# (Dimethylamino)methylene Hydantoins as Building Blocks in the Synthesis of Oxoaplysinopsins and Parabanic Acids with Antifungal Activity

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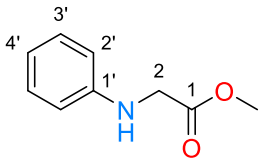
## Supplementary Information

### Contents

## 1. Experimental Section

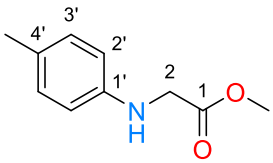
**General:** Melting points were determined on a Krüss KSP 1N capillary melting point apparatus. IR spectra were recorded on Perkin-Elmer 2000 and Smiths Detection IlluminatIR (ATR) spectrophotometers. $^{1}$H (300, 400, 500, 600 or 750 MHz) and $^{13}$C (75.4, 100, 125, 150 or 187.5 MHz) NMR spectra were obtained on Varian Mercury (300 MHz) MHz), Bruker Ascend 400 (400 MHz), Varian VNMR System (500 MHz), Bruker 600AVANCE III (600 MHz), and Bruker Avance III HD (750 MHz) spectrometers, with TMS and $CDCl_3$ as internal standards. Signal assignments were based on 2D NMR spectra (HSQC and HMBC). Mass spectra (MS) were acquired (ionization mode) on Thermo Polaris Q-Trace GC Ultra and Hewlett-Packard 5971A spectrometers. High-resolution mass spectra (HRMS) were captured (ionization mode) on Jeol JSM-GcMateII, Jeol JMS T100-LC AccuTOF DART, and and Bruker Compass micrOTOF-Q spectrometers. MW irradiation was achieved in a CEM MW reactor. A Multi-Therm Benchmark, Model H5000-HC was utilized as a heating and cooling shaker in enzymatic stability assays. Yeast growth was quantified in a Multiskan™ GO microplate spectrophotometer at 620 nm. Analytical thin-layer chromatography was carried out with silica gel 60 F254 coated 0.25 plates (E. Merck), which were visualized by a long- and short-wavelength UV lamp. Flash column chromatography was performed over silica gel (230-400 mesh, Natland). All air moisture sensitive reactions were conducted under an $N_2$ atmosphere in oven-dried glassware. Acetone was freshly distilled over $KMnO_4$ prior to use, as was $CH_2Cl_2$ and MeCN over 4Å molecular sieves, followed by over $CaH_2$. All other reagents were utilized without further purification.

**Methyl 2-(phenylamino)acetate (6a).**[1]



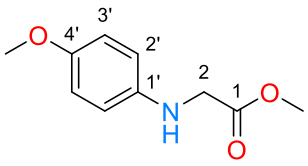

In a threaded ACE glass pressure tube sealed with a Teflon screw cap and equipped with a magnetic stirring bar, a solution of methyl 2-bromoacetate (**5**) (0.181 g, 1.20 mmol) in anhydrous MeCN (2.0 mL) was added dropwise at rt to a mixture of aniline (**4a**) (0.100 g, 1.07 mmol) and DIPEA (0.070 g, 0.54 mmol) in anhydrous MeCN (3.0 mL). The mixture was heated at 80 °C for 12 h. Afterwards, an aqueous solution of $Na_2S_2O_3$ (1.0 N, 10 mL) was added, and the mixture was stirred at rt for 10 min, and then extracted with EtOAc (2 x 15 mL). The organic layer was dried ($Na_2SO_4$), the solvent removed under vacuum, and the residue purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 95:5) to give **6a** (0.16 g, 90%) as an amber solid. $R_f$ 0.60 (hexane/EtOAc, 7:3); mp 44–45 ºC [Lit.[1] 46 ºC]. IR (film): $\bar{\upsilon}$ = 3395, 3374, 1735, 1609, 1585, 1518, 1441, 1370, 1261, 1229, 1141, 870, 754, 741, 694 cm$^{-1}$. $^{1}$H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H, $CO_2CH_3$), 3.92 (s, 2H, $CH_2CO_2$), 4.22 (br s, 1H, N*H*), 6.61 (d, *J* = 7.5 Hz, 2H, H-2'), 6.75 (tm, *J* = 7.5 Hz, 1H, H-4'), 7.16-7.24 (m, 2H, H-3'). $^{13}$C NMR (75.4 MHz, $CDCl_3$): δ 51.9 ($CH_2N$), 53.1 ($CO_2CH_3$), 112.2 (C-2'), 118.2 (C-4'), 129.1 (C-3'), 147.5 (C-1'), 171.2 ($CO_2$Me). MS (70 eV): *m/z* 165 ($M^+$, 8), 133 (18), 120 (24), 106 (22), 87 (34), 85 (100), 77 (60). HRMS (EI, [$M^+$]): *m/z* calcd for $C_9H_{11}NO_2$: 165.0790; found: 165.0791.

**Methyl 2-(*p*-tolylamino)acetate (6b).**[2,3]



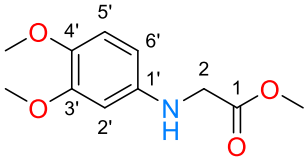

Following the procedure for **6a**, a mixture of *p*-toluidine (**4b**) (0.100 g, 0.93 mmol), **5** (0.157 g, 1.03 mmol), and DIPEA (0.060 g, 0.47 mmol) afforded **6b** (0.159 g, 95%) as an amber solid. $R_f$ 0.43 (hexane/EtOAc, 7:3); mp 76–77 ºC. IR (film): $\bar{\upsilon}$ = 3376, 1738, 1616, 1525, 1443, 1360, 1319, 1226, 1208, 1180, 1142, 810 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 2.24 (s, 3H, $CH_3$Ar), 3.77 (s, 3H, $CO_2CH_3$), 3.89 (s, 2H, $CH_2CO_2$), 4.13 (br s, 1H, N*H*), 6.51−6.56 (m, 2H, H-2'), 6.97−7.03 (m, 2H, H-3'). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 20.4 ($CH_3$Ar), 46.1 ($CH_2N$), 52.1 ($CO_2CH_3$), 113.1 (C-2'), 127.5 (C-4'), 129.8 (C-3'), 144.7 (C-1'), 171.8 ($CO_2$Me). MS (70 eV): *m/z* 179 ($M^+$, 92), 120 (100), 91 (60), 77 (24), 65 (40). HRMS (EI, [$M^+$]) *m/z* calcd for $C_{10}H_{13}NO_2$: 179.0946; found: 179.0952.

**Methyl 2-((4-methoxyphenyl)amino)acetate (6c).**[2]



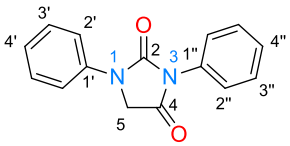
Following the procedure for **6a**, a mixture of *p*-anisidine (**4c**) (0.100 g, 0.81 mmol), **5** (0.137 g, 0.89 mmol), and DIPEA (0.052 g, 0.40 mmol) provided **6c** (0.138 g, 87%) as an amber solid, $R_f$ 0.50 (hexane/EtOAc, 7:3); mp 83–84 ºC. IR (film): ῡ = 3409, 2956, 2838, 1739, 1521, 1436, 1365, 1215, 1144, 1034, 823 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 3.74 (s, 3H, C*H*$_3$Oar), 3.77 (s, 3H, $CO_2CH_3$), 3.88 (s, 2H, C*H*$_2$CO$_2$), 6.56−6.61 (m, 2H, H-2'), 6.76−6.82 (m, 2H, H-3'). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 46.6 (*C*H$_2$N), 52.1 ($CO_2CH_3$), 55.7 (*C*H$_3$Oar), 114.3 (C-2'), 114.8 (C-3'), 141.1 (C-1'), 152.6 (C-4'), 171.9 (*C*O$_2$Me). MS (70 eV): *m/z* 195 ($M^+$, 28), 136 (100), 108 (15), 94 (5). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{10}H_{13}NO_3$: 195.0895; found: 195.0895.

**Methyl 2-((3,4-dimethoxyphenyl)amino)acetate (6d).**



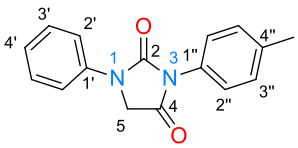
Following the procedure for **6a**, a mixture of 3,4-dimethoxyaniline (**4d**) (0.100 g, 0.65 mmol), **5** (0.110 g, 0.72 mmol), and DIPEA (0.043 g, 0.33 mmol) yielded **6d** (0.137 g, 93%) as a reddish brown solid, $R_f$ 0.50 (hexane/EtOAc, 7:3); mp 60.0–61.5 ºC. IR (film): ῡ = 3432, 3005, 2968, 1777, 1709, 1675, 1510, 1448, 1400, 1381, 1295, 1249, 1154, 1025, 813, 743 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 3.77 (s, 3H, $CO_2CH_3$), 3.80 (s, 3H, C*H*$_3$O-4'), 3.84 (s, 3H, C*H*$_3$O-3'), 3.89 (s, 2H, C*H*$_2$CO$_2$), 6.11 (dd, *J* = 8.6, 2.7 Hz, 1H, H-6'), 6.28 (d, *J* = 2.7 Hz, 1H, H-2'), 6.74 (d, *J* = 8.6 Hz, 1H, H-5'). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 46.2 (*C*H$_2$N), 52.0 ($CO_2CH_3$), 55.5 (C*H*$_3$O-3'), 56.3 (C*H*$_3$O-4'), 99.1 (C-2'), 103.1 (C-6'), 112.8 (C-5'), 141.7 (C-1'), 141.9 (C-4'), 149.8 (C-3'), 171.7 (*C*O$_2$CH$_3$). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{11}H_{15}NO_4$: 225.1001; found: 225.0998.

**1,3-Diphenylimidazolidine-2,4-dione (8a).**



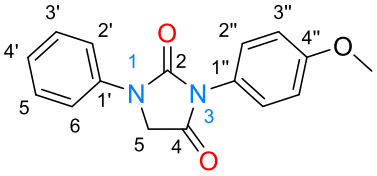
In a MW glass vial equipped with a magnetic stirring bar and sealed with a cap, a mixture of **6a** (0.100 g, 0.60 mmol) and **7a** (0.086 g, 0.72 mmol) was heated at 140 ºC for 2 h under $N_2$ atmosphere and MW irradiation (200 W). The crude mixture was extracted with $CH_2Cl_2$ (2 x 15 mL) and the organic layer was dried ($Na_2SO_4$). The solvent was removed under vacuum and the residue was purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 95:5) to generate **8a** (0.145 g, 95%) as a white solid. $R_f$ 0.46 (hexane/EtOAc, 7:3); mp 131–132 ºC. IR (KBr): ῡ = 2927, 1709, 1649, 1595, 1492, 1415, 1210, 753, 690 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 4.43 (s, 2H, H-5), 7.20 (t, *J* = 7.3 Hz, 1H, H-4'), 7.39−7.47 (m, 5H, H-3', H-2", H-4"), 7.48−7.52 (m, 2H, H-3"), 7.60−7.62 (m, 2H, H-2'). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 49.6 (C-5), 118.4 (C-2'), 124.6 (C-4'), 126.2 (C-2"), 128.4 (C-4"), 129.1 (C-3' or C-3"), 129.3 (C-3" or C-3'), 131.1 (C-1"), 137.3 (C-1'), 153.1 (C-2), 167.3 (C-4). MS (ESI): *m/z* 253 ($M^+$+H, 100), 150 (6), 134 (21), 106 (72). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{15}H_{12}N_2O_2$: 252.0899; found: 252.0905.

**1-Phenyl-3-(*p*-tolyl)imidazolidine-2,4-dione (8b).**



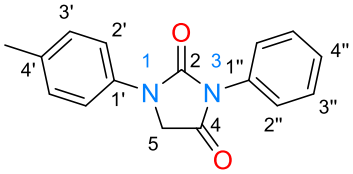
Following the procedure for **8a**, a mixture of **6a** (0.100 g, 0.60 mmol) and **7b** (0.097 g, 0.73 mmol) formed **8b** (0.156 g, 97%) as a white solid. $R_f$ 0.46 (hexane/EtOAc, 7:3); mp 149–150 ºC. IR (film): ῡ = 2958, 2938, 1776, 1697, 1520, 1500, 1441, 1406, 1256, 1149, 1031, 874, 823, 779, 740 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.42 (s, 3H, C*H*$_3$), 4.44 (s, 2H, H-5), 7.21 (tm, *J* = 7.4 Hz, 1H, H-4'), 7.29–7.37 (m, 4H, H-2", H-3"), 7.41–7.47 (m, 2H, H-3'), 7.61–7.66 (m, 2H, H-2'). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 21.3 (*C*H$_3$), 49.8 (C-5), 118.6 (C-2'), 124.6 (C-4'), 126.2 (C-2"), 128.6 (C-1"), 129.4 (C-3'), 129.9 (C-3"), 137.5 (C-1'), 138.6 (C-4"), 153.4 (C-2), 167.6 (C-4). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{16}H_{14}N_2O_2$: 266.1055; found: 266.1053.

**3-(4-Methoxyphenyl)-1-phenylimidazolidine-2,4-dione (8c).**



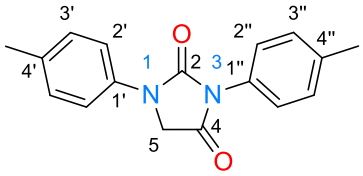
Following the procedure for **8a**, a mixture of **6a** (0.100 g, 0.60 mmol) and **7c** (0.109 g, 0.73 mmol) gave **8c** (0.166 g, 97%) as a white solid. $R_f$ 0.42 (hexane/EtOAc, 7:3); mp 130–131 ºC. IR (KBr): $\bar{\upsilon}$ = 3070, 2930, 1775, 1713, 1597, 1521, 1505, 1438, 1415, 1375, 1258, 1200, 1157, 1027, 819, 760 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 3.83 (s, 3H, C$H_3$O), 4.44 (s, 2H, H-5), 6.90–7.02 (m, 2H, H-3"), 7.19 (t, *J* = 7.5 Hz, 1H, H-4'), 7.31–7.36 (m, 2H, H-2"), 7.41 (t, *J* = 7.5 Hz, 2H, H-3'), 7.59-7.62 (m, 2H, H-2'). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 47.2 (C-5), 53.0 (*C*$H_3$O), 112.0 (C-3"), 115.9 (C-2'), 121.2 (C-1"), 122.1 (C-4'), 125.2 (C-2"), 126.8 (C-3'), 134.9 (C-1'), 150.9 (C-2), 156.9 (C-4"), 165.1 (C-4). MS (70 eV): *m/z* 282 ($M^+$, 100), 149 (44), 134 (13), 105 (73), 77 (19). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{16}H_{14}N_2O_3$: 282.1005; found: 282.1009.

**3-Phenyl-1-(*p*-tolyl)imidazolidine-2,4-dione (8d).**



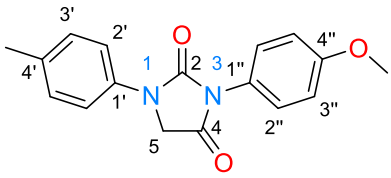
Following the procedure for **8a**, a mixture of **6b** (0.100 g, 0.56 mmol) and **7a** (0.080 g, 0.67 mmol) provided **8d** (0.147 g, 99%) as a white solid. $R_f$ 0.43 (hexane/EtOAc, 7:3); mp 144–145 ºC. IR (film): $\bar{\upsilon}$ = 2927, 1746, 1698, 1638, 1515, 1441, 1386, 1250, 1174, 1134, 1029, 802, 766, 698 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 2.36 (s, 3H, C$H_3$), 4.46 (s, 2H, H-5), 7.23 (d, *J* = 8.5 Hz, 2H, H-3'), 7.40–7.43 (m, 1H, H-4"), 7.45–7.52 (m, 6H, H-2', H-2", H-3"). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 20.8 (*C*$H_3$), 50.0 (C-5), 118.8 (C-2'), 126.3 (C-2"), 128.5 (C-4"), 129.1 (C-3"), 129.9 (C-3'), 131.4 (C-1"), 134.6 (C-4'), 134.9 (C-1'), 153.6 (C-2), 167.5 (C-4). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{16}H_{14}N_2O_2$: 266.1055; found: 266.1060.

**1,3-Di-*p*-tolylimidazolidine-2,4-dione (8e).**



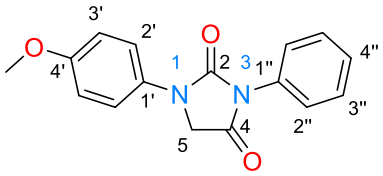
Following the procedure for **8a**, a mixture of **6b** (0.100 g, 0.56 mmol) and **7b** (0.089 g, 0.67 mmol) yielded **8e** (0.147 g, 94%) as a white solid. $R_f$ 0.43 (hexane/EtOAc, 7:3); mp 158–159 ºC. IR (film): $\bar{\upsilon}$ = 2937, 2843, 1769, 1709, 1509, 1446, 1412, 1301, 1243, 1153, 1023, 825 $cm^{-1}$. $^1H$ NMR (750 MHz, $CDCl_3$): δ 2.34 (s, 3H, C$H_3$-4'), 2.38 (s, 3H, C$H_3$-4"), 4.40 (s, 2H, H-5), 7.18–7.21 (m, 2H, H-3'), 7.26–7.29 (m, 2H, H-3"), 7.30–7.32 (m, 2H, H-2"), 7.46–7.49 (m, 2H, H-2'). $^{13}C$ NMR (187.5 MHz, $CDCl_3$): δ 20.8 (*C*$H_3$-4'), 21.2 (*C*$H_3$-4"), 50.0 (C-5), 118.7 (C-2'), 126.2 (C-2"), 128.7 (C-1"), 129.8 (C-3"), 129.9 (C-3'), 134.5 (C-4'), 135.0 (C-1'), 138.6 (C-4"), 153.4 (C-2), 167.7 (C-4). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{17}H_{16}N_2O_2$: 280.1212; found: 280.1213.

**3-(4-Methoxyphenyl)-1-(*p*-tolyl)imidazolidine-2,4-dione (8f).**



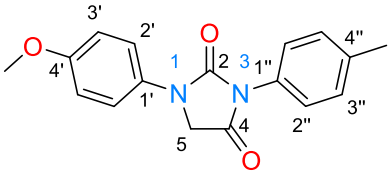
Following the procedure for **8a**, a mixture of **6b** (0.100 g, 0.56 mmol) and **7c** (0.100 g, 0.67 mmol) afforded **8f** (0.144 g, 87%) as a white solid. $R_f$ 0.40 (hexane/EtOAc, 7:3); mp 169–170 ºC. IR (KBr): $\bar{\upsilon}$ = 2965, 2940, 1769, 1715, 1616, 1513, 1435, 1411, 1380, 1302, 1256, 1158, 1035, 818 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 2.36 (s, 3H, C$H_3$), 3.85 (s, 3H, C$H_3$O), 4.44 (s, 2H, H-5), 6.99–7.03 (m, 2H, H-3"), 7.21–7.24 (m, 2H, H-3'), 7.34–7.37 (m, 2H, H-2"), 7.49–7.51 (m, 2H, H-2'). $^{13}C$ NMR (125 MHz, $CDCl_3$)**:** δ 20.8 (*C*$H_3$), 49.9 (C-5), 55.5 (*C*$H_3$O), 114.5 (C-3"), 118.7 (C-2'), 123.9 (C-1"), 127.7 (C-2"), 129.9 (C-3'), 134.5 (C-4'), 134.9 (C-1'), 153.5 (C-2), 159.4 (C-4"), 167.8 (C-4). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{17}H_{17}N_2O_3$: 297.1239; found: 297.1234.

**1-(4-Methoxyphenyl)-3-phenylimidazolidine-2,4-dione (8g).**



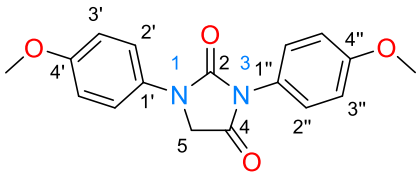
Following the procedure for **8a**, a mixture of **6c** (0.100 g, 0.51 mmol) and **7a** (0.073 g, 0.61 mmol) produced **8g** (0.140 g, 97%) as a white solid. $R_f$ 0.38 (hexane/EtOAc, 7:3); mp 150–151 ºC. IR (film): $\bar{\upsilon}$ = 2945, 1745, 1691, 1632, 1506, 1441, 1374, 1242, 1130, 968, 818, 759 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H, C*H*$_3$O), 4.41 (s, 2H, H-5), 6.91–6.97 (m, 2H, H-3'), 7.37–7.42 (m, 1H, H-4"), 7.43–7.52 (m, 6H, H-2', H-2", H-3"). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 50.3 (C-5), 55.5 (*C*H$_3$O), 114.6 (C-3'), 120.8 (C-2'), 126.3 (C-2"), 128.4 (C-4"), 129.2 (C-3"), 130.4 (C-1'), 131.4 (C-1"), 153.3 (C-2), 156.9 (C-4'), 167.6 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{16}H_{14}N_2O_3$: 282.1005; found: 282.1006.

**1-(4-Methoxyphenyl)-3-(*p*-tolyl)imidazolidine-2,4-dione (8h).**



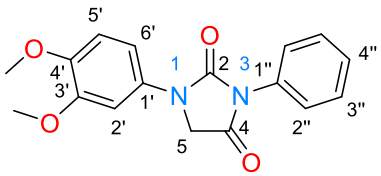
Following the procedure for **8a**, a mixture of **6c** (0.100 g, 0.51 mmol) and **7b** (0.081 g, 0.61 mmol) furnished **8h** (0.146 g, 96%) as a white solid. $R_f$ 0.28 (hexane/EtOAc, 7:3); mp 130–131 ºC. IR (film): $\bar{\upsilon}$ = 2965, 2934, 1774, 1711, 1510, 1444, 1405, 1378, 1245, 1147, 1030, 814, 744 cm$^{-1}$. $^1$H NMR (750 MHz, $CDCl_3$): δ 2.38 (s, 3H, C*H*$_3$), 3.80 (s, 3H, C*H*$_3$O), 4.38 (s, 2H, H-5), 6.91–6.94 (m, 2H, H-3'), 7.26–7.28 (m, 2H, H-3"), 7.29–7.32 (m, 2H, H-2"), 7.47–7.50 (m, 2H, H-2'). $^{13}$C NMR (187.5 MHz, $CDCl_3$): δ 21.2 (*C*H$_3$), 50.3 (C-5), 55.5 (*C*H$_3$O), 114.6 (C-3'), 120.8 (C-2'), 126.2 (C-2"), 128.8 (C-1"), 129.8 (C-3"), 130.5 (C-1'), 138.5 (C-4"), 153.5 (C-2), 156.8 (C-4'), 167.8 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{17}H_{16}N_2O_3$: 296.1161; found: 296.1162.

**1,3-Bis(4-methoxyphenyl)imidazolidine-2,4-dione (8i).**



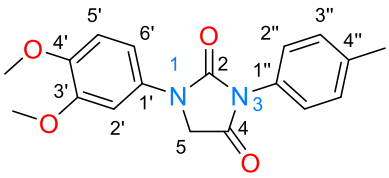
Following the procedure for **8a**, a mixture of **6c** (0.100 g, 0.51 mmol) and **7c** (0.091 g, 0.61 mmol) generated **8i** (0.150 g, 94%) as a white solid. $R_f$ 0.37 (hexane/EtOAc, 7:3); mp 131–132 ºC. IR (film): $\bar{\upsilon}$ = 2974, 2832, 1772, 1610, 1512, 1445, 1410, 1291, 1244, 1146, 1024, 819 cm$^{-1}$. $^1$H NMR (750 MHz, $CDCl_3$): δ 3.81 (s, 3H, C*H*$_3$O-4'), 3.83 (s, 3H, C*H*$_3$O-4"), 4.41 (s, 2H, H-5), 6.92–6.95 (m, 2H, H-3'), 6.98–7.01 (m, 2H, H-3"), 7.32–7.36 (m, 2H, H-2"), 7.48–7.51 (m, 2H, H-2'). $^{13}$C NMR (187.5 MHz, $CDCl_3$): δ 50.4 (C-5), 55.6 (*C*H$_3$O-4', *C*H$_3$O-4"), 114.5 (C-3"), 114.6 (C-3'), 120.7 (C-2'), 124.1 (C-1"), 127.7 (C-2"), 130.5 (C-1'), 153.6 (C-2), 156.8 (C-4'), 159.5 (C-4"), 167.9 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{17}H_{16}N_2O_4$: 312.1110; found: 312.1116.

**1-(3,4-Dimethoxyphenyl)-3-phenylimidazolidine-2,4-dione (8j).**



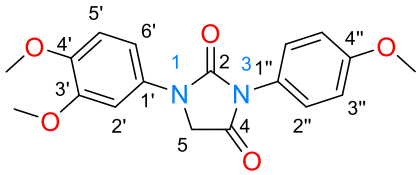
Following the procedure for **8a**, a mixture of **6d** (0.100 g, 0.44 mmol) and **7a** (0.063 g, 0.53 mmol) formed **8j** (0.135 g, 98%) as a yellow oil. $R_f$ 0.03 (hexane/EtOAc, 1:1). IR (film): $\bar{\upsilon}$ = 2928, 1746, 1694, 1642, 1498, 1452, 1387, 1240, 1135, 1034, 979, 844, 739 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 3.89 (s, 3H, C*H*$_3$O), 3.92 (s, 3H, C*H*$_3$O), 4.39 (s, 2H, H-5), 6.91 (d, *J* = 8.4 Hz, 1H, H-5'), 6.97–7.01 (m, 1H, H-4"), 7.03–7.07 (m, 2H, H-2', H-6'), 7.21–7.25 (m, 2H, H-3"), 7.28–7.32 (m, 2H, H-2"). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 51.3 (C-5), 56.1 (*C*H$_3$O), 56.1 (*C*H$_3$O), 111.6 (C-2'), 111.7 (C-5'), 119.2 (C-2"), 120.9 (C-6'), 123.1 (C-4"), 128.8 (C-3"), 133.9 (C-1'), 138.6 (C-1"), 149.2 (C-4'), 149.9 (C-3'), 154.4 (C-2), 170.7 (C-4). HRMS (ESI-TOF, [M$^+$]): *m/z* calcd for $C_{17}H_{16}N_2O_4$: 312.1110; [M$^+$+Na(23)]: 335.1008; found [M$^+$+Na(23)]: 335.1002.

**1-(3,4-Dimethoxyphenyl)-3-(*p*-tolyl)imidazolidine-2,4-dione (8k).**



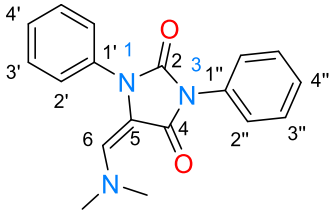
Following the procedure for **8a**, a mixture of **6d** (0.100 g, 0.44 mmol) and **7b** (0.071 g, 0.53 mmol) delivered **8k** (0.137 g, 95%) as a yellow solid. $R_f$ 0.03 (hexane/EtOAc, 1:1); mp 181–182 ºC. IR (film): $\bar{\upsilon}$ = 2930, 1736, 1698, 1645, 1504, 1450, 1378, 1298, 1252, 1134, 1028, 978, 844, 738 cm$^{-1}$. $^1$H NMR (750 MHz, $CDCl_3$): δ 2.39 (s, 3H, C$H_3$), 3.88 (s, 3H, C$H_3$O-4'), 3.89 (s, 2H, C$H_3$O-3'), 4.41 (s, 2H, H-5), 6.76 (dd, *J* = 8.6, 2.6 Hz, 1H, H-6'), 6.87 (d, *J* = 8.6 Hz, 1H, H-5'), 7.26–7.33 (m, 4H, H-2", H-3"), 7.60 (d, *J* = 2.6 Hz, 1H, H-2'). $^{13}$C NMR (187.5 MHz, $CDCl_3$): δ 21.2 (*C*$H_3$-4''), 50.2 (C-5), 56.0 (*C*$H_3$O-4'), 56.1 (*C*$H_3$O-3'), 104.2 (C-2'), 110.0 (C-6'), 111.3 (C-5'), 126.2 (C-2"), 128.6 (C-1"), 129.9 (C-3"), 131.1 (C-1'), 138.7 (C-4"), 146.3 (C-4'), 149.4 (C-3'), 153.5 (C-2), 167.6 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{18}H_{18}N_2O_4$: 326.1267; found: 326.1267.

**1-(3,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)imidazolidine-2,4-dione (8l).**



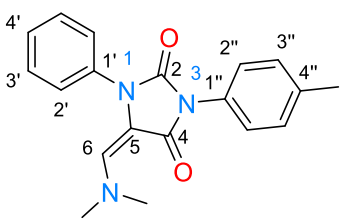
Following the procedure for **8a**, a mixture of **6d** (0.100 g, 0.44 mmol) and **7c** (0.079 g, 0.53 mmol) yielded **8l** (0.140 g, 92%) as a yellow oil. $R_f$ 0.01 (hexane/EtOAc, 1:1). IR (film): $\bar{\upsilon}$ = 2926, 1733, 1689, 1642, 1595, 1489, 1374, 1311, 1244, 1136, 964, 918, 744, 696 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 3.82 (s, 3H, C$H_3$O-4"), 3.88 (s, 3H, C$H_3$O-4'), 3.89 (s, 3H, C$H_3$O-3'), 4.42 (s, 2H, H-5), 6.75 (dd, *J* = 8.7, 2.6 Hz, 1H, H-6'), 6.86 (d, *J* = 8.7 Hz, 1H, H-5'), 6.97–7.02 (m, 2H, H-3"), 7.30–7.36 (m, 2H, H-2"), 7.61 (d, *J* = 2.6 Hz, 1H, H-2'). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 50.3 (C-5), 55.6 (*C*$H_3$O-4"), 56.1 (*C*$H_3$O), 56.2 (*C*$H_3$O), 104.2 (C-2'), 110.0 (C-6'), 111.3 (C-5'), 114.6 (C-3"), 124.0 (C-1"), 127.8 (C-2"), 131.2 (C-1'), 146.3 (C-4'), 149.5 (C-3'), 153.7 (C-2), 159.6 (C-4"), 167.8 (C-4). HRMS (ESI-TOF, [M$^+$]): *m/z* calcd for $C_{18}H_{18}N_2O_5$: 342.1216; [M$^+$+Na(23)]: 365.1113; found [M$^+$+Na(23)]: 365.1108.

**(*E*)-5-((Dimethylamino)methylene)-1,3-diphenylimidazolidine-2,4-dione (9a).**



In a MW glass vial equipped with a magnetic stirring bar and sealed with a cap, a mixture of **6a** (0.100 g, 0.606 mmol) and **7a** (0.087 g, 0.73 mmol) was subjected to MW irradiation (200 W) at 140 °C for 1.0 h under an $N_2$ atmosphere. Subsequently, DMFDMA (0.216 g, 1.82 mmol) was added, followed by MW (200 W) irradiated at 140 °C for 30 min. The crude was extracted with $CH_2Cl_2$ (2 x 25 mL), the organic layer was dried ($Na_2SO_4$), and the solvent removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 9:1), resulting in **9a** (0.170 g, 91%) as white crystals. $R_f$ 0.31 (hexane/EtOAc, 7:3); mp 186–187 ºC. IR (film): $\bar{\upsilon}$ = 3054, 1746, 1698, 1640, 1432, 1379, 1254, 1133, 768, 745, 695, 635 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 2.62 (s, 6H, N(C$H_3$)$_2$), 6.99 (s, 1H, C*H*=), 7.25–7.36 (m, 2H, H-4', H-4"), 7.38–7.52 (m, 8H, ArH). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 43.2 (N(*C*$H_3$)$_2$), 102.3 (C-5), 124.6 (C-2'), 126.3 (C-4'), 126.4 (C-2"), 127.7 (C-4"), 128.8 (C-3' or C-3"), 129.0 (C-3" or C-3'), 132.5 (C-1"), 133.3 (*C*H=), 138.1 (C-1'), 153.5 (C-2), 164.0 (C-4). EM (70 eV): *m/z* 307 (M$^+$, 100), 292 (28), 160 (32), 159 (28), 104 (14), 83 (17), 77 (13). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{18}H_{17}N_3O_2$: 307.1321; found: 307.1326.

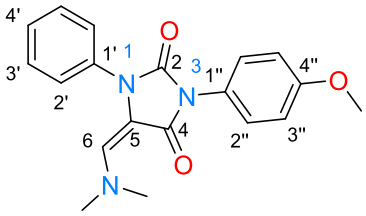
**(*E*)-5-((Dimethylamino)methylene)-1-phenyl-3-(*p*-tolyl)imidazolidine-2,4-dione (9b).**



Following the procedure for **9a**, a mixture of **6a** (0.100 g, 0.606 mmol), **7b** (0.097 g, 0.73 mmol), and DMFDMA (0.216 g, 1.82 mmol) gave **9b** (0.187 g, 96%) as a pale yellow solid. $R_f$ 0.29 (hexane/EtOAc, 7:3); mp 143.5–144.2 °C. IR (film): $\bar{\upsilon}$ = 3327, 3283, 1711, 1646, 1593, 1546, 1497, 1440, 1315, 1230, 751, 694 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H, C$H_3$), 2.63 (s, 6H, N(C$H_3$)$_2$), 6.99 (s, 1H, C*H*=), 7.23–7.31 (m, 3H, H-4', H-3"), 7.35–7.39 (m, 2H, H-2"), 7.40–7.44 (m, 4H, H-2', H-3'). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.2 (*C*$H_3$-4"), 43.1 (N(*C*$H_3$)$_2$), 102.4 (C-5),

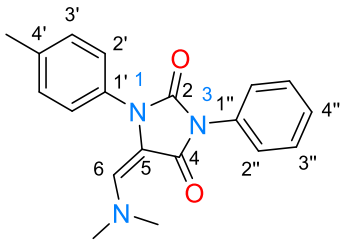
124.6 (C-2'), 126.2 (C-4'), 126.3 (C-2"), 129.0 (C-3'), 129.6 (C-3"), 129.8 (C-1"), 133.2 (*C*H=), 137.6 (C-4"), 138.2 (C-1'), 153.7 (C-2), 164.2 (C-4). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{19}H_{19}N_3O_2$: 321.1477; found: 321.1477.

**(*E*)-5-((Dimethylamino)methylene)-3-(4-methoxyphenyl)-1-phenylimidazolidine-2,4-dione (9c).**



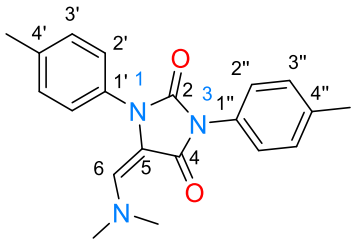
Following the procedure for **9a**, a mixture of **6a** (0.100 g, 0.606 mmol), **7c** (0.109 g, 0.73 mmol), and DMFDMA (0.216 g, 1.82 mmol) afforded **9c** (0.201 g, 98%) as a pale yellow solid. $R_f$ 0.25 (hexane/EtOAc, 7:3); mp 158–159 ºC. IR (film): $\bar{\upsilon}$ = 2922, 1778, 1716, 1502, 1444, 1405, 1377, 1200, 1159, 811, 754, 692 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 2.64 (s, 6H, N(C*H*$_3$)$_2$), 3.83 (s, 3H, C*H*$_3$O), 6.96–6.99 (m, 2H, H-3"), 6.99 (s, 1H, C*H*=), 7.27–7.30 (m, 1H, H-4'), 7.36–7.39 (m, 2H, H-2"), 7.39–7.41 (m, 2H, H-2'), 7.41–7.44 (m, 2H, H-3'). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 43.2 (N(*C*H$_3$)$_2$), 55.5 (*C*H$_3$O), 102.3 (C-5), 114.3 (C-3"), 124.5 (C-2'), 125.1 (C-1"), 126.2 (C-4'), 127.8 (C-2"), 128.9 (C-3'), 133.2 (*C*H=), 138.1 (C-1'), 153.8 (C-2), 158.9 (C-4"), 164.3 (C-4). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{19}H_{19}N_3O_3$: 337.1426; found: 337.1426.

**(*E*)-5-((Dimethylamino)methylene)-3-phenyl-1-(*p*-tolyl)imidazolidine-2,4-dione (9d).**



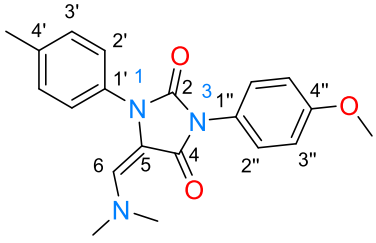
Following the procedure for **9a**, a mixture of **6b** (0.100 g, 0.56 mmol), **7a** (0.080 g, 0.67 mmol), and DMFDMA (0.200 g, 1.67 mmol) yielded **9d** (0.165 g, 92%) as a white solid. $R_f$ 0.26 (hexane/EtOAc, 7:3); mp 175–176 °C. IR (film): $\bar{\upsilon}$ = 2923, 1743, 1698, 1643, 1375, 1247, 1128, 1061, 967, 918, 745 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H, C*H*$_3$), 2.65 (s, 6H, N(C*H*$_3$)$_2$), 7.00 (s, 1H, C*H*=), 7.21–7.25 (m, 2H, H-3'), 7.27–7.31 (m, 2H, H-2'), 7.32–7.37 (m, 1H, H-4"), 7.43–7.49 (m, 2H, H-3"), 7.50–7.55 (m, 2H, H-2"). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 21.1 (*C*H$_3$), 43.3 (N(*C*H$_3$)$_2$), 102.6 (C-5), 124.5 (C-2'), 126.4 (C-2"), 127.6 (C-4"), 128.9 (C-3"), 129.6 (C-3'), 132.6 (C-1"), 133.1 (*C*H=), 135.6 (C-4'), 136.2 (C-1'), 153.6 (C-2), 164.0 (C-4). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{19}H_{19}N_3O_2$: 321.1477; found: 321.1473.

**(*E*)-5-((Dimethylamino)methylene)-1,3-di-*p*-tolylimidazolidine-2,4-dione (9e).**



Following the procedure for **9a**, a mixture of **6b** (0.100 g, 0.56 mmol), **7b** (0.089 g, 0.67 mmol), and DMFDMA (0.200 g, 1.67 mmol) furnished **9e** (0.178 g, 95%) as a white solid. $R_f$ 0.24 (hexane/EtOAc, 7:3); mp 132–133 °C. IR (film): $\bar{\upsilon}$ = 2922, 1745, 1697, 1637, 1511, 1377, 1252, 1131, 815 $cm^{-1}$. $^1H$ NMR (750 MHz, $CDCl_3$): δ 2.36 (s, 6H, 2C*H*$_3$), 2.62 (s, 6H, (NC*H*$_3$)$_2$), 6.95 (s, 1H, C*H*=), 7.19–7.22 (m, 2H, H-3'), 7.23–7.25 (m, 2H, H-3"), 7.25–7.27 (m, 2H, H-2'), 7.34–7.36 (m, 2H, H-2"). $^{13}C$ NMR (187.5 MHz, $CDCl_3$): δ 21.1 (*C*H$_3$), 21.3 (*C*H$_3$), 43.3 (N(*C*H$_3$)$_2$), 102.7 (C-5), 124.5 (C-2'), 126.3 (C-2"), 129.59 (C-3' or C-3"), 129.64 (C-3" or C-3'), 129.9 (C-1"), 133.0 (*C*H=), 135.7 (C-1'), 136.2 (C-4'), 137.6 (C-4"), 153.8 (C-2), 164.3 (C-4). HRMS (ESI-TOF, [$M^+$]): *m/z* calcd for $C_{20}H_{21}N_3O_2$: 335.1634; [$M^+$+Na(23)]: 358.1531; found [$M^+$+Na(23)]: 358.1526.

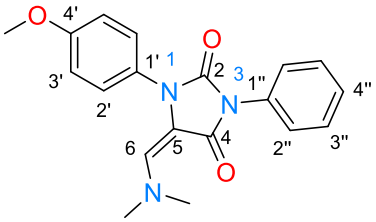
**(*E*)-5-((Dimethylamino)methylene)-3-(4-methoxyphenyl)-1-(*p*-tolyl)imidazolidine-2,4-dione (9f).**



Following the procedure for **9a**, a mixture of **6b** (0.100 g, 0.56 mmol), **7c** (0.100 g, 0.67 mmol), and DMFDMA (0.200 g, 1.67 mmol) provided **9f** (0.192 g, 98%) as a white solid. $R_f$ 0.19 (hexane/EtOAc, 7:3); mp 161–163 °C. IR (film): $\bar{\upsilon}$ = 2957, 2923, 1767, 1705, 1512, 1440, 1403, 1373, 1194, 1157, 812, 770, 747 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H, C*H*$_3$), 2.63 (s, 6H, (NC*H*$_3$)$_2$), 3.82 (s, 3H, C*H*$_3$O), 6.91–6.96 (m, 2H, H-3"), 6.93 (s, 1H, C*H*=), 7.22–7.26 (m, 2H, H-3'), 7.27–7.32 (m, 2H, H-2"), 7.33–7.38 (m, 2H, H-2'). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 21.2 (*C*H$_3$), 43.3 (N(*C*H$_3$)$_2$), 55.5 (*C*H$_3$O), 103.0 (C-5), 114.3 (C-3"), 126.0 (C-2"), 126.2 (C-2'), 129.5 (C-3'), 129.9 (C-1'), 131.1 (C-

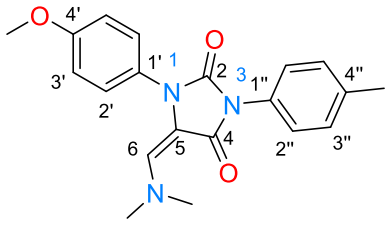
1”), 132.7 (*C*H=), 137.5 (C-4’), 154.0 (C-2), 158.0 (C-4”), 164.2 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{20}H_{21}N_3O_3$: 351.1583; found: 351.1583.

**(*E*)-5-((Dimethylamino)methylene)-1-(4-methoxyphenyl)-3-phenylimidazolidine-2,4-dione (9g).**



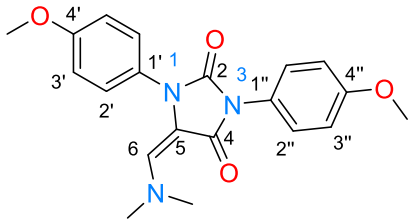
Following the procedure for **9a**, a mixture of **6c** (0.100 g, 0.51 mmol), **7a** (0.073 g, 0.61 mmol), and DMFDMA (0.183 g, 1.54 mmol) furnished **9g** (0.163 g, 95%) as a white solid. $R_f$ 0.20 (hexane/EtOAc, 7:3); mp 159–160 °C. IR (film): $\bar{\upsilon}$ = 2964, 2939, 1768, 1708, 1509, 1445, 1411, 1302, 1244, 1175, 1154, 1022, 825 cm$^{-1}$. $^1$H NMR (750 MHz, $CDCl_3$): δ 2.63 (s, 6H, N(C*H*$_3$)$_2$), 3.82 (s, 3H, C*H*$_3$O), 6.93–6.96 (m, 3H, C*H*=, H-3’), 7.28–7.31 (m, 2H, H-2’), 7.31–7.34 (m, 1H, H-4”), 7.42–7.46 (m, 2H, H-3”), 7.48–7.51 (m, 2H, H-2”). $^{13}$C NMR (187.5 MHz, $CDCl_3$): δ 43.4 (N(*C*H$_3$)$_2$), 55.6 (*C*H$_3$O), 102.9 (C-5), 114.3 (C-3’), 126.0 (C-2’), 126.4 (C-2”), 127.6 (C-4”), 129.0 (C-3”), 131.1 (C-1’), 132.6 (C-1”), 132.8 (*C*H=), 153.9 (C-2), 158.1 (C-4’), 164.1 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{20}H_{21}N_3O_4$: 337.1426; found: 337.1427.

**(*E*)-5-((Dimethylamino)methylene)-1-(4-methoxyphenyl)-3-(*p*-tolyl)imidazolidine-2,4-dione (9h).**



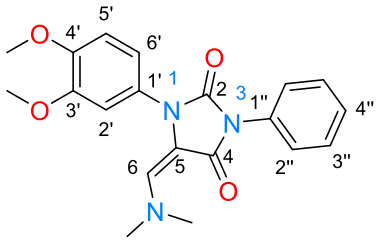
Following the procedure for **9a**, a mixture of **6c** (0.100 g, 0.51 mmol), **7b** (0.081 g, 0.61 mmol), and DMFDMA (0.183 g, 1.54 mmol) generated **9h** (0.178 g, 99%) as a white solid. $R_f$ 0.18 (hexane/EtOAc, 7:3); mp 160–161 °C. IR (film): $\bar{\upsilon}$ = 2936, 1742, 1692, 1634, 1509, 1375, 1244, 1138, 1028, 970, 819, 779, 760 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H, C*H*$_3$), 2.63 (s, 6H, N(C*H*$_3$)$_2$), 3.82 (s, 3H, C*H*$_3$O), 6.92–6.96 (m, 2H, H-3’), 6.93 (m, 1H, C*H*=), 7.22–7.26 (m, 2H, H-3”), 7.27–7.32 (m, 2H, H-2’), 7.33–7.38 (m, 2H, H-2”). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.2 (*C*H$_3$), 43.3 (N(*C*H$_3$)$_2$), 55.5 (*C*H$_3$O), 103.0 (C-5), 114.3 (C-3’), 126.0 (C-2’), 126.2 (C-2”), 129.5 (C-3”), 130.0 (C-1”) 131.1 (C-1’), 132.7 (*C*H=), 137.6 (C-4”), 154.0 (C-2), 158.0 (C-4’), 164.2 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{20}H_{21}N_3O_3$: 351.1583; found: 351.1587.

**(*E*)-5-((Dimethylamino)methylene)-1,3-bis(4-methoxyphenyl)imidazolidine-2,4-dione (9i).**



Following the procedure for **9a**, a mixture of **6c** (0.100 g, 0.51 mmol), **7c** (0.091 g, 0.61 mmol), and DMFDMA (0.183 g, 1.54 mmol) provided **9i** (0.182 g, 97%) as a white solid. $R_f$ 0.15 (hexane/EtOAc, 7:3); mp 140–141 °C. IR (film): $\bar{\upsilon}$ = 2932, 2836, 1742, 1684, 1633, 1509, 1440, 1381, 1240, 1127, 1023, 759 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 2.61 (s, 6H, N(C*H*$_3$)$_2$), 3.79 (s, 3H, C*H*$_3$O), 3.80 (s, 3H, C*H*$_3$O), 6.90–6.97 (m, 4H, H-3’, H-3”), 6.92 (s, 1H, C*H*=), 7.27–7.30 (m, 2H, H-2’), 7.35–7.38 (m, 2H, H-2”). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 43.2 (N(*C*H$_3$)$_2$), 55.4 (*C*H$_3$O), 55.5 (*C*H$_3$O), 102.9 (C-5), 114.23 (C-3’ or C-3”), 114.25 (C-3” or C-3’), 125.3 (C-1”), 126.0 (C-2”), 127.7 (C-2’), 131.1 (C-1’), 132.7 (*C*H=), 154.0 (C-2), 158.0 (C-4’ or C-4”), 159.0 (C-4” or C-4’), 164.2 (C-4). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{20}H_{21}N_3O_4$: 367.1532; found: 367.1528.

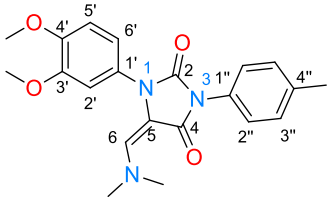
**(*E*)-1-(3,4-Dimethoxyphenyl)-5-((dimethylamino)methylene)-3-phenylimidazolidine-2,4-dione (9j). (*Z*)-1-(3,4-Dimethoxyphenyl)-5-((dimethylamino)methylene)-3-phenylimidazolidine-2,4-dione (9j’).**



Following the procedure for **9a**, a mixture of **6d** (0.100 g, 0.44 mmol), **7a** (0.063 g, 0.53 mmol), and DMFDMA (0.158 g, 1.33 mmol) afforded a mixture of **9j**/**9j’** (70:30) (0.157 g, 96%) as a yellow oil. $R_f$ 0.35 (hexane/EtOAc, 1:1). IR (film): $\bar{\upsilon}$ = 2923, 1746, 1677, 1630, 1511, 1439, 1375, 1229, 1127, 1022, 760, 737, 682 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 2.65 (s, 6H, N(C*H*$_3$)$_2$), 3.88 (s, 3H, C*H*$_3$O), 3.89 (s, 3H, C*H*$_3$O), 6.86–6.92 (m, 2H, H-5’, H-6’), 6.95 (s, 1H,

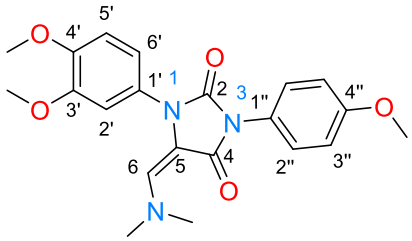
C*H*=), 6.94–6.98 (m, 2H, H-2'). 7.30–7.35 (m, 1H, H-4"), 7.42–7.46 (m, 2H, H-3"), 7.46–7.50 (m, 2H, H-2"). Signals attributed to the minor isomer **19j'**: δ 3.19 (s, N(C$H_3$)$_2$), 3.90 (s, C$H_3$O). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 43.3 (N(*C*$H_3$)$_2$), 56.1 (2*C*$H_3$O), 102.7 (C-5), 108.8 (C-2'), 111.0 (C-5'), 116.7 (C-6'), 126.3 (C-2"), 127.7 (C-4"), 128.9 (C-3"), 131.2 (C-1'), 132.5 (C-1"), 133.0 (*C*H=), 147.5 (C-3' or C-4'), 149.1 (C-4' or C-3'), 153.8 (C-2), 164.0 (C-4). Signals attributed to the minor isomer **19j'**: δ 44.9, 105.6, 111.5, 111.8, 120.9, 127.1, 127.5, 132.7, 137.0, 148.8, 149.7, 150.9, 158.8. HRMS (EI, [M$^+$]): *m/z* calcd for $C_{20}H_{21}N_3O_4$: 367.1532; found: 367.1526.

**(*E*)-1-(3,4-Dimethoxyphenyl)-5-((dimethylamino)methylene)-3-(*p*-tolyl)imidazolidine-2,4-dione (9k). (Z)-1-(3,4-dimethoxyphenyl)-5-((dimethylamino)methylene)-3-(p-tolyl)imidazolidine-2,4-dione (9k').**



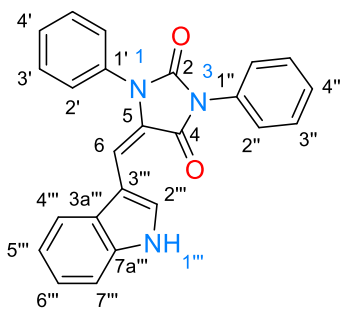
Following the procedure for **9a**, a mixture of **6d** (0.100 g, 0.44 mmol), **7b** (0.071 g, 0.53 mmol), and DMFDMA (0.158 g, 1.33 mmol) resulted in a mixture of **9k**/**9k'** (80:20) (0.160 g, 94%) as a yellow oil. $R_f$ 0.30 (hexane/EtOAc, 1:1). IR (film): ῡ = 2923, 1716, 1637, 1593, 1513, 1439, 1405, 1152, 812, 750, 691 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H, C$H_3$), 2.64 (s, 6H, N(C$H_3$)$_2$), 3.87 (s, 3H, C$H_3$O), 3.89 (s, 3H, C$H_3$O), 6.85–6.92 (m, 2H, H-5', H-6'), 6.94 (s, 1H, C*H*=), 6.97 (d, *J* = 2.0 Hz 2H, H-2'), 7.22–7.26 (m, 2H, H-3"), 7.32–7.36 (m, 2H, H-2"). Signals attributed to the minor isomer **19k'**: δ 3.19 (s, N(C$H_3$)$_2$), 3.90 (s, C$H_3$O). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.2 (*C*$H_3$), 43.2 (N(*C*$H_3$)$_2$), 56.10 (*C*$H_3$O), 56.12 (*C*$H_3$O), 102.9 (C-5), 108.9 (C-2'), 111.1 (C-5'), 116.7 (C-6'), 126.2 (C-2"), 129.6 (C-3"), 129.8 (C-1"), 131.3 (C-1'), 132.9 (*C*H=), 137.6 (C-4"), 147.5 (C-3' or C-4'), 149.2 (C-4' or C-3'), 154.0 (C-2), 164.1 (C-4). Signals attributed to the minor isomer **19k'**: δ 44.9, 56.14, 111.6, 111.9, 120.9, 126.6, 129.4, 136.7, 137.4, 148.9, 149.7, 159.0. HRMS (EI, [M$^+$]): *m/z* calcd for $C_{21}H_{23}N_3O_4$: 381.1689; found: 381.1687.

**(*E*)-1-(3,4-Dimethoxyphenyl)-5-((dimethylamino)methylene)-3-(4-methoxyphenyl)imidazolidine-2,4-dione (9l). (Z)-1-(3,4-dimethoxyphenyl)-5-((dimethylamino)methylene)-3-(4-methoxyphenyl)imidazolidine-2,4-dione (9l').**



Following the procedure for **9a**, a mixture of **6d** (0.100 g, 0.44 mmol), **7c** (0.080 g, 0.53 mmol), and DMFDMA (0.158 g, 1.33 mmol) delivered a mixture of **9l**/**9l'** (75:25) (0.164 g, 93%) as a yellow oil. $R_f$ 0.25 (hexane/EtOAc, 1:1). IR (film): ῡ = 2929, 2835, 1743, 1685, 1634, 1509, 1380, 1239, 1125, 1024, 758 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.65 (s, 6H, N(C$H_3$)$_2$), 3.80 (s, 3H, C$H_3$O-4"), 3.87 (s, 3H, C$H_3$O), 3.89 (s, 3H, C$H_3$O), 6.86–6.89 (m, 2H, H-5', H-6'), 6.92–6.98 (m, 3H, H-2', H-3"), 6.94 (s, 1H, C*H*=), 7.35–7.38 (m, 2H, H-2"). Signals attributed to the minor isomer **19l'**: δ 3.19 (s, N(C$H_3$)$_2$), 3.90 (s, C$H_3$O). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 43.2 (N(*C*$H_3$)$_2$), 55.5 (*C*$H_3$O-4"), 56.10 (*C*$H_3$O), 56.13 (*C*$H_3$O), 102.8 (C-5), 108.9 (C-2'), 111.1 (C-5'), 114.3 (C-3"), 116.7 (C-6'), 125.2 (C-1"), 127.7 (C-2"), 131.3 (C-1'), 132.8 (*C*H=), 147.5 (C-3' or C-4'), 149.2 (C-4' or C-3'), 154.1 (C-2), 159.0 (C-4"), 164.3 (C-4). Signals attributed to the minor isomer **19l'**: δ 44.9, 105.8, 111.6, 111.9, 114.2, 120.9, 125.4, 127.2, 128.0, 136.7, 148.9, 149.7, 158.8, 159.2. HRMS (EI, [M$^+$]): *m/z* calcd for $C_{21}H_{23}N_3O_5$: 397.1638; found: 397.1639.

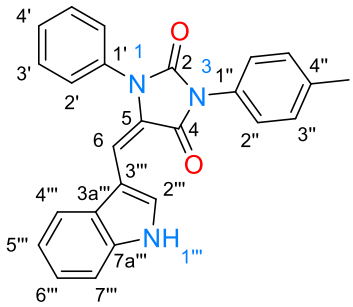
**(*E*)-5-((1*H*-Indol-3-yl)methylene)-1,3-diphenylimidazolidine-2,4-dione (11a).**



In a MW glass vial equipped with a magnetic stirring bar and sealed with a cap, a mixture of **9a** (0.100 g, 0.33 mmol) and **10a** (0.042 g, 0.36 mmol) in AcOH (0.5 mL) was subjected to MW (150 W) irradiation at 100 °C for 2.0 h under an $N_2$ atmosphere. Absolute EtOH (5.0 mL) was added to the crude, and the precipitate was filtered, washed with absolute EtOH (2 x 5 mL), and dried under vacuum, leading to **11a** (0.115 g, 93%) as a green solid. $R_f$ 0.57 (hexane/EtOAc, 7:3); mp 257–258 °C. IR (film): ῡ = 3260, 3158, 1741, 1689, 1618, 1499, 1388, 1216, 1179, 1127, 939, 730, 678 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 6.84 (s, 1H, C*H*=), 7.15 (br t, *J* = 7.6 Hz, 1H, H-5'"), 7.22 (br t, *J* = 8.5 Hz, 1H, H-6'"), 7.26 (br d, *J* = 8.7 Hz, 1H, H-4'"), 7.43 (br d, *J* = 7.6 Hz, 1H, H-7'"), 7.45–7.50 (m, 1H, ArH), 7.52–7.60 (m, 5H,

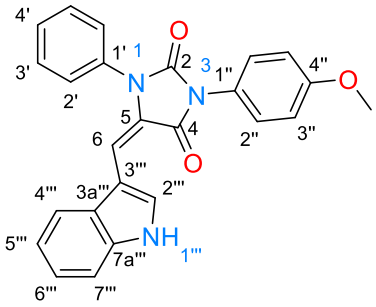
ArH), 7.60–7.66 (m, 4H, ArH), 8.96 (br s, 1H, N*H*), 9.06 (d, *J* = 2.9 Hz, 1H, H-2'''). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 109.3 (C-5), 111.2 (*C*H=), 111.7 (C-4'''), 117.5 (C-7'''), 120.9 (C-5'''), 122.9 (C-6'''), 124.8 (C-3'''), 126.6 (2ArH), 127.8 (C-3a'''), 128.3 (ArH), 128.4 (2ArH), 128.9 (ArH), 129.2 (2ArH), 129.7 (C-2'''), 130.0 (2ArH), 131.8 (Ar), 133.1 (Ar), 135.5 (C-7a'''), 151.4 (C-2), 161.2 (C-4). HRMS (ESI-TOF, [M$^+$]): *m/z* calcd for $C_{24}H_{17}N_3O_2$: 379.1321; [M$^+$+Na(23)]: 402.1218; found [M$^+$+Na(23)]: 402.1213.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-1-phenyl-3-(*p*-tolyl)imidazolidine-2,4-dione (11b).**



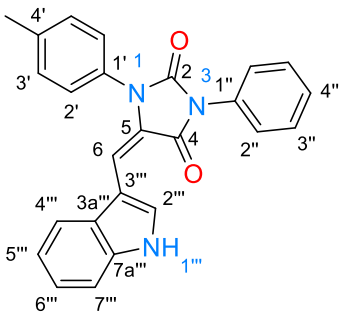
Following the procedure for **11a**, a mixture of **9b** (0.100 g, 0.31 mmol) and **10a** (0.040 g, 0.34 mmol) gave **11b** (0.113 g, 92%) as a green solid. $R_f$ 0.55 (hexane/EtOAc, 7:3); mp 156–157 °C. IR (film): ῡ = 3320, 3050, 1752, 1687, 1628, 1518, 1399, 1215, 1176, 1123, 1102, 939, 805, 728, 677 cm$^{-1}$. $^1$H NMR (500 MHz, DMSO-$d_6$): δ 2.38 (s, 3H, C*H*$_3$), 6.57 (s, 1H, C*H*=), 7.07 (t, *J* = 7.5 Hz, 1H, H-5'''), 7.16 (t, *J* = 7.5 Hz, 1H, H-6'''), 7.28 (d, *J* = 7.8 Hz, 1H, H-4'''), 7.33–7.37 (m, 2H, H-3"), 7.42–7.44 (m, 2H, H-2"), 7.46 (d, *J* = 7.8 Hz, 1H, H-7'''), 7.57 (t, *J* = 7.3 Hz, 1H, H-4'), 7.61 (d, *J* = 7.3 Hz, 2H, H-2'), 7.66 (t, *J* = 7.3 Hz, 2H, H-3'), 8.86 (s, 1H, H-2'''), 11.83 (s, 1H, N*H*). $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ 20.8 (*C*H$_3$), 107.9 (C-5), 108.9 (*C*H=), 112.3 (C-4'''), 116.9 (C-7'''), 120.3 (C-5'''), 122.3 (C-6'''), 125.1 (C-3'''), 127.1 (C-2"), 127.4 (C-3a'''), 128.77 (C-4'), 128.84 (C-2'), 129.4 (C-3"), 129.45 (C-1"), 129.50 (C-2'''), 129.9 (C-3'), 133.4 (C-1'), 135.7 (C-7a'''), 137.7 (C-4"), 151.1 (C-2), 160.8 (C-4). HRMS (ESI-TOF, [M$^+$]): *m/z* calcd for $C_{25}H_{19}N_3O_2$: 393.1477; [M$^+$+Na(23)]: 416.1375; found [M$^+$+Na(23)]: 416.1369.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-3-(4-methoxyphenyl)-1-phenylimidazolidine-2,4-dione (11c).**



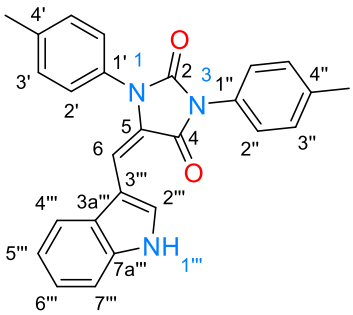
Following the procedure for **11a**, a mixture of **9c** (0.100 g, 0.30 mmol) and **10a** (0.038 g, 0.32 mmol) provided **11c** (0.110 g, 90%) as a green solid. $R_f$ 0.49 (hexane/EtOAc, 7:3); mp 258–259 °C. IR (film): ῡ = 3310, 1753, 1692, 1517, 1492, 1400, 1250, 1210, 1163, 1127, 1102, 939, 810, 730, 687 cm$^{-1}$. $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.82 (s, 3H, C*H*$_3$O), 6.58 (s, 1H, C*H*=), 7.04–7.12 (m, 3H, H-3", H-5'''), 7.17 (t, *J* = 7.7 Hz, 1H, H-6'''), 7.28 (d, *J* = 8.0 Hz, 1H, H-4'''), 7.42–7.48 (m, 3H, H-2", H-7'''), 7.57 (t, *J* = 7.5 Hz, 1H, H-4'), 7.61 (d, *J* = 7.5 Hz, 2H, H-2'), 7.66 (t, *J* = 7.5 Hz, 2H, H-3'), 8.87 (s, 1H, H-2'''), 11.83 (s, 1H, N*H*). $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ 55.4 (*C*H$_3$O), 107.9 (C-5), 108.9 (*C*H=), 112.3 (C-4'''), 114.1 (C-3"), 116.9 (C-7'''), 120.4 (C-5'''), 122.3 (C-6'''), 124.6 (C-1"), 125.2 (C-3'''), 127.4 (C-3a'''), 128.70 (C-2"), 128.77 (C-4'), 128.85 (C-2'), 129.5 (C-2'''), 129.9 (C-3'), 133.4 (C-1'), 135.7 (C-7a'''), 151.3 (C-2), 158.9 (C-4"), 161.0 (C-4). HRMS (ESI-TOF, [M$^+$]): *m/z* calcd for $C_{25}H_{19}N_3O_3$: 409.1426; [M$^+$+Na(23)]: 432.1324; found [M$^+$+Na(23)]: 432.1319.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-3-phenyl-1-(*p*-tolyl)imidazolidine-2,4-dione (11d).**



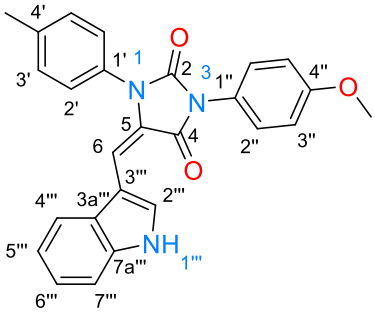
Following the procedure for **11a**, a mixture of **9d** (0.100 g, 0.31 mmol) and **10a** (0.040 g, 0.34 mmol) afforded **11d** (0.115 g, 94%) as a green solid. $R_f$ 0.46 (hexane/EtOAc, 7:3); mp 159–160 °C. IR (film): ῡ = 3323, 1744, 1689, 1631, 1512, 1498, 1399, 1216, 1166, 1122, 1106, 937, 746, 691 cm$^{-1}$. $^1$H NMR (500 MHz, DMSO-$d_6$): δ 2.44 (s, 3H, C*H*$_3$), 6.59 (s, 1H, C*H*=), 7.08 (t, *J* = 7.5 Hz, 1H, H-5'''), 7.17 (t, *J* = 7.5 Hz, 1H, H-6'''), 7.30 (d, *J* = 8.0 Hz, 1H, H-4'''), 7.43–7.51 (m, 6H, H-2', H-3', H-4", H-7'''), 7.51–7.59 (m, 4H, H-2", H-3"), 8.87 (s, 1H, H-2'''), 11.85 (s, 2H, N*H*). $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ 20.9 (*C*H$_3$), 108.0 (C-5), 109.0 (*C*H=), 112.3 (C-4'''), 117.0 (C-7'''), 120.4 (C-5'''), 122.3 (C-6'''), 125.1 (C-3'''), 127.3 (C-2"), 127.4 (C-3a'''), 128.1 (C-4"), 128.6 (C-2'), 128.9 (C-3"), 129.5 (C-2'''), 130.4 (C-3'), 130.7 (C-1'), 132.1 (C-1"), 135.7 (C-7a'''), 138.4 (C-4'), 151.1 (C-2), 160.8 (C-4). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{25}H_{19}N_3O_2$: 394.1556; found: 394.1573.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-1,3-di-*p*-tolylimidazolidine-2,4-dione (11e).**



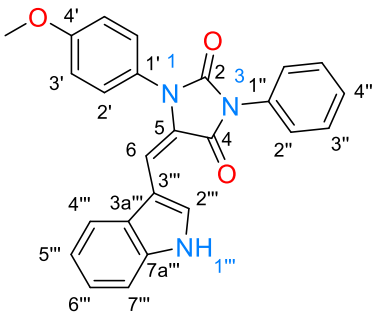
Following the procedure for **11a**, a mixture of **9e** (0.100 g, 0.30 mmol) and **10a** (0.038 g, 0.33 mmol) yielded **11e** (0.118 g, 97%) as a green solid. $R_f$ 0.46 (hexane/EtOAc, 7:3); mp 277–278 °C. IR (film): $\bar{\upsilon}$ = 3325, 1750, 1695, 1611, 1515, 1399, 1211, 1161, 1125, 1103, 823, 735 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 2.42 (s, 3H, C*H*$_3$-4”), 2.48 (s, 3H, C*H*$_3$-4’), 6.79 (s, 1H, C*H*=), 7.14 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, H-5’”), 7.21 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H, H-6’”), 7.28 (dt, *J* = 8.1, 1.1 Hz, 1H, H-4’”), 7.31–7.34 (m, 2H, H-3’), 7.37–7.42 (m, 4H, H-2”, H-3”), 7.42–7.47 (m, 3H, H-2’, H-7’”), 8.79 (br s, 1H, N*H*), 9.04 (d, *J* = 2.9 Hz, 1H, H-2’”). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 21.4 (*C*H$_3$-4”), 21.5 (*C*H$_3$-4’), 109.5 (C-5), 110.8 (*C*H=), 111.8 (C-4’”), 117.7 (C-7’”), 120.9 (C-5’”), 123.0 (C-6’”), 125.4 (C-3’”), 126.6 (C-2”), 128.0 (C-3a’”), 128.3 (C-2’), 129.3 (C-1”), 129.6 (C-2’”), 130.0 (C-3”), 130.6 (C-1’), 130.7 (C-3’), 135.6 (C-7a’”), 138.4 (C-4”), 139.0 (C-4’), 151.8 (C-2), 161.6 (C-4). HRMS (ESI, $[M+H]^+$): *m/z* calcd for $C_{26}H_{22}N_3O_2$: 408.1712; found: 408.1718.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-3-(4-methoxyphenyl)-1-(*p*-tolyl)imidazolidine-2,4-dione (11f).**



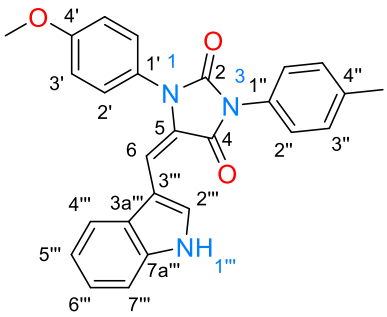
Following the procedure for **11a**, a mixture of **9f** (0.100 g, 0.28 mmol) and **10a** (0.037 g, 0.31 mmol) furnished **11f** (0.115 g, 95%) as a green solid. $R_f$ 0.45 (hexane/EtOAc, 7:3); mp 274–275 °C. IR (film): $\bar{\upsilon}$ = 3323, 1750, 1707, 1646, 1517, 1394, 1213, 1173, 1099, 1032, 828, 734 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 2.49 (s, 3H, C*H*$_3$), 3.86 (s, 3H, C*H*$_3$O), 6.79 (s, 1H, C*H*=), 7.02–7.07 (m, 2H, H-3”), 7.14 (tm, *J* = 7.6 Hz, 1H, H-5’”), 7.21 (tm, *J* = 7.6 Hz, 1H, H-6’”), 7.30 (br d, *J* = 8.0 Hz, 1H, H-4’”), 7.37–7.43 (m, 4H, H-2’, H-3’), 7.45 (br d, *J* = 8.0 Hz, 1H, H-7’”), 7.47–7.51 (m, 2H, H-2”), 8.77 (br s, 1H, N*H*), 9.03 (br s, 1H, H-2’”). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 21.4 (*C*H$_3$), 55.6 (*C*H$_3$O), 109.4 (C-5), 110.7 (C-6), 111.7 (C-4’”), 114.5 (C-3”), 117.6 (C-7’”), 120.8 (C-5’”), 122.9 (C-6’”), 124.5 (C-1”), 125.3 (C-3’”), 127.8 (C-3a’”), 127.9 (C-2”), 128.2 (C-2’), 129.5 (C-2’”), 130.4 (C-1’), 130.6 (C-3’), 135.5 (C-7a’”), 138.9 (C-4’), 151.7 (C-2), 159.3 (C-4”), 161.5 (C-4). HRMS (ESI-TOF, $[M^+]$): *m/z* calcd for $C_{26}H_{21}N_3O_3$: 423.1583; $[M^+$+Na(23)]: 446.1481; found $[M^+$+Na(23)]: 446.1475.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-1-(4-methoxyphenyl)-3-phenylimidazolidine-2,4-dione (11g).**



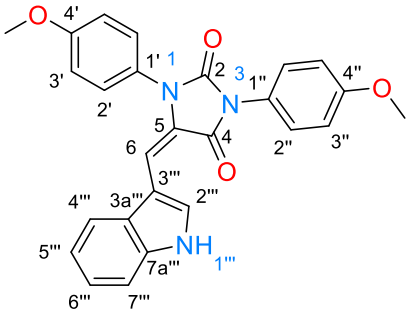
Following the procedure for **11a**, a mixture of **9g** (0.100 g, 0.30 mmol) and **10a** (0.036 g, 0.31 mmol) produced **11g** (0.111 g, 91%) as a green solid. $R_f$ 0.38 (hexane/EtOAc, 7:3); mp 251–252 °C. IR (film): $\bar{\upsilon}$ = 3329, 1741, 1693, 1611, 1502, 1379, 1249, 1214, 1170, 1133, 1020, 730, 683 $cm^{-1}$. $^1H$ NMR (500 MHz, DMSO-$d_6$): δ 3.87 (s, 3H, C*H*$_3$O), 6.52 (s, 1H, C*H*=), 7.08 (tm, *J* = 7.5 Hz, 1H, H-5’”), 7.17 (tm, *J* = 7.5 Hz, 1H, H-6’”), 7.18–7.22 (m, 2H, H-3’), 7.30 (br d, *J* = 8.0 Hz, 1H, H-4’”), 7.43–7.47 (m, 2H, H-4”, H-7’”), 7.50–7.53 (m, 2H, H-2’), 7.54–7.57 (m, 4H, H-2”, H-3”), 8.84 (d, *J* = 2.6 Hz, 1H, H-2’”), 11.82 (br s, 1H, N*H*). $^{13}C$ NMR (125 MHz, DMSO-$d_6$): δ 55.5 (*C*H$_3$O), 108.0 (C-5), 109.0 (*C*H=), 112.3 (C-4’”), 115.1 (C-3’), 117.3 (C-7’”), 120.4 (C-5’”), 122.3 (C-6’”), 125.6 (C-3’”), 125.7 (C-1’), 127.3 (C-3”), 127.4 (C-3a’”), 128.1 (C-4”), 128.9 (C-2”), 129.4 (C-2’”), 130.2 (C-2’), 132.2 (C-1”), 135.7 (C-7a’”), 151.2 (C-2), 159.3 (C-4’), 160.8 (C-4). HRMS (ESI, $[M+H]^+$): *m/z* calcd for $C_{25}H_{20}N_3O_3$: 410.1505; found: 410.1513.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-1-(4-methoxyphenyl)-3-(*p*-tolyl)imidazolidine-2,4-dione (11h).**



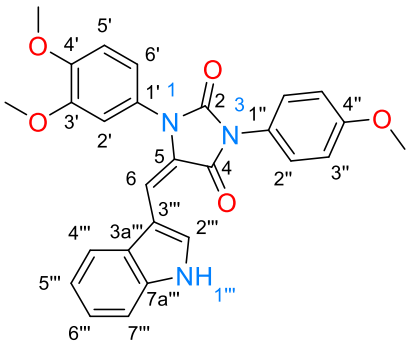
Following the procedure for **11a**, a mixture of **9h** (0.100 g, 0.28 mmol) and **10a** (0.037 g, 0.31 mmol) generated **11h** (0.116 g, 96%) as a green solid. $R_f$ 0.48 (hexane/EtOAc, 7:3); mp 263.5-265.0 °C. IR (film): $\bar{\upsilon}$ = 3321, 1748, 1694, 1614, 1513, 1396, 1256, 1215, 1164, 1125, 1103, 944, 824, 727 cm$^{-1}$. $^1$H NMR (500 MHz, DMSO-$d_6$): δ 2.38 (s, 3H, C$H_3$), 3.87 (s, 3H, C$H_3$O), 6.52 (s, 1H, C*H*=), 7.07 (t, *J* = 7.5 Hz, 1H, H-5'"), 7.16 (t, *J* = 7.5 Hz, 1H, H-6'"), 7.17–7.21 (m, 2H, H-3'), 7.31 (d, *J* = 8.0 Hz, 1H, H-4'"), 7.33–7.36 (m, 2H, H-3"), 7.40–7.43 (m, 2H, H-2"), 7.46 (d, *J* = 8.0 Hz, 1H, H-7'"), 7.49–7.53 (m, 2H, H-2'), 8.85 (s, 1H, H-2'"), 11.79 (s, 1H, N*H*). $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ 20.8 (*C*H$_3$), 55.5 (*C*H$_3$O), 108.0 (C-5), 108.8 (*C*H=), 112.2 (C-4'"), 115.0 (C-3'), 117.0 (C-7'"), 120.3 (C-5'"), 122.2 (C-6'"), 125.5 (C-3'"), 125.7 (C-1'), 127.0 (C-2"), 127.4 (C-3a'"), 129.3 (C-3", C-2'"), 129.5 (C-1"), 130.2 (C-2'), 135.7 (C-7a'"), 137.6 (C-4"), 151.3 (C-2), 159.2 (C-4'), 160.8 (C-4). HRMS (ESI-TOF, [M$^+$]): *m/z* calcd for $C_{26}H_{21}N_3O_3$: 423.1583; [M$^+$+Na(23)]: 446.1481; found [M$^+$+Na(23)]: 446.1475.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-1,3-bis(4-methoxyphenyl)imidazolidine-2,4-dione (11i).**



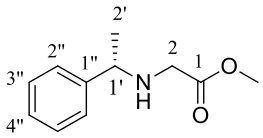
Following the procedure for **11a**, a mixture of **9i** (0.100 g, 0.27 mmol) and **10a** (0.035 g, 0.30 mmol) formed **11i** (0.116 g, 97%) as a green solid. $R_f$ 0.41 (hexane/EtOAc, 7:3); mp 259–260 °C. IR (film): $\bar{\upsilon}$ = 3342, 1748, 1694, 1513, 1392, 1300, 1243, 1208, 1160, 1122, 1024, 830, 818, 738 cm$^{-1}$. $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.81 (s, 3H, C$H_3$O), 3.86 (s, 3H, C$H_3$O), 6.50 (s, 1H, C*H*=), 7.03–7.10 (m, 3H, H-3', H-5'"), 7.13–7.20 (m, 3H, H-3", H-6'"), 7.29 (br d, *J* = 8.0 Hz, 1H, H-4'"), 7.40–7.46 (m, 3H, H-2', H-7'"), 7.46–7.53 (m, 2H, H-2"), 8.84 (d, *J* = 2.9 Hz, 1H, H-2'"), 11.80 (br s, 1H, N*H*). $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ 55.8 (*C*H$_3$O), 55.9 (*C*H$_3$O), 108.4 (C-5), 109.2 (*C*H=), 112.7 (C-4'"), 114.6 (C-3'), 115.5 (C-3"), 117.4 (C-7'"), 120.8 (C-5'"), 122.7 (C-6'"), 125.0 (C-1'), 126.0 (C-3'"), 126.1 (C-1"), 127.8 (C-3a'"), 129.1 (C-2'), 129.7 (C-2'"), 130.6 (C-2"), 136.1 (C-7a'"), 151.9 (C-2), 159.3 (C-4'), 159.7 (C-4"), 161.5 (C-4). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{26}H_{22}N_3O_4$: 440.1610; found: 440.1626.

**(*E*)-5-((1*H*-Indol-3-yl)methylene)-1-(3,4-dimethoxyphenyl)-3-(4-methoxyphenyl)imidazolidine-2,4-dione (11j).**



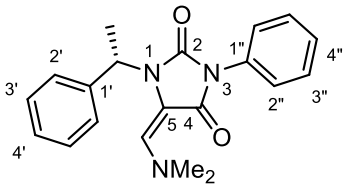
Following the procedure for **11a**, a mixture of **9l** (0.100 g, 0.25 mmol) and **10a** (0.032 g, 0.28 mmol) delivered **11j** (0.114 g, 96%) as a green solid. $R_f$ 0.15 (hexane/EtOAc, 7:3); mp 222.5–224.0 °C. IR (film): $\bar{\upsilon}$ = 3339, 1750, 1693, 1508, 1399, 1410, 1252, 1236, 1211, 1163, 1125, 1026, 738 cm$^{-1}$. $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.78 (s, 3H, C$H_3$O), 3.81 (s, 3H, C$H_3$O), 3.87 (s, 3H, C$H_3$O), 6.53 (s, 1H, C*H*=), 7.05–7.21 (m, 7H, H-2', H-5', H-6', H-3", H-5'", H-6'"), 7.31 (br d, *J* = 8.0 Hz, 1H, H-4'"), 7.40–7.46 (m, 3H, H-2", H-7'"), 8.83 (br s, 1H, H-2'"), 11.80 (br s, 1H, N*H*). $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ 55.5 (*C*H$_3$O), 55.7 (*C*H$_3$O), 55.8 (*C*H$_3$O), 108.1 (C-5), 108.9 (*C*H=), 112.1 (C-2'), 112.3 (C-4'"), 112.5 (C-6'), 114.2 (C-3"), 117.1 (C-7'"), 120.4 (C-5'"), 121.4 (C-5'), 122.3 (C-6'"), 124.7 (C-1"), 125.7 (C-3'"), 125.8 (C-1'), 127.5 (C-3a'"), 128.7 (C-2"), 129.3 (C-2'"), 135.7 (C-7a'"), 149.0 (C-3' or C-4'), 149.4 (C-4' or C-3'), 151.4 (C-2), 158.9 (C-4"), 161.1 (C-4). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{27}H_{24}N_3O_5$: 470.1716; found: 470.1729.

**Methyl (*S*)-(1-phenylethyl)glycinate** (**13**).



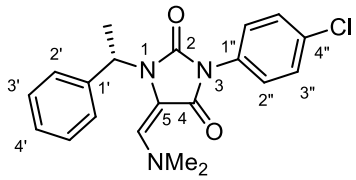
At rt and under $N_2$ atmosphere, **5** (1.26 g, 8.26 mmol) was added to a mixture of **12** (1.00 g, 8.26 mmol) and $K_2CO_3$ (2.28 g, 16.50 mmol) in anhydrous acetone (5 mL). After heating at 60 °C for 5 h, the mixture was filtered, and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 95:5) to provide **13** (1.39 g, 88%) as a yellow oil. $R_f$ 0.41 (hexane/EtOAc, 7:3). $[\alpha]_D^{25}$ = –602.3 (*c* 0.37, $CHCl_3$). IR (film): $\bar{\upsilon}$ = 3446, 3413, 2956, 1722, 1613, 1525, 1438, 1368, 1219, 1199, 1147, 988, 727, 701 $cm^{-1}$. $^1H$ RMN (300 MHz, $CDCl_3$): δ 1.36 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH), 2.03 (br s, 1H, NH), 3.20–3.30 (m, 2H, H-2), 3.67 (s, 3H, $CO_2CH_3$), 3.78 (q, *J* = 7.0, 1H, $CH_3CH$), 7.23–7.32 (m, 5H, ArH). $^{13}C$ RMN (75.4 MHz, $CDCl_3$): δ 24.0 (*C*$H_3$CH), 48.4 (C-2), 51.4 ($CO_2CH_3$), 57.4 ($CH_3CH$), 126.5 (C-2'), 126.9 (C-4'), 128.3 (C-3'), 144.3 (C-1'), 172.7 (*C*$O_2$Me). HRMS (ESI, $[M+H]^+$): *m/z* calcd for $C_{11}H_{16}NO_2$: 194.1181; found: 194.1177.

**(*S*,*E*)-5-((Dimethylamino)methylene)-3-phenyl-1-(1-phenylethyl)imidazolidine-2,4-dione (14a).**



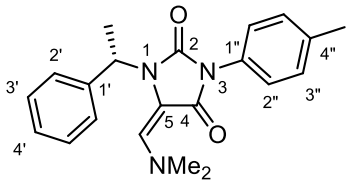
In a threaded ACE glass pressure tube equipped with a magnetic stirring bar and sealed with a Teflon screw cap, a mixture of **13** (1.00 g, 5.18 mmol) and **7a** (0.924 g, 7.76 mmol) was heated at 80 °C for 12 h. At rt and under $N_2$ atmosphere, DMFDMA (1.847 g, 15.52 mmol) was added, and the reaction mixture was heated at 120 °C for 12 h. The crude was extracted with $CH_2Cl_2$ (2 x 25 mL), the organic layer was dried ($Na_2SO_4$), the solvent was removed under vacuum, and the residue purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 9:1), leading to **14a** (1.58 g, 90%) as yellow crystals. $R_f$ 0.30 (hexane/EtOAc, 7:3); mp 219–221 °C. $[\alpha]_D^{25}$ = –302.0 (c 0.021, $CHCl_3$). IR (KBr): $\bar{\upsilon}$ = 1729, 1680, 1635, 1492, 1393, 1134, 1105, 948, 912, 811 $cm^{-1}$. $^1H$ RMN (600 MHz, $CDCl_3$) δ 1.80 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 3.06 (s, 6H, N(C*H*$_3$)$_2$), 5.88 (q, *J* = 7.2 Hz, 1H, $CH_3CH$), 6.08 (s, 1H, C*H*=), 7.27–7.34 (m, 2H, H-4', H-4"), 7.36–7.41 (m, 4H, H-2', H-3'), 7.43 (t, *J* = 7.8 Hz, 1H, H-3"), 7.51 (br d, *J* = 7.8 Hz, 1H, H-2"). $^{13}C$ RMN (150 MHz, $CDCl_3$): δ 16.9 (*C*$H_3$CH), 44.9 (N(*C*$H_3$)$_2$), 49.7 ($CH_3CH$), 101.5 (C-5), 126.5 (C-2"), 126.6 (C-2'), 127.4 (C-4' or C-4"), 127.5 (C-4" or C-4'), 128.8 (C-3', C-3"), 132.8 (C-1"), 137.3 (*C*H=), 140.4 (C-1'), 152.1 (C-2), 158.9 (C-4). HRMS (EI, $[M^+]$): *m/z* calcd for: $C_{20}H_{21}N_3O_2$: 335.1634; found: 335.1646.

**(*S*,*E*)-3-(4-Chlorophenyl)-5-((dimethylamino)methylene)-1-(1-phenylethyl)imidazolidine-2,4-dione (14b).**



Following the procedure for **14a**, a mixture of **13** (1.00 g, 5.18 mmol), **7d** (1.191 g, 7.76 mmol), and DMFDMA (1.847 g, 15.52 mmol) gave **14b** (1.77 g, 93%) as yellow crystals. $R_f$ 0.23 (hexane/AcOEt, 7:3); mp 170–171 °C. $[\alpha]_D^{25}$ = –12.4 (c 0.020, $CHCl_3$). IR (film): $\bar{\upsilon}$ = 2983, 2929, 1727, 1677, 1629, 1496, 1407, 1362, 1132, 1085, 1034, 947, 913, 837, 825, 757, 700, 662 $cm^{-1}$. $^1H$ RMN (500 MHz, $CDCl_3$): δ 1.77 (d, *J* = 7.5 Hz, 3H, C*H*$_3$CH), 3.03 (s, 6H, N(C*H*$_3$)$_2$), 5.84 (q, *J* = 7.5 Hz, 1H, $CH_3CH$), 6.07 (s, 1H, C*H*=), 7.26–7.32 (m, 1H, H-4'), 7.33–7.40 (m, 4H, H-2', H-3'), 7.40–7.44 (m, 2H, H-2"), 7.48–7.53 (m, 2H, H-3"). $^{13}C$ RMN (125 MHz, $CDCl_3$): δ 16.8 (*C*$H_3$CH), 44.9 (N(*C*$H_3$)$_2$), 49.8 ($CH_3CH$), 101.2 (C-5), 126.4 (C-2'), 127.5 (C-4'), 127.6 (C-2"), 128.8 (C-3'), 128.9 (C-3"), 131.4 (C-4"), 132.8 (C-1"), 137.6 (*C*H=), 140.2 (C-1'), 151.7 (C-2), 158.5 (C-4). HRMS (ESI, $[M+H]^+$): *m/z* calcd for $C_{20}H_{21}ClN_3O_2$: 370.1322; found: 370.1336.

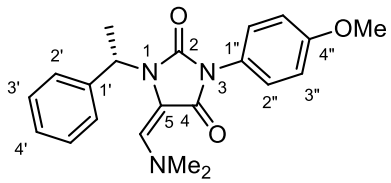
**(*S*,*E*)-5-((Dimethylamino)methylene)-1-(1-phenylethyl)-3-(*p*-tolyl)imidazolidine-2,4-dione (14c).**



Following the procedure for **14a**, a mixture of **13** (1.00 g, 5.18 mmol), **7b** (1.032 g, 7.76 mmol), and DMFDMA (1.847 g, 15.52 mmol) afforded **14c** (1.76 g, 97%) as yellow crystals. $R_f$ 0.19 (hexane/AcOEt, 7:3); mp 109–110 ºC. $[\alpha]_D^{25}$ = –80.3 (c 0.07, MeOH). IR (film): $\bar{\upsilon}$ = 2980, 1721, 1669, 1611, 1516, 1389, 1357, 1139, 1097, 1074, 1035, 994, 911, 820, 758, 703, 667 $cm^{-1}$. $^1H$ RMN

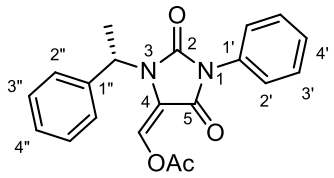
(600 MHz, $CDCl_3$): δ 1.77 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 2.37 (s, 3H, C*H*$_3$Ar), 3.02 (s, 6H, N(C*H*$_3$)$_2$), 5.85 (q, *J* = 7.2 Hz, 1H, CH$_3$C*H*), 6.04 (s, 1H, C*H*=), 7.24 (br d, *J* = 7.8 Hz, 2H, H-3"), 7.26–7.31 (m, 1H, H-4'), 7.34–7.39 (m, 6H, H-2', H-3', H-2"). $^{13}$C RMN (150 MHz, $CDCl_3$): δ 17.0 (*C*H$_3$CH), 21.3 (*C*H$_3$Ar), 44.9 (N(*C*H$_3$)$_2$), 49.8 (CH$_3$*C*H), 101.6 (C-5), 126.5 (C-2'), 126.6 (C-2"), 127.5 (C-4'), 128.9 (C-3'), 129.5 (C-3"), 130.2 (C-1"), 137.3 (*C*H=), 137.4 (C-4"), 140.5 (C-1'), 152.3 (C-2), 159.1 (C-4). HRMS (ESI-TOF, [M$^+$+H]): *m/z* calcd for $C_{21}H_{24}N_3O_2$: 350.1869; found: 350.1863.

**(*S*,*E*)-5-((Dimethylamino)methylene)- 3-(4-methoxyphenyl)-1-(1-phenylethyl)imidazolidine-2,4-dione (14d).**



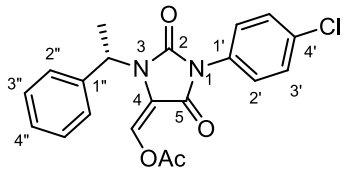

Following the procedure for **14a**, a mixture of **13** (1.00 g, 5.18 mmol), **7c** (1.156 g, 7.76 mmol), and DMFDMA (1.85 g, 15.52 mmol) provided **14d** (1.80 g, 95%) as a brown resin. $R_f$ 0.12 (hexane/AcOEt, 7:3); $[\alpha]_D^{25}$ = –43.5 (c 0.05, MeOH). IR (film): ῡ = 2951, 1728, 1650, 1513, 1402, 1367, 1302, 1249, 1201, 1171, 1022, 836, 752, 696 cm$^{-1}$. $^1$H RMN (600 MHz, $CDCl_3$): δ 1.77 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 3.01 (s, 6H, N(C*H*$_3$)$_2$), 3.80 (s, 3H, *C*H$_3$O), 5.83 (q, *J* = 7.2 Hz, 1H, CH$_3$C*H*), 6.04 (s, 1H, C*H*=), 6.97 (br d, *J* = 9.0 Hz, 2H, H-3"), 7.25–7.31 (m, 1H, H-4'), 7.34–7.42 (m, 6H, H-2', H-3', H-2"). $^{13}$C RMN (150 MHz, $CDCl_3$): δ 17.0 (*C*H$_3$CH), 44.9 (N(*C*H$_3$)$_2$), 49.8 (CH$_3$*C*H), 55.6 (*C*H$_3$O), 101.6 (C-5), 114.3 (C-3"), 125.6 (C-1"), 126.5 (C-2'), 127.5 (C-4'), 128.0 (C-2"), 128.9 (C-3'), 137.3 (*C*H=), 140.4 (C-1'), 152.4 (C-2), 158.8 (C-4"), 159.2 (C-4). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{21}H_{24}N_3O_3$: 366.1818; found: 366.1825.

**(*S*,*E*)-(2,5-Dioxo-1-phenyl-3-(1-phenylethyl)14yrrolidine14e-4-yliden)methyl acetate (15a).**



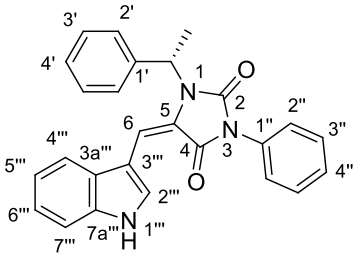

In a round-bottom flask (50 mL), a mixture of **14a** (0.100 g, 0.30 mmol) and acetic anhydride (0.060 g, 0.59 mmol) was heated at rt for 12 h. The crude was filtered and the residue purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 95:5) to obtain **15a** (0.09 g, 87%) as white crystals. $R_f$ 0.57 (hexane/EtOAc, 7:3); mp 135–136 °C. $[\alpha]_D^{25}$ = +20.7 (c 0.14, MeOH). IR (film): ῡ = 1766, 1731, 1687, 1502, 1406, 1369, 1186, 1164, 1127, 893, 850, 761, 744, 691, 641 cm$^{-1}$. $^1$H RMN (500 MHz, $CDCl_3$): δ 1.64 (s, 3H, C*H*$_3$CO$_2$), 1.65 (d, *J* = 7.3 Hz, 3H, C*H*$_3$CH), 5.71 (q, *J* = 7.3 Hz, 1H, CH$_3$C*H*), 7.02–7.07 (m, 1H, H-4'), 7.08–7.11 (m, 2H, H-2'), 7.11–7.17 (m, 3H, H-3', H-4"), 7.24–7.27 (m, 4H, H-2", H-3"), 7.50 (s, 1H, C*H*=). $^{13}$C RMN (125 MHz, $CDCl_3$): δ 18.5 (*C*H$_3$CH), 20.2 (*C*H$_3$CO$_2$), 50.9 (CH$_3$*C*H), 114.5 (C-4), 122.7 (*C*H=), 125.8 (C-2'), 126.0 (C-2"), 127.2 (C-4'), 128.2 (C-4"), 128.5 (C-3'), 129.0 (C-3"), 131.4 (C-1'), 140.6 (C-1"), 153.1 (C-2), 162.5 (C-5), 165.4 (CH$_3$*C*O$_2$). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{20}H_{18}N_2O_4$: 350.1267; found: 350.1263.

**(*S*,*E*)-(1-(4-Chlorophenyl)-2,5-dioxo-3-(1-phenylethyl)14yrrolidine14e-4-yliden)methyl acetate (15b).**



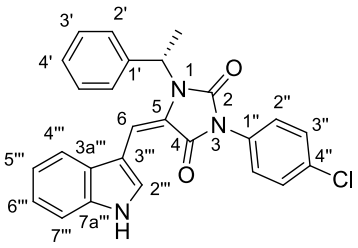

Following the procedure for **14a**, a mixture of **14b** (0.100 g, 0.27 mmol) and acetic anhydride (0.055 g, 0.54 mmol) yielded **15b** (0.087 g, 84%) as white crystals. $R_f$ 0.60 (hexane/EtOAc, 7:3); mp 131-132 °C. $[\alpha]_D^{25}$ = –37.2 (c 0.140, MeOH). IR (film): ῡ = 1767, 1732, 1688, 1497, 1408, 1370, 1186, 1165, 1229, 1091, 896, 852, 829, 758, 698 cm$^{-1}$. $^1$H RMN (500 MHz, $CDCl_3$): δ 1.87 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH), 1.88 (s, 3H, C*H*$_3$CO$_2$), 5.93 (q, *J* = 7.0 Hz, 1H, CH$_3$C*H*), 7.26–7.30 (m, 1H, H-4"), 7.31 (br d, *J* = 7.5 Hz, 2H, H-2"), 7.34–7.39 (m, 2H, H-3"), 7.43–7.49 (m, 4H, H-2', H-3'), 7.73 (s, 1H, *C*H=). $^{13}$C RMN (125 MHz, $CDCl_3$): δ 18.5 (*C*H$_3$CH), 20.2 (*C*H$_3$CO$_2$), 51.0 (CH$_3$*C*H), 114.3 (C-4), 122.9 (*C*H=), 125.7 (C-2"), 127.1 (C-2'), 127.3 (C-4"), 128.5 (C-3"), 129.2 (C-3'), 130.0 (C-1'), 133.8 (C-4'), 140.4 (C-1"), 152.7 (C-1'), 162.3 (C-5), 165.4 (CH$_3$*C*O$_2$). HRMS (ESI-TOF, [M$^+$]): *m/z* calcd for $C_{20}H_{17}ClN_2O_4$: 384.0877; [M$^+$+Na(23)]: 407.0775; found [M$^+$+Na(23)]: 407.0769.

**(*S,E*)-5-((1*H*-Indol-3-yl)methylene)-3-phenyl-1-(1-phenylethyl)imidazolidine-2,4-diona (16a). (*S,Z*)-5-((1*H*-Indol-3-yl)methylene)-3-phenyl-1-(1-phenylethyl)imidazolidine-2,4-diona (17a).**



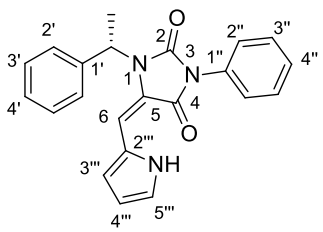
In a round-bottom flask (50 mL), a mixture of **14a** (0.100 g, 0.30 mmol) and **10a** (0.051 g, 0.44 mmol) in glacial AcOH (2 mL) was heated at 110 °C for 4 h. The crude was extracted with $CH_2Cl_2$ (2 x 25 mL), the organic layer dried ($Na_2SO_4$), the solvent removed under vacuum, and the residue purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 95:5) to generate a mixture of **16a**/**17a** (90:10, 0.99 g, 85%) as a yellow solid. $R_f$ 0.61 (hexane/EtOAc, 7:3); mp 219–221 °C. $[\alpha]_D^{25}$ = +4.5° (c 0.16, MeOH). IR (KBr): $\bar{\upsilon}$ = 3328, 1741, 1698, 1627, 1492, 1396, 1216, 1128, 770, 744, 690, 640 $cm^{-1}$. $^1H$ RMN (500 MHz, $CDCl_3$): δ 1.98 (d, *J* = 7.5 Hz, 3H, C*H*$_3$CH), 6.04 (q, *J* = 7.5 Hz, 1H, CH$_3$C*H*), 6.62 (s, 1H, C*H*=), 7.12–7.16 (m, 1H, H-5'"), 7.18–7.21 (m, 2H, H-6'", H-7'"), 7.23–7.25 (m, 1H, H-4'"), 7.34 (t, *J* = 7.6 Hz, 1H, H-4'), 7.41–7.45 (m, 1H, H-4"), 7.45–7.49 (br t, *J* = 7.6, 2H, H-3'), 7.52–7.59 (m, 6H, H-2', H-2", H-3"), 8.72 (br s, 1H, NH), 8.88 (d, *J* = 2.2 Hz, 1H, H-2'"). Signals attributed to the minor isomer **17a**: δ 1.87 (d, *J* = 7.2 Hz, C*H*$_3$CH), 5.51 (q, *J* = 7.2 Hz, CH$_3$C*H*). $^{13}C$ RMN (125 MHz, $CDCl_3$): δ 16.5 (*C*H$_3$CH), 49.8 (CH$_3$*C*H), 109.4 (C-3'"), 111.6 (C-7'"), 112.2 (C*H*=), 117.4 (C-4'"), 120.8 (C-5'"), 121.4 (C-5), 122.8 (C-6'"), 126.5 (C-2"), 126.7 (C-2'), 127.9 (C-4'), 128.0 (C-3a'"), 128.1 (C-4"), 129.0 (C-3'), 129.1 (C-2'"), 129.2 (C-3"), 131.9 (C-1"), 135.3 (C-7a'"), 139.2 (C-1'), 152.5 (C-2), 161.4 (C-4). Signals attributed to the minor isomer **17a**: δ 18.3, 53.2, 106.9, 119.5, 123.5, 125.2, 150.5, 163.0. HRMS (EI, [$M^+$]): *m/z* calcd for $C_{26}H_{21}N_3O_2$: 407.1634; found: 407.1636.

**(*S,E*)-5-((1*H*-Indol-3-yl)methylene)-3-(4-chlorophenyl)-1-(1-phenylethyl)imidazolidine-2,4-dione (16b). (*S,Z*)-5-((1*H*-Indol-3-yl)methylene)-3-(4-chlorophenyl)-1-(1-phenylethyl)imidazolidine-2,4-dione (17b).**



Following the procedure for **16a**/**17a**, a mixture of **14b** (0.100 g, 0.27 mmol) and **10a** (0.047 g, 0.40 mmol) furnished a mixture of **16b**/**17b** (92:8, 0.10 g, 90%) as green crystals. $R_f$ 0.58 (hexane/EtOAc, 7:3); mp 214-216 °C. $[\alpha]_D^{25}$ = +209.4 (c 0.20, MeOH). IR (film): $\bar{\upsilon}$ = 3338, 3061, 2981, 2931, 1742, 1698, 1624, 1495, 1395, 1217, 1201, 1127, 1091, 1016, 950, 877, 822, 743, 698 $cm^{-1}$. $^1H$ RMN (500 MHz, $CDCl_3$): δ 1.97 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH), 6.03 (q, *J* = 7.0 Hz, 1H, CH$_3$C*H*), 6.65 (s, 1H, C*H*=), 7.13–7.22 (m, 4H, H-4'", H-5'", H-6'", H-7'"), 7.35 (t, *J* = 7.3 Hz, 1H, H-4'), 7.45–7.51 (m, 4H, H-3', H-3"), 7.53–7.57 (m, 4H, H-2', H-2"), 8.86 (d, *J* = 2.2 Hz, 1H, H-2'"), 8.90 (br, 1H, NH). Signals attributed to the minor isomer **17b**: δ 1.66 (d, *J* = 6.9 Hz, C*H*$_3$CH), 5.58 (q, *J* = 7.1 Hz, CH$_3$C*H*). $^{13}C$ RMN (125 MHz, $CDCl_3$): δ 13.9 (*C*H$_3$CH), 47.4 (CH$_3$*C*H), 106.8 (C-3'"), 109.1 (C-7'"), 110.2 (*C*H=), 114.8 (C-4'"), 118.3 (C-5'"), 118.4 (C-5), 120.3 (C-6'"), 124.1 (C-2'), 125.0 (C-2"), 125.39 (C-4'), 125.40 (C-3a'"), 126.5 (C-3'), 126.7 (C-2'"), 126.8 (C-3"), 127.9 (C-1"), 131.2 (C-4"), 132.8 (C-7a'"), 136.5 (C-1'), 149.6 (C-2), 158.6 (C-4). Signals attributed to the minor isomer **17b**: δ 14.3, 126.3, 128.4, 150.2. HRMS (EI, [$M^+$]): *m/z* calcd for $C_{26}H_{21}ClN_3O_2$: 441.1244; found: 441.1253.

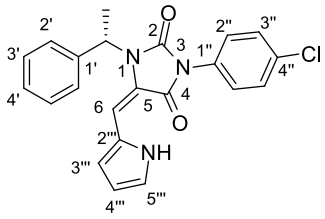
**(*S,E*)-5-((1*H*-Pyrrol-2-yl)methylene)-3-phenyl-1-(1-phenylethyl)imidazolidine-2,4-dione (18a). (*S,Z*)-5-((1*H*-Pyrrol-2-yl)methylene)-3-phenyl-1-(1-phenylethyl)imidazolidine-2,4-dione (19a).**



Following the procedure for **16a**/**17a**, a mixture **14a** (0.100 g, 0.30 mmol) and **10b** (0.030 g, 0.45 mmol) produced a mixture of **18a**/**18b** (88:12, 0.09 g, 85%) as a brown oil. $R_f$ 0.71 (hexane/EtOAc, 7:3). $[\alpha]_D^{25}$ = –71.9 (c 0.18, MeOH). IR (film): $\bar{\upsilon}$ = 3257, 1741, 1695, 1611, 1502, 1408, 1364, 1307, 1200, 1128, 1089, 1035, 772, 748, 691, 639, 601 $cm^{-1}$. $^1H$ RMN (500 MHz, $CDCl_3$): δ 1.92 (d, *J* = 7.3 Hz, 3H, C*H*$_3$CH), 5.88 (q, *J* = 7.3 Hz, 1H, CH$_3$C*H*), 6.22–6.25 (m, 2H, C*H*=, H-4'"), 6.30–6.34 (m, 1H, H-3'"), 6.93 (br s, 1H, H-5'"), 7.30–7.35 (m, 1H, H-4'), 7.39–7.46 (m, 5H, H-3', H-2", H-4"), 7.52–7.56 (m,

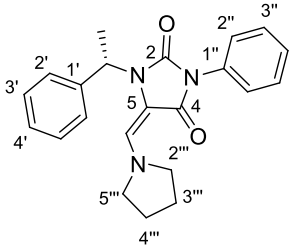
4H, H-2', H-3"), 12.20 (br s, 1H, NH). Signals attributed to the minor isomer **19a**: δ 1.98 (d, *J* = 7.3 Hz, C*H*$_3$CH), 7.70–7.74 (m, ArH). $^{13}$C RMN (125 MHz, $CDCl_3$): δ 16.9 (*C*H$_3$CH), 50.2 (CH$_3$*C*H), 110.8 (C-4'"), 112.4 (*C*H=), 118.1 (C-3'"), 119.1 (C-5), 122.8 (C-5'"), 126.4 (C-2"), 126.5 (C-2'), 126.6 (C-2'"), 127.9 (C-4'), 128.4 (C-4"), 129.0 (C-3'), 129.2 (C-3"), 131.5 (C-1"), 138.9 (C-1'), 152.1 (C-2), 162.6 (C-4). Signals attributed to the minor isomer **19a**: δ 14.1, 125.6, 126.0, 132.4, 167.8. HRMS (EI, [M$^+$]): *m/z* calcd for $C_{22}H_{19}N_3O_2$: 357.1477; found: 357.1490.

**(*S*,*E*)-5-((1H-Pyrrol-2-yl)methylene)-3-(4-chlorophenyl)-1-(1-phenylethyl)imidazolidine-2,4-dione (18b). (*S*,*Z*)-5-((1H-Pyrrol-2-yl)methylene)-3-(4-chlorophenyl)-1-(1-phenylethyl)imidazolidine-2,4-dione (19b).**



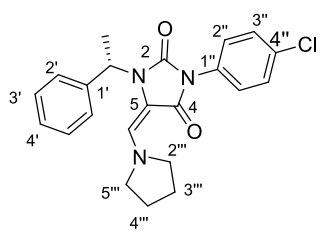
Following the procedure for **16a**/**17a**, a mixture of **14b** (0.100 g, 0.27 mmol) and **10b** (0.027 g, 0.40 mmol) yielded a mixture of **18b**/**19b** (89:11, 0.085 g, 80%) as a brown oil. $R_f$ 0.77 (hexane/EtOAc, 7:3). $[\alpha]_D^{25}$ = –104.3 (c 0.020, MeOH). IR (film): $\bar{\upsilon}$ = 3258, 1744, 1698, 1611, 1496, 1412, 1364, 1310, 1219, 1128, 1090, 1033, 1016, 945, 813, 770, 739, 697 cm$^{-1}$. $^1$H RMN (500 MHz, $CDCl_3$): δ 1.93 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 5.87 (q, *J* = 7.2 Hz, 1H, CH$_3$C*H*), 6.24–6.27 (m, 2H, C*H*=, H-4'"), 6.33–6.35 (m, 1H, H-3'"), 6.96 (br s, 1H, H-5'"), 7.32–7.36 (m, 1H, H-4'), 7.40–7.45 (m, 4H, H-2', H-3'), 7.49–7.55 (m, 4H, H-2'', H-3''), 12.14 (br s, 1H, NH). Signals attributed to the minor isomer **19b**: δ 1.99 (d, *J* = 7.3 Hz, C*H*$_3$CH), 6.04 (q, *J* = 7.3 Hz, CH$_3$C*H*), 6.64 (s, H-5'"). $^{13}$C RMN (125 MHz, $CDCl_3$): δ 16.8 (*C*H$_3$CH), 50.3 (CH$_3$*C*H), 110.9 (C-4'"), 112.8 (C-6), 118.4 (C-3'"), 118.8 (C-5), 123.0 (C-5'"), 126.5 (C-2'), 126.6 (C-2'"), 127.5 (C-2"), 127.9 (C-4'), 129.0 (C-3'), 129.3 (C-3"), 130.0 (C-4"), 134.0 (C-1"), 138.7 (C-1'), 151.7 (C-2), 162.3 (C-4). Signals attributed to the minor isomer **19b**: δ 16.5 (*C*H$_3$CH), 49.9 (CH$_3$*C*H). HRMS (EI, [M$^+$]): *m/z* calcd for $C_{22}H_{18}ClN_3O_2$: 391.1088; found: 391.1095.

**(*S*,*E*)-3-Phenyl-1-(1-phenylethyl)-5-(16yrrolidine-1-ylmethylene)imidazolidine-2,4-dione (20a). (*S*,*Z*)-3-Phenyl-1-(1-phenylethyl)-5-(16yrrolidine-1-ylmethylene)imidazolidine-2,4-dione (21a).**



Following the procedure for **16a**/**17a**, a mixture of **14a** (0.100 g, 0.30 mmol) and **10c** (0.021 g, 0.30 mmol) delivered a mixture of **20a**/**21a** (90:10, 0.099 g, 92%) as a red oil. $R_f$ 0.25 (hexane/EtOAc, 7:3). $[\alpha]_D^{25}$ = –51.1 (c 0.200, MeOH). IR (film): $\bar{\upsilon}$ = 1736, 1682, 1614, 1500, 1400, 1337, 1227, 1121, 949, 762, 694 cm$^{-1}$. $^1$H RMN (500 MHz, $CDCl_3$): δ 1.79 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 1.80–1.86 (m, 4H, H-3'", H-4'"), 3.33–3.39 (m, 2H, H2'", H-5'"), 3.45-3.53 (m, 2H, H-2'", H-5'"), 5.83 (q, *J* = 7.2 Hz, 1H, CH$_3$C*H*), 6.25 (s, 1H, C*H*=), 7.26–7.34 (m, 2H, H-4', H-4"), 7.35–7.41 (m, 4H, H-2', H-3'), 7.43–7.47 (m, 2H, H-3"), 7.50–7.54 (m, 2H, H-2"). Signals attributed to the minor isomer **21a**: δ 1.74 (d, *J* = 7.3 Hz, C*H*$_3$CH), 5.55 (q, *J* = 7.3 Hz, CH$_3$C*H*). $^{13}$C RMN (125 MHz, $CDCl_3$): δ 16.9 (*C*H$_3$CH), 25.4 (C-3'", C-4'"), 49.7 (CH$_3$*C*H), 53.7 (C-2'", C-5'"), 102.0 (C-5), 126.4 (C-2"), 126.5 (C-2'), 127.2 (C-4' or C-4"), 127.4 (C-4" or C-4'), 128.6 (C-3'), 128.7 (C-3"), 132.8 (C-1"), 133.1 (*C*H=), 140.2 (C-1'), 152.0 (C-2), 158.8 (C-4). Signals attributed to the minor isomer **21a**: δ 14.2, 25.7, 125.6, 126.2, 126.8, 128.4. HRMS (EI, [M$^+$]): m/z calcd for $C_{22}H_{23}N_3O_2$: 361.1790; found: 361.1790.

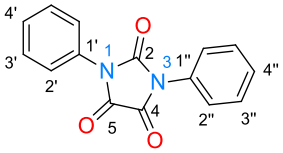
**(*S*,*E*)-3-(4-Chlorophenyl)-1-(1-phenylethyl)-5-(16yrrolidine-1-ylmethylene)imidazolidine-2,4-dione (20b). (*S*,*Z*)-3-(4-Chlorophenyl)-1-(1-phenylethyl)-5-(16yrrolidine-1-ylmethylene)imidazolidine-2,4-dione (21b).**



Following the procedure for **16a**/**17a**, a mixture of **14b** (0.100 g, 0.27 mmol) and **10c** (0.019 g, 0.27 mmol) gave a mixture of **20b**/**21b** (88:12, 0.089 g, 83%) as a red oil. $R_f$ 0.25 (hexane/EtOAc, 7:3). $[\alpha]_D^{25}$ = –36.0 (c 0.300, MeOH). IR (film): $\bar{\upsilon}$ = 1738, 1685, 1614, 1495, 1402, 1337, 1130, 1091, 949, 758, 699, 660 cm$^{-1}$. $^1$H RMN (500 MHz, $CDCl_3$): δ 1.78 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 1.80–1.87 (m, 4H, H-3'", H-4'"), 3.33–3.39 (m, 2H, H-2'", H-5'"), 3.45-3.53 (m, 2H, H-2'", H-5'"), 5.82 (q, *J* = 7.2

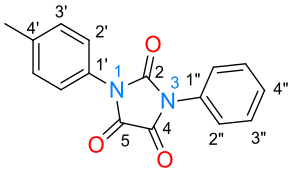
Hz, 1H, $CH_3CH$), 6.27 (s, 1H, C*H*=), 7.27–7.31 (m, 1H, H-4'), 7.32–7.40 (m, 4H, H-2', H-3'), 7.40–7.43 (m, 2H , H-3"), 7.49–7.52 (m, 2H, H-2"). Signals attributed to the minor isomer **21b**: δ 1.75 (d, *J* = 7.2 Hz, $CH_3CH$). $^{13}$C RMN (125 MHz, $CDCl_3$): δ 16.9 ($CH_3CH$), 25.4 (C-3'", C-4'"), 49.8 ($CH_3CH$), 53.8 (C-2'", C-5'"), 101.7 (C-5), 126.5 (C-2'), 127.5 (C-4'), 127.6 (C-2"), 128.8 (C-3'), 128.9 (C-3"), 131.5 (C-4"), 132.7 (C-1"), 133.5 (*C*H=), 140.0 (C-1'), 151.7 (C-2), 158.5 (C-4). Signals attributed to the minor isomer **21b**: δ 52.2, 127.7, 129.4. HRMS (EI, [$M^+$]): *m/z* calcd for $C_{22}H_{22}ClN_3O_2$: 395.1401; found: 395.1405.

**1,3-Diphenylimidazolidine-2,4,5-trione (22a).**



In a round-bottom flask, a mixture of **9a** (0.100 g, 0.32 mmol) and *m*CPBA (70%) (0.152 g, 0.89 mmol) in dry $CH_2Cl_2$ (10 mL) was stirred at rt for 4 h. The crude mixture was extracted with $CH_2Cl_2$ (2 x 15 mL) and the organic layer was dried ($Na_2SO_4$). The solvent was removed under vacuum and the residue purified by column chromatography over silica gel (30 g/g mixture, hexane/EtOAc, 90:10), resulting in **22a** (0.074 g, 86%) as a white solid. $R_f$ 0.61 (hexane/EtOAc, 7:3); mp 203–204 °C. IR (film): $\bar{\upsilon}$ = 1792, 1731, 1593, 1498, 1390, 1197, 748, 687, 607 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.45–7.50 (m, 6H, H-2', H-2", H-4', H-4"), 7.51–7.55 (m, 4H, H-3', H-3"). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 125.8 (C-2', C-2"), 129.3 (C-4', C-4"), 129.5 (C-3', C-3"), 129.7 (C-1', C-1"), 151.7 (C-2), 155.0 (C-4, C-5). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{15}H_{11}N_2O_3$: 267.0770; found: 267.0776.

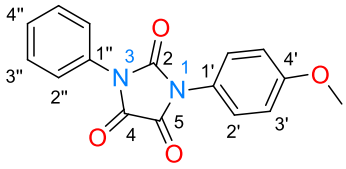
**3-Phenyl-1-(*p*-tolyl)imidazolidine-2,4,5-trione (22b).**



Method A: Following the procedure for **22a**, a mixture of **9b** (0.100 g, 0.31 mmol) and *m*CPBA (70%) (0.152 g, 0.89 mmol) afforded **22b** (0.072 g, 82%) as a white solid.

Method B: Following the procedure for **22a**, a mixture of **9d** (0.100 g, 0.31 mmol) and *m*CPBA (70%) (0.152 g, 0.89 mmol) yielded **22b** (0.070 g, 80%) as a white solid. $R_f$ 0.60 (hexane/EtOAc, 7:3); mp 125–126 °C. IR (film): $\bar{\upsilon}$ = 1729, 1606, 1517, 1500, 1399, 1291, 1265, 1210, 1150, 795, 746, 715, 689 $cm^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.42 (s, 3H, C*H*$_3$), 7.30–7.38 (m, 4H, H-2', H-3'), 7.45–7.55 (m, 5H, H-2", H-3", H-4"). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.3 ($CH_3$), 125.7 (C-2'), 125.8 (C-2"), 127.1 (C-1'), 129.2 (C-4"), 129.5 (C-3"), 129.8 (C-1"), 130.1 (C-3'), 139.5 (C-4'), 151.9 (C-2), 155.1 (C-4 or C-5), 155.2 (C-5 or C-4). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{16}H_{12}N_2O_3$: 280.0848; found: 280.0853.

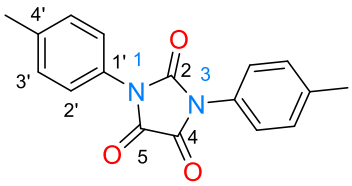
**1-(4-Methoxyphenyl)-3-phenylimidazolidine-2,4,5-trione (22c).**



Method A: Following the procedure for **22a**, a mixture of **9c** (0.100 g, 0.30 mmol) and *m*CPBA (70%) (0.146 g, 0.85 mmol) furnished **22c** (0.075 g, 85%) as a white solid.

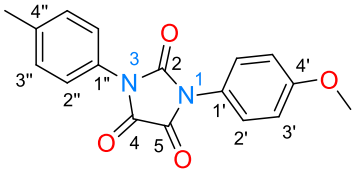
Method B: Following the procedure for **22a**, a mixture of **9g** (0.100 g, 0.30 mmol) and *m*CPBA (70%) (0.147 g, 0.8 mmol) provided **22c** (0.077 g, 87%) as a white solid. $R_f$ 0.55 (hexane/EtOAc, 7:3); mp 142–143 °C. IR (film): $\bar{\upsilon}$ = 1727, 1620, 1505, 1499, 1392, 1246, 1204, 1163, 1105, 851, 807, 751, 691 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): δ 3.86 (s, 3H, C*H*$_3$O), 6.98–7.03 (m, 2H, H-3'), 7.34–7.38 (m, 2H, H-2'), 7.43–7.37 (m, 3H, H-2", H-4"), 7.49–7.54 (m, 2H, H-3"). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 55.6 ($CH_3$O), 114.8 (C-3'), 122.2 (C-1'), 125.8 (C-2"), 127.3 (C-2'), 129.2 (C-4"), 129.5 (C-3"), 129.8 (C-1"), 152.0 (C-2), 155.2 (C-4 or C-5), 155.3 (C-5 or C-4), 160.0 (C-4'). HRMS (ESI-TOF, [$M^+$]): *m/z* calcd for $C_{16}H_{12}N_2O_4$: 296.0797; [$M^+$+Na(23)]: 319.0695; found [$M^+$+Na(23)]: 319.0689.

**1,3-Di(*p*-tolyl)imidazolidine-2,4,5-trione (22d).**



Following the procedure for **22a**, a mixture of **9e** (0.100 g, 0.30 mmol) and *m*CPBA (70%) (0.146 g, 0.85 mmol) rendered **22d** (0.081 g, 92%) as a white solid. $R_f$ 0.56 (hexane/EtOAc, 7:3); mp 124–125 °C. IR (film): $\bar{\upsilon}$ = 2928, 1729, 1685, 1569, 1516, 1414, 1401, 1285, 1257, 1210, 1135, 799, 848, 721 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 6H, 2C*H*$_3$), 7.30–7.37 (m, 8H, H-2', H-3', H-2", H-3"). $^{13}C$ NMR (100 MHz, CDCl): δ 21.2 (2*C*H$_3$), 125.7 (C-2', C-2"), 127.1 (C-1', C-1"), 130.1 (C-3', C-3"), 139.5 (C-4', C-4"), 152.0 (C-2), 155.2 (C-4, C-5). HRMS (EI, [$M^+$]): *m/z* calcd for $C_{17}H_{14}N_2O_3$: 294.1005; found: 294.1003.

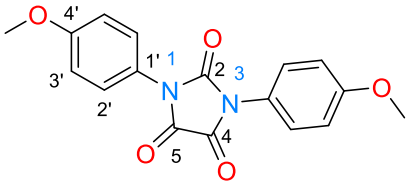
**1-(4-Methoxyphenyl)-3-(*p*-tolyl)imidazolidine-2,4,5-trione (22e).**



Method A: Following the procedure for **22a**, a mixture of **9f** (0.100 g, 0.28 mmol) and *m*CPBA (70%) (0.140 g, 0.81 mmol) produced **22e** (0.077 g, 87%).

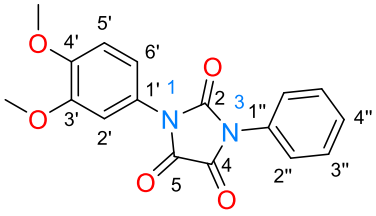
Method B: Following the procedure for **22a**, a mixture of **9h** (0.100 g, 0.28 mmol) and *m*CPBA (70%) (0.140 g, 0.81 mmol) generated **22e** (0.079 g, 89%) as a white solid. $R_f$ 0.47 (hexane/EtOAc, 7:3); mp 127–128 °C. IR (film): $\bar{\upsilon}$ = 1769, 1711, 1597, 1505, 1436, 1398, 1375, 1153, 785, 757, 690 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 3H, C*H*$_3$Ar), 3.84 (s, 3H, C*H*$_3$O), 6.97–7.03 (m, 2H, H-3'), 7.28–7.33 (m, 4H, H-2", H-3"), 7.33–7.38 (m, 2H, H-2'). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 21.3 (*C*H$_3$), 55.6 (*C*H$_3$O), 114.7 (C-3'), 122.3 (C-1'), 125.7 (C-2"), 127.1 (C-1"), 127.3 (C-2'), 130.1 (C-3"), 139.4 (C-4"), 152.1 (C-2), 155.3 (C-4 or C-5), 155.4 (C-5 or C-4), 160.0 (C-4'). HRMS (ESI-TOF, [$M^+$]): *m/z* calcd for $C_{17}H_{14}N_2O_4$: 310.0954; [$M^+$+Na(23)]: 333.0851; found [$M^+$+Na(23)]: 333.0846.

**1,3-Bis(4-methoxyphenyl)imidazolidine-2,4,5-trione (22f).**



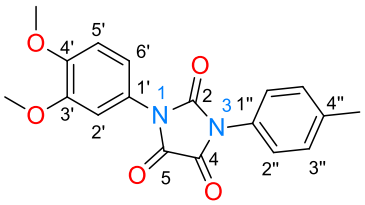
Following the procedure for **22a**, a mixture of **9i** (0.100 g, 0.27 mmol) and *m*CPBA (70%) (0.134 g, 0.78 mmol) provided **22f** (0.077 g, 86%) as a white solid. $R_f$ 0.41 (hexane/EtOAc, 7:3); mp 172–173 °C. IR (film): $\bar{\upsilon}$ = 1770, 1729, 1612, 1505, 1401, 1306, 1237, 1210, 1152, 1024, 797, 748 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 3.83 (s, 6H, 2C*H*$_3$O), 6.97–7.01 (m, 4H, H-3', H-3"), 7.31–7.35 (m, 4H, H-2', H-2"). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 55.6 (2*C*H$_3$O), 114.8 (C-3', C-3"), 122.3 (C-1', C-1"), 127.3 (C-2', C-2"), 152.1 (C-2), 155.5 (C-4, C-5), 160.0 (C-4', C-4"). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{17}H_{15}N_2O_5$: 327.0981; found: 327.0971.

**1-(3,4-Dimethoxyphenyl)-3-phenylimidazolidine-2,4,5-trione (22g).**



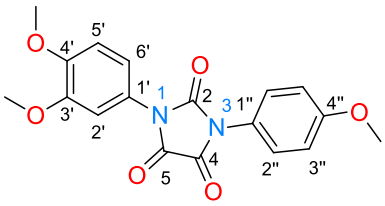
Following the procedure for **22a**, a mixture of **9j** (0.100 g, 0.27 mmol) and *m*CPBA (70%) (0.134 g, 0.78 mmol) afforded **22g** (0.082 g, 92%) as a white solid. $R_f$ 0.38 (hexane/EtOAc, 7:3); mp 156–157 °C. IR (film): $\bar{\upsilon}$ = 1735, 1599, 1505, 1450, 1396, 1259, 1235, 1210, 1131, 1008, 803, 754, 740, 691 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 3.88 (s, 3H, C*H*$_3$O), 3.92 (s, 3H, C*H*$_3$O), 6.94–6.97 (m, 2H, H-2', H-5'), 7.03 (dd, *J* = 8.6, 2.4 Hz, 1H, H-6'), 7.43–7.47 (m, 3H, H-2", H-4"), 7.49–7.55 (m, 2H, H-3"). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 56.11 (*C*H$_3$O), 56.13 (*C*H$_3$O), 109.3 (C-2'), 111.1 (C-5'), 118.7 (C-6'), 122.2 (C-1'), 125.8 (C-2"), 129.3 (C-4"), 129.5 (C-3"), 129.7 (C-1"), 149.4 (C-3' or C-4'), 149.7 (C-4' or C-3'), 152.0 (C-2), 155.1 (C-4 or C-5), 155.3 (C-5 or C-4). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{17}H_{15}N_2O_5$: 327.0981; found: 327.0970.

**1-(3,4-Dimethoxyphenyl)-3-(*p*-tolyl)imidazolidine-2,4,5-trione (22h).**



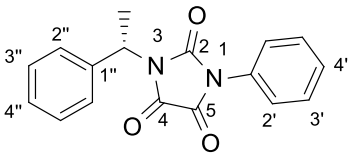
Following the procedure for **22a**, a mixture of **9k** (0.100 g, 0.26 mmol) *m*CPBA (70%) (0.117 g, 0.52 mmol) provided **22h** (0.079 g, 88%) as a white solid. $R_f$ 0.32 (hexane/EtOAc, 7:3); mp 140–141 °C. IR (film): $\bar{\upsilon}$ = 2925, 1734, 1513, 1399, 1256, 1236, 1204, 1139, 1009, 794, 742 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 2.40 (s, 3H, C*H*$_3$), 3.87 (s, 3H, C*H*$_3$O), 3.92 (s, 3H, C*H*$_3$O), 6.95 (d, *J* = 7.0 Hz, 1H, H-5'), 6.96 (d, *J* = 2.0 Hz, 1H, H-2'), 7.02 (dd, *J* = 7.0, 2.0 Hz, 1H, H-6'), 7.27–7.35 (m, 4H, H-2", H-3"). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 21.3 (*C*H$_3$), 56.20 (*C*H$_3$O), 56.22 (*C*H$_3$O), 109.5 (C-2'), 111.3 (C-5'), 118.8 (C-6'), 122.4 (C-1'), 125.8 (C-2"), 127.2 (C-1"), 130.2 (C-3"), 139.6 (C-4"), 149.5 (C-3'), 149.7 (C-4'), 152.2 (C-2), 155.3 (C-4 or C-5), 155.5 (C-5 or C-4). HRMS (ESI-TOF, [$M^+$]): *m/z* calcd for $C_{18}H_{16}N_2O_5$: 340.1059; [$M^+$+Na(23)]: 363.0957; found [$M^+$+Na(23)]: 363.0951.

**1-(3,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)imidazolidine-2,4,5-trione (22i).**



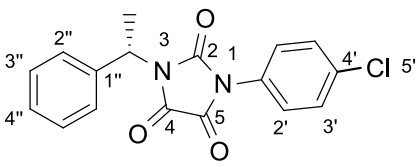
Following the procedure for **22a**, a mixture of **9l** (0.100 g, 0.25 mmol) *m*CPBA (70%) (0.124 g, 0.72 mmol) yielded **22i** (0.083 g, 92%) as a white solid. $R_f$ 0.28 (hexane/EtOAc, 7:3); mp 136–137 °C. IR (film): $\bar{\upsilon}$ = 1737, 1602, 1507, 1455, 1402, 1258, 1237, 1203, 1132, 1025, 838, 791, 743 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): δ 3.85 (s, 3H, C*H*$_3$O-4"), 3.89 (s, 3H, C*H*$_3$O), 3.92 (s, 3H, C*H*$_3$O), 6.95 (d, *J* = 2.4 Hz, 1H, H-2'), 6.96 (d, *J* = 8.6 Hz, 1H, H-5'), 7.00–7.03 (m, 2H, H-3"), 7.03 (dd, *J* = 8.6, 2.4 Hz, 1H, H-6'), 7.34–7.39 (m, 2H, H-2"). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 55.7 (*C*H$_3$O-4"), 56.23 (*C*H$_3$O), 56.25 (*C*H$_3$O), 109.4 (C-2'), 111.3 (C-5'), 114.9 (C-3"), 118.7 (C-6'), 122.3 (C-1"), 122.4 (C-1'), 127.4 (C-2"), 149.5 (C-3' or C-4'), 149.7 (C-4' or C-3'), 152.4 (C-2), 155.4 (C-4 or C-5), 155.5 (C-5 or C-4), 160.1 (C-4"). HRMS (ESI, [M+H]$^+$): *m/z* calcd for $C_{18}H_{17}N_2O_6$: 357.1087; found: 357.1075.

**(S)-1-Phenyl-3-(1-phenylethyl)imidazolidine-2,4,5-trione (23a).**



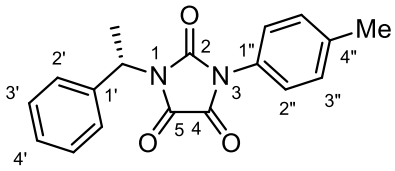
Following the procedure for **22a**, a mixture of **14a** (0.100 g, 0.30 mmol) and *m*CPBA (70%) (0.148 g, 0.86 mmol) furnished **23a** (0.080 g, 91%) as a colorless oil. $R_f$ 0.66 (hexane/EtOAc, 7:3). $[\alpha]_D^{25}$ = –24.7 (c 6.00, MeOH). IR (film): $\bar{\upsilon}$ = 2938, 1731, 1500, 1396, 1194, 758, 687 $cm^{-1}$. $^1H$ RMN (600 MHz, $CDCl_3$): δ 1.97 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 5.56 (q, *J* = 7.2 Hz, 1H, CH$_3$C*H*), 7.32–7.36 (m, 1H, H-4"), 7.36–7.43 (m, 5H, H-2', H-4', H-3"), 7.48 (t, *J* = 7.8 Hz, 2H, H-3'), 7.54 (br d, *J* = 7.8 Hz, 2H, H-2"). $^{13}C$ RMN (150 MHz, $CDCl_3$): δ 17.5 (*C*H$_3$CH), 52.3 (CH$_3$*C*H), 125.7 (C-2'), 127.8 (C-2"), 128.7 (C-4"), 129.0 (C-3"), 129.1 (C-4'), 129.5 (C-3'), 130.0 (C-1'), 138.6 (C-1"), 152.5 (C-2), 155.3 (C-5), 155.9 (C-4). HRMS (ESI-TOF, [$M^+$]): *m/z* calcd for $C_{17}H_{14}N_2O_3$: 294.1004; [$M^+$+Na(23)]: 317.0902; found [$M^+$+Na(23)]: 317.0897.

**(*S*)-1-(4-Chlorophenyl)-3-(1-phenylethyl)imidazolidine-2,4,5-trione (23b).**



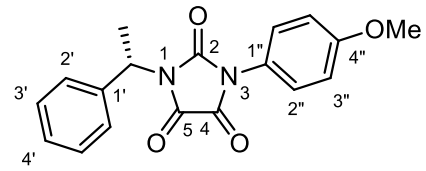
Following the procedure for **22a**, a mixture of **14b** (0.100 g, 0.27 mmol) and *m*CPBA (70%) (0.148 g, 0.858 mmol) produced **23b** (0.079 g, 89%) as white crystals. $R_f$ 0.56 (hexane/AcOEt, 7:3); mp 103–104 ºC. $[\alpha]_D^{25}$ = –239.7 (c 0.06, MeOH). IR (film): $\bar{\upsilon}$ = 1728, 1493, 1402, 1376, 1354, 1201, 1080, 833, 755, 693 $cm^{-1}$. $^1H$ RMN (600 MHz, $CDCl_3$): δ 1.96 (d, *J* = 7.2 Hz, 1H, C*H*$_3$CH), 5.54 (q, *J* = 7.2 Hz, 1H, CH$_3$C*H*), 7.31–7.40 (m, 5H, H-3', H-3", H-4"), 7.42–7.45 (m, 2H, H-2'), 7.50–7.54 (m, 2H, H-2"). $^{13}C$ RMN (150 MHz, $CDCl_3$): δ 17.4 (*C*H$_3$CH), 52.3 (CH$_3$*C*H), 126.8 (C-2'), 127.8 (C-2"), 128.4 (C-4'), 128.7 (C-4"), 129.0 (C-3"), 129.6 (C-3'), 134.8 (C-1'), 138.5 (C-1"), 152.2 (C-2), 155.0 (C-5), 155.7 (C-4). HRMS (ESI-TOF, [$M^+$]): *m/z* calcd for $C_{17}H_{13}ClN_2O_3$: 328.0615; [$M^+$+Na(23)]: 351.0512; found [$M^+$+Na(23)]: 351.0564.

**(*S*)-1-(1-Phenylethyl)-3-(*p*-tolyl)imidazolidine-2,4,5-trione (23c).**




Following the procedure for **22a**, a mixture of **14c** (0.100 g, 0.29 mmol) and *m*CPBA (70%) (0.139 g, 0.81 mmol) generated **23c** (0.080 g, 90%) as white crystals. $R_f$ 0.55 (hexane/AcOEt, 7:3); mp 91–92 ºC. $[\alpha]_D^{25}$ = –33.6 (c 0.06, MeOH). IR (film): $\bar{\upsilon}$ = 1777, 1715, 1513, 1399, 1360, 1194, 1054, 950, 833, 794, 758, 742, 696 $cm^{-1}$. $^1$H RMN (600 MHz, $CDCl_3$): δ 1.96 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 2.39 (s, 1H, C*H*$_3$Ar), 5.55 (q, *J* = 7.2 Hz, 1H. $CH_3$C*H*), 7.23–7.29 (m, 4H, H-2", H-3"), 7.32–7.36 (m, 1H, H-4'), 7.38 (br t, *J* = 7.2 Hz, 2H, H-3'), 7.53 (br d, *J* = 7.2 Hz, 2H, H-2'). $^{13}$C RMN (150 MHz, $CDCl_3$): δ 17.5 (*C*H$_3$CH), 21.3 (*C*H$_3$Ar), 52.2 (CH$_3$*C*H), 125.6 (C-2"), 127.2 (C-1"), 127.8 (C-2'), 128.7 (C-4'), 129.0 (C-3'), 130.1 (C-3"), 138.7 (C-1'), 139.3 (C-4"), 152.6 (C-2), 155.4 (C-4), 156.0 (C-5). HRMS (ESI, $[M+H]^+$): *m/z* calcd for $C_{18}H_{17}N_2O_3$: 309.1239; found: 309.1243.

**(*S*)-1-(1-Phenylethyl)-3-(4-methoxyphenyl)imidazolidine-2,4,5-trione (23d).**




Following the procedure for **22a**, a mixture of **14d** (0.100 g, 0.27 mmol) and *m*CPBA (70%) (0.132 g, 0.77 mmol) formed **23d** (0.082 g, 92%) as a pale-yellow oil. $R_f$ 0.42 (hexane/AcOEt, 7:3). $[\alpha]_D^{25}$ = –157.2 (c 6.00, MeOH). IR (film): $\bar{\upsilon}$ = 2928, 1725, 1672, 1617, 1507, 1402, 1295, 1246, 1171, 1136, 1097, 1025, 944, 823, 758, 696 $cm^{-1}$. $^1$H RMN (600 MHz, $CDCl_3$): δ 1.96 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH), 3.82 (s, 1H, C*H*$_3$O), 5.53 (q, *J* = 7.2 Hz, 1H. $CH_3$C*H*), 6.96 (br d, *J* = 7.8 Hz, 2H, H-3"), 7.26 (br d, *J* = 7.8 Hz, 2H, H-2"), 7.32–7.35 (m, 1H, H-4'), 7.38 (t, *J* = 7.8 Hz, 2H, H-3'), 7.53 (br d, *J* = 7.8 Hz, 2H, H-2'). $^{13}$C RMN (150 MHz, $CDCl_3$): δ 17.4 (*C*H$_3$CH), 52.1 (CH$_3$*C*H), 55.6 (*C*H$_3$O), 114.7 (C-3"), 122.4 (C-1"), 127.1 (C-2"), 127.7 (C-2'), 128.6 (C-4'), 128.9 (C-3'), 138.6 (C-1'), 152.7 (C-2), 155.5 (C-5), 156.0 (C-4), 159.8 (C-4"). HRMS (ESI-TOF, $[M^+]$): *m/z* calcd for $C_{18}H_{16}N_2O_4$: 324.1110; $[M^+$+Na(23)]: 347.1008; found $[M^+$+Na(23)]: 347.0972.

Single crystal X-Ray Crystallography

Compound **16b** were obtained as pale-yellow crystals and crystallized on MeOH, which were mounted on glass fibers. Crystallographic measurements were performed by utilizing an area-detector with Mo Kα radiation (λ = 71073 Å; graphite monochromator) at rt. Unit cell parameters were obtained from a least-squares refinement. Intensities were corrected for Lorentz and polarization effects. Absorption correction was applied by "multi-scan" method. Anisotropic temperature factors were introduced for all non-hydrogen atoms. Hydrogen atoms were placed in idealized positions and their atomic coordinates refined by employing unit weights. After the structure was solved using SHELXT,[4] it was visualized and plotted on the MERCURY program.[5] Data for **16b**: (CCDC **2371941**) Formula: $C_{26}H_{21}ClN_3O_2$; molecular weight: 407.46; cryst. Syst.: orthorhombic; space group: P 21 21 21; unit cell parameters: *a*, 6.5034(4), *b*, 18.5739(13), *c*, 18.5540(10) (Å); α, 90º, *β*, 90º, *γ*, 90º; temp. (K): 293(2); Z: 4; No. of reflections collected: 13817; no. of independent reflections: 7033; no. of reflections observed: 2088; data collection range: 3.104 < θ < 32.506; *R*: 0.0944; GOF: 1.125.

Evaluation of Antifungal Activity

The compounds herein prepared were submitted to the CLSI M27-A3 microdilution method, and an evaluation was made of the sensitivity of *Candida* spp. (*C. albicans* ATCC 10231, *C. glabrata* CBS 138 (sensitive), *C. glabrata* 43 (resistant), *C. krusei* ATCC 6258, and *C. dubliniensis* CD36) to various concentrations of the antifungal compounds,[6] applied at 187–0.01 μg/mL. The reference drug was fluconazole. The inoculum of *Candida* spp. was adjusted in a spectrophotometer to 620 nm, with a 1:1000 dilution made with RPMI medium. The 96-well microplates were inoculated with the yeast suspension (75 μL) and the compound (75 μL) to be tested. RPMI (without the addition of an antifungal agent) served as the sterility control and DMSO as the growth control. The microplates

were incubated at 37 °C for 24 h. Growth was quantified in a microplate spectrophotometer at 620 nm and expressed as the average of three independent assays.

References


1. J. D. McKerrow, J. M. A. Al-Rawi and P. Brooks, *Synth. Commun.*, 2010, **40**, 1161−1179.
2. S. J. Gu, J. K. Lee, A. N. Pae, H. J. Chung, H. Rhim, S. Y. Han, S.-J. Min and Y. S. Cho, *Bioorg. Med. Chem. Lett*., 2010, **20**, 2705−2708.
3. P. Y. S. Lam, D. Bonne, G. Vincent, C. G. Clark and A. P. Combs, *Tetrahedron Lett.* 2003, **44**, 1691−1694.
4. G. M. Sheldrick, *Acta Crystallogr. C*, 2015, **A71**, 3−8.
5. C. F. Macrae, P. R. Edgington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor, M. Towler and J. van de Streek, *J. Appl. Crystallogr.*, 2006, **39**, 453−457.
6. M. Cuenca-Estrella, W. Lee-Yang, M. A. Ciblak, B. A. Arthington-Skaggs, E. Mellado, D. W. Warnock and J. L. Rodríguez-Tudela, J. L. *Antimicrob. Agents Chemother*., 2002, **46**, 3644–4647.

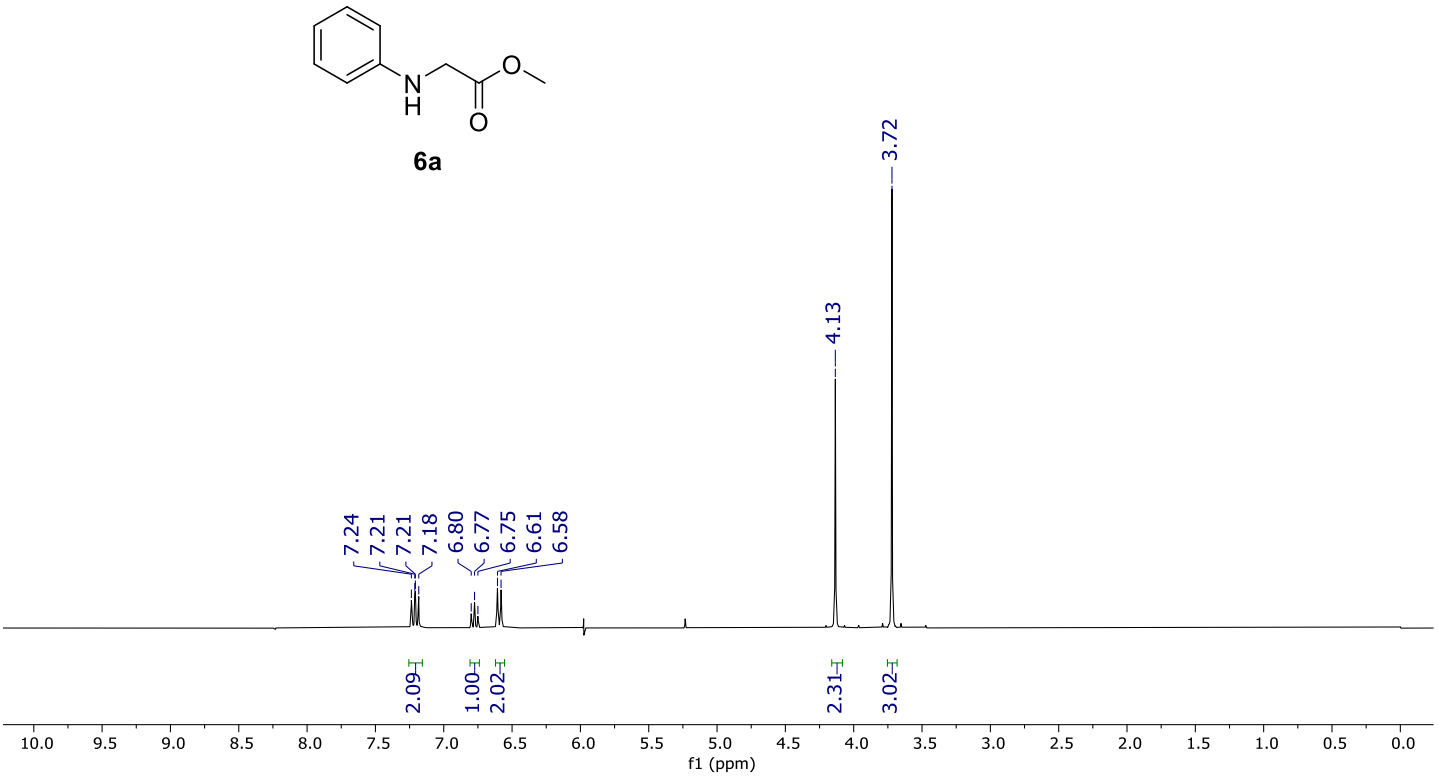



Figure S1. $^{1}H$ NMR (300 MHz, $CDCl_3$) spectrum of compound **6a**.

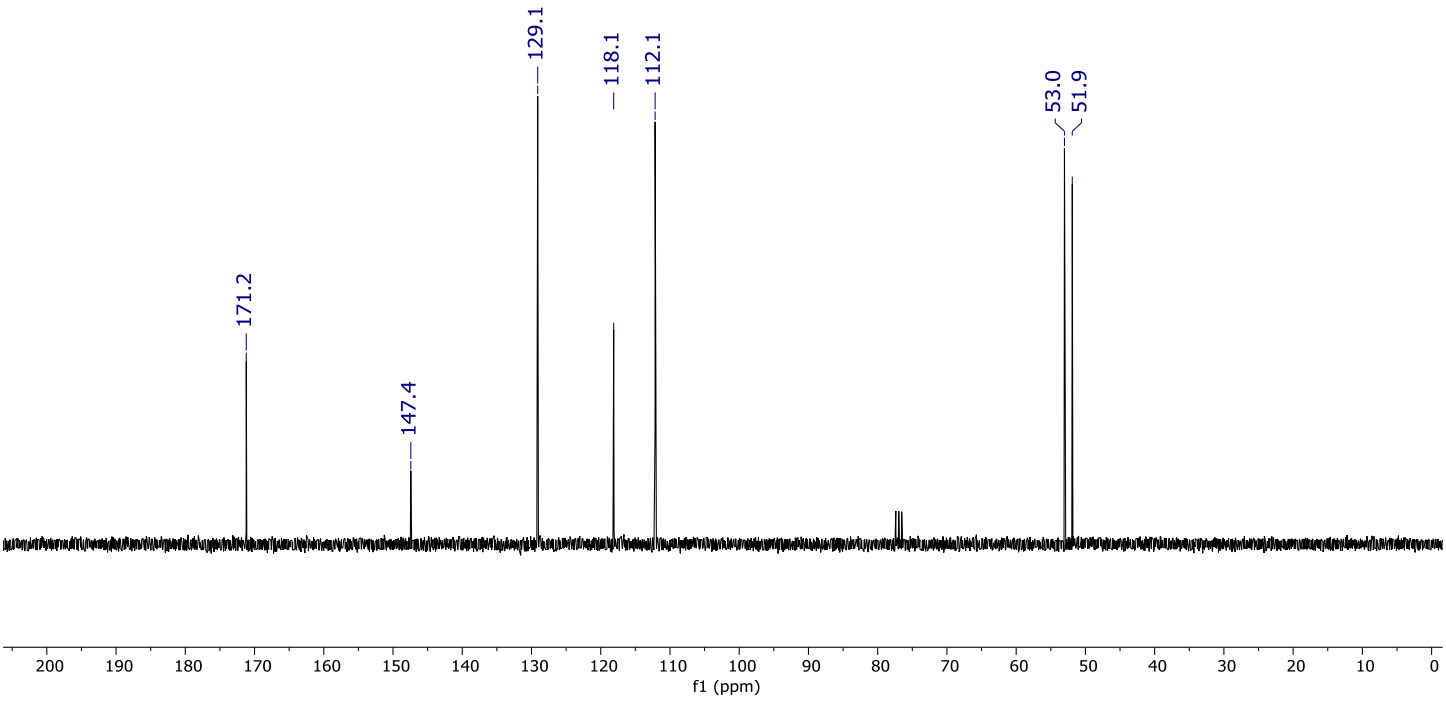



Figure S2. $^{13}C$ NMR (75.4 MHz, $CDCl_3$) spectrum of compound **6a**.

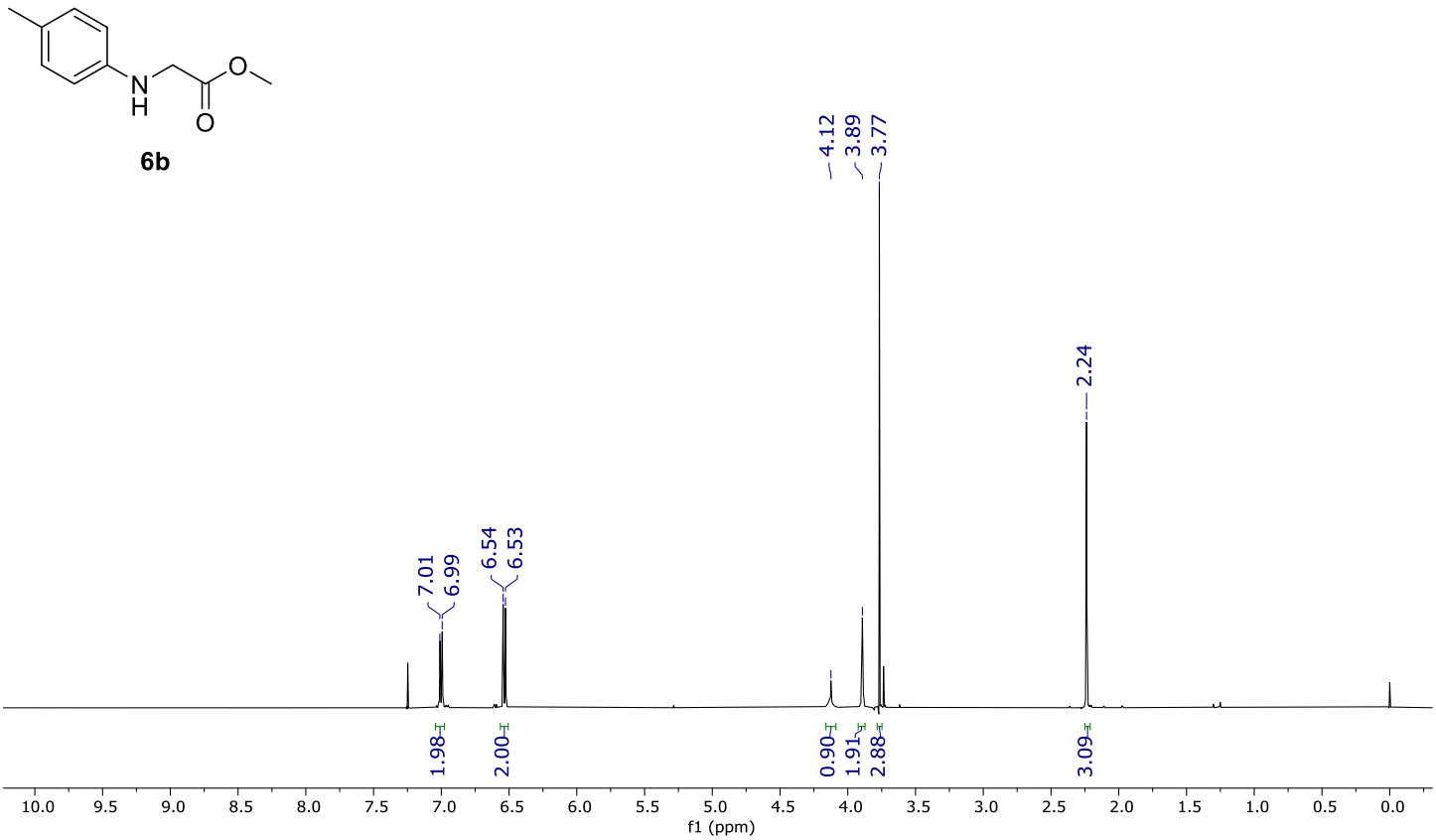



Figure S3. $^{1}H$ NMR (500 MHz, $CDCl_3$) spectrum of compound **6b**.

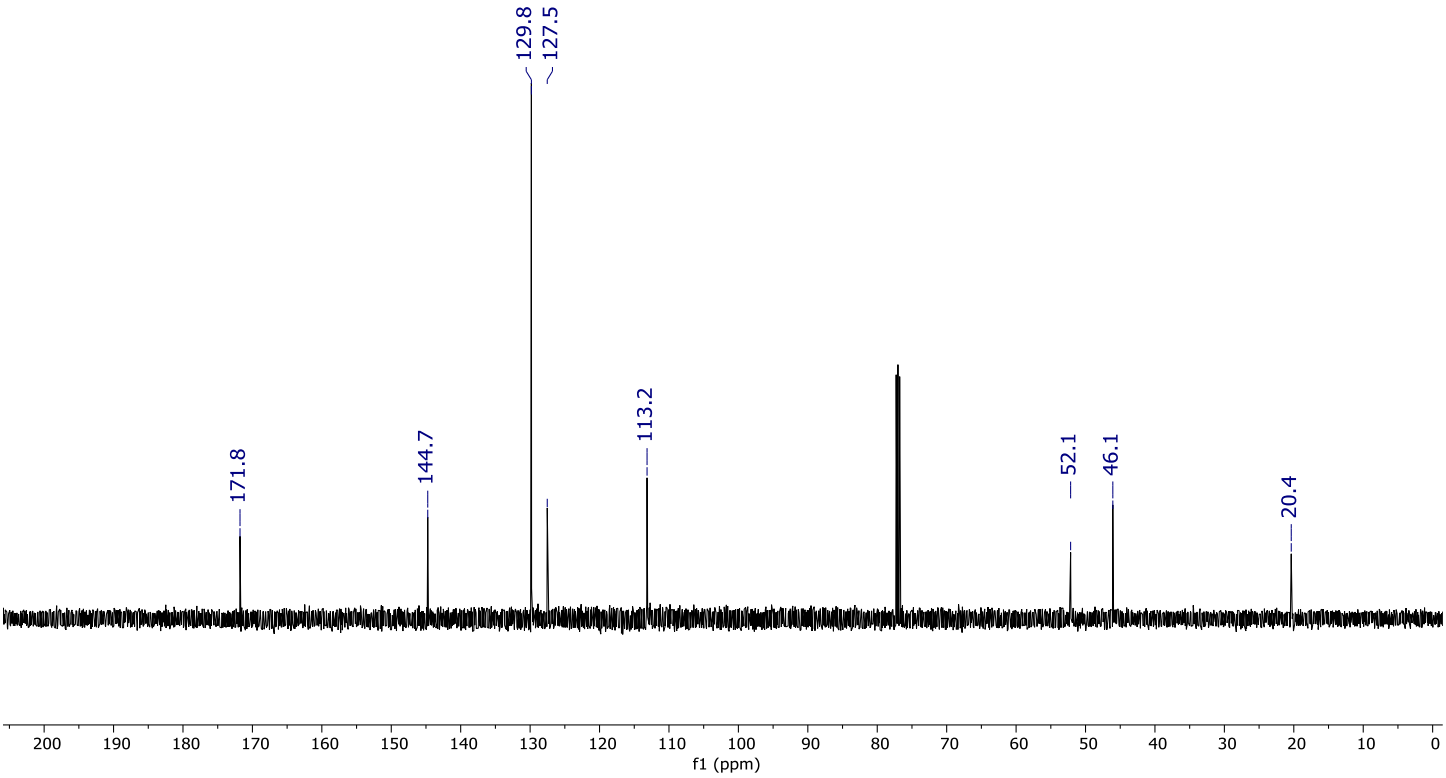



Figure S4. $^{13}C$ NMR (125 MHz, $CDCl_3$) spectrum of compound **6b**.

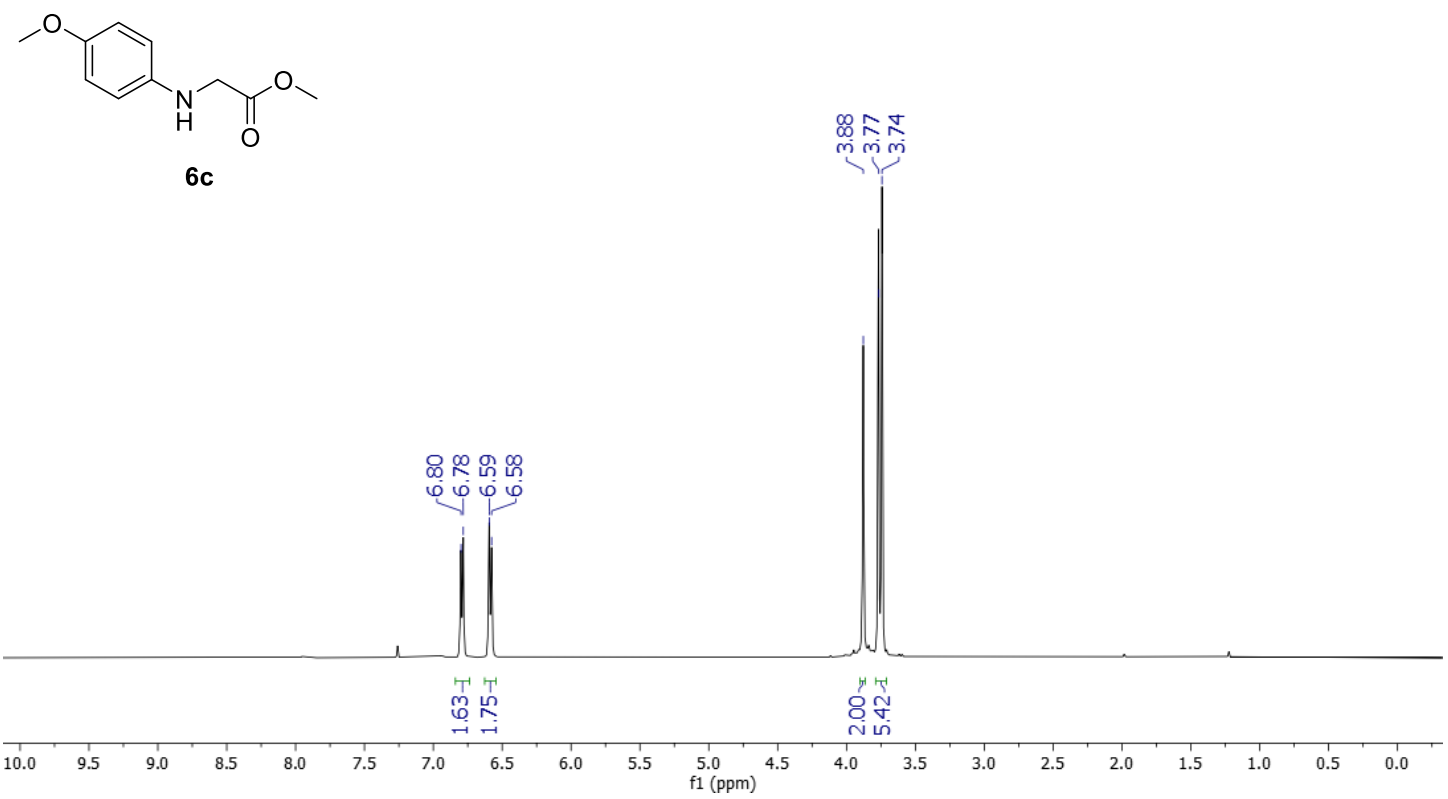



Figure S5. $^{1}H$ NMR (500 MHz, $CDCl_3$) spectrum of compound **6c**.

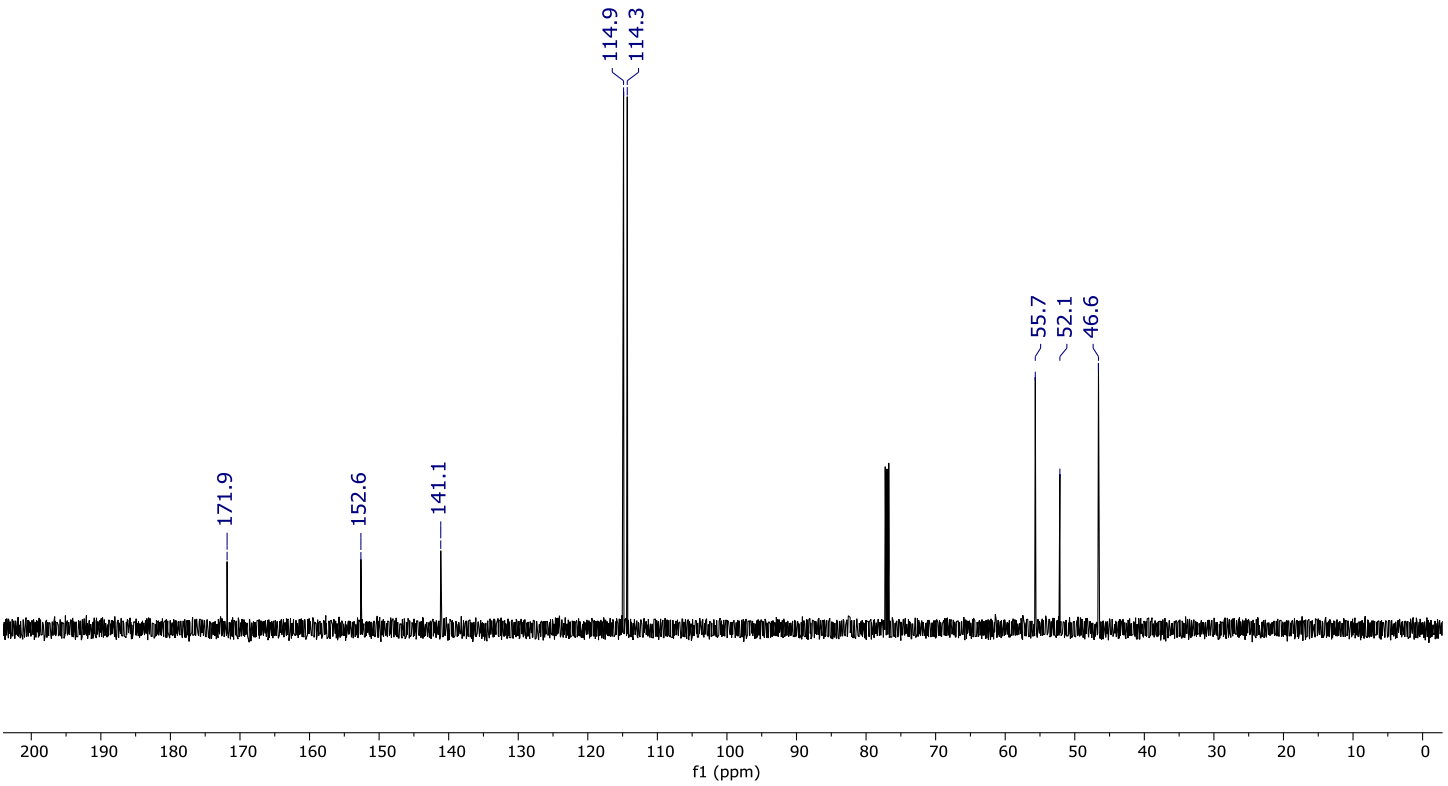



Figure S6. $^{13}C$ NMR (125 MHz, $CDCl_3$) spectrum of compound **6c**.

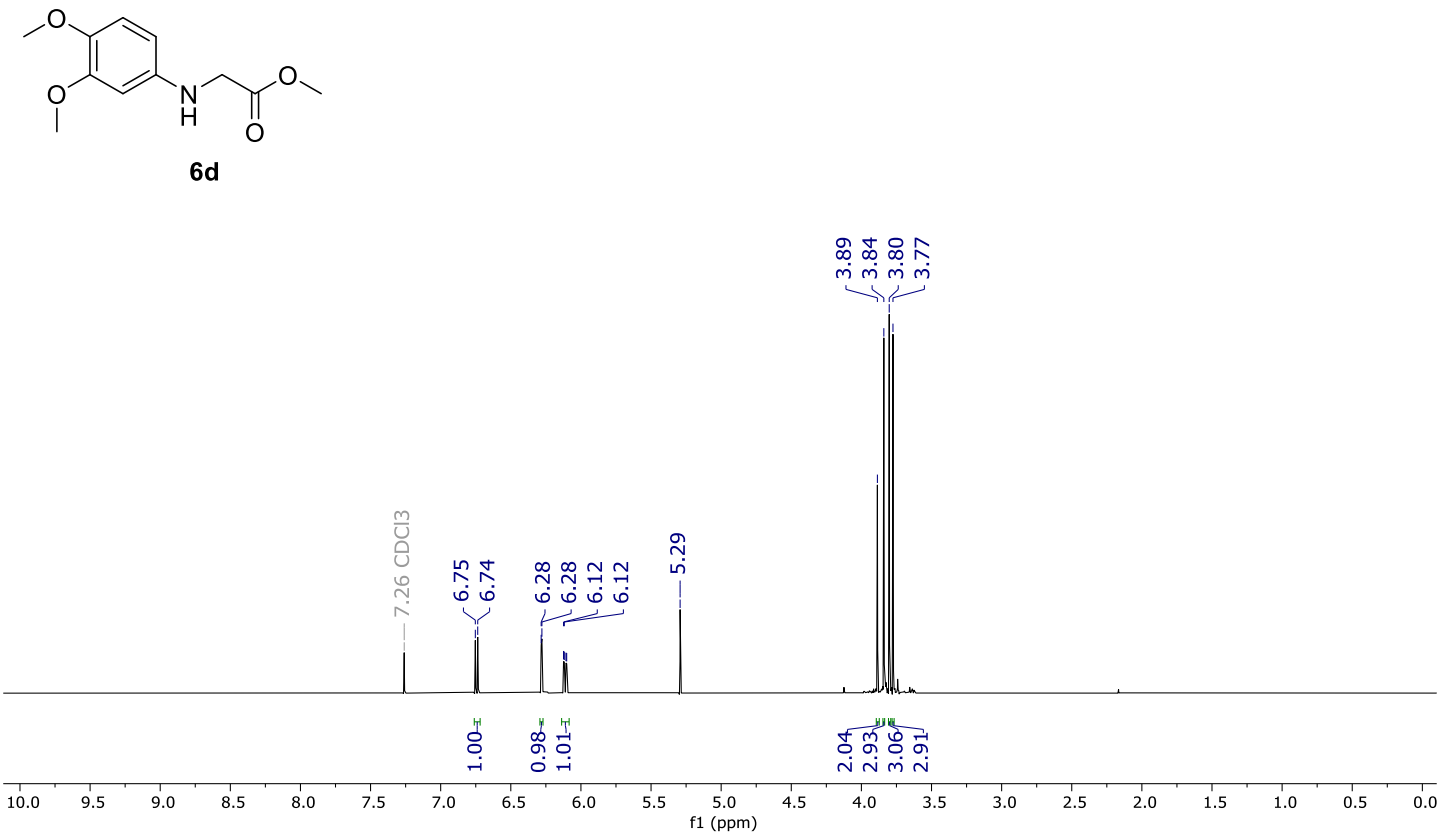



Figure S7. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **6d**.

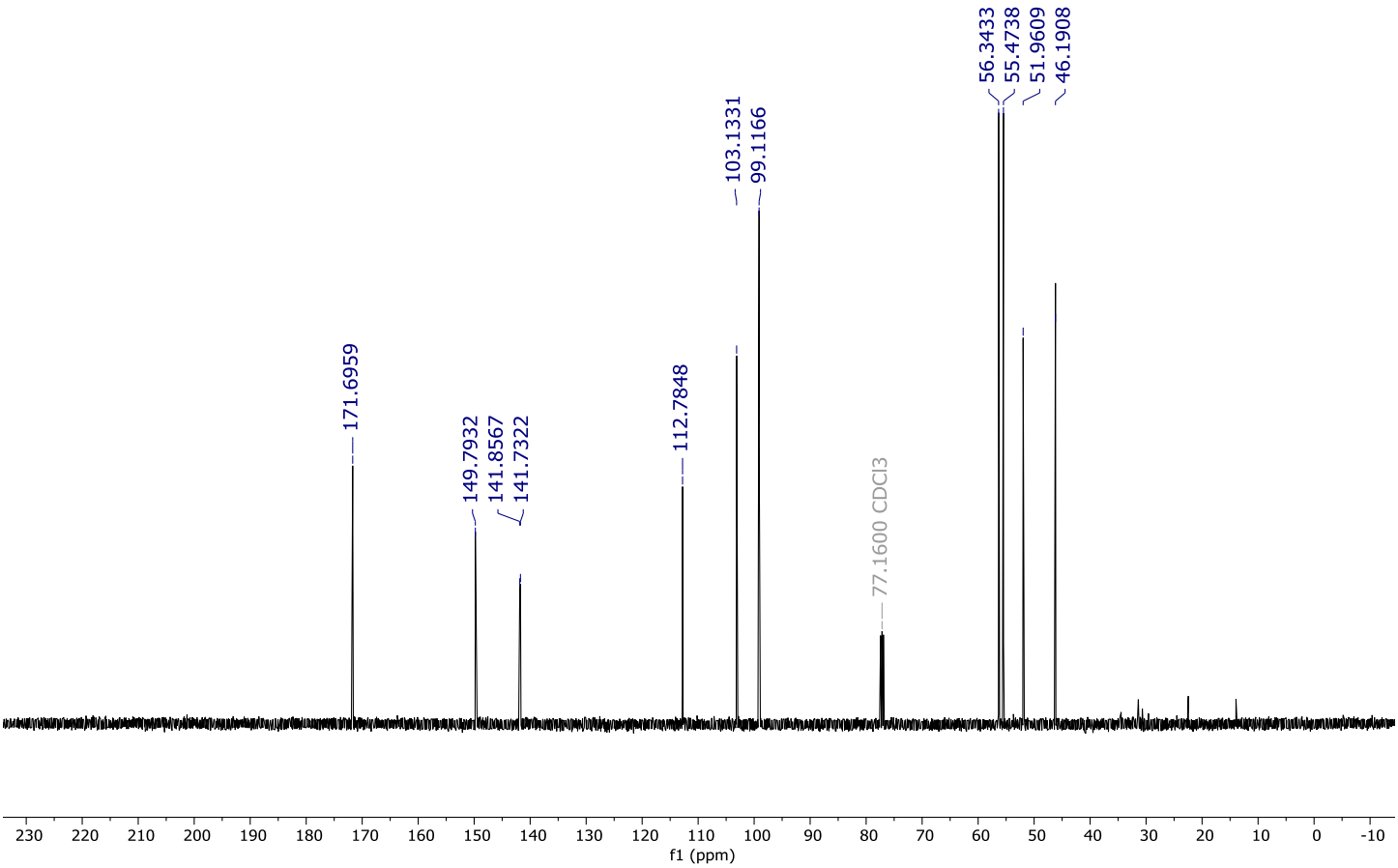
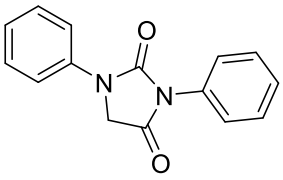



Figure S8. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **6d**.



**8a**

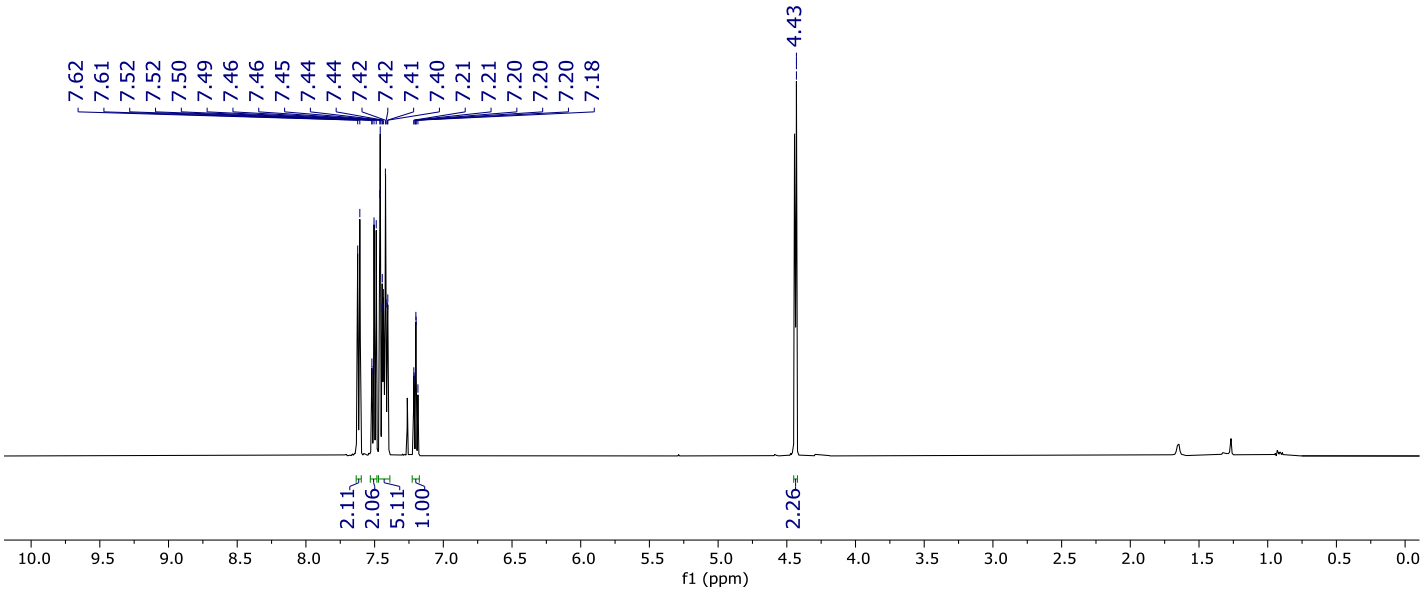



Figure S9. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **8a**.

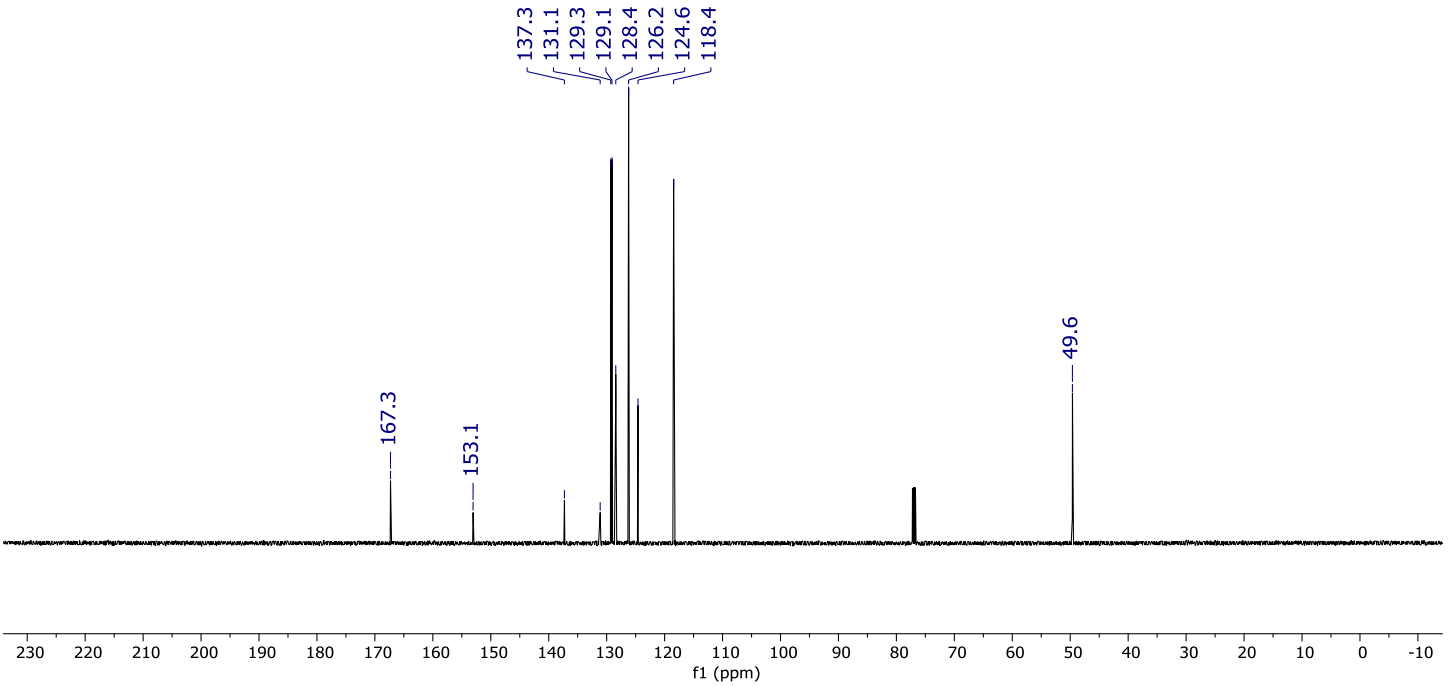



Figure S10. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **8a**.

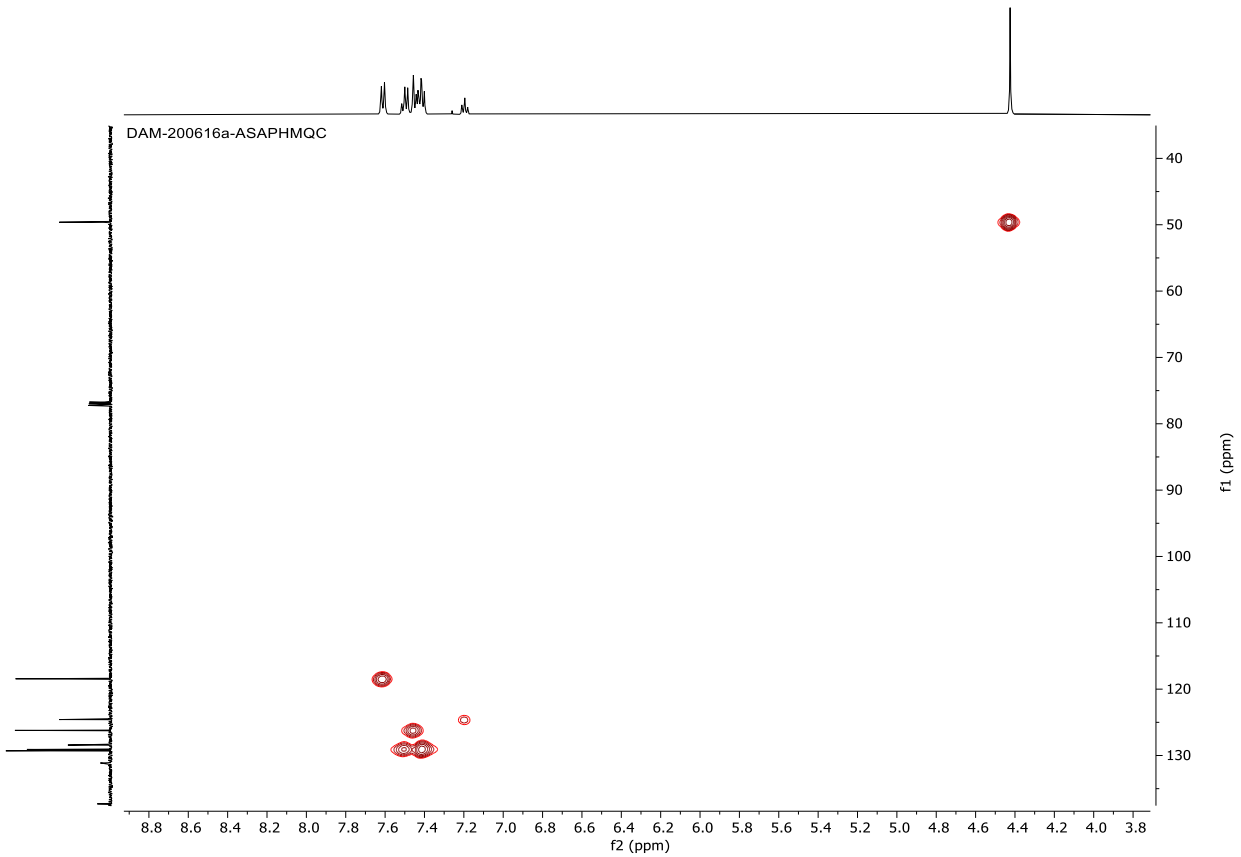



Figure S11. HMQC (500 MHz, $CDCl_3$) spectrum of compound **8a.**

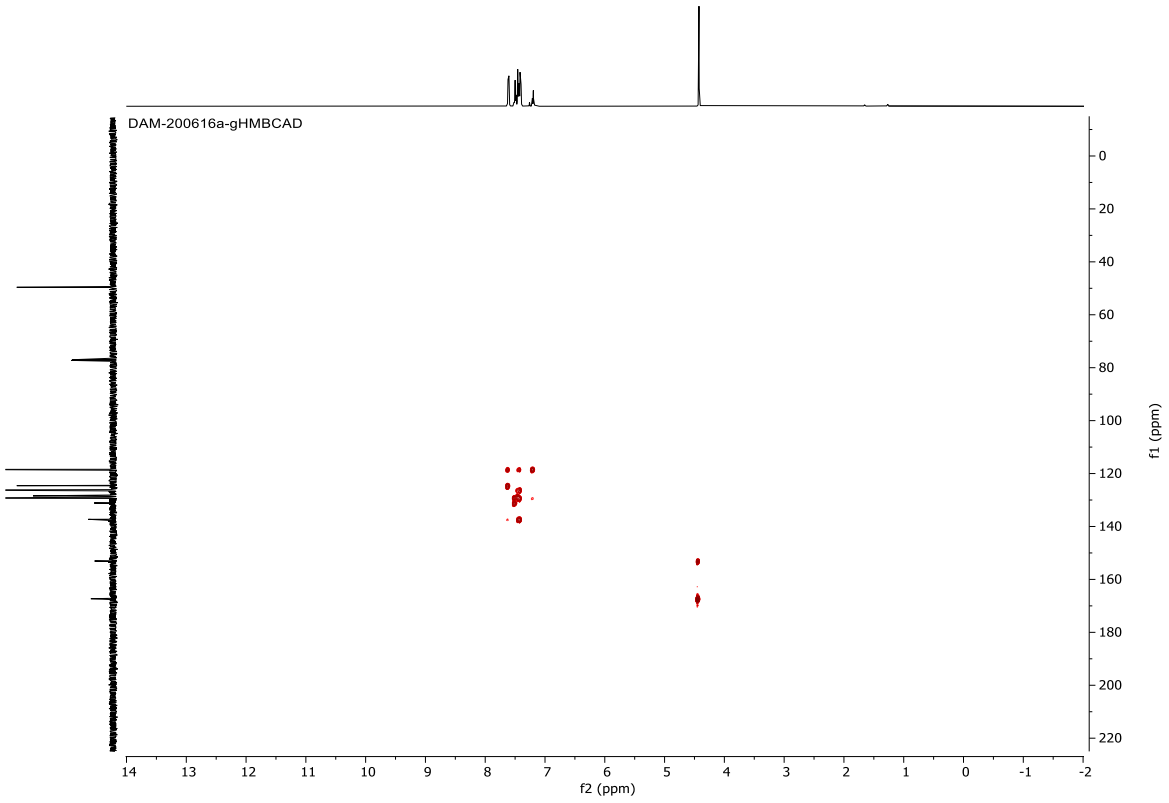



Figure S12. HMBC (500 MHz, $CDCl_3$) spectrum of compound **8a.**

File: JT-DAM-200616-3
Sample: JT-DAM-200616-3
Instrument: JEOL GCmate
Inlet: Direct Probe

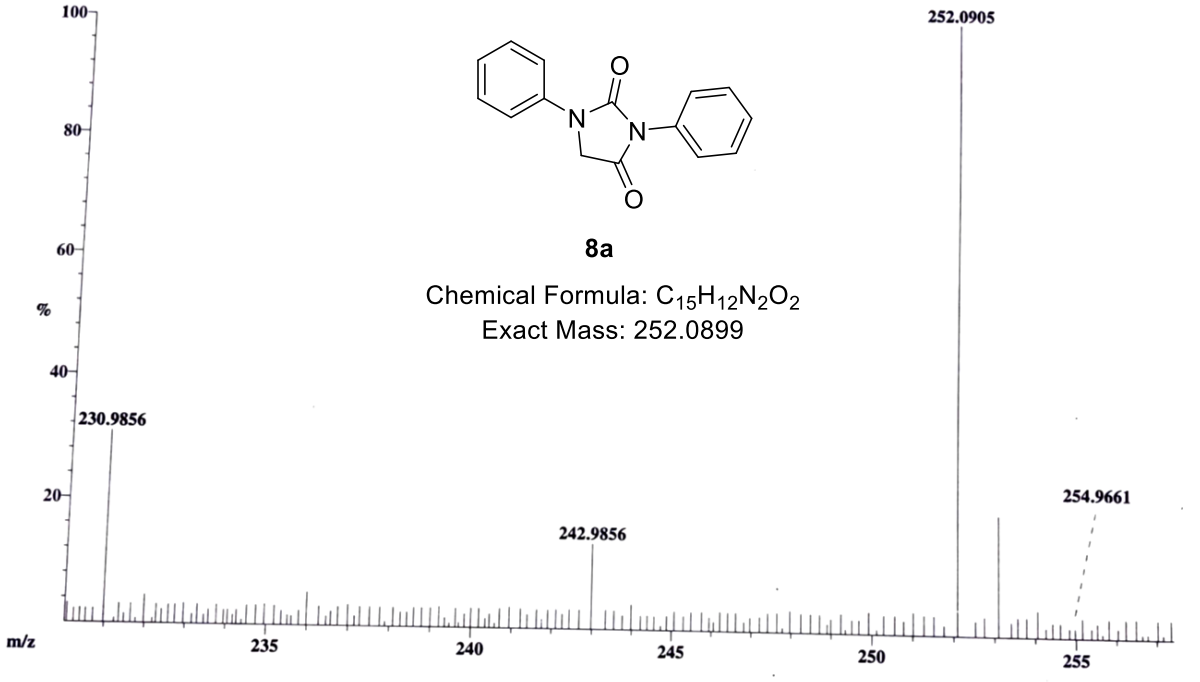
Date Run: 09-07-2017 (Time Run: 16:11:05)

Ionization mode: EI+

Scan: 168-171
Base: m/z 252; 1.7%FS TIC: 229636

R.T.: 2.26

#Ions: 445






**8a**

Chemical Formula: $C_{15}H_{12}N_2O_2$
Exact Mass: 252.0899

Selected Isotopes : $C_{0-15}H_{0-12}N_{0-2}O_{0-2}$

Error Limit : 5 ppm

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 252.0905 | 100.0% | $C_{15}H_{12}N_2O_2$ | 252.0899 | 2.5 |

Figure S13. HRMS of compound **8a.**

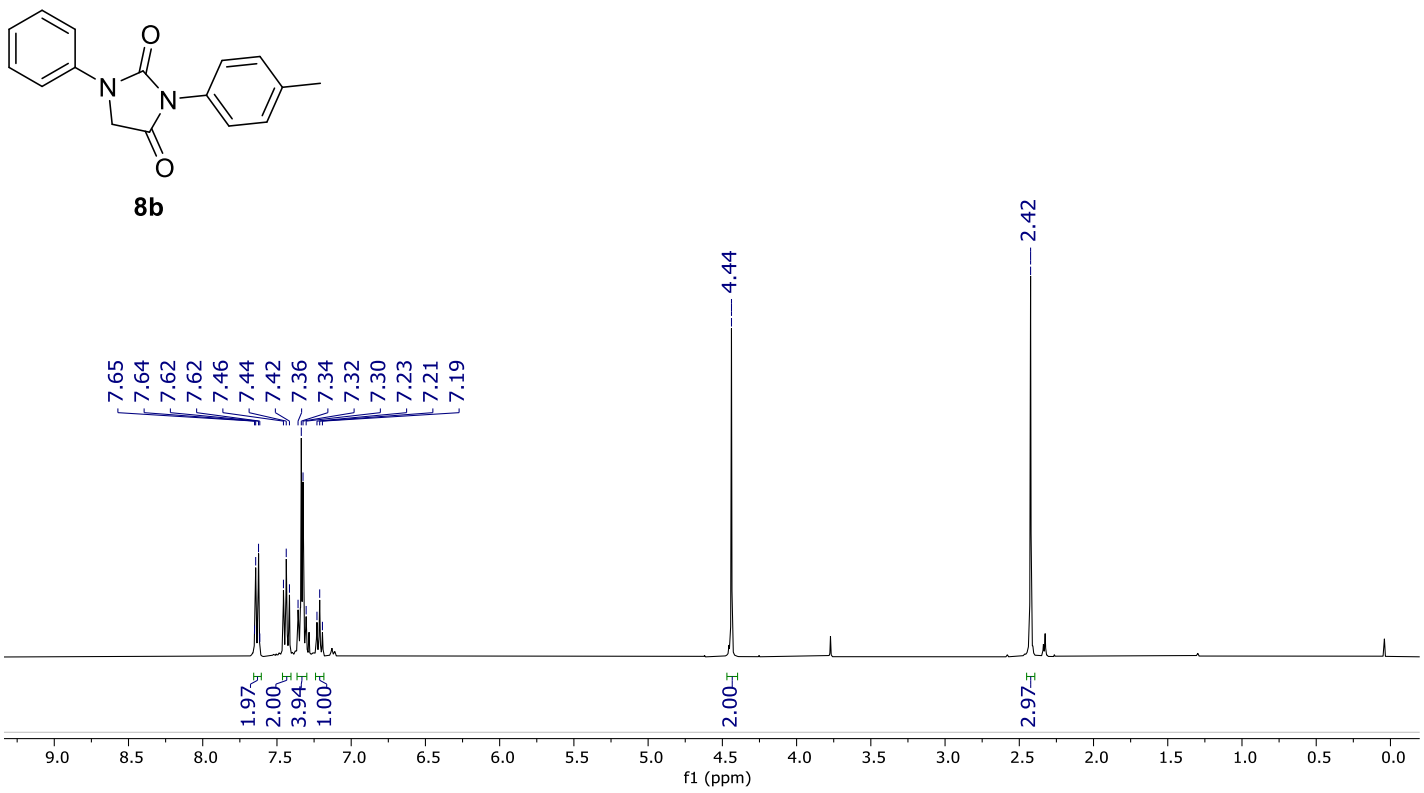



Figure S14. $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **8b**.

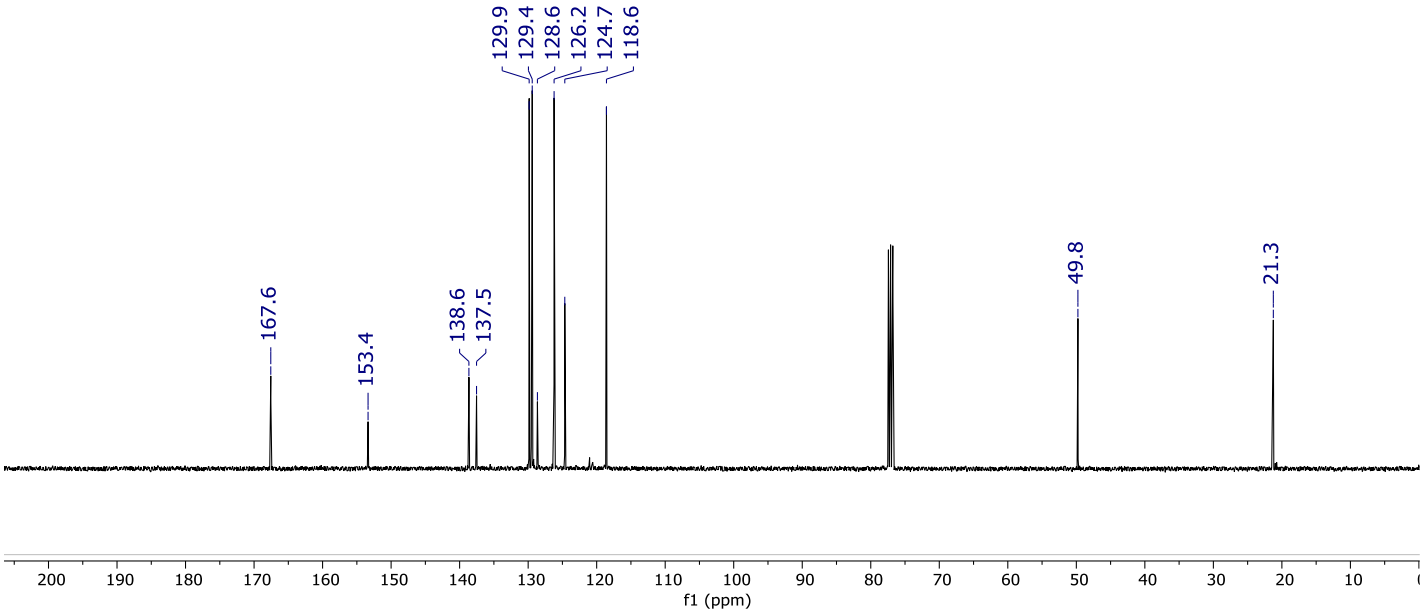



Figure S15. $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **8b**.

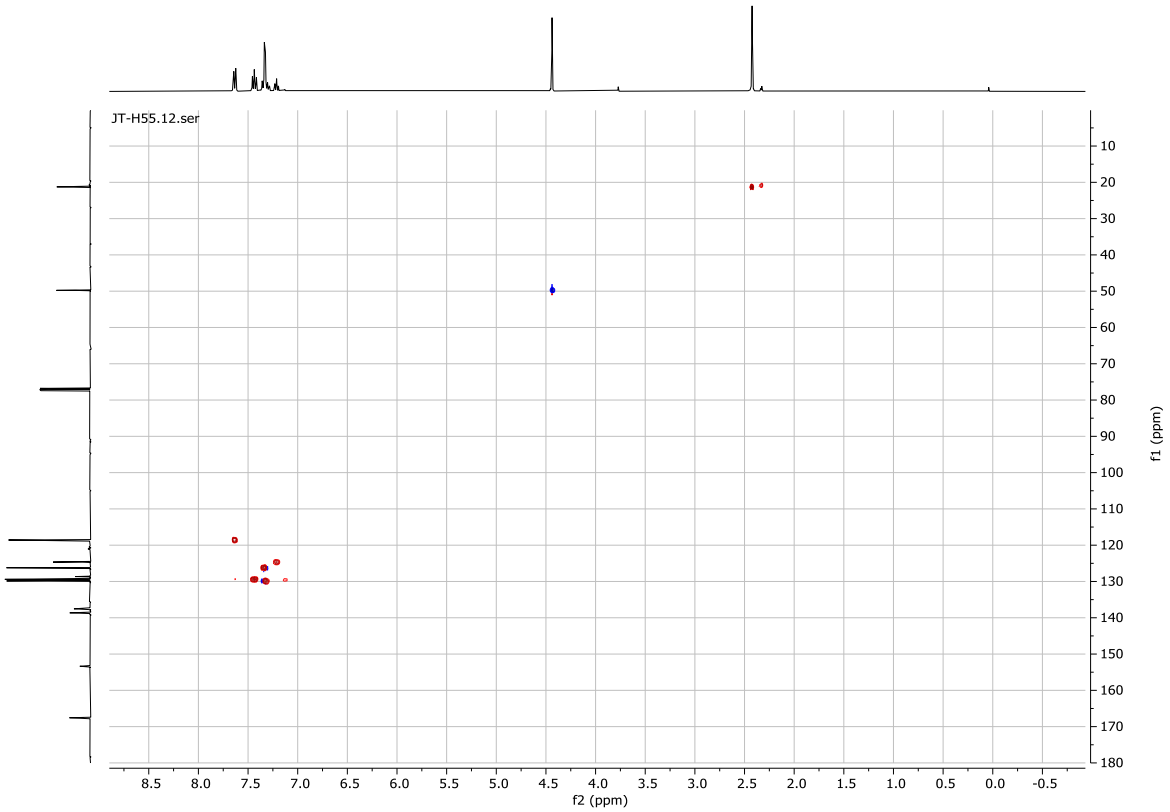



Figure S16. HSQC (400 MHz, $CDCl_3$) spectrum of compound **8b.**

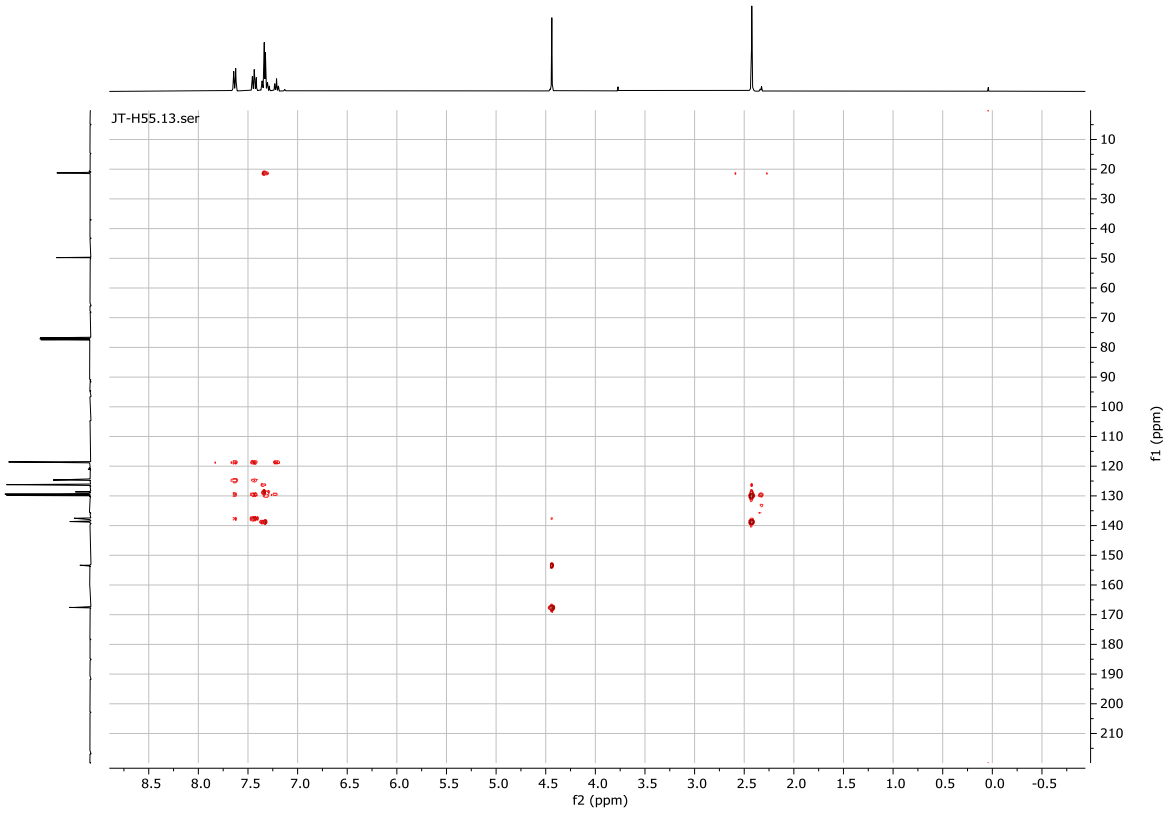
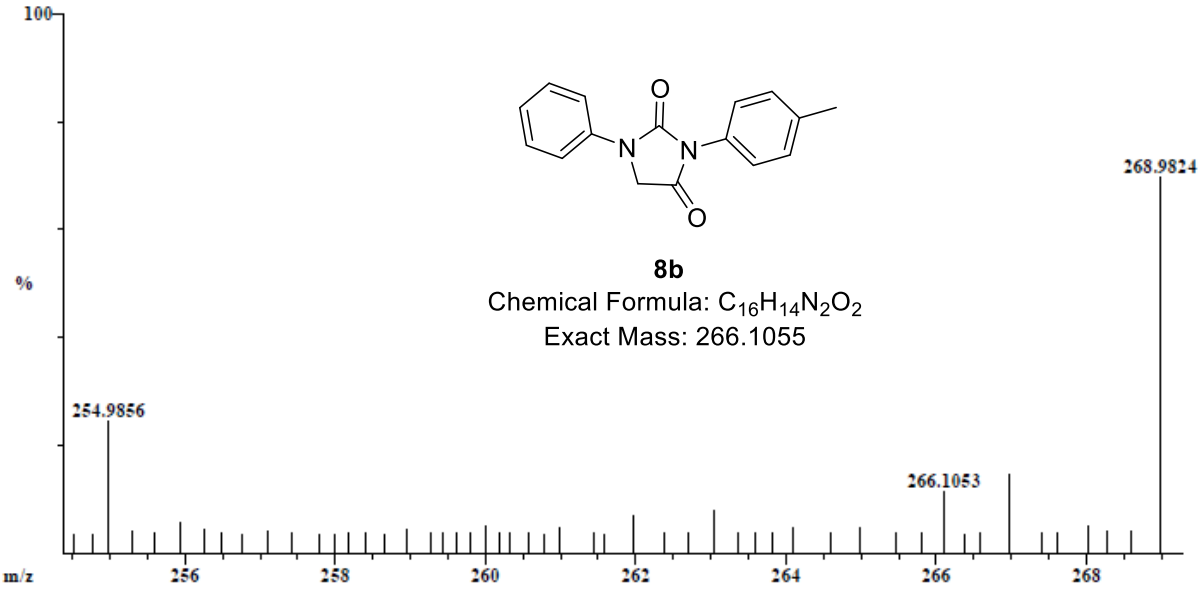



Figure S17. HMBC (400 MHz, $CDCl_3$) spectrum of compound **8b.**

**File: JT-H55-1** **Date Run: 02-11-2023 (Time Run: 13:01:06)**
**Sample: JT-H55-1**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 237** **R.T.: 2.74**
**Base: m/z 281; 2%FS TIC: 235648** **#Ions: 181**

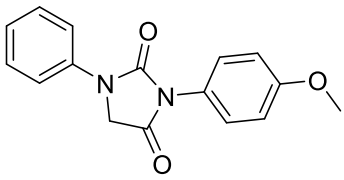



**8b**
Chemical Formula: $C_{16}H_{14}N_2O_2$
Exact Mass: 266.1055

**Selected Isotopes : $H_{0-14}C_{0-16}N_{0-2}O_{0-2}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 266.1053 | 11.2% | $C_{16}H_{14}N_2O_2$ | 266.1055 | -0.9 | 11.0 |

Figure S18. HRMS of compound **8b.**



**8c**

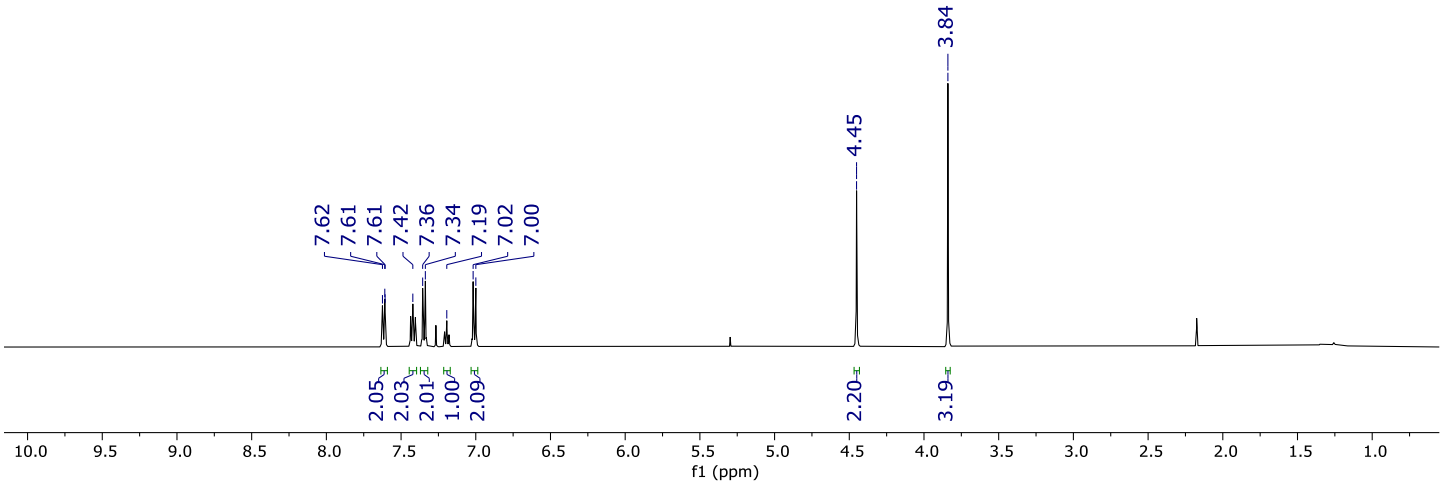



Figure S19. $^{1}H$ NMR (500 MHz, $CDCl_3$) spectrum of compound **8c**.

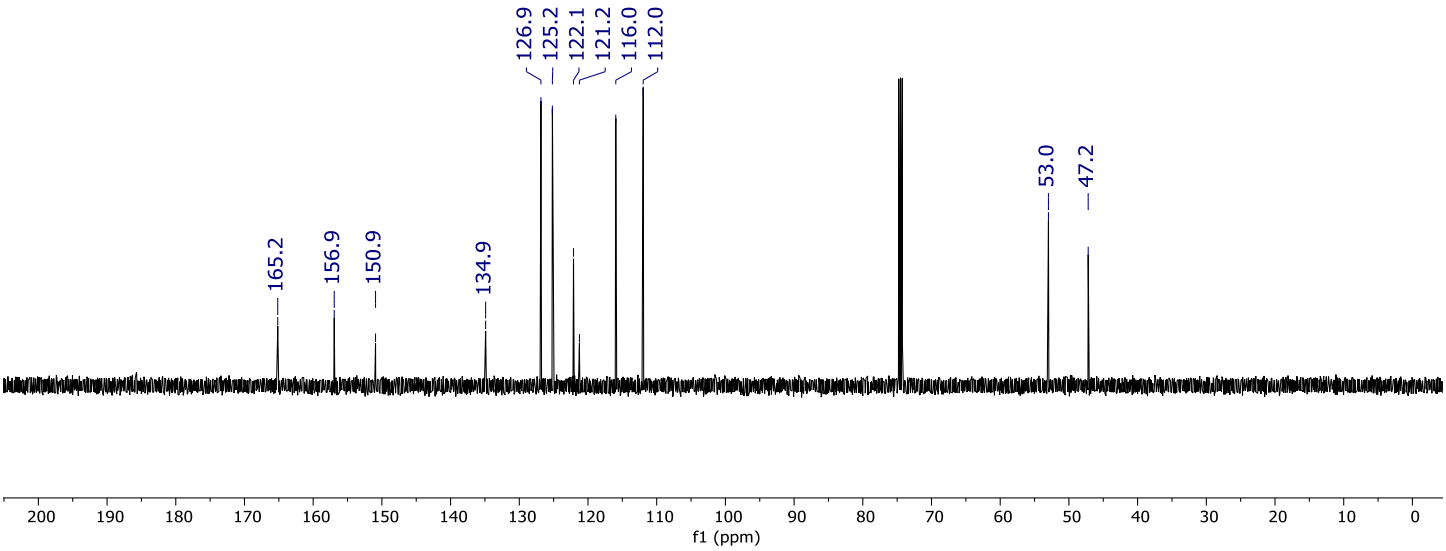



Figure S20. $^{13}C$ NMR (125 MHz, $CDCl_3$) spectrum of compound **8c.**

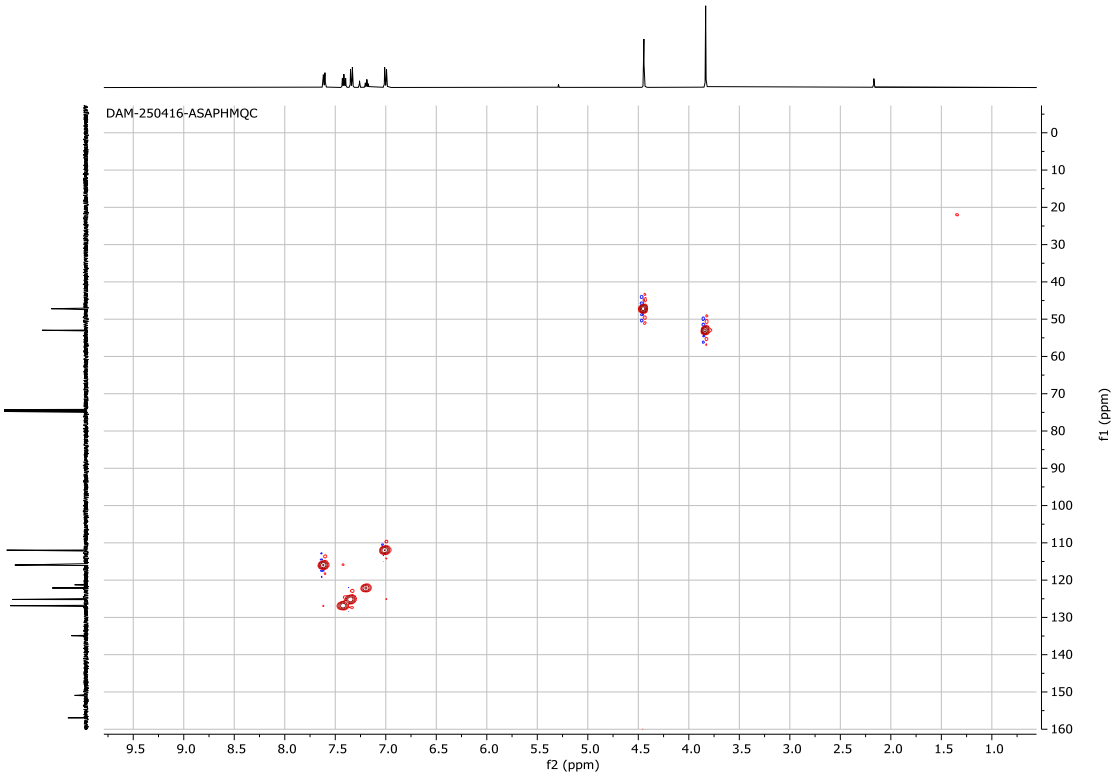



Figure S21. HMQC (500 MHz, $CDCl_3$) spectrum of compound **8c.**

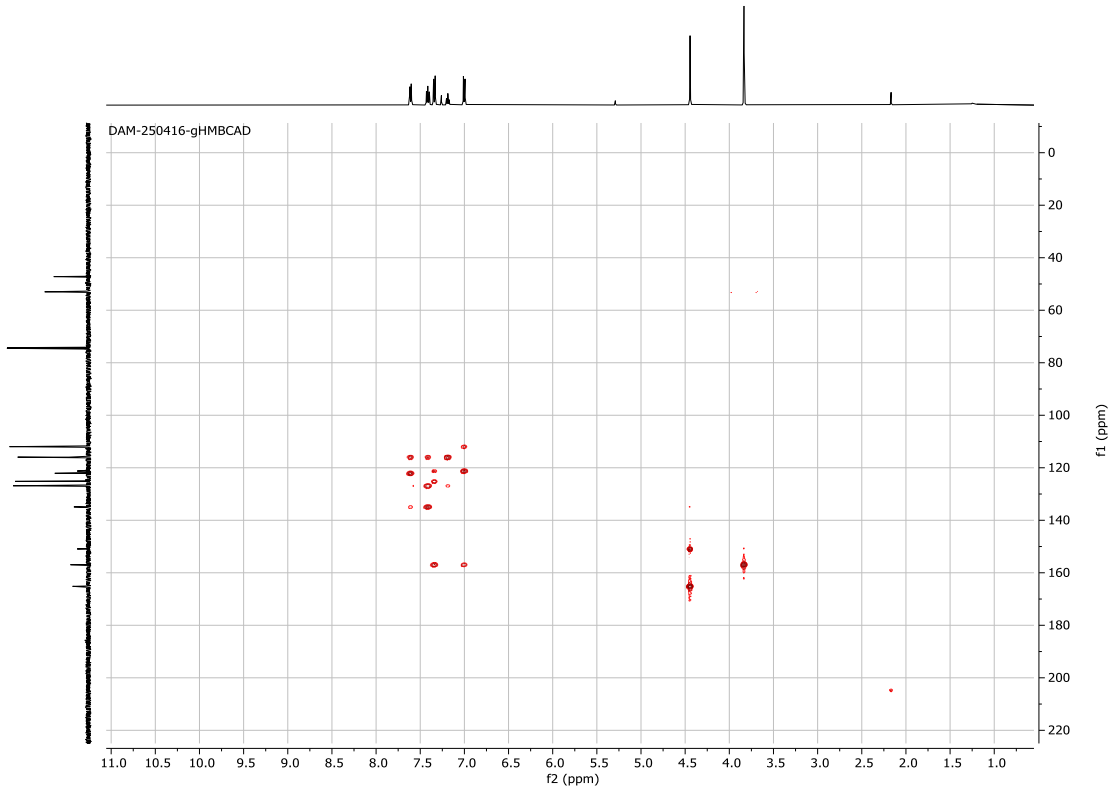



Figure S22. HMBC (500 MHz, $CDCl_3$) spectrum of compound **8c.**

File: JT-DAM-250416
Sample: JT-DAM-250416
Instrument: JEOL GCmate
Inlet: Direct Probe

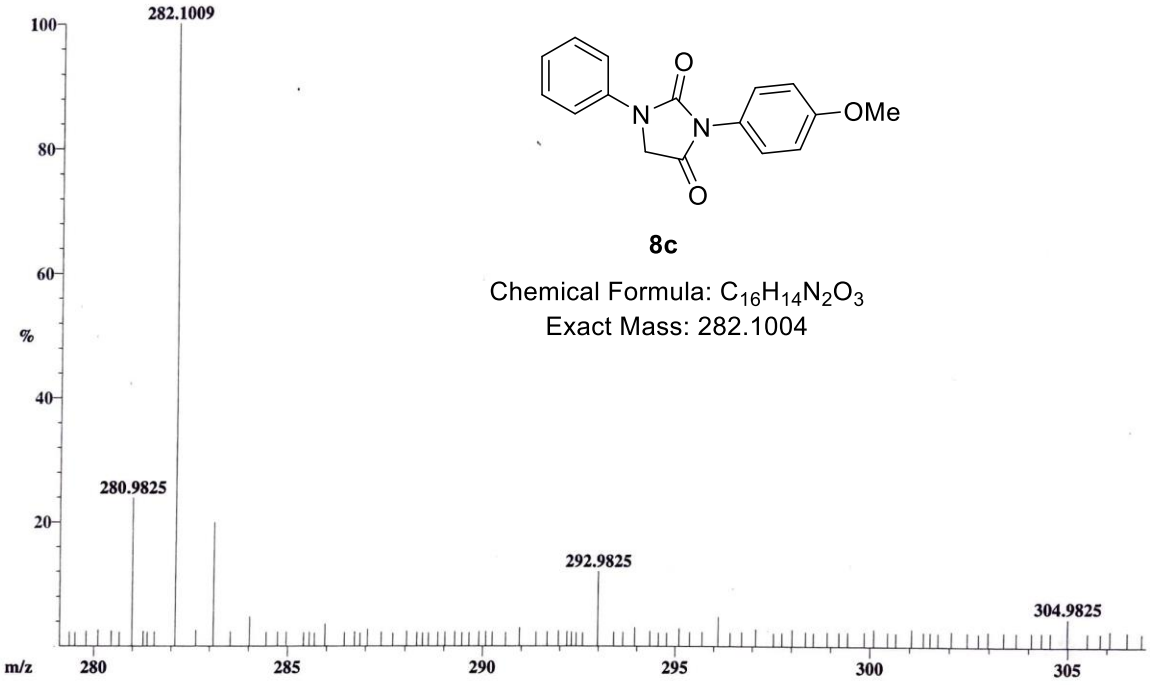
Date Run: 08-30-2017 (Time Run: 16:03:56)

Ionization mode: EI+

Scan: 70
Base: m/z 282; 2.2%FS TIC: 162752

R.T.: .93

#Ions: 215







**8c**

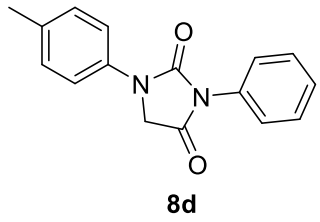
Chemical Formula: $C_{16}H_{14}N_2O_3$
Exact Mass: 282.1004

Selected Isotopes : $H_{0-14}C_{0-16}N_{0-2}O_{0-3}$

Error Limit : 5 ppm

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 282.1009 | 100.0% | $C_{16}H_{14}N_2O_3$ | 282.1005 | 1.6 |

Figure S23. HRMS of compound **8c.**



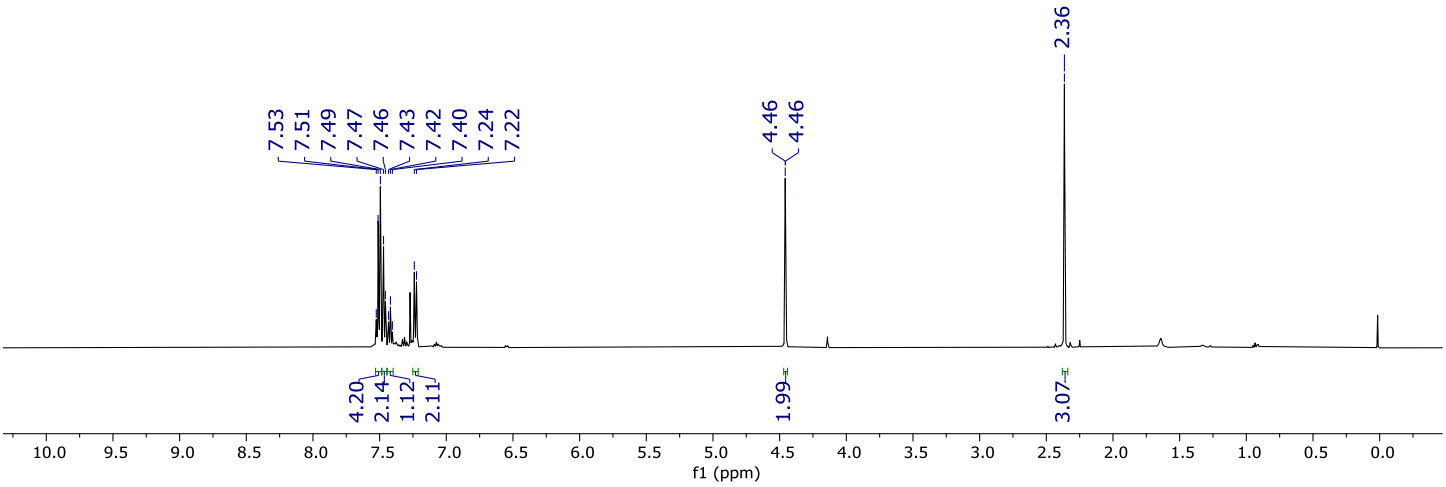




Figure S24. $^{1}H$ NMR (500 MHz, $CDCl_3$) spectrum of compound **8d**.

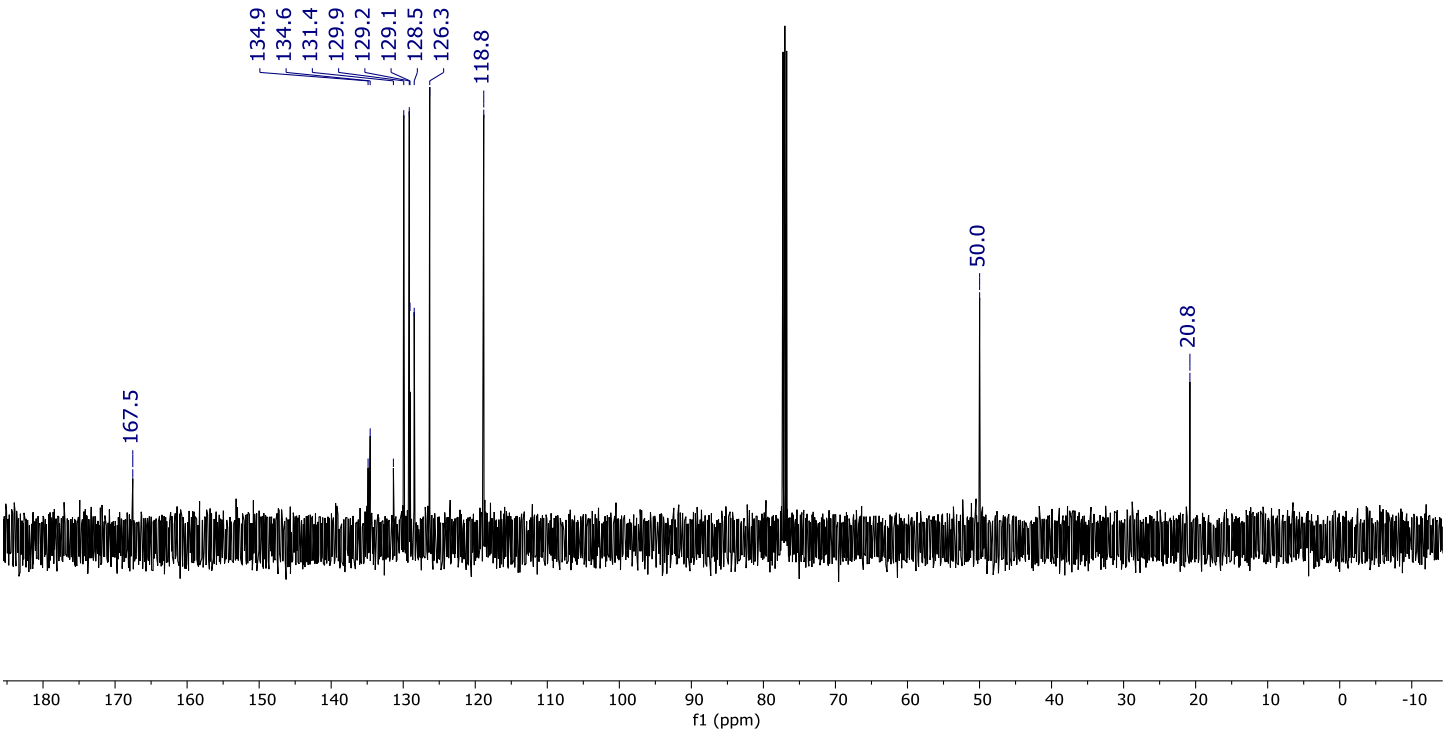



Figure S25. $^{13}C$ NMR (125 MHz, $CDCl_3$) spectrum of compound **8d.**

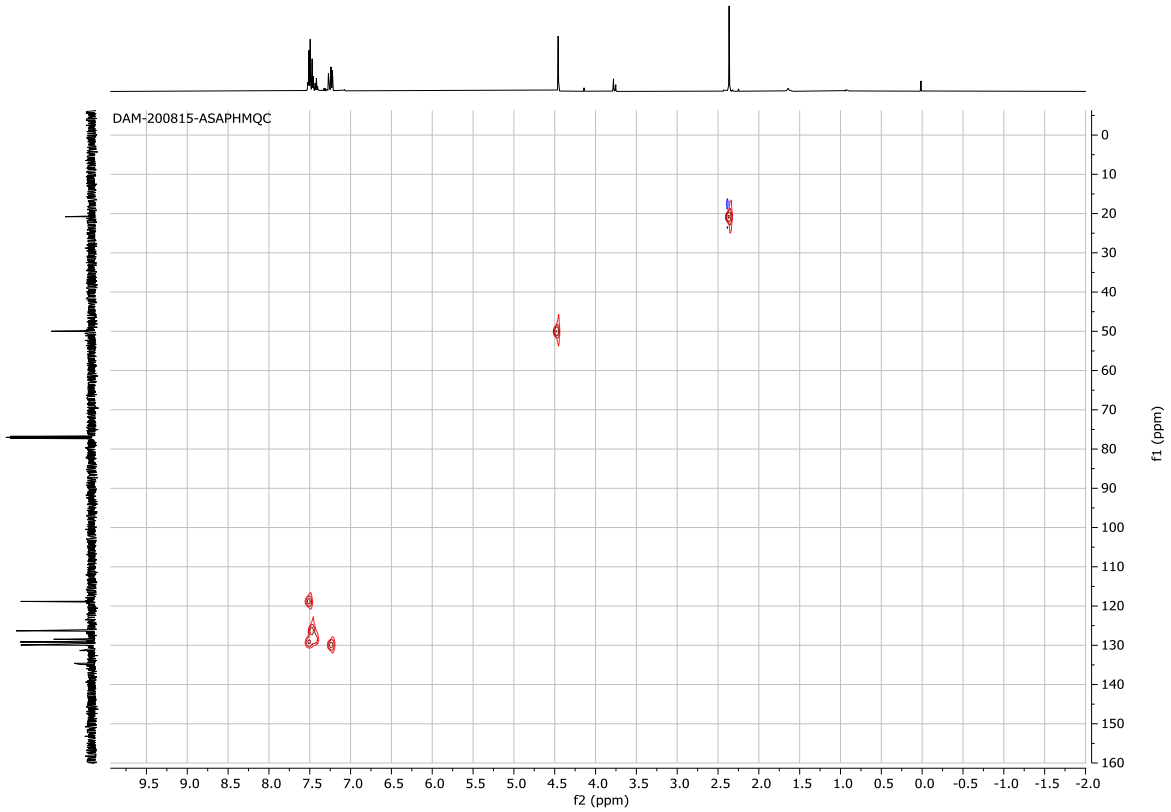



Figure S26. HMQC (500 MHz, $CDCl_3$) spectrum of compound **8d.**

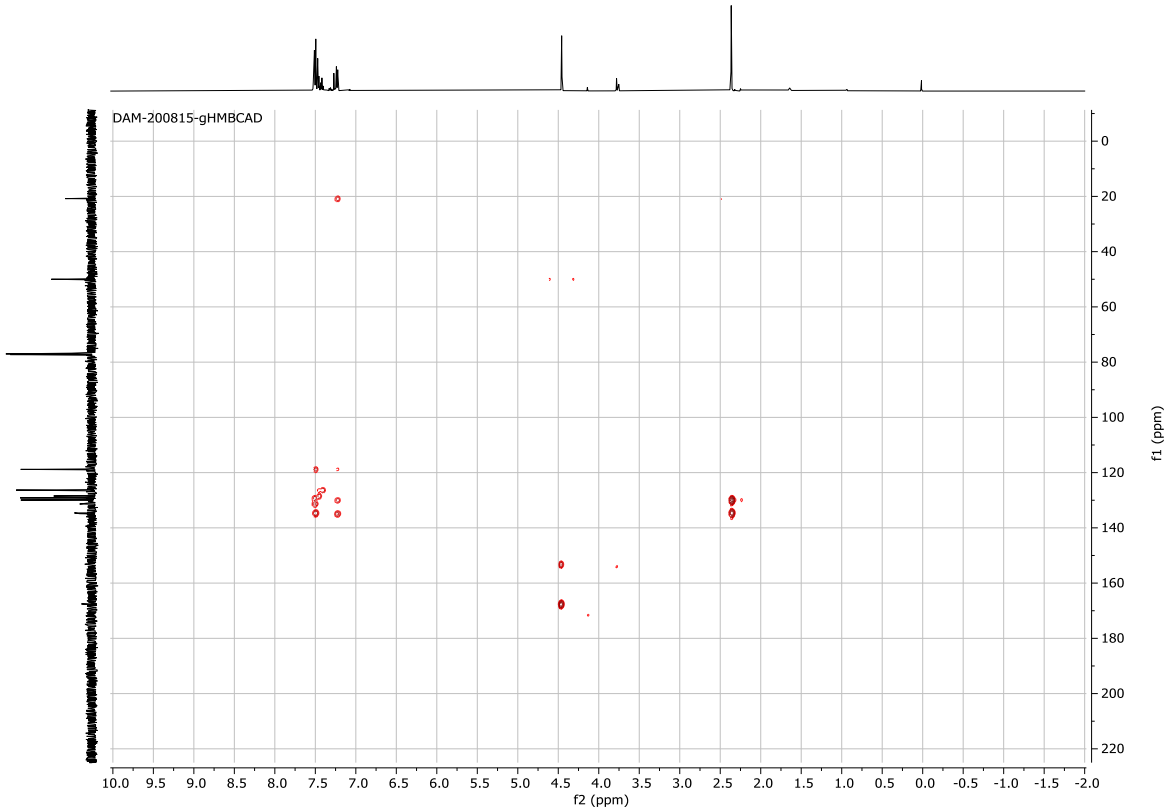



Figure S27. HMBC (500 MHz, $CDCl_3$) spectrum of compound **8d.**

File: JT-DAM-200815-3
Sample: JT-DAM-200815-3
Instrument: JEOL GCmate
Inlet: Direct Probe

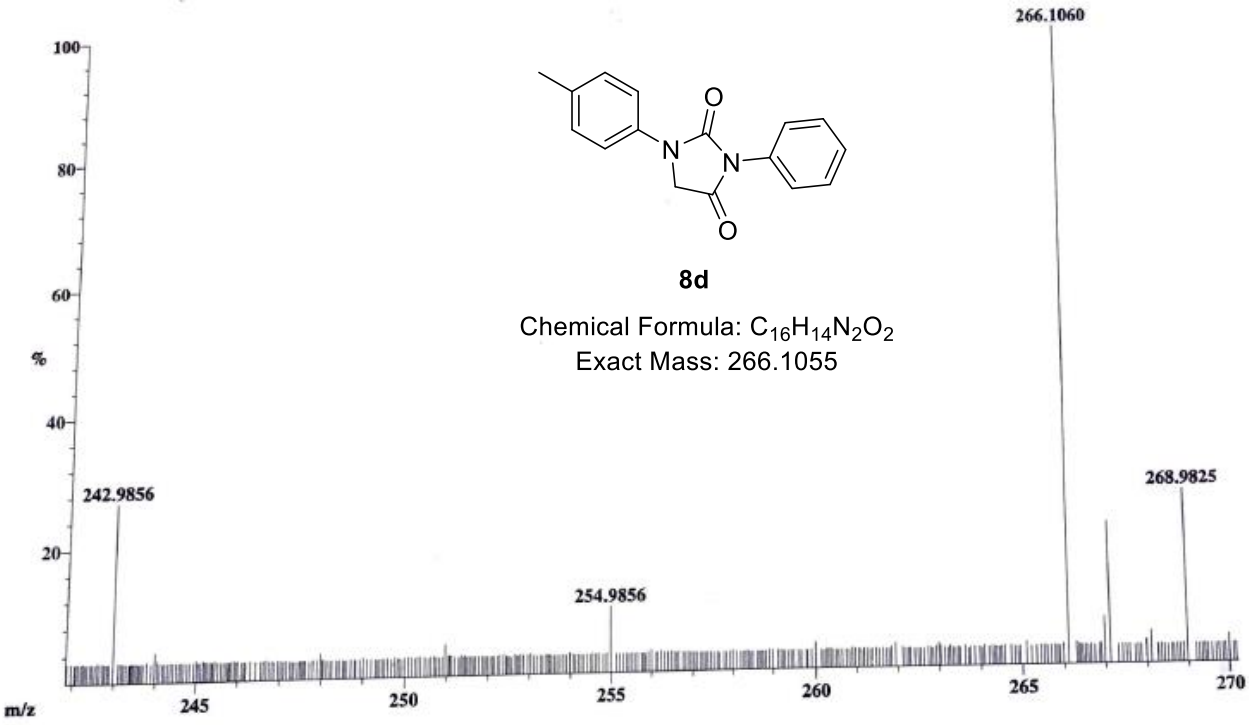
Date Run: 11-04-2017 (Time Run: 18:58:38)

Ionization mode: EI+

Scan: 176
Base: m/z 266; 1.9%FS TIC: 449088

R.T.: 2.35

#Ions: 697







**8d**

Chemical Formula: $C_{16}H_{14}N_2O_2$
Exact Mass: 266.1055

Error Limit : 5 ppm

Selected Isotopes : $H_{0-14}C_{0-16}N_{0-2}O_{0-2}$

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 266.1060 | 100.0% | $C_{16}H_{14}N_2O_2$ | 266.1055 | 1.8 |

Figure S28. HRMS of compound **8d.**

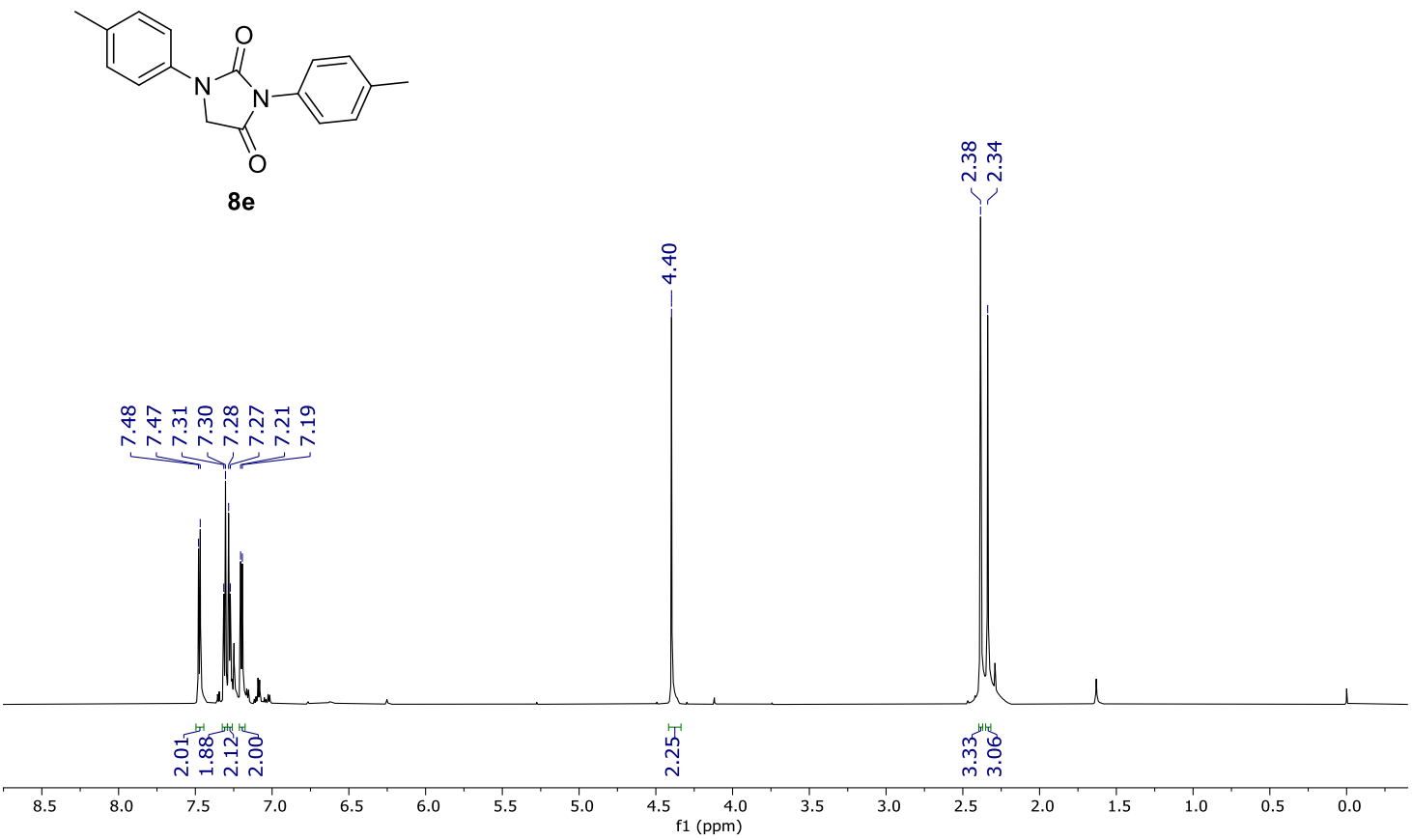



Figure S29. $^{1}$H NMR (750 MHz, $CDCl_3$) spectrum of compound **8e**.

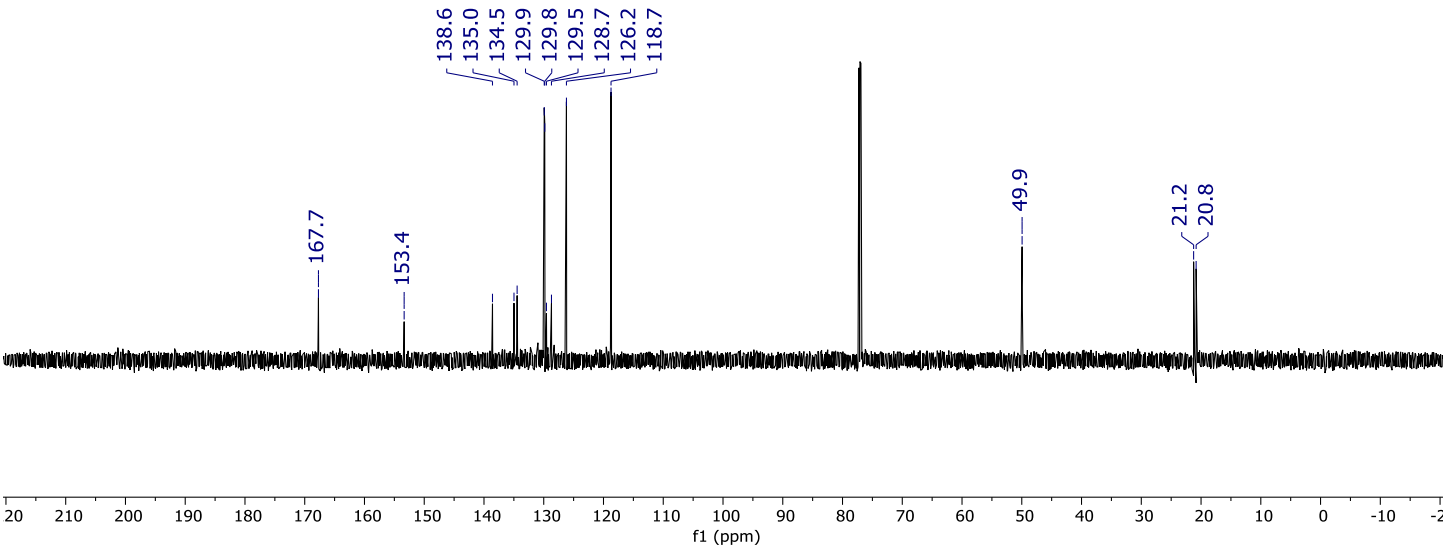



Figure S30. $^{13}$C NMR (187.5 MHz, $CDCl_3$) spectrum of compound **8e**.

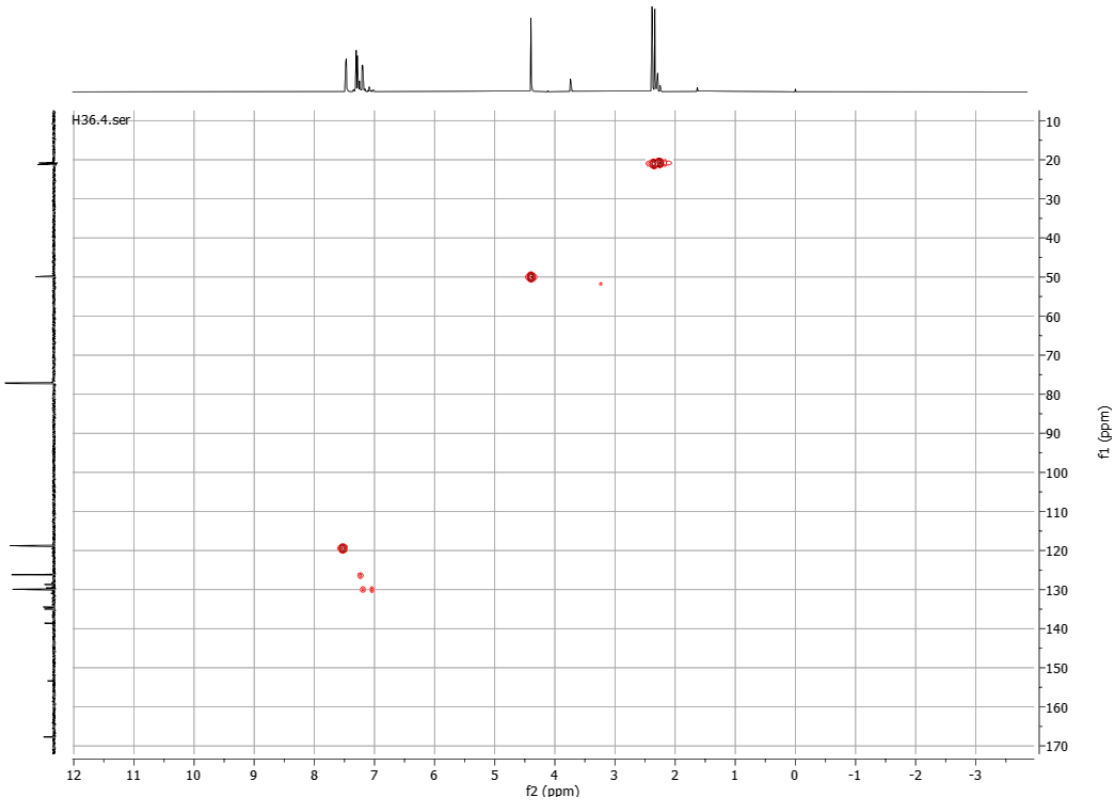



Figure S31. HSQC (750 MHz, $CDCl_3$) spectrum of compound **8e.**

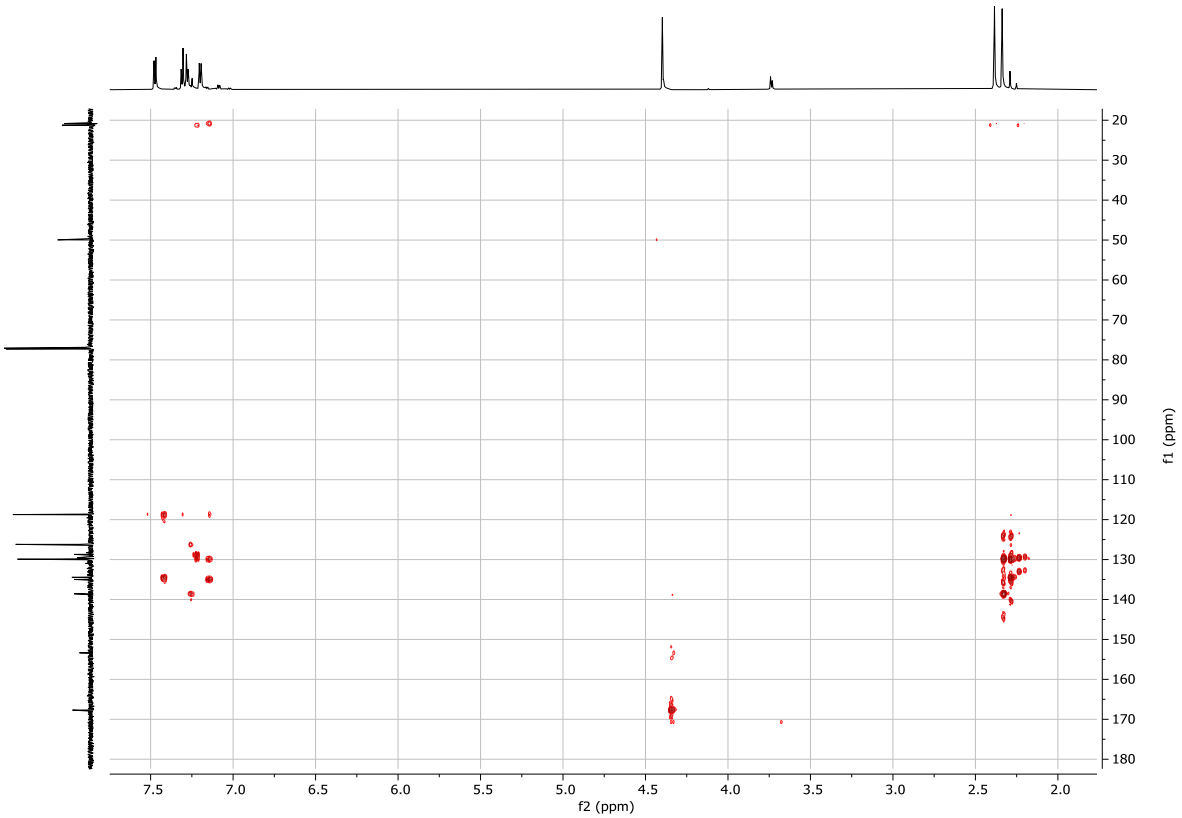



Figure S32. HMBC (750 MHz, $CDCl_3$) spectrum of compound **8e.**

***IPN***

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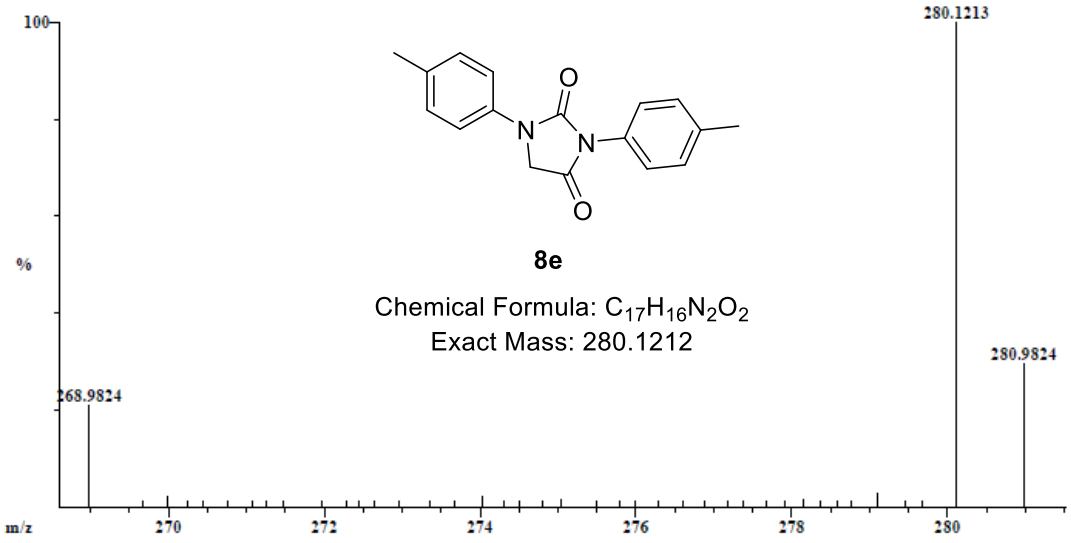
**File: JT-EBC-H17** **Date Run: 02-11-2023 (Time Run: 13:21:45)**
**Sample: JT-EBC-H17**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 174** **R.T.: 2.01**
**Base: m/z 280; 6.3%FS TIC: 295568** **#Ions: 196**




**8e**

Chemical Formula: $C_{17}H_{16}N_2O_2$
Exact Mass: 280.1212

**Selected Isotopes : $H_{0-16}C_{0-17}N_{0-2}O_{0-2}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 280.1213 | 100.0% | $C_{17}H_{16}N_2O_2$ | 280.1212 | 0.4 | 11.0 |

Figure S33. HRMS of compound **8e.**

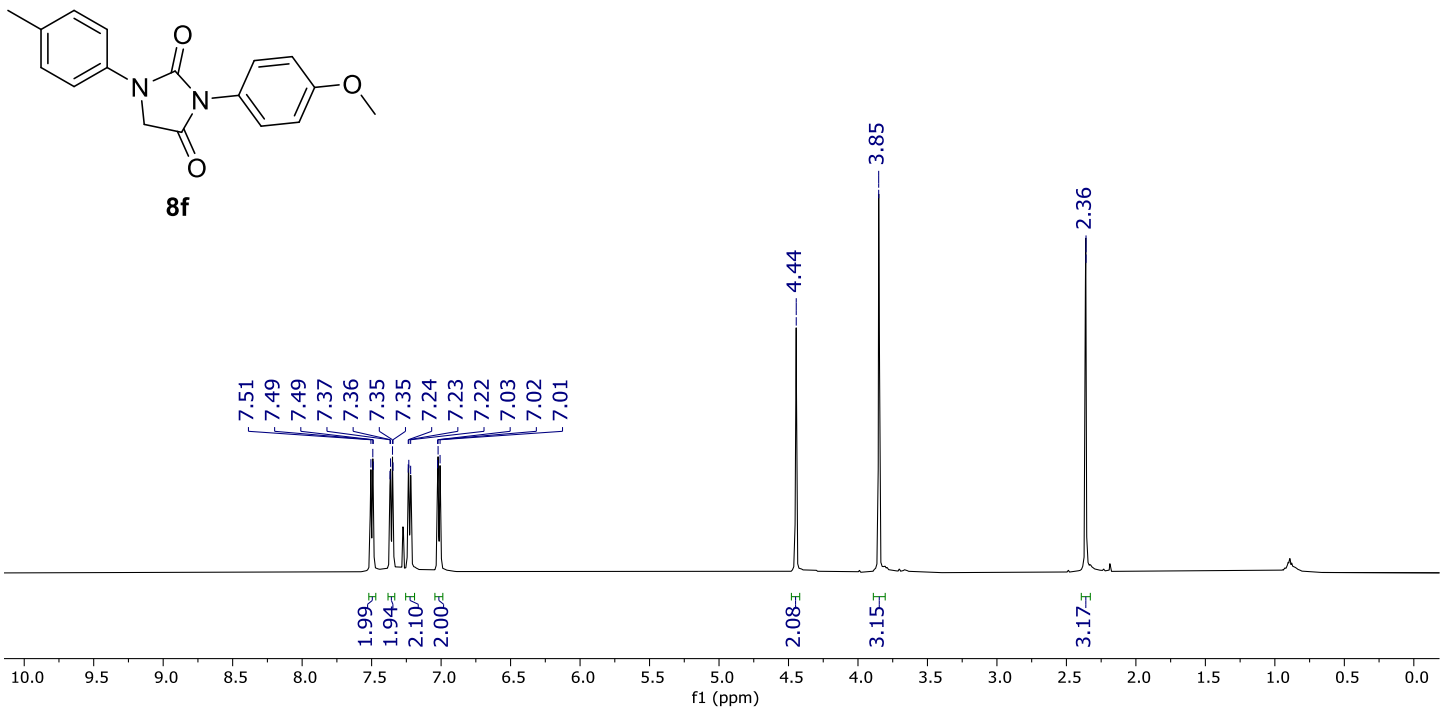



Figure S34. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **8f**.

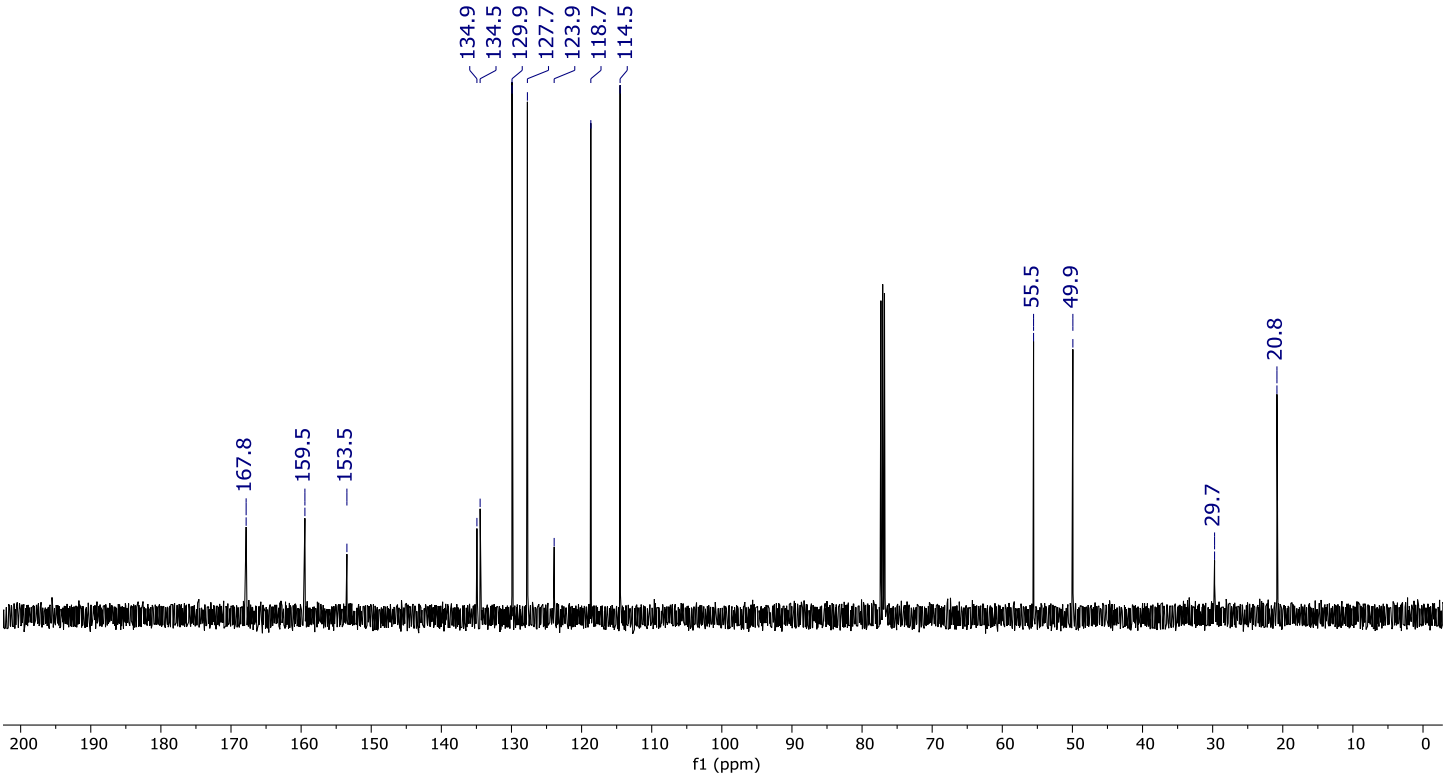



Figure S35. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **8f**.

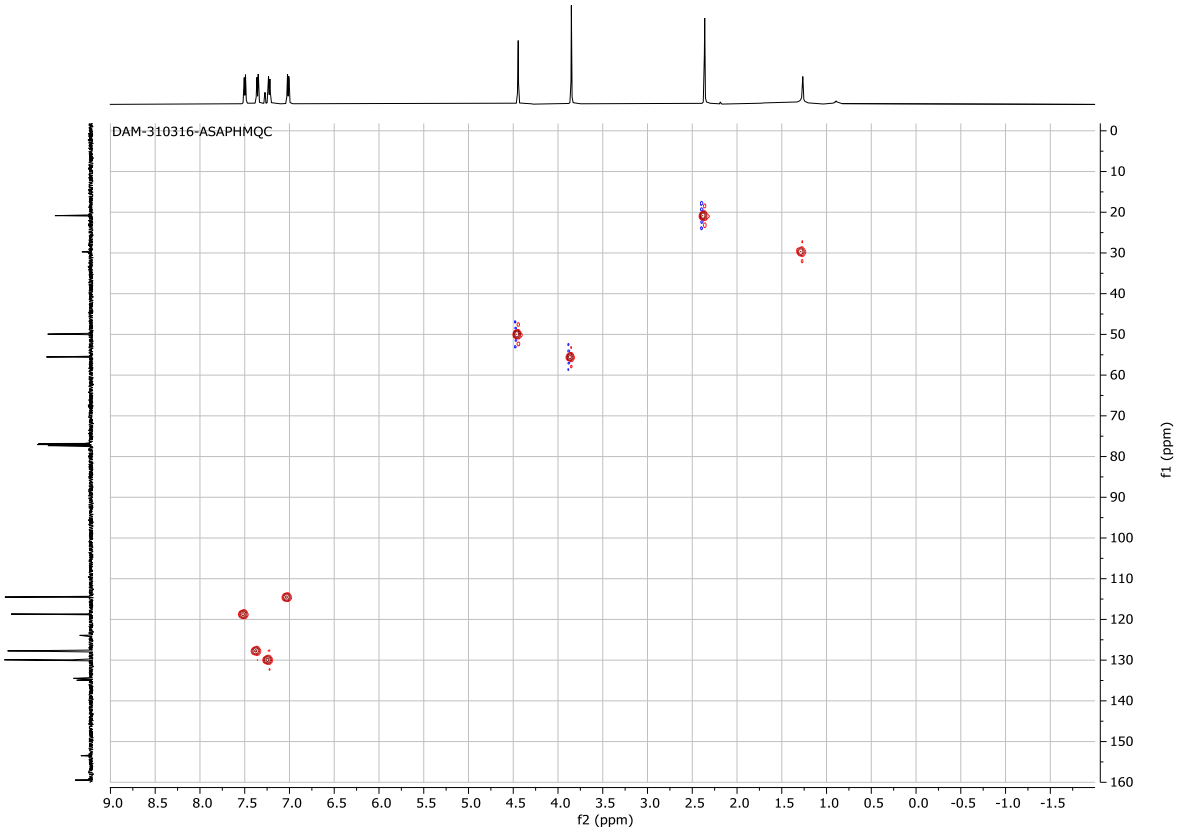



Figure S36. HSQC (500 MHz, $CDCl_3$) spectrum of compound **8f.**

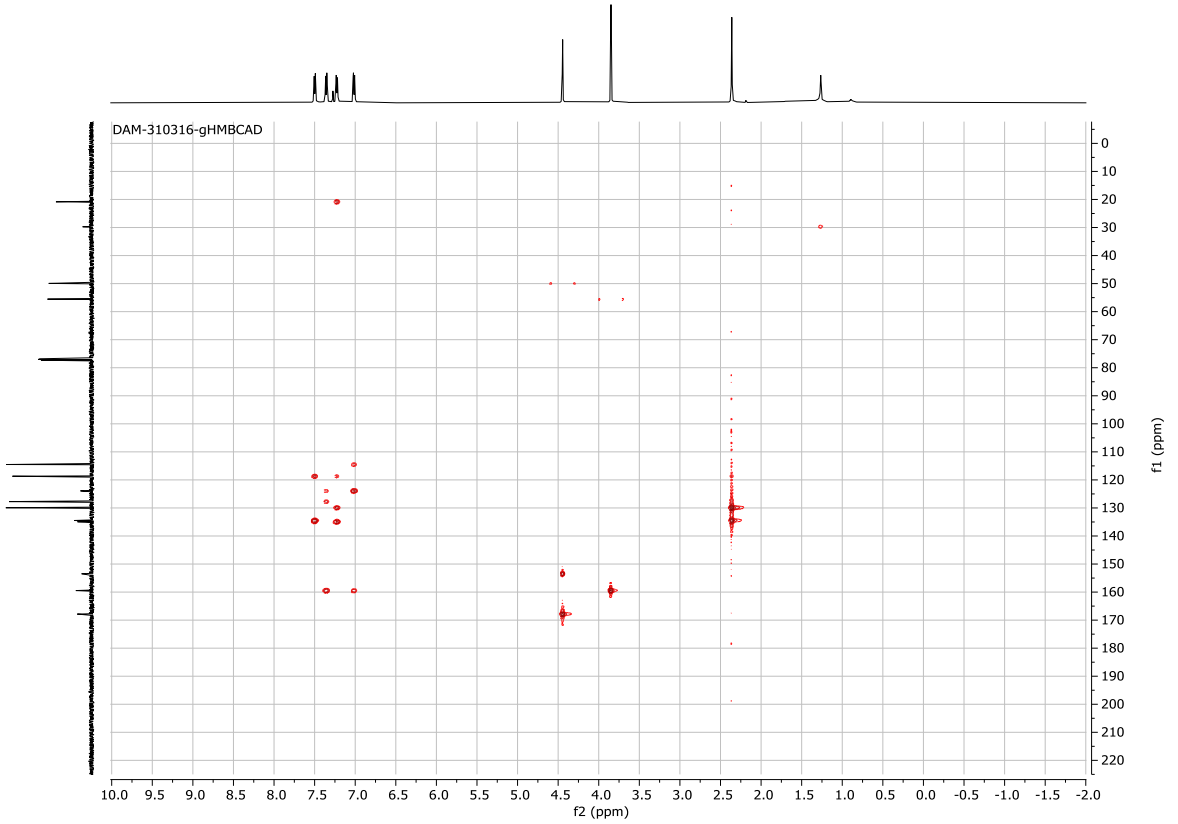



Figure S37. HMBC (500 MHz, $CDCl_3$) spectrum of compound **8f.**

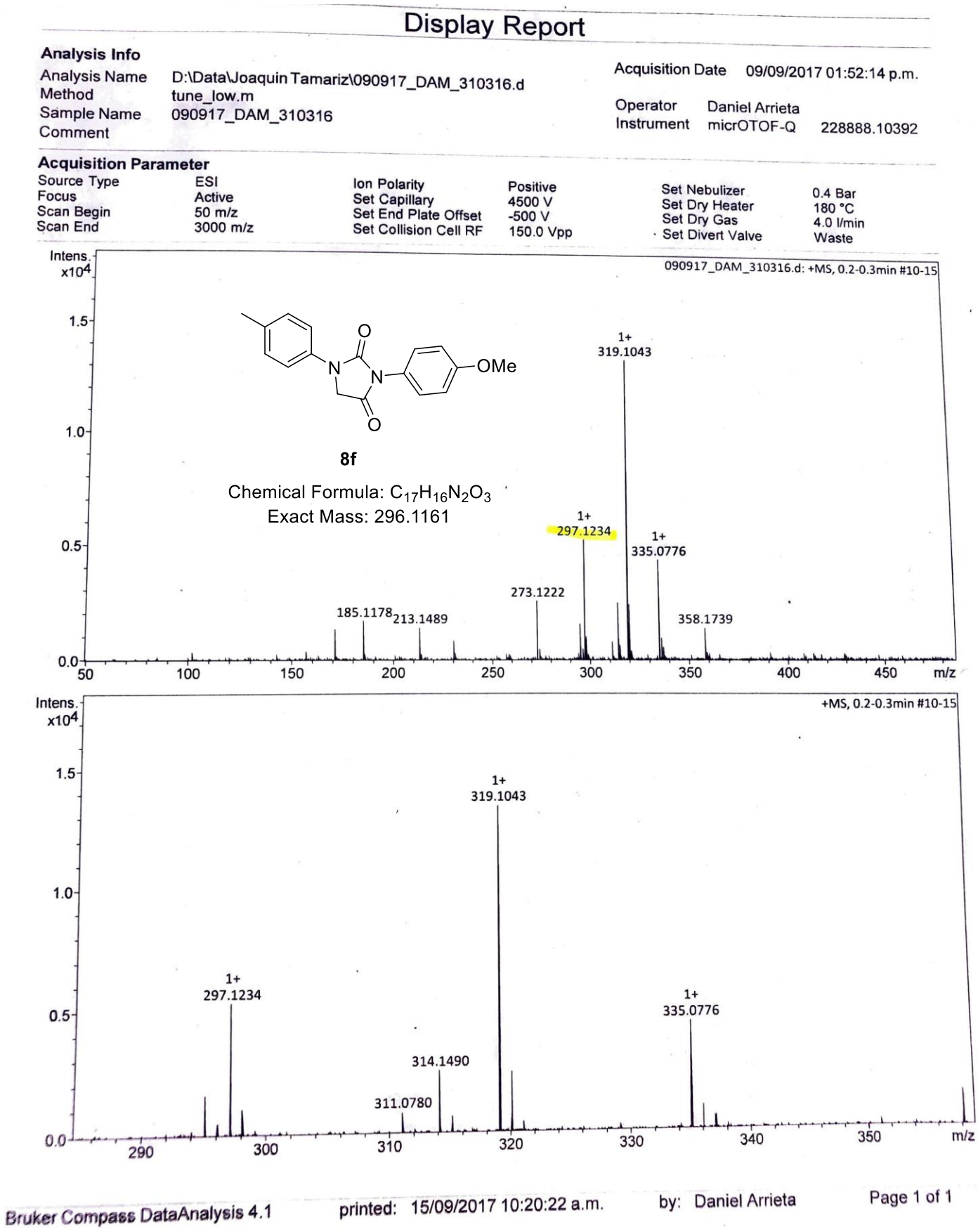



Figure S38. HRMS of compound **8f.**

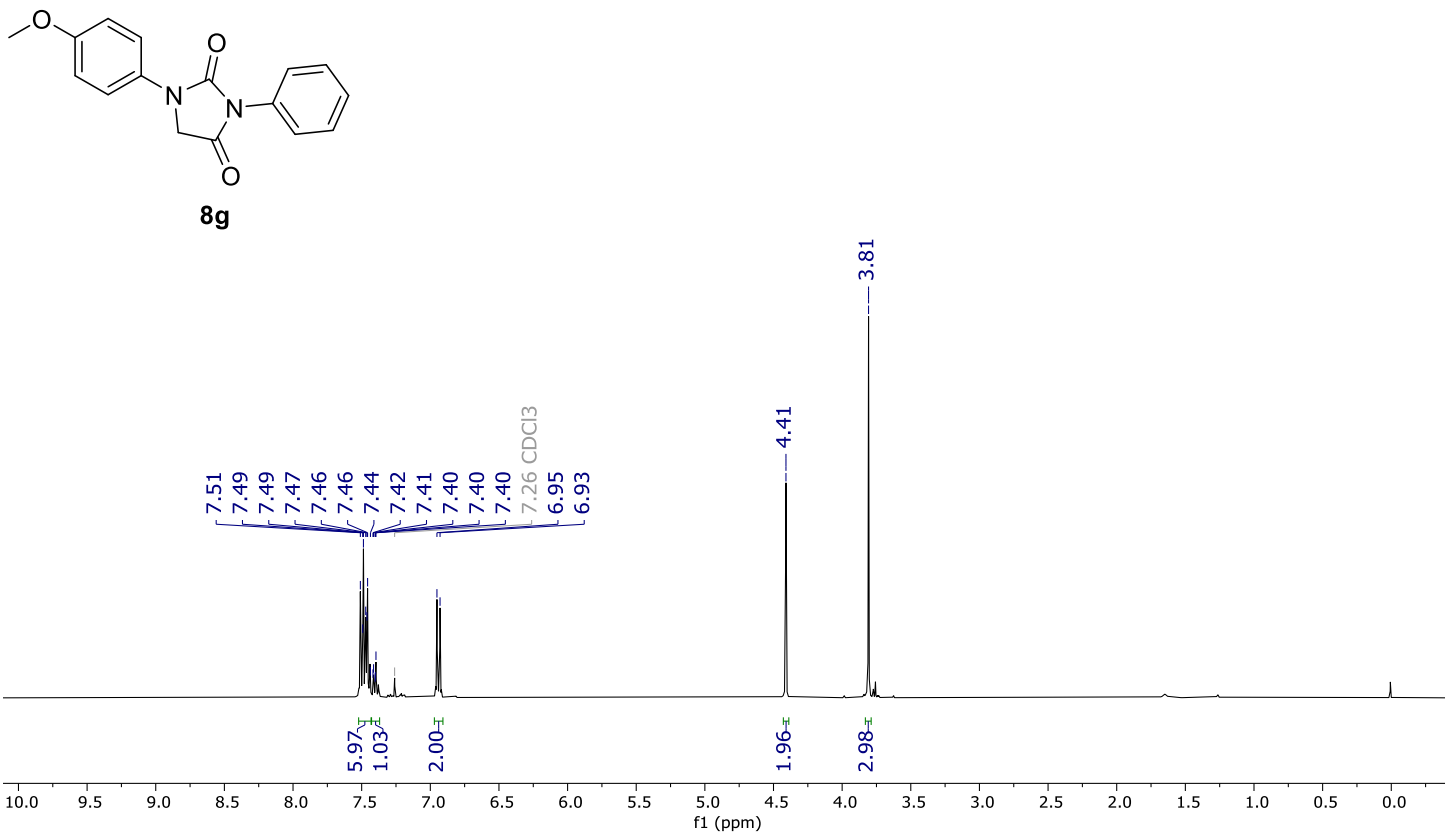



Figure S39. $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **8g**.

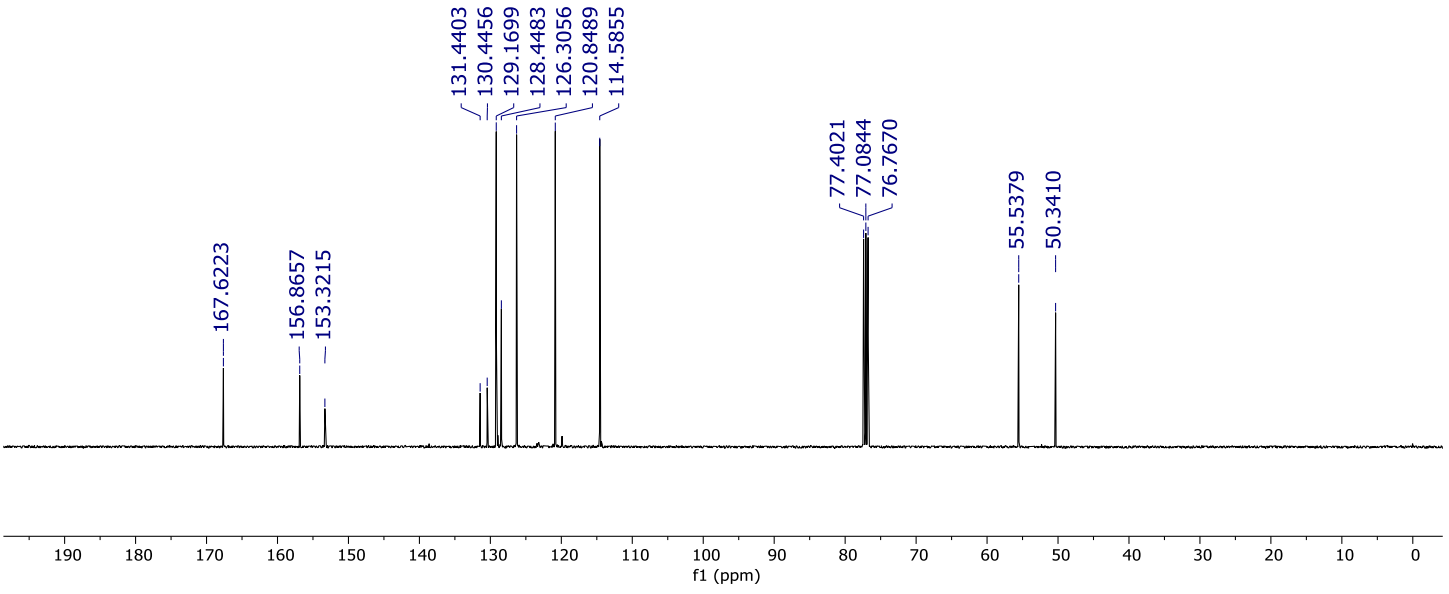



Figure S40. $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **8g**,

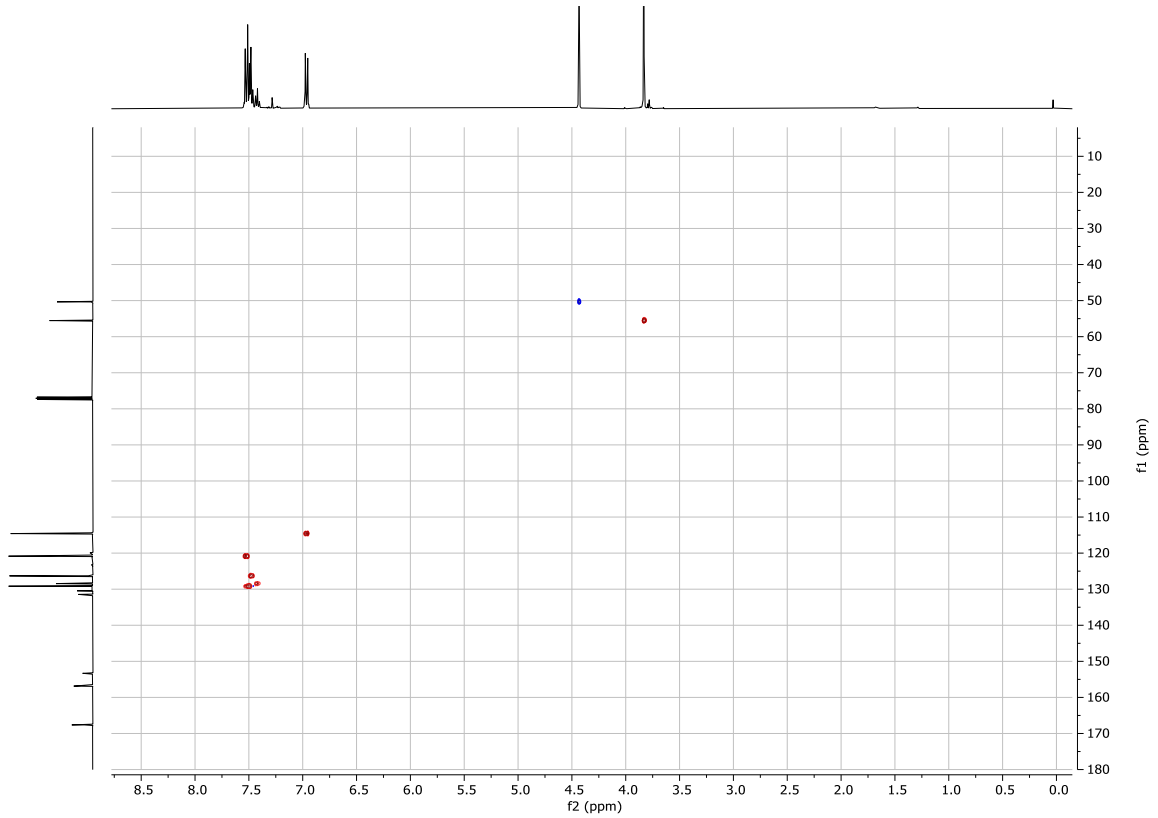



Figure S41. HSQC (400 MHz, $CDCl_3$) spectrum of compound **8g.**

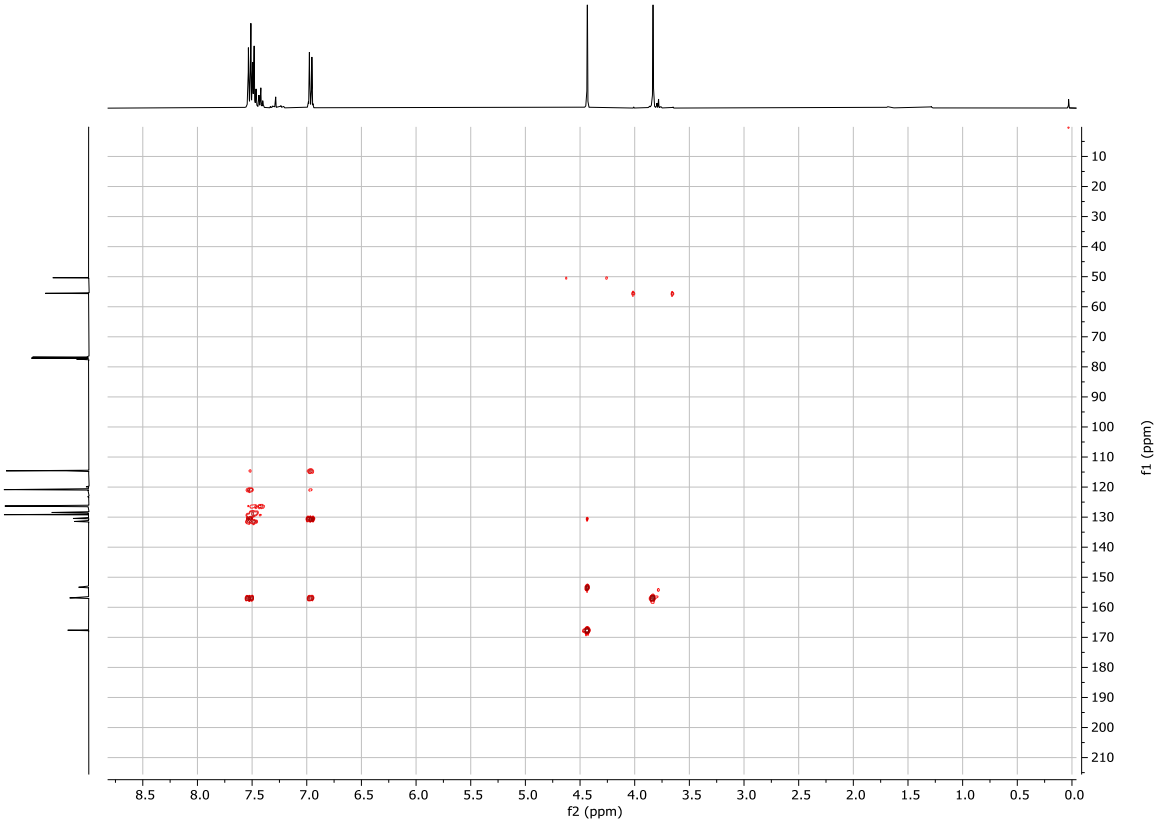
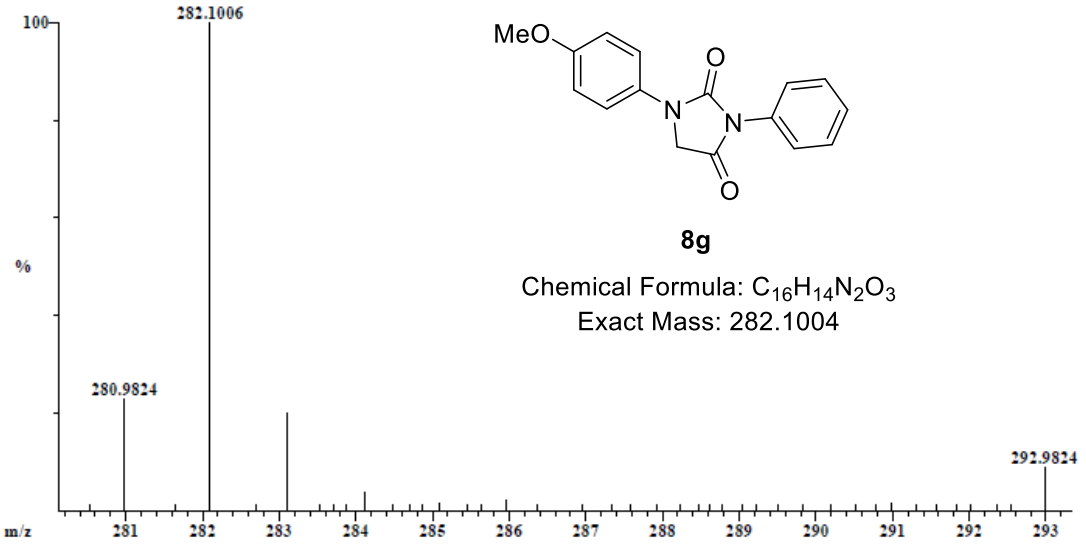



Figure S42. HMBC (400 MHz, $CDCl_3$) spectrum of compound **8g.**

**File: JT-EBC-H59** **Date Run: 02-11-2023 (Time Run: 14:20:23)**
**Sample: JT-EBC-H59**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 192** **R.T.: 2.22**
**Base: m/z 282; 6.4%FS TIC: 238496** **#Ions: 160**




**8g**

Chemical Formula: $C_{16}H_{14}N_2O_3$
Exact Mass: 282.1004

**Selected Isotopes : $H_{0-14}C_{0-16}N_{0-2}O_{0-3}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 282.1006 | 100.0% | $C_{16}H_{14}N_2O_3$ | 282.1005 | 0.5 | 11.0 |

Figure S43. HRMS of compound **8g.**

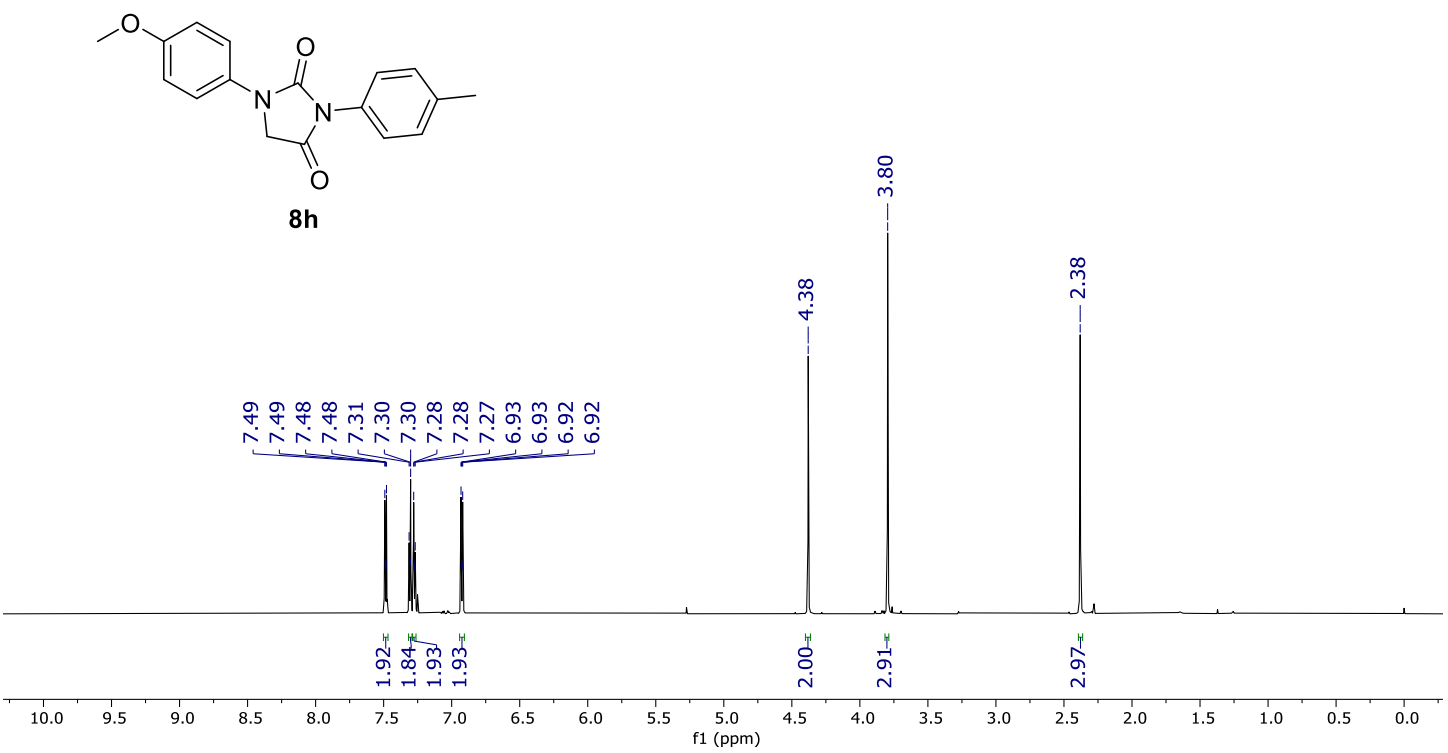



Figure S44. $^{1}$H NMR (750 MHz, $CDCl_3$) spectrum of compound **8h**.

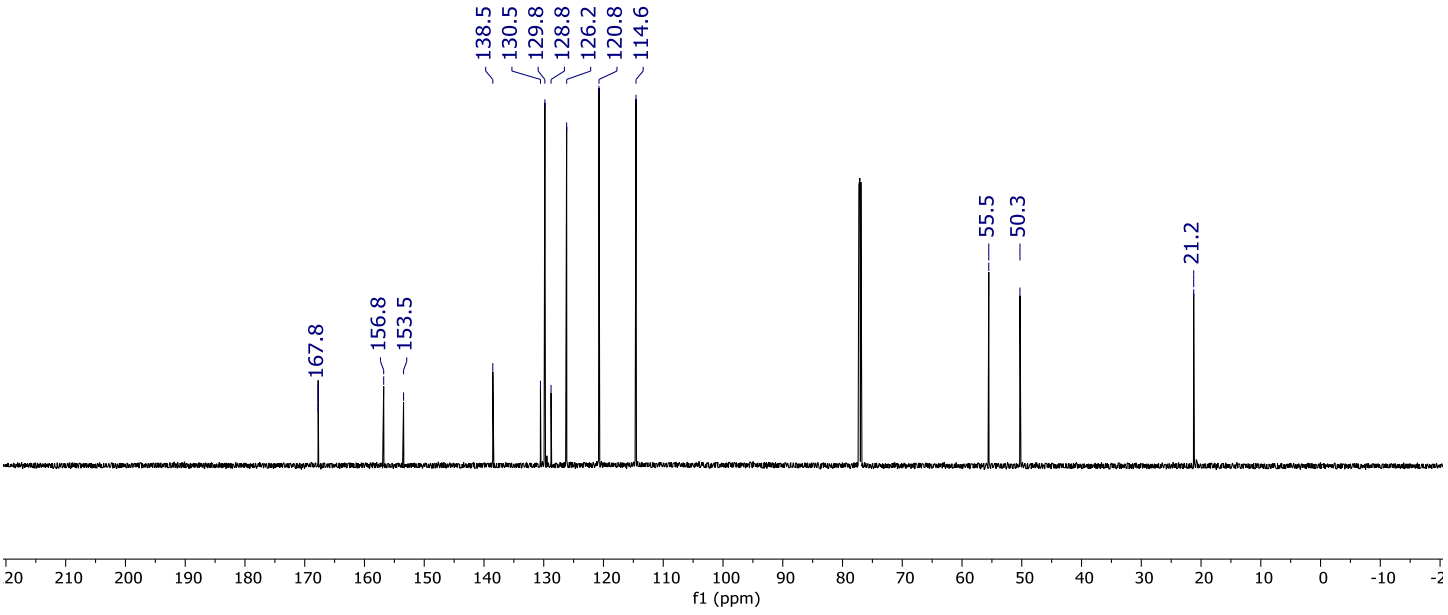



Figure S45. $^{13}$C NMR (187.5 MHz, $CDCl_3$) spectrum of compound **8h**.

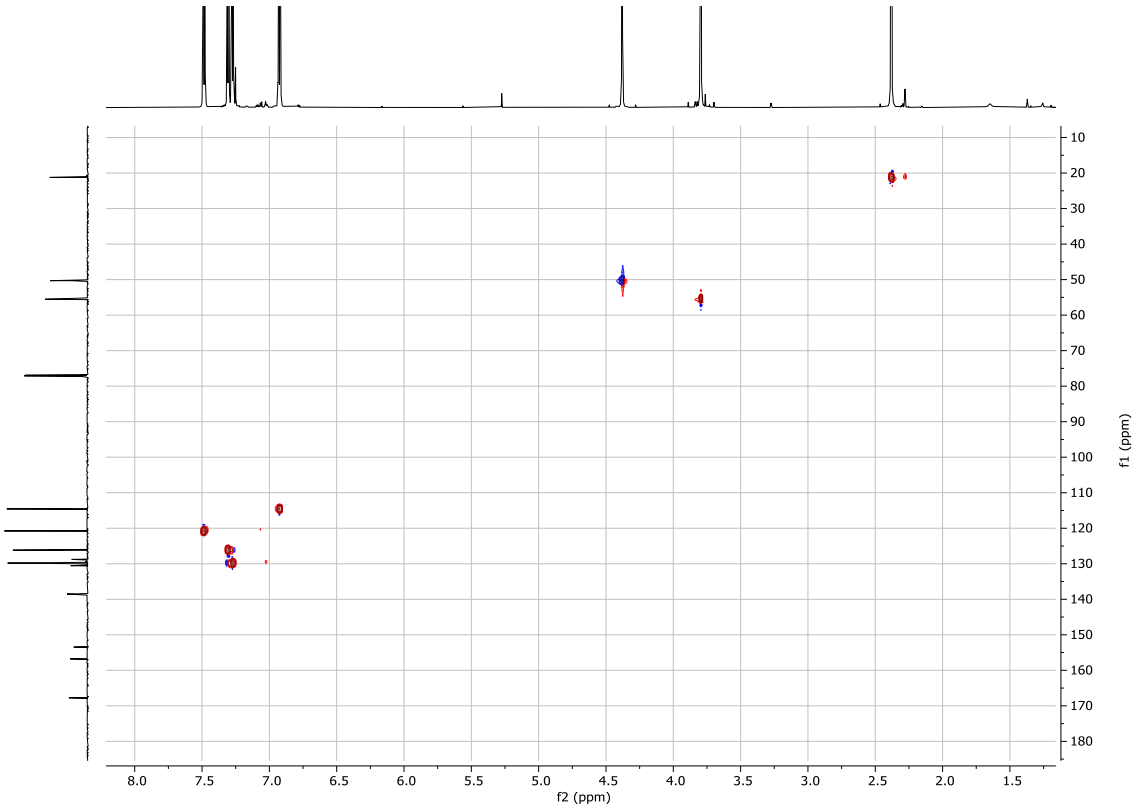



Figure S46. HSQC (750 MHz, $CDCl_3$) spectrum of compound **8h.**

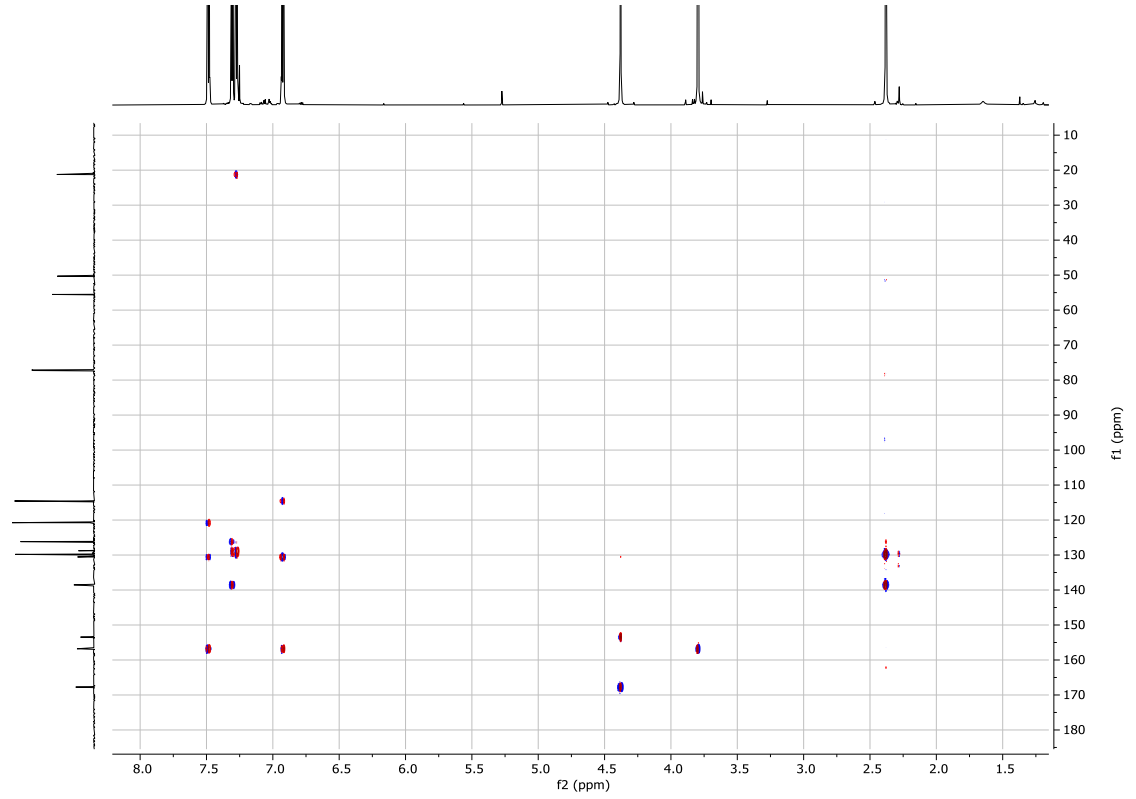
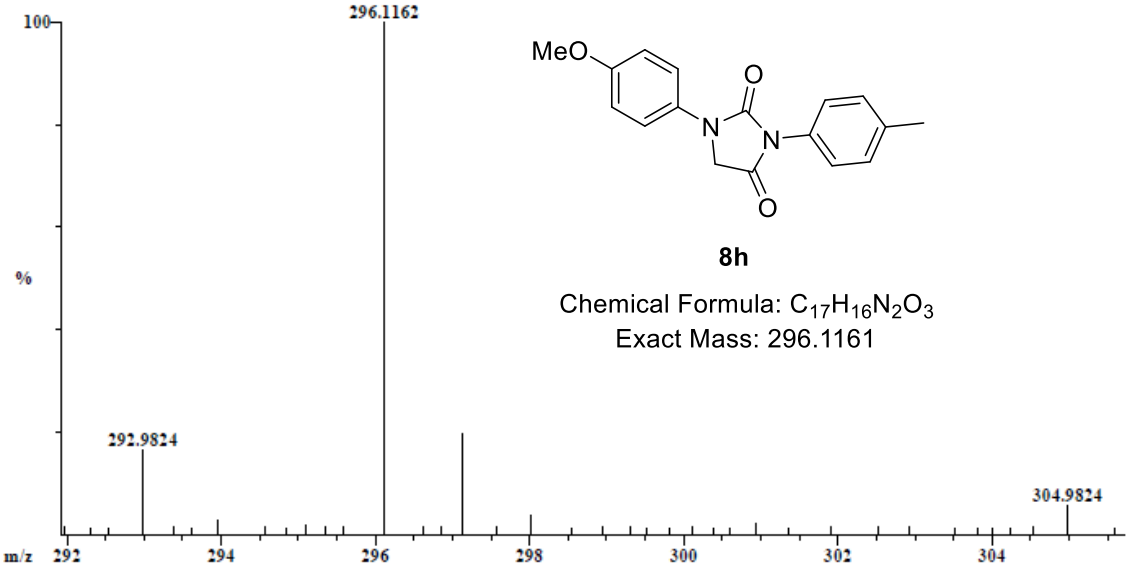



Figure S47. HMBC (750 MHz, $CDCl_3$) spectrum of compound **8h.**

**File: JT-EBC-H15** **Date Run: 02-11-2023 (Time Run: 14:37:03)**
**Sample: JT-EBC-H15**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 189** **R.T.: 2.49**
**Base: m/z 296; 5.6%FS TIC: 278480** **#Ions: 187**




**8h**

Chemical Formula: $C_{17}H_{16}N_2O_3$
Exact Mass: 296.1161

**Selected Isotopes : $H_{0-16}C_{0-17}N_{0-2}O_{0-3}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 296.1162 | 100.0% | $C_{17}H_{16}N_2O_3$ | 296.1161 | 0.3 | 11.0 |

Figure S48. HRMS of compound **8h.**

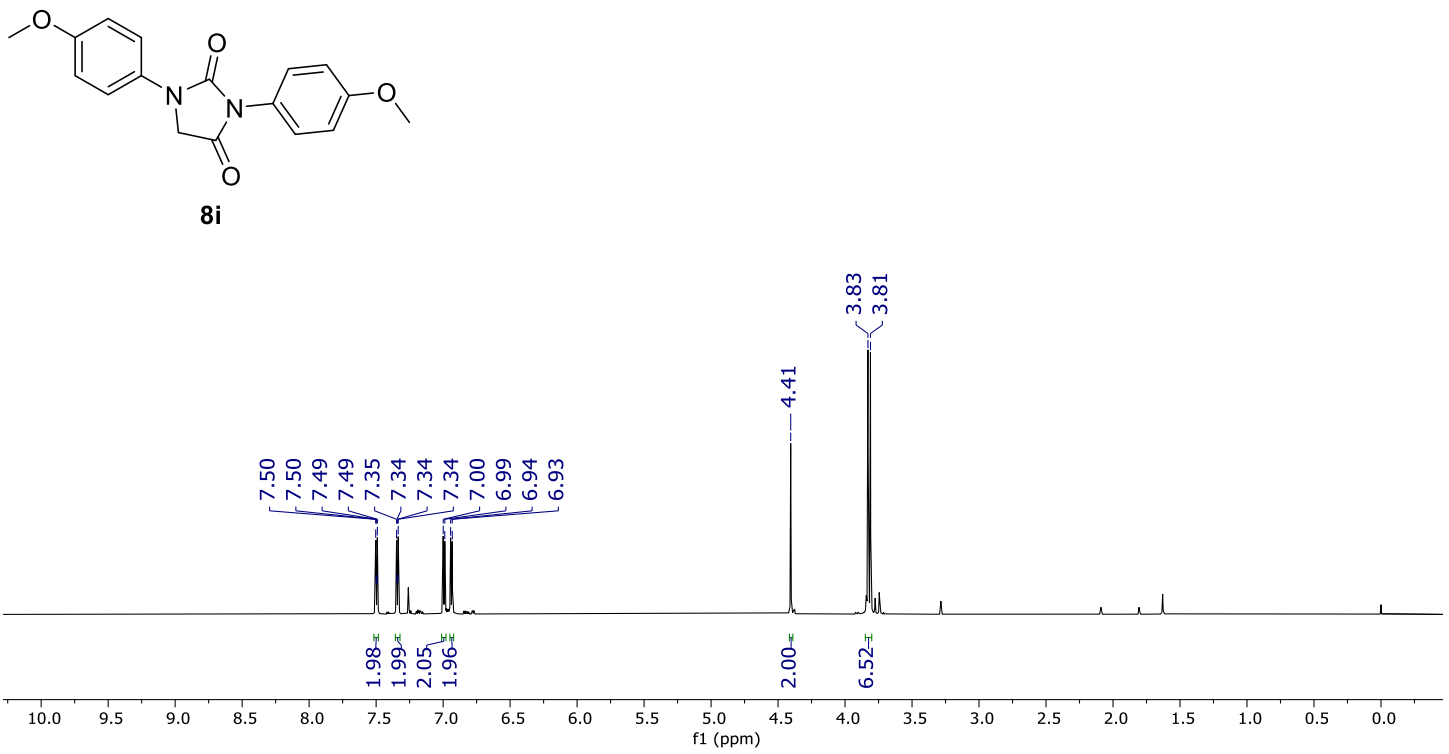



Figure S49. $^{1}$H NMR (750 MHz, $CDCl_3$) spectrum of compound **8i**.

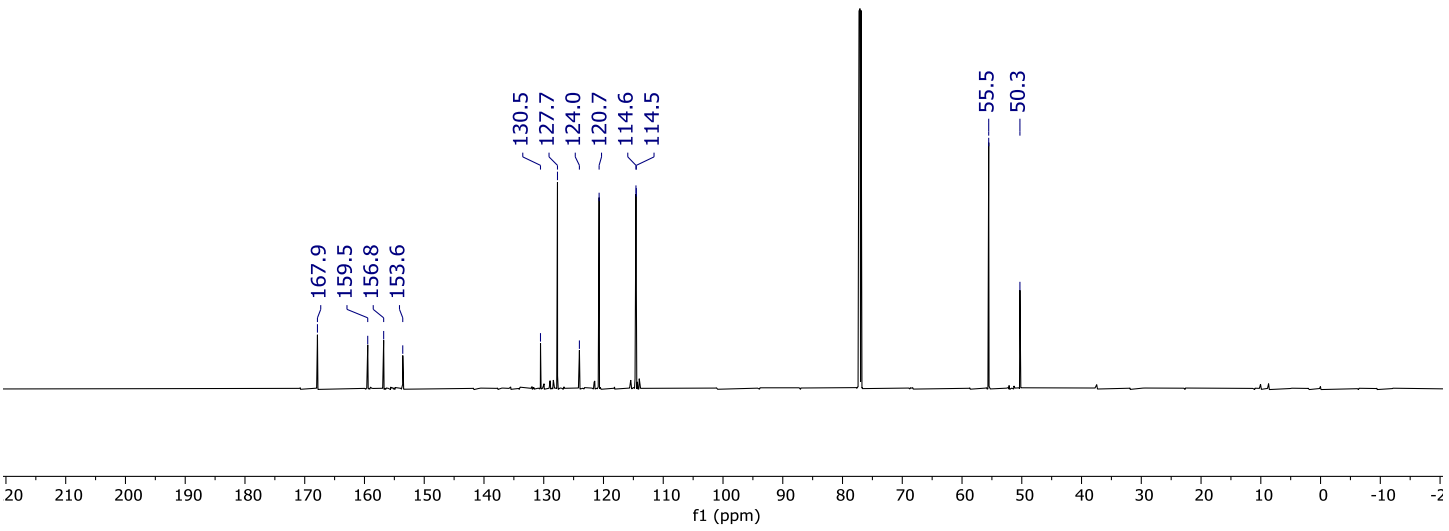



Figure S50. $^{13}$C NMR (187.5 MHz, $CDCl_3$) spectrum of compound **8i**.

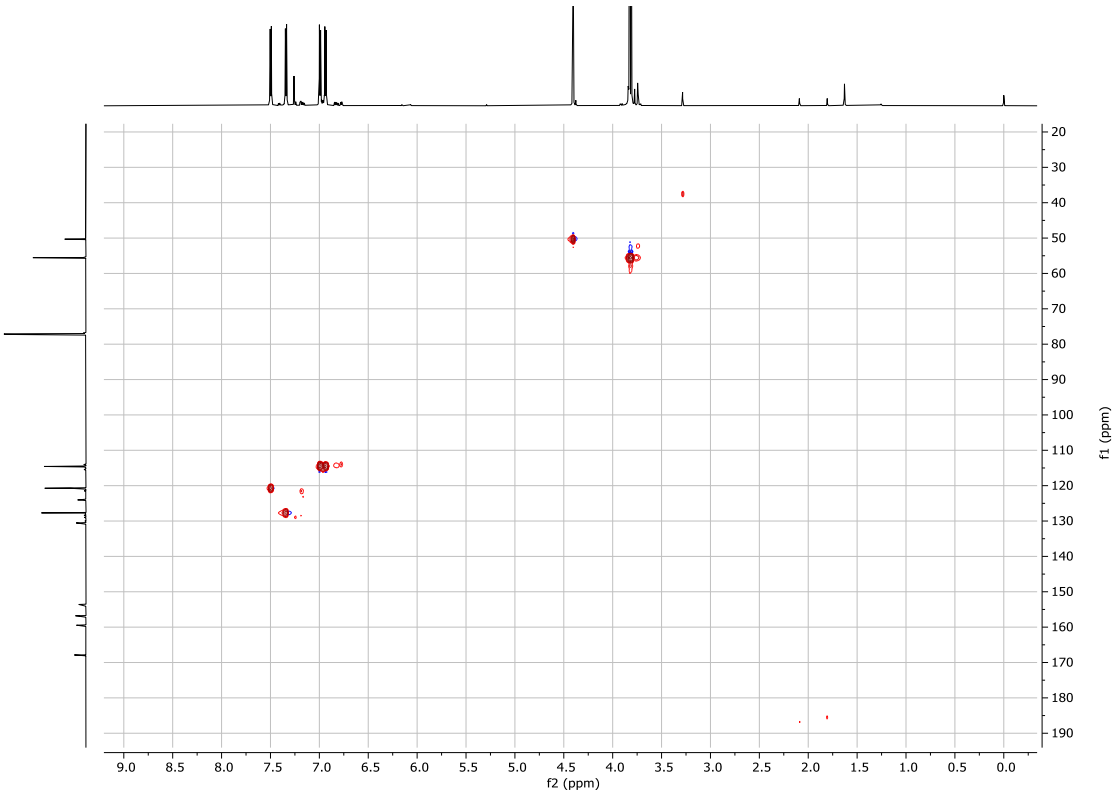



Figure S51. HSQC (750 MHz, $CDCl_3$) spectrum of compound **8i.**

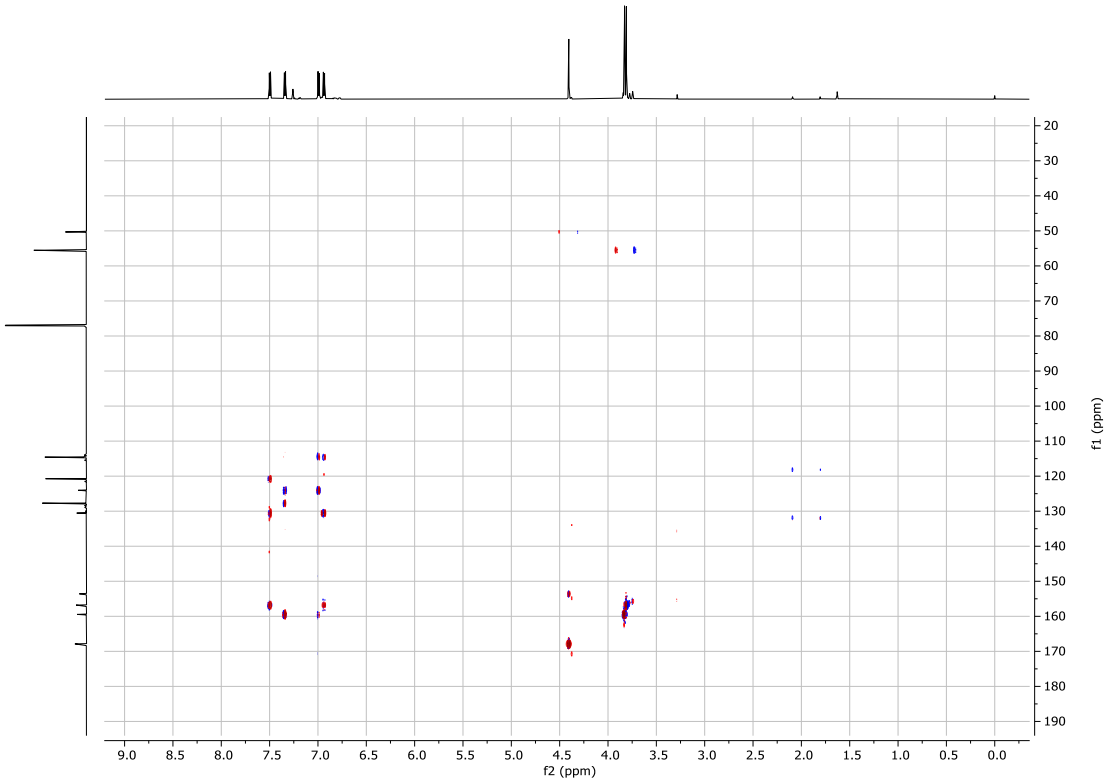
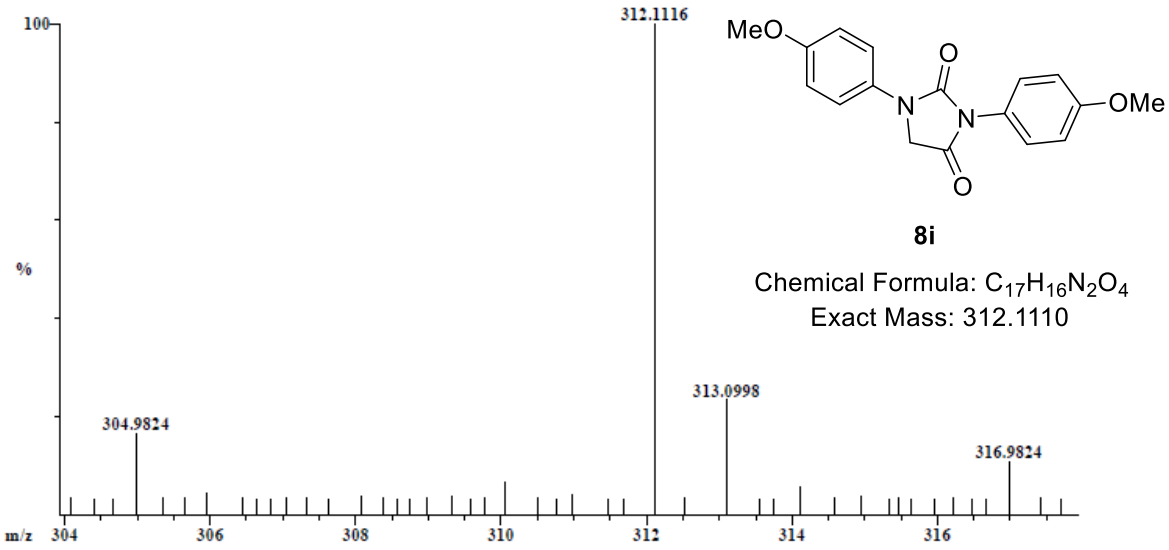



Figure S52. HMBC (750 MHz, $CDCl_3$) spectrum of compound **8i.**

**File: JT-EBC-H42** **Date Run: 03-05-2023 (Time Run: 12:27:35)**
**Sample: JT-EBC-H42**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 189** **R.T.: 2.53**
**Base: m/z 312; 2.2%FS TIC: 226800** **#Ions: 210**




**8i**

Chemical Formula: $C_{17}H_{16}N_2O_4$
Exact Mass: 312.1110

**Selected Isotopes : $H_{0-16}C_{0-17}N_{0-2}O_{0-4}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 312.1116 | 100.0% | $C_{17}H_{16}N_2O_4$ | 312.1110 | 1.9 | 11.0 |

Figure S53. HRMS of compound **8i.**

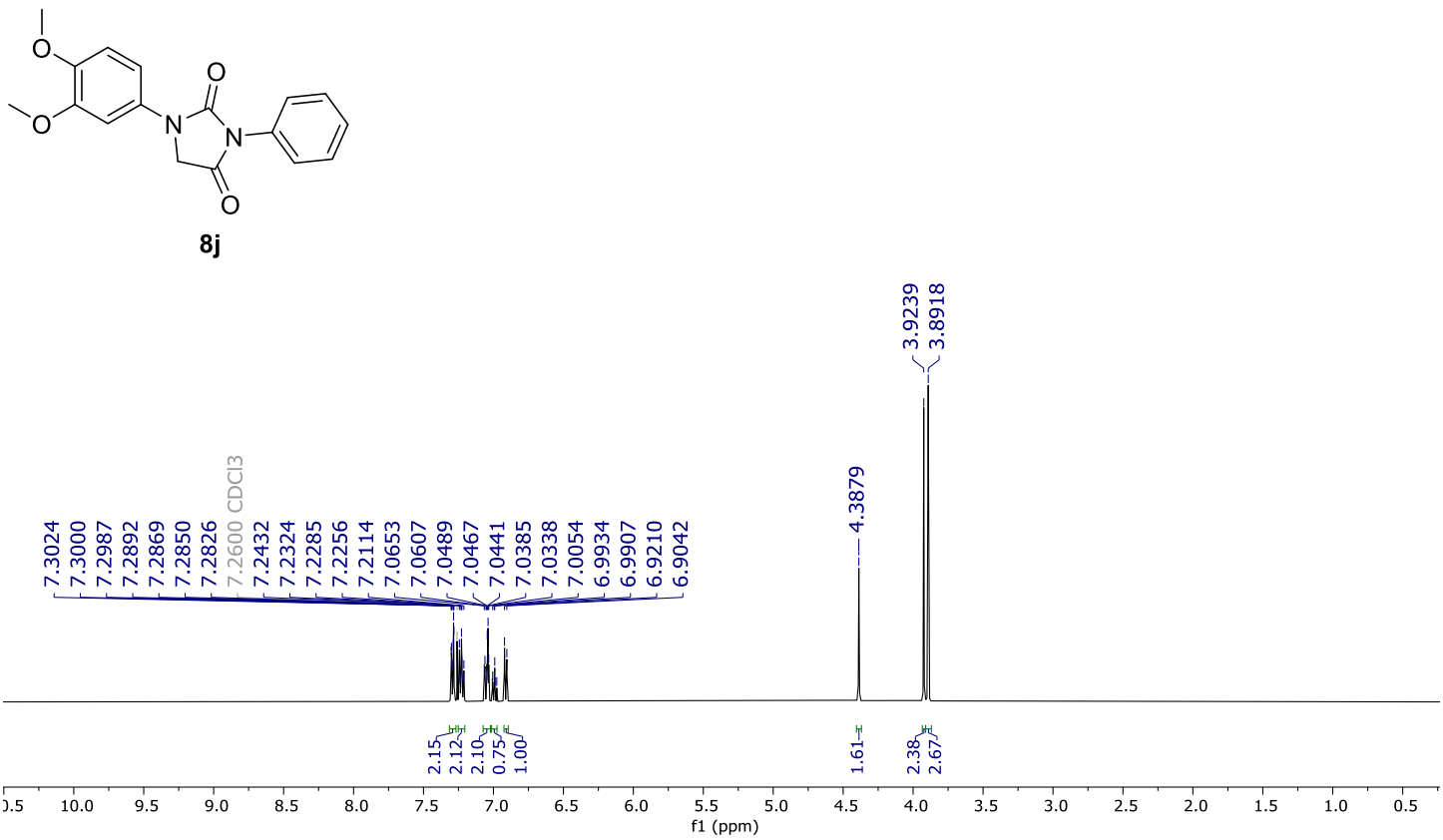



Figure S54. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **8j**.

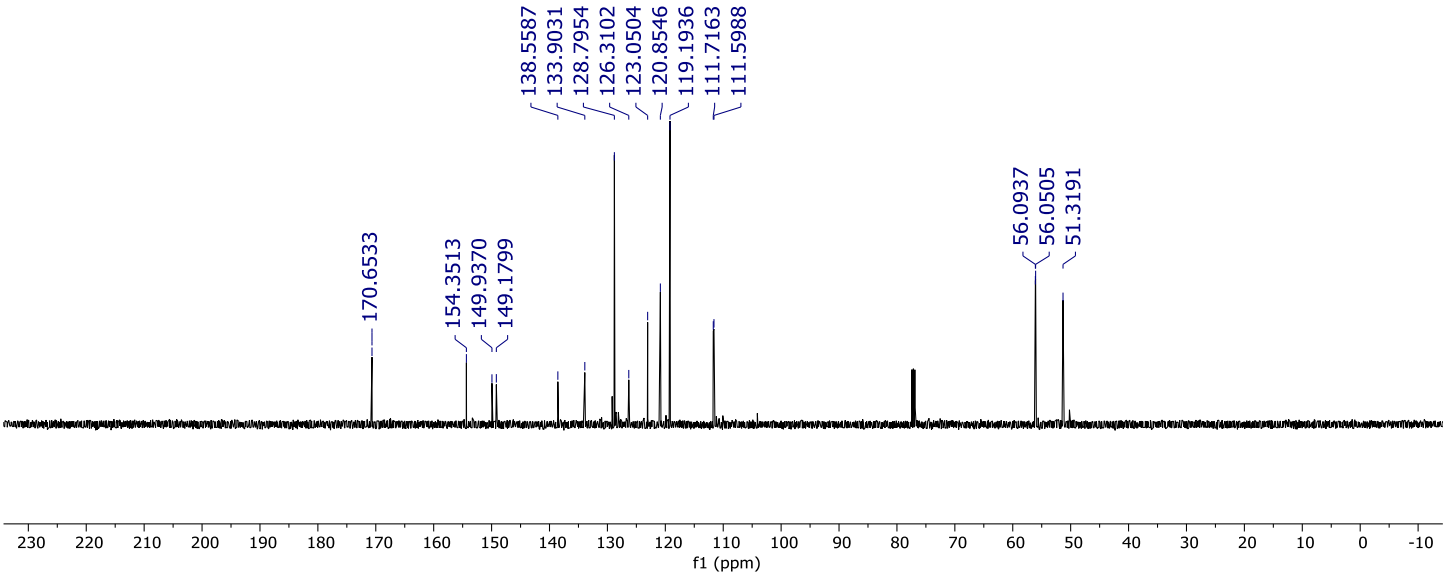



Figure S55. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **8j**.

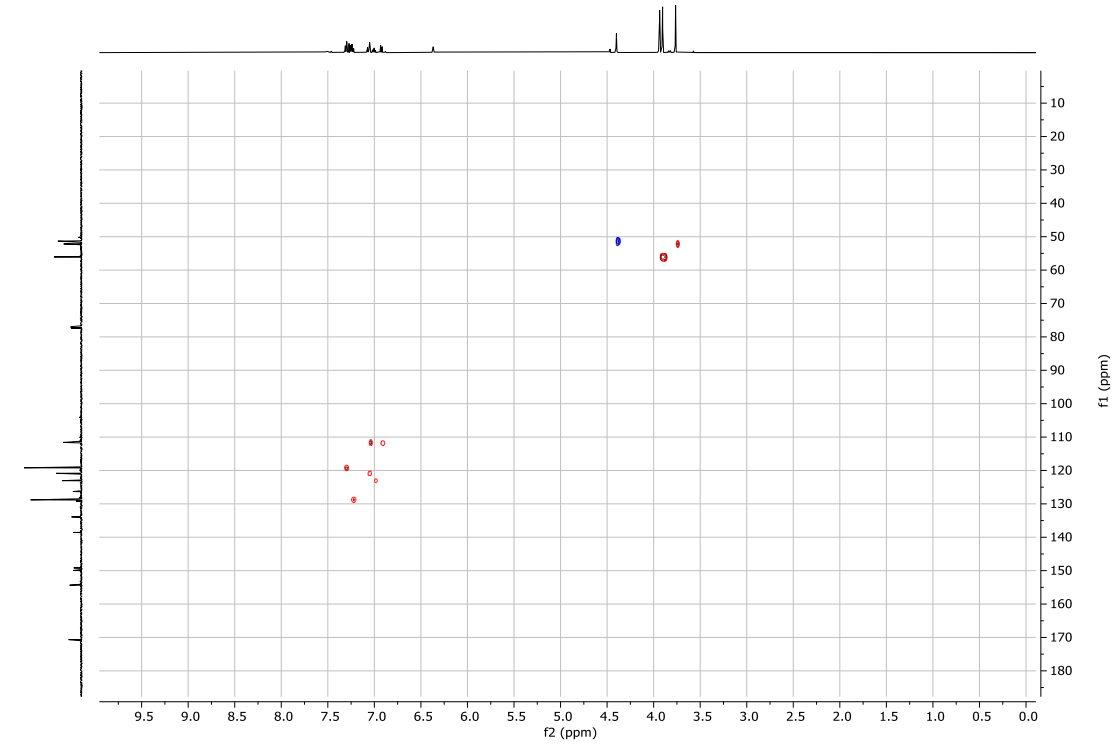



Figure S56. HSQC (500 MHz, $CDCl_3$) spectrum of compound **8j.**

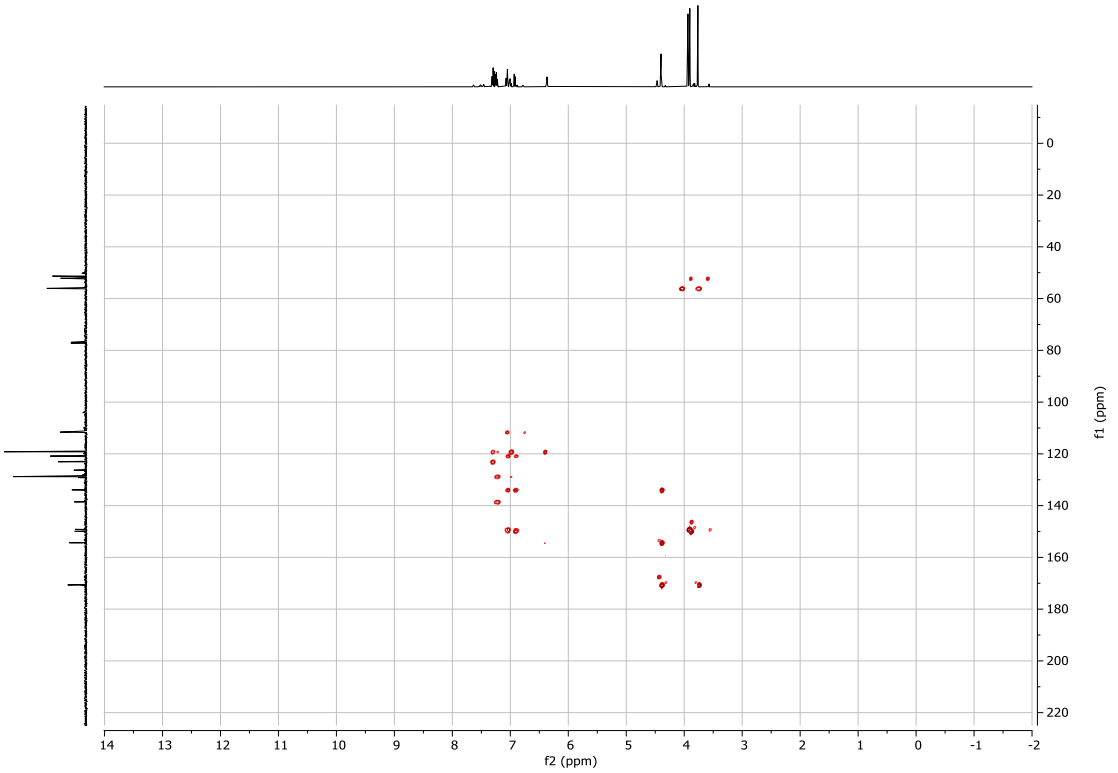



Figure S57. HMBC (500 MHz, $CDCl_3$) spectrum of compound **8j.**

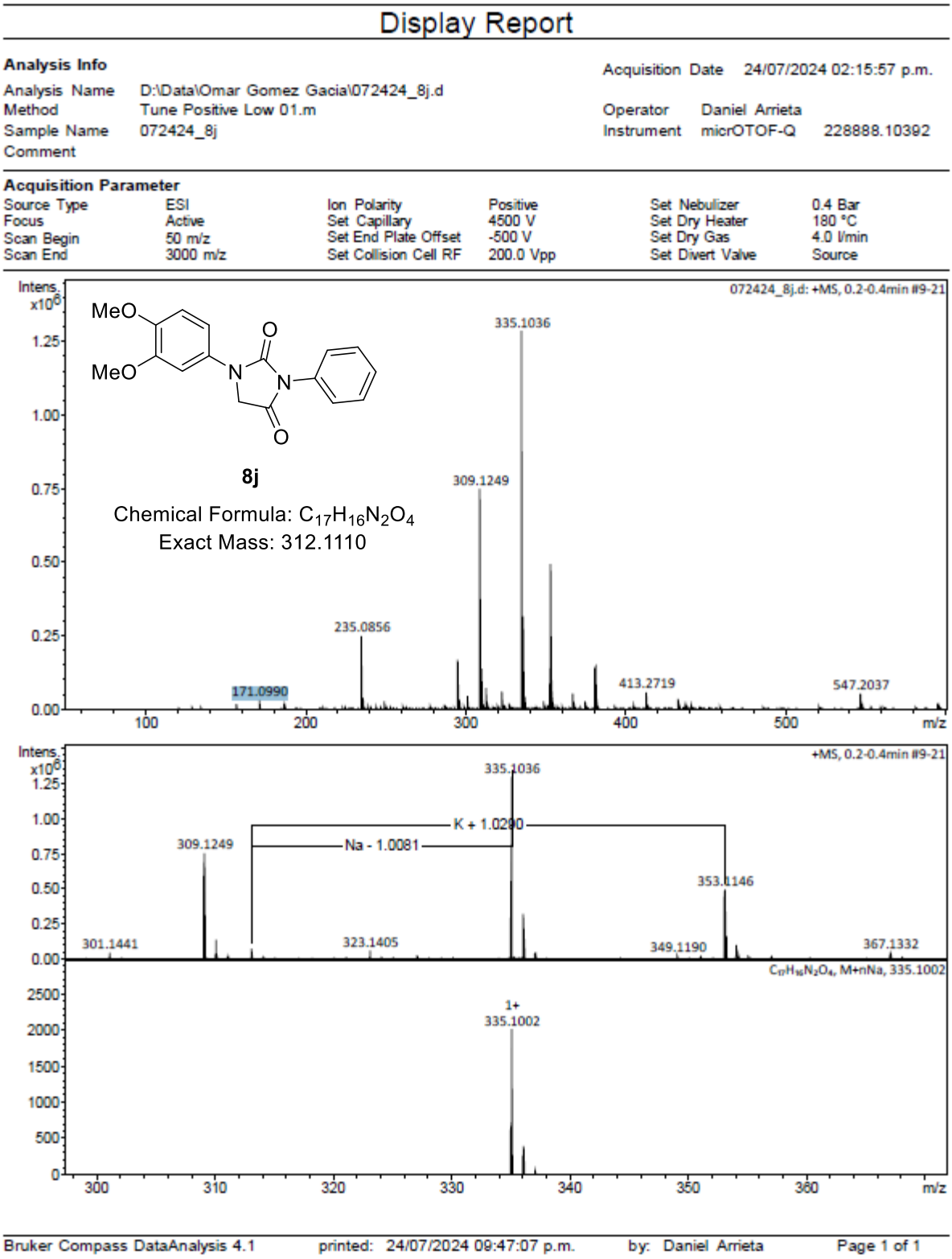



Figure S58. HRMS of compound **8j.**

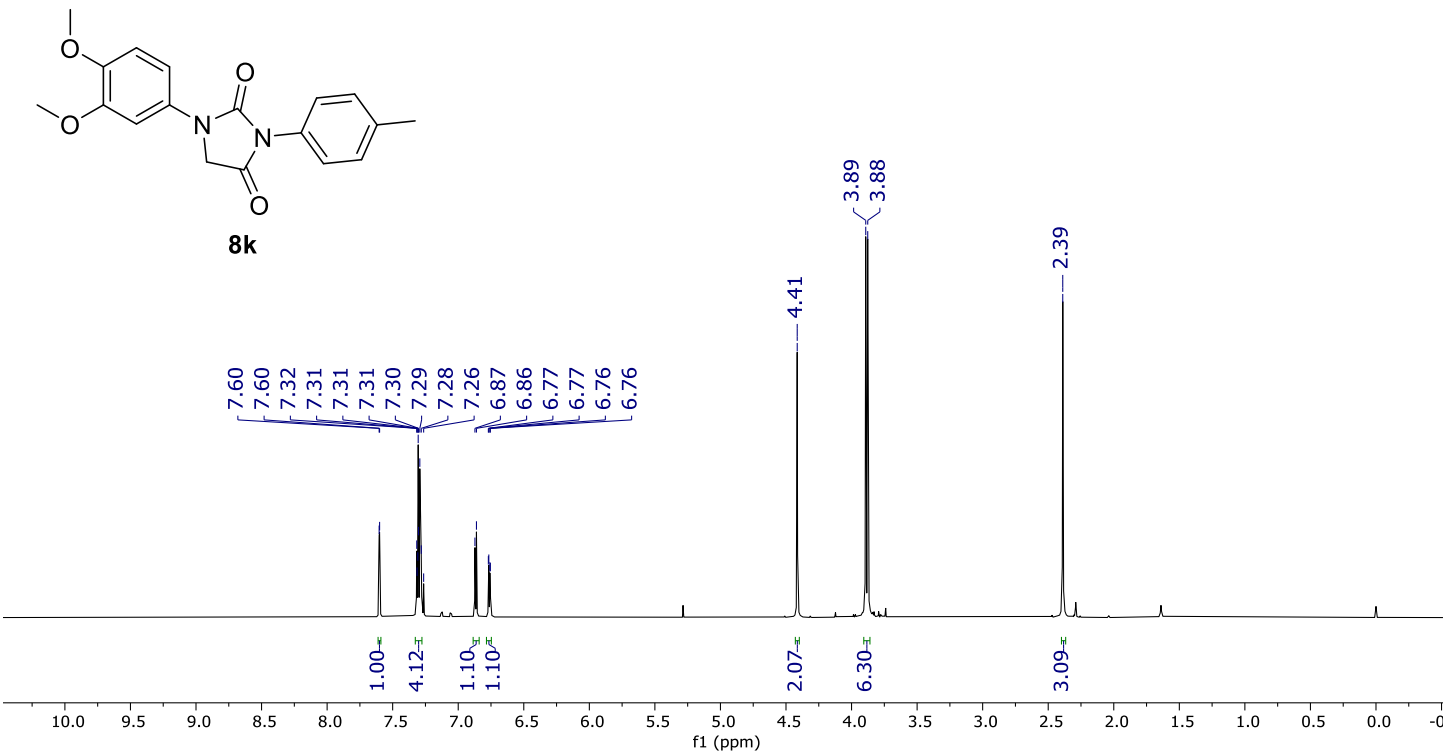



Figure S59. $^{1}$H NMR (750 MHz, $CDCl_3$) spectrum of compound **8k**.

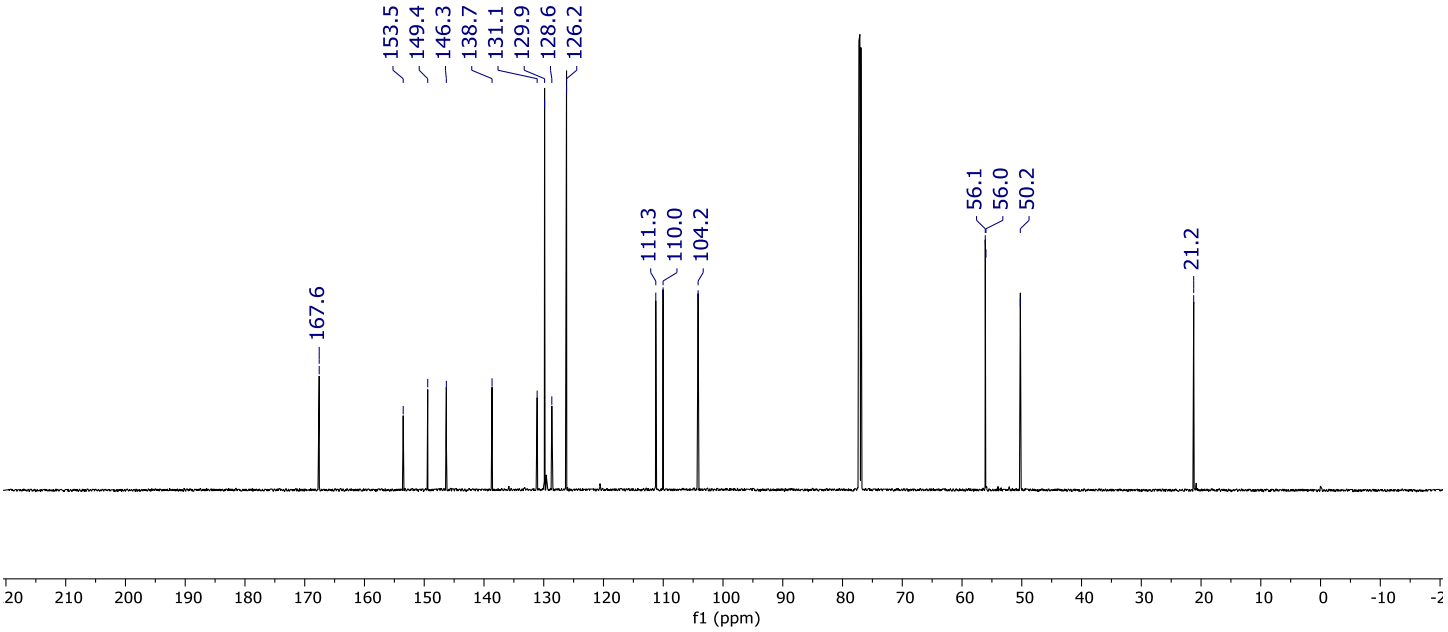



Figure S60. $^{13}$C NMR (187.5 MHz, $CDCl_3$) spectrum of compound **8k**.

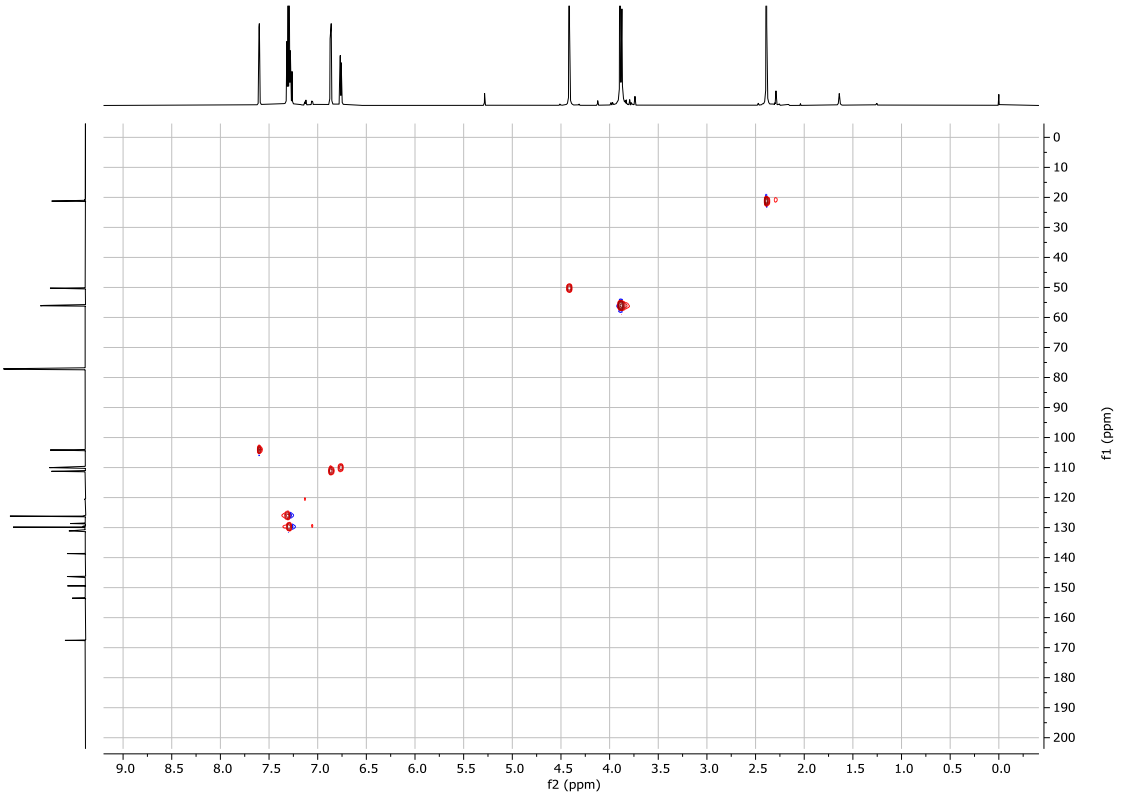



Figure S61. HSQC (750 MHz, $CDCl_3$) spectrum of compound **8k.**

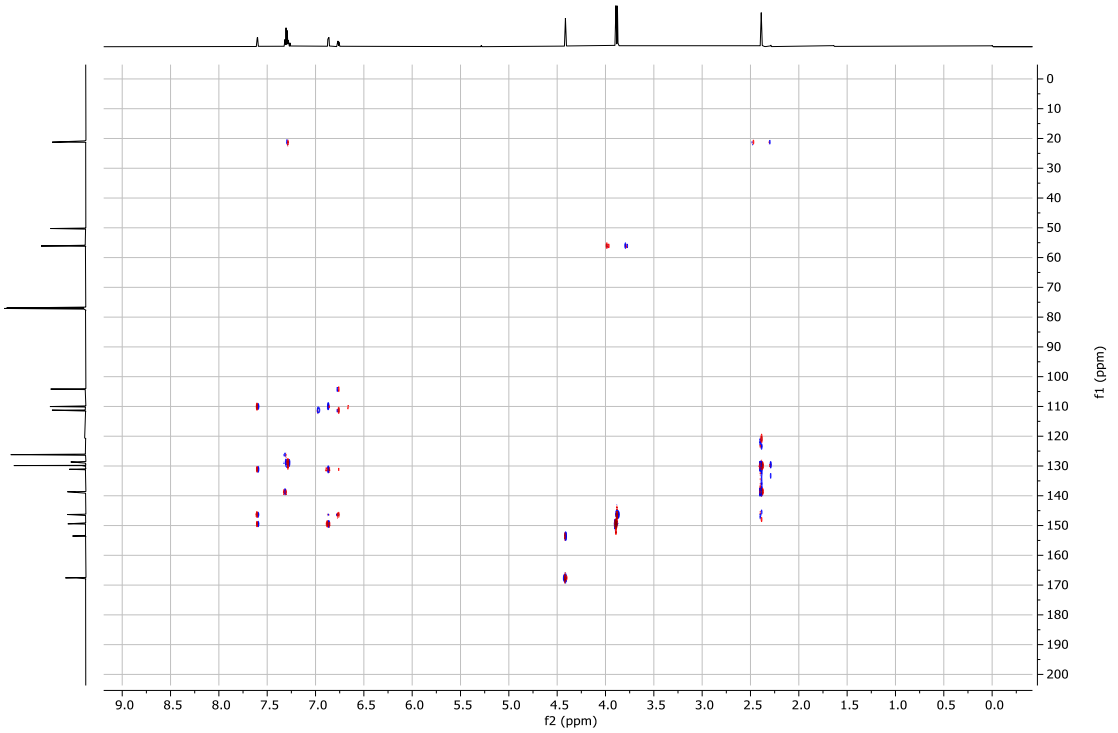



Figure S62. HMBC (750 MHz, $CDCl_3$) spectrum of compound **8k.**

***IPN***

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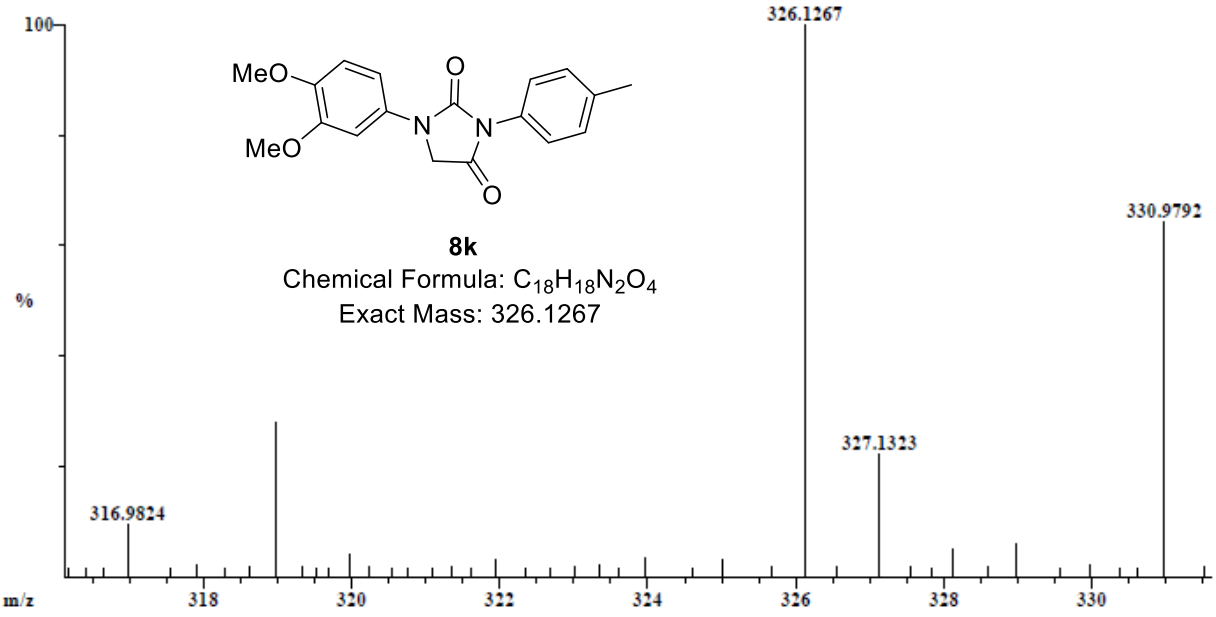
**File: JT-H33** **Date Run: 10-29-2022 (Time Run: 14:21:29)**
**Sample: JT-H33**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 440** **R.T.: 5.9**
**Base: m/z 326; 4.6%FS TIC: 321920** **#Ions: 193**




**8k**
Chemical Formula: $C_{18}H_{18}N_2O_4$
Exact Mass: 326.1267

**Selected Isotopes : $H_{0-18}C_{0-18}N_{0-2}O_{0-4}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 326.1267 | 100.0% | $C_{18}H_{18}N_2O_4$ | 326.1267 | 0.1 | 11.0 |

Figure S63. HRMS of compound **8k.**

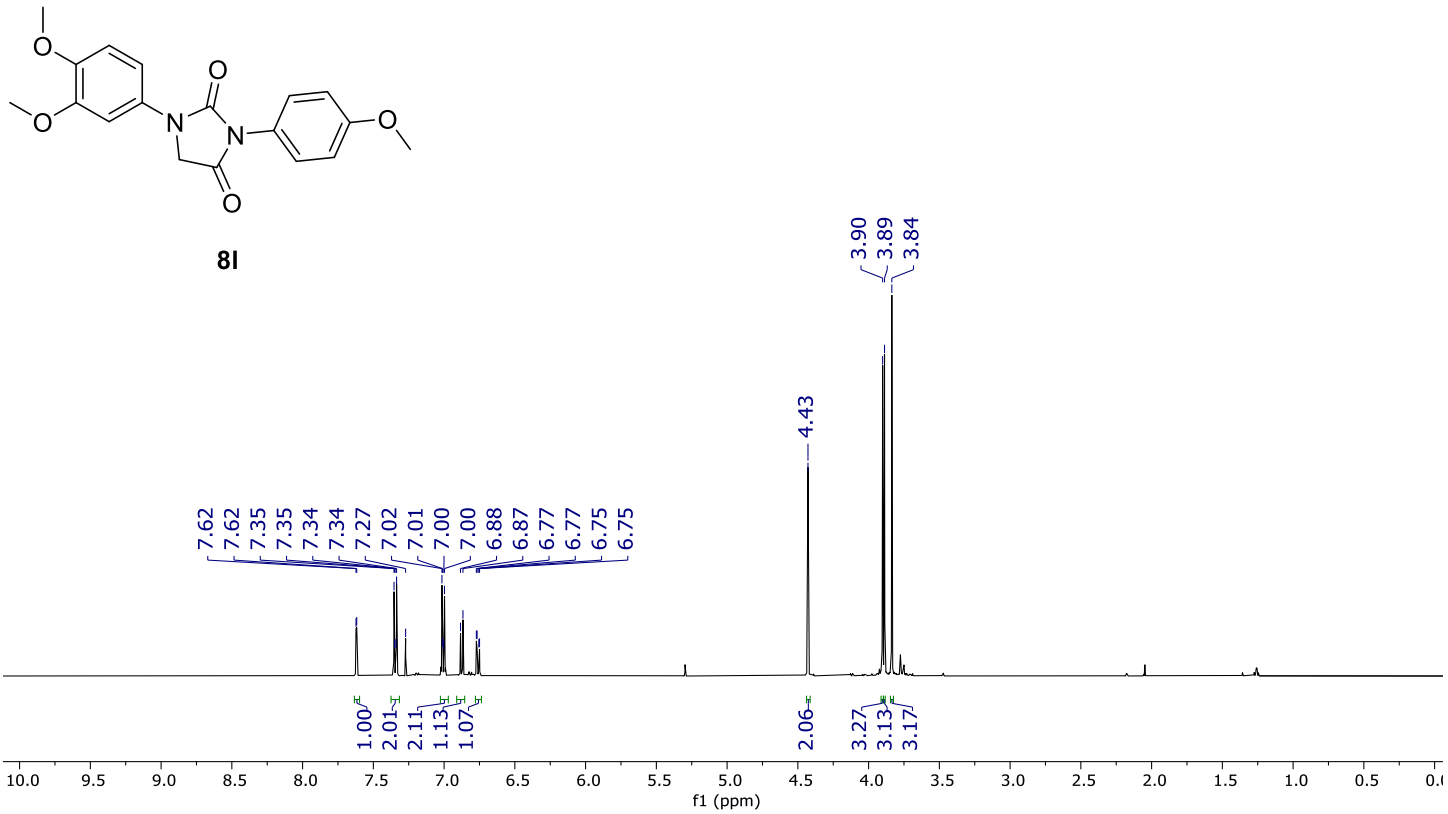



Figure S64. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **8l**.

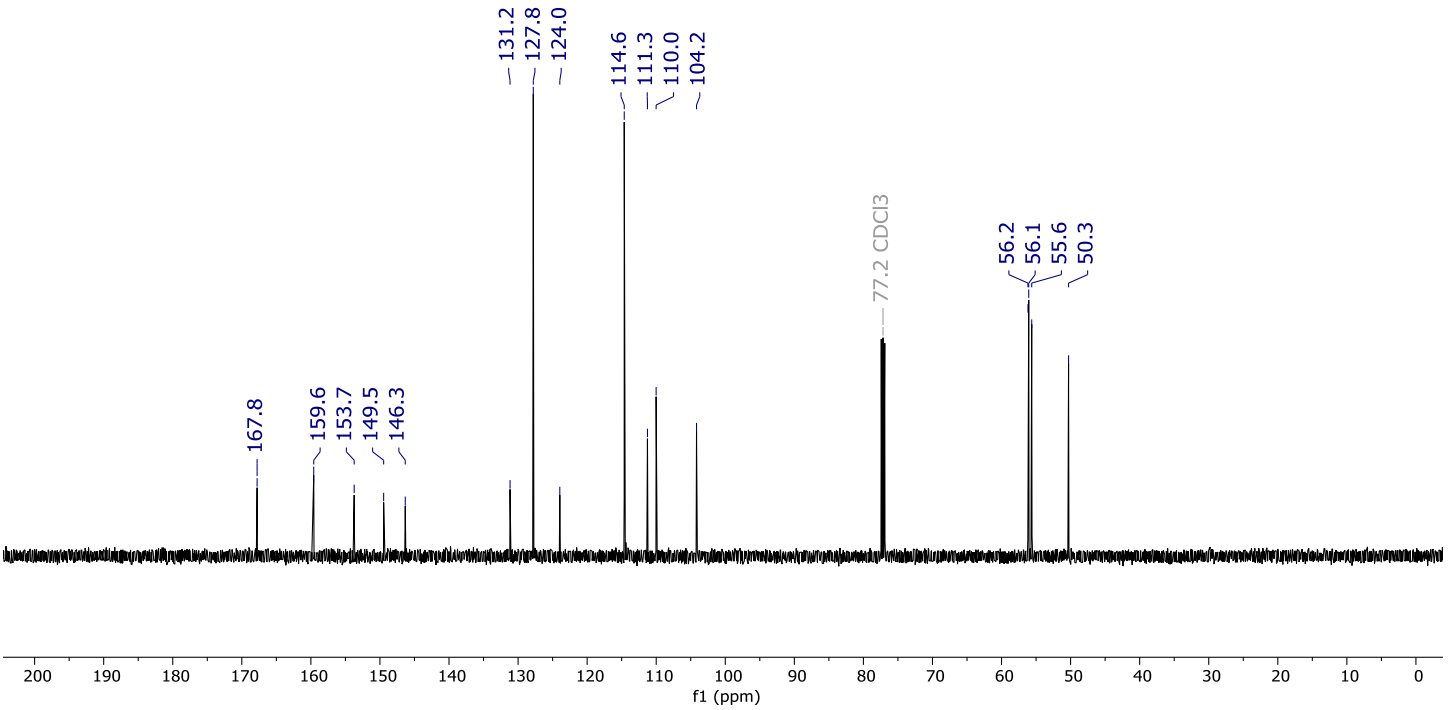



Figure S65. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **8l**.

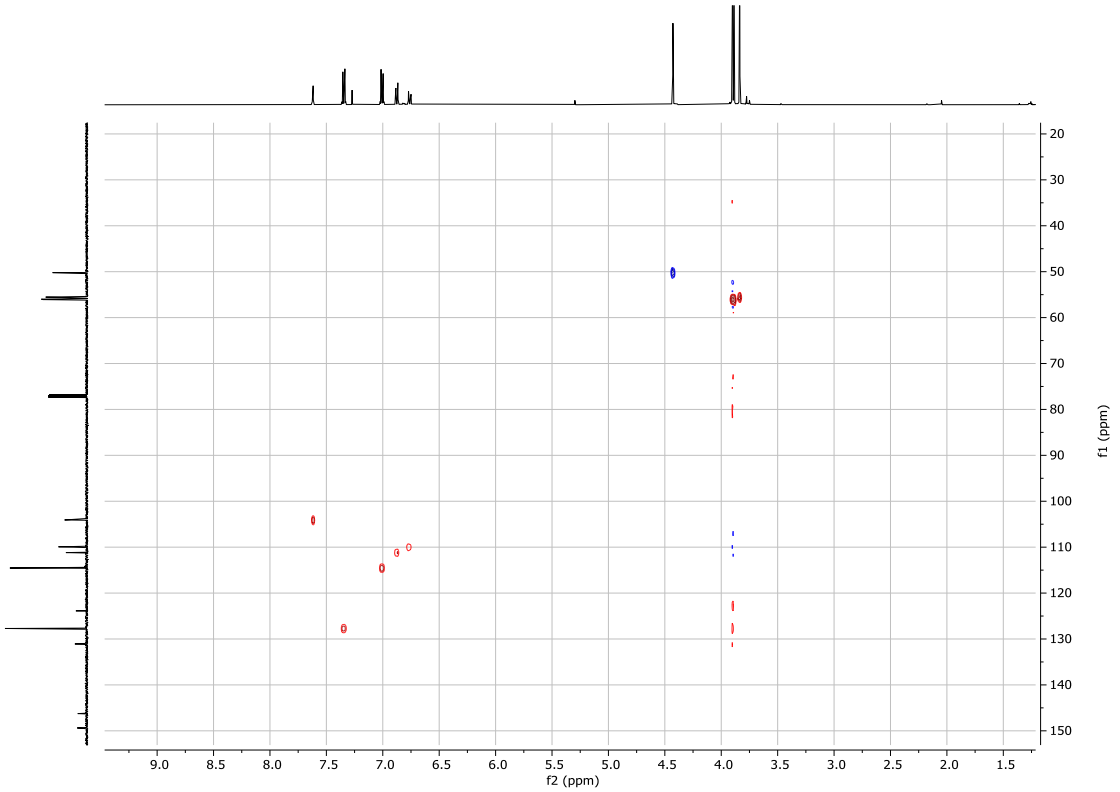



Figure S66. HSQC (500 MHz, $CDCl_3$) spectrum of compound **8l.**

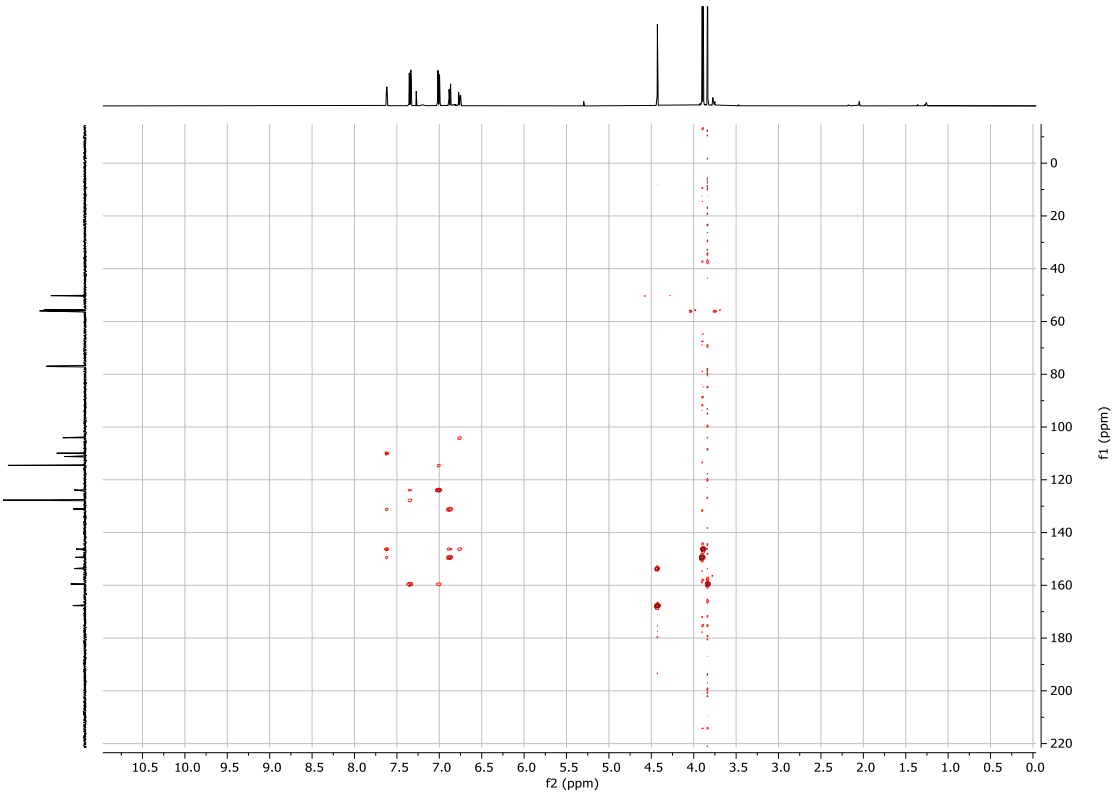



Figure S67. HMBC (500 MHz, $CDCl_3$) spectrum of compound **8l.**

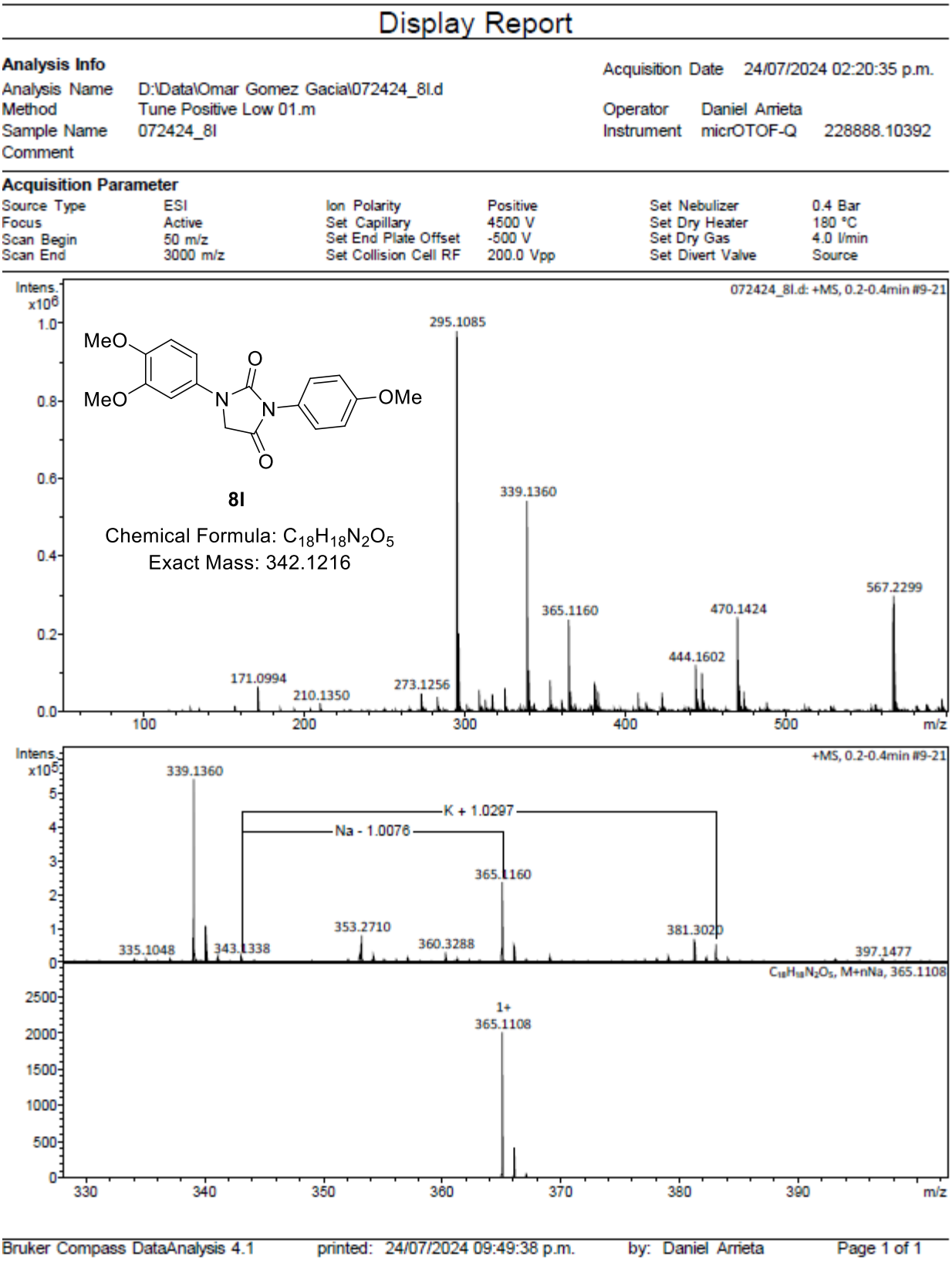



Figure S68. HRMS of compound **8l.**

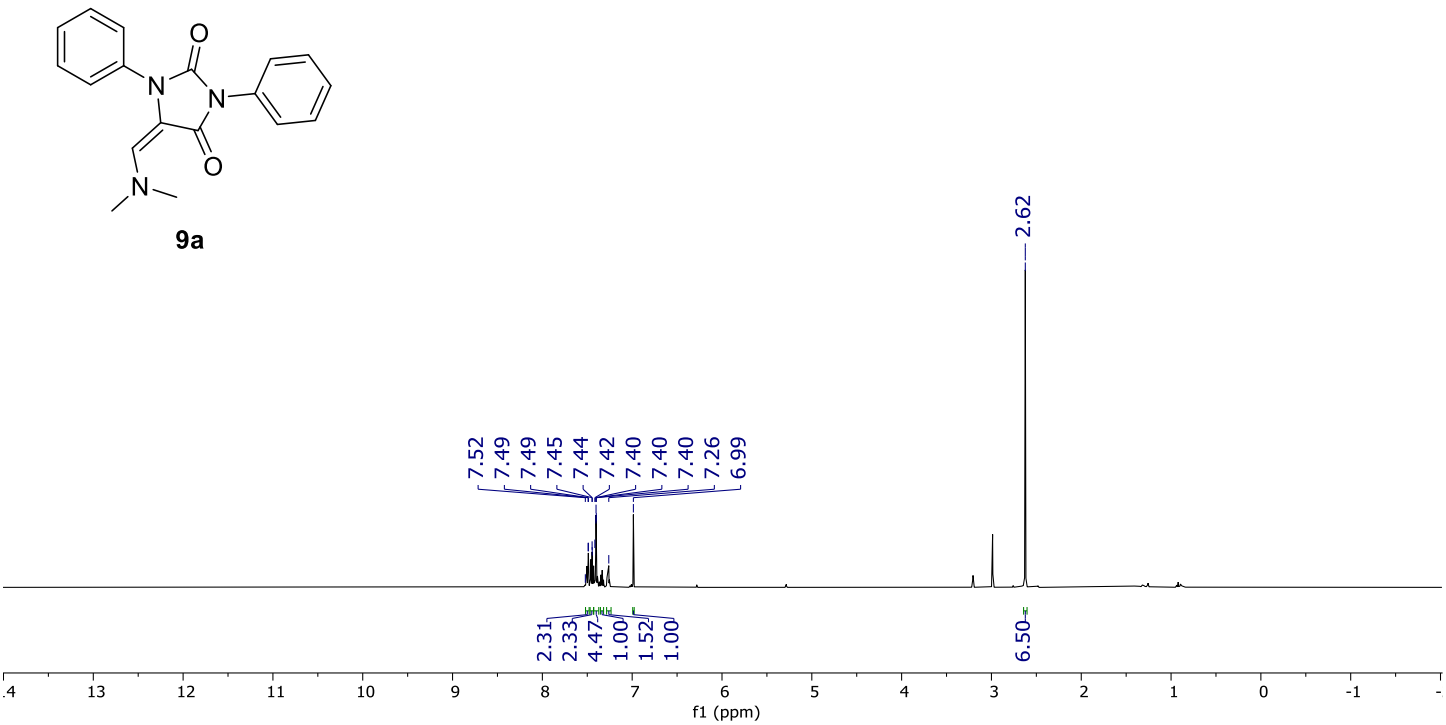



Figure S69. $^{1}H$ NMR (500 MHz, $CDCl_3$) spectrum of compound **9a**.

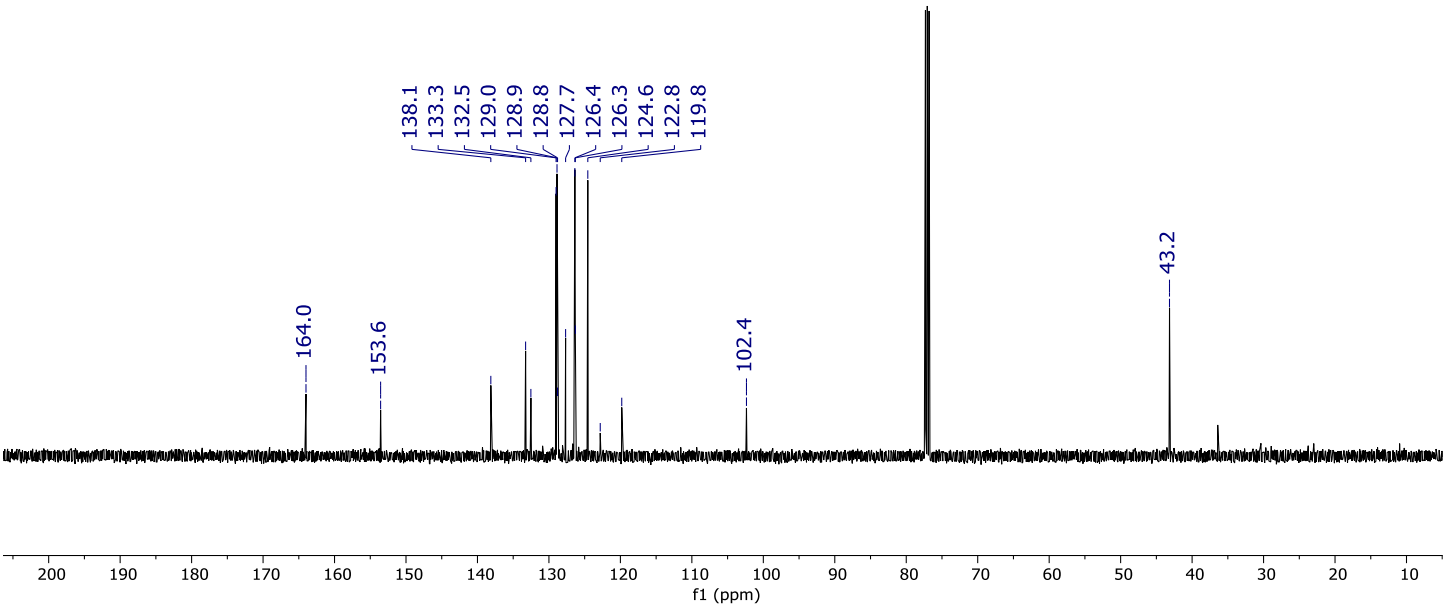



Figure S70. $^{13}C$ NMR (125 MHz, $CDCl_3$) spectrum of compound **9a**.

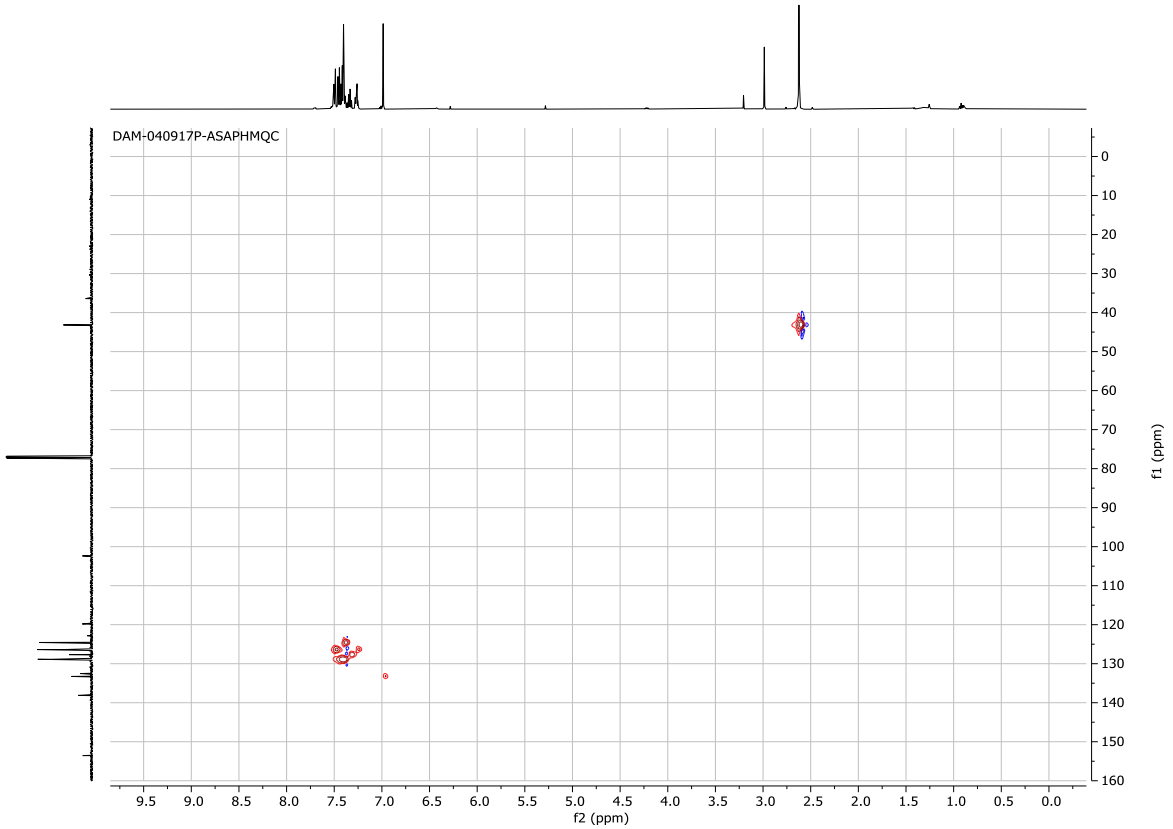



Figure S71. HSQC (500 MHz, $CDCl_3$) spectrum of compound **9a.**

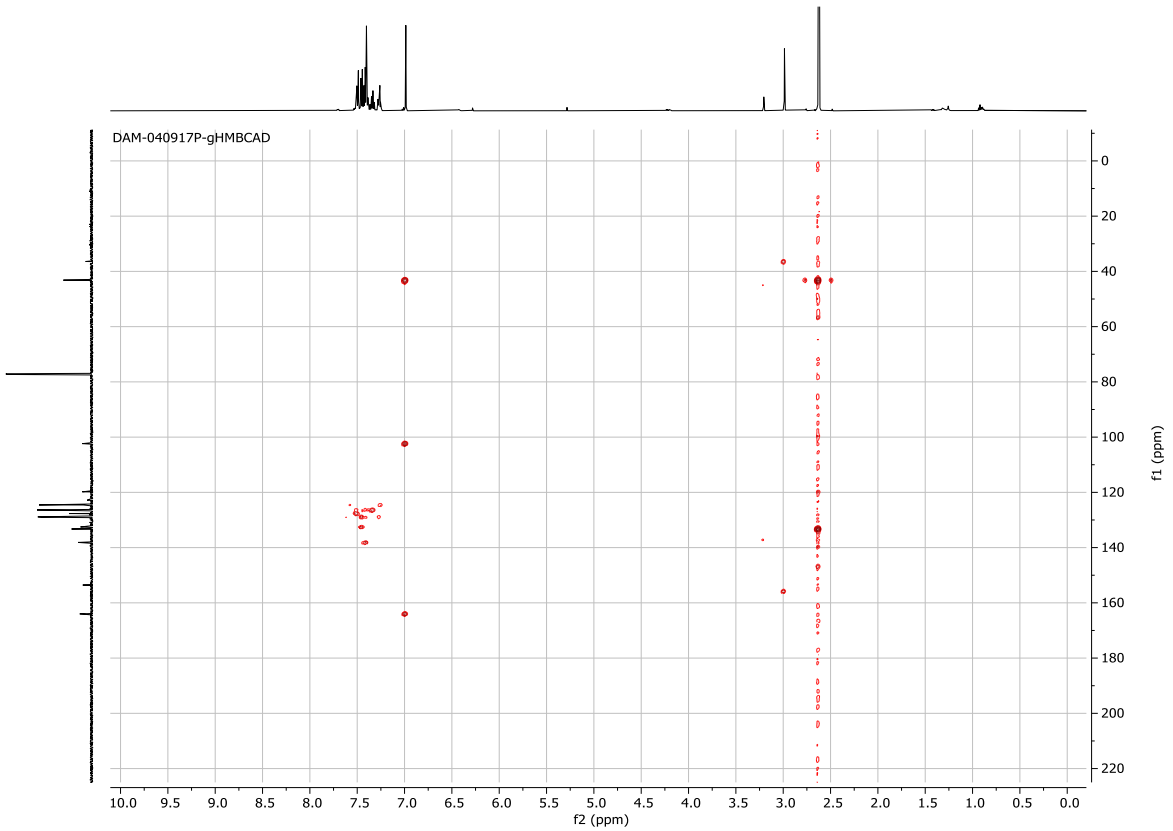
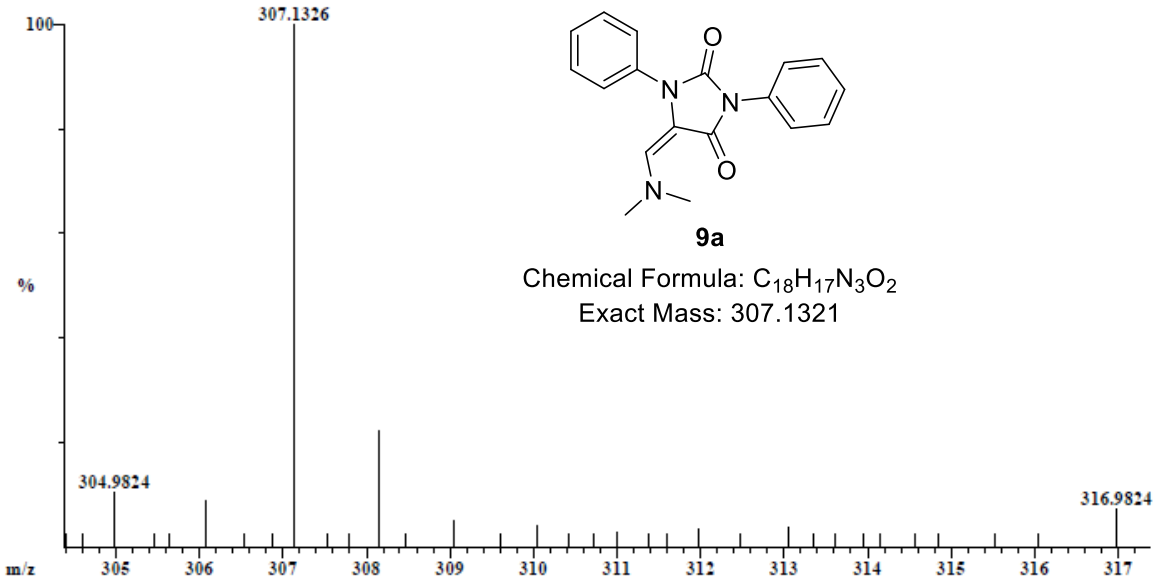



Figure S72. HMBC (500 MHz, $CDCl_3$) spectrum of compound **9a.**

**File: JT-EBC-H51** **Date Run: 02-11-2023 (Time Run: 14:57:24)**
**Sample: JT-EBC-H51**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 207** **R.T.: 2.39**
**Base: m/z 307; 2.9%FS TIC: 232784** **#Ions: 158**







**9a**

Chemical Formula: $C_{18}H_{17}N_3O_2$
Exact Mass: 307.1321

**Selected Isotopes : $H_{0-17}C_{0-18}N_{0-3}O_{0-2}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 307.1326 | 100.0% | $C_{18}H_{17}N_3O_2$ | 307.1321 | 1.7 | 12.0 |

Figure S73. HRMS of compound **9a.**

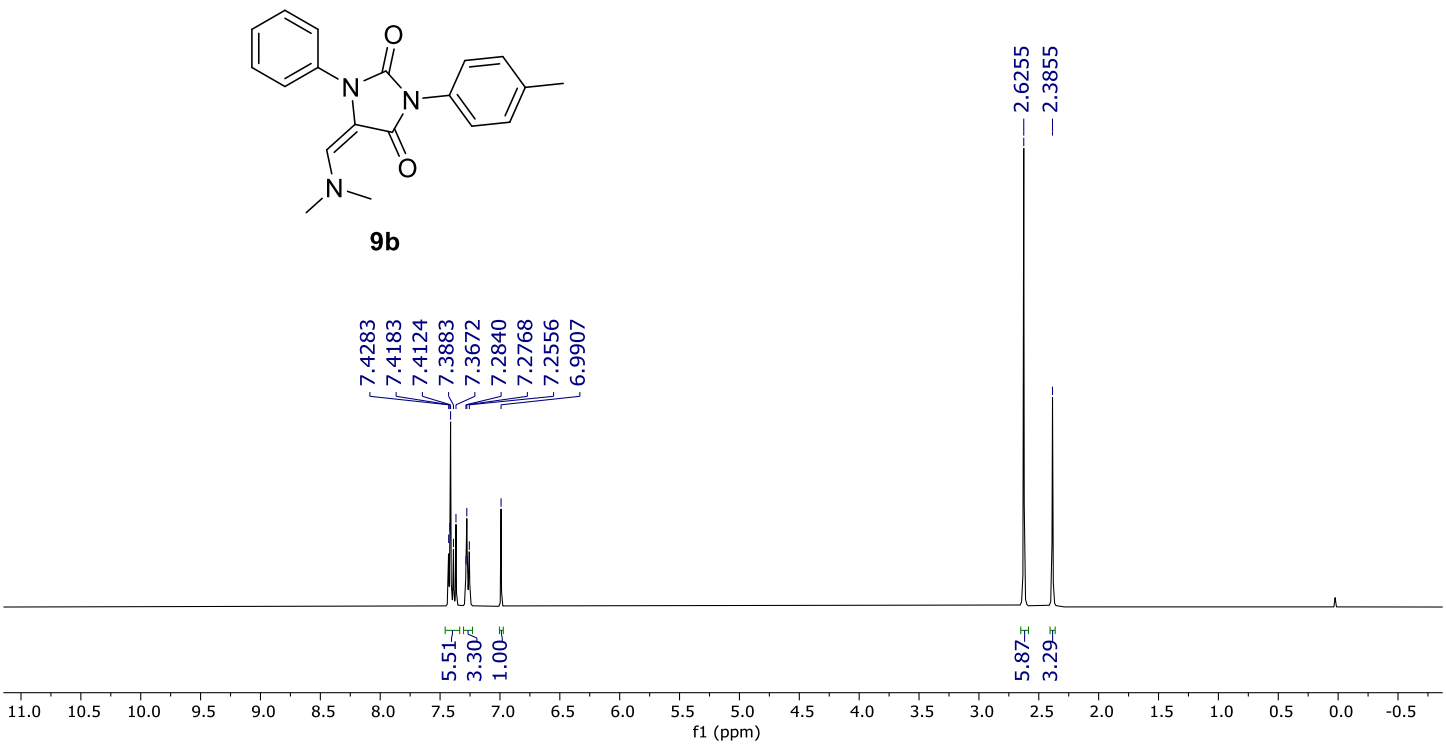



Figure S74. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **9b**.

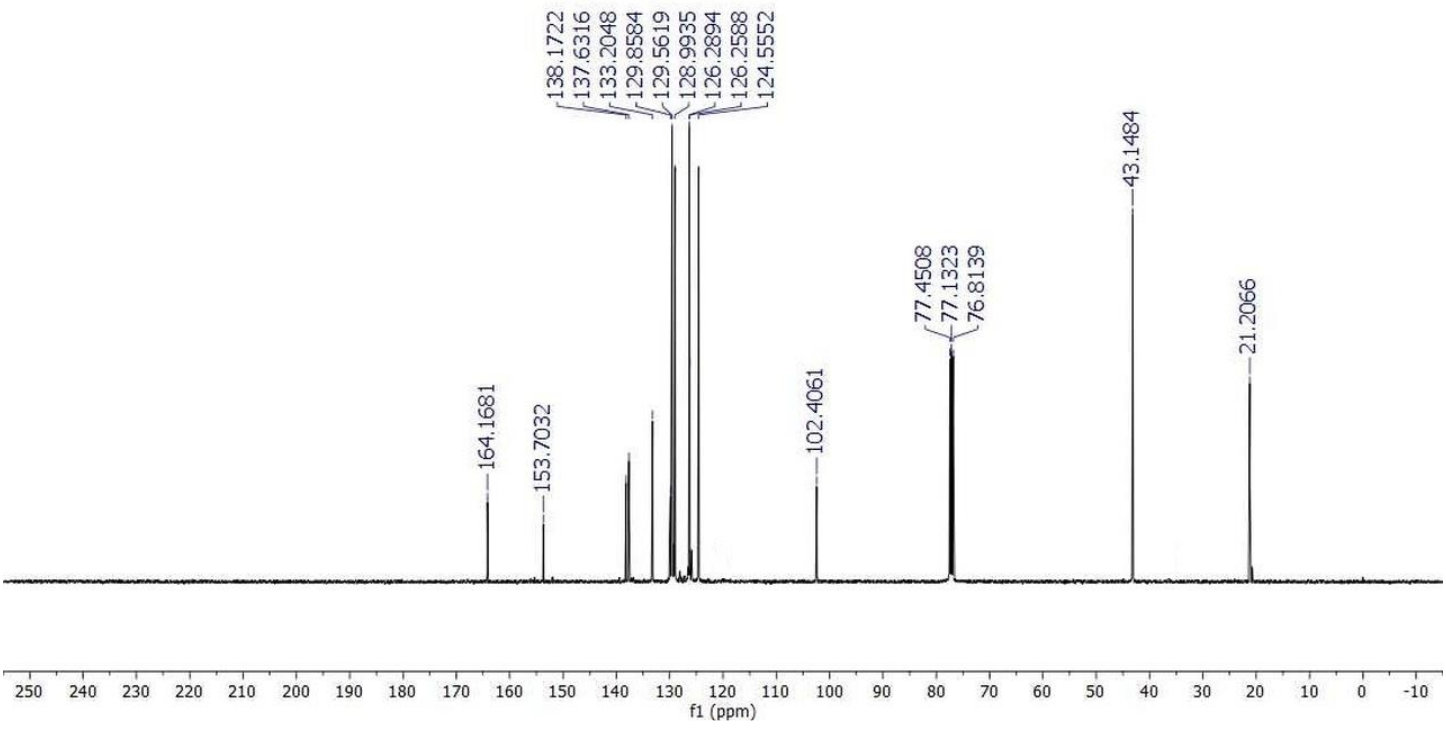



Figure S75. $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **9b**.

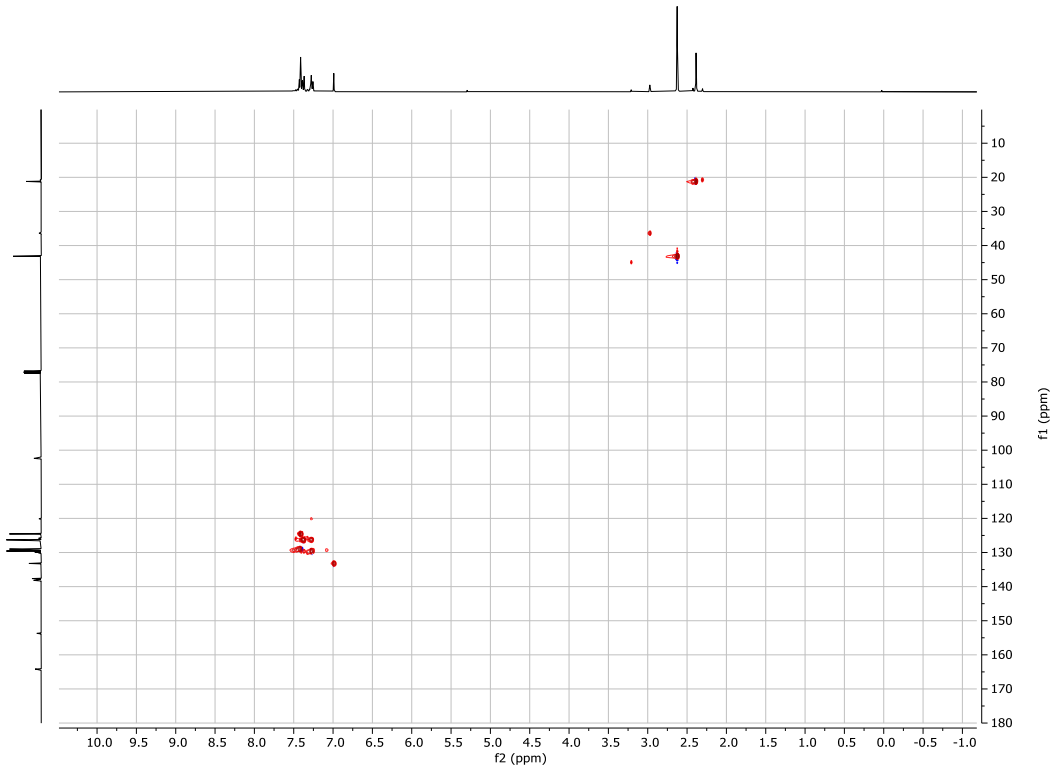



Figure S76. HSQC (400 MHz, $CDCl_3$) spectrum of compound **9b.**

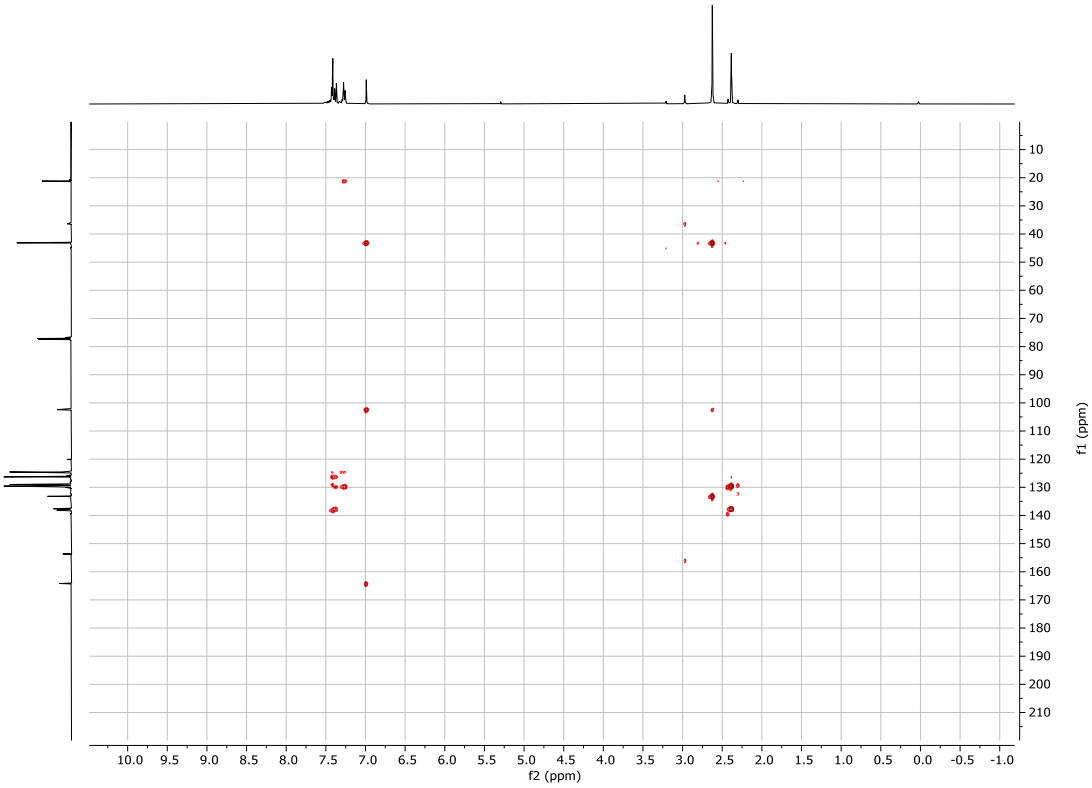
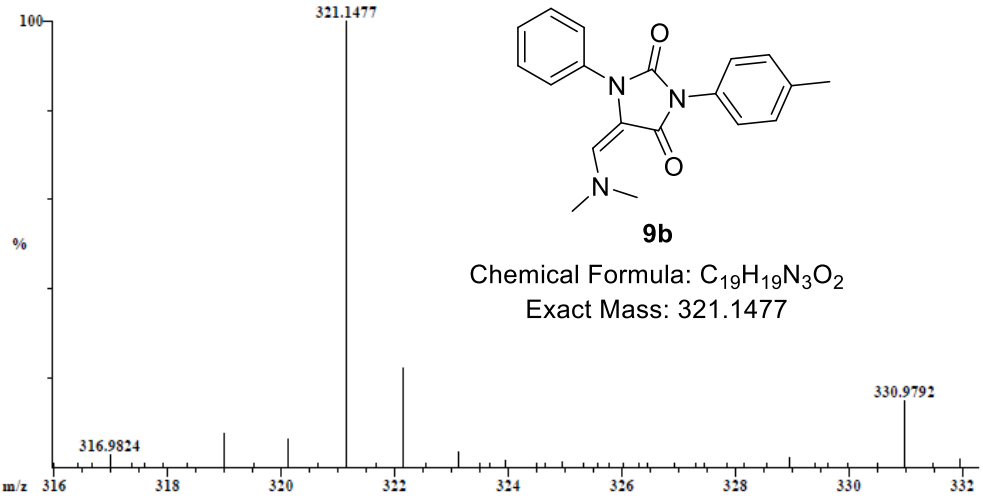



Figure S77. HMBC (400 MHz, $CDCl_3$) spectrum of compound **9b.**

**File: JT-EBC-49** **Date Run: 02-11-2023 (Time Run: 15:17:57)**
**Sample: JT-EBC-49**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 245** **R.T.: 3.28**
**Base: m/z 321; 8.6%FS TIC: 331776** **#Ions: 193**






**9b**

Chemical Formula: $C_{19}H_{19}N_3O_2$
Exact Mass: 321.1477

**Selected Isotopes : $H_{0-19}C_{0-19}N_{0-3}O_{0-2}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 321.1477 | 100.0% | $C_{19}H_{19}N_3O_2$ | 321.1477 | -0.1 | 12.0 |

Figure S78. HRMS of compound **9b.**

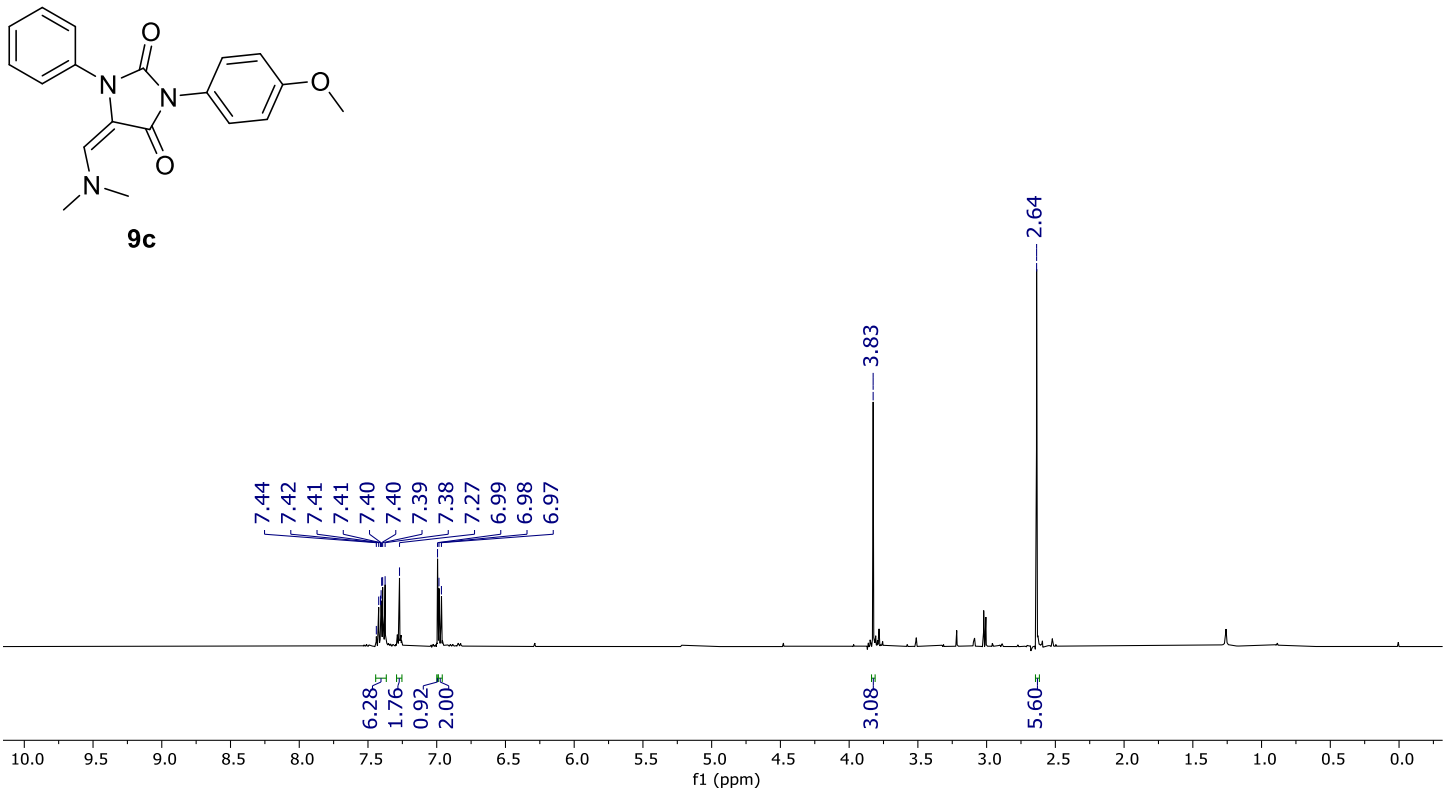



Figure S79. $^{1}H$ NMR (500 MHz, $CDCl_3$) spectrum of compound **9c**.

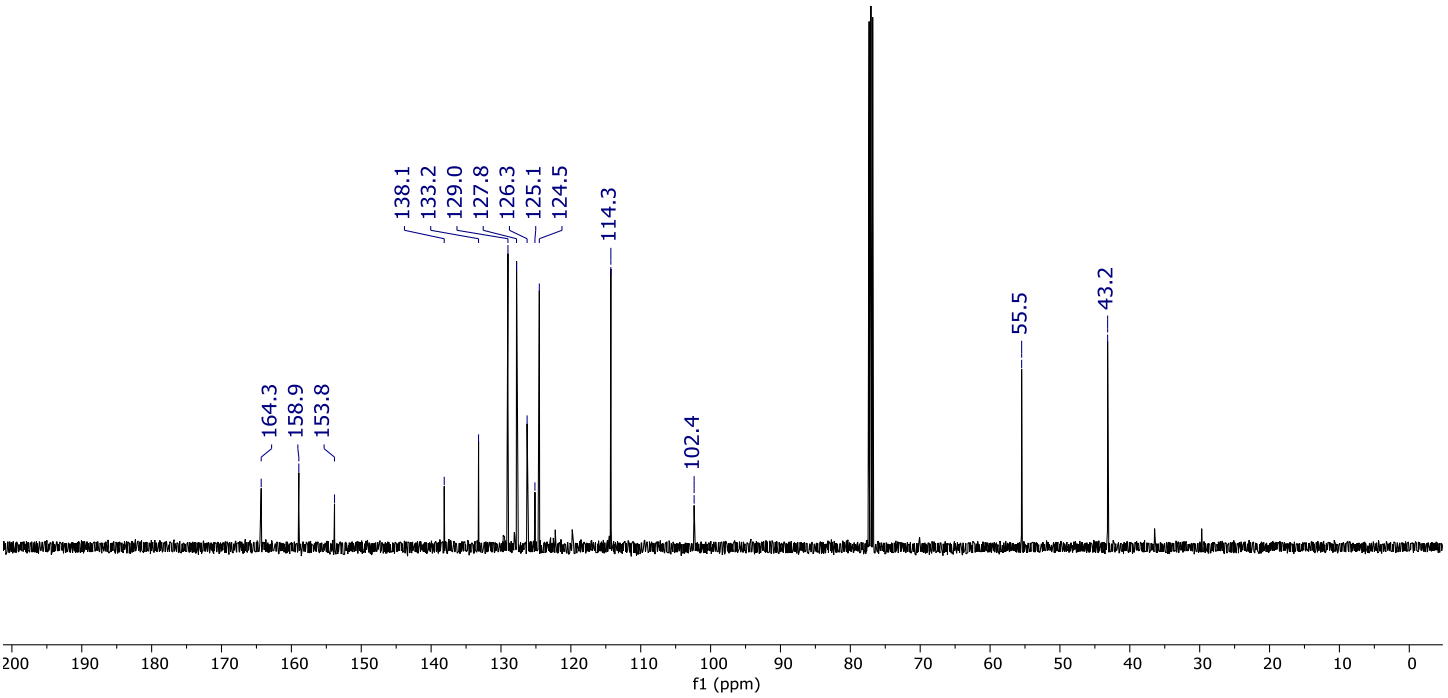



Figure S80. $^{13}C$ NMR (125 MHz, $CDCl_3$) spectrum of compound **9c**.

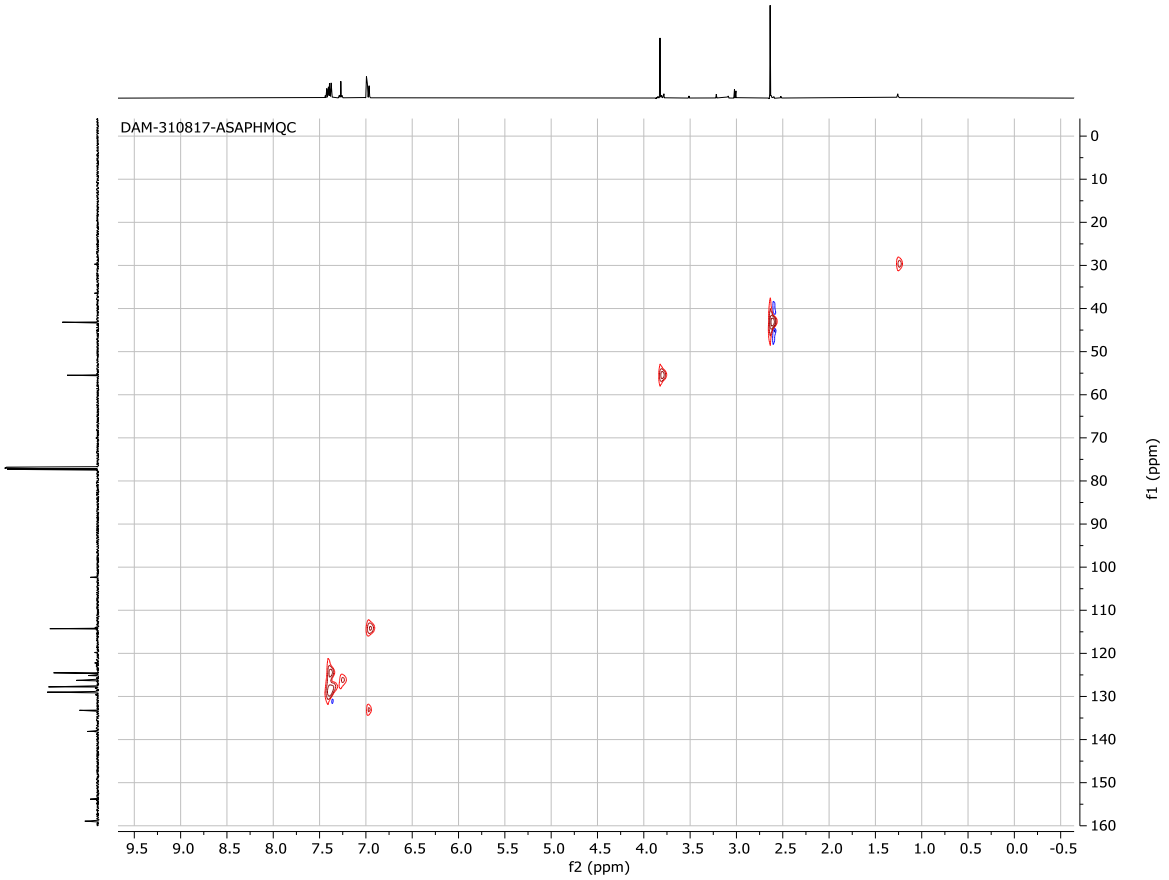



Figure S81. HSQC (500 MHz, $CDCl_3$) spectrum of compound **9c.**

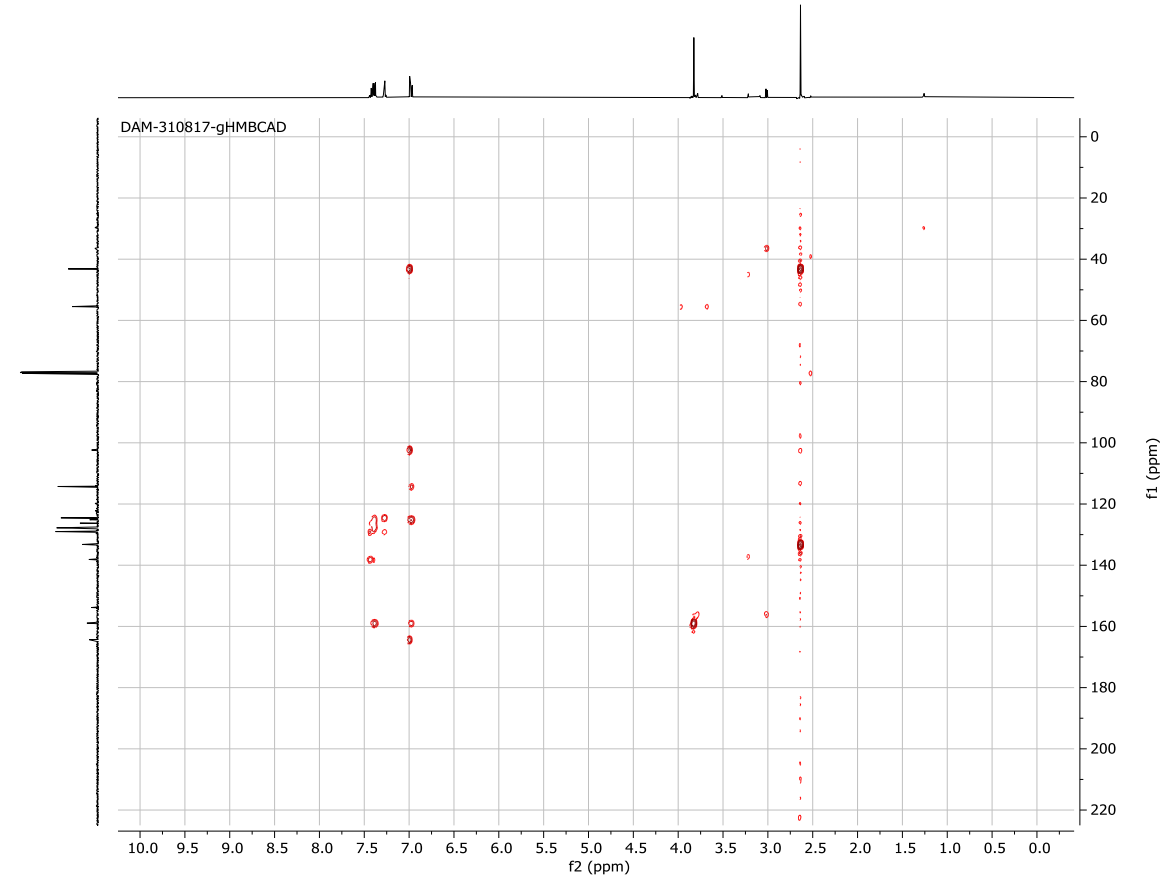



Figure S82. HMBC (500 MHz, $CDCl_3$) spectrum of compound **9c.**

*IPN*
**11/4/2017**



**File: JT-DAM-310817-2**
**Sample: JT-DAM-310817-2**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe**

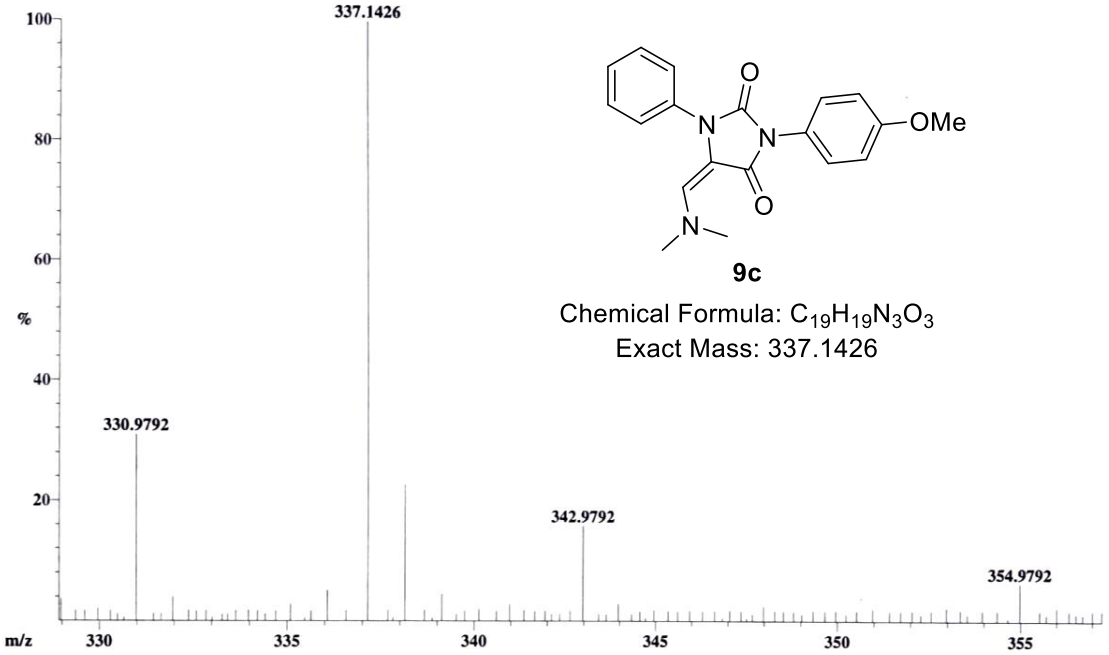
**Date Run: 11-04-2017 (Time Run: 17:19:55)**

**Ionization mode: EI+**

**Scan: 334-336**
**Base: m/z 337; 3%FS TIC: 199052**

**R.T.: 4.47**

**#Ions: 253**







**9c**

Chemical Formula: $C_{19}H_{19}N_3O_3$
Exact Mass: 337.1426

**Selected Isotopes : $H_{0-19}C_{0-19}N_{0-3}O_{0-3}$**

**Error Limit : 5 ppm**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 337.1426 | 100.0% | $C_{19}H_{19}N_3O_3$ | 337.1426 | -0.1 |

Figure S83. HRMS of compound **9c.**

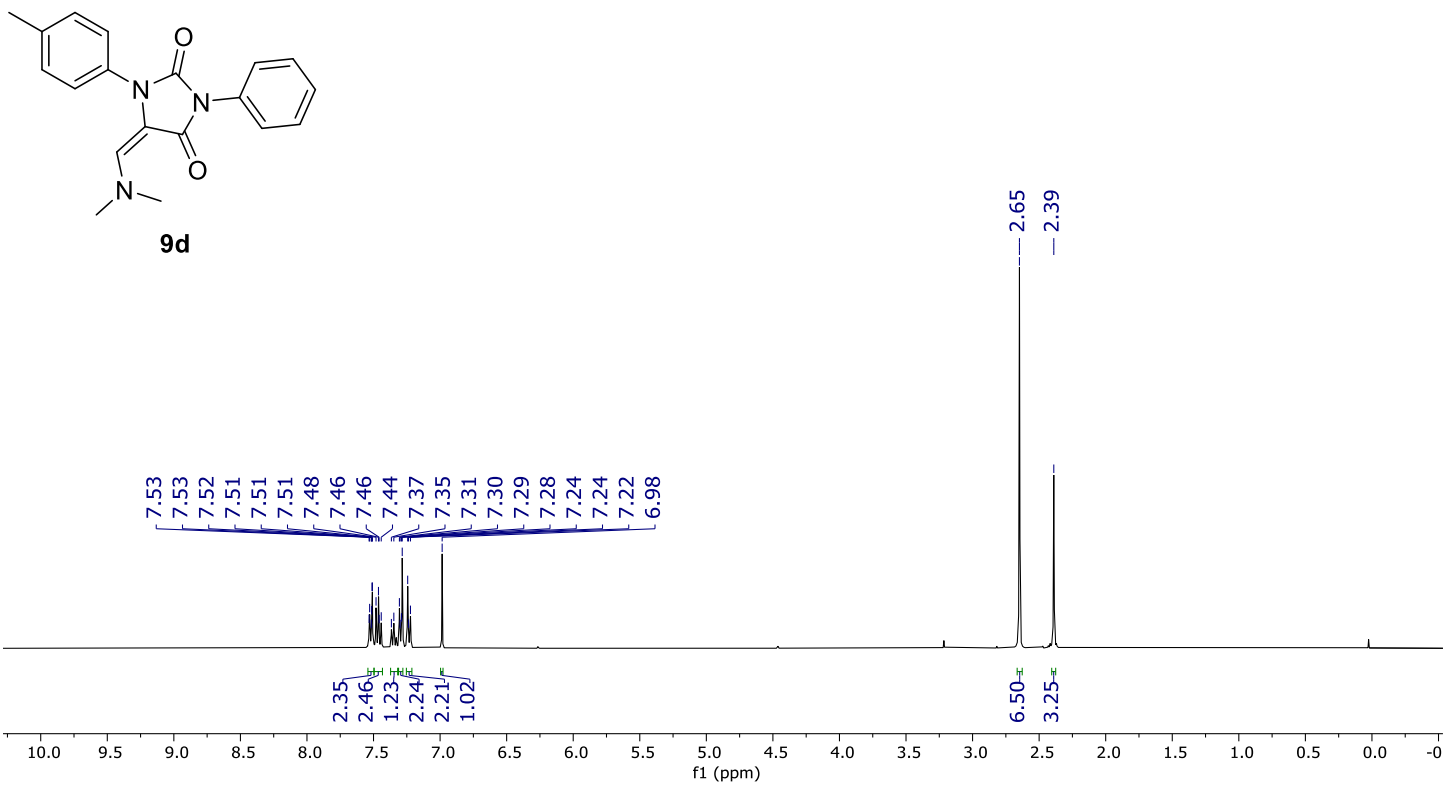



Figure S84. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **9d**.

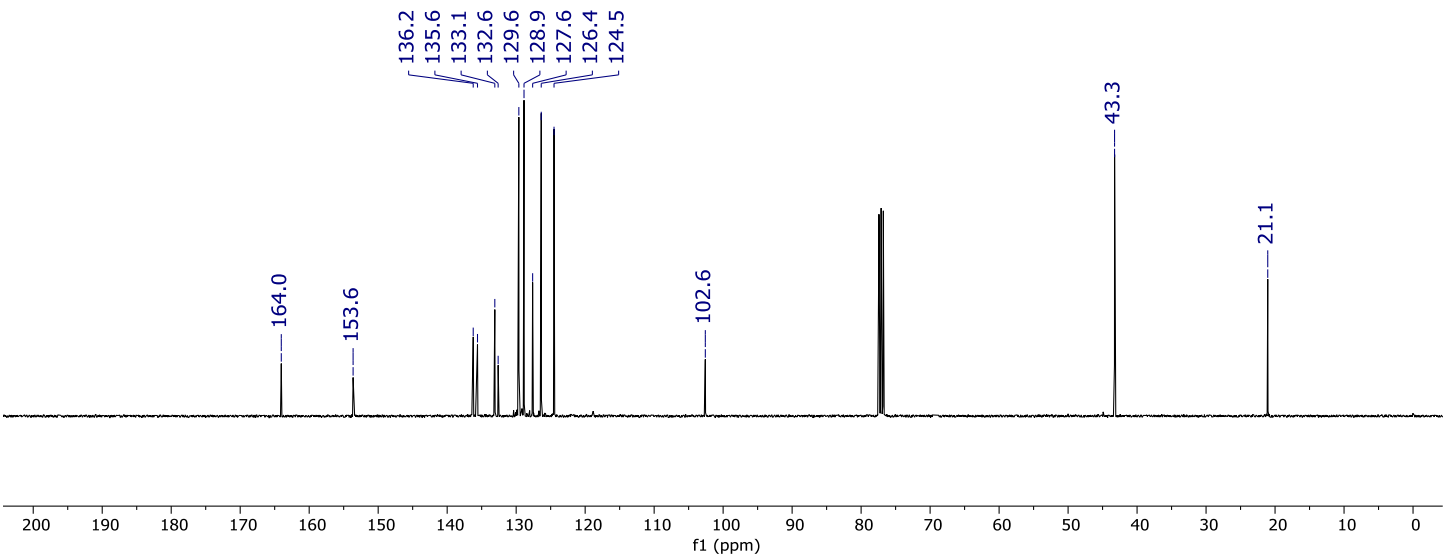



Figure S85. $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **9d**.

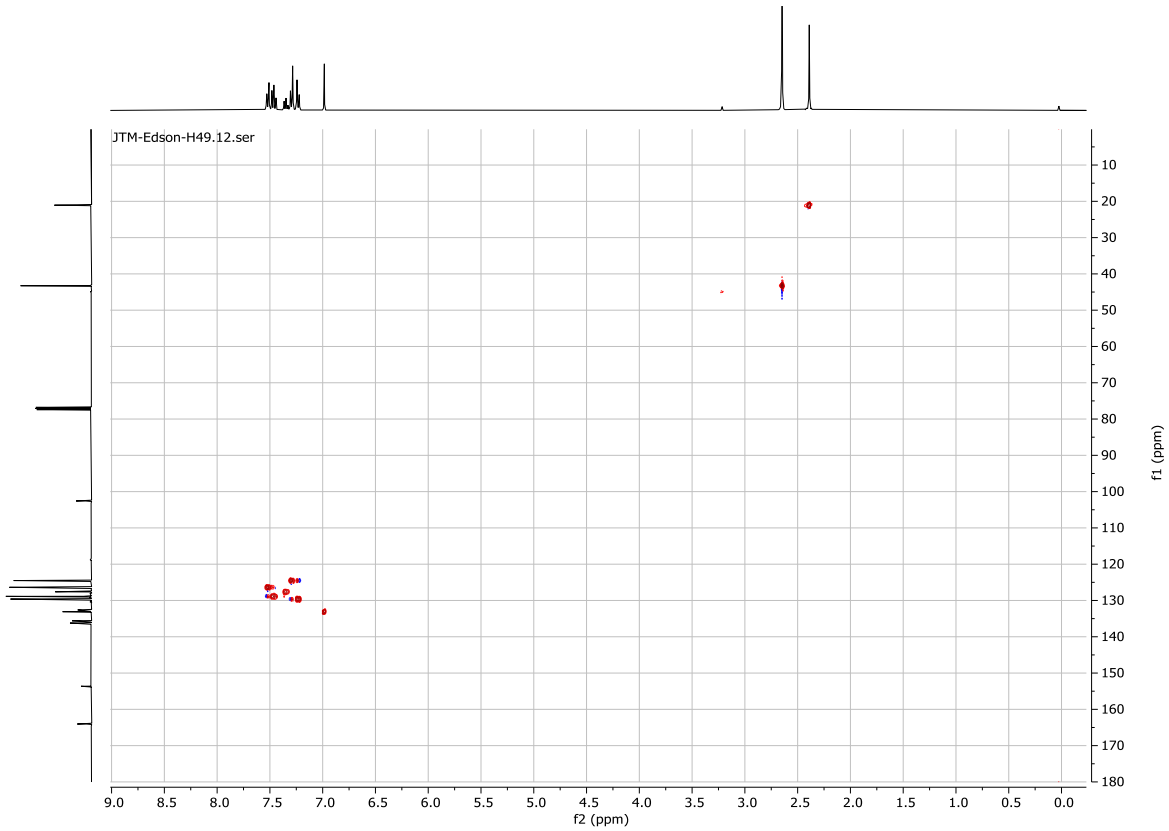



Figure S86. HSQC (400 MHz, $CDCl_3$) spectrum of compound **9d.**

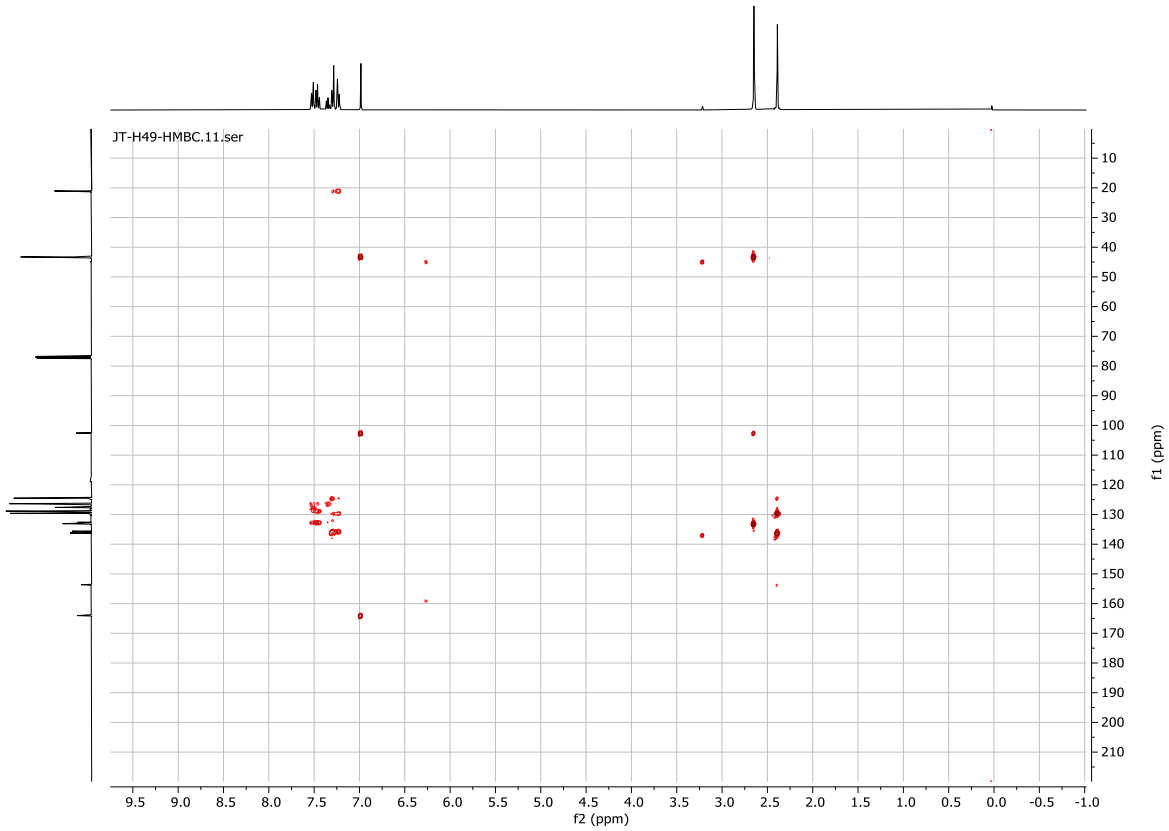



Figure S87. HMBC (400 MHz, $CDCl_3$) spectrum of compound **9d.**

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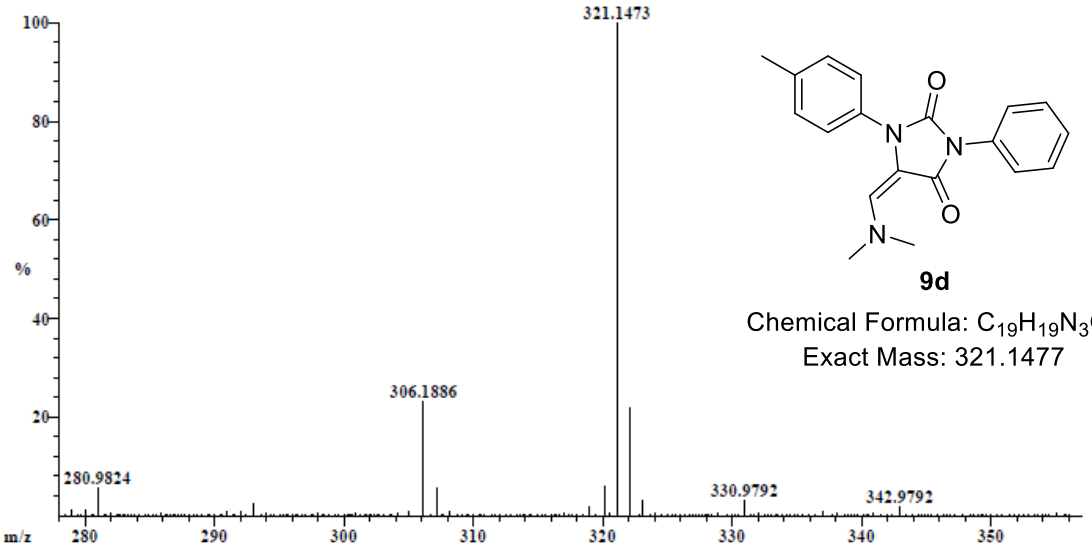
**File: JT-EBC-H165B-120923 Date Run: 09-12-2023 (Time Run: 18:18:41)**
**Sample: JT-EBC-H165b-120923**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe Ionization mode: EI+**

**Scan: 690 R.T.: 9.14**
**Base: m/z 321; 33.8%FS TIC: 820576 #Ions: 225**







**9d**

Chemical Formula: $C_{19}H_{19}N_3O_2$
Exact Mass: 321.1477

**Selected Isotopes : $N_{0-3}O_{0-2}H_{0-19}C_{0-19}$ Error Limit : 500 ppm Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 321.1473 | 100.0% | $C_{19}H_{19}N_3O_2$ | 321.1477 | -1.3 | 12.0 |

Figure S88. HRMS of compound **9d.**

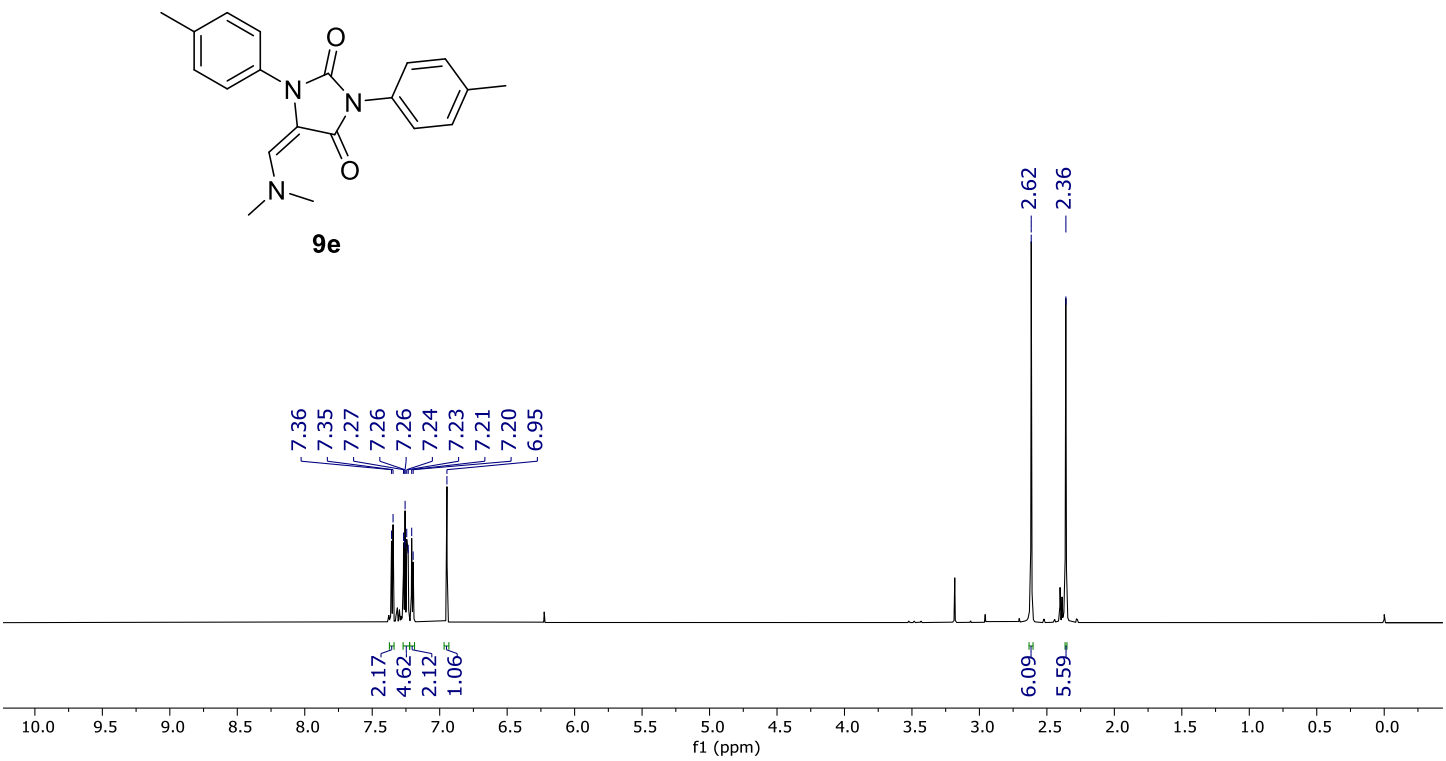



Figure S89. $^{1}$H NMR (750 MHz, $CDCl_3$) spectrum of compound **9e**.

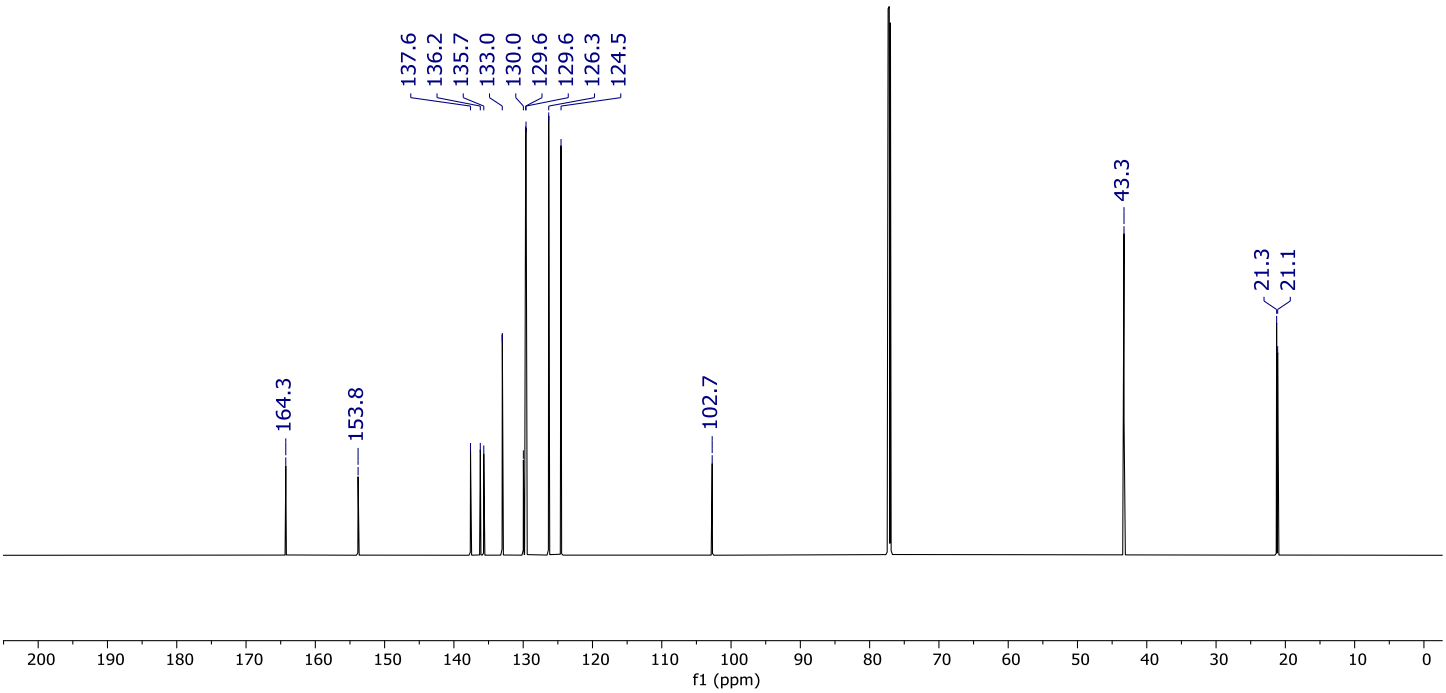



Figure S90. $^{13}$C NMR (187.5 MHz, $CDCl_3$) spectrum of compound **9e**.

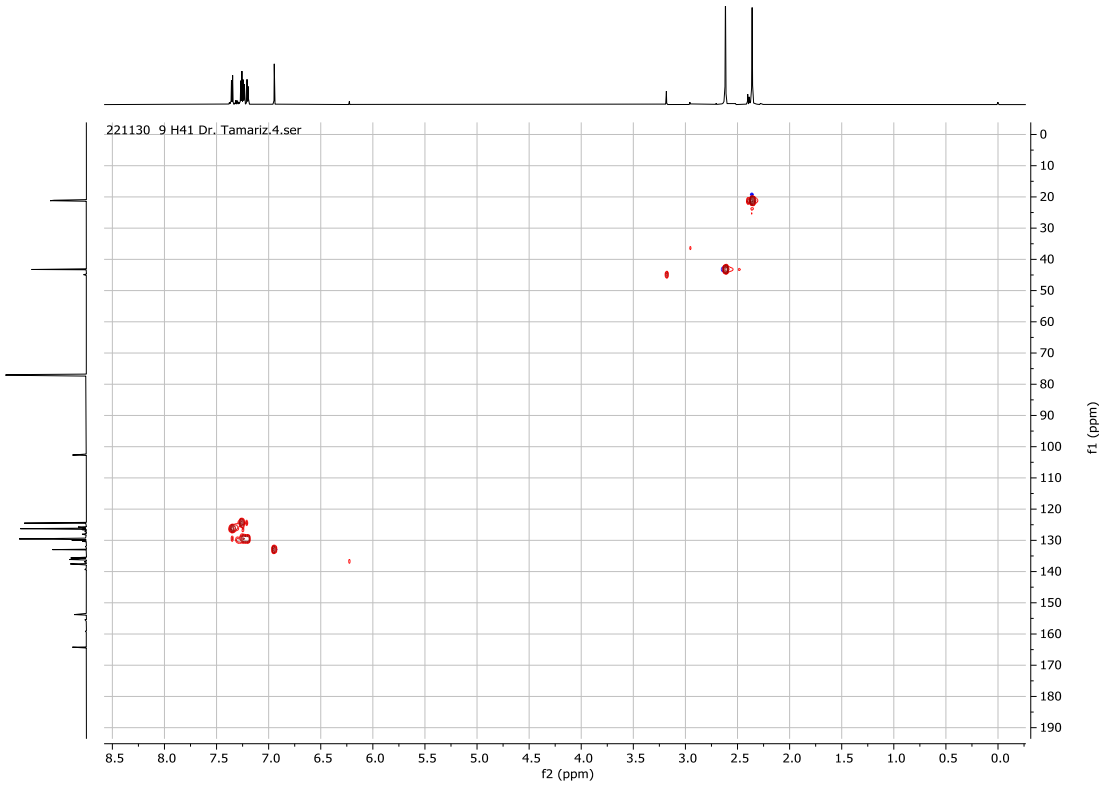



Figure S91. HSQC (750 MHz, $CDCl_3$) spectrum of compound **9e.**

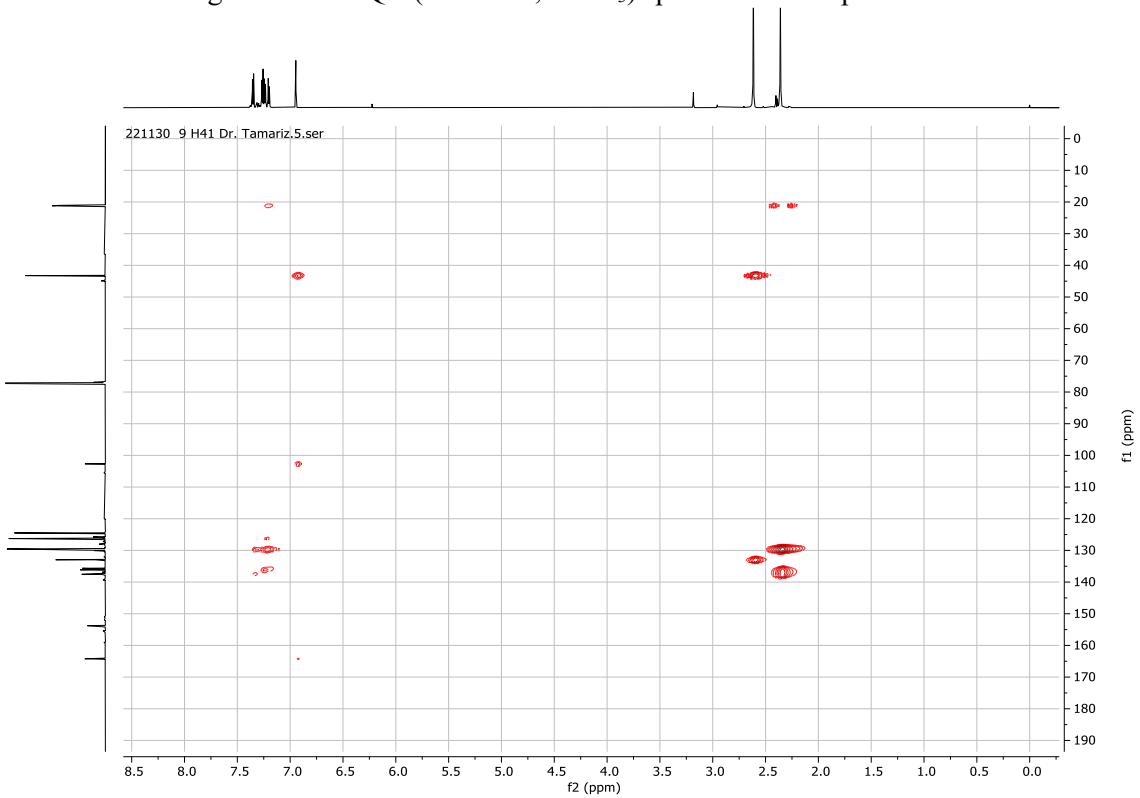



Figure S92. HMBC (750 MHz, $CDCl_3$) spectrum of compound **9e.**

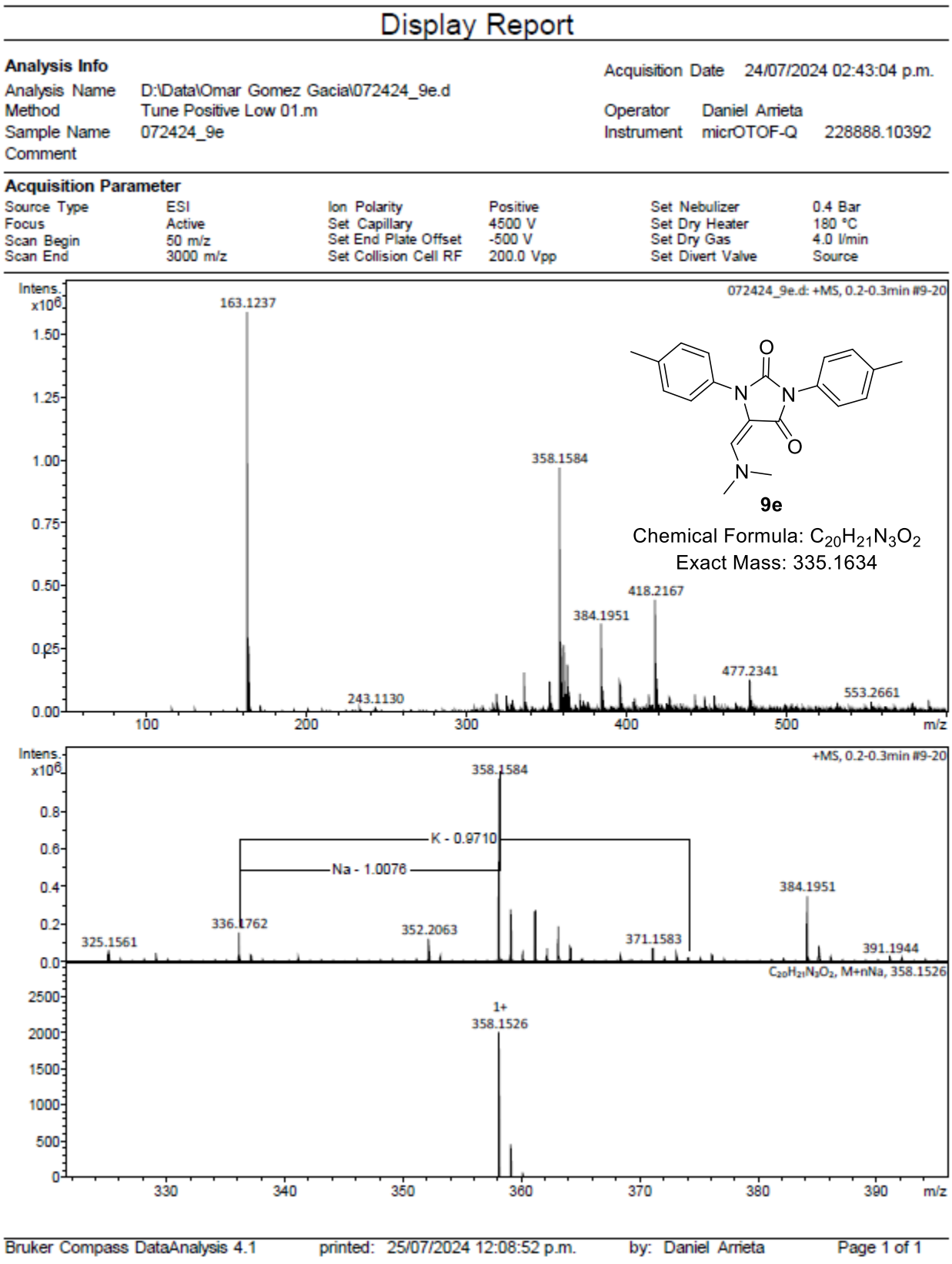



Figure S93. HRMS of compound **9e.**

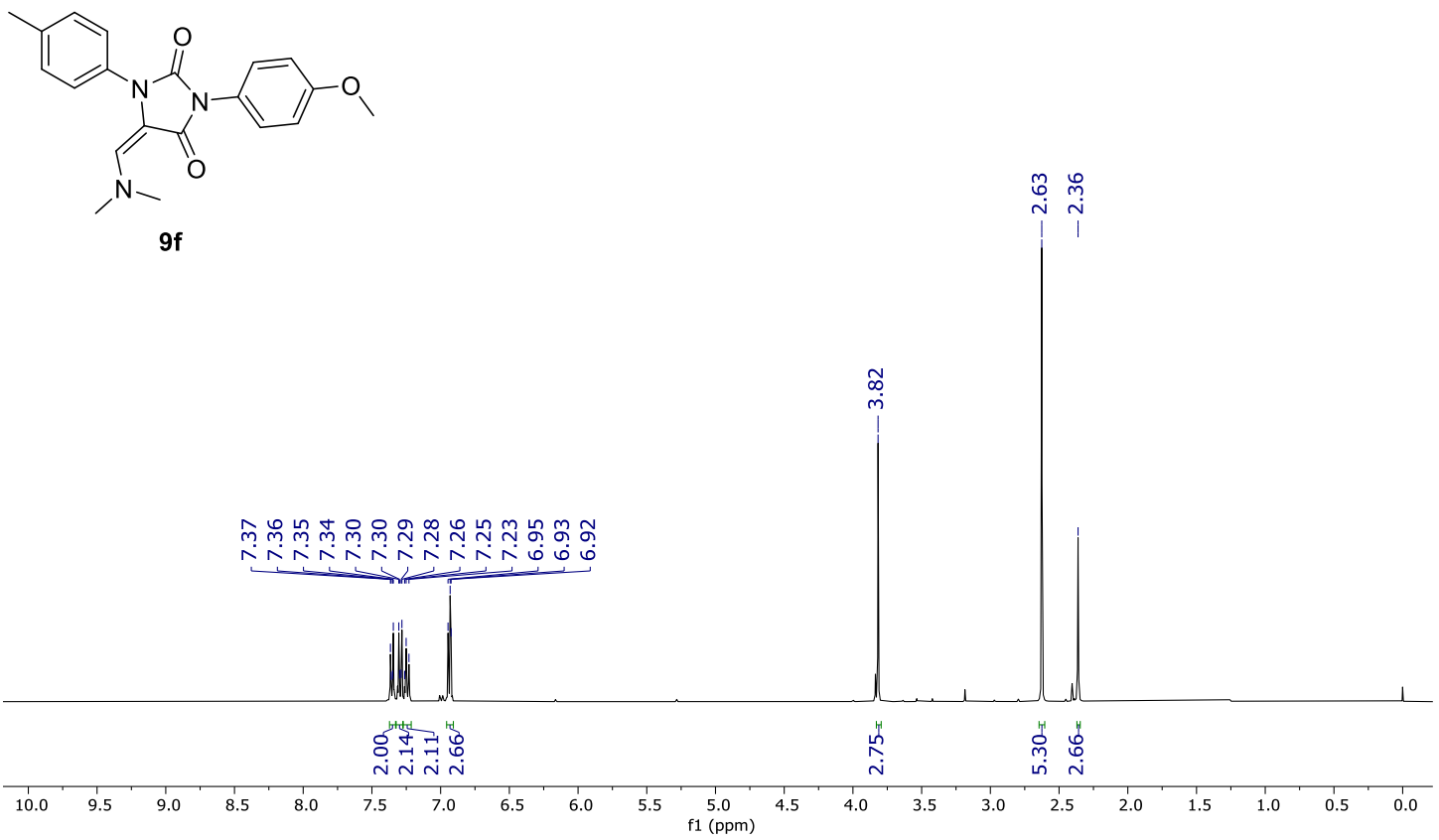



Figure S94. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **9f**.

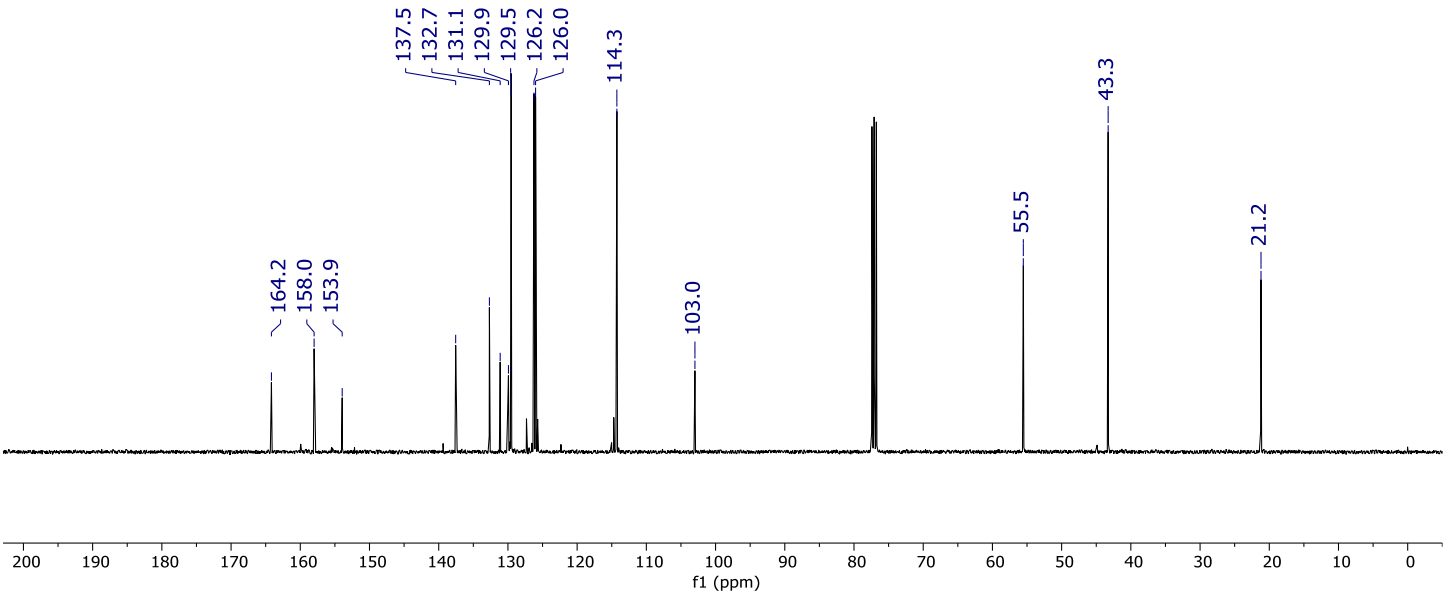



Figure S95. $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **9f**.

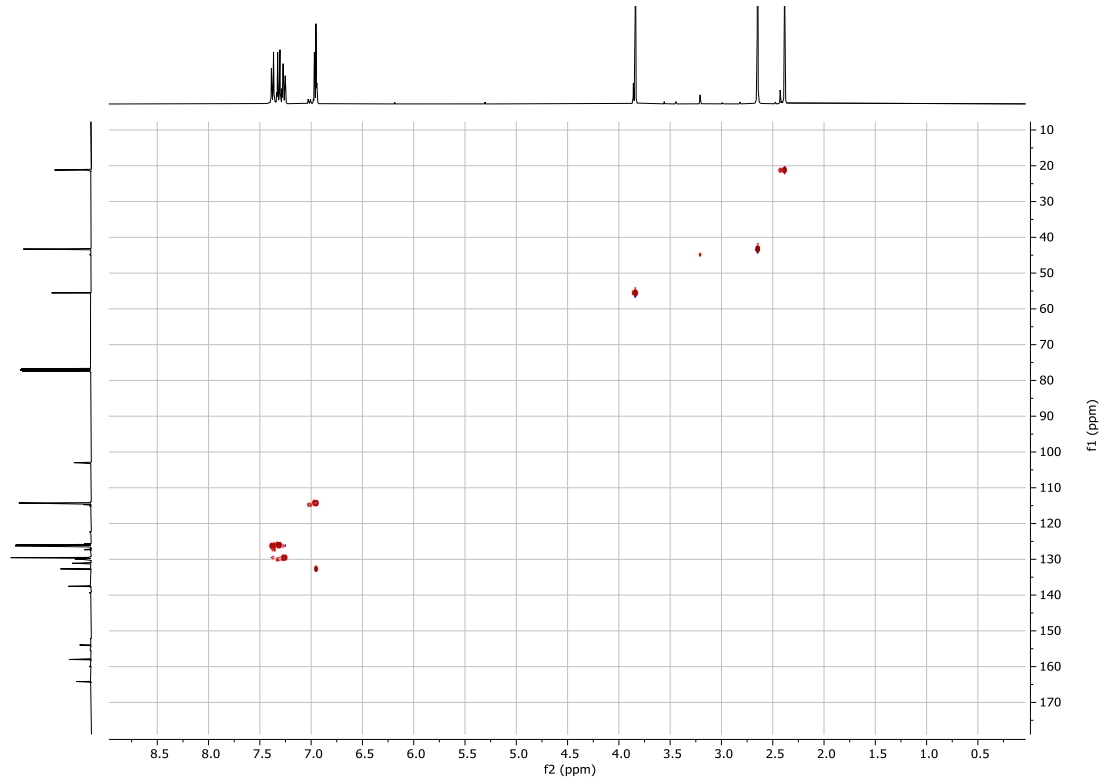



Figure S96. HSQC (400 MHz, $CDCl_3$) spectrum of compound **9f.**

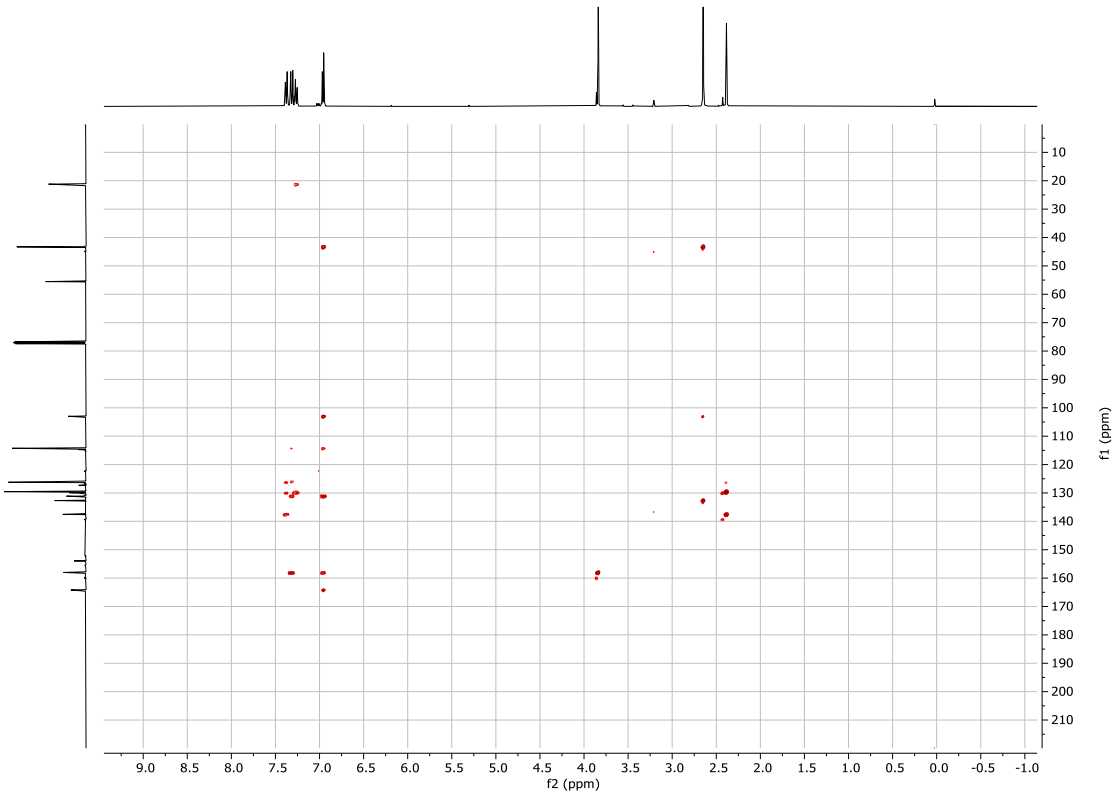
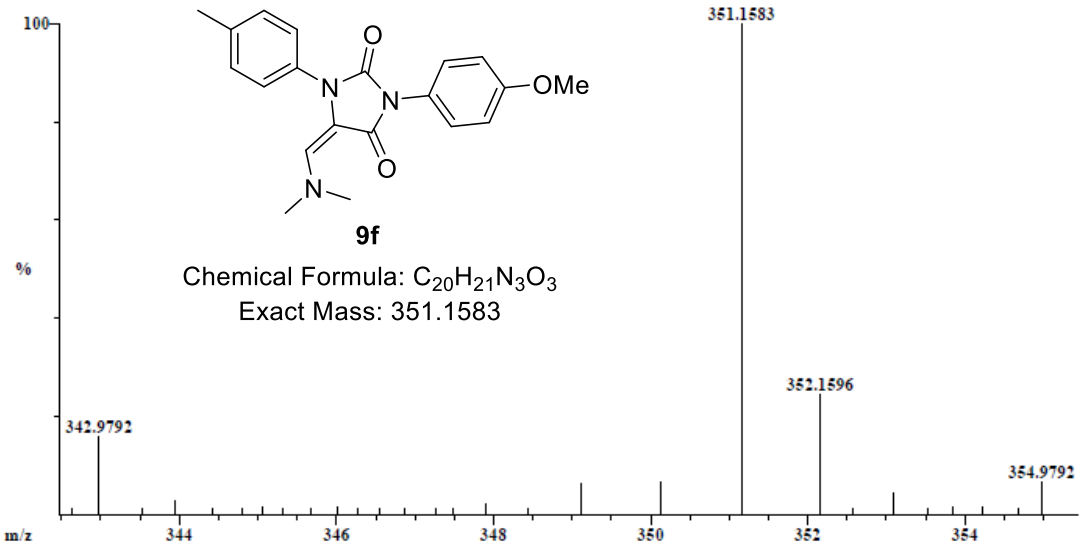



Figure S97. HMBC (400 MHz, $CDCl_3$) spectrum of compound **9f.**

**File: JT-EBC-H43** **Date Run: 03-05-2023 (Time Run: 12:07:30)**
**Sample: JT-EBC-H43**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 418** **R.T.: 5.6**
**Base: m/z 351; 5.7%FS TIC: 250112** **#Ions: 162**




**Selected Isotopes : $H_{0-21}C_{0-20}N_{0-3}O_{0-3}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 351.1583 | 100.0% | $C_{20}H_{21}N_3O_3$ | 351.1583 | 0.0 | 12.0 |

Figure S98. HRMS of compound **9f.**

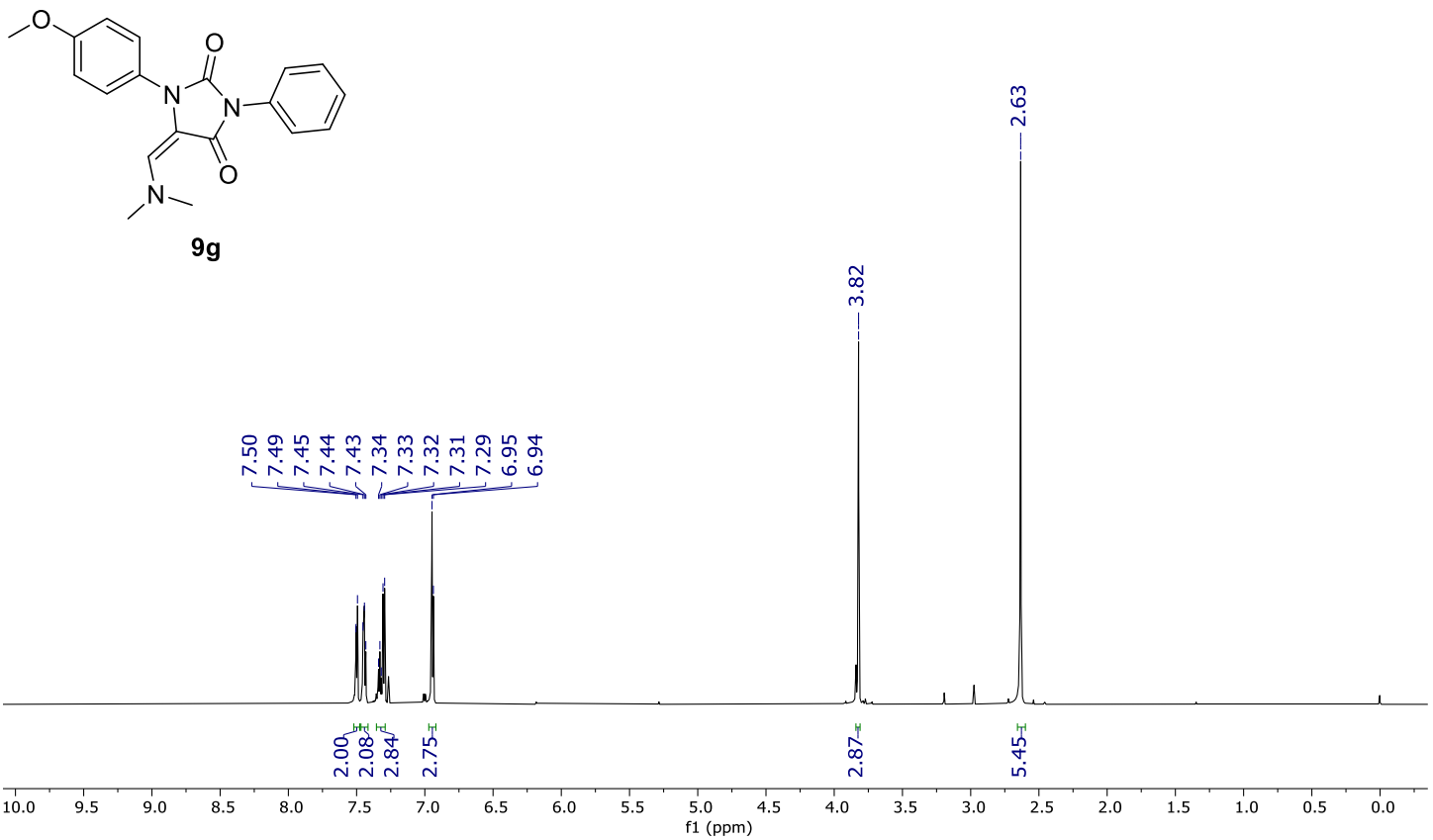



Figure S99. $^{1}$H NMR (750 MHz, $CDCl_3$) spectrum of compound **9g**.

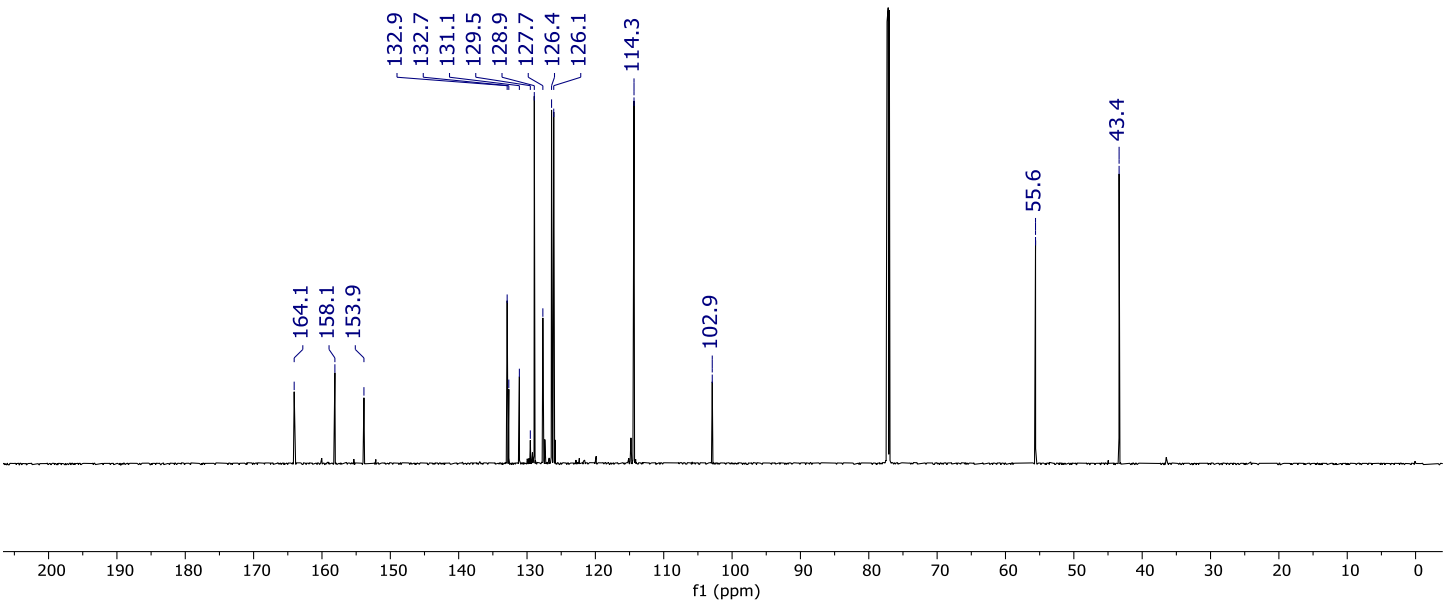



Figure S100. $^{13}$C NMR (187.5 MHz, $CDCl_3$) spectrum of compound **9g**.

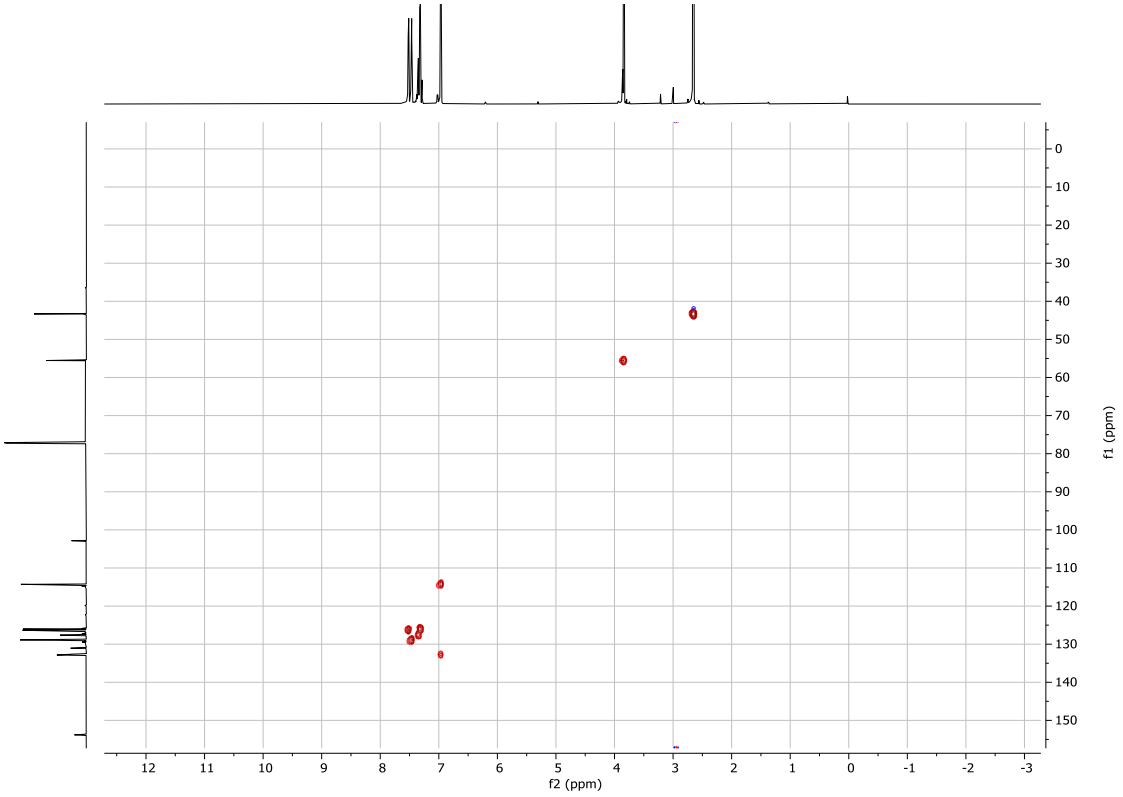



Figure S101. HSQC (750 MHz, $CDCl_3$) spectrum of compound **9g.**

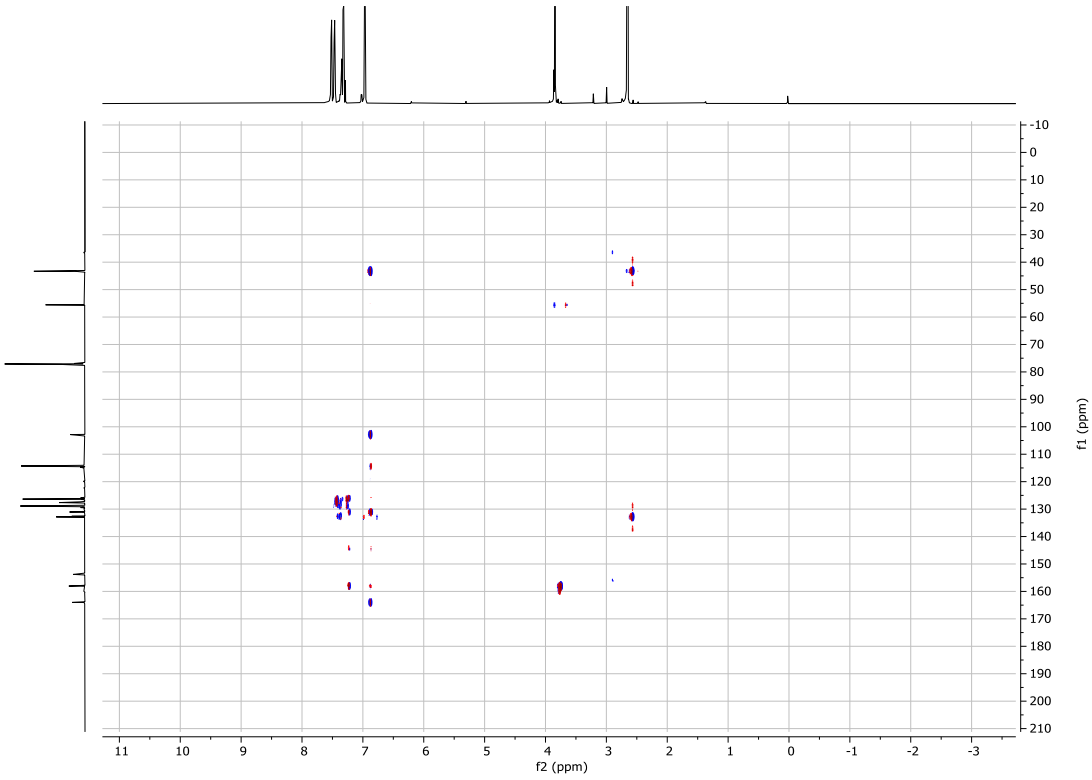



Figure S102. HMBC (750 MHz, $CDCl_3$) spectrum of compound **9g.**

***IPN***

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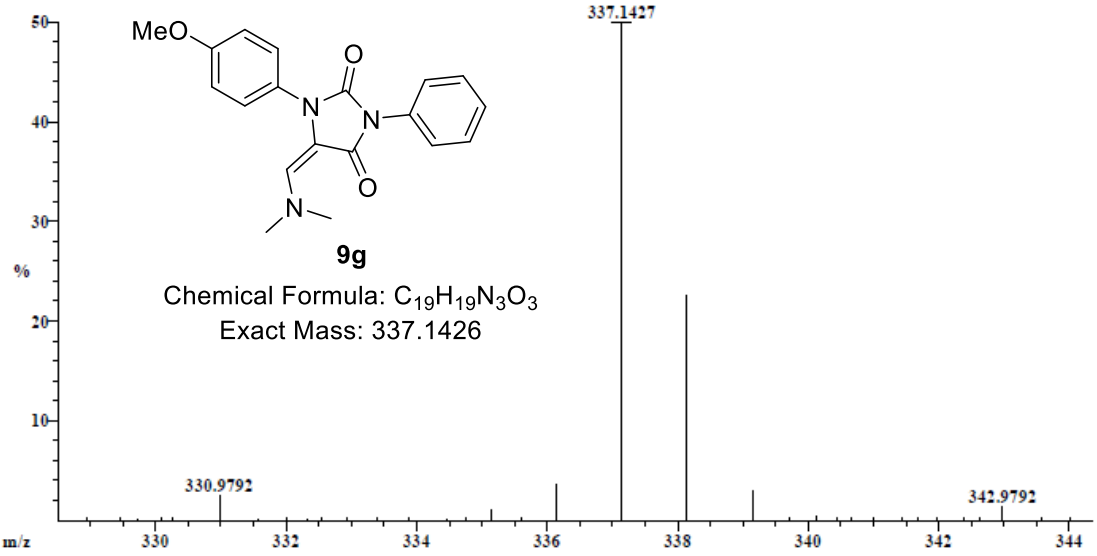
**File: JT-EBC-H165G-120923 Date Run: 09-12-2023 (Time Run: 15:32:08)**
**Sample: JT-EBC-H165g-120923**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe Ionization mode: EI+**

**Scan: 902 R.T.: 11.95**
**Base: m/z 337; 45.2%FS TIC: 1029200 #Ions: 230**




**Selected Isotopes : $N_{0-3}O_{0-3}C_{0-19}H_{0-19}$ Error Limit : 500 ppm Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 337.1427 | 100.0% | $C_{19}H_{19}N_3O_3$ | 337.1426 | 0.2 | 12.0 |

Figure S103. HRMS of compound **9g.**

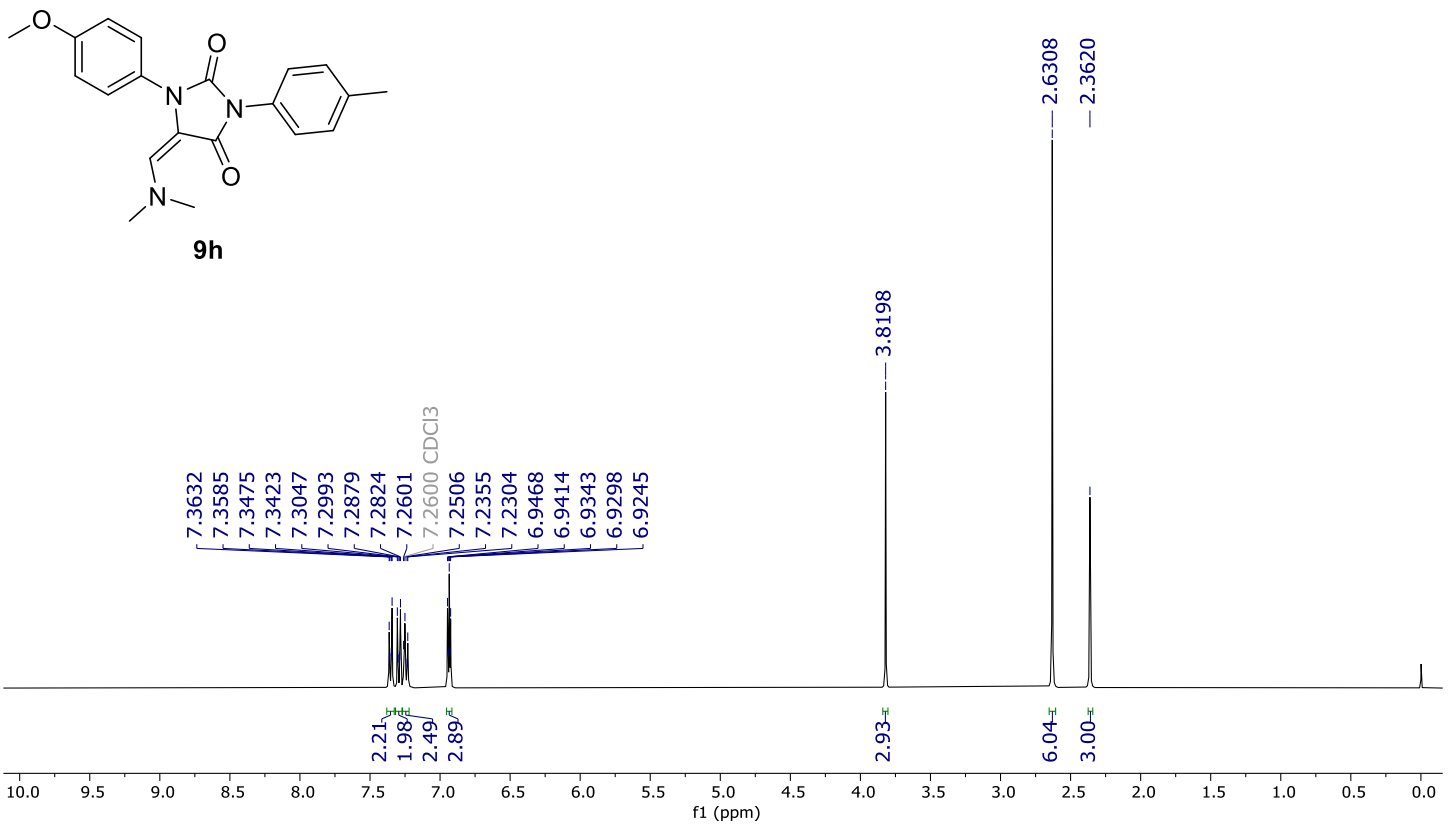



Figure S104. $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **9h**.

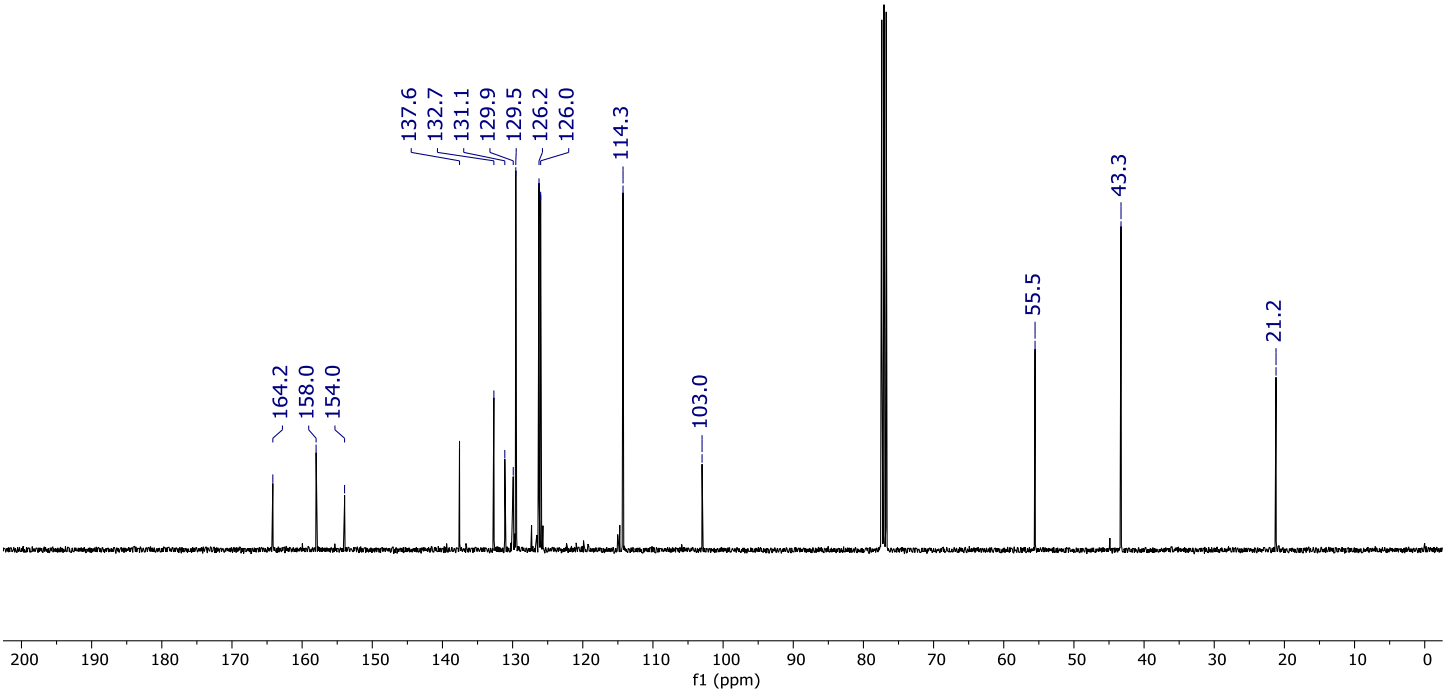



Figure S105. $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **9h**.

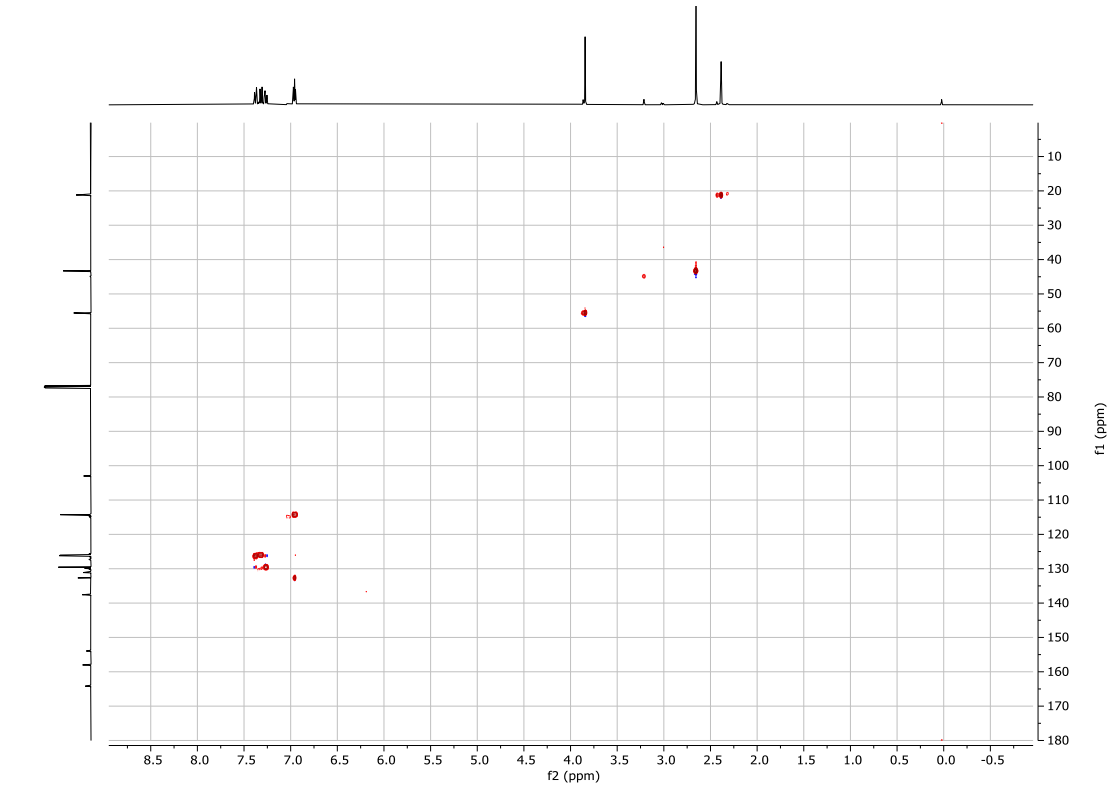



Figure S106. HSQC (400 MHz, $CDCl_3$) spectrum of compound **9h.**

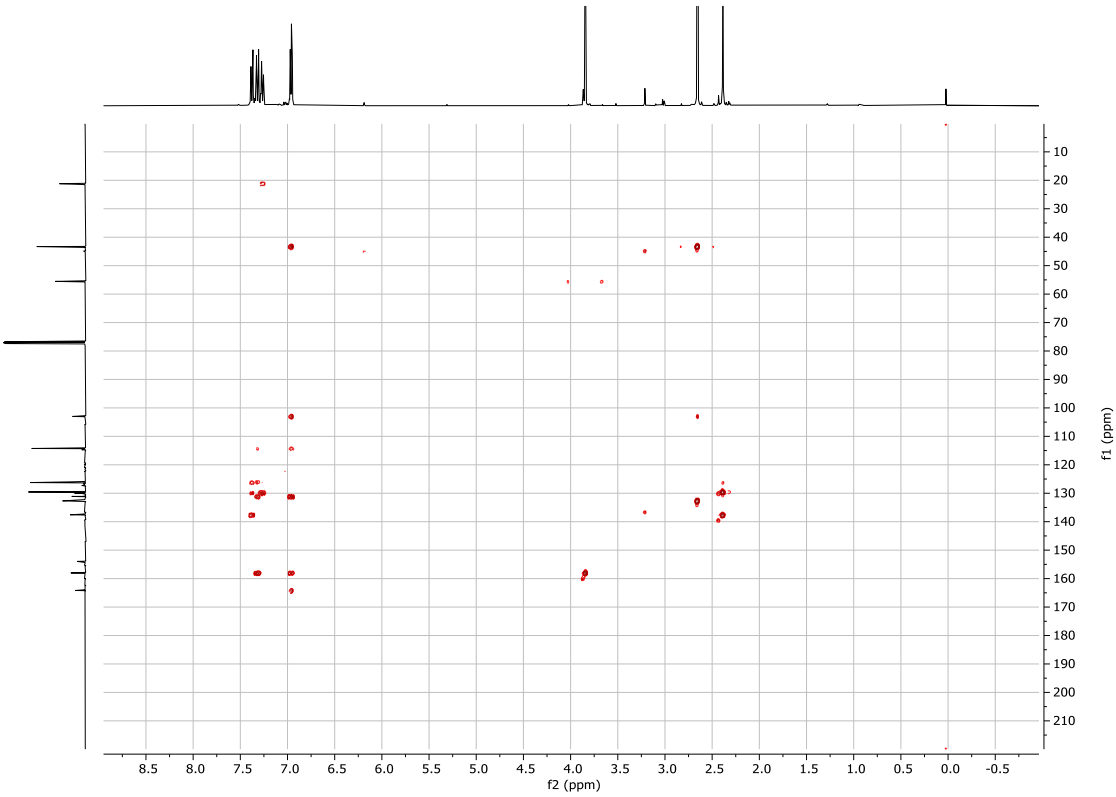
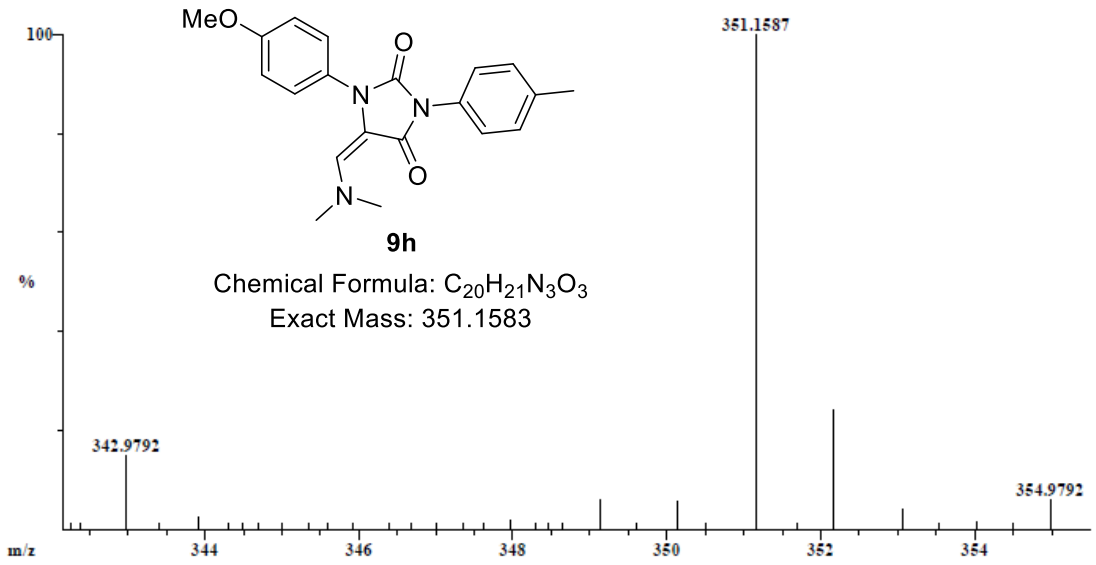



Figure S107. HMBC (400 MHz, $CDCl_3$) spectrum of compound **9h.**

**File: JT-EBC-H50-250323** **Date Run: 03-25-2023 (Time Run: 12:44:52)**
**Sample: JT-EBC-H50-250323**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 270** **R.T.: 9.05**
**Base: m/z 351; 6.4%FS TIC: 235104** **#Ions: 144**




**Selected Isotopes : $H_{0-21}C_{0-20}N_{0-3}O_{0-3}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 351.1587 | 100.0% | $C_{20}H_{21}N_3O_3$ | 351.1583 | 1.2 | 12.0 |

Figure S108. HRMS of compound **9h.**

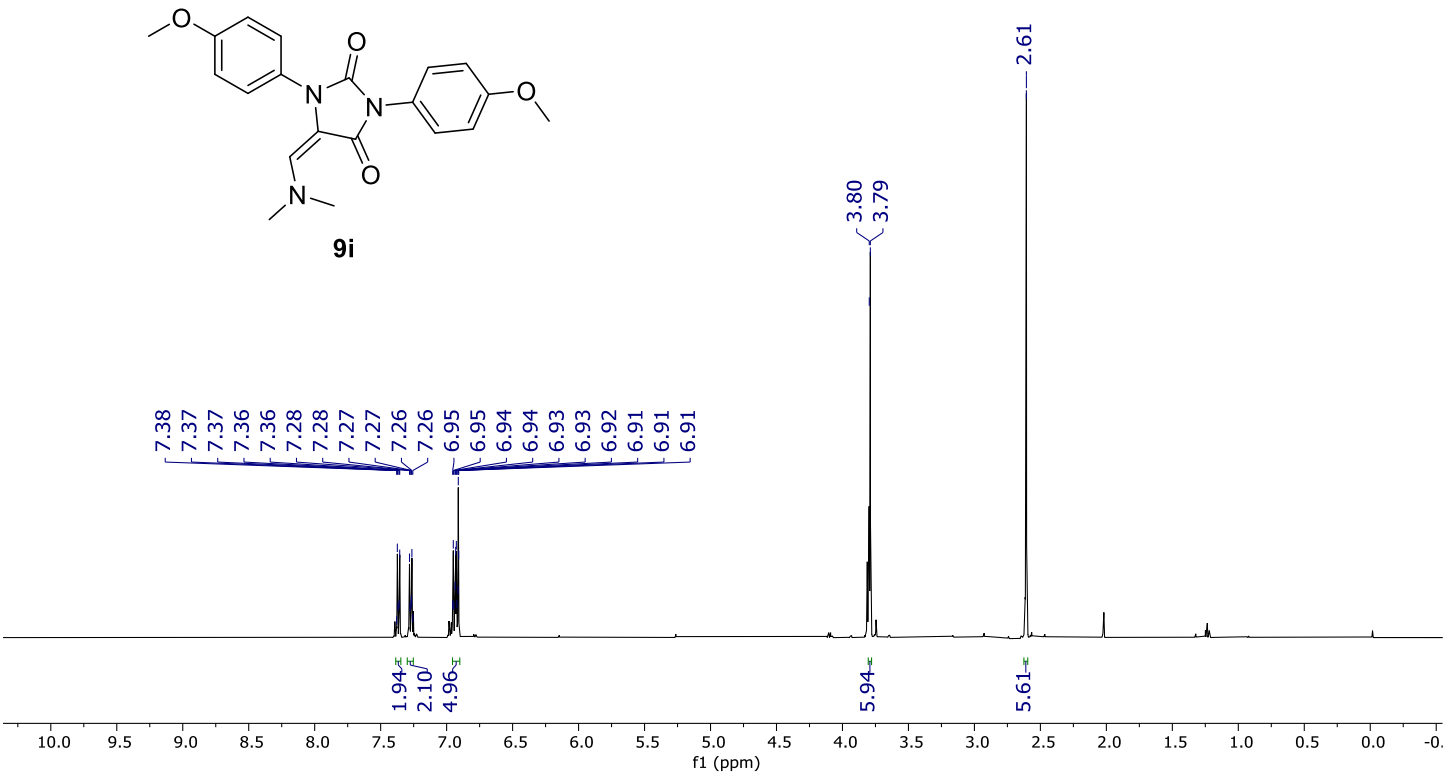



Figure S109. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound 9**i**.

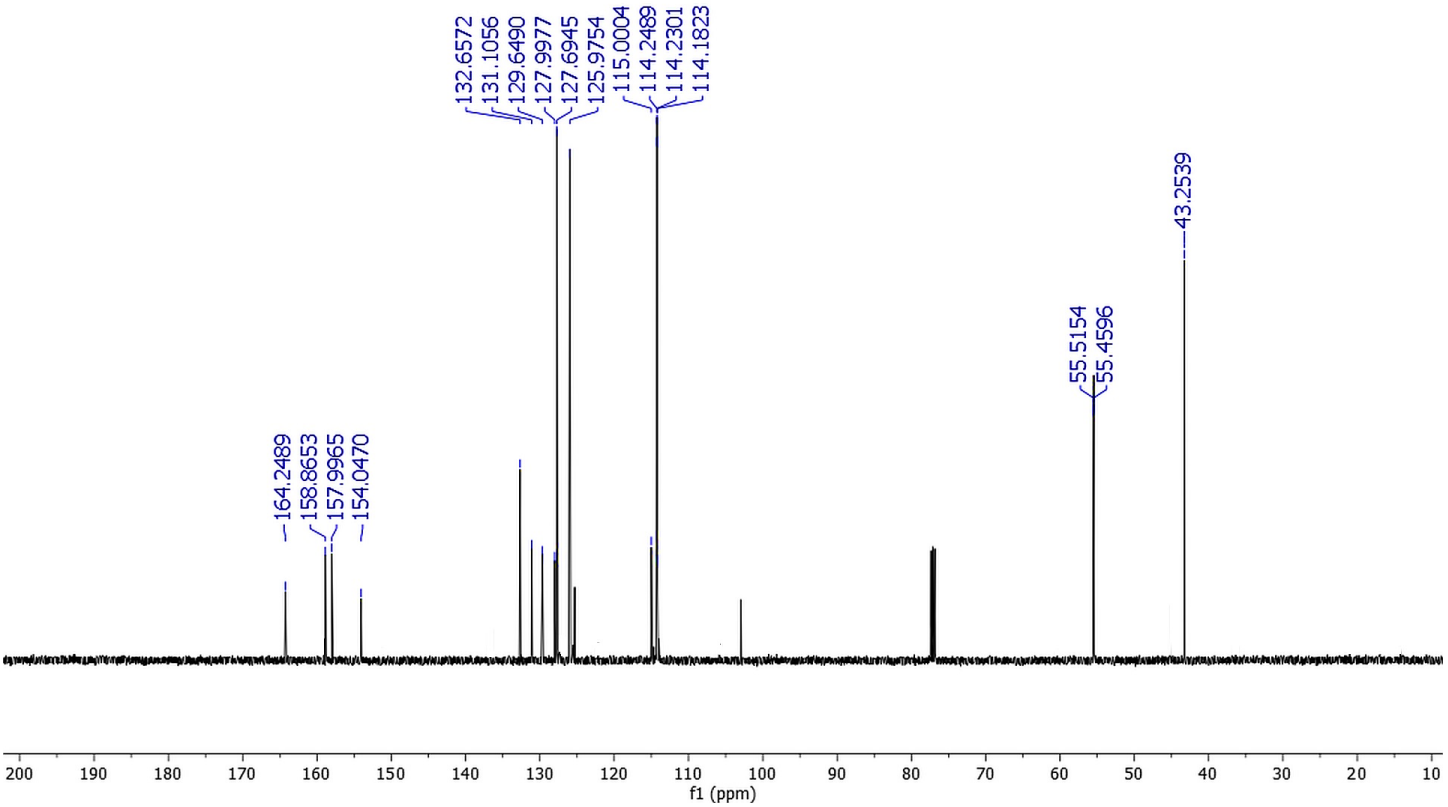



Figure S110. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **9i**.

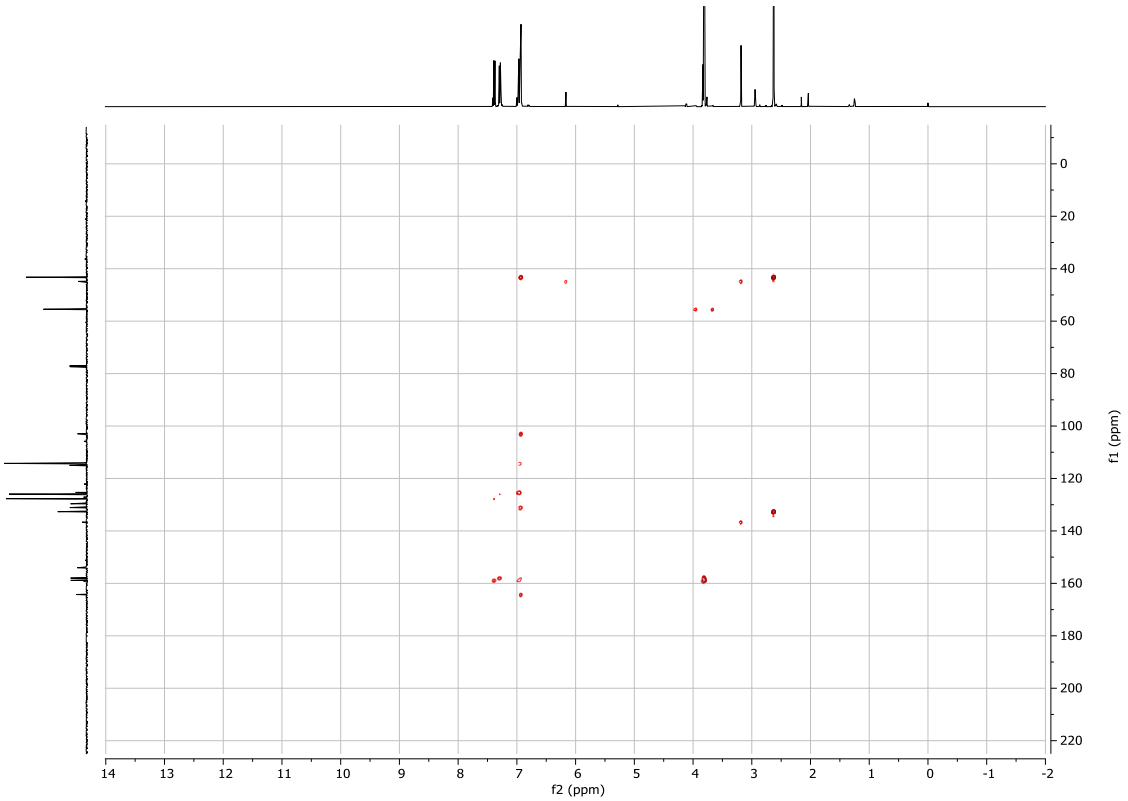



Figure S111. HMBC (500 MHz, $CDCl_3$) spectrum of compound **9i.**

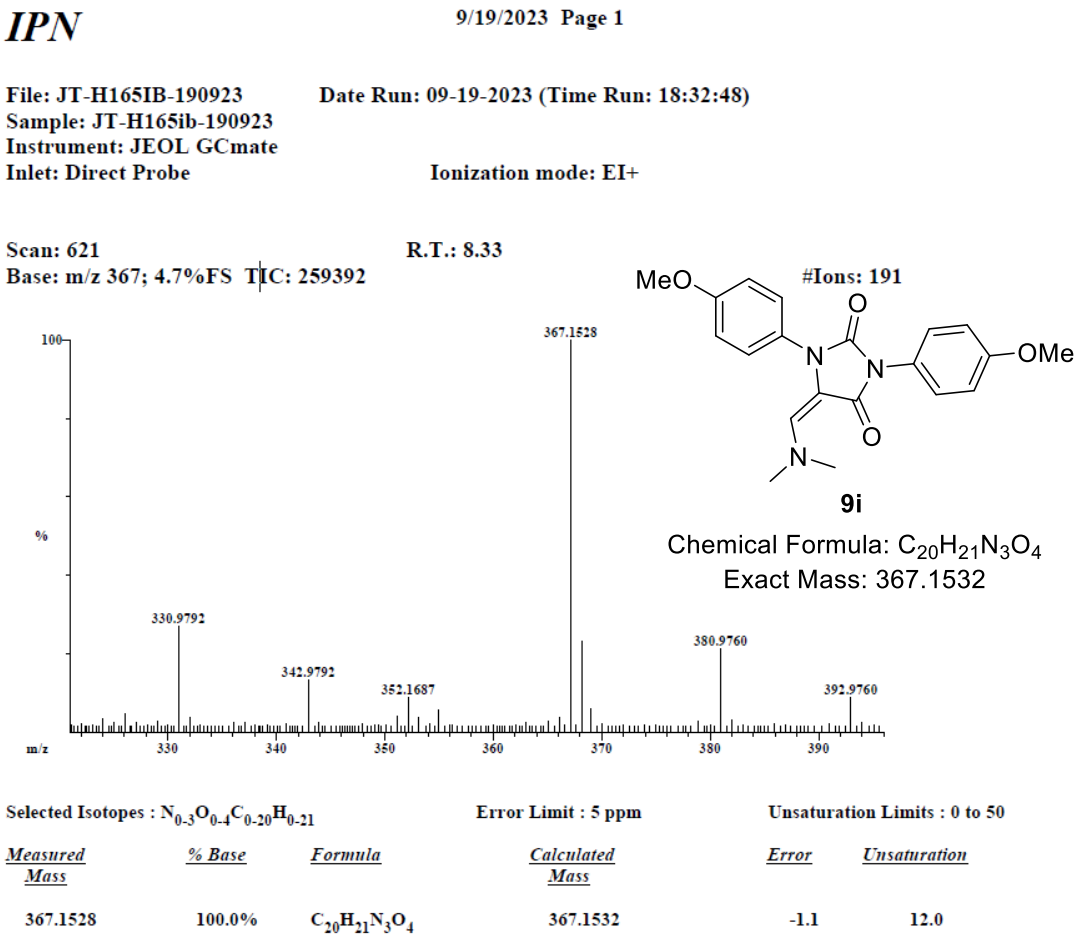



Figure S112. HRMS of compound **9i.**

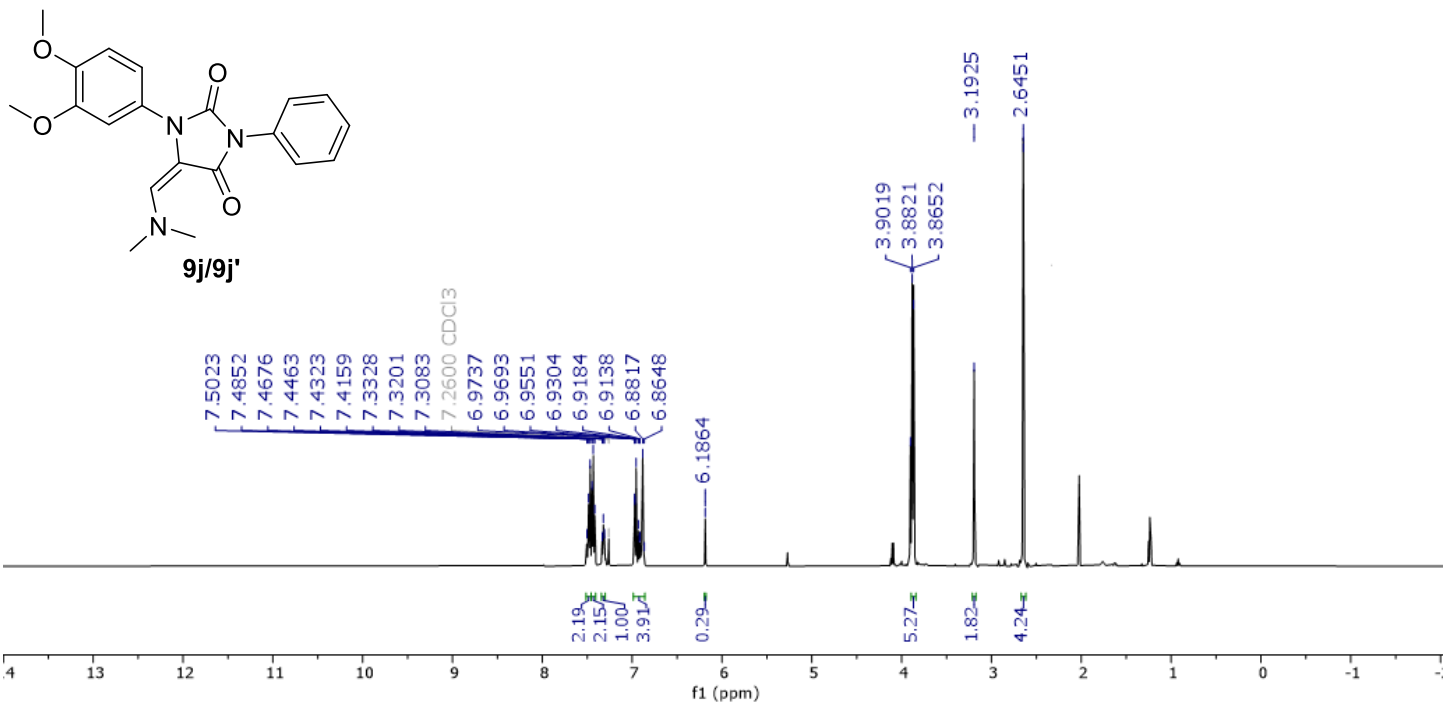



Figure S113. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **9j/9j'**.

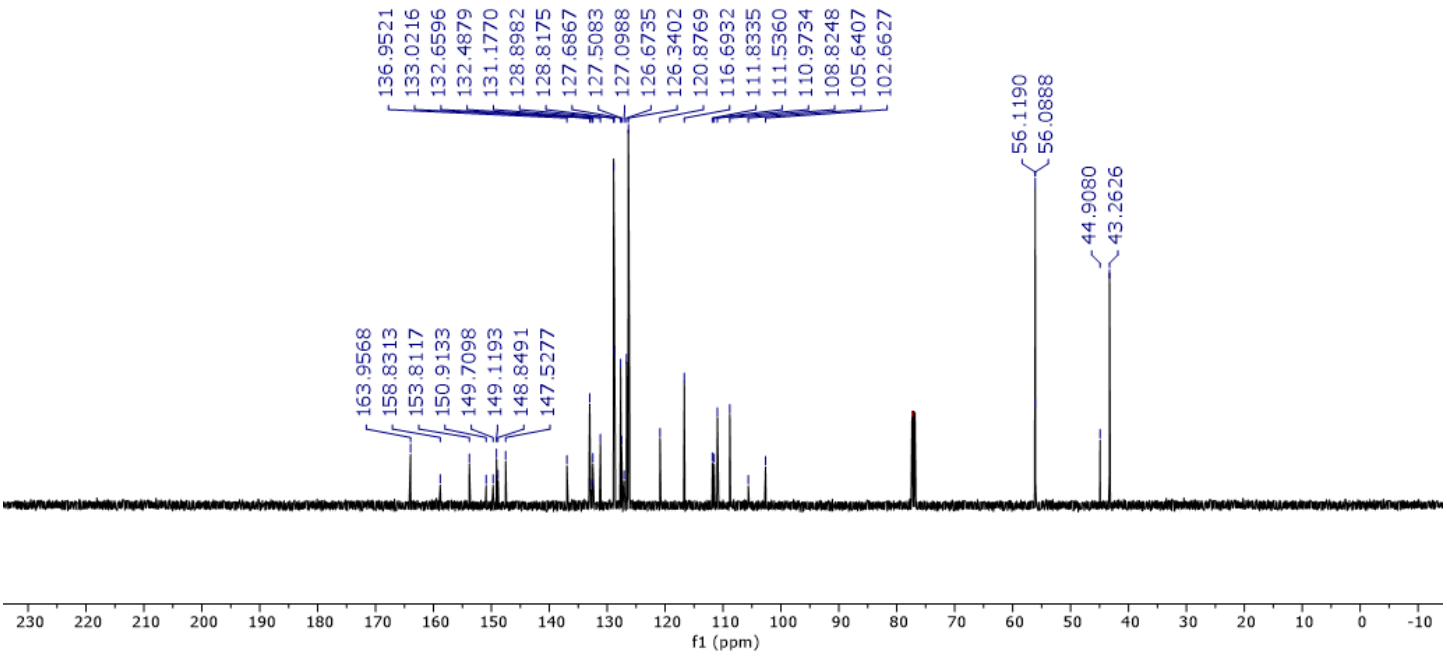



Figure S114. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **9j/9j'**.

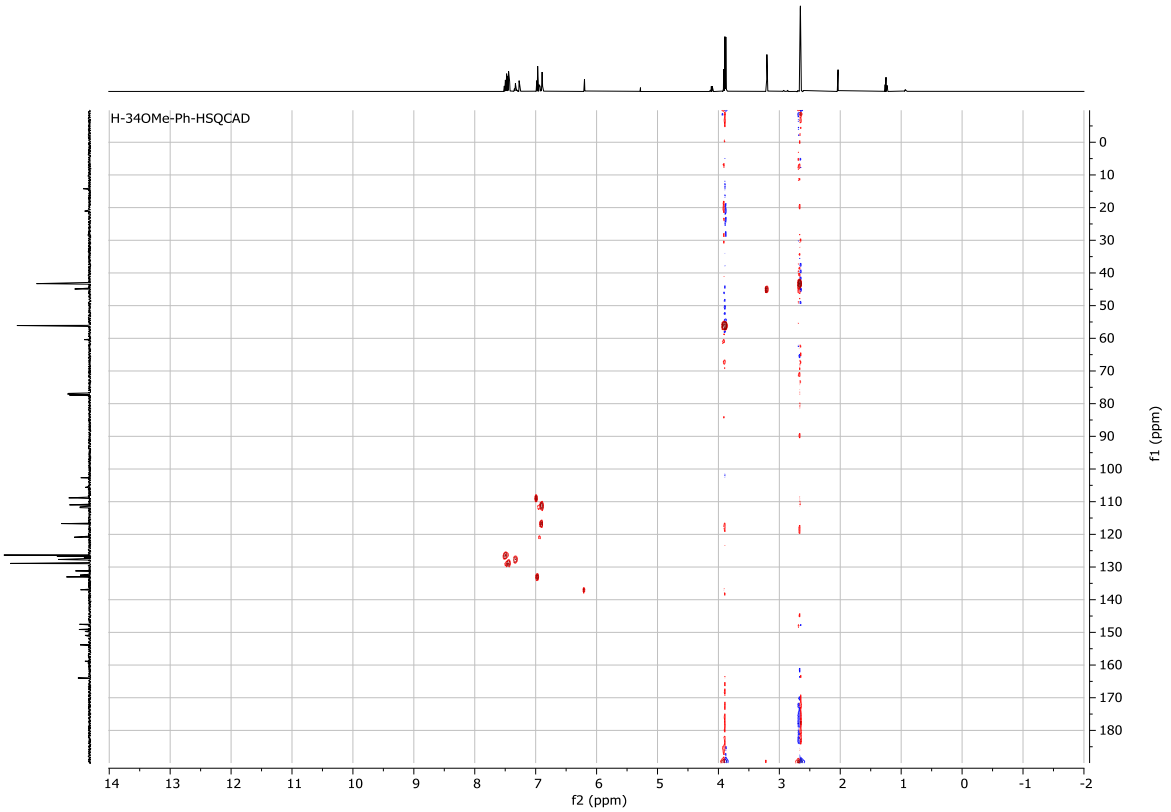



Figure S115. HSQC (500 MHz, $CDCl_3$) spectrum of compound **9j/9j'.**

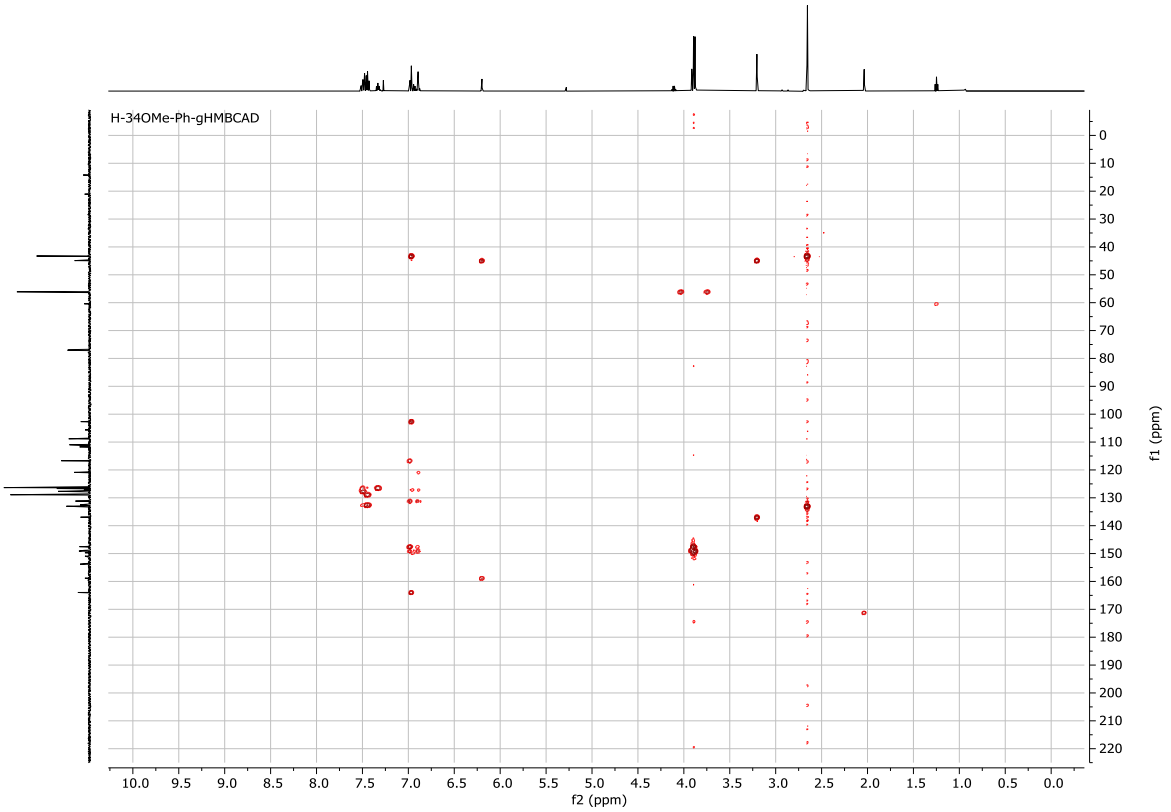
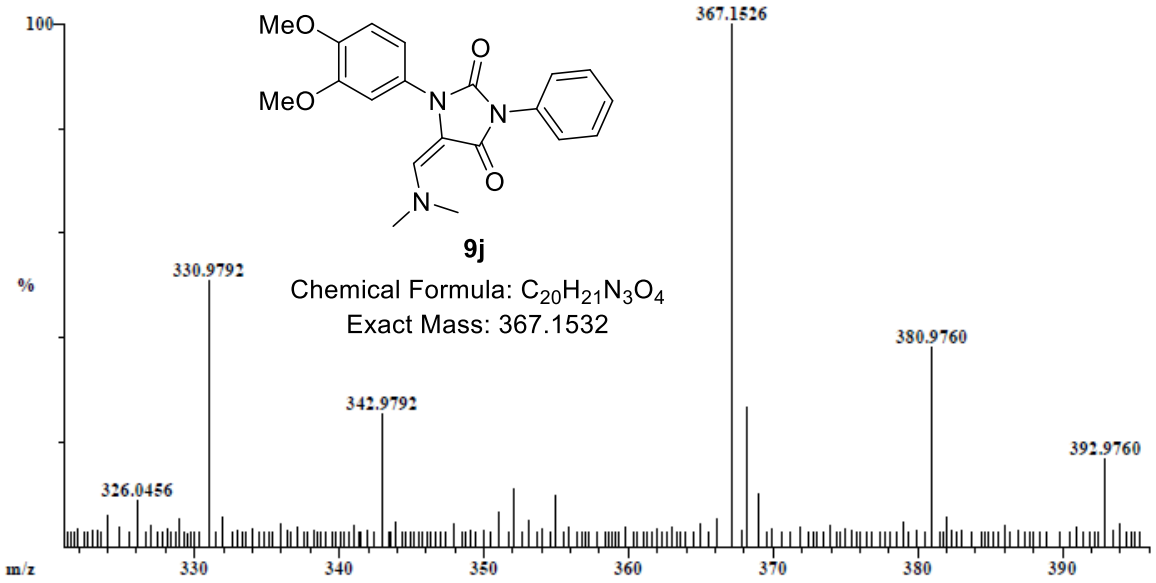



Figure S116. HMBC (500 MHz, $CDCl_3$) spectrum of compound **9j/9j'.**

**File: JT-H165IB-190923** **Date Run: 09-19-2023 (Time Run: 18:32:48)**
**Sample: JT-H165ib-190923**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 584** **R.T.: 7.85**
**Base: m/z 367; 2.6%FS TIC: 223056** **#Ions: 184**




**Selected Isotopes : $N_{0-3}O_{0-4}C_{0-20}H_{0-21}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 367.1526 | 100.0% | $C_{20}H_{21}N_3O_4$ | 367.1532 | -1.6 | 12.0 |

Figure S117. HRMS of compound **9j.**

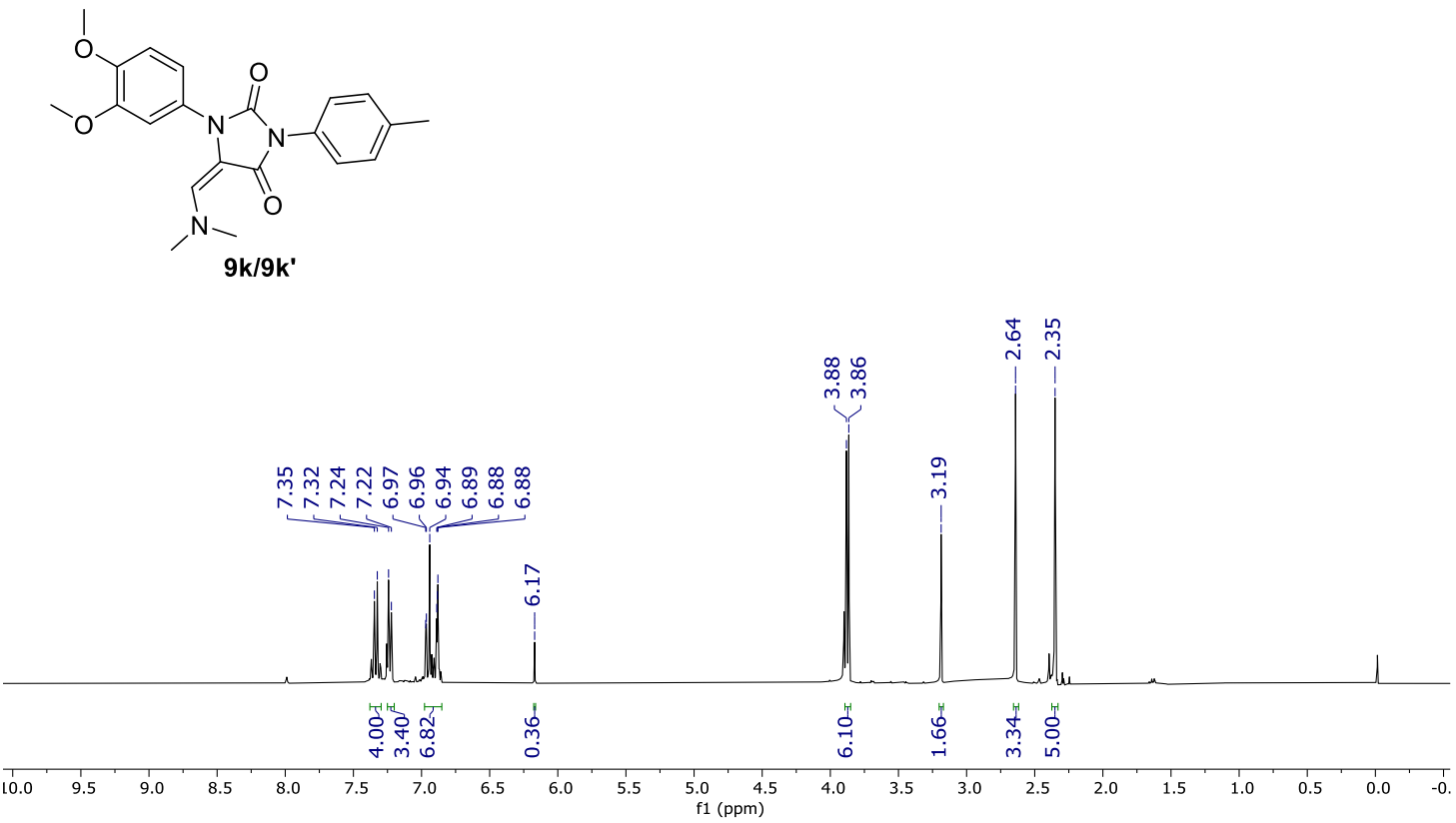



Figure S118. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **9k/9k'**.

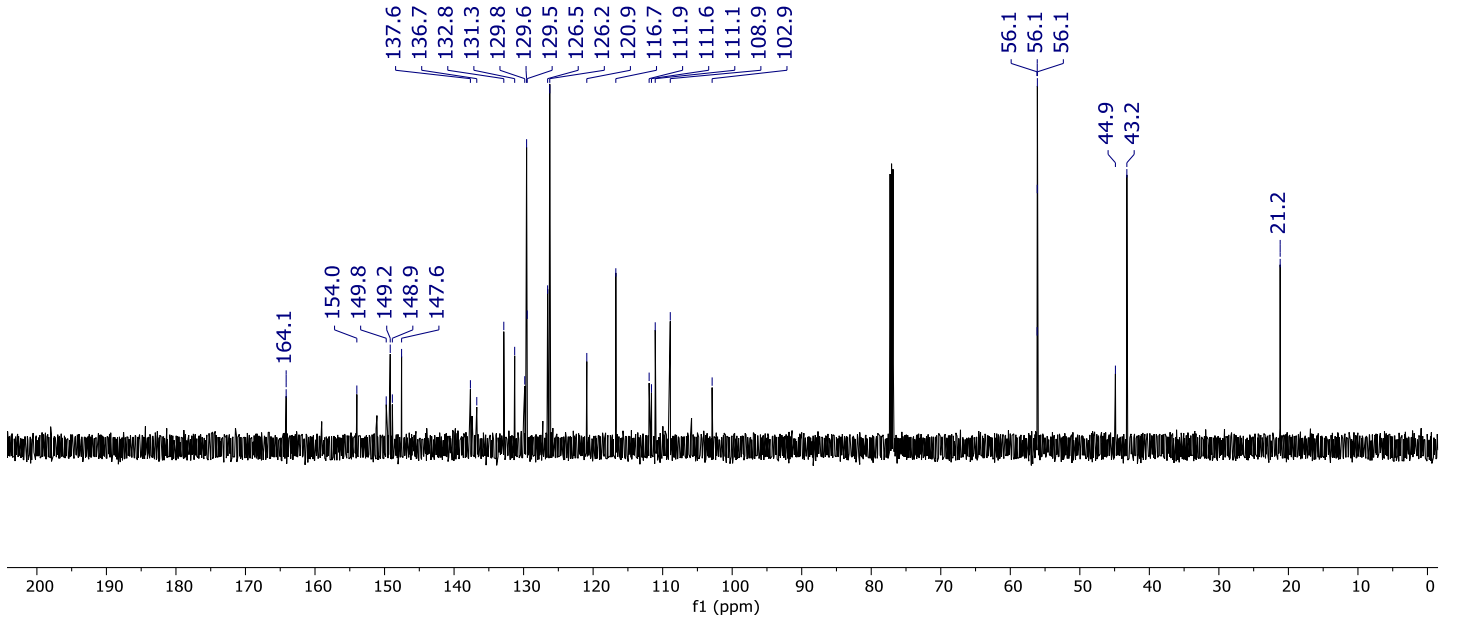



Figure S119. $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **9k/9k'**.

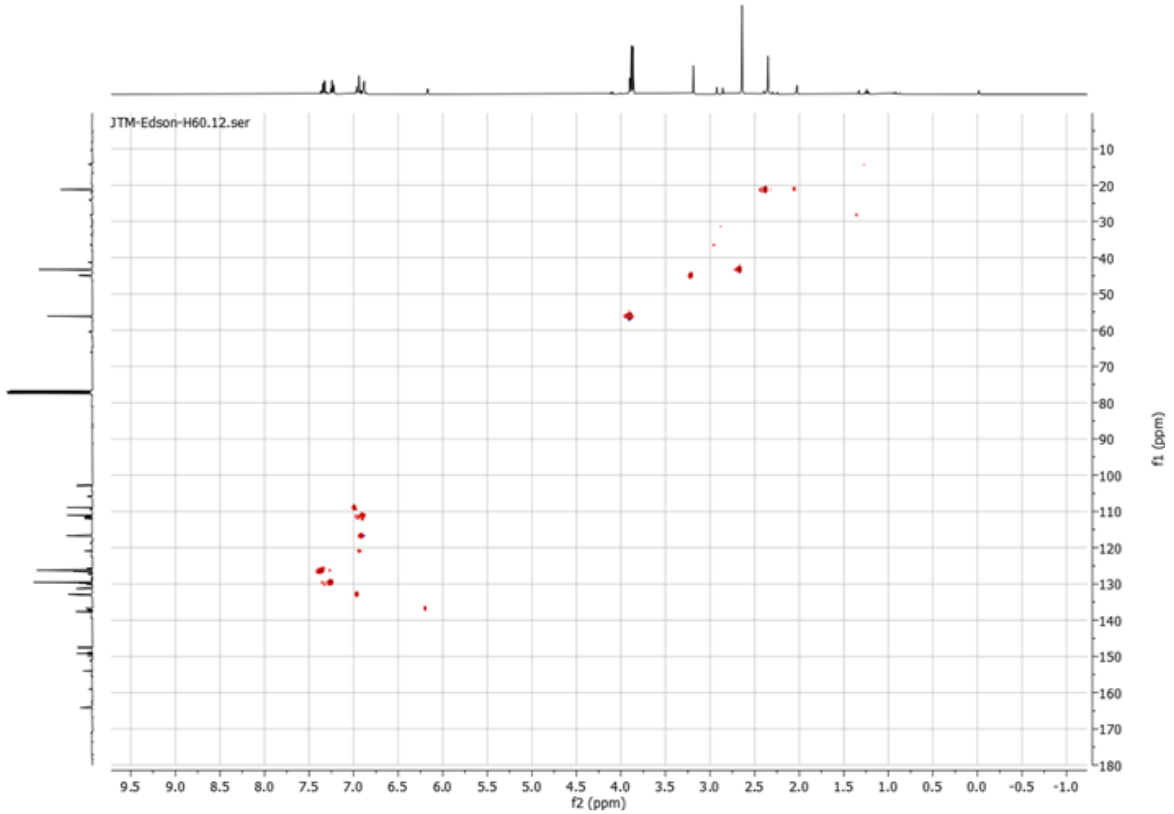



Figure S120. HSQC (400 MHz, $CDCl_3$) spectrum of compound **9k/9k'.**

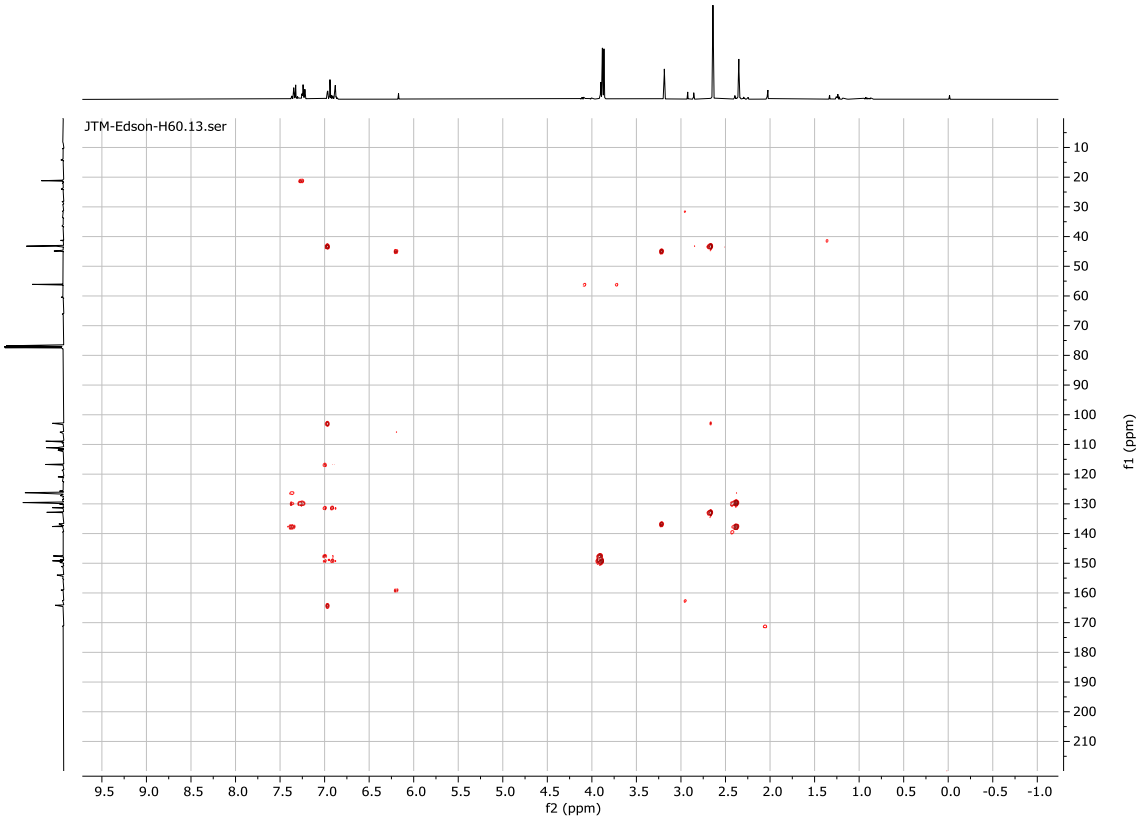
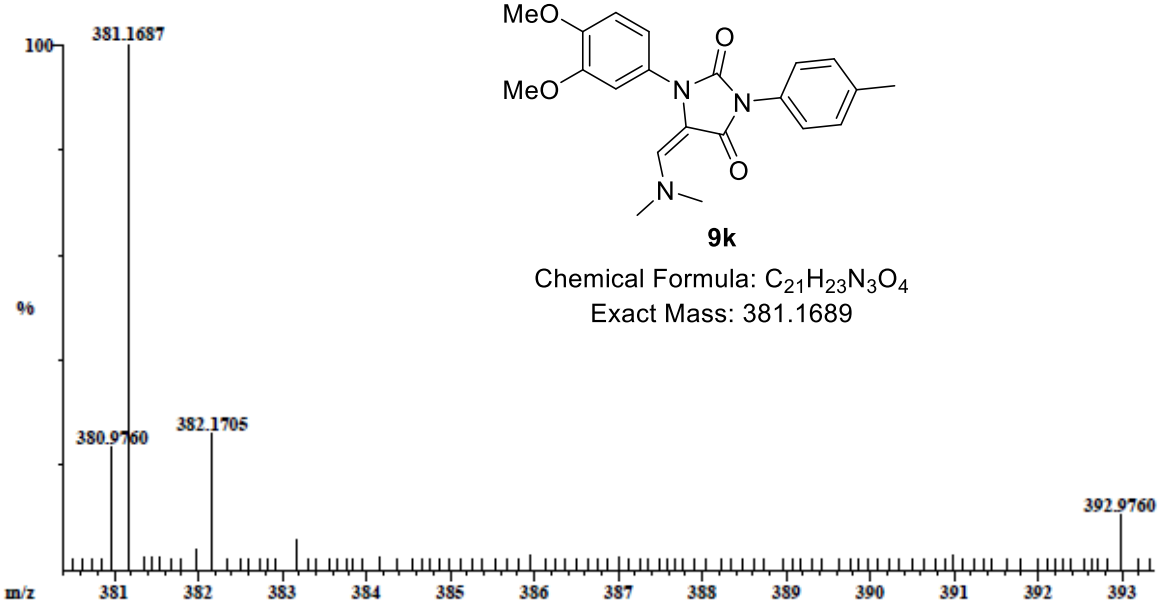



Figure S121. HMBC (400 MHz, $CDCl_3$) spectrum of compound **9k/9k'.**

**File: JT-EBC-H60** **Date Run: 03-25-2023 (Time Run: 15:00:30)**
**Sample: JT-EBC-H60**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 159** **R.T.: 4**
**Base: m/z 381; 3.3%FS TIC: 350864** **#Ions: 387**







**9k**

Chemical Formula: $C_{21}H_{23}N_3O_4$
Exact Mass: 381.1689

**Selected Isotopes : $H_{0-23}C_{0-21}N_{0-3}O_{0-4}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 381.1687 | 100.0% | $C_{21}H_{23}N_3O_4$ | 381.1689 | -0.4 | 12.0 |

Figure S122. HRMS of compound **9k.**

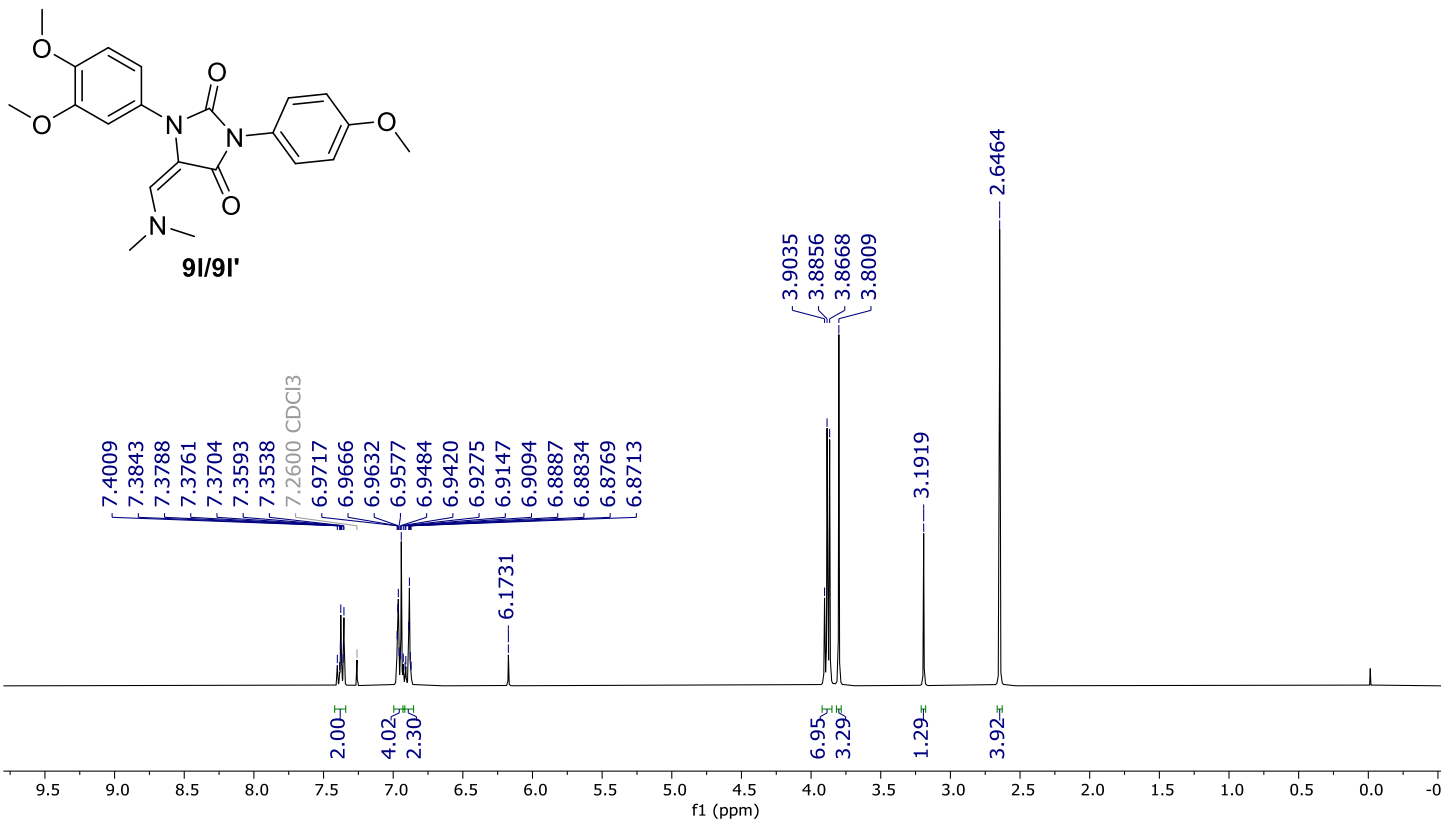



Figure S123. $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **9l/9l'**.

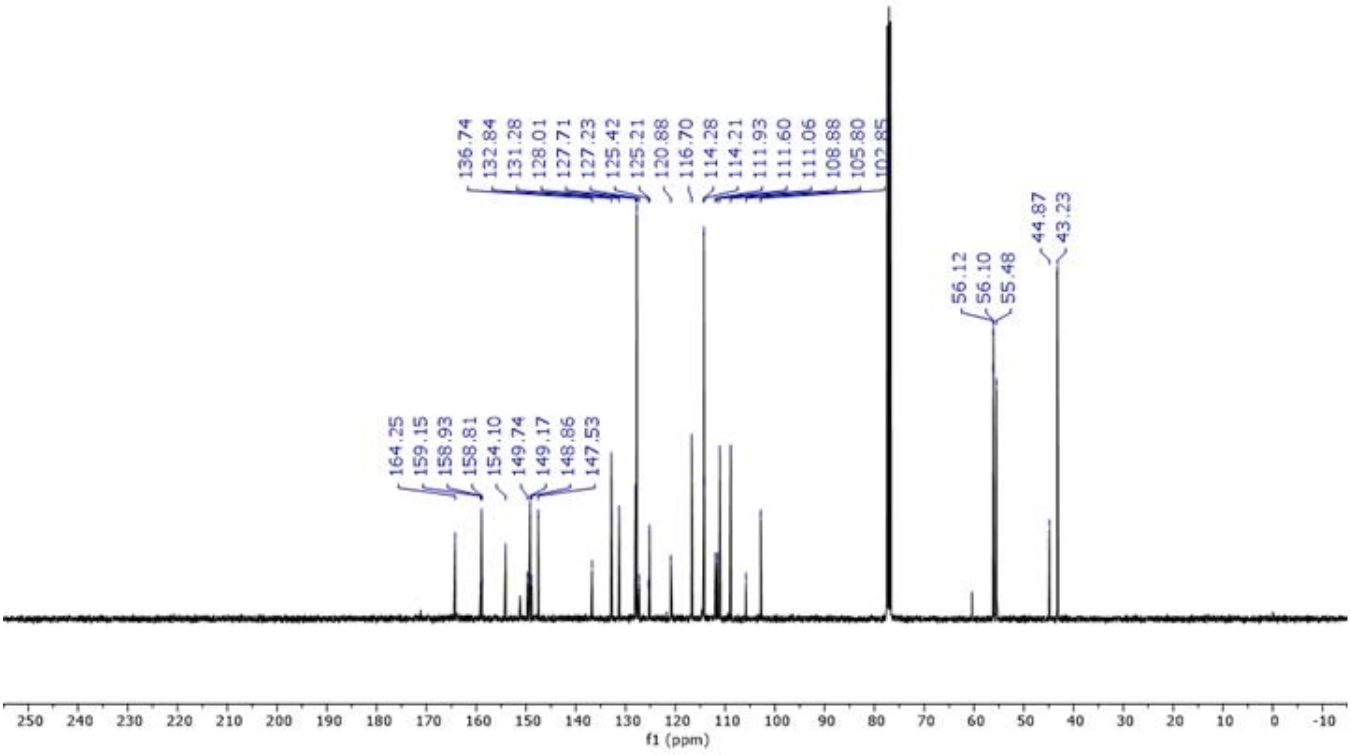



Figure S124. $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **9l/9l'**.

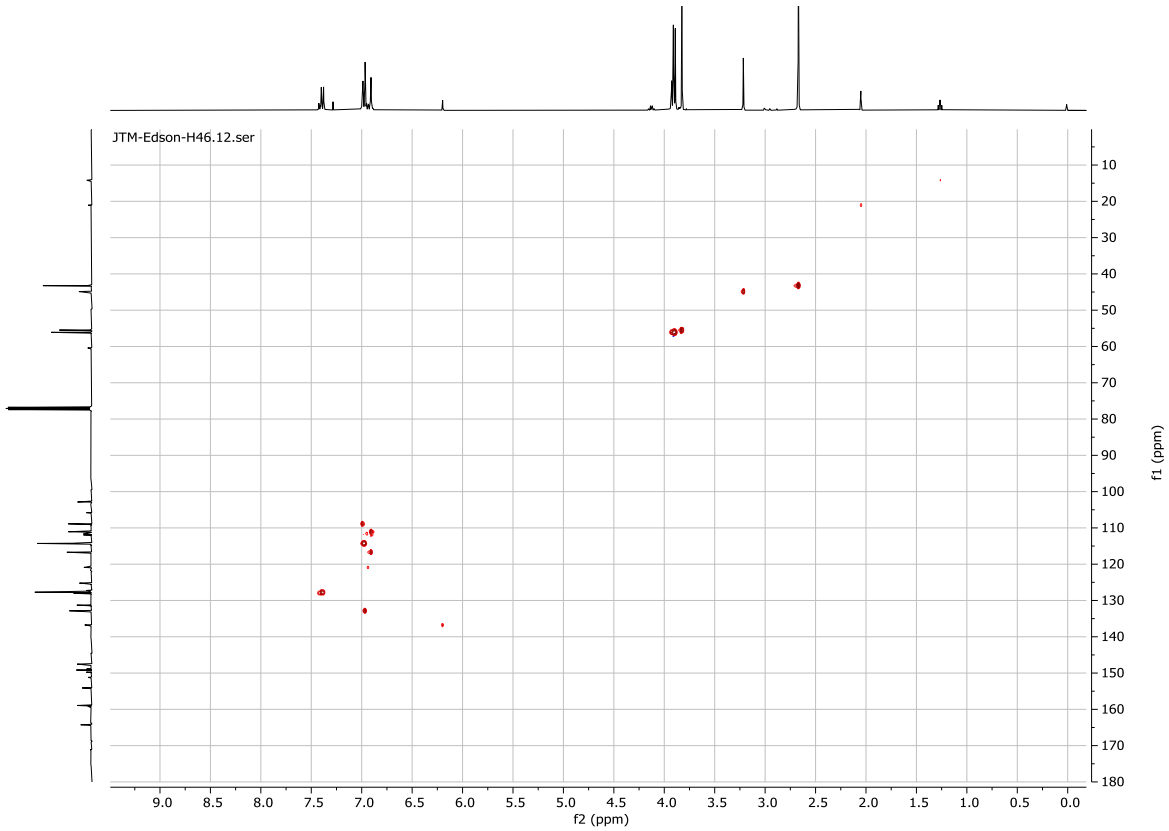



Figure S125. HSQC (400 MHz, $CDCl_3$) spectrum of compound **9l/9l'.**

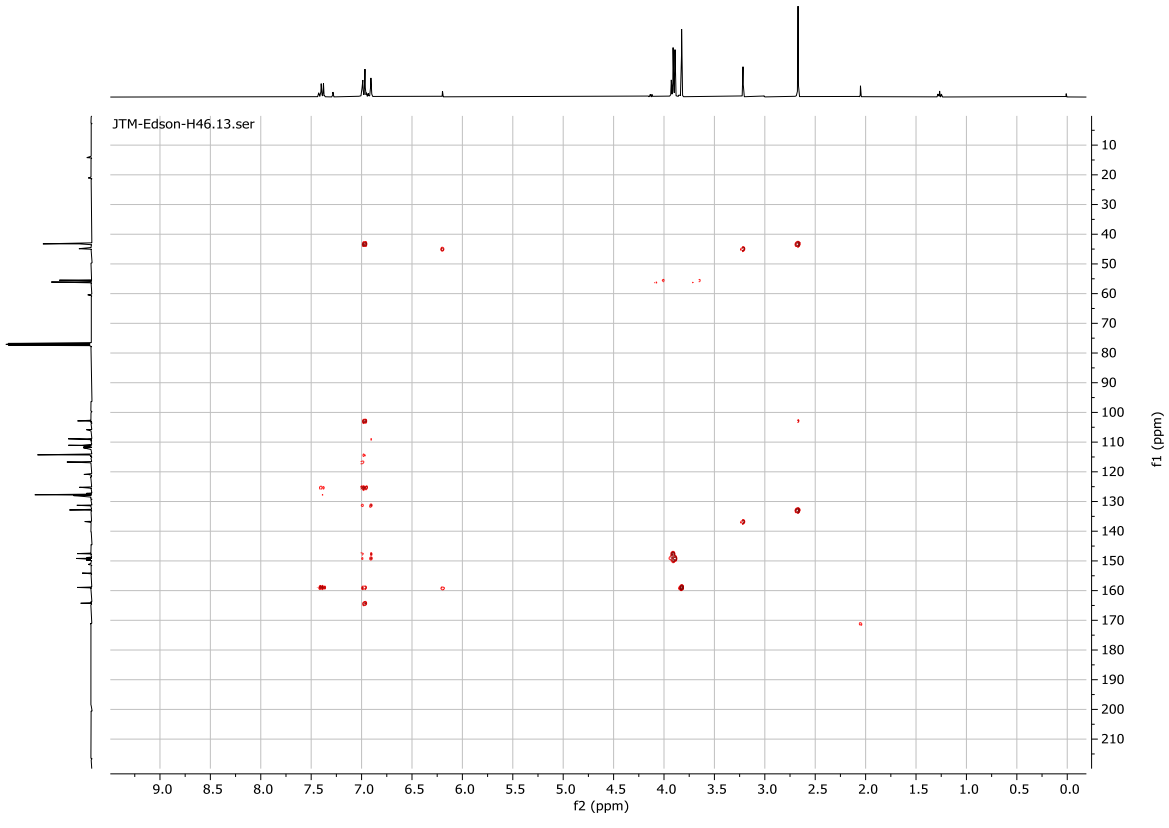



Figure S126. HMBC (400 MHz, $CDCl_3$) spectrum of compound **9l/9l'.**

***IPN***

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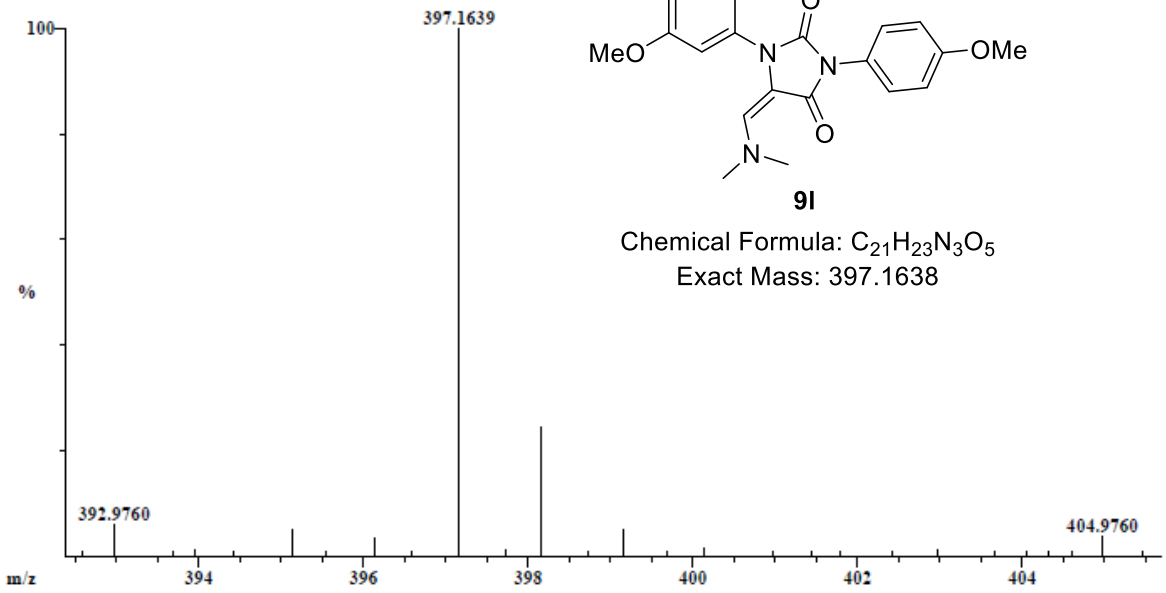
**File: JT-EBC-H53-25032023 Date Run: 03-25-2023 (Time Run: 14:10:00)**
**Sample: JT-EBC-H53-25032023**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe Ionization mode: EI+**

**Scan: 407 R.T.: 5.41**
**Base: m/z 397; 10.4%FS TIC: 329712 #Ions: 164**







**9l**

Chemical Formula: $C_{21}H_{23}N_3O_5$
Exact Mass: 397.1638

**Selected Isotopes : $H_{0-23}C_{0-21}N_{0-3}O_{0-5}$ Error Limit : 5 ppm Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 397.1639 | 100.0% | $C_{21}H_{23}N_3O_5$ | 397.1638 | 0.3 | 12.0 |

Figure S127. HRMS of compound **9l.**

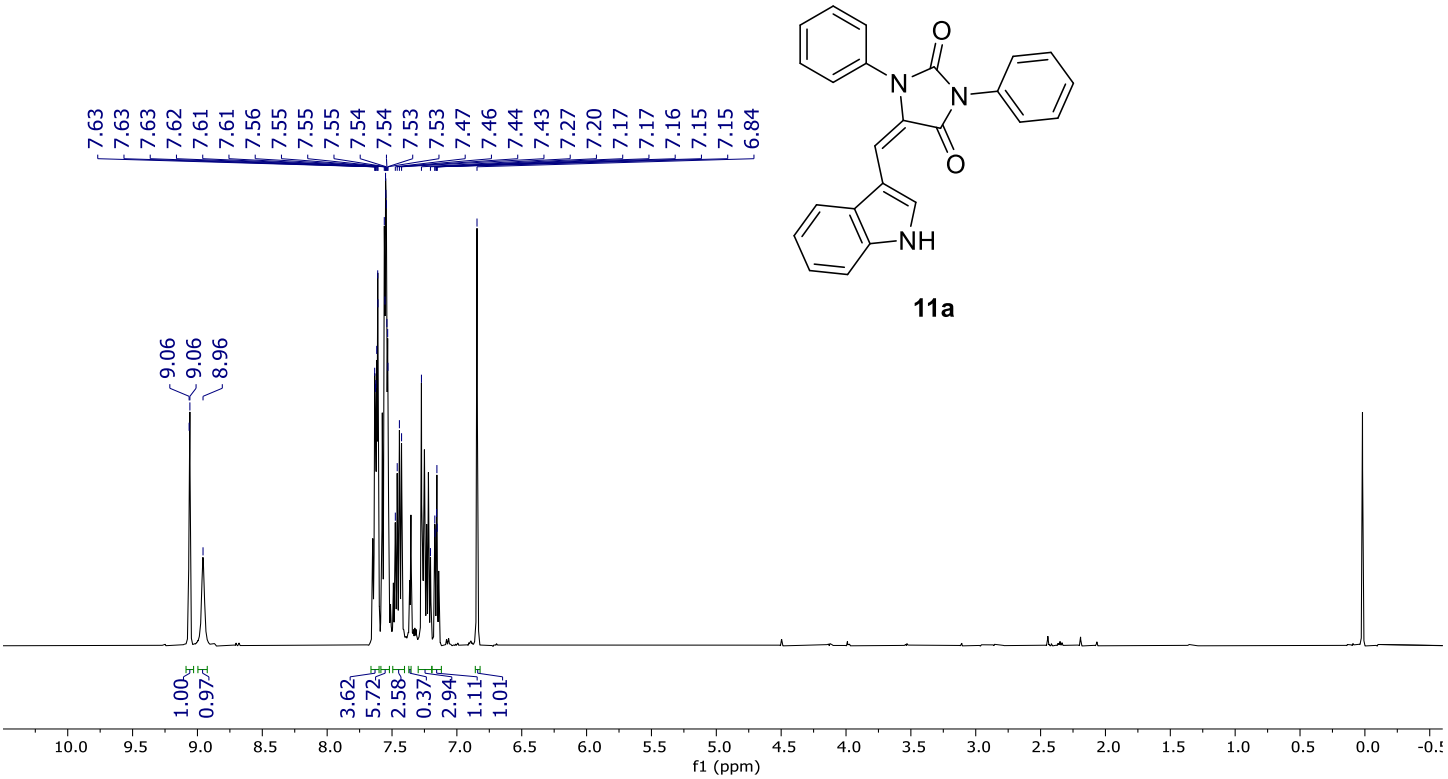



Figure S128. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **11a**.

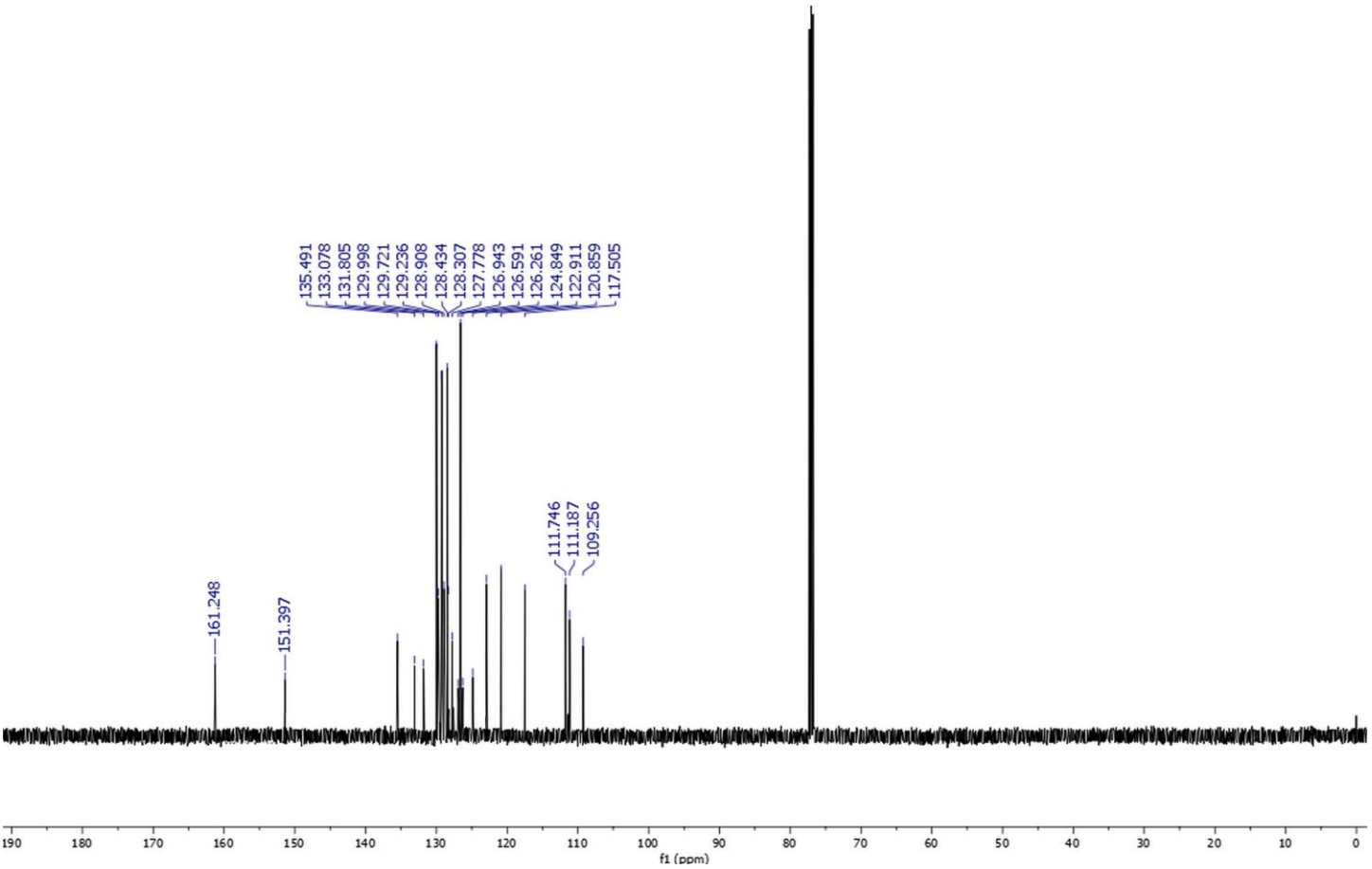



Figure S129. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **11a**.

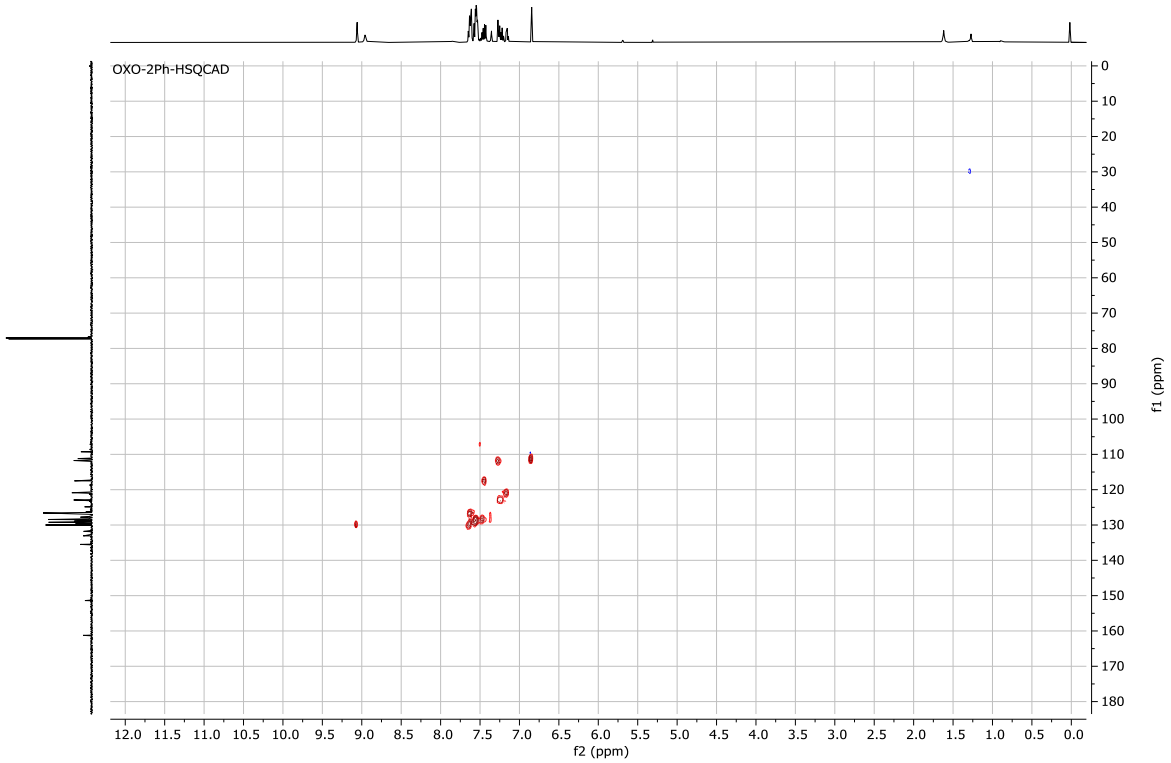



Figure S130. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11a.**

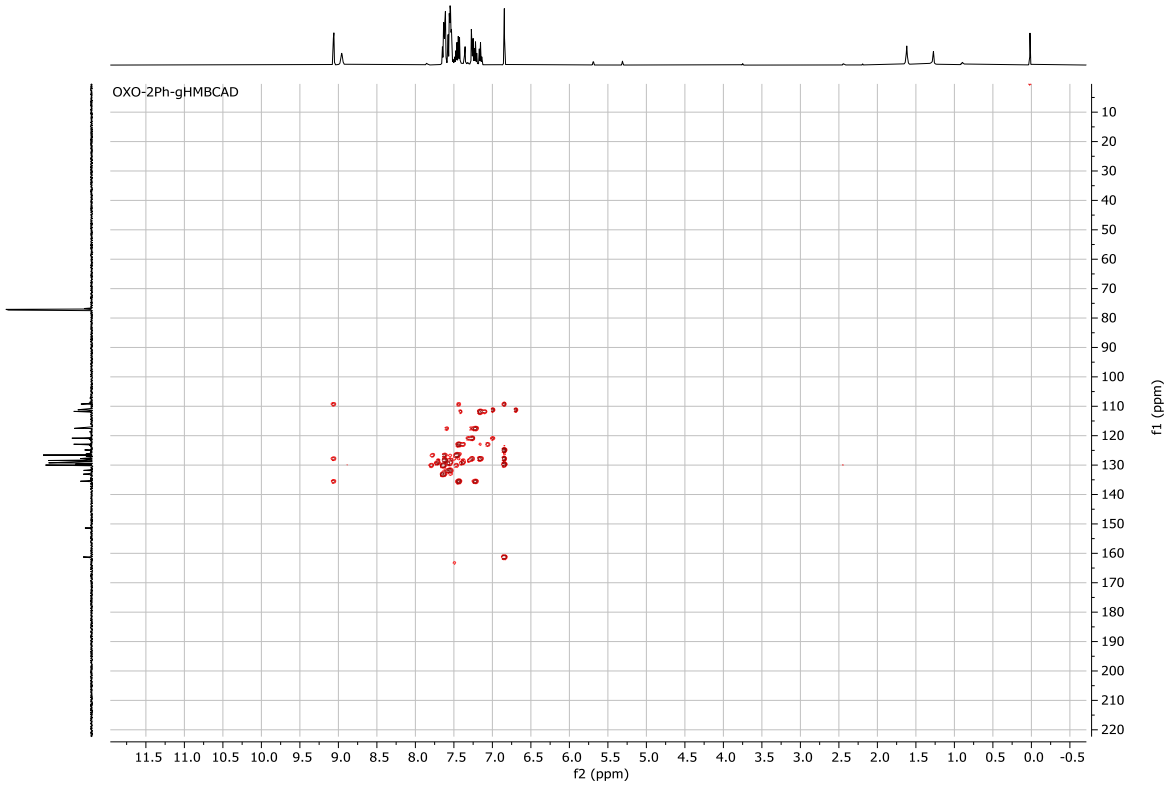



Figure S131. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11a.**

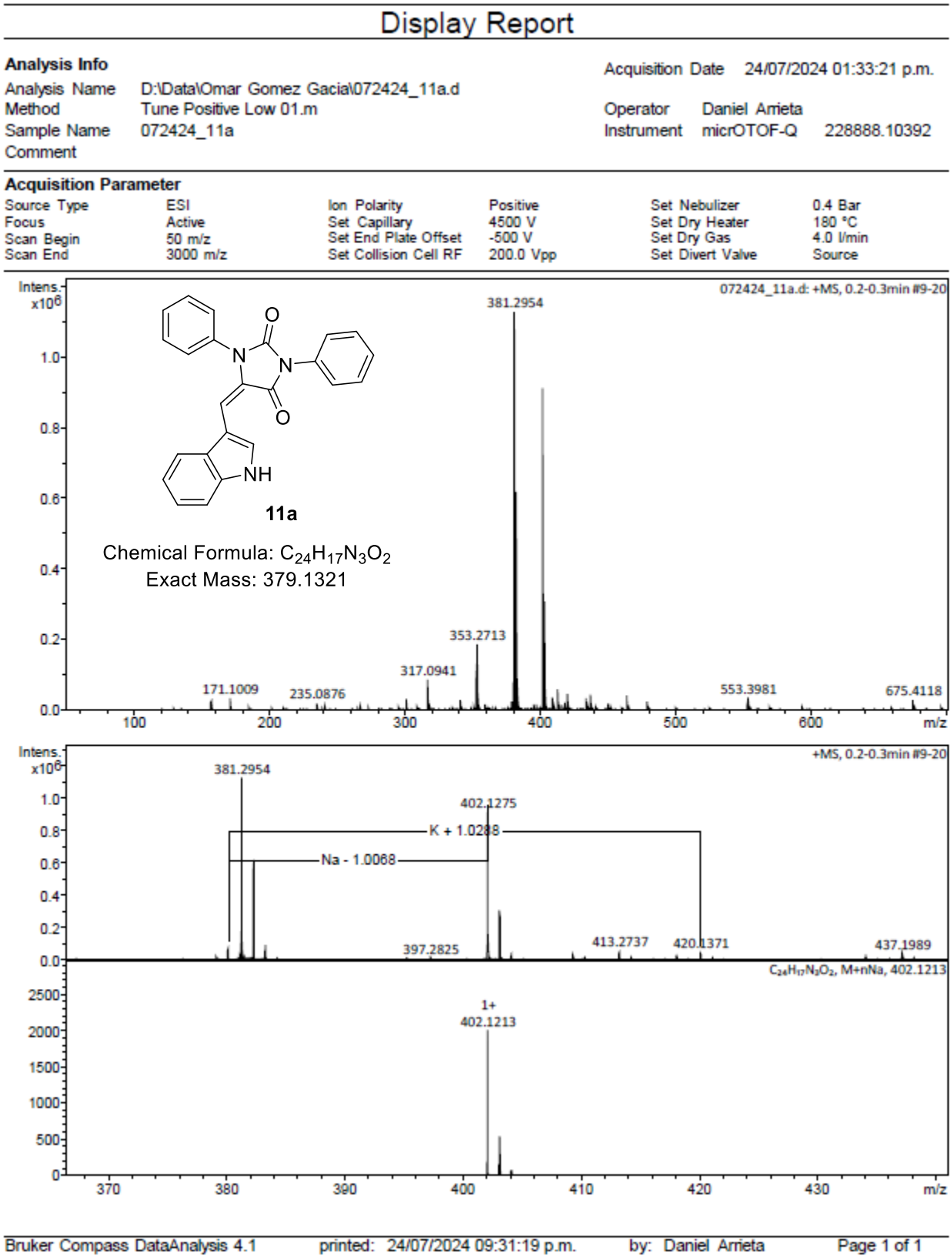



Figure S132. HRMS of compound **11a.**

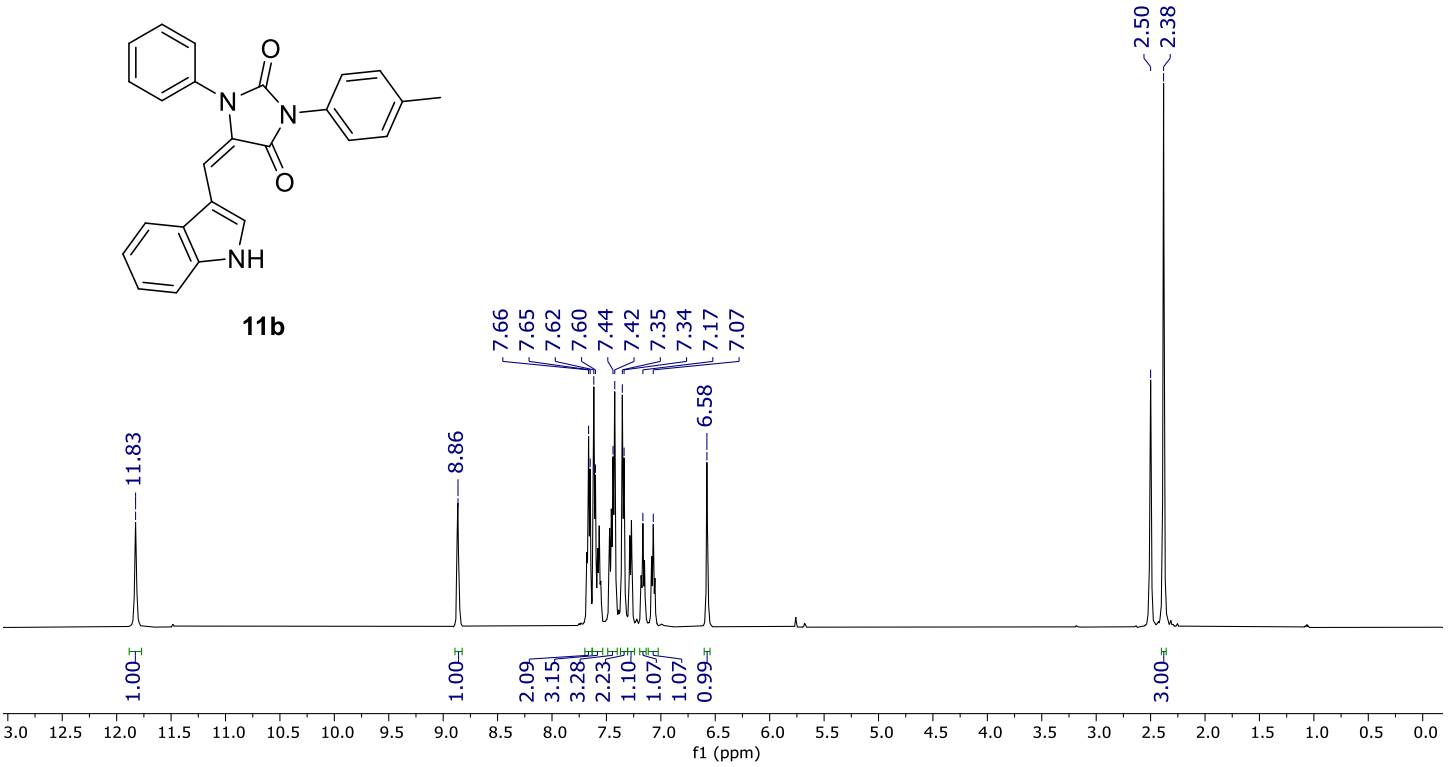



Figure S133. $^{1}$H NMR (500 MHz, DMSO-$d_6$) spectrum of compound **11b**.

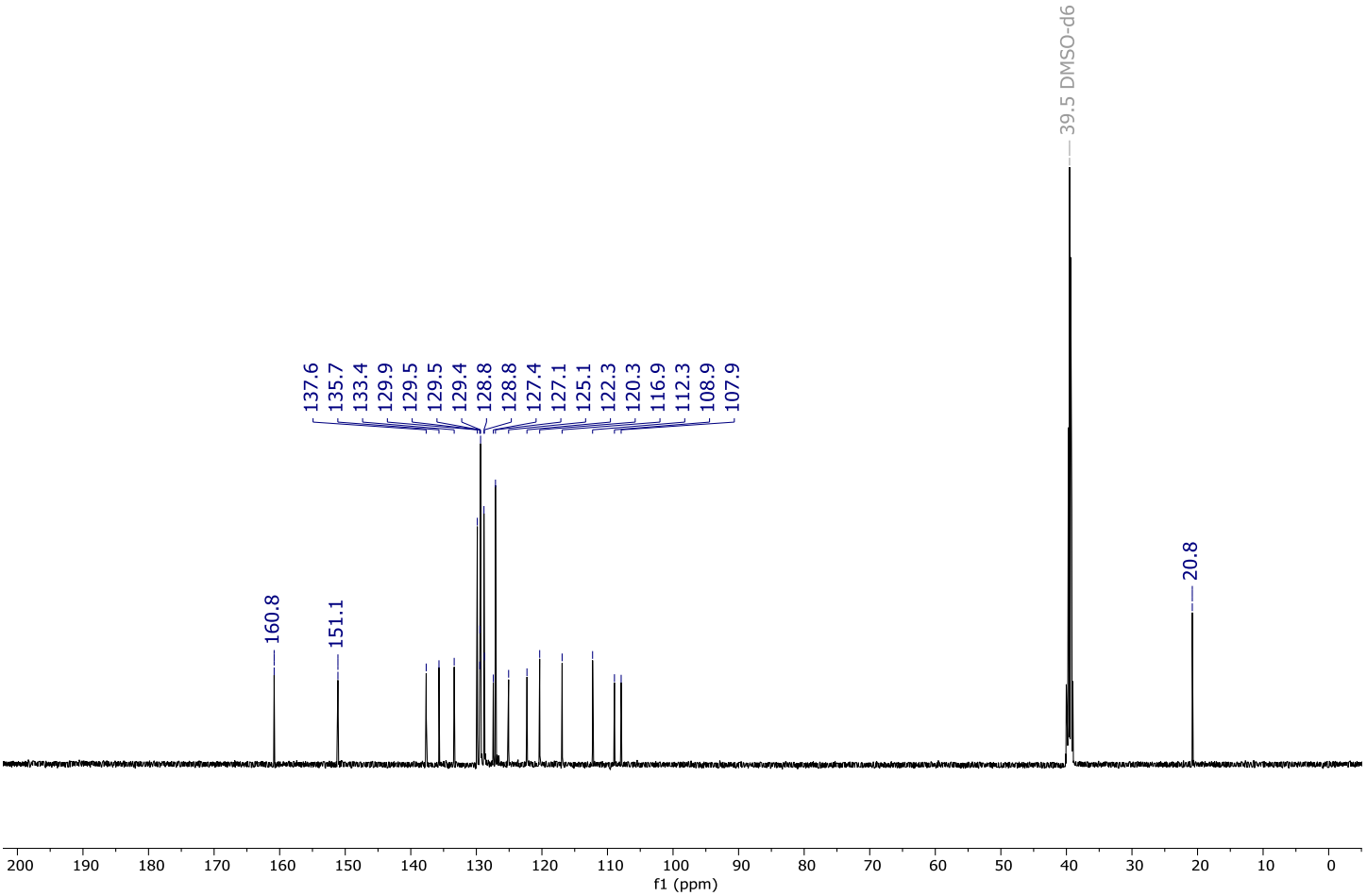



Figure S134. $^{13}$C NMR (125 MHz, DMSO-$d_6$) spectrum of compound **11b**.

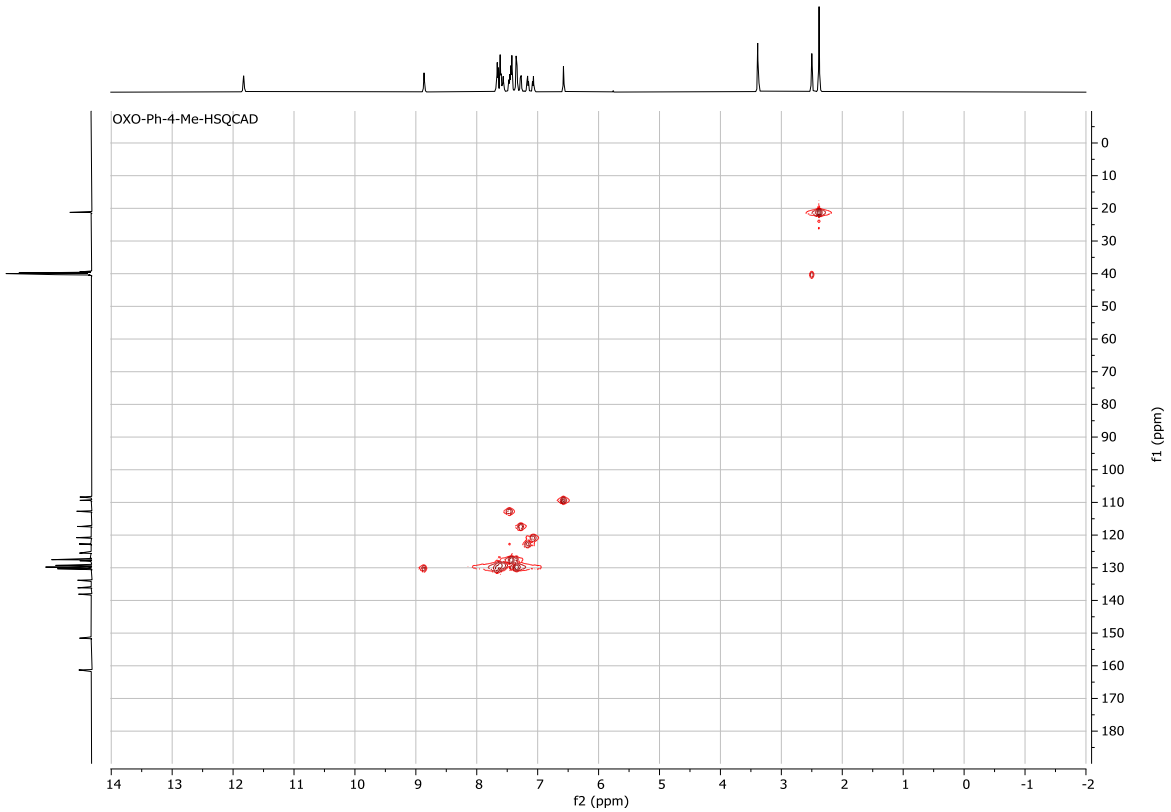



Figure S135. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11b.**

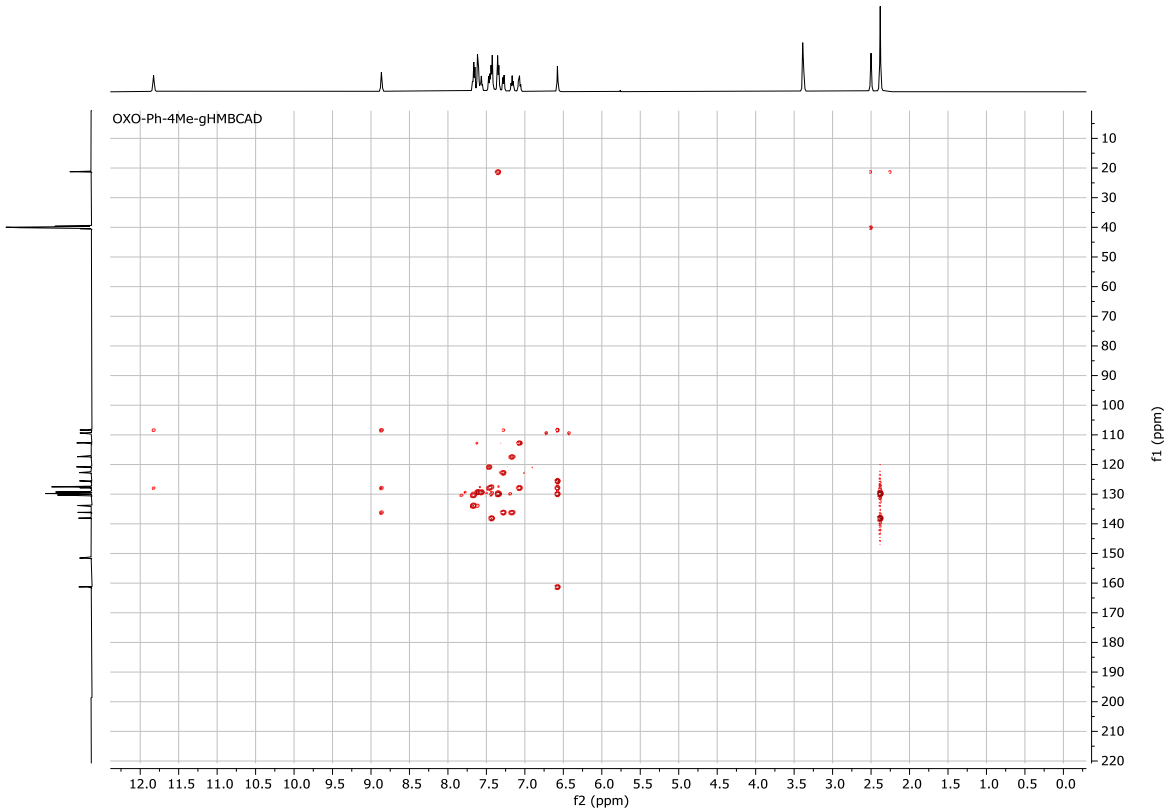



Figure S136. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11b.**

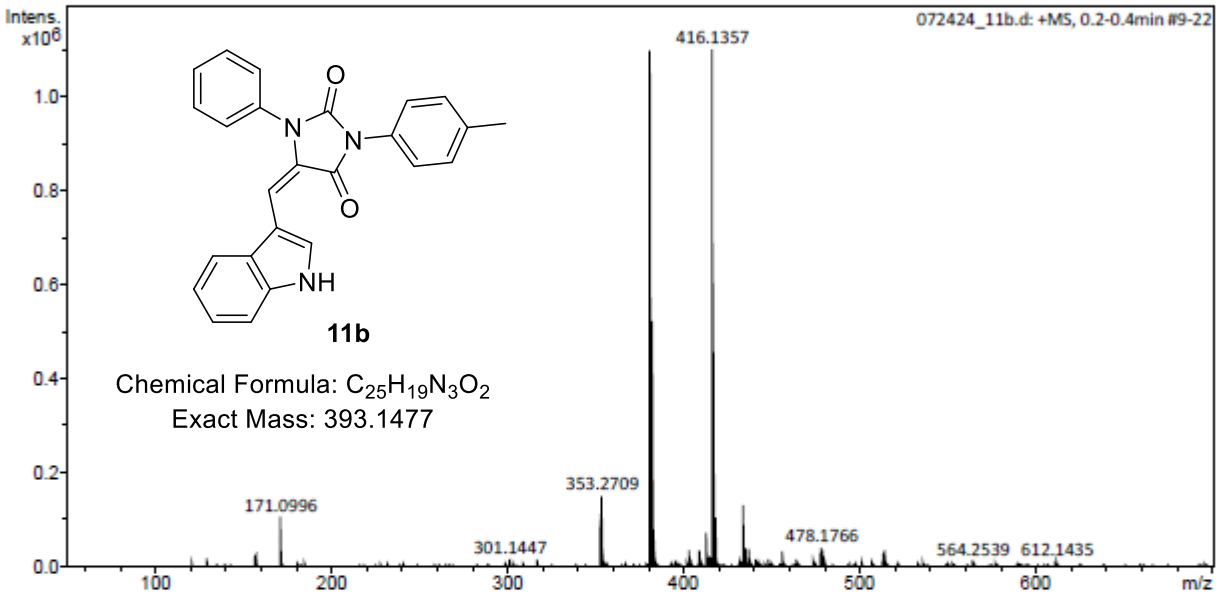
# Display Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\Omar Gomez Gacia\072424_11b.d | Acquisition Date | 24/07/2024 01:49:13 p.m. |
| Method | Tune Positive Low 01.m | Operator | Daniel Arrieta |
| Sample Name | 072424_11b | Instrument | micrOTOF-Q 228888.10392 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.4 Bar |
| Focus | Active | Set Capillary | 4500 V | Set Dry Heater | 180 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 200.0 Vpp | Set Divert Valve | Source |




**11b**

Chemical Formula: $C_{25}H_{19}N_3O_2$

Exact Mass: 393.1477

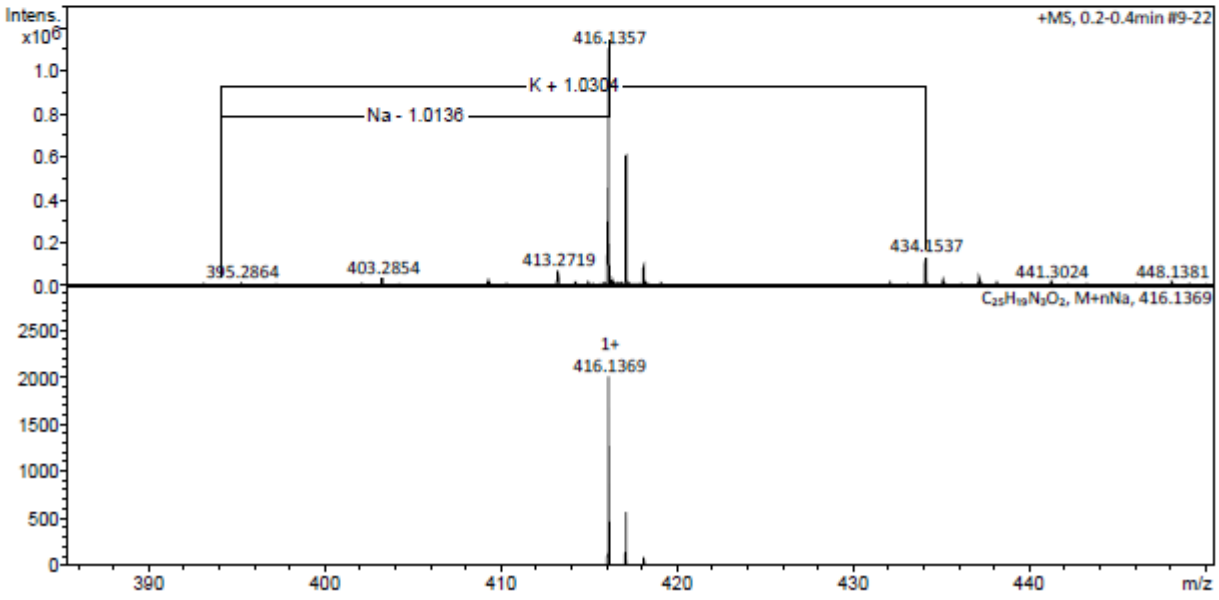





Figure S137. HRMS of compound **11b.**

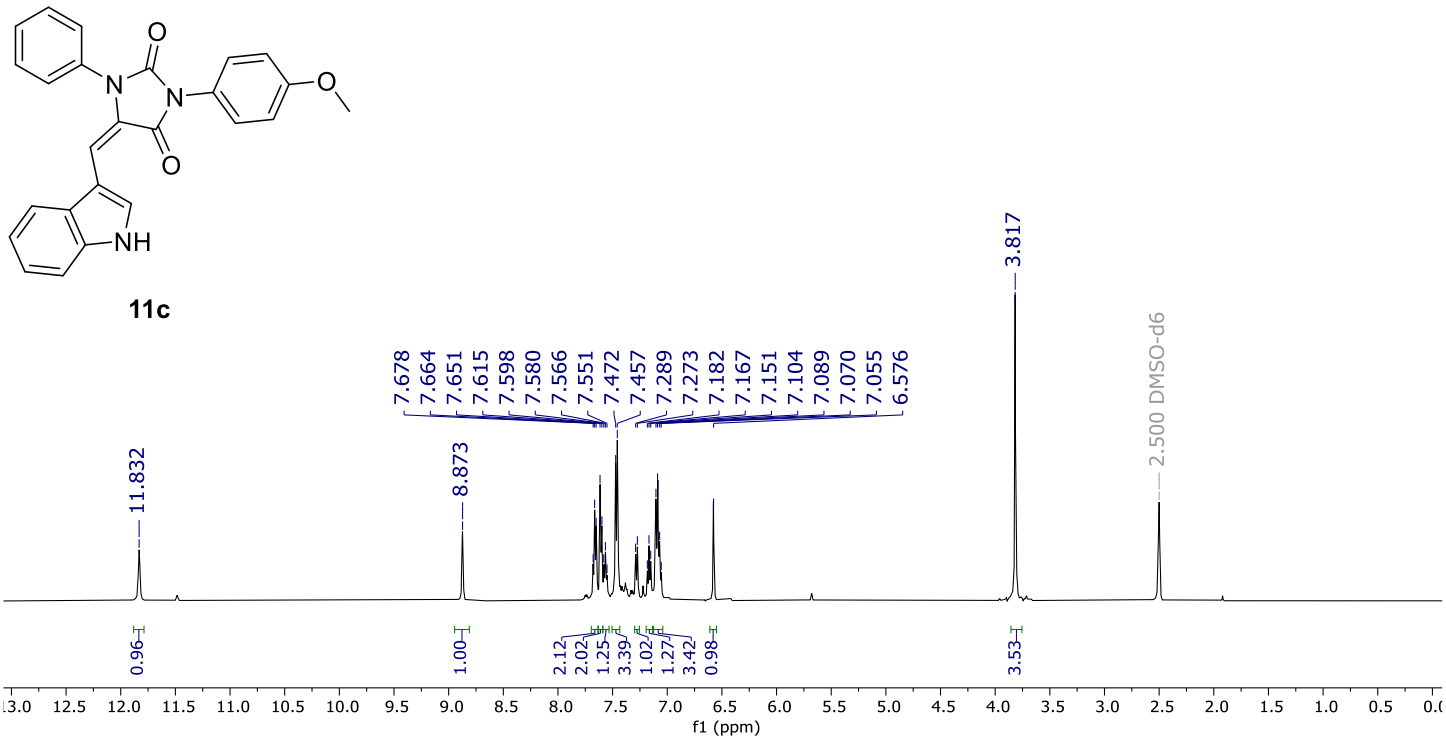



Figure S138. $^{1}$H NMR (500 MHz, DMSO-$d_6$) spectrum of compound **11c**.

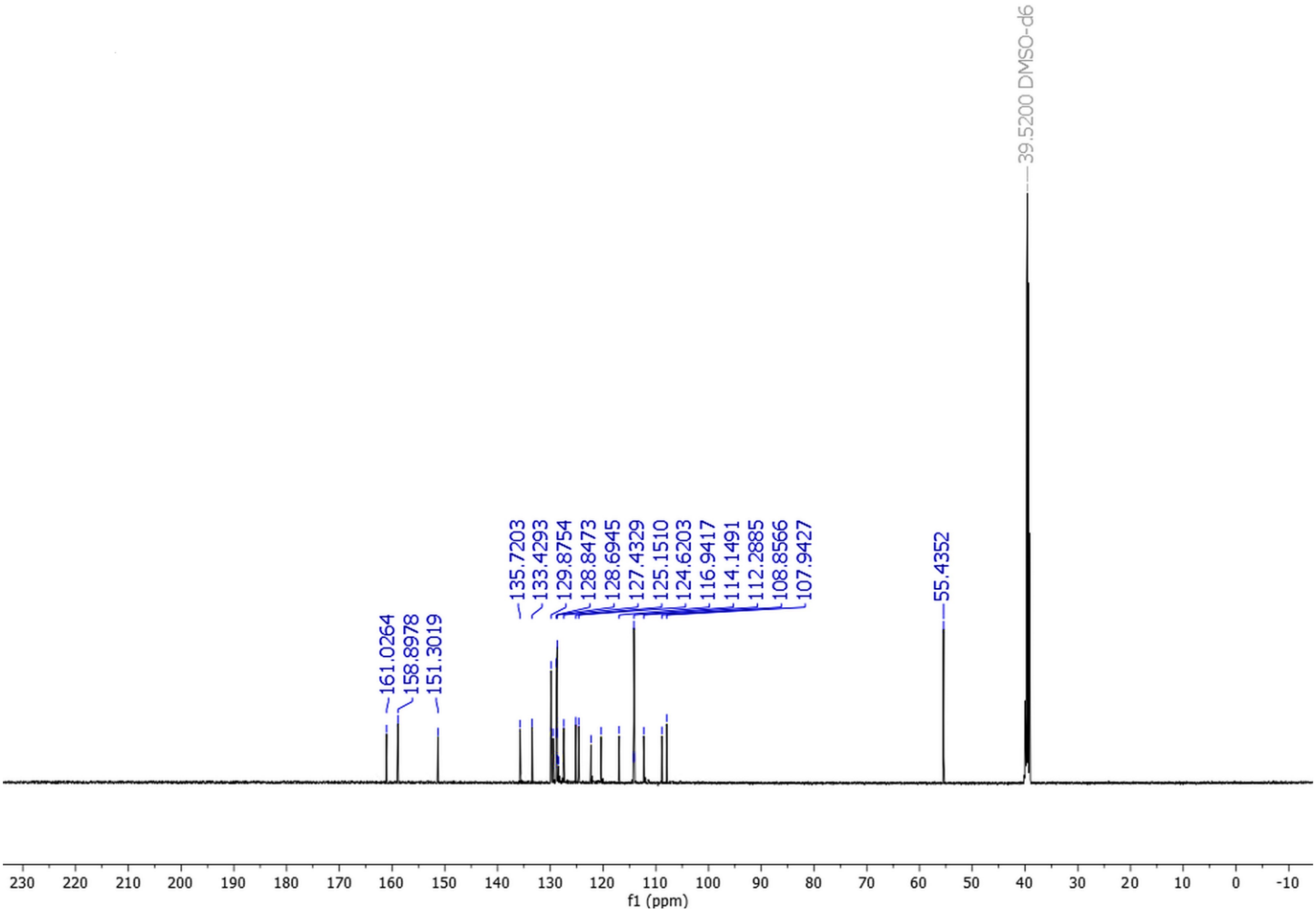



Figure S139. $^{13}$C NMR (125 MHz, DMSO-$d_6$) spectrum of compound **11c**.

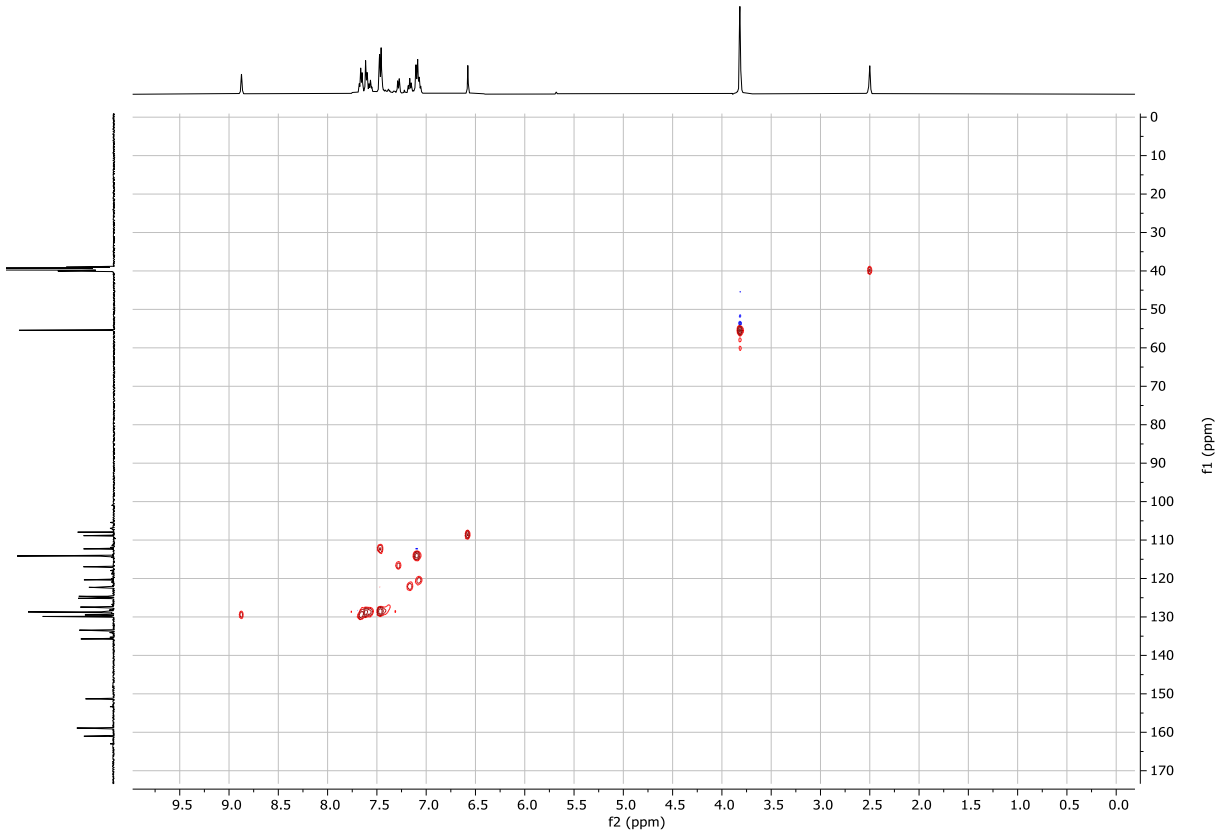



Figure S140. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11c.**

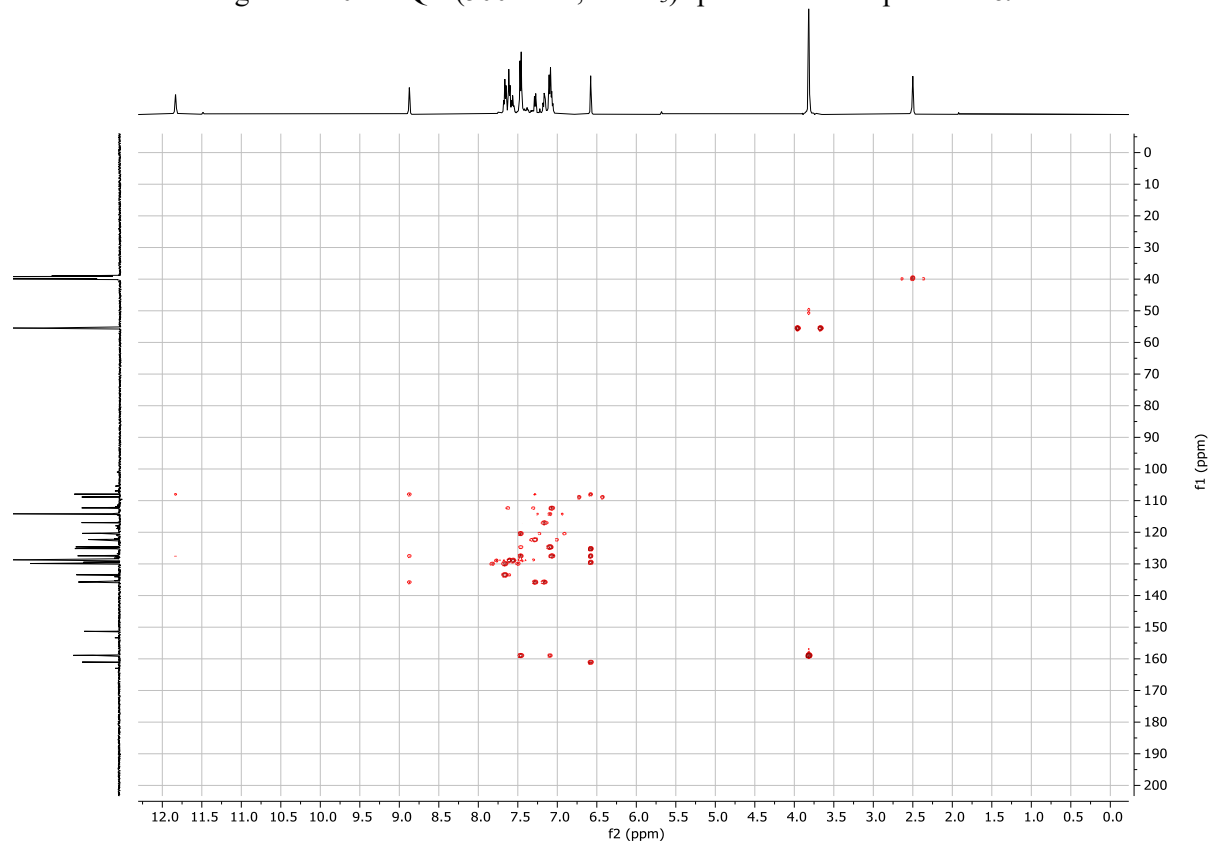



Figure S141. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11c.**

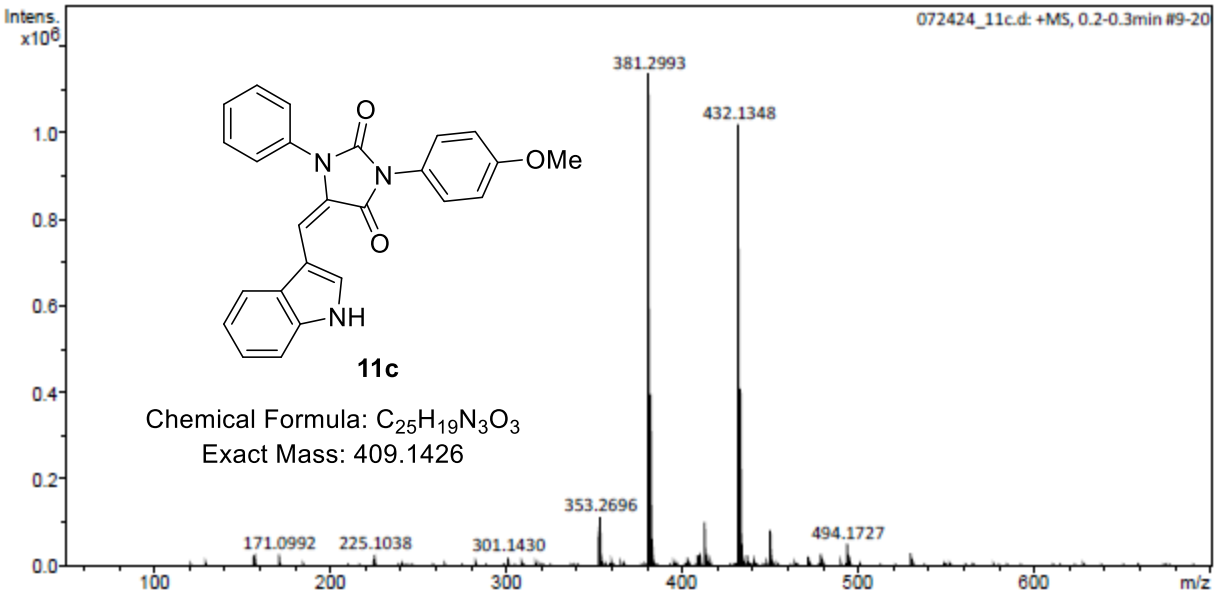
# Display Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\Omar Gomez Gacia\072424_11c.d | Acquisition Date | 24/07/2024 01:53:12 p.m. |
| Method | Tune Positive Low 01.m | Operator | Daniel Arrieta |
| Sample Name | 072424_11c | Instrument | micrOTOF-Q 228888.10392 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.4 Bar |
| Focus | Active | Set Capillary | 4500 V | Set Dry Heater | 180 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 200.0 Vpp | Set Divert Valve | Source |



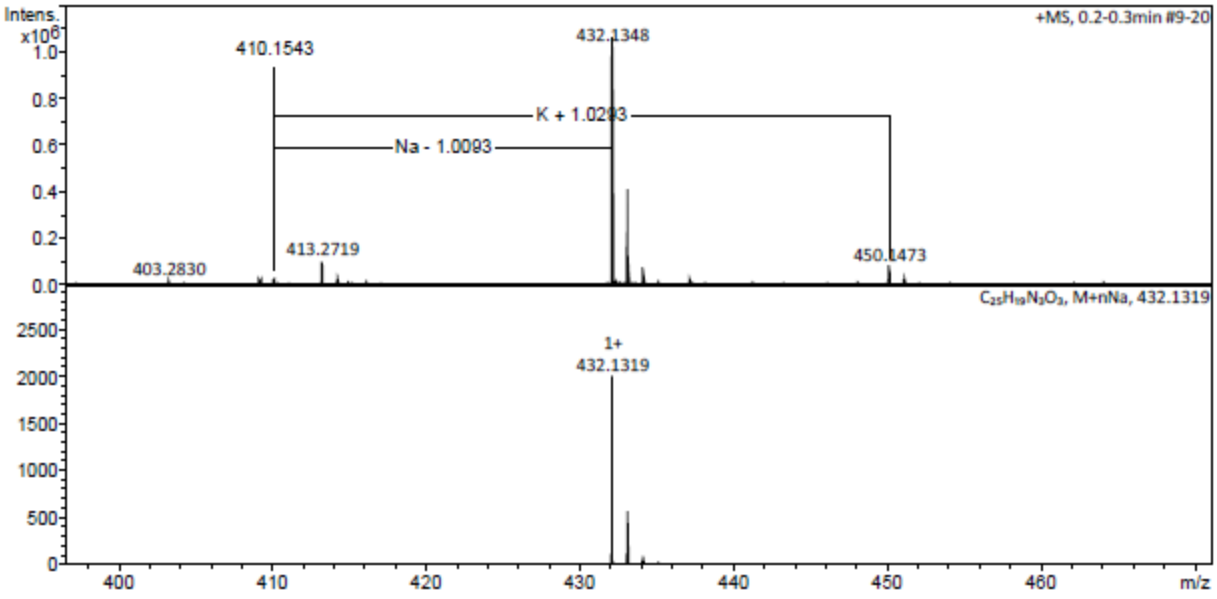




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Figure S142. HRMS of compound **11c.**

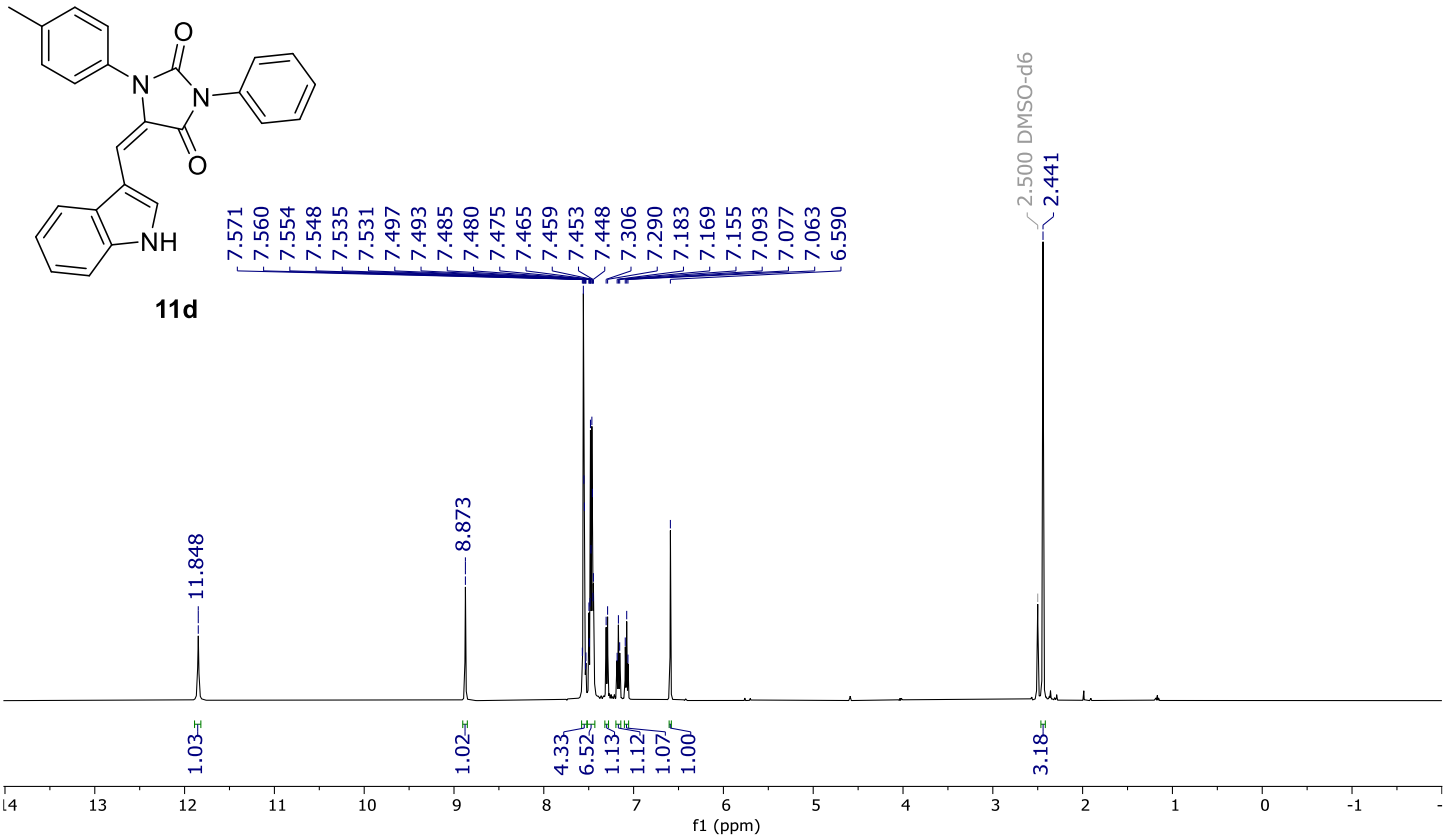



Figure S143. $^{1}$H NMR (500 MHz, DMSO-$d_6$) spectrum of compound **11d**.

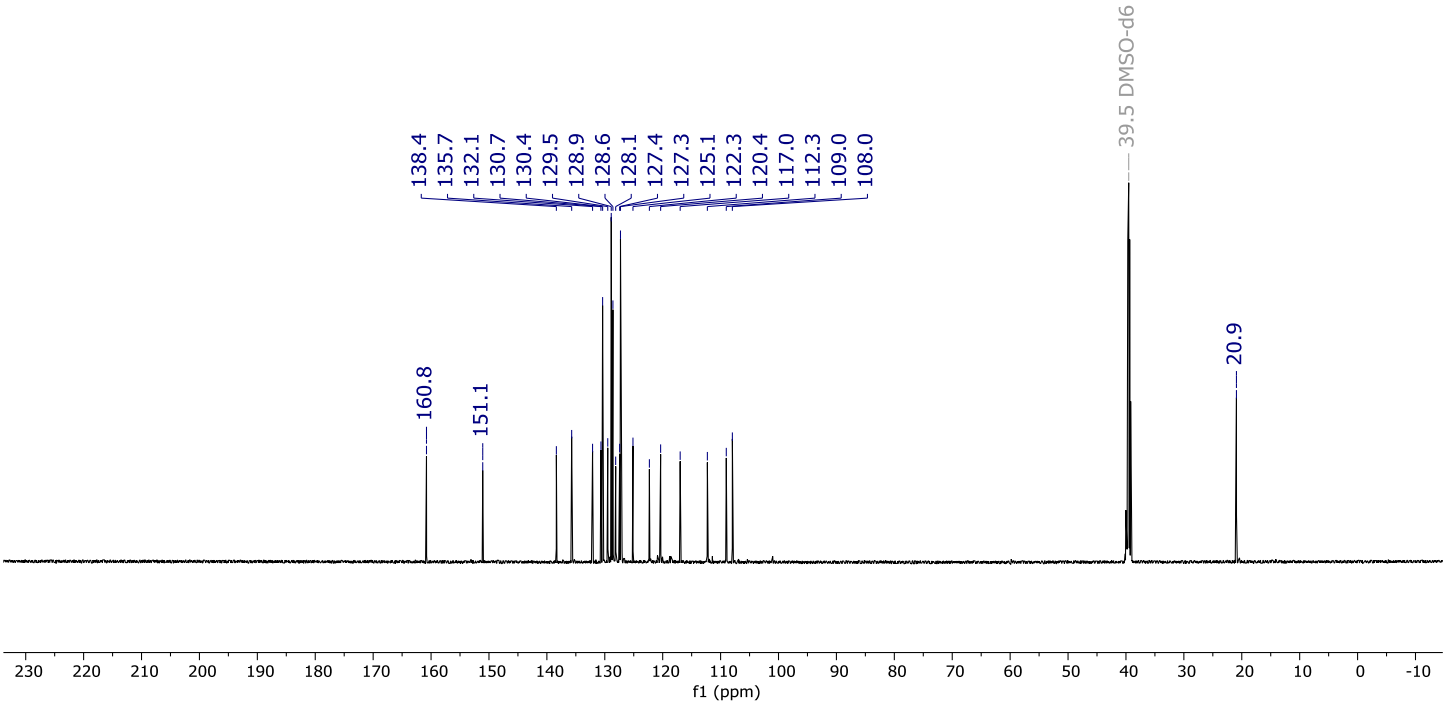



Figure S144. $^{13}$C NMR (125 MHz, DMSO-$d_6$) spectrum of compound **11d**.

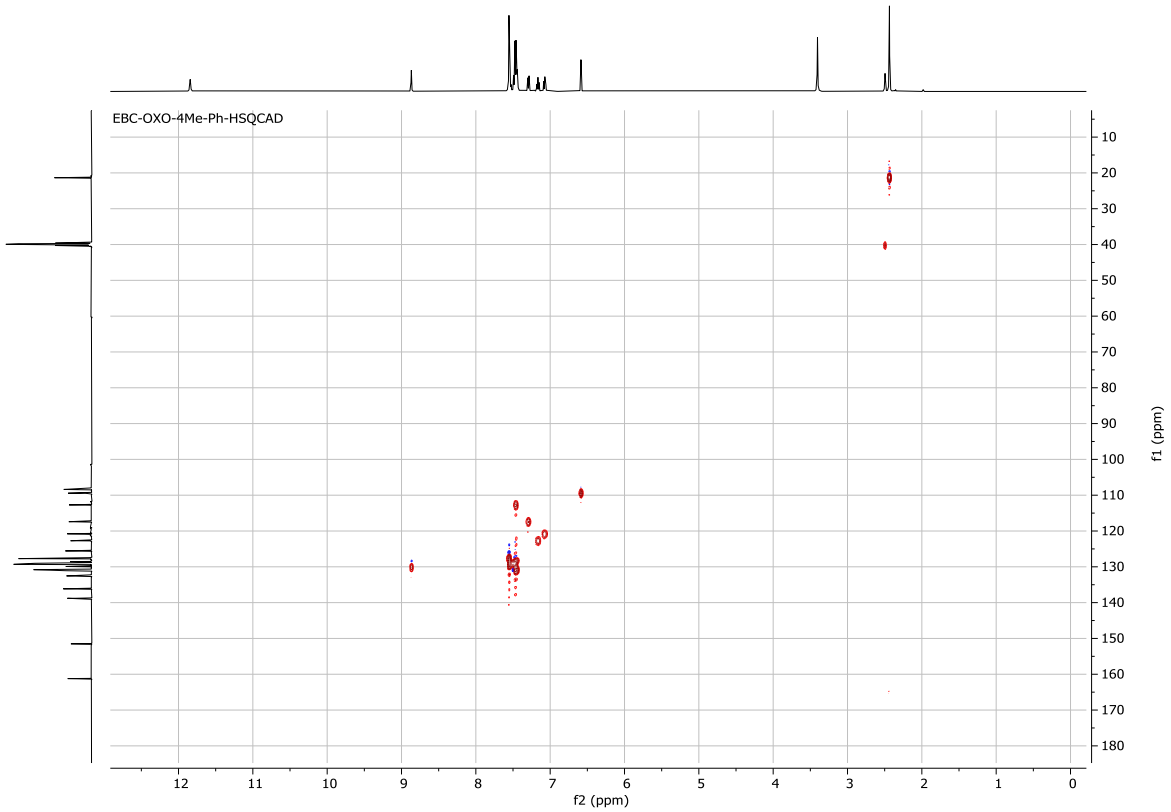



Figure S145. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11d.**

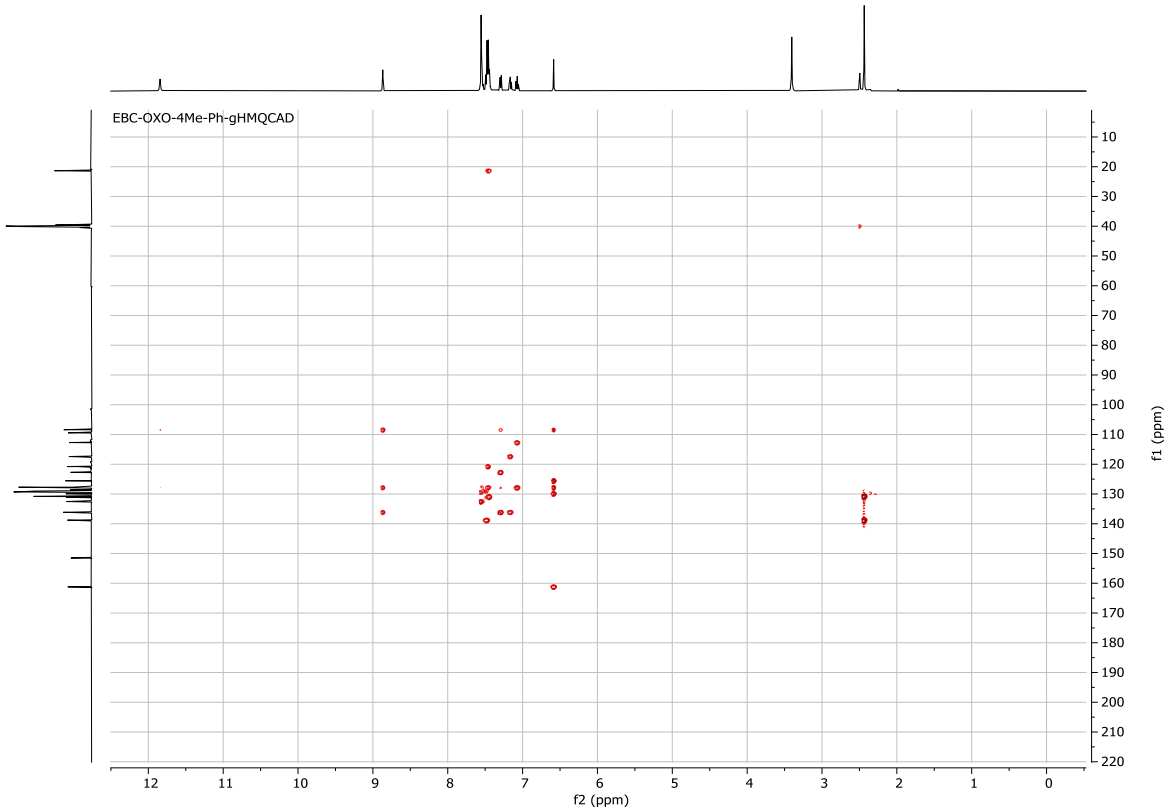
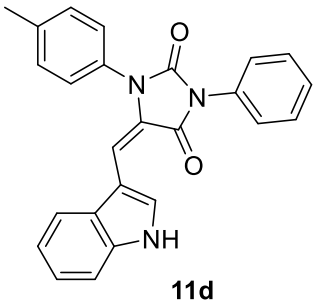



Figure S146. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11d.**




**11d**

Chemical Formula: $C_{25}H_{19}N_3O_2$
Exact Mass: 393.1477

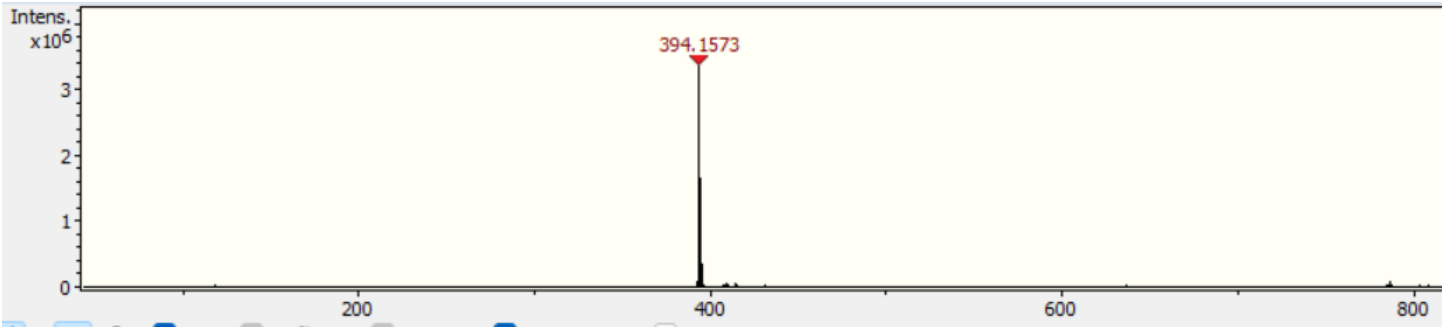



Figure S147. HRMS of compound **11d.**

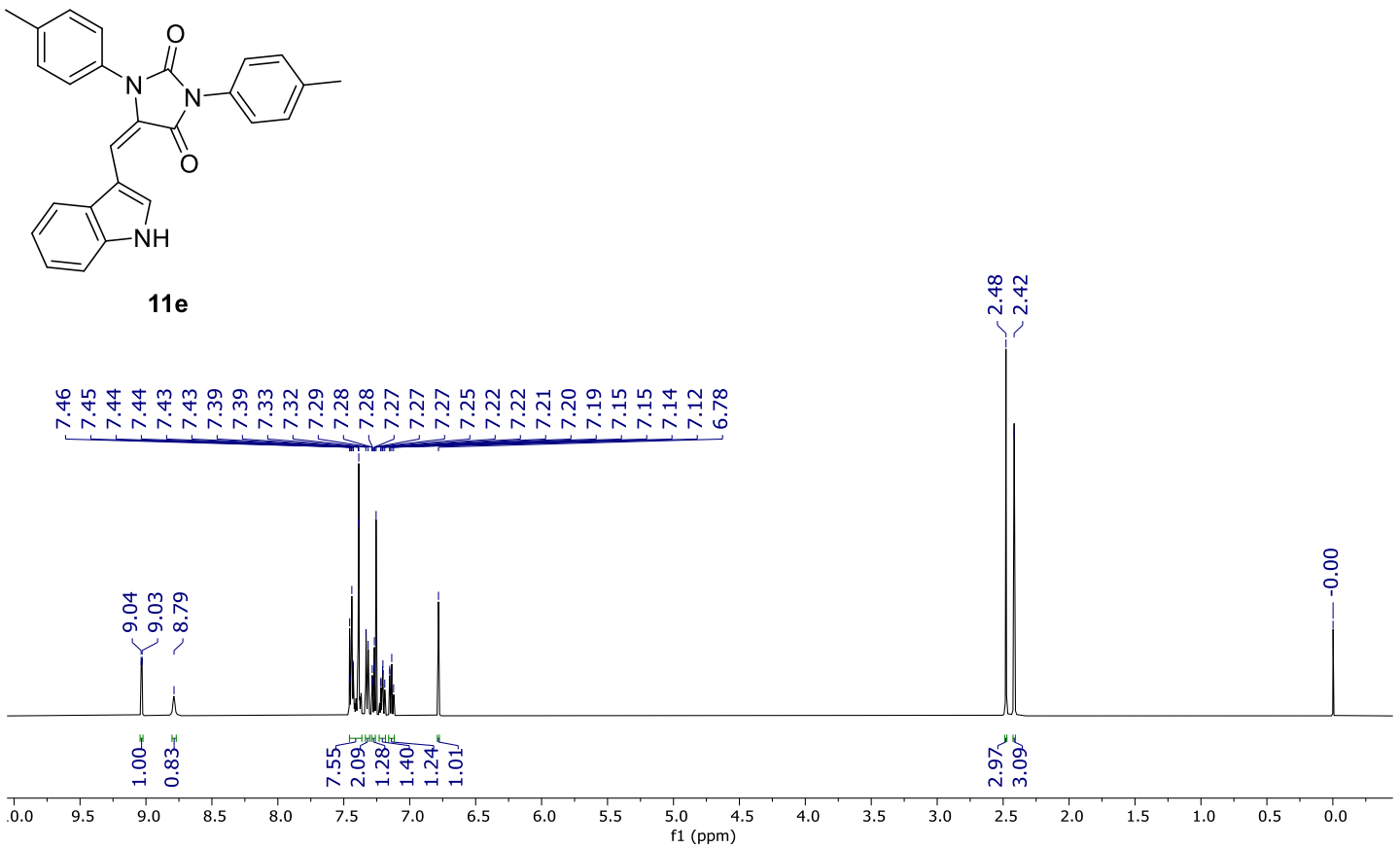



Figure S148. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **11e**.

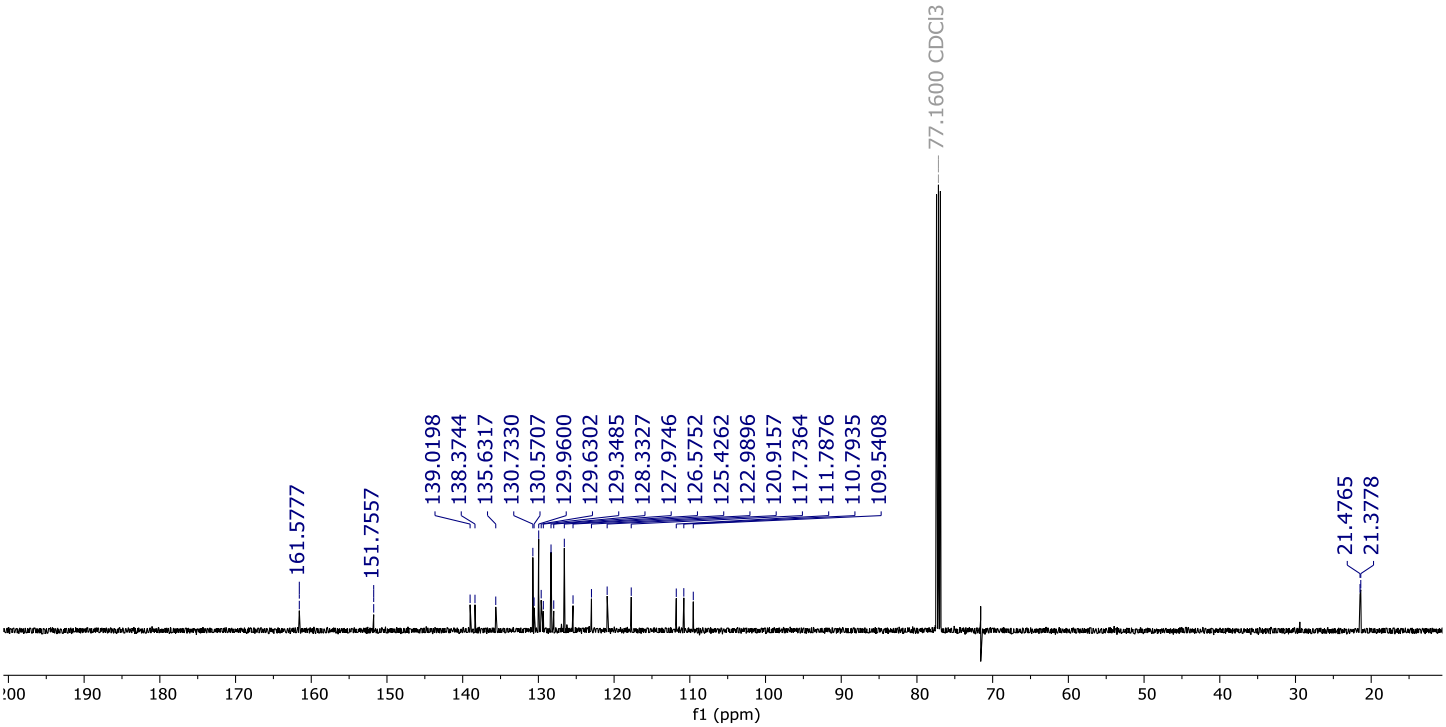



Figure S149. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **11e**.

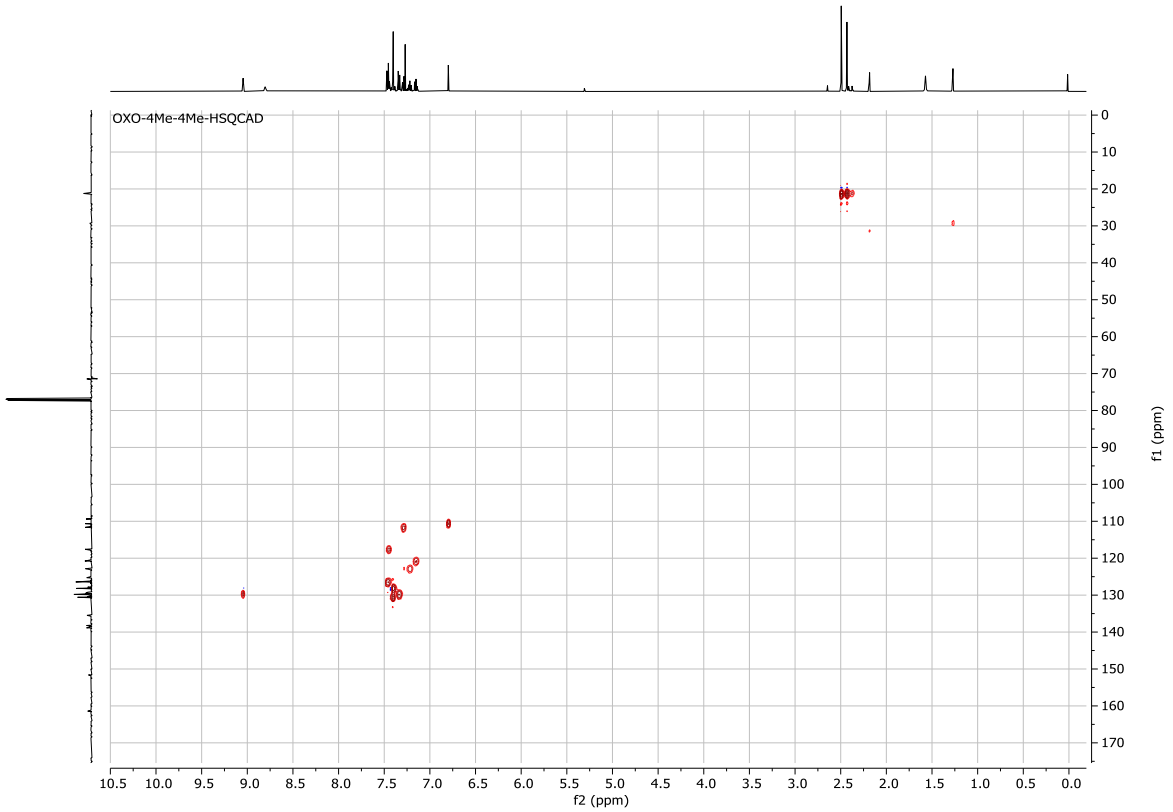



Figure S150. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11e.**

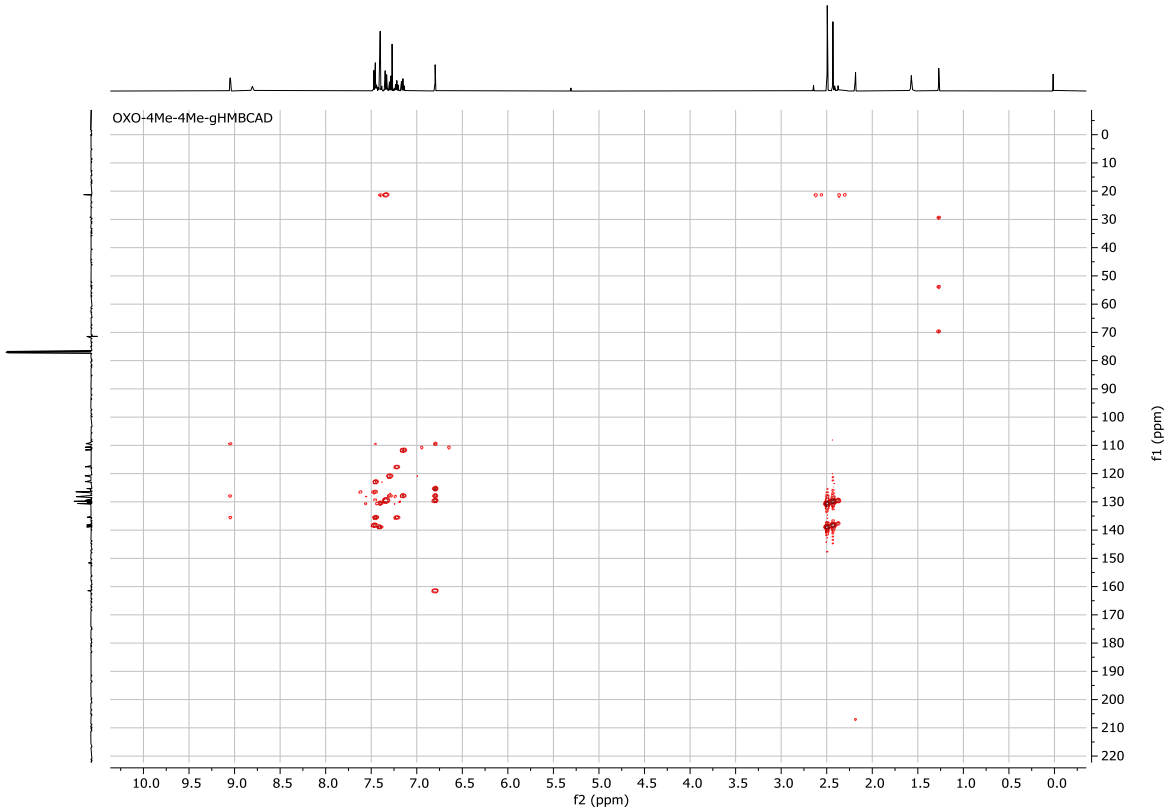
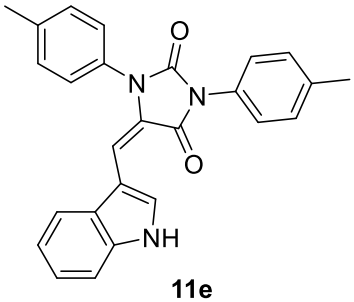



Figure S151. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11e.**




**11e**

Chemical Formula: $C_{26}H_{21}N_3O_2$
Exact Mass: 407.1634

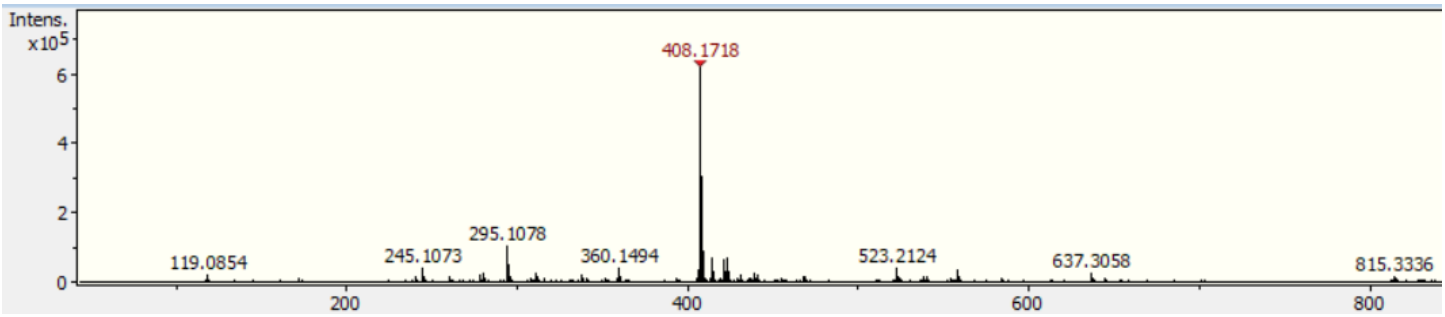



Figure S152. HRMS of compound **11e.**

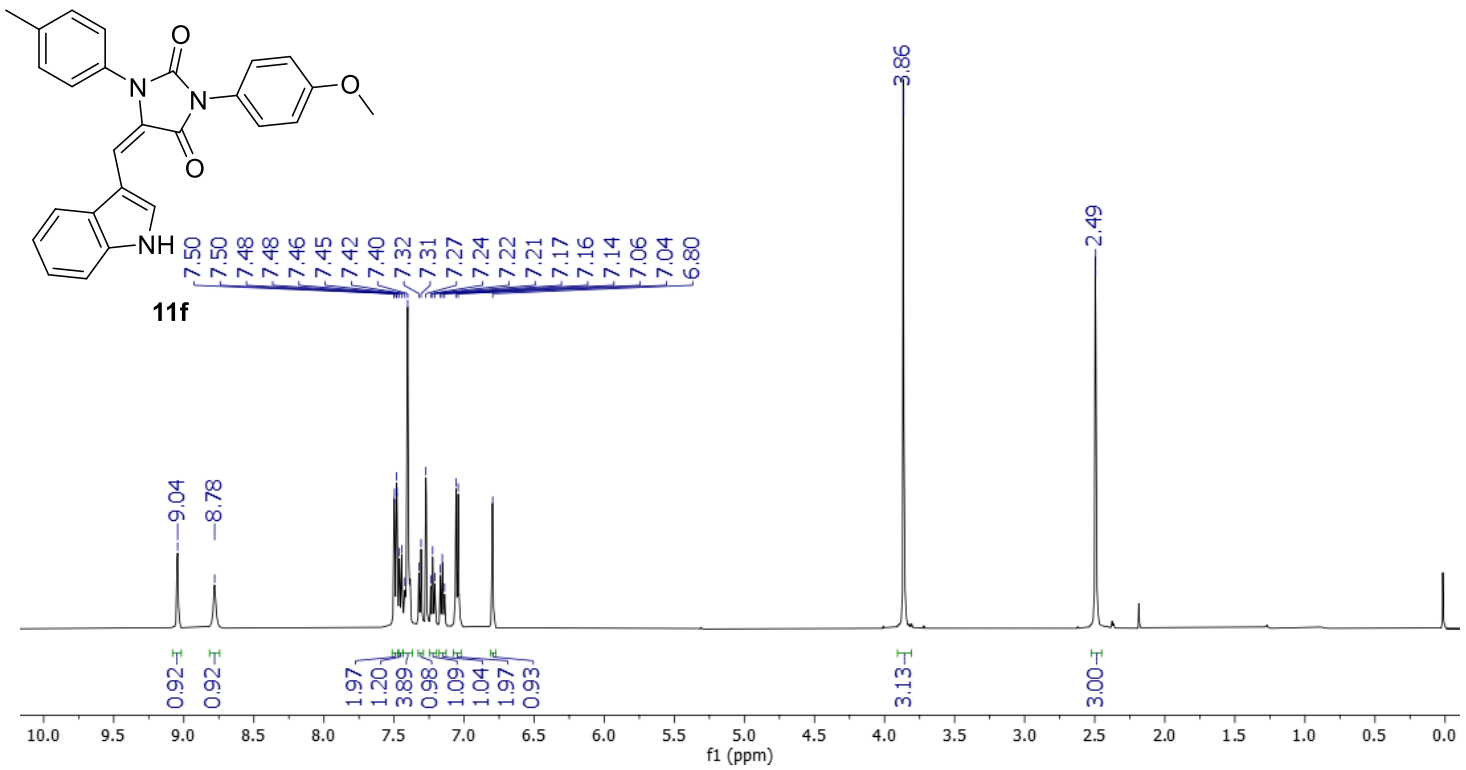



Figure S153. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **11f**.

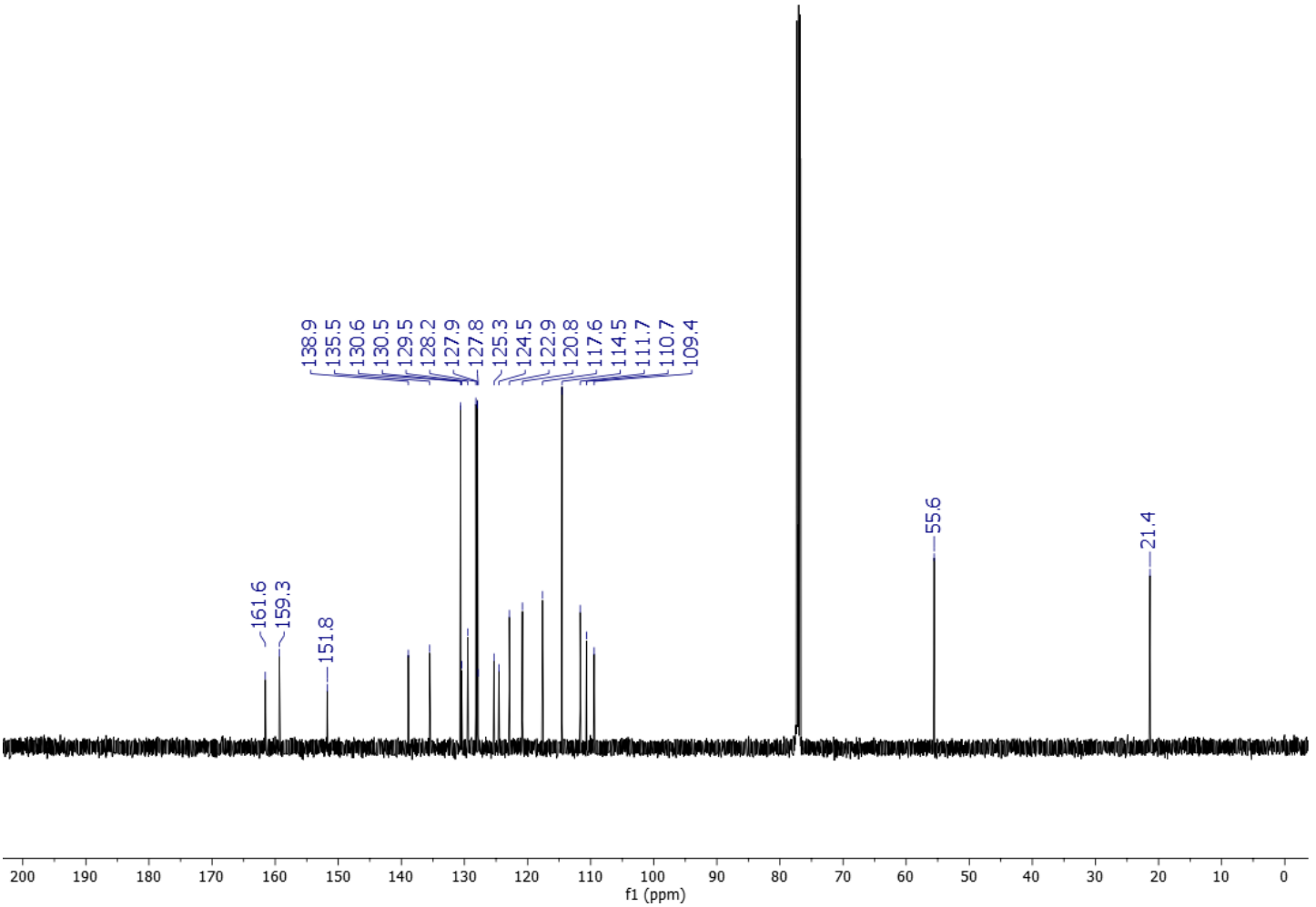



Figure S154. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **11f**.

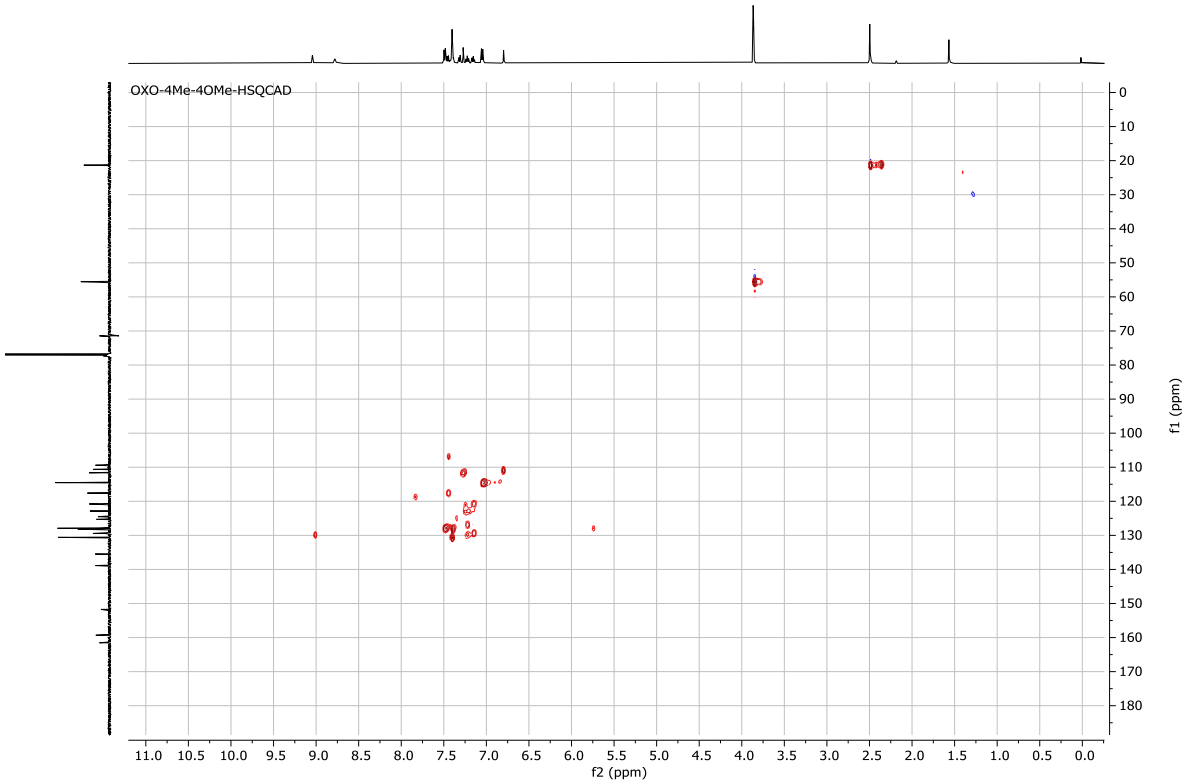



Figure S155. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11f.**

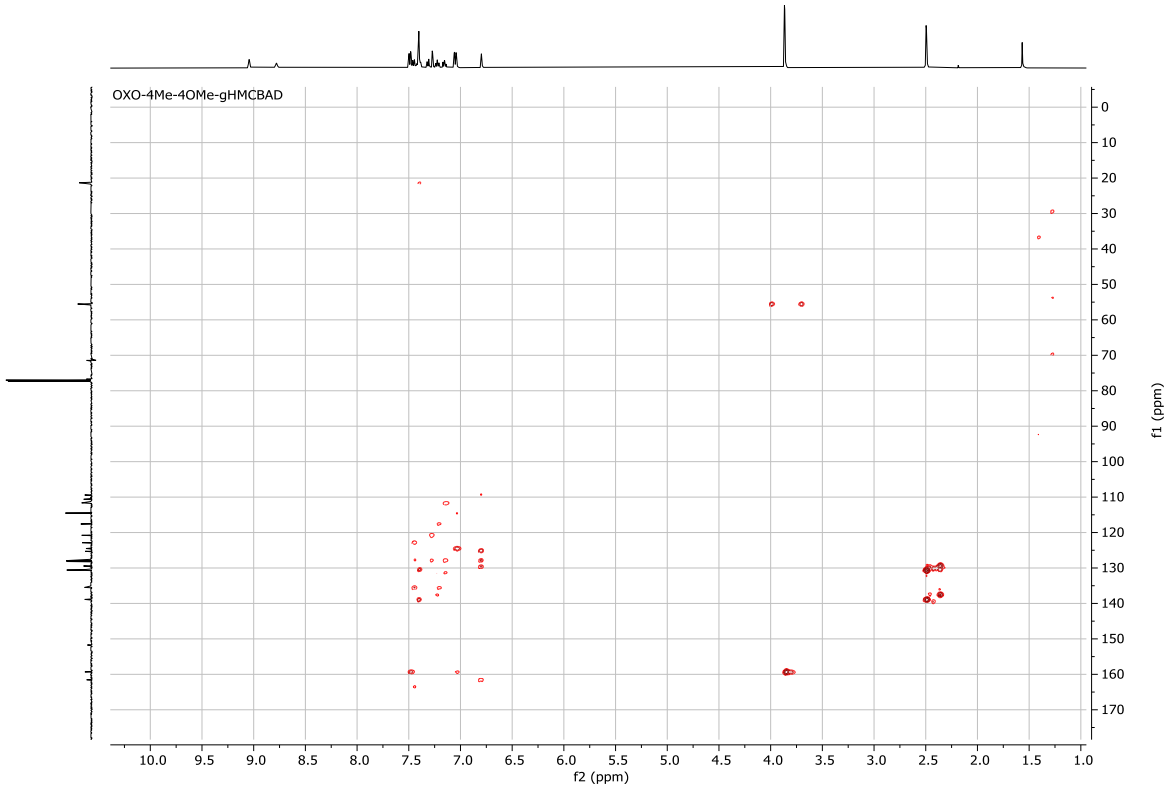



Figure S156. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11f.**

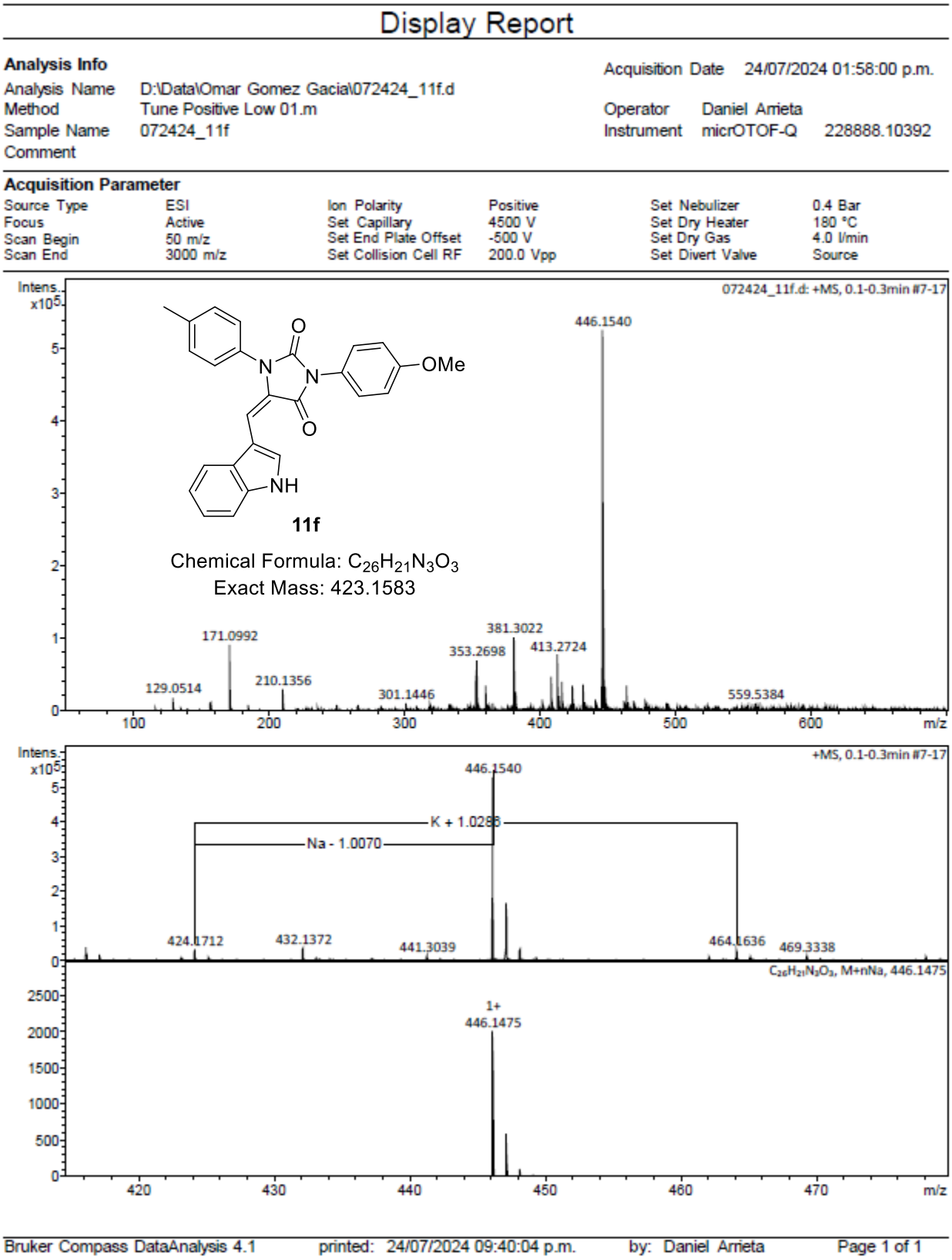



Figure S157. HRMS of compound **11f.**

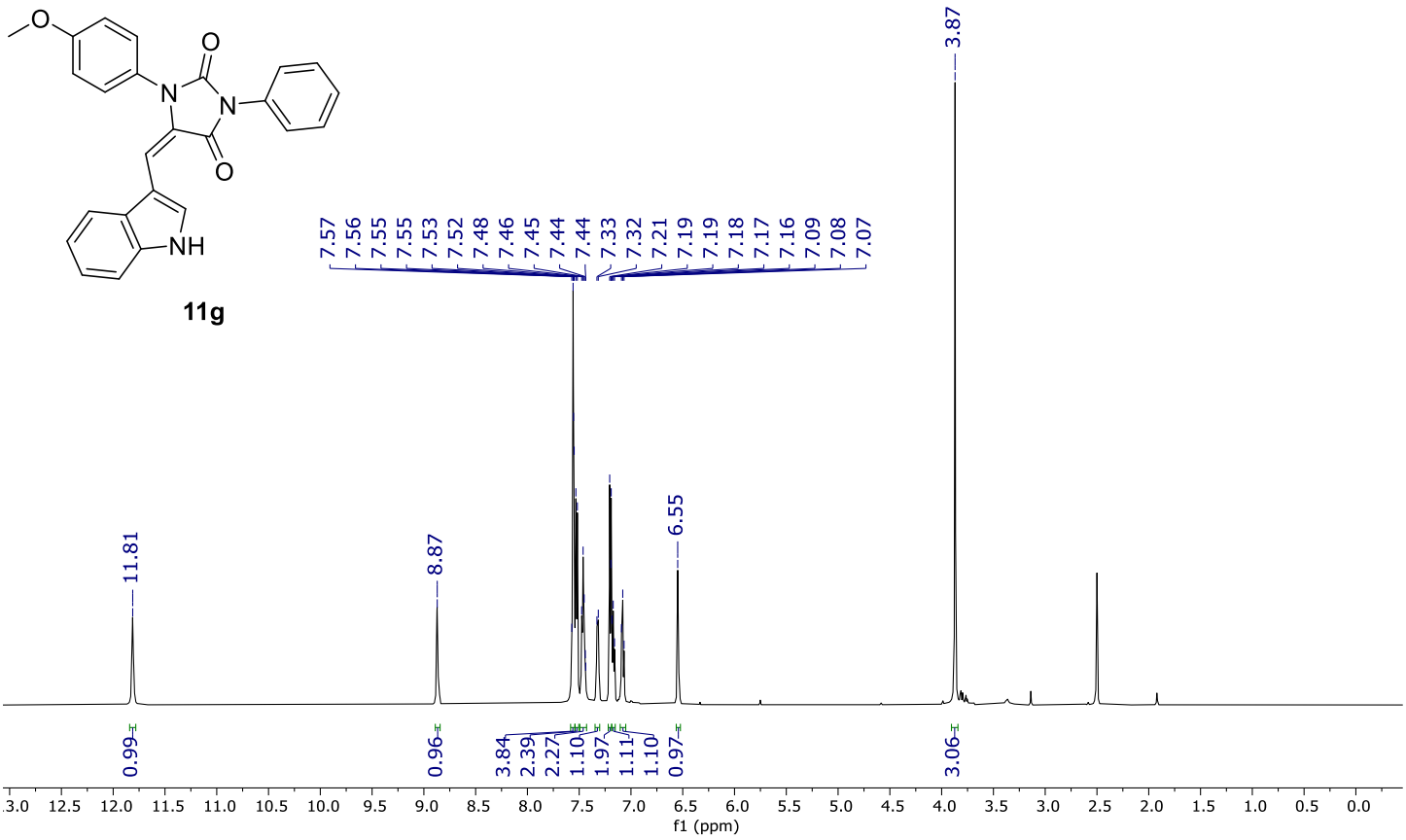



Figure S158. $^{1}$H NMR (500 MHz, DMSO-$d_6$) spectrum of compound **11g**.

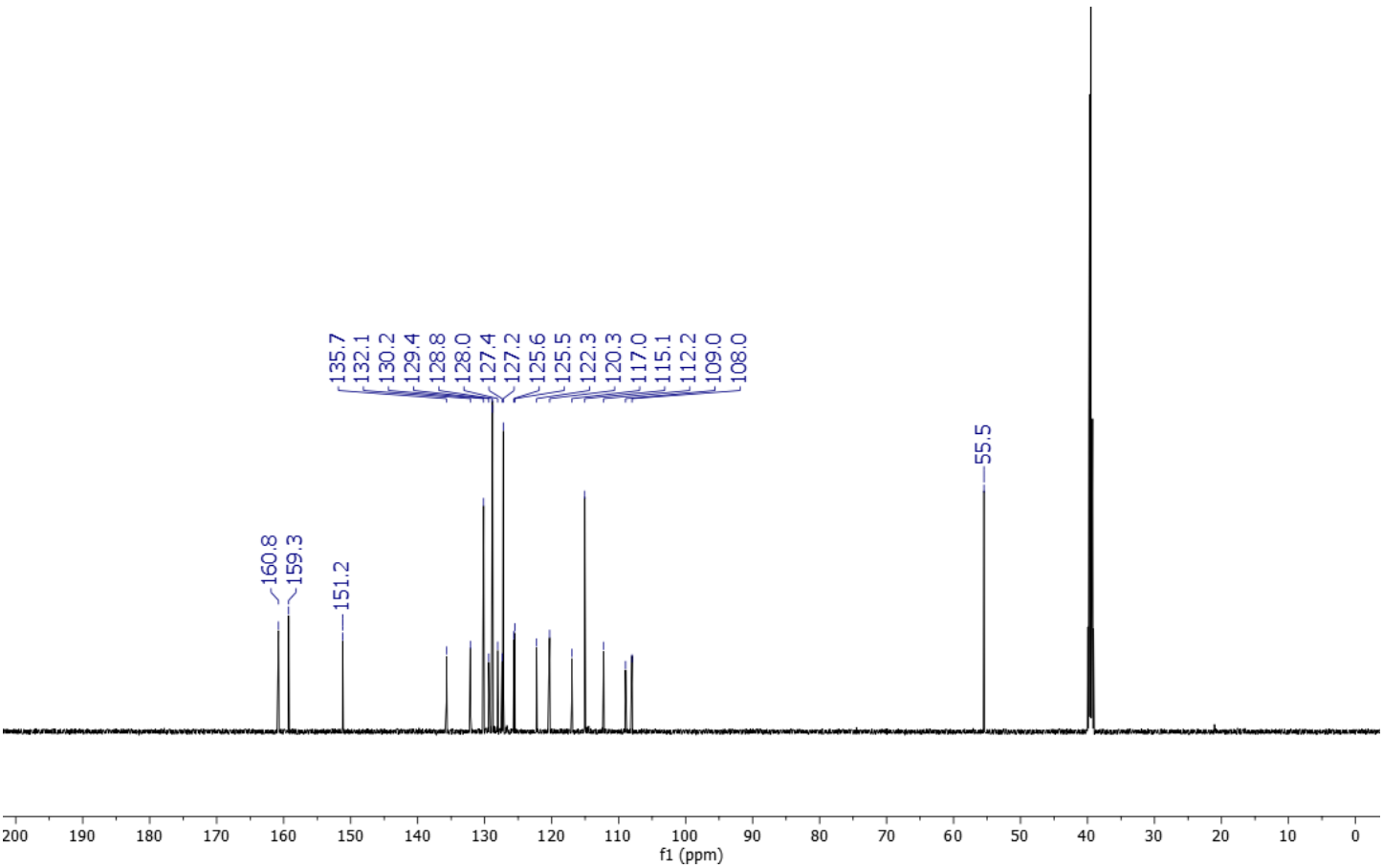



Figure S159. $^{13}$C NMR (125 MHz, DMSO-$d_6$) spectrum of compound **11g**.

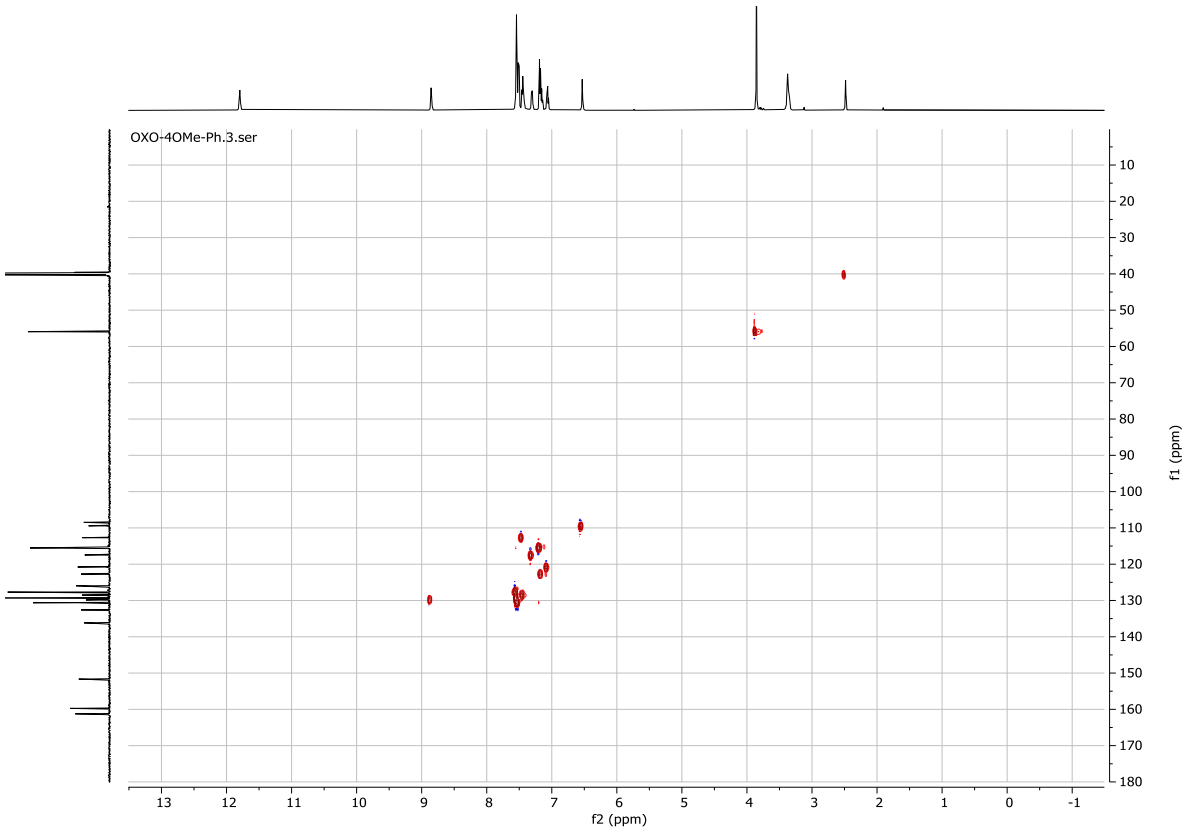



Figure S160. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11g.**

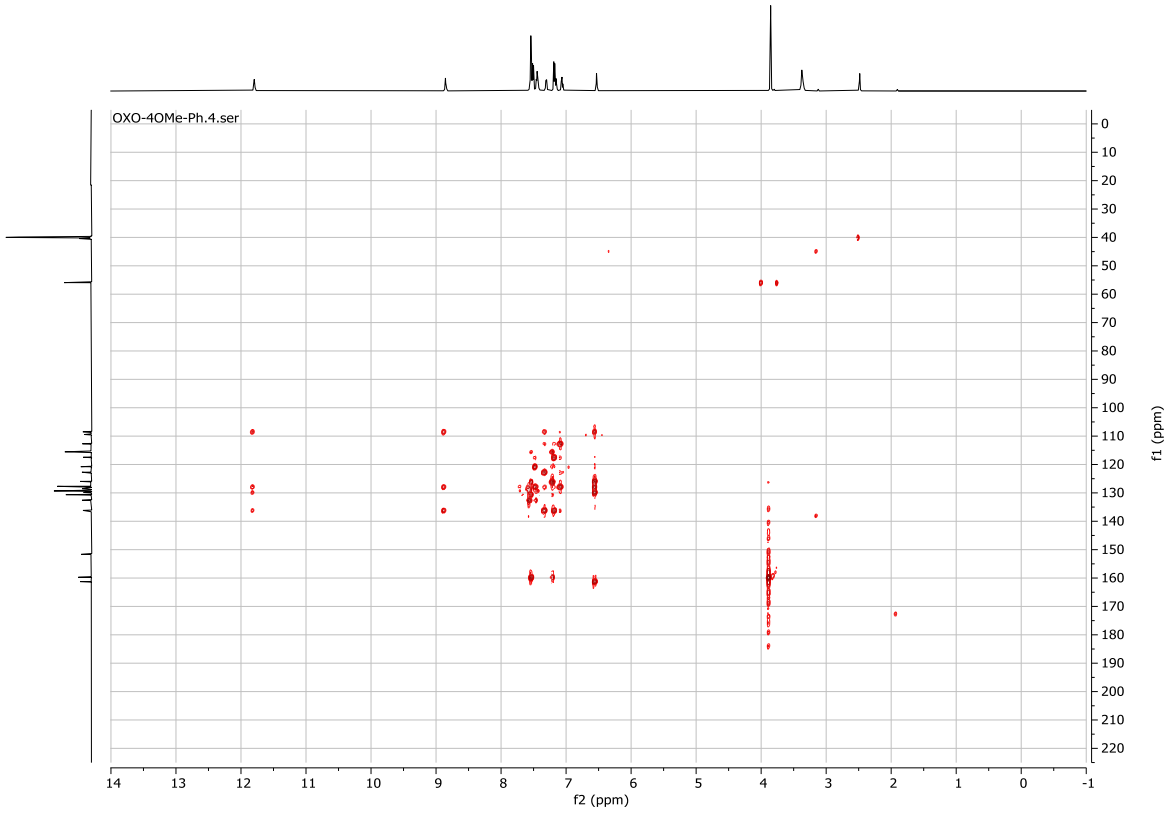
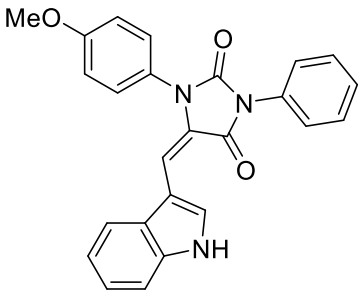



Figure S161. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11g.**




**11g**

Chemical Formula: $C_{25}H_{19}N_3O_3$
Exact Mass: 409.1426

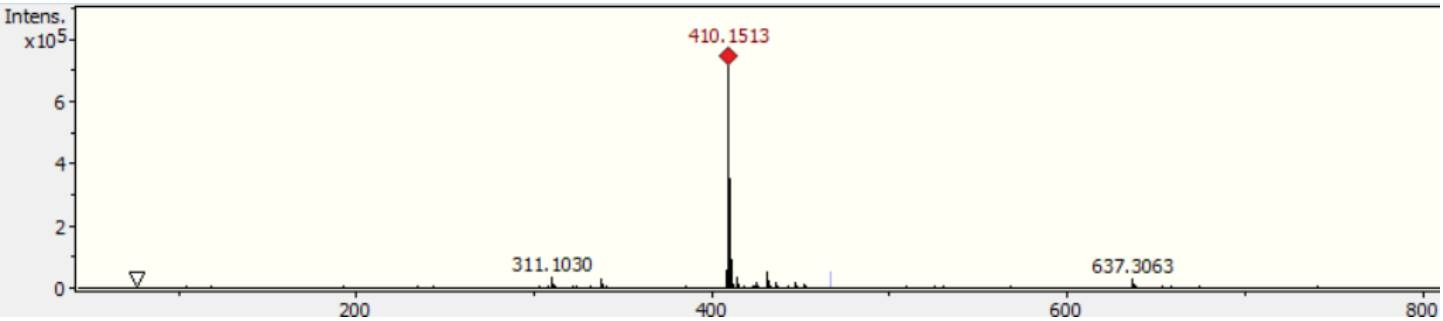



Figure S162. HRMS of compound **11g.**

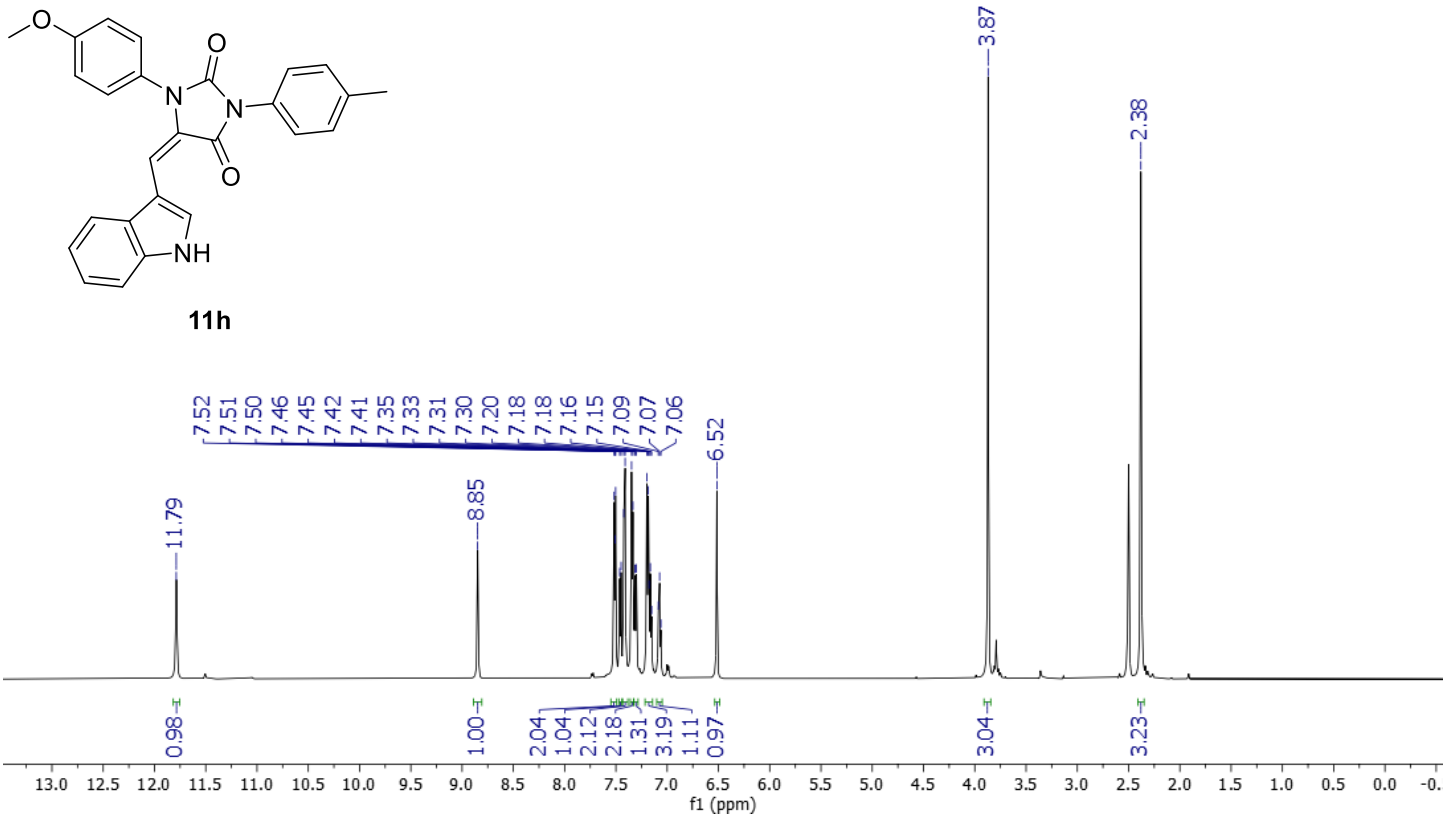



Figure S163. $^{1}$H NMR (500 MHz, DMSO-$d_6$) spectrum of compound **11h**.

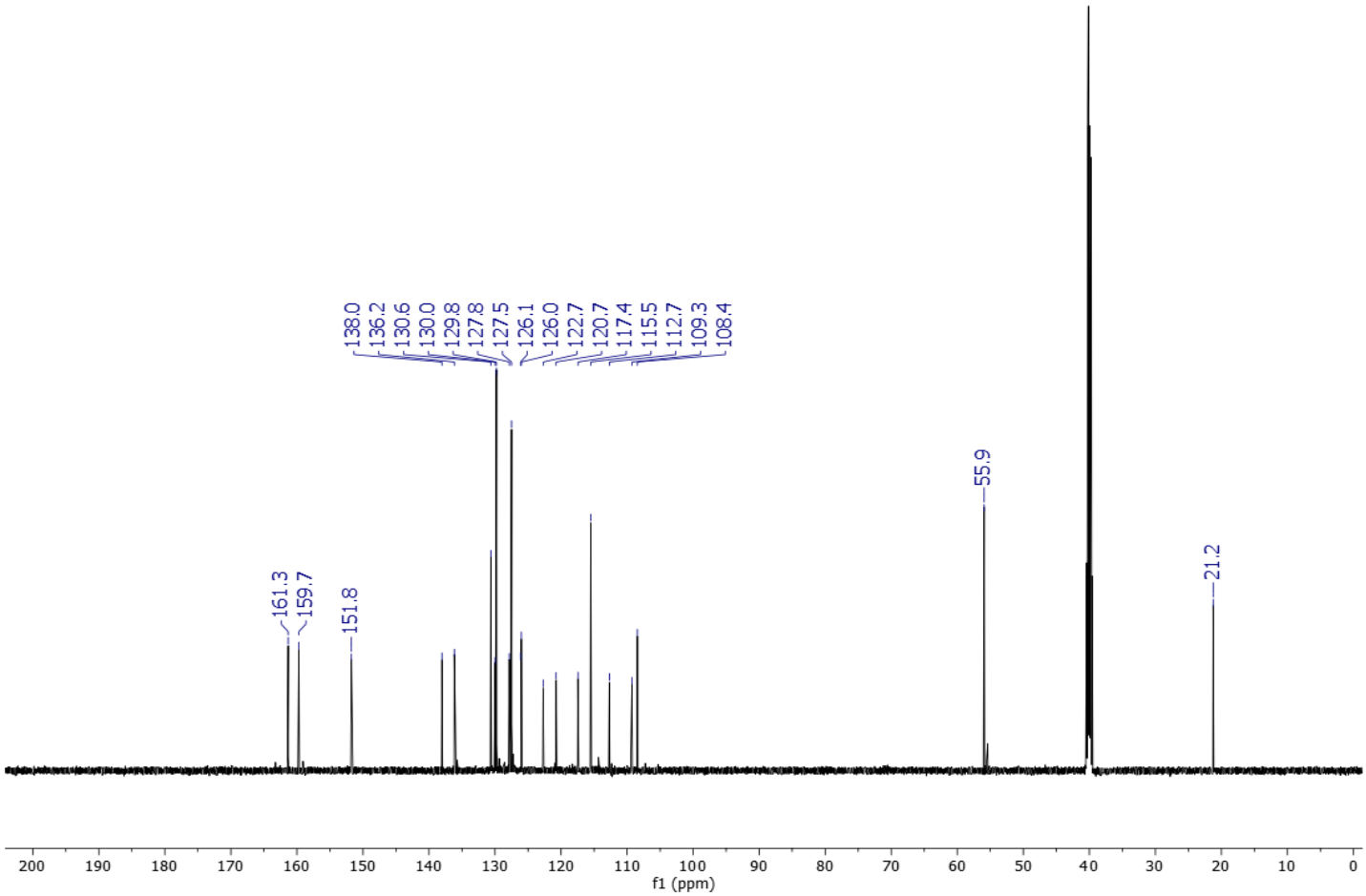



Figure S164. $^{13}$C NMR (125 MHz, DMSO-$d_6$) spectrum of compound **11h**.

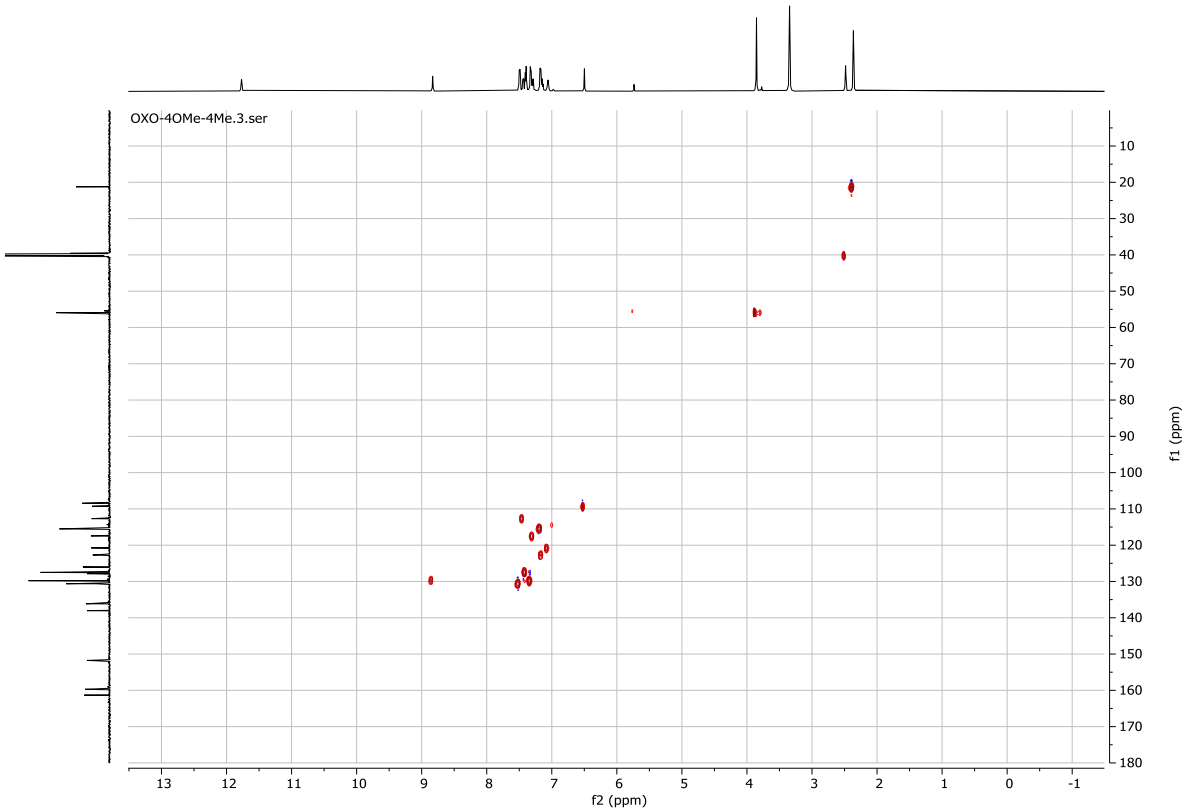



Figure S165. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11h.**

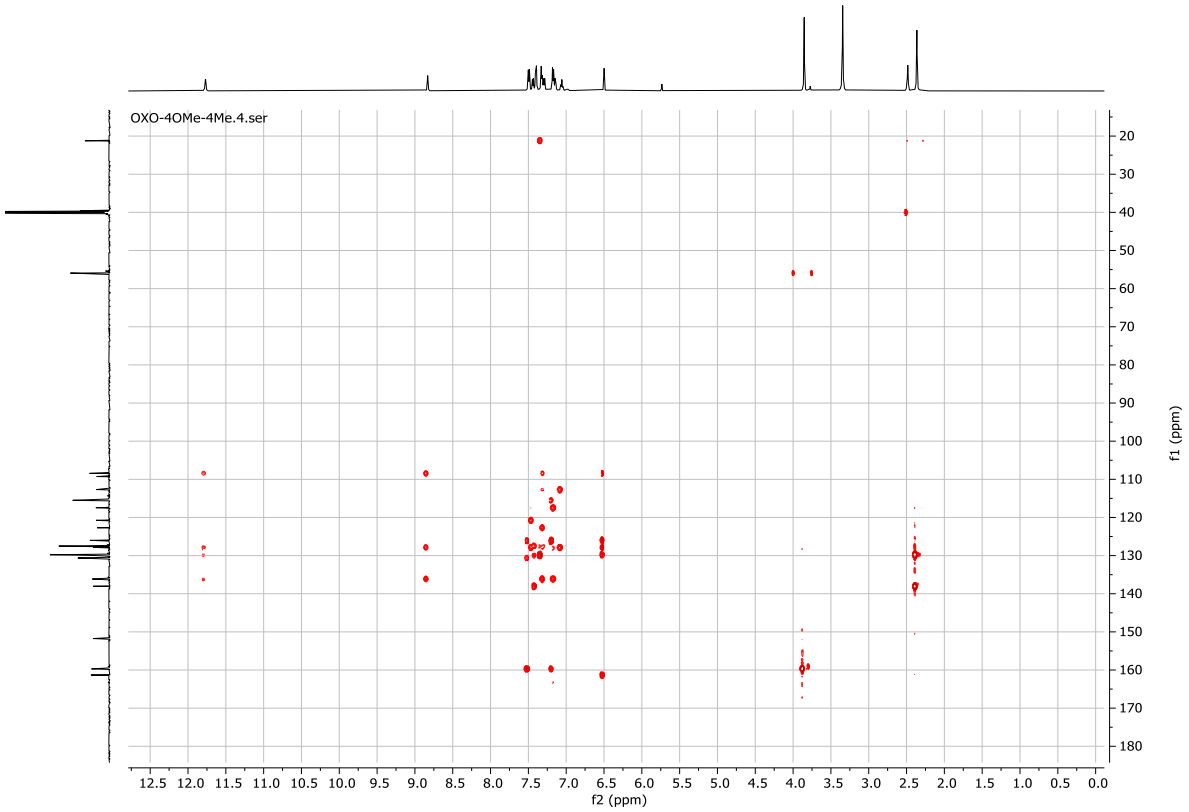



Figure S166. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11h.**

# Display Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\Omar Gomez Gacia\072424_11h.d | Acquisition Date | 24/07/2024 03:27:00 p.m. |
| Method | Tune Positive Low 01.m | Operator | Daniel Arrieta |
| Sample Name | 072424_11h | Instrument | micrOTOF-Q 228888.10392 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.4 Bar |
| Focus | Active | Set Capillary | 4500 V | Set Dry Heater | 180 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 200.0 Vpp | Set Divert Valve | Source |

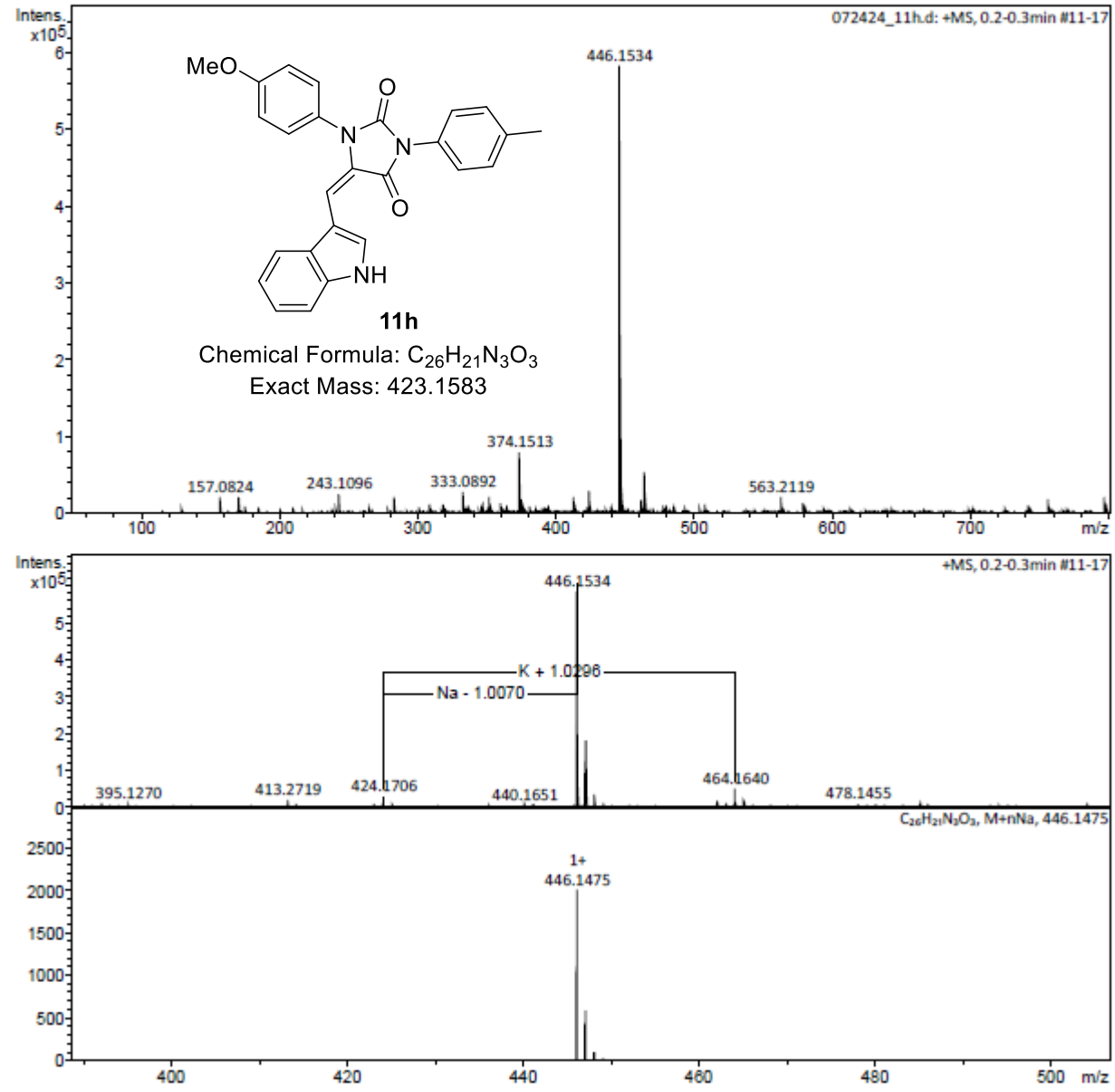





Figure S167. HRMS of compound **11h.**

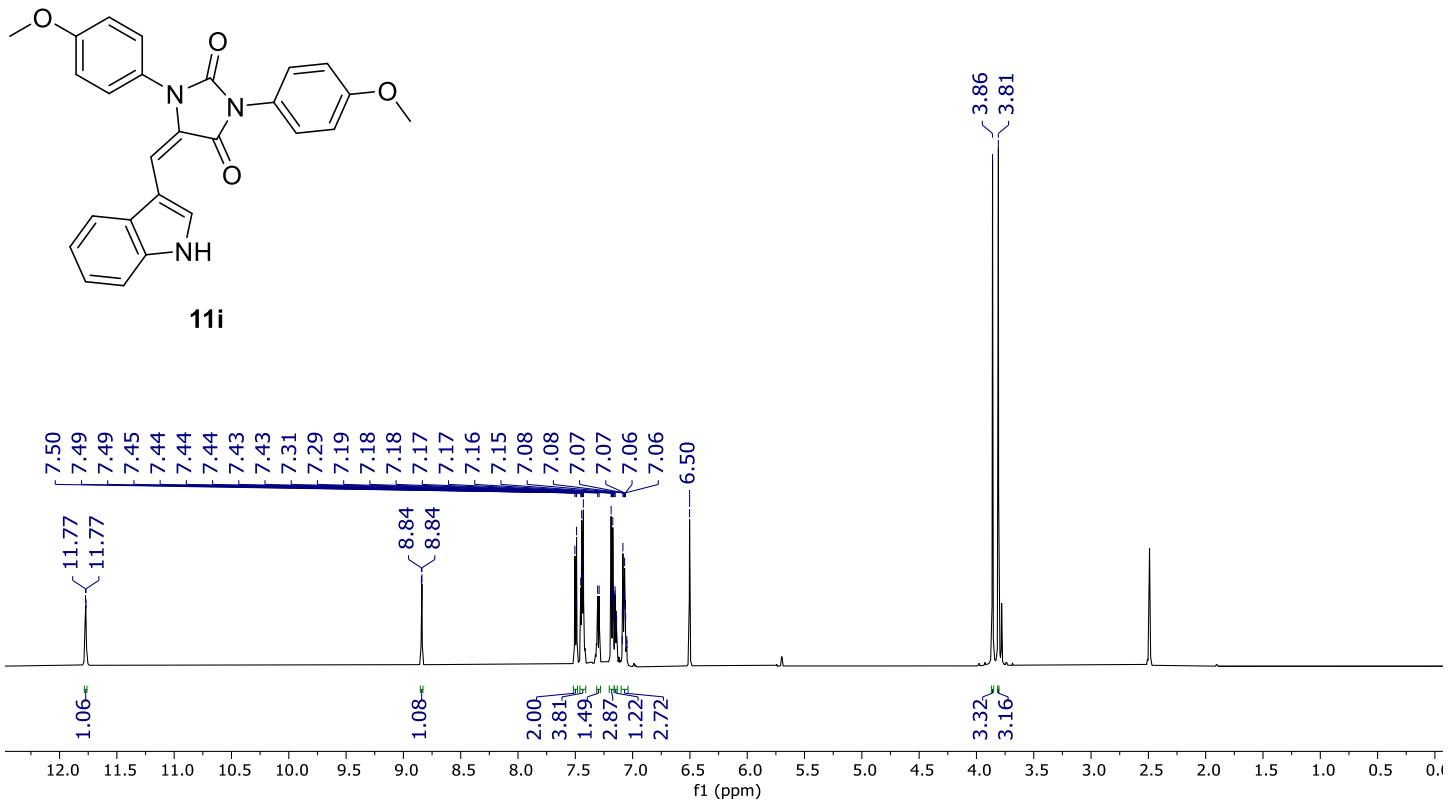



Figure S168. $^{1}$H NMR (500 MHz, DMSO-$d_6$) spectrum of compound **11i**.

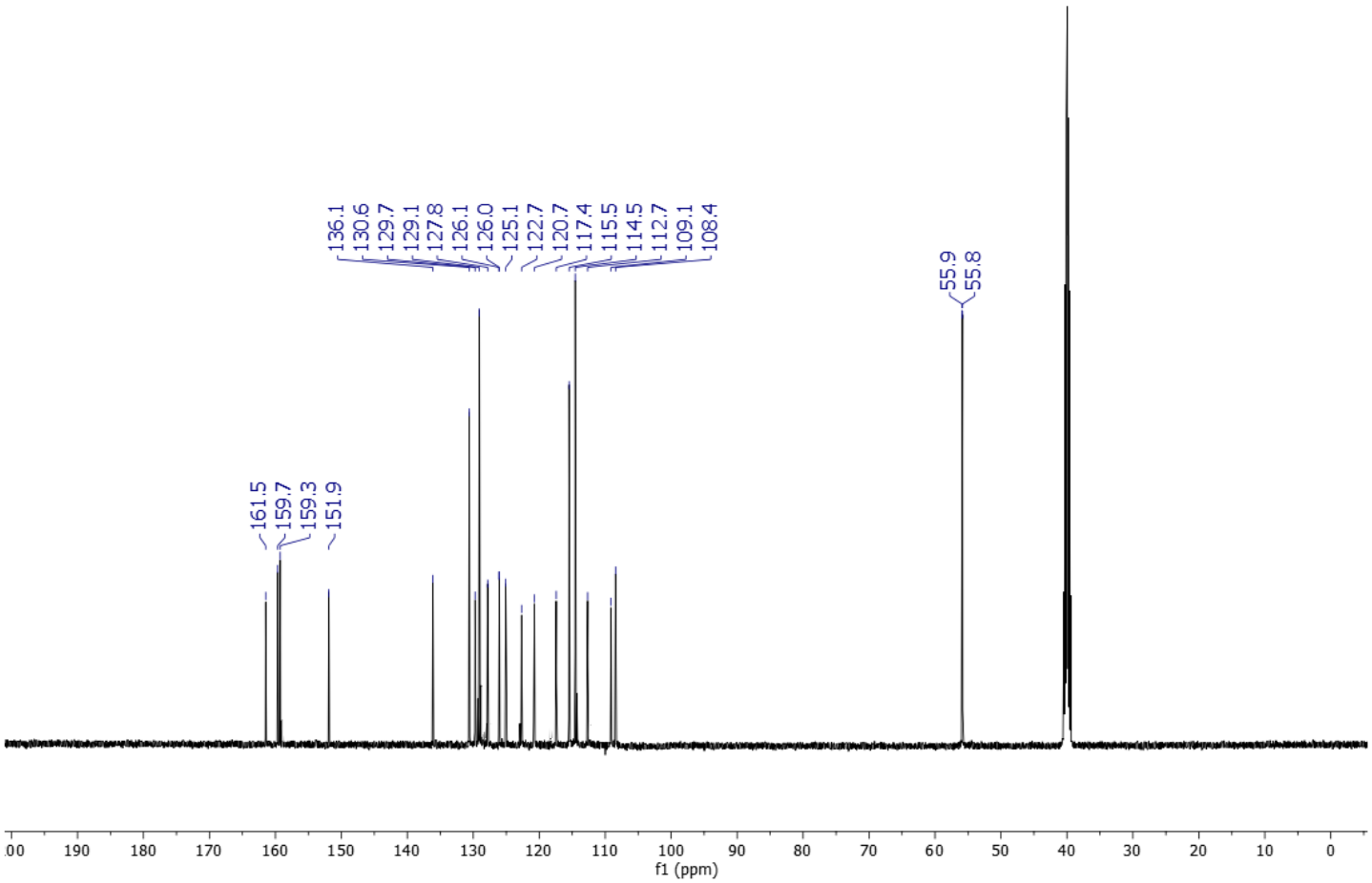



Figure S169. $^{13}$C NMR (125 MHz, DMSO-$d_6$) spectrum of compound **11i**.

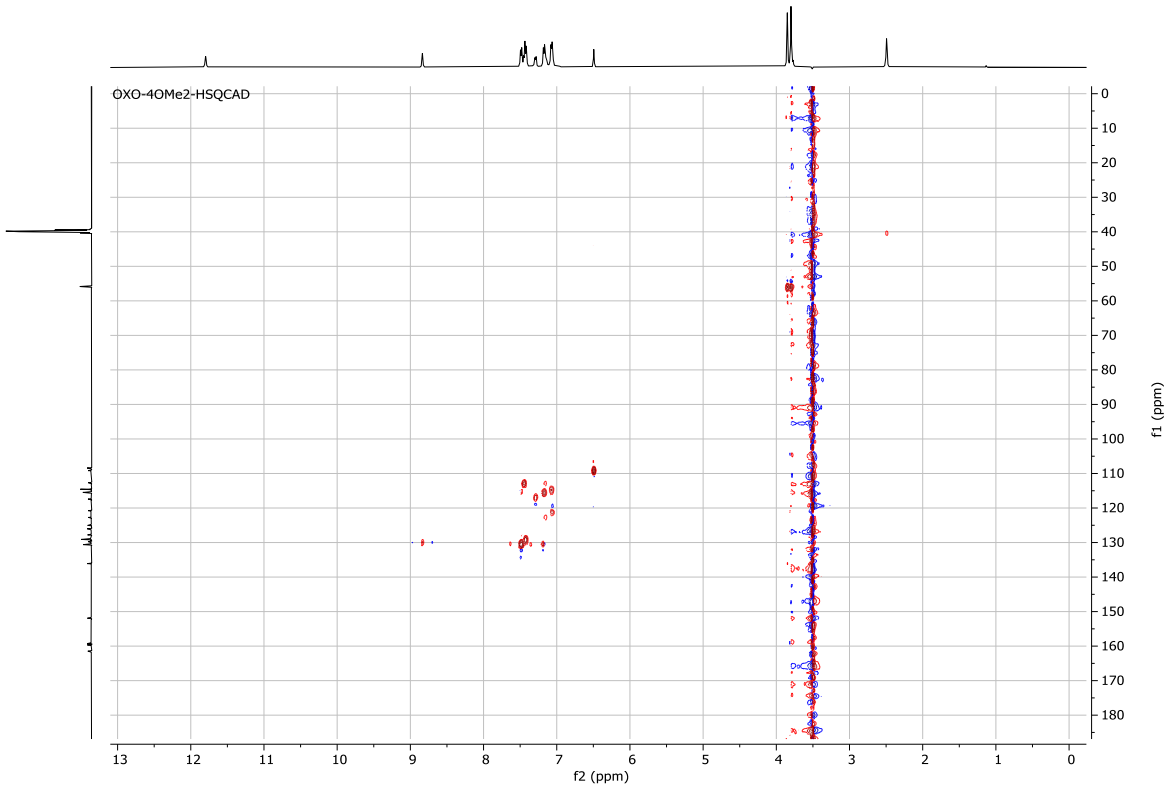



Figure S170. HSQC (500 MHz, $CDCl_3$) spectrum of compound **11i.**

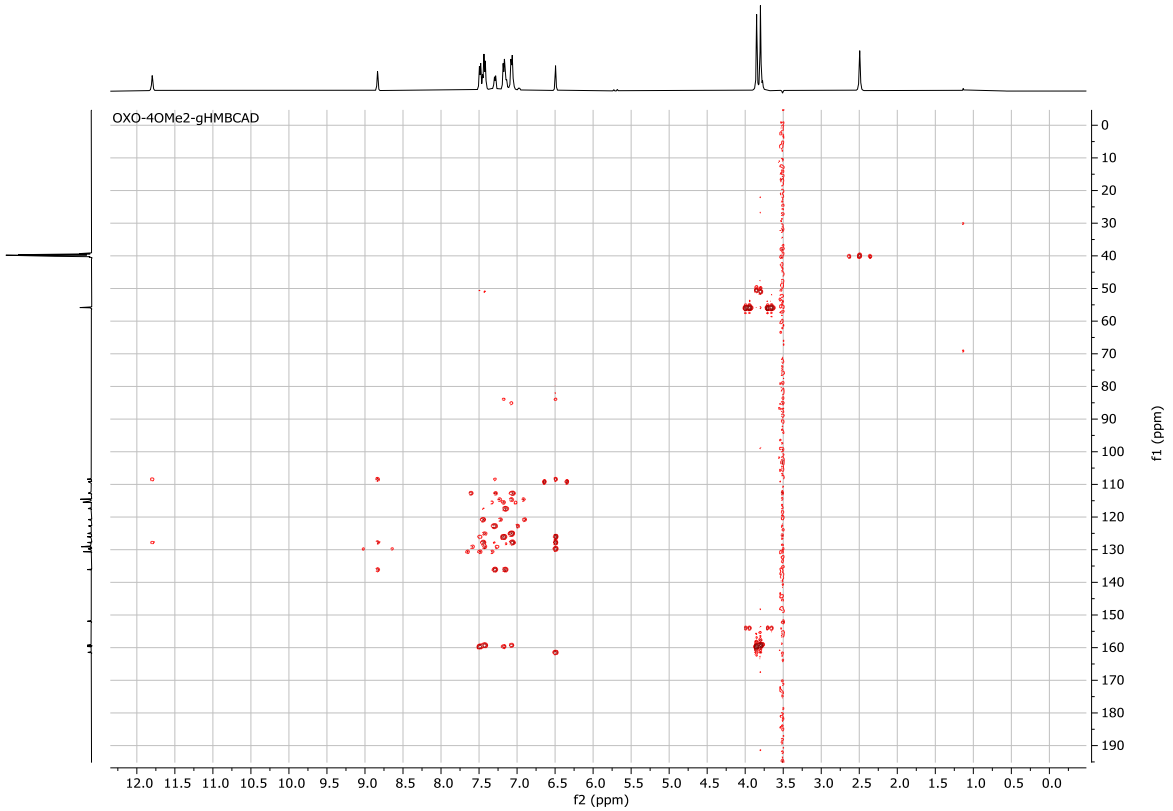
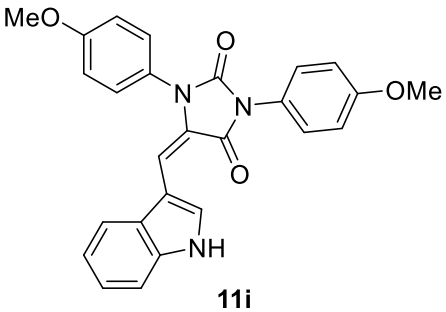



Figure S171. HMBC (500 MHz, $CDCl_3$) spectrum of compound **11i.**




**11i**

Chemical Formula: $C_{26}H_{21}N_3O_4$

Exact Mass: 439.1532

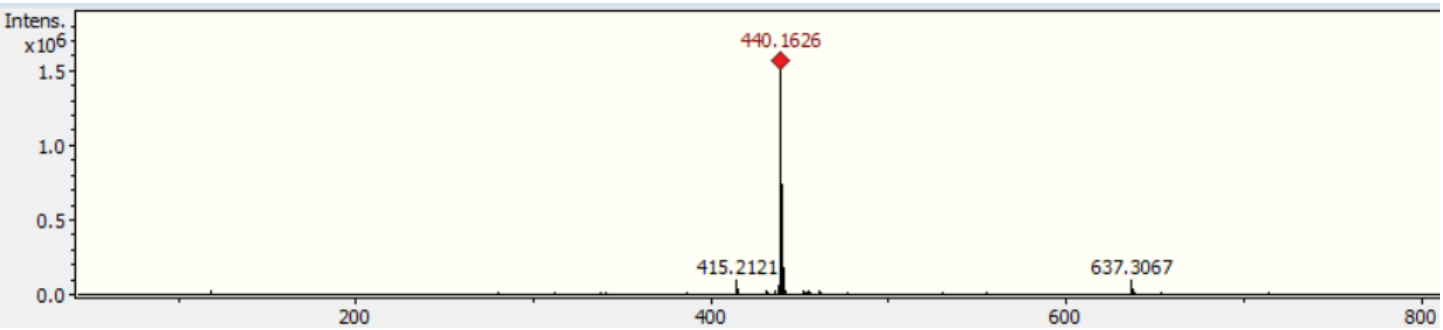



Figure S172. HRMS of compound **11i.**

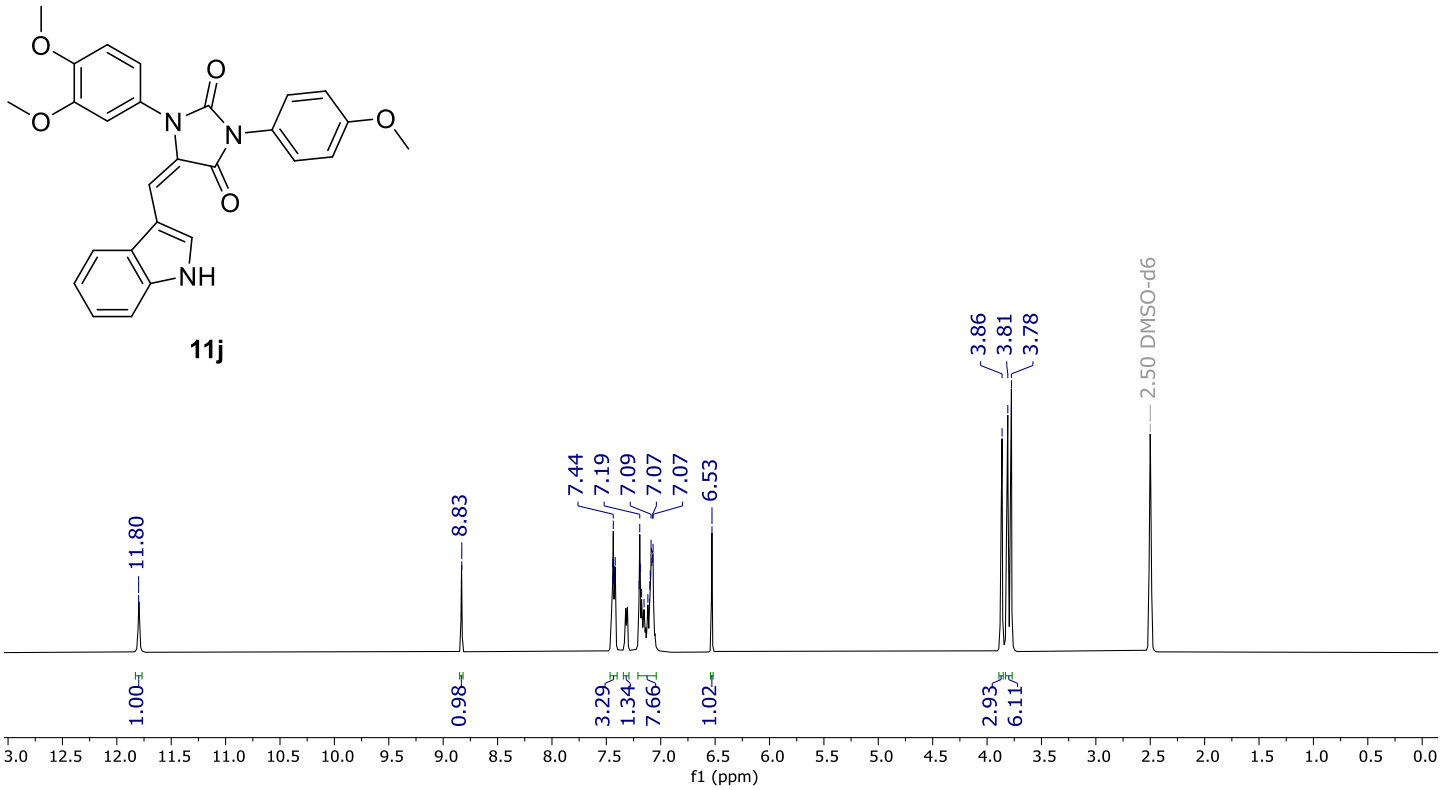



Figure S173. $^{1}$H NMR (500 MHz, DMSO-$d_6$) spectrum of compound **11j**.

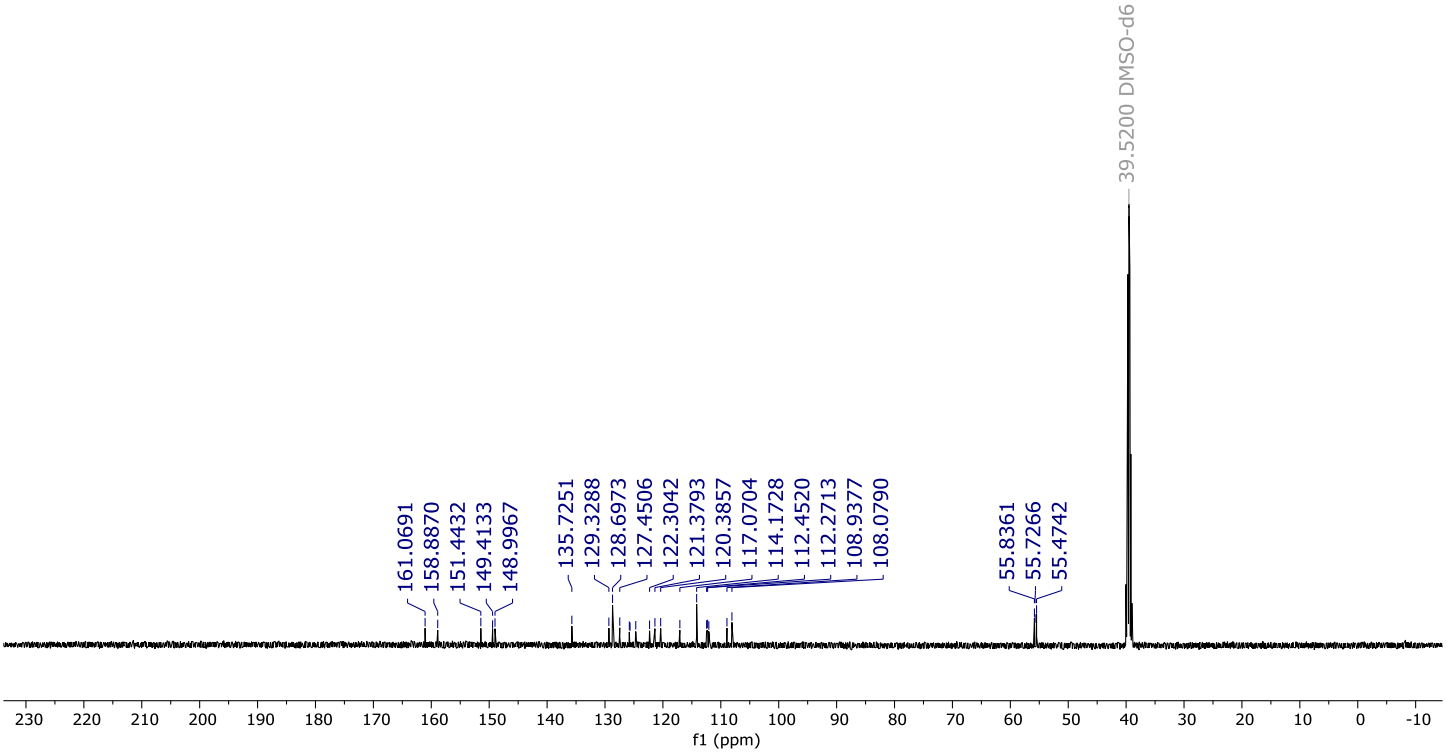



Figure S174. $^{13}$C NMR (125 MHz, DMSO-$d_6$) spectrum of compound **11j**.

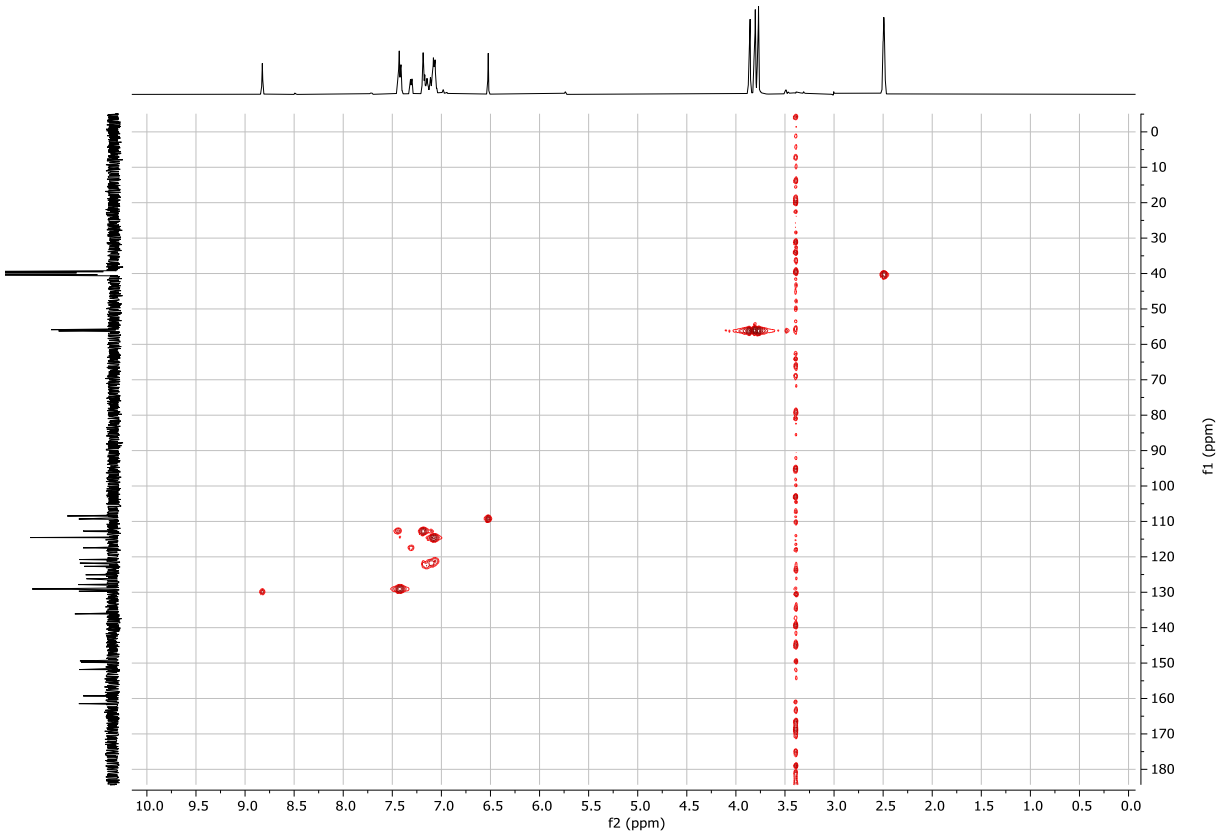



Figure S175. HSQC (500 MHz, DMSO-$d_6$) spectrum of compound **11j.**

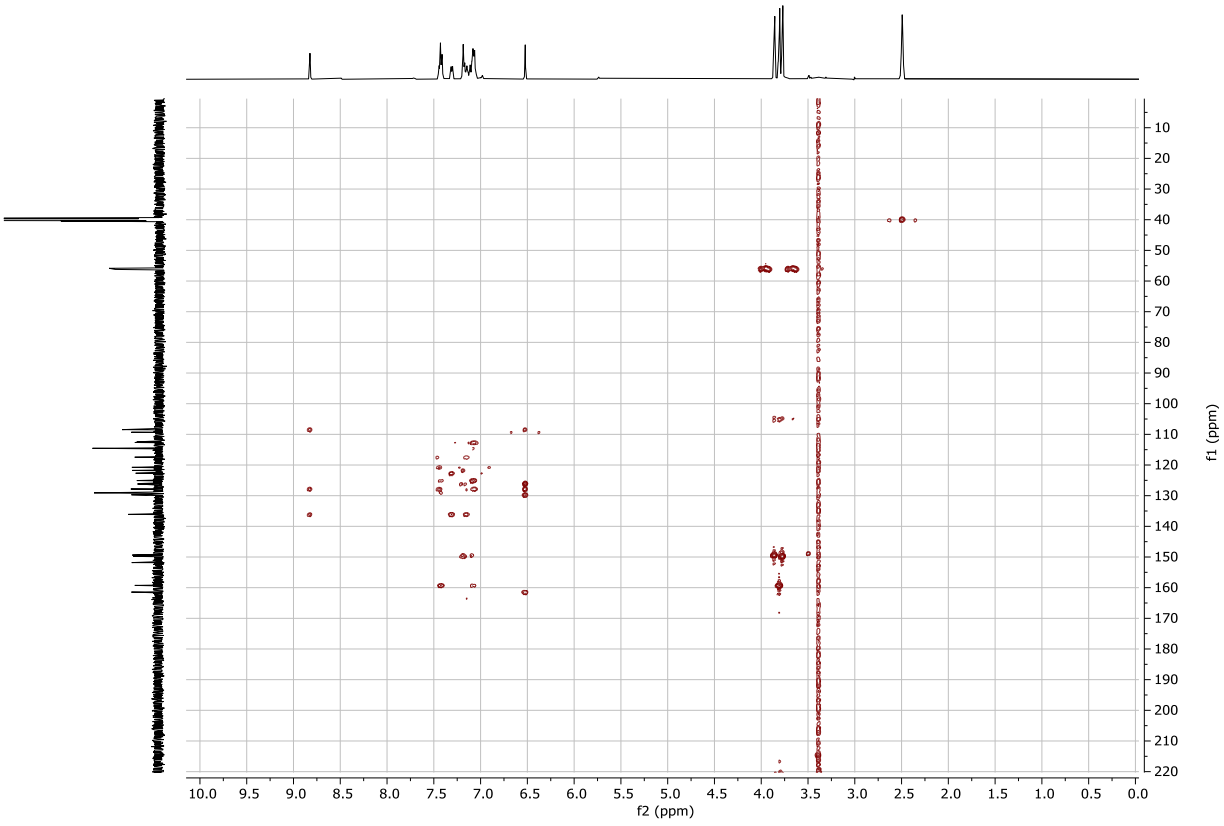
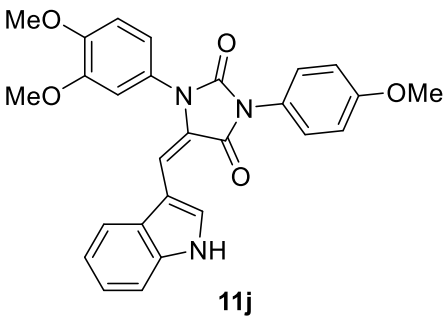



Figure S176. HMBC (500 MHz, DMSO-$d_6$) spectrum of compound **11j.**




**11j**

Chemical Formula: $C_{27}H_{23}N_3O_5$

Exact Mass: 469.1638

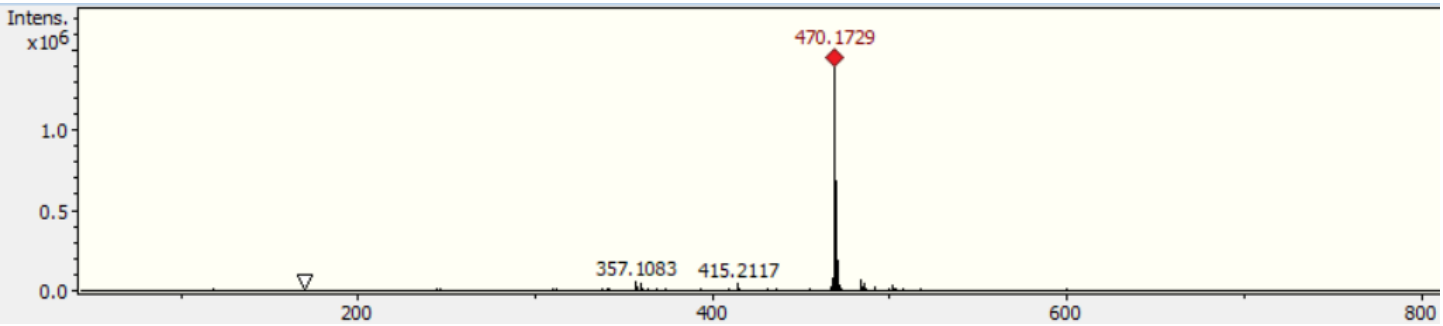



Figure S177. HRMS of compound **11j.**

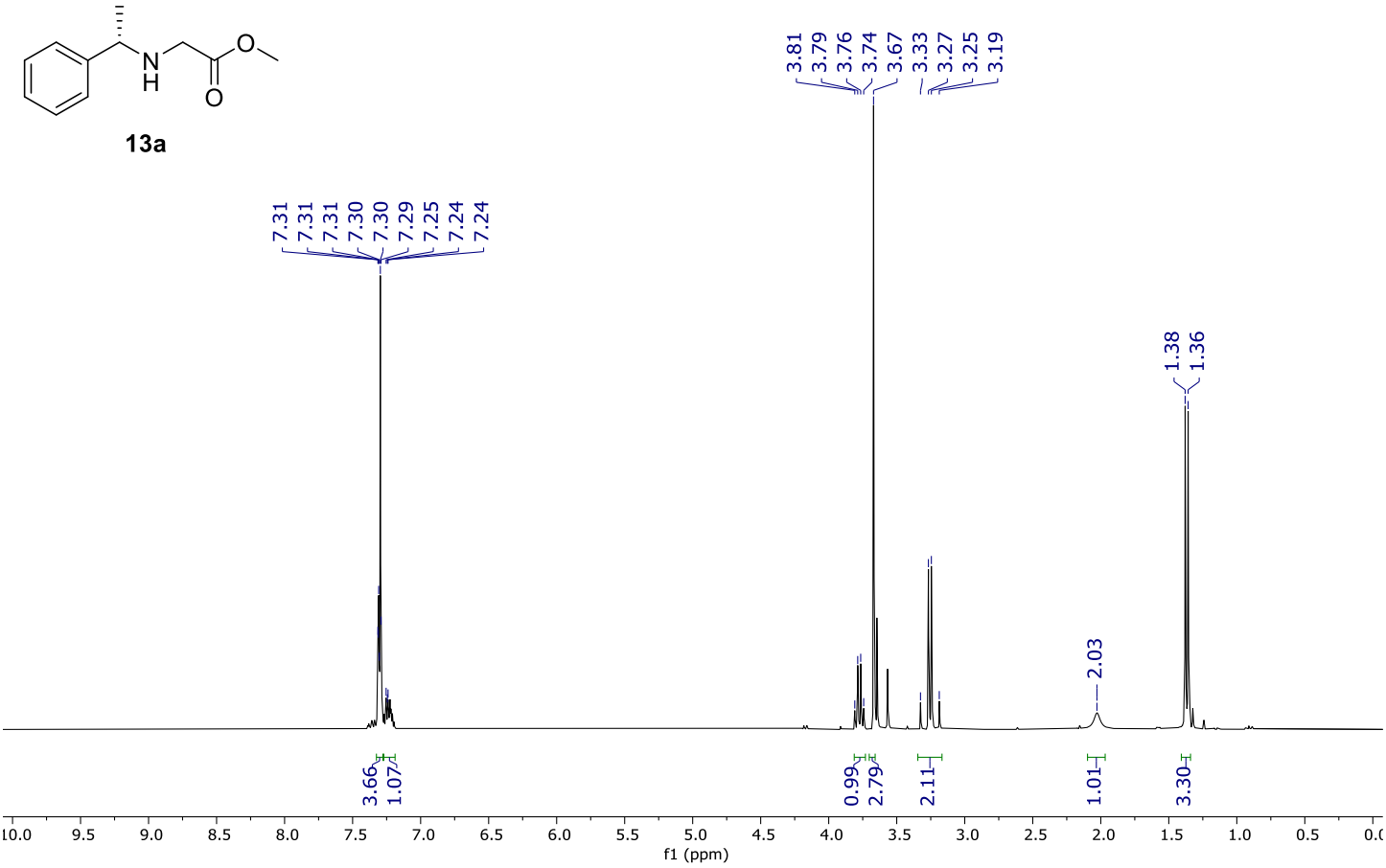



Figure S178. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **13**.

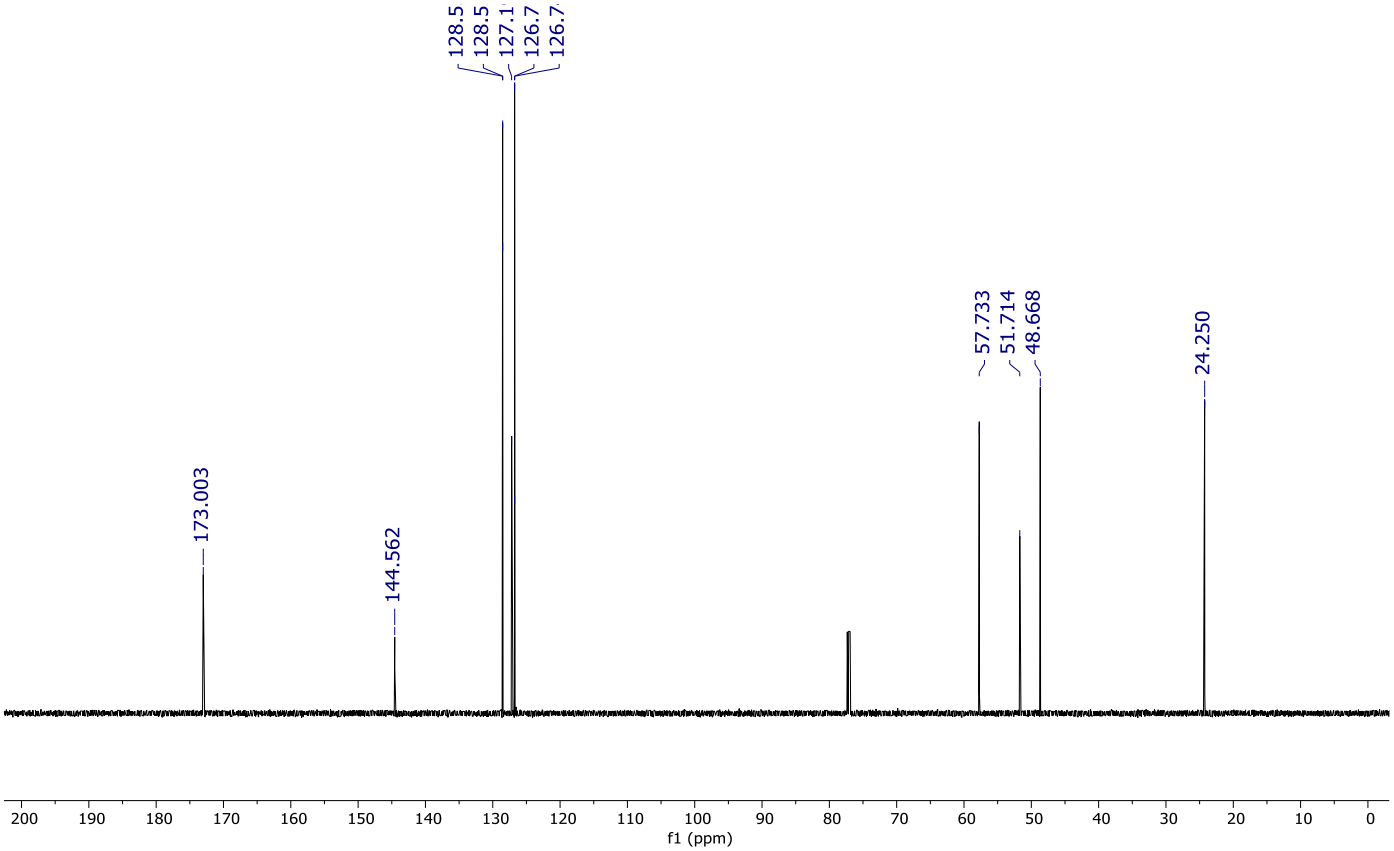
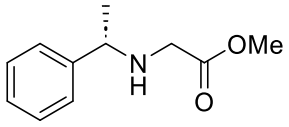



Figure S179. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **13**.




**13**

Chemical Formula: $C_{11}H_{15}NO_2$
Exact Mass: 193.1103

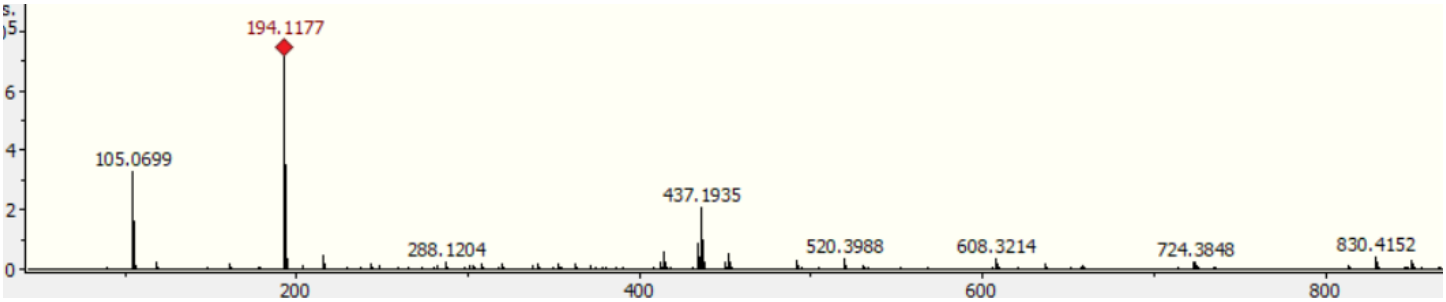



Figure S180. HRMS of compound **13.**

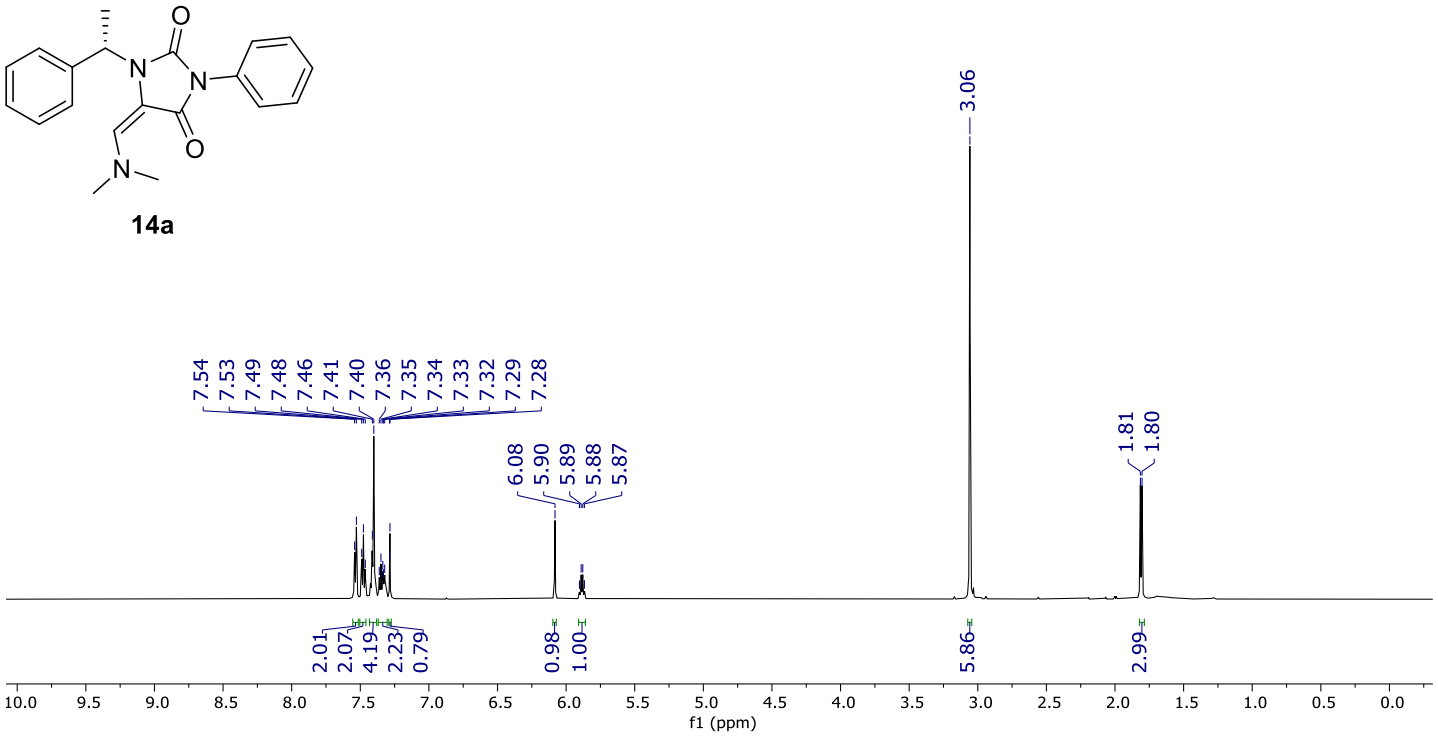



Figure S181. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **14a**.

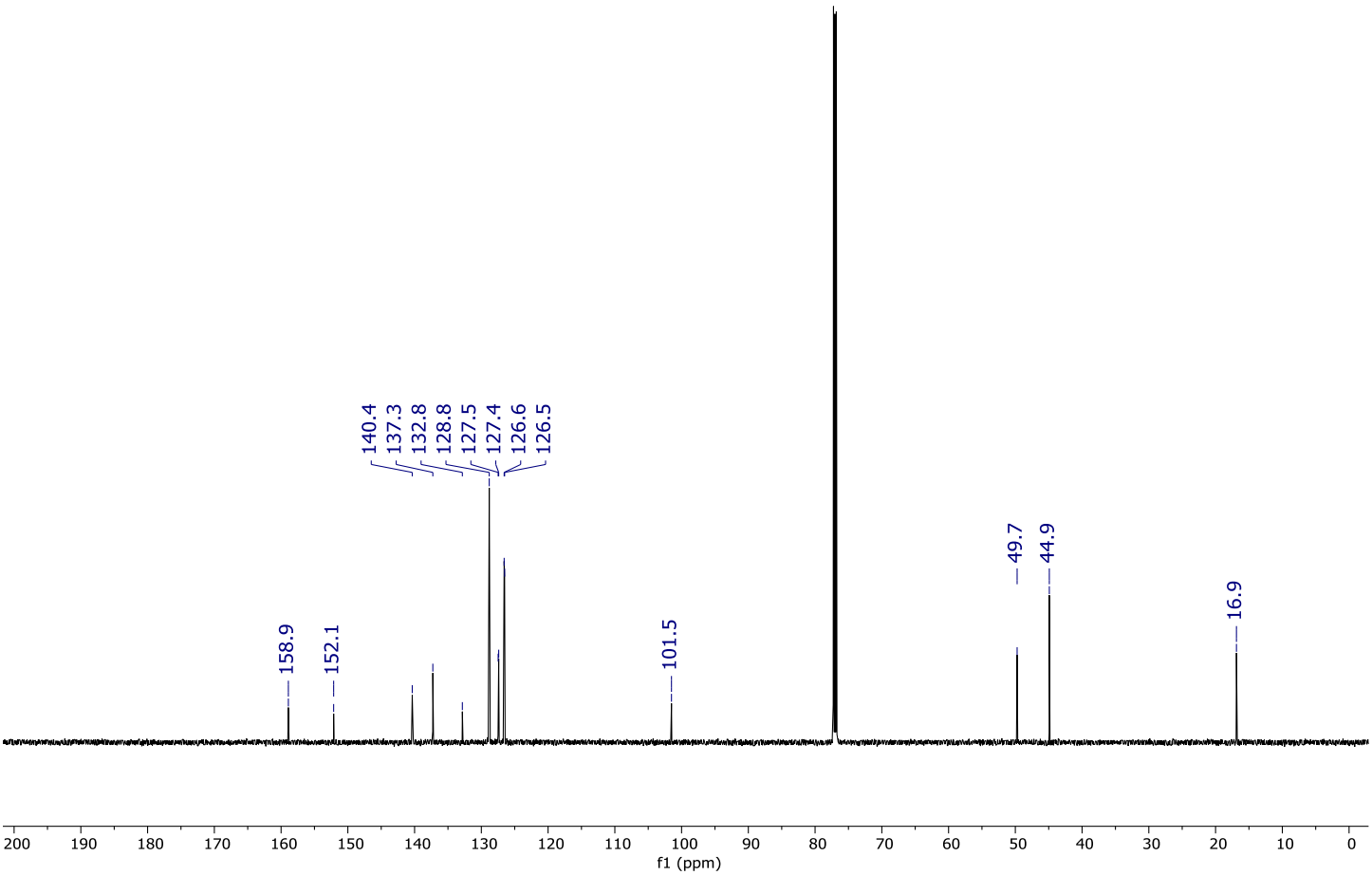



Figure S182. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **14a**.

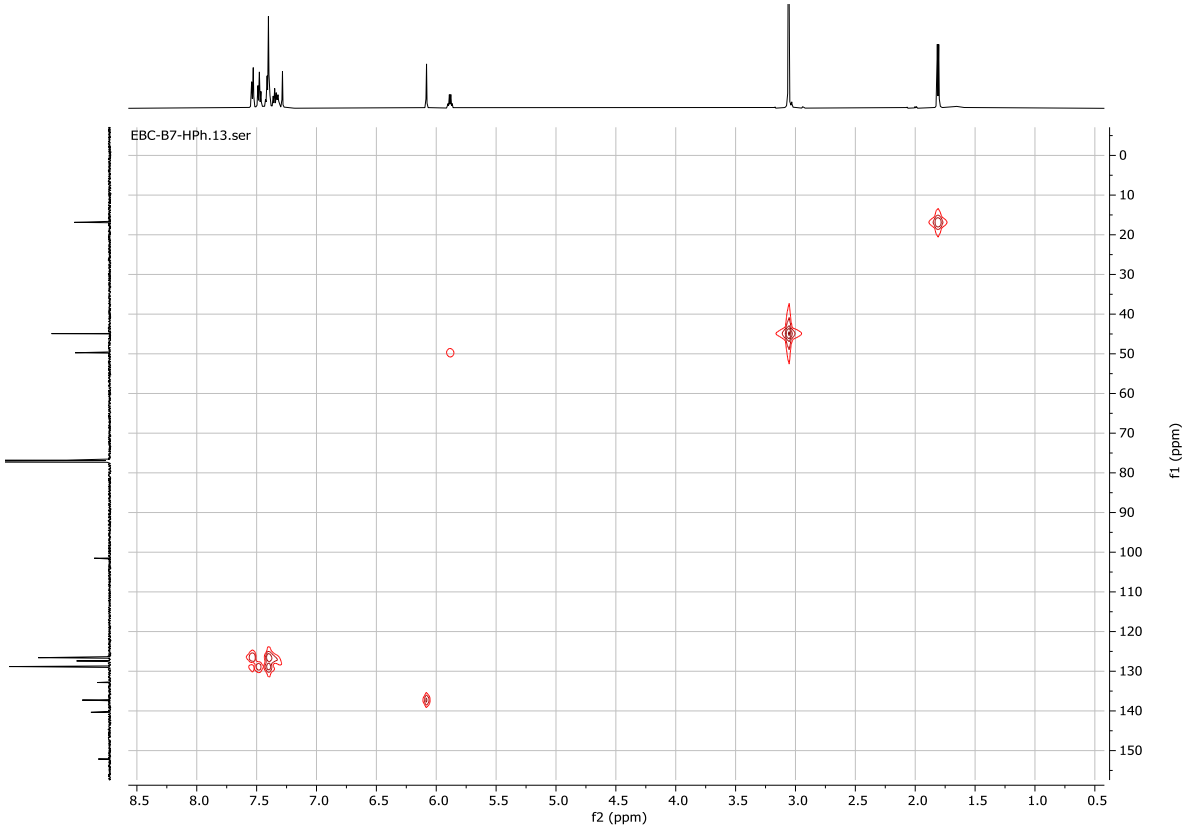



Figure S183. HSQC (600 MHz, $CDCl_3$) spectrum of compound **14a.**

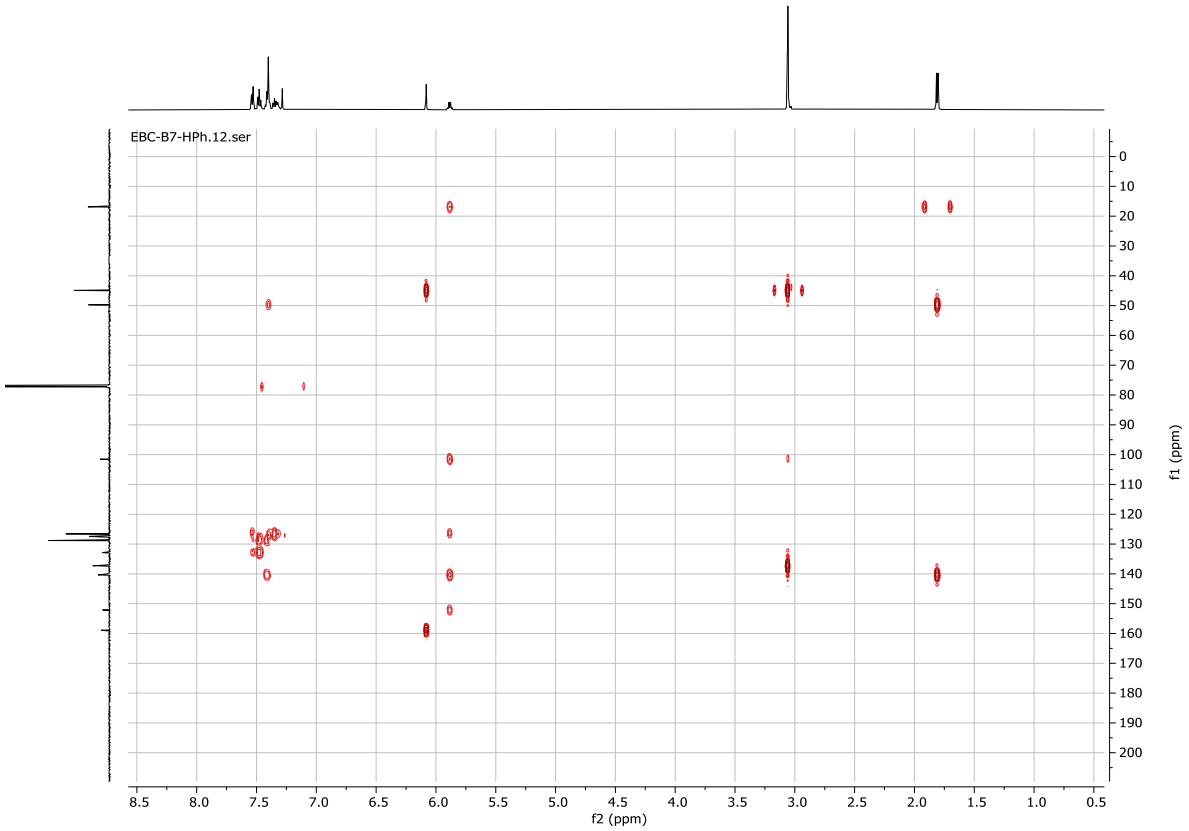
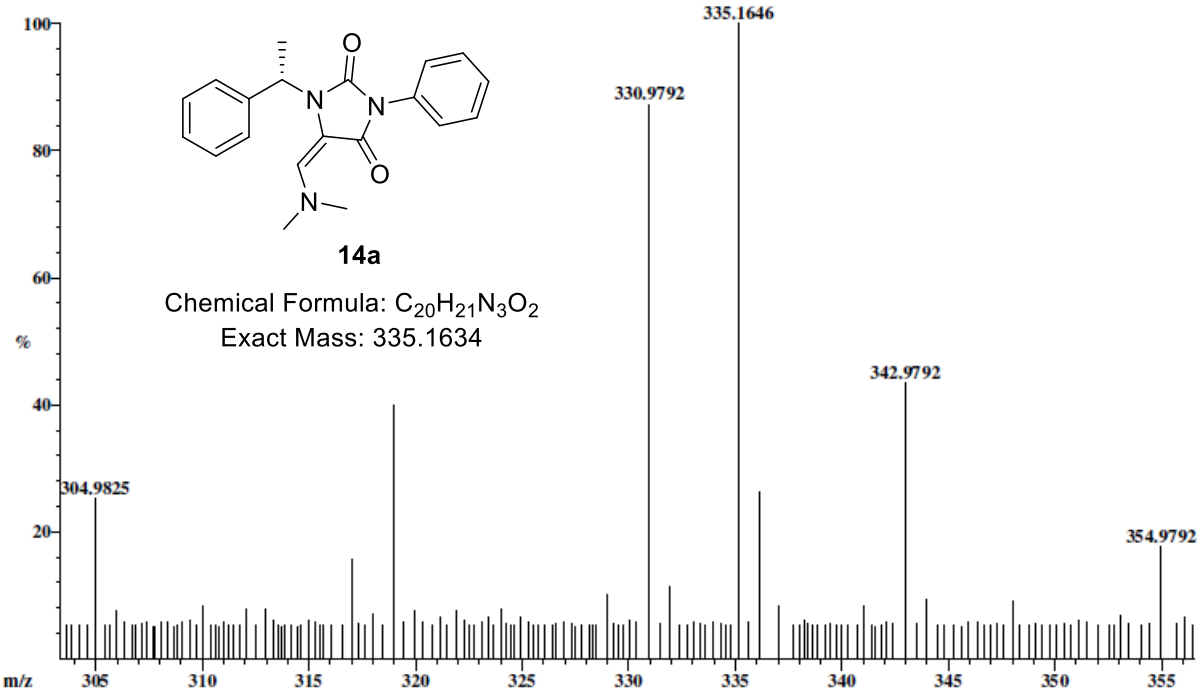



Figure S184. HMBC (600 MHz, $CDCl_3$) spectrum of compound **14a.**

**File: JT-EBC-B1-155** **Date Run: 02-22-2018 (Time Run: 11:08:00)**
**Sample: JT-EBC-B1-155**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 73** **R.T.: 1.2**
**Base: m/z 335; 1%FS TIC: 154672** **#Ions: 204**




**Selected Isotopes : $H_{0-21}C_{0-20}N_{0-3}O_{0-2}$** **Error Limit : 5 ppm**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 335.1646 | 100.0% | $C_{20}H_{21}N_3O_2$ | 335.1634 | 3.7 |

Figure S185. HRMS of compound **14a.**

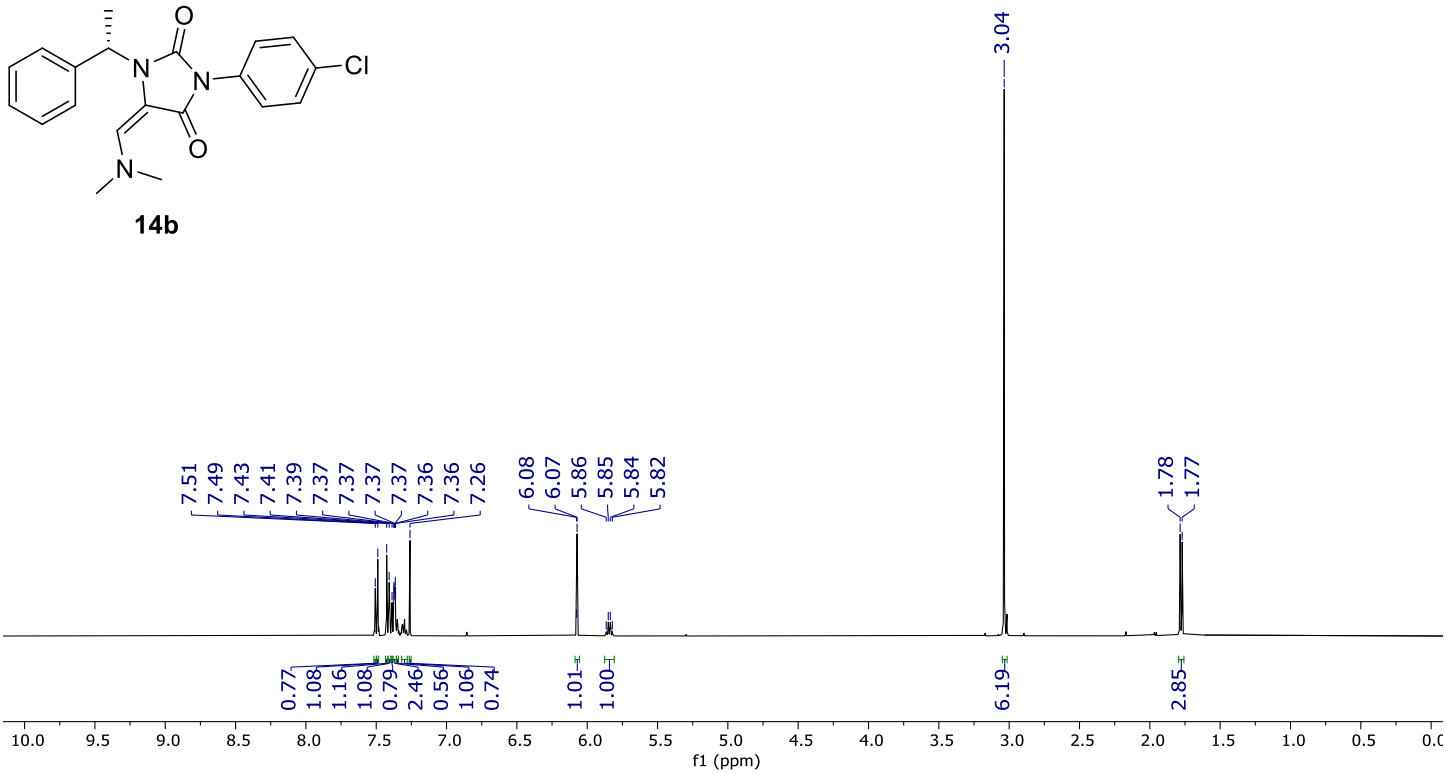



Figure S186. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **14b**.

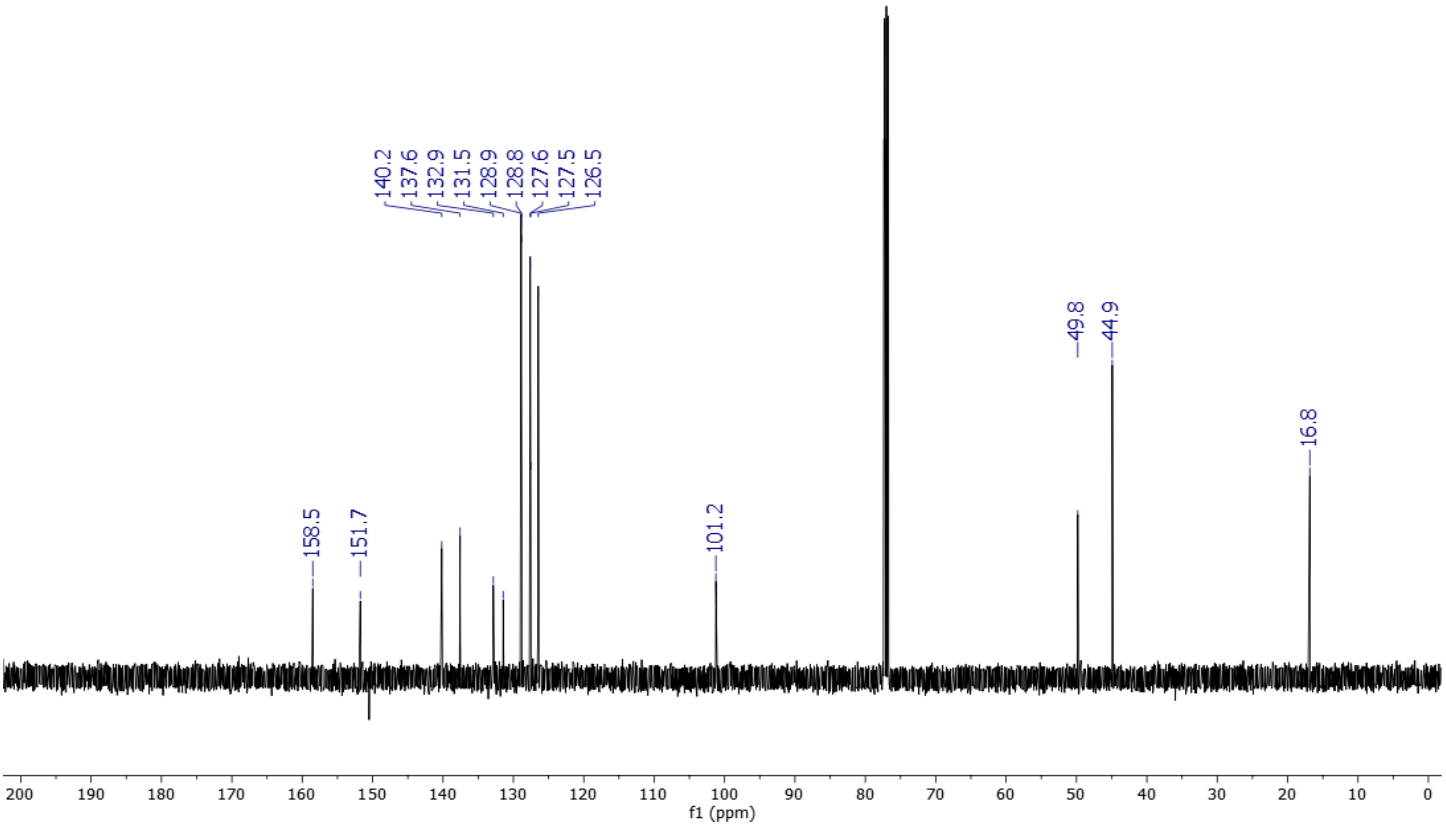



Figure S187. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **14b**.

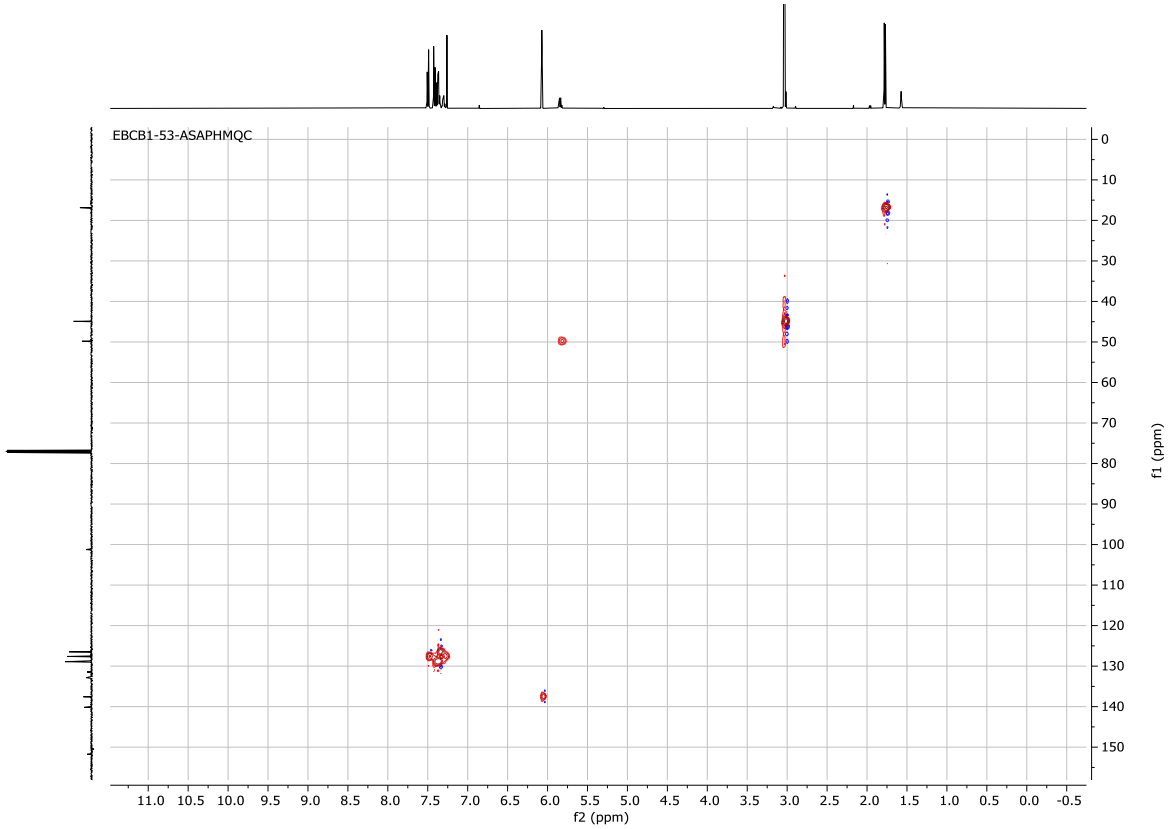



Figure S188. HSQC (500 MHz, $CDCl_3$) spectrum of compound **14b.**

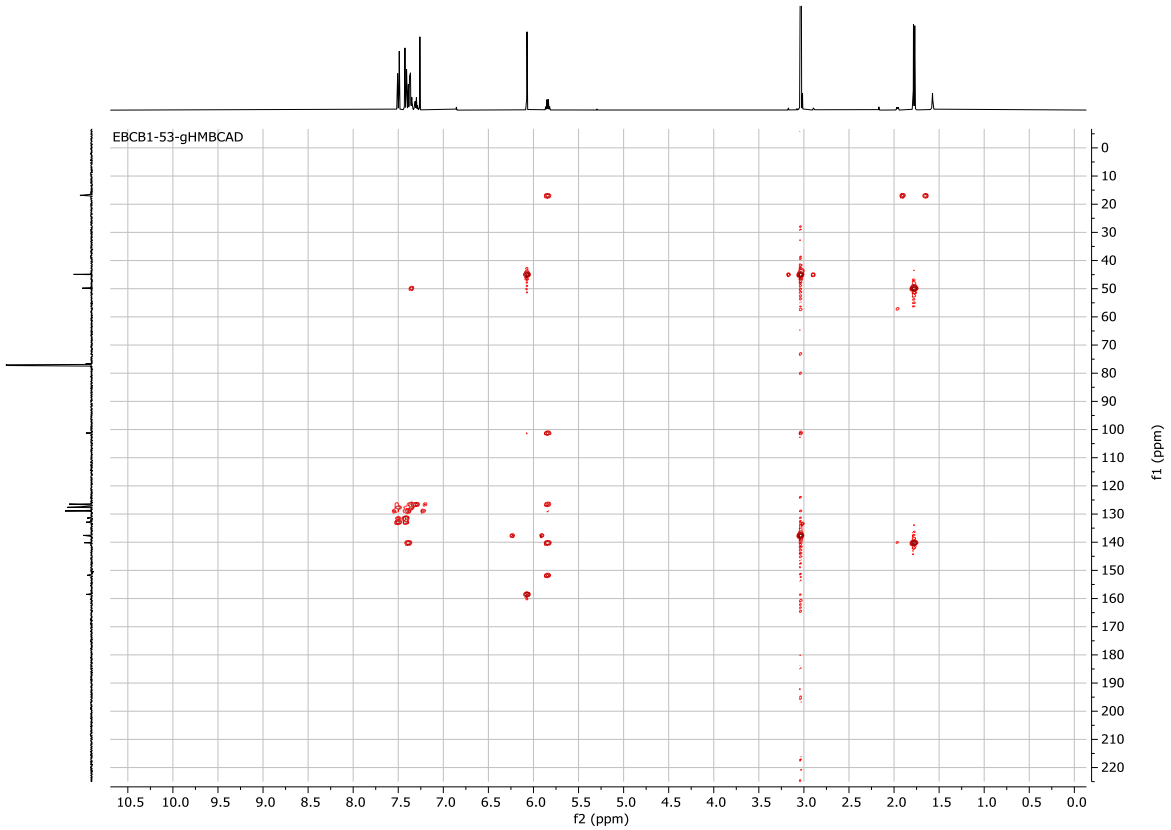
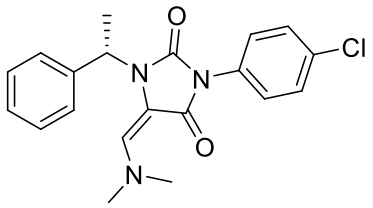



Figure S189. HMBC (00 MHz, $CDCl_3$) spectrum of compound **14b.**




**14b**

Chemical Formula: $C_{20}H_{20}ClN_3O_2$
Exact Mass: 369.1244

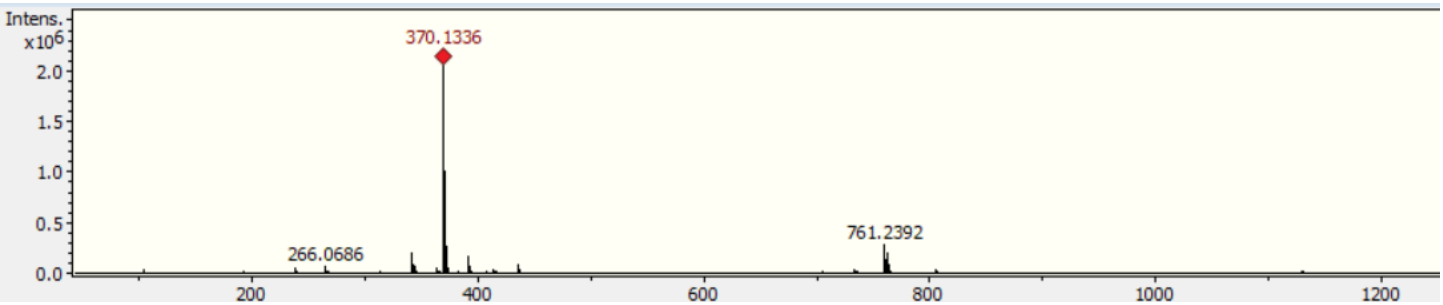
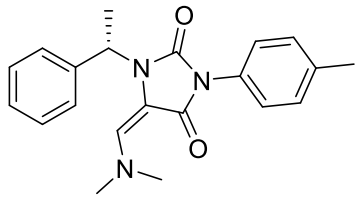



Figure S190. HRMS of compound **14b.**



**14c**

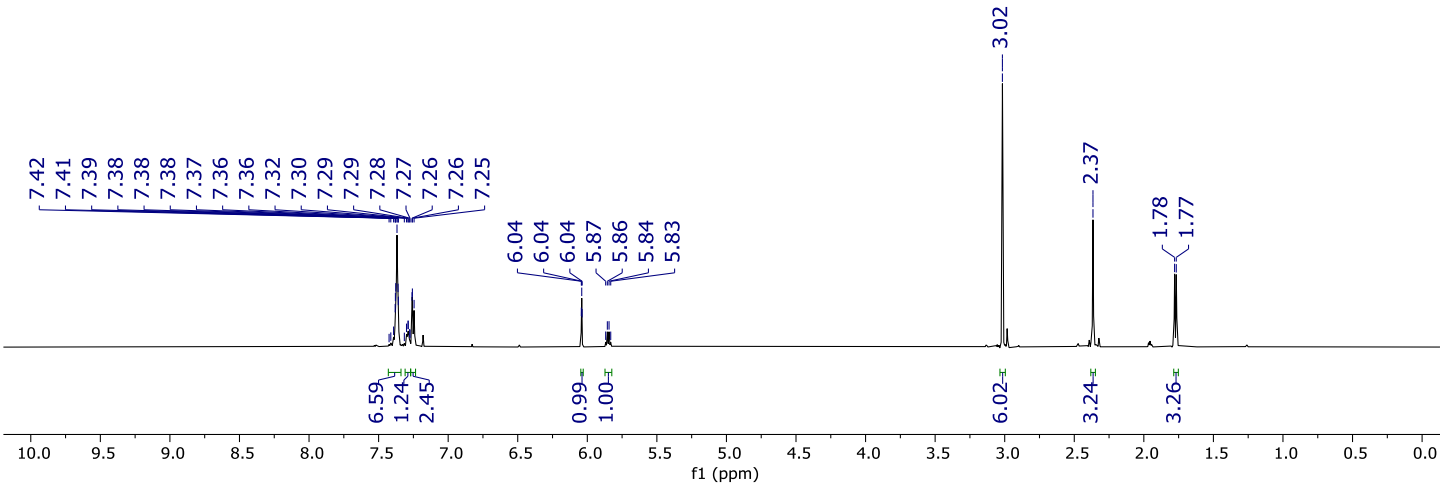



Figure S191. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **14c**.

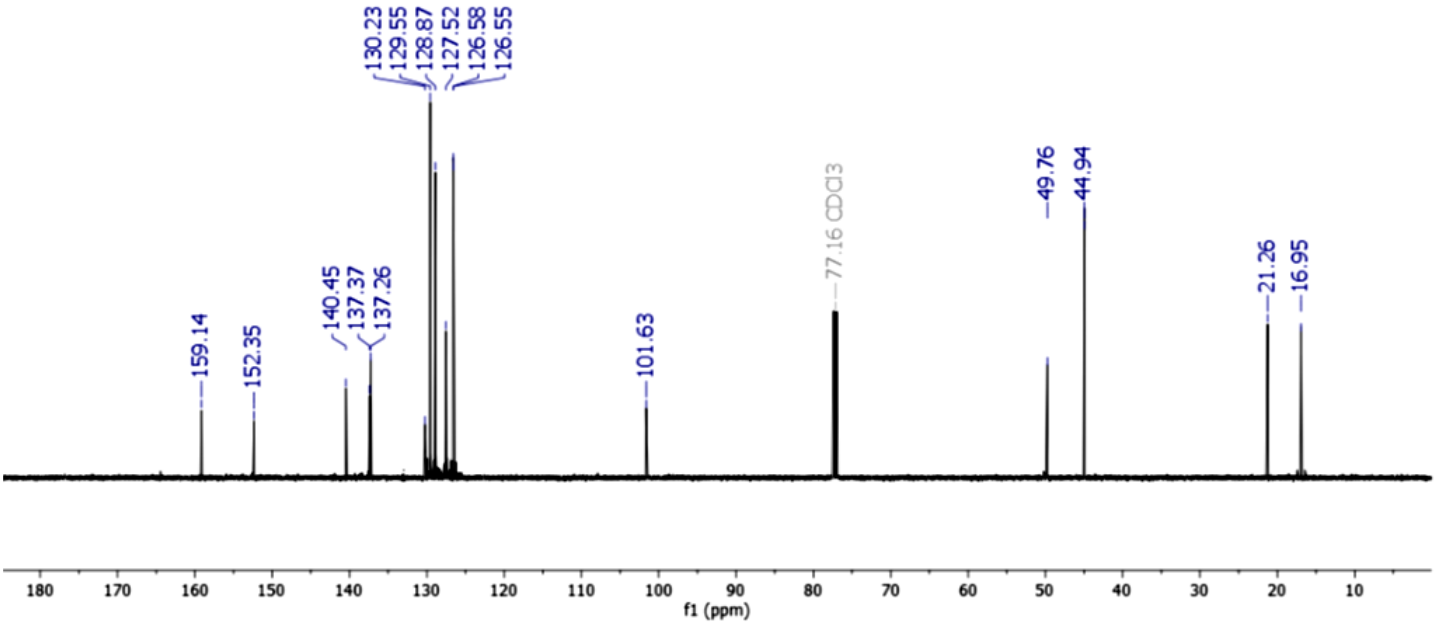



Figure S192. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **14c**.

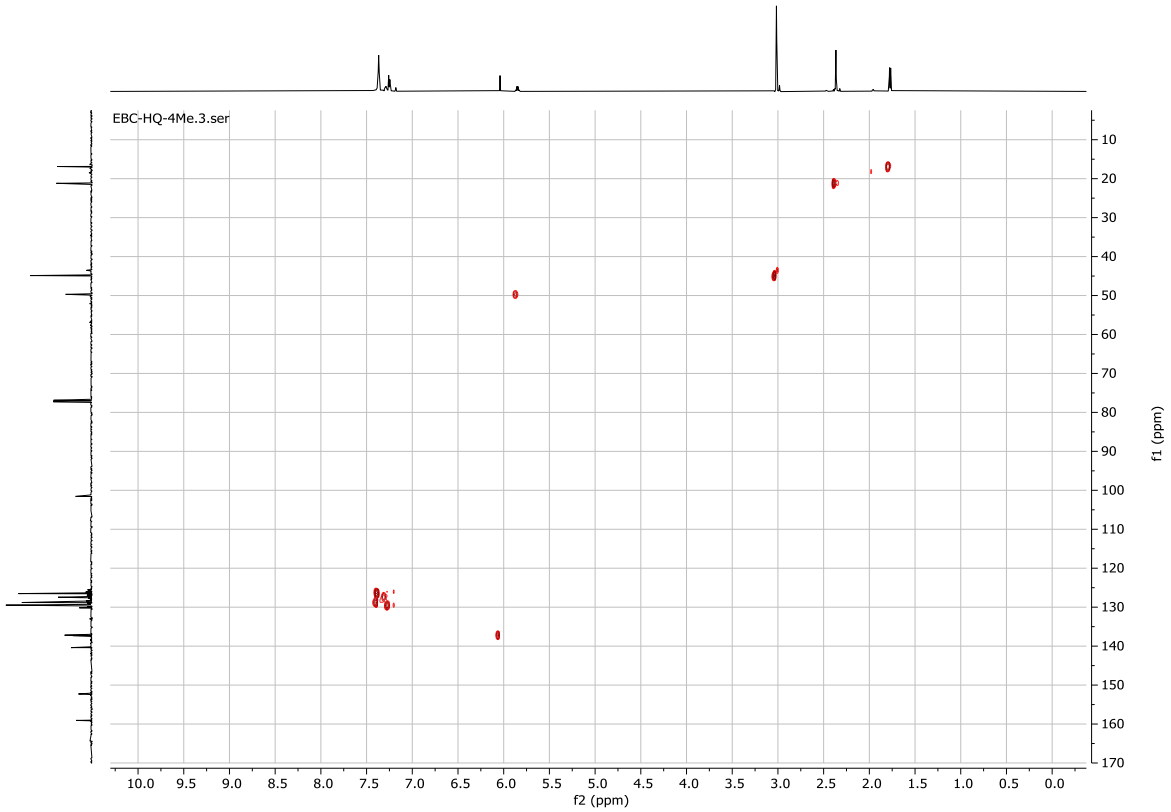



Figure S193. HSQC (600 MHz, $CDCl_3$) spectrum of compound **14c.**

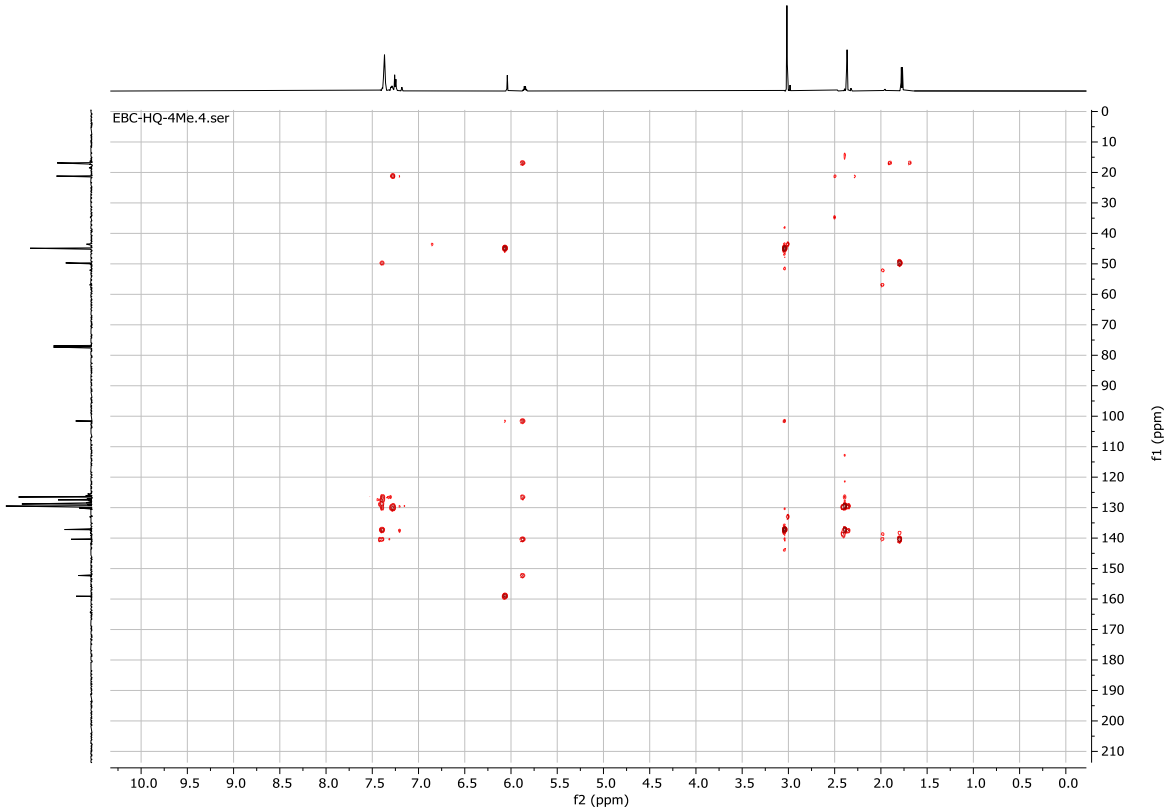



Figure S194. HMBC (600 MHz, $CDCl_3$) spectrum of compound **14c.**

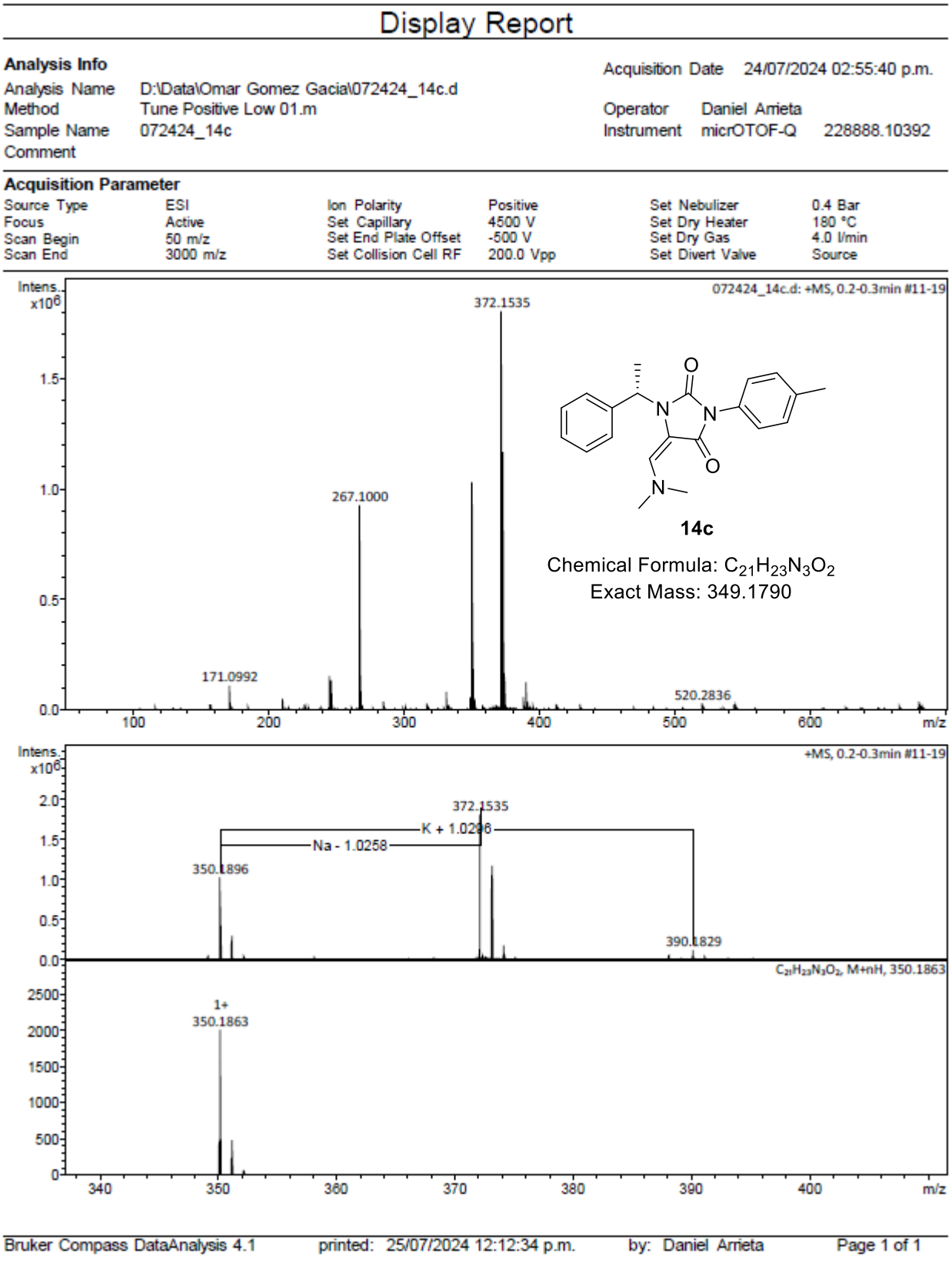



Figure S195. HRMS of compound **14c.**

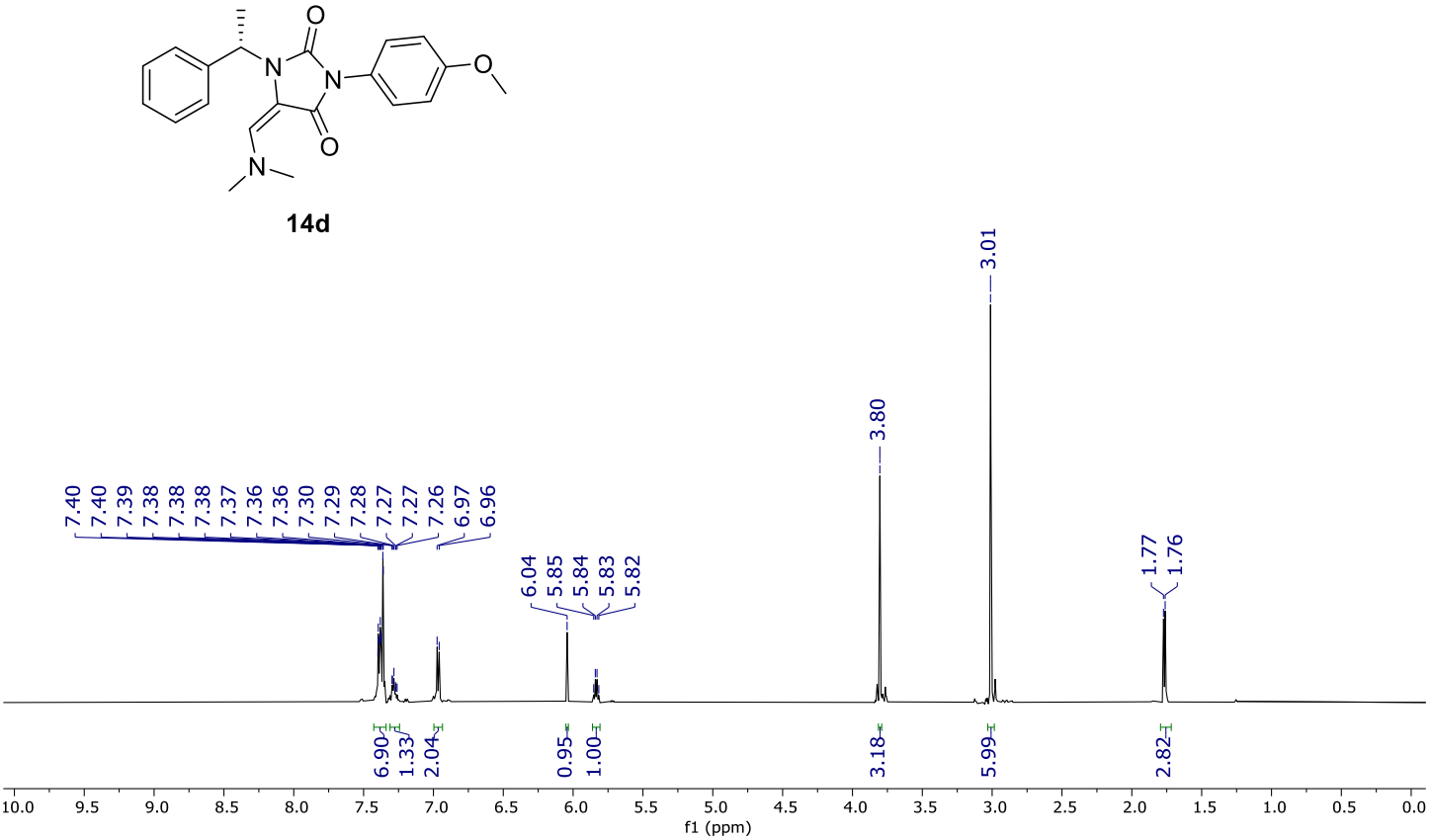



Figure S196. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **14d**.

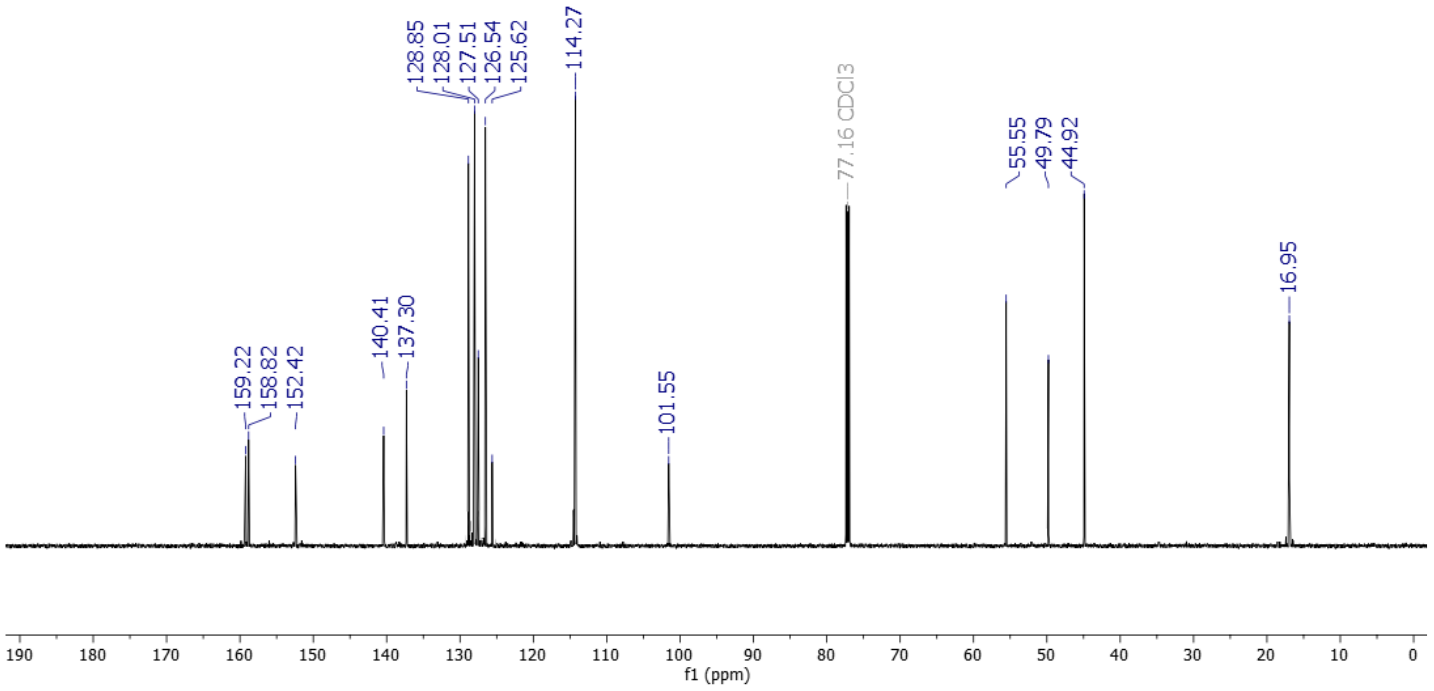



Figure S197. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **14d**.

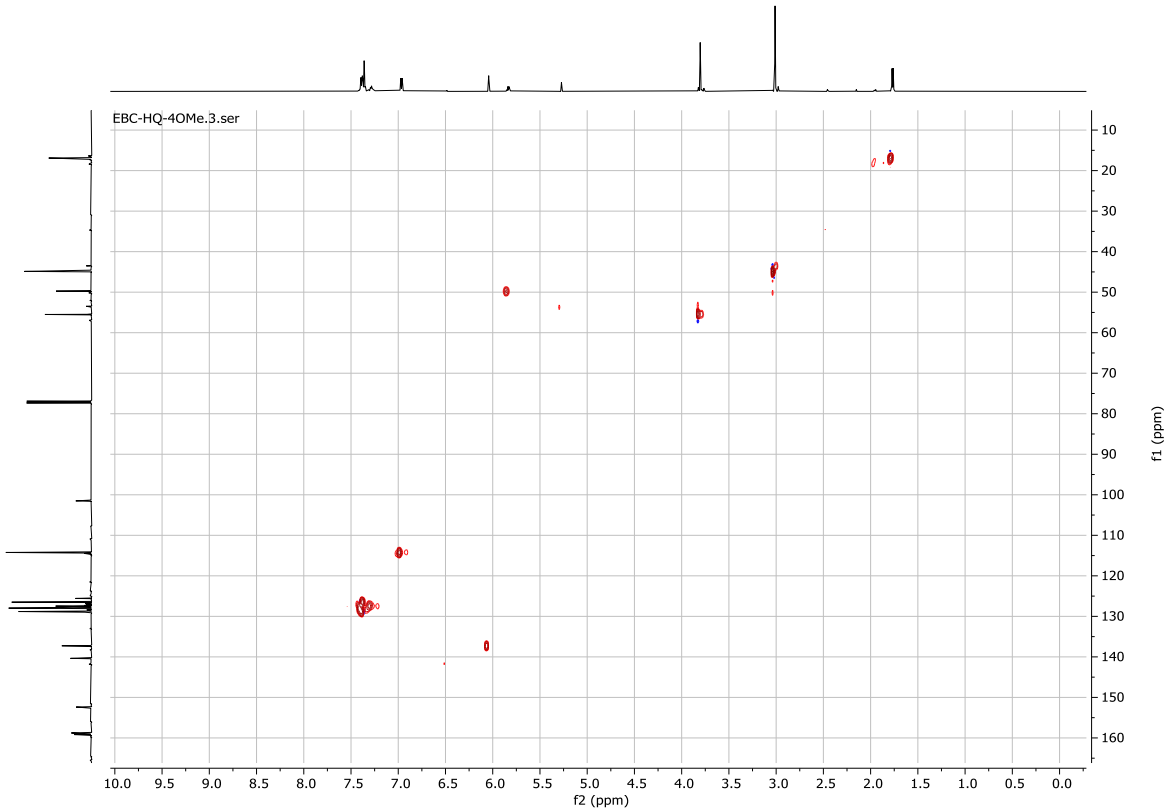



Figure S198. HSQC (600 MHz, $CDCl_3$) spectrum of compound **14d.**

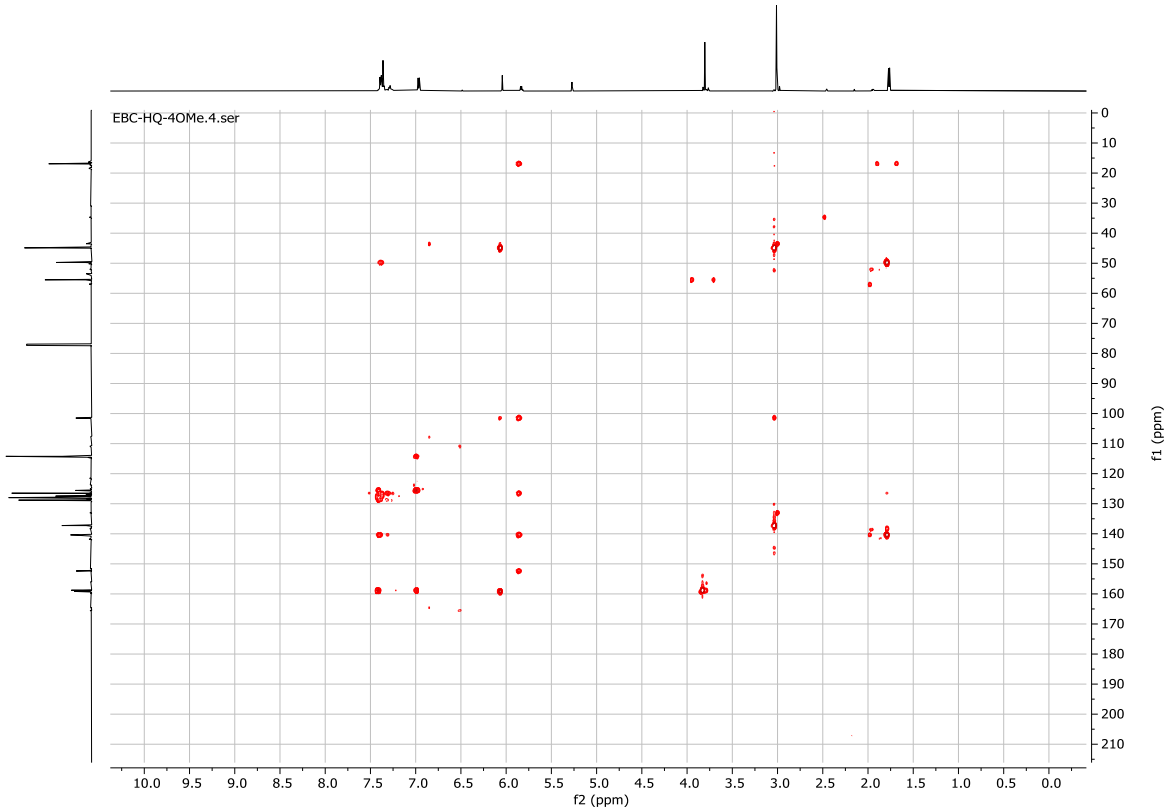
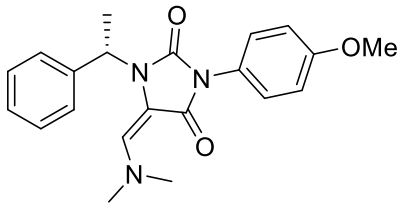



Figure S199. HMBC (600 MHz, $CDCl_3$) spectrum of compound **14d.**




**14d**

Chemical Formula: $C_{21}H_{23}N_3O_3$
Exact Mass: 365.1739

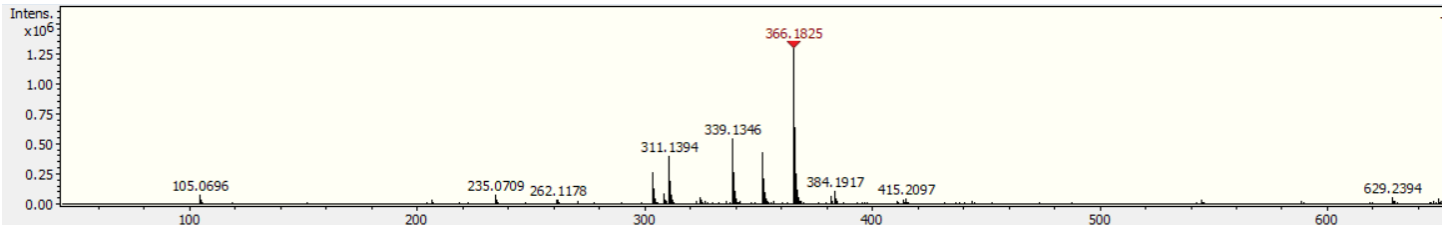



Figure S200. HRMS of compound **14d.**

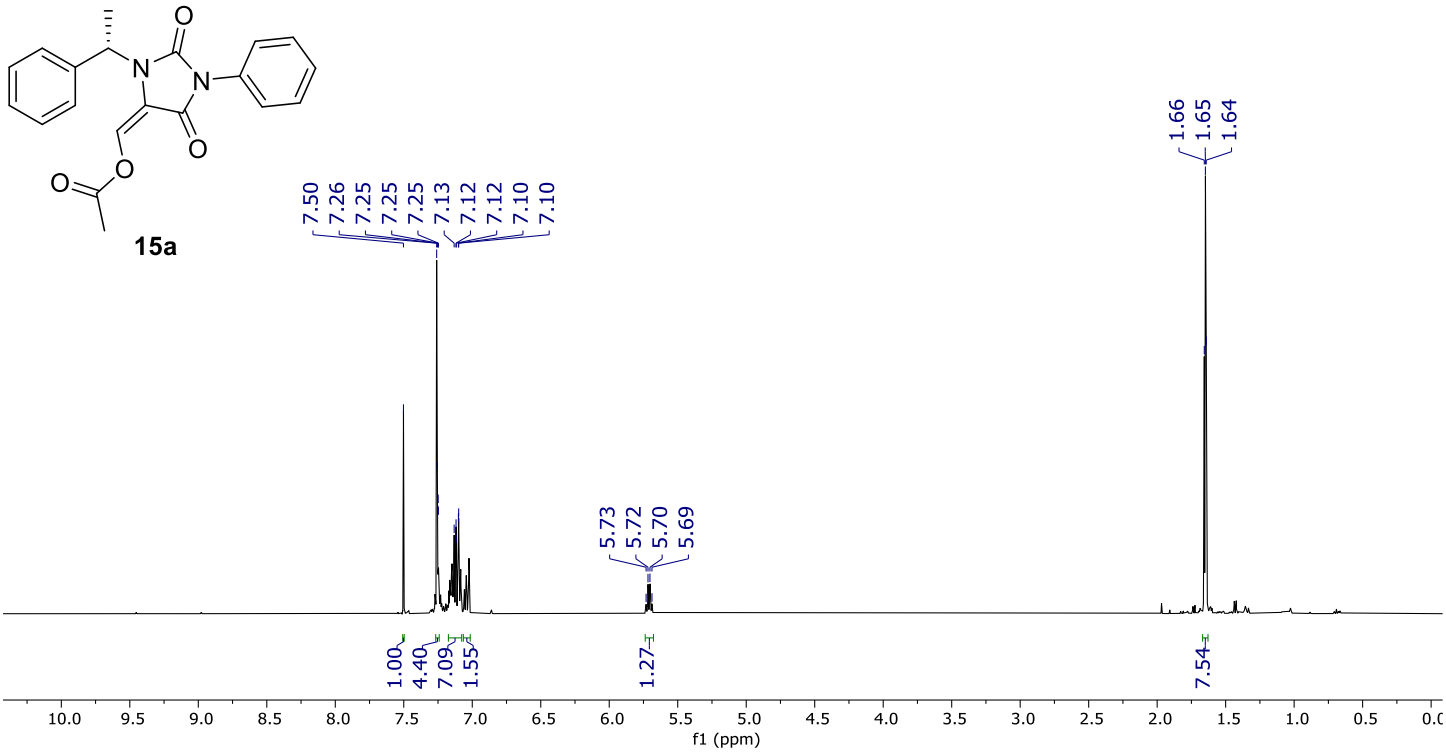



Figure S201. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **15a**.

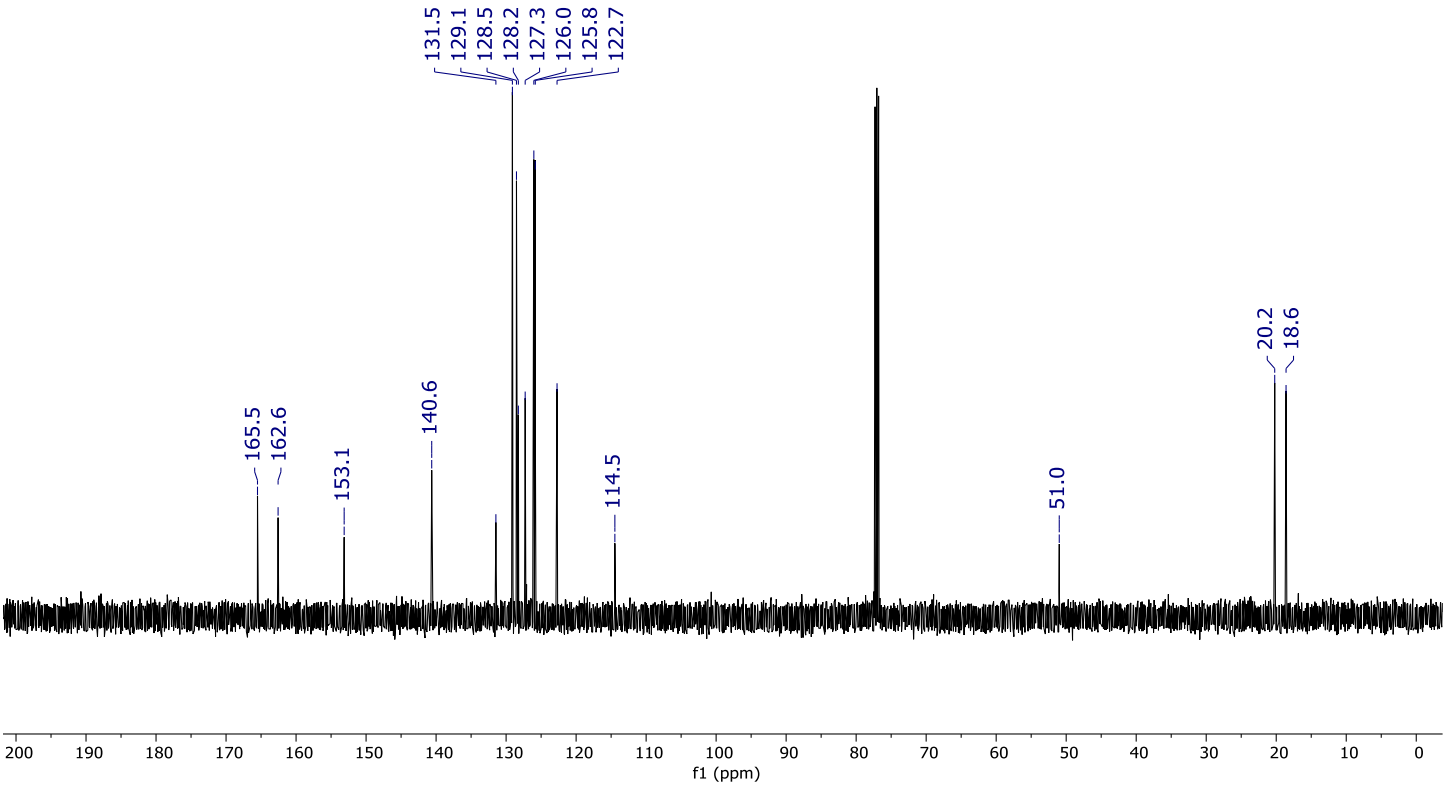



Figure S202. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **15a**.

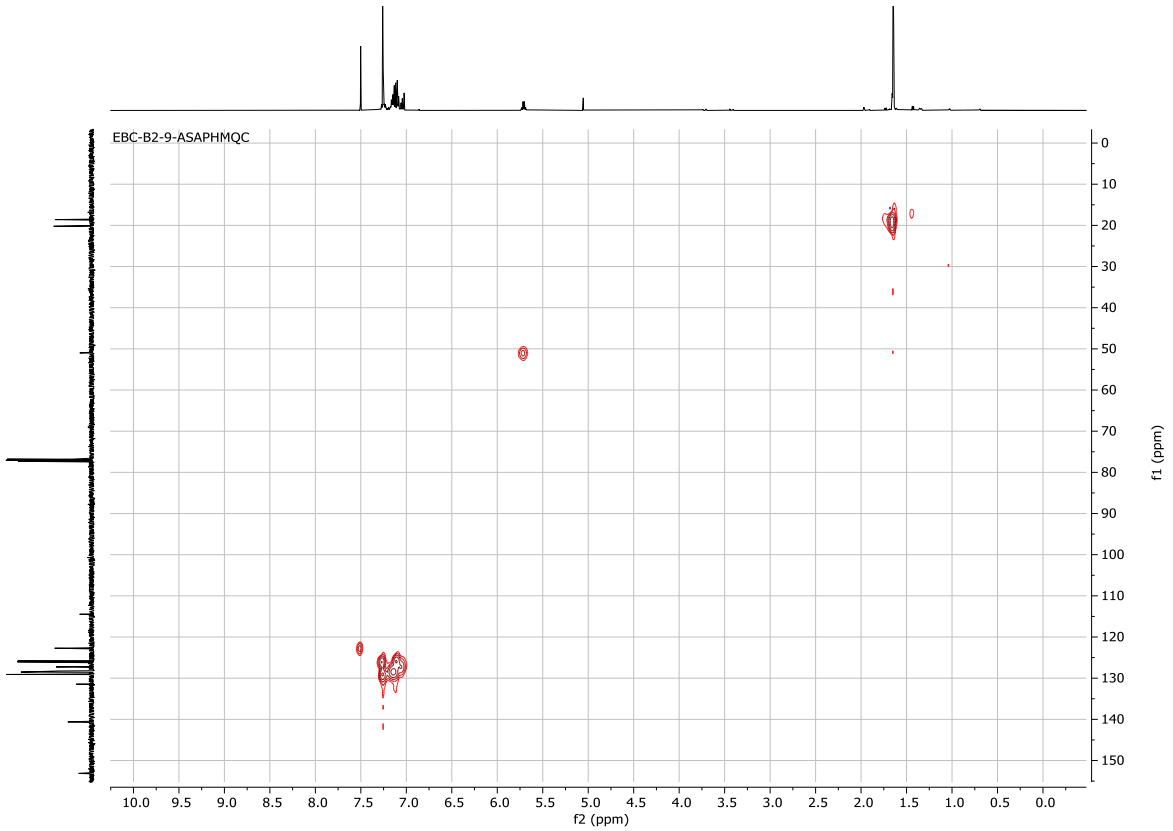



Figure S203. HSQC (500 MHz, $CDCl_3$) spectrum of compound **15a.**

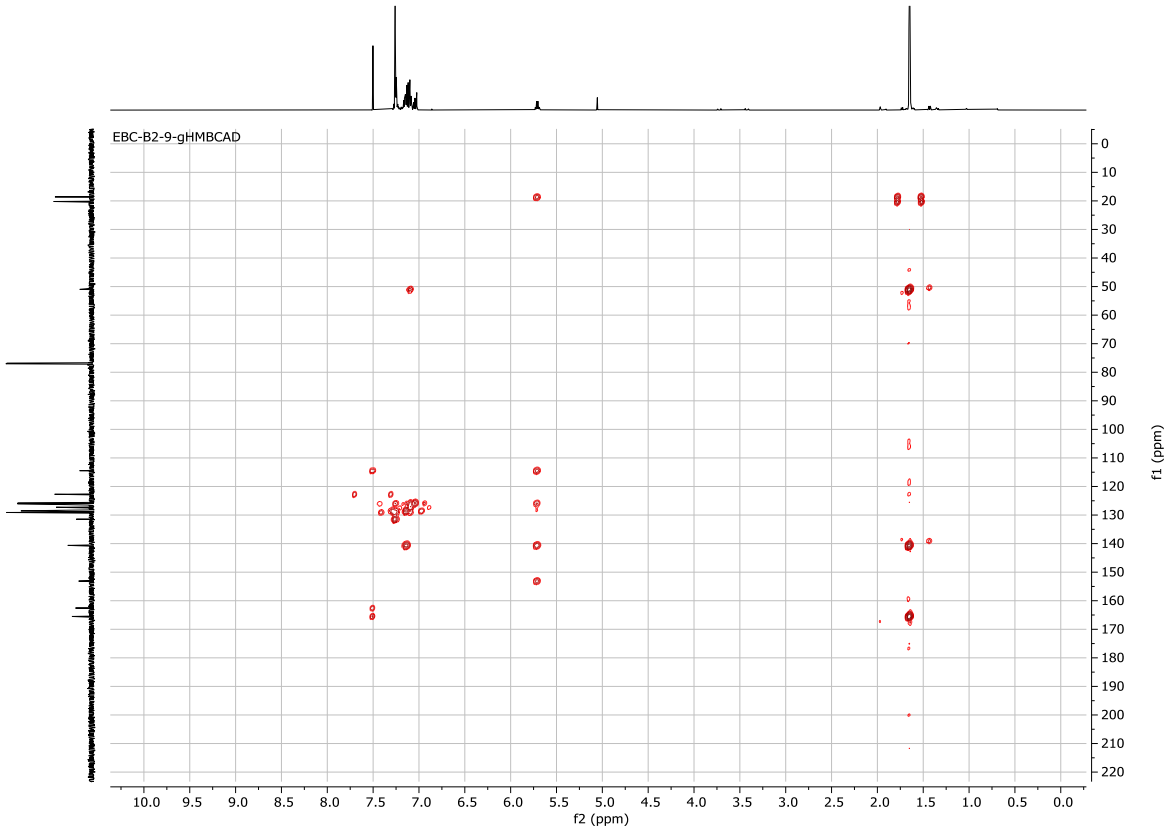


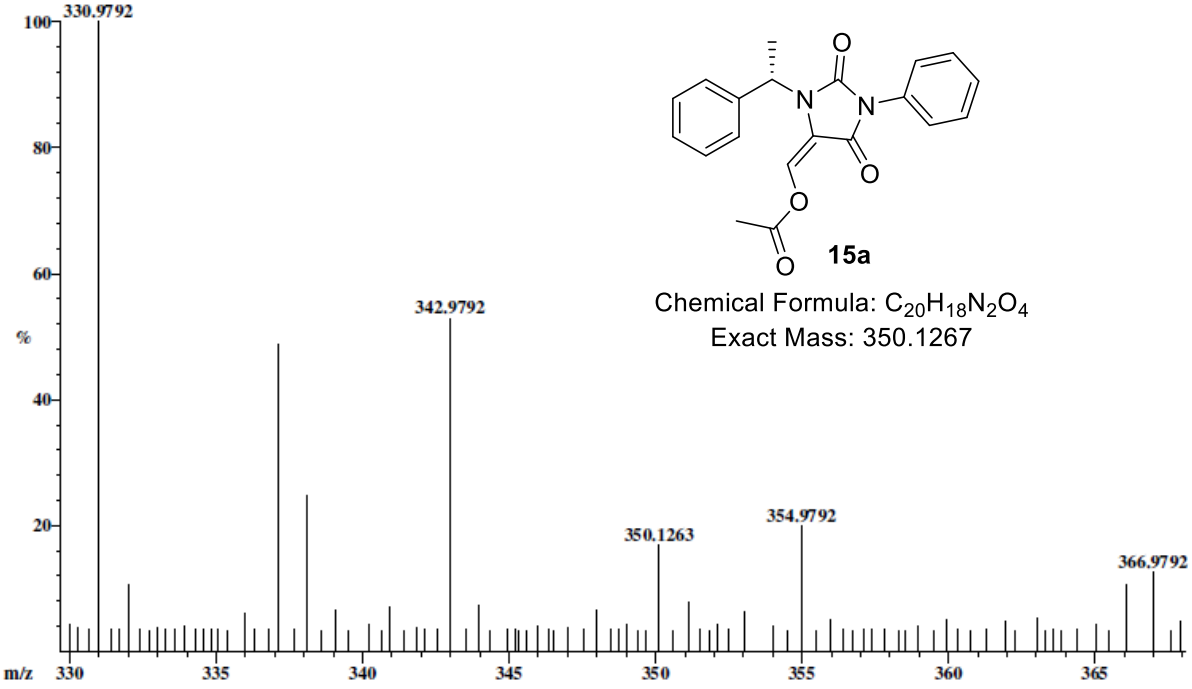

Figure S204. HMBC (500 MHz, $CDCl_3$) spectrum of compound **15a.**

*IPN*
9/7/2018



File: JT-EBC-B2-15 Date Run: 09-07-2018 (Time Run: 12:12:39)
Sample: JT-EBC-B2-15
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 116 R.T.: 1.92
Base: m/z 331; 1.6%FS TIC: 197216 #Ions: 191






**15a**

Chemical Formula: $C_{20}H_{18}N_2O_4$
Exact Mass: 350.1267

Selected Isotopes : $H_{0-18}C_{0-20}N_{0-2}O_{0-4}$ Error Limit : 5 ppm

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 350.1263 | 16.8% | $C_{20}H_{18}N_2O_4$ | 350.1267 | -1.0 |

Figure S205. HRMS of compound **15a.**

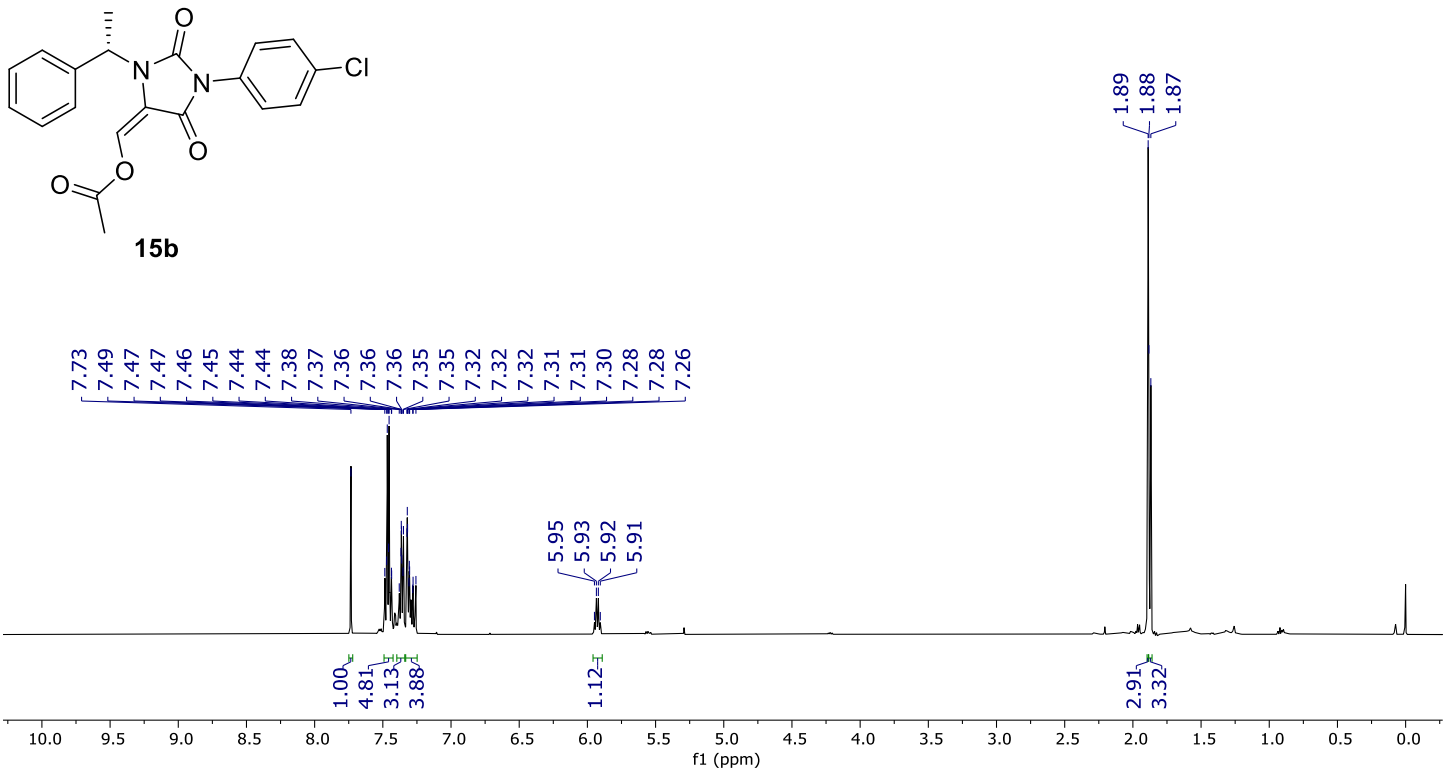



Figure S206. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **15b**.

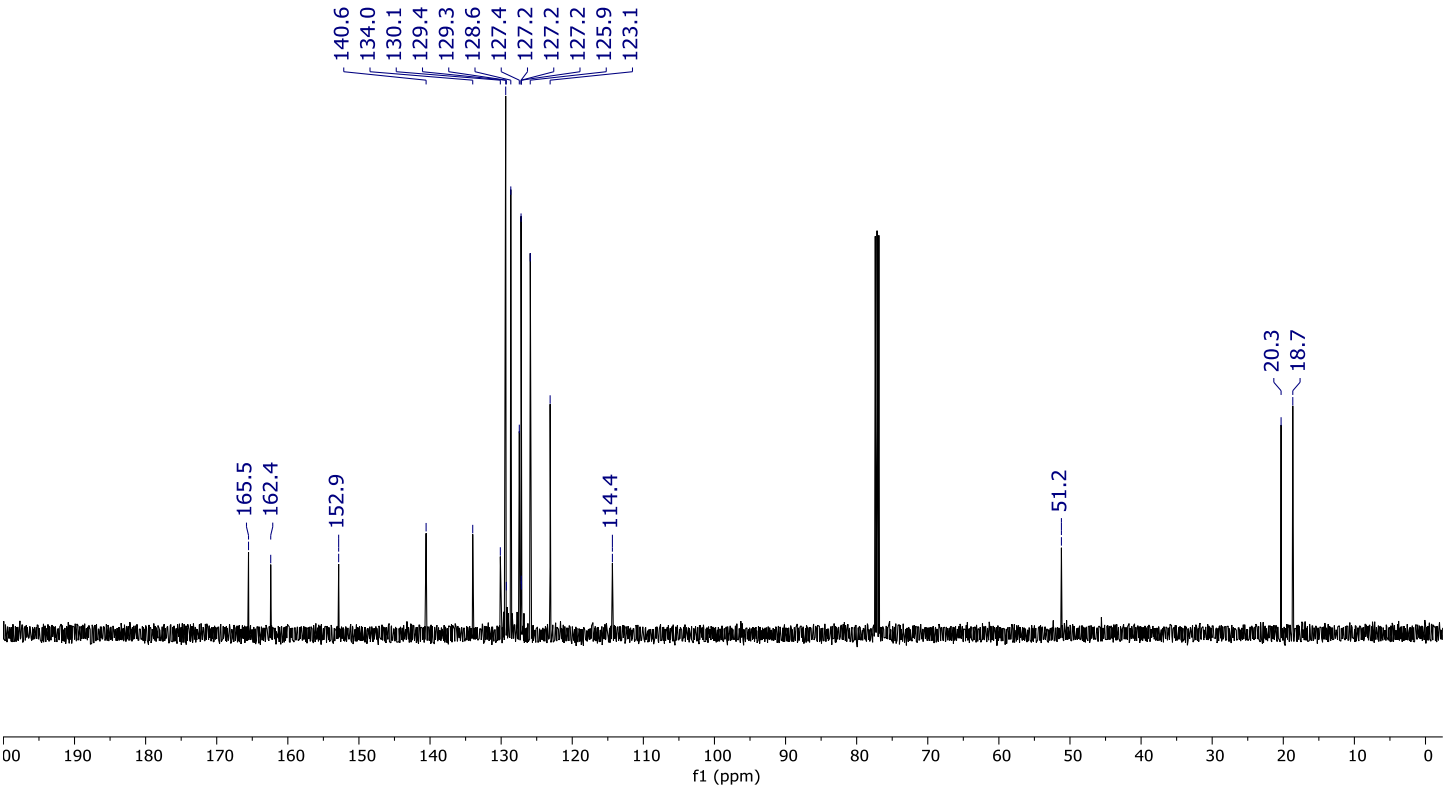



Figure S207. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **15b**.

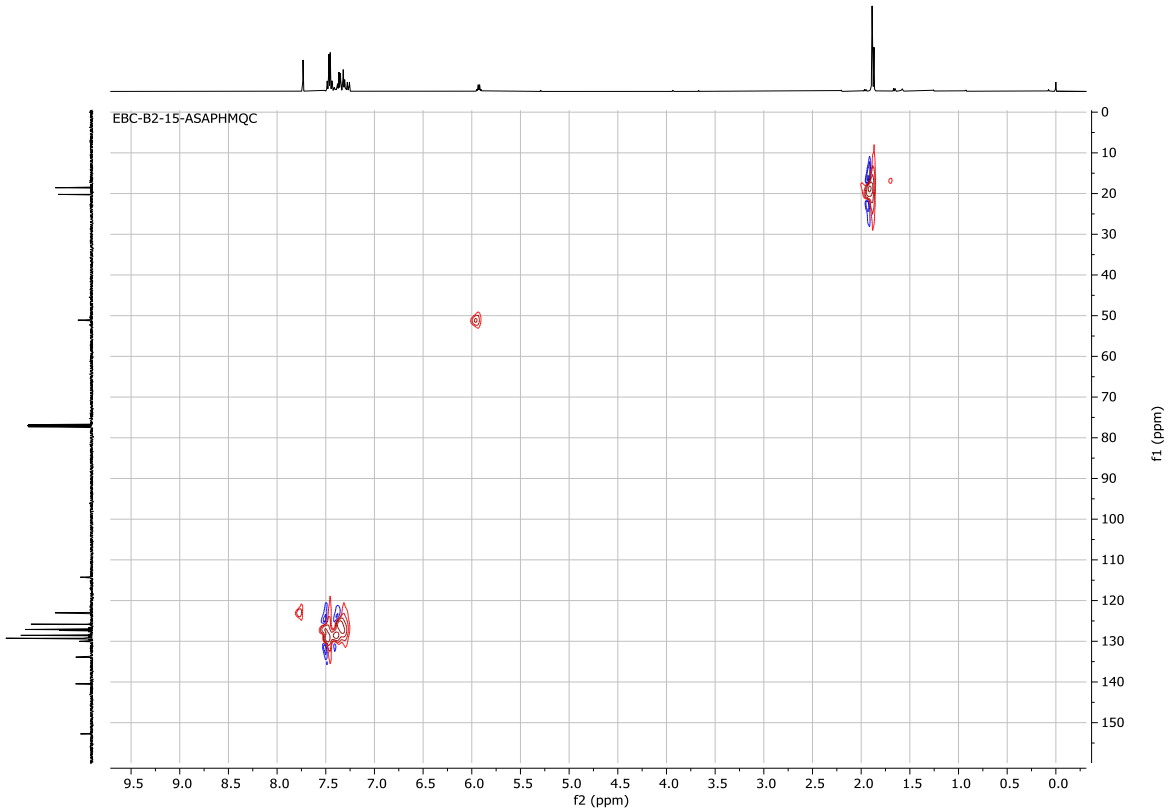



Figure S208. HSQC (500 MHz, $CDCl_3$) spectrum of compound **15b.**

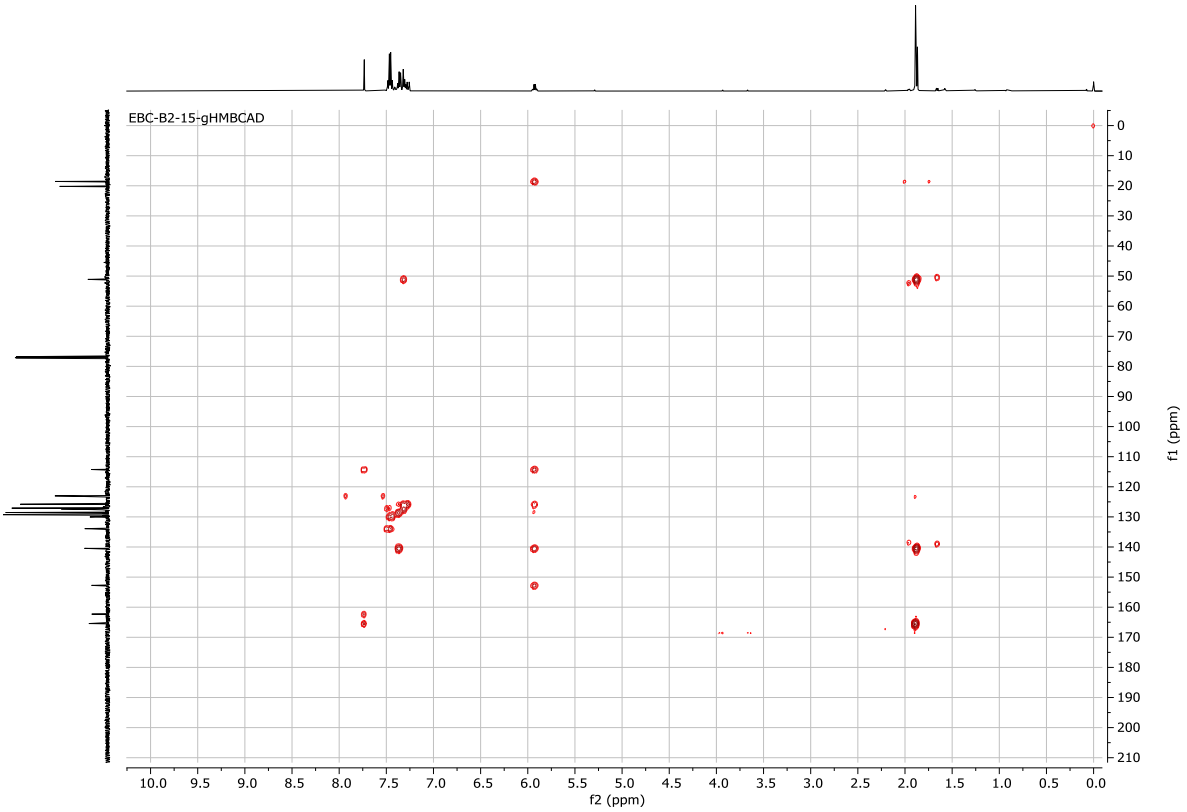



Figure S209. HMBC (500 MHz, $CDCl_3$) spectrum of compound **15b.**

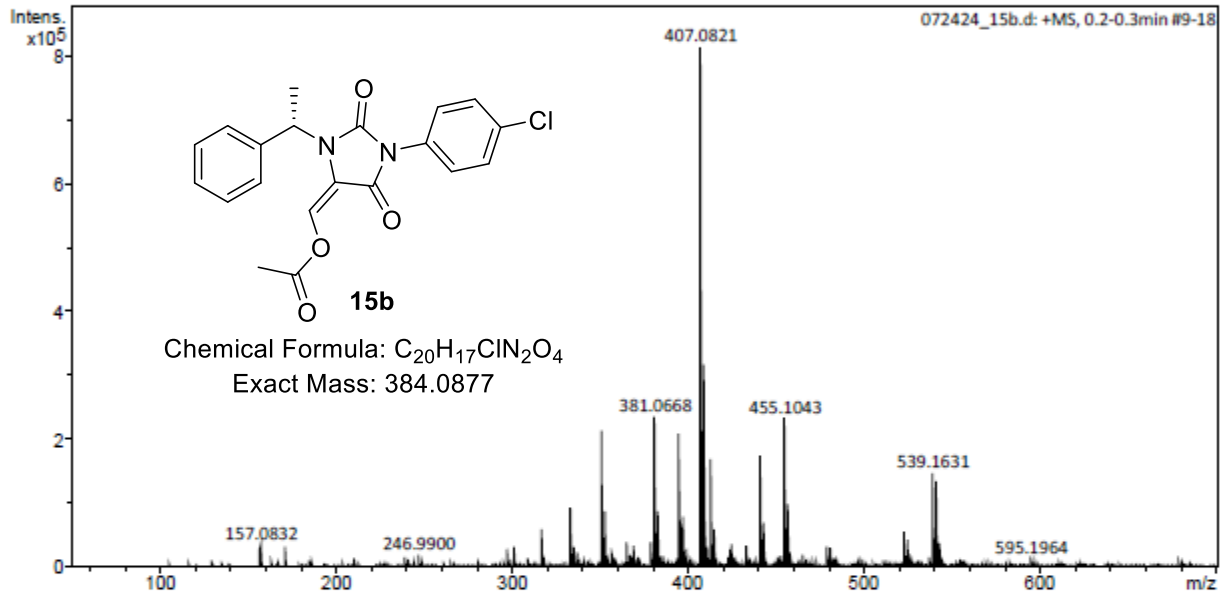
# Display Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\Omar Gomez Gacia\072424_15b.d | Acquisition Date | 24/07/2024 02:51:19 p.m. |
| Method | Tune Positive Low 01.m | Operator | Daniel Arrieta |
| Sample Name | 072424_15b | Instrument | micrOTOF-Q 228888.10392 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.4 Bar |
| Focus | Active | Set Capillary | 4500 V | Set Dry Heater | 180 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 200.0 Vpp | Set Divert Valve | Source |







**15b**

Chemical Formula: $C_{20}H_{17}ClN_2O_4$

Exact Mass: 384.0877

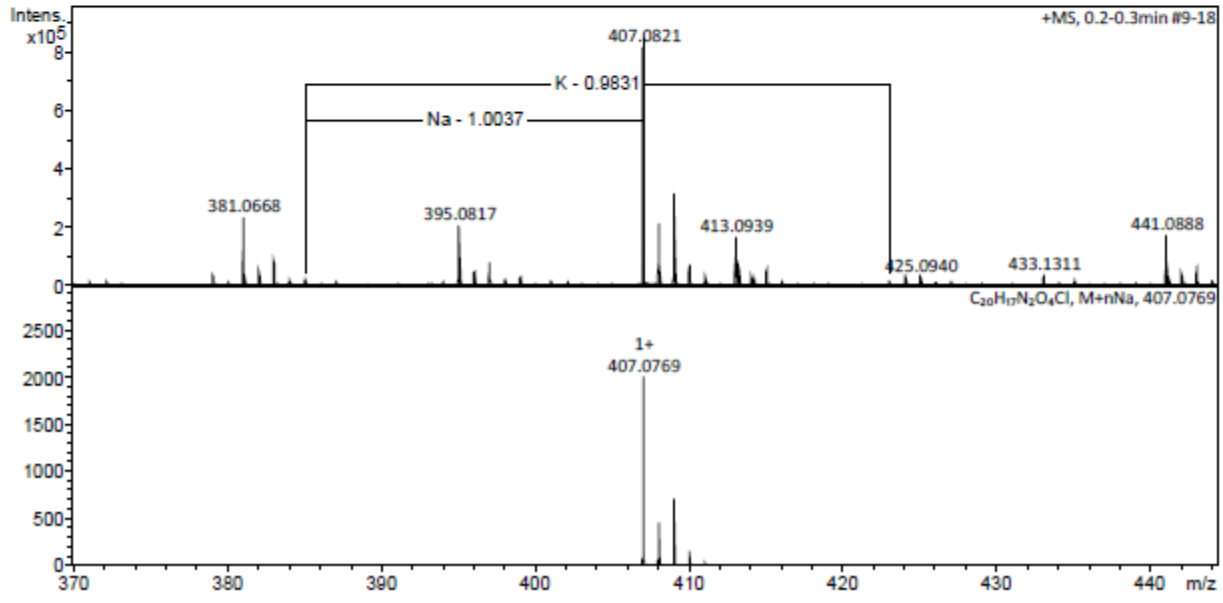






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Figure S210. HRMS of compound **15b.**

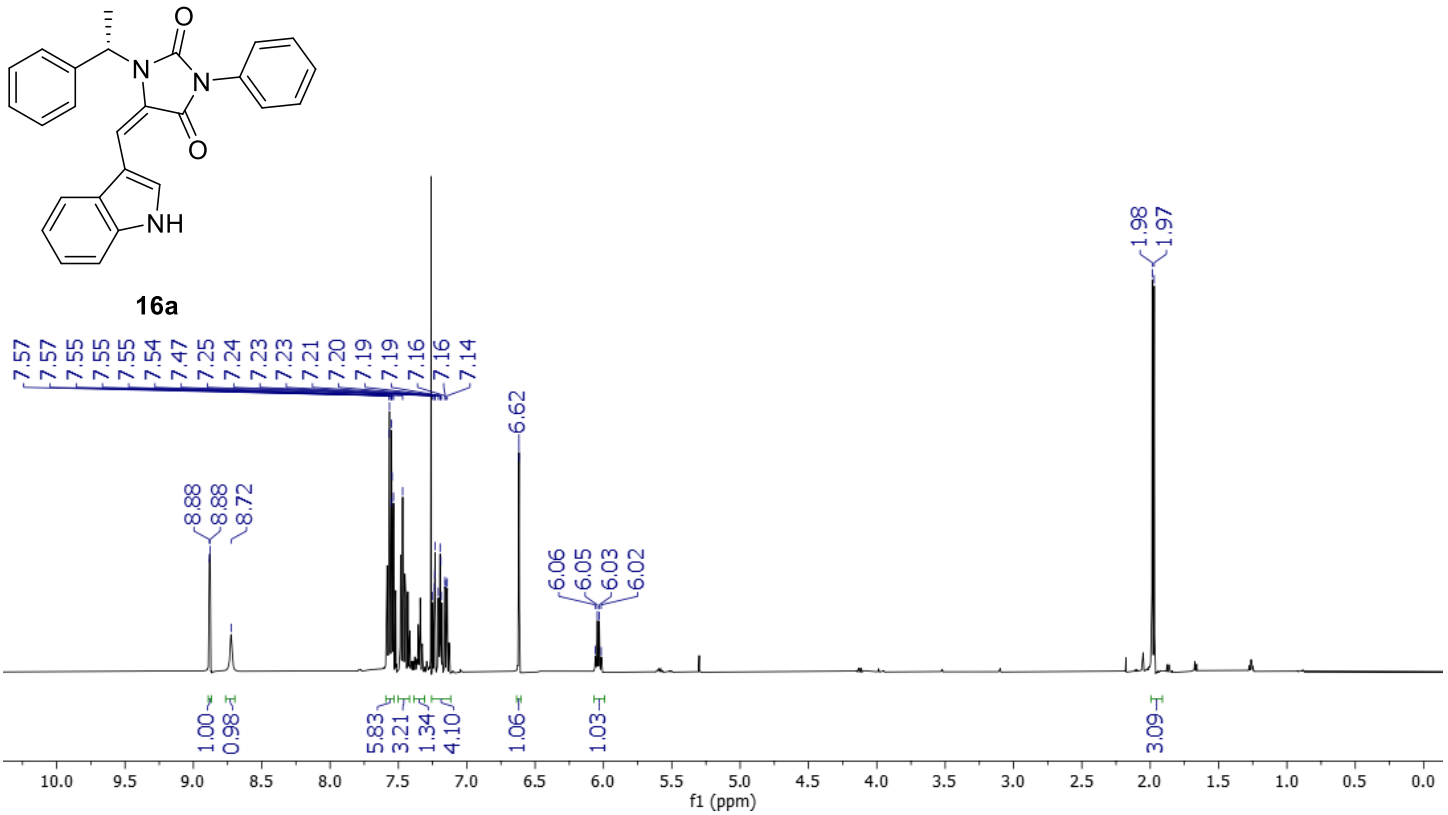



Figure S211. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **16a**.

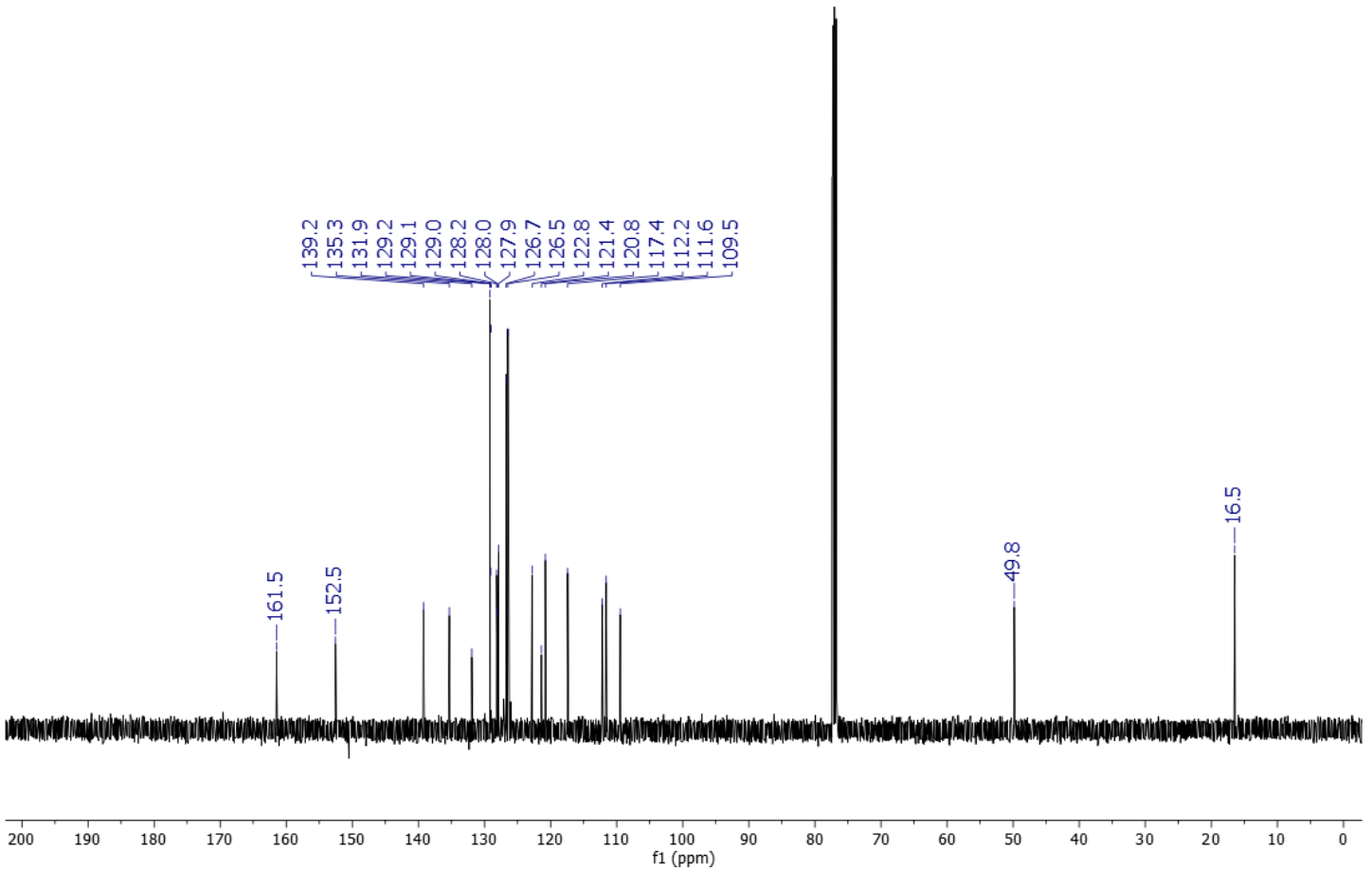



Figure S212. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **16a**.

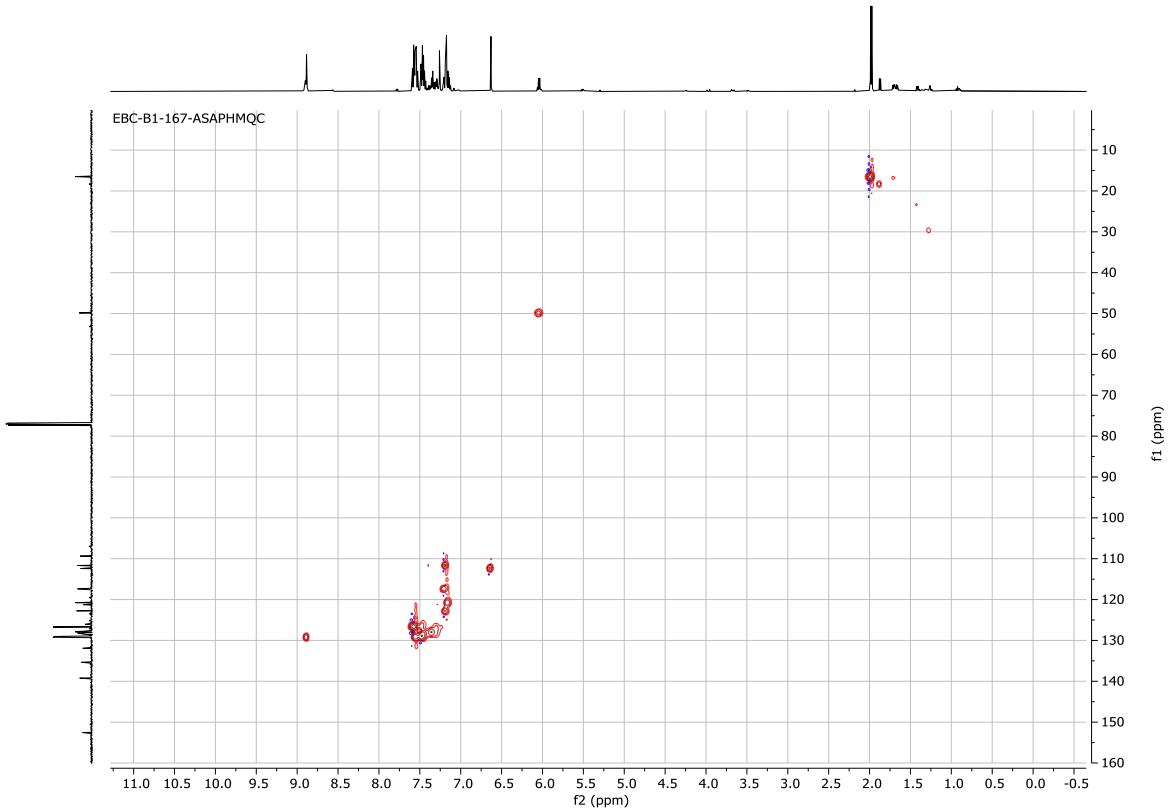



Figure S213. HSQC (500 MHz, $CDCl_3$) spectrum of compound **16a.**

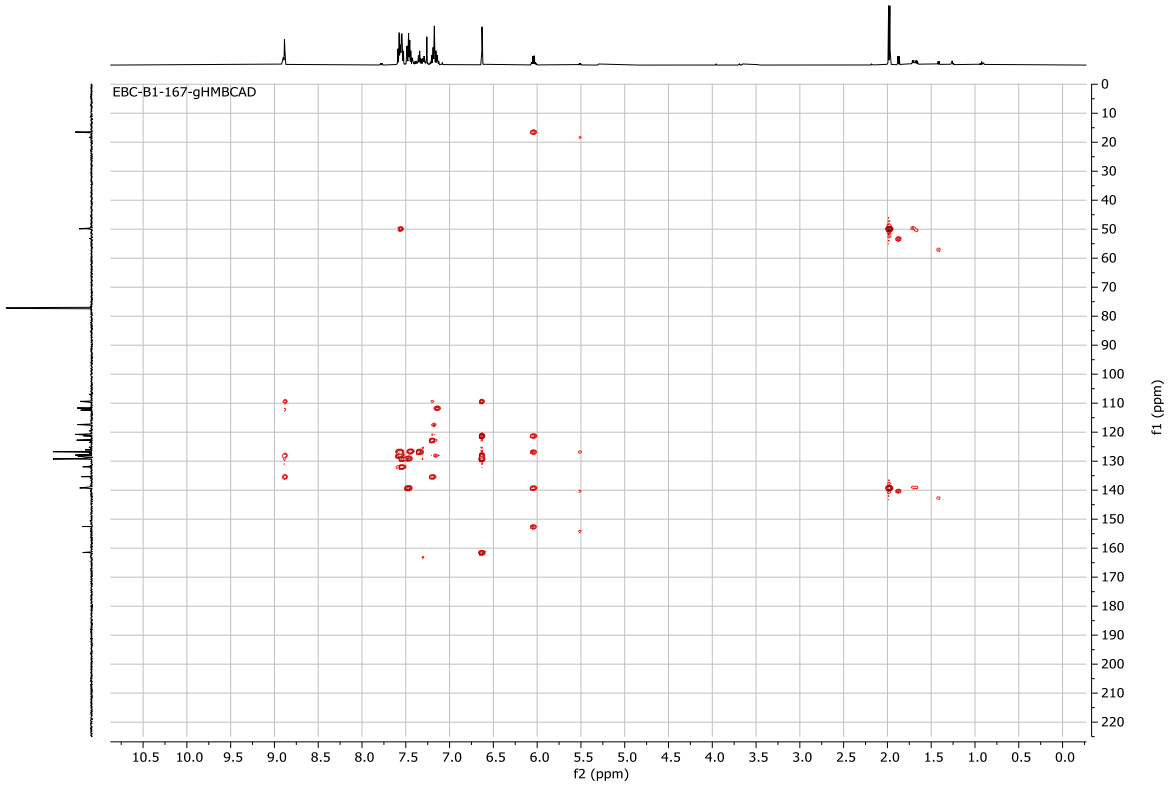
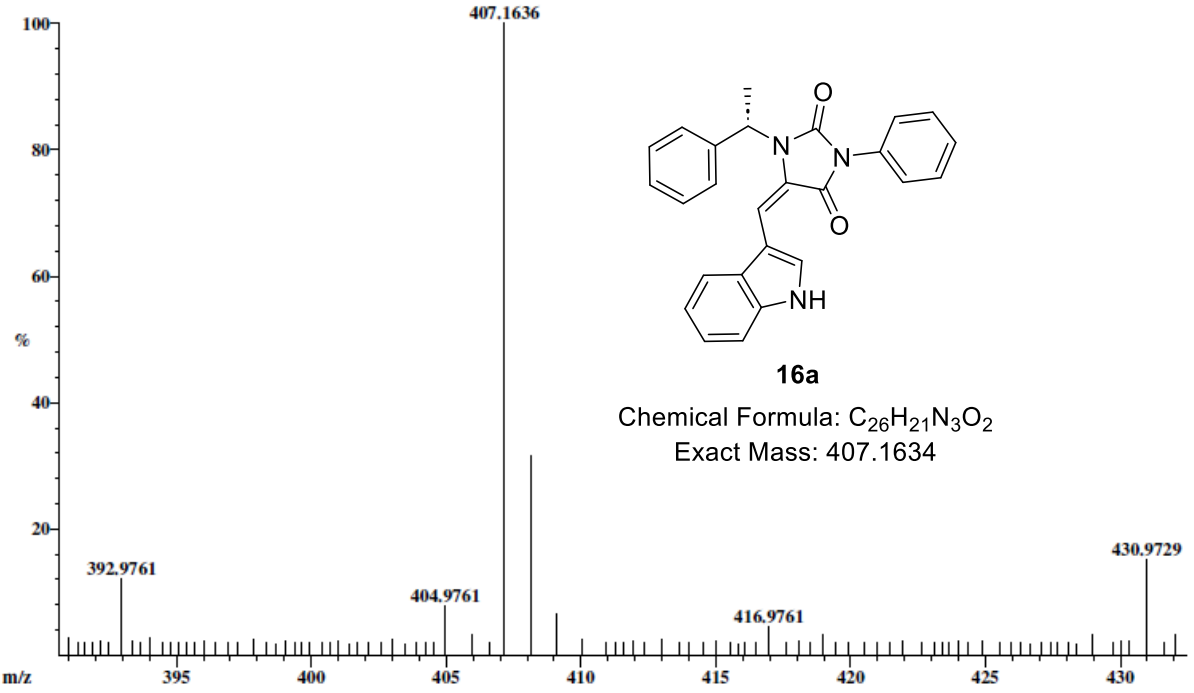



Figure S214. HMBC (500 MHz, $CDCl_3$) spectrum of compound **16a.**

**File: JT-EBC-B1-167** **Date Run: 02-03-2018 (Time Run: 11:46:39)**
**Sample: JT-EBC-B1-167**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 596** **R.T.: 7.92**
**Base: m/z 407; 2.8%FS TIC: 139664** **#Ions: 145**




**16a**

Chemical Formula: $C_{26}H_{21}N_3O_2$
Exact Mass: 407.1634

**Selected Isotopes : $H_{0-21}C_{0-26}N_{0-3}O_{0-2}$** **Error Limit : 5 ppm**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 407.1636 | 100.0% | $C_{26}H_{21}N_3O_2$ | 407.1634 | 0.6 |

Figure S215. HRMS of compound **156a**.

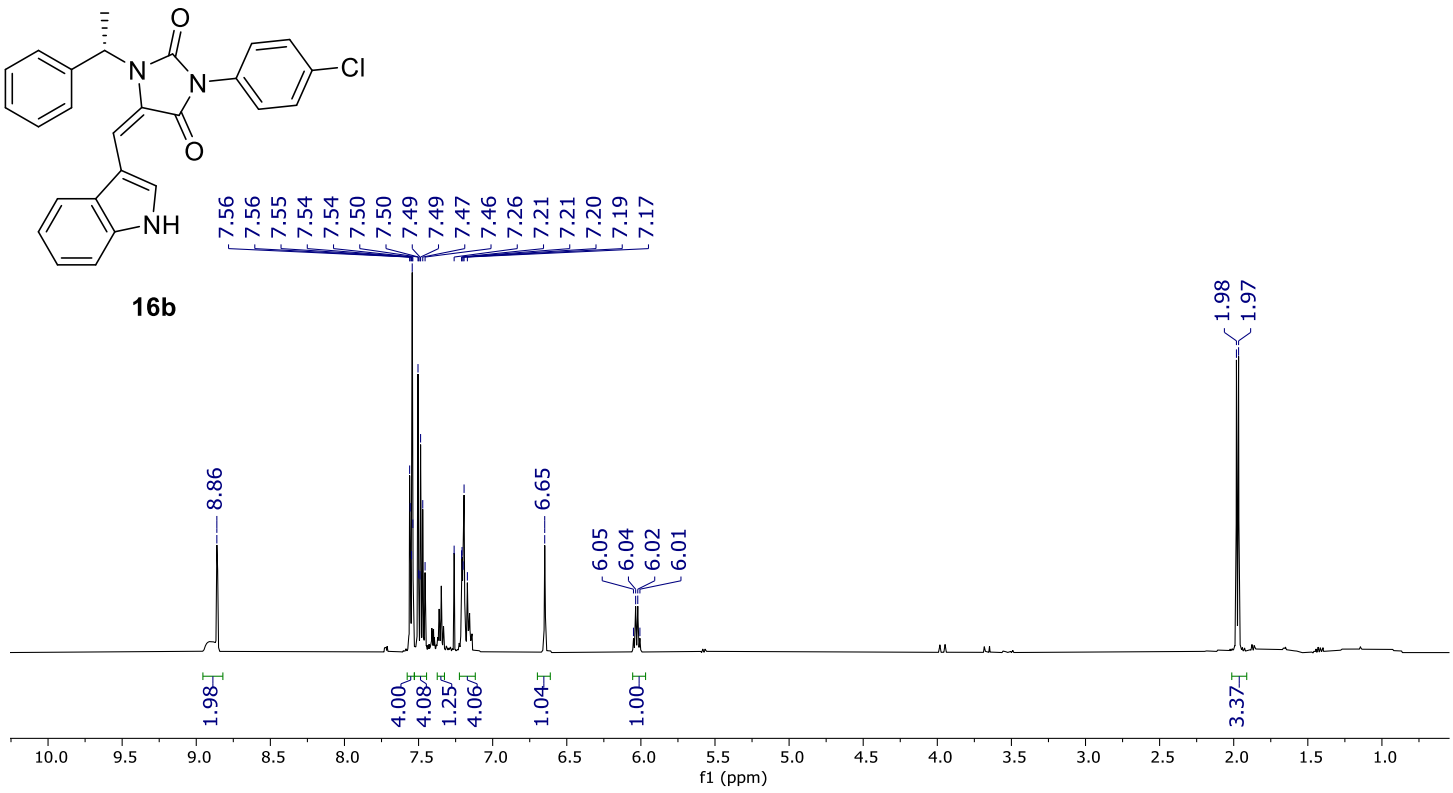



Figure S216. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **16b**.

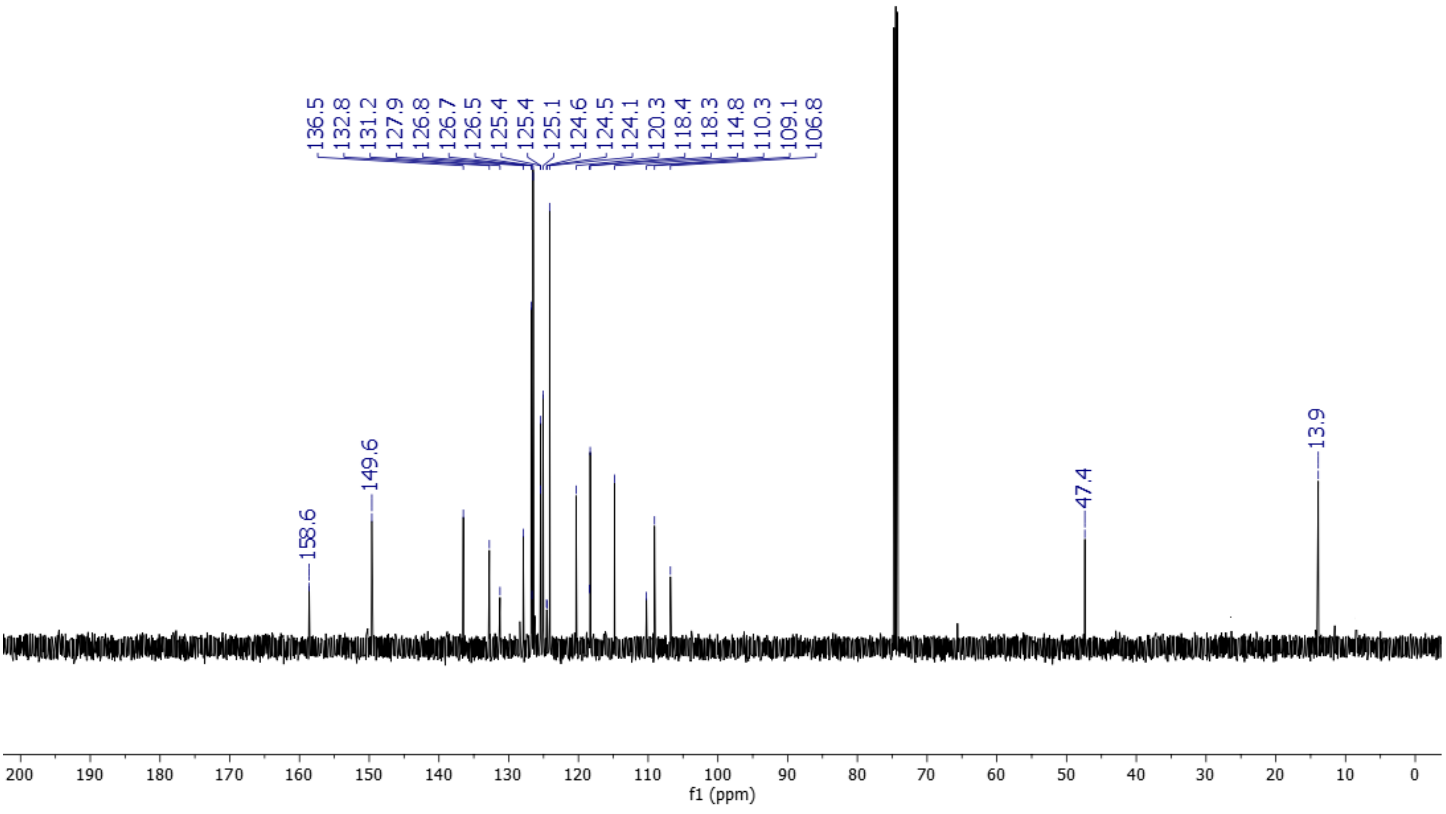



Figure S217. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **16b**.

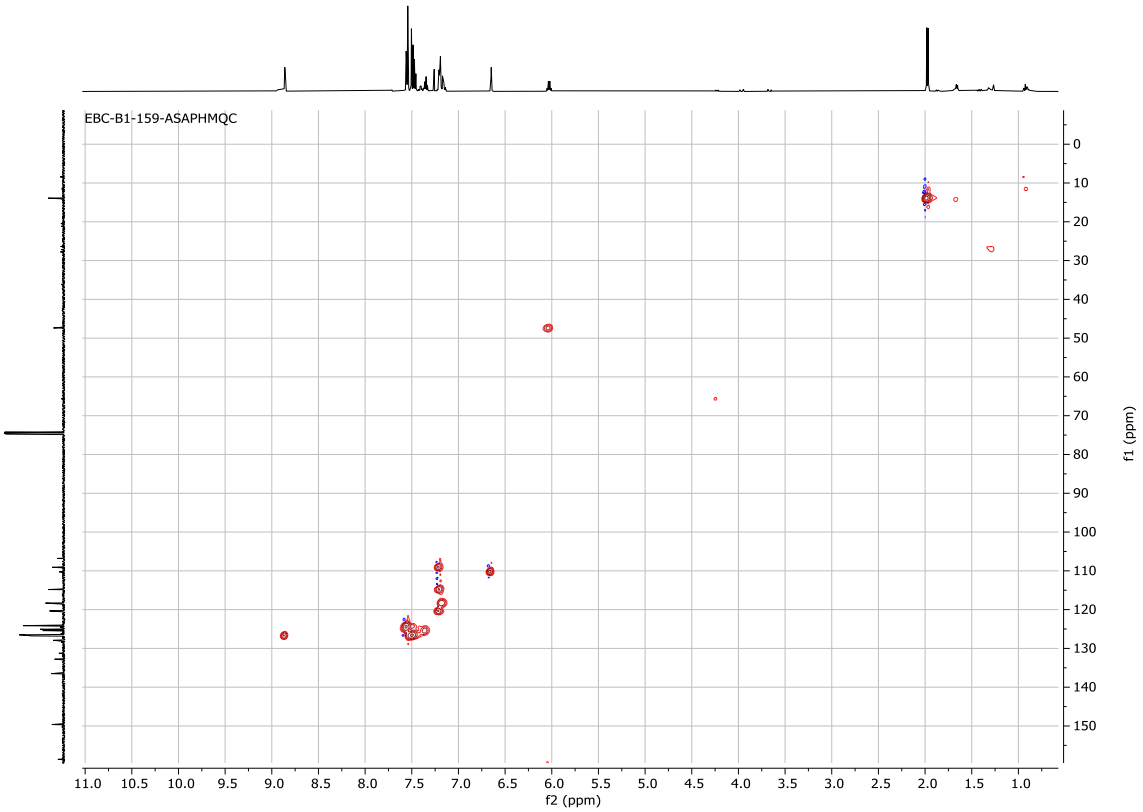



Figure S218. HSQC (500 MHz, $CDCl_3$) spectrum of compound **16b.**

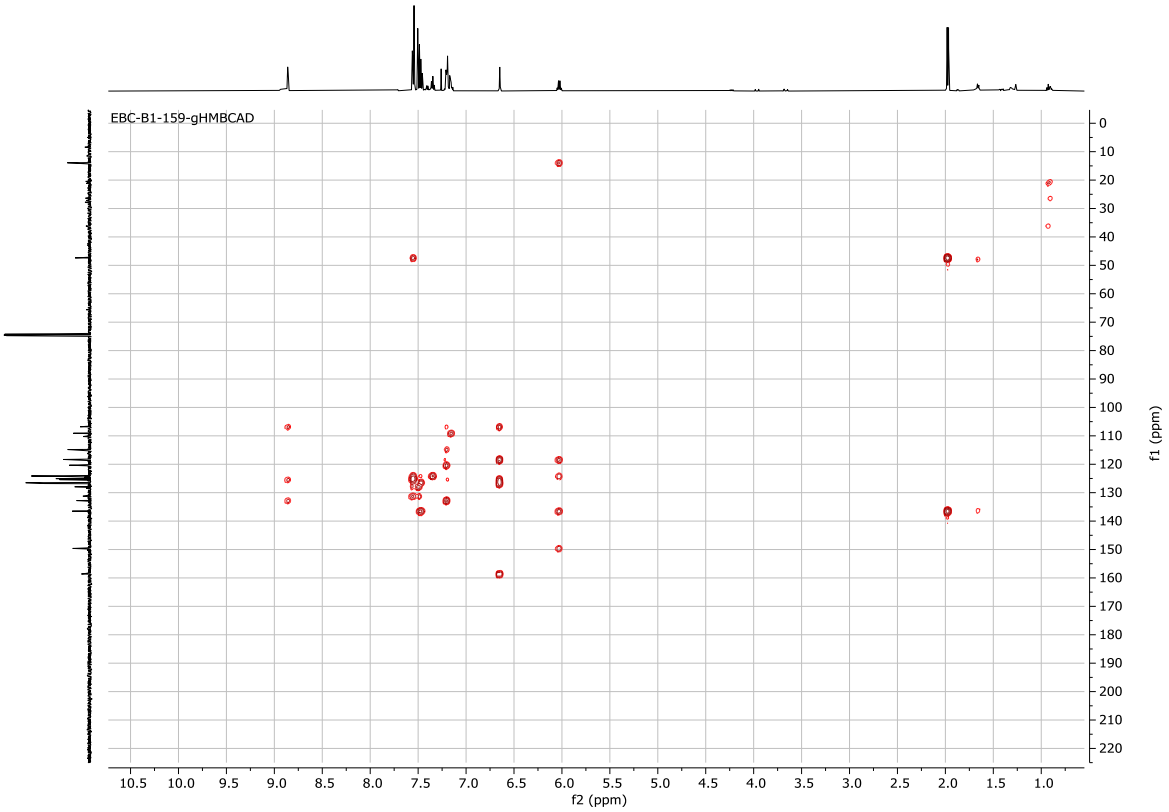
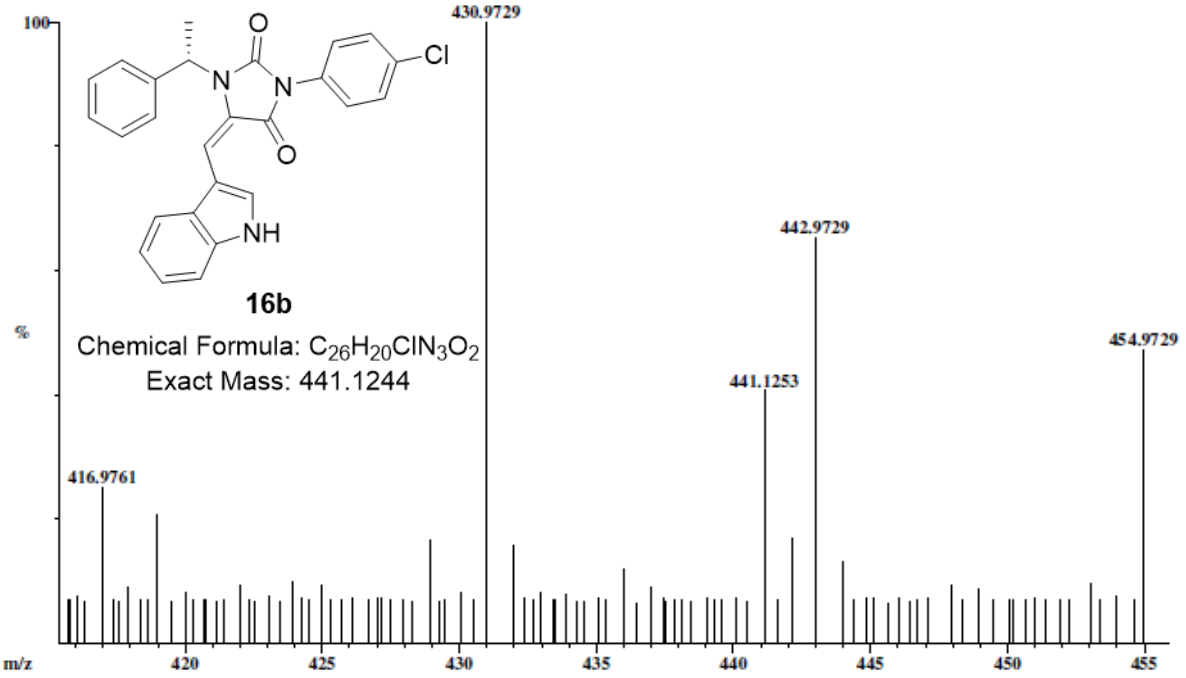



Figure S219. HMBC (500 MHz, $CDCl_3$) spectrum of compound **16b.**

File: JT-EBC-B1-159 Date Run: 04-23-2018 (Time Run: 17:29:52)
Sample: JT-EBC-B1-159
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 568 R.T.: 7.57
Base: m/z 431; .8%FS TIC: 107696 #Ions: 129




Selected Isotopes : $C_{0-26}H_{0-20}Cl_{0-1}N_{0-3}O_{0-2}$ Error Limit : 5 ppm

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 441.1253 | 40.6% | $C_{26}H_{20}ClN_3O_2$ | 441.1244 | 2.0 |

Figure S220. HRMS of compound **16b.**

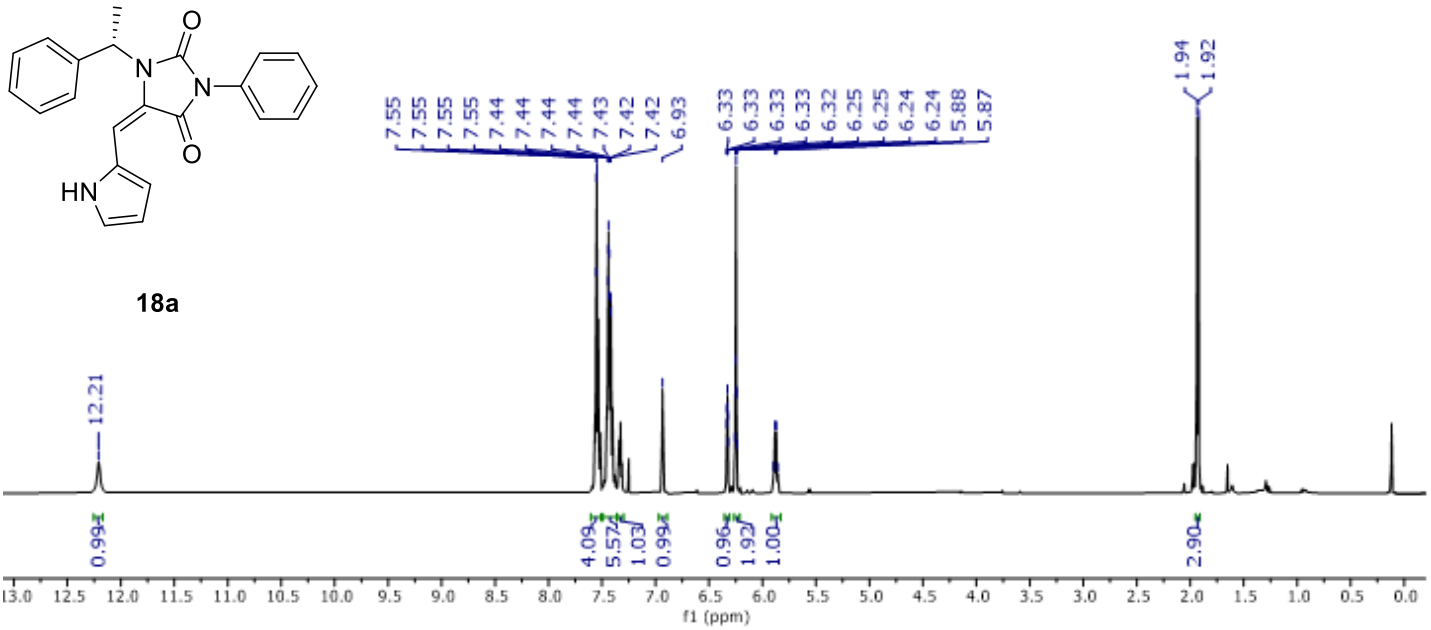



Figure S221. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **18a**.

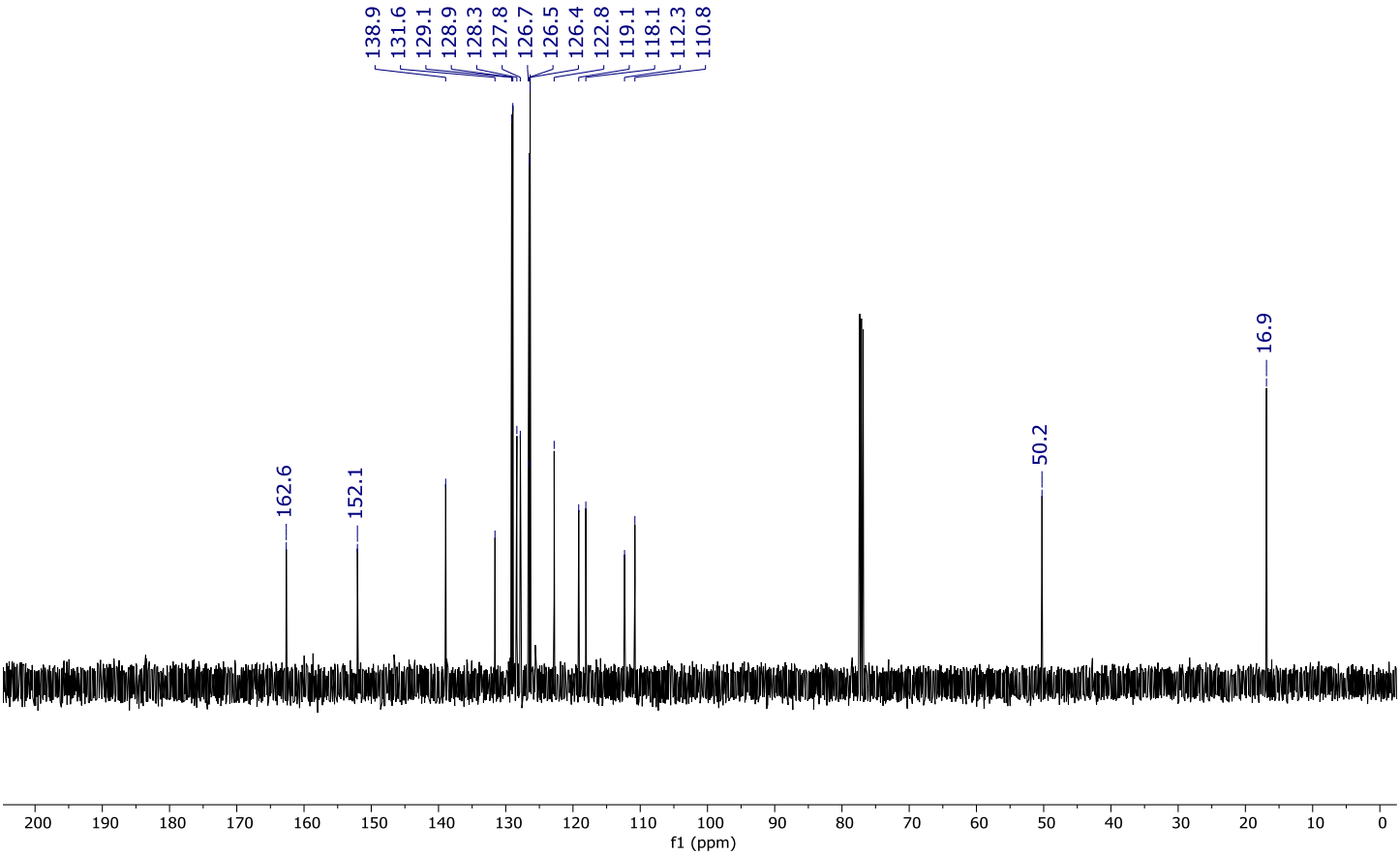



Figure S222. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **18a**.

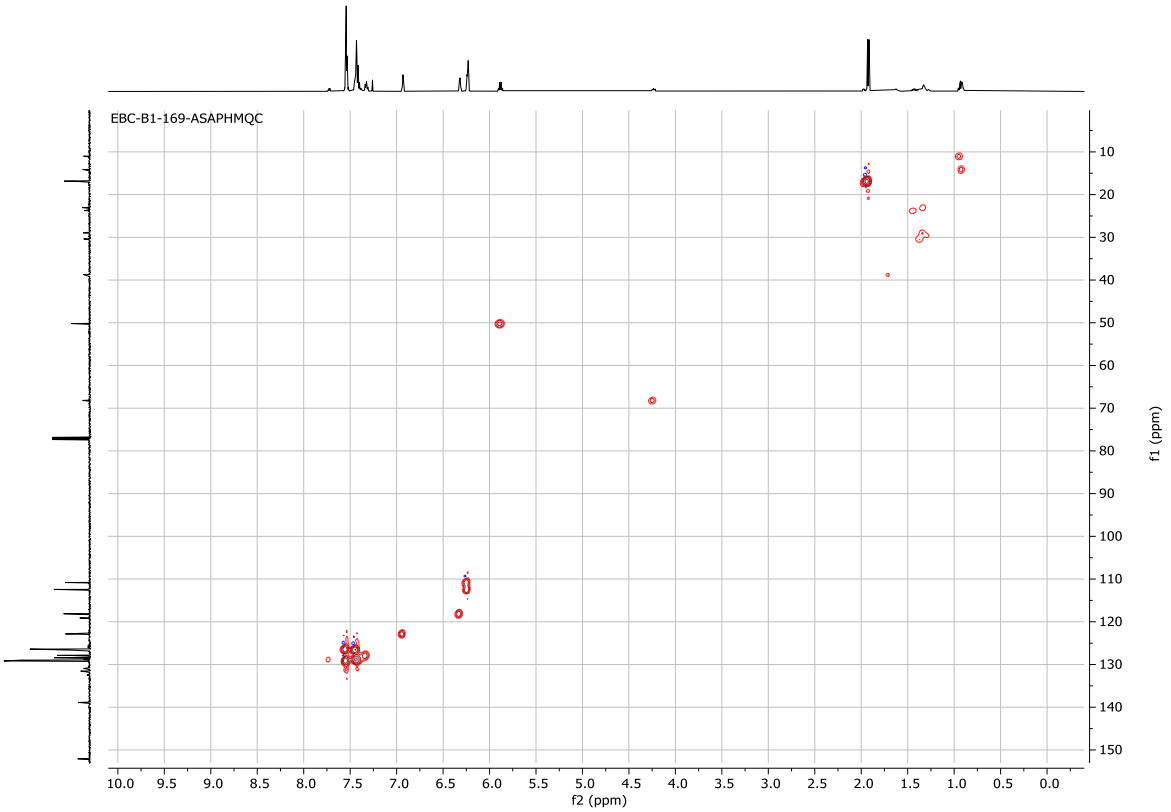



Figure S223. HSQC (500 MHz, $CDCl_3$) spectrum of compound **18a.**

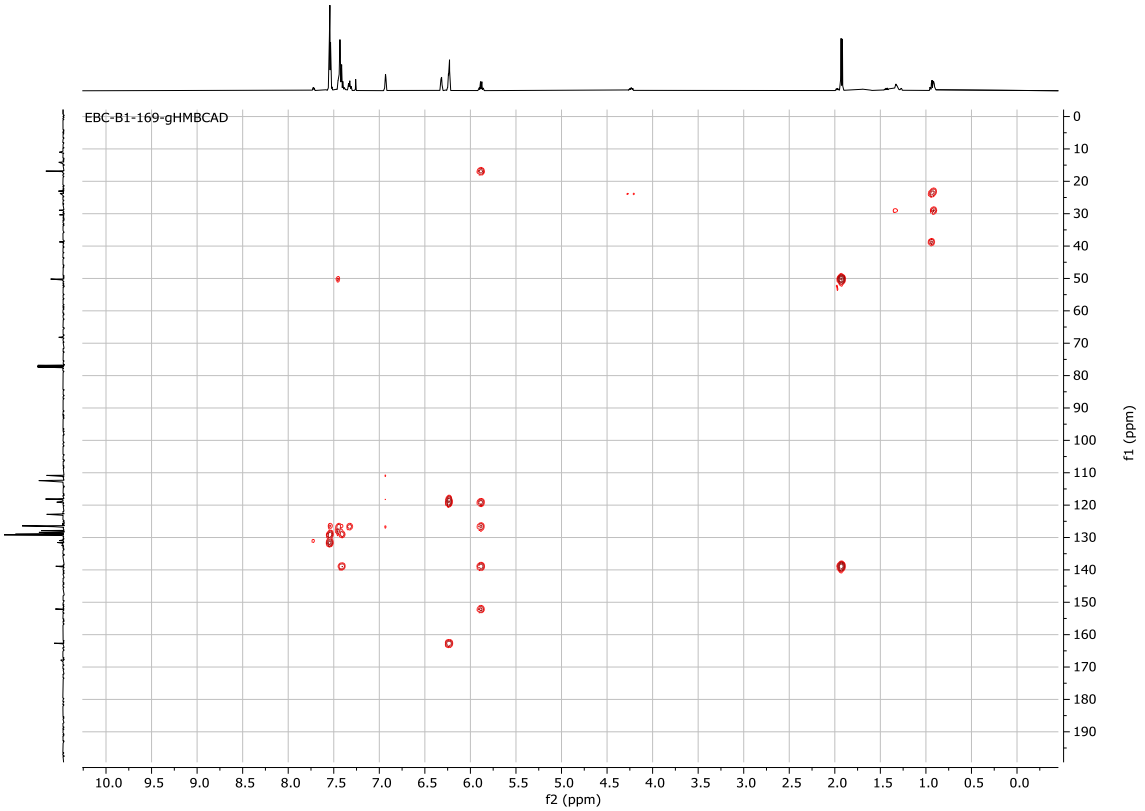
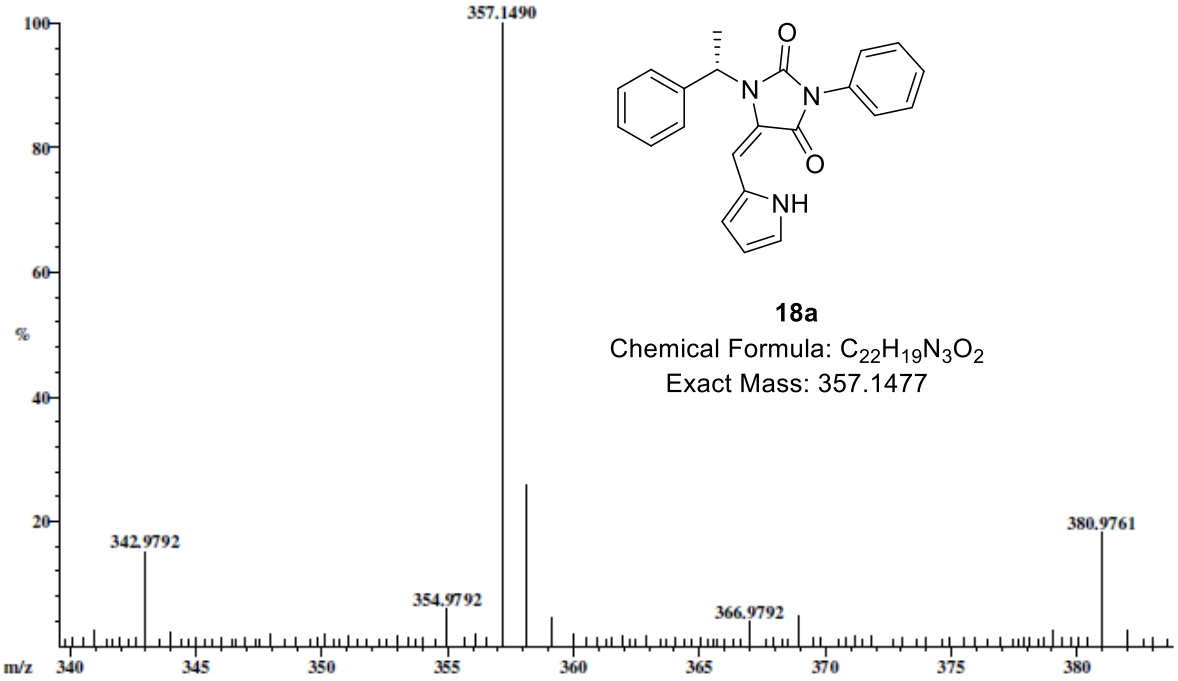



Figure S224. HMBC (500 MHz, $CDCl_3$) spectrum of compound **18a.**

File: JT-EBC-B1-169 Date Run: 04-23-2018 (Time Run: 17:10:07)
Sample: JT-EBC-B1-169
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 400 R.T.: 5.34
Base: m/z 357; 4.8%FS TIC: 238160 #Ions: 216




**18a**
Chemical Formula: $C_{22}H_{19}N_3O_2$
Exact Mass: 357.1477

Selected Isotopes : $C_{0-22}H_{0-19}N_{0-3}O_{0-2}$ Error Limit : 5 ppm

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 357.1490 | 100.0% | $C_{22}H_{19}N_3O_2$ | 357.1477 | 3.6 |

Figure S225. HRMS of compound **18a.**

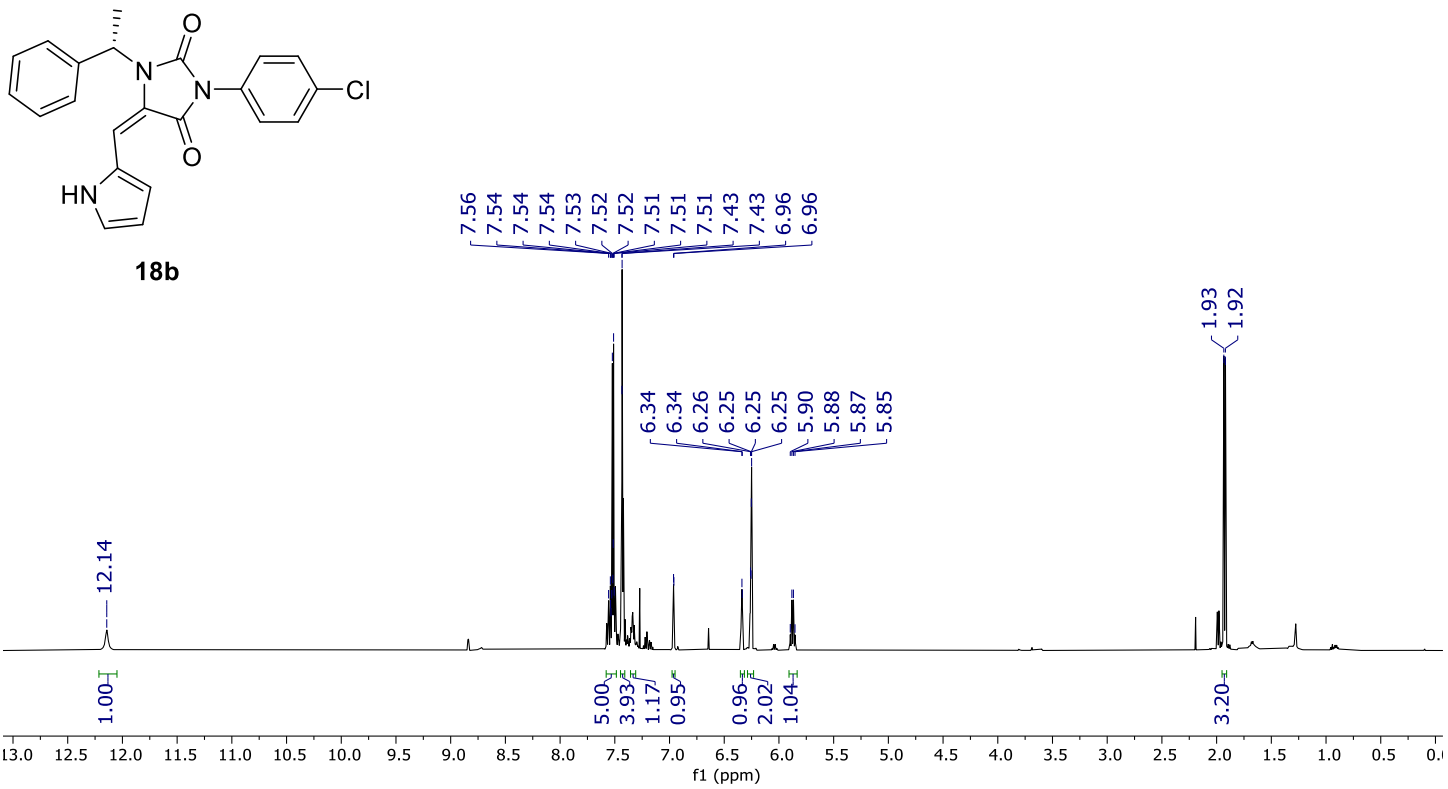



Figure S226. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compounds **18b**/**19b**.

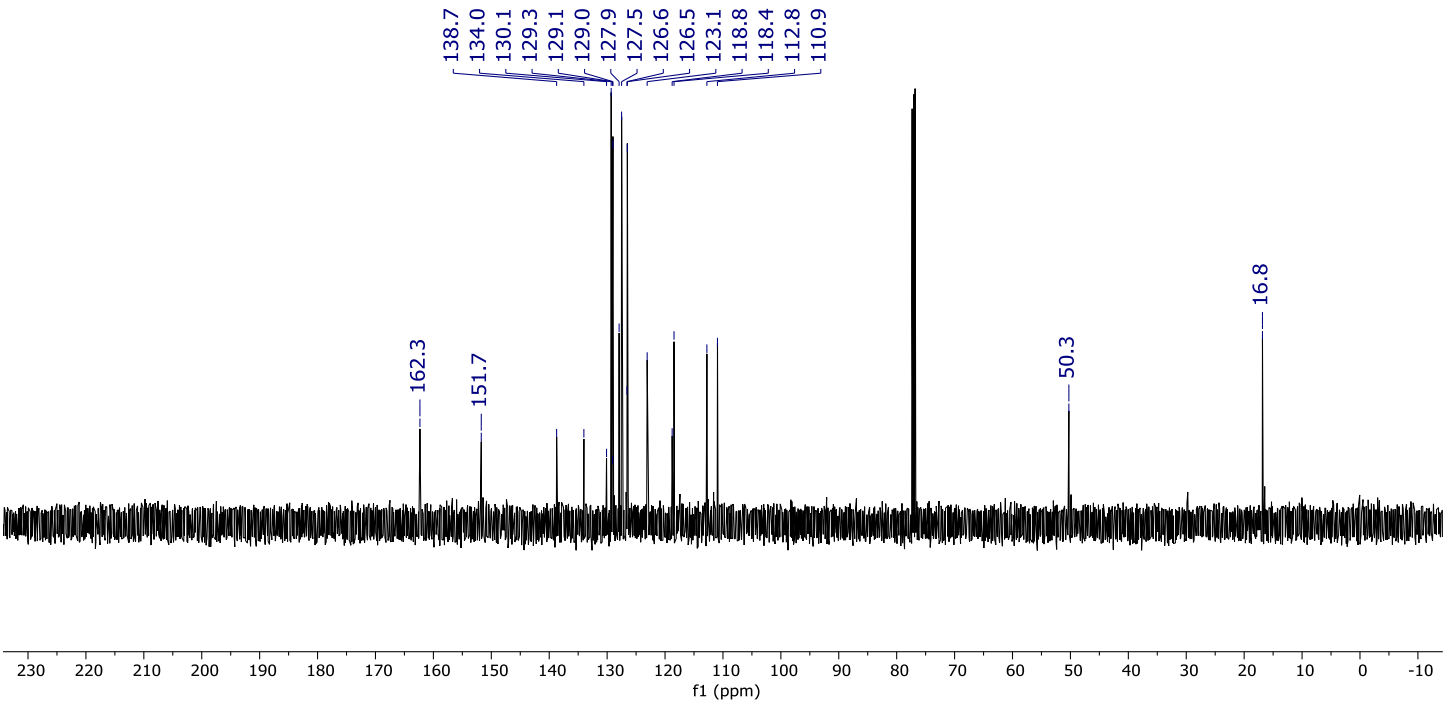



Figure S227. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compounds **18b**/**19b**.

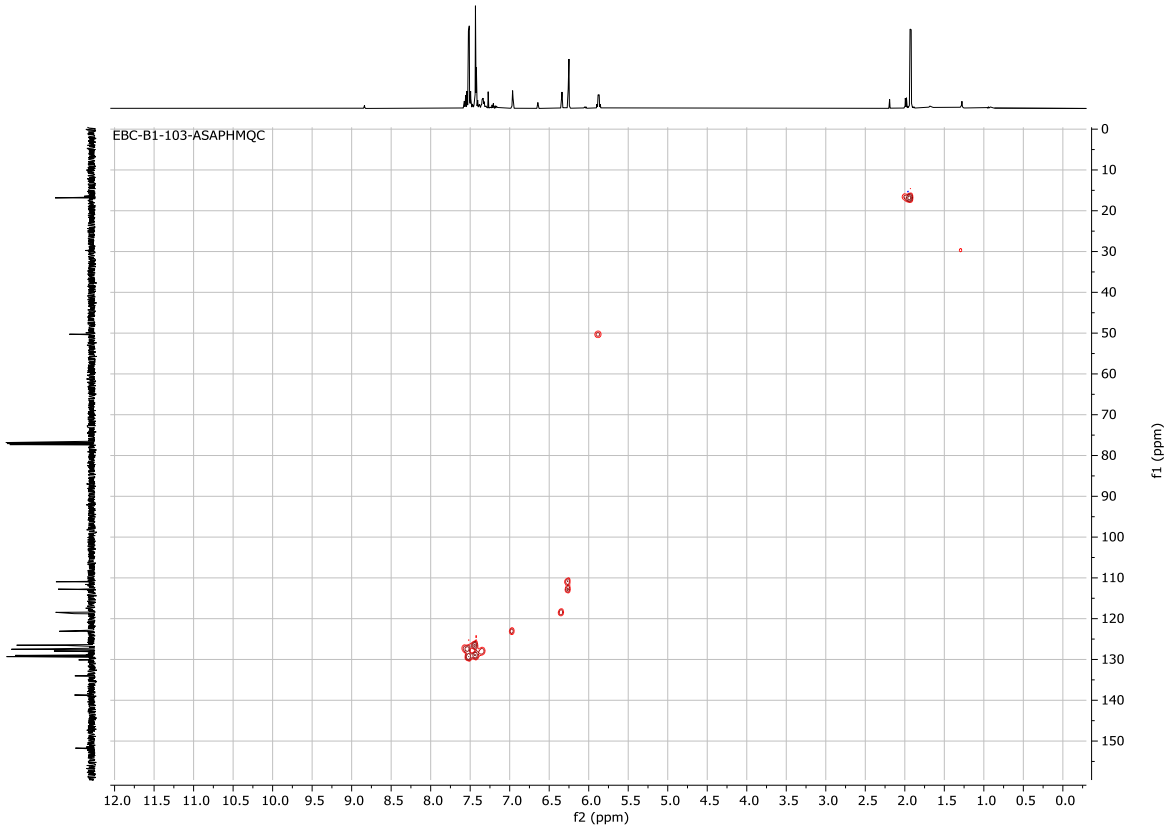



Figure S228. HSQC (500 MHz, $CDCl_3$) spectrum of compound **18b/19b.**

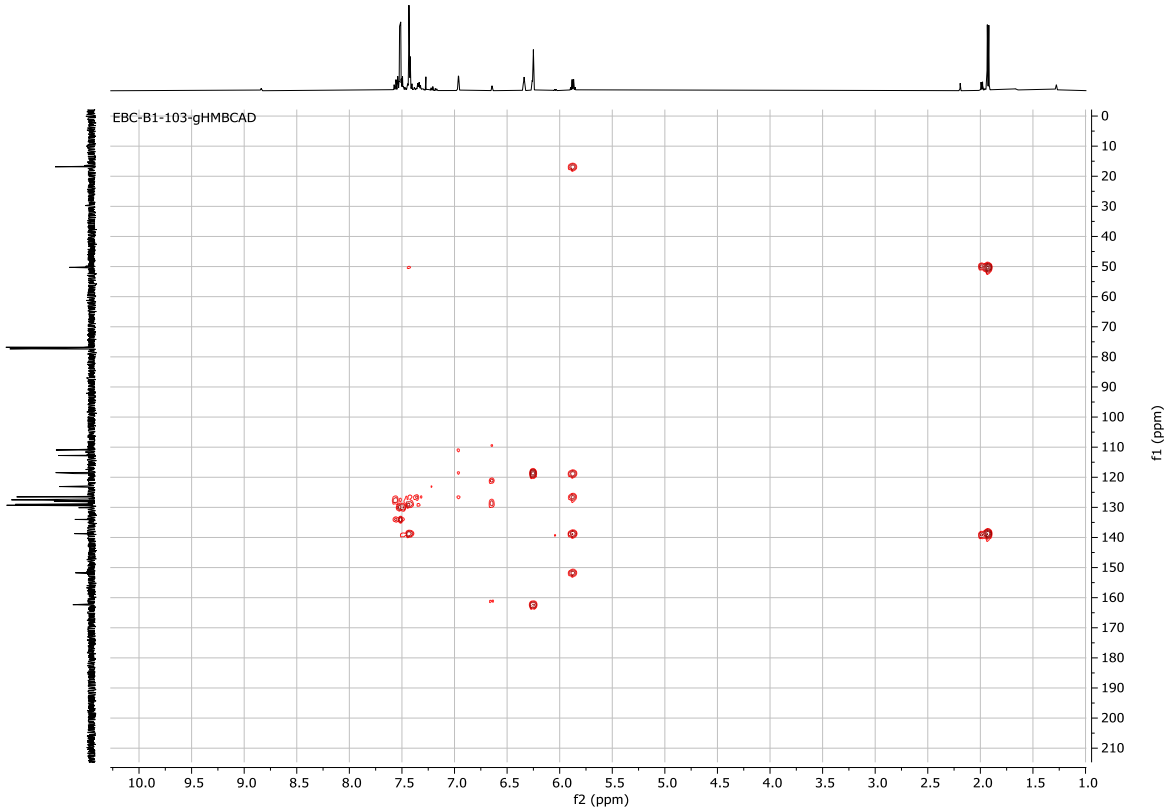
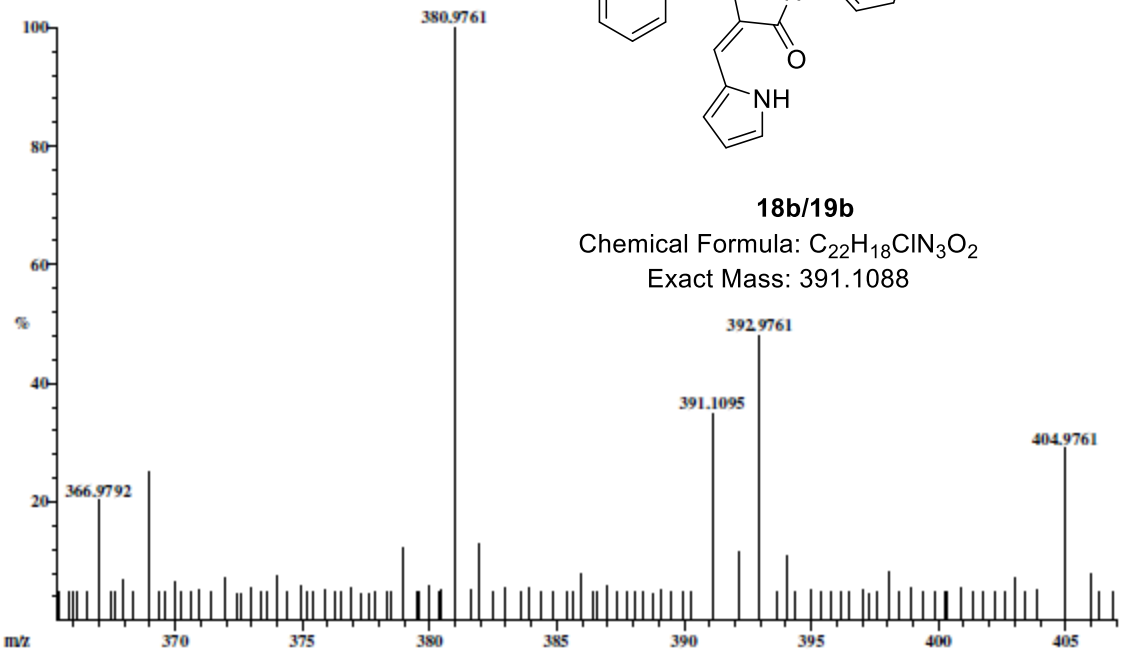



Figure S229. HMBC (500 MHz, $CDCl_3$) spectrum of compound **18b/19b.**

File: JT-EBC-B1-103 Date Run: 04-23-2018 (Time Run: 16:41:44)
Sample: JT-EBC-B1-103
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 476 R.T.: 6.32
Base: m/z 381; 1.1%FS TIC: 119888 #Ions: 141







**18b/19b**
Chemical Formula: $C_{22}H_{18}ClN_3O_2$
Exact Mass: 391.1088

Selected Isotopes : $C_{0-22}H_{0-18}Cl_{0-1}N_{0-3}O_{0-2}$ Error Limit : 5 ppm

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 391.1095 | 34.9% | $C_{22}H_{18}ClN_3O_2$ | 391.1088 | 1.9 |

Figure S230. HRMS of compound **18b/19b.**

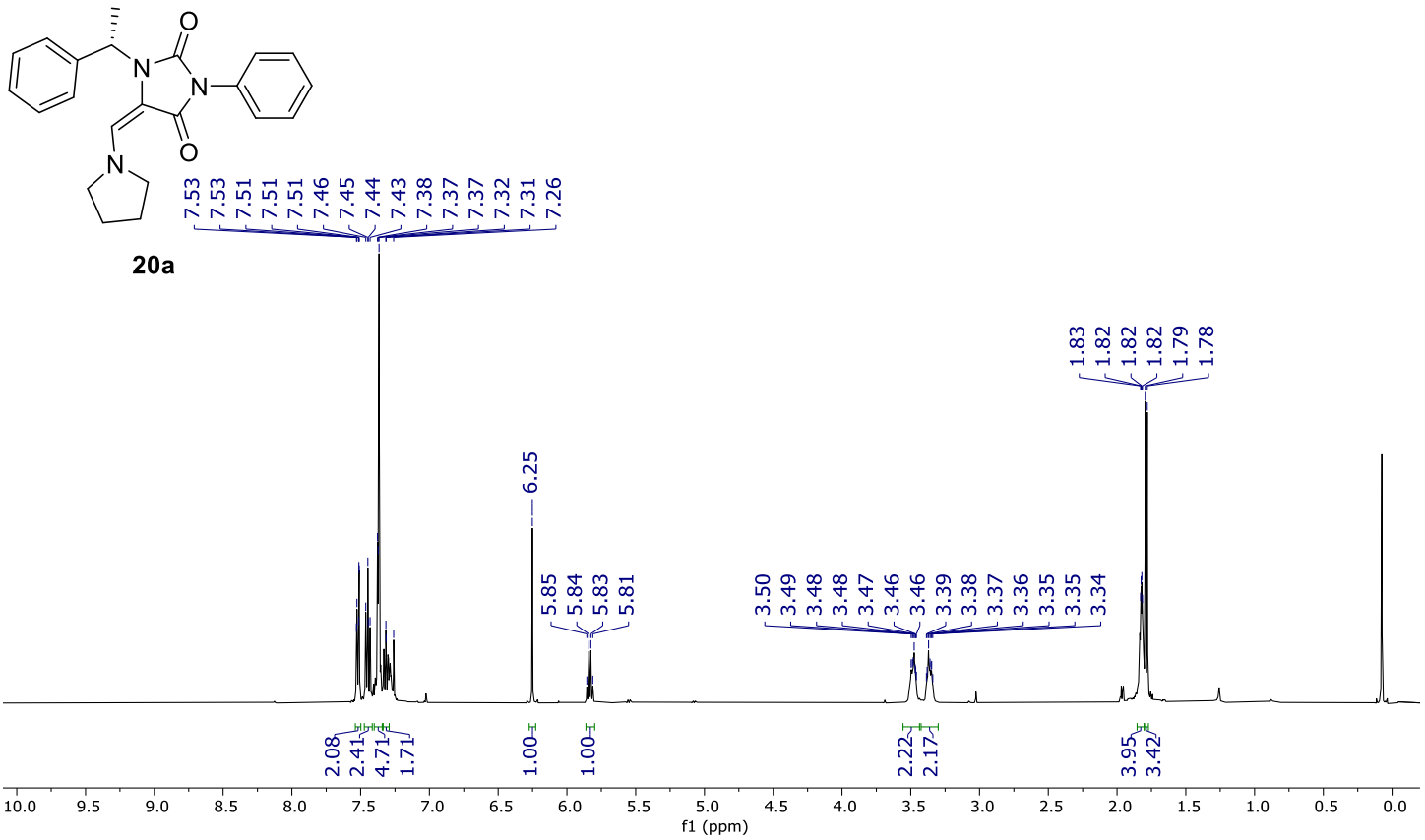



Figure S231. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **20a**.

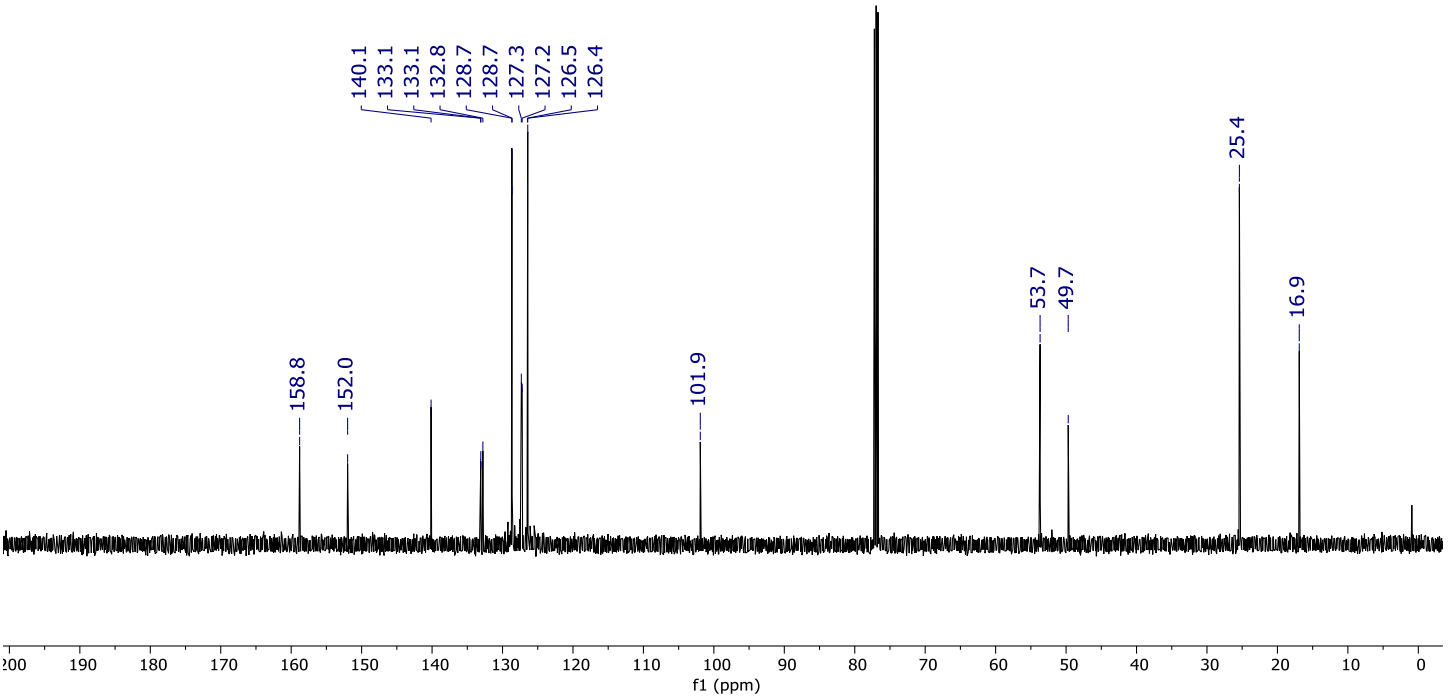



Figure S232. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **20a**.

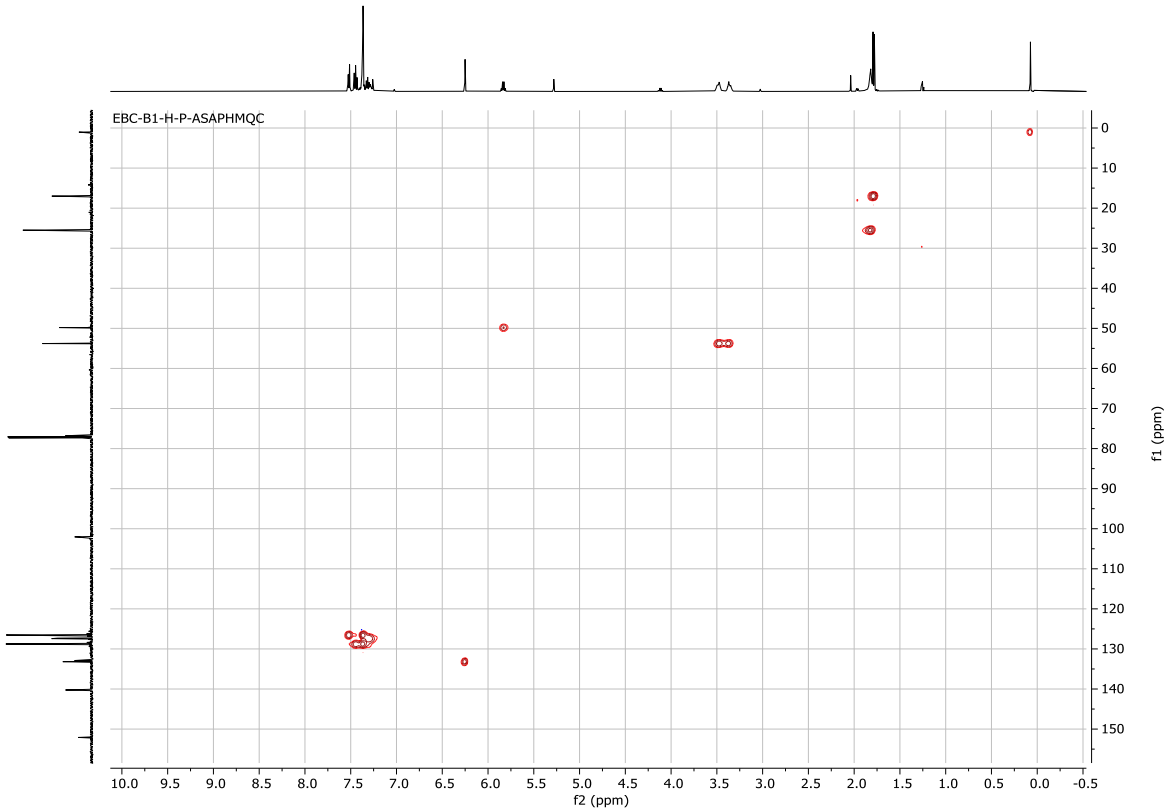



Figure S233. HSQC (500 MHz, $CDCl_3$) spectrum of compound **20a.**

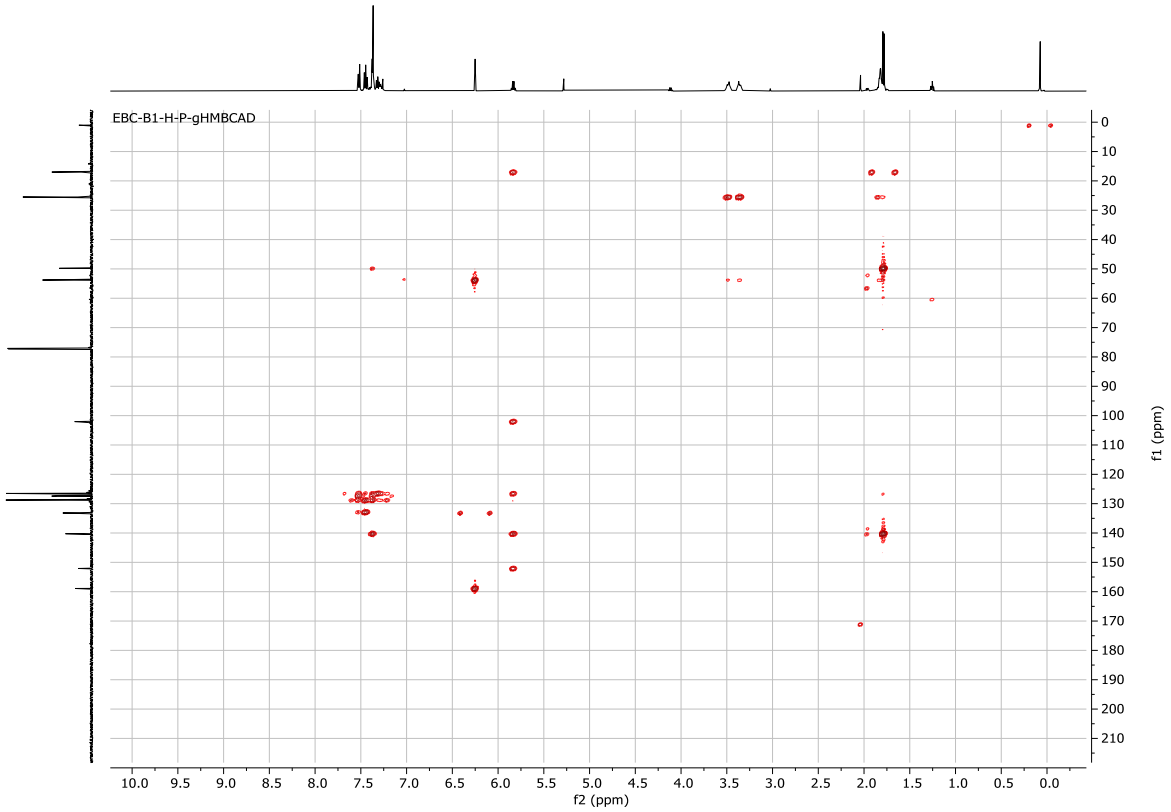
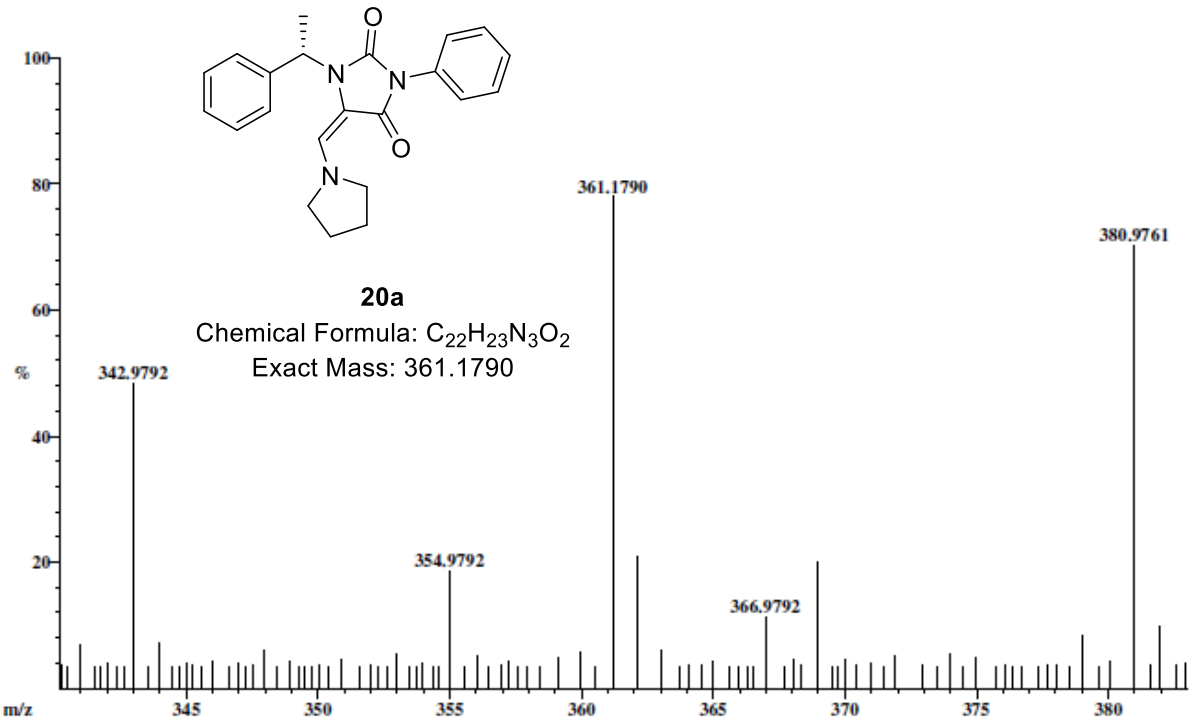



Figure S234. HMBC (500 MHz, $CDCl_3$) spectrum of compound **20a.**

File: JT-EBC-B1-185 Date Run: 05-29-2018 (Time Run: 12:46:01)
Sample: JT-EBC-B1-185
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 306 R.T.: 4.1
Base: m/z 331; 1.6%FS TIC: 157136 #Ions: 156




Selected Isotopes : $H_{0-23}C_{0-22}N_{0-3}O_{0-2}$ Error Limit : 5 ppm

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 361.1790 | 78.0% | $C_{22}H_{23}N_3O_2$ | 361.1790 | -0.1 |

Figure S235. HRMS of compound **20a.**

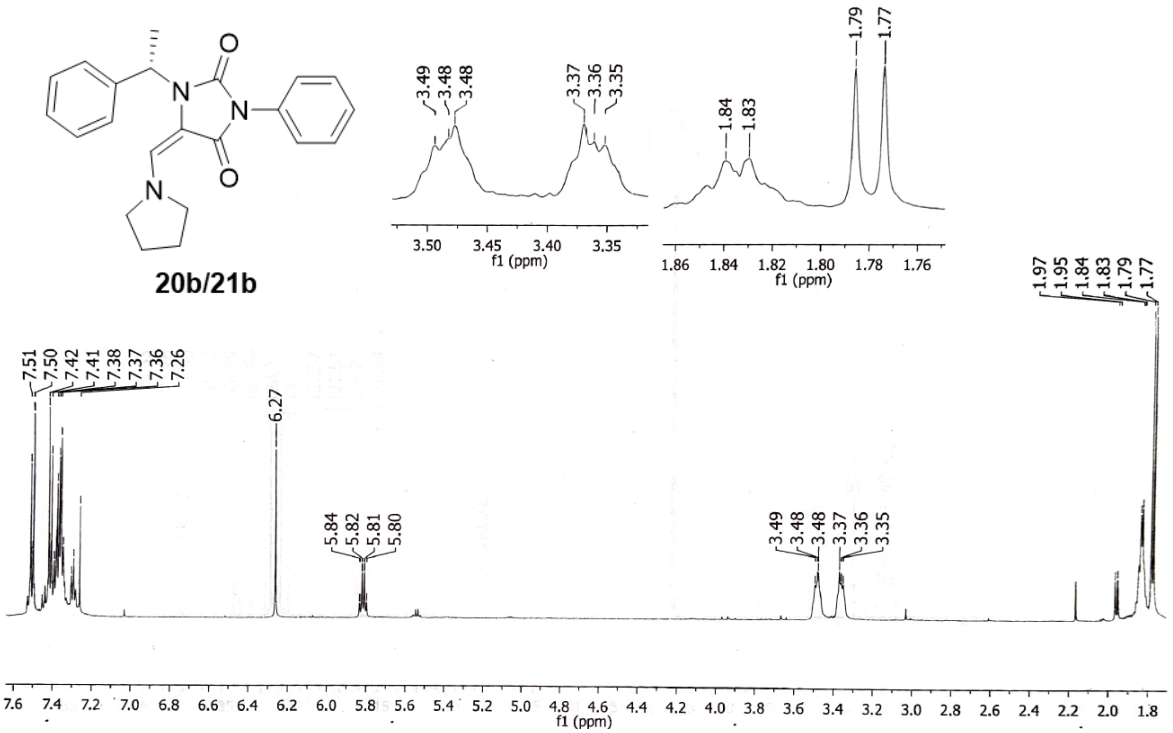



Figure S236. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **20b**/**21b**.

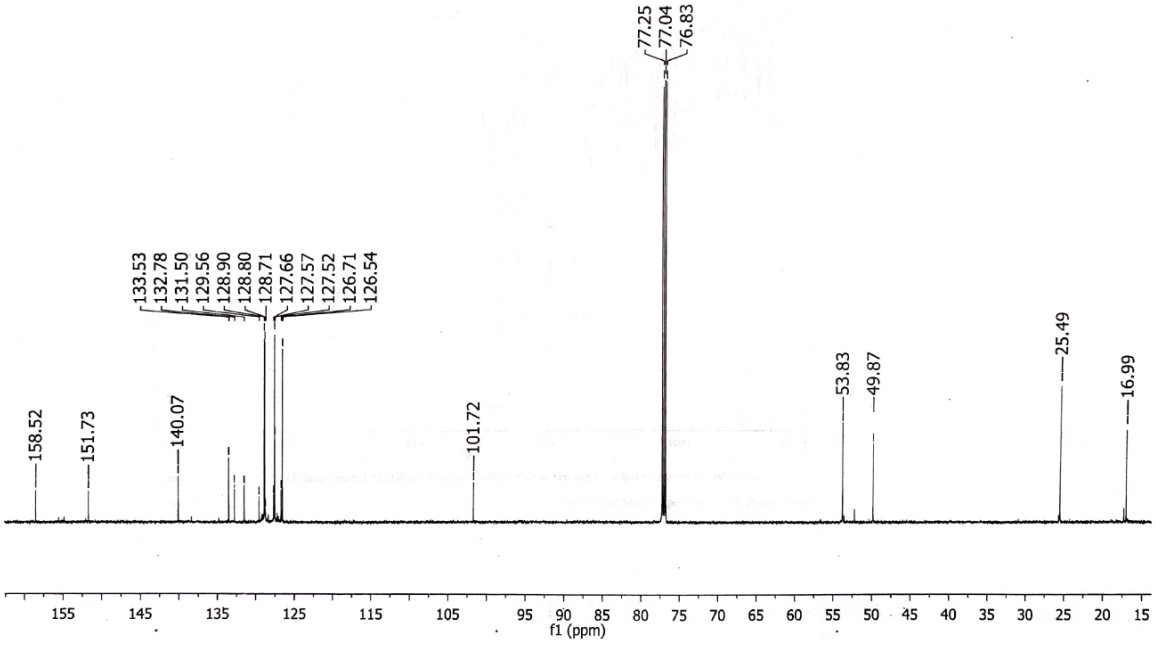



Figure S237. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **20b**/**21b**.

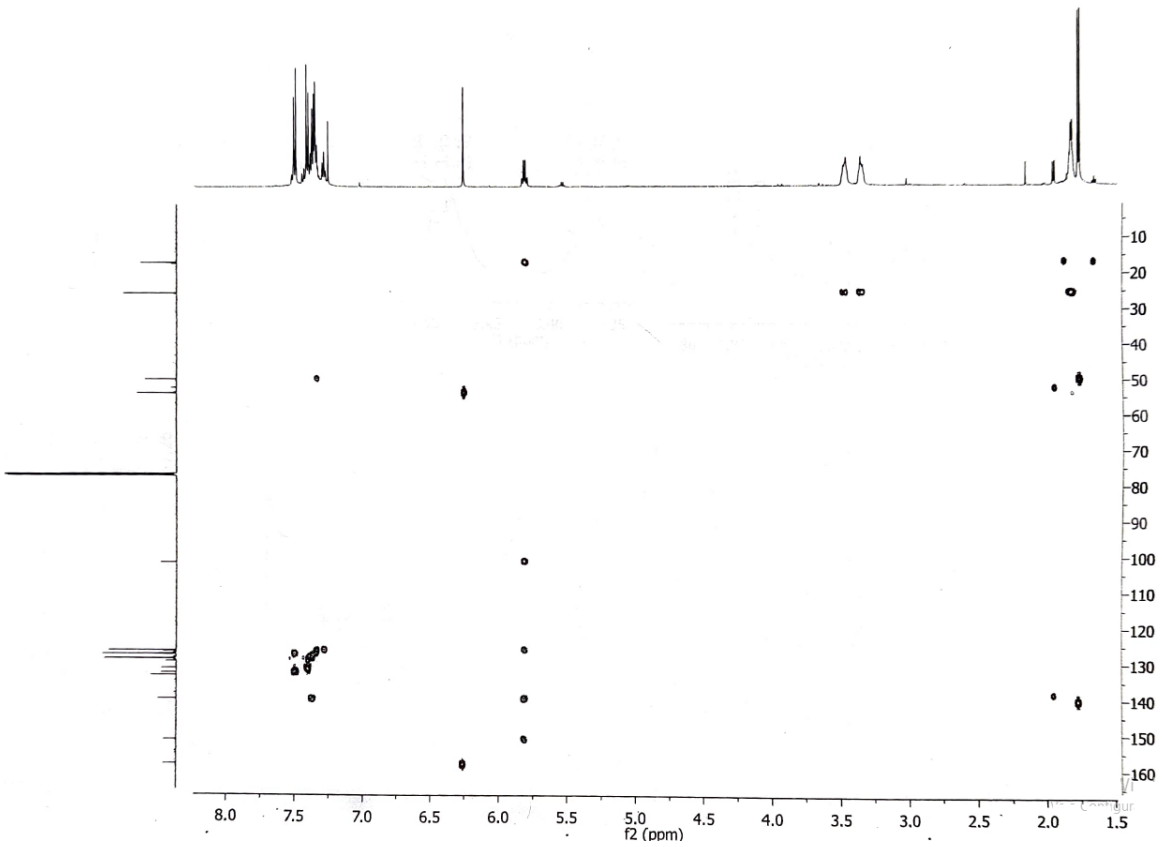
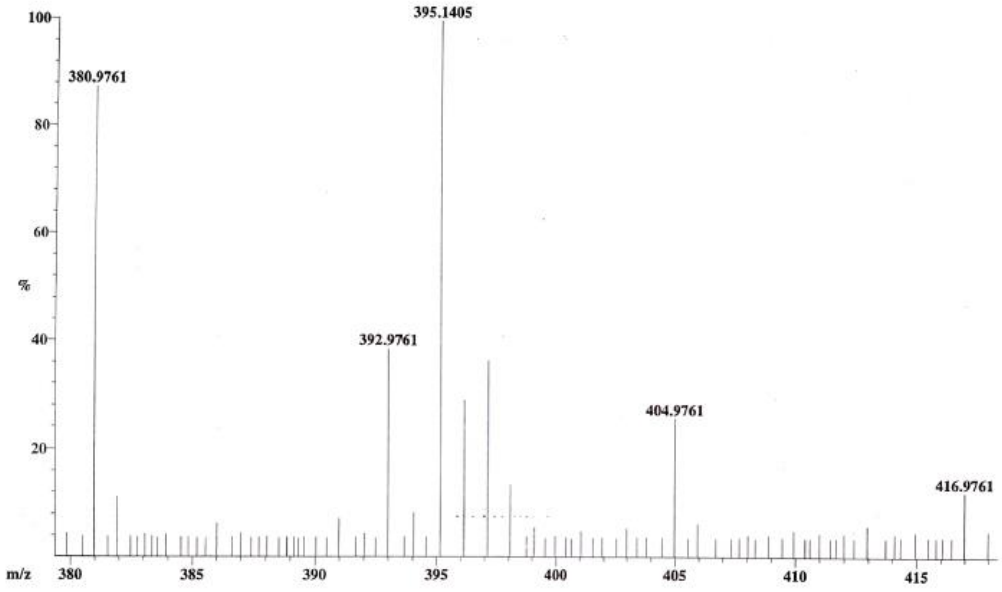



Figure S238. HMBC (500 MHz, $CDCl_3$) spectrum of compound **20b**/**21b.**

**File: JT-EBC-B1-189** **Date Run: 05-29-2018 (Time Run: 13:01:35)**
**Sample: JT-EBC-B1-189**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 490** **R.T.: 6.51**
**Base: m/z 395; 1.5%FS TIC: 141552** **#Ions: 128**




**Selected Isotopes : $H_{0-22}C_{0-22}N_{0-3}O_{0-2}Cl_{0-1}$** **Error Limit : 5 ppm**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* |
|---|---|---|---|---|
| 395.1405 | 100.0% | $C_{22}H_{22}N_3O_2Cl$ | 395.1401 | 1.1 |

Figure S239. HRMS of compound **20b**/**21b.**

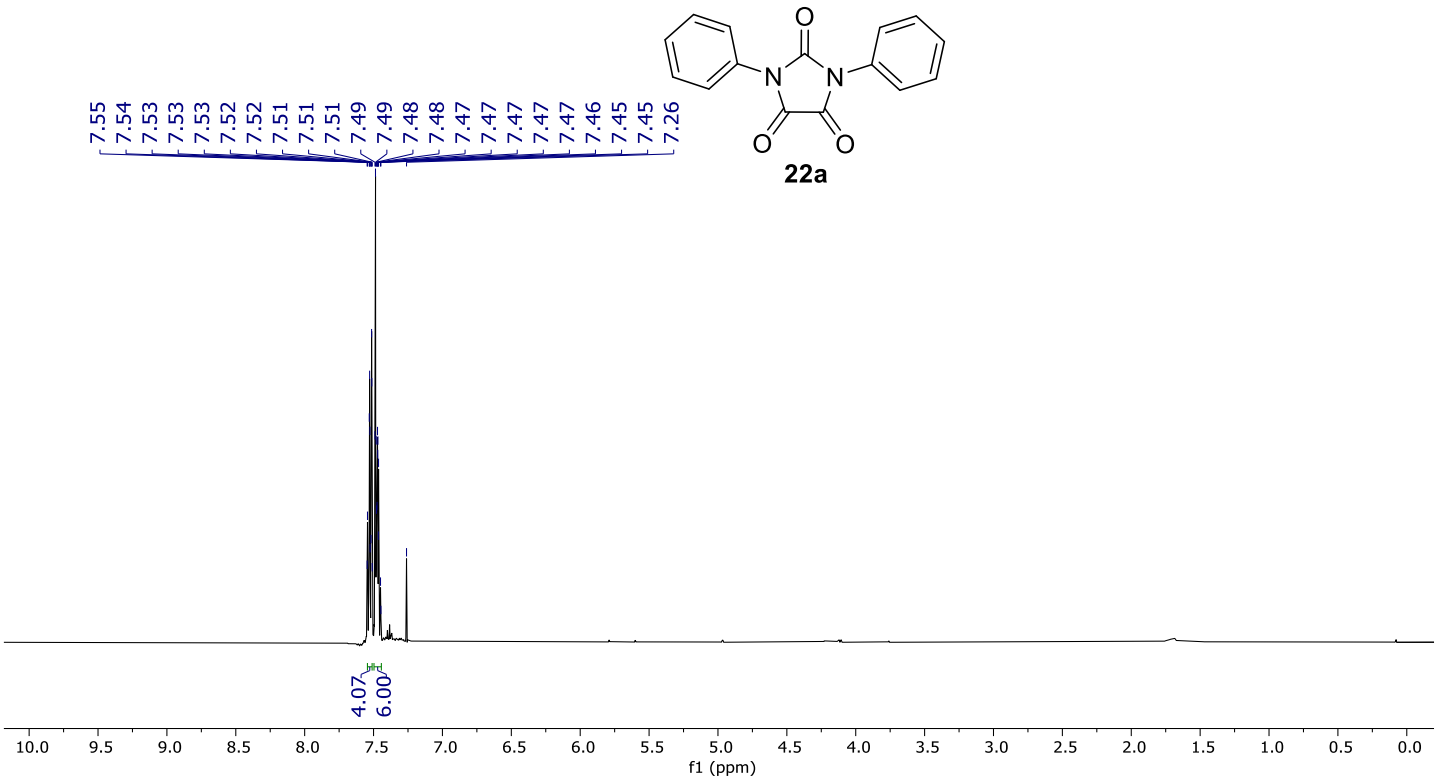



Figure S240. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **22a**.

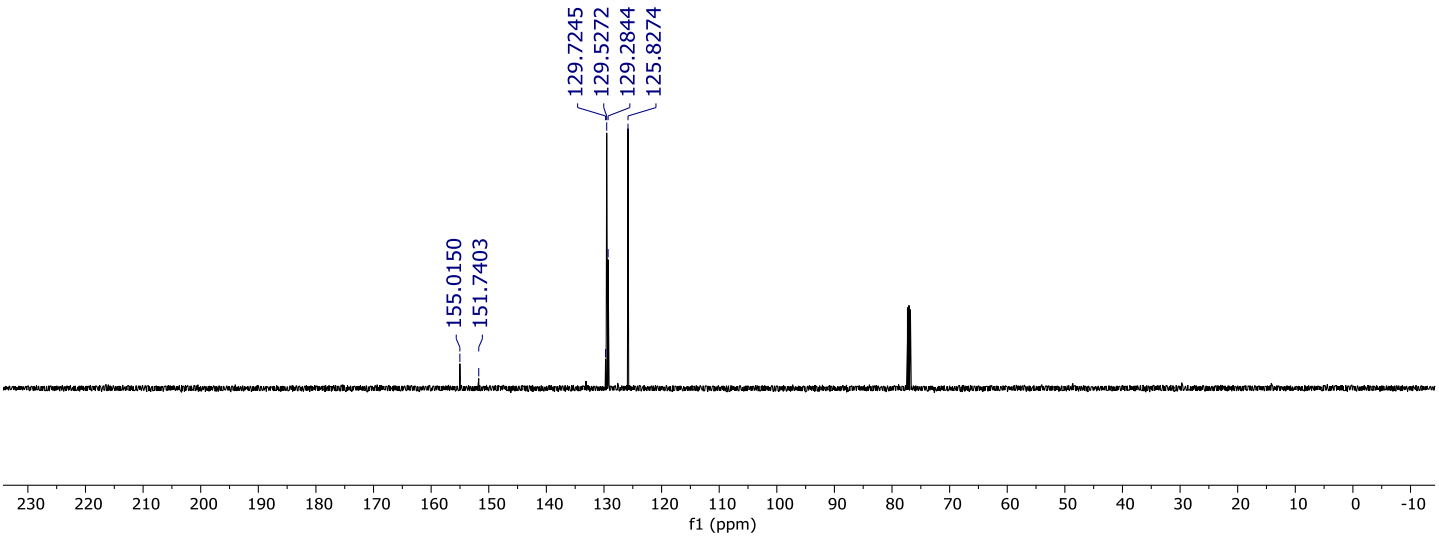



Figure S241. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **22a**.

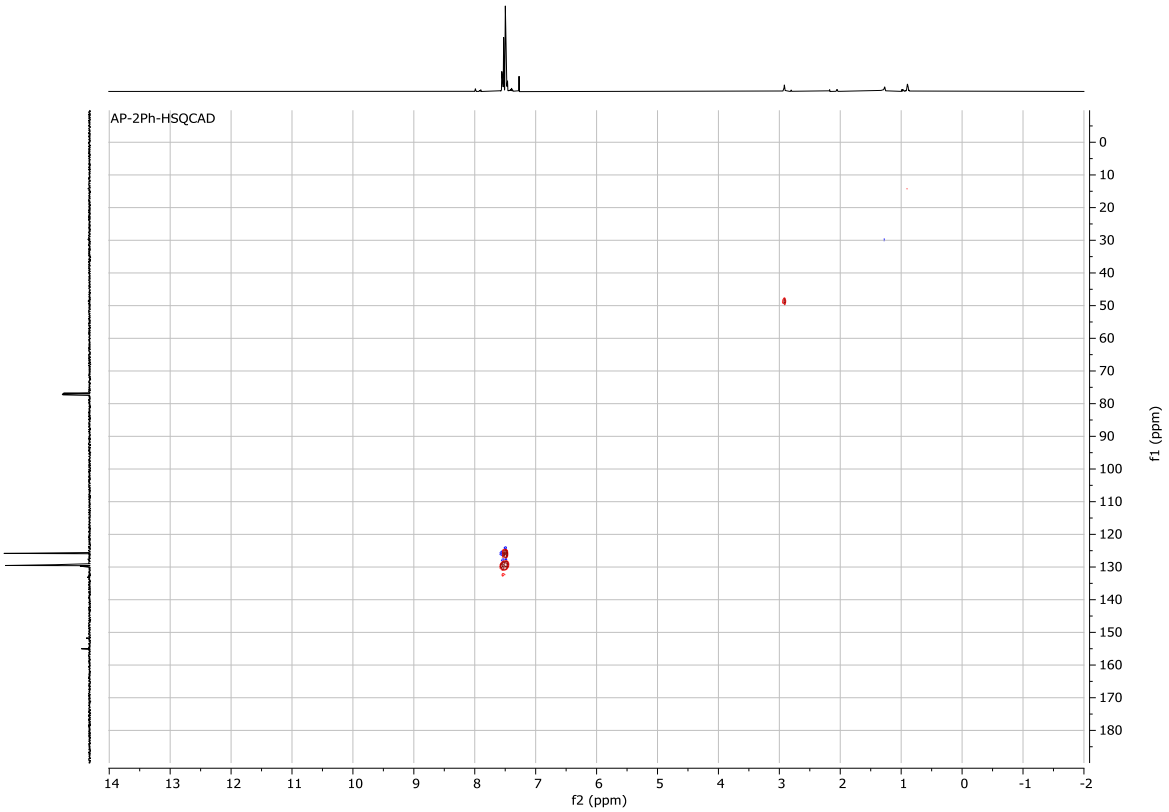



Figure S242. HSQC (500 MHz, $CDCl_3$) spectrum of compound **22a.**

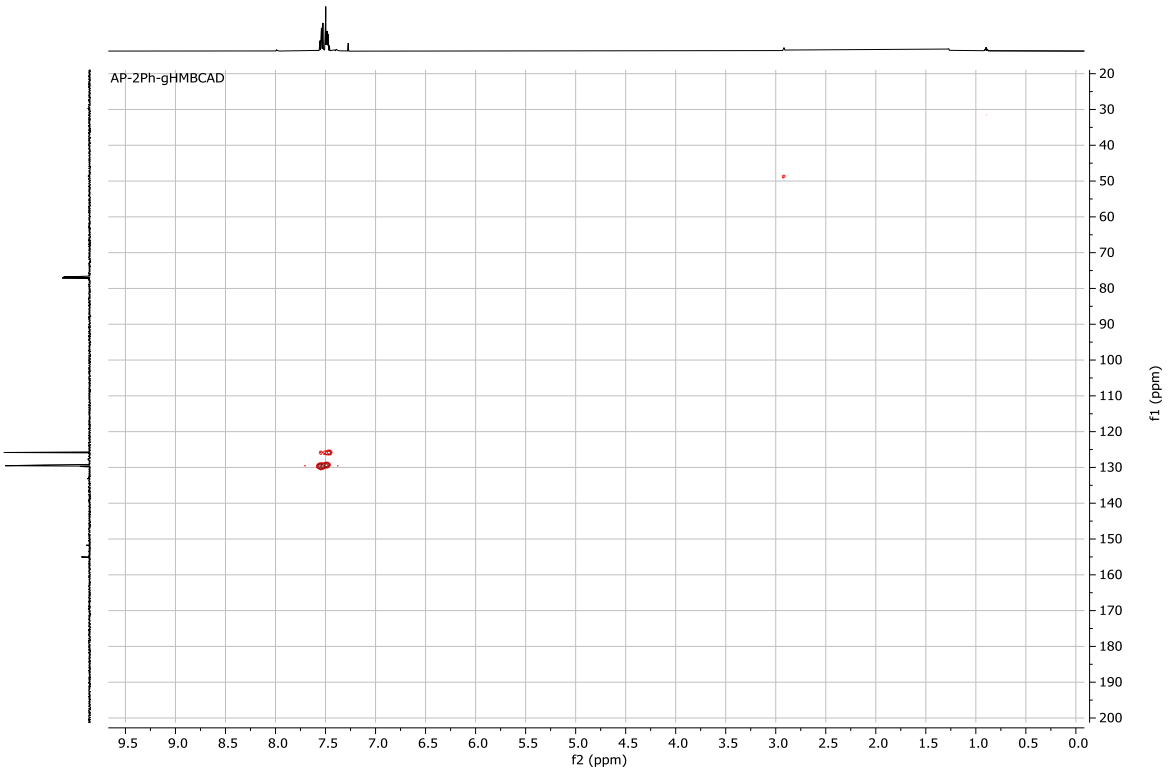
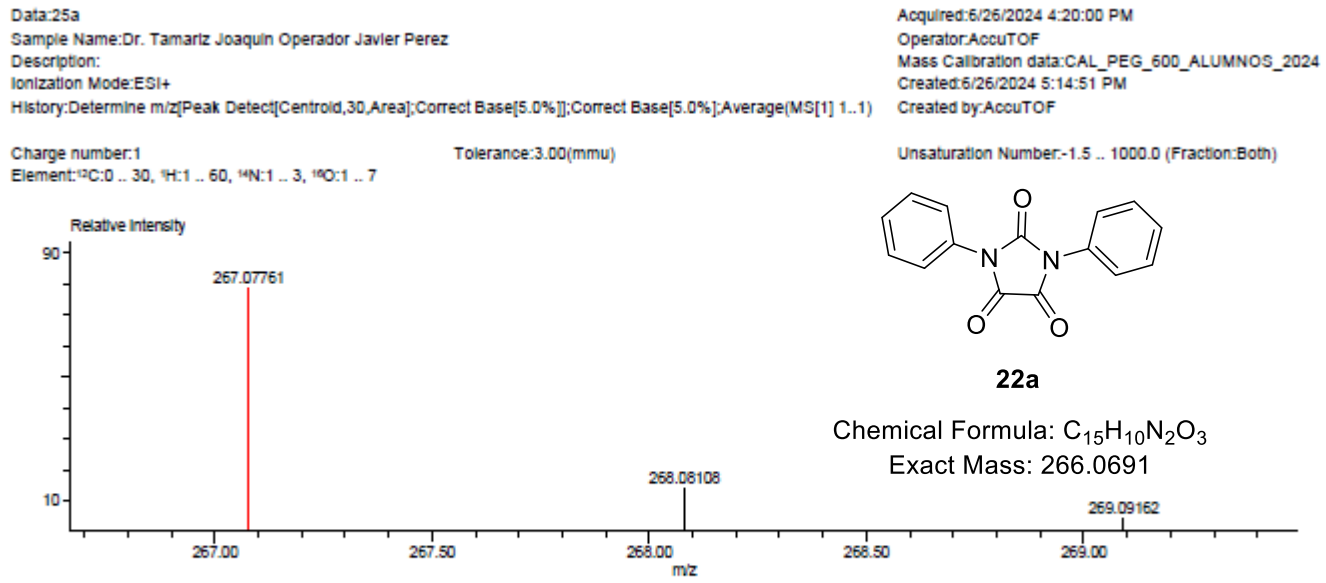



Figure S243. HMBC (500 MHz, $CDCl_3$) spectrum of compound **22a.**




| Mass | Intensity | Calc. Mass | Mass Difference (mmu) | Mass Difference (ppm) | Possible Formula | Unsaturation Number |
|---|---|---|---|---|---|---|
| 267.07761 | 313843.96 | 267.07697 | 0.64 | 2.40 | $^{12}C_{15}{}^{1}H_{11}{}^{14}N_{2}{}^{16}O_{3}$ | 11.5 |

Figure S244. HRMS of compound **22a.**

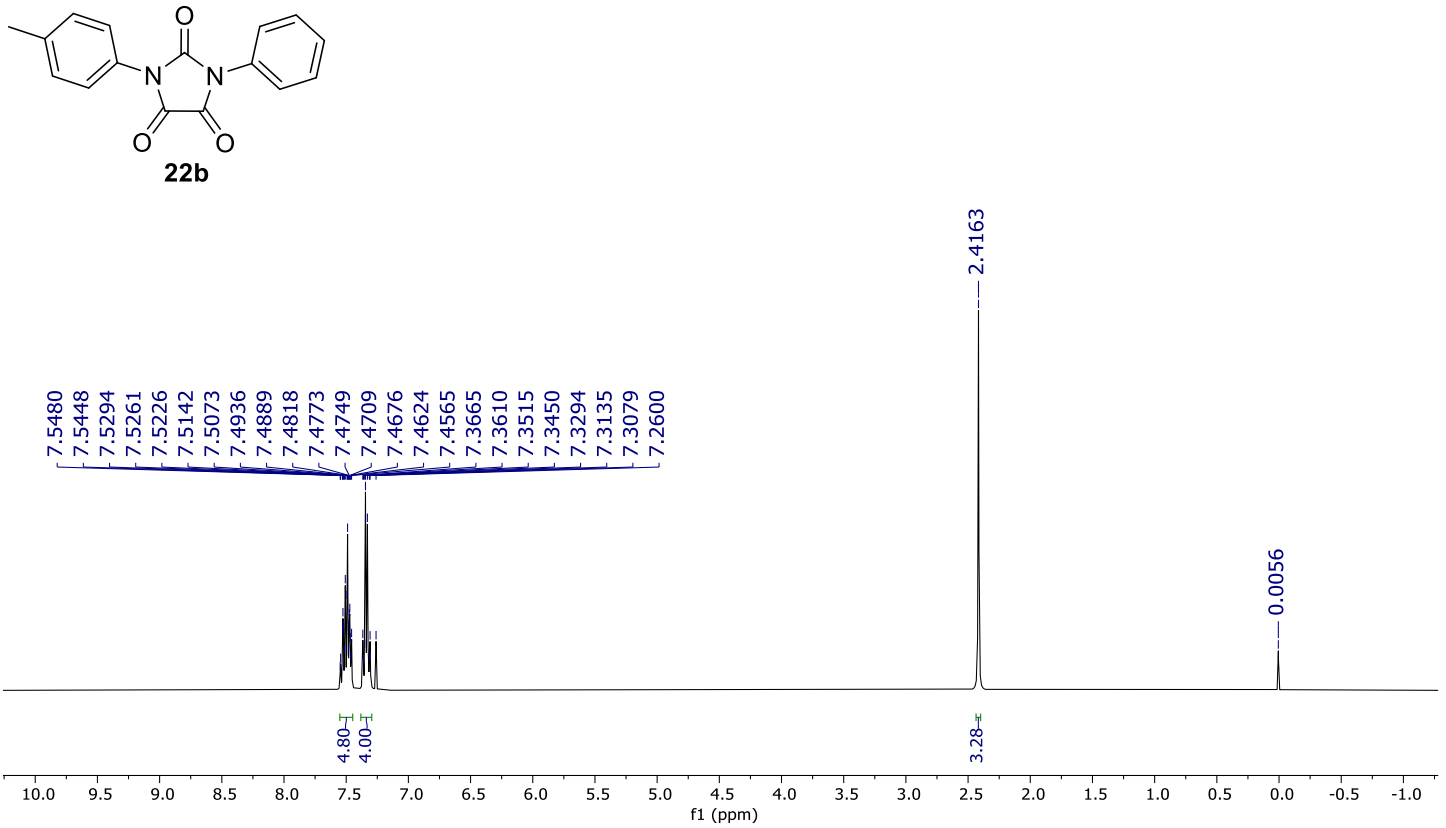



Figure S245. $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **22b**.

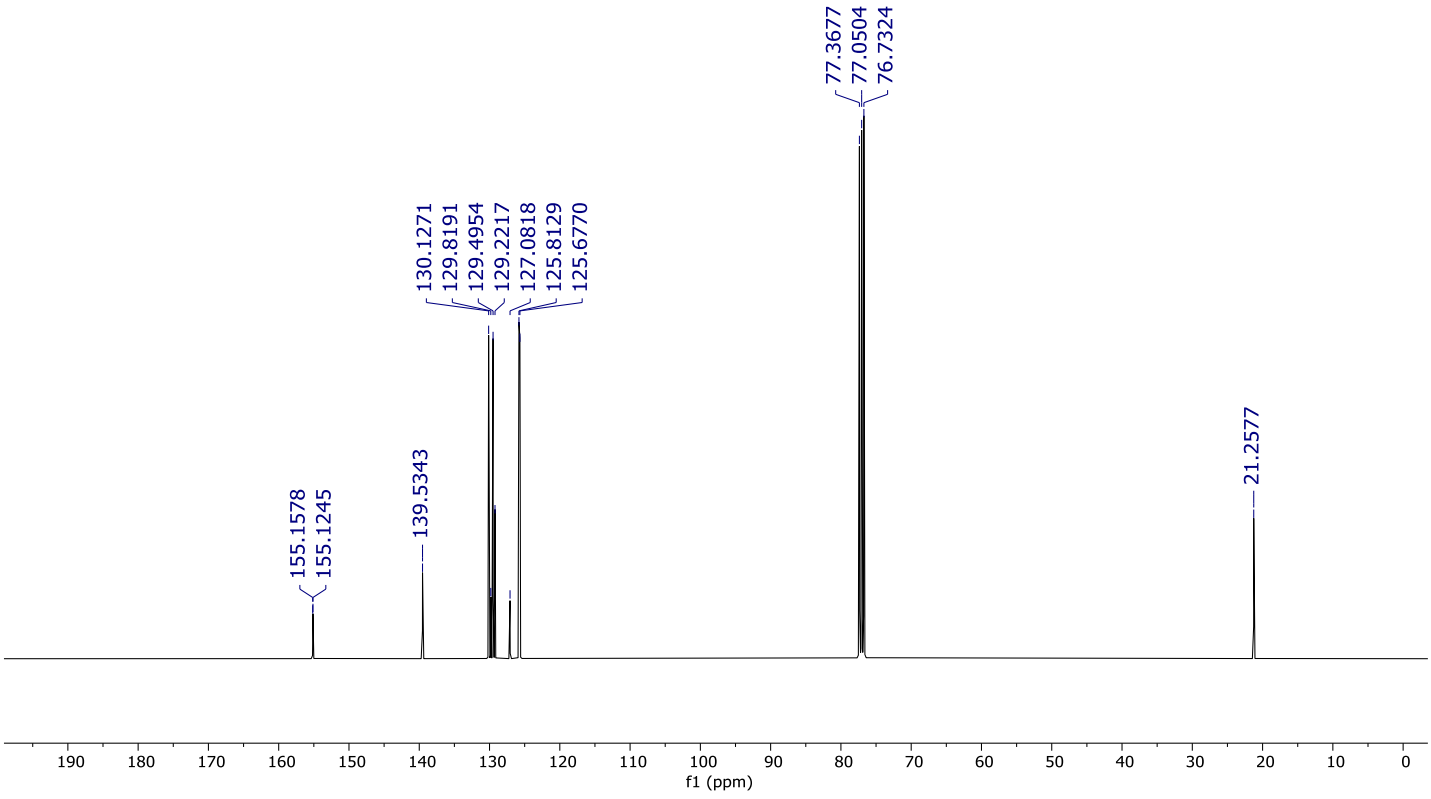



Figure S246. $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **22b**.

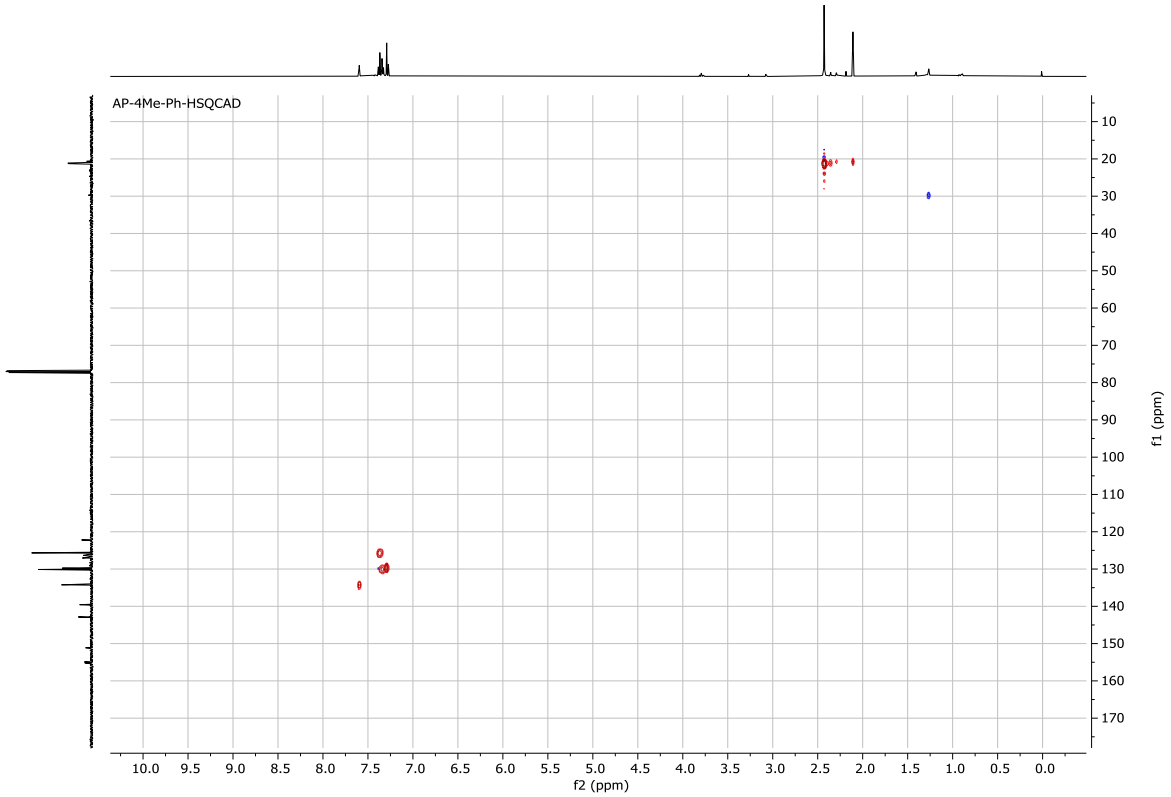



Figure S247. HSQC (400 MHz, $CDCl_3$) spectrum of compound **22b.**

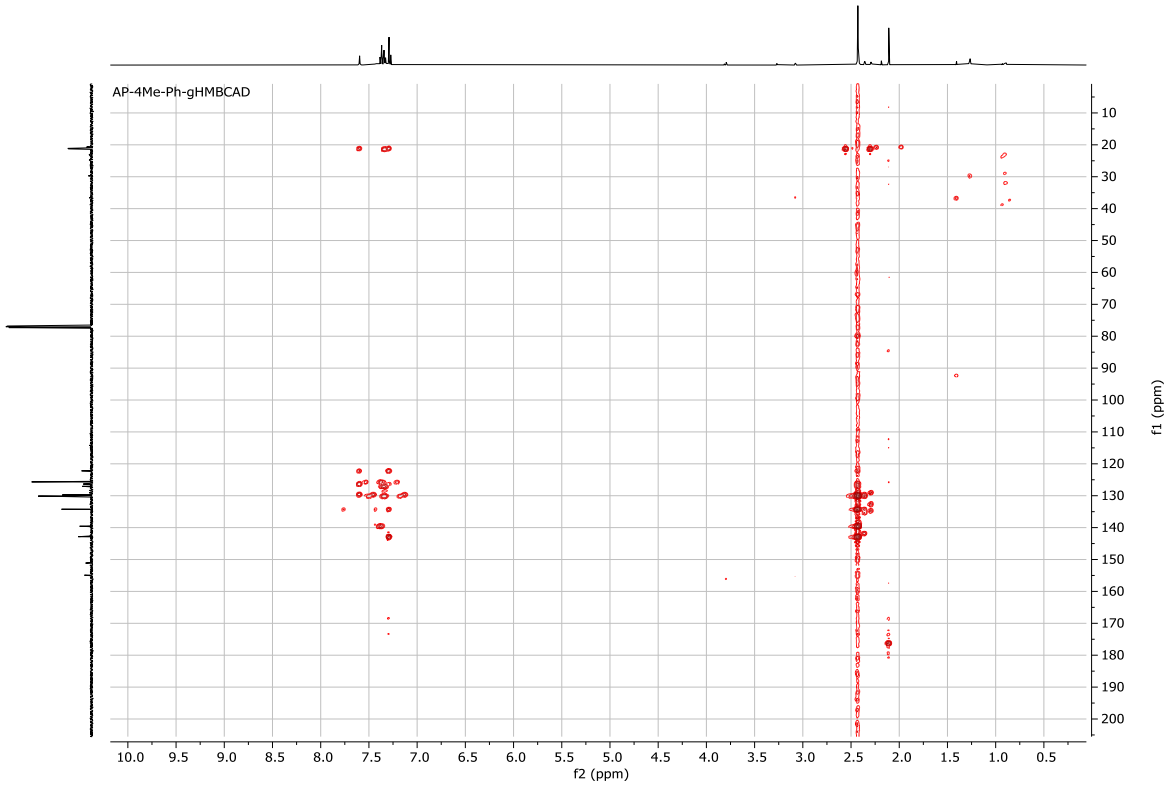



Figure S248. HMBC (400 MHz, $CDCl_3$) spectrum of compound **22b.**

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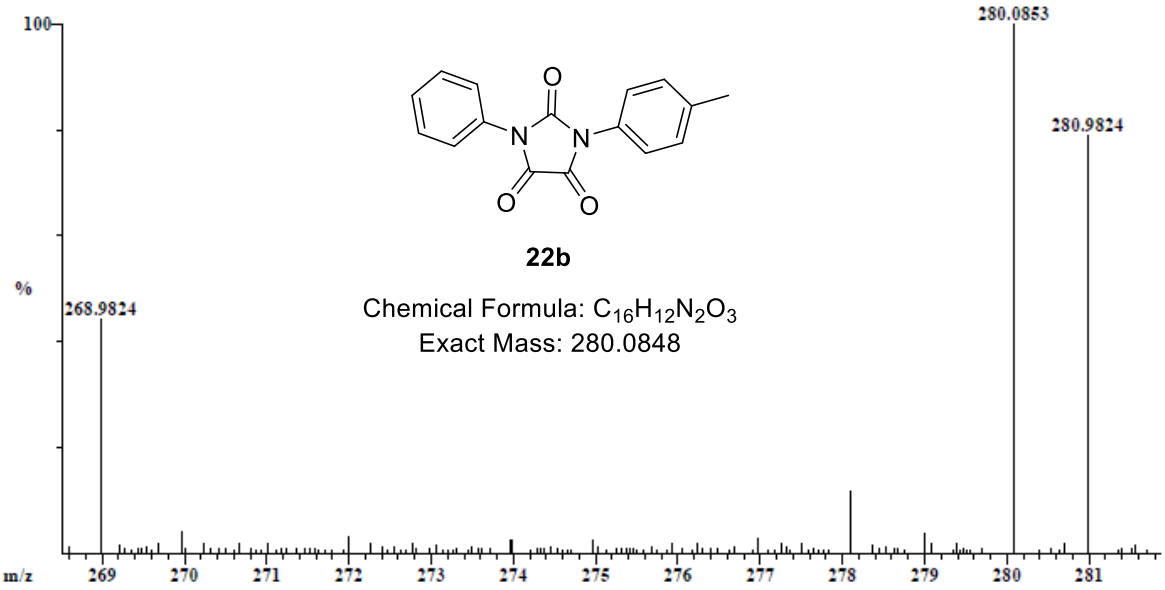
**File: JT-EBC-H62** **Date Run: 03-25-2023 (Time Run: 14:29:51)**
**Sample: JT-EBC-H62**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 81-86** **R.T.: 1.1**
**Base: m/z 280; 2.8%FS TIC: 234824** **#Ions: 577**




**22b**

Chemical Formula: $C_{16}H_{12}N_2O_3$
Exact Mass: 280.0848

**Selected Isotopes : $H_{0-12}C_{0-16}N_{0-2}O_{0-3}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 280.0853 | 100.0% | $C_{16}H_{12}N_2O_3$ | 280.0848 | 1.8 | 12.0 |

Figure S249. HRMS of compound **22b.**

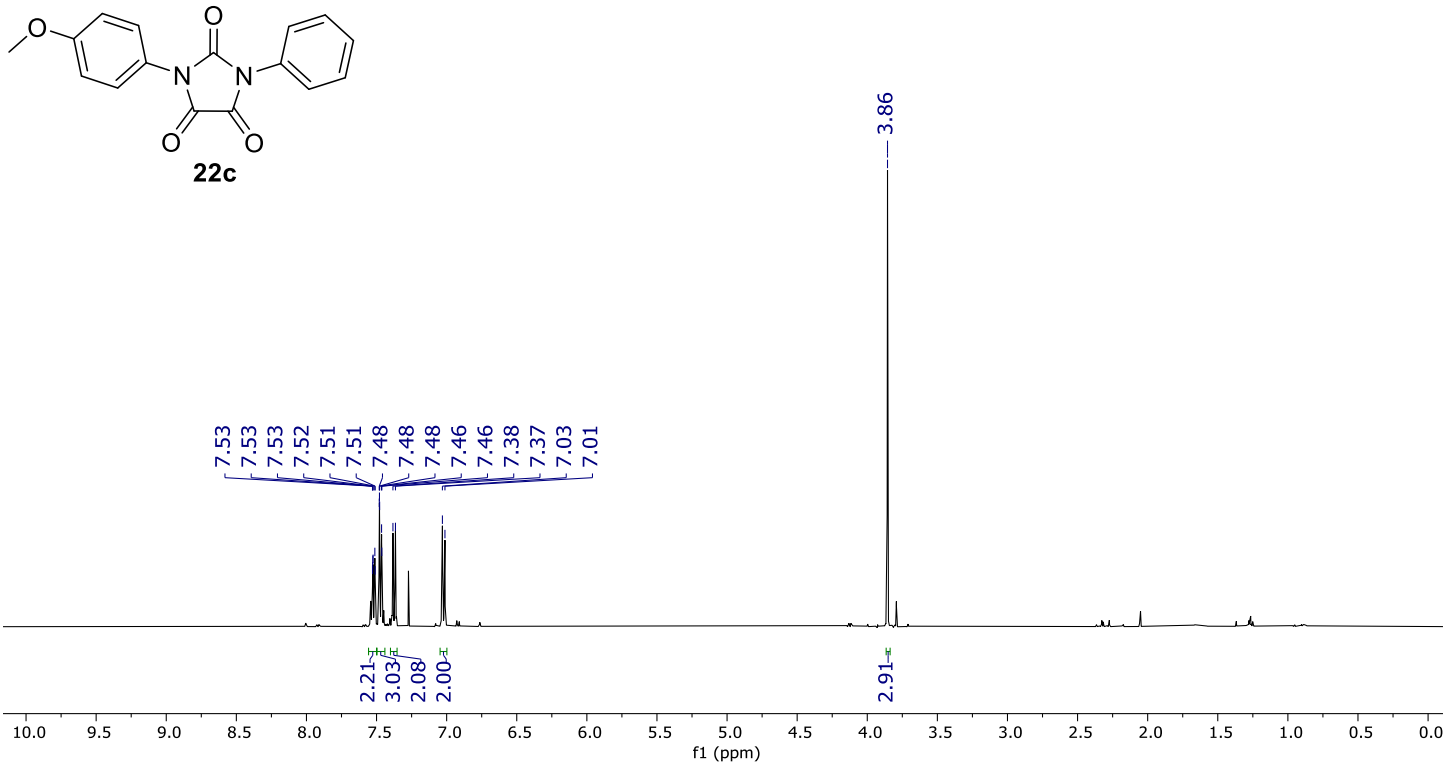



Figure S250. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **22c**.

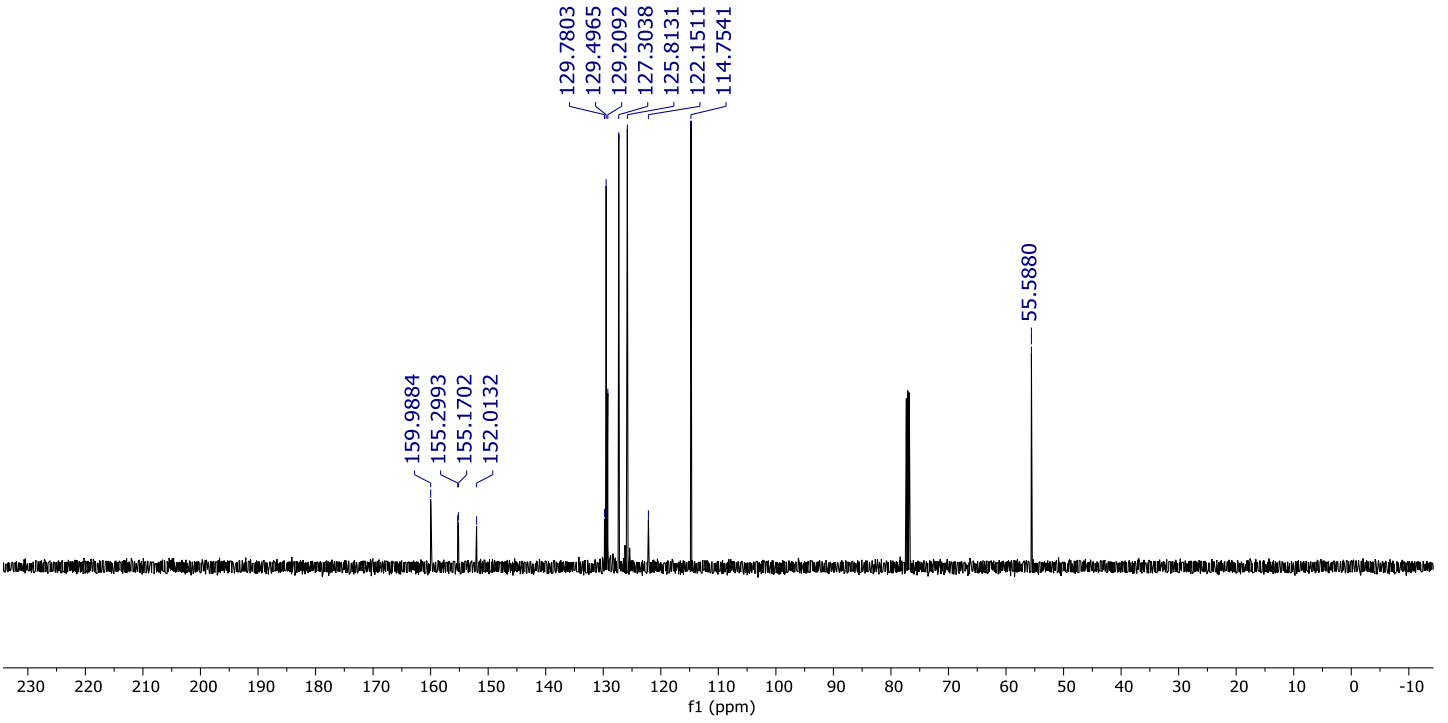



Figure S251. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **22c**.

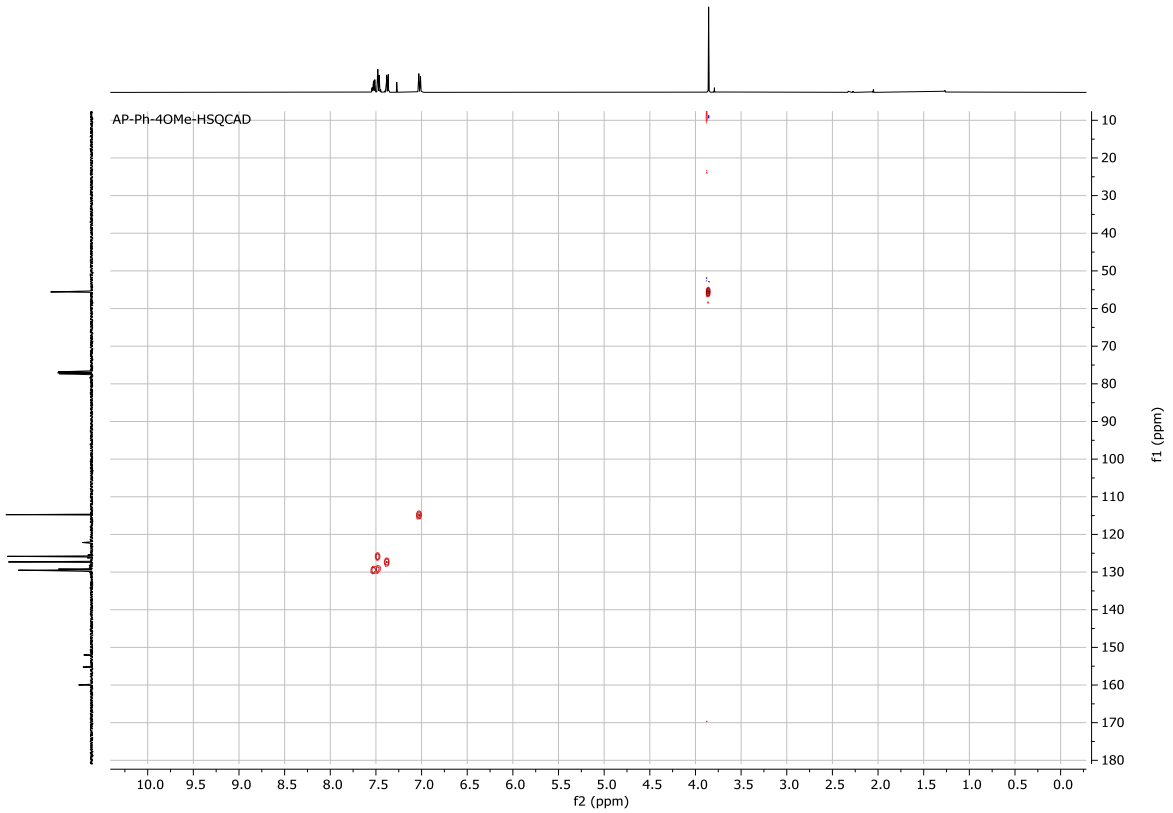



Figure S252. HSQC (500 MHz, $CDCl_3$) spectrum of compound **22c.**

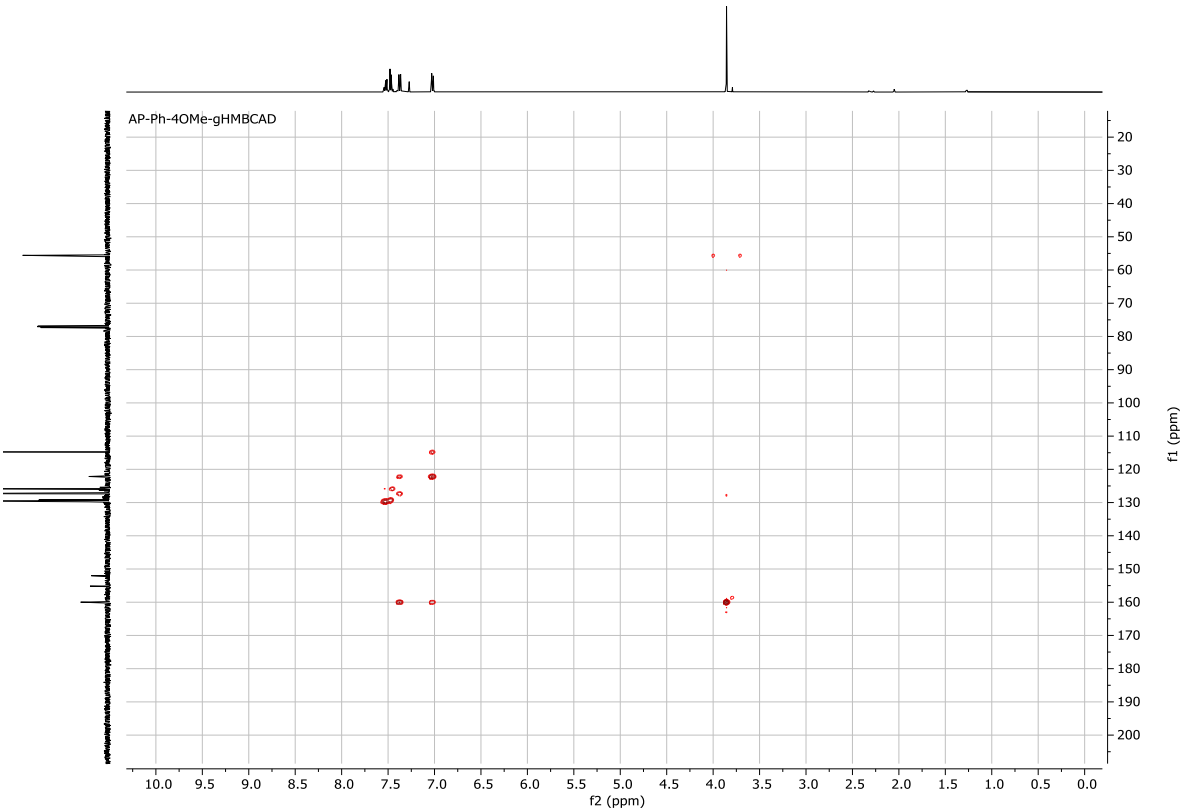



Figure S253. HMBC (500 MHz, $CDCl_3$) spectrum of compound **22c.**

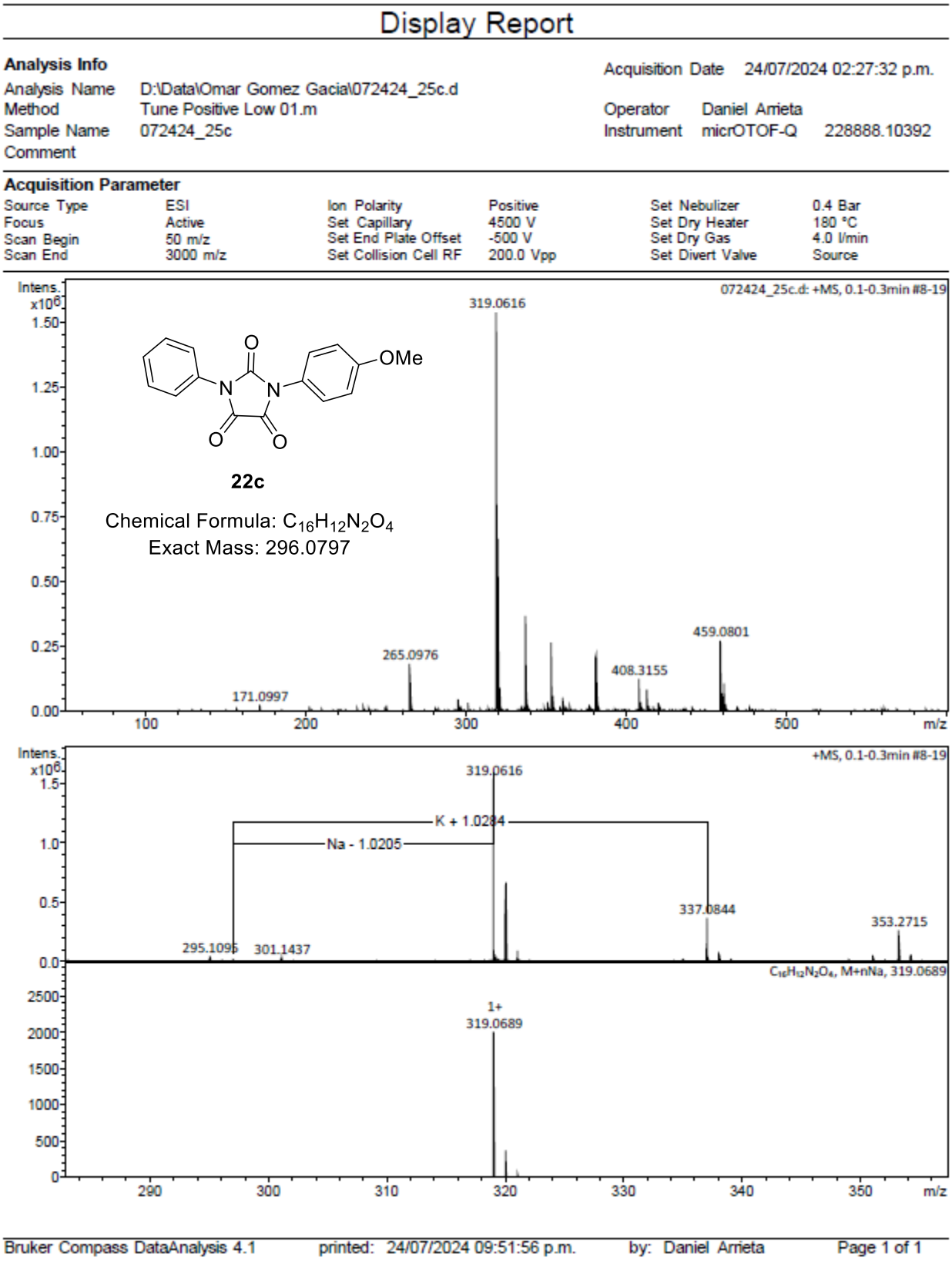



Figure S254. HRMS of compound **22c.**

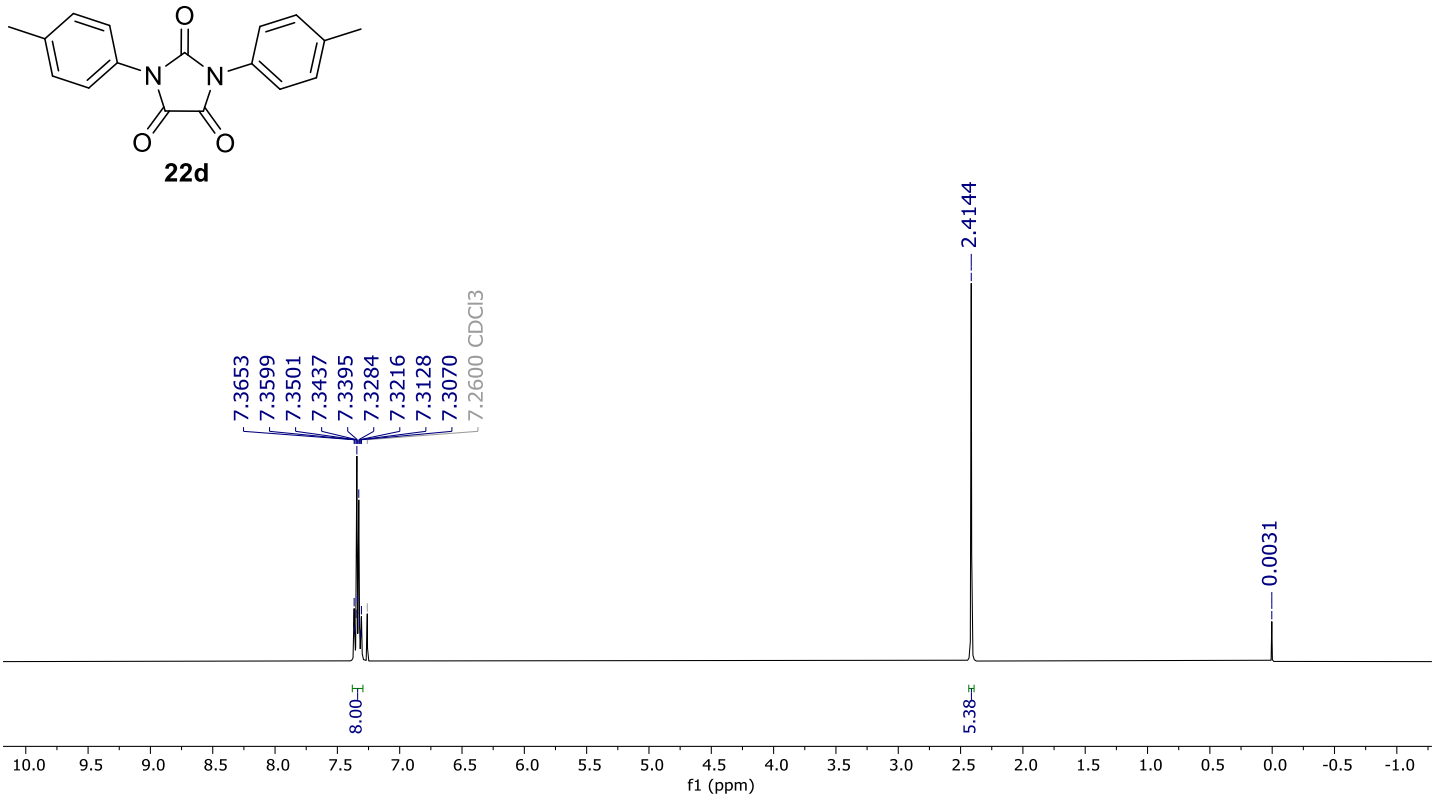



Figure S255. $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **22d**.

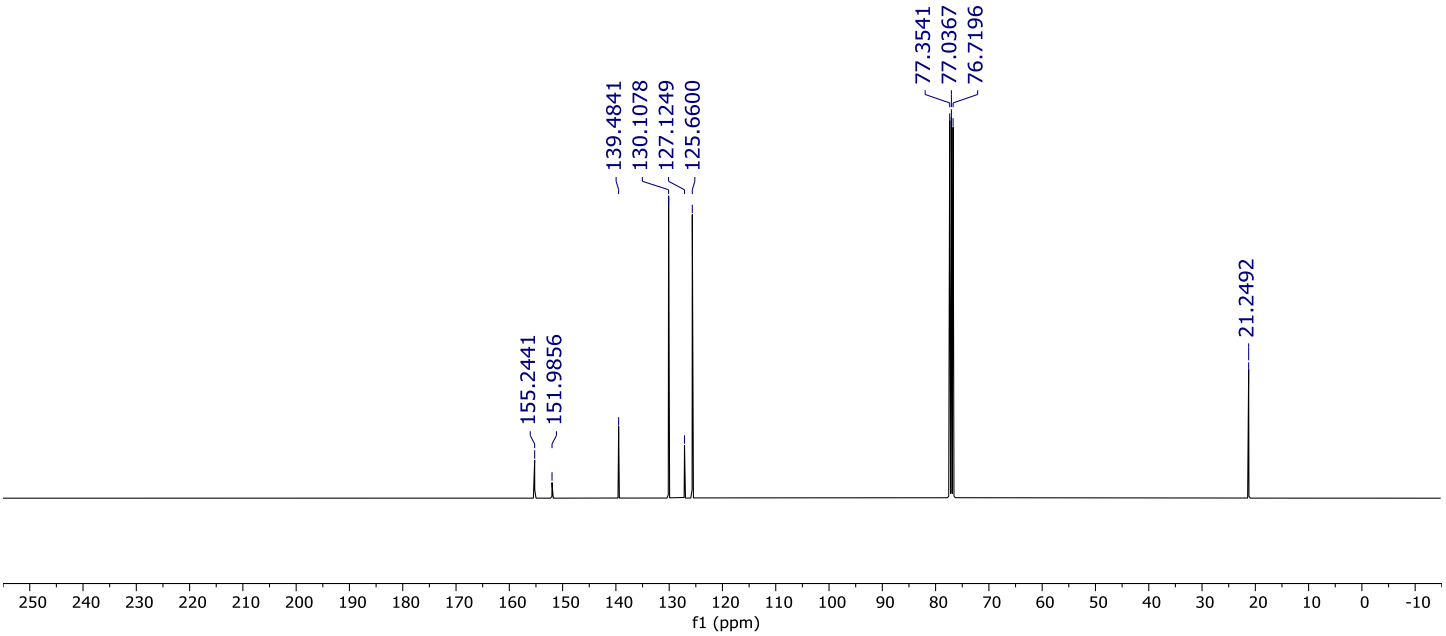



Figure S256. $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **22d**.

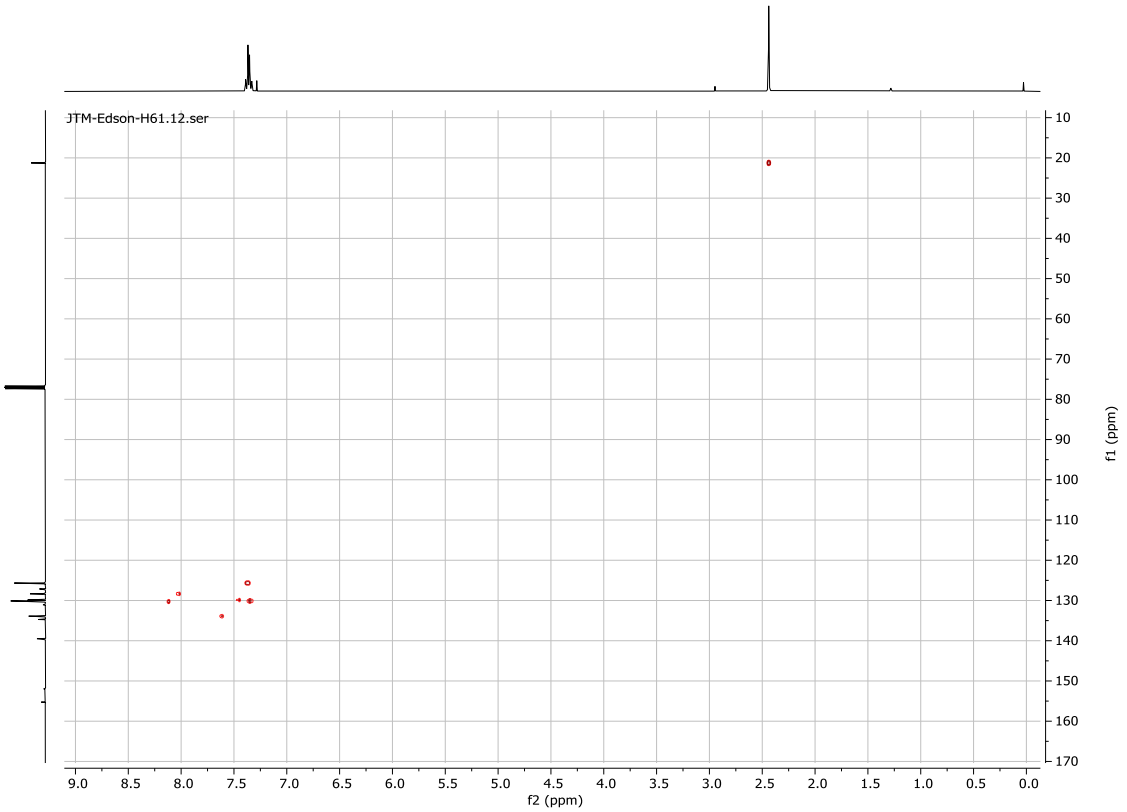



Figure S257. HSQC (400 MHz, $CDCl_3$) spectrum of compound **22d.**

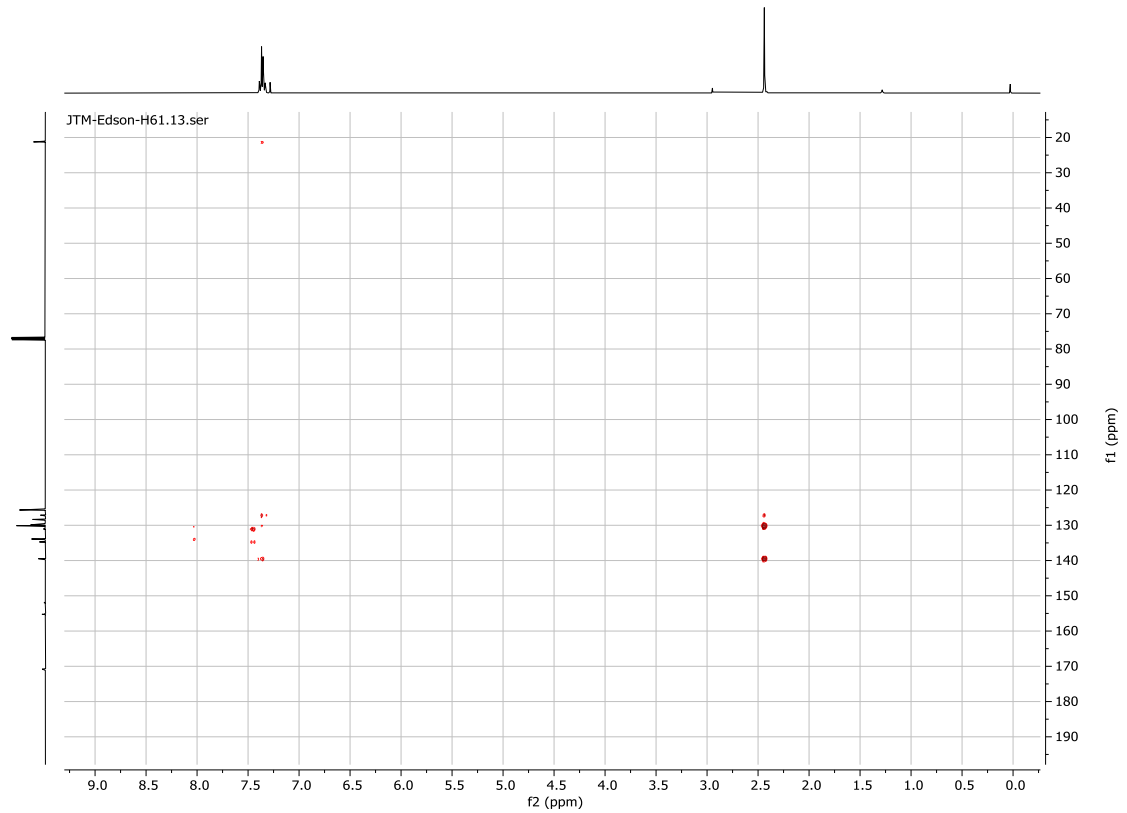



Figure S258. HMBC (400 MHz, $CDCl_3$) spectrum of compound **22d.**

***IPN***

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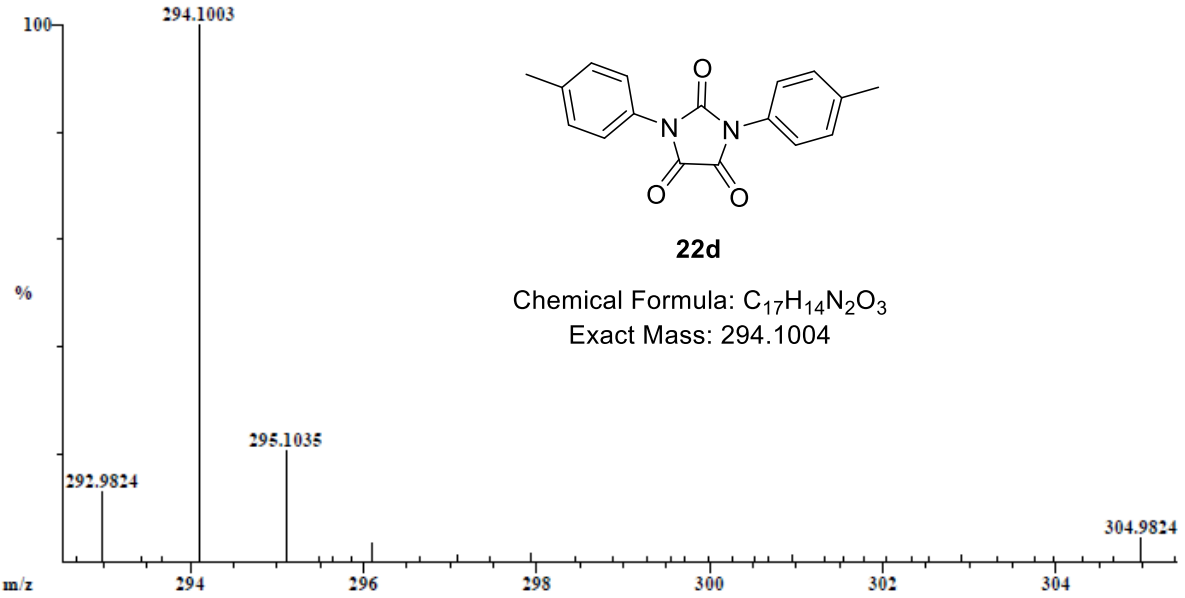
**File: JT-EBC-H61** **Date Run: 03-25-2023 (Time Run: 14:43:47)**
**Sample: JT-EBC-H61**
**Instrument: JEOL GCmate**
**Inlet: Direct Probe** **Ionization mode: EI+**

**Scan: 256** **R.T.: 3.37**
**Base: m/z 294; 8.6%FS TIC: 327840** **#Ions: 194**







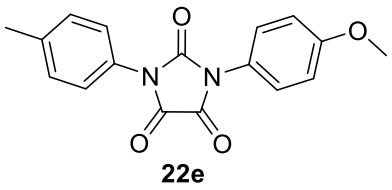
**22d**

Chemical Formula: $C_{17}H_{14}N_2O_3$
Exact Mass: 294.1004

**Selected Isotopes : $H_{0-14}C_{0-17}N_{0-2}O_{0-3}$** **Error Limit : 5 ppm** **Unsaturation Limits : 0 to 50**

| *Measured Mass* | *% Base* | *Formula* | *Calculated Mass* | *Error* | *Unsaturation* |
|---|---|---|---|---|---|
| 294.1003 | 100.0% | $C_{17}H_{14}N_2O_3$ | 294.1005 | -0.5 | 12.0 |

Figure S259. HRMS of compound **22d.**



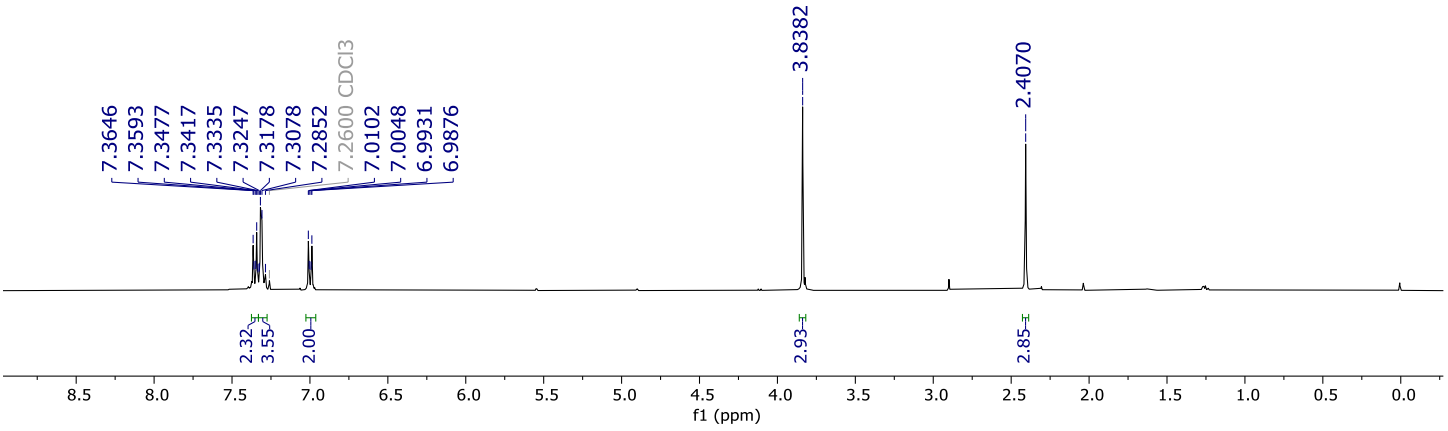




Figure S260. $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **22e**.

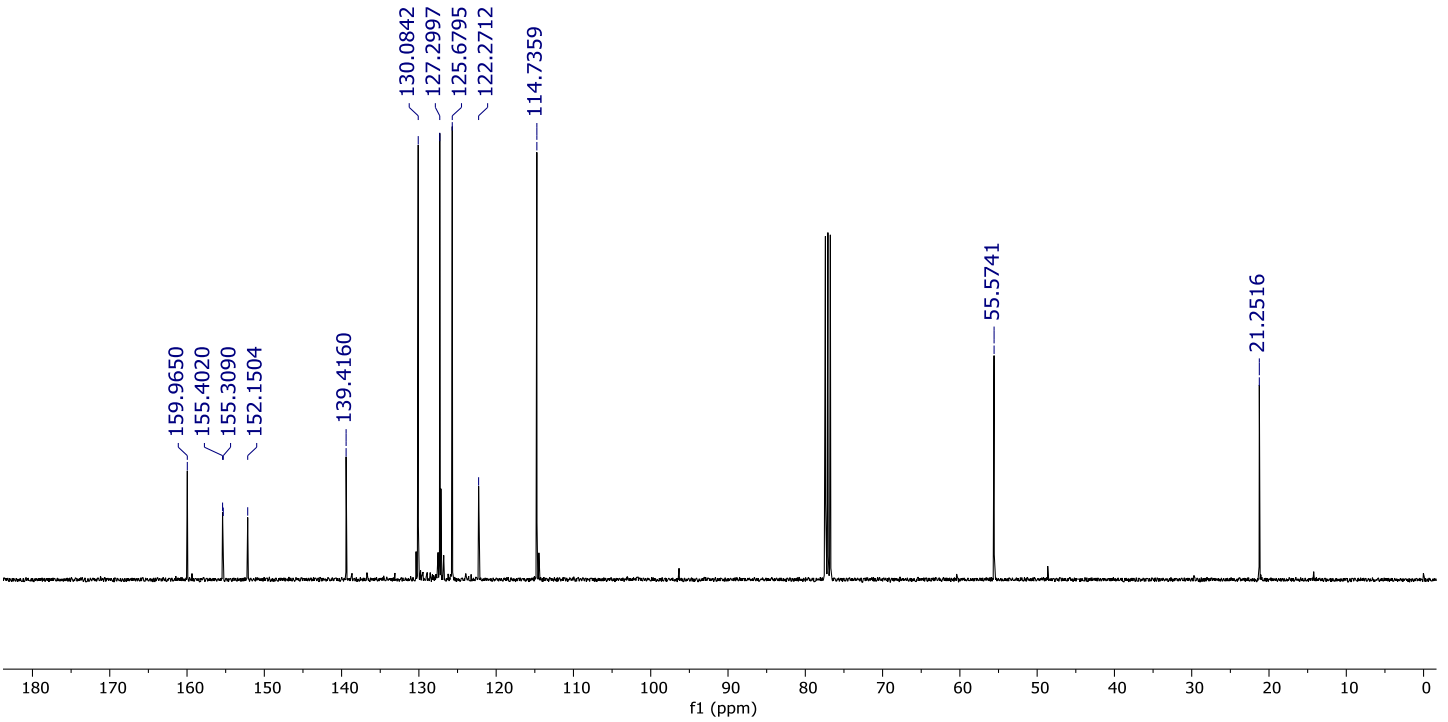



Figure S261. $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **22e**.

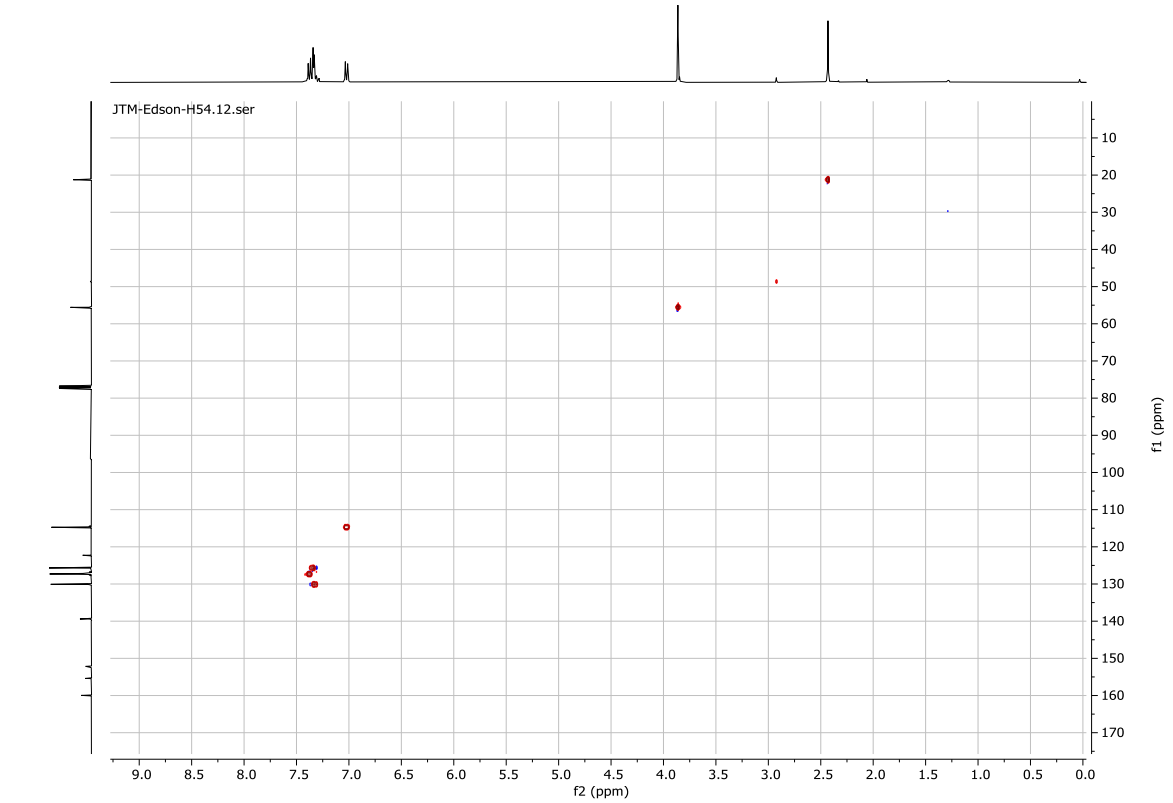



Figure S262. HSQC (400 MHz, $CDCl_3$) spectrum of compound **22e.**

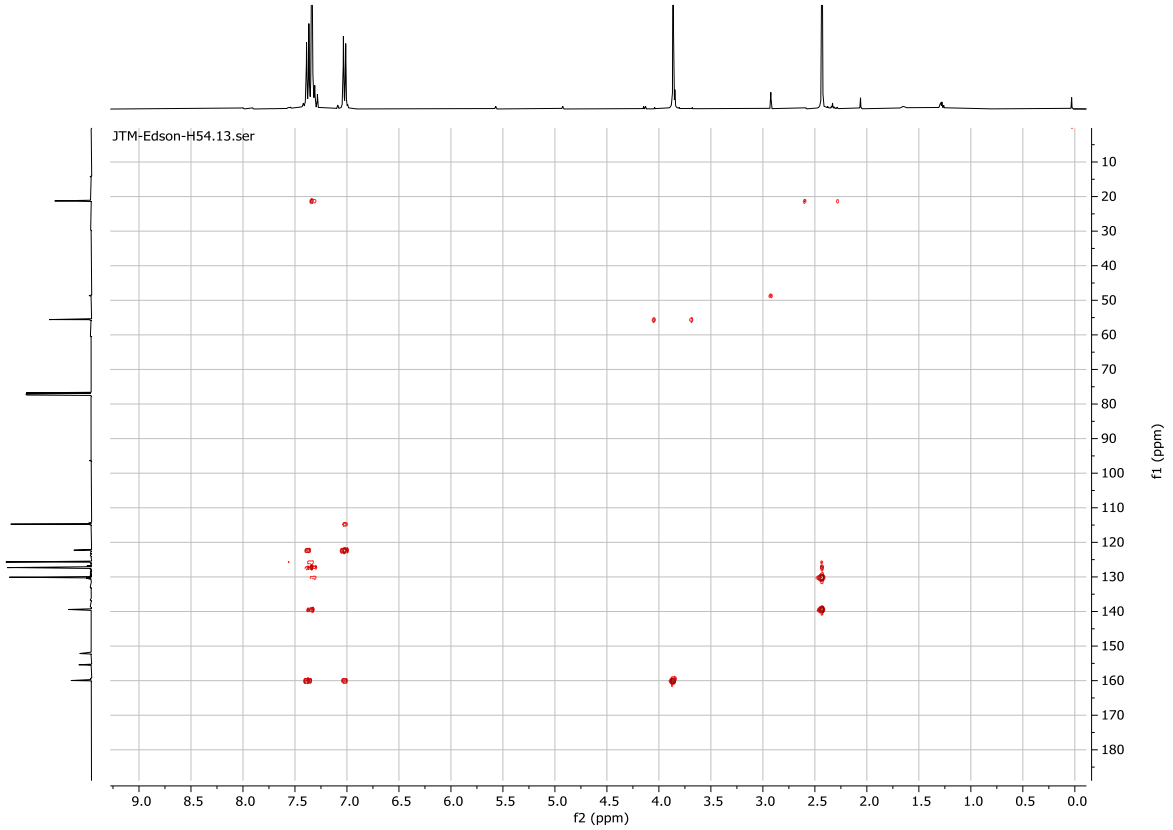



Figure S263. HMBC (400 MHz, $CDCl_3$) spectrum of compound **22e.**

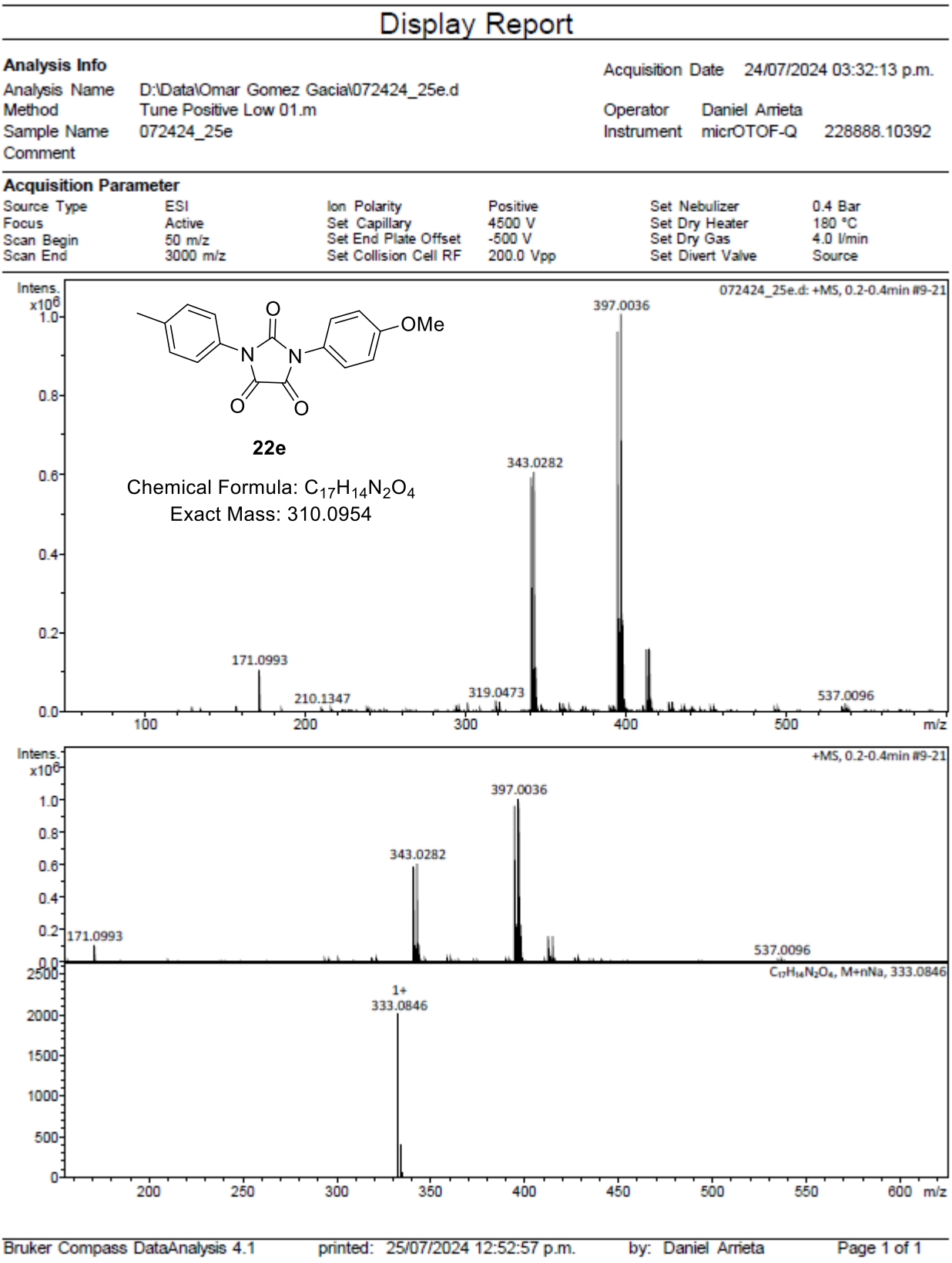



Figure S264. HRMS of compound **22e.**

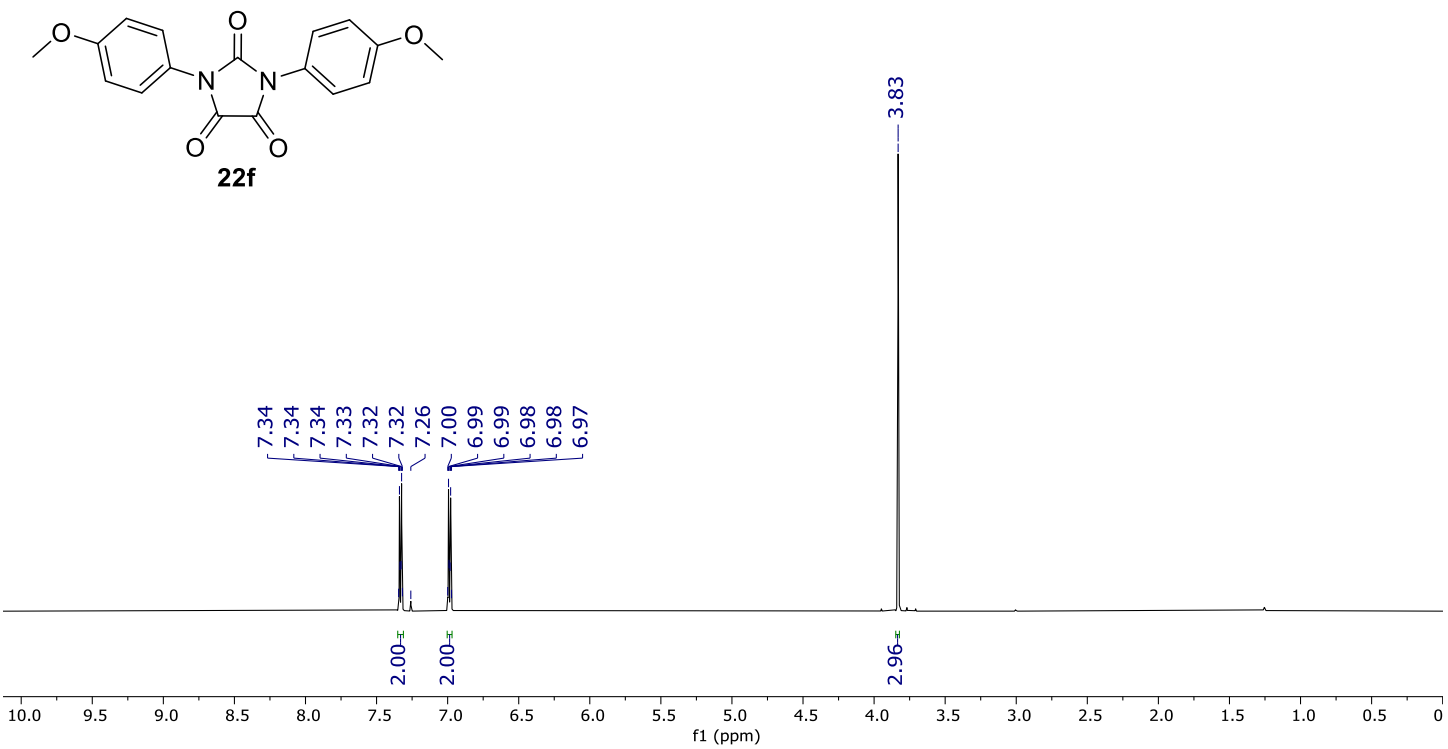



Figure S265. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **22f**.

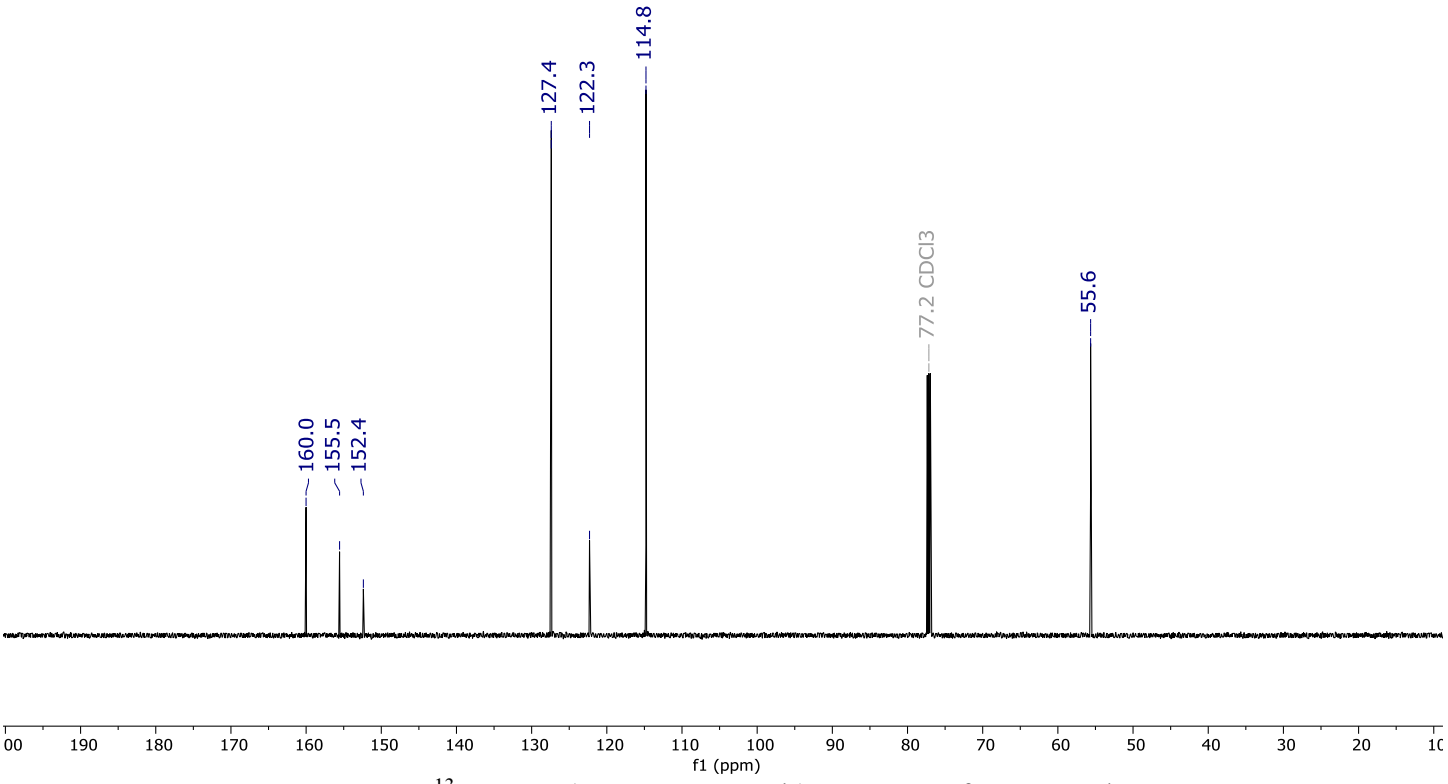



Figure S266. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **22f**.

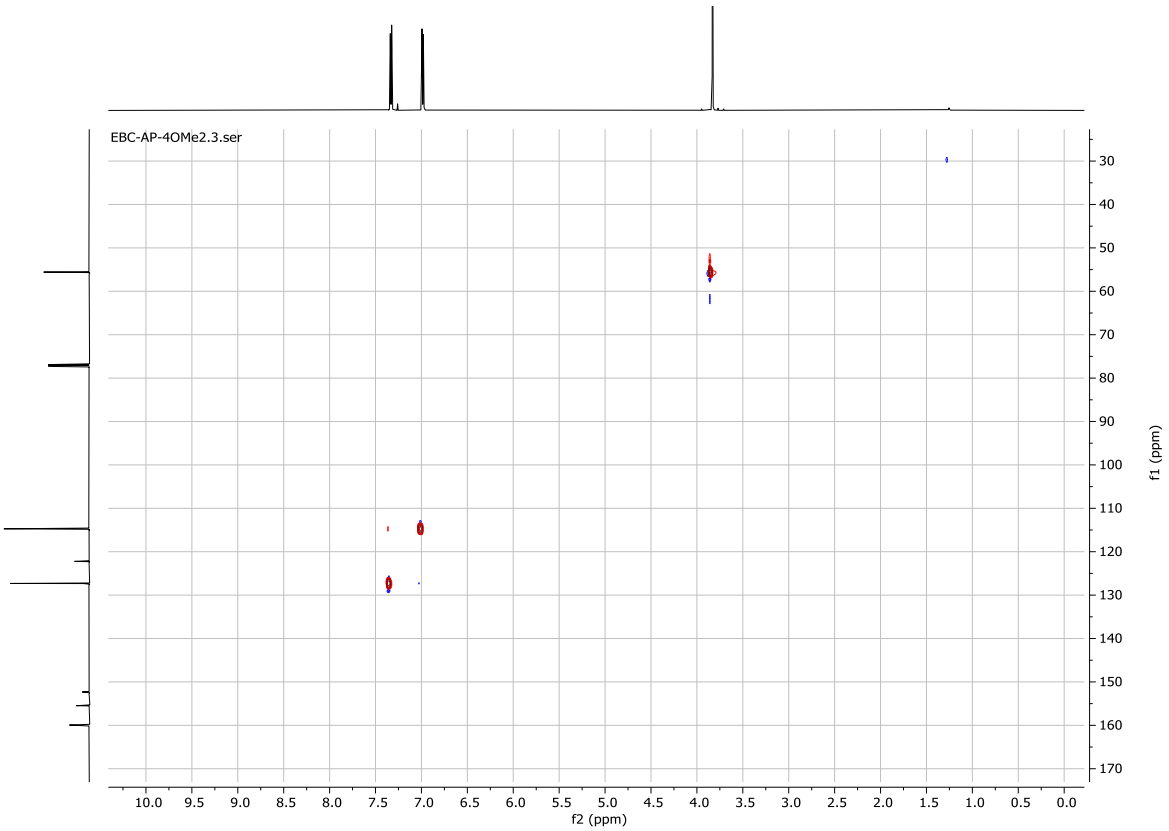



Figure S267. HSQC (500 MHz, $CDCl_3$) spectrum of compound **22f.**

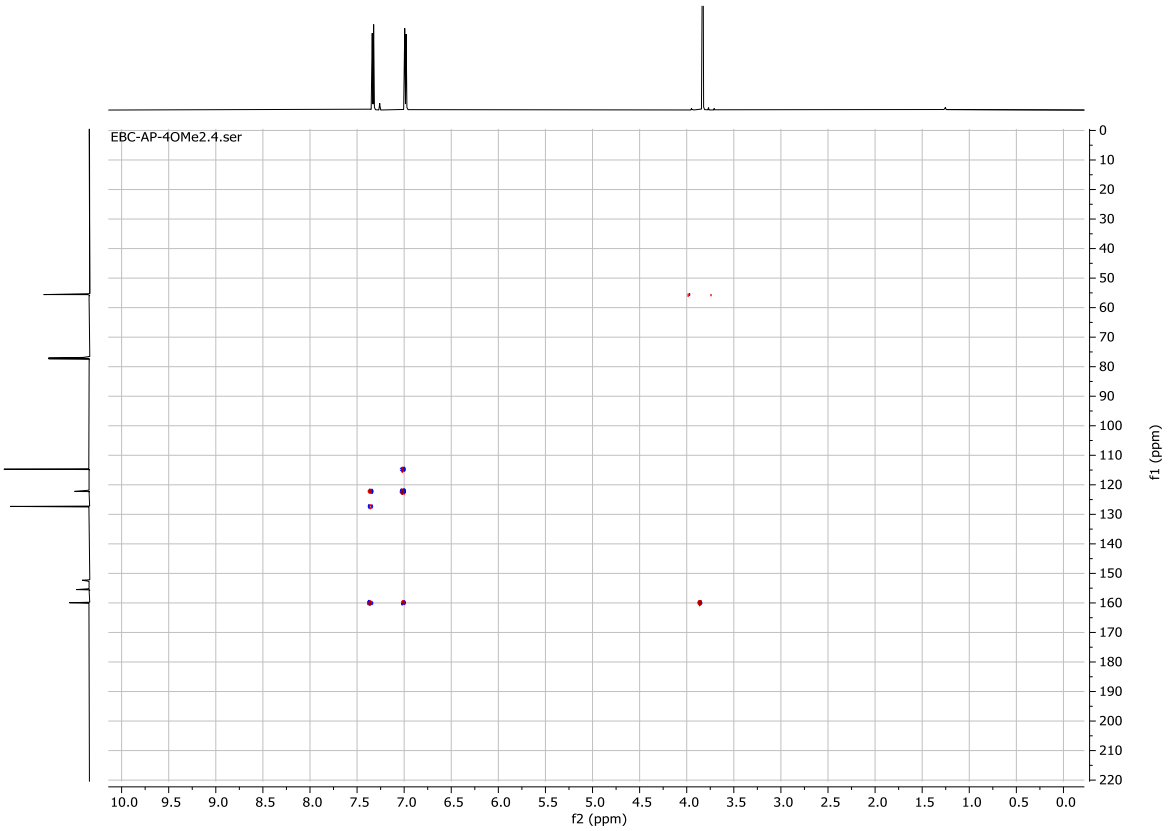



Figure S268. HMBC (500 MHz, $CDCl_3$) spectrum of compound **22f.**

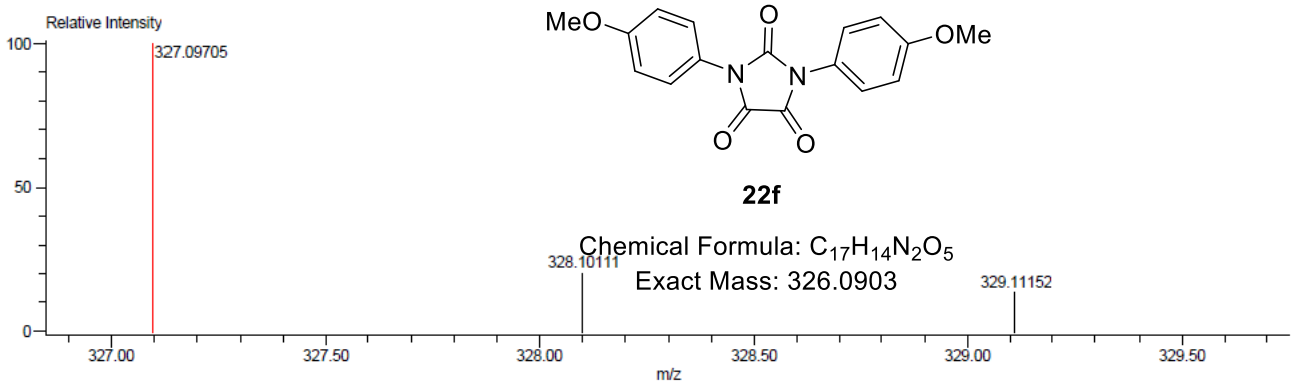
Data:25f
Sample Name:Dr. Tamariz Joaquin Operador Javier Perez
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1..1)

Acquired:6/26/2024 4:33:23 PM
Operator:AccuTOF
Mass Calibration data:CAL_PEG_600_ALUMNOS_2024
Created:6/26/2024 6:03:11 PM
Created by:AccuTOF

Charge number:1
Element:$^{12}$C:0 .. 30, $^{1}$H:1 .. 60, $^{14}$N:1 .. 4, $^{16}$O:1 .. 5

Tolerance:3.00(mmu)

Unsaturation Number:-1.5 .. 1000.0 (Fraction:Both)




| Mass | Intensity | Calc. Mass | Mass Difference (mmu) | Mass Difference (ppm) | Possible Formula | Unsaturation Number |
|---|---|---|---|---|---|---|
| 327.09705 | 169566.76 | 327.09810 | -1.05 | -3.20 | $^{12}C_{17}{}^{1}H_{15}{}^{14}N_2{}^{16}O_5$ | 11.5 |

Figure S269. HRMS of compound **22f.**

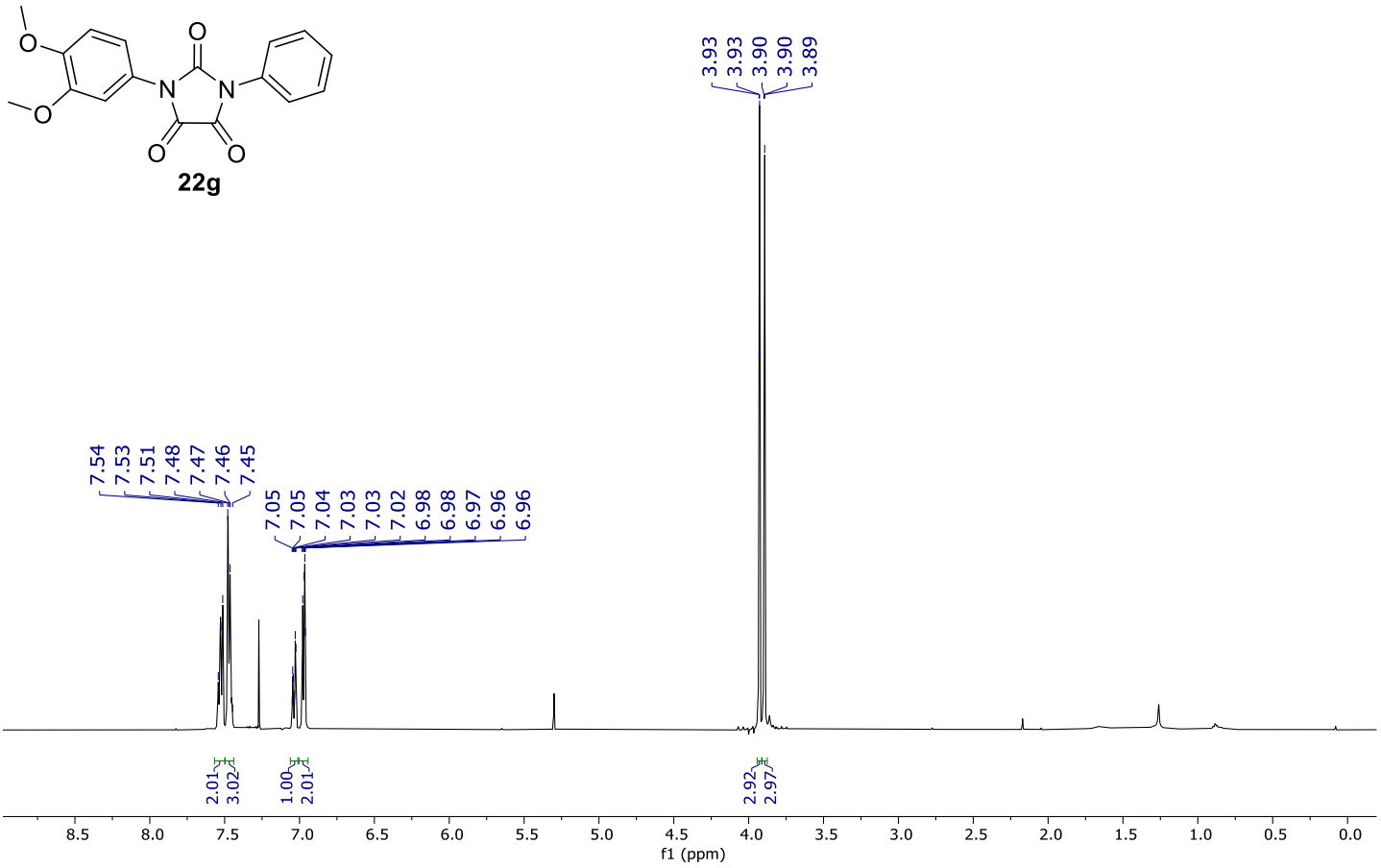



Figure S270. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **22g**.

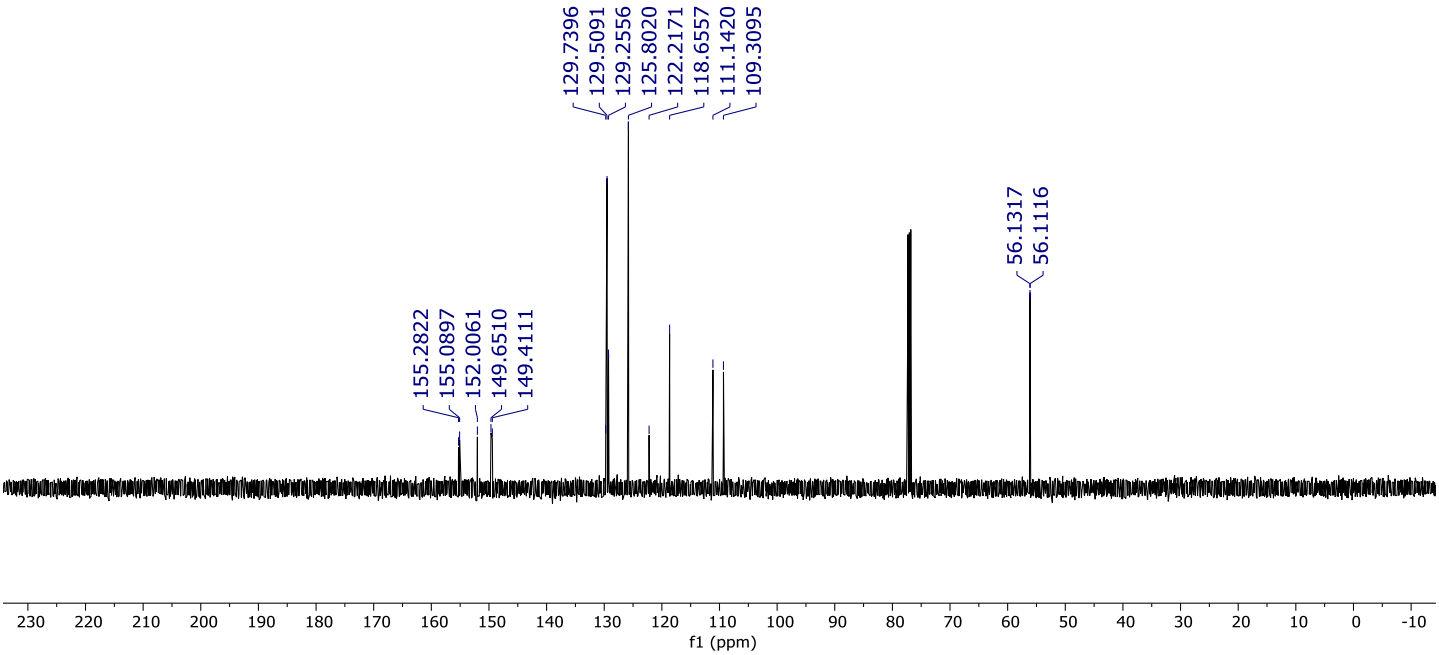



Figure S271. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **22g**.

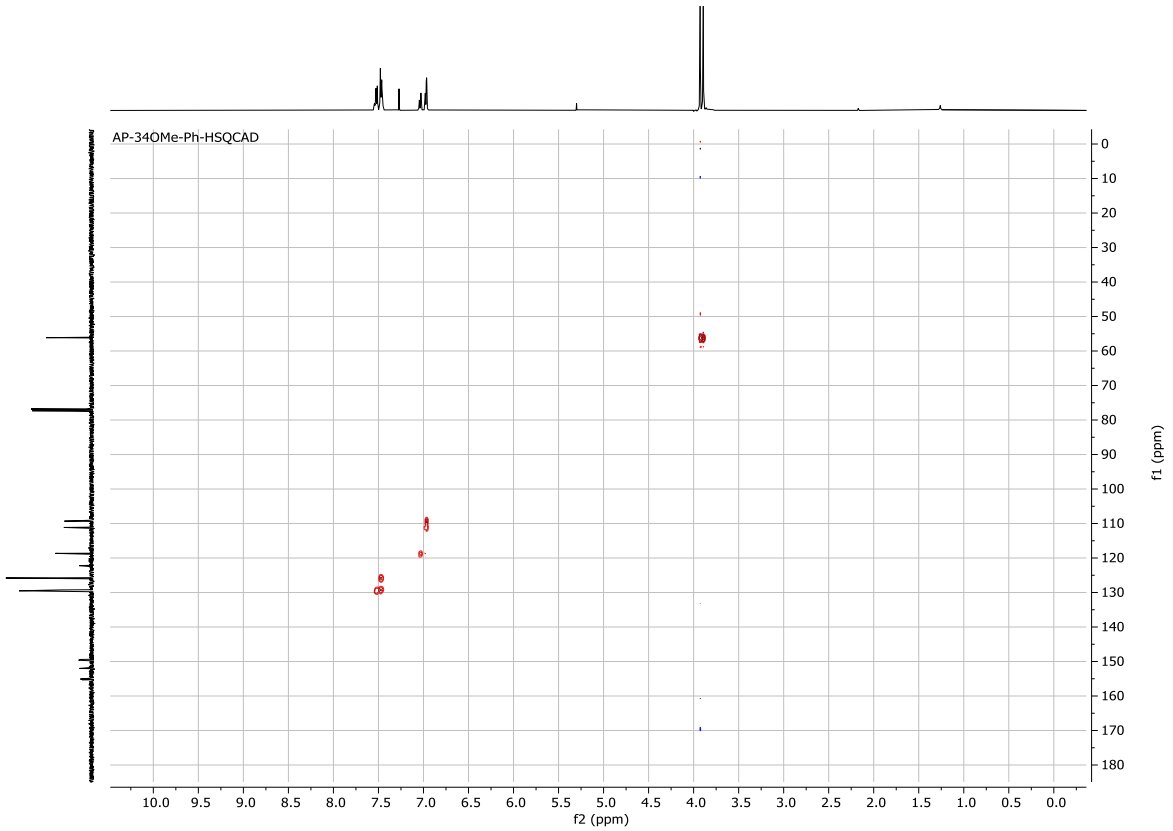



Figure S272. HSQC (500 MHz, $CDCl_3$) spectrum of compound **22g.**

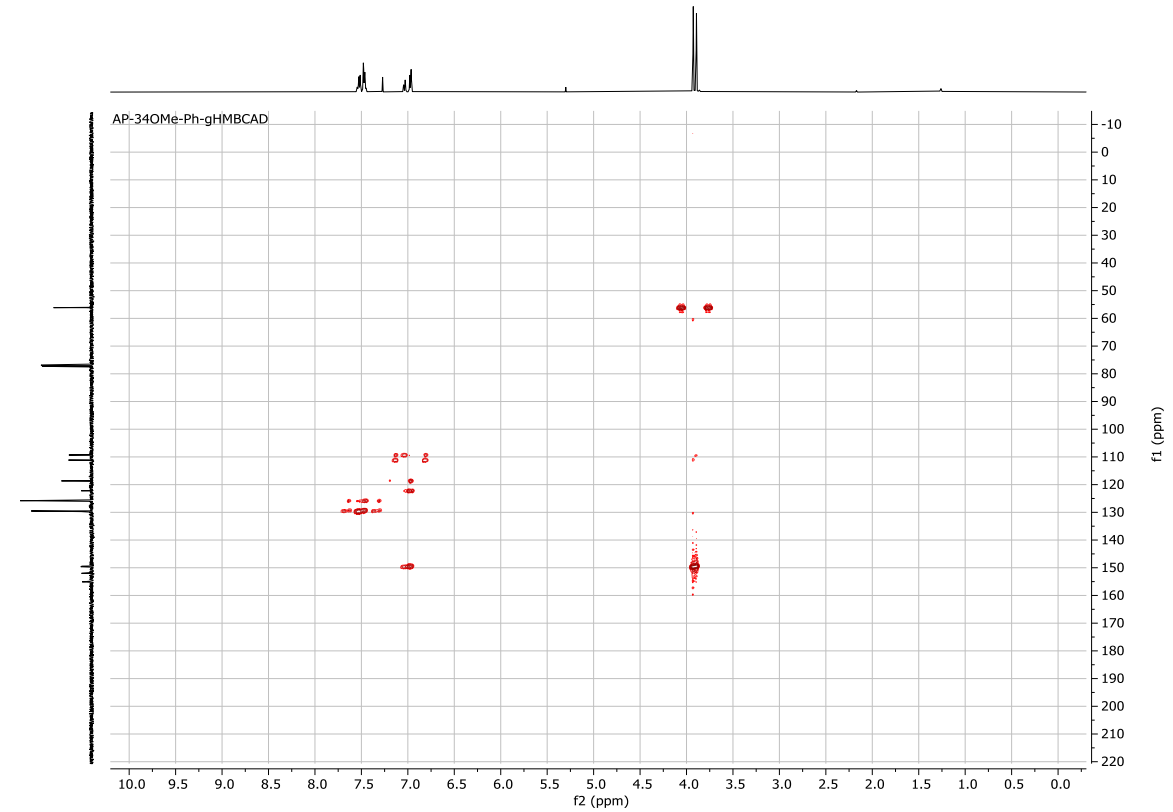



Figure S273. HMBC (500 MHz, $CDCl_3$) spectrum of compound **22g.**

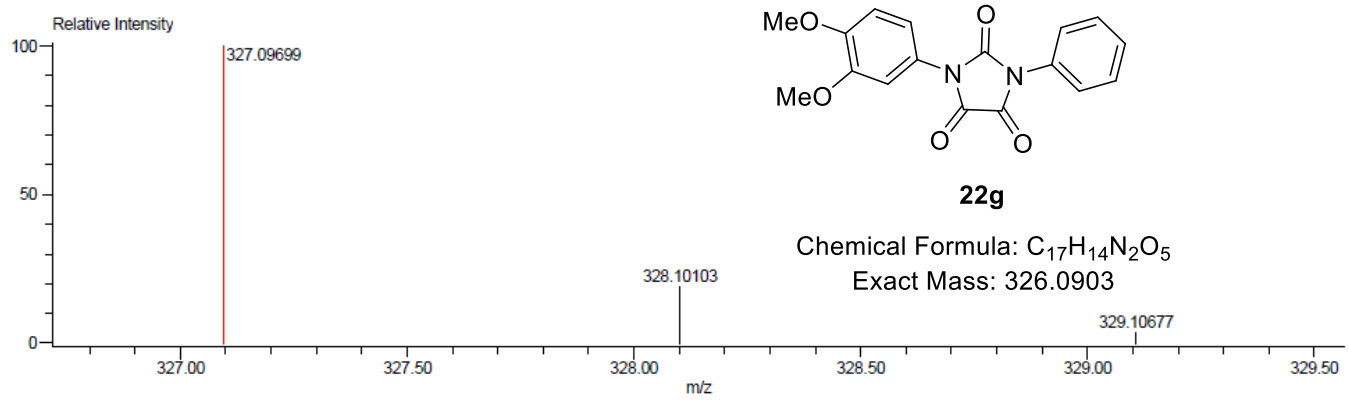
Data:25g
Sample Name:Dr. Tamariz Joaquin Operador Javier Perez
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1..1)

Acquired:6/26/2024 4:36:53 PM
Operator:AccuTOF
Mass Calibration data:CAL_PEG_600_ALUMNOS_2024
Created:6/26/2024 5:23:43 PM
Created by:AccuTOF

Charge number:1
Element:$^{12}$C:0 .. 30, $^{1}$H:1 .. 60, $^{14}$N:1 .. 3, $^{16}$O:1 .. 6

Tolerance:3.00(mmu)

Unsaturation Number:-1.5 .. 1000.0 (Fraction:Both)







**22g**

Chemical Formula: $C_{17}H_{14}N_2O_5$
Exact Mass: 326.0903

| Mass | Intensity | Calc. Mass | Mass Difference (mmu) | Mass Difference (ppm) | Possible Formula | Unsaturation Number |
|---|---|---|---|---|---|---|
| 327.09699 | 340053.46 | 327.09810 | -1.10 | -3.37 | $^{12}C_{17}{}^{1}H_{15}{}^{14}N_2{}^{16}O_5$ | 11.5 |

Figure S274. HRMS of compound **22g.**

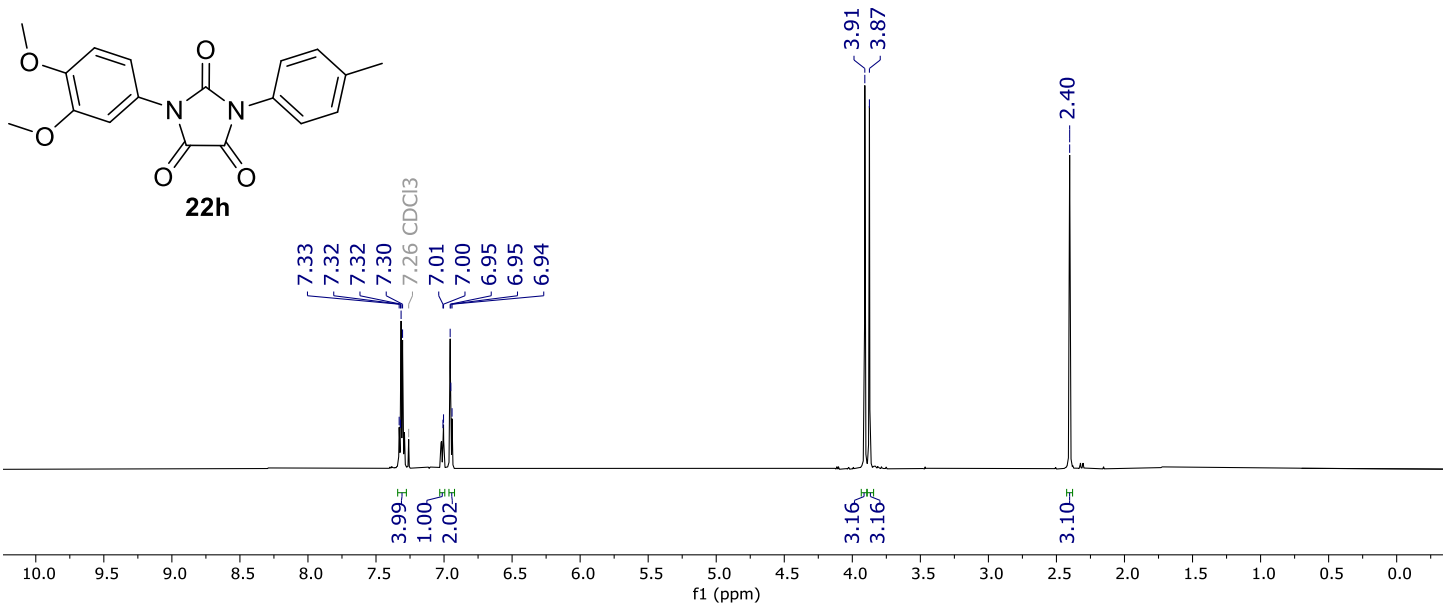



Figure S275. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **22h**.

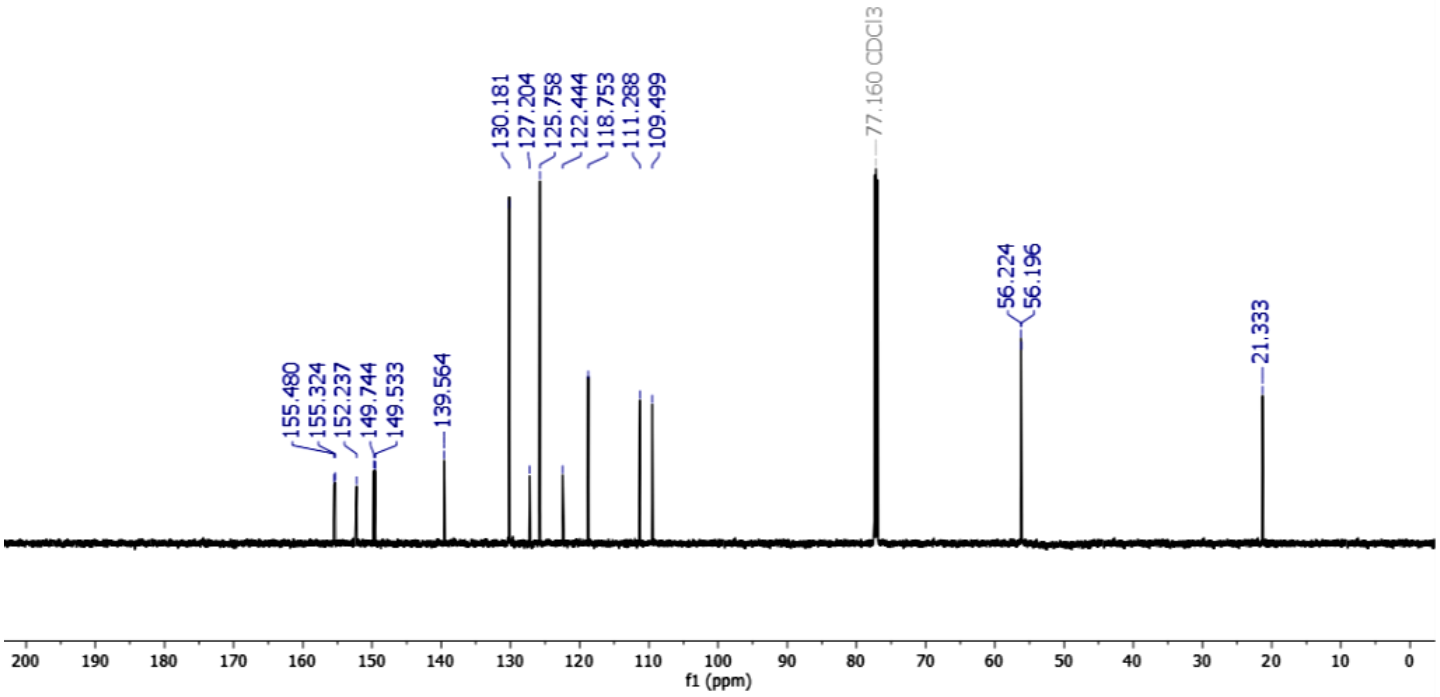



Figure S276. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **22h**.

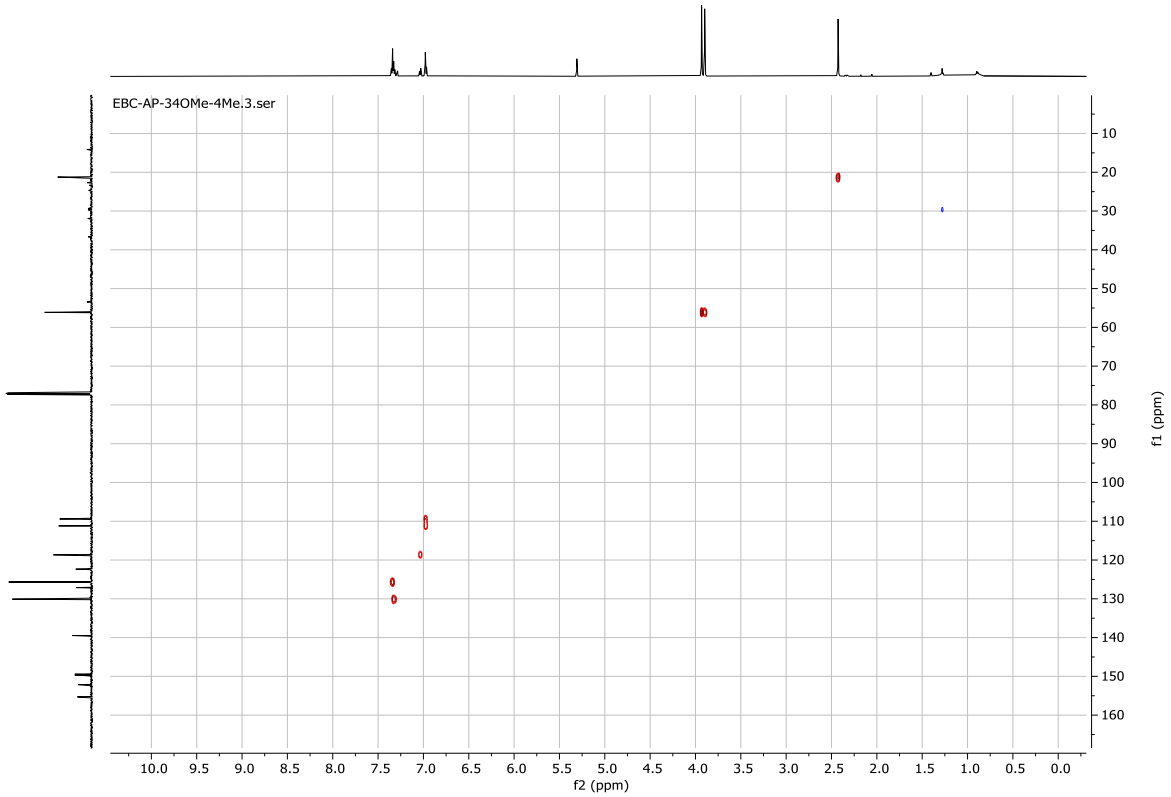



Figure S277. HSQC (600 MHz, $CDCl_3$) spectrum of compound **22h.**

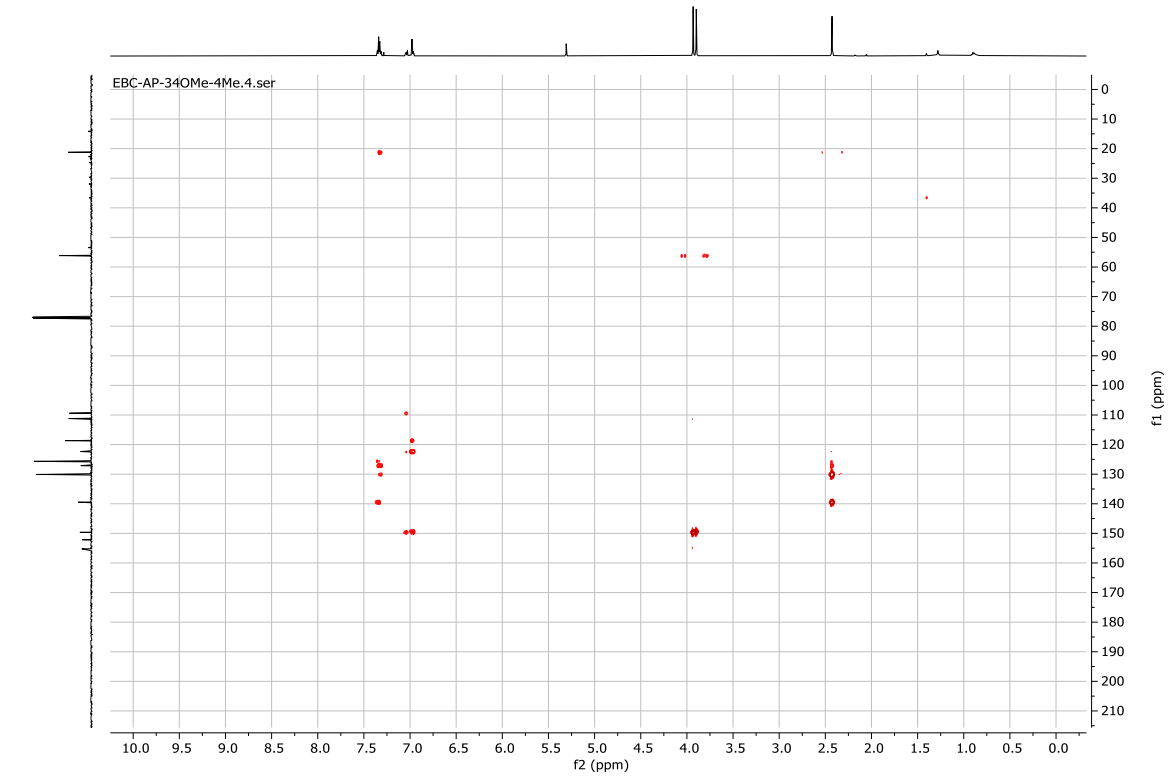



Figure S278. HMBC (600 MHz, $CDCl_3$) spectrum of compound **22h.**

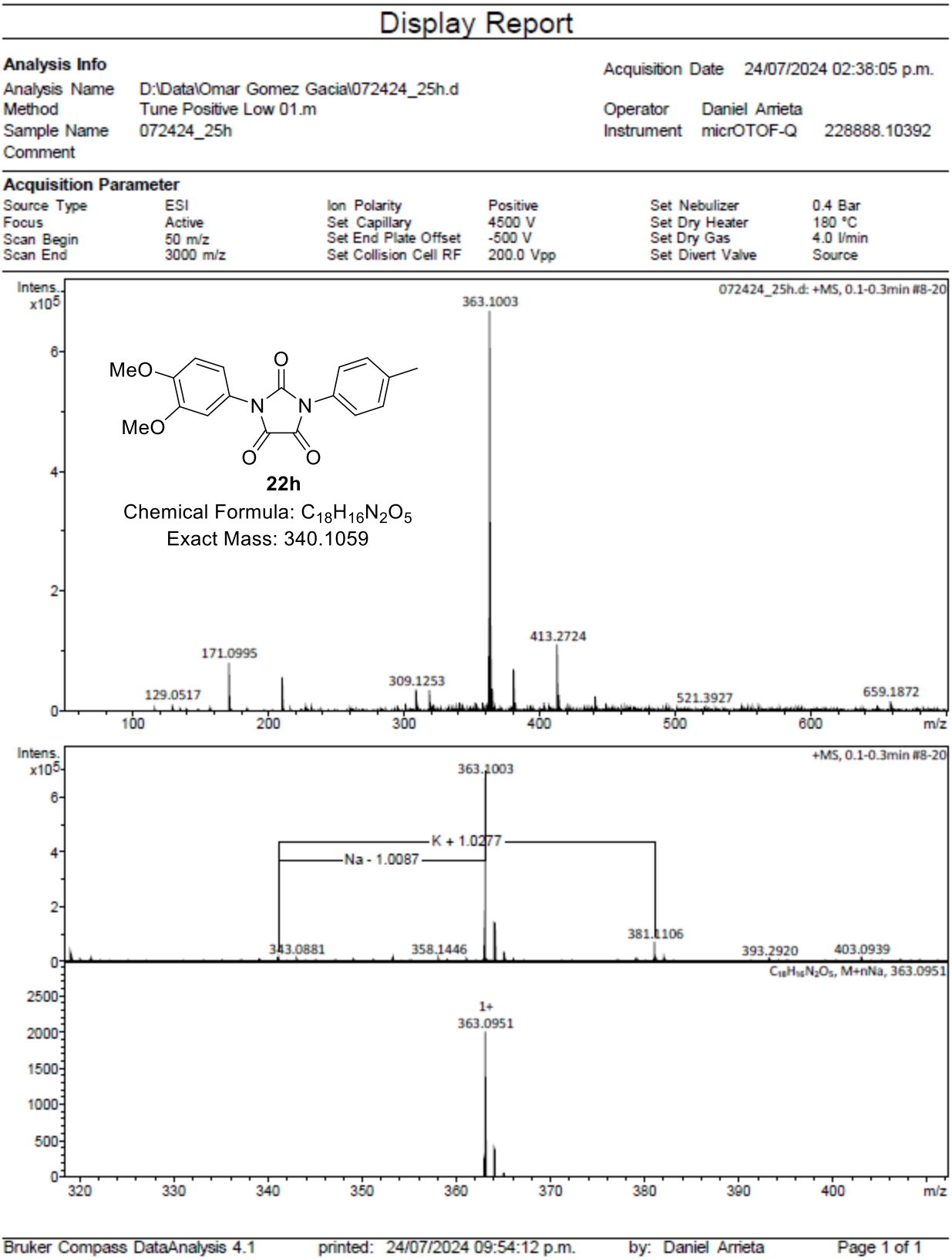



Figure S279. HRMS of compound **22h.**

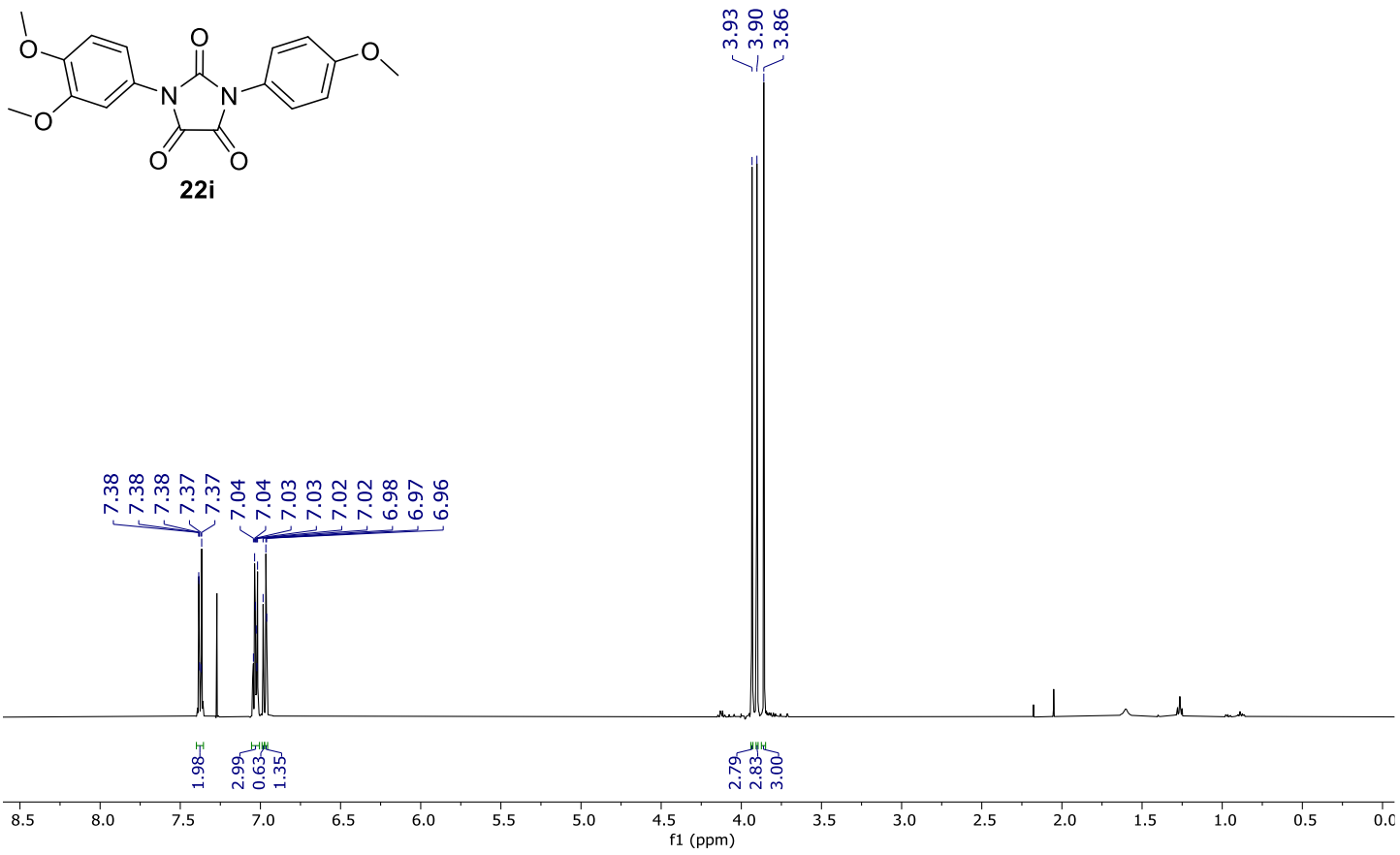



Figure S280. $^{1}$H NMR (500 MHz, $CDCl_3$) spectrum of compound **22i**.

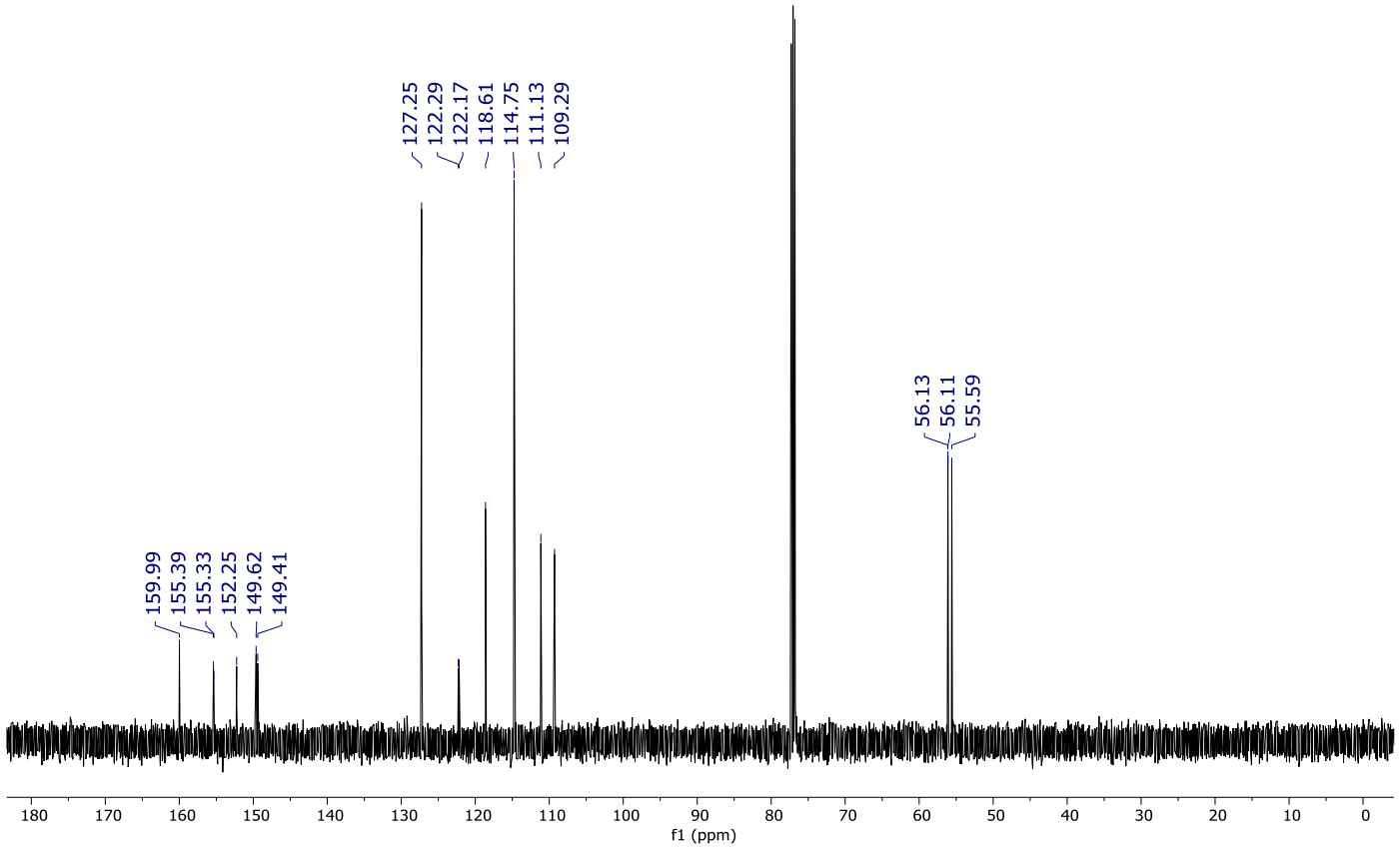



Figure S281. $^{13}$C NMR (125 MHz, $CDCl_3$) spectrum of compound **22i**.

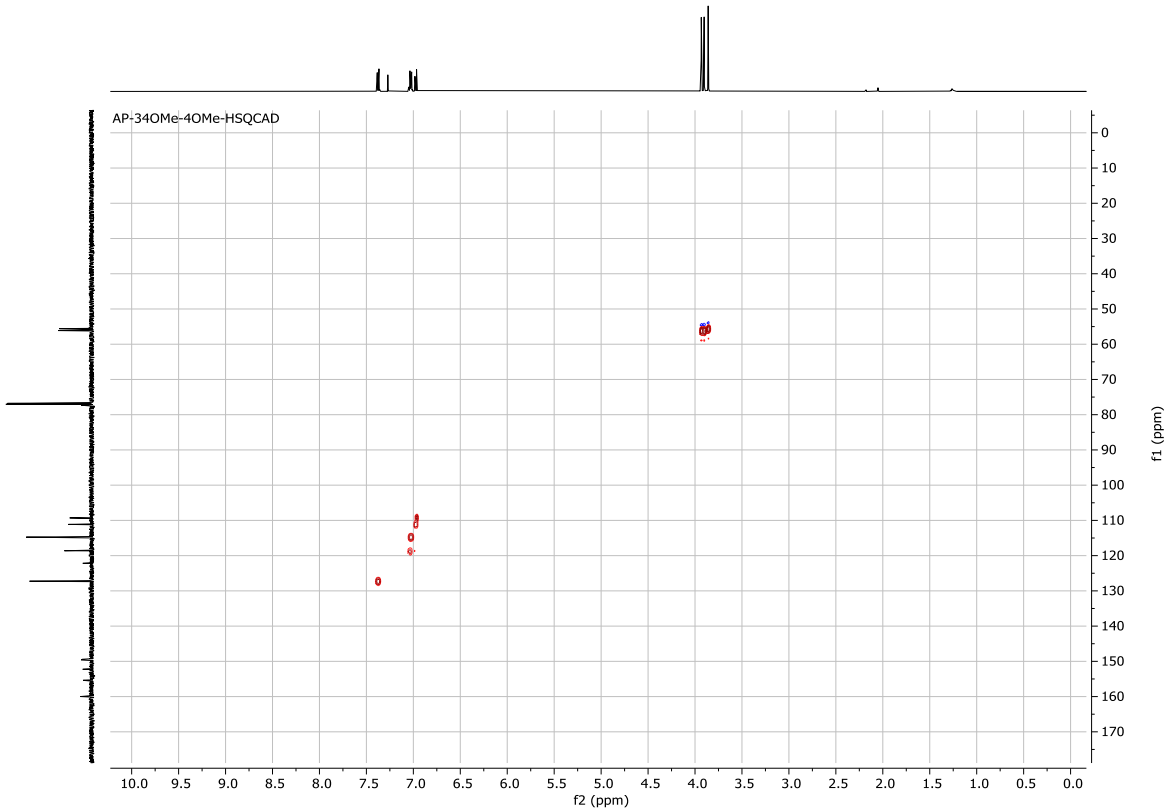



Figure S282. HSQC (500 MHz, $CDCl_3$) spectrum of compound **22i.**

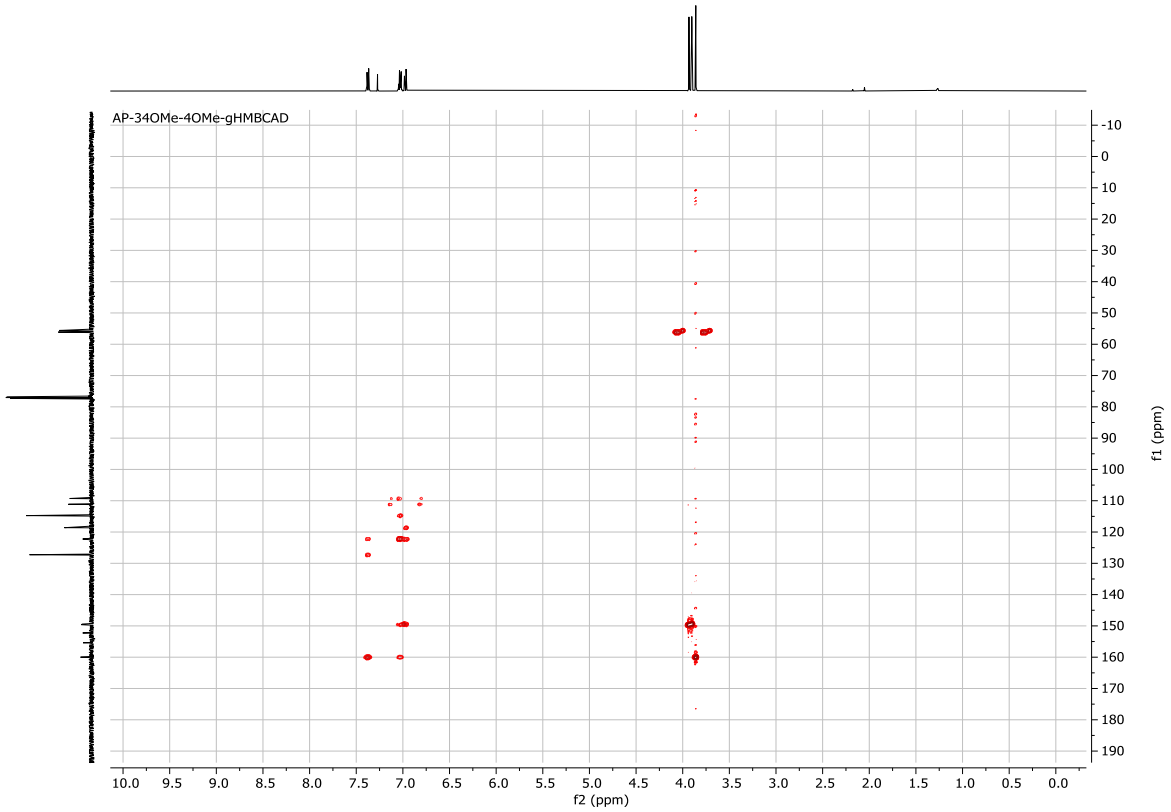



Figure S283. HMBC (500 MHz, $CDCl_3$) spectrum of compound **22i.**

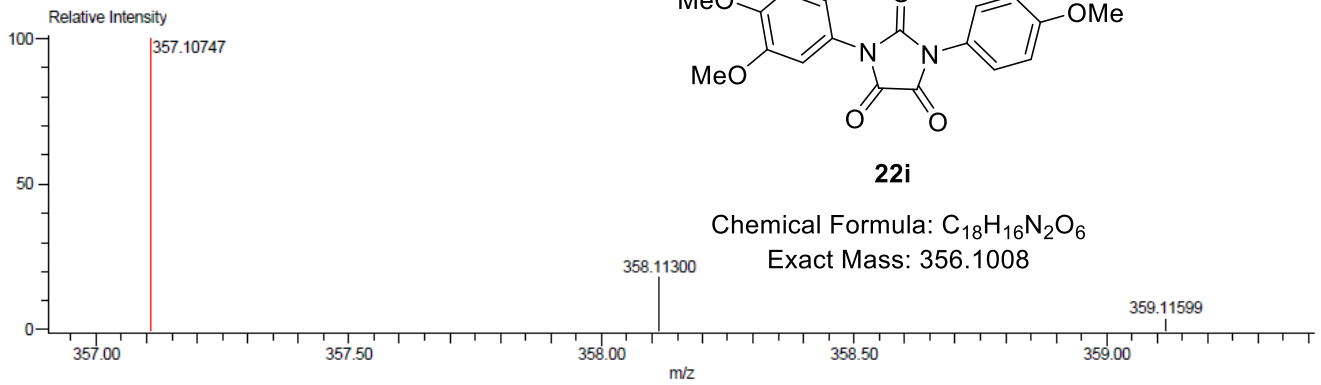
Data:25i
Sample Name:Dr. Tamariz Joaquin Operador Javier Perez
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1..1)

Acquired:6/26/2024 4:40:25 PM
Operator:AccuTOF
Mass Calibration data:CAL_PEG_600_ALUMNOS_2024
Created:6/26/2024 5:06:45 PM
Created by:AccuTOF

Charge number:1
Element:$^{12}$C:0 .. 30, $^{1}$H:1 .. 60, $^{14}$N:1 .. 3, $^{16}$O:3 .. 7

Tolerance:3.00(mmu)

Unsaturation Number:-1.5 .. 1000.0 (Fraction:Both)





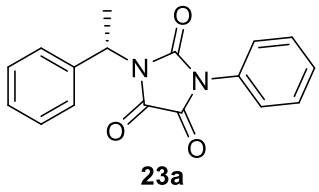


**22i**

Chemical Formula: $C_{18}H_{16}N_2O_6$
Exact Mass: 356.1008

| Mass | Intensity | Calc. Mass | Mass Difference (mmu) | Mass Difference (ppm) | Possible Formula | Unsaturation Number |
|---|---|---|---|---|---|---|
| 357.10747 | 402594.42 | 357.10866 | -1.19 | -3.32 | $^{12}C_{18}{}^{1}H_{17}{}^{14}N_2{}^{16}O_6$ | 11.5 |

Figure S284. HRMS of compound **22i.**



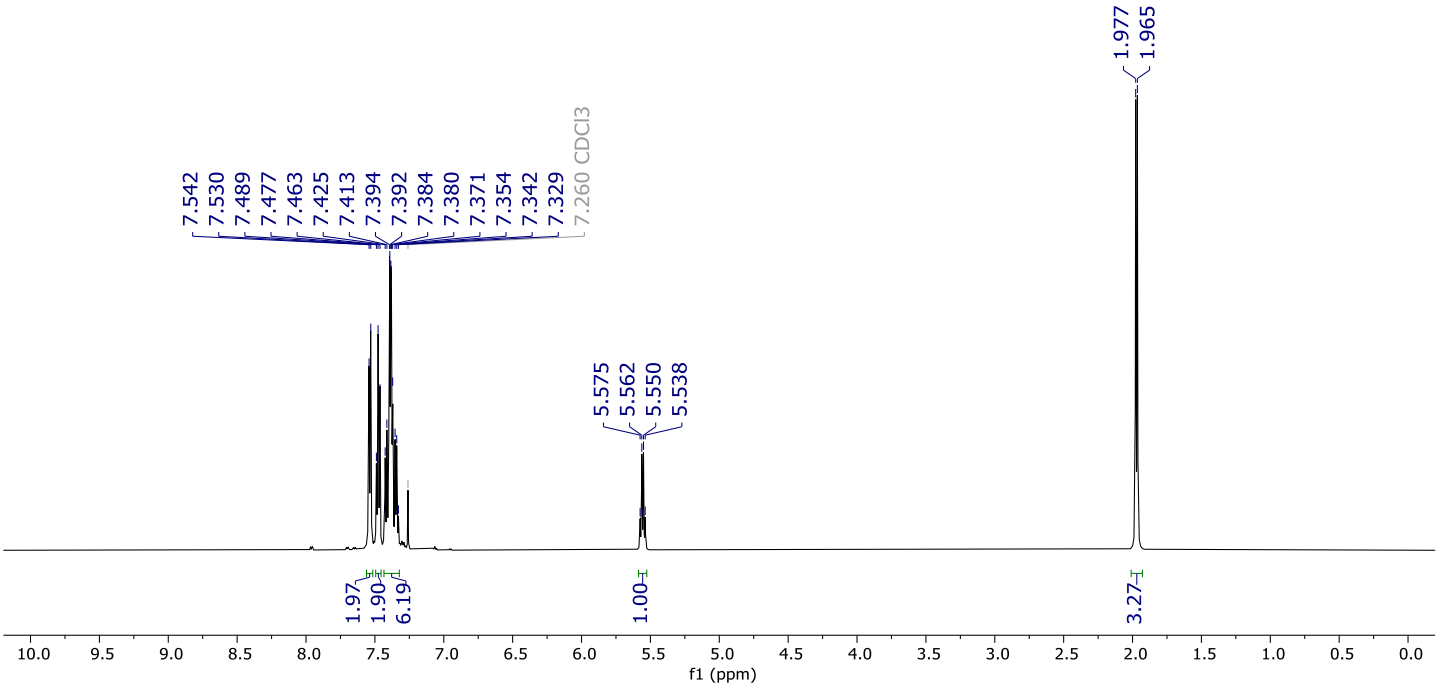




Figure S285. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **23a**.

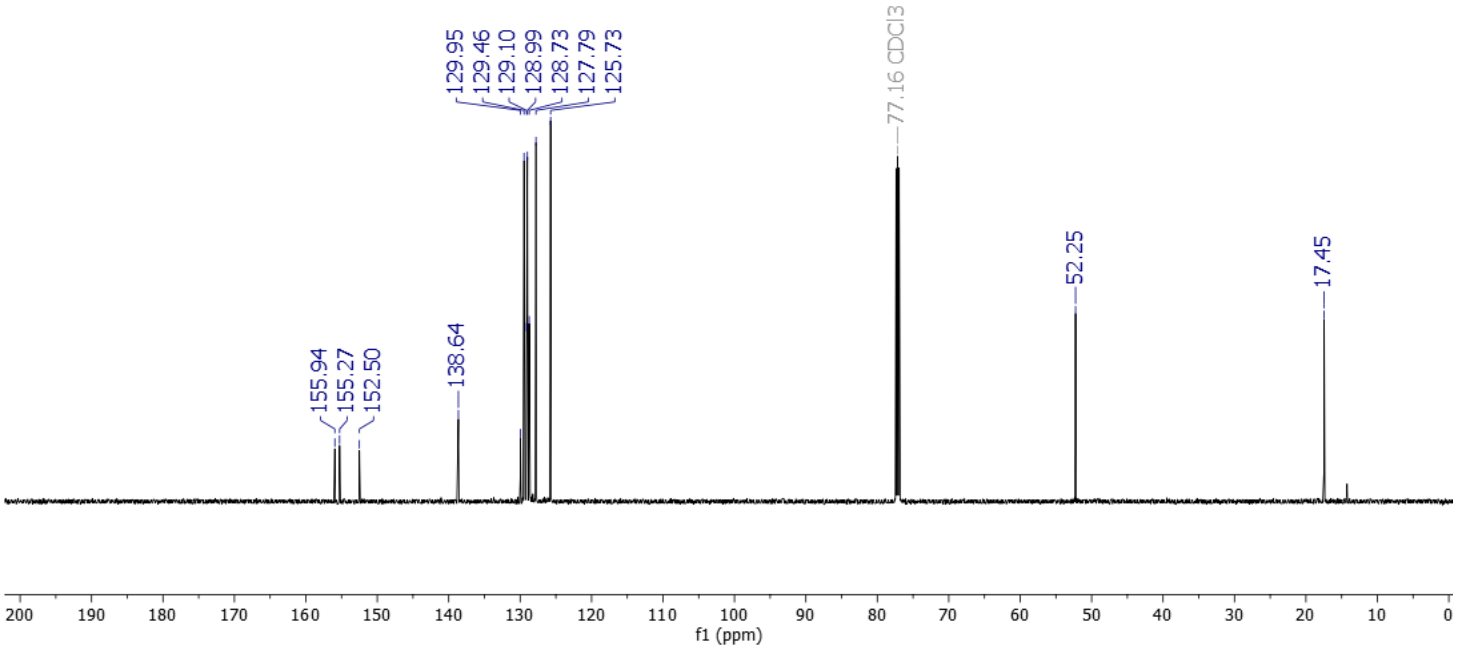



Figure S286. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **23a**.

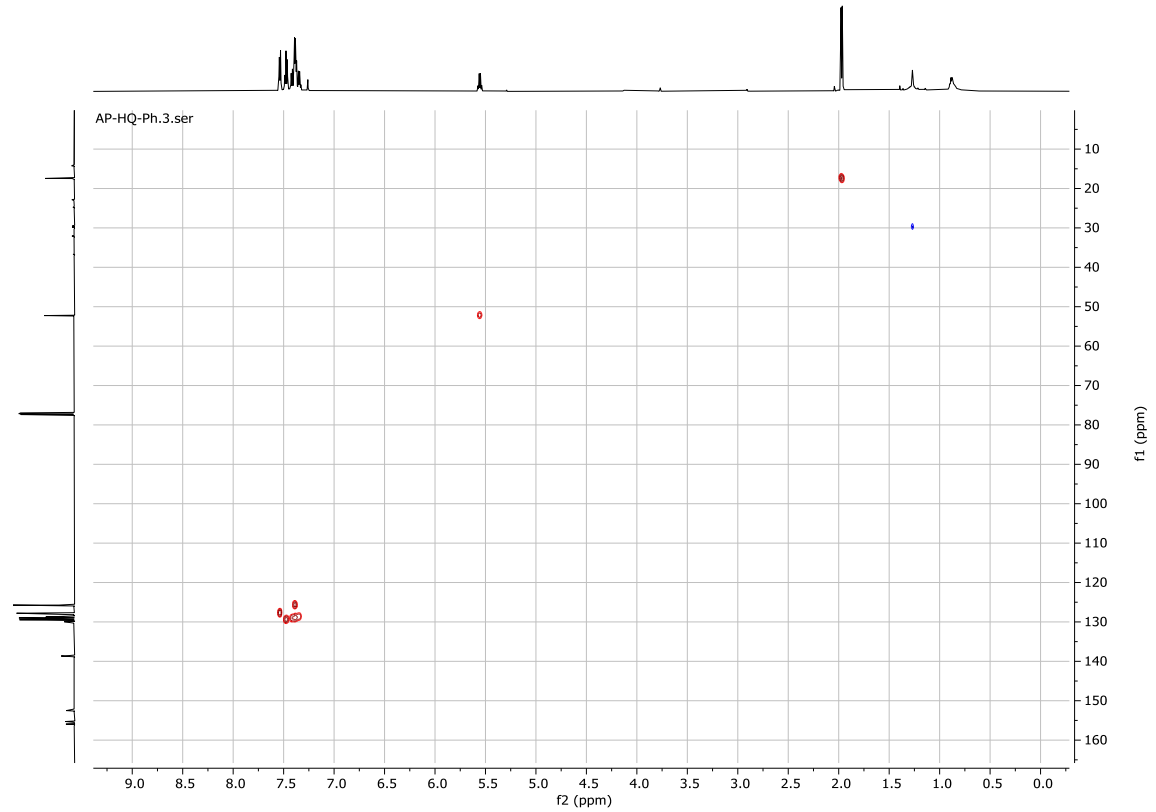



Figure S287. HSQC (600 MHz, $CDCl_3$) spectrum of compound **23a.**

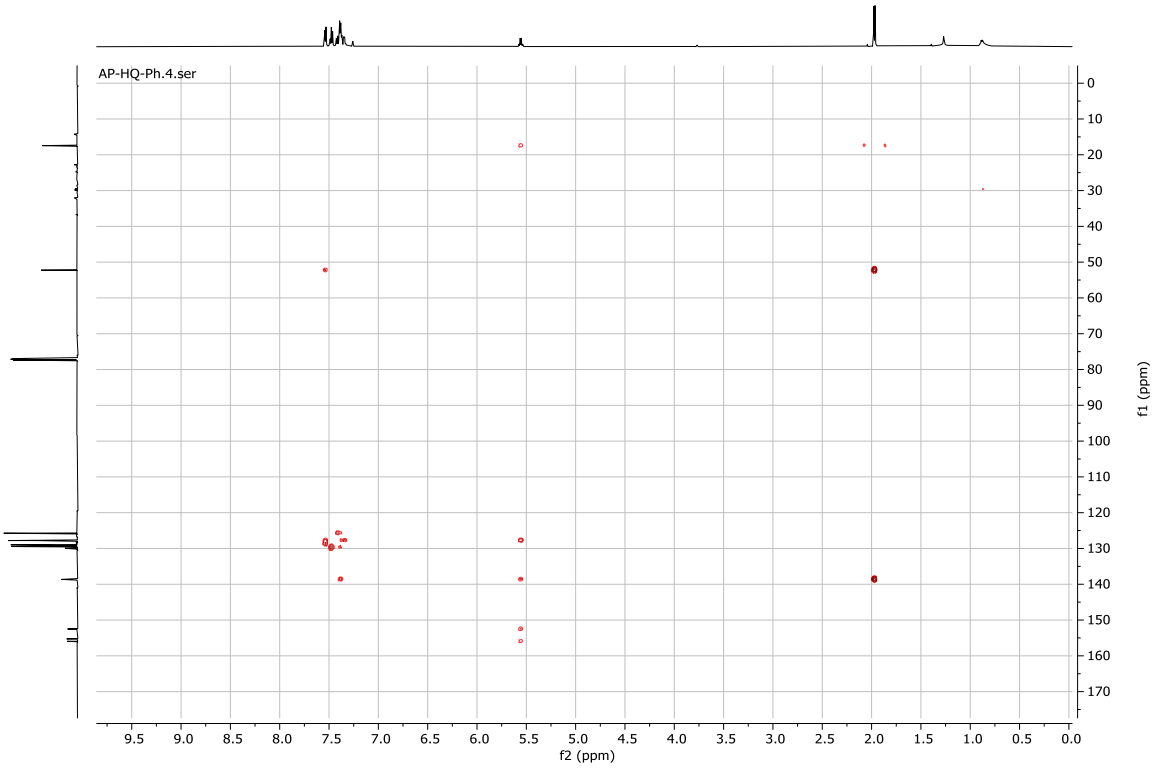



Figure S288. HMBC (600 MHz, $CDCl_3$) spectrum of compound **23a.**

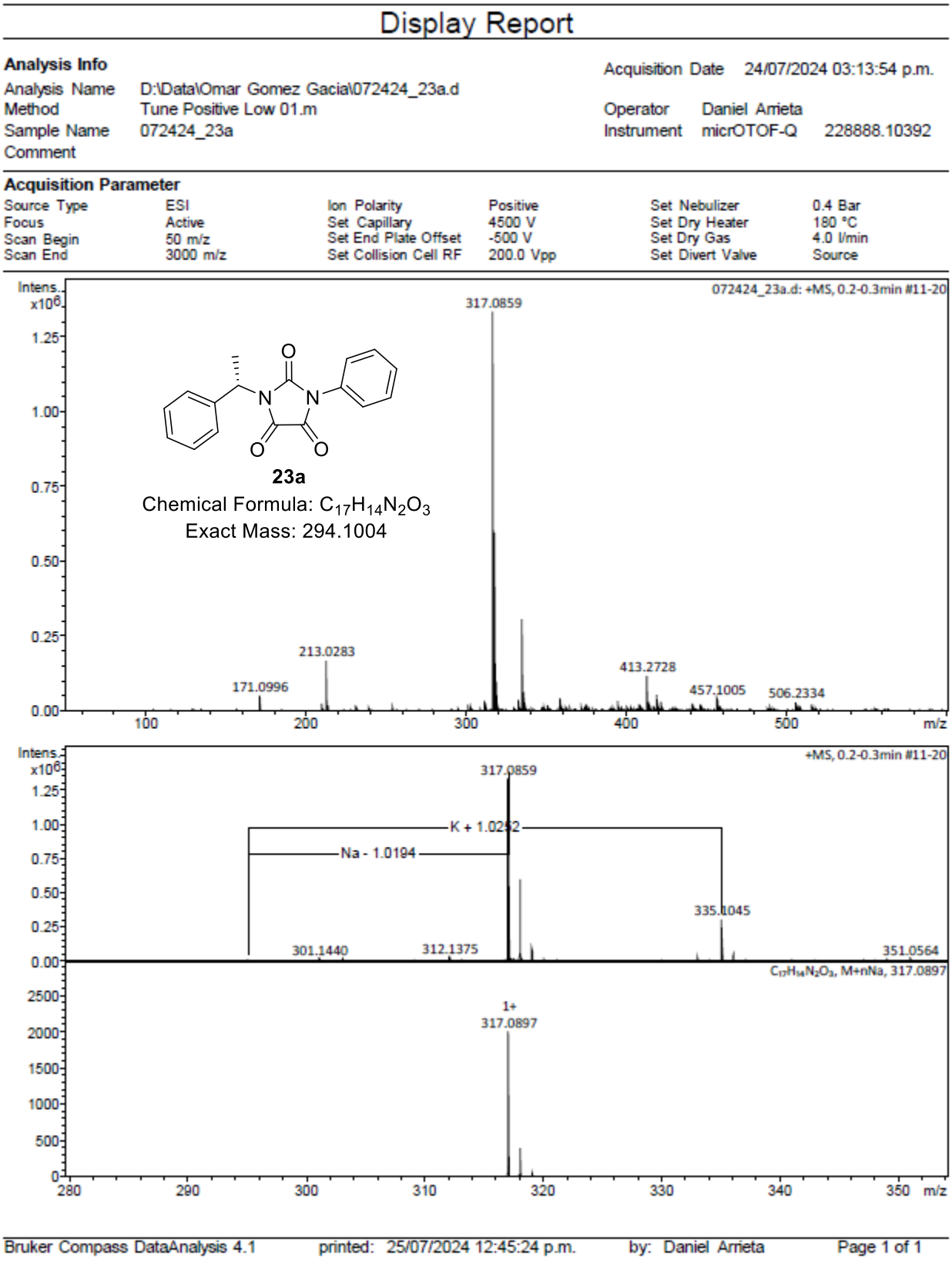
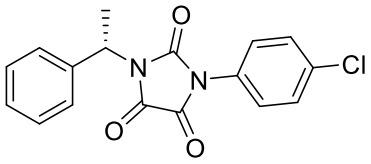



Figure S289. HRMS of compound **23a.**




**23b**

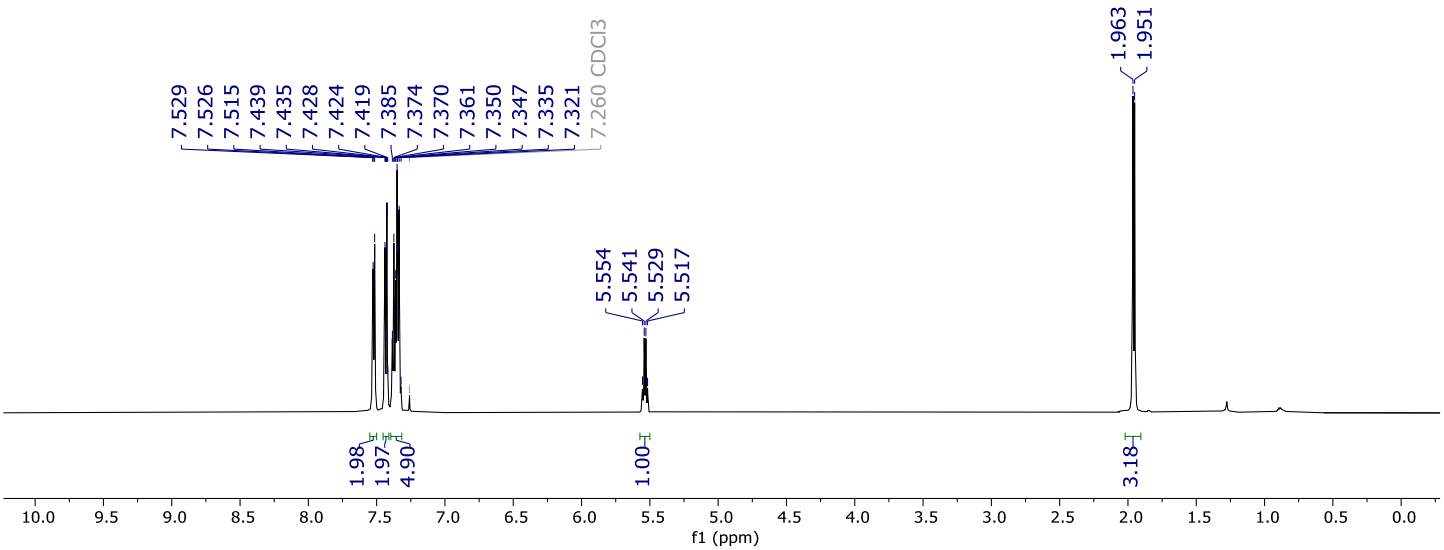



Figure S290. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **23b**.

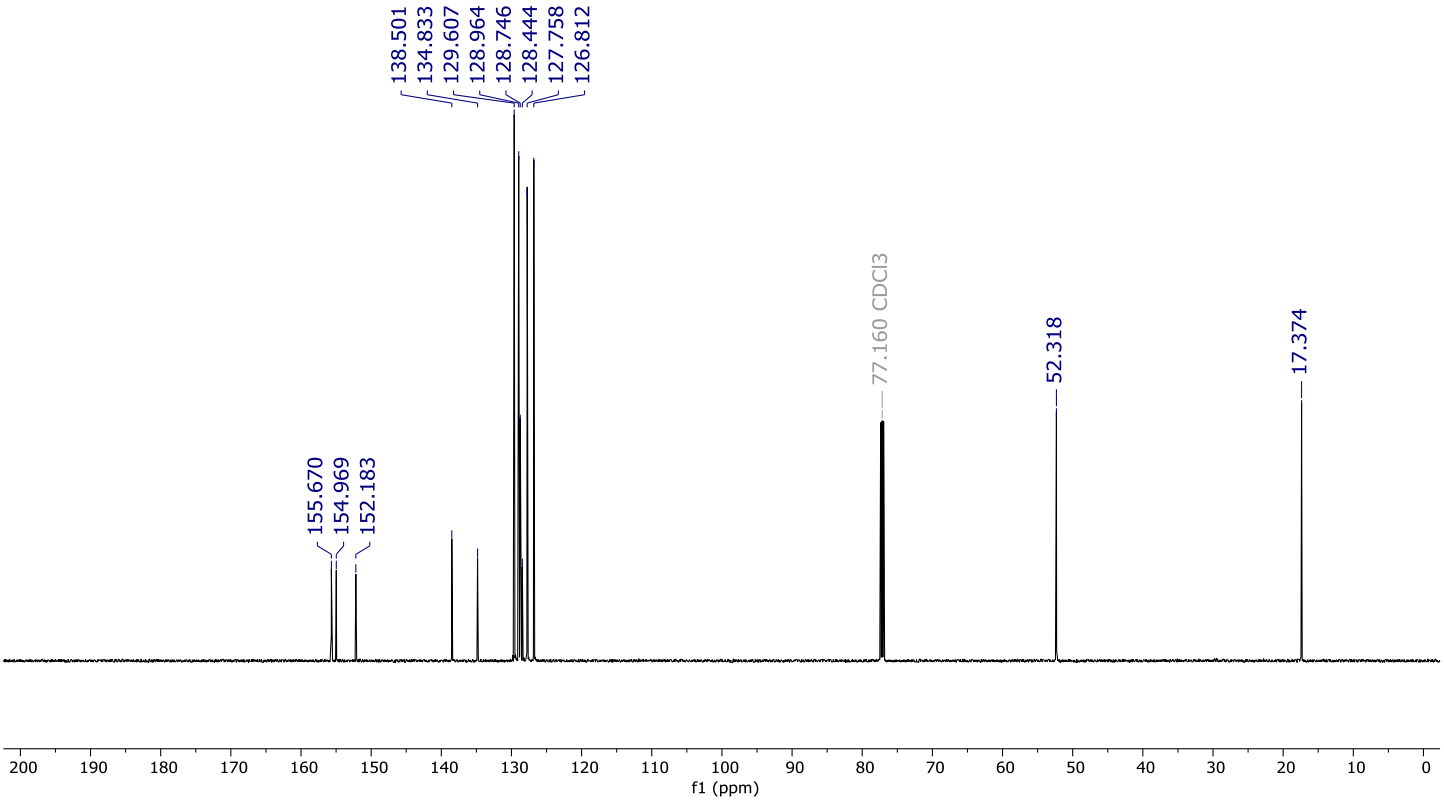



Figure S291. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **23b**.

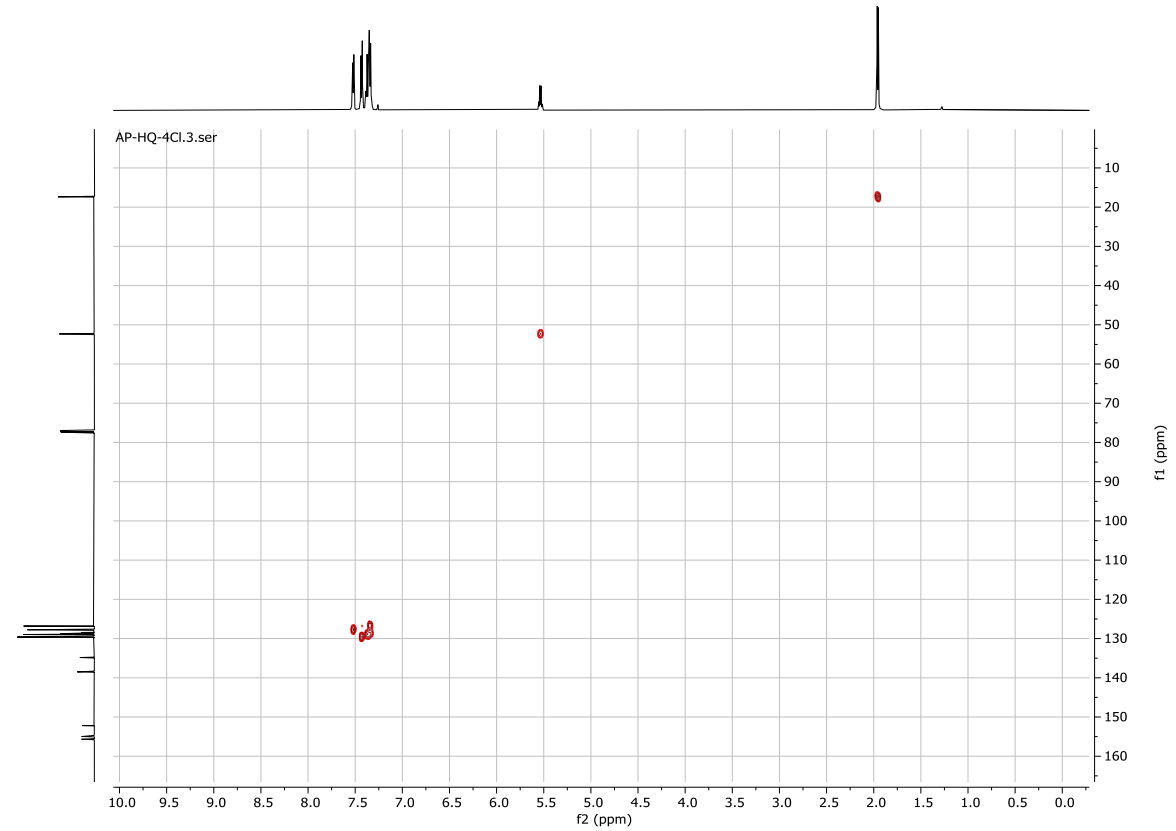



Figure S292. HSQC (600 MHz, $CDCl_3$) spectrum of compound **23b.**

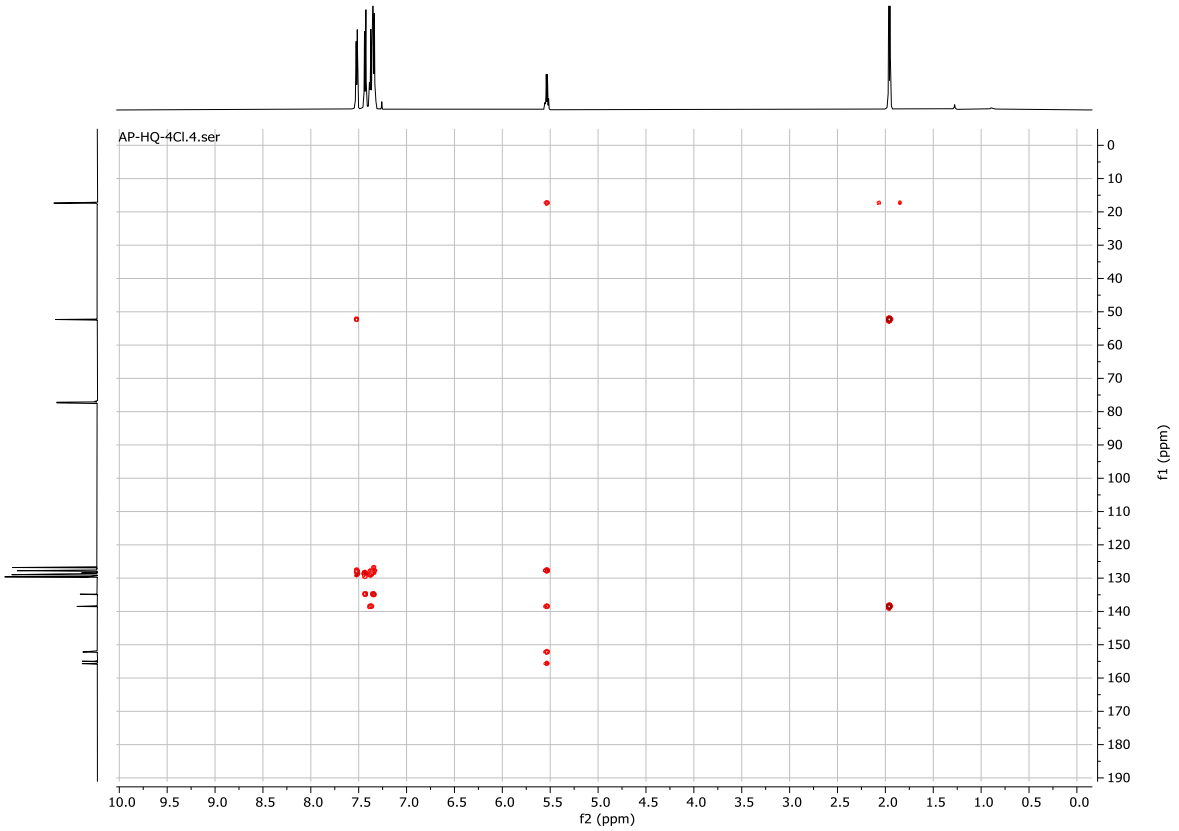



Figure S293. HMBC (600 MHz, $CDCl_3$) spectrum of compound **23b.**

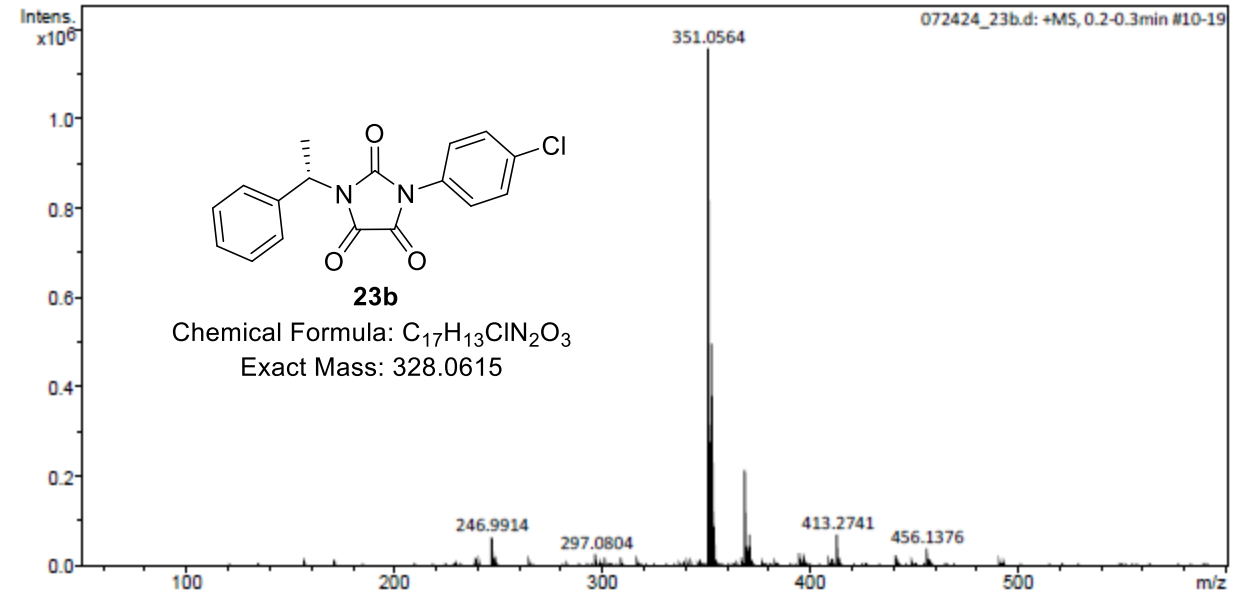
# Display Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | D:\Data\Omar Gomez Gacia\072424_23b.d | Acquisition Date | 24/07/2024 03:36:05 p.m. |
| Method | Tune Positive Low 01.m | Operator | Daniel Arrieta |
| Sample Name | 072424_23b | Instrument | micrOTOF-Q 228888.10392 |
| Comment | | | |

**Acquisition Parameter**

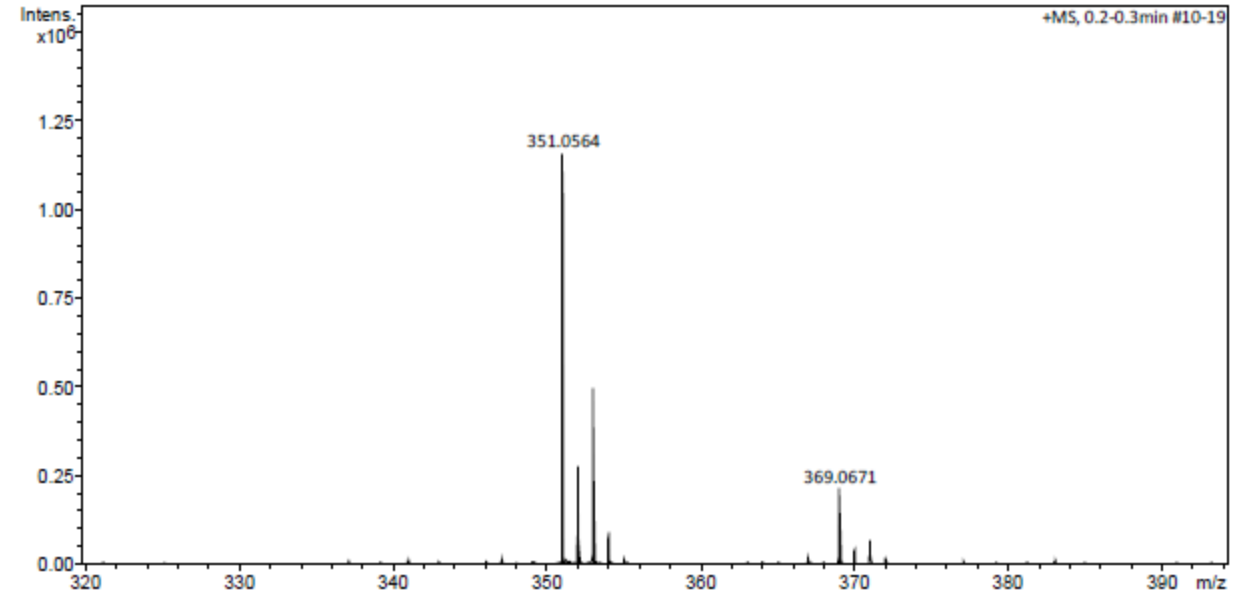
| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.4 Bar |
| Focus | Active | Set Capillary | 4500 V | Set Dry Heater | 180 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 3000 m/z | Set Collision Cell RF | 200.0 Vpp | Set Divert Valve | Source |




**23b**

Chemical Formula: $C_{17}H_{13}ClN_2O_3$

Exact Mass: 328.0615




Bruker Compass DataAnalysis 4.1 printed: 25/07/2024 12:50:13 p.m. by: Daniel Arrieta Page 1 of 1

Figure S294. HRMS of compound **23b.**

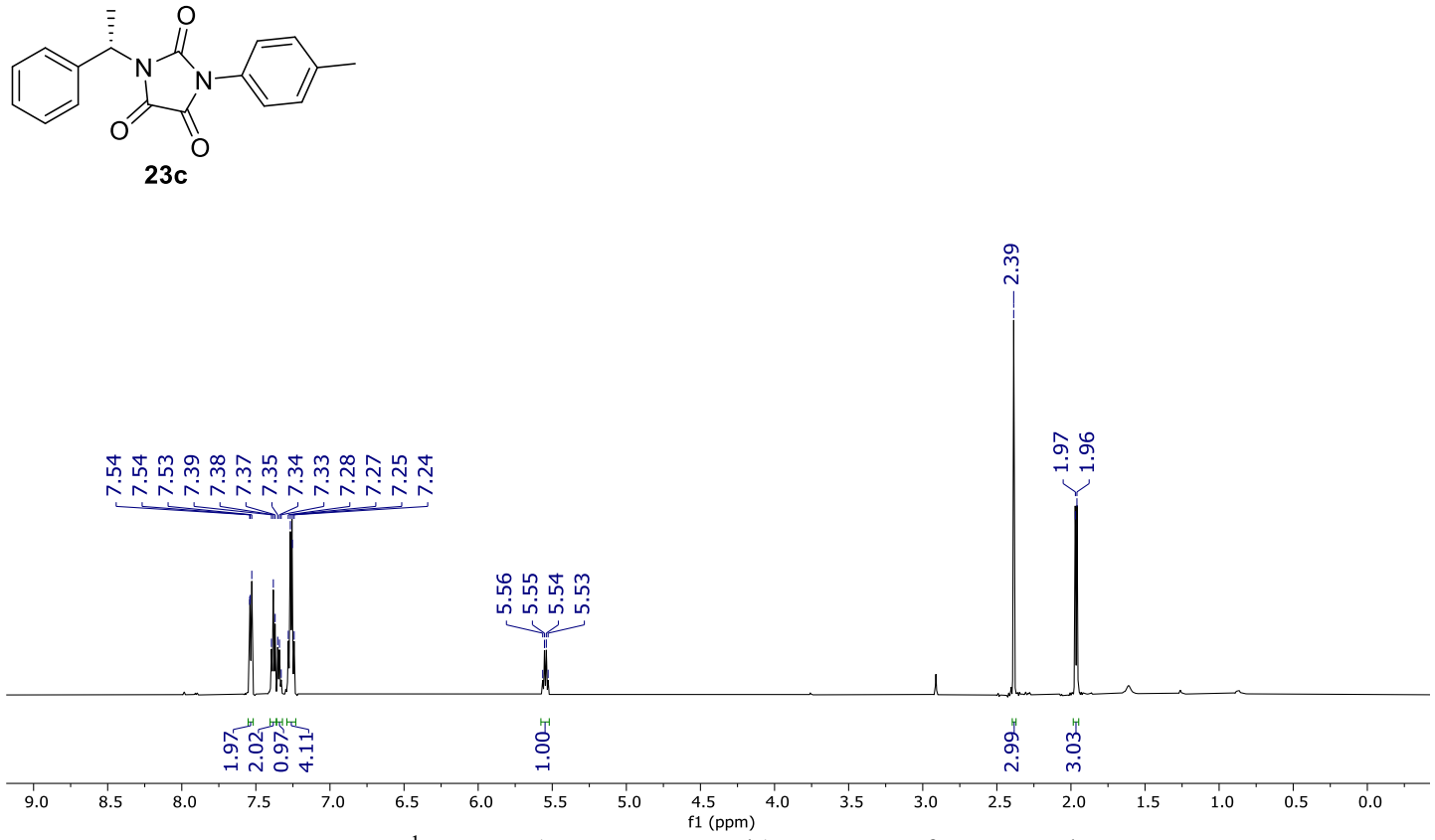



Figure S295. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **23c**.

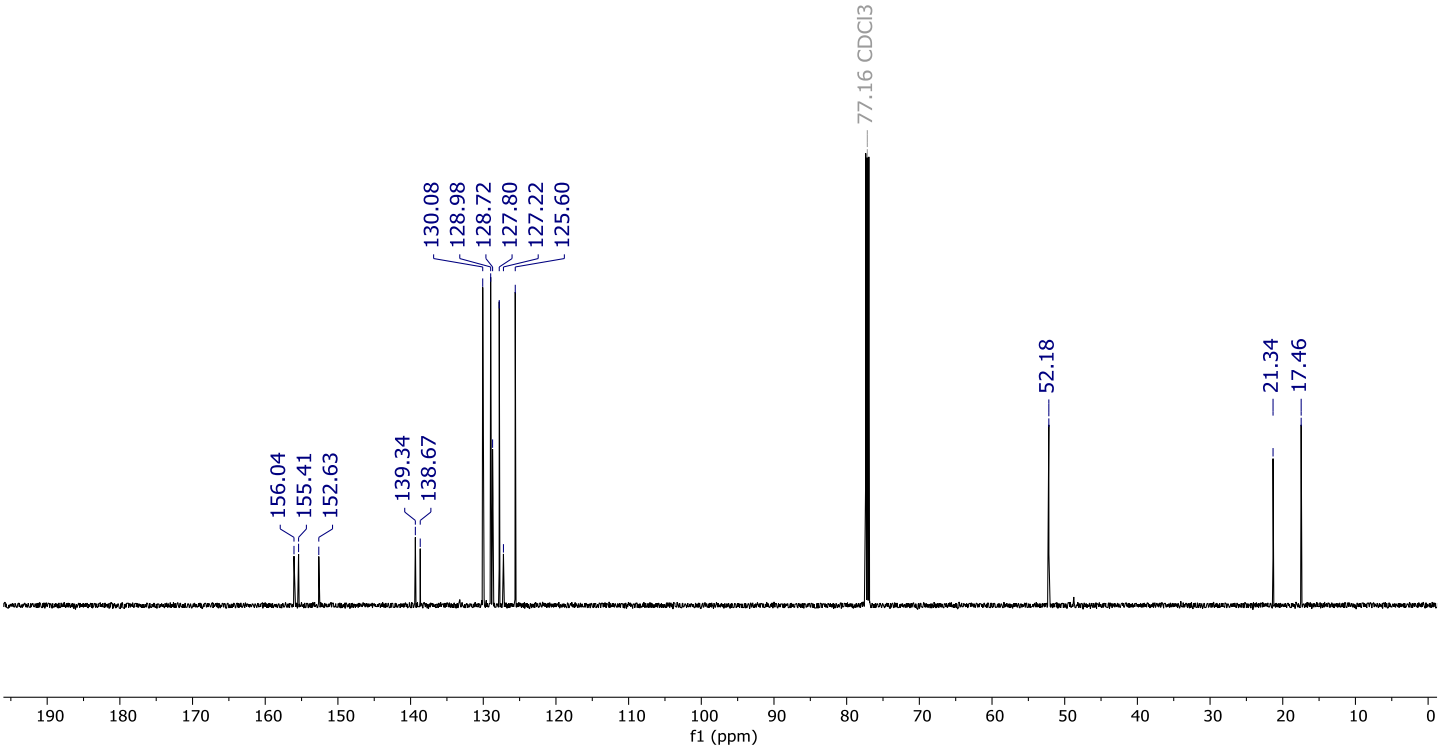



Figure S296. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **23c**.

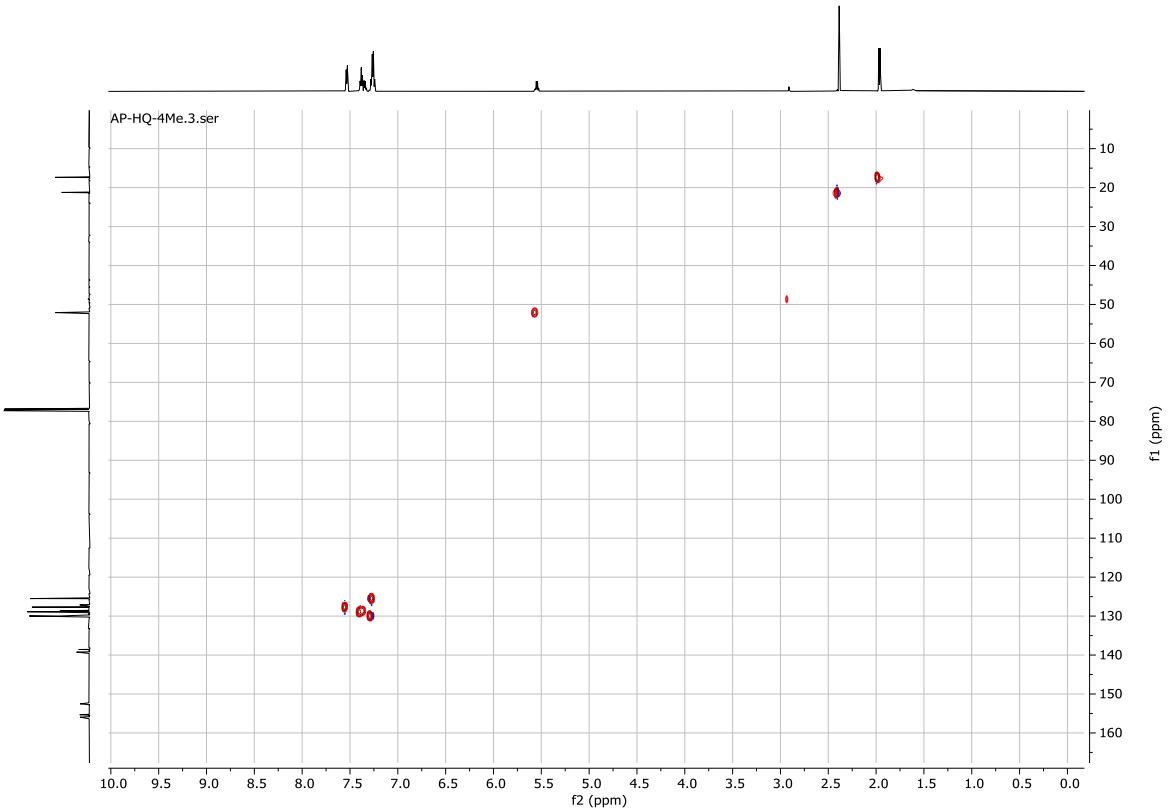



Figure S297. HSQC (600 MHz, $CDCl_3$) spectrum of compound **23c.**

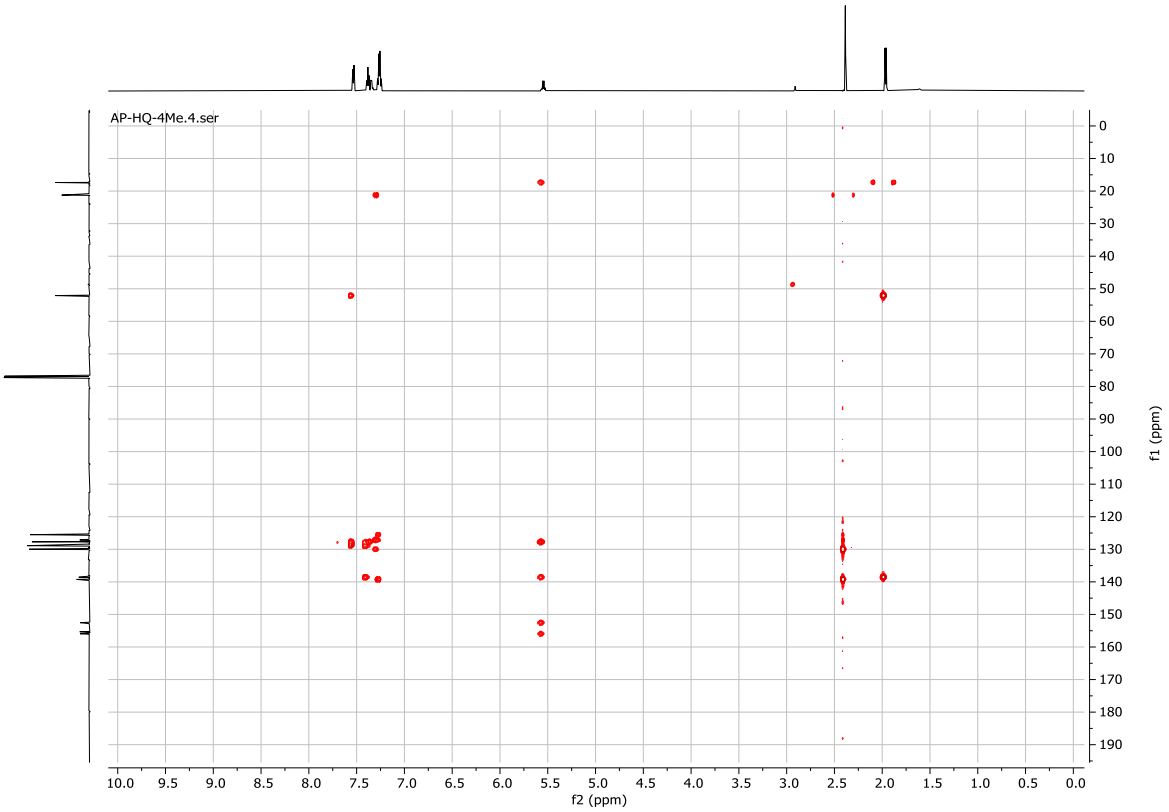
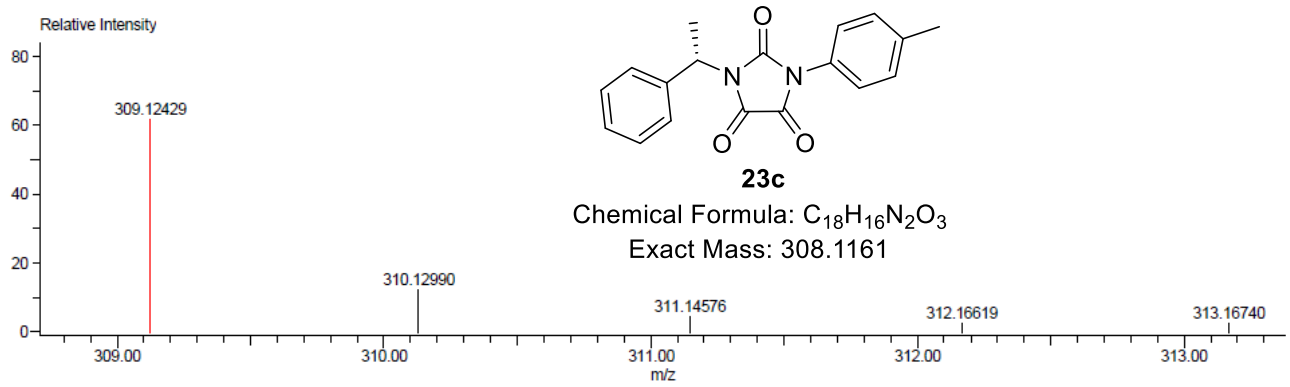



Figure S298. HMBC (600 MHz, $CDCl_3$) spectrum of compound **23c.**

Data:26c
Sample Name:Dr. Tamariz Joaquin Operador Javier Perez
Description:
Ionization Mode:ESI+
History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[5.0%]];Correct Base[5.0%];Average(MS[1] 1..1)

Acquired:6/26/2024 4:26:29 PM
Operator:AccuTOF
Mass Calibration data:CAL_PEG_600_ALUMNOS_2024
Created:6/26/2024 5:39:17 PM
Created by:AccuTOF

Charge number:1
Tolerance:3.00(mmu)
Unsaturation Number:-1.5 .. 1000.0 (Fraction:Both)
Element:$^{12}$C:0 .. 30, $^{1}$H:1 .. 60, $^{14}$N:1 .. 4, $^{16}$O:1 .. 6






**23c**

Chemical Formula: $C_{18}H_{16}N_2O_3$
Exact Mass: 308.1161

| Mass | Intensity | Calc. Mass | Mass Difference (mmu) | Mass Difference (ppm) | Possible Formula | Unsaturation Number |
|---|---|---|---|---|---|---|
| 309.12429 | 83080.92 | 309.12392 | 0.37 | 1.20 | $^{12}C_{18}{}^{1}H_{17}{}^{14}N_2{}^{16}O_3$ | 11.5 |

Figure S299. HRMS of compound **23c.**

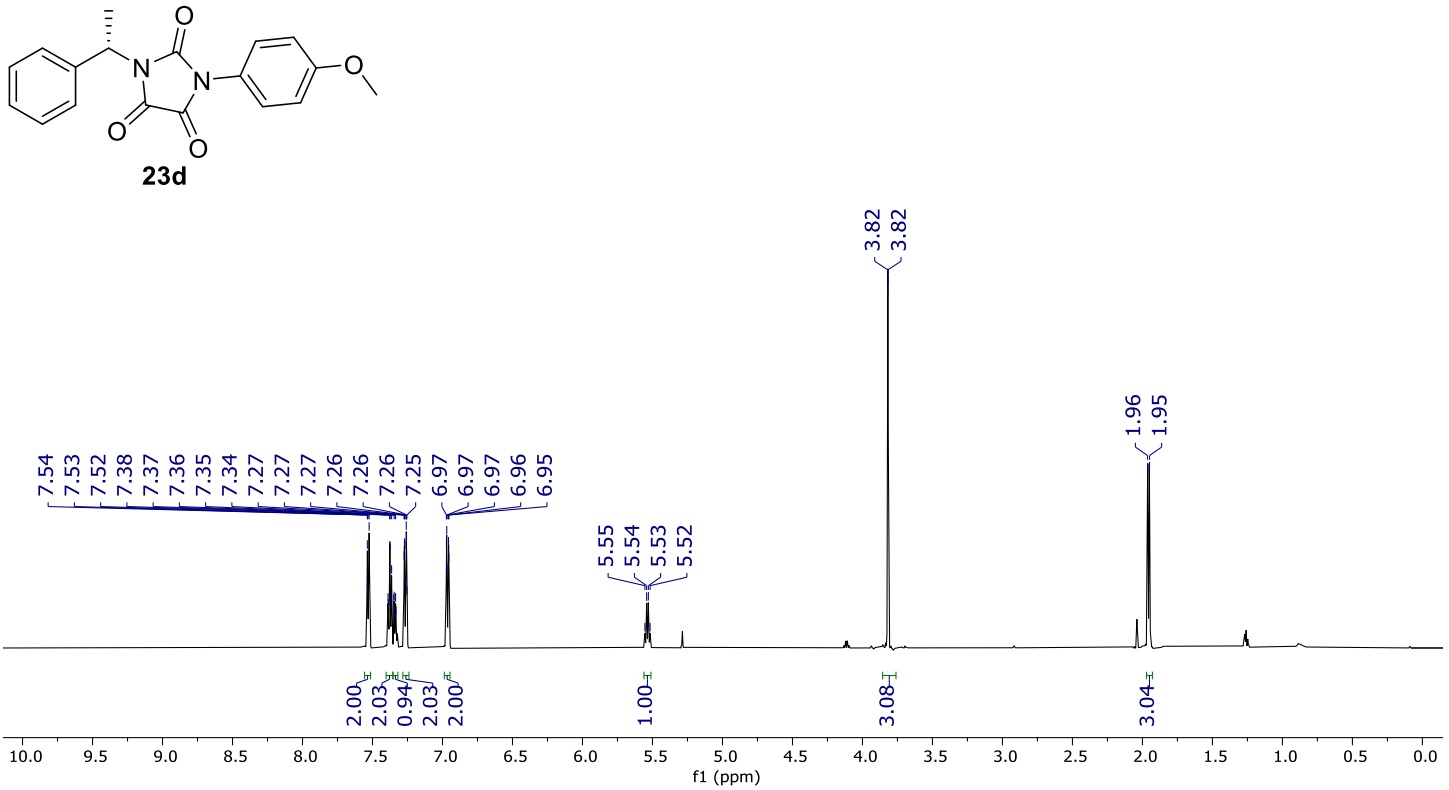



Figure S300. $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **23d**.

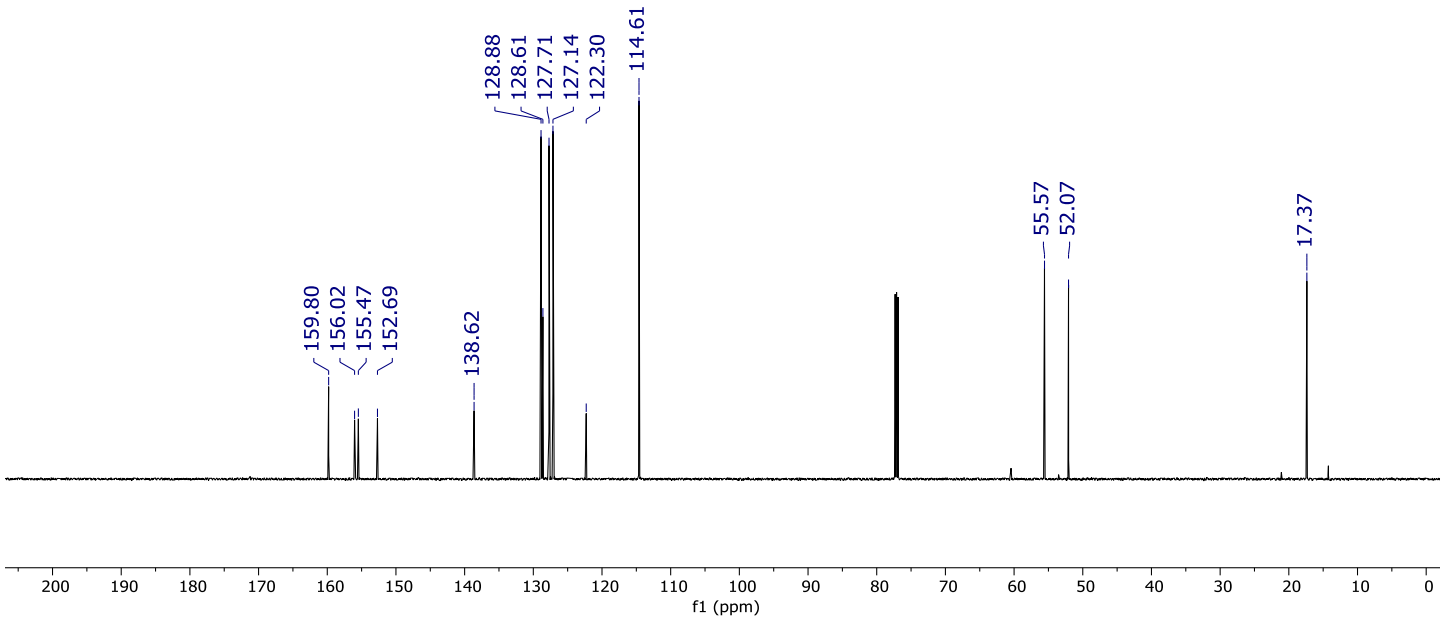



Figure S301. $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **23d**.

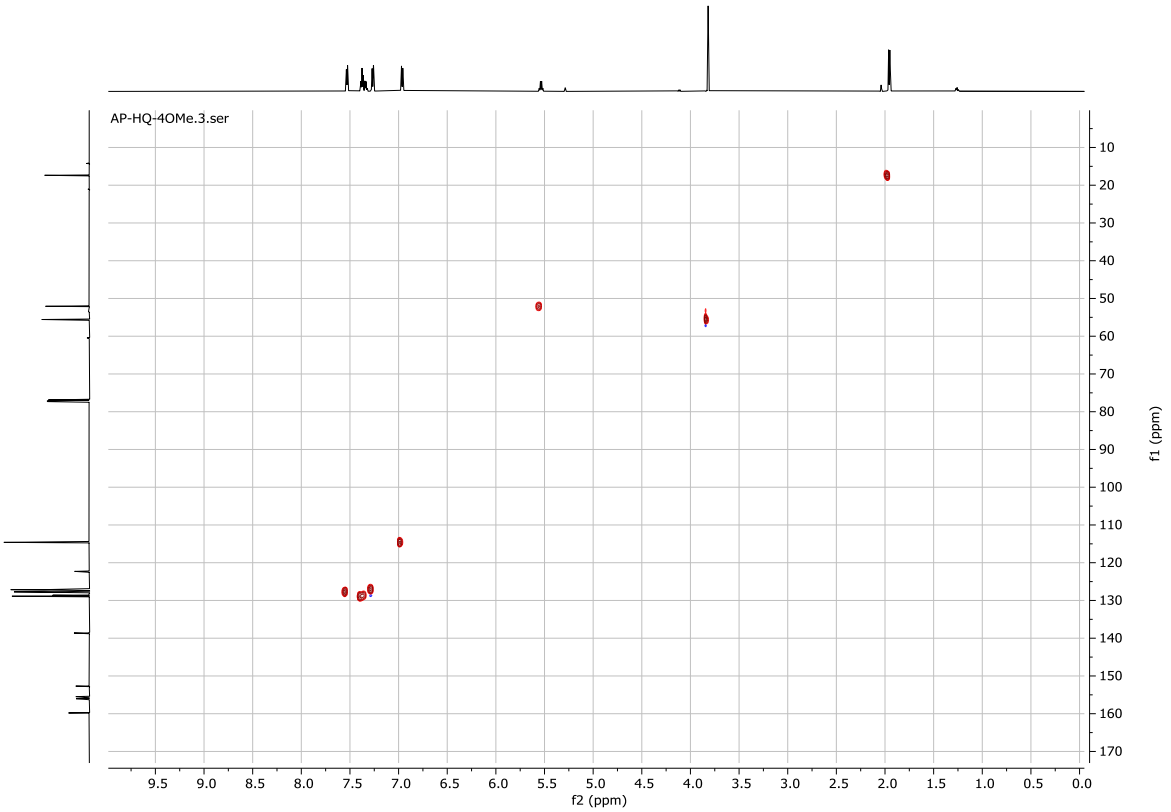



Figure S302. HSQC (600 MHz, $CDCl_3$) spectrum of compound **23d.**

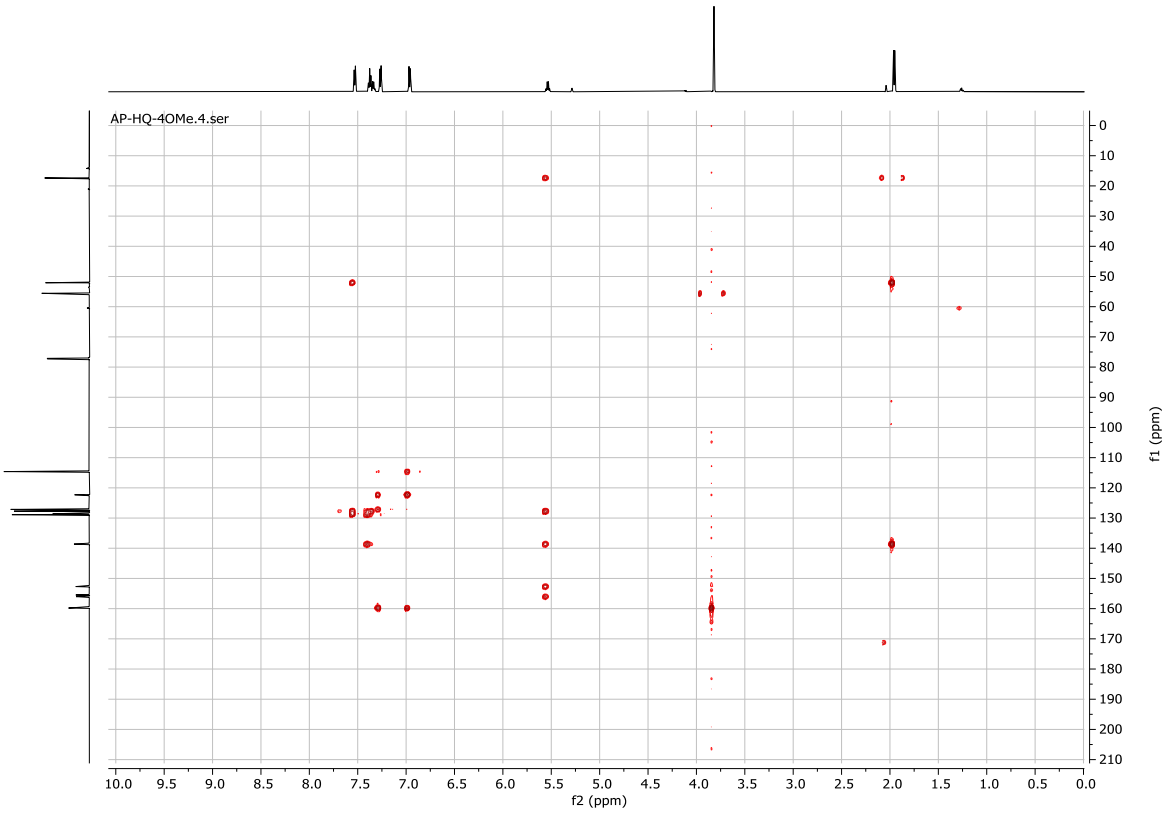



Figure S303. HMBC (600 MHz, $CDCl_3$) spectrum of compound **23d.**

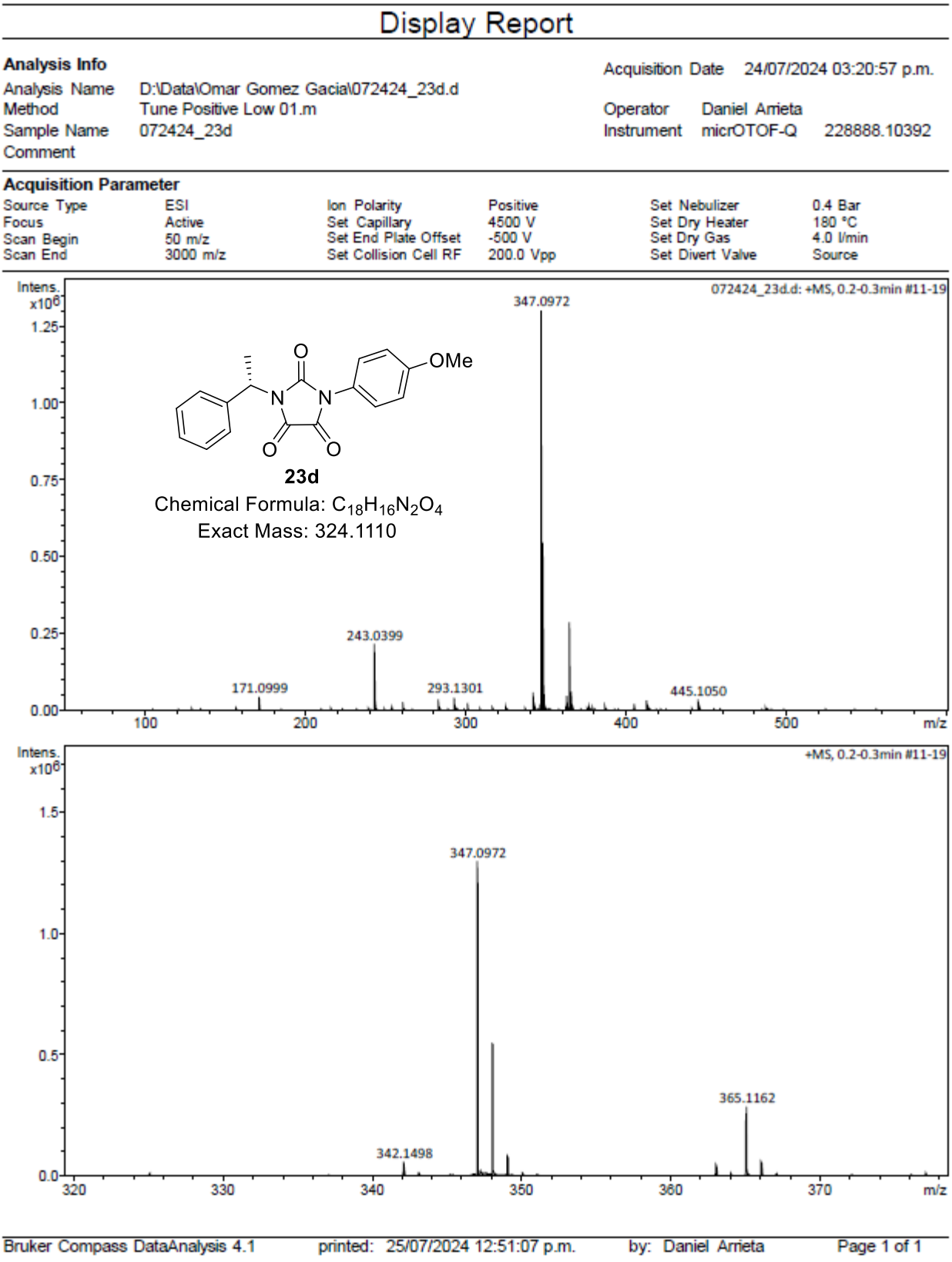
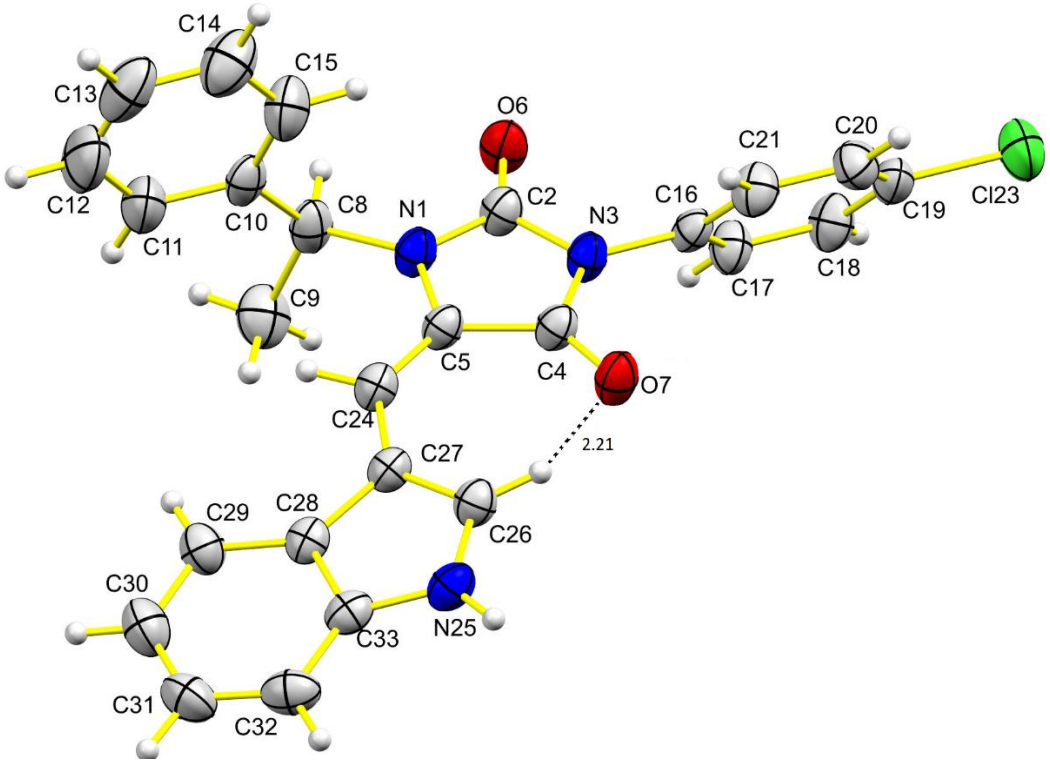



Figure S304. HRMS of compound **23d.**

## 3. X-Ray structure and crystallographic data of **16b**.

### 3.1 X-Ray structure of **16b**.




### 3.2 Crystallographic data of **16b (CCDC 2371941)**.

**Table S1.** Crystal data and structure refinement for **16b**.

| | | |
|---|---|---|
| Identification code | shelx | |
| Empirical formula | C26 H21 Cl0 N3 O2 | |
| Formula weight | 407.46 | |
| Temperature | 293(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Orthorhombic | |
| Space group | P 21 21 21 | |
| Unit cell dimensions | a = 6.5034(4) Å | α= 90°. |
| | b = 18.5739(13) Å | β= 90°. |
| | c = 18.5540(10) Å | γ = 90°. |
| Volume | 2241.2(2) Å$^3$ | |
| Z | 4 | |
| Density (calculated) | 1.208 Mg/m$^3$ | |

| | |
|---|---|
| Absorption coefficient | 0.078 $mm^{-1}$ |
| F(000) | 856 |
| Crystal size | 0.5 x 0 x 0 $mm^3$ |
| Theta range for data collection | 3.104 to 32.506°. |
| Index ranges | -9<=h<=9, -24<=k<=26, -27<=l<=26 |
| Reflections collected | 13817 |
| Independent reflections | 7033 [R(int) = 0.0460] |
| Completeness to theta = 25.242° | 99.6 % |
| Absorption correction | None |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 7033 / 0 / 290 |
| Goodness-of-fit on $F^2$ | 1.125 |
| Final R indices [I>2sigma(I)] | R1 = 0.0944, wR2 = 0.1205 |
| R indices (all data) | R1 = 0.1941, wR2 = 0.1495 |
| Absolute structure parameter | -0.03(6) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.202 and -0.135 $e.Å^{-3}$ |

**Table S2.** Torsion angles [°] for **16b**.

| | |
|---|---|
| C(24)-C(5)-C(4)-O(7) | -2.8(7) |
| N(1)-C(5)-C(4)-O(7) | 179.6(5) |
| C(24)-C(5)-C(4)-N(3) | 175.2(4) |
| N(1)-C(5)-C(4)-N(3) | -2.4(4) |
| N(1)-C(8)-C(10)-C(15) | 43.5(6) |
| C(9)-C(8)-C(10)-C(15) | 172.0(5) |
| N(1)-C(8)-C(10)-C(11) | -139.8(5) |
| C(9)-C(8)-C(10)-C(11) | -11.3(7) |
| C(15)-C(10)-C(11)-C(12) | -1.5(8) |
| C(8)-C(10)-C(11)-C(12) | -178.3(5) |
| C(10)-C(11)-C(12)-C(13) | 0.8(10) |
| C(11)-C(12)-C(13)-C(14) | 0.1(10) |
| C(12)-C(13)-C(14)-C(15) | -0.3(10) |
| C(21)-C(16)-C(17)-C(18) | -0.9(6) |
| N(3)-C(16)-C(17)-C(18) | -179.6(4) |
| C(16)-C(17)-C(18)-C(19) | 0.3(7) |
| C(17)-C(18)-C(19)-C(20) | 0.6(7) |
| C(17)-C(18)-C(19)-Cl(23) | 179.6(3) |

| | |
|---|---|
| C(18)-C(19)-C(20)-C(21) | -0.9(7) |
| Cl(23)-C(19)-C(20)-C(21) | -179.9(3) |
| C(17)-C(16)-C(21)-C(20) | 0.7(7) |
| N(3)-C(16)-C(21)-C(20) | 179.4(4) |
| C(19)-C(20)-C(21)-C(16) | 0.2(7) |
| N(1)-C(5)-C(24)-C(27) | 174.8(4) |
| C(4)-C(5)-C(24)-C(27) | -2.3(7) |
| N(25)-C(26)-C(27)-C(24) | -179.3(4) |
| N(25)-C(26)-C(27)-C(28) | 0.0(4) |
| C(5)-C(24)-C(27)-C(26) | 15.0(7) |
| C(5)-C(24)-C(27)-C(28) | -164.1(4) |
| C(26)-C(27)-C(28)-C(33) | -0.6(4) |
| C(24)-C(27)-C(28)-C(33) | 178.7(4) |
| C(26)-C(27)-C(28)-C(29) | 179.3(4) |
| C(24)-C(27)-C(28)-C(29) | -1.5(7) |
| C(33)-C(28)-C(29)-C(30) | -0.4(6) |
| C(27)-C(28)-C(29)-C(30) | 179.8(4) |
| C(28)-C(29)-C(30)-C(31) | 0.1(7) |
| C(29)-C(30)-C(31)-C(32) | 0.4(8) |
| C(30)-C(31)-C(32)-C(33) | -0.5(7) |
| C(31)-C(32)-C(33)-N(25) | 179.1(4) |
| C(31)-C(32)-C(33)-C(28) | 0.2(6) |
| C(29)-C(28)-C(33)-N(25) | -178.8(3) |
| C(27)-C(28)-C(33)-N(25) | 1.1(4) |
| C(29)-C(28)-C(33)-C(32) | 0.2(6) |
| C(27)-C(28)-C(33)-C(32) | -179.9(4) |
| C(11)-C(10)-C(15)-C(14) | 1.4(8) |
| C(8)-C(10)-C(15)-C(14) | 178.2(5) |
| C(13)-C(14)-C(15)-C(10) | -0.5(9) |
| O(6)-C(2)-N(1)-C(5) | 177.8(4) |
| N(3)-C(2)-N(1)-C(5) | -1.8(4) |
| O(6)-C(2)-N(1)-C(8) | 4.7(7) |
| N(3)-C(2)-N(1)-C(8) | -174.9(4) |
| C(24)-C(5)-N(1)-C(2) | -175.0(4) |
| C(4)-C(5)-N(1)-C(2) | 2.7(4) |
| C(24)-C(5)-N(1)-C(8) | -2.5(6) |
| C(4)-C(5)-N(1)-C(8) | 175.2(4) |
| C(10)-C(8)-N(1)-C(2) | -123.0(4) |
| C(9)-C(8)-N(1)-C(2) | 105.9(4) |
| C(10)-C(8)-N(1)-C(5) | 65.2(5) |

| | |
|---|---|
| C(9)-C(8)-N(1)-C(5) | -66.0(5) |
| O(7)-C(4)-N(3)-C(2) | 179.6(4) |
| C(5)-C(4)-N(3)-C(2) | 1.4(4) |
| O(7)-C(4)-N(3)-C(16) | -2.9(7) |
| C(5)-C(4)-N(3)-C(16) | 178.9(3) |
| O(6)-C(2)-N(3)-C(4) | -179.4(4) |
| N(1)-C(2)-N(3)-C(4) | 0.2(5) |
| O(6)-C(2)-N(3)-C(16) | 3.0(7) |
| N(1)-C(2)-N(3)-C(16) | -177.4(3) |
| C(17)-C(16)-N(3)-C(4) | 119.7(5) |
| C(21)-C(16)-N(3)-C(4) | -59.0(6) |
| C(17)-C(16)-N(3)-C(2) | -63.1(5) |
| C(21)-C(16)-N(3)-C(2) | 118.2(5) |
| C(27)-C(26)-N(25)-C(33) | 0.7(5) |
| C(32)-C(33)-N(25)-C(26) | 179.9(4) |
| C(28)-C(33)-N(25)-C(26) | -1.1(5) |

Symmetry transformations used to generate equivalent atoms:

**Table S3.** Hydrogen bonds for **16b** [Å and °].

| D−H···A | d (D−H) | d (H···A) | d (D···A) | < (D−H···A) |
|---|---|---|---|---|
| C(18)-H(18)...Cl(23)#1 | 0.93 | 2.96 | 3.818(5) | 154.4 |
| C(26)-H(26)...O(7) | 0.93 | 2.21 | 2.913(5) | 132.0 |
| N(25)-H(25)...O(6)#2 | 0.86 | 2.02 | 2.837(5) | 159.4 |
| C(18)-H(18)...Cl(23)#1 | 0.93 | 2.96 | 3.818(5) | 154.4 |
| C(26)-H(26)...O(7) | 0.93 | 2.21 | 2.913(5) | 132.0 |
| N(25)-H(25)...O(6)#2 | 0.86 | 2.02 | 2.837(5) | 159.4 |

Symmetry transformations used to generate equivalent atoms:

#1 x+1/2,-y+3/2,-z+2  #2 -x+1,y-1/2,-z+3/2