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Ruthenium(II)-Catalyzed Acyloxylation of the *ortho* C-H Bonds in 2-Aroyl-Imidazoles with Carboxylic Acids

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Contents

I. General Information.

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$ with tetramethylsilane as the internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, and m = multiplet), coupling constant (Hz), and integration. In some cases, it was not possible to assign some of the peaks in the ^{13}C NMR spectra because of overlapping. Infrared spectra (IR) were recorded on a JASCO FT/IR-4000 spectrometer using the ATR method. Absorption data are reported in reciprocal centimeters from 800 to 3500 cm^{-1} with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra and high resolution mass spectra (HRMS) were obtained using a JEOL JMS-700 or JMS-T100LP spectrometer. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with SiO_2 (Silicycle SiliaFlash F60 (230-400 mesh). Some of the compounds that were prepared were purified by LC-908 HPLC (GPC). Medium-pressure liquid chromatography (MPLC) was performed with Biotage Isolera® equipped with Biotage® SNAP Ultra flash chromatography cartridges.

II. Materials

Ruthenium source: $[Ru(p\text{-cymene})Cl_2]_2$ (Sigma-Aldrich Co.)

Additives: Ag_2CO_3 (Wako Pure Chemicals Industries, Ltd), AgOAc (Wako Pure Chemicals Industries, Ltd), Ag_2O (Wako Pure Chemicals Industries, Ltd), Na_3PO_4 (Sigma-Aldrich Co.),

$AgSbF_6$ (Tokyo Chemical Industry Co., Ltd), $AgNO_3$, (Nacalai Tesque, Inc.), MnO_2 (Wako Pure Chemicals Industries, Ltd)

Benzoic acid:

2,6-dimethylbenzoic acid, 4-methylbenzoic acid, 4-acetoxybenzoic acid, 4-fluorobenzoic acid, 4-chlorobenzoic acid, 3-(trifluoromethyl) benzoic acid, trans-cinnamic acid, 2-thiophenecarboxylic acid, 2-furoic acid, benzofuran-2-carboxylic acid, 2-naphthoic acid (Tokyo Chemical Industry Co., Ltd)

2,4,6-trimethylbenzoic acid (Sigma-Aldrich Co.)

4-bromobenzoic acid, 3-methoxybenzoic acid (Kanto Chemical Co., Inc.), acetic acid (Nacalai Tesque, Inc.)

III. Synthesis of Starting Materials.

All of the 2-acyl imidazole derivatives were prepared by reacting the corresponding acids or the corresponding acid chlorides with 1-methylimidazole.[1]

To a stirred solution of 1-methylimidazole (30 mmol) in CH_3CN (120 mL) at 0 °C, a solution of acid chlorides (45 mmol) and triethylamine (36 mmol) was added dropwise. The resulting mixture was allowed to warm to room temperature and then stirred overnight. The crude product was washed with saturated aqueous $NaHCO_3$ (20 mL), brine (50 mL), and EtOAc (3x50 mL). The organic phases were dried over anhydrous Na_2SO_4 and the solvent was removed by evaporation under reduced pressure. The residue was purified by MPLC (rate: 40 mL/min., eluent: hexane/EtOAc = 3/1).

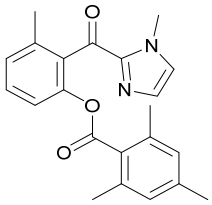
IV. General Procedure for the Ru-Catalyzed Acyloxylation of 2-Aroyl-Imidazoles with Carboxylic Acids.

To an oven-dried 5 mL screw-capped vial, (1-methyl-1H-imidazol-2-yl)(2-methylphenyl)methanone (**1a**, 60.1 mg, 0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (9.2 mg, 0.015mmol), 2,6-dimethylbenzoic acid (90.1mg, 0.6 mmol), Ag_2CO_3 (124.1 mg, 0.45mmol), and PhCl (1.5 mL) were added. The mixture was stirred for 18 h at 110 °C and then allowed to cool to room temperature. The resulting mixture was filtered through a celite pad and the filtrate concentrated in vacuo. The residue was purified by MPLC (rate: 36 mL/min., eluent: hexane/EtOAc = 3/1 to 1/1) to afford the acyloxylation product **3aa** (88.6 mg, 85%) as a white powder.

1. S. K. Mahato, N. Chatani. *ACS Catal*., **2020**, *10*, 5173.

V. Spectroscopic Data.

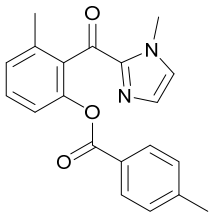
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 2,4,6-trimethylbenzoate



3ab

73.4 mg, 68% yield, R_f 0.43 (hexane/EtOAc = 1:1). white solid, m.p. 180.6-180.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (m, 12H), 4.03 (s, 3H), 6.80-6.81 (m, 2H), 7.03 (s, 1H), 7.14-7.21 (m, 3H), 7.39 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 19.8, 21.2, 36.2, 120.0, 127.4, 127.8, 128.6, 129.8, 130.0, 130.8, 132.9, 135.9, 136.9, 139.9, 143.4, 147.6, 168.0, 186.7; IR (ATR): 3109 w, 2958 w, 2922 w, 2863 w, 2363 w, 1746 s, 1655 s, 1609 m, 1576 w, 1507 w, 1460 m, 1429 w, 1395 s, 1293 w, 1254 m, 1218 s, 1161 s, 1053 s, 1011 w, 936 s, 900 m, 851 w, 773 w, 733 w, 699 w; MS *m/z* (relative intensity, %) 362 (4, M^+), 148 (11), 147 (100), 119 (11); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{22}H_{22}N_2O_3$: 362.1630; Found: 362.1628.

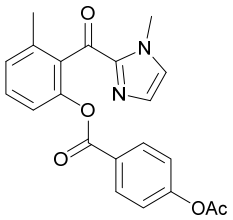
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 4-methylbenzoate



3ac

67.1 mg, 67% yield, R_f 0.35 (hexane/EtOAc = 10:1). white solid, m.p. 108.8-109.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.39 (s, 3H), 3.95 (s, 3H), 6.95 (s, 1H), 7.12 (s, 1H), 7.15-7.21 (m, 4H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.69-7.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 21.8, 35.9, 120.2, 126.5, 127.0, 128.0, 129.1, 130.0, 130.3, 130.5, 132.3, 137.4, 143.8, 144.3, 148.2, 164.2, 186.6; IR (ATR) 3016 w, 2968 w, 1740 s, 1657 m, 1610 m, 1397 s, 1263 w, 1225 s, 1073 w, 1019 w, 936 w, 901 w, 836 w, 775 w, 746 w; MS *m/z* (relative intensity, %) 334 (4, M^+), 200 (11), 199 (76), 119 (100), 91 (23); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{18}N_2O_3$: 334.1314; Found: 334.1317.

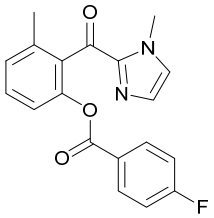
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 4-acetoxybenzoate



3ad

76.2 mg, 67% yield, R_f 0.24 (hexane/EtOAc = 1:1). white solid, m.p. 108.5-108.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.34 (s, 3H), 3.96 (s, 3H), 6.96 (s, 1H), 7.09-7.13 (m, 3H), 7.18-7.21 (m, 2H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.87 (dt, *J* = 9.0, 2.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 21.3, 36.0, 120.2, 121.7, 126.9, 127.2, 128.2, 130.3, 130.6, 131.6, 132.4, 137.5, 143.7, 148.0, 154.7, 163.4, 169.0, 186.5; IR (ATR) 3399 w, 2925 w, 2361 w, 1741 s, 1655 m, 1604 w, 1578 w, 1504 w, 1462 w, 1397 s, 1371 w, 1261 m, 1222 s, 1195 s, 1160s, 1053 m, 1024 m, 1008 m, 935 w, 901 w, 857 w, 825 w, 769 w, 732 w, 700 w, 680 w, 663 w; MS *m/z* (relative intensity, %) 378 (4, M^+), 215 (10), 200 (14), 199 (98), 163 (13), 121 (100); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{18}N_2O_5$: 378.1216; Found: 378.1212.

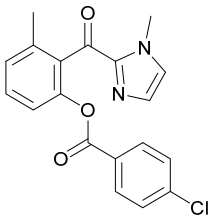
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 4-fluorobenzoate



3ae

66.9 mg, 66% yield, R_f 0.38 (hexane/EtOAc = 1:1). white solid, m.p. 112.2-112.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.97 (s, 3H), 6.96 (s, 1H), 7.02-7.06 (m, 2H), 7.12 (d, *J* = 0.9 Hz, 1H), 7.17-7.21 (m, 2H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.83-7.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.49, 35.97, 115.64 (d, *J* = 22.04 Hz), 120.145, 125.52 (d, *J* = 2.82 Hz), 127.09, 128.1881, 130.34, 130.55, 132.25, 132.52 (d, *J* = 9.59 Hz), 137.48, 143.66. 147.95, 163.23, 166.04 (d, *J* = 254.0 Hz); IR (ATR) 3468 w, 3111 w, 3073 w, 3006 w, 2962 w,1741 s, 1603 s. 1579 w, 1506 w, 1462 w, 1397 s, 1262 m,1224 s, 1154 m, 1073 m, 1013w, 934 w, 900 w, 855w, 762 w, 732 w, 685 w; MS *m/z* (relative intensity, %) 337 (1, M^+), 215 (12), 200 (14), 199 (100), 123 (72), 95 (20); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{19}H_{15}FN_2O_3$: 338.1067; Found: 338.1069.

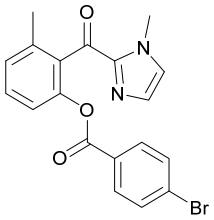
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 4-chlorobenzoate



3af

74.0 mg, 70% yield, R_f 0.43 (hexane/EtOAc = 1:1). white solid, m.p. 98.3-98.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.97 (s, 3H), 6.97 (s, 1H), 7.12 (s, 1H), 7.19 (dd, *J* = 7.8, 5.0 Hz, 2H), 7.33-7.36 (m, 2H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.75-7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 36.0, 120.1, 127.1, 127.8, 128.3, 128.8, 130.4, 130.5, 131.3, 132.2, 137.5, 140.0, 143.6, 147.9, 163.4, 186.3; IR (ATR) 3461 w, 3107 w, 2959 w, 2926 w, 1741s, 1655 m, 1594 m, 1462m, 1397 s, 1261 s, 1224 s, 1172 w, 1151 w, 1087 w, 1013 w, 935 w, 900 w, 851 w, 777 w, 753 w, 724 w, 700 w, 681 w, 665 w; MS *m/z* (relative intensity, %) 354 (1, M^+), 215 (12), 200 (13), 199 (100), 141 (18), 139 (59), 111 (16); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{19}H_{15}ClN_2O_3$: 354.0771; Found: 354.0775.

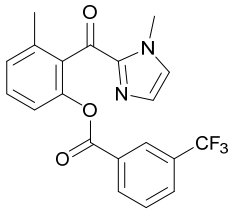
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 4-bromobenzoate



3ag

75.6 mg, 63% yield, R_f 0.45(hexane/EtOAc = 1:1). white solid, m.p. 120.6-120.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.97 (s, 3H), 6.98 (s, 1H), 7.12 (s, 1H), 7.18-7.21 (m, 2H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.51-7.53 (m, 2H), 7.69 (dd, *J* = 6.8, 1.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 36.1, 120.1, 127.1, 128.2, 128.3, 128.8, 130.4, 131.4, 131.8, 132.1, 137.6, 143.6, 147.9, 163.5, 186.3; IR (ATR) 3470 w, 3105 w, 3035 w, 2959 w, 2924 w, 1739 s, 1711 w, 1653 s, 1604 w, 1589 w, 1507 w, 1482 w, 1461 m, 1395 s, 1260 s, 1222 s, 1173 m, 1149 w, 1071 s, 1009 m, 934 w, 899 m, 847 w, 776 w, 748 m, 715 w, 699 w, 678 w, 664 w; MS *m/z* (relative intensity, %) 398 (1, M^+), 215 (11), 200 (13), 199 (100), 185 (32), 183 (33); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{19}H_{15}BrN_2O_3$: 398.0266; Found: 398.0261.

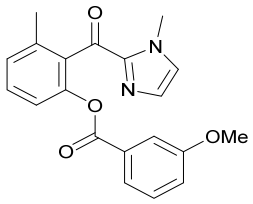
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 3-(trifluoromethyl)benzoate



3ah

87.1 mg, 75% yield, R_f 0.46 (hexane/EtOAc = 1:1). white solid, m.p. 133.0-133.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.99 (s, 3H), 6.97 (s, 1H), 7.10 (s, 1H), 7.21 (d, *J* = 7.7 Hz, 1H), 7.26-7.28 (m, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.91 (s, 1H), 8.10 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.52, 36.06, 119.99, 123.60 (q, *J* = 271.2 Hz); 126.46 (q, *J* = 3.83 Hz), 127.31, 128.42, 129.25, 129.97 (q, *J* = 3.83 Hz), 130.32, 130.40, 130.57, 131.04 (q, *J* = 32.6 Hz), 132.01, 133.32, 137.68, 143.53, 147.79, 162.83, 186.23; IR (ATR) 3107 w, 2962 w, 2927 w, 2868 w, 1745 m, 1654 m, 1609 w, 1577 w, 1508 w, 1462 w, 1443 w, 1396 m, 1334 m, 1294 w, 1240 m, 1218 s, 1169 m, 1127 m, 1070 m, 1003 w, 934 w, 899 m, 868 w, 810 w, 771w, 747 w, 696 w, 665 w; MS *m/z* (relative intensity, %) 388 (1, M^+), 215 (11), 200 (14), 199 (100), 173 (35), 145 (28); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{15}F_3N_2O_3$: 388.1035; Found: 388.1030.

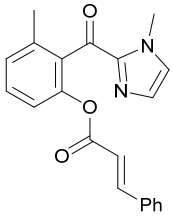
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 3-methoxybenzoate



3ai

66.3 mg, 63% yield, R_f 0.34 (hexane/EtOAc = 1:1). white solid, m.p. 104.5-104.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.79 (s, 3H), 3.96 (s, 3H), 6.96 (s, 1H), 7.08 (dd, *J* = 8.1, 2.6 Hz, 1H), 7.12 (s, 1H), 7.19 (dd, *J* = 11.7, 7.8 Hz, 2H), 7.26 (t, *J* = 7.9 Hz, 1H), 7.36-7.42 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 35.9, 55.5, 114.2, 120.1, 122.3, 127.1, 128.1, 129.4, 130.3, 130.5, 132.3, 137.4, 143.7, 148.1, 159.6, 164.1, 186.5; IR (ATR) 3107 w, 3006 w, 2958 w, 2837 w, 1738 m, 1654 m, 1602 w, 1586 w, 1485 w, 1460 w, 1432 w, 1396 s, 1333 w, 1274 s, 1212 s, 1175 m, 1150 w, 1130 w, 1091 w, 1065 w, 1039 w, 995 w, 934 w, 899 w, 829 w, 772 w, 747 w, 699 w, 680 w, 665 w; MS *m/z* (relative intensity, %) 350 (4, M^+), 215 (12), 200 (14), 199 (100), 135 (97), 107 (20), 77 (10); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{18}N_2O_4$: 350.1267; Found: 350.1266.

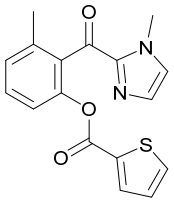
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl cinnamate



3aj

76.3 mg, 74% yield, R_f 0.32 (hexane/EtOAc = 1:1). white solid, m.p. 137.7-137.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H), 4.04 (s, 3H), 6.35 (d, *J* = 15.9 Hz, 1H), 7.03 (s, 1H), 7.12-7.16 (m, 2H), 7.17 (d, *J* = 0.8 Hz, 1H), 7.35-7.39 (m, 4H), 7.45 (dd, *J* = 4.6, 3.0 Hz, 2H), 7.54 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 36.1, 116.9, 120.1, 127.2, 127.9, 128.2, 129.0, 130.2, 130.5, 130.7, 132.4, 134.1, 137.2, 143.6, 146.2, 147.8, 164.5, 186.5; IR (ATR) 3299 w, 3106 w, 3062 w, 3027 w, 2959 w, 2924 w, 2362 w, 1733 m, 1654 m, 1635 w, 1605 w, 1576 w, 1461 w, 1396 s, 1330 w, 1308 w, 1257 w, 1220 s, 1199 m, 1173 w, 1133 s, 1076 w, 1028 w, 979 w, 936 w, 900 w, 863 w, 766 w, 703 w, 683 w, 665 w; MS *m/z* (relative intensity, %) 347 (4, M^++1), 346 (16, M^+), 216 (37), 215 (17), 199 (45), 188 (15), 187 (14), 132 (10), 131 (100), 105 (10), 103 (40), 77 (18); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{18}N_2O_3$: 346.1317; Found: 346.1315.

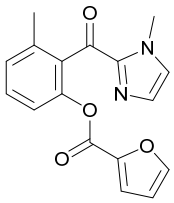
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl thiophene-2-carboxylate



3ak

74.5 mg, 76% yield, R_f 0.29 (hexane/EtOAc = 1:1). white solid, m.p. 98.2-98.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 4.02 (s, 3H), 6.97 (d, *J* = 0.5 Hz, 1H), 7.05 (dd, *J* = 4.9, 3.8 Hz, 1H), 7.11 (d, *J* = 0.9 Hz, 1H), 7.17 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.27-7.28 (m, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.53 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.68 (dd, *J* = 3.8, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 36.0, 120.0, 127.0, 127.9, 128.1, 130.2, 130.5, 132.1, 132.5, 133.4, 134.5, 137.4, 143.6, 147.7, 159.4, 186.3; IR (ATR) 3105 w, 2956 w, 2925 w, 2868 w, 1730 s, 1653 s, 1606 w, 1579 w, 1521 w, 1461 w, 1396 s, 1358 w, 1335 w, 1252 m, 1221 s, 1173 w, 1150 w, 1083 w, 1062 w, 1008 w, 936 w, 900 m, 861 w, 838 w, 773 w, 735 m, 700 w, 663 w; MS *m/z* (relative intensity, %) 326 (1, M^+), 215 (11), 200 (14), 199 (100), 111 (70); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{14}N_2O_3S$: 326.0725; Found: 326.0729.

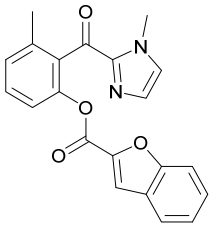
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl furan-2-carboxylate



3al

72.9 mg, 78% yield, R_f0.24 (hexane/EtOAc = 1:1). yellow solid, m.p. 108.4-108.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 4.03 (s, 3H), 6.44-6.46 (m, 1H), 6.93-6.94 (m, 1H), 7.00 (s, 1H), 7.11 (d, *J* = 0.9 Hz, 1H), 7.16-7.22 (m, 2H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.55-7.56 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 36.0, 112.0, 118.9, 120.1, 127.0, 128.2, 130.3, 130.5, 132.2, 137.5, 143.7, 143.7, 147.1, 147.4, 155.9, 186.2; IR (ATR) 3455 w, 3133 w, 2959 w, 2926 w, 2857 w, 2334 w, 1742s, 1654 s, 1607 w, 1569 w,1463 w, 1396 s, 1336 w, 1293 w, 1256 w, 1225 s, 2282 m, 1097 s, 1012 w, 935 w, 900 w, 842 w, 769 w, 730 w, 699 w, 665 w; MS *m/z* (relative intensity, %) 310 (0, M^+), 200 (15), 199 (100), 95 (32); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{14}N_2O_4$: 310.0954; Found: 310.0950.

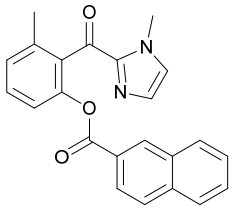
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl benzofuran-2-carboxylate



3am

73.1 mg, 68% yield, R_f0.31 (hexane/EtOAc = 1:1). white solid, m.p.139.2-139.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 3.94 (s, 3H), 6.86 (s, 1H), 7.03 (d, *J* = 0.9 Hz, 1H), 7.12 (*d*, *J* = 7.8 Hz, 1H), 7.17-7.24 (m, 3H), 7.31-7.39 (m, 2H), 7.45-7.48 (m, 1H), 7.56-7.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 36.0, 112.4, 114.9, 120.0, 123.0, 124.0, 126.8, 127.1, 128.1, 128.4, 130.4, 130.5, 132.2, 137.7, 143.7, 144.6, 147.5, 156.0, 156.9, 186.1; IR (ATR) 3299 w, 3105 w, 3067 w, 3026 w, 2957 w, 2925 w, 2358 w, 1745 s, 1654 s, 1609 w, 1562 w, 1508 w, 1461 w, 1397 s, 1349 w, 1330 s, 1294m, 1257 w, 1224 m, 1167 s, 1143 m, 1081 w, 958 w, 936 w, 900 w, 846 w, 749 w, 699 w, 664 w; MS *m/z* (relative intensity, %) 360 (1, M^+), 304, 200 (13), 199 (100), 145 (35), 89 (11); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{16}N_2O_4$: 360.1110; Found: 360.1114.

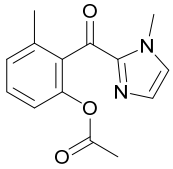
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 2-naphthoate



3an

80.6 mg, 73% yield, R_f 0.38 (hexane/EtOAc = 1:1). white solid, m.p.115.8-116.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.89 (s, 3H), 6.89 (s, 1H), 7.14 (s, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 7.1 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.51-7.60 (m, 2H), 7.79-7.86 (m, 4H), 8.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 35.9, 120.2, 125.2, 126.5, 126.9, 127.0, 127.9, 128.1, 128.2, 128.6, 129.4, 130.3, 130.5, 131.6, 132.3, 132.4, 135.7, 137.5, 143.8, 148.2, 164.3, 186.5; IR (ATR) 3458w, 3108 w, 3061 w, 2959 w, 1736 s, 1654 m, 1605 w, 1461 m, 1396 s, 1356 w, 1279 m, 1261 m, 1219 s, 1188 s, 1149 w, 1128 m, 1070 m, 957 w, 936 w, 900 m, 868 w, 828 w, 774 m, 763 m, 729 m; MS *m/z* (relative intensity, %) 370 (6, M^+), 199 (57), 156 (12) 155 (100), 127 (43); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{23}H_{18}N_2O_3$: 370.1317; Found: 370.1317.

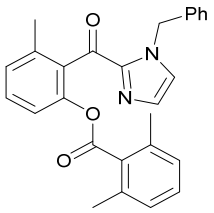
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl acetate



3ao

27.6 mg, 36% yield, R_f 0.22 (hexane/EtOAc = 1:1). colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.25 (s, 3H), 4.12 (s, 3H), 7.06 (d, *J* = 8.2 Hz, 1H), 7.11-7.14 (m, 2H), 7.18 (d, *J* = 0.7 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 20.8, 36.3, 120.3, 127.3, 128.0, 130.2, 130.7, 132.2, 137.3, 143.6, 147.8, 168.7, 186.6; IR (ATR) 3110 w, 3023 w, 2960 w, 2362 w, 2334 w, 1770 m, 1655 s, 1606 w, 1577 w, 1508 w, 1462 w, 1397 s, 1369 w, 1292 w, 1257 w, 1217 s, 1197 w, 1148 w, 1178 w, 1031 w, 901 w, 868 w, 792 w, 777 w, 702 w, 663 w; MS *m/z* (relative intensity, %) 258 (2, M^+), 216 (26), 200 (14), 199 (100), 188 (29), 187 (57), 105 (56); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{14}H_{14}N_2O_3$: 258.1004; Found: 258.1007.

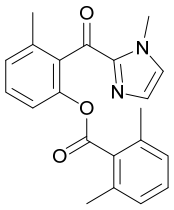
2-(1-benzyl-1*H*-imidazole-2-carbonyl)-3-methylphenyl 2,6-dimethylbenzoate



3ba

101.3 mg, 80% yield, R_f0.62 (hexane/EtOAc = 1:1). white solid, m.p. 115.8-116.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.24 (s, 6H), 5.64 (s, 2H), 6.97 (d, *J* = 7.5 Hz, 2H), 7.06-7.25 (m, 10H), 7.38 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 19.8, 51.7, 119.8, 126.5, 127.5, 127.8, 128.1, 128.8, 129.7, 129.9, 131.2, 132.5, 132.8, 135.8, 136.2, 136.8, 142.9, 147.5, 167.7, 186.6; IR (ATR) 3030 w, 2959 w, 2924 w, 1745 s, 1657 s, 1607 w, 1578 w, 1496 w, 1461 m, 1430 w, 1399 s, 1381m, 1296 w, 1259 w, 1240 w, 1217 s, 1162 w, 1135 w, 1103 m,1052 s, 1013 w, 930 w, 899 m, 858 w, 776 m, 715 m, 695 w, 668 w; MS *m/z* (relative intensity, %) 424 (10, M^+), 275 (12), 134 (10), 133 (100), 105 (14), 91 (12); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{27}H_{24}N_2O_3$: 424.1787; Found: 424.1786.

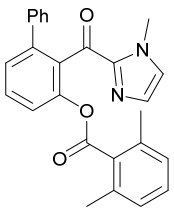
3-methyl-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 2,6-dimethylbenzoate



3aa

88.6 mg, 85% yield, R_f0.31 (hexane/EtOAc = 1:1). white solid, m.p. 150.8-160.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.28 (s, 6H), 4.03 (s, 3H), 6.99 (d, *J* = 7.5 Hz, 2H), 7.03 (s, 1H), 7.14-7.18 (m, 3H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 19.7, 36.1, 119.9, 127.5, 127.7, 127.9, 129.8, 130.0, 130.9, 132.8, 132.9, 135.6, 136.9, 143.4, 147.5, 167.8, 186.7; IR (ATR) 3107 w, 3067 w, 2959 w, 2925 w, 1746 m, 1655 m, 1607 w, 1577 w, 1506 w, 1461 w, 1424 w, 1395 s, 1292 w, 1258 m, 1240 w, 1216 s, 1174 w, 1149 w, 1103 m, 1052 s, 1014 w, 935 w, 900 m, 858 w, 776 m, 720 w, 700 w, 667 w; MS *m/z* (relative intensity, %) 348 (6, M^+), 134 (10), 133 (100), 105 (16); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{20}N_2O_3$: 348.1474; Found: 348.1479.

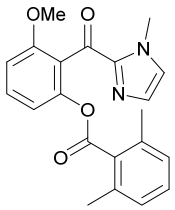
2-(1-methyl-1*H*-imidazole-2-carbonyl)-[1,1'-biphenyl]-3-yl 2,6-dimethylbenzoate



3ca

82.3 mg, 67% yield, R_f 0.46 (hexane/EtOAc = 1:1). colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 6H), 3.77 (s, 3H), 6.77 (d, *J* = 0.5 Hz, 1H), 6.94 (d, *J* = 0.7 Hz, 1H), 6.99-7.01 (m, 2H), 7.15-7.24 (m, 4H), 7.28-7.33 (m, 3H), 7.42 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.55-7.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 35.6, 121.6, 126.5, 127.5, 127.8, 128.0, 129.1, 129.9, 130.2, 130.3, 132.2, 132.6, 135.8, 139.7, 142.3, 143.9, 147.8, 167.9, 185.9; IR (ATR) 3303 w, 3105 w, 3063 w, 3027 w, 2965 w, 1746 s, 1658 m, 1599 w, 1566 w, 1460 m, 1397 s, 1256 w, 1237 m, 1217 s, 1166 w, 1103 m, 1046 m, 937 w, 902 w, 861 w, 769 w, 702 w, 667 w; MS *m/z* (relative intensity, %) 410 (5, M^+), 134 (10), 133 (100), 105 (14); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{25}H_{22}N_2O_3$: 410.1630; Found: 410.1623.

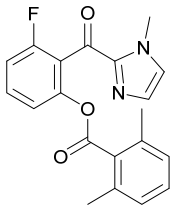
3-methoxy-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 2,6-dimethylbenzoate



3da

89.1 mg, 82% yield, R_f 0.34 (hexane/EtOAc = 1:1). white solid, m.p. 203.8-204.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 6H), 3.78 (s, 3H), 4.05 (s, 3H), 6.90 (d, *J* = 8.6 Hz, 1H), 6.98-7.03 (m, 4H), 7.14-7.19 (m, 2H), 7.46 (t, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 36.2, 56.4, 109.1, 115.1, 122.9, 127.2, 127.7, 129.8, 130.6, 130.8, 132.7, 135.6, 143.7, 148.3, 158.0, 167.7, 184.1; IR (ATR) 3106 w, 3069 w, 3007 w, 2963 w, 1748 w, 1658 s, 1606 m, 1585 w, 1467 m, 1436 w, 1398 s, 1268 m, 1257 m, 1240 m, 1220 s, 1169 w, 1103 m, 1077 s, 1047 w, 937 w, 901 m, 780 w, 749 w; MS *m/z* (relative intensity, %) 364 (4, M^+), 213 (11), 133 (100), 105 (16); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{20}N_2O_4$: 364.1423; Found: 364.1426.

3-fluoro-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 2,6-dimethylbenzoate

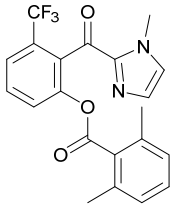


3ea

83.1 mg, 79% yield, R_f 0.4 (hexane/EtOAc = 1:1). white solid, m.p. 114.5-114.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 6H), 4.03 (s, 3H), 7.01 (d, *J* = 7.5 Hz, 2H), 7.07-7.11 (m, 2H), 7.17-7.21 (m, 3H), 7.47-7.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.86, 36.14, 133.41, 133.62, 118.74 (d, *J* = 3.84 Hz), 122.06 (d, *J* = 21.08 Hz),127.49, 127.84, 130.06, 130.85, 131.37 (d, *J* = 9.58 Hz), 132.31, 135.78, 143.10, 148.57, 148.64, 159.93 (d, *J* = 248.2 Hz), 167.47, 180.50; IR (ATR) 3449 w, 3107 w, 3066 w, 2965 w, 2927 w, 2361 w, 1752 w, 1660 m, 1617 w, 1585 w, 1507 w, 1461 m, 1398 s, 1293 w, 1256 m, 1218 s, 1174 w, 1153 w, 1102 w, 1049 s, 979 w, 936 w, 901 m, 856 w, 777 w, 718 w, 698 w, 665 w; MS *m/z* (relative

intensity, %) 352 (1, M^+), 134 (10), 133 (100), 105 (19); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{17}FN_2O_3$: 352.1223; Found: 352.1217.

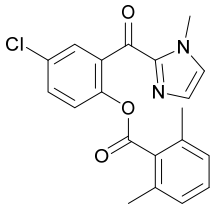
2-(1-methyl-1*H*-imidazole-2-carbonyl)-3-(trifluoromethyl)phenyl 2,6-dimethylbenzoate



3fa

70 mg, 58% yield, R_f 0.51 (hexane/EtOAc = 1:1). white solid, m.p. 137.0-137.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 6H), 4.02 (s, 3H), 6.99-7.00 (m, 2H), 7.05 (s, 1H), 7.14 (d, *J* = 0.9 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.64 (t, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.82, 35.97, 123.41 (q, *J* = 273.1 Hz), 123.97 (q, *J* = 4.8 Hz), 126.50, 127.63, 127.90, 129.28 (q, *J* = 31.58 Hz), 130.16, 130.38, 131.39, 132.01, 135.82, 143.23, 148.10, 167.30, 183.11; IR (ATR) 3108 w, 3067 w, 2965 w, 2928 w, 2356 w, 1752 s, 1666 w, 1592 w, 1508 w, 1463 w, 1399 s,1319 s, 1294 w, 1255 w,1221 s, 1167 m, 1131m, 1077 w, 1035 m, 938 w, 901 w, 860 w, 777 w, 737 ,w 701 ,w 682 ,w 669 w; MS *m/z* (relative intensity, %) 402 (4, M^+), 258 (12), 134 (13), 133 (100), 118 (72), 117 (12), 105 (22), 91 (15), 57 (21); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{17}F_3N_2O_3$: 402.1191; Found: 402.1198.

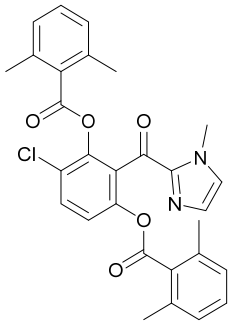
4-chloro-2-(1-methyl-1*H*-imidazole-2-carbonyl)phenyl 2,6-dimethylbenzoate



3ga

66.5 mg, 60 % yield, R_f 0.54 (hexane/EtOAc = 1:1). white solid, m.p. 102.5-102.7 °C; ^{1}H NMR(400 MHz, $CDCl_3$) δ 2.32 (s, 6H), 3.96 (s, 3H), 6.95-6.97 (m, 2H), 7.00 (s, 1H), 7.11-7.15 (m, 2H), 7.22 (d, *J* = 8.7 Hz, 1H), 7.44 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.71 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 36.4, 124.4, 127.8, 128.0, 130.2, 130.5, 130.9, 131.1, 131.8, 132.0, 133.3, 136.2, 142.6, 147.1, 167.6, 182.3; IR (ATR) 3107 w, 3069 w, 3025 w, 2962 w, 2927 w, 1746 s, 1713 w, 1657 s, 1595 w, 1506 w, 1466 m, 1396 s, 1280 w, 1255 s, 1280 w, 1255 m, 1236 m, 1198 s, 1170 w, 1152 w, 1117 m, 1105 w, 1045 s, 948 w, 910 w, 875 w, 828 w, 808 w, 775 s, 718 w, 689 w, 654 w; MS *m/z* (relative intensity, %) 368 (2, M^+), 134 (10) 133 (100), 105 (15); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{17}ClN_2O_3$: 368.0928; Found: 368.0927.

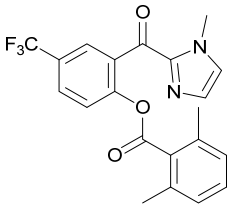
4-chloro-2-(1-methyl-1*H*-imidazole-2-carbonyl)-1,3-phenylene



3ga`

31.1 mg, 20% yield, R_f 0.49 (hexane/EtOAc = 1:1). white solid, m.p. 190.0-190.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (s, 6H), 2.29 (s, 6H), 3.86 (s, 3H), 6.90-6.95 (m, 5H), 7.08-7.14 (m, 3H), 7.32 (d, *J* = 8.9 Hz, 1H), 7.57 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ19.8, 20.9, 36.0, 121.4, 125.3, 127.9, 127.9, 128.4, 128.9, 130.1, 130.6, 130.7, 131.2, 131.3, 132.1, 135.8, 137.6, 142.9, 145.0, 146.9, 165.4, 166.9, 181.3; IR (ATR) 3068 w, 2966 w, 2928 w, 1752 s, 1659 s, 1596 w, 1463 w, 1396 s, 1254 w, 1222 m, 1206 m, 1172 w, 1102 w, 1046 m, 973 w, 950 w, 903 w, 870 w, 777 w, 719 w, 659 w; MS *m/z* (relative intensity, %) 516 (3, M^+), 134 (10), 133 (100), 105 (16); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{29}H_{25}ClN_2O_5$: 516.1452; Found: 516.1442.

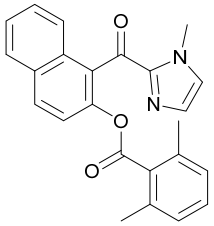
2-(1-methyl-1*H*-imidazole-2-carbonyl)-4-(trifluoromethyl)phenyl 2,6-dimethylbenzoate



3ha

52.8 mg, 44 % yield, R_f 0.62 (hexane/EtOAc = 1:1). white solid, m.p. 115.5-115.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 6H), 4.06 (s, 3H), 7.04-7.06 (m, 2H), 7.10 (s, 1H), 7.21-7.25 (m, 2H), 7.50 (d, *J* = 8.6 Hz, 1H), 7.83 (dd, *J* = 8.6, 2.2 Hz, 1H), 8.06-8.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.14, 36.43, 123.61(q, *J* = 271.19 Hz), 123.76, 127.61 (q, *J* = 32.58 Hz), 127.88, 128.10, 128.38 (q, *J* = 3.84 Hz), 128.90 (q, *J* = 3.84 Hz), 130.36, 130.48, 131.67, 132.50, 136.30, 142.40, 151.04, 167.24, 182.27; IR (ATR) 3111 w, 3070 w, 2965 w, 2931 w, 1748 m, 1657 m, 1616 w, 1593 w, 1465 w, 1396 s, 1332 s, 1299 w, 1250 m, 1238 m, 1203 s, 1167 s, 1120 s, 1079 w, 1034 m, 952 w, 909 w, 878 w, 835 w, 776 w, 726 w, 685 w; MS *m/z* (relative intensity, %) 402 (0.4, M^+), 213 (11), 133 (100), 132 (10) 105 (15); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{17}F_3N_2O_3$: 402.1191; Found: 402.1194.

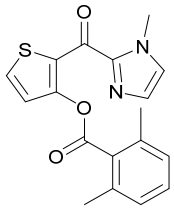
1-(1-methyl-1*H*-imidazole-2-carbonyl)naphthalen-2-yl 2,6-dimethylbenzoate



3ia

59.5 mg, 52% yield, R_f 0.33 (hexane/EtOAc = 1:1). white solid, m.p. 237.5-237.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 6H), 4.15 (s, 3H), 7.01-7.03 (m, 2H), 7.08-7.12 (m, 2H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.43-7.53 (m, 3H), 7.62-7.65 (m, 1H), 7.91 (dd, *J* = 7.3, 2.1 Hz, 1H), 8.01 (d, *J* = 8.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 36.4, 121.4, 125.1, 126.1, 127.4, 127.7, 127.8, 128.5, 128.6, 129.9, 131.0, 131.1, 131.5, 131.6, 132.7, 135.7, 143.9, 145.4, 167.9, 186.3; IR (ATR) 3108 w, 3065 w, 2959 w, 2925 w, 1745 s ,1655 s, 1604 w, 1509 w, 1463 w, 1432 w, 1400 w, 1400 s, 1333 w, 1293 w, 1258 w, 1222 m, 1205 m, 1168 w, 1137 w, 1101 w, 1073 w, 1050 m, 935 w, 899 w, 809 w, 772 w, 701 w; MS *m/z* (relative intensity, %) 384 (5, M^+), 235 (24), 134 (10), 133 (100), 105 (20); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{24}H_{20}N_2O_3$: 384.1474; Found: 384.1471.

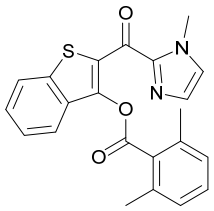
2-(1-methyl-1*H*-imidazole-2-carbonyl)thiophen-3-yl 2,6-dimethylbenzoate



3ja

63.4 mg, 62% yield, R_f 0.60 (hexane/EtOAc = 1:1). white solid, m.p. 156.4-156.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (s, 6H), 4.02 (s, 3H), 7.05-7.11 (m, 4H), 7.19 (d, *J* = 0.8 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 36.5, 122.8, 124.3, 127.4, 128.2, 129.0, 130.3, 131.9, 133.3, 136.8, 142.6, 151.9, 167.1, 174.0; IR (ATR) 3108 w, 3019 w, 2959 w, 2926 w, 1747 m, 1633 m, 1593 w, 1516 w, 1465 w, 1413 s, 1292 w, 1259 w, 1237 m, 1216 m, 1165 w, 1142 w, 1103 w, 1052 m, 988 w, 926 w, 887 m, 858 w, 833 w, 777 w, 728 w, 681 w, 665 w; MS *m/z* (relative intensity, %) 340 (4, M^+), 213 (10), 133 (100), 105 (21); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{18}H_{16}N_2O_3S$: 340.0882; Found: 340.0887.

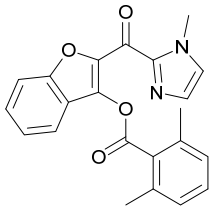
2-(1-methyl-1*H*-imidazole-2-carbonyl)benzo[*b*]thiophen-3-yl 2,6-dimethylbenzoate



3ka

65.4 mg, 56% yield, R_f0.65 (hexane/EtOAc = 1:1). yellow solid, m.p. 171.2-171.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.69 (s, 6H), 4.02 (s, 3H), 7.06 (s, 1H), 7.16 (d, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 0.9 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.42-7.44 (m, 1H), 7.48-7.50 (m, 1H), 7.84-7.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 36.5, 122.6, 123.0, 124.1, 125.1, 127.7, 128.2, 128.6, 129.2, 130.6, 131.2, 132.3, 137.8, 140.7, 142.8, 146.1, 166.4, 175.2; IR (ATR) 3467 w, 3114 w, 3019 w, 2968 w, 2361 m, 2338 w, 1742 s, 1640 m, 1596 w, 1563 w, 1501 w, 1463 w, 1401 m 1365 m, 1263 w, 1224 s, 1167 w, 1105 w, 1053 w, 1000 w, 972 w, 938 w, 900 w, 831 w, 767 w, 708 w, 658 w; MS *m/z* (relative intensity, %) 390 (14, M^+), 134 (10), 133 (100), 105 (19); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{22}H_{18}N_2O_3S$: 390.1038; Found: 390.1040.

2-(1-methyl-1*H*-imidazole-2-carbonyl)benzofuran-3-yl 2,6-dimethylbenzoate



3la

53.3 mg, 48% yield, R_f0.29 (hexane/EtOAc = 1:1). yellow solid, m.p. 113.5-113.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (s, 6H), 4.05 (s, 3H), 7.09 (s, 1H), 7.11-7.13 (m, 2H), 7.23 (d, *J* = 0.9 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.33-7.38, 1H), 7.50-7.54 (m, 1H), 7.69 (dd, *J* = 8.2, 0.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 36.2, 113.4, 120.8, 122.4, 124.1, 127.3, 128.3, 128.8, 130.3, 130.6, 131.3, 137.1, 138.7, 141.3, 142.5, 153.6, 165.7, 173.2; IR (ATR) 3108 w, 3067 w, 2967 w, 2928 w, 1756 m, 1639 s, 1593 w, 1563 w, 1449 w, 1415 m, 1366 w, 1345 w, 1283 w, 1260 w, 1230 s, 1189w, 1155 s, 1138 m, 1109 w, 1018 s, 993 m, 972 m, 916 w, 868 w, 868 m, 791 w, 772 w, 749 m, 698 w, 674 w; MS *m/z* (relative intensity, %) 374 (12, M^+), 134 (10), 133 (100), 105 (15); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{22}H_{18}N_2O_4$: 374.1267; Found: 374.1263.

VI. Mechanistic Studies

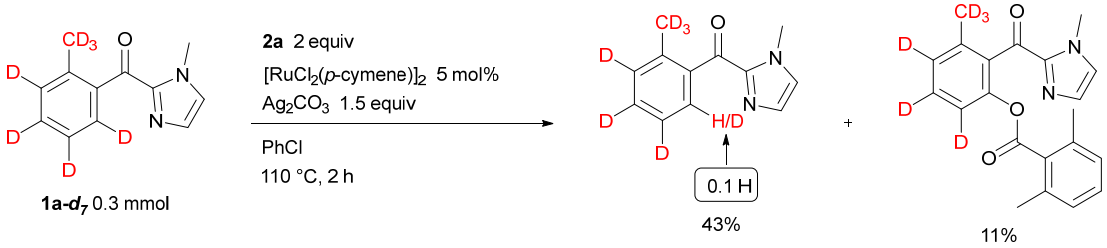
(I) Experiment with TEMPO

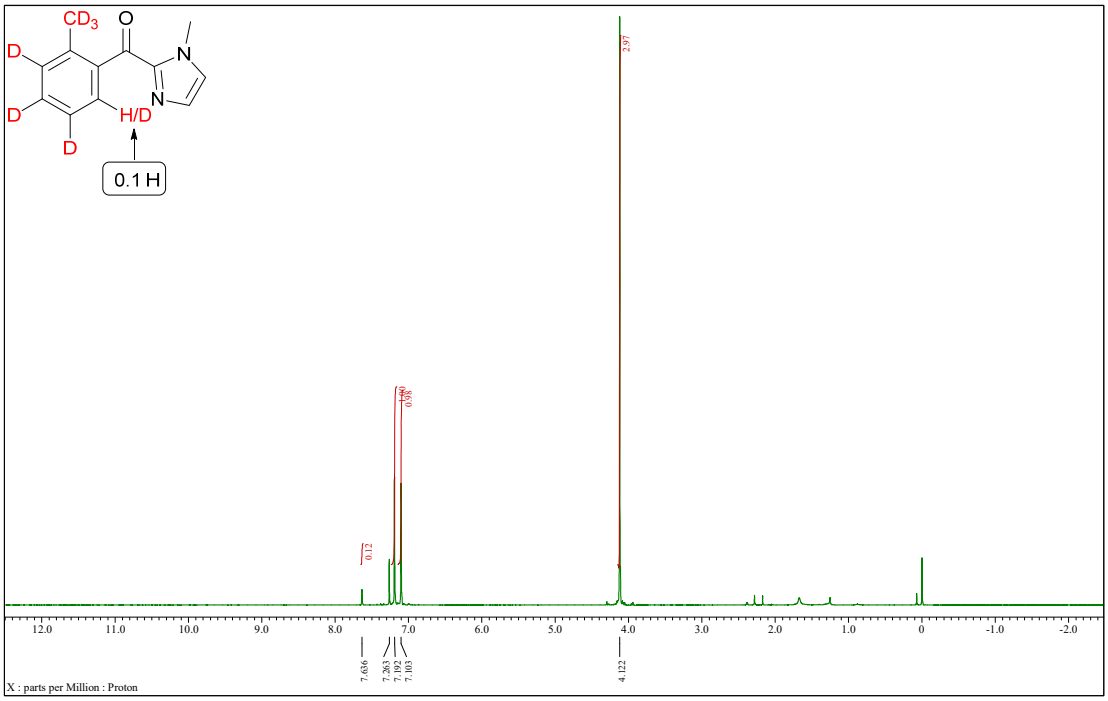
To an oven-dried 5 mL screw-capped vial, (1-methyl-1H-imidazol-2-yl)(2-methylphenyl)methanone (**1a**, 60.1 mg, 0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (9.2 mg, 0.015mmol), 2,6-dimethylbenzoic acid (90.1mg, 0.6 mmol), Ag_2CO_3 (124.1 mg, 0.45 mmol), TEMPO (46.9 mg, 0.3 mmol), and PhCl (1.5 mL) were added. The mixture was stirred for 18 hours at 110 °C and then allowed to cool to room temperature. The resulting mixture was filtered through a celite pad and the filtrate concentrated in vacuo. The residue was purified by MPLC (rate: 36 mL/min., eluent: hexane/EtOAc = 3/1 to 1/1) to afford the acyloxylation product **3aa** (47 mg, 45%) as a white powder.

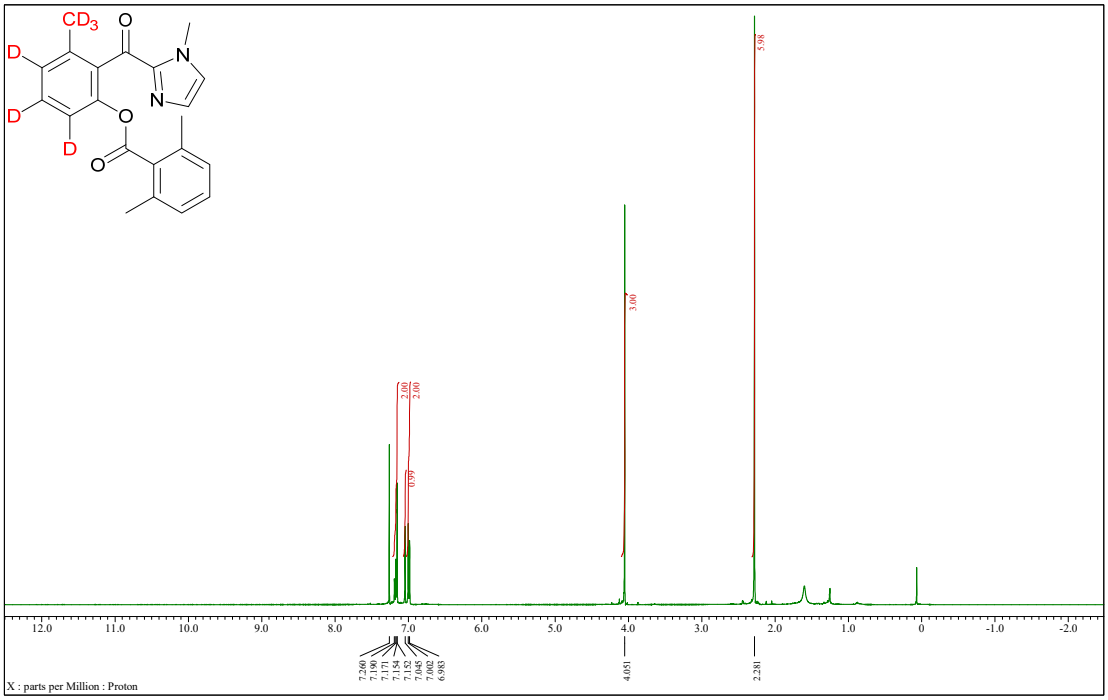
(II) KIE Experiments

Two parallel reactions using **1a** and **1a-*d*$_7$** were carried out in two different oven-dried 5 mL screw-capped vial. In the vial, **1a** or **1a-*d*$_7$** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (9.2 mg, 0.015 mmol), 2,6-dimethylbenzoic acid (90.1mg, 0.6 mmol), Ag_2CO_3 (124.1 mg, 0.45 mmol), and PhCl (1.5 mL) were added. The mixture was stirred for 2 hours at 110 °C and then allowed to cool to room temperature. The resulting mixture was filtered through a celite pad and the filtrate concentrated in vacuo. The residue was purified by MPLC (rate: 40 mL/min., eluent: hexane/EtOAc = 3/1 to 1/1) to afford the acyloxylation product **3aa** (24.4 mg, 23%) or **3aa-*d*$_6$** (11.3 mg, 11%) as white powder. The KIE value was determined to be 2.11, suggesting that the C–H activation step is a rate limiting step.

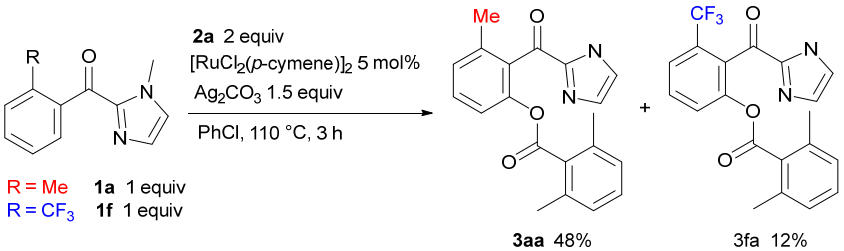
(III) Deuterium Scrambling Experiments







(IV) Competition Experiments

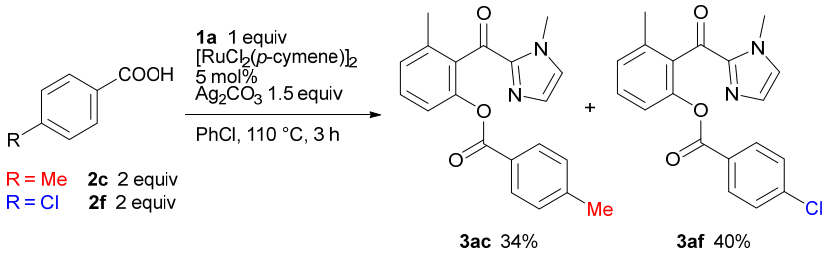


R = Me **1a** 1 equiv
R = CF_3 **1f** 1 equiv

3aa 48%

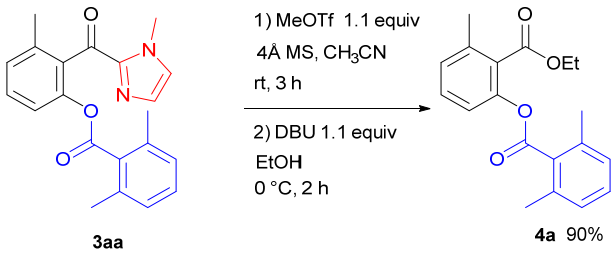
3fa 12%

To an oven-dried 5 mL screw-capped vial, (1-methyl-1H-imidazol-2-yl)(2-methylphenyl)methanone (**1a**, 60.1 mg, 0.3 mmol), (1-methyl-1H-imidazol-2-yl)(2-(trifluoromethyl)phenyl)methanone (**1f,** 76.3 mg, 0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (9.2 mg, 0.015mmol), 2,6-dimethylbenzoic acid (90.1mg, 0.6 mmol), Ag_2CO_3 (124.1 mg, 0.45 mmol), and PhCl (1.5 mL) were added. The mixture was stirred for 3 hours at 110 °C and then allowed to cool to room temperature. The resulting mixture was filtered through a celite pad and the filtrate concentrated in vacuo. The conversion of **1a** and **1f** and the yields of **3aa** and **3fa** were determined by ^{1}H NMR spectroscopy with respect to the internal standard (1,1,2,2-tetrachloroethane). The reaction gave **3aa** and **3fa** in 48% and 12% NMR yields, along with **1a** (47%) and **1f** (84%) recovered, respectively.



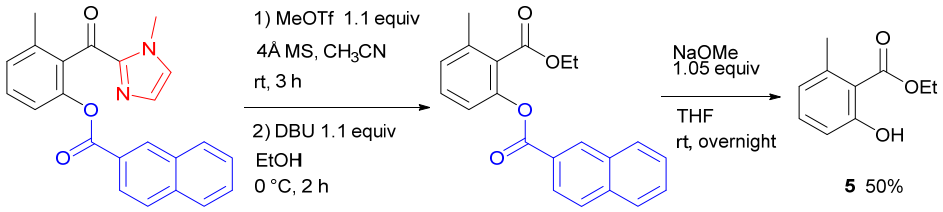
To an oven-dried 5 mL screw-capped vial, (1-methyl-1H-imidazol-2-yl)(2-methylphenyl)methanone (**1a**, 60.1 mg, 0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (9.2 mg, 0.015mmol), 4-methylbenzoic acid (**2a**, 93.9 mg, 0.6 mmol), 4-chlorobenzoic acid (**2f,** 81.7 mg, 0.6 mmol), Ag_2CO_3 (124.1 mg, 0.45 mmol), and PhCl (1.5 mL) were added. The mixture was stirred for 3 hours at 110 °C and then allowed to cool to room temperature. The resulting mixture was filtered through a celite pad and the filtrate concentrated in vacuo. The yields of **3ac** and **3af** were determined by ^{1}H NMR spectroscopy with respect to the internal standard (1,1,2,2-tetrachloroethane). The reaction gave **3ac** and **3af** in 34% and 40% NMR, respectively.

VII. Removal of a Directing Group



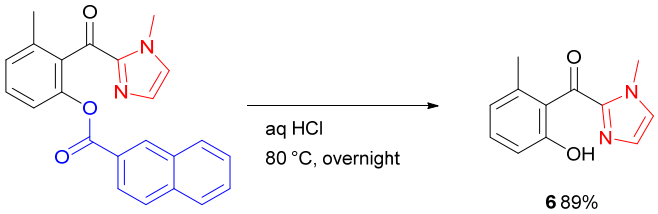
In a 25ml J-Young Schlenk, 4Å MS (200 mg; 100 mg/0.1 mmol) was heated under a vacuum for 30 minutes and was then allow to cool to room temperature under a nitrogen atmosphere. To the Schlenk tube, **3aa** (69.5 mg, 0.2 mmol) and anhydrous CH_3CN (2 mL) were added. The

resulting suspension was stirred for 3 h at room temperature under a nitrogen atmosphere. Methyl trifluoromethanesulfonate (34.8 mg, 0.22 mmol) was then slowly added at room temperature and the reaction mixture was stirred for 3 h. After stirring for 3 h, the reaction mixture was allowed to cool to 0 °C and ethanol (2 mL) and DBU (33.5 mg, 0.22 mmol) were added. The reaction was then stirred for an additional 2 h at 0 °C and the progress of the reaction was monitored by TLC (10% ethyl acetate -hexane). The crude product was washed with brine (25 mL) and EtOAc (3x25 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and the solvent was removed by evaporation. The residue was purified by MPLC (rate: 40 mL/min., eluent: hexane/EtOAc = 10/1) to afford the ester **4n** (56.4 mg, 90%) as a white powder.



In a 25ml J-Young Schlenk, 4Å MS (400 mg; 100 mg/0.1 mmol) was heated under a vacuum for 30 minutes and was then allow to cool to room temperature under a nitrogen atmosphere. To the Schlenk tube, **3an** (148 mg, 0.4 mmol) and anhydrous CH_3CN (4 mL) were added. The resulting suspension was stirred for 3 h at room temperature under a nitrogen atmosphere. Methyl trifluoromethanesulfonate (72 mg, 0.44 mmol) was then slowly added at room temperature and the reaction mixture was stirred for 3 h. After stirring for 3 h, the reaction mixture was allowed to cool to 0 °C and ethanol (2 mL) and DBU (67 mg, 0.44 mmol) were added. The reaction was then stirred for an additional 2 h at 0 °C and the progress of the reaction was monitored by TLC (10% ethyl acetate -hexane). The crude product was washed with brine (50 mL) and EtOAc (3x50 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and the solvent was removed by evaporation. The residue was purified by MPLC (rate: 40 mL/min., eluent: hexane/EtOAc = 10/1) to afford the ester **4n** (106.5 mg, 80%) as a white powder.

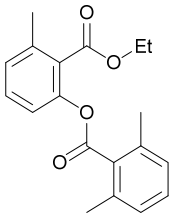
To an oven-dried 5 mL screw-capped vial, **4n** (37.5 mg, 0.1 mmol,), NaOMe (5.7 mg, 0.0105 mmol), THF (1 mL), and MeOH (0.02 ml) were added. The mixture was then stirred for overnight at room temperature. The resulting mixture was filtered through a celite pad and then concentrated in vacuo. The residue was purified by MPLC (rate: 40 mL/min., eluent: hexane/EtOAc = 10/1) to afford ethyl 2-hydroxy-6-methylbenzoate (**5**) (9.1 mg, 50%) as a white powder.



3an **6** 89%

To an oven-dried 5 mL screw-capped vial, **3an** (37.5 mg, 0.1 mmol), 12 N HCI (1 mL) was added. The mixture was then stirred overnight at 80 °C. The crude product was washed with brine (20 mL) and extracted with EtOAc (3x20 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and the solvent was removed by evaporation. The residue was purified by MPLC (rate: 40 mL/min., eluent: hexane/EtOAc = 2/1) to afford **6** (19.2 mg, 89%) as a white powder.

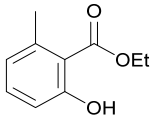
2-(ethoxycarbonyl)-3-methylphenyl 2,6-dimethylbenzoate



4a

56.4 mg, 90% yield. R_f 0.50 (hexane/EtOAc = 5:1). white solid, m.p. 82.8-83.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26-1.30 (m, 3H), 2.41 (s, 3H), 2.48 (s, 6H), 4.32 (q, *J* = 7.1 Hz, 2H), 7.08 (d, *J* = 7.7 Hz, 2H), 7.13-7.17 (m, 2H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 19.9, 20.3, 61.5, 120.2, 127.6, 128.1, 128.1, 130.2, 130.5, 132.4, 136.1, 137.6, 147.9, 166.8, 168.0; IR (ATR) 3069 w, 2980 w, 2931 w, 2359 w, 2337 w, 1730 s, 1661 w, 1608 w, 1582 w, 1464 m, 1426 w, 1384 w, 1366 w, 1333 w, 1267 s, 1240 m, 1219 s, 1167 w, 1105 m, 1076 m, 1047 s, 938 w, 900 w, 857 w, 775 w, 735 w, 714 w; MS *m/z* (relative intensity, %) 312 (1, M^+), 134 (10), 133 (100), 105 (13); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{19}H_{20}O_4$: 312.1362; Found:312.1361.

2-(ethoxycarbonyl)-3-methylphenyl 2-naphthoate

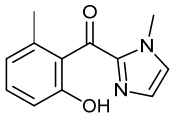


5

106.5 mg, 80% yield. R_f 0.44 (hexane/EtOAc = 5:1). white solid, m.p. 61.0-61.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, *J* = 7.1 Hz, 3H), 2.46 (s, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 7.16 (t, *J*

= 7.4 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.56-7.65 (m, 2H), 7.90-8.00 (m, 3H), 8.17 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.1, 61.5, 120.7, 125.6, 126.6, 126.9, 127.0, 128.0, 128.4, 128.6, 128.8, 129.6, 130.8, 132.1, 132.6, 136.0, 138.4, 148.7, 165.1, 166.7; IR (ATR) 3460 w, 3062 w, 2981 w, 2932 w, 1737 s, 1630 w, 1607 w, 1462 w, 1395 w, 1365 w, 1272 s, 1247 m, 1220 s, 1188 s, 1082 w, 1063 w, 1017 w, 957 w, 868 w, 829 w, 774 w, 763 w; MS *m/z* (relative intensity, %) 334 (10, M^+), 156 (12), 155 (100), 127 (28); HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{18}O_4$: 334.1205; Found: 334.1202.

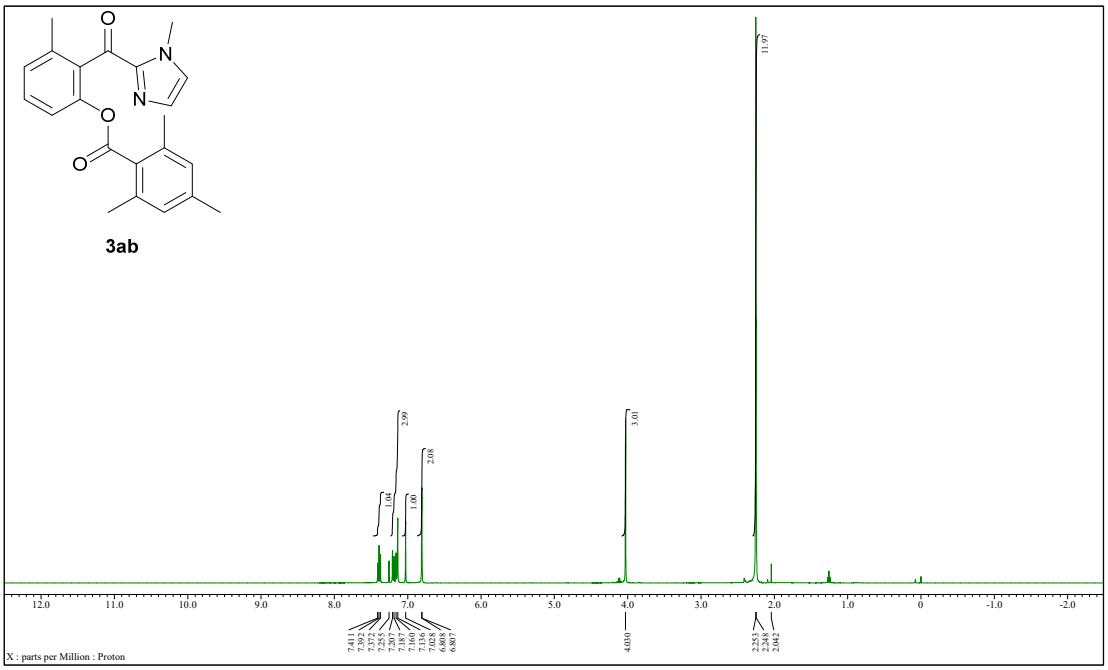
(2-hydroxy-6-methylphenyl)(1-methyl-1H-imidazol-2-yl)methanone

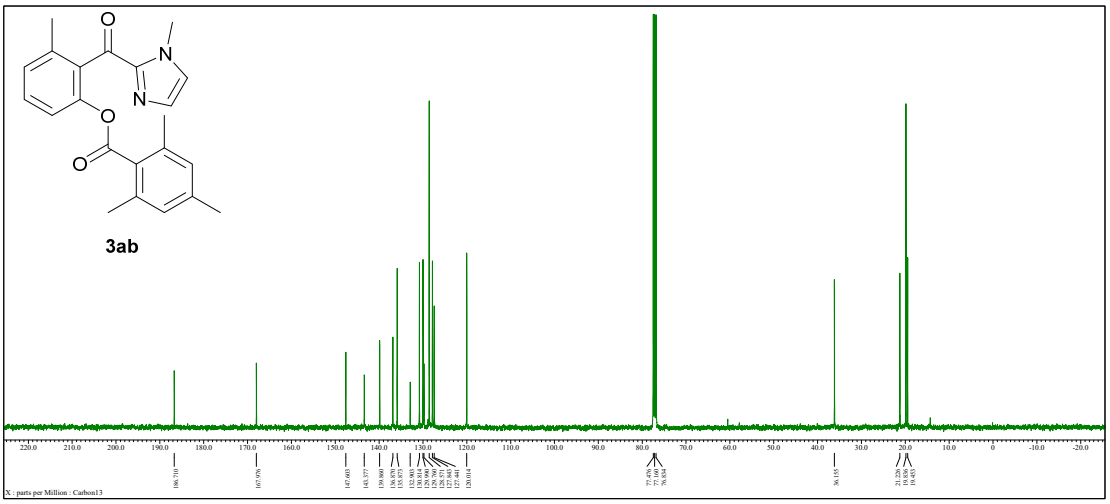


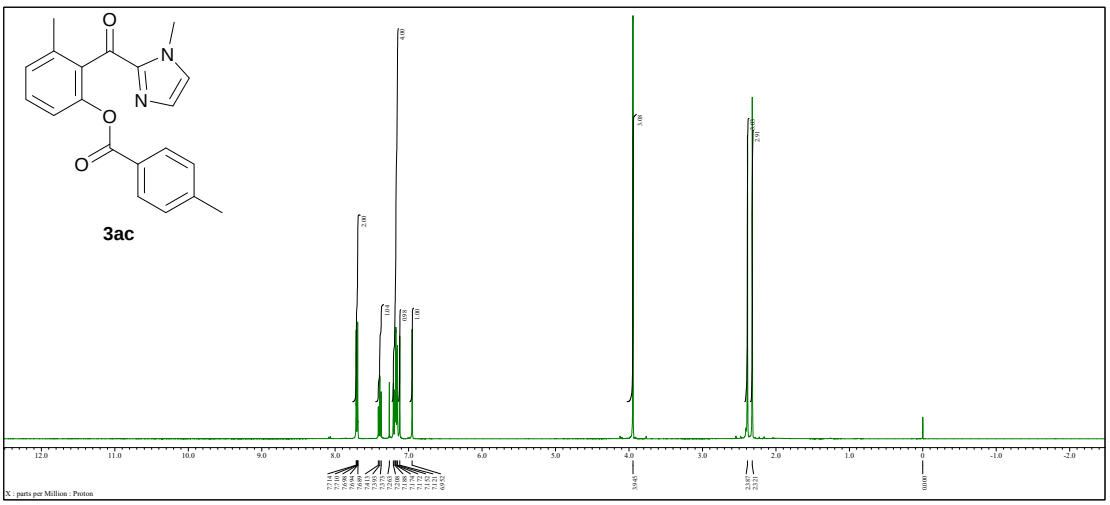
6

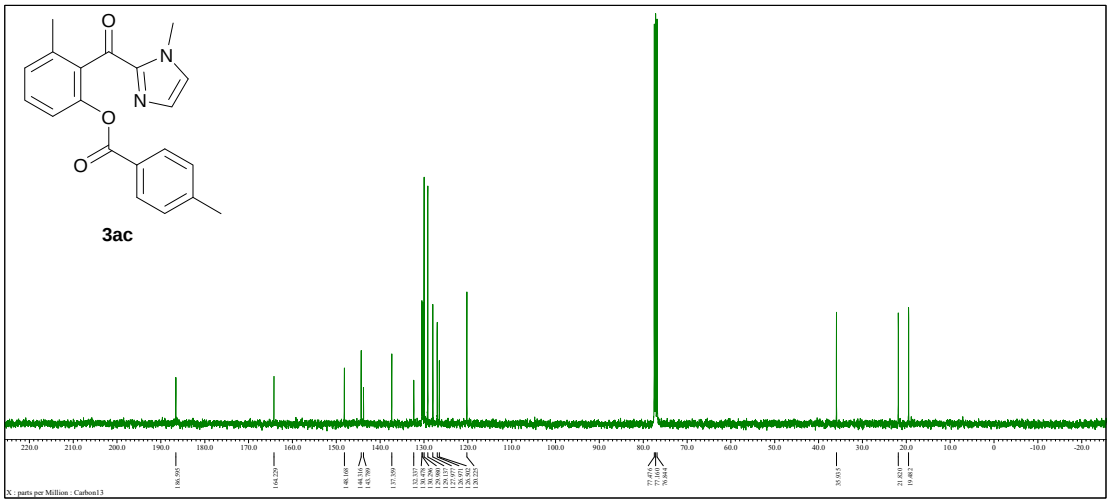
19.2 mg, 89% yield. R_f 0.35 (hexane/EtOAc = 1:1). white solid, m.p. 151.8-152.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.03 (s, 3H), 4.01 (s, 3H), 6.65-6.68 (m, 2H), 7.03 (d, *J* = 0.9 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.51 (s, 1H), 9.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 36.4, 117.4, 123.6, 127.0, 127.5, 128.4, 132.5, 139.7, 144.7, 155.9, 186.9; IR (ATR) 3312 w, 3108 w, 3072 w, 3024 w, 2965 w, 2857 w, 1754 w, 1740 w, 1725 w, 1710 w, 1658 m, 1602 w, 1586 w, 1550 w, 1463 m, 1400 s, 1367 w, 1289 w, 1261 w, 1224 w, 1172 w, 1150 w, 1084 w, 1029 w, 938 w, 907 s, 873 w, 785 w, 731 w, 703 w, 662 w; HRMS (DART) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{13}N_2O_2$ ($[M+H]^+$): 217.09715. Found: 217.09975.

VIII. Copies of ^{1}H and ^{13}C NMR Spectra


3ab
X : parts per Million : Proton


3ab
X : parts per Million : Carbon13


3ac
X : parts per Million : Proton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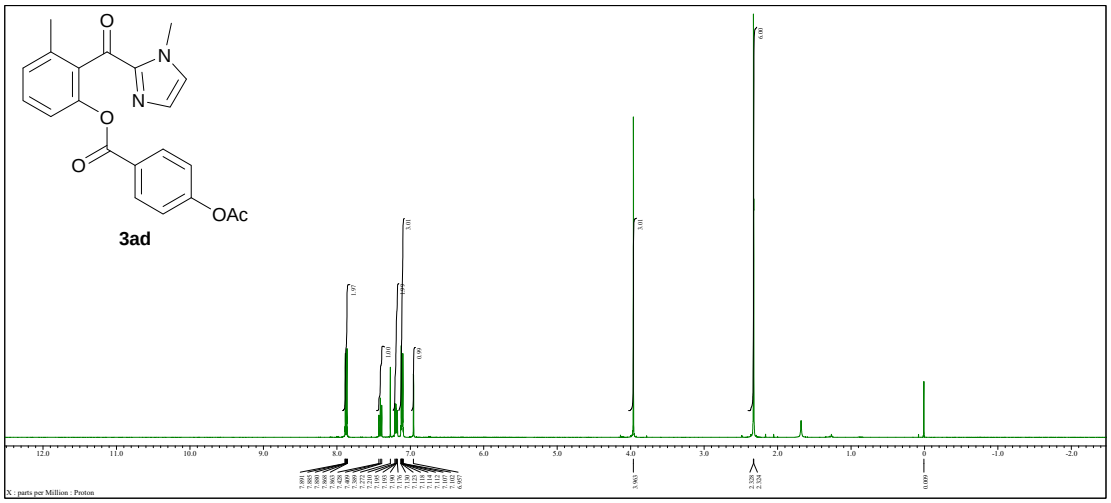
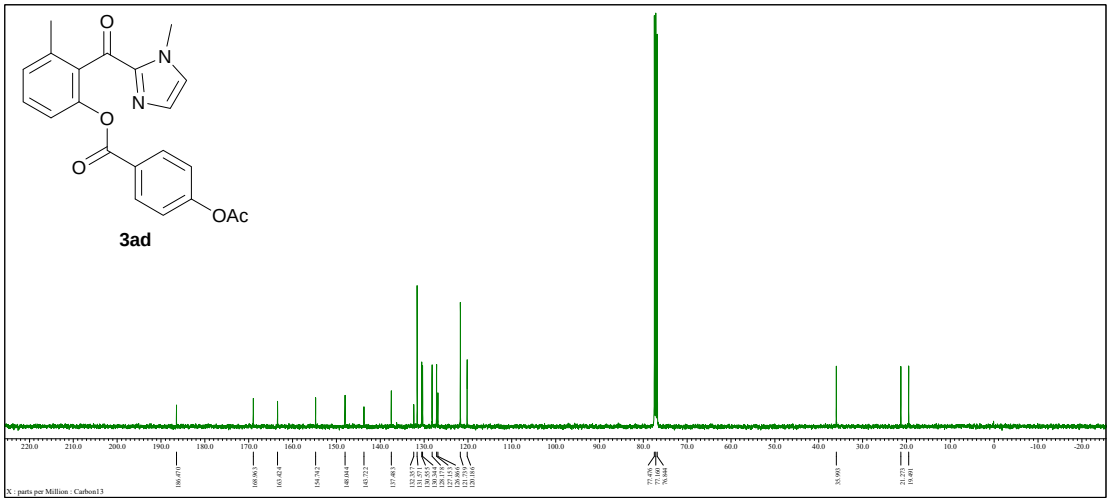

OAc
3ad
X : parts per Million : Proton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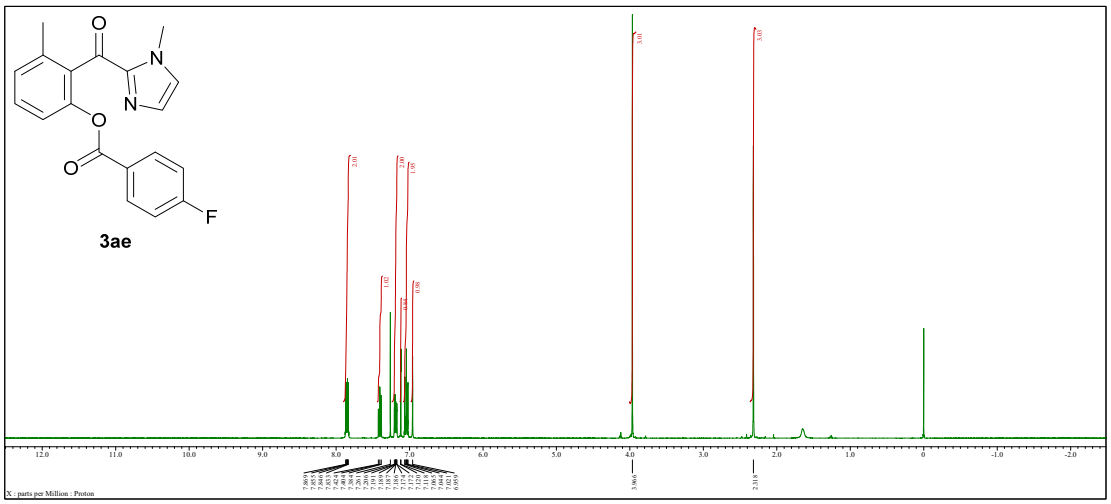
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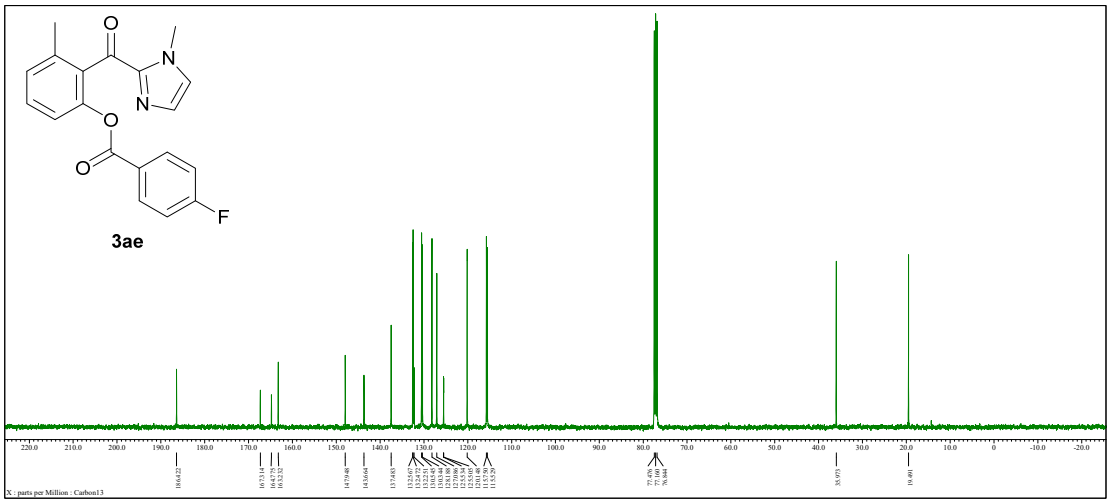
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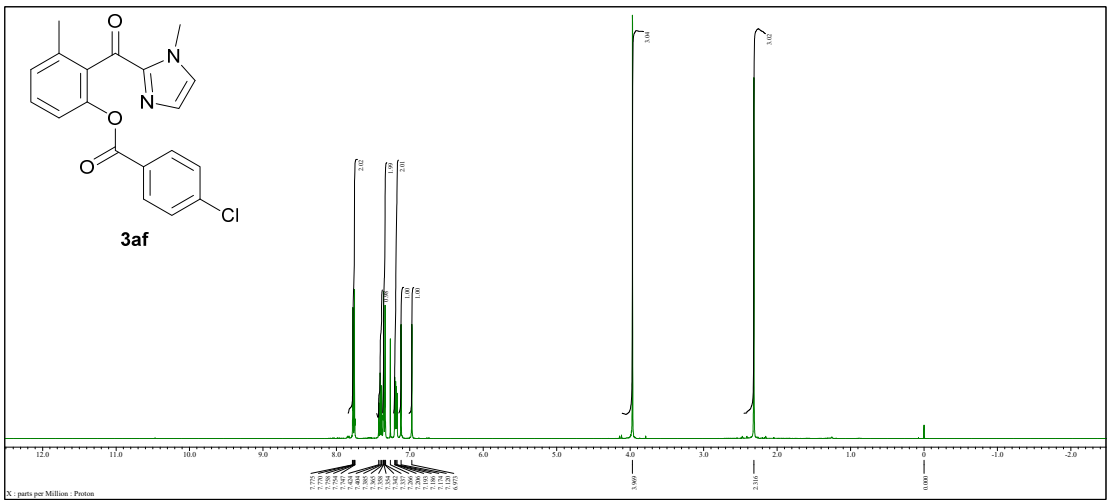
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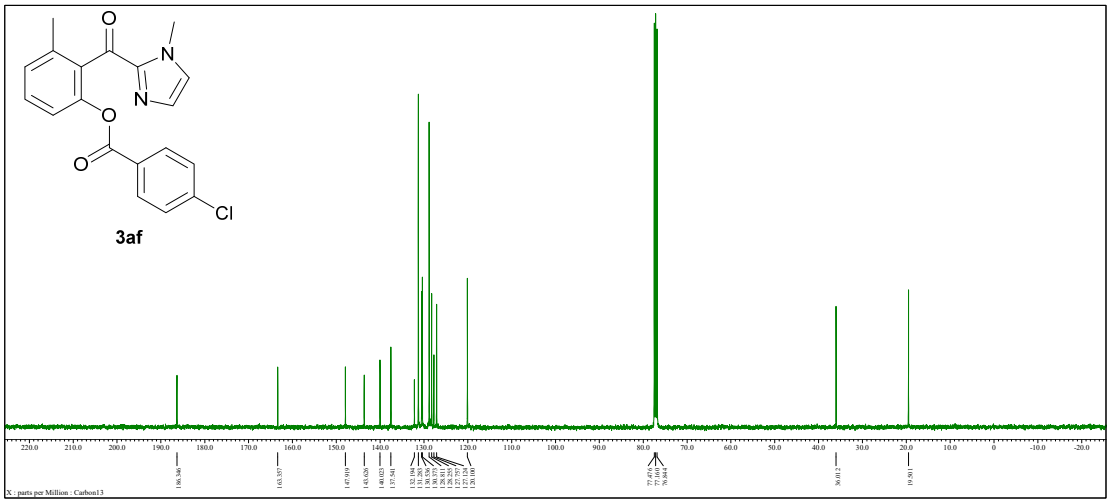
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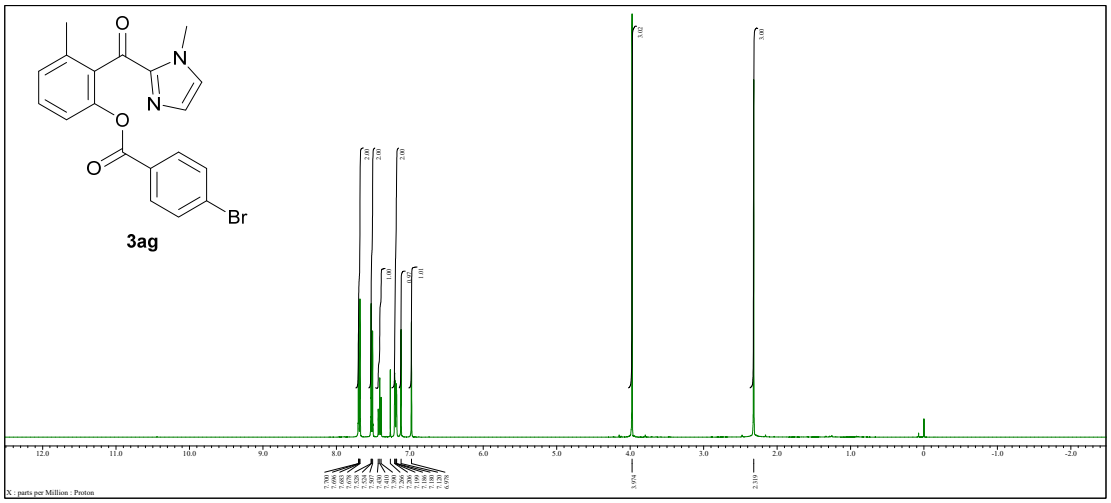
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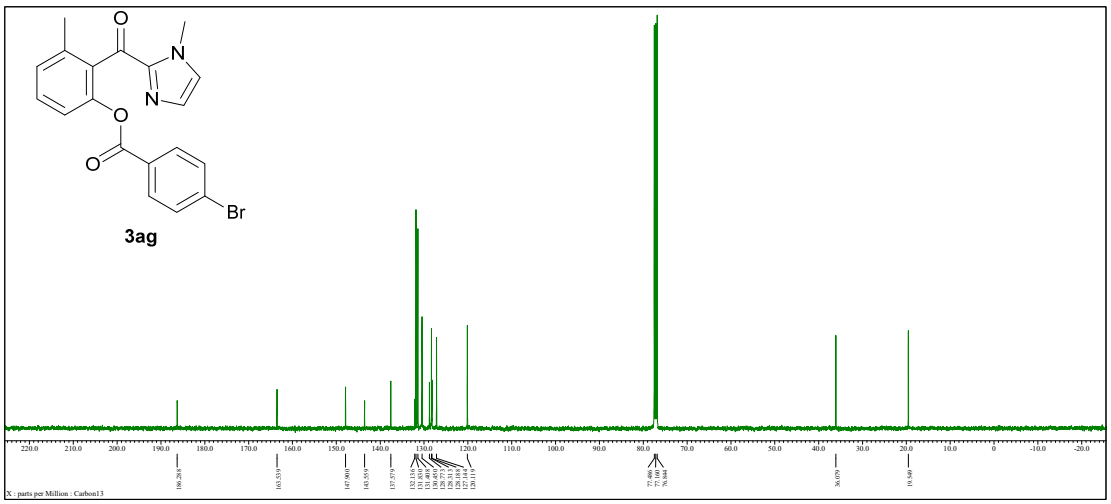
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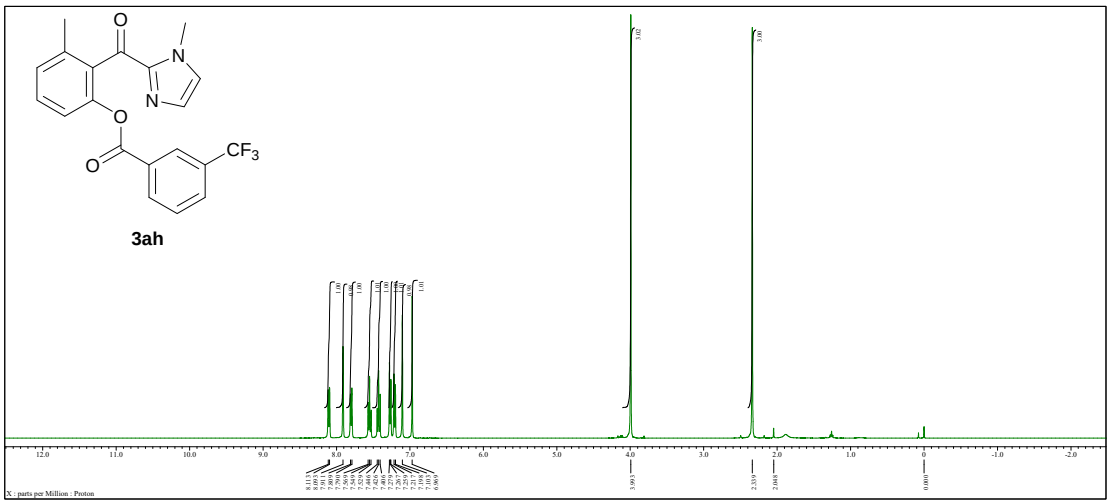
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CF3
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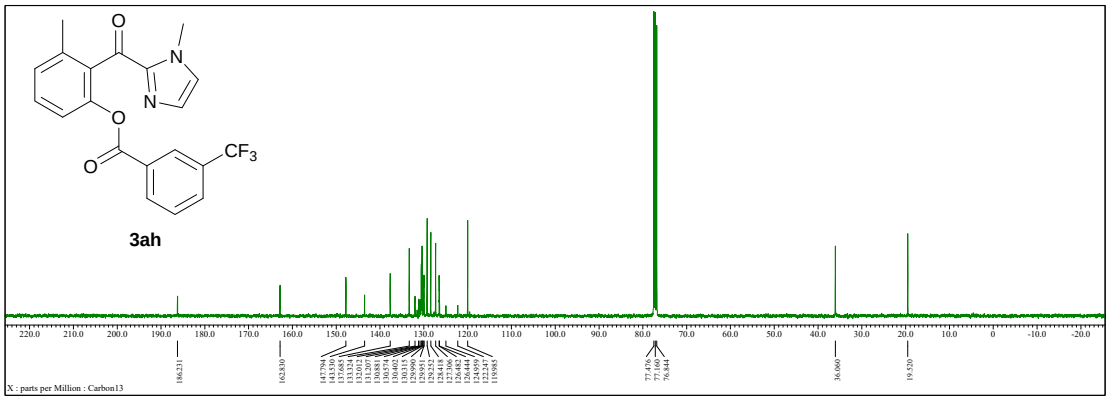
X : parts per Million : Proton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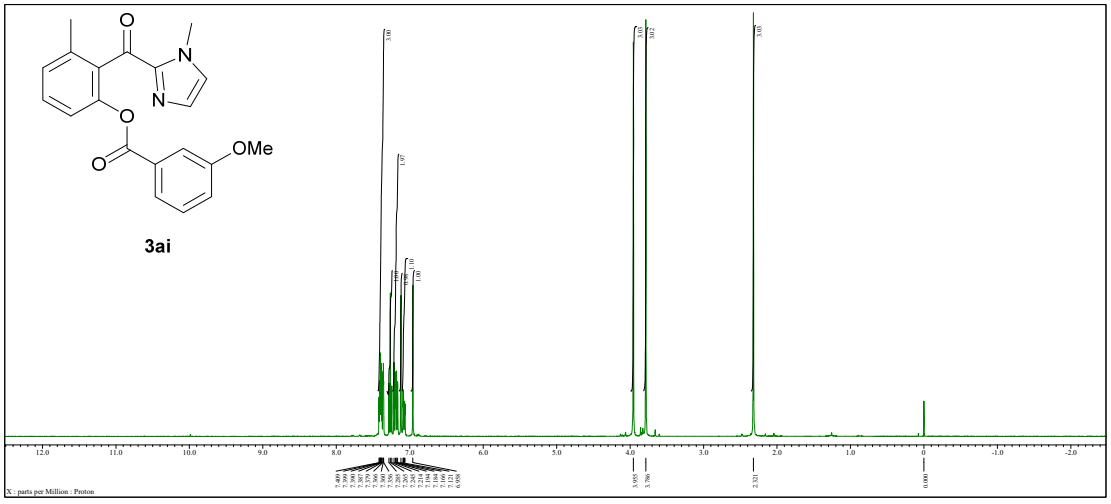
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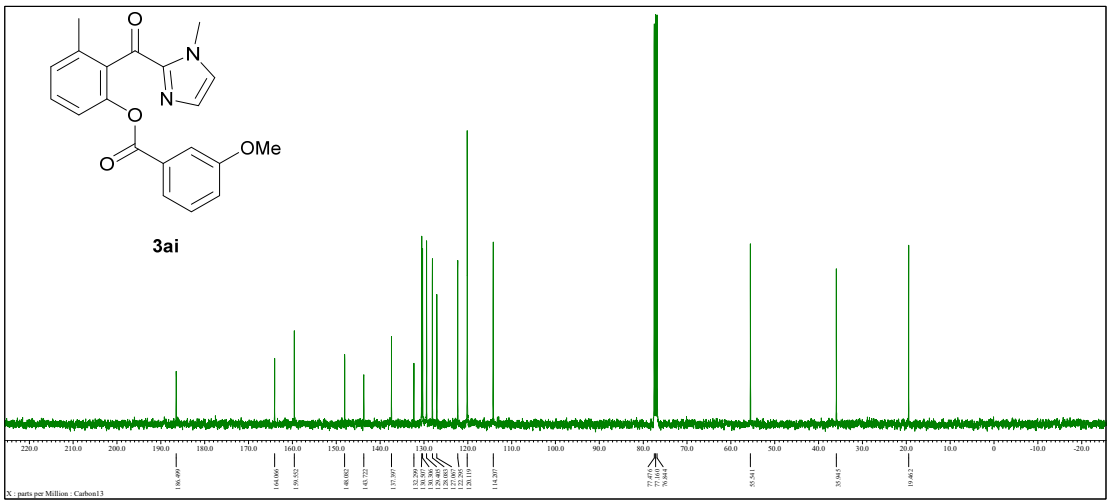
X : parts per Million : Proton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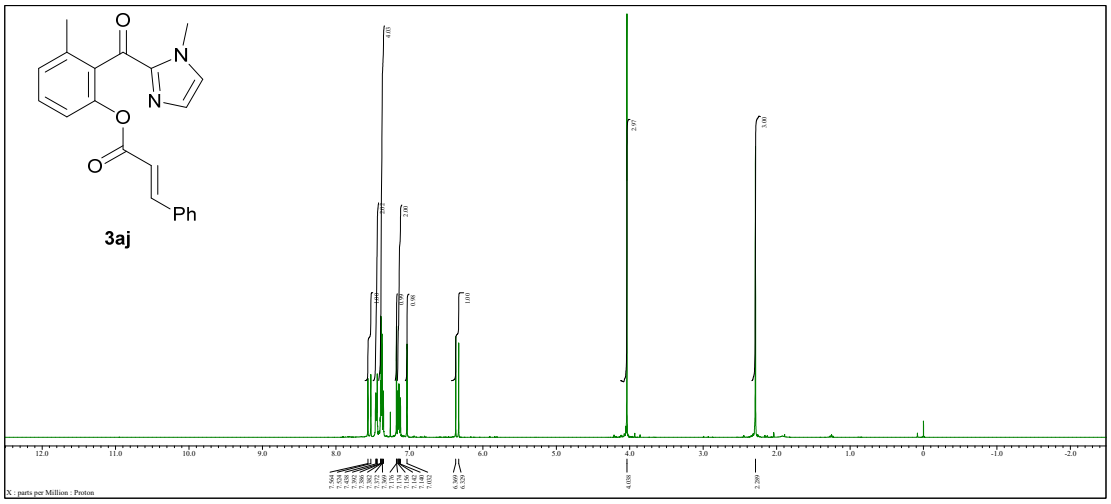
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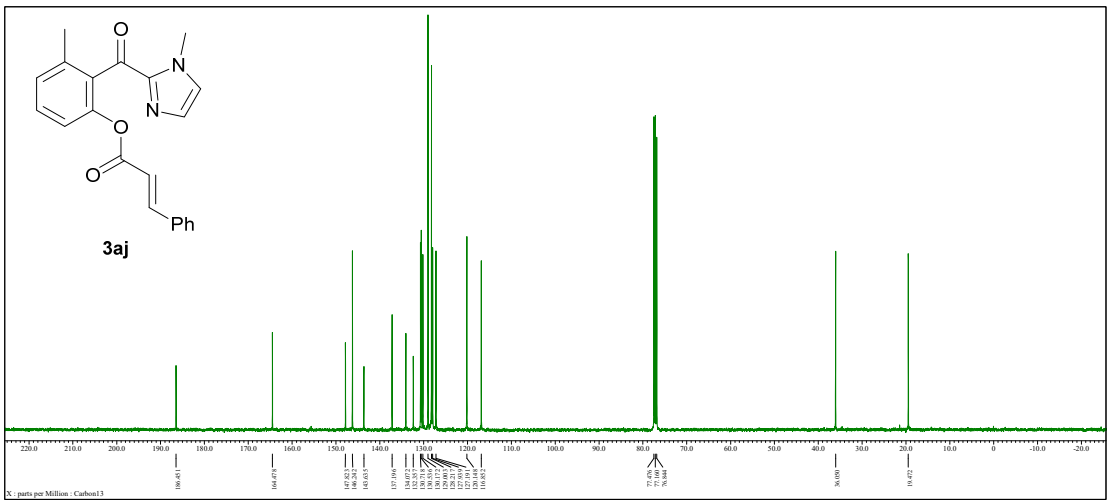
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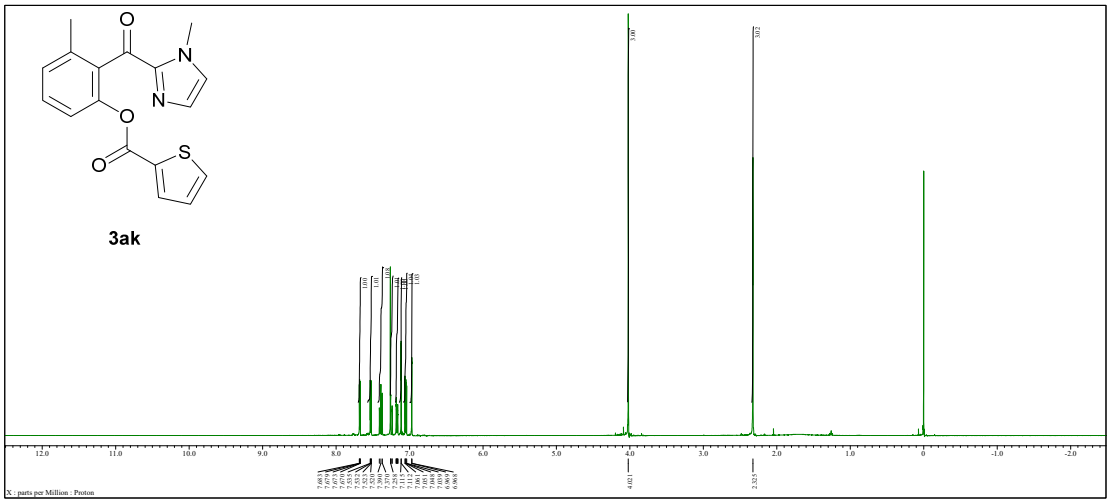
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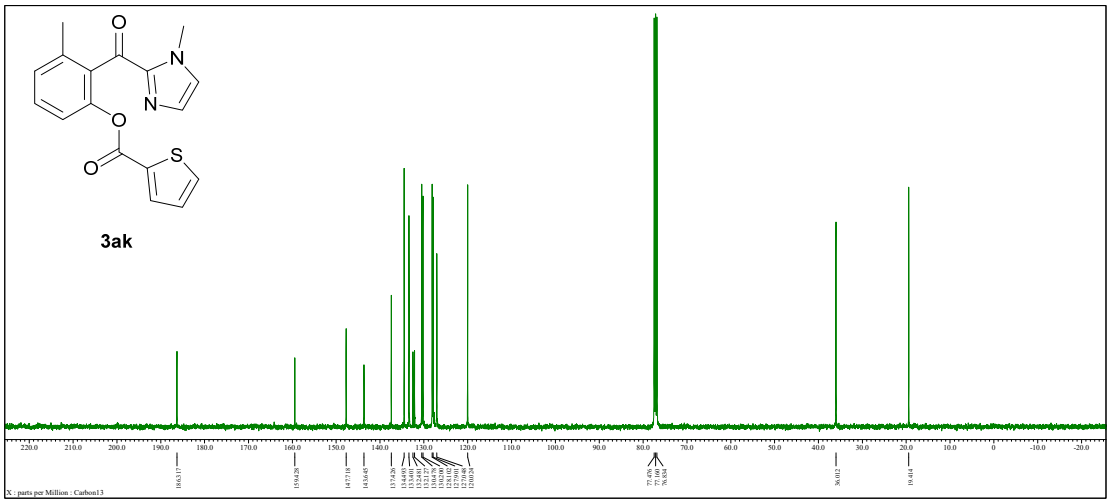
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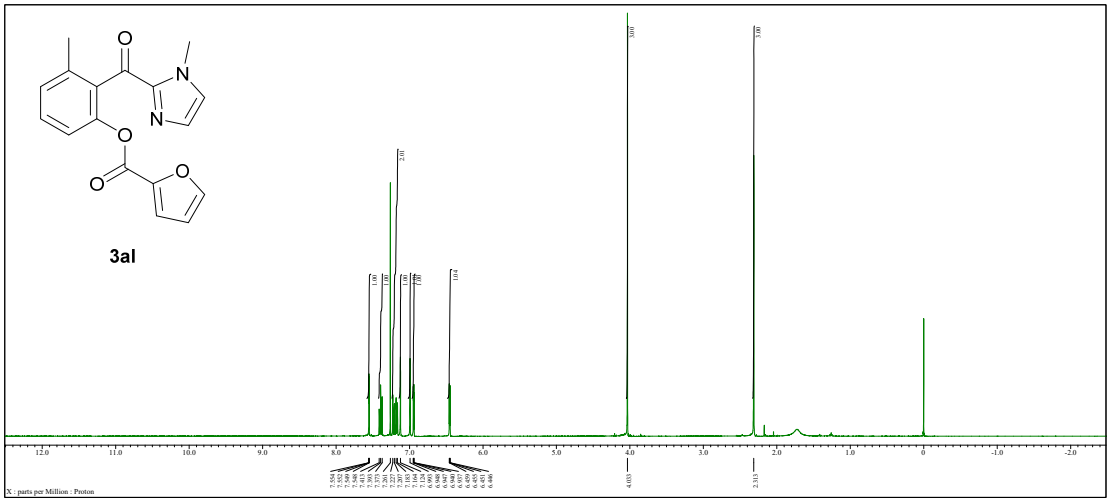
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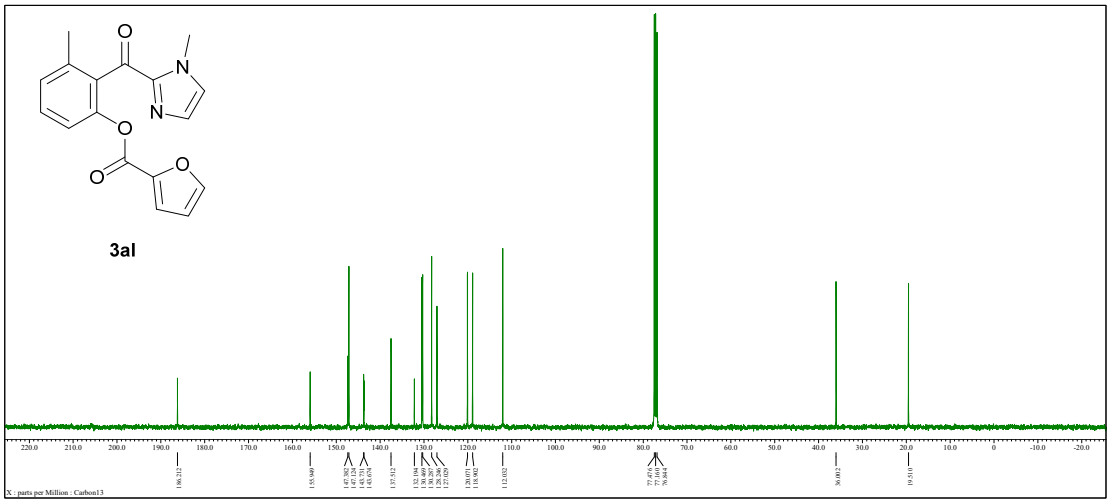
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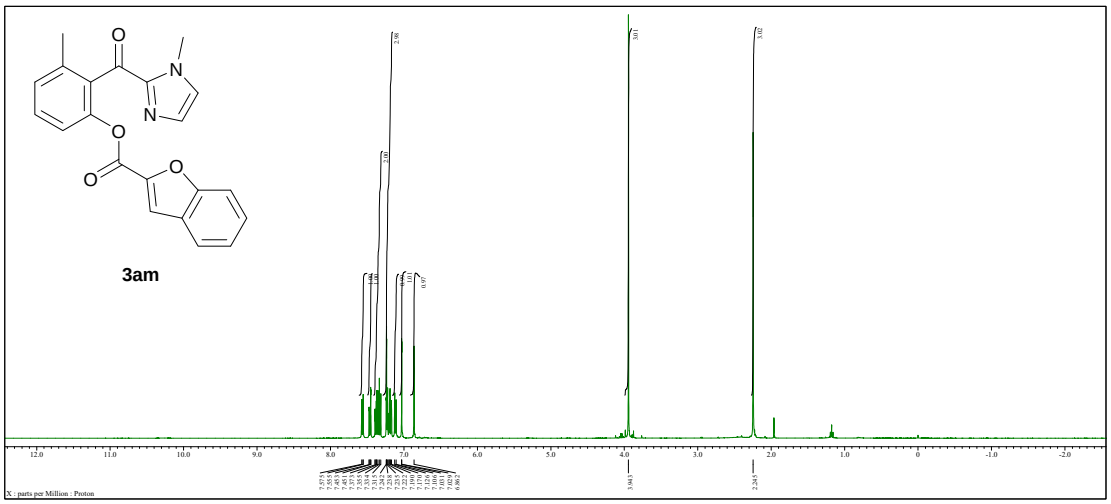
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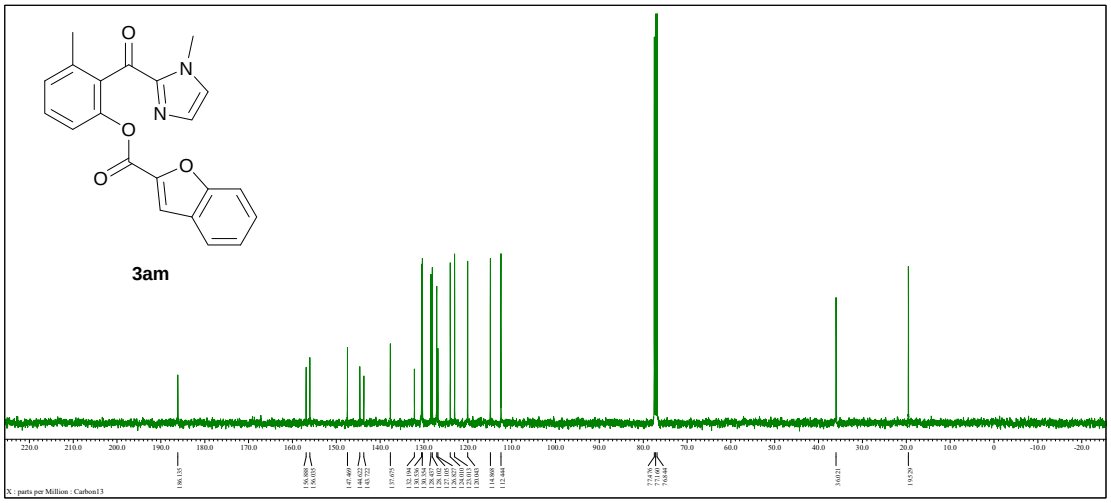
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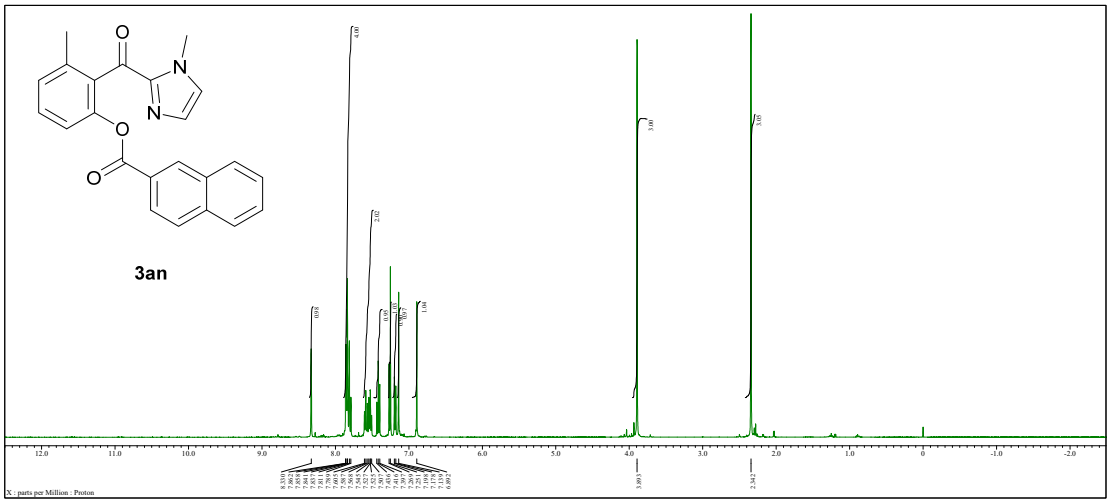
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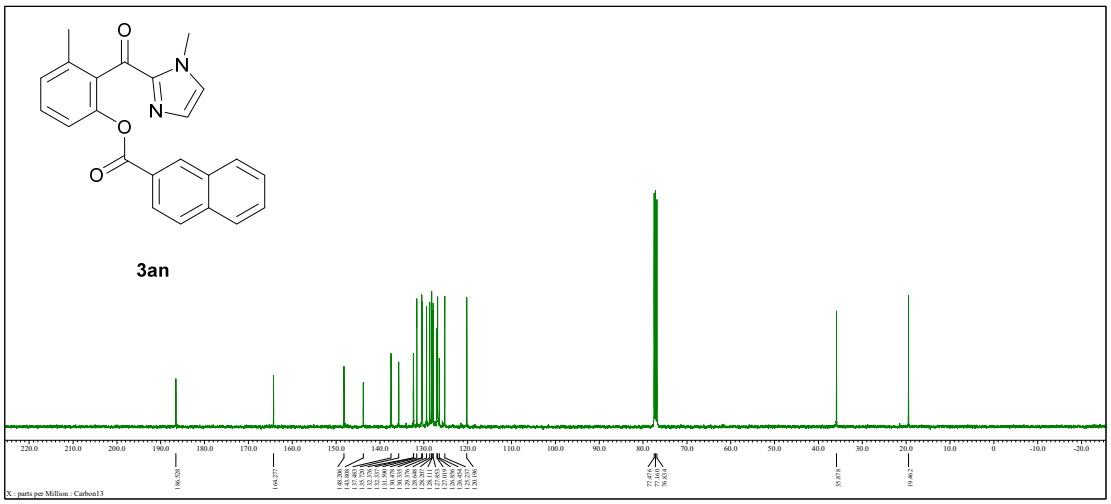
X : parts per Million : Proton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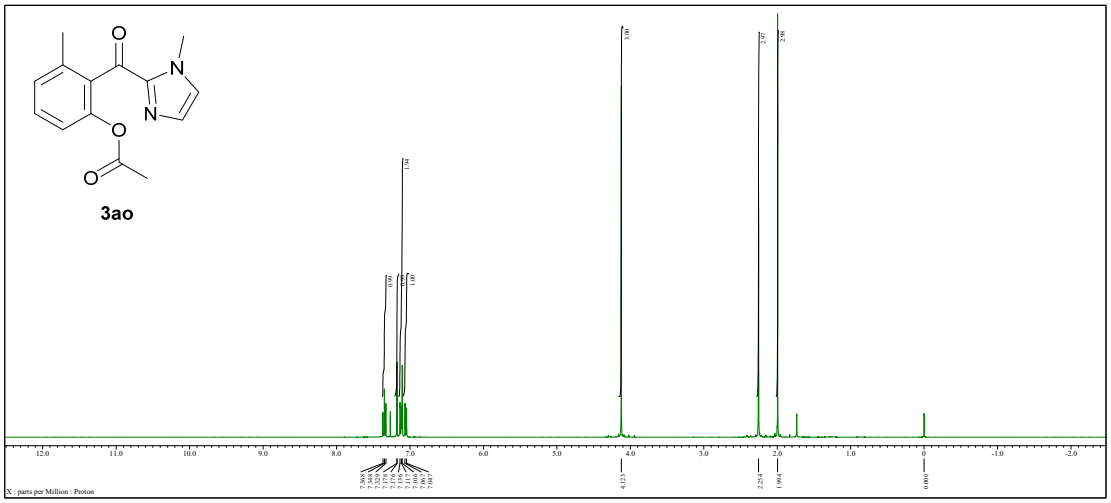
X : parts per Million : Carbon13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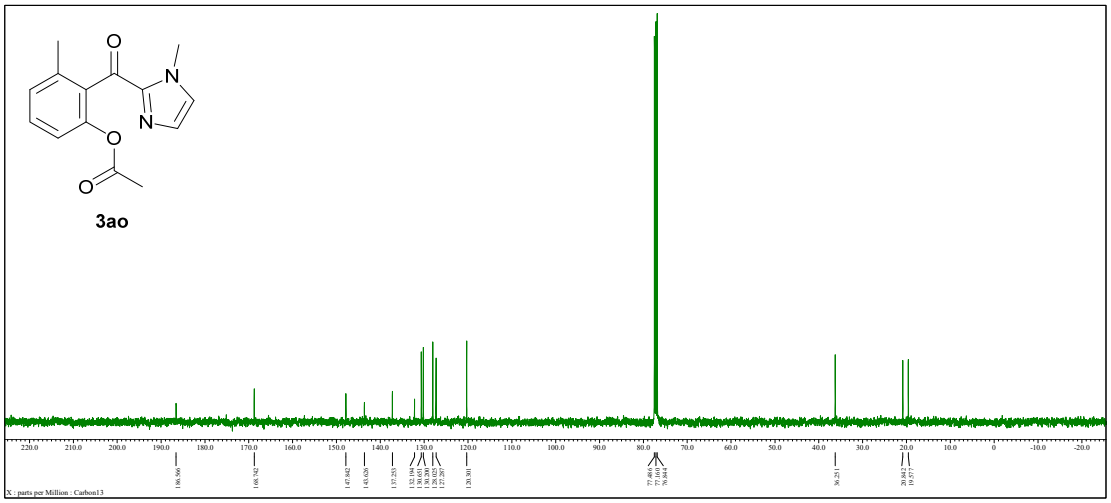
X : parts per Million : Proton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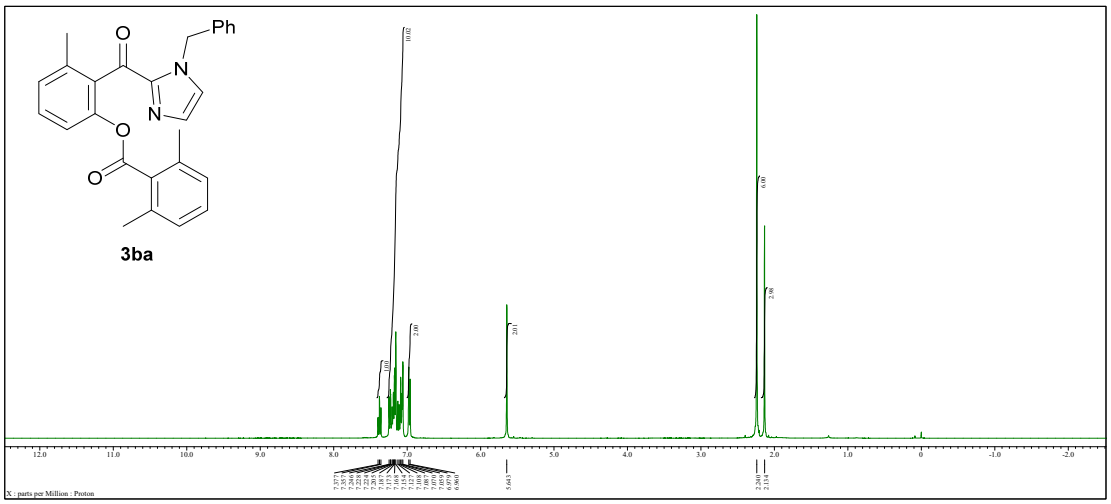
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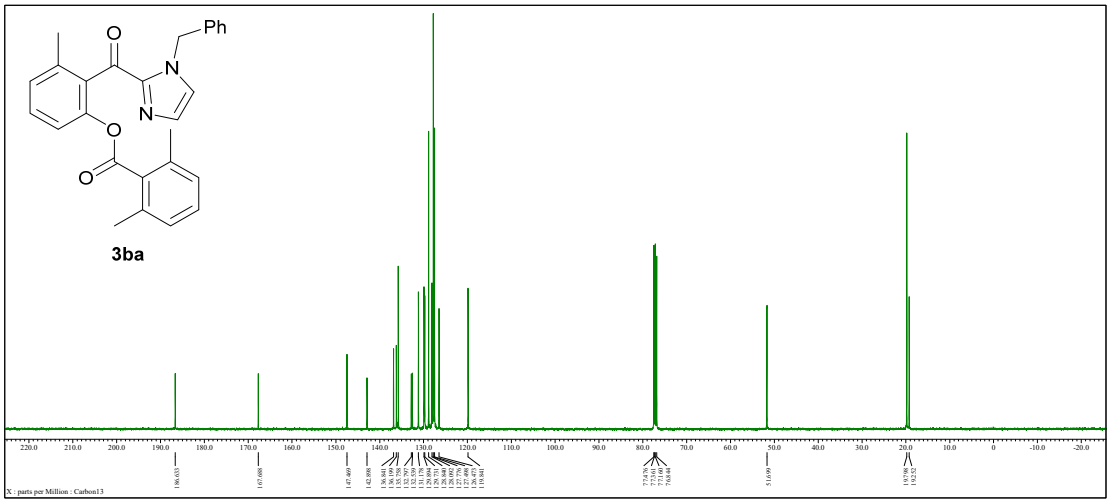
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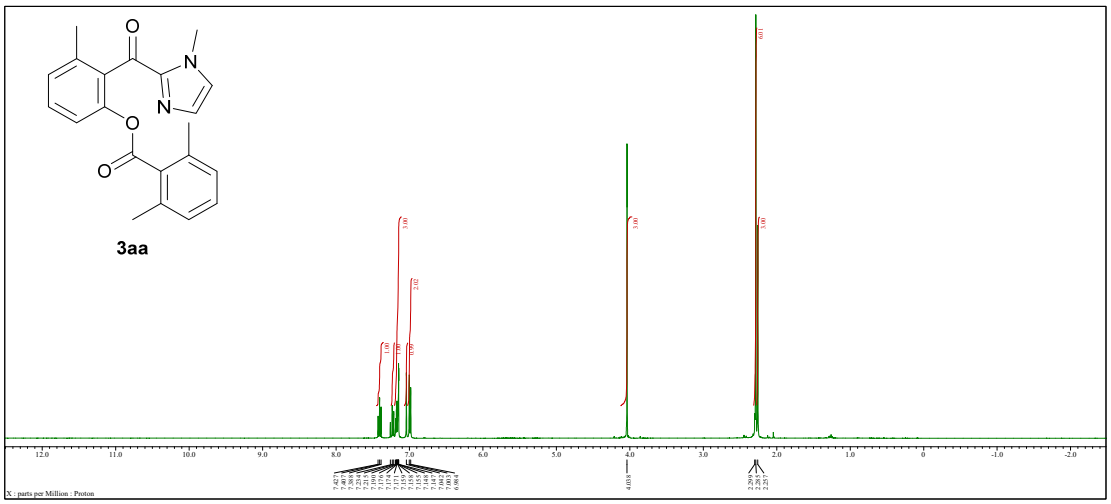
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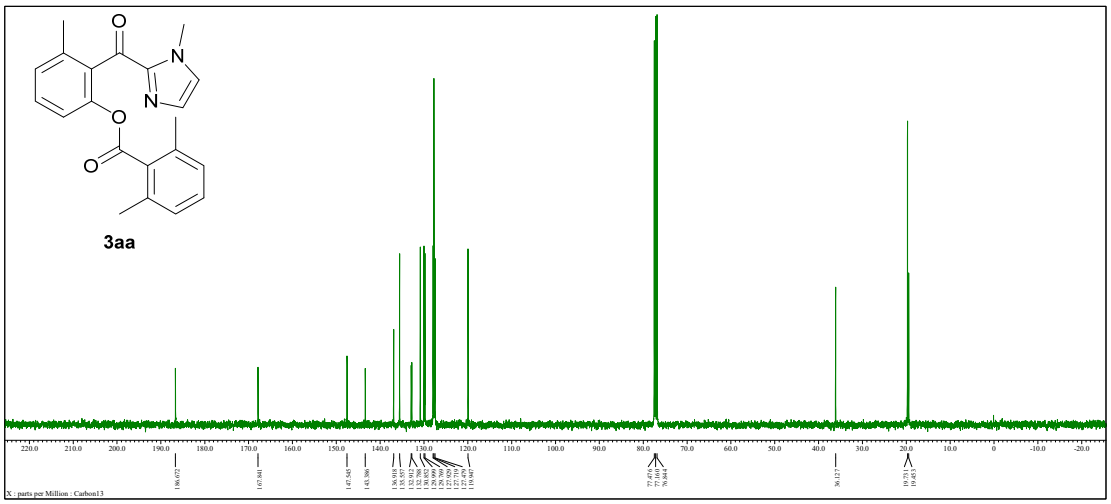
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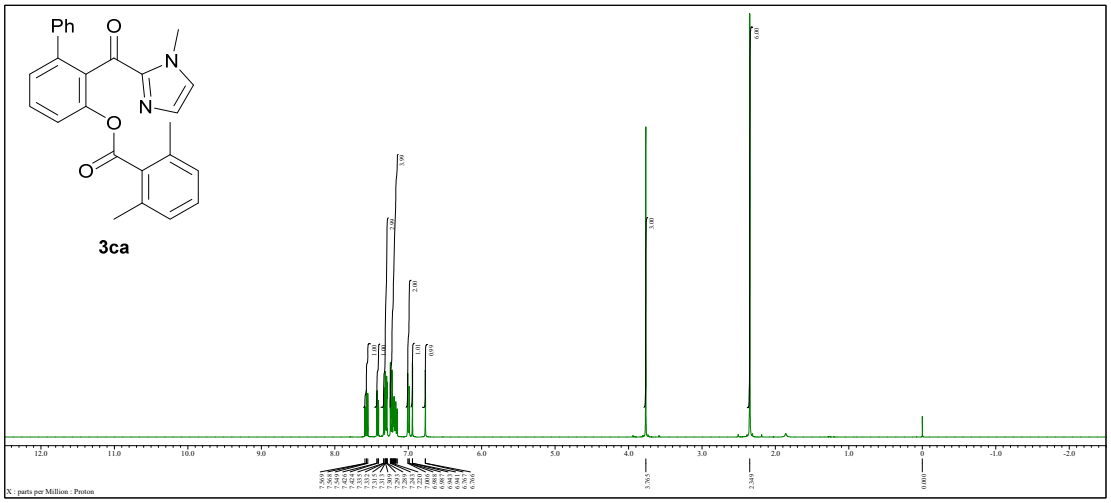
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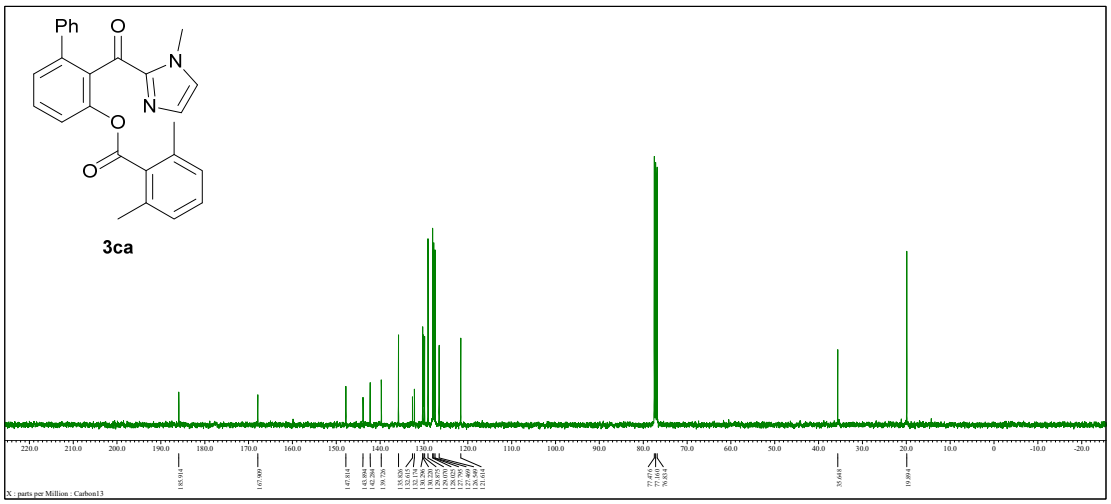
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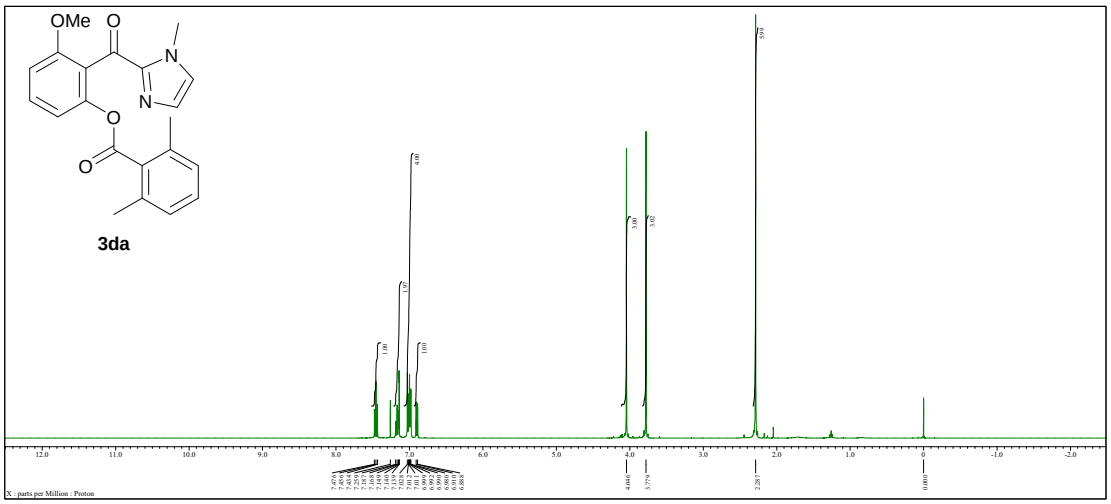
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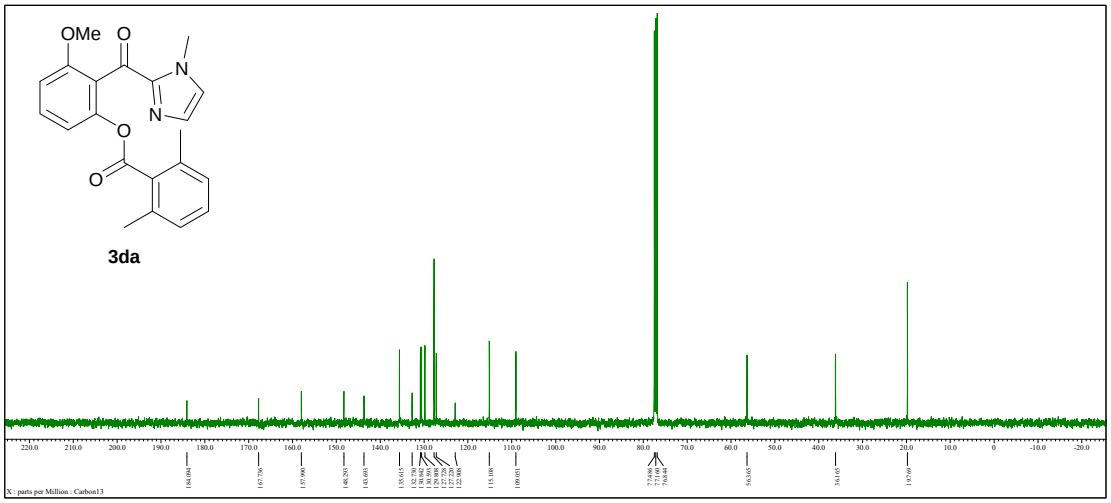
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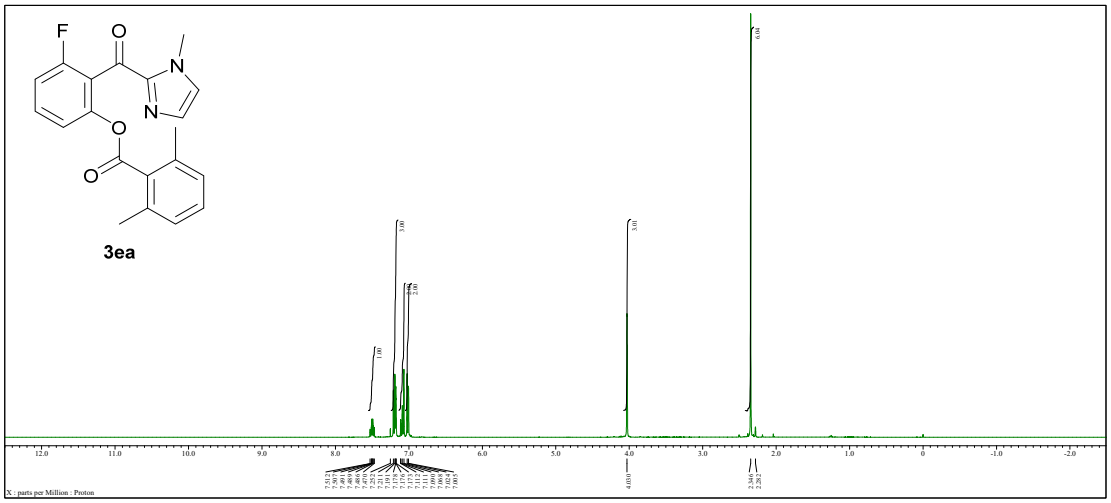
F
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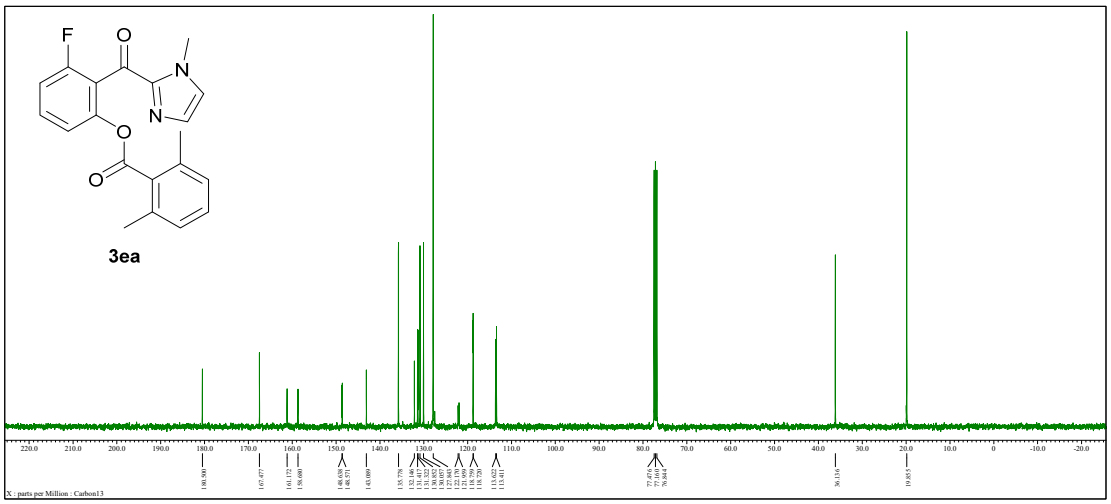
X : parts per Million : Proton


F
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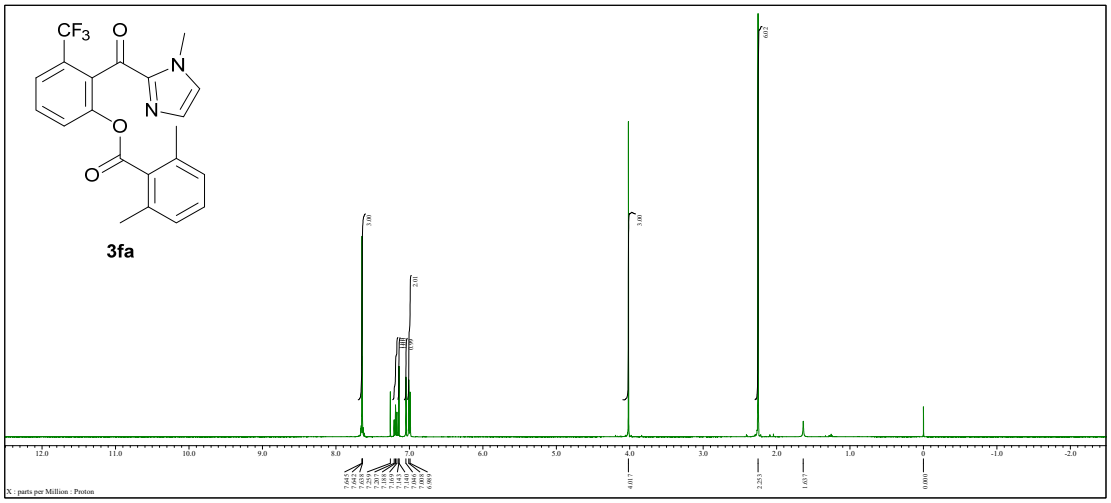
X : parts per Million : Carbon13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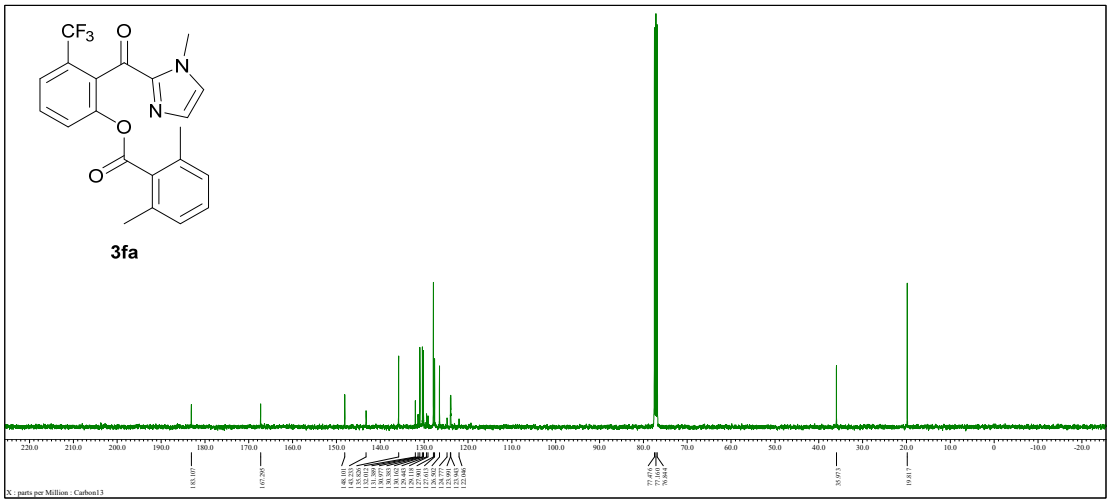
X : parts per Million : Proton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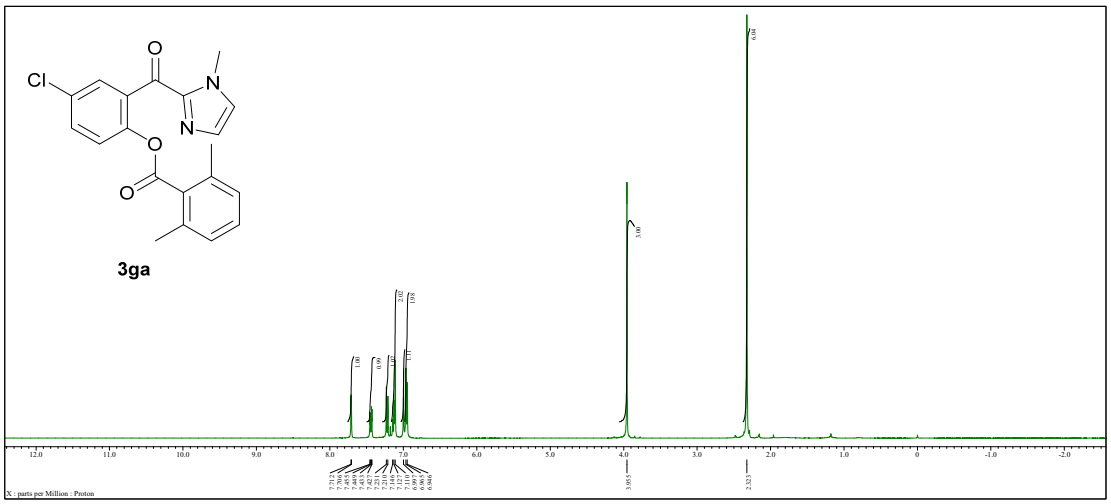
3fa


Cl
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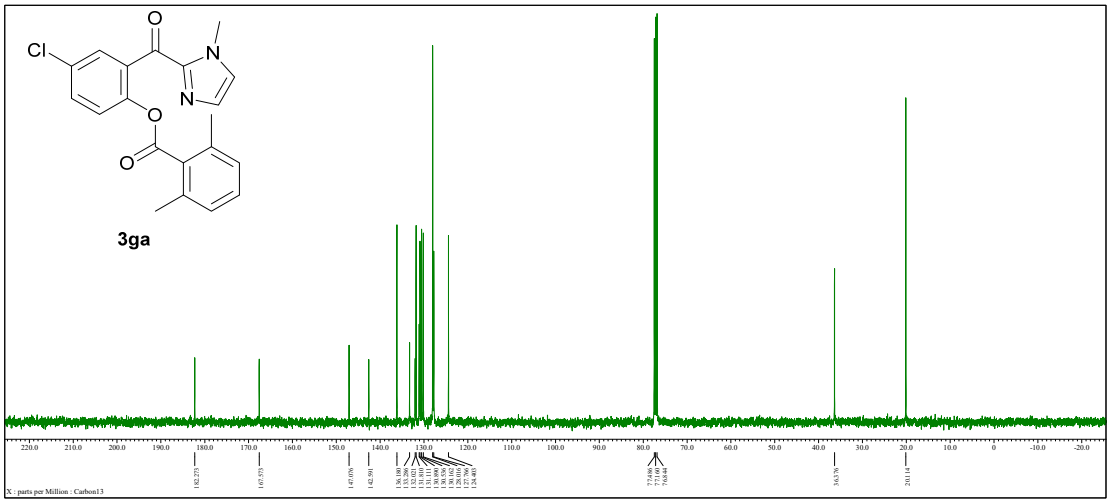
3ga


Cl
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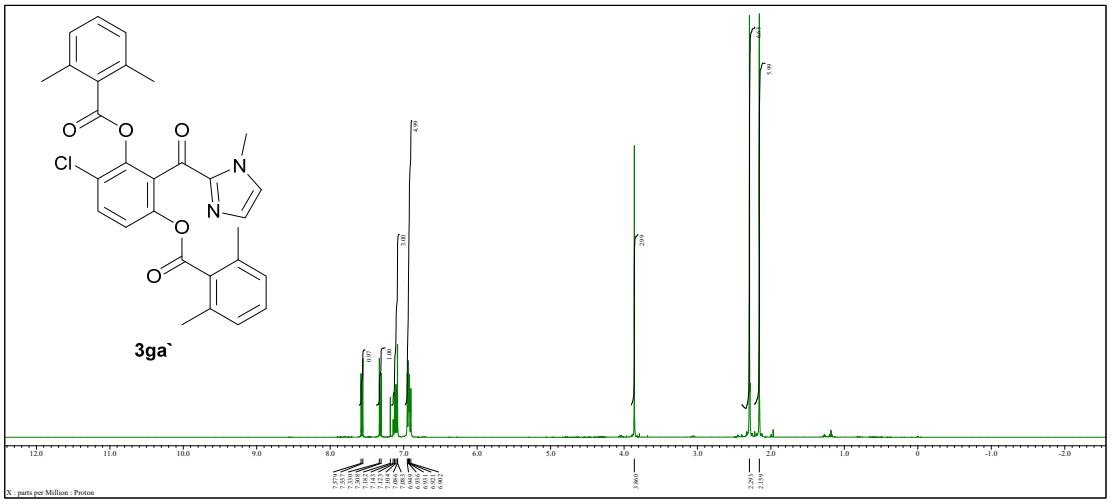
3ga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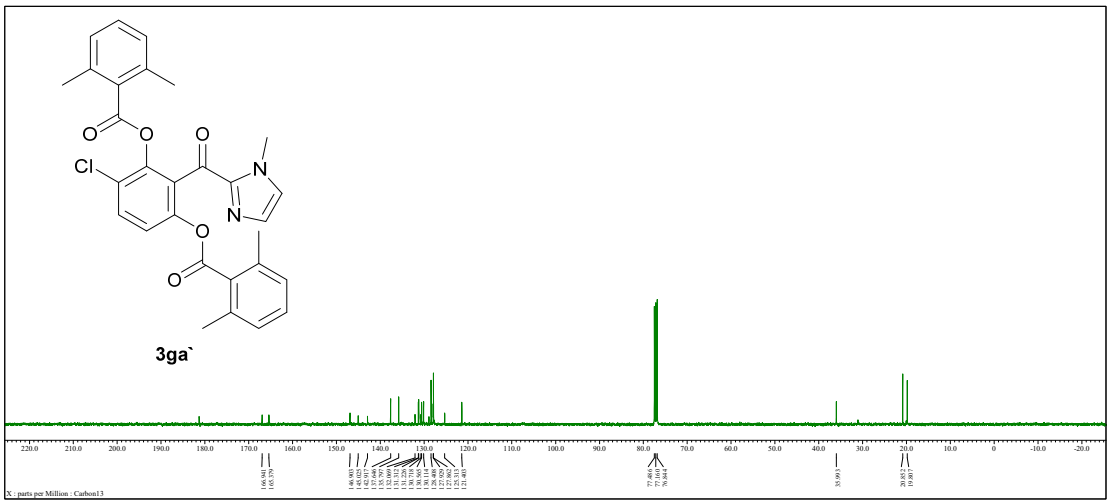
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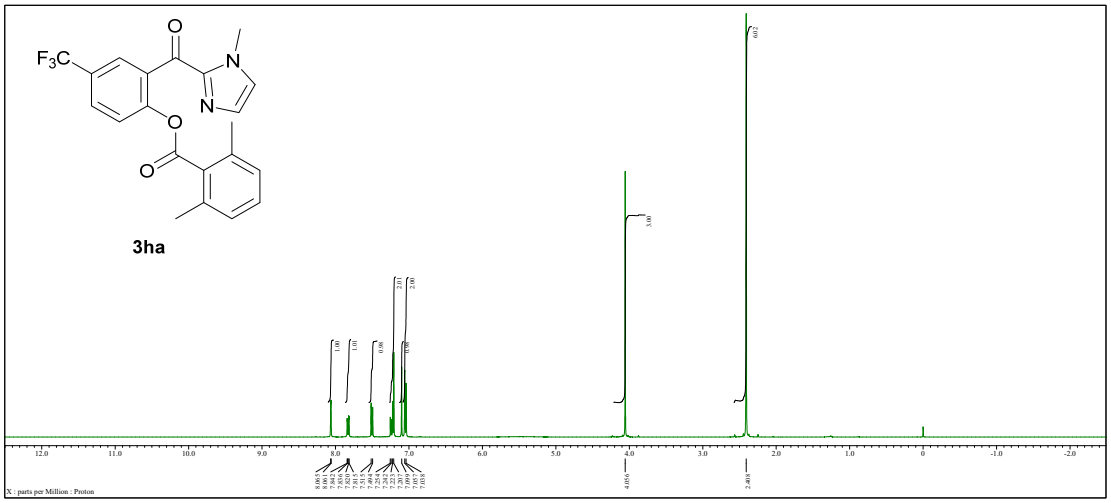
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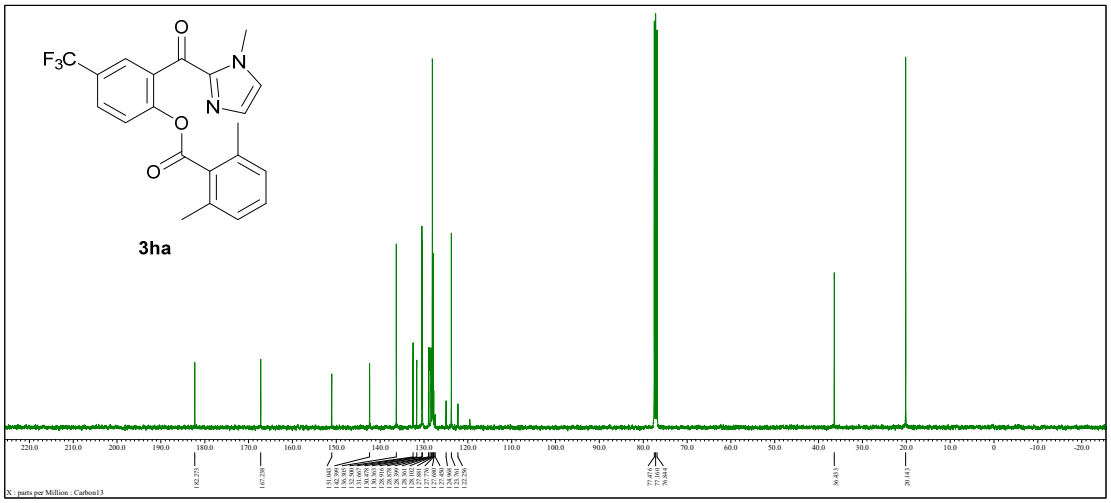
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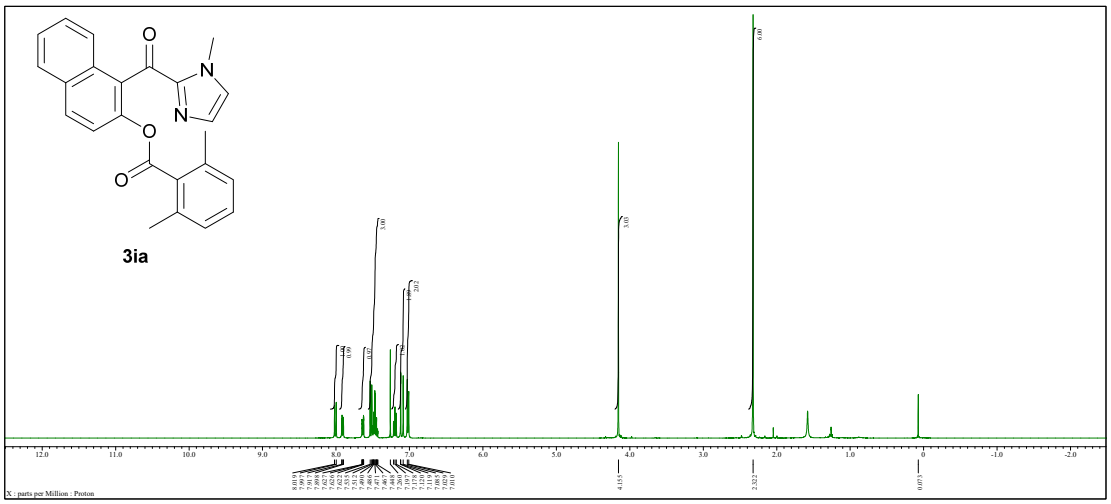
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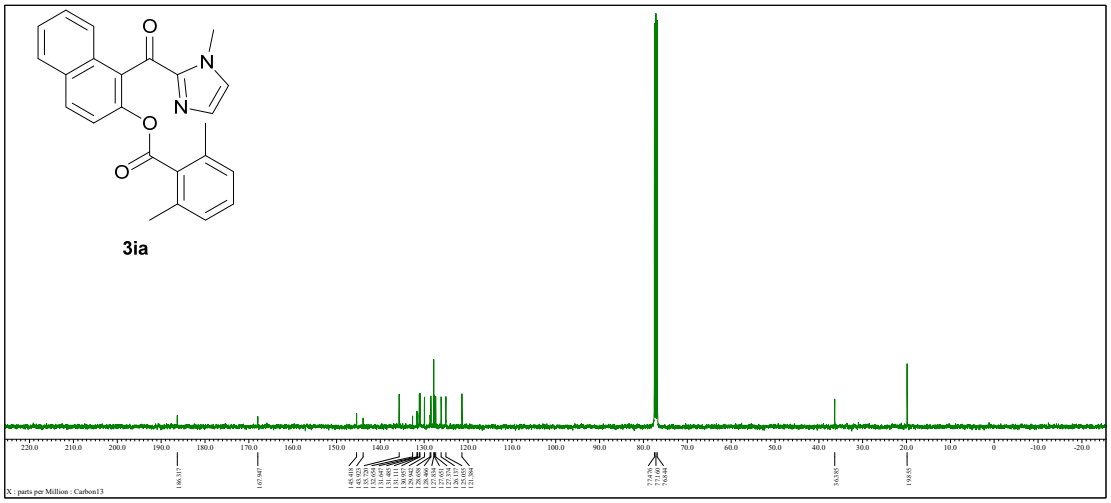
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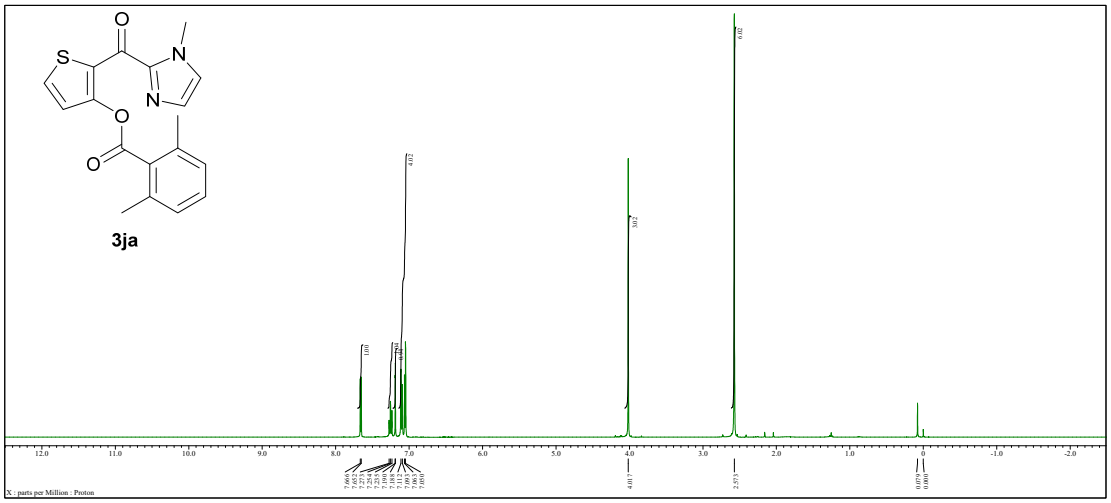
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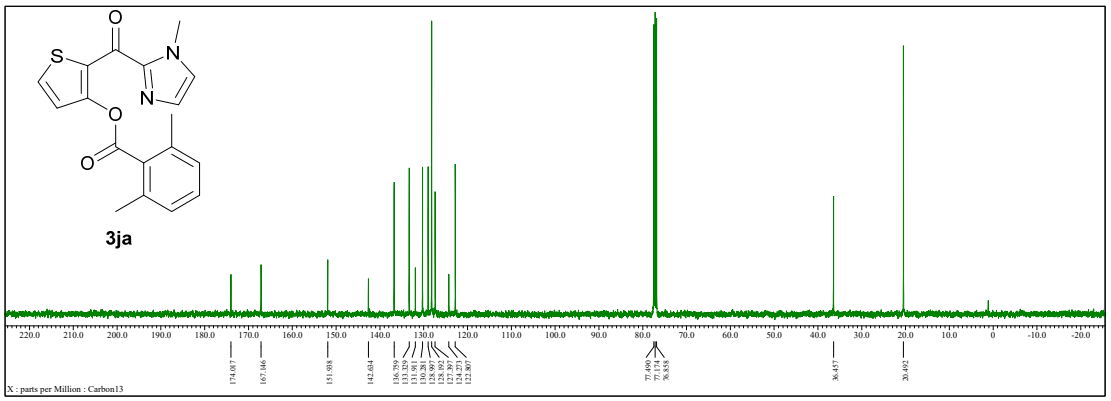
X : parts per Million : Proton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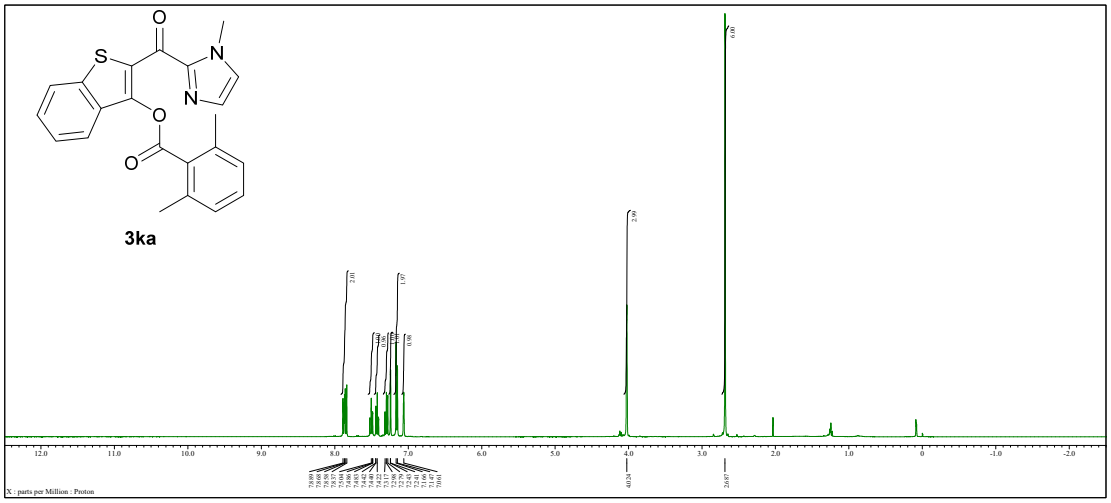
X : parts per Million : Carbon13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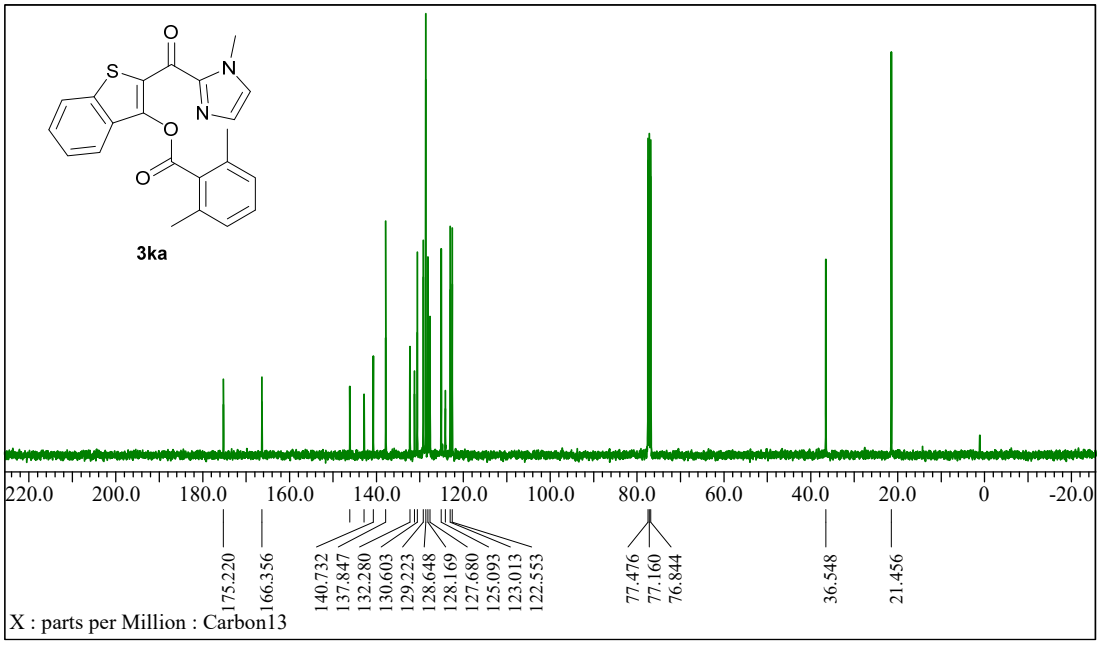
X : parts per Million : Proton


3ka
220.0
200.0
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0
-20.0
175.220
166.356
140.732
137.847
132.280
130.603
129.223
128.648
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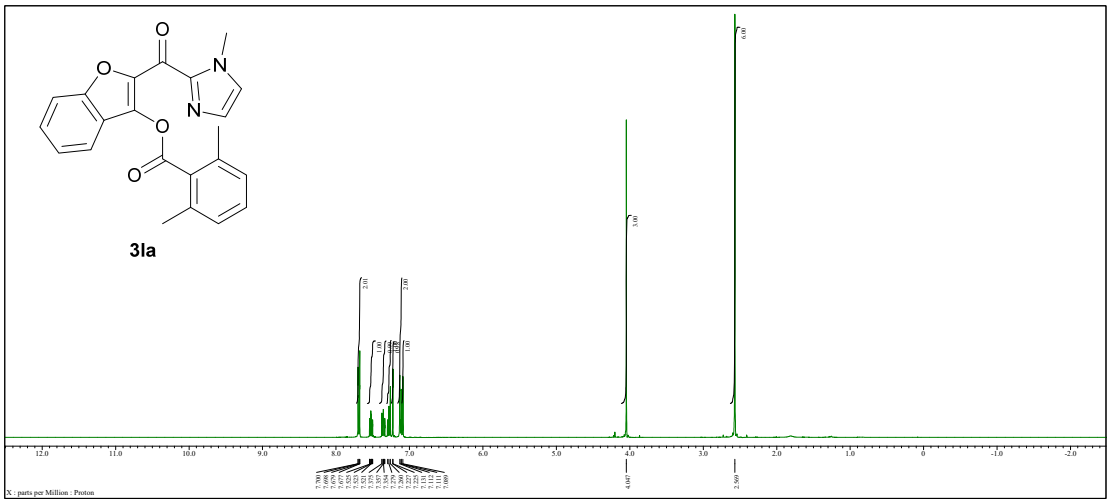
X : parts per Million : Carbon13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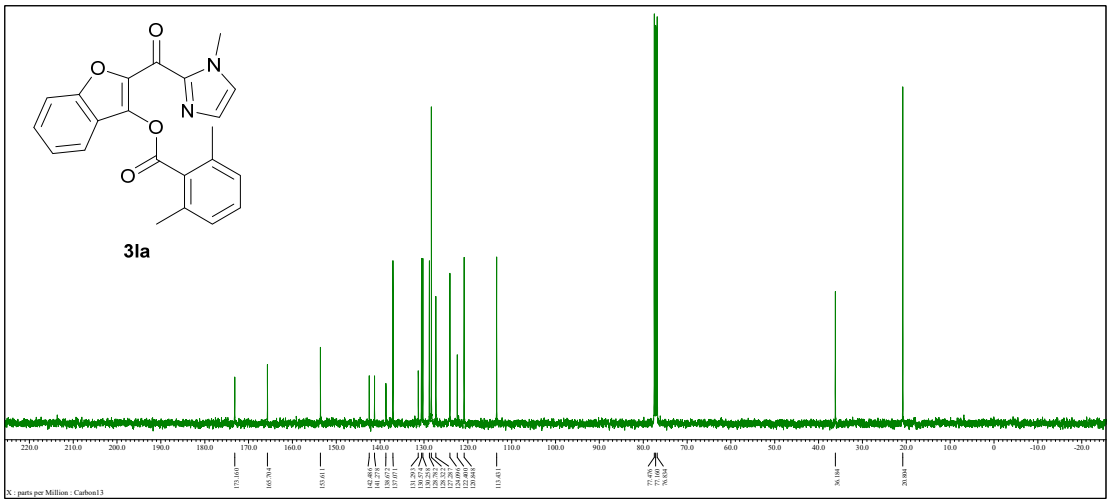
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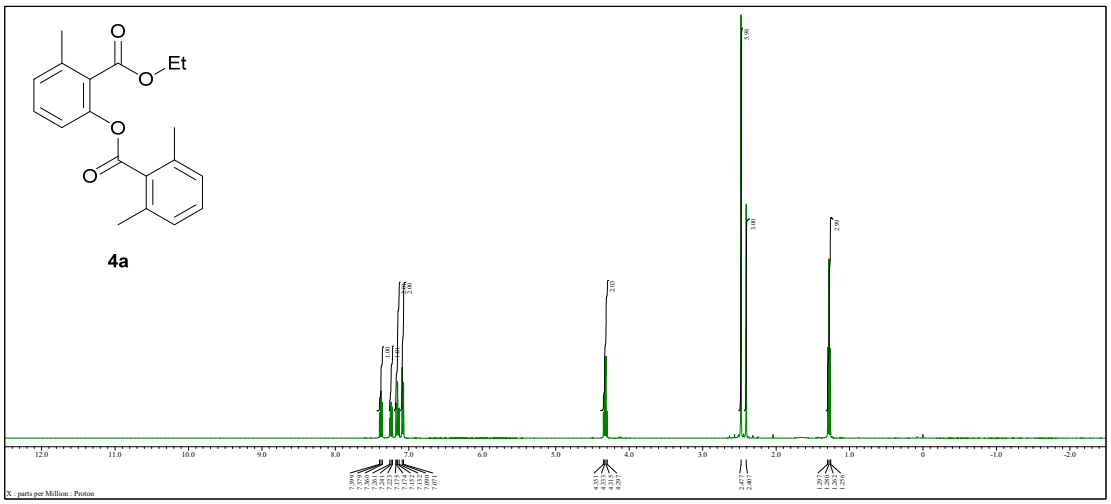
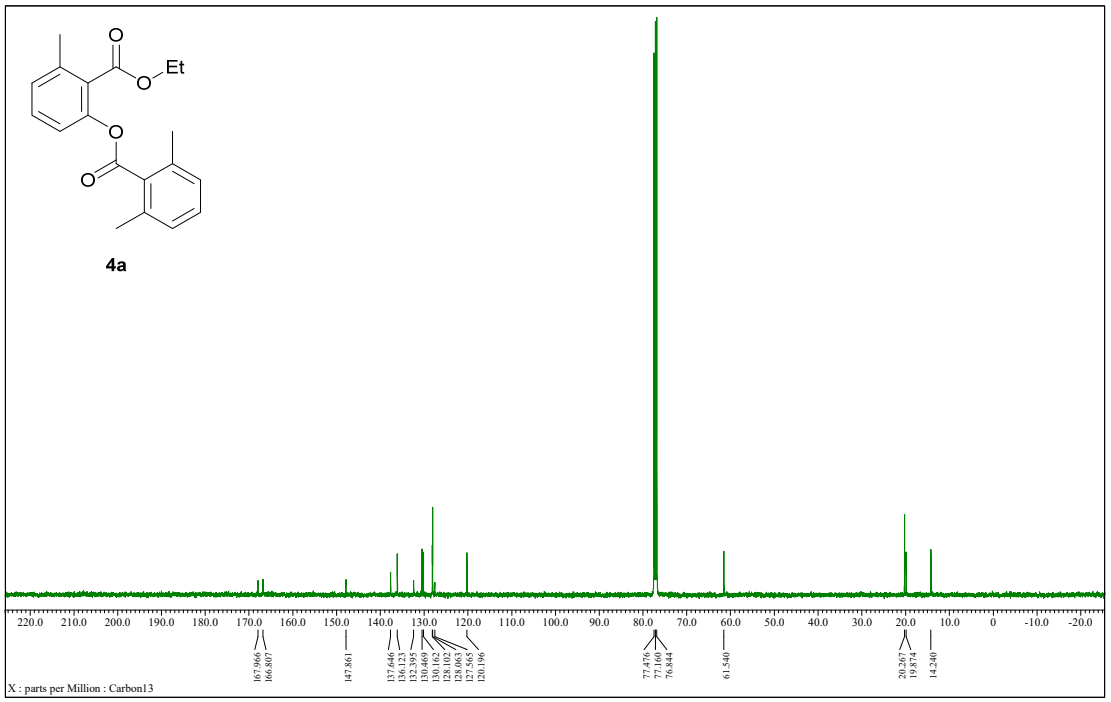
X : parts per Million : Carbon13


Et
4a
X : parts per Million : Proton


Et
4a
167.966
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137.646
136.123
132.395
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130.167
128.102
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20.267
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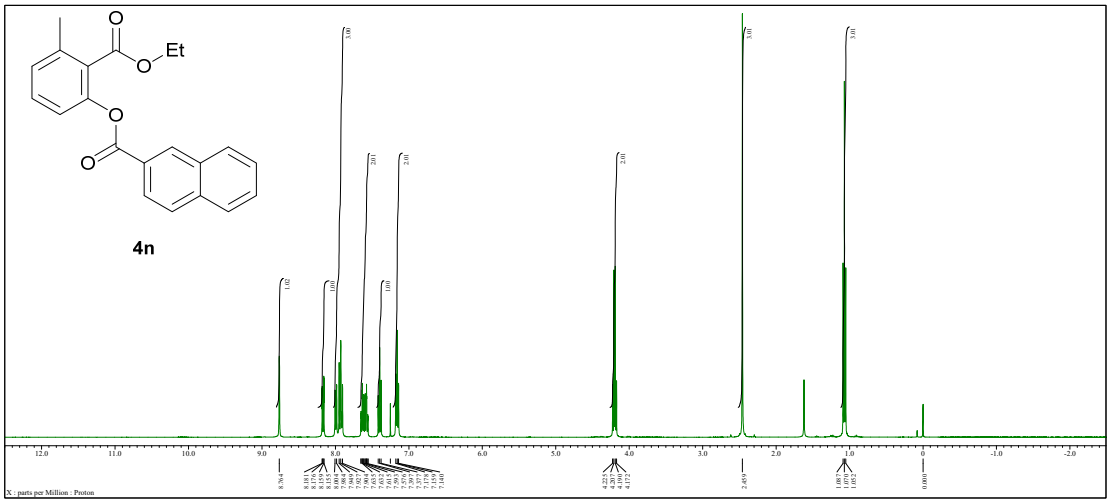
Et
4n
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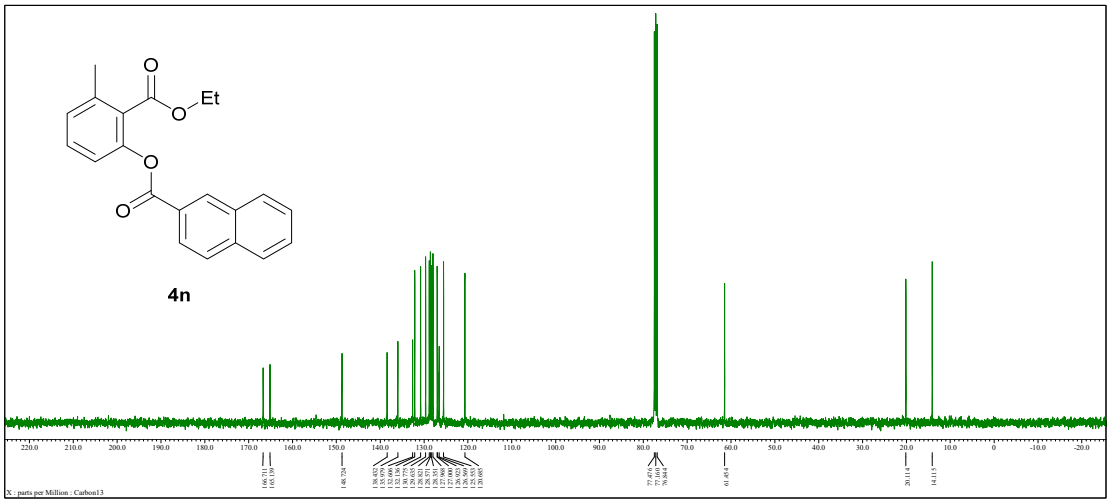
O
Et
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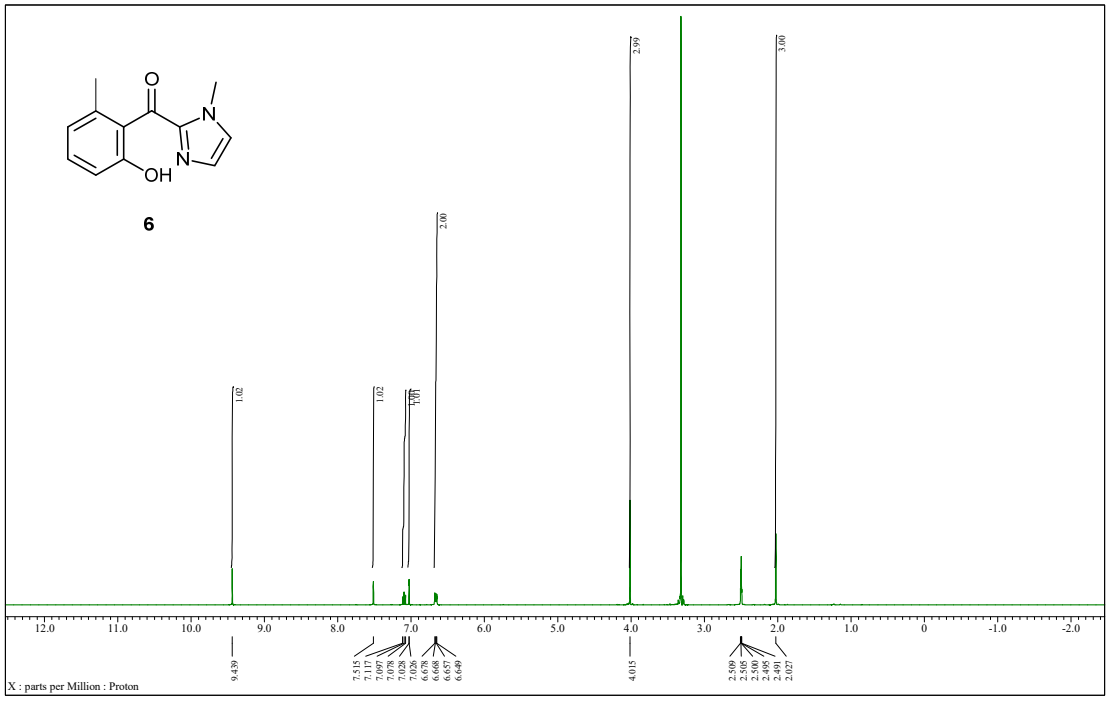
X : parts per Million : Carbon13


O
N
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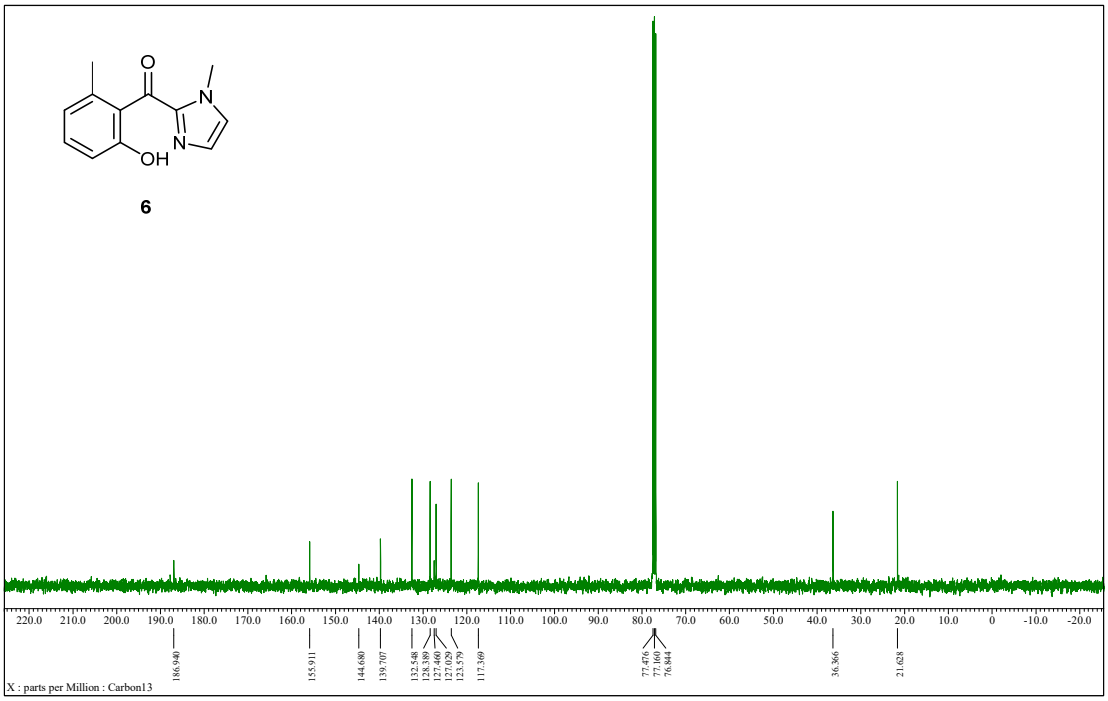
OH
6
2.99
3.00
2.00
1.02
1.02
1.00
X : parts per Million : Proton


O
N
N
OH
6
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
186.940
155.911
144.680
139.707
132.548
128.389
127.440
121.979
123.579
117.369
77.476
77.160
76.844
36.366
21.628
X : parts per Million : Carbon13