Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

Converting Oxazoles into Imidazoles: New Opportunities for Diversity-Oriented Synthesis

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1. General Information on Analytical Compound Characterization

^{1}H Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance III 600 MHz spectrometer. In the ^{1}H NMR spectra, signal positions (δ) are given in parts per million (ppm) from tetramethylsilane ($\delta = 0$) and were measured relative to the signal of $CDCl_3$ ($\delta =$ 7.26 ppm). Resonances in the ^{1}H NMR spectra are reported to the nearest 0.01 ppm. ^{13}C NMR spectra were recorded using the same spectrometer (150 MHz), and signal positions (δ) are given in parts per million (ppm) from tetramethylsilane ($\delta = 0$) and were measured relative to the signal of $CDCl_3$ (δ = 77.16 ppm) and reported to the nearest 0.1 ppm. ^{19}F NMR resonances are reported in ppm and the chemical shift of the lock solvent ($CDCl_3$) was used as an internal reference. The multiplicities of signals are given as s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, br = broadened and combinations thereof. Coupling constants (J) are reported to the nearest 0.1 Hz.

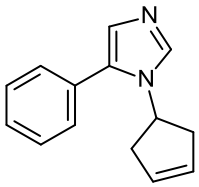
High resolution mass spectrometry (HRMS) was performed on a Finnigan LTQ FT MS or a Agilent 6520 spectrometer using time of flight (TOF) with positive ESI at 70 eV within a tolerance of ± 5 ppm of the theoretical value.

IR spectra were recorded using attenuated total reflectance (ATR) on a Nicolet 6700 from Thermo Scientific.

All compounds in this study have been isolated by MPLC (medium pressure liquid chromatography, CombiFlash Companion, Isco Inc.) for the purpose of analytical characterization.

2. Experimental Procedures for Reactions and Characterization Data

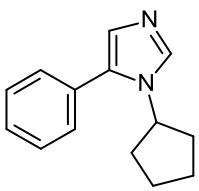
1-(Cyclopent-3-en-1-yl)-5-phenyl-1*H*-imidazole (9)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and *tert*-butyl cyclopent-3-enylcarbamate (1.26 g, 6.89 mmol, 10 equiv) in *o*-dichlorobenzene (5 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 180 °C and maintained at this temperature for 2 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown oil (79 mg, 55%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.62 – 2.65 (m, 2H), 2.88 – 2.93 (m, 2H), 4.82 (tt, J = 8.2, 3.4 Hz, 1H), 5.84 – 5.87 (m, 2H), 7.03 (s, 1H), 7.35 – 7.37 (m, 2H), 7.38 – 7.41 (m, 1H), 7.43 – 7.46 (m, 2H), 7.65 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 42.1 (2C), 53.4, 127.5, 128.2, 128.9 (2C), 129.1 (2C), 129.5 (2C), 130.4, 133.1, 135.1 ppm. IR (ATR): ν 3108, 3058, 2920, 2849, 1605, 1575, 1550, 1486, 1471, 761, 698 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{14}N_2$ 210.1157, found 210.1157.

1-Cyclopentyl-5-phenyl-1*H*-imidazole (14)

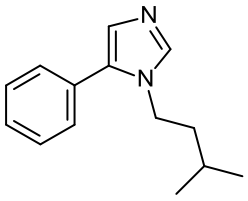


To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was

heated by microwave irradiation to 200 °C and maintained at this temperature for 2 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (116 mg, 79%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.65 – 1.69 (m, 2H), 1.81 – 1.89 (m, 4H), 2.08 – 2.13 (m, 2H), 4.49 (quin, J = 7.2 Hz, 1H), 7.03 (d, J = 0.9 Hz, 1H), 7.35 – 7.40 (m, 3H), 7.43 – 7.45 (m, 2H), 7.66 (d, J = 0.9 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.3 (2C), 34.5 (2C), 56.4, 128.0, 128.1, 128.8 (2C), 129.4 (2C), 130.7, 133.5, 135.1 ppm. IR (ATR): ν 3110, 3060, 2956, 2871, 1605, 1575, 1551, 1487, 1473, 760, 699 cm^{-1}. HRMS ESI+ (m/z): $[M]^+$ calcd for $C_{14}H_{16}N_2$ 212.1313, found 212.1324.

1-(3-Methyl-butyl)-5-phenyl-1*H*-imidazole (15)

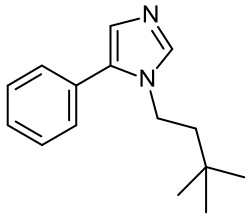


To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and 3-methyl-butylamine (120 mg, 161 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (46 mg, 31%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.82 (d, J = 6.5 Hz, 6H), 1.44 – 1.50 (m, 1H), 1.51 – 1.54 (m, 2H), 3.97 (m, 2H), 7.05 (s, 1H), 7.35 – 7.39 (m, 3H), 7.42 – 7.45 (m, 2H), 7.55 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 22.3 (2C), 25.6, 40.0, 43.8, 128.1, 128.3, 128.8 (2C), 128.9

(2C), 130.4, 133.1, 138.1 ppm. IR (ATR): ν 2955, 2870, 1605, 1551, 1481, 1366, 762, 698 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{18}N_2$ 214.1469, found 214.1481.

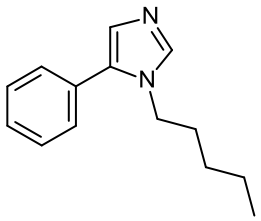
1-(3,3-Dimethyl-butyl)-5-phenyl-1*H*-imidazole (16)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and 3,3-dimethyl-butylamine (140 mg, 186 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (58 mg, 37%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.85 (s, 9H), 1.55 – 1.57 (m, 2H), 3.95 – 3.98 (m, 2H), 7.05 (d, J = 1.1 Hz, 1H), 7.36 – 7.39 (m, 3H), 7.42 – 7.45 (m, 2H), 7.55 (d, J = 1.1 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 29.2 (3C), 30.0, 41.1, 45.0, 128.1, 128.3, 128.8 (2C), 128.9 (2C), 130.3, 133.0, 138.1 ppm. IR (ATR): ν 3117, 3099, 3076, 2998, 2953, 2867, 1605, 1552, 1489, 1476, 1363, 761, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{20}N_2$ 228.1626, found 228.1631.

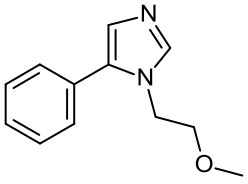
1-Pentyl-5-phenyl-1*H*-imidazole (17)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and pentylamine (120 mg, 160 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (77 mg, 52%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.82 (t, J = 7.1 Hz, 3H), 1.15 – 1.26 (m, 4H), 1.62 (quin, J = 7.4 Hz, 2H), 3.95 (m, 2H), 7.05 (s, 1H), 7.35 – 7.39 (m, 3H), 7.42 – 7.45 (m, 2H), 7.55 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 13.9, 22.2, 28.7, 30.7, 45.5, 128.1, 128.3, 128.8 (2C), 128.9 (2C), 130.4, 133.1, 138.2 ppm. IR (ATR): ν 2928, 2859, 1605, 1551, 1481, 1364, 762, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{18}N_2$ 214.1469, found 214.1479.

1-(2-Methoxy-ethyl)-5-phenyl-1*H*-imidazole (18)

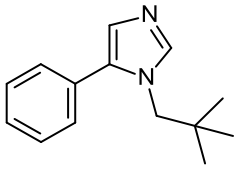


To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and 2-methoxy-ethylamine (104 mg, 119 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture

was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (98 mg, 70%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.29 (s, 3H), 3.53 (t, J = 5.4 Hz, 2H), 4.11 (t, J = 5.4 Hz, 2H), 7.06 (s, 1H), 7.37 – 7.39 (m, 3H), 7.42 – 7.45 (m, 2H), 7.67 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 45.1, 59.1, 71.6, 128.1, 128.2, 128.9 (2C), 129.2 (2C), 130.1, 133.0, 138.9 ppm. IR (ATR): ν 3114, 3057, 2989, 2928, 2900, 2828, 1605, 1576, 1553, 1480, 1112, 763, 698 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{12}H_{14}N_2O$ 202.1106, found 202.1109.

1-(2,2-Dimethyl-propyl)-5-phenyl-1*H*-imidazole (19)

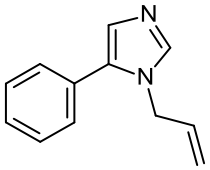


To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and 2,2-dimethyl-propylamine (120 mg, 163 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 1.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow solid (67 mg, 45%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.73 (s, 9H), 3.85 (s, 2H), 7.03 (d, J = 1.0 Hz, 1H), 7.32 – 7.38 (m, 3H), 7.41 – 7.44 (m, 2H), 7.55 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 27.8 (3C), 33.5, 56.3, 128.0, 128.3, 128.8 (2C), 129.6 (2C), 131.0, 133.8, 139.3

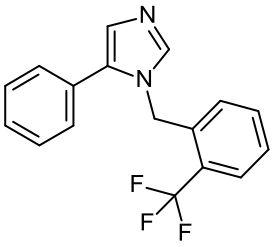
ppm. IR (ATR): ν 3114, 2961, 2865, 1606, 1555, 1477, 1368, 769, 701 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{18}N_2$ 214.1469, found 214.1478.

1-Allyl-5-phenyl-1*H*-imidazole (20)



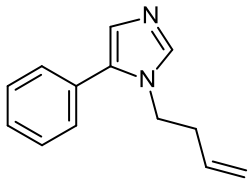
To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and allylamine (79 mg, 106 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (42 mg, 33%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 4.57 (dt, J = 5.1, 1.7 Hz, 2H), 5.04 (ddt, J = 17.1, 1.0, 0.9 Hz, 1H), 5.25 (ddt, J = 10.4, 1.3, 0.9 Hz, 1H), 5.91 – 5.97 (m, 1H), 7.12 (s, 1H), 7.36 – 7.39 (m, 3H), 7.41 – 7.44 (m, 2H), 7.59 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 47.6, 118.2, 128.0, 128.2, 128.8 (2C), 128.9 (2C), 129.8, 133.3, 133.4, 138.5 ppm. IR (ATR): ν 3082, 2923, 2847, 1644, 1605, 1577, 1552, 1490, 911, 766, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{12}H_{12}N_2$ 184.1000, found 184.1004.

5-Phenyl-1-(2-trifluoromethyl-benzyl)-1*H*-imidazole (21)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and 2-trifluoromethyl-benzylamine (242 mg, 193 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (88 mg, 42%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.39 (s, 2H), 6.78 (d, J = 7.7 Hz, 1H), 7.22 (d, J = 1.1 Hz, 1H), 7.24 – 7.25 (m, 2H), 7.31 – 7.35 (m, 3H), 7.39 (t, J = 7.7 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 7.57 (d, J = 1.1 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 45.4 (q, J_{CF} = 3.5 Hz), 124.2 (q, J_{CF} = 272.6 Hz), 126.4 (q, J_{CF} = 8.3 Hz), 127.1 (q, J_{CF} = 31.1 Hz), 127.5, 128.1, 128.4, 128.68, 128.70 (2C), 128.9 (2C), 129.3, 132.8, 133.7, 135.8, 139.2 ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -60.8 ppm. IR (ATR): ν 3066, 1585, 1553, 1493, 1479, 1458, 1310, 1159, 762, 754, 698 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{17}H_{13}F_3N_2$ 302.1031, found 302.1043.

1-But-3-enyl-5-phenyl-1*H*-imidazole (22)

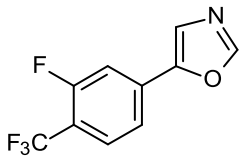


To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and but-3-enylamine (98 mg, 129 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced

pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (78 mg, 57%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.35 (qt, J = 7.3, 1.4 Hz, 2H), 4.04 (t, J = 7.3 Hz, 2H), 4.99 (dq, J = 17.1, 1.4 Hz, 1H), 5.03 (dq, J = 10.2, 1.4 Hz, 1H), 5.59 – 5.66 (m, 1H), 7.06 (d, J = 1.0 Hz, 1H), 7.36 – 7.40 (m, 3H), 7.43 – 7.45 (m, 2H), 7.55 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 35.1, 44.9, 118.2, 128.2, 128.5, 128.9 (2C), 129.0 (2C), 130.3, 133.0, 133.6, 138.3 ppm. IR (ATR): ν 3077, 2977, 2921, 2855, 1640, 1606, 1576, 1552, 1401, 1480, 914, 763, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157, found 198.1163.

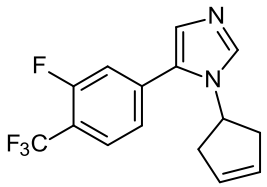
5-(3-Fluoro-4-trifluoromethyl-phenyl)-oxazole



A solution of 3-fluoro-4-trifluoromethyl-benzaldehyde (1.40 g, 7.07 mmol, 1 equiv; CAS[204339-72-0]) and *p*-toluene-sulfonylmethyl-isocyanide (1.53 g, 7.68 mmol, 1 equiv; TosMIC) in MeOH (100 mL) was treated with potassium carbonate (1.97 g, 14.14 mmol, 2 equiv) and the suspension heated to reflux for 14 h. After being cooled to room temperature, the solvent was removed under reduced pressure and the crude product triturated with water at 0°C (2 x 25 mL). The slightly orange precipitate was collected by filtration and dried under vacuum (4.46 g, 92%).

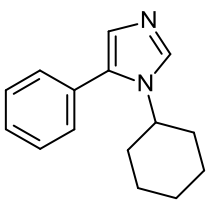
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.48 – 7.50 (m, 2H), 7.53 (d, J = 8.2 Hz, 1H), 7.67 (t, J = 7.7 Hz, 1H), 7.99 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 112.7 (d, J_{CF} = 23.7 Hz), 118.2 (dd, J_{CF} = 33.1, 12.6 Hz), 119.8 (d, J_{CF} = 3.6 Hz), 122.5 (qd, J_{CF} = 272.4, 1.0 Hz), 124.3, 128.2 (qd, J_{CF} = 4.7, 2.1 Hz), 133.4 (dd, J_{CF} = 9.0, 0.9 Hz), 149.3 (d, J_{CF} = 2.6 Hz), 151.7, 160.3 (dq, J_{CF} = 257.0, 2.2 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -61.3, -113.0 ppm. IR (ATR): ν 3158, 3130, 3039, 1628, 1595, 1574, 1510, 1318, 1118 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{10}H_5F_4N_2O$ 231.0307, found 231.0291.

1-(Cyclopent-3-en-1-yl)-5-(3-fluoro-4-(trifluoromethyl)phenyl)-1*H*-imidazole (23)



To a solution of 5-(3-fluoro-4-trifluoromethyl-phenyl)-oxazole (50 mg, 0.22 mmol, 1 equiv) and *tert*-butyl cyclopent-3-enylcarbamate (79 mg, 0.43 mmol, 2 equiv) in *o*-dichlorobenzene (3 mL) was added trifluoroacetic acid (49 mg, 33 µL, 0.43 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 2 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (24 mg, 38%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 2.61 – 2.67 (m, 2H), 2.96 (dd, J = 16.0, 8.1 Hz, 2H), 4.79 – 4.83 (m, 1H), 5.86 – 5.90 (m, 2H), 7.11 (s, 1H), 7.21 (d, J = 11.2 Hz, 1H), 7.24 (d, J = 8.2 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.68 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 42.1 (2C), 53.7, 117.2 (d, J_{CF} = 22.0 Hz), 117.8 (dd, J_{CF} = 34.1, 11.9 Hz), 122.6 (qd, J_{CF} = 272.6, 1.0 Hz), 124.5 (d, J_{CF} = 3.6 Hz), 127.8 (qd, J_{CF} = 3.6, 2.2 Hz), 129.0 (2C), 129.1, 130.5 (d, J_{CF} = 1.7 Hz), 136.4, 136.5 (d, J_{CF} = 8.8 Hz), 159.7 (dq, J_{CF} = 257.6, 2.1 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -61.3, -113.3 ppm. IR (ATR): ν 3110, 3060, 2956, 2871, 1605, 1575, 1551, 1487, 1473, 760, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{12}F_4N_2$ 296.0937, found 297.1018.

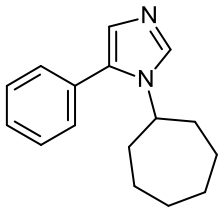
1-Cyclohexyl-5-phenyl-1*H*-imidazole (24)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and cyclohexylamine (137 mg, 158 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (64 mg, 41%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.19 – 1.32 (m, 3H), 1.62 – 1.71 (m, 3H), 1.84 – 1.87 (m, 2H), 2.04 – 2.06 (m, 2H), 3.94 (tt, J = 12.0, 3.7 Hz, 1H), 7.02 (d, J = 0.8 Hz, 1H), 7.32 – 7.34 (m, 2H), 7.37 – 7.40 (m, 1H), 7.43 – 7.46 (m, 2H), 7.66 (d, J = 0.8 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 25.3, 25.9 (2C), 35.0 (2C), 54.7, 127.8, 128.1, 128.8 (2C), 129.3 (2C), 130.6, 132.7, 135.2 ppm. IR (ATR): ν 2930, 2855, 1575, 1488, 1472, 1450, 1360, 763, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{18}N_2$ 226.1469, found 226.1474.

1-Cycloheptyl-5-phenyl-1*H*-imidazole (25)

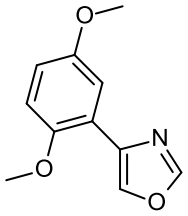


To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and cycloheptylamine (156 mg, 182 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting

with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown oil (135 mg, 81%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.38 – 1.44 (m, 2H), 1.56 – 1.64 (m, 4H), 1.73 – 1.79 (m, 2H), 1.86 – 1.92 (m, 2H), 2.05 – 2.09 (m, 2H), 4.11 – 4.16 (m, 1H), 7.01 (s, 1H), 7.32 – 7.34 (m, 2H), 7.39 (tt, J = 7.4, 1.6 Hz, 1H), 7.45 (tt, J = 7.4, 1.6 Hz, 2H), 7.67 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.7 (2C), 27.5 (2C), 36.9 (2C), 56.6, 127.5, 128.0, 128.7 (2C), 129.2 (2C), 130.5, 132.5, 135.3 ppm. IR (ATR): ν 3029, 2924, 2855, 1604, 1575, 1548, 762, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{16}H_{20}N_2$ 240.1626, found 240.1646.

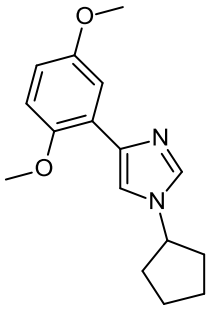
4-(2,5-Dimethoxy-phenyl)-oxazole



2-Bromo-1-(2,5-dimethoxy-phenyl)-ethanone (1.0 g, 3.86 mmol, 1 equiv; CAS [1204-21-3]) and formamide (17.4 g, 15.4 mL, 386.0 mmol, 100 equiv) were heated by microwave irradiation to 110 °C and maintained at this temperature for 2 h. After being cooled to room temperature, the crude reaction mixture was poured into a sat. solution of $NaHCO_3$ (15 mL) and water (10 mL), stirred for 15 min and then extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane / ethyl acetate (0 to 50%). The title compound was isolated as white solid (0.60 g, 76%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.86 (s, 3H), 3.92 (s, 3H), 6.85 (dd, J = 8.8, 3.0 Hz, 1H), 6.90 (d, J = 8.8 Hz, 1H), 7.71 (d, J = 3.1 Hz, 1H), 7.92 (d, J = 1.0 Hz, 1H), 8.22 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 56.0, 56.1, 111.9, 112.4, 114.7, 120.5, 135.7, 137.7, 150.1, 150.9, 154.0 ppm. IR (ATR): ν 3192, 3132, 3078, 2922, 2853, 1620, 1570, 1523, 1498, 1273, 1239, 1181, 1151 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{11}H_{11}NO_3$ 205.0739, found 205.0745.

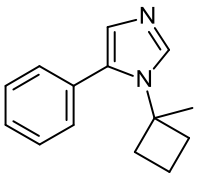
1-Cyclopentyl-4-(2,5-dimethoxy-phenyl)-1*H*-imidazole (26)



To a solution of 4-(2,5-dimethoxy-phenyl)-oxazole (142 mg, 0.69 mmol, 1 equiv) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 1 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (131 mg, 70%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.74 – 1.77 (m, 2H), 1.87 – 1.96 (m, 4H), 2.21 – 2.26 (m, 2H), 3.85 (s, 3H), 3.90 (s, 3H), 4.49 (quin, J = 7.1 Hz, 1H), 6.76 (dd, J = 8.9, 3.2 Hz, 1H), 6.88 (d, J = 8.9 Hz, 1H), 7.57 – 7.58 (m, 2H), 7.79 (d, J = 3.2 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0 (2C), 33.8 (2C), 56.0, 56.1, 58.7, 111.4, 112.4, 113.6, 118.2, 123.9, 135.0, 137.4, 150.3, 154.1 ppm. IR (ATR): ν 3175, 3108, 3045, 3003, 2965, 2951, 2873, 2843, 1611, 1587, 1552, 1540, 1502, 1275, 1162, 1021 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{16}H_{20}N_2O_2$ 272.1525, found 272.1534.

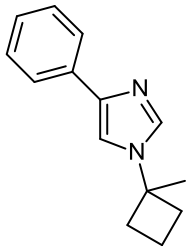
1-(1-Methyl-cyclobutyl)-5-phenyl-1*H*-imidazole (27)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and 1-methyl-cyclobutylamine (118 mg, 134 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 14 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow solid (53 mg, 36%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.63 (s, 3H), 1.76 – 1.90 (m, 2H), 1.97 – 2.02 (m, 2H), 2.45 – 2.50 (m, 2H), 6.94 (d, J = 1.3 Hz, 1H), 7.34 – 7.38 (m, 5H), 7.48 (d, J = 1.3 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 15.6, 28.6, 36.1, 58.0, 128.1 (2C), 128.3 (2C), 129.1, 130.5 (2C), 131.4, 132.4, 135.4 ppm. IR (ATR): ν 3109, 3050, 2983, 2939, 2858, 1650, 1603, 1576, 1546, 1489, 1469, 762, 700 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{16}N_2$ 212.1313, found 212.1320.

1-(1-Methyl-cyclobutyl)-4-phenyl-1*H*-imidazole (28)

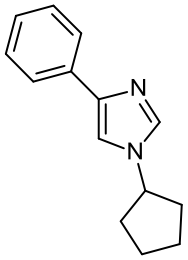


To a solution of 4-phenyloxazole (155 mg, 0.69 mmol, 1 equiv; CAS [20662-89-9]) and 1-methyl-cyclobutylamine (118 mg, 134 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C. After 1 h, another 2 equiv of 1-methylcyclobutanamine were added and heating continued for 2 h. The reaction mixture was allowed to cool to room temperature, poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product

purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (117 mg, 80%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.69 (s, 3H), 1.96 – 2.06 (m, 2H), 2.26 – 2.30 (m, 2H), 2.56 – 2.61 (m, 2H), 7.21 – 7.24 (m, 1H), 7.23 (d, J = 1.4 Hz, 1H), 7.35 – 7.38 (m, 2H), 7.56 (d, J = 1.4 Hz, 1H), 7.77 – 7.79 (m, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.5, 28.1, 35.1 (2C), 57.6, 112.1, 124.8 (2C), 126.8, 128.7 (2C), 134.5, 134.7, 142.2 ppm. IR (ATR): ν 3117, 3084, 3055, 2974, 2966, 2873, 2857, 1605, 1581, 1552, 1494, 1480, 767, 694 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{16}N_2$ 212.1313, found 212.1321.

1-Cyclopentyl-4-phenyl-1*H*-imidazole (29)

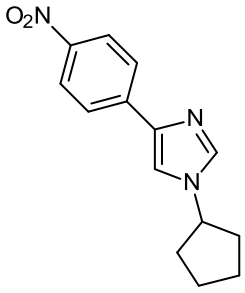


To a solution of 4-phenyloxazole (155 mg, 0.69 mmol, 1 equiv; CAS [20662-89-9]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 1 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (135 mg, 93%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.74 – 1.78 (m, 2H), 1.88 – 1.93 (m, 4H), 2.21 – 2.25 (m, 2H), 4.48 (quin, J = 7.0 Hz, 1H), 7.21 – 7.23 (m, 1H), 7.24 (d, J = 1.3 Hz, 1H), 7.35 – 7.38 (m, 2H), 7.56 (d, J = 1.3 Hz, 1H), 7.76 – 7.78 (m, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0 (2C), 33.8 (2C), 56.7, 113.4, 124.8 (2C), 126.7, 128.7 (2C), 134.5, 136.3, 142.3 ppm. IR

(ATR): ν 3112, 3083, 2961, 2909, 2867, 1656, 1606, 1582, 1550, 1491, 1443, 758, 691 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{16}N_2$ 213.1313, found 212.1321.

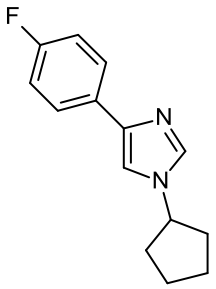
1-Cyclopentyl-4-(4-nitro-phenyl)-1*H*-imidazole (30)



To a solution of 4-(4-nitro-phenyl)-oxazole (132 mg, 0.69 mmol, 1 equiv; CAS [13382-61-1]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 1 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as dark green solid (146 mg, 82%).

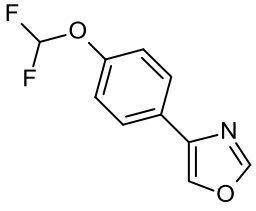
^{1}H NMR (600 MHz, $CDCl_3$): δ 1.77 – 1.81 (m, 2H), 1.89 – 1.94 (m, 4H), 2.24 – 2.29 (m, 2H), 4.51 (quin, J = 7.0 Hz, 1H), 7.40 (d, J = 1.3 Hz, 1H), 7.62 (d, J = 1.3 Hz, 1H), 7.90 (dt, J = 9.2, 2.2 Hz, 2H), 8.23 (dt, J = 9.3, 2.2 Hz, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0 (2C), 33.9 (2C), 59.0, 116.0, 124.4 (2C), 125.0 (2C), 137.3, 140.2, 140.9, 146.4 ppm. IR (ATR): ν 3123, 2952, 2873, 1598, 1553, 1510, 1336, 853 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{15}N_3O_2$ 257.1177, found 257.1164.

1-Cyclopentyl-4-(4-fluoro-phenyl)-1*H*-imidazole (31)



To a solution of 4-(4-fluoro-phenyl)-oxazole (113 mg, 0.69 mmol, 1 equiv; CAS [620633-04-7]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (125 mg, 79%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 1.74 – 1.79 (m, 2H), 1.86 – 1.93 (m, 4H), 2.21 – 2.25 (m, 2H), 4.47 (quin, J = 7.0 Hz, 1H), 7.03 – 7.07 (m, 2H), 7.18 (d, J = 1.3 Hz, 1H), 7.55 (d, J = 1.3 Hz, 1H), 7.71 – 7.74 (m, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0 (2C), 33.8 (2C), 58.7, 113.1, 115.5 (d, J_{CF} = 21.5 Hz, 2C), 126.3 (d, J_{CF} = 7.8 Hz, 2C), 130.8 (d, J_{CF} = 2.7 Hz), 136.3, 141.5, 162.0 (d, J_{CF} = 245.7 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -116.3 ppm. IR (ATR): ν 3135, 3110, 3067, 3038, 2922, 2855, 1656, 1604, 1595, 1555, 1492, 1219, 844 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{15}FN_2$ 230.1219, found 230.1228.

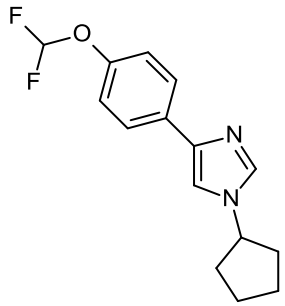
4-(4-Difluoromethoxy-phenyl)-oxazole



2-Bromo-1-(4-difluoromethoxy-phenyl)-ethanone (0.97 g, 3.66 mmol, 1 equiv; CAS [141134-24-9]) and formamide (16.5 g, 14.6 mL, 366.0 mmol, 100 equiv) were heated by microwave irradiation to 110 °C and maintained at this temperature for 5 h. After being cooled to room temperature, the crude reaction mixture was poured into a sat. solution of $NaHCO_3$ (15 mL) and water (10 mL), stirred for 15 min and then extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane / ethyl acetate (0 to 50%). The title compound was isolated as white solid (0.22 g, 28%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.54 (t, J_{HF} = 73.8 Hz, 1H), 7.16 – 7.19 (m, 2H), 7.75 (dt, J = 9.3, 2.4 Hz, 2H), 7.92 – 7.95 (m, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 116.0 (t, J_{CF} = 259.4 Hz), 120.0 (2C), 127.2 (2C), 128.3, 133.8, 139.7, 151.1 (t, J_{CF} = 2.9 Hz), 151.6 ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -80.9 ppm. IR (ATR): ν 3163, 3147, 3007, 1618, 1601, 1576, 1540, 1515, 1502, 1410, 1226, 1114, 1104, 1023, 1014, 839 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{10}H_7F_2NO_2$ 211.0445, found 211.0444.

1-Cyclopentyl-4-(4-difluoromethoxy-phenyl)-1*H*-imidazole (32)

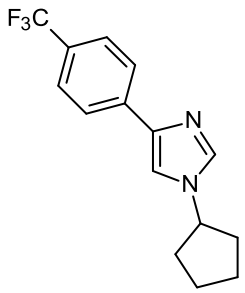


To a solution of 4-(4-difluoromethoxy-phenyl)-oxazole (146 mg, 0.69 mmol, 1 equiv) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting

with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (148 mg, 77%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.74 – 1.80 (m, 2H), 1.86 – 1.93 (m, 4H), 2.20 – 2.26 (m, 2H), 4.48 (quin, J = 7.0 Hz, 1H), 6.51 (t, J_{HF} = 74.2 Hz, 1H), 7.10 – 7.13 (m, 2H), 7.20 (d, J = 1.3 Hz, 1H), 7.56 (d, J = 1.3 Hz, 1H), 7.75 (dt, J = 9.2, 2.5 Hz, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0 (2C), 33.8 (2C), 58.7, 113.4, 116.3 (t, J_{CF} = 257.8 Hz), 119.8 (2C), 126.2 (2C), 132.1, 136.4, 141.3, 150.1 (t, J_{CF} = 2.8 Hz) ppm. ^{19}F NMR (375 Hz, $CDCl_3$): δ -80.4 ppm. IR (ATR): ν 3122, 2973, 2874, 1651, 1591, 1557, 1501, 1399, 1218, 1111, 1028, 845 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{16}F_2N_2O$ 278.1231, found 278.1244.

1-Cyclopentyl-4-(4-trifluoromethyl-phenyl)-1*H*-imidazole (33)

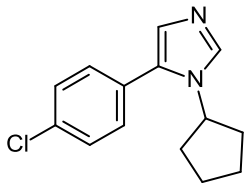


To a solution of 4-(4-trifluoromethyl-phenyl)-oxazole (147 mg, 0.69 mmol, 1 equiv; CAS [1126636-40-5]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichloro-benzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as white solid (153 mg, 79%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.76 – 1.81 (m, 2H), 1.87 – 1.94 (m, 4H), 2.21 – 2.28 (m, 2H), 4.50 (quin, J = 7.0 Hz, 1H), 7.32 (d, J = 1.2 Hz, 1H), 7.59 (d, J = 1.2 Hz, 1H), 7.61 (d, J = 8.1 Hz, 2H), 7.86 (d, J = 8.1 Hz, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0 (2C), 33.9 (2C), 58.8, 114.6, 124.8 (2C), 125.5, 125.7 (q, J_{CF} = 3.8 Hz), 128.5 (q, J_{CF} = 33.2 Hz), 136.8 (2C),

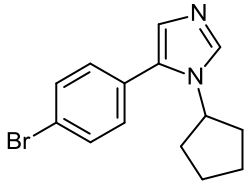
138.0, 140.9 ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -62.3 ppm. IR (ATR): ν 3127, 2970, 2876, 1616, 1562, 1505, 1491, 1413, 1371, 1319, 1125, 843 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{15}F_3N_2$ 280.1187, found 280.1198.

5-(4-Chloro-phenyl)-1-cyclopentyl-1*H*-imidazole (34)



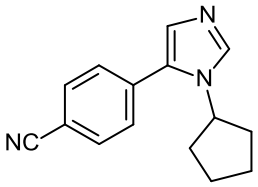
To a solution of 5-(4-chloro-phenyl)-oxazole (124 mg, 0.69 mmol, 1 equiv; CAS [1008-94-2]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 1 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (127 mg, 75%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 1.66 – 1.71 (m, 2H), 1.81 – 191 (m, 4H), 2.07 – 2.12 (m, 2H), 4.43 (quin, J = 7.3 Hz, 1H), 7.02 (d, J = 1.0 Hz, 1H), 7.30 (dt, J = 8.9, 2.3 Hz, 2H), 7.41 (dt, J = 8.9, 2.3 Hz, 2H), 7.66 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.2 (2C), 34.5 (2C), 56.5, 128.3, 129.1 (2C), 129.2, 130.7 (2C), 132.3, 134.3, 135.4 ppm. IR (ATR): ν 3109, 2950, 2863, 1599, 1542, 1485, 1470, 808 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{15}ClN_2$ 246.0924, found 246.0932.

5-(4-Bromo-phenyl)-1-cyclopentyl-1*H*-imidazole (35)



To a solution of 5-(4-bromo-phenyl)-oxazole (155 mg, 0.69 mmol, 1 equiv; CAS [72571-06-3]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 1 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (117 mg, 58%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 1.67 – 1.71 (m, 2H), 1.80 – 1.90 (m, 4H), 2.07 – 2.12 (m, 2H), 4.43 (quin, J = 7.3 Hz, 1H), 7.03 (d, J = 0.9 Hz, 1H), 7.23 (dt, J = 8.8, 2.2 Hz, 2H), 7.57 (dt, J = 8.8, 2.2 Hz, 2H), 7.66 (d, J = 0.9 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.3 (2C), 34.5 (2C), 56.6, 122.4, 128.3, 129.6 (2C), 130.9 (2C), 132.0, 132.3, 135.5 ppm. IR (ATR): ν 3110, 2948, 2864, 1594, 1539, 807 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{15}BrN_2$ 290.0419, found 290.0424.

4-(3-Cyclopentyl-3*H*-imidazol-4-yl)-benzonitrile (36)

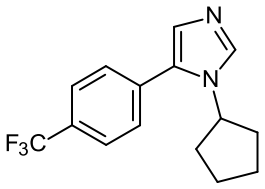


To a solution of 4-oxazol-5-yl-benzonitrile (117 mg, 0.69 mmol, 1 equiv; CAS [87150-13-8]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 1 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting

with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (131 mg, 80%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.70 – 1.75 (m, 2H), 1.83 – 1.93 (m, 4H), 2.11 – 2.16 (m, 2H), 4.49 (quint, J = 7.2 Hz, 1H), 7.12 (d, J = 1.0 Hz, 1H), 7.49 (dt, J = 8.4, 1.8 Hz, 2H), 7.72 (d, J = 1.0 Hz, 1H), 7.73 (dt, J = 8.4, 1.8 Hz, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.3 (2C), 34.6 (2C), 56.9, 111.6, 118.7, 129.4 (2C), 129.6, 131.8, 132.7 (2C), 135.3, 136.5 ppm. IR (ATR): ν 3109, 2949, 2876, 2224, 1606, 1560, 1544, 1493, 1470, 815 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{15}N_3$ 237.1266, found 237.1274.

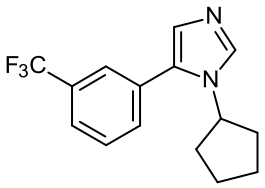
1-Cyclopentyl-5-(4-trifluoromethyl-phenyl)-1*H*-imidazole (37)



To a solution of 5-(4-trifluoromethyl-phenyl)-oxazole (147 mg, 0.69 mmol, 1 equiv; CAS [87150-14-9]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichloro-benzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (151 mg, 78%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 1.67 – 1.73 (m, 2H), 1.83 – 1.93 (m, 4H), 2.10 – 2.14 (m, 2H), 4.48 (quin, J = 7.2 Hz, 1H), 7.09 (d, J = 1.0 Hz, 1H), 7.49 – 7.50 (m, 2H), 7.69 – 7.71 (m, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.3 (2C), 34.6 (2C), 56.7, 124.2 (q, J_{CF} = 271.4 Hz), 125.8 (q, J_{CF} = 3.6 Hz), 129.0 (2C), 129.4 (2C), 130.1 (q, J_{CF} = 33.2 Hz), 132.1, 134.3, 135.9 ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -62.6 ppm. IR (ATR): ν 2944, 2875, 1618, 1553, 1322, 1102, 1067, 844 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{15}F_3N_2$ 280.1187, found 280.1196.

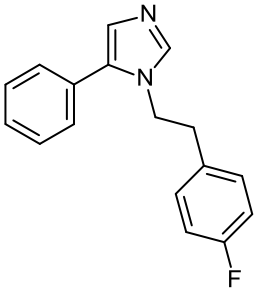
1-Cyclopentyl-5-(3-trifluoromethyl-phenyl)-1*H*-imidazole (38)



To a solution of 5-(3-trifluoromethyl-phenyl)-oxazole (147 mg, 0.69 mmol, 1 equiv; CAS [175205-48-8]) and cyclopentylamine (118 mg, 136 µL, 1.38 mmol, 2 equiv) in *o*-dichloro-benzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 2 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown solid (133 mg, 69%).

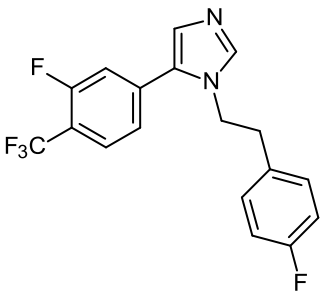
^{1}H NMR (600 MHz, $CDCl_3$): δ 1.68 – 1.73 (m, 2H), 1.83 – 1.92 (m, 4H), 2.10 – 2.16 (m, 2H), 4.44 (quin, J = 7.1 Hz, 1H), 7.09 (d, J = 1.0 Hz, 1H), 7.55 – 7.59 (m, 2H), 7.63 – 7.66 (m, 2H), 7.70 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.3 (2C), 34.6 (2C), 56.7, 123.1, 124.9 (q, J_{CF} = 3.9 Hz), 126.0 (q, J_{CF} = 3.9 Hz), 128.8, 129.4, 131.4 (q, J_{CF} = 32.4 Hz), 131.5, 132.0, 132.5 (d, J_{CF} = 1.1 Hz), 135.7 ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -62.7 ppm. IR (ATR): ν 3114, 2960, 2874, 1616, 1601, 1550, 1325, 1119, 903, 802, 701 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{15}H_{15}F_3N_2$ 280.1187, found 280.1196.

1-[2-(4-Fluoro-phenyl)-ethyl]-5-phenyl-1*H*-imidazole (39)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and 2-(4-fluoro-phenyl)-ethylamine (192 mg, 181 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (101 mg, 55%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 2.81 (t, J = 7.2 Hz, 2H), 4.18 (t, J = 7.2 Hz, 2H), 6.83 – 6.86 (m, 2H), 6.88 – 6.92 (m, 2H), 7.04 (d, J = 1.0 Hz 1H), 7.29 – 7.30 (m, 2H), 7.37 (d, J = 1.0 Hz, 1H), 7.39 (m, 1H), 7.42 – 7.44 (m, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 36.7, 46.9, 115.7 (d, J_{CF} = 21.5 Hz, 2C), 128.2, 128.5, 128.9 (4C), 130.2 (d, J_{CF} = 8.1 Hz, 2C), 130.2, 132.9, 133.0 (d, J_{CF} = 3.3 Hz), 138.2, 162.0 (d, J_{CF} = 245.0 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -115.8 ppm. IR (ATR): ν 3037, 2929, 2860, 1602, 1492, 1480, 1440, 1358, 1219, 822, 761, 699 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{17}H_{15}FN_2$ 266.1219, found 266.1230.

1-[2-(4-Fluoro-phenyl)-ethyl]-5-(3-fluoro-4-trifluoromethyl-phenyl)-1*H*-imidazole (40)

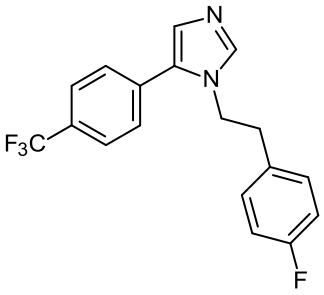


To a solution of 5-(3-fluoro-4-trifluoromethyl-phenyl)-oxazole (160 mg, 0.69 mmol, 1 equiv) and 2-(4-fluoro-phenyl)-ethylamine (192 mg, 181 µL, 1.38 mmol, 2 equiv) in *o*-dichloro-benzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C. After 1 h, another 2 equiv of 2-(4-fluoro-phenyl)-ethylamine were added and heating continued for 2 h. The

reaction mixture was allowed to cool to room temperature, poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (201 mg, 83%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.87 (t, J = 6.8 Hz, 2H), 4.23 (t, J = 6.9 Hz, 2H), 6.82 – 6.85 (m, 2H), 6.89 – 6.92 (m, 2H), 7.04 (d, J = 11.0 Hz, 1H), 7.11 – 7.13 (m, 2H), 7.45 (d, J = 0.8 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 36.9, 47.1, 115.6, 115.8 (d, J_{CF} = 22.4 Hz, 2C), 116.5 (d, J_{CF} = 22.2 Hz), 123.9 (d, J_{CF} = 3.6 Hz), 127.8 (dq, J_{CF} = 4.5, 2.2 Hz), 130.1, 130.2 (d, J_{CF} = 8.1 Hz, 2C), 130.3 (d, J_{CF} = 8.1 Hz), 130.6, 132.5 (d, J_{CF} = 3.0 Hz), 136.3, 139.6, 161.2, 162.0 (d, J_{CF} = 245.0 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -61.3, -113.2, -115.3 ppm. IR (ATR): ν 3040, 2933, 2863, 1628, 1601, 1576, 1510, 1321, 1122, 822 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{18}H_{13}F_5N_2$ 352.0999, found 352.1005.

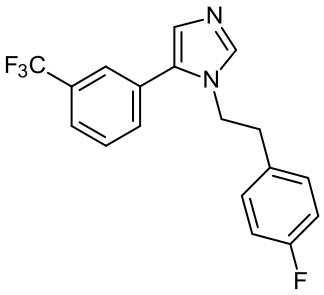
1-[2-(4-Fluoro-phenyl)-ethyl]-5-(4-trifluoromethyl-phenyl)-1*H*-imidazole (41)



To a solution of 5-(4-trifluoromethyl-phenyl)-oxazole (147 mg, 0.69 mmol, 1 equiv; CAS [87150-14-9]) and 2-(4-fluoro-phenyl)-ethylamine (192 mg, 181 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C for 2 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown oil (94 mg, 41%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.84 (t, J = 7.0 Hz, 2H), 4.22 (t, J = 7.0 Hz, 2H), 6.81 – 6.84 (m, 2H), 6.89 (tt, J = 7.8, 3.1 Hz, 2H), 7.10 (d, J = 0.8 Hz, 1H), 7.36 – 7.38 (m, 2H), 7.44 (d, J = 0.8 Hz, 1H), 7.66 – 7.68 ppm (m, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 36.9, 47.0, 115.8 (d, J_{CF} = 21.8 Hz, 2C), 124.1 (q, J_{CF} = 273.4 Hz), 125.9 (q, J_{CF} = 3.7 Hz, 2C), 128.8 (2C), 129.5, 130.12 (q, J_{CF} = 32.8 Hz), 130.15 (d, J_{CF} = 8.1 Hz, 2C), 131.7, 132.7 (d, J_{CF} = 3.3 Hz), 133.8 (d, J_{CF} = 1.0 Hz), 139.1, 162.1 (d, J_{CF} = 245.1 Hz) ppm. ^{19}F NMR: (375 MHz, $CDCl_3$): δ -62.7, -115.5 ppm. IR (ATR): ν 3106, 3040, 2935, 1619, 1510, 1482, 1323, 1107, 823 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{18}H_{14}F_4N_2$ 334.1093, found 334.1102.

1-[2-(4-Fluoro-phenyl)-ethyl]-5-(3-trifluoromethyl-phenyl)-1*H*-imidazole (42)

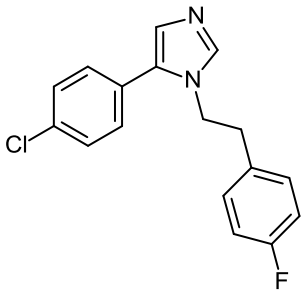


To a solution of 5-(3-trifluoromethyl-phenyl)-oxazole (147 mg, 0.69 mmol, 1 equiv; CAS [175205-48-8]) and 2-(4-fluoro-phenyl)-ethylamine (192 mg, 181 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C. After 1 h, another 2 equiv of 2-(4-fluoro-phenyl)-ethylamine were added and heating continued for 2 h. The reaction mixture was allowed to cool to room temperature, poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (119 mg, 52%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.85 (t, J = 7.0 Hz, 2H), 4.19 (t, J = 7.0 Hz, 2H), 6.81 – 6.84 (m, 2H), 6.89 (tt, J = 8.9, 2.4 Hz, 2H), 7.08 (d, J = 1.1 Hz, 1H), 7.41 – 7.43 (m, 1H), 7.47 (br s, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.62 – 7.64 (m, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 37.0, 46.9, 115.8 (d, J_{CF} = 21.5 Hz, 2C), 123.1, 124.9 (q, J_{CF} = 3.7 Hz), 125.4 (q, J_{CF} = 3.7 Hz), 129.3, 129.5, 130.2 (d, J_{CF} = 8.1 Hz, 2C), 131.0, 131.4 (q, J_{CF} = 32.8 Hz), 131.7,

132.1, 132.7 (d, J_{CF} = 3.2 Hz), 138.8, 162.1 (d, J_{CF} = 245.8 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -62.7, -115.5 ppm. IR (ATR): ν 3042, 2945, 1601, 1553, 1510, 1326, 1119, 802 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{18}H_{14}F_4N_2$ 334.1093, found 334.1102.

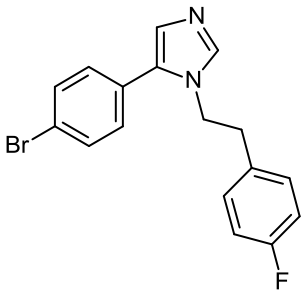
5-(4-Chloro-phenyl)-1-[2-(4-fluoro-phenyl)-ethyl]-1*H*-imidazole (43)



To a solution of 5-(4-chloro-phenyl)-oxazole (124 mg, 0.69 mmol, 1 equiv; CAS [1008-94-2]) and 2-(4-fluoro-phenyl)-ethylamine (192 mg, 181 µL, 1.38 mmol, 2 equiv) in *o*-dichloro-benzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C. After 1 h, another 2 equiv of 2-(4-fluoro-phenyl)-ethylamine were added and heating continued for 2 h. The reaction mixture was allowed to cool to room temperature, poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (156 mg, 75%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.82 (t, J = 7.0 Hz, 2H), 4.16 (t, J = 7.0 Hz, 2H), 6.83 – 6.86 (m, 2H), 6.91 (tt, J = 8.2, 3.1 Hz, 2H), 7.03 (d, J = 0.9 Hz, 1H), 7.19 (dt, J = 8.9, 2.3 Hz, 2H), 7.38 – 7.40 (m, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 39.8, 46.9, 115.8 (d, J_{CF} = 21.4 Hz, 2C), 128.6, 128.9, 129.2 (2C), 130.1 (2C), 130.2 (d, J_{CF} = 8.1 Hz, 2C), 131.8, 132.9 (d, J_{CF} = 3.5 Hz), 134.3, 138.5, 162.0 (d, J_{CF} = 245.8 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -115.6 ppm. IR (ATR): ν 3083, 2930, 2860, 1601, 1550, 1508, 1476, 1218, 1092, 817 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{17}H_{14}ClFN_2$ 300.0830, found 300.0835.

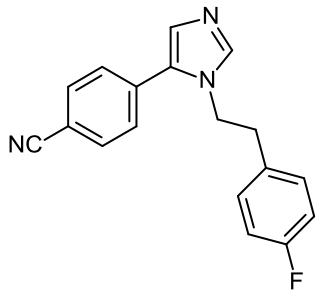
5-(4-Bromo-phenyl)-1-[2-(4-fluoro-phenyl)-ethyl]-1*H*-imidazole (44)



To a solution of 5-(4-bromo-phenyl)-oxazole (155 mg, 0.69 mmol, 1 equiv; CAS [72571-06-3]) and 2-(4-fluoro-phenyl)-ethylamine (192 mg, 181 µL, 1.38 mmol, 2 equiv) in *o*-dichloro-benzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (148 mg, 62%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.82 (t, J = 7.0 Hz, 2H), 4.17 (t, J = 7.0 Hz, 2H), 6.83 – 6.86 (m, 2H), 6.89 – 6.92 (m, 2H), 7.03 (d, J = 1.0 Hz, 1H), 7.12 (dt, J = 8.8, 2.2 Hz, 2H), 7.40 (d, J = 1.0 Hz, 1H), 7.55 (dt, J = 8.8, 2.2 Hz, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 36.8, 46.9, 115.7 (d, J_{CF} = 21.3 Hz, 2C), 122.5, 128.8, 129.0, 130.2 (d, J_{CF} = 8.1 Hz, 2C), 130.4 (2C), 131.8, 132.1 (2C), 132.8 (d, J_{CF} = 3.5 Hz), 138.6, 162.0 (d, J_{CF} = 245.8 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -115.6 ppm. IR (ATR): ν 3038, 2931, 2859, 1675, 1601, 1549, 1509, 1478, 1221, 1007, 823 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{17}H_{14}BrFN_2$ 344.0324, found 344.0330.

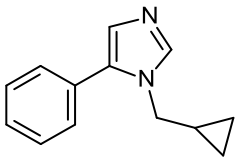
4-{3-[2-(4-Fluoro-phenyl)-ethyl]-3*H*-imidazol-4-yl}-benzonitrile (45)



To a solution of 4-oxazol-5-yl-benzonitrile (117 mg, 0.69 mmol, 1 equiv; CAS [87150-13-8]) and 2-(4-fluoro-phenyl)-ethylamine (192 mg, 181 µL, 1.38 mmol, 2 equiv) in *o*-dichloro-benzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C. After 1 h, another 2 equiv of 2-(4-fluoro-phenyl)-ethylamine were added and heating continued for 2 h. The reaction mixture was allowed to cool to room temperature, poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (127 mg, 63%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.84 (t, J = 7.0 Hz, 2H), 4.23 (t, J = 7.0 Hz, 2H), 6.80 – 6.83 (m, 2H), 6.90 (tt, J = 8.9, 2.4 Hz, 2H), 7.12 (d, J = 1.0 Hz, 1H), 7.35 (dt, J = 8.4, 1.8 Hz, 2H), 7.46 (d, J = 1.0 Hz, 1H), 7.70 (dt, J = 8.3 , 1.8 Hz, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 36.9, 47.2, 111.7, 115.8 (d, J_{CF} = 21.8 Hz, 2C), 118.6, 128.8 (2C), 130.0, 130.1 (d, J_{CF} = 8.1 Hz, 2C), 131.3, 132.7 (d, J_{CF} = 3.4 Hz), 132.7 (2C), 134.8, 139.6, 162.1 (d, J_{CF} = 245.8 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -115.3 ppm. IR (ATR): ν 3041, 2929, 2226, 1608, 1563, 1546, 1509, 1219, 822 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{18}H_{14}FN_3$ 291.1172, found 291.1183.

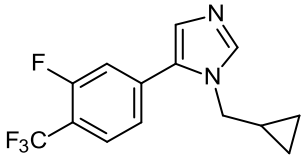
1-Cyclopropylmethyl-5-phenyl-1*H*-imidazole (46)



To a solution of 5-phenyloxazole (100 mg, 0.69 mmol, 1 equiv; CAS[1006-68-4]) and cyclopropyl-methylamine (98 mg, 120 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown oil (111 mg, 81%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.19 – 0.26 (m, 2H), 0.54 – 0.62 (m, 2H), 1.05 – 1.12 (m, 1H), 3.80 (d, J = 7.0 Hz, 2H), 7.08 (d, J = 1.1 Hz, 1H), 7.36 – 7.39 (m, 3H), 7.42 – 7.45 (m, 2H), 7.71 (d, J = 1.1 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.4 (2C), 11.7, 50.2, 128.1, 128.2, 128.8 (2C), 129.1 (2C), 130.4, 133.0, 137.8 ppm. IR (ATR): ν 3080, 3002, 2874, 1605, 1576, 1552, 1480, 1364, 916, 762, 698 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157, found 198.1166.

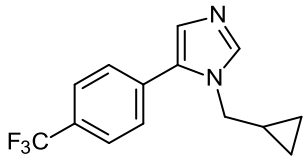
1-Cyclopropylmethyl-5-(3-fluoro-4-trifluoromethyl-phenyl)-1*H*-imidazole (47)



To a solution of 5-(3-fluoro-4-trifluoromethyl-phenyl)-oxazole (160 mg, 0.69 mmol, 1 equiv) and cyclopropyl-methylamine (98 mg, 120 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for

0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (133 mg, 68%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 0.27 – 0.30 (m, 2H), 0.64 – 0.67 (m, 2H), 1.07 – 1.14 (m, 1H), 3.85 (d, J = 7.0 Hz, 2H), 7.19 (d, J = 1.0 Hz, 1H), 7.24 (dd, J = 10.9, 0.9 Hz, 1H), 7.27 – 7.28 (m, 1H), 7.67 (t, J = 7.8 Hz, 1H), 7.76 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.5 (2C), 11.6, 50.6, 116.7 (d, J_{CF} = 21.6 Hz), 117.5 (d, J_{CF} = 13.8 Hz), 122.6 (q, J_{CF} = 272.4 Hz), 124.0 (d, J_{CF} = 3.1 Hz), 127.8 (q, J_{CF} = 2.4 Hz), 130.0, 130.6, 136.6 (d, J_{CF} = 8.7 Hz), 139.2, 159.9 (dq, J_{CF} = 256.8, 2.1 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -61.3, -113.3 ppm. IR (ATR): ν 3086, 1627, 1575, 1499, 1321, 1121, 926, 826 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{12}F_4N_2$ 284.0937, found 284.0946.

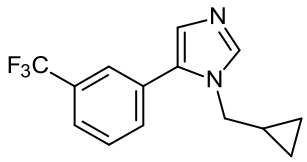
1-Cyclopropylmethyl-5-(4-trifluoromethyl-phenyl)-1*H*-imidazole (48)



To a solution of 5-(4-trifluoromethyl-phenyl)-oxazole (147 mg, 0.69 mmol, 1 equiv; CAS [87150-14-9]) and cyclopropyl-methylamine (98 mg, 120 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown oil (125 mg, 68%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.22 – 0.29 (m, 2H), 0.58 – 0.66 (m, 2H), 1.06 – 1.12 (m, 1H), 3.83 (d, J = 2.0 Hz, 2H), 7.15 (d, J = 1.1 Hz, 1H), 7.50 – 7.52 (m, 2H), 7.69 – 7.71 (m, 2H), 7.75 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.5 (2C), 11.7, 50.5, 124.2 (q, J_{CF} = 273.4 Hz), 125.9 (q, J_{CF} = 3.6 Hz), 129.0 (2C), 129.3, 130.1 (d, J_{CF} = 32.8 Hz), 131.7, 134.0 (d, J_{CF} = 1.3 Hz), 138.7 (2C) ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -62.2 ppm. IR (ATR): ν 3080, 3008, 2936, 2877, 1618, 1576, 1556, 1483, 1322, 1106, 826 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{13}F_3N_2$ 266.1030, found 266.1037.

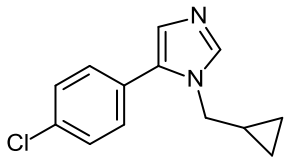
1-Cyclopropylmethyl-5-(3-trifluoromethyl-phenyl)-1*H*-imidazole (49)



To a solution of 5-(3-trifluoromethyl-phenyl)-oxazole (147 mg, 0.69 mmol, 1 equiv; CAS [175205-48-8]) and cyclopropyl-methylamine (98 mg, 120 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 4 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light brown oil (96 mg, 52%).

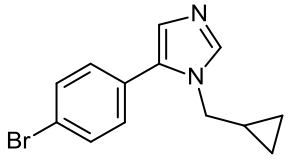
^{1}H NMR (600 MHz, $CDCl_3$): δ 0.21 – 0.28 (m, 2H), 0.58 – 0.66 (m, 2H), 1.05 – 1.12 (m, 1H), 3.80 (d, J = 7.0 Hz, 2H), 7.14 (d, J = 1.1 Hz, 1H), 7.56 – 7.59 (m, 2H), 7.63 – 7.65 (m, 2H), 7.75 (d, J = 1.1 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.5 (2C), 11.7, 50.4, 123.1, 124.8 (q, J_{CF} = 3.8 Hz), 125.7 (q, J_{CF} = 3.9 Hz), 129.1, 129.4, 131.3, 131.4 (q, J_{CF} = 32.4 Hz), 131.6, 132.2 (d, J_{CF} = 1.1 Hz), 138.5 ppm. ^{19}F NMR (375 MHz, $CDCl_3$): δ -62.7 ppm. IR (ATR): ν 3084, 3008, 1617, 1592, 1551, 1491, 1326, 1119, 903, 802 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{13}F_3N_2$ 266.1030, found 266.1041.

5-(4-Chloro-phenyl)-1-cyclopropylmethyl-1*H*-imidazole (50)



To a solution of 5-(4-chloro-phenyl)-oxazole (124 mg, 0.69 mmol, 1 equiv; CAS [1008-94-2]) and cyclopropyl-methylamine (98 mg, 120 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (132 mg, 86%).
^{1}H NMR (600 MHz, $CDCl_3$): δ 0.22 – 0.25 (m, 2H), 0.58 – 0.62 (m, 2H), 1.04 – 1.10 (m, 1H), 3.78 (d, J = 7.0 Hz, 2H), 7.08 (d, J = 1.0 Hz, 1H), 7.31 (dt, J = 8.9, 2.3 Hz, 2H), 7.41 (dt, J = 8.9, 2.3 Hz, 2H), 7.71 (d, J = 1.0 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.4 (2C), 11.7, 50.3, 128.6, 128.9, 129.1 (2C), 130.3 (2C), 131.9, 134.2, 138.1 ppm. IR (ATR): ν 3084, 3004, 2873, 1600, 1569, 1549, 1091, 915, 817 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{13}H_{13}ClN_2$ 232.0767, found 232.0775.

5-(4-Bromo-phenyl)-1-cyclopropylmethyl-1*H*-imidazole (51)

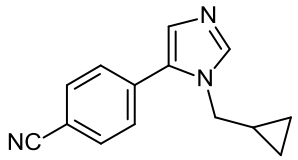


To a solution of 5-(4-bromo-phenyl)-oxazole (155 mg, 0.69 mmol, 1 equiv; CAS [72571-06-3]) and cyclopropyl-methylamine (98 mg, 120 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this

temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (102 mg, 53%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.22 – 0.25 (m, 2H), 0.59 – 0.62 (m, 2H), 1.04 – 1.10 (m, 1H), 3.78 (d, J = 7.1 Hz, 2H), 7.08 (d, J = 1.1 Hz, 1H), 7.25 (dt, J = 8.8, 2.2 Hz, 2H), 7.57 (dt, J = 8.8, 2.2 Hz, 2H), 7.71 (d, J = 1.1 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.4 (2C), 11.7, 50.3, 122.3, 128.6, 129.3, 130.6 (2C), 131.9 (2C), 132.1, 138.2 ppm. IR (ATR): ν 3080, 3007, 1598, 1545, 1007, 933, 818 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{13}H_{13}BrN_2$ 276.0262, found 276.0270.

4-(3-Cyclopropylmethyl-3*H*-imidazol-4-yl)-benzonitrile (52)



To a solution of 4-oxazol-5-yl-benzonitrile (117 mg, 0.69 mmol, 1 equiv; CAS [87150-13-8]) and cyclopropyl-methylamine (98 mg, 120 µL, 1.38 mmol, 2 equiv) in *o*-dichlorobenzene (10 mL) was added trifluoroacetic acid (157 mg, 106 µL, 1.38 mmol, 2 equiv) and the reaction mixture was heated by microwave irradiation to 200 °C and maintained at this temperature for 0.5 h. After being cooled to room temperature, the crude reaction mixture was poured into a mixture of 1 M NaOH (20 mL) and a sat. solution of NaCl (40 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by medium pressure liquid chromatography eluting with a gradient of heptane (containing 1% triethylamine) / ethyl acetate (0 to 60%). The title compound was isolated as light yellow oil (99 mg, 64%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 0.25 – 0.28 (m, 2H), 0.60 – 0.68 (m, 2H), 1.06 – 1.12 (m, 1H), 3.84 (d, J = 7.0 Hz, 2H), 7.19 (d, J = 1.1 Hz, 1H), 7.51 (dt, J = 8.4, 1.8 Hz, 2H), 7.73 (dt, J = 8.4, 1.8 Hz, 2H), 7.77 (d, J = 1.1 Hz, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.5 (2C),

11.7, 50.7, 111.6, 118.7, 129.0 (2C), 130.0, 131.3, 132.7 (2C), 135.0, 139.2 ppm. IR (ATR): ν 3083, 3004, 2225, 1608, 1563, 1545, 1495, 1480, 828 cm^{-1}. HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{14}H_{13}N_3$ 223.1109, found 223.1116.

General Experimental Procedure for Coupling of Amino Acids

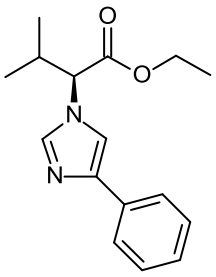
In a microwave reaction tube**,** the substituted oxazole (1 equiv), amino acid (4 equiv) and trifluoroacetic acid (2 equiv) were taken and toluene was added. The reaction mixture was heated at 100 °C for 0.5 h. The crude reaction mixture was purified on silica gel column chromatography using hexanes and ethyl acetate as eluents to afford the desired product.

Table S1. Enantiomeric purity of imidazolyl esters **54-57**.

entry	product	solvent	temp (°C)	time (min)	yield (%)	ee (%) [a]
1	**54**	*o*-DCB	160	45	25	0
2	**54**	$PhCH_3$	100	30	47	92
3	**55**	$PhCH_3$	100	30	57	40
4	**55**	$PhCH_3$	100	10	38 [b]	89
5	**56**	$PhCH_3$	100	30	56	68 [c]
6	**57**	$PhCH_3$	100	30	50	32
7	**57**	$PhCH_3$	100	10	32[b]	58

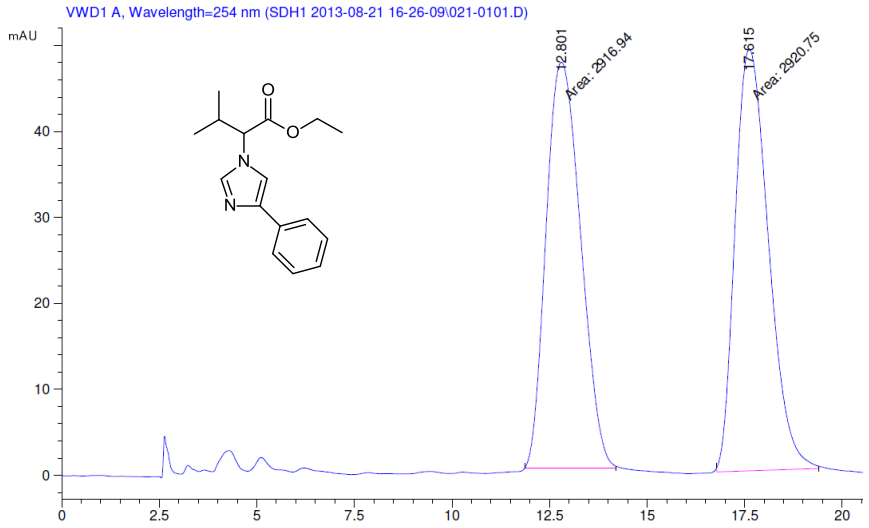
[a] Determined by chiral HPLC (see chromatograms below); [b] 1 equiv of TFA used; [c] diastereomeric excess (de).

(*S*)-3-Methyl-2-(4-phenyl-imidazol-1-yl)-butyric acid ethyl ester (54)

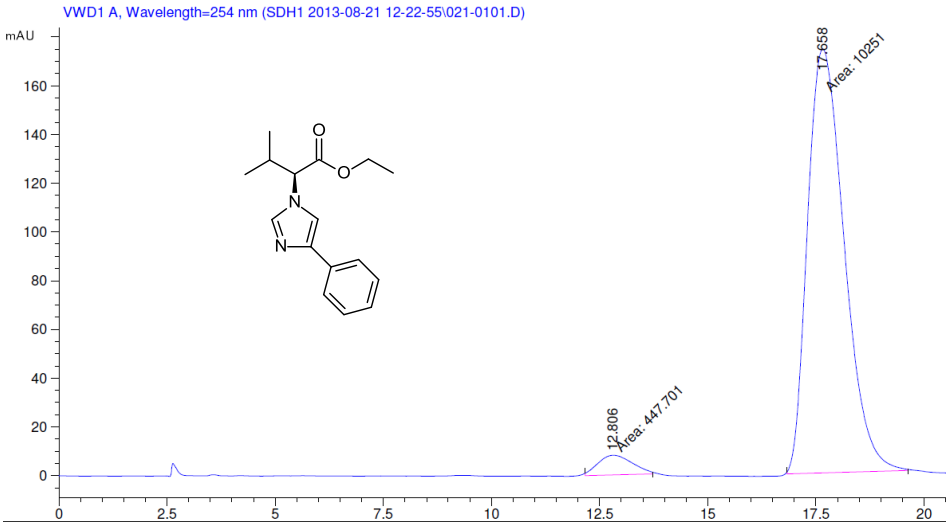


The above general experimental procedure was used. A solution of 4-phenyloxazole (36.3 mg, 0.25 mmol, 1 equiv), valine ethyl ester (145 mg, 1.0 mmol, 4 equiv) and trifluoroacetic acid (57 mg, 39 μL, 0.5 mmol, 2 equiv) in toluene (1 mL) were heated by microwave irradiation to 100 °C and maintained at this temperature for 0.5 h. The crude reaction mixture was purified directly by column chromatography eluting with hexanes / ethyl acetate (6:4). The title compound was isolated as colorless oil (32 mg, 47%). The enantiomeric purity of **54** (92% ee) was determined by chiral HPLC analysis using a Chiralcel® OD column (flow rate = 1.2 ml/min, 95:5 hexanes / isopropyl alcohol). The retention time for the (*R*)-enantiomer was ~12.8 min and for the (*S*)-enantiomer was ~17.6 min. See HPLC chromatogram below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (d, J = 6.6 Hz, 3H), 1.04 (d, J = 6.6 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H), 2.41 – 2.50 (m, 1H), 4.19 – 4.30 (m, 3H), 7.23 (tt, J = 7.3, 1.4 Hz, 1H), 7.35 – 7.39 (m, 2H), 7.40 (d, J = 1.2 Hz, 1H), 7.60 (d, J = 1.4 Hz, 1H), 7.77 – 7.80 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 18.6, 19.3, 32.1, 61.9, 66.9, 114.1, 124.8 (2C), 126.9, 128.6 (2C), 134.0, 137.3, 142.4, 169.4 ppm. IR: ν 2969, 2945, 1740, 1189, 750, 695 cm^{-1}. $[\alpha]_D^{20}$ = +31.9 (c = 0.1, $CHCl_3$). HRMS ESI+ (m/z): $[M]^+$ calcd for $C_{16}H_{20}N_2O_2$ 272.1525, found 272.1530.

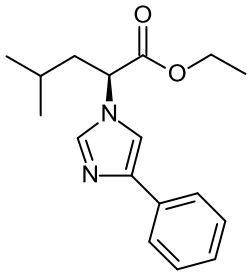


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.801	MM T	1.0283	2916.94336	47.27604	49.9674
2	17.615	MM T	0.9923	2920.75464	49.05781	50.0326



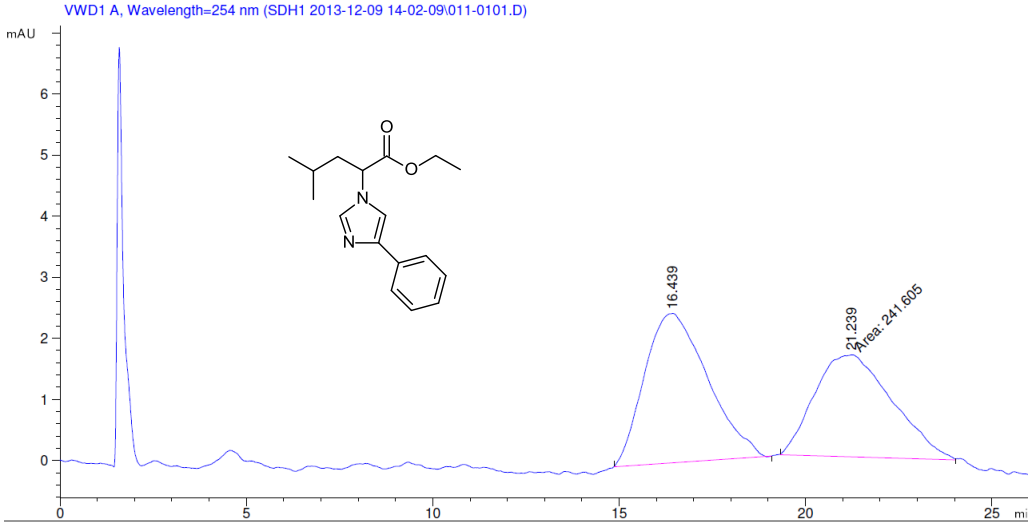
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.806	MM T	0.9220	447.70099	8.09255	4.1846
2	17.658	MM T	0.9821	1.02510e4	173.96346	95.8154

(*S*)-4-Methyl-2-(4-phenyl-imidazol-1-yl)-pentanoic acid ethyl ester (55)

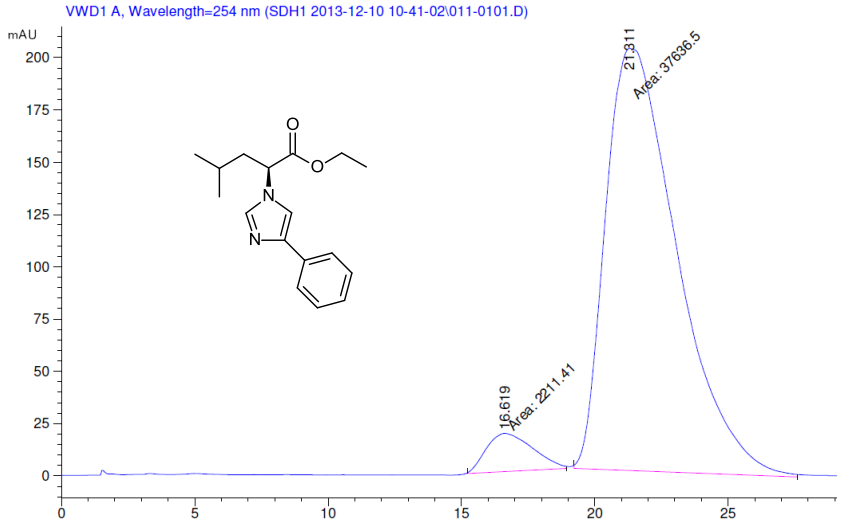


The above general experimental procedure was used. 4-Phenyloxazole (36.3 mg, 0.25 mmol, 1 equiv), leucine ethyl ester (159 mg, 1.0 mmol, 4 equiv) and trifluoroacetic acid (57 mg, 39 µL, 0.5 mmol, 2 equiv) in toluene (1 mL) were heated by microwave irradiation to 100 °C and maintained at this temperature for 0.5 h. The crude reaction mixture was purified directly by column chromatography eluting with hexanes / ethyl acetate (6:4). The title compound was isolated as colorless oil (41 mg, 57%). The enantiomeric purity of **55** (89% ee) was determined by chiral HPLC analysis using a Chiralpak® AD column (2 ml/min, 95:5 hexanes / isopropyl alcohol). The retention time for the (*R*)-enantiomer was ~16.5 min and for the (*S*)-enantiomer was ~21.3 min. See HPLC chromatogram below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (d, J = 6.6 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H), 1.27 (t, J = 7.2 Hz, 3H), 1.40 – 1.51 (m, 1H), 1.95 – 2.00 (m, 2H), 4.21 (qd, J = 7.2, 0.8 Hz, 2H), 4.76 (dd, J = 9.4, 6.4 Hz, 1H), 7.22 – 7.26 (m, 1H), 7.34 – 7.39 (m, 3H), 7.64 (s, 1H), 7.77 – 7.79 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 21.6, 22.8, 24.6, 41.6, 58.6, 62.2, 113.9, 124.9 (2C), 127.1, 128.7 (2C), 133.9, 137.2, 142.2, 170.0 ppm. IR: ν 2959, 2871, 1740, 1187, 746, 696 cm^{-1}. $[\alpha]_D^{20}$ = +10.2 (c = 0.1, $CHCl_3$). HRMS ESI+ (m/z): $[M]^+$ calcd for C17H22N2O2 286.1681, found 286.1698.

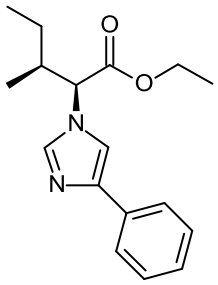


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.439	BB	1.3998	287.70688	2.44618	54.3549
2	21.239	MM	2.4125	241.60500	1.66912	45.6451



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.619	MM	2.0133	2211.41064	18.30639	5.5496
2	21.311	MM	3.1068	3.76365e4	201.90094	94.4504

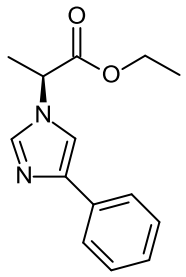
(2*S*,3*S*)-3-Methyl-2-(4-phenyl-imidazol-1-yl)-pentanoic acid ethyl ester (56)



The above general experimental procedure was used. A solution of 4-phenyloxazole (36.3 mg, 0.25 mmol, 1 equiv), isoleucine ethyl ester (159 mg, 1.0 mmol, 4 equiv) and trifluoroacetic acid (57 mg, 39 μL, 0.5 mmol, 2 equiv) in toluene (1 mL) was heated by microwave irradiation to 100 °C and maintained at this temperature for 0.5 h. The crude reaction mixture was purified directly by column chromatography eluting with hexanes / ethyl acetate (6:4). The title compound was isolated as colorless oil (40 mg, 56%). The diastereomeric purity of **56** (68% de) was determined by analysis of ^{1}H NMR spectra acquired on the crude reaction product. The (2*R*)- and (2*S*)-diastereomers exhibit distinct resonances for H2 at δ 4.45 and δ 4.39 ppm, respectively.

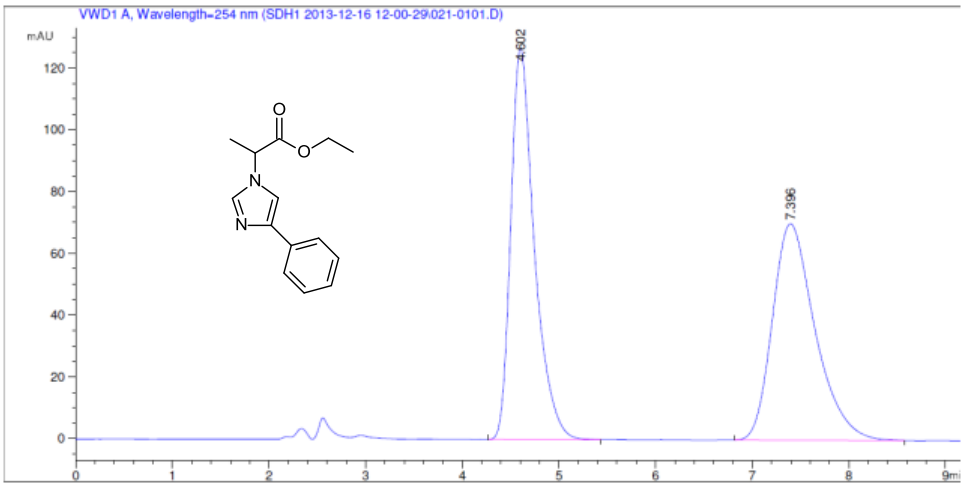
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, J = 7.2 Hz, 3H), 1.00 (d, J = 6.8 Hz, 3H), 1.25 – 1.30 (m, 4H), 1.42 – 1.51 (m, 1H), 2.19 – 2.23 (m, 1H), 4.18 – 4.30 (m, 2H), 4.36 (d, J = 10.2 Hz, 1H), 7.21 – 7.25 (m, 1H), 7.34 – 7.40 (m, 3H), 7.61 (s, 1H), 7.78 (dd, J = 8.2, 1.2 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.7, 14.2, 15.6, 24.9, 38.1, 62.0, 65.7, 114.3, 124.9 (2C), 127.0, 128.7 (2C), 134.0, 137.5, 142.2, 169.6 ppm. IR: ν 2966, 2877, 1738, 1185, 730, 695 cm^{-1}. $[\alpha]_D^{20}$ = +21.3 (c = 0.1, $CHCl_3$). HRMS ESI+ (*m/z*): $[M]^+$ calcd for $C_{17}H_{22}N_2O_2$ 286.1681, found 286.1704.

(*S*)-2-(4-Phenyl-imidazol-1-yl)-propionic acid ethyl ester (57)

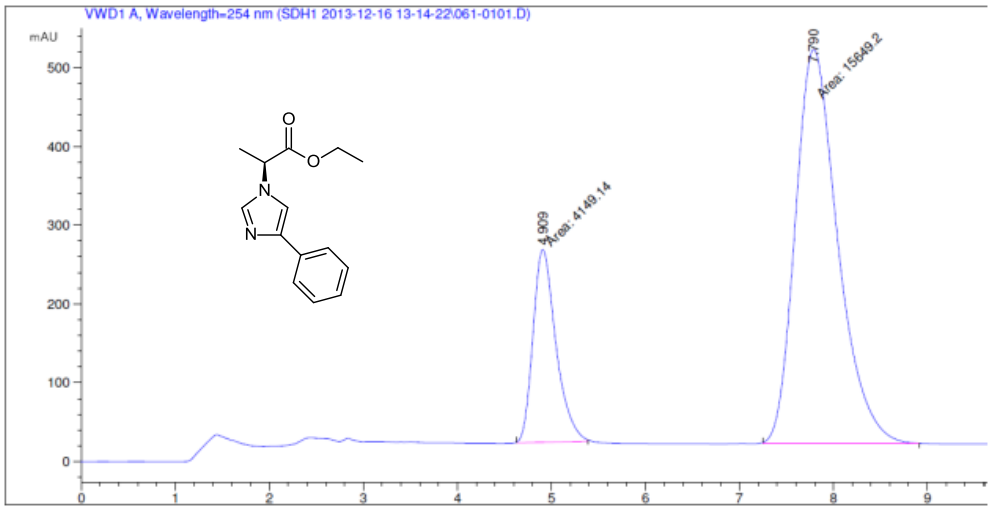


The above general experimental procedure was used. A solution of 4-phenyloxazole (36.3 mg, 0.25 mmol, 1equiv), alanine ethyl ester (116 mg, 1.0 mmol, 4 equiv) and trifluoroacetic acid (57 mg, 39 μL, 0.5 mmol, 2 equiv) in toluene (1 mL) was heated by microwave irradiation to 100 °C and maintained at this temperature for 0.5 h. The crude reaction mixture was purified directly by column chromatography eluting with hexanes / ethyl acetate (6:4). The title compound was isolated as colorless oil (31 mg, 50%). The enantiomeric purity of **57** (58% ee) was determined by chiral HPLC analysis using a Chiralcel® OD column (flow rate = 1.5 mL/min, mobile phase = 75:25 hexanes / isopropyl alcohol). The retention time for the (*R*)-enantiomer was ~4.9 min and for the (*S*)-enantiomer was ~7.8 min. See HPLC chromatogram below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, J = 7.2 Hz, 3H), 1.77 (d, J = 7.4 Hz, 3H), 4.21 (qd, J = 7.2, 1.2 Hz, 2H), 4.85 (q, J = 7.2 Hz, 1H), 7.21 – 7.25 (m, 1H), 7.31 (s, 1H), 7.36 (t, J = 7.6 Hz, 2H), 7.62 (s, 1H), 7.77 (d, J = 7.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 18.6, 55.4, 62.3, 113.7, 124.9 (2C), 127.0, 128.7 (2C), 134.1, 136.8, 142.4, 170.1 ppm. IR: ν 2985, 2920, 1738, 1192, 1068, 745, 696 cm^{-1}. $[\alpha]_D^{20}$ = +9.4 (c = 0.1, $CHCl_3$). HRMS ESI+ (m/z): $[M]^+$ calcd for $C_{14}H_{16}N_2O_2$ 244.1212, found 244.1226.



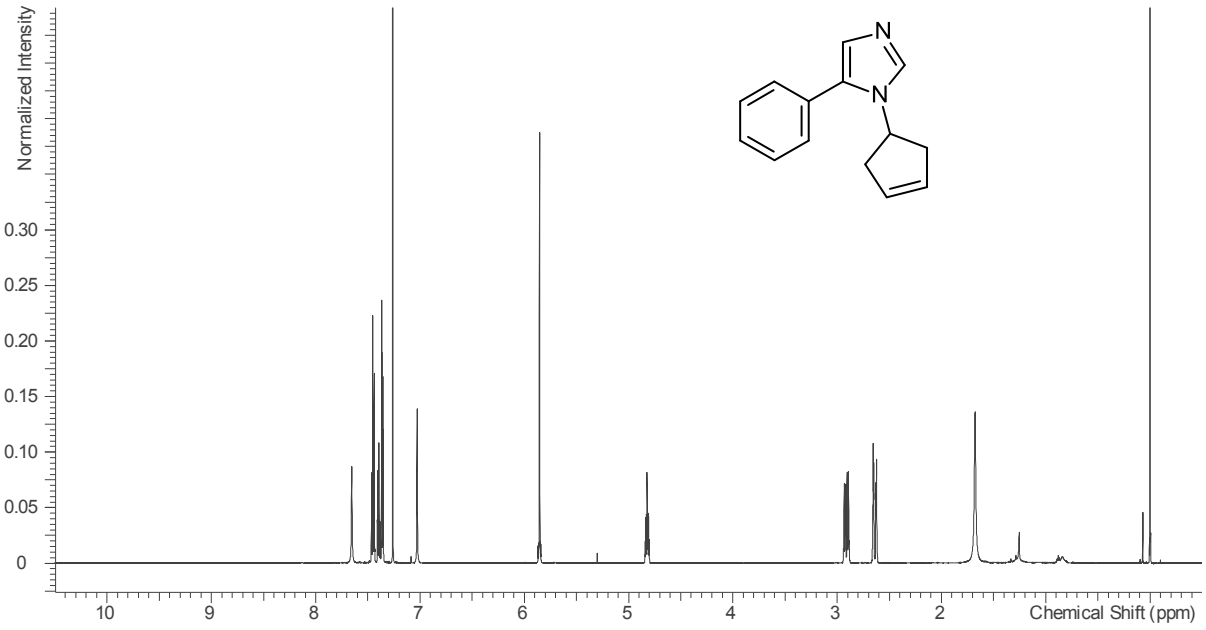
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.602	BB	0.2534	2152.36963	126.79349	49.9623
2	7.396	BB	0.4648	2155.61475	70.14021	50.0377

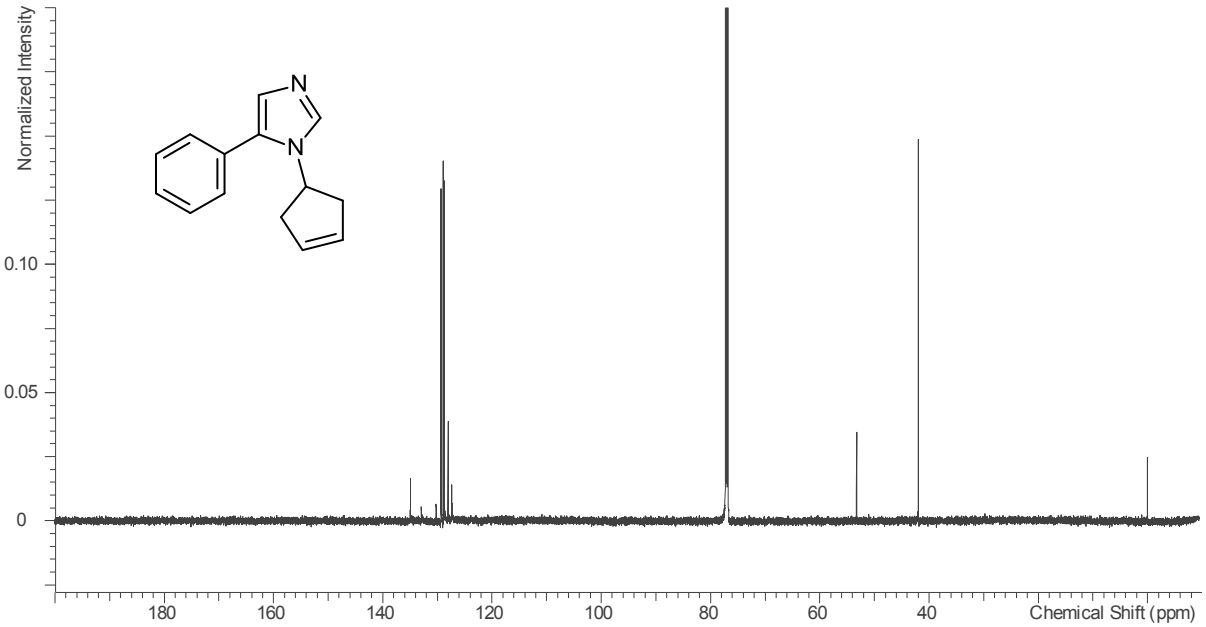


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.909	MM	0.2828	4149.14062	244.49332	20.9571
2	7.790	MM	0.5226	1.56492e4	499.10986	79.0429

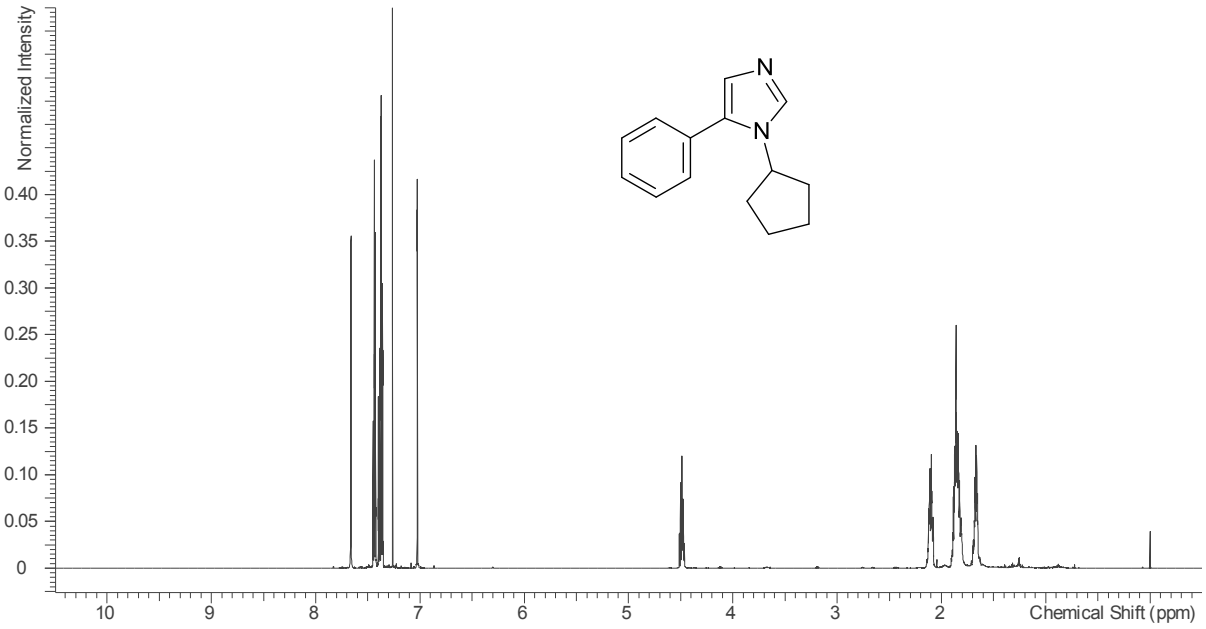
3. ^{1}H, ^{13}C and ^{19}F NMR Spectra for All New Compounds

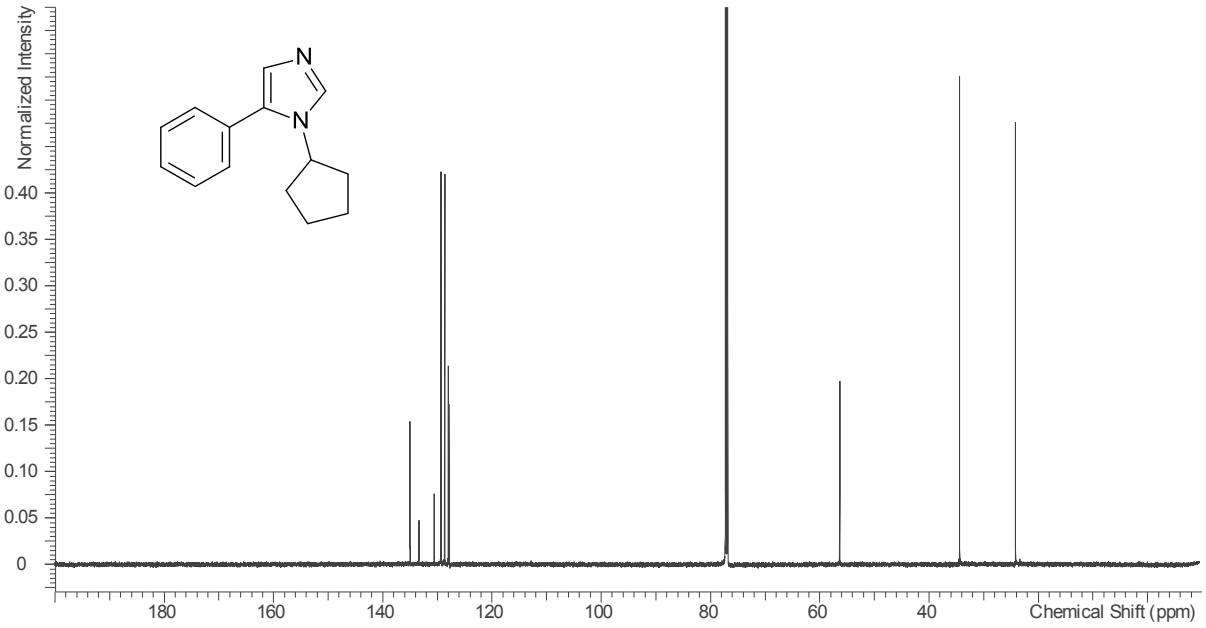
1-(Cyclopent-3-en-1-yl)-5-phenyl-1*H*-imidazole (9)



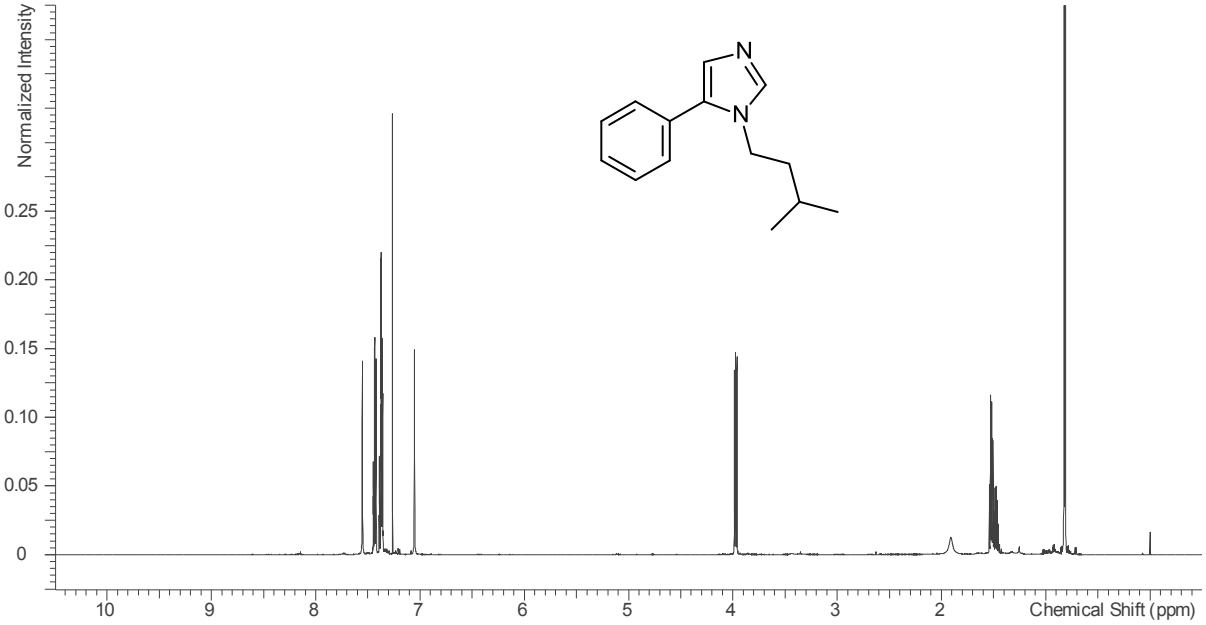


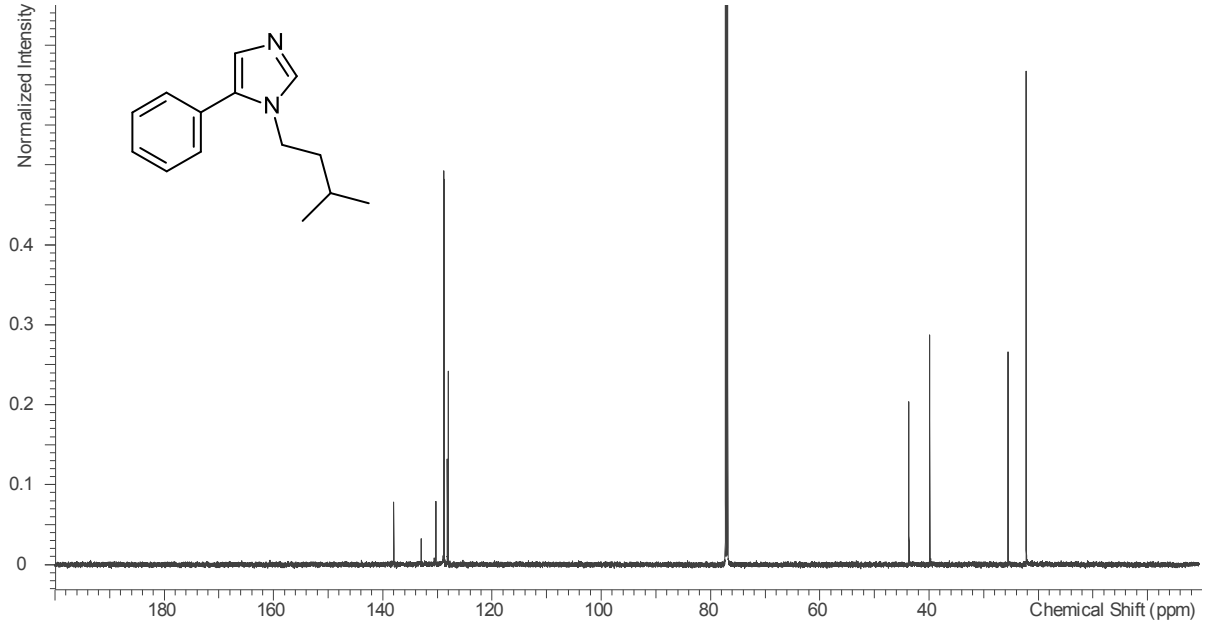
1-Cyclopentyl-5-phenyl-1*H*-imidazole (14)



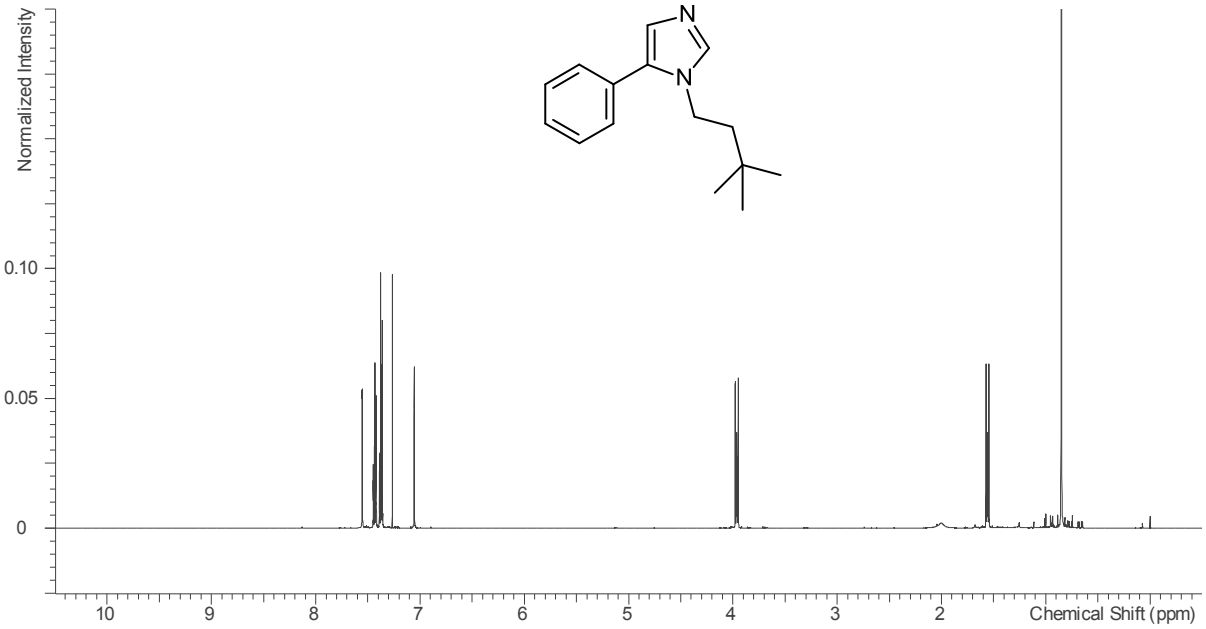


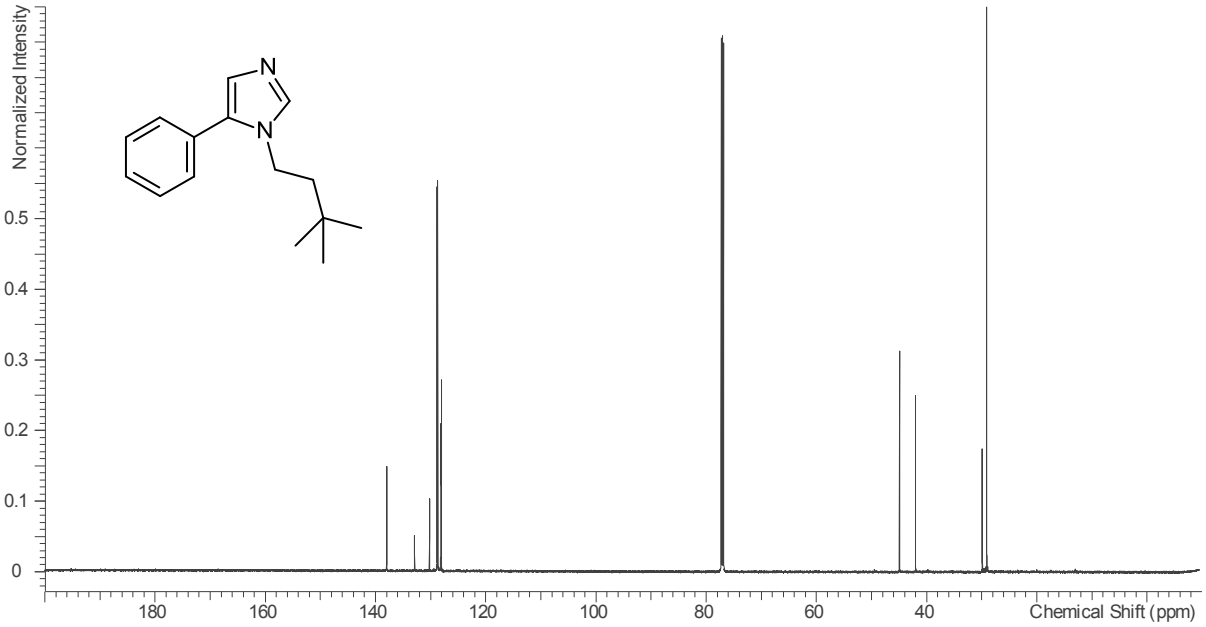
1-(3-Methyl-butyl)-5-phenyl-1*H*-imidazole (15)



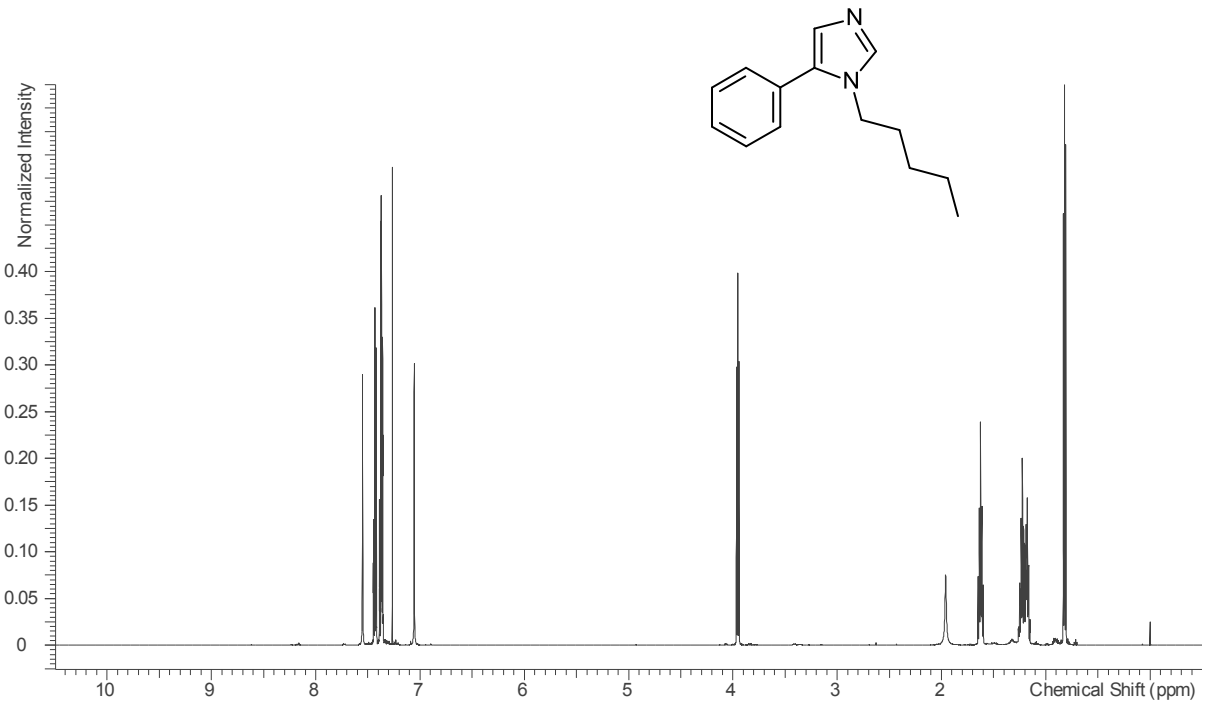


1-(3,3-Dimethyl-butyl)-5-phenyl-1*H*-imidazole (16)

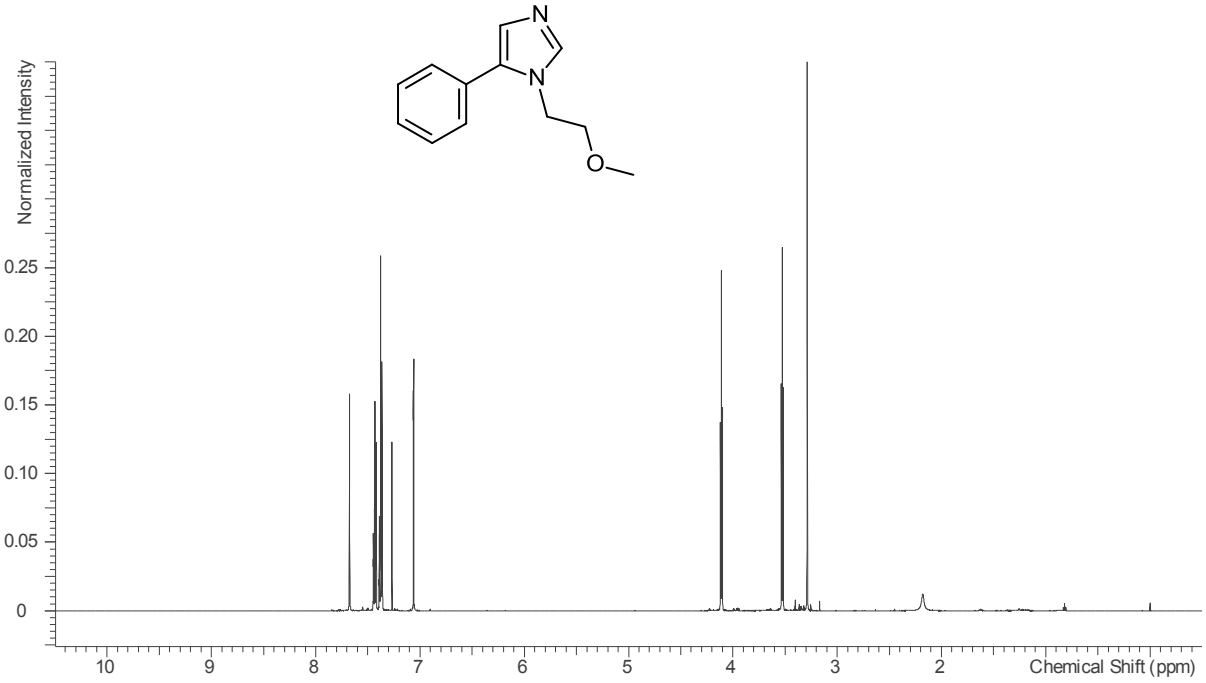


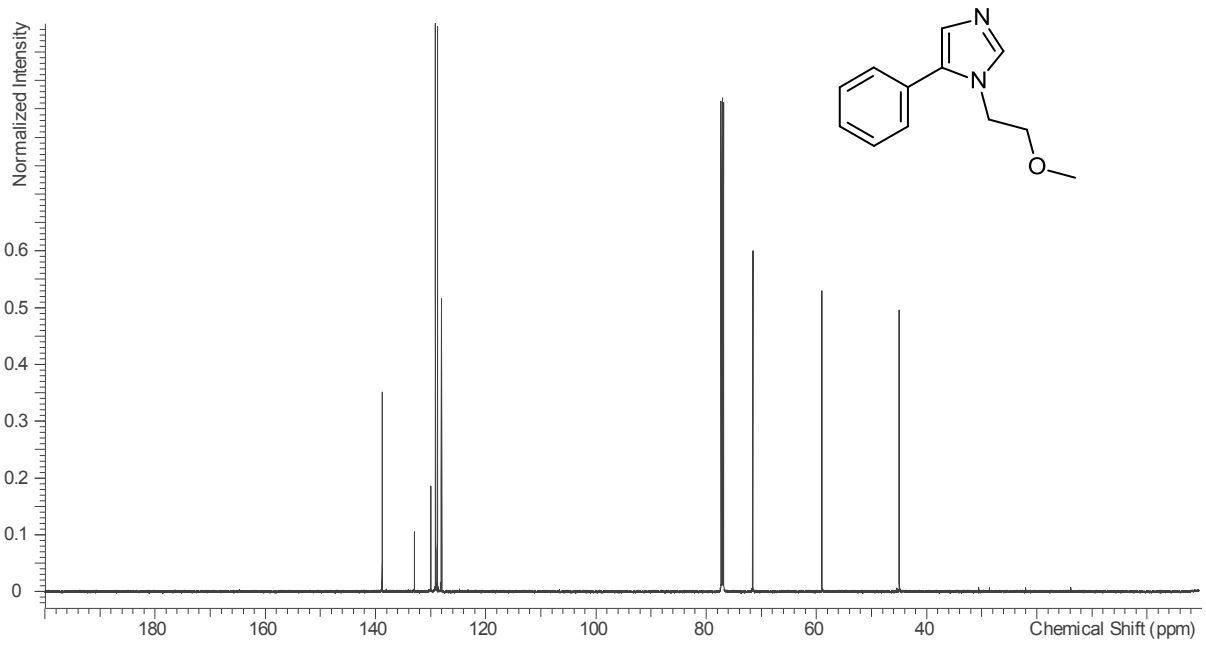


1-Pentyl-5-phenyl-1*H*-imidazole (17)

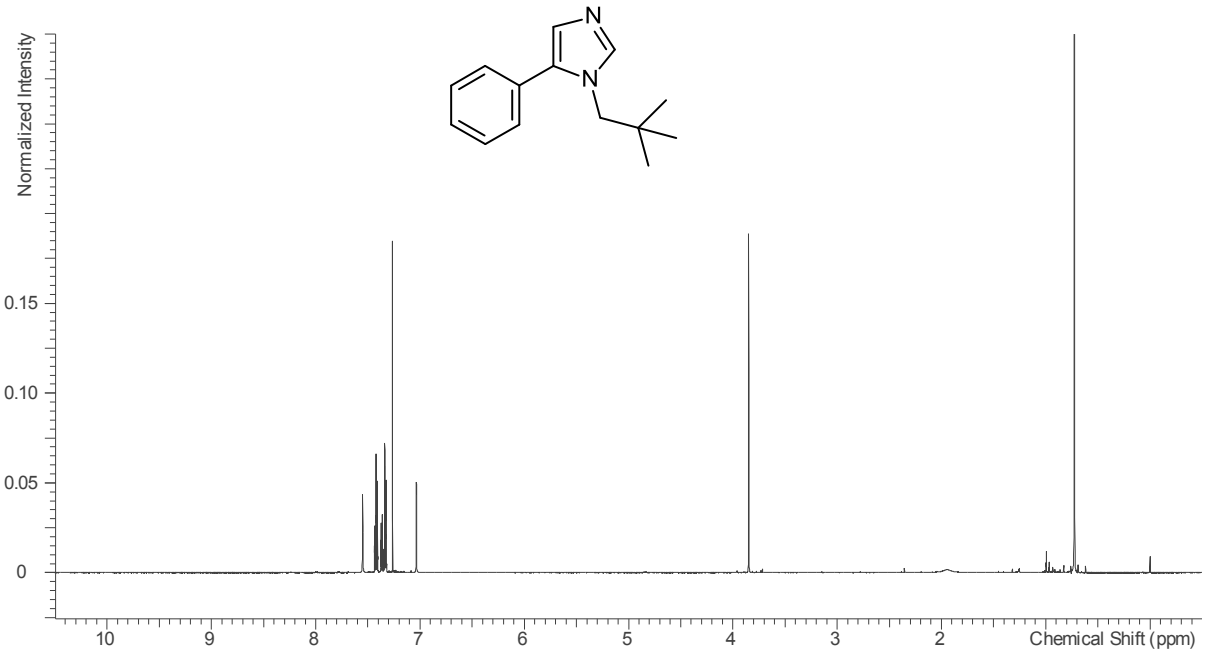


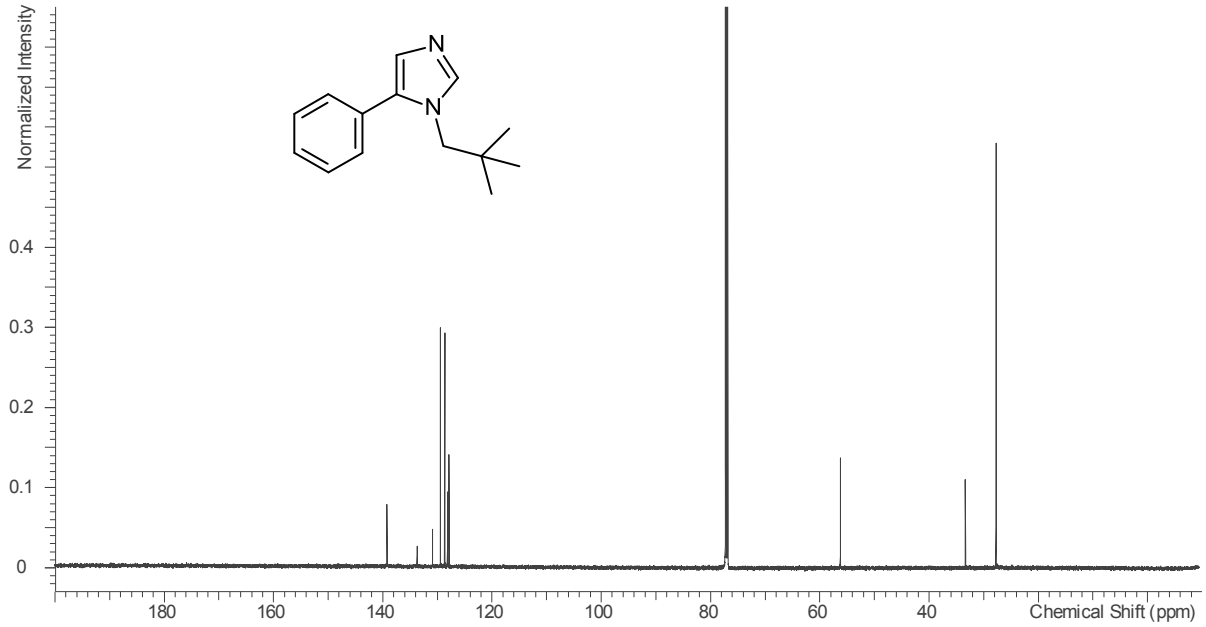
1-(2-Methoxy-ethyl)-5-phenyl-1*H*-imidazole (18)



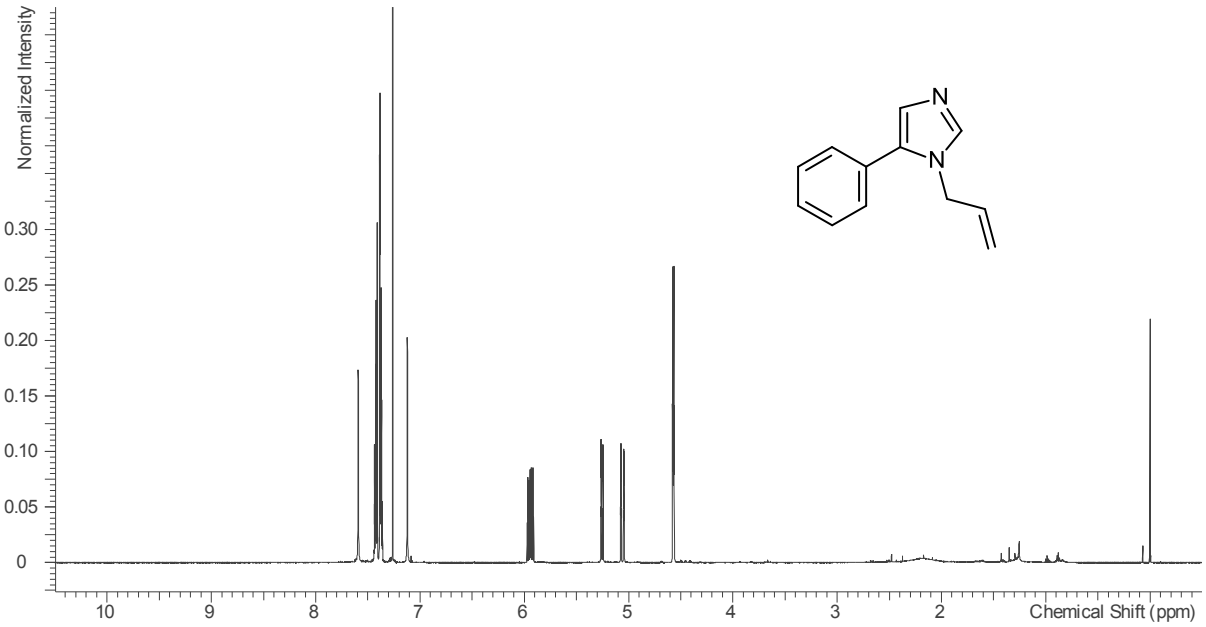


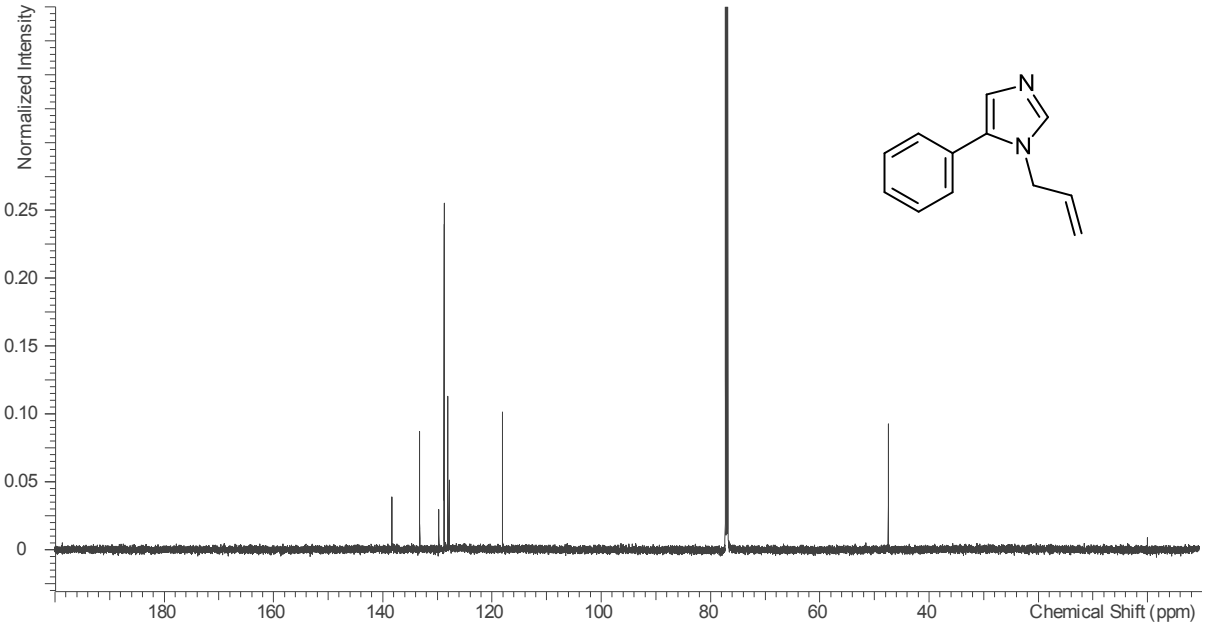
1-(2,2-Dimethyl-propyl)-5-phenyl-1*H*-imidazole (19)



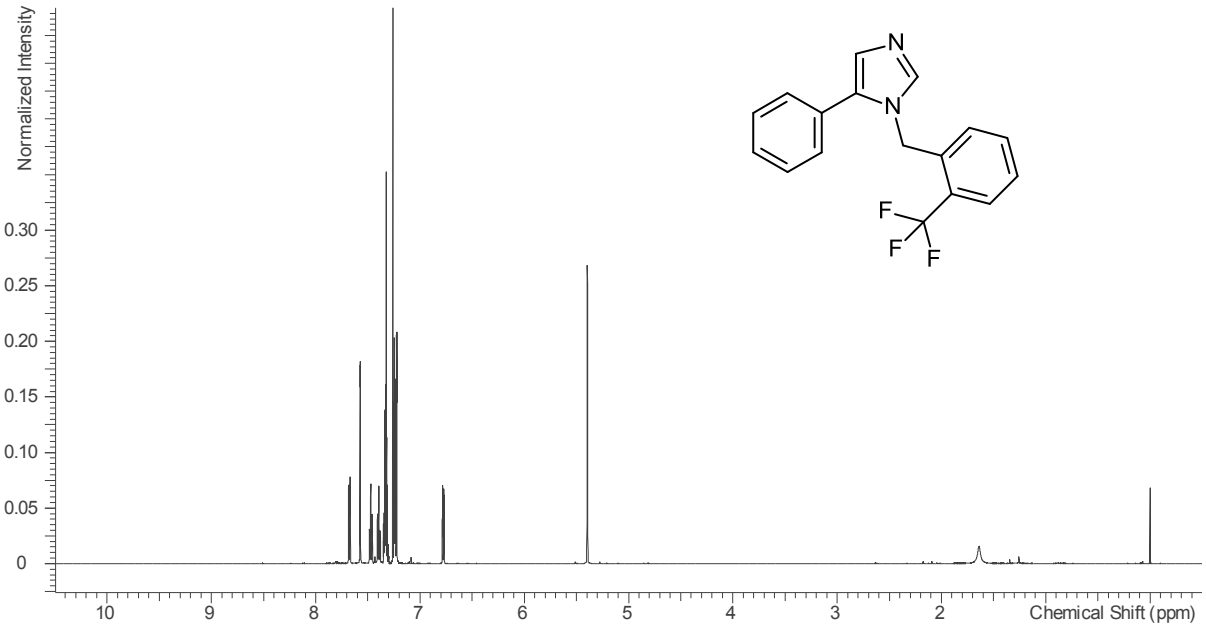


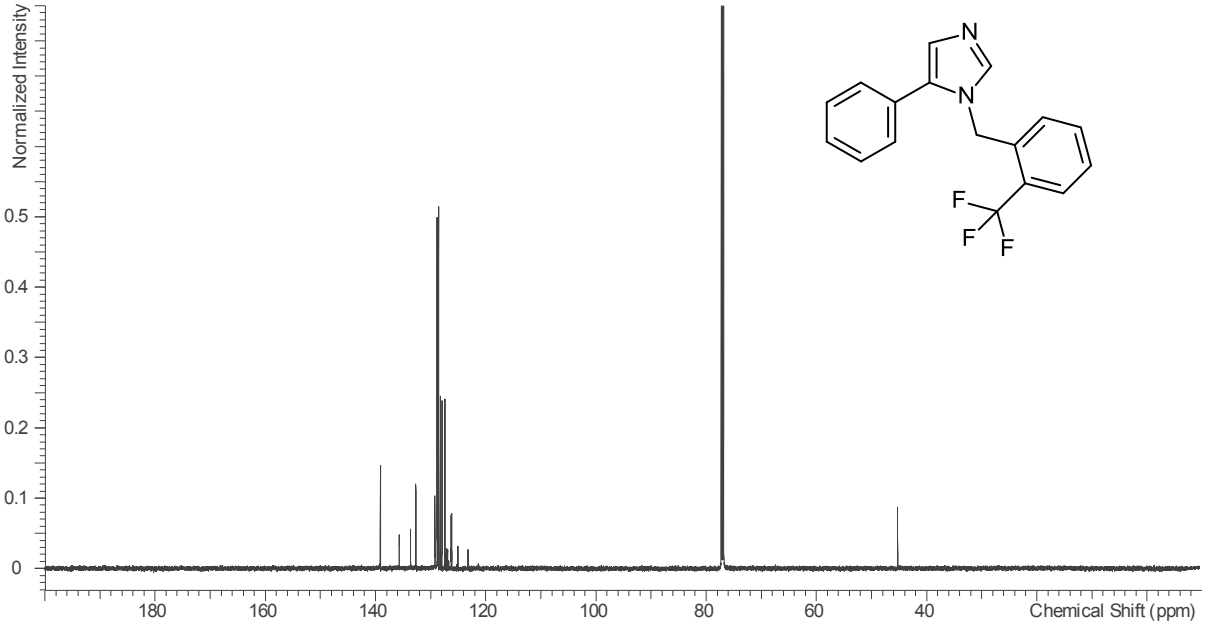
1-Allyl-5-phenyl-1*H*-imidazole (20)

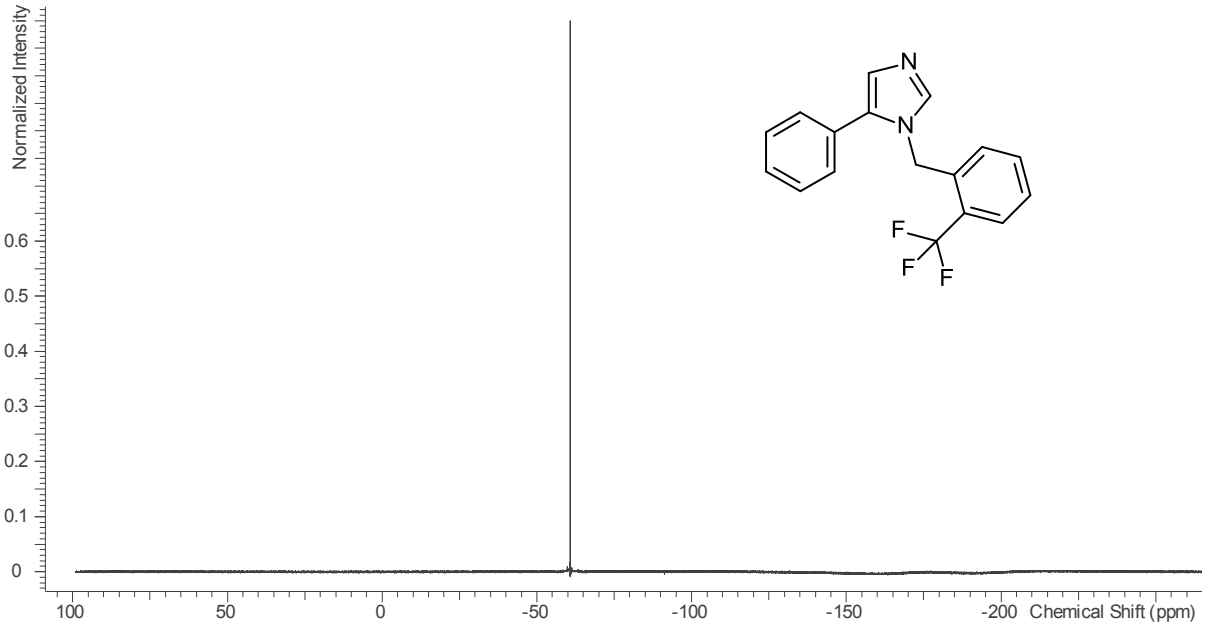




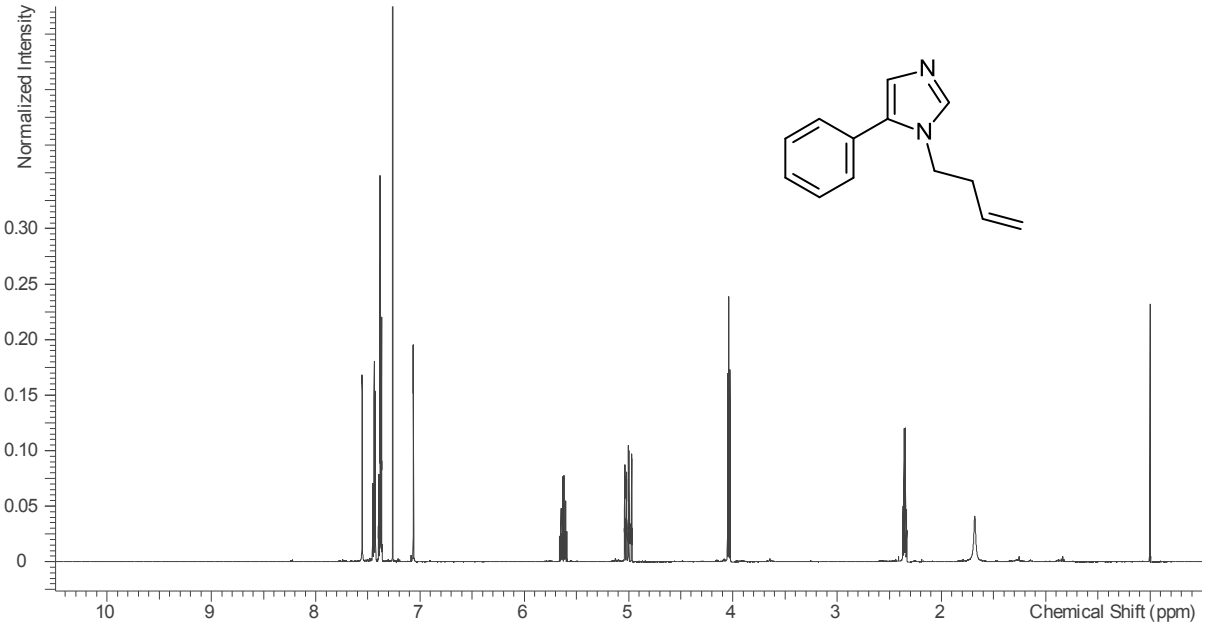
5-Phenyl-1-(2-trifluoromethyl-benzyl)-1*H*-imidazole (21)

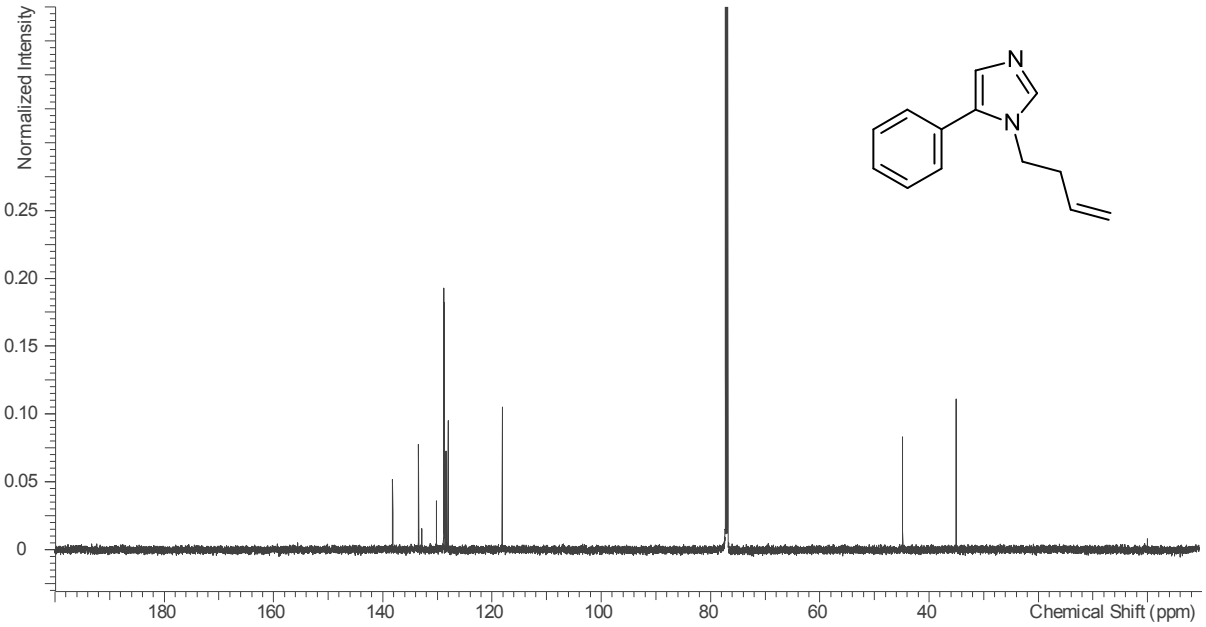




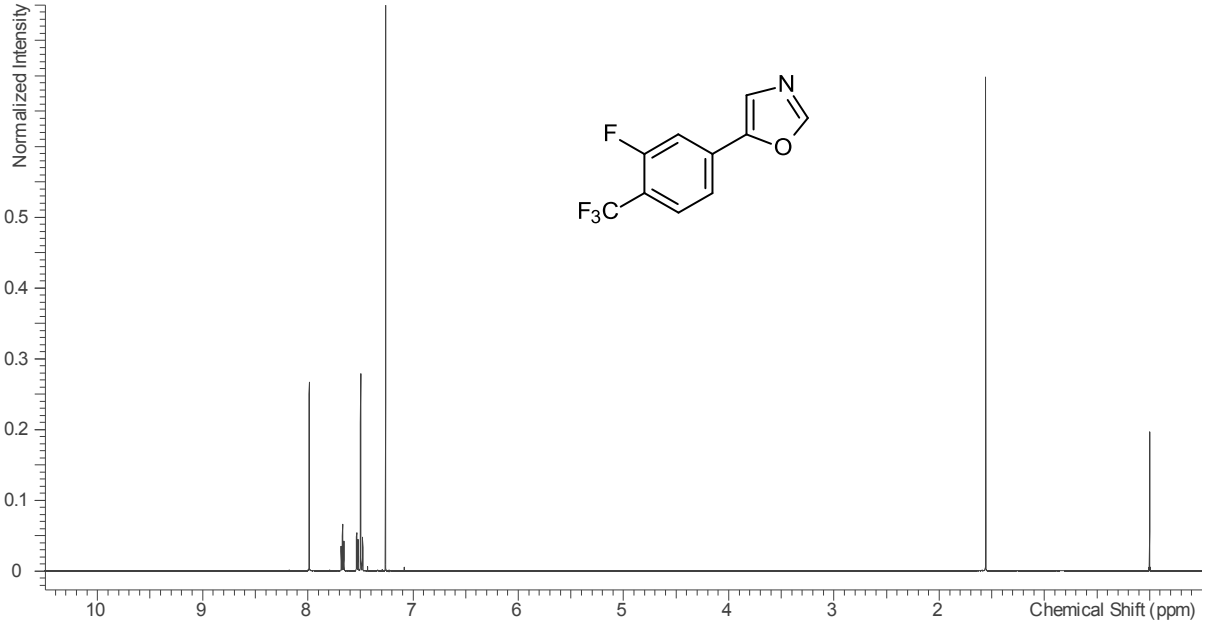

Normalized Intensity
0.6
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
N
N
F
F
F

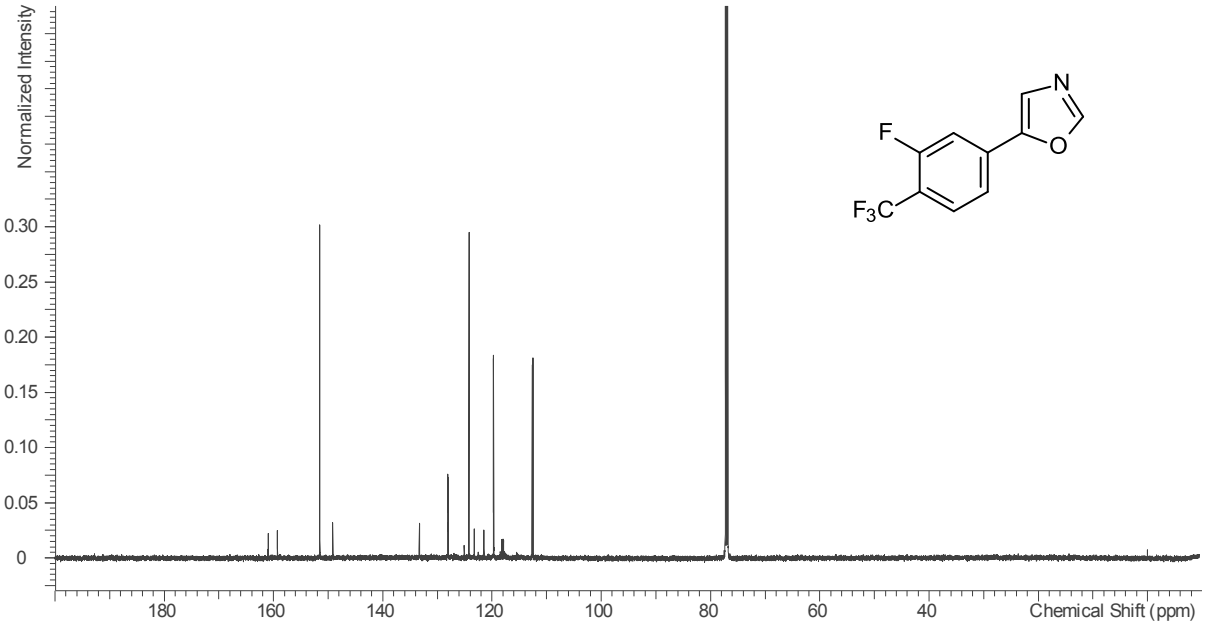
1-But-3-enyl-5-phenyl-1*H*-imidazole (22)

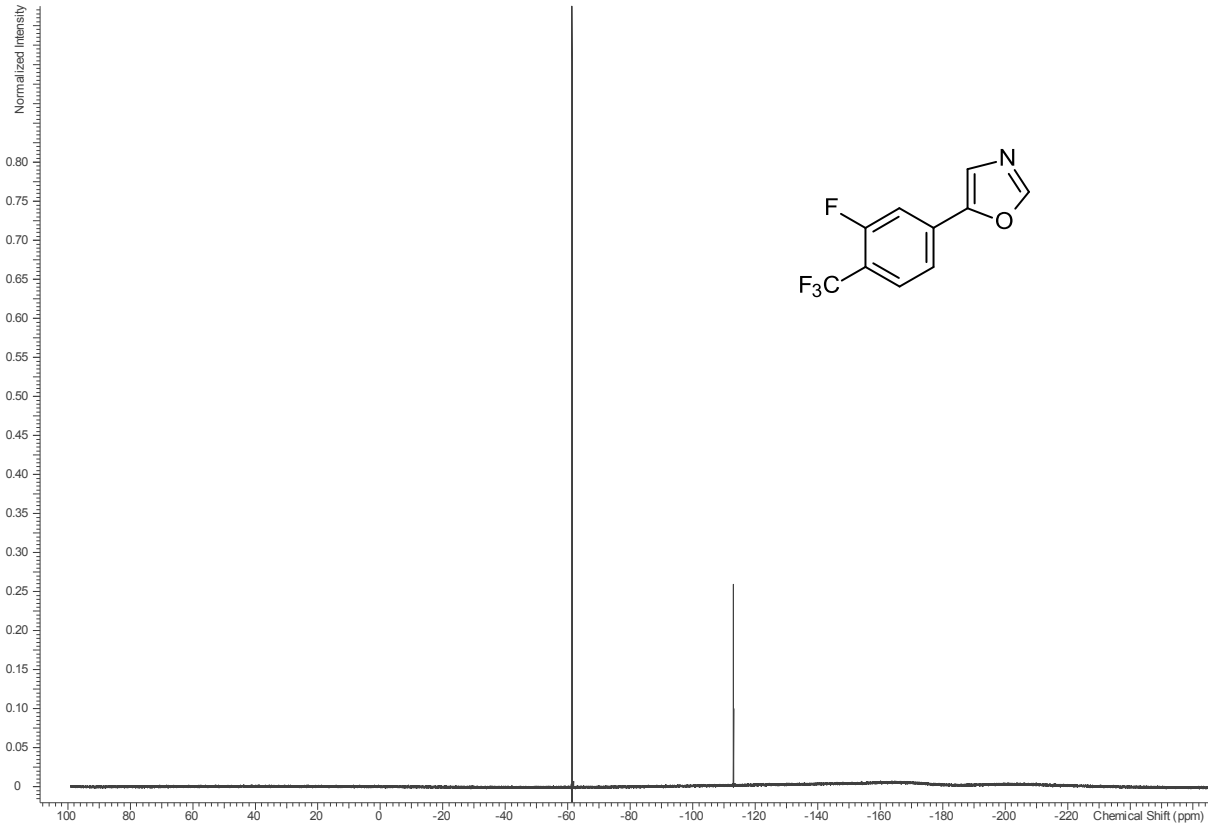




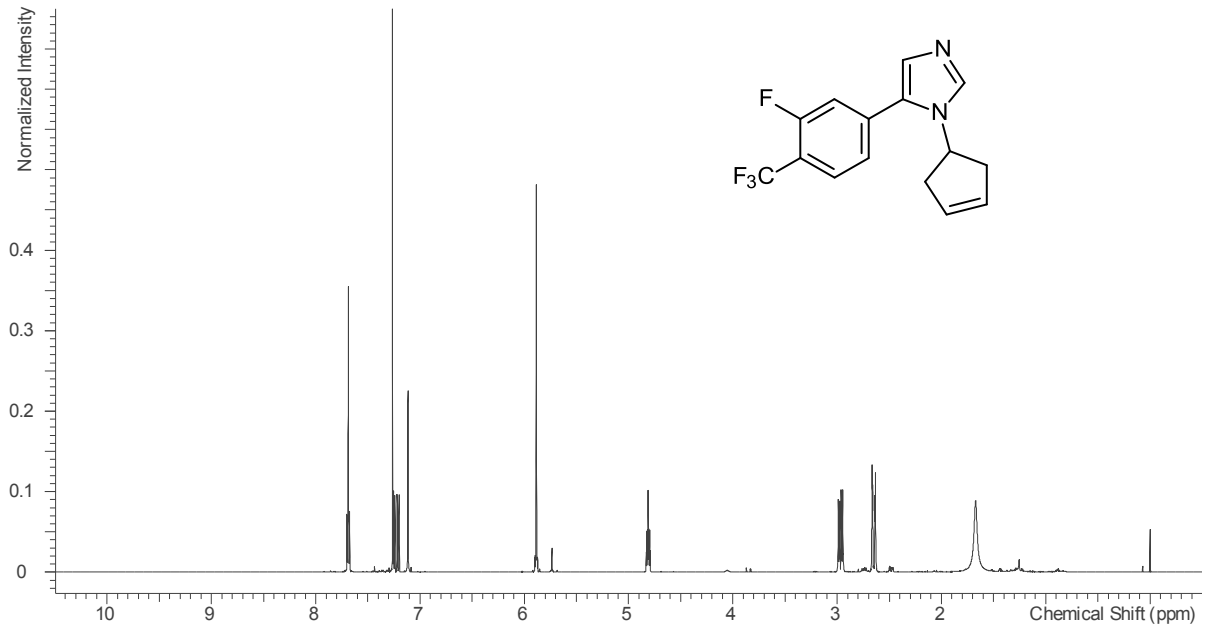
5-(3-Fluoro-4-trifluoromethyl-phenyl)-oxazole

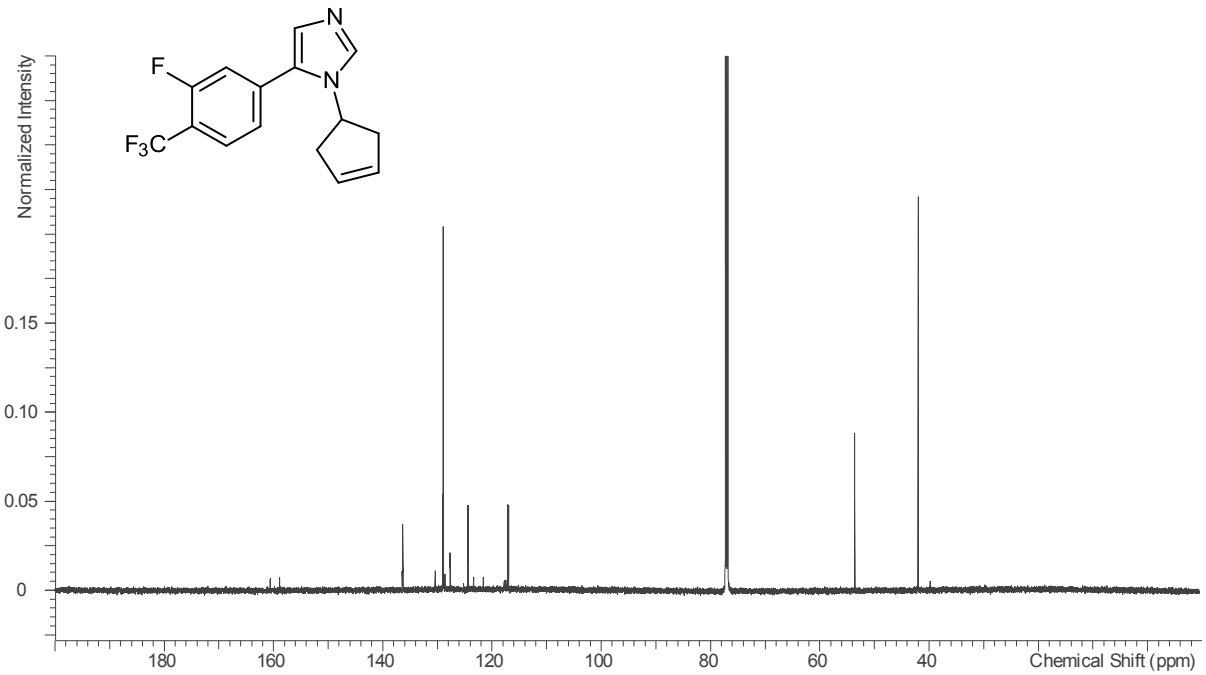


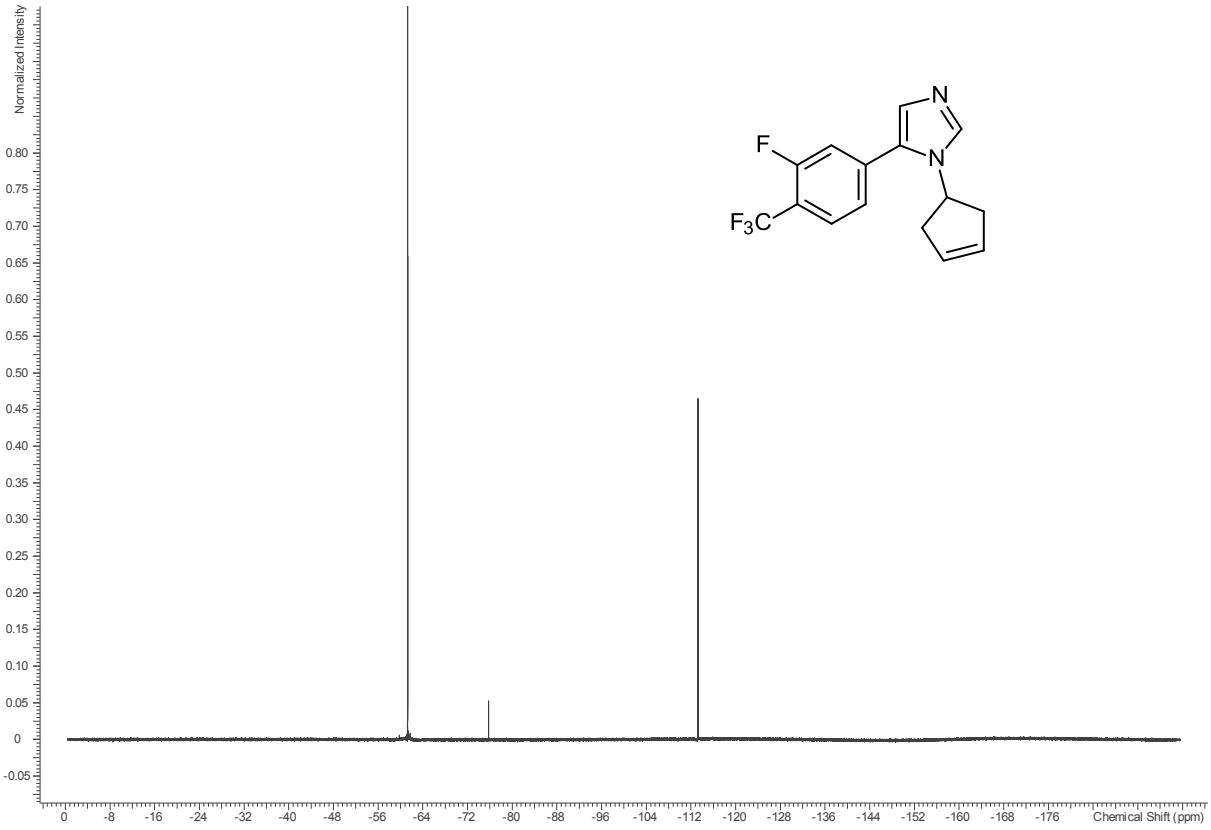



Normalized Intensity
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
Chemical Shift (ppm)
N
O
F
F3C

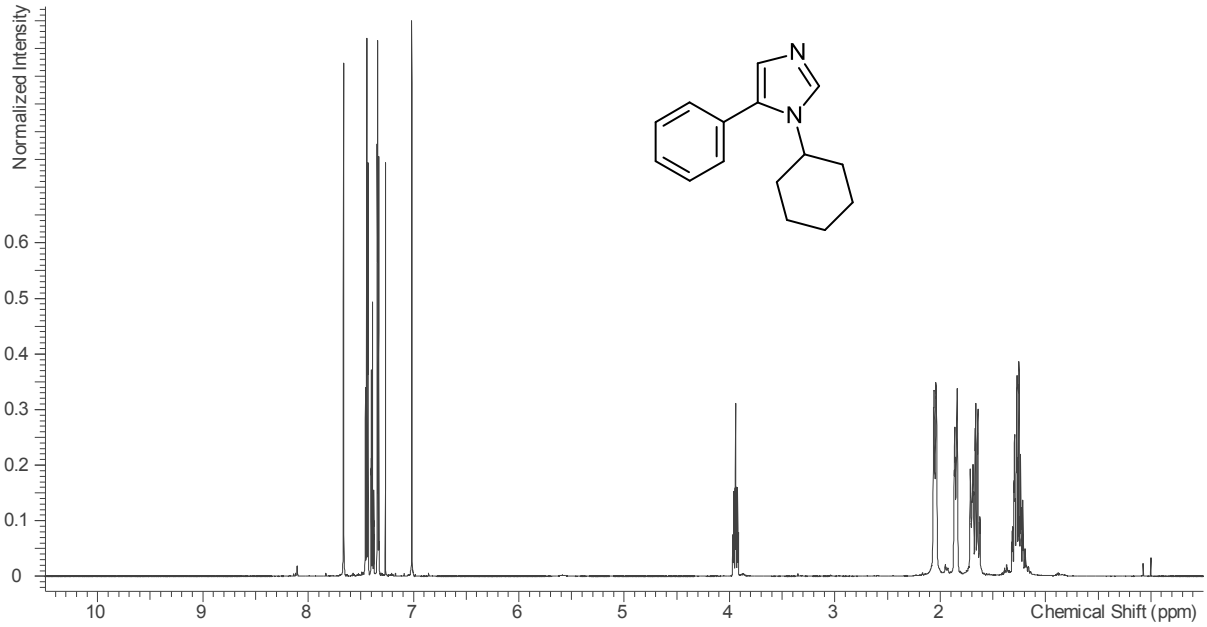
1-(Cyclopent-3-en-1-yl)-5-(3-fluoro-4-(trifluoromethyl)phenyl)-1*H*-imidazole (23)

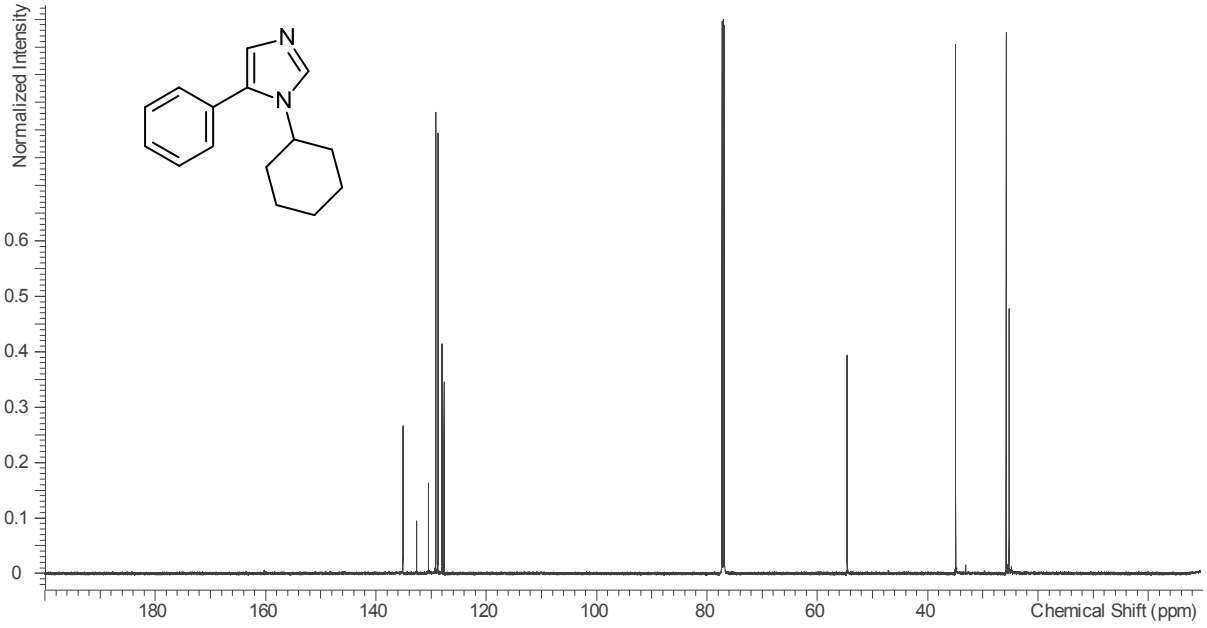




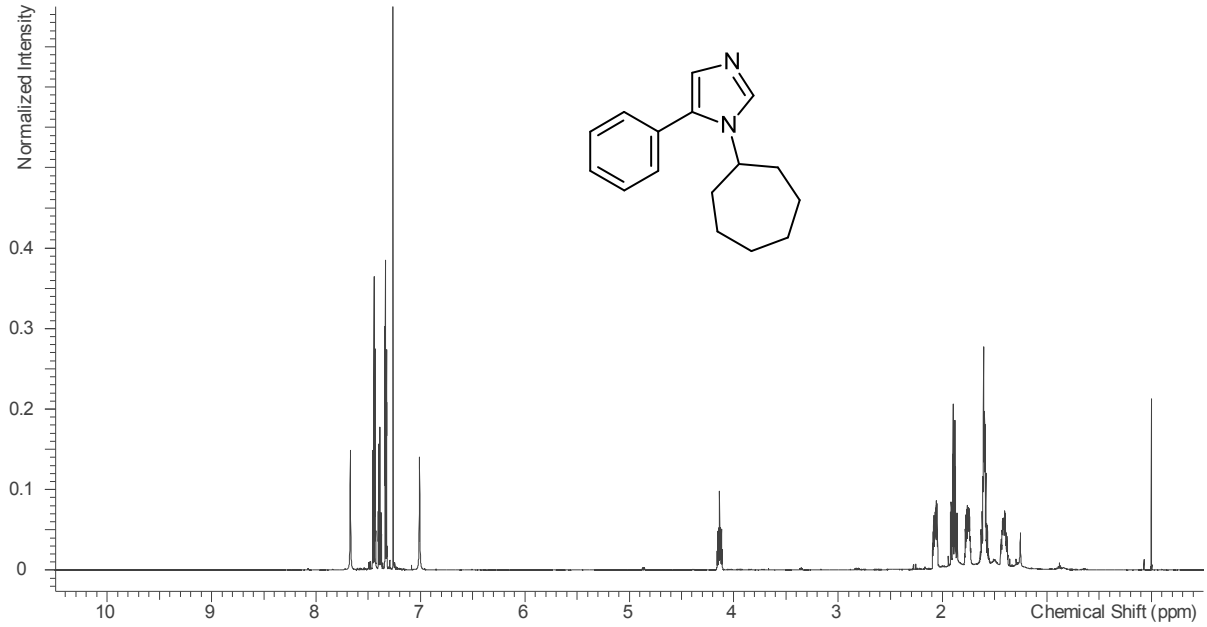

Normalized Intensity
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-8
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
Chemical Shift (ppm)
F
F3C
N
N

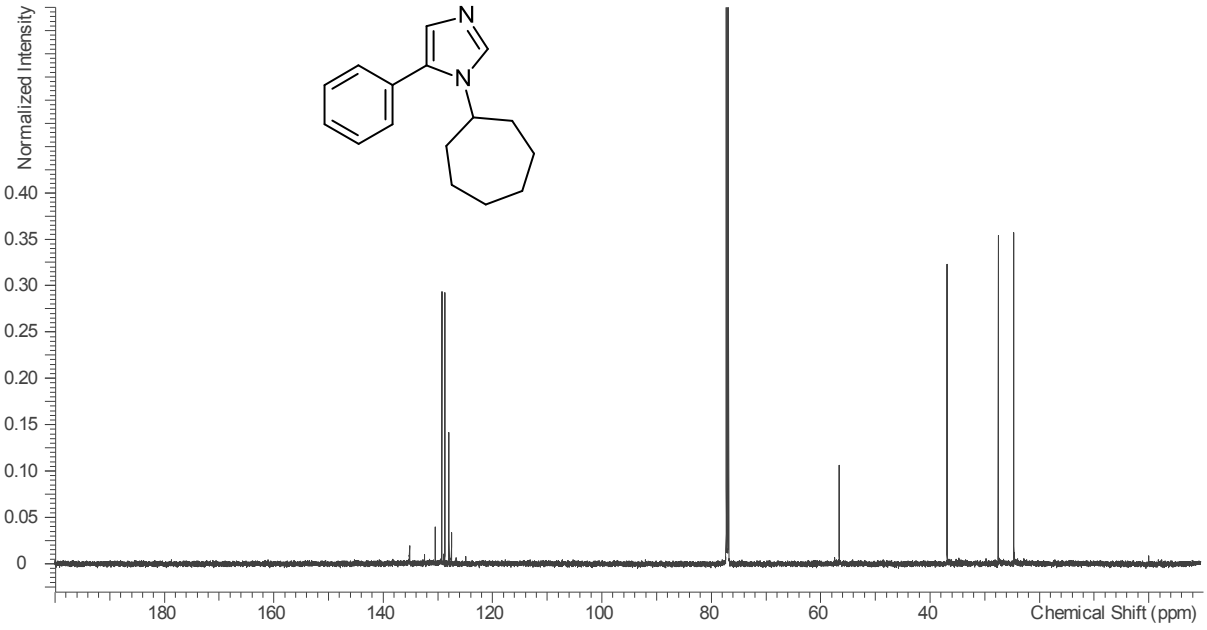
1-Cyclohexyl-5-phenyl-1*H*-imidazole (24)



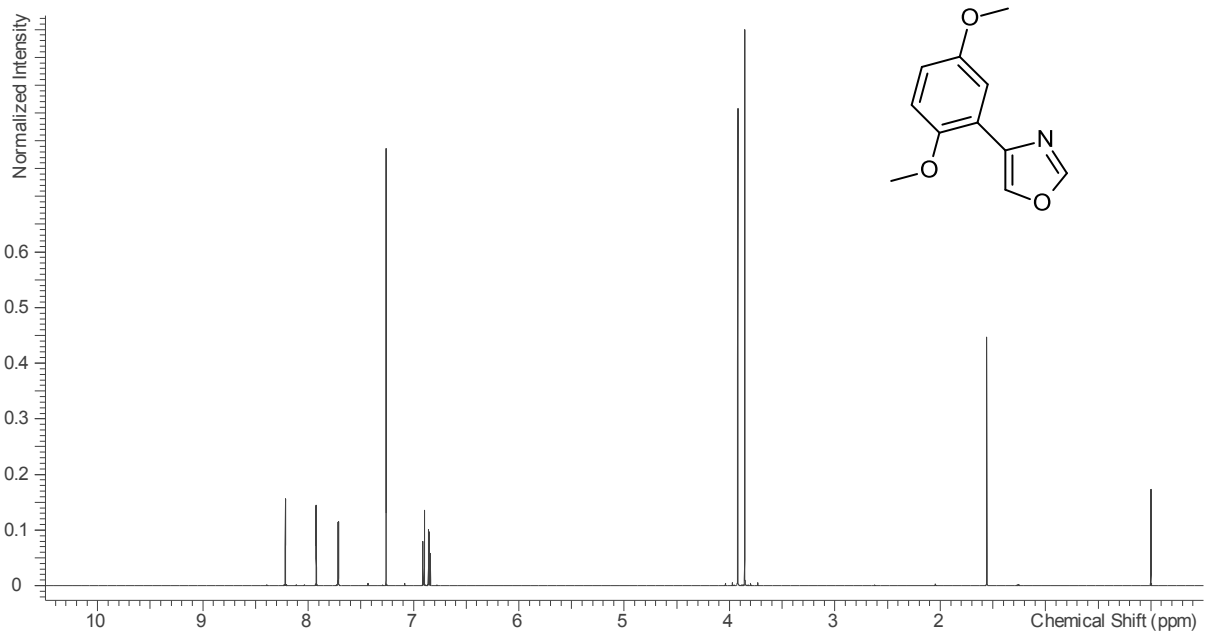


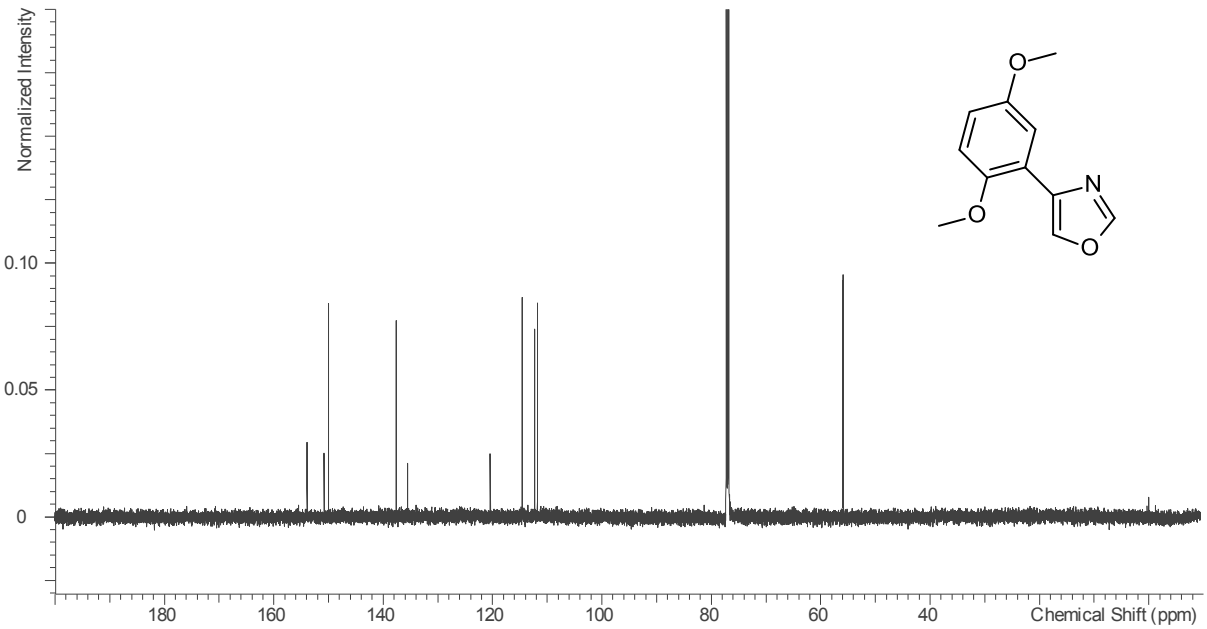
1-Cycloheptyl-5-phenyl-1*H*-imidazole (25)



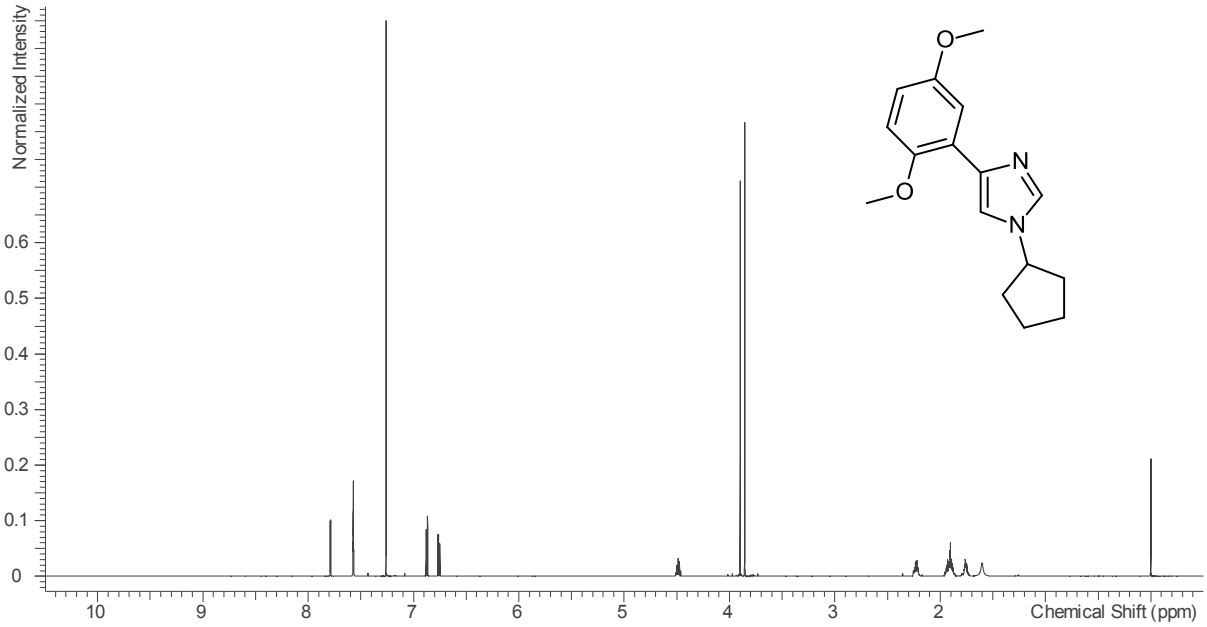


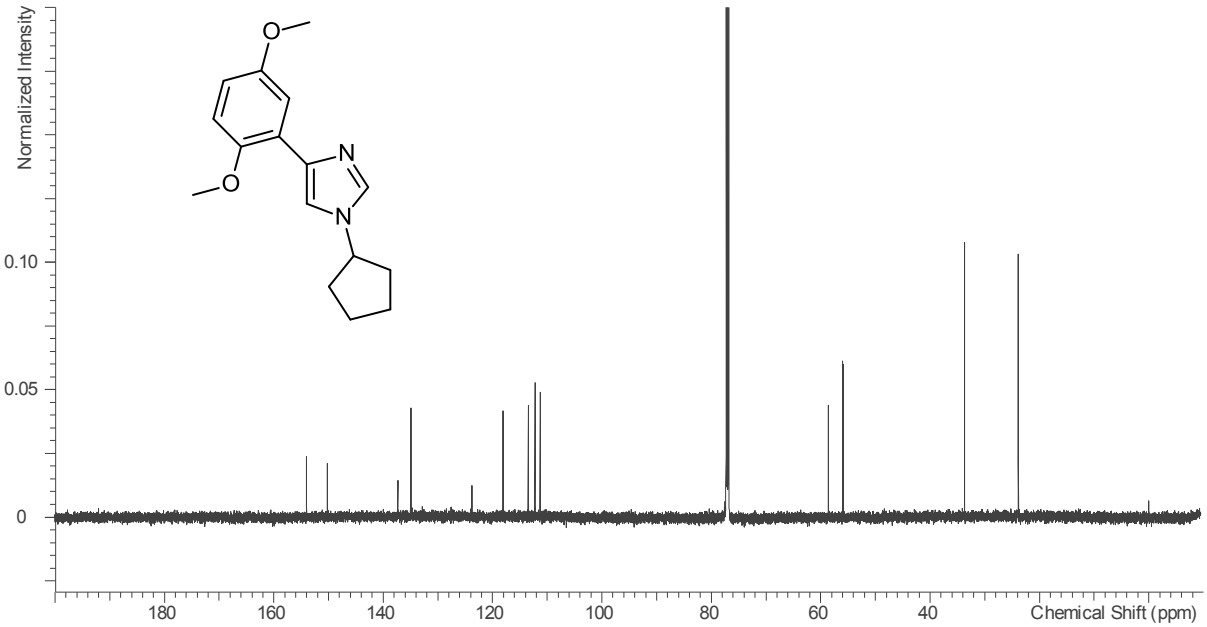
4-(2,5-Dimethoxy-phenyl)-oxazole



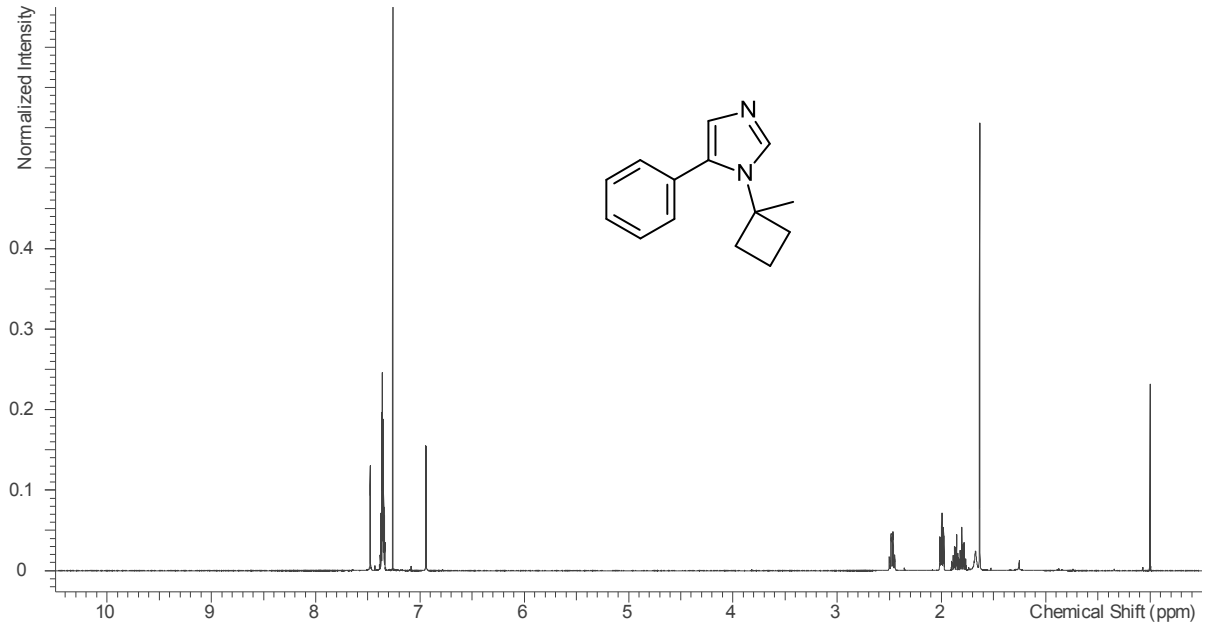


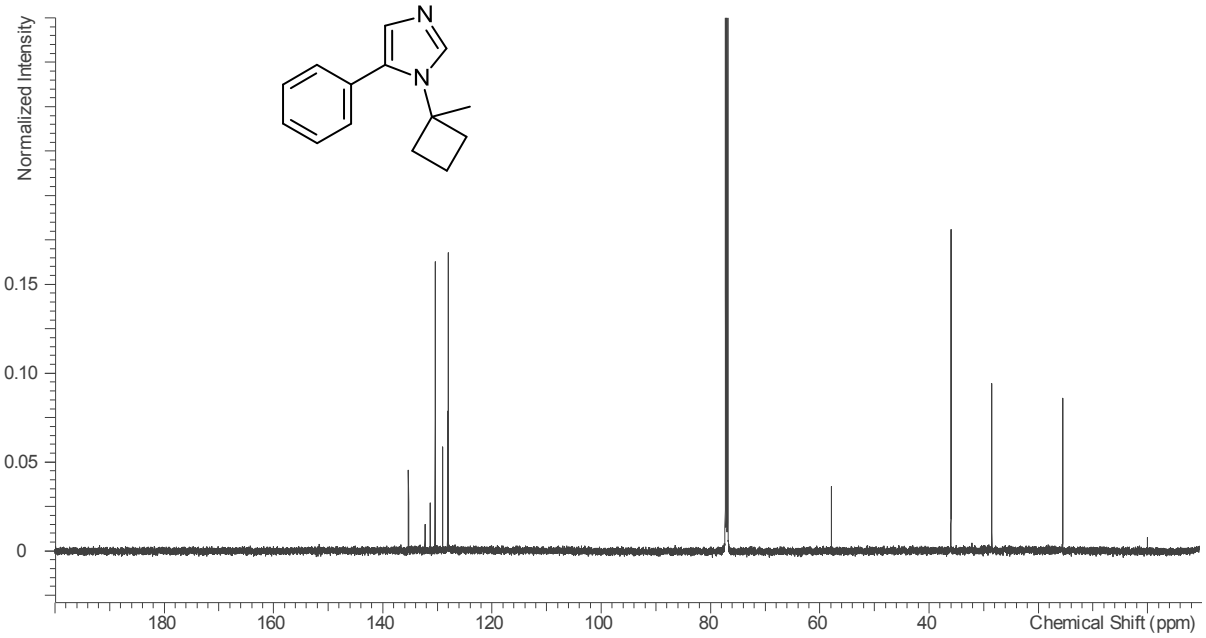
1-Cyclopentyl-4-(2,5-dimethoxy-phenyl)-1*H*-imidazole (26)



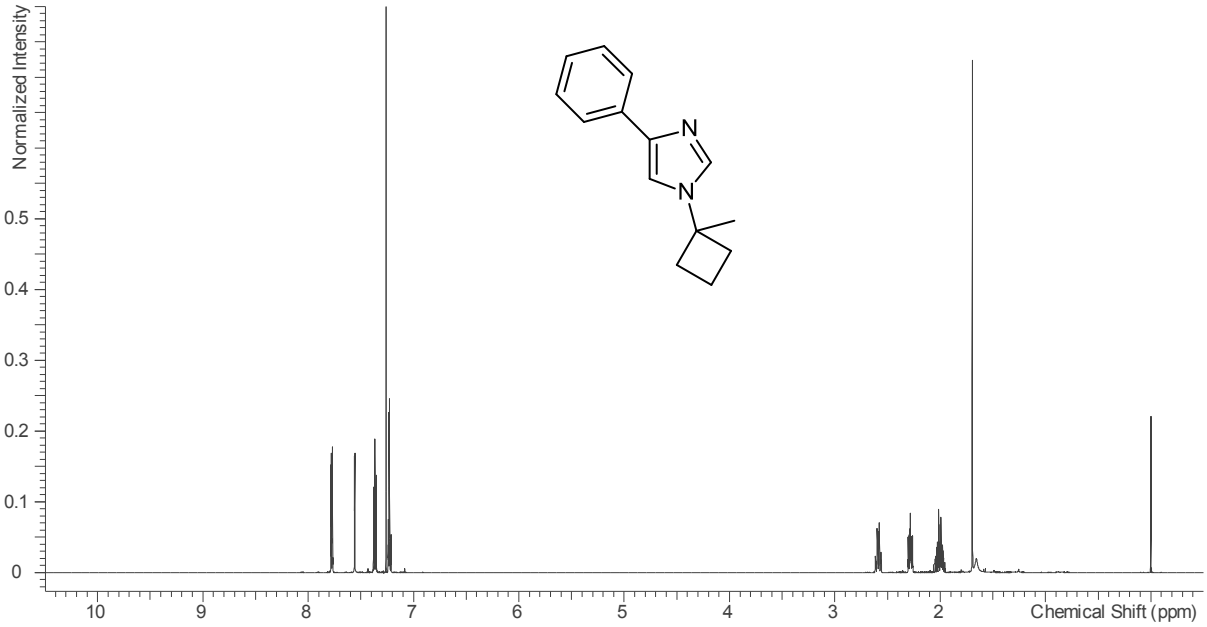


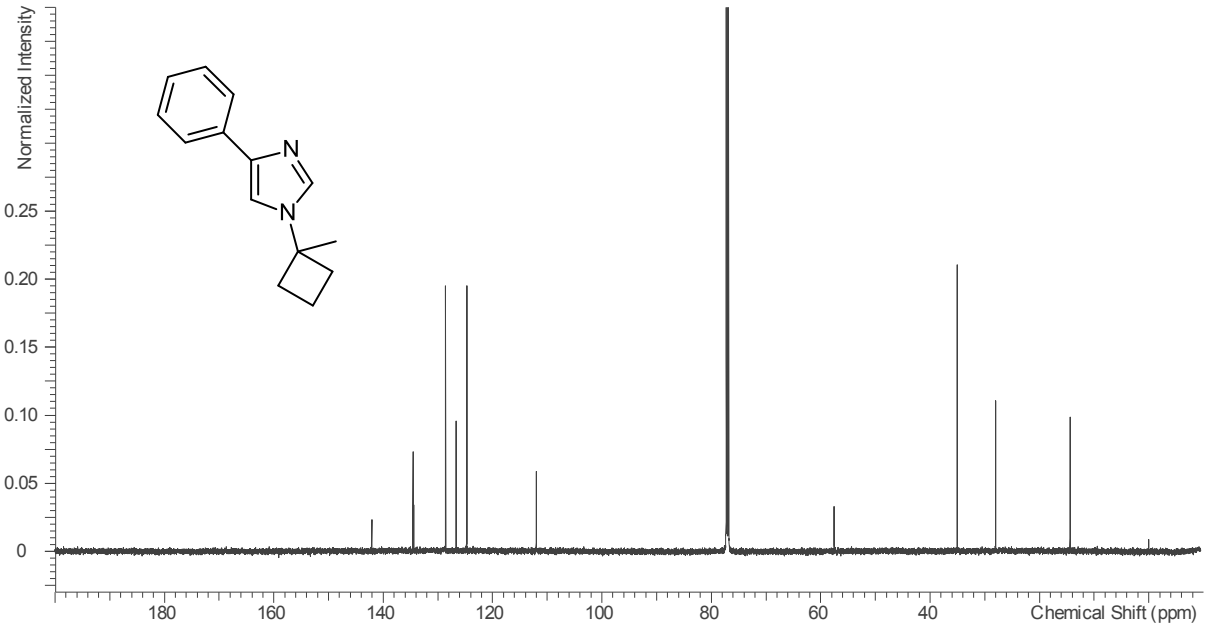
1-(1-Methyl-cyclobutyl)-5-phenyl-1*H*-imidazole (27)



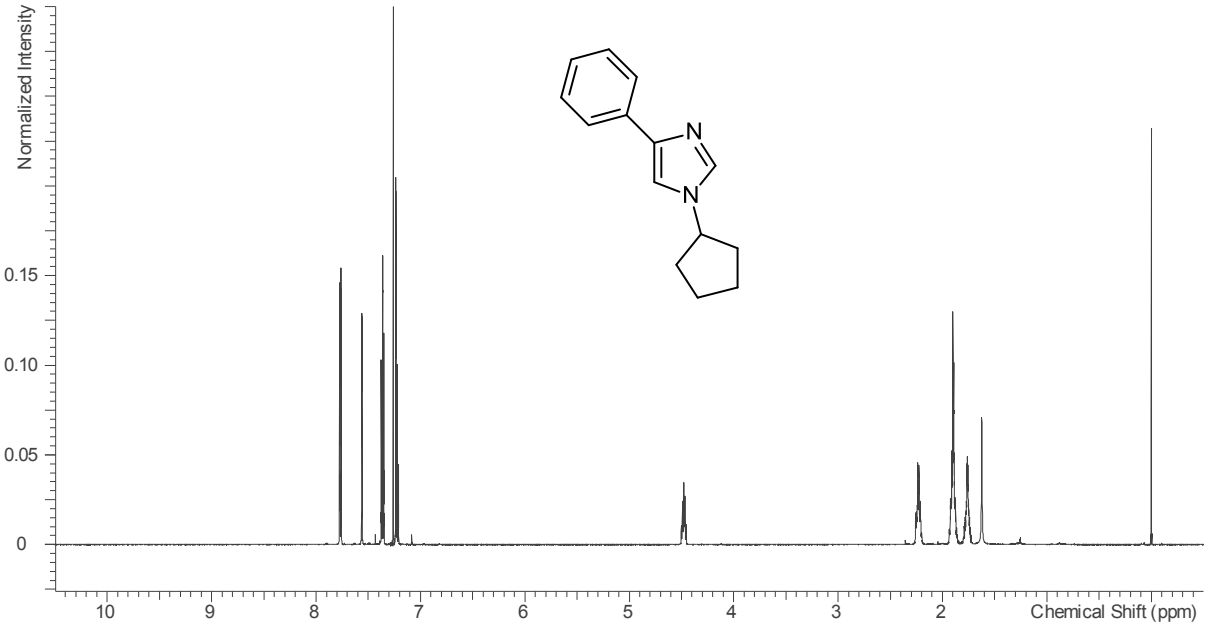


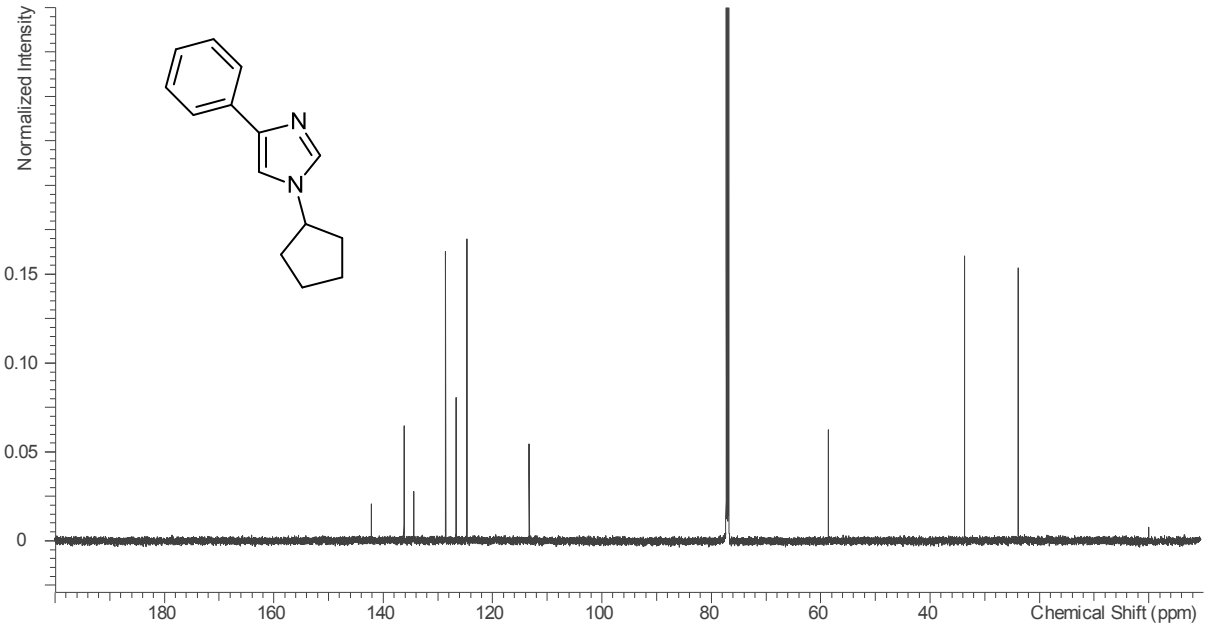
1-(1-Methyl-cyclobutyl)-4-phenyl-1*H*-imidazole (28)



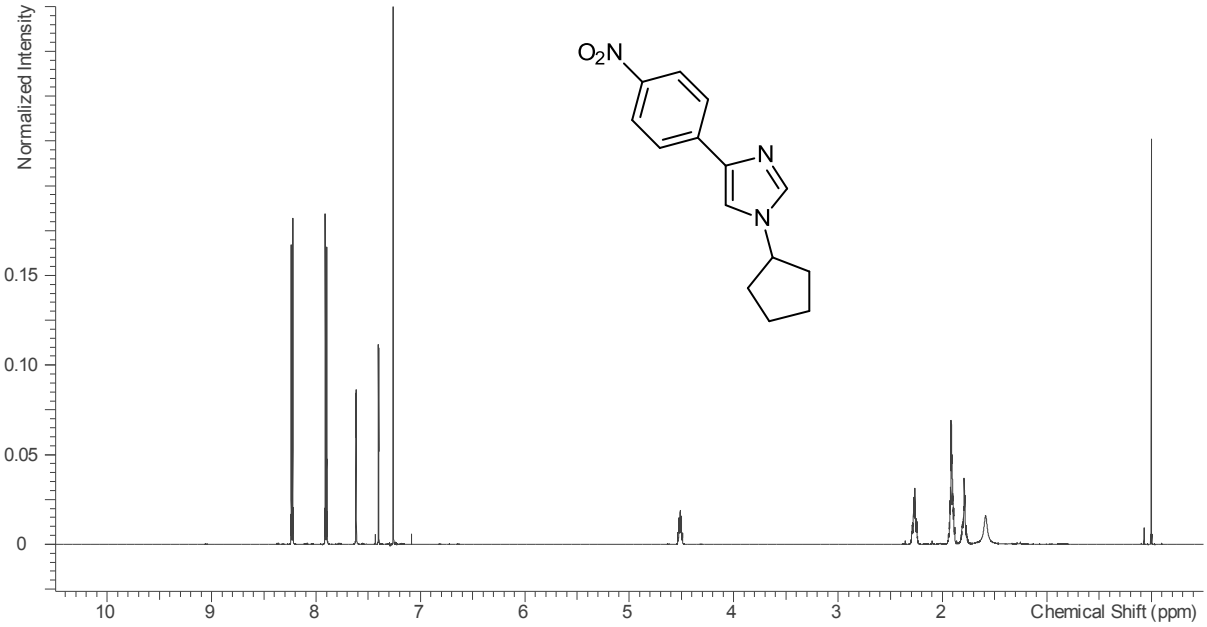


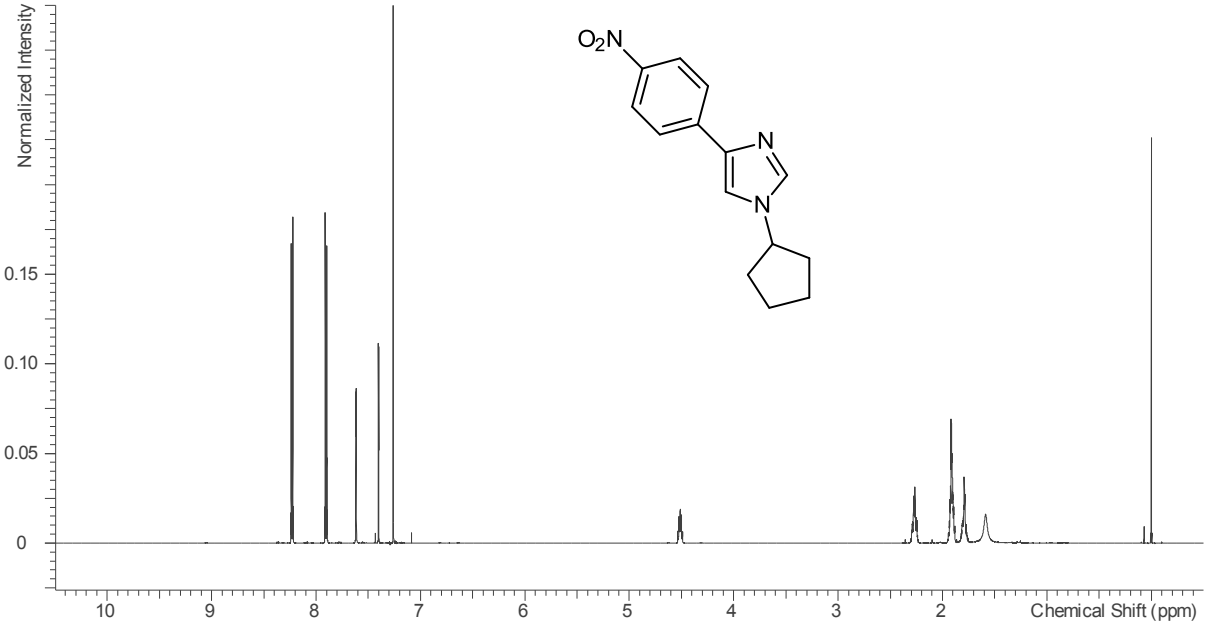
1-Cyclopentyl-4-phenyl-1*H*-imidazole (29)



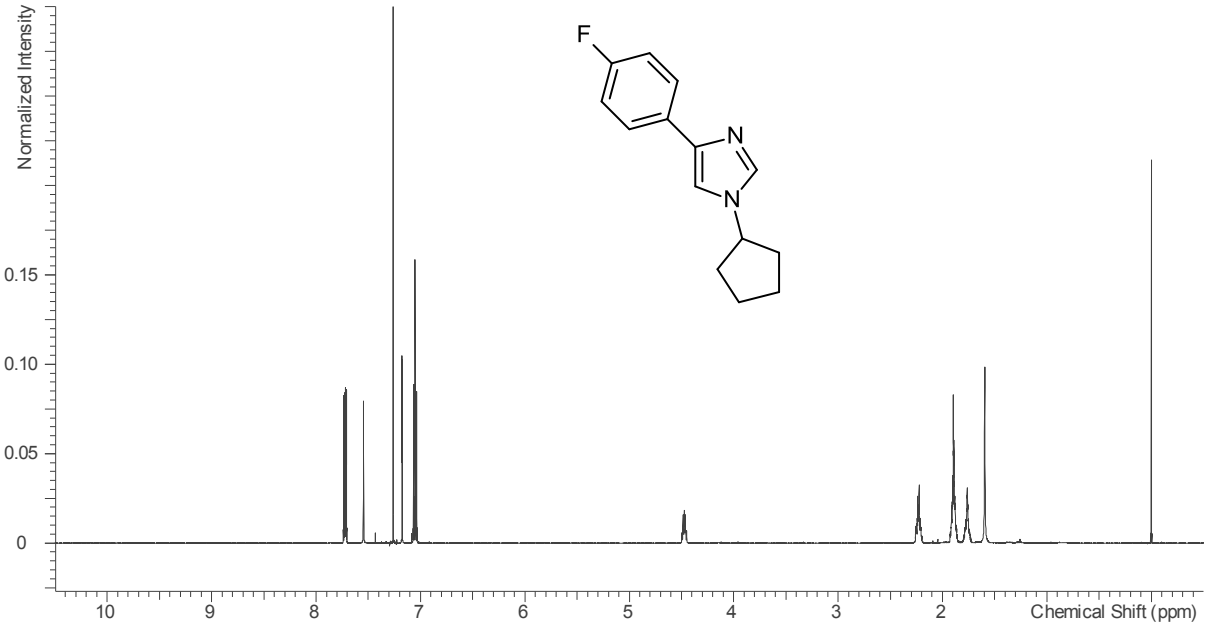


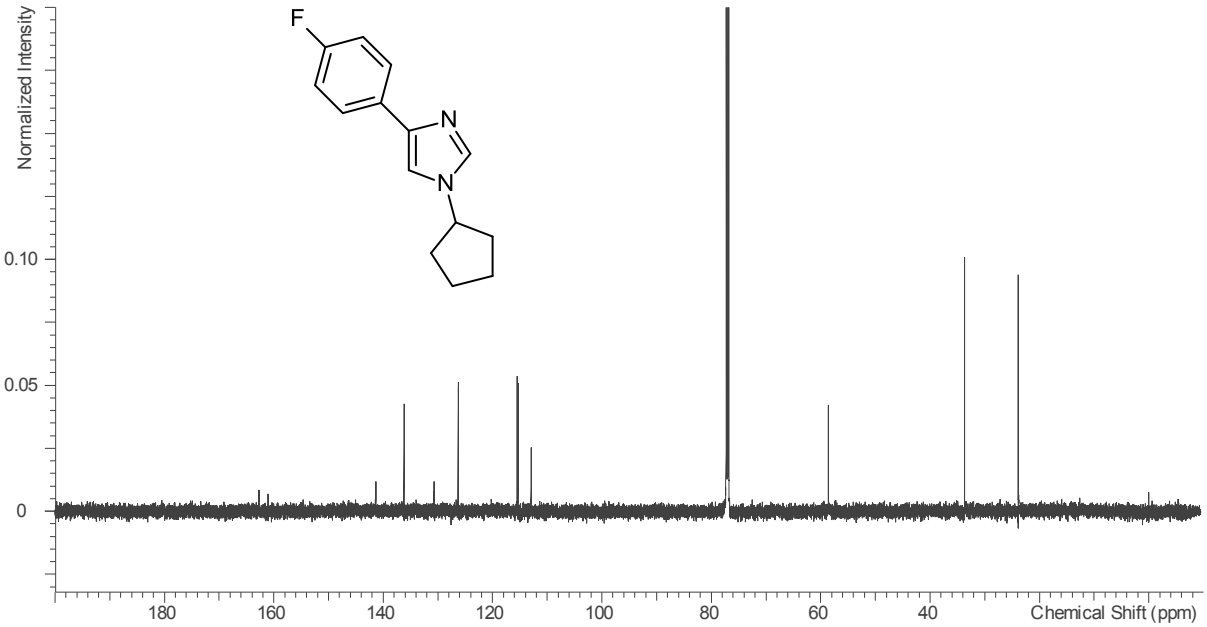
1-Cyclopentyl-4-(4-nitro-phenyl)-1*H*-imidazole (30)

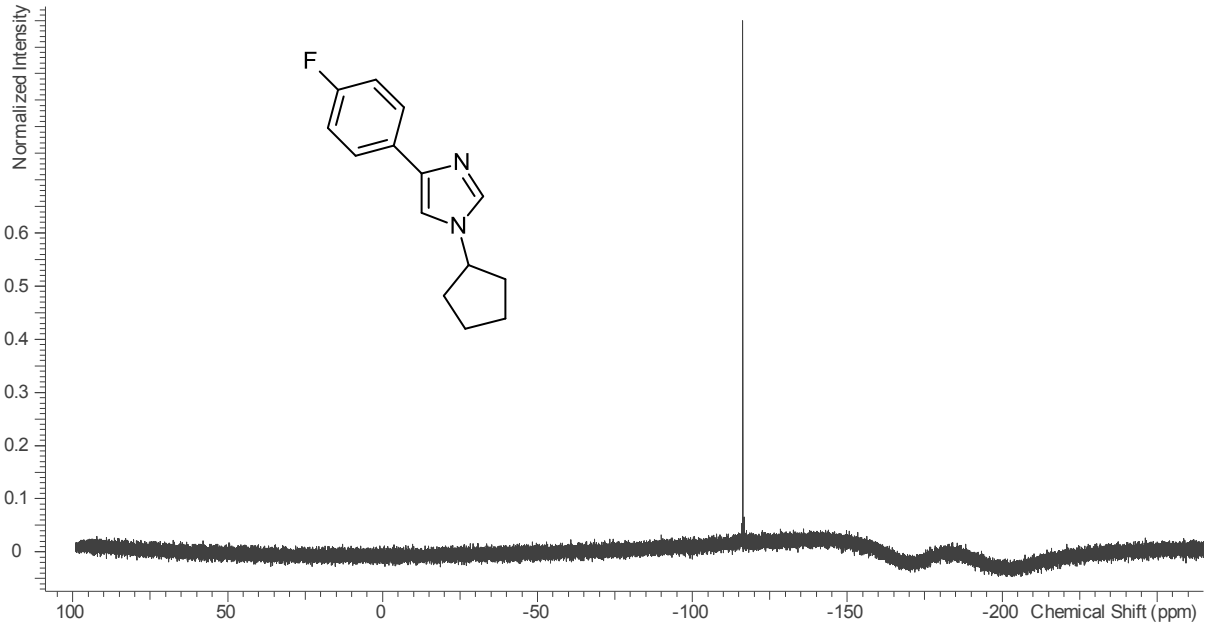




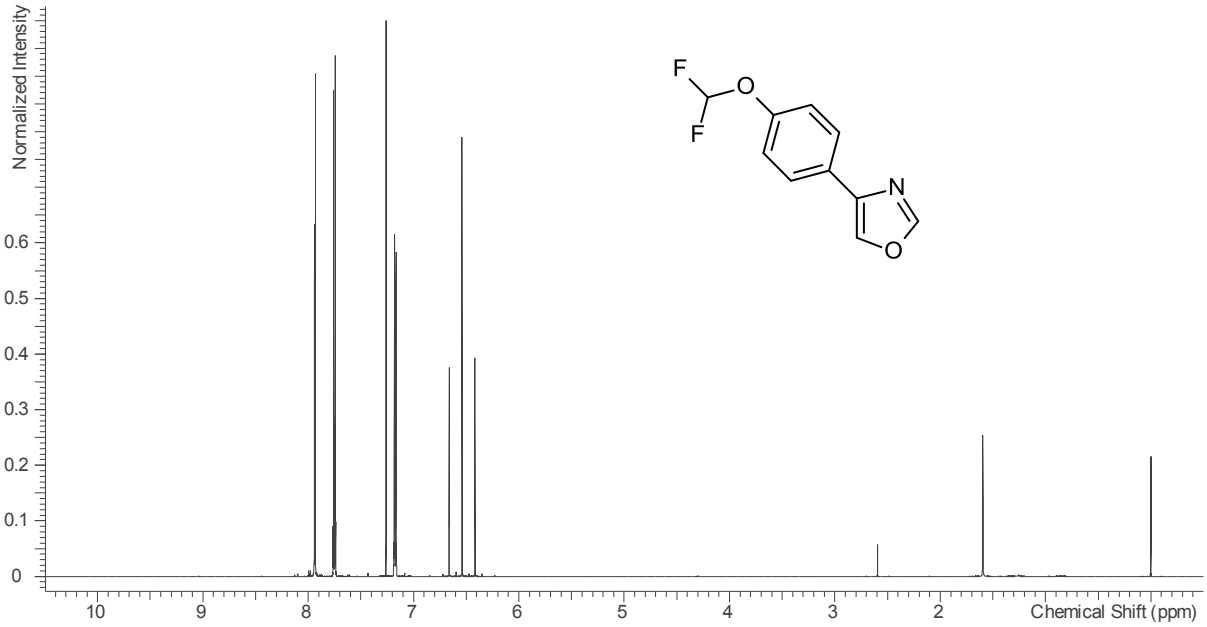
1-Cyclopentyl-4-(4-fluoro-phenyl)-1*H*-imidazole (31)

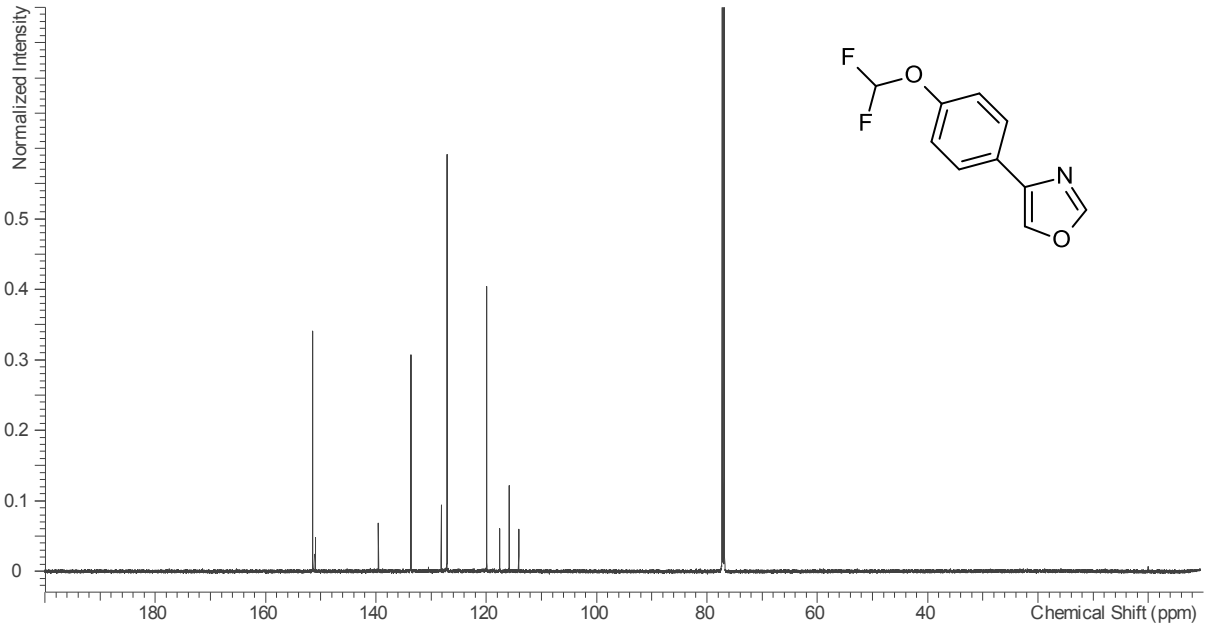


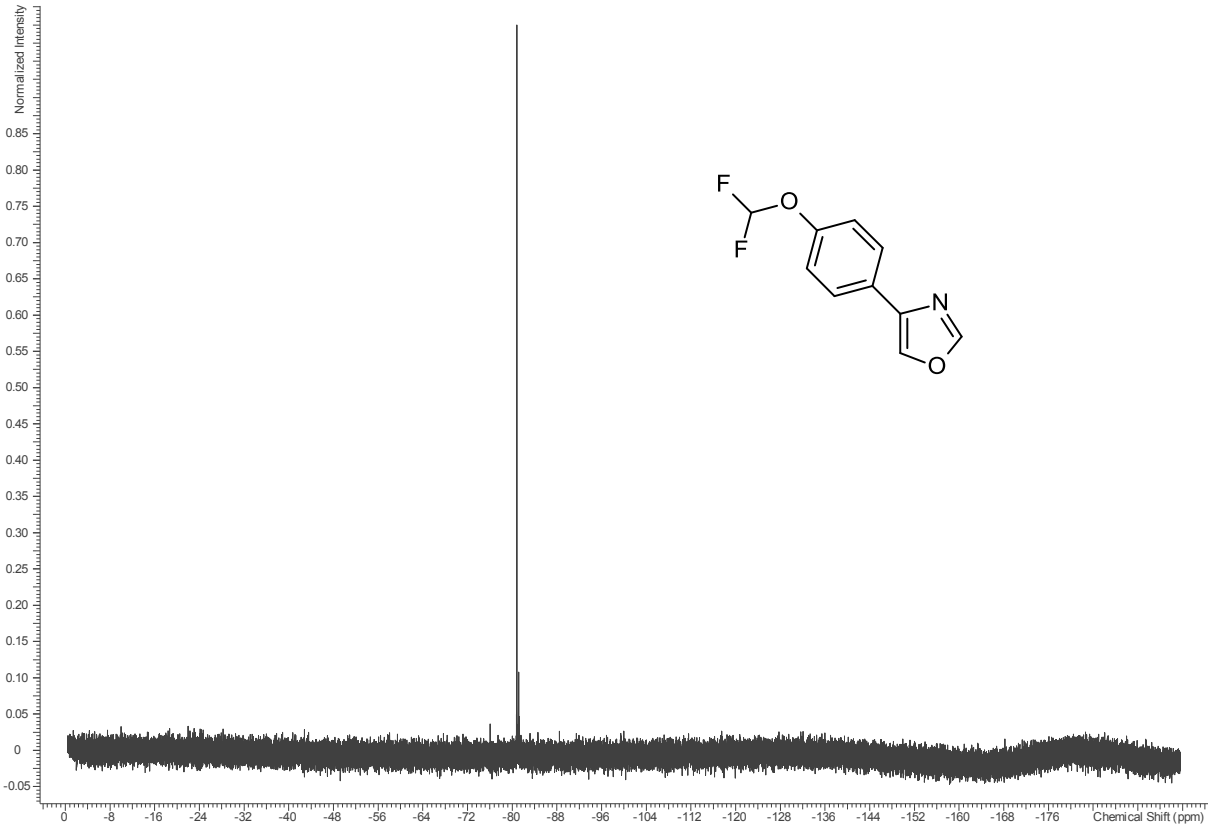



F
N
N
Normalized Intensity
0.6
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)

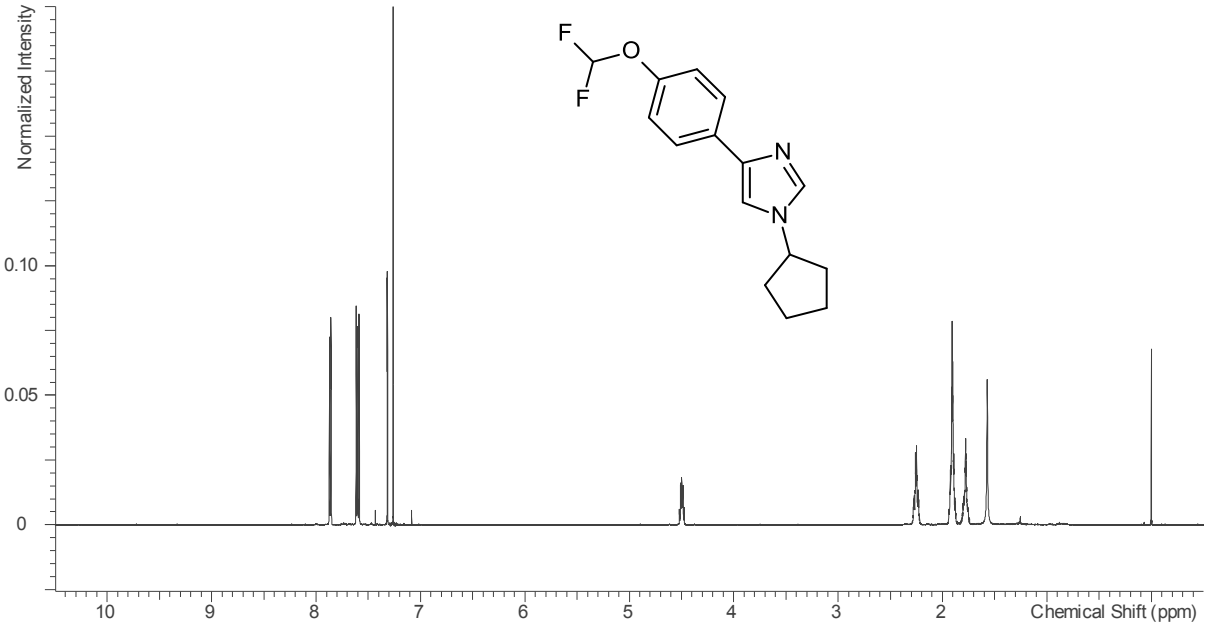
4-(4-Difluoromethoxy-phenyl)-oxazole

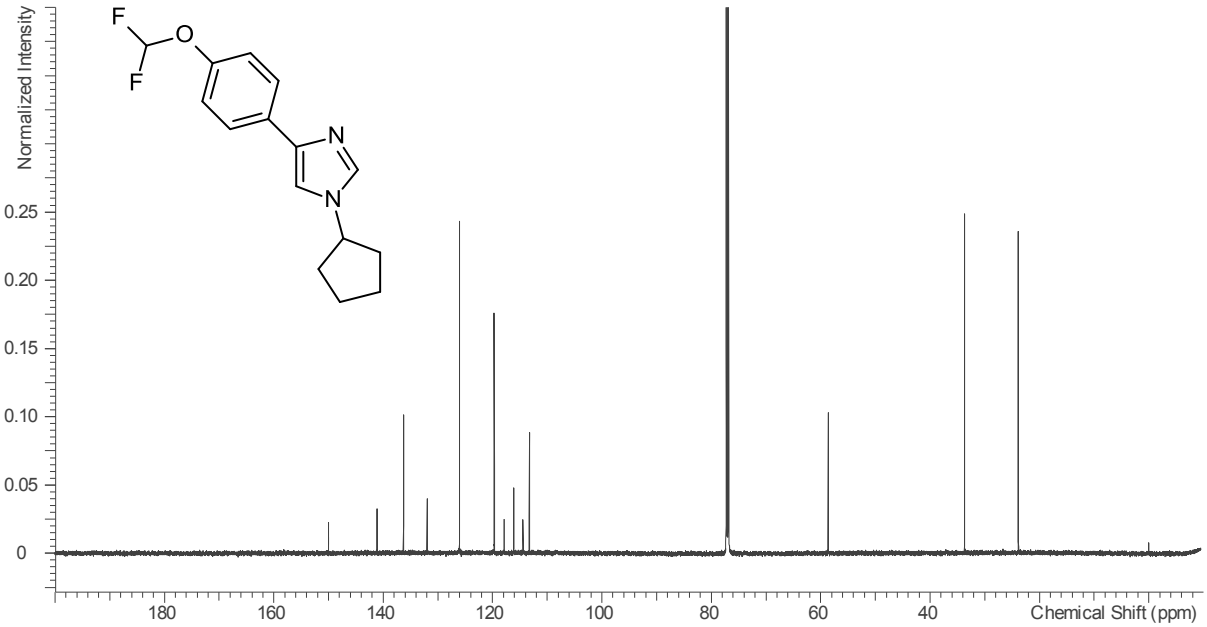


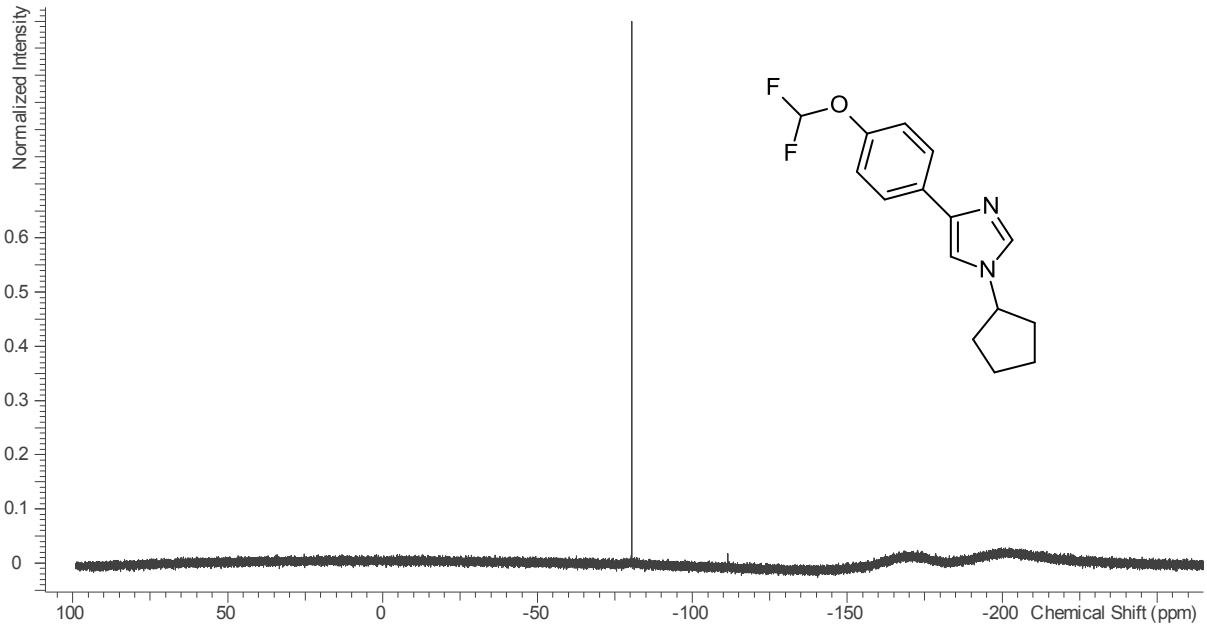



Normalized Intensity
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
-8
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
Chemical Shift (ppm)
F
O
F
N
O

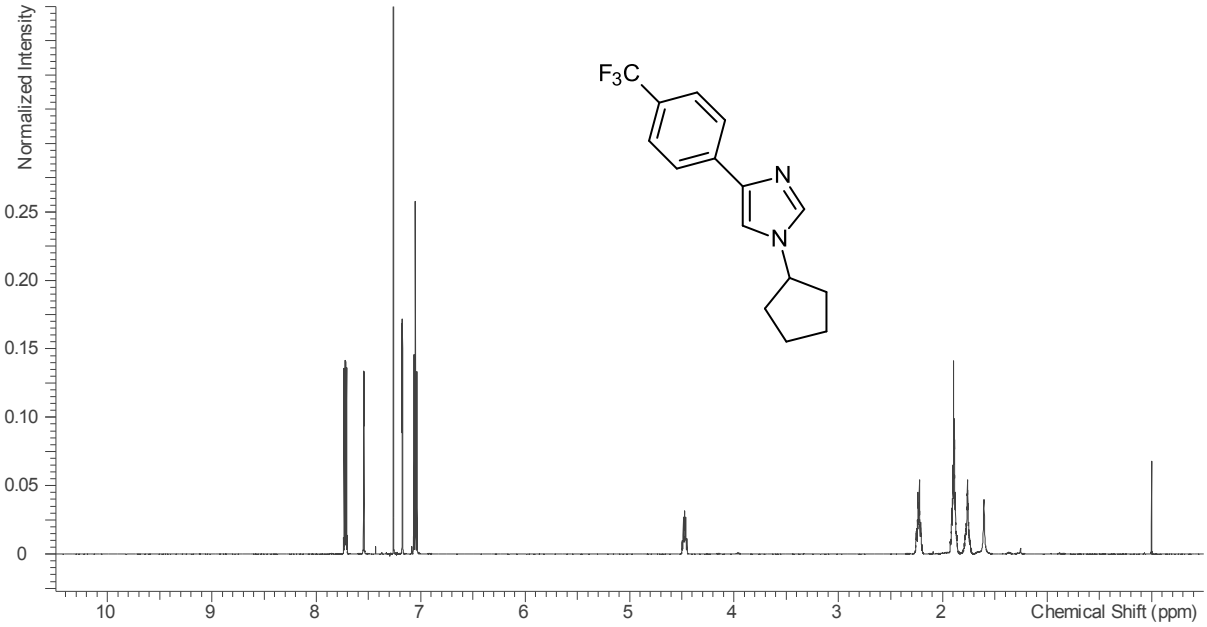
1-Cyclopentyl-4-(4-difluoromethoxy-phenyl)-1*H*-imidazole (32)

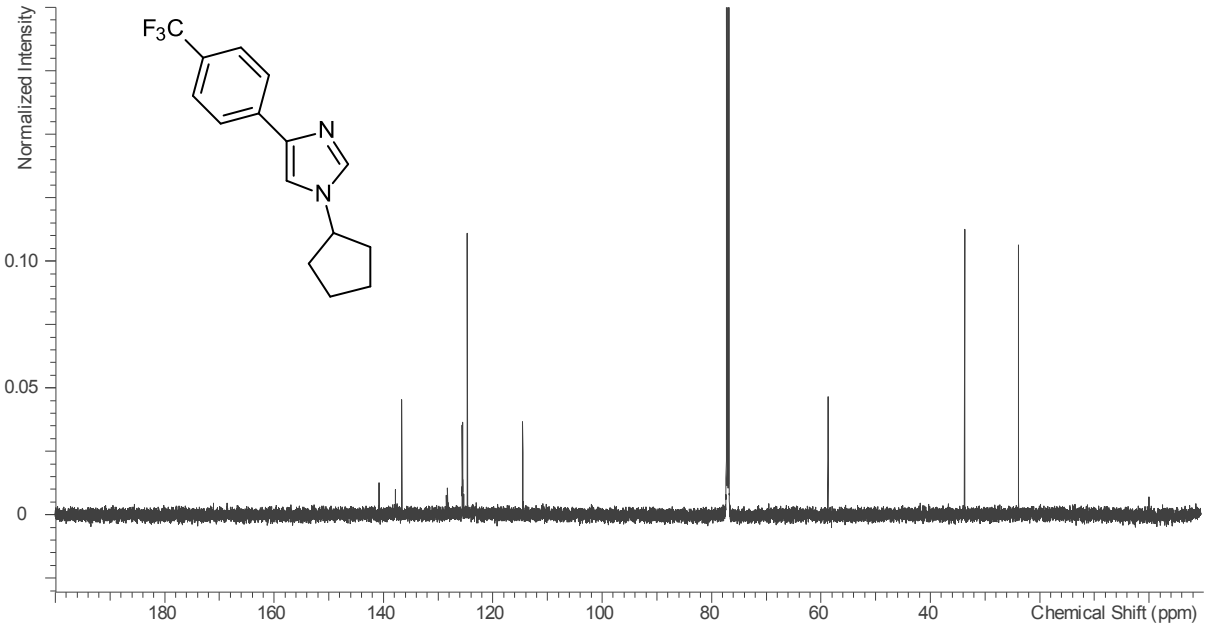


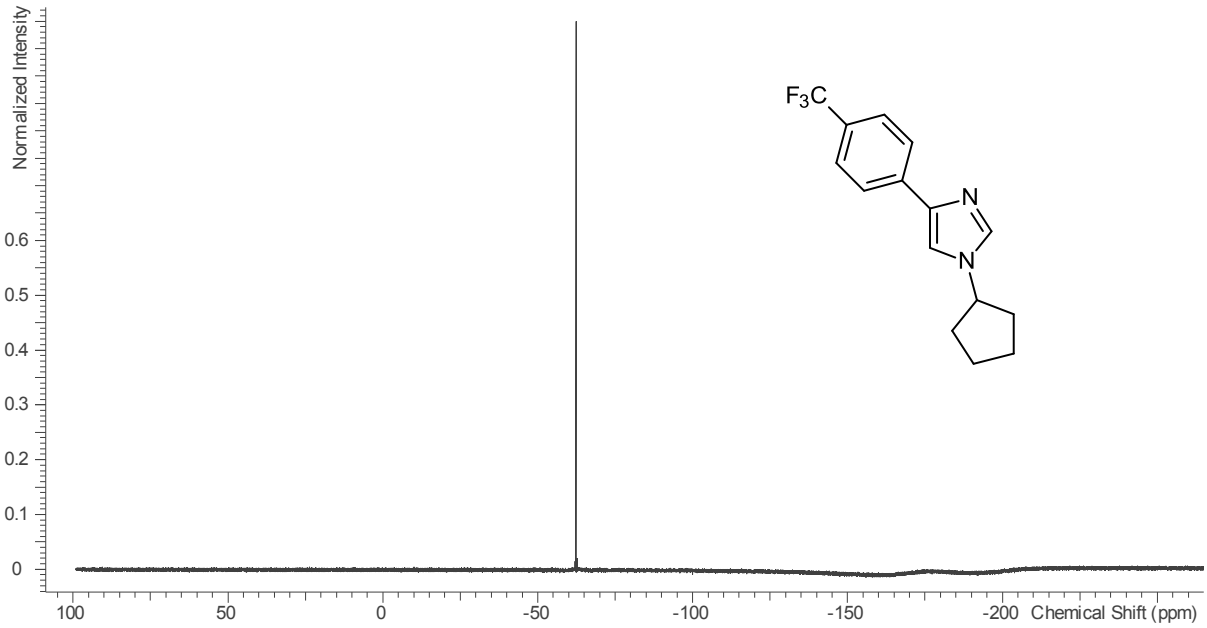



Normalized Intensity
0.6
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
F
O
F
N
N

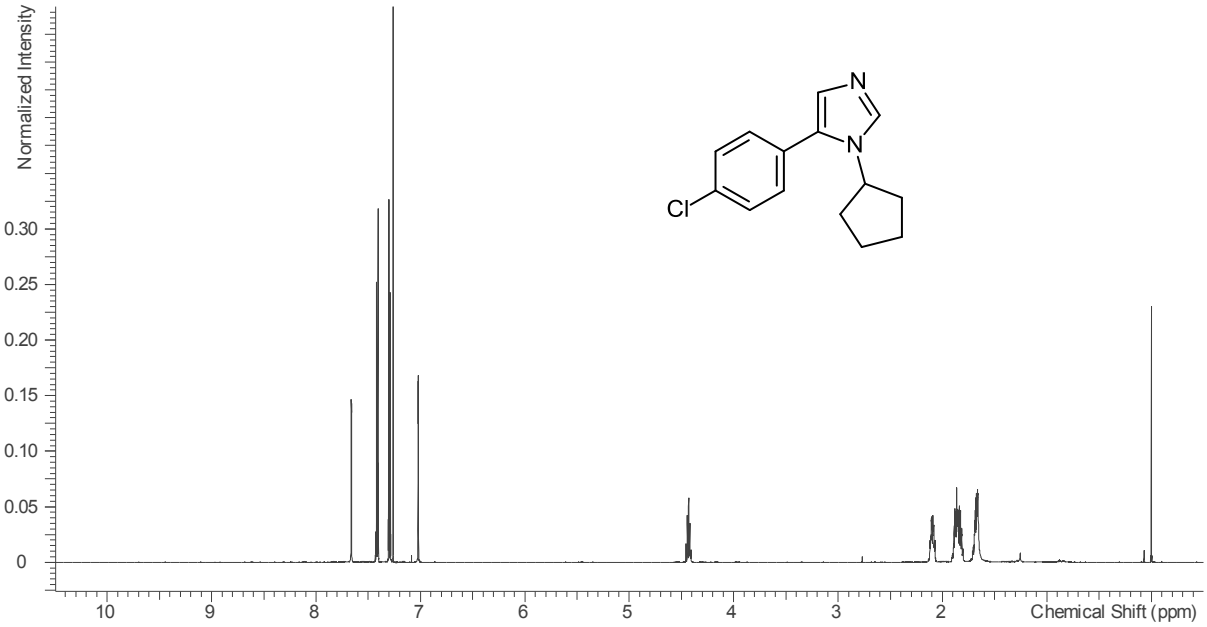
1-Cyclopentyl-4-(4-trifluoromethyl-phenyl)-1*H*-imidazole (33)

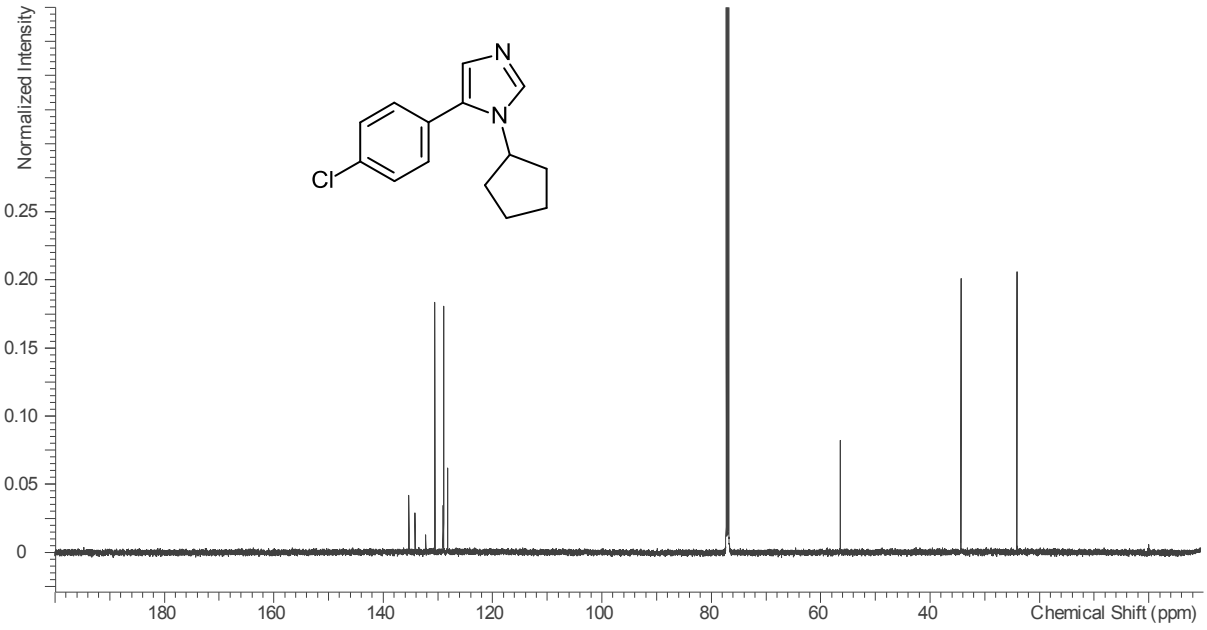




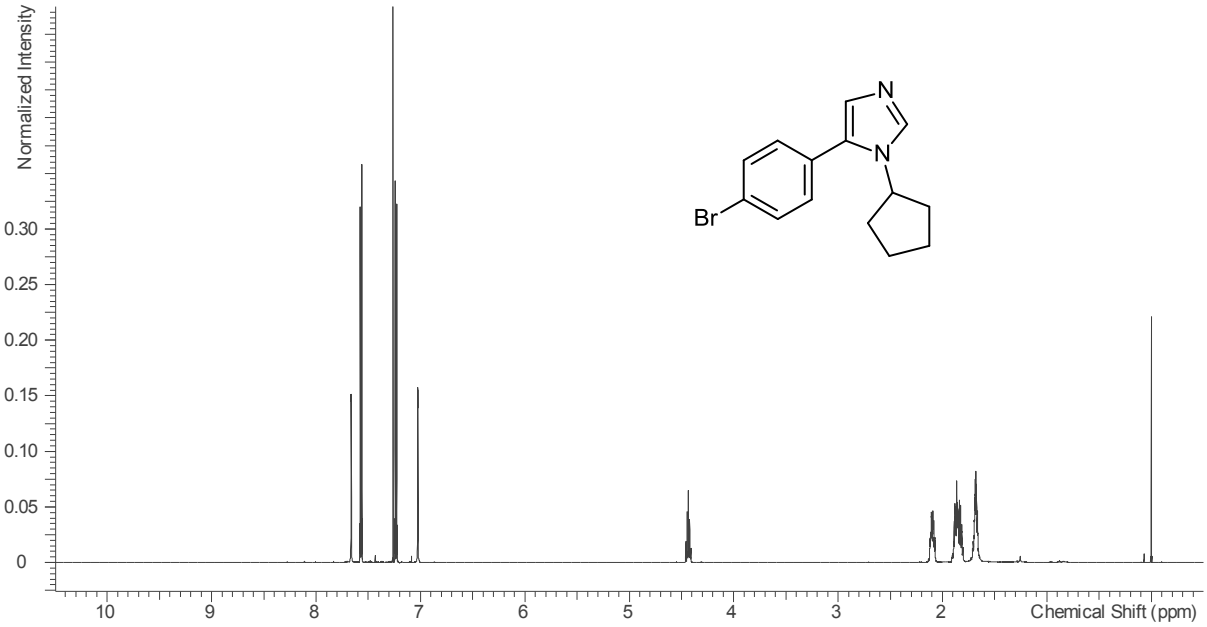

Normalized Intensity
0.6
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
F3C
N
N

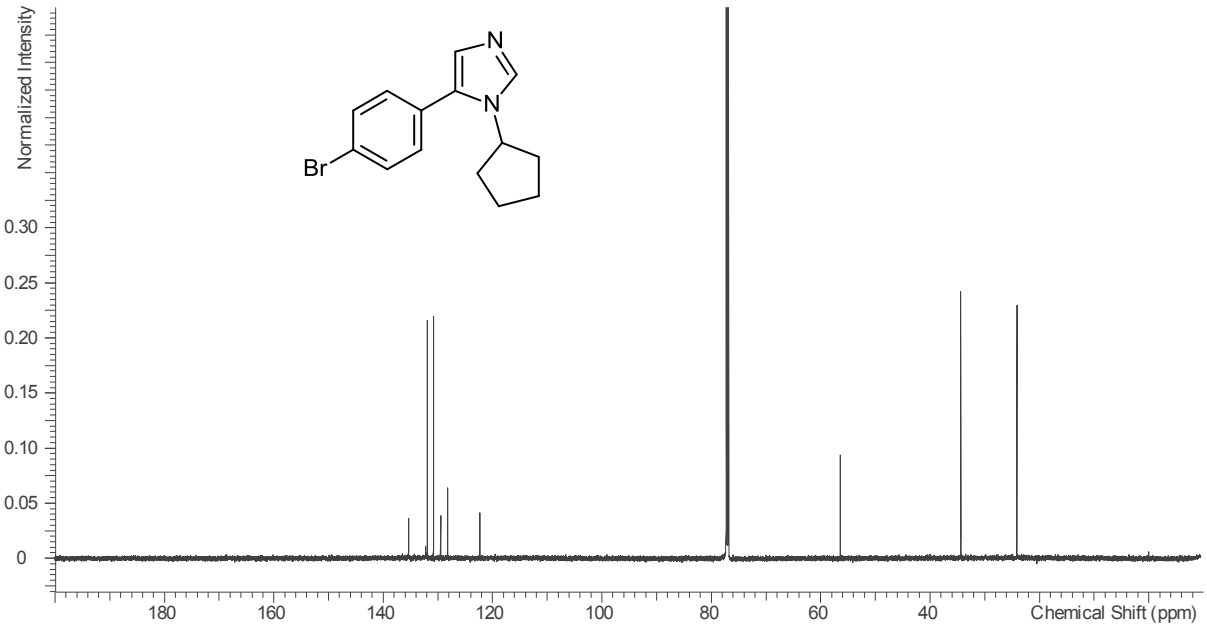
5-(4-Chloro-phenyl)-1-cyclopentyl-1*H*-imidazole (34)



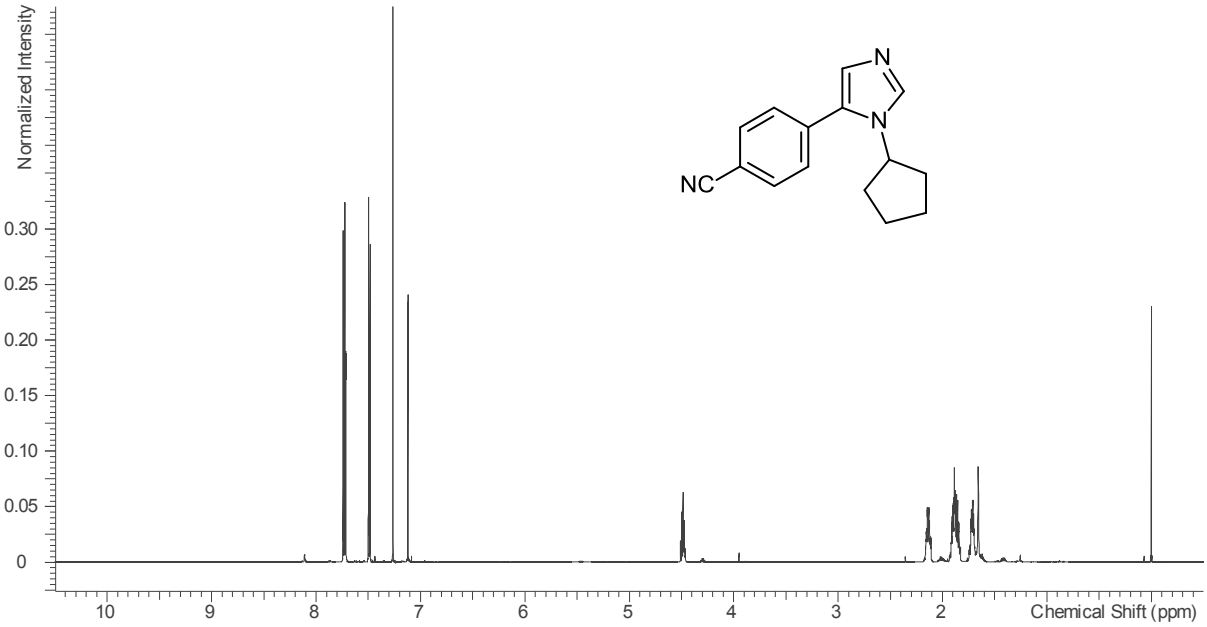


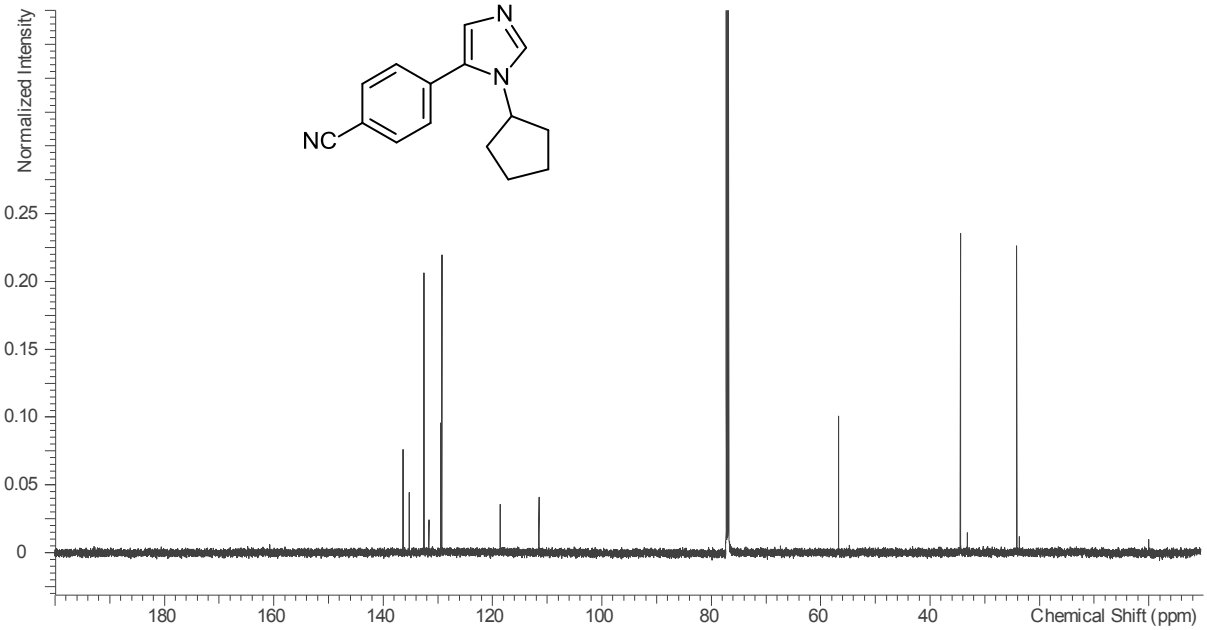
5-(4-Bromo-phenyl)-1-cyclopentyl-1*H*-imidazole (35)



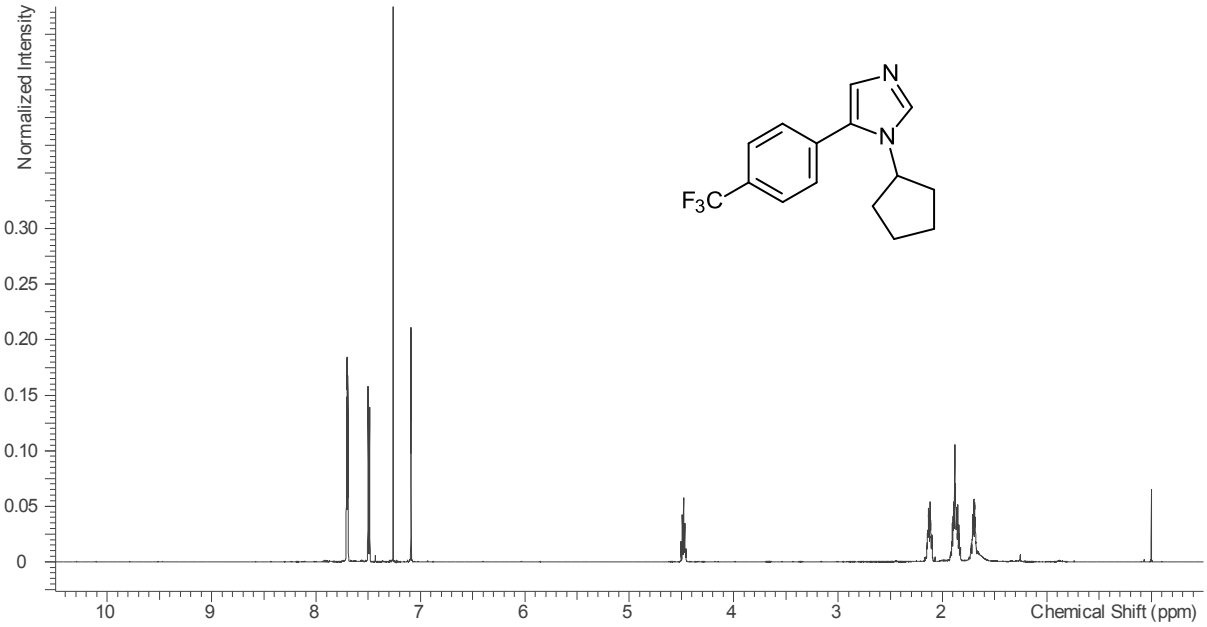


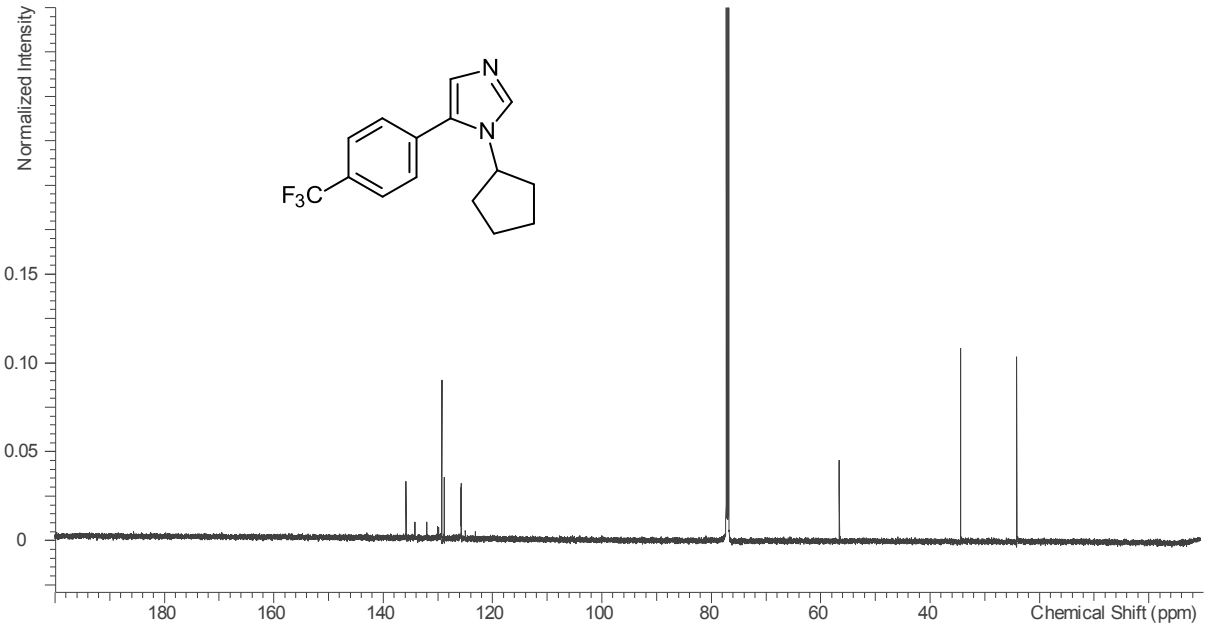
4-(3-Cyclopentyl-3*H*-imidazol-4-yl)-benzonitrile (36)

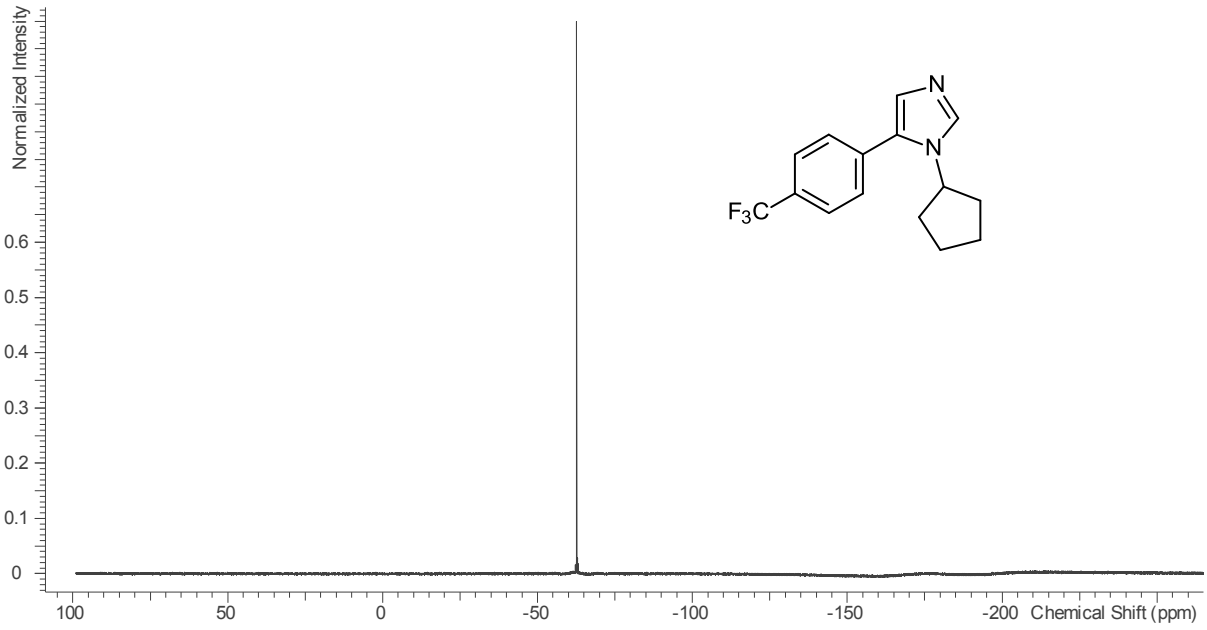




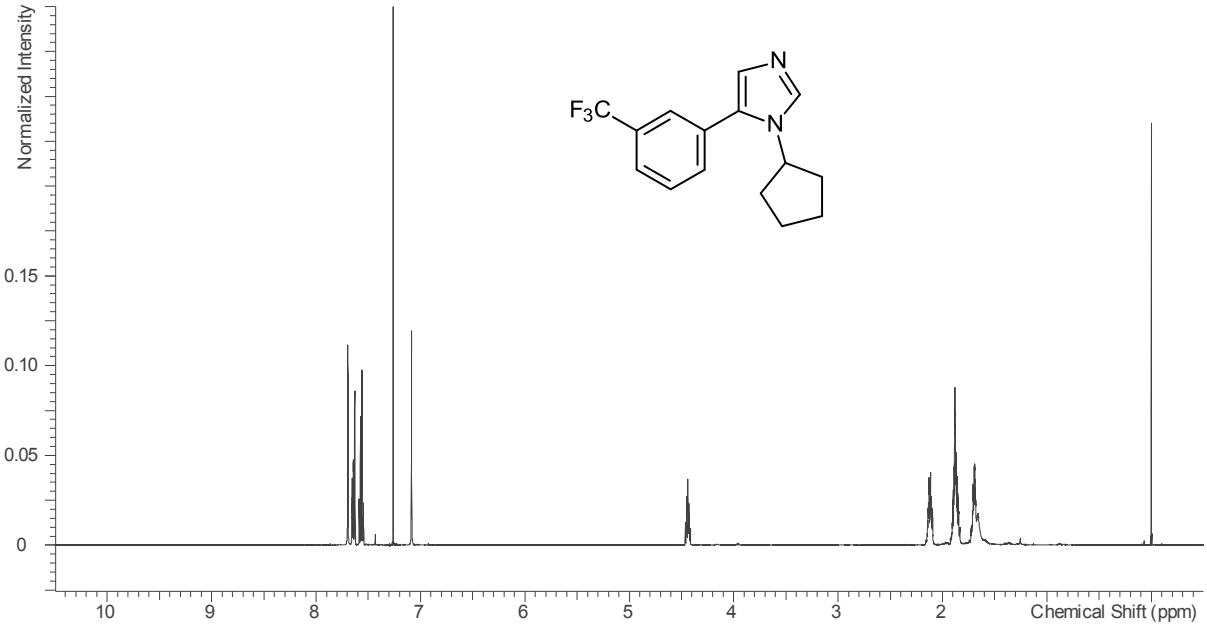
1-Cyclopentyl-5-(4-trifluoromethyl-phenyl)-1*H*-imidazole (37)

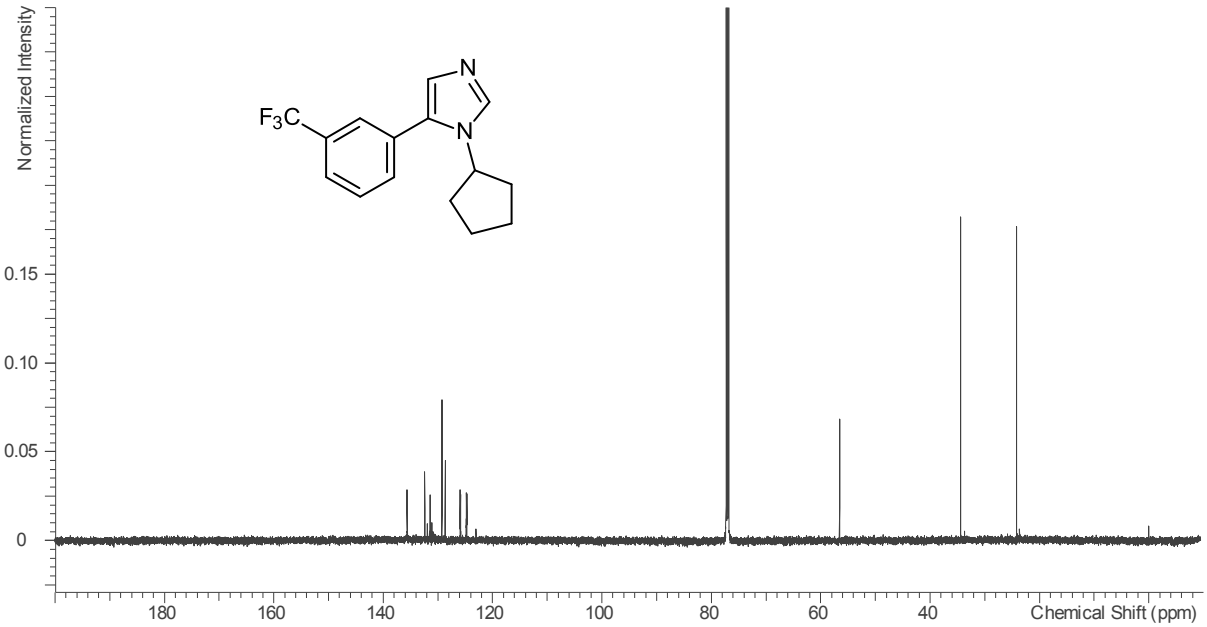


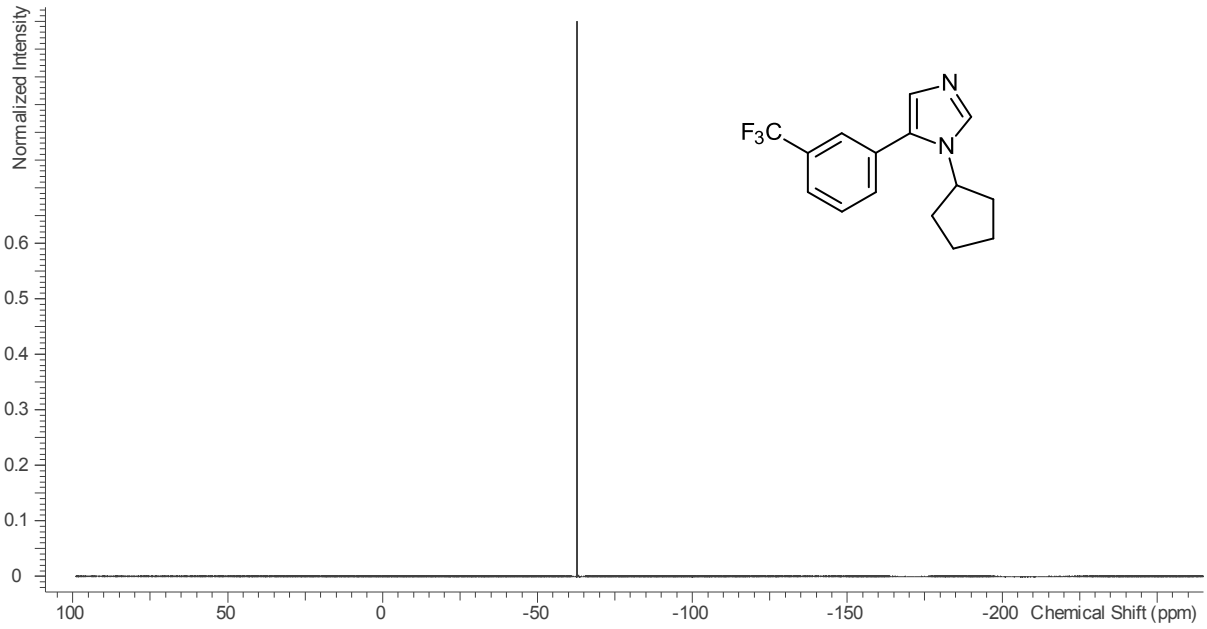



Normalized Intensity
0.6
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
N
N
F3C

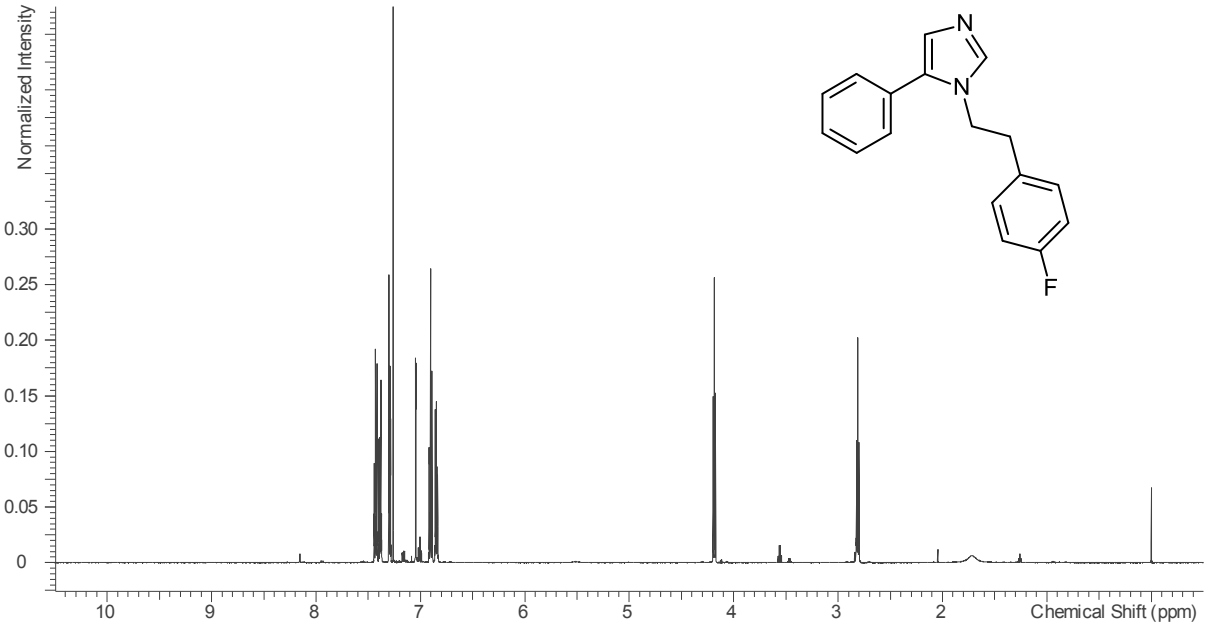
1-Cyclopentyl-5-(3-trifluoromethyl-phenyl)-1*H*-imidazole (38)

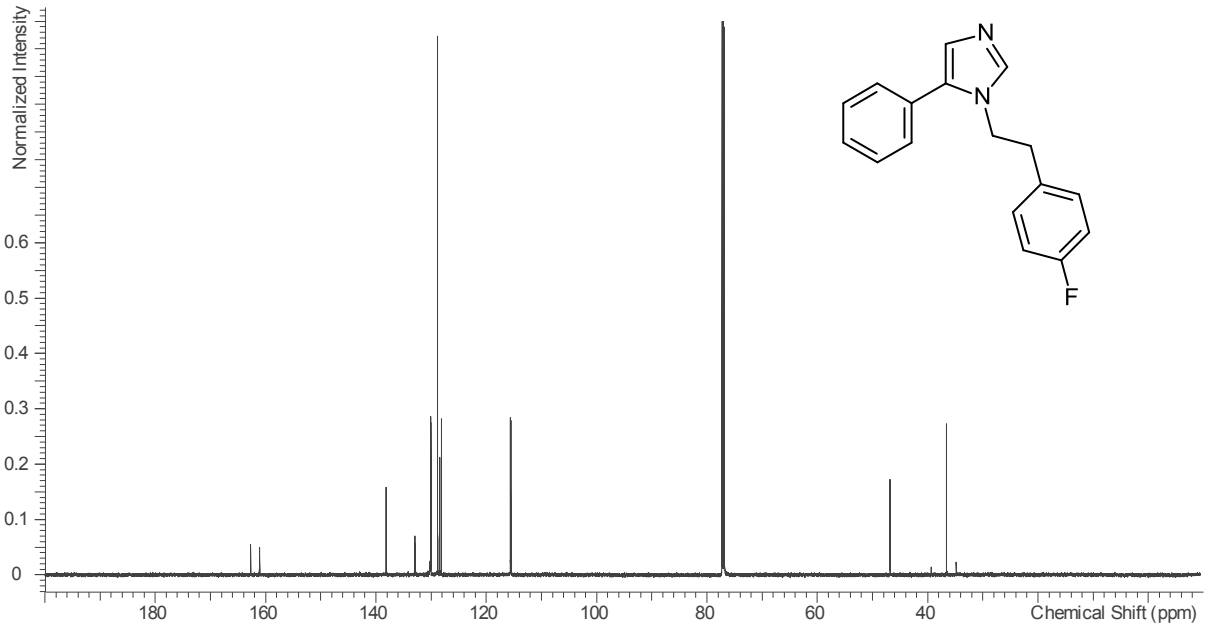


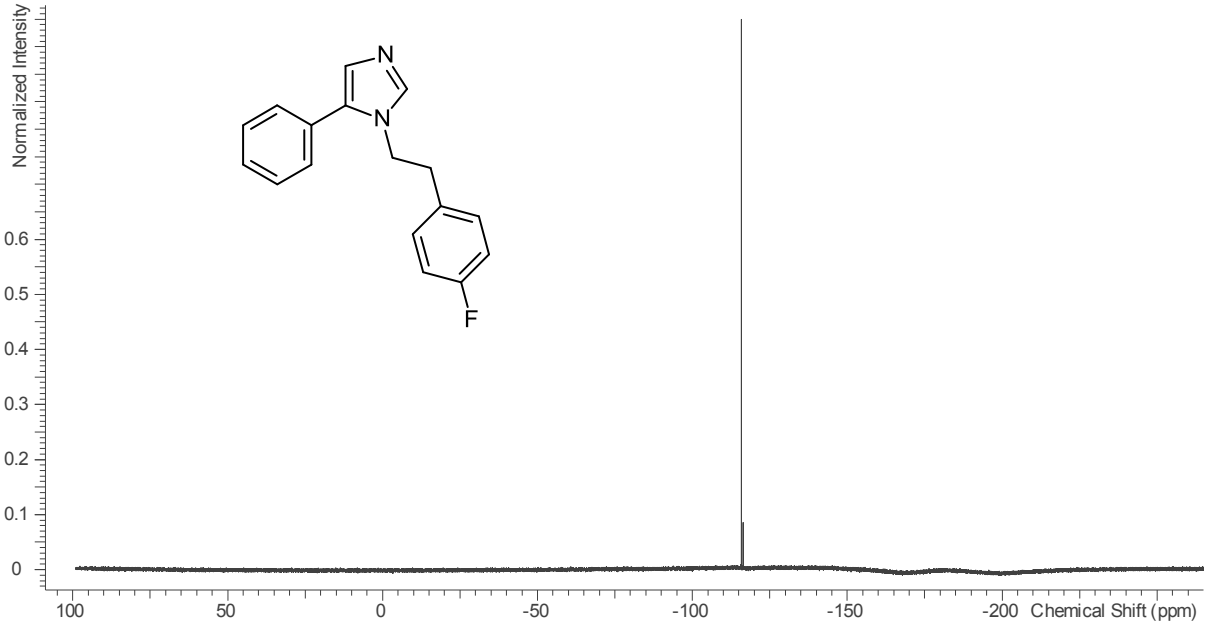




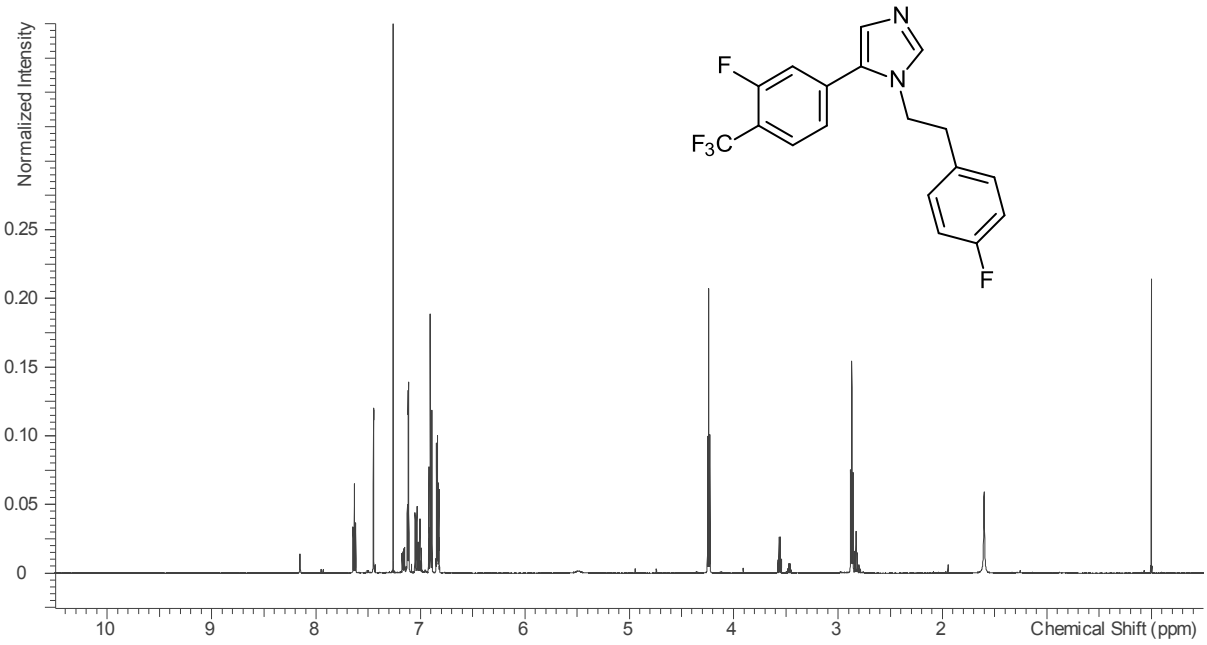
1-[2-(4-Fluoro-phenyl)-ethyl]-5-phenyl-1*H*-imidazole (39)

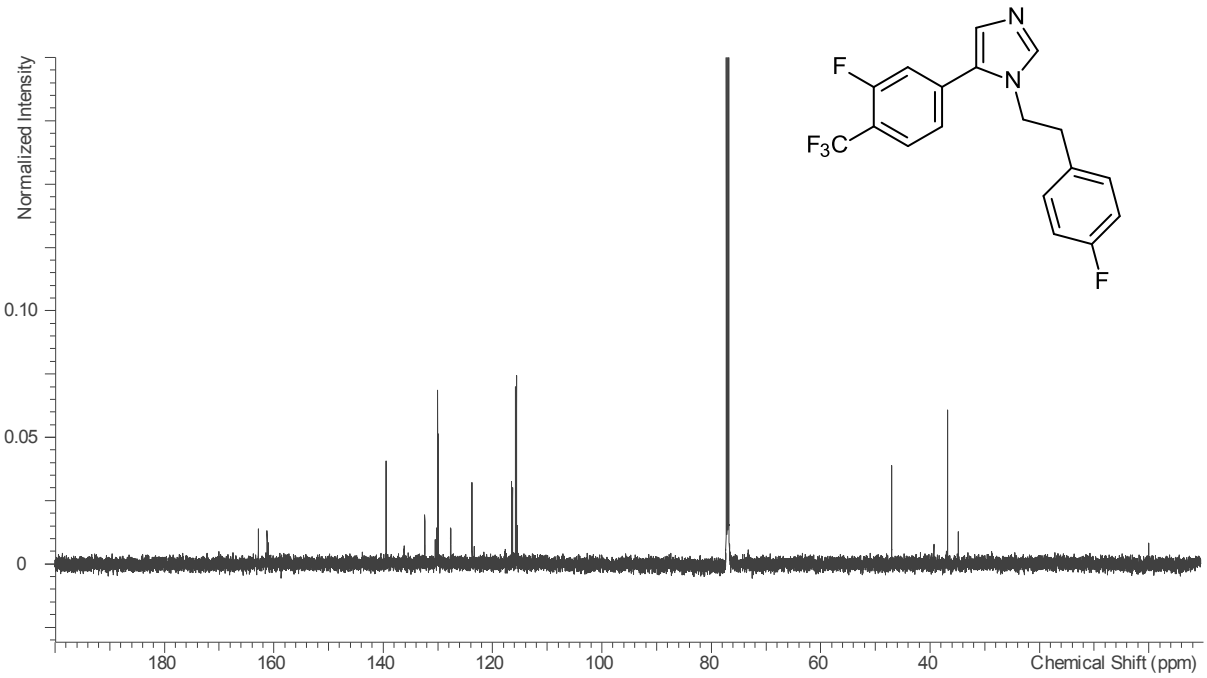


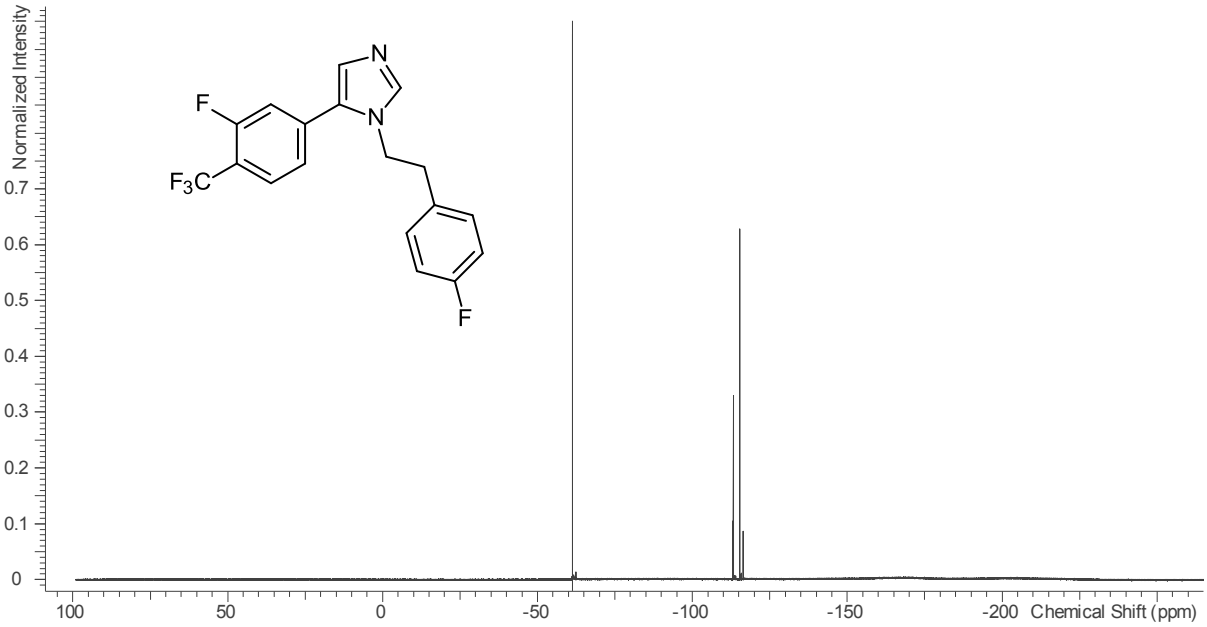



Normalized Intensity
0.6
0.5
0.4
0.3
0.2
0.1
0
N
N
F
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)

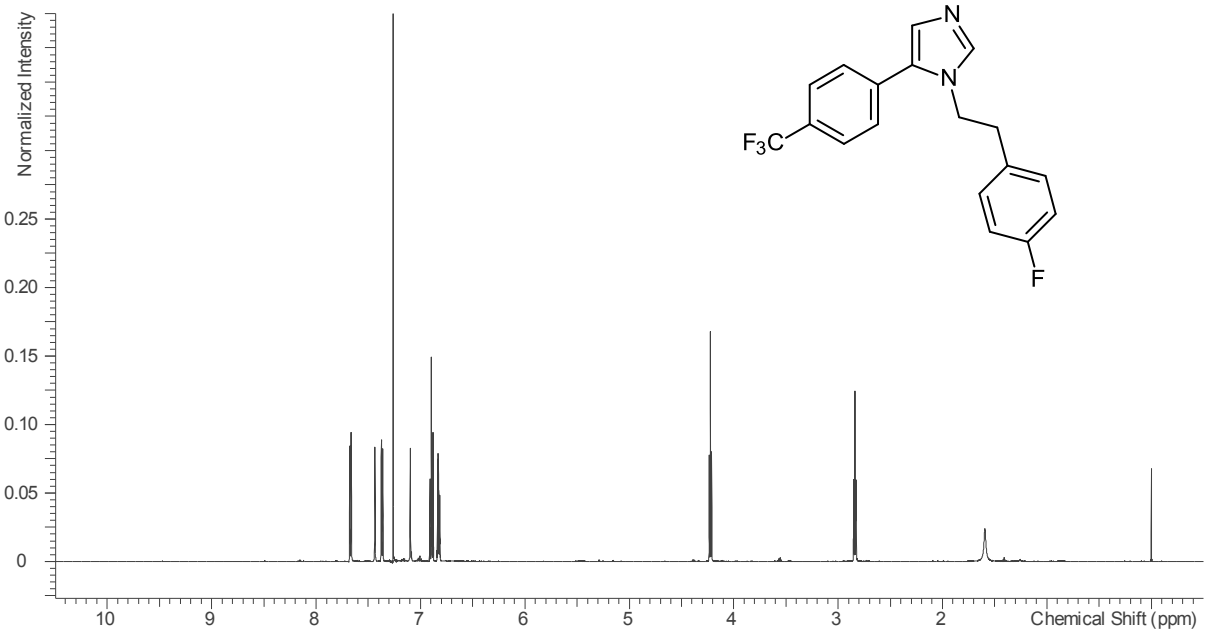
1-[2-(4-Fluoro-phenyl)-ethyl]-5-(3-fluoro-4-trifluoromethyl-phenyl)-1*H*-imidazole (40)

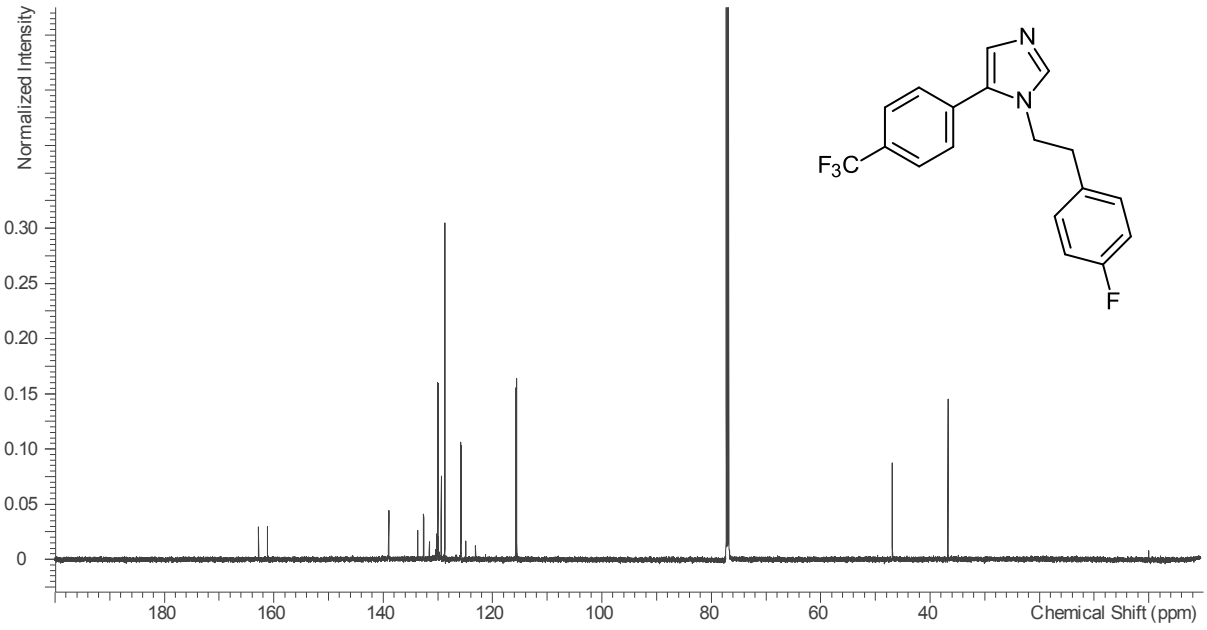


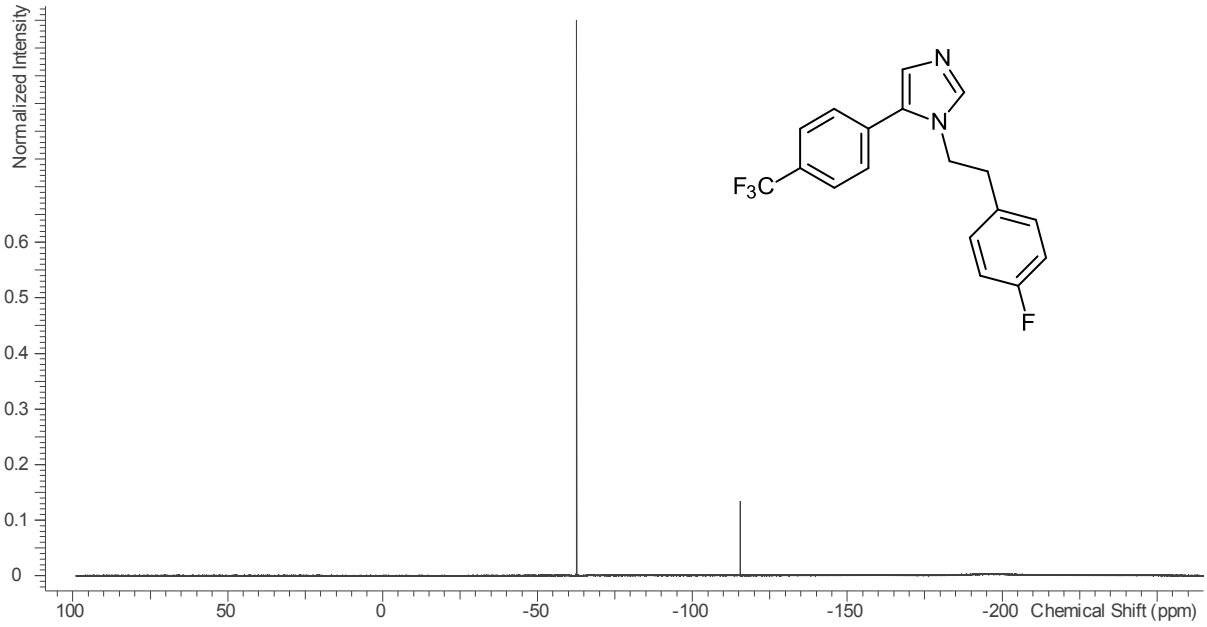



Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
F
F3C
N
N
F

1-[2-(4-Fluoro-phenyl)-ethyl]-5-(4-trifluoromethyl-phenyl)-1*H*-imidazole (41)






Normalized Intensity
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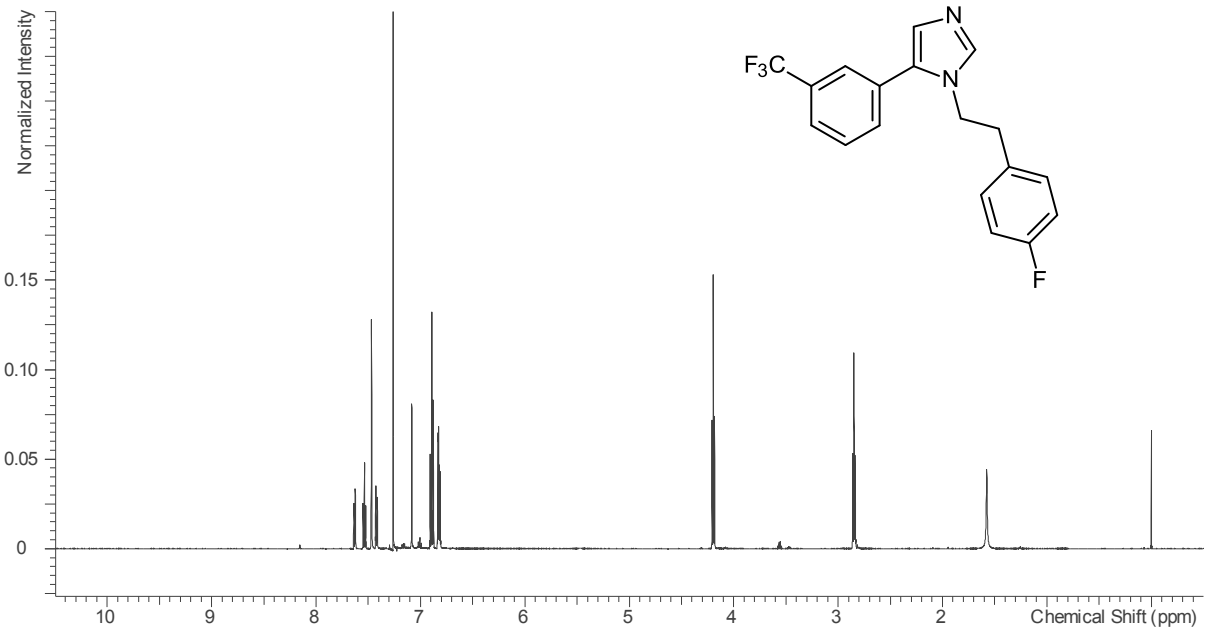
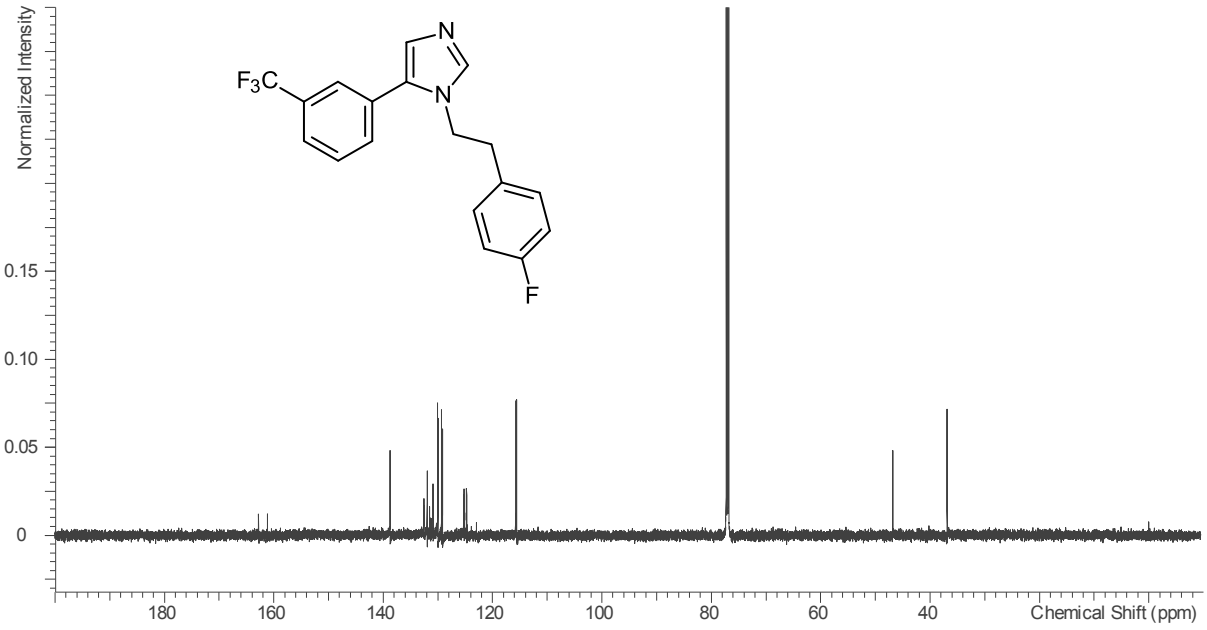
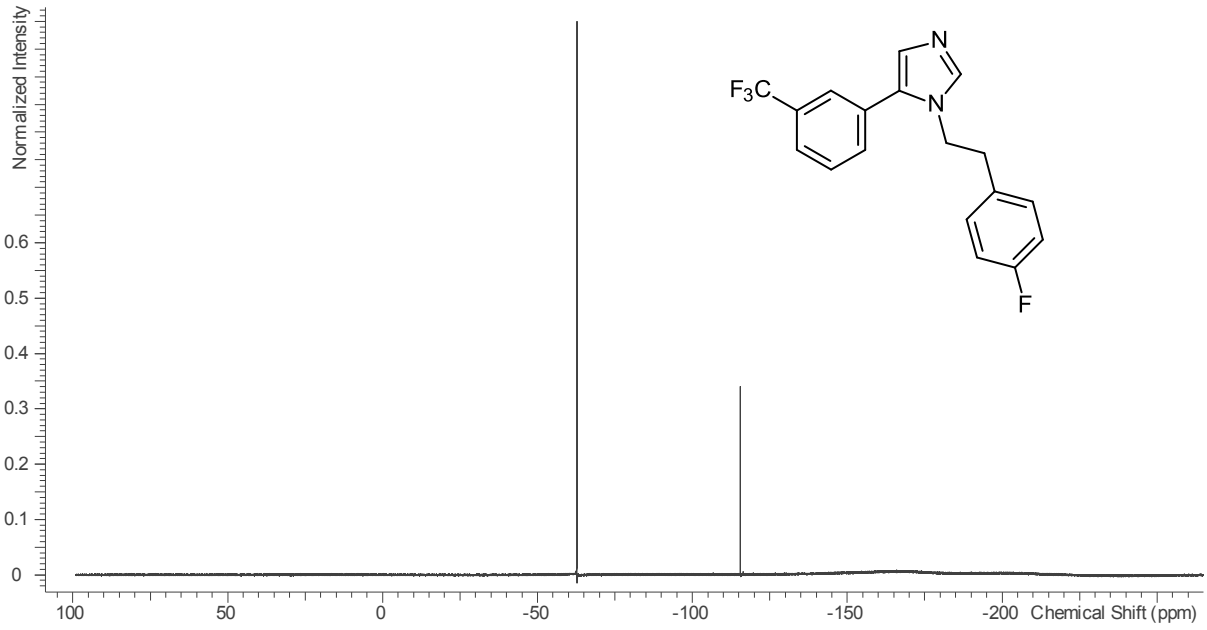
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
N
N
F3C
F

1-[2-(4-Fluoro-phenyl)-ethyl]-5-(3-trifluoromethyl-phenyl)-1*H*-imidazole (42)






Normalized Intensity
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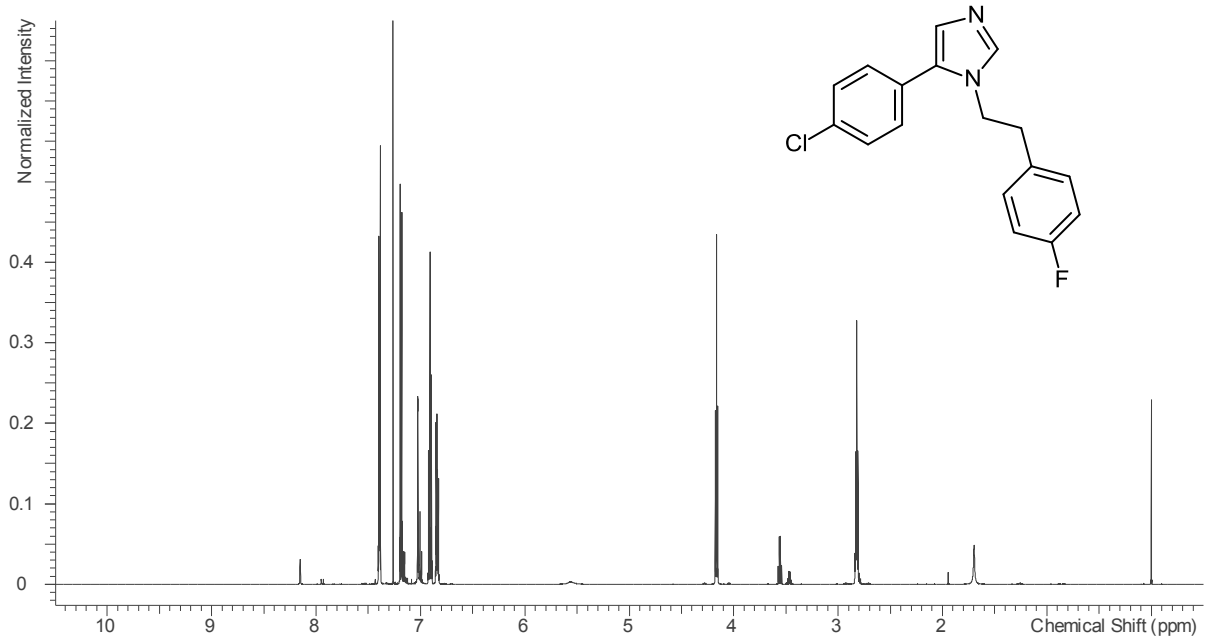
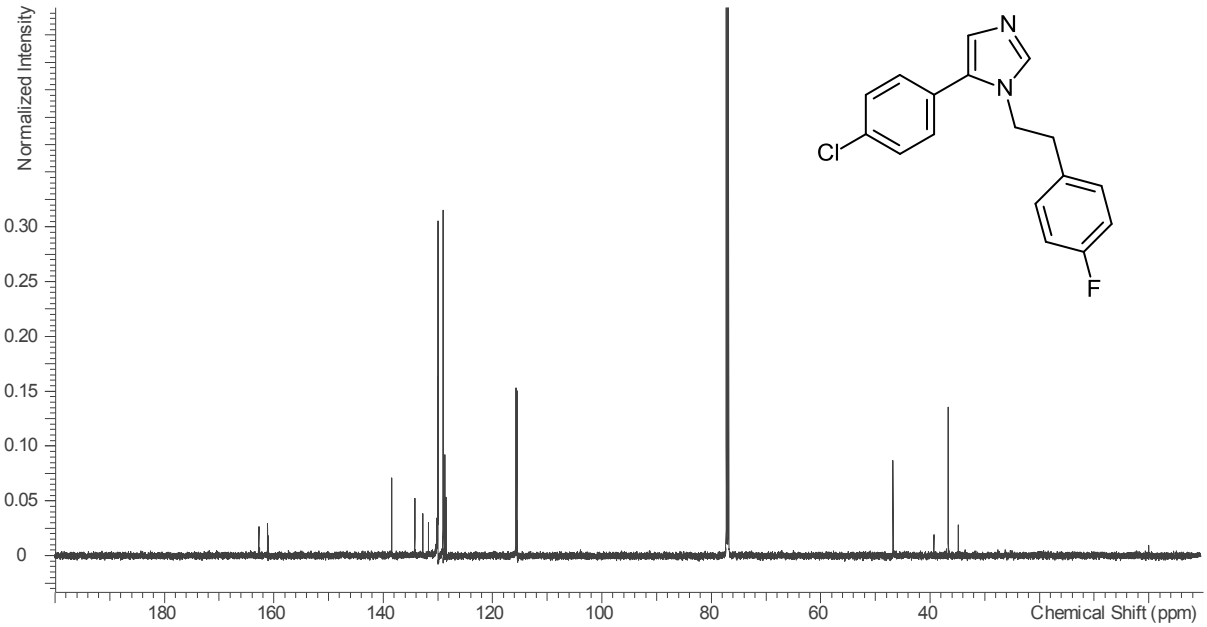
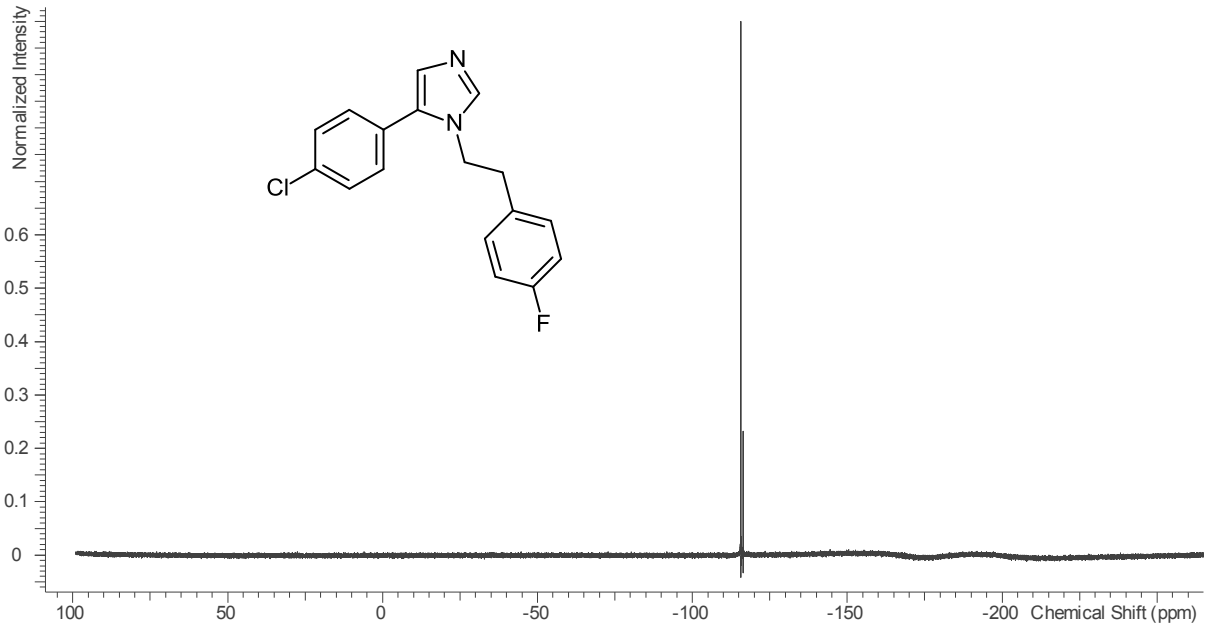
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
F3C
N
N
F

5-(4-Chloro-phenyl)-1-[2-(4-fluoro-phenyl)-ethyl]-1*H*-imidazole (43)






Normalized Intensity
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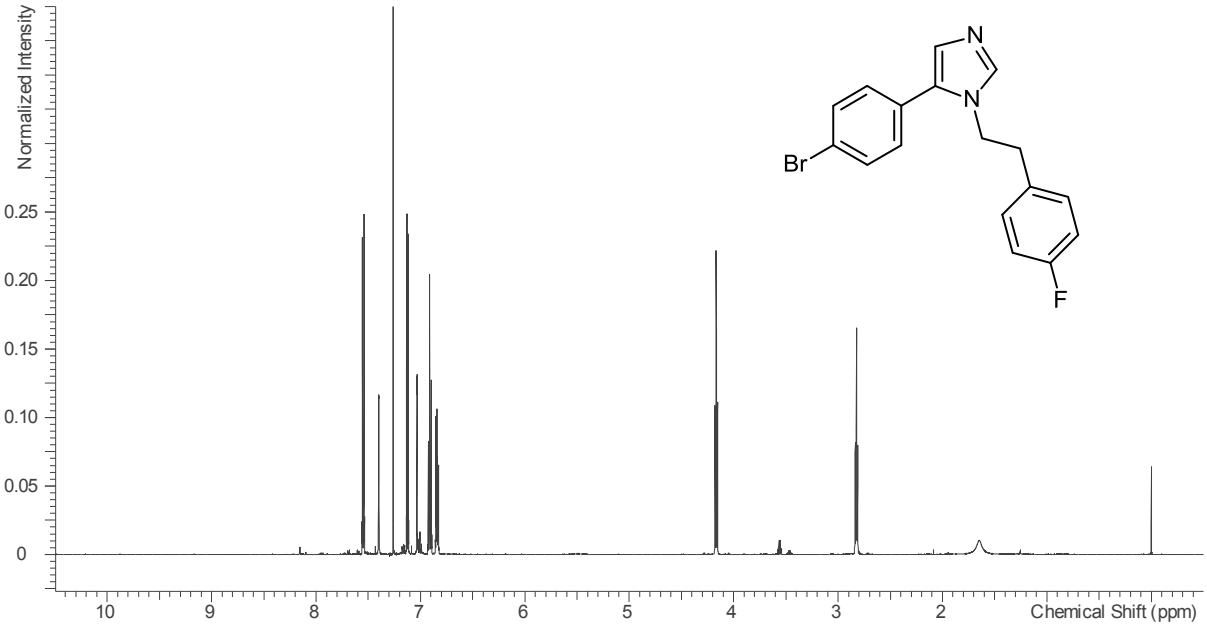
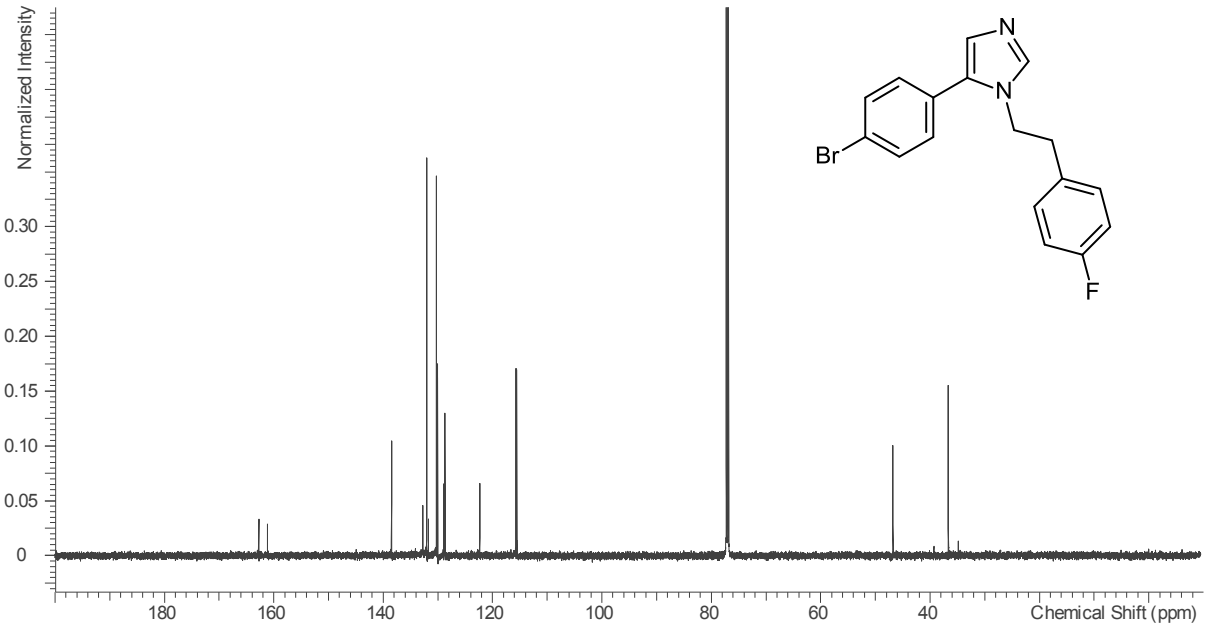
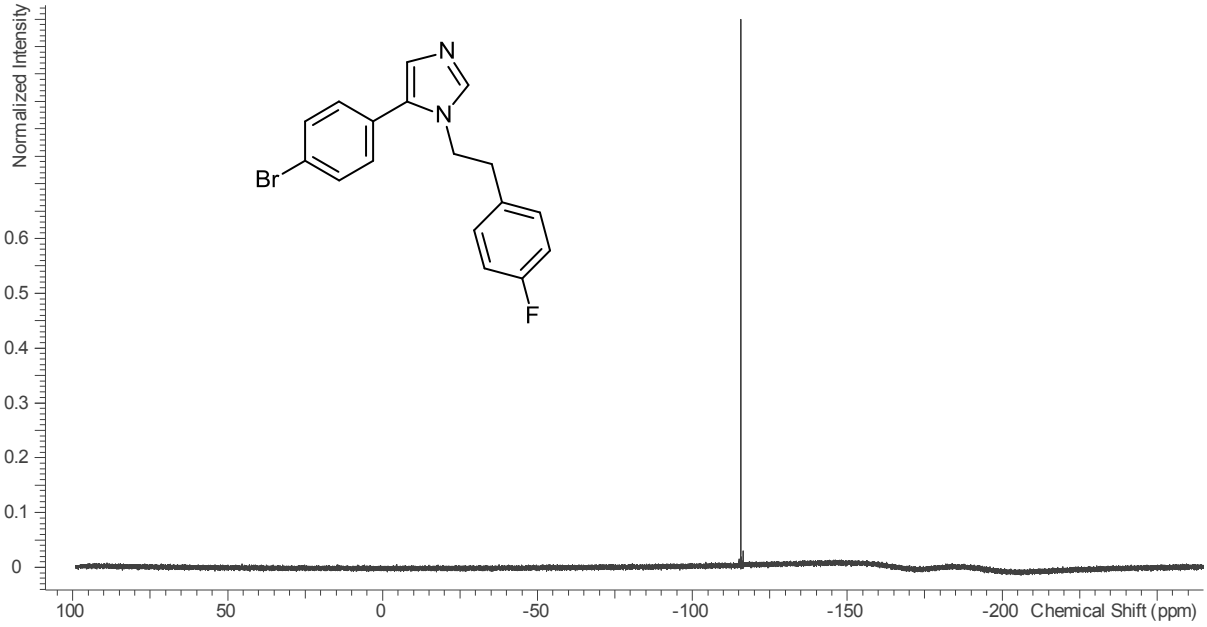
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
N
N
Cl
F

5-(4-Bromo-phenyl)-1-[2-(4-fluoro-phenyl)-ethyl]-1*H*-imidazole (44)






Normalized Intensity
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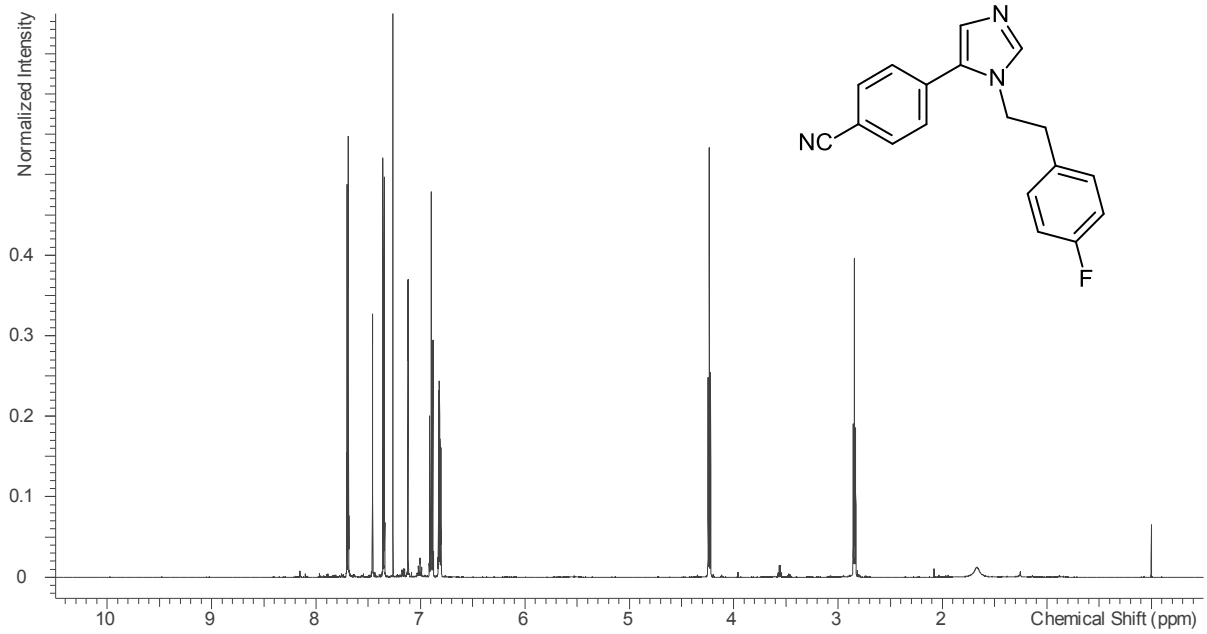
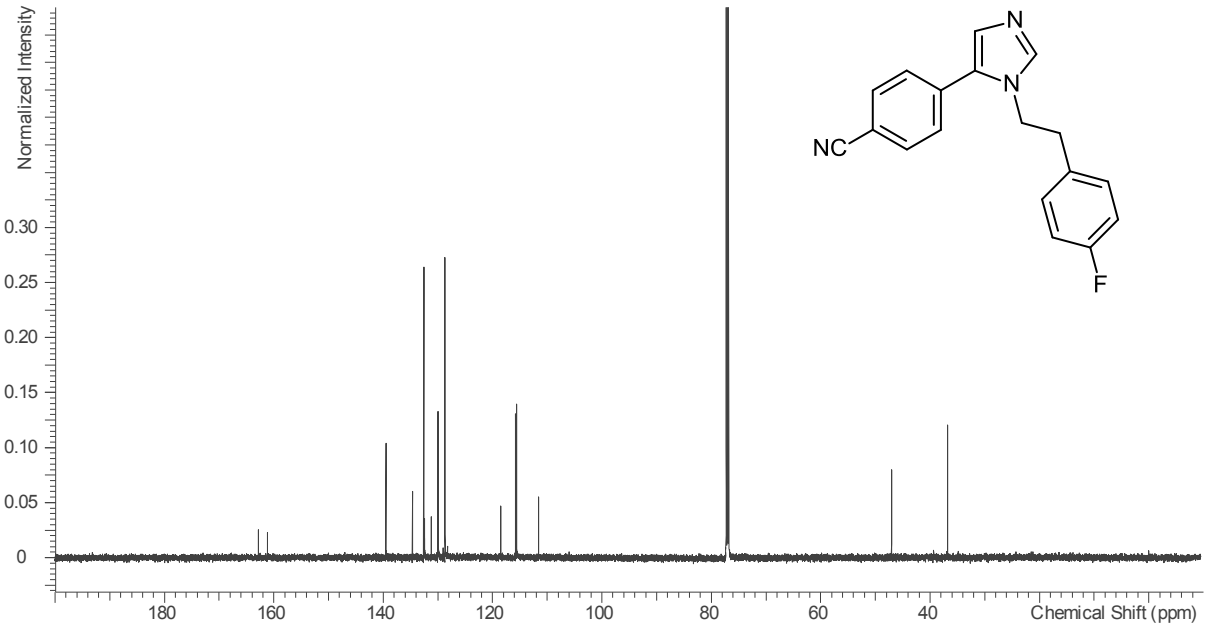
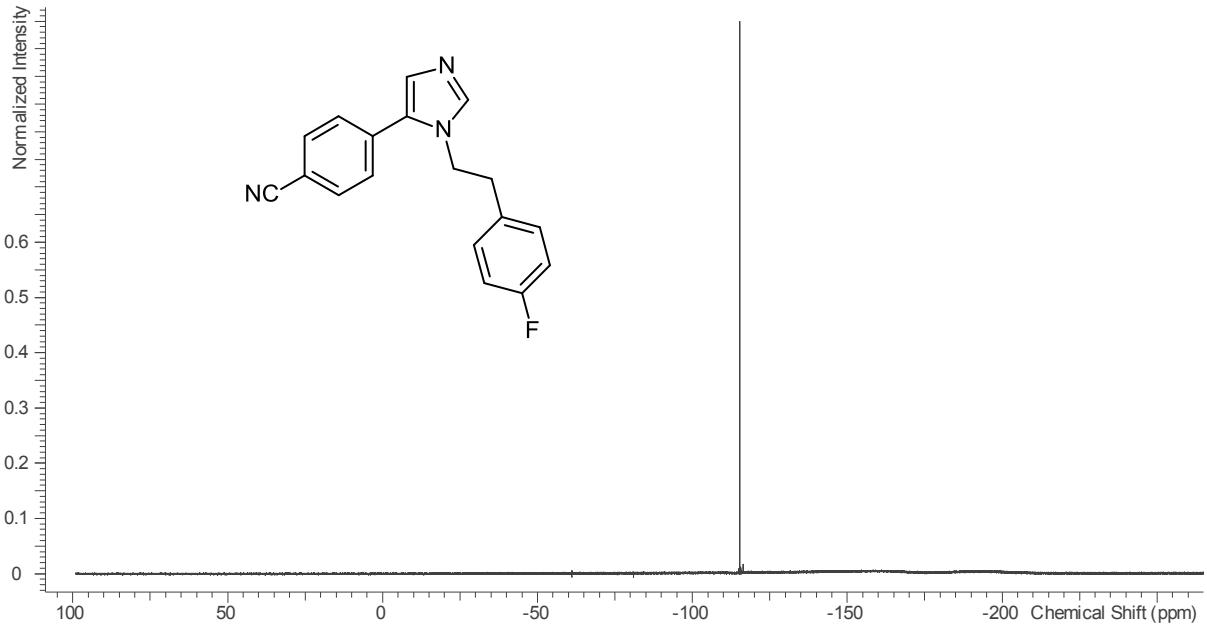
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
N
N
Br
F

4-{3-[2-(4-Fluoro-phenyl)-ethyl]-3*H*-imidazol-4-yl}-benzonitrile (45)






Normalized Intensity
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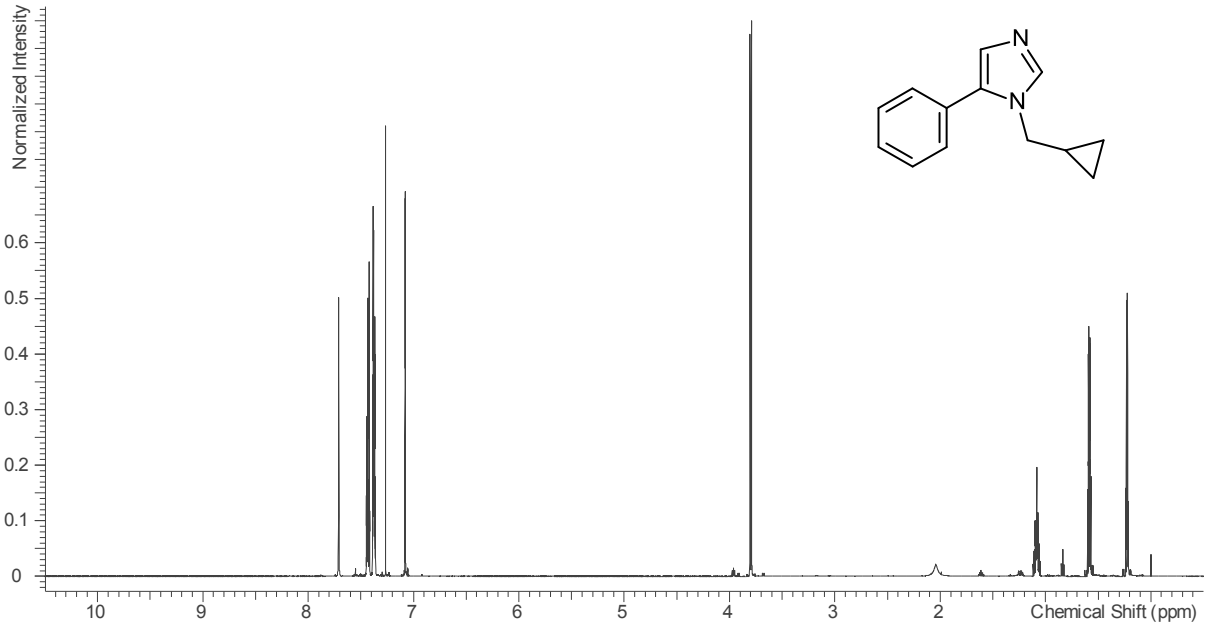
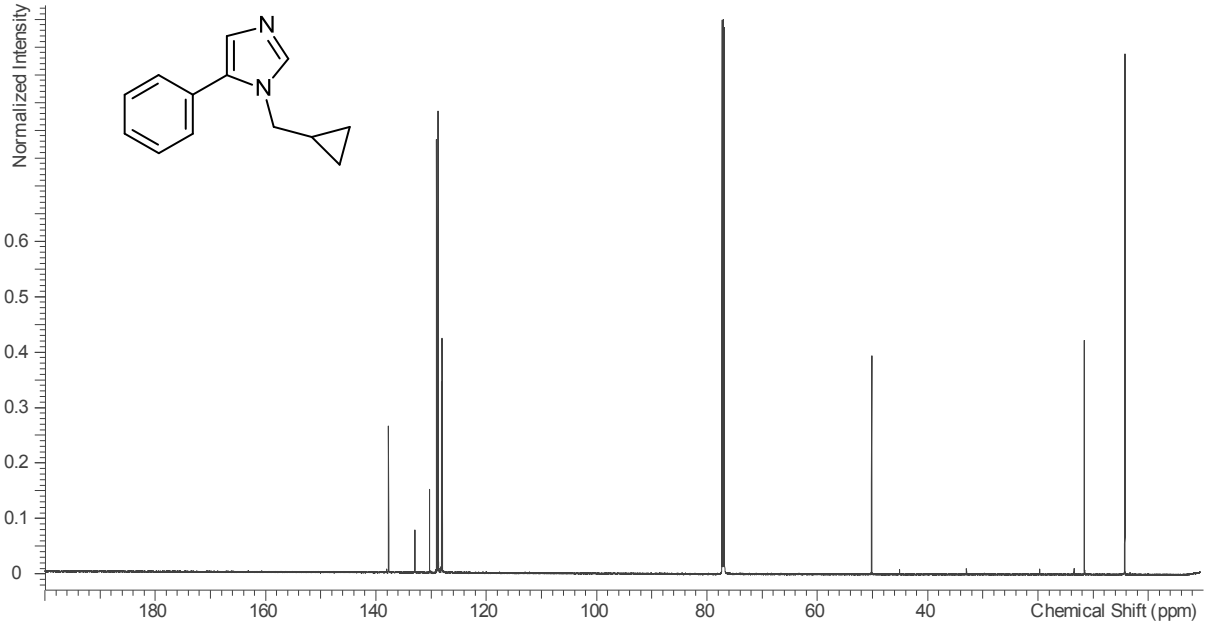
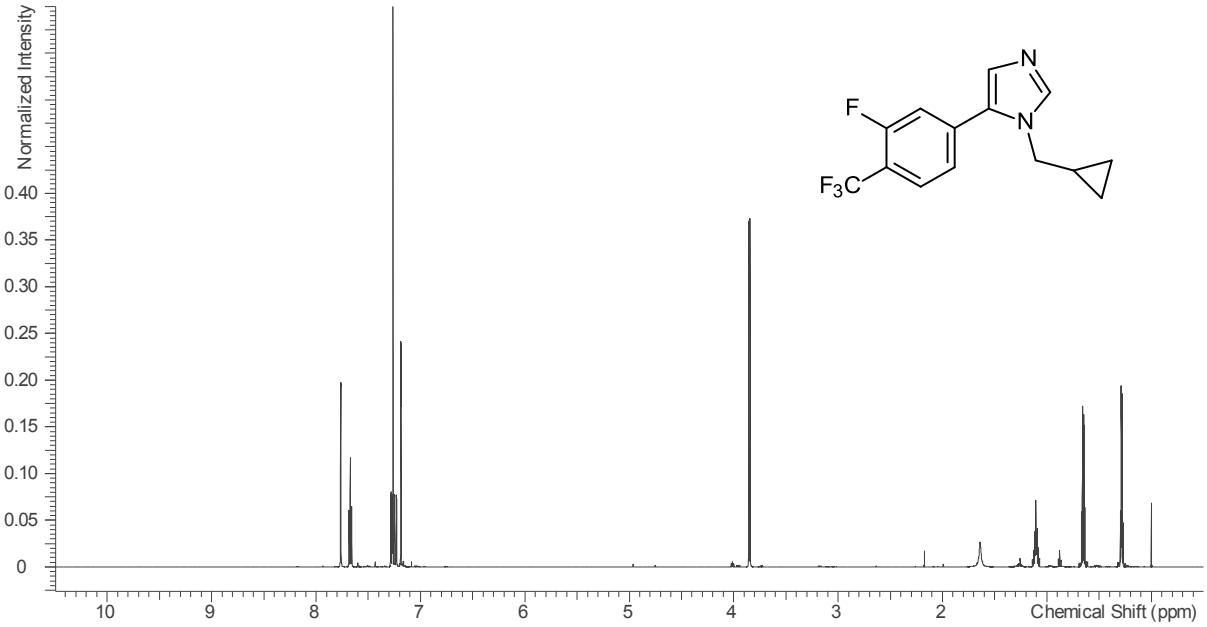
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
N
N
NC
F

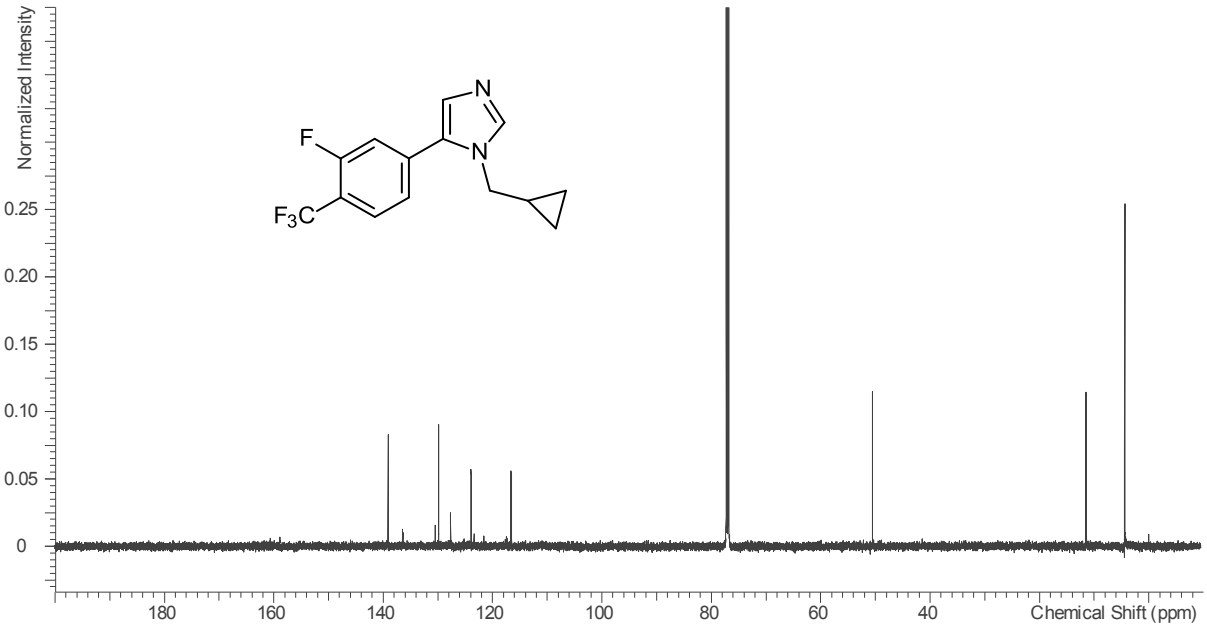
1-Cyclopropylmethyl-5-phenyl-1*H*-imidazole (46)

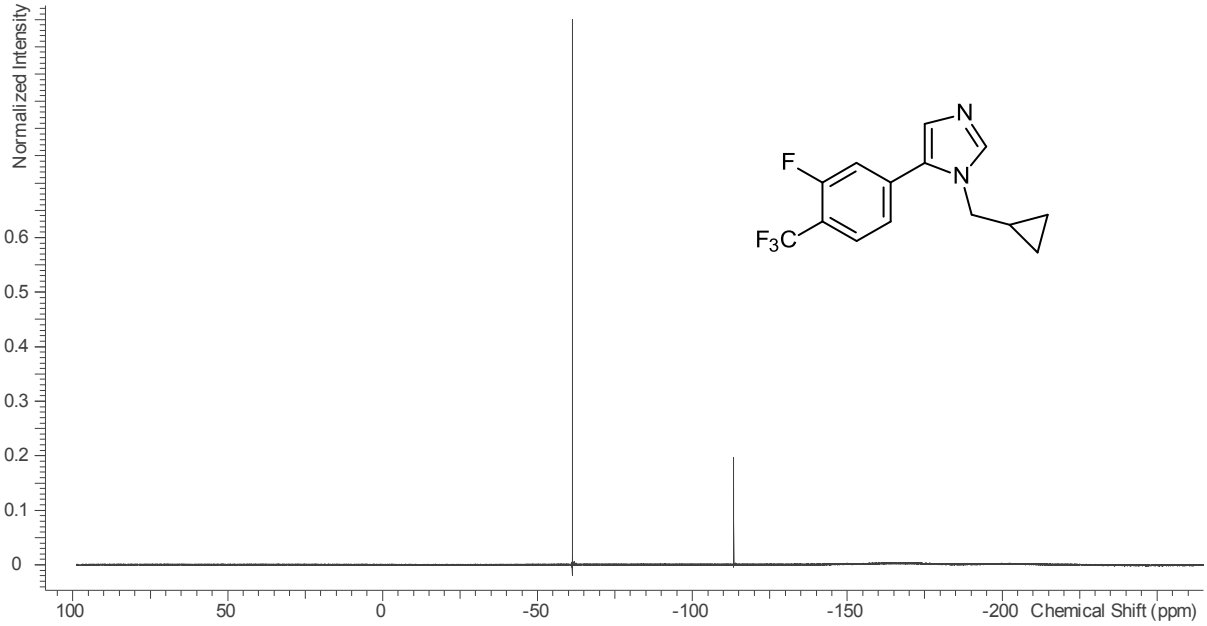




1-Cyclopropylmethyl-5-(3-fluoro-4-trifluoromethyl-phenyl)-1*H*-imidazole (47)






Normalized Intensity
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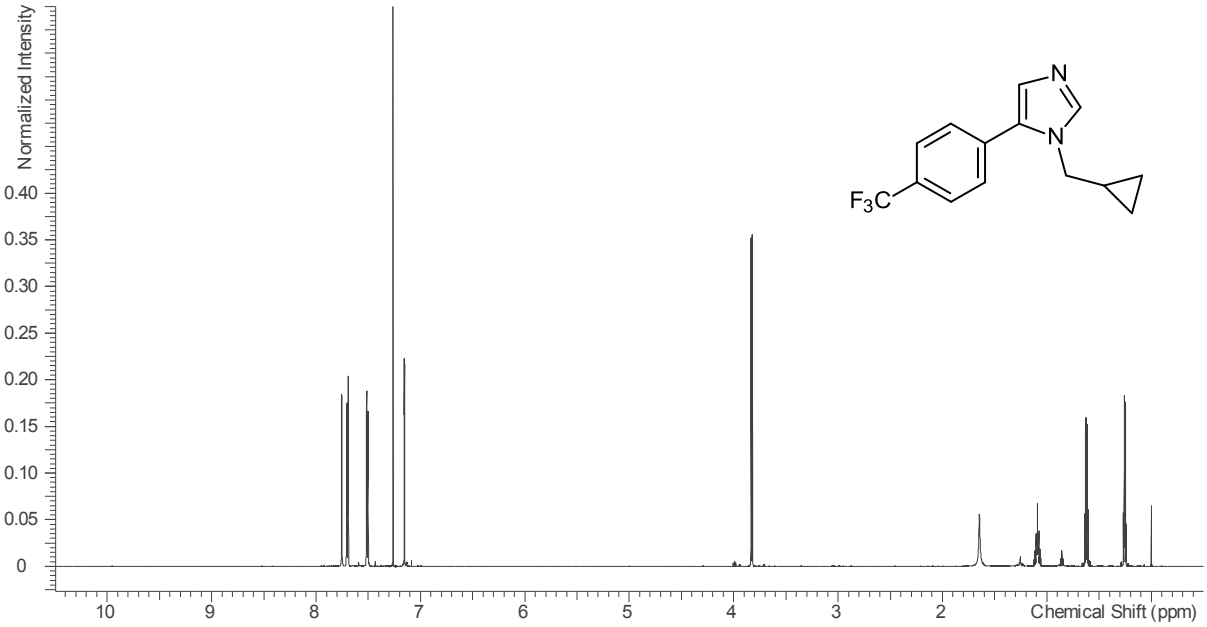
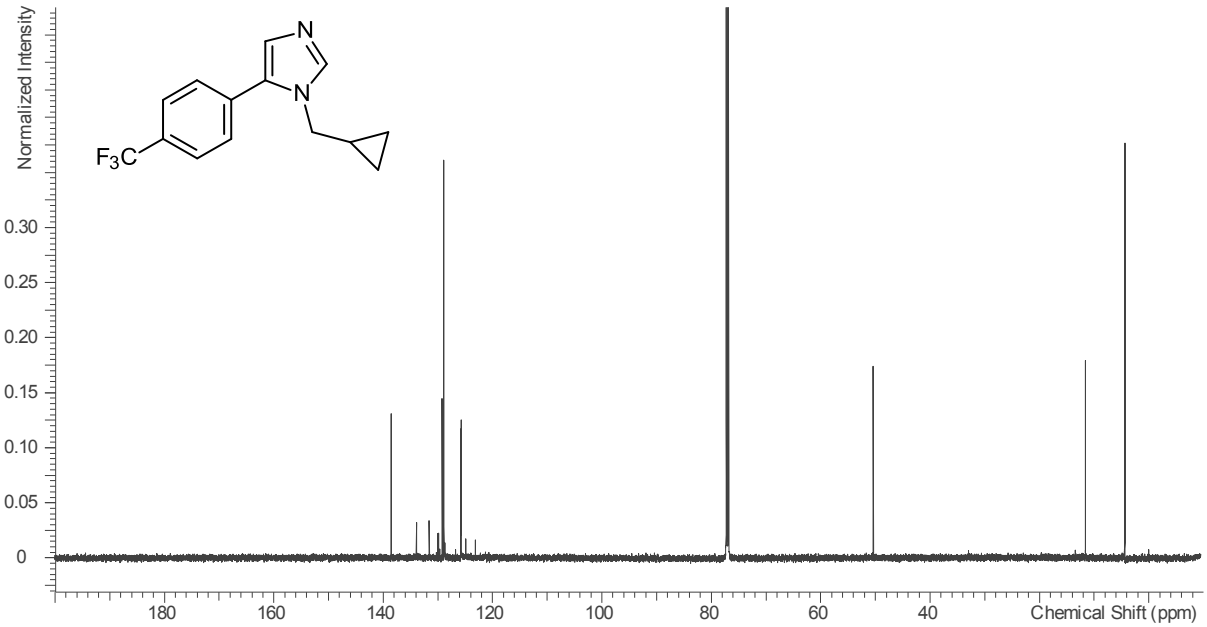
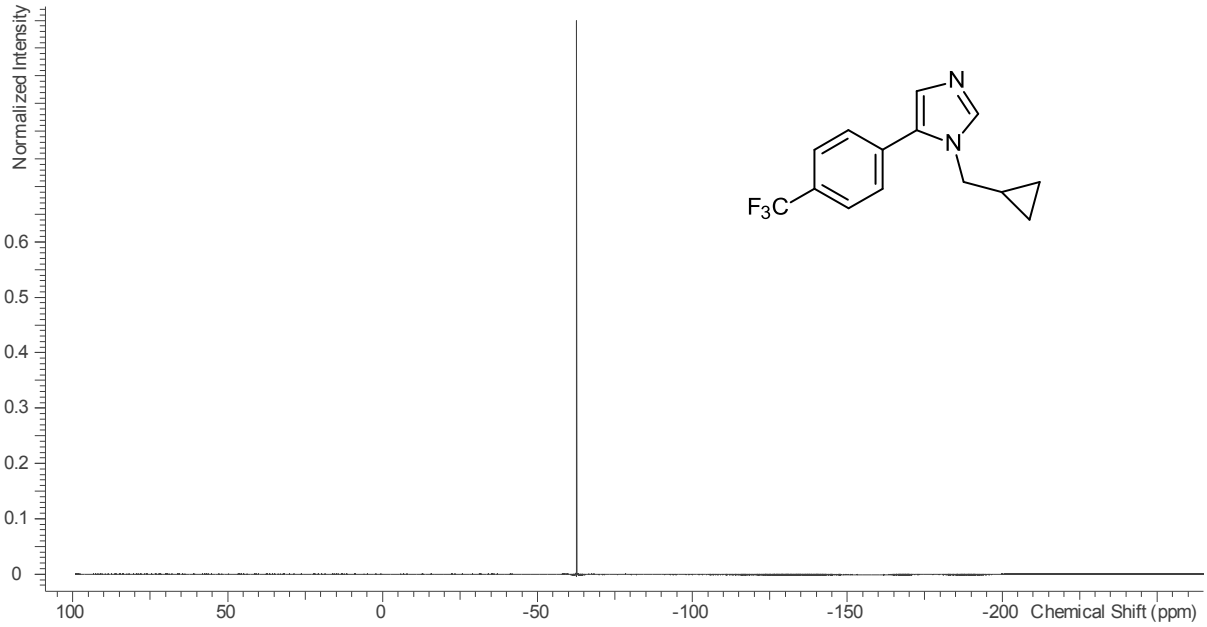
0.5
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
F
F3C
N
N

1-Cyclopropylmethyl-5-(4-trifluoromethyl-phenyl)-1*H*-imidazole (48)






Normalized Intensity
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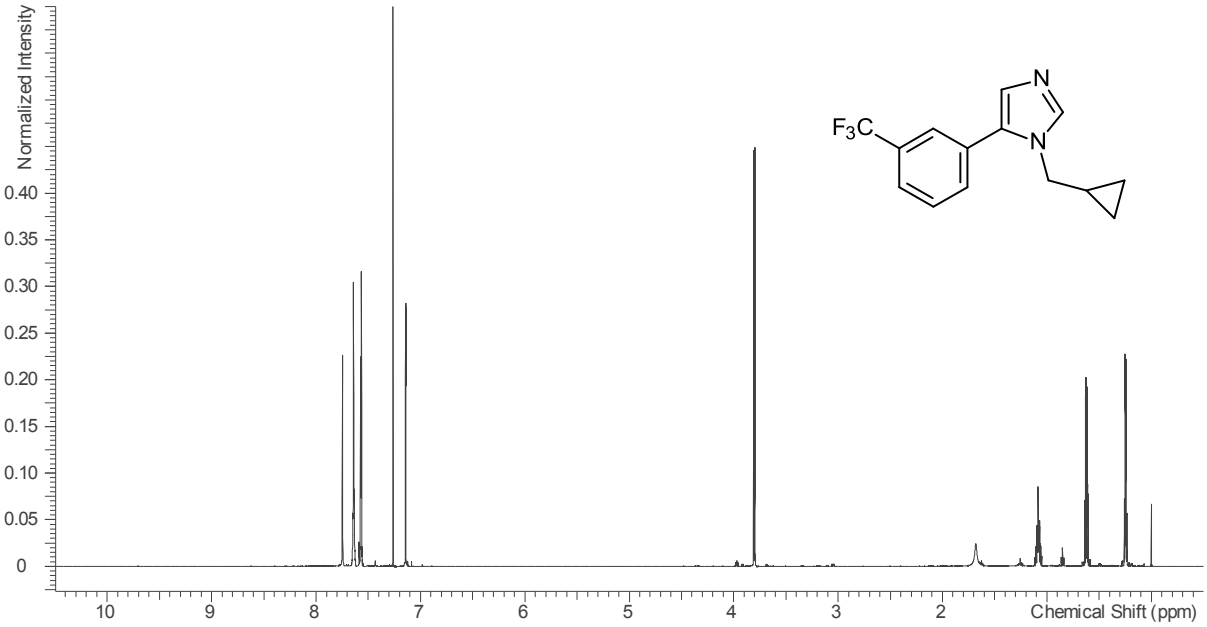
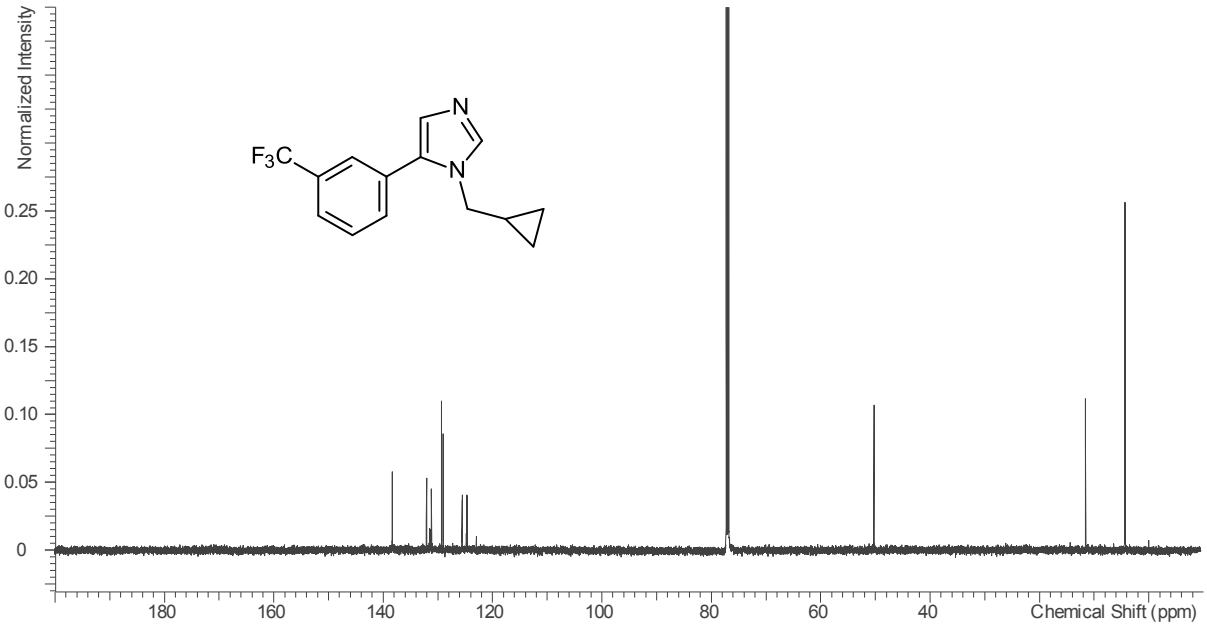
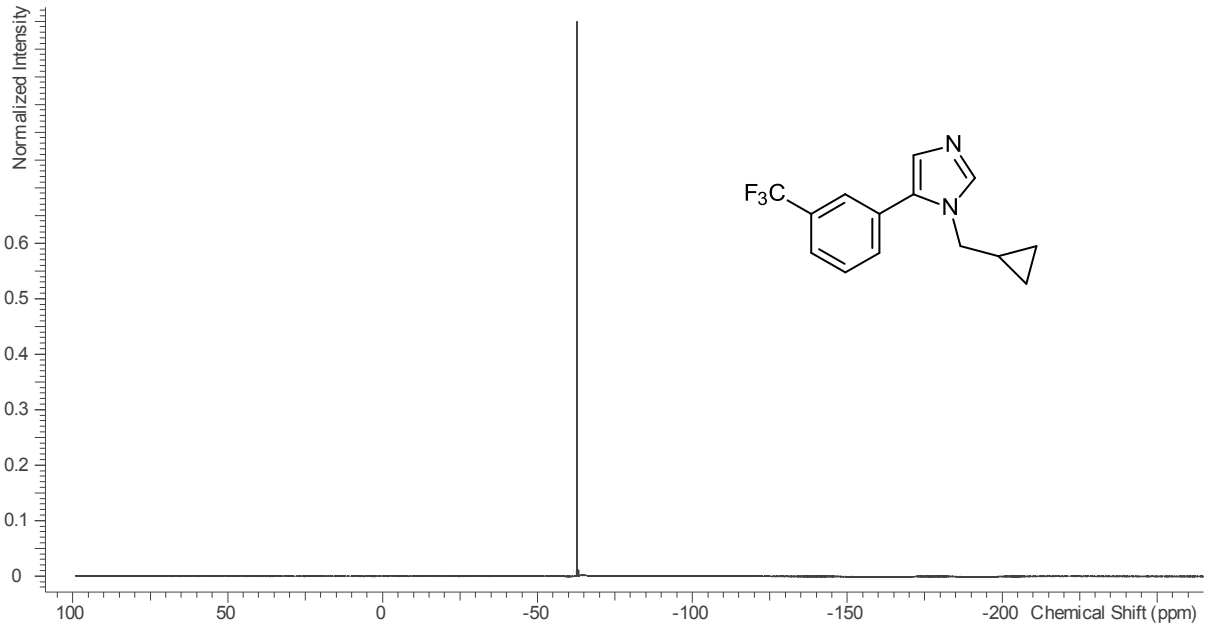
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
N
N
F3C

1-Cyclopropylmethyl-5-(3-trifluoromethyl-phenyl)-1*H*-imidazole (49)






Normalized Intensity
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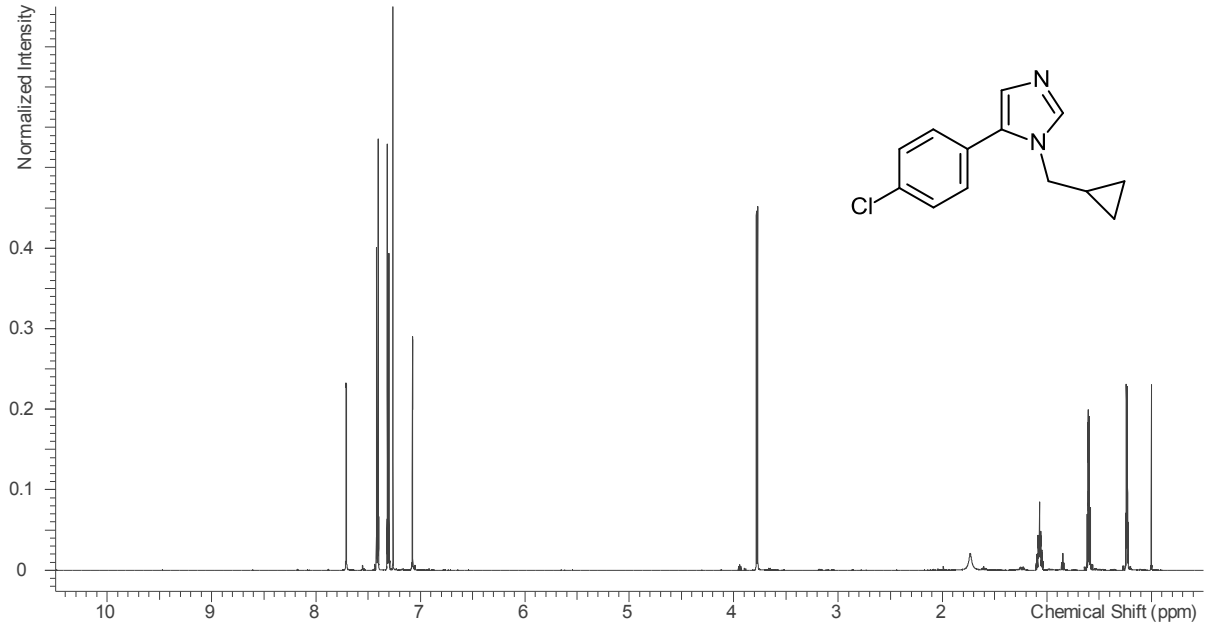
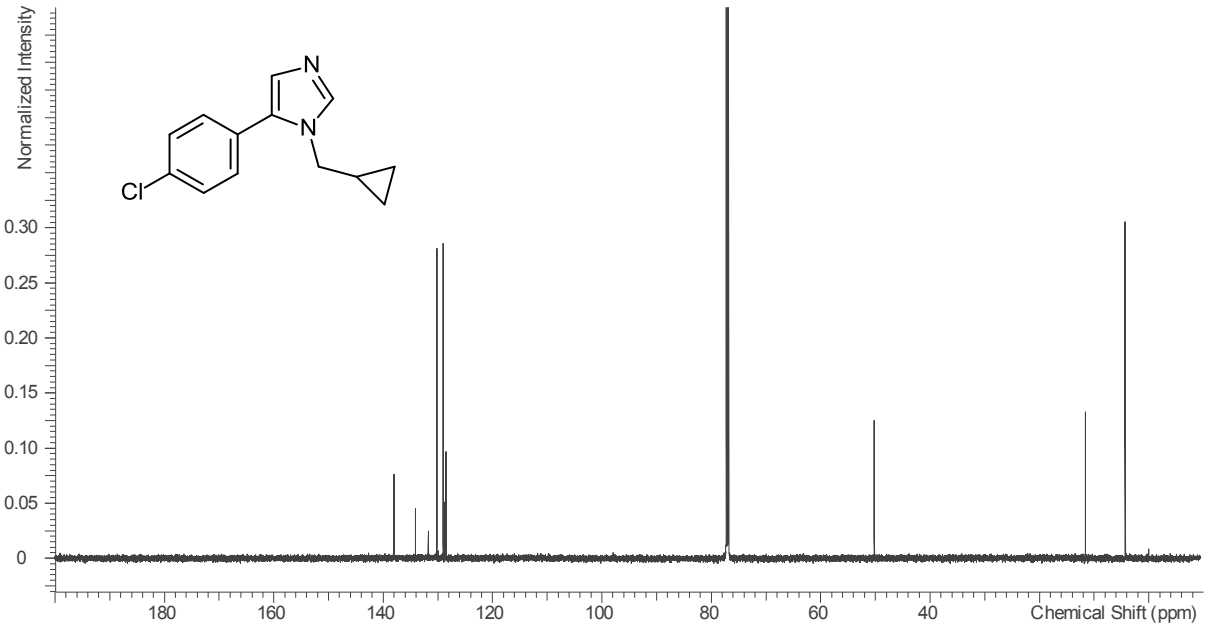
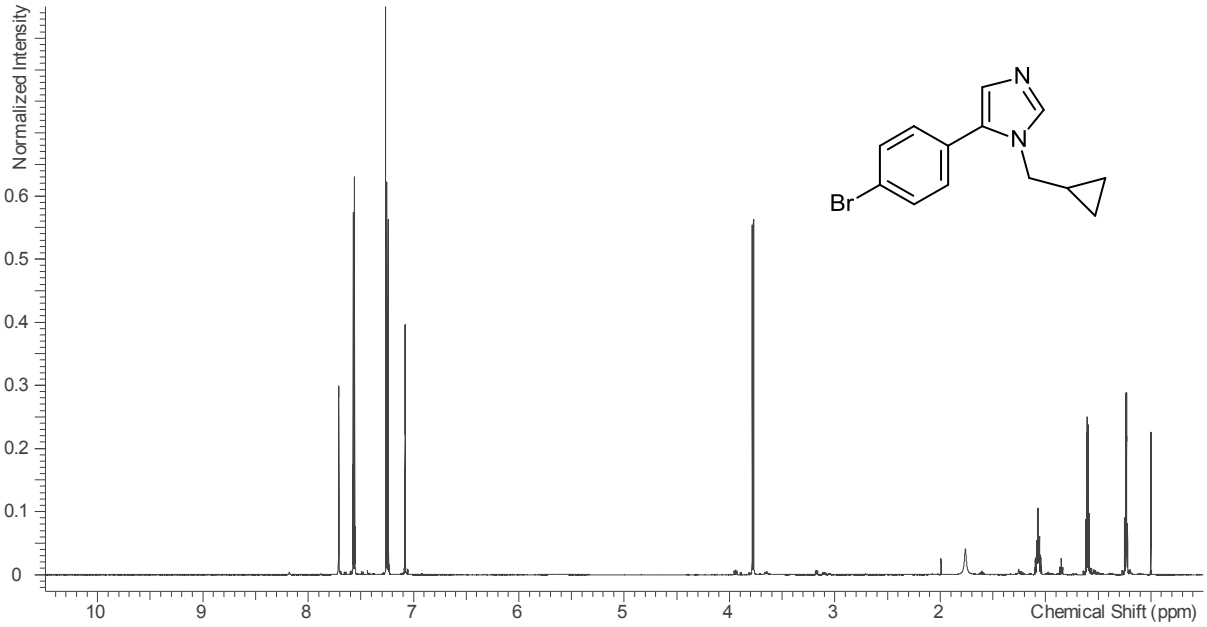
0.4
0.3
0.2
0.1
0
100
50
0
-50
-100
-150
-200
Chemical Shift (ppm)
F3C
N
N

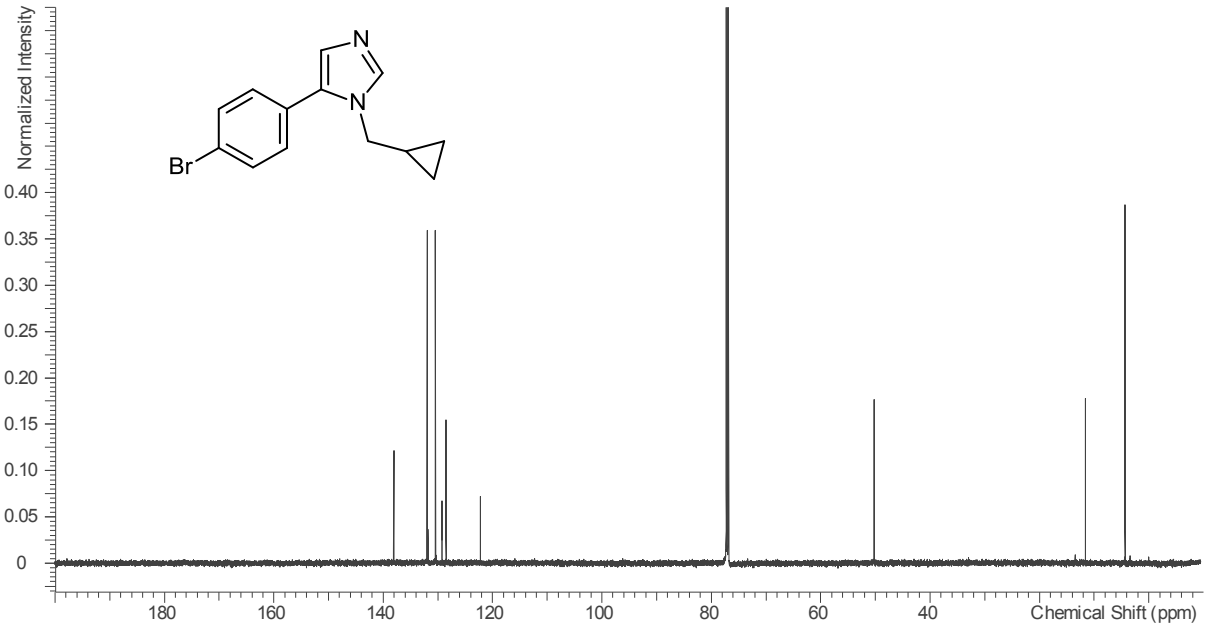
5-(4-Chloro-phenyl)-1-cyclopropylmethyl-1*H*-imidazole (50)



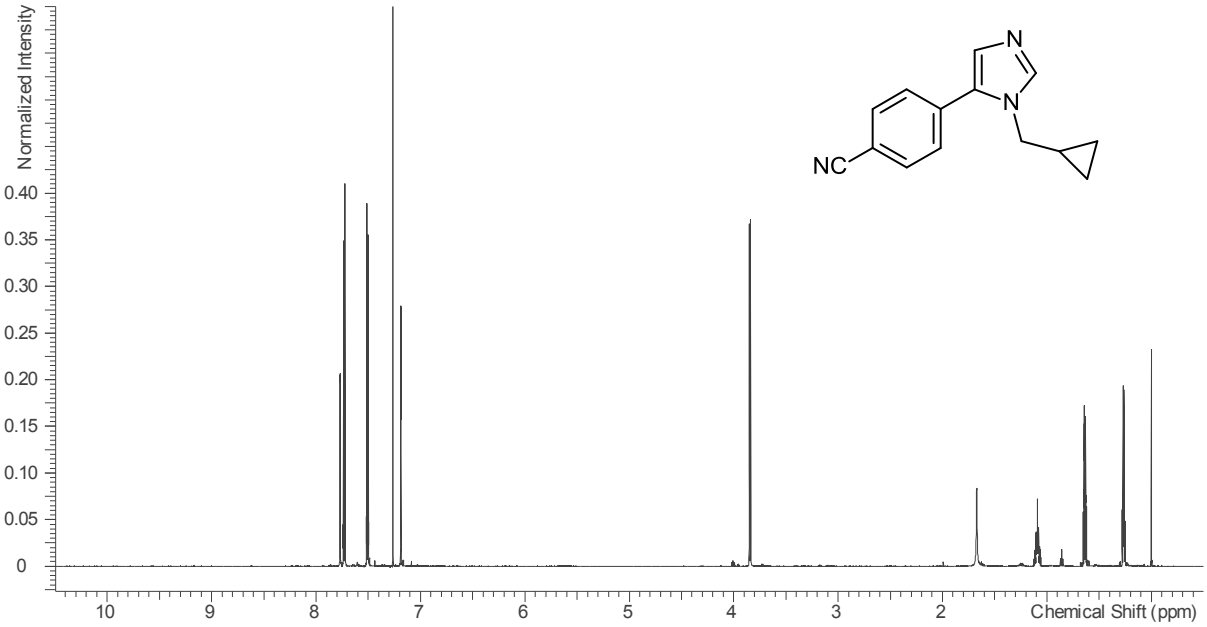


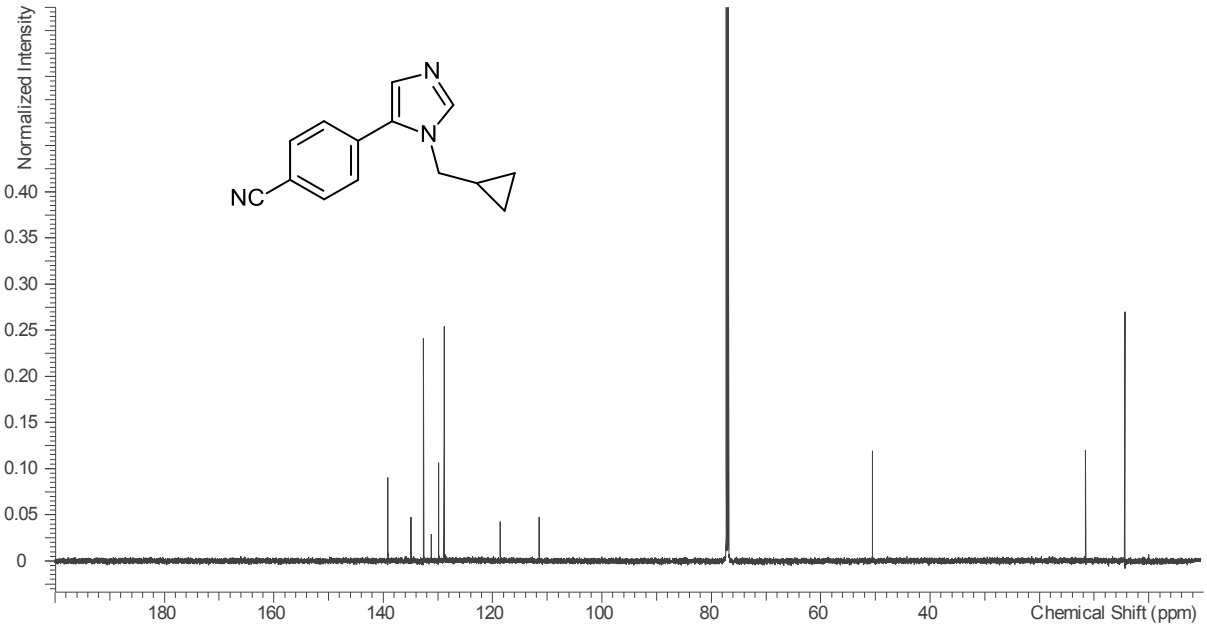
5-(4-Bromo-phenyl)-1-cyclopropylmethyl-1*H*-imidazole (51)



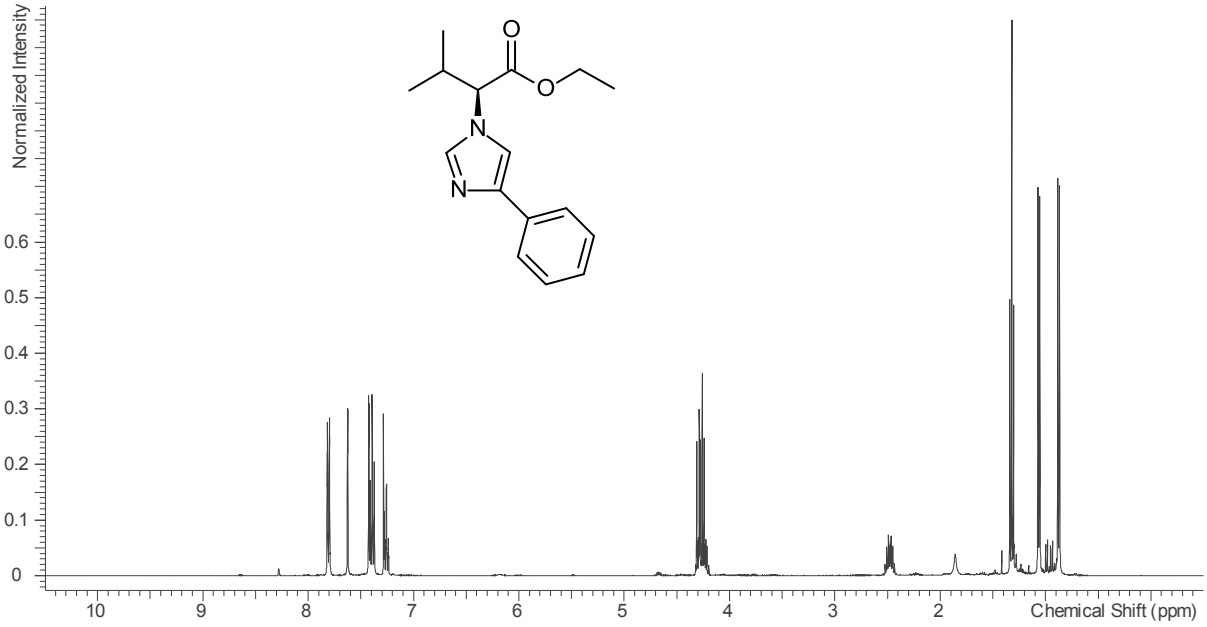


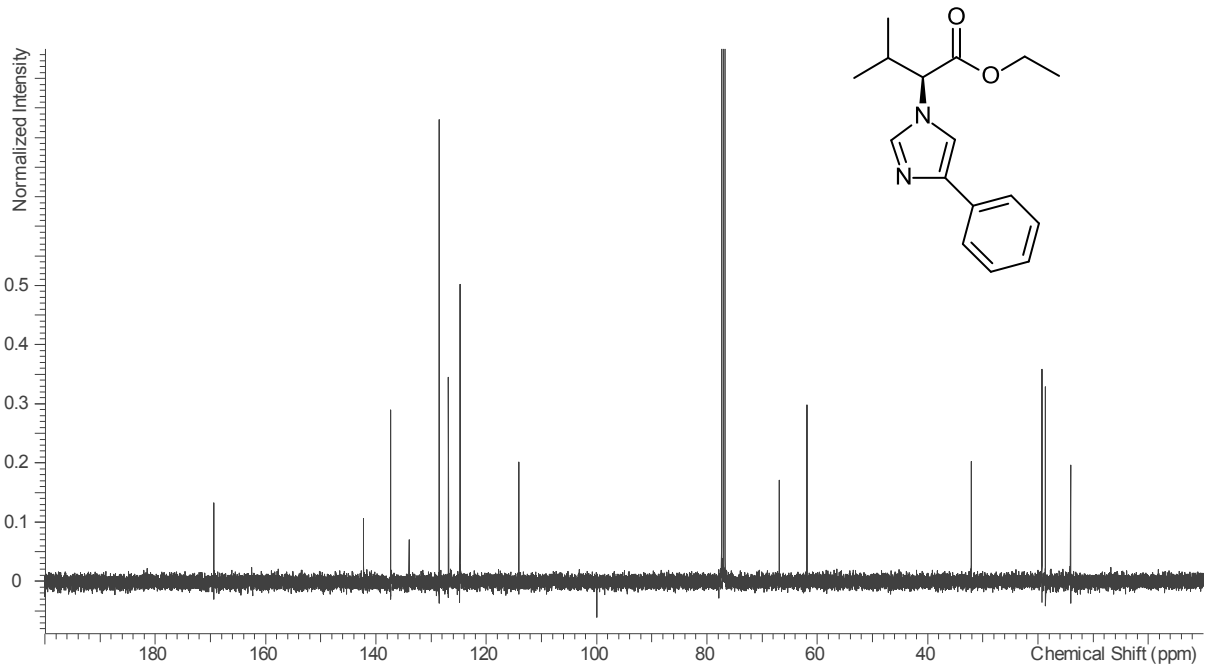
4-(3-Cyclopropylmethyl-3*H*-imidazol-4-yl)-benzonitrile (52)



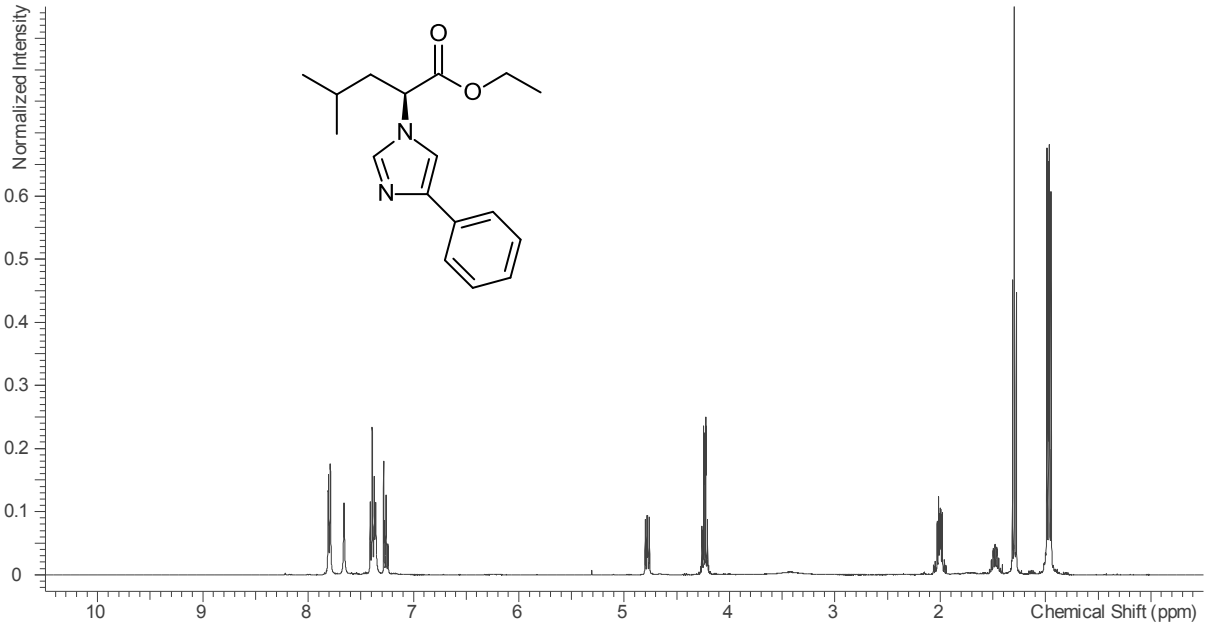


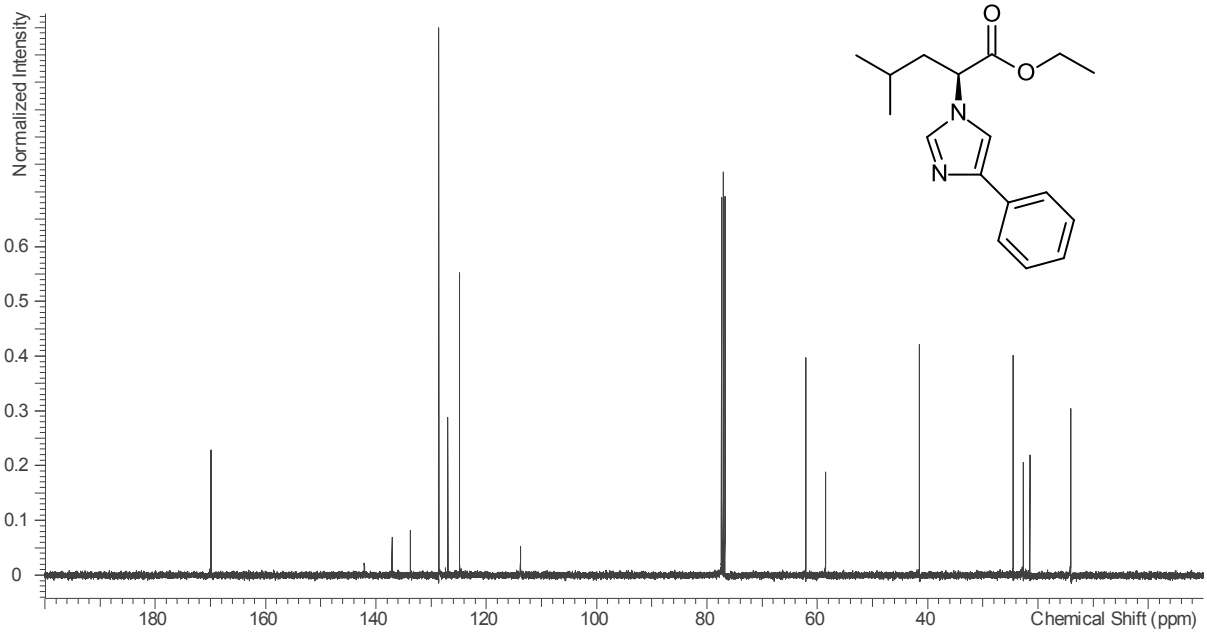
(*S*)-3-Methyl-2-(4-phenyl-imidazol-1-yl)-butyric acid ethyl ester (54)



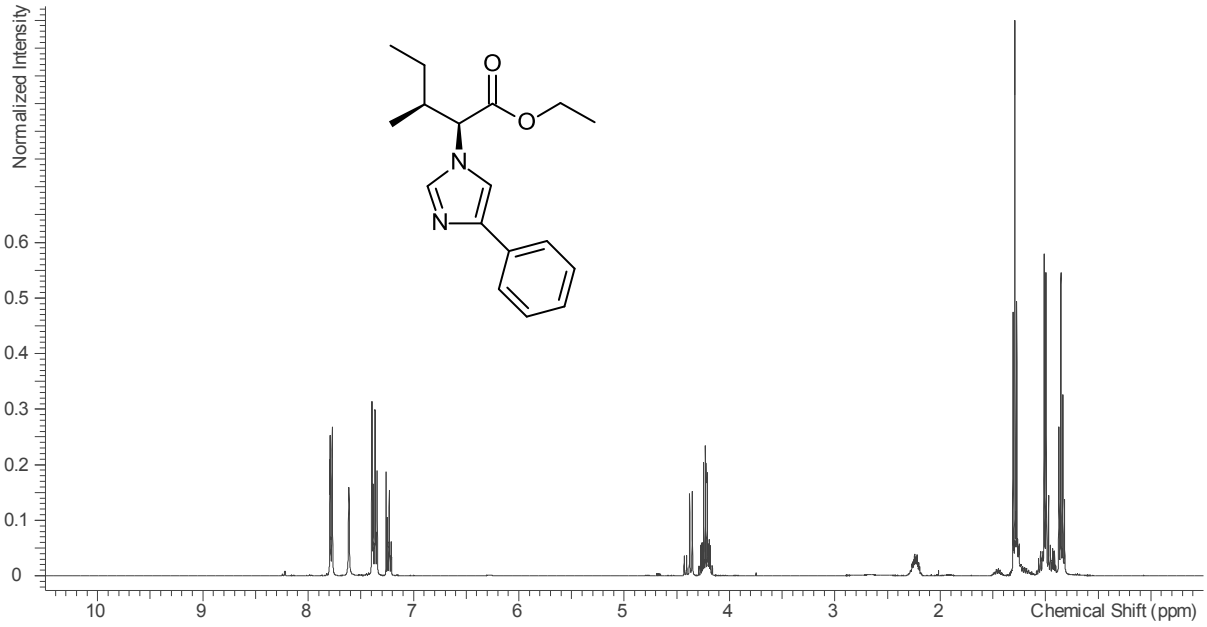


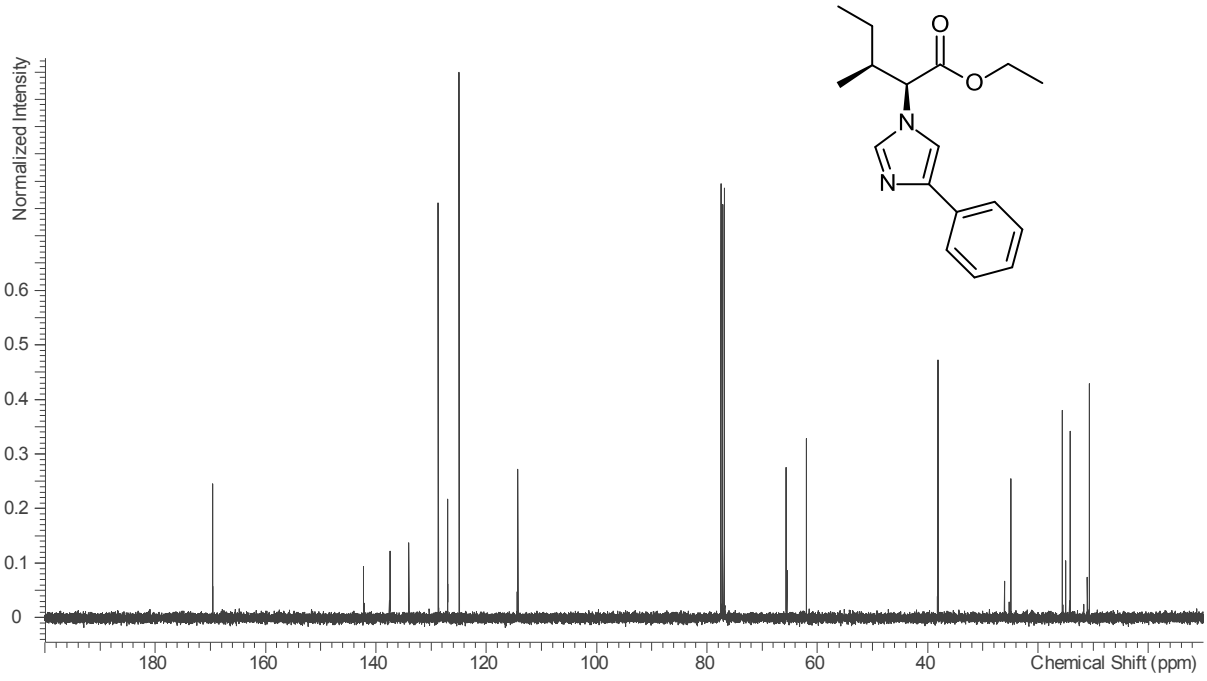
(*S*)-4-Methyl-2-(4-phenyl-imidazol-1-yl)-pentanoic acid ethyl ester (55)





(2*S*,3*S*)-3-Methyl-2-(4-phenyl-imidazol-1-yl)-pentanoic acid ethyl ester (56)





(*S*)-2-(4-Phenyl-imidazol-1-yl)-propionic acid ethyl ester (57)