$Ce(SO_4)_2$-Catalysed the Highly Diastereoselective Synthesis of Tetrahydroquinolines Via imino Diels Alder ABB´ Type Reaction and their In Vivo Toxicity and Imaging in Zebrafish Embryos

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ELECTRONIC SUPPORTING INFORMATION

1. Reagents

Aniline: Was purchased from Merck and used as received.
4'-Aminoacetanilide: Was purchased from Merck and used as received.
***p*-Anisidine:** Was purchased from Aldrich and used as received.
4-Aminobenzoic acid: Was purchased from Aldrich and used as received.
***N*-Vinylacetamide:** Was purchased from Aldrich and used as received.
***N*-Vinylformamide:** Was purchased from Aldrich and used as received.
1-Vinyl-2-pyrrolidone: Was purchased from Merck and used as received.
Ceric ammonium nitrate: Was purchased from Merck and used as received.
Cerium(IV) sulfate: Was purchased from Merck and used as received.
Methanol: Was purchased from Merck and used as received.
Acetonitrile: Was purchased from J.T.Baker and used as received.
Dimethyl sulfoxide: Was purchased from Aldrich and used as received.
Silica gel 60 (0.063-0.200 mm) 70-230 mesh: Was purchased from Merck and used as received.

2. Characterization data of all synthesized 2-methyltetrahydroquinolines 3a-l

***cis*-4-Acetamido-6-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline (3a):** White solid (0.43 g, 1.78 mmol, 89 %), R_f [hexane-EtOAc] = 0.5; mp: 225-228 °C; FT-IR (KBr disk, cm^{-1}): 3363, 3239, 3070, 1635, 1589, 1434, 1280, 817; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 8.18 (d, *J* = 8.8 Hz, 1H, 4-NH), 7.55 (d, *J* = 8.3 Hz, 1H, 7-H_{Ar}), 7.52 (s, 1H, 5-H_{Ar}), 6.73 (s, 1H, 1-NH), 6.48 (d, *J* = 8.3 Hz, 1H, 8-H_{Ar}), 5.02 (ddd, *J* = 11.5, 8.8, 5.4 Hz, 1H, 4-H_{ax}), 3.55 (dqd, *J* = 11.5, 6.3, 2.6 Hz, 1H, 2-H_{ax}), 2.35 (s, 3H, 6-$COCH_3$), 2.02-1.96 (m, 1H, 3-H_{eq}), 1.94 (s, 3H, 4-$COCH_3$), 1.38 (q, *J* = 11.5 Hz, 1H, 3-H_{ax}), 1.17 (d, *J* = 6.3 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 194.9, 169.4, 149.9, 129.3 (+), 127.2 (+), 124.4, 120.2, 112.0 (+), 45.9 (+), 44.9 (+), 36.6 (-), 25.8 (+), 22.8 (+), 21.5 (+); COSY correlation [δ_H/δ_H]: 1.17/3.55 [2-CH_3/2-H_{ax}], 1.38/5.02/2.02-1.96 [3-H_{ax}/4-H_{ax}/3-H_{eq}], 2.02-1.96/5.02/1.38 [3-H_{eq}/4-H_{ax}/3-H_{ax}], 3.55/2.02-1.96/1.38/1.17 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.02/2.02-1.96/1.38 [4-H_{ax}/3-H_{eq}/3-H_{ax}], 6.48/7.55 [8-H_{Ar}/7-H_{Ar}], 7.55/6.48 [7-H_{Ar}/8-H_{Ar}], 8.18/5.02 [4-NH/4-H_{ax}]; HSQC correlation [δ_H/δ_C]: 1.17/21.5 [2-CH_3/C-11], 1.38/36.6 [3-H_{ax}/C-3], 1.94/22.8 [4-$COCH_3$/C-14], 2.02-1.96/36.6 [3-H_{eq}/C-3], 2.35/25.8 [6-$COCH_3$/C-16], 3.55/46.0 [2-H_{ax}/C-2], 5.02/44.9 [4-H_{ax}/C-4], 6.48/112.0 [8-H_{Ar}/C-8], 7.52/127.2 [5-H_{Ar}/C-5], 7.55/129.3 [7-H_{Ar}/C-7]; HMBC correlation [δ_H/δ_C]: 1.17/46.0/36.6 [2-CH_3/C-2/C-3], 1.38/46.0/44.9/21.5 [3-H_{ax}/C-2/C-4/C-11], 1.94/169.4 [4-$COCH_3$/C-13], 2.02-1.96/44.9 [3-H_{eq}/C-4], 2.35/194.7/124.4 [6-$COCH_3$/C-12/C-6], 5.02/36.6/120.2 [4-H_{ax}/C-3/C-9], 6.48/124.4/120.2/44.9 [8-H_{Ar}/C-6/C-9/C-4], 6.73/ 149.9/120.2/112.0/46.0/36.6/21.5 [1-NH/C-10/C-9/C-8/C-2/C-3/C-11], 7.52/194.7/149.9 /129.3/44.9 [5-H_{Ar}/C-12/C-10/C-7/C-4], 7.55/194.7/149.9/127.2 [7-H_{Ar}/C-12/C-10/C-5], 8.18/ 169.4/44.9 [4-NH/C-13/C-4]; GC: R_t= 24.3 min, MS (EI), *m/z* (%): 246 ($M^{+\cdot}$, 5),

231 (5), 215 (2), 203 (12), 186 (80), 172 (100), 77 (3); HRMS (ESI+): *m/*z: calcd for $C_{14}H_{19}N_2O_2$ ($[M+H]^+$) 247,1441, found: 247,1437; calcd for $C_{14}H_{18}N_2NaO_2$ ($[M+Na]^+$) 269,1260, found: 269,1263.

cis-4-Acetamido-2-methyl-1,2,3,4-tetrahydroquinoline (3b): White solid (0.33 g, 1.6 mmol, 80 %), R_f [hexane-EtOAc 1:1] = 0.7; mp: 170-172 °C; FT-IR (KBr disk, cm^{-1}): 3347, 3255, 3070, 2962, 1635, 1496, 1311, 971, 755; ^{1}H NMR (400 MHz, $CDCl_3$), δ(ppm): 8.12 (d, *J* = 8.9 Hz, 1H, 4-NH), 6.92-6.86 (m, 2H, 8-H_{Ar}), 6.49-6.44 (m, 2H, 7-H_{Ar} and 5-H_{Ar}), 5.66 (s, 1H, 1-NH), 5.02 (ddd, *J* = 11.8, 8.9, 6.0 Hz, 1H, 4-H_{ax}), 3.44-3.38 (m, 1H, 2-H_{ax}), 1.95-1.89 (m, 1H, 2-H_{ax}), 1.88 (s, 3H, 4-$COCH_3$), 1.38 (q, *J* = 11.8 Hz, 1H, 3-H_{ax}), 1.12 (d, *J* = 6.2 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, $CDCl_3$), $\delta_{(ppm)}$: 169.2, 145.7, 127.4 (+), 126.6 (+), 121.3, 115.5 (+), 113.4 (+), 46.1 (+), 45.2 (+), 37.5 (-), 22.8 (+), 22.0 (+); COSY correlation [δ_H/δ_H]: 1.12/3.44-3.38 [2-CH_3/2-H_{ax}], 1.38/5.02/3.44-3.38/1.95-1.89 [3-H_{ax}/4-H_{ax}/2-H_{ax}/3-H_{eq}], 1.95-1.89/5.02/3.44-3.38/1.38 [3-H_{eq}/4-H_{ax}/2-H_{ax}/3-H_{ax}], 3.44-3.38/1.95-1.89/1.38/1.12 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.02/8.12/1.95 /1.38-1.89 [4-H_{ax}/4-NH/3-H_{ax}/3-H_{eq}], 8.12/5.02 [4-NH/4-H_{ax}]; HSQC correlation [δ_H/δ_C]: 1.12/22.0 [2-CH_3/C-11], 1.38/37.5 [3-H_{ax}/C-3], 1.88/22.8 [4-$COCH_3$/C-14], 1.95-1.89/37.5 [3-H_{eq}/C-3], 3.44-3.38/46.1 [2-H_{ax}/C-2], 5.02/45.7 [4-H_{ax}/C-4], 6.49-6.44/ 113.4,115.5 [7-H_{Ar},5-H_{Ar}/C-5,C-7], 6.92-6.86/127.4,126.7 [6-H_{Ar},8-H_{Ar}/C-8,C-6]; HMBC correlation [δ_H/δ_C]: 1.12/46.1/37.5 [2-CH_3/C-2/C-3], 1.38/46.1/45.2/22.0 [3-H_{ax}/C-2/C-4/C-11], 1.88/169.2 [4-$COCH_3$/C-13], 1.95-1.89/121.4/45.2 [3-H_{eq}/C-9/C-4], 5.66/121.4/113.4/37.5 [1-NH/C-9/C-8/C-3], 6.49-6.44/121.4/115.5,113.4 [7-H_{Ar},5-H_{Ar} /C-9/C-6,C-8], 6.92-6.86/127.4,126.6/145.8/45.2 [6-H_{Ar},8-H_{Ar}/C-7,C-5/C-10/C-4], 8.12/ 169.2 [4-NH/C-13]; GC: R_t= 16.7 min, MS (EI), *m/z* (%): 204 ($M^{+\cdot}$, 25), 187 (2), 173 (2), 161 (5), 114 (60), 130 (100), 77 (5); HRMS (ESI+): *m/*z: calcd for $C_{12}H_{17}N_2O$ ($[M+H]^+$) 205,1335, found: 205,1339; calcd for $C_{12}H_{16}N_2NaO$ ($[M+Na]^+$) 227,1155, found: 227,1152.

cis-4-Acetamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (3c): White solid (0.36 g, 1.54 mmol, 77 %), R_f [hexane-EtOAc 1:1] = 0.7; mp: 176-178 °C; FT-IR (KBr disk, cm^{-1}): 3378, 3286, 2962, 1727, 1635, 1542, 1295, 1234, 1157, 1033, 817; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 8.15 (d, 1H, *J* = 8.7 Hz, 4-NH), 6.58 (d, 1H, *J* = 8.5 Hz, 7-H_{Ar}), 6.51 (s, 1H, 5-H_{Ar}), 6.43 (d, 1H, *J* = 8.5 Hz, 8-H_{Ar}), 5.28 (s, 1H, 1-NH), 5.05-4.98 (m, 1H, 4-H_{ax}), 3.60 (s, 3H, 6-OCH_3), 3.30-3.37 (m, 1H, 2-H_{ax}), 1.96-1.90 (m, 1H, 3-H_{eq}), 1.89 (s, 3H, 4-$COCH_3$), 1.36 (q, 1H, *J* = 11.7 Hz, 3-H_{ax}), 1.10 (d, 3H, *J* = 6.0 Hz, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 169.3, 150.7, 140.1, 122.7, 114.6 (+), 113.6 (+), 112.4 (+), 55.4 (+), 46.4 (+), 45.4 (+), 37.7 (-), 22.8 (+), 22.0 (+); GC: R_t= 20.7 min, MS (EI), *m/z* (%): 234 ($M^{+\cdot}$, 25), 234 (25), 219 (2), 203 (2), 174 (55), 160 (100); HRMS (ESI+): *m/*z: calcd for $C_{13}H_{19}N_2O_2$ ($[M+H]^+$) 235,1441, found: 235,1439; calcd for $C_{13}H_{18}N_2NaO_2$ ($[M+Na]^+$) 257,1260, found: 257,1261.

cis-4-Acetamido-6-carboxy-2-methyl-1,2,3,4-tetrahydroquinoline (3d): White solid (0.37 g, 1.5 mmol, 75 %), R_f [hexane-EtOAc 1:2] = 0.4; mp: 259-262 °C; FT-IR (KBr disk, cm^{-1}): 3363, 3301, 3270, 2962, 2591, 1666, 1604, 1511, 1295, 833, 771; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 11.9 (br., s, 1H, 6-COOH), 8.21 (d, *J* = 9.0 Hz, 1H, 4-NH), 7.52 (s, 1H, 5-H_{Ar}), 7.50-7.52 (m, 1H, 7-H_{Ar}), 6.54 (s, 1H, 1-NH), 6.47 (d, *J* = 9.0 Hz, 1H, 8-H_{Ar}), 5.01 (dd, *J* = 11.8, 9.0 Hz, 1H, 4-H_{ax}), 3.53 (dqd, *J* = 11.8, 6.3, 2.5 Hz, 1H, 2-H_{ax}), 1.95-198 (m, 1H, 3-H_{eq}), 1.93 (s, 3H, 4-$COCH_3$), 1.38 (q, *J* = 11.8 Hz, 1H, 3-H_{ax}), 1.16 (d, *J* = 6.3 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 169.5, 167.7, 149.6, 129.7 (+), 128.5 (+), 120.3, 116.5, 112.3 (+), 46.0 (+), 45.0 (+), 36.8 (-), 22.9 (+), 21.6 (+); COSY correlation [δ_H/δ_H]: 1.16/3.53 [2-CH_3/2-H_{ax}], 1.38/5.01/3.53 /1.95-1.98 [3-H_{ax}/4-H_{ax}/2-H_{ax}/3-H_{eq}], 1.95-1.98/5.01/3.53/1.38 [3-H_{eq}/4-H_{ax}/2-H_{ax}/3-H_{ax}], 3.53/1.95-198/1.38/1.16 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.01/8.21/ 1.95-198/1.38 [4-H_{ax}/4-NH/3-H_{eq}/3-H_{ax}], 6.47/7.50-7.52 [8-H_{Ar}/7-H_{Ar}], 6.54/1.95-1.98 [1-NH/3-H_{eq}], 7.50-7.52/6.47 [7-H_{Ar}/8-H_{Ar}], 7.52/5.01 [5-H_{Ar}/4-H_{ax}], 8.21/5.01 [4-NH/4-H_{ax}]; HSQC correlation [δ_H/δ_C]: 1.16/21.6 [2-CH_3/C-11], 1.93/22.7 [4-$COCH_3$/C-14], 1.95-1.98/1.4 [3-H_{eq}/3-H_{ax}/C-3], 3.53/46.0 [2-H_{ax}/C-2], 5.01/45.0 [4-H_{ax}/C-4], 6.47/112.3 [8-H_{Ar}/C-8], 7.50-7.52/129.7 [7-H_{Ar}/C-7], 7.52/128.5 [5-H_{Ar}/C-5]; HMBC correlation [δ_H/δ_C]: 1.16/46.0/36.8 [2-CH_3/C-2/C-3], 1.38/46.0/45.0/21.6 [3-H_{ax}/C-2/C-4/C-11], 1.93/169.5 [4-$COCH_3$/C-13], 1.95-1.98/45.0 [3-H_{eq}/C-4], 5.01/169.5/120.3/36.8 [4-H_{ax}/C-13/C-10/C-3], 6.47/167.7/128.5/120.3/116.5/45.9 [8-H_{Ar}/C-15/C-5/C-10/C-6/C-4], 6.54/149.6/ 128.5/120.3/112.4/46.0/36.8/21.64 [1-NH/C-9/C-5/C-10/C-8/C-2/C-3/C-11], 7.50-7.52/167.7/149.6/112.3 [7-H_{Ar}/C-15/C-9/C-8], 7.52/167.7/129.7/45.0 [5-H_{Ar}/C-15/C-7/C-4], 8.21/169.5/120.3/45.0/36.8 [4-NH/C-13/C-10/C-4/C-3]; GC: R_t= 17.6 min, MS (EI), *m/z* (%): 204 ($M^{+\cdot}$-44, 5), 161 (5), 144 (60), 130 (100), 77 (10); HRMS (ESI+): *m/z*: calcd for $C_{13}H_{17}N_2O_3$ ($[M+H]^+$) 249,1234, found: 249,1237; calcd for $C_{13}H_{16}N_2NaO_3$ ($[M+Na]^+$) 271,1053, found: 271,1049.

cis-6-Acetyl-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline (3e): Pale yellow solid (0.32 g, 1.38 mmol, 69 %), R_f [hexane-EtOAc 1:1] = 0.5; mp: 235-237 °C; FT-IR (KBr disk, cm^{-1}): 3348, 3255, 3039, 1650, 1589, 1434, 1249, 817; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 8.28 (d, *J* = 9.3 Hz, 1H, 4-NH), 8.23 (s, 1H, 4-COH), 7.56 (d, *J* = 1.3 Hz, 1H, 5-H_{Ar}), 7.51 (dd, *J* = 8.5, 1.3 Hz, 1H, 7-H_{Ar}), 6.51-6.42 (m, 2H, 1-NH and 8-H_{Ar}), 5.12 (ddd, *J* = 12.2, 9.3, 4.2 Hz, 1H, 4-H_{ax}), 3.55 (dqd, *J* = 12.2, 6.3, 2.1 Hz, 1H, 2-H_{ax}), 2.35 (s, 3H, 2-H_{ax}), 2.04 (td, *J* = 12.2, 4.2, 2.1 Hz, 1H, 3-H_{eq}), 1.42 (q, *J* = 12.2 Hz, 1H, 3-H_{ax}), 1.18 (d, *J* = 6.3 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 194.5, 161.0 (+), 149.6, 128.9 (+), 127.1 (+), 124.4, 119.1, 112.0 (+), 45.8 (+), 43.6 (+), 36.4 (-), 25.5 (+), 21.3 (+); GC: R_t= 24.3 min, MS (EI), *m/z* (%): 232 ($M^{+\cdot}$, 25), 217 (10), 186 (60), 172 (100), 161 (10), 144 (25), 129 (8); HRMS (ESI+): *m/z*: calcd for $C_{13}H_{17}N_2O_2$ ($[M+H]^+$) 233,1285, found: 233,1288; calcd for $C_{13}H_{16}N_2NaO_2$ ($[M+Na]^+$) 255,1104, found: 255,1106.

cis-4-Formamido-2-methyl-1,2,3,4-tetrahydroquinoline (3f): White solid (0.26 g, 1.40 mmol, 70 %), R_f [hexane-EtOAc 1:1] = 0.6; mp: 151-153 °C; FT-IR (KBr disk, cm^{-1}): 3286, 3023, 1666, 1527, 1496, 755; ^{1}H NMR (400 MHz, $CDCl_3$), δ(ppm): 8.29 (1H, s, 4-COH), 7.10 (1H, dd, *J* = 7.7, 0.84 Hz, 5-H_{Ar}), 7.03 (1H, td, *J* = 7.7, 7.5, 0.58 Hz, 6-H_{Ar}), 6.67 (1H, td, *J* = 7.5, 0.84 Hz, 7-H_{Ar}), 6.49 (1H, dd, *J* = 7.5, 0.58 Hz, 8-H_{Ar}), 5.87 (1H, d, *J* = 8.4 Hz, 4-NH), 5.39 (1H, ddd, *J* = 11.4, 8.4, 6.2 Hz, 4-H_{ax}), 3.78 (1H, s, 1-NH), 3.53 (1H, dqd, *J* = 11.4, 6.3, 2.1 Hz, 2-H_{ax}), 2.26 (1H, ddd, *J* = 11.4, 6.2, 2.1 Hz, 3-H_{eq}), 1.45 (1H, q, *J* = 11.4 Hz, 3-H_{ax}), 1.20 (3H, d, *J* = 6.3 Hz, 2-CH_3); ^{13}C NMR (101 MHz, $CDCl_3$), $\delta_{(ppm)}$: 161.3 (+),145.3, 128.53 (+),127.02 (+), 120.87, 117.87 (+), 114.53 (+), 46.69 (+), 44.96 (+), 37.96 (-), 22.20 (+); GC: R_t= 16.7 min, MS (EI), *m/z* (%):190 ($M^{+\cdot}$, 25), 161 (10), 144 (45), 130 (100), 77 (15); HRMS (ESI+): *m/*z: calcd for $C_{11}H_{15}N_2O$ ($[M+H]^+$) 191,1178, found: 191,1182; calcd for $C_{11}H_{14}N_2NaO$ ($[M+Na]^+$) 213,0998, found: 213,1001.

cis-4-Formamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (3g): White solid (0.28 g, 1.26 mmol, 63 %), R_f [hexane-EtOAc 1:1] = 0.6; mp: 151-153 °C; FT-IR (KBr disk, cm^{-1}): 3286, 3239, 3023, 2838, 1666, 1542, 1265, 1234, 1033, 725; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 8.35 (d, *J* = 8.4 Hz, 1H, 4-NH), 8.19 (s, 1H, 4-COH), 6.59 (d, *J* = 8.4 Hz, 1H, 7-H_{Ar}), 6.53 (s, 1H, 5-H_{Ar}), 6.45 (d, *J* = 8.4 Hz, 1H, 8-H_{Ar}), 5.30 (s, 1H, 1-NH), 5.12 (ddd, *J* = 11.5, 8.4, 3.5 Hz, 1H, 4-H_{ax}), 3.60 (s, 3H, 6-OCH_3), 3.36-3.34 (m, 1H, 2-H_{ax}), 1.98-1.94 (m, 1H, 3-H_{eq}), 1.39 (q, *J* = 11.5 Hz, 1H, 3-H_{ax}), 1.11 (d, *J* = 5.7 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 161.2 (+), 150.7, 140.1, 121.9, 114.8 (+), 114.0 (+), 112.1 (+), 55.4 (+), 46.3 (+), 44.2 (+), 37.6 (-), 22.0 (+); COSY correlation [δ_H/δ_H]: 1.11/3.36-3.34 [2-CH_3/2-H_{ax}], 1.39/3.36-3.34/1.96/5.12 [3-H_{ax}/2-H_{ax}/3-H_{eq}/4-H_{ax}], 1.96/3.36-3.34/1.39/5.12 [3-H_{eq}/2-H_{ax}/3-H_{ax}/4-H_{ax}], 3.36-3.34/1.96/1.39/1.11 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.12/8.35/1.96/1.39 [4-H_{ax}/4-NH/3-H_{eq}/3-H_{ax}], 6.45/6.59 [8-H_{Ar}/7-H_{Ar}], 6.59/6.45 [7-H_{Ar}/8-H_{Ar}], 8.35/5.12 [4-NH/4-H_{ax}]; HSQC correlation [δ_H/δ_C]: 1.11/46.3 [2-CH_3/C-11], 1.39/37.6 [3-H_{ax}/C-3], 1.96/37.6 [3-H_{eq}/C-3], 3.36-3.34/46.3 [2-H_{ax}/C-2], 3.60/55.4 [6-OCH_3/C-15], 5.12/44.2 [4-H_{ax}/C-4], 6.45/114.8 [8-H_{Ar}/C-8], 6.53/112.1 [5-H_{Ar}/C-5], 6.59/114.0 [7-H_{Ar}/C-7]; HMBC correlation [δ_H/δ_C]: 1.11/46.3/37.6 [2-CH_3/C-2/C-3], 1.39/121.8/46.3/44.2/22.0 [3-H_{ax}/C-9/C-2/C-4/C-11], 1.96/121.8/44.2 [3-H_{eq}/C-9/C-4], 3.60/150.7 [6-OCH_3/C-6], 5.12/161.2/121.8/37.9 [4-H_{ax}/C-13/C-9/C-3], 5.30/121.8/114.8/37.6/22.0 [1-NH/C-9/C-8/C-3/C-11], 6.45/150.7/121.8/112.1/44.2 [8-H_{Ar}/C-6/C-9/C-5/C-4], 6.53/150.7/140.1/114.0/44.2 [5-H_{Ar}/C-6/C-10/C-7/C-4], 6.59/150.7/140.1/112.1 [7-H_{Ar}/C-6/C-10/C-5], 8.19/44.2 [4-COH/C-4], 8.3/161.2/44.2 [4-NH/C-13/C-4]; GC: R_t= 20.4 min, MS (EI), *m/z* (%): 220 ($M^{+\cdot}$, 35), 160 (100), 145 (10), 130 (15), 117 (15); HRMS (ESI+): *m/*z: calcd for $C_{12}H_{17}N_2O_2$ ($[M+H]^+$) 221,1285, found: 221,1282; calcd for $C_{12}H_{16}N_2NaO_2$ ($[M+Na]^+$) 243,1104, found: 243,1101.

cis-6-Carboxy-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline (3h): White solid (0.38 g, 1.62 mmol, 81 %), R_f [hexane-EtOAc 1:2] = 0.4; mp: 208-210 °C; FT-IR (KBr disk, cm^{-1}): 3394, 2962, 2653, 2561, 1666, 1604, 1527, 1419, 1280, 1172, 833, 771; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 12.05 (br., s, 1H, 6-COOH), 8.41 (d, *J* = 8.9 Hz, 1H, 4-NH), 8.25 (s, 1H, 4-COH), 7.53 (s, 1H, 5-H_{Ar}), 7.50-7.52 (m, 1H, 7-H_{Ar}), 6.57 (s, 1H, 1-NH), 6.48 (d, *J* = 8.3 Hz, 1H, 8-H_{Ar}), 5.11 (ddd, *J* = 11.8, 8.9, 6.5 Hz, 1H, 4-H_{ax}), 3.59-3.51 (m, 1H, 2-H_{ax}), 2.02-1.93 (m, 1H, 3-H_{eq}), 1.41 (q, *J* = 11.8 Hz, 1H, 3-H_{ax}), 1.17 (d, *J* = 6.1 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 167.6, 161.3 (+), 149.5, 129.8 (+), 128.5 (+), 119.5, 116.7, 112.4 (+), 45.9 (+), 43.6 (+), 36.5 (-), 21.5 (+); COSY correlation [δ_H/δ_H]: 1.17/3.59-3.51 [2-CH_3/2-H_{ax}], 1.41/5.11/3.59-3.51/2.02-1.93 [3-H_{ax}/4-H_{ax}/2-H_{ax}/3-H_{eq}], 2.02-1.93/5.11/3.59-3.51/1.41 [3-H_{eq}/4-H_{ax}/2-H_{ax}/3-H_{ax}], 3.59-3.51/2.02-1.93/1.41/1.17 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.11/8.41/1.93-2.02/1.41 [4-H_{ax}/4-NH/3-H_{eq}/3-H_{ax}], 7.50-7.52/6.48 [7-H_{Ar}/8-H_{Ar}], 8.41/5.11 [4-NH/4-H_{ax}]; HSQC correlation [δ_H/δ_C]: 1.17/21.5 [2-CH_3/C-11], 2.02-1.9/1.41/36.5 [3-H_{eq}/3-H_{ax}/C-3], 3.59-3.51/45.9 [2-H_{ax}/C-2], 5.11/43.6 [4-H_{ax}/C-4], 6.48/112.4 [8-H_{Ar}/C-8], 7.50-7.52/129.8 [7-H_{Ar}/C-7], 7.53/128.5 [5-H_{Ar}/C-5], 8.25/161.3 [4-COH/C-13]; HMBC correlation [δ_H/δ_C]: 1.17/36.5/45.9 [2-CH_3/C-3/C-2], 1.41/45.9/43.6/21.5 [3-H_{ax}/C-2/C-4/C-11], 2.02-1.93/43.6/119.5 [3-H_{eq}/C-4/C-9], 5.11/36.6 [4-H_{ax}/C-3], 6.48/119.5/116.7 [8-H_{Ar}/C-9/C-6], 6.57/149.5/119.5/112.4/45.9/36.5/21.5 [1-NH/C-10/C-9/C-8/C-2/C-3/C-11], 7.50-7.52/167.6/149.5/128.5/112.4 [7-H_{Ar}/C-14/C-10/C-5/C-8], 7.53/149.5/129.8/43.6 [5-H_{Ar}/C-10/C-7/C-4], 8.25/43.6 [4-COH/C-4], 8.41/161.3/43.6/36.5 [4-NH/C-13/C-4/C-3]; GC: R_t= 23.3 min, MS (EI), *m/z* (%): 190 ($M^{+\cdot}$-44, 30), 161 (5) 145 (63), 130 (100), 103 (5), 77 (15); HRMS (ESI+): *m/z*: calcd for $C_{12}H_{15}N_2O_3$ ($[M+H]^+$) 235,1077, found: 235,1081; calcd for $C_{12}H_{14}N_2NaO_3$ ($[M+Na]^+$) 257,0897, found: 257,0897.

cis-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline (3i): White solid (0.44 g, 1.62 mmol, 81 %), R_f [hexane-EtOAc 1:1] = 0.5; mp: 165-167 °C; FT-IR (KBr disk, cm^{-1}): 3332, 2962, 2915, 2885, 1681, 1573, 1434, 956, 833; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 7.57 (dd, *J* = 8.5, 1.7 Hz, 1H, 7-H_{Ar}), 7.21 (s, 1H, 5-H_{Ar}), 6.77 (s, 1H, 1-NH), 6.53 (d, *J* = 8.5 Hz, 1H, 8-H_{Ar}), 5.25 (dd, *J* = 11.9, 5.2 Hz, 1H, 4-H_{ax}), 3.61 (ddd, *J* = 11.9, 6.3, 2.3 Hz, 1H, 2-H_{ax}), 3.26-3.19 (m, 1H, 5´-H_b), 3.03-2.96 (m, 1H, 5´-H_a), 2.41-2.34 (m, 2H, 3´-H_a and 3´-H_b), 2.36 (s, 3H, 6-$COCH_3$), 2.02-1.89 (m, 2H, 4´-H_a and 4´-H_b), 1.81 (ddd, *J* = 11.9, 5.2, 2.3 Hz, 1H, 3-H_{eq}), 1.63 (q, *J* = 11.9 Hz, 1H, 3-H_{ax}), 1.19 (d, *J* = 6.3 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 194.9, 174.8, 150.6, 129.5 (+), 126.3 (+), 124.6, 116.8, 112.5 (+), 47.2 (+), 46.0 (+), 41.7 (+), 39.5 (-), 33.1 (-), 30.8 (-), 25.9 (+), 21.4 (+), 18.1 (-); NOESY correlation [δ_H/δ_H]: 1.81/1.63 [3-H_{eq}/3-H_{ax}], 3.03-2.96/2.02-1.89 [5´-H_a/4´-H_a and 4´-H_b], 3.26-3.19/2.02-1.89 [5´-H_b, 4´-H_a and 4´-H_b], 3.61/1.19/1.63 [2-H_{ax}/2-CH_3/3-H_{ax}], 5.25/1.63/1.81 [4-H_{ax}/3-H_{ax}/3-H_{eq}], 7.57/6.53 [7-H_{Ar}/8-H_{Ar}]; COSY correlation [δ_H/δ_H]: 1.19/3.61 [2-CH_3/2-H_{ax}], 1.63/5.25/3.61/1.81 [3-H_{ax}/4-H_{ax}/2-H_{ax}/3-H_{eq}], 1.81/5.25/3.61/1.63 [3-H_{eq}/4-H_{ax}/2-H_{ax}/3-H_{ax}], 2.02-

1.89/3.26-3.19/3.03-2.96/2.41-2.34 [4´-H_a,4´-H_b/5´-H_b/5'-H_a/3´-H_a,3´-H_b], 2.41-2.34/ 2.02-1.89 [3´-H_a,3´-H_b/4´-H_a,4´-H_b], 3.03-2.96/3.26-3.19/2.02-1.89 [5'-H_a/5´-H_b/4´-H_a,4´-H_b], 3.26-3.19/3.03-2.96/2.02-1.89 [5´-H_b/5'-H_a/4´-H_a,4´-H_b], 3.61/1.81/1.63/1.19 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.25/1.81/1.63 [4-H_{ax}/3-H_{eq}/3-H_{ax}], 6.53/7.57 [8-H_{Ar}/7-H_{Ar}], 7.21/7.57 [5-H_{Ar}/7-H_{Ar}], 7.57/7.21/6.53 [7-H_{Ar}/5-H_{Ar}/8-H_{Ar}]; HSQC correlation [δ_H/δ_C]: 1.19/21.4 [2-CH_3/C-11], 1.81/1.63/33.1 [3-H_{eq}/3-H_{ax}/C-3], 2.02-1.89/18.1 [4´-H_a,4´-H_b/C-15], 2.36/25.9 [6-$COCH_3$/C-18], 3.26-3.19, 3.03-2.96/41.7 [5´-H_b, 5´-H_a/C-16], 3.61/46.0 [2-H_{ax}/C-2], 5.25/47.2 [4-H_{ax}/C-4], 6.53/112.5 [8-H_{Ar}/C-8], 7.21/126.3 [5-H_{Ar}/C-5], 7.57/129.5 [7-H_{Ar}/C-7]; HMBC correlation [δ_H/δ_C]: 1.19/47.2/46.0/33.1/30.8 [2-CH_3/C-4/C-2/C-3/C-14], 1.63/47.2/46.0/21.4 [3-H_{ax}/C-4/C-2/C-11], 1.81/47.2/46.0 [3-H_{eq}/C-4/C-2], 2.02-1.89/174.8/41.7/30.8 [4´-H_a,4´-H_b/C-13/C-16/C-14], 2.36/194.9 [6-$COCH_3$/C-17], 2.41-2.34/174.8/41.7/18.1 [3´-H_a,3´-H_b/C-13/C-16/C-15], 3.26-3.19,3.03-2.96/174.8/30.8/18.1 [5´-H_b,5´-H_a/C-13/C-14/C-15], 5.25/174.8 /116.8/41.7/33.1 [4-H_{ax}/C-13/C-9/C-16/C-3], 6.53/124.6/116.8/47.2 [8-H_{Ar}/C-10/C-9/C4], 6.77/116.8/112.5/ 46.0/33.1/21.4 [1-NH/C-9/C-8/C-2/C-3/C-11], 7.21/194.9/150.6/129.6 /47.2 [5-H_{Ar}/C-17/C-6/C-7/C-4], 7.57/194.9/150.6/126.3 [7-H_{Ar}/C-17/C-6/C-5]; GC: R_t= 23.6 min, MS (EI), *m/z* (%): 272 ($M^{+\cdot}$,5), 257 (3), 243(3), 187 (65), 172 (100); HRMS (ESI+): *m/*z: calcd for $C_{16}H_{21}N_2O_2$ ($[M+H]^+$) 273,1598, found: 273,1601; calcd for $C_{16}H_{20}N_2NaO_2$ ($[M+Na]^+$) 295,1417, found: 295,1419.

cis-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline (3j): White solid (0.32 g, 1.4 mmol, 70 %), R_f [hexane-EtOAc 1:1] = 0.6; mp: 190-192 °C; FT-IR (KBr disk, cm^{-1}): 3317, 3039, 2977, 2946, 2885, 1666, 1604, 1496, 1265, 755; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 6.91 (td, *J* = 7.5, 7.5, 0.9 Hz, 1H, 7-H_{Ar}), 6.62 (d, *J* = 7.5 Hz, 1H, 5-H_{Ar}), 6.53-6.44 (m, 2H, 6-H_{Ar} and 8-H_{Ar}), 5.72 (s, 1H, 1-NH), 5.27 (dd, *J* = 11.8, 5.7 Hz, 1H, 4-H_{ax}), 3.48 (dqd, *J* = 11.8, 6.2, 2.1 Hz, 1H, 2-H_{ax}), 3.19 (dt, *J* = 9.4, 7.2 Hz, 1H, 5´-H_b), 2.95 (dt, *J* = 9.4, 6.7 Hz, 1H, 5´-H_a), 2.42-2.26 (m, 2H, 3´-H_a and 3´-H_b), 1.96-1.87 (m, 2H, 4´-H_a and 4´-H_b), 1.75 (ddd, *J* = 11.8, 5.7, 2.1 Hz, 1H, 3-H_{eq}), 1.62 (q, *J* = 11.8 Hz, 1H, 3-H_{ax}), 1.15 (d, *J* = 6.2 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 174.7, 146.5, 127.7 (+), 125.8 (+), 117.8, 115.8 (+), 114.0 (+), 47.5 (+), 46.1 (+), 41.6 (-), 33.7 (-), 30.8 (-), 21.9 (+), 17.8 (-);COSY correlation [δ_H/δ_H]: 3.19/2.95/1.96-1.87 [5´-H_b/5´-H_a/3´-H_a, 3´-H_b], 3.48/1.75/1.62/1.15 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.27/1.75/1.62 [4-H_{ax}/3-H_{eq}/3-H_{ax}], 6.91/ 6.53-6.44 [7-H_{Ar}/6-H_{Ar},8-H_{Ar}], HSQC correlation [δ_H/δ_C]: 1.15/21.9 [2-CH_3/C-11], 1.62/33.7 [3-H_{ax}/C-3], 1.75/33.7 [3-H_{eq}/C-3], 1.96-1.87/17.8 [4´-H_a, 4´-H_b/C-15], 2.42-2.26/30.8 [3´-H_a, 3´-H_b/C-14], 2.95/41.6 [5´-H_a/C-16], 3.19/41.6 [5´-H_b/C-16], 3.48/46.1 [2-H_{ax}/C-2], 5.72/47.5 [4-H_{ax}/C-4], 6.53-6.44/115.8,114.0 [6-H_{Ar}, 8-H_{Ar} /C-6, C-8], 6.62/125.8 [5-H_{Ar}/C-5], 6.91/127.7 [7-H_{Ar}/C-7]; HMBC correlation [δ_H/δ_C]: 1.15/146.5/46.1/33.7 [2-CH_3/C-10/C-2/C-3], 1.62/ 117.8/47.5/46.1/21.9 [3-H_{ax}/C-9/C-4/C-2/C-11], 1.75/125.8/117.8/47.5/21.9/17.8 [3-H_{eq}/C-5/C-9/C-4/C-11/C-15], 1.96-1.87/174.7/41.6/33.7/30.8 [4´-H_a,4´-H_b/C-13/C-16/C-3/C-14], 2.42-2.26/174.7/

41.6/17.8 [3´-H_a, 3´-H_b/C-13/C-16/C-15], 2.95/174.7/30.8/17.8 [5´-H_a/C-13/C-14/C-15], 3.19/174.7/30.8/17.8 [5´-H_b/C-13/C-14/C-15], 5.27/117.8/41.6/33.7 [4-H_{ax}/C-9/C-16/C-3], 5.72/117.8/114.9/46.1/33.7/21.9 [1-NH/C-9/C-8/C-2/C-3/C-11], 6.53-6.44/127.6/117.8/115.8/114.0 [6-H_{Ar},8-H_{Ar}/C-7/C-9/C-6/C-8], 6.62/146.5/127.6/47.5 [5-H_{Ar}/C-10/C-7/C-4], 6.91/146.5/125.8/117.8/114.0 [7-H_{Ar}/C-10/C-5/C-9/C-8]; GC: R_t= 21.1 min, MS (EI), *m/z* (%): 230 ($M^{+\cdot}$, 8), 201 (4), 144 (52), 130 (100), 77 (10); HRMS (ESI+): *m/*z: calcd for $C_{14}H_{19}N_2O$ ($[M+H]^+$) 231,1492, found: 231,1495; calcd for $C_{14}H_{18}N_2NaO$ ($[M+Na]^+$) 253,1311, found: 253,1311.

cis-6-Methoxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline (3k): Yellow oil (0.44 gr, 1.68 mmol, 84 %), R_f [hexane-EtOAc 1:1] = 0.7; FT-IR (liquid film, cm^{-1}): 3332, 2962, 1666, 1496, 1434, 1280, 1033, 817; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 6.59 (dd, *J* = 8.7, 2.7 Hz, 1H, 7-H_{Ar}), 6.47 (d, *J* = 8.7 Hz, 1H, 8-H_{Ar}), 6.22 (d, *J* = 2.7 Hz, 1H, 5-H_{Ar}), 5.31 (s, 1H, 1-NH), 5.27 (dd, *J* = 11.9, 6.1 Hz, 1H, 4-H_{ax}), 3.59 (s, 3H, 6-OCH_3), 3,42-3.34 (m, 1H, 2-H_{ax}), 3.19 (1H, dt, *J* = 9.6, 7.4 Hz, 5´-H_b), 2.95 (dt, *J* = 9.6, 6.7 Hz, 1H, 5´-H_a), 2.43-2.26 (m, 2H, 3´-H_a and 3´-H_b), 1.96-1.88 (m, 2H, 4´-H_a and 4´-H_b), 1.73 (ddd, 1H, *J* = 11.9, 6.1, 1.80 Hz, 3-H_{eq}), 1.60 (q, *J* = 11.9 Hz, 1H, 3-H_{ax}), 1.13 (d, *J* = 6.2 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 174.7, 150.9, 140.8, 119.2, 115.3 (+), 113.9 (+), 111.2 (+), 55.3 (+), 47.7 (+), 46.5 (+), 41.7 (-), 33.9 (-), 30.8 (-), 21.9 (+), 17.9 (-);COSY correlation [δ_H/δ_H]: 1.13/3,42-3.34 [2-CH_3/2-H_{ax}], 1.60/5.27/1.73 [3-H_{ax}/4-H_{ax}/3-H_{eq}], 1.73/5.27/1.60 [3-H_{eq}/4-H_{ax}/3-H_{ax}], 1.96-1.88/3.23-3.15/2.95/2.43-2.26 [4´-H_a, 4´-H_b/5´-H_b/5´-H_a/3´-H_a, 3´-H_b], 2.43-2.26/1.96-1.88 [3´-H_a, 3´-H_b/4´-H_a, 4´-H_b], 2.95/3.19/1.96-1.88 [5´-H_a/5´-H_b/4´-H_a, 4´-H_b], 3.23-3.15/2.95/1.96-1.88 [5´-H_b/5´-H_a/4´-H_a, 4´-H_b], 3,42-3.34/1.60/1.13 [2-H_{ax}/3-H_{ax}/2-CH_3], 5.27/1.73/1.60 [4-H_{ax}/3-H_{eq}/3-H_{ax}], 6.22/6.59 [5-H_{Ar}/7-H_{Ar}], 6.47/6.59 [8-H_{Ar}/7-H_{Ar}], 6.59/6.47/6.22 [7-H_{Ar}/8-H_{Ar}/5-H_{Ar}]; HSQC correlation [δ_H/δ_C]: 1.13/21.9 [2-CH_3/C-11], 1.73/1.60/33.9 [3-H_{eq}/3-H_{ax}/C-3], 1.96-1.88/17.9 [4´-H_a, 4´-H_b/C-15], 2.43-2.26/30.8 [3´-H_a, 3´-H_b/C-14], 3.23-3.15/2.95/41.7 [5´-H_b/5´-H_a/C-16], 3.42-3.34/46.5 [2-H_{ax}/C-2], 3.59/55.3 [6-OCH_3/C-18], 5.27/47.7 [4-H_{ax}/C-4], 6.22/111.2 [5-H_{Ar}/C-5], 6.47/115.3 [8-H_{Ar}/C-8], 6.59/113.9 [7-H_{Ar}/C-7]; HMBC correlation [δ_H/δ_C]: 1.13/46.5/33.9 [2-CH_3/C-2/C-3], 1.73,1.60/ 47.7/46.5/21.9 [3-H_{eq}, 3-H_{eq}/C-4/C-2/C-11], 1.96-1.88/30.8/41.7/174.7 [4´-H_a, 4´-H_b/C-14/C-16/C-13], 2.43-2.26/17.9/41.7/174.7 [3´-H_a, 3´-H_b/C-15/C-16/C-13], 3.23-3.15,2.95/17.9/30.8/174.7 [5´-H_b, 5´-H_b/C-15/C-14/C-13], 3.59/150.9 [6-OCH_3/C-6], 5.27/174.7/140.7/119.2/111.2/41.7/33.9 [4-H_{ax}/C-13/C-10/C-9/C-5/C-16/C-3], 5.31/ 119.2/33.9 [1-NH/C-9/C-3], 6.22/47.7/113.9/119.2/140.8/150.9 [5-H_{Ar}/C-4/C-7/C-9/C-10/C-6], 6.47/47.7/111.2/119.2/140.8/150.9 [8-H_{Ar}/C-4/C-5/C-9/C-10/C-6], 6.59/ 111.2/119.2/140.8/150.9 [7-H_{Ar}/C-5/C-9/C-10/C-6]; GC: R_t= 23.2 min, MS (EI), *m/z* (%): 260 ($M^{+\cdot}$, 45), 245 (3), 175 (20), 174 (60), 160 (100), 77 (4); HRMS (ESI+): *m/*z: calcd for $C_{15}H_{21}N_2O_2$ ($[M+H]^+$) 261,1598, found: 261,1595; calcd for $C_{15}H_{20}N_2NaO_2$ ($[M+Na]^+$) 283,1417, found: 283,1419.

cis-6-Carboxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline (3l): White solid (0.4 gr, 1.44 mmol, 72 %), R_f [hexane-EtOAc 1:2] = 0.3; mp: 233-237 °C; FT-IR (KBr disk, cm^{-1}): 3347, 2962, 2854, 1697, 1635, 1527, 1326, 1172, 771; ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm): 12.04 (s, 1H, 6-COOH), 7.51 (d, 1H, 7-H_{Ar}), 7.22 (s, 1H, 5-H_{Ar}), 6.59 (s, 1H, 1-NH), 6.52 (d, *J* = 8.4 Hz, 1H, 8-H_{Ar}), 5.25 (dd, *J* = 12.0, 4.7 Hz, 1H, 4-H_{ax}), 3.62-3.54 (m, 1H, 2-H_{ax}), 3.26-3.19 (m, 1H, 5´-H_b), 2.98 (td, *J* = 8.3, 4.5 Hz, 1H, 5´-H_a), 2.38-2.34 (m, 2H, 3´-H_a and 3´-H_b), 2.00-1.89 (m, 2H, 4´-H_a and 4´-H_b), 1.79 (ddd, *J* = 12.0, 4.7, 2.6 Hz, 1H, 3-H_{eq}), 1.63 (q, *J* = 12.0 Hz, 1H, 3-H_{ax}), 1.18 (d, *J* = 6.1 Hz, 3H, 2-CH_3); ^{13}C NMR (101 MHz, DMSO-d_6), $\delta_{(ppm)}$: 174.8, 167.6, 150.2, 129.8 (+), 127.5 (+), 116.8, 112.8 (+), 47.2 (+), 46.0 (+), 41.7 (-), 33.1 (-), 30.8 (-), 21.5, 18.0 (-); COSY correlation [δ_H/δ_H]: 1.18/3.62-3.54 [2-CH_3/2-H_{ax}], 1.63/5.25/3.62-3.54/1.79 [3-H_{ax}/4-H_{ax}/2-H_{ax}/3-H_{eq}], 1.79/5.25/3.62-3.54/1.63 [3-H_{eq}/4-H_{ax}/2-H_{ax}/3-H_{ax}], 2.00-1.89/3.26-3.19/2.98/2.38-2.34 [4´-H_a,4´-H_b/5´-H_b/5´-H_a/3´-H_a, 3´-H_b], 2.38-2.34/2.00-1.89 [3´-H_a,3´-H_b/4´-H_a, 4´-H_b], 2.98/3.26-3.19/2.00-1.89 [5´-H_a/5´-H_b/4´-H_a,4´-H_b], 3.26-3.19/2.98/2.00-1.89 [5´-H_b/5´-H_a/4´-H_a, 4´-H_b], 3.62-3.54/1.79/1.63/1.18 [2-H_{ax}/3-H_{eq}/3-H_{ax}/2-CH_3], 5.25/1.79/1.63 [4-H_{ax}/3-H_{eq}/3-H_{ax}], 6.52/7.51 [8-H_{Ar}/7-H_{Ar}], 7.51/6.52 [7-H_{Ar}/8-H_{Ar}]; HSQC correlation [δ_H/δ_C]: 1.18/21.5 [2-CH_3/C-11], 1.79, 1.63/33.1 [3-H_{eq}, 3-H_{ax}/C-3], 2.00-1.89/18.0 [4´-H_a, 4´-H_b/C-15], 2.38-2.34/30.8 [3´-H_a,3´-H_b/C-14], 3.26-3.19, 2.98/41.7 [5´-H_b, 5´-H_b/C-16], 3.62-3.54/46.0 [2-H_{ax}/C-2], 5.25/47.2 [4-H_{ax}/C-4], 6.52/112.8 [8-H_{Ar}/C-8], 7.22/127.5 [5-H_{Ar}/C-5], 7.51/129.8 [7-H_{Ar}/C-7]; HMBC correlation [δ_H/δ_C]: 1.18/46.0/33.1 [2-CH_3/C-2/C-3], 1.63/46.0/47.2/21.5 [3-H_{ax}/C-2/C-4/C-11], 1.79/47.2/46.0 [3-H_{eq}/C-4/C-2], 2.00-1.89/174.8/41.7/30.8 [4´-H_a,4´-H_b/C-13/C-16/C-14], 2.38-2.34/174.8/41.7/18.0 [3´-H_a,3´-H_b/C-13/C-16/C-15], 3.26-3.19,2.98/174.8/18.0 [5´-H_b,5´-H_a/C-13/C-15], 5.25/116.8/33.1 [4-H_{ax}/C-9/C-3], 6.52/129.8/116.8 [8-H_{Ar}/C-7/C-9], 6.59/116.8/112.8/46.0/33.1/21.5 [1-NH/C-9/C-8/C-2/C-3/C-11], 7.22/167.6/150.2/129.8/47.2 [5-H_{Ar}/C-17/C-6/C-7/C-4], 7.51/167.6/150.2/127.5/112.8 [7-H_{Ar}/C-17/C-6/C-5/C-8]; GC: R_t= 24.9 min, MS (EI), *m/z* (%):230 ($M^{+\cdot}$-44, 30), 201 (10), 159 (5), 145 (70), 130 (100), 103 (8), 77 (12); HRMS (ESI+): *m/*z: calcd for $C_{15}H_{19}N_2O_3$ ($[M+H]^+$) 275,1390, found: 275,1394; calcd for $C_{15}H_{18}N_2NaO_3$ ($[M+Na]^+$) 297,1210, found: 297,1207.

3. Copies of ^{1}H NMR, ^{13}C NMR, DEPT-135, COSY, HSQC and HMBC charts of the synthesized 2-methyltetrahydroquinolines 3a-l.

Figure ESI 1. ^{1}H-NMR spectrum of *cis*-4-Acetamido-6-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline **3a**.

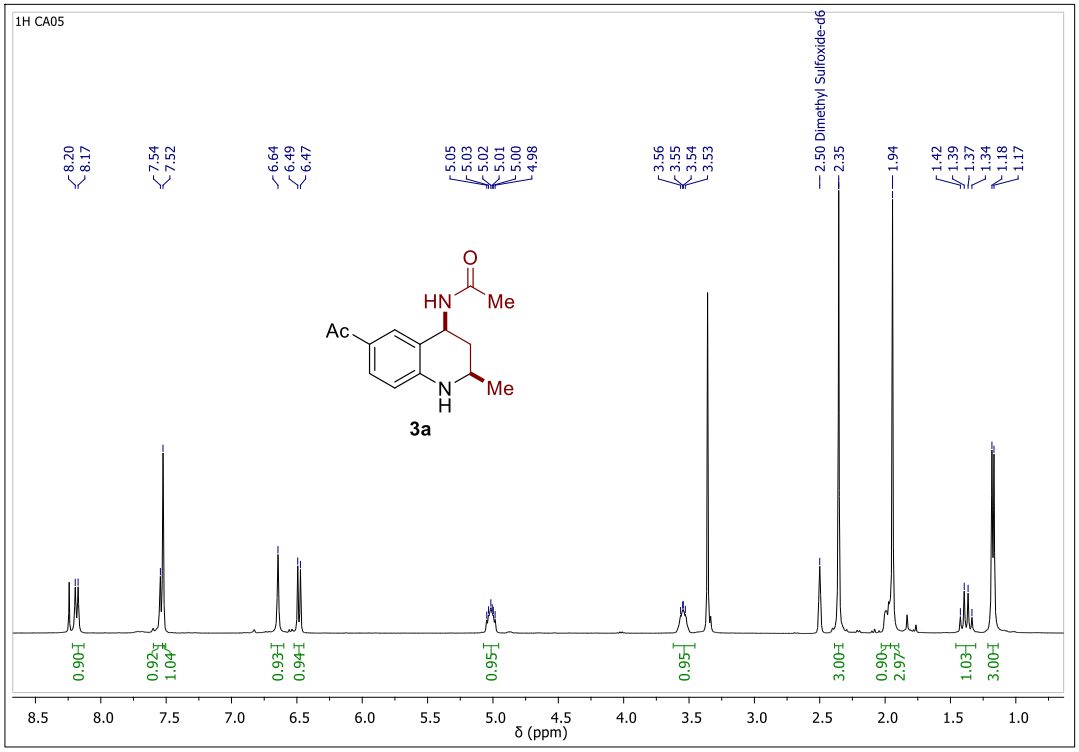


Figure ESI 2. ^{13}C-NMR spectrum of *cis*-4-Acetamido-6-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline **3a**.

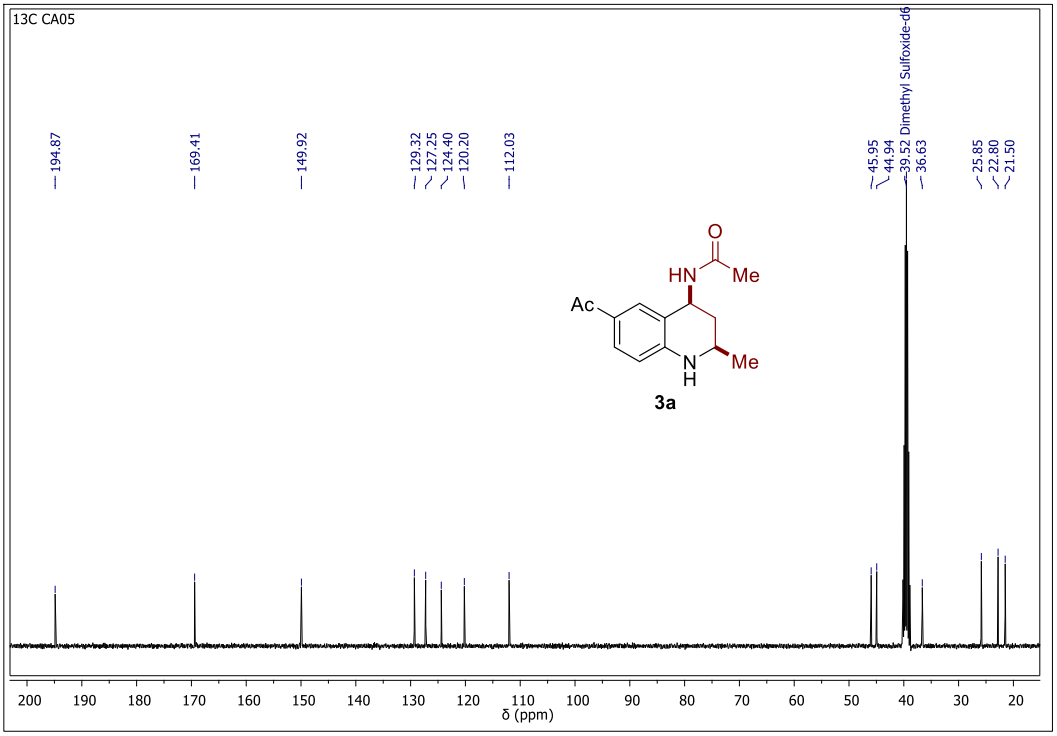


Figure ESI 3. DEPT-135 spectrum of *cis*-4-Acetamido-6-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline **3a**.

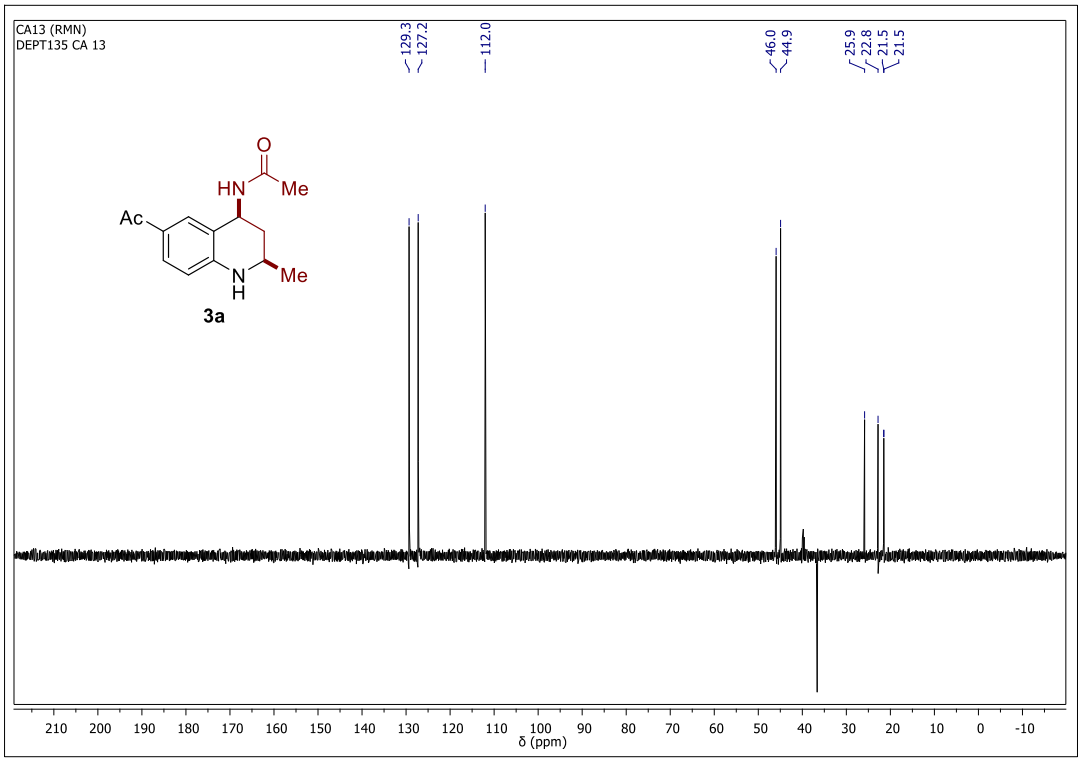


Figure ESI 4. COSY spectrum of *cis*-4-Acetamido-6-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline **3a**.

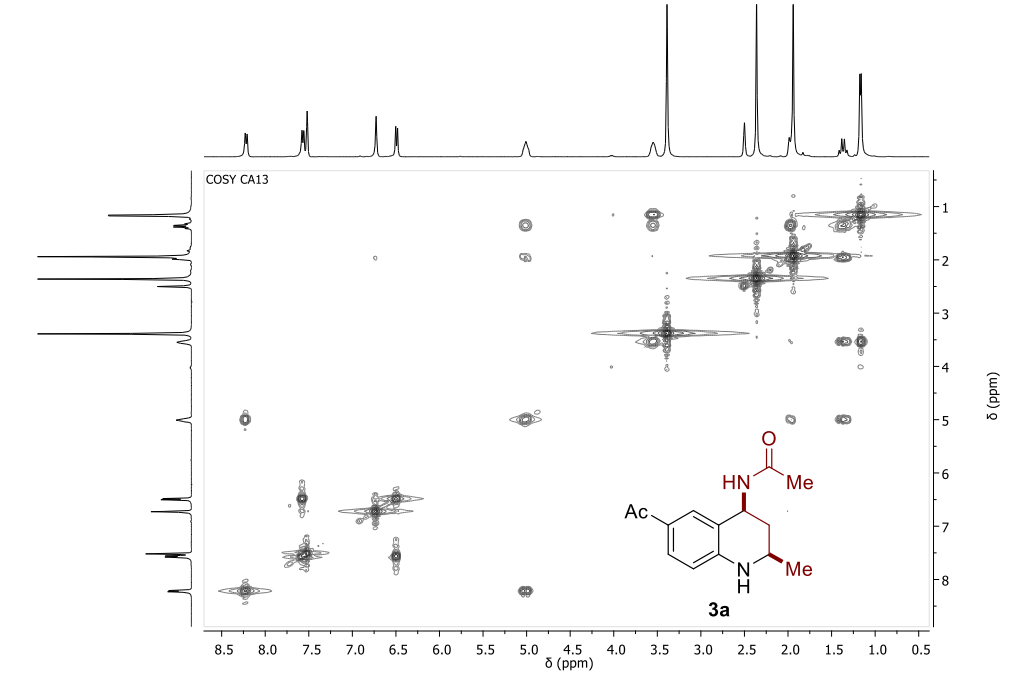


Figure ESI 5. HSQC spectrum of *cis*-4-Acetamido-6-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline **3a**.

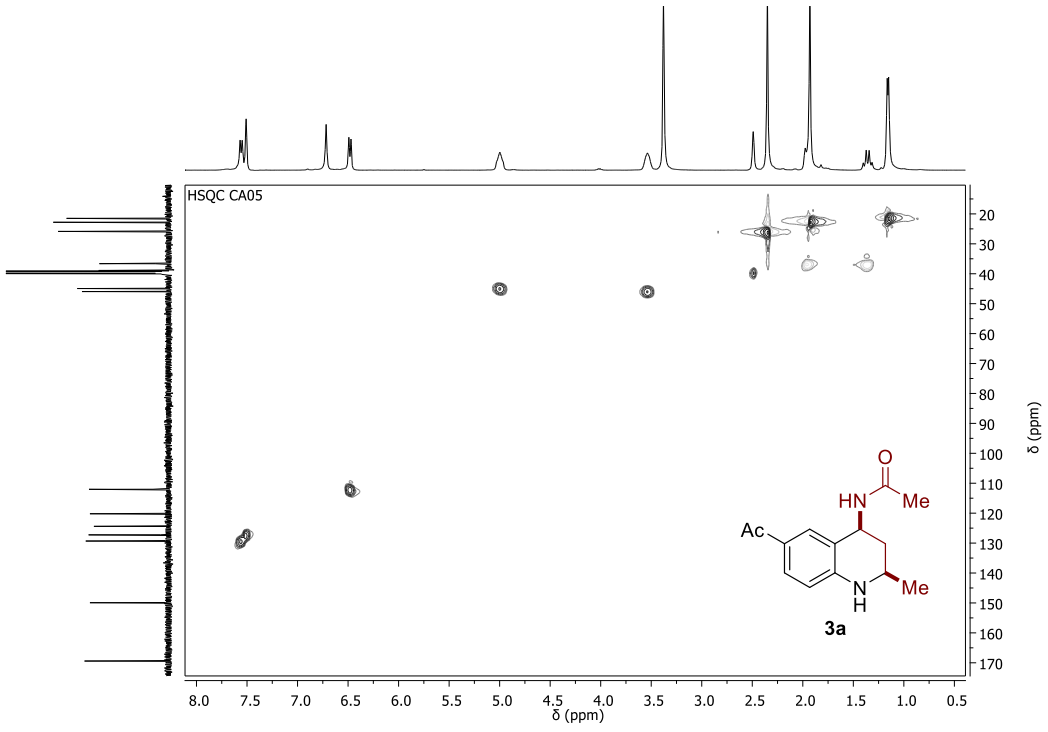


Figure ESI 6. HMBC spectrum of *cis*-4-Acetamido-6-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline **3a**.

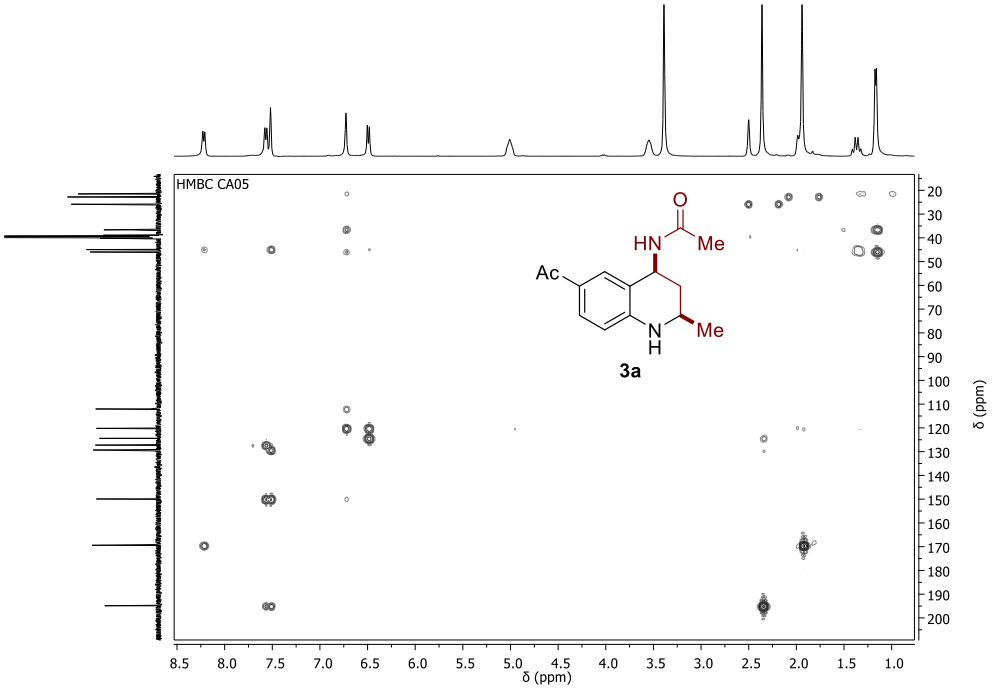


Figure ESI 7. ^{1}H-NMR spectrum of *cis*-4-Acetamido-2-methyl-1,2,3,4-tetrahydroquinoline **3b**.

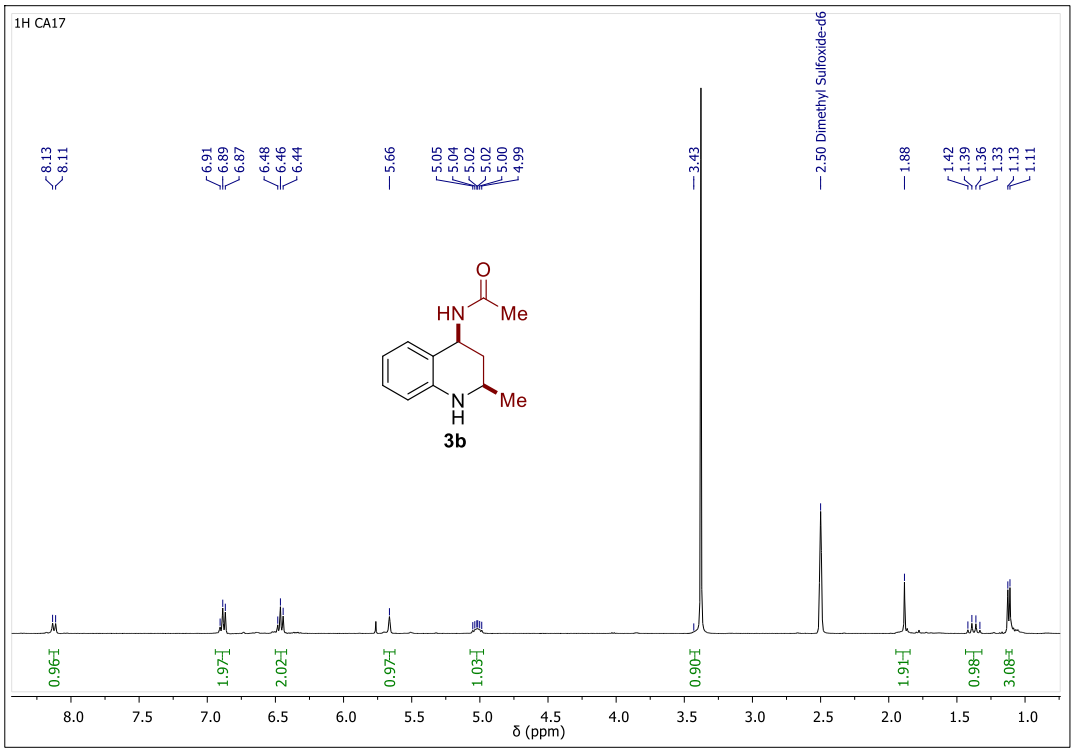


Figure ESI 8. ^{13}C-NMR spectrum of *cis*-4-Acetamido-2-methyl-1,2,3,4-tetrahydroquinoline **3b**.

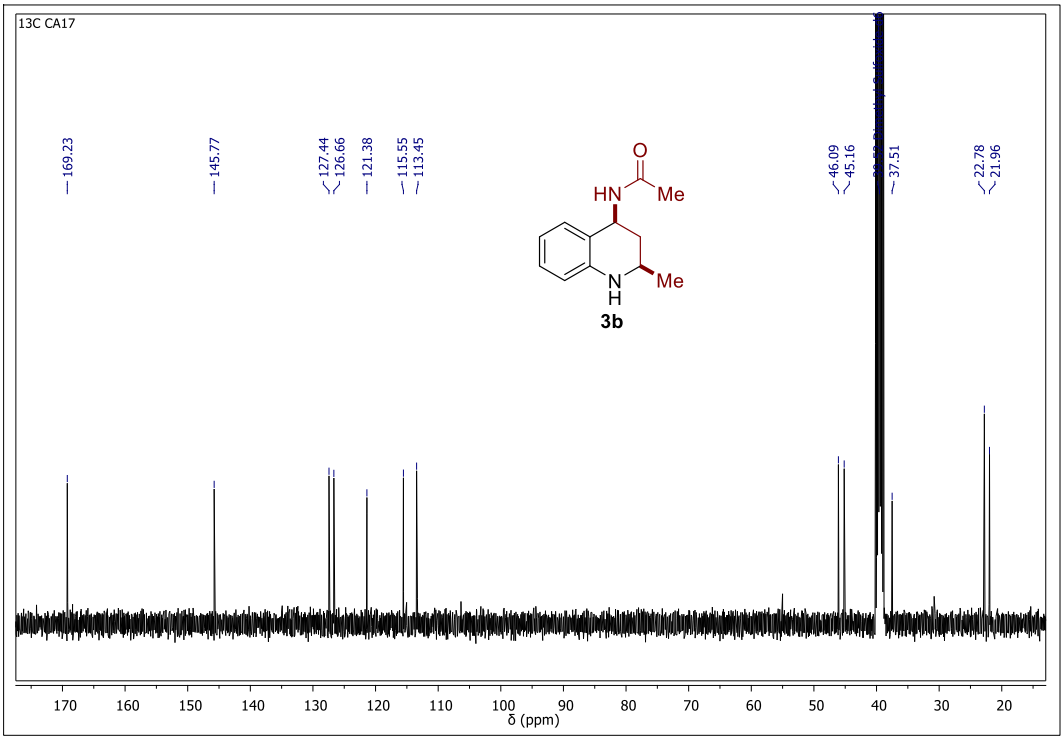


Figure ESI 9. DEPT-135 spectrum of *cis*-4-Acetamido-2-methyl-1,2,3,4-tetrahydroquinoline **3b**.

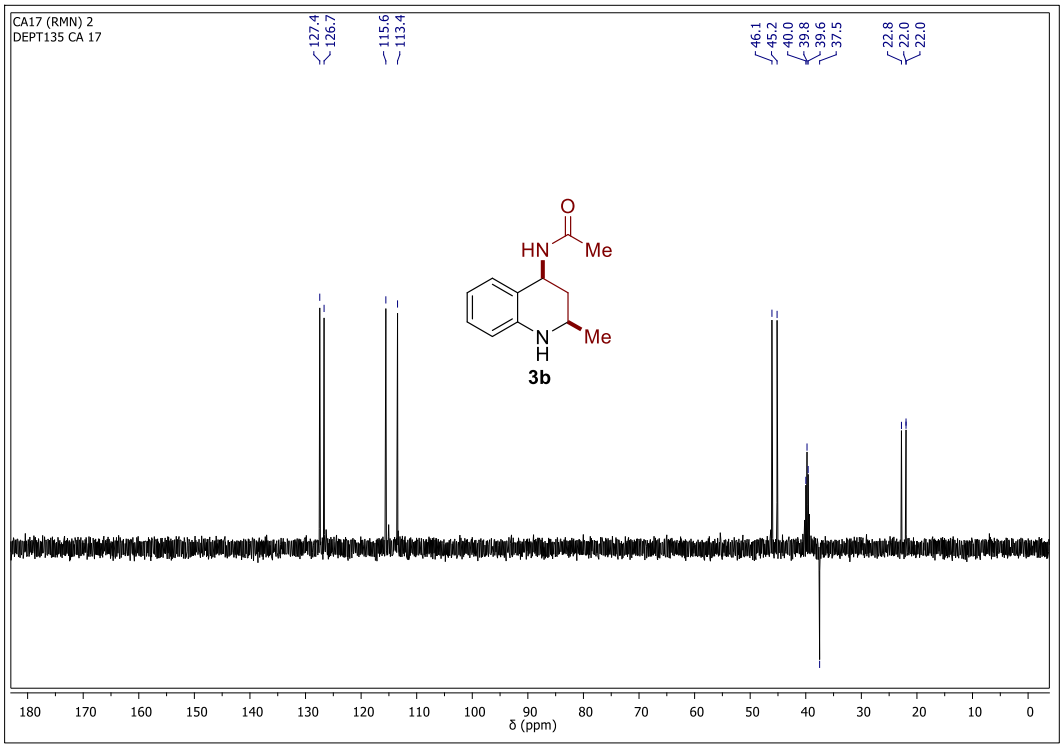


Figure ESI 10. COSY spectrum of *cis*-4-Acetamido-2-methyl-1,2,3,4-tetrahydroquinoline **3b**.

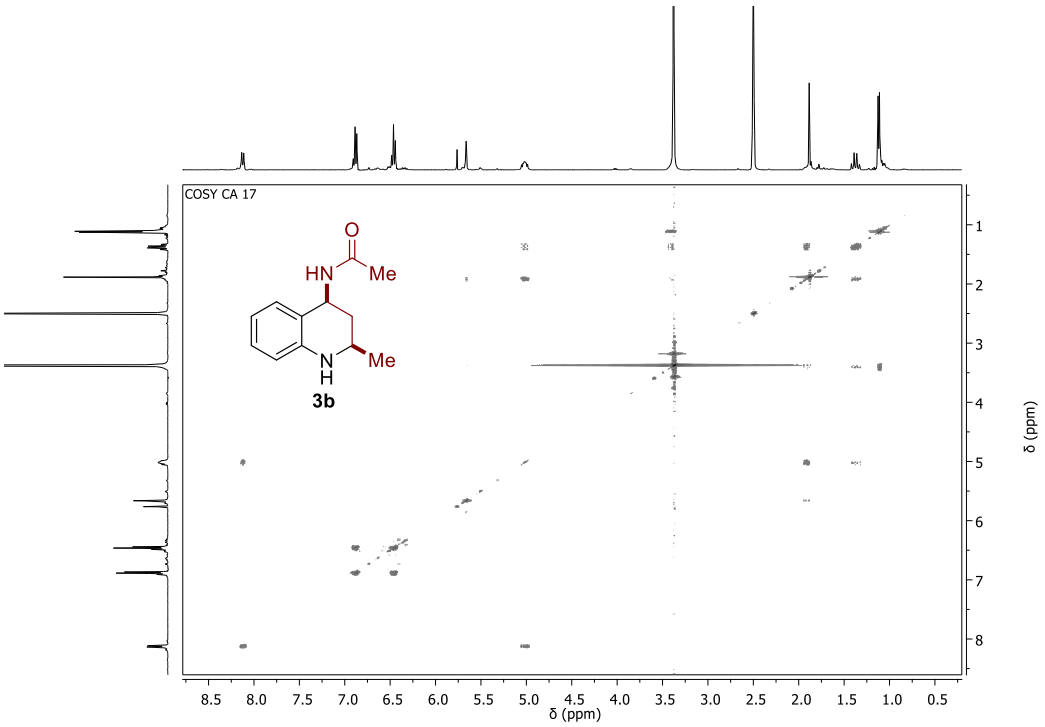


Figure ESI 11. HSQC spectrum of *cis*-4-Acetamido-2-methyl-1,2,3,4-tetrahydroquinoline **3b**.

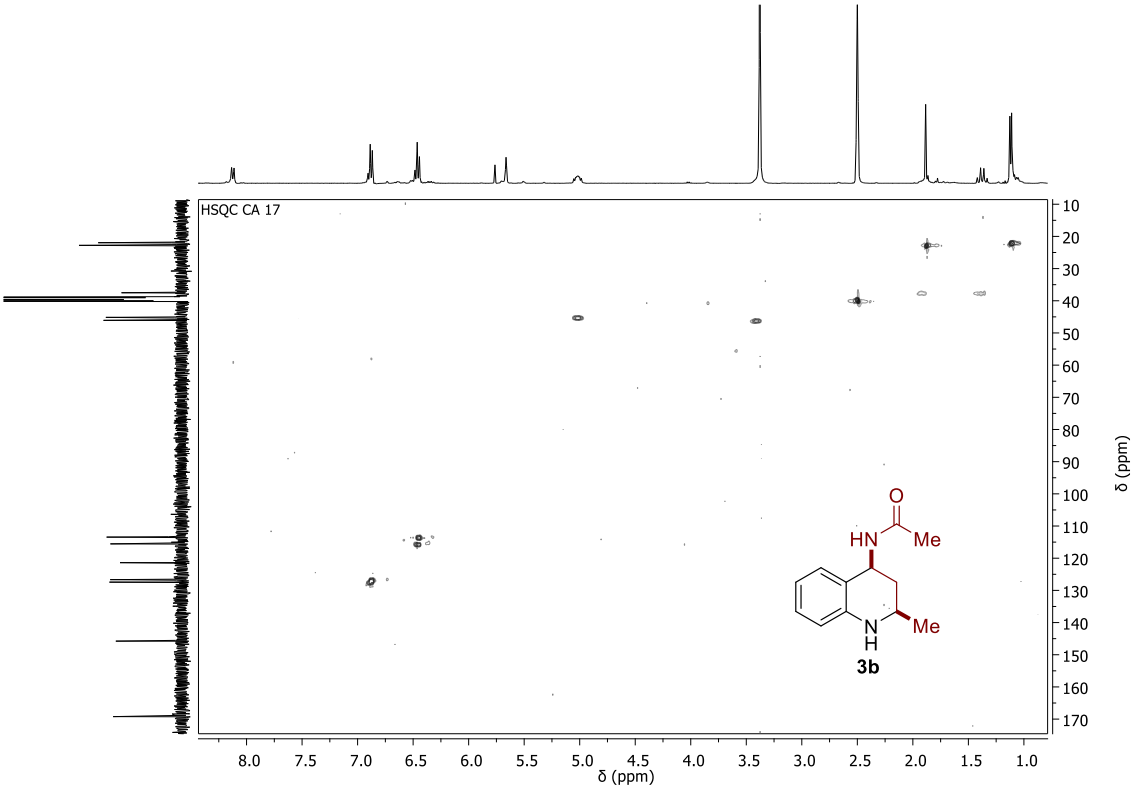


Figure ESI 12. HMBC spectrum of *cis*-4-Acetamido-2-methyl-1,2,3,4-tetrahydroquinoline **3b**.

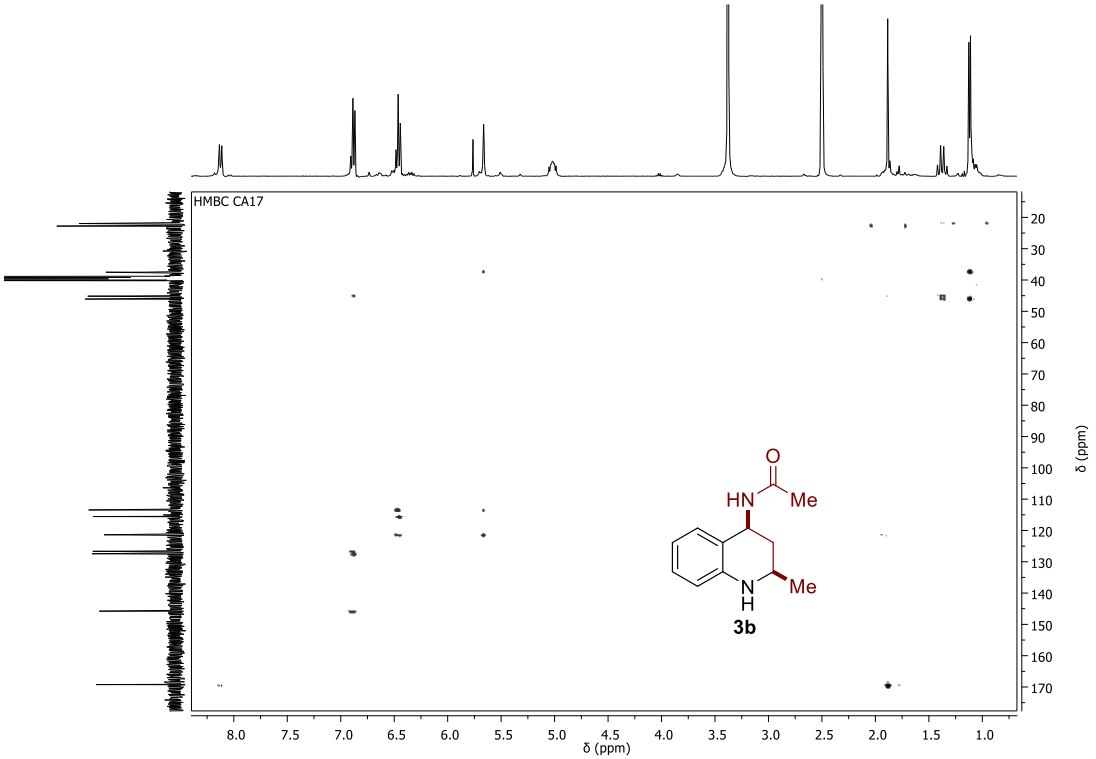


Figure ESI 13. ^{1}H-NMR spectrum of *cis*-4-Acetamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3c**.

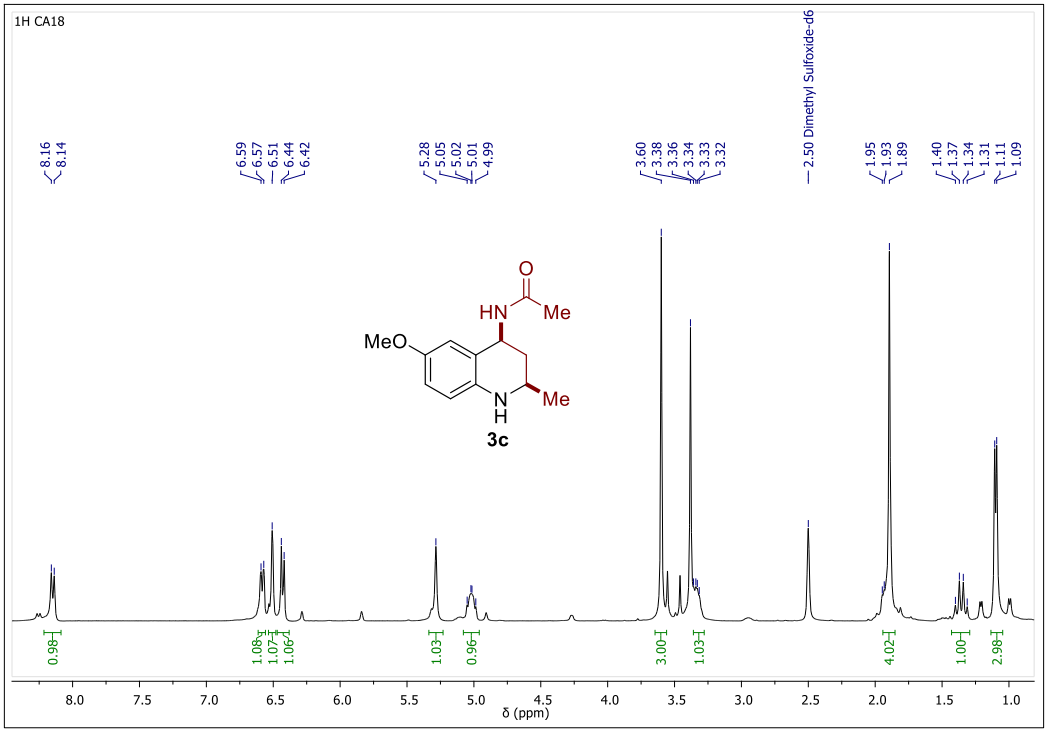


Figure ESI 14. ^{13}C-NMR spectrum of *cis*-4-Acetamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3c**.

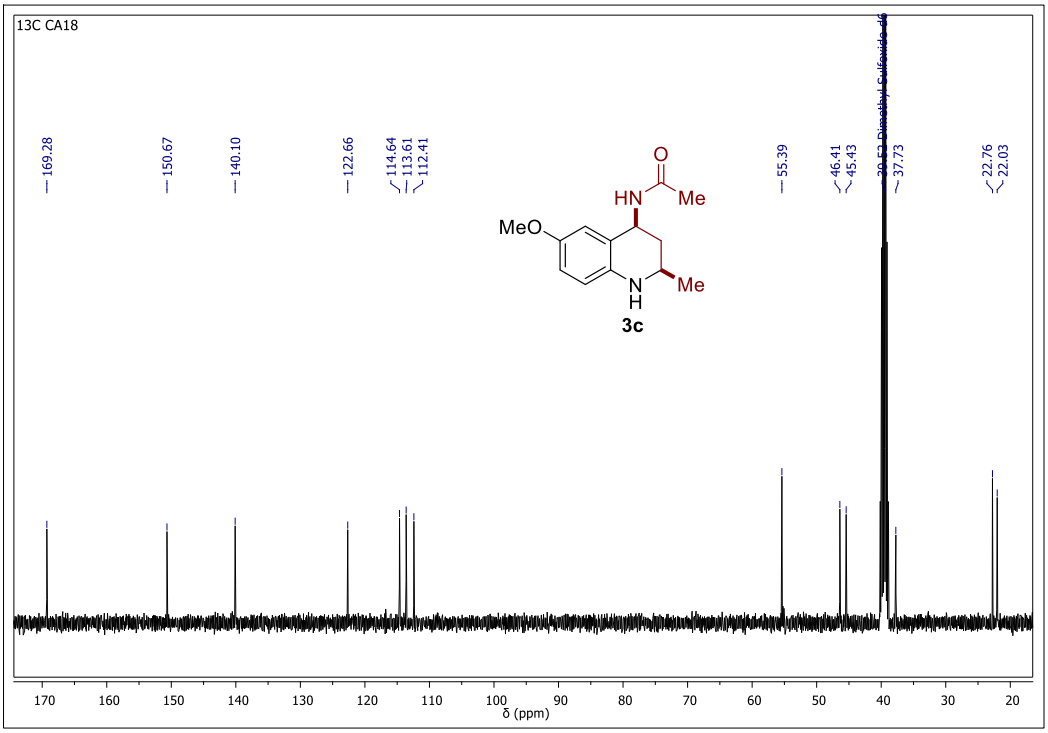


Figure ESI 15. DEPT-135 spectrum of *cis*-4-Acetamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3c**.

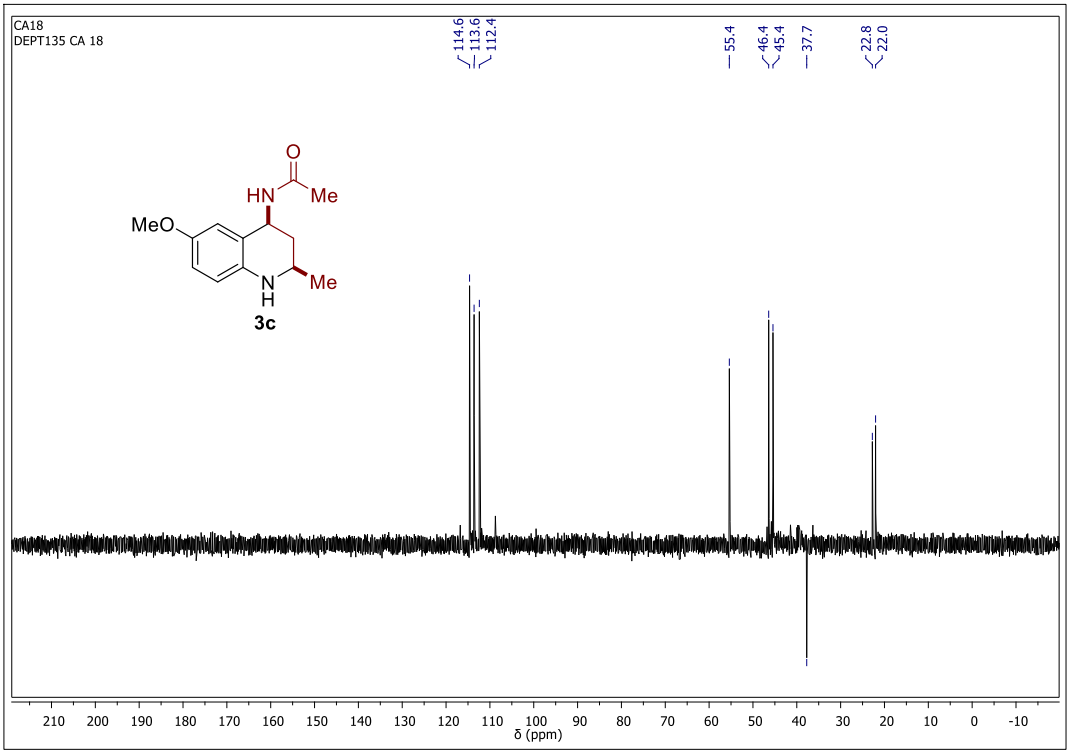


Figure ESI 16. ^{1}H-NMR spectrum of *cis*-4-Acetamido-6-carboxy-2-methyl-1,2,3,4-tetrahydroquinoline **3d**.

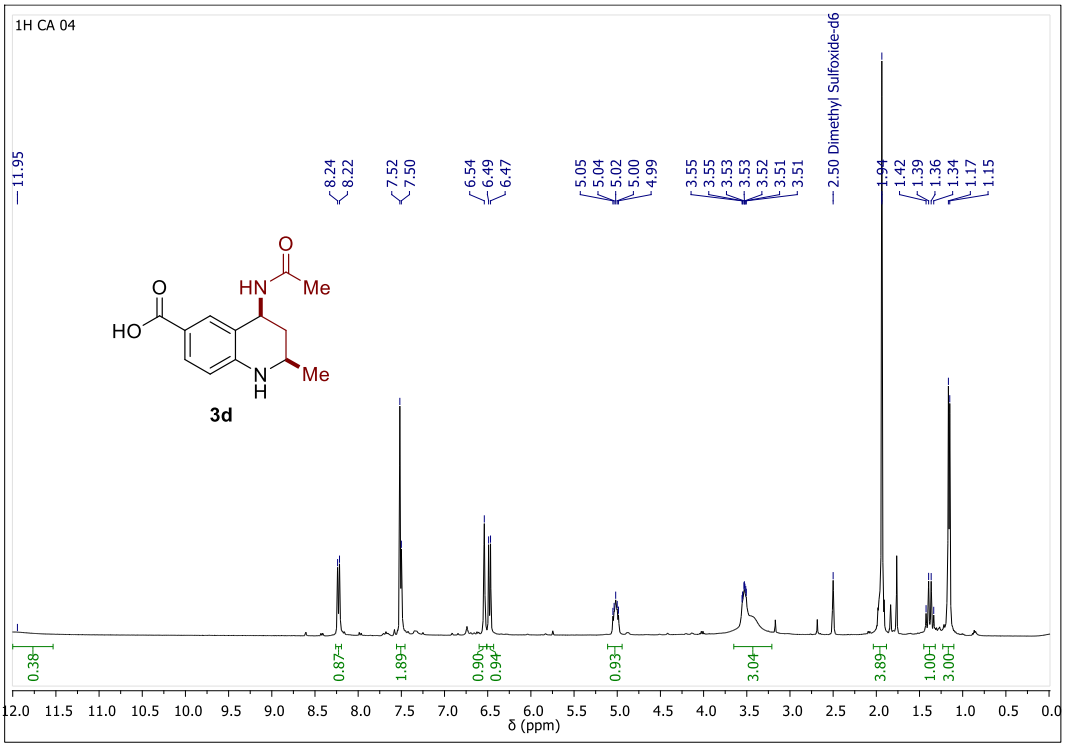


Figure ESI 17. ^{13}C-NMR spectrum of *cis*-4-Acetamido-6-carboxy-2-methyl-1,2,3,4-tetrahydroquinoline **3d**.

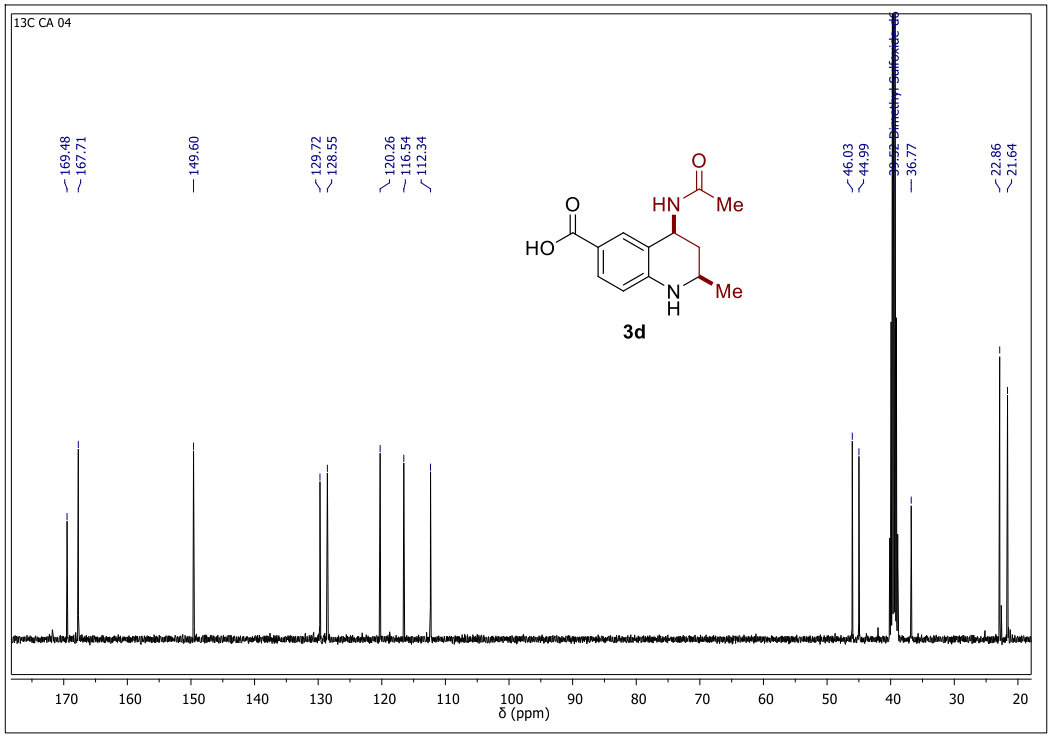


Figure ESI 18. DEPT-135 spectrum of *cis*-4-Acetamido-6-carboxy-2-methyl-1,2,3,4-tetrahydroquinoline **3d**.

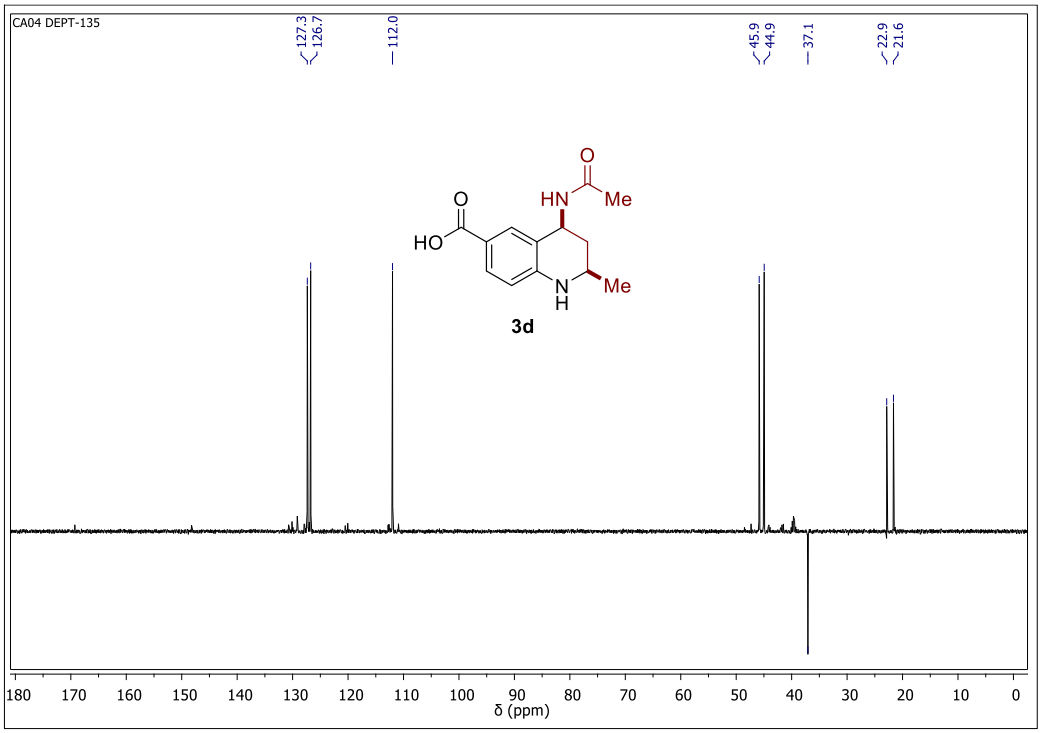


Figure ESI 19. COSY spectrum of *cis*-4-Acetamido-6-carboxy-2-methyl-1,2,3,4-tetrahydroquinoline **3d**.

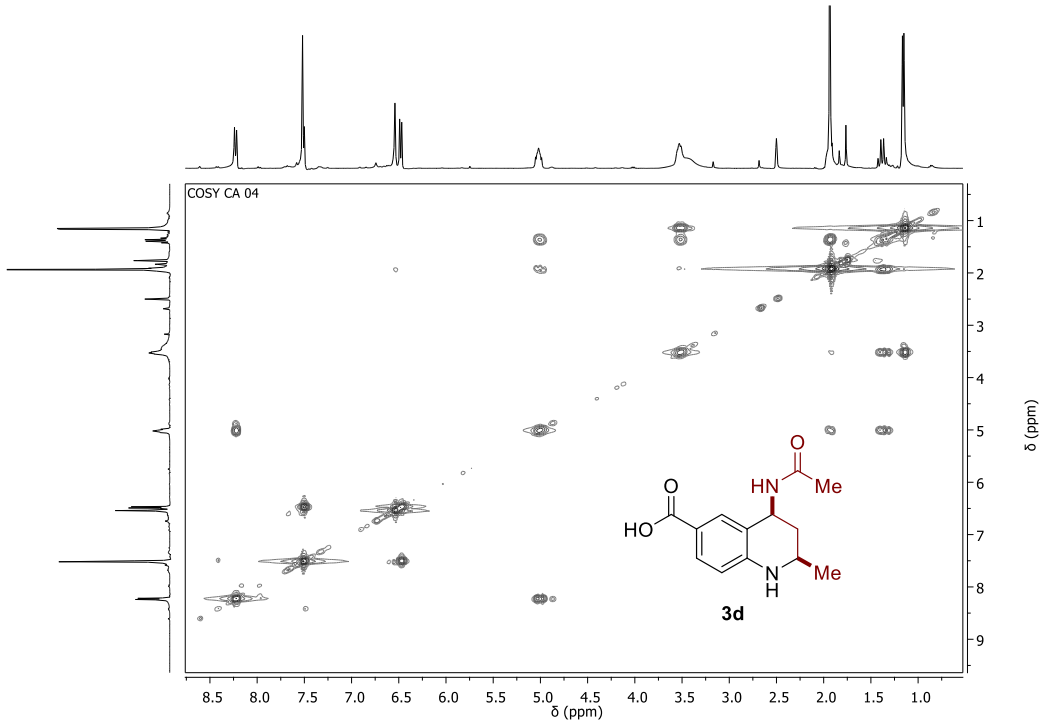


Figure ESI 20. HSQC spectrum of *cis*-4-Acetamido-6-carboxy-2-methyl-1,2,3,4-tetrahydroquinoline **3d**.

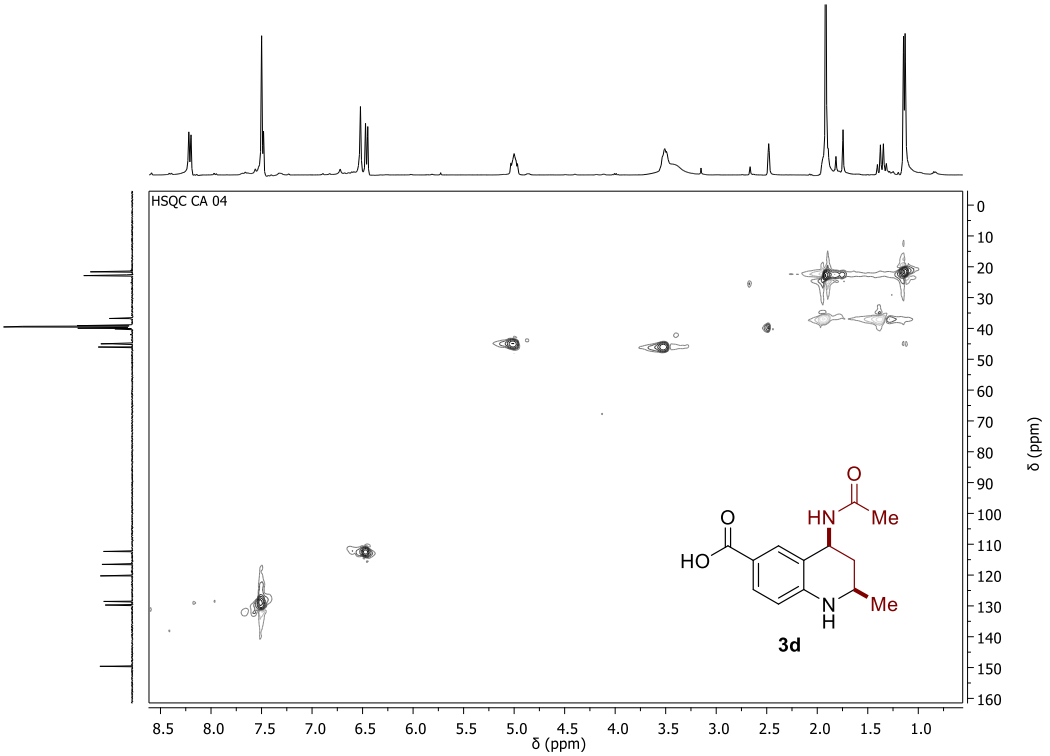


Figure ESI 21. HMBC spectrum of *cis*-4-Acetamido-6-carboxy-2-methyl-1,2,3,4-tetrahydroquinoline **3d**.

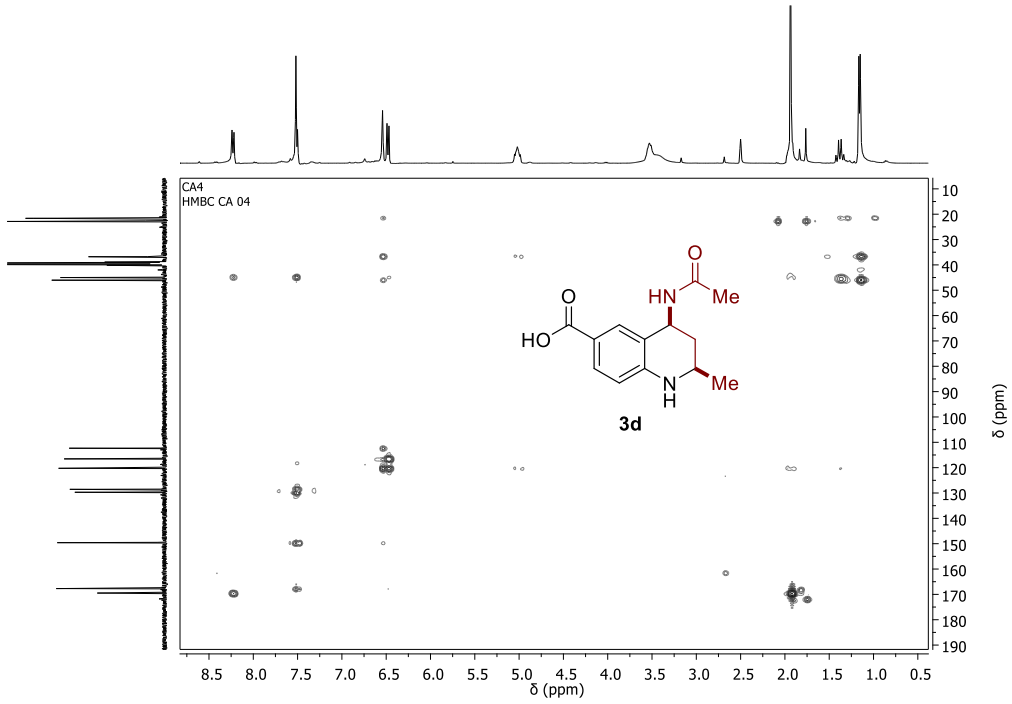


Figure ESI 22. ^{1}H-NMR spectrum of *cis*-6-Acetyl-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3e**.

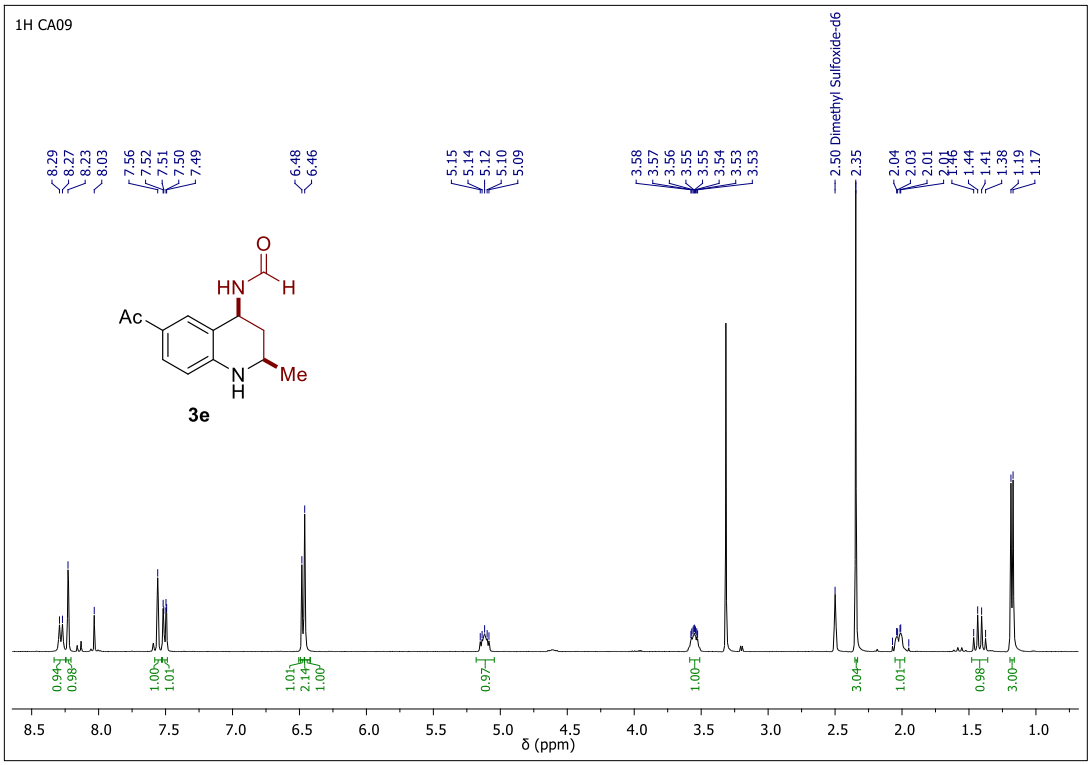


Figure ESI 23. ^{13}C-NMR spectrum of *cis*-6-Acetyl-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3e**.

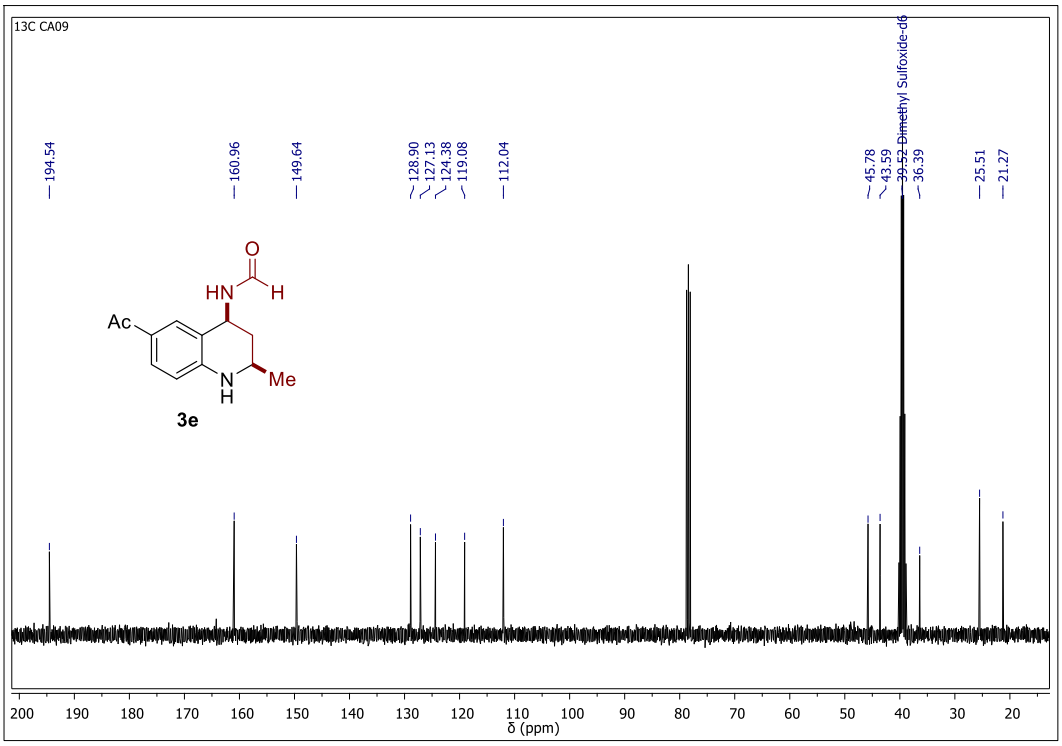


Figure ESI 24. DEPT-135 spectrum of *cis*-6-Acetyl-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3e**.

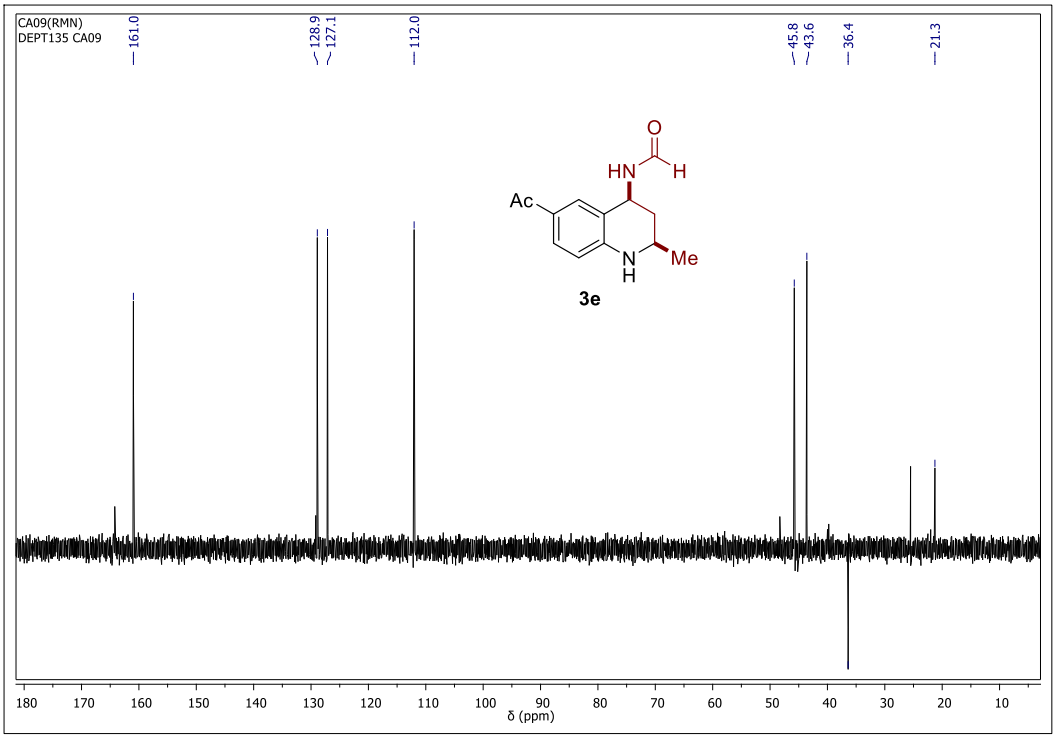


Figure ESI 25. ^{1}H-NMR spectrum of *cis*-4-Formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3f**.

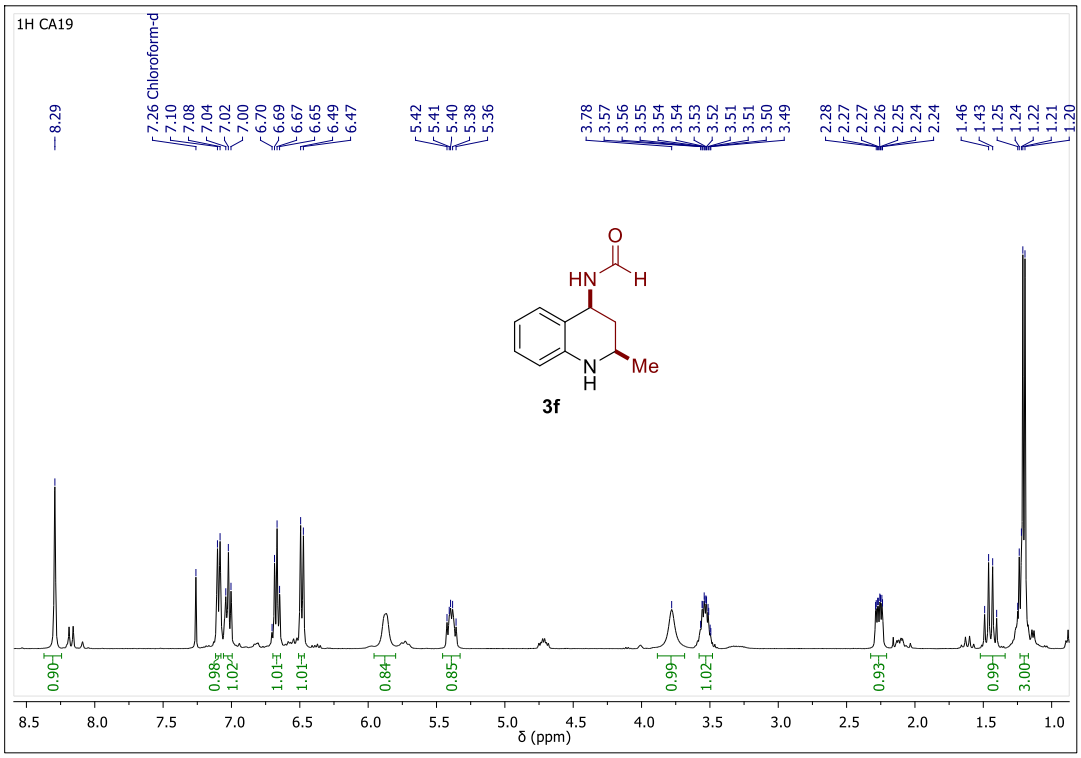


Figure ESI 26. ^{13}C-NMR spectrum of *cis*-4-Formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3f**.

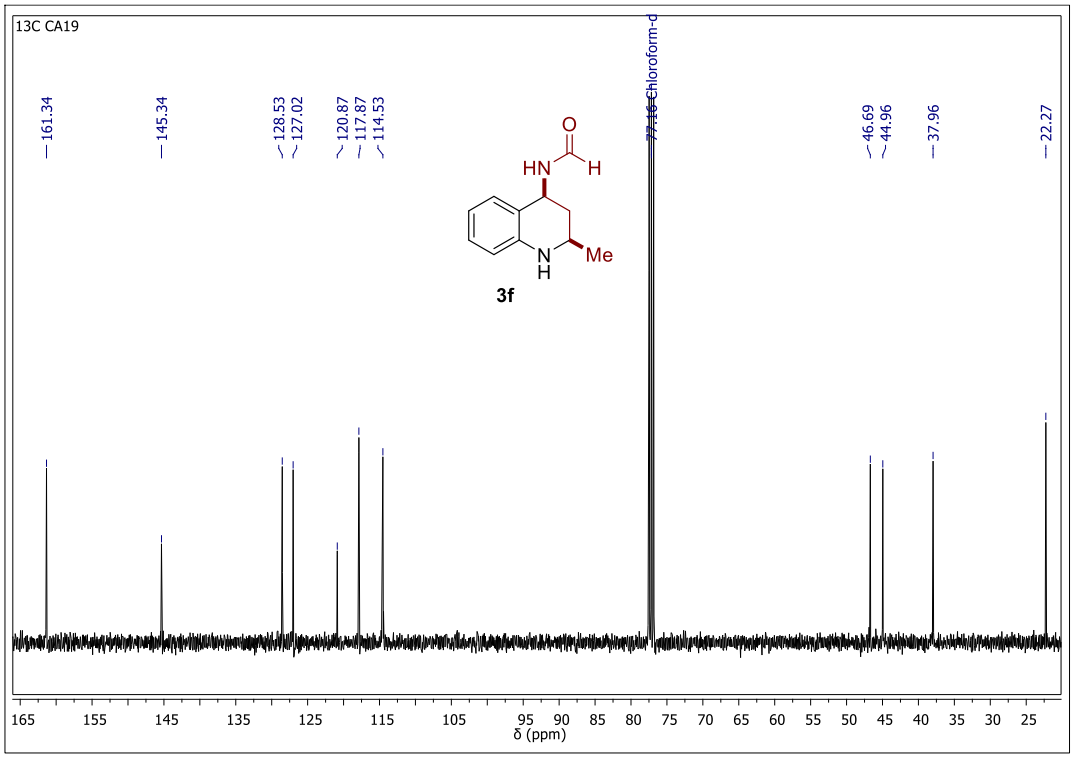


Figure ESI 27. DEPT-135 spectrum of *cis*-4-Formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3f**.

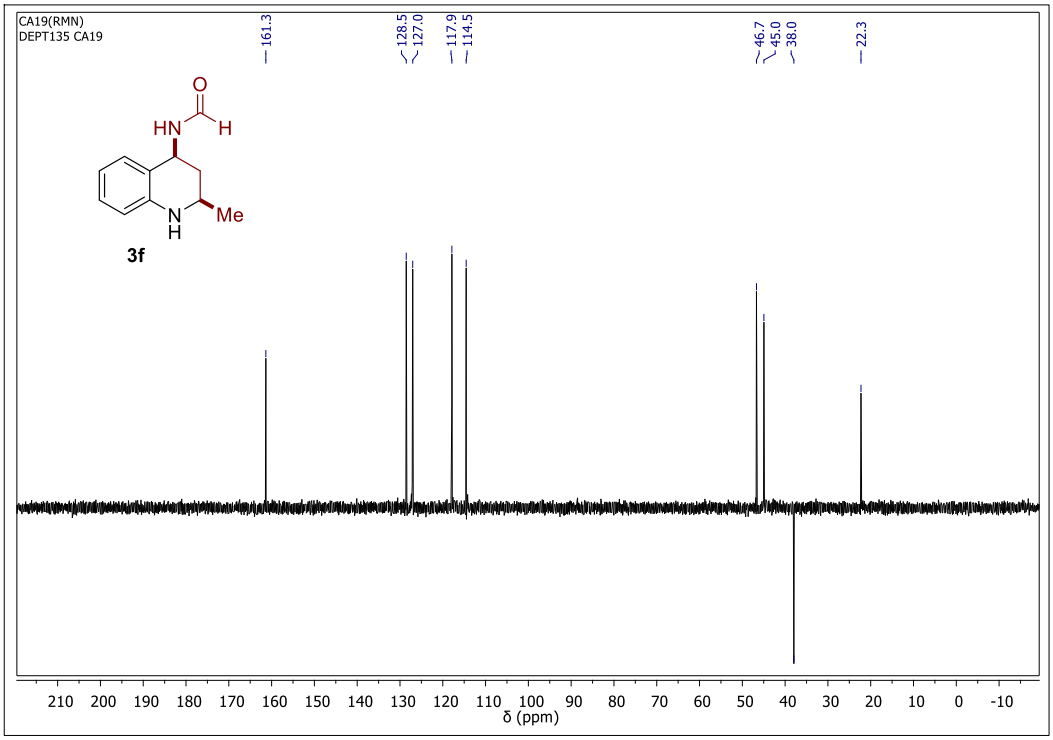


Figure ESI 28. ^{1}H-NMR spectrum of *cis*-4-Formamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3g**.

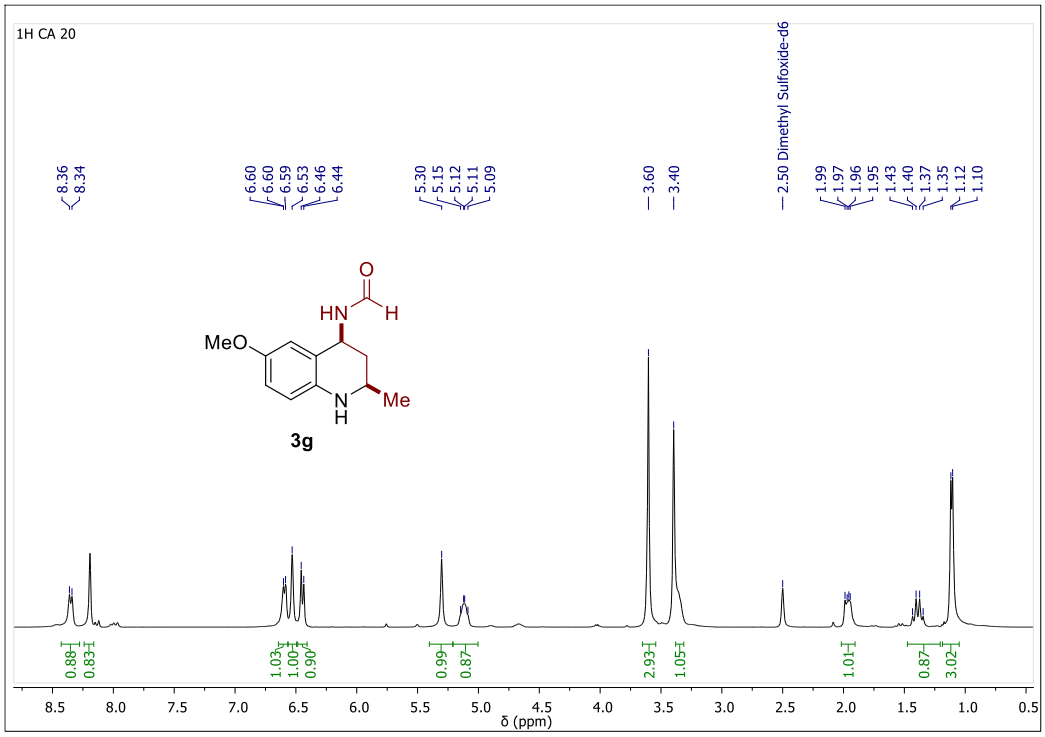


Figure ESI 29. ^{13}C-NMR spectrum of *cis*-4-Formamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3g**.

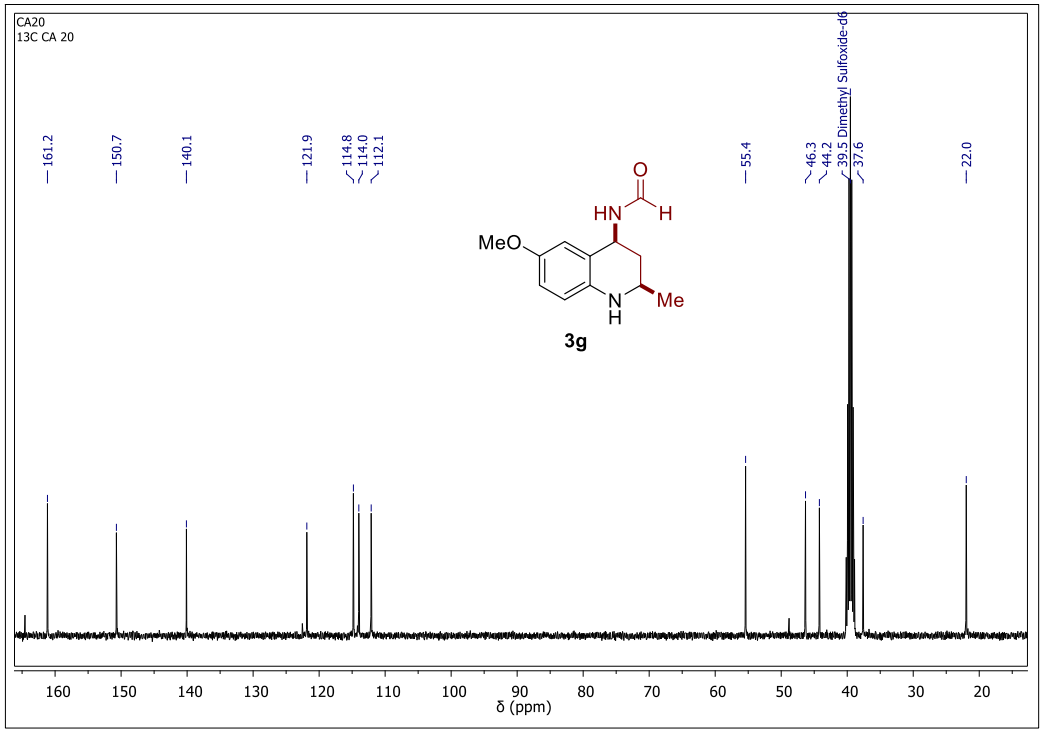


Figure ESI 30. DEPT-135 spectrum of *cis*-4-Formamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3g**.

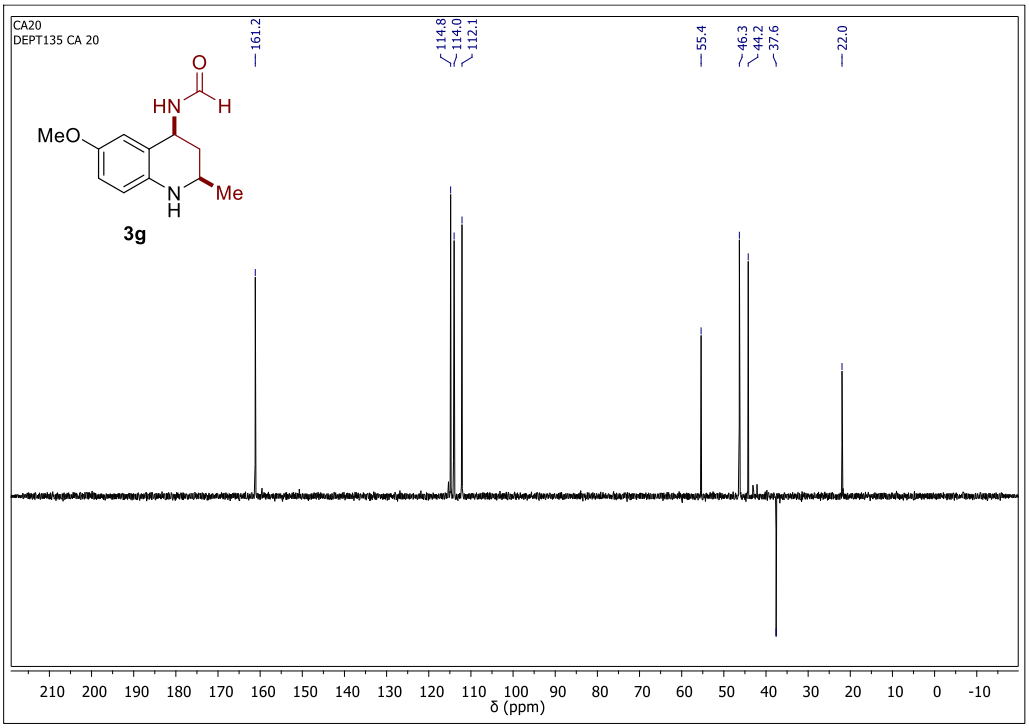


Figure ESI 31. COSY spectrum of *cis*-4-Formamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3g**.

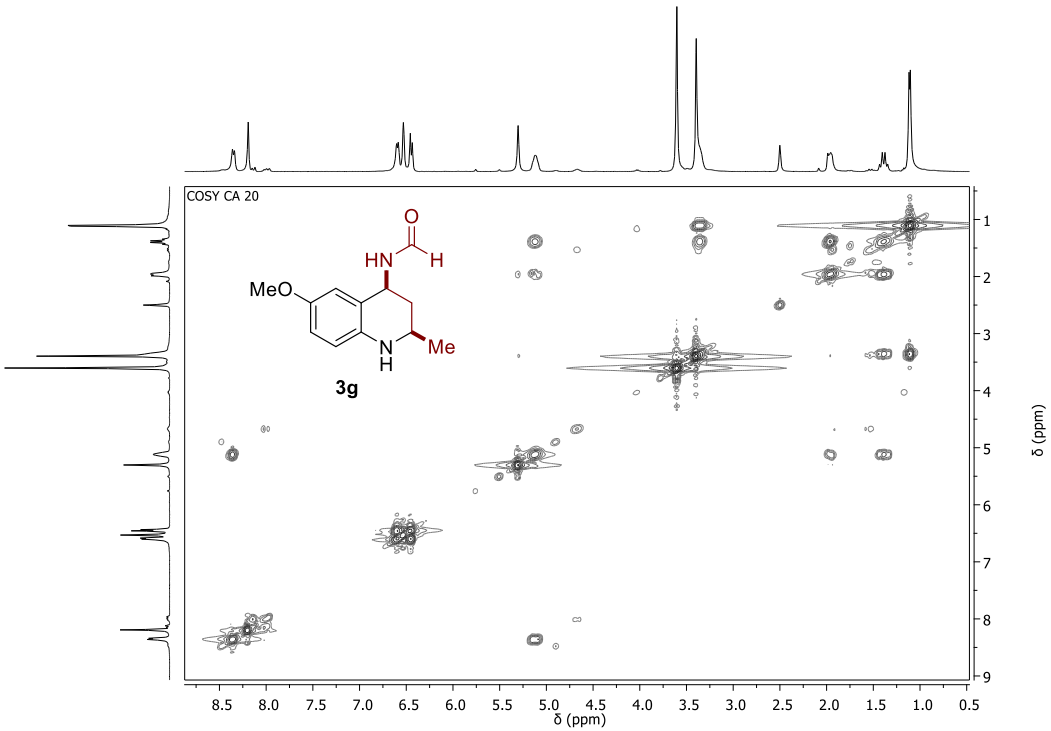


Figure ESI 32. HSQC spectrum of *cis*-4-Formamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3g**.

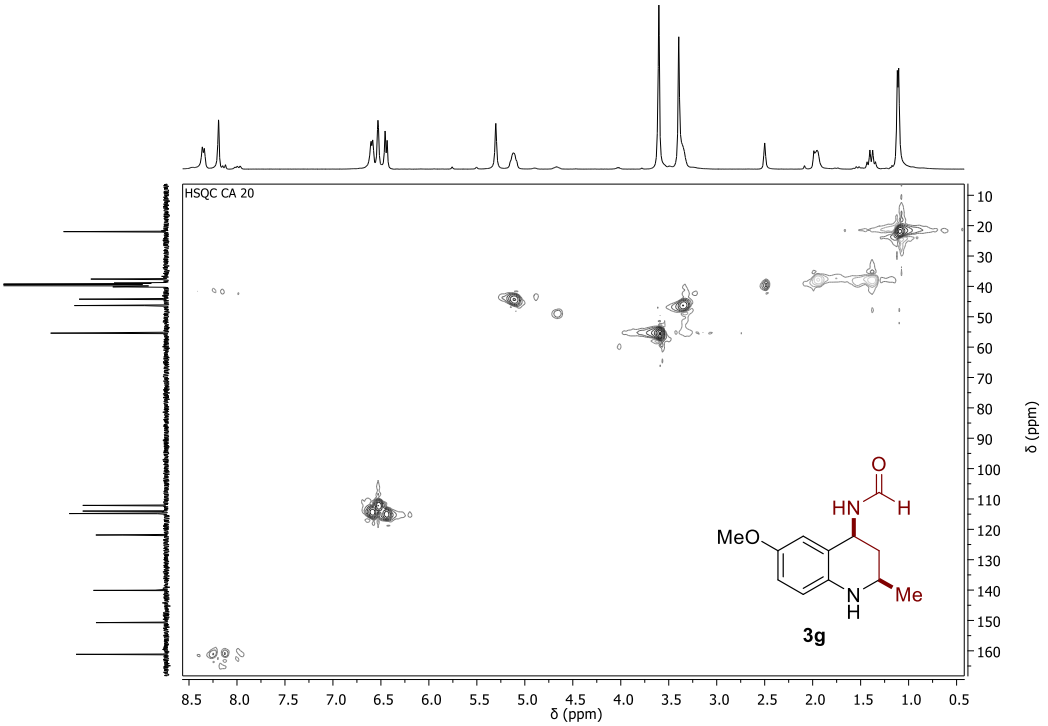


Figure ESI 33. HMBC spectrum of *cis*-4-Formamido-6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline **3g**.

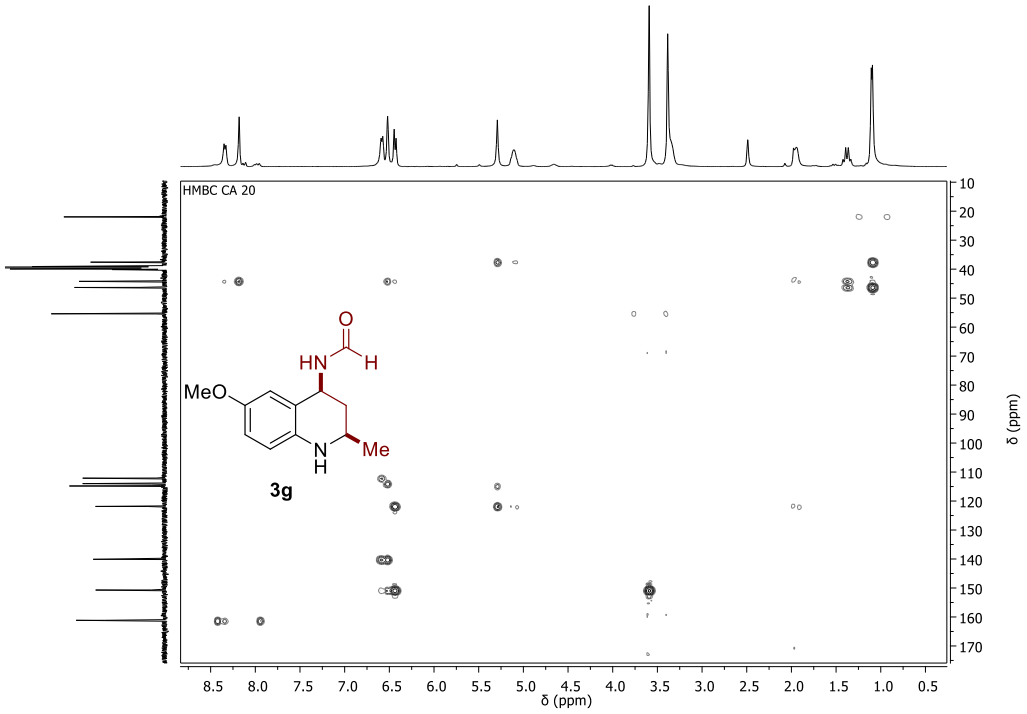


Figure ESI 34. ^{1}H-NMR spectrum of *cis*-6-Carboxy-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3h**.

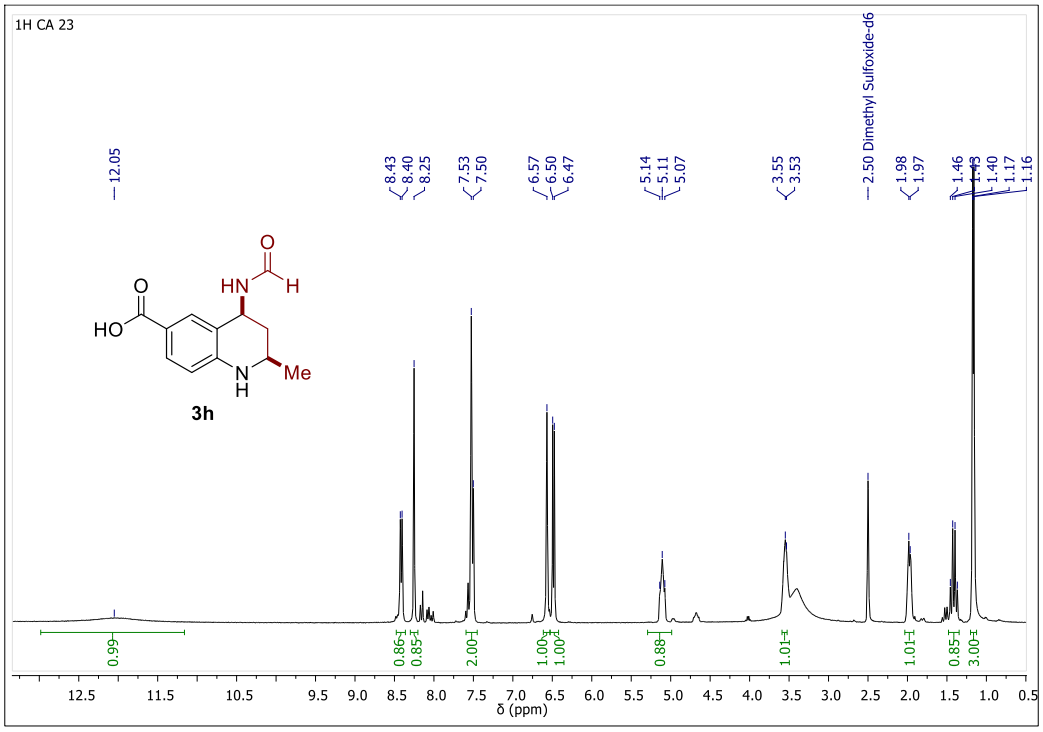


Figure ESI 35. ^{13}C-NMR spectrum of *cis*-6-Carboxy-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3h**.

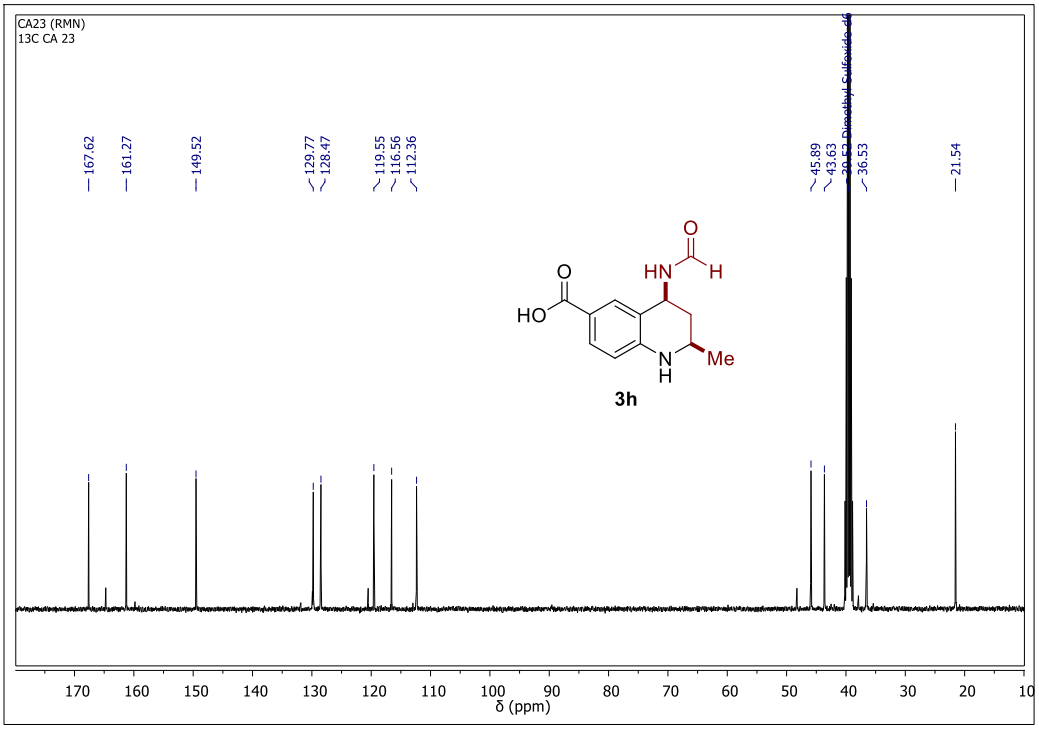


Figure ESI 36. DEPT-135 spectrum of *cis*-6-Carboxy-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3h**.

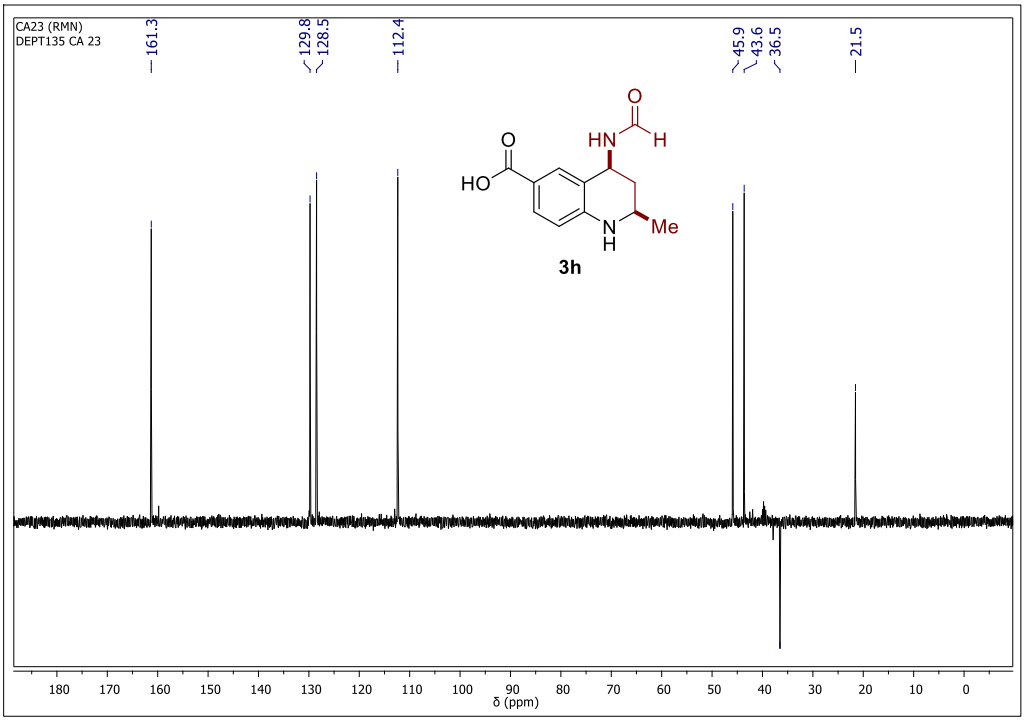


Figure ESI 37. COSY spectrum of *cis*-6-Carboxy-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3h**.

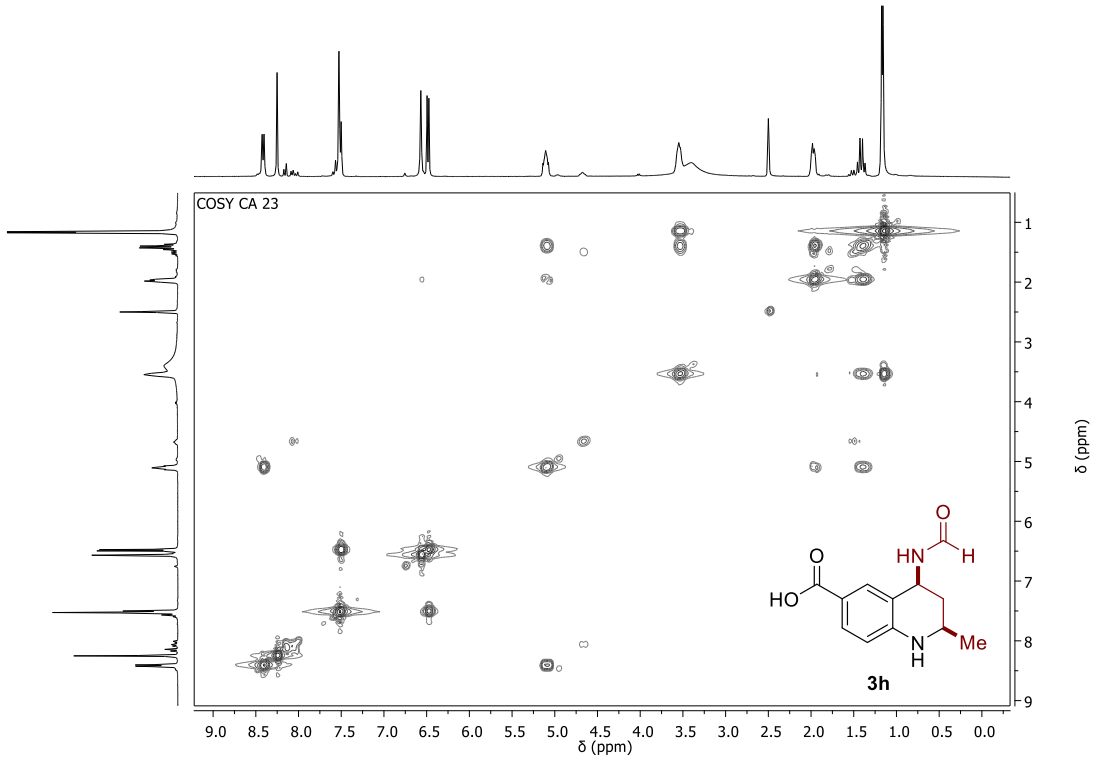


Figure ESI 38. HSQC spectrum of *cis*-6-Carboxy-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3h**.

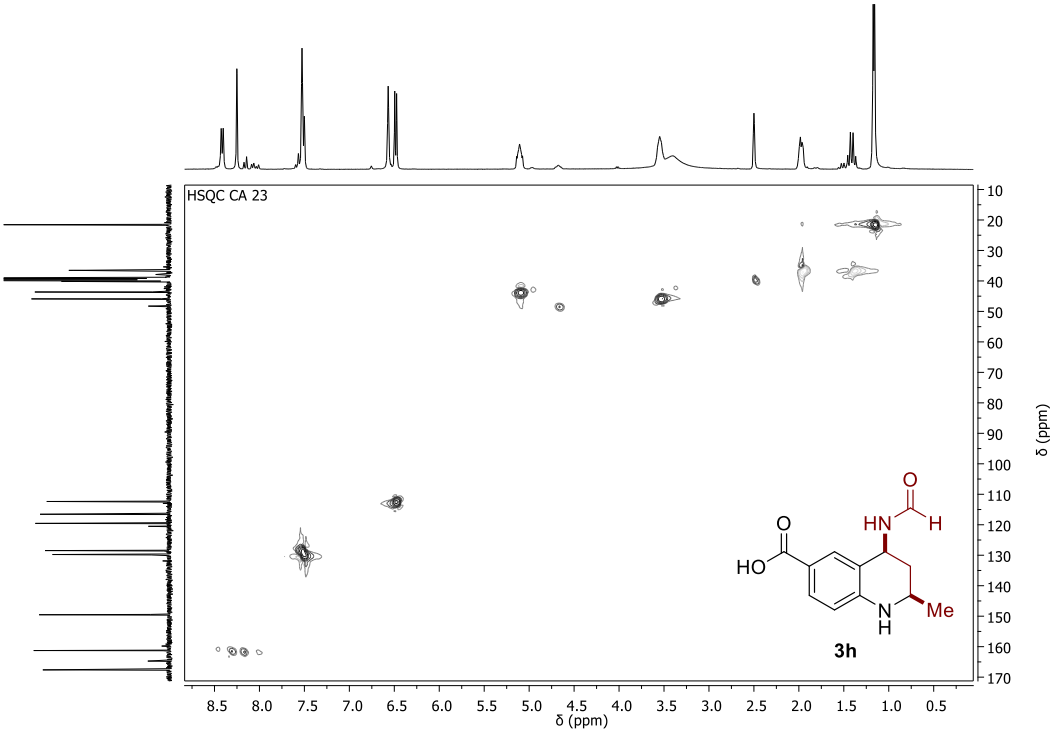


Figure ESI 39. HMBC spectrum of *cis*-6-Carboxy-4-formamido-2-methyl-1,2,3,4-tetrahydroquinoline **3h**.

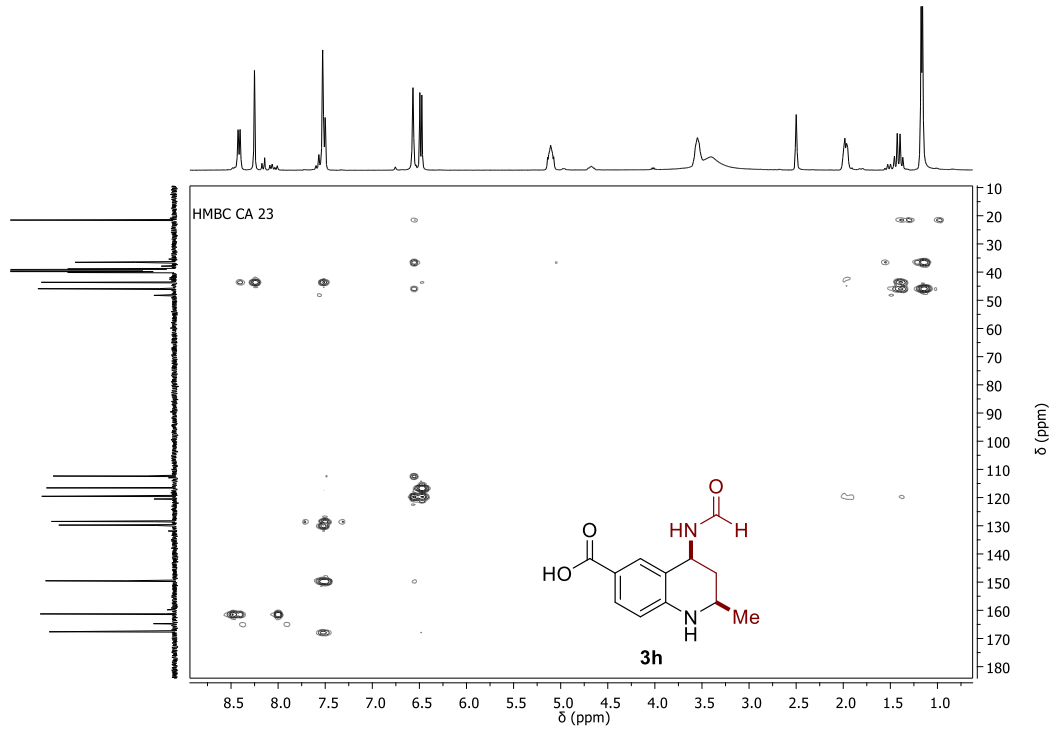


Figure ESI 40. ^{1}H-NMR spectrum of *cis*-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3i**.

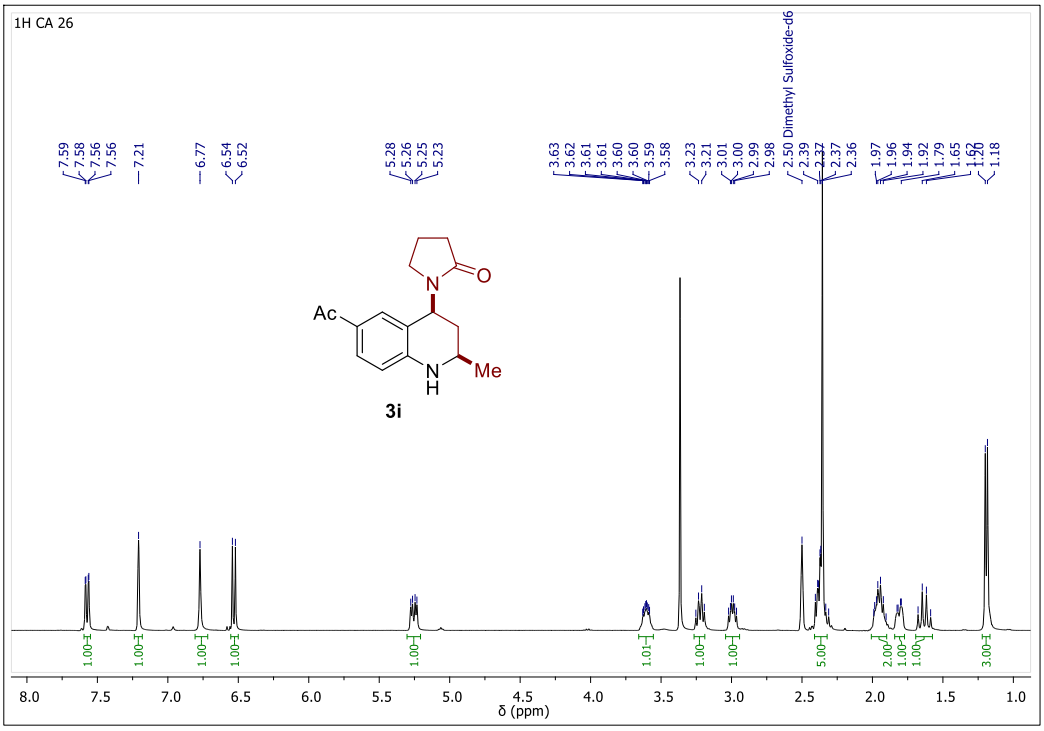


Figure ESI 41. ^{13}C-NMR spectrum of *cis*-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3i**.

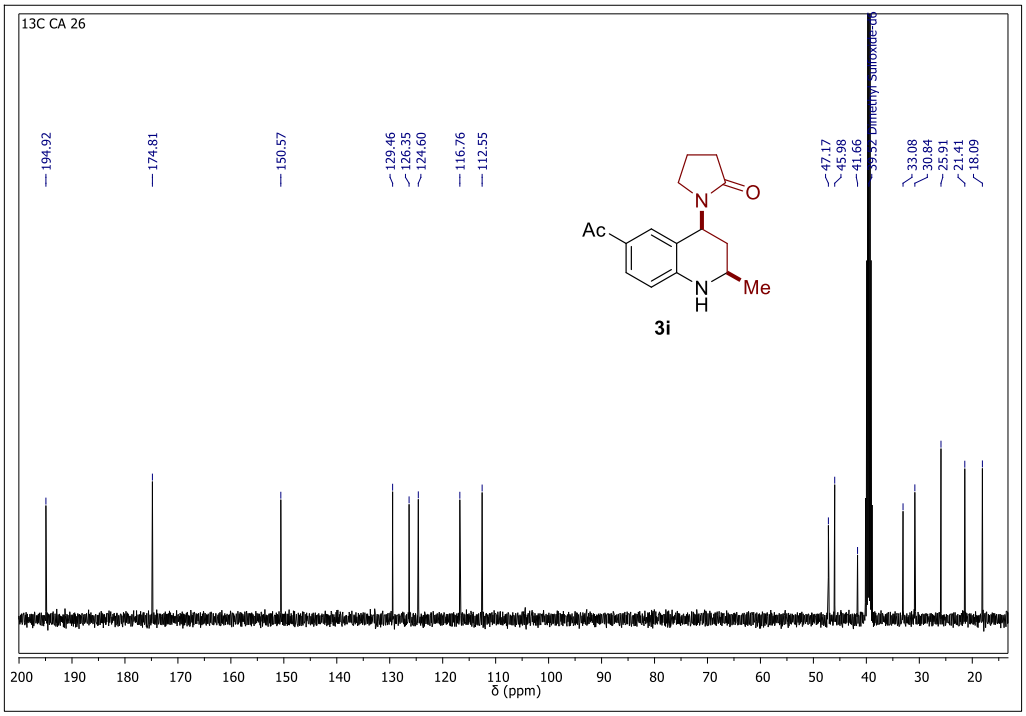


Figure ESI 42. DEPT-135 spectrum of *cis*-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3i**.

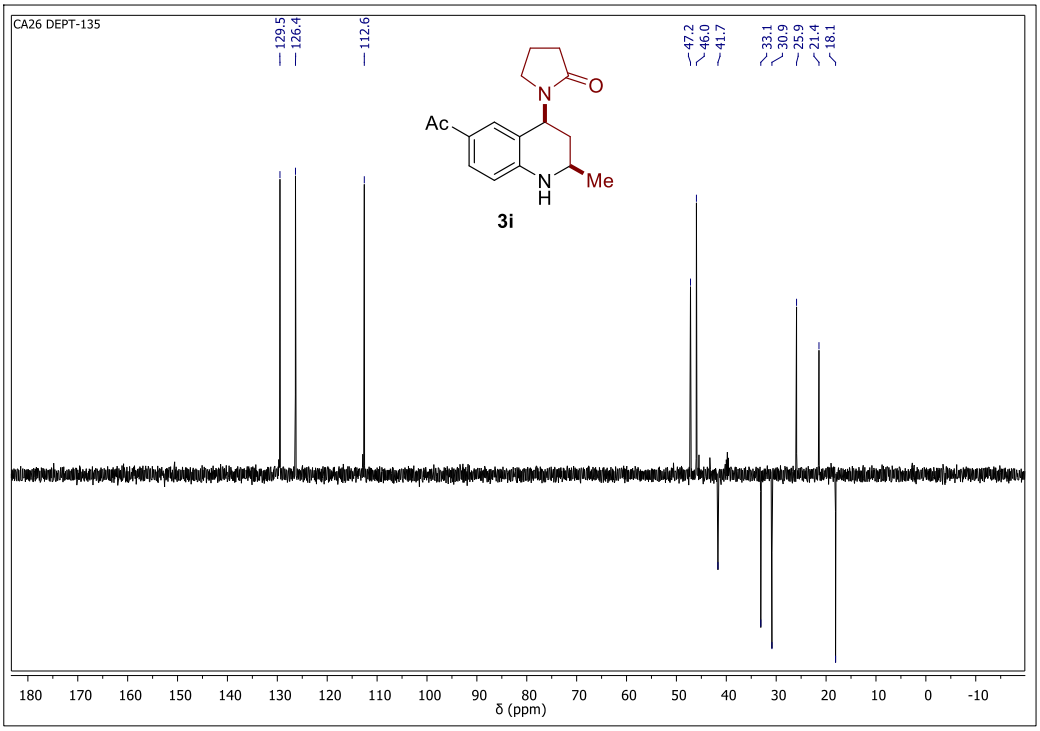


Figure ESI 43. NOESY spectrum of *cis*-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3i**.

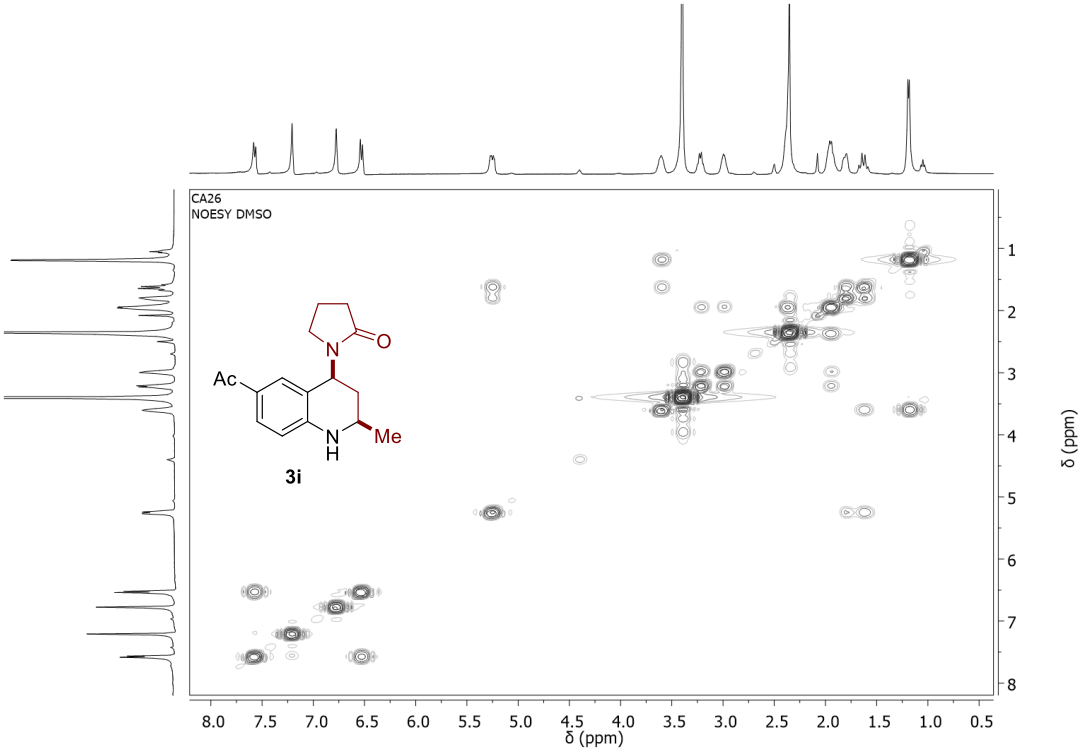


Figure ESI 44. COSY spectrum of *cis*-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3i**.

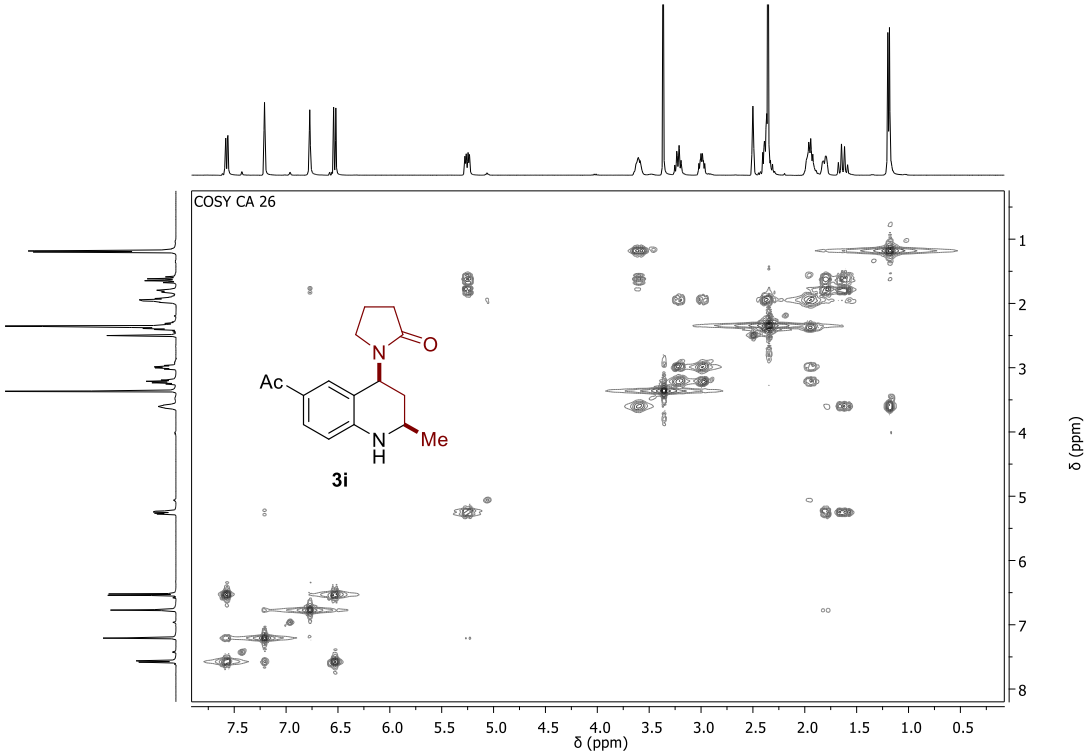


Figure ESI 45. HSQC spectrum of *cis*-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3i**.

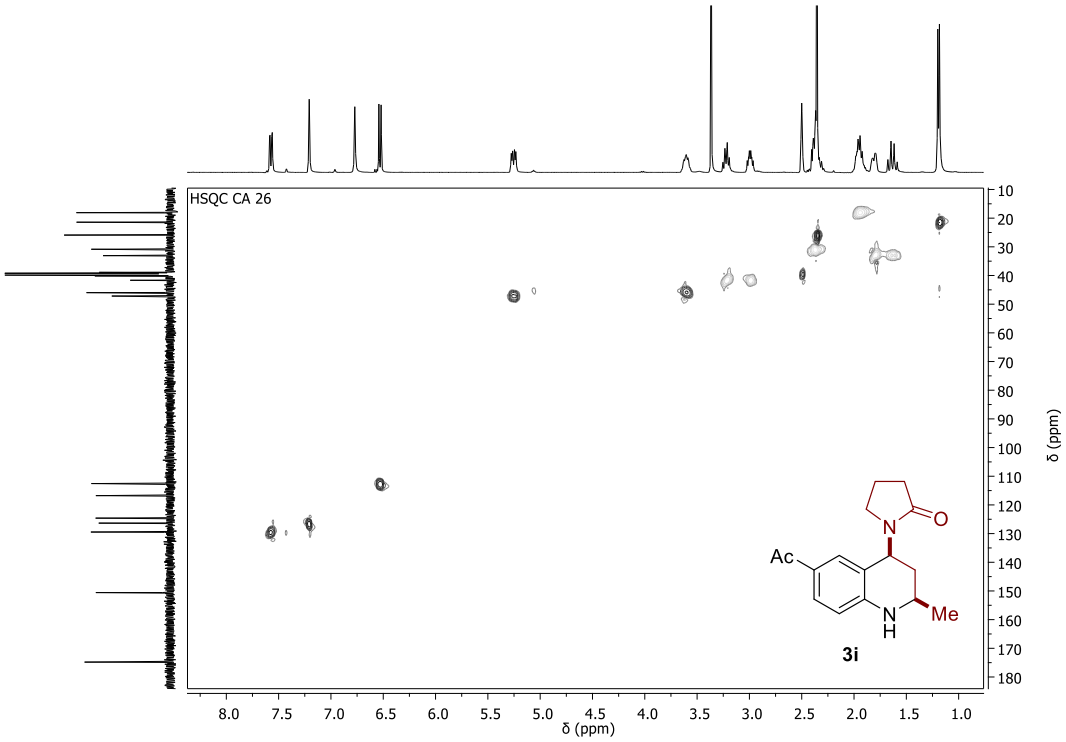


Figure ESI 46. HMBC spectrum of *cis*-6-Acetyl-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3i**.

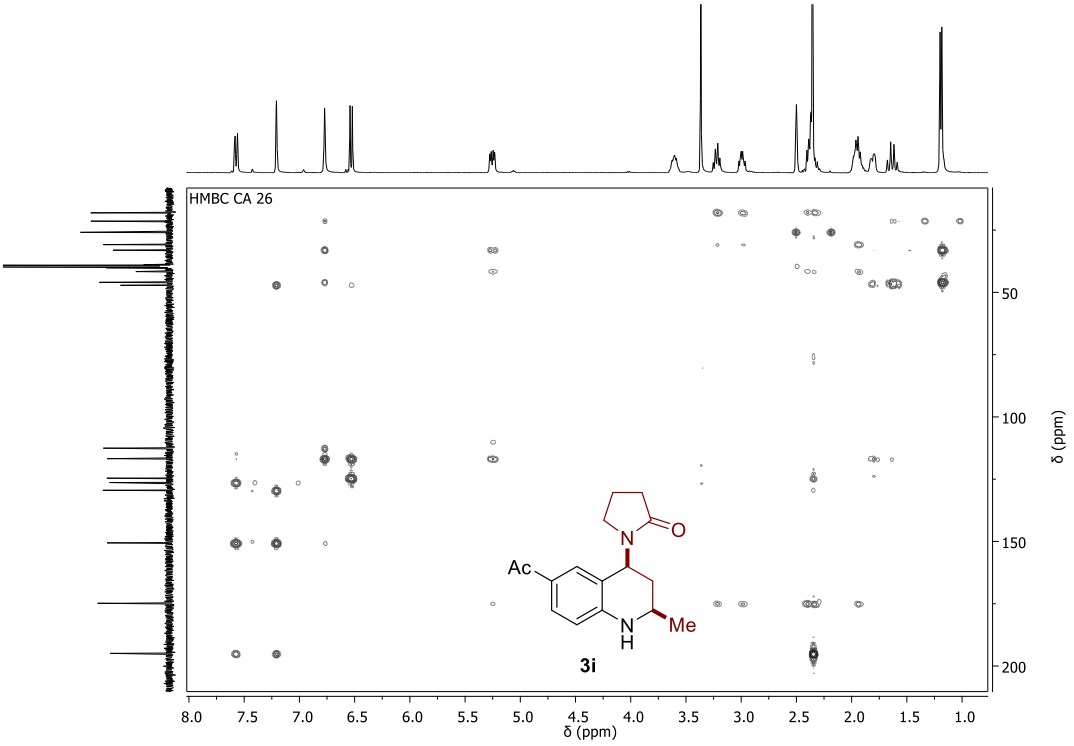


Figure ESI 47. ^{1}H-NMR spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3j**.

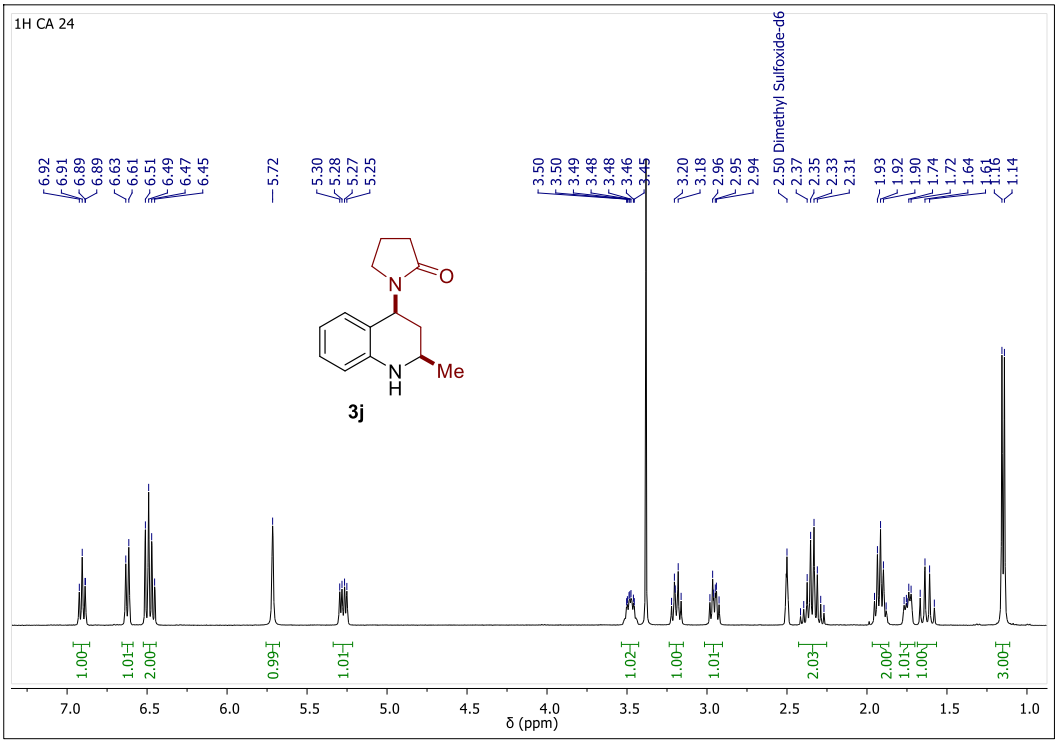


Figure ESI 48. ^{13}C-NMR spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3j**.

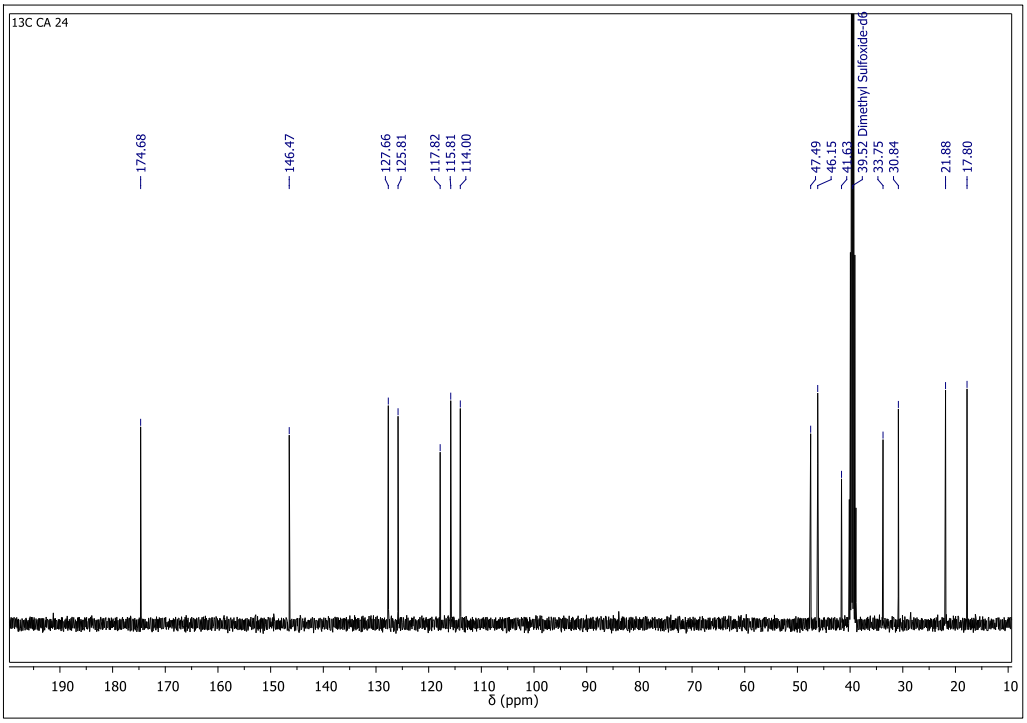


Figure ESI 49. DEPT-135 spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3j**.

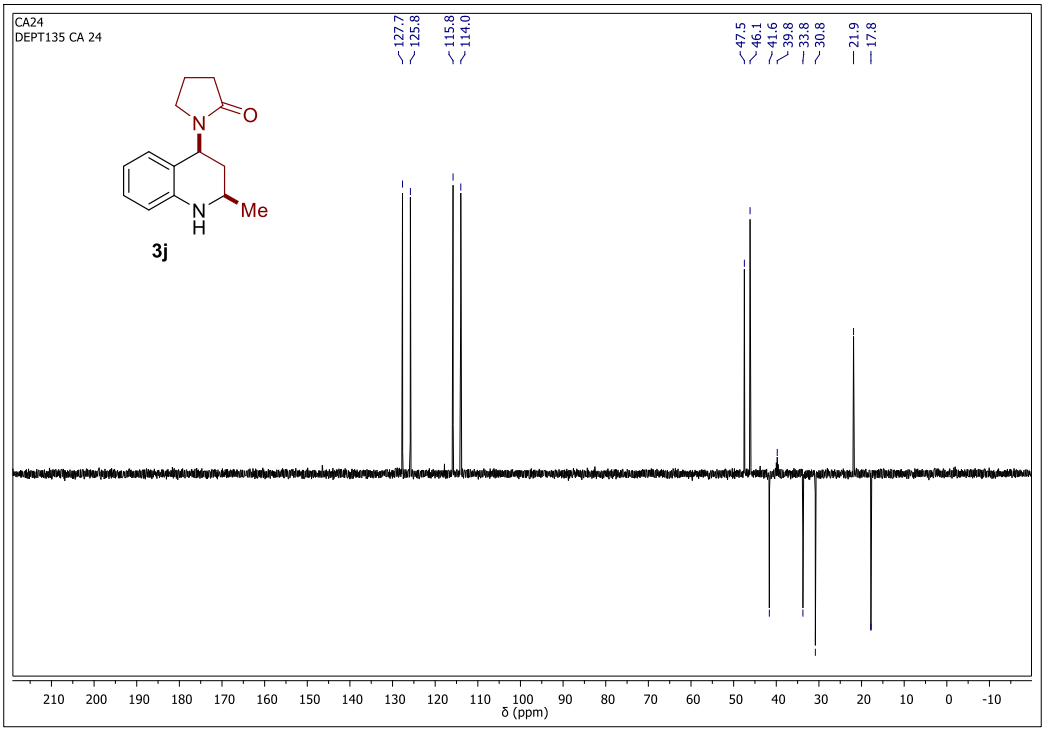


Figure ESI 50. COSY spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3j**.

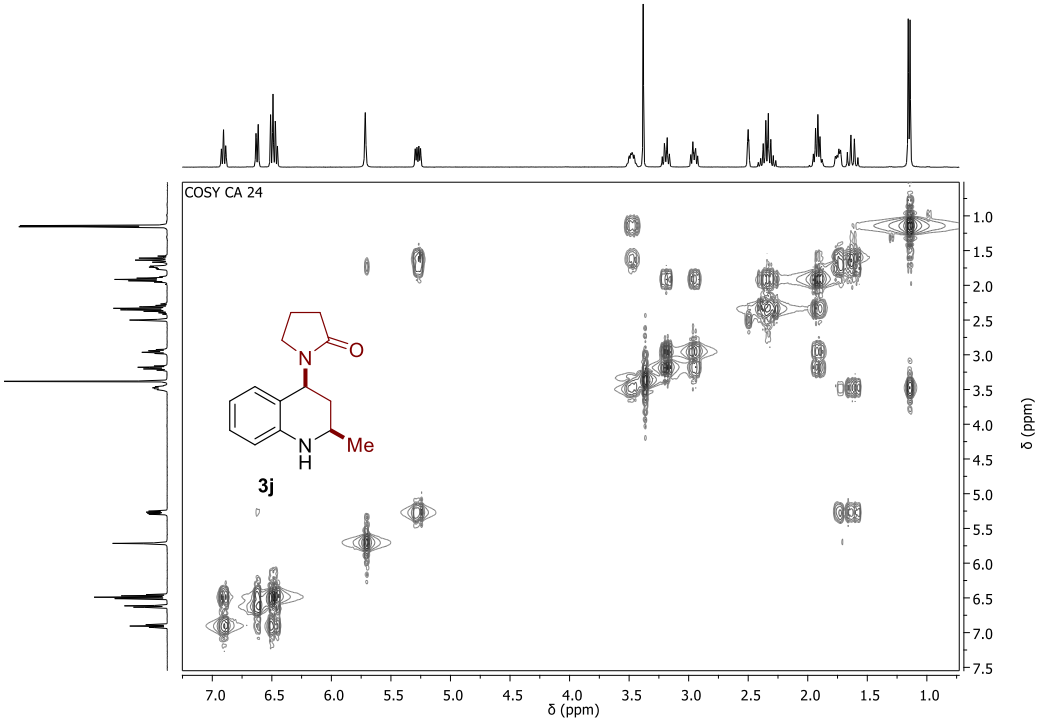


Figure ESI 51. HSQC spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3j**.

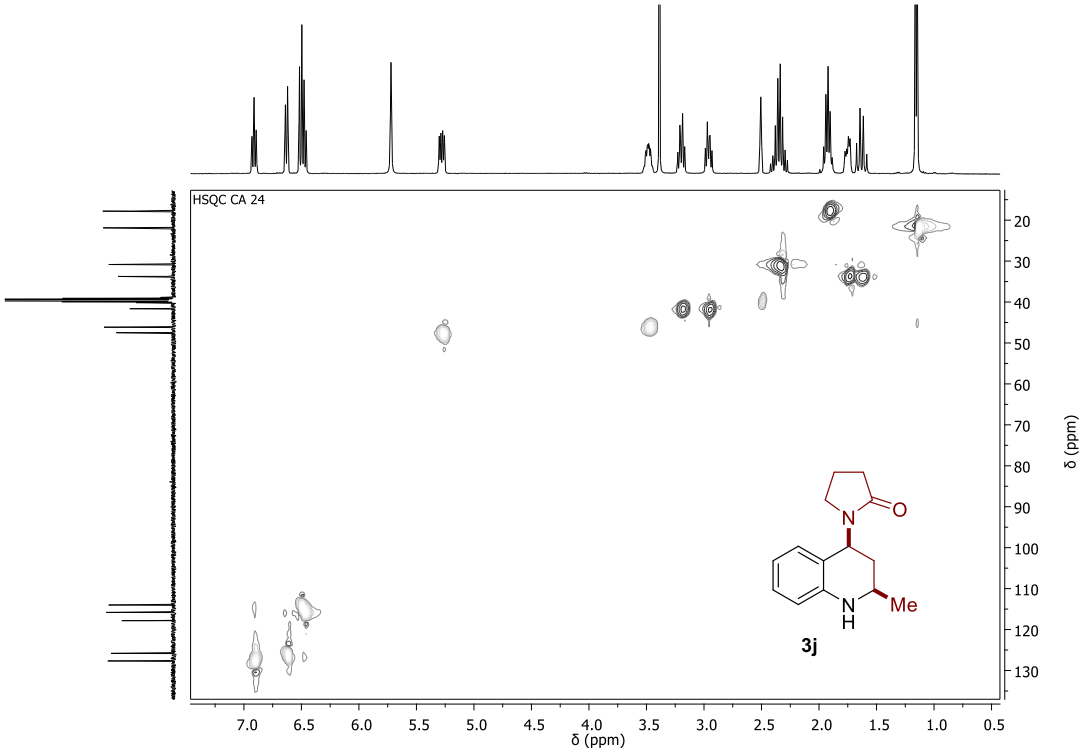


Figure ESI 52. HMBC spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3j**.

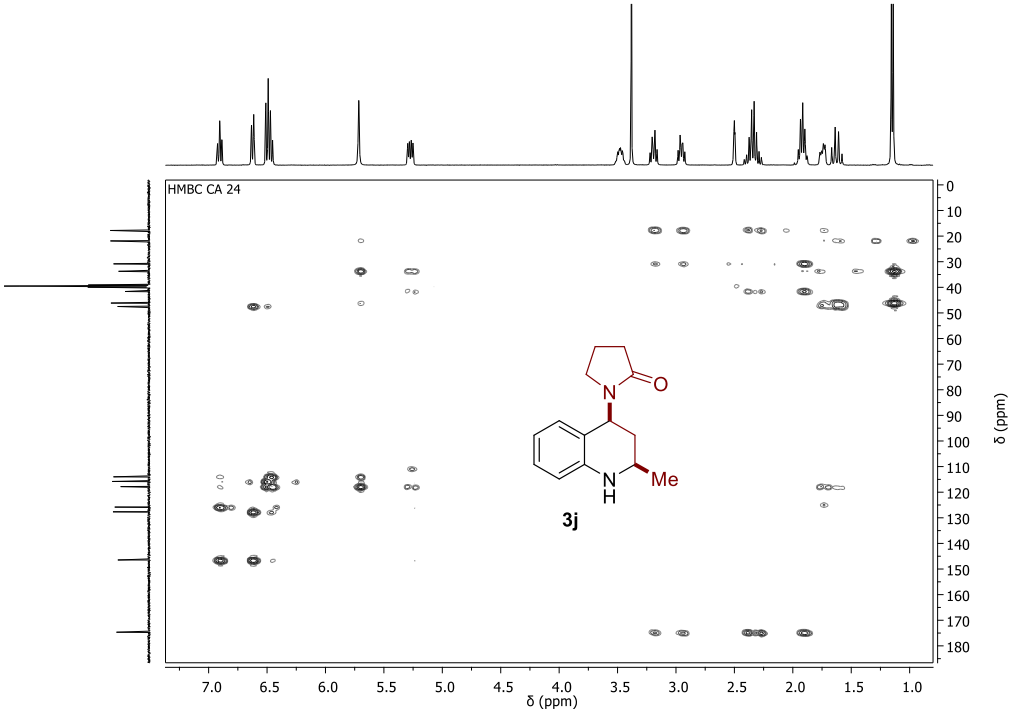


Figure ESI 53. ^{1}H-NMR spectrum of *cis*-6-Methoxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3k**.

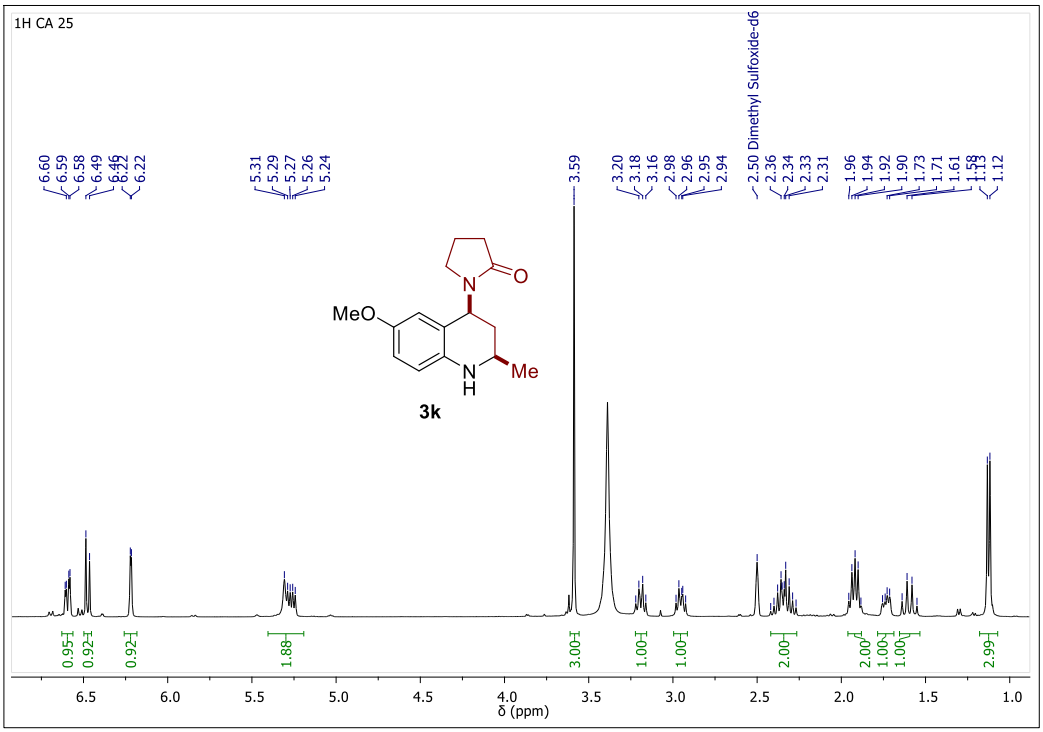


Figure ESI 54. ^{13}C-NMR spectrum of *cis*-6-Methoxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3k**.

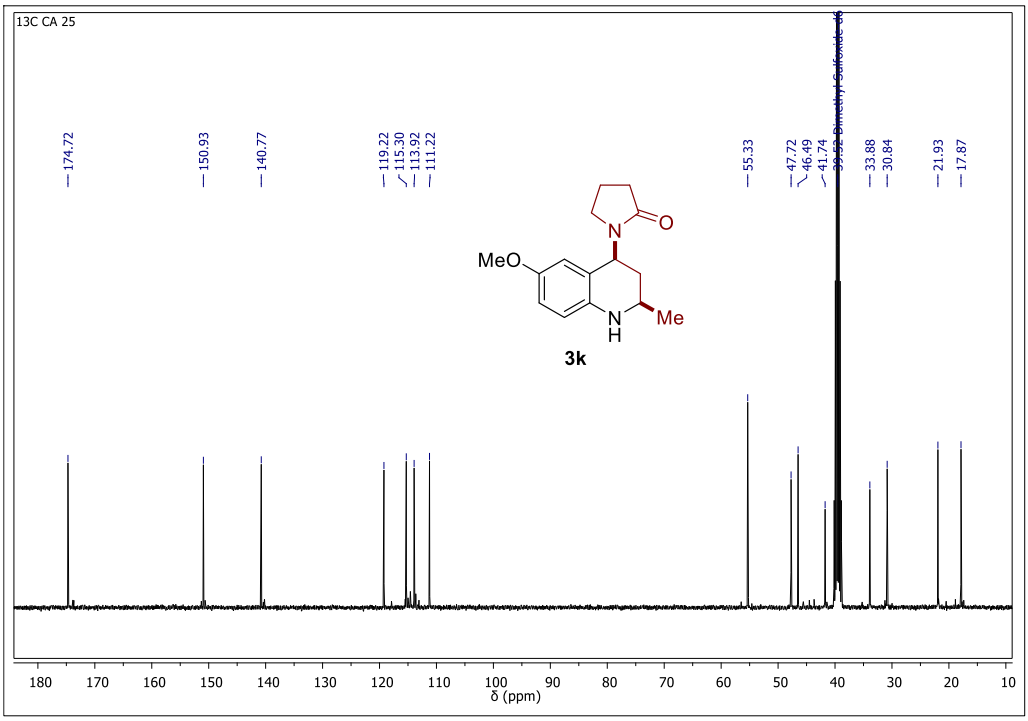


Figure ESI 55. DEPT-135 spectrum of *cis*-6-Methoxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3k**.

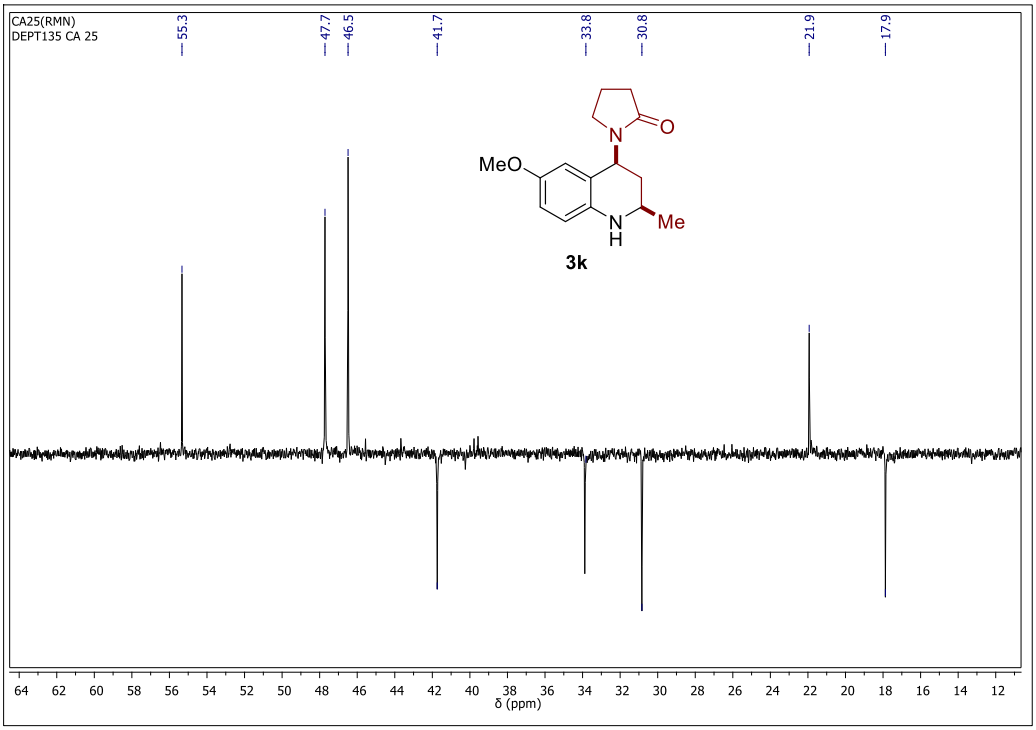


Figure ESI 56. COSY spectrum of *cis*-6-Methoxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3k**.

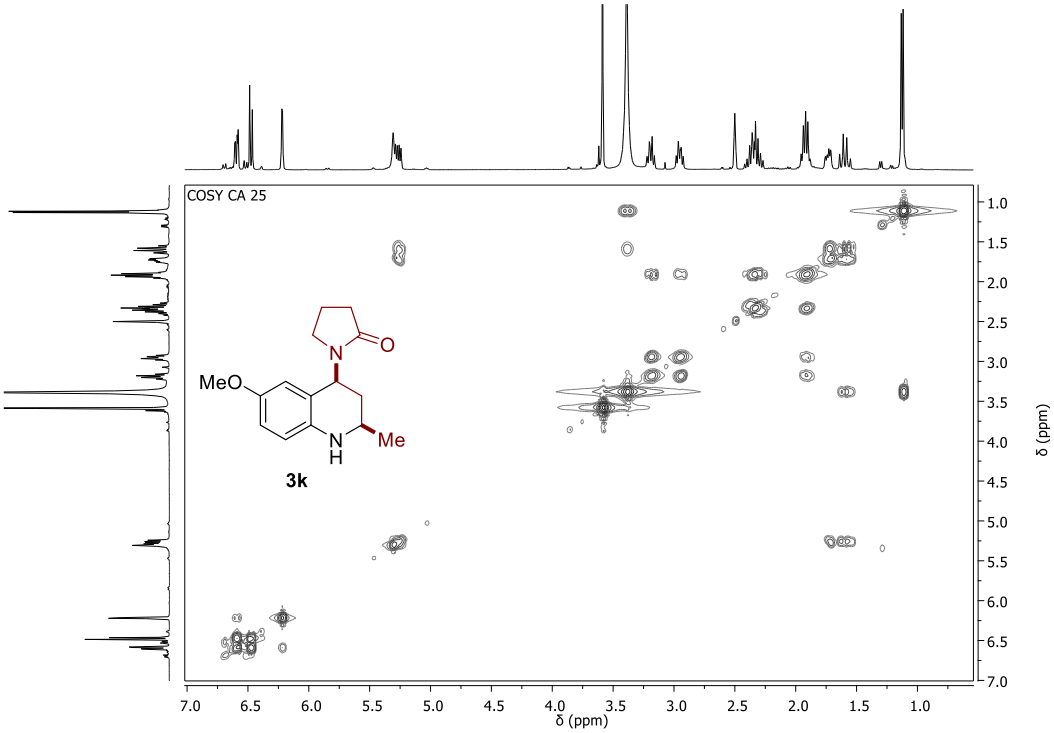


Figure ESI 57. HSQC spectrum of *cis*-6-Methoxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3k**.

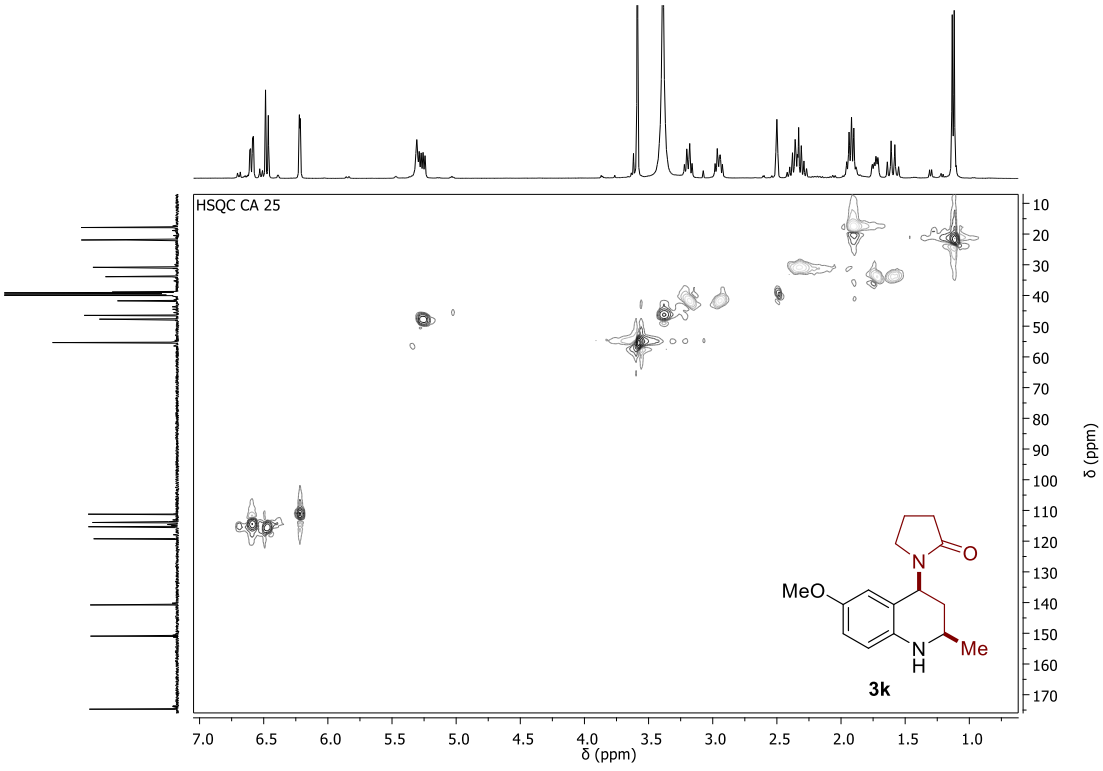


Figure ESI 58. HMBC spectrum of *cis*-6-Methoxy-4-(pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3k**.

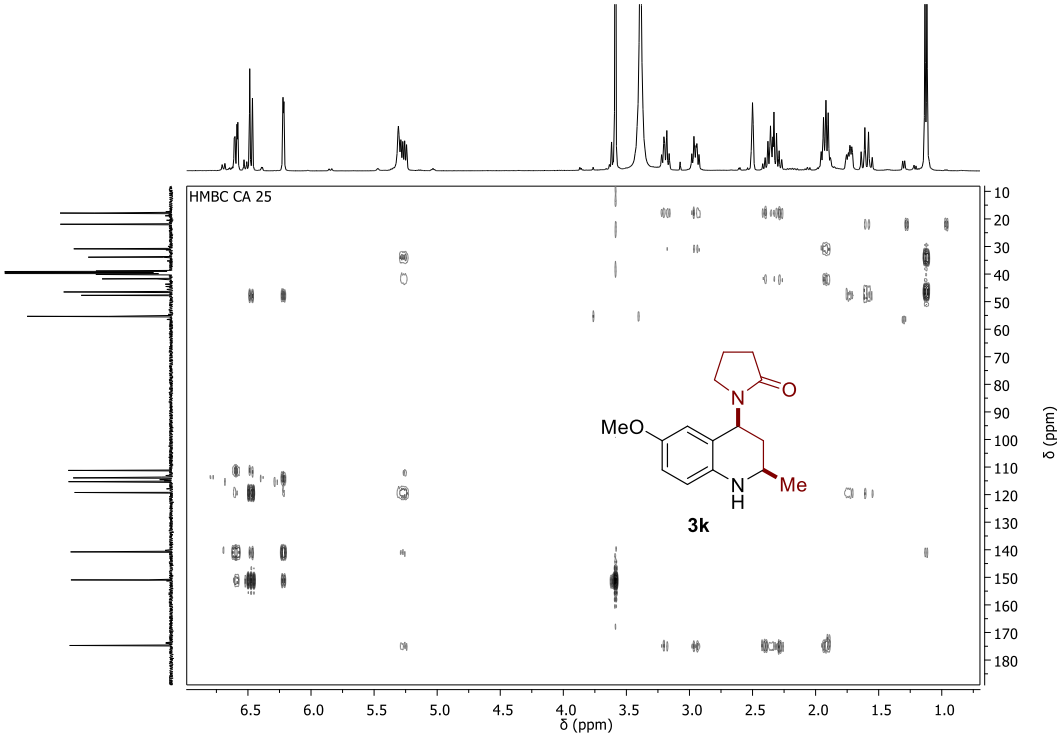


Figure ESI 59. ^{1}H-NMR spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3l**.

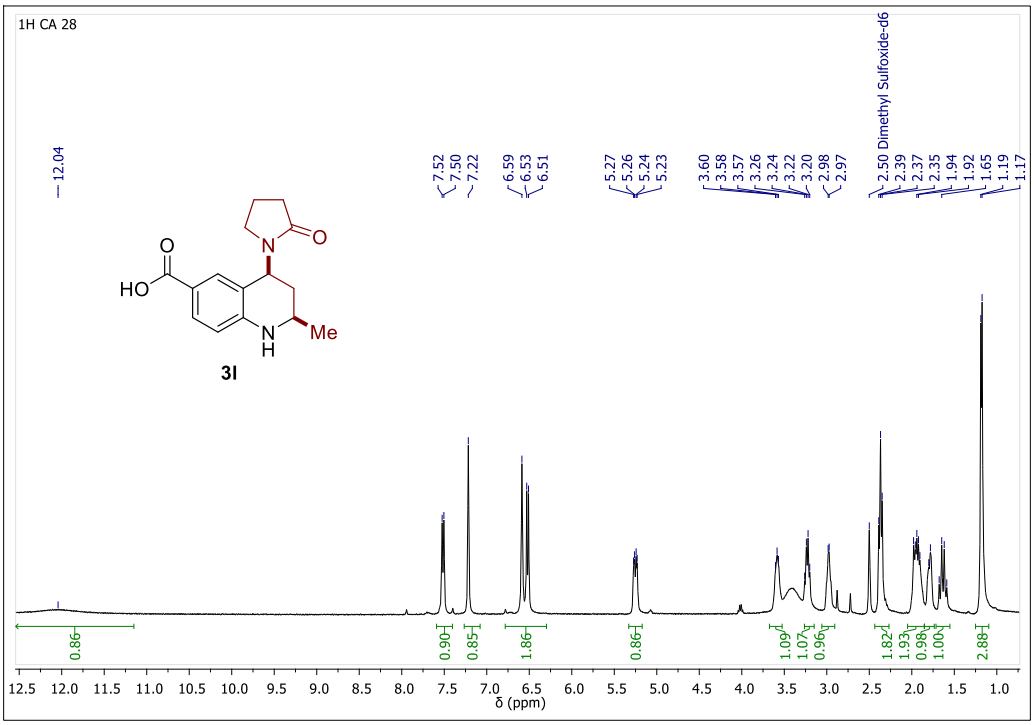


Figure ESI 60. ^{13}C-NMR spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3l**.

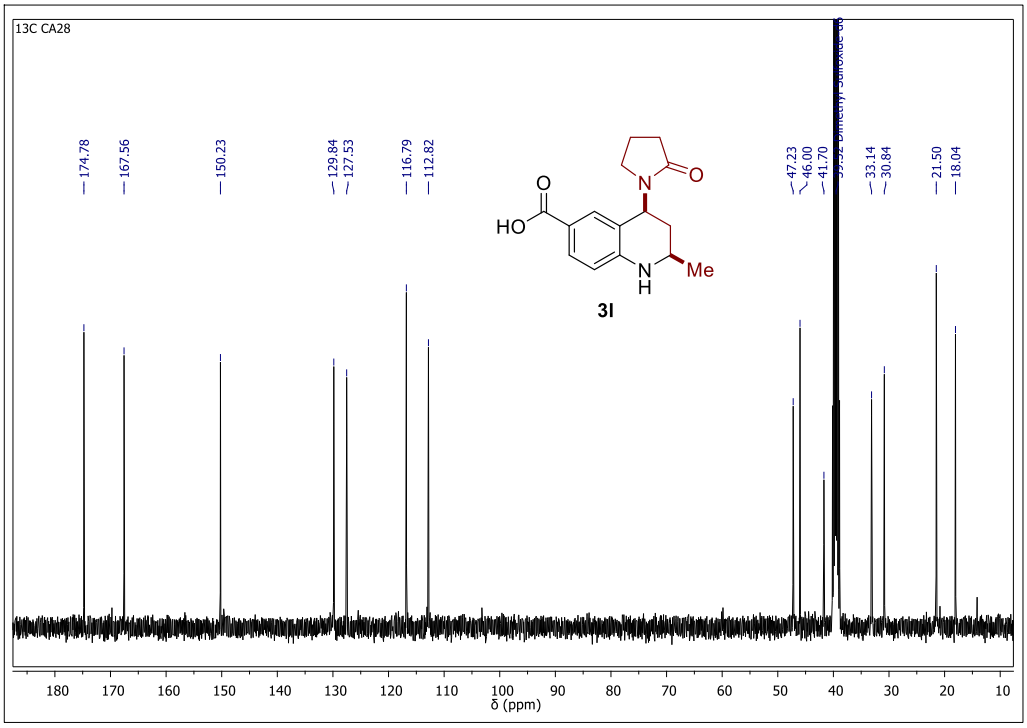


Figure ESI 61. DEPT-135 spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3l**.

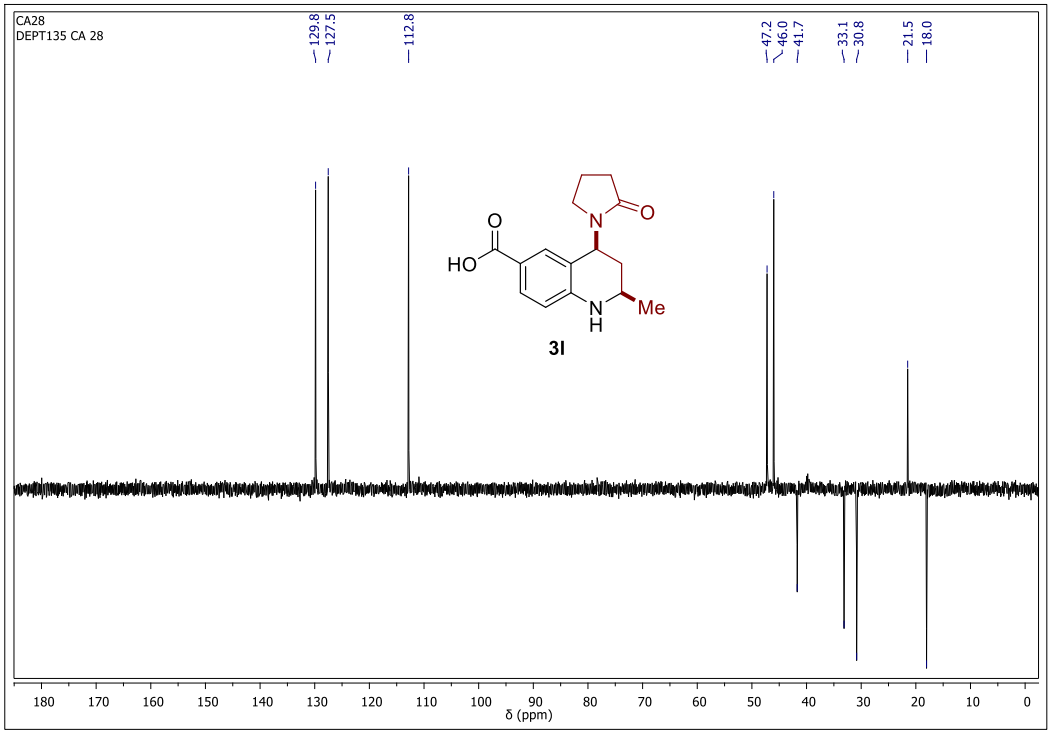


Figure ESI 62. COSY spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3l**.

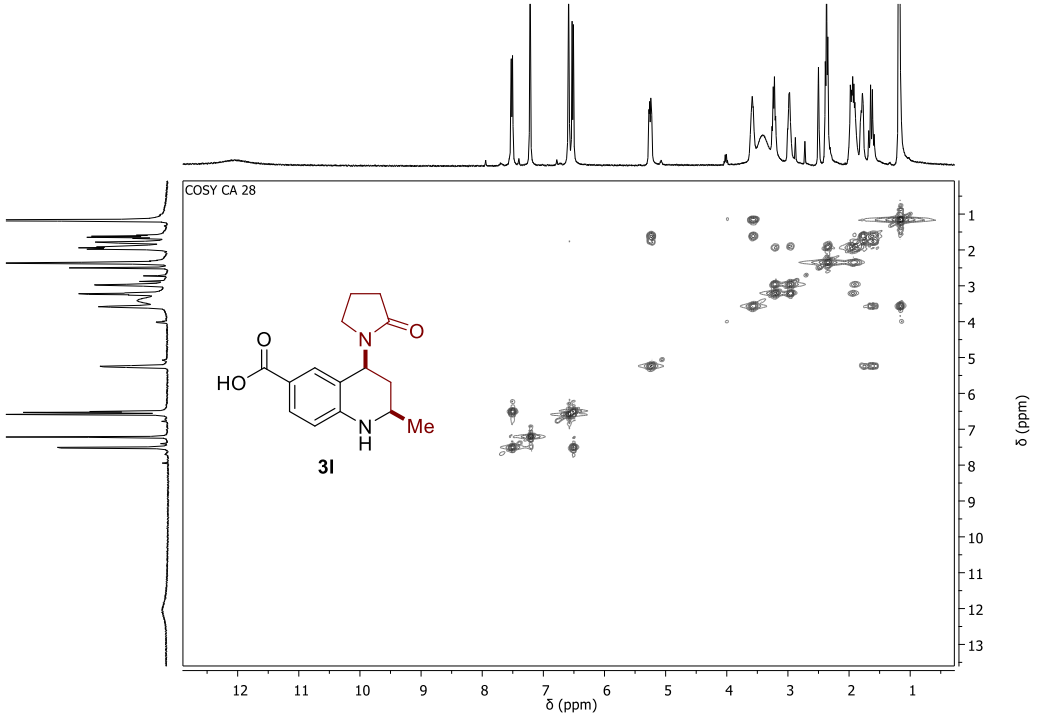


Figure ESI 63. HSQC spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3l**.

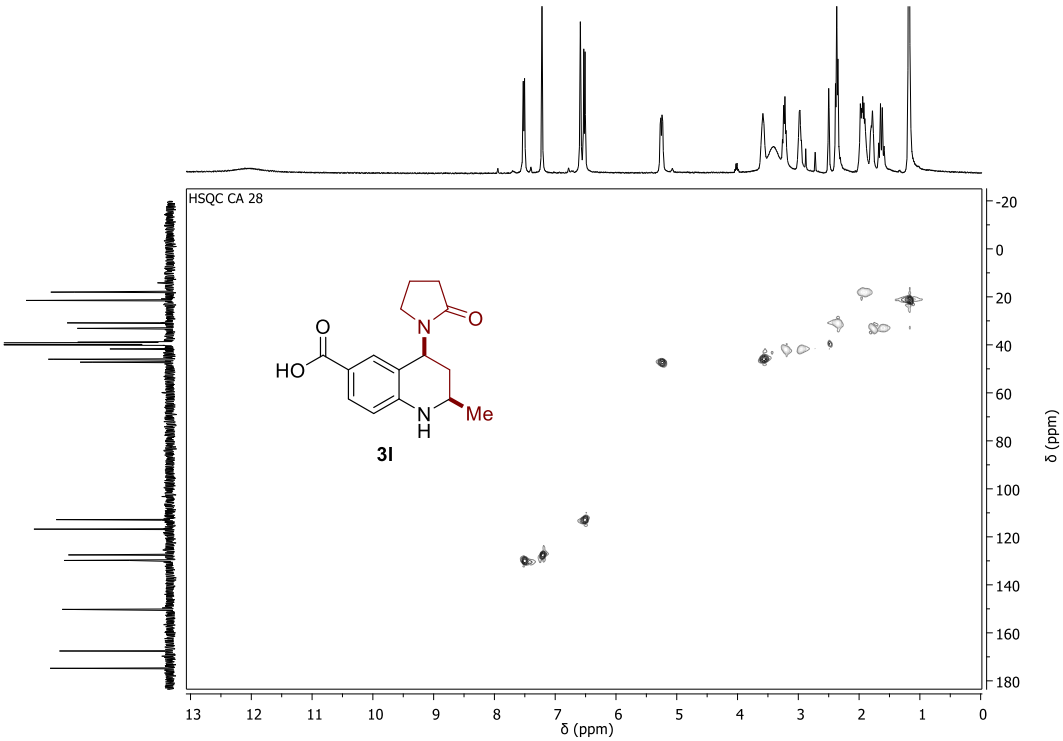
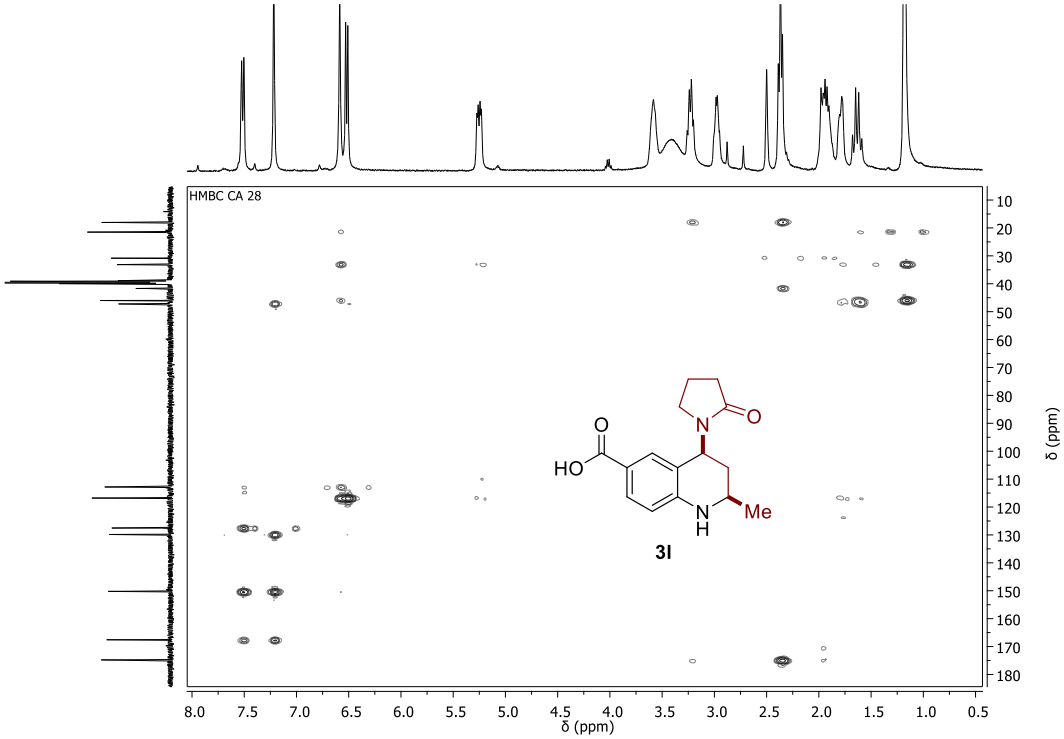
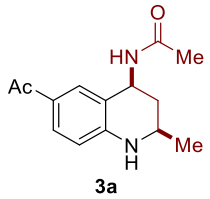
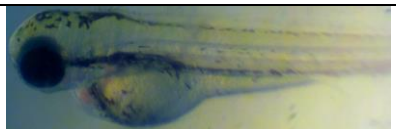
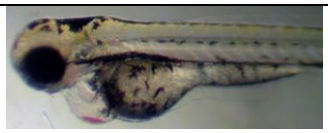
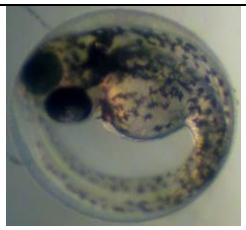
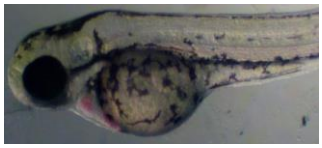
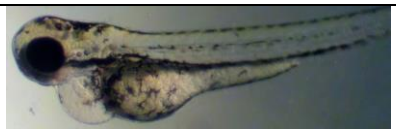
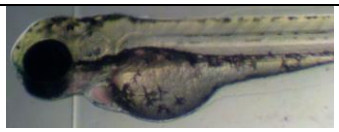
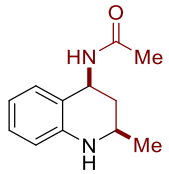
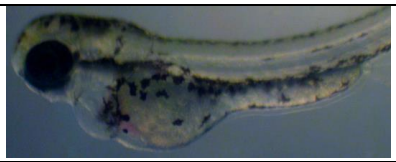
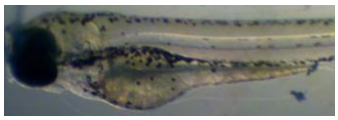


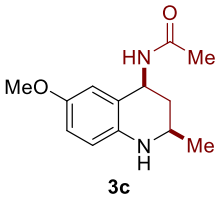
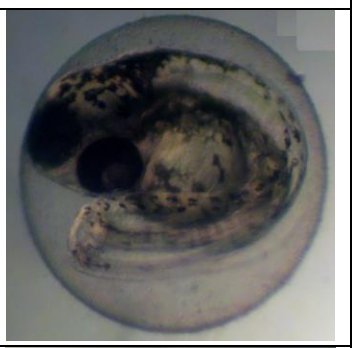
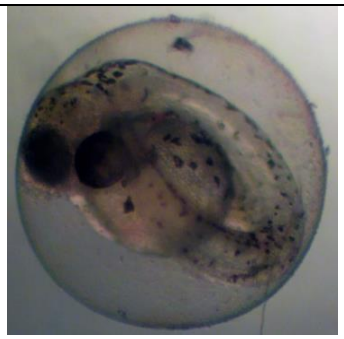
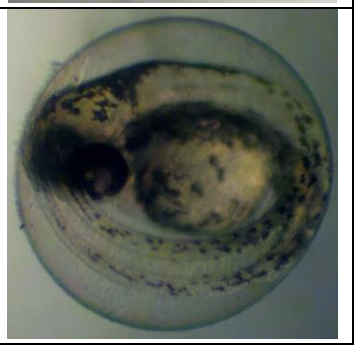
Figure ESI 64. HMBC spectrum of *cis*-4-(Pyrrolidinyl-2-one)-2-methyl-1,2,3,4-tetrahydroquinoline **3l**.

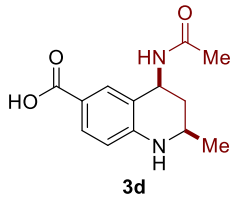
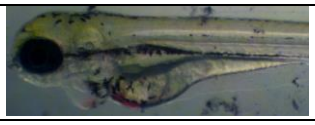
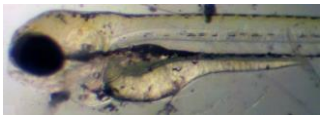
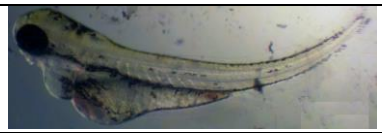
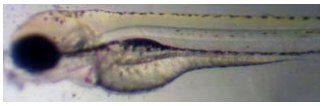


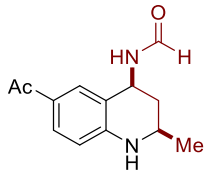
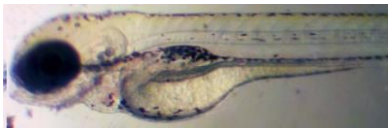
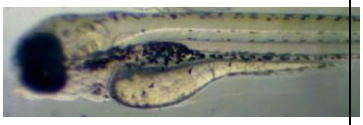
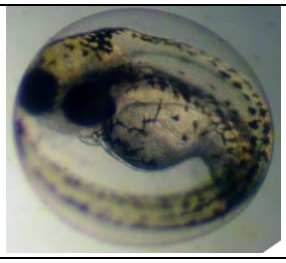
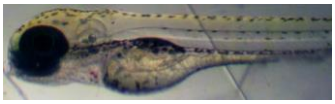
4. Photographic records of the phenotypic changes during the development of the zebrafish embryo tretated with compounds 3a-l after 96 hpf.

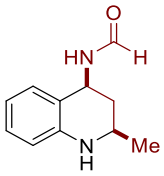
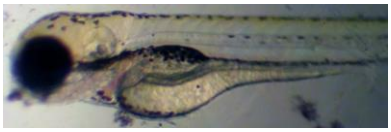
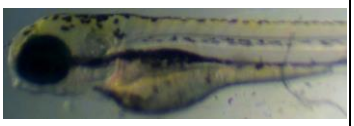
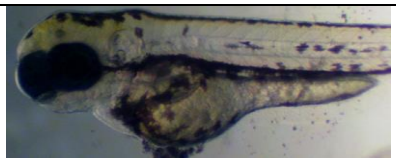
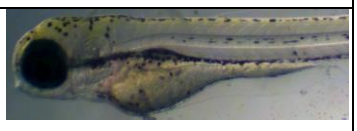
Compound	Concentration in µM (96 hpf)			
 **3a**	**Control**		**75**	
	150		**50**	
LC_{50} (µmol/L ± SEM) 351.2 ± 5.7	**100**		**25**	

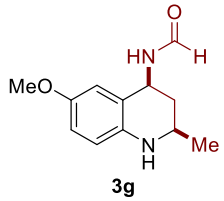
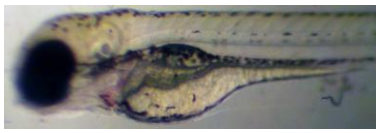
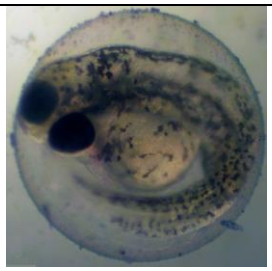
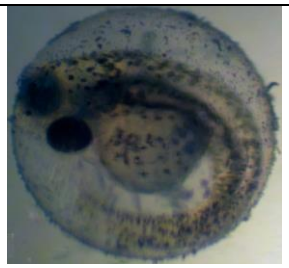
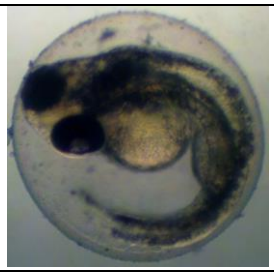
Compound	**Concentration in µM (96 hpf)**			
 **3b**	**Control**		**100**	
LC_{50} (µmol/L ± SEM) 223.8 ± 7.1	**150**		**50**	

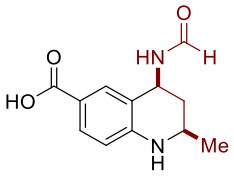
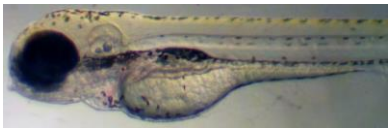
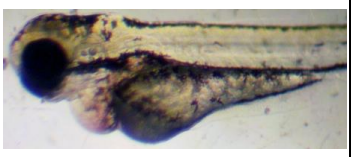
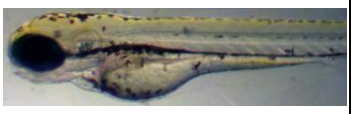
Compound	**Concentration in µM (96 hpf)**			
 **3c**	**Control**		**75**	
LC_{50} (µmol/L ± SEM) 400.4 ± 7.2	**200**		**50**	

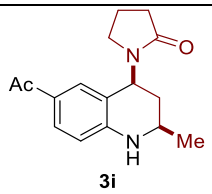
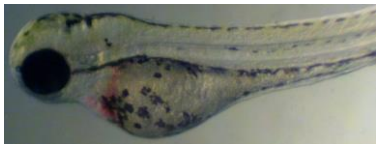
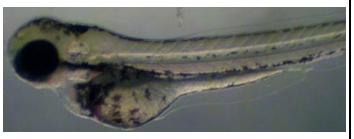
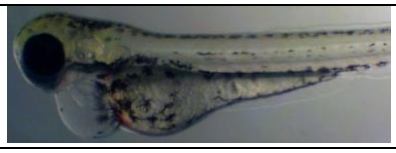
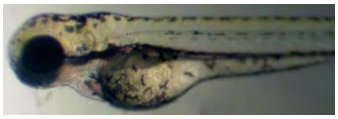
Compound	Concentration in µM (96 hpf)			
 3d	Control		200	
	400		125	
LC_{50} (µmol/L ± SEM) 429.7 ± 0.3	250		62	

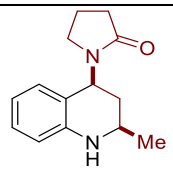
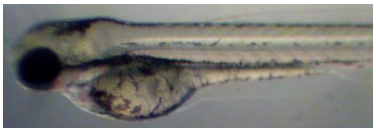
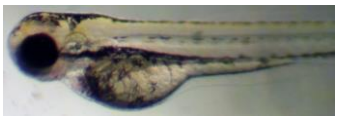
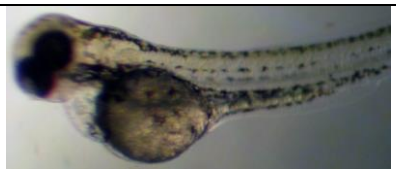
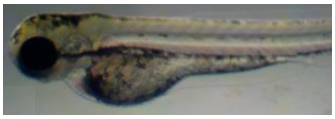
Compound	Concentration in µM (96 hpf)			
 3e	Control		100	
LC_{50} (µmol/L ± SEM) 429.3 ± 0.4	125		31	

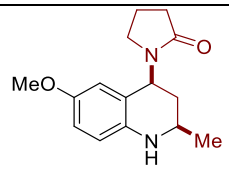
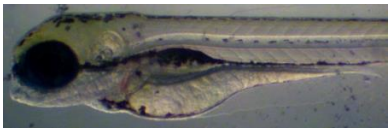
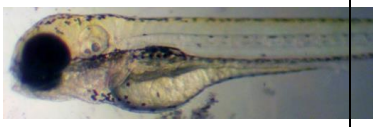
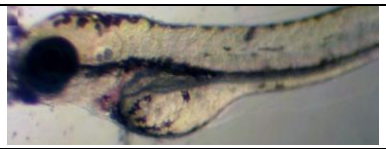
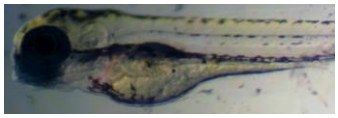
Compound	Concentration in µM (96 hpf)			
 3f	Control		100	
LC_{50} (µmol/L ± SEM) 216.0 ± 7.1	150		75	

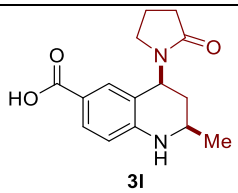
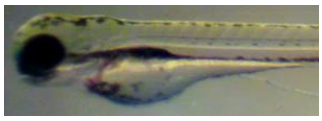
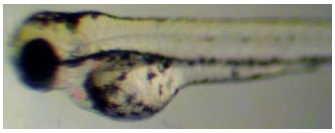
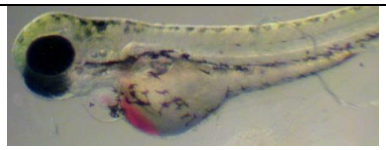
Compound	Concentration in µM (96 hpf)			
 3g	Control		200	
LC_{50} (µmol/L ± SEM) 435.9 ± 3.7	250		125	

Compound	Concentration in µM (96 hpf)			
 3h	Control		200	
LC_{50} (µmol/L ± SEM) 449.2 ± 10.2	250		125	

Compound	Concentration in µM (96 hpf)			
 3i	Control		75	
LC_{50} (µmol/L ± SEM) 426.3 ± 7.0	100		50	

Compound	Concentration in µM (96 hpf)			
 3j	Control		100	
LC_{50} (µmol/L ± SEM) 330.7 ± 13.7	200		75	

Compound	Concentration in µM (96 hpf)			
 3k	Control		18	
LC_{50} (µmol/L ± SEM) 94.9 ± 3.7	25		10	

Compound	Concentration in µM (96 hpf)			
 3l	Control		150	
LC_{50} (µmol/L ± SEM) 358.4 ± 9.0	200		100