Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Cu(I)-Catalyzed double C-H Amination: Synthesis of 2-iodo-Imidazo [1, 2-a] pyridines

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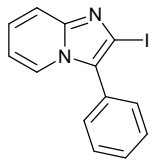
General Information Melting points were uncorrected. ^{1}H and ^{13}C NMR spectra in $CDCl_3$ and CD_3OD were recorded on Bruker Avance III-400 MHz, using $(CH_3)_4Si$ as an internal standard. Chemical shifts (δ) are expressed in parts per million referenced to the residual solvent (i.e., ^{1}H 7.24 ppm, ^{13}C 77.1 ppm for $CDCl_3$; ^{1}H 3.35, 4.78 ppm, ^{13}C 49.3 ppm for CD_3OD). Signal multiplicity is expressed as follows: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet). *J* values are given in hertz (Hz). For the HRMS measurement, Q-TOF was used. All reactions and purity of the synthesized compounds were monitored by TLC using silica gel 60 F254 aluminium plates. Visualization was accomplished by UV light, exposure to iodine vapours and by treating the plates with dragendorff reagent followed by heating. Unless otherwise indicated, materials and solvents were purchased and used without further purification.

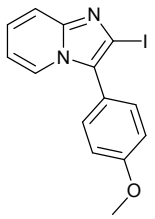
General procedures

Typical Experimental Procedure

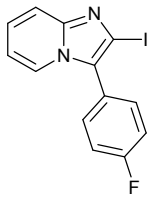
A suspension of 2-aminopyridine **1a** (1.0 eq), phenylacetylene **2a** (1.5 eq), I_2 (1.5 eq) and CuI (10 mol %) in acetonitrile (5 mL) was stirred for 10 min at room temprature, a red homogeneous solution was formed, which was transferred to stir at 80 ^{o}C under an oxygen atmosphere for 8h (reaction progress was monitored by TLC). After reaction was finished, the mixture was quenched by water to stop the reaction. The aqueous solution was extracted with EtOAc (3 x 10 mL) and combined organic layer was washed with saturated Na_2SO_3 solution, dried over anhydrous Na_2SO_4, and evaporated in vacuum. The residue was purified by column (silica gel, 5% EtOAc in petroleum ether) to afford the desired product.



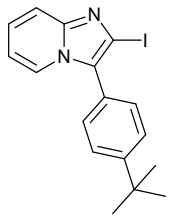
Synthesis of 2-iodo-3-phenylimidazo[1,2-a]pyridine(3a): IR (KBr): ν =2924, 2852, 1465, 1312, 1298, 1185, 1074, 737, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 6.9 Hz, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.55-7.48 (m, 4H), 7.47-7.41 (m, 1H), 7.19-7.11 (m, 1H), 6.68 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.9 (C), 130.0 (2CH), 129.2 (2CH), 128.2 (C), 127.0 (C3), 125.0 (CH), 123.1(CH), 117.1(CH), 112.9 (CH), 93.6 (C2) ppm; HRMS (ESI): calcd. for $C_{17}H_{13}NO$ $[M+H]^{+}$, 320.9844; found:. 320.9849.



2-Iodo-3-(4-methoxyphenyl)imidazo[1,2-a]pyridine (**3b**): IR (KBr) : *v* = 2927, 2850, 1458, 1307, 1285, 1172, 1029, 837, 761, 656 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 6.9 Hz, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.20-7.13 (m, 1H), 7.08 (d, *J* = 8.7 Hz, 2H), 6.73 (t, *J* = 6.8 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2 (C), 146.8 (C), 131.6 (2CH), 126.7 (C), 124.6(CH), 123.1(CH), 120.4(C3), 116.9 (CH), 114.7(2CH), 112.4(CH), 93.3(C2), 55.3(OCH_3) ppm; HRMS (ESI): calcd. for $C_{14}H_{11}IN_2O$, 350.9950; found: 350.9953.

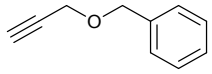


3-(4-Fluorophenyl)-2-iodoimidazo[1,2-a]pyridine (3c): IR (KBr) : *v* = 2924, 2853, 1605, 1541, 1481, 1344, 1227, 1158, 970, 843, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 6.9 Hz, 1H), 7.65 (d, *J* = 9.1 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.28 – 7.18 (m, 3H), 6.79 (t, *J* = 6.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5 (d, *J* = 250.1 Hz), 148.2(C), 133.6 (d, *J* = 8.4 Hz, CH), 127.5(C), 126.7(d, *J* = 6.7 Hz, CH), 125.6(C3), 124.5(CH), 118.5(CH), 117.9 (dd, *J* = 21.8, 2.0 Hz, CH), 114.6 (d, *J* = 4.0 Hz, CH), 94.8(C2) ppm ; HRMS (ESI): calcd. for $C_{14}H_{11}IN_2O$, 338.9750; found: 338.9759.

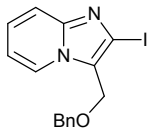


3-(4-(tert-butyl)phenyl)-2-iodoimidazo[1,2-a]pyridine (3d): IR (KBr) : *v* = 2961, 2925, 2854, 1682, 1537, 1300, 1016, 843, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 6.9 Hz, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.22 – 7.14 (m, 1H), 6.74 (t, *J* = 6.8 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3(C),

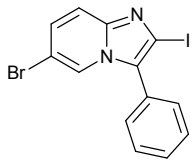
146.6(C), 129.6(2CH), 127.1(C), 126.2(2CH), 125.2(CH), 125.0(C), 123.3(CH), 116.9(CH), 112.9(CH), 92.7(C), 34.9(C), 31.2(CH_3) ppm; HRMS (ESI): calcd. for $C_{17}H_{17}IN_2[M+H]^+$, 377.0470; found: 377.0475.



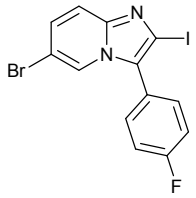
((Prop-2-yn-1-yloxy)methyl)benzene: IR (KBr) : ν = 3444, 3297, 2925, 1651, 1496, 1454, 1355, 1207, 742, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 5H), 4.70 (s, 2H), 4.25 (s, 2H), 2.56 (s, 1H).



3-((Benzyloxy)methyl)-2-iodoimidazo[1,2-a]pyridine (3e): IR (KBr) : ν = 2923, 2853, 1633, 1495, 1453, 1307, 1339, 1216, 1060, 747, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 6.8 Hz, 1H), 7.47 (d, J = 9.1 Hz, 1H), 7.30 – 7.17 (m, 5H), 7.15 – 7.07 (m, 1H), 6.72 (t, J = 6.8 Hz, 1H), 4.76 (s, 2H), 4.40 (s, 2H).); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6(C), 137.5(C), 128.4(2CH), 127.9(2CH), 125.4(CH), 124.0 (CH), 122.6 (C3), 116.9 (CH), 112.9 (CH), 96.0 (C2), 71.7(CH_2), 62.0(CH_2) ppm; ESI-HRMS (m/z): $[M+H]^+$ calcd. for $C_{15}H_{13}IN_2O$, 365.0106; found: 365.0111.

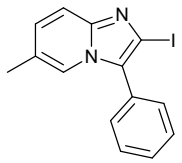


6-Bromo-2-iodo-3-phenylimidazo[1,2-a]pyridine (3f): IR (KBr) : ν = 2924, 2852, 1644, 1490, 1322, 1222, 1058, 929, 797, 760, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 6.9 Hz, 1H), 7.65 (d, J = 9.1 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.28-7.26 (m, 3H), 6.82-6.75 (m, 1H).^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9(C), 130.0(2CH), 129.7(CH), 129.4(2CH), 128.9(CH), 127.5(C4), 127.3(C3), 123.2(CH), 117.5(CH), 108.3(C6), 93.2(C2) ppm; HRMS (ESI): calcd. for $C_{13}H_8BrIN_2[M+H]^+$, 398.8949; found: 398.8956.

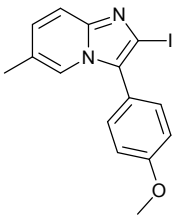


6-Bromo-3-(4-fluorophenyl)-2-iodoimidazo[1,2-a]pyridine(3g): IR (KBr) : ν = 2924, 2853, 1606, 1538, 1479, 1320, 1158, 842, 797 cm^{-1}**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.54 – 7.49 (m, 3H), 7.31-7.27 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2 (d, J = 251.0 Hz, C), 144.1(C), 131.1(CH) (d, J = 8.4 Hz), 127.6(CH), 125.4(C), 122.5(C), 121.9(CH), 116.7(CH), 115.8 (CH) (d, J = 21.9Hz), 107.2(C6), 93.2(C1) ppm; HRMS (ESI): calcd. for $C_{13}H_7BrFIN_2[M+H]^+$, 416.8855; found: 416.8863.

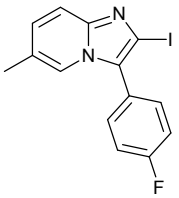
3-((Benzyloxy)methyl)-6-bromo-2-iodoimidazo[1,2-a]pyridine (3h): IR (KBr) : ν = 2921, 2851, 1515, 1486, 1325, 1217, 1027, 938, 837, 744, 698, 642 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.38 (d, J = 9.5 Hz, 1H), 7.28-7.18 (m, 6H), 4.75 (s, 2H), 4.44 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9(C), 137.1(C), 129.0(CH), 128.5(2CH), 128.1(CH), 128.0(2CH), 124.2(CH) 123.1(C3), 117.4(CH), 107.9(C6), 96.2(C2), 71.9(CH_2), 61.6 (CH_2) ppm; HRMS (ESI): calcd. for $C_{15}H_{12}BrIN_2O$ $[M+H]^+$, 442.9211; found: 442.9222.



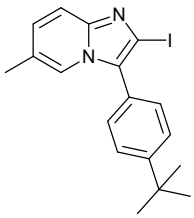
2-Iodo-6-methyl-3-phenylimidazo[1,2-a]pyridine (3i): IR (KBr) : ν = 2923, 2853, 1741, 1444, 1405, 1227, 1158, 1074, 799, 757, 700, 596 cm^{-1}**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.59– 7.48 (m, 6H), 7.05 (d, J = 7.8 Hz, 1H), 2.28 (d, J = 0.8 Hz 3H)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9(C), 130.1, 129.2, 129.0, 128.1, 122.7, 120.8, 116.4, 92.7(C2), 18.2(CH_3) ppm; HRMS (ESI): calcd. for $C_{14}H_{11}IN_2O[M+H]^+$, 335.0000; found: 335.0009.



2-Iodo-3-(4-methoxyphenyl)-6-methylimidazo[1,2-a]pyridine(3j): IR (KBr) : ν = 2954, 2924, 2853, 1543, 1441, 1301, 1225, 1176, 1031, 966, 831, 799, 601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.46 (d, J = 9.2 Hz, 1H), 7.36 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 9.2 Hz, 1H), 3.83 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2(C), 145.4(C), 131.6 (2CH), 128.4(CH), 126.7(C), 122.9(C), 120.8(CH), 120.1(C), 116.0(CH), 114.7(2CH), 91.8(C), 55.3(OCH_3), 17.9(CH_3) ppm; HRMS (ESI): calcd. for $C_{15}H_{13}IN_2O[M+H]^+$, 365.0106; found: 365.1015.

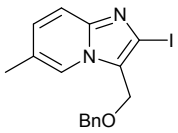


3-(4-Fluorophenyl)-2-iodo-6-methylimidazo[1,2-a]pyridine (3k): IR (KBr) : ν = 2924, 2853, 1606, 1481, 1332, 1224, 1158, 833, 799 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.62 (d, J = 9.1 Hz, 1H), 7.51 (dd, J = 8.6, 5.3 Hz, 2H), 7.27 (t, J = 8.6 Hz, 2H), 7.12 (d, J = 8.9 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ163.0 (d, J = 252 Hz), 145.6(C), 132.2(2CH), 128.6(CH), 125.8(C), 124.2(C), 122.9(C), 120.7(CH), 116.6(CH), 116.4(CH), 116.3(CH), 92.5(C), 18.5(CH_3) ppm; HRMS (ESI): calcd. for $C_{14}H_{10}FIN_2[M+H]^+$, 352.9906; found: 352.9911.

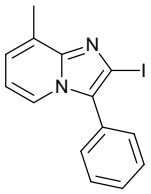


3-(4-(tert-butyl)phenyl)-2-iodo-6-methylimidazo[1,2-a]pyridine (3l): IR (KBr) : ν = 2961, 2925, 2866, 1648, 1504, 1332, 1298, 1226, 1127, 1022, 967, 754, 606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 9.1 Hz, 1H), 7.39 (d, J = 8.5 Hz, 2H), 6.96 (dd, J = 9.2, 1.5 Hz, 1H), 2.20 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (125 MHz,

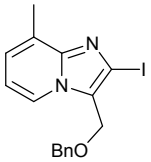
$CDCl_3$) δ 152.1(C), 145.8(C), 129.7(2CH), 128.0(CH), 126.1(2CH), 125.3(C), 122.5(C), 120.9(CH), 116.3(CH), 92.6(C), 34.8(C), 31.3($3CH_3$), 18.2(CH_3) ppm; ESI-HRMS (m/z): $[M+H]^+$ calcd for $C_{18}H_{19}IN_2$, 391.0626; found: 391.0635.



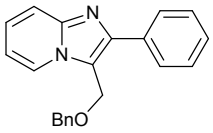
3-((Benzyloxy)methyl)-2-iodo-6-methylimidazo[1,2-a]pyridine (3m): IR (KBr) : ν = 2923, 2853, 1674, 1581, 1453, 1311, 1228, 1123, 1084, 801 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.41 (d, J = 9.2 Hz, 1H), 7.30 – 7.21 (m, 5H), 7.01 (d, J = 9.2 Hz, 1H), 4.76 (s, 2H), 4.43 (s, 2H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 146.1(C), 137.6, 129.7, 128.0, 127.6, 127.5, 126.5, 123.5, 122.2, 114.3, 92.8, 71.5(CH_2), 61.0(CH_2), 16.4(CH_3) ppm; ESI-HRMS (m/z): $[M+H]^+$ calcd for $C_{16}H_{15}IN_2O[M+H]^+$, 379.0263; found: 379.0267.



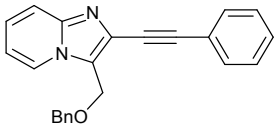
2-Iodo-8-methyl-3-phenylimidazo[1,2-a]pyridine(3n) : IR (KBr) : ν = 2923, 2853, 1740, 1490, 1348, 1298, 1082, 858, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 6.9 Hz, 1H), 7.52 – 7.39 (m, 5H), 6.93 (d, J = 7.8 Hz, 1H), 6.61 (t, J = 6.9 Hz, 1H), 2.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.4(C), 130.1, 129.0, 128.6, 127.3, 127.0, 123.7, 121.1, 112.8, 93.0(C2), 17.0(CH_3) ppm; ESI-HRMS (m/z): $[M+H]^+$ calcd for $C_{14}H_{11}IN_2$, 335.0000; found: 335.0005.



3-((benzyloxy)methyl)-2-iodo-8-methylimidazo[1,2-a]pyridine(3o): IR (KBr) : ν = 2923, 2852, 1702, 1631, 1489, 1309, 1221,1158, 1063, 745, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 6.8 Hz, 1H), 7.28 – 7.20 (m, 5H), 6.94 (d, J = 8.0 Hz, 1H), 6.67 (t, J = 6.9 Hz, 1H), 4.79 (s, 2H), 4.41 (s, 2H), 2.53 (s, 3H)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1(C), 137.5(C), 128.4(2CH), 128.0(2CH), 127.9(CH), 126.8(C), 124.4(CH), 122.8(C), 121.9(CH), 113.0(CH), 95.4(C), 71.5(CH_2), 62.1(CH_2), 17.0(CH_3) ppm; ESI-HRMS (m/z): calcd for $C_{16}H_{15}IN_2O[M+H]^+$, 379.0263; found: 379.0268.

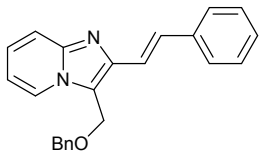


3-((Benzyloxy)methyl)-2-phenylimidazo[1,2-a]pyridine (8): A mixture of **3e** (0.5 mmol), phenylboronic acid (0.7 mmol), K_2CO_3 (70 mg, 0.7 mmol), and $Pd(PPh_3)_2Cl_2$ (0.025 mmol) in DMF−H_2O (4:1, 3 mL) was stirred for 24 h at 80 °C. Then the resultant mixture was poured into H_2O (15 mL) and was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. The solvent was removed on a under vacuum, and the residue was purified by column chromatography [silica gel, 5% EtOAc in petroleum ether] to give **8** (90%)**;** IR (KBr) : ν = 2924, 2853, 1634, 1504, 1453, 1361, 1058, 1027, 847, 773, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 6.9 Hz, 1H), 7.64 (t, J = 8.6 Hz, 3H), 7.42-7.21 (m, 8H), 7.18 (t, J = 7.9 Hz, 1H), 6.77 (t, J = 6.3 Hz, 1H), 4.84 (s, 2H), 4.49 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.4(C), 145.1(C), 137.4(C), 133.7(C), 128.7(2CH), 128.6(2CH), 128.5(2CH), 128.2(2CH), 128.1(CH), 128.0(CH), 125.4(CH), 124.3(CH), 117.3(CH), 116.7(C), 112.6(CH), 72.0(CH_2), 60.8(CH_2) ppm; ESI-HRMS (m/z): calcd for $C_{21}H_{18}N_2O$ $[M+H]^+$, 315.1453; found: 315.1462.

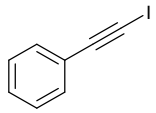


3-((Benzyloxy)methyl)-2-(phenylethynyl)imidazo[1,2-a]pyridine (9): A mixture of **3a** (0.5 mmol), phenylacetylene (1 mmol), $Pd(PPh_3)_2Cl_2$ (0.01 mmol) and CuI (0.1 mmol) in Et_3N (2 mL) was stirred for 12 h at 80 °C under N_2(reaction progress was monitored by TLC). Then the resultant mixture was poured into H_2O (15 mL) and was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by column chromatography [silica gel, 5% EtOAc in petroleum ether] to give (95%) of desired compound **9**; IR (KBr) : ν = 2959, 2923, 2853, 2221, 1635, 1497, 1352, 1261, 1205, 1158, 1066, 801, 691, 625 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 6.7 Hz, 1H), 7.52 (d, J = 9.1 Hz, 1H), 7.44 (dd, 2H), 7.29-7.17 (m, 9H), 6.80 (d, J = 6.8 Hz, 1H), 4.90 (s, 2H), 4.44 (s, 2H); ^{13}C NMR (125 MHz, CD_3Cl_3) δ 144.8(C), 137.5(C), 131.2(2CH), 128.8(CH), 128.2(2CH), 128.0(2CH), 127.7(2CH), 127.54(CH), 127.51(CH), 126.8(C), 125.0(CH),

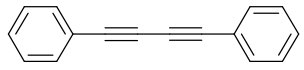
124.2(C), 122.0(C), 115.6(CH), 113.6(CH), 93.4(C), 80.4(C), 71.4(CH_2), 59.3(CH_2) ppm; ESI-HRMS (m/z): calcd for $C_{23}H_{18}N_2O$ $[M+H]^+$, 339.1453; found: 339.1461.



3-((Benzyloxy)methyl)-2-styrylimidazo[1,2-a]pyridine (10): A mixture of **3a** (0.5 mmol), Na_2CO_3 (1.25 mmol), n-Bu_4NBr (0.5 mmol), $Pd(OAc)_2$ (0.05 mmol), and styrene (2.0 mmol) in DMF (2 mL) in a DMF, was stirred for 24 h at 85 °C under N_2. Then the resultant mixture was poured into H_2O (15 mL) and was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by column chromatography [silica gel, 5% EtOAc in petroleum ether] to give **10** (90%); IR (KBr) : ν = 2924, 2853, 1730, 1633, 1503, 1452, 1361, 1063, 964, 757, 738, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 6.8 Hz, 1H), 7.60 (dd, J = 12.5, 9.5 Hz, 2H), 7.46 (d, J = 7.3 Hz, 2H), 7.32-7.19 (m, 9H), 6.97 (d, J = 15.9 Hz, 1H), 6.76 (t, J = 6.7 Hz, 1H), 4.86 (s, 2H), 4.44 (s, 2H)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.7(C), 142.5(C), 137.4(C), 137.0(C), 131.8(CH), 128.7(2CH), 128.6(2CH), 128.1(2CH), 128.0(CH), 127.9(CH), 126.8(2CH), 126.1(CH), 124.4(CH), 117.6(C), 117.2(CH), 116.8(CH), 112.5(CH), 71.1(CH_2), 59.2(CH_2) ppm; ESI-HRMS (m/z): calcd for $C_{23}H_{20}N_2O$ $[M+H]^+$, 341.1609; found: 341.1618.



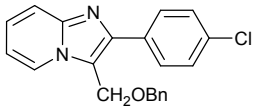
(Iodoethynyl)benzene (5): A mixture of phenylacetylene, CuI and I_2 in acetonitrile was stirred at room temperature for 10 min (reaction progress was monitored by TLC). After reaction was finished, the mixture was evaporated in vacuum. The residue was purified by column (silica gel, 5% EtOAc in petroleum ether) to afford the desired product IR (KBr) : ν = 3049, 2853, 2681,2248, 1485, 1440, 1242, 915, 756, 687 cm^{-1}; ^{1} H NMR (400 MHz, $CDCl_3$): δ = 7.29 – 7.33 (m, 3H), 7.43 – 7.46 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 132.4, 129.2, 128.2, 121.7, 81.5, 73.8ppm.



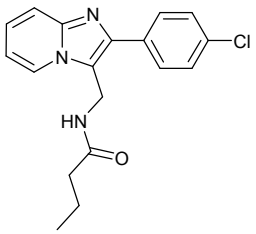
1,4-diphenylbuta-1,3-diyne: A mixture of iodophenylacetylene(**5**), CuI and I_2 in acetonitrile was stirred at 80 ^oC for 6 h under O_2 atmosphere (reaction progress was monitored by TLC). After reaction was finished, the mixture was evaporated in vacuum. The residue was purified

by column (silica gel, 5% EtOAc in petroleum ether) to afford the desired product IR (KBr) : ν = 3049, 2853, 2681,2248, 1485, 1440, 1242, 915, 756, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 – 7.52 (m, 4H), 7.37 – 7.32 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 131.49, 128.19, 127.43, 120.79, 80.55, 72.91 ppm.

Total synthesis of Saripidem

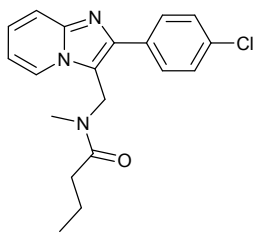


3-((benzyloxy)methyl)-2-(4-chlorophenyl)H-imidazo[1,2-a]pyridine(11): A mixture of **3e** (200 mg, 0.54 mmol), 4-chlorophenylboronic acid (129 mg, 0.82 mmol), K_2CO_3 (1.35 mmol), and $Pd(PPh_3)_2Cl_2$ (0.025 mmol, 10 mol%) in DMF−H_2O (5:1, 3 mL) was stirred for 24 h at 80 °C. Then the resultant mixture was poured into H_2O (15 mL) and was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. The solvent was removed on a under vacuum, and the residue was purified by column chromatography [silica gel, 5% EtOAc in petroleum ether] to give 180 mg of product **11** (90%); IR (KBr) : ν = 2923, 2855, 1635, 1502, 1488, 1360, 1055, 1012, 838, 752, 737, 699 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 6.9 Hz, 1H), 7.72-7.60 (m, 3H), 7.40 – 7.31 (m, 6H), 7.26 (d, J = 3.0 Hz, 2H), 6.86 (td, J = 6.8, 1.1 Hz, 1H), 4.89 (s, 2H), 4.59 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2(C), 144.6(C), 137.7(C), 134.7(C), 133.0(C), 129.8(2CH), 128.8(2CH), 128.6(2CH), 128.2(2CH), 128.1(CH), 128.0(CH), 125.4(CH), 124.2(CH), 117.5(CH), 116.8(C), 112.6(CH), 72.1(CH_2), 60.6(CH_2) ppm; ESI-HRMS (m/z): calcd. for $C_{21}H_{17}ClN_2O$ $[M+H]^+$, 349.1102; found: 349.1103.



N-((2-(4-chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)methyl)butyramide(13): A solution of **11** (150 mg, 0.57 mmol) in DCM (5 ml) equipped with nitrogen inlet-outlet was cooled to -78 ^{o}C. After 10 minutes, BCl_3 (1M, 6 eqvt) was added into the reaction mixture at a rate so

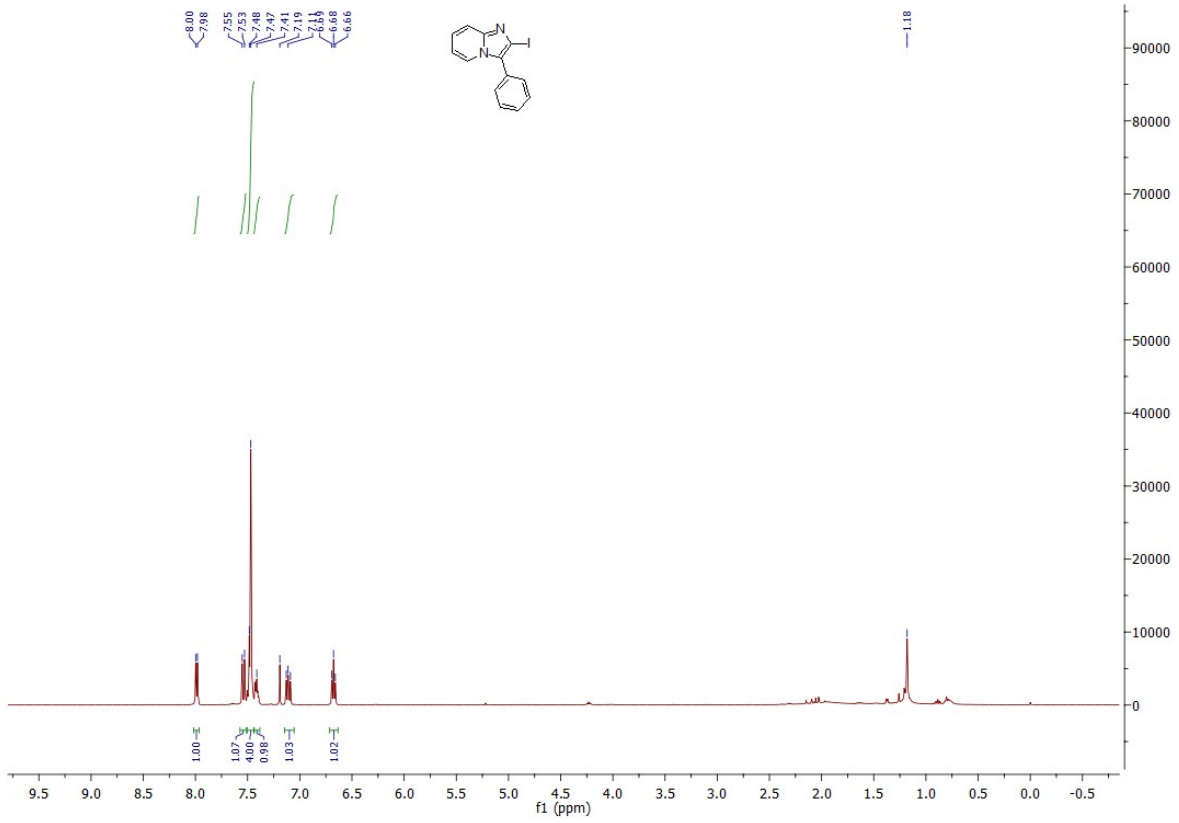
that the reaction temperature did not exceed -65^{o}C. The reaction mixture was stirred at -78 ^{o}C for 0.5h and then it was warmed upto -20 ^{o}C and stirred for 2-3 hrs. After the completion of the reaction, MeOH (10 mL) was added into the mixture. This was stirred for 10 minutes and later concentrated in vacuo to remove methanol to afford yellowish white solid. This was dissolved in water (20 ml) and extracted with ethyl acetate (2x30 ml). Crude was further purified on silica gel (5% MeOH/DCM) to give 80 mg of alcohol, that was proceed for next step without column purification. In next step, a solution of butyronitrile (0.06 mL, 0.58 mmol) at 0 ^{o}C, concentrated H_2SO_4 (0.3 mL, 20 equiv) was added slowly and the mixture was stirred for 30 min. A solution of alcohol (75 mg, 0.29 mmol) in MeOH (2 mL) was added dropwise to the above mixture at 0 ^{o}C during these 30 min. Then the mixture was warmed to room temperature and stirred for 1h. After completion of the reaction, the reaction mixture was concentrated under vacuum to remove methanol to afford white solid. Further it was dissolved in water, basified with potassium carbonate solution till pH 8, extracted with Dichloro methane (3 x 30 mL). The solid crude was purified on silica gel (2% MeOH/DCM) to give white crystallized compound **13** (90 %). IR (KBr) : ν = 3418, 2961, 2924, 1634, 1503, 1405, 1266, 1093, 1013, 836, 757, 514 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 6.8 Hz, 1H), 7.60 (d, J = 8.2 Hz, 3H), 7.39 (d, J = 6.9 Hz, 2H), 7.27 (s, 1H), 6.87 (t, J = 6.8 Hz, 1H), 5.93 (s, 1H), 4.93 (d, J = 5.2 Hz, 2H), 2.21 (t, J = 7.4 Hz, 2H), 1.71 – 1.65 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5 (CO), 145.0 (C8a), 143.3 (C2) , 134.0 (C1'), 132.2 (C4'), 129.5 (2C, C3', C5'), 128.9 (2C, C2', C6'), 125.4 (C5), 124.6 (C7), 117.3 (C8), 116.7 (C3), 112.9 (C6), 38.5 (CH_2), 32.4 (CO*C*H_2), 18.9 (CH_2), 13.7 (CH_3)ppm; ESI-HRMS (m/z): calcd. for $C_{21}H_{17}ClN_2O$ $[M+H]^+$, 328.1211; found: 328.1234.

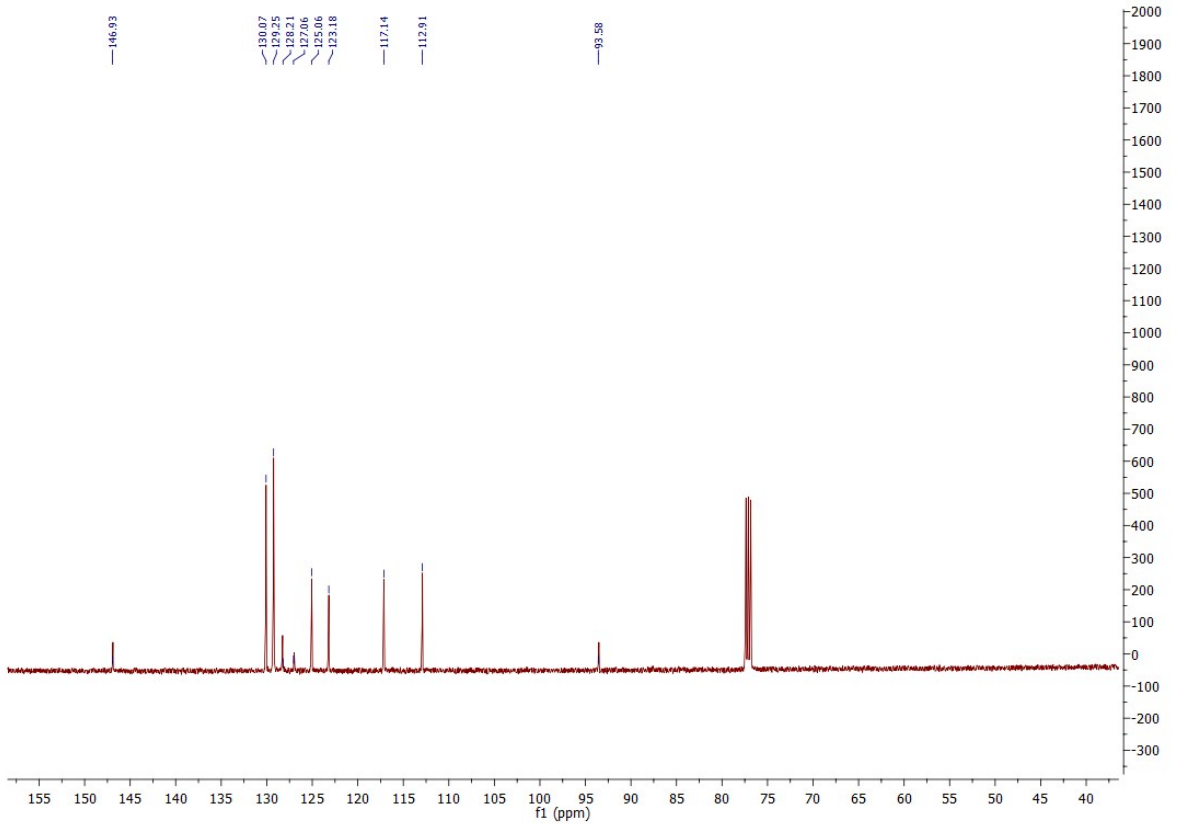


N-((2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methyl)-N-methylbutyramide(Saripidem). To a solution of **13** (91 mg, 0.28 mmol) in DMF (2 mL) cooled to 5 ºC (ice bath) sodium hydride (60% in mineral oil) (20 mg, 0.42 mmol) was added portionwise. The mixture was stirred at rt for 30 min. To the resulting orange solution was added methyl iodide (100 mg, 0.42 mmol), and the mixture stirred at rt for 1 h. Then, the solvent was removed under reduced pressure,

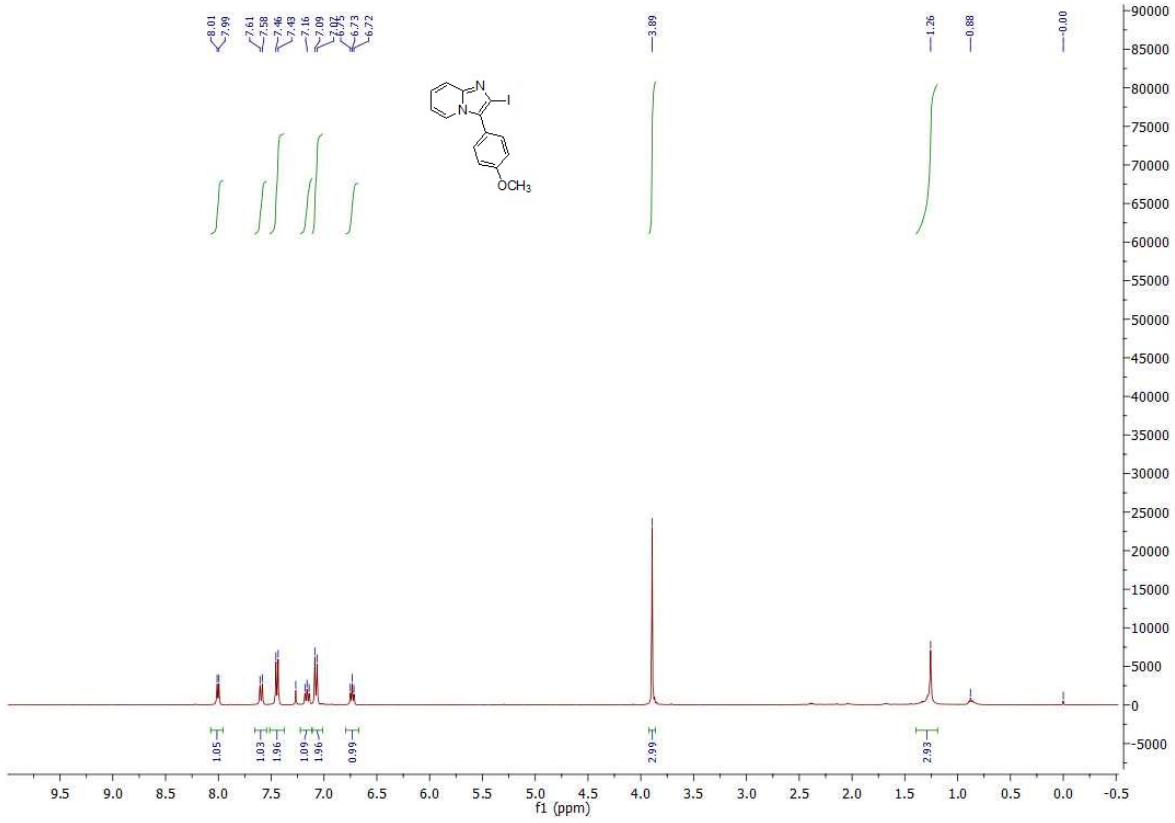
water was added and the mixture was extracted with CH_2Cl_2. The organic phase was dried over sodium sulphate and the solvent was removed under reduced pressure. The solid was recrystallized from ether to give saripidem (90 mg, 95%) as a white solid: mp 171-3 ºC; IR (KBr) : ν = 2922, 2851, 1733, 1634, 1404, 1134, 1013, 841, 737, 719, 594 cm-1; ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 6.9 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.26 – 7.23 (m, 1H), 6.84 (td, *J* = 6.8, 1.1 Hz, 1H), 5.18 (s, 2H), 2.60 (s, 3H, NCH_3), 2.28 (t, *J* = 7.4 Hz, 2H), 1.73 – 1.64 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6 (CO), 145.2, 144.8, 134.1, 132.8, 130.0, 128.9, 125.5, 125.4, 117.3, 116.0, 112.8, 38.5, 35.4, 33.6, 18.4, 13.9; ESI-HRMS (m/z): calcd. for $C_{21}H_{17}ClN_2O$ $[M+H]^+$, 342.1375 ; found: 342.1382.

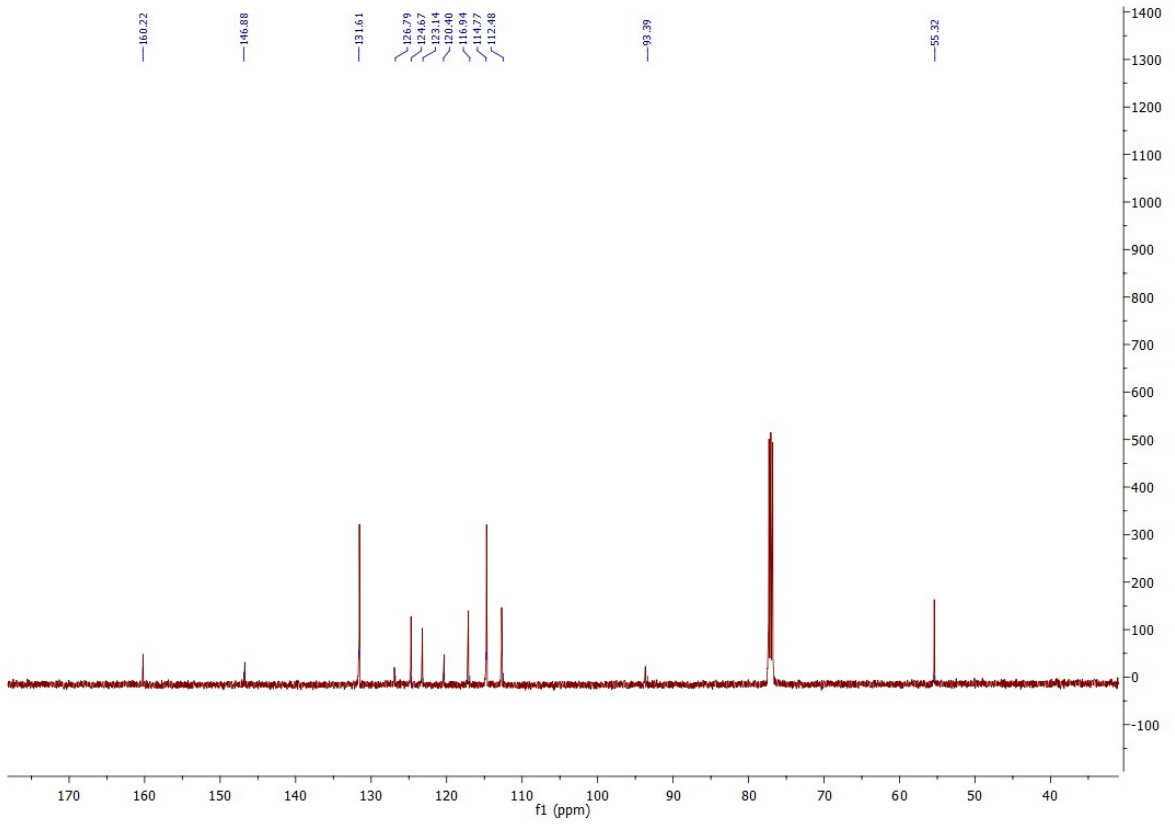
2-iodo-3-phenylimidazo[1,2-a]pyridine(3a)



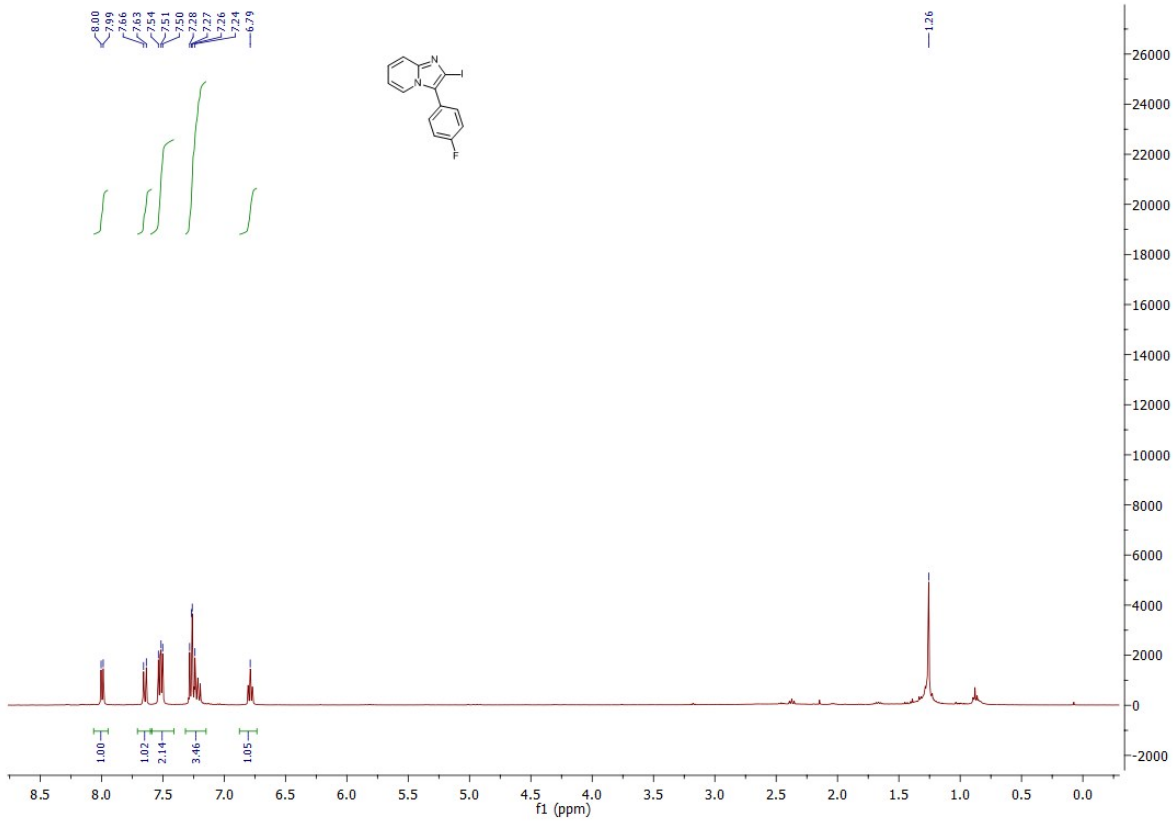


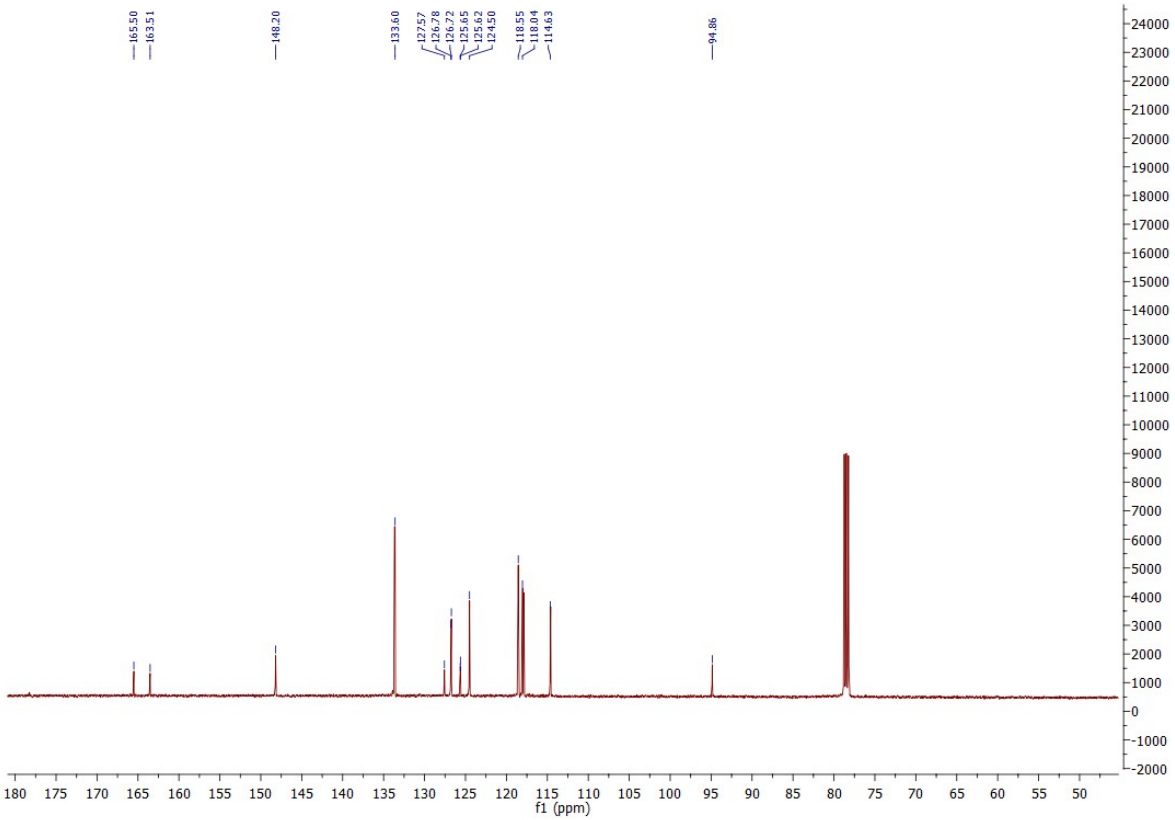
2-Iodo-3-(4-methoxyphenyl)imidazo[1,2-a]pyridine (3b)



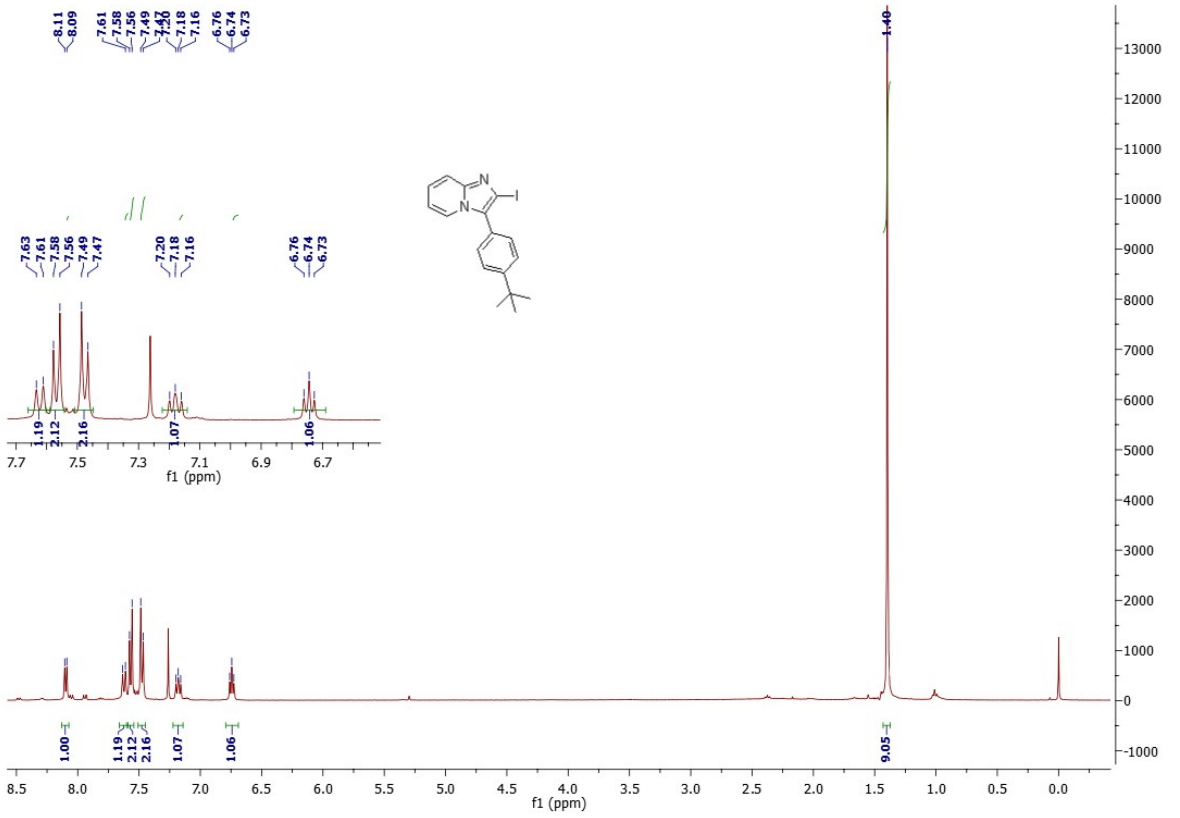


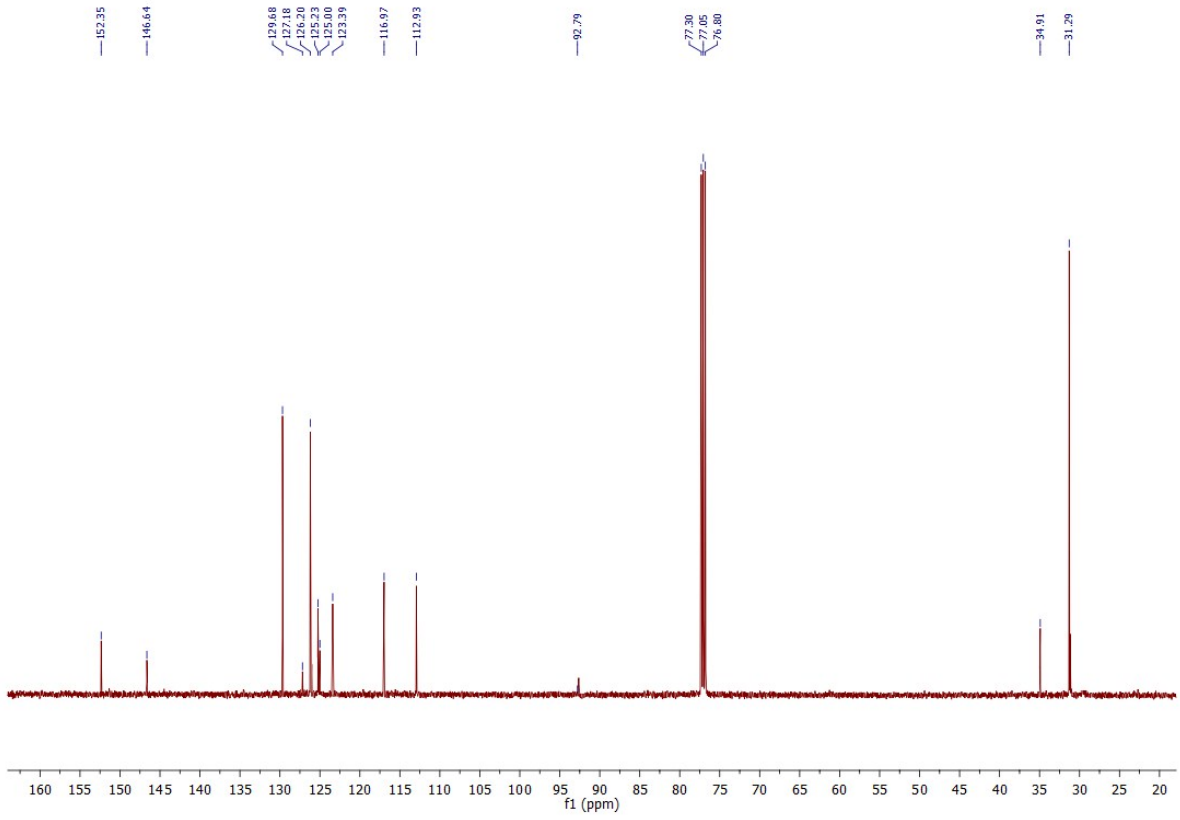
3-(4-Fluorophenyl)-2-iodoimidazo[1,2-a]pyridine (3c)



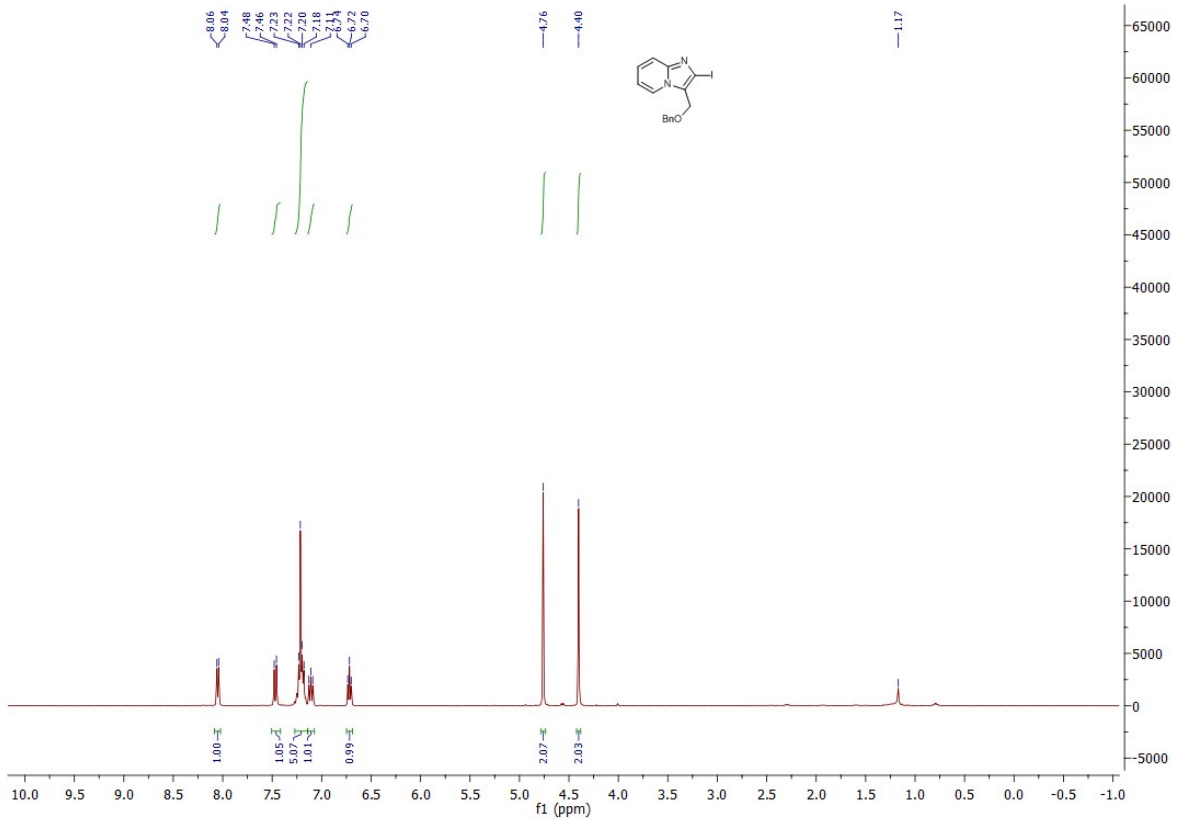


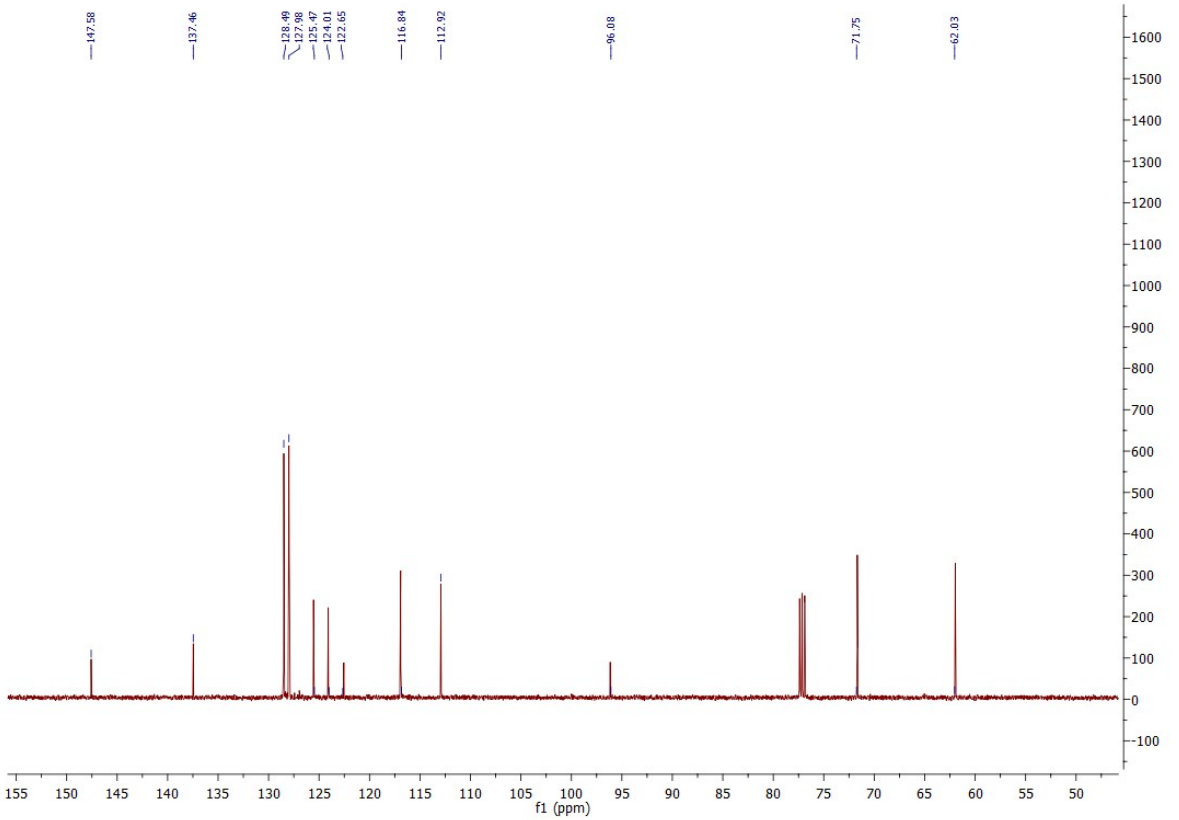
3-(4-(tert-butyl)phenyl)-2-iodoimidazo[1,2-a]pyridine (3d)



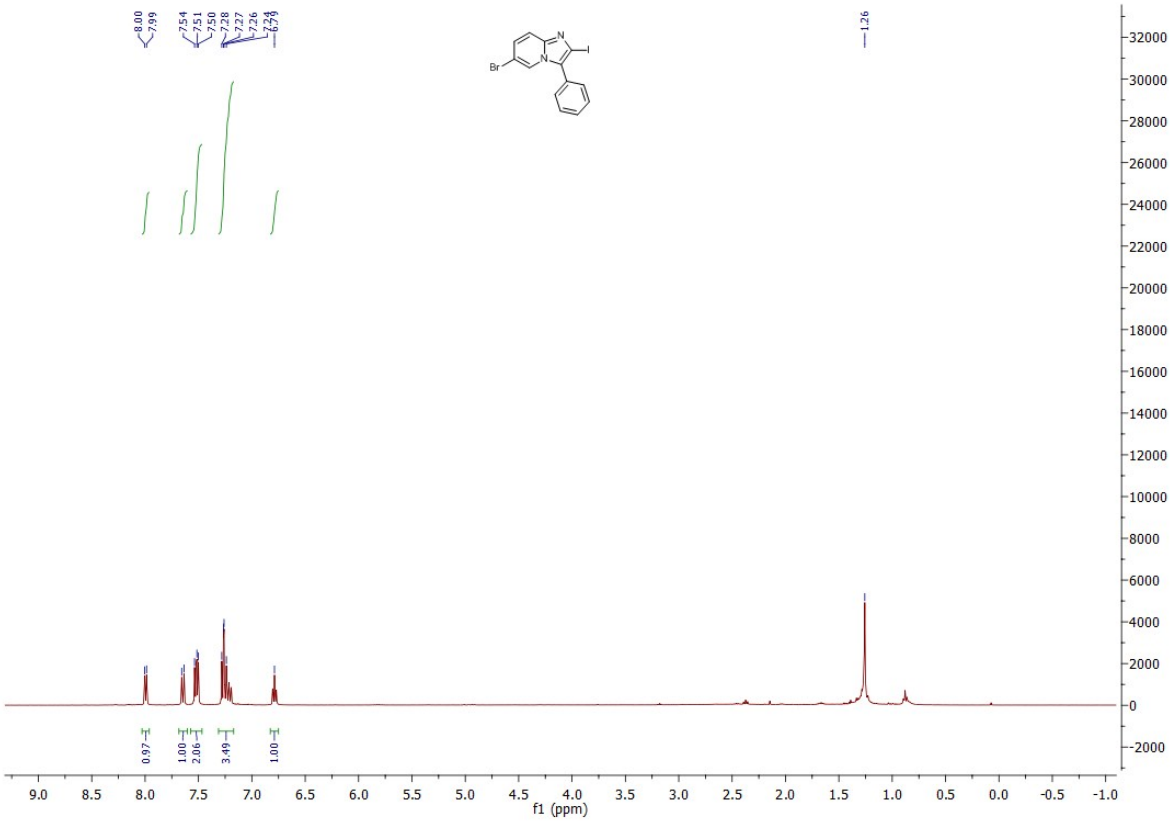


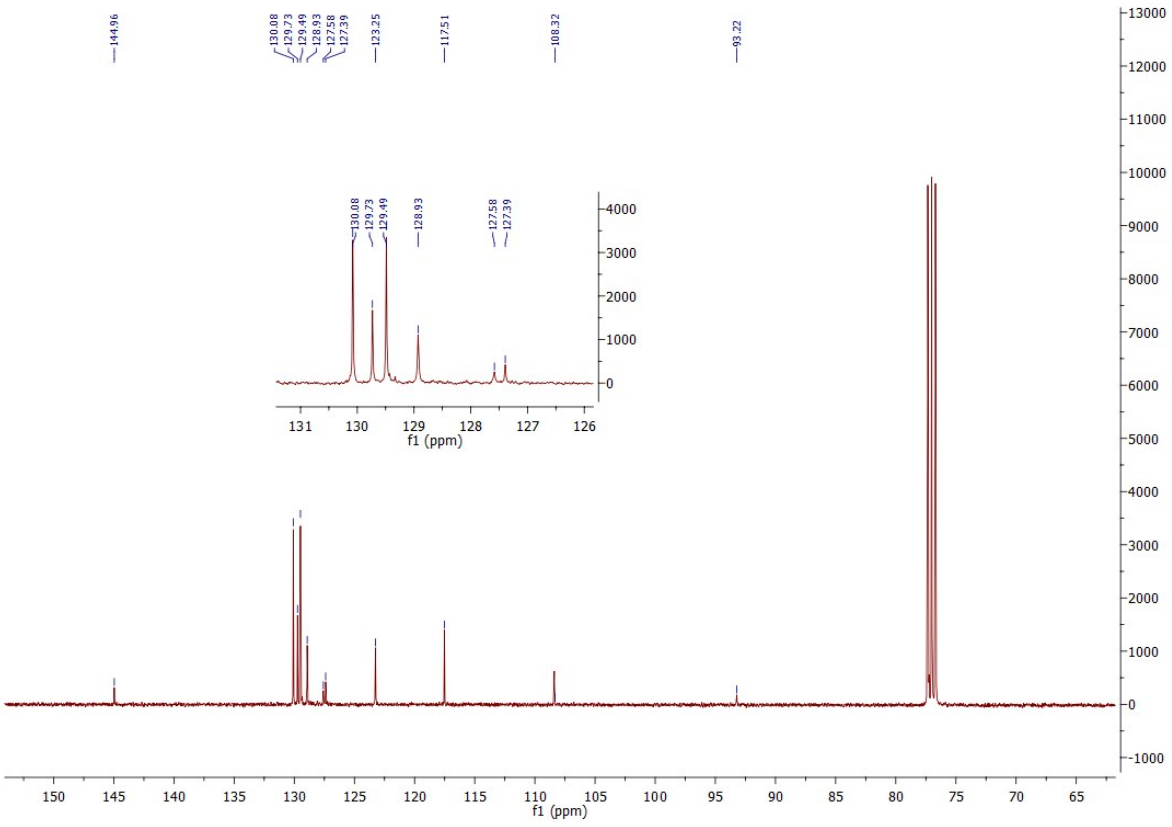
3-((Benzyloxy)methyl)-2-iodoimidazo[1,2-a]pyridine (3e):



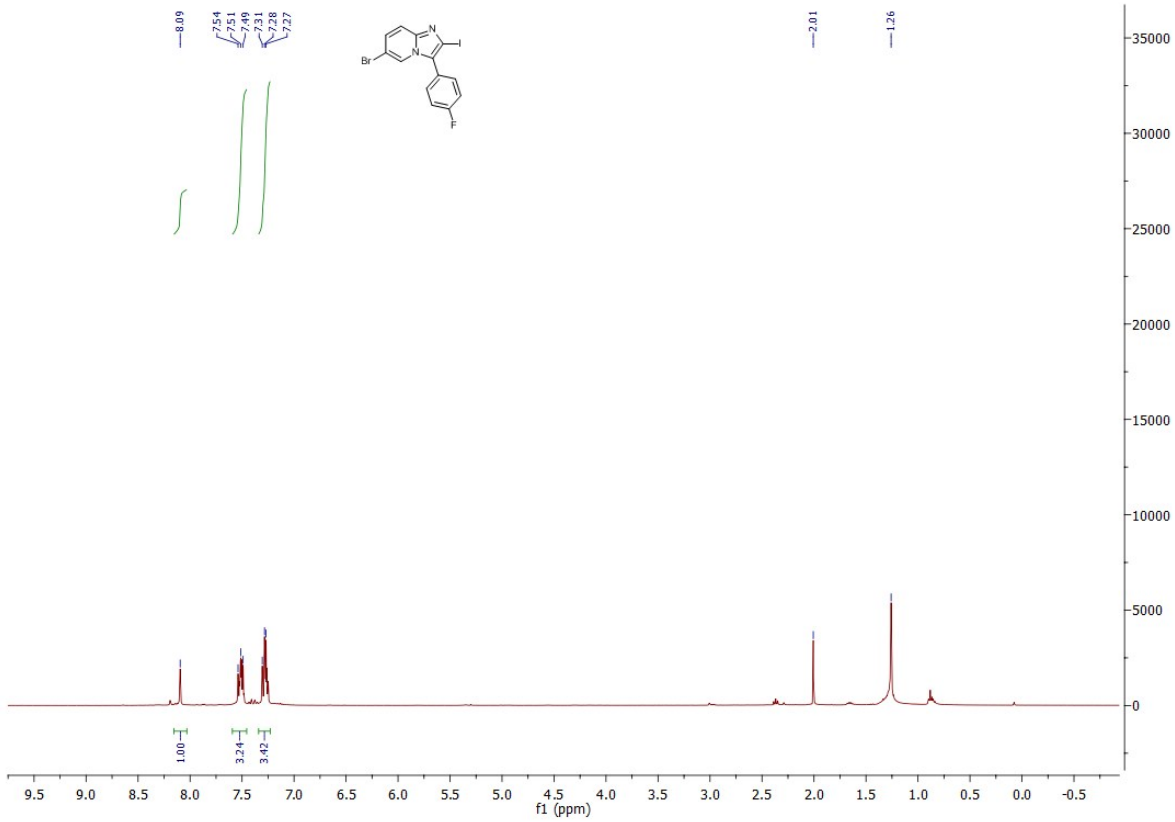


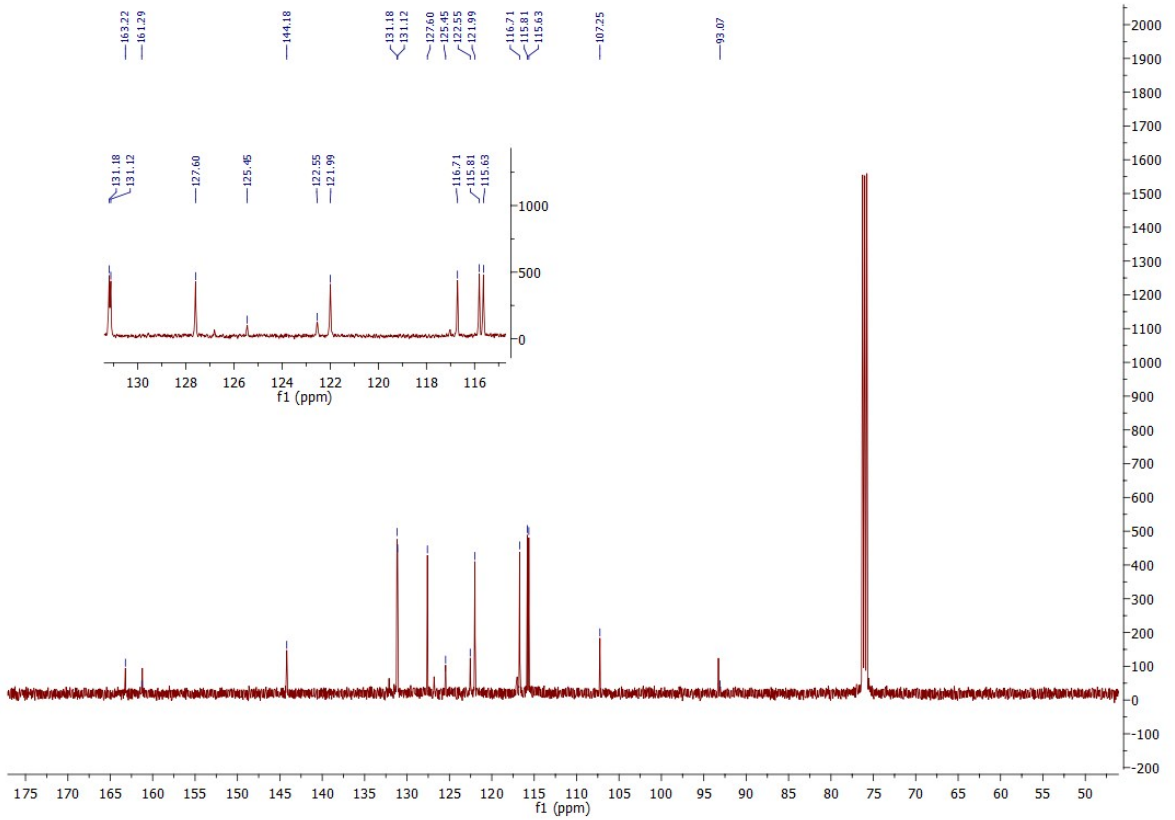
6-Bromo-2-iodo-3-phenylimidazo[1,2-a]pyridine (3f)



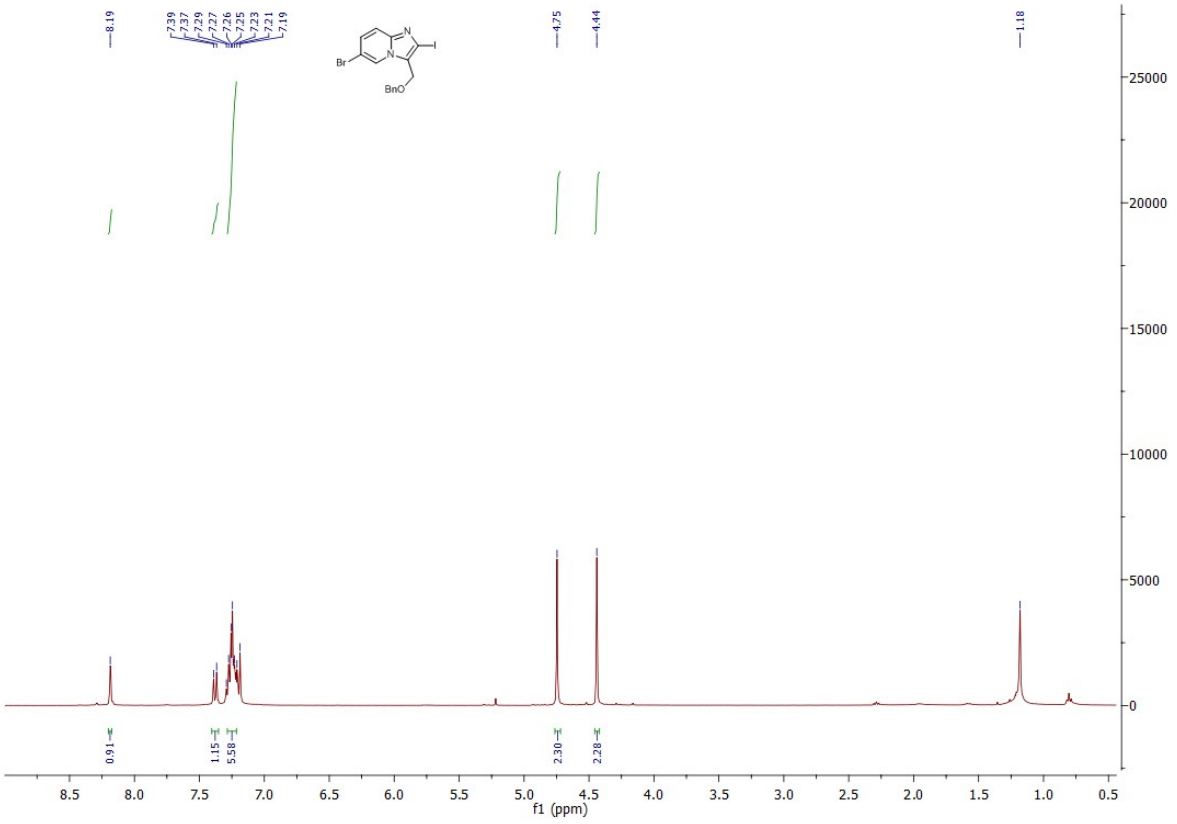


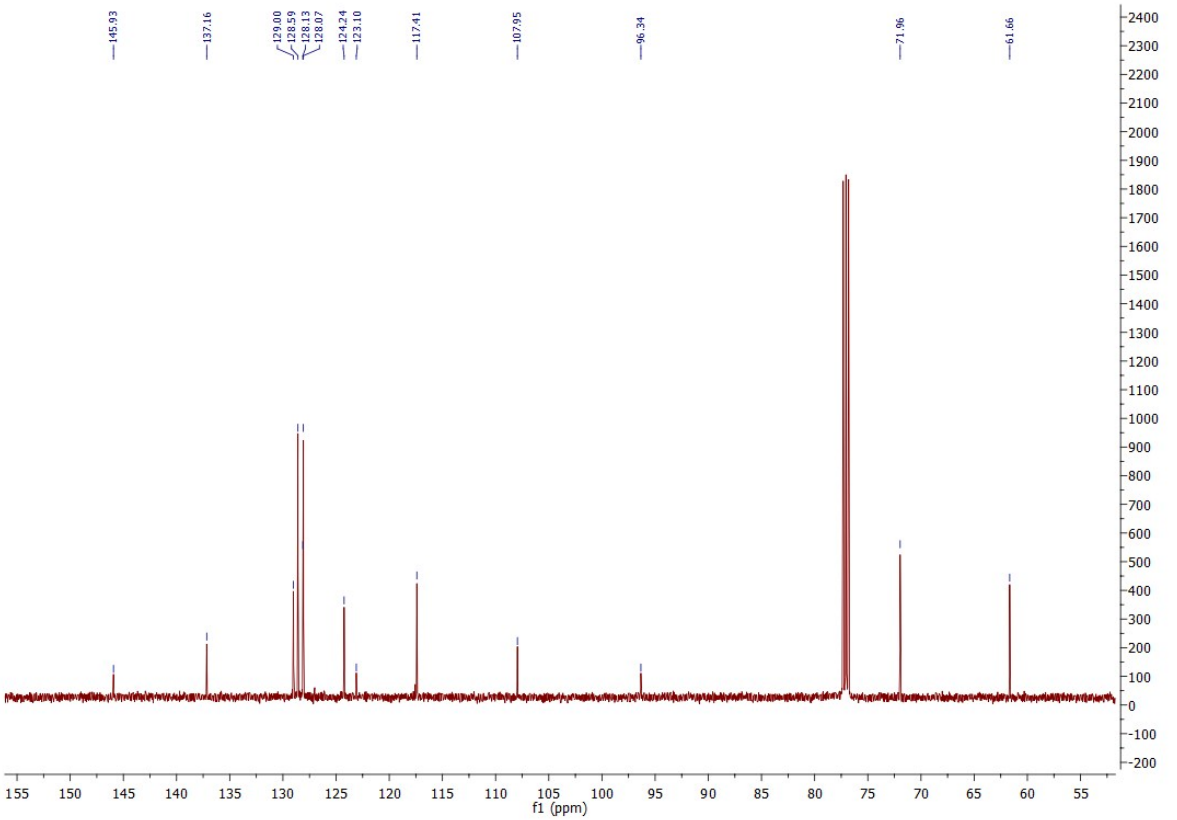
6-Bromo-3-(4-fluorophenyl)-2-iodoimidazo[1,2-a]pyridine(3g)



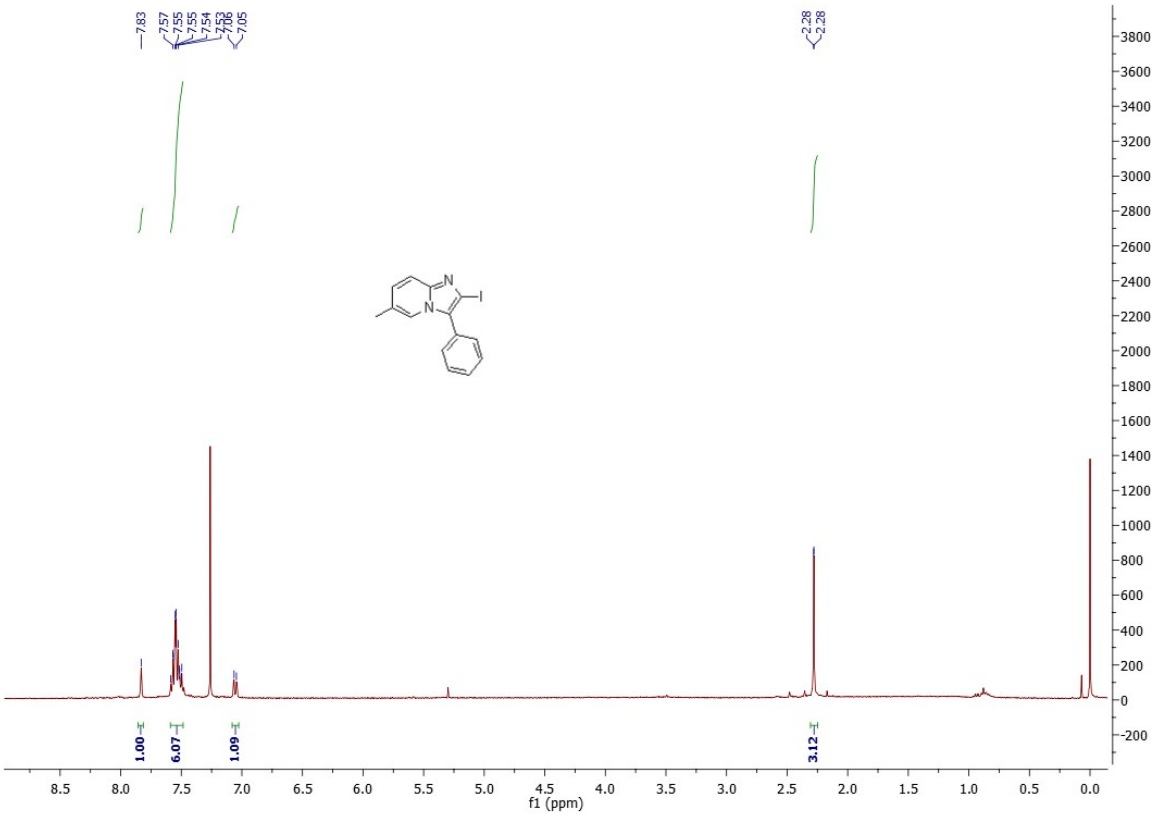


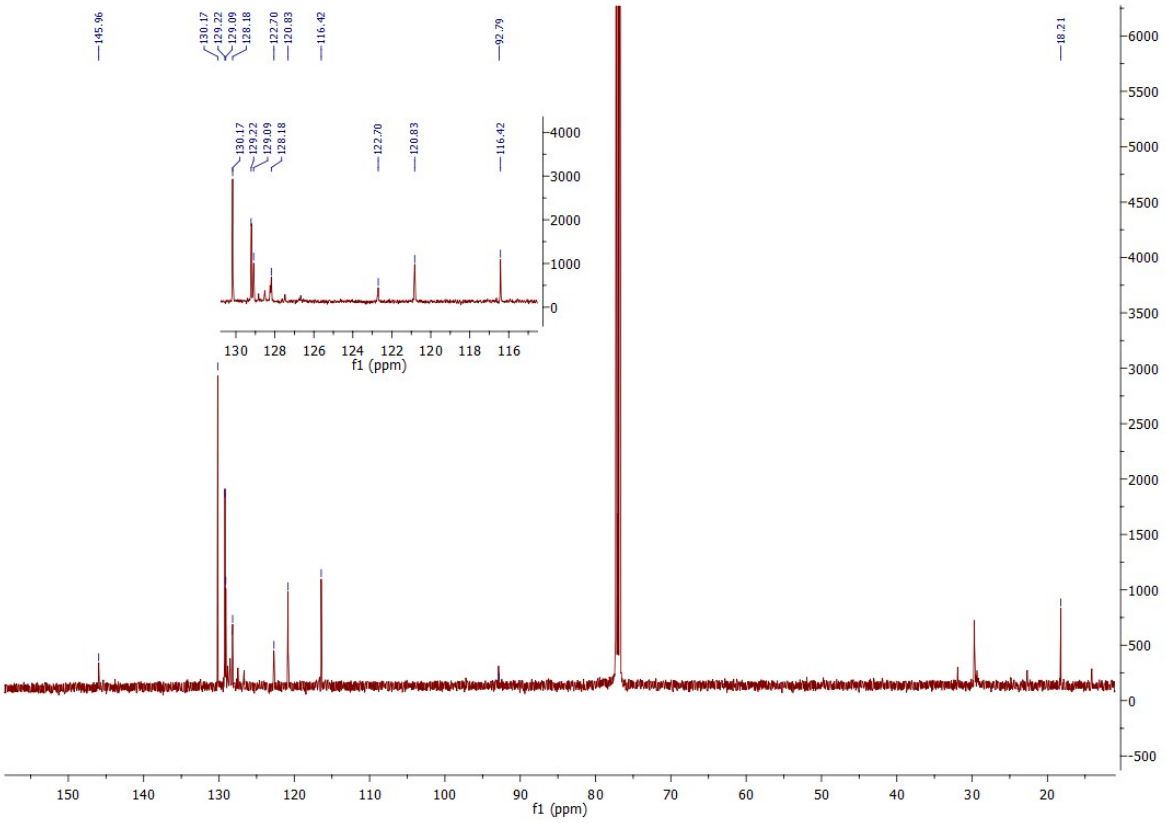
3-((Benzyloxy)methyl)-6-bromo-2-iodoimidazo[1,2-a]pyridine (3h)



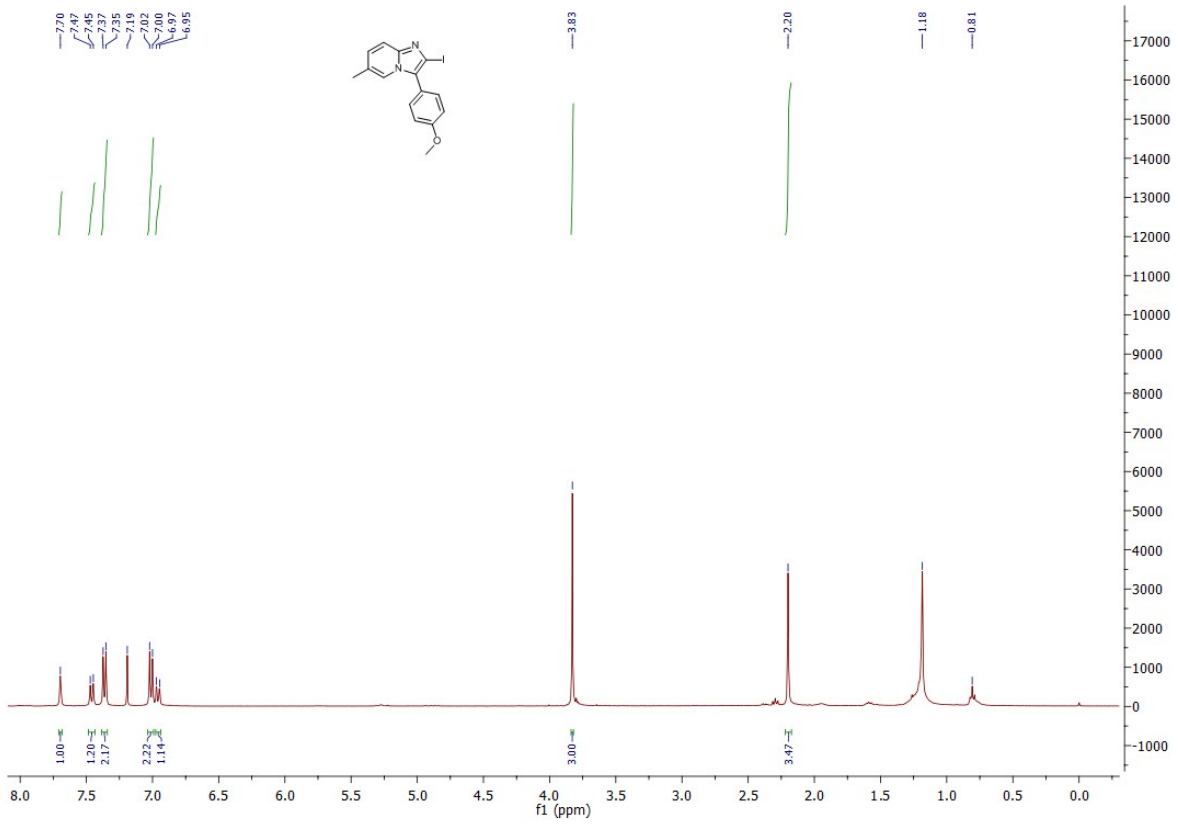


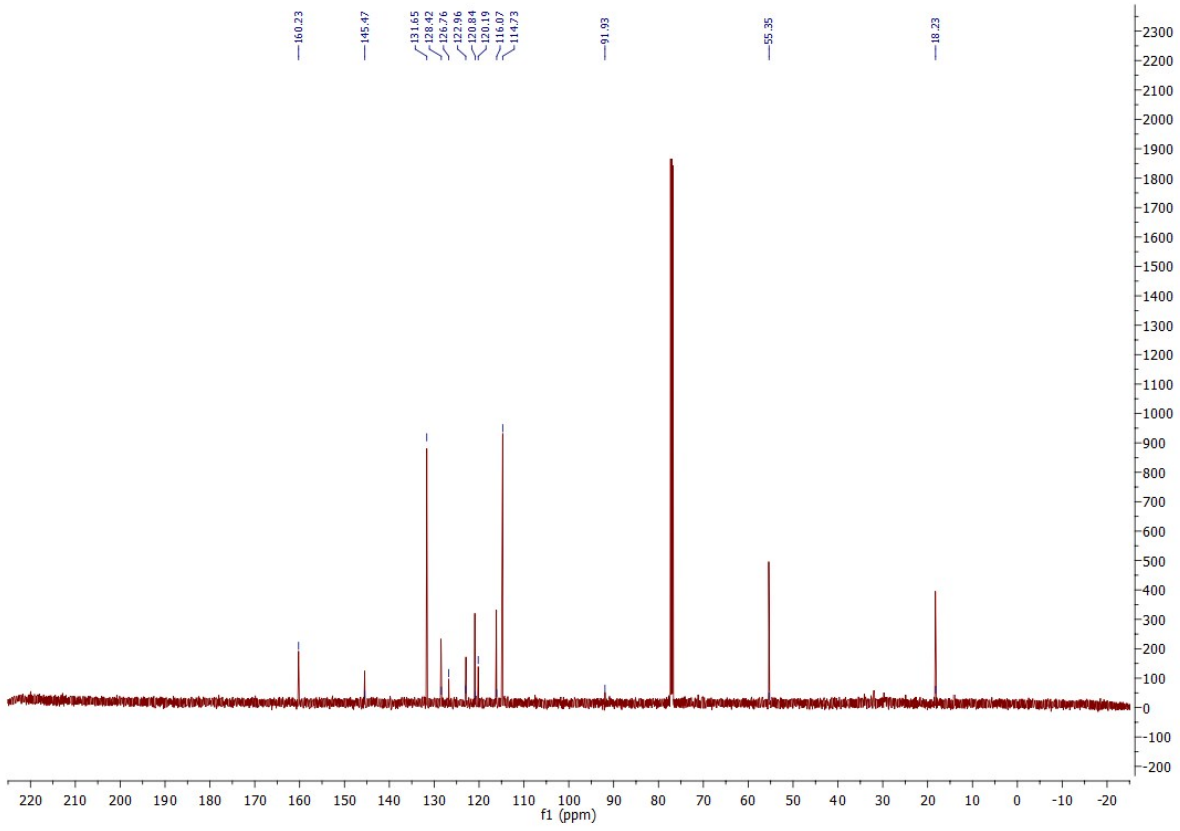
2-Iodo-6-methyl-3-phenylimidazo[1,2-a]pyridine (3i)



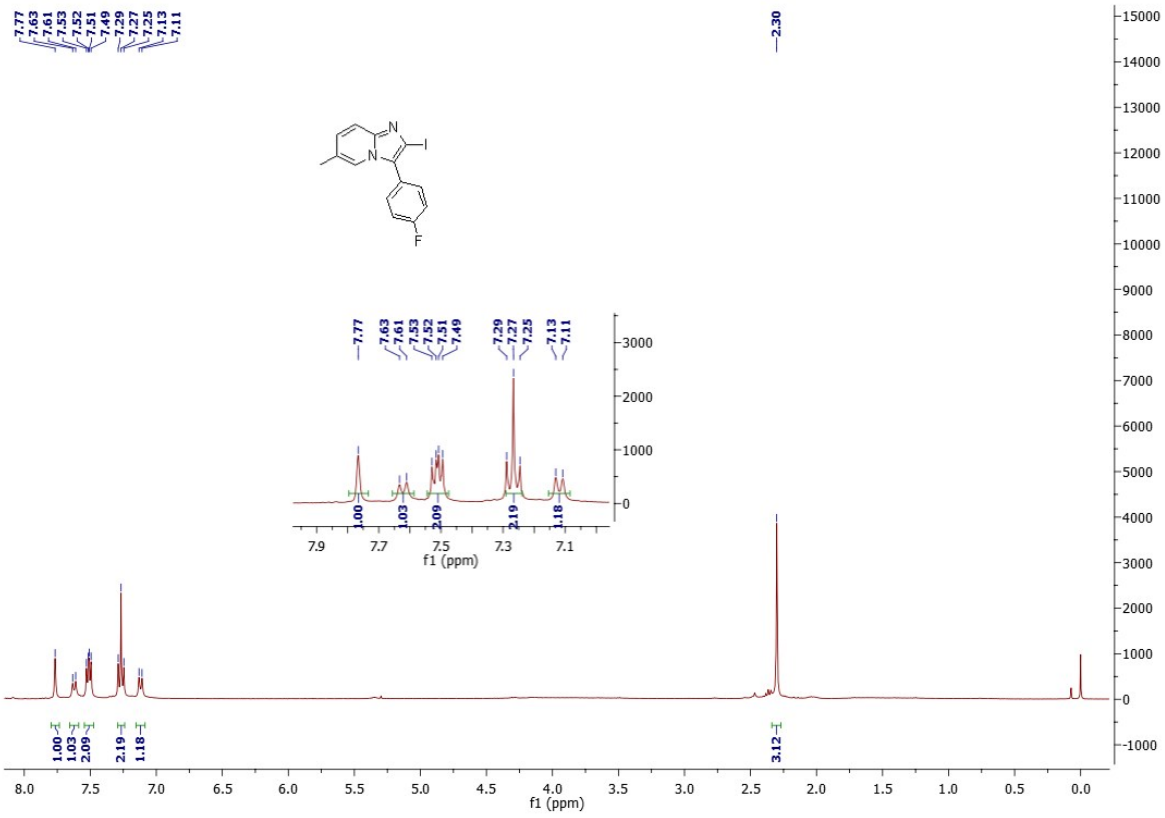


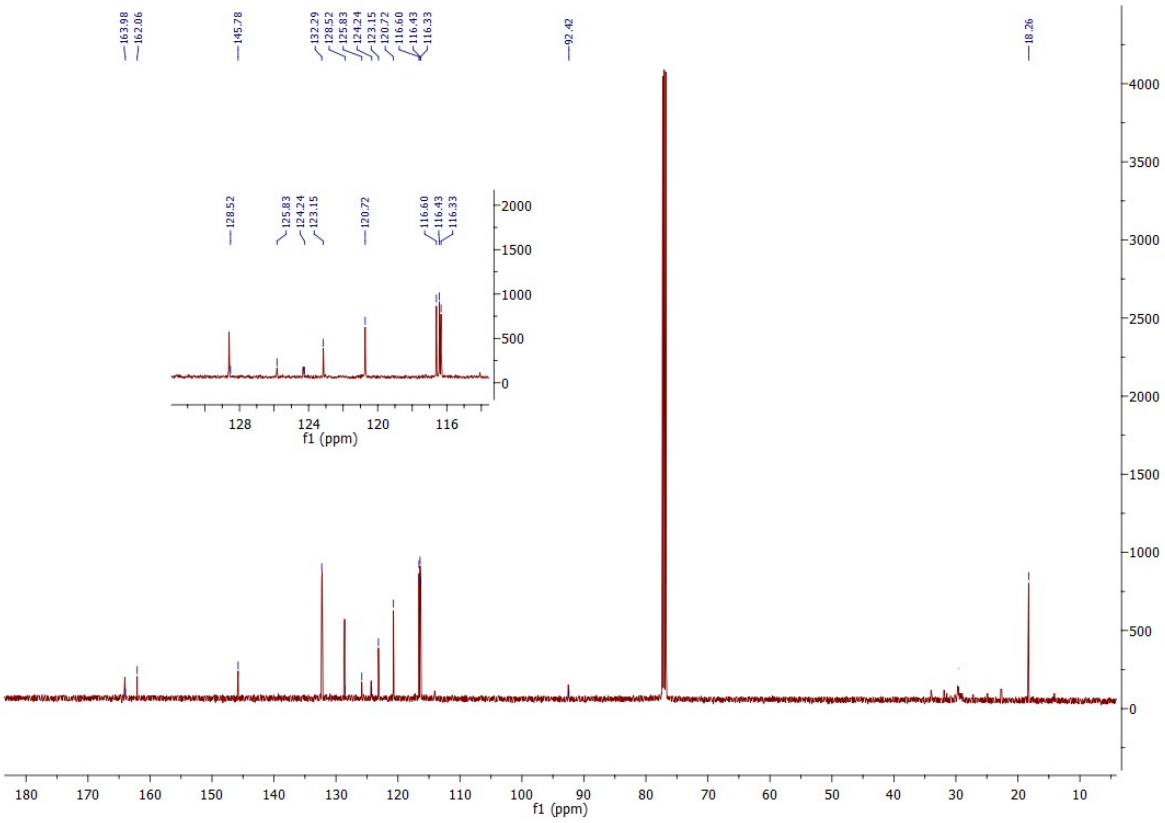
2-Iodo-3-(4-methoxyphenyl)-6-methylimidazo[1,2-a]pyridine(3j)



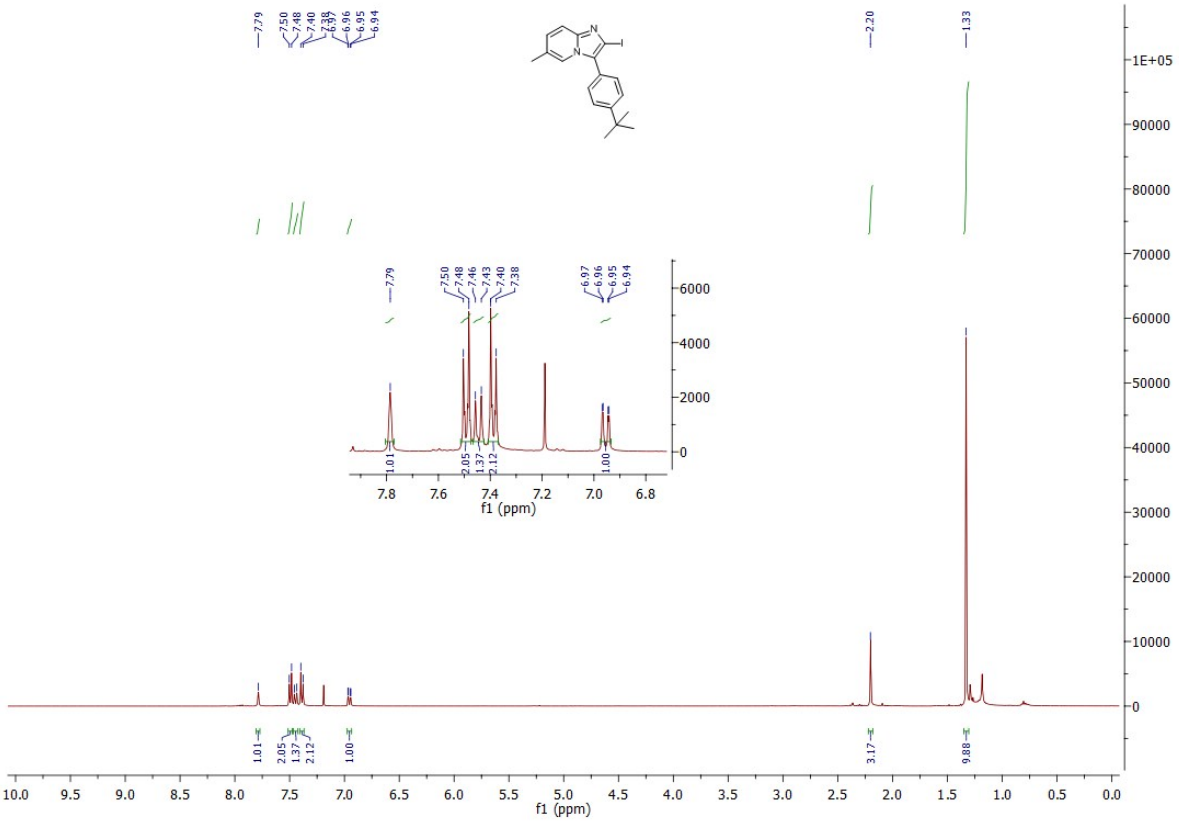


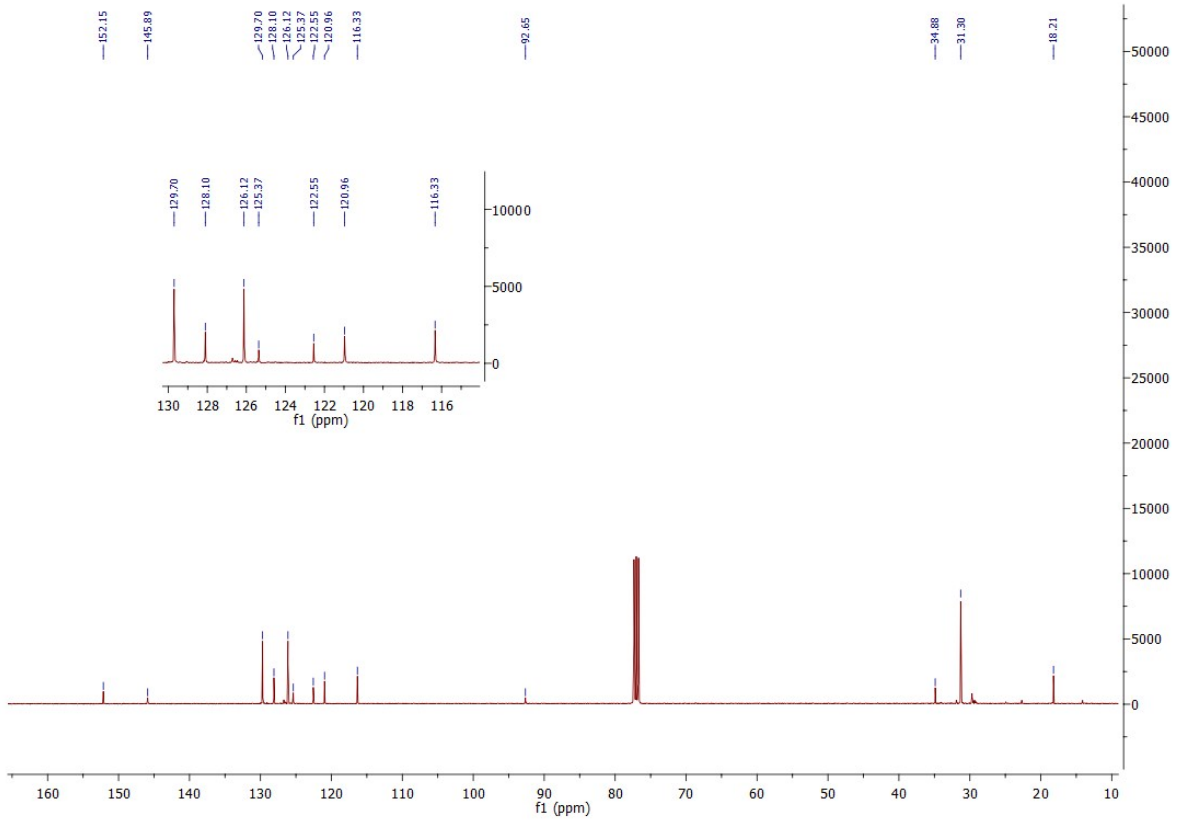
3-(4-Fluorophenyl)-2-iodo-6-methylimidazo[1,2-a]pyridine (3k)



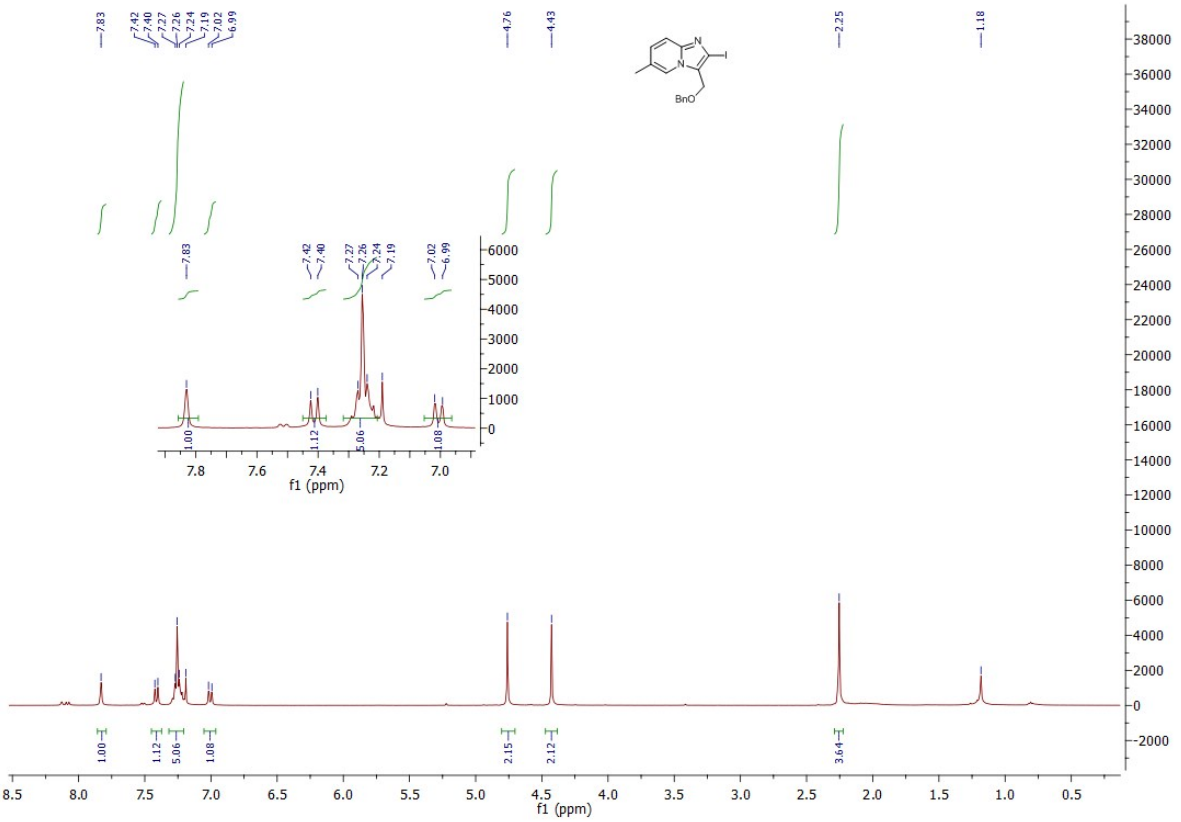


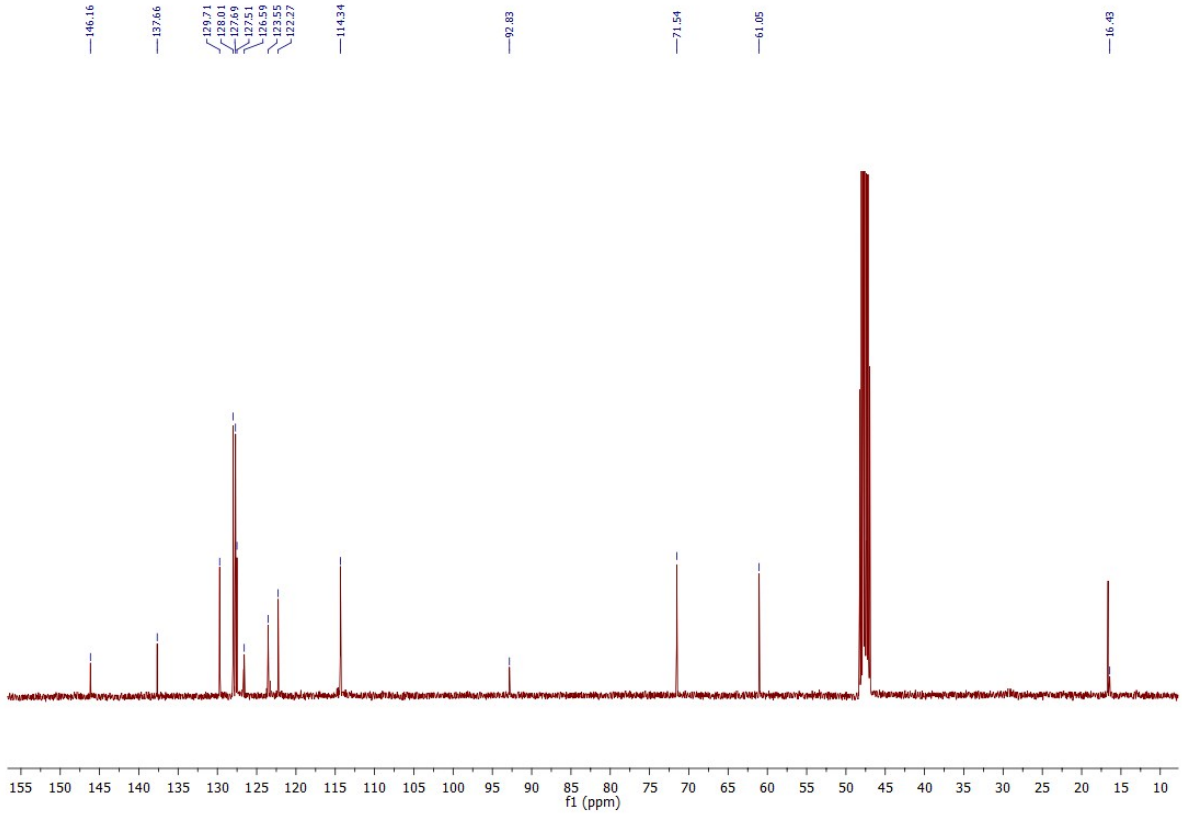
3-(4-(tert-butyl)phenyl)-2-iodo-6-methylimidazo[1,2-a]pyridine (3l)



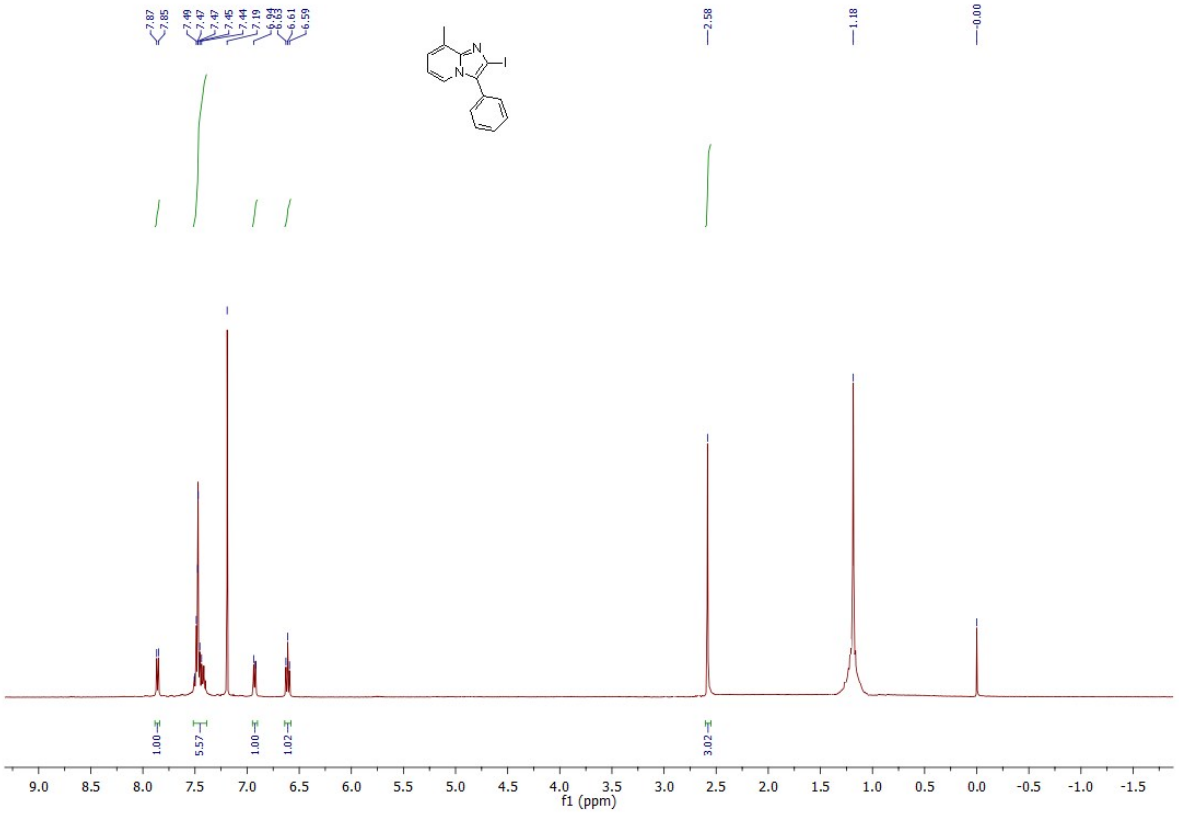


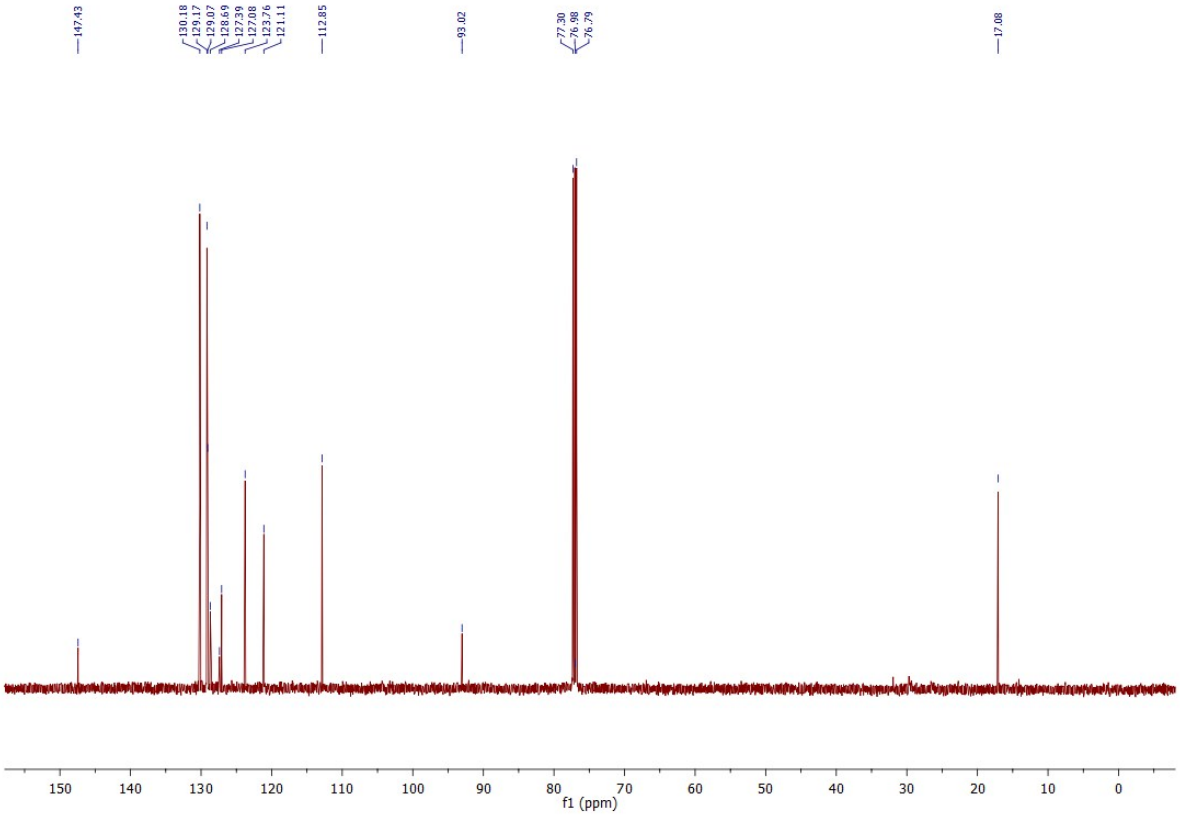
3-((Benzyloxy)methyl)-2-iodo-6-methylimidazo[1,2-a]pyridine (3m):



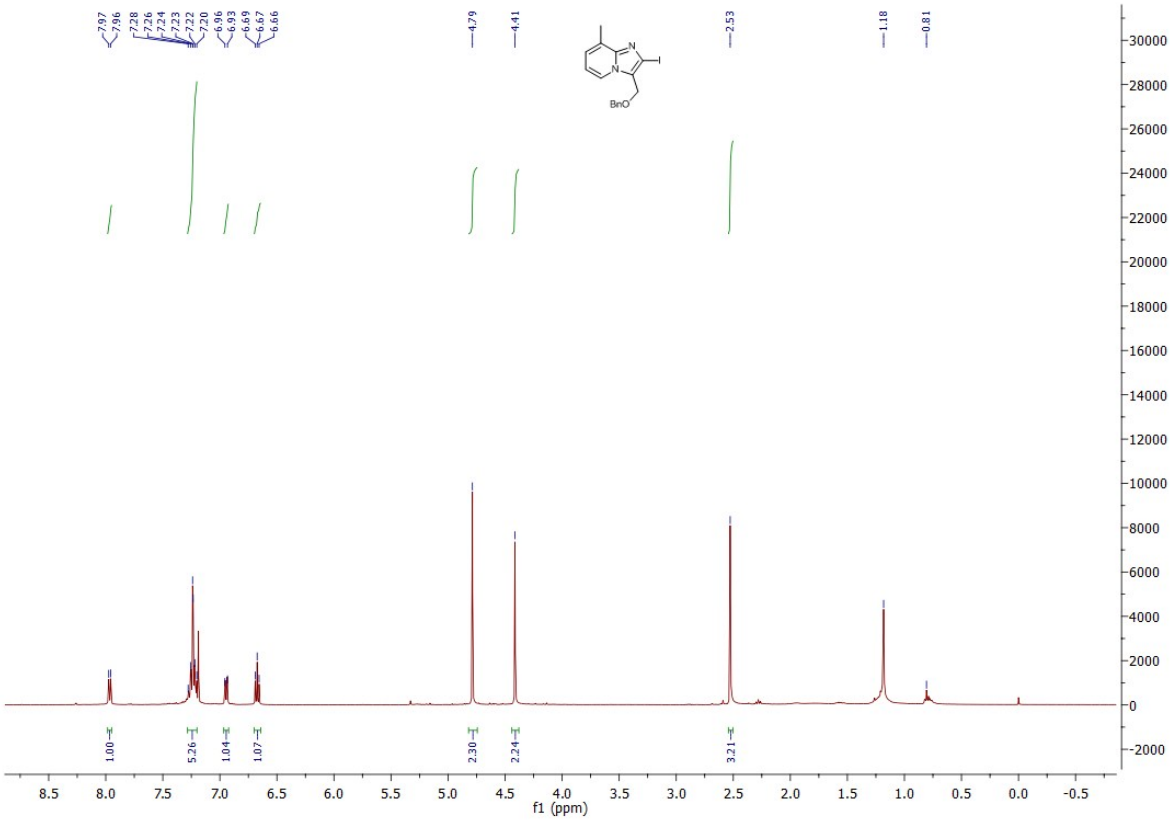


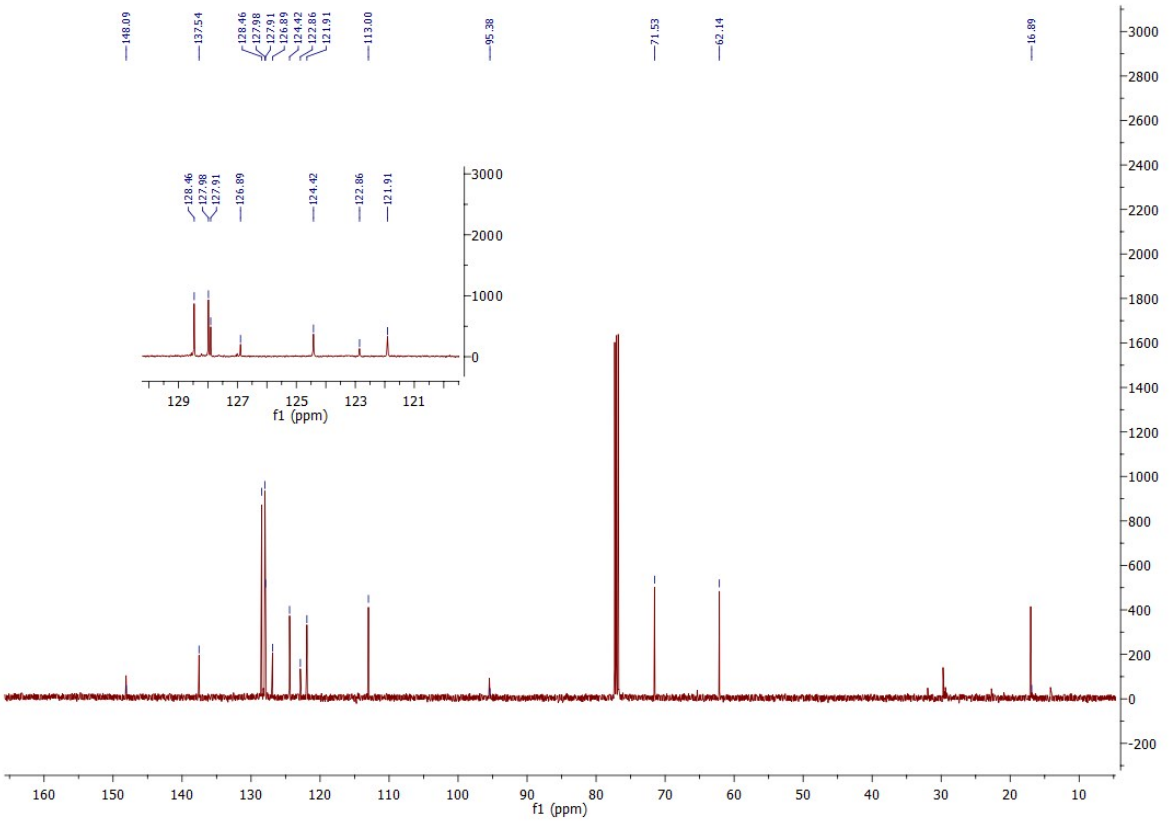
2-Iodo-8-methyl-3-phenylimidazo[1,2-a]pyridine(3n) :



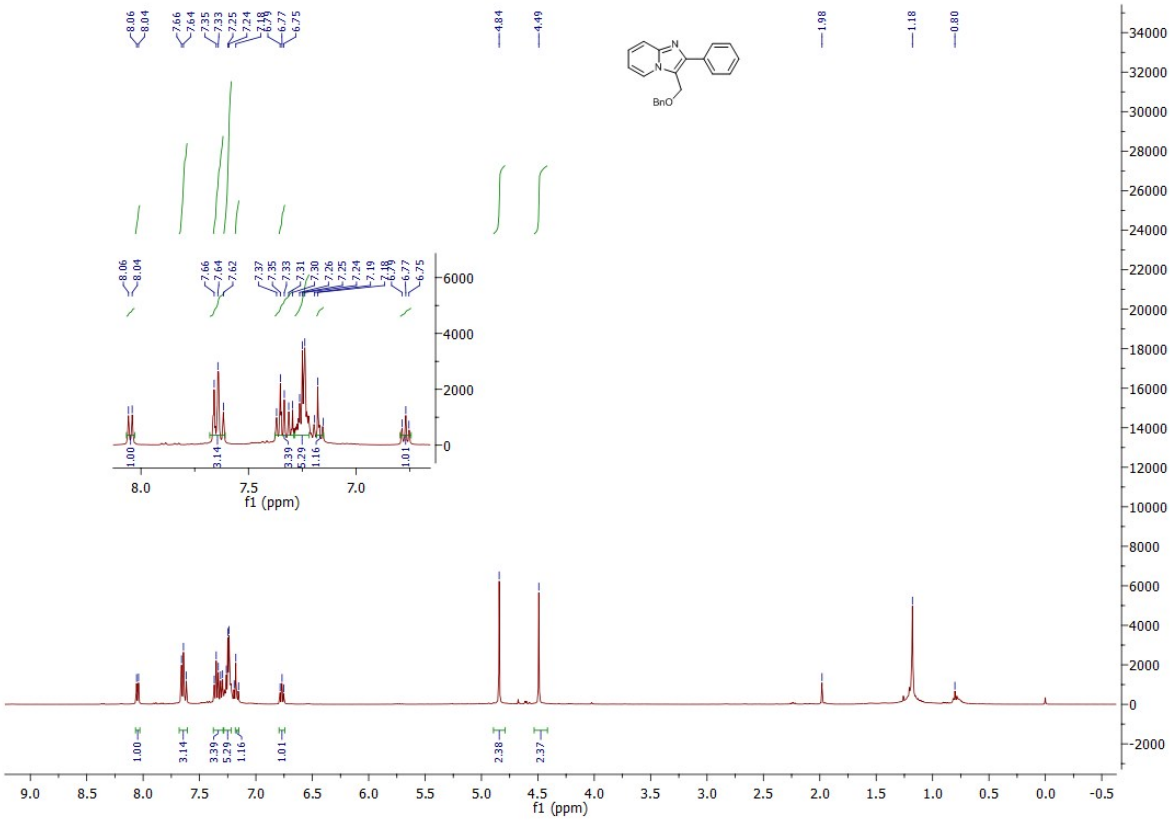


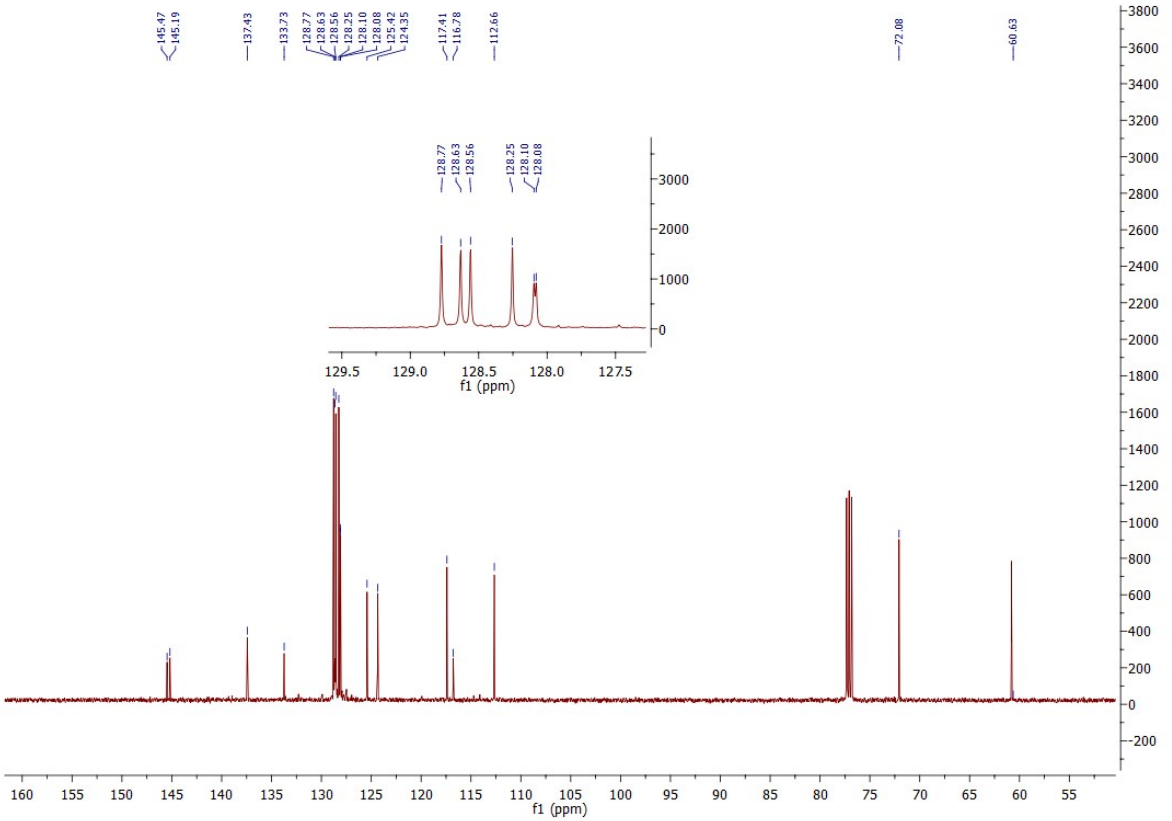
3-((benzyloxy)methyl)-2-iodo-8-methylimidazo[1,2-a]pyridine(3o):



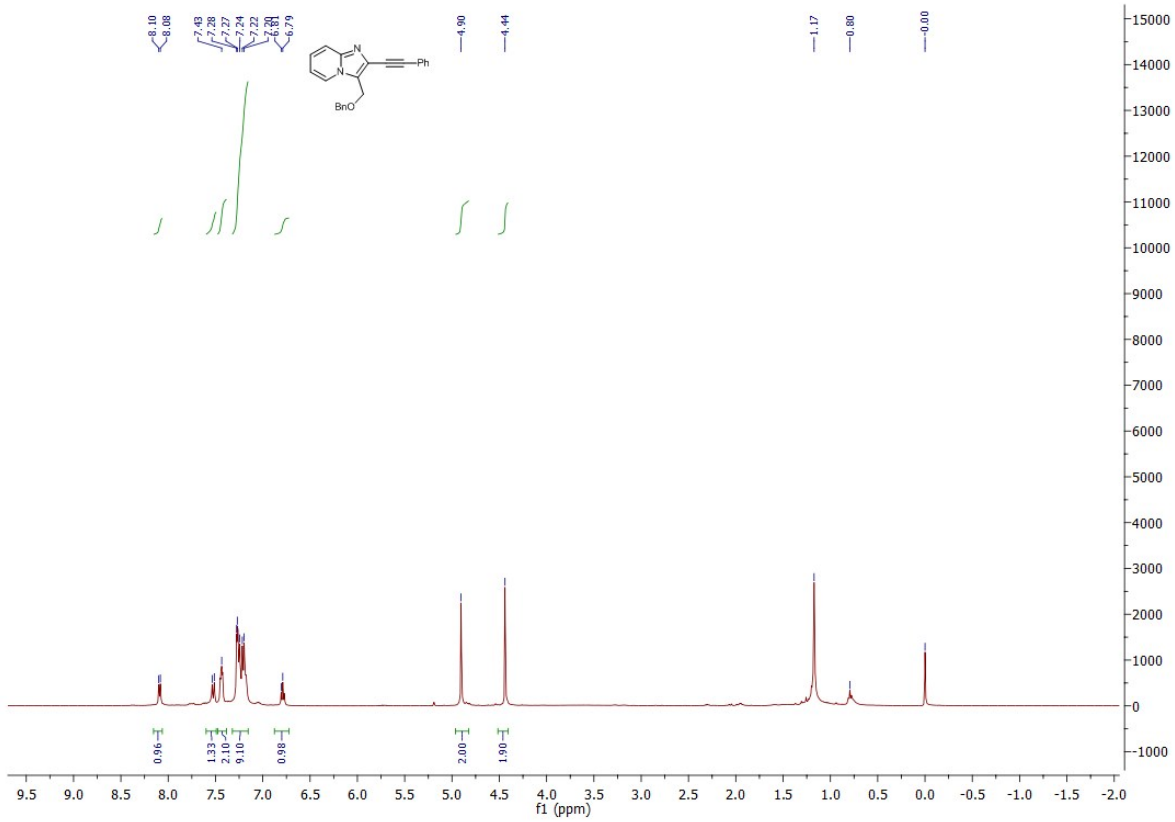


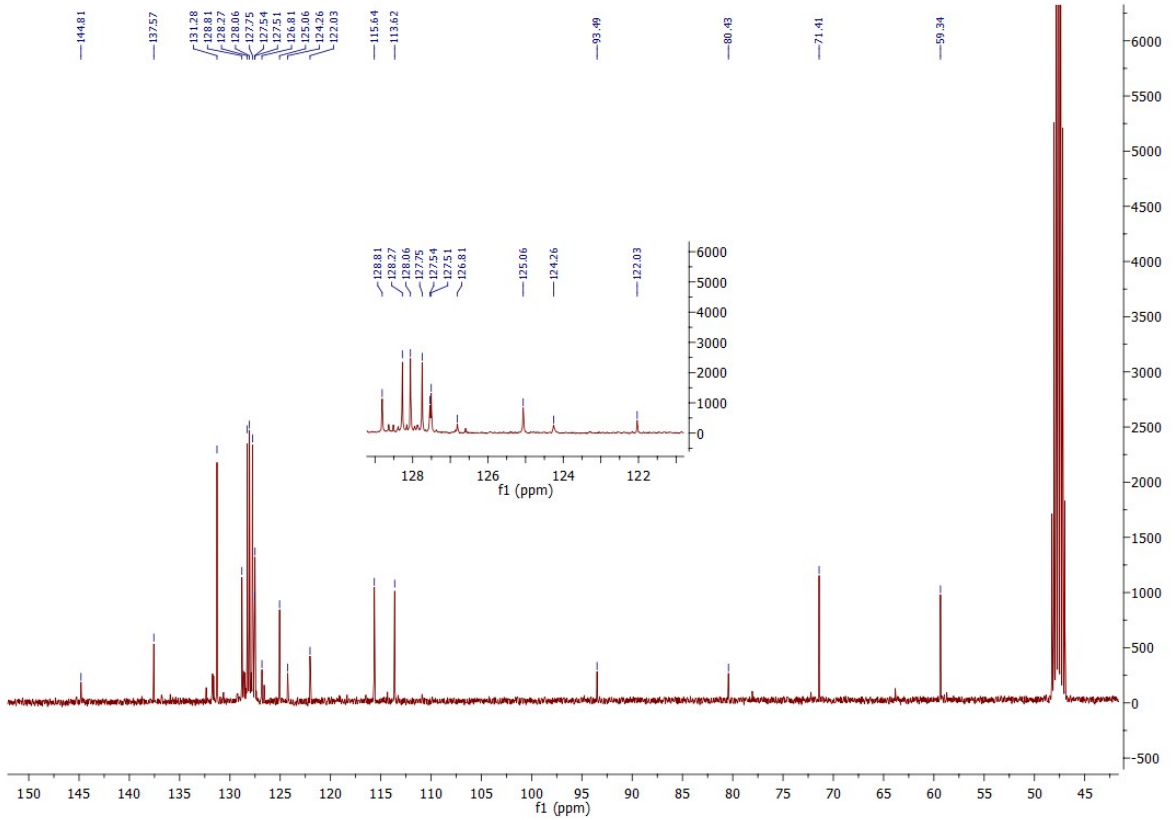
3-((Benzyloxy)methyl)-2-phenylimidazo[1,2-a]pyridine (8)



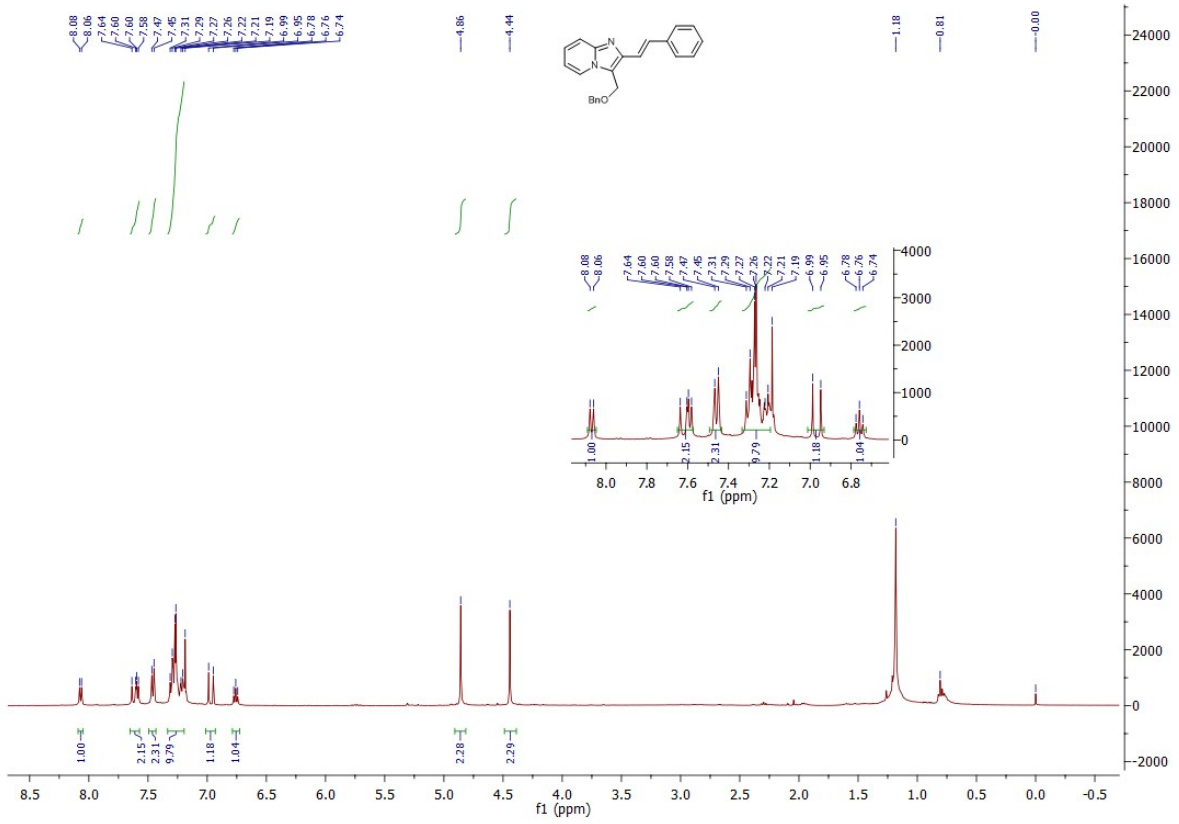


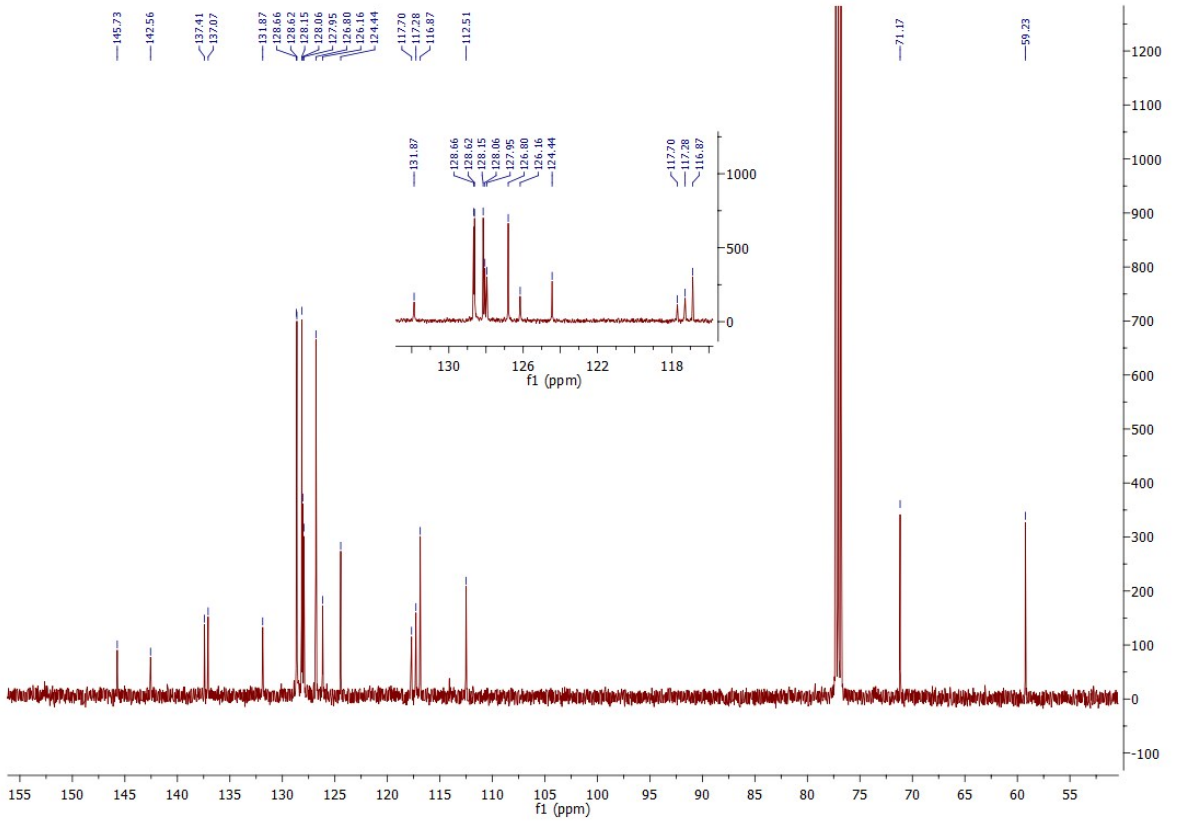
3-((Benzyloxy)methyl)-2-(phenylethynyl)imidazo[1,2-a]pyridine (9):



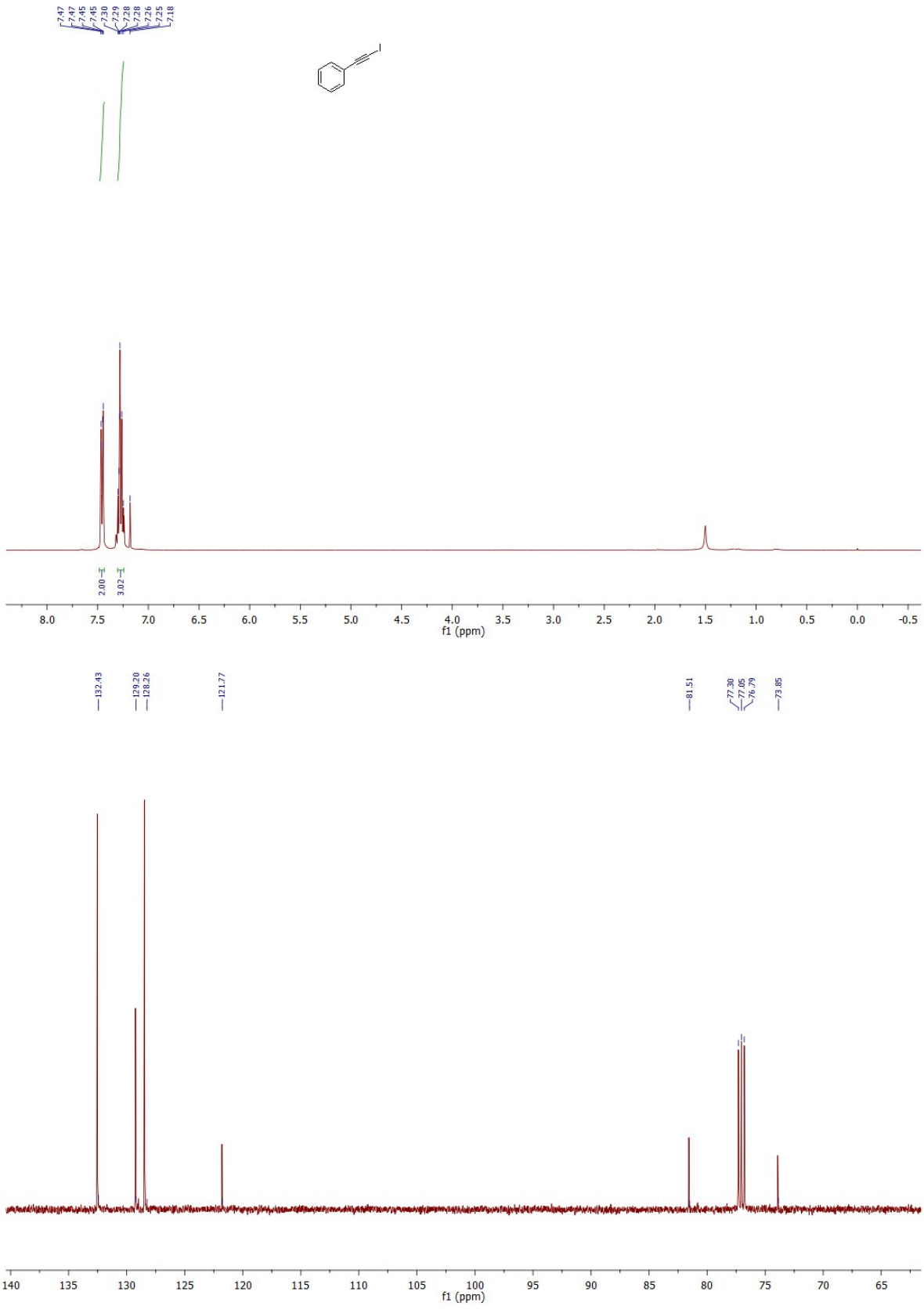


3-((Benzyloxy)methyl)-2-styrylimidazo[1,2-a]pyridine (10):

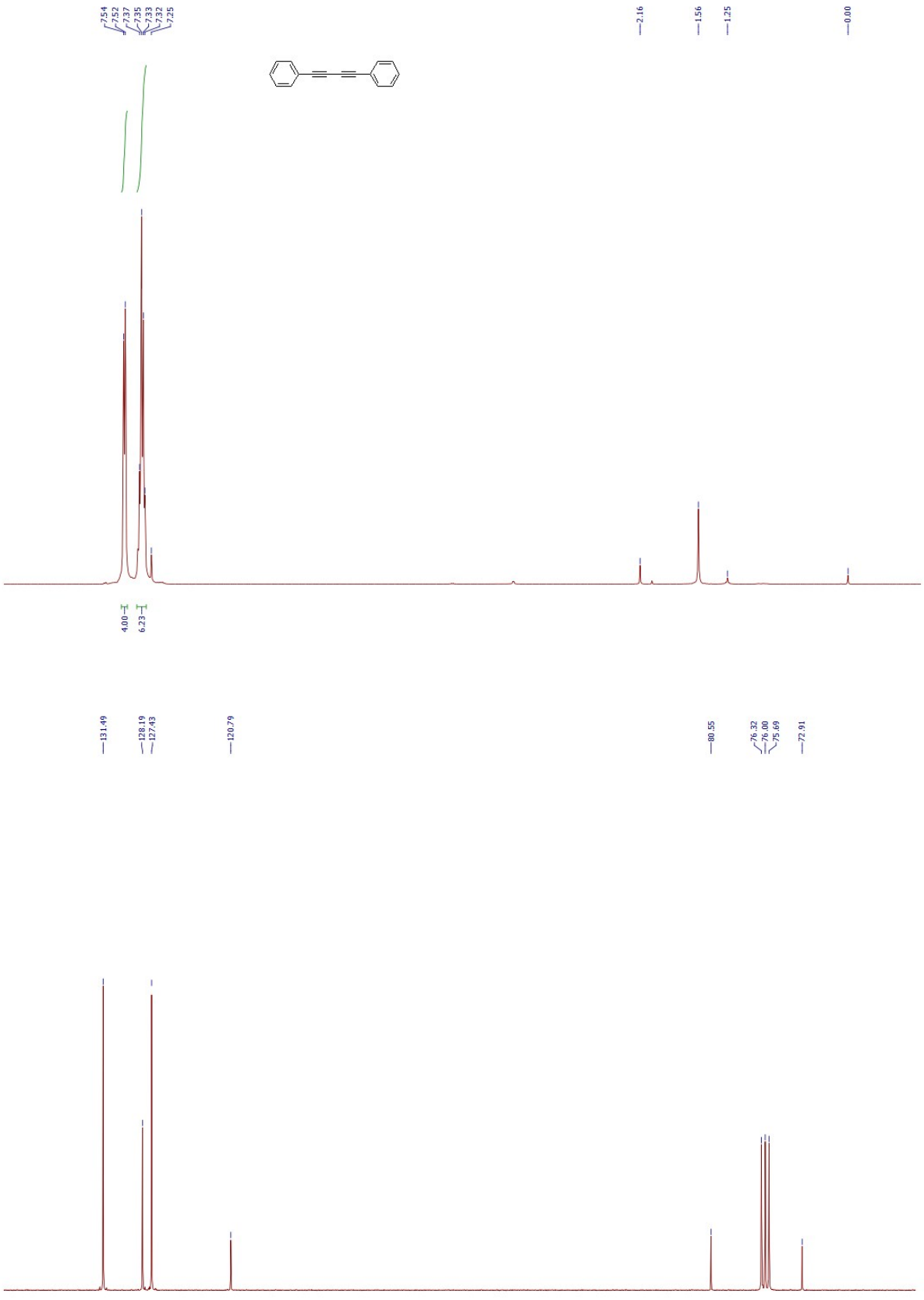




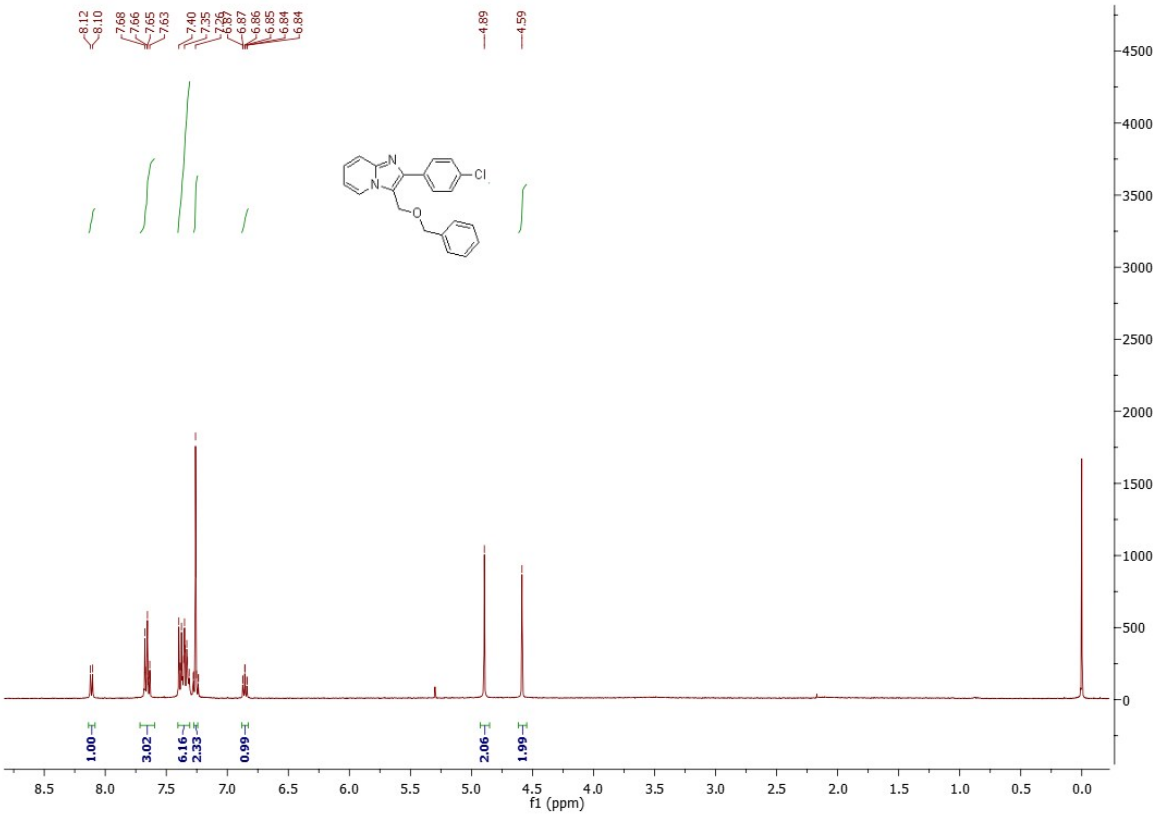
(Iodoethynyl)benzene (5):

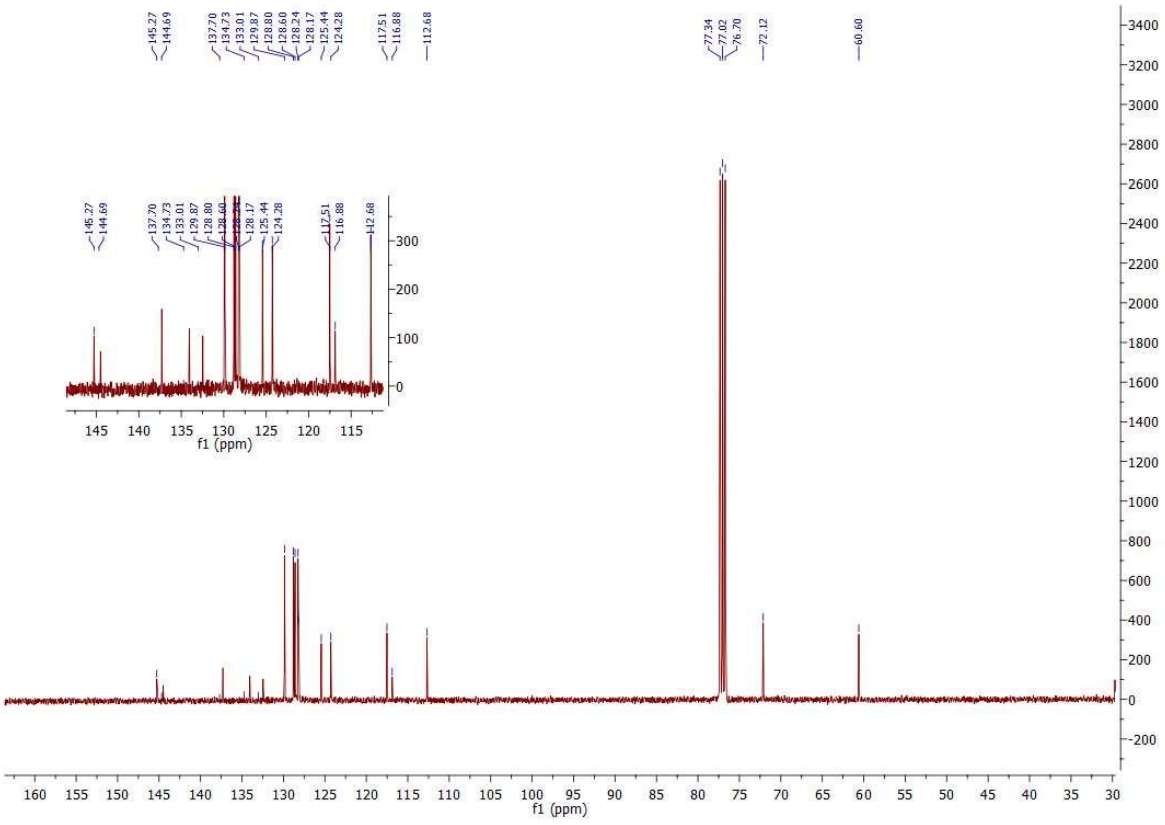


1,4-diphenylbuta-1,3-diyne

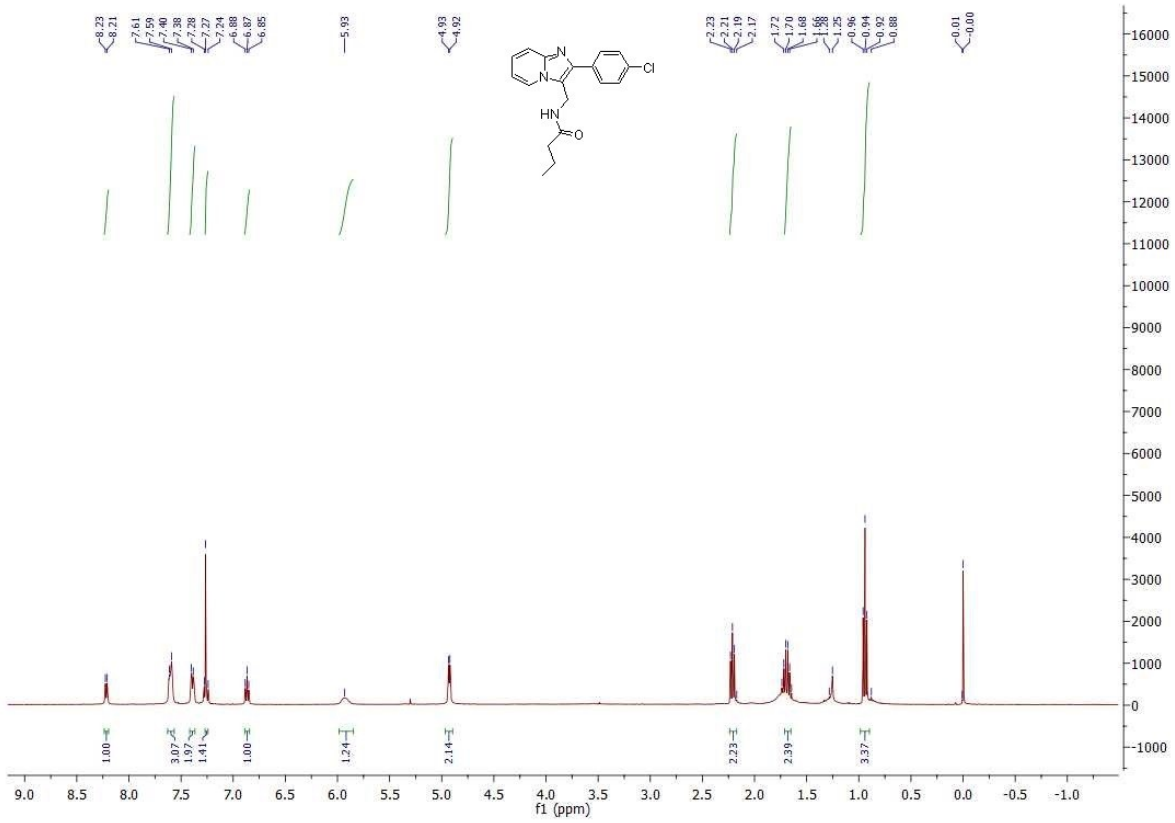


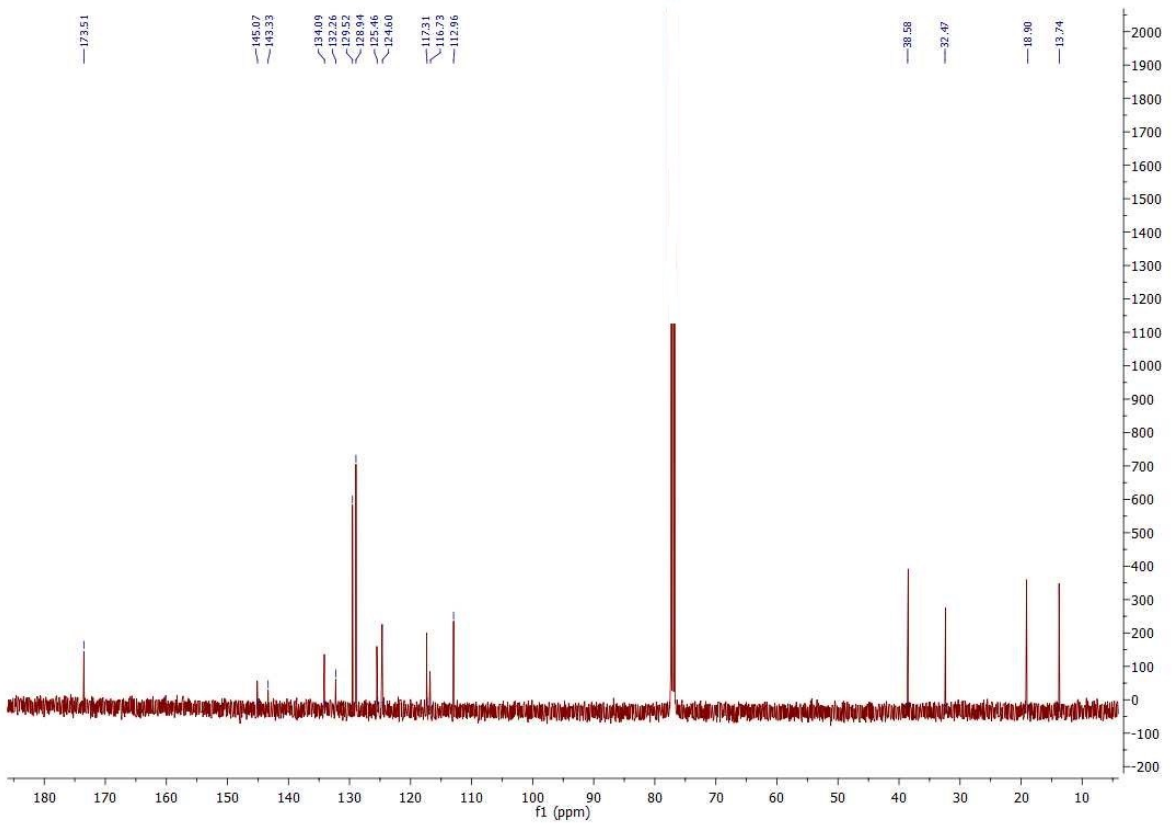
3-((benzyloxy)methyl)-2-(4-chlorophenyl)H-imidazo[1,2-a]pyridine(11)





N-((2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methyl)butyramide (12)





N-((2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methyl)-N-methylbutyramide(Saripidem)