Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

$Yb(NTf_2)_3$-Catalyzed［3+3］Cycloaddition between Isatin Ketonitrones and Cyclopropanes to Construct Novel Spiro[tetrahydro-1,2-oxazine]oxindoles

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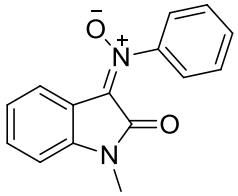
Contents

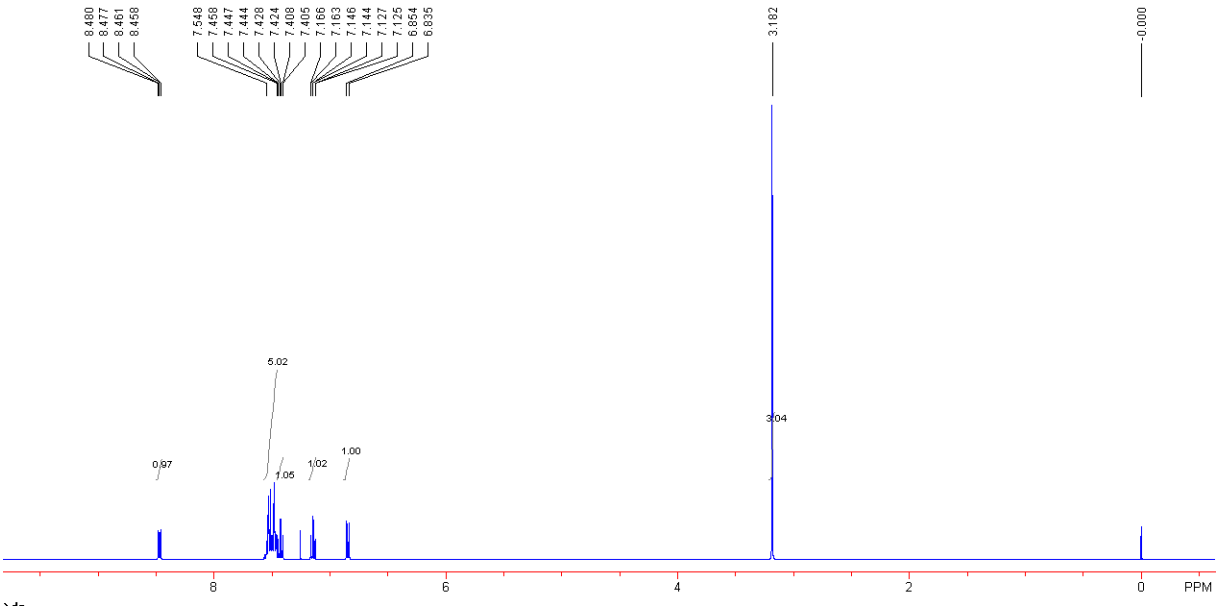
General Remarks. ^{1}H and ^{13}C NMR spectra were recorded at 400 (or 300) MHz, respectively. HRMS spectra were recorded by ESI method. The employed solvents were dry up by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with silica gel coated plates. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure.

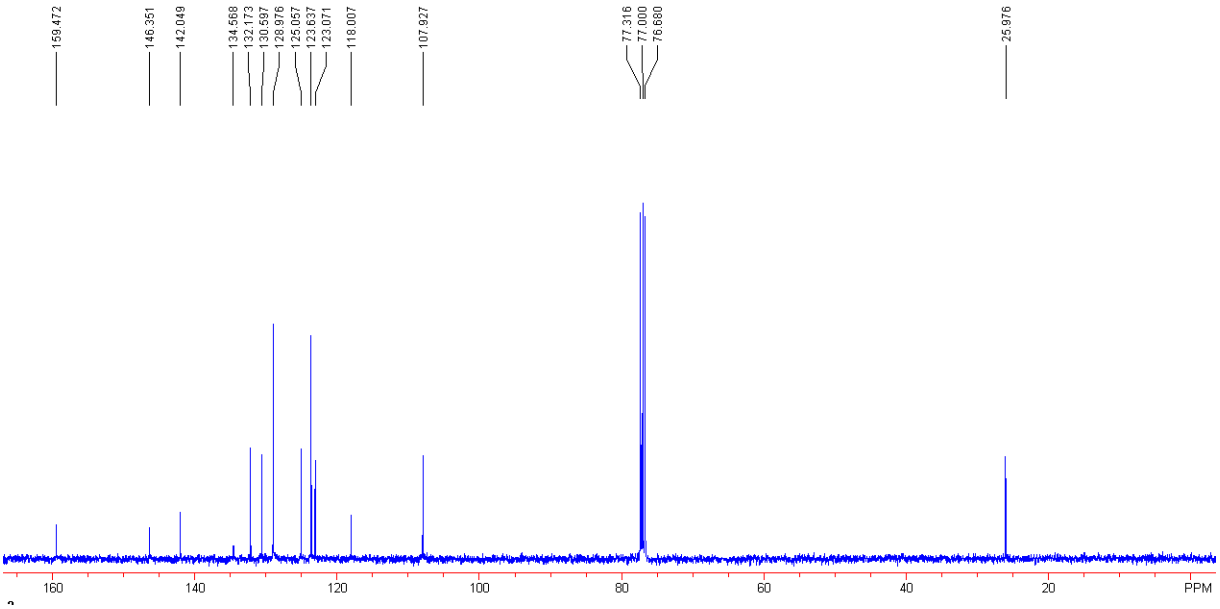
General procedure for preparing isatin ketonitrones. N-protected isatin (1.0 equiv), N-phenylhydroxylamines (2.5 equiv), 2,2,2-trifluoroacetic acid (0.01 equiv) and 4Å MS was stirred in 1,2-dichloromethane until TLC showed that N-protected isatins disappeared completely. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding products **1**.

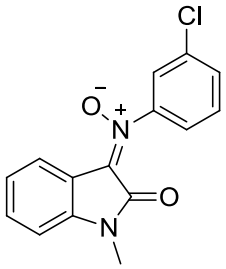
General procedure for $Yb(NTf_2)_3$-catalyzed [3+3] cycloaddition between isatin ketonitrones and cyclopropanes under the standard reaction conditions. Under an argon atmosphere, isatin ketonitrones **1** (0.1 mmol, 1.0 equiv), cyclopropanes **2** (0.2 mmol, 2.0 equiv), $Yb(NTf_2)_3$ (0.02 mmol, 0.2 equiv) and 4Å MS was mixed in 1,2-dichloroethane (DCE) (1.0 mL) in an Schlenk tube. Then, the reaction mixture was stirred at 80 ^{o}C until the reaction completed. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (SiO_2) to give the corresponding products **3** in moderate to good yields.



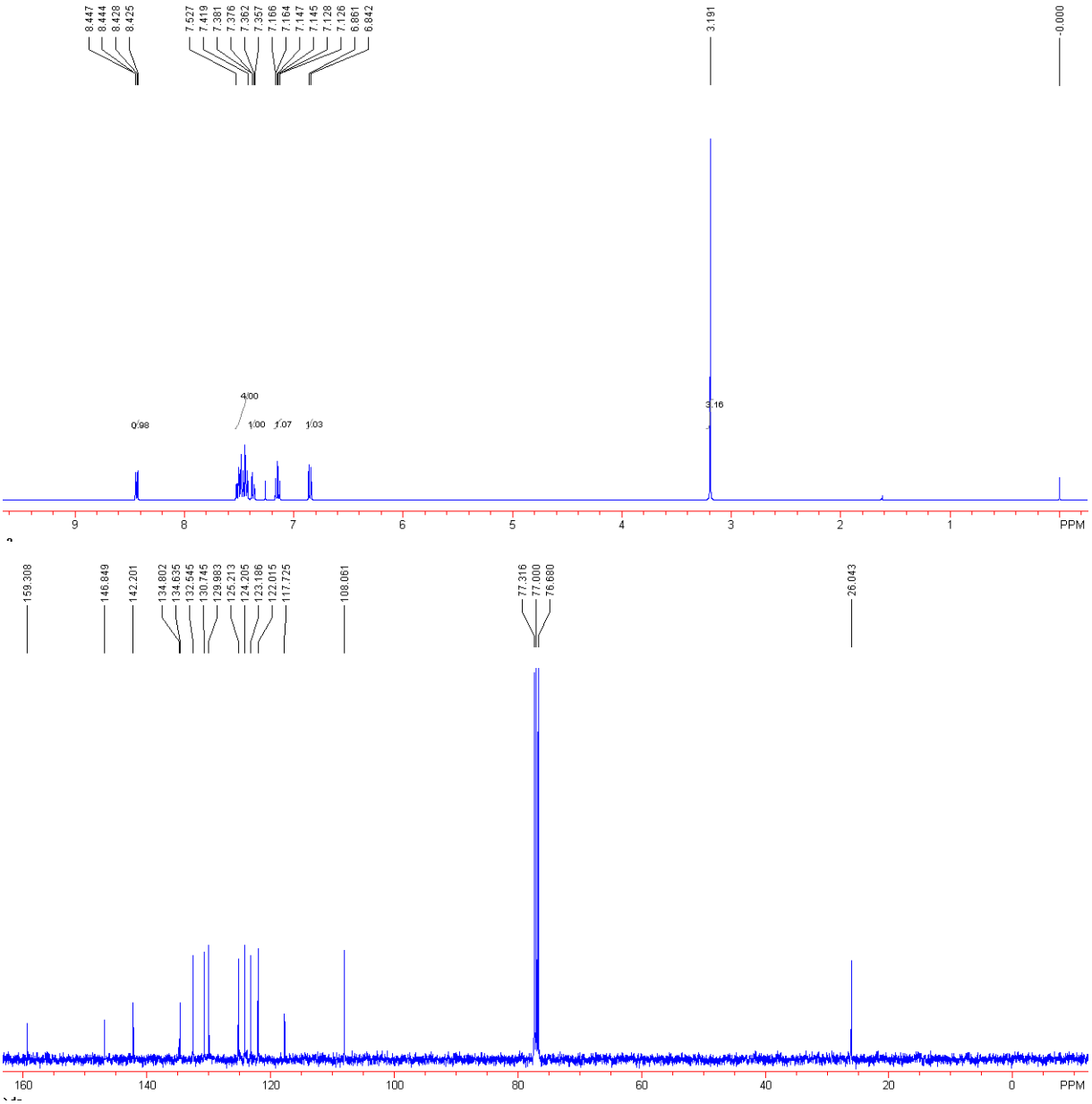
Compound 1a: Yield: 73%. A yellow solid. m. p.: 160-162 ^{o}C. IR (neat) ν 3059, 3021, 1695, 1608, 1467, 1373, 1328, 1098, 1080, 983 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.18 (s, 3H), 6.84 (d, *J* = 7.6 Hz, 1H), 7.15 (td, *J* = 7.6 Hz, 0.8 Hz, 1H), 7.43 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.46-7.55 (m, 5H), 8.47 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 26.0, 107.9, 118.0, 123.1, 123.6, 125.1, 129.0, 130.6, 132.2, 134.6, 142.0, 146.4, 159.5; HRMS (MALDI) Calcd. for $C_{15}H_{12}N_2O_2$ requires (M^++H): 253.0977, Found: 253.0976.

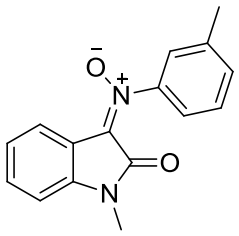






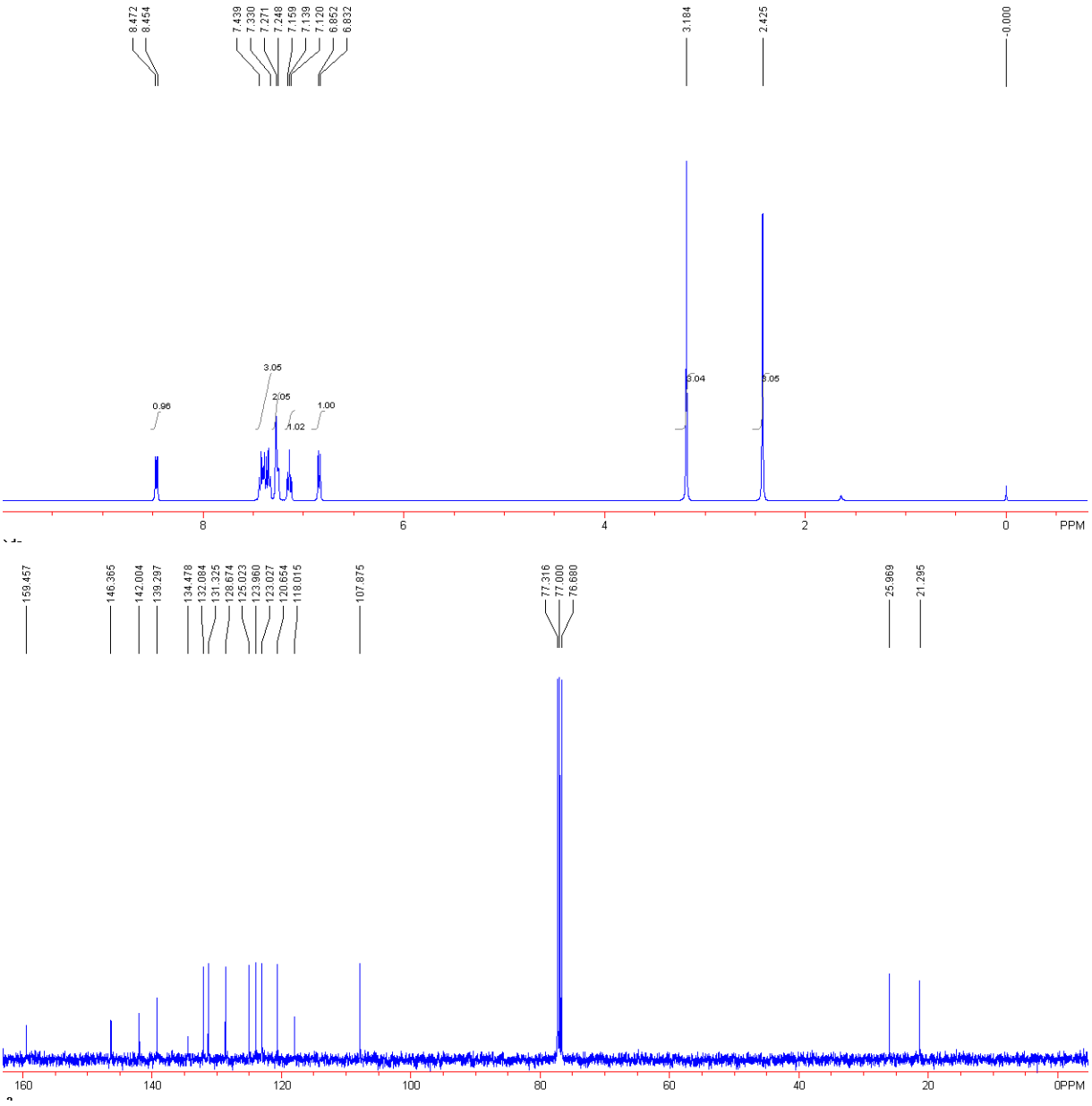
Compound 1b: Yield: 99%. A yellow solid. m. p.: 209-211 ^{o}C. IR (neat) ν 3072, 2935, 1704, 1605, 1541, 1468, 1327, 1243, 1103, 987, 898 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.19 (s, 3H), 6.85 (d, *J* = 7.6 Hz, 1H), 7.15 (td, *J* = 7.6 Hz, 0.8 Hz, 1H), 7.37 (dd, *J* = 7.6 Hz, 2.0 Hz, 1H), 7.42-7.53 (m, 4H), 8.44 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 26.0, 108.1, 117.7, 122.0, 123.2, 124.2, 125.2, 130.0, 130.7, 132.5, 134.6, 134.8, 142.2, 146.8, 159.3; HRMS (MALDI) Calcd. for $C_{15}H_{11}ClN_2O_2$ requires (M^++H): 287.0587, Found: 287.0593.

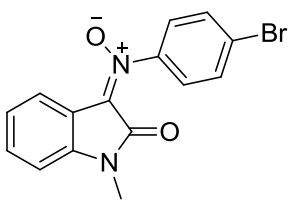




Compound 1c: Yield: 63%. A red solid. m. p.: 162-164 ^{o}C. IR (neat) ν 3056, 2928, 1702, 1607, 1469, 1375, 1327, 1096, 1023, 985, 873 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 3.18 (s, 3H), 6.84 (d, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.25-7.27 (m, 2H),

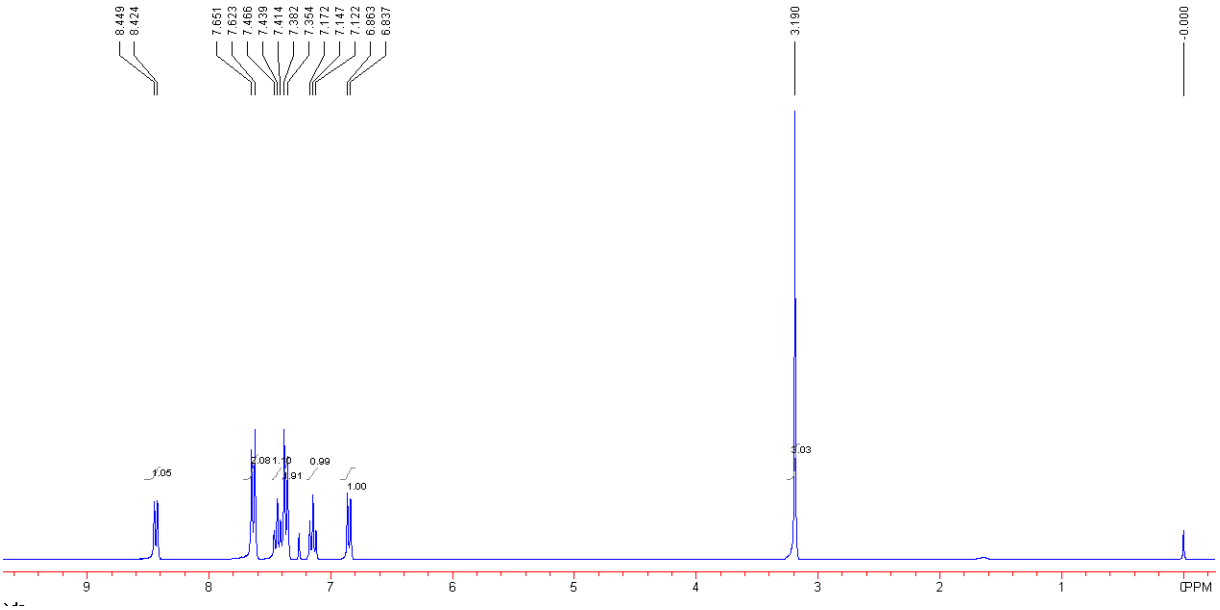
7.33-7.44 (m, 3H), 8.46 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 21.3, 26.0, 107.9, 118.0, 120.7, 123.0, 124.0, 125.0, 128.7, 131.3, 132.1, 134.5, 139.3, 142.0, 146.4, 159.5; HRMS (MALDI) Calcd. for $C_{16}H_{14}N_2O_2$ requires (M^++H): 267.1134, Found: 267.1138.

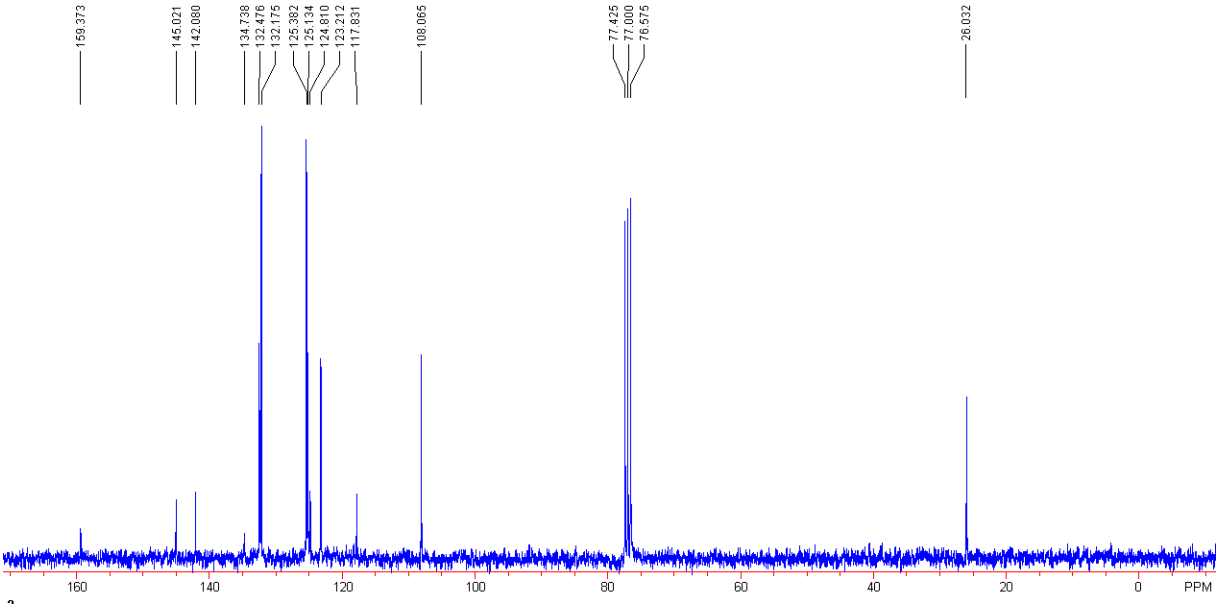


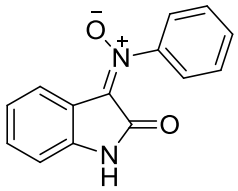


Compound 1d: Yield: 58%. A yellow solid. m. p.: 212-214 ^{o}C. IR (neat) ν 3093, 3055, 2927,

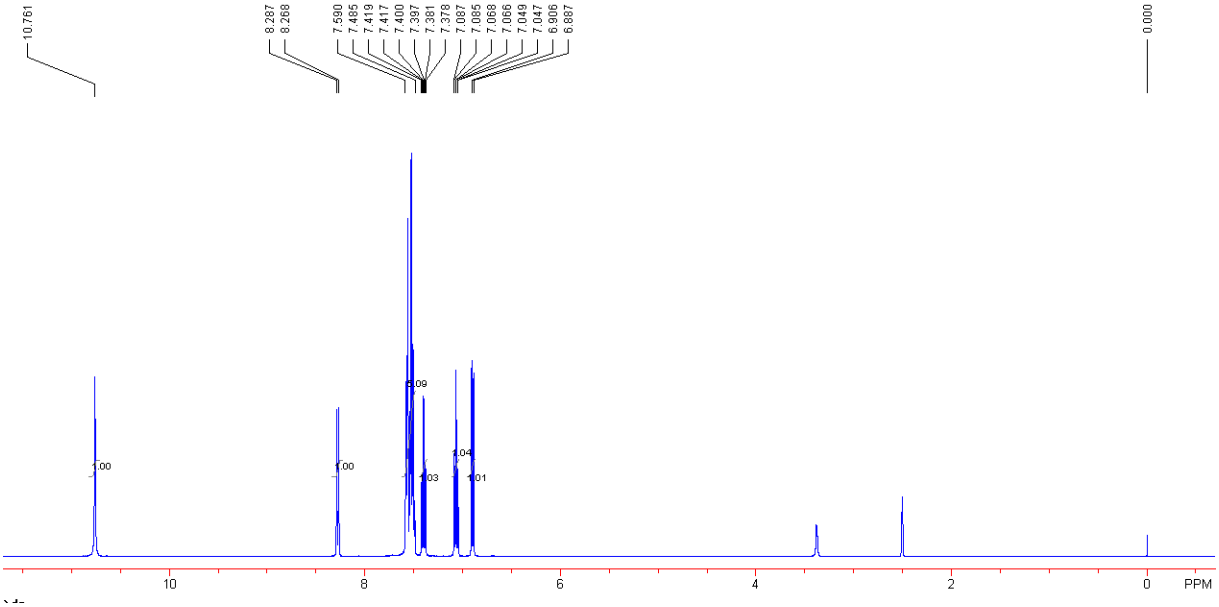
1698, 1677, 1606, 1466, 1243, 1095, 1067, 1013, 982 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 3.19 (s, 3H), 6.85 (d, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 8.44 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ 26.0, 108.1, 117.8, 123.2, 124.8, 125.1, 125.4, 132.2, 132.5, 134.7, 142.1, 145.0, 159.4; HRMS (MALDI) Calcd. for $C_{15}H_{11}BrN_2O_2$ requires (M^++H): 331.0082, Found: 331.0079.

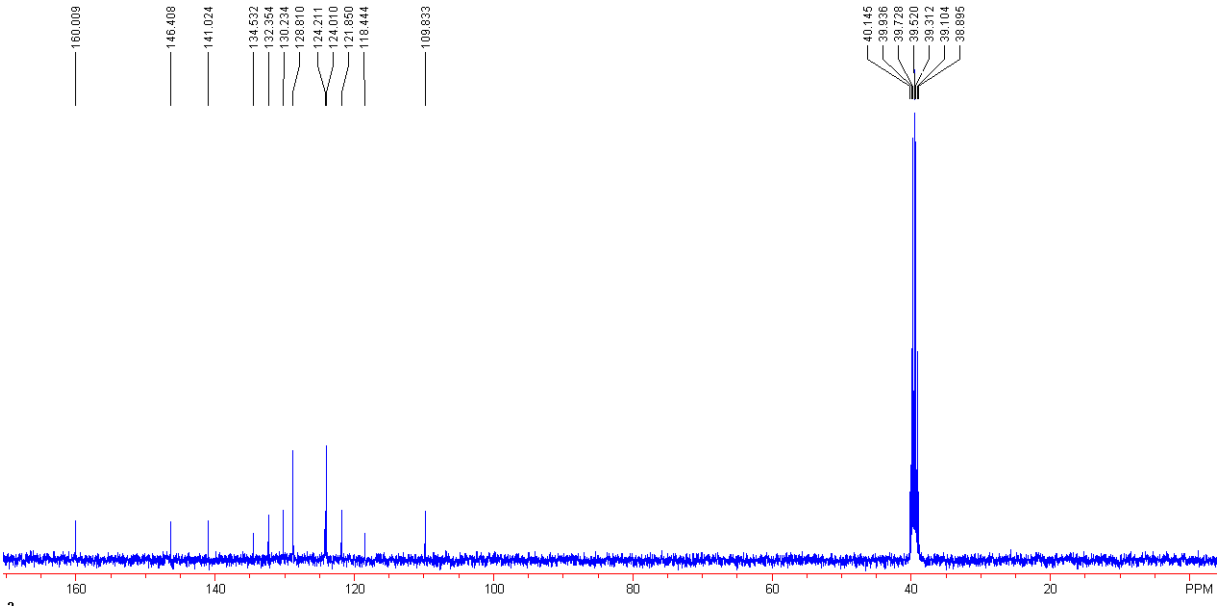


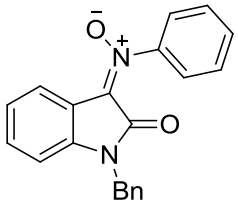




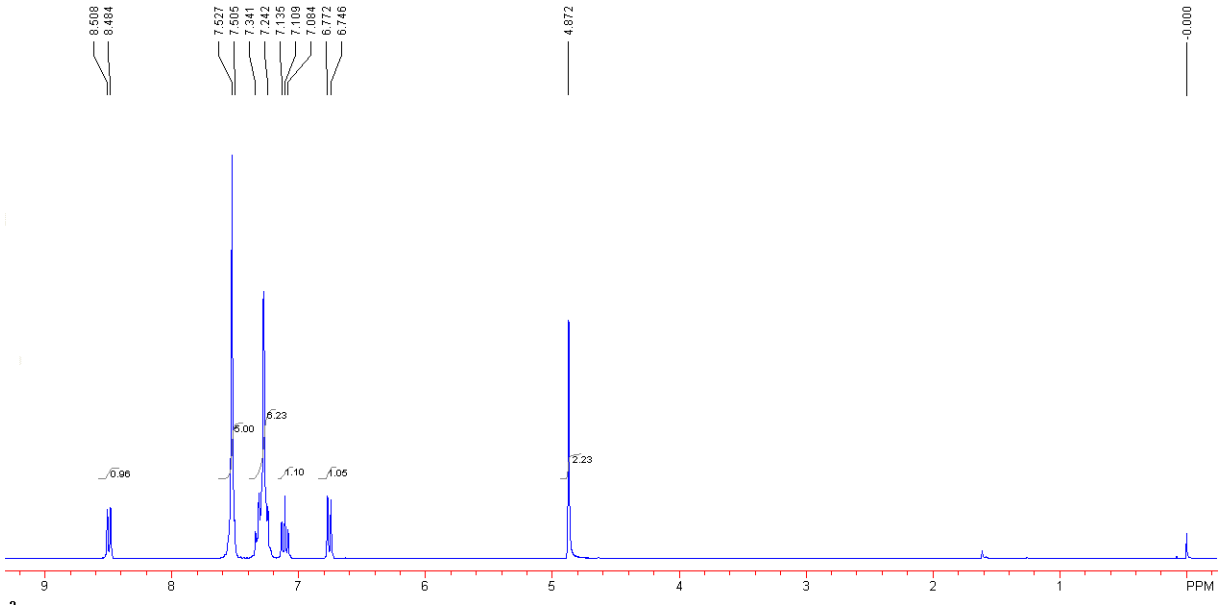
Compound 1e: Yield: 62%. A yellow solid. m. p.: 258-260 ^{o}C. IR (neat) ν 3149, 3066, 3028, 2828, 1701, 1539, 1459, 1351, 1256, 1237, 1139, 925, 857 cm^{-1}; ^{1}H NMR (400 MHz, d^{6}-DMSO, TMS) δ 6.90 (d, *J* = 7.6 Hz, 1H), 7.07 (td, *J* = 7.6 Hz, 0.8 Hz, 1H), 7.40 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.49-7.59 (m, 5H), 8.28 (d, *J* = 7.6 Hz, 1H), 10.8 (s, 1H); ^{13}C NMR (100 MHz, d^{6}-DMSO, TMS) δ 109.8, 118.4, 121.9, 124.0, 124.2, 128.8, 130.2, 132.4, 134.5, 141.0, 146.4, 160.0; HRMS (MALDI) Calcd. for $C_{14}H_{10}N_2O_2$ requires (M^{+}+H): 239.0821, Found: 239.0806.

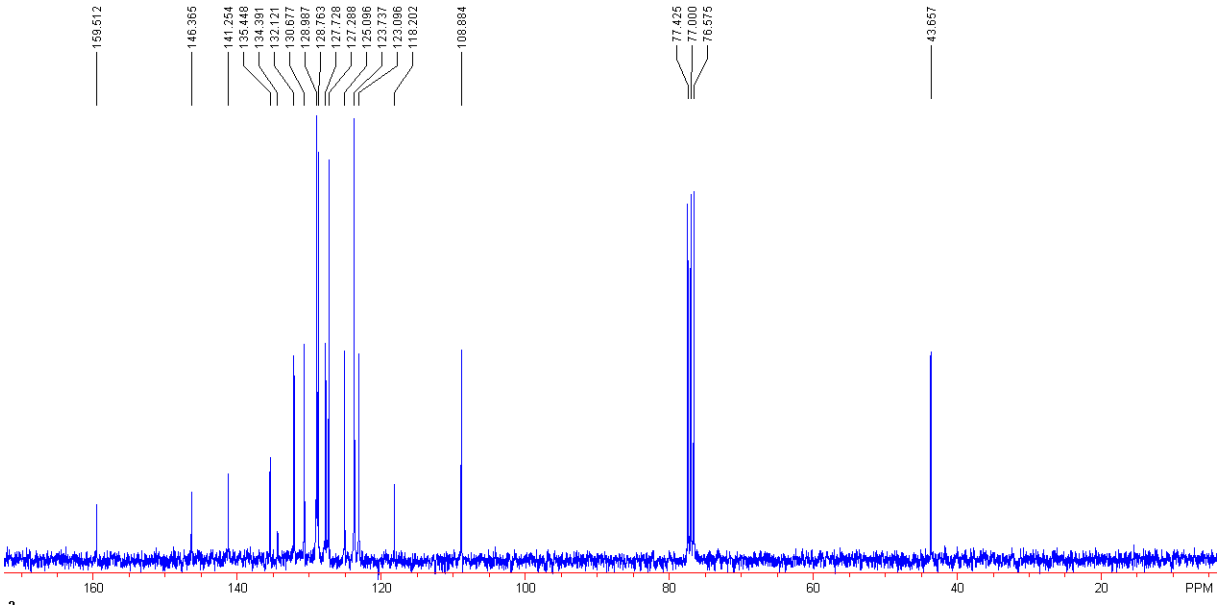


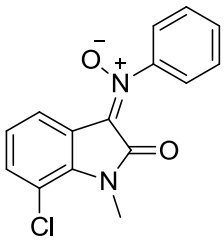




Compound 1f: Yield: 75%. A yellow solid. m. p.: 208-210 ^{o}C. IR (neat) ν 3067, 3030, 2939, 1696, 1605, 1541, 1463, 1258, 1162, 948, 871 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 4.87 (s, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.24-7.34 (m, 6H), 7.51-7.53 (m, 5H), 8.50 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ 43.7, 108.9, 118.2, 123.1, 123.7, 125.1, 127.3, 127.7, 128.8, 129.0, 130.7, 132.1, 134.4, 135.4, 141.3, 146.4, 159.5; HRMS (MALDI) Calcd. for $C_{21}H_{16}N_2O_2$ requires (M^++H): 329.1290, Found: 329.1280.

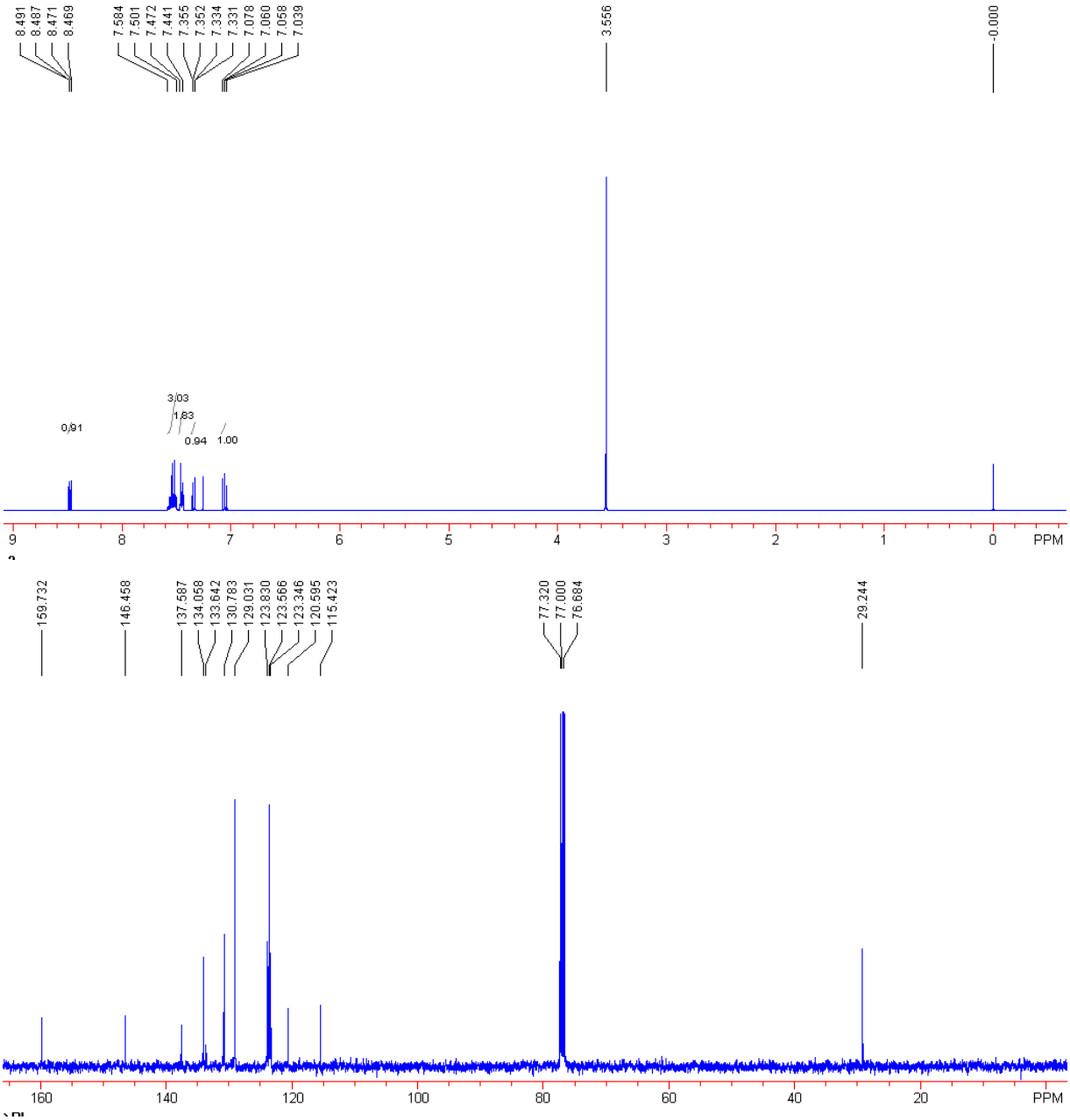


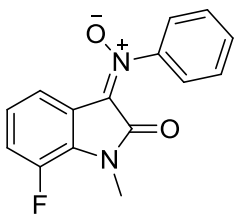




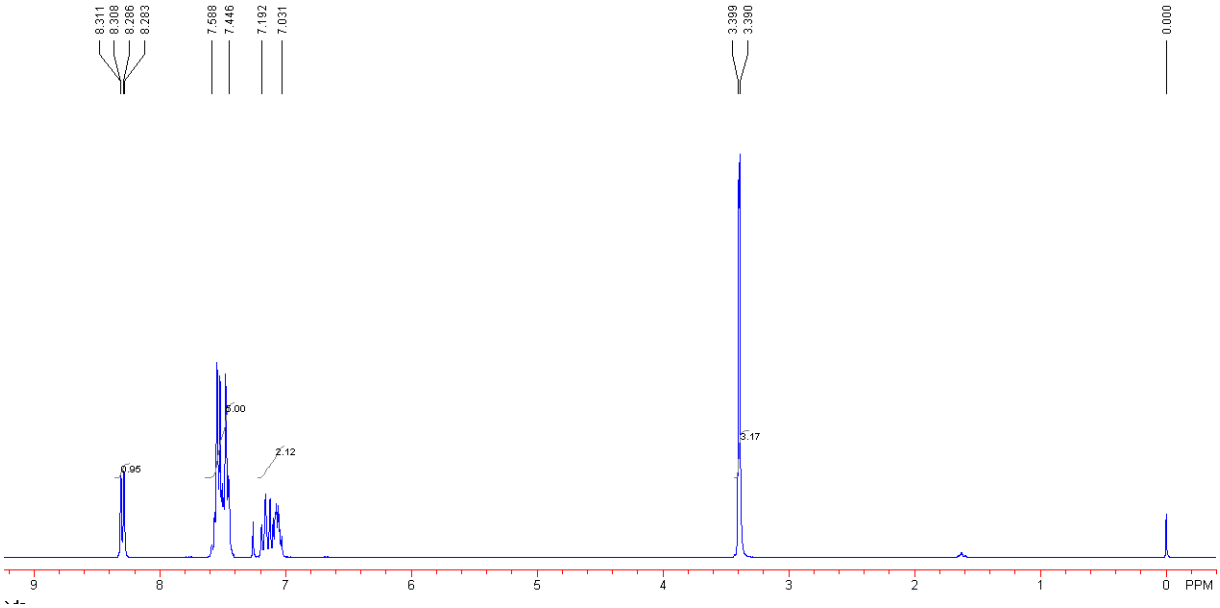
Compound 1g: Yield: 64%. A red solid. m. p.: 237-240 ^{o}C. IR (neat) ν 3053, 2953, 1702, 1599, 1535, 1450, 1370, 1316, 1110, 1056, 989 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.56 (s, 3H), 7.06 (dd, *J* = 8.4 Hz, 7.6 Hz, 1H), 7.34 (dd, *J* = 8.4 Hz, 1.2 Hz, 1H), 7.44-7.47 (m,

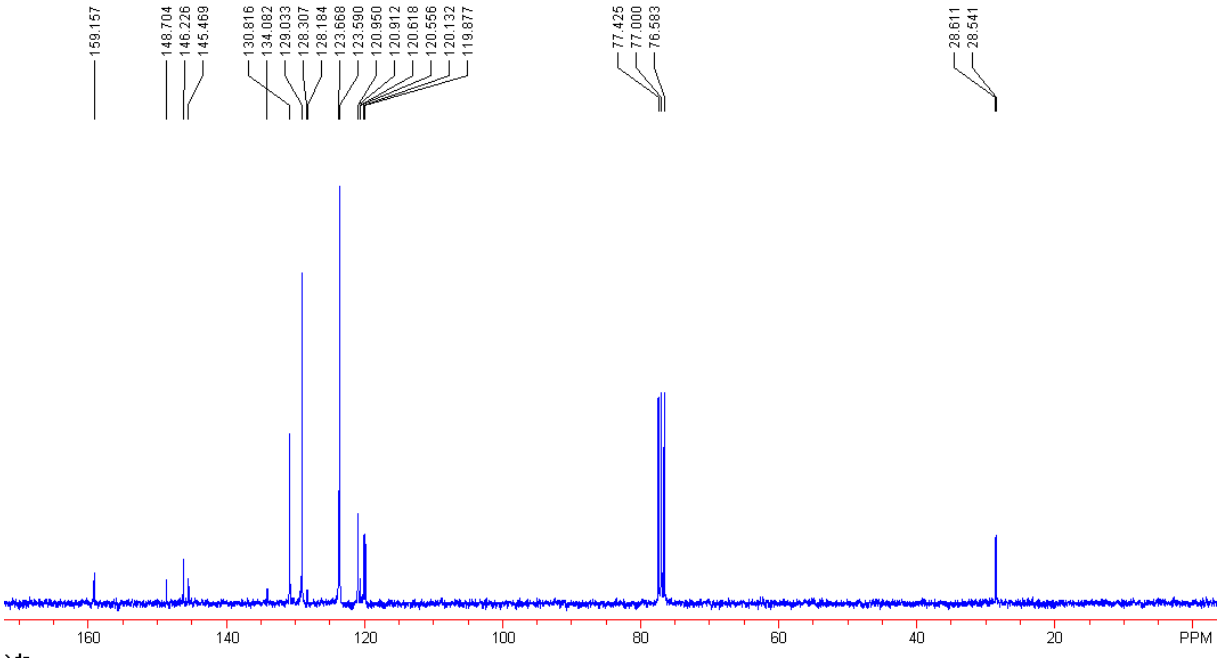
2H), 7.50-7.58 (m, 3H), 8.48 (dd, J = 8.0 Hz, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 29.2, 115.4, 120.6, 123.3, 123.6, 123.8, 129.0, 130.8, 133.6, 134.1, 137.6, 146.5, 159.7; HRMS (MALDI) Calcd. for $C_{15}H_{11}ClN_2O_2$ requires (M^++H): 287.0587, Found: 287.0581.

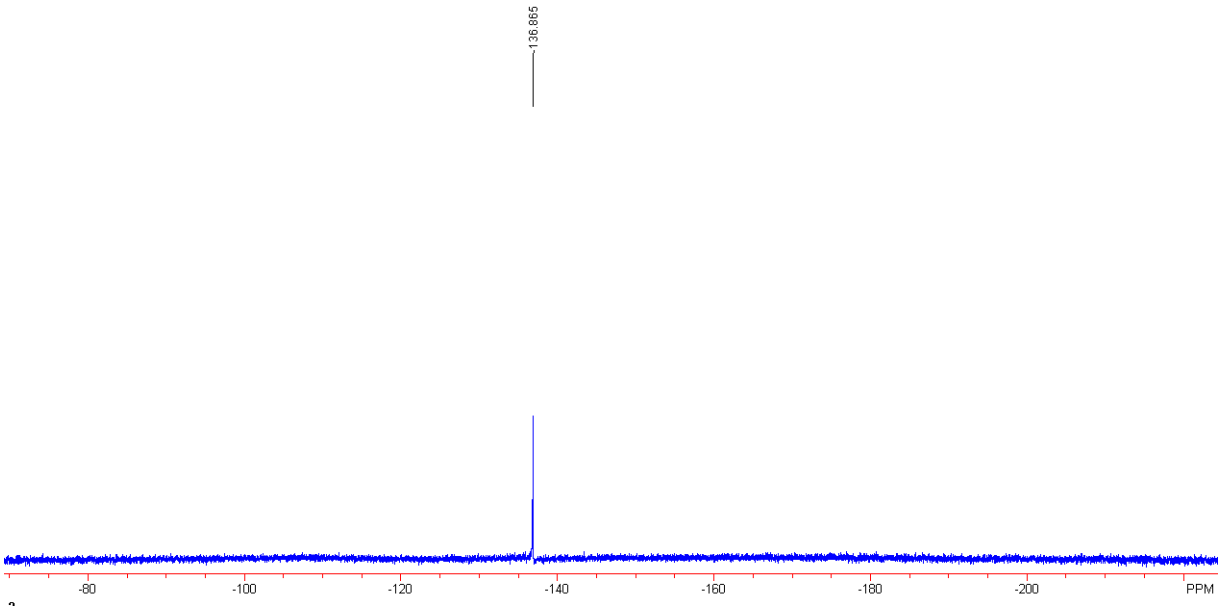


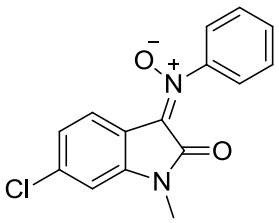


Compound 1h: Yield: 59%. A red solid. m. p.: 170-172 ^{o}C. IR (neat) ν 3051, 2937, 1706, 1626, 1548, 1461, 1372, 1230, 791 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 3.99-3.40 (m, 3H), 7.03-7.19 (m, 2H), 7.45-7.59 (m, 5H), 8.29 (dd, J = 7.5 Hz, 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ 28.6 (d, $J_{C\text{-}F}$ = 5.3 Hz), 120.0 (d, $J_{C\text{-}F}$ = 19.1 Hz), 120.6 (d, $J_{C\text{-}F}$ = 1.6 Hz), 120.9 (d, $J_{C\text{-}F}$ = 2.9 Hz), 123.6, 123.7, 128.2 (d, $J_{C\text{-}F}$ = 9.2 Hz), 129.0, 130.8, 134.1, 146.2, 147.1 (d, $J_{C\text{-}F}$ = 242.6 Hz), 159.2; ^{19}F NMR (282 MHz, $CDCl_3$, $CFCl_3$) δ -136.87 (brs, 1F); HRMS (MALDI) Calcd. for $C_{15}H_{11}FN_2O_2$ requires (M^++H): 271.0883, Found: 271.0875.

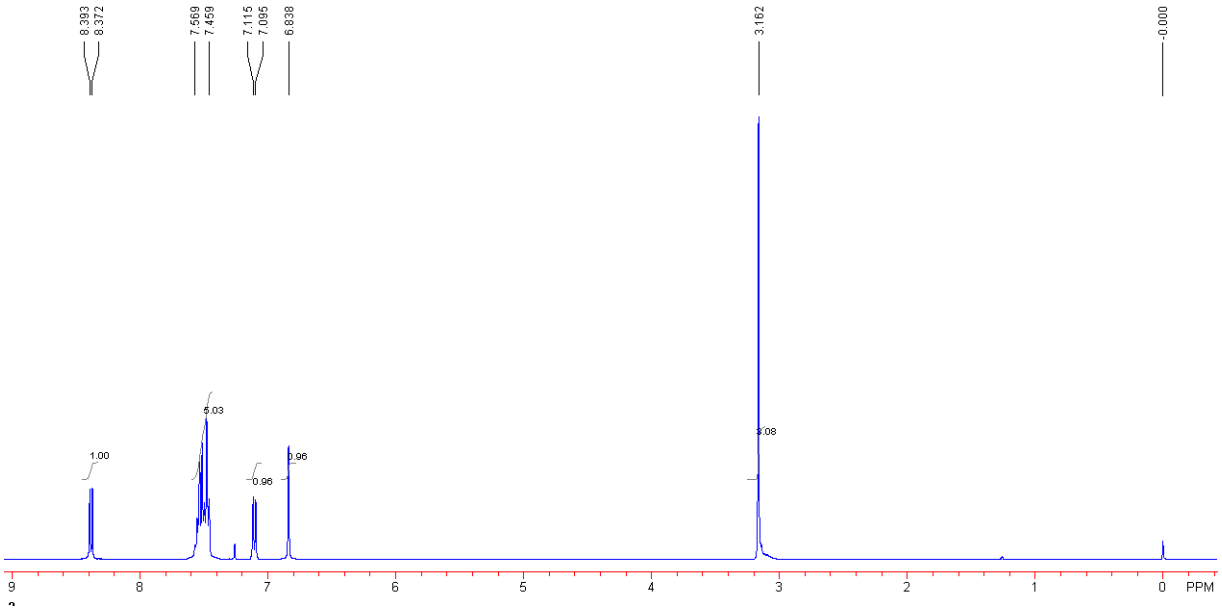


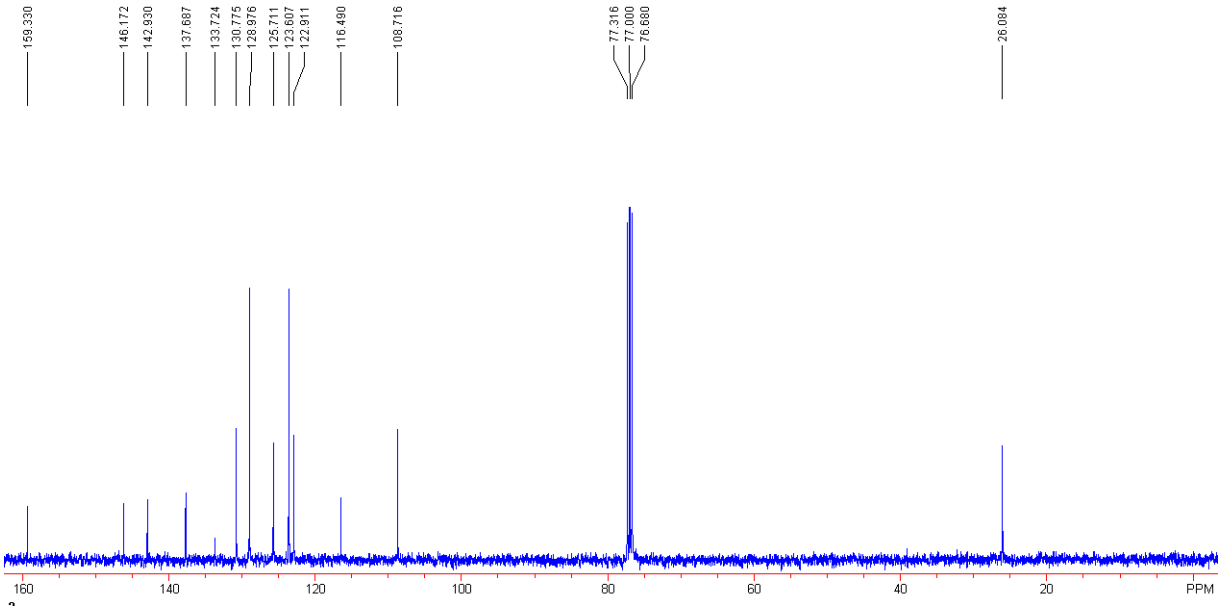


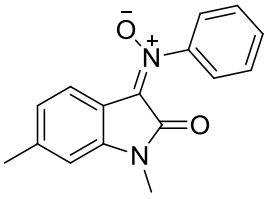




Compound 1i: Yield: 78%. A red solid. m. p.: 218-220 ^{o}C. IR (neat) ν 3056, 3015, 1702, 1601, 1531, 1479, 1371, 1284, 1238, 1107, 1072, 995 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.16 (s, 3H), 6.84 (s, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 7.46-7.57 (m, 5H), 8.38 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 26.1, 108.7, 116.5, 122.9, 123.6, 125.7, 129.0, 130.8, 133.7, 137.7, 142.9, 146.2, 159.3; HRMS (MALDI) Calcd. for $C_{15}H_{11}ClN_2O_2$ requires (M^++H): 287.0587, Found: 287.0578.

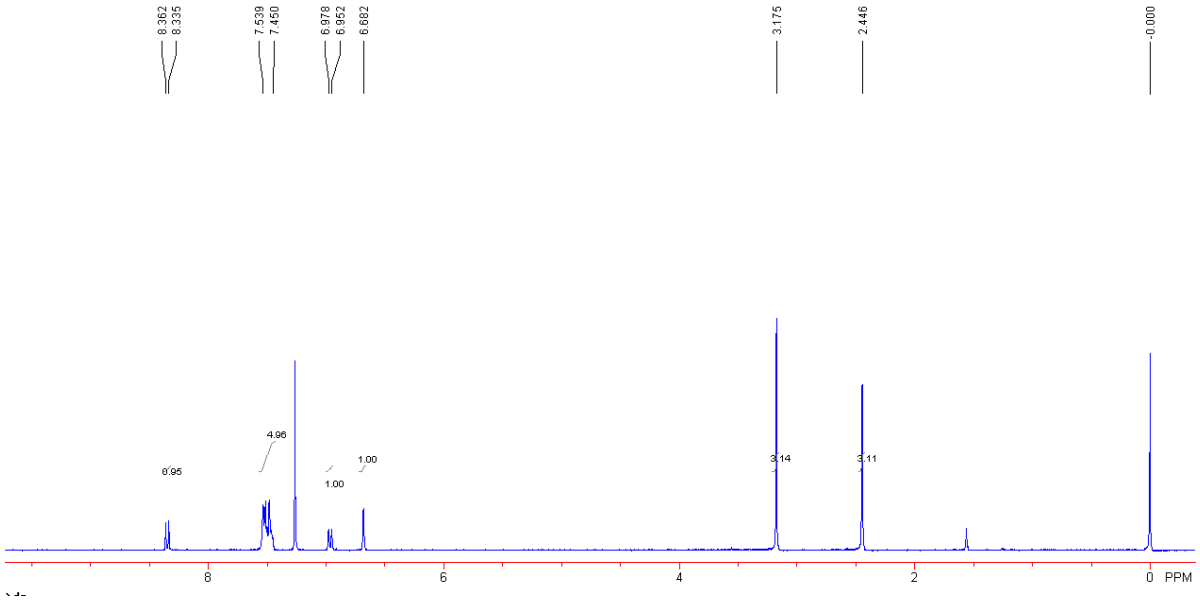


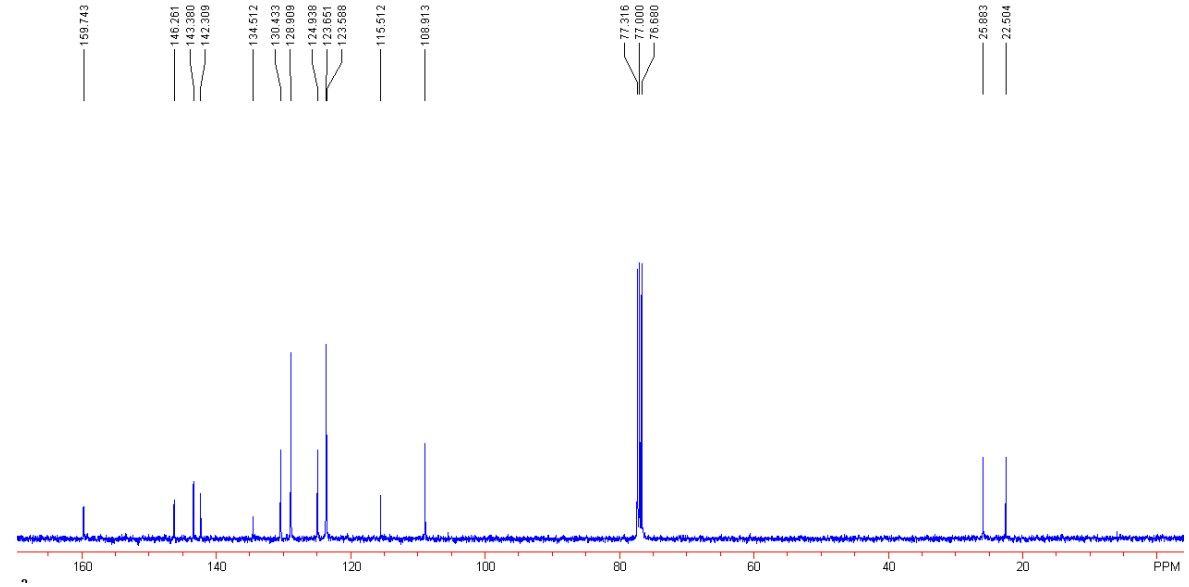


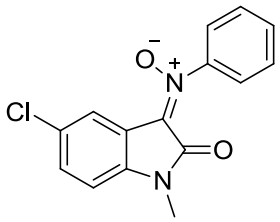


Compound 1j: Yield: 86%. A red solid. m. p.: 214-216 ^{o}C. IR (neat) ν 3032, 2916, 2857, 1701, 1614, 1454, 1378, 1244, 1078, 923 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.45 (s, 3H), 3.18 (s, 3H), 6.68 (s, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 7.45-7.54 (m, 5H), 8.35 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ 22.5, 25.9, 108.9, 115.5, 123.6, 123.7, 124.9, 128.9,

130.4, 134.5, 142.3, 143.4, 146.3, 159.7; HRMS (MALDI) Calcd. for $C_{16}H_{14}N_2O_2$ requires (M^++H): 267.1134, Found: 267.1136.

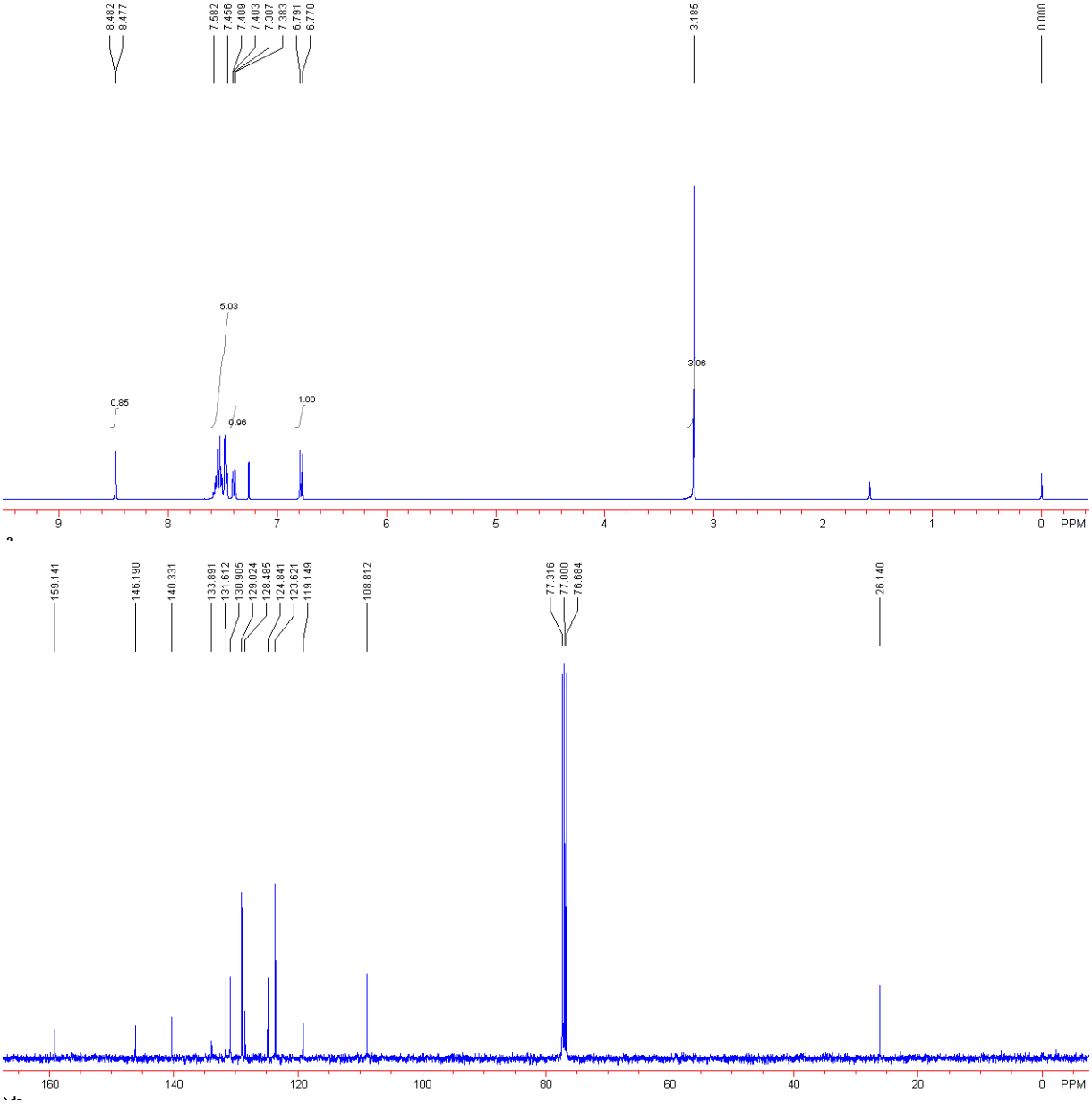


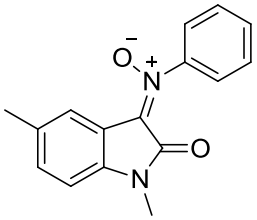




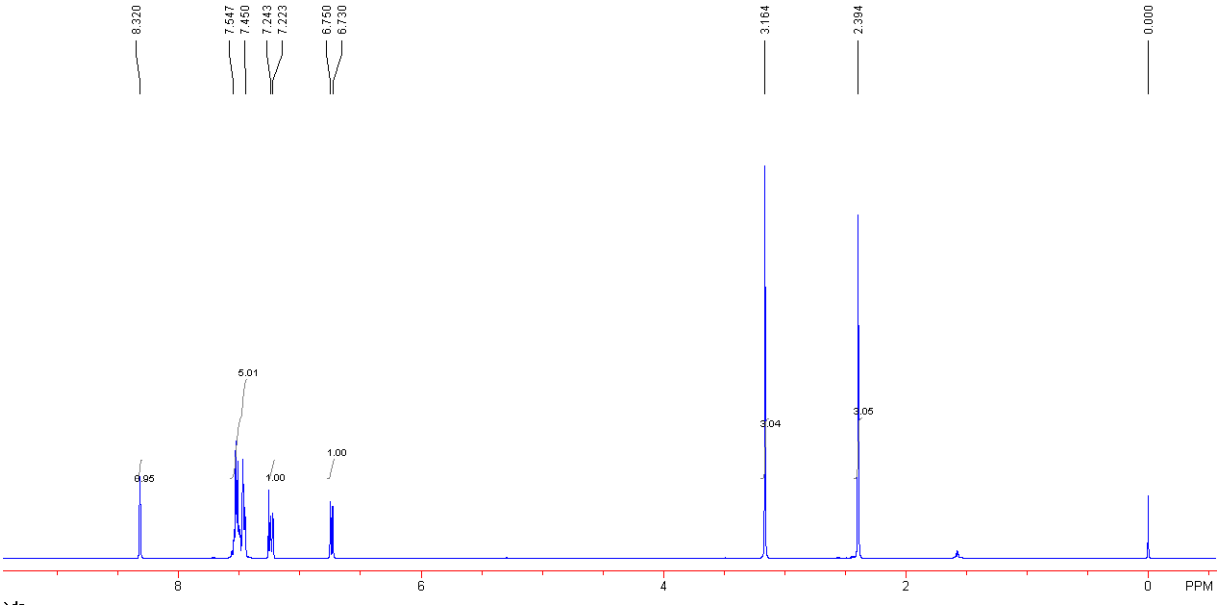
Compound 1k: Yield: 59%. A red solid. m. p.: 210-212 ^oC. IR (neat) ν 3108, 3084, 3019, 1701, 1536, 1471, 1290, 1234, 1101, 1076, 994 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ

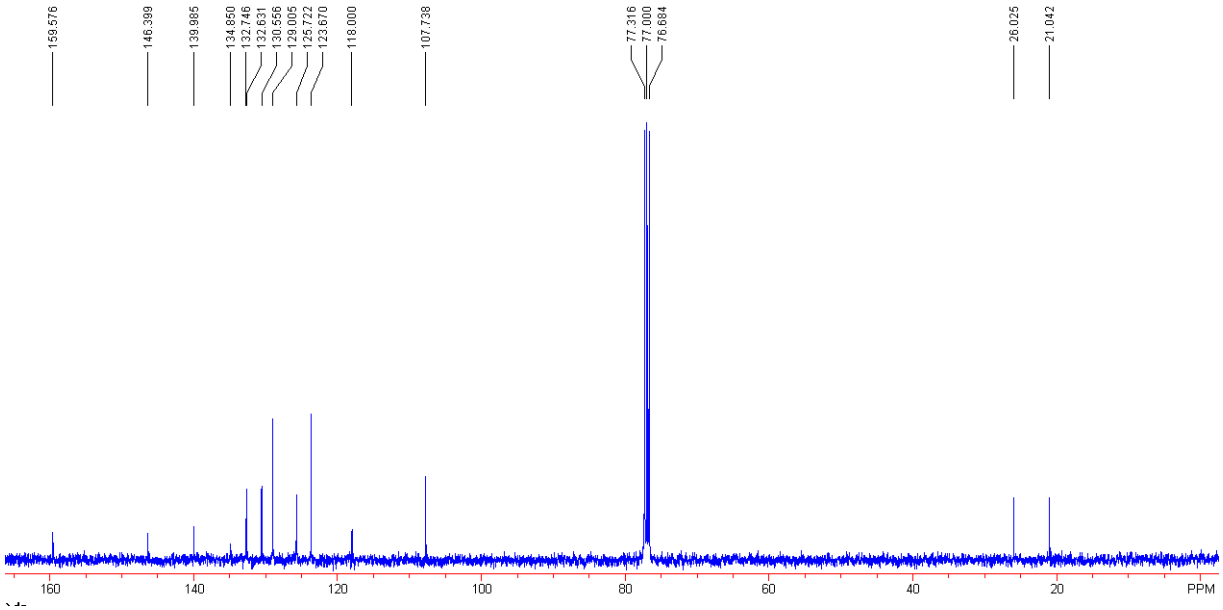
3.19 (s, 3H), 6.78 (d, *J* = 8.4 Hz, 1H), 7.40 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.46-7.58 (m, 5H), 8.48 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 26.1, 108.8, 119.1, 123.6, 124.8, 128.5, 129.0, 130.9, 131.6, 133.9, 140.3, 146.2, 159.1; HRMS (MALDI) Calcd. for $C_{15}H_{11}ClN_2O_2$ requires (M^++H): 287.0587, Found: 287.0587.

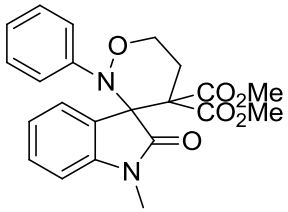




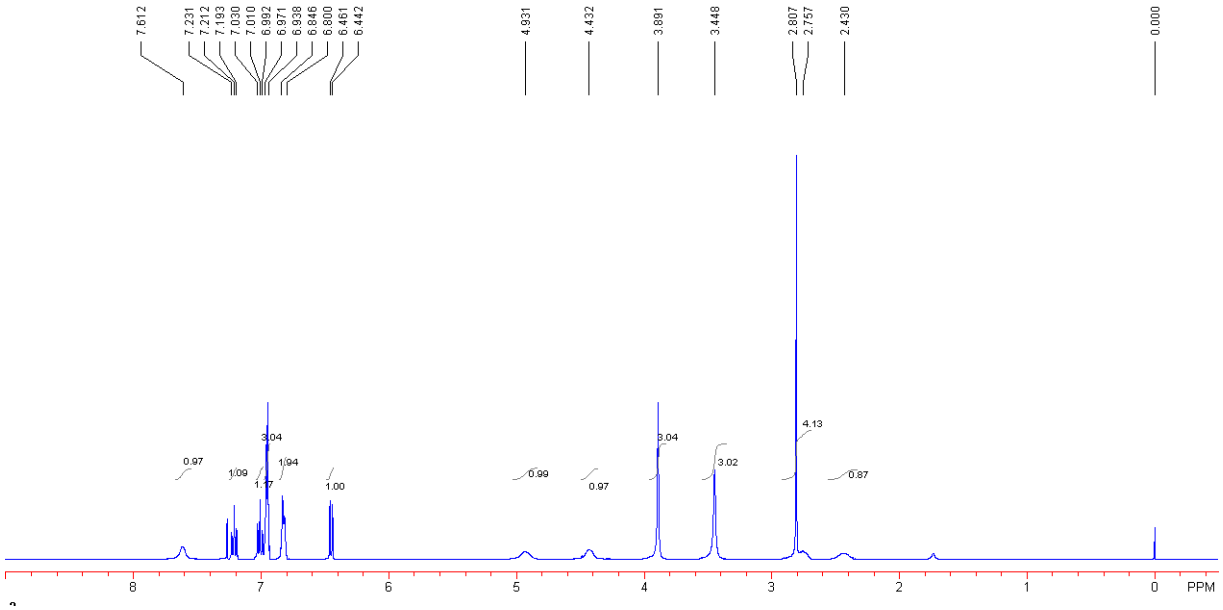
Compound 1l: Yield: 82%. A red solid. m. p.: 190-192 ^{o}C. IR (neat) ν 3063, 3010, 2911, 1694, 1612, 1538, 1483, 1299, 1101, 1008, 930 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 3.16 (s, 3H), 6.74 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.45-7.55 (m, 5H), 8.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 21.0, 26.0, 107.7, 118.0, 123.7, 125.7, 129.0, 130.6, 132.6, 132.7, 134.9, 140.0, 146.4, 159.6; HRMS (MALDI) Calcd. for $C_{16}H_{14}N_2O_2$ requires (M^++H): 267.1134, Found: 267.1132.

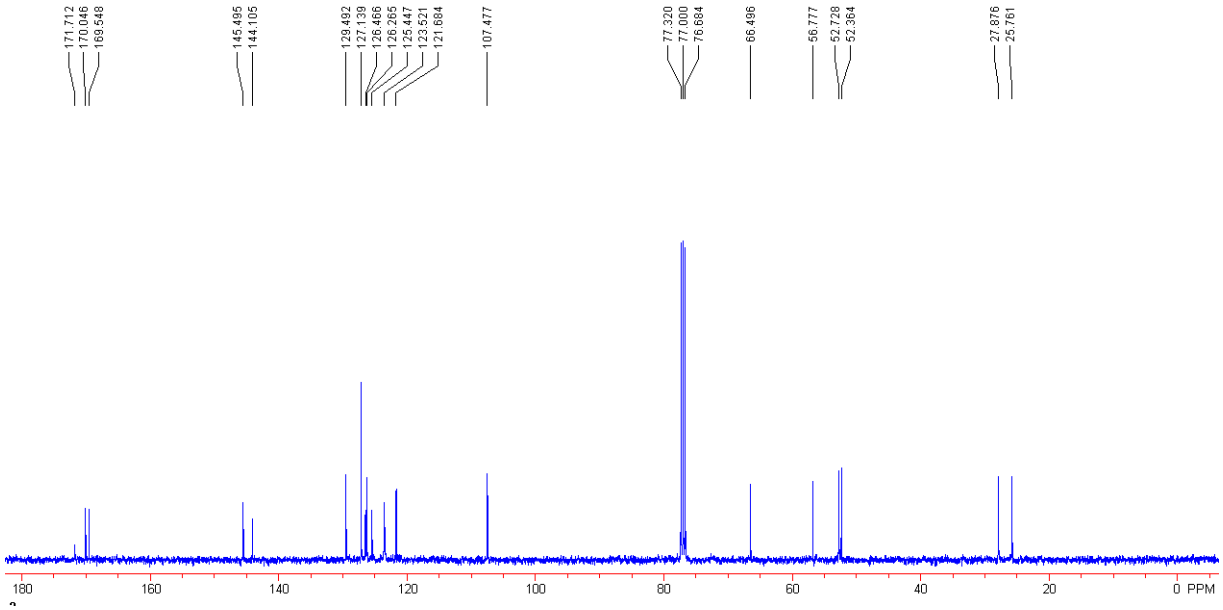


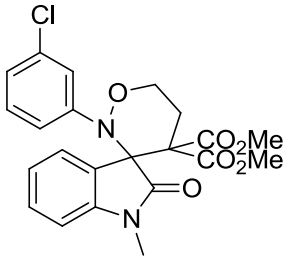




Compound 3a: Yield: 34 mg, 82%. A white solid. m. p.: 168-170 ^{o}C. IR (neat) ν 2955, 1746, 1714, 1607, 1486, 1433, 1264, 1218, 1046, 990, 973 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (brs, 1H), 2.76 (brs, 1H), 2.81 (s, 3H), 3.45 (s, 3H), 3.89 (s, 3H), 4.43 (brs, 1H), 4.93 (brs, 1H), 6.45 (d, *J* = 7.6 Hz, 1H), 6.80-6.85 (m, 2H), 6.94-6.97 (m, 3H), 7.01 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.61 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.8, 27.9, 52.4, 52.7, 56.8, 66.5, 107.5, 121.7, 123.5, 125.4, 126.3, 126.5, 127.1, 129.5, 144.1, 145.5, 169.5, 170.0, 171.7; HRMS (MALDI) Calcd. for $C_{22}H_{22}N_2O_6$ requires (M^++H): 411.1556, Found: 411.1552.

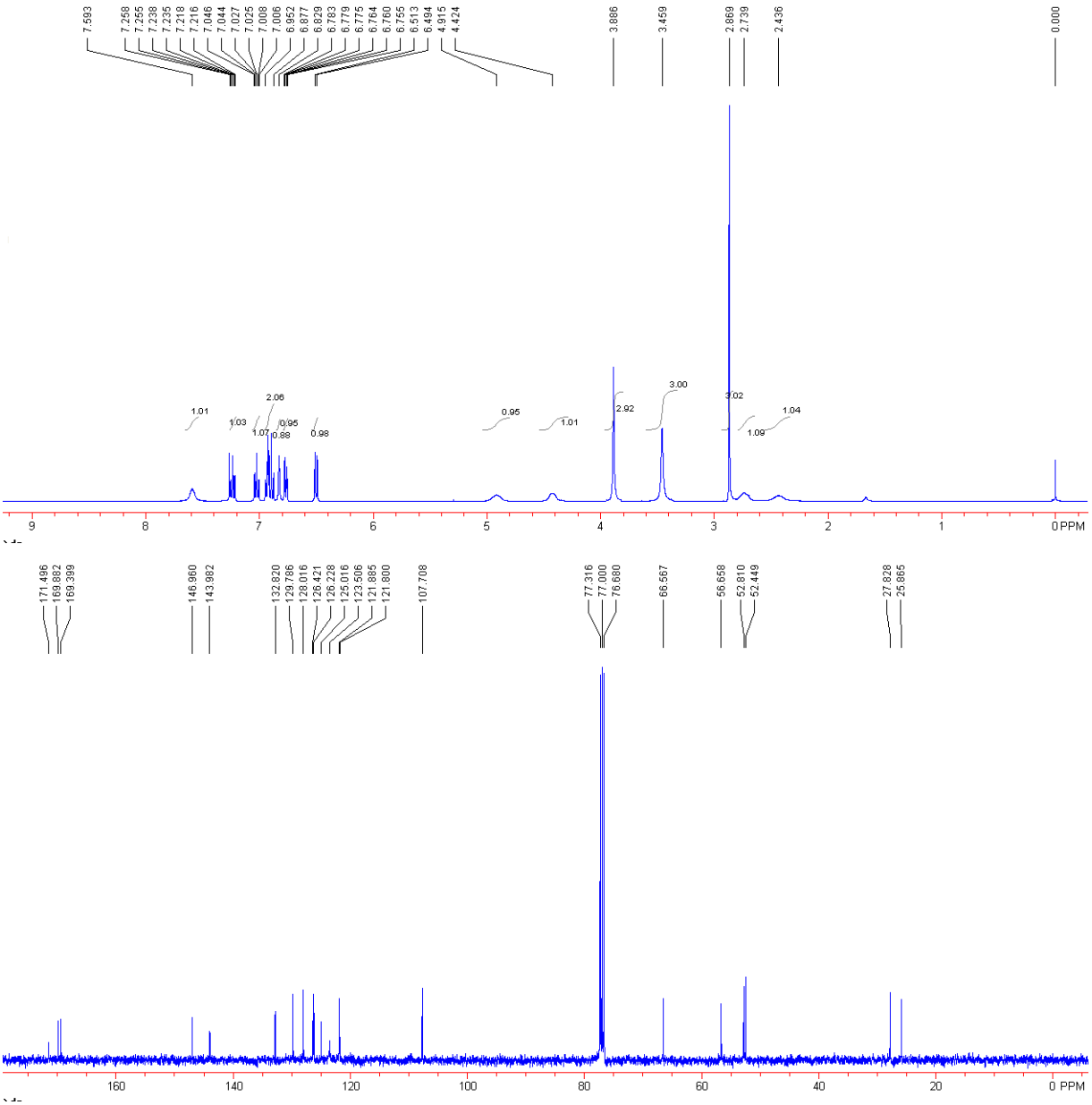


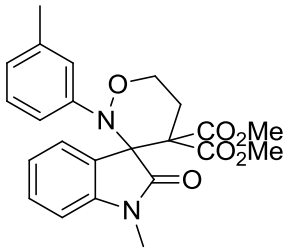




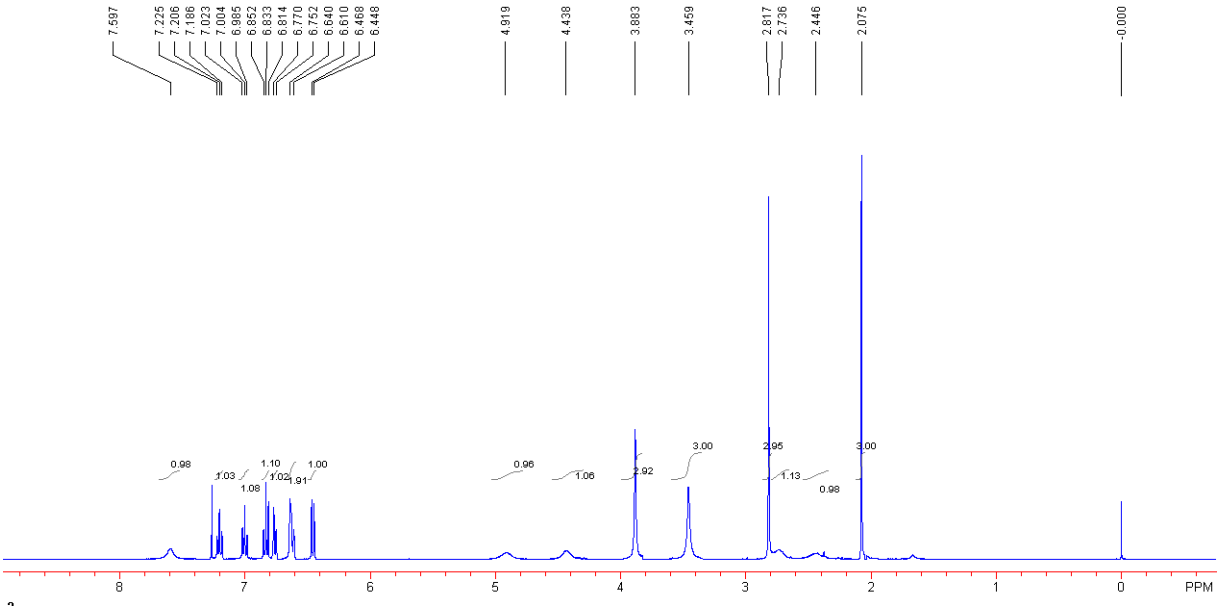
Compound 3b: Yield: 24 mg, 55%. A white solid. m. p.: 165-167 ^{o}C. IR (neat) ν 2960, 1740, 1719, 1464, 1264, 1219, 1086, 1049, 972, 955 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.44 (brs, 1H), 2.74 (brs, 1H), 2.87 (s, 3H), 3.46 (s, 3H), 3.89 (s, 3H), 4.42 (brs, 1H), 4.92 (brs, 1H),

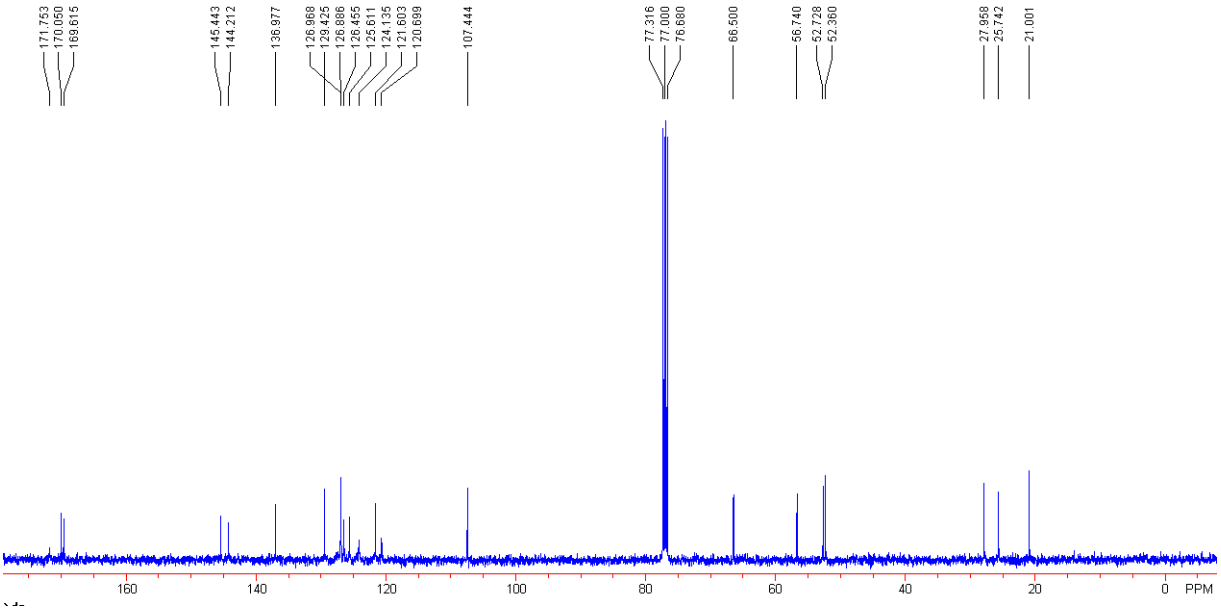
6.50 (d, *J* = 7.6 Hz, 1H), 6.77 (td, *J* = 7.6 Hz, 2.0 Hz, 1H), 6.83 (s, 1H), 6.88-6.95 (m, 2H), 7.03 (dt, *J* = 7.6 Hz, 0.8 Hz, 1H), 7.24 (dt, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.59 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.9, 27.8, 52.4, 52.8, 56.7, 66.6, 107.7, 121.8, 121.9, 123.5, 125.0, 126.2, 126.4, 128.0, 129.8, 132.8, 144.0, 147.0, 169.4, 169.9, 171.5; HRMS (MALDI) Calcd. for $C_{22}H_{21}ClN_2O_6$ requires (M^++H): 445.1166, Found: 445.1164.

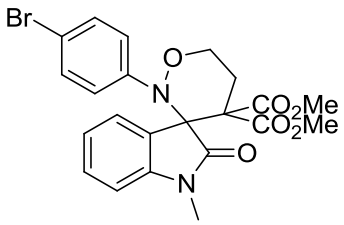




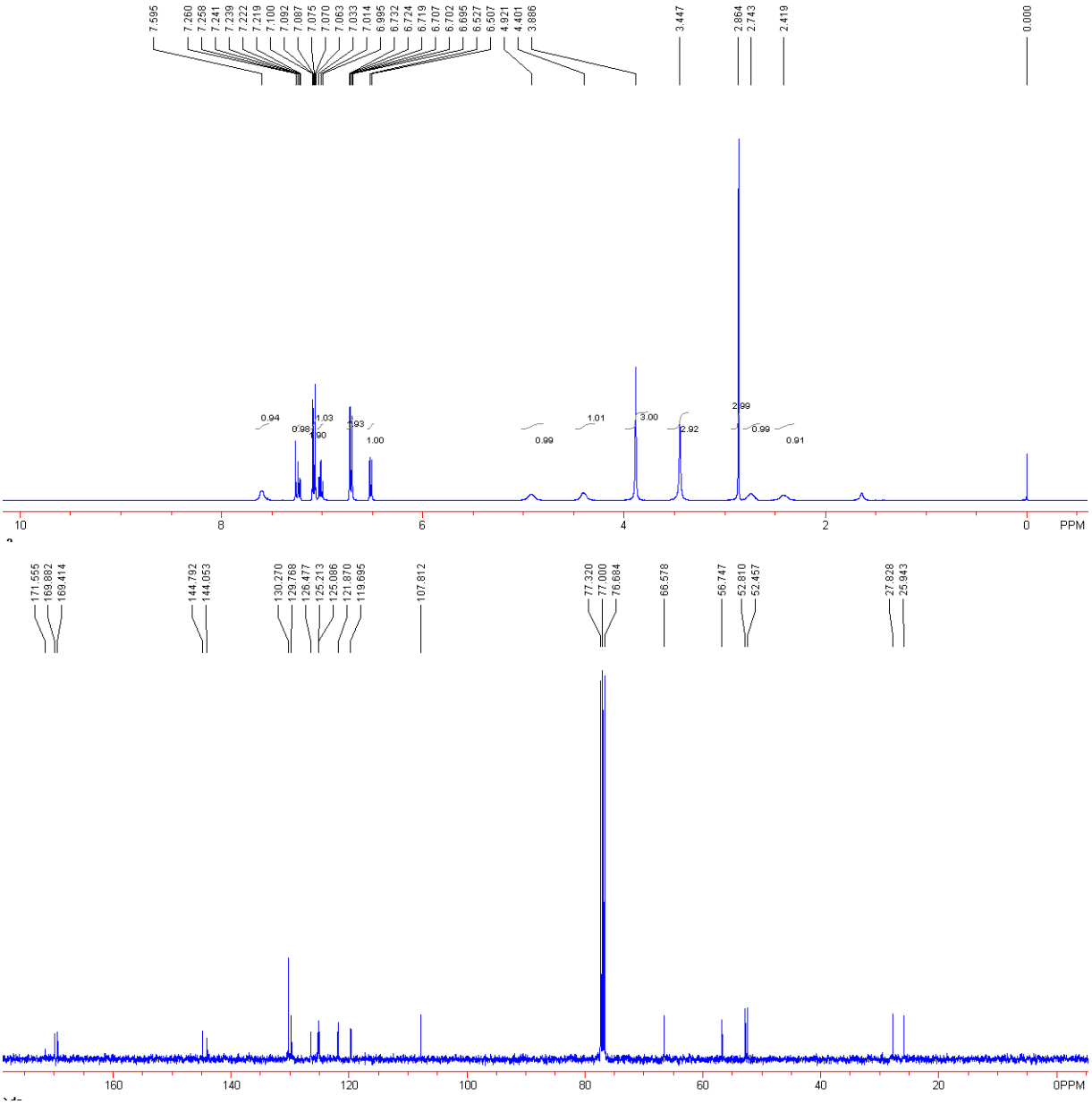
Compound 3c: Yield: 21 mg, 50%. A white solid. m. p.: 172-174 ^{o}C. IR (neat) ν 2951, 1740, 1717, 1608, 1428, 1371, 1221, 1085, 1048, 987, 972 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.08 (s, 3H), 2.45 (brs, 1H), 2.74 (brs, 1H), 2.82 (s, 3H), 3.46 (s, 3H), 3.88 (s, 3H), 4.44 (brs, 1H), 4.92 (brs, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 6.61-6.64 (m, 2H), 6.75-6.77 (m, 1H), 6.83 (t, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.60 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 21.0, 25.7, 28.0, 52.4, 52.7, 56.7, 66.5, 107.4, 120.7, 121.6, 124.1, 125.6, 126.5, 126.9, 127.0, 129.4, 137.0, 144.2, 145.4, 169.6, 170.1, 171.8; HRMS (MALDI) Calcd. for $C_{23}H_{24}N_2O_6$ requires (M^++H): 425.1713, Found: 425.1705.

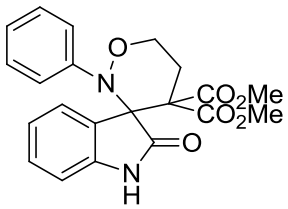






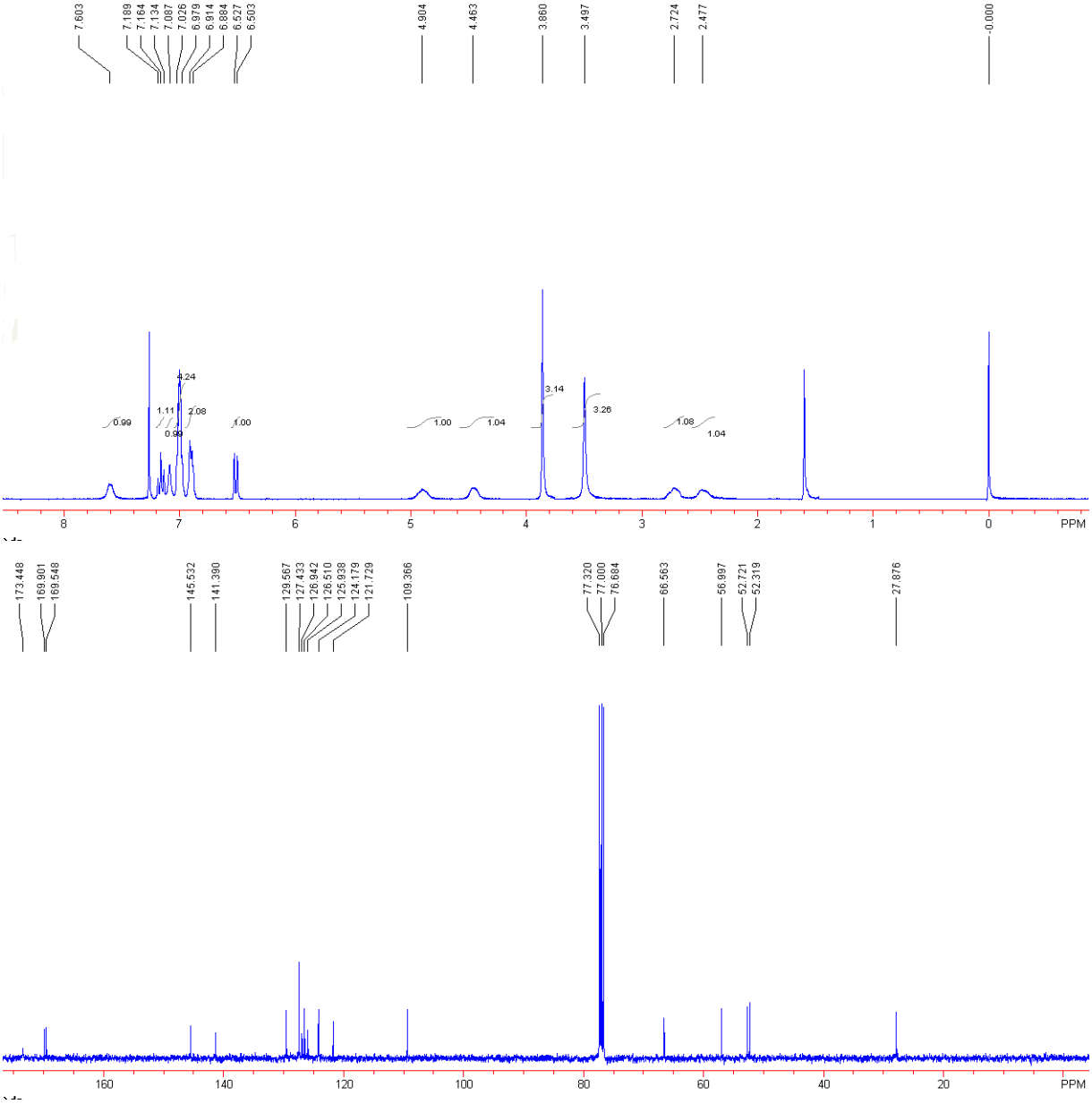
Compound 3d: Yield: 15 mg, 31%. A white solid. m. p.: 194-196 ^{o}C. IR (neat) ν 2948, 1741, 1717, 1609, 1483, 1469, 1263, 1214, 1096, 1053, 1008, 974 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (brs, 1H), 2.74 (brs, 1H), 2.86 (s, 3H), 3.45 (s, 3H), 3.89 (s, 3H), 4.40 (brs, 1H), 4.92 (brs, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 6.71 (dt, *J* = 8.8 Hz, 2.4 Hz, 2H), 7.01 (t, *J* = 7.6 Hz, 1H), 7.08 (dt, *J* = 8.8 Hz, 2.4 Hz, 2H), 7.24 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.60 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.9, 27.8, 52.5, 52.8, 56.7, 66.6, 107.8, 119.7, 121.9, 125.1, 125.2, 126.5, 129.8, 130.3, 144.1, 144.8, 169.4, 169.9, 171.6; HRMS (MALDI) Calcd. for $C_{22}H_{21}BrN_2O_6$ requires (M^++H): 489.0661, Found: 489.0656.

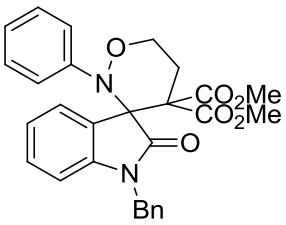




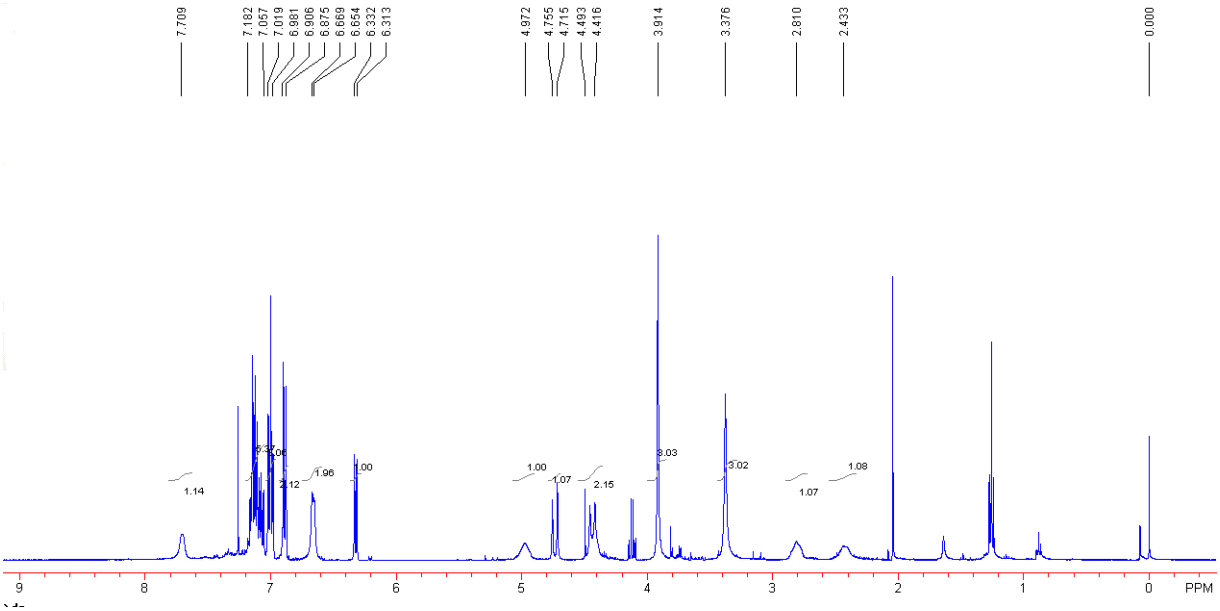
Compound 3e: Yield: 25 mg, 63%. A white solid. m. p.: 250-252 ^{o}C. IR (neat) ν 3092, 2946, 2887, 1744, 1717, 1620, 1467, 1265, 1213, 1049, 970 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.48 (brs, 1H), 2.72 (brs, 1H), 3.50 (s, 3H), 3.86 (s, 3H), 4.46 (brs, 1H), 4.90 (brs, 1H), 6.52

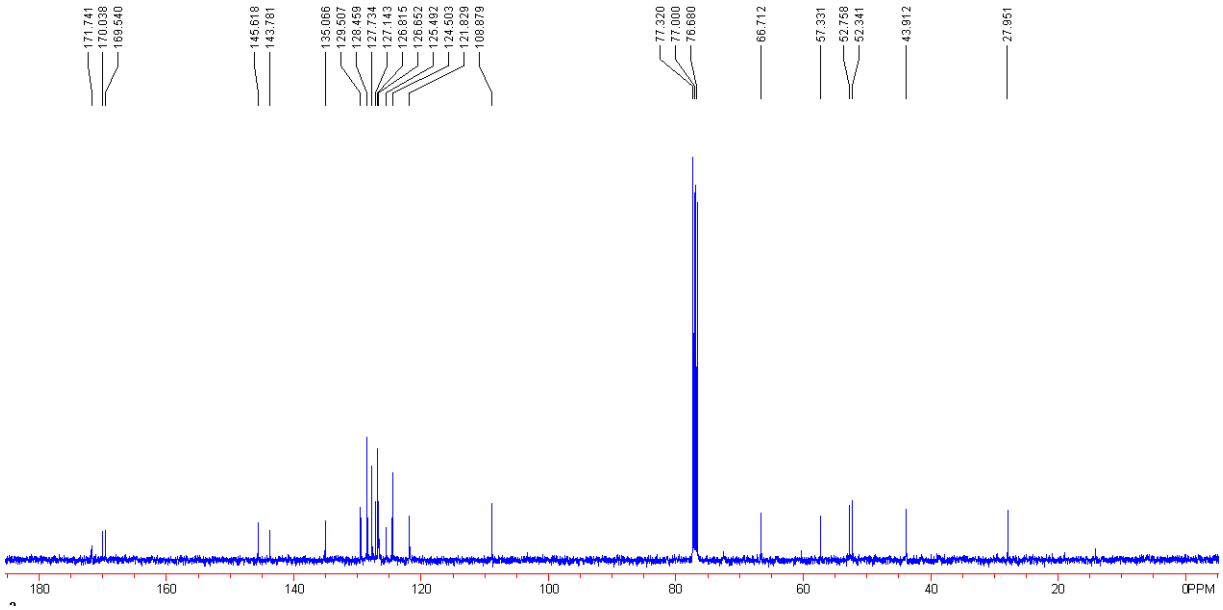
(d, *J* = 7.2 Hz, 1H), 6.88-6.91 (m, 2H), 6.98-7.03 (m, 4H), 7.09 (brs, 1H), 7.16 (t, *J* = 7.5 Hz, 1H) , 7.60 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 27.9, 52.3, 52.7, 57.0, 66.6, 109.4, 121.7, 124.2, 125.9, 126.5, 126.9, 127.4, 129.6, 141.4, 145.5, 169.5, 169.9, 173.4; HRMS (MALDI) Calcd. for $C_{21}H_{20}N_2O_6$ requires (M^++H): 397.1400, Found: 397.1394.

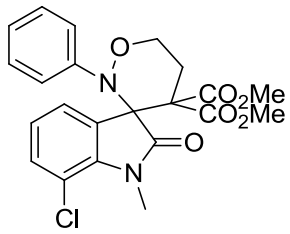




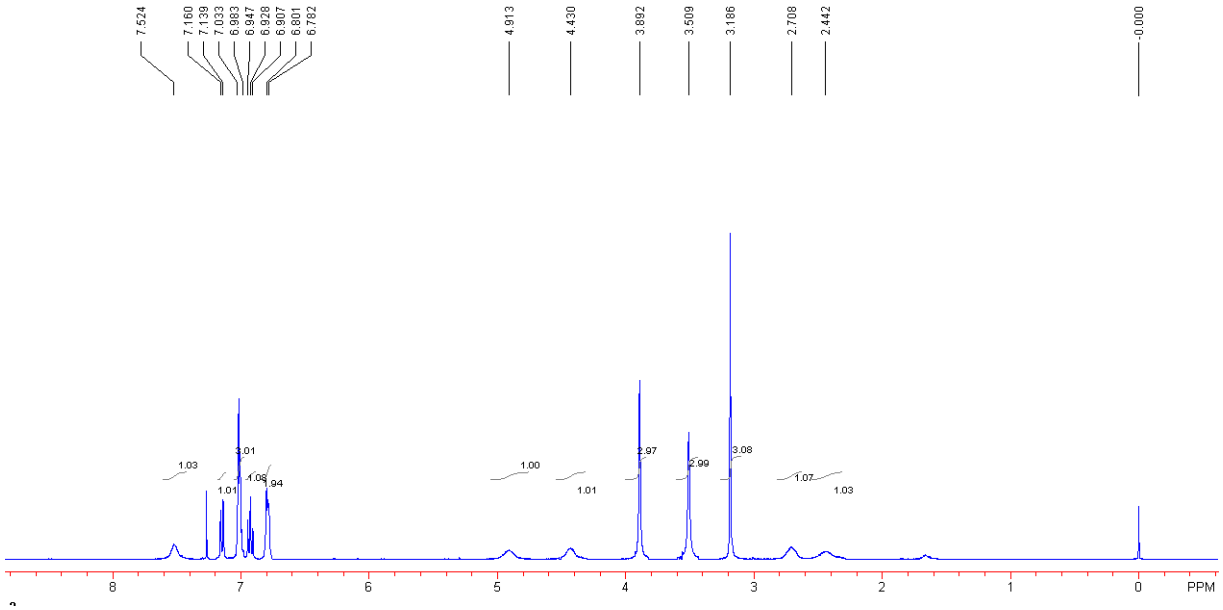
Compound 3f: Yield: 29 mg, 80%. A white solid. m. p.: 146-148 ^{o}C. IR (neat) ν 2954, 2941, 1746, 1720, 1609, 1486, 1365, 1275, 1215, 1044, 978 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (brs, 1H), 2.81 (brs, 1H), 3.38 (s, 3H), 3.91 (s, 3H), 4.42-4.49 (m, 2H), 4.74 (d, *J* = 16.0 Hz, 1H), 4.97 (brs, 1H), 6.32 (d, *J* = 7.6 Hz, 1H), 6.65-6.67 (m, 2H), 6.88-6.91 (m, 2H), 6.98-7.02 (m, 3H), 7.06-7.17 (m, 5H), 7.71 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 28.0, 43.9, 52.3, 52.8, 57.3, 66.7, 108.9, 121.8, 124.5, 125.5, 126.7, 126.8, 127.1, 127.7, 128.5, 129.5, 135.1, 143.8, 145.6, 169.5, 170.0, 171.7; HRMS (MALDI) Calcd. for $C_{28}H_{26}N_2O_6$ requires (M^++H): 487.1869, Found: 487.1856.

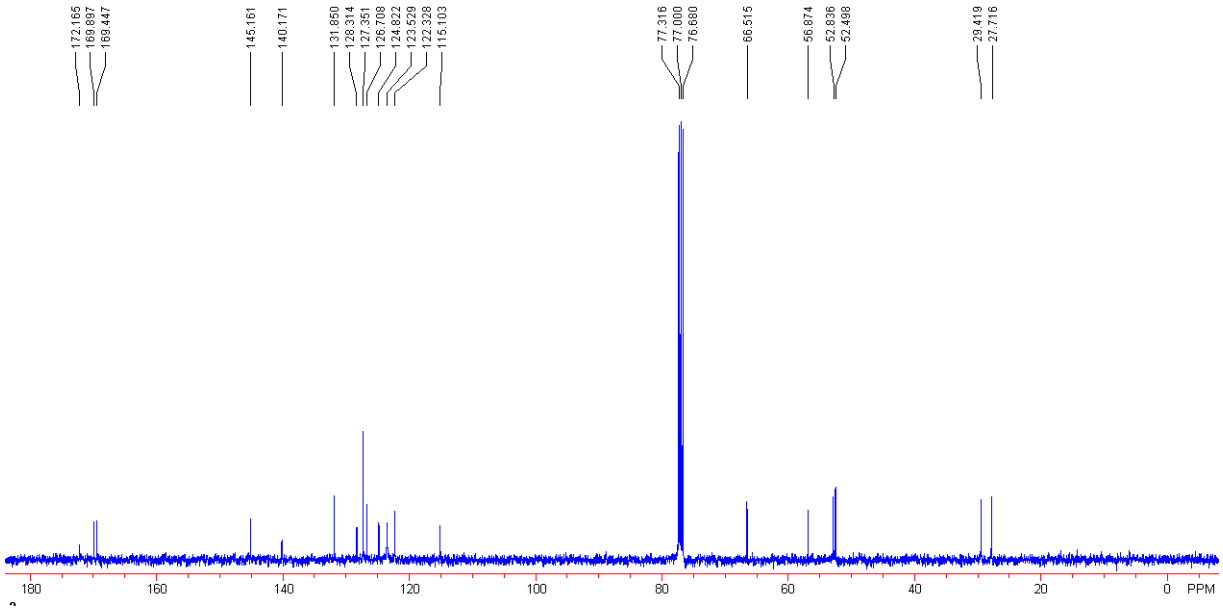


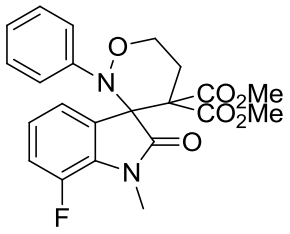




Compound 3g: Yield: 27 mg, 61%. A white solid. m. p.: 136-138 ^{o}C. IR (neat) ν 2954, 1747, 1726, 1708, 1463, 1277, 1216, 1111, 1078, 984 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.44 (brs, 1H), 2.71 (brs, 1H), 3.19 (s, 3H), 3.51 (s, 3H), 3.89 (s, 3H), 4.43 (brs, 1H), 4.91 (brs, 1H), 6.78-6.80 (m, 2H), 6.93 (t, *J* = 8.4 Hz, 1H), 6.98-7.03 (m, 3H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.52 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 27.7, 29.4, 52.5, 52.8, 56.9, 66.5, 115.1, 122.3, 123.5, 124.8, 126.7, 127.4, 128.3, 131.9, 140.2, 145.2, 169.4, 169.9, 172.2; HRMS (MALDI) Calcd. for $C_{22}H_{21}ClN_2O_6$ requires (M^++H): 445.1166, Found: 445.1162.

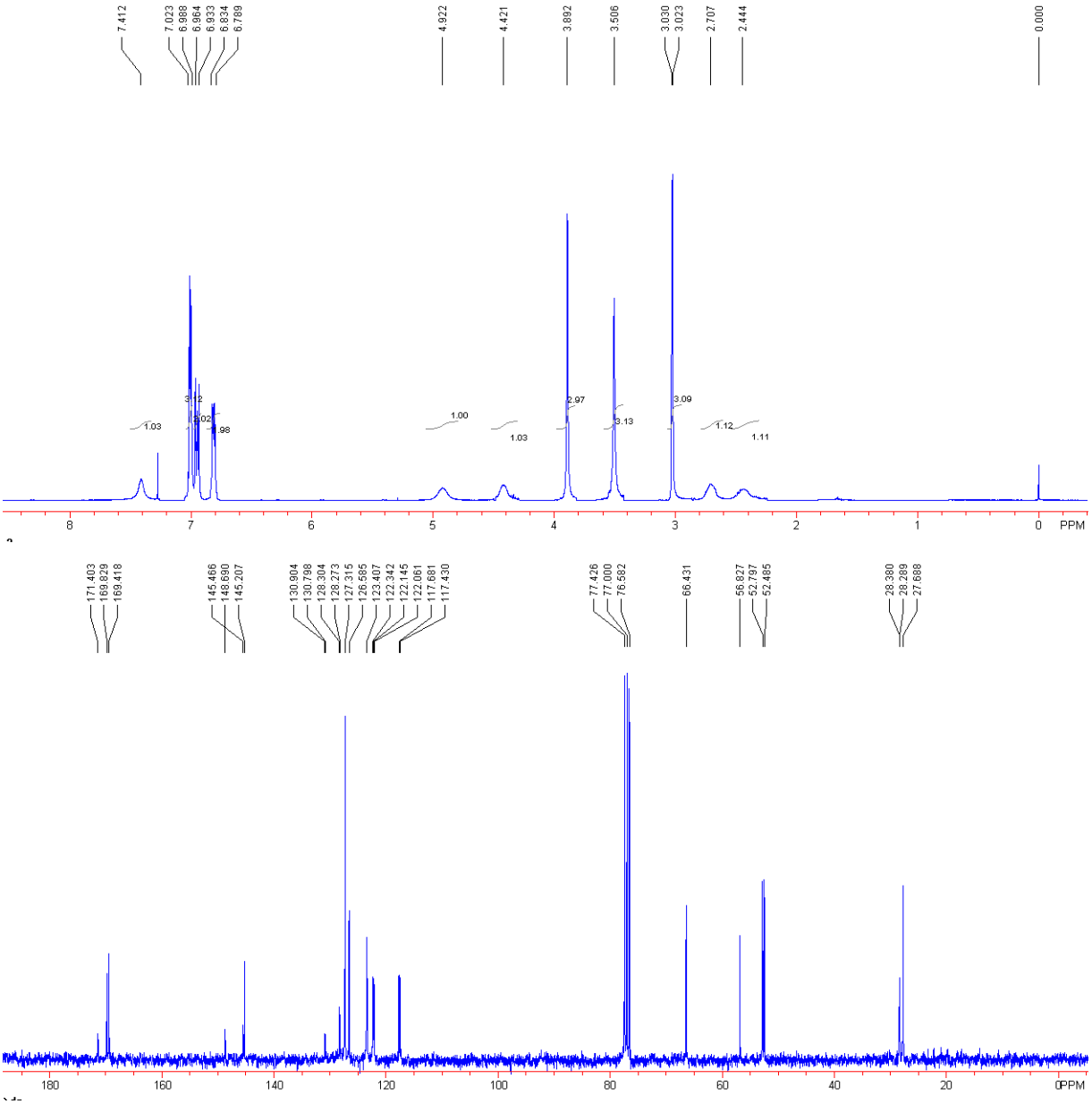


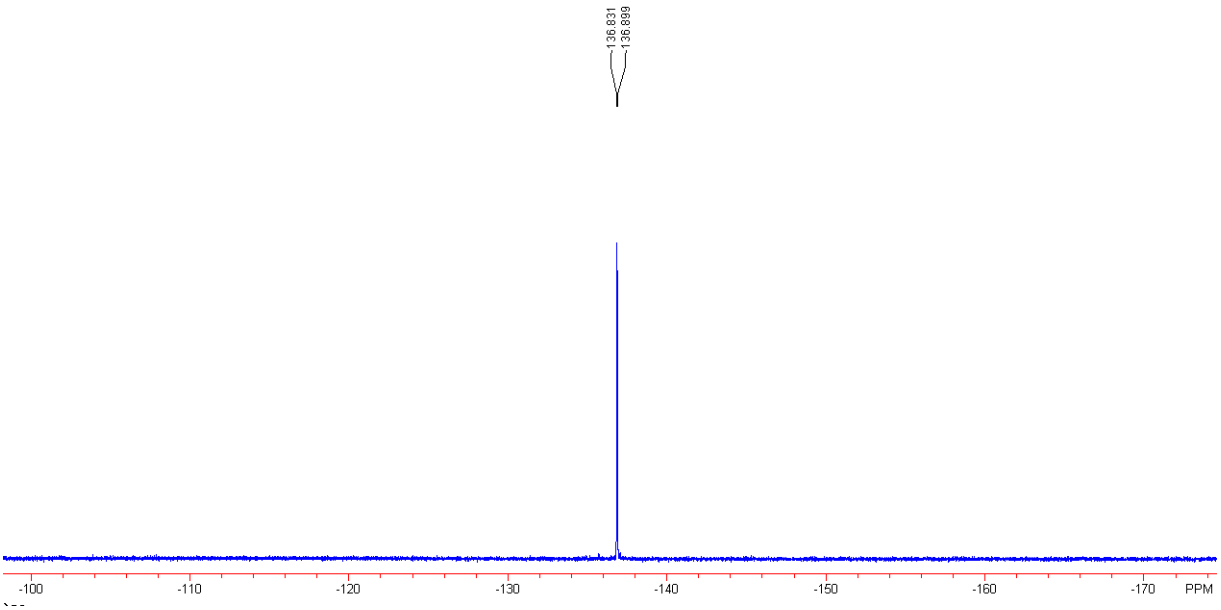


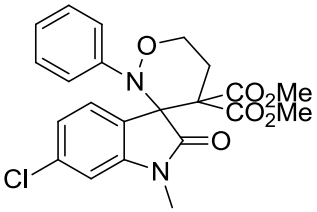


Compound 3h: Yield: 51 mg, 60%. A white solid. m. p.: 190-192 ^{o}C. IR (neat) ν 2949, 1725, 1719, 1626, 1596, 1476, 1432, 1337, 1282, 1214, 1119, 1041, 870 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.44 (brs, 1H), 2.71 (brs, 1H), 3.03 (d, *J* = 2.1 Hz, 3H), 3.51 (s, 3H), 3.89 (s,

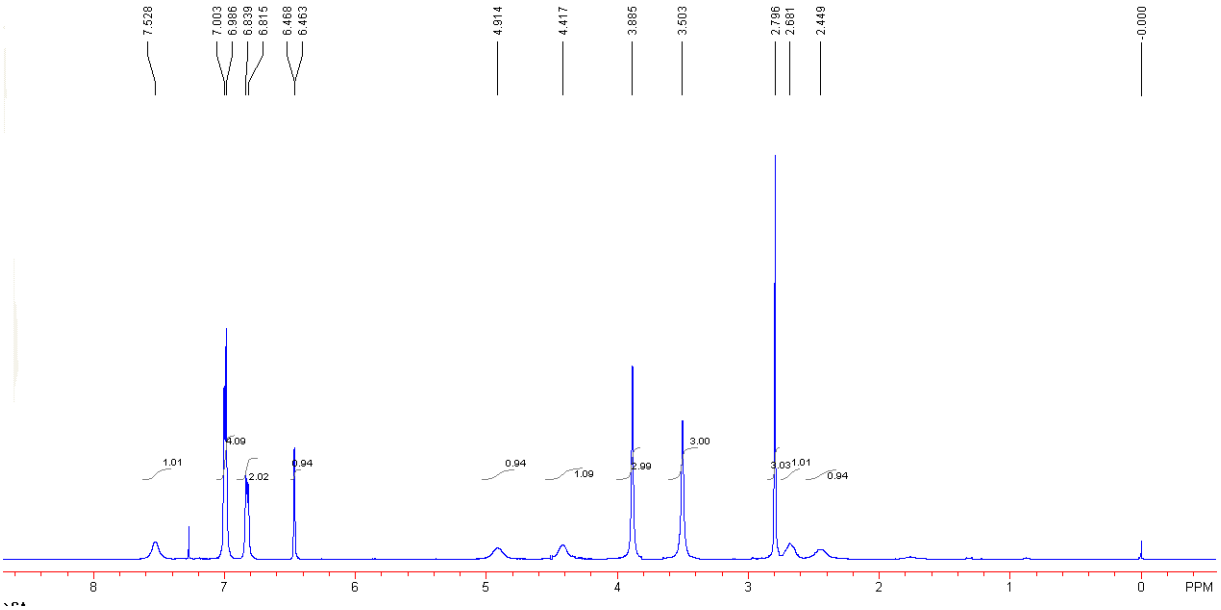
3H), 4.42 (brs, 1H), 4.92 (brs, 1H), 6.79-6.83 (m, 2H), 6.93-6.96 (m, 2H), 6.99-7.02 (m, 3H), 7.41 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ 27.7, 28.3 (d, *J* = 6.8 Hz), 52.5, 52.8, 56.8, 66.4, 117.6 (d, *J* = 18.8 Hz), 122.1 (d, *J* = 6.3 Hz), 122.3, 123.4, 126.6, 127.3, 128.3 (d, *J* = 2.3 Hz), 130.9 (d, *J* = 8.0 Hz), 145.2, 147.1 (d, *J* = 241.8 Hz), 169.4, 169.8, 171.4; ^{19}F NMR (282 MHz, $CDCl_3$, $CFCl_3$) δ -136.83--136.90 (m, 1F); HRMS (MALDI) Calcd. for $C_{22}H_{21}FN_2O_6$ requires (M^++H): 429.1462, Found: 429.1455.

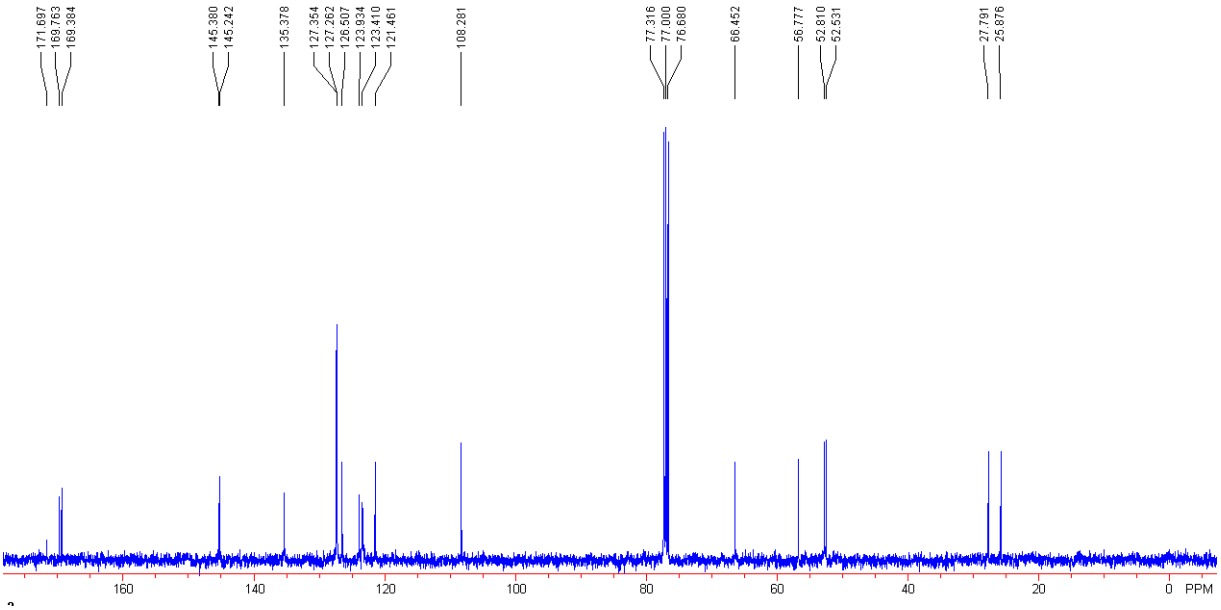


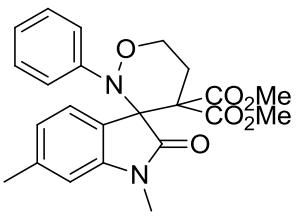




Compound 3i: Yield: 27 mg, 60%. A white solid. m. p.: 200-202 ^{o}C. IR (neat) ν 2956, 1725, 1605, 1592, 1432, 1372, 1250, 1211, 1073, 968 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.45 (brs, 1H), 2.68 (brs, 1H), 2.80 (s, 3H), 3.50 (s, 3H), 3.89 (s, 3H), 4.42 (brs, 1H), 4.91 (brs, 1H), 6.47 (d, *J* = 2.0 Hz, 1H), 6.82-6.84 (m, 2H), 6.99-7.00 (m, 4H), 7.53 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.9, 27.8, 52.5, 52.8, 56.8, 66.5, 108.3, 121.5, 123.4, 123.9, 126.5, 127.3, 127.4, 135.4, 145.2, 145.4, 169.4, 169.8, 171.7; HRMS (MALDI) Calcd. for $C_{22}H_{21}ClN_2O_6$ requires (M^++H): 445.1166, Found: 445.1157.

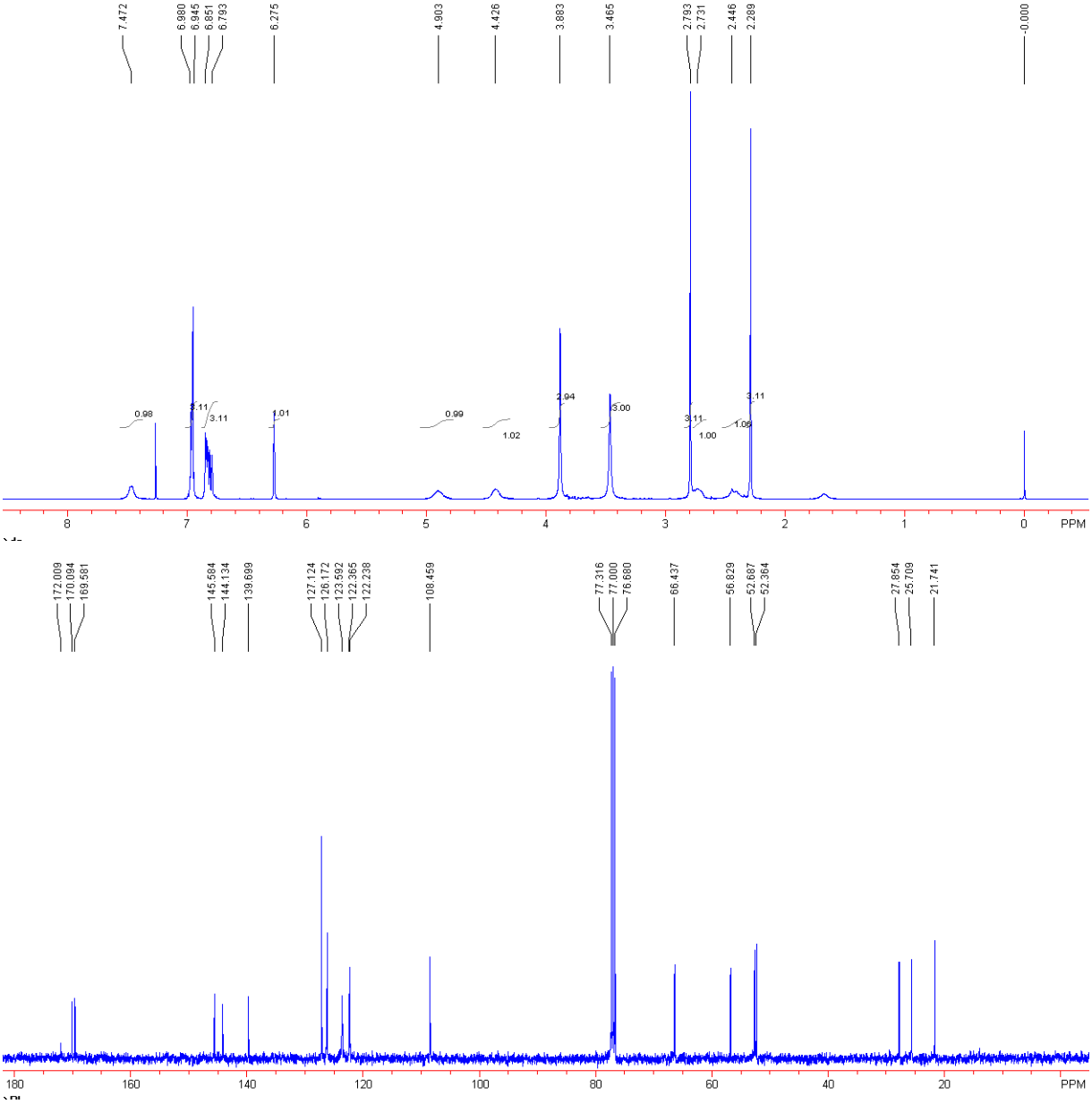


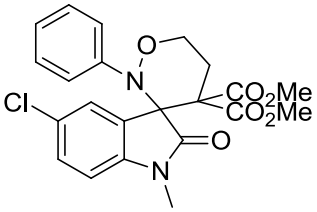




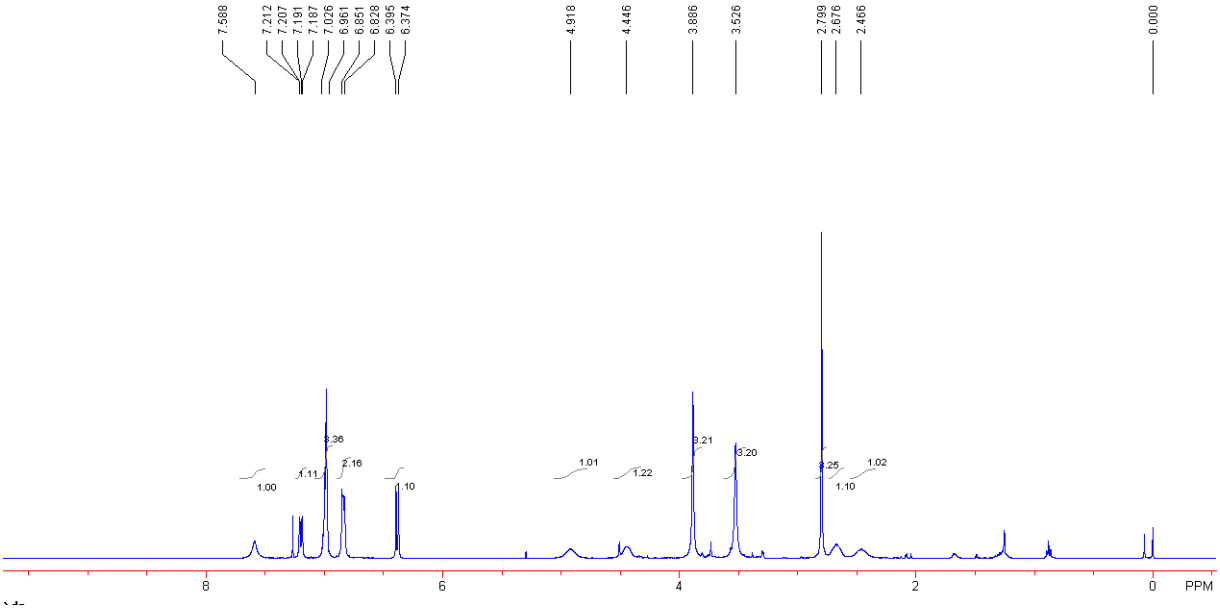
Compound 3j: Yield: 22mg, 52%. A white solid. m. p.: 178-180 ^{o}C. IR (neat) ν 3008, 2955, 1732, 1718, 1618, 1594, 1438, 1379, 1279, 1201, 1084, 969 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.29 (s, 3H), 2.45 (brs, 1H), 2.73 (brs, 1H), 2.79 (s, 3H), 3.47 (s, 3H), 3.88 (s, 3H),

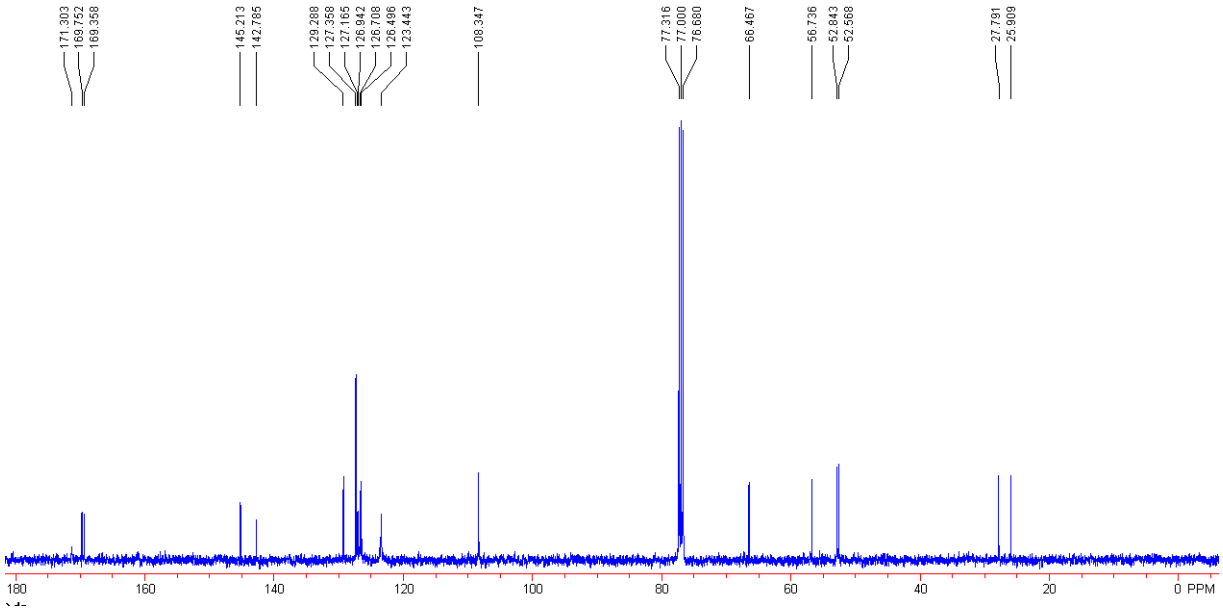
4.43 (brs, 1H), 4.90 (brs, 1H), 6.28 (s, 1H), 6.79-6.85 (m, 3H), 6.95-6.98 (m, 3H), 7.47 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 21.7, 25.7, 27.9, 52.4, 52.7, 56.8, 66.4, 108.5, 122.2, 122.4, 123.6, 126.2, 127.1, 139.7, 144.1, 145.6, 169.6, 170.1, 172.0; HRMS (MALDI) Calcd. for $C_{23}H_{24}N_2O_6$ requires (M^++H): 425.1713, Found: 425.1706.

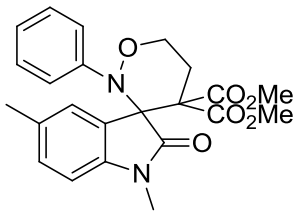




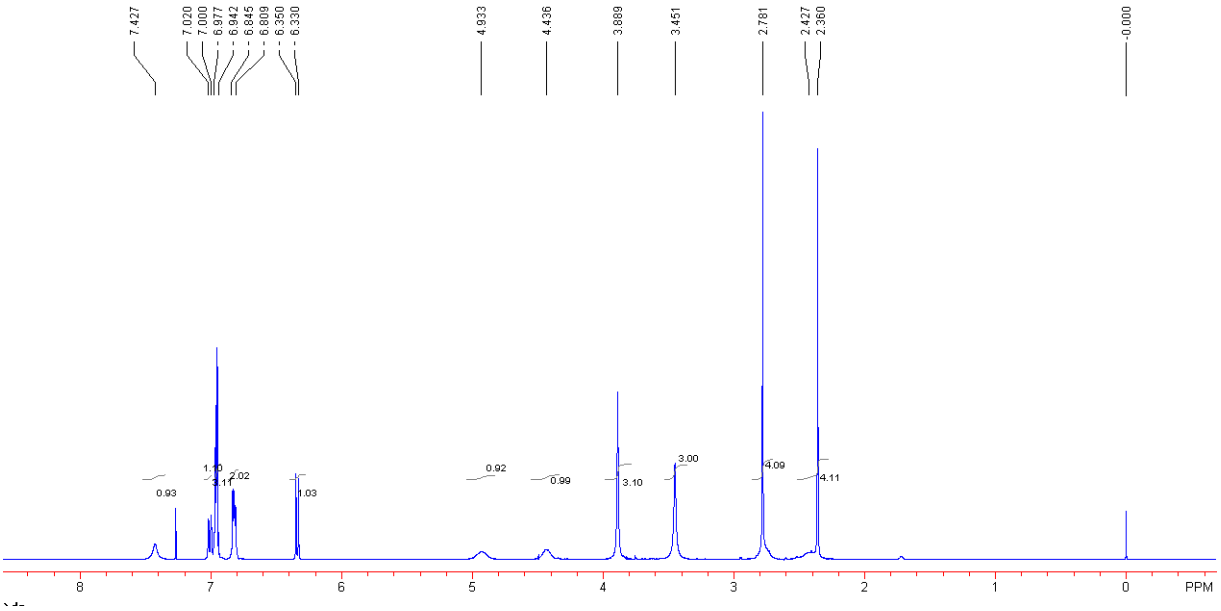
Compound 3k: Yield: 28 mg, 63%. A white solid. m. p.: 196-198 ^{o}C. IR (neat) ν 2951, 1756, 1736, 1716, 1609, 1488, 1428, 1279, 1202, 1086, 977, 944 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.47 (brs, 1H), 2.68 (brs, 1H), 2.80 (s, 3H), 3.53 (s, 3H), 3.89 (s, 3H), 4.45 (brs, 1H), 4.92 (brs, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 6.83-6.85 (m, 2H), 6.96-7.03 (m, 3H), 7.20 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.59 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.9, 27.8, 52.6, 52.8, 56.7, 66.5, 108.3, 123.4, 126.5, 126.7, 126.9, 127.2, 127.4, 129.3, 142.8, 145.2, 169.4, 169.8, 171.3; HRMS (MALDI) Calcd. for $C_{22}H_{21}ClN_2O_6$ requires (M^++H): 445.1166, Found: 445.1156.

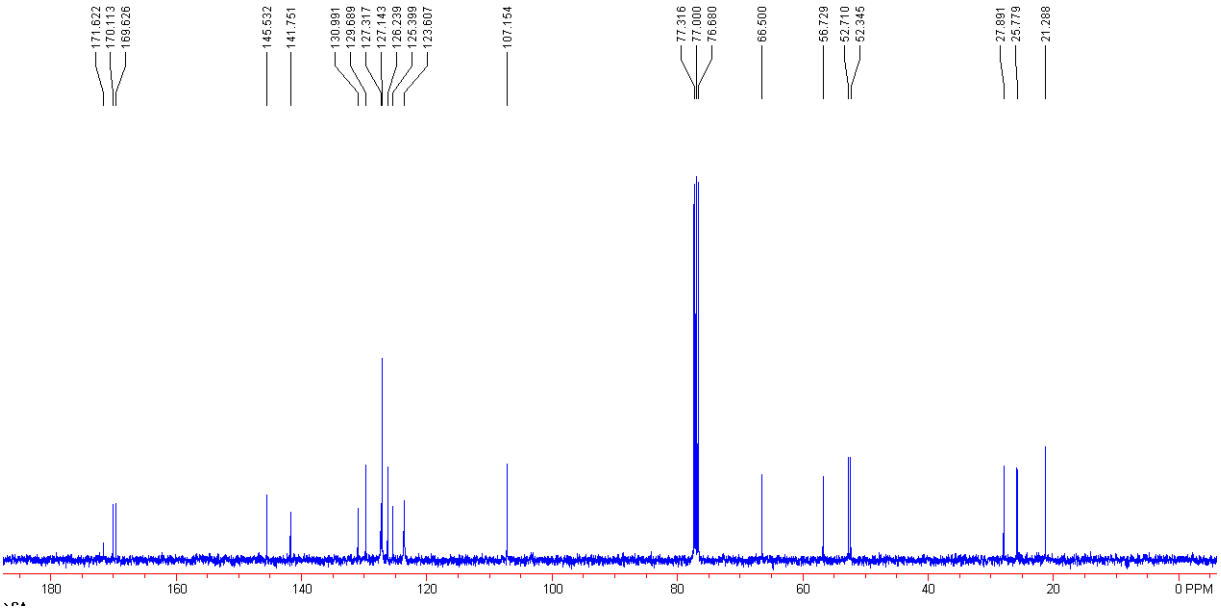


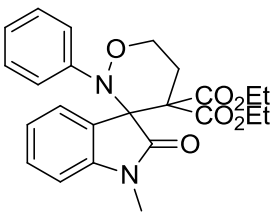




Compound 3l: Yield: 31 mg, 73%. A white solid. m. p.: 175-177 ^{o}C. IR (neat) ν 2947, 1738, 1717, 1495, 1433, 1353, 1263, 1213, 1099, 1045, 989 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.36 (s, 3H), 2.43 (brs, 1H), 2.78 (brs, 4H), 3.45 (s, 3H), 3.89 (s, 3H), 4.44 (brs, 1H), 4.93 (brs, 1H), 6.34 (d, *J* = 8.0 Hz, 1H), 6.81-6.83 (m, 2H), 6.94-6.98 (m, 3H), 7.01 (d, *J* = 7.6 Hz, 1H), 7.43 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 21.3, 25.8, 27.9, 52.3, 52.7, 56.7, 66.5, 107.2, 123.6, 125.4, 126.2, 127.1, 127.3, 129.7, 131.0, 141.8, 145.5, 169.6, 170.1, 171.6; HRMS (MALDI) Calcd. for $C_{23}H_{24}N_2O_6$ requires (M^++H): 425.1713, Found: 425.1717.

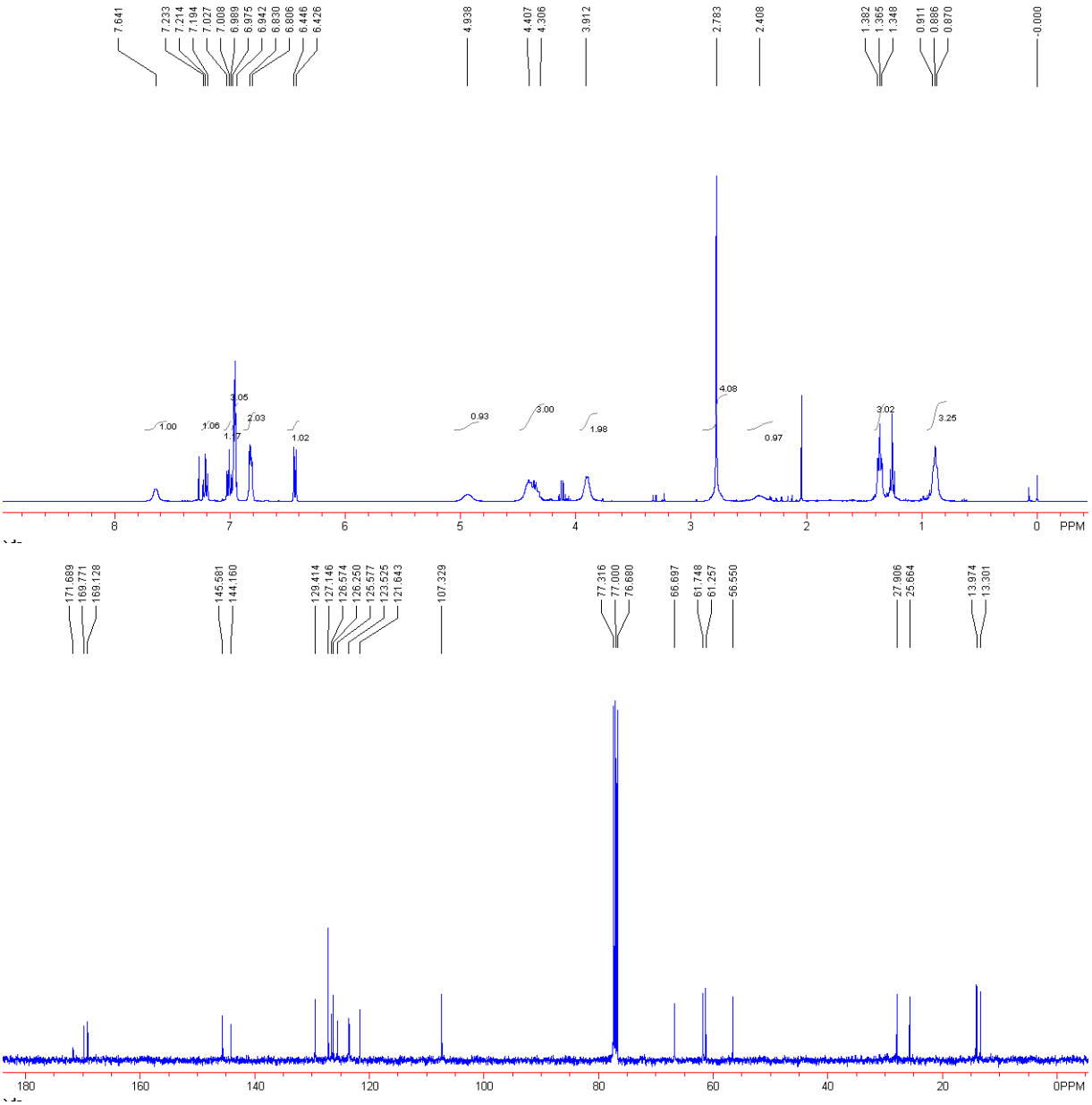


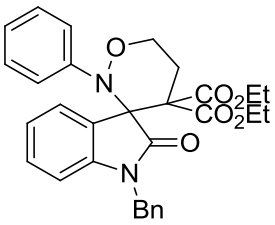




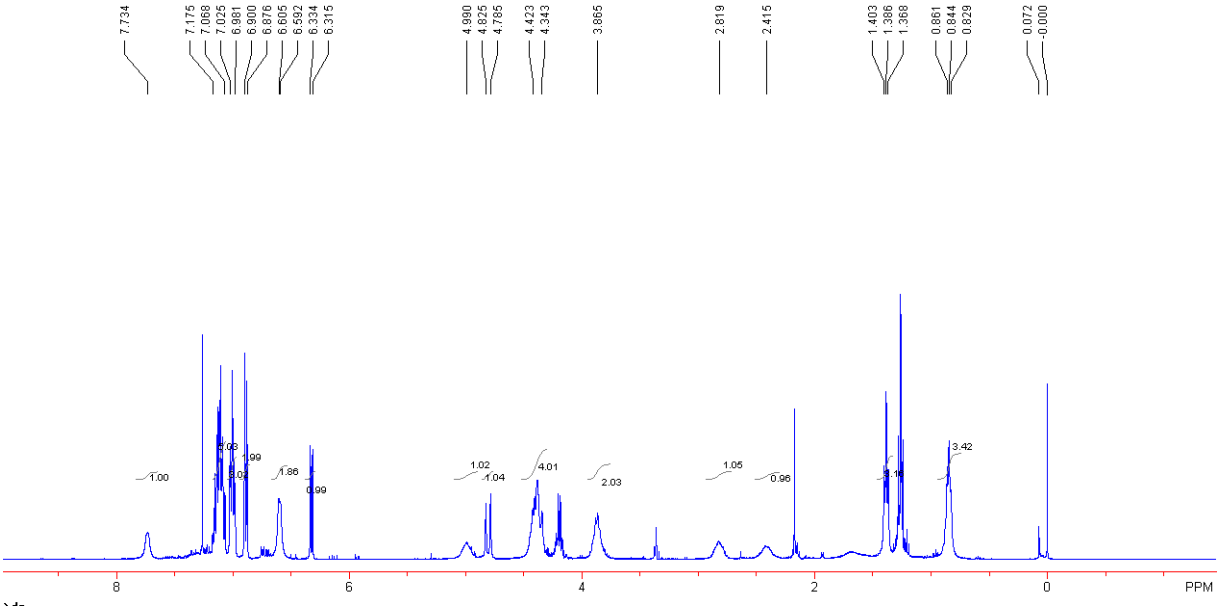
Compound 3m: Yield: 29 mg, 62%. A white solid. m. p.: 140-142 ^{o}C. IR (neat) ν 2974, 2939, 2892, 1725, 1712, 1612, 1491, 1468, 1260, 1214, 1044, 990 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.89 (t, *J* = 6.4 Hz, 3H), 1.37 (t, *J* = 6.8 Hz, 3H), 2.41 (brs, 1H), 2.78 (brs, 4H), 3.91

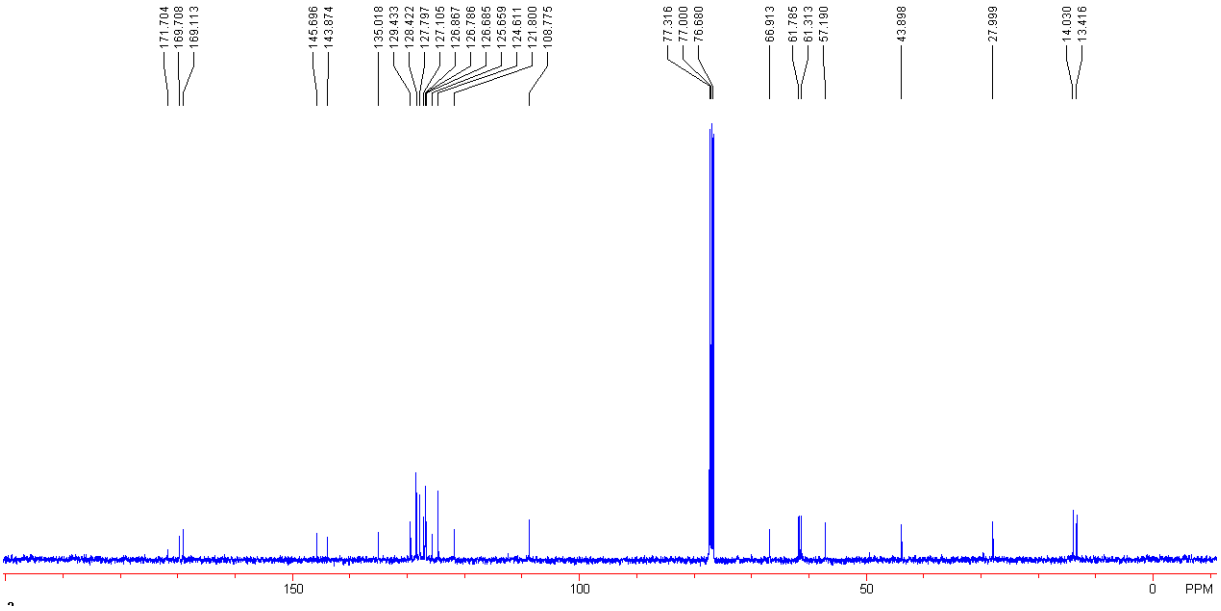
(brs, 2H), 4.31-4.41 (m, 3H), 4.94 (brs, 1H), 6.44 (d, *J* = 8.0 Hz, 1H), 6.81-6.83 (m, 2H), 6.94-6.98 (m, 3H), 7.01 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.64 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 13.3, 14.0, 25.7, 27.9, 56.6, 61.3, 61.7, 66.7, 107.3, 121.6, 123.5, 125.6, 126.3, 126.6, 127.1, 129.4, 144.2, 145.6, 169.1, 169.8, 171.7; HRMS (MALDI) Calcd. for $C_{24}H_{26}N_2O_6$ requires (M^++H): 439.1869, Found: 439.1858.

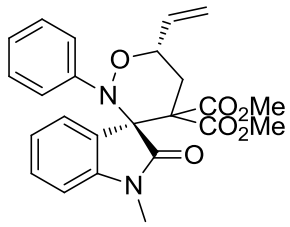




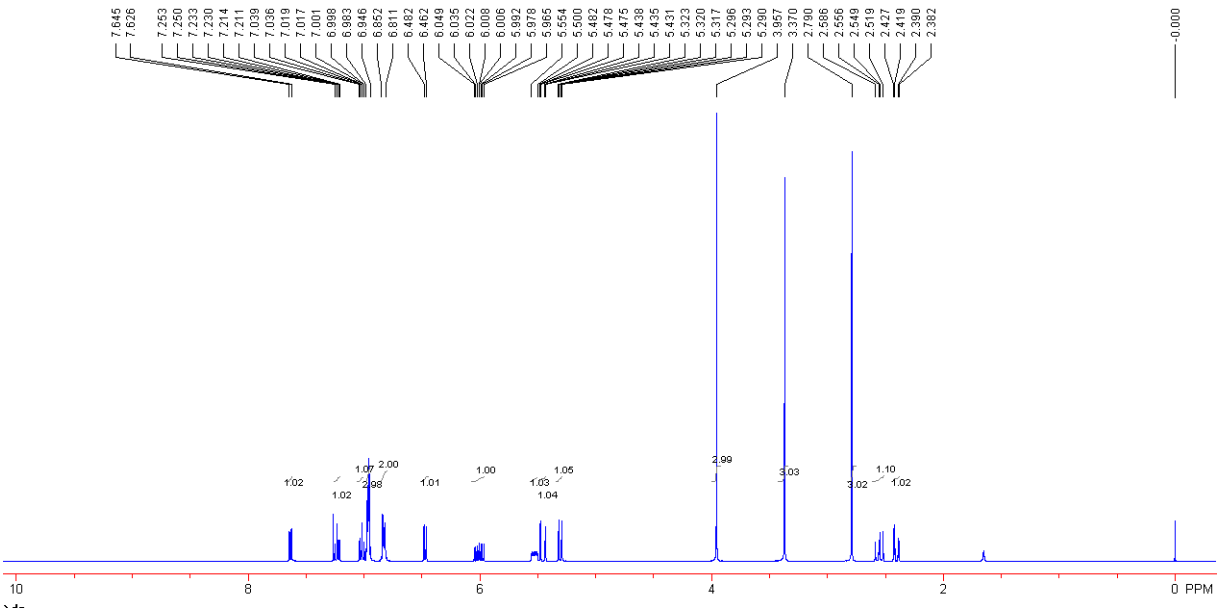
Compound 3n: Yield: 23 mg, 44%. A white solid. m. p.: 192-194 ^{o}C. IR (neat) ν 2969, 2927, 2849, 1721, 1711, 1609, 1466, 1367, 1226, 1047, 1022 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.84 (t, *J* = 6.0 Hz, 3H), 1.39 (t, *J* = 7.2 Hz, 3H), 2.42 (brs, 1H), 2.82 (brs, 1H), 3.87 (brs, 2H), 4.34-4.42 (m, 4H), 4.81 (d, *J* = 16.0 Hz, 1H), 4.99 (brs, 1H), 6.32 (d, *J* = 7.6 Hz, 1H), 6.60 (d, *J* = 5.2 Hz, 2H), 6.88-6.90 (m, 2H), 6.98-7.03 (m, 3H), 7.07-7.18 (m, 5H), 7.73 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 13.4, 14.0, 28.0, 43.9, 57.2, 61.3, 61.8, 66.9, 108.8, 121.8, 124.6, 125.7, 126.7, 126.8, 126.9, 127.1, 127.8, 128.4, 129.4, 135.0, 143.9, 145.7, 169.1, 169.7, 171.7; HRMS (MALDI) Calcd. for $C_{30}H_{30}N_2O_6$ requires (M^++H): 515.2182, Found: 515.2186.

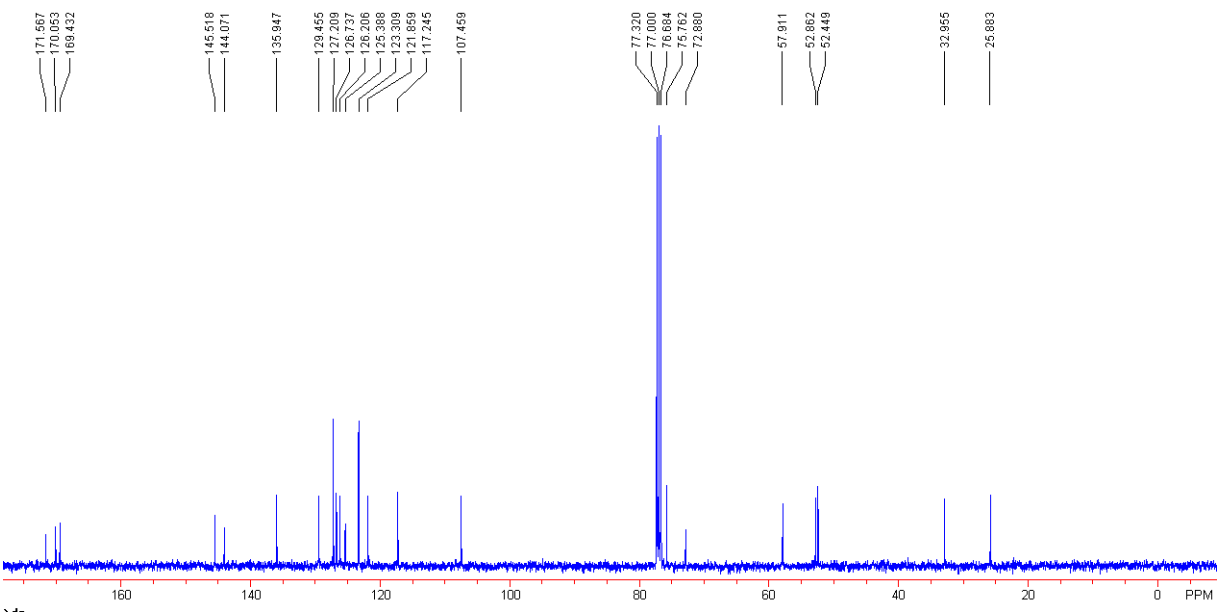


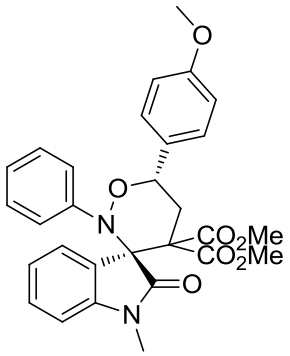




Compound 3o: Yield: 22 mg, 51%. A white solid. m. p.: 164-166 ^{o}C. IR (neat) ν 2953, 1750, 1725, 1610, 1471, 1254, 1200, 1043, 973, 949 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (dd, *J* = 14.8 Hz, 3.2 Hz, 1H), 2.55 (dd, *J* = 14.8 Hz, 12.0 Hz, 1H), 2.79 (s, 3H), 3.37 (s, 3H), 3.96 (s, 3H), 5.31 (dt, *J* = 10.8 Hz, 1.2 Hz, 1H), 5.46 (dt, *J* = 17.2 Hz, 1.2 Hz, 1H), 5.50-5.55 (m, 1H), 6.01 (ddd, *J* = 17.2 Hz, 10.8 Hz, 5.2 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 6.81-6.85 (m, 2H), 6.95-6.98 (m, 3H), 7.02 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.23 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.9, 33.0, 52.4, 52.9, 57.9, 72.9, 75.8, 107.5, 117.2, 121.9, 123.3, 125.4, 126.2, 126.7, 127.2, 129.5, 135.9, 144.0, 145.5, 169.4, 170.1, 171.6; HRMS (MALDI) Calcd. for $C_{24}H_{24}N_2O_6$ requires (M^++H): 437.1713, Found: 437.1705.

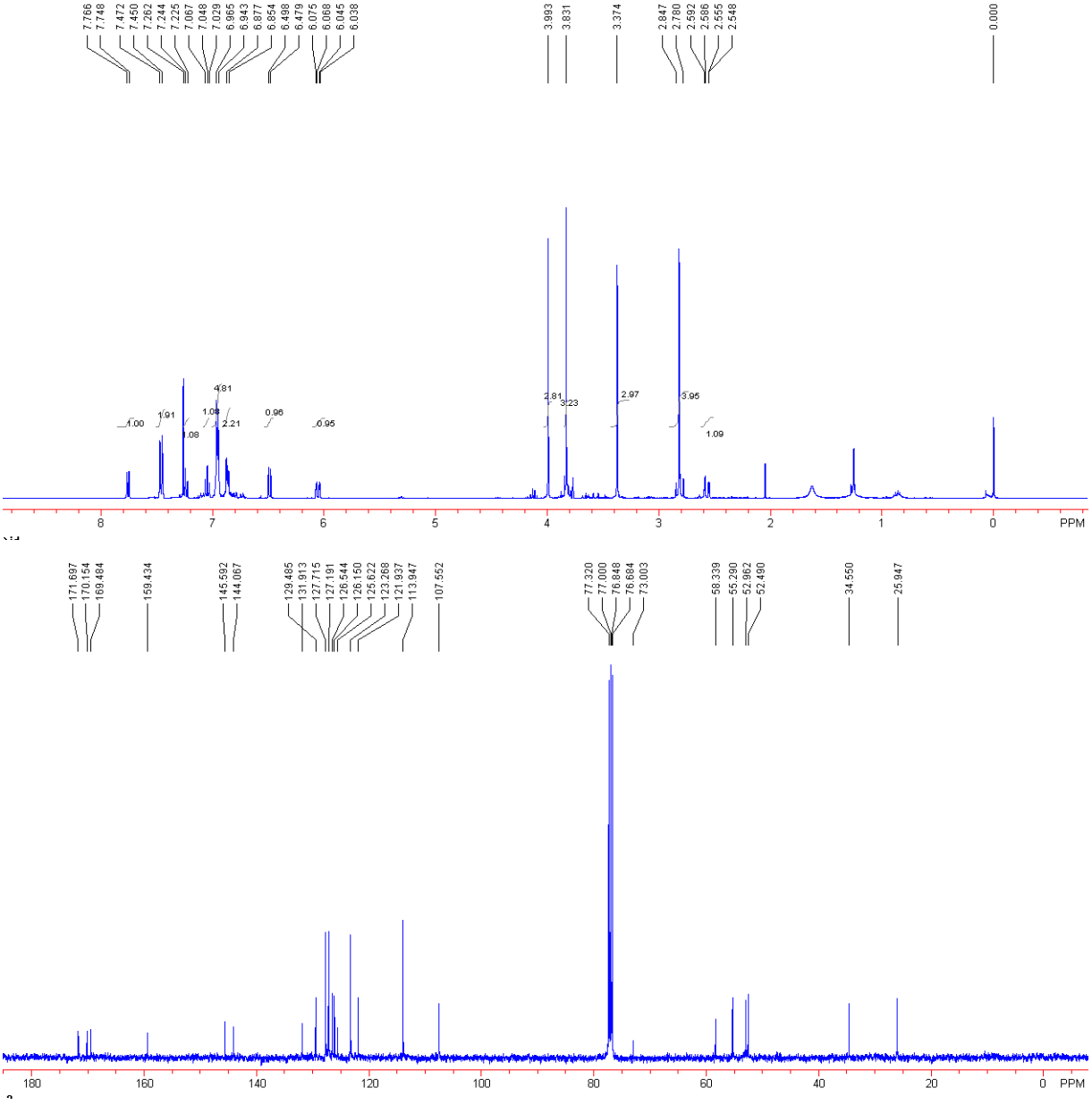


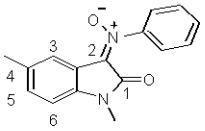




Compound 3p: Yield: 12 mg, 12%. A white solid. m. p.: 190-192 ^{o}C. IR (neat) ν 2952, 2917, 1750, 1724, 1611, 1514, 1246, 1178, 1030, 972 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ

2.57 (dd, *J* = 14.8 Hz, 2.8 Hz, 1H), 2.78-2.85 (m, 4H), 3.37 (s, 3H), 3.83 (s, 3H), 3.99 (s, 3H), 6.06 (dd, *J* = 12.0 Hz, 2.8 Hz, 1H), 6.49 (d, *J* = 7.6 Hz, 1H), 6.85-6.88 (m, 2H), 6.94-6.97 (m, 5H), 7.05 (t, *J* = 7.6 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.76 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.9, 34.6, 52.5, 53.0, 55.3, 58.3, 73.0, 76.8, 107.6, 113.9, 121.9, 123.3, 125.6, 126.2, 126.5, 127.2, 127.7, 129.5, 131.9, 144.1, 145.6, 159.4, 169.5, 170.2, 171.7; HRMS (MALDI) Calcd. for $C_{29}H_{28}N_2O_7$ requires (M^++H): 517.1975, Found: 517.1964.




O
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3
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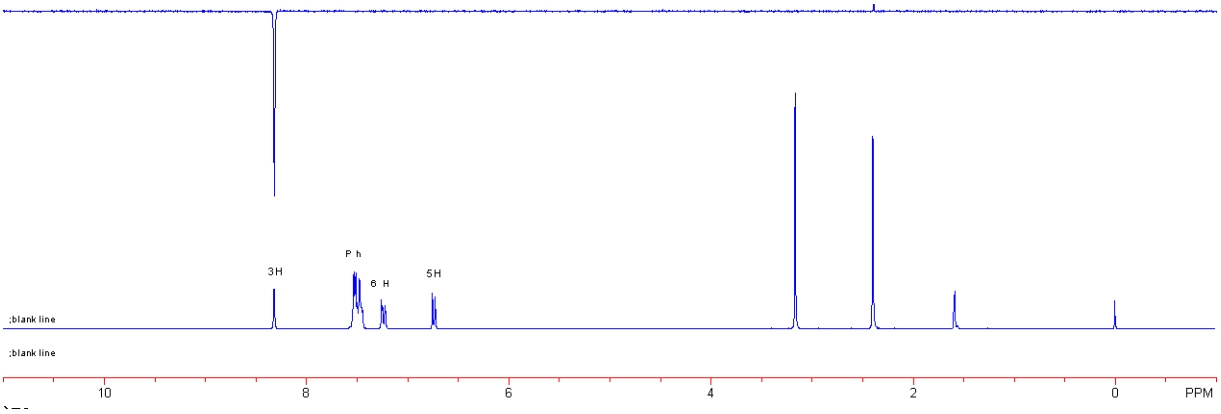
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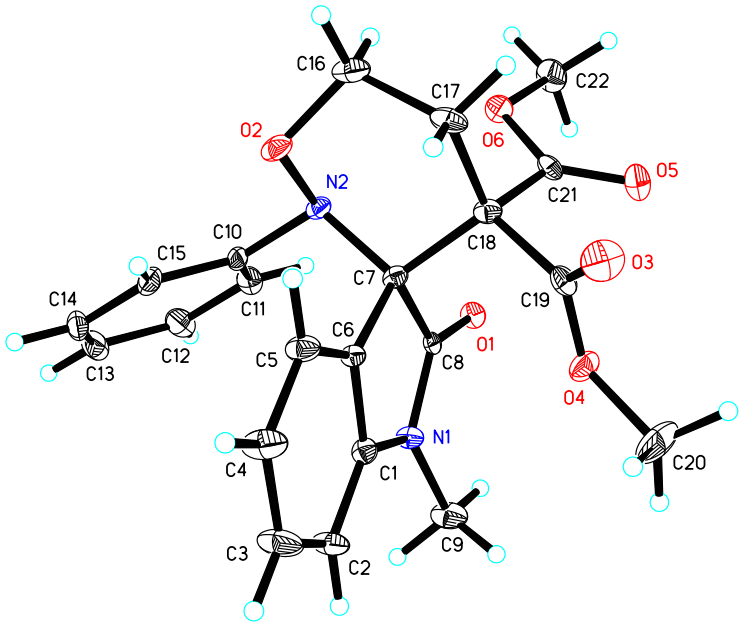
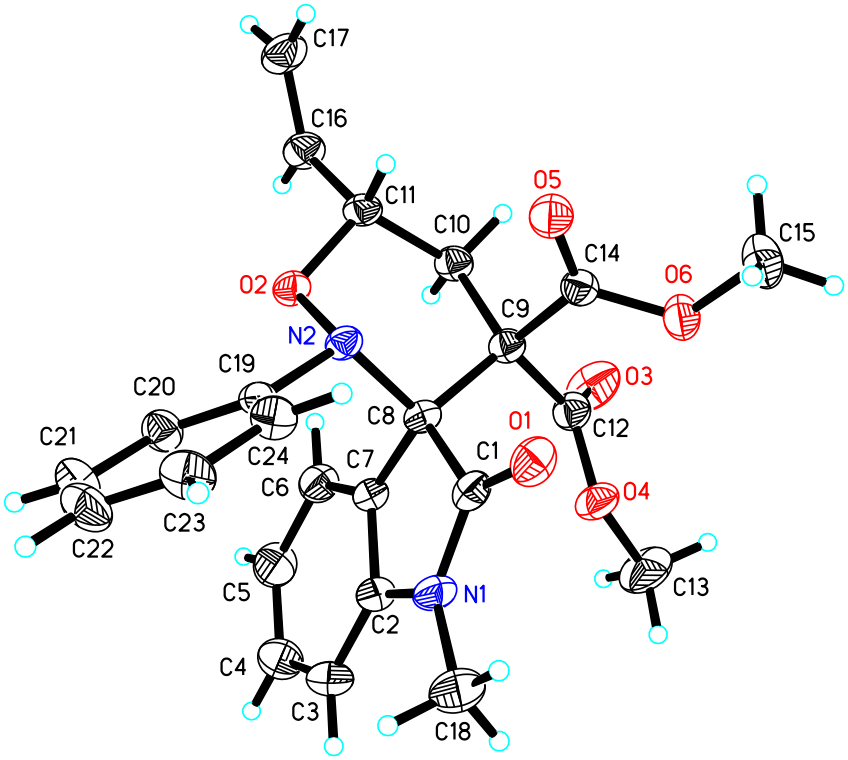


The crystal data of **3a** have been deposited in CCDC with number 858690. Empirical Formula: $C_{22}H_{22}N_2O_6$; Formula Weight: 410.42; Crystal Color, Habit: colorless; Crystal Dimensions: 0.22 x 0.20 x 0.10 mm; Crystal System: Monoclinic; Lattice Parameters: a = 20.206(4)Å, b = 8.8525(16)Å, c = 22.032(4)Å, $\alpha = 90^o$, $\beta = 94.898(3)^o$, $\gamma = 90^o$, V = 3926.7(12)Å^3; Space group: P2(1)/c; Z = 8; D_{calc} = 1.388 g/cm^3; F_{000} = 1728; Final R indices [I>2sigma(I)] R1 = 0.0487, wR2 = 0.1397.



The crystal data of **3o** have been deposited in CCDC with number 880875. Empirical Formula: $C_{24}H_{24}N_2O_6$; Formula Weight: 436.45; Crystal Color, Habit: colorless; Crystal Dimensions: 0.35 x 0.25 x 0.20 mm; Crystal System: Triclinic; Lattice Parameters: a = 8.7826(18)Å, b = 9.574(2)Å, c = 13.717(3)Å, α = 89.306(4)°, β = 81.155(4)°, γ = 83.165(4)°, V = 1131.6(4)Å^3; Space group: P-1; Z = 2; D_{calc} = 1.281 g/cm^3; F_{000} = 460; Final R indices [I>2sigma(I)] R1 = 0.0500, wR2 = 0.1324.