Unique Regioselectivity in the C(sp^3)–H α-Alkylation of Amines: The Benzoxazole Moiety as a Removable Directing Group

Günther Lahm and Till Opatz*

Institute of Organic Chemistry, Johannes Gutenberg-University, Duesbergweg 10–14, 55128 Mainz, Germany

Email: opatz@uni-mainz.de

Supporting Information

General Methods

Reaction conditions
All reactions requiring anhydrous conditions were performed in dried glassware under argon atmosphere.

Solvents and reagents
All reagents and solvents were obtained from commercial suppliers without further purification. Anhydrous DME was distilled from potassium / benzophenone under argon.

Melting points
Melting points were determined in open capillary tubes with a KRÜSS OPTRONIC KSP 1N apparatus.

NMR spectra
NMR spectra were recorded with a Bruker AC 300 (300 MHz ^{1}H and 75.5 MHz ^{13}C), a Bruker ARX 400 or Avance-II 400 (400 MHz ^{1}H and 100.6 MHz ^{13}C) and with a Bruker Avance-III 600 (600 MHz ^{1}H and 151 MHz ^{13}C). Deuterated solvents were used as internal standard. The δ values are reported in parts per million (ppm) downfield from TMS and were referenced to the residual solvent signal ($CDCl_3$, D_2O, DMSO-d_6)[1] Coupling constants *J* are given in Hertz (Hz).

Infrared spectra
IR spectra were recorded on a Tensor 27 or on a Vector 22 (both Bruker) FTIR-spectrometer using a diamond ATR and are reported in terms of frequency of absorption (ν, cm^{-1}).

Mass spectra
ESI-HRMS spectra were recorded on a Q-TOF Ultima-III spectrometer (Waters) with a dual source and a suitable external calibrant.

Thin-layer chromatography
Thin-layer chromatography was carried out on 0.2-mm silica gel plates (F-254 Merck). They were detected by UV light (254 and 360 nm).

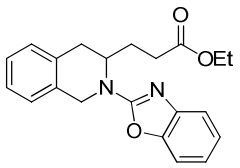
Preparative thin-layer chromatography
Preparative thin-layer chromatography was performed on silica gel plates (SIL G-200 UV_{254} Macherey-Nagel).

Experimental procedures and spectroscopic data

General experimental procedure for C(sp^3)–H alkylation:

N-(Benzoxazol-2-yl)amine (1 equiv) and catalyst ([Ir(cod)$_2$]BARF or [Ir(cod)$_2$]BF$_4$, 7 mol %) were placed in a microwave reaction vessel (10 mL) with a septum (conditions A) or in an oven-dried Schlenk tube (conditions B). The vial was evacuated and flushed with argon (three times). To the reaction vessel were added dry and degassed dimethoxyethane (0.2 M) and olefin (8 equiv). The sealed reaction vessel was heated either under microwave irradiation to 140 °C for 1–2 h (300 W, conditions A) or in an oil bath to 85 °C for 4–48 h (conditions B). After cooling to room temperature, the volatiles were removed under reduced pressure. The resulting crude product was purified by preparative TLC unless noted otherwise

Ethyl 3-[2-(1,3-benzoxazol-2-yl)-1,2,3,4-tetrahydroisoquinolin-3-yl]propanoate (2a)



Reaction conditions **B** were applied using benzoxazole **1** (23.0 mg, 0.092 mmol), ethylacrylate (80.4 ul, 0.74 mmol, 8.0 equiv) and [Ir(cod)$_2$]BF$_4$ (7 mol %). After 48 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 8/1) afforded the title compound (27.1 mg, 84%) as a colourless amorphous solid.

R$_f$= 0.20 (cyclohexane/AcOEt = 8/1)

IR (ATR): 3061 (w), 2979 (w), 2842 (w), 1731 (m), 1633 (s), 1572 (s), 1459 (m), 1244 (s).

^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ = 7.41–7.37 (m, 1H, Ar-H), 7.30–7.26 (m, 1H, Ar-H), 7.25–7.13 (m, 5H, Ar-H), 7.04 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 5.10 (d, *J* = 16.9 Hz, 1H, H$_a$-1'), 4.85–4.74 (m, 1H, H-3'), 4.58 (d, *J* = 16.9 Hz, 1H, H$_b$-1'), 4.10–3.98 (m, 2H, CH_2-ethyl), 3.28 (dd, *J* = 16.0, 5.8 Hz, 1H, H$_a$-4'), 2.79 (dd, *J* = 16.0, 1.9 Hz, 1H, H$_b$-1'), 2.44–2.30 (m, 2H, H-2), 2.01–1.9 (m, 1H, H-3), 1.89–1.78 (m, 1H), 1.13 (t, *J* = 7.1 Hz, 3H, CH_3-ethyl).

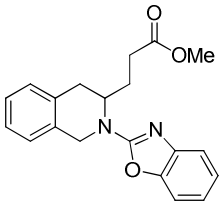
^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 173.0 (C1), 161.8 (C=N), 148.6, 142.4, 132.0, 131.4 (4 x C_q), 129.6, 127.2, 126.8, 126.3, 124.3, 120.9, 116.3, 108.9 (8 x Ar-C), 60.7 (CH_2-ethyl), 51.3 (C3'), 44.2 (C1'), 33.1 (C4'), 31.2 (C2), 27.2 (C3), 14.2 (CH_3-ethyl).

161.8, 142.4 out of HMBC

ESI-MS: *m/z* (%) = 351.2 (100) $[M+H]^+$

ESI-HRMS: calcd for $[C_{21}H_{22}N_2O_3Na]^+$: *m/z* = 373.1528, found: 373.1523

Methyl 3-[2-(1,3-benzoxazol-2-yl)-1,2,3,4-tetrahydroisoquinolin-3-yl]propanoate (2b)



Reaction conditions **B** were applied using benzoxazole **1** (74.3 mg, 0.30 mmol), methylacrylate (222 µl, 2.4 mmol, 8.0 equiv) and [Ir(cod)$_2$]BF$_4$ (7 mol %). After 48 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 8/2) afforded the title compound (77.6 mg, 78%) as a colourless amorphous solid.

R$_f$= 0.19 (cyclohexane/AcOEt = 8/2)

IR (ATR): 2981 (w), 2928 (w), 2854 (w), 1734 (m), 1637 (s), 1576 (s), 1460 (m), 1241 (br, sh).

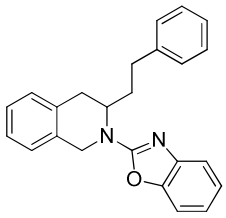
^{1}H NMR, COSY (300 MHz, $CDCl_3$): *δ* = 7.41–736 (m, 1H, Ar-H), 7.31–7.13 (m, 6H, 6 x Ar-H), 7.03 (pseudo-td, *J* = 7.7, 1.3 Hz, Ar-H), 5.09 (d, *J* = 16.8 Hz, 1H, H$_a$-1'), 4.84–473 (m, 1H, H-3'), 4.57 (d, *J* = 16.8 Hz, 1H, H$_b$-1'), 3.58 (s, 3H, OMe), 3.28 (dd, *J* = 16.0, 5.8 Hz, 1H, H$_a$-4'), 2.79 (dd, *J* = 16.0, 2.0 Hz, 1H, H$_b$-4'), 2.43–2.33 (m, 2H, H-2), 2.07–1.72 (m, 2H, H-3).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 173.4 (C1), 162.0 (C=N), 148.7, 143.1, 132.0, 131.5 (4 x C_q), 129.6, 127.2, 126.7, 126.3, 124.2, 120.8, 116.4, 108.9 (8 x Ar-C), 51.8 (OCH_3), 51.2 (C3'), 44.2 (C1'), 33.1 (C4'), 31.0 (C2), 27.2 (C3).

ESI-MS: *m/z* (%)= 337.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{20}H_{20}N_2O_3Na]^+$: *m/z* = 359.1372, found: 359.1369

2-(1,3-Benzoxazol-2-yl)-3-(2-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (2c)



Reaction conditions **A** were applied using benzoxazole **1** (89.5 mg, 0.36 mmol), styrene (328.5 ul, 2.9 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 8/2) afforded the title compound (102.4 mg, 81%) as a colourless amorphous solid.

R_f= 0.53 (cyclohexane/AcOEt = 8/2)

IR (ATR): 3026 (w), 2931 (w), 2855 (w), 1628 (s), 1566 (s), 1458 (s), 1245 (s), 739 (s, sh).

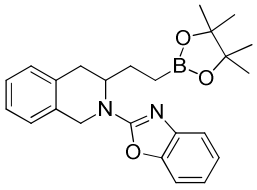
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.43–7.37(m, 1H, Ar-H), 7.30–7.25 (m, 1H, Ar-H), 7.25–7.08 (m, 10H, Ar-H), 7.04 (pseudo-td, *J* = 7.7, 1.3 Hz, 1H, Ar-H), 5.12 (d, *J* = 16.9 Hz, 1H, H_a-1), 4.82–4.72 (m, 1H, H-3), 4.58 (d, *J* = 16.9 Hz, 1H, H_b-1), 3.27 (dd, *J* = 16.0, 5.7 Hz, 1H, H_a-4), 2.81 (dd, *J* = 16.0, 2.0 Hz, 1H, H_b-4), 2.75–2.61 (m, 2H, H-2'), 2.07–1.91 (m, 1H, H_a-1'), 1.89–1.69 (m, 1H, H_b-1').

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.2 (C=N), 148.8, 143.3, 141.3, 132.3, 131.7 (5 x C_q), 129.6, 128.5 (4 x), 127.1, 126.6, 126.2, 126.1, 124.2, 120.6, 116.3, 108.9 (13 x Ar-C), 51.7 (C3), 44.2 (C1), 33.6 (C1'), 33.0, 32.8.

ESI-MS: *m/z* (%) = 355.2 (100) $[M+H]^+$

ESI-HRMS: calcd for $[C_{24}H_{23}N_2O]^+$: *m/z* = 355.1810, found: 355.1819

2-(1,3-Benzoxazol-2-yl)-3-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-1,2,3,4-tetrahydroisoquinoline (2d)



Reaction conditions **A** were applied using benzoxazole **1** (26.0 mg, 0.10 mmol), 2-vinylboronic acid pinacolester (141 µl, 0.83 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by HPLC (ACE 5 C18, 125 x 21.2 mm, isocratic: water/acetonitrile (50/50), 30 mL/min, 18.2 min) afforded the title compound (25.6 mg, 61%) as a colourless amorphous solid.

R_f= 0.64 (cyclohexane/AcOEt = 7/3)

IR (ATR): 2977 (w), 2932 (w), 2854 (w), 1633 (s), 1573 (s), 1460 (m), 1354 (m), 1261 (m).

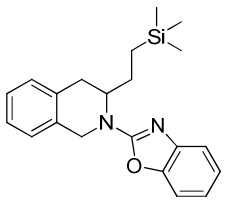
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.39–7.33 (m, 1H, Ar-H), 7.28–7.12 (m, 6H, Ar-H), 7.00 (pseudo-td, *J* = 7.7, 1.3 Hz, 1H, Ar-H), 5.08 (d, *J* = 16.8 Hz, 1H, H_a-1), 4.70–4.60 (m, 1H, H-3), 4.56 (d, *J* = 16.8 Hz, 1H, H_b-1), 3.23 (dd, *J* = 16.1, 5.9 Hz, 1H, H_a-4), 2.82 (dd, *J* = 16.1, 1.9 Hz, 1H, H_b-4), 1.87–1.46 (m, 2H, H-1'), 1.20 (s, 12H, 4 x CH_3), 0.82 (ddd, *J* = 10.0, 6.4, 3.4 Hz, 2H, H-2').

^{13}C NMR, HMBC, HSQC (75 MHz, CDCl3): δ = 162.4 (C=N), 148.8, 143.5, 132.5, 131.9, (4 x Cq), 129.7, 126.9, 126.4, 126.2, 124.0,120.4, 116.2, 108.8, (8 x Ar-C), 83.3 (2 x $OC(CH_3)_2$, 53.7 (C3), 44.1 (C1), 32.4 (C4), 26.1 (C1'), 25.0, 24.9 (4 x CH_3). Carbon C2' is missing

ESI-MS: *m/z* (%)= 405.3 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C24H30BN_2O3]^+$: *m/z* =405.2349, found: 405.2361

2-(1,3-Benzoxazol-2-yl)-3-[2-(trimethylsilyl)ethyl]-1,2,3,4-tetrahydroisoquinoline (2e)



Reaction conditions **B** were applied using benzoxazole **1** (34.0 mg, 0.14 mmol), vinyltrimethylsilane (171 µl, 1.1 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 12 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound (19.6 mg, 41%) as a colourless amorph solid.

R_f = 0.79 (cyclohexane/AcOEt = 7/3)

IR (ATR): 3069 (w), 2952 (m), 2925 (w), 1694 (m), 1634 (s), 1572 (s, sh), 1459 (s), 1244 (s).

^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.41–7.36 (m, 1H, Ar-H), 7.32–7.13 (m, 6H, Ar-H), 7.02 (pseudo-td, *J* = 7.7, 1.3 Hz, 1H, Ar-H), 5.10 (d, *J* = 16.8 Hz, 1H, H_a-1), 4.65–4.54 (m, 1H, H-3), 4.52 (d, *J* = 16.8 Hz, 1H, H_b-1), 3.24 (dd, *J* = 16.1, 5.8 Hz, 1H, H_a-4), 2.84 (dd, *J* = 16.2, 1.9 Hz, 1H, H_b-4), 1.69–1.34 (m, 2H, H-1'), 0.61–0.43 (m, 2H, H-2'), –0.09 (s, 9H, 3 x CH_3).

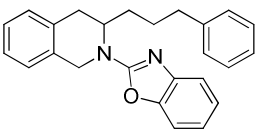
^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.4 (C=N), 148.7, 143.1, 132.5, 131.9, (4 x Cq), 129.6, 127.0, 126.5, 126.2, 124.1, 120.5, 116.2, 108.8, (8 x Ar-C), 54.5 (C3), 44.1 (C1), 32.3 (C4), 26.1 (C1'), 13.1 (C2'), –1.7 (3 x CH_3).

143.1 out of HMBC

ESI-MS: *m/z* (%)= 351.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{21}H_{27}N_2OSi]^+$: *m/z* = 351.1893, found: 351.1897

2-(4,5-Dihydro-1,3-benzoxazol-2-yl)-3-(3-phenylpropyl)-1,2,3,4-tetrahydroisoquinoline (2f)



Reaction conditions **A** were applied using benzoxazole **1** (38.3 mg, 0.15 mmol), allylbenzene (162 µl, 1.2 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 1 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound (43.9 mg, 78%) as pale brown oil.

R_f = 0.71 (cyclohexane/AcOEt = 7/3)

IR (ATR): 3025 (w), 2934 (w), 2857 (w), 1634 (s), 1572 (s), 1459 (s), 1245 (s), 740 (s, sh).

^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ = 7.41–7.36 (m, 1H, Ar-H), 7.31–7.26 (m, 1H, Ar-H), 7.26–7.09 (m, 10 H, Ar-H), 7.03 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 5.09 (d, *J* = 16.8 Hz, 1H, H_a-1), 4.79–4.69 (m, 1H, H-3), 4.53 (d, *J* = 16.8 Hz, 1H, H_b-1), 3.25 (dd, *J* = 16.0, 5.8 Hz, 1H, H-3'), 2.77 (dd, *J* = 16.0, 1.9 Hz, 1H, H_b-4), 2.65–2.54 (m, 2H, H-3'), 1.77–1.62 (m, 3H, H-2', H_a-1'), 1.57–1.45 (m, 1H, H_b-1').

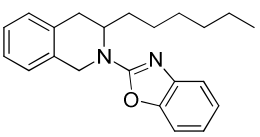
^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 162.1 (C=N), 148.7, 143.1, 142.1, 132.4, 131.8 (5 x C_q), 129.6, 128.5 (2x), 128.5 (2 x), 127.1, 126.6, 126.2, 126.0, 124.2, 120.6, 116.3, 108.9 (13 x Ar-C), 51.7 (C3), 44.1 (C1), 35.7 (C3'), 32.8 (C4), 31.2 (C1'), 28.1 (C2').

HMBC 143.1 out of HMBC

ESI-MS: *m/z* (%) = 369.2 (100) $[M+H]^+$

ESI-HRMS: calcd for $[C_{25}H_{25}N_2O]^+$: *m/z* = 369.1967, found: 369.1979

2-(4,5-Dihydro-1,3-benzoxazol-2-yl)-3-hexyl-1,2,3,4-tetrahydroisoquinoline (2g)



Reaction conditions **A** were applied using benzoxazole **1** (61.0 mg, 0.24 mmol), hex-1-ene (256 µl, 2.0 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound

(67.7 mg, 83%) as pale yellow oil.

R_f= 0.81 (cyclohexane/AcOEt = 7/3)

IR (ATR): 3069 (w), 2955 (m), 2855 (w), 1634 (s), 1572 (s), 1460 (m), 1245 (s), 754 (m, sh).

^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.41–7.36 (m, 1H, Ar-H), 7.31–7.26 (m, 1H, Ar-H), 7.25–7.12 (m, 5H, Ar-H), 7.02 (pseudo-td, *J* = 7.7, 1.3 Hz, 1H, Ar-H), 5.09 (d, *J* = 16.8 Hz, 1H, H_a-1), 4.76–7.64 (m, 1H, H-3), 4.55 (d, *J* = 16.8 Hz, 1H, H_b-1), 3.24 (dd, *J* = 16.0, 5.8 Hz, 1H, H_a-4), 2.79 (dd, *J* = 16.0, 1.9 Hz, 1H, H_b-4), 1.75–1.53 (m, 1H, CH_2), 1.53–1.10 (m, 9 H, CH_2), 0.92–0.71 (m, 3H, CH_3).

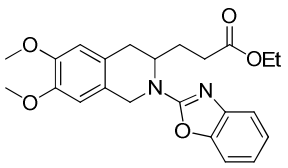
^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.09 (C=N), 148.6, 143.2, 132.4, 131.7 (4 x C_q), 129.5, 126.9, 126.4, 126.1, 124.0, 120.4, 116.1, 108.7 (8 x Ar-C), 51.7 (C3), 44.0 (C1), 32.6 (C4), 31.7, 31.5, 29.1, 26.2, 22.6 (5 x CH_2), 14.0 (CH_3).

ESI-MS: *m/z* (%) = 335.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{22}H_{27}N_2O]^+$: *m/z* = 335.2123, found: 335.2124

Ethyl 3-[2-(1,3-benzoxazol-2-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-3-yl]propanoate (4a)

Reaction conditions **A** were applied using benzoxazole **3** (39.1 mg, 0.13 mmol), ethylacrylate (110 µl, 1.0 mmol, 8.0 equiv) and $[Ir(cod)_2]$BARF (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound (32.6 mg, 63%) as a colourless amorphous solid.



R_f= 0.25 (cyclohexane/AcOEt = 7/3)

IR (ATR): 2978 (w, sh), 2907 (w, sh), 2836 (w), 1730 (m), 1632 (s), 1573 (s), 1518 (s), 1460 (s), 1283 (s, sh).

^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.41–7.37 (m, 1H, Ar-H), 7.31–7.25 (m, 1H, Ar-H), 7.19 (pseud-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 7.04 (pseudo-td, *J* = 7.7, 1.3 Hz, 1H, Ar-H), 6.68 (s, 1H, H-8'), 6.65 (s, 1H, H-5'), 5.05 (d, *J* = 16.5 Hz, 1H, H-1'), 4.84–4.74 (m, 1H, H-3'), 4.50 (d, *J* = 16.5 Hz, 1H, H-1'), 4.14–4.03 (m, 2H, CH_2-ethyl), 3.89 (s, 6H, 2 x OCH_3), 3.25 (dd, *J* = 16.0, 5.9 Hz, 1H, H_a-4'), 2.70 (dd, *J* = 16.0, 1.7 Hz, 1H, H_b-4'), 2.46–2.32 (m, 2H, H-2), 2.09–1.78 (m, 2H, H-3), 1.16 (t, *J* = 7.2 Hz, 3H, CH_3-ethyl).

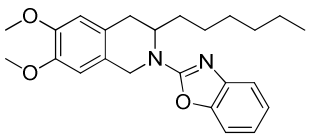
^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 173.0 (C1), 162.2 (C=N), 148.7, 148.2, 148.0, 143.3, (4 x C_q), 124.2, 123.8, 123.1, 120.7, 116.4 (5 x Ar-C), 112.2 (C5'), 109.0, (C8'), 108.8 (Ar-C), 60.7 (CH_2-ethyl), 56.1 (2 x OCH_3), 51.2 (C3'), 43.7 (C1'), 32.6 (C4'), 31.3 (C2), 27.0 (C3), 14.2 (CH_3-ethyl).

ESI-MS: *m/z* (%) = 411.3 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{23}H_{27}N_2O_5]^+$: *m/z* = 411.1920, found: 411.1917

2-(1,3-Benzoxazol-2-yl)-3-hexyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4b)

Reaction conditions **A** were applied using benzoxazole **3** (45.9 mg, 0.15 mmol), hex-1-ene (156 µl, 1.2 mmol, 8.0 equiv) and $[Ir(cod)_2]$BARF (7 mol %). After 2 h, purification by HPLC (ACE 5 C18, 125 x 21.2 mm, gradient: 50 % water/acetonitrile for 10 min, → 100% acetonitrile in 10 min 30 mL/min, 14.4 min) afforded the title compound (27.4 mg, 47%) as a colourless amorphous solid.



R_f= 0.53 (cyclohexane/AcOEt = 8/2)

IR (ATR): 2953 (m, sh), 2929 (m), 2855 (w), 1633 (s), 1574 (s), 1517 (m), 1258 (m, sh), 741 (w, sh).

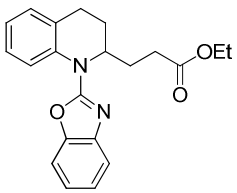
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.39–7.34 (m, 1H, Ar-H), 7.30–7.26 (m, 1H, Ar-H), 7.17 (pseudo-td, J = 7.7, 1.2 Hz, 1H, Ar-H), 7.01 (td, J = 7.7, 1.2 Hz, 1H, Ar-H), 6.66 (s, 1H, H-8), 6.63 (s, 1H, H-5), 5.03 (d, J = 16.5 Hz, 1H, H_a-1), 4.74–4.61 (m, 1H, H-3), 4.45 (d, J = 16.5 Hz, 1H, H_b-1), 3.87 (s, 6H, 2 x CH_3), 3.19 (dd, J = 15.8, 5.9 Hz, 1H, H_a-4), 2.71–2.62 (m, 1H, H_b-4), 1.77–1.09 (m, 10H), 0.94–0.72 (m, 3H).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.3 (C=N), 148.8, 148.1, 147.8, 143.5, (4 x Cq), 124.3, 124.1, 123.5, 120.5, 116.2 (5 x Ar-C), 112.3 (C5), 108.9 (C8), 108.8 (Ar-C), 56.1 (2 x OCH_3), 51.8 (C3), 43.6 (C1), 32.2 (C4), 31.8, 31.6, 29.3, 26.5, 22.7 (5 x CH_2), 14.2 (CH_3).

ESI-MS: m/z (%) = 395.3 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{24}H_{31}N_2O_3]^+$: m/z = 395.2335, found: 395.2344

Ethyl 3-[1-(1,3-benzoxazol-2-yl)-1,2,3,4-tetrahydroquinolin-2-yl]propanoate (6a)



Reaction conditions **A** were applied using benzoxazole **5** (21.7 mg, 0.087 mmol), ethylacrylate (76.0 µl, 0.69 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 9/1) afforded the title compound (28.8 mg, 95%) as a colourless amorphous solid.

$\mathbf{R}_f$ = 0.15 (cyclohexane/AcOEt = 9/1)

IR (ATR): 2977 (w, sh), 2934 (w, sh), 2855 (w), 1732 (m), 1624 (m), 1559 (s), 1459 (m,), 755 (w, sh).

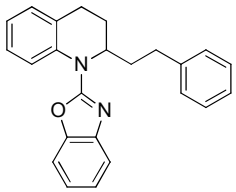
^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ = 7.77 (dd, J = 8.2 Hz, 1.2, 1H, Ar-H), 7.47–740 (m, 1H, Ar-H), 7.31–7.24 (m, 2H, Ar-H), 7.23–7.14 (m, 2H, Ar-H), 7.12–7.05 (m, 2H, Ar-H), 4.94–4.83 (m, 1H, H-2'), 4.11 (qd, J = 7.1, 1.6 Hz, 2H, CH_2-ethyl), 2.96–2.75 (m, 2H, H-4'), 2.60–2.36 (m, 2H, H-2), 2.32–2.21 (m, 1H, H_a-3'), 2.08–1.82 (m, 3H, H_b-3', H-3), 1.21 (t, J = 7.1 Hz, 3H, CH_3-ethyl).

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 173.3 (C1), 160.7 (C=N), 148.4, 142.6, 136.0 (3 x C_q), 129.2,(Ar-C) 129.2 (C_q), 126.8, 124.3, 124.3, 123.7, 121.5, 117.0, 109.2 (7 x Ar-C) 60.6 (CH_2-ethyl), 54.8 (C2'), 31.0 (C2), 27.1 (C3'), 26.8 (C3), 23.6 (C4'), 14.3 (CH_3-ethyl).

ESI-MS: m/z (e%) = 351.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{21}H_{23}N_2O_3]^+$: m/z = 351.1709, found: 351.1715

1-(1,3-Benzoxazol-2-yl)-2-(2-phenylethyl)-1,2,3,4-tetrahydroquinoline (6b)



Reaction conditions **A** were applied using benzoxazole **5** (44.7 mg, 0.18 mmol), styrene (164 µl, 1.4 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 9/1) afforded the title compound (46.2 mg, 73%) as a colourless amorphous solid.

$\mathbf{R}_f$ = 0.24 (cyclohexane/AcOEt = 9/1)

IR (ATR): 2931 (w, sh), 2861 (w, sh), 2855 (w), 1624 (m), 1558 (s), 1458 (m,), 754 (w, sh).

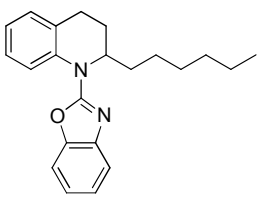
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.79 (dd, J = 8.2, 1.1 Hz, 1H, Ar-H), 7.40–744 (m, 1H, Ar-H), 7.3–6.97 (m, 11 H, Ar-H), 5.01–4.83 (m, 1H, H-2), 2.97–2.67 (m, 4H, H-4, H-2'), 2.37–2.22 (m, 1H, H_a-3), 2.14–1.99 (m, 1H, H_a-1'), 2.00–1.78 (m, 2H, H_b-3, H_b-1').

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 160.7 (C=N), 148.4, 142.7, 141.8, 136.3, 129.5 (5 x C_q), 129.1, 128.5 (4 x), 126.7, 126.0, 124.3, 124.2, 123.8, 121.4, 117.0, 109.1 (13 x Ar-C), 55.3 (C2), 33.6 (C1'), 32.5 (C2'), 27.1 (C3), 23.8 (C4).

ESI-MS: m/z (%) = 355.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{21}H_{23}N_2O_3]^+$: *m/z* = 355.1810, found: 355.1818

1-(1,3-Benzoxazol-2-yl)-2-hexyl-1,2,3,4-tetrahydroquinoline (6c)



Reaction conditions **A** were applied using benzoxazole **5** (43.7 mg, 0.17 mmol), hex-1-ene (184 µl, 1.4 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 9/1) afforded the title compound (38.5 mg, 66%) as a colourless amorphous solid.

$\mathbf{R}_f$ = 0.37 (cyclohexane/AcOEt = 9/1)

IR (ATR): 2952 (w, sh), 2927 (m, sh), 2856 (w), 1622 (m), 1554 (s), 1457 (m,), 754 (m, sh).

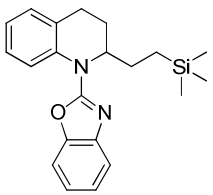
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 8.2, 1.1 Hz, 1H, Ar-H), 7.49–7.42 (m, 1H, Ar-H), 7.33–7.24 (m, 2H, Ar-H), 7.24–7.13 (m, 2H, Ar-H), 7.13–7.03 (m, 2H, Ar-H), 4.87–4.76 (m, 1H, H-2), 2.98–2.63 (m, 2H, H-4), 2.3–2.16 (m, 1H, H_a-3), 1.95–1.80 (m, 1H, H_b-3), 1.82–1.65 (m, 1H, H_a-1'), 1.61–1.15 (m, 9H, CH_2-hexyl), 0.94–0.75 (m, 3H, CH_3-hexyl).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 160.7 (C=N), 148.4, 142.8, 136.5, 129.6 (4 x C_q), 129.0, 126.6, 124.1, 124.1, 123.7, 121.3, 116.9, 109.1 (8 x Ar-C), 55.6 (C2), 31.9, 31.7 (C1'), 29.3, 26.9 (C3), 26.0, 23.9 (C4), 22.7, 14.2 (CH_3-hexyl).

ESI-MS: *m/z* (%) = 335.3 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{22}H_{27}N_2O]^+$: *m/z* = 335.2123, found: 335.2125

1-(1,3-Benzoxazol-2-yl)-2-[2-(trimethylsilyl)ethyl]-1,2,3,4-tetrahydroquinoline (6d)



Reaction conditions **A** were applied using benzoxazole **5** (39.3 mg, 0.16 mmol), vinyltrimethylsilane (197 µl, 1.3 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 9.5/0.5) afforded the title compound (44.4 mg, 81%) as a colourless amorphous solid.

$\mathbf{R}_f$ = 0.36 (cyclohexane/AcOEt = 9/1)

IR (ATR): 2951 (w, sh), 2929 (w, sh), 1624 (m), 1558 (s), 1459 (m), 1248 (m), 754 (m, sh).

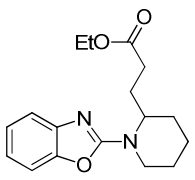
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 8.2, 1.2 Hz, 1H, Ar-H), 7.49–7.41 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar-H), 7.33–7.25 (m, 2H, Ar-H), 7.25–7.14 (m, 2H, Ar-H), 7.13–7.01 (m, 2H, Ar-H), 4.78–4.62 (m, 1H, H-2), 2.87–2.69 (m, 2H, H-4), 2.34–2.15 (m, 1H, H_a-3), 1.99–181 (m, 1H, H_b-3), 1.80–1.64 (m, 1H, H_a-1'), 1.63–1.44 (m, 1H, H_b-1'), 0.64–0.52 (m, 2H, H-2'), –0.06 (s, 9H, 3 x CH_3).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 160.8 (C=N), 148.4, 142.7, 136.6, 130.1 (4 x C_q), 128.8, 126.6, 124.2, 124.1, 123.7, 121.3, 116.8, 109.1 (8 x Ar-C), 58.1 (C2), 26.7 (C3), 26.3 (C1'), 24.1 (C4), 12.5 (C2'), –1.7 (3 x CH_3).

ESI-MS: *m/z* (%) = 351.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{21}H_{27}N_2OSi]^+$: *m/z* = 351.1893, found: 351.1886

Ethyl 3-[1-(1,3-Benzoxazol-2-yl)piperidin-2-yl]propanoate (8a)



Reaction conditions **A** were applied using benzoxazole **7** (100.6 mg, 0.50 mmol), ethylacrylate (433 µl, 4.0 mmol, 8.0 equiv) and $[Ir(cod)_2]BF_4$ (7 mol %). After 2 h, purification by thin-layer

chromatography (cyclohexane/AcOEt = 8/2) afforded the title compound (85.3 mg, 81%) as a colourless oil.

$\mathbf{R}_f$= 0.34 (cyclohexane/AcOEt = 8/2)

IR (ATR): 2978 (w, sh), 2938 (m, sh), 2867 (w, sh), 1733 (m), 1633 (s), 1575 (s), 1461 (m), 1247 (m), 741 (w, sh).

^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ = 7.33–7.29 (m, 1H, Ar-H), 7.23–7.19 (m, 1H, Ar-H), 7.14 (pseudo-td, J = 7.7, 1.2 Hz, 1H, Ar-H), 6.98 (pseudo-td, J = 7.7, 1.2 Hz, 1H, Ar-H), 4.54–4.43 (m, 1H, H-2'), 4.22–4.15 (m, 1H, H_a-6'), 4.07 (qd, J = 7.2, 2.0 Hz, 2H, CH_2-ethyl), 3.18 (td, J = 13.3, 2.7 Hz, 1H, H_b-6'), 2.43–2.31 (m, 2H, H-2), 2.32–2.18 (m, 1H, H_a-3), 1.93–1.46 (m, 7H), 1.15 (t, J = 7.1 Hz, 3H, CH_3-ethyl).

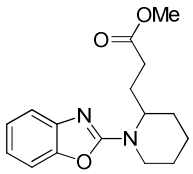
Ethyl acetate could not be removed

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 173.4 (C1), 162.5 (C=N), 148.6, 143.5 (2 x C_q), 124.0, 120.3, 116.0, 108.6 (4 x Ar-C), 60.6 (CH_2-ethyl), 52.6 (C2'), 41.0 (C6'), 31.4 (C2), 28.5, 25.3, 24.9 (C3), 19.0, 14.2 (CH_3-ethyl).

ESI-MS: m/z (%) = 303.1 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{17}H_{23}N_2O_3]^+$: m/z = 303.1709, found: 303.1718

Methyl 3-[1-(1,3-benzoxazol-2-yl)piperidin-2-yl]propanoate (8b)



Reaction conditions **A** were applied using benzoxazole **7** (65.1 mg, 0.32 mmol), methylacrylate (241 µl, 2.6 mmol, 8.0 equiv) and $[Ir(cod)_2]BF_4$ (7 mol %). After 2 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 8/2) afforded the title compound (47.0 mg, 51%) as a colourless oil.

$\mathbf{R}_f$ = 0.30 (cyclohexane/AcOEt = 8/2)

IR (ATR): 2945 (m), 2863 (w), 1737 (m), 1633 (s), 1575 (s), 1460 (m), 1247 (m), 742 (w, sh).

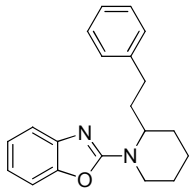
^{1}H NMR, COSY (400 MHz, $CDCl_3$): δ = 7.33–7.29 (m, 1H, Ar-H), 7.23–7.19 (m, 1H, Ar-H), 7.14 (pseudo-td, J = 7.7, 1.1 Hz, 1H, Ar-H), 6.98 (pseudo-td, J = 7.7, 1.1 Hz, 1H, Ar-H), 4.52–4.44 (m, 1H, H2'), 4.24–4.10 (m, 1H, H_a-6'), 3.6 (s, 3H, OCH_3), 3.17 (td, J = 13.3, 2.7 Hz, 1H, H_b-6'), 2.40–2.34 (m, 2H, H-2), 2.33–2.20 (m, 1H, H_a-3), 1.94–1.49 (m, 7H).

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 173.8 (C1), 162.5 (C=N), 148.6, 143.5 (2 x C_q), 124.0, 120.3, 116.0, 108.6 (4 x Ar-C), 52.6 (C2'), 51.8 (OCH_3), 41.0 (C6'), 31.1 (C2), 28.5, 25.3, 24.9 (C3), 19.0.

ESI-MS: m/z (%) = 289.1 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{16}H_{21}N_2O_3]^+$: m/z =289.1552, found: 289.1557

2-[2-(2-Phenylethyl)piperidin-1-yl]-1,3-benzoxazole (8c)



Reaction conditions **A** were applied using benzoxazole **7** (25.1 mg, 0.12 mmol), styrene (113 µl, 1.0 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 1 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound (18.3 mg, 48%) as a colourless oil.

$\mathbf{R}_f$= 0.66 (cyclohexane/AcOEt = 7/3)

IR (ATR): 2938 (m), 2860 (w), 1737 (m), 1633 (s), 1574 (s), 1460 (m), 1247 (m), 741 (w, sh).

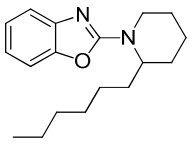
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.36–7.31 (m, 1H, Ar-H), 7.30–7.11 (m, 7H, Ar-H), 6.99 (pseudo-td, J = 7.7, 1.3 Hz, 1H, Ar-H), 4.59–4.39 (m, 1H, H-2'), 4.26–4.16 (m, 1H, H_a-6'), 3.29–3.06 (m, 1H, H_b-6'), 2.76–2.51 (m, 2H, H-2"), 2.2–2.10 (m, 1H, H_a-1"), 1.99–1.78 (m, 1H, H_b-1"), 1.79–1.46 (m, 6H).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.7 (C=N), 148.6, 143.6, 141.8 (3 x C_q), 128.5 (4 x), 126.1, 124.0, 120.2, 116.0, 108.7 (9 x Ar-C), 53.0 (C2'), 41.2 (C6'), 32.8 (C2''), 31.7 (C1''), 28.3, 25.4, 19.0.

ESI-MS: *m/z* (%) = 307.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{20}H_{23}N_2O]^+$: *m/z* = 307.1810, found: 307.1809

2-(2-Hexylpiperidin-1-yl)-1,3-benzoxazole (8d)



Reaction conditions **A** were applied using benzoxazole **7** (39.3 mg, 0.19 mmol), hex-1-ene (204 µl, 1.6 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 1 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound (23.3 mg, 42%) as a colourless oil.

R_f = 0.72 (cyclohexane/AcOEt = 7/3)

IR (ATR): 2928 (s), 2856 (m), 1737 (m), 1629 (s), 1571 (s), 1459 (m), 1246 (m), 739 (s, sh).

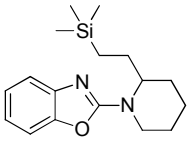
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.35–7.29 (m, 1H, Ar-H), 7.24–7.19 (m, 1H, Ar-H), 7.13 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 6.97 (pseudo-td, *J* = 7.7, 1.3 Hz, 1H, Ar-H), 4.47–4.34 (m, 1H, H-2'), 4.123–4.09 (m, 1H, H_a-6'), 3.23–3.10 (m, 1H, H_b-6'), 1.90–1.47 (m, 8H), 1.38–1.12 (m, 8H), 0.92–0.77 (m, 3H, CH_3).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.7 (C=N), 148.6, 143.7 (2 x C_q), 123.9, 120.1, 115.9, 108.5 (4 x Ar-C), 53.1 (C2'), 41.1 (C6'), 31.9, 29.5, 29.4, 28.1, 26.4, 25.4, 22.8, 18.9 (8 x CH_2), 14.2 (CH_3).

ESI-MS: *m/z* (%) = 287.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{18}H_{27}N_2O]^+$: *m/z* = 287.2123, found: 287.2117

2-{2-[2-(Trimethylsilyl)ethyl]piperidin-1-yl}-1,3-benzoxazole (8e)



Reaction conditions **B** were applied using benzoxazole **7** (42.4 mg, 0.21 mmol), vinyltrimethylsilane (263 µl, 1.7 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 48 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound (24.7 mg, 39%) as a pale brown oil.

R_f = 0.67 (cyclohexane/AcOEt = 7/3)

IR (ATR): 2947 (m, sh), 2862 (w), 1737 (m), 1634 (s), 1575 (s), 1460 (m), 1247 (m), 740 (m, sh).

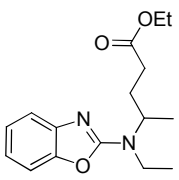
^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.35–7.30 (m, 1H, Ar-H), 7.24–7.19 (m, 1H, Ar-H), 7.14 (pseudo-td, *J* = 7.6, 1.2 Hz, 1H, Ar-H), 6.97 (pseudo-td, *J* = 7.6, 1.2 Hz, 1H, Ar-H), 4.43–4.26 (m, 1H, H-2'), 4.23–4.13 (m, 1H, H_a-6'), 3.19–3.04 (m, 1H, H_b-6'), 1.87–1.38 (m, 8H), 0.58–0.33 (m, 2H, H-2''), –0.02 (s, 9H).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.8 (C=N), 148.6, 143.7 (2 x C_q), 123.9, 120.1, 115.8, 108.6 (4 x Ar-C), 55.7 (C2'), 41.1 (C6'), 27.5, 25.4, 23.7, 18.9, 13.0 (C2''), –1.6 (3 x CH_3).

ESI-MS: *m/z* (%) = 303.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{17}H_{27}N_2OSi]^+$: *m/z* = 303.1893, found: 303.1889

Ethyl 4-[1,3-benzoxazol-2-yl(ethyl)amino]pentanoate (12a)



Reaction conditions **B** were applied using benzoxazole **11** (21.5 mg, 0.11 mmol), ethylacrylate (98.4 µl, 0.90 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 4 h, purification by thin-layer chromatography (cyclohexane/AcOEt = 7/3) afforded the title compound (21.0 mg, 64%) as colorless amorphous solid

R_f = 0.52 (cyclohexane/AcOEt = 7/3)

IR (ATR): 2977 (m. sh), 2937 (w, sh), 1734 (m), 1633 (s), 1576 (s), 1461 (m), 1248 (m), 742 (w, sh).

^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.37–7.32 (m, 1H, Ar-H), 7.27–7.21 (m, 1H, Ar-H), 7.14 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 6.99 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 4.43–4.24 (m, 1H, H-4), 4.09 (q, *J* = 7.2, Hz, 2H, OCH_2CH_3), 3.60–3.36 (m, 2H, CH, NCH_2CH_3), 2.41–2.22 (m, 2H, H-2), 2.15–1.79 (m, 2H, H-3), 1.35–1.27 (m, 6H), 1.18 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3).

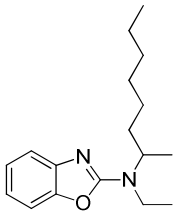
^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 173.3 (C1), 162.5 (C=N), 148.7, 143.3 (2 x C_q), 124.0, 120.2, 116.0, 108.7 (4 x Ar-C), 60.7 (OCH_2CH_3), 53.7 (C4), 39.1 (NCH_2CH_3), 31.5 (C2), 29.7 (C3), 19.3, 15.1, 14.3 (OCH_2CH_3).

ESI-MS: *m/z* (%) = 291.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{16}H_{22}N_2O_3Na]^+$: *m/z* = 313.1528, found: 313.1524

162.5, 143.3 out of HMBC

N-Ethyl-N-(octan-2-yl)-1,3-benzoxazol-2-amine (12b)



Reaction conditions **A** were applied using benzoxazole **11** (48.4 mg, 0.25 mmol), hex-1-ene (277 µl, 2.0 mmol, 8.0 equiv) and $[Ir(cod)_2]BARF$ (7 mol %). After 2 h, purification by thin-layer chromatography (Cyclohexan/AcOEt = 7/3) afforded the title compound (36.9 mg, 53%) as colorless oil.

R_f = 0.71 (cyclohexane/AcOEt = 7/3)

IR (ATR): 2957 (w, sh), 2929 (w, sh), 2857 (w, sh), 1631 (s), 1575 (s), 1461 (m), 1283 (m), 904 (m), 739 (s, sh).

^{1}H NMR, COSY (300 MHz, $CDCl_3$): δ = 7.38–7.33 (m, 1H, Ar-H), 7.28–7.20 (m, 1H, Ar-H), 7.14 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 6.98 (pseudo-td, *J* = 7.7, 1.3 Hz, 1H, Ar-H), 4.40–4.24 (m, 1H, H2), 3.56–3.35 (m, 2H, H-2'), 1.76–1.59 (m, 1H, H_a-3'), 1.59–1.42 (m, 1H, H_b-3'), 1.39–1.07 (m, 14H), 0.96–0.72 (m, 3H, H-8 H_a-3').

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.7 (C=N), 148.7, 143.4 (2 x C_q), 123.9, 120.0, 115.9, 108.6 (4 x Ar-C), 54.2 (C2'), 38.7 (CH_2-ethyl), 34.9 (C3'), 31.9, 29.4, 26.7, 22.7, 19.4 (C1'), 15.2 CH_3-ethyl, 14.2 (C8').

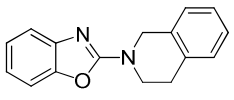
143.4 out of HMBC

ESI-MS: *m/z* (%) = 275.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{17}H_{27}N_2O]^+$: *m/z* =275.2123, found: 275.2134

Introduction of the benzoxazol-2-yl (Bo-) group

2-(1,3-Benzoxazol-2-yl)-1,2,3,4-tetrahydroisoquinoline (1)



Method A: To a mixture of acetic acid (3.54 g, 59 mmol 3.0 equiv) and *tert*-butyl-hydroperoxide (70% in water, 3.86 g, 30 mmol, 1.5 equiv) in acetonitrile (12.0 mL), *tetra*-butylammonium iodide (350 mg, 0.95 mmol, 5 mol %), 1,2,3,4-tetrahydroisoquinoline (3.15 g, 24 mmol, 1.2 equiv) and benzoxazole (2.35 g, 20 mmol) in acetonitrile (12.0 mL) were added. The reaction mixture was stirred for 4.5 h at 80 °C .Then the mixture was cooled to room temperature and quenched by the addition of an aqueous solution of sodium disulfite (120 mL) and a saturated solution of sodium hydrogen carbonate (300 mL). The mixture was extracted with DCM (5 × 200 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (cyclohexane/AcOEt = 10/1) to afforded the title compound (4.30 g, 87%) as a white solid, mp 95.2–97.0. °C (dec.), lit. mp 85–88 °C.[2]

R_f = 0.22 (cyclohexane/AcOEt = 10/1)

IR (ATR): 1634 (m, sh), 1576 (m), 1457 (m), 1371 (m), 1257 (m), 738 (s).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ = 7.42–737 (m, 1H, Ar-H), 7.31–7.27 (m, 1H, Ar-H), 7.26–7.15 (m, 5H, Ar-H), 7.03 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 4.86 (s, 2H, H-1), 3.96 (t, *J* = 6.0 Hz, 2H, H-3), 3.01 (t, *J* = 5.9 Hz, 2H, H-4).

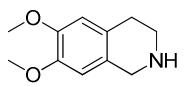
^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 162.2 (C=N), 148.9, 143.3, 134.2, 132.5 (4 x Cq), 128.9, 126.9, 126.7, 126.5, 124.1, 120.7, 116.4, 108.9 (8 x Ar-C), 47.3 (C1), 43.2 (C3), 28.6 (C4).

ESI-MS: *m/z* (%) = 251.1 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{16}H_{15}N_2O]^+$: *m/z* =251.1184, found: 251.1191

Method B: To a mixture of 2-chlorobenzoxazole (2.00 g, 13 mmol, 1.2) in dry THF (30 mL) was added 1,2,3,4-tetrahydroisoquinoline (1.47 g, 11 mmol) and triethylamine (1.98 g, 20 mmol, 1.8 equiv) under an argon atmosphere. The reaction mixture was stirred for 2 h at 70 °C .Then the mixture was cooled to room temperature and quenched by the addition of water (50 mL). The mixture was extracted with DCM (3 × 100 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (Cyclohexan/AcOEt = 10/1) to afforded the title compound (2.64 g , 96%) as a pale yellow solid, mp 97.1–98.3 °C (dec.), lit. mp 85–88 °C.[2] The spectroscopic data were identically with the sample prepared by method **A**.

6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline (16)



Compound **16** was prepared in 92% yield by the method Min Wang, et al. (2010).[3] To 2-(3,4-dimethoxyphenyl)ethylamine (25.0 g, 137 mmol) was added formic acid (70 mL) at 0 °C. After stirring at 0 °C for 10 min, paraformaldehyde (8.14 g, 137 mmol, 1.0 equiv) was added. The reaction mixture was stirred for 14 h at 50 °C. Excess formic acid was evaporated under reduced pressure, and the residue was poured into ice-water. After basification with 1N NaOH to pH 11, the mixture was extracted with DCM (3 x 200 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was recrystallized from DCM to afforded the title compound (24.5 g, 92%) as pale yellow solid, mp 79.1–80.2.°C (dec.), lit. mp 78–79 °C.[3]

R_f = 0.28 (CH_2Cl_2/MeOH = 3/1)

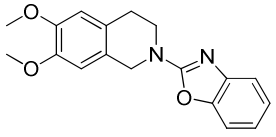
IR (ATR): 2953 (m), 2792 (m), m1523 (w), 1227 (m), 1120 (m), 903 (s), 727 (s), 650 (w).

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ = 6.61 (s, 1H, Ar-H), 6.56 (s, 1H, Ar-H), 4.25 (s, 2H, 1-H), 3.85 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.41 (t, *J* = 6.2 Hz, 2H, H-3), 3.09 (t, *J* = 6.1 Hz, 2H, H-4).

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 149.0, 148.5, 123.5, 119.3 (4 x C_q), 111.6, 109.2 (2 x Ar-C), 56.2, 56.1 (2 x OCH_3), 44.0 (C1), 41.7 (C3), 25.1 (C4).

ESI-MS: *m/z* (%) = 194.1 (100) $[M+H]^+$

2-(1,3-Benzoxazol-2-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3)



To a mixture of 2-chlorobenzoxazole (350 mg, 3.6 mmol) in dry THF (15 mL) was added 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**16:** 1.03 g, 5.3 mmol, 1.5 equiv) and Hünig's base (0.69 g, 5.3 mmol, 1.5 equiv) under an argon atmosphere. The reaction mixture was stirred for 20 h at 60 °C .Then the mixture was cooled to room temperature and quenched by the addition of water (30 mL). The mixture was extracted with DCM (3 × 50 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (petroleum ether /AcOEt = 2/1) to afforded the title compound (1.10 g, 96%) as a pale yellow solid, mp 110.9–111.4 °C.

R_f = 0.53 (petroleum ether/AcOEt = 1/1)

IR (ATR): 2935 (m), 2836 (m), 1634 (s), 1575 (s), 1515 (s), 1458 (s), 1202 (s), 1115 (s), 739 (s),.

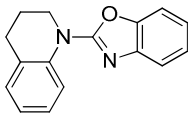
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ = 7.45–7.40 (m, 1H, Ar-H), 7.31–7.27 (m, 1H, Ar-H), 7.20 (pseudo-td, *J* = 7.8, 1.1 Hz, 1H, Ar-H), 7.06 (pseudo-td, *J* = 7.8, 1.1 Hz, 1H, Ar-H), 6.68 (s, 1H, Ar-H), 6.66 (s, 1H, Ar-H), 4.83 (s, 2H, H-1), 3.99 (t, *J* = 5.9 Hz, 2H, H-3), 3.87 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 2.94 (t, *J* = 6.2 Hz, 2H, H-4).

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 161.3 (C=N), 148.4, 148.1, 148.0, 141.3, 125.8 (5 x C_q), 124.5 (Ar-C), 123.8 (C_q), 121.3, 116.1, 111.6, 109.2, 109.1 (5 x Ar-C), 56.1, (2 x OCH_3), 47.2 (C1), 43.6 (C3), 28.0 (C4).

ESI-MS: *m/z* (%) = 311.1 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{18}H_{19}N_2O_3]^+$: *m/z* = 311.1396, found: 311.1395

1-(1,3-Benzoxazol-2-yl)-1,2,3,4-tetrahydroquinoline (5)



To a mixture of 2-chlorobenzoxazole (2.00 g, 13 mmol) in dry THF (30 mL) was added 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (2.60 g, 20 mmol, 1.5 equiv) and Hünig's base (2.53 g, 20 mmol, 1.5 equiv) under an argon atmosphere. The reaction mixture was stirred for 40 h under reflux.Then the mixture was cooled to room temperature and quenched by the addition of water (50 mL). The mixture was extracted with DCM (3 × 100 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (petroleum ether /AcOEt = 12/1) to afforded the title compound (2.84 g, 87%) as a pale yellow solid, mp 63.2–64.6 °C.

R_f = 0.53 (petroleum ether/AcOEt = 5/1)

IR (ATR): 3037 (w), 2947 (m), 1622 (s), 1552 (s), 1235 (m), 1455 (s), 802 (m), 741(s).

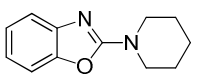
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ = 7.99–7.94 (m, 1H, Ar-H), 7.52–7.46 (m, 1H, Ar-H), 7.37–7.32 (m, 1H, Ar-H), 7.31–7.26 (m, 1H, Ar-H), 7.23 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 7.18–7.14 (m, 1H, Ar-H), 7.14–7.03 (m, 2H, Ar-H), 4.10 (t, *J* = 6.1 Hz, 2H, H-2), 2.86 (t, *J* = 6.4 Hz, 2H, H-4), 2.17–1.91 (m, 2H, H-3).

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 160.4 (C=N), 148.4, 142.5, 137.7, 129.2 (4 x C_q), 129.1, 126.7, 124.2, 123.6, 121.7, 121.6, 117.0, 109.2 (8 x Ar-C), 47.3 (C2), 27.5 (C4), 23.0 (C3).

ESI-MS: *m/z* (%) = 251.1 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{16}H_{15}N_2O]^+$: *m/z* = 251.1184, found: 251.1194

2-(Piperidin-1-yl)-1,3-benzoxazole (7)



Method A: To a mixture of 2-chlorobenzoxazole (2.00 g, 13 mmol) in dry THF (40 mL) was added piperidine (1.66 g, 20 mmol, 1.5 equiv) and Hünig's base (2.53 g, 20 mmol, 1.5 equiv) under an argon atmosphere. The reaction mixture was stirred for 2 h at 70 °C.Then the mixture was cooled to room temperature and quenched by the addition of water (50 mL). The mixture was extracted with DCM (3 × 100 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (cyclohexane/AcOEt = 5/1) to afforded the title compound (2.47 g, 93%) as a white amorphous solid.

R_f = 0.35 (cyclohexane/AcOEt = 5/1)

IR (ATR): 2938 (m), 2853 (m), 1631 (s), 1574 (s), 1458 (s), 1278 (m, sh), 1226 (m, sh), 740 (s).

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ = 7.36–7.29 (m, 1H, Ar-H), 7.23–7.19 (m, 1H, Ar-H), 7.12 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 6.96 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 3.82–3.23 (m, 4H, H-2', H-6'), 1.71–156 (m, 6H, H-3', H-4'. H-5').

^{13}C NMR, HMBC, HSQC (75 MHz, $CDCl_3$): δ = 162.4 (C=N), 148.7, 143.4 (2 x Cq), 123.8, 120.3, 116.0, 108.6, (4 x Ar-C), 46.6 (C2', C6'), 25.3 (C3', C5'), 24.1 (C4').

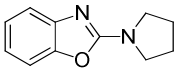
ESI-MS: *m/z* (%) = 203.2 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{12}H_{15}N_2O]^+$: *m/z* = 203.1184, found: 203.1178

Method B: Compound **7** was prepared in 69% yield by the method Froehr et al. (2011).[4] To a mixture of acetic acid (3.00 g, 50 mmol 3.0 equiv) and *tert*-butyl-hydroperoxide (70% in water, 3.58 g, 28 mmol, 1.6 equiv) in acetonitrile (18.0 mL), *tetra*-butylammonium iodide (308 mg, 0.83 mmol, 5 mol %), piperidine (1.70 g, 20 mmol, 1.2 equiv) and benzoxazole (2.00 g, 17 mmol) were added. The reaction mixture was stirred for 1.75 h at 80 °C .Then the mixture was cooled to room temperature and quenched by the addition of an aqueous solution of sodium disulfite (250 mL) and a saturated solution of sodium hydrogen carbonate (250 mL). The mixture was extracted with DCM (3 × 300 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (cyclohexane/AcOEt = 15/1) afforded the title compound (2.33 g, 69%) as white amorphous solid. The spectroscopic data were identically with the sample prepared by method **A**.

2-(pyrrolidin-1-yl)-1,3-benzoxazole (9)

Compound **9** was prepared in 49% yield by the method Froehr et al. (2011).[4]



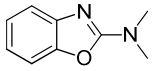
R_f = 0.31 (cyclohexane/AcOEt = 5/1)

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 1H, Ar-H), 7.25–7.22 (m, 1H, Ar-H), 7.14 (pseudo-td, *J* = 7.7, 1.1 Hz, 1H, Ar-H), 6.98 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 3.71–3.54 (m, 4H, H-2', H-5'), 2.08–1.94 (m, 4H, H-3', H-4').

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 161.1 (C=N), 149.1, 143.8 (2 x C_q), 123.9, 120.1, 116.1, 108.7 (4 x Ar-C), 47.5 (C2', C5'), 25.7 (C3', C4').

***N*,*N*-dimethyl-1,3-benzoxazol-2-amine (10)**

To a mixture of 2-chlorobenzoxazole (2.00 g, 13 mmol) in dry THF (40 mL) was added dimethylamine (40% in water, 14.65 g, 0.13 mol, 10 equiv) under an argon atmosphere. Then the reaction mixture was stirred for 10 min at room temperature, filtered and washed with water to afforded the title compound in quantitative yield as a colorless solid mp 82.1–83.0 °C (dec), lit. mp 80–82 °C.[5]



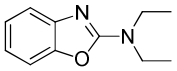
R_f = 0.27 (cyclohexane/AcOEt = 6/4)

IR (ATR): 3053 (m), 2932 (w), 2878 (w), 1656 (s), 1580 (s), 1462 (s), 1422 (s), 1267 (s), 1237 (s), 811 (m), 733 (s).

^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 1H, Ar-H), 7.27–7.22 (m, 1H, Ar-H), 7.15 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 6.99 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 3.20 (s, 6H, 2 x CH_3).

***N*,*N*-Diethyl-1,3-benzoxazol-2-amine (11)**

To a mixture of 2-chlorobenzoxazole (2.00 g, 13 mmol) in dry THF (10 mL) was added triethylamine (1.98 g, 20 mmol, 1.5 equiv) under an argon atmosphere. The reaction mixture was stirred for 14 h under reflux. Then the mixture was cooled to room temperature and quenched by the addition of water (50 mL). The mixture was extracted with DCM (3 × 100 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (petroleum ether /AcOEt = 10/1) to afforded the title compound (1.67 g, 67%) as a pale brown liquid.



R_f = 0.19 (petroleum ether /AcOEt = 10/1)

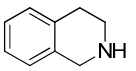
IR (ATR): 2974 (m), 1634 (s), 1575 (s), 1459 (s), 1245 (s), 779 (m), 738 (s, sh).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ = 7.36–7.35 (m, 1H, Ar-H), 7.34–7.33 (m, 1H, Ar-H), 7.13 (pseudo-td, *J* = 7.7, 1.1 Hz, 1H, Ar-H), 6.97 (pseudo-td, *J* = 7.7, 1.2 Hz, 1H, Ar-H), 3.57 (q, *J* = 7.1 Hz, 4H, 2 x CH_2-ethyl), 1.27 (t, *J* = 7.1 Hz, 6H, 2 x CH_3-ethyl).

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 162.3 (C=N), 148.9, 143.8 (2 x C_q), 123.8, 120.0, 115.9, 108.6 (4 x Ar-C), 43.0 (2 x CH_2), 13.6 (2 x CH_3).

ESI-MS: *m/z* (%) = 191.1 (100) $[M+H]^+$

1,2,3,4-tetrahydroisoquinoline (13)



Method A: To a mixture of benzoxazole (**1:** 84.0 mg, 0.34 mmol) in ethylene glycol (53 mL) was added KOH (6.30 g). The reaction mixture was stirred for 24 h at 140 °C.Then the mixture was cooled to room temperature and water (150 mL) was added. The aqueous phase was extracted with DCM (3 × 150 mL) . The combined organic layers where washed with water (150 mL), dried over Na_2SO_4 and concentrated *in vacuo*, to afford the title compound (29.0 mg, 65%) as a pale brown liquid.

$\mathbf{R_f}$ = 0.77 (AcOEt/EtOH = 2/1, 1 % NEt_3)

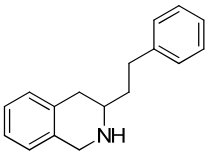
IR (ATR): 330 (m, br), 3056 (m, br), 2737 (m, sh), 1590 (m, sh), 1512 (s, sh), 1265 (s) 741 (s).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.18–7.05 (m, 3H, Ar-H), 7.06–6.92 (m, 1H, Ar-H), 4.02 (s, 2H, H-1), 3.15 (t, *J* = 6.0 Hz, 2H, CH_2), 2.81 (t, *J* = 6.0 Hz, 2H, CH_2), 2.27 (s, 1H, NH).

ESI-MS: *m/z* (%) = 134.1 (100) $[M+H]^+$

Method B: To benzoxazole (**1:** 24.0 mg, 0.096 mmol) in dry THF (2 mL) was added LAH (144 µl, 2 M solution in THF, 0. 29 mmol, 3.0 equiv) under an argon atmosphere. The reaction mixture was stirred for 20 h under reflux.Then the mixture was cooled to room temperature and quenched by the addition of 2 N NaOH (1 mL) and water (1 mL). The suspension was filtrated and washed with DCM 50 (mL). The aqueous phase was extracted with DCM (3 × 10 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to afforded the title compound (11.3 mg, 88%) as brown liquid. The spectroscopic data were identically with the sample prepared by method **A**.

3-(2-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (14)



To tetrahydroisoquinoline (**2c:** 56.0 mg, 0.16 mmol) in dry THF (5 mL) was added LAH (240 µl, 2 M solution in THF, 0. 47 mmol, 3.0 equiv) under an argon atmosphere. The reaction mixture was stirred for 48 h under reflux.Then the mixture was cooled to room temperature and quenched by the addition of 2 N NaOH (1.5 mL) and water (1.5 mL). The suspension was filtrated and washed with DCM 50 (mL). The aqueous phase was extracted with DCM (3 × 10 mL) The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo.* The residue was purified by flash column chromatography (cyclohexane/AcOEt = 5/3, 1 % NEt_3) to afforded the title compound (21.0 mg, 57%) as a pale brown oil.

$\mathbf{R_f}$ = 0.13 (cyclohexane/AcOEt = 5/3, 1 % NEt_3)

IR (ATR): 3023 (m), 2919 (s), 1495 (m), 1452 (m), 744 (s), 699 (s).

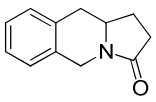
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ = 7.38–7.33 (m, 2H, Ar-H), 7.27–7.16 (m, 3H, Ar-H),7.16–7.06 (m, 3H, Ar-H), 7.05–6.99 (m, 1H, Ar-H), 4.07 (s, 2H, H-1), 2.97–2.70 (m, 4H), 2.57 (dd, *J* = 16.2, 10.4 Hz, 1H, H_b-4), 1.90–1.79 (m, 2H, H-1'), 1.69 (br, s, 1H, NH).

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 142.2, 135.9, 134.8 (3 x C_q), 129.4, 128.5 (4 x), 126.2, 126.1, 126.0, 125.9 (9 x Ar-C), 53.3 (C3), 48.6 (C1), 38.6 (C1'), 35.6 (C4), 32.5 (C2').

ESI-MS: *m/z* (%) = 238.1 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{17}H_{20}N]^+$: *m/z* = 238.1596, found: 238.1607

1,5,10,10a-Tetrahydropyrrolo[1,2-*b*]isoquinolin-3(2*H*)-one (15)



A mixture of propanoate (**2a:** 62.0 mg, 0.18 mmol) and KOH (5.20 g) in ethylene glycol (44 ml) was immersed in a pre-heated oil bad at 190 °C and refluxed for 24 h. Then the mixture was cooled to room temperature and water (100 mL) was added. The aqueous phase was extracted with DCM (3 × 100 mL). The combined organic layers where washed with water (150 mL), dried over Na_2SO_4 and concentrated *in vacuo*, to afford the title compound (24.1 mg, 73%) as a colourless amorph solid.

$\mathbf{R_f}$ = 0.32 (cyclohexane/AcOEt = 8/2)

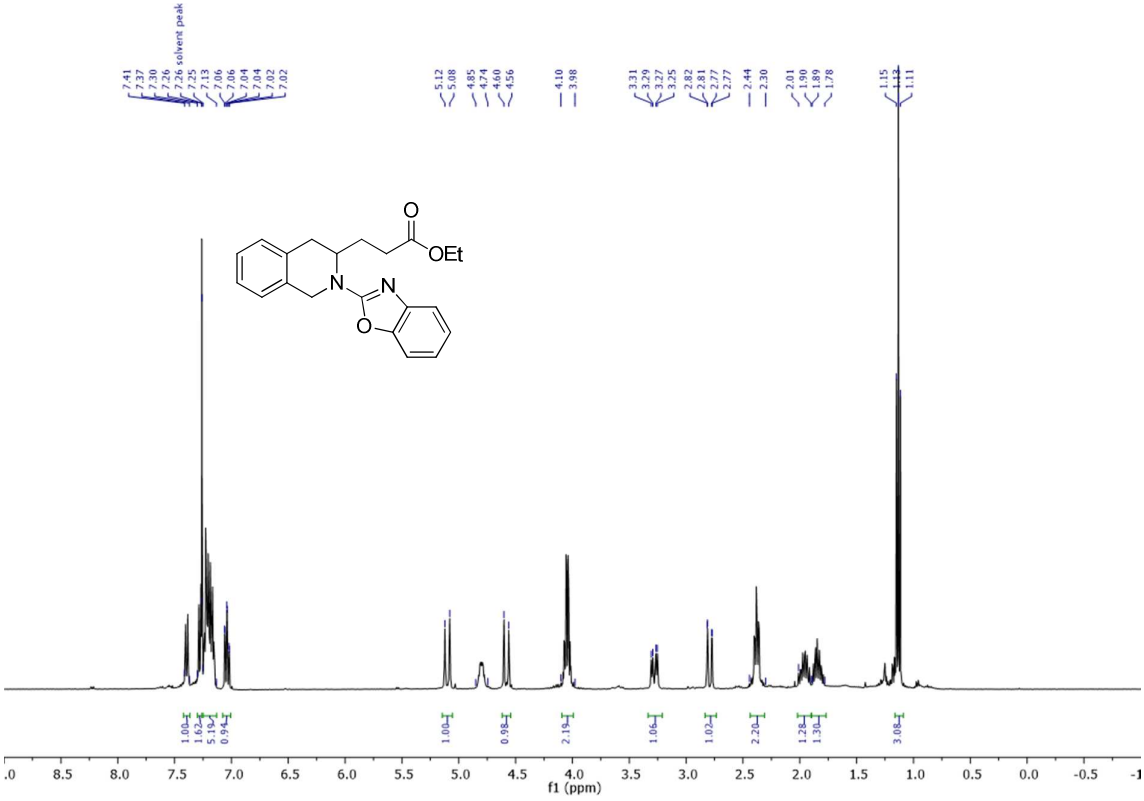
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ = 7.26–7.03 (m, 4H, Ar-H), 4.94 (d, J = 17.5 Hz, 1H, H_a-5), 4.27 (d, J = 17.5 Hz, 1H, H_b-5), 3.84–3.73 (m, 1H, H-10a), 2.97 (dd, J = 15.4, 3.8 Hz, 1H, H_a-10), 2.75–2.65 (m, 1H, H_b-10), 2.51–2.32 (m, 3H, CH_2), 1.89–1.67 (m, 1H, CH_2).

^{13}C NMR, HMBC, HSQC (101 MHz, $CDCl_3$): δ = 174.4 (C3), 133.3, 131.9 (2 x C_q), 129.2, 126.9, 126.8, 126.7 (4 x Ar-C), 54.1 (C10a), 42.7 (C5), 37.0 (C10), 30.3 (CH_2), 25.4 (CH_2).

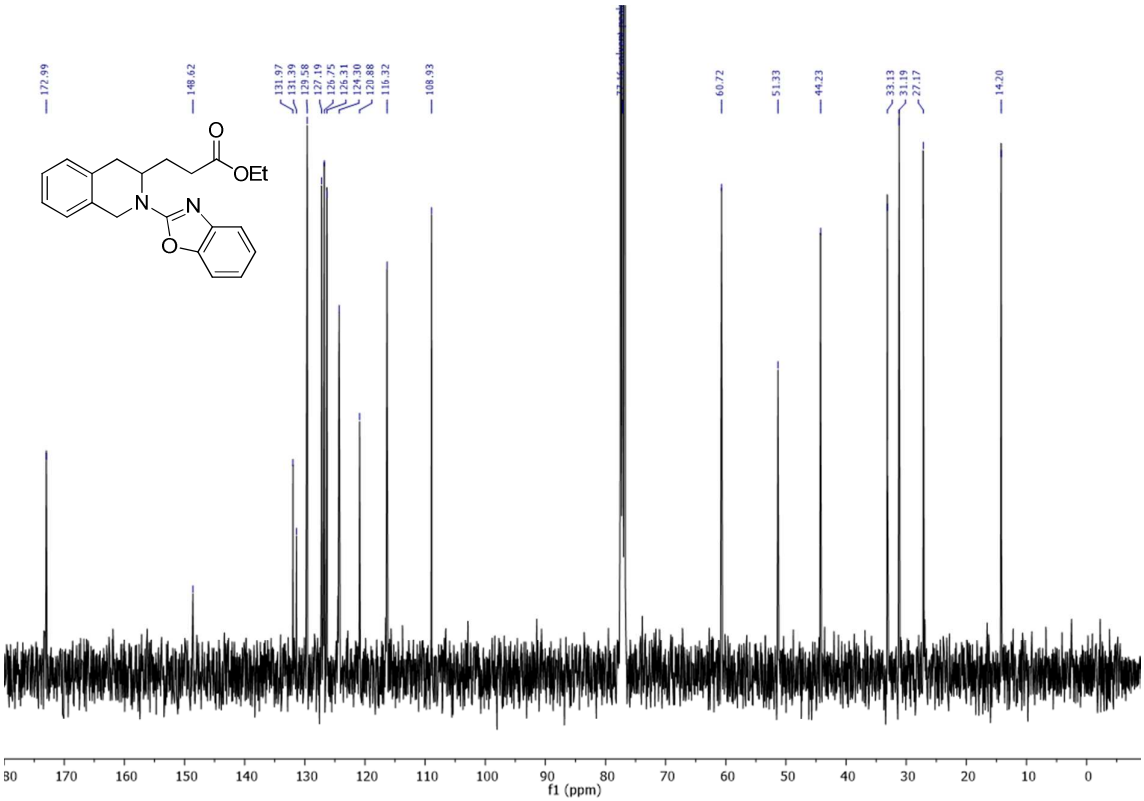
ESI-MS: *m/z* (%) = 188.1 (100) $[M+H]^+$

ESI-HRMS: calculated for $[C_{12}H_{132}ONa]^+$: *m/z* = 210.0895, found: 210.0904

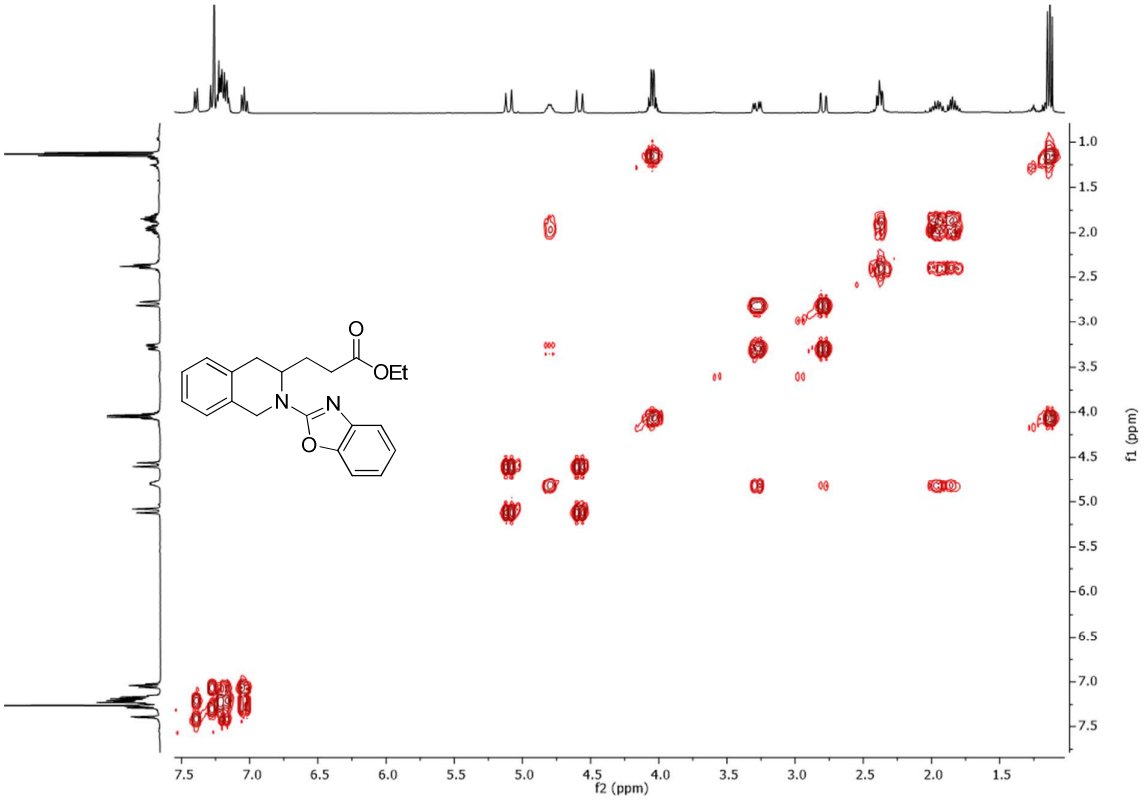
Spectra



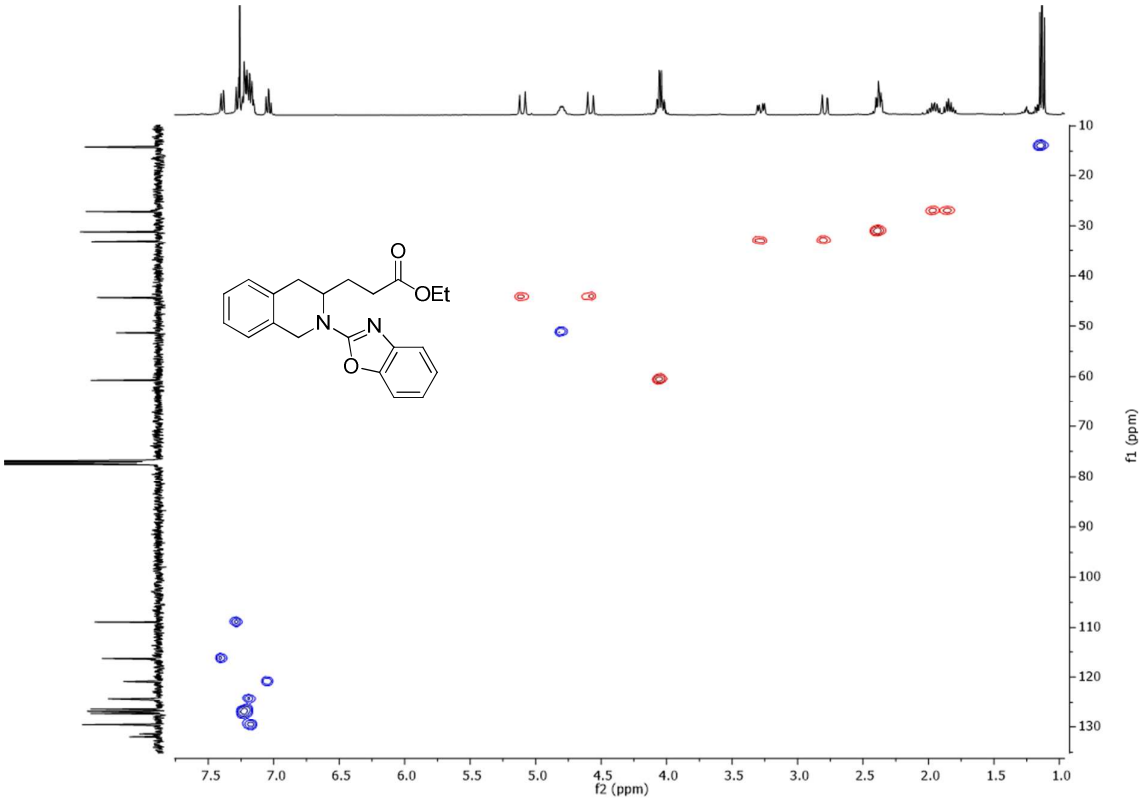
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 2a



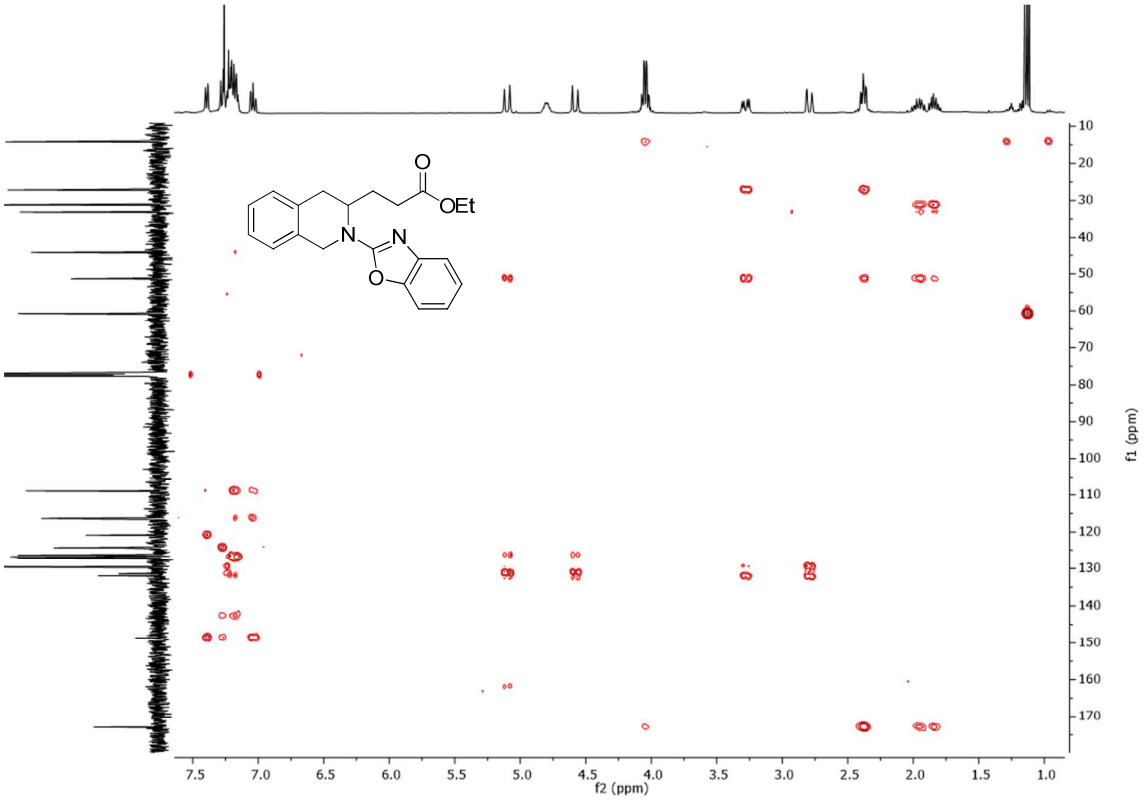
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 2a



COSY of compound 2a

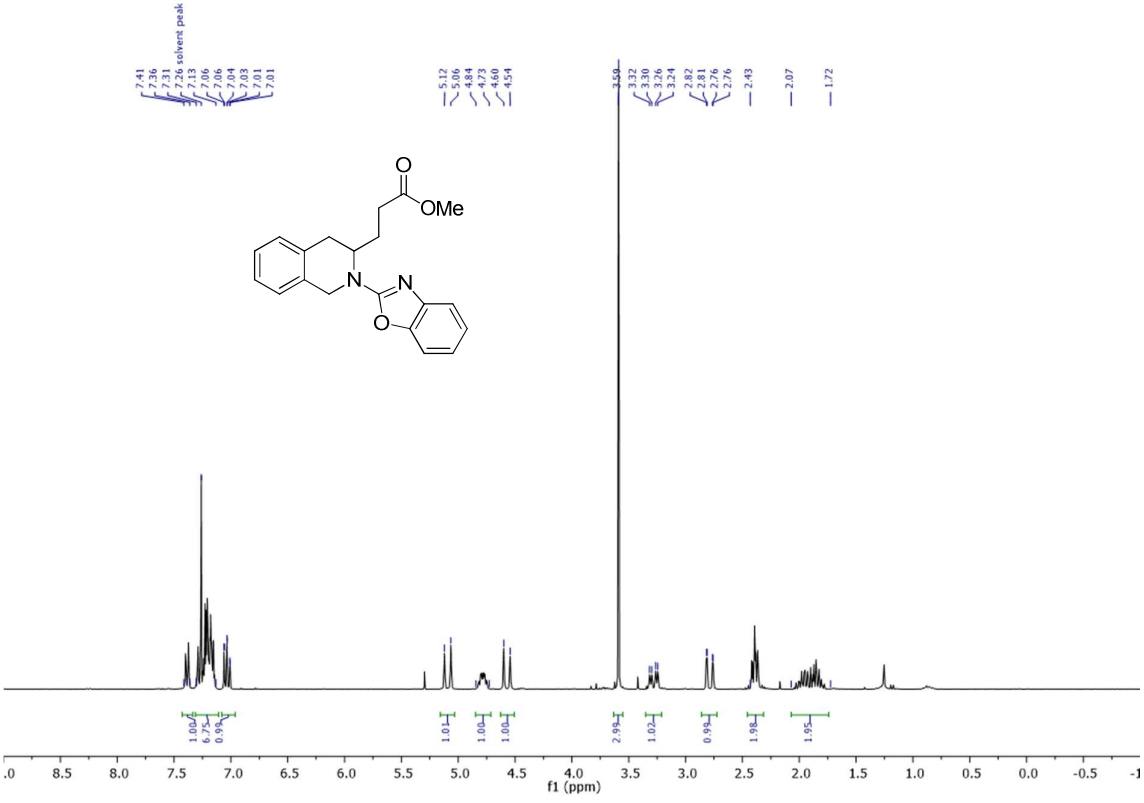


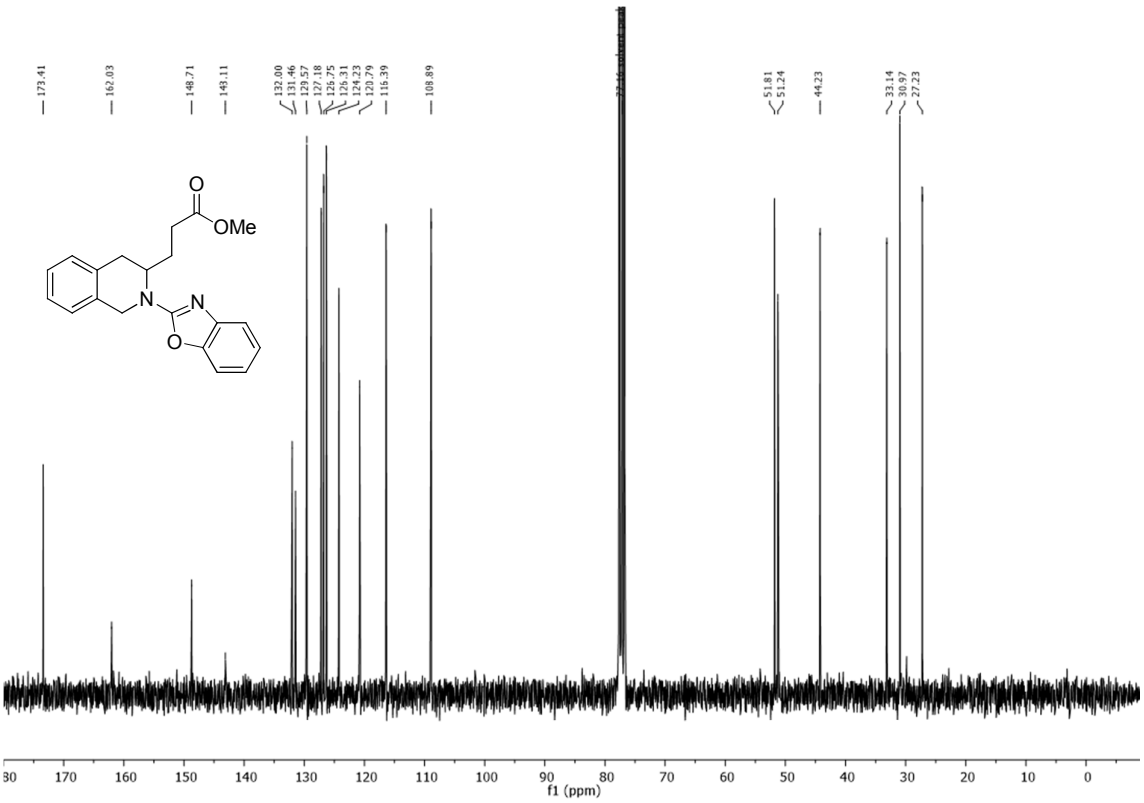
HSQC of compound 2a



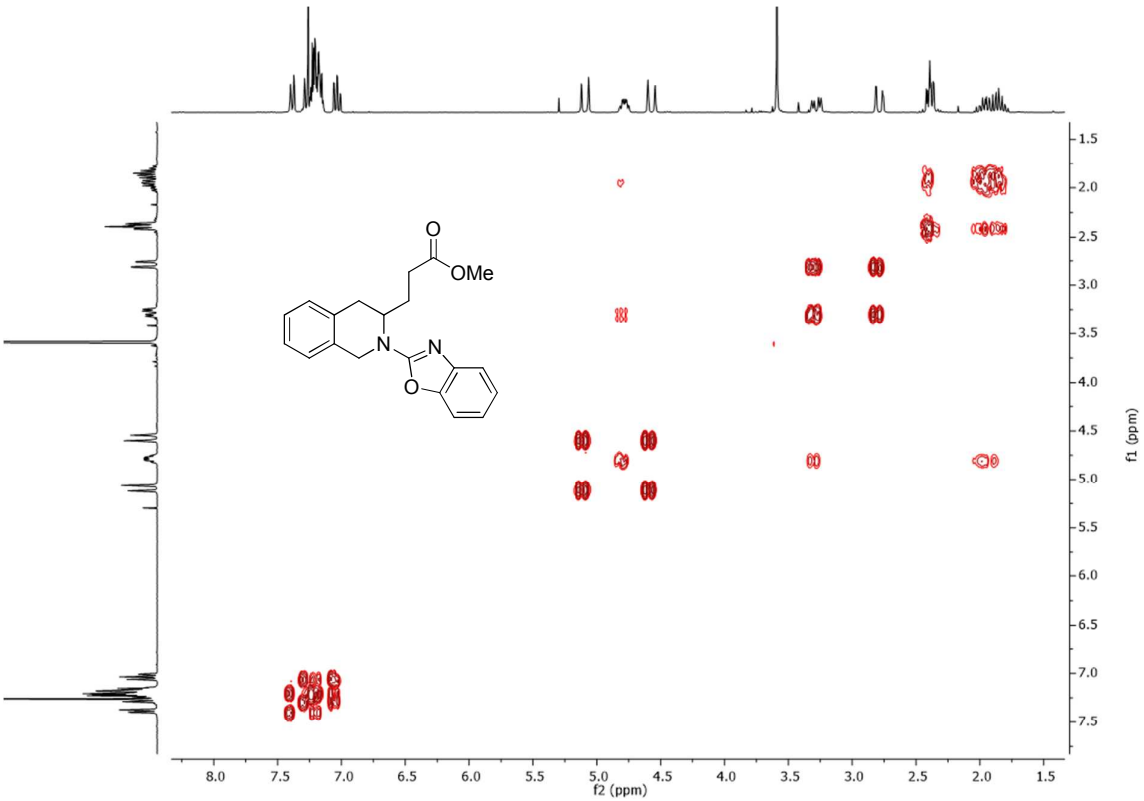
HMBC of compound 2a

^{1}H-NMR (300 MHz, $CDCl_3$) of compound 2b

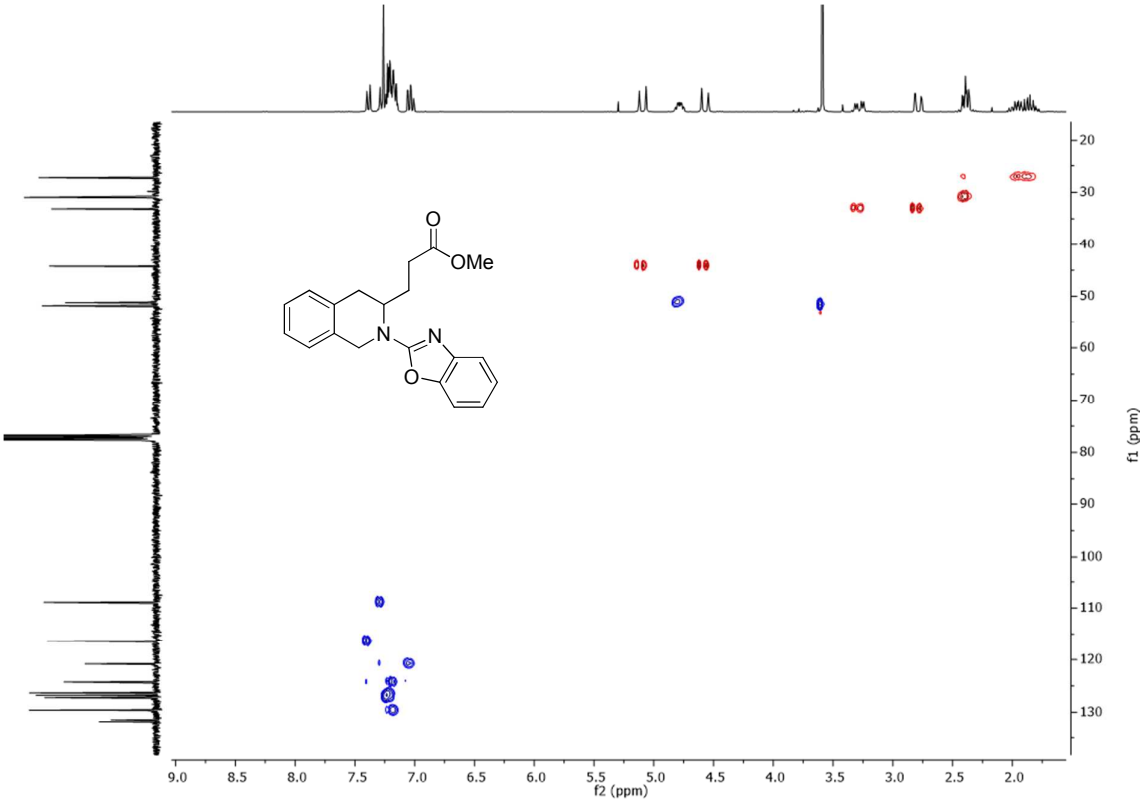




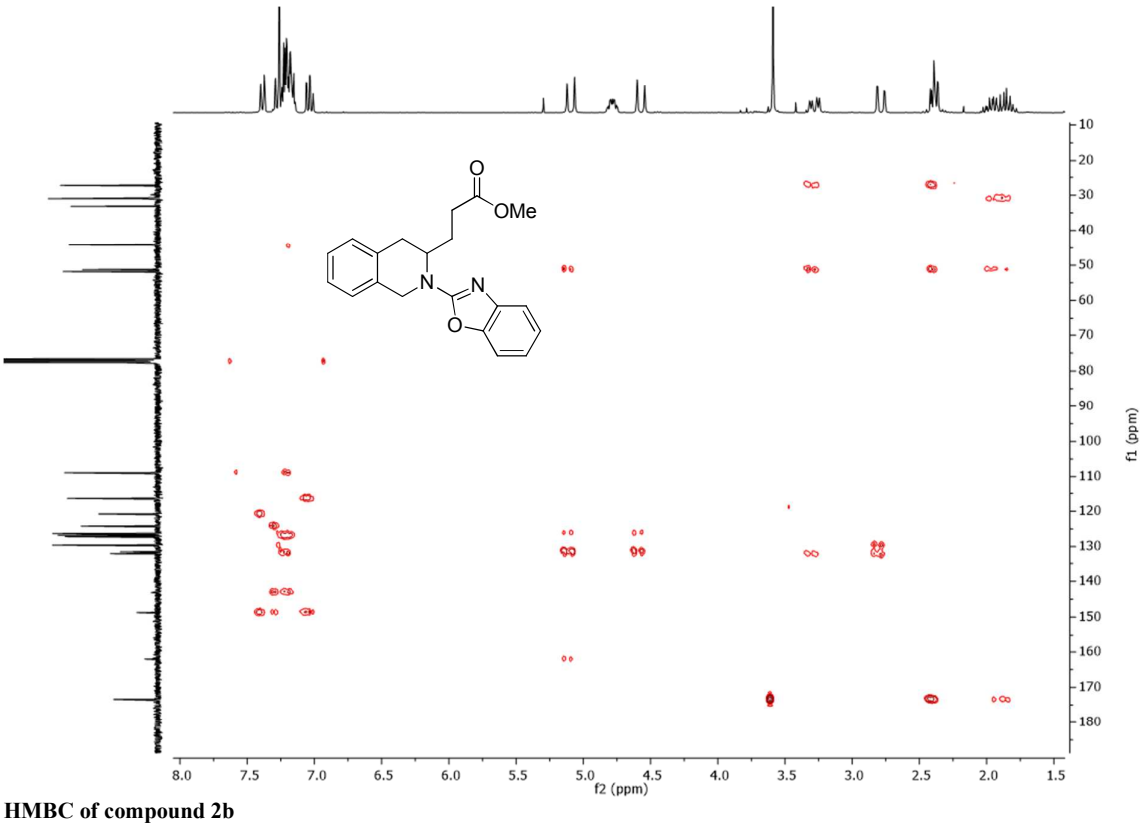
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 2b



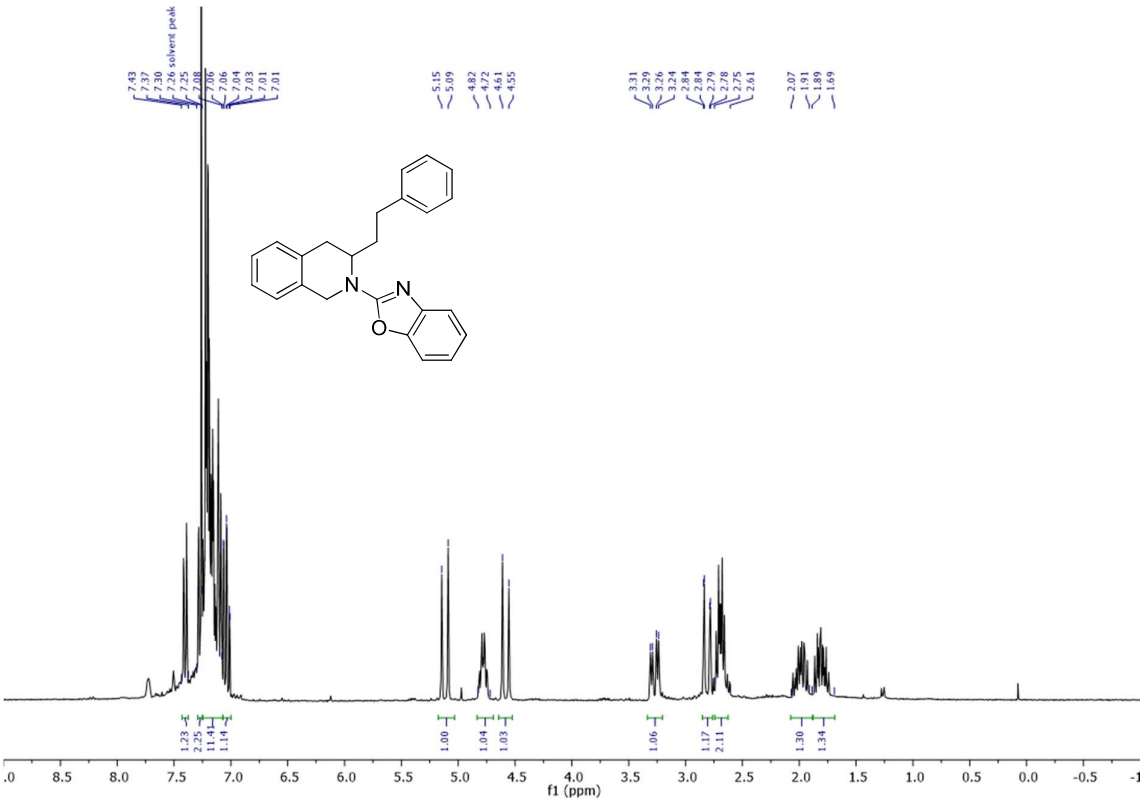
COSY of compound 2b



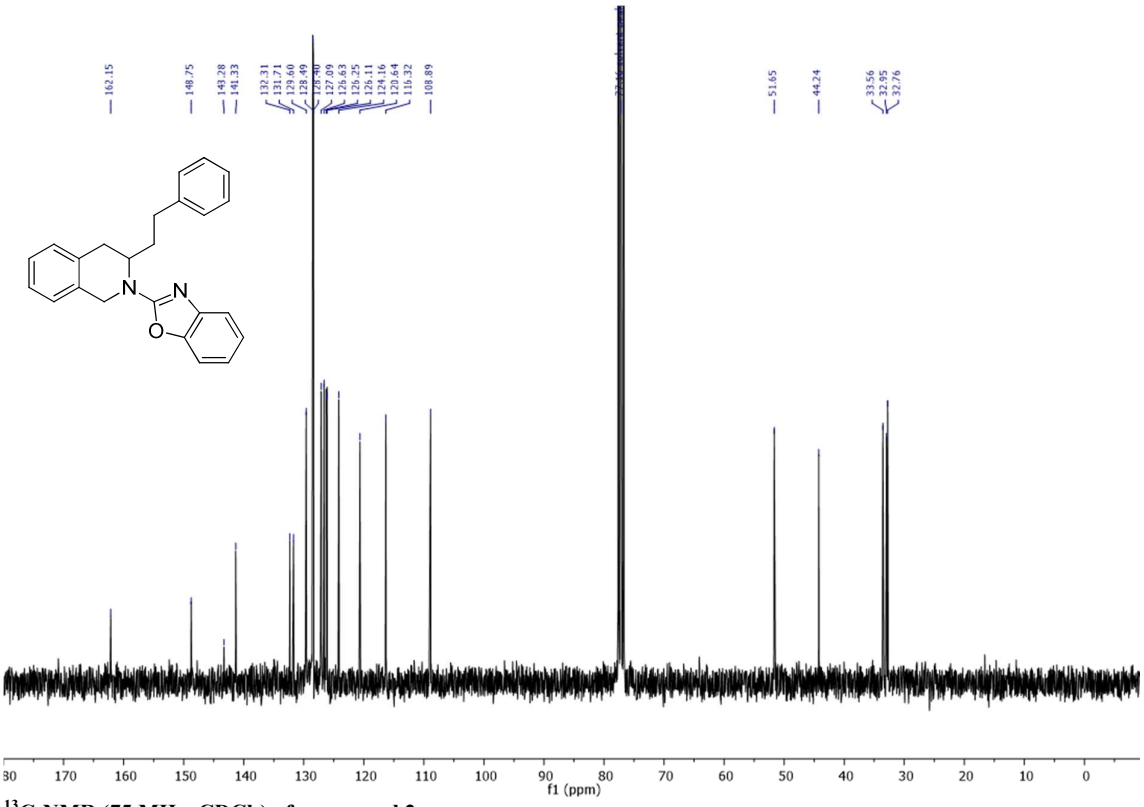
HSQC of compound 2b



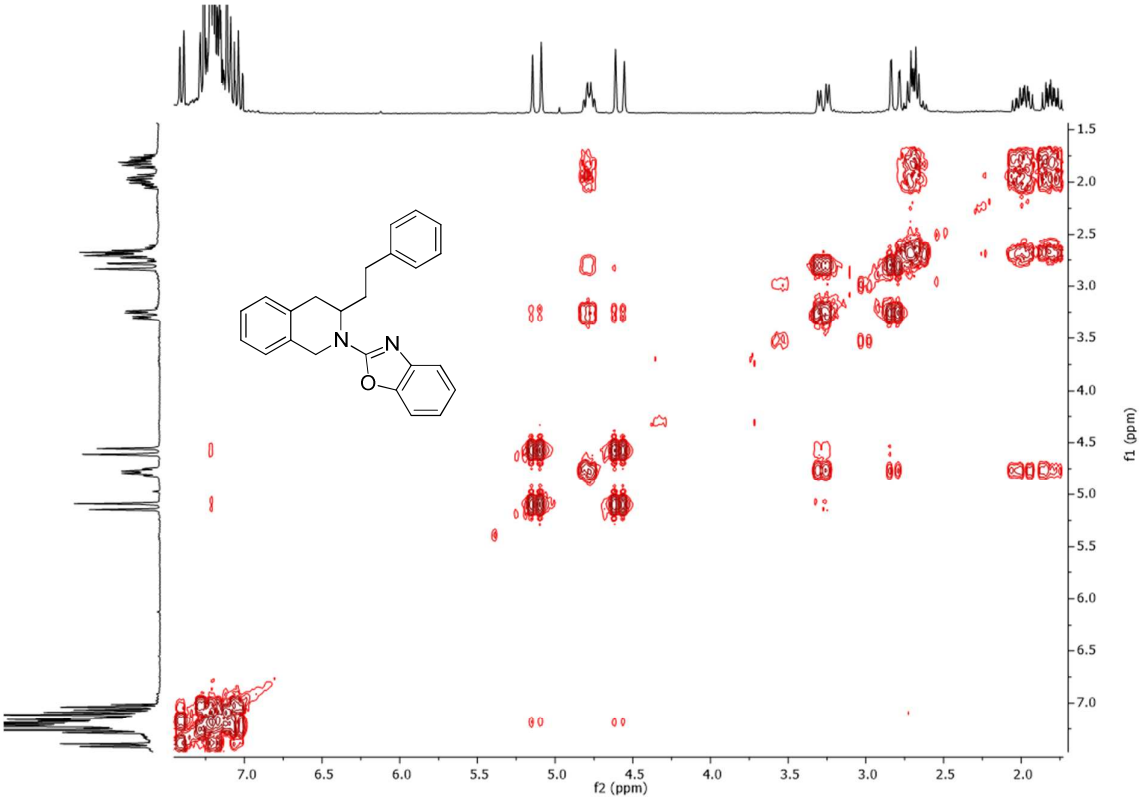
HMBC of compound 2b



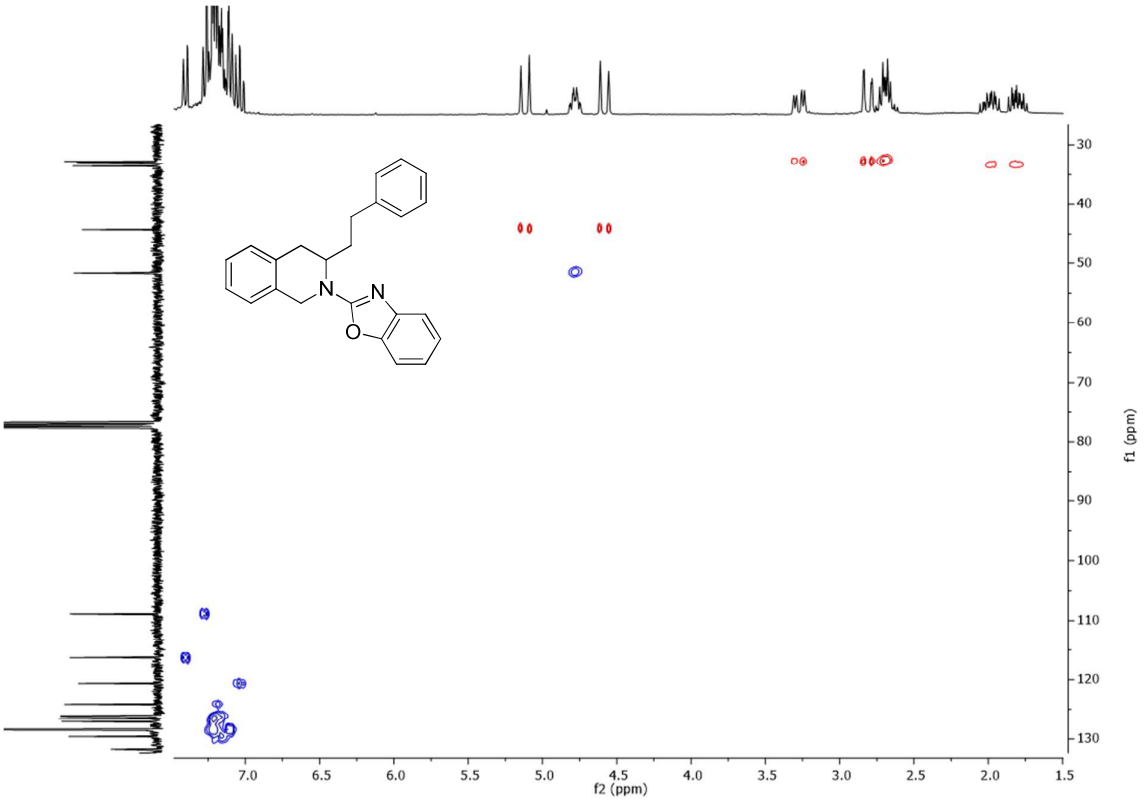
[1]H-NMR (300 MHz, $CDCl_3$) of compound 2c



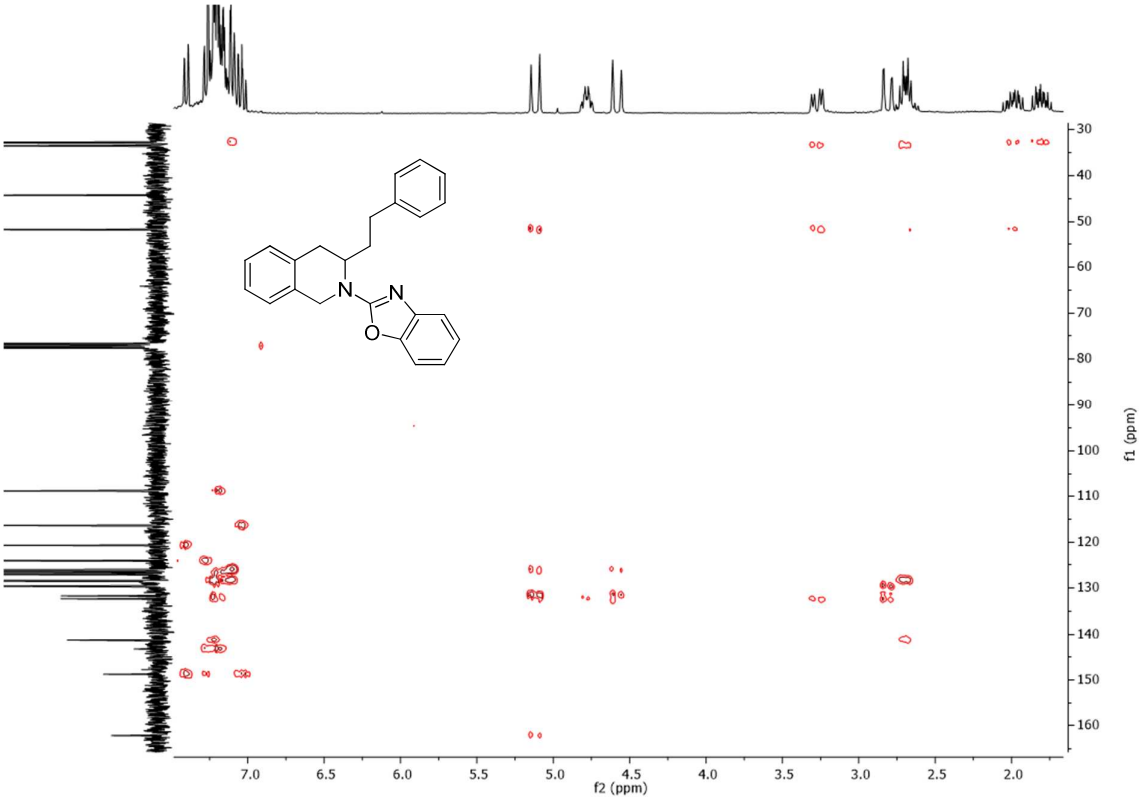
[13]C-NMR (75 MHz, $CDCl_3$) of compound 2c



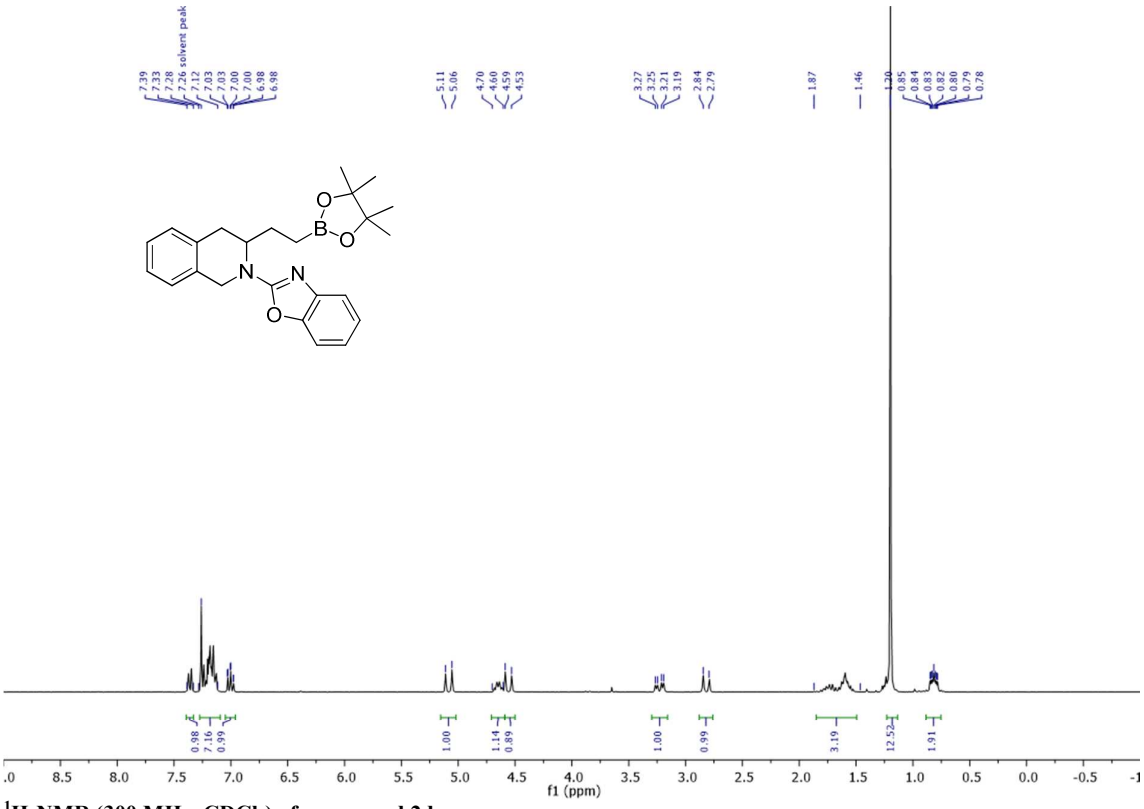
COSY of compound 2c



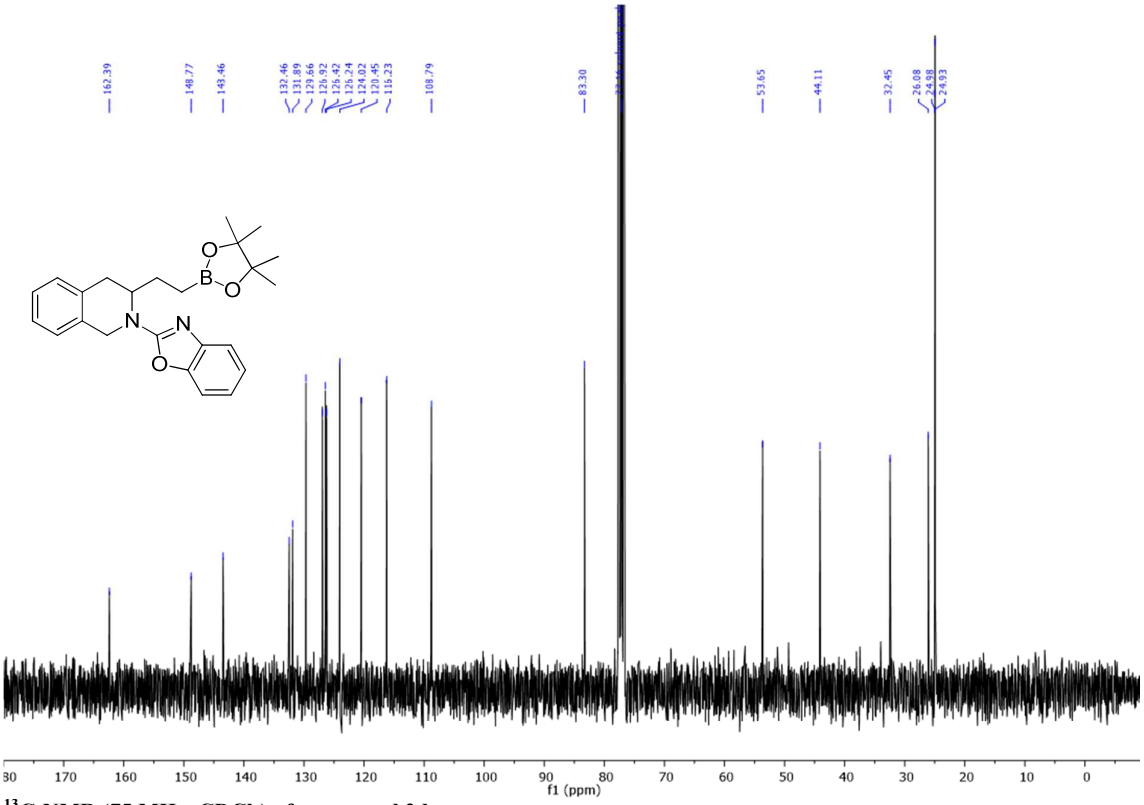
HSQC of compound 2c



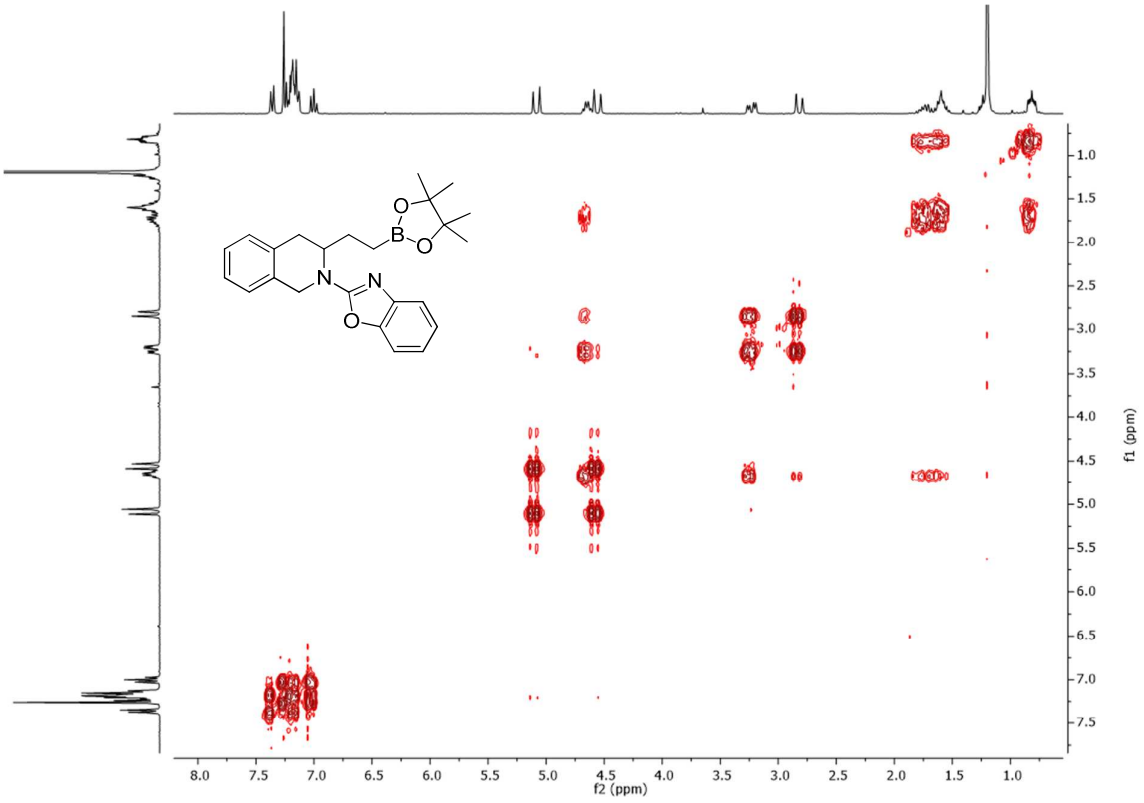
HMBC of compound 2c



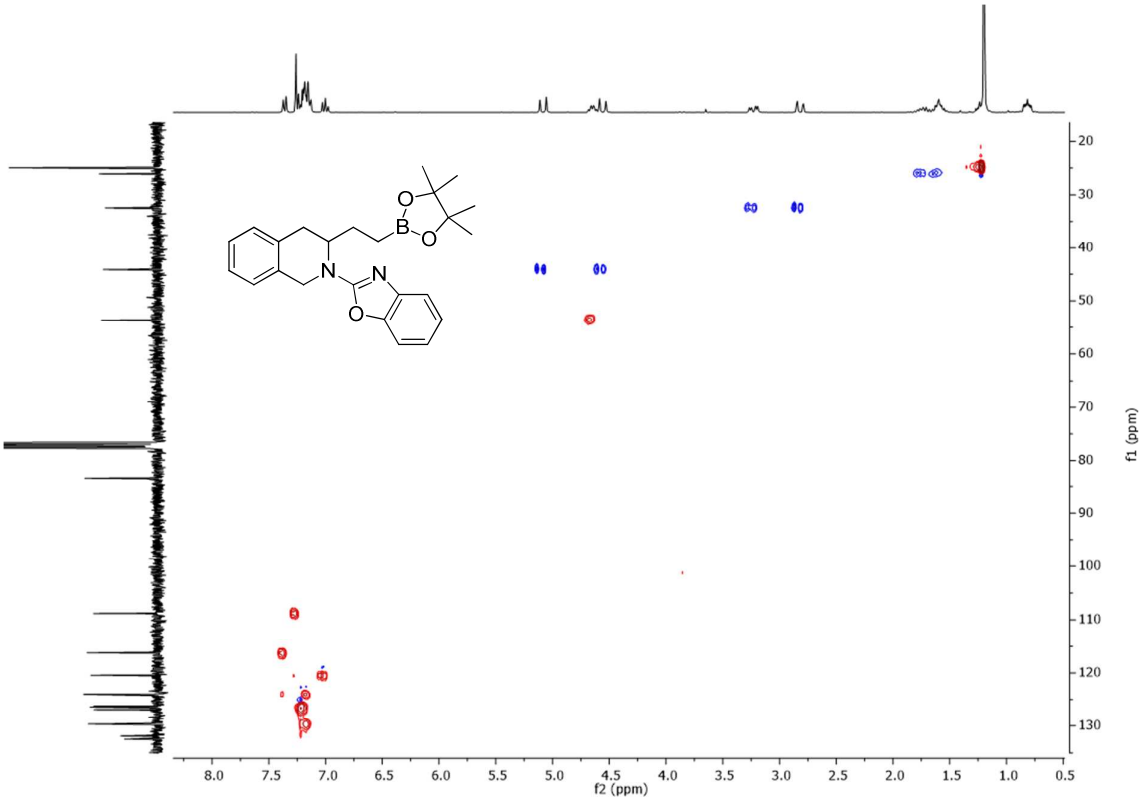
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 2d



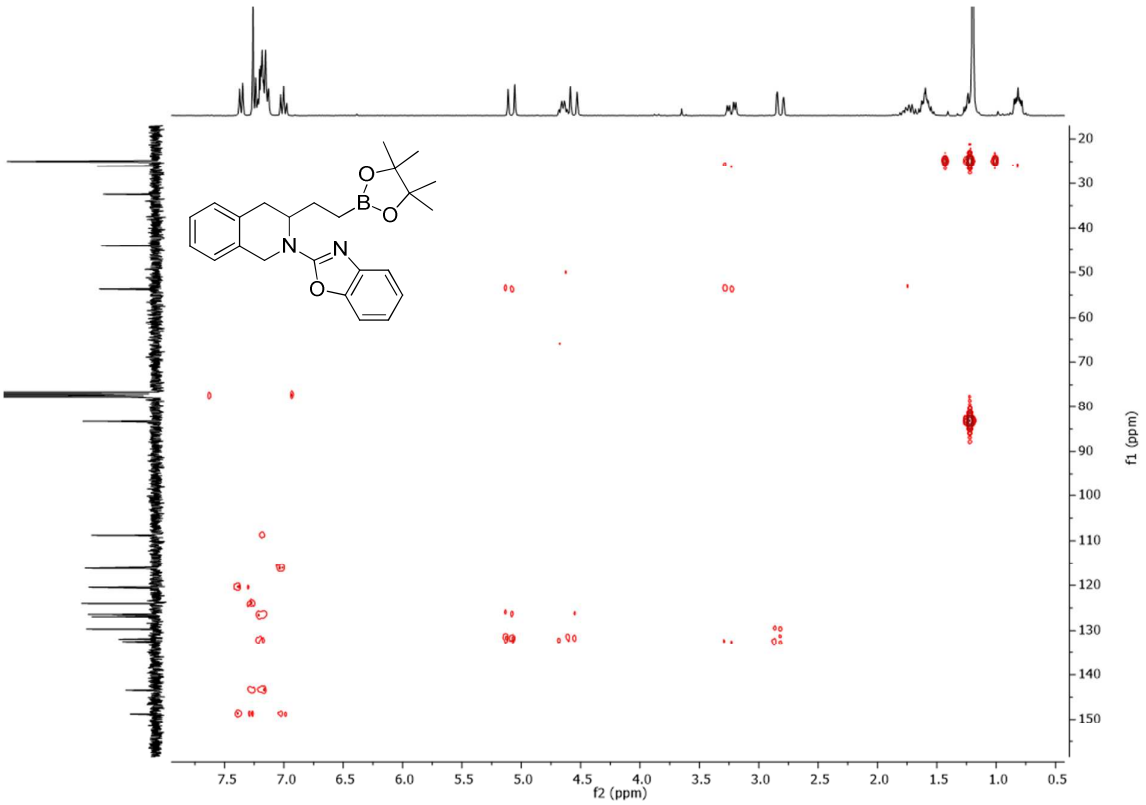
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 2d



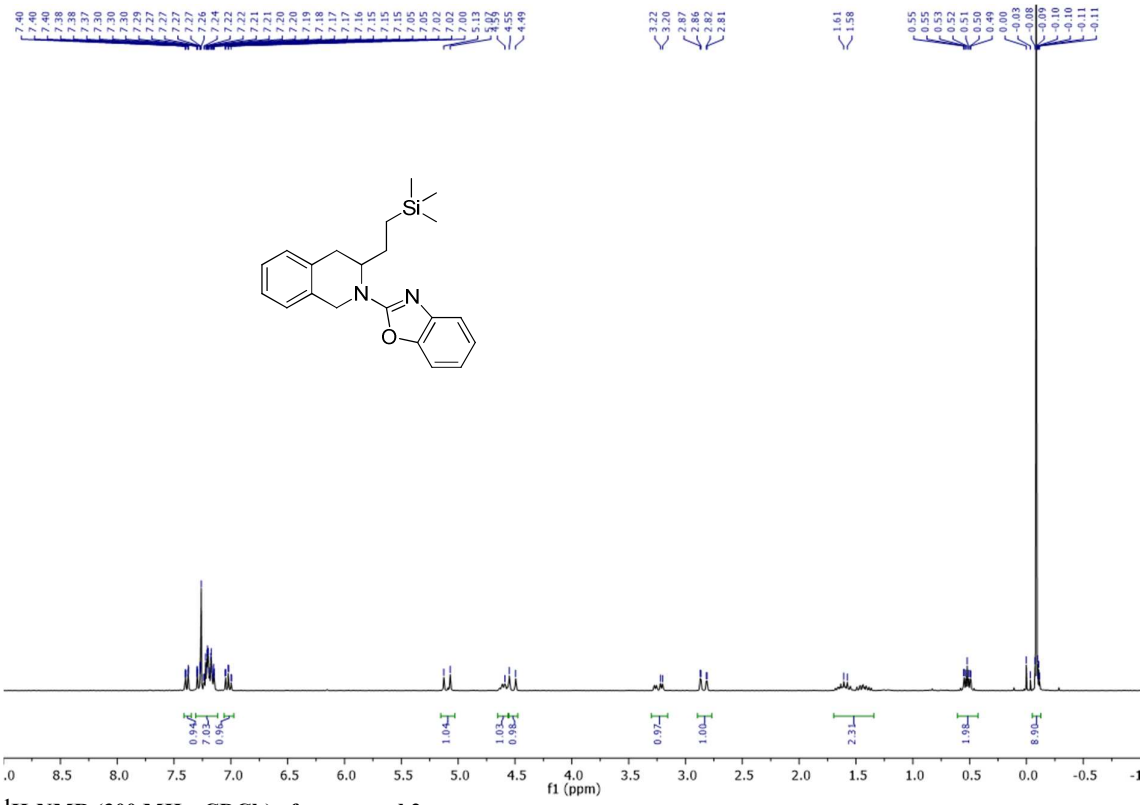
COSY of compound 2d



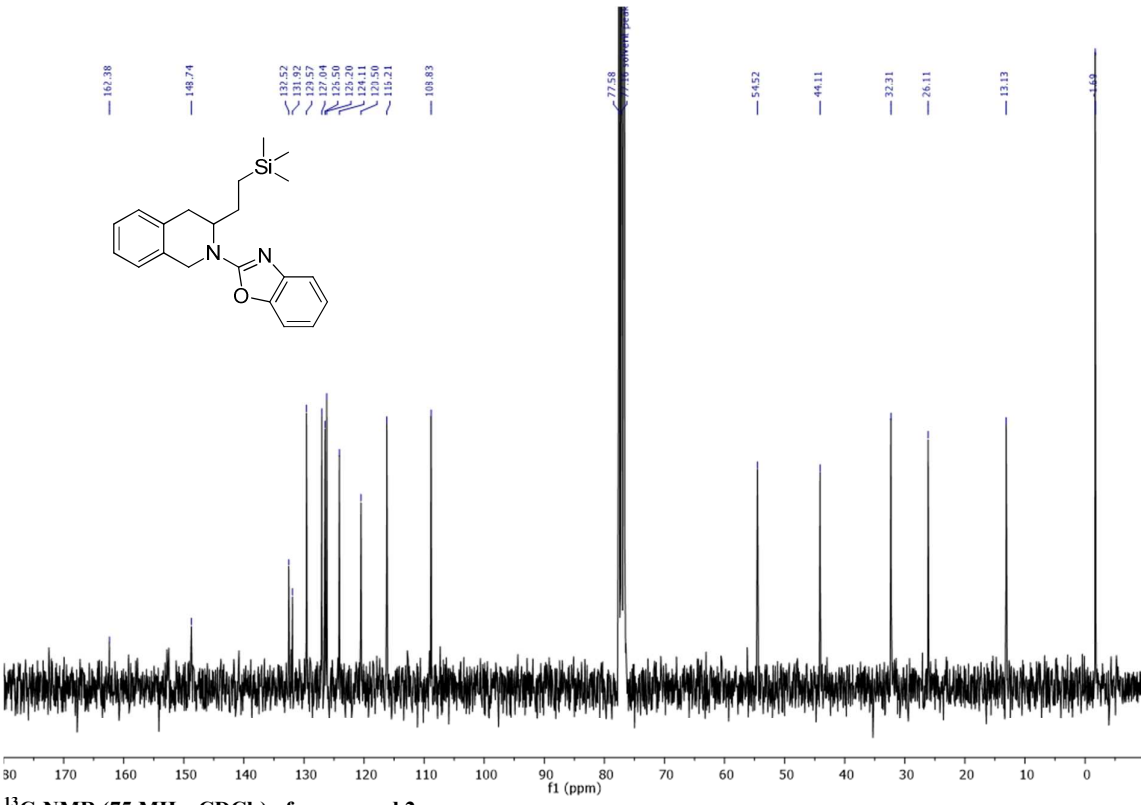
HSQC of compound 2d



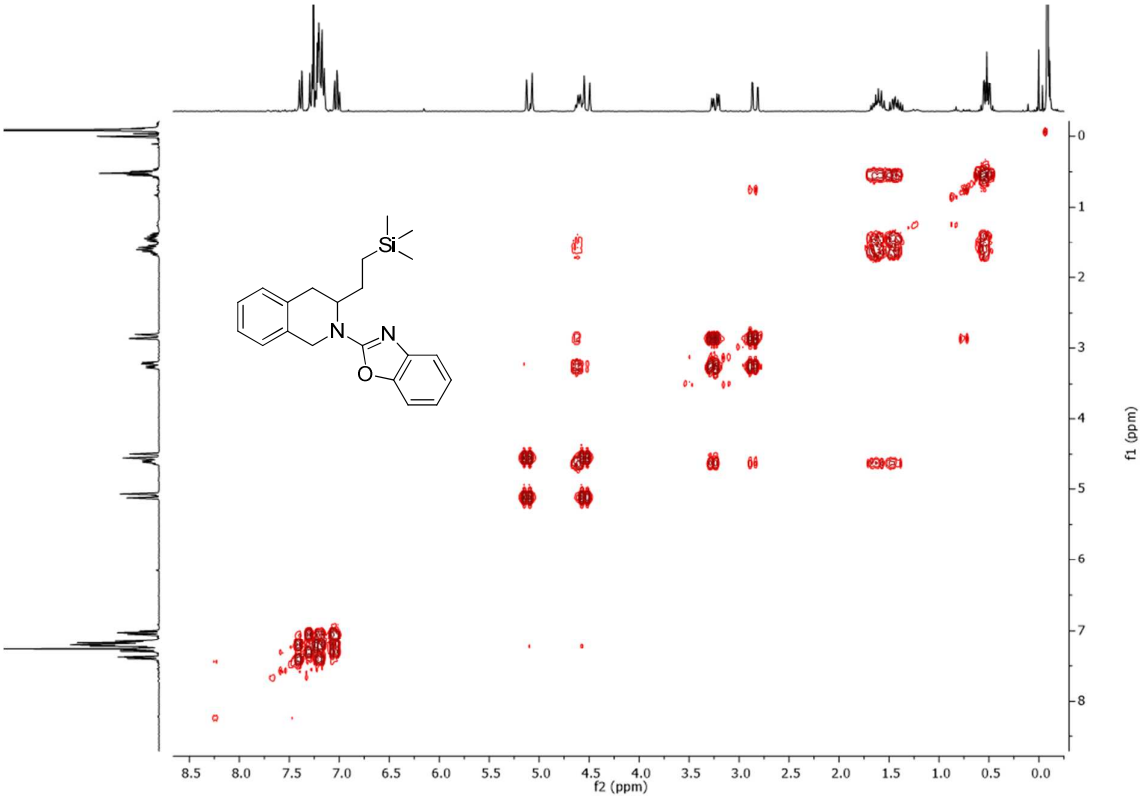
HMBC of compound 2d



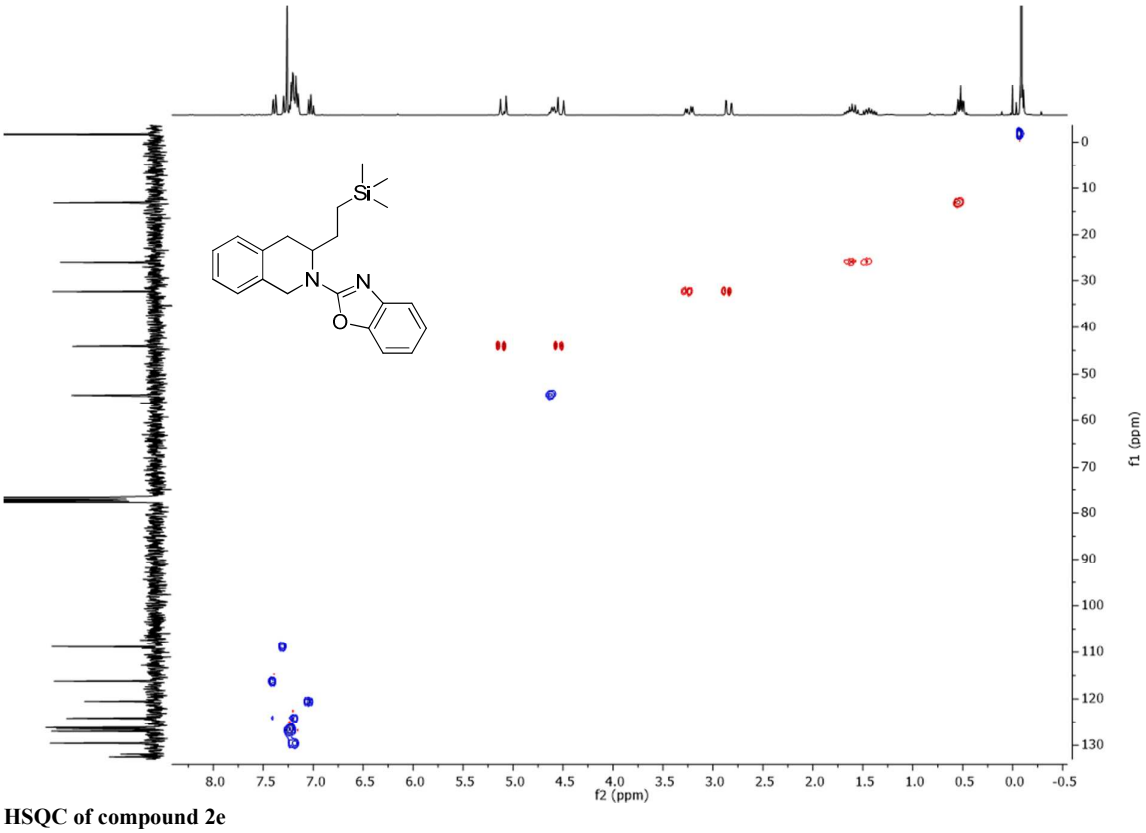
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 2e



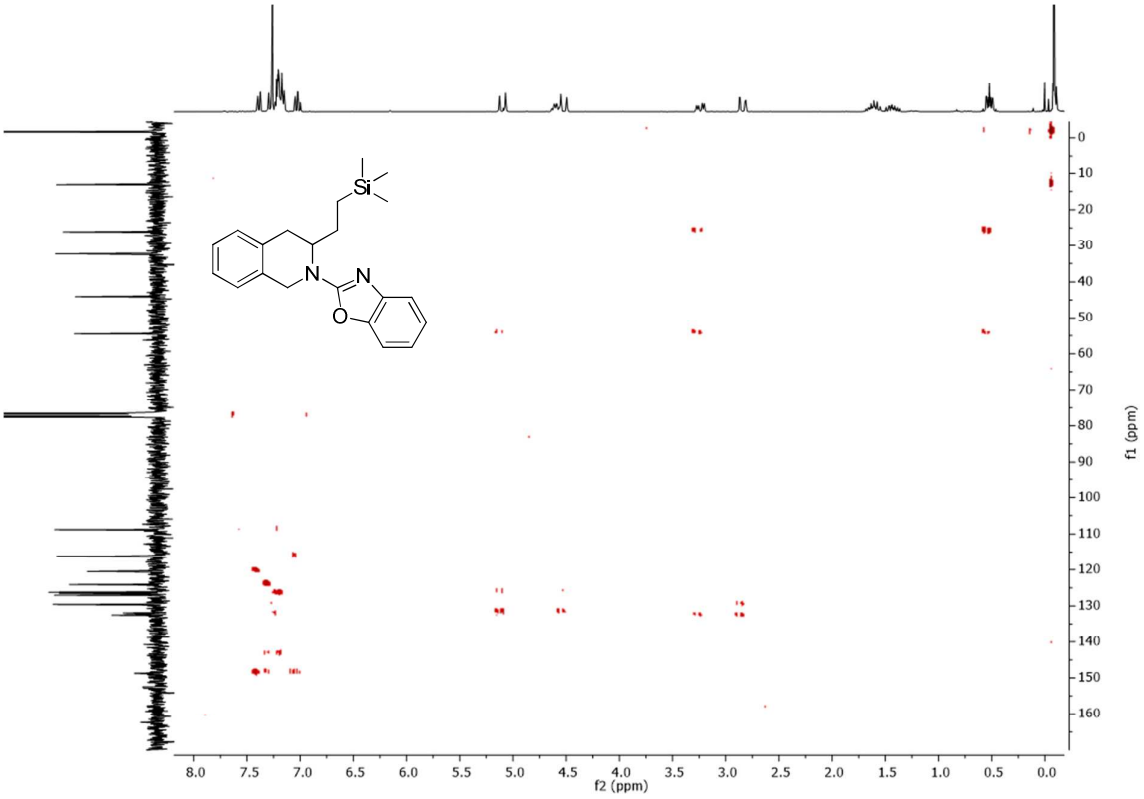
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 2e



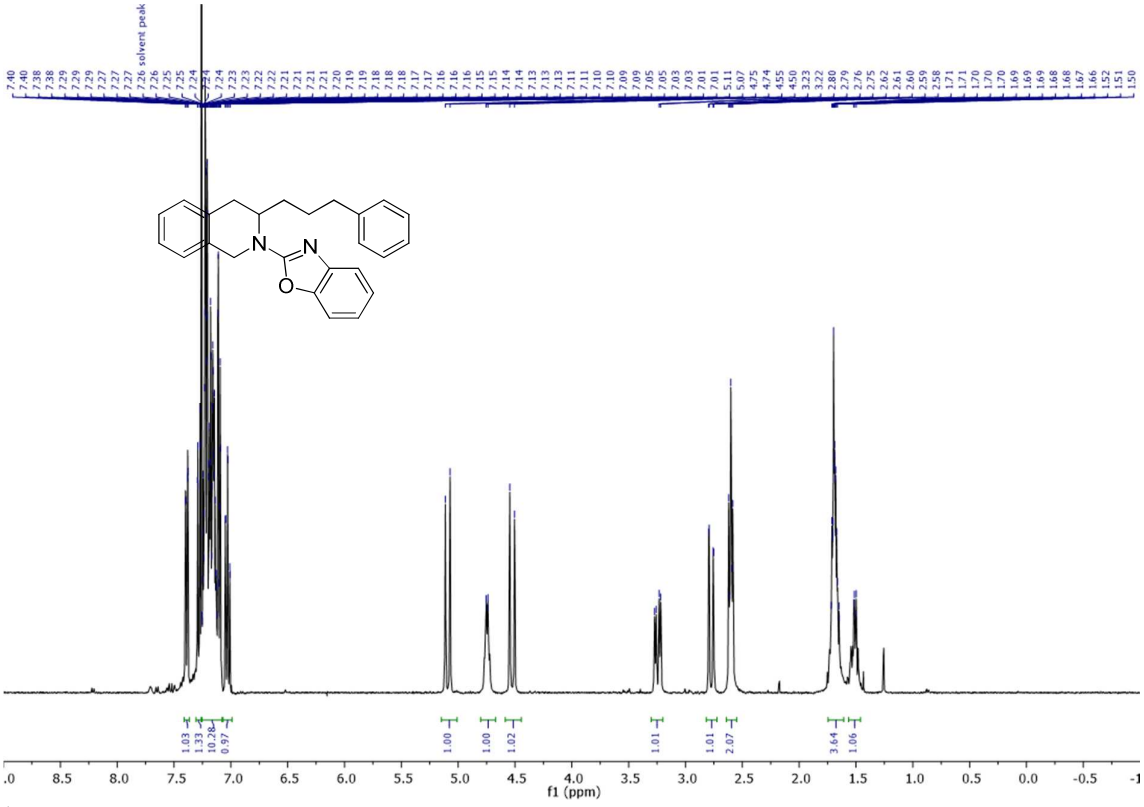
COSY of compound 2e



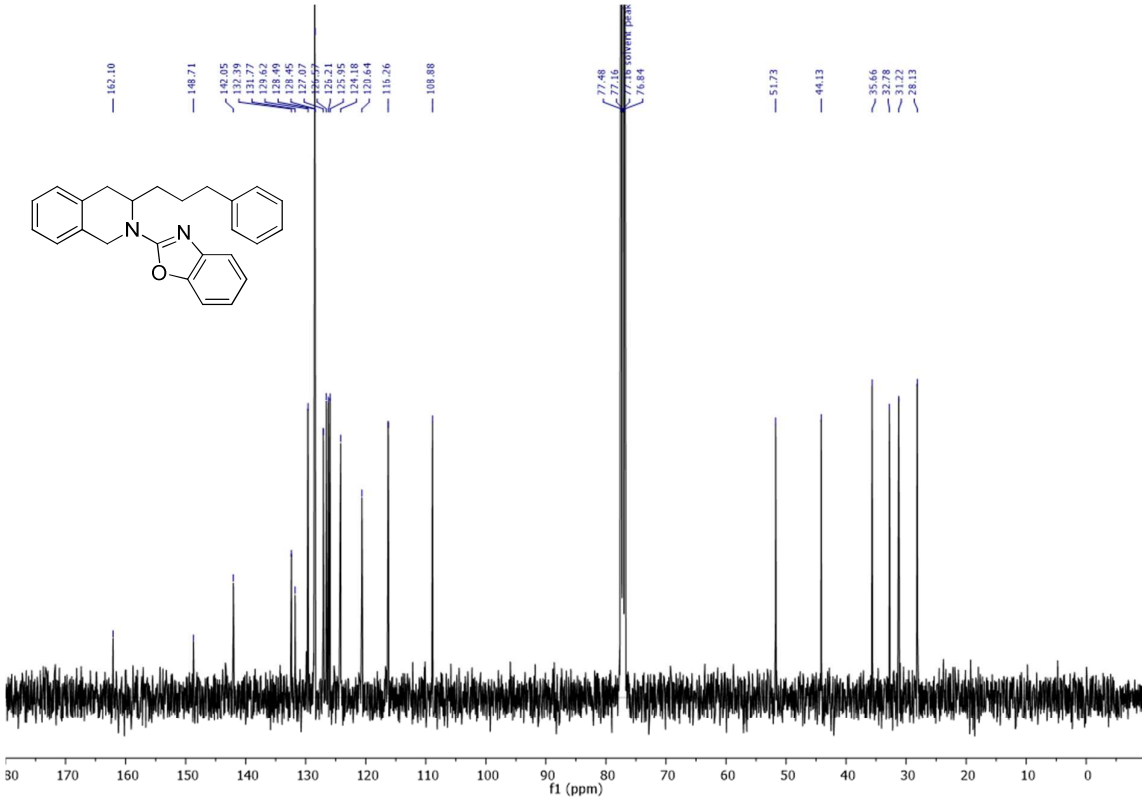
HSQC of compound 2e



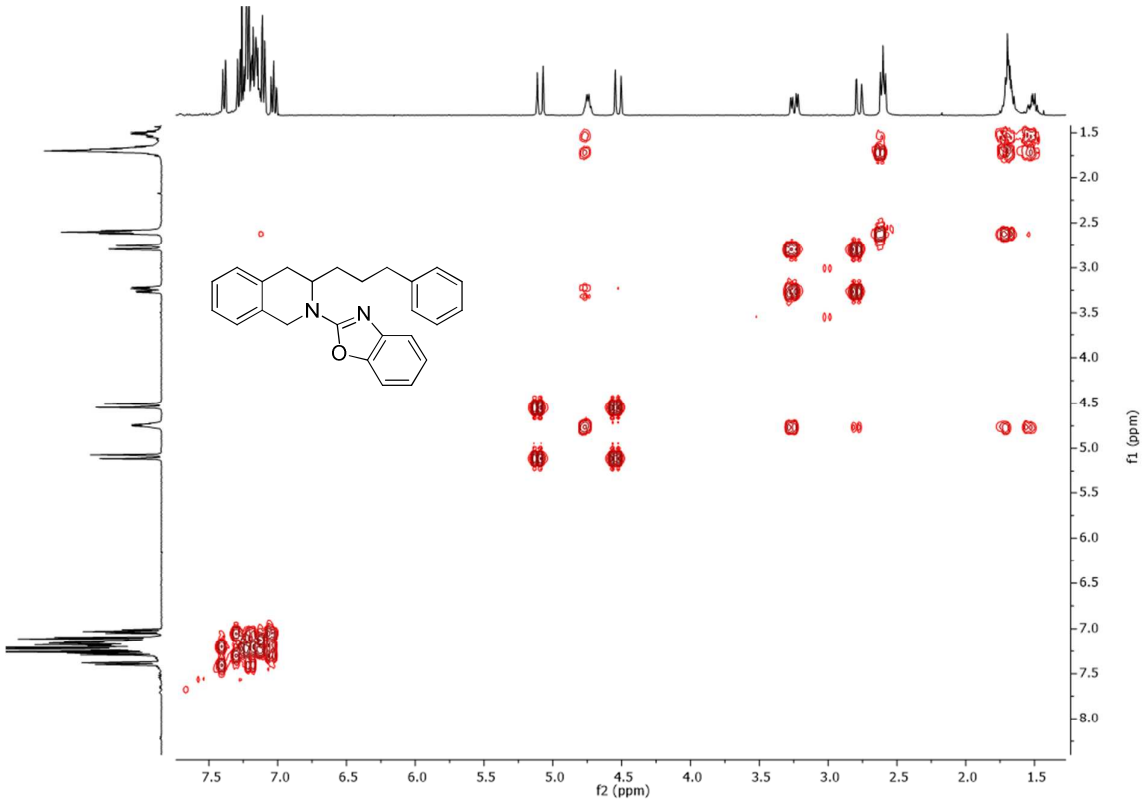
HMBC of compound 2e



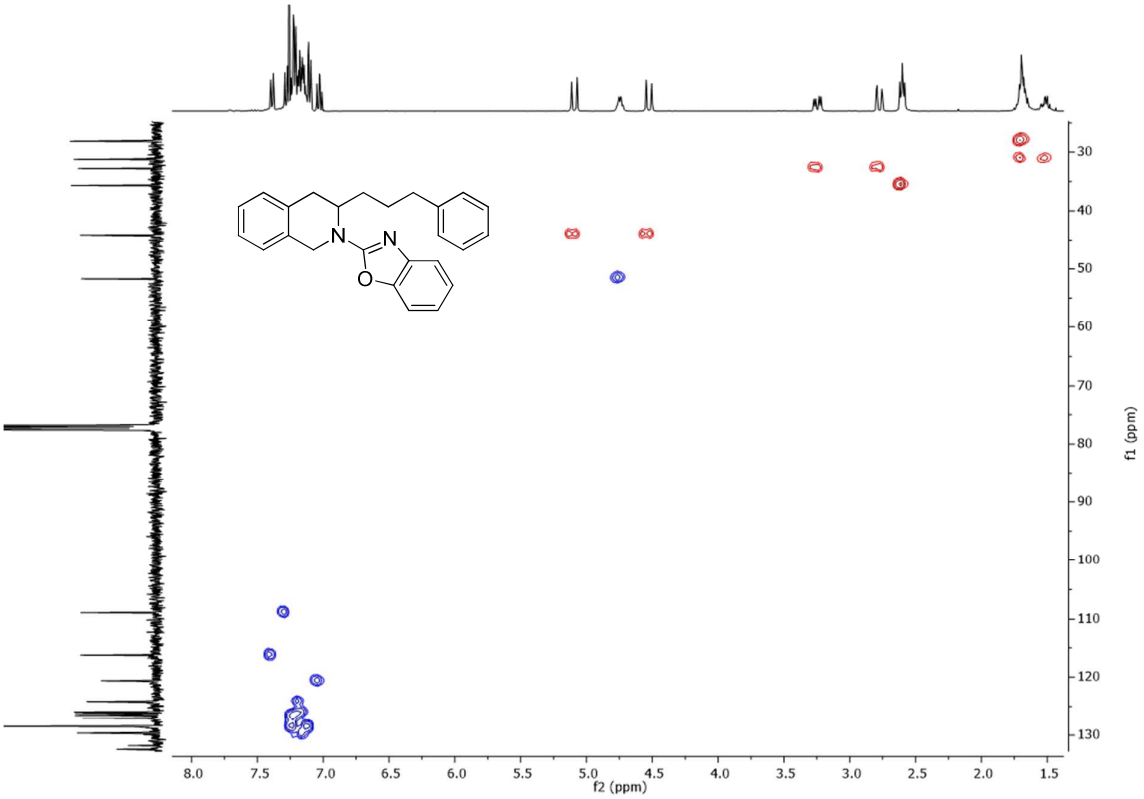
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 2f



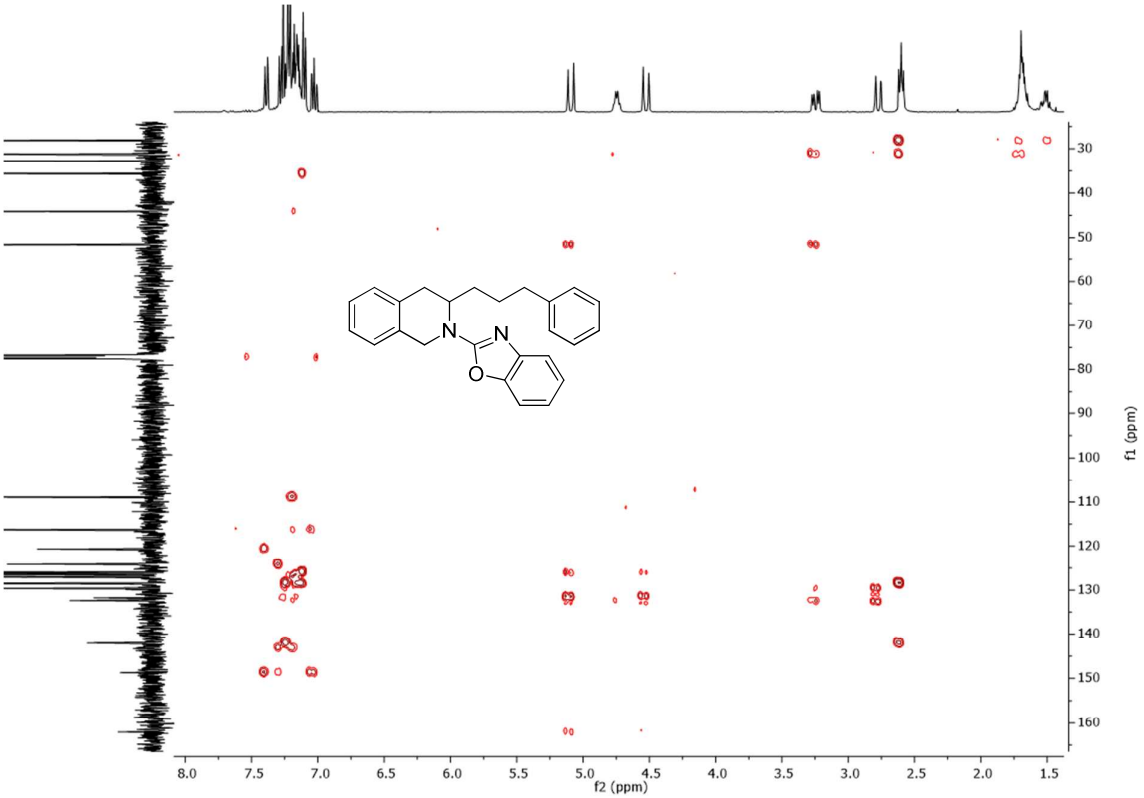
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 2f



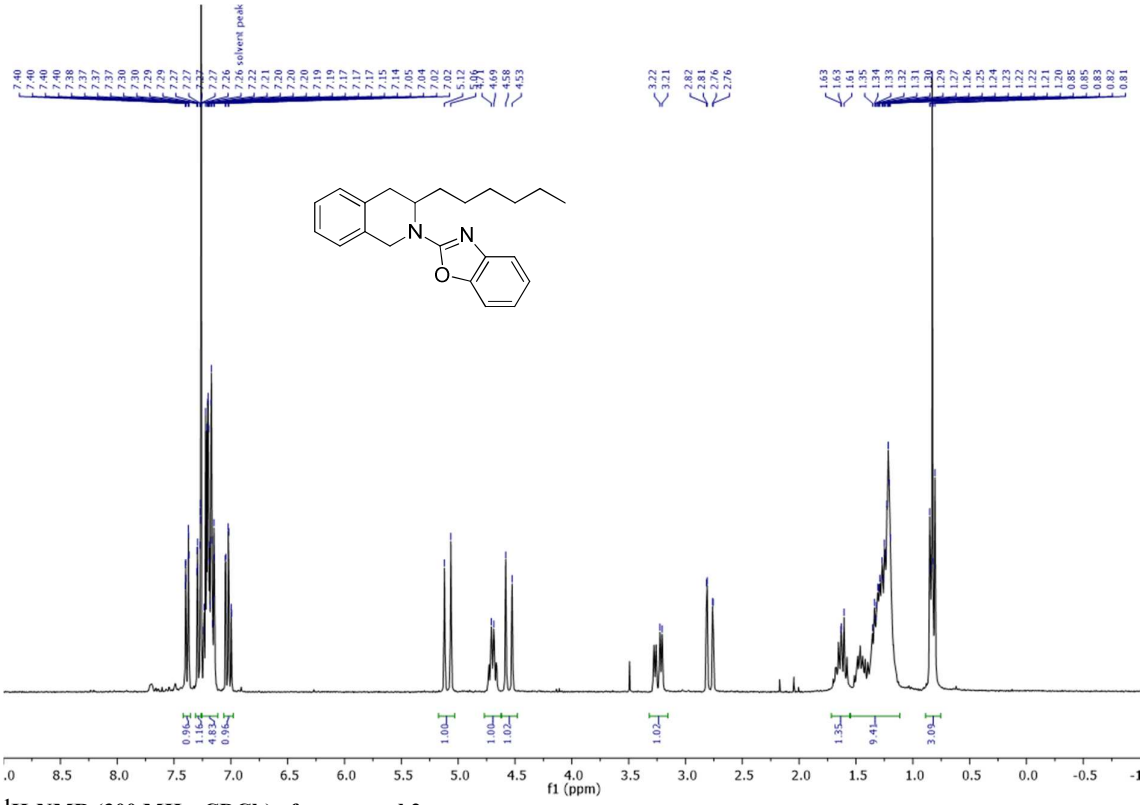
COSY of compound 2f



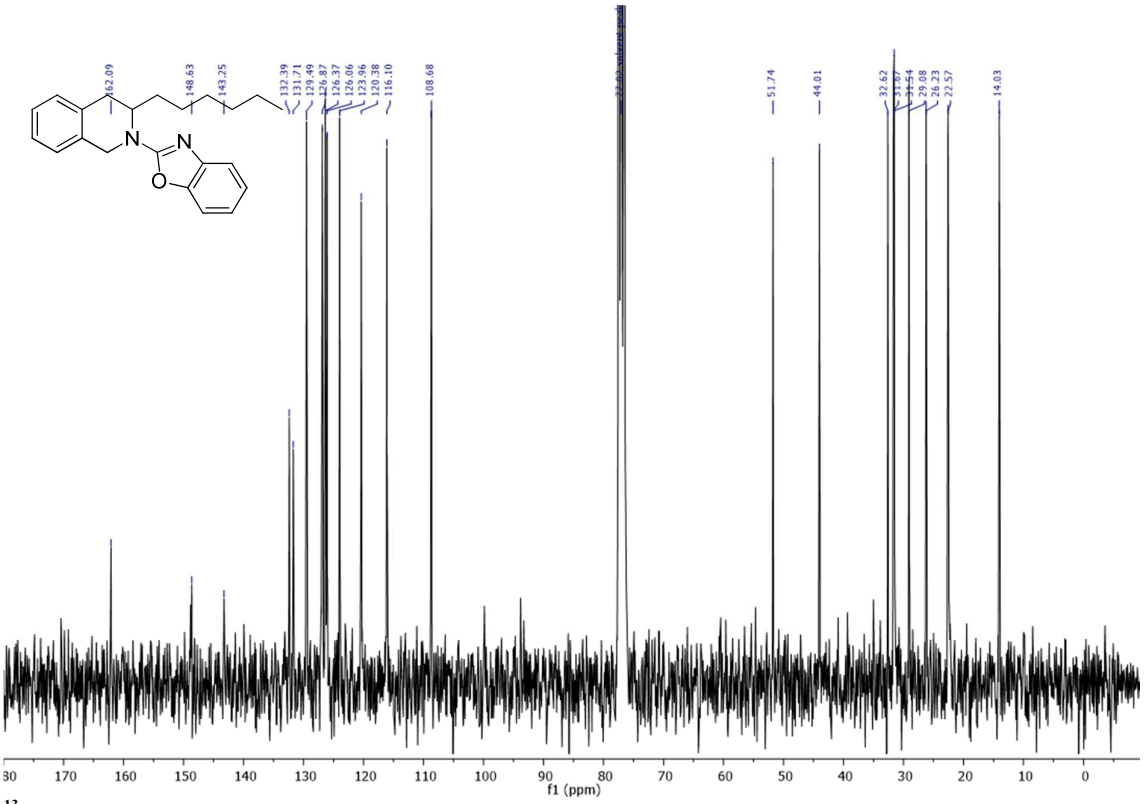
HSQC of compound 2f



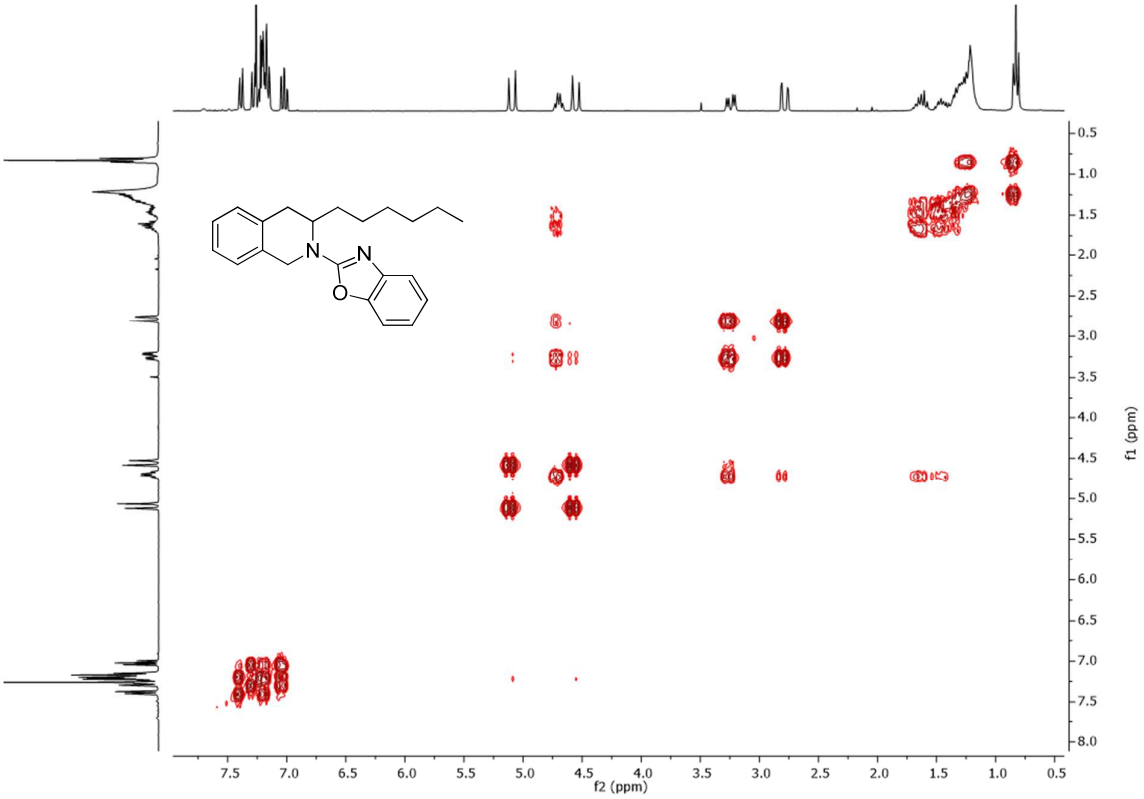
HMBC of compound 2f



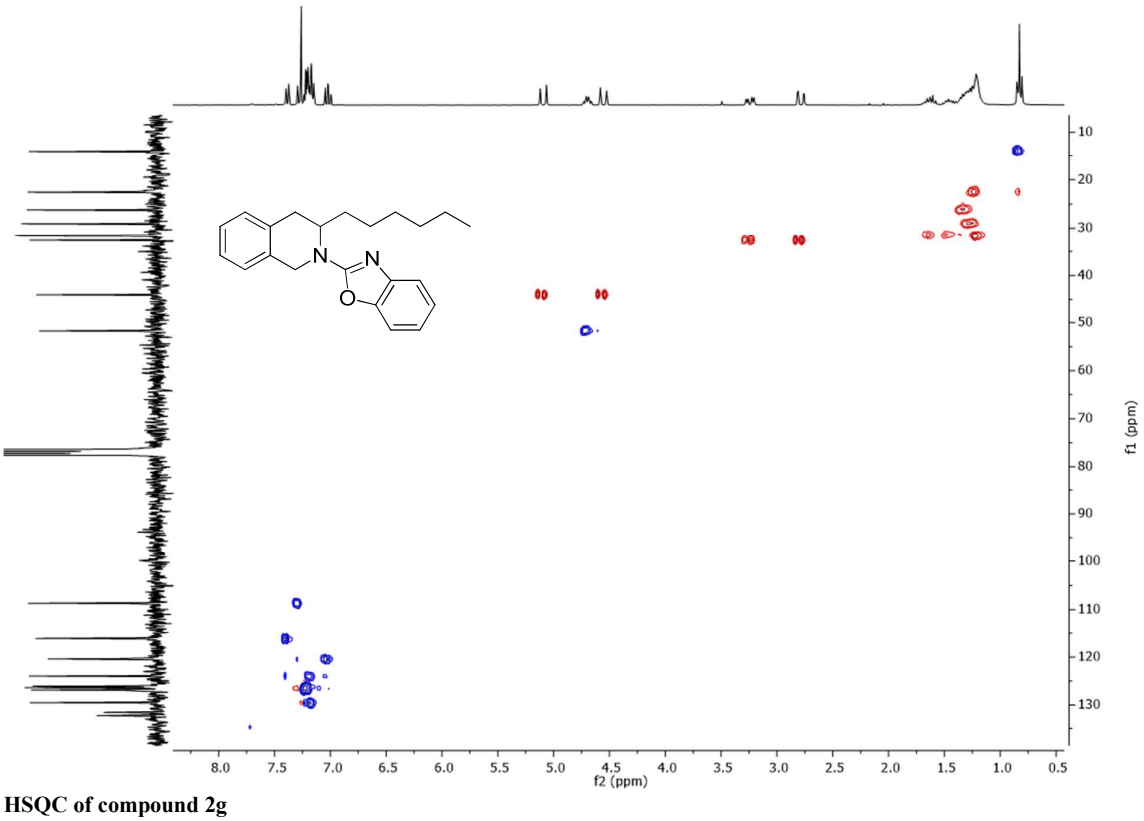
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 2g



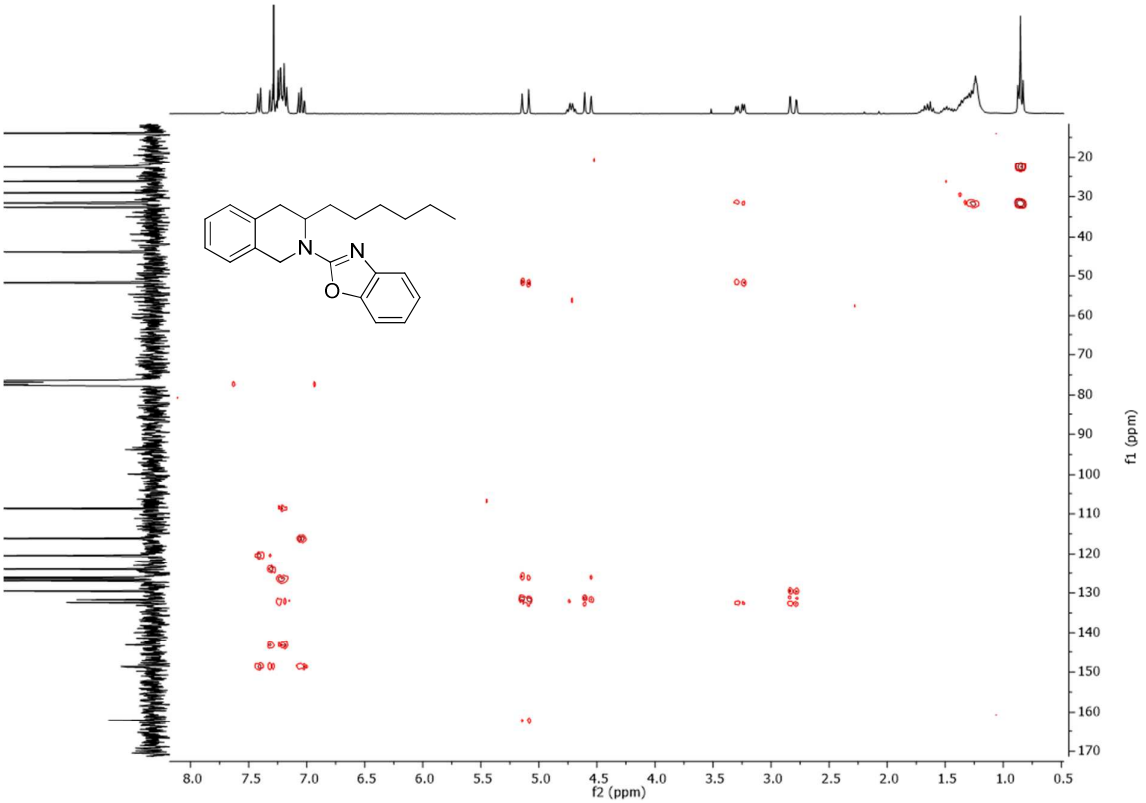
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 2g



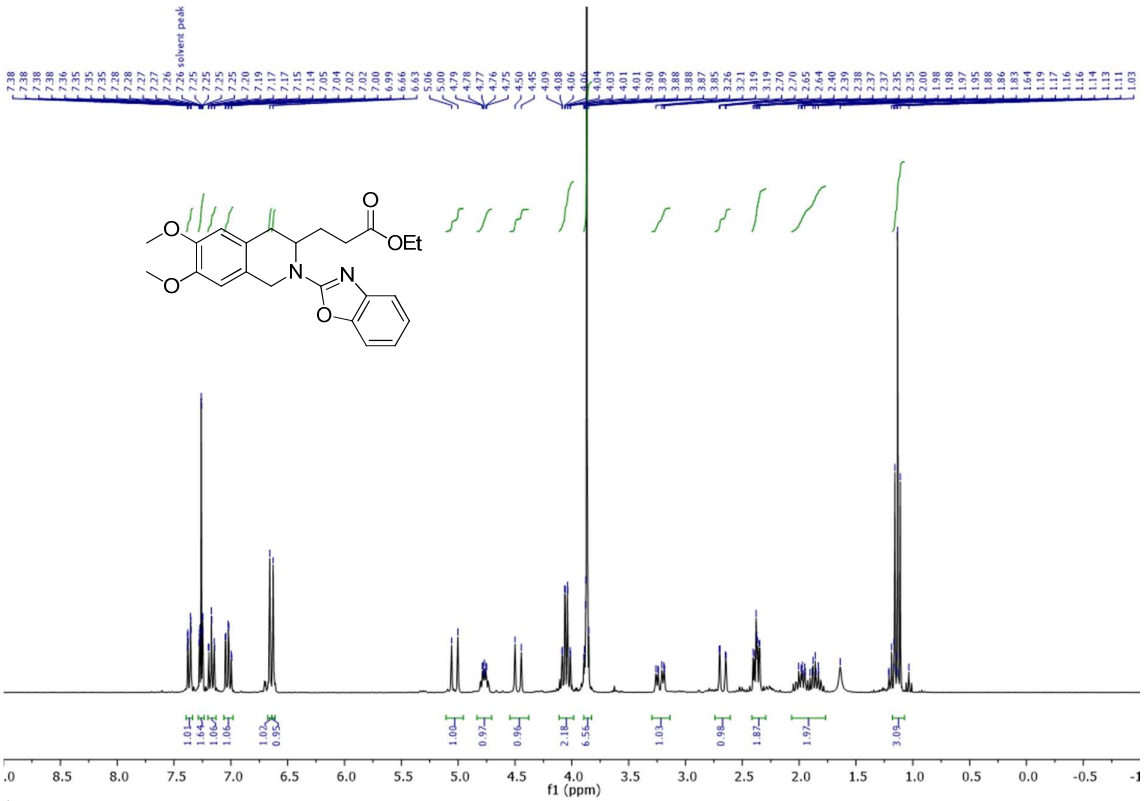
COSY of compound 2g



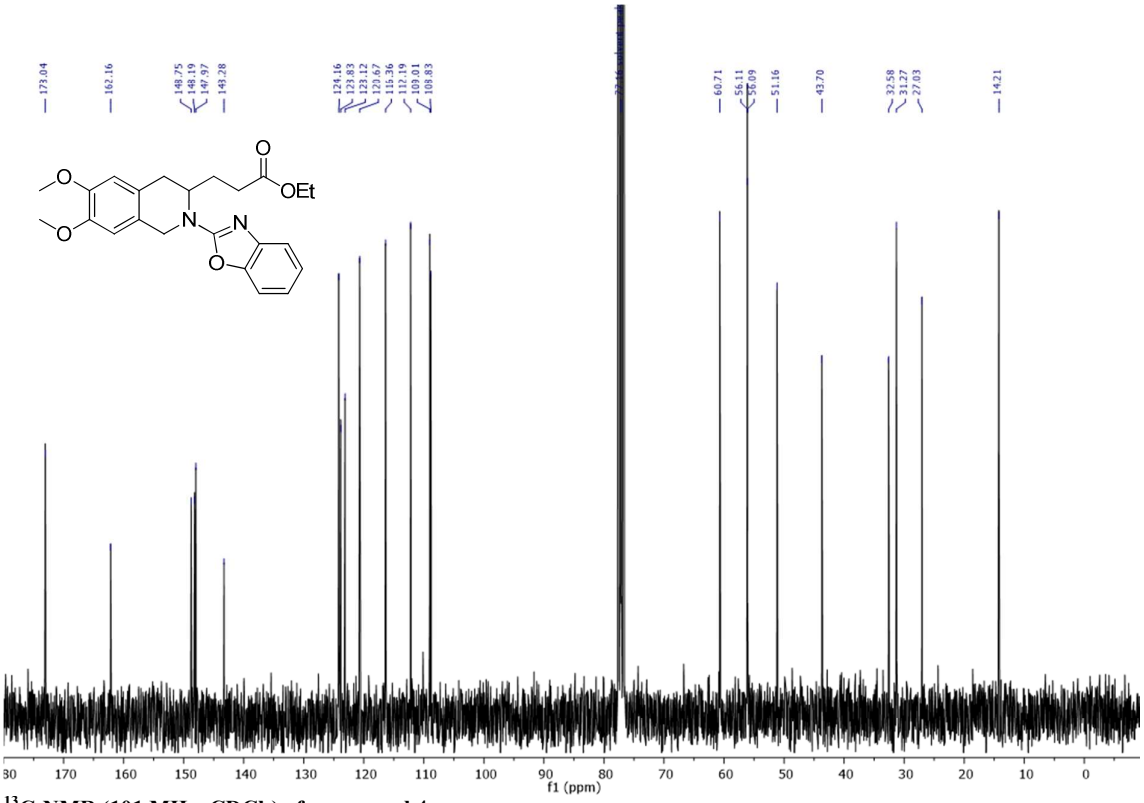
HSQC of compound 2g



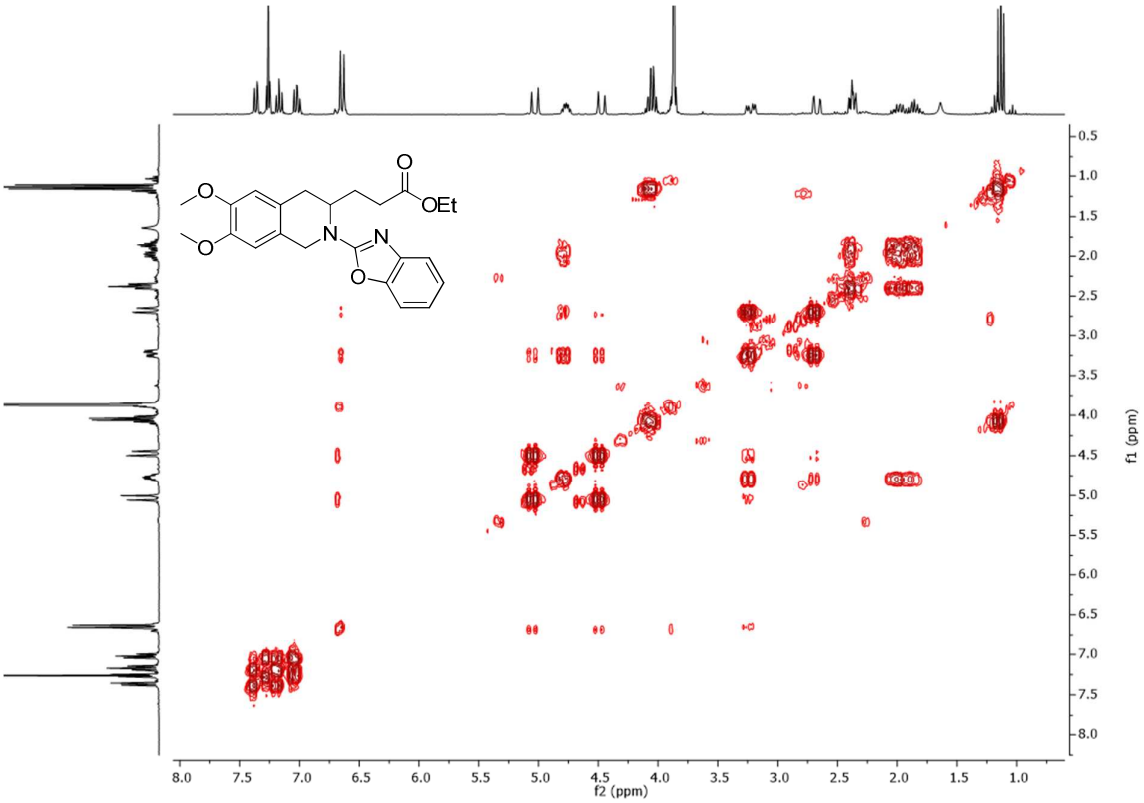
HMBC of compound 2g



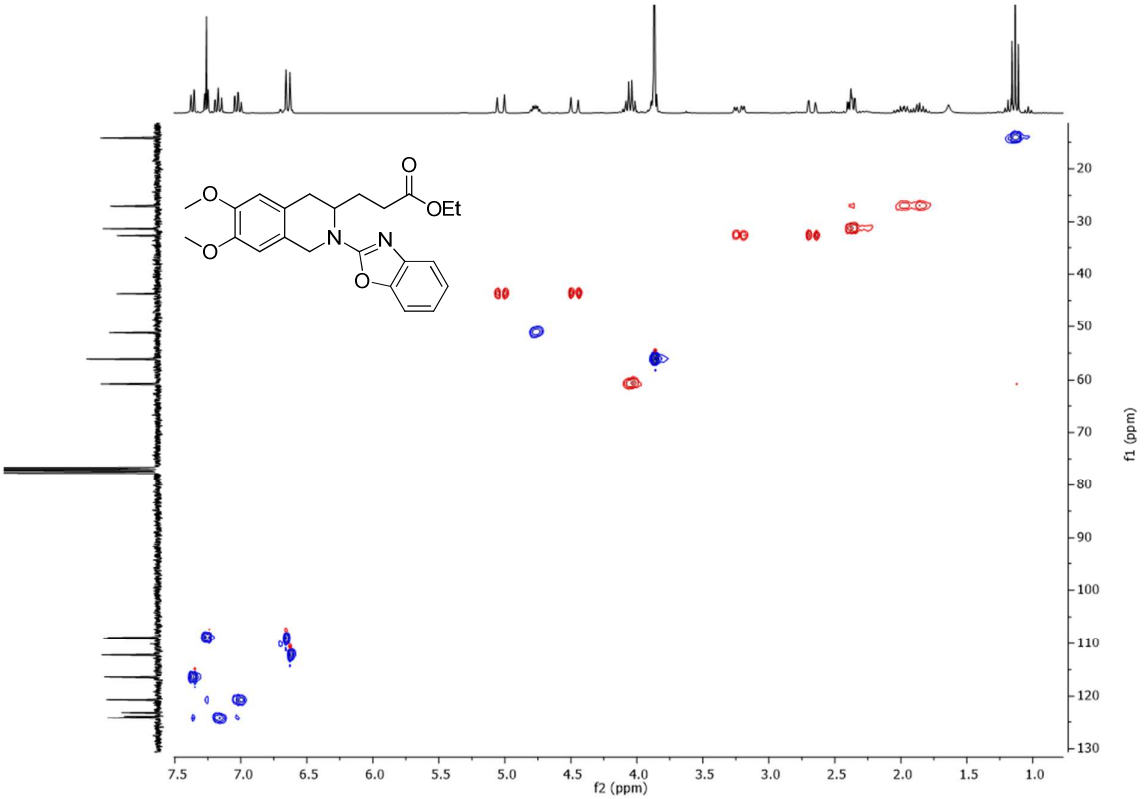
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 4a



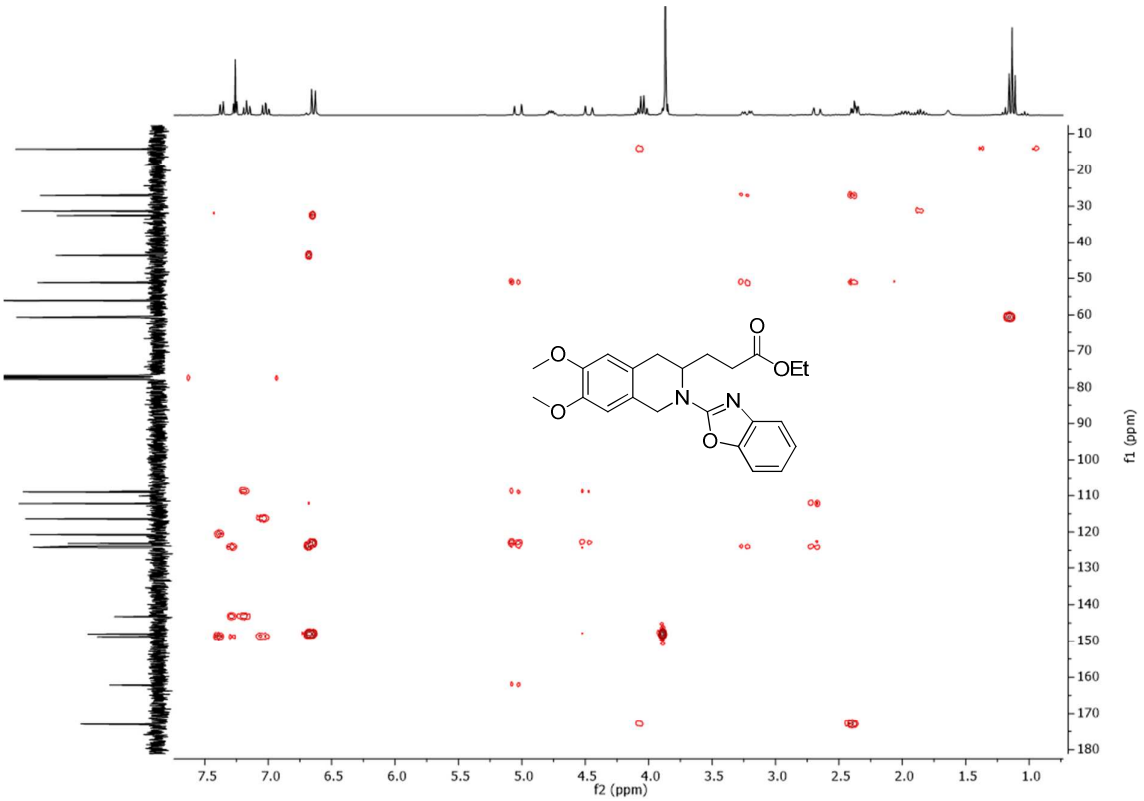
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 4a



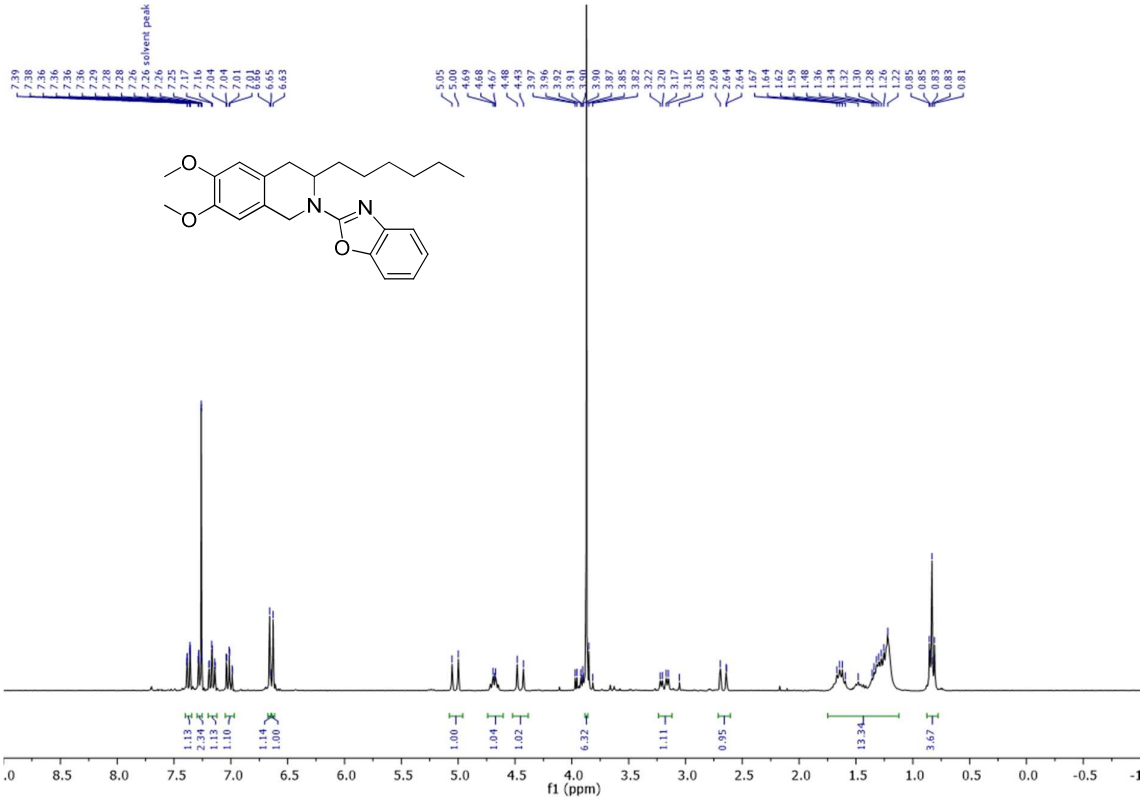
COSY of compound 4a



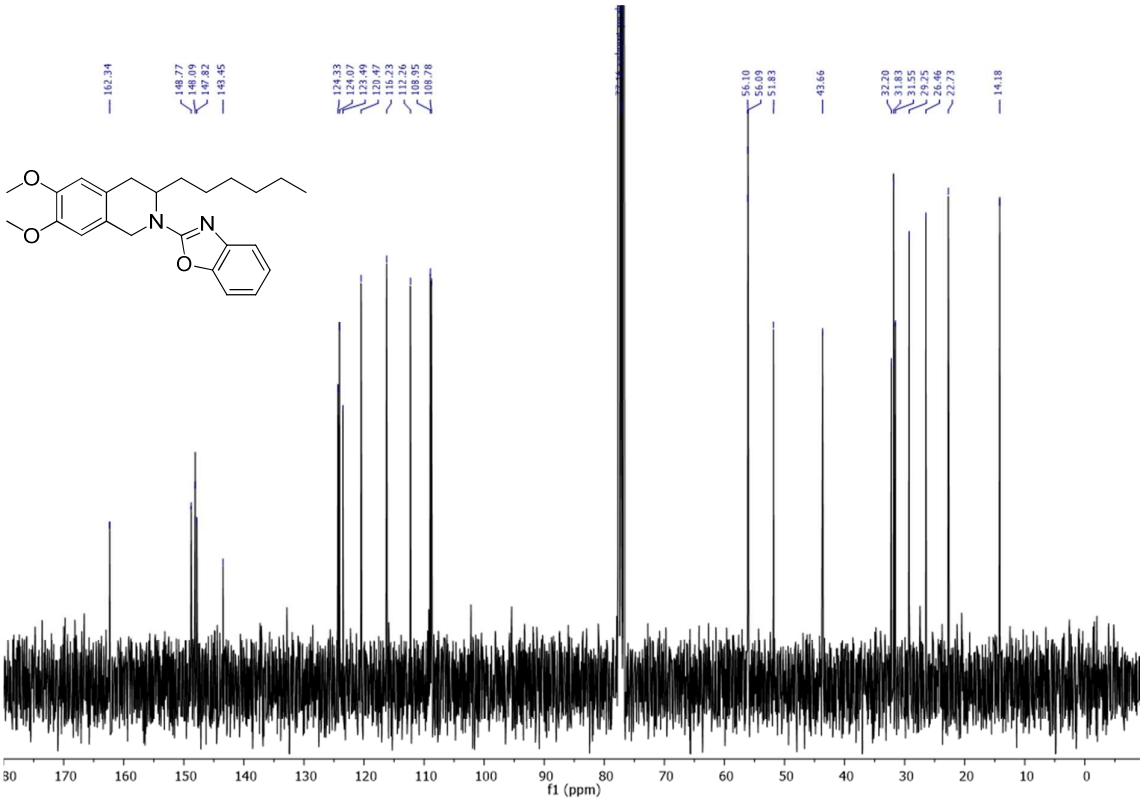
HSQC of compound 4a



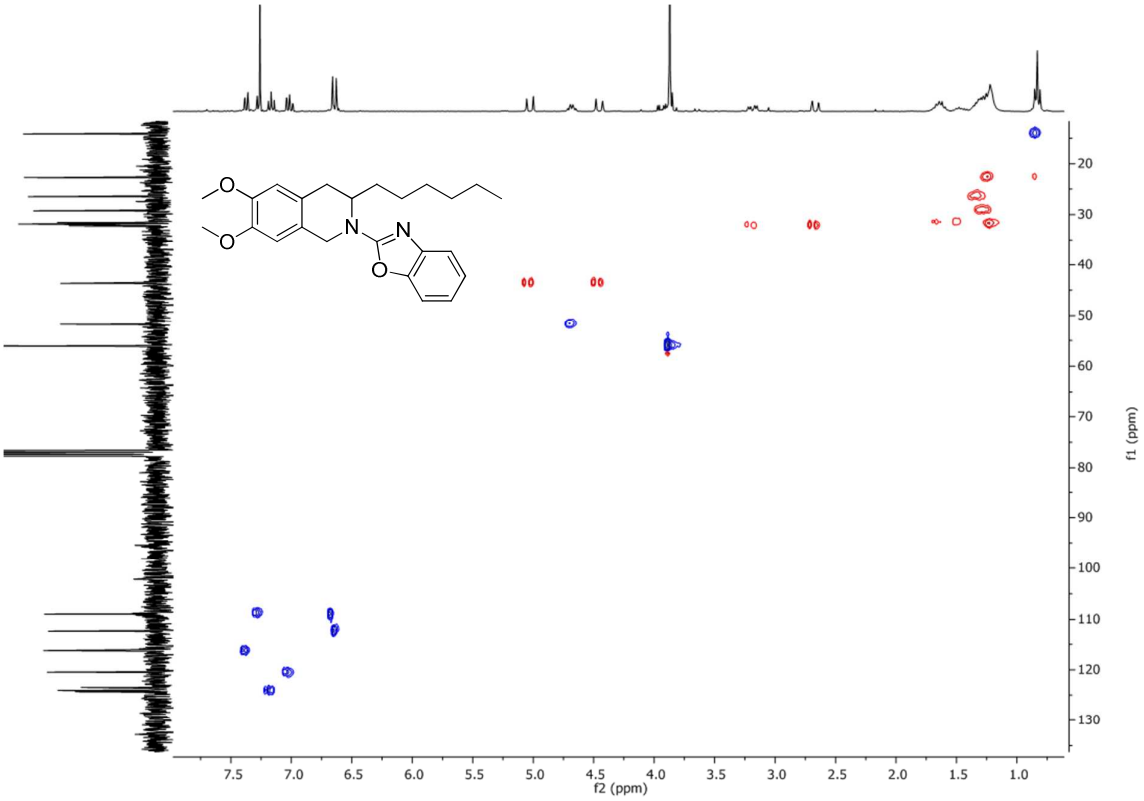
HMBC of compound 4a



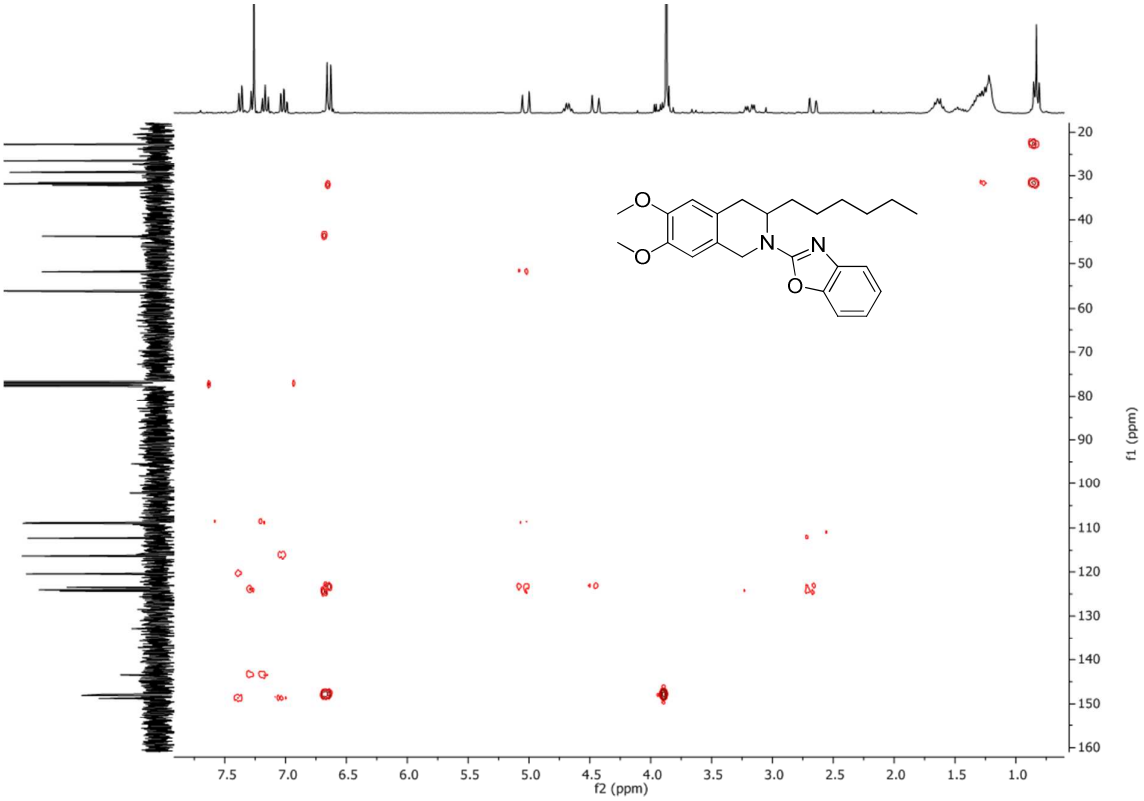
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 4b



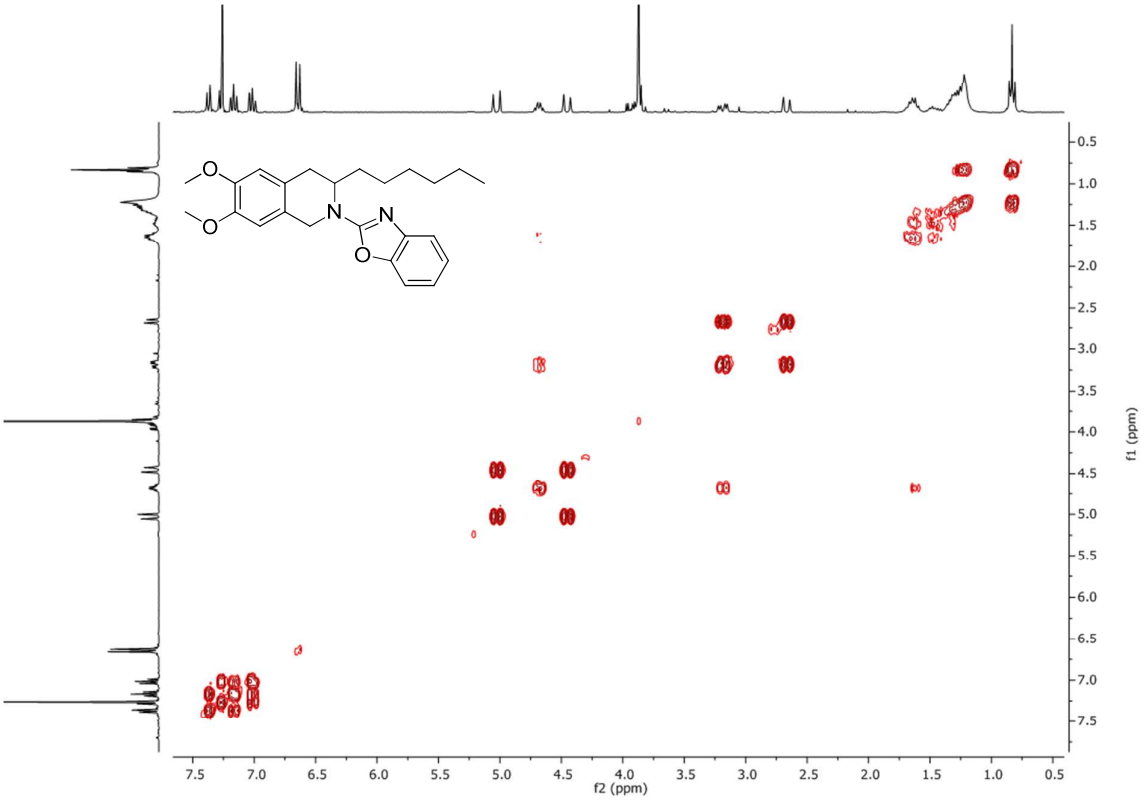
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 4b



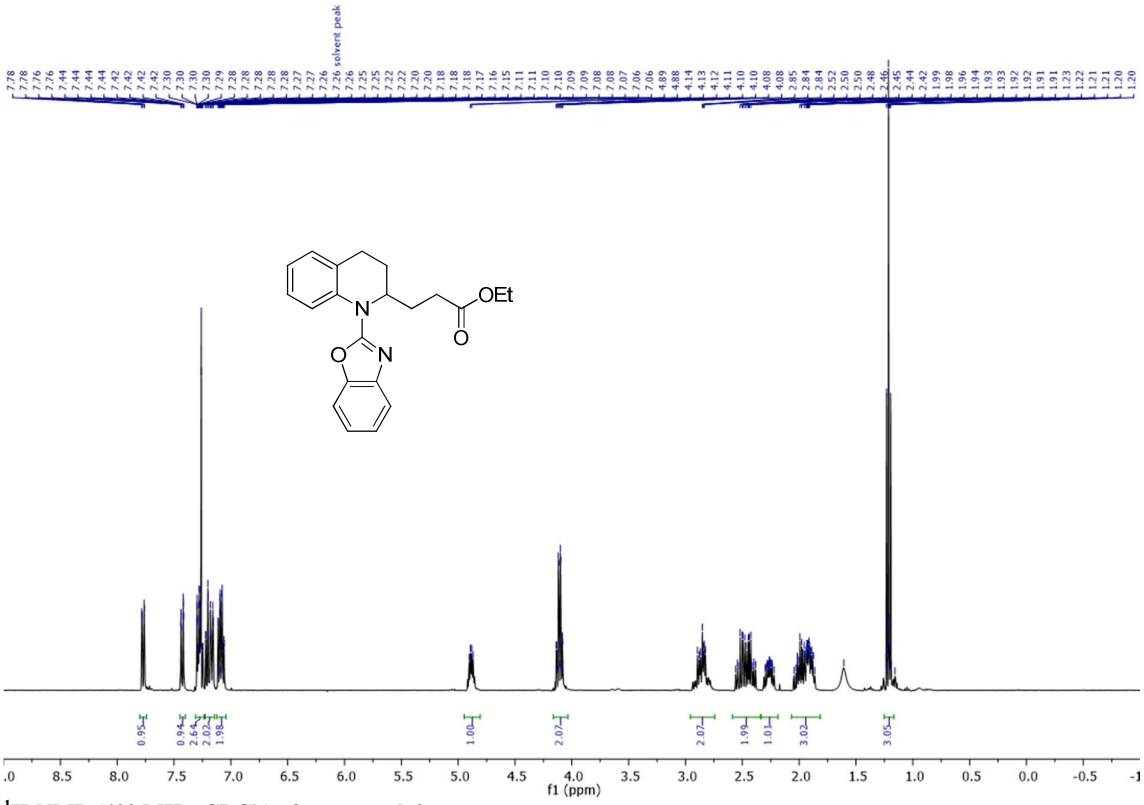
COSY of compound 4b



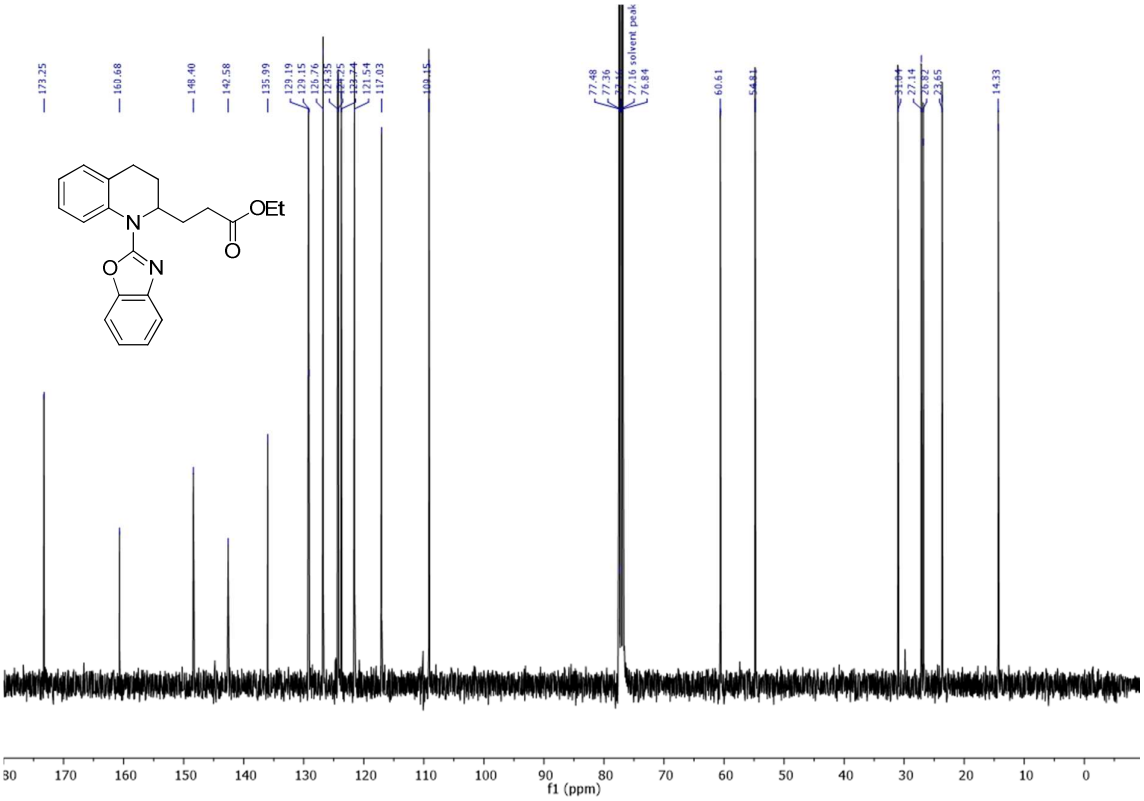
HSQC of compound 4b



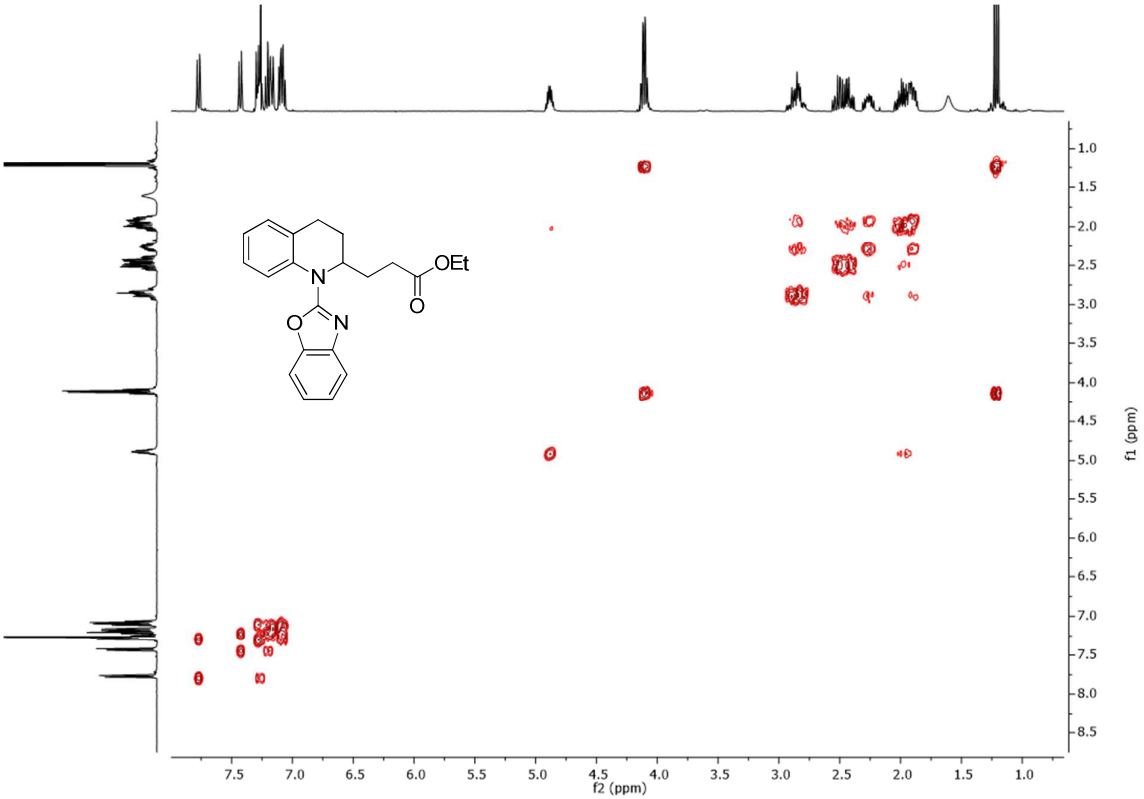
HMBC of compound 4b



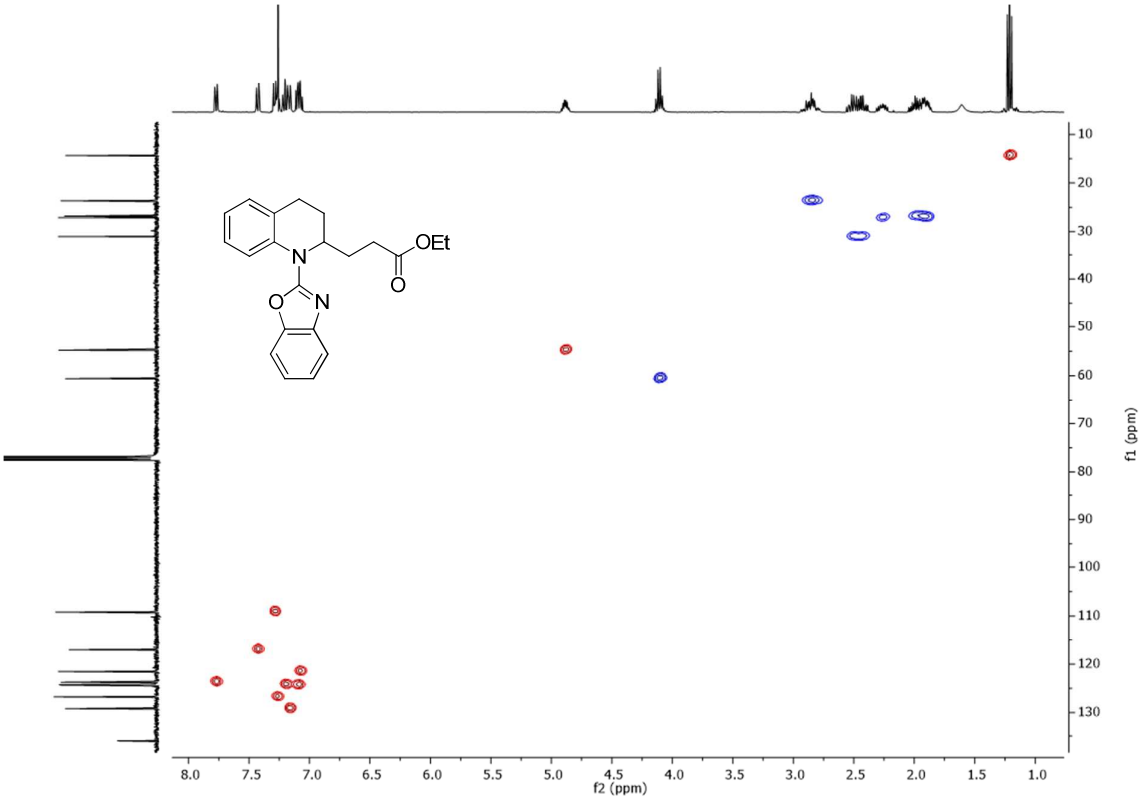
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 6a



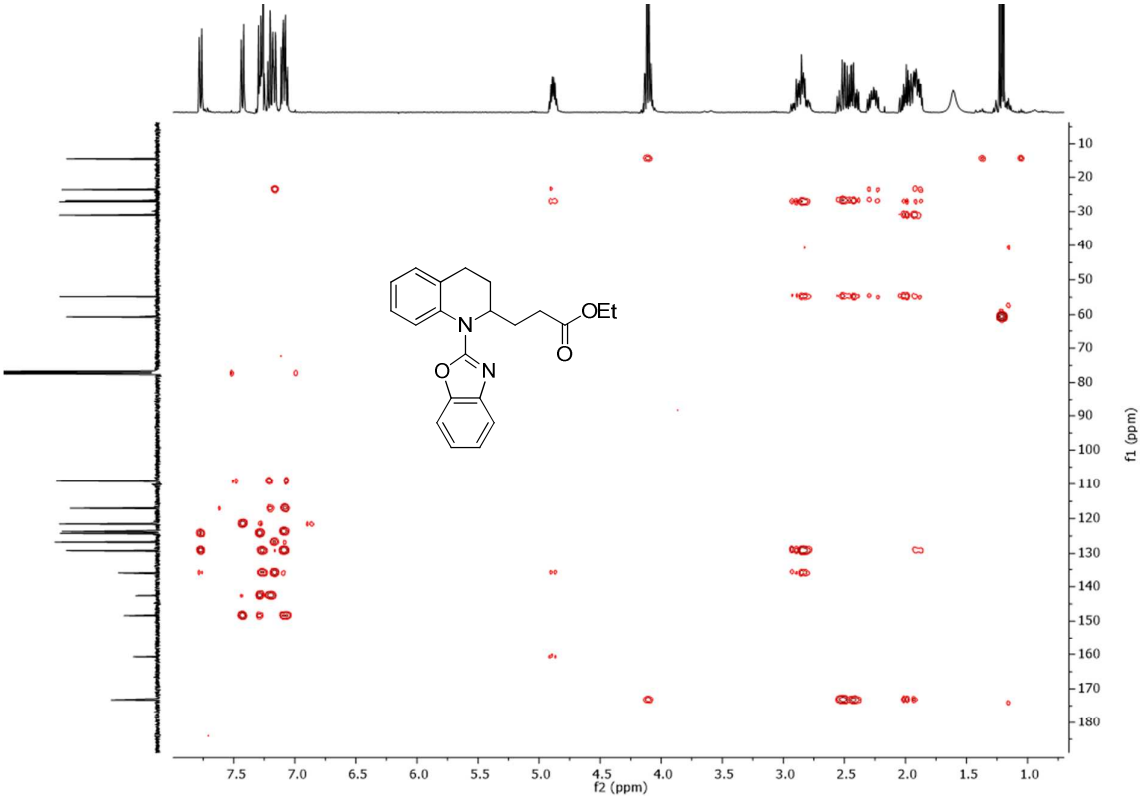
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 6a



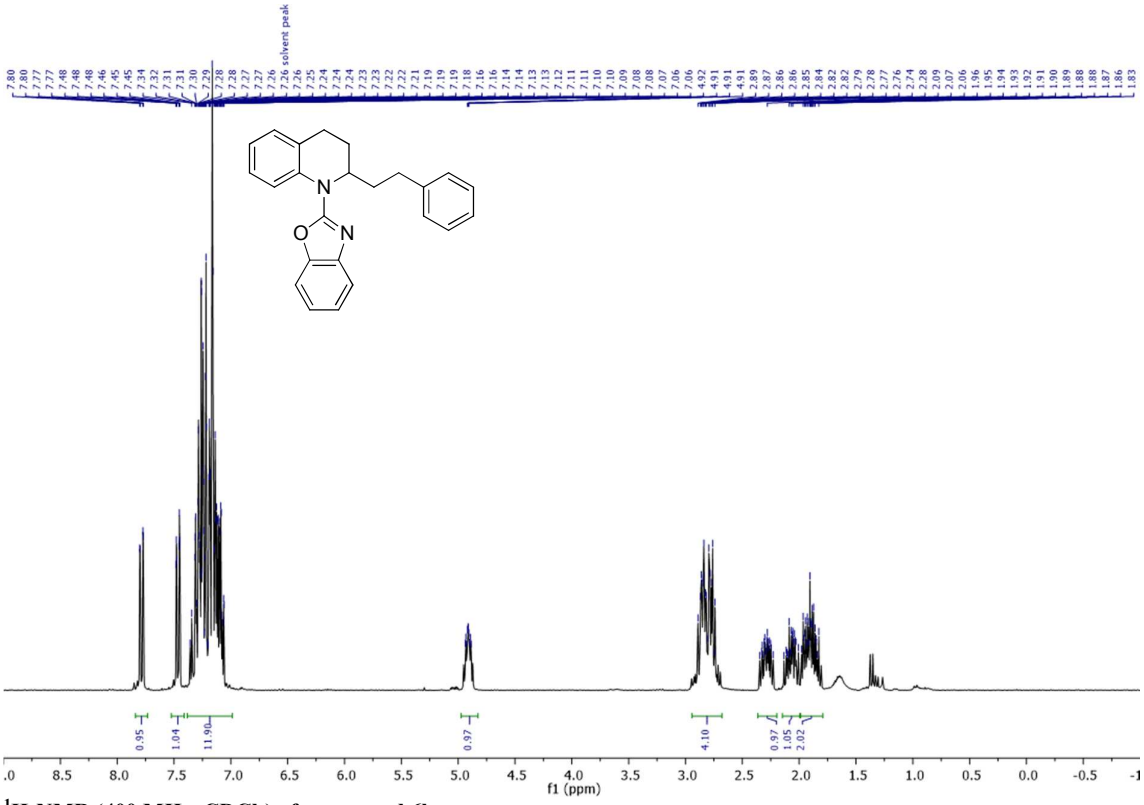
COSY of compound 6a



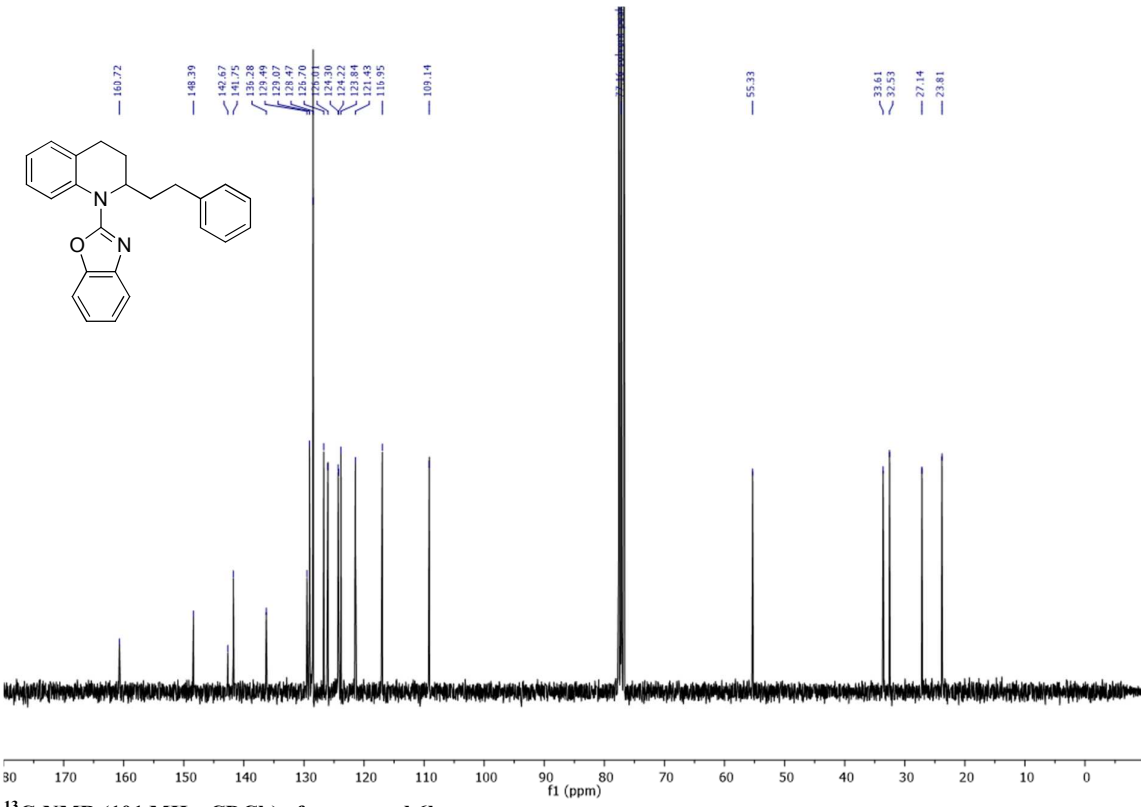
HSQC of compound 6a



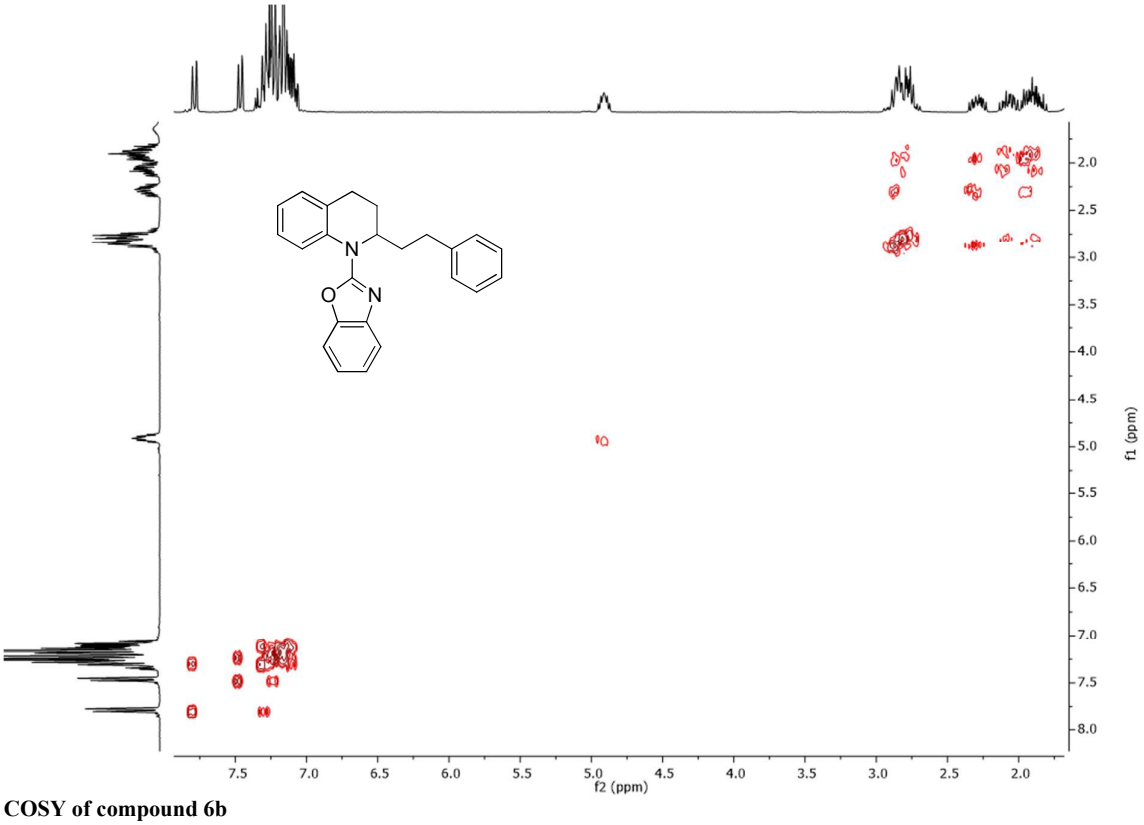
HMBC of compound 6a



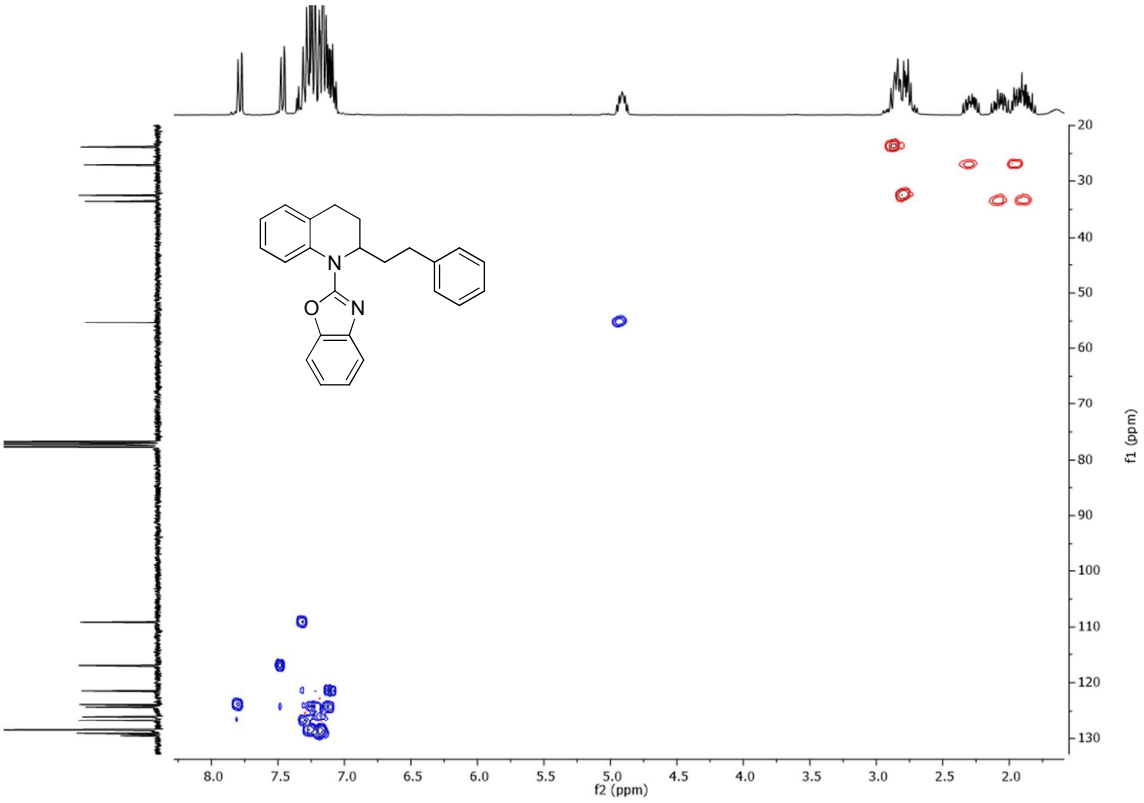
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 6b



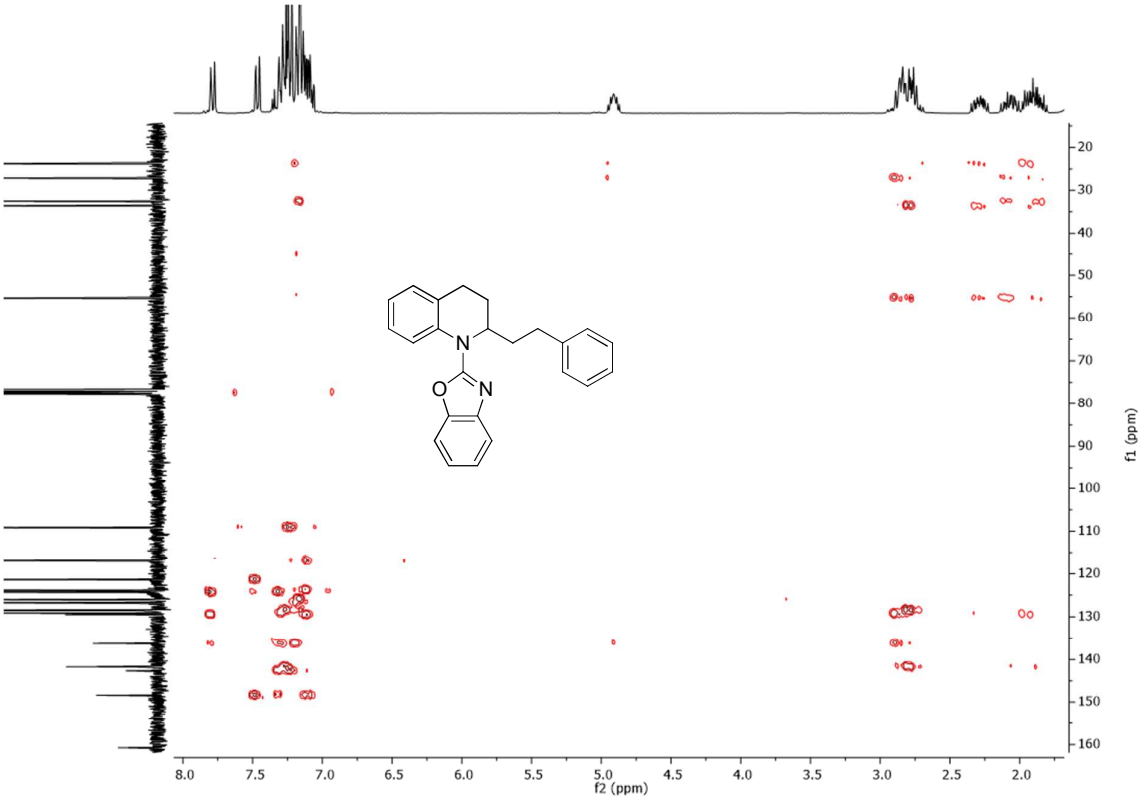
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 6b



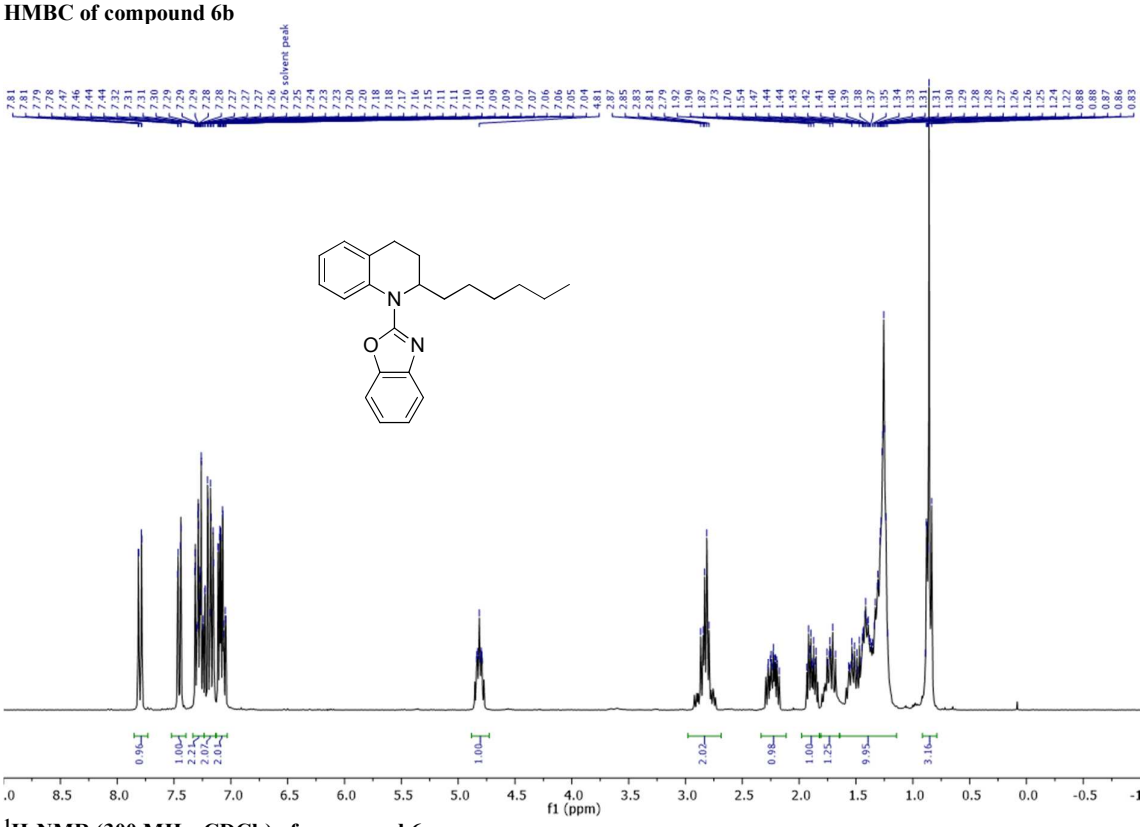
COSY of compound 6b



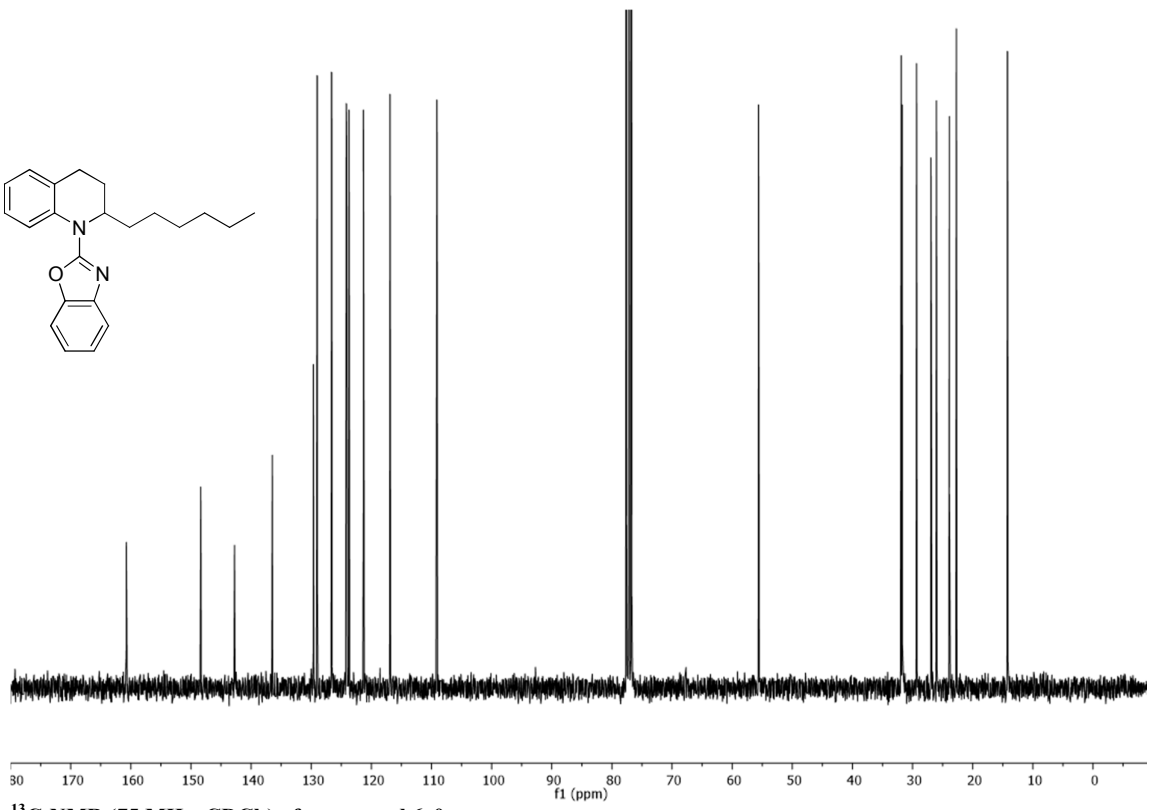
HSQC of compound 6b



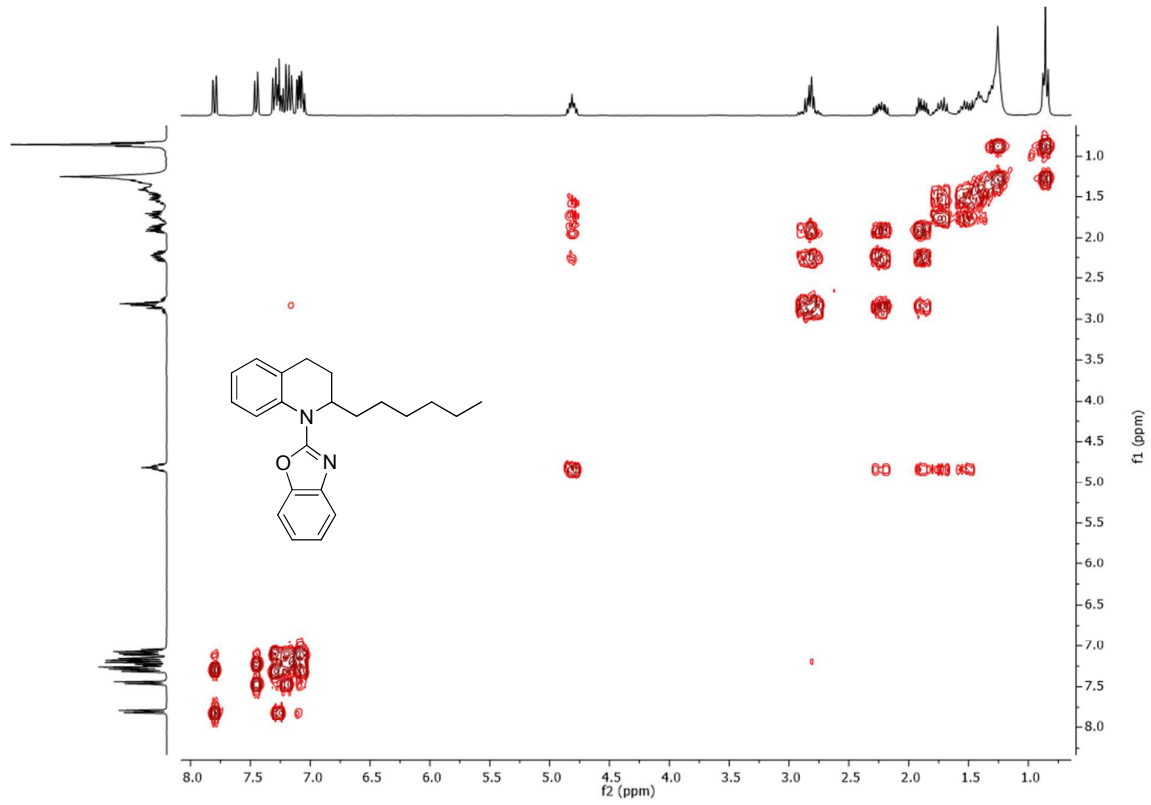
HMBC of compound 6b



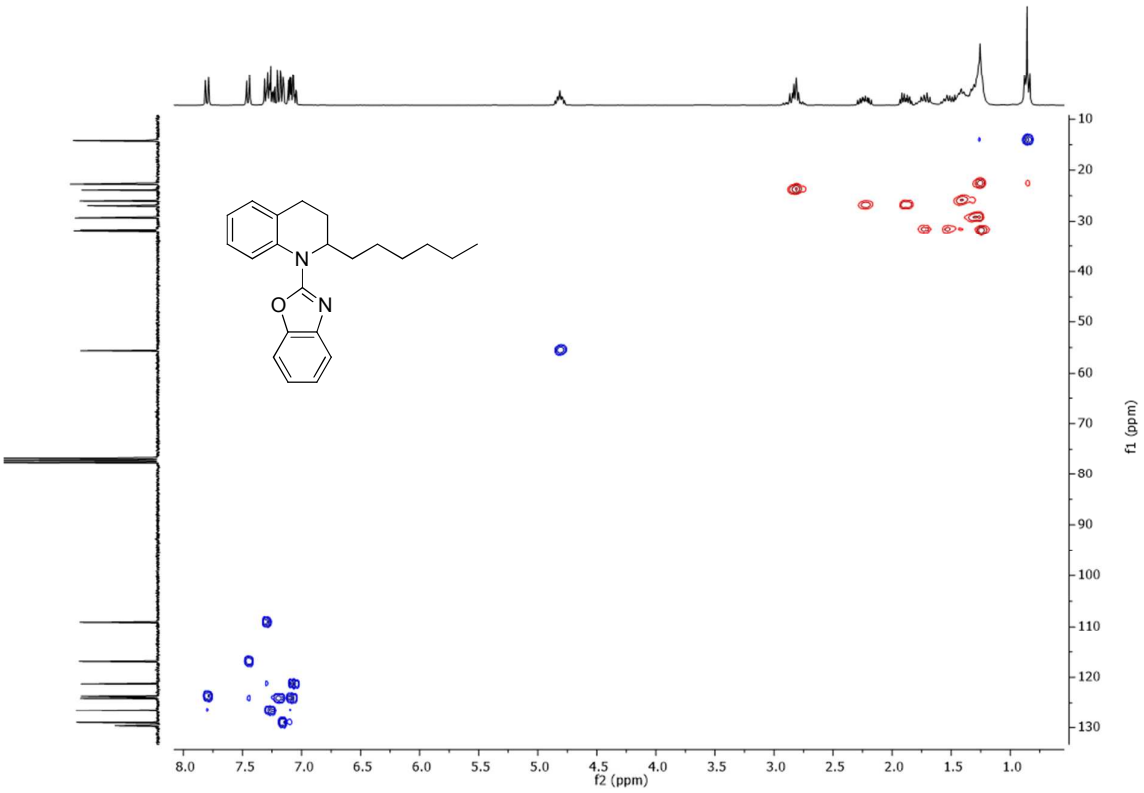
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 6c



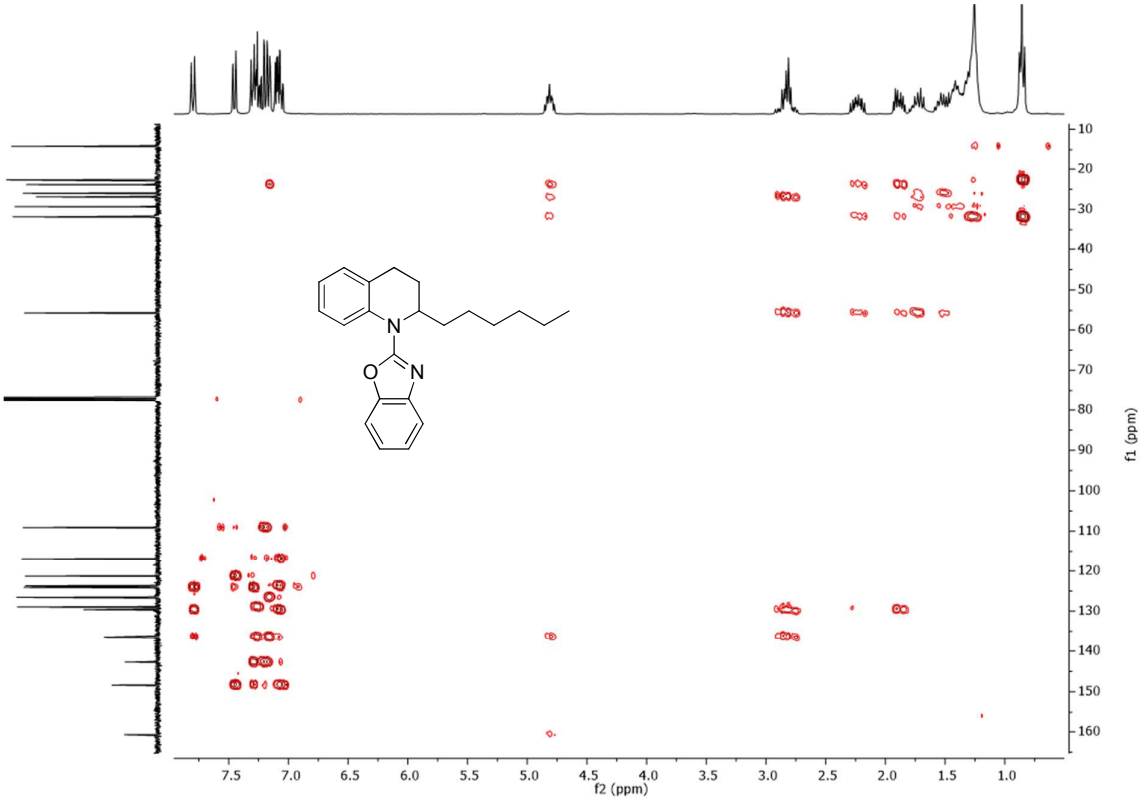
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 6c0



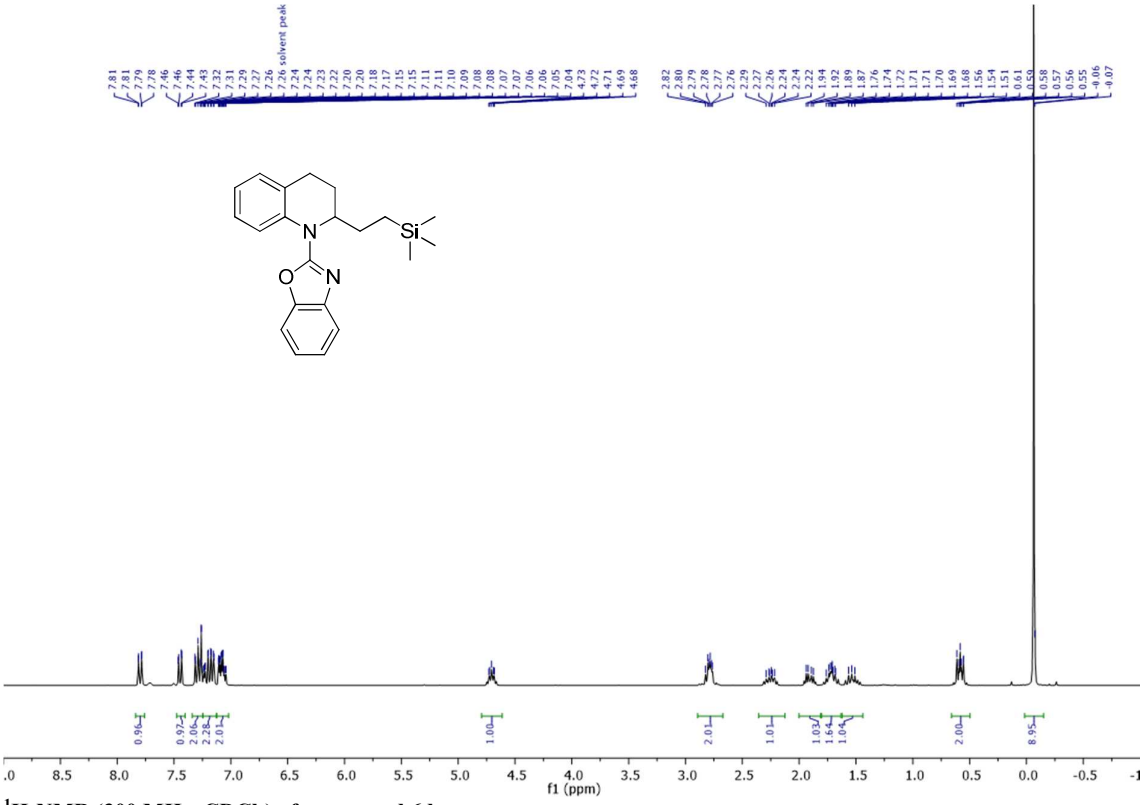
COSY of compound 6c



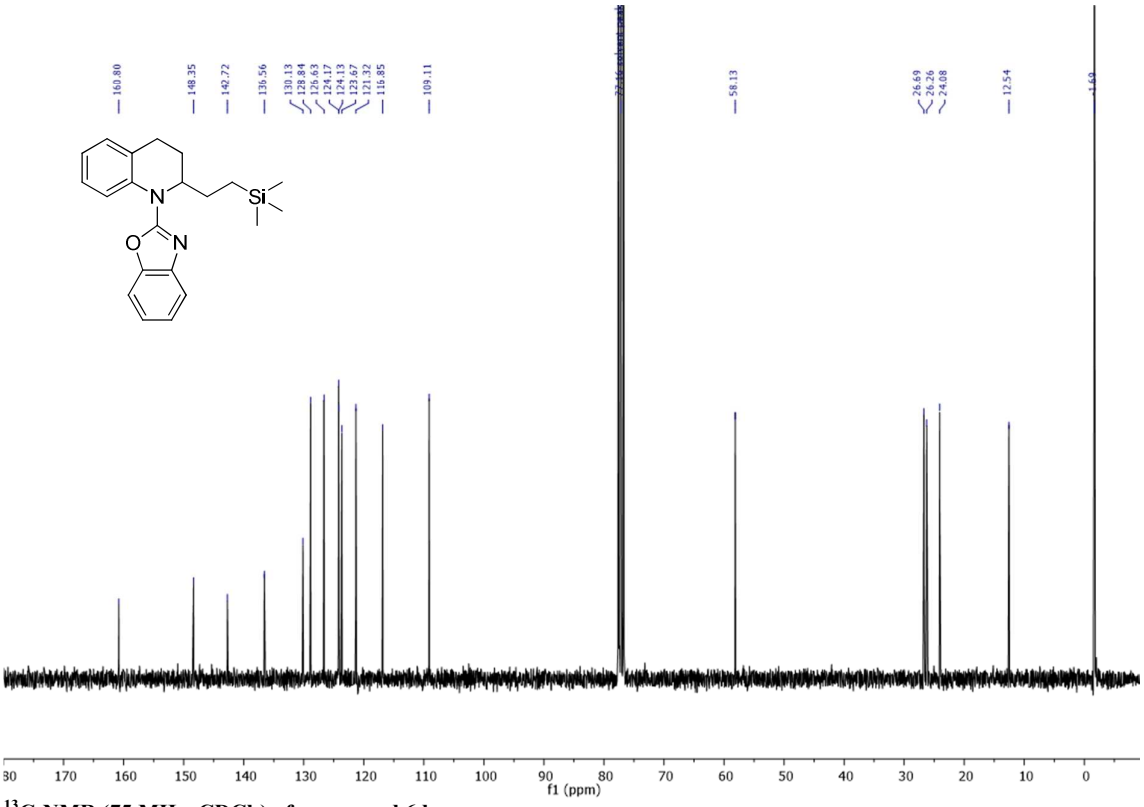
HSQC of compound 6c



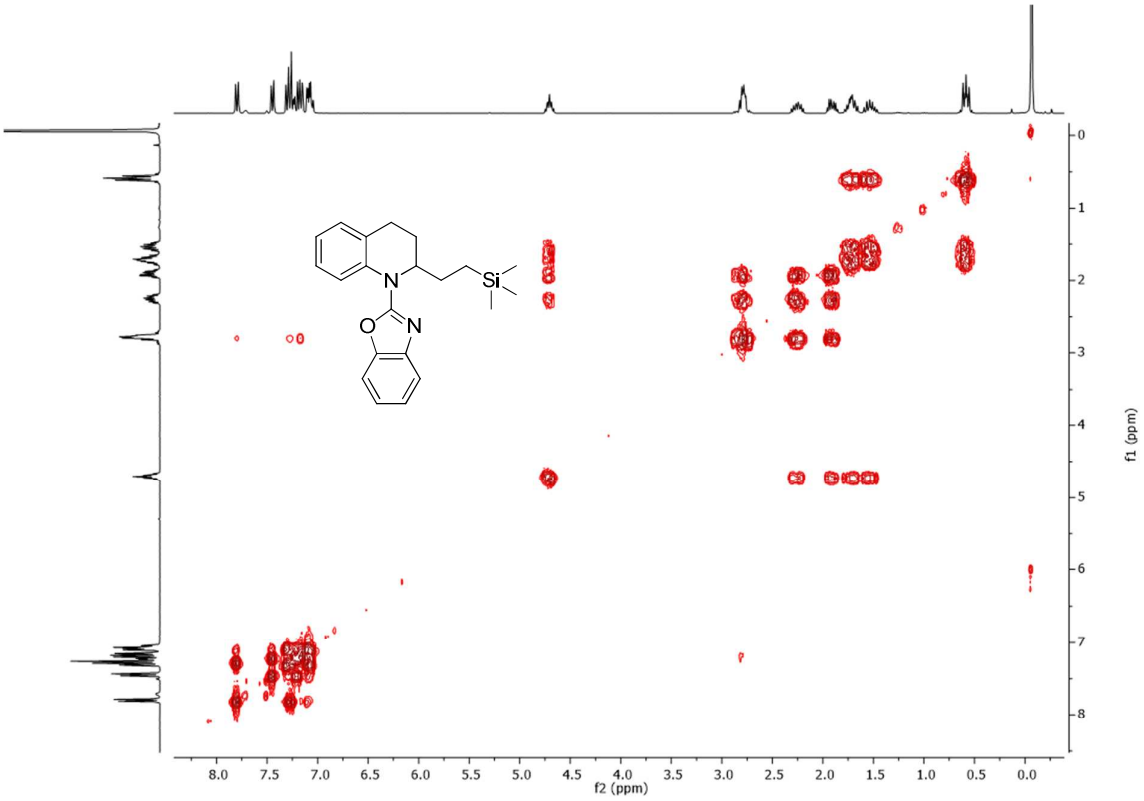
HMBC of compound 6c



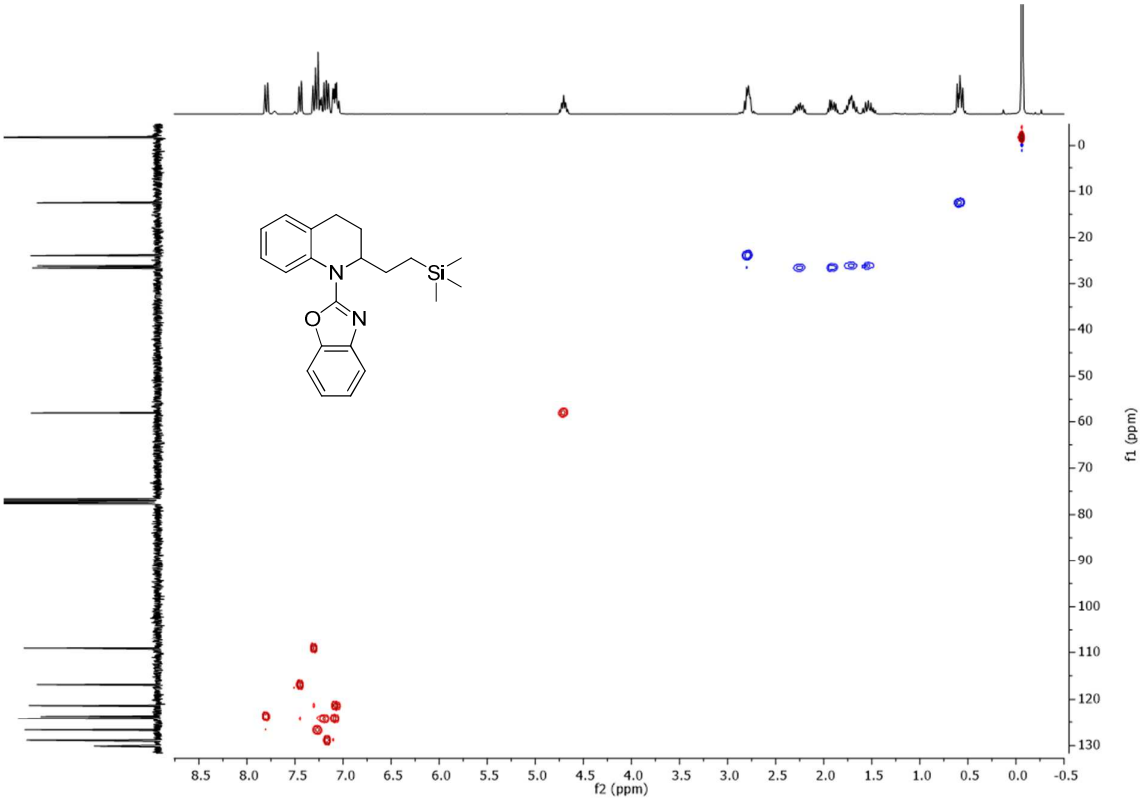
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 6d



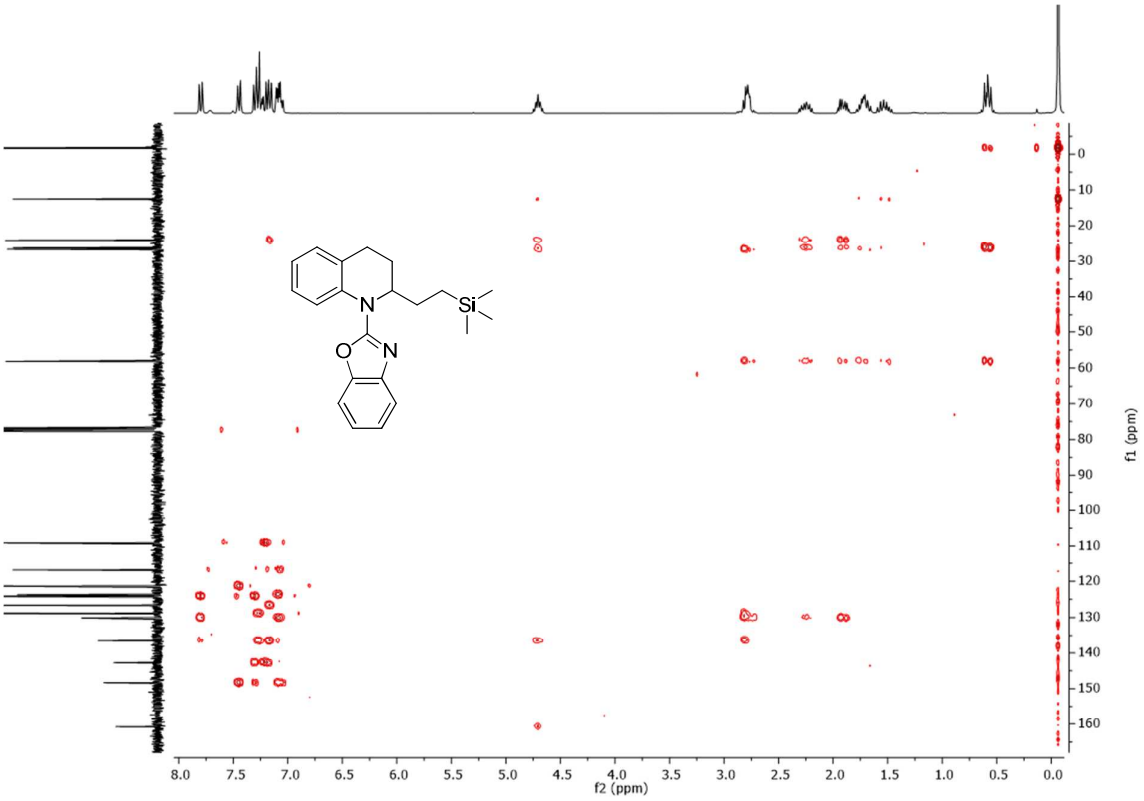
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 6d



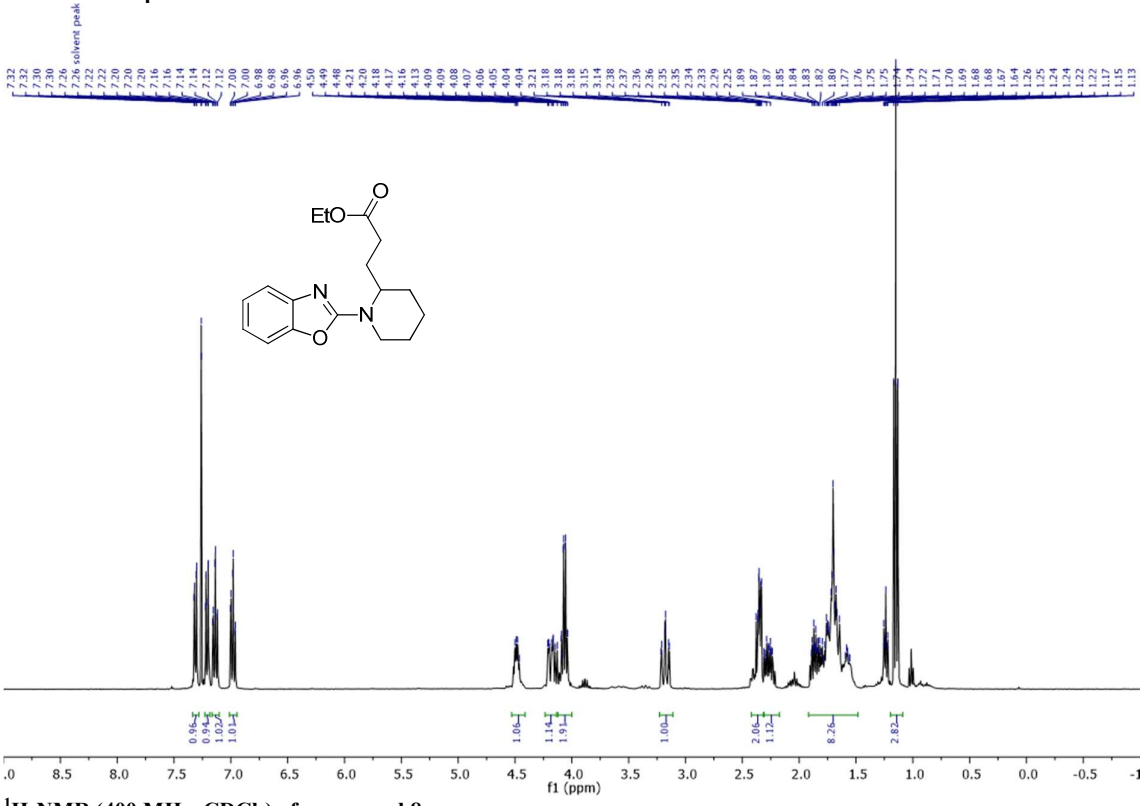
COSY of compound 6d



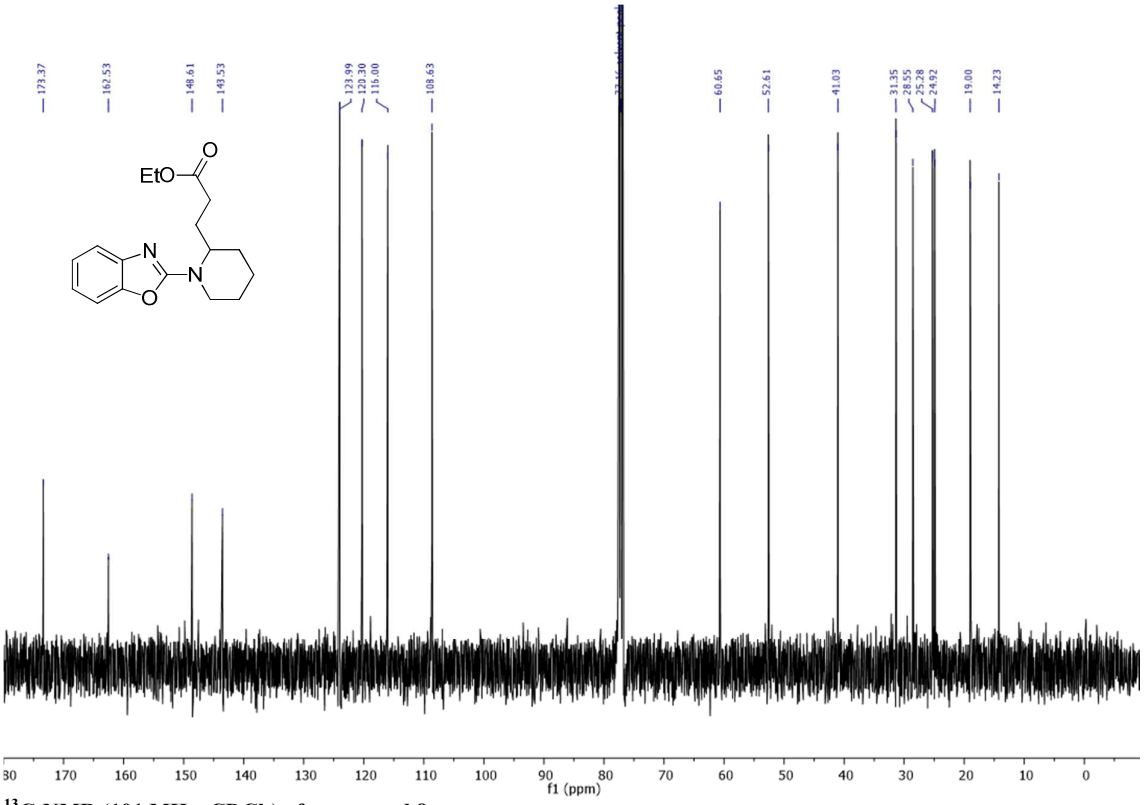
HSQC of compound 6d



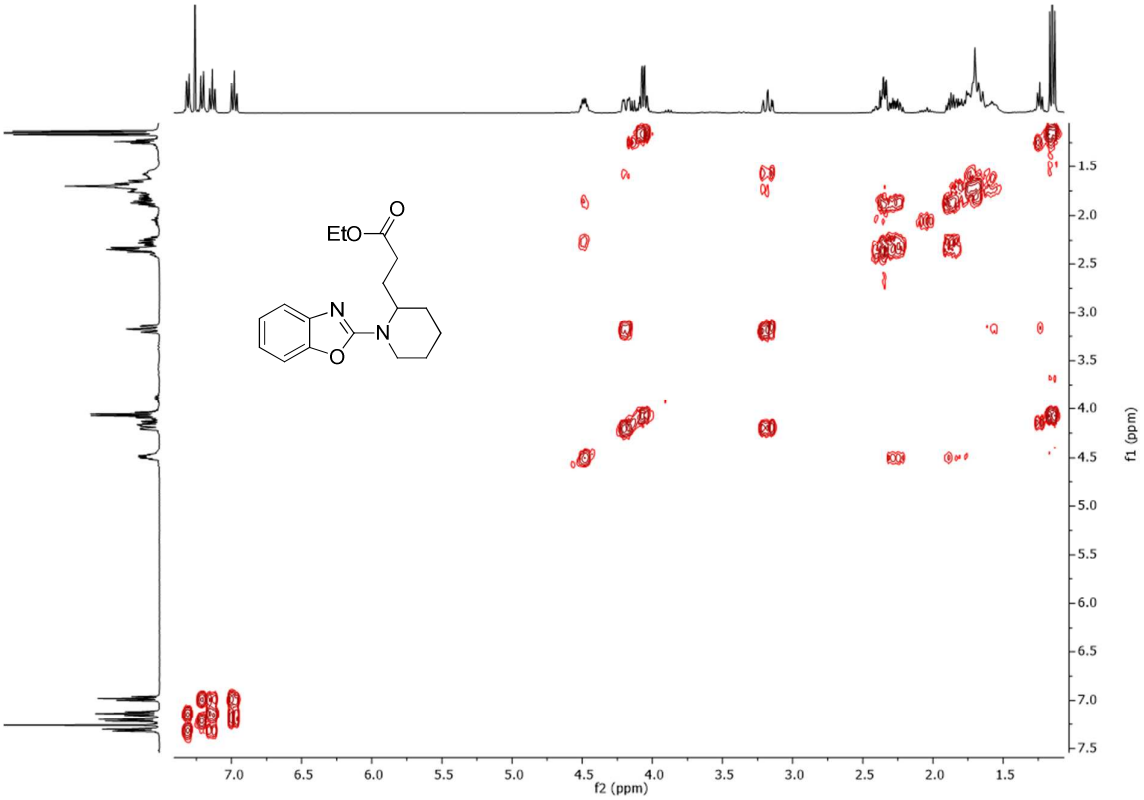
HMBC of compound 6d



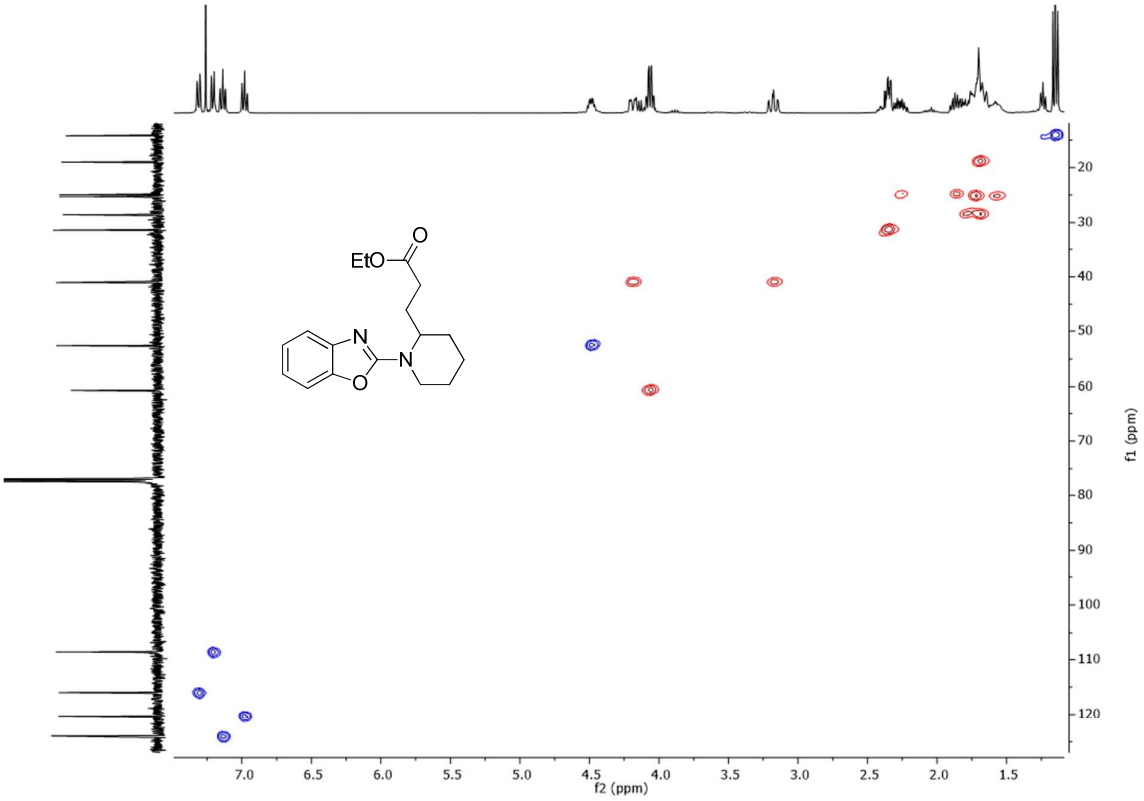
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 8a



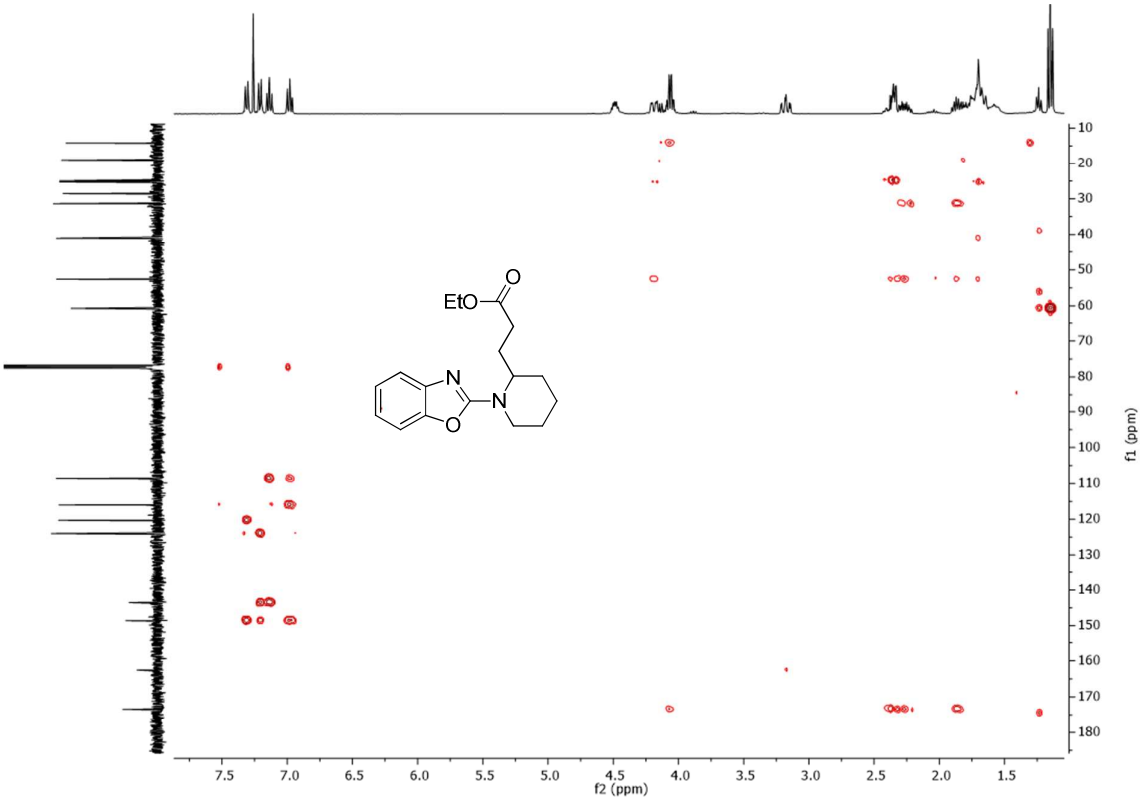
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 8a



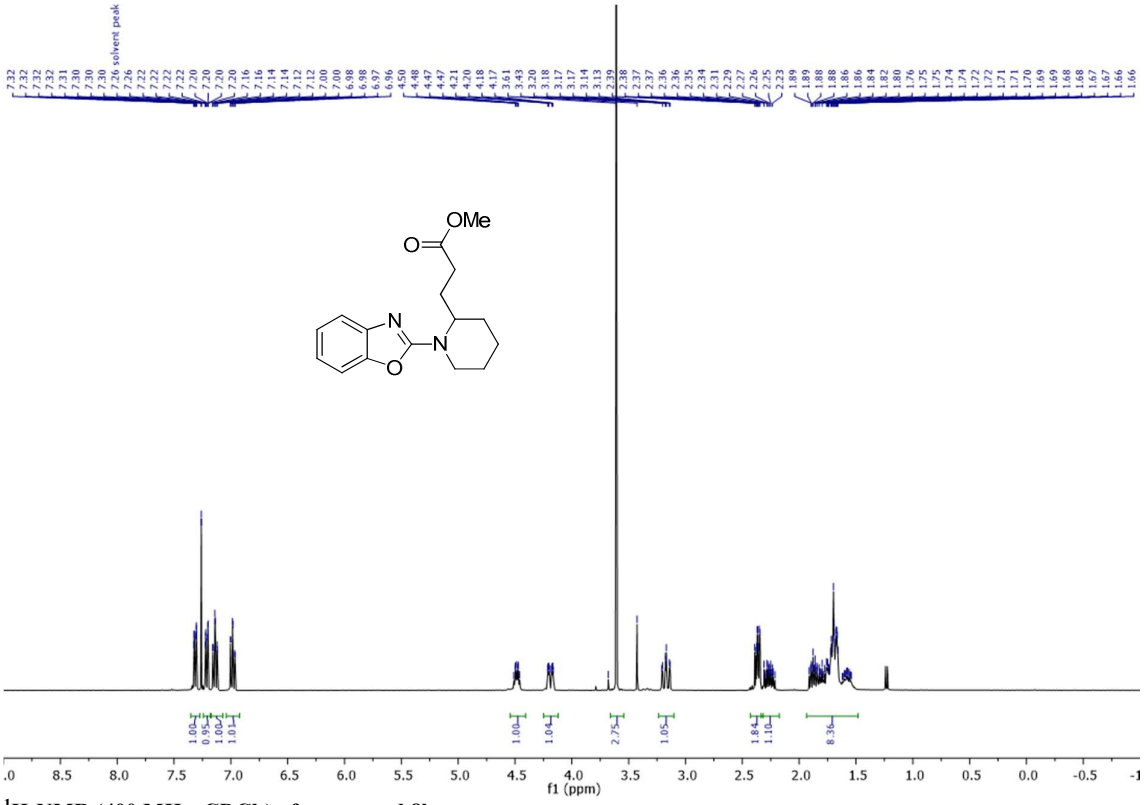
COSY of compound 8a



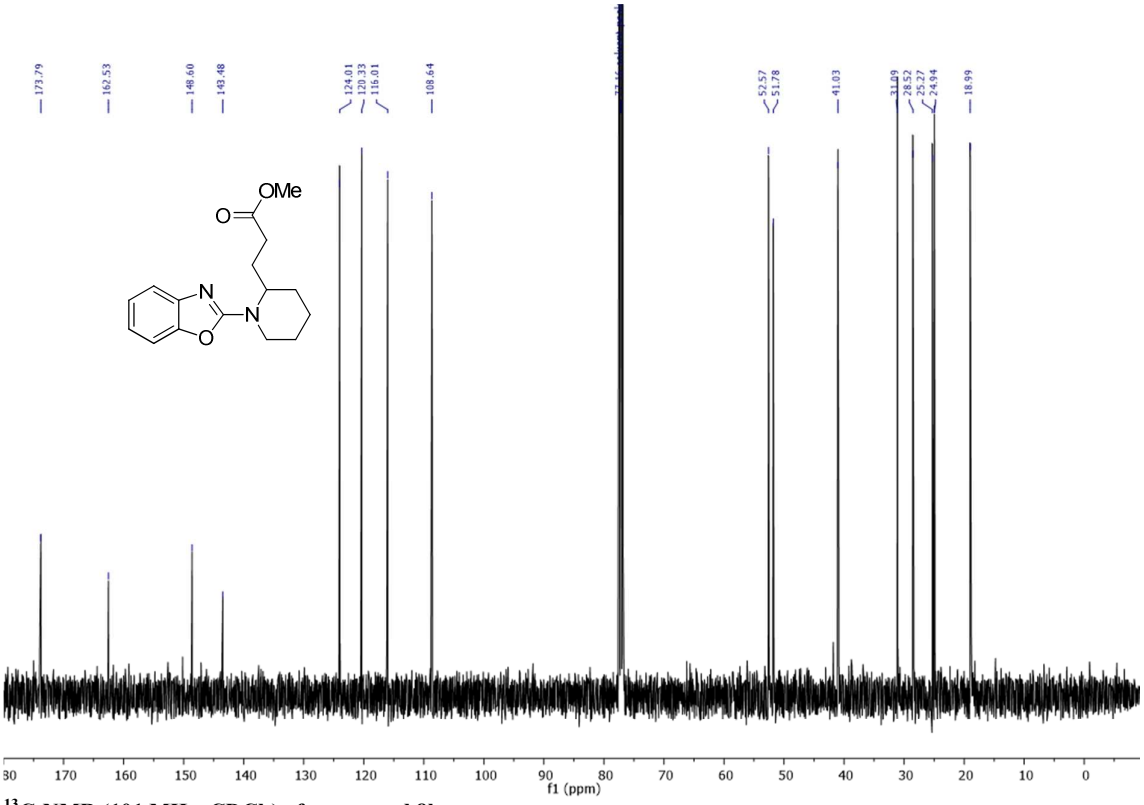
HSQC of compound 8a



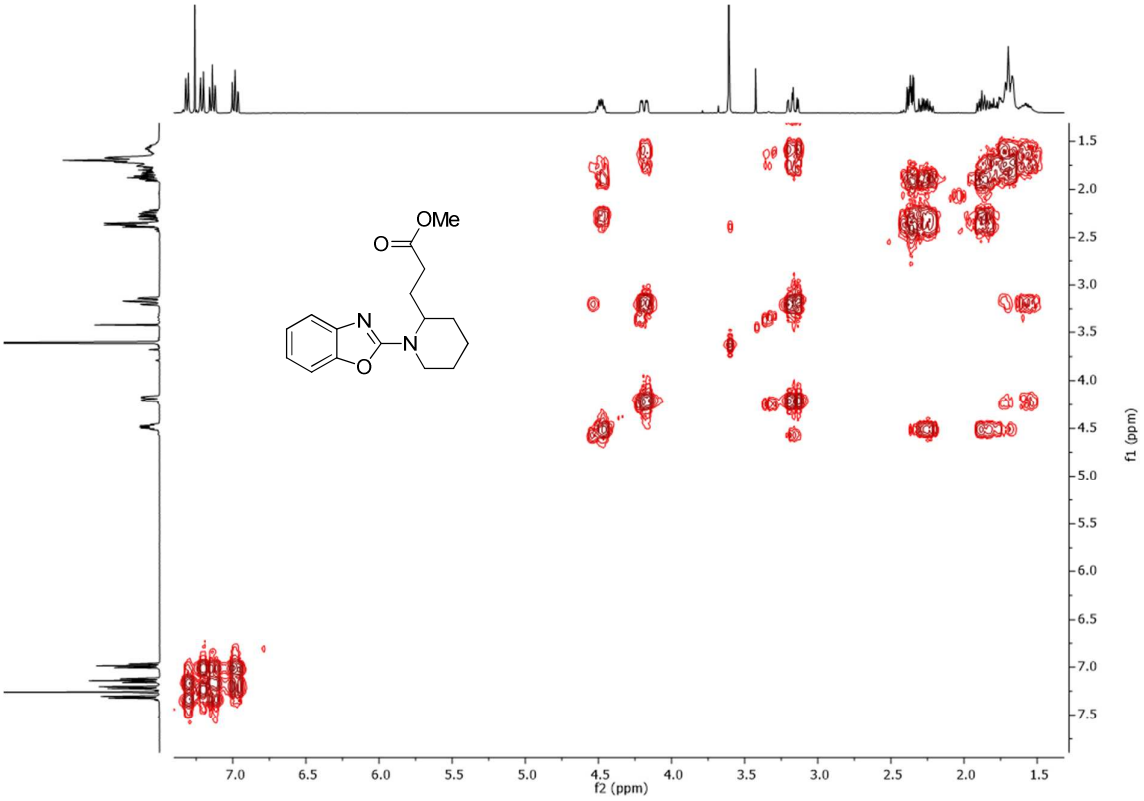
HMBC of compound 8a



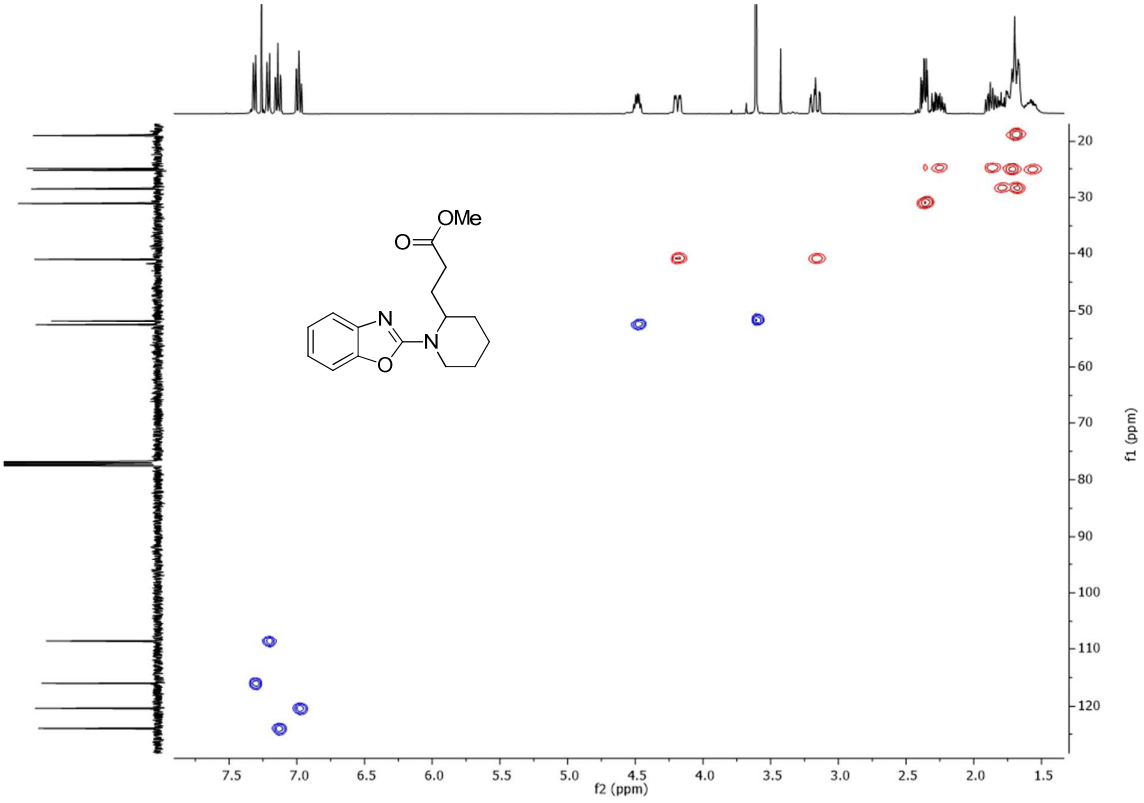
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 8b



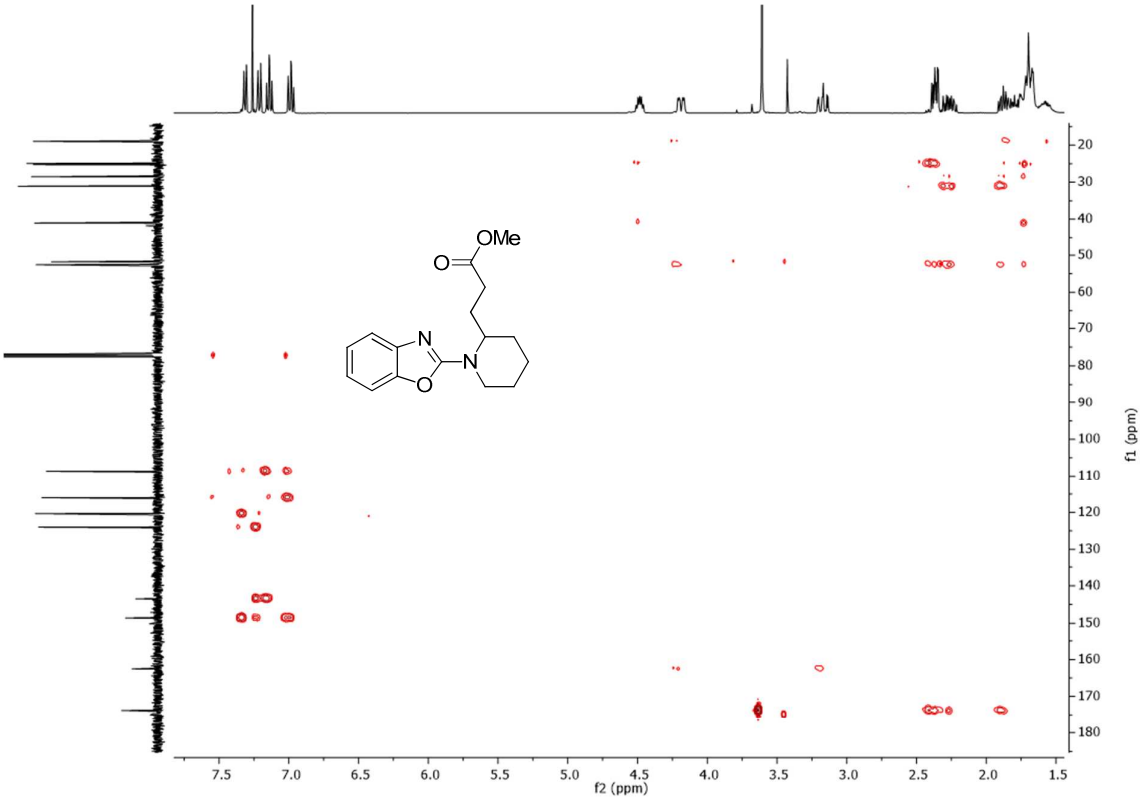
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 8b



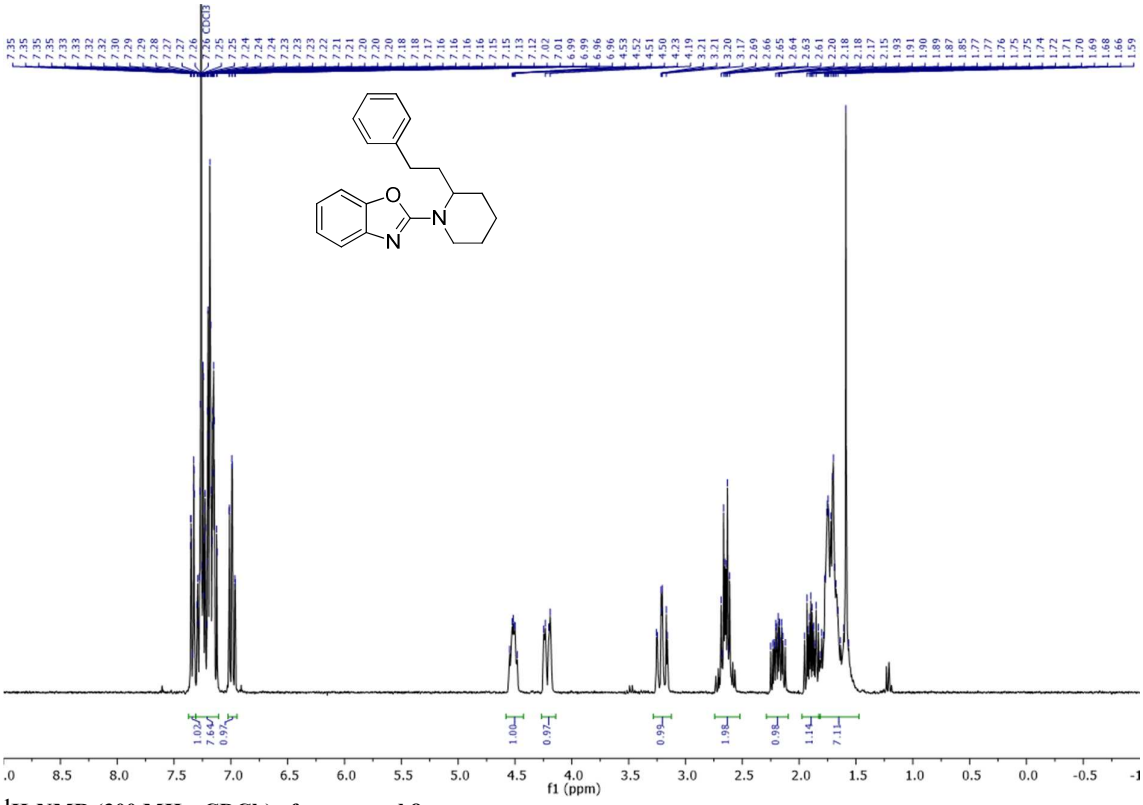
COSY of compound 8b



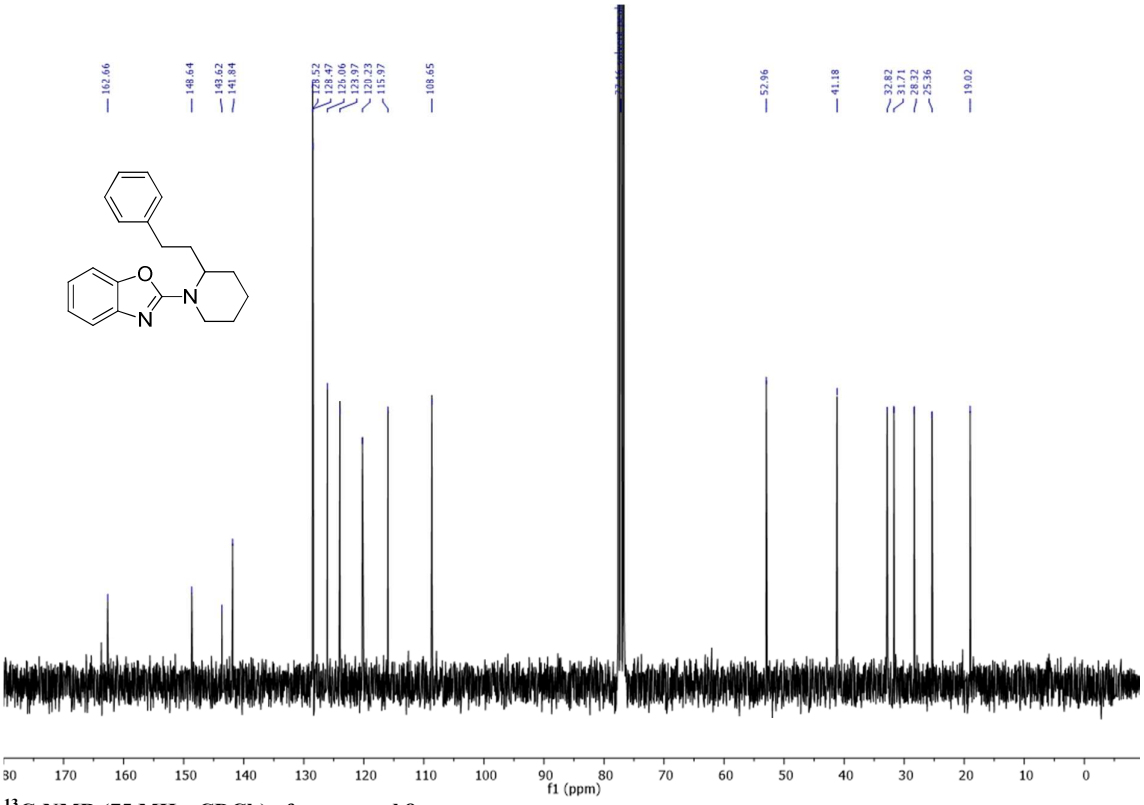
HSQC of compound 8b



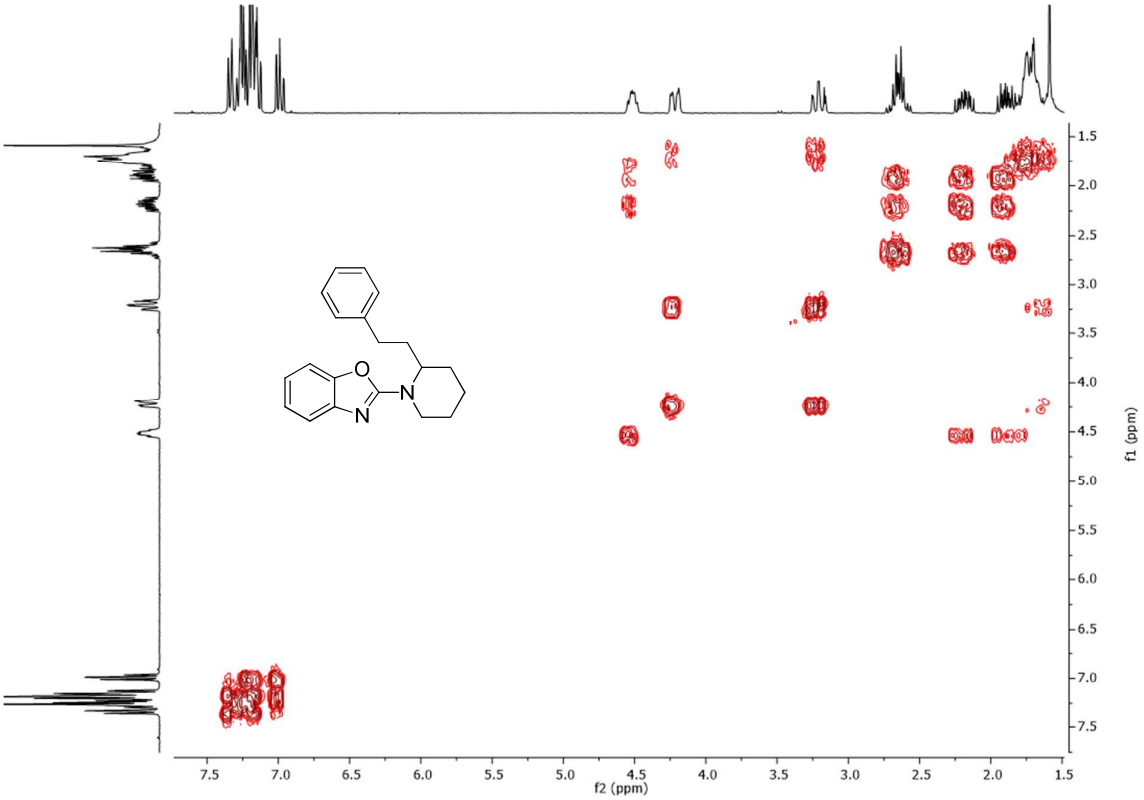
HMBC of compound 8b



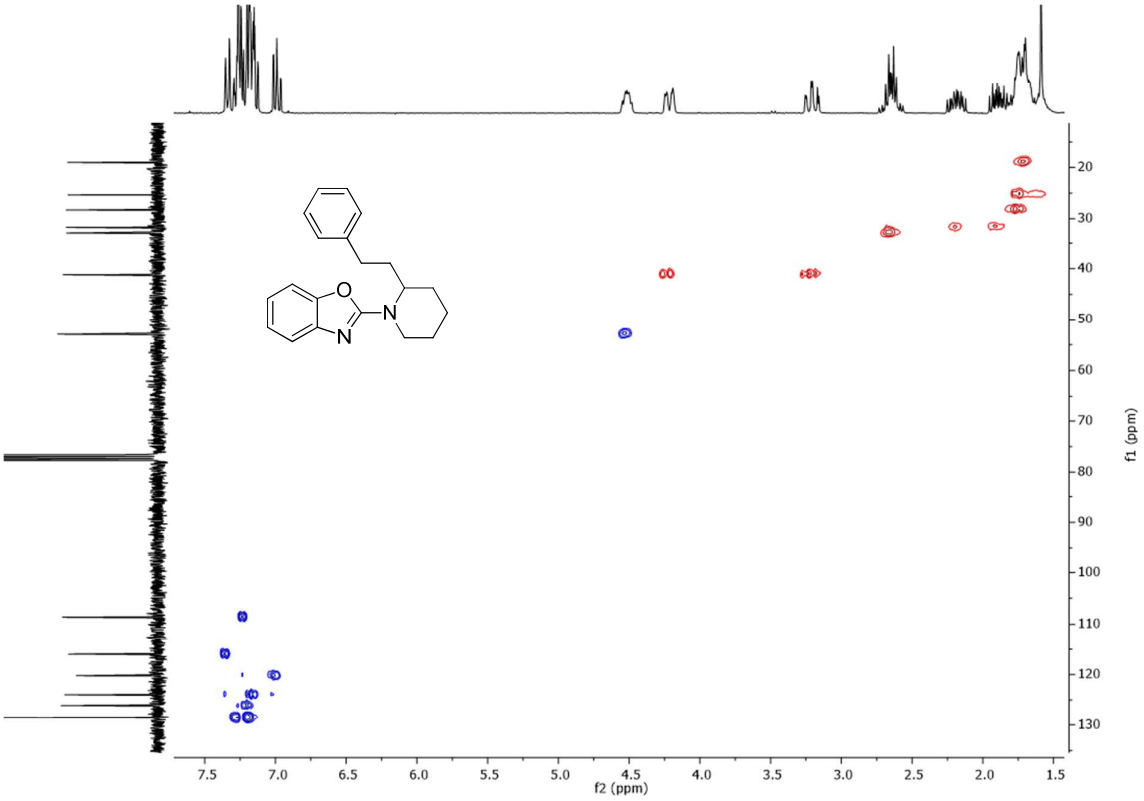
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 8c



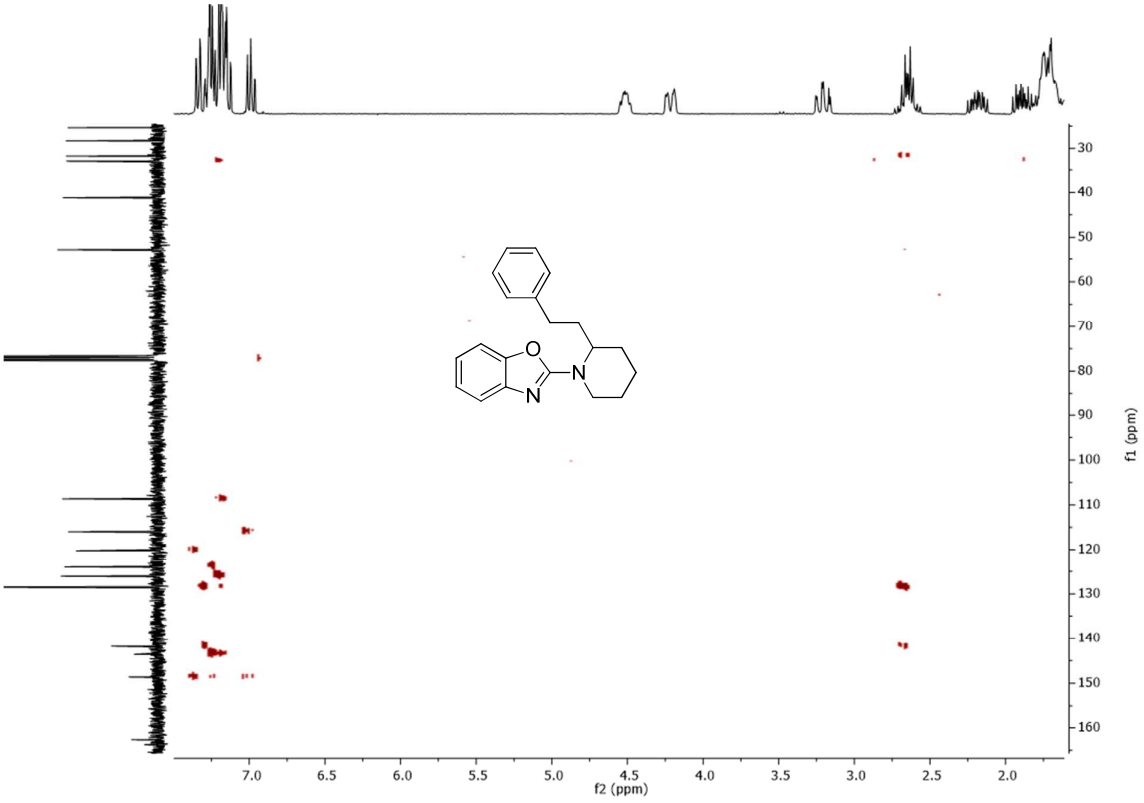
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 8c



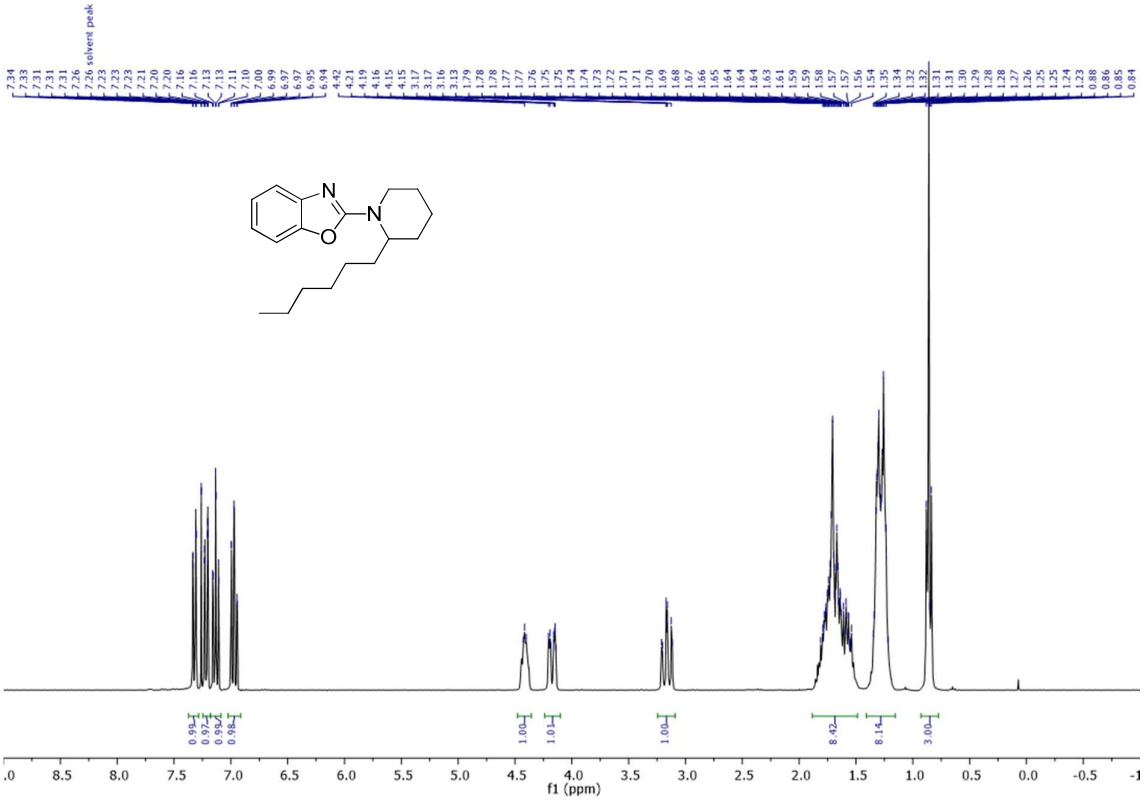
COSY of compound 8c



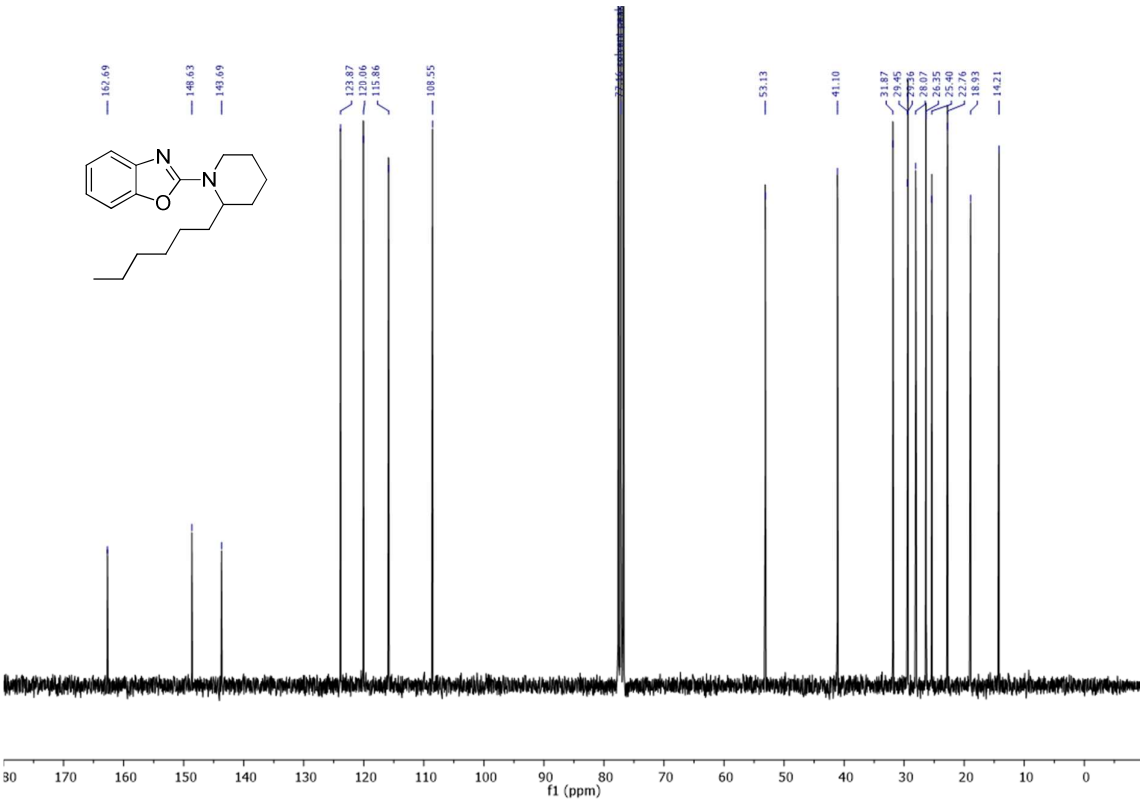
HSQC of compound 8c



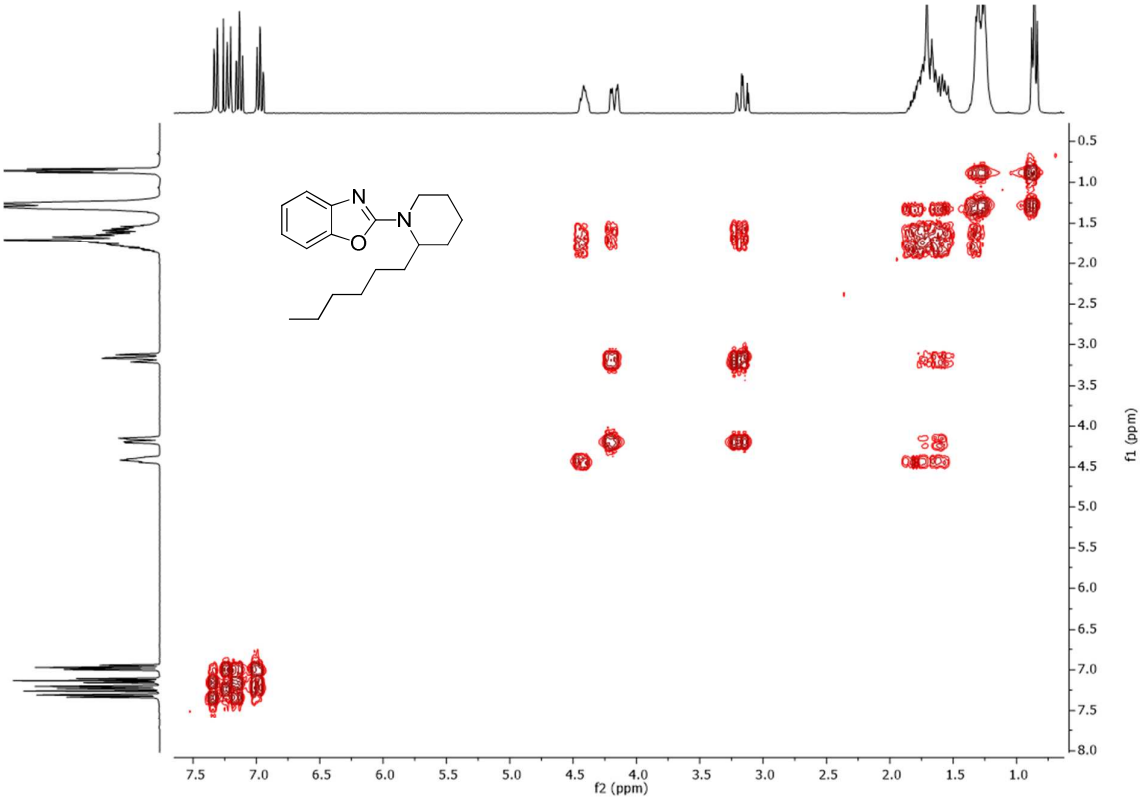
HMBC of compound 8c



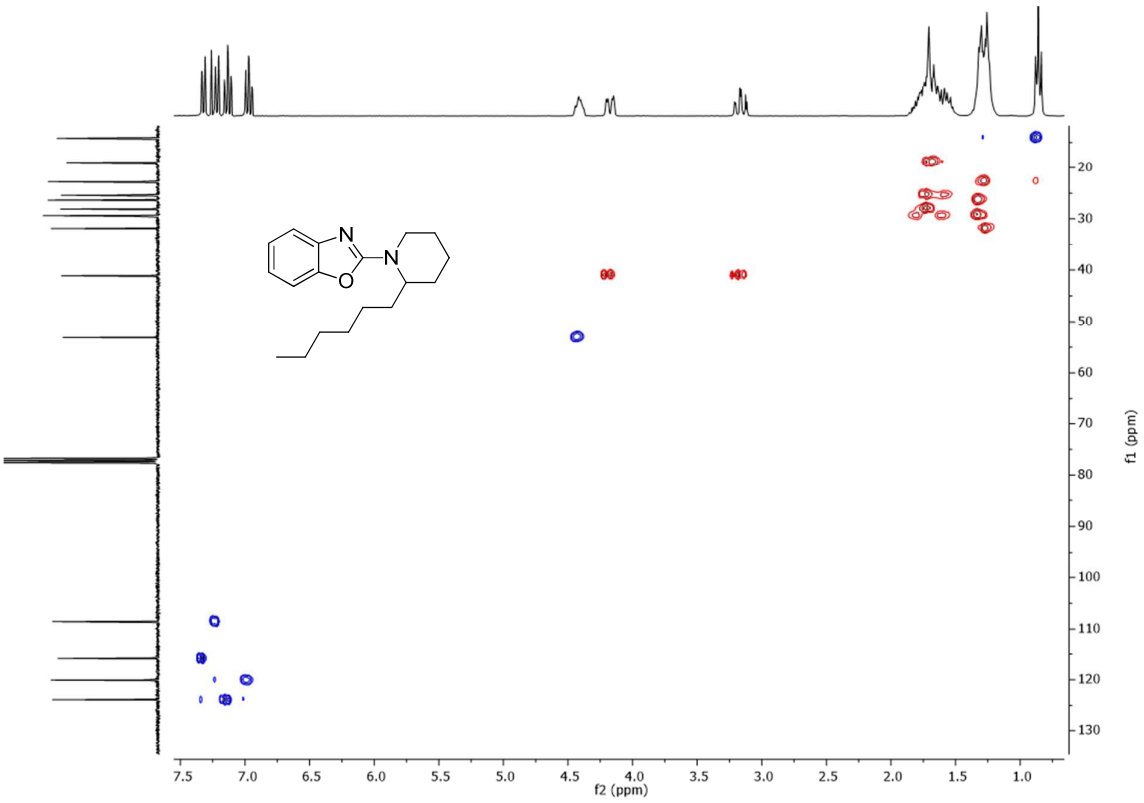
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 8d



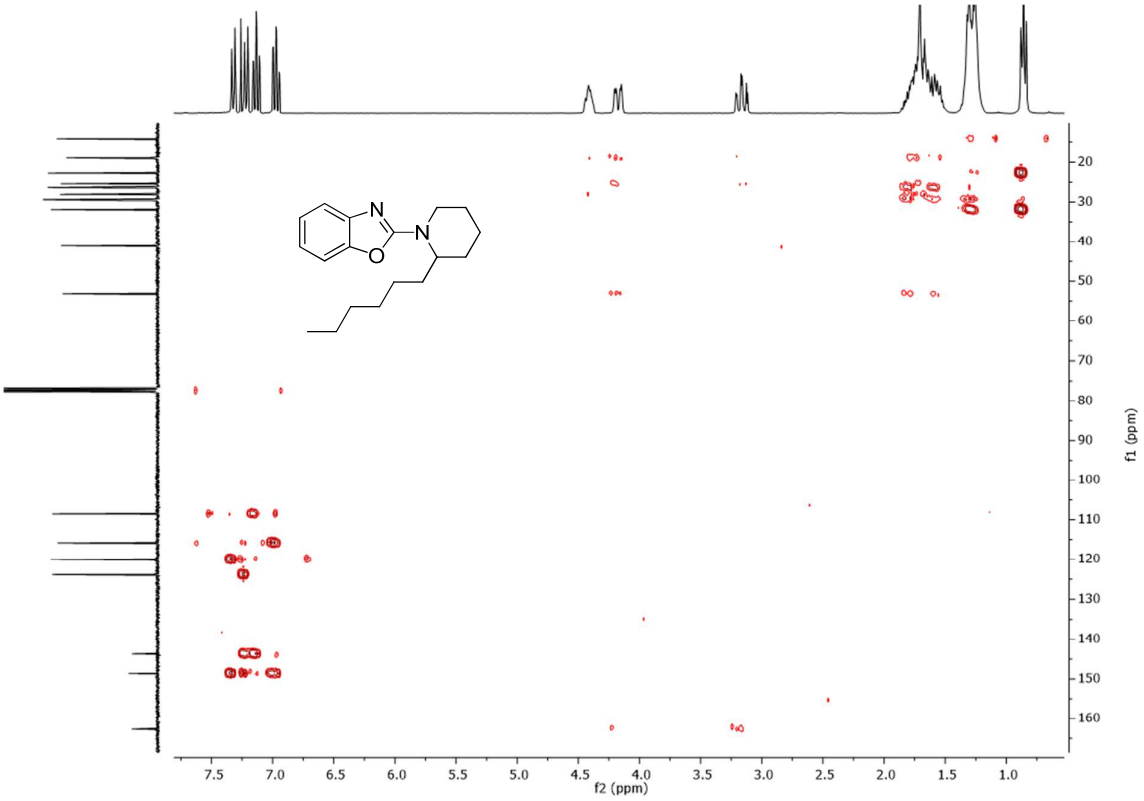
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 8d



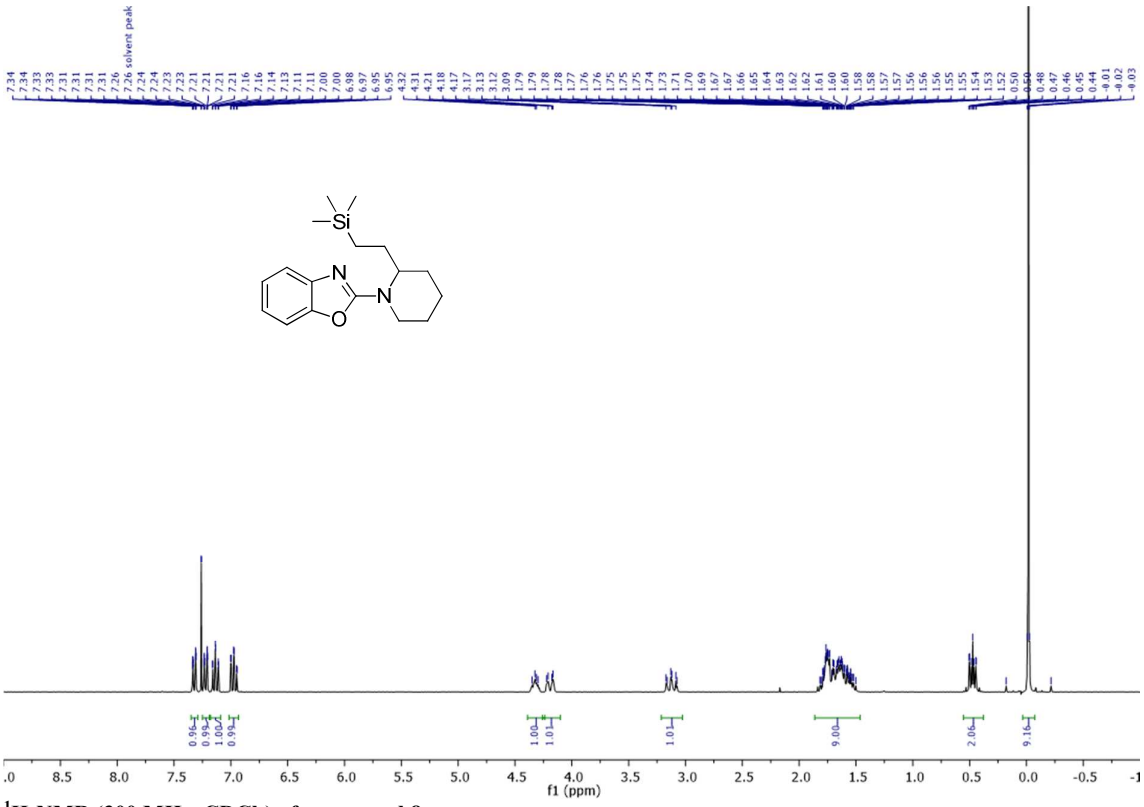
COSY of compound 8d



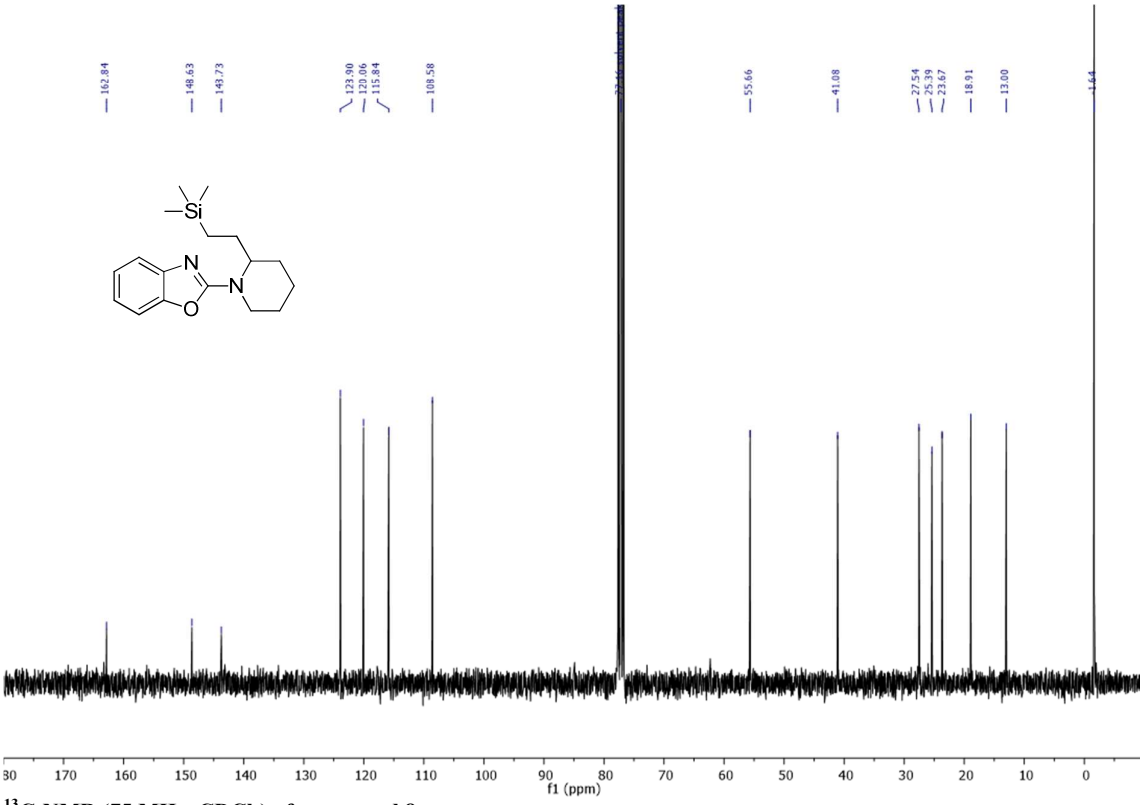
HSQC of compound 8d



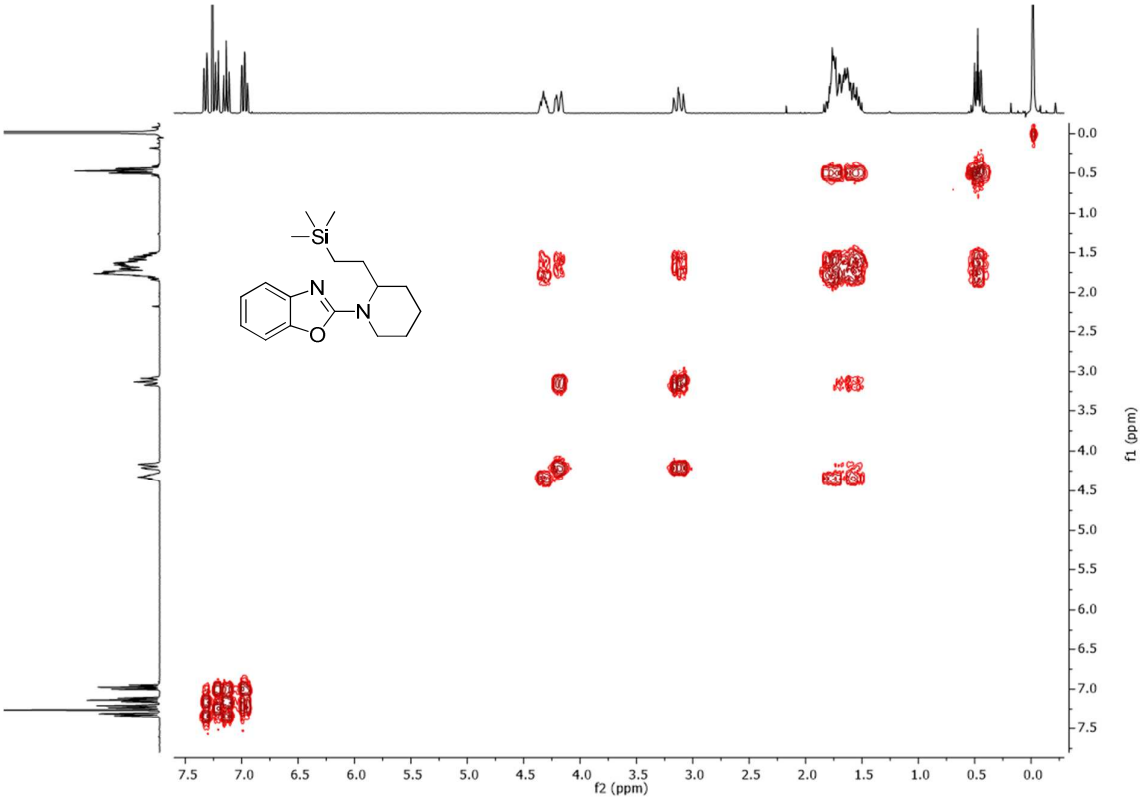
HMBC of compound 8d



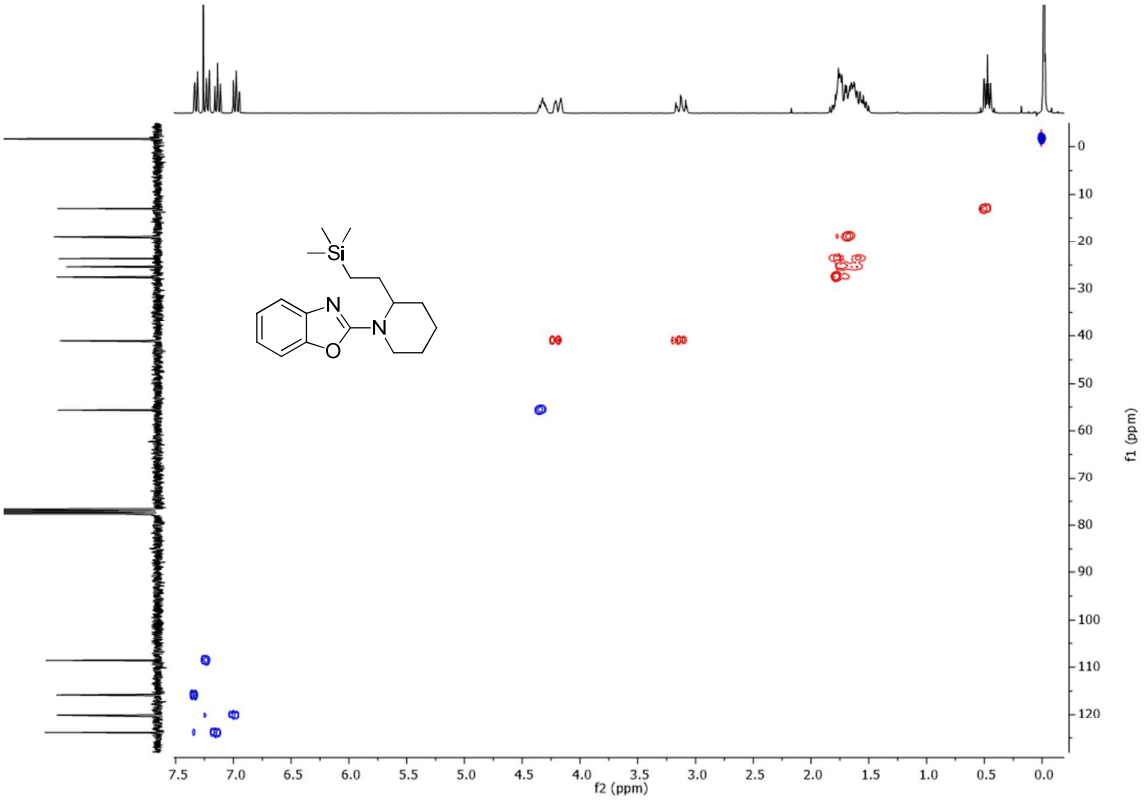
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 8e



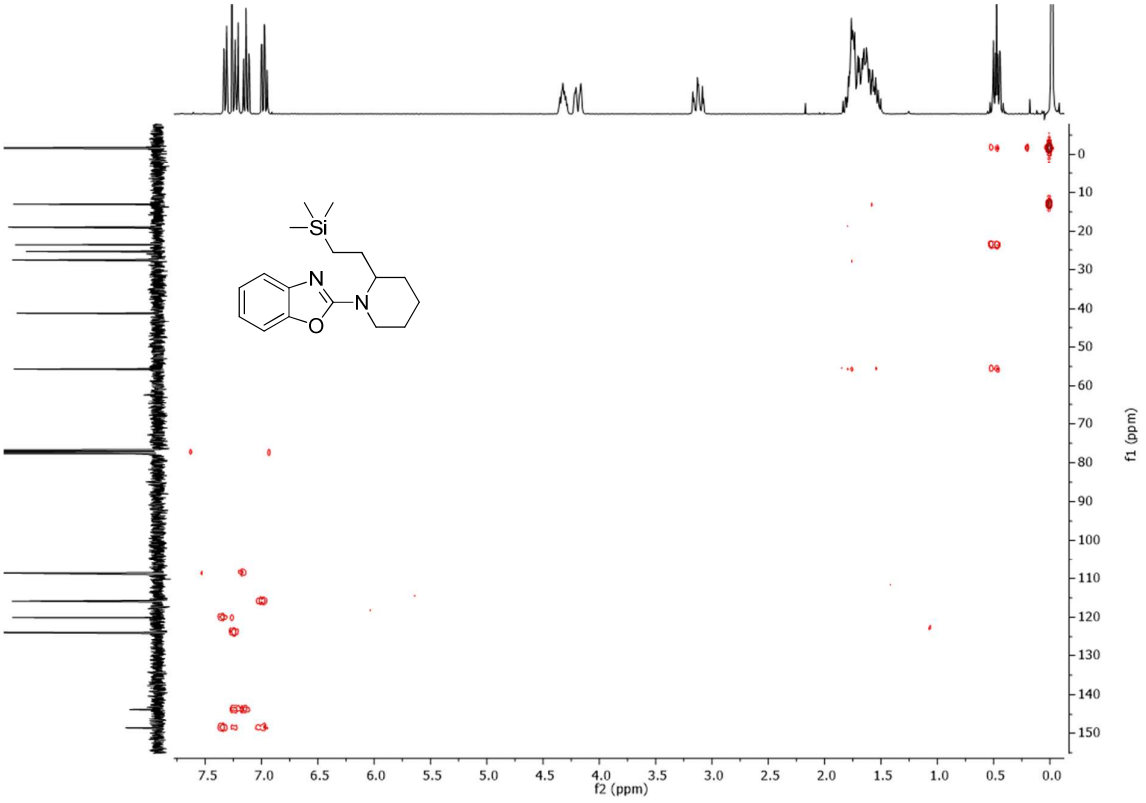
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 8e



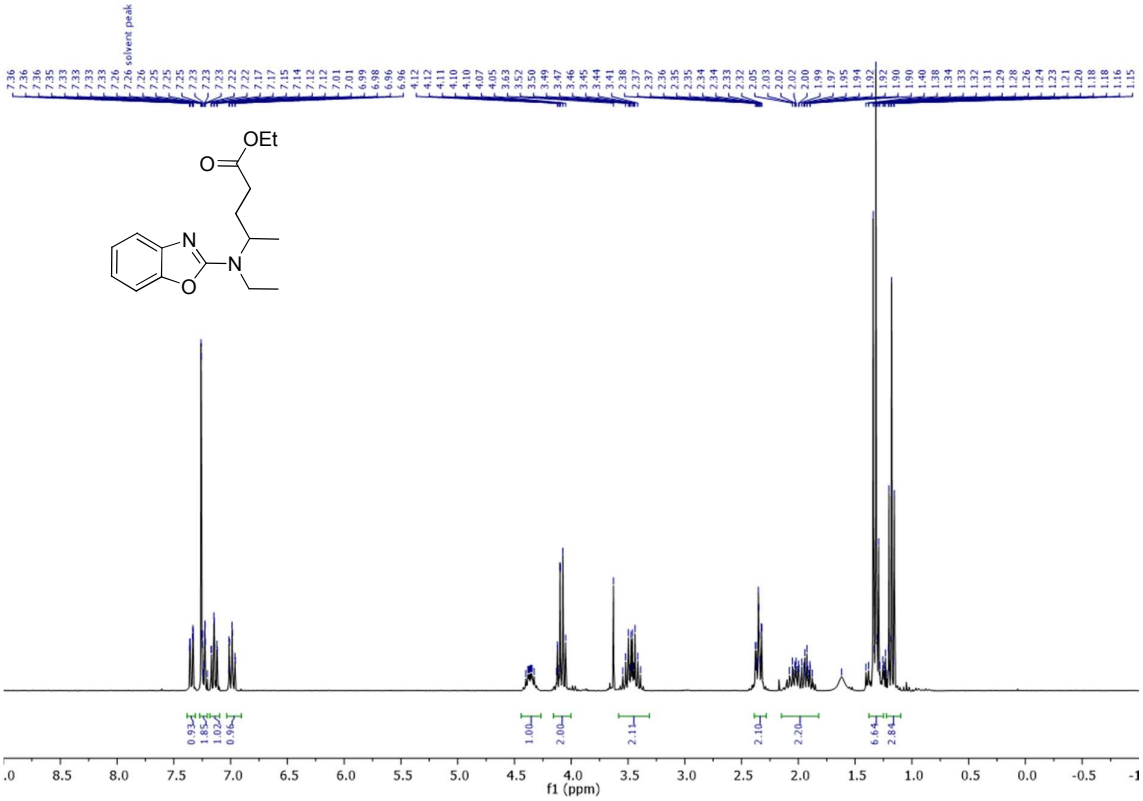
COSY of compound 8e



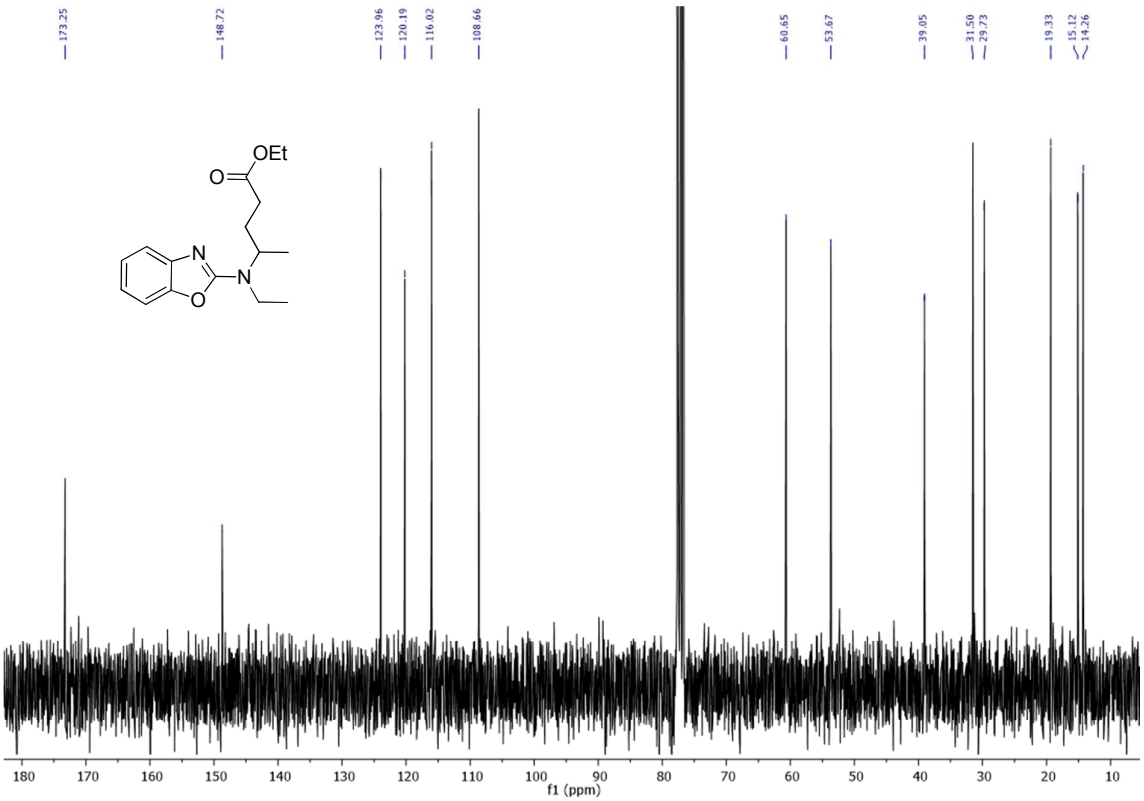
HSQC of compound 8e



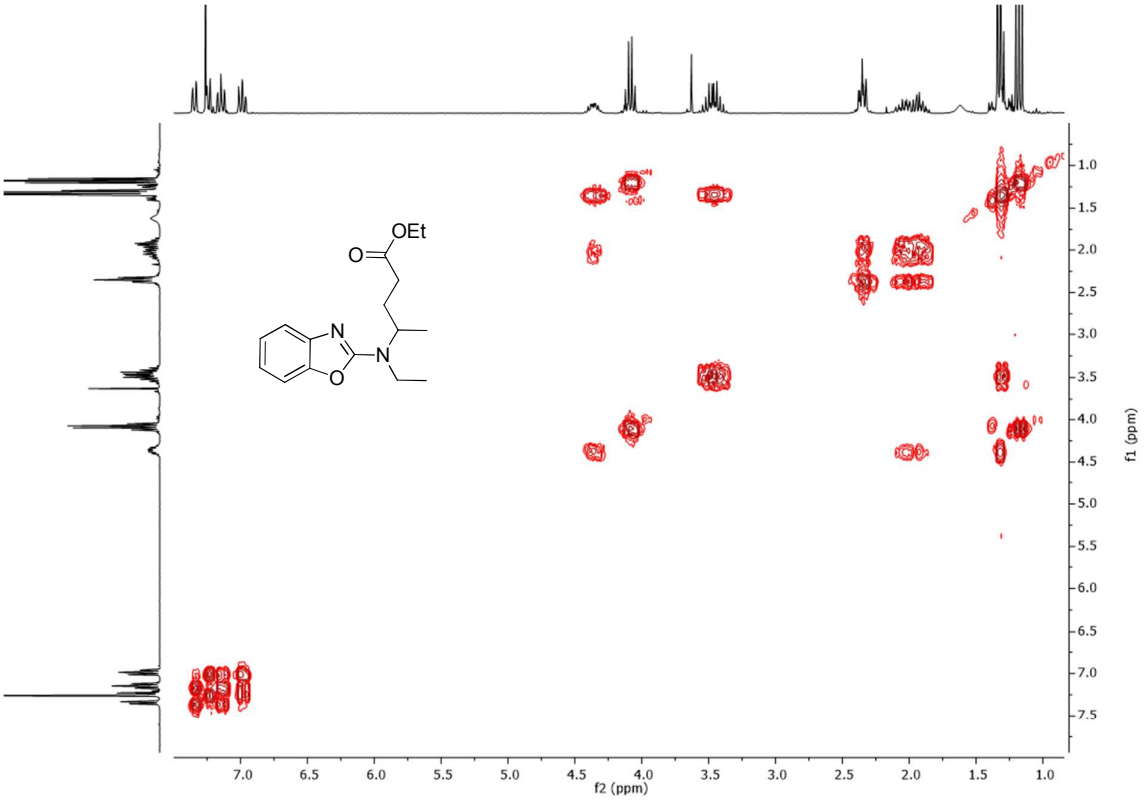
HMBC of compound 8e



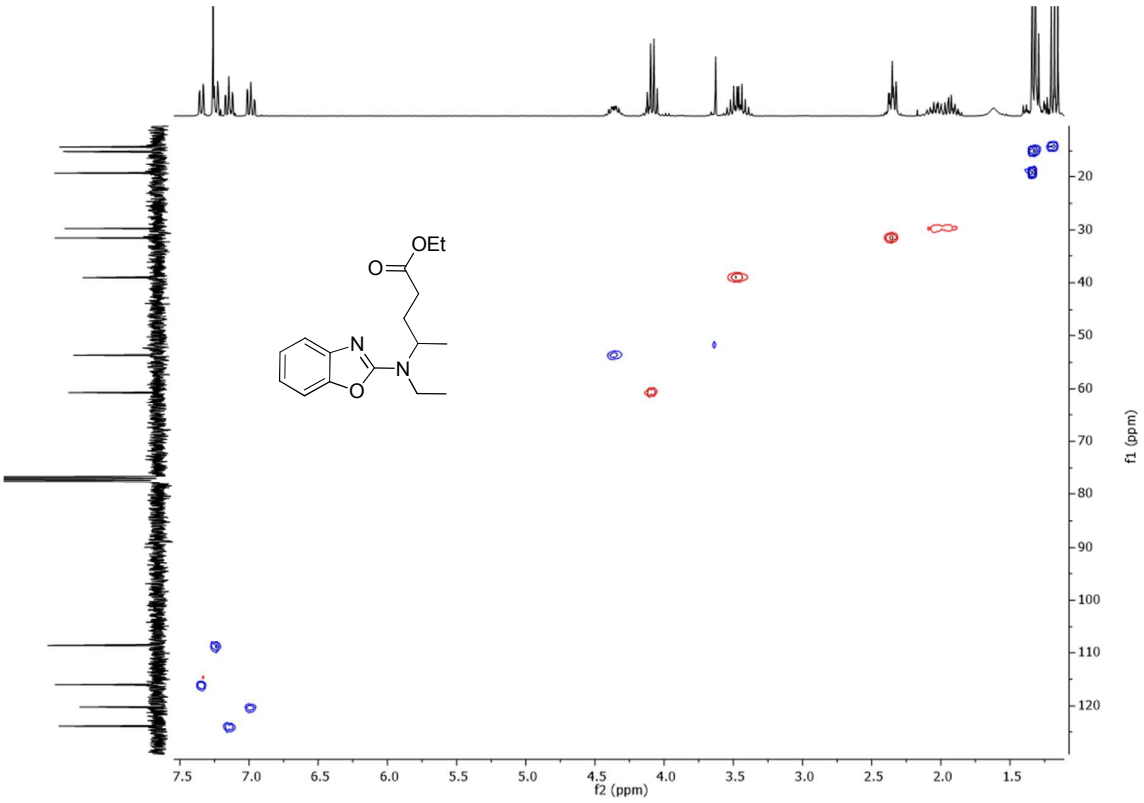
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 12a



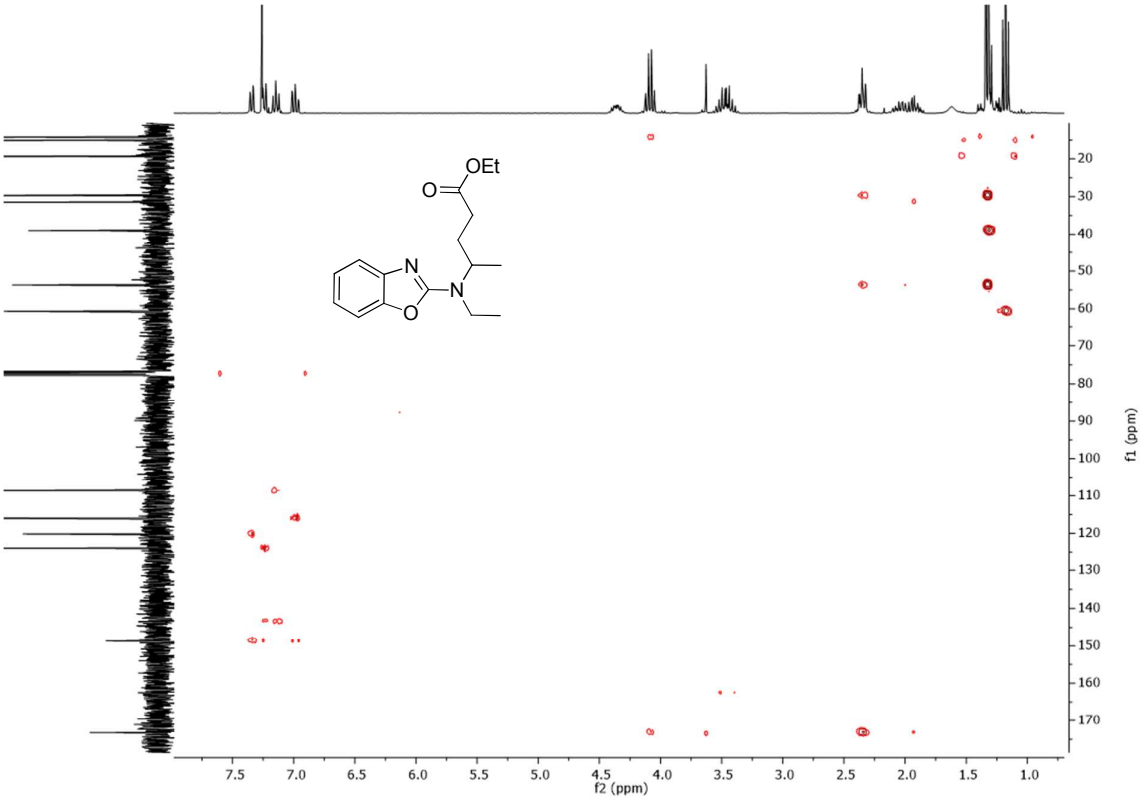
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 12a



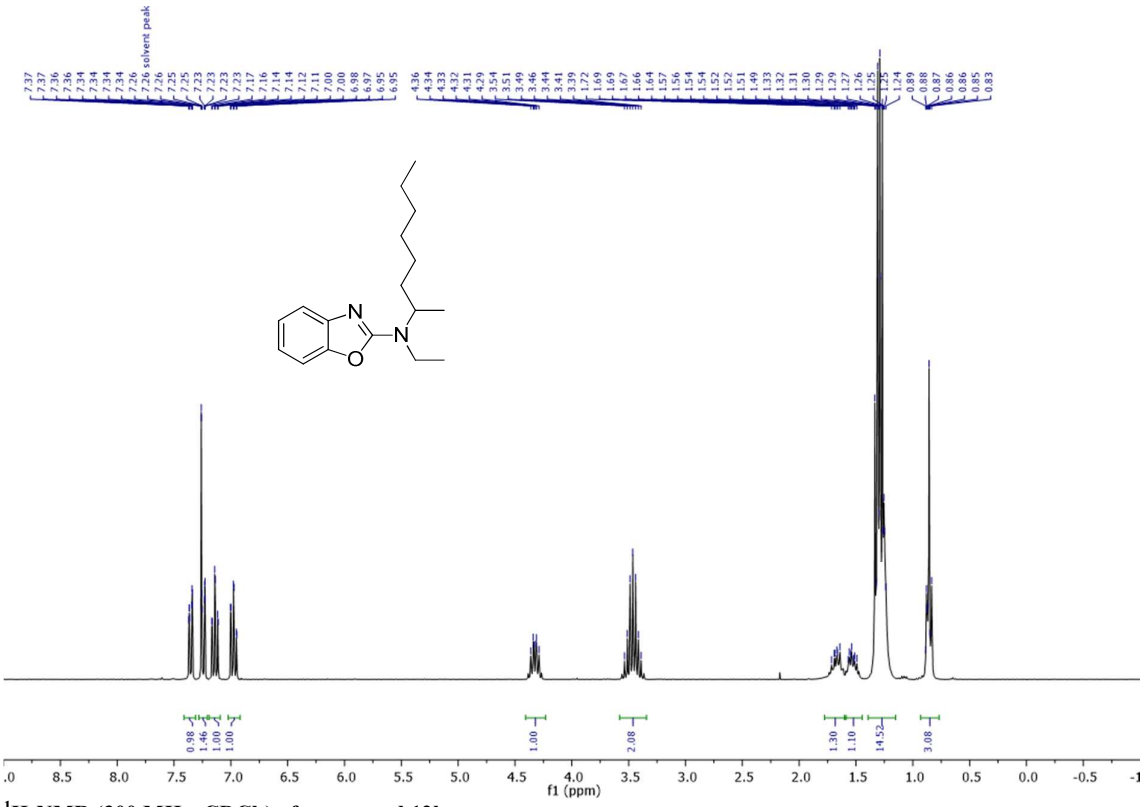
COSY of compound 12a



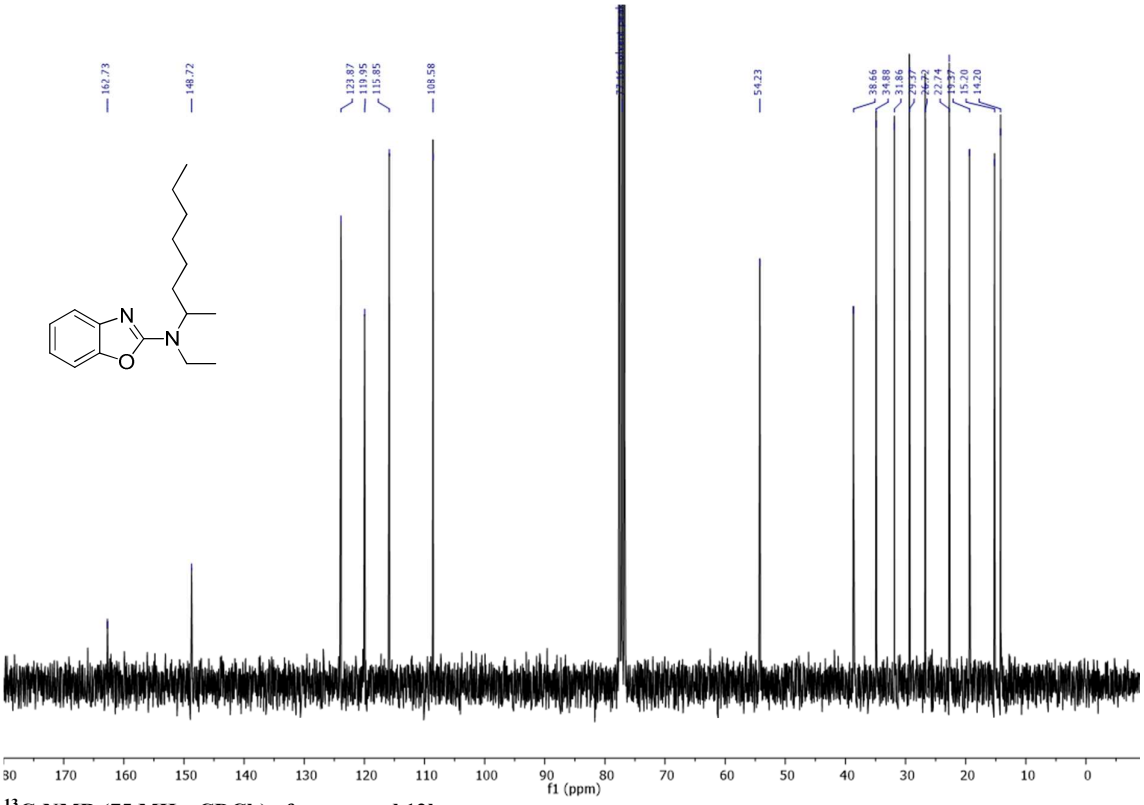
HSQC of compound 12a



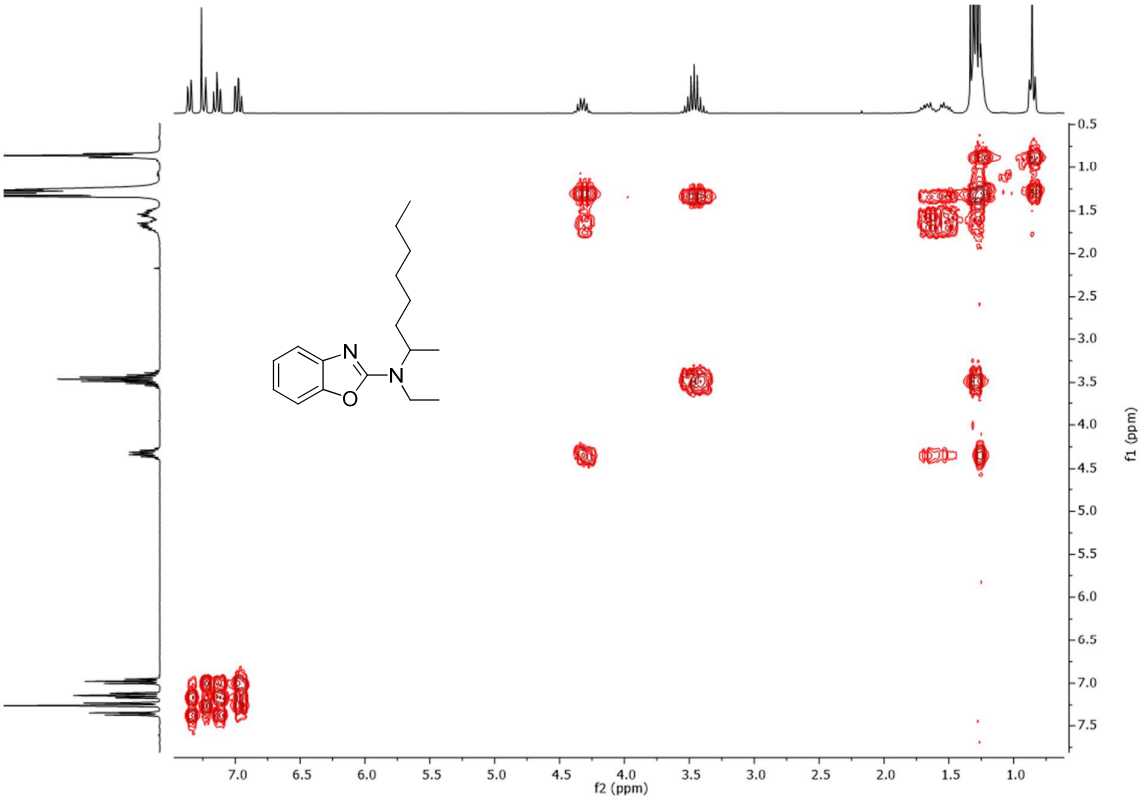
HMBC of compound 12a



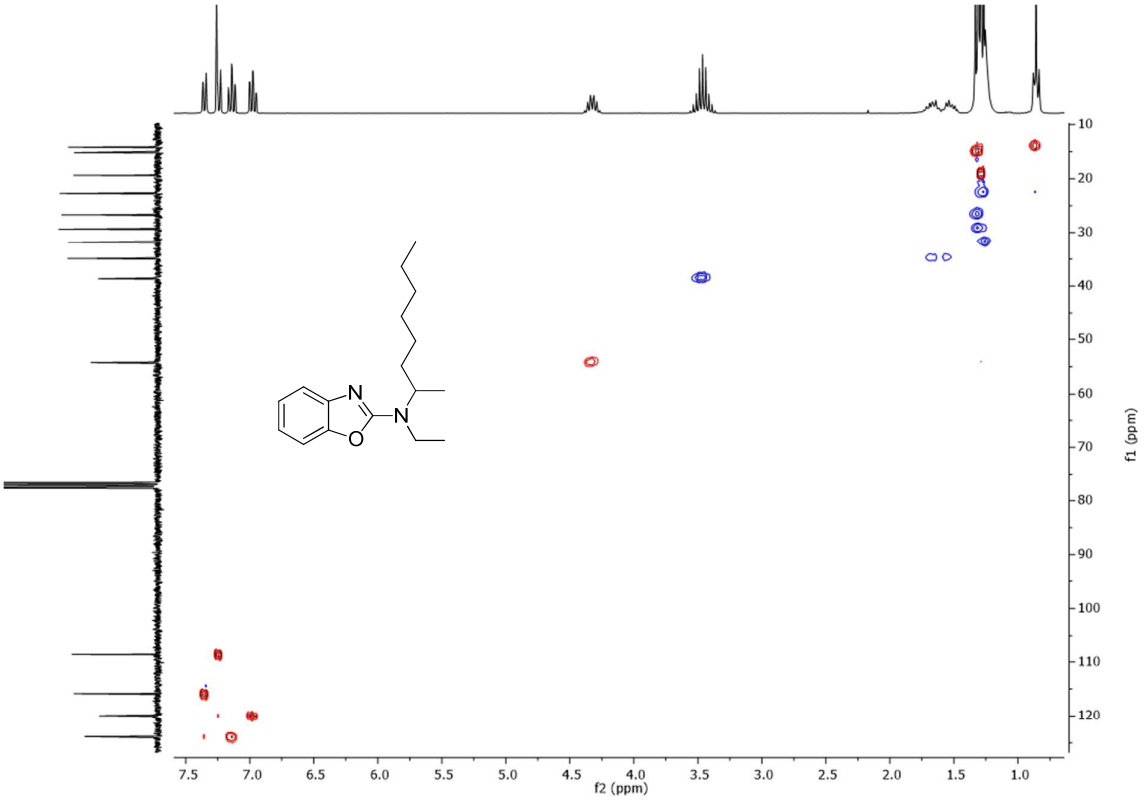
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 12b



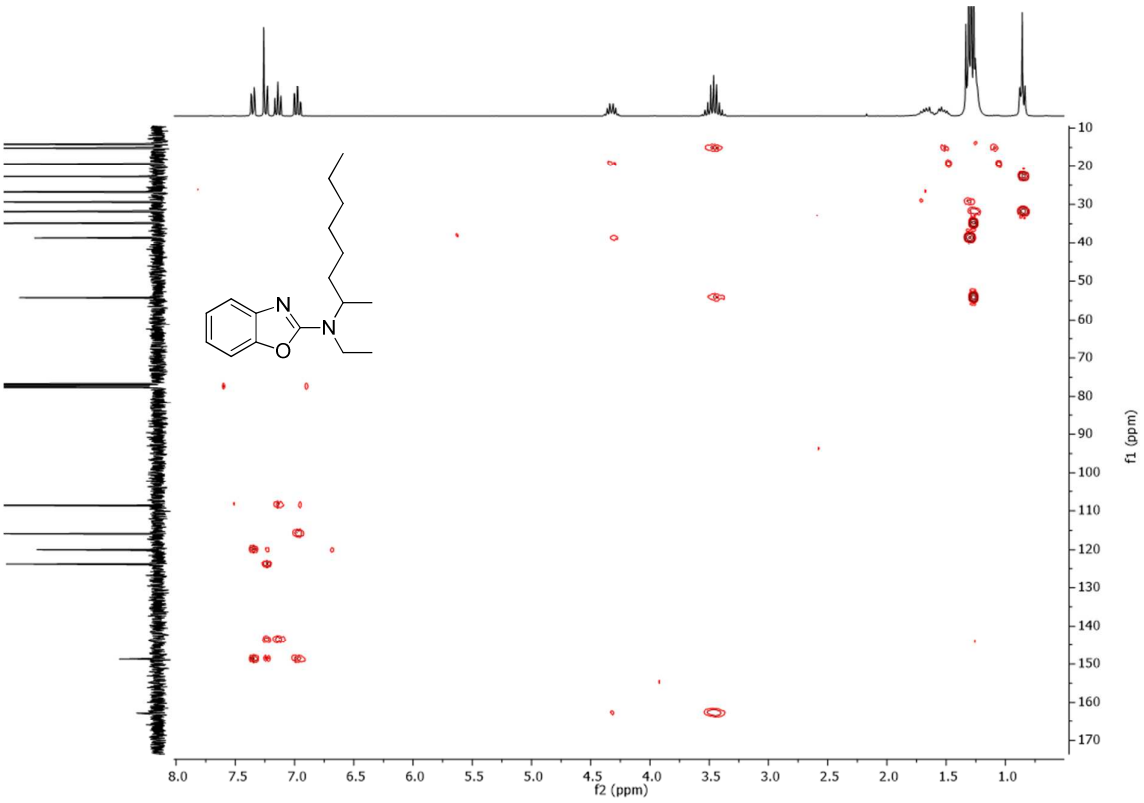
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 12b



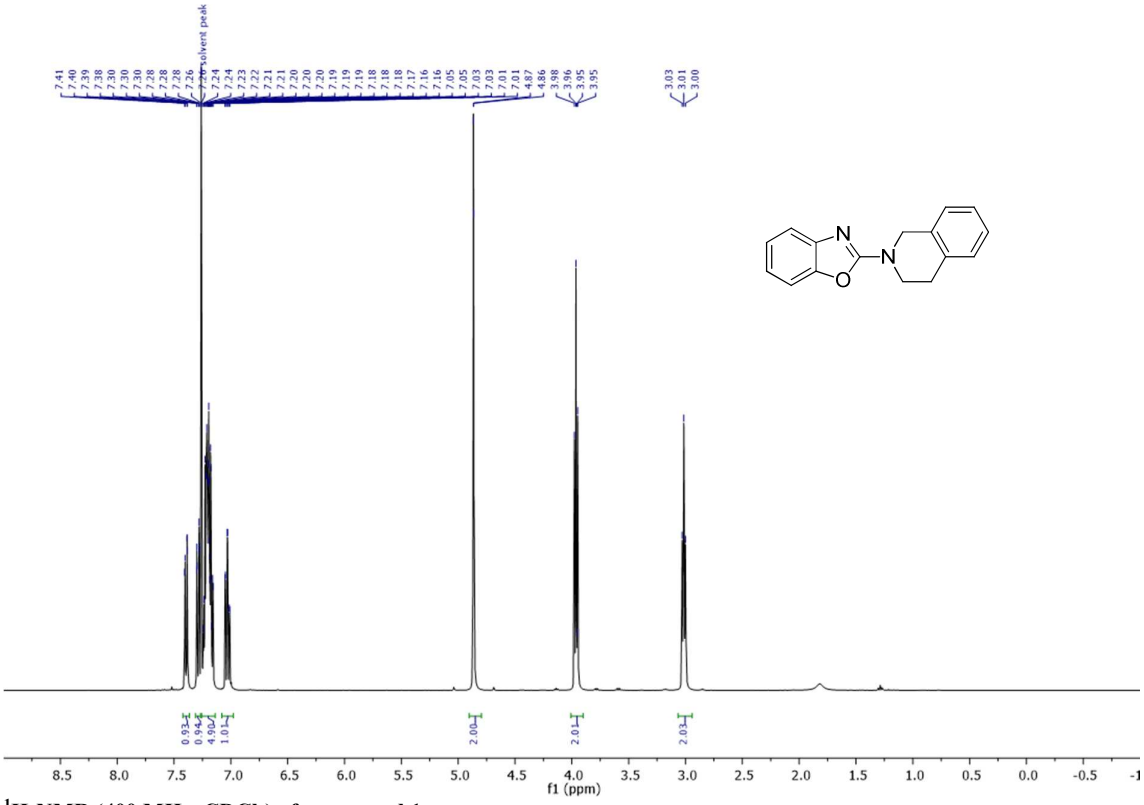
COSY of compound 12b



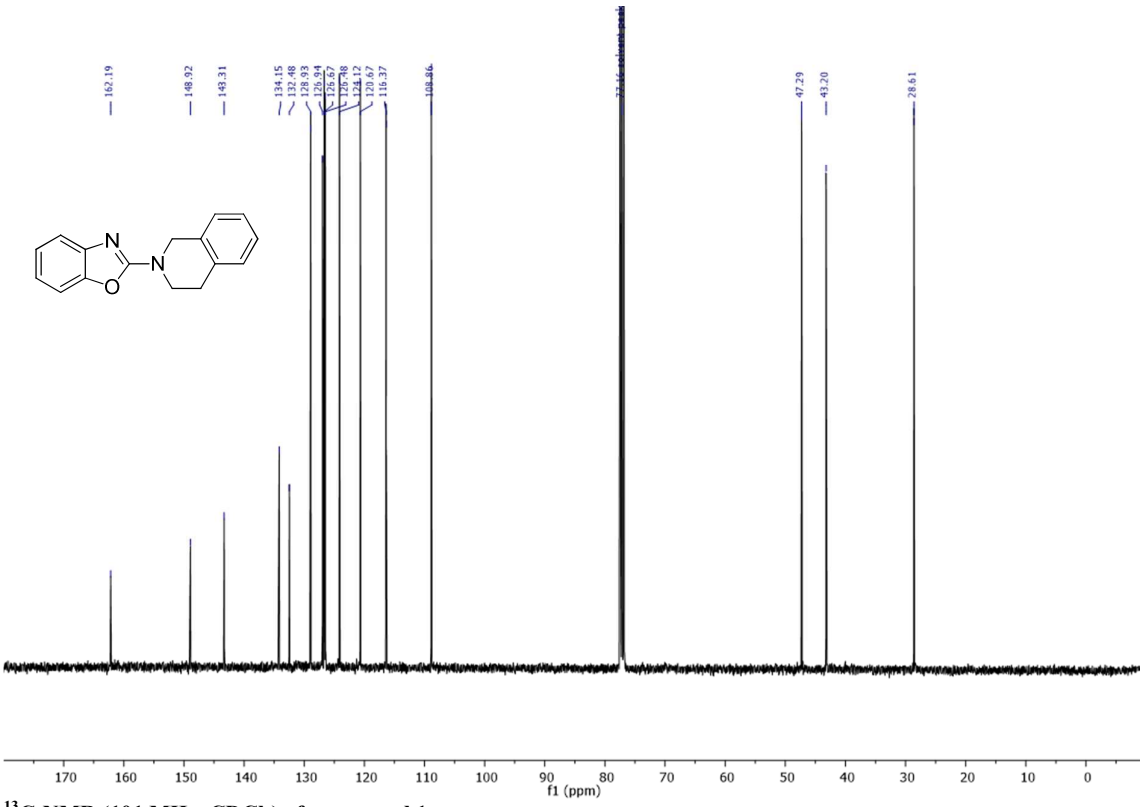
HSQC of compound 12b



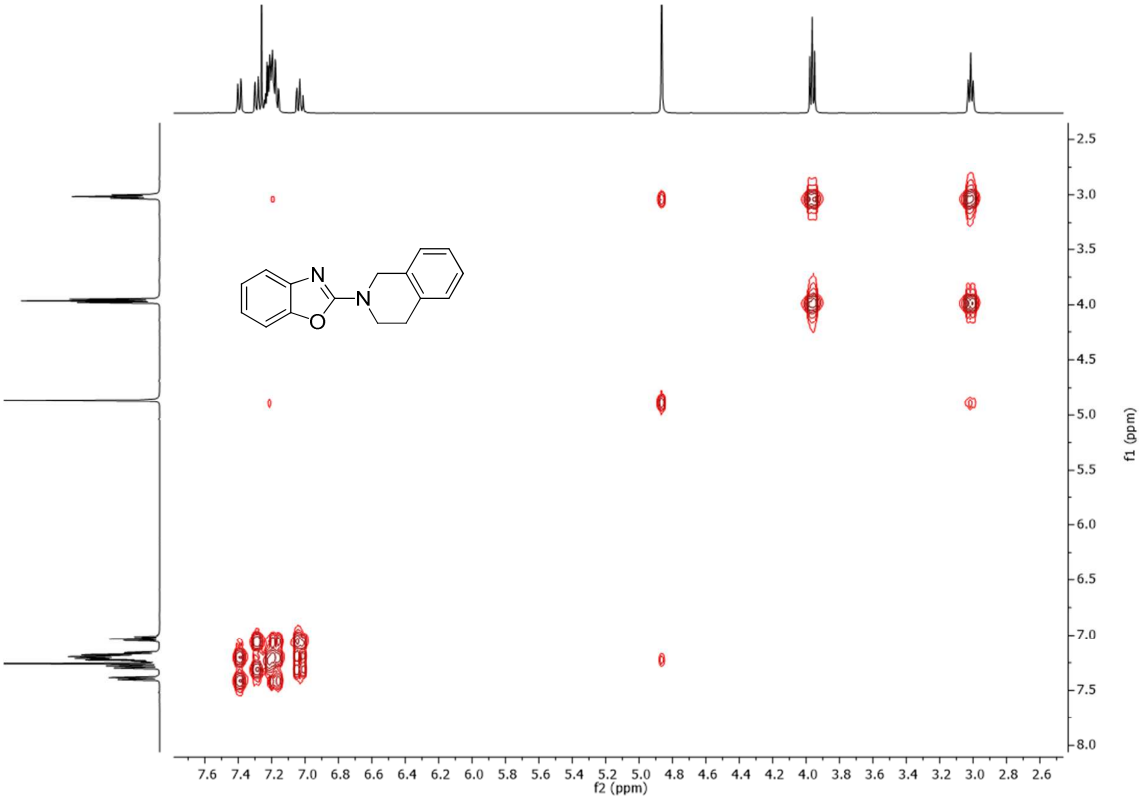
HMBC of compound 12b



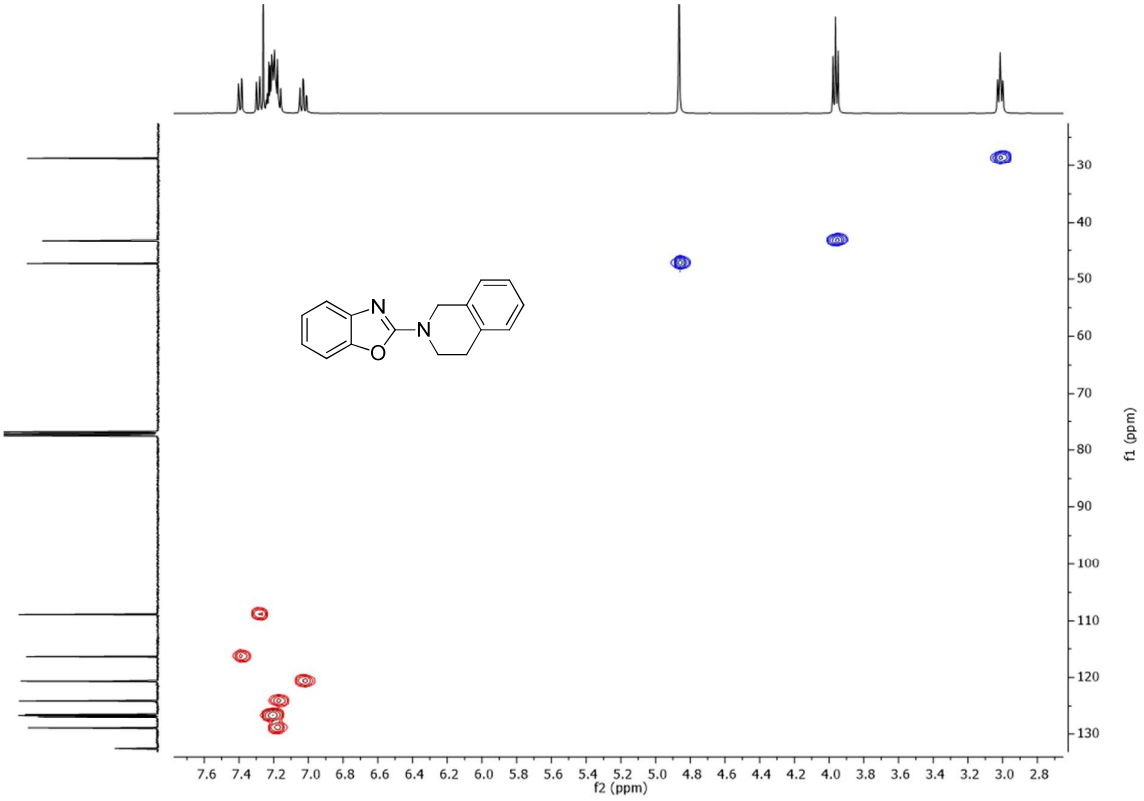
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 1



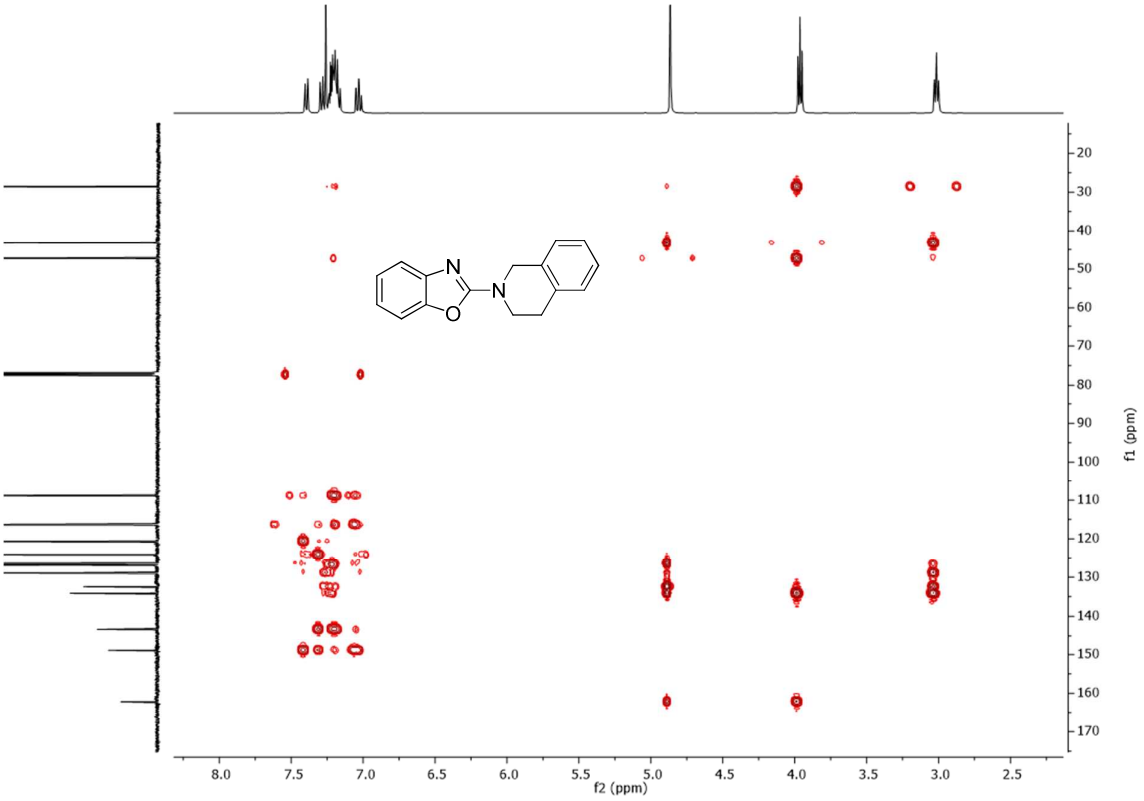
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 1



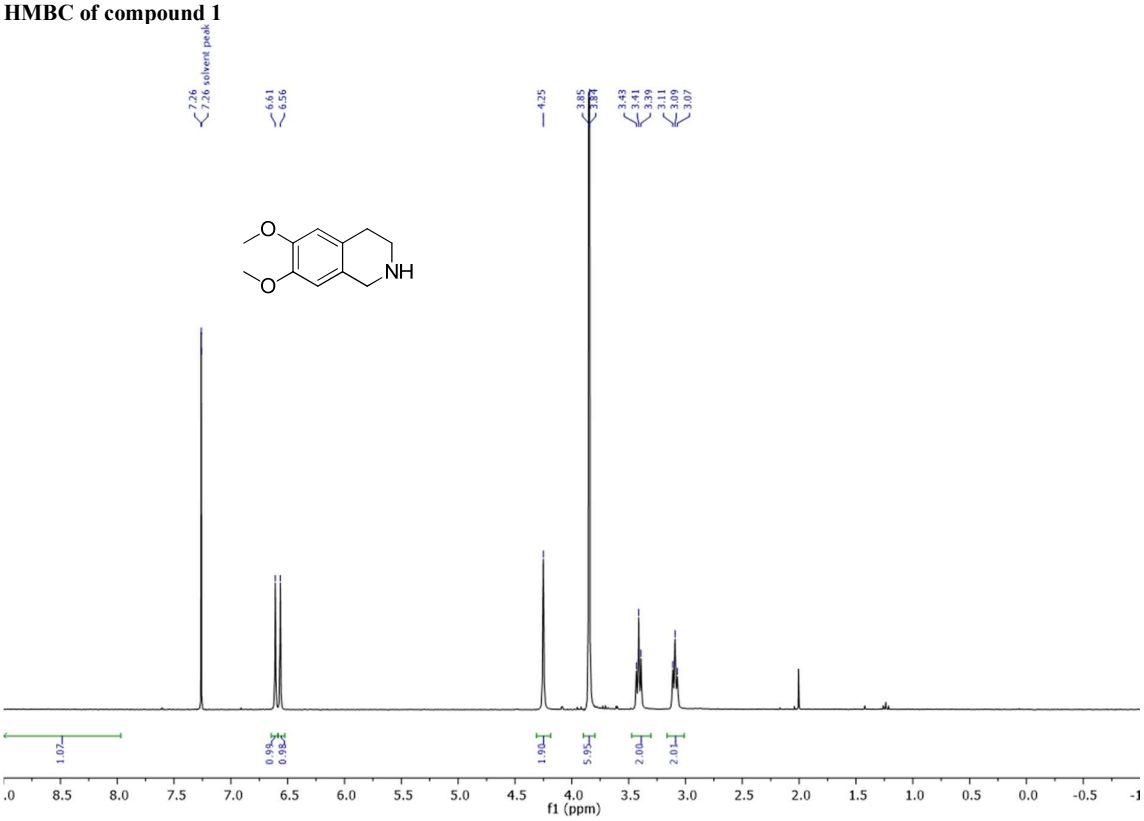
COSY of compound 1



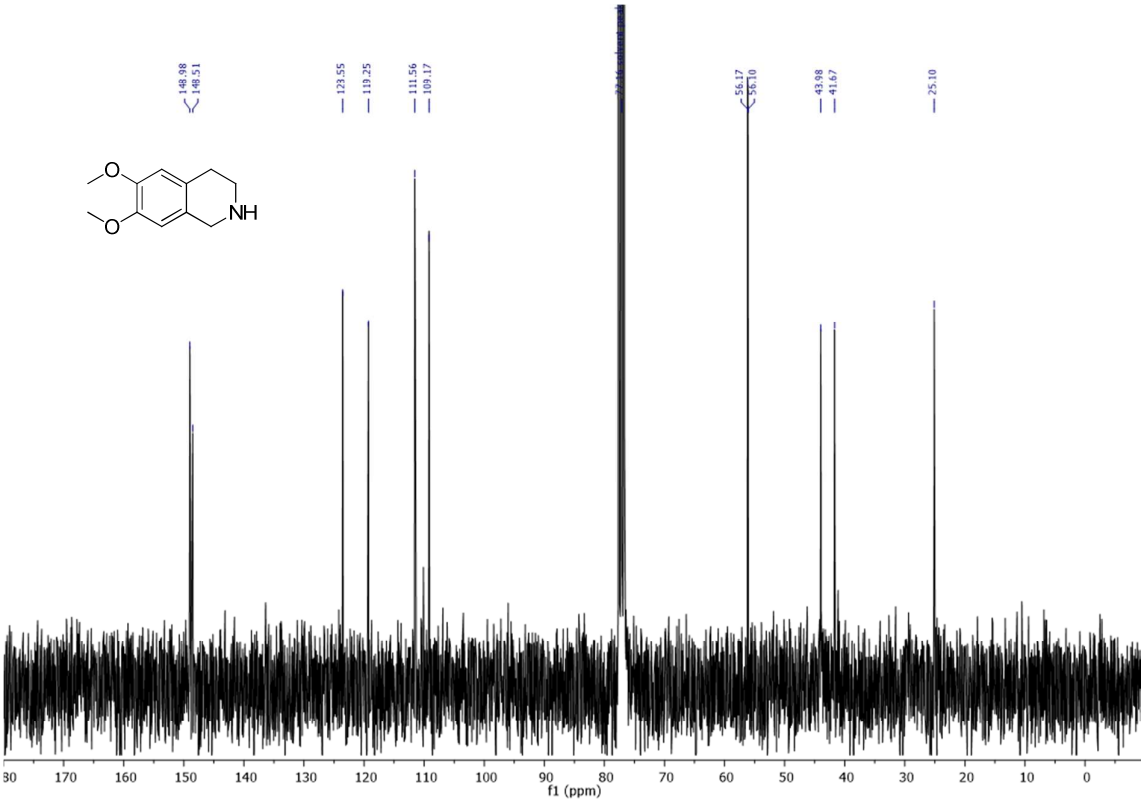
HSQC of compound 1



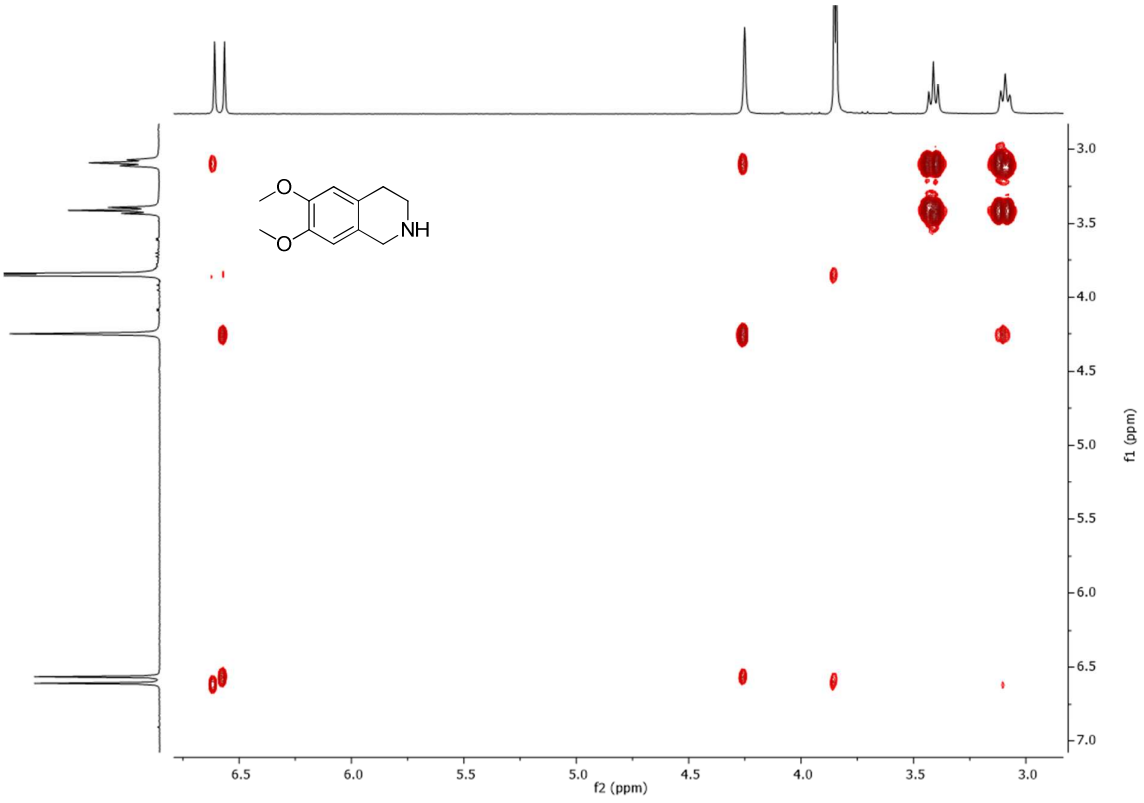
HMBC of compound 1



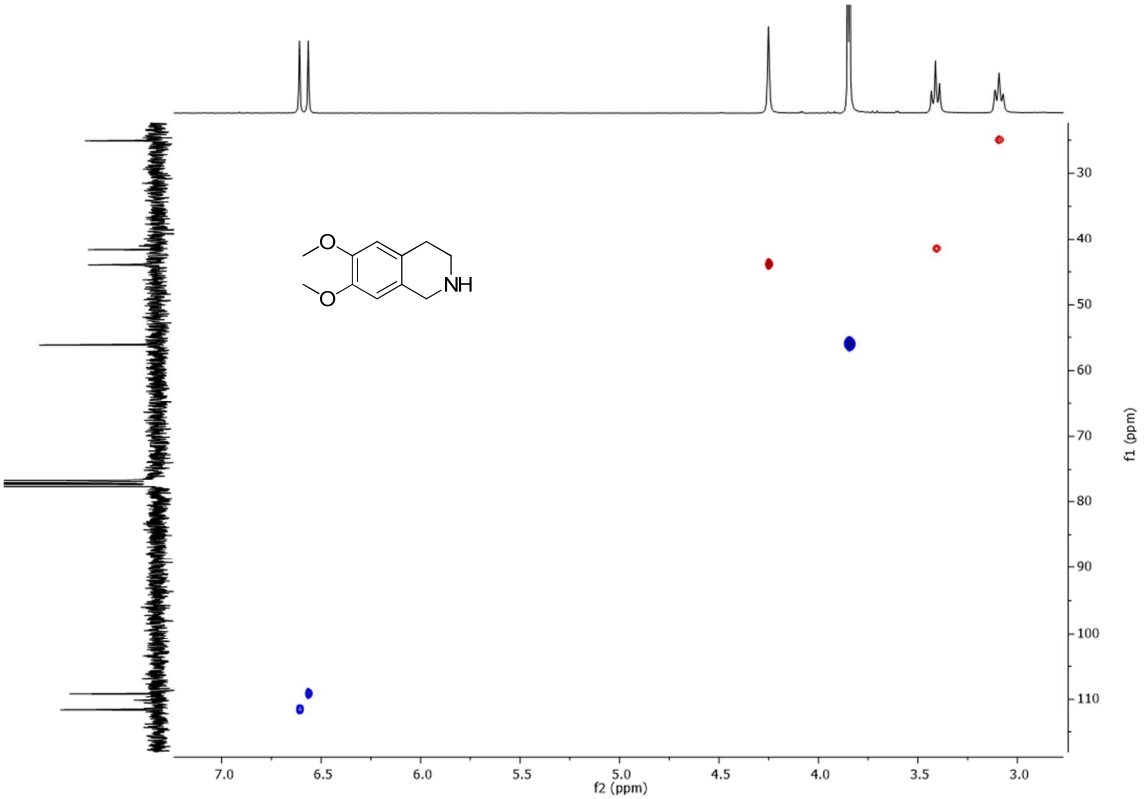
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 16



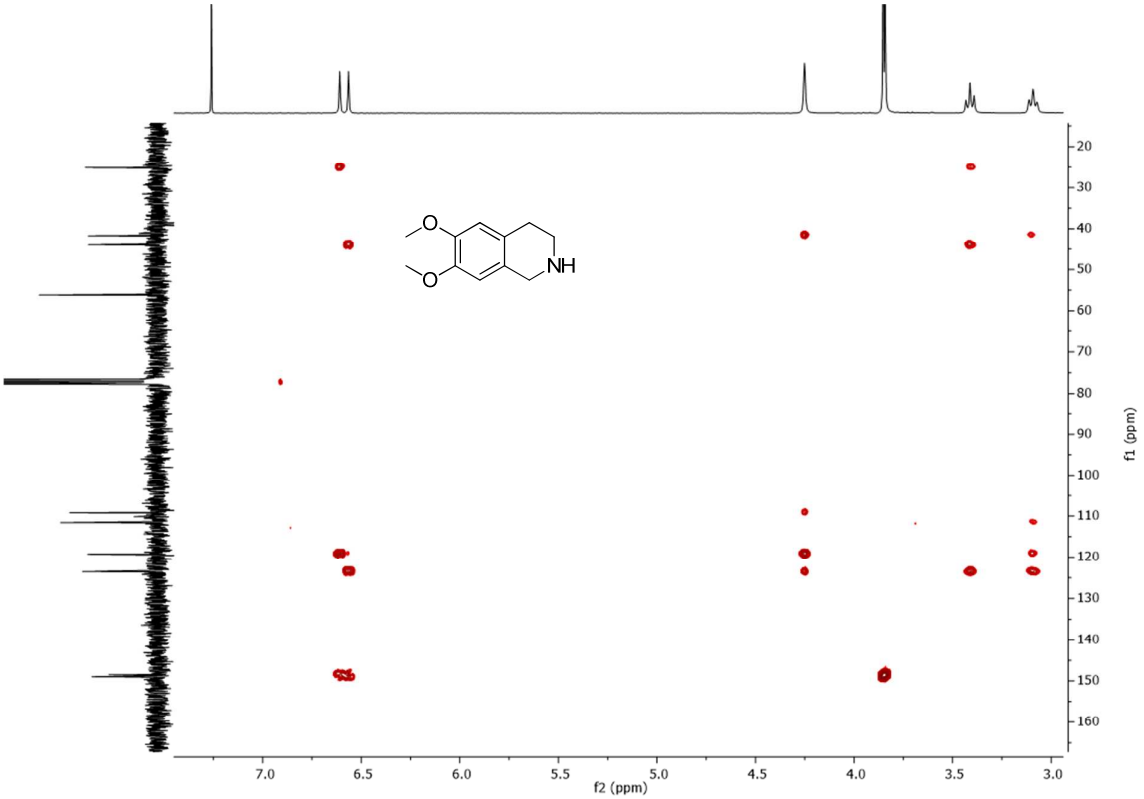
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 16



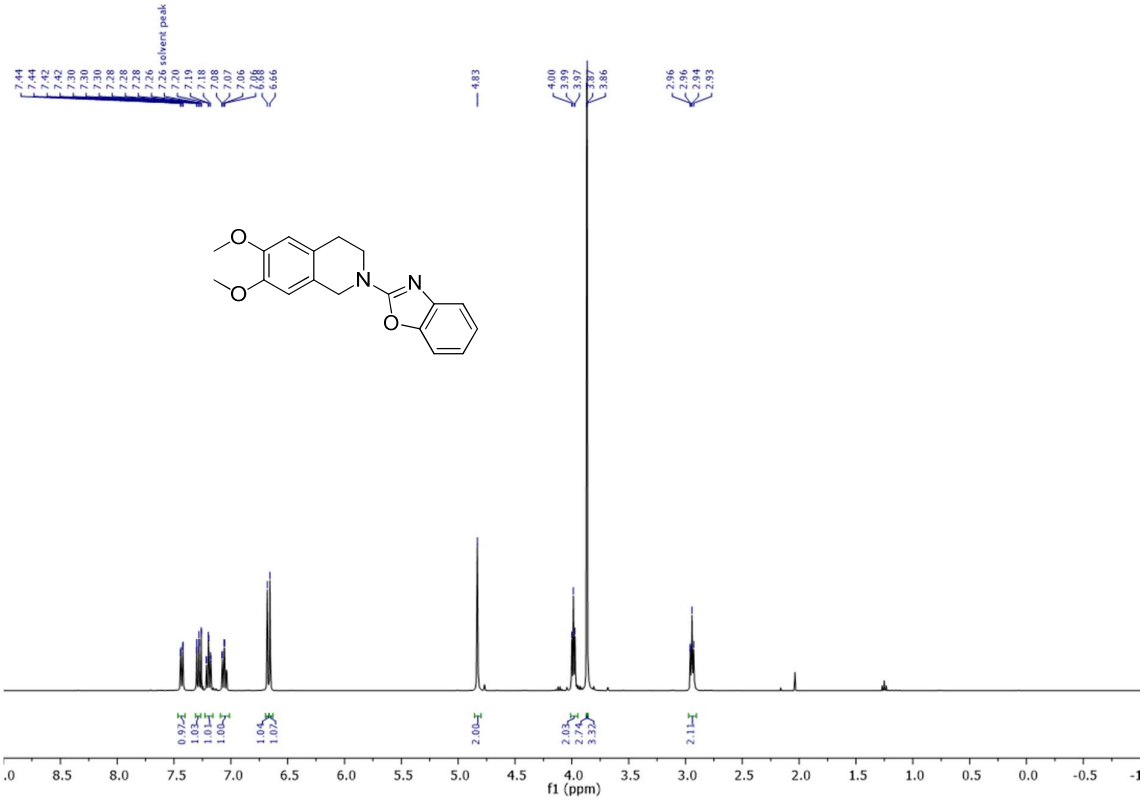
COSY of compound 16



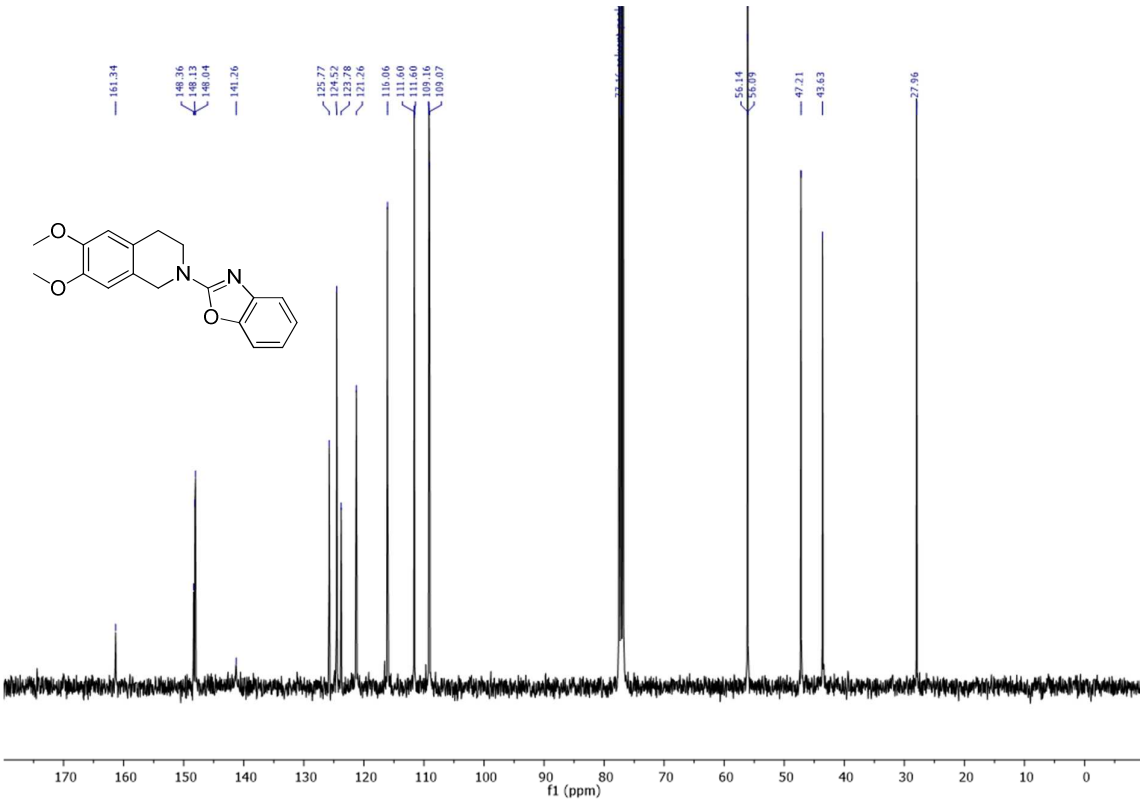
HSQC of compound 16



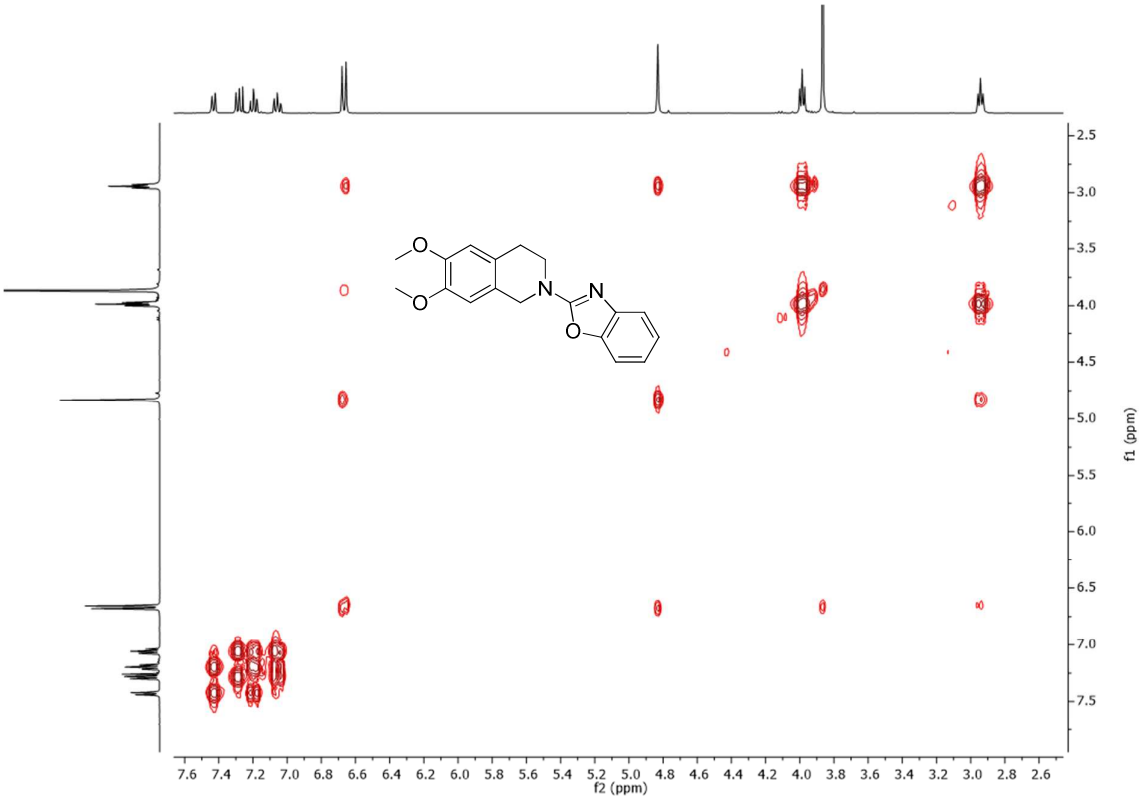
HMBC of compound 16



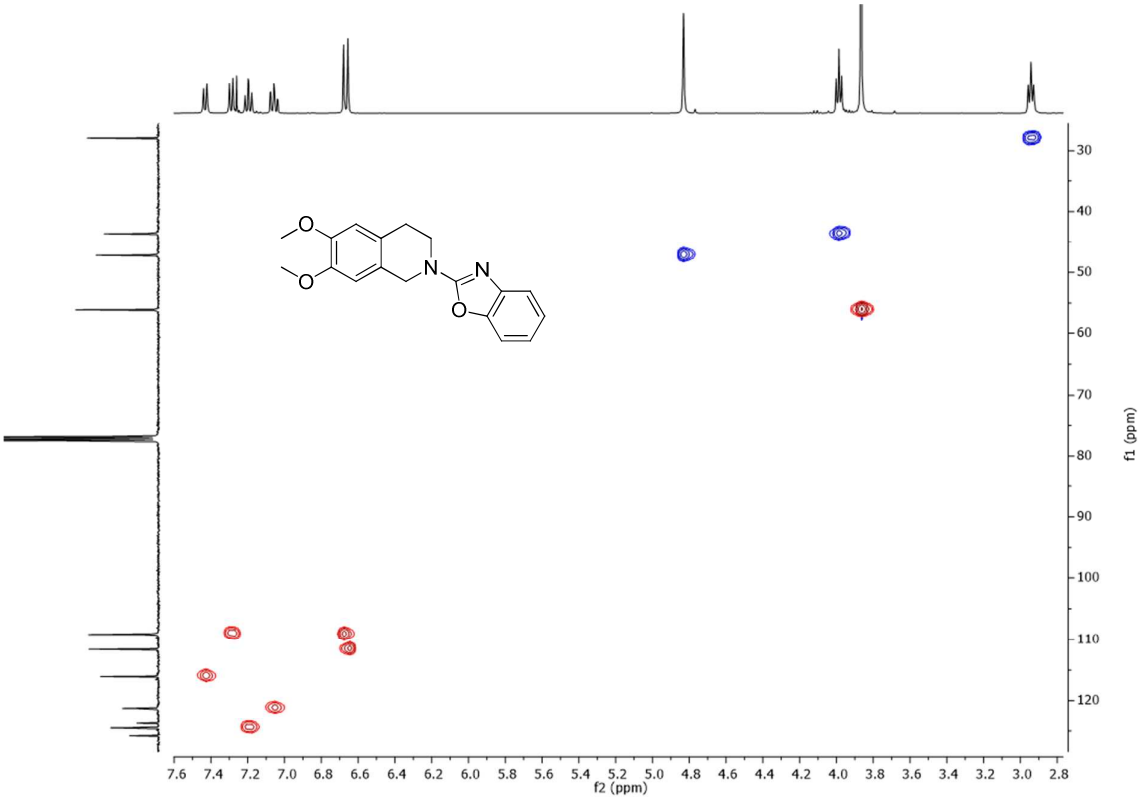
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 3



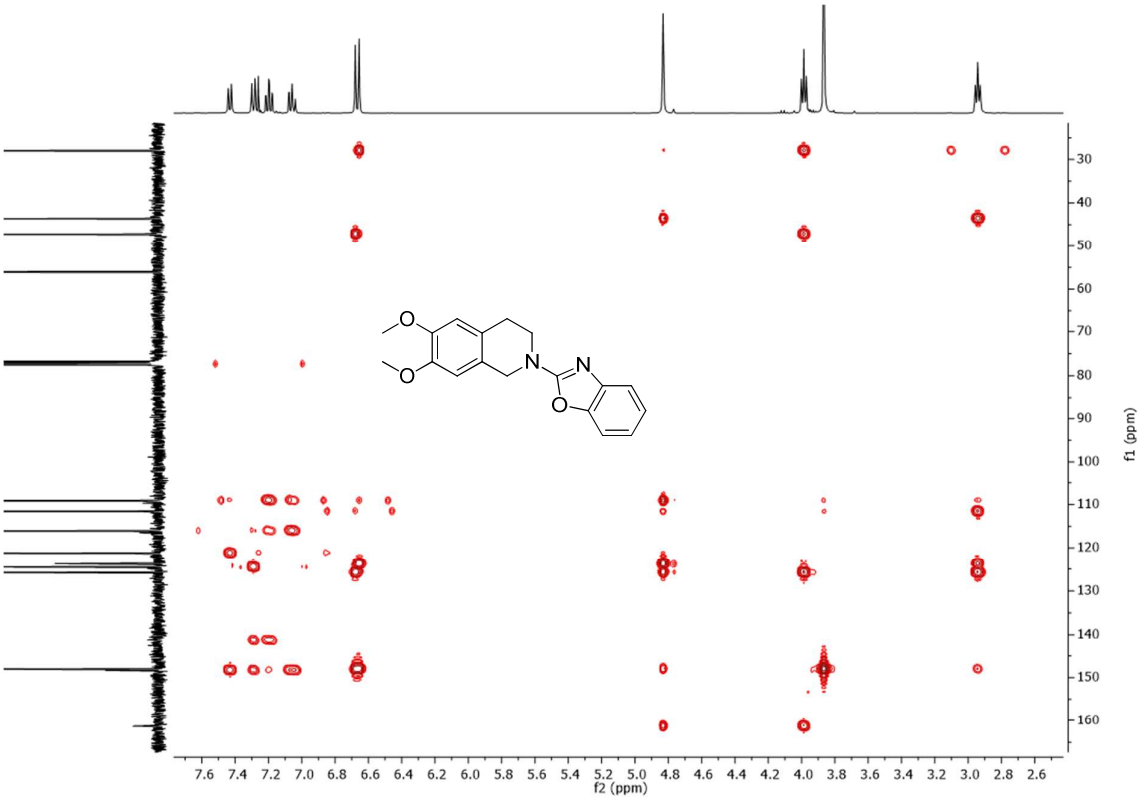
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 3



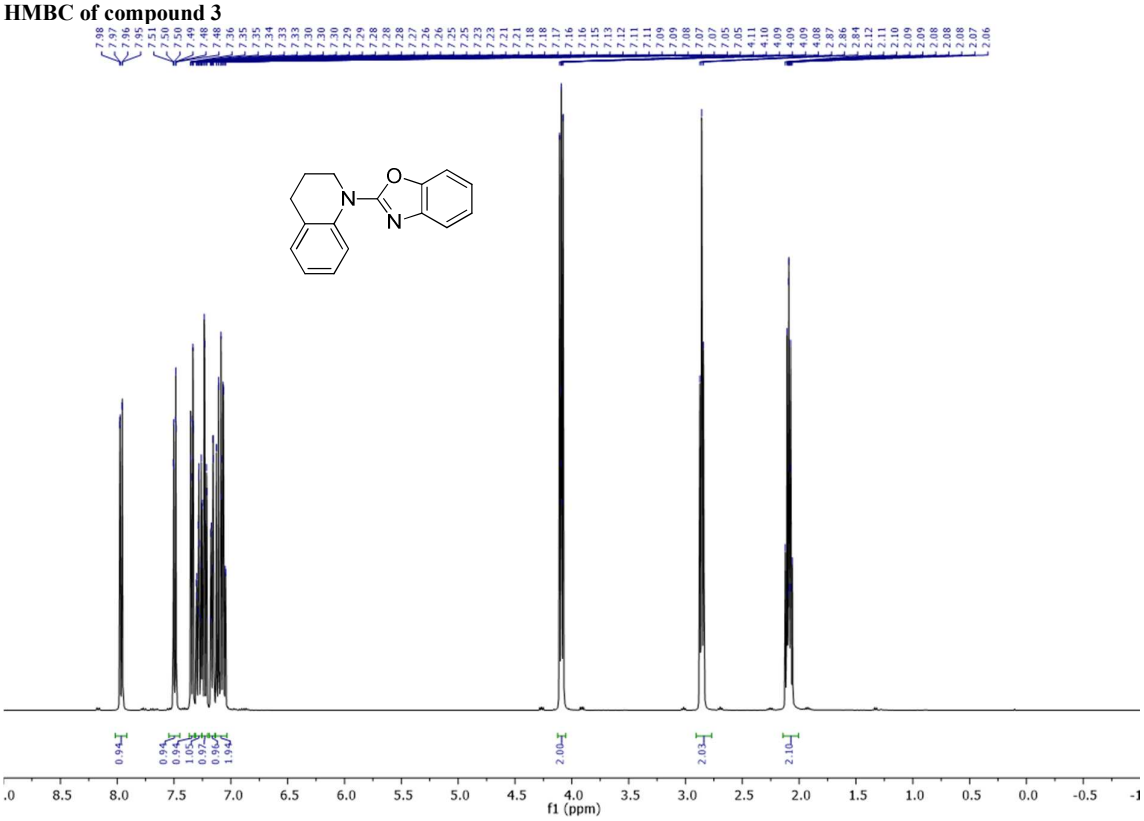
COSY of compound 3



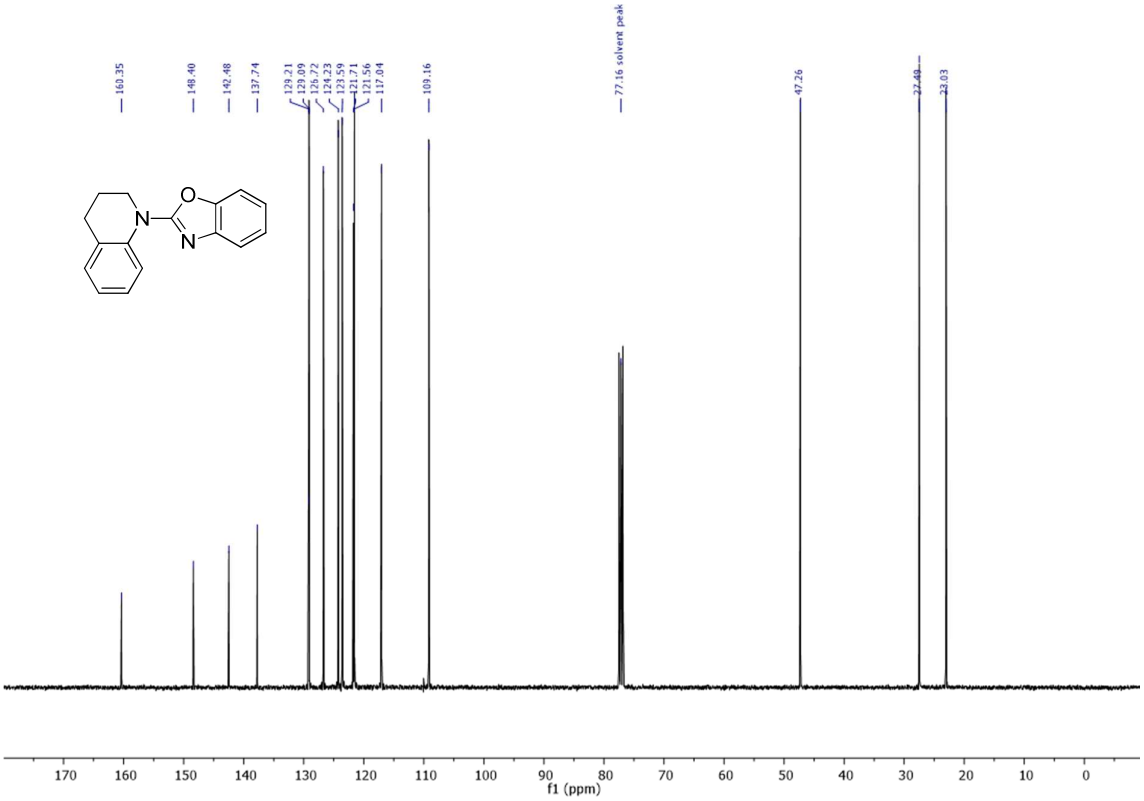
HSQC of compound 3



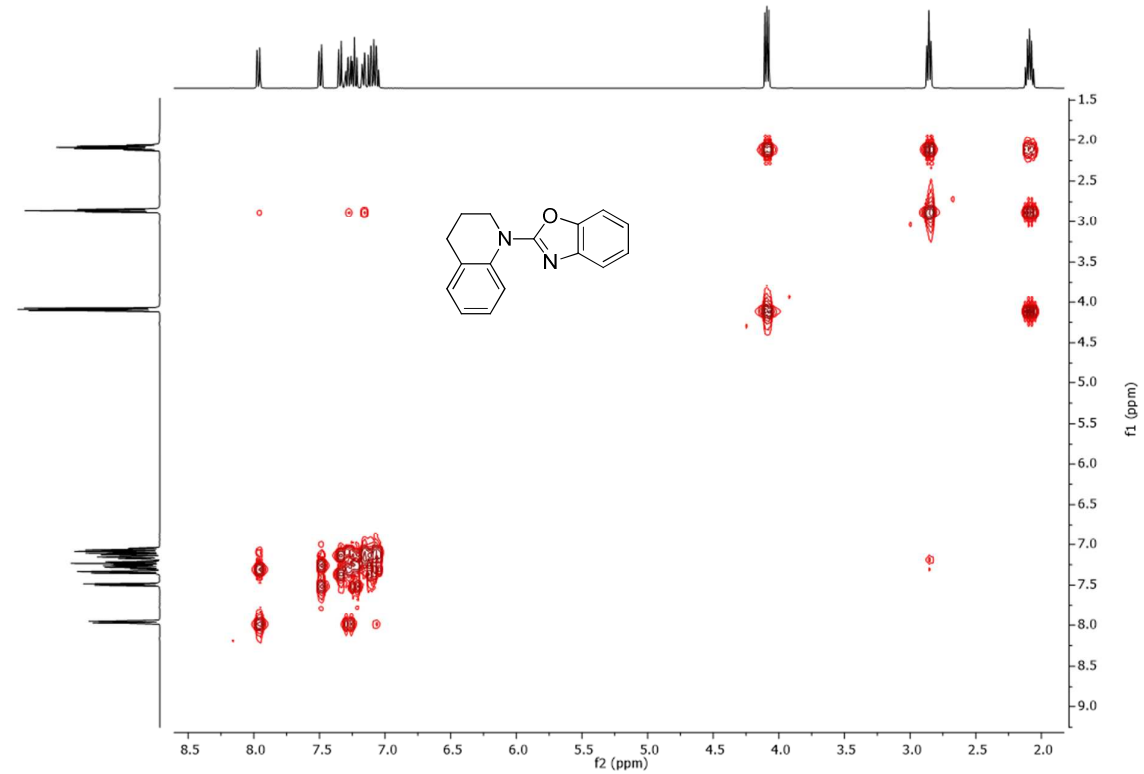
HMBC of compound 3



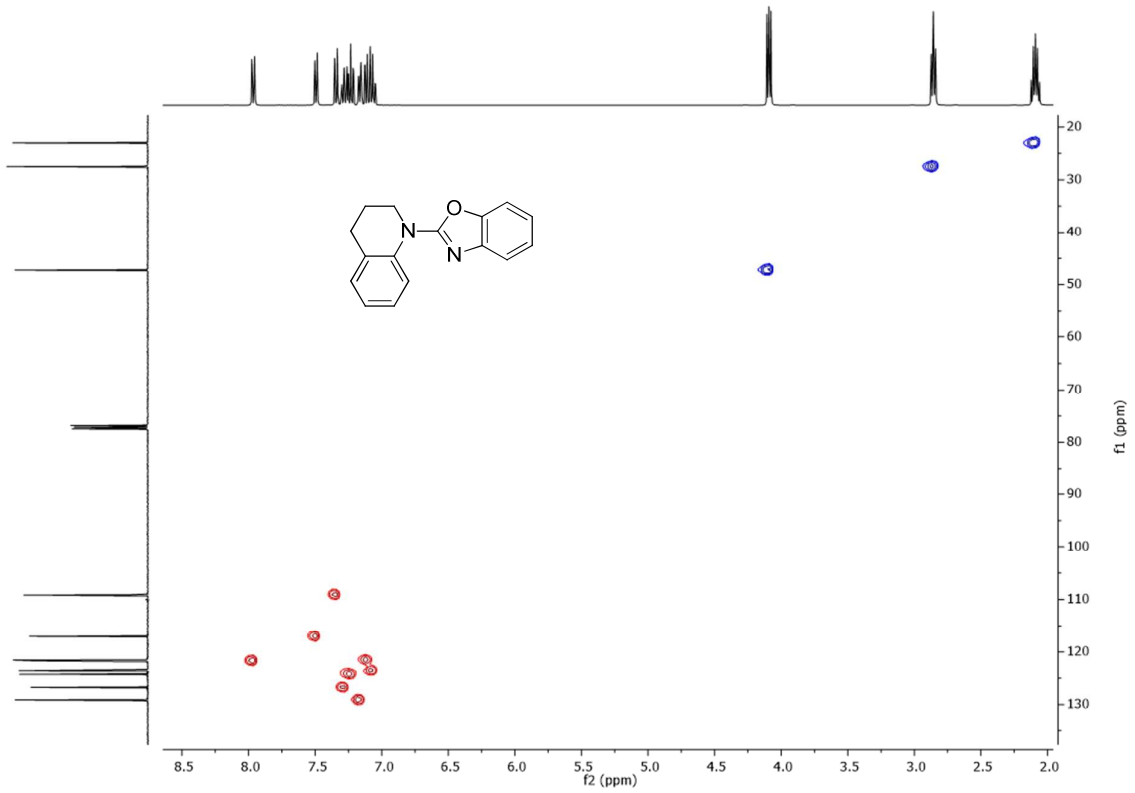
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 5



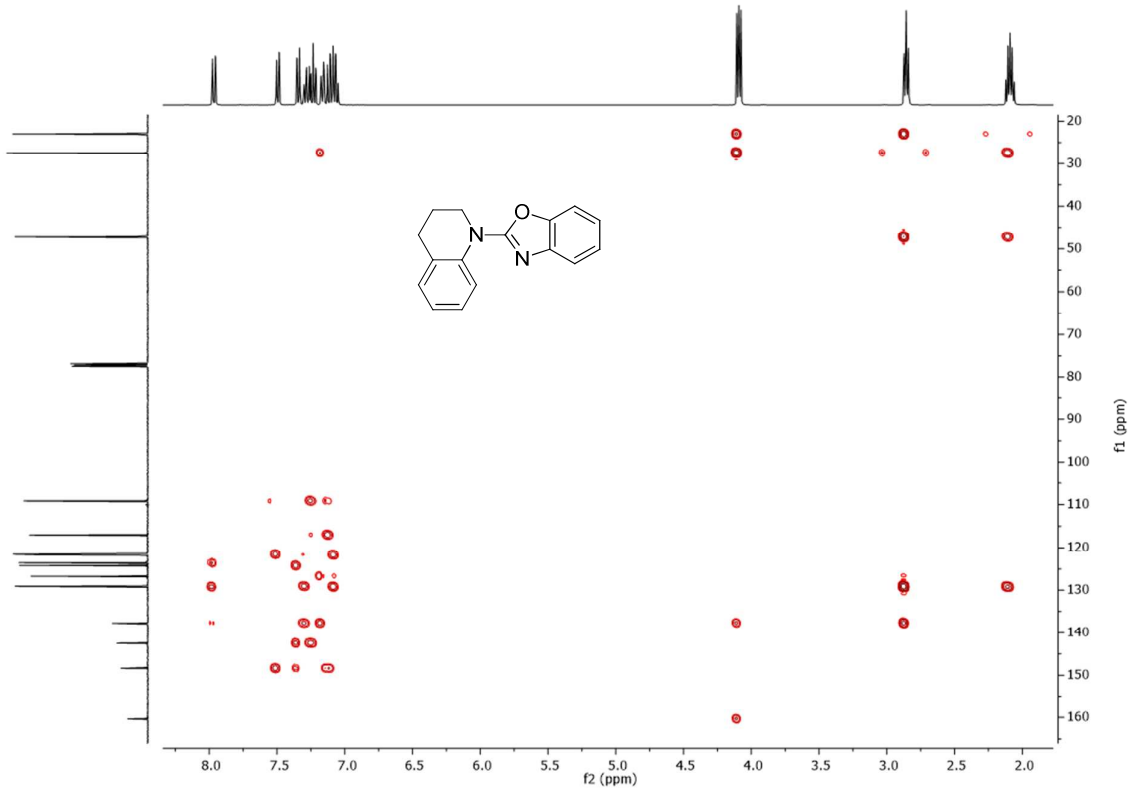
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 5



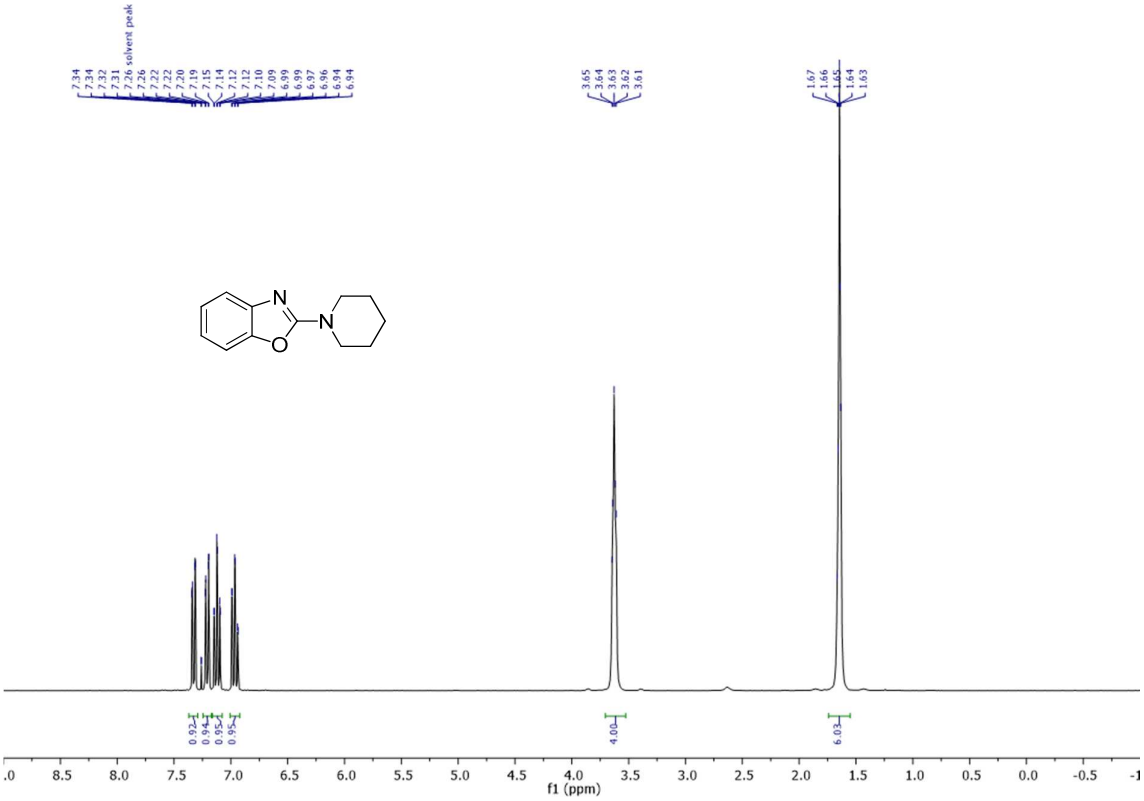
COSY of compound 5



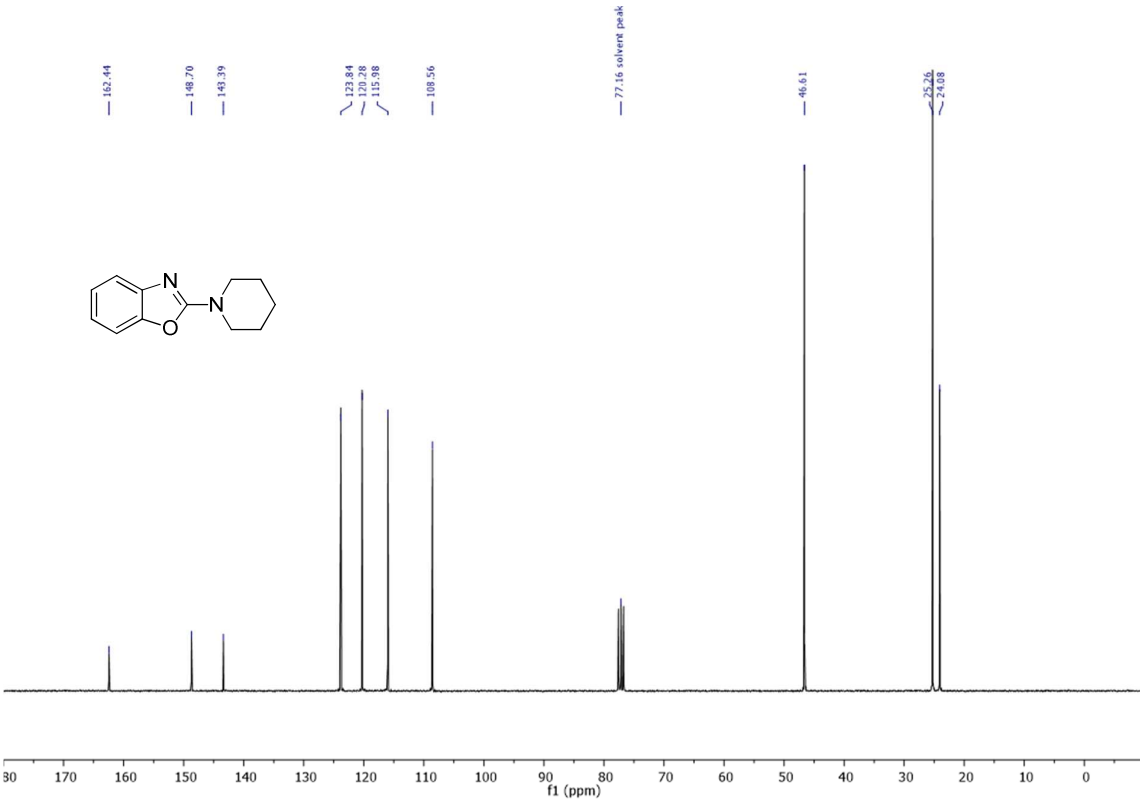
HSQC of compound 5



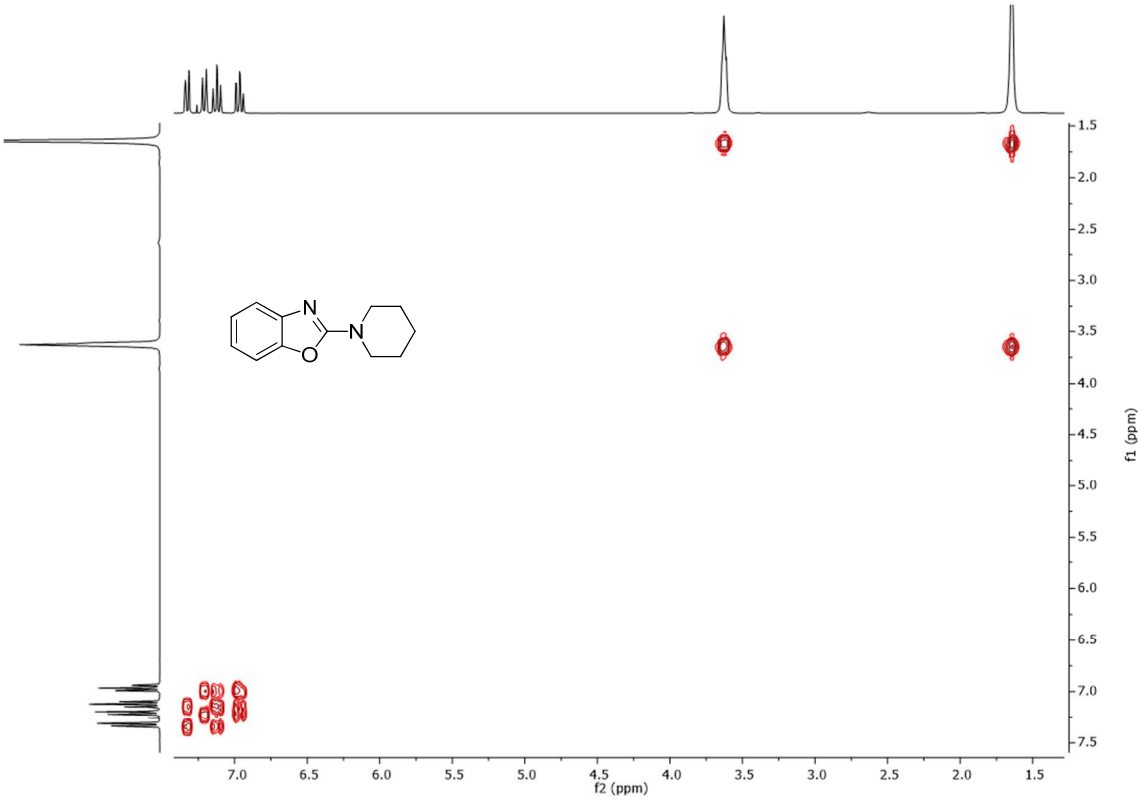
HMBC of compound 5



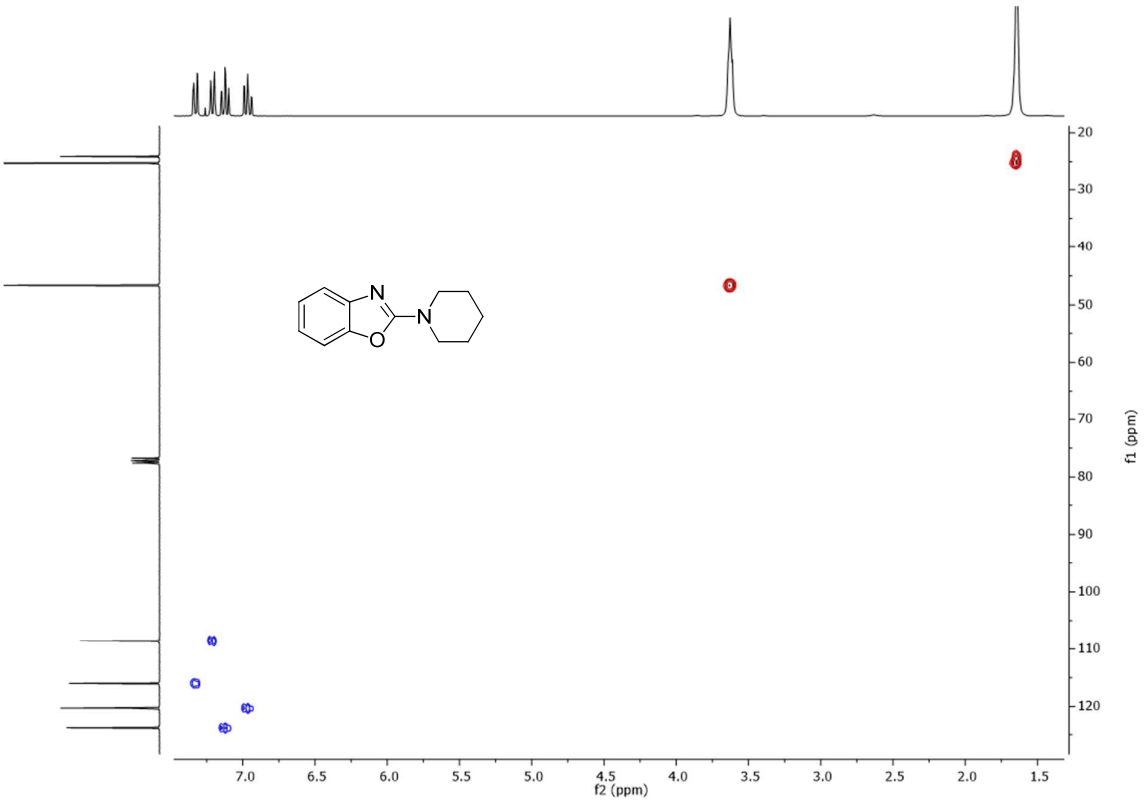
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 7



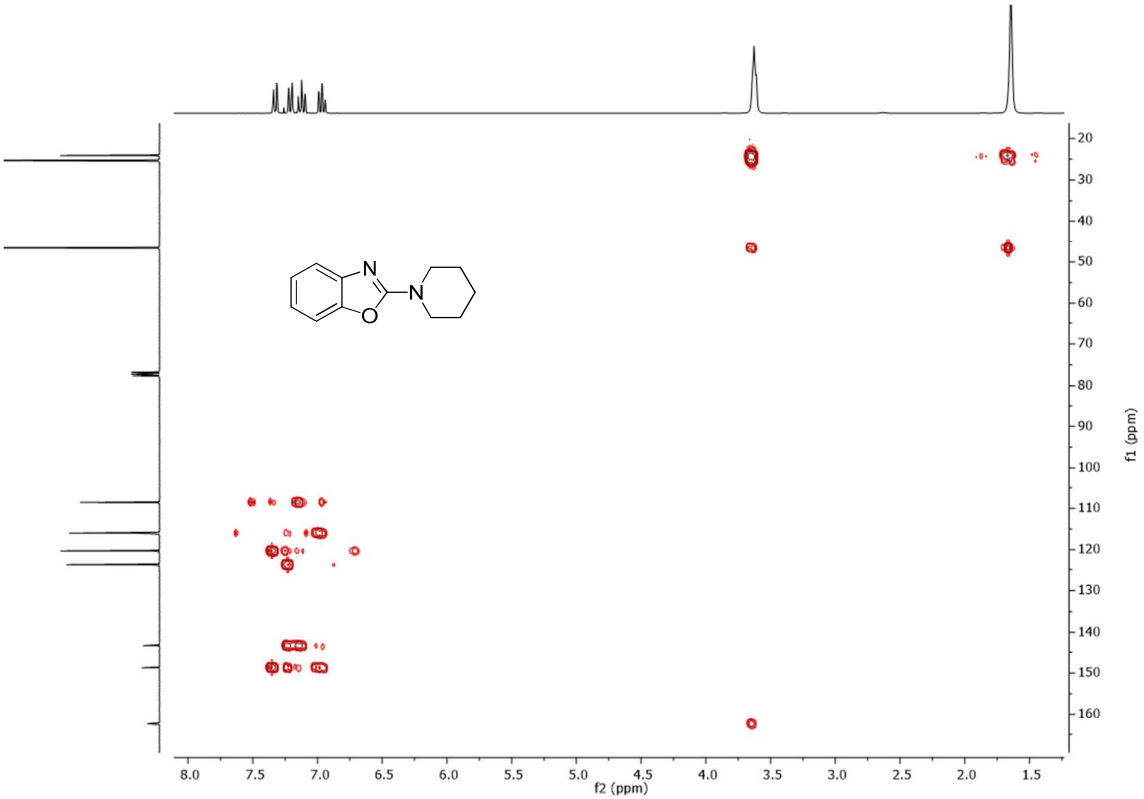
^{13}C-NMR (75 MHz, $CDCl_3$) of compound 7



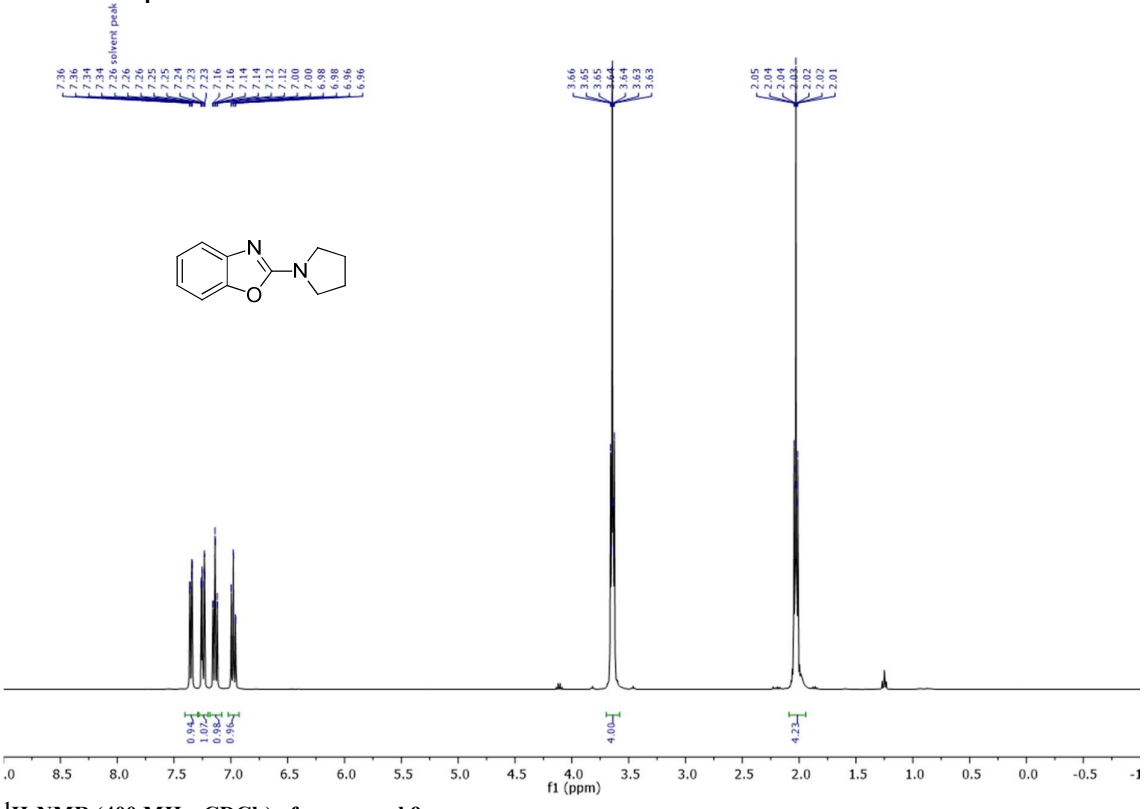
COSY of compound 7



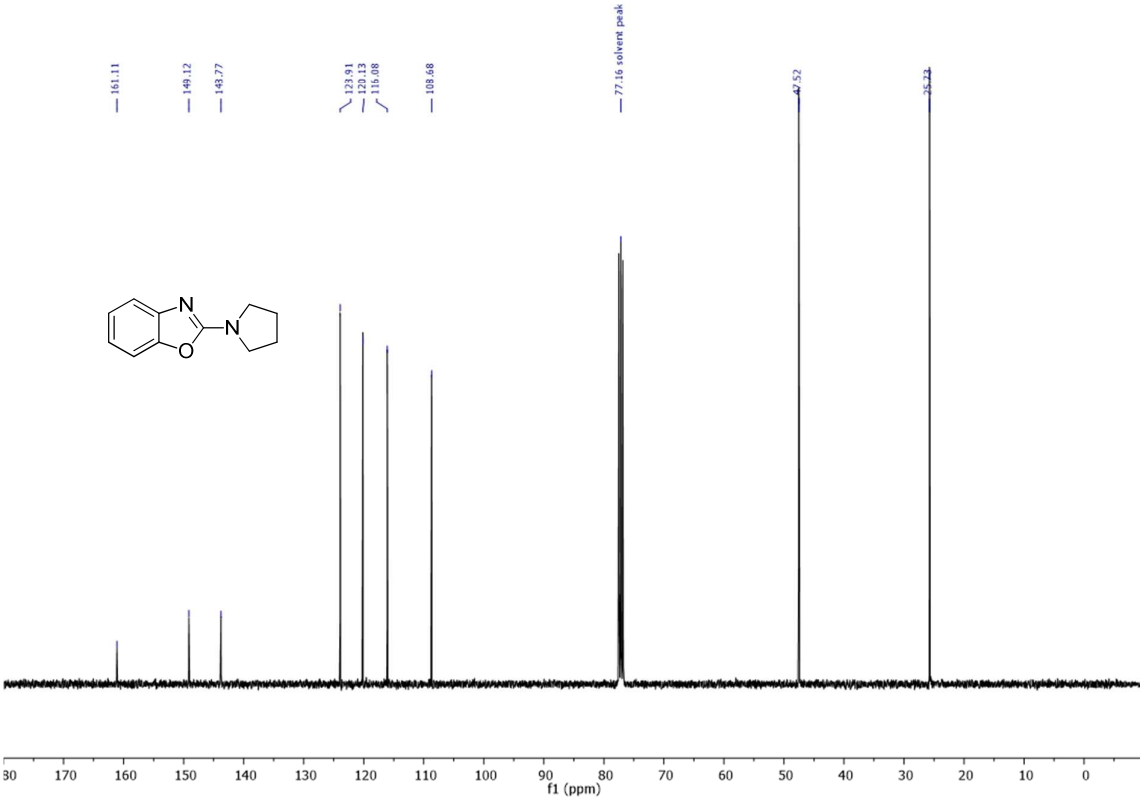
HSQC of compound 7



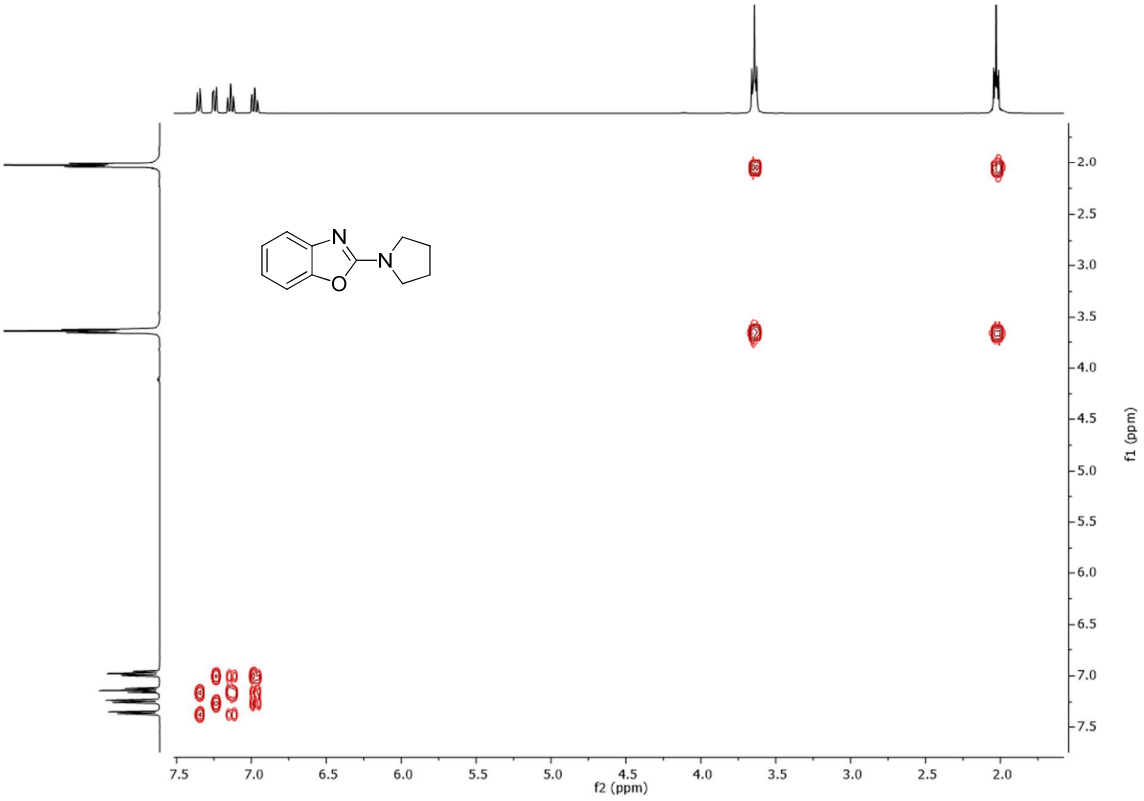
HMBC of compound 7



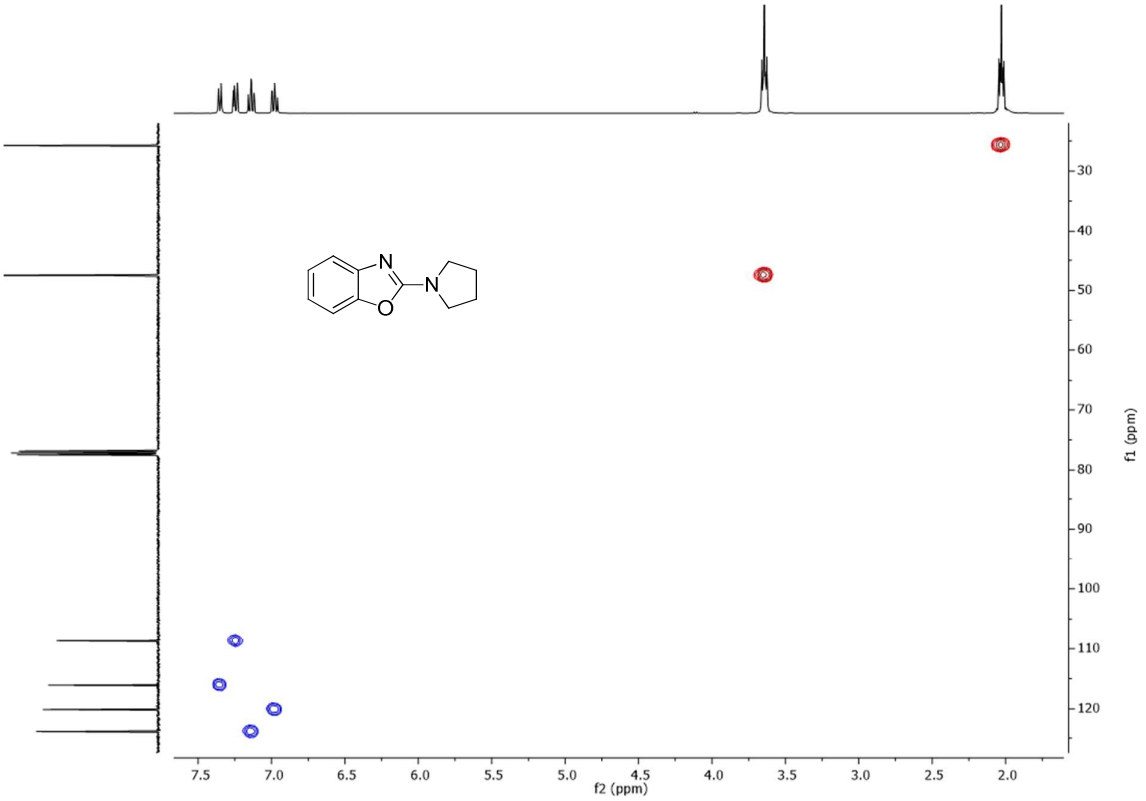
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 9



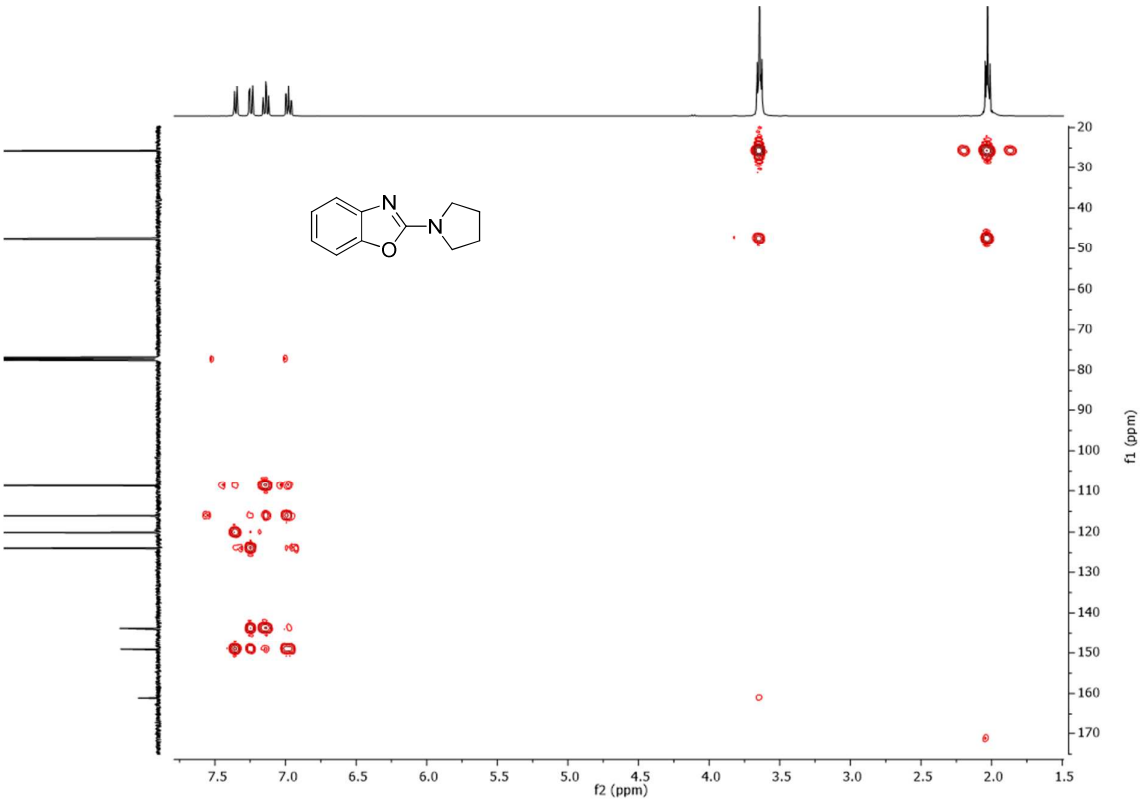
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 9



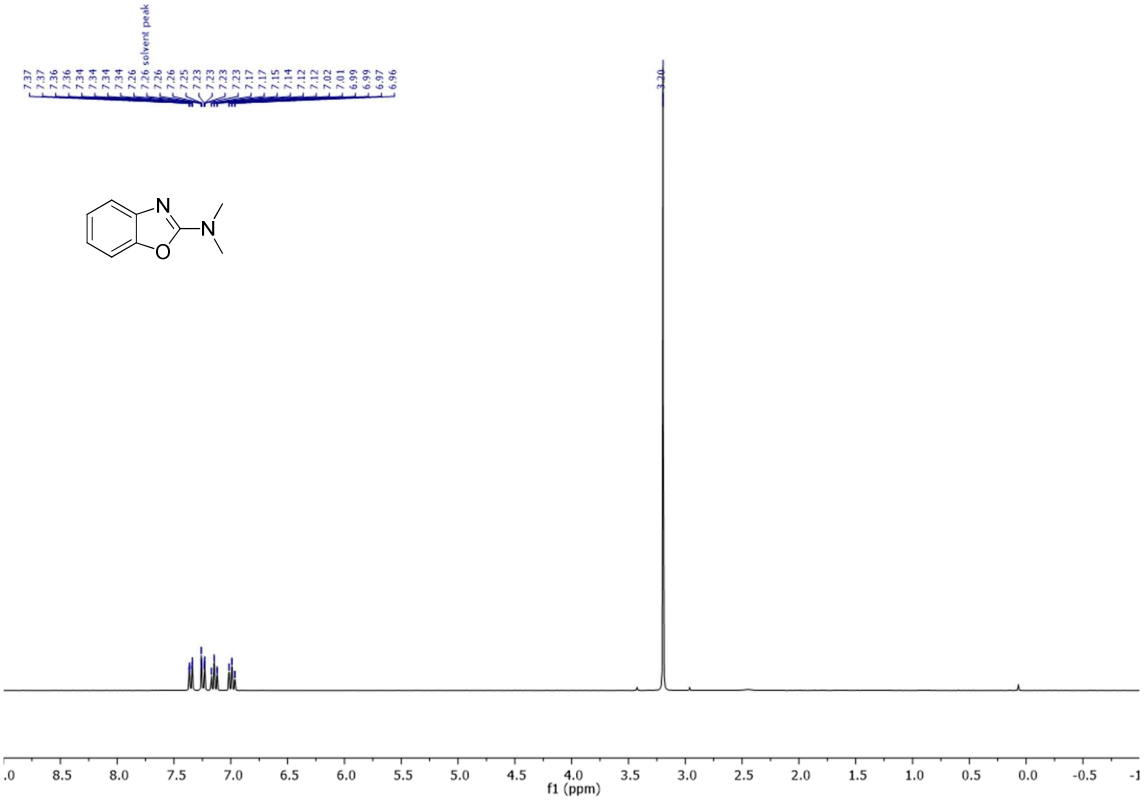
COSY of compound 9



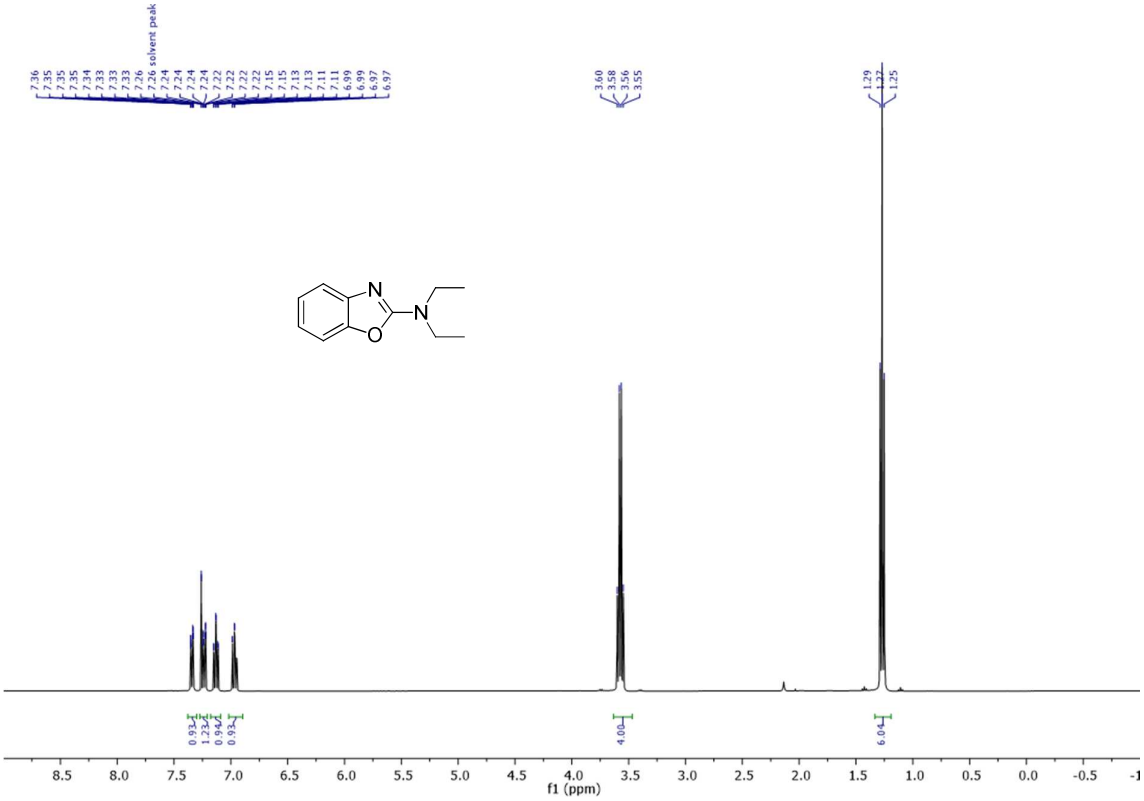
HSQC of compound 9



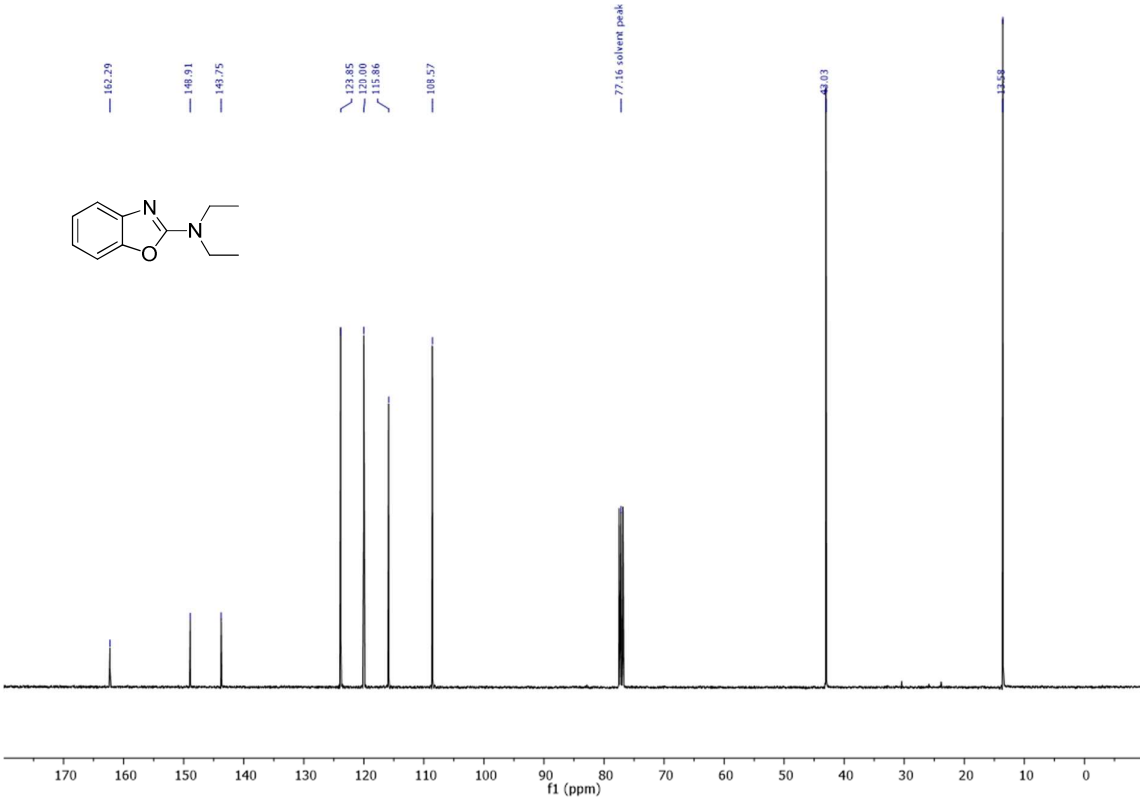
HMBC of compound 9



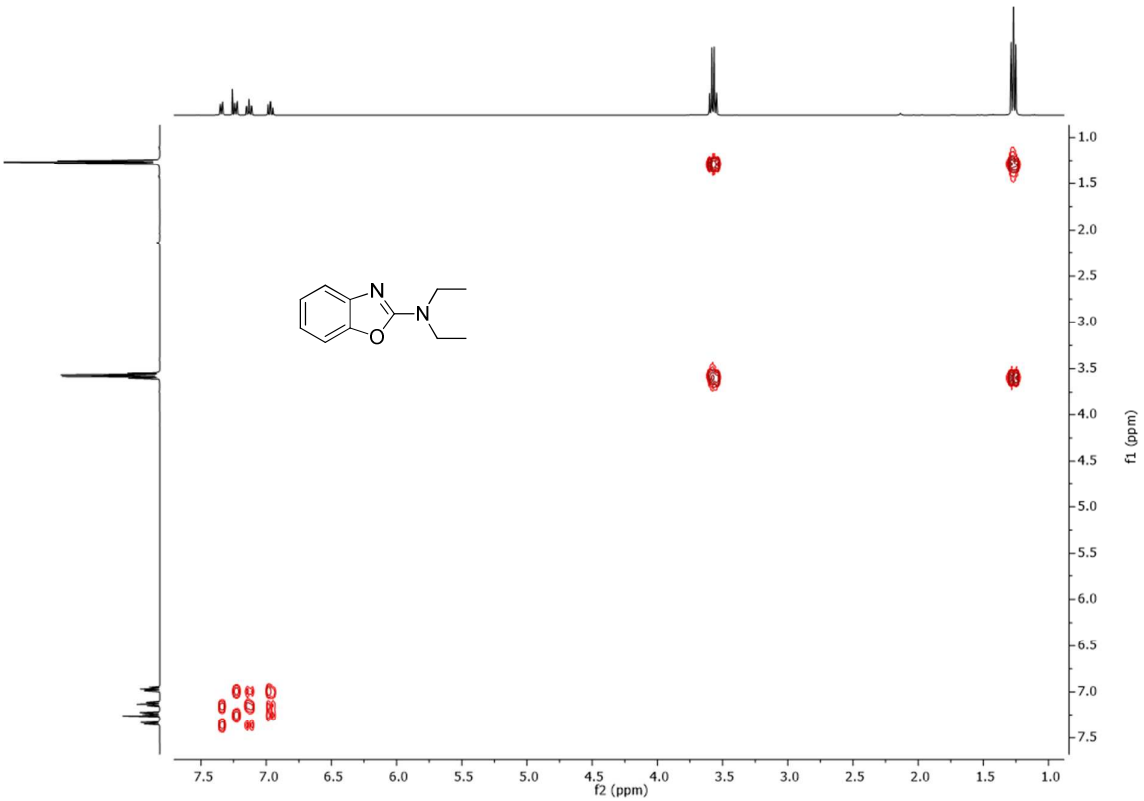
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 10



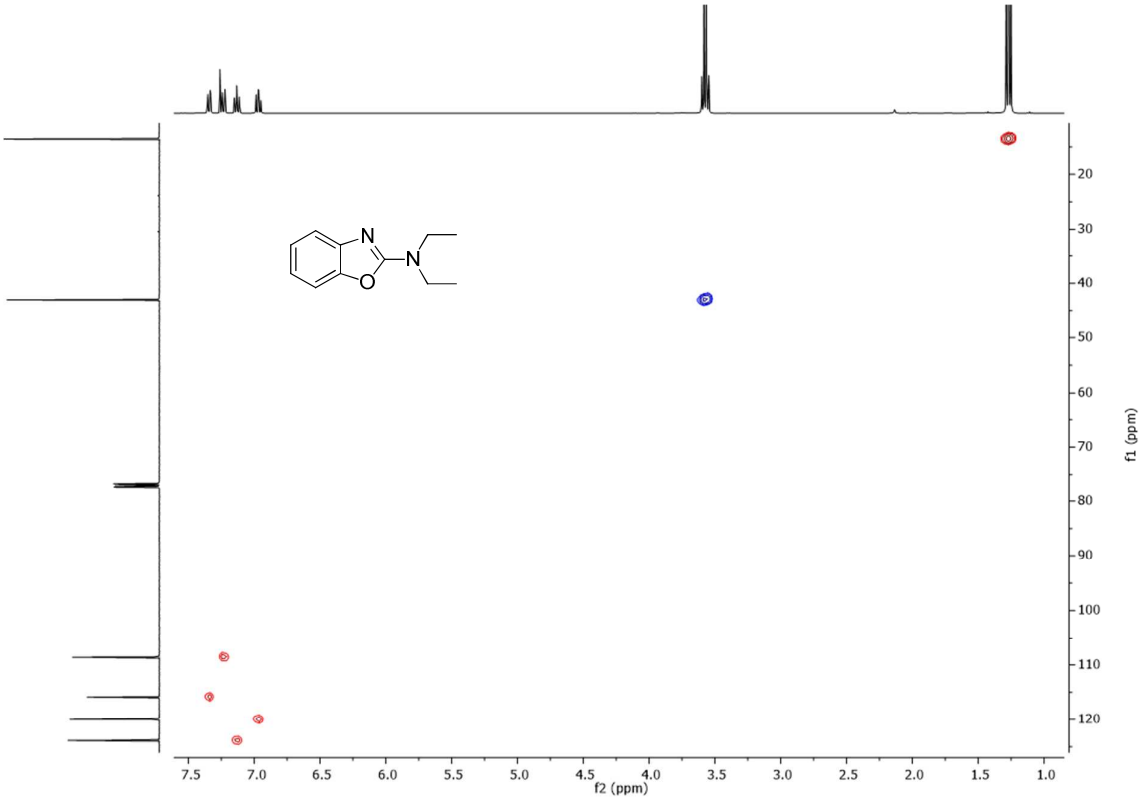
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 11



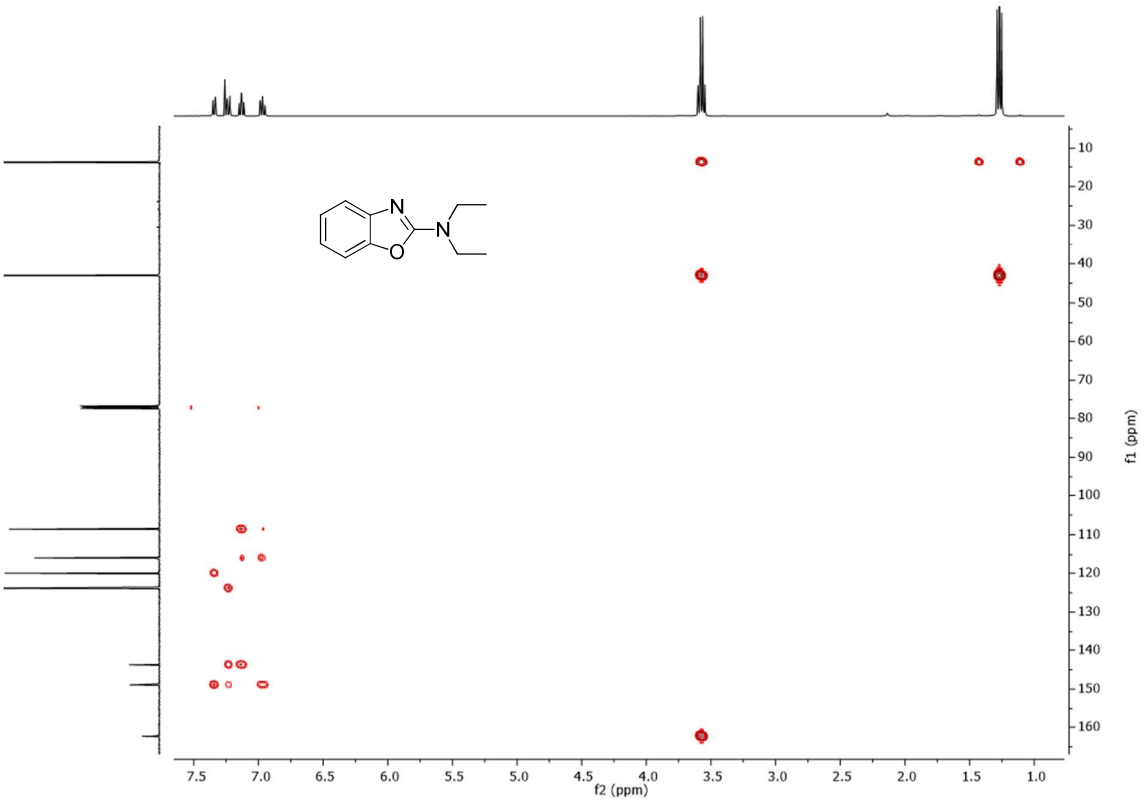
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 11



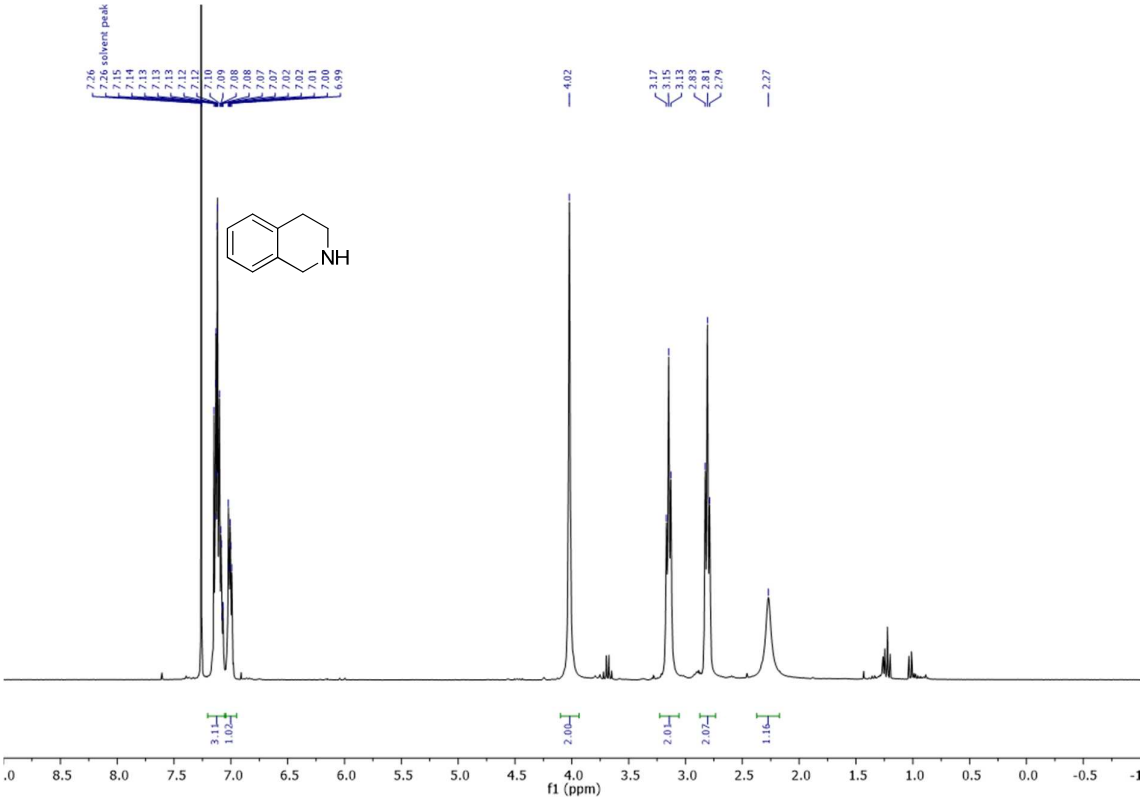
COSY of compound 11



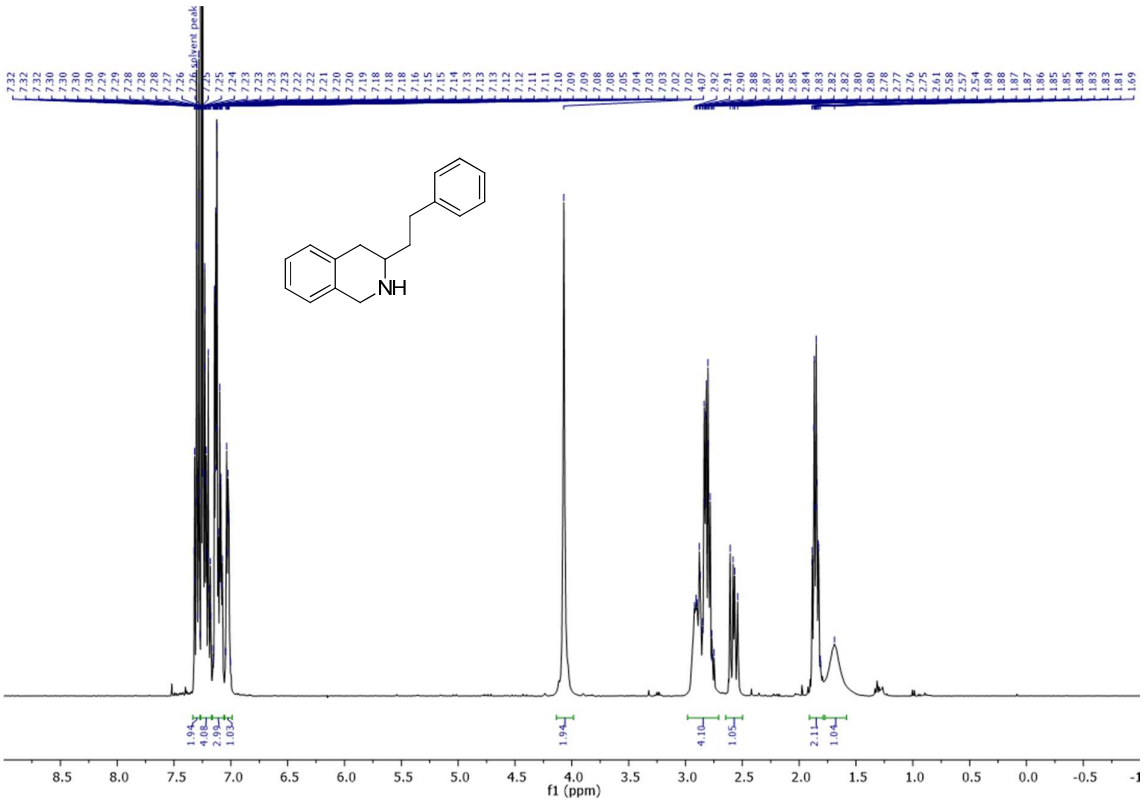
HSQC of compound 11



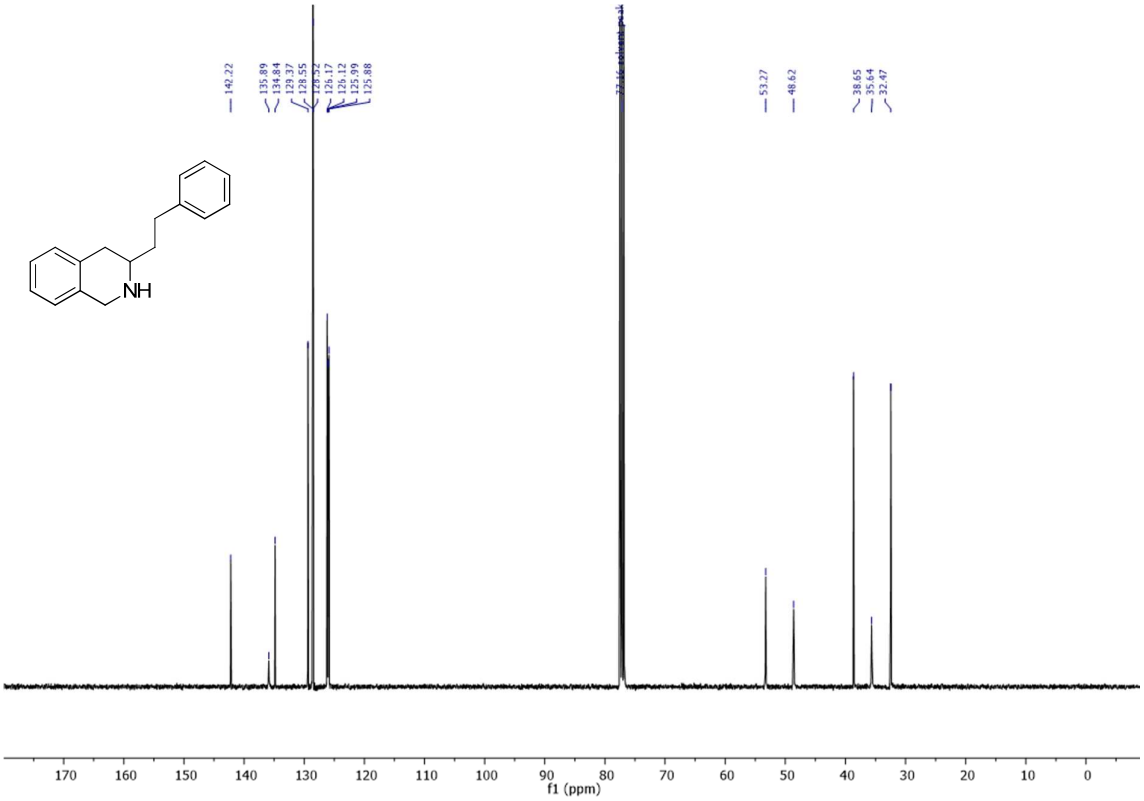
HMBC of compound 11



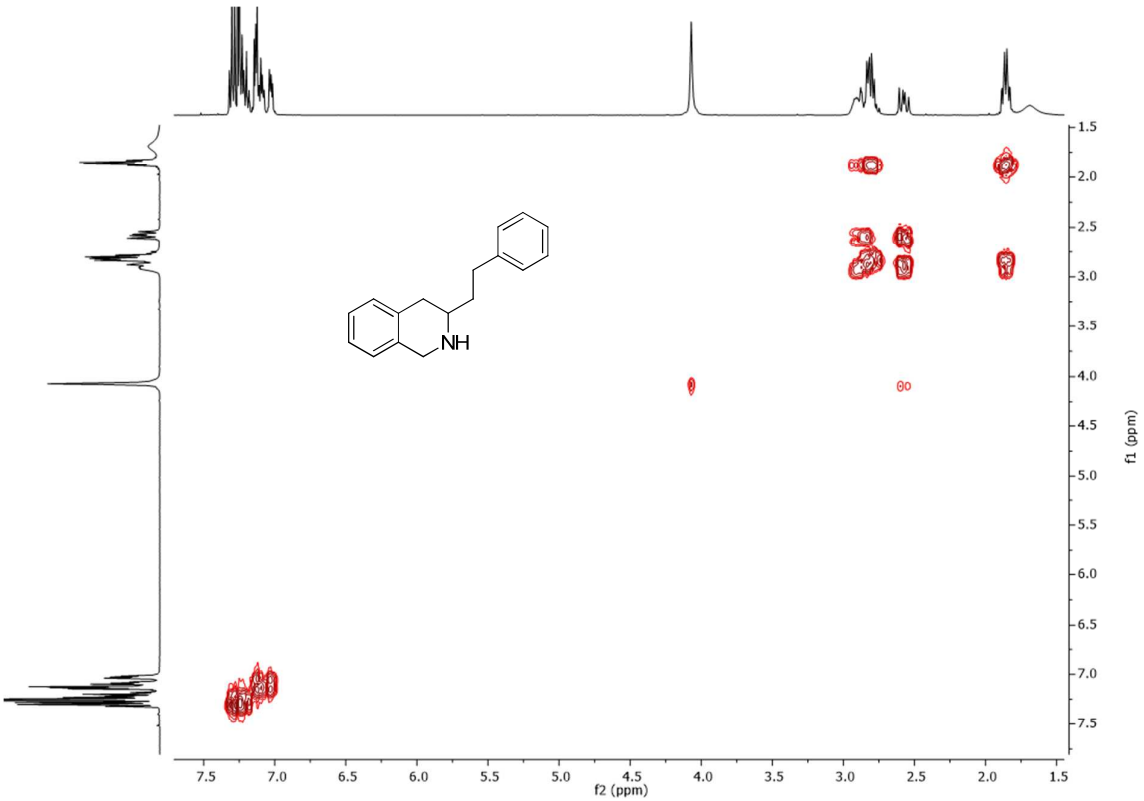
^{1}H-NMR (300 MHz, $CDCl_3$) of compound 13



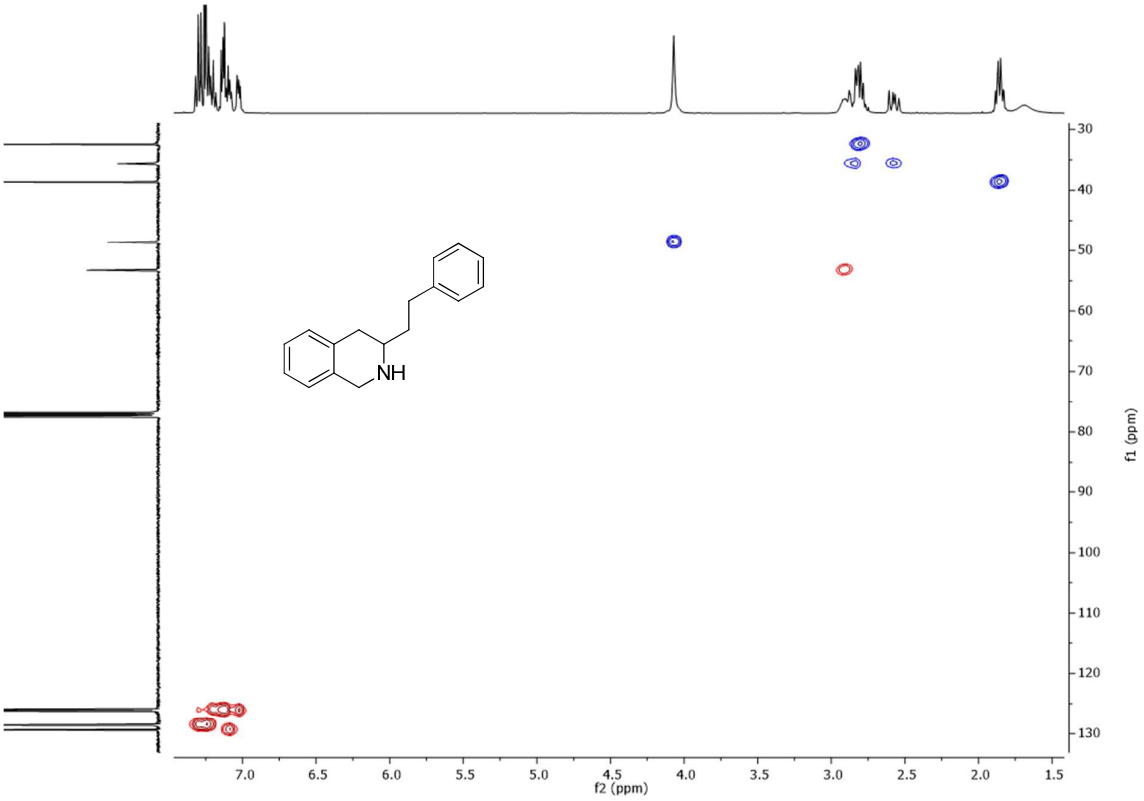
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 14



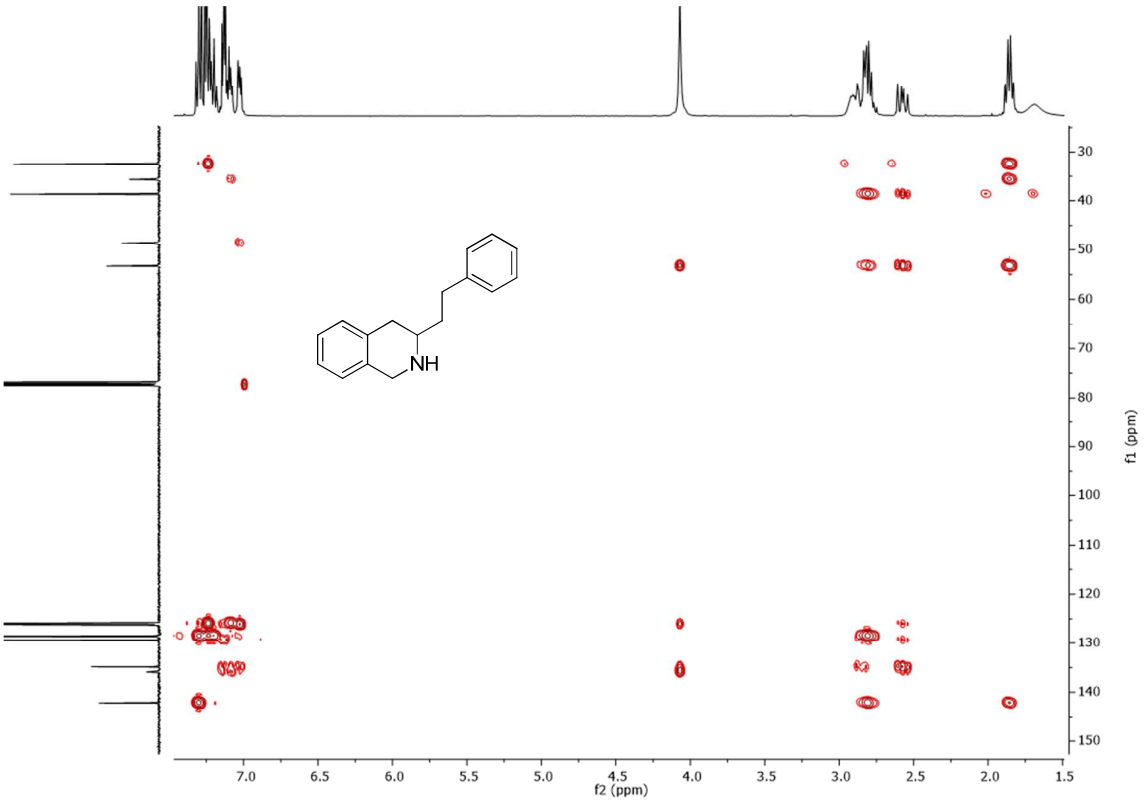
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 14



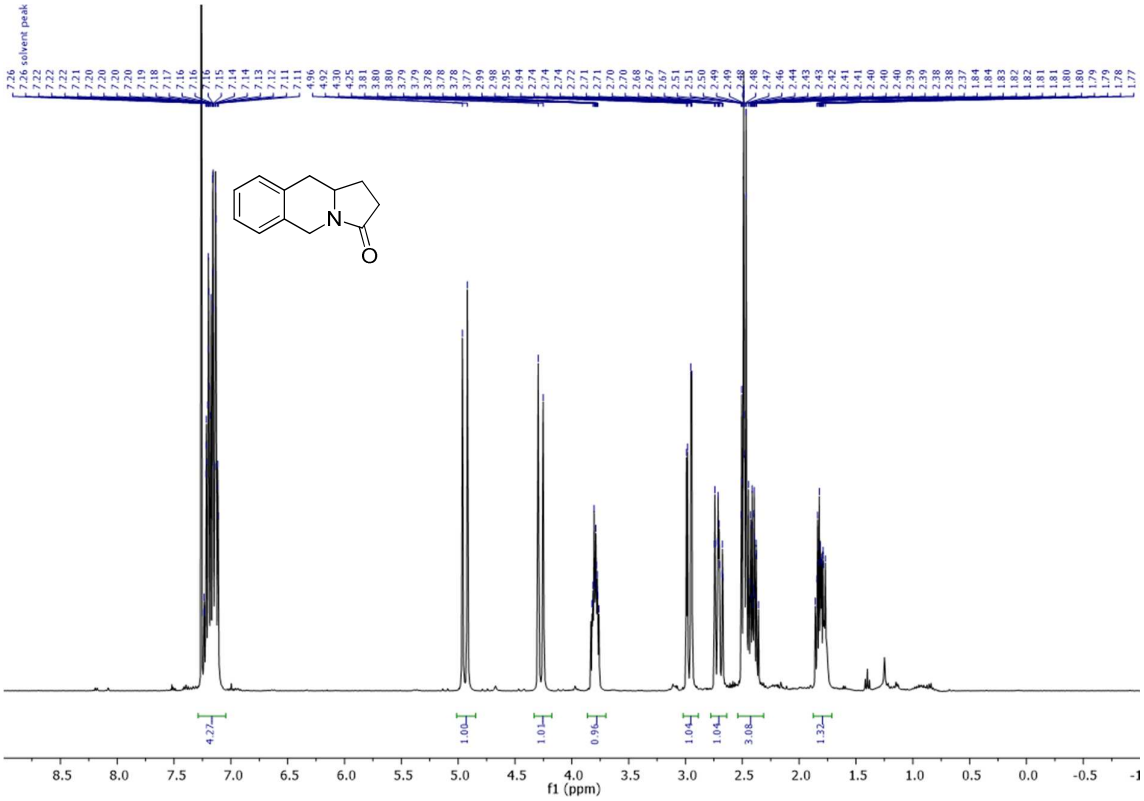
COSY of compound 14



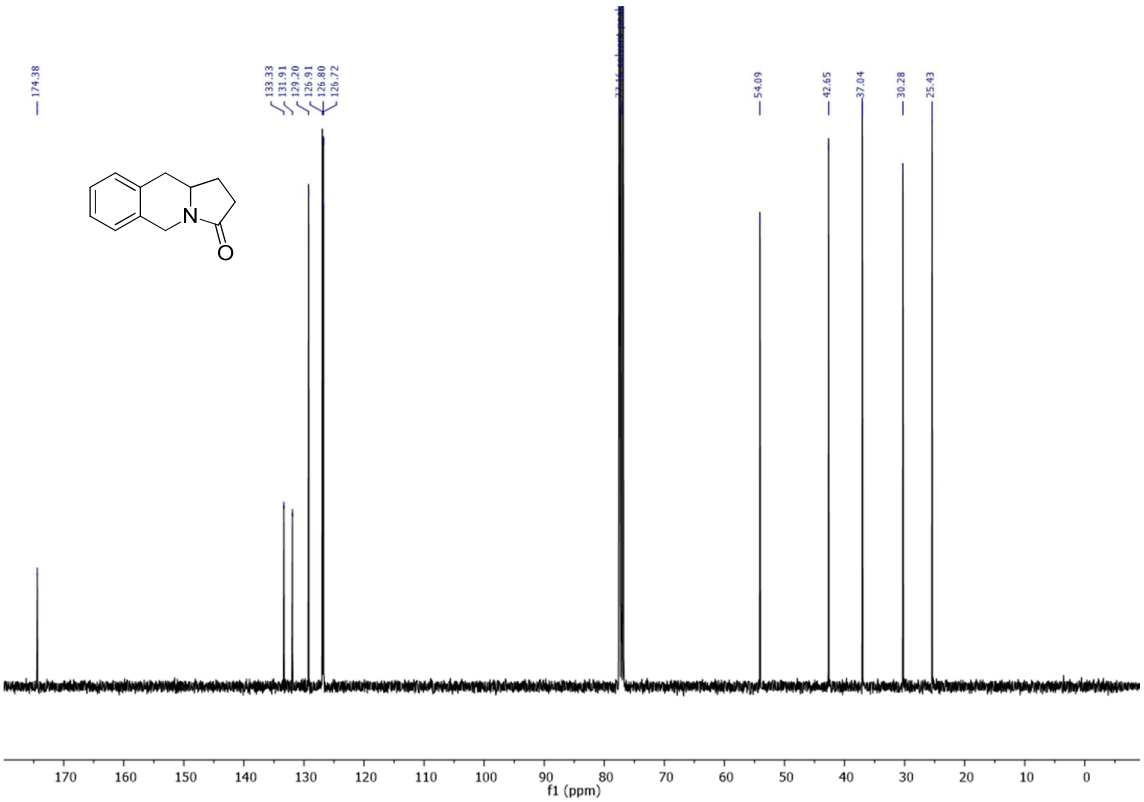
HSQC of compound 14



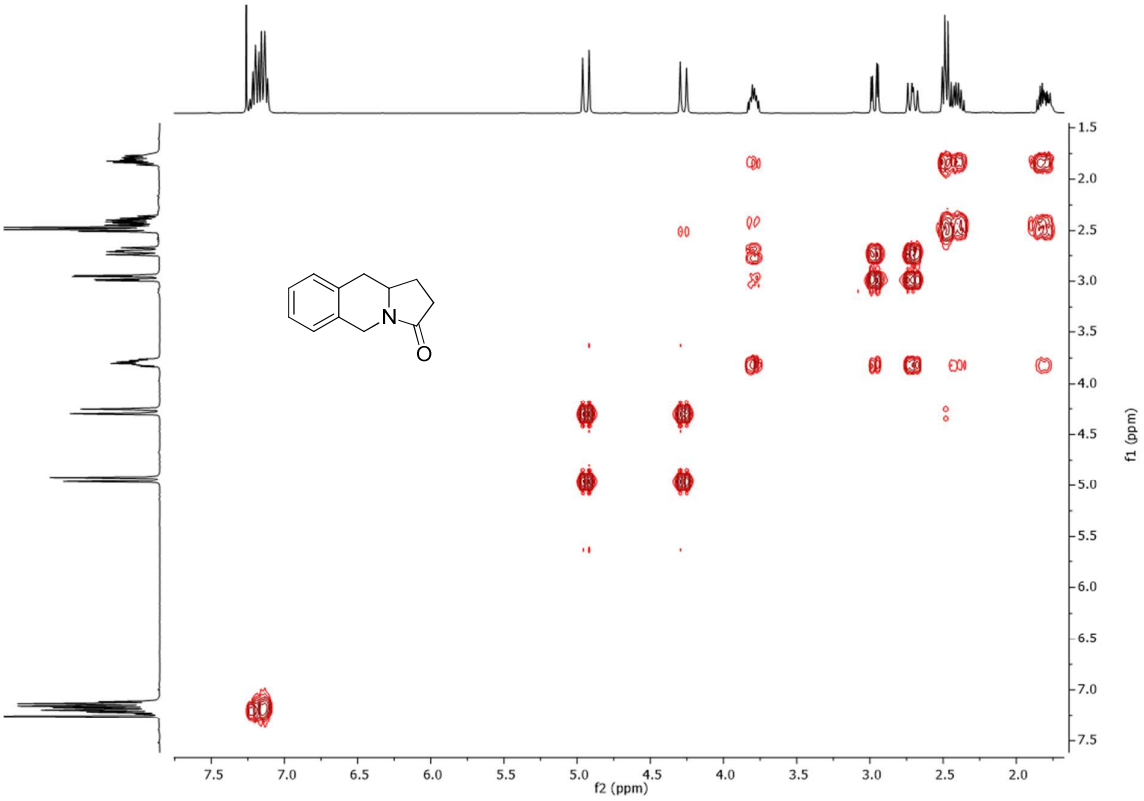
HMBC of compound 14



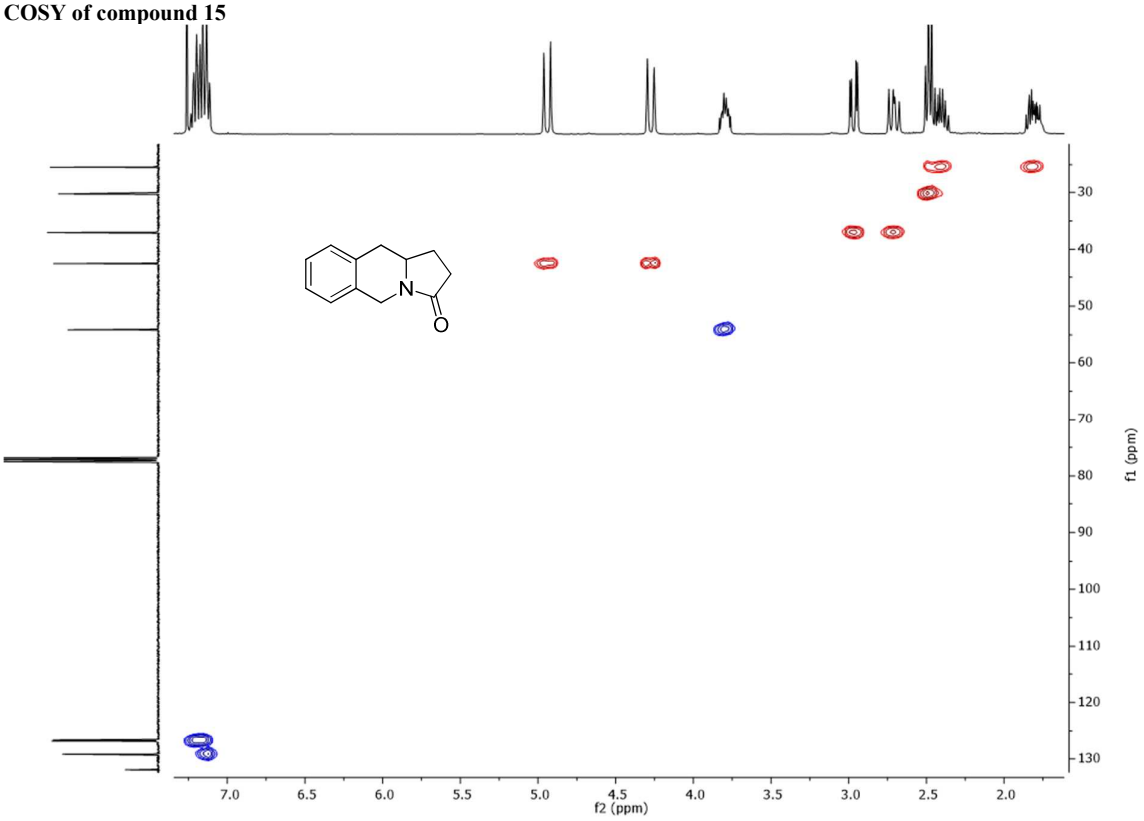
^{1}H-NMR (400 MHz, $CDCl_3$) of compound 15



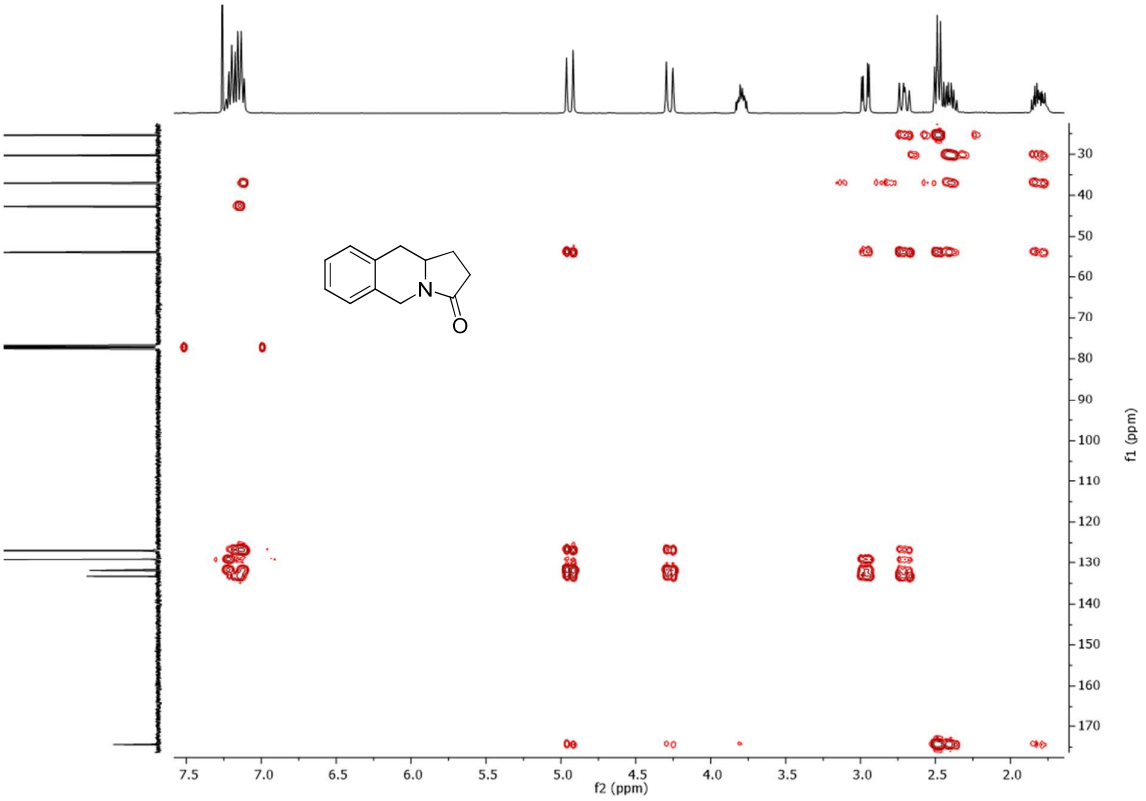
^{13}C-NMR (101 MHz, $CDCl_3$) of compound 15



COSY of compound 15



HSQC of compound 15



HMBC of compound 15

References

(1) Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics.* **2010,** *29*, 2176.
(2) Lamani, M.; Prabhu, K. R. *J. Org. Chem.* **2011,** *76*, 7938.
(3) Wang, M.; Zheng, D. X.; Luo, M. B.; Gao, M.; Miller, K. D.; Hutchins, G. D.; Zheng, Q.-H. *Appl. Radiat. Isot.* **2010,** *68*, 1098.
(4) Froehr, T.; Sindlinger, C. P.; Kloeckner, U.; Finkbeiner, P.; Nachtsheim, B. J. *Org. Lett.* **2011,** *13*, 3754.
(5) Cho, S. H.; Kim, J. Y.; Lee, S. Y.; Chang, S. *Angew. Chem. Int. Ed.* **2009,** *48*, 9127.