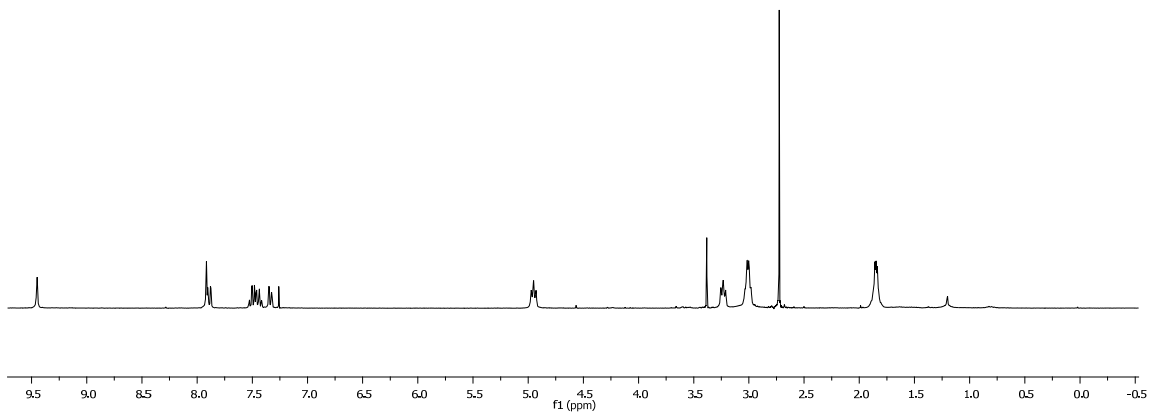
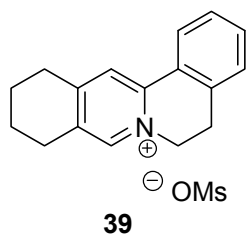
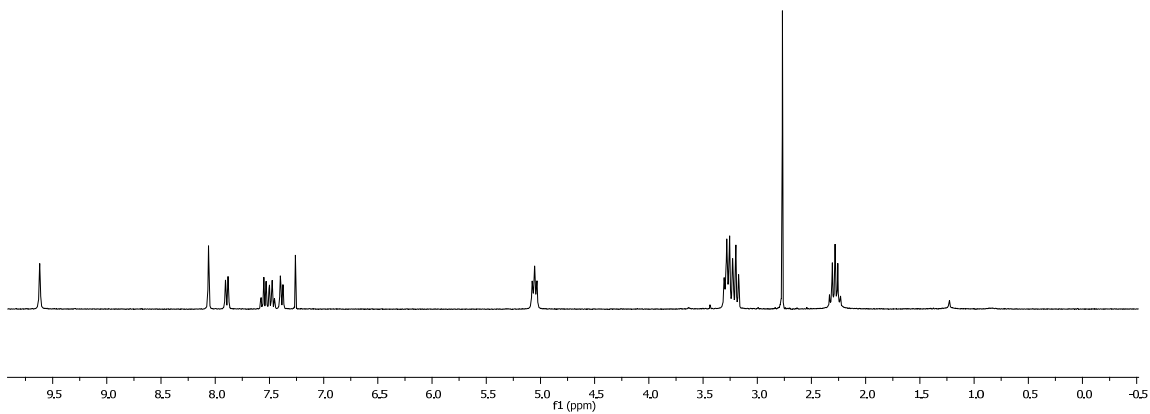
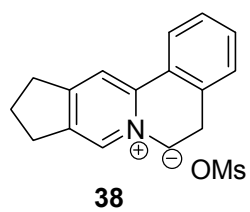


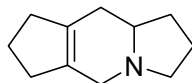




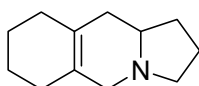
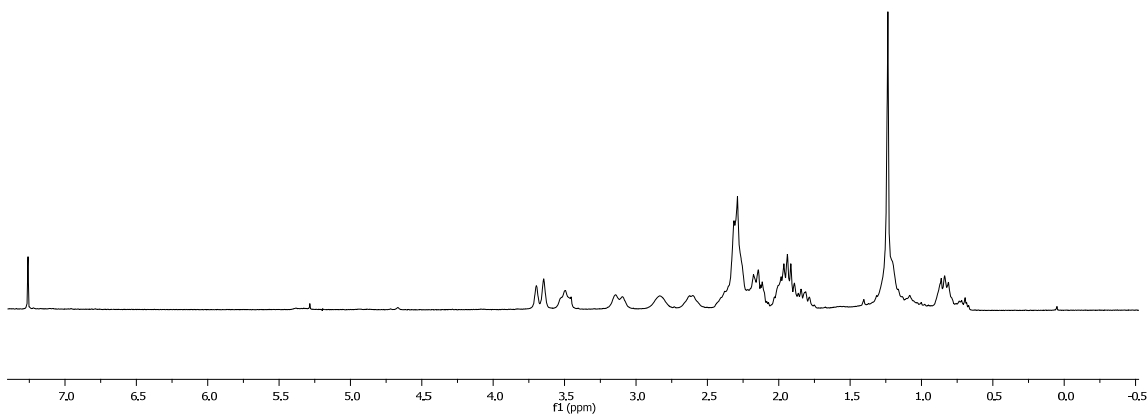




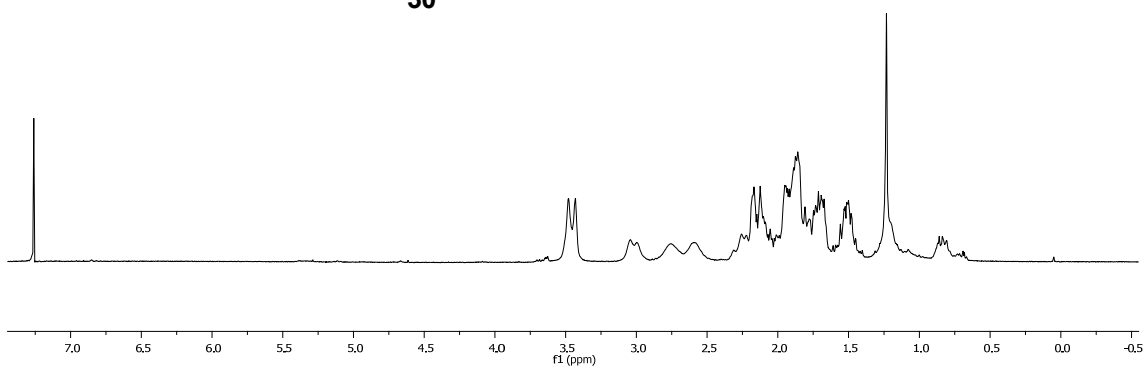


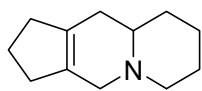


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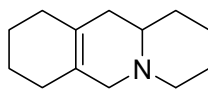
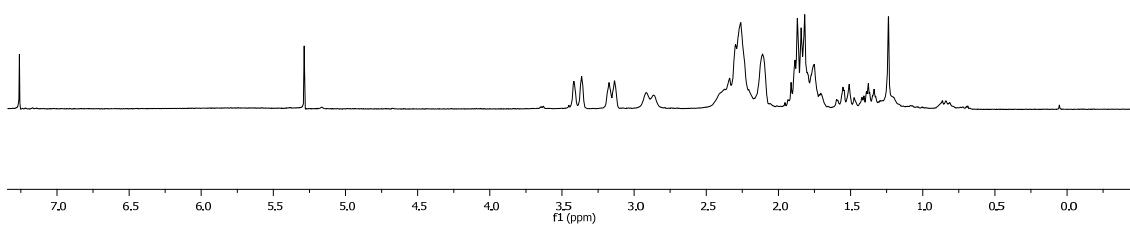


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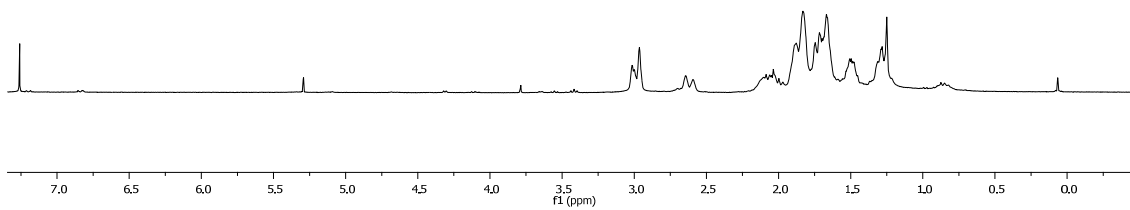


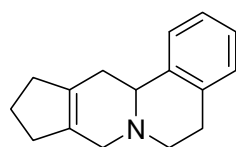


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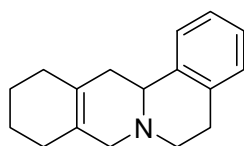
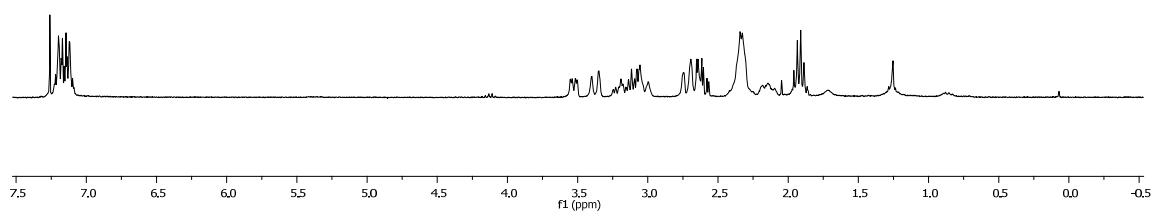


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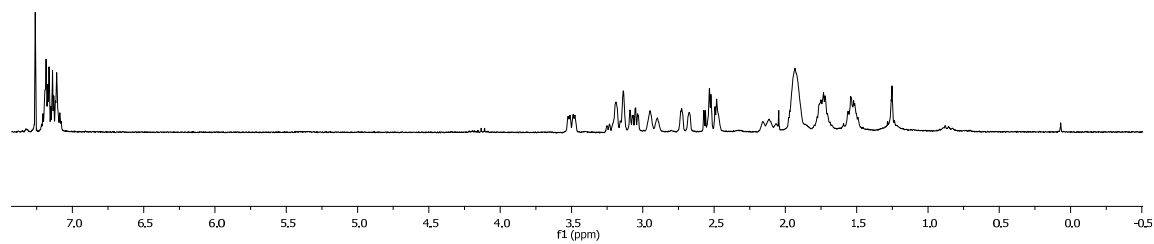


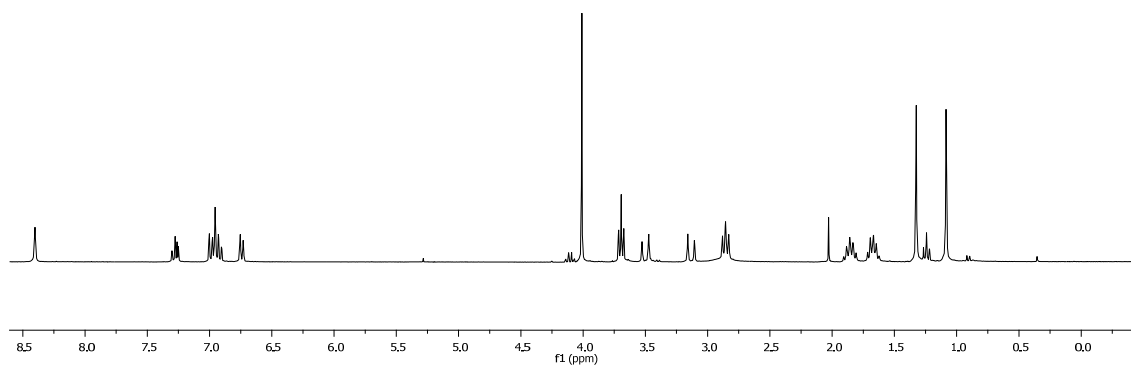
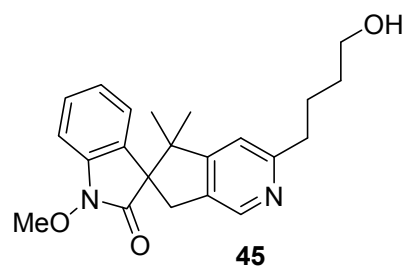
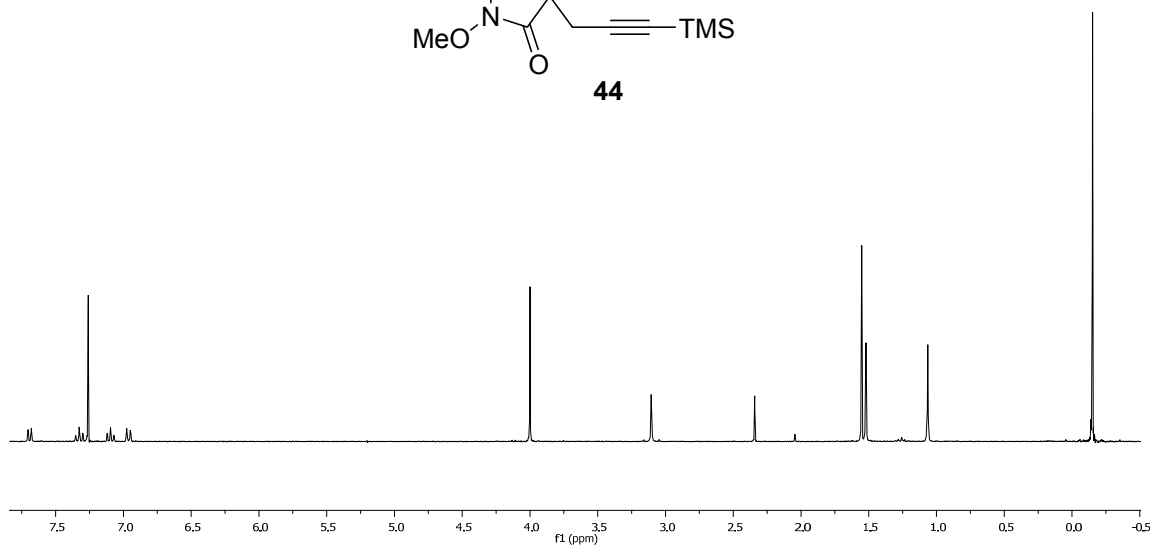
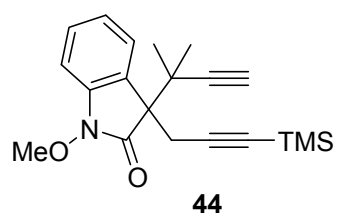


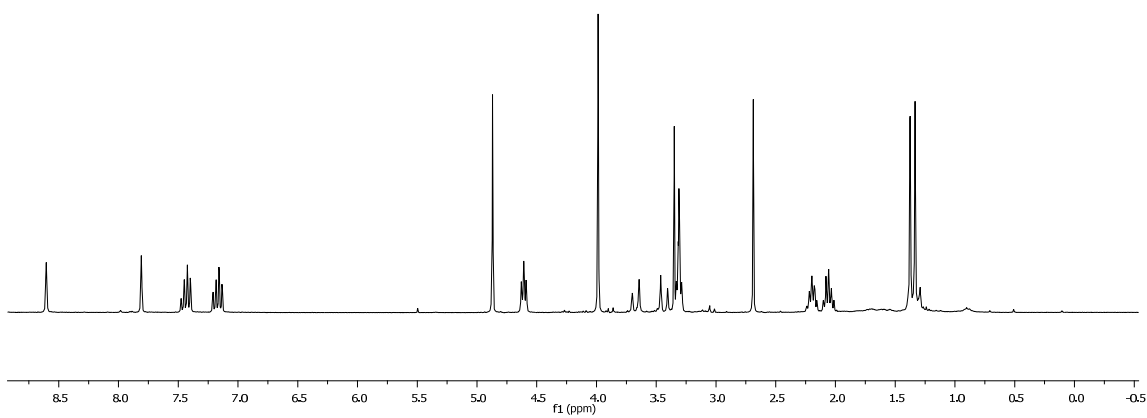
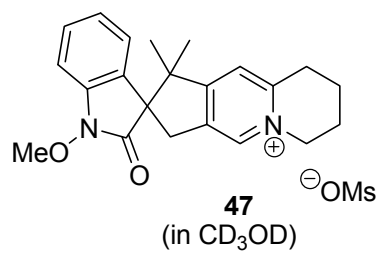
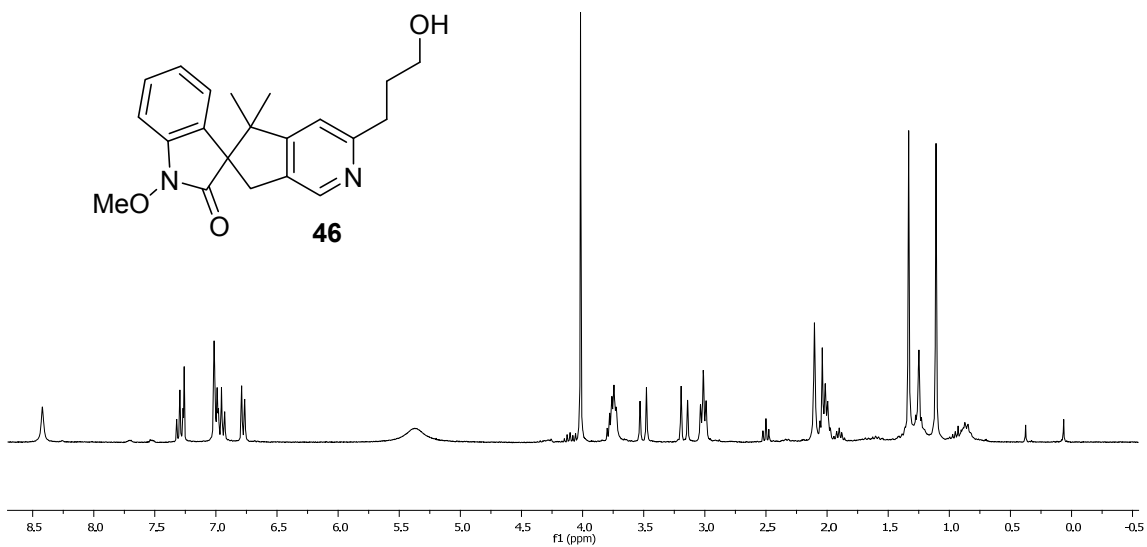
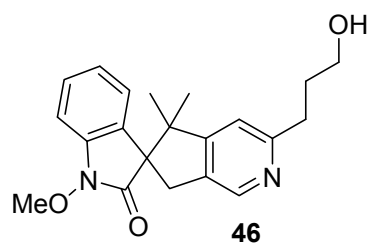
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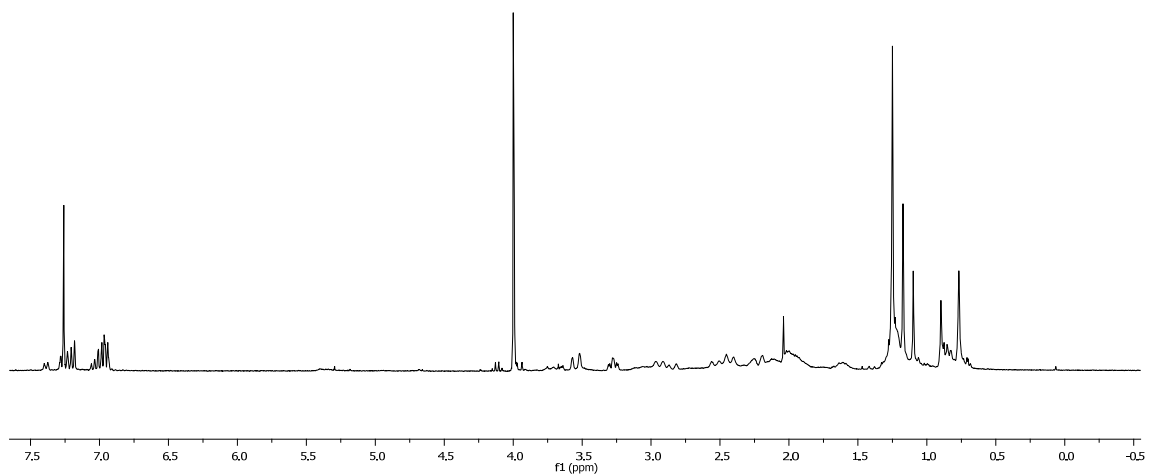
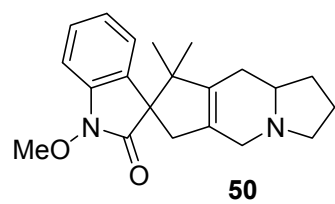
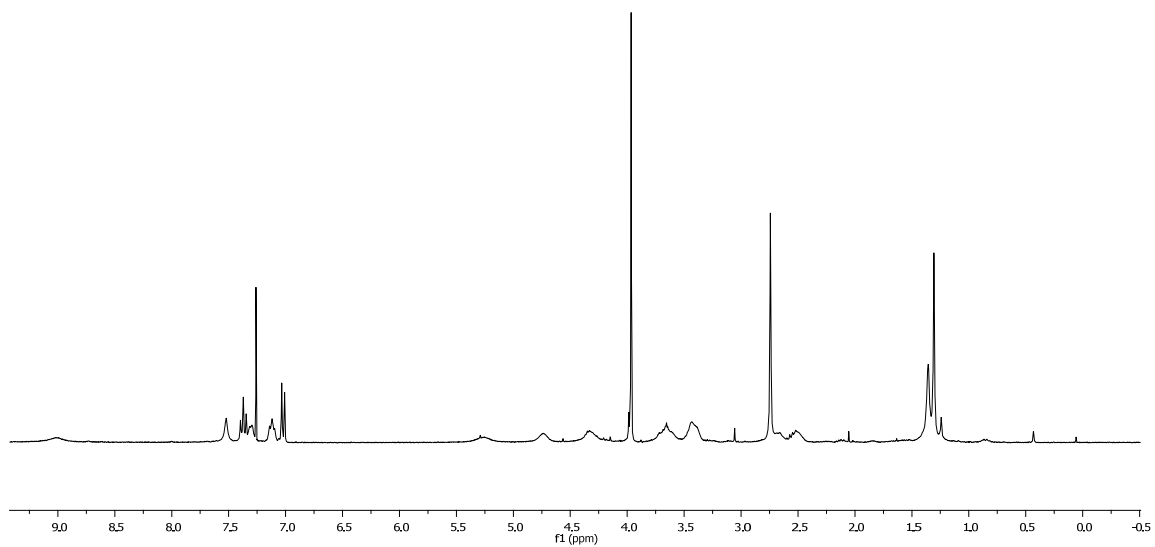
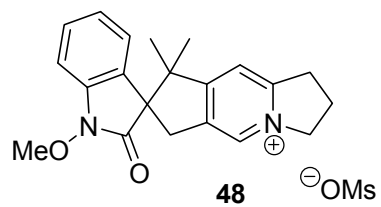


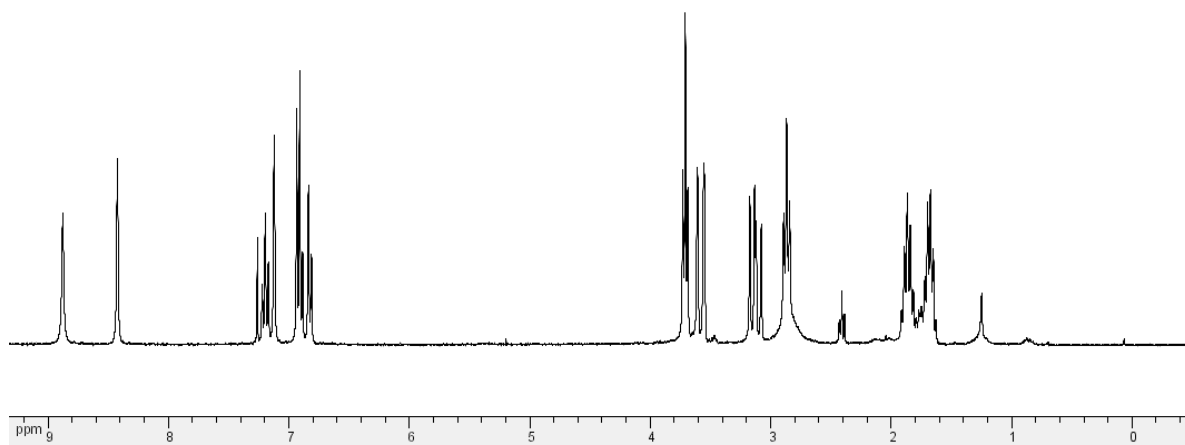
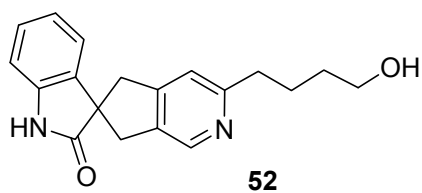
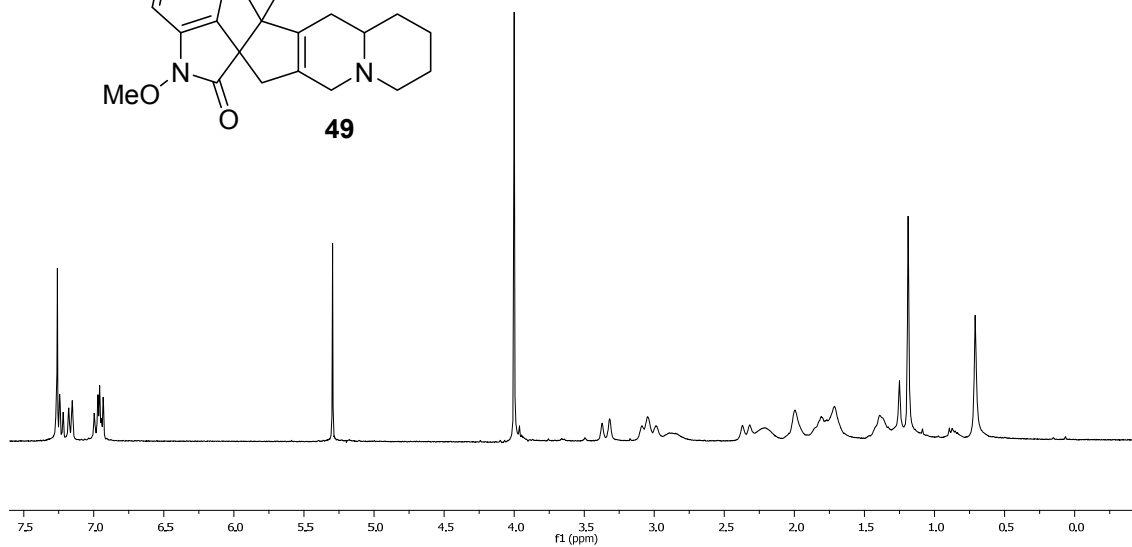
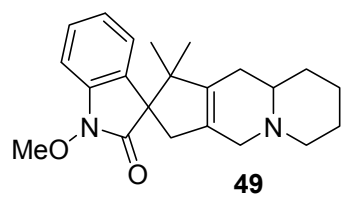
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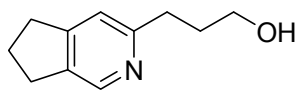




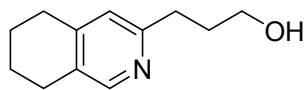
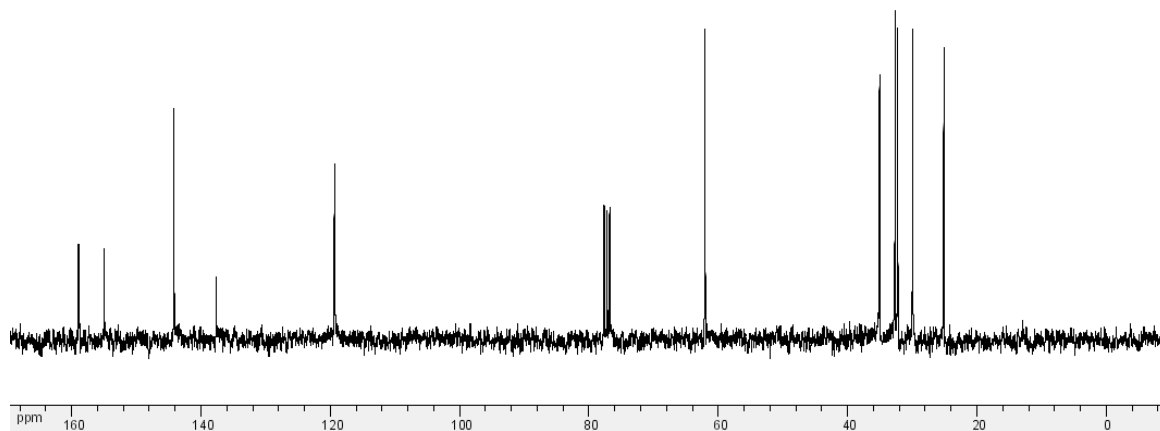


¹³C NMR Spectra for Compounds 15-18, 21-32, 34-41, and 44-50

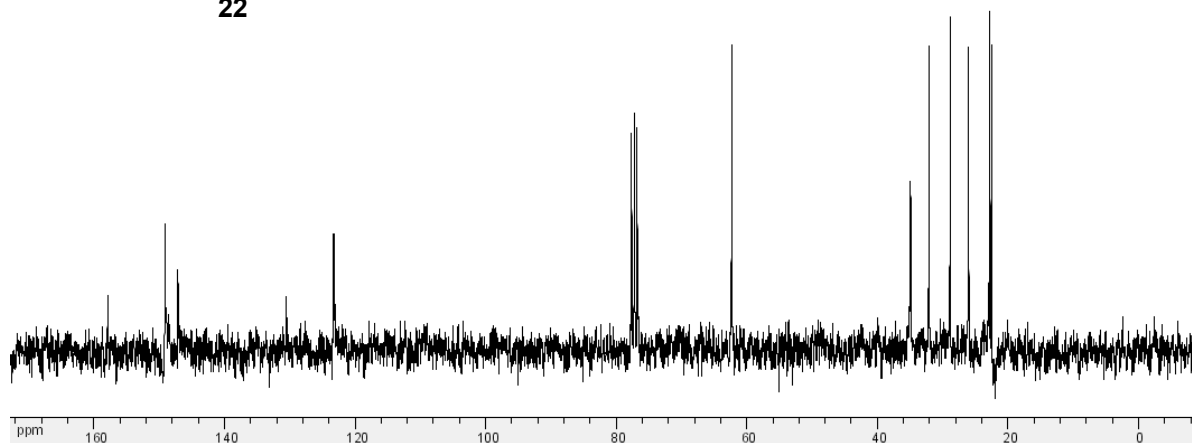
All spectra were recorded at 75 MHz in CDCl₃ unless noted otherwise.

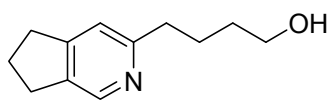


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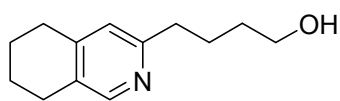
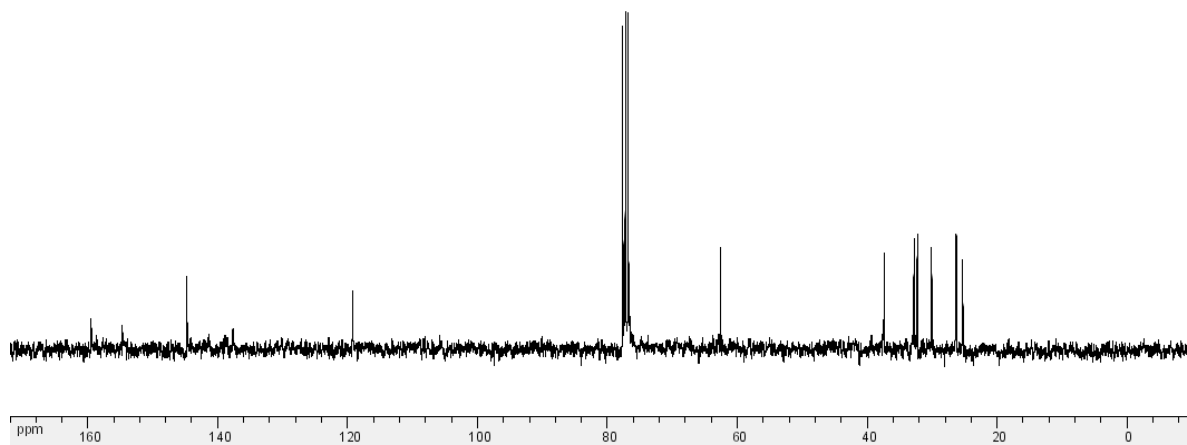


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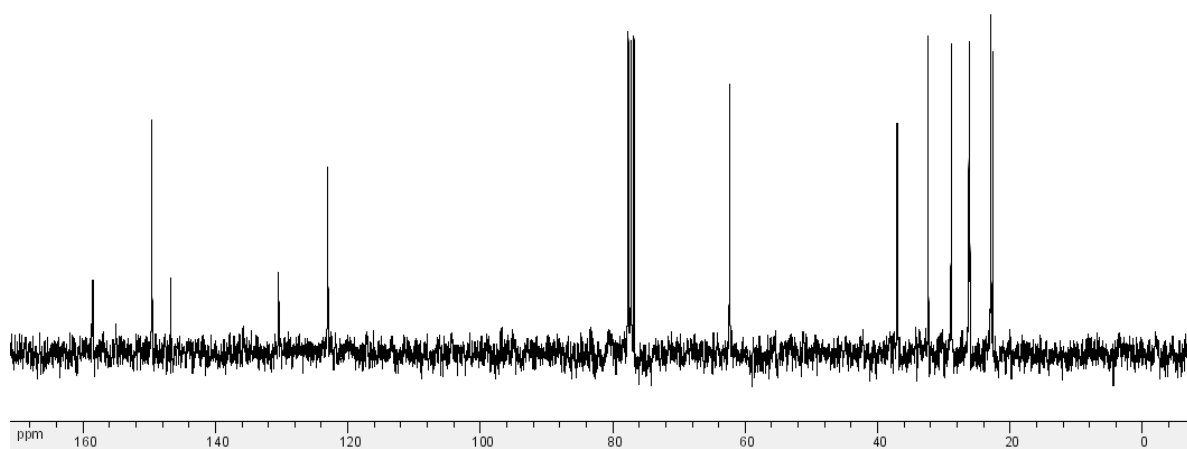


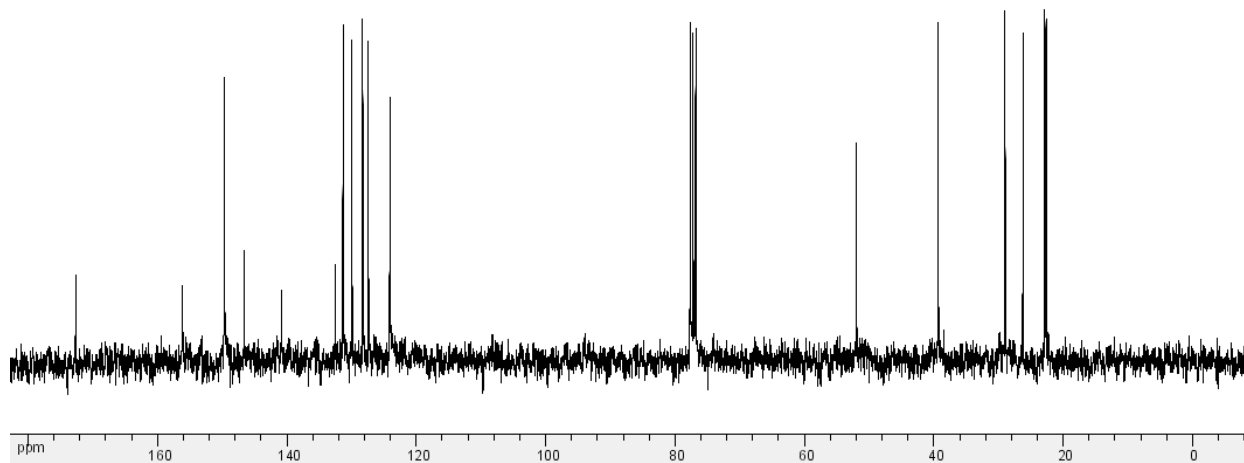
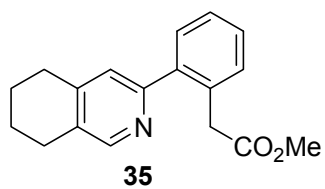
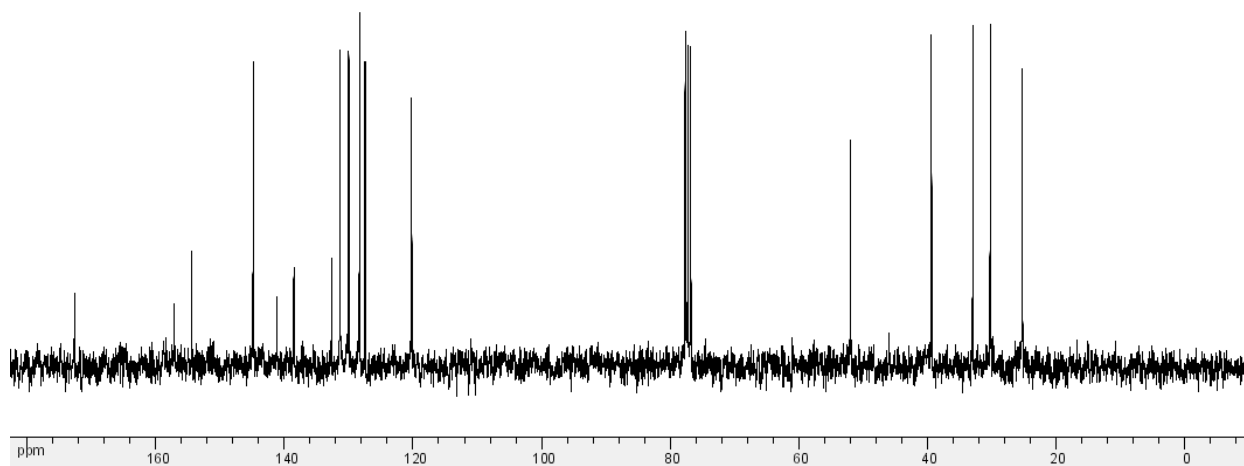
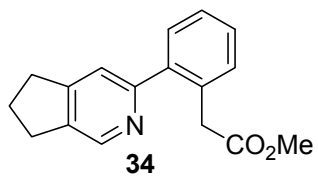


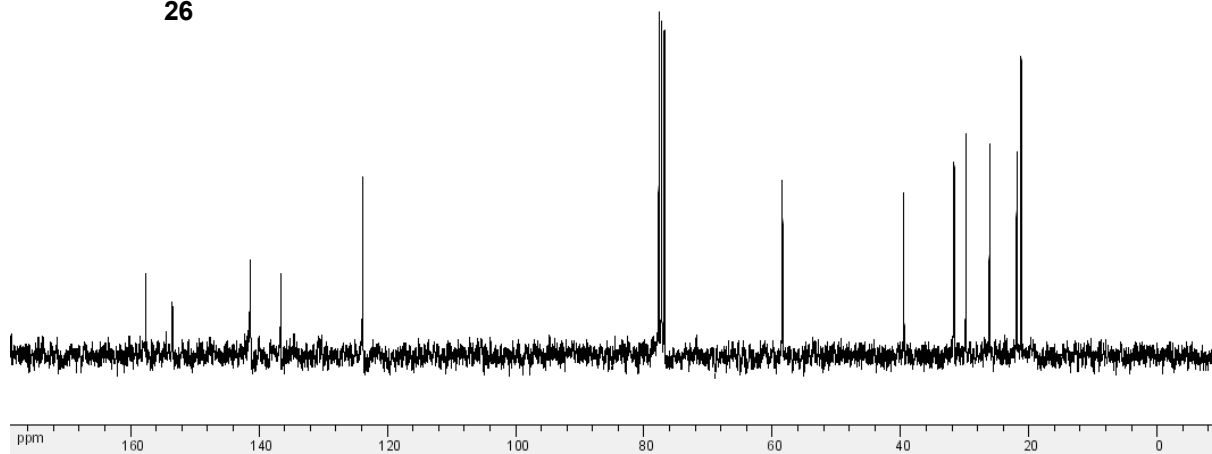
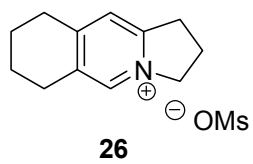
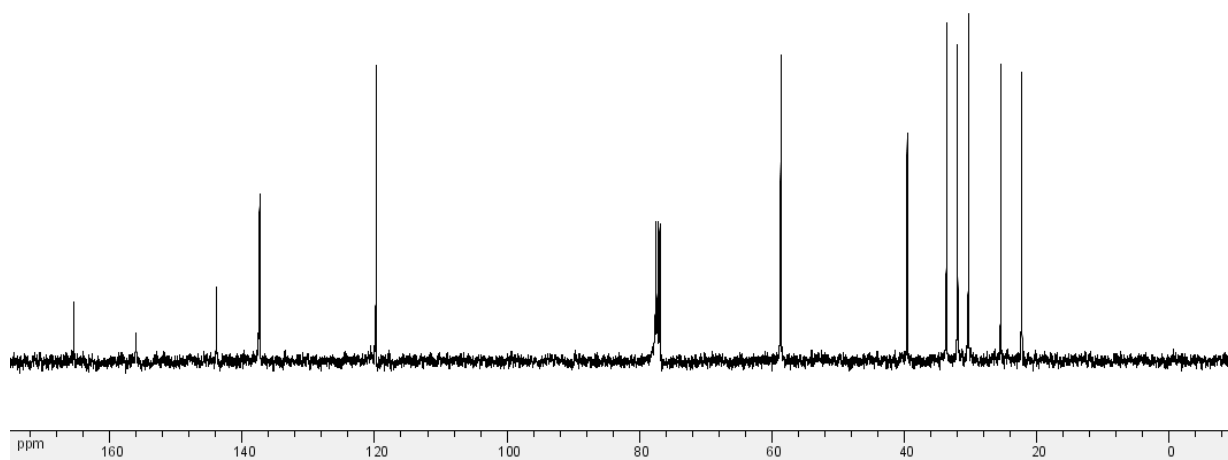
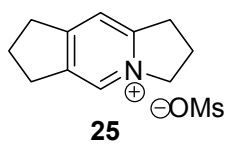
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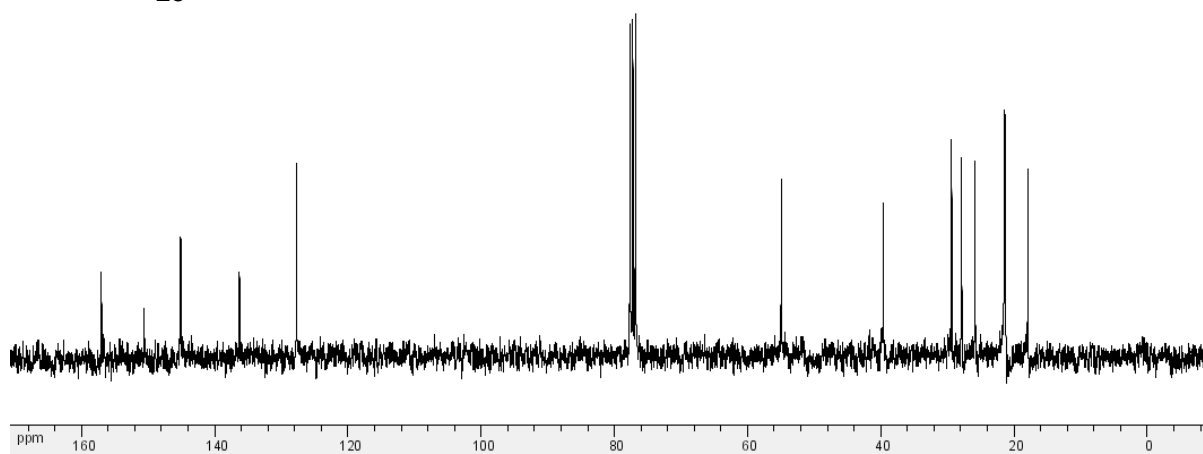
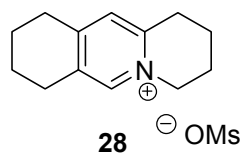
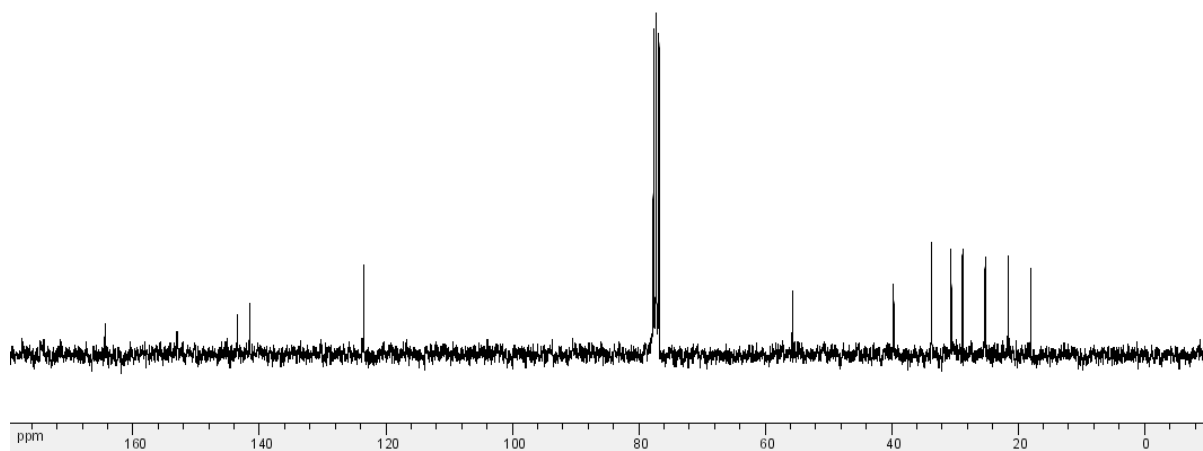
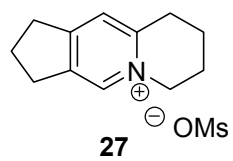


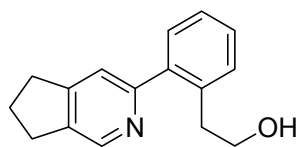
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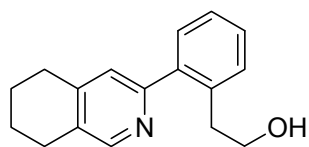
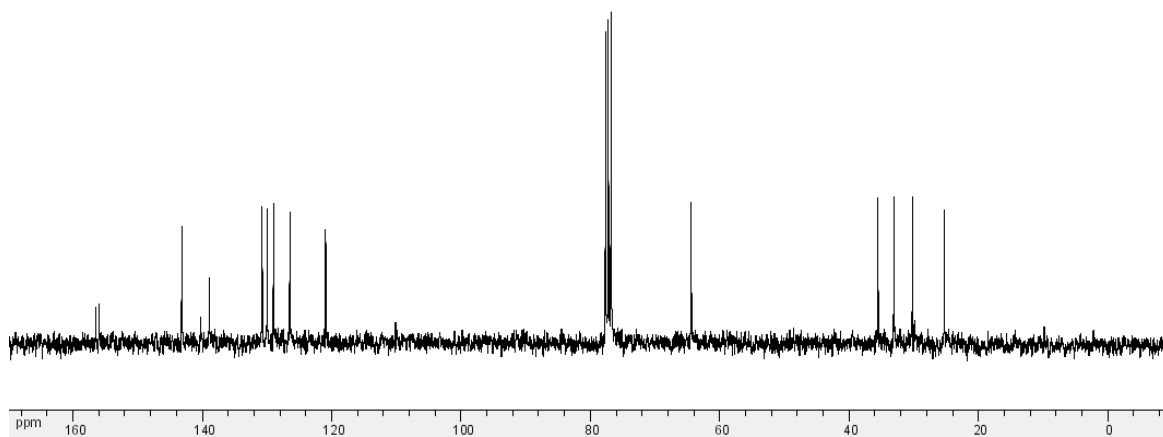




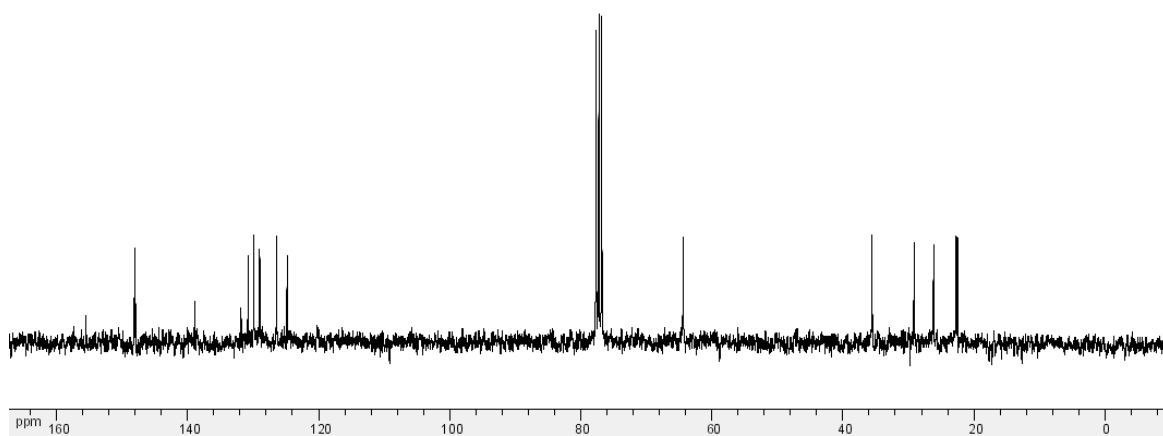


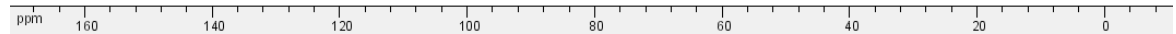
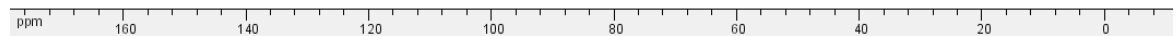


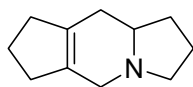
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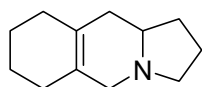
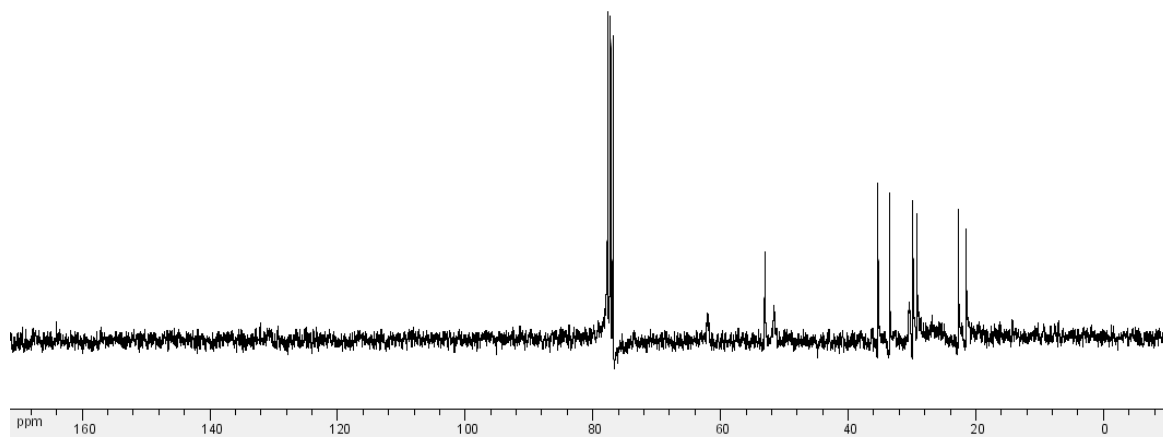
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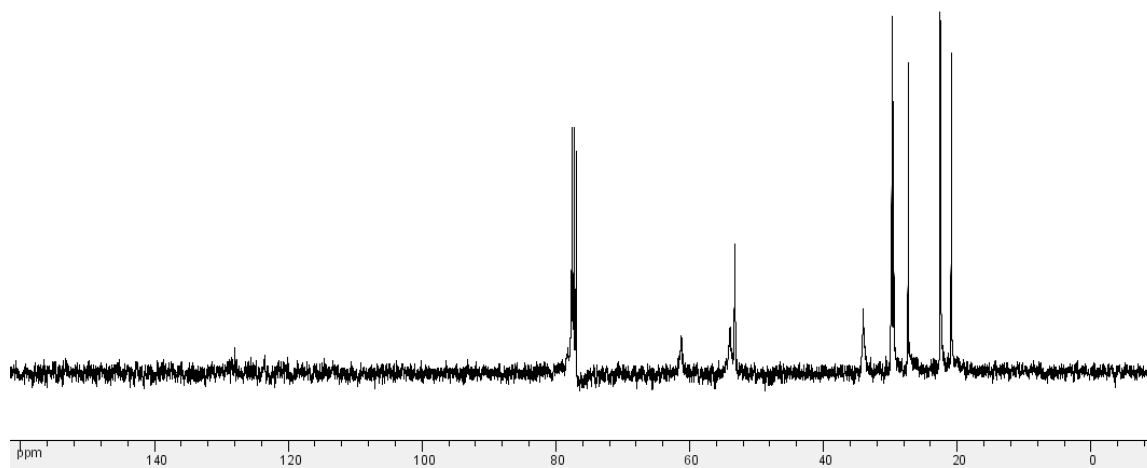


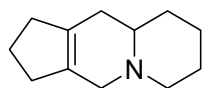


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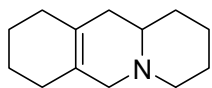
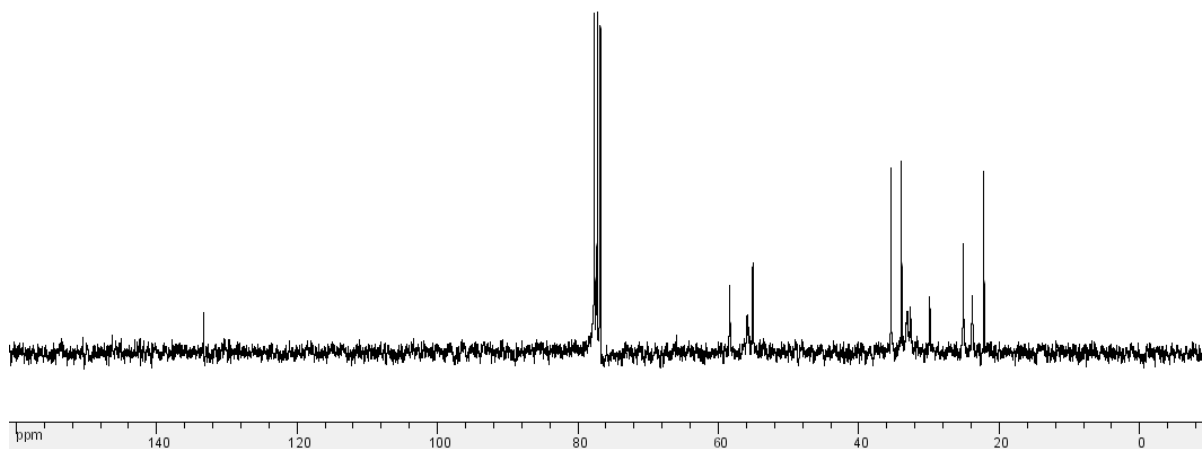


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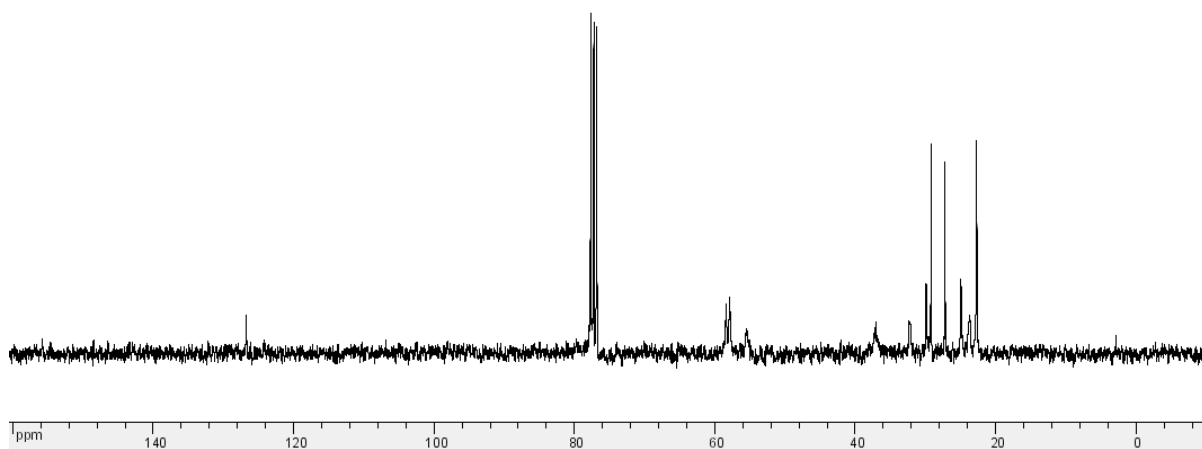


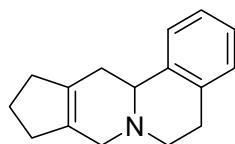


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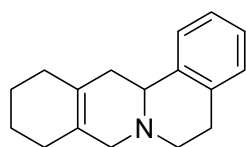
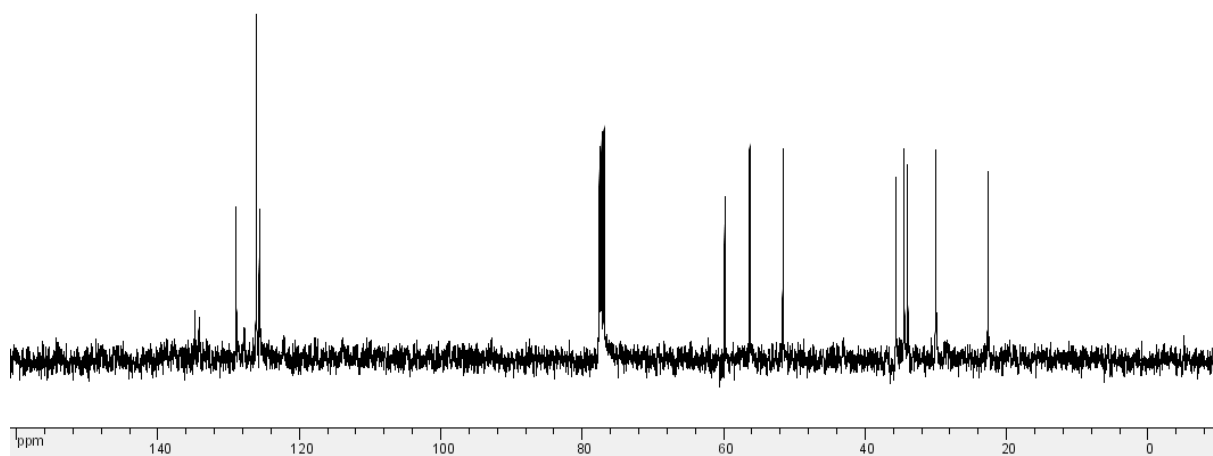


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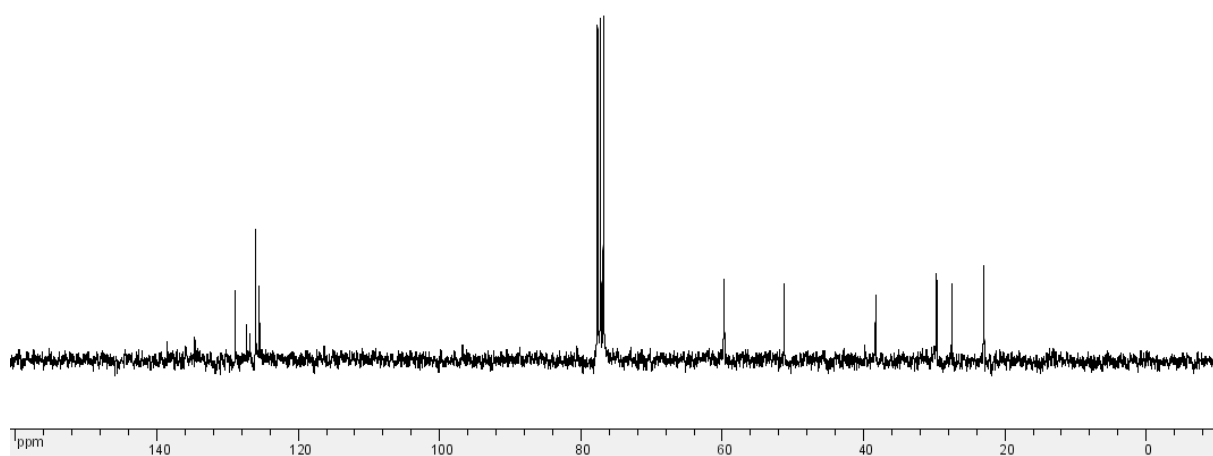


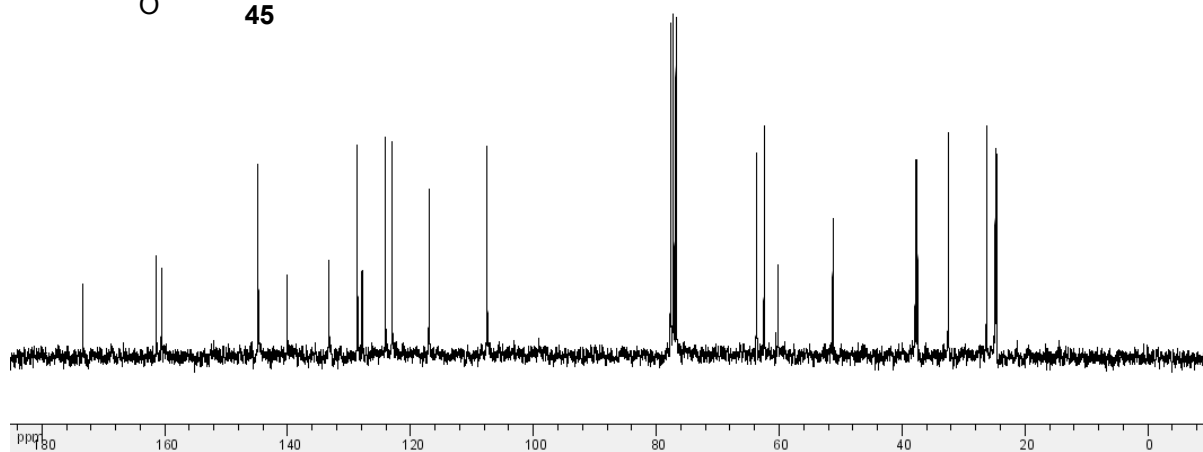
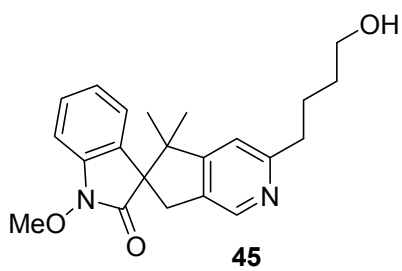
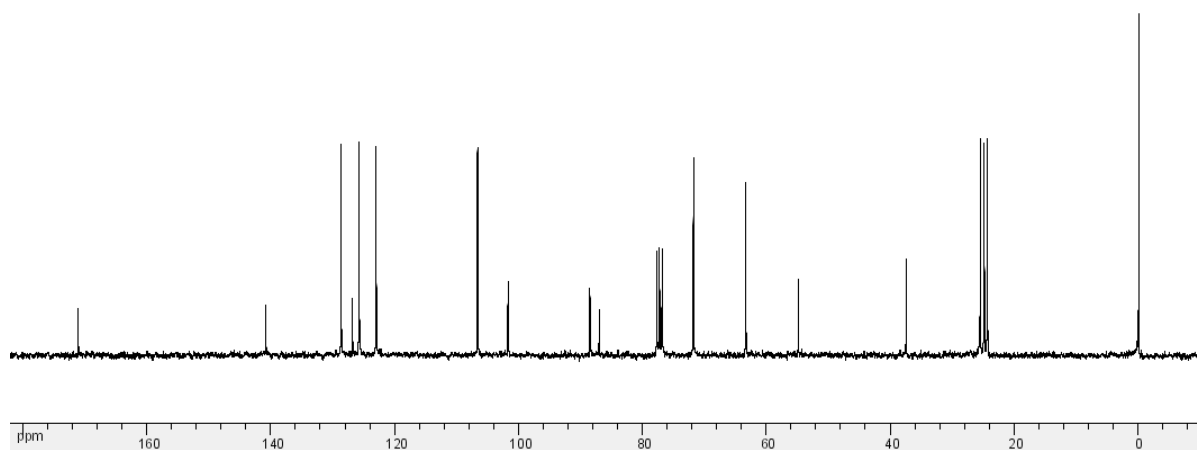
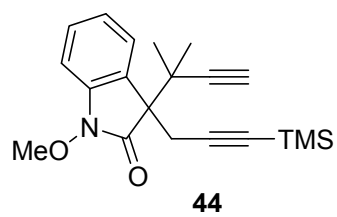


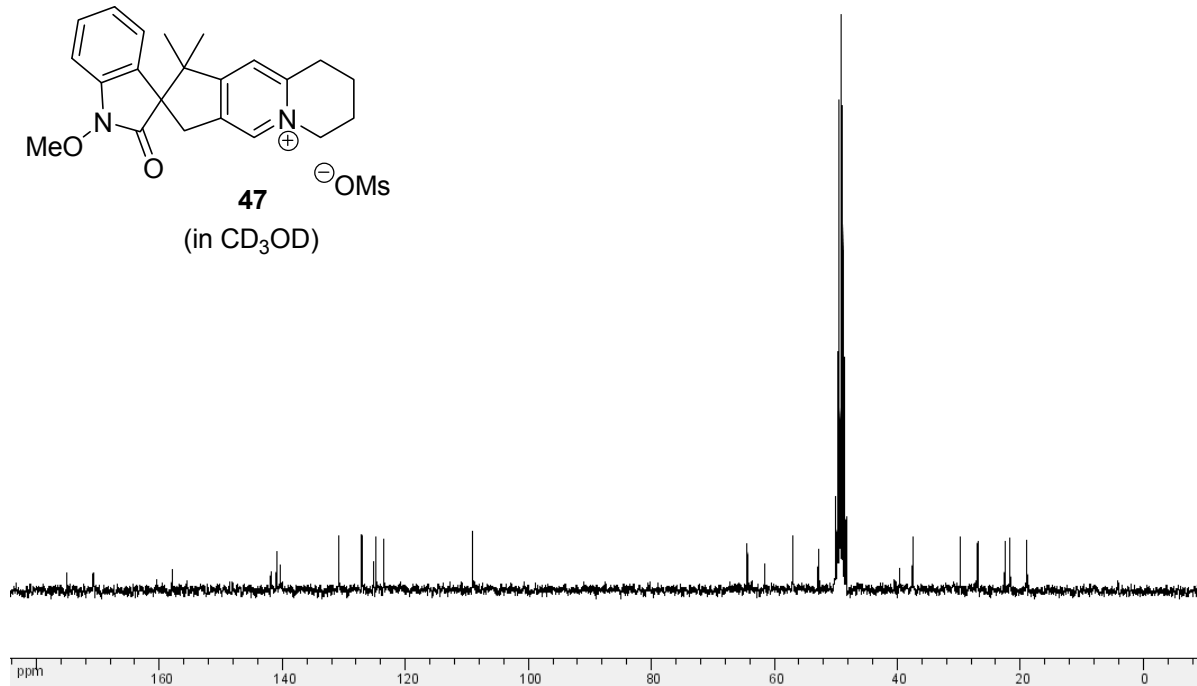
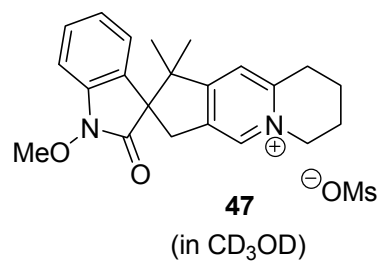
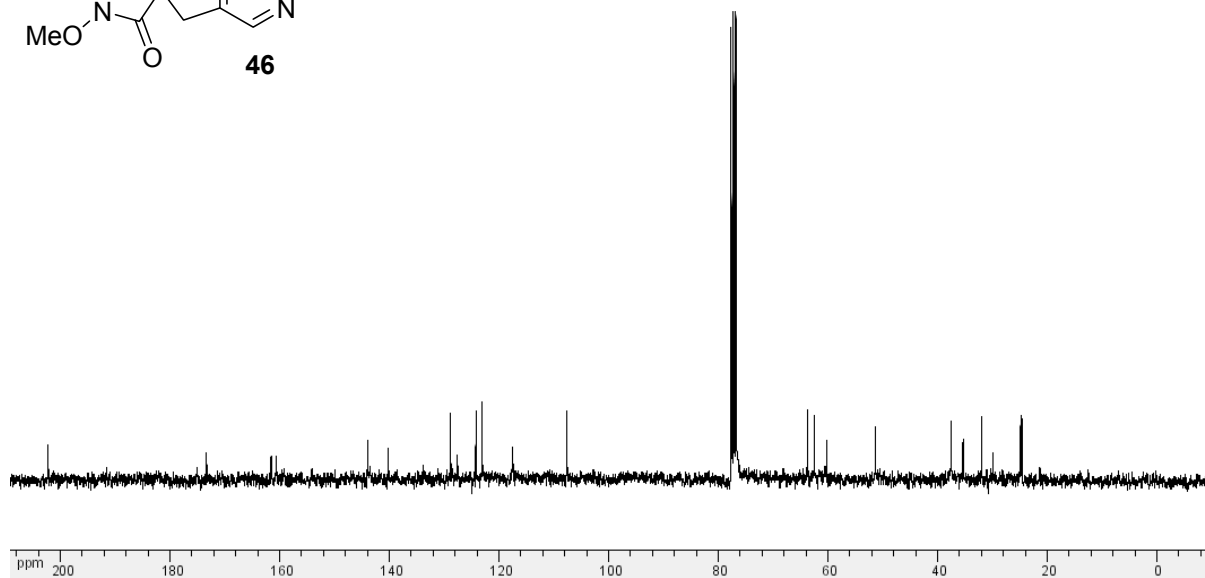
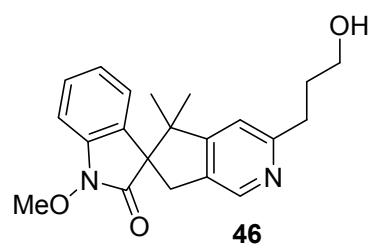
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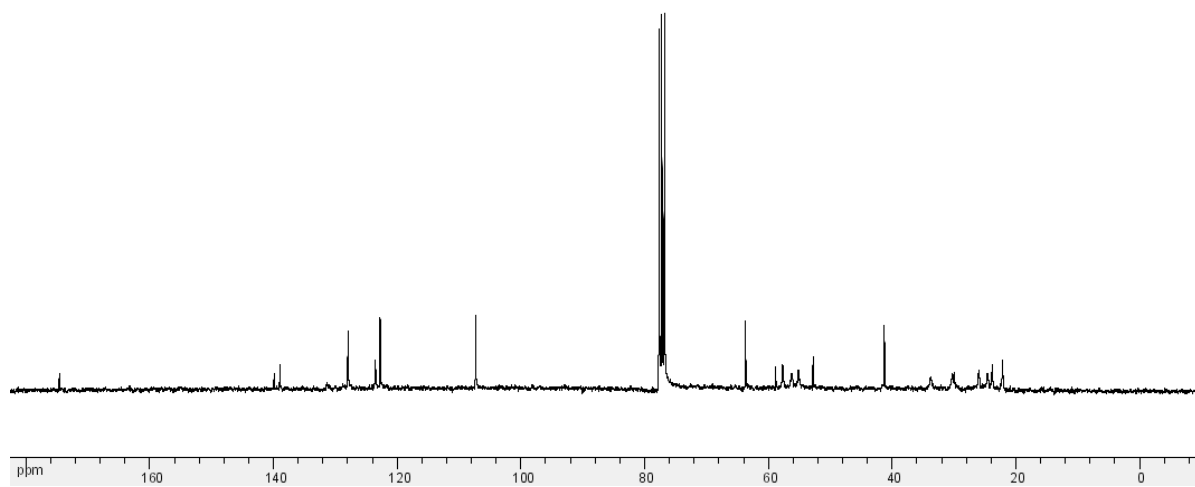
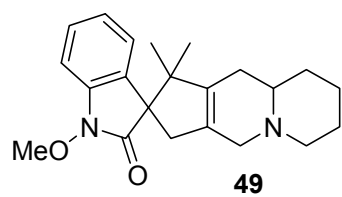
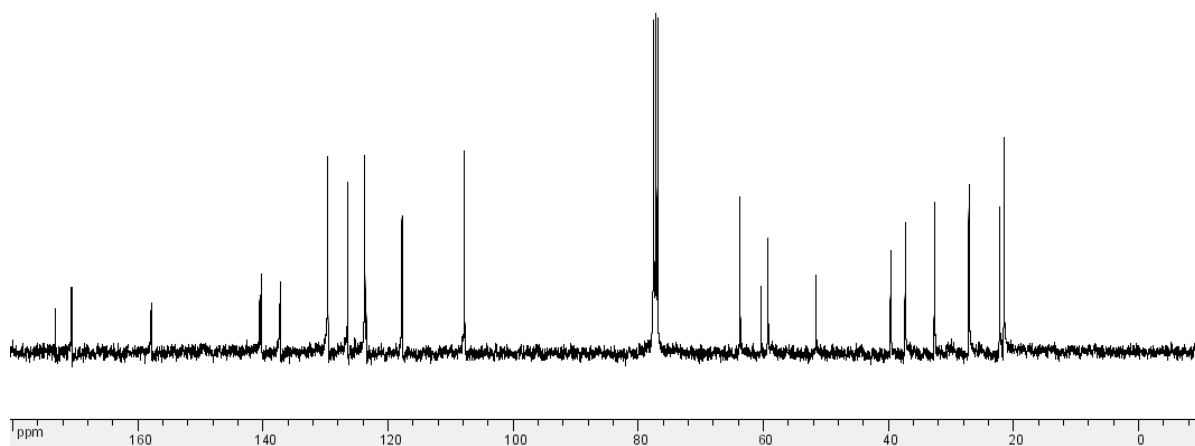
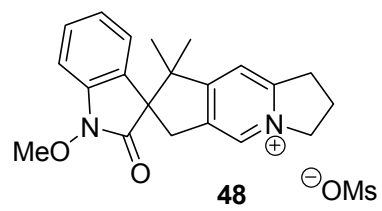


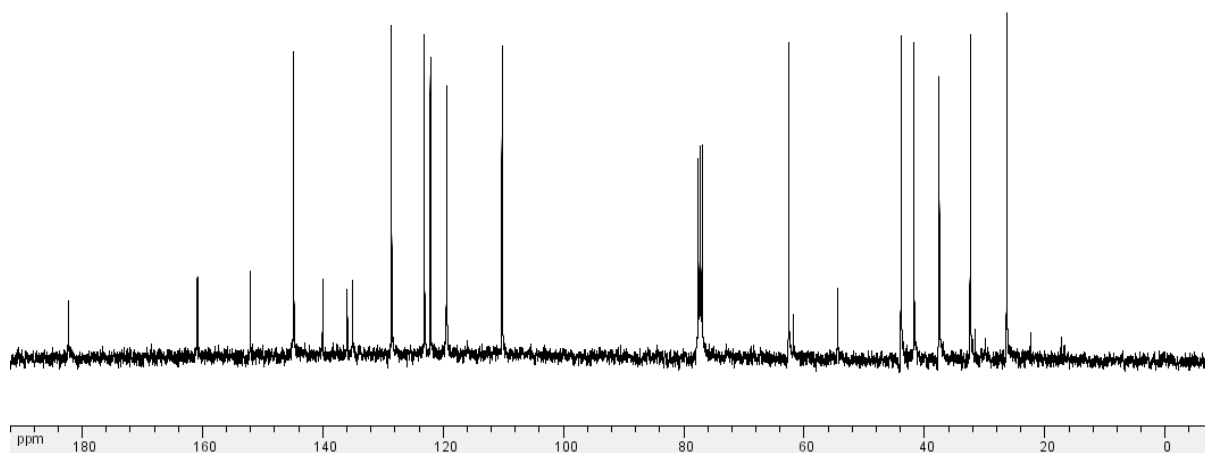
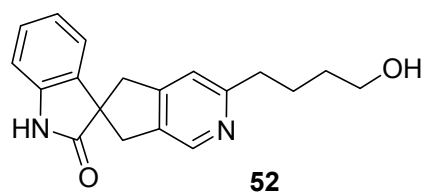
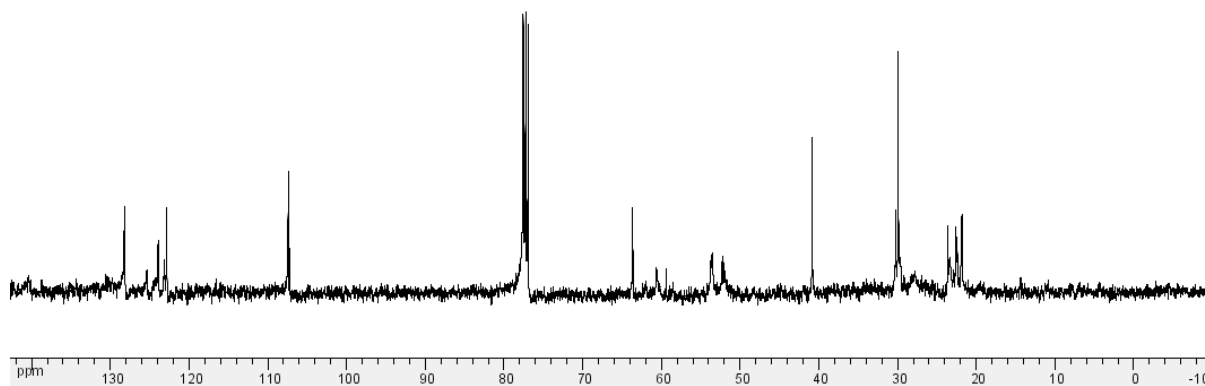
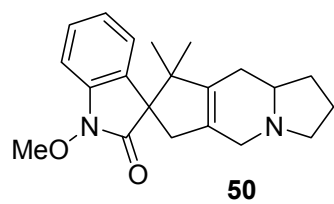
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