Supporting information

For

Catalyst free, C-3 Functionalization of Imidazo[1,2-*a*]pyridines to Rapidly Access New Chemical Space for Drug Discovery Efforts

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I. General Experimental Methods

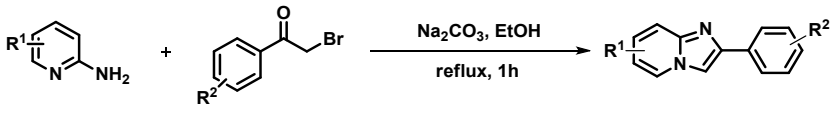
Glassware was dried in an oven (120 °C), heated under reduced pressure, and cooled in a desiccator before use. Materials obtained from commercial suppliers were used without further purification. Reactions were monitored by thin-layer chromatography on silica gel plates using UV-light for visualization. All compounds were purified using silica gel (0.035-0.070 mm, 60 Å) flash chromatography using hexanes and ethyl acetate as eluent. Evaporation of solvents was conducted under reduced pressure at 50 °C. FTIR spectra were recorded neat on a Perkin-Elmer Spectrum 65. NMR spectra were recorded on an Agilent 400 NMR spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C). Deuterated chloroform and deuterated dimethyl sulfoxide were used as solvents, and spectra were calibrated against the residual solvent peak or TMS. Chemical shifts (δ) and coupling constants (*J*) are given in ppm (parts per million) and Hz (Hertz). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet. Purity of final compounds was assessed using a Thermo Finnigan LCQ Deca with Thermo Surveyor LCMS System at variable wavelengths of 254 nm and 214 nm and final compound purity was >95%.

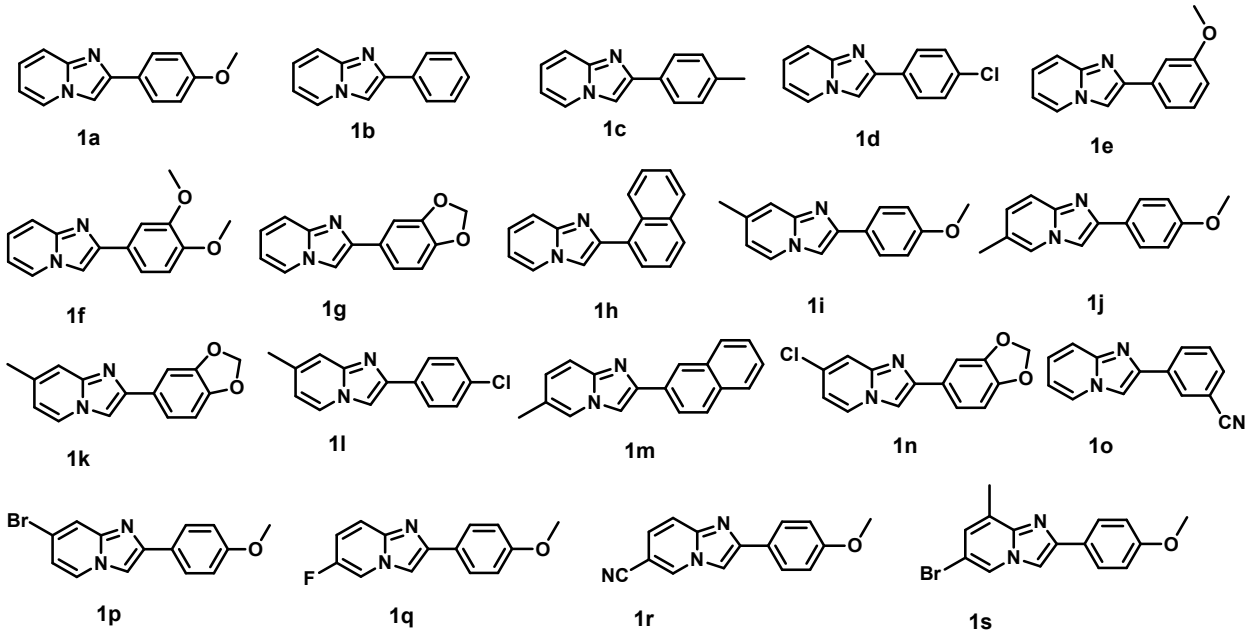
II. General experimental procedure and data for the synthesis of imidazo[1,2-*a*]pyridine starting material

IIA. General experimental procedure for synthesis of imidazo(1,2-*a*)pyridine derivatives (1a-1s):[1]

Imidazo[1,2-*a*]pyridines (**1a-1s**, fig.1) were synthesized by condensation of substituted 2-aminopyridines (1.0 mmol) with various acetophenone-2-bromides (1.0 mmol) in ethanol at reflux for 1 h in the presence of Na_2CO_3 (1.0 mmol). Upon cooling, the ethanol was evaporated under reduced pressure and the crude reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was dried over sodium sulfate and the dichloromethane was removed under reduced pressure. The crude product was used directly in the next step without further purification.

Supplemental Figure 1:

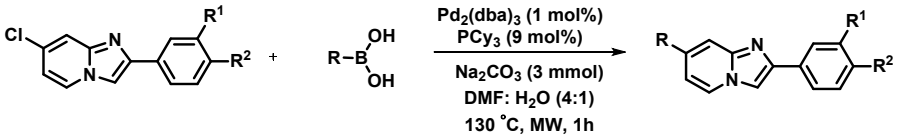


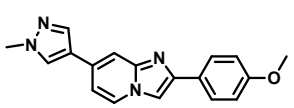


IIB. General experimental procedure for synthesis of imidazo[1,2-*a*]pyridine derivatives (1t-1w):

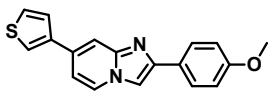
A 20 mL oven dried microwave vial was charged with 7-chloro-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (1.0 mmol), corresponding boronic acid/pinacol ester (1.5 mmol), sodium carbonate (3.0 mmol) and DMF:H_2O (4:1) 15 ml. The reaction mixture was vigorously degassed with nitrogen for ten minutes. Following, 3.0 mol% of $Pd_2(dba)_3$ and 9.0 mol% of tricyclohexylphosphine was added and the reaction was irradiated (Biotage 400 MW) at 130 °C for 1h. Reaction progress was monitored with TLC and, after completion, the reaction was filtered through Celite® and washed with DMF. The solvent was evaporated under reduced pressure and the crude reaction mixture was purified via column chromatography using dichloromethane and methanol as eluents.

Supplemental Figure 2:

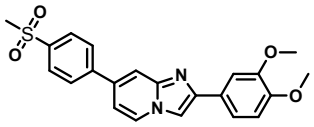




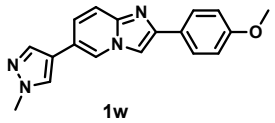
1t



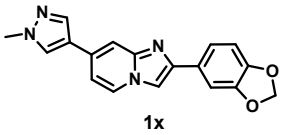
1u



1v

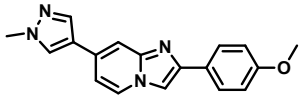


1w



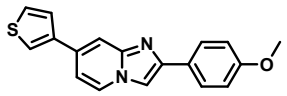
1x

2-(4-methoxyphenyl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine (1t):



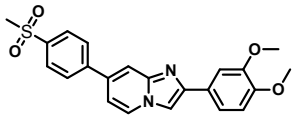
Compound **1t** was synthesized by following the general procedure for IIB with 7-chloro-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (500 mg , 1.93 mmol) and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (603 mg, 2.90 mmol); Yield: 353 mg (60%), White solid, mp = 248-250 °C; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.41 (d, *J* = 7.1 Hz, 1H), 8.25 (s, 1H), 8.15 (s, 1H), 8.00 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.73 (s, 1H), 7.09 (dd, *J* = 7.0, 1.7 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 159.37, 145.81, 145.17, 136.92, 129.63, 128.91, 127.20, 127.07, 127.04, 120.83, 114.52, 111.10, 110.14, 108.05, 55.54, 40.57, 40.36, 40.15, 39.20; FTIR (neat): 2944, 1612, 1481, 1374, 1241, 1172, 1029, 919, 851, 781, 742, 643 cm-1; LC-MS (ESI): *m/z* 305.2710 $(M+H)^{+}$.

2-(4-methoxyphenyl)-7-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (**1u**):



Compound **1u** was synthesized by following the general procedure for IIB with 7-chloro-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (500 mg , 1.93 mmol) and thiophen-3-ylboronic acid (371 mg, 2.90 mmol); Yield: 300 mg (51%), Pale white solid, mp = 236-238 °C; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.51 (d, *J* = 7.1 Hz, 1H), 8.26 (s, 1H), 8.09 (s, 1H), 7.95 (s, 1H), 7.90 (d, *J* = 8.7 Hz, 2H), 7.75 (d, *J* = 5.0 Hz, 1H), 7.68 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.32 (dd, *J* = 7.1, 1.4 Hz, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 159.45, 145.64, 145.59, 139.98, 131.70, 127.87, 127.25, 127.03, 126.95, 126.45, 122.66, 114.57, 112.14, 111.49, 108.36, 55.56; FTIR (neat): 3094, 2939, 1610, 1482, 1372, 1239, 1078, 839, 773, 713, 645, 601 cm^{-1}; LC-MS (ESI): *m/z* 307.2392 $(M+H)^{+}$.

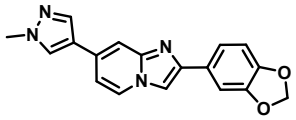
2-(3,4-dimethoxyphenyl)-7-(4-(methylsulfonyl)phenyl)imidazo[1,2-*a*]pyridine (**1v**):



Compound **1v** was synthesized by following the general procedure for IIB with 7-chloro-2-(3,4-dimethoxyphenyl)imidazo[1,2-*a*]pyridine (500 mg , 1.93 mmol) and (4-(methylsulfonyl)phenyl)boronic acid (520 mg, 2.90 mmol); Yield: 389 mg (55%), Pale green solid, mp = 223-225 °C; ^{1}H NMR

(400 MHz, DMSO-*d6*): δ 8.60 (dd, *J* = 7.1, 0.7 Hz, 1H), 8.40 (s, 1H), 8.10 – 8.01 (m, 5H), 7.60 (d, *J* = 1.9 Hz, 1H), 7.53 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.32 (dd, *J* = 7.1, 1.9 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.28(s, 3H); ^{13}C NMR (101 MHz, DMSO-*d6*): δ 149.37, 149.22, 146.33, 145.26, 143.33, 140.41, 134.49, 128.62, 128.16, 128.10, 127.76, 127.35, 126.96, 118.51, 114.43, 112.41, 111.54, 109.59, 109.05, 55.96, 55.88, 43.94; FTIR (neat): 2919, 1588, 1484, 1328, 1238, 1144, 1024, 774, 740, 670 cm^{-1}; LC-MS (ESI): *m/z* 409.2536 $(M+H)^+$.

2-(benzo[*d*][1,3]dioxol-5-yl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine (**1x**):

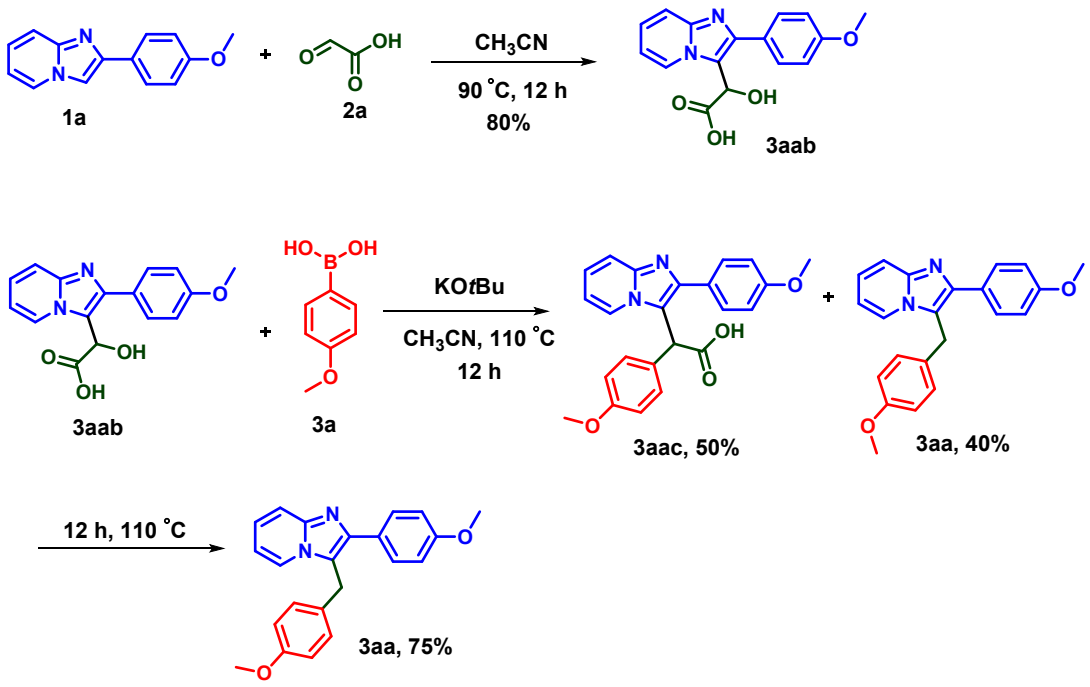


Compound **1x** was synthesized by following the general procedure for IIB with 2-(benzo[*d*][1,3]dioxol-5-yl)-7-chloroimidazo[1,2-*a*]pyridine (500 mg , 1.93 mmol) and 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrole (380 mg, 2.90 mmol); Yield: 350 mg (60%), Pale white solid, mp = 235-237 °C; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.45 (d, *J* = 7.1 Hz, 1H), 8.29 (s, 1H), 8.21 (s, 1H), 8.04 (s, 1H), 7.75 (s, 1H), 7.50 – 7.47 (m, 2H), 7.13 (dd, *J* = 7.1, 1.7 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.05 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 148.09, 147.29, 145.65, 144.91, 136.95, 136.31, 129.87, 128.97, 128.63, 127.17, 127.13, 120.76, 119.58, 111.27, 110.05, 108.99, 108.50, 106.26, 101.45, 39.20; FTIR (neat): 2955, 1611, 1500, 1354, 1244, 1172, 1029, 904, 750, 732, 576 cm^{-1}; LC-MS (ESI): *m/z* 319.2899 $(M+H)^+$.

III. Control experiments to elucidate the arylomethylation reaction mechanism

After extensive analysis of the substrate scope, we completed control experiments to determine the reaction mechanism for arylomethylation of imidazo[1,2-*a*]pyridine (Supplemental Scheme 1). To complete this, we isolated intermediates from the reaction mixture. Based on our reaction optimization conditions, we performed the reaction with 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) 1mmol, 2-oxoacetic acid (glyoxylic acid) 1.5 mmol and 1.5 mmol of (4-methoxyphenyl)boronic acid in DMF at 110 °C for 24 h and identified 3 products based on LCMS analysis, which had molecular weights that corresponded to **3aa**, **3aab**, and **3aac**. At this stage, to better understanding the reaction pathway, we slightly modified reaction conditions and performed control experiments as shown in Supplemental Scheme 1. Initially, we conducted a reaction with 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) 1mmol and glyoxylic acid (**2a**) 1.5 mmol in acetonitrile without any base at 110 °C for 12 h. Reaction progress was monitored with LCMS and we identified intermediate **3aab,** along with unknown by-products, so the reaction was conducted at a lower temperature. At 90 °C for 12 hours, we identified clean conversion to intermediate **3aab** through LCMS analysis. We then isolated intermediate **3aab** and added (4-methoxyphenyl) boronic acid 1.5 mmol and 1.0 mmol KO*t*Bu in acetonitrile and heated the reaction to 110 °C for 12 h. After, we identified intermediate **3aac** and the decarboxylated product **3aa**. The reaction was heated for an additional 12 h, which resulted in complete conversion of intermediate **3aac** to the decarboxylated product **3aa**. These experiments clearly support the proposed reaction mechanism for the arylomethylation of imidazo[1,2-*a*]pyridines.

Supplemental Scheme 1: Control experiments with key intermediates



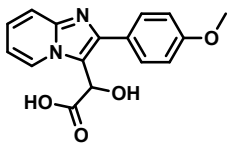
IV. General Procedure and experimental data of intermediates and final compounds

IVA. General procedure for the arylomethylation of imidazo(1,2-*a*)pyridine derivatives:

An oven dried 2-5 mL microwave reaction vial was charged with 0.45 mmol (1.0 equiv.) of respective imidazo(1,2-*a*)pyridine (**1a-1t**), 0.67 mmol (1.5 equiv.) of glyoxylic acid (**2a**), 0.67 mmol (1.5 equiv.) of respective boronic acid (**3a-3q**), 0.45 mmol (1.0 equiv.) of KO*t*Bu and 4 mL of CH_3CN. The reaction mixture was tightly sealed and heated to 110 °C for 24 h and was monitored through LCMS. After completion, the solvent was evaporated under reduced pressure, diluted with dichloromethane (50 mL), washed with water (2 x 25.0 mL), brine (25.0 mL), and then dried with $MgSO_4$. Evaporation of the solvent under reduced pressure provided the crude product, which was purified by column chromatography (hexane/EtOAc 4:1) to afford the final product.

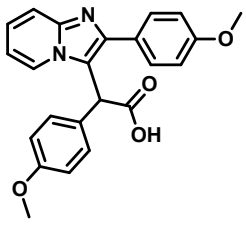
IVB. Experimental data:

2-hydroxy-2-(2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)acetic acid (3aab):



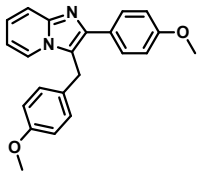
Pale brown semi solid; Yield: 75%; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.99 (s, 1H), 8.79 (t, *J* = 7.0 Hz, 1H), 7.92 (d, *J* = 8.9 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 3H), 7.43 (t, *J* = 6.8 Hz, 1H), 7.17 (d, *J* = 8.8 Hz, 2H), 5.71 (s, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 172.53, 171.78, 160.92, 140.99, 131.67, 130.83, 128.13, 119.27, 116.33, 115.04, 113.86, 87.18, 64.23, 55.85; LC-MS (ESI): *m/z* 299.2531 $(M+H)^+$.

2-(4-methoxyphenyl)-2-(2-(4-methoxyphenyl)imidazo[1,2- *a*]pyridin-3-yl)acetic acid (3aac):



Pale white semi solid; Yield; 50 % ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.9 Hz, 1H), 7.70 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.24 – 7.17 (m, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.2 Hz, 4H), 6.63 (t, *J* = 6.9 Hz, 1H), 5.60 (s, 1H), 3.73 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.98, 159.97, 158.54, 142.16, 139.48, 130.38, 128.87, 127.92, 127.84, 127.20, 122.16, 119.06, 114.49, 114.14, 114.09, 113.22, 55.21, 55.17, 48.26; LC-MS (ESI): *m/z* 389.1750 $(M+H)^+$.

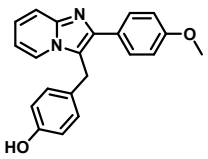
(3-(4-methoxybenzyl)-2-(4-methoxyphenyl)imidazo[1,2- *a*]pyridine) (3aa):[2]



Compound **3ac** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2- *a*]pyridine **(1a)** (100 mg 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (102 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 115 mg, (75%) ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.63 (m, 4H), 7.15 (dd, *J* = 8.4, 7.4 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 2H), 6.69 (t, *J* = 6.8 Hz, 1H), 4.39 (s, 2H), 3.82 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.32, 158.49, 144.66, 143.66, 129.34, 128.63, 128.59, 126.95,

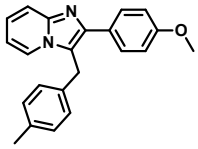
124.04, 123.31, 117.36, 117.18, 114.65, 114.38, 114.08, 112.05, 55.24, 28.98; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{20}N_2O_2$ 345.16030, found 345.15970

4-((2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)phenol (**3ab**):



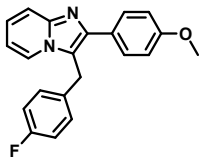
Compound **3ab** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) (100 mg 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol) and (4-hydroxyphenyl)boronic acid (**3b**) (92 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as white solid, Yiled: 88 mg, (60%); mp = 68-70 °C; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 9.28 (s, 1H), 8.09 (d, *J* = 6.9 Hz, 1H), 7.71 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 9.0 Hz, 1H), 7.27 – 7.19 (m, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.92 – 6.81 (m, 3H), 6.67 (d, *J* = 8.4 Hz, 2H), 4.40 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (1000 MHz, DMSO-*d6*): δ 163.91, 161.17, 148.86, 147.20, 133.89, 133.66, 132.41, 132.30, 129.27, 129.23, 123.20, 121.74, 120.76, 119.25, 117.06, 60.29, 33.08; FTIR (neat): 2898, 2592, 1500, 1426, 1362, 1244, 1168, 1027, 831, 761, 742, 636, 517 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{19}N_2O_2$ 331.14465, found 331.14401.

2-(4-methoxyphenyl)-3-(4-methylbenzyl)imidazo[1,2-*a*]pyridine (**3ac**):[2]



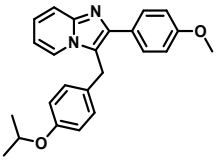
Compound 3ac was prepared by following the general procedure for the arylo-methylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) (100 mg 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol), p-tolylboronic acid (**3c**) (91 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale white solid, Yield: 95 mg, (65%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 – 7.62 (m, 4H), 7.19 – 7.13 (m, 1H), 7.11 (d, *J* = 7.9 Hz, 2H), 7.03 (d, *J* = 7.9 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.69 (t, *J* = 6.7 Hz, 1H), 4.43 (s, 2H), 3.83 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.29, 144.69, 143.84, 136.45, 133.67, 129.66, 129.33, 127.54, 127.08, 123.92, 123.30, 117.27, 117.17, 114.05, 111.98, 55.26, 29.47, 20.99; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{21}N_2O$ 329.16539, found 329.16476.

3-(4-fluorobenzyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3ad**):[2]



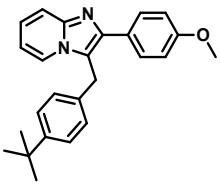
Compound **3ad** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) (100 mg 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol), (4-fluorophenyl)boronic acid (**3d**) (94 mg 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 82 mg (55%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.66 (m, 4H), 7.22 – 7.15 (m, 1H), 7.09 (dd, *J* = 8.2, 5.6 Hz, 2H), 6.99 (t, *J* = 9.2 Hz, 4H), 6.72 (t, *J* = 6.8 Hz, 1H), 4.44 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.99, 160.55, 159.38, 144.75, 143.96, 132.41, 132.38, 129.31, 129.13, 129.05, 126.85, 124.13, 123.10, 117.37, 116.73, 115.97, 115.76, 114.11, 112.17, 55.27, 29.11; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{18}FN_2O$ 333.14032, found 333.13922.

3-(4-isopropoxybenzyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3ae**):



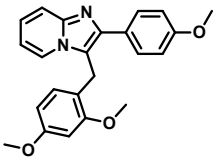
Compound **3ae** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-isopropoxyphenyl)boronic acid (**3e**) (120 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale brown semi solid, Yield: 133 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 – 7.63 (m, 4H), 7.15 (dd, *J* = 8.3, 7.5 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.68 (t, *J* = 6.8 Hz, 1H), 4.48 (dq, *J* = 12.1, 6.0 Hz, 1H), 4.39 (s, 2H), 3.83 (s, 3H), 1.31 (d, *J* = 6.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.28, 156.77, 144.67, 143.73, 129.33, 128.64, 128.38, 127.09, 123.92, 123.35, 117.37, 117.23, 116.25, 114.05, 111.95, 69.84, 55.26, 29.01, 22.02; FTIR (neat): 2974, 1610, 1501, 1356, 1240, 1171, 1105, 1028, 834, 749, 729 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_2$ 373.19160, found 373.19107.

3-(4-(tert-butyl)benzyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3af**):



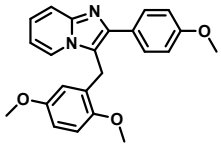
Compound **3af** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-(tert-butyl)phenyl)boronic acid (**3f**) (119 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow semi solid, Yield: 127 mg (77%) ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 – 7.63 (m, 4H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.18 – 7.11 (m, 1H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.68 (t, *J* = 6.8 Hz, 1H), 4.42 (s, 2H), 3.82 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.28, 149.72, 144.68, 143.81, 133.70, 129.34, 127.32, 127.10, 125.87, 123.92, 123.38, 117.22, 114.06, 111.97, 55.26, 34.42, 31.32, 29.36; FTIR (neat): 2959, 1501, 1245, 1172, 1030, 834, 749, 729, 557, 547, 529 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{25}H_{27}N_2O$ 371.21234, found 371.21179.

3-(2,4-dimethoxybenzyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3ag**):



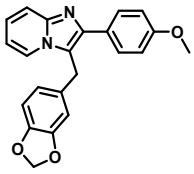
Compound **3ag** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (2,4-dimethoxyphenyl)boronic acid (**3g**) (122 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as brown semi solid, Yield: 134 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 – 7.68 (m, 3H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.19 – 7.12 (m, 1H), 6.95 (d, *J* = 8.6 Hz, 2H), 6.70 (t, *J* = 6.8 Hz, 1H), 6.55 (dd, *J* = 11.0, 5.3 Hz, 2H), 6.28 (dd, *J* = 8.4, 2.2 Hz, 1H), 4.31 (s, 2H), 3.89 (s, 3H), 3.83 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.81, 159.21, 158.22, 144.56, 143.62, 129.28, 128.26, 127.06, 123.89, 123.41, 117.23, 117.11, 117.03, 114.00, 111.94, 103.89, 98.65, 55.36, 55.32, 55.24, 23.35; FTIR (neat): 2932, 1958, 1503, 1455, 1357, 1246, 1206, 1155, 1114, 1026, 833, 751, 734, 506 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}N_2O_3$ 375.17087, found 375.17007.

3-(2,5-dimethoxybenzyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3ah**):



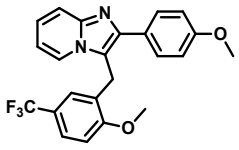
Compound **3ac** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (2,5-dimethoxyphenyl)boronic acid (**3h**) (122 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 125 mg (75%); mp = 121-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.6 Hz, 3H), 7.65 (dd, *J* = 9.1, 0.8 Hz, 1H), 7.18 – 7.11 (m, 1H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.76 – 6.66 (m, 2H), 6.29 (d, *J* = 2.9 Hz, 1H), 4.38 (s, 2H), 3.87 (s, 3H), 3.82 (d, *J* = 0.7 Hz, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.20, 153.77, 151.54, 144.72, 144.04, 129.30, 127.23, 126.33, 123.83, 123.35, 117.22, 116.77, 114.83, 114.00, 111.92, 111.39, 110.97, 55.84, 55.51, 55.24, 24.00. FTIR (neat): 2934, 1492, 1356, 1243, 1220, 1173, 1107, 1025, 834, 811, 759, 732, 719, 703, 581, 516 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}N_2O_3$ 375.17087, found 375.17001.

3-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3ai**):



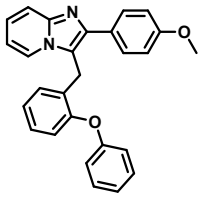
Compound **3ac** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** 3,4-(methylenedioxy)phenylboronic acid (**3i**) (111 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale white solid, Yield: 128 mg (80%); mp = 134-136 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.68 (m, 3H), 7.65 (d, *J* = 9.0 Hz, 1H), 7.20 – 7.13 (m, 1H), 6.98 (t, *J* = 5.7 Hz, 2H), 6.76 – 6.67 (m, 2H), 6.63 – 6.56 (m, 2H), 5.92 (s, 2H), 4.37 (s, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.31, 148.24, 146.48, 144.74, 143.92, 130.55, 129.32, 127.04, 123.96, 123.26, 120.47, 117.33, 117.03, 114.07, 112.02, 108.60, 108.09, 101.04, 55.27, 29.56; FTIR (neat): 2878, 1710, 1540, 1450, 1310, 1226, 1206, 1160, 1025, 750, 535 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{19}N_2O_3$ 359.13957, found 359.13882.

(3-(2-methoxy-5-(trifluoromethyl)benzyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3aj**):



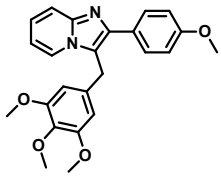
Compound **3aj** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (2-methoxy-5-(trifluoromethyl)phenyl)boronic acid (**3j**) (147 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 120 mg (65%); mp = 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 – 7.62 (m, 4H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.24 – 7.17 (m, 1H), 7.02 – 6.91 (m, 4H), 6.75 (t, *J* = 7.1 Hz, 1H), 4.40 (s, 2H), 3.95 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.73, 159.34, 129.33, 126.00, 125.62, 125.59, 125.55, 125.51, 125.00, 124.96, 124.92, 124.89, 124.11, 123.03, 117.44, 115.73, 114.05, 112.19, 109.96, 55.69, 55.26, 24.15; FTIR (neat): 2923, 1613, 1495, 1423, 1354, 1311, 1173, 1159, 896, 751,744, 623, 576, 521 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{20}F3N_2O_2$ 413.14762, found 413.14700.

(2-(4-methoxyphenyl)-3-(2-phenoxybenzyl)imidazo[1,2-*a*]pyridine (**3ak**):



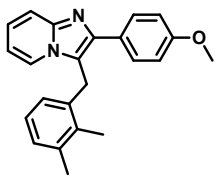
Compound **3ac** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (2-phenoxyphenyl)boronic acid (**3k**) (143 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow semi solid, Yield: 127 mg (70%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 6.9 Hz, 1H), 7.68 (t, *J* = 8.7 Hz, 3H), 7.35 (t, *J* = 7.9 Hz, 2H), 7.24 – 7.14 (m, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.04 – 6.92 (m, 6H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.73 (t, *J* = 6.8 Hz, 1H), 4.45 (s, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.28, 157.31, 154.39, 144.68, 131.15, 129.85, 129.29, 128.83, 128.32, 128.25, 126.93, 124.40, 124.00, 123.22, 123.04, 119.64, 117.59, 117.26, 116.45, 114.38, 114.04, 112.49, 112.09, 55.26, 24.04; FTIR (neat): 2924, 1633, 1501, 1481, 1451, 1356, 1229, 1172, 1028, 874, 747, 730, 690, 520 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{27}H_{23}N_2O_2$ 407.17595, found 407.17523.

(2-(4-methoxyphenyl)-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**3al**):



Compound **3al** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (142 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow semi solid, Yield: 148 mg (82%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (t, *J* = 7.9 Hz, 3H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.18 (dd, *J* = 8.3, 7.5 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.73 (t, *J* = 6.8 Hz, 1H), 6.34 (s, 2H), 4.40 (s, 2H), 3.83 (d, *J* = 2.6 Hz, 6H), 3.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.36, 153.66, 144.76, 144.03, 136.75, 132.56, 129.26, 126.97, 124.12, 123.34, 117.22, 116.76, 114.11, 112.09, 104.40, 60.80, 56.07, 55.25, 30.10; FTIR (neat): 2935, 1588, 1500, 1419, 1329, 1234, 1120, 1004, 835, 751, 729 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_4$ 405.18143, found 405.18109.

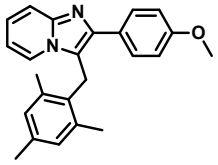
(3-(2, 3-dimethylbenzyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3am**):



Compound **3am** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (2,3-dimethylphenyl)boronic acid (**3m**) (100 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale white solid, Yield: 95 mg (62%); mp = 163-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 9.0 Hz, 1H), 7.64 (d, *J* = 8.7 Hz, 2H), 7.21 – 7.15 (m, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 3H), 6.70 (t, *J* = 6.6 Hz, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 4.35 (s, 2H), 3.82 (s, 3H), 2.38 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.27, 144.77, 144.11, 137.18, 134.80, 134.42, 131.15, 129.28, 128.70, 127.04, 125.94, 124.49, 123.93, 123.27, 117.27, 116.98,

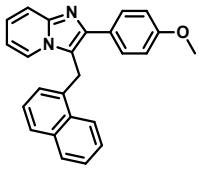
114.06, 112.04, 55.25, 28.30, 20.67, 15.13; FTIR (neat): 2928, 1630, 1499, 1413, 1362, 1259, 1238, 1176, 1028, 855, 774, 751, 739, 634, 555 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}N_2O$ 343.18104, found 343.18063.

2-(4-methoxyphenyl)-3-(2, 4, 6-trimethylbenzyl)imidazo[1,2-*a*]pyridine (**3an**):



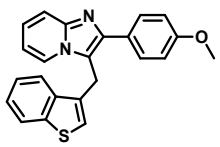
Compound **3an** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** mesitylboronic acid (**3n**) (110 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale brown semi solid, Yield: 116 mg (73%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 9.0 Hz, 1H), 7.45 (d, *J* = 7.0 Hz, 1H), 7.08 – 7.04 (m, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.79 (s, 2H), 6.56 (t, *J* = 6.8 Hz, 1H), 4.45 (s, 2H), 3.86 (s, 3H), 2.23 (s, 3H), 2.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.09, 144.19, 136.81, 136.24, 130.07, 129.69, 129.60, 128.28, 127.31, 123.63, 123.25, 117.66, 117.24, 113.77, 111.85, 77.30, 76.98, 76.66, 55.26, 25.41, 22.40, 21.14, 20.75, 20.55; FTIR (neat): 2917, 1607, 1500, 1431, 1245, 1172, 1028, 834, 749, 732, 558 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{25}N_2O$ 357.19669, found 357.19617.

2-(4-methoxyphenyl)-3-(naphthalen-1-ylmethyl)imidazo[1,2-*a*]pyridine (**3ao**):[3]



Compound **3ao** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1a)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** naphthalen-1-ylboronic acid (**3o**) (115 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 111 mg (68)%; mp = 168-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.1 Hz, 1H), 7.96 – 7.91 (m, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.71 (d, *J* = 9.0 Hz, 1H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.63 – 7.53 (m, 3H), 7.26 (dd, *J* = 11.1, 4.1 Hz, 1H), 7.20 – 7.14 (m, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 7.1 Hz, 1H), 6.63 (t, *J* = 6.8 Hz, 1H), 4.81 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.34, 144.98, 144.43, 133.98, 131.86, 131.85, 129.23, 128.99, 127.66, 126.95, 126.47, 126.01, 125.81, 124.25, 124.06, 123.29, 122.99, 117.33, 116.22, 114.12, 112.12, 55.23, 27.25; FTIR (neat): 3033, 1613, 1596, 1522, 1503, 1420, 1355, 1245, 1174, 832, 787, 748, 736, 729, 523 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{25}H_{21}N_2O$ 365.16539, found 365.16467.

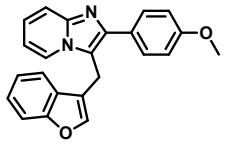
3-(benzo[*b*]thiophen-3-ylmethyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3ap**):



Compound **3ap** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** benzo[*b*]thiophen-3-ylboronic acid (**3p**) (119 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 99 mg, (60%); mp = 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.5 Hz, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.70 (dd, *J* = 9.1, 2.9 Hz, 4H), 7.48 – 7.41 (m, 2H), 7.21 – 7.17 (m, 1H), 6.94 (d, *J* = 8.3 Hz, 2H),

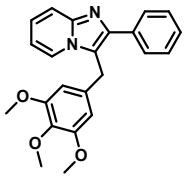
6.75 (s, 1H), 6.71 (t, J = 6.8 Hz, 1H), 4.56 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.38, 144.91, 143.87, 141.09, 138.22, 131.06, 129.31, 126.89, 124.76, 124.31, 124.08, 123.29, 123.11, 122.78, 121.39, 117.41, 115.92, 114.16, 112.16, 55.26, 24.14; FTIR (neat): 3101, 2923, 1611, 1562, 1401, 1361, 1269, 1243, 1170, 1103, 1019, 839, 783, 748, 730, 636 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}N_2OS$ 371.12181, found 345.371.12061.

3-(benzofuran-3-ylmethyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**3aq**):



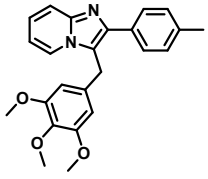
Compound **3aq** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (**1a**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol), benzofuran-3-ylboronic acid (**3q**) (108 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 103 mg (65%); mp = 143-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 6.8 Hz, 1H), 7.77 (d, J = 8.6 Hz, 2H), 7.68 (d, J = 9.1 Hz, 1H), 7.45 (dd, J = 7.7, 3.5 Hz, 2H), 7.27 – 7.17 (m, 3H), 7.00 (d, J = 8.6 Hz, 2H), 6.79 (t, J = 6.8 Hz, 1H), 6.34 (s, 1H), 4.53 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.47, 155.05, 153.90, 144.90, 144.15, 129.56, 128.39, 126.70, 124.24, 123.93, 123.27, 122.85, 120.62, 117.44, 114.14, 113.99, 112.26, 111.02, 103.66, 77.32, 77.00, 76.68, 55.28, 24.30; FTIR (neat): 2917, 1634, 1614, 1500, 1451, 1362, 1246, 1173, 1106, 1034, 825, 746, 733, 629 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}N_2O_2$ 355.14465, found 355.14386.

2-phenyl-3-(3, 4, 5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**3ar**):



Compound **3ar** was prepared by following the general procedure for the arylomethylation of IIIA from 2-phenylimidazo[1,2-*a*]pyridine (**1b**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (164 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 135 mg (70%); mp = 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 7.6 Hz, 2H), 7.74 (d, J = 6.8 Hz, 1H), 7.69 (d, J = 9.1 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 7.22 – 7.18 (m, 1H), 6.75 (t, J = 6.8 Hz, 1H), 6.35 (s, 2H), 4.43 (s, 2H), 3.83 (s, 3H), 3.72 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$): δ 153.69, 144.89, 144.24, 136.81, 134.47, 132.47, 128.66, 128.11, 127.76, 124.26, 123.47, 117.51, 117.47, 112.21, 104.44, 60.82, 56.09, 30.11; FTIR (neat): 2939, 2838, 1589, 1504, 1447, 1353, 1238, 1114, 1014, 750, 702, 693 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}N_2O_3$ 375.17087, found 375.17004.

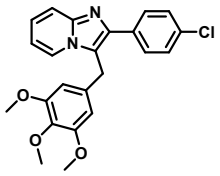
2-(*p*-tolyl)-3-(3, 4, 5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**3as**):



Compound **3as** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(*p*-tolyl)imidazo[1,2-*a*]pyridine (**1c**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (153 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 140 mg (75%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.67 (m, 4H), 7.27 (d, J

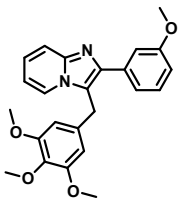
= 2.4 Hz, 2H), 7.22 – 7.18 (m, 1H), 6.75 (t, *J* = 6.7 Hz, 1H), 6.35 (s, 2H), 4.43 (s, 2H), 3.83 (s, 3H), 3.72 (s, 6H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.68, 144.84, 144.30, 137.58, 136.76, 132.58, 131.51, 129.39, 127.98, 124.17, 123.40, 117.42, 117.16, 112.14, 104.42, 77.31, 76.99, 76.68, 60.84, 56.09, 30.18, 21.25; FTIR (neat): 3021, 2765, 1450, 1314, 1245, 1140, 1026, 750, 726, 686 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_3$ 389.18652, found 389.18570.

2-(4-chlorophenyl)-3-(3, 4, 5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**3at**):



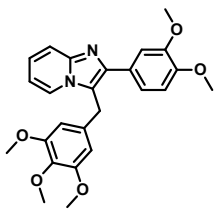
Compound **3at** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-chlorophenyl)imidazo[1,2-*a*]pyridine **(1d)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (139 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 107mg (60%); mp = 106-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.6 Hz, 3H), 7.69 (d, *J* = 9.1 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.25 – 7.21 (m, 1H), 6.78 (t, *J* = 6.8 Hz, 1H), 6.32 (s, 2H), 4.41 (s, 2H), 3.83 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.77, 144.92, 143.05, 136.94, 133.77, 132.90, 132.12, 129.29, 128.88, 124.60, 123.48, 117.60, 117.53, 112.45, 104.38, 60.84, 56.12, 30.08; FTIR (neat): 2930, 2836, 1504, 1456, 1327, 1234, 1122, 1094, 1009, 832, 750, 736, 693 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{22}ClN_2O_3$ 409.13190, found 409.13089.

2-(3-methoxyphenyl)-3-(3, 4, 5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**3au**):



Compound **3au** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(3-methoxyphenyl)imidazo[1,2-*a*]pyridine **(1e)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (142 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale brown semi solid, Yield: 114 mg (63%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 6.7 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.40 (d, *J* = 0.7 Hz, 1H), 7.35 (t, *J* = 5.4 Hz, 2H), 7.20 (dd, *J* = 8.3, 7.4 Hz, 1H), 6.92 (dt, *J* = 5.4, 2.5 Hz, 1H), 6.76 (t, *J* = 6.8 Hz, 1H), 6.34 (s, 2H), 4.44 (s, 2H), 3.82 (s, 6H), 3.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.87, 153.68, 144.79, 144.04, 136.80, 135.78, 132.47, 129.63, 124.33, 123.45, 120.43, 117.67, 117.49, 113.97, 113.23, 112.29, 104.44, 77.36, 77.04, 76.72, 60.82, 56.08, 55.27, 30.12; FTIR (neat): 2936, 1503, 1455, 1357, 1329, 1230, 1120, 1038, 1003, 782, 750, 732, 692 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_4$ 405.18143, found 405.18057.

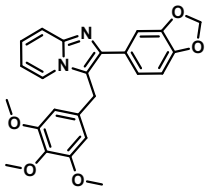
2-(3,4-dimethoxyphenyl)-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**3av**):



Compound **3av** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(3,4-dimethoxyphenyl)imidazo[1,2-*a*]pyridine **(1f)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (125 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as orange semi solid, Yield: 137 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* =

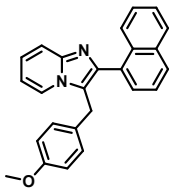
6.8 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.44 (s, 1H), 7.31 – 7.25 (m, 1H), 7.24 – 7.17 (m, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 6.76 (t, *J* = 6.8 Hz, 1H), 6.35 (s, 2H), 4.43 (s, 2H), 3.91 (d, *J* = 5.8 Hz, 6H), 3.83 (s, 3H), 3.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.69, 149.15, 148.84, 144.75, 144.14, 136.79, 132.62, 127.28, 124.20, 123.28, 120.18, 117.29, 116.94, 112.20, 111.42, 111.13, 104.39, 60.82, 56.09, 55.88, 55.86, 30.16; FTIR (neat): 2934, 1587, 1502, 1455, 1355, 1243, 1120, 1023, 814, 750, 728, 643 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{25}H_{27}N_2O_5$ 435.19200, found 435.19080.

2-(benzo[*d*][1,3]dioxol-5-yl)-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**3aw**):



Compound **3aw** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(benzo[*d*][1,3]dioxol-5-yl)imidazo[1,2-*a*]pyridine **(1g)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (133 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as a brown solid, Yield: 126 mg (72%); mp = 123-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 6.8 Hz, 1H), 7.65 (d, *J* = 9.1 Hz, 1H), 7.31 (s, 1H), 7.26 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.15 (m, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.74 (t, *J* = 6.8 Hz, 1H), 6.32 (s, 2H), 5.98 (s, 2H), 4.40 (s, 2H), 3.83 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.68, 147.93, 147.32, 144.67, 143.98, 136.79, 132.39, 128.53, 124.22, 123.37, 121.76, 117.28, 116.91, 112.16, 108.60, 108.51, 104.39, 101.07, 60.79, 56.07, 30.04; FTIR (neat): 2929, 1631, 1500, 1455, 1353, 1235, 1123, 1035, 934, 829, 817, 750, 738, 618 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{23}N_2O_5$ 419.16070, found 345.15964.

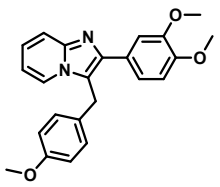
3-(4-methoxybenzyl)-2-(naphthalen-1-yl)imidazo[1,2-*a*]pyridine (**3ax**):



Compound **3ax** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(naphthalen-1-yl)imidazo[1,2-*a*]pyridine **(1h)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (93 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale brown solid, Yield: 112 mg (75%); mp = 82-85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.96 – 7.89 (m, 2H), 7.85 (dd, *J* = 6.1, 3.3 Hz, 2H), 7.76 – 7.72 (m, 2H), 7.47 (dd, *J* = 6.2, 3.2 Hz, 2H), 7.24 – 7.18 (m, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.74 (t, *J* = 6.8 Hz, 1H), 4.51 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.54, 144.87, 143.72, 133.49, 132.84, 131.86, 128.71, 128.54, 128.31, 128.23, 127.63, 127.07, 126.19, 126.11, 126.00, 124.30, 123.43, 118.50, 117.48, 114.44, 112.26, 55.26, 29.14; FTIR (neat): 2923, 2179, 1607, 1505, 1460, 1355, 1241, 1167, 1030, 819, 749, 721, 638 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{25}H_{21}N_2O$ 365.16539, found 365.16519.

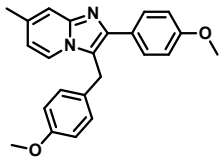
2-(3,4-dimethoxyphenyl)-3-(4-methoxybenzyl)imidazo[1,2-*a*]pyridine (**3ay**):

Compound **3ay** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(3,4-dimethoxyphenyl)imidazo[1,2-*a*]pyridine **(1f)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (90 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow semi solid, Yield:



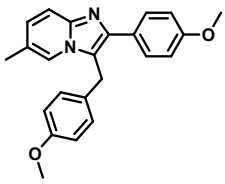
118 mg, (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 6.8 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.41 (s, 1H), 7.26 (dd, *J* = 7.3, 1.9 Hz, 2H), 7.22 – 7.15 (m, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.73 (t, *J* = 6.8 Hz, 1H), 4.43 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.50, 149.10, 148.78, 144.59, 143.72, 128.63, 128.59, 127.25, 124.11, 123.24, 120.25, 117.52, 117.26, 114.39, 112.16, 111.44, 111.09, 55.87, 55.85, 55.25, 29.03; FTIR (neat): 2930, 1608, 1506, 1462, 1355, 1242, 1224, 1137, 1022, 813, 749, 732, 641 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}N_2O_3$ 375.17087, found 375.17035.

3-(4-methoxybenzyl)-2-(4-methoxyphenyl)-7-methylimidazo[1,2-*a*]pyridine (**4a**):



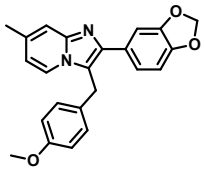
Compound **4a** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)-7-methylimidazo[1,2-*a*]pyridine **(1i**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (96 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale brown semi solid, Yield: 120 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.7 Hz, 2H), 7.56 (d, *J* = 9.1 Hz, 1H), 7.47 (s, 1H), 7.03 (dd, *J* = 14.9, 8.9 Hz, 3H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 4.37 (s, 2H), 3.83 (s, 3H), 3.78 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.18, 158.43, 143.78, 143.55, 129.18, 128.85, 128.62, 127.26, 127.06, 121.58, 120.87, 117.01, 116.62, 114.35, 114.01, 55.25, 55.24, 28.98, 18.38; FTIR (neat): 2926, 1610, 1501, 1460, 1387, 1298, 1242, 1172, 1028, 834, 797, 728, 640 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}N_2O_2$ 359.17595, found 359.17651.

3-(4-methoxybenzyl)-2-(4-methoxyphenyl)-6-methylimidazo[1,2-*a*]pyridine (**4b**):



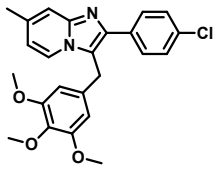
Compound **4b** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)-6-methylimidazo[1,2-*a*]pyridine **(1j**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (96 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 98 mg (65%); mp = 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.6 Hz, 2H), 7.60 (d, *J* = 9.1 Hz, 1H), 7.48 (s, 1H), 7.04 (t, *J* = 7.8 Hz, 3H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.37 (s, 2H), 3.83 (s, 3H), 3.79 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.26, 158.46, 143.58, 129.24, 128.73, 128.61, 127.37, 121.83, 120.90, 117.04, 116.49, 114.37, 114.04, 113.95, 113.53, 55.26, 55.25, 28.94, 18.39; FTIR (neat): 3255, 2927, 1675, 1607, 1506, 1461, 1243, 1174, 1027, 834, 799, 631 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}N_2O_2$ 359.17595, found 359.17551.

2-(benzo[*d*][1,3]dioxol-5-yl)-3-(4-methoxybenzyl)-7-methylimidazo[1,2-*a*]pyridine (**4c**):



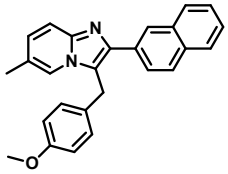
Compound **4c** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(benzo[*d*][1,3]dioxol-5-yl)-7-methylimidazo[1,2-*a*]pyridine **(1k)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (90 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 89 mg (60%); mp = 140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 7.0 Hz, 1H), 7.40 (s, 1H), 7.28 (s, 1H), 7.22 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.84 (dd, *J* = 11.7, 8.2 Hz, 3H), 6.52 (d, *J* = 7.0 Hz, 1H), 5.97 (d, *J* = 0.8 Hz, 2H), 4.36 (s, 2H), 3.77 (d, *J* = 0.6 Hz, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.45, 147.84, 147.14, 144.99, 143.25, 135.03, 128.75, 128.71, 128.60, 122.58, 121.73, 116.84, 115.71, 114.69, 114.36, 108.65, 108.44, 101.01, 55.24, 28.93, 21.29; FTIR (neat): 2915, 1609, 1503, 1445, 1242, 1232, 1177, 1027, 815, 775, 698, 601 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{23}H_{21}N_2O_3$ 373.15522, found 373.15720.

2-(4-chlorophenyl)-7-methyl-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**4d**):



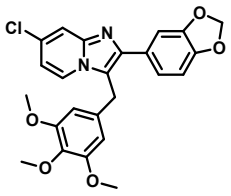
Compound **4d** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-chlorophenyl)-7-methylimidazo[1,2-*a*]pyridine **(1l)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (131 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 113 mg (65%); mp = 173-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 7.0 Hz, 1H), 7.42 – 7.39 (m, 3H), 6.59 (d, *J* = 7.0 Hz, 1H), 6.31 (s, 2H), 4.37 (s, 2H), 3.82 (s, 3H), 3.72 (s, 6H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.73, 145.37, 142.69, 136.86, 135.55, 133.55, 133.11, 132.39, 129.90, 129.20, 128.89, 128.81, 122.68, 116.96, 115.90, 115.05, 104.36, 60.84, 56.10, 30.07, 21.34; FTIR (neat): 2938, 1644, 1505, 1456, 1235, 1125, 1093, 834, 774, 730, 687, 637 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{24}ClN_2O_3$ 423.14755, found 423.14700.

3-(4-methoxybenzyl)-6-methyl-2-(naphthalen-2-yl)imidazo[1,2-*a*]pyridine (**4e**):



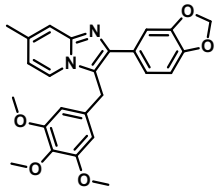
Compound **4e** was prepared by following the general procedure for the arylomethylation of IIIA from 6-methyl-2-(naphthalen-2-yl)imidazo[1,2-*a*]pyridine **(1m)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (88 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale red solid, Yield: 103 mg (70%); mp = 250-252 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.92 – 7.81 (m, 3H), 7.63 (d, *J* = 6.8 Hz, 1H), 7.46 (dd, *J* = 6.1, 3.1 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.99 (d, *J* = 6.8 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.65 (t, *J* = 6.8 Hz, 1H), 4.47 (s, 2H), 3.78 (s, 3H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.46, 145.34, 143.38, 133.50, 132.79, 132.26, 128.89, 128.73, 128.31, 128.16, 127.63, 127.47, 127.16, 126.52, 125.99, 125.85, 123.00, 121.29, 118.86, 114.37, 112.20, 55.25, 29.24, 17.21; FTIR (neat): 2920, 1608, 1380, 1359, 1030, 860, 816, 740 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{23}N_2O$ 379.18104, found 379.18048.

2-(benzo[*d*][1,3]dioxol-5-yl)-7-chloro-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**4f**)



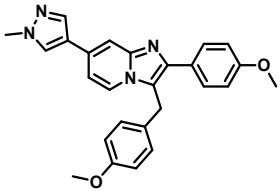
Compound **4f** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(benzo[*d*][1,3]dioxol-5-yl)-7-chloroimidazo[1,2-*a*]pyridine **(1n)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (117 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow semi solid, Yield: 120 mg (72%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (dd, *J* = 9.9, 4.4 Hz, 2H), 7.26 (dd, *J* = 12.7, 6.6 Hz, 3H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.73 (dd, *J* = 7.2, 2.0 Hz, 1H), 6.30 (s, 2H), 6.00 (s, 2H), 4.39 (s, 2H), 3.83 (s, 3H), 3.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.69, 149.15, 148.84, 144.75, 144.14, 136.79, 132.62, 127.28, 124.20, 123.28, 120.18, 117.29, 116.94, 112.20, 111.42, 111.13, 104.39, 60.82, 56.09, 55.88, 55.86, 30.16; FTIR (neat): 2950, 1645, 1550, 1470, 1240, 1222, 1155, 1035, 826, 742, 679 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{22}ClN_2O_5$ 453.12172, found 453.12165.

3-(benzo[*d*][1,3]dioxol-5-yl)-7-methyl-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**4g**):



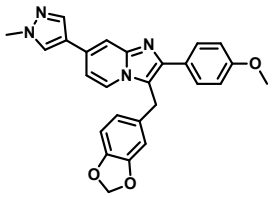
Compound **4g** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(benzo[*d*][1,3]dioxol-5-yl)-7-methylimidazo[1,2-*a*]pyridine **(1k)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (126 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 129 mg (75%); mp = 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 7.0 Hz, 1H), 7.40 (s, 1H), 7.29 (s, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.57 (d, *J* = 7.0 Hz, 1H), 6.32 (s, 2H), 5.99 (d, *J* = 0.5 Hz, 2H), 4.37 (s, 2H), 3.84 – 3.80 (m, 3H), 3.73 (s, 6H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.67, 147.89, 147.20, 145.14, 143.69, 136.76, 135.15, 132.66, 128.77, 122.61, 121.68, 116.25, 115.77, 114.76, 108.58, 108.49, 104.39, 101.04, 60.82, 56.09, 30.09, 21.31; FTIR (neat): 2925, 1646, 1592, 1452, 1225, 1125, 1037, 826, 777, 665, 579 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{25}H_{25}N_2O_5$ 433.17635, found 433.17542.

3-(4-methoxybenzyl)-2-(4-methoxyphenyl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine (**4h**):



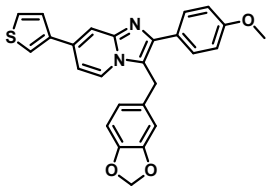
Compound **4h** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine **(1t)** (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (4-methoxyphenyl)boronic acid (**3a**) (74.9 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale white solid, Yield: 95 mg (68%) ; mp = 93-95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.74 – 7.68 (m, 3H), 7.63 (d, *J* = 7.9 Hz, 2H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.86 – 6.78 (m, 3H), 4.38 (s, 2H), 3.94 (s, 3H), 3.83 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.29, 158.48, 145.11, 143.98, 136.74, 129.22, 128.86, 128.68, 128.64, 127.23, 127.00, 123.32, 121.34, 117.18, 114.38, 114.07, 111.26, 111.01, 55.27, 55.25, 39.19, 28.97; FTIR (neat): 3234, 1611, 1507, 1387, 1266, 1244, 1031, 779, 609 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{25}N_4O_2$ 425.19775, found 425.19647.

3-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-(4-methoxyphenyl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine (**4i**):



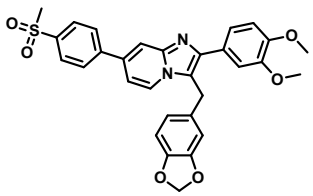
Compound **4i** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine **(1t**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** 3,4-(methylenedioxy)phenylboronic acid(**3i**) (82 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 94 mg (65%); mp = 113-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.72 (d, *J* = 8.8 Hz, 3H), 7.66 (d, *J* = 7.6 Hz, 2H), 6.98 (d, *J* = 8.7 Hz, 2H), 6.84 (dd, *J* = 7.1, 1.4 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.64 – 6.58 (m, 2H), 4.37 (s, 2H), 3.96 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.35, 148.27, 146.51, 145.12, 144.07, 136.78, 130.57, 129.24, 129.01, 127.22, 126.87, 123.30, 121.34, 120.49, 116.89, 114.09, 111.34, 111.12, 108.61, 108.10, 101.06, 55.28, 39.23, 29.55; FTIR (neat): 3243, 1645, 1485, 1244, 1171, 1033, 831, 780, 665, 637, 612 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{23}N_4O_3$ 439.17702, found 439.17599.

3-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-(4-methoxyphenyl)-7-(thiophen-3-yl)imidazo[1,2-*a*]pyridine (**4j**):



Compound **4k** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)-7-(thiophen-3-yl)imidazo[1,2-*a*]pyridine **(1u**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol), 3,4-(methylenedioxy)phenylboronic acid (**3i**) (81 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale brown solid, Yield: 86 mg (60%); mp = 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.71 (dd, *J* = 10.6, 7.8 Hz, 3H), 7.52 (s, 1H), 7.43 (q, *J* = 5.3 Hz, 2H), 6.99 (dd, *J* = 6.8, 4.8 Hz, 3H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.65 – 6.59 (m, 2H), 4.39 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.40, 148.29, 146.54, 145.02, 144.40, 140.05, 131.81, 130.51, 129.27, 126.88, 126.80, 125.74, 123.19, 121.26, 120.50, 117.10, 114.12, 112.94, 111.58, 108.63, 108.11, 101.07, 55.28, 29.58; FTIR (neat): 3220, 1630, 1435, 1226, 1156, 1022, 827, 745, 676 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{21}N_2O_3S$ 441.12729, found 441.12003.

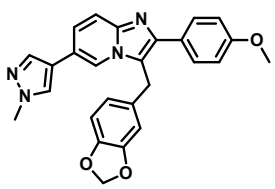
3-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-(3,4-dimethoxyphenyl)-7-(4-(methylsulfonyl)phenyl)imidazo[1,2-*a*]pyridine (**4k**):



Compound **4k** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(3,4-dimethoxyphenyl)-7-(4-(methylsulfonyl)phenyl)imidazo[1,2-*a*]pyridine **(1v**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** 3,4-(methylenedioxy)phenylboronic acid(**3i**) (61 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale yellow solid, Yield: 84 mg (62%); mp = 168-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 7.1 Hz, 2H), 7.94 (s, 1H), 7.83 (t, *J* = 7.3 Hz, 3H), 7.43 (s, 1H), 7.28 (d, *J* = 6.8 Hz, 2H), 7.03 (d, *J* = 7.1 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.63 (d, *J* = 8.2 Hz, 2H), 5.94 (s, 2H), 4.45 (s, 2H), 3.92 (s, 6H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.22, 149.07, 148.36, 146.63, 145.32, 144.60, 144.21, 139.78, 134.69, 130.20, 128.21, 127.50, 127.32, 126.82, 123.56, 120.48,

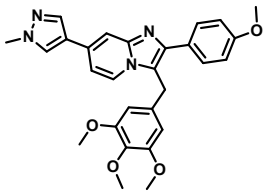
120.30, 117.83, 115.12, 111.56, 111.39, 111.16, 108.70, 108.02, 101.13, 55.91, 44.55, 29.63; FTIR (neat): 3149, 2912, 1504, 1487, 1299, 1241, 1143, 1130, 1022, 921, 776, 765, 739, 634 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{30}H_{27}N_2O_6S$ 543.15898, found 543.15808.

3-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-(4-methoxyphenyl)-6-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine (**4l**):



Compound **4l** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)-6-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine **(1w**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** 3,4-(methylenedioxy)phenylboronic acid(**3i**) (82 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as pale green solid, Yield: 79 mg (55%); mp = 160-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.71 (d, *J* = 8.7 Hz, 2H), 7.66 (d, *J* = 9.2 Hz, 1H), 7.60 (s, 1H), 7.50 (s, 1H), 7.28 (dd, *J* = 10.1, 2.0 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 5.7 Hz, 2H), 5.93 (s, 2H), 4.39 (s, 2H), 3.93 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.33, 148.31, 146.54, 144.18, 143.80, 136.51, 130.49, 129.25, 126.98, 126.94, 124.05, 120.48, 119.55, 118.51, 118.19, 117.33, 117.28, 114.08, 108.63, 108.05, 101.06, 55.27, 39.14, 29.61; FTIR (neat): 3033, 2879, 1611, 1573, 1441, 1238, 1174, 1095, 1025, 813, 803, 777, 664 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{23}N_4O_3$ 439.17702, found 439.17615.

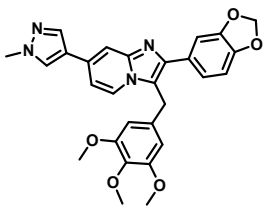
2-(4-methoxyphenyl)-7-(1-methyl-1*H*-pyrazol-4-yl)-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**4m**):



Compound **4m** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(4-methoxyphenyl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine **(1t**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (104 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as brown semi solid, Yield: 127 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.66 (dd, *J* = 14.6, 7.4 Hz, 3H), 6.98 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 7.1 Hz, 1H), 6.35 (s, 2H), 4.35 (s, 2H), 3.91 (s, 3H), 3.82 (s, 6H), 3.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.38, 153.66, 145.13, 144.06, 136.75, 136.66, 132.58, 129.18, 129.16, 127.33, 126.75, 123.36, 121.12, 116.65, 114.14, 111.13, 110.99, 104.42, 60.78, 56.06, 55.24, 39.11, 29.99; FTIR (neat): 2936, 1643, 1588, 1504, 1418, 1329, 1234, 1121, 1003, 835, 725, 643 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{20}N_2O_2$ 345.15248, found 345.15970.

2-(benzo[*d*][1,3]dioxol-5-yl)-7-(1-methyl-1*H*-pyrazol-4-yl)-3-(3,4,5-trimethoxybenzyl)imidazo[1,2-*a*]pyridine (**4n**):

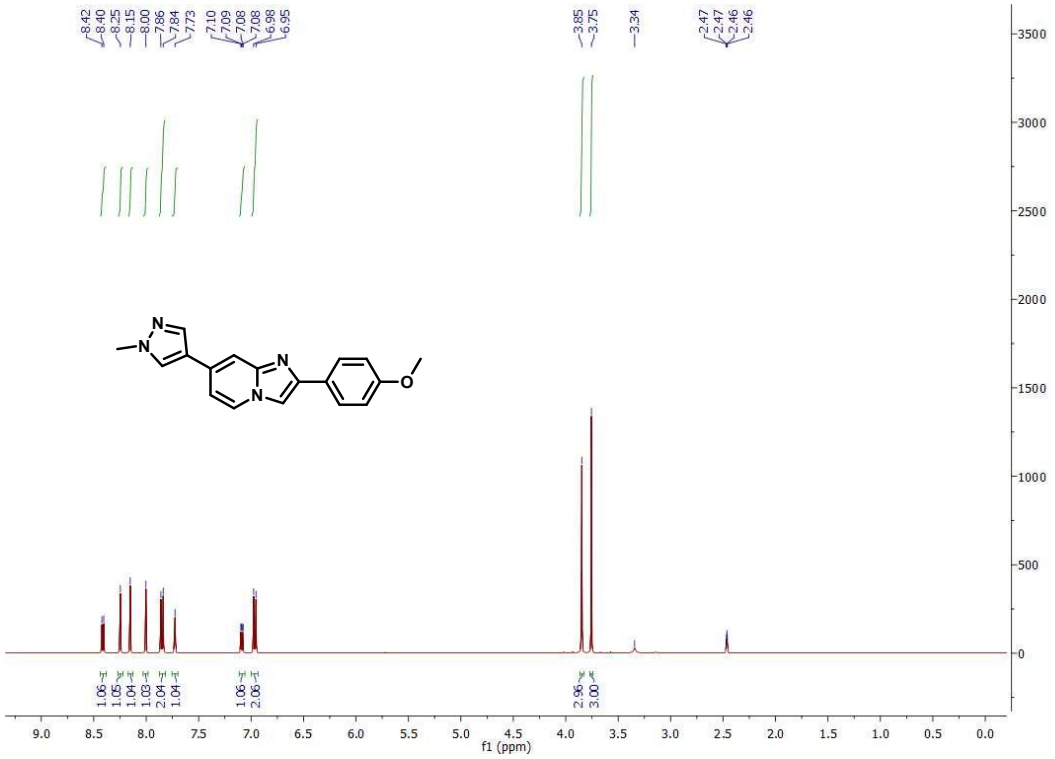
Compound **4n** was prepared by following the general procedure for the arylomethylation of IIIA from 2-(benzo[*d*][1,3]dioxol-5-yl)-7-(1-methyl-1*H*-pyrazol-4-yl)imidazo[1,2-*a*]pyridine **(1x**) (100 mg, 0.45 mmol), 2-oxoacetic acid (**2a**) (73.9 µL 0.67 mmol)**,** (3,4,5-trimethoxyphenyl)boronic acid (**3l**) (100 mg, 0.67 mmol) and KO*t*Bu (95 mg, 0.45 mmol), isolated as brown semi solid,



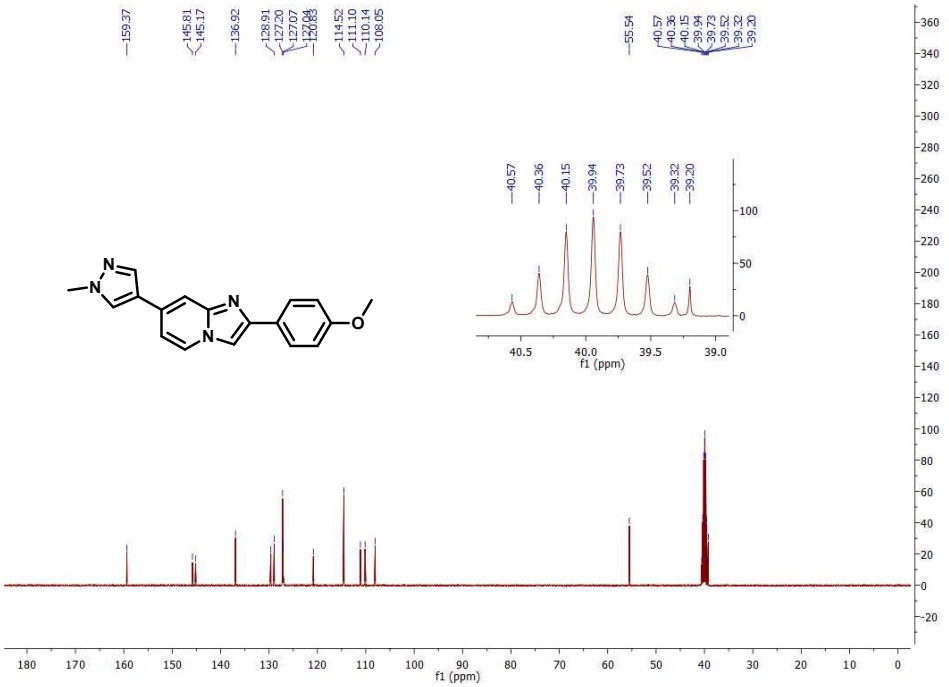
Yield: 110 mg (70%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.63 (m, 4H), 7.15 (dd, *J* = 8.4, 7.4 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 2H), 6.69 (t, *J* = 6.8 Hz, 1H), 4.39 (s, 2H), 3.82 (s, 3H), 3.76 (s, 3H) ;^{13}C NMR (100 MHz, $CDCl_3$): δ 153.72, 147.96, 147.35, 145.13, 144.27, 136.83, 136.77, 132.46, 129.20, 128.47, 127.25, 123.42, 121.71, 121.25, 116.74, 111.31, 111.22, 108.54, 104.40, 101.09, 60.83, 56.11, 39.23, 30.10; FTIR (neat): 2934, 1588, 1502, 1446, 1329, 1230, 1121, 1034, 908, 815, 726, 608 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{28}H_{27}N_4O_5$ 499.19814, found 499.19540.

V. ^{1}H and ^{13}C NMR Spectra for Key intermediates & All final Compounds:

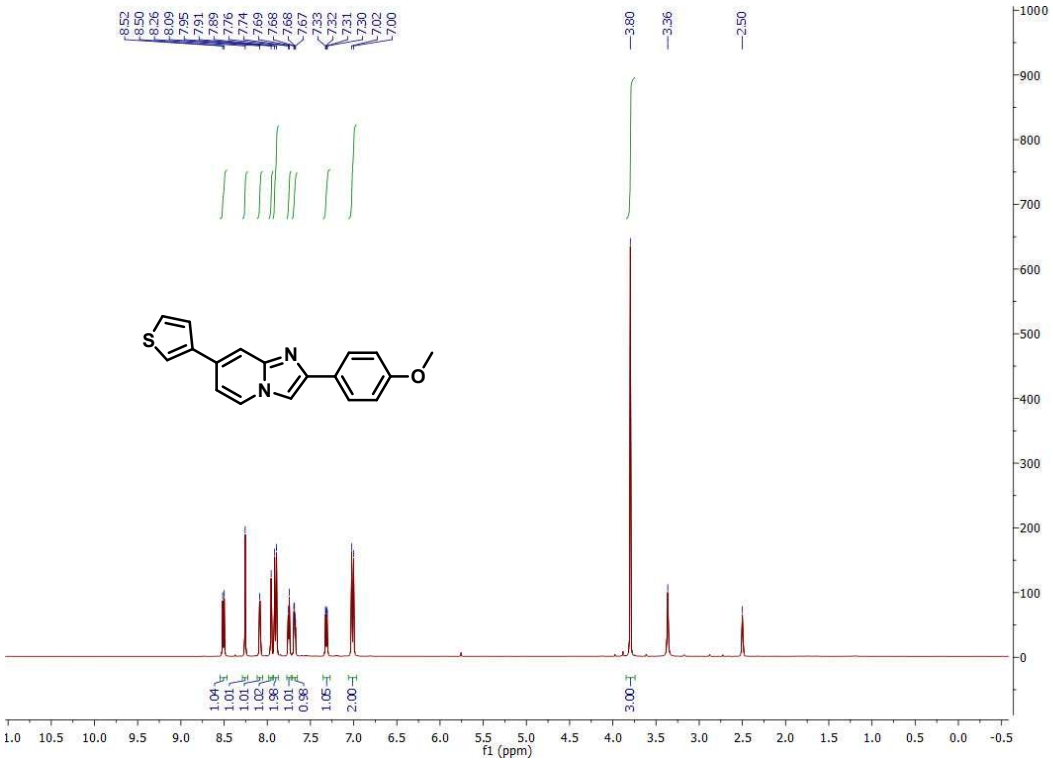
^{1}H NMR spectrum of compound **1t** (DMSO-*d6*, 400 MHz)

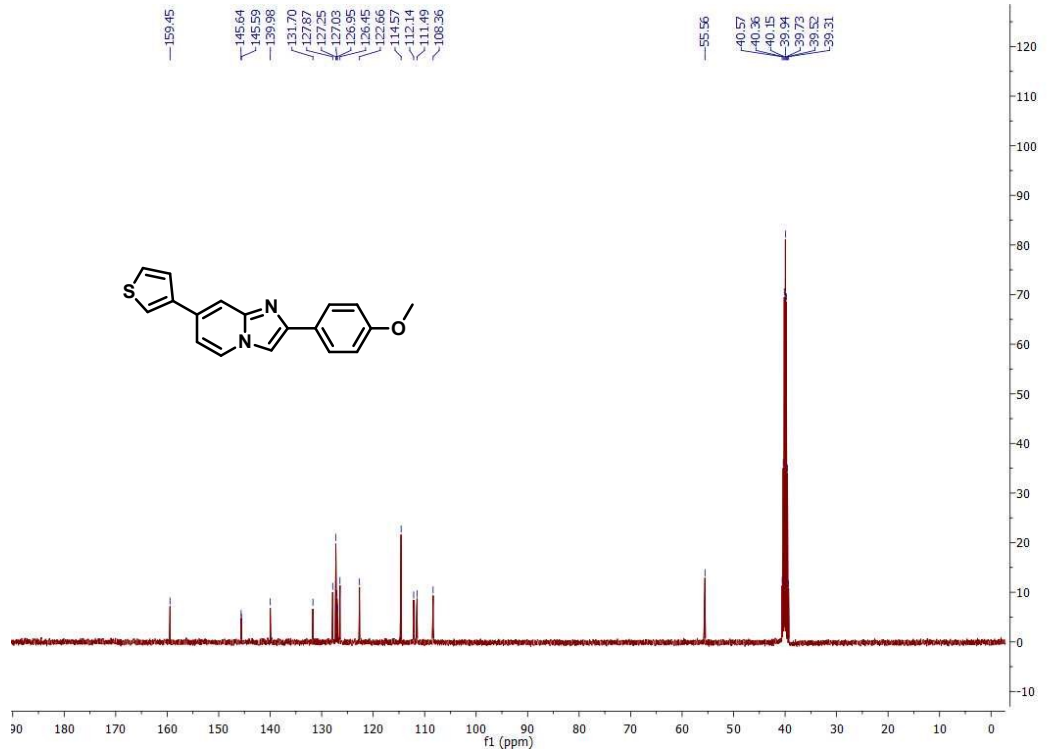


^{13}CNMR spectrum of compound **1t** (DMSO-*d6*, 100 MHz)



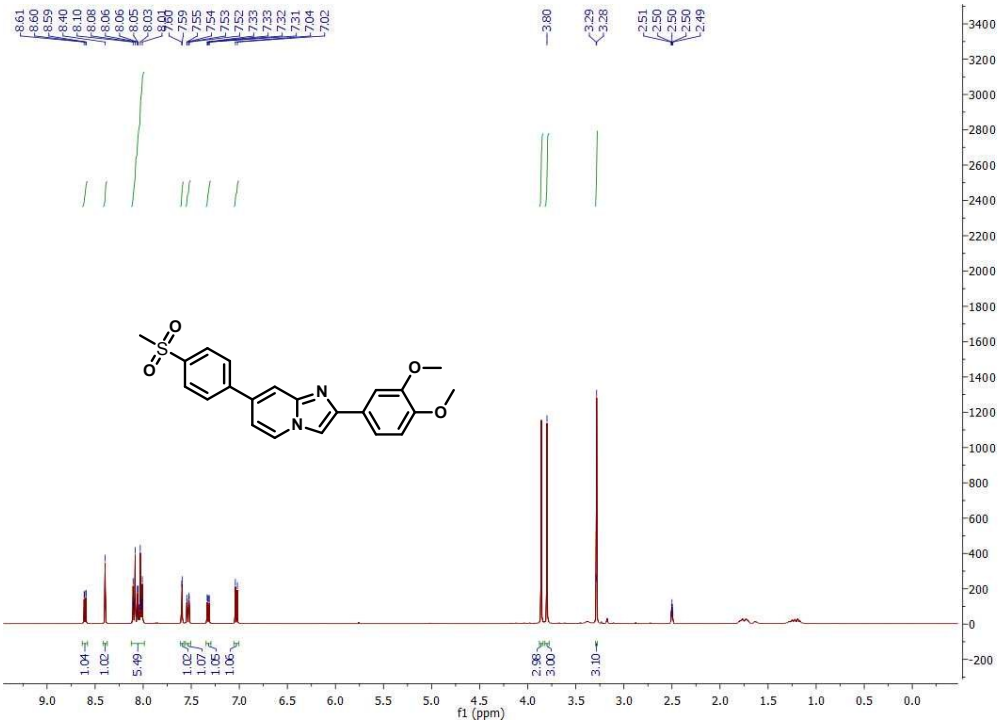
^{1}H NMR spectrum of compound **1u** (DMSO-*d6*, 400 MHz)

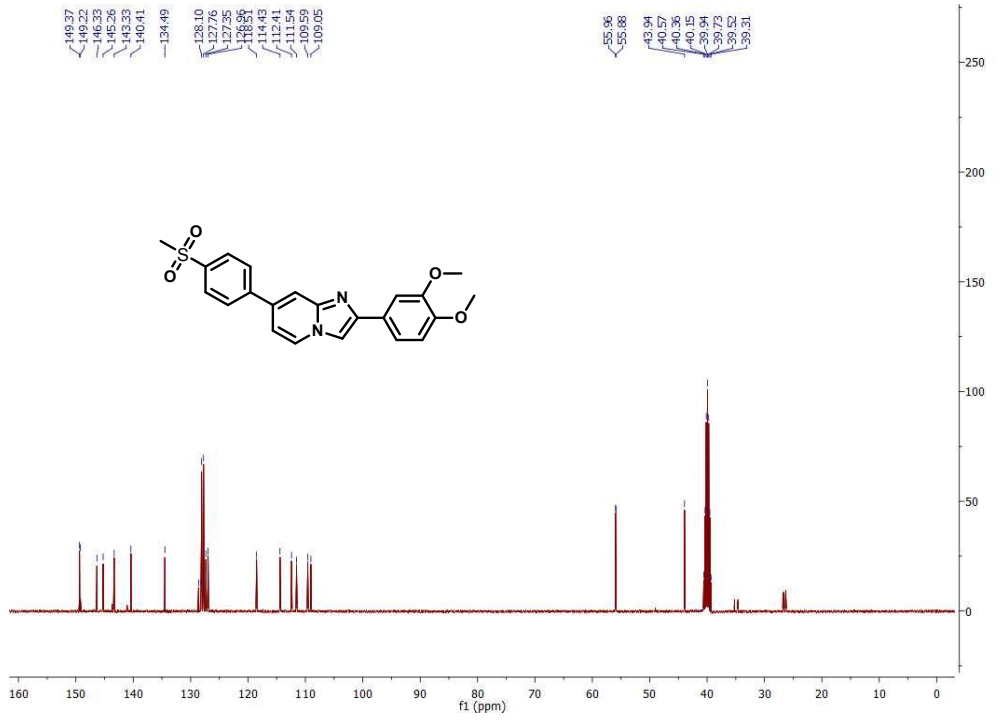




^{13}CNMR spectrum of compound **1u** (DMSO-*d6*, 100 MHz)

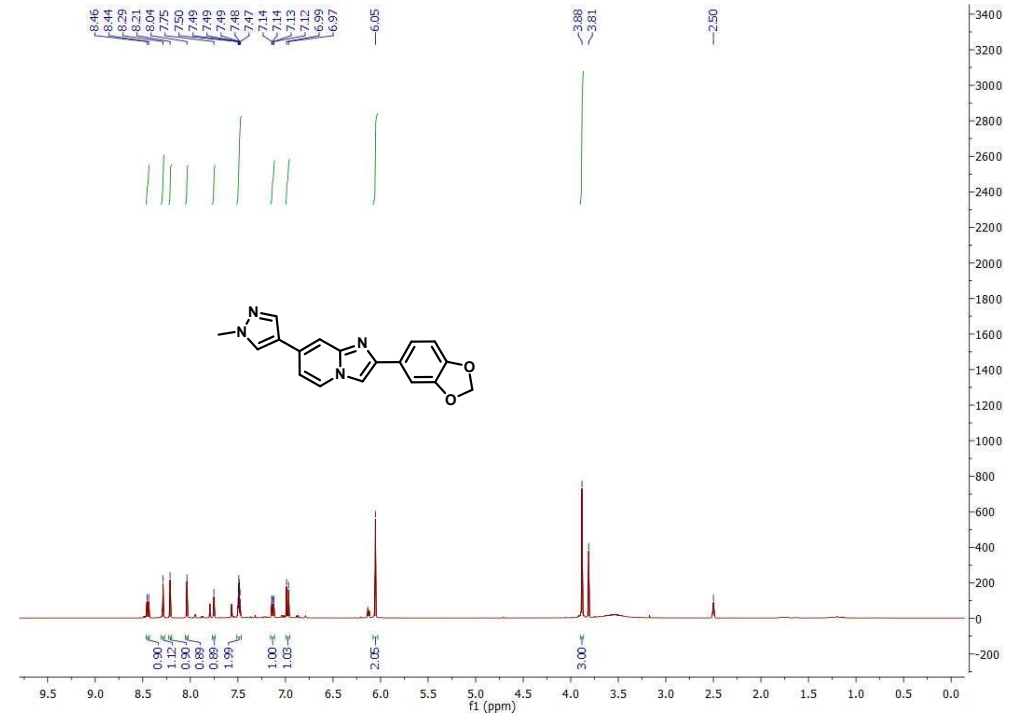
^{1}H NMR spectrum of compound **1v** (DMSO-*d6*, 400 MHz)



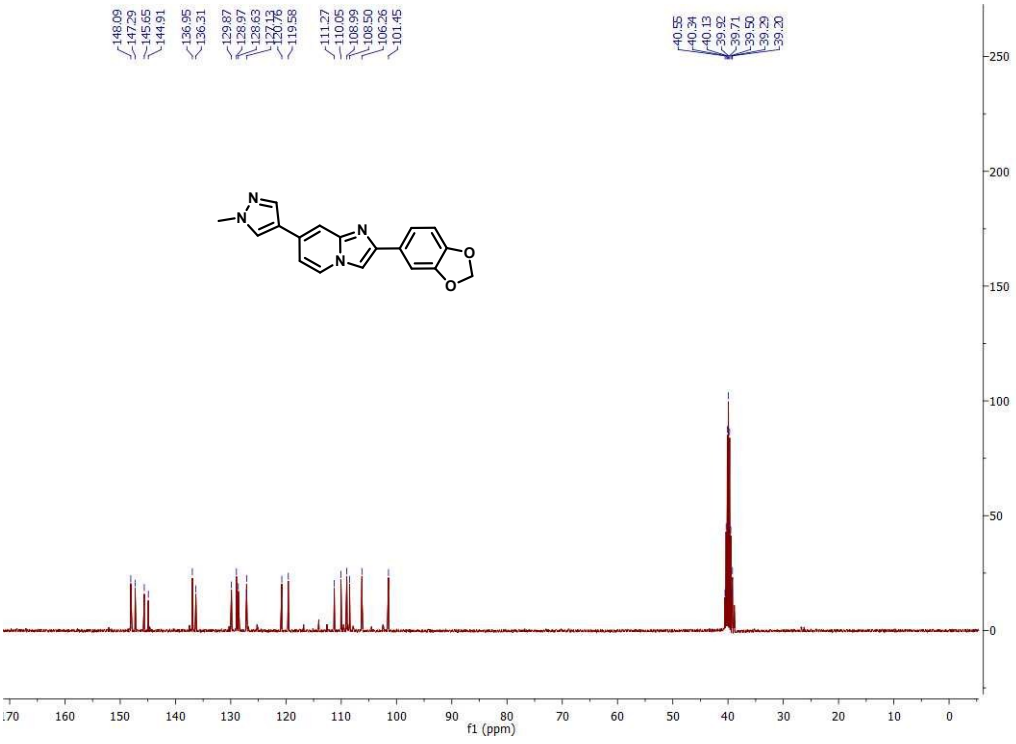


^{13}CNMR spectrum of compound **1v** (DMSO-*d6*, 100 MHz)

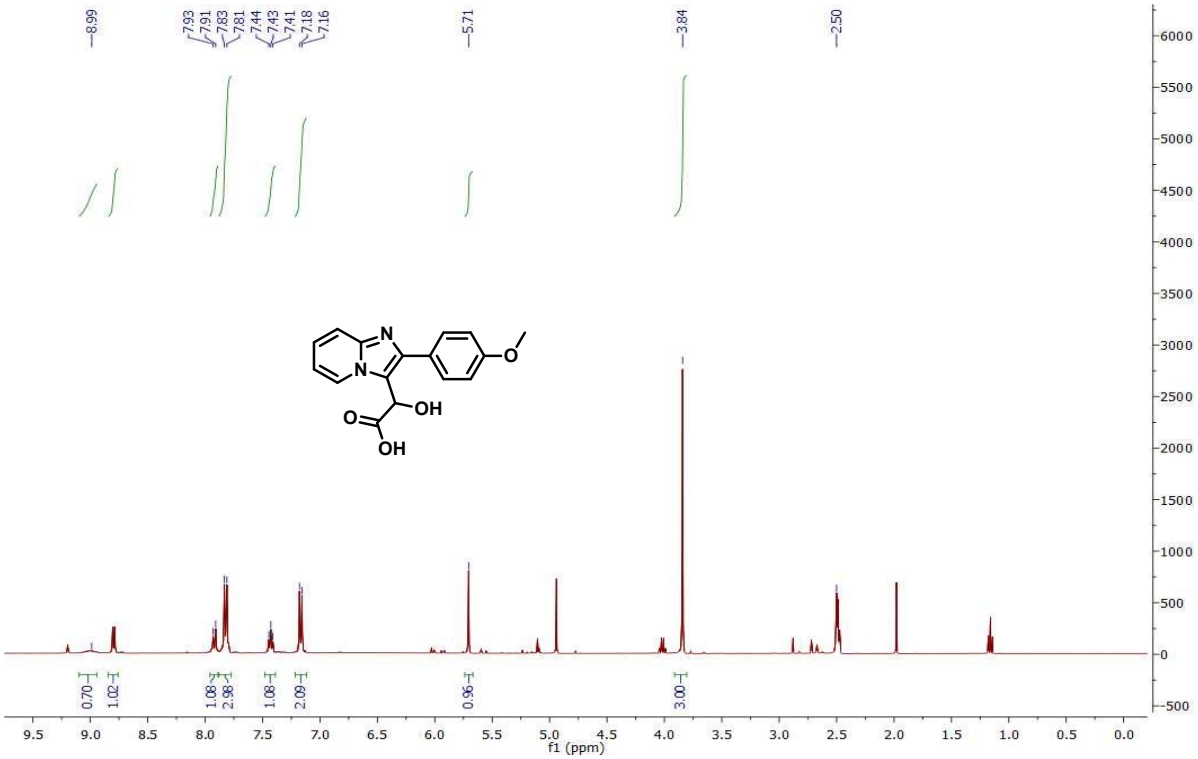
^{1}H NMR spectrum of compound **1x** (DMSO-*d6*, 400 MHz)

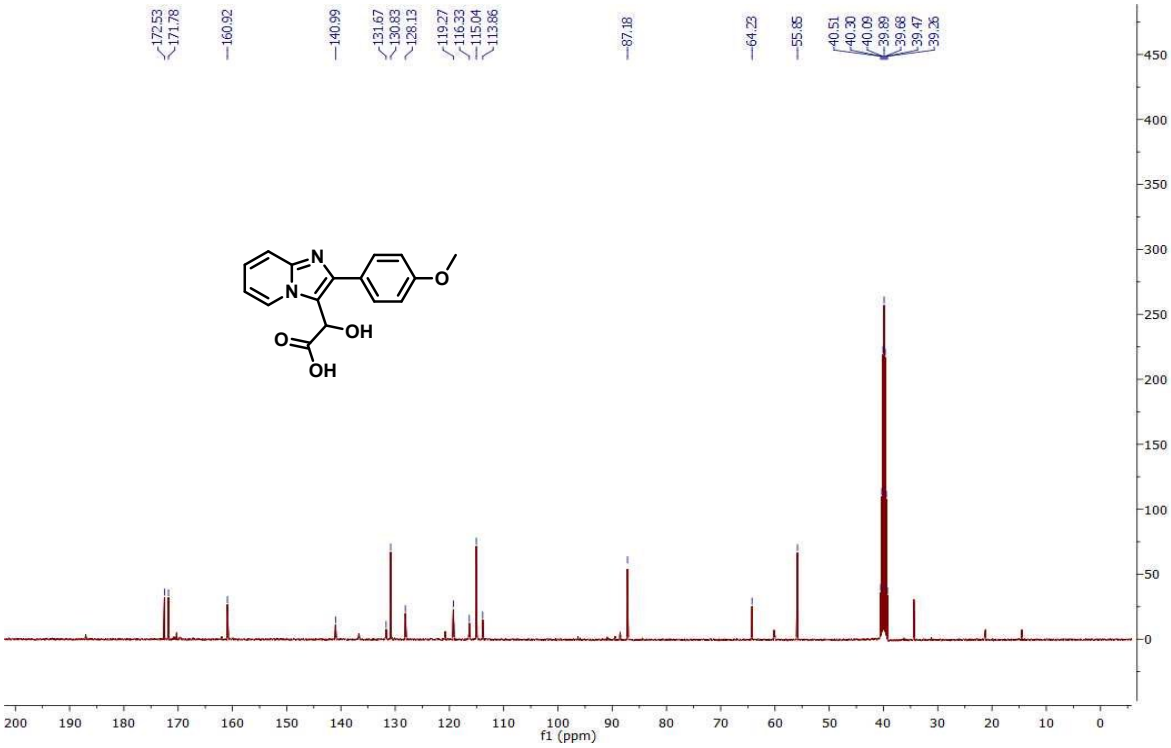


^{13}CNMR spectrum of compound **1u** (DMSO-*d6*, 100 MHz)



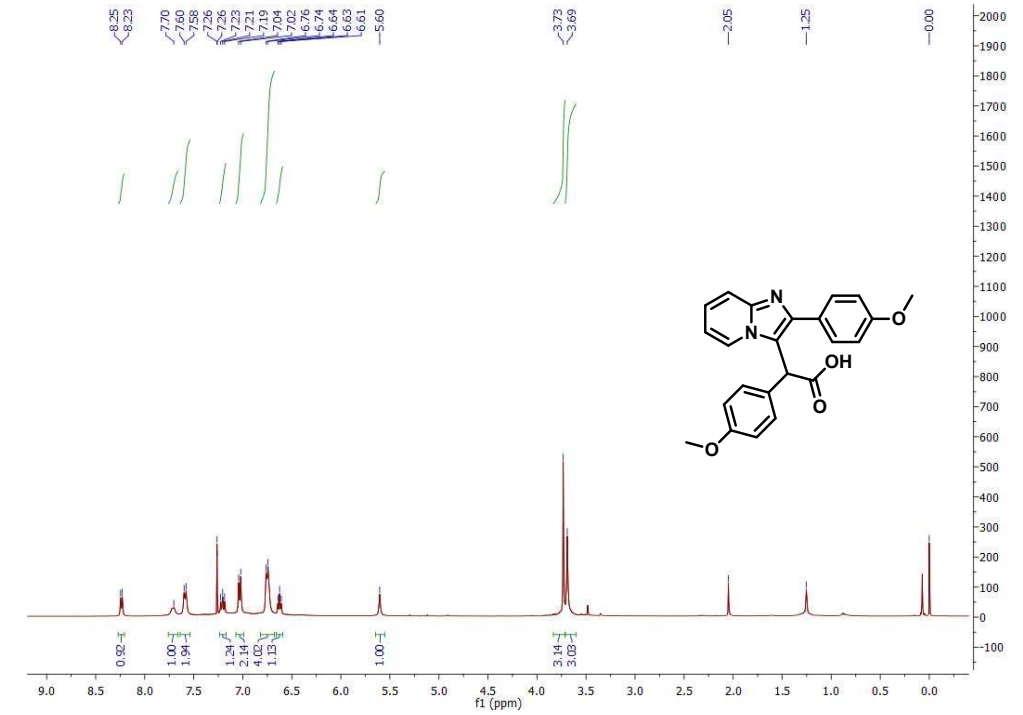
^{1}H NMR spectrum of compound **3aab** (DMSO-*d6*, 400 MHz)

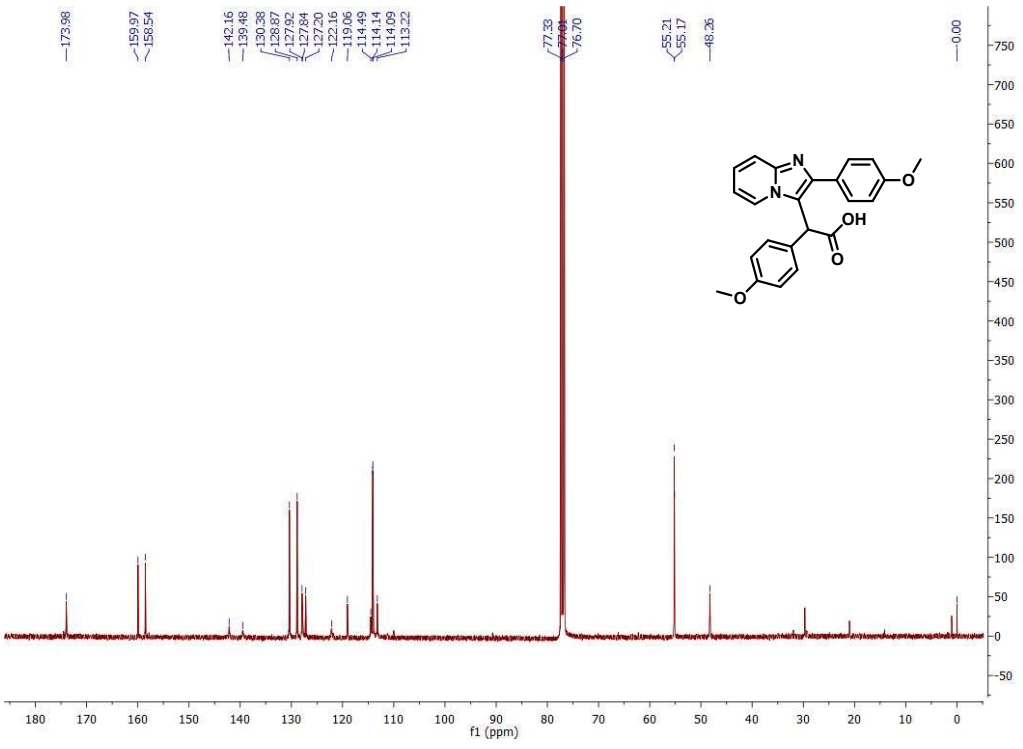




CNMR spectrum of compound **3aab** (DMSO-*d6*, 100 MHz)

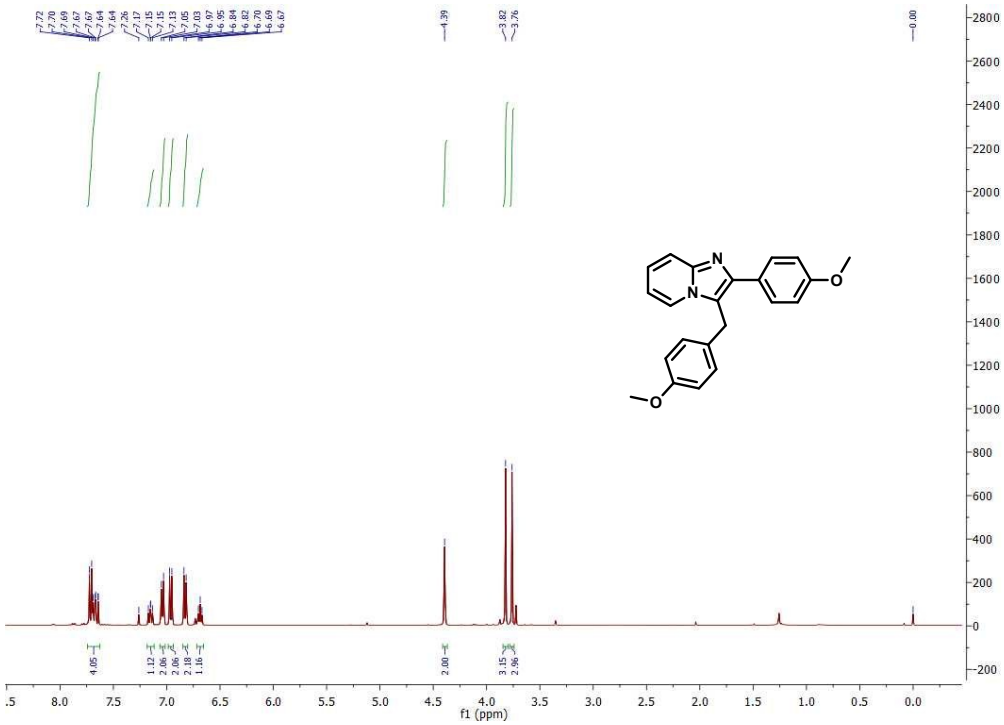
^{1}H NMR spectrum of compound **3aac** ($CDCl_3$, 400 MHz)

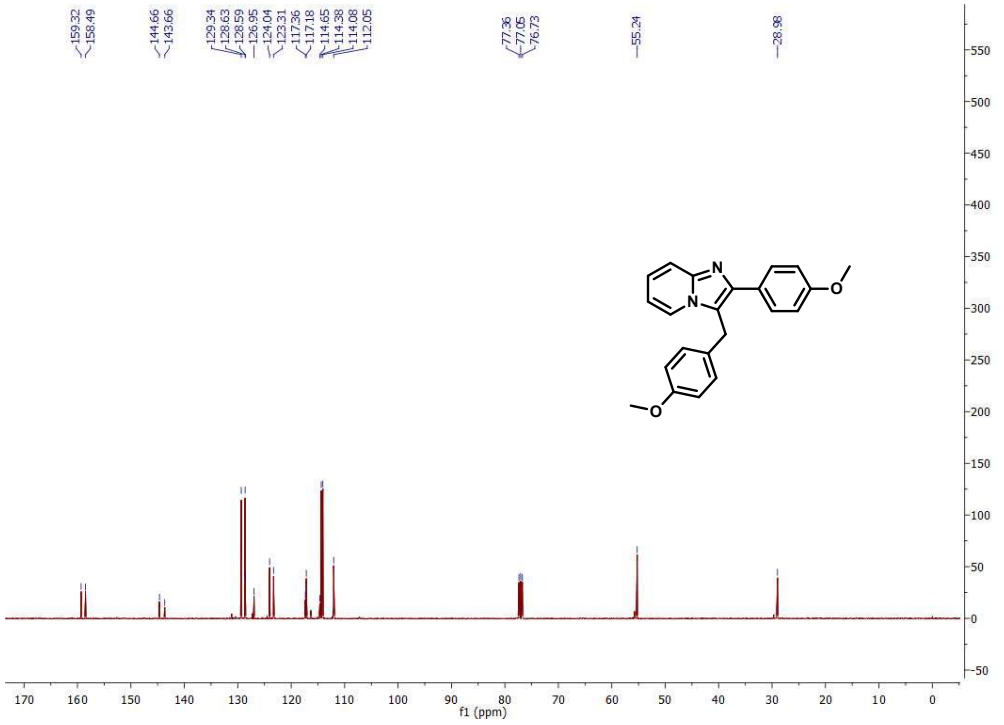




^{13}CNMR spectrum of compound **3aac** ($CDCl_3$, 100 MHz)

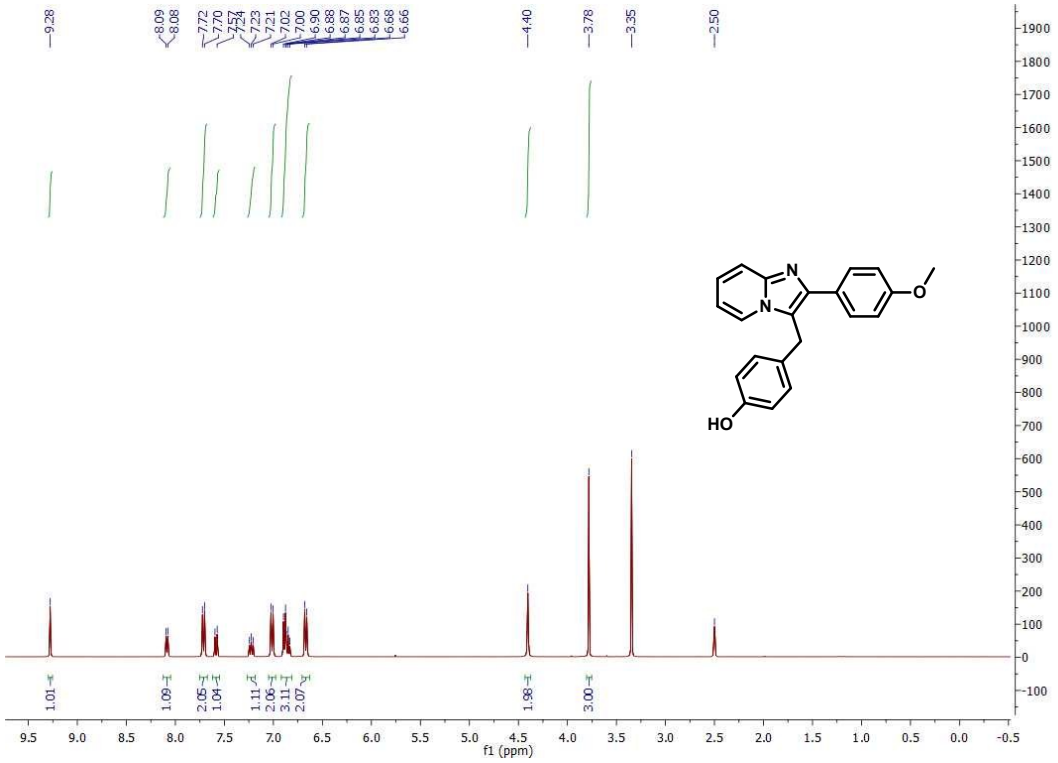
^{1}H NMR spectrum of compound **3aa** ($CDCl_3$, 400 MHz)

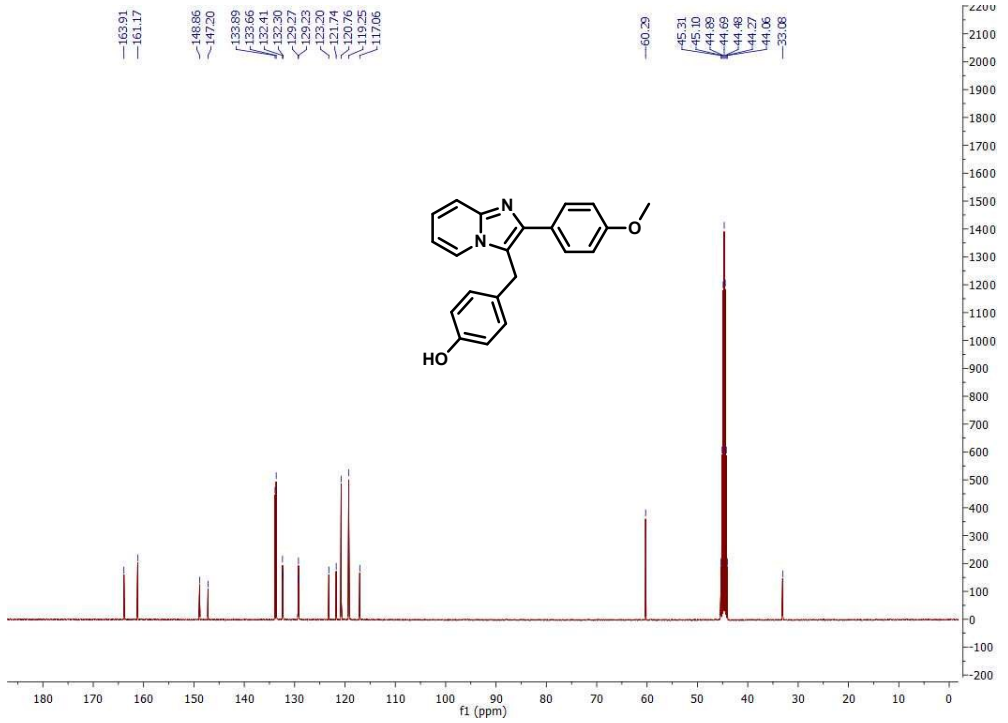




^{13}CNMR spectrum of compound **3aa** ($CDCl_3$, 100 MHz)

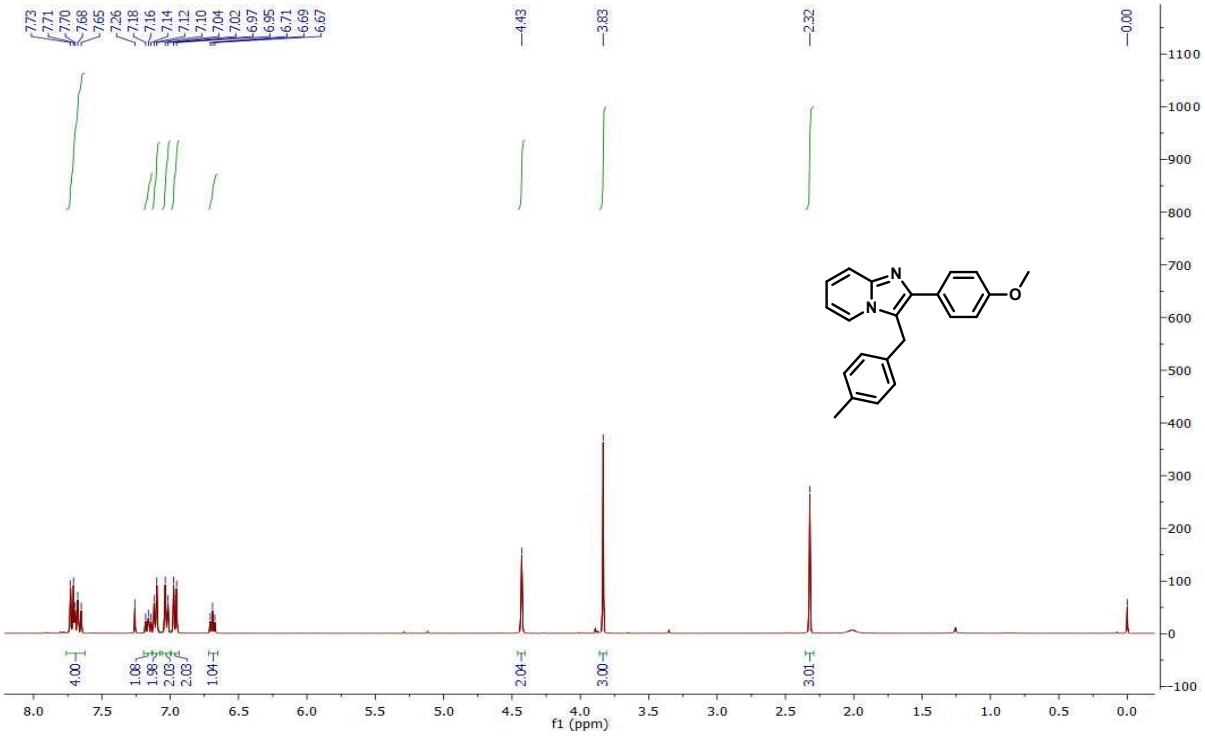
^{1}H NMR spectrum of compound **3ab** (DMSO-*d6*, 400 MHz)

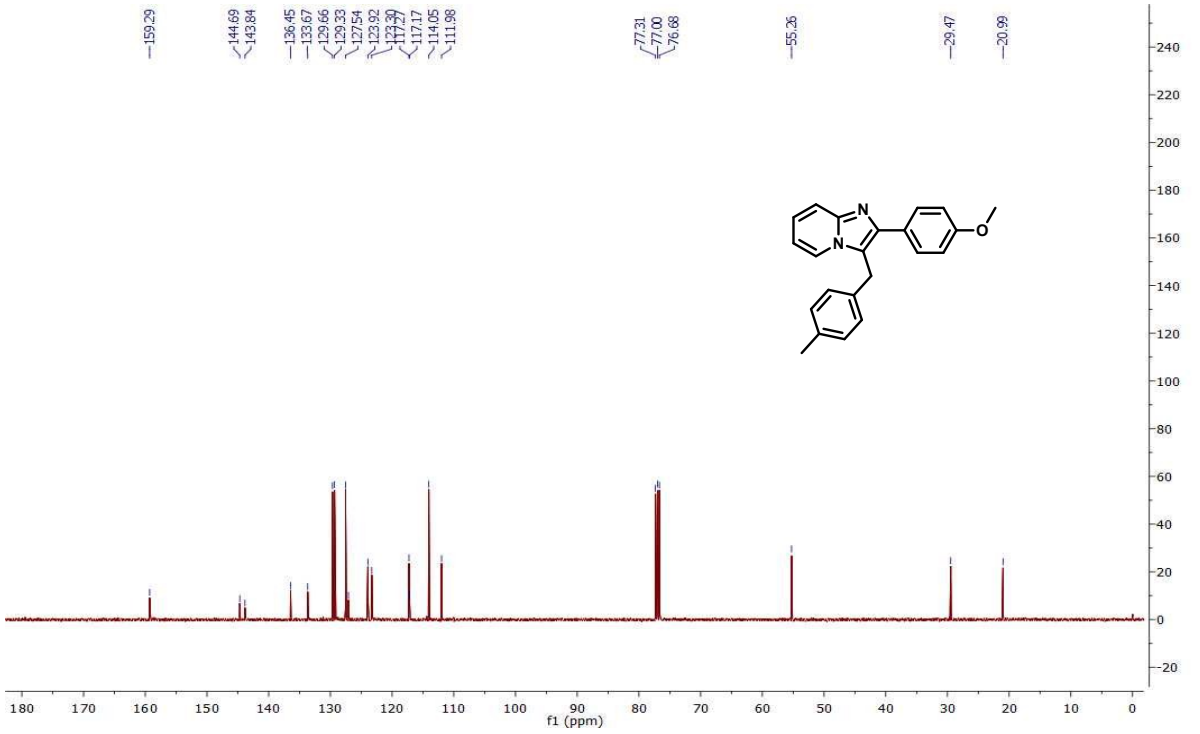




^{13}CNMR spectrum of compound **3ab** (DMSO-*d6*, 100 MHz)

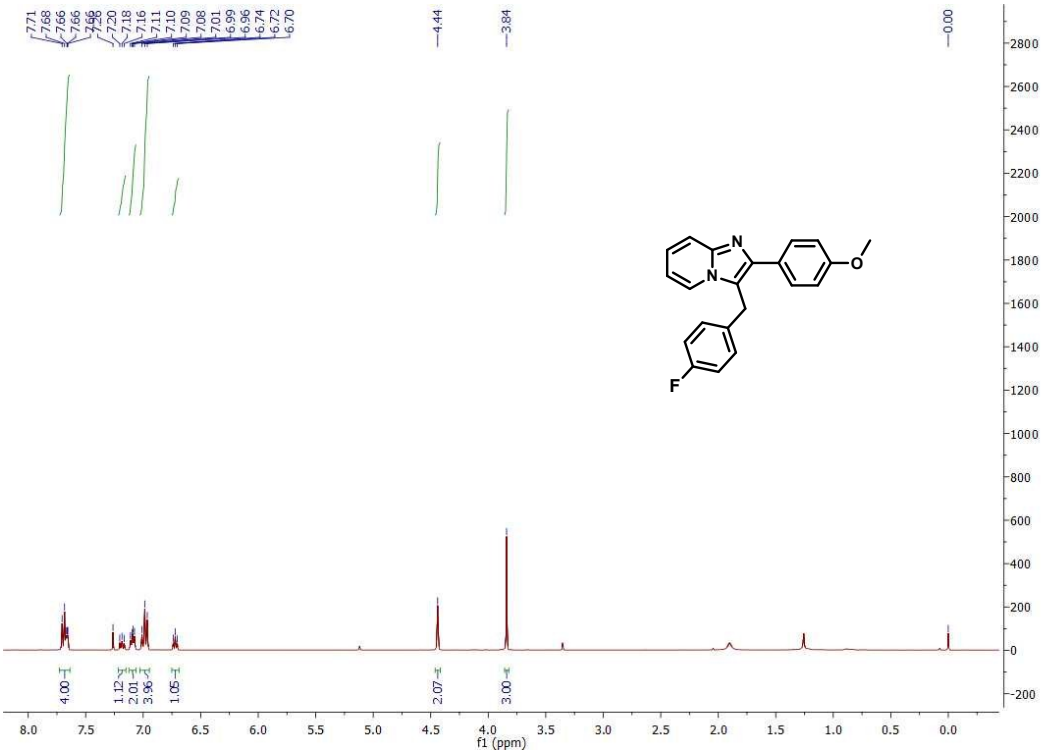
^{1}H NMR spectrum of compound **3ac** ($CDCl_3$, 400 MHz)

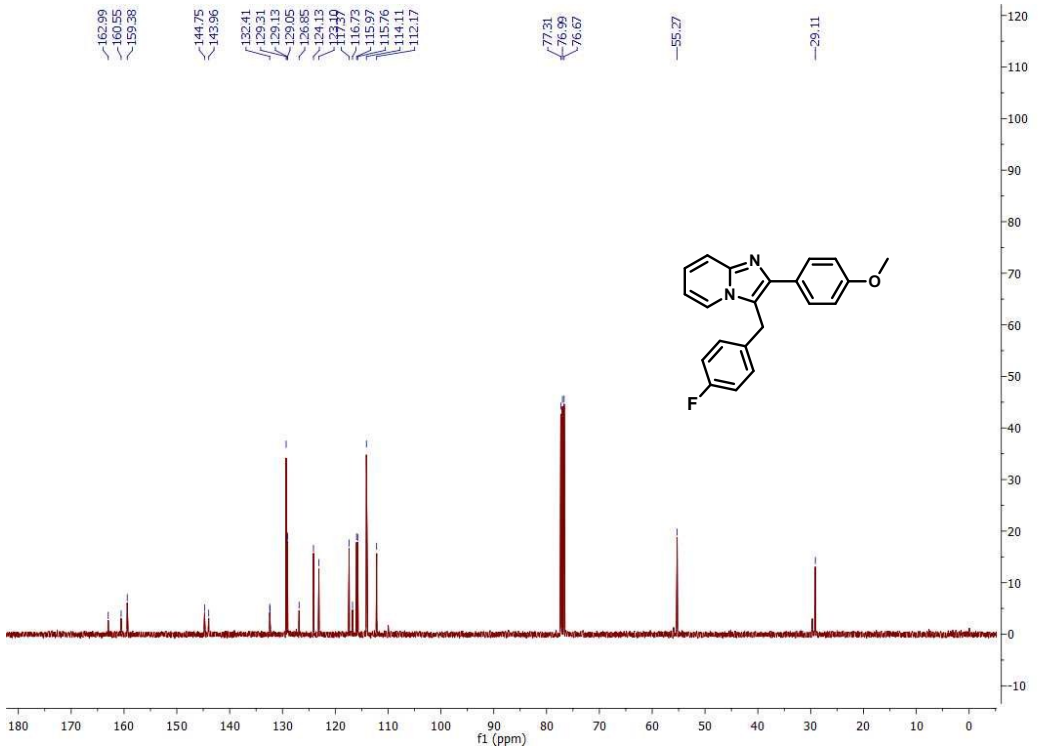




^{13}CNMR spectrum of compound **3ac** ($CDCl_3$, 100 MHz)

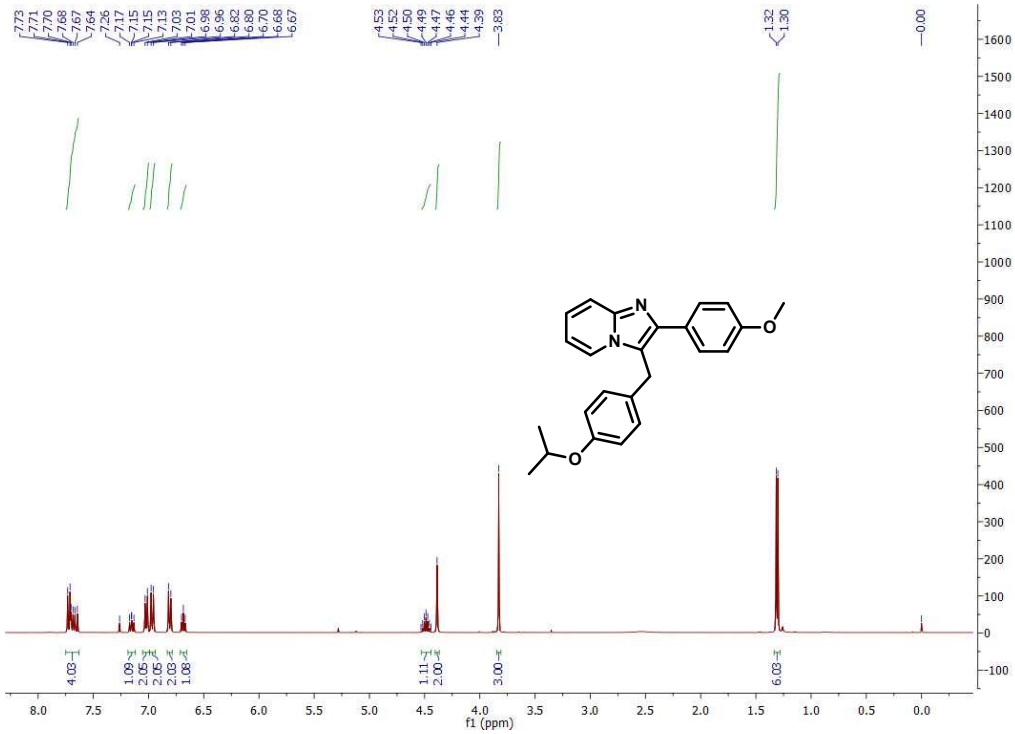
^{1}H NMR spectrum of compound **3ad** ($CDCl_3$, 400 MHz)

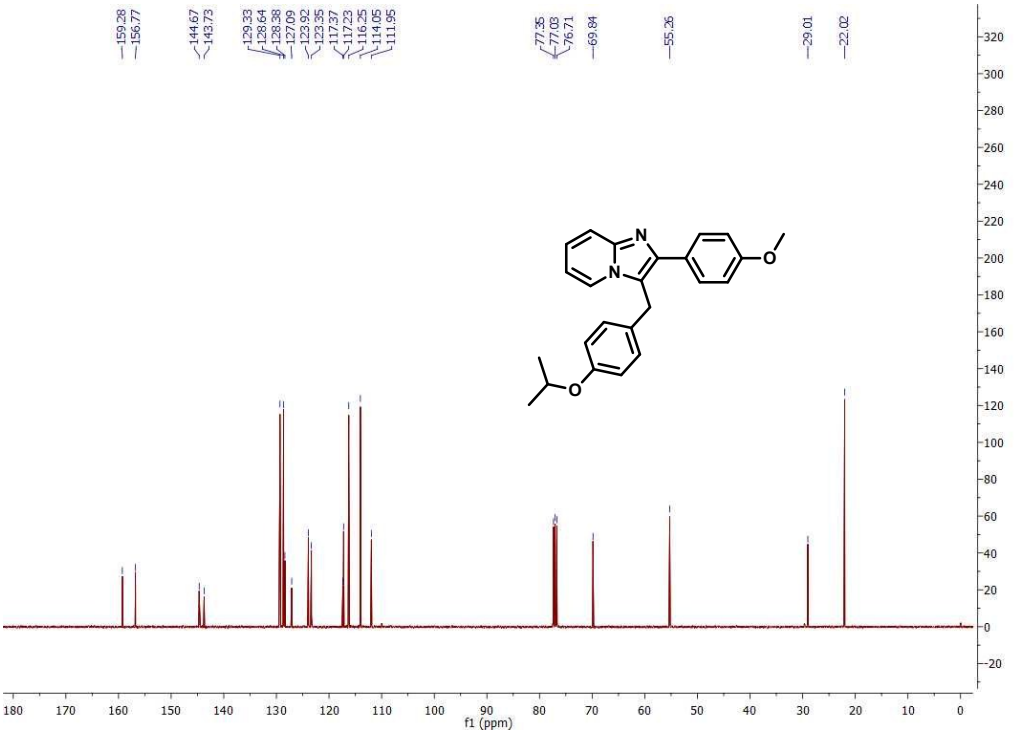




^{13}CNMR spectrum of compound **3ad** ($CDCl_3$, 100 MHz)

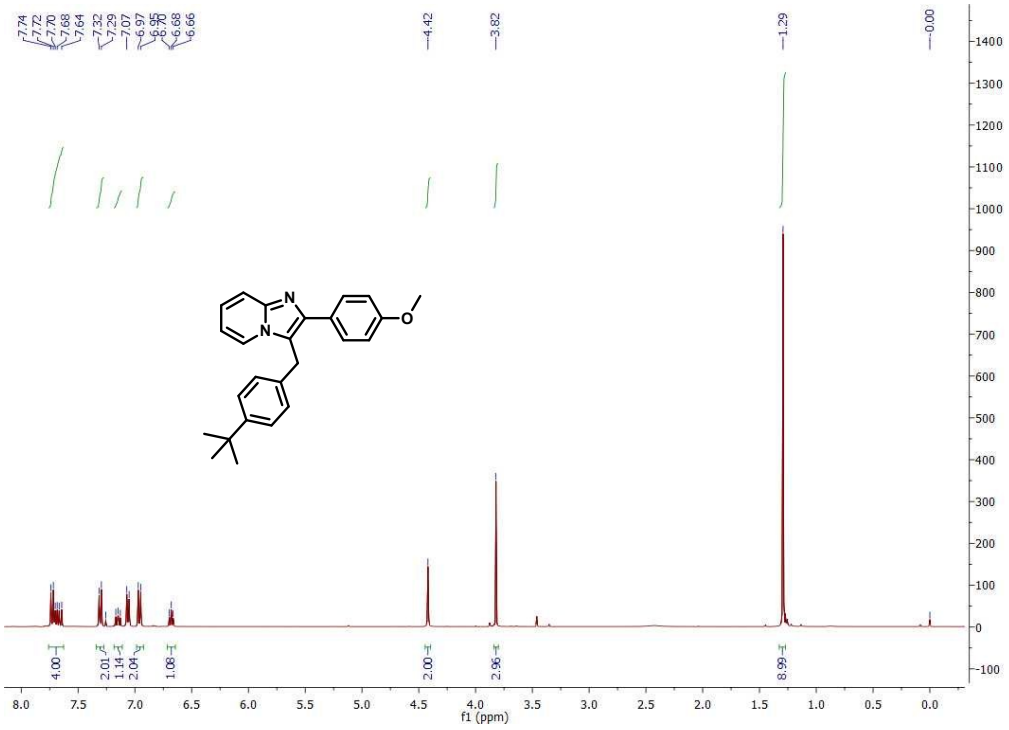
^{1}H NMR spectrum of compound **3ae** ($CDCl_3$, 400 MHz)

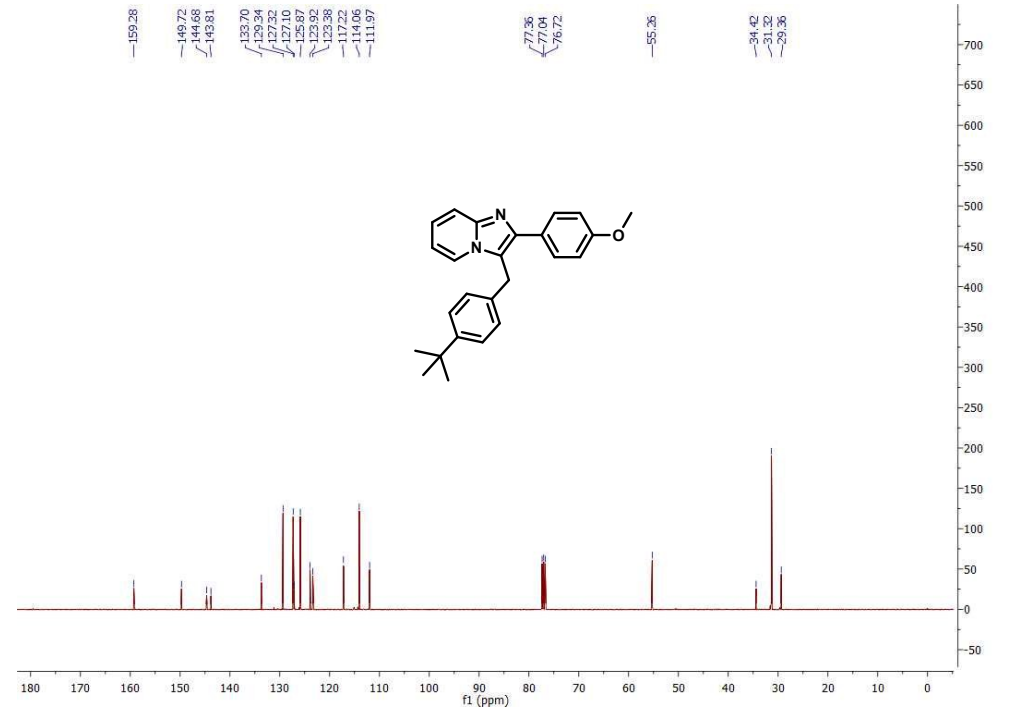




^{13}CNMR spectrum of compound **3ae** ($CDCl_3$, 100 MHz)

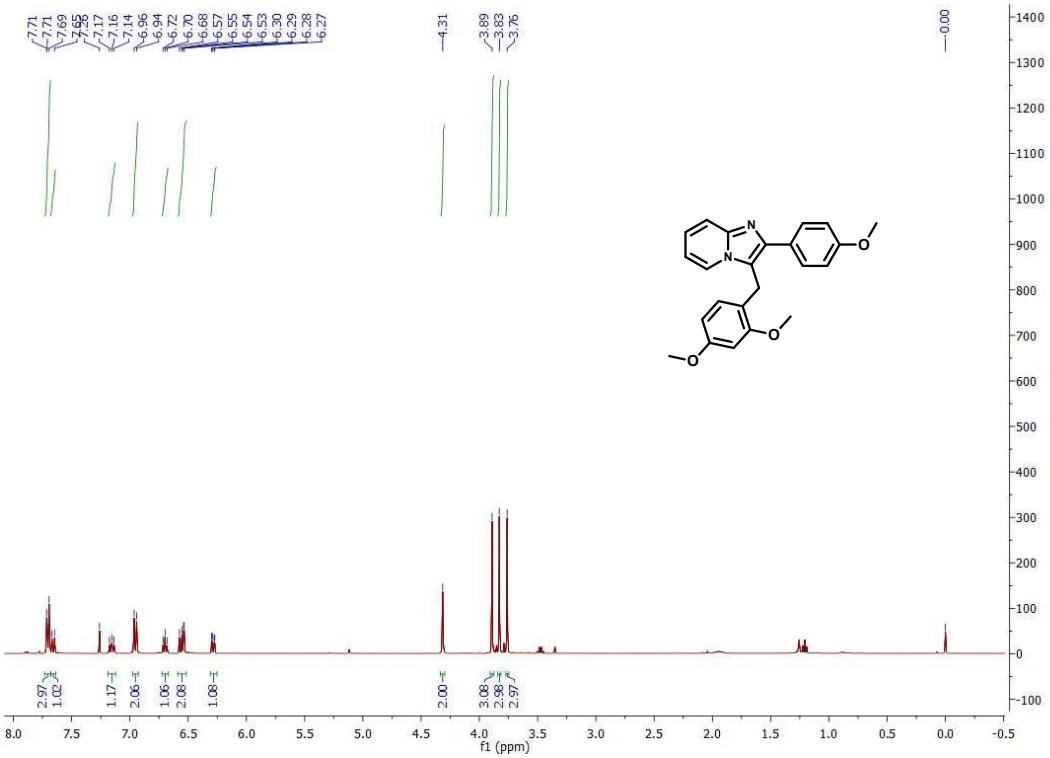
^{1}H NMR spectrum of compound **3af** ($CDCl_3$, 400 MHz)

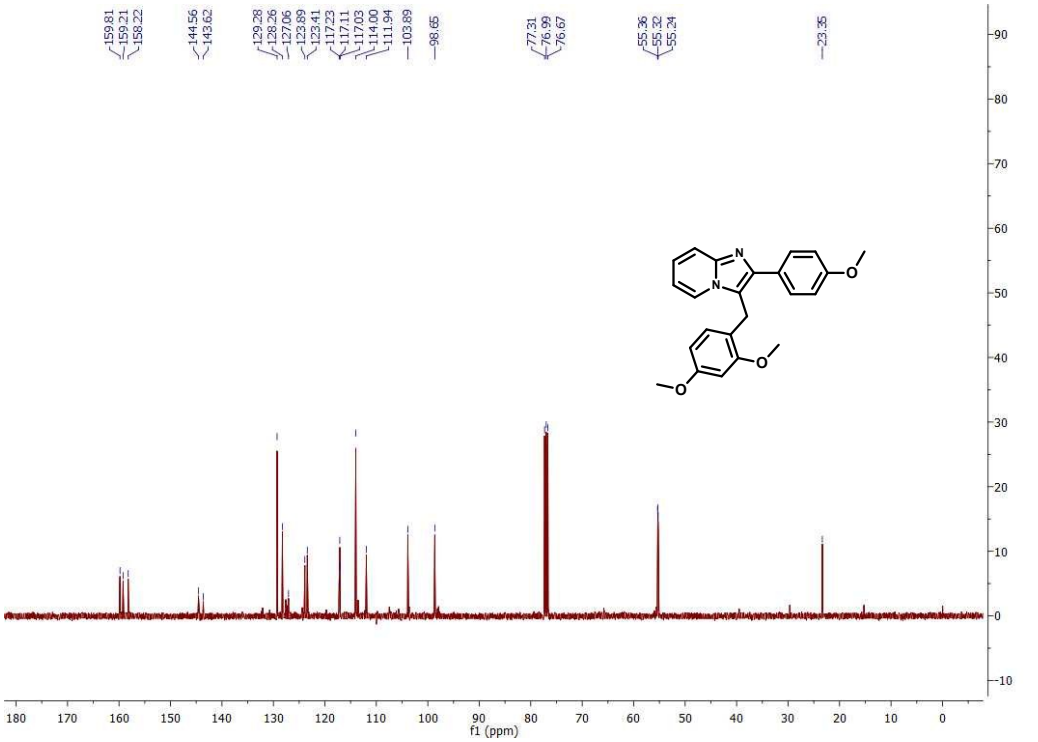




^{13}CNMR spectrum of compound **3af** ($CDCl_3$, 100 MHz)

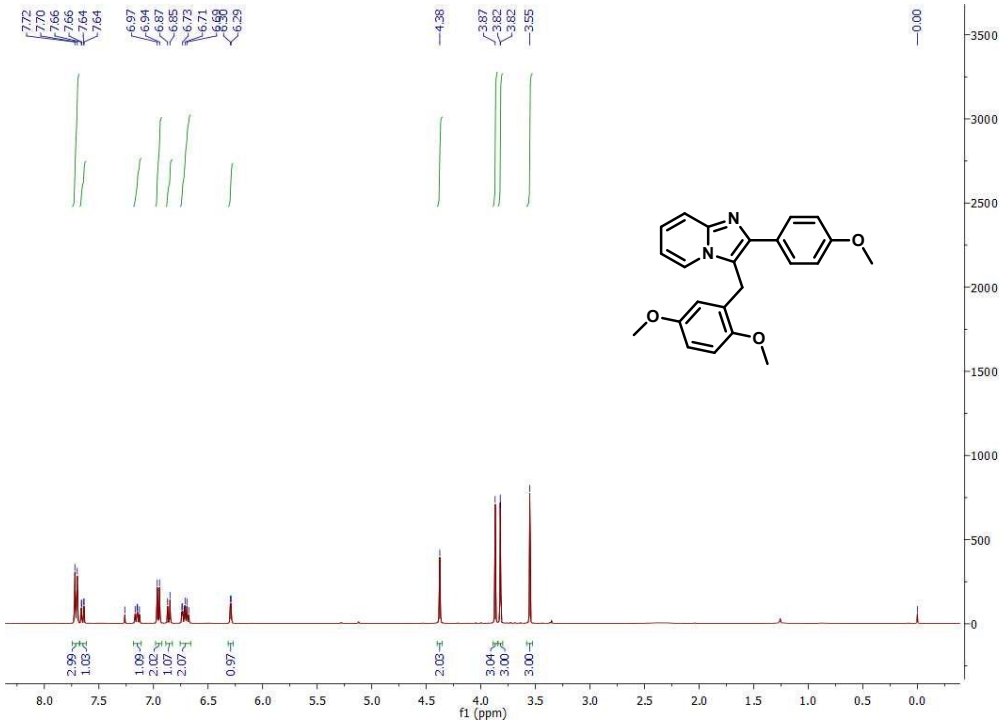
^{1}H NMR spectrum of compound **3ag** ($CDCl_3$, 400 MHz)

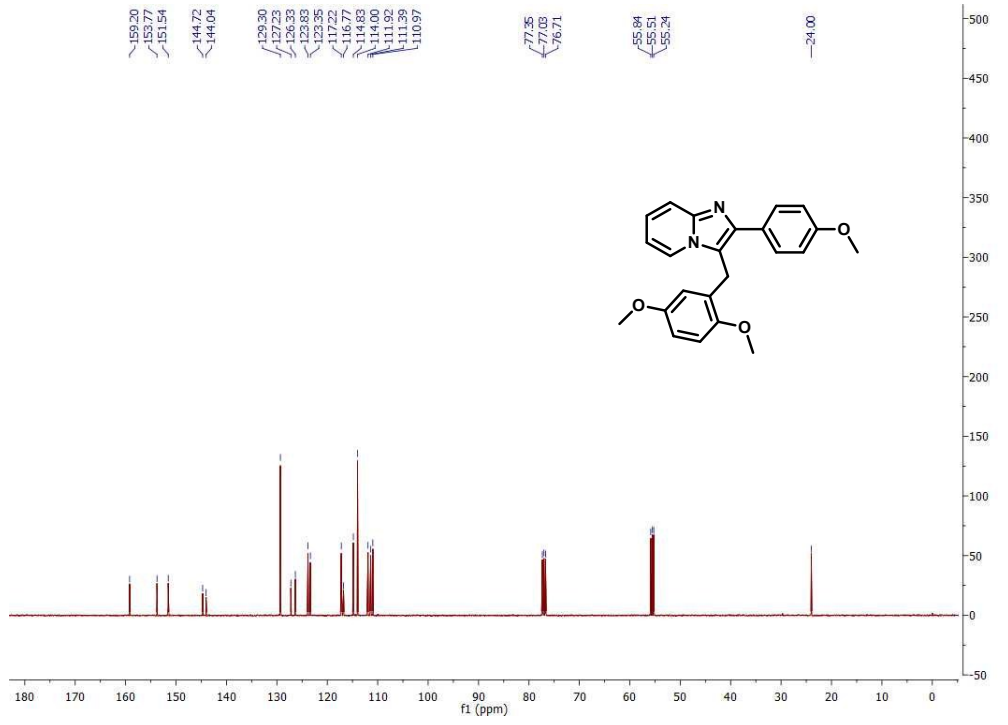




^{13}CNMR spectrum of compound **3ag** ($CDCl_3$, 100 MHz)

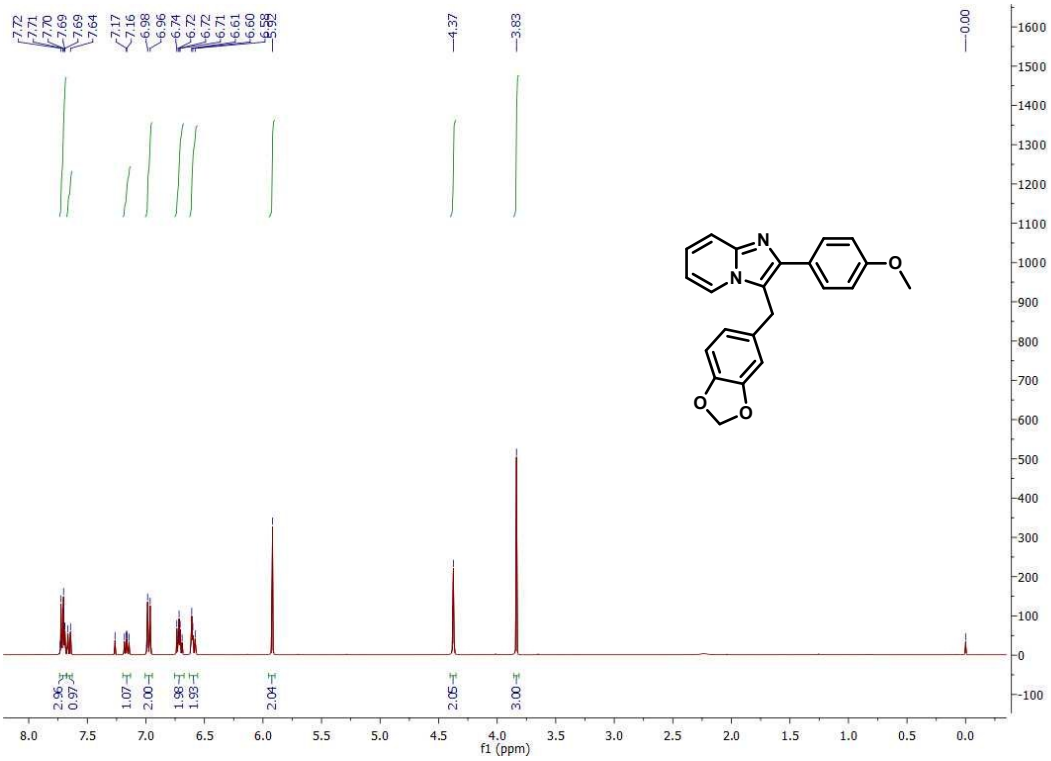
^{1}H NMR spectrum of compound **3ah** ($CDCl_3$, 400 MHz)

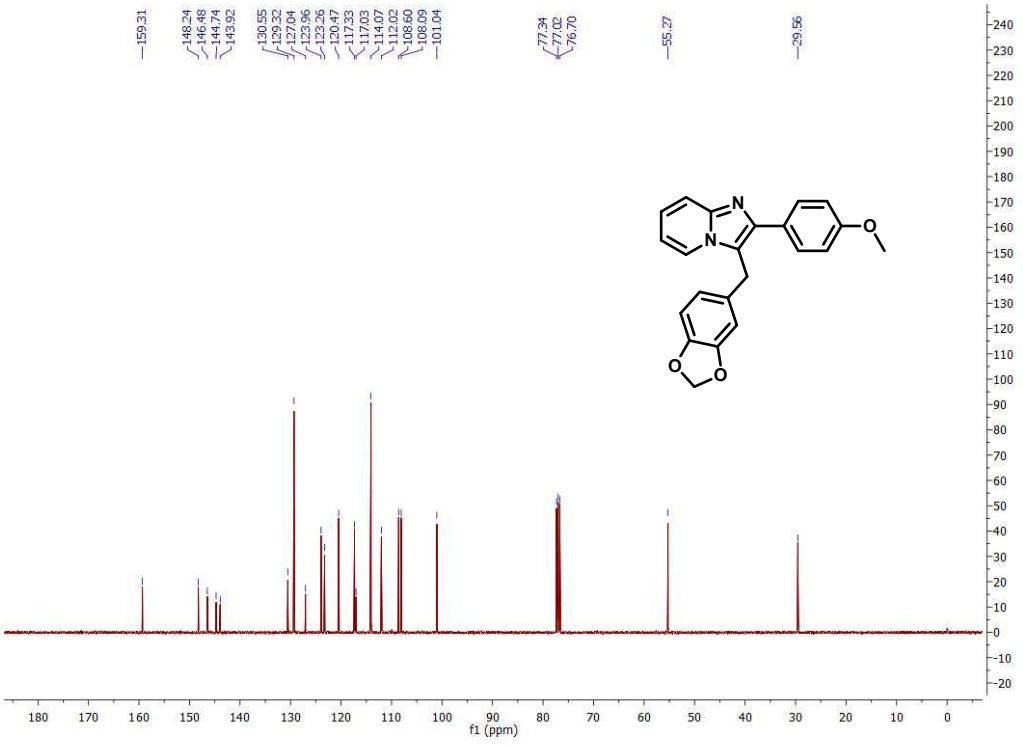




^{13}CNMR spectrum of compound **3ah** ($CDCl_3$, 100 MHz)

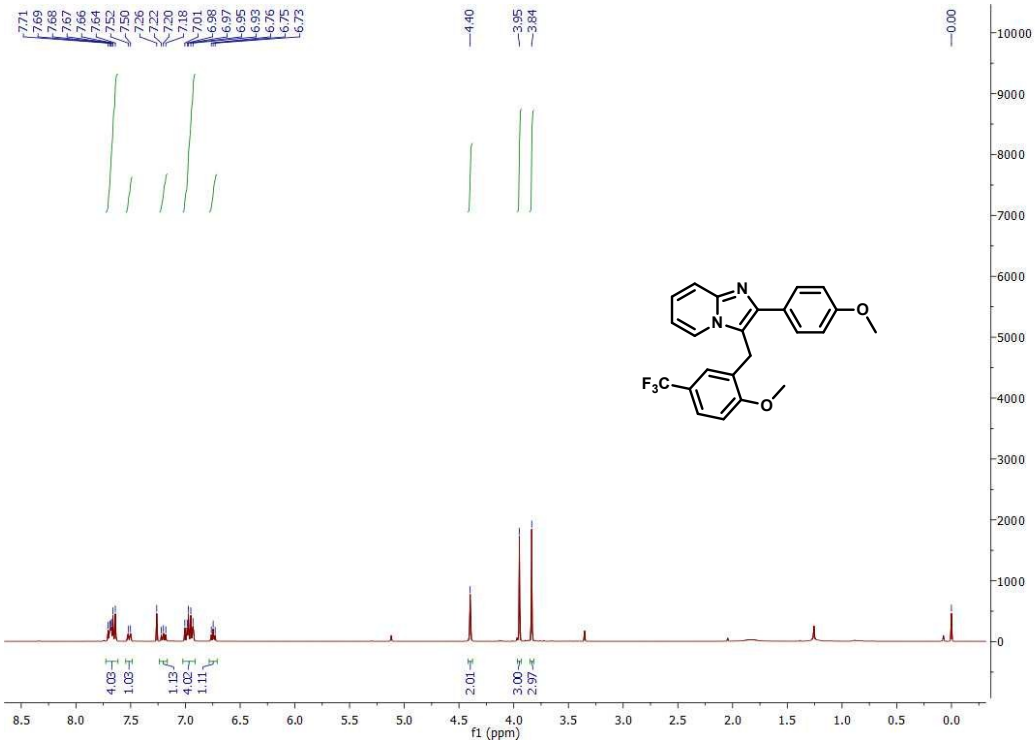
^{1}H NMR spectrum of compound **3ai** ($CDCl_3$, 400 MHz)

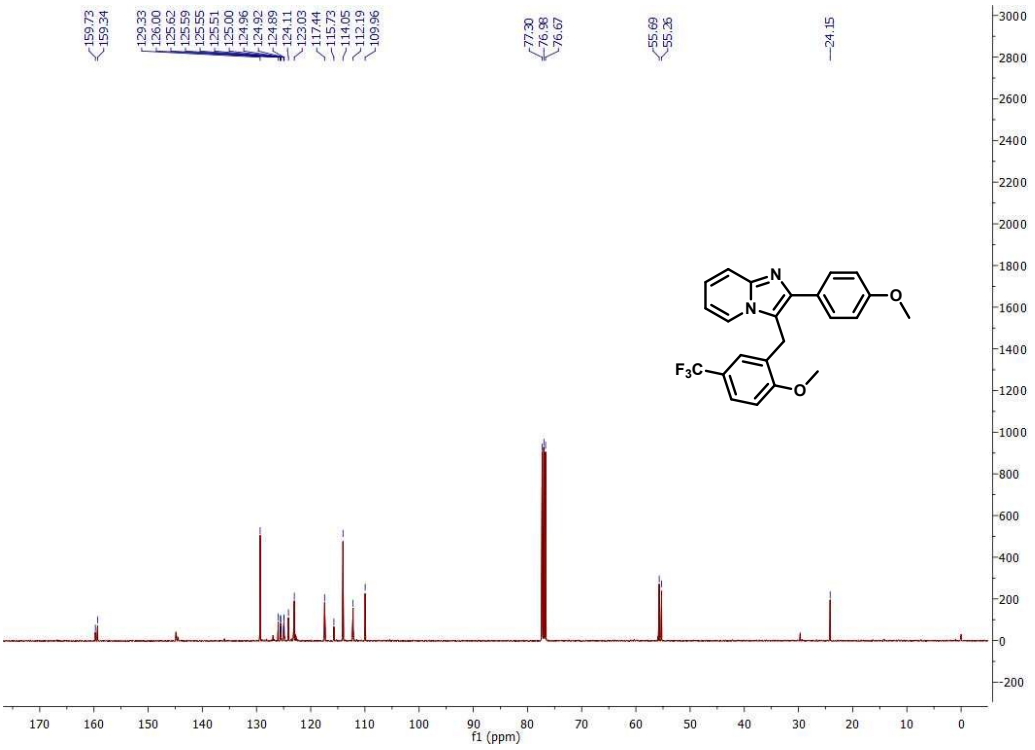




^{13}CNMR spectrum of compound **3ai** ($CDCl_3$, 100 MHz)

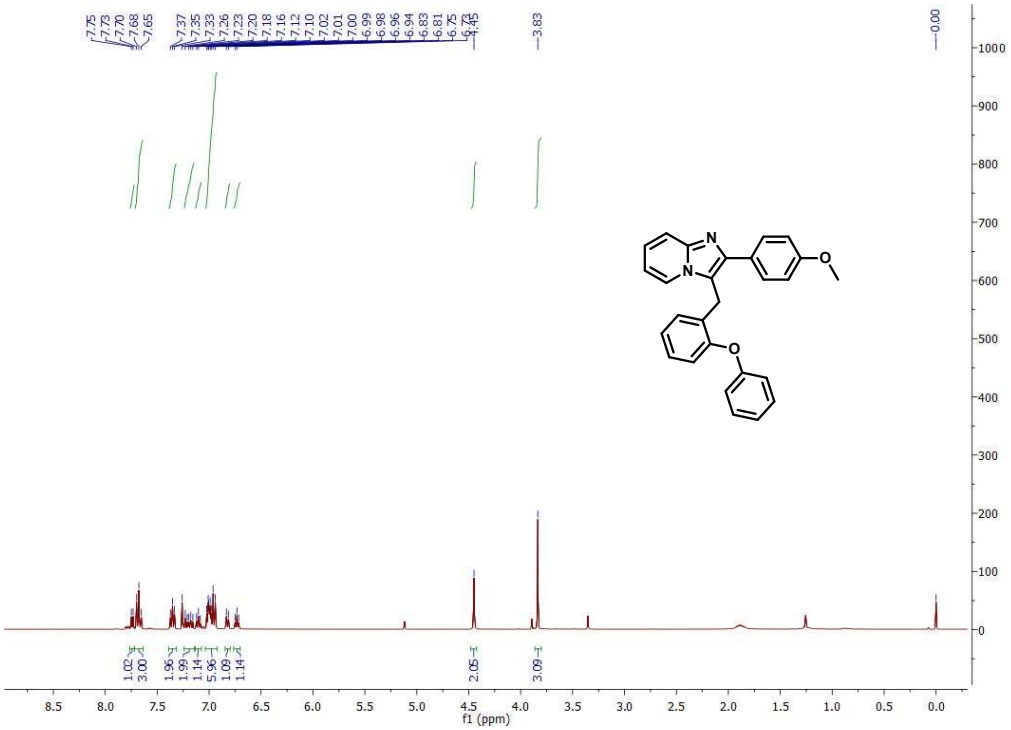
^{1}H NMR spectrum of compound **3aj** ($CDCl_3$, 400 MHz)

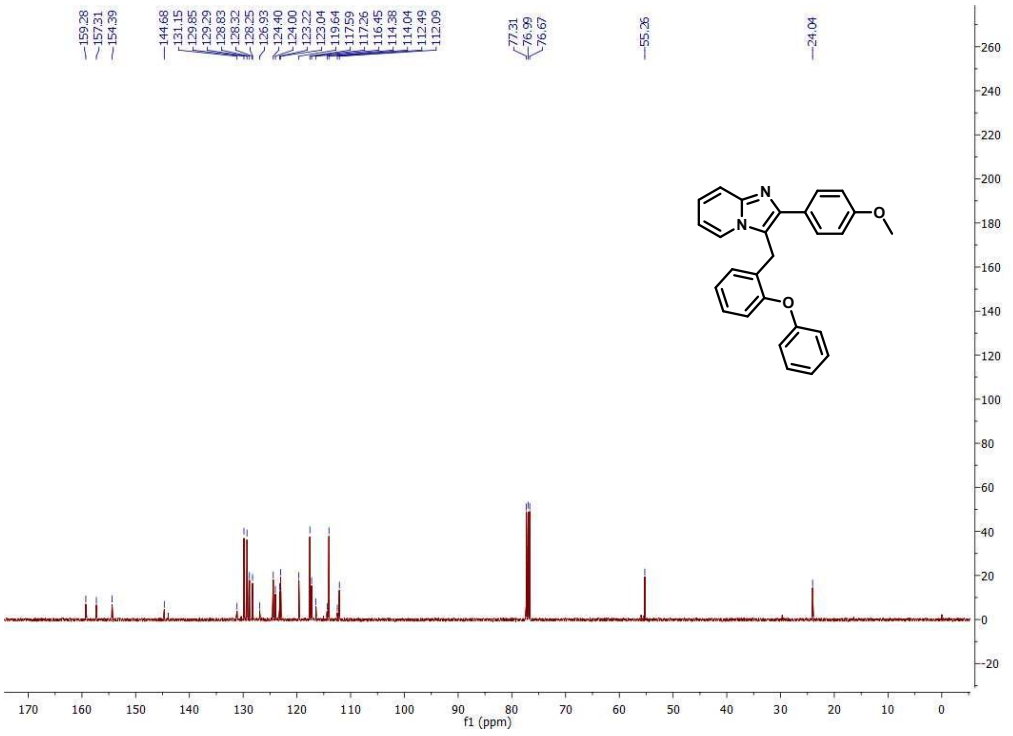




^{13}CNMR spectrum of compound **3aj** ($CDCl_3$, 100 MHz)

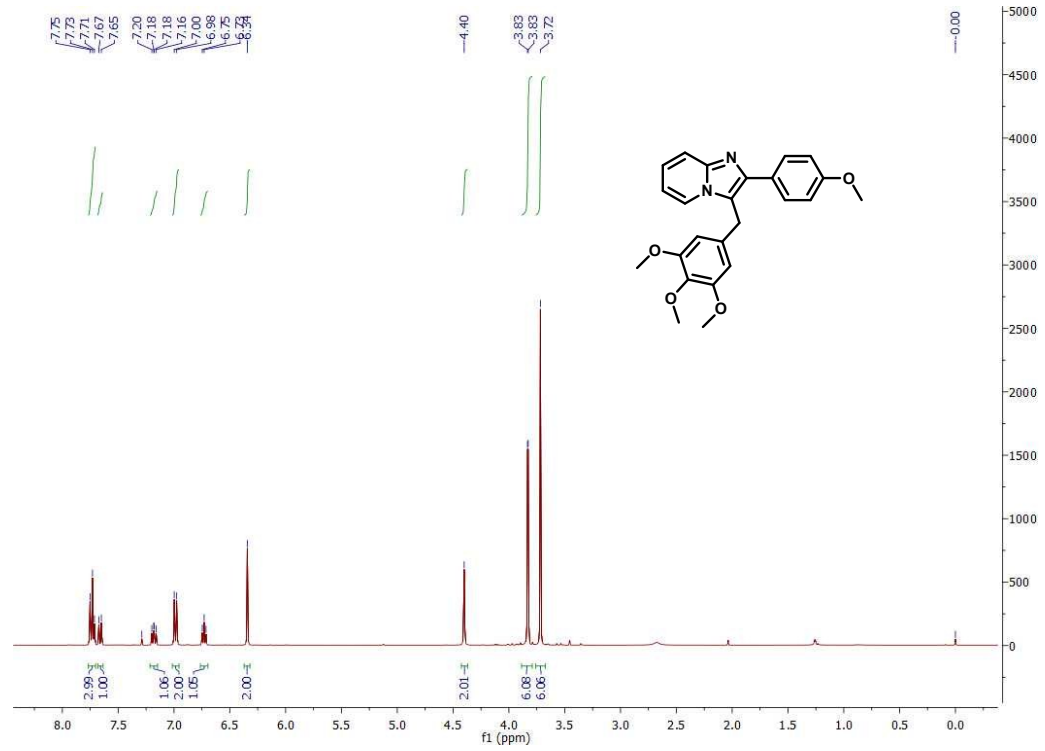
^{1}H NMR spectrum of compound **3ak** ($CDCl_3$, 400 MHz)

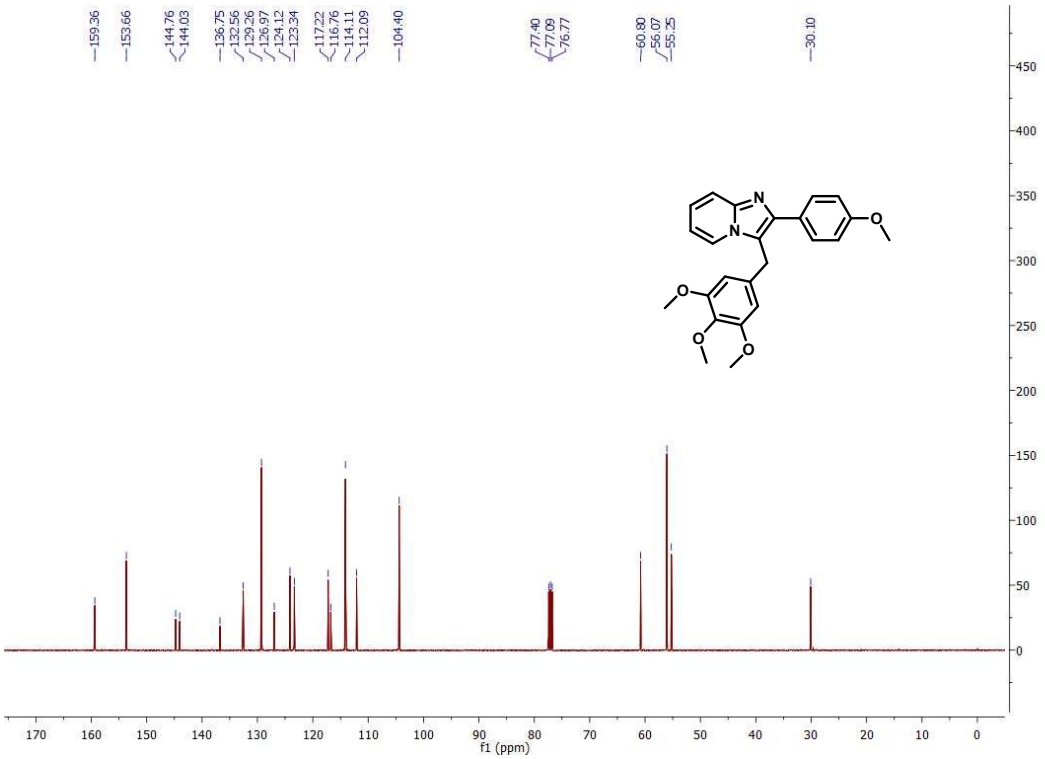




^{13}CNMR spectrum of compound **3ak** ($CDCl_3$, 100 MHz)

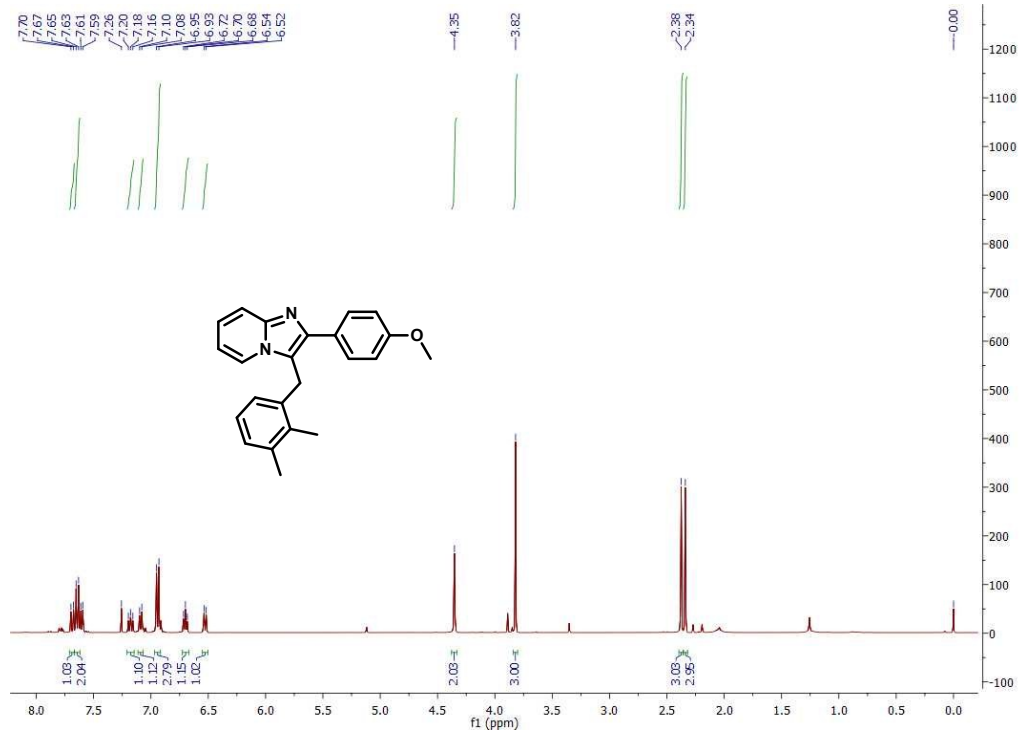
^{1}H NMR spectrum of compound **3al** ($CDCl_3$, 400 MHz)

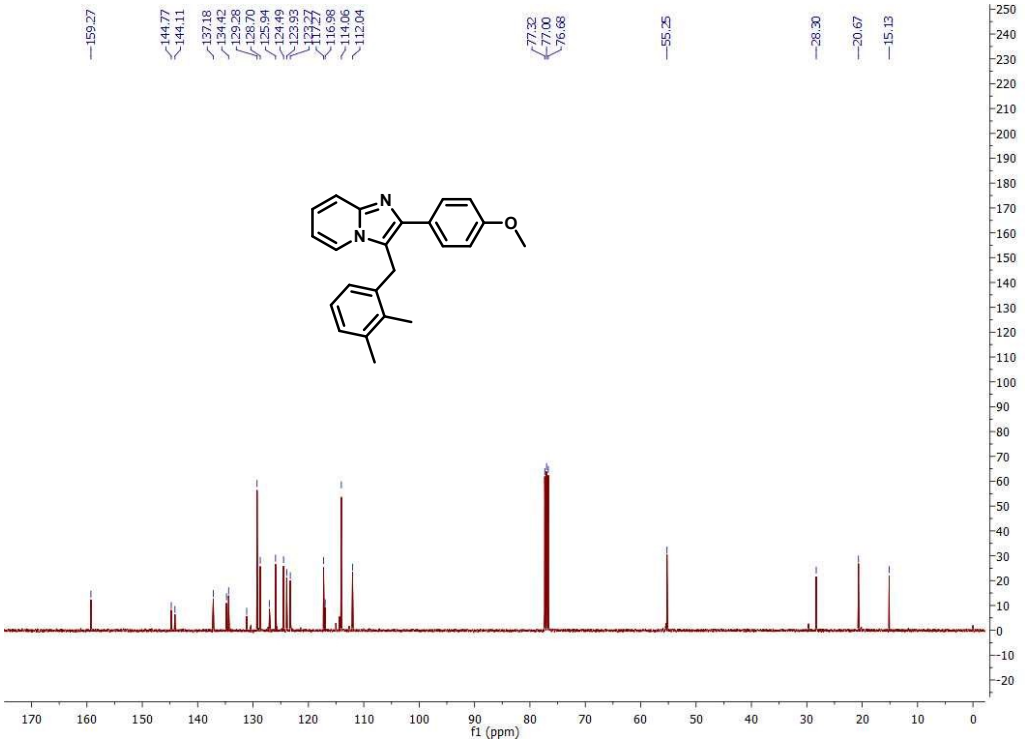




^{13}CNMR spectrum of compound **3al** ($CDCl_3$, 100 MHz)

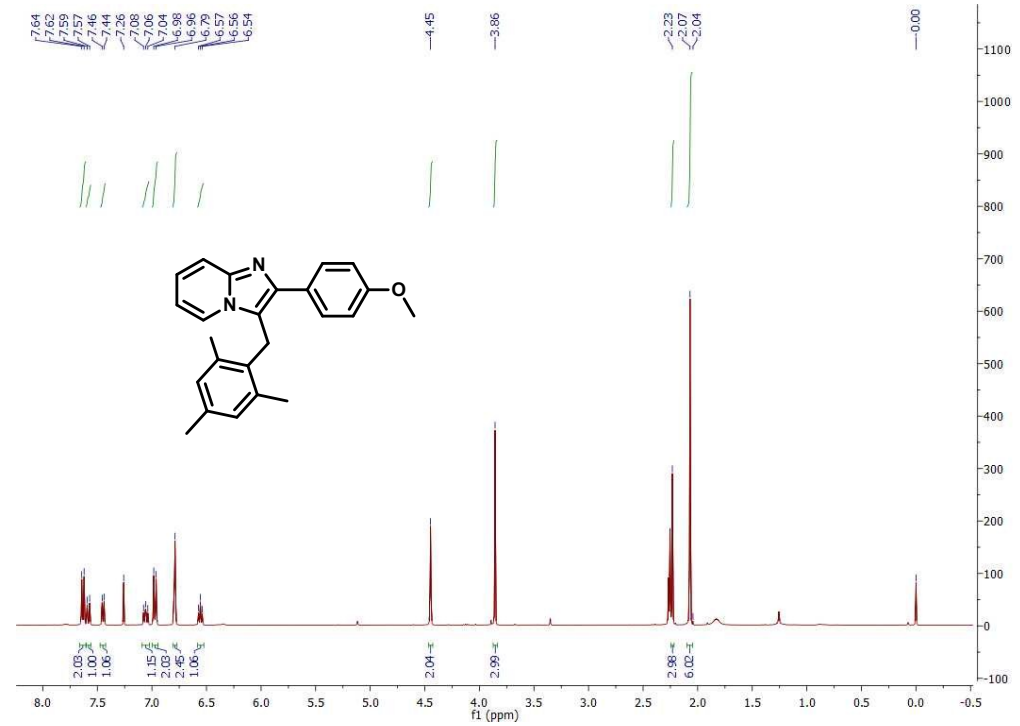
^{1}H NMR spectrum of compound **3am** ($CDCl_3$, 400 MHz)

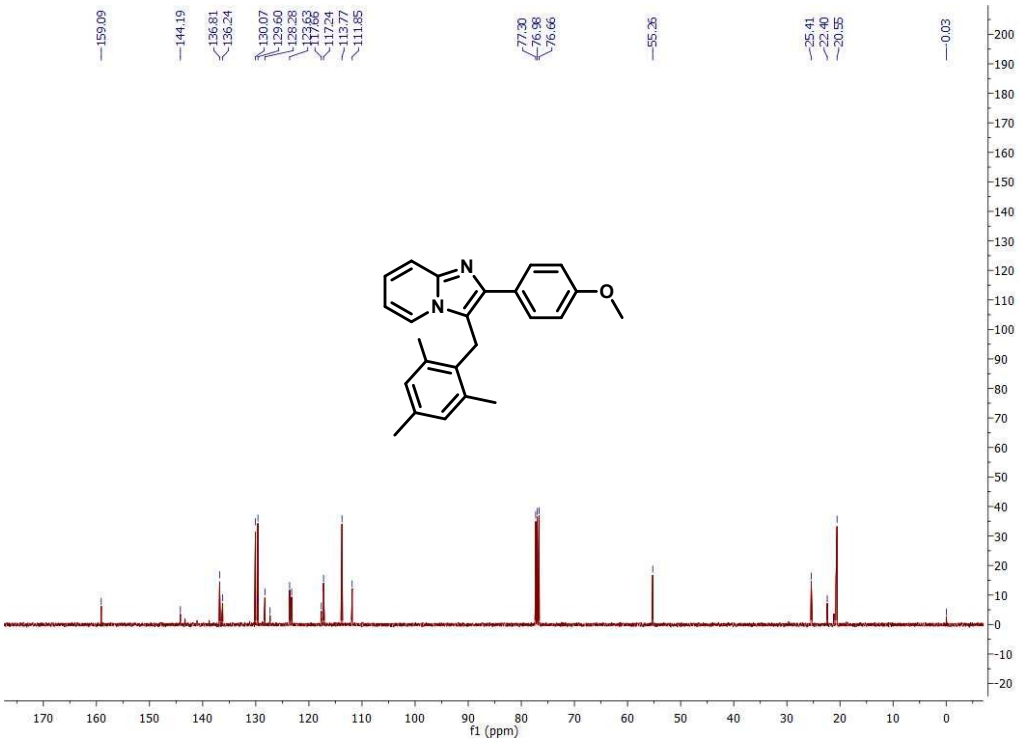




^{13}CNMR spectrum of compound **3am** ($CDCl_3$, 100 MHz)

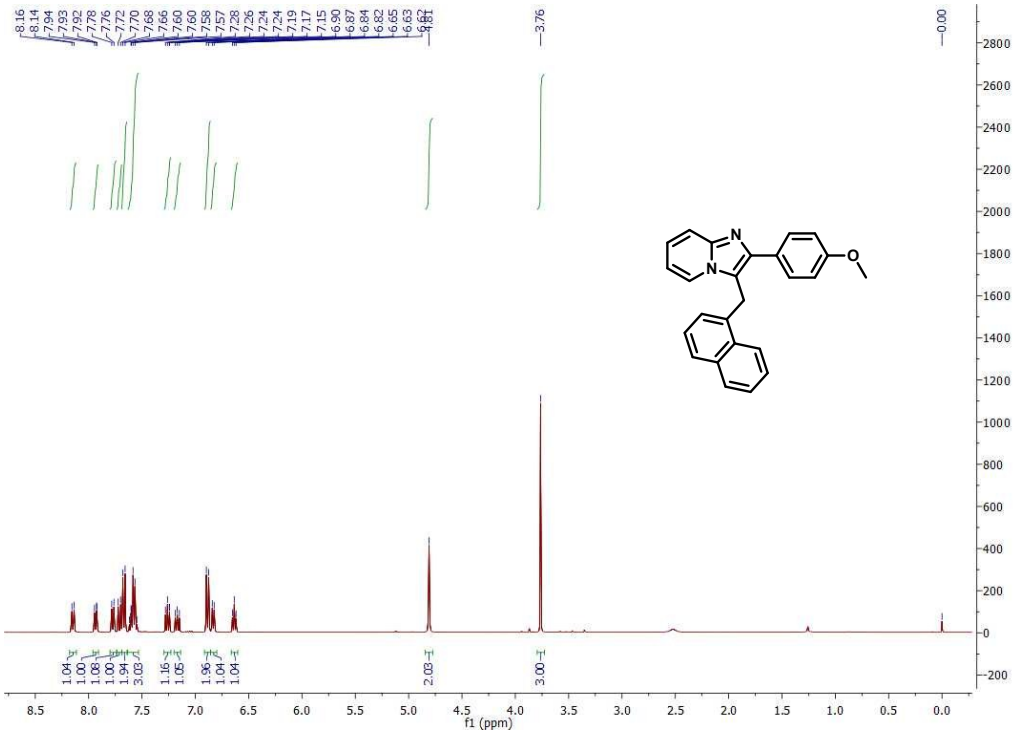
^{1}H NMR spectrum of compound **3an** ($CDCl_3$, 400 MHz)

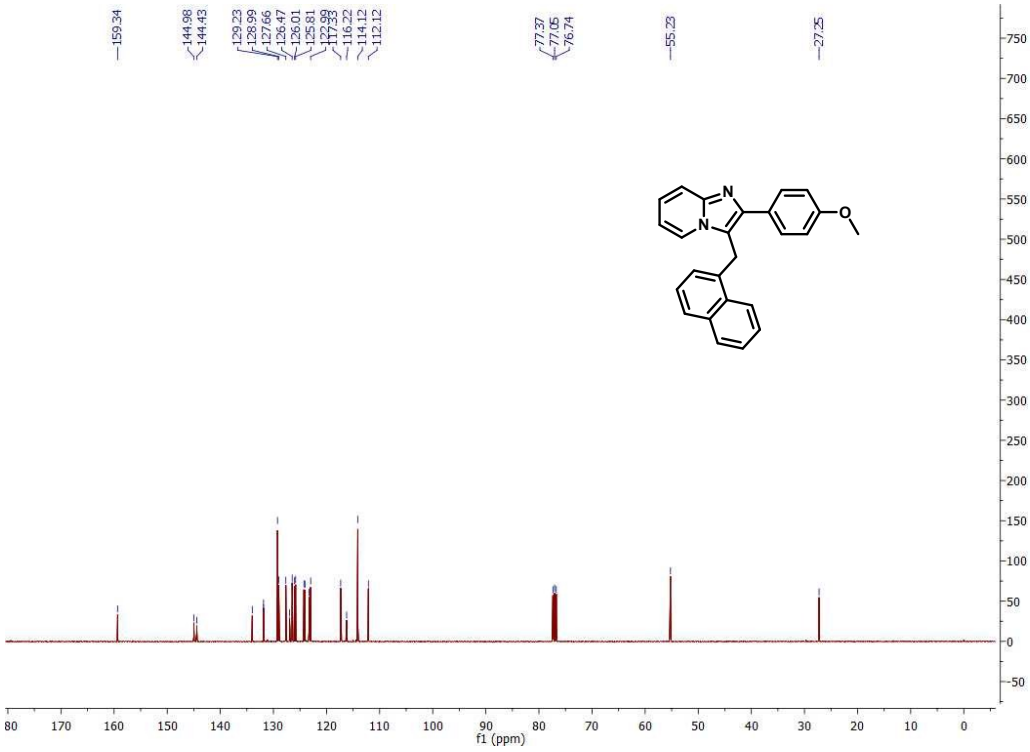




^{13}CNMR spectrum of compound **3an** ($CDCl_3$, 100 MHz)

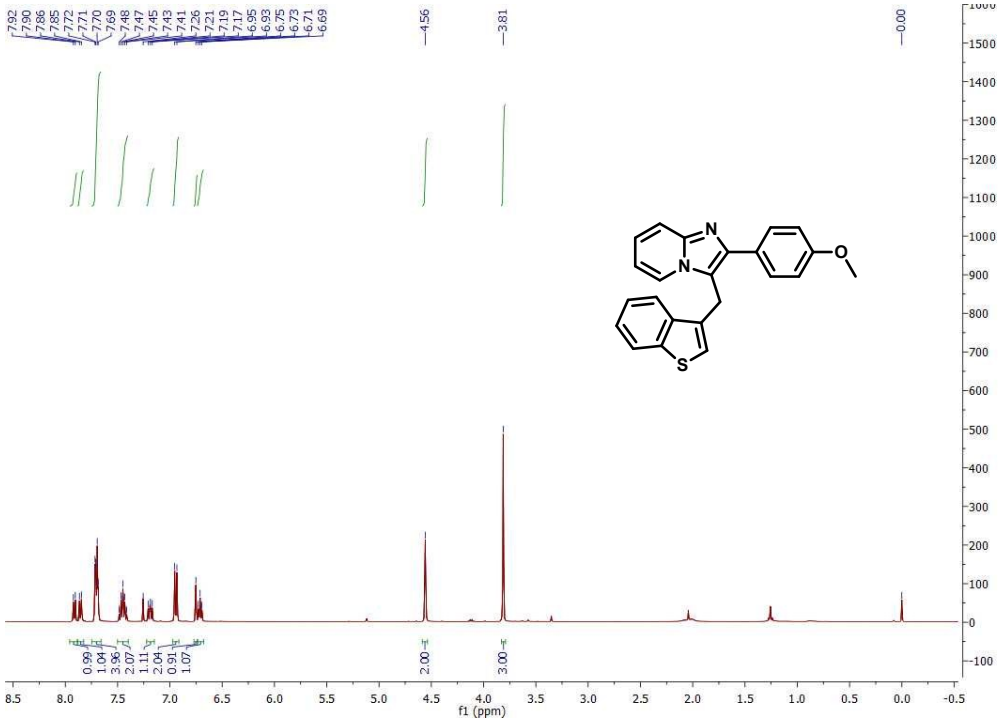
^{1}H NMR spectrum of compound **3ao** ($CDCl_3$, 400 MHz)

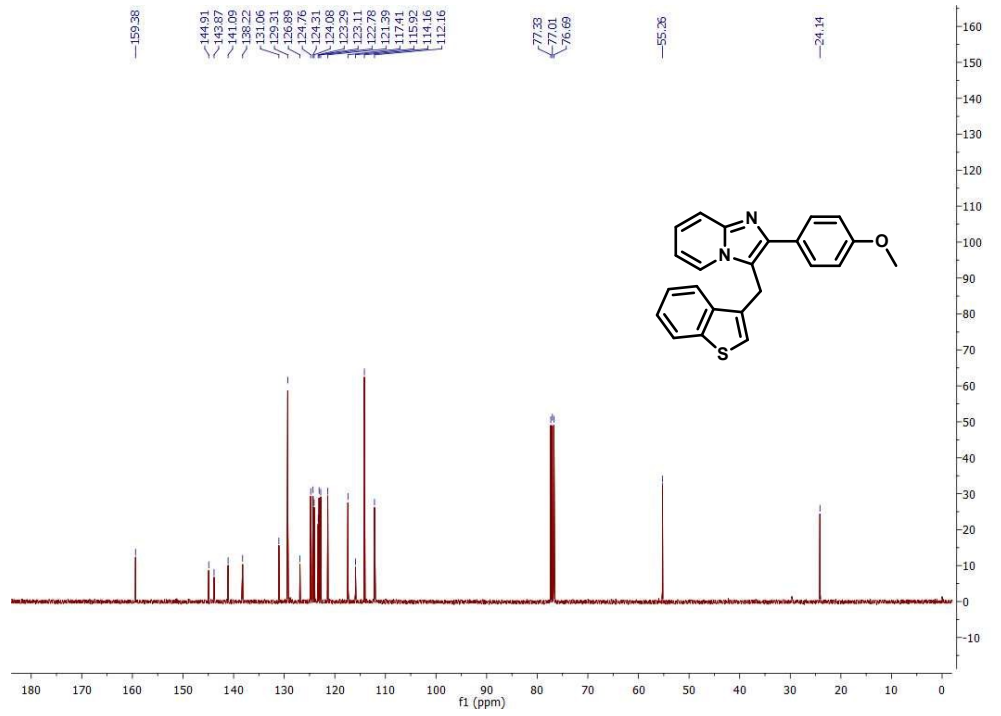




^{13}CNMR spectrum of compound **3ao** ($CDCl_3$, 100 MHz)

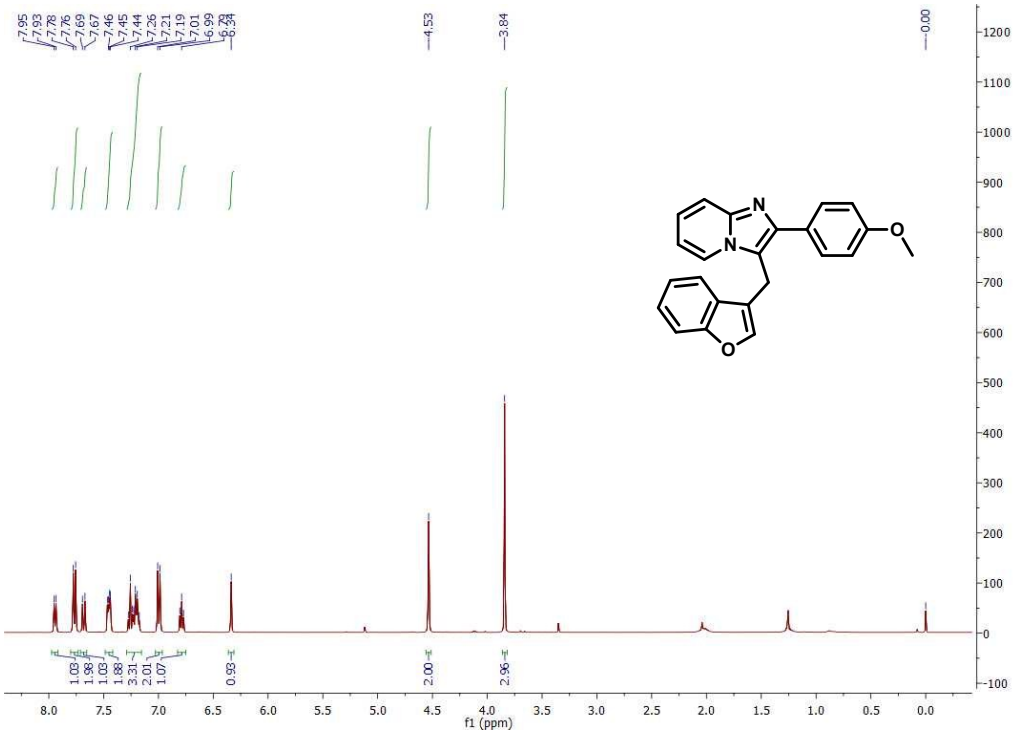
^{1}H NMR spectrum of compound **3ap** ($CDCl_3$, 400 MHz)

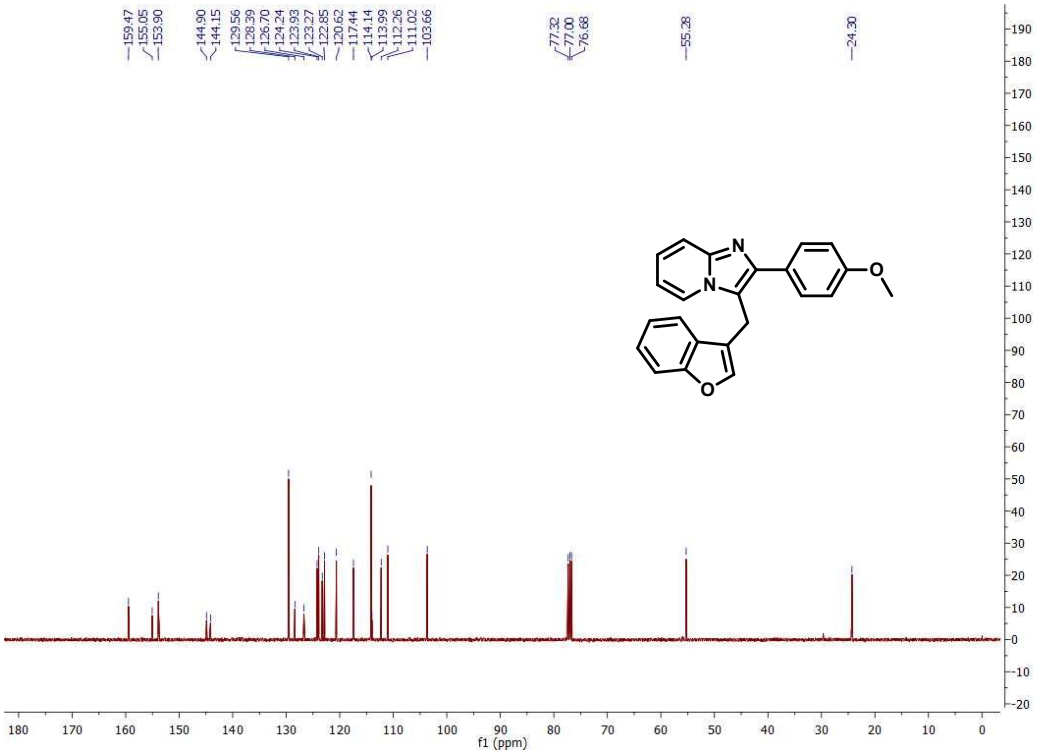




^{13}CNMR spectrum of compound **3ap** ($CDCl_3$, 100 MHz)

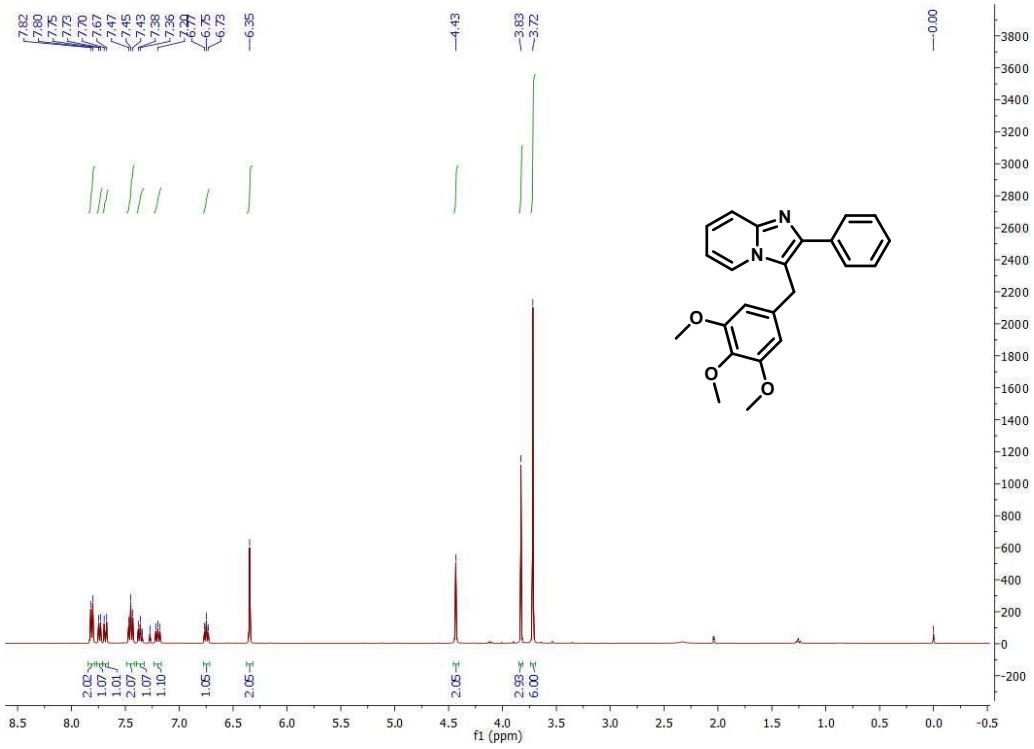
^{1}H NMR spectrum of compound **3aq** ($CDCl_3$, 400 MHz)

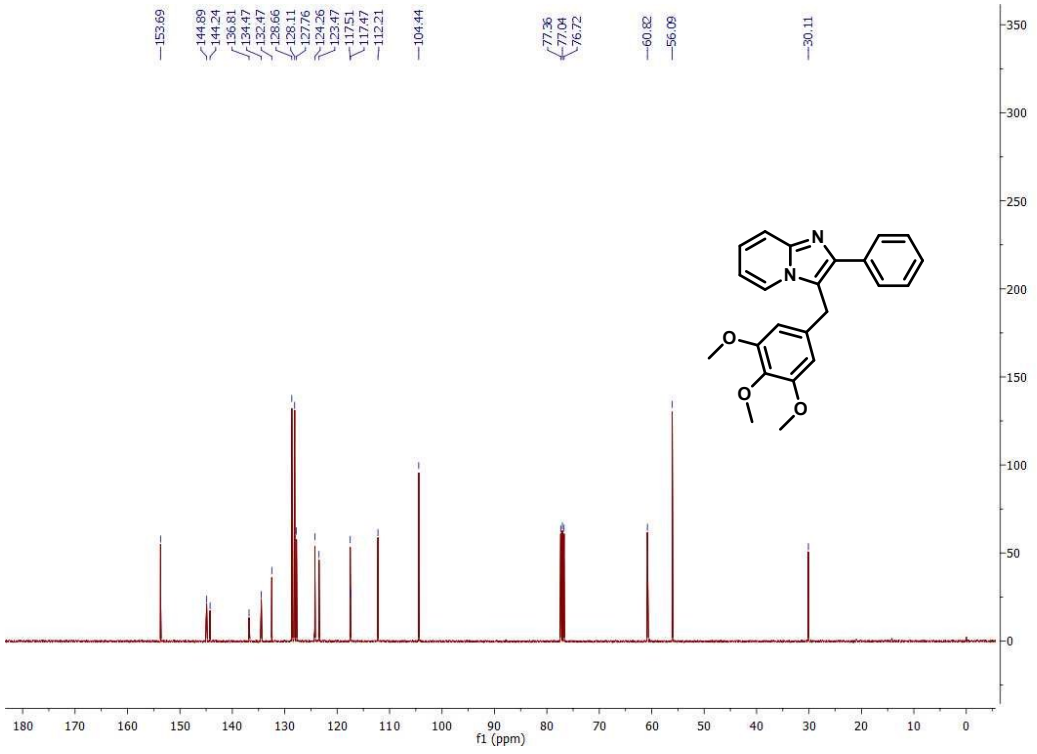




^{13}CNMR spectrum of compound **3aq** ($CDCl_3$, 100 MHz)

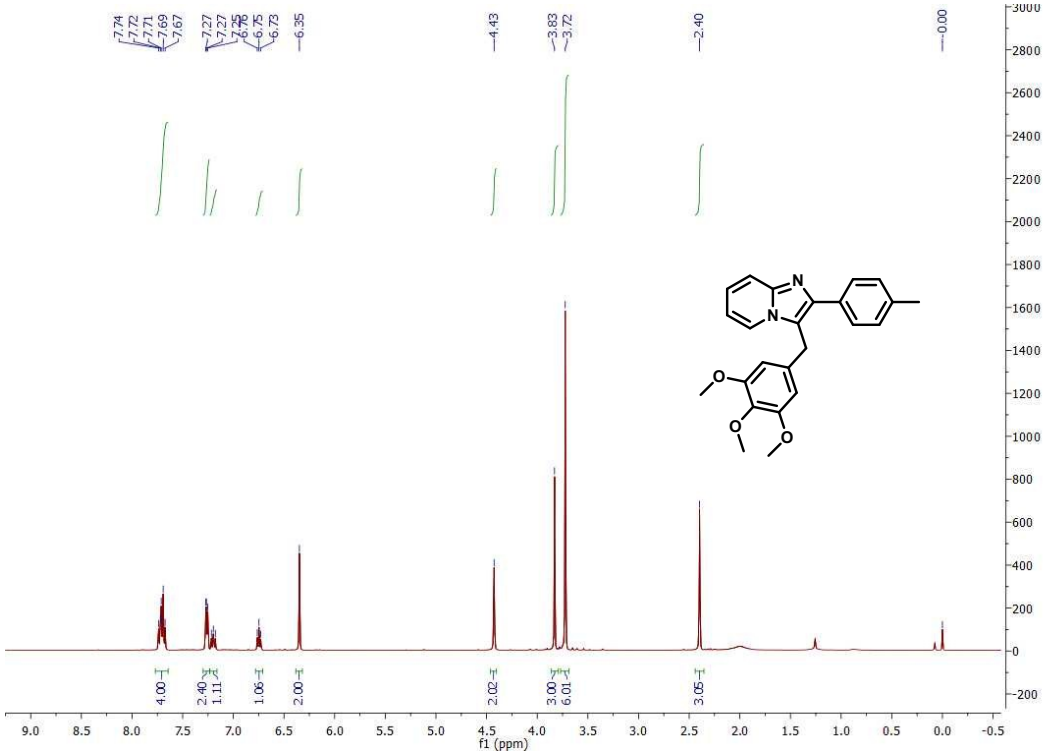
^{1}H NMR spectrum of compound **3ar** ($CDCl_3$, 400 MHz)

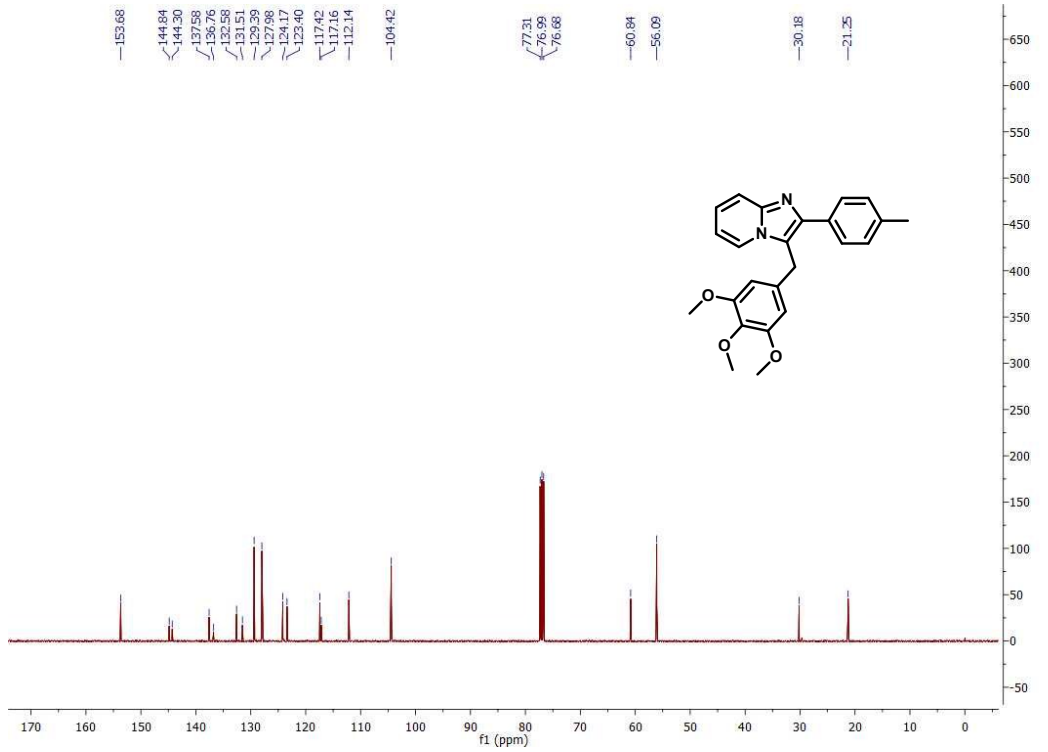




^{13}CNMR spectrum of compound **3ar** ($CDCl_3$, 100 MHz)

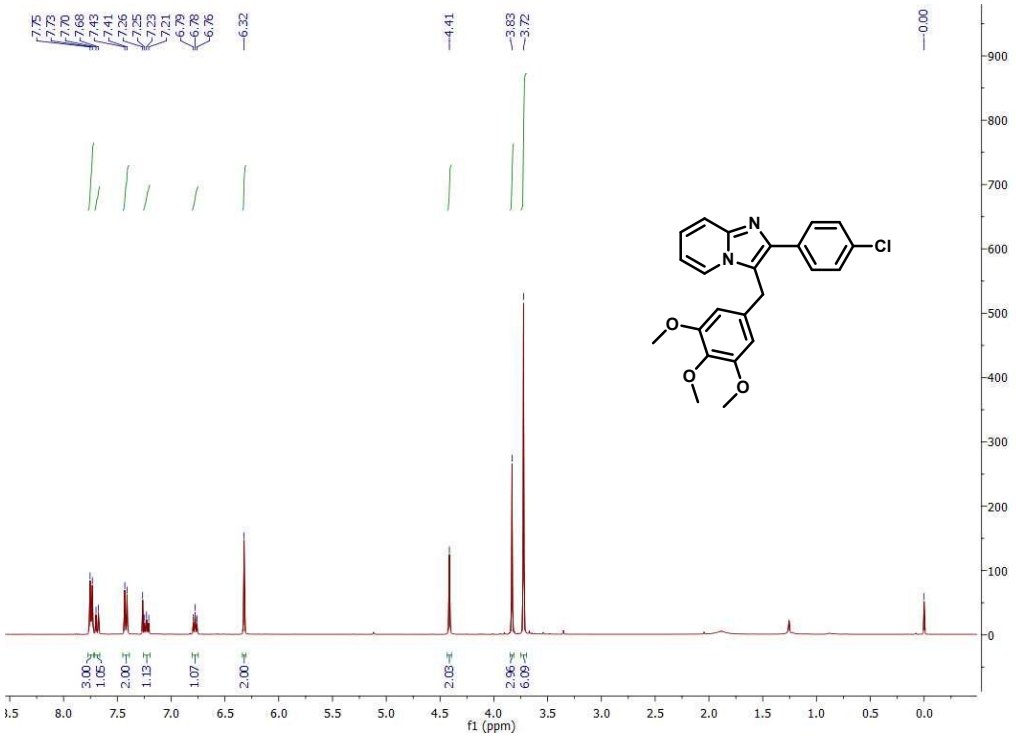
^{1}H NMR spectrum of compound **3as** ($CDCl_3$, 400 MHz)

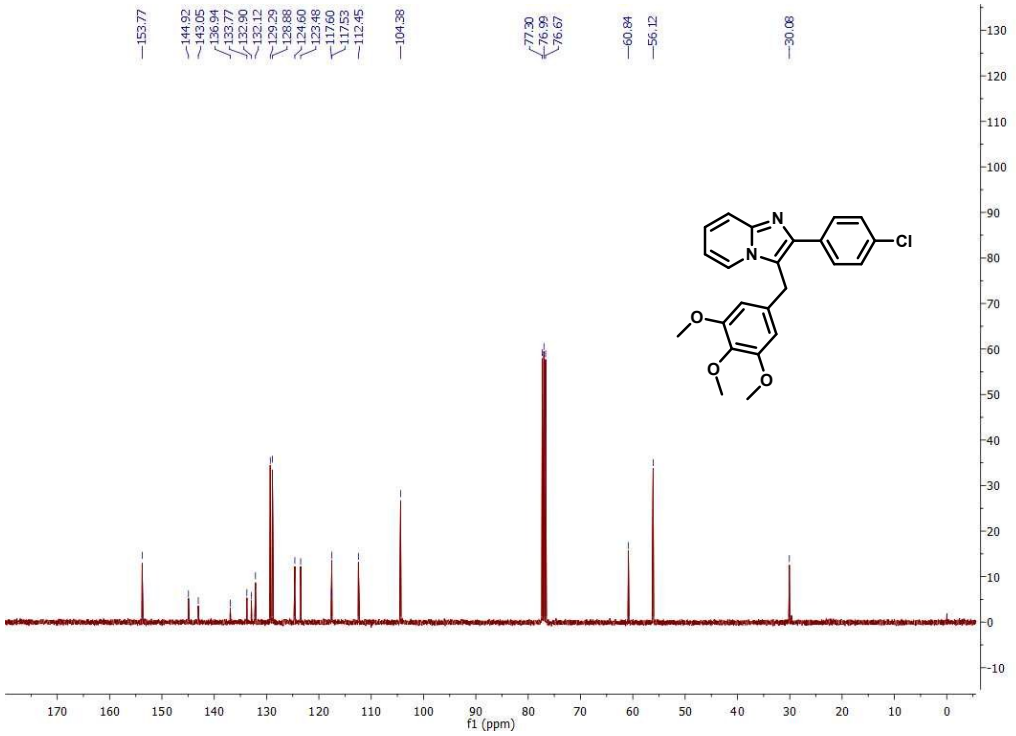




^{13}CNMR spectrum of compound **3as** ($CDCl_3$, 100 MHz)

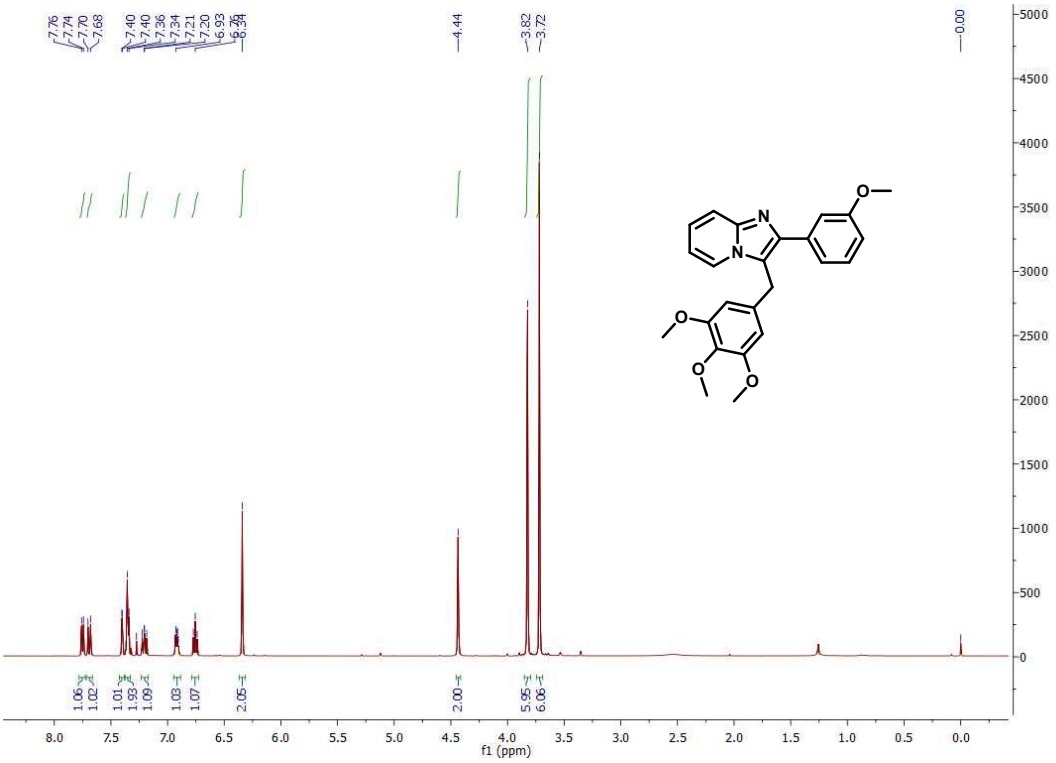
^{1}H NMR spectrum of compound **3at** ($CDCl_3$, 400 MHz)

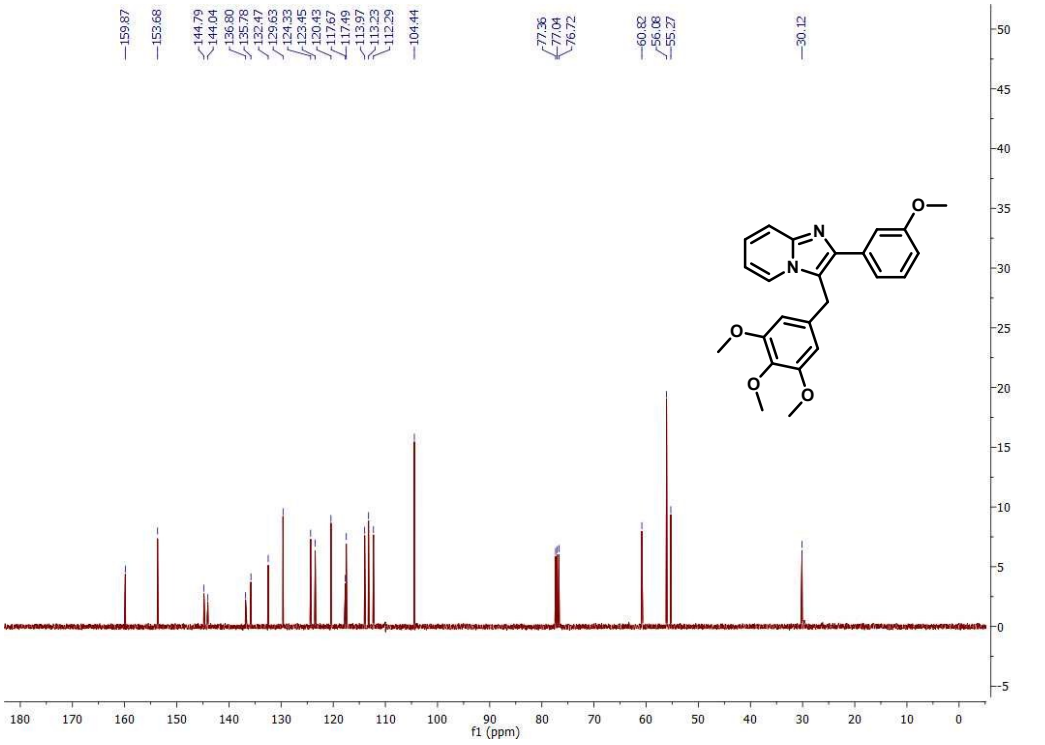




^{13}CNMR spectrum of compound **3at** ($CDCl_3$, 100 MHz)

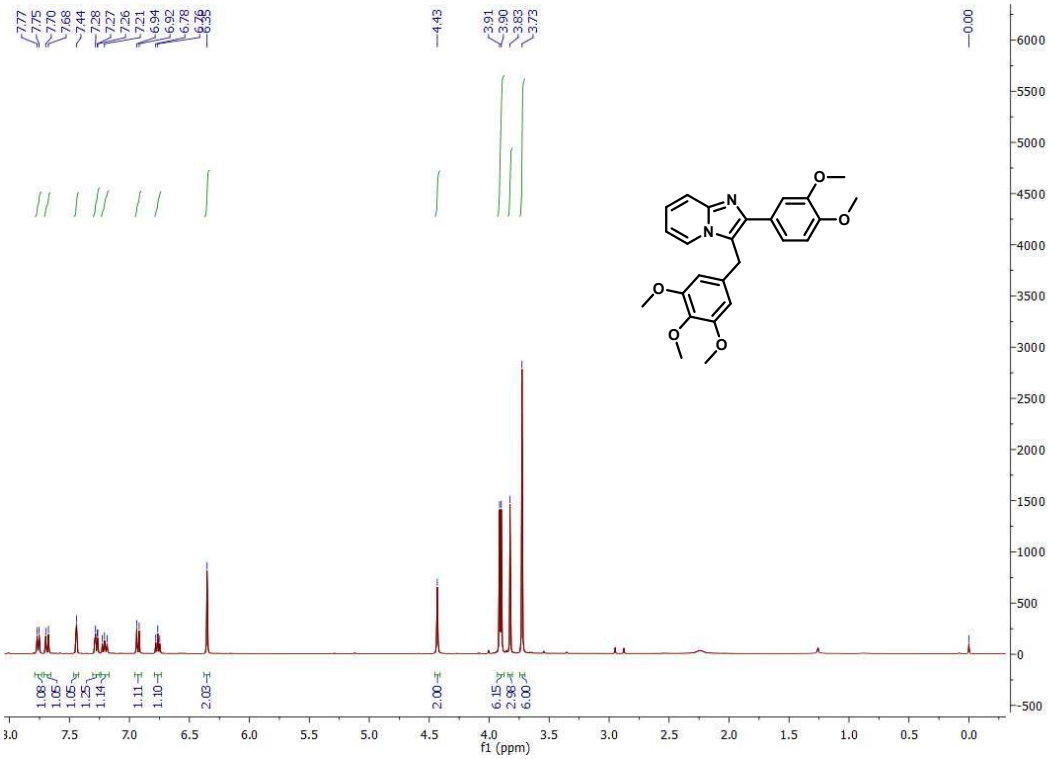
^{1}H NMR spectrum of compound **3au** ($CDCl_3$, 400 MHz)

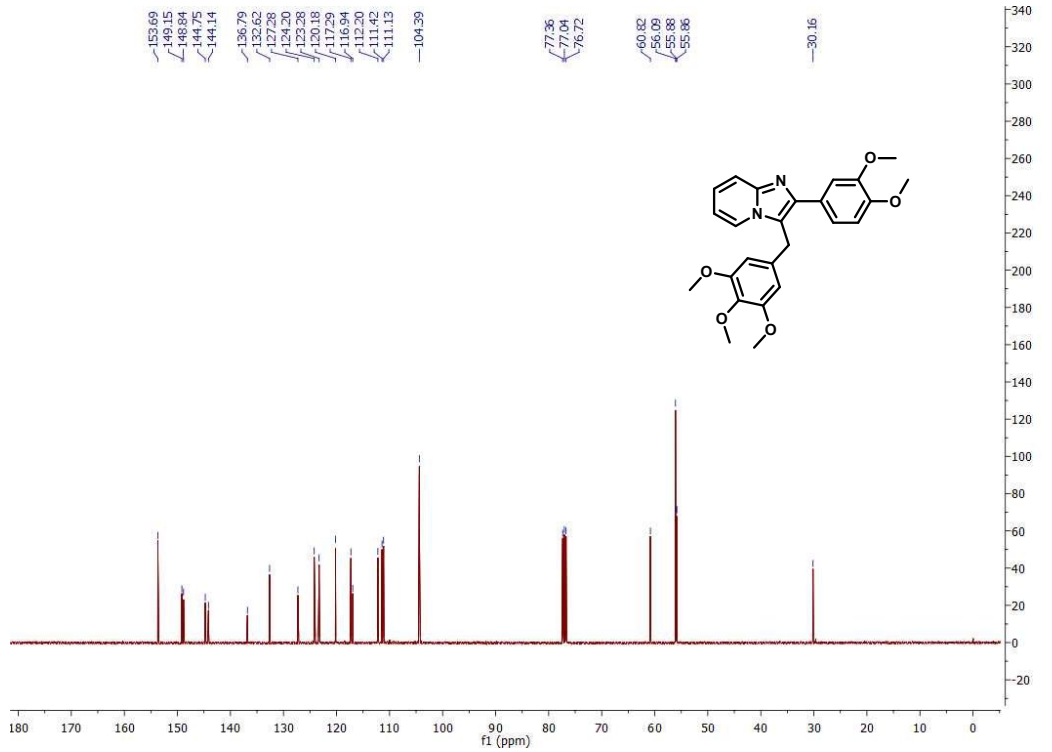




^{13}CNMR spectrum of compound 3**au** ($CDCl_3$, 100 MHz)

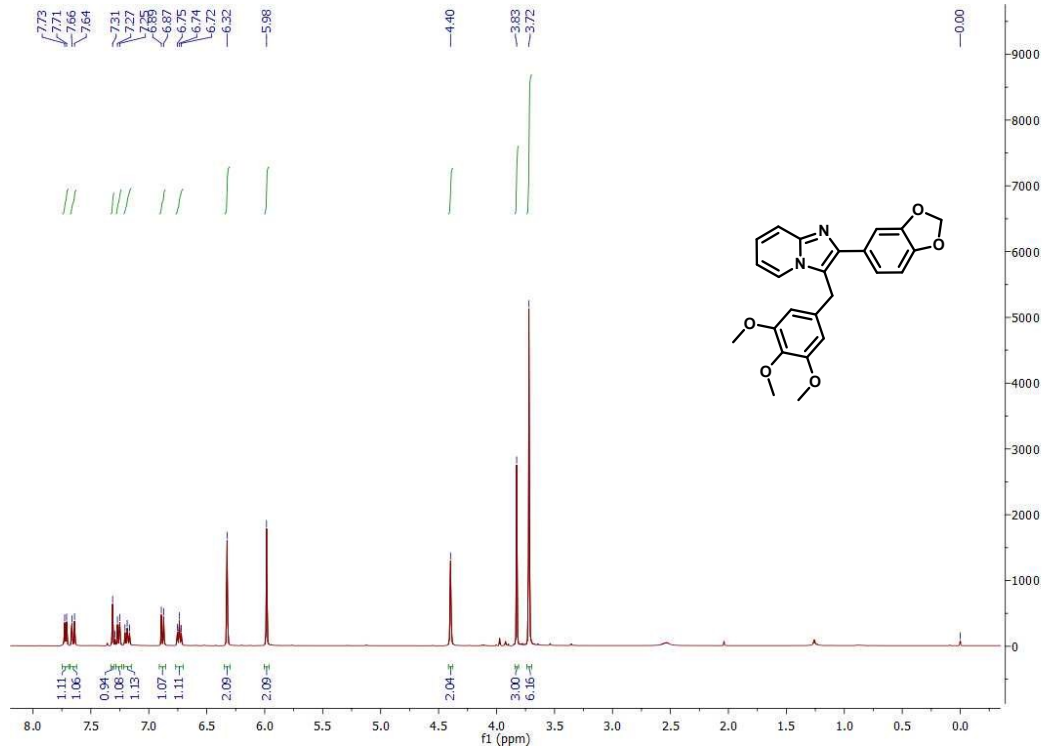
^{1}H NMR spectrum of compound **3av** ($CDCl_3$, 400 MHz)

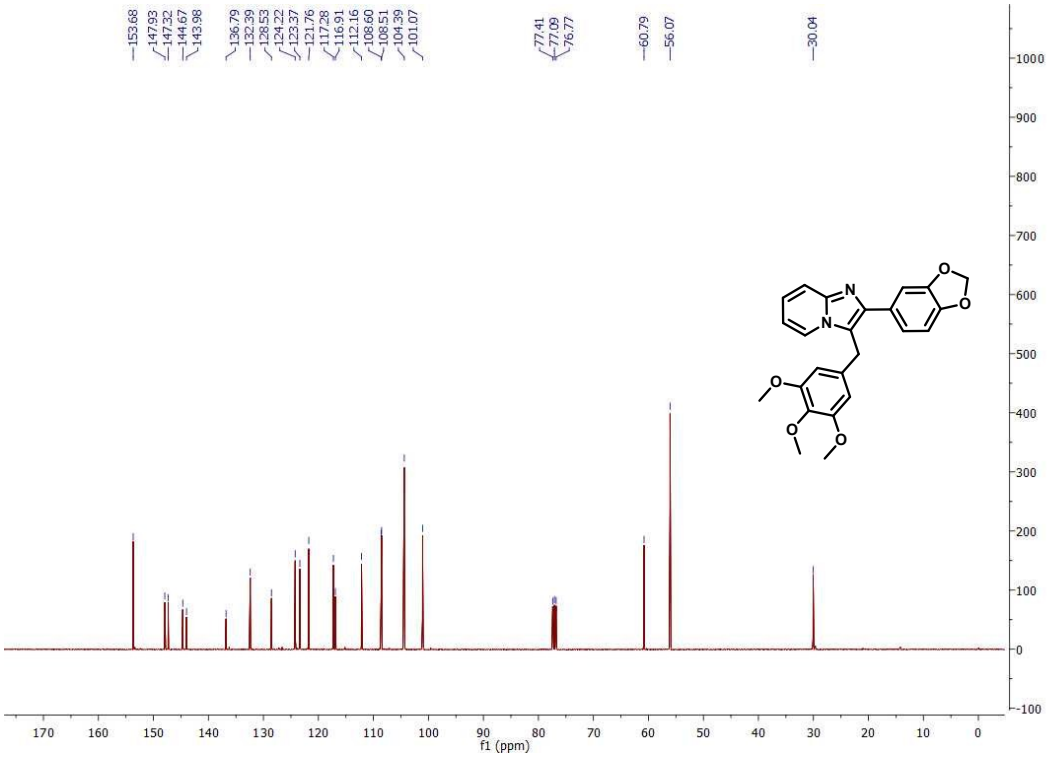




^{13}CNMR spectrum of compound **3av** ($CDCl_3$, 100 MHz)

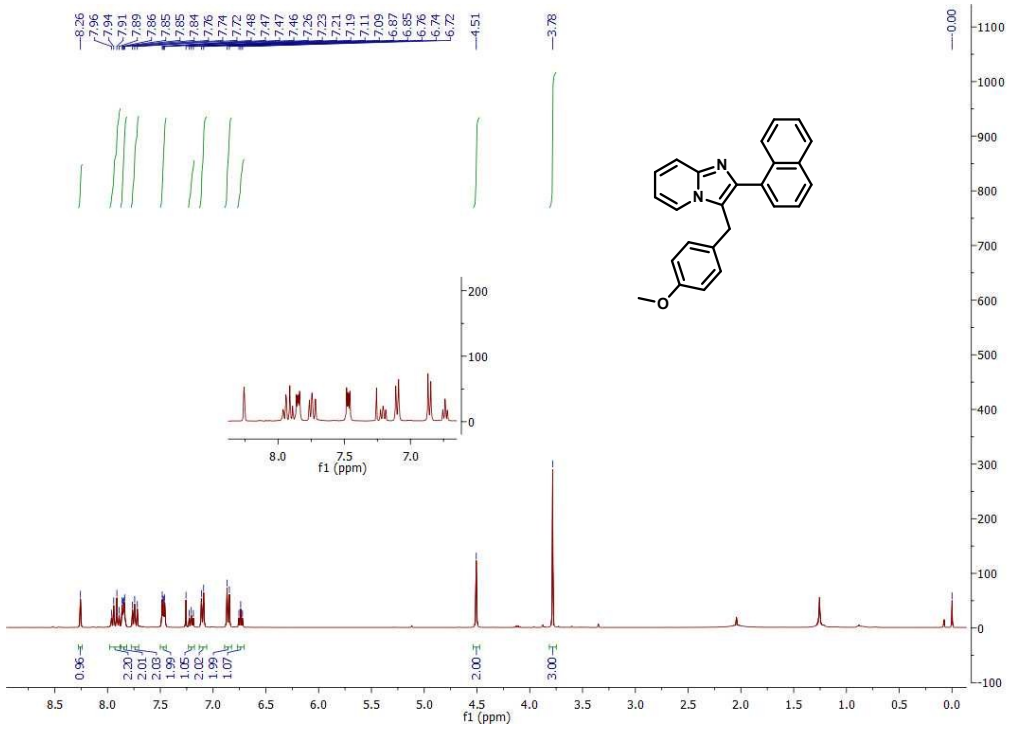
^{1}H NMR spectrum of compound **3aw** ($CDCl_3$, 400 MHz)

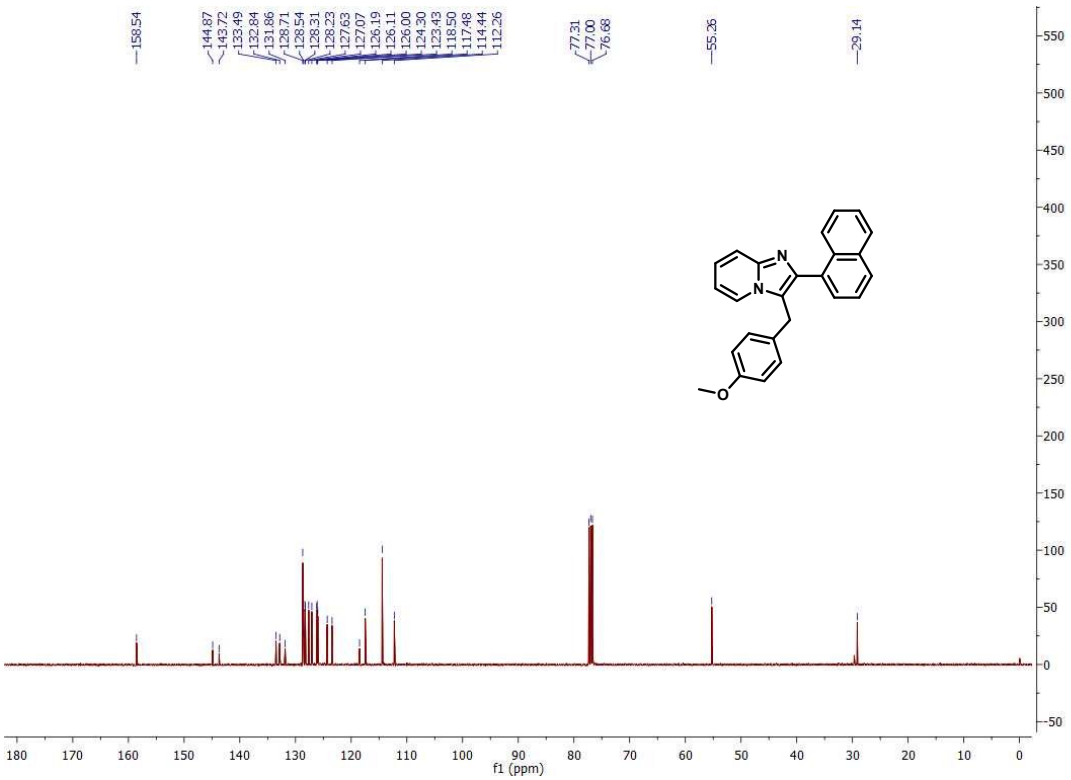




^{13}CNMR spectrum of compound **3aw** ($CDCl_3$, 100 MHz)

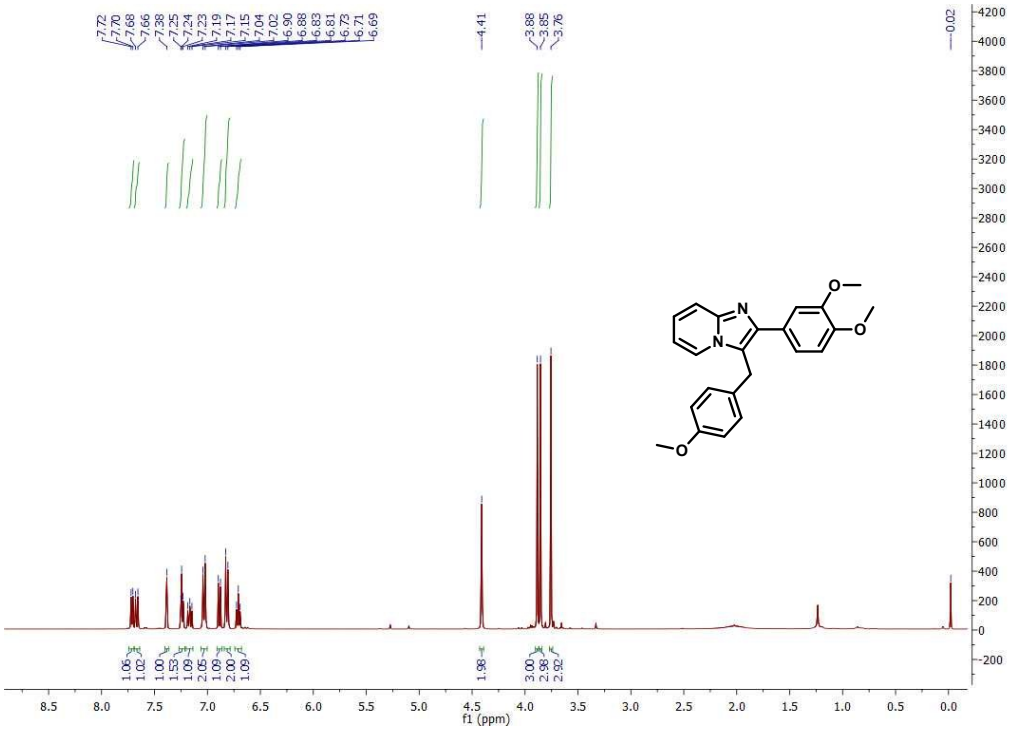
^{1}H NMR spectrum of compound **3ax** ($CDCl_3$, 400 MHz)

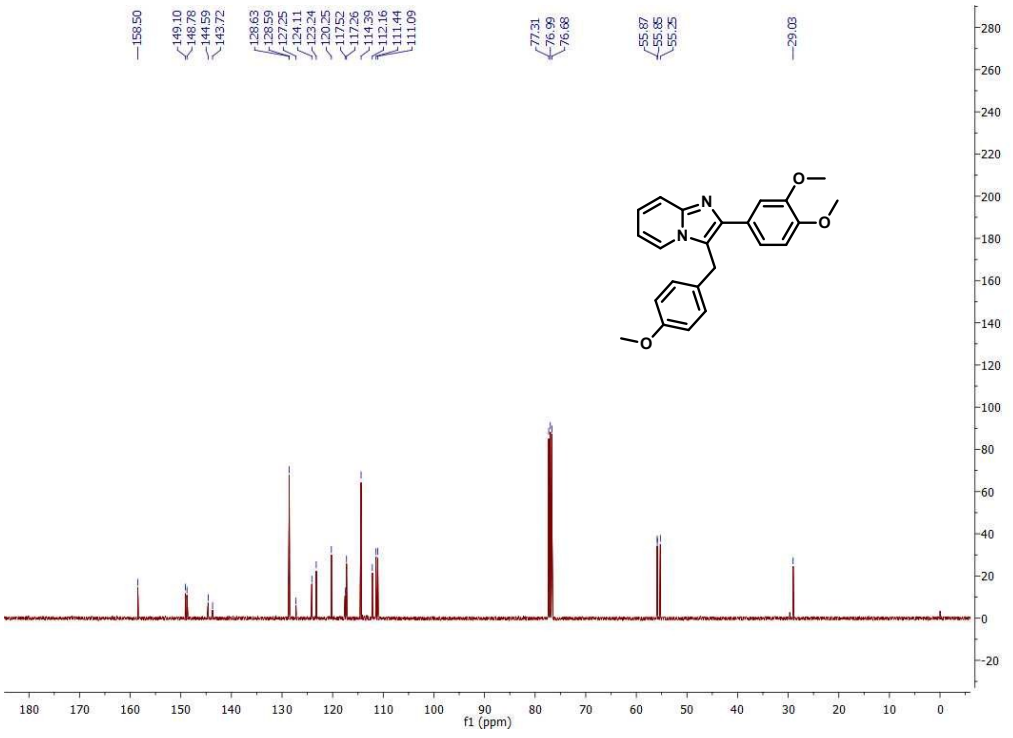




^{13}CNMR spectrum of compound **3ax** ($CDCl_3$, 100 MHz)

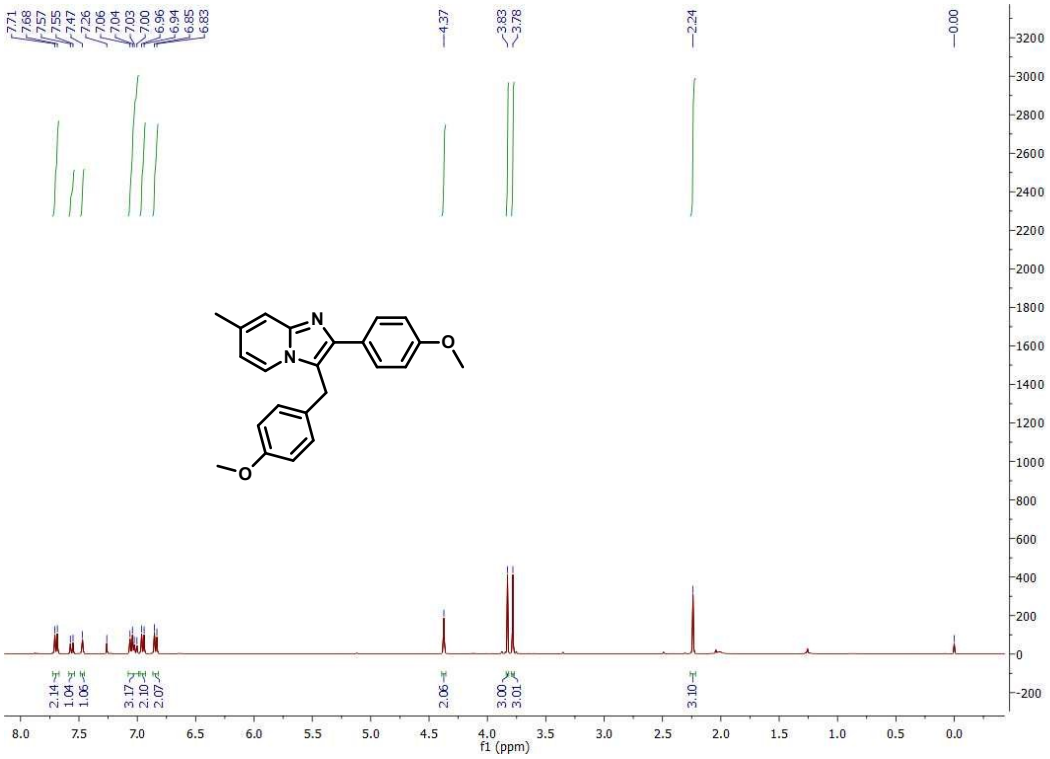
^{1}H NMR spectrum of compound **3ay** ($CDCl_3$, 400 MHz)

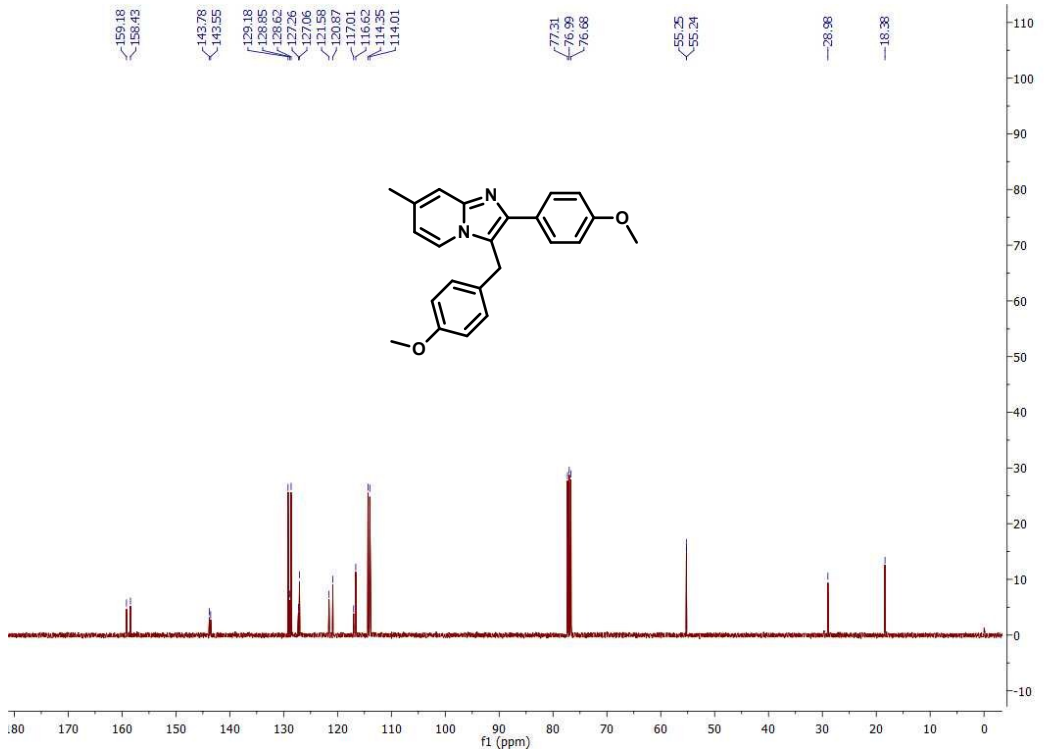




^{13}CNMR spectrum of compound **3ay** ($CDCl_3$, 100 MHz)

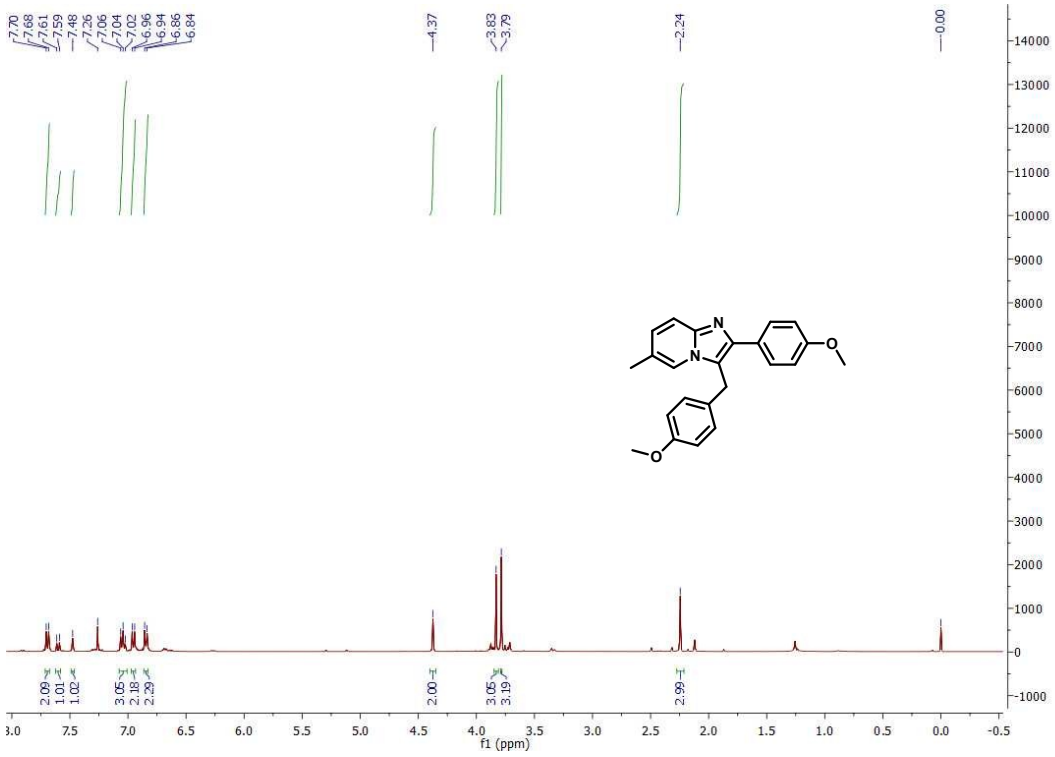
^{1}H NMR spectrum of compound **4a** ($CDCl_3$, 400 MHz)

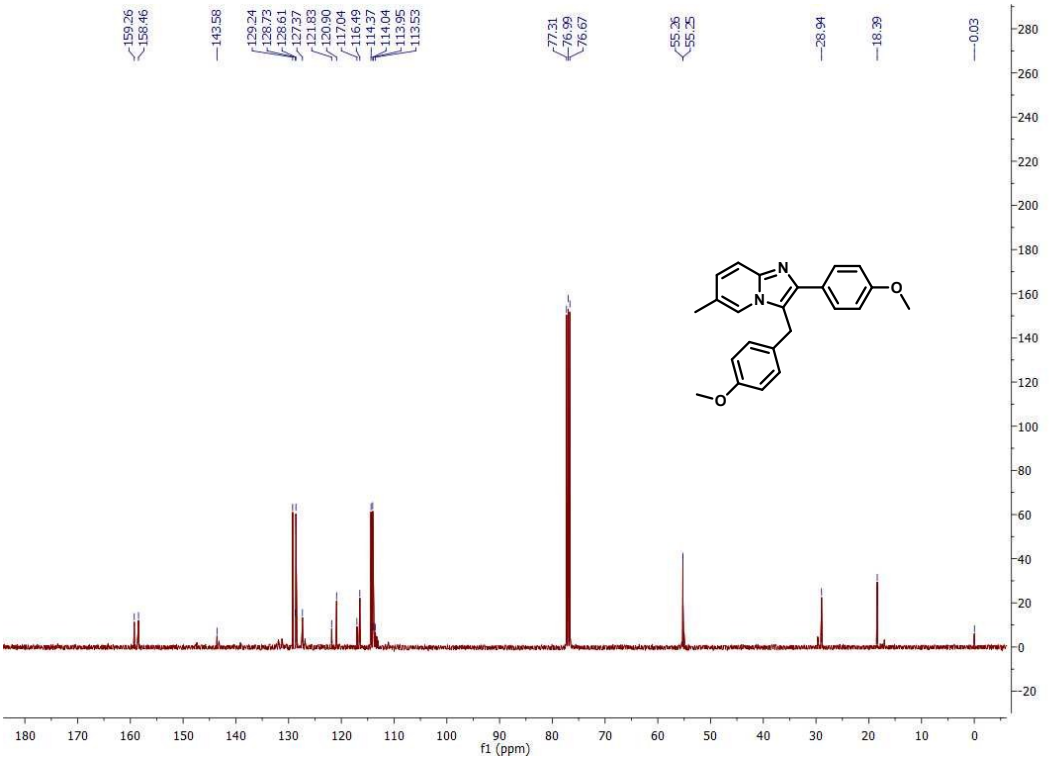




^{13}CNMR spectrum of compound **4a** ($CDCl_3$, 100 MHz)

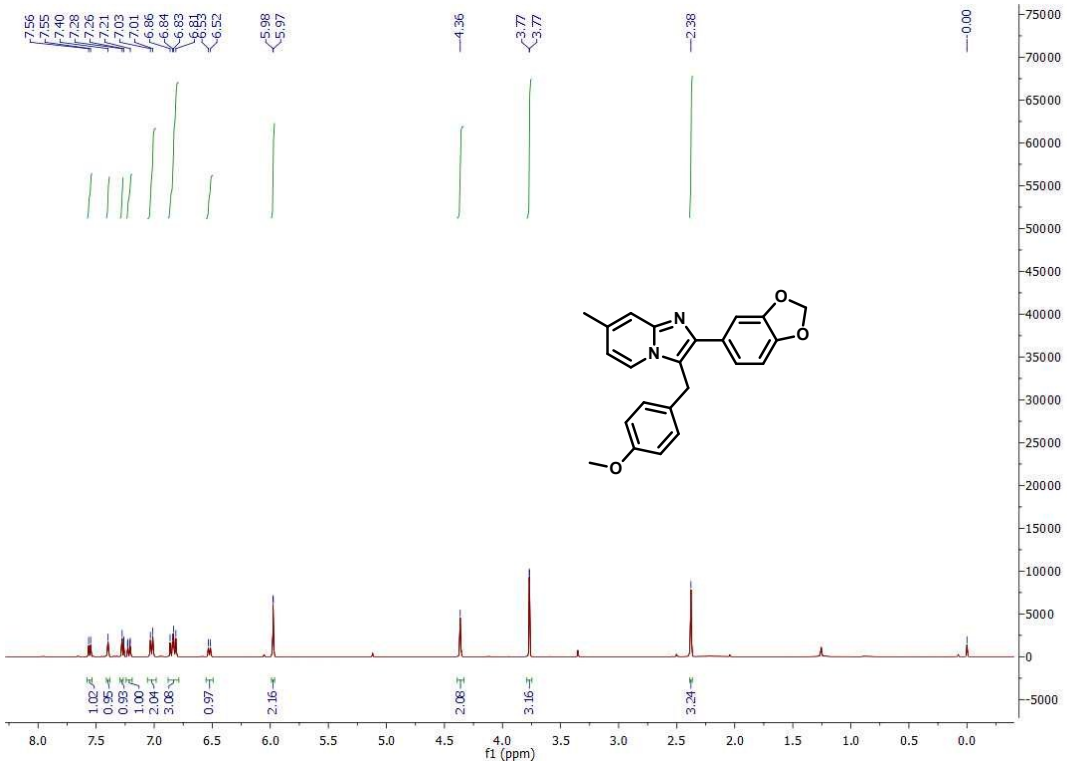
^{1}H NMR spectrum of compound **4b** ($CDCl_3$, 400 MHz)

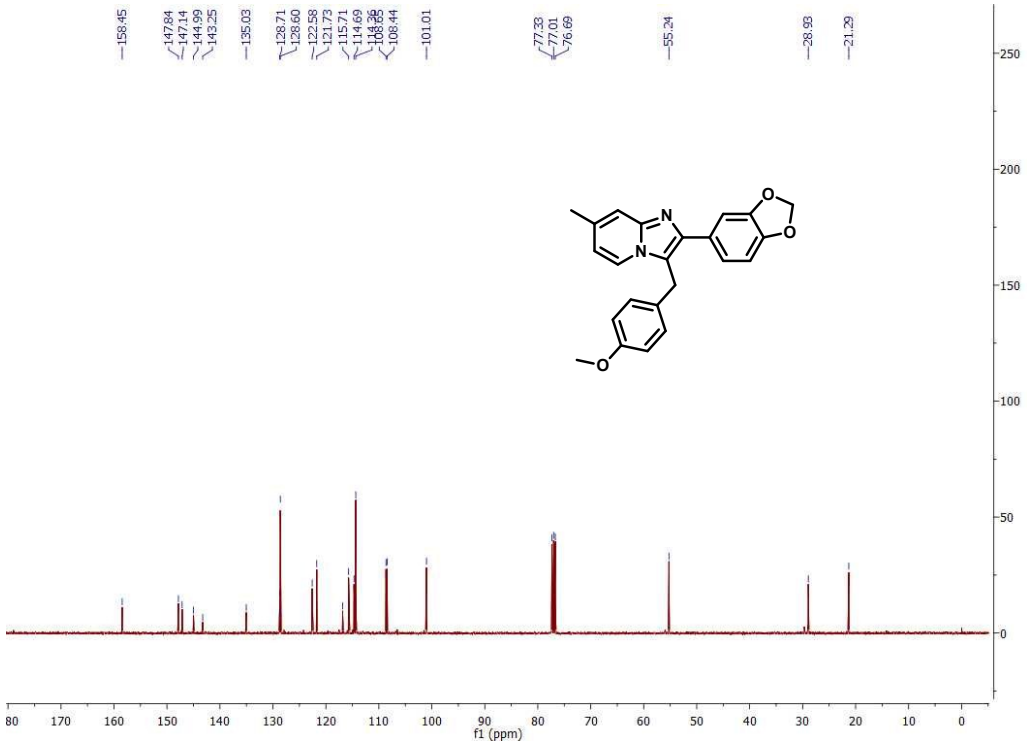




^{13}CNMR spectrum of compound **4b** ($CDCl_3$, 100 MHz)

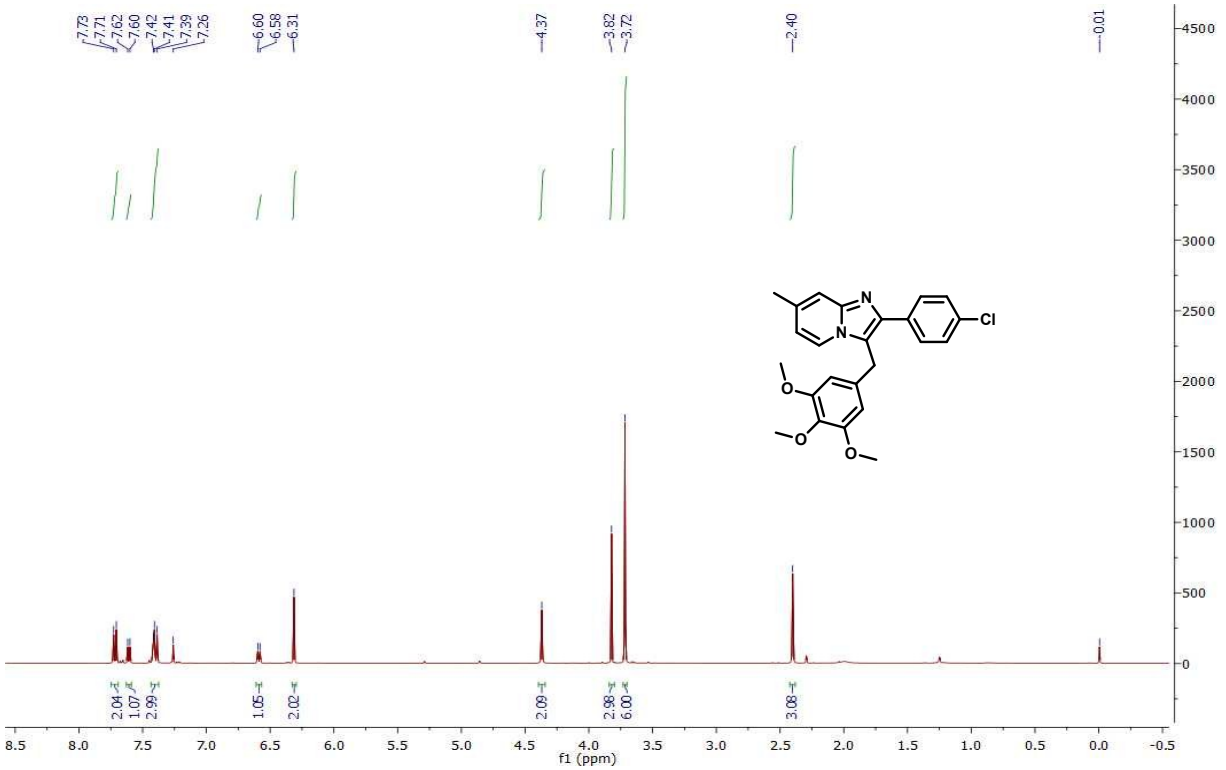
^{1}H NMR spectrum of compound **4c** ($CDCl_3$, 400 MHz)

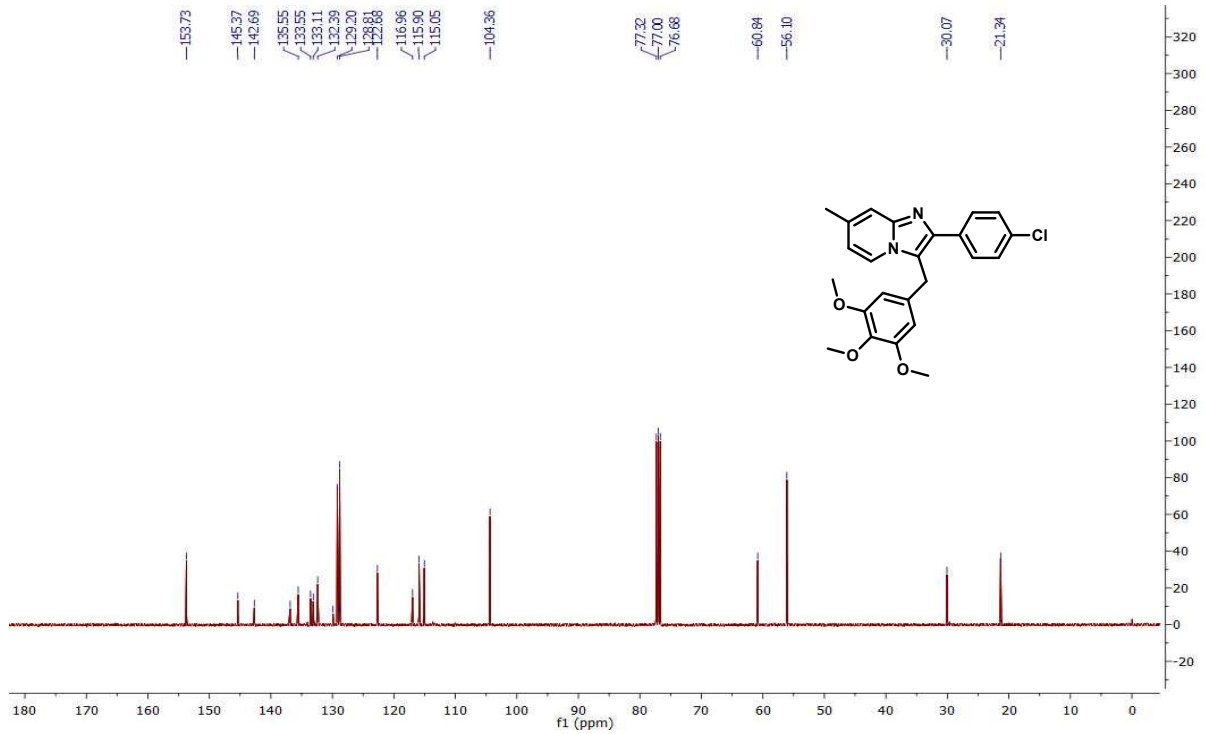




^{13}CNMR spectrum of compound **4c** ($CDCl_3$, 100 MHz

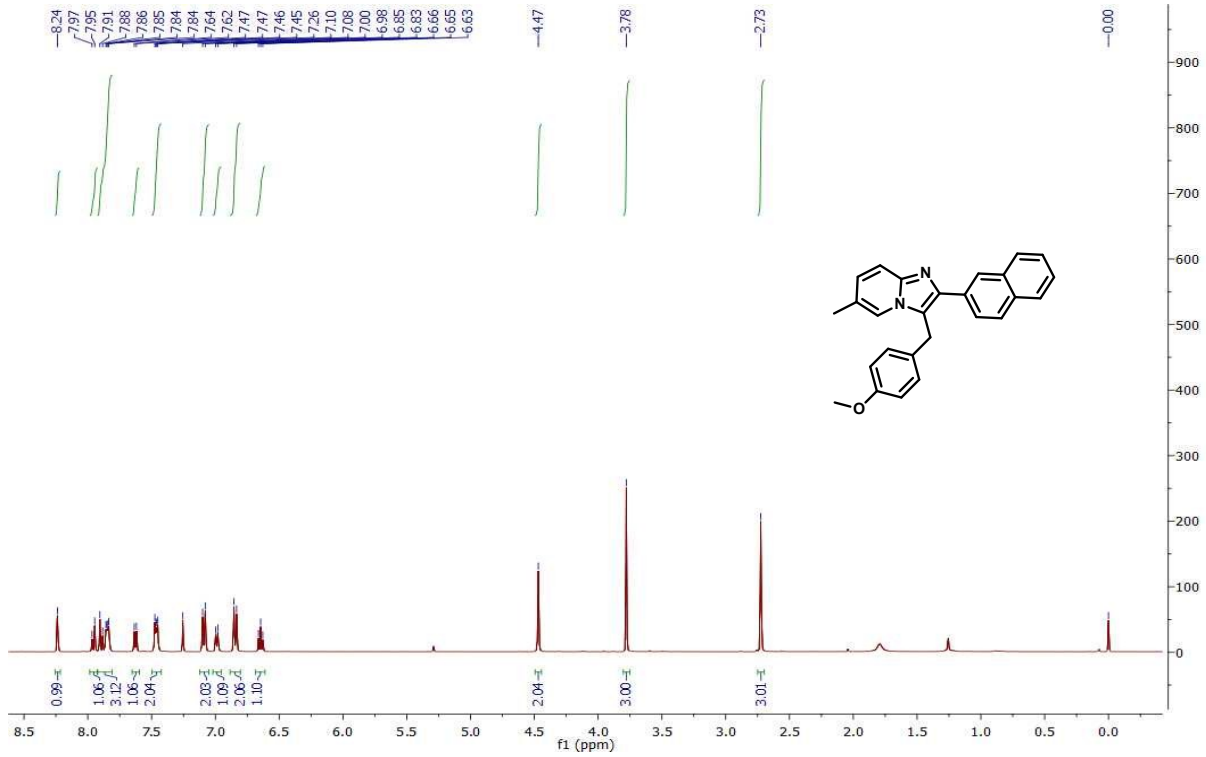
^{1}H NMR spectrum of compound **4d** ($CDCl_3$, 400 MHz)

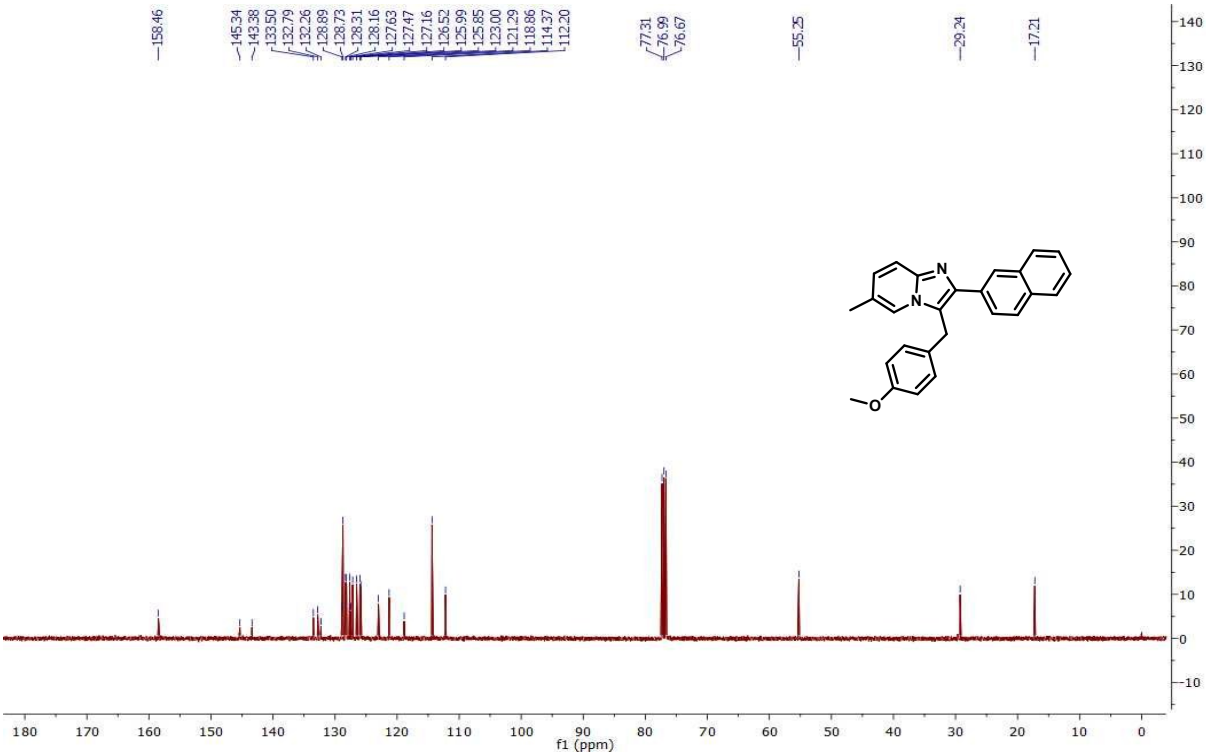




^{13}CNMR spectrum of compound **4d** ($CDCl_3$, 100 MHz)

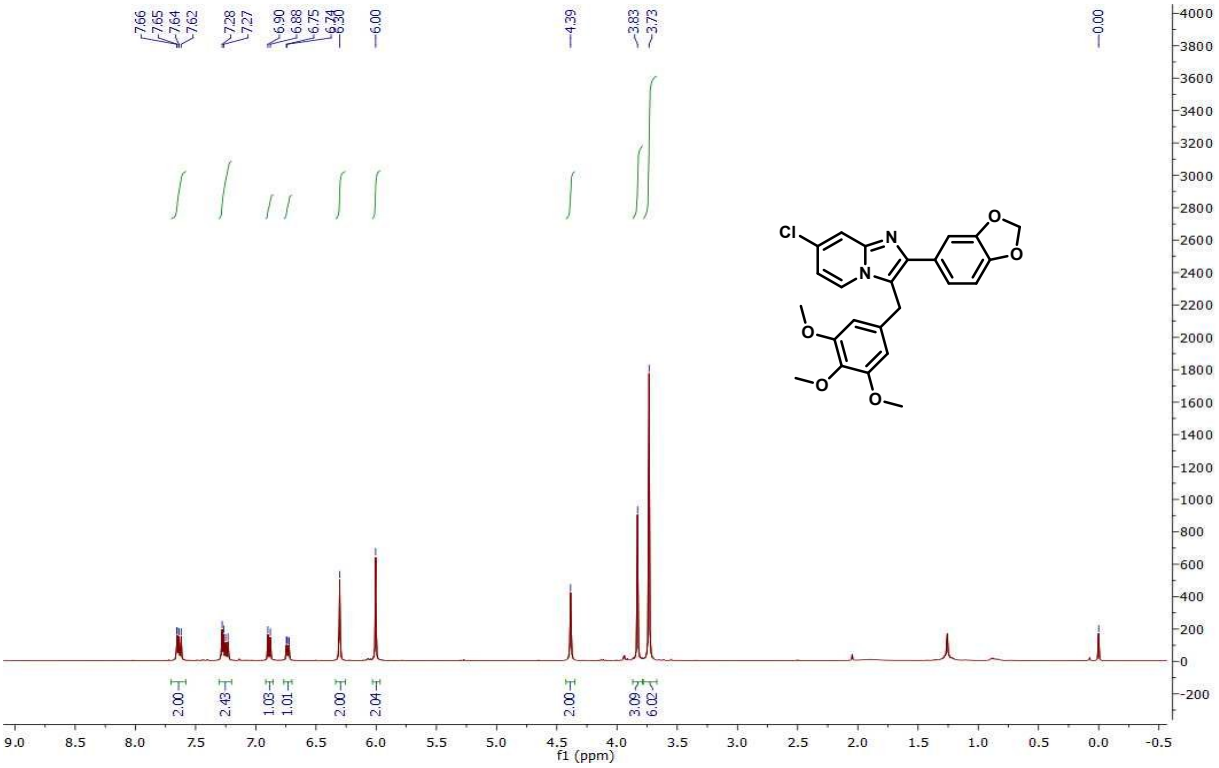
^{1}H NMR spectrum of compound **4e** ($CDCl_3$, 400 MHz)

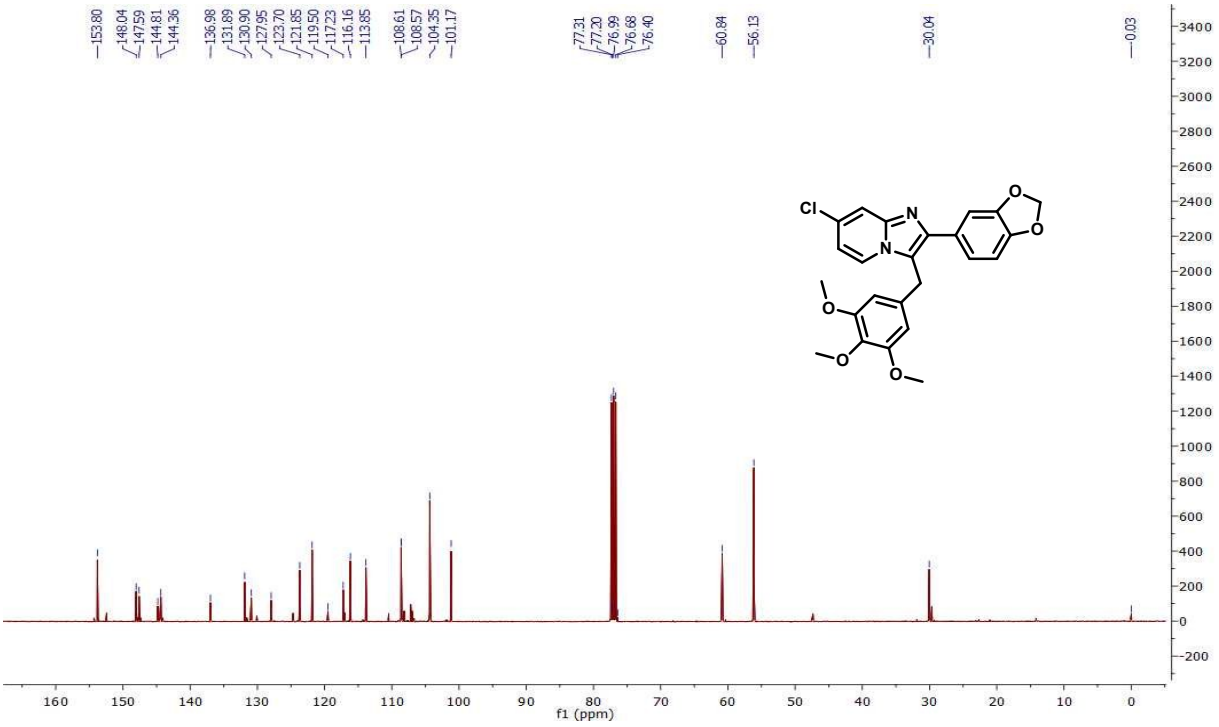




^{13}CNMR spectrum of compound **4e** ($CDCl_3$, 100 MHz)

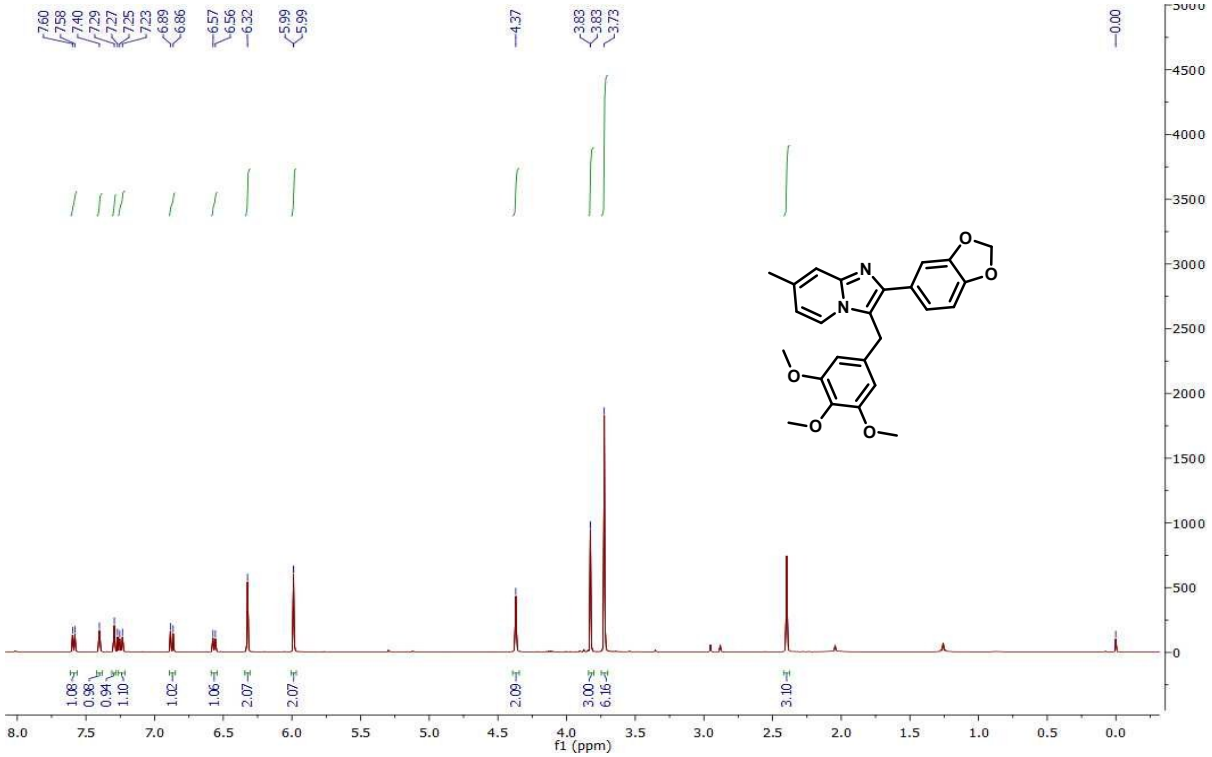
^{1}H NMR spectrum of compound **4f** ($CDCl_3$, 400 MHz)

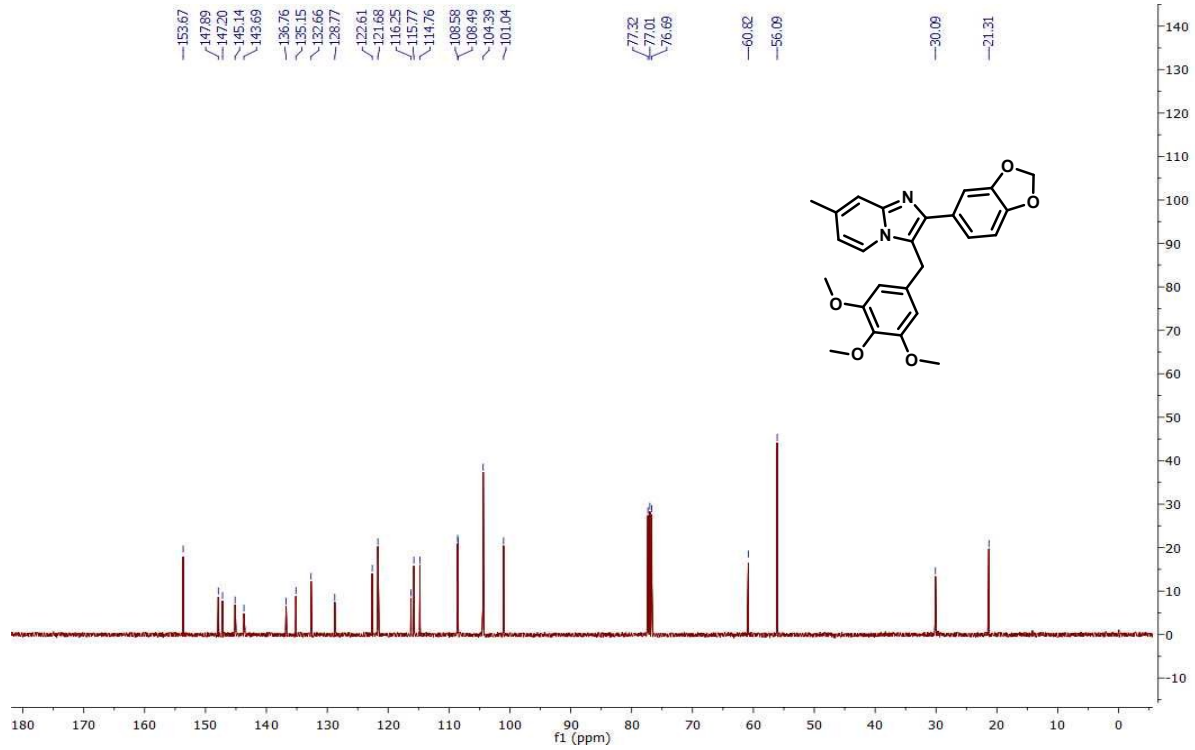




^{13}CNMR spectrum of compound **4f** ($CDCl_3$, 100 MHz)

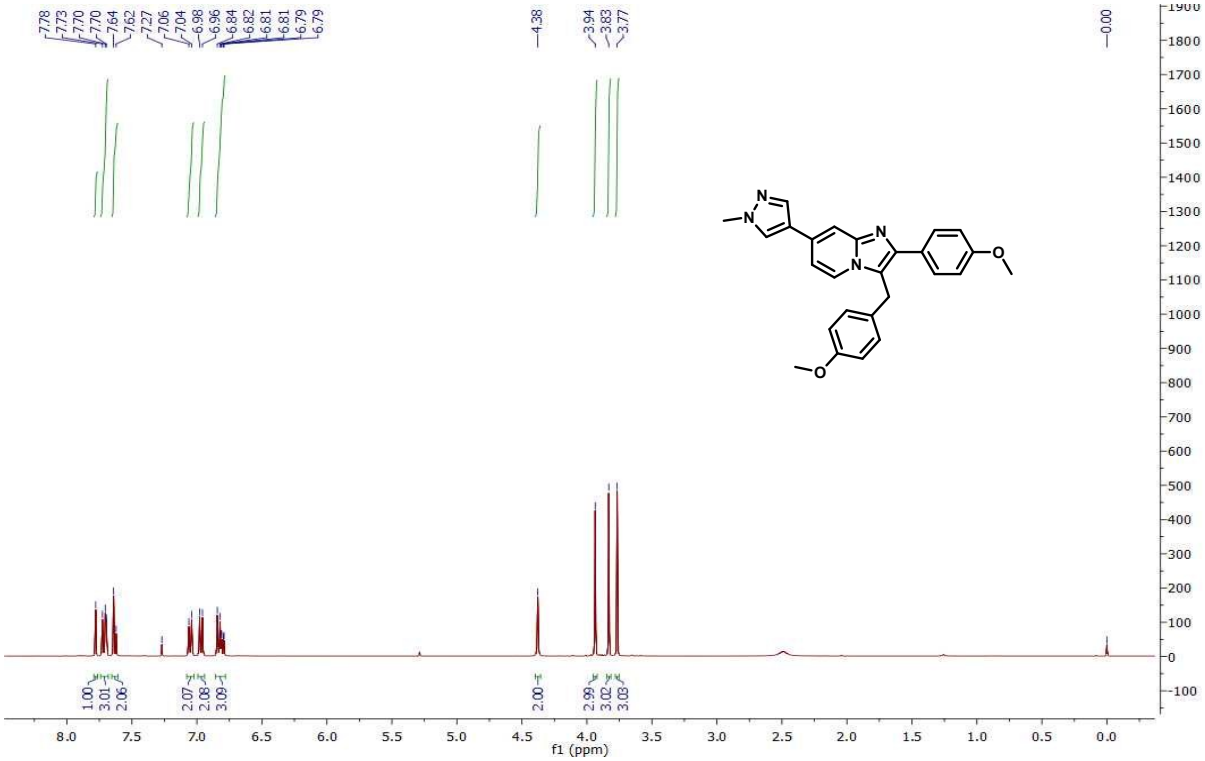
^{1}H NMR spectrum of compound **4g** ($CDCl_3$, 400 MHz)

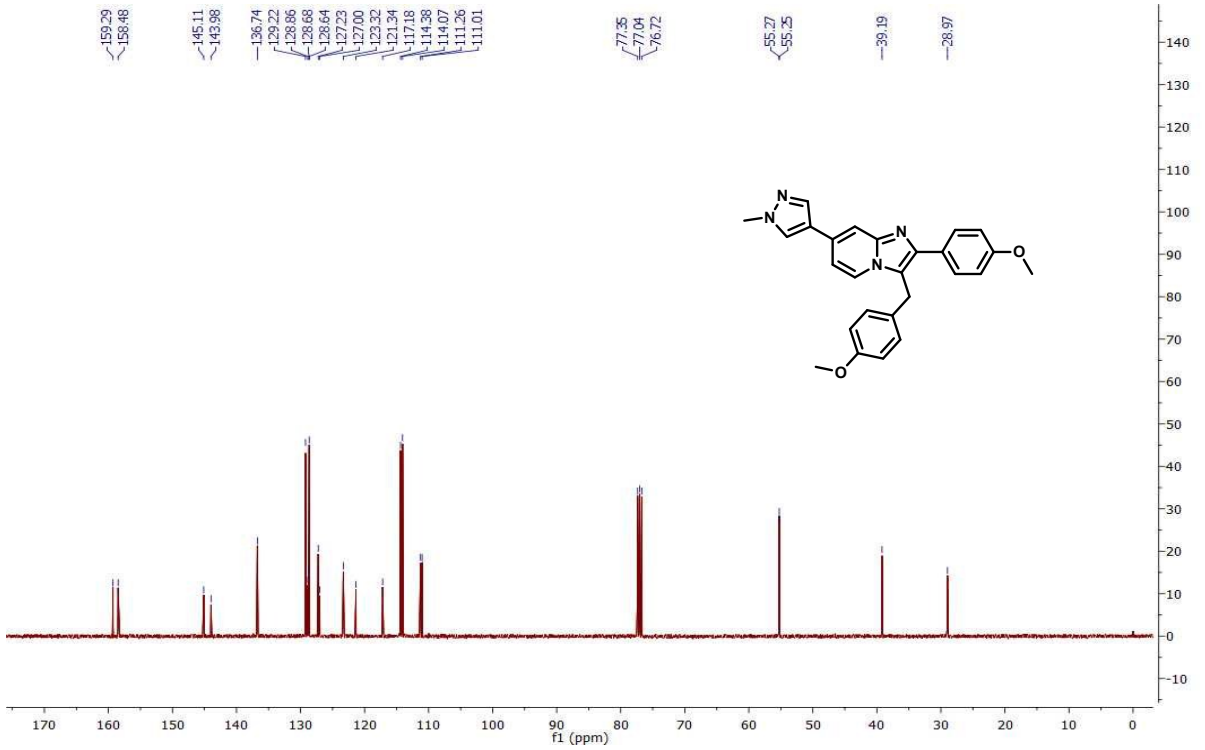




^{13}CNMR spectrum of compound **4g** ($CDCl_3$, 100 MHz)

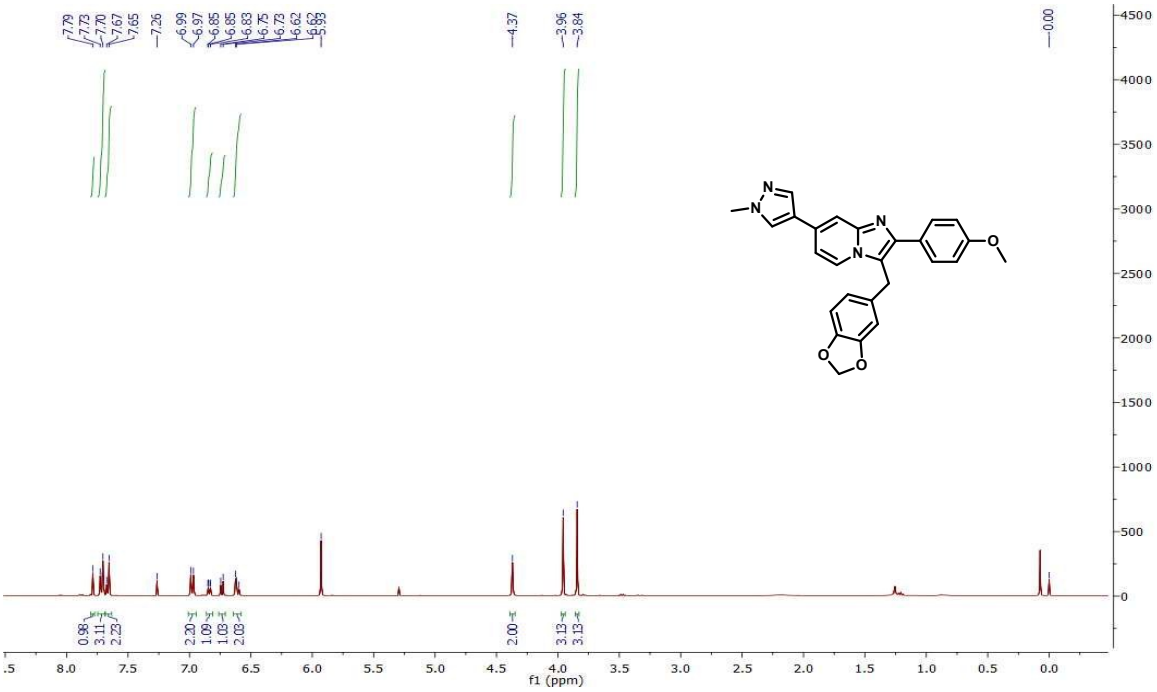
^{1}H NMR spectrum of compound **4h** ($CDCl_3$, 400 MHz)

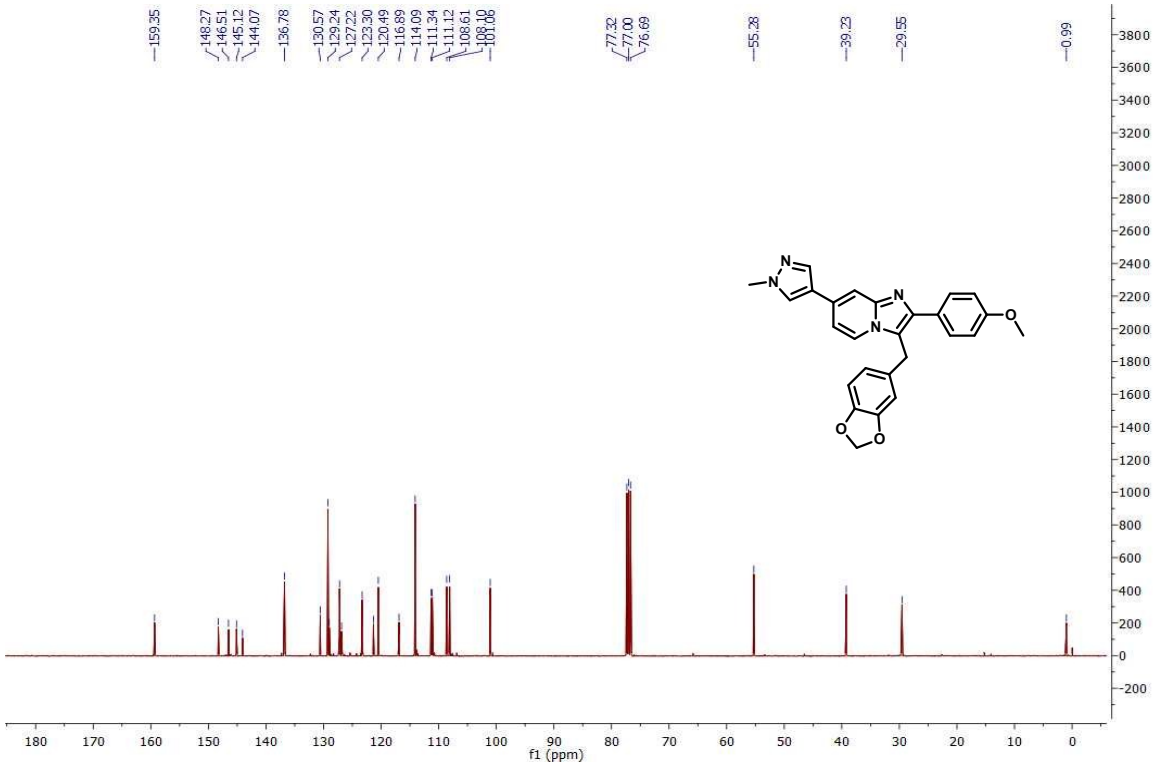




^{13}CNMR spectrum of compound **4h** ($CDCl_3$, 100 MHz)

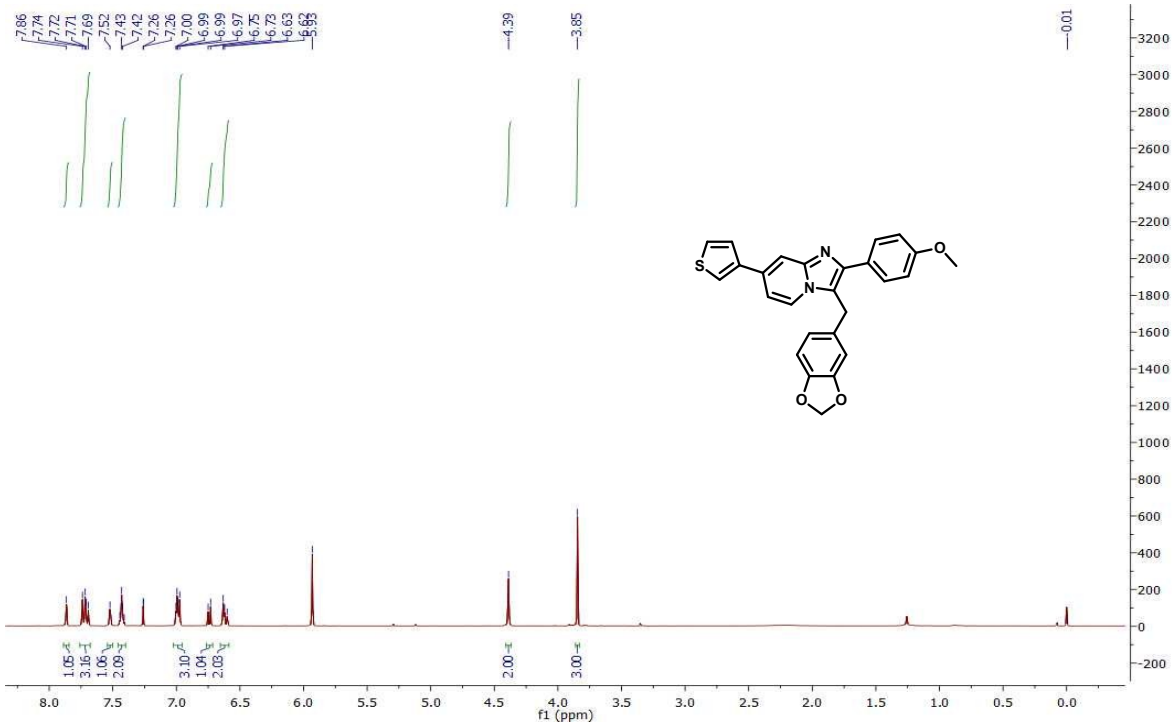
^{1}H NMR spectrum of compound **4i** ($CDCl_3$, 400 MHz)

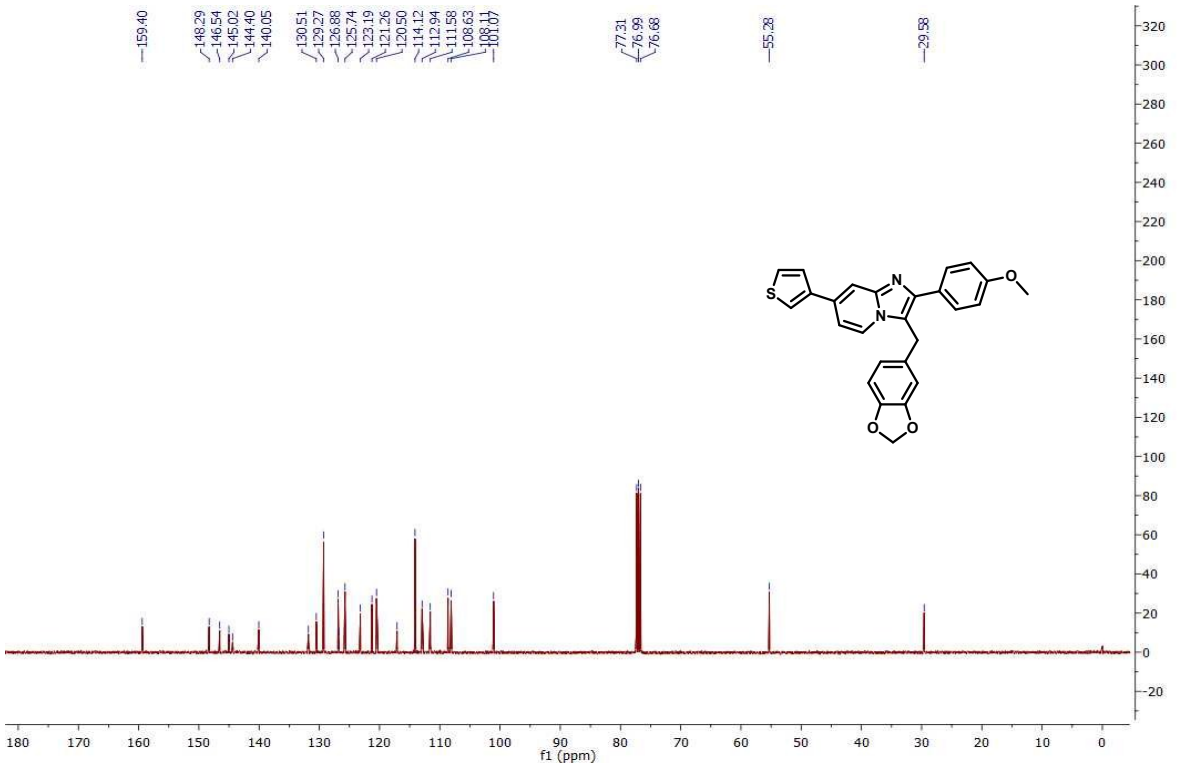




^{13}CNMR spectrum of compound **4i** ($CDCl_3$, 100 MHz)

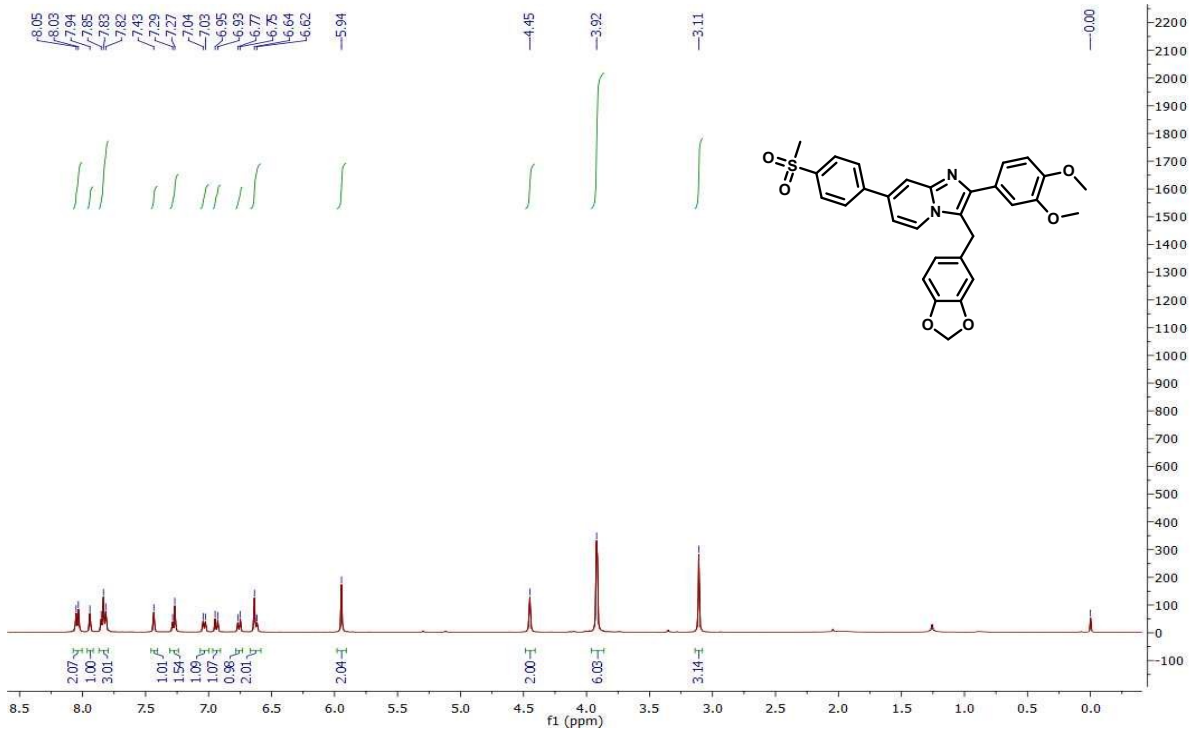
^{1}H NMR spectrum of compound **4j** ($CDCl_3$, 400 MHz)

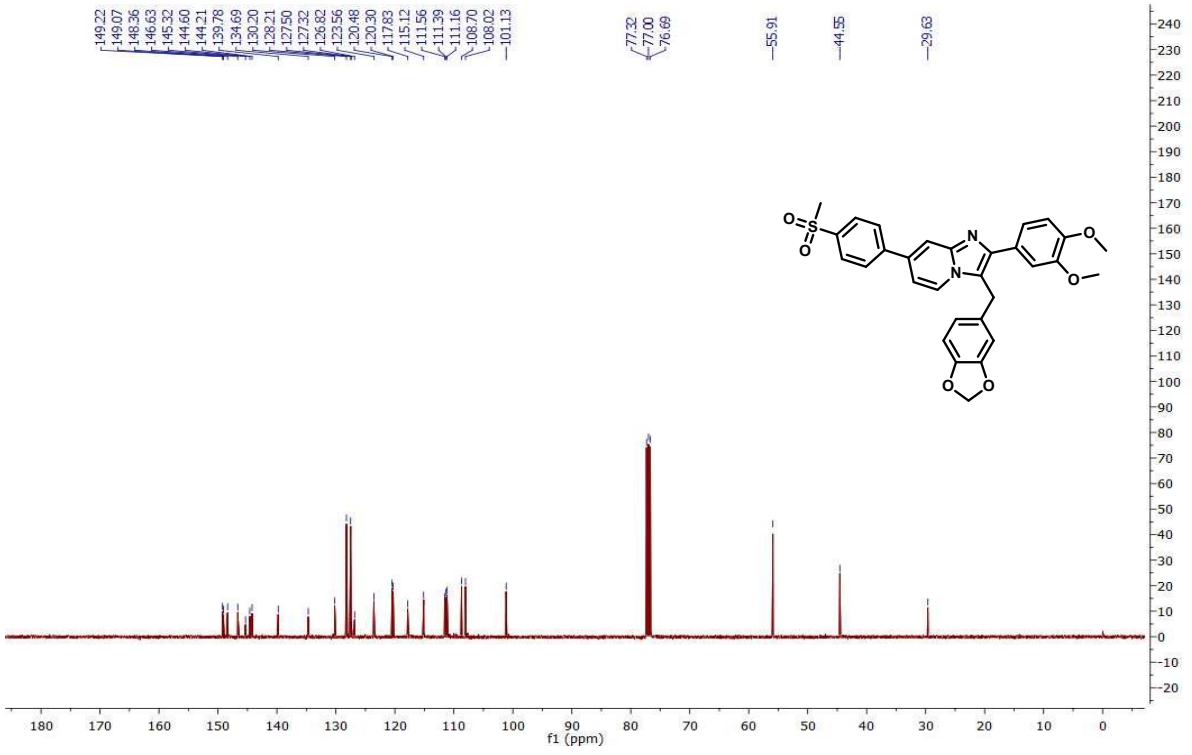




^{13}CNMR spectrum of compound **4j** ($CDCl_3$, 100 MHz)

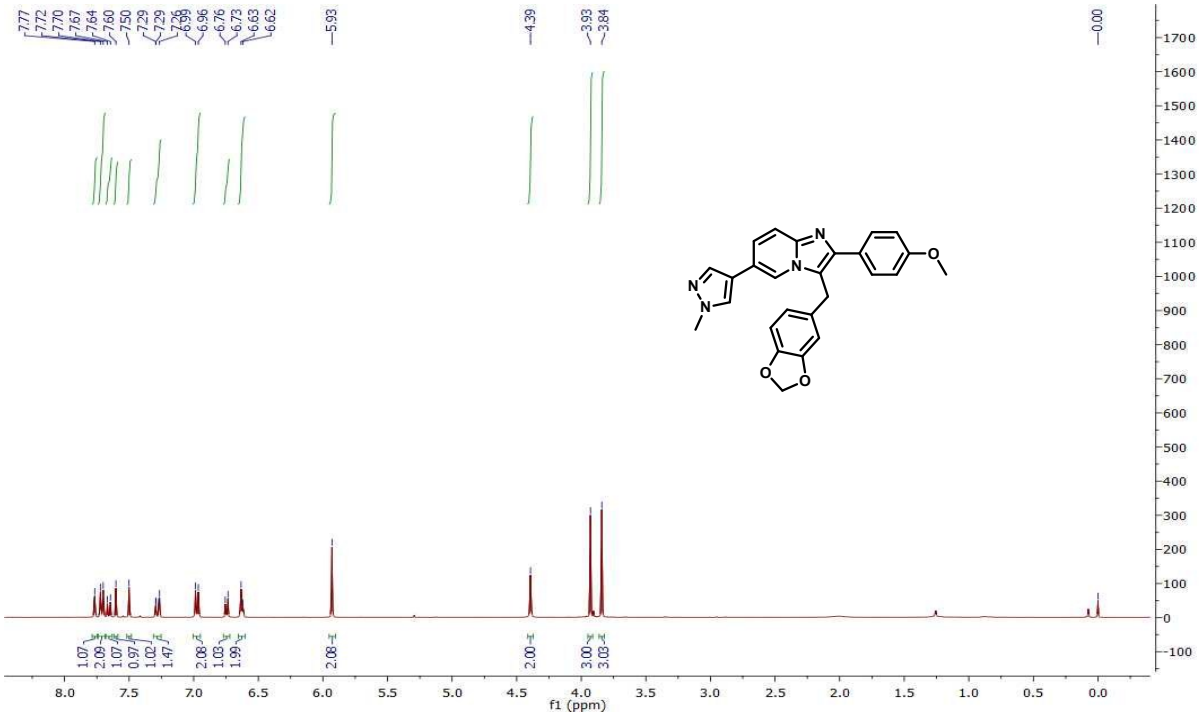
^{1}H NMR spectrum of compound **4k** ($CDCl_3$, 400 MHz)

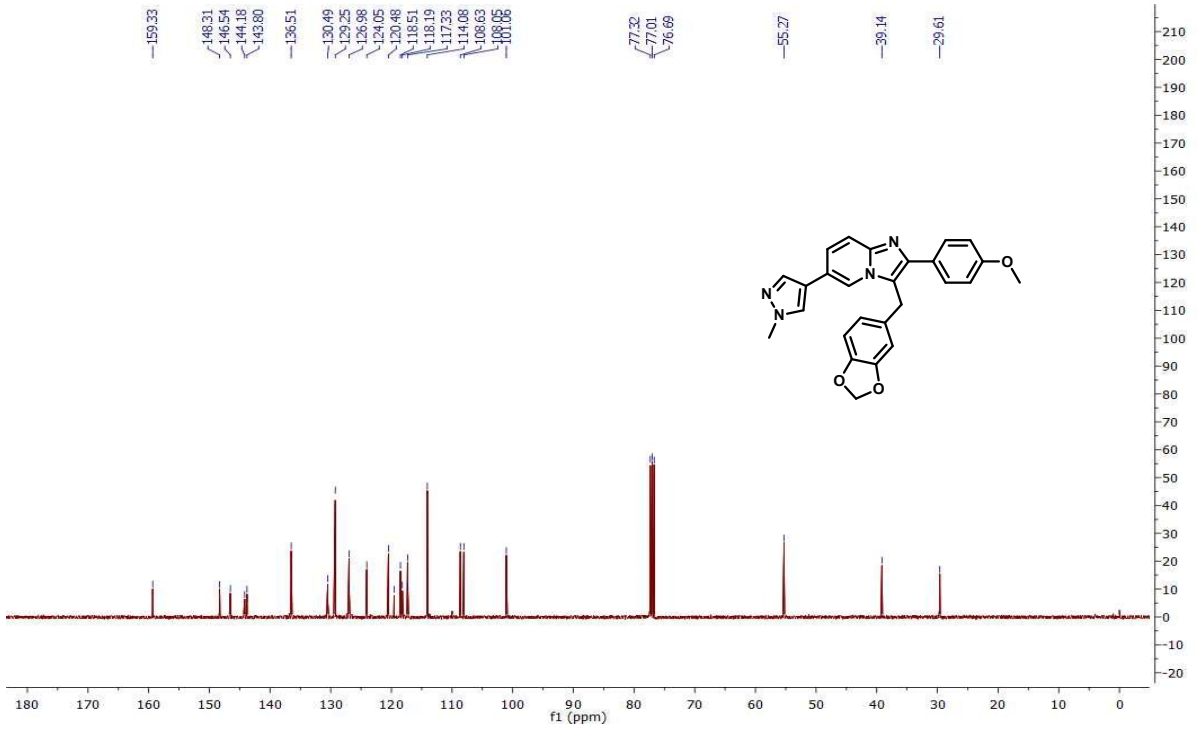




^{13}CNMR spectrum of compound **4k** ($CDCl_3$, 100 MHz)

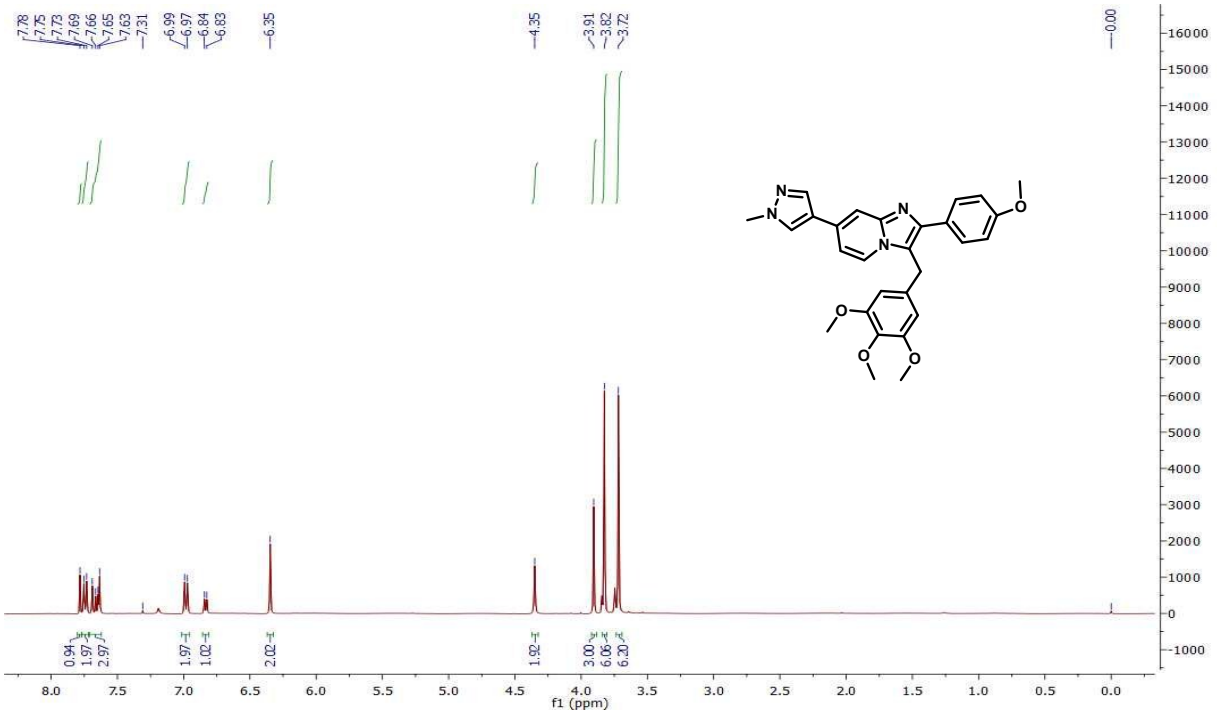
^{1}H NMR spectrum of compound **4l** ($CDCl_3$, 400 MHz)

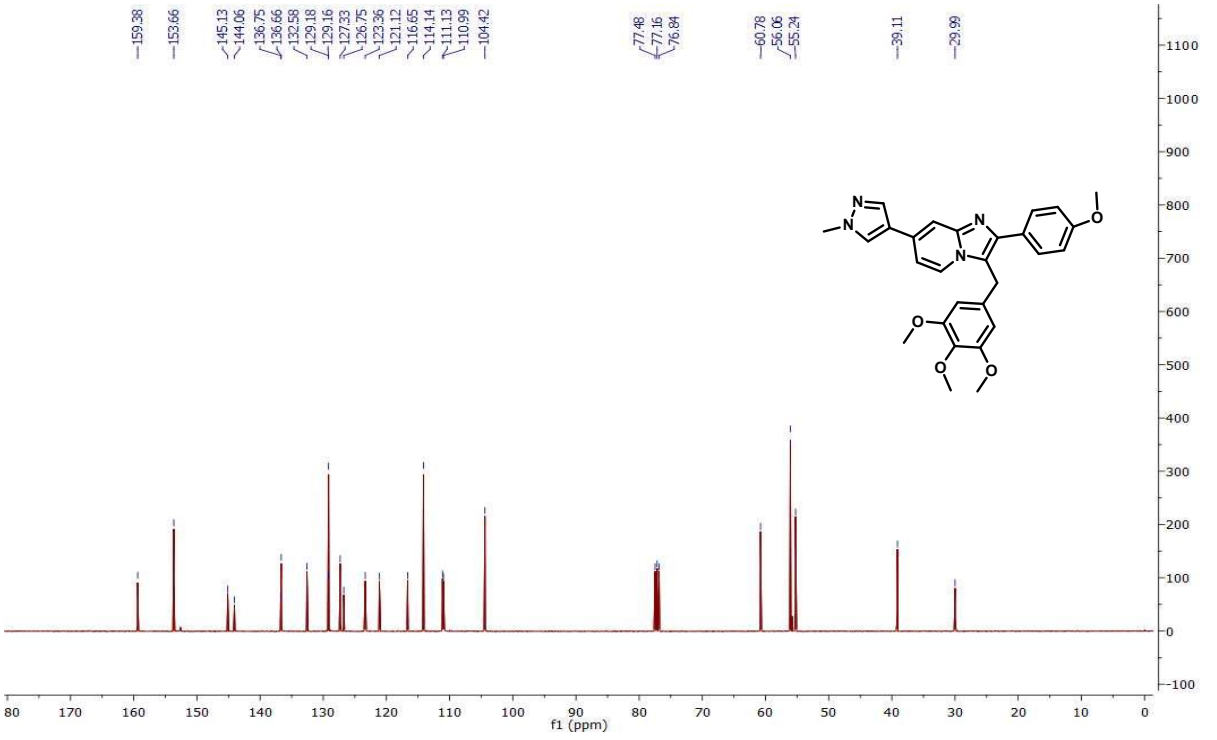




^{13}CNMR spectrum of compound **4l** ($CDCl_3$, 100 MHz)

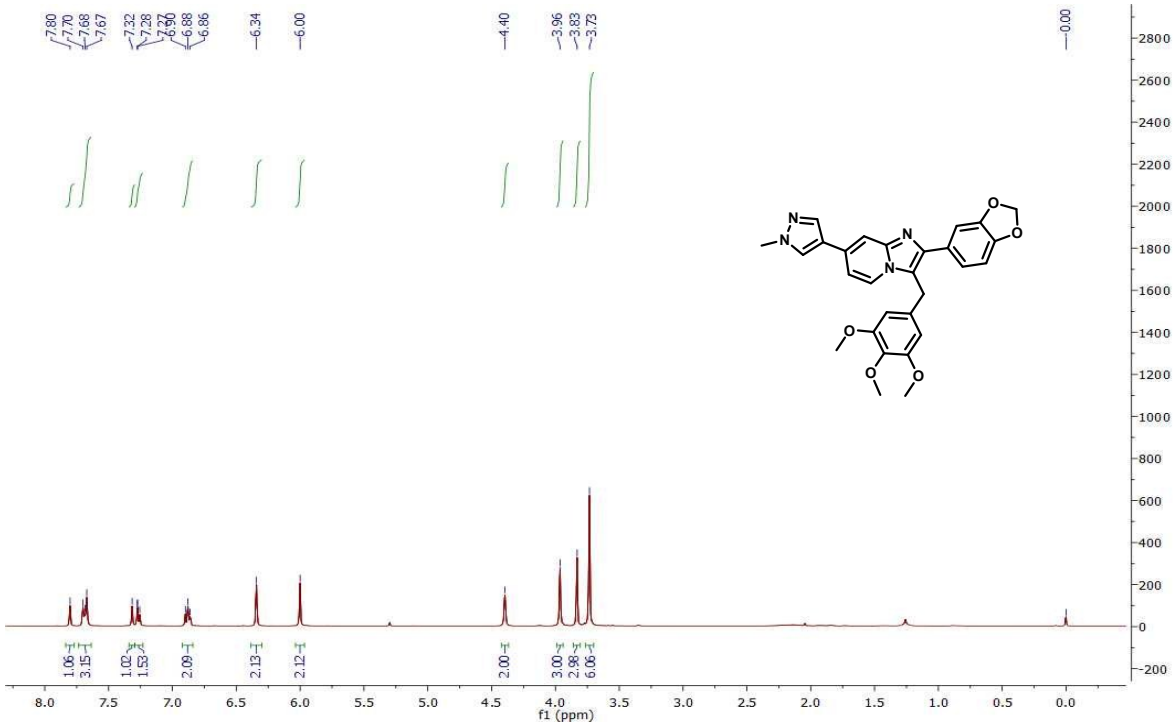
^{1}H NMR spectrum of compound **4m** ($CDCl_3$, 400 MHz)

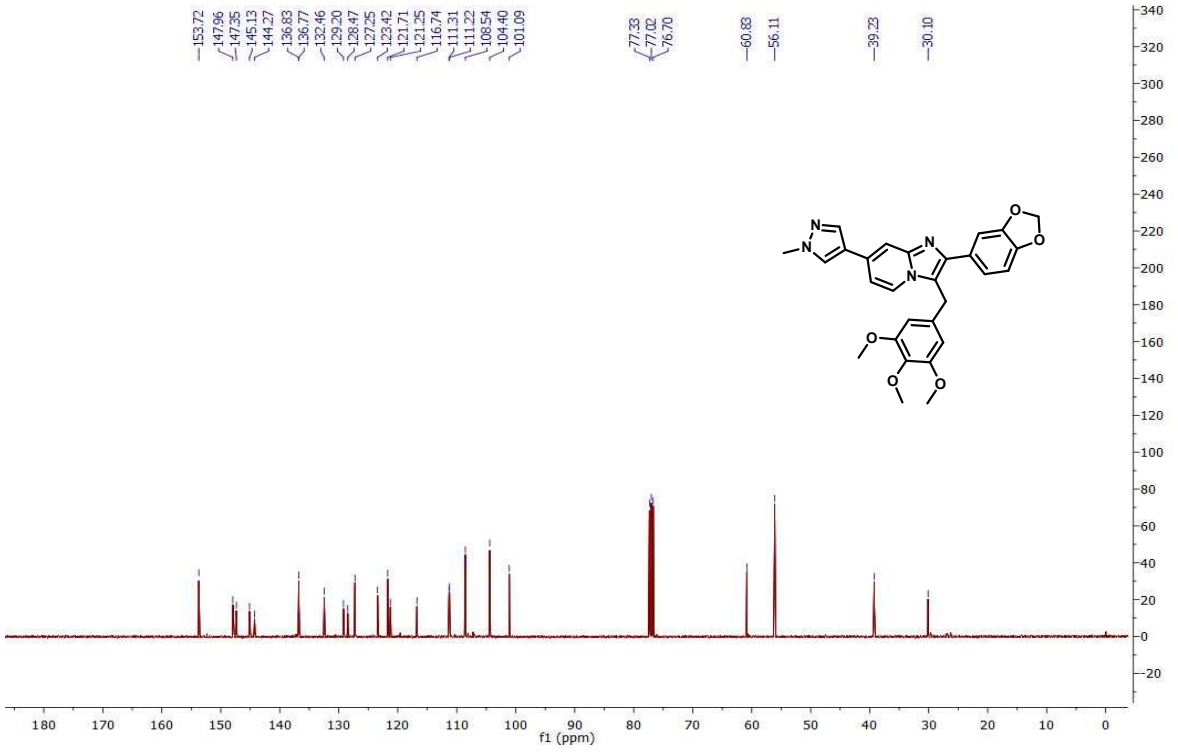




^{13}CNMR spectrum of compound **4m** ($CDCl_3$, 100 MHz)

^{1}H NMR spectrum of compound **4n** ($CDCl_3$, 400 MHz)



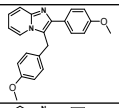
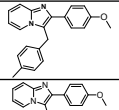
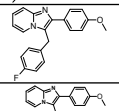
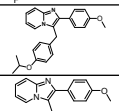
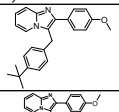
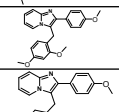
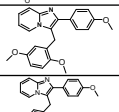
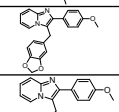
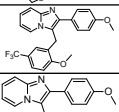
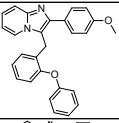
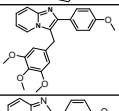
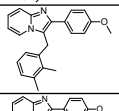
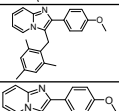
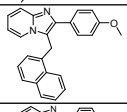
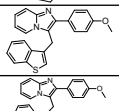
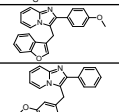
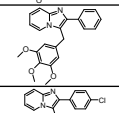
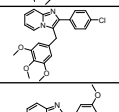
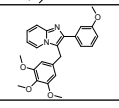


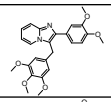
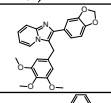
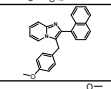
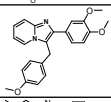
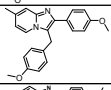
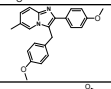
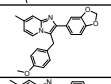
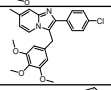
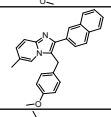
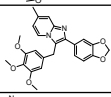
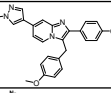
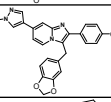
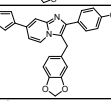
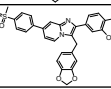
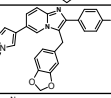
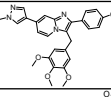
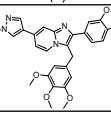
^{13}CNMR spectrum of compound **4n** ($CDCl_3$, 100 MHz)

VI. Cellular Assay Procedure

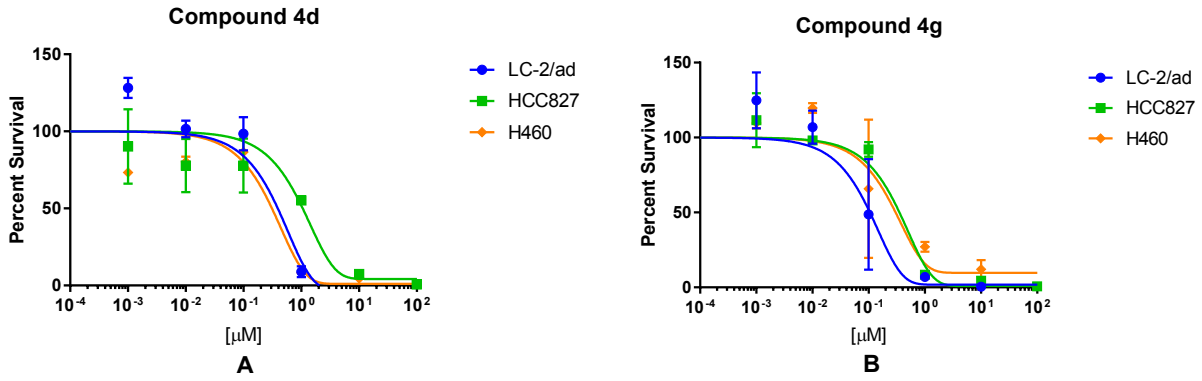
The LC-2/ad cell line was obtained from Sigma-Aldrich. HCC827 and H460 cell lines were obtained from American Type Culture Collection (ATCC). LC-2/ad cells were cultured using a 1:1 ratio of RPMI-1640 and F12K medium, supplemented with 10% fetal bovine serum (FBS). HCC827 and H460 cells were cultured using RPMI-1640 medium, supplemented with 10% fetal bovine serum. The cells were maintained at 37 °C in a humidified atmosphere with 5% CO_2 and were sub-cultured as necessary. Cell viability assays were performed in 96-well plates (Sigma-Aldrich). Briefly, LC-2/ad cells were seeded at approximately 5 x 10^3 cells per well and incubated for 24 hours. After 24 hours, the cells were treated with compounds at doses of 100 μM, 10 μM and 1 μM for 10 days. At the end of treatment, the medium was removed, cells were washed with PBS (3x, 200μL/well), and treated with a solution of resazurin (50 μL) for six hours [4]. Resazurin can be converted to highly fluorescent resorufin in viable cells, which can be monitored by measuring the excitation/emission profile at 540/590 nm using a microplate reader (Synergy H4 Biotek INC, Winooski, VT) [5, 6]. Background fluorescence was measured at 540/590 nm with resazurin and culture medium only. The experiment was repeated three (3) times independently. A similar viability protocol was utilized for HCC827 and H460 cells. HCC827 cells were treated with compounds for 5 days and H460 cells were treated with compounds for 7 days. Generated data was analyzed in GraphPad Prism 7, and compounds exhibiting over 50% inhibition at 1 μM were screened in further viability assays. A similar protocol was applied in the follow-on assay, and cells were treated with compounds in a 6-point, full log dilutions ranging from 200 to 0.002 μM. Dose response curves were generated in GraphPad Prism 7 and analyzed using non-liner, one phase decay. GI_{50} values are reported as the half-life of the curve and error was calculated from the standard deviation of each GI_{50} measurement from three independent experiments.

VII. Antiproliferative activities of synthesized compounds (3aa - 3ay & 4a - 4n):

Compound Information		*Cell IC_{50} (μM)*		
Code	Structure	LC-2/ad	HCC827	H460
3aa		>1	>1	>1
3ac		>1	>1	>1
3ad		>1	>1	>1
3ae		>1	>1	>1
3af		>1	>1	>1
3ag		>1	>1	>1
3ah		>1	>1	>1
3ai		>1	>1	>1
3aj		>1	>1	>1
3ak		>1	>1	>1
3al		1.85 ± 0.18	>1	>1
3am		>1	>1	>1
3an		>1	>1	>1
3ao		>1	>1	>1
3ap		>1	>1	>1
3aq		>1	>1	>1
3ar		>1	>1	>1
3at		>1	>1	>1
3au		>1	>1	>1

3av		>1	>1	>1
3aw		>1	>1	>1
3ax		>1	>1	>1
3ay		>1	>1	>1
4a		>1	>1	>1
4b		>1	>1	>1
4c		>1	>1	>1
4d		0.28 ± 0.040	2.03 ± 0.56	0.39 ± 0.07
4e		>1	>1	>1
4g		0.063 ± 0.029	0.60 ± 0.18	0.15 ± 0.01
4h		>1	>1	>1
4i		>1	>1	>1
4j		>1	>1	>1
4k		>1	>1	>1
4l		1.39 ± 0.41	>1	>1
4m		>1	>1	>1
4n		>1	>1	>1

VIII. Representative dose response curves for 4d and 4g



Supplemental Figure 1. Cell-based activities of compounds **4d** and **4g**.

IX. Supplemental References

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