Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Iridium-Catalysed Reductive Coupling Reaction of Tertiary Lactams/Amides with Isocyanoacetates

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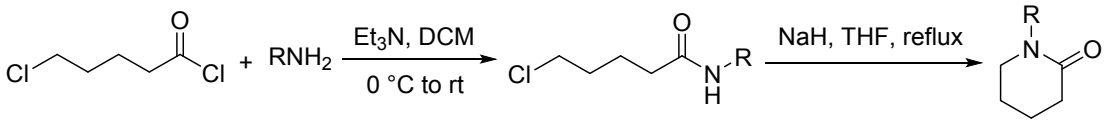
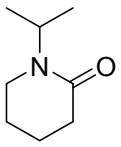
General: ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker spectrometer at 400 (500) and 100 (125) MHz, respectively. Chemical shifts (δ) are reported in ppm and referenced to internal standard Me_4Si and solvent signals respectively (Me_4Si, 0 ppm for ^{1}H NMR and $CDCl_3$, 77.0 ppm for ^{13}C NMR). HRMS spectra were recorded on an ESI-TOF mass spectrometer. Melting points were determined on a Büchi M560 Automatic Melting Point apparatus. Infrared spectra were measured with a Nicolet Avatar 330 FT-IR spectrometer using film KBr pellet technique. Silica gel (300-400 mesh) was used for flash column chromatography (FC), eluting (unless otherwise stated) with ethyl acetate/ hexane mixture. Dichloromethane and dichloroethane were distilled over calcium hydride under N_2. Tetrahydrofuran, ethylene glycol diethyl ether and toluene were distilled over Na under argon atmosphere.

General procedure for the synthesis of piperidin-2-one: General Procedure A



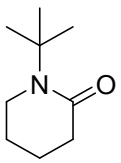
To a solution of amine (15.0 mmol) and triethylamine (20.0 mmol) in dry CH_2Cl_2 (50 mL) at 0 °C was added dropwise 5-chloropentanoyl chloride (2.12 mL, 16.5 mmol). The mixture was warmed to room temperature and stirred for 4 h. After being cooled to 0 °C, the reaction was quenched with 20 mL of 1.0 M HCl and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed successively with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. After the crude compound was redissolved in THF (150 mL), NaH (1.80 g, 75mmol, 60% dispersion on mineral oil) was added at 0 °C and refluxed overnight. Then water (60 mL) was added at 0 °C and the aqueous phase was extracted with Et_2O (3 × 40 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The reaction mixture was purified by flash chromatography on silica gel to give the desired compound.

Isopropylpiperidin-2-one (1a)



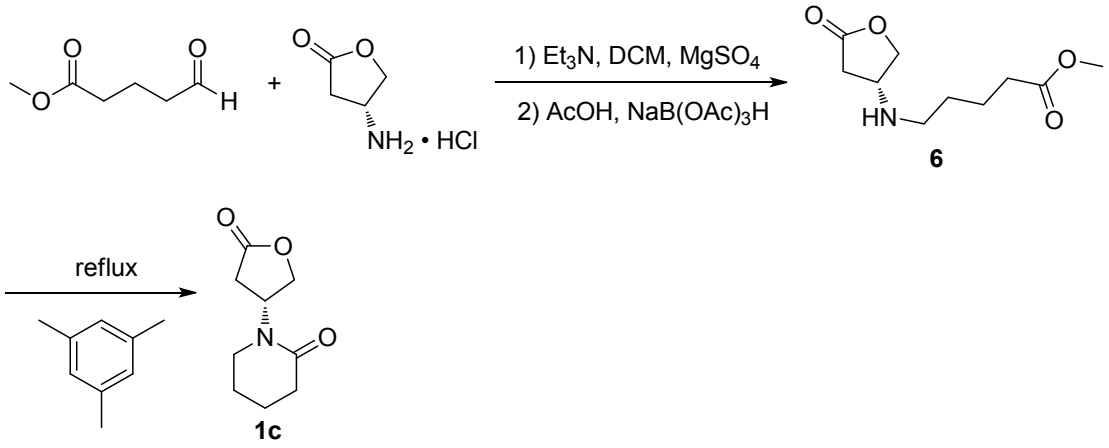
Following the general procedure A, the reaction of the propan-2-amine (0.887 g, 15.0 mmol) with 5-chloropentanoyl chloride (2.12 mL, 16.5 mmol) to give the known isopropylpiperidin-2-one (**1a**)[1] (1.792 g, yield: 85%) as a colorless oil after purified by flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 1). IR (film) ν_{max} 2931, 2866, 1636, 1209 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.10 (d, J = 6.9 Hz, 6H), 1.70-1.82 (m, 4H), 2.39 (t, J = 6.3 Hz, 2H), 3.16 (t, J = 5.8 Hz, 2H), 4.92 (heptet, J = 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1 (2C), 20.9, 23.2, 32.5, 40.3, 43.4, 169.0; MS (ESI, *m/z*): 164 ($M + Na^+$, 100%).

1-(*t*-Butyl)piperidin-2-one (1b)



Following the general procedure A, the reaction of the 2-methylpropan-2-amine (1.157 g, 15.0 mmol) with 5-chloropentanoyl chloride (2.12 mL, 16.5 mmol) to give the known 1-(*t*-butyl)piperidin-2-one (**1b**) [2](1.700 g, yield: 73%) as a colorless oil after purified by flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 2). IR (film) ν_{max} 2955, 2863, 1638, 1206 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.65-1.78 (m, 4H), 2.35 (t, J = 6.7 Hz, 2H), 3.30 (t, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 24.2, 28.2 (3C), 34.8, 44.1, 57.1, 171.1; HRMS (ESI, *m/z*) calcd for $C_9H_{17}NO$ [$M+Na^+$]: 178.1202; found: 178.1202.

(*R*)-1-(5-Oxotetrahydrofuran-3-yl)piperidin-2-one (1c)

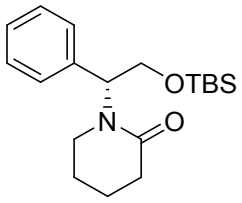


To a solution of methyl 5-oxopentanoate (0.650 g, 5.0 mmol), (*R*)-4-aminodihydro furan-2(3*H*)-one hydrochloride (0.688 g, 5.0 mmol) and $MgSO_4$ (0.750 g) in dry CH_2Cl_2 (50 mL) was added dropwise triethylamine (850 μL, 6.0 mmol) at room temperature. The mixture was stirred for 1 h. To the mixture was added dropwise AcOH (425 μL, 7.5 mmol) and $NaB(OAc)_3H$ (1.065 g, 5.0 mmol) was added. After being stirred for 2 h at room temperature, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (5.0 mL) and extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed successively with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: EtOAc) to afford an unstable compound **6** (0.570 g, yield: 53%) as a colorless oil. IR (film) ν_{max} 3302, 2951, 2869, 1775, 1734, 1636, 1172 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29-1.39 (br s, 1H), 1.40-1.49 (m, 2H), 1.55-1.65 (m, 2H), 2.22-2.32 (m, 3H), 2.48-2.58 (m, 2H), 2.64 (dd, J = 7.2, 17.5 Hz, 1H), 3.53-3.65 (m, 4H), 4.02 (dd, J = 3.9, 9.4 Hz, 1H), 4.32 (dd, J = 5.9, 9.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 29.5, 33.6, 35.6, 47.0, 51.4, 54.3, 73.3, 173.7, 176.0; HRMS (ESI, *m/z*) calcd for $C_{10}H_{17}NO_4$ [M+Na^+]: 238.1050; found: 238.1049.

The solution of compound **6** (0.916 g, 5 mmol) in mesitylene (50 mL) was refluxed at 165 ºC overnight. The mixture was then cooled to room temperature. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: MeOH/ *n*-hexane = 1/ 10) to give the desired compound **1c** (0.843 g, yield: 92%) as a white solid. Mp 92-94 °C. IR (film) ν_{max}

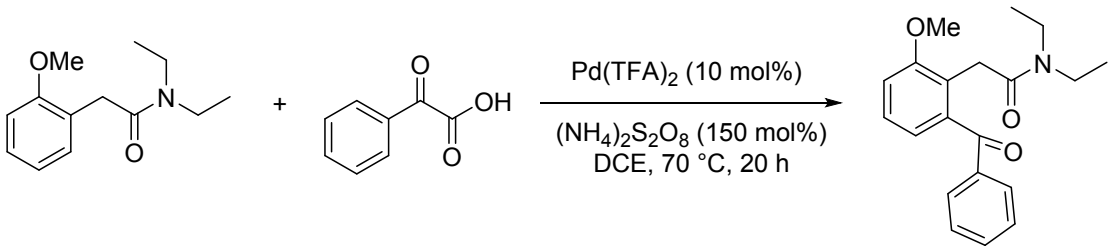
2948, 2869, 1774, 1635, 1497, 1251, 1175, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.75-1.92 (m, 4H), 2.42 (t, J = 6.6 Hz, 2H), 2.58 (dd, J = 3.8, 18.3 Hz, 1H), 2.80 (dd, J = 9.3, 18.3 Hz, 1H), 3.19-3.33 (m, 2H), 4.29 (dd, J = 3.3, 10.2 Hz, 1H), 4.53 (dd, J = 7.3, 10.2 Hz, 1H), 5.30-5.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 23.1, 31.9, 32.5, 43.9, 50.0, 71.3, 170.2, 175.4; HRMS (ESI, *m/z*) calcd for $C_9H_{13}NO_3$ [M+Na^+]: 206.0788; found: 206.0790. $[\alpha]_D^{20}$ = +43.0 (*c* 1.0, $CHCl_3$).

(*R*)-1-(2-((*t*-Butyldimethylsilyl)oxy)-1-phenylethyl)piperidin-2-one (1d)



Following the general procedure A, the reaction of the 2-((*t*-butyldimethylsilyl)oxy)-1-phenylethan-1-amine (3.772 g, 15.0 mmol) with 5-chloropentanoyl chloride (2.12 mL, 16.5 mmol) to give the known 1-(2-((*t*-butyldimethylsilyl)oxy)-1-phenylethyl)piperidin-2-one (**1d**)[3] (2.901 g, yield: 58%) as a white solid after purified by flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 50). Mp 69-70 °C. IR (film) ν_{max} 3058, 3030, 2951, 2929, 2856, 1642, 1463, 1256, 1176, 1104, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 1.59-1.69 (m, 1H), 1.72-1.80 (m, 3H), 2.44-2.50 (m, 2H), 2.95-3.03 (m, 1H), 3.23-3.32 (m, 1H), 4.10 (d, J = 6.6 Hz, 2H), 5.89 (t, J = 6.6 Hz, 1H), 7.25-7.28 (m, 1H), 7.29-7.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.6, -5.4, 18.0, 21.1, 23.3, 25.8 (3C), 32.6, 43.5, 56.6, 61.7, 127.3, 128.0 (2C), 128.3 (2C), 138.0, 170.1; MS (ESI, *m/z*): 356 (M + Na^+, 100%). $[\alpha]_D^{20}$ = -79.8 (*c* 1.0, $CHCl_3$).

2-(2-Benzoyl-6-methoxyphenyl)-*N*,*N*-diethylacetamide (1v)



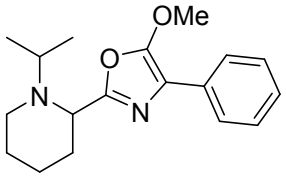
To an oven-dried sealed tube charged with *N*,*N*-diethyl-2-(2 -methoxyphenyl)acetamide (266 mg, 1.2 mmol), $Pd(TFA)_2$ (40 mg, 0.12 mmol), and $(NH_4)_2S_2O_8$ (411 mg, 1.8 mmol) in DCE (4.0 mL) was added phenylglyoxylic acid (270 mg, 1.8 mmol). The reaction mixture was stirred for 20 h at 70 °C. The reaction mixture was diluted with EtOAc (20 mL) and washed with a saturated aqueous solution of Na_2CO_3 (6.0 mL). The aqueous layer was extracted with EtOAc (10 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (eluent: EtOAc/ *n*-hexanes = 1/ 3) to afford the acylated product **1v**[4] (286 mg, yield: 73%). IR (film) ν_{max} 3048, 2972, 2933, 2837, 1642, 1602, 1495, 1462, 1380, 1246, 1136, 1051, 1029, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H), 3.25 (q, J = 7.1 Hz, 2H), 3.35 (q, J = 7.1 Hz, 2H), 3.85 (s, 3H), 3.88 (s, 2H), 6.89-6.93 (m, 1H), 6.99-7.03 (m, 1H), 7.22-7.29 (m, 1H), 7.38-7.45 (m, 2H), 7.49-7.56 (m, 1H), 7.83-7.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0, 14.1, 30.1, 40.5, 42.2, 55.9, 112.6, 121.3, 124.6, 126.8, 128.1 (2C), 130.5 (2C), 132.7, 137.9, 140.6, 158.0, 169.5, 198.5; MS (ESI, *m/z*): 348 ($M + Na^+$, 100%)

General procedure for the synthesis of 5-methoxy-4-phenyloxazol: General Procedure B

To a solution of $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol) and lactam/amide (0.5 mol) in 1,2-diethoxyethane (DEE) (4.0 mL) was added dropwise TMDS (134 mg, 1.0 mmol) at room temperature. The reaction mixture was stirred for 30 min, then the 2-isocyano-2-arylacetate (0.6 mmol) and 1,4-diaza[2.2.2]bicyclooctane (DABCO) (73 mg, 0.65 mmol) was added successively. After stirring for 30 min, the reaction

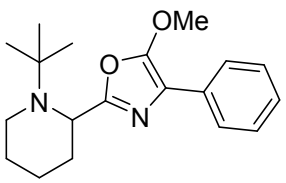
mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired 5-methoxy-4-aryloxazole derivative.

2-(1-Isopropylpiperidin-2-yl)-5-methoxy-4-phenyloxazole (3a)



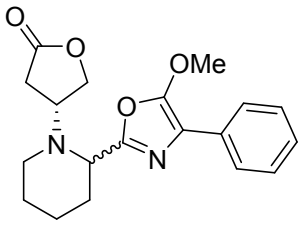
Following the general procedure B, the reaction of the 1-isopropylpiperidin-2-one **1a** (71 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3a** (145 mg, yield: 96%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 4). IR (film) ν_{max} 3055, 2965, 2936, 2855, 2799, 1644, 1604, 1499, 1448, 1372, 1037, 1016, 767, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, J = 6.5 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H), 1.31-1.44 (m, 1H), 1.60-1.75 (m, 2H), 1.80-1.96 (m, 3H), 2.29 (ddd, J = 3.5, 10.8, 10.8 Hz, 1H), 2.72 (qq, J = 6.5, 6.8 Hz, 1H), 2.98 (ddd, J = 4.0, 4.0, 10.8 Hz, 1H), 3.71 (dd, J = 3.5, 9.3 Hz, 1H), 4.06 (s, 3H), 7.17-7.23 (m, 1H), 7.33-7.40 (m, 2H), 7.78-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.7, 23.7, 25.6, 31.6, 44.2, 51.2, 58.7, 60.2, 114.1, 124.9 (2C), 126.2, 128.4 (2C), 131.4, 154.3, 155.5; HRMS (ESI, *m/z*) calcd for $C_{18}H_{24}N_2O_2$ [M+H^+]: 301.1911; found: 301.1912.

2-(1-(*t*-Butyl)piperidin-2-yl)-5-methoxy-4-phenyloxazole (3b)



Following the general procedure B, the reaction of the 1-(*t*-butyl)piperidin-2-one **1b** (78 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3b** (130 mg, yield: 83%) as a white solid after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 5). Mp 77-78 °C. IR (film) ν_{max} 3058, 2971, 2938, 2869, 2850, 1645, 1604, 1499, 1449, 1366, 1219, 1071, 1038, 1018, 959, 767, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.02 (s, 9H), 1.51-1.64 (m, 2H), 1.75-1.97 (m, 4H), 2.85 (ddd, J = 3.8, 3.8, 11.7 Hz, 1H), 3.01 (ddd, J = 2.4, 11.7, 11.7 Hz, 1H), 4.04 (s, 3H), 4.43 (dd, J = 2.5, 4.4 Hz, 1H), 7.18-7.24 (m, 1H), 7.34-7.41 (m, 2H), 7.79-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 26.8, 27.2(3C), 31.0, 41.1, 51.1, 54.6, 60.1, 114.0, 125.0 (2C), 126.2, 128.4 (2C), 131.6, 154.2, 157.4; HRMS (ESI, *m/z*) calcd for $C_{19}H_{26}N_2O_2$ [$M+H^+$]: 315.2067; found: 315.2066.

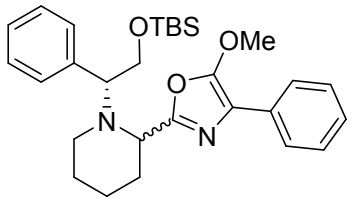
(*R*)-4-(2-(5-Methoxy-4-phenyloxazol-2-yl)piperidin-1-yl)dihydrofuran-2(3H)-one (3c)



Following the general procedure B, the reaction of the (*R*)-1-(5-oxotetrahydrofuran-3-yl)piperidin-2-one **1c** (92 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3c** (146 mg, yield: 83%, dr: 1.1:1) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 1). IR (film) ν_{max} 3058, 2941, 2856, 1781, 1685, 1643, 1499, 1448, 1373, 1171, 1016, 767, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.45-1.58 (m, 2H (major + minor)), 1.62-1.78 (m, 4H (major + minor)), 1.81-2.05 (m, 6H (major + minor)), 2.32-2.40 (m, 1H (major)), 2.41-2.49 (m, 2H (major + minor)),

2.54 (dd, J = 8.2, 17.8 Hz, 1H (minor)), 2.60-2.66 (m, 2H (major + minor)), 2.84-2.97 (m, 2H (major + minor)), 3.51-3.63 (m, 2H (major + minor)), 3.74-3.83 (m, 2H (major + minor)), 4.07 (m, 6H (major + minor)), 4.15 (dd, J = 5.8, 9.5 Hz, 1H (major)), 4.28-4.36 (m, 2H (major + minor)), 4.40 (dd, J = 6.9, 9.5 Hz, 1H (major)), 7.20-7.25 (m, 2H (major + minor)), 7.35-7.41 (m, 4H (major + minor)), 7.75-7.82 (m, 4H (major + minor)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5 (minor), 21.6 (major), 25.3 (major), 25.4 (minor), 29.9 (minor), 30.0 (major), 30.7 (major), 33.0 (minor), 45.5 (major), 45.6 (minor), 57.2 (minor), 57.4 (major), 57.8 (major), 58.0 (minor), 60.1(2C, major+minor), 69.8 (minor), 71.8 (major), 114.4 (2C, major+minor), 125.0 (2C, major+minor), 126.6 (2C, major+minor), 128.5 (2C, major+minor), 131.0 (2C, major+minor), 153.6 (2C, major+minor), 154.4 (2C, major+minor), 175.7 (major), 176.0 (minor); HRMS (ESI, *m/z*) calcd for $C_{19}H_{22}N_2O_2$ [M+H$^+$]: 343.1652; found: 343.1652.

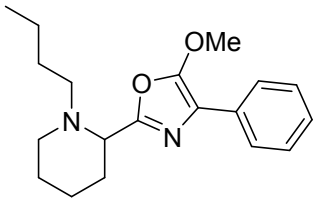
(*R*)-2-(1-(2-((*t*-Butyldimethylsilyl)oxy)-1-phenylethyl)piperidin-2-yl)-5-methoxy-4-phenyloxazole (3d)



Following the general procedure B, the reaction of the (*R*)-1-(2-((*t*-butyldimethylsilyl)oxy)-1-phenylethyl)piperidin-2-one **1d** (167 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3d** (180 mg, yield: 73%, dr: 3:1 decided by NMR) after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 50). IR (film) ν_{max} 3060, 3027, 2931, 2855, 1645, 1603, 1498, 1449, 1371, 1310, 1255, 1106, 1018, 836, 775, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.07--0.03 (m, 8H, major+minor), -0.02—0.00 (m, 4H, major+minor), 0.80 (s, 9H, minor), 0.87 (s, 9H,

major), 1.44-2.09 (m, 12H, major+minor), 2.36-2.46 (m, 1H, minor), 2.53-2.63 (m, 1H, major), 2.86-2.96 (m, 1H, major), 3.04-3.14 (m, 1H, minor), 3.78-3.89 (m, 2H, major+minor), 3.95-4.11 (m, 11H, major+minor), 4.37 (dd, J = 4.4, 6.4 Hz, 1H, major), 7.20-7.27 (m, 4H, major+minor), 7.27-7.33 (m, 4H, major+minor), 7.32-7.37 (m, 2H, major+minor), 7.38-7.47 (m, 6H, major+minor), 7.82-7.93 (m, 4H, major+minor); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.6 (2C, major), -5.6 (2C, minor), 18.1 (2C, major+minor), 22.3 (2C, major+minor), 25.7 (2C, minor), 25.8 (4C, major+minor), 25.9(major), 30.9 (major), 31.0 (minor), 46.0 (major), 46.9 (minor), 56.9 (major), 57.3 (minor), 59.7 (major), 60.0 (minor), 63.4 (major), 64.5 (minor), 66.2 (major), 66.7 (minor), 113.7 (major), 114.0 (minor), 124.9 (2C, major), 125.0 (2C, minor), 126.1 (major), 126.2 (minor), 126.5 (major), 126.9 (minor), 127.7 (4C, major+minor), 128.4 (6C, major+minor), 129.3 (2C, minor), 131.6 (minor), 131.7(major), 138.2 (minor), 141.8 (major), 154.1 (major), 154.2 (minor), 155.3 (minor), 155.7 (major); HRMS (ESI, *m/z*) calcd for $C_{29}H_{40}N_2O_2Si$ [M+H$^+$]: 493.2881; found: 493.2878.

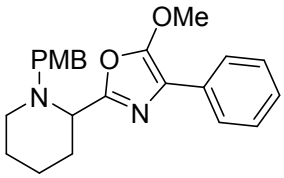
2-(1-Butylpiperidin-2-yl)-5-methoxy-4-phenyloxazole (3e)



Following the general procedure B, the reaction of the 1-butylpiperidin-2-one **1e** (78 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3e** (101 mg, yield: 64%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 5). IR (film) ν_{max} 3084, 2936, 2859, 2808, 1644, 1603, 1498, 1373, 1038, 1017, 767, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, J = 7.4 Hz, 3H), 1.14-1.30 (m, 2H), 1.32-1.56 (m, 3H), 1.65-1.74 (m, 2H), 1.80-1.93 (m, 3H), 2.15-2.26 (m, 2H), 2.44 (ddd, J =

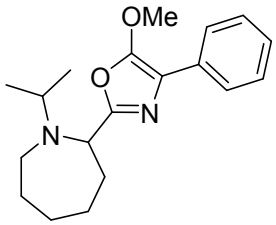
5.9, 10.1, 12.7 Hz, 1H), 3.10 (ddd, J = 4.1, 4.1, 11.6 Hz, 1H), 3.47 (dd, J = 4.6, 8.2 Hz, 1H), 4.06 (s, 3H), 7.18-7.24 (m, 1H), 7.33-7.41 (m, 2H), 7.78-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 20.7, 23.3, 25.5, 28.3, 31.1, 52.1, 55.9, 60.1, 61.2, 114.1, 124.9 (2C), 126.2, 128.4 (2C), 131.4, 154.3, 155.5; HRMS (ESI, *m/z*) calcd for $C_{19}H_{26}N_2O_2$ [M+H$^+$]: 315.2067; found: 315.2067.

5-Methoxy-2-(1-(4-methoxybenzyl)piperidin-2-yl)-4-phenyloxazole (3f)



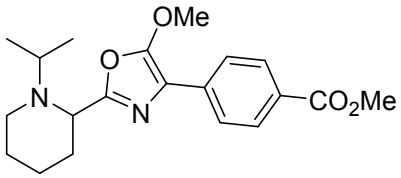
Following the general procedure B, the reaction of the 1-(4-methoxybenzyl)piperidin -2-one **1f** (110 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3f** (53 mg, yield: 28%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 5). IR (film) ν_{max} 3062, 2937, 2855, 2834, 1644, 1611, 1511, 1448, 1372, 1246, 1171, 1037, 1018, 1017, 767, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30-1.44 (m, 1H), 1.57-1.69 (m, 2H), 1.77-1.87 (m, 1H), 1.87-1.99 (m, 2H), 2.07-2.17 (m, 1H), 2.95 (ddd, J = 3.8, 3.8, 11.3 Hz, 1H), 3.28 (d, J = 13.4 Hz, 1H), 3.53 (dd, J = 4.7, 8.3 Hz, 1H), 3.63 (d, J = 13.4 Hz, 1H), 3.76 (s, 3H), 4.05 (s, 3H), 6.78-6.85 (m, 2H), 7.18-7.26 (m, 3H), 7.34-7.41 (m, 2H), 7.78-7.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 25.4, 31.1, 51.8, 55.2, 59.6, 60.0, 60.9, 113.4 (2C), 114.0, 124.9 (2C), 126.2, 128.4 (2C), 130.2, 130.3 (2C), 131.4, 154.3, 155.4, 158.6; HRMS (ESI, *m/z*) calcd for $C_{23}H_{26}N_2O_2$ [M+H$^+$]: 379.2016; found: 379.2016.

2-(1-Isopropylazepan-2-yl)-5-methoxy-4-phenyloxazole (3g)



Following the general procedure B, the reaction of the 1-isopropylazepan-2-one **1g** (78 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3g** (134 mg, yield: 92%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 40). IR (film) ν_{max} 3058, 2962, 2926, 2853, 1644, 1604, 1500, 1449, 1371, 1172, 1037, 1017, 767, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, J = 6.5 Hz, 3H), 0.97 (d, J = 6.6 Hz, 3H), 1.39-1.56 (m, 2H), 1.58-1.72 (m, 3H), 1.76-1.86 (m, 1H), 1.87-1.97 (m, 1H), 2.02-2.13 (m, 1H), 2.60-2.70 (m, 1H), 2.89-3.00 (m, 2H), 4.00-4.05 (m, 4H), 7.17-7.23 (m, 1H), 7.33-7.40 (m, 2H), 7.77-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 20.0, 24.8, 30.1, 31.9, 33.8, 43.0, 52.7, 58.9, 60.0, 114.1, 125.0 (2C), 126.1, 128.4 (2C), 131.7, 154.2, 158.5; HRMS (ESI, *m/z*) calcd for $C_{19}H_{26}N_2O_2$ [M+H^+]: 315.2067; found: 315.2069.

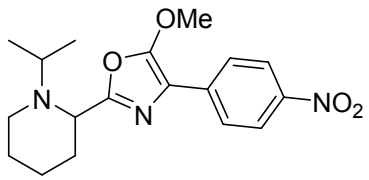
Methyl 4-(2-(1-isopropylpiperidin-2-yl)-5-methoxyoxazol-4-yl)benzoate (3i)



Following the general procedure B, the reaction of the 1-isopropylpiperidin-2-one **1a** (71 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 4-(1-isocyano-2-methoxy-2-oxoethyl)benzoate (140 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3i** (167 mg, yield: 93%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 2/ 3). IR (film) ν_{max} 2946, 2856, 1720, 1638, 1612, 1435, 1375,

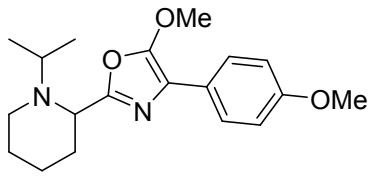
1278, 1107, 1026, 1015, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, J = 6.6 Hz, 3H), 1.09 (d, J = 6.6 Hz, 3H), 1.31-1.44 (m, 1H), 1.58-1.76 (m, 2H), 1.79-1.98 (m, 3H), 2.29 (ddd, J = 3.2, 11.2, 11.2 Hz, 1H), 2.72 (qq, J = 6.6, 6.6 Hz, 1H), 2.98 (ddd, J = 3.8, 3.8, 11.2 Hz, 1H), 3.71 (dd, J = 3.5, 9.3 Hz, 1H), 3.91 (s, 3H), 4.11 (s, 3H), 7.84-7.89 (m, 2H), 8.01-8.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 20.7, 23.7, 25.6, 31.6, 44.2, 51.3, 51.9, 58.6, 59.9, 112.9, 124.5 (2C), 127.4, 129.8 (2C), 136.1, 155.4, 155.6, 167.1; HRMS (ESI, *m/z*) calcd for $C_{20}H_{26}N_2O_4$ [M+H^+]: 359.1965; found: 359.1963.

2-(1-Isopropylpiperidin-2-yl)-5-methoxy-4-(4-nitrophenyl)oxazole (3j)



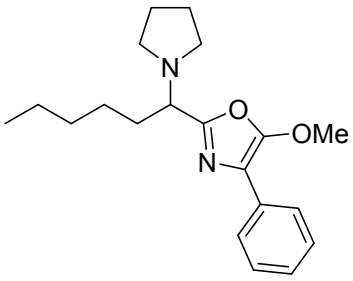
Following the general procedure B, the reaction of the 1-isopropylpiperidin-2-one **1a** (71 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), Methyl 2-isocyano-2-(4-nitrophenyl)acetate (132 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3j** (72 mg, yield: 42%) as a yellow solid after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 2/ 3). Decompose at 93 °C. IR (film) ν_{max} 3074, 2935, 2855, 2805, 1633, 1601, 1513, 1458, 1383, 1336, 1109, 1024, 966, 854, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (d, J = 6.6 Hz, 3H), 1.09 (d, J = 6.6 Hz, 3H), 1.33-1.45 (m, 1H), 1.59-1.76 (m, 2H), 1.81-1.99 (m, 3H), 2.31 (ddd, J = 3.3, 11.2, 11.2 Hz, 1H), 2.72 (qq, J = 6.6, 6.6 Hz, 1H), 2.98 (ddd, J = 3.9, 3.9, 11.2 Hz, 1H), 3.73 (dd, J = 3.6, 9.2 Hz, 1H), 4.16 (s, 3H), 7.90-7.95 (m, 2H), 8.18-8.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 20.7, 23.6, 25.6, 31.6, 44.2, 51.3, 58.4, 59.7, 111.7, 123.9 (2C), 124.9 (2C), 138.3, 145.4, 155.7, 156.0; HRMS (ESI, *m/z*) calcd for $C_{18}H_{23}N_3O_4$ [M+H^+]: 346.1761; found: 346.1758.

2-(1-Isopropylpiperidin-2-yl)-5-methoxy-4-(4-methoxyphenyl)oxazole (3k)



Following the general procedure B, the reaction of the 1-isopropylpiperidin-2-one **1a** (71 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-(4-methoxyphenyl)acetate (123 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3k** (145 mg, yield: 60%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 4). IR (film) ν_{max} 3064, 2933, 2853, 1649, 1609, 1516, 1457, 1368, 1298, 1247, 1173, 1020, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.94 (d, J = 6.6 Hz, 3H), 1.08 (d, J = 6.7 Hz, 3H), 1.30-1.44 (m, 1H), 1.58-1.75 (m, 2H), 1.80-1.98 (m, 3H), 2.28 (ddd, J = 3.4, 11.0, 11.0 Hz, 1H), 2.72 (qq, J = 6.6, 6.7 Hz, 1H), 2.98 (ddd, J = 4.0, 4.0, 11.0 Hz, 1H), 3.69 (dd, J = 3.6, 9.4 Hz, 1H), 3.82 (s, 3H), 4.03 (s, 3H), 6.90-6.94 (m, 2H), 7.71-7.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.7, 23.8, 25.7, 31.7, 44.2, 51.2, 55.3, 58.7, 60.3, 113.9 (2C), 114.3, 124.2, 126.3 (2C), 153.6, 155.6, 158.2; HRMS (ESI, *m/z*) calcd for $C_{19}H_{26}N_2O_3$ [$M+H^+$]: 331.2016; found: 331.2015.

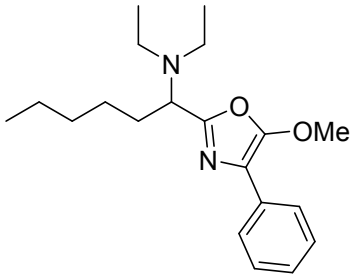
5-Methoxy-4-phenyl-2-(1-(pyrrolidin-1-yl)hexyl)oxazole (3l)



Following the general procedure B, the reaction of the 1-(pyrrolidin-1-yl)hexan-1-one **1l** (85 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg,

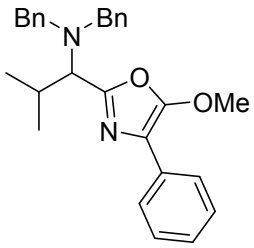
0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3l** (146 mg, yield: 90%) as a yellow oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 5). IR (film) ν_{max} 3058, 2962, 2932, 2859, 1644, 1603, 1500, 1449, 1369, 1170, 1070, 1038, 1017, 767, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, J = 6.9 Hz, 3H), 1.14-1.37 (m, 6H), 1.72-1.82 (m, 4H), 1.85-2.01 (m, 2H), 2.49-2.58 (m, 2H), 2.67-2.77 (m, 2H), 3.56 (dd, J = 5.2, 9.8 Hz, 1H), 4.05 (s, 3H), 7.18-7.24 (m, 1H), 7.35-7.40 (m, 2H), 7.80-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.4, 23.3 (2C), 25.8, 31.6, 32.5, 51.1 (2C), 60.1, 62.3, 114.1, 125.0 (2C), 126.3, 128.4 (2C), 131.5, 154.4, 154.7; HRMS (ESI) calcd for $C_{20}H_{28}N_2O_2$ [M+H^+]: 329.2224; found: 329.2219.

***N*,*N*-Diethyl-1-(5-methoxy-4-phenyloxazol-2-yl)hexan-1-amine (3m)**

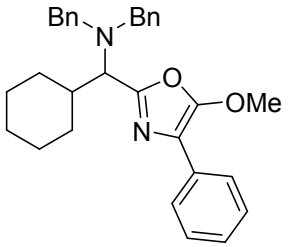


Following the general procedure B, the reaction of the *N*,*N*-diethylhexanamide **1m** (86 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3m** (161 mg, yield: 97%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 10). IR (film) ν_{max} 3058, 2962, 2932, 2859, 1644, 1500, 1449, 1369, 1202, 1170, 1070, 1017, 767, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 6.8, Hz, 3H), 1.09 (t, J = 7.1 Hz, 6H), 1.26-1.49 (m, 6H), 1.78-1.89 (m, 1H), 1.91-2.01 (m, 1H), 2.39-2.49 (m, 2H), 2.74-2.84 (m, 2H), 3.84 (dd, J = 6.8, 8.2 Hz, 1H), 4.06 (s, 3H), 7.20-7.26 (m, 1H), 7.37-7.43 (m, 2H), 7.81-7.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (2C), 14.0, 22.5, 26.2, 30.8, 31.7, 44.4 (2C), 58.5, 59.9, 114.0, 125.0 (2C), 126.2, 128.4 (2C), 131.6, 154.2, 155.1; HRMS (ESI, *m/z*) calcd for $C_{20}H_{30}N_2O_2$ [M+H^+]: 331.2380; found: 331.2377.

***N*,*N*-Dibenzyl-1-(5-methoxy-4-phenyloxazol-2-yl)-2-methylpropan-1-amine (3n)**



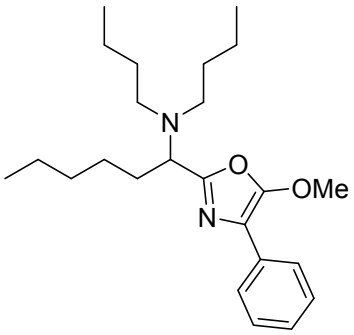
Following the general procedure B, the reaction of the *N*,*N*-dibenzylisobutyramide **1n** (134 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3n** (187 mg, yield: 88%) as a white solid after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 40). Mp 84-85 °C. IR (film) ν_{max} 3062, 3028, 2959, 2869, 2839, 1643, 1603, 1495, 1449, 1372, 1211, 1070, 1017, 768, 747, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.76 (d, J = 6.5 Hz, 3H), 1.13 (d, J = 6.5 Hz, 3H), 2.38-2.48 (m, 1H), 3.22 (d, J = 13.8 Hz, 2H), 3.31 (d, J = 11.0 Hz, 1H), 4.01 (d, J = 13.8 Hz, 2H), 4.10 (s, 3H) , 7.22-7.27 (m, 3H), 7.31-7.36 (m, 4H), 7.39-7.47 (m, 6H), 7.87-7.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 20.4, 28.2, 54.6 (2C), 59.9, 63.4, 114.0, 125.1 (2C), 126.3, 126.9 (2C), 128.2 (4C), 128.5 (2C), 129.0 (4C), 131.7, 139.6 (2C), 153.4, 154.3; HRMS (ESI, *m/z*) calcd for $C_{28}H_{30}N_2O_2$ [M+H$^+$]: 427.2380; found: 427.2380.***N*,*N*-Dibenzyl-1-cyclohexyl-1-(5-methoxy-4-phenyloxazol-2-yl)methanamine (3o)**



Following the general procedure B, the reaction of the *N*,*N*-dibenzylcyclohexanecarboxamide **1o** (134 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105

mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3o** (210 mg, yield: 90%) as a white solid after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 40). Mp 104-105 °C. IR (film) ν_{max} 3061, 3028, 2926, 2850, 1643, 1602, 1495, 1449, 1371, 1070, 1037, 1017, 767, 746, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.71-0.93 (m, 2H), 1.02-1.30 (m, 3H), 1.31-1.40 (m, 1H), 1.54-1.66 (m, 2H), 1.68-1.79 (m, 1H), 2.12 (m, 1H), 2.36-2.46 (m, 1H), 3.23 (d, J = 13.8 Hz, 2H), 3.44 (d, J = 11.0 Hz, 1H), 4.01 (d, J = 13.8 Hz, 2H), 4.09 (s, 3H), 7.21-7.28 (m, 3H), 7.30-7.37 (m, 4H), 7.39-7.46 (m, 6H), 7.86-7.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 26.0, 26.6, 30.3, 30.7, 37.4, 54.6 (2C), 60.0, 62.2, 114.1, 125.1 (2C), 126.3, 126.9 (2C), 128.2 (4C), 128.5 (2C), 129.0 (4C), 131.7, 139.7 (2C), 153.3, 154.3; HRMS (ESI, *m/z*) calcd for $C_{31}H_{34}N_2O_2$ [M+H^+]: 467.2693; found: 467.2693.

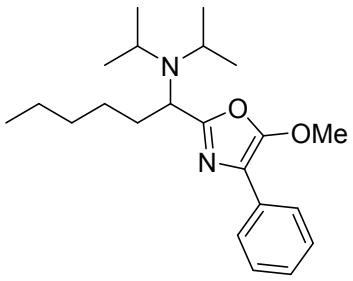
***N*,*N*-Dibutyl-1-(5-methoxy-4-phenyloxazol-2-yl)hexan-1-amine (3p)**



Following the general procedure B, the reaction of the *N*,*N*-dibutylhexanamide **1p** (114 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3p** (192 mg, yield: 99%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 50). IR (film) ν_{max} 3058, 2956, 2931, 2860, 1644, 1604, 1500, 1460, 1370, 1170, 1093, 1018, 804, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86-0.94 (m, 9H),

1.25-1.49 (m, 14H), 1.74-1.84 (m, 1H), 1.84-1.94 (m, 1H), 2.29-2.38 (m, 2H), 2.57-2.66 (m, 2H), 3.76 (dd, J = 7.5, 7.5 Hz, 1H), 4.03(s, 3H), 7.17-7.23 (m, 1H), 7.34-7.40 (m, 2H), 7.78-7.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1 (2C), 20.5 (2C), 22.5, 26.2, 30.5, 30.9 (2C), 31.7, 50.7 (2C), 58.7, 59.9, 113.9, 125.0 (2C), 126.1, 128.4 (2C), 131.7, 154.2, 155.3; HRMS (ESI, *m/z*) calcd for $C_{24}H_{38}N_2O_2$ [M+H$^+$]: 387.3006; found: 387.3004.

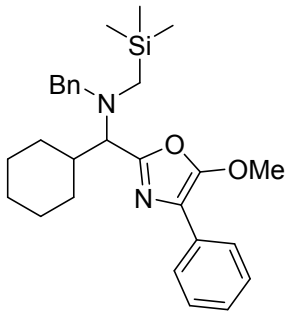
_N_,_N_-Diisopropyl-1-(5-methoxy-4-phenyloxazol-2-yl)hexan-1-amine (3q)



Following the general procedure B, the reaction of the *N*,*N*-diisopropylhexanamide **1q** (100 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3q** (170 mg, yield: 95%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 100). IR (film) ν_{max} 3058, 2962, 2931, 2860, 1644, 1604, 1450, 1460, 1371, 1261, 1186, 1019, 804, 767, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, J = 6.9 Hz, 3H), 0.97 (d, J = 6.8 Hz, 6H), 1.09 (d, J = 6.8 Hz, 6H), 1.28-1.40 (m , 5H), 1.41-1.52 (m, 1H), 1.71-1.82 (m, 1H), 1.87-1.98 (m, 1H), 3.35 (hept, J = 6.8 Hz, 2H), 3.91 (dd, J = 7.6, 7.6 Hz, 1H), 4.04 (s, 3H), 7.20-7.25 (m, 1H), 7.37-7.42 (m, 2H), 7.81-7.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 21.7 (2C), 22.6, 23.7 (2C), 26.4, 31.8, 32.9, 45.2 (2C), 52.0, 59.9, 114.0, 125.0 (2C), 126.0, 128.4 (2C), 131.9, 153.8, 157.3; HRMS (ESI, *m/z*) calcd for $C_{22}H_{34}N_2O_2$ [M+H$^+$]: 359.2693; found: 359.2690.

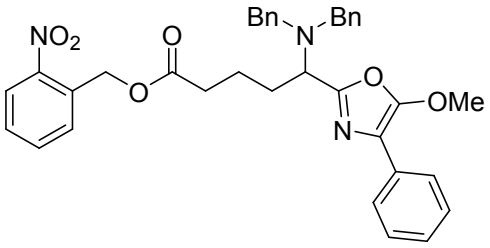
_N_-Benzyl-1-cyclohexyl-1-(5-methoxy-4-phenyloxazol-2-yl)-N-

((trimethylsilyl)methyl)methanamine (3r)



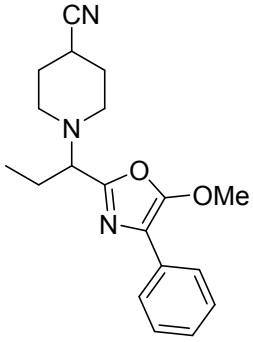
Following the general procedure B, the reaction of the *N*-benzyl-*N*-((trimethylsilyl)methyl)cyclohexanecarboxamide **1r** (152 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3r** (182 mg, yield: 79%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 100). IR (film) ν_{max} 3062, 3028, 2926, 2851, 2796, 1745, 1683, 1644, 1603, 1496, 1449, 1370, 1248, 1218, 1070, 1017, 853, 737, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.10 (s, 9H), 0.71-0.91 (m, 2H), 1.03-1.31 (m, 3H), 1.33-1.42 (m , 1H), 1.57-1.67 (m, 2H), 1.69-1.79 (m, 2H), 1.91-2.04 (m, 1H), 2.22-2.34 (m, 2H), 3.23 (d, J = 13.9 Hz, 1H), 3.34 (d, J = 10.9 Hz, 1H), 3.94 (d, J = 13.9 Hz, 1H), 4.07 (s, 3H), 7.19-7.28 (m, 2H), 7.31-7.37 (m, 2H), 7.37-7.45 (m, 4H), 7.83-7.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -1.0 (3C), 26.0, 26.1, 26.7, 30.4, 30.9, 37.7, 41.7, 58.1, 59.9, 64.8, 113.9, 125.0 (2C), 126.2, 126.8, 128.2 (2C), 128.4 (2C), 129.0 (2C), 131.8, 140.0, 154.3, 154.2; HRMS (ESI, *m/z*) calcd for $C_{28}H_{38}N_2O_2Si$ $[M+Na^+]$: 485.2595; found: 485.2592.

2-Nitrobenzyl 5-(dibenzylamino)-5-(5-methoxy-4-phenyloxazol-2-yl)pentanoate (3s)



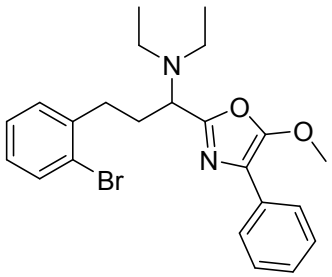
Following the general procedure B, the reaction of the 2-nitrobenzyl 5-(dibenzylamino)-5-oxopentanoate **1s** (223 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3s** (238 mg, yield: 79%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 5). IR (film) ν_{max} 3061, 3028, 2943, 2853, 1741, 1643, 1603, 1578, 1528, 1495, 1450, 1372, 1343, 1208, 1158, 1071, 1017, 959, 729, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.62-1.74 (m, 1H), 1.84-1.98 (m, 2H), 2.02-2.15 (m, 1H), 2.29 (dd, J = 7.3, 7.3 Hz, 2H), 3.37 (d, J = 13.8 Hz, 2H), 3.78 (dd, J = 6.0, 8.7 Hz, 1H), 3.92 (d, J = 13.8 Hz, 2H), 4.11 (s, 3H), 5.49 (s, 2H), 7.20-7.26 (m, 3H), 7.28-7.35 (m, 4H), 7.37-7.44 (m, 6H), 7.44-7.48 (m, 1H), 7.52-7.56 (m, 1H), 7.56-7.62 (m, 1H), 7.82-7.88 (m, 2H), 8.05-8.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 29.2, 33.5, 54.5, 55.5 (2C), 59.9, 62.7, 114.1, 125.0 (2C), 126.3, 127.0 (2C), 128.3 (4C), 128.5 (2C), 128.7 (2C), 129.0 (4C), 131.5, 132.2, 133.6 (2C), 139.5, 147.5, 153.8, 154.3, 172.6; HRMS (ESI, *m/z*) calcd for $C_{36}H_{35}N_3O_6$ [M+Na^+]: 628.2418; found: 628.2414.

1-(1-(5-Methoxy-4-phenyloxazol-2-yl)propyl)piperidine-4-carbonitrile (3t)



Following the general procedure B, the reaction of the 1-propionylpiperidine-4-carbonitrile **1t** (83 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3t** (102 mg, yield: 63%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 7/ 10). IR (film) ν_{max} 3055, 3023, 2949, 2876, 2815, 2762, 2239, 1643, 1604, 1498, 1448, 1372, 1331, 1313, 1212, 1172, 1138, 1098, 1016, 955, 769, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, J = 7.4 Hz, 3H), 1.75-2.02 (m, 6H), 2.27-2.39 (m, 1H), 2.43-2.62 (m, 2H), 2.71-2.83 (m, 1H), 2.83-2.94 (m, 1H), 3.54 (dd, J = 6.6, 8.7 Hz, 1H), 4.05 (s, 3H), 7.18-7.24 (m, 1H), 7.34-7.41 (m, 2H), 7.76-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.0, 23.2, 26.4, 29.2 (2C), 47.2, 48.8, 60.0, 64.6, 114.2, 121.7, 125.0 (2C), 126.3, 128.4 (2C), 131.3, 153.5, 154.4; HRMS (ESI, *m/z*) calcd for $C_{19}H_{23}N_3O_2$ [M+Na^+]: 348.1682; found: 348.1672.

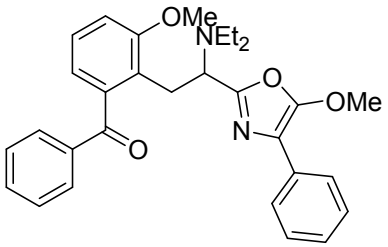
3-(2-Bromophenyl)-*N*,*N*-diethyl-1-(5-methoxy-4-phenyloxazol-2-yl)propan-1-amine (3u)



Following the general procedure B, the reaction of the 3-(2-bromophenyl)-N,N-diethylpropanamide **1u** (142 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3u** (204 mg, yield: 92%) as a colorless oil after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 10). IR (film) ν_{max} 3058, 2967, 2934, 2868, 2812, 1643, 1603, 1559, 1500, 1471, 1448, 1372, 1202, 1170, 1070, 1017, 752, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, J = 7.2 Hz, 6H), 2.11-2.28 (m, 2H), 2.39-2.51

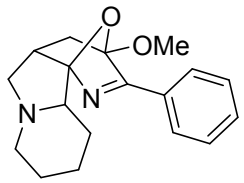
(m, 2H), 2.70-2.85 (m, 3H), 2.89-3.00 (m, 1H), 3.88 (dd, J = 7.5, 7.5 Hz, 1H), 4.03 (s, 3H), 7.00-7.07 (m, 1H), 7.17-7.29 (m, 3H), 7.33-7.41 (m, 2H), 7.49-7.57 (m, 1H), 7.77-7.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8 (2C), 30.7, 33.4, 44.4 (2C), 57.9, 59.9, 114.1, 124.4, 125.0 (2C), 126.2, 127.4, 127.6, 128.4 (2C), 130.6, 131.6, 132.8, 141.4, 154.3, 154.6; HRMS (ESI, *m/z*) calcd for $C_{23}H_{27}BrN_2O_2$ [M+Na$^+$]: 467.1128; found: 467.1127.

(2-(2-(Diethylamino)-2-(5-methoxy-4-phenyloxazol-2-yl)ethyl)-3-methoxyphenyl)(phenyl)methanone (3v)



Following the general procedure B, the reaction of the 2-(2-benzoyl-6-methoxyphenyl)-*N*,*N*-diethylacetamide **1v** (117 mg, 0.5 mmol) with $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol), TMDS (134 mg, 1.0 mmol), methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) afforded 5-methoxy-4-phenyloxazole **3v** (122 mg, yield: 50%) as a white solid after flash column chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 1/ 100). Mp 84-85 °C. IR (film) ν_{max} 3060, 2968, 2937, 2836, 1665, 1642, 1597, 1578, 1457, 1373, 1317, 1274, 1070, 1017, 713, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.1 Hz, 6H), 2.32-2.44 (m, 2H), 2.61-2.73 (m, 2H), 3.31 (dd, J = 4.9, 13.3 Hz, 1H), 3.63 (dd, J = 9.4, 13.3 Hz, 1H), 3.74 (s, 3H), 3.88 (s, 3H), 4.15 (dd, J = 4.9, 9.4 Hz, 1H), 6.74-6.84 (m, 1H), 6.92-6.99 (m, 1H), 7.09-7.31 (m, 6H), 7.36-7.44 (m, 1H), 7.52-7.59 (m, 2H), 7.59-7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4 (2C), 27.5, 44.2 (2C), 55.5, 58.3, 59.2, 112.0, 113.3, 121.3, 124.8 (2C), 125.7, 126.4, 126.9, 128.0 (2C), 128.1 (2C), 130.3 (2C), 131.6, 132.8, 137.6, 140.4, 153.7, 154.0, 158.4, 197.7; HRMS (ESI, *m/z*) calcd for $C_{30}H_{32}N_2O_4$ [M+H$^+$]: 485.2435; found: 485.2434.

3-Methoxy-2-phenyl-3,4,4a,5,8,9,10,10a-octahydro-7H-3,10b-epoxypyrido[2,3-2]indolizine (5)

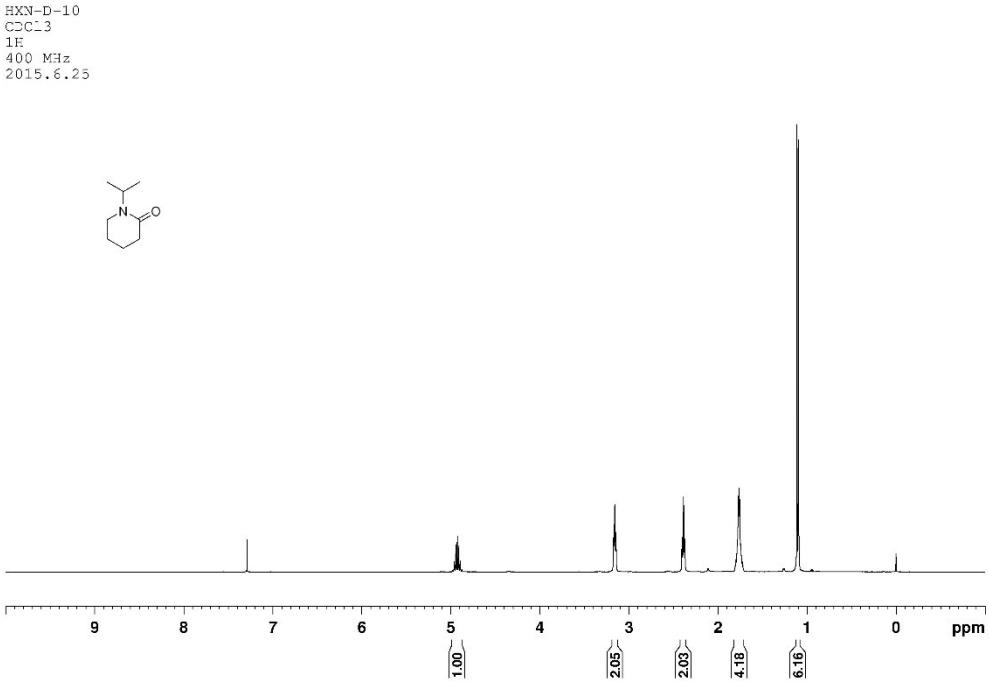


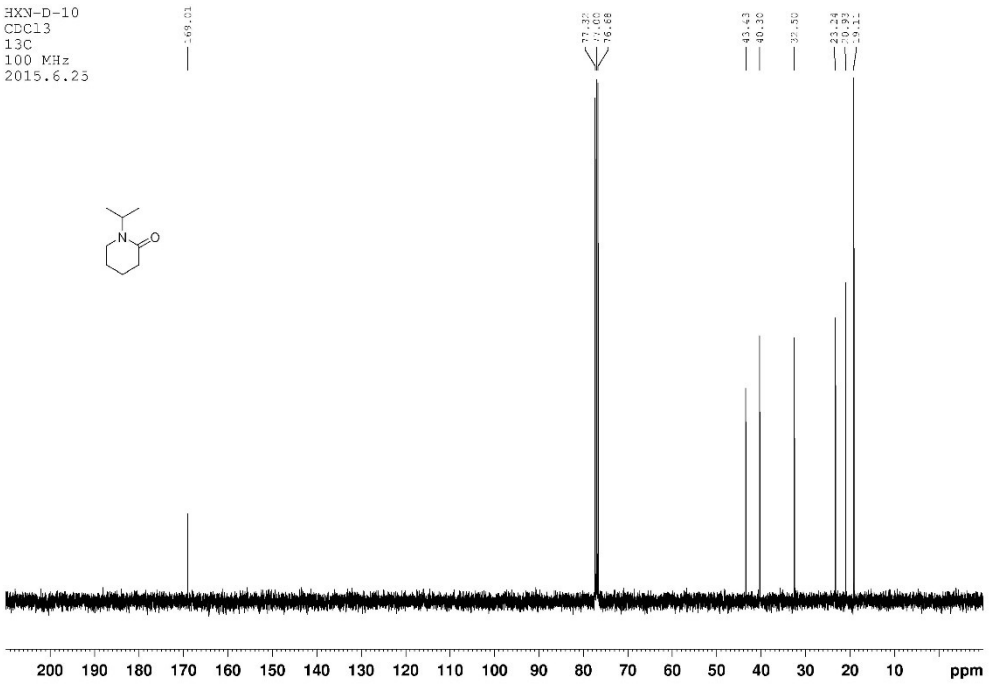
To a solution of $IrCl(CO)(PPh_3)_2$ (4 mg, 0.005 mmol) and 1-allylpiperidin-2-one **1w** (70 mg, 0.5 mmol) in 1,2-diethoxyethane (DEE) (4.0 mL) was added dropwise TMDS (134 mg, 1.0 mmol) at room temperature. The reaction mixture was stirred for 30 min, then methyl 2-isocyano-2-phenylacetate (105 mg, 0.6 mmol) and DABCO (73 mg, 0.65 mmol) was added successively. After stirring for 30 min, the reaction mixture was concentrated under reduced pressure in 50 ^{o}C. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/ *n*-hexane = 3/ 1) to afford 3-methoxy-2-phenyl-3,4,4a,5,8,9,10,10a-octahydro-7H-3,10b-epoxypyrido[2,3-2]indolizine **5** (74 mg, yield: 50%) as a white solid. Mp 74-76 °C. IR (film) ν_{max} 3058, 2938, 2852, 2785, 1563, 1494, 1448, 1300, 1280, 1251, 1028, 903, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35-1.48 (m, 1H), 1.58-1.71 (m, 3H), 1.78-1.91 (m, 2H), 1.93-2.01 (m, 1H), 2.03-2.12 (m, 1H), 2.15-2.24 (m, 1H), 2.30 (dd, J = 8.2, 9.8 Hz, 1H), 2.41-2.54 (m, 2H), 3.06 (ddd, J = 3.1, 3.1, 11.0 Hz, 1H), 3.15 (dd, J = 6.5, 8.2 Hz, 1H), 3.48 (s, 3H), 7.39-7.50 (m, 3H), 7.94-8.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 25.0, 26.8, 29.8, 47.3, 51.7, 54.9, 56.9, 65.4, 105.7, 114.4, 126.9 (2C), 128.7 (2C), 131.1, 131.2, 172.9; HRMS (ESI, *m/z*) calcd for $C_{18}H_{22}N_2O_2$ [M+H$^+$]: 299.1754; found: 299.1753.

Reference:

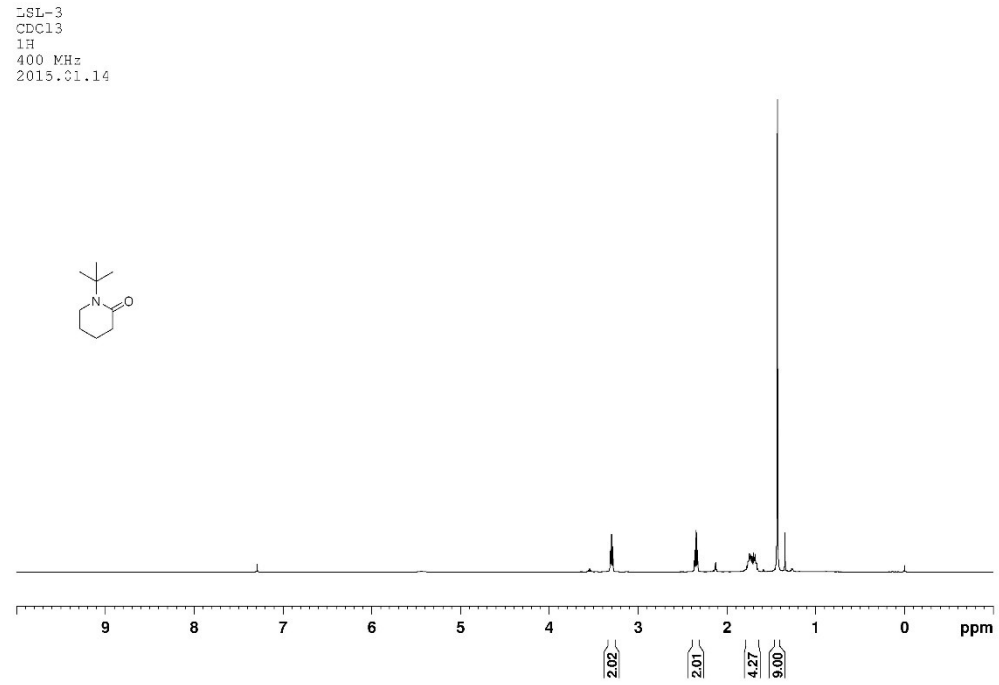
1. A. Nova, D. Balcells, N. D. Scheley, G. E. Dobereiner, R. H. Crabtree, O. Eisenstein, *Organometallics*, 2010, **29**, 6548–6558.
2. P. Magnus, J. Moursounidis, *J. Org. Chem.*, 1991, **56**, 1529–1534.
3. X. Huang, W. Zhou, X. Liu, H. Li, G. Sun, M. Mandal, M.Vicarel, X. Zhu, C. Bennett, T. McCraken, D. Pissarnitski, Z. Zhao, D. Cole, G. Gallo, Z. Zhu, A. Palani, R. Aslanian, J. Clader, M. Czarniecki, W. Greenlee, D. Burnett, M. Cohen-Williams, L. Hyde, L. Song, L. Zhang, I. Chu, A. Buevich. *ACS Med. Chem. Lett.*, 2012, **3**, 931−935.
4. J. Park, M. Kim, S. Sharma, E. Park, A. Kim, S. H. Lee, J. H. Kwak, Y. H. Jung, I. S. Kim, *Chem. Commun.*, 2013, **49**, 1654−1656.

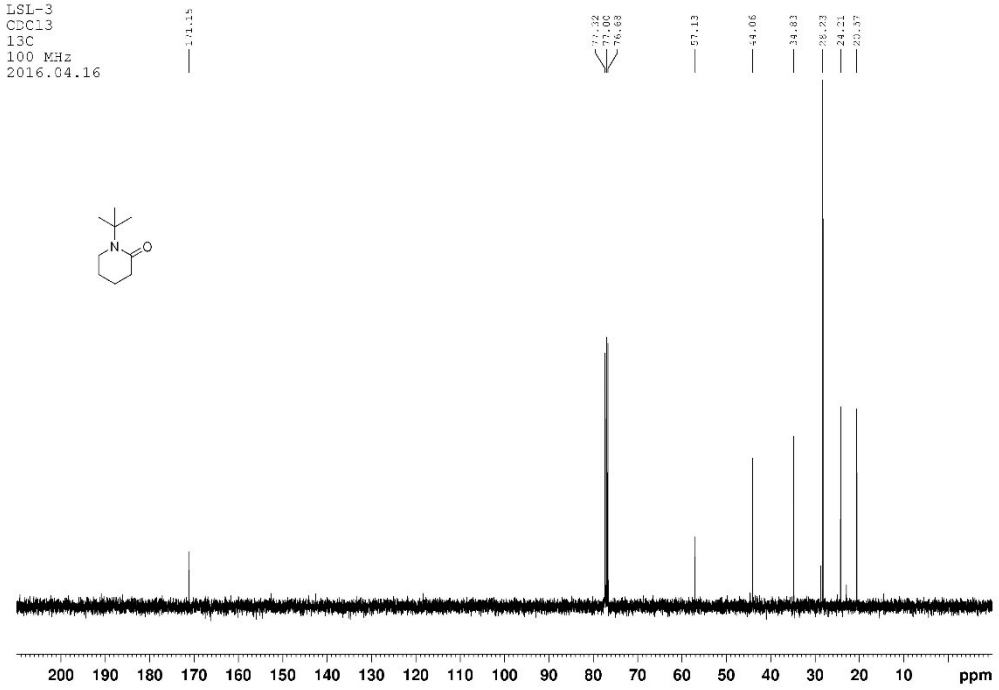
^{1}H and ^{13}C NMR spectra of **1a**



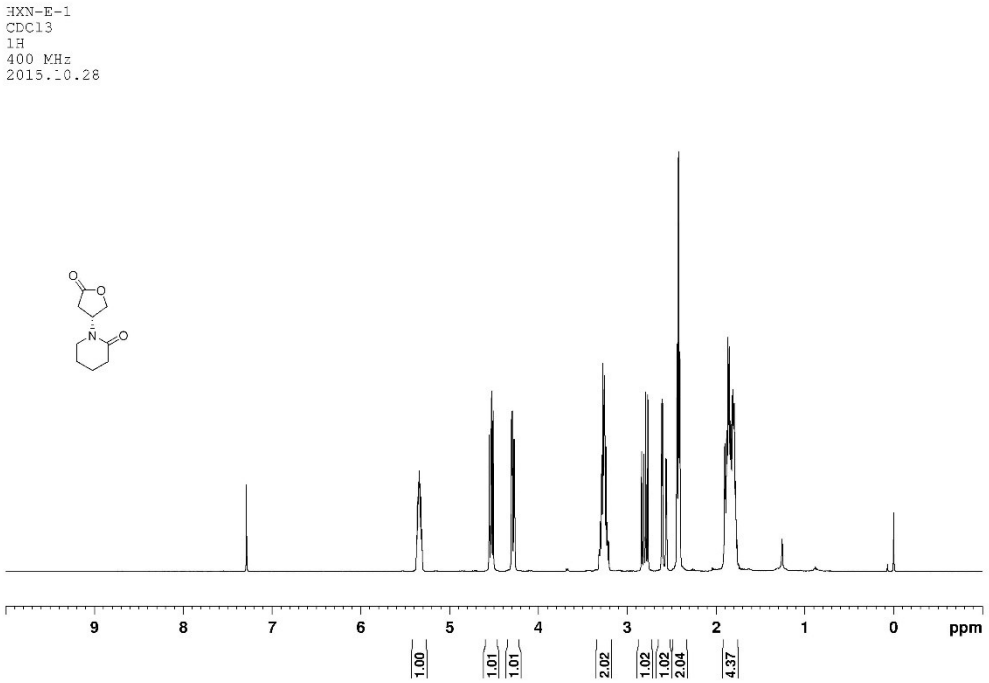


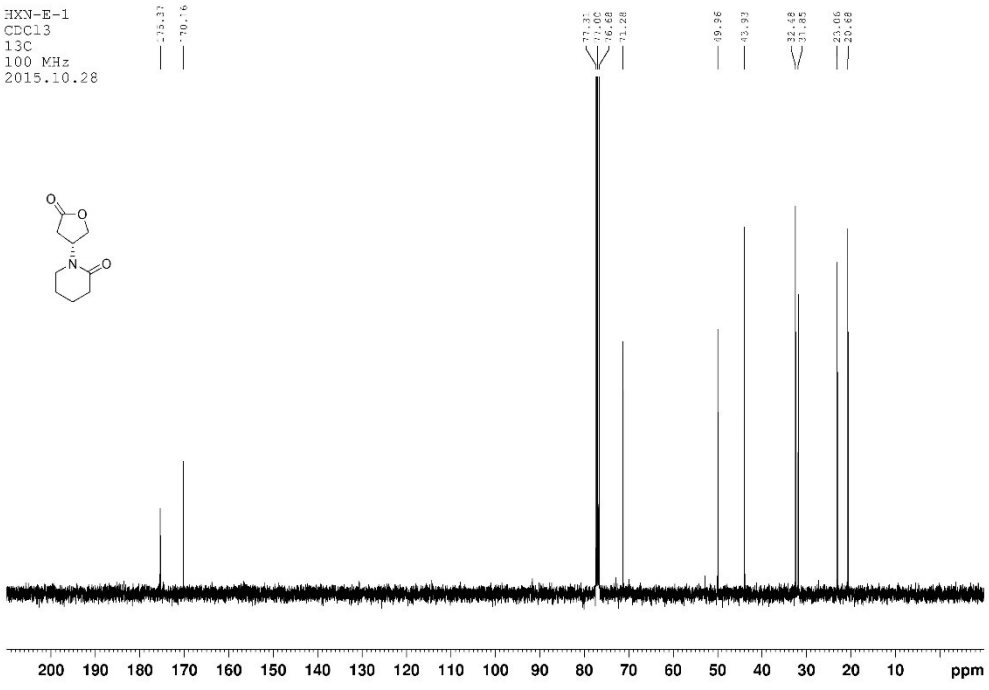
^{1}H and ^{13}C NMR spectra of **1b**



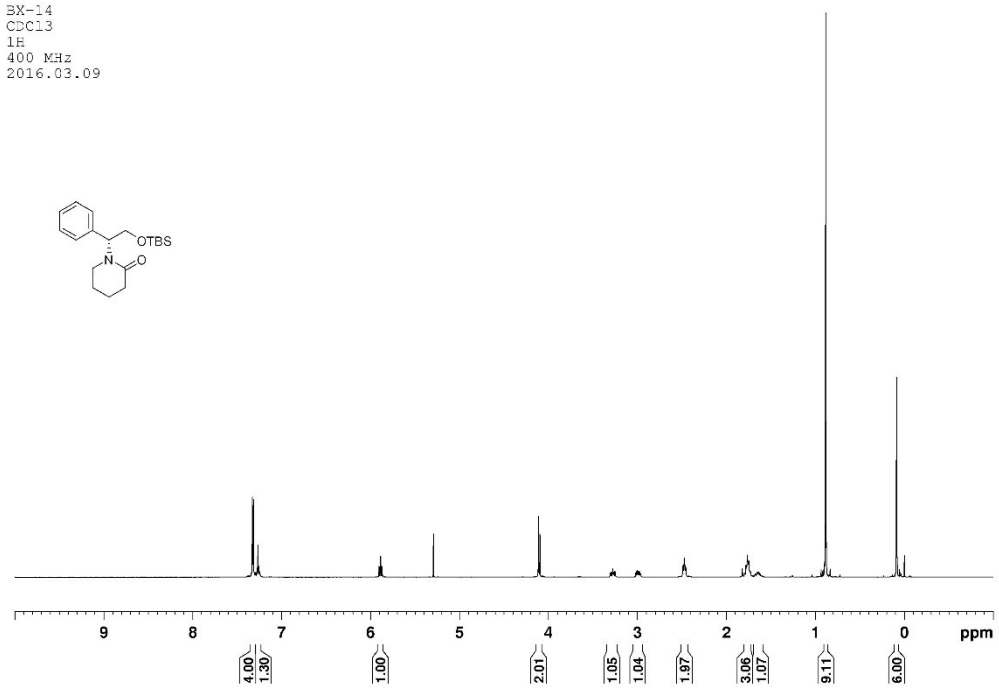


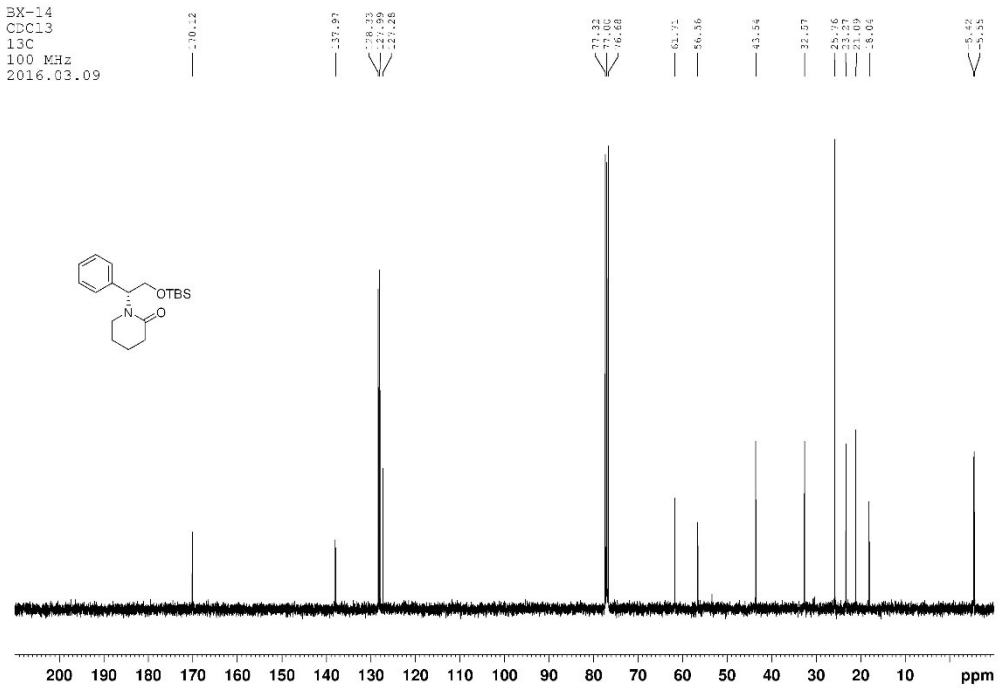
^{1}H and ^{13}C NMR spectra of **1c**



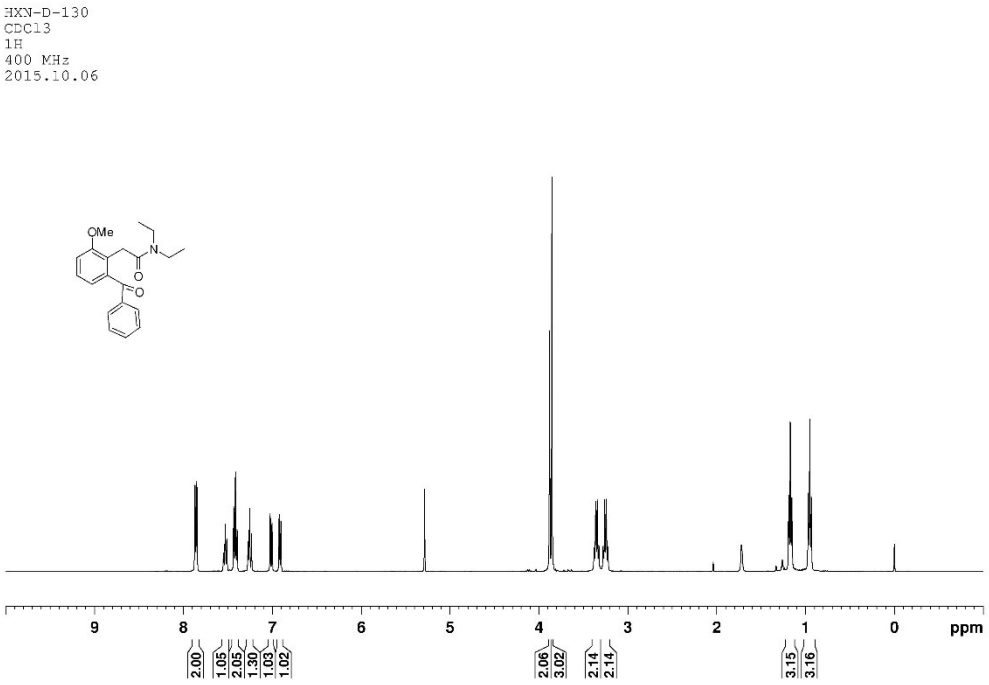


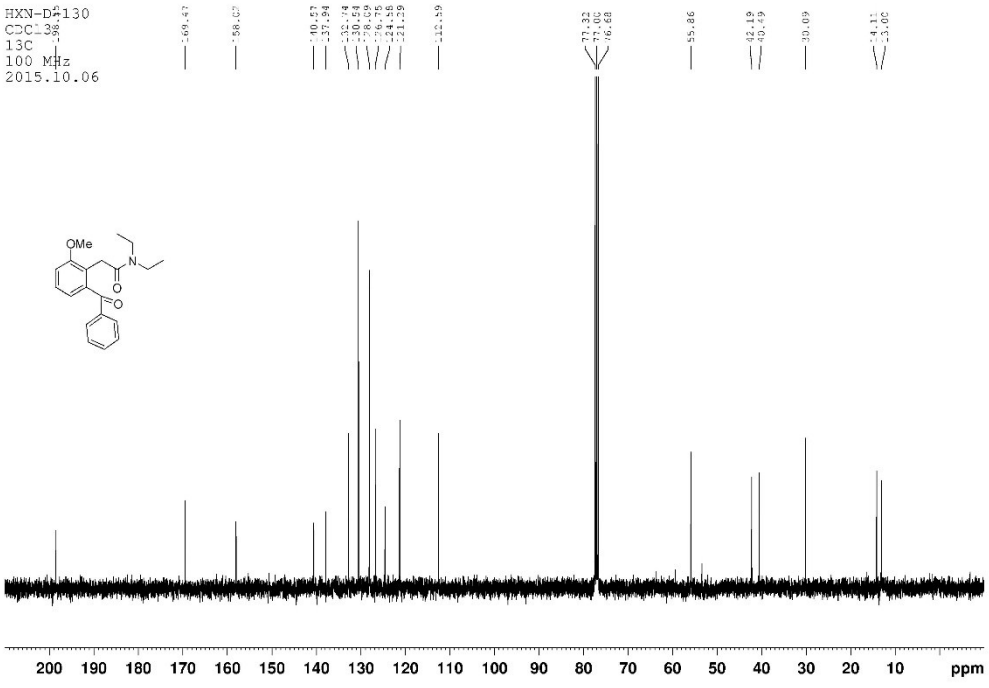
^{1}H and ^{13}C NMR spectra of **1d**



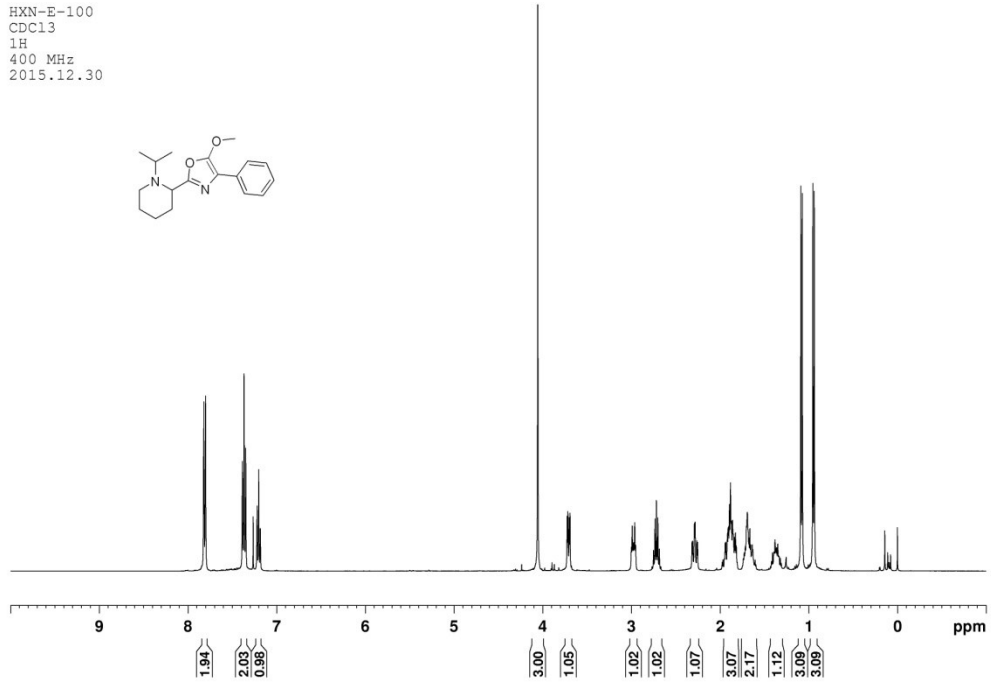


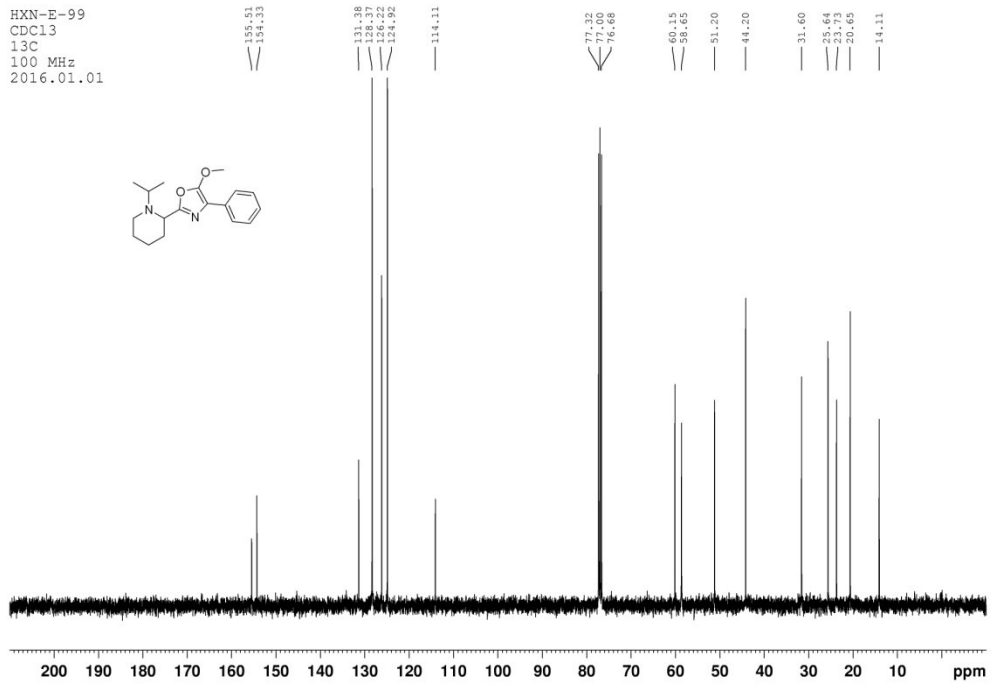
^{1}H and ^{13}C NMR spectra of **1u**



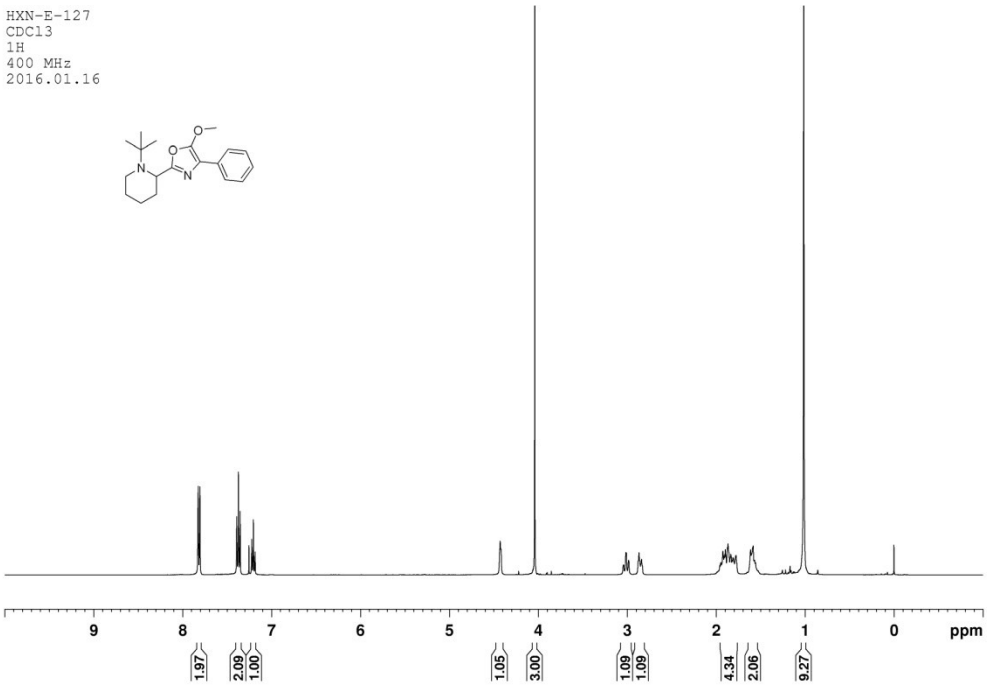


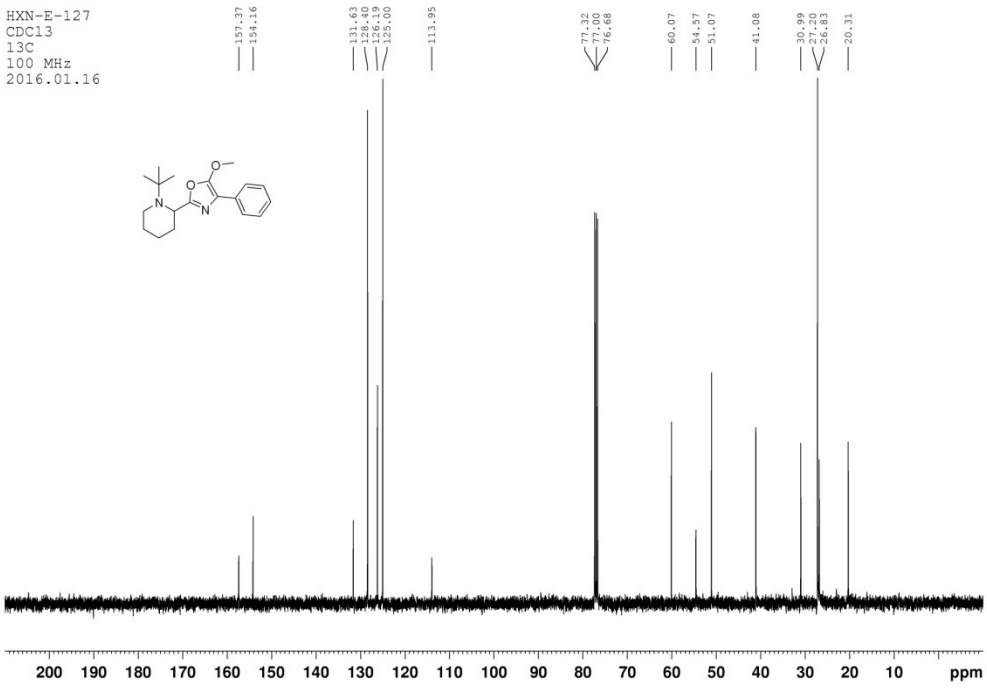
^{1}H and ^{13}C NMR spectra of **3a**



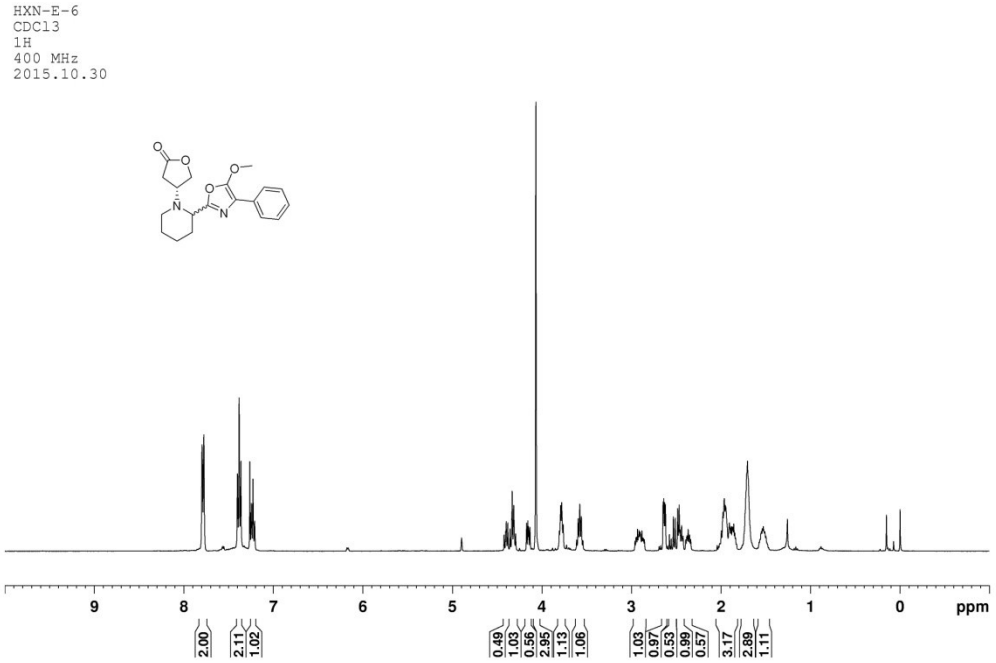


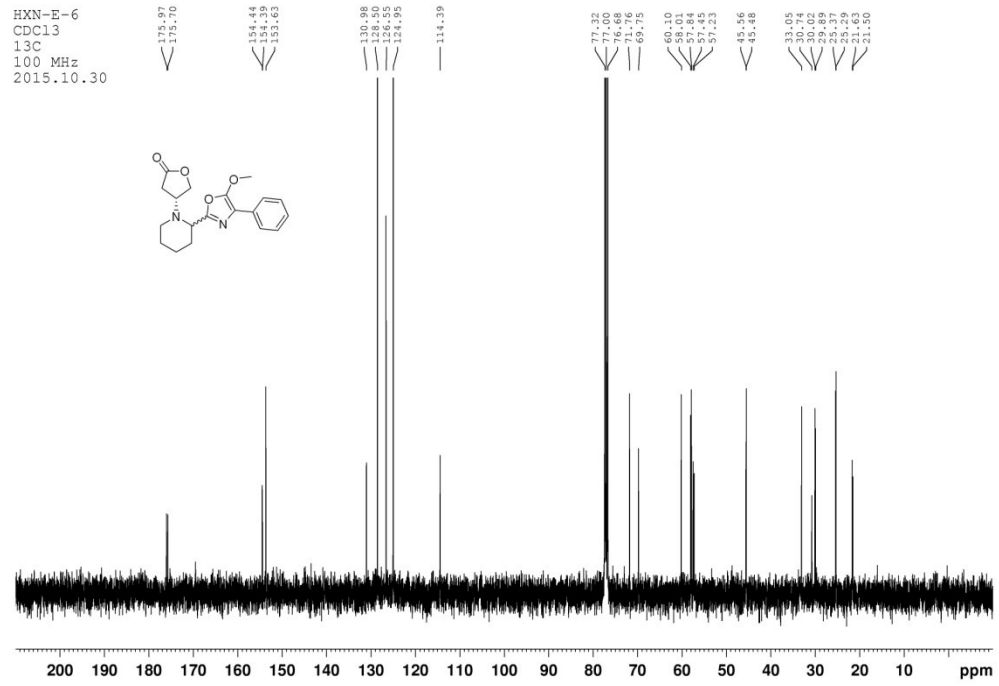
^{1}H and ^{13}C NMR spectra of **3b**



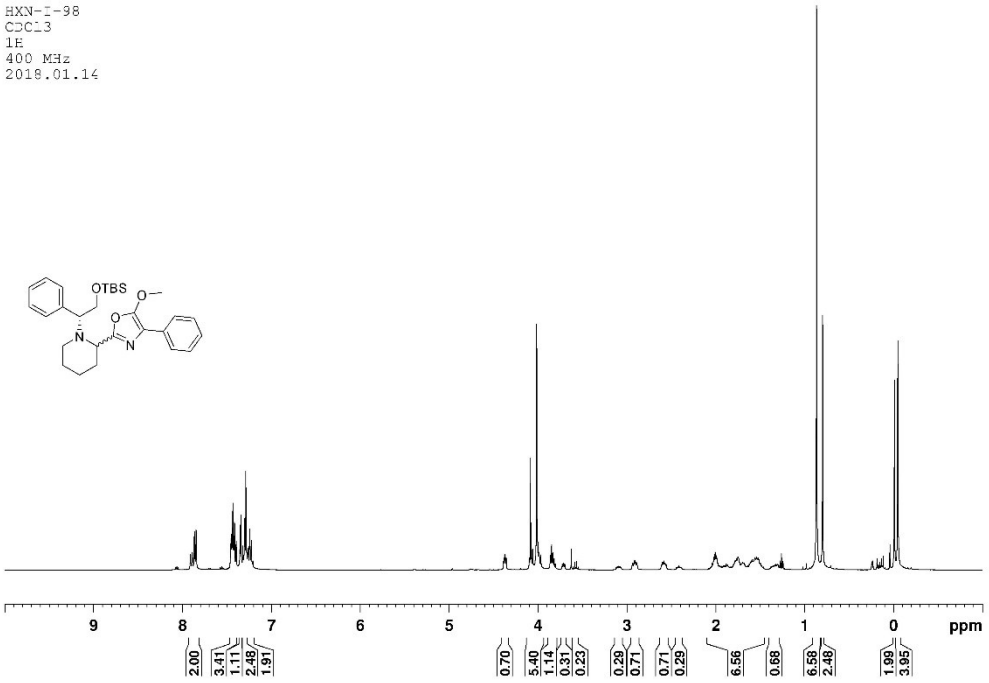


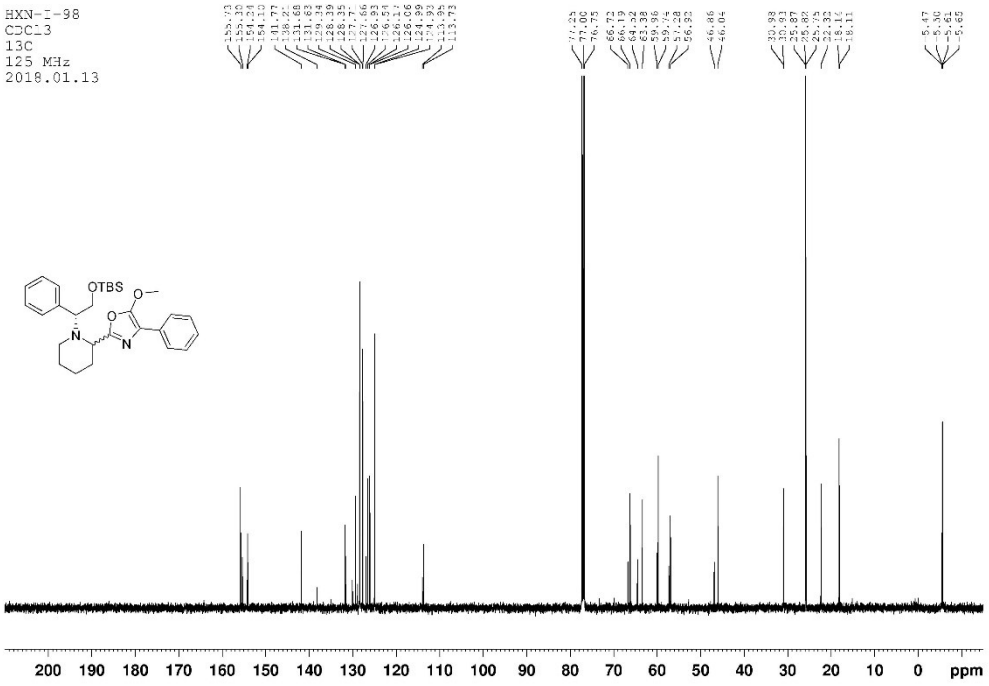
^{1}H and ^{13}C NMR spectra of **3c** (the mixture of major and minor)



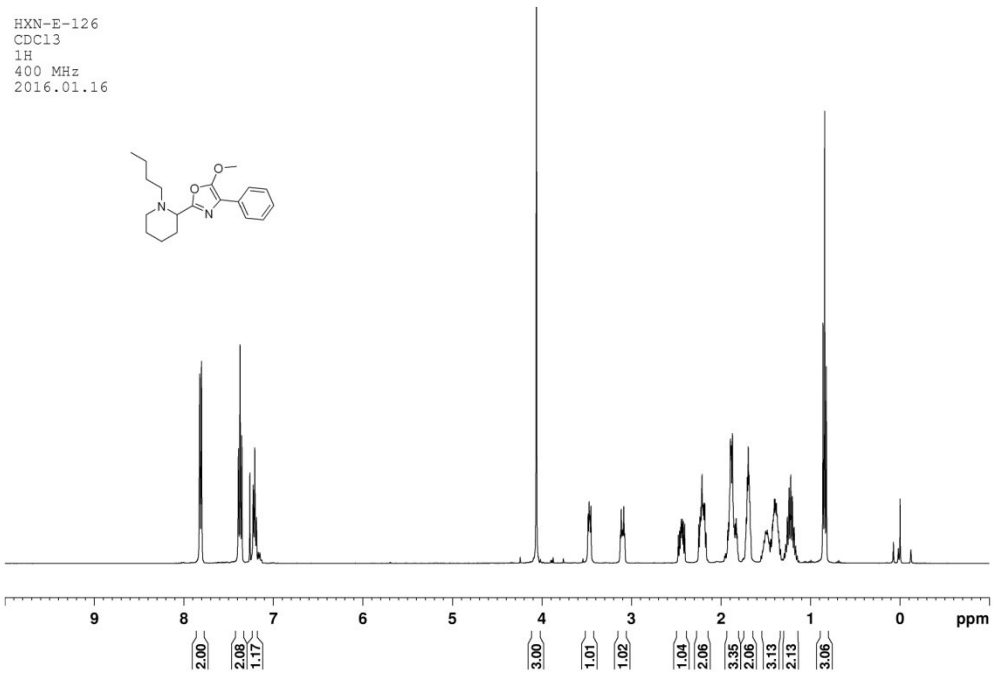


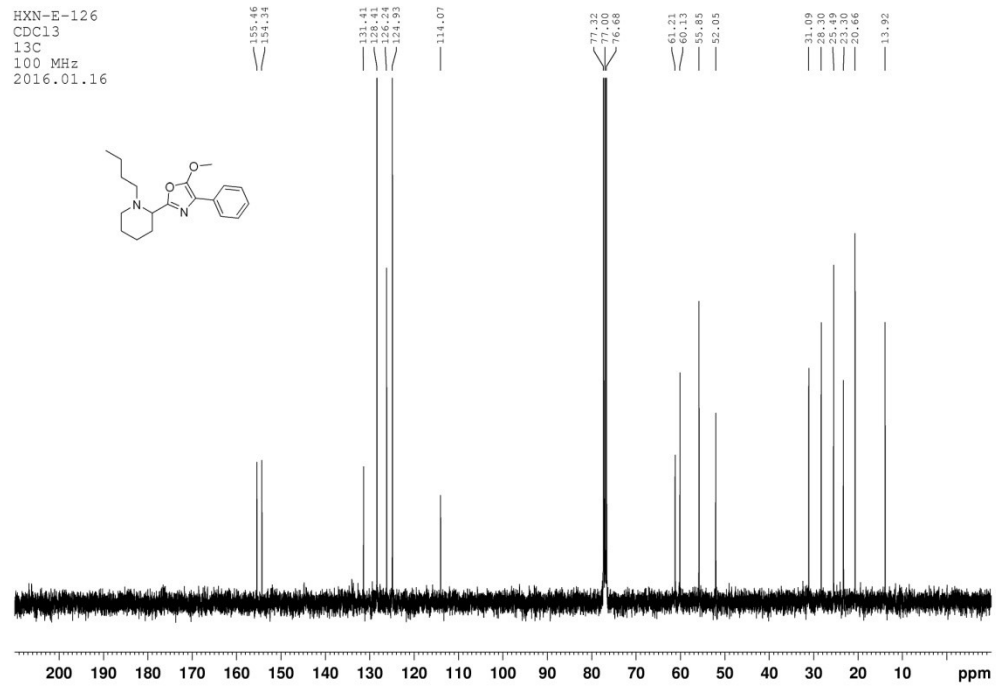
^{1}H and ^{13}C NMR spectra of **3d** (the mixture of major and minor)



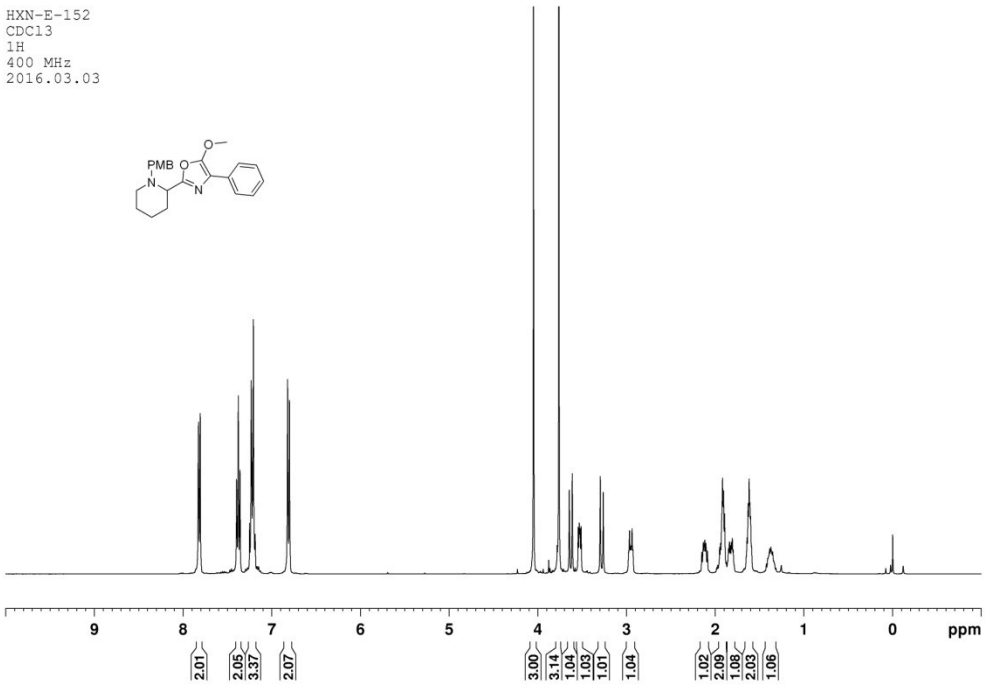


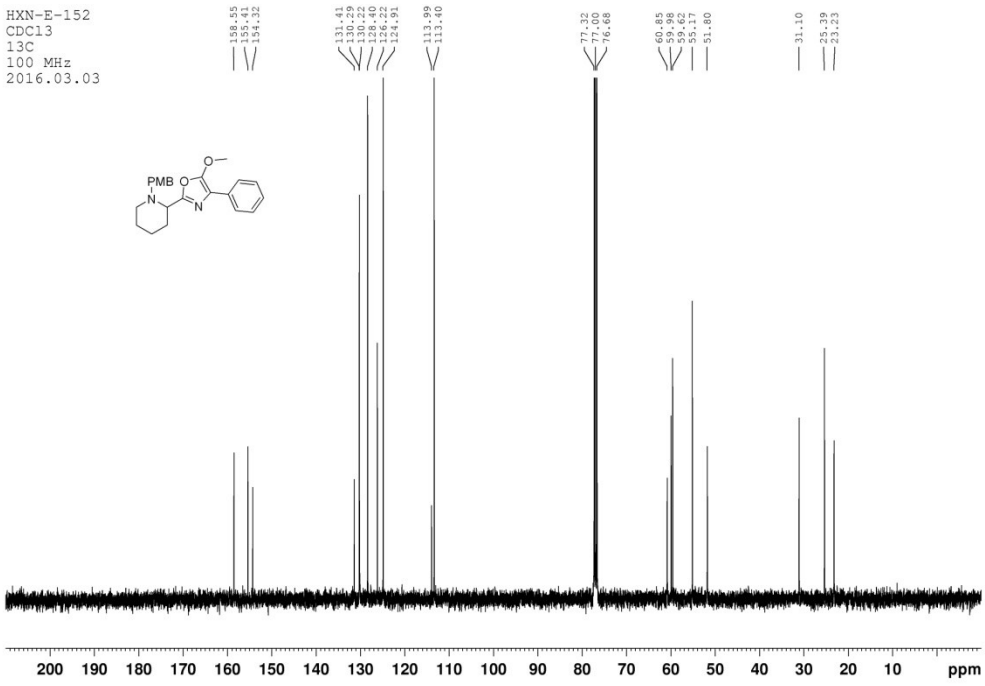
^{1}H and ^{13}C NMR spectra of **3e**



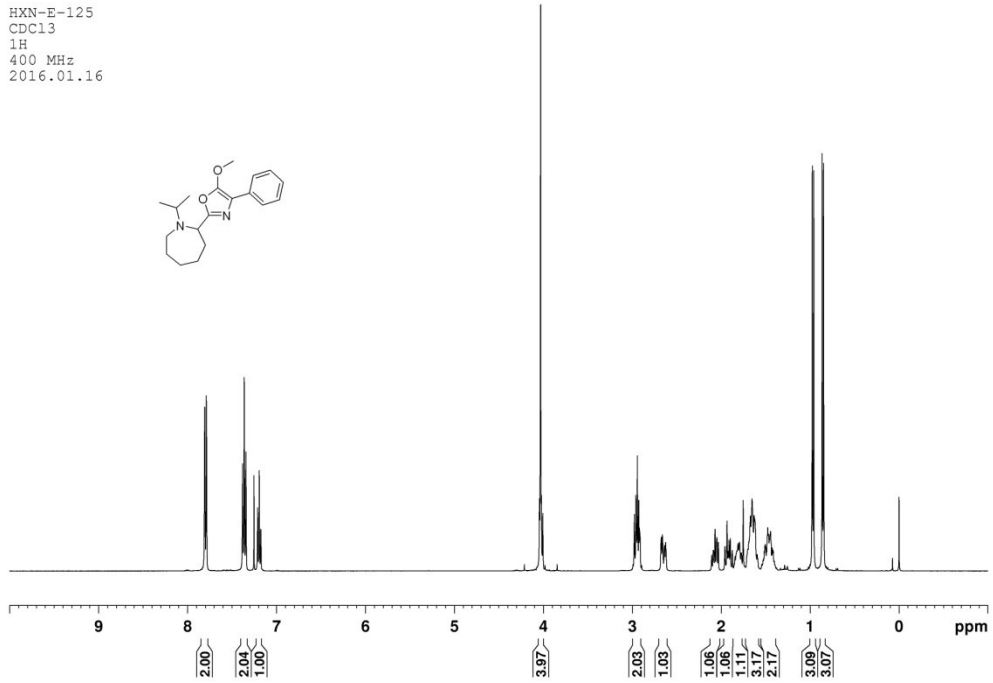


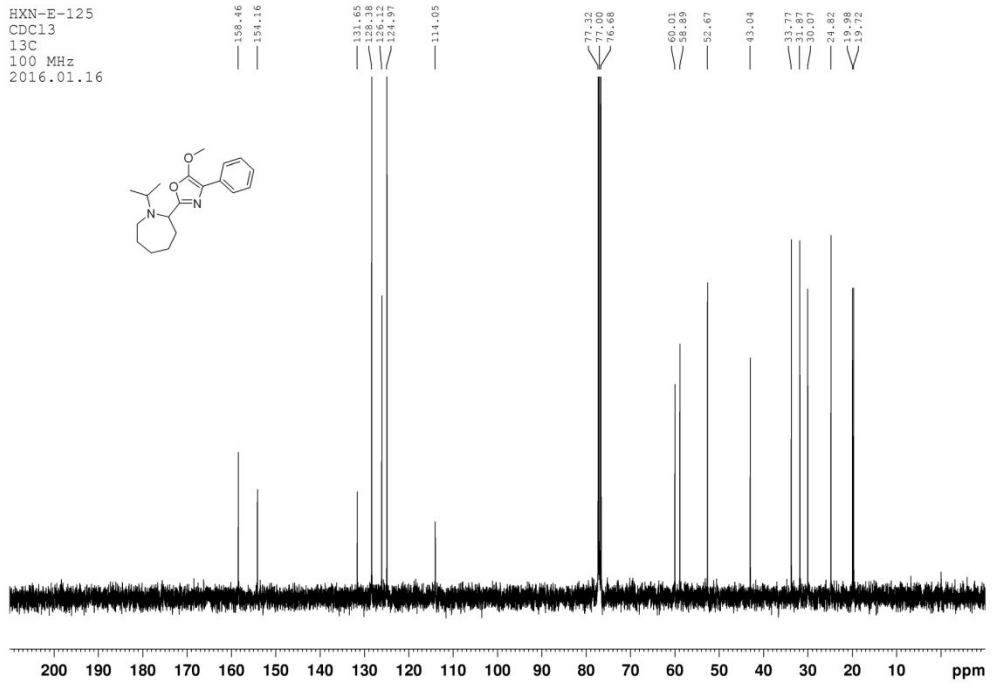
^{1}H and ^{13}C NMR spectra of **3f**



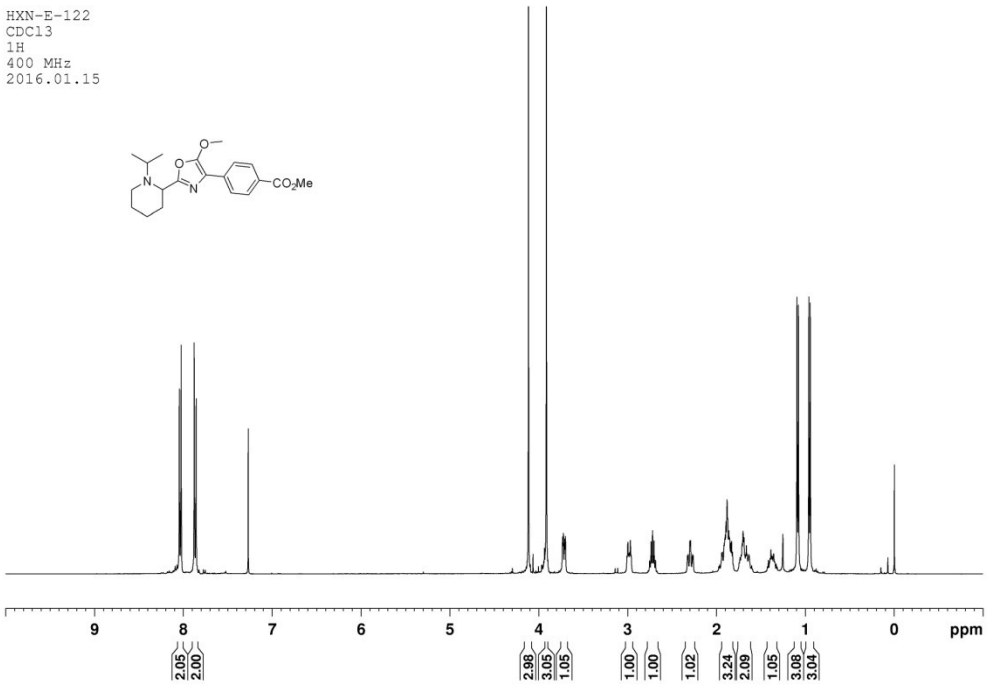


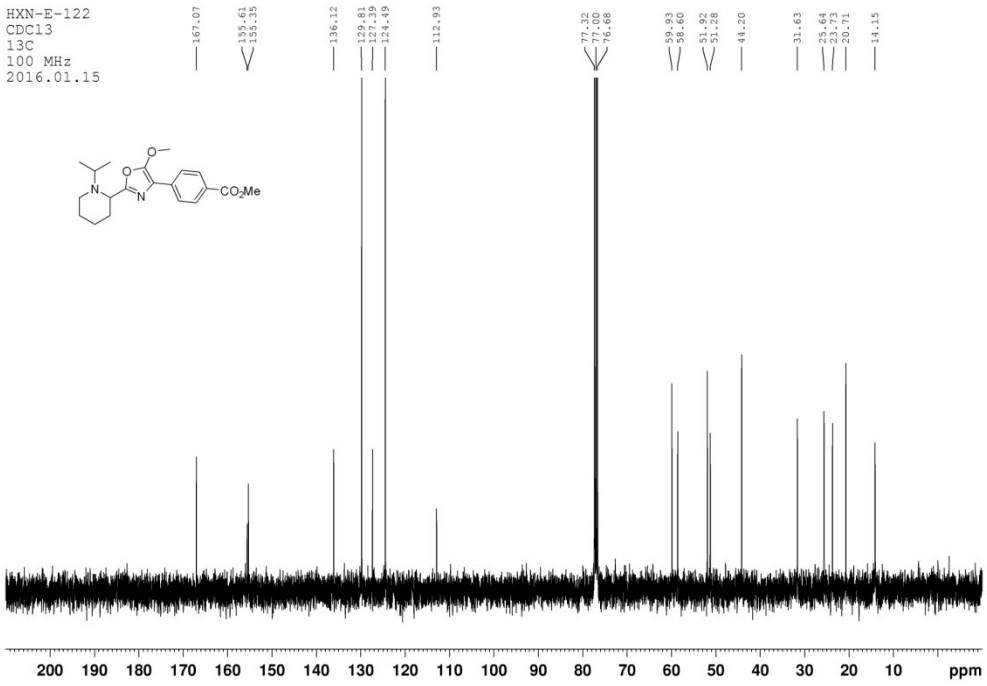
^{1}H and ^{13}C NMR spectra of **3g**



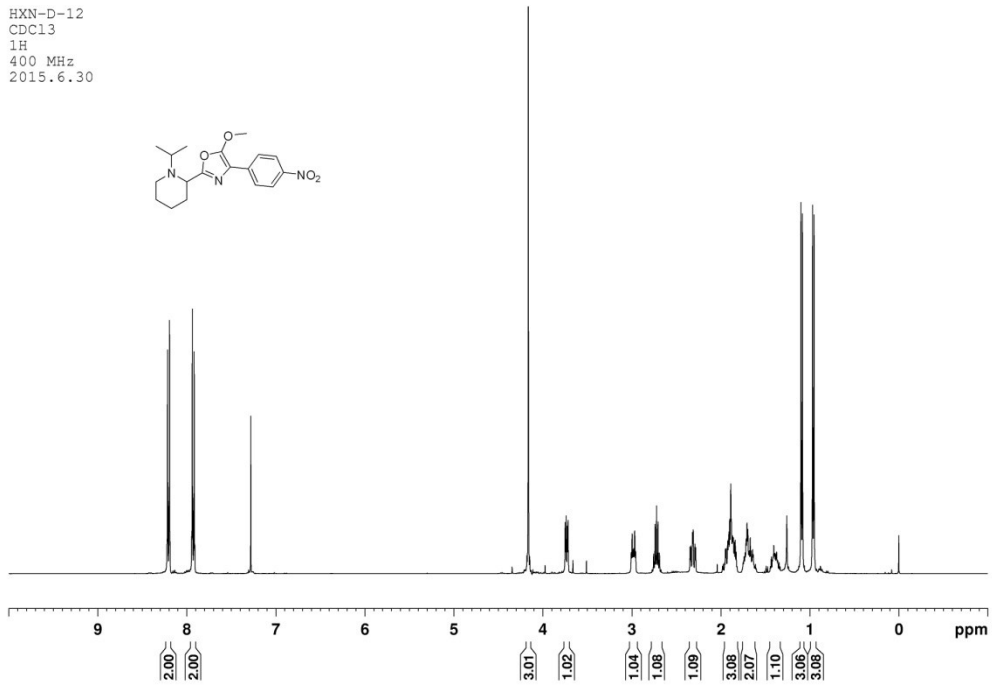


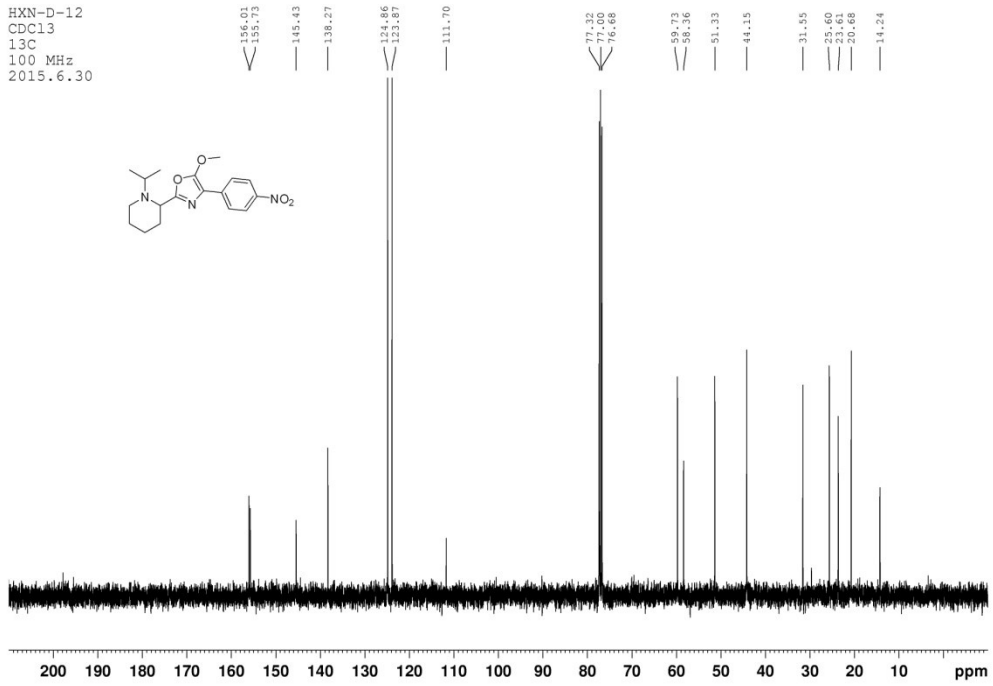
^{1}H and ^{13}C NMR spectra of **3i**



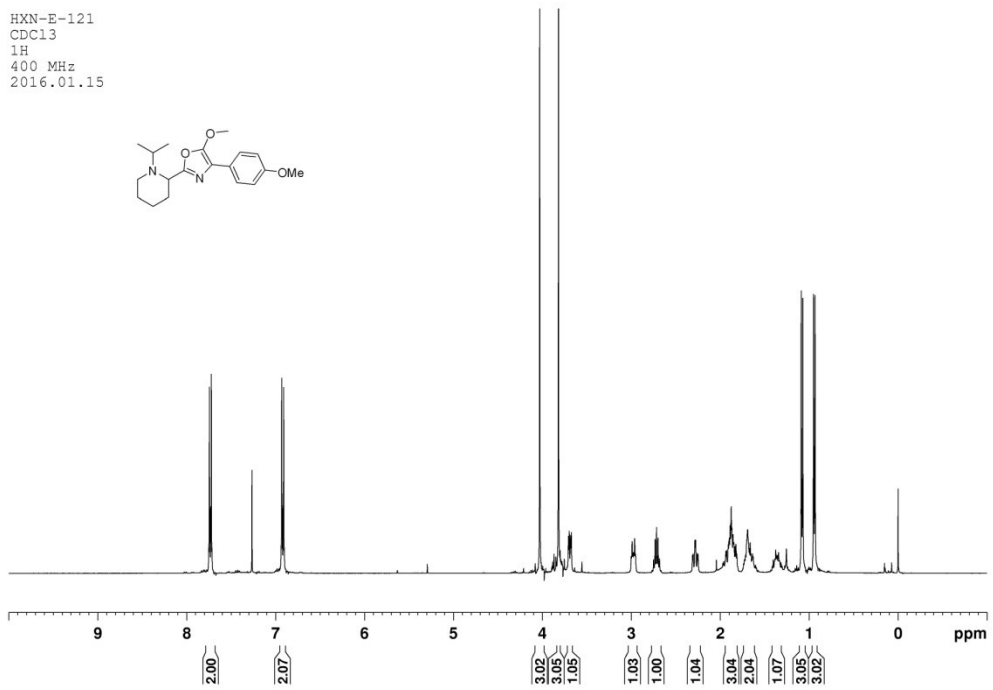


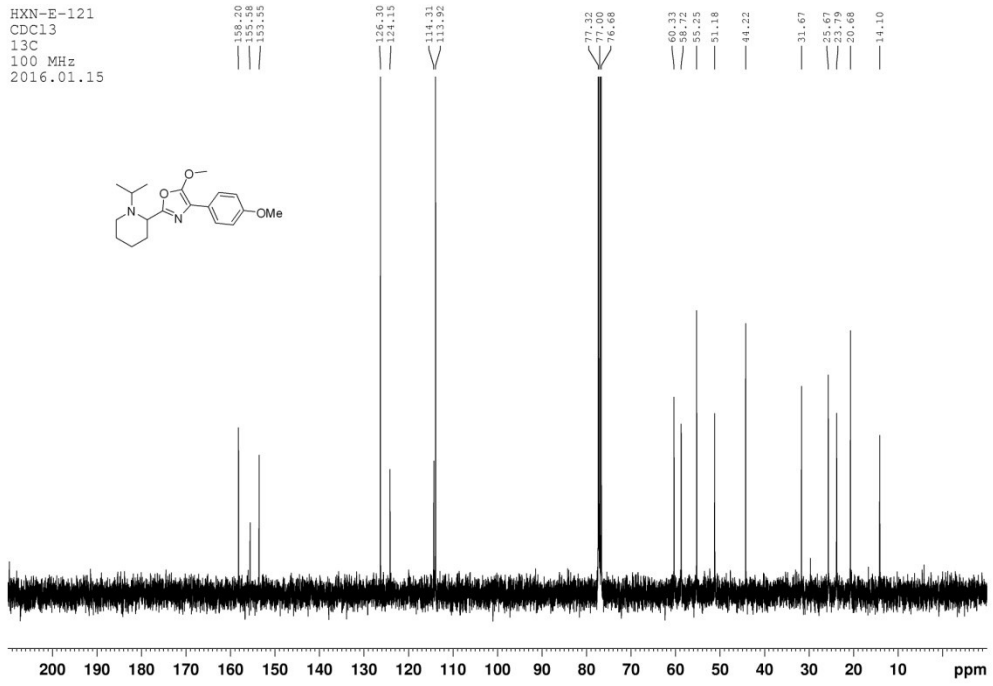
^{1}H and ^{13}C NMR spectra of **3j**



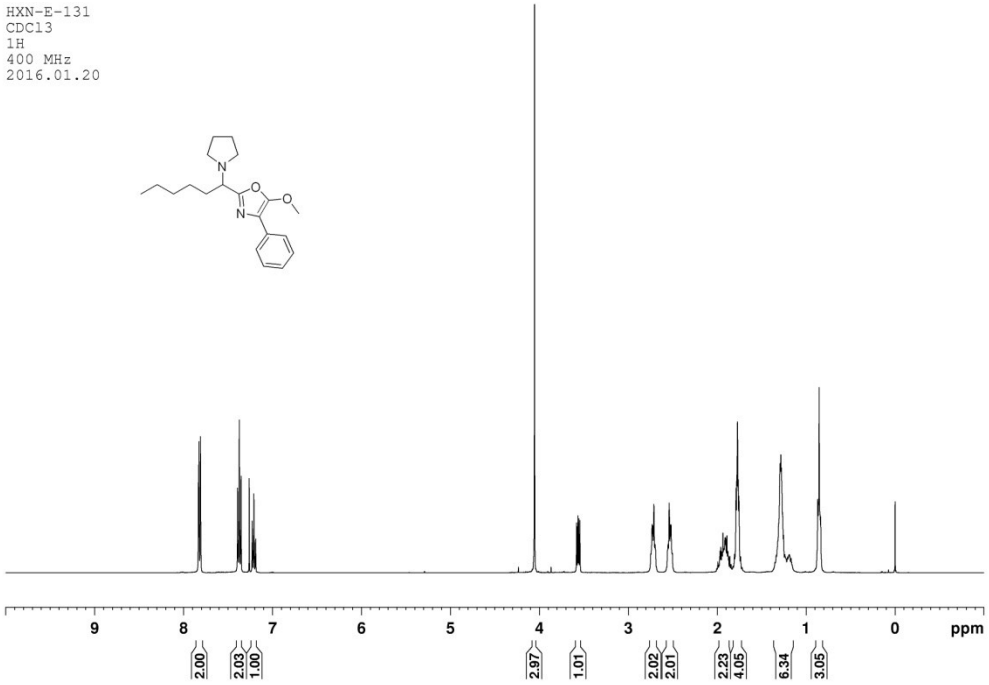


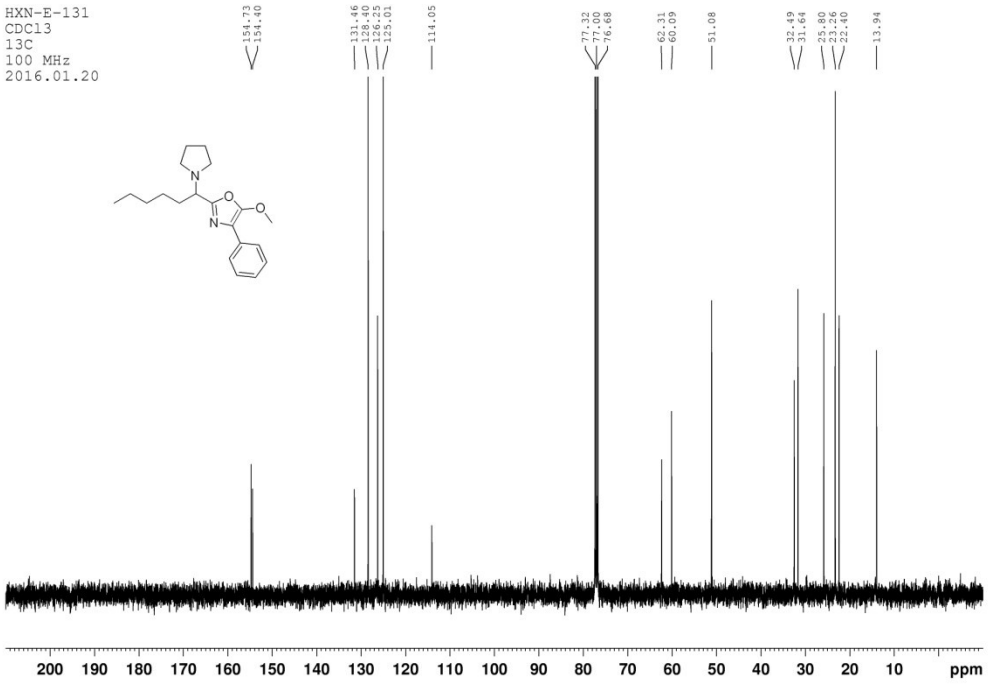
^{1}H and ^{13}C NMR spectra of **3k**



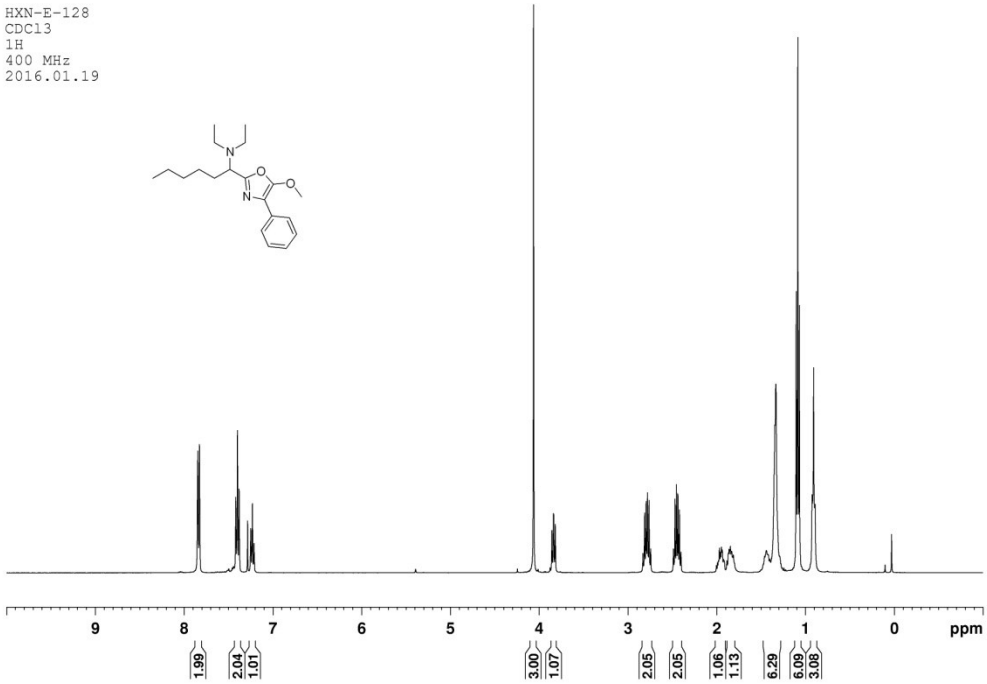


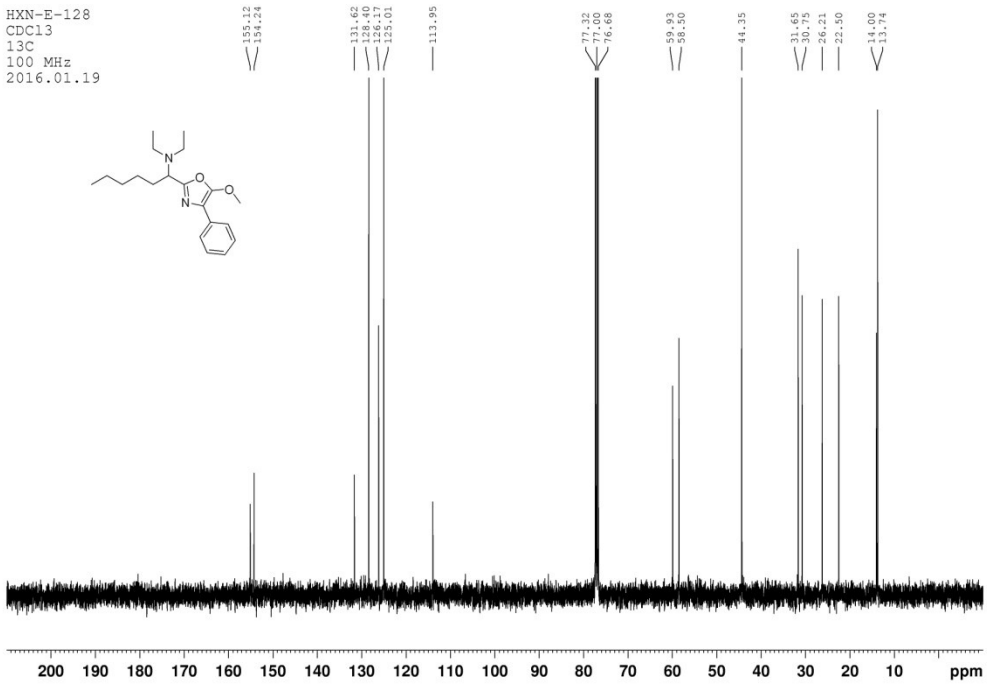
^{1}H and ^{13}C NMR spectra of **3l**



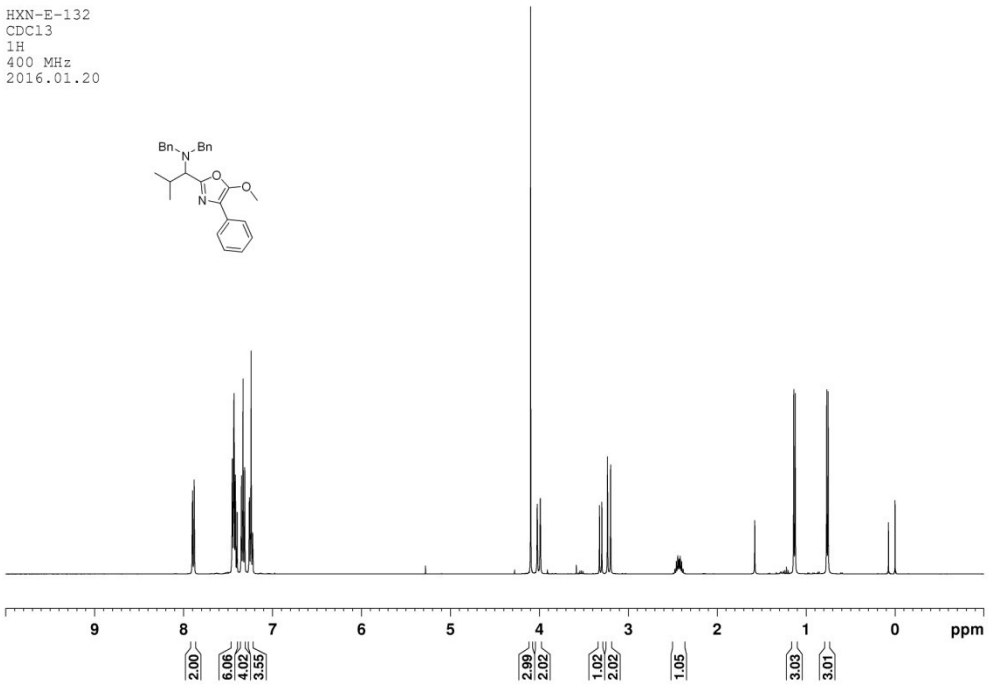


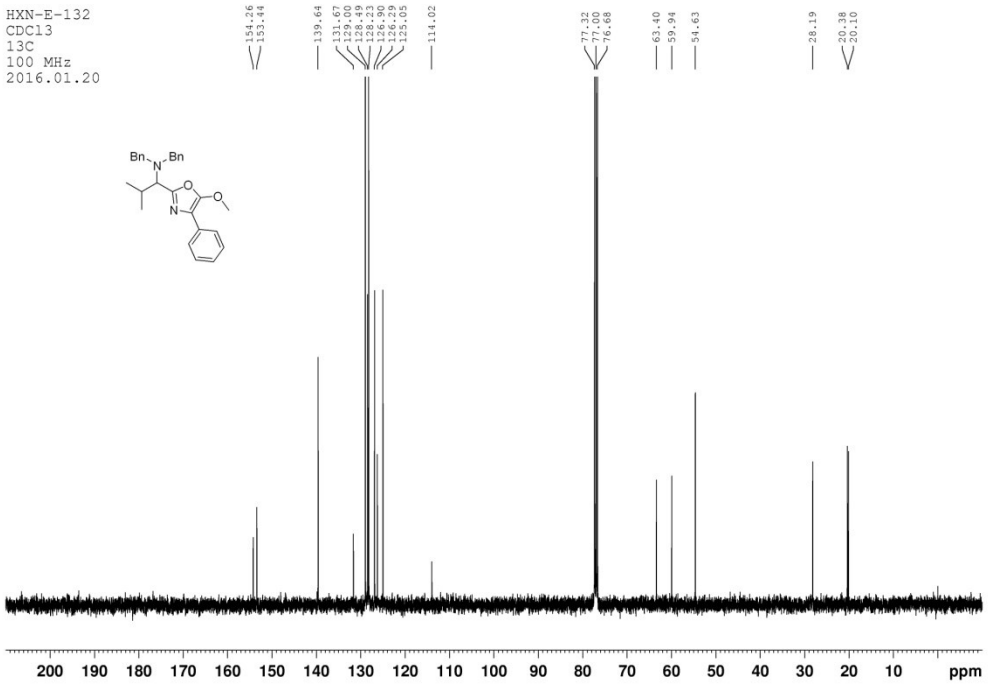
^{1}H and ^{13}C NMR spectra of **3m**



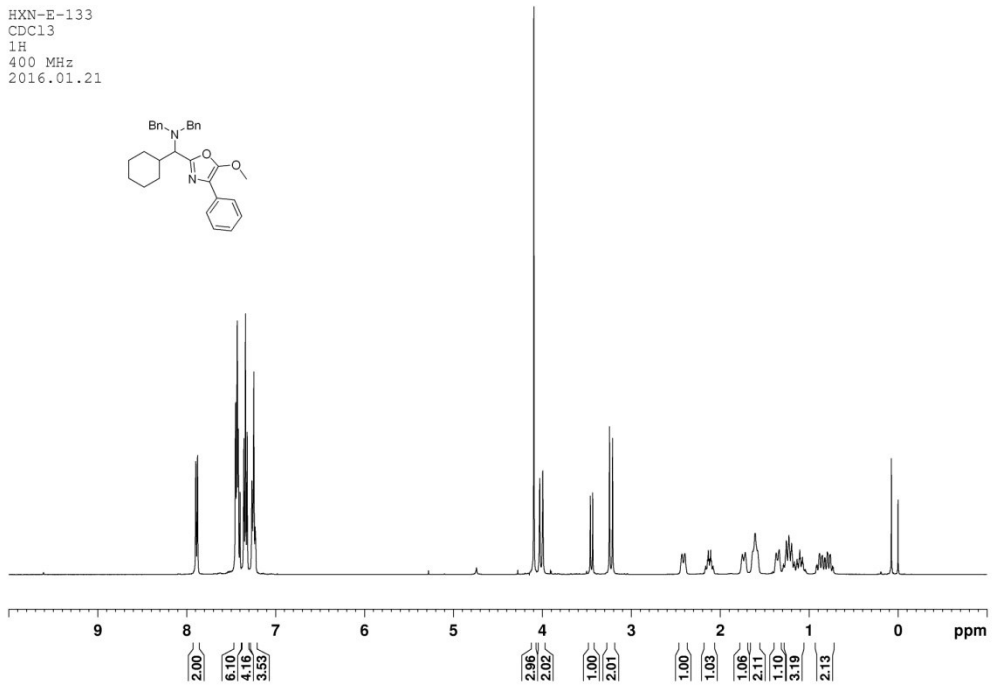


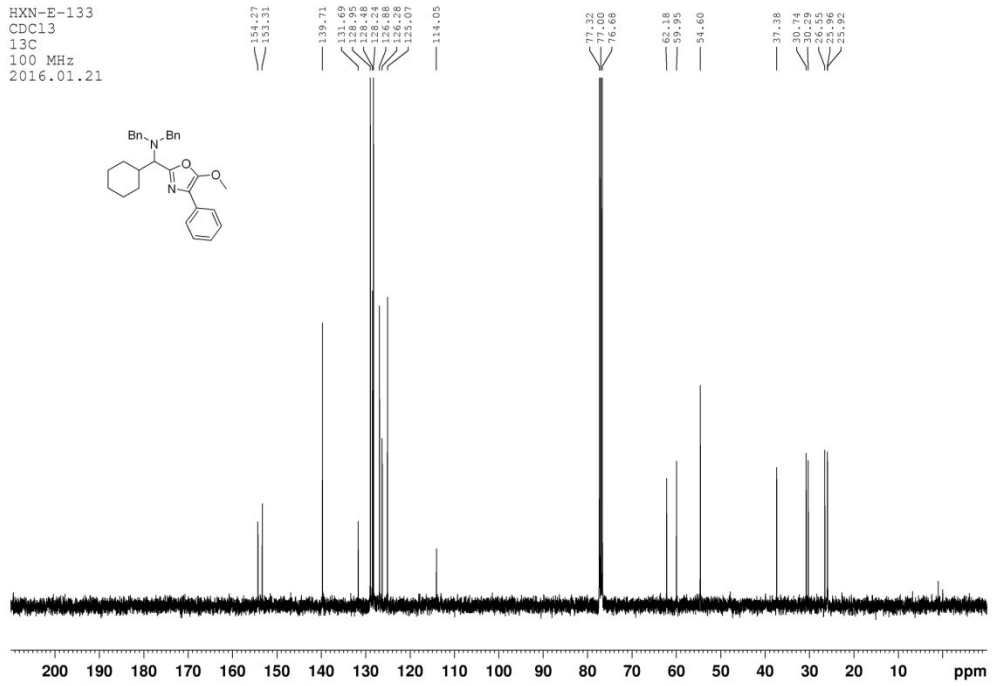
^{1}H and ^{13}C NMR spectra of **3n**



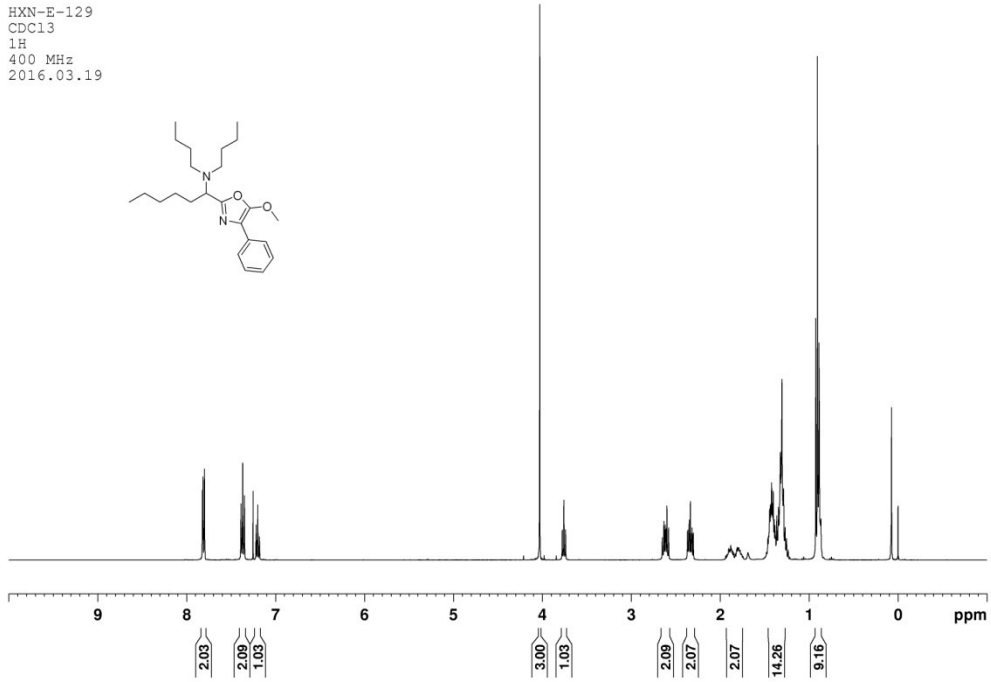


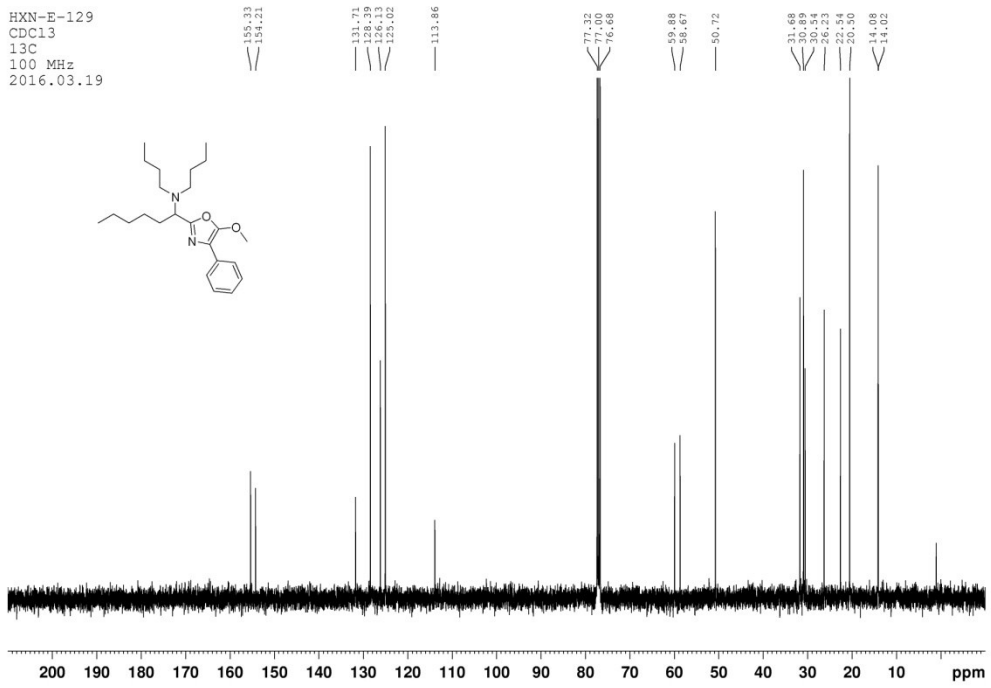
^{1}H and ^{13}C NMR spectra of **3o**



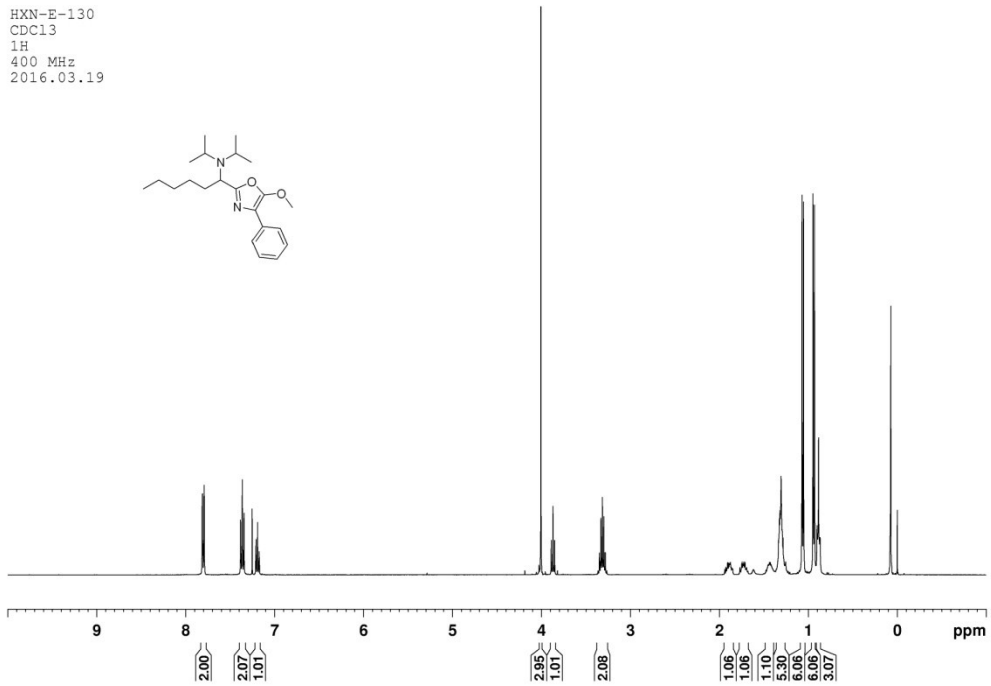


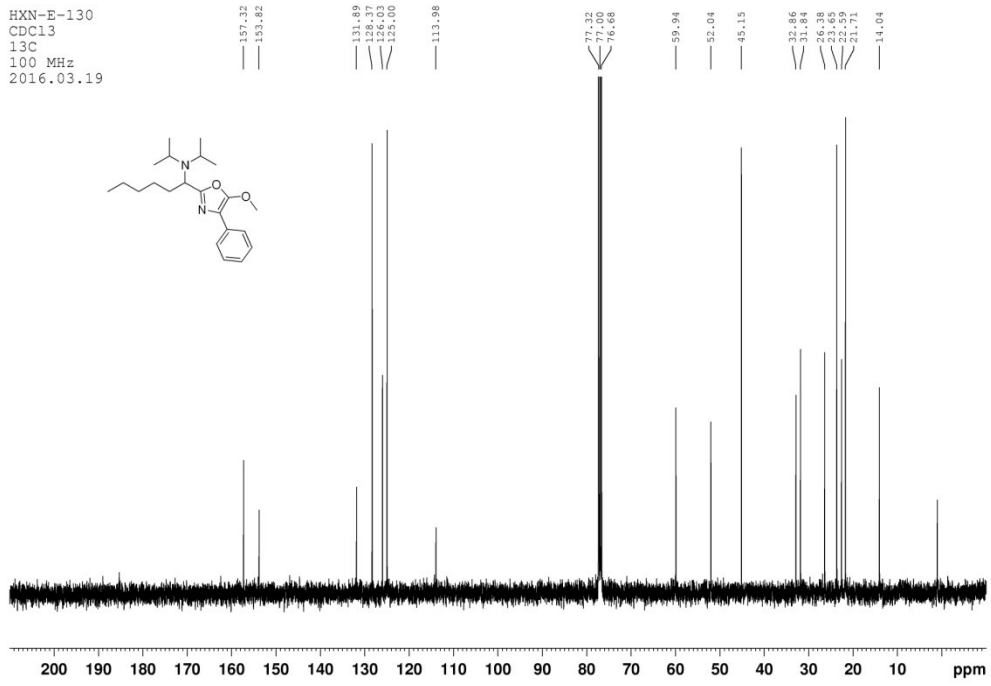
^{1}H and ^{13}C NMR spectra of **3p**



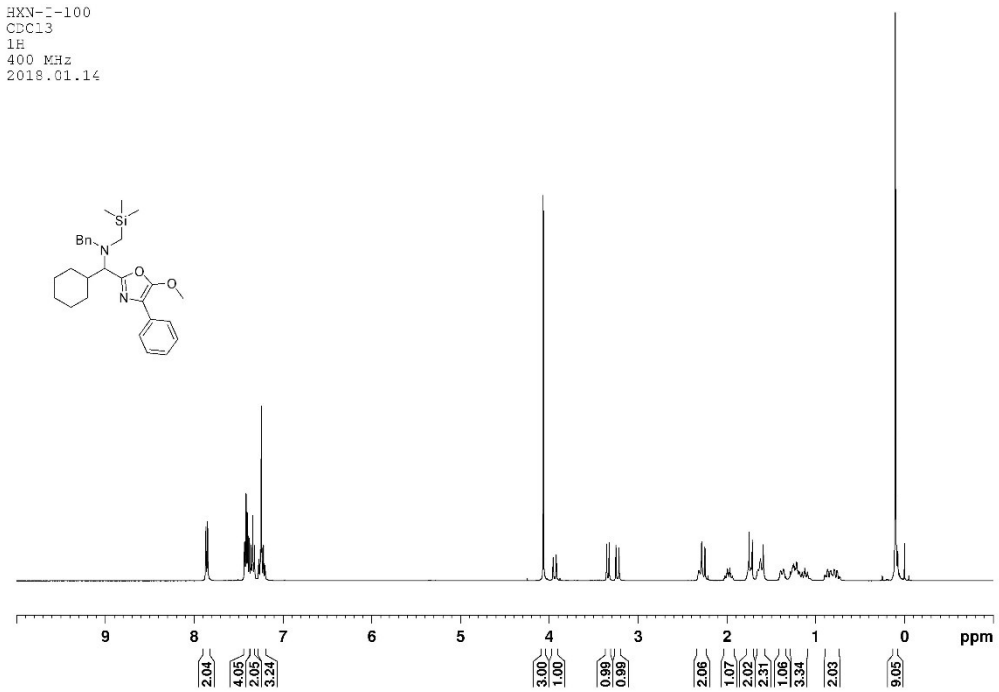


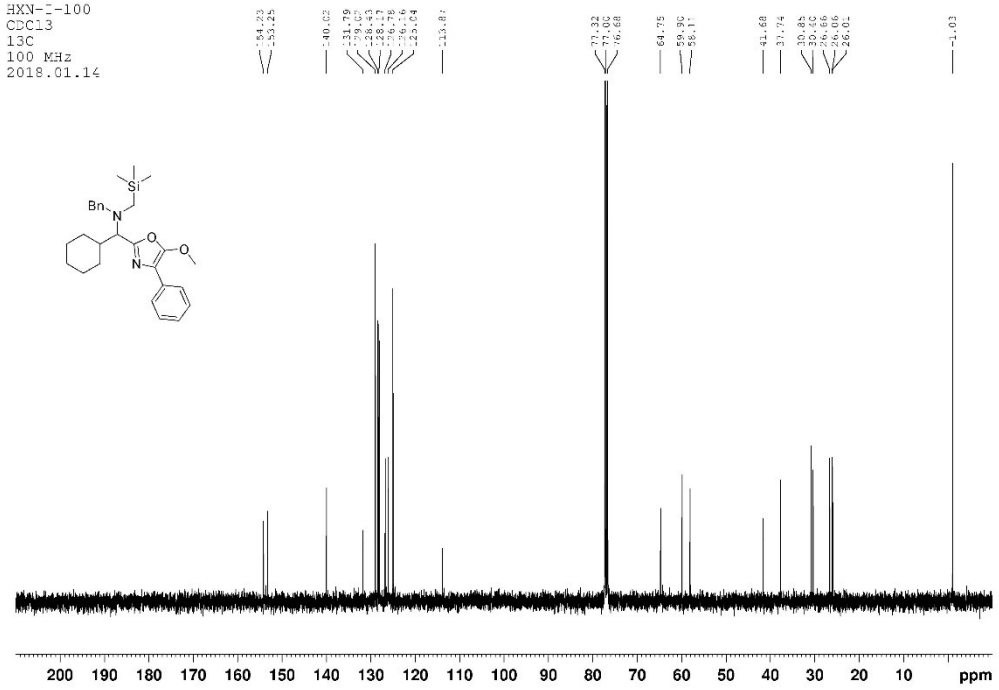
^{1}H and ^{13}C NMR spectra of **3q**



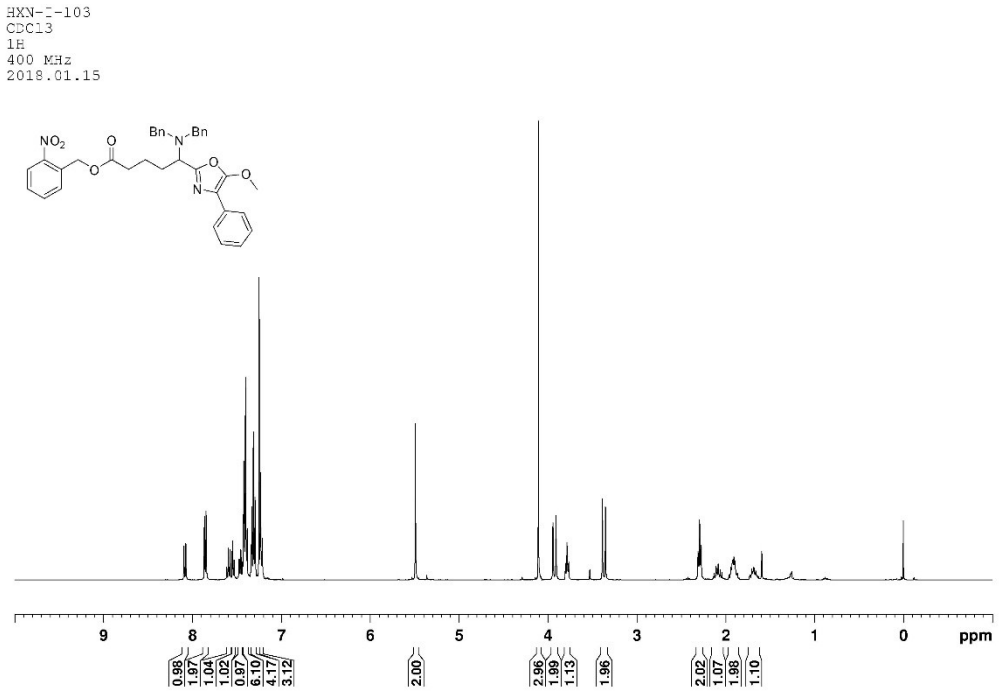


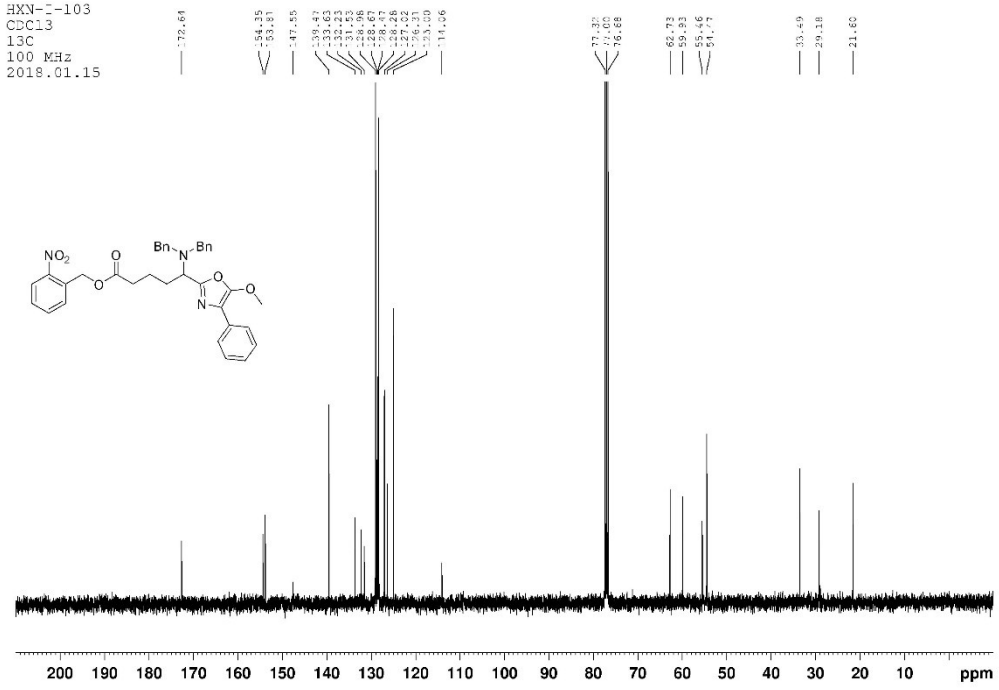
^{1}H and ^{13}C NMR spectra of **3r**



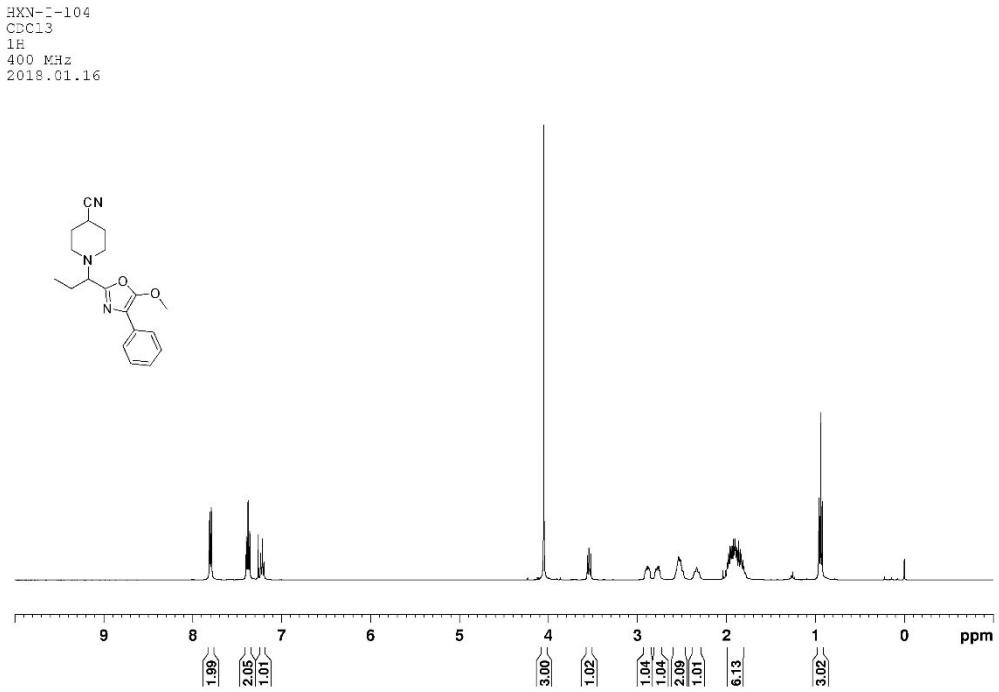


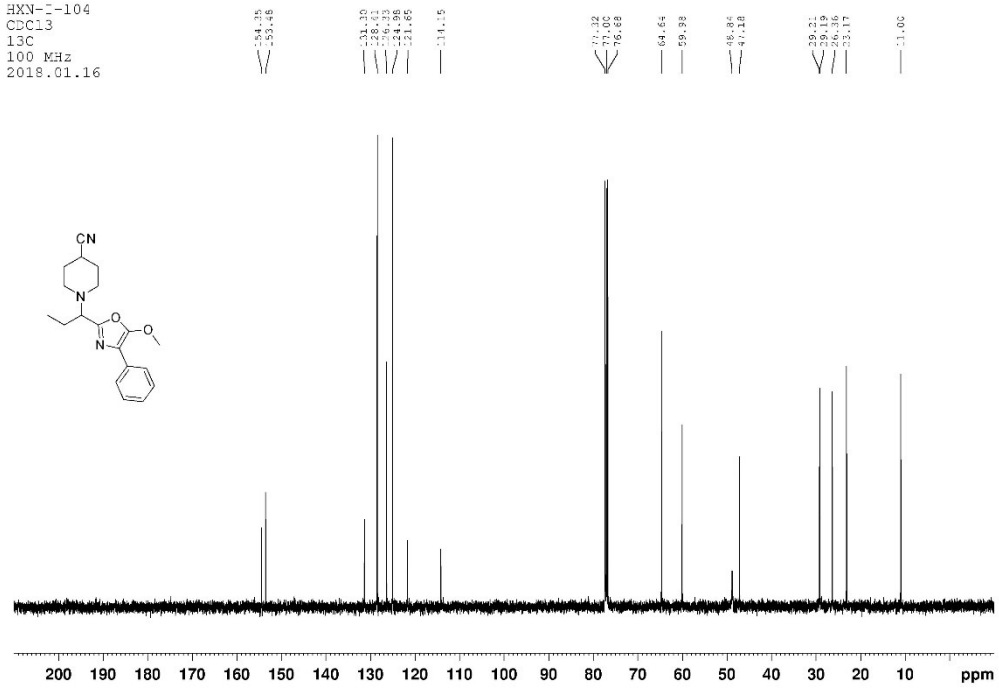
^{1}H and ^{13}C NMR spectra of **3s**



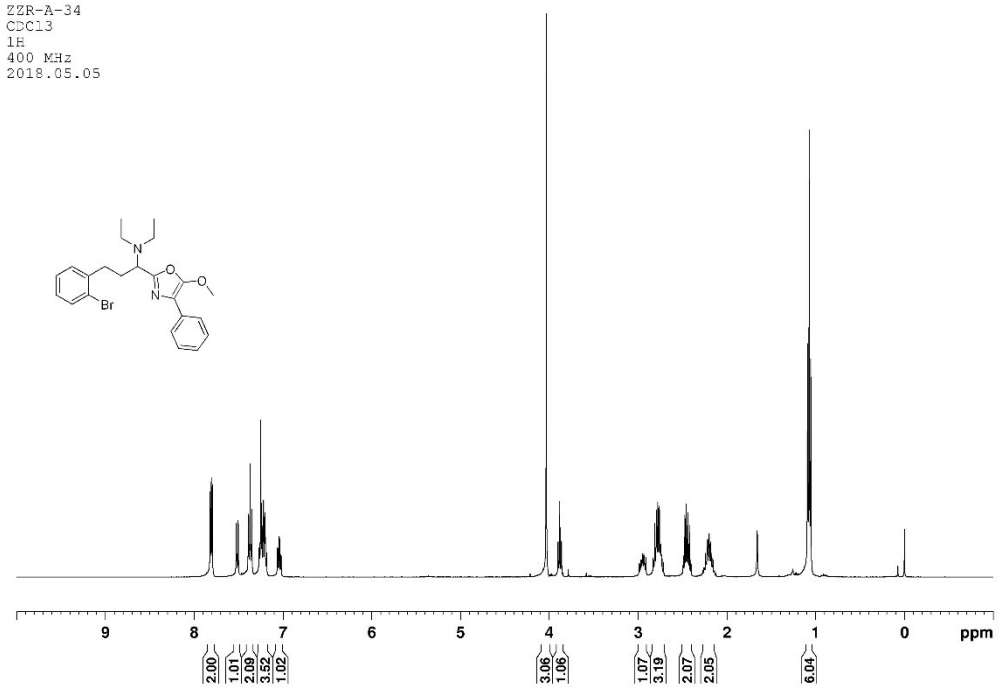


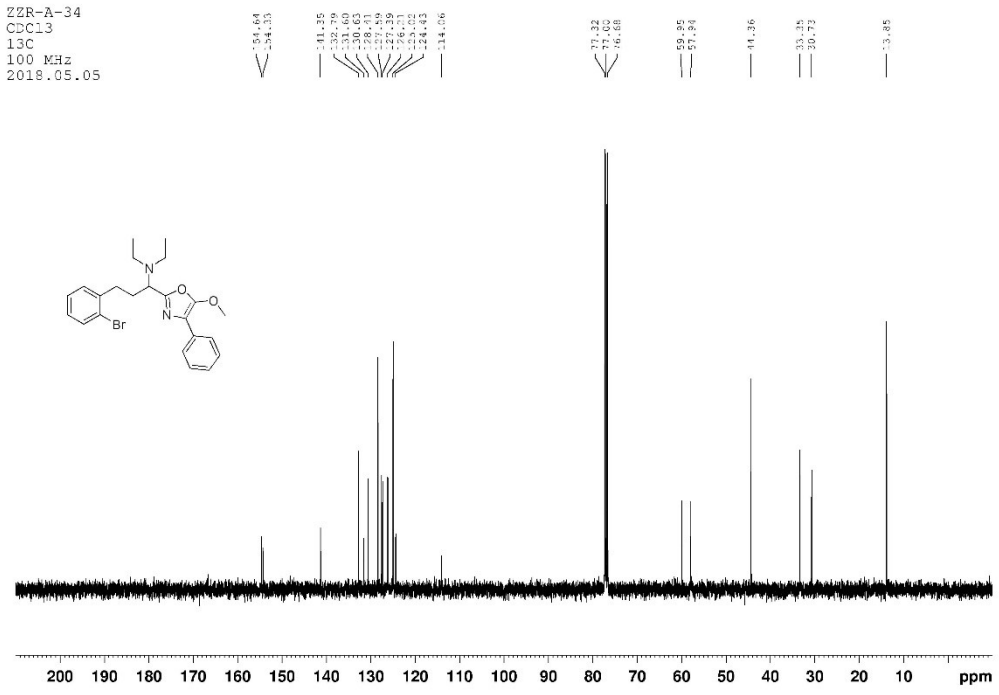
^{1}H and ^{13}C NMR spectra of **3t**



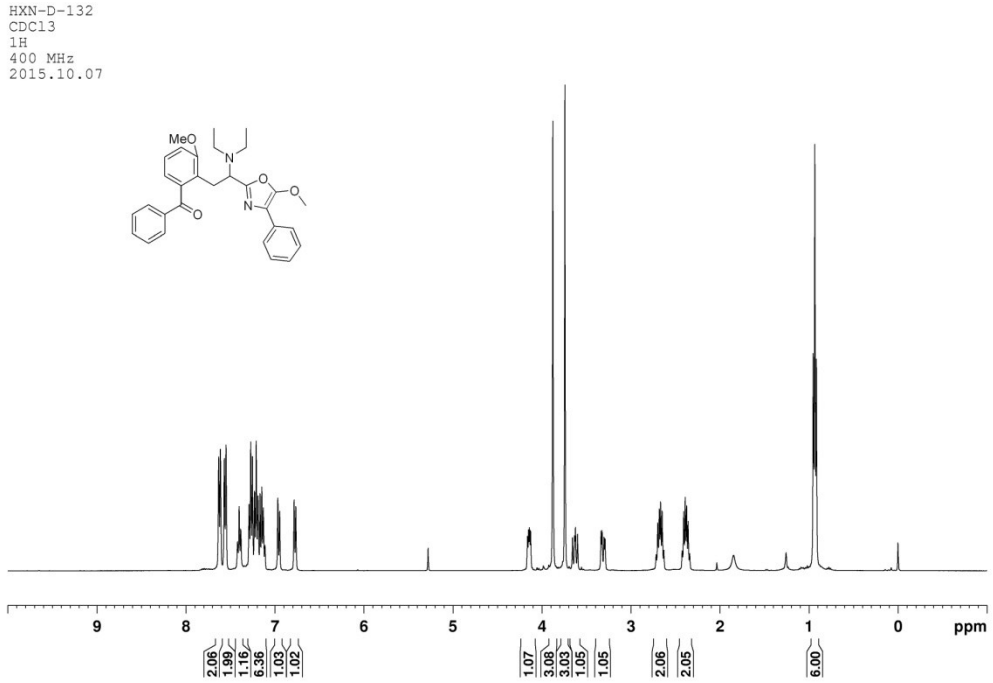


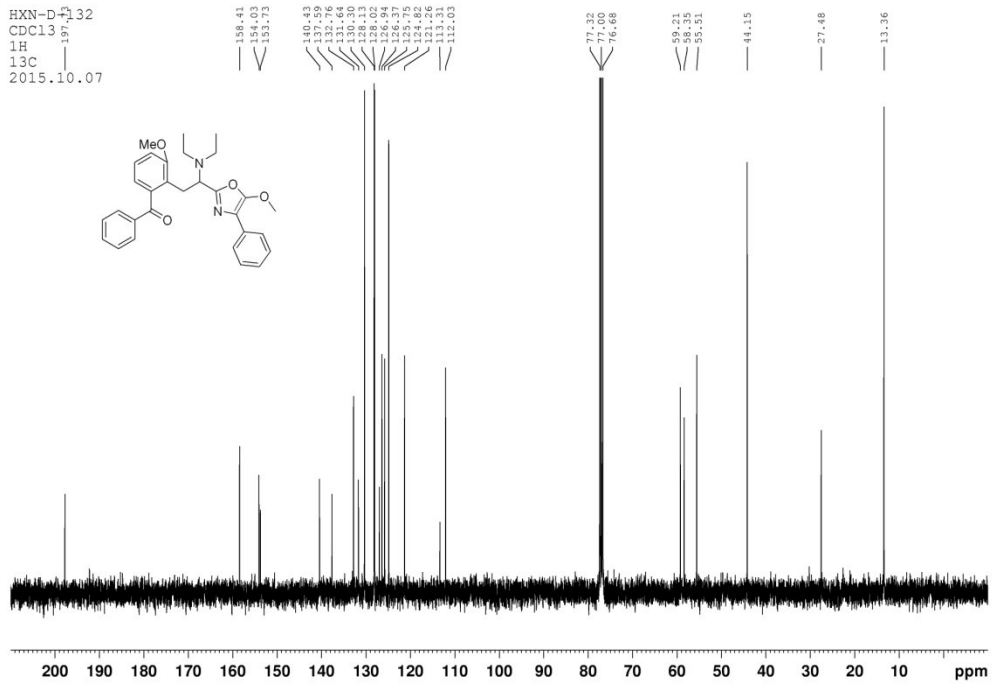
^{1}H and ^{13}C NMR spectra of **3u**



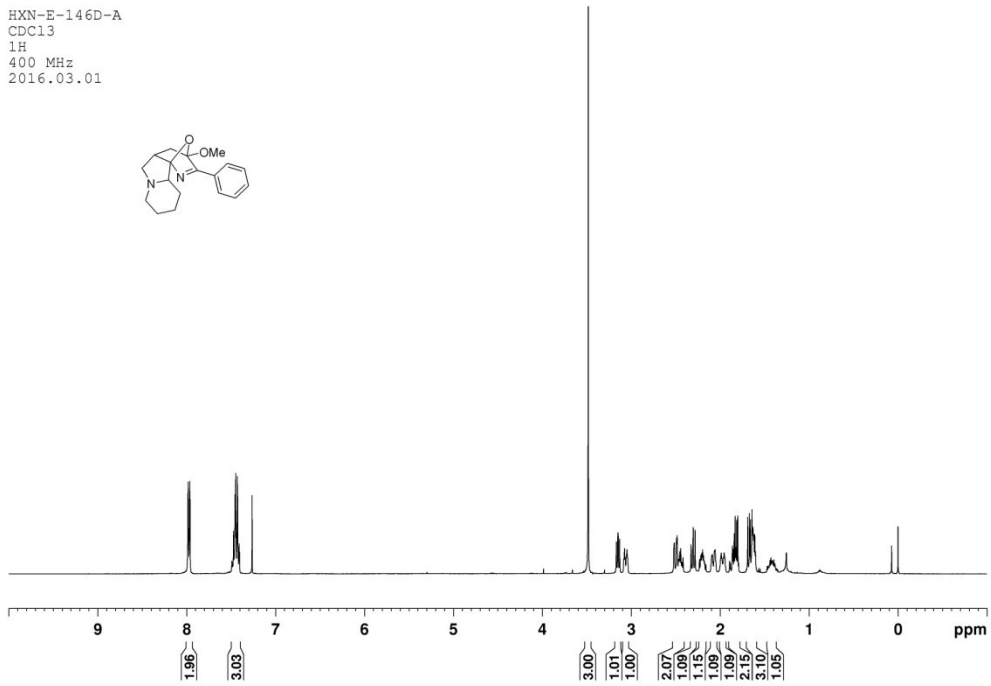


^{1}H and ^{13}C NMR spectra of **3v**





^{1}H and ^{13}C NMR spectra of **5**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OMe
N
N
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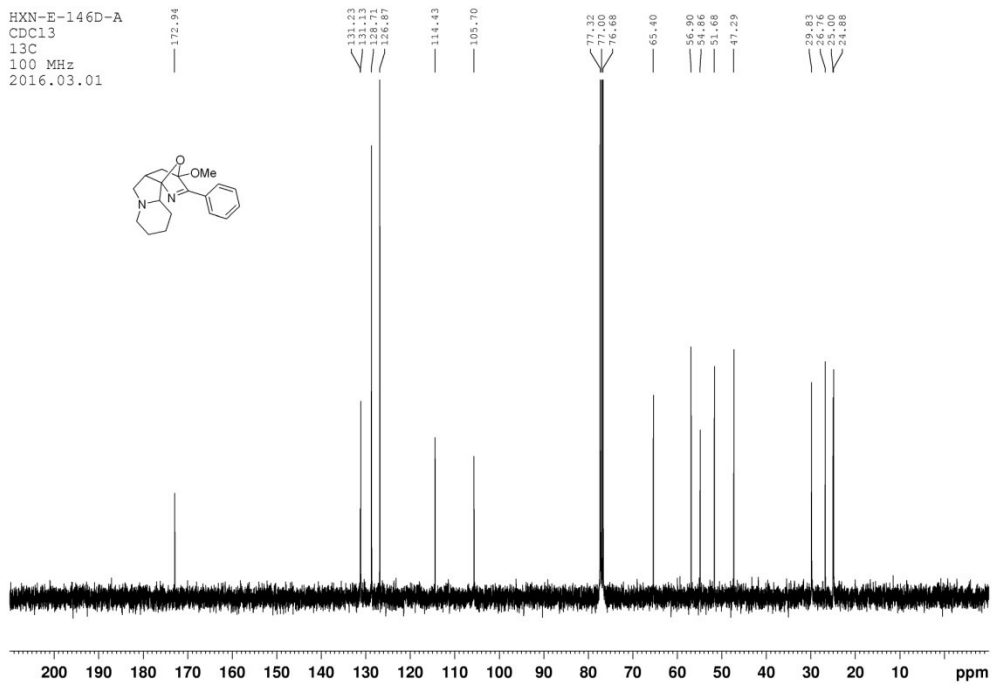
8
7
6
5
4
3
2
1
0
ppm
1.96
3.03
3.00
1.01
1.00
2.07
1.09
1.15
1.09
1.09
2.15
3.10
1.05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100 MHz
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131.23
131.13
128.71
126.87
114.43
105.70
77.32
77.00
76.68
65.40
56.90
54.86
51.68
47.29
29.83
25.66
25.00
24.88
O
OMe
N
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm