Supporting Information

Palladium(0)-Catalyzed Direct C-H Hetero-Arylation of 2-arylimidazo[1,2-a]pyridines with (*E*)-1-(5-bromothiophen-2-yl)-3-arylprop-2-en-1-ones and Their Anticancer Activity

Mari Vellakkaran,[a] Rajaka Lingayya,[a,b] Bejjanki Naveen Kumar,[a] Kommu Nagaiah,*[a,b] Y. Poornachandra,[c] C. Ganesh Kumar[c]

[a] *Organic and Biomolecular Chemistry Division, CSIR- Indian Institute of Chemical Technology, Tarnaka, Hyderabad, India-500007. E-mail:nagaiah@iict.res.in*

[b] *Academy of Scientific and Innovative Research (AcSIR), CSIR - Indian Institute of Chemical Technology, Hyderabad, India.*

[c] *Medicinal Chemistry and Pharmacology Division, CSIR-Indian Institute of Chemical Technology, Uppal Road, Hyderabad 500 007, India.*

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1.1 General Experimental Details:

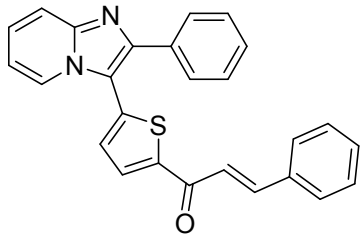
All solvents and reagents were used, as received from the suppliers. TLC was performed on Merck Kiesel gel 60, F_{254} plates with the layer thickness of 0.25 mm. Column chromatography was performed on silica gel (60-120 mesh) using a gradient of ethyl acetate and hexane as mobile phase. Melting points were determined on a Fisher John's melting point apparatus and are uncorrected. IR spectra were recorded on a Brucker Alpha Spectrometer FT-IR system. ^{1}H NMR spectral data were collected at 300 (AVANCE & JCAMP), 400 (INOVA) & 500 (INOVA & AVANCE) MHz, while ^{13}C NMR were recorded at 75, 100 & 125 MHz. ^{1}H NMR spectral data are given as chemical shifts in ppm followed by multiplicity (s- singlet; d- doublet; t- triplet; q- quartet; m- multiplet), number of protons and coupling constants. ^{13}C NMR chemical shifts are expressed in ppm. HRMS (ESI) spectral data were collected using ORBITRAP High Resolution Mass Spectrometer. Starting materials [2-arylimidazo[1,2-a]pyridines[1] and (*E*)-1-(5-bromothiophen-2-yl)-3-arylprop-2-en-1-ones[2]] were prepared as previously reported literatures.

1.2 General Procedure for Synthesis of (*E*)-3-aryl-1-(5-(2-arylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one derivatives from 2-arylimidazo[1,2-*a*]pyridines:

A solution of 2-arylimidazo[1,2-a]pyridine (0.5 mmol) and $Pd(OAc)_2$ (0.025 equiv.), $P(Cy)_3$ (0.05 equiv.), K_2CO_3 (2.0 equiv.) and (*E*)-1-(5-bromothiophen-2-yl)-3-arylprop-2-en-1-ones (0.6 mmol) in DMA (4.0 mL) was taken in a 10.0 mL RB flask, which was then attached to N_2 atmosphere. The mixture was vigorously stirred at 90 °C for 18 h. The completion of reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was partitioned between ethyl acetate (25.0 mL) and water (25.0 mL) in a separatory funnel. The organic layer was washed with water, and brine, dried over anhydrous Na_2SO_4 (s) and concentrated *in vacuo*. The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product.

1.3 Analytical data for products

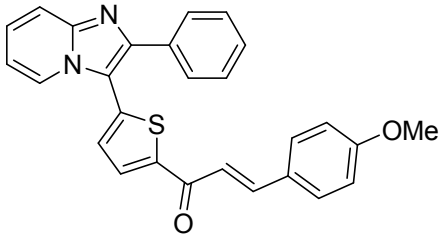
(*E*)-3-phenyl-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3a)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.197 g, 97%). M.p. 130-131 ^{o}C; ^{1}H NMR (300

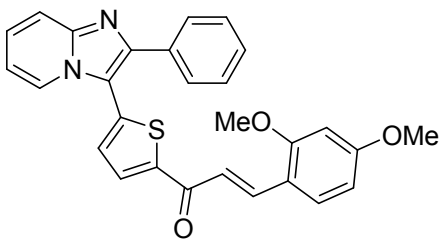
MHz, $CDCl_3$) δ 8.22 (d, J = 6.9 Hz, 1H), 7.92 (t, J = 9.9 Hz, 2H), 7.75 – 7.64 (m, 5H), 7.44 (dd, J = 8.9, 5.7 Hz, 4H), 7.37 – 7.23 (m, 5H), 6.88 (dd, J = 6.8, 0.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.6, 147.0, 145.9, 144.6, 138.5, 134.6, 133.4, 132.4, 130.8, 130.7, 129.0, 128.6, 128.5, 128.5, 128.3, 125.8, 123.8, 121.1, 117.8, 113.2; (IR, Neat): 3056, 1640,1435, 1220, 752, 697 cm^{-1}; HRMS (ESI): Calculated for $[C_{26}H_{19}ON_2S]^+$ 407.12126; Found 407.11890.

(*E*)-3-(4-methoxyphenyl)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3b)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.190 g, 87%). M.p. 182-183 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 6.8 Hz, 1H), 7.90 (dd, J = 13.1, 9.7 Hz, 2H), 7.72 (d, J = 5.0 Hz, 3H), 7.62 (d, J = 8.4 Hz, 2H), 7.37 – 7.23 (m, 6H), 6.95 (d, J = 8.3 Hz, 2H), 6.87 (t, J = 6.7 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.7, 161.9, 147.4, 145.8, 144.5, 138.1, 133.4, 132.1, 130.7, 130.5, 128.5, 128.4, 128.2, 127.3, 125.8, 123.8, 118.7, 117.7, 114.5, 113.2, 55.5; (IR, Neat): 2934, 1641, 1436, 1216, 749, 696 cm^{-1}; HRMS (ESI): Calculated for $[C_{27}H_{21}O_2SN_2]^+$ 437.13183; Found 437.12885.

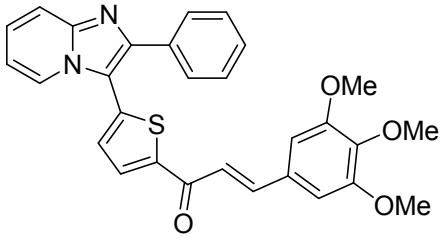
(*E*)-3-(2,4-dimethoxyphenyl)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3c)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 20% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.217 g, 93%). M.p. 135-137 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 6.8 Hz, 1H), 8.12 (d, J = 15.6 Hz, 1H), 7.90 (d, J = 3.6 Hz, 1H), 7.72 (t, J = 6.7 Hz, 3H), 7.57 (d, J = 8.5 Hz, 1H), 7.48 (d, J = 15.6 Hz, 1H), 7.36 – 7.21 (m,

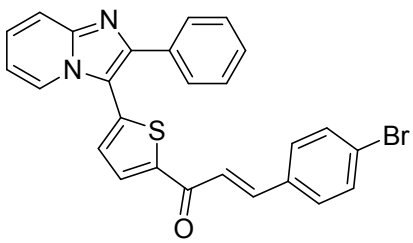
5H), 6.86 (t, J = 6.7 Hz, 1H), 6.56 – 6.47 (m, 2H), 3.91 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.3, 163.3, 160.7, 147.8, 145.8, 145.3, 140.4, 137.5, 133.5, 131.8, 131.5, 130.7, 128.5, 128.4, 128.2, 125.7, 123.8, 119.5, 117.7, 116.9, 113.3, 113.1, 105.6, 98.5, 55.6, 55.5; (IR, Neat): 2962, 1639, 1436, 1212, 735, 697 cm^{-1}; HRMS (ESI): Calculated for $[C_{28}H_{23}O_3N_2S]^+$ 467.14239; Found 467.13904.

(*E*)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (3d)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 30% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.228 g, 92%). M.p. 145-146 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 – 8.20 (m, 1H), 7.96 (d, J = 3.9 Hz, 1H), 7.82 (d, J = 15.5 Hz, 1H), 7.73 (dd, J = 5.2, 3.1 Hz, 3H), 7.38 – 7.30 (m, 5H), 7.25 (d, J = 3.9 Hz, 1H), 6.90 – 6.86 (m, 3H), 3.93 (s, 6H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.5, 153.5, 147.0, 145.8, 145.4, 144.8, 140.8, 138.3, 133.3, 132.4, 130.8, 130.0, 128.5, 128.5, 128.3, 126.0, 123.8, 120.4, 117.7, 113.3, 105.9, 61.1, 56.3; (IR, Neat): 2938, 1645, 1435, 1280, 753, 699 cm^{-1}; HRMS (ESI): Calculated for $[C_{29}H_{25}O_4N_2S]^+$ 497.15295; Found 497.14944. Elemental Analysis: Calculated C, 70.14; H, 4.87; N, 5.64; S, 6.46; Found C, 69.83; H, 5.37; N, 3.97; S, 5.77.

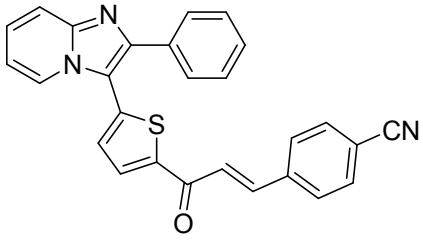
(*E*)-3-(4-bromophenyl)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3e)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.208 g, 86%). M.p. 165-166 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 6.9 Hz, 1H), 7.93 (d, J = 3.9 Hz, 1H), 7.83 (d, J = 15.6 Hz, 1H), 7.73

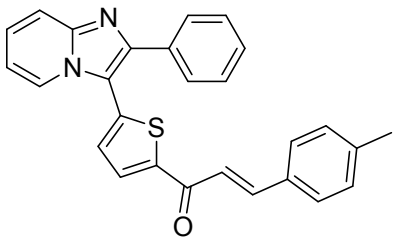
– 7.70 (m, 2H), 7.58 – 7.51 (m, 5H), 7.42 (d, *J* = 15.6 Hz, 1H), 7.37 – 7.31 (m, 4H), 7.30 – 7.27 (m, 1H), 6.88 (td, *J* = 6.8, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.3, 146.7, 145.9, 143.2, 138.8, 133.5, 133.4, 132.5, 132.3, 131.5, 130.7, 129.9, 128.7, 128.6, 128.5, 128.3, 125.8, 125.2, 123.8, 121.7, 117.8, 113.2; (IR, Neat): 2960, 1648, 1405, 1238, 751, 664 cm^{-1}; HRMS (ESI): Calculated for $[C_{26}H_{18}ON_2SBr]^+$ 485.03177; Found 485.02863.

(*E*)-4-(3-oxo-3-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-1-en-1-yl)benzonitrile (3f)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.174 g, 81%). M.p. 152-154 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.9 Hz, 1H), 7.96 (d, *J* = 3.9 Hz, 1H), 7.87 (d, *J* = 15.6 Hz, 1H), 7.78 – 7.68 (m, 5H), 7.50 (d, *J* = 15.6 Hz, 1H), 7.37 (dd, *J* = 11.0, 4.9 Hz, 5H), 7.23 – 7.11 (m, 2H), 6.91 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.3, 146.0, 144.6, 141.9, 139.4, 132.9, 132.7, 132.5, 132.4, 130.7, 129.5, 128.8, 128.6, 128.5, 128.4, 128.3, 126.0, 124.2, 123.7, 118.4, 117.8, 113.6, 113.3; (IR, Neat): 3017, 2227, 1648, 1436, 1223,752, 696 cm^{-1}; HRMS (ESI): Calculated for $[C_{27}H_{18}ON_3S]^+$ 432.11651; Found 432.11343.

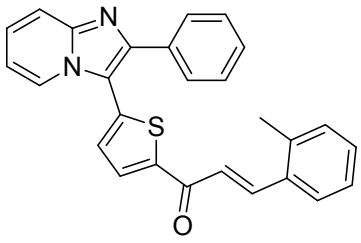
(*E*)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)-3-(p-tolyl)prop-2-en-1-one (3g)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.199 g, 95%). M.p. 163-164 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 6.7 Hz, 1H), 7.93 (d, *J* = 3.6 Hz, 1H), 7.88 (d, *J* = 15.5 Hz, 1H), 7.72 (t, *J* = 6.9 Hz, 3H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 15.6 Hz, 1H), 7.37 – 7.22 (m, 7H), 6.87 (t, *J* = 6.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.7, 147.2, 145.8, 145.5, 144.7,

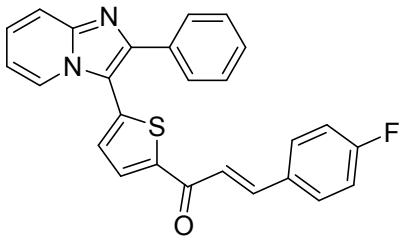
141.5, 138.3, 133.4, 132.3, 131.8, 130.7, 129.8, 128.6, 128.5, 128.4, 128.2, 125.8, 123.8, 120.1, 117.7, 113.2, 21.6; (IR, Neat): 2959, 1643, 1435, 1224, 749, 697 cm^{-1}; HRMS (ESI): Calculated for $[C_{27}H_{21}ON_2S]^+$ 421.13691; Found 421.13416.

(*E*)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)-3-(o-tolyl)prop-2-en-1-one (3h)



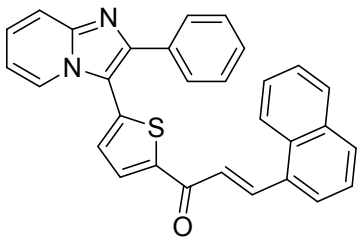
Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.197 g, 94%). M.p. 173-174 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.27 – 8.18 (m, 2H), 7.95 (d, *J* = 3.7 Hz, 1H), 7.72 (d, *J* = 6.5 Hz, 4H), 7.47 – 7.19 (m, 10H), 6.88 (t, *J* = 6.8 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.6, 147.0, 145.8, 145.5, 142.2, 138.6, 138.5, 133.6, 133.4, 132.7, 132.4, 131.0, 130.7, 130.6, 128.5, 128.4, 128.3, 126.4, 125.8, 123.8, 122.2, 117.7, 113.2, 19.9; (IR, Neat): 3019, 1649, 1437, 1214, 746, 666 cm^{-1}; HRMS (ESI): Calculated for $[C_{27}H_{21}ON_2S]^+$ 421.13691; Found 421.13397.

(*E*)-3-(4-fluorophenyl)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3i)



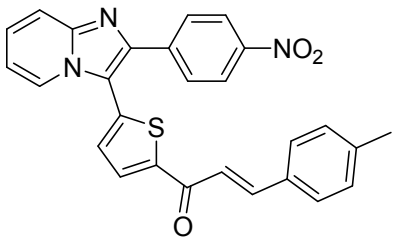
Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.189 g, 89%). M.p. 160-161 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, *J* = 6.9 Hz, 1H), 7.93 (d, *J* = 3.9 Hz, 1H), 7.85 (d, *J* = 15.5 Hz, 1H), 7.74 – 7.68 (m, 3H), 7.64 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.39 – 7.30 (m, 5H), 7.24 (d, *J* = 3.9 Hz, 1H), 7.11 (t, *J* = 8.5 Hz, 2H), 6.86 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.4, 162.5, 146.9, 145.9, 145.6, 143.2, 138.6, 133.4, 132.4, 130.9, 130.7, 130.6, 130.5, 128.5, 128.3, 125.8, 123.8, 120.9, 117.8, 116.4, 116.1, 113.2; (IR, Neat): 3013, 1647, 1435, 1216, 748, 694 cm^{-1}; HRMS (ESI): Calculated for $[C_{26}H_{18}ON_2SF]^+$ 425.11184; Found 425.10886.

(*E*)-3-(naphthalen-1-yl)-1-(5-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3j)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 20% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.207 g, 91%). M.p. 158-159 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75 (d, *J* = 15.3 Hz, 1H), 8.26 (dd, *J* = 15.5, 7.6 Hz, 2H), 7.97 – 7.88 (m, 4H), 7.75 – 7.69 (m, 3H), 7.62 – 7.51 (m, 4H), 7.40 – 7.29 (m, 4H), 7.26 (d, *J* = 1.3 Hz, 1H), 6.87 (td, *J* = 6.8, 1.0 Hz, 1H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.5, 147.0, 145.9, 141.5, 138.7, 133.8, 133.4, 132.5, 132.0, 131.8, 131.1, 130.7, 128.8, 128.6, 128.5, 128.3, 127.1, 126.4, 125.8, 125.5, 125.2, 123.8, 123.7, 123.5, 117.8, 113.2; (IR, Neat): 3010, 1642, 1434, 1218, 749, 697 cm^{-1}; HRMS (ESI): Calculated for $[C_{30}H_{21}ON_2S]^+$ 457.13691; Found 457.13362. Elemental Analysis: Calculated C, 78.92; H, 4.42; N, 6.14; S, 7.02; Found C, 79.28; H, 4.49; N, 5.34; S, 7.11.

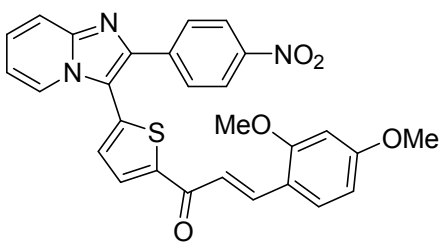
(*E*)-1-(5-(2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)-3-(p-tolyl)prop-2-en-1-one (3k)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 30% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.211 g, 91%). M.p. 191-192 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.8 Hz, 1H), 8.18 (d, *J* = 3.1 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 1H), 8.01 – 7.97 (m, 2H), 7.91 (dd, *J* = 12.1, 3.3 Hz, 3H), 7.73 (d, *J* = 9.1 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 15.6 Hz, 1H), 7.31 (d, *J* = 10.2 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 6.92 (t, *J* = 6.4 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.6, 148.4, 147.3, 146.1, 145.2, 141.7, 140.0, 136.8, 132.2, 131.8, 131.3, 129.8, 128.8, 128.7, 126.5, 126.4, 125.6, 124.2, 124.0, 123.8, 119.9, 118.0, 113.7, 113.2, 21.6; (IR, Neat): 3020, 1646, 1410, 1219, 750, 665 cm^{-1}; HRMS

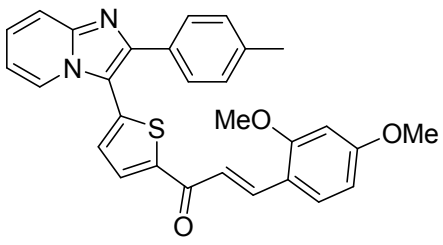
(ESI): Calculated for $[C_{27}H_{20}O_3N_3S]^+$ 466.12199; Found 466.12190. Elemental Analysis: Calculated C, 69.66; H, 4.11; N, 9.03; S, 6.89; Found C, 70.18; H, 3.61; N, 8.78; S, 5.35.

(*E*)-3-(2,4-dimethoxyphenyl)-1-(5-(2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3l)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 30% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.222 g, 87%). M.p. 177-179 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 13.4, 7.5 Hz, 3H), 8.10 (t, *J* = 13.8 Hz, 1H), 7.93 (t, *J* = 6.5 Hz, 3H), 7.72 (d, *J* = 8.9 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.50 (d, *J* = 15.6 Hz, 1H), 7.41 – 7.24 (m, 1H), 6.91 (t, *J* = 6.7 Hz, 1H), 6.55 (d, *J* = 8.6 Hz, 1H), 6.49 (d, *J* = 1.8 Hz, 3H), 3.93 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.2, 163.5, 160.8, 149.0, 147.3, 146.0, 142.6, 140.9, 140.1, 136.1, 131.8, 131.6, 131.3, 128.8, 126.5, 124.0, 123.8, 119.2, 118.0, 116.8, 114.7, 113.7, 105.6, 98.5, 55.6, 55.5; (IR, Neat): 2962, 1639, 1438, 1209, 744, 664 cm^{-1}; HRMS (ESI): Calculated for $[C_{28}H_{22}O_5N_3S]^+$ 512.12747; Found 512.12627.

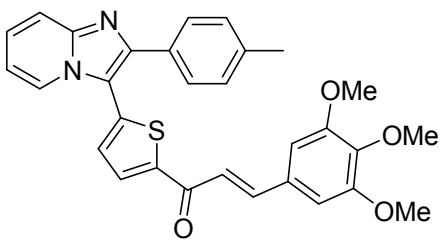
(*E*)-3-(2,4-dimethoxyphenyl)-1-(5-(2-(*p*-tolyl)imidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3m)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 30% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.211 g, 88%). M.p. 131-132 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 – 8.05 (m, 2H), 7.90 (d, *J* = 3.9 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.60 (dd, *J* = 12.7, 8.4 Hz, 3H), 7.49 (dd, *J* = 16.2, 3.3 Hz, 1H), 7.24 – 7.12 (m, 3H), 6.90 – 6.80 (m, 1H), 6.59 – 6.44 (m, 3H), 3.91 (d, *J* = 3.3 Hz, 3H), 3.86 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.3, 163.3, 160.7, 147.7, 145.7, 145.5, 140.4, 138.1, 137.8, 131.8, 131.5,

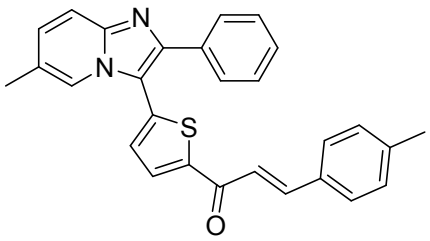
130.7, 130.6, 129.2, 128.3, 125.6, 123.8, 119.5, 117.6, 116.9, 113.0, 105.5, 98.5, 55.6, 55.5, 21.3; (IR, Neat): 2937, 1637, 1438, 1211, 749, 663 cm^{-1}; HRMS (ESI): Calculated for $[C_{27}H_{26}O_3N_2S]^+$ 481.15563; Found 481.15627.

(*E*)-1-(5-(2-(*p*-tolyl)imidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (3n)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 30% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.214 g, 84%). M.p. 136-137 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, *J* = 6.9 Hz, 1H), 7.97 (d, *J* = 3.9 Hz, 1H), 7.84 (d, *J* = 15.5 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.65 – 7.60 (m, 1H), 7.36 – 7.29 (m, 2H), 7.19 (dd, *J* = 15.2, 9.5 Hz, 3H), 6.93 – 6.83 (m, 4H), 3.95 (s, 6H), 3.93 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.7, 153.6, 147.1, 145.6, 144.8, 144.7, 140.8, 139.5, 138.2, 132.4, 131.8, 131.3, 130.6, 129.3, 128.3, 127.4, 125.7, 123.7, 120.4, 117.7, 113.1, 106.0, 61.0, 56.3, 21.3; (IR, Neat): 2937, 1642, 1413, 1242, 748, 664 cm^{-1}; HRMS (ESI): Calculated for $[C_{30}H_{27}O_4N_2S]^+$ 511.16860; Found 511.16752.

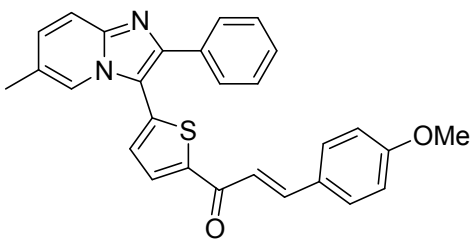
(*E*)-1-(5-(6-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)-3-(*p*-tolyl)prop-2-en-1-one (3o)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.208 g, 96%). M.p. 148-149 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.1 Hz, 1H), 7.93 (d, *J* = 4.0 Hz, 1H), 7.87 (s, 1H), 7.72 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 13.1 Hz, 2H), 7.39 – 7.34 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 3H), 6.72 (dd, *J* = 7.1, 1.5 Hz, 1H), 2.46 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz,

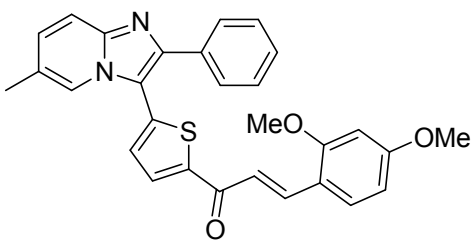
$CDCl_3$) δ 181.7, 146.8, 146.3, 144.6, 141.4, 138.7, 137.0, 135.8, 135.2, 133.6, 132.3, 131.9, 130.4, 129.8, 128.6, 128.5, 128.4, 128.1, 123.0, 120.1, 116.1, 115.8, 21.6, 21.4; (IR, Neat): 2926, 1643, 1435, 1213, 750, 665 cm^{-1}; HRMS (ESI): Calculated for $[C_{28}H_{23}ON_2S]^+$ 435.15256; Found 435.15110.

(*E*)-3-(4-methoxyphenyl)-1-(5-(6-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3p)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 15% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.211 g, 94%). M.p. 181-182 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, J = 7.0 Hz, 1H), 7.90 (t, J = 9.7 Hz, 2H), 7.76 – 7.70 (m, 2H), 7.64 (d, J = 8.7 Hz, 2H), 7.47 (s, 1H), 7.39 – 7.30 (m, 4H), 7.22 (d, J = 3.8 Hz, 1H), 6.96 (d, J = 8.7 Hz, 2H), 6.72 (d, J = 7.0 Hz, 1H), 3.88 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.6, 161.9, 147.0, 146.3, 145.3, 144.3, 138.4, 136.9, 133.6, 132.0, 130.4, 128.5, 128.4, 128.1, 127.3, 123.0, 118.8, 116.1, 115.7, 114.5, 55.5, 21.4; (IR, Neat): 2916, 1642, 1435, 1215, 748, 696 cm^{-1}; HRMS (ESI): Calculated for $[C_{28}H_{23}O_2N_2S]^+$ 451.14748; Found 451.14557. Elemental Analysis: Calculated C, 74.64; H, 4.92; N, 6.22; S, 7.12; Found C, 73.27; H, 4.84; N, 5.55; S, 6.96.

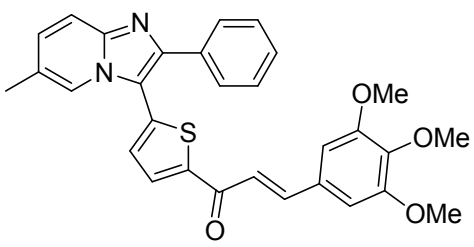
(*E*)-3-(2,4-dimethoxyphenyl)-1-(5-(6-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)prop-2-en-1-one (3q)



Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 20% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.214 g, 89%). M.p. 121-123 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 – 8.09 (m, 2H), 7.90 (d, J = 3.9 Hz, 1H), 7.73 (dd, J =

7.9, 1.5 Hz, 2H), 7.61 – 7.52 (m, 2H), 7.47 (s, 1H), 7.35 (q, *J* = 6.3 Hz, 3H), 7.21 (d, *J* = 3.9 Hz, 1H), 6.74 – 6.68 (m, 1H), 6.56 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.50 (d, *J* = 2.2 Hz, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.3, 163.3, 160.7, 147.5, 146.2, 145.2, 140.3, 137.9, 136.8, 133.7, 131.8, 131.4, 130.4, 128.4, 128.4, 128.0, 123.1, 119.6, 116.9, 116.1, 115.7, 113.5, 112.8, 105.5, 98.5, 55.6, 55.5, 21.4; (IR, Neat): 3019, 1643, 1439, 1214, 745, 667 cm^{-1}; HRMS (ESI): Calculated for $[C_{29}H_{25}O_3N_2S]^+$ 481.15804; Found 481.15631.

(*E*)-1-(5-(6-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)thiophen-2-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (3r)



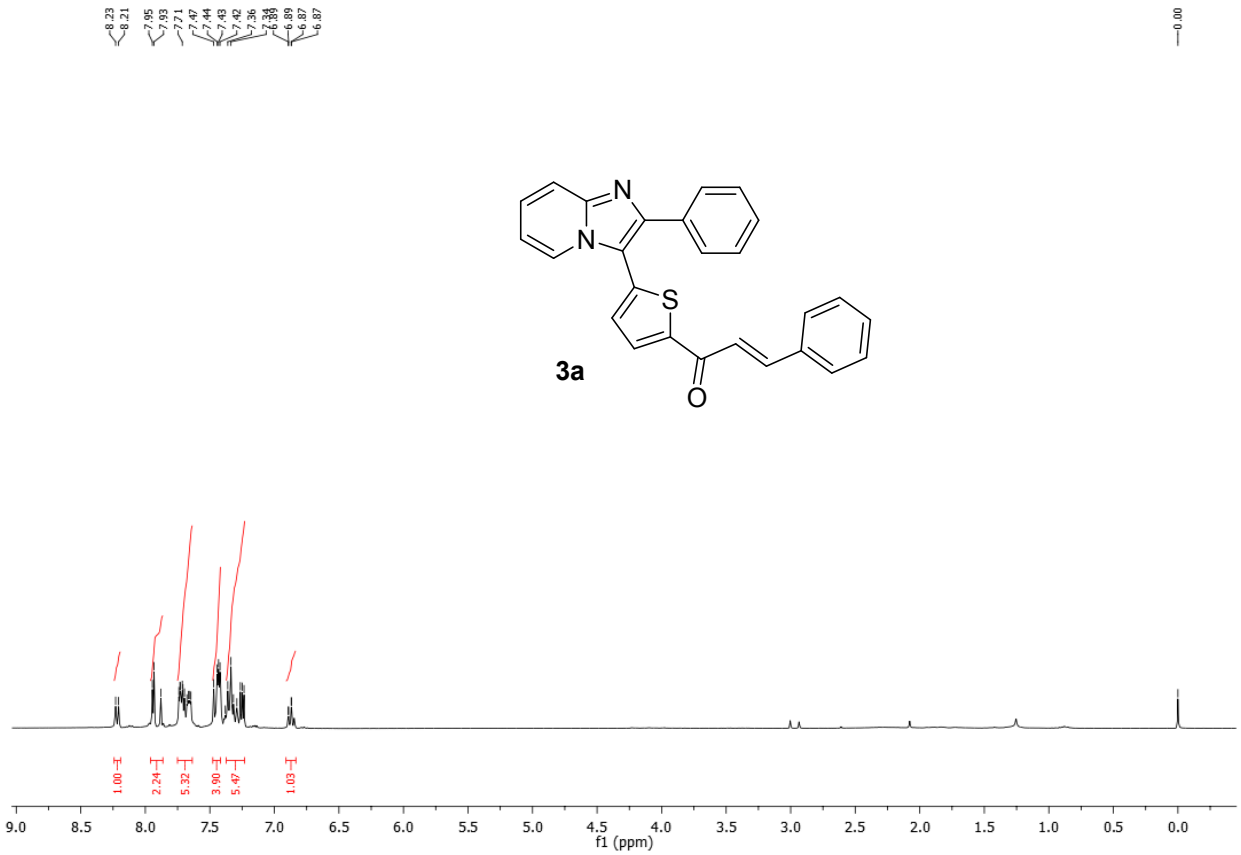
Following the general procedure, the residue was purified by column chromatography (silica gel 60-120 mesh, 30% ethyl acetate in hexane as the eluent) to afford the title product as a yellow solid (0.217 g, 85%). M.p. 158-159 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.0 Hz, 1H), 7.94 (d, *J* = 3.9 Hz, 1H), 7.82 (d, *J* = 15.5 Hz, 1H), 7.71 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.46 (s, 1H), 7.37 – 7.29 (m, 4H), 7.22 (d, *J* = 3.9 Hz, 1H), 6.88 (s, 2H), 6.71 (dd, *J* = 7.1, 1.6 Hz, 1H), 3.93 (s, 6H), 3.91 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.4, 153.5, 146.6, 146.3, 145.4, 144.6, 140.8, 138.8, 136.9, 133.7, 132.3, 130.4, 130.1, 128.4, 128.1, 123.0, 120.4, 116.2, 115.7, 112.6, 105.9, 61.0, 56.3, 21.4; (IR, Neat): 3011, 1644, 1417, 1217, 746, 696 cm^{-1}; HRMS (ESI): Calculated for $[C_{30}H_{27}O_4N_2S]^+$ 511.16860; Found 511.16752. Elemental Analysis: Calculated C, 70.57; H, 5.13; N, 5.49; S, 6.28; Found C, 69.54; H, 5.21; N, 4.13; S, 5.53.

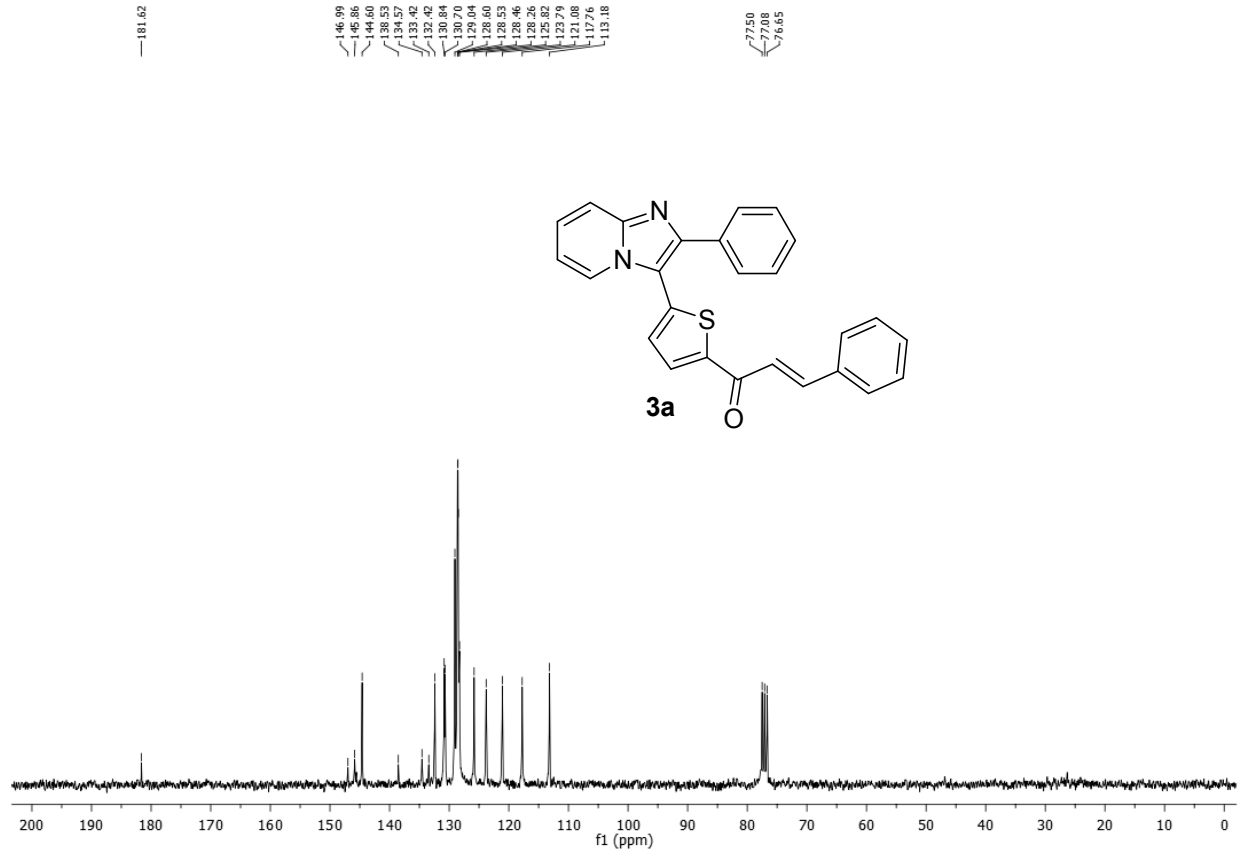
1.4 References

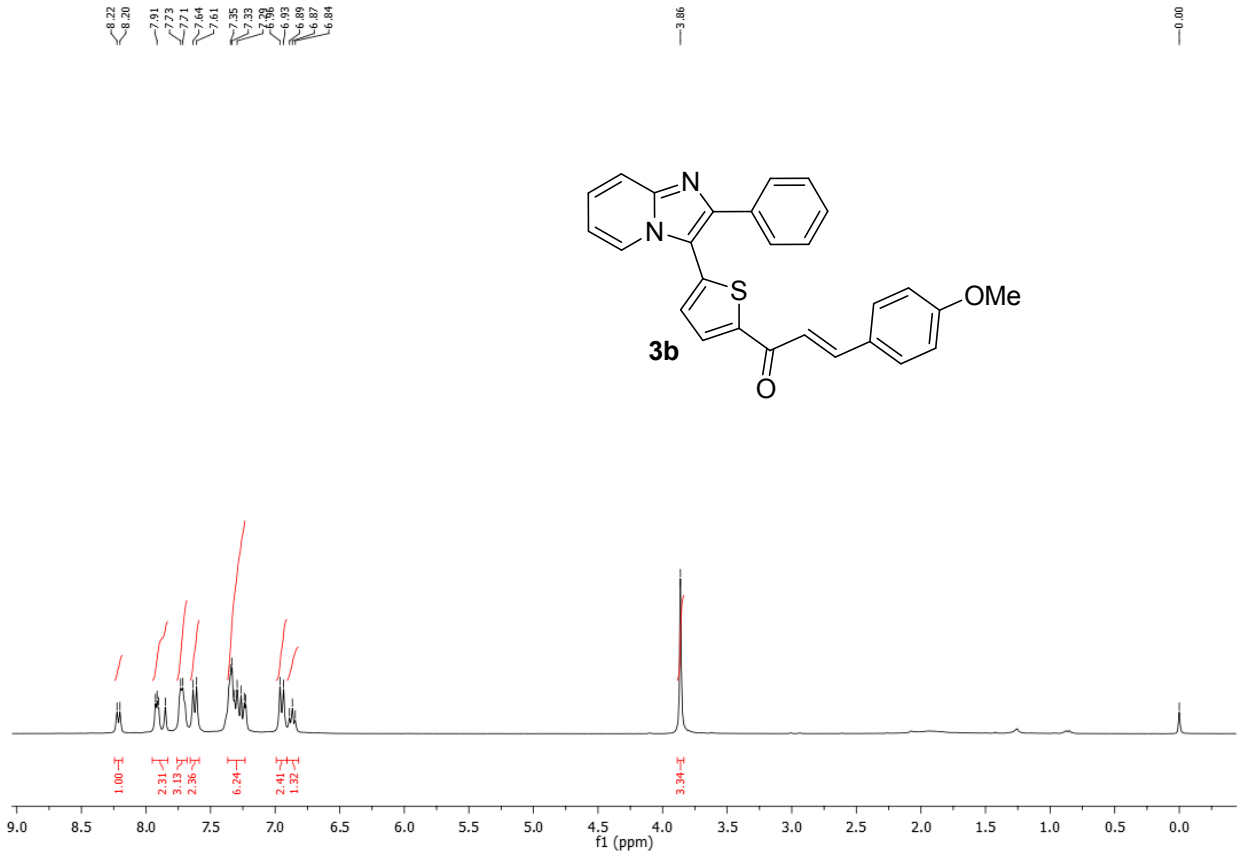
1. K. S. Gudmundsson and B. A. Johns, *Bioorg. Med. Chem. Lett*. **2007**, *17*, 2735–2739.

2. B. Ramesh, and B. Someswara Rao, *E-Journal of Chemistry*, **2010**, *7*, 433-436.

1.5 ^{1}H and ^{13}C NMR spectra for compounds 3a-3r



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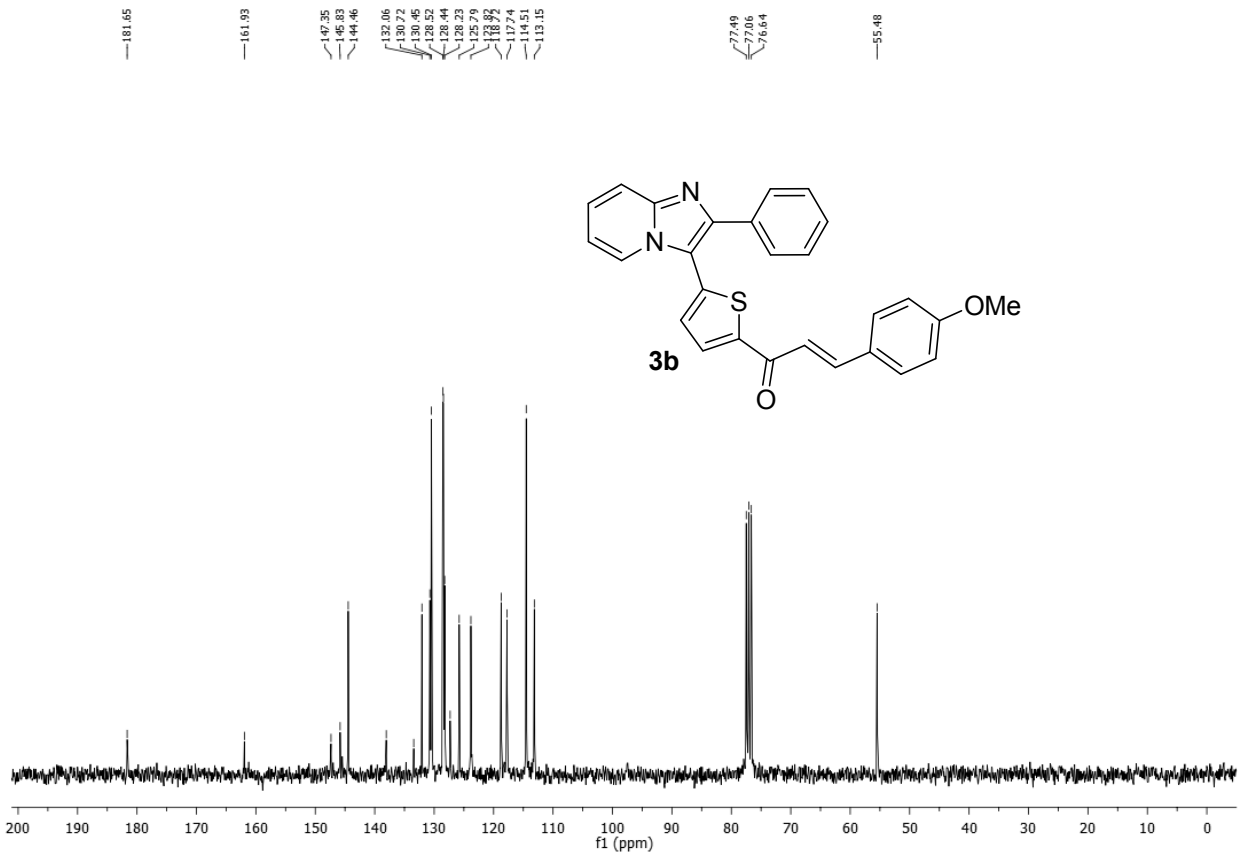
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OMe
O
3b
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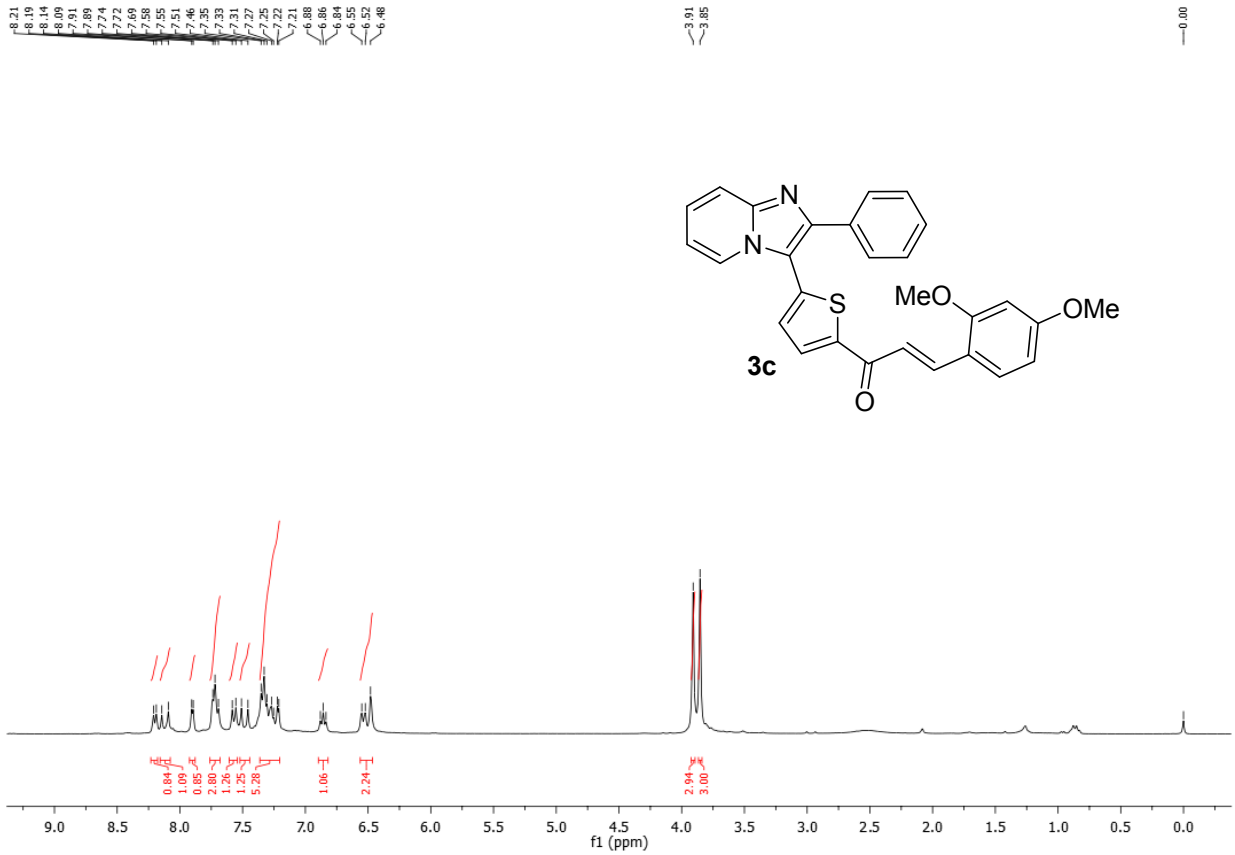
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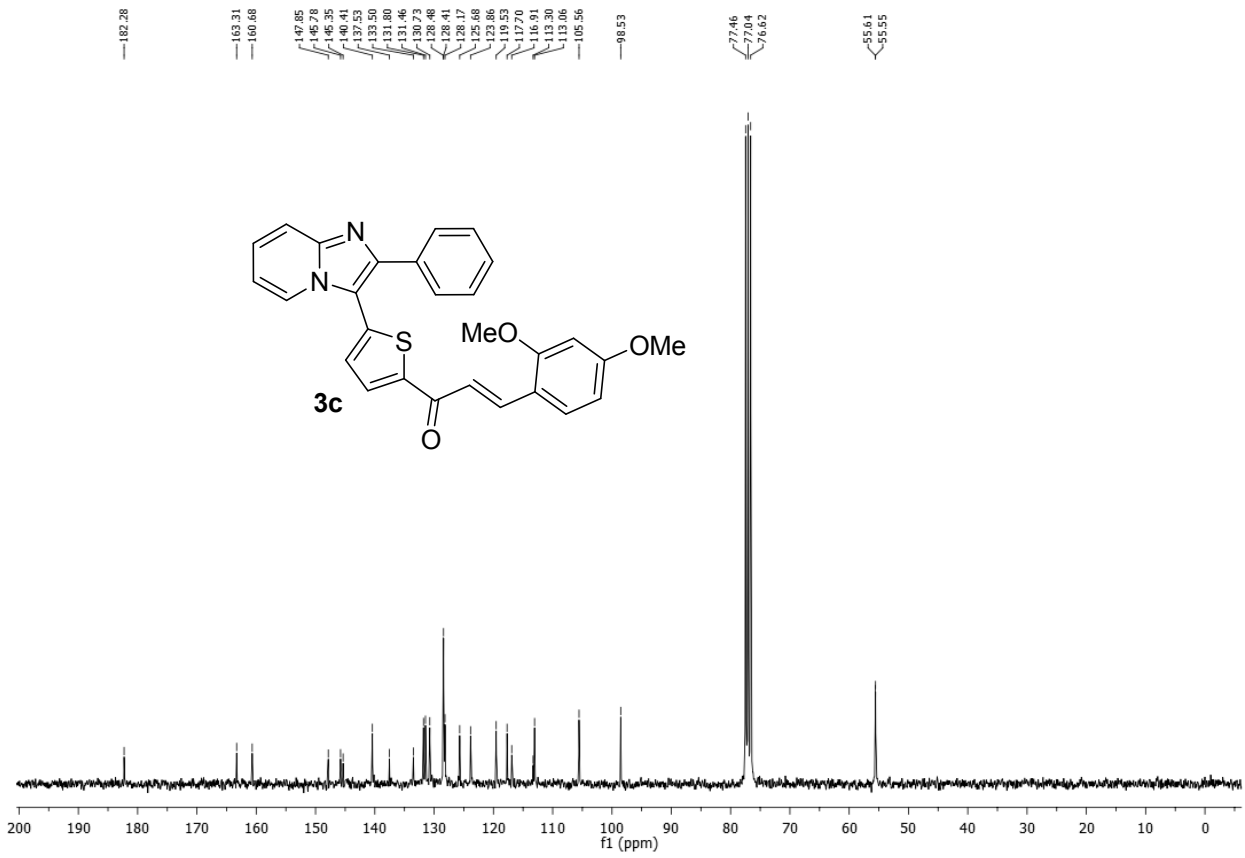
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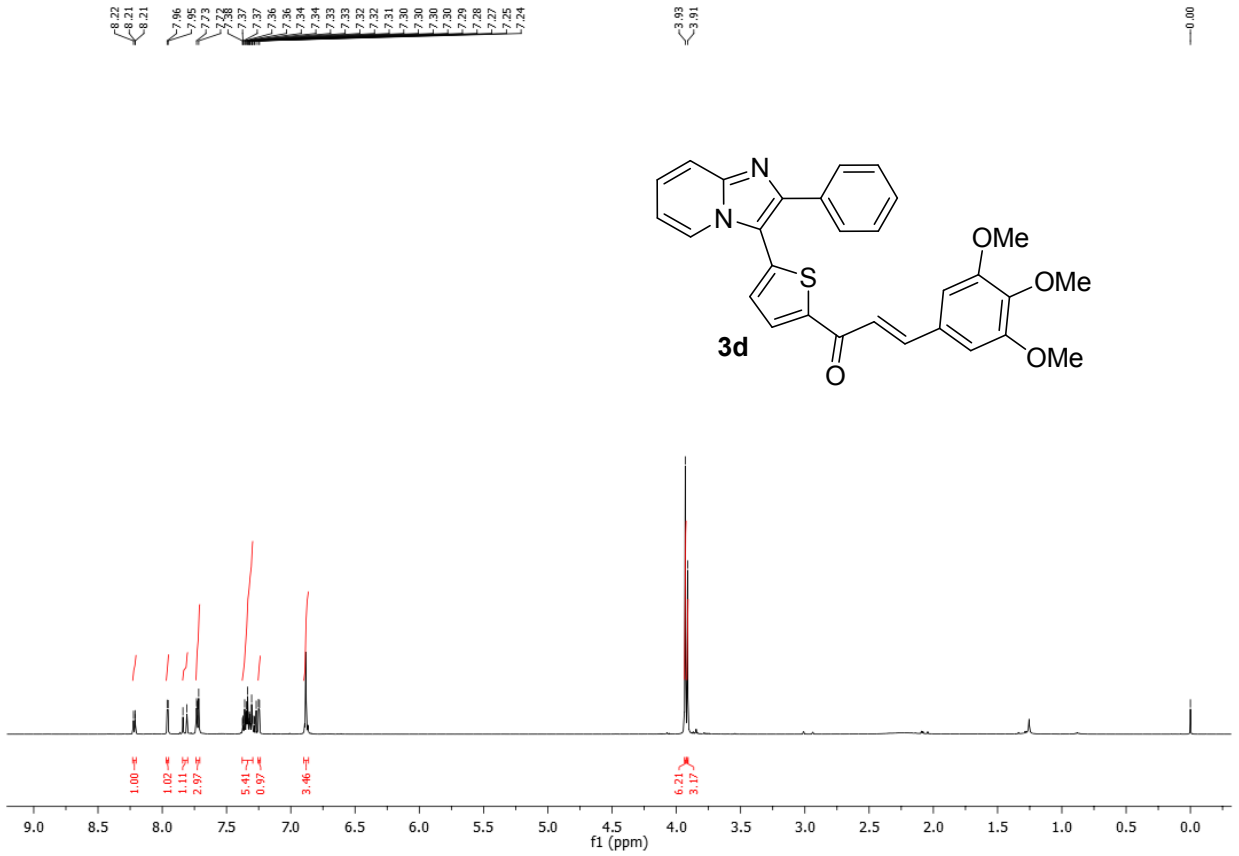
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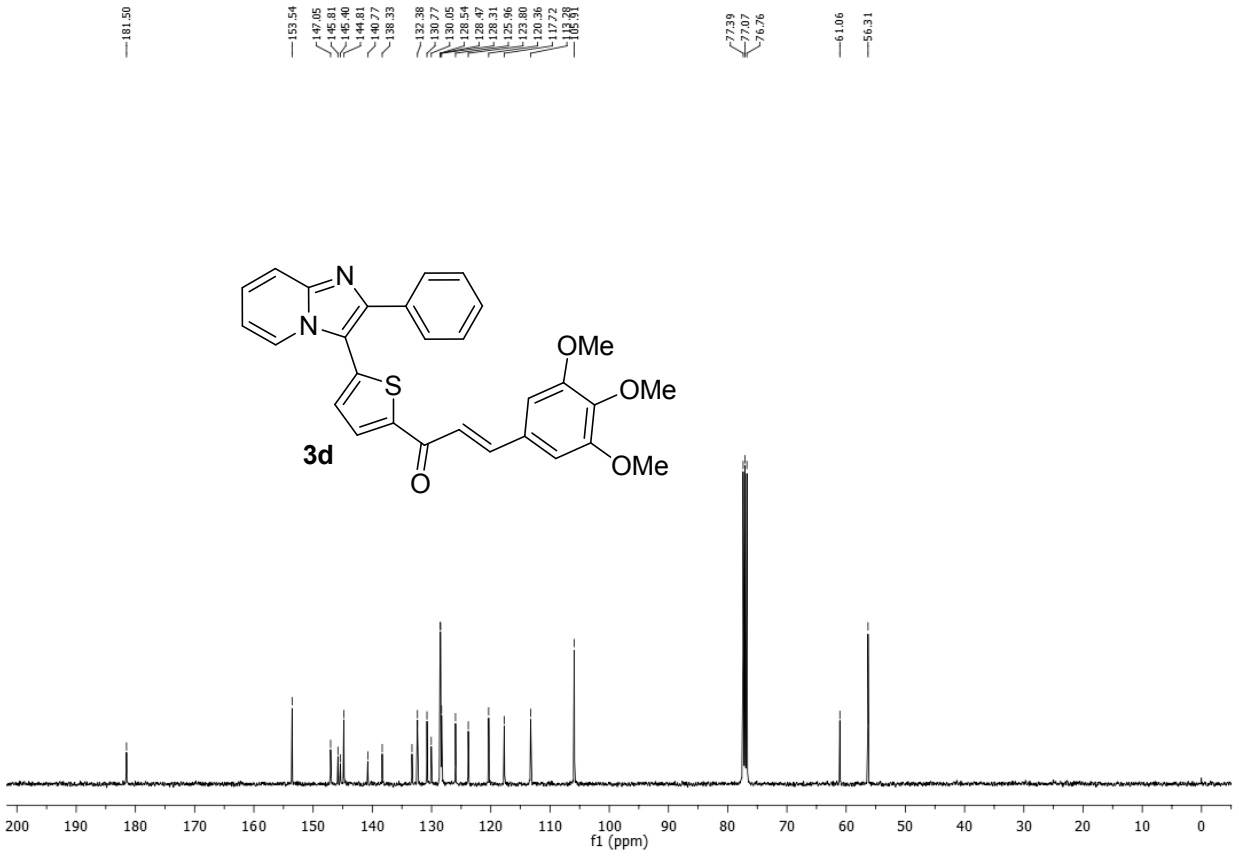
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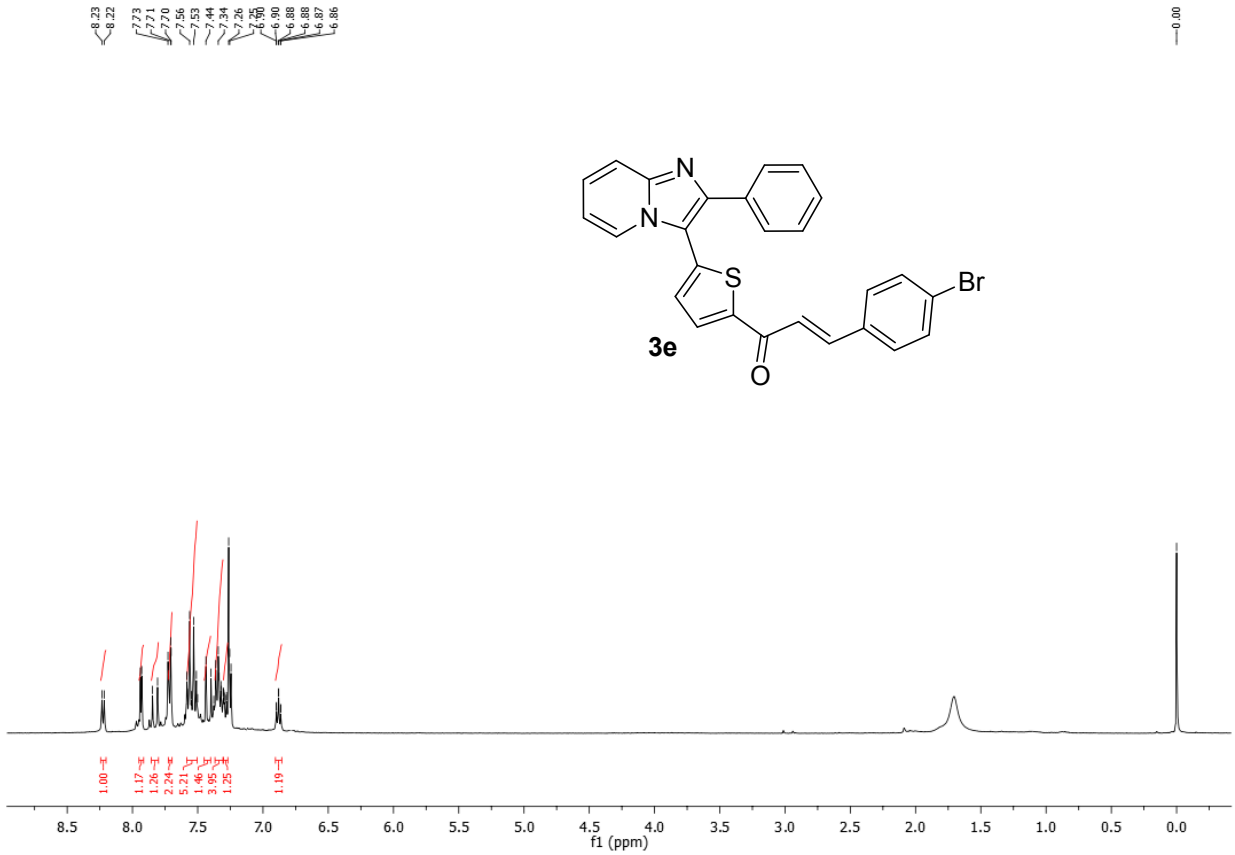
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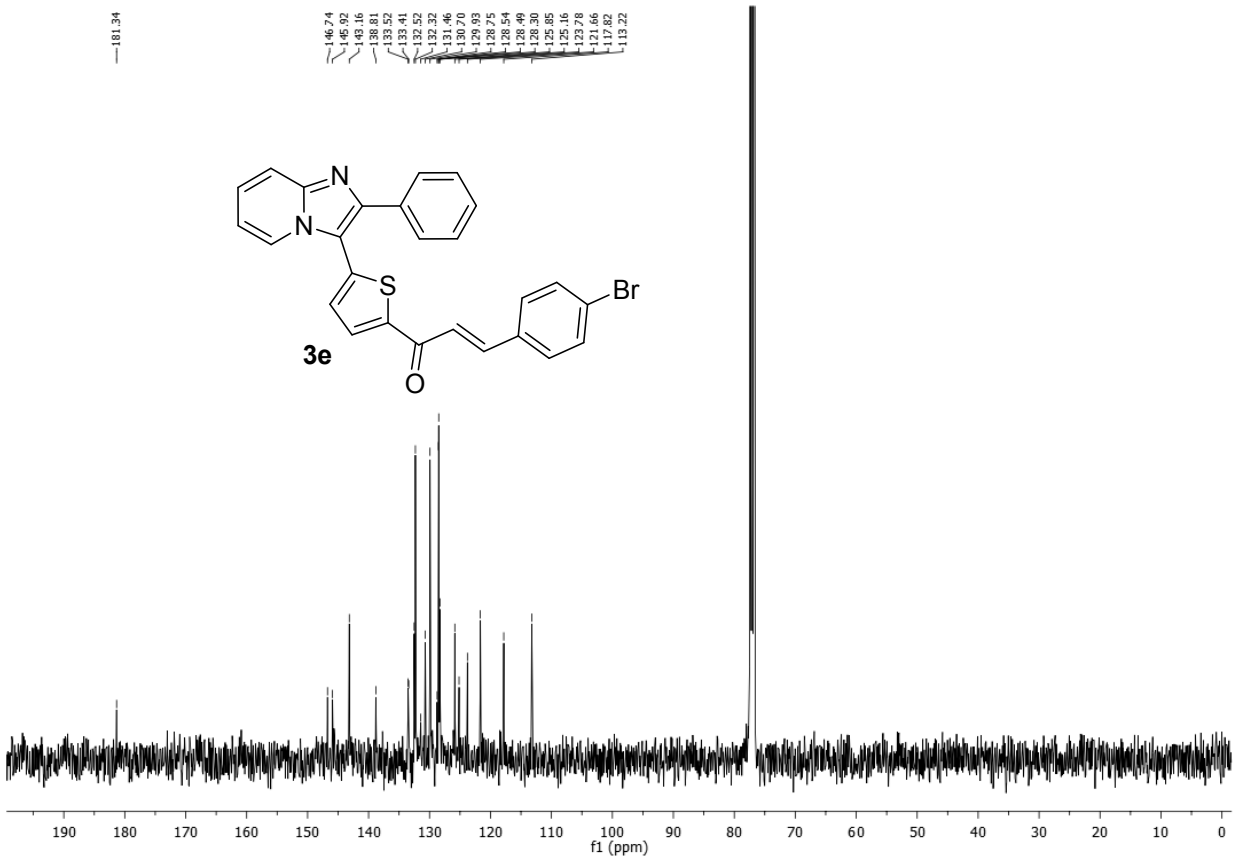
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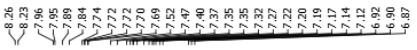
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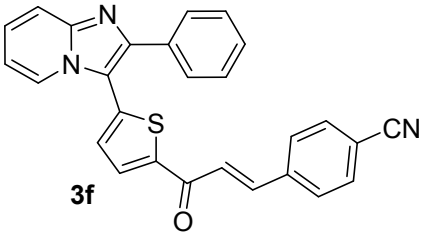
6.92
6.90
6.87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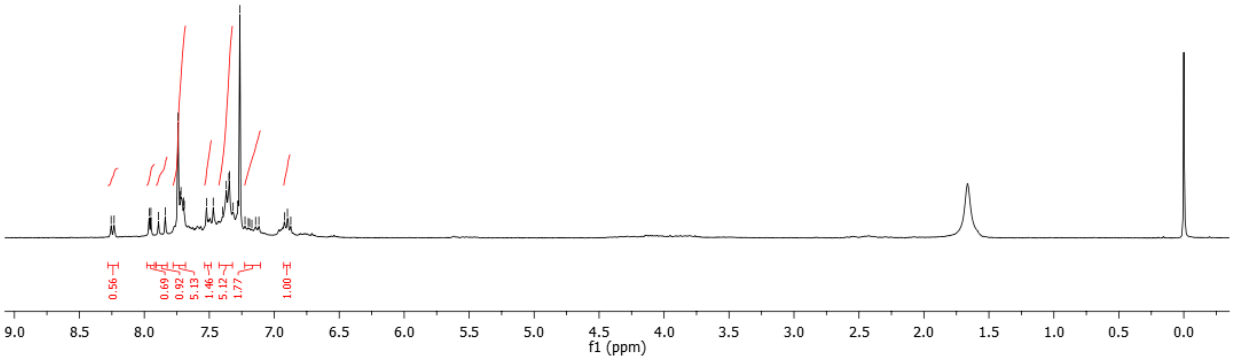
S
CN
O

3f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6.0
5.5
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3.0
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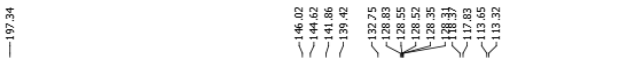
f1 (ppm)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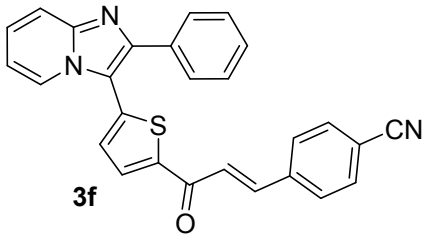
113.32
77.47
77.05
76.62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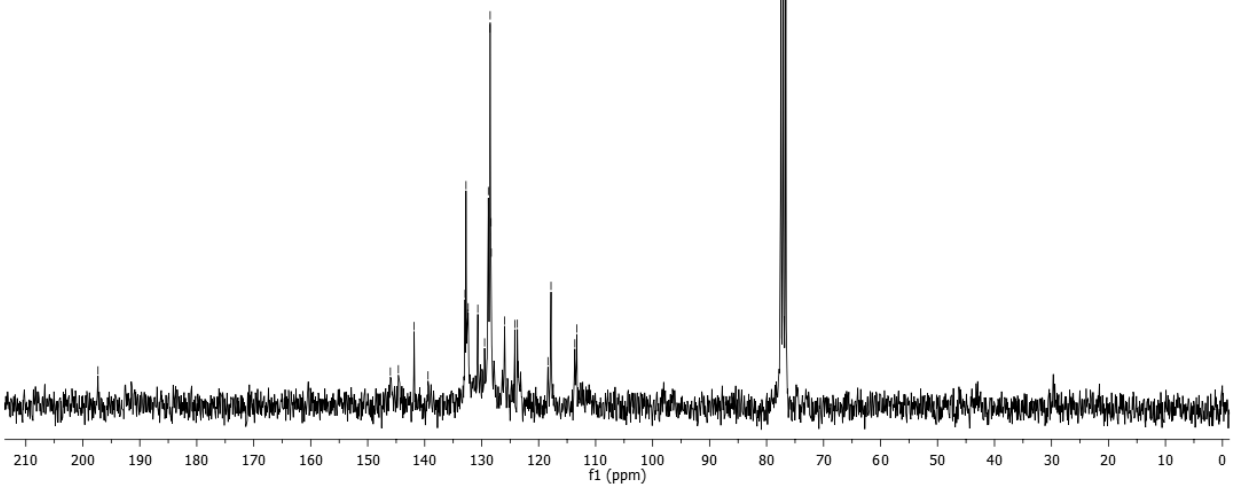
S
CN
O

3f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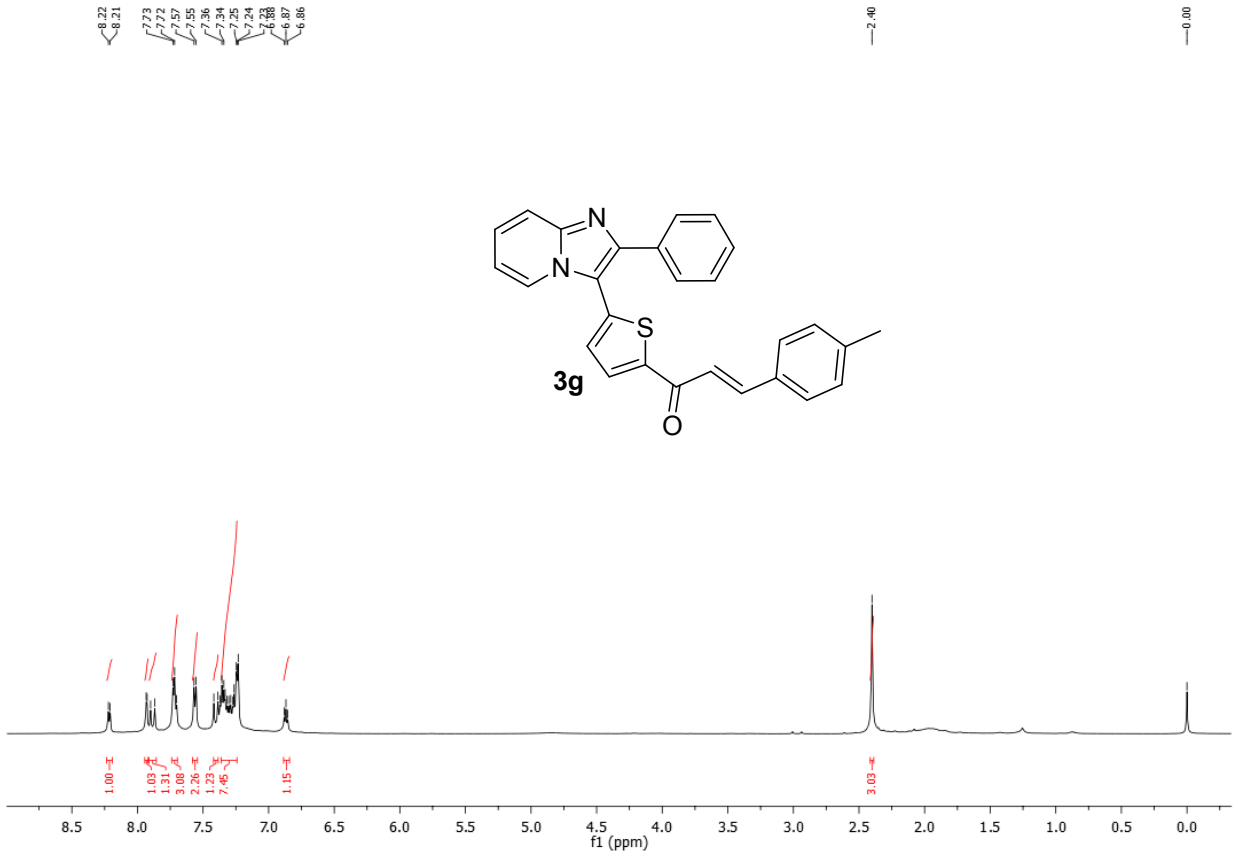
f1 (ppm)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7.34
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7.24
6.87
6.86
2.40
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1.31
3.08
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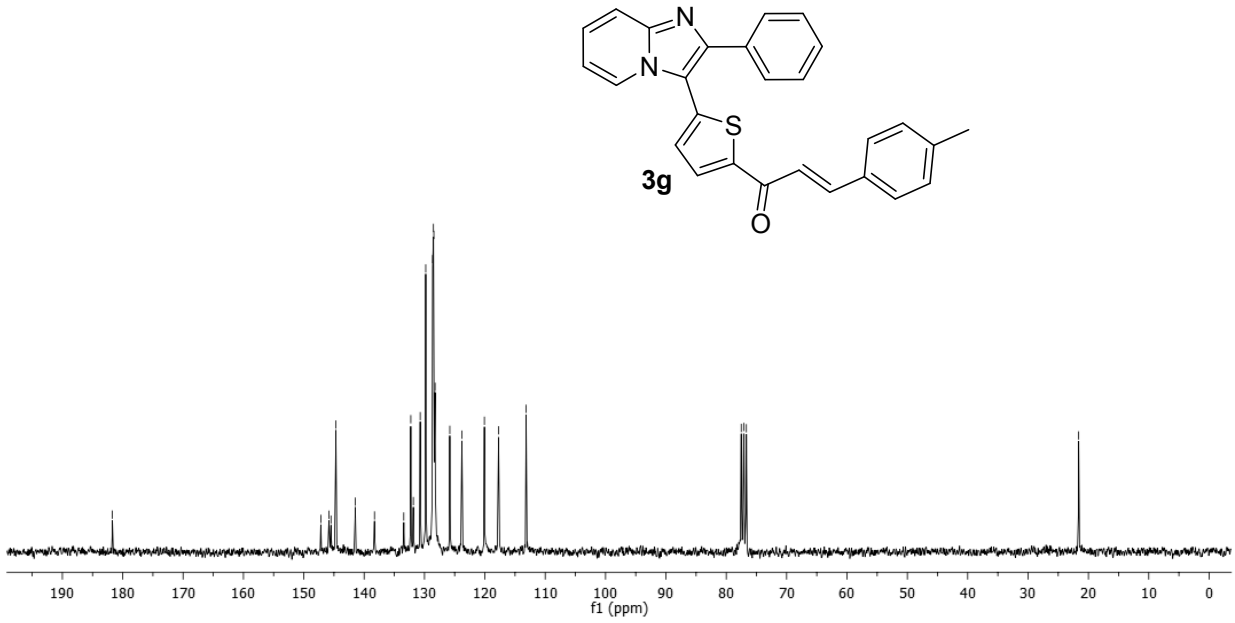
1.23
7.46
1.15
3.03
f1 (ppm)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133.43
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129.79
128.65
128.52
128.45
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120.08
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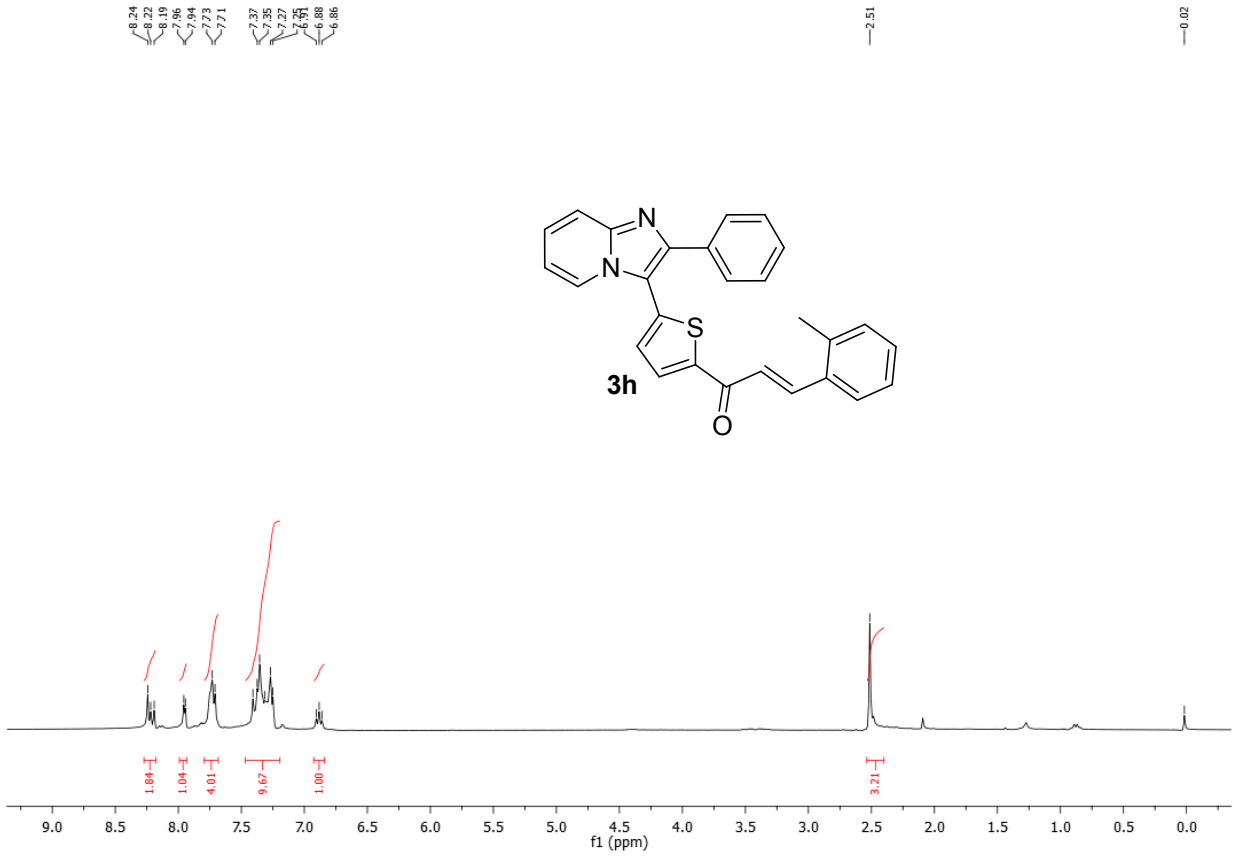
113.17
77.52
77.09
76.67
21.61
3g
f1 (ppm)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7.73
7.71
7.37
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7.27
6.91
6.88
6.86
2.51
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N
S
O
3h
1.84
1.04
4.01
9.67
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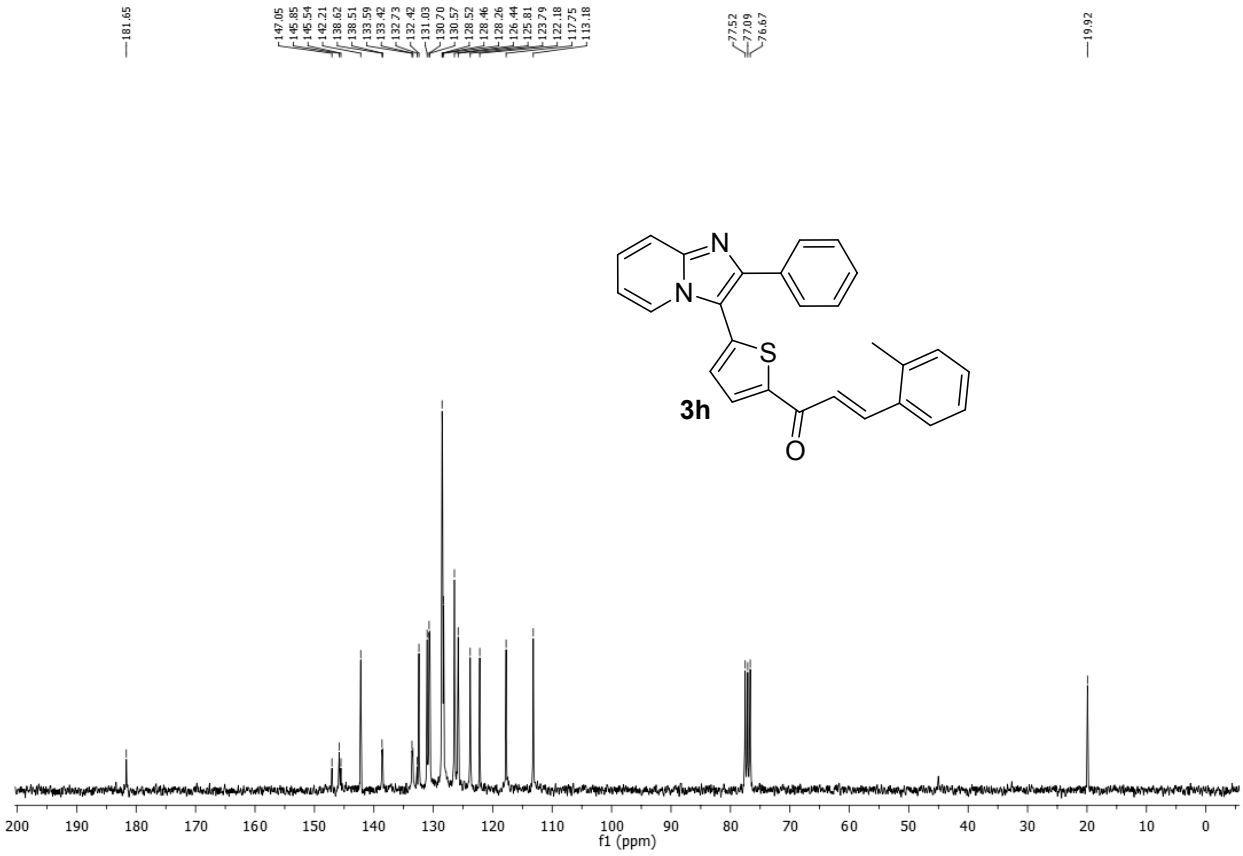
3.21
f1 (ppm)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130.57
128.52
128.46
128.26
126.44
125.81
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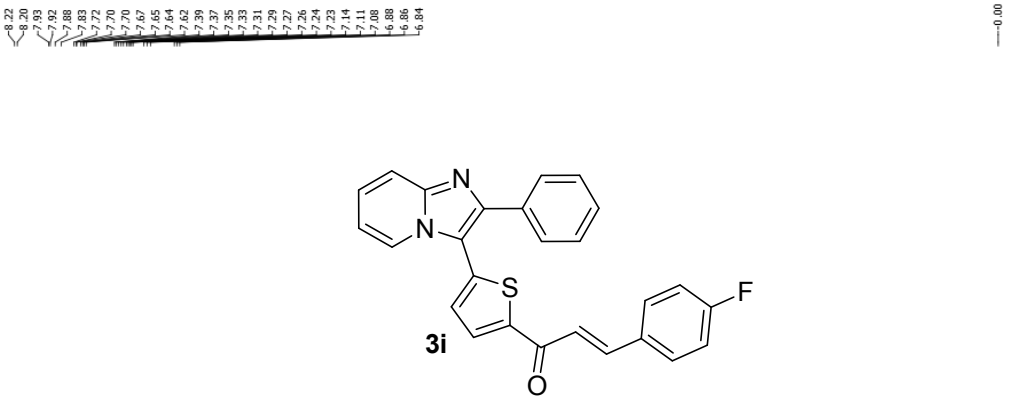
113.18
77.52
77.09
76.67
19.92
N
N
S
O
3h
f1 (ppm)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7.83
7.72
7.70
7.70
7.67
7.65
7.64
7.62
7.39
7.37
7.35
7.33
7.31
7.29
7.27
7.26
7.24
7.23
7.14
7.11
7.08
6.88
6.86
6.84
0.00
N
N
S
F
O
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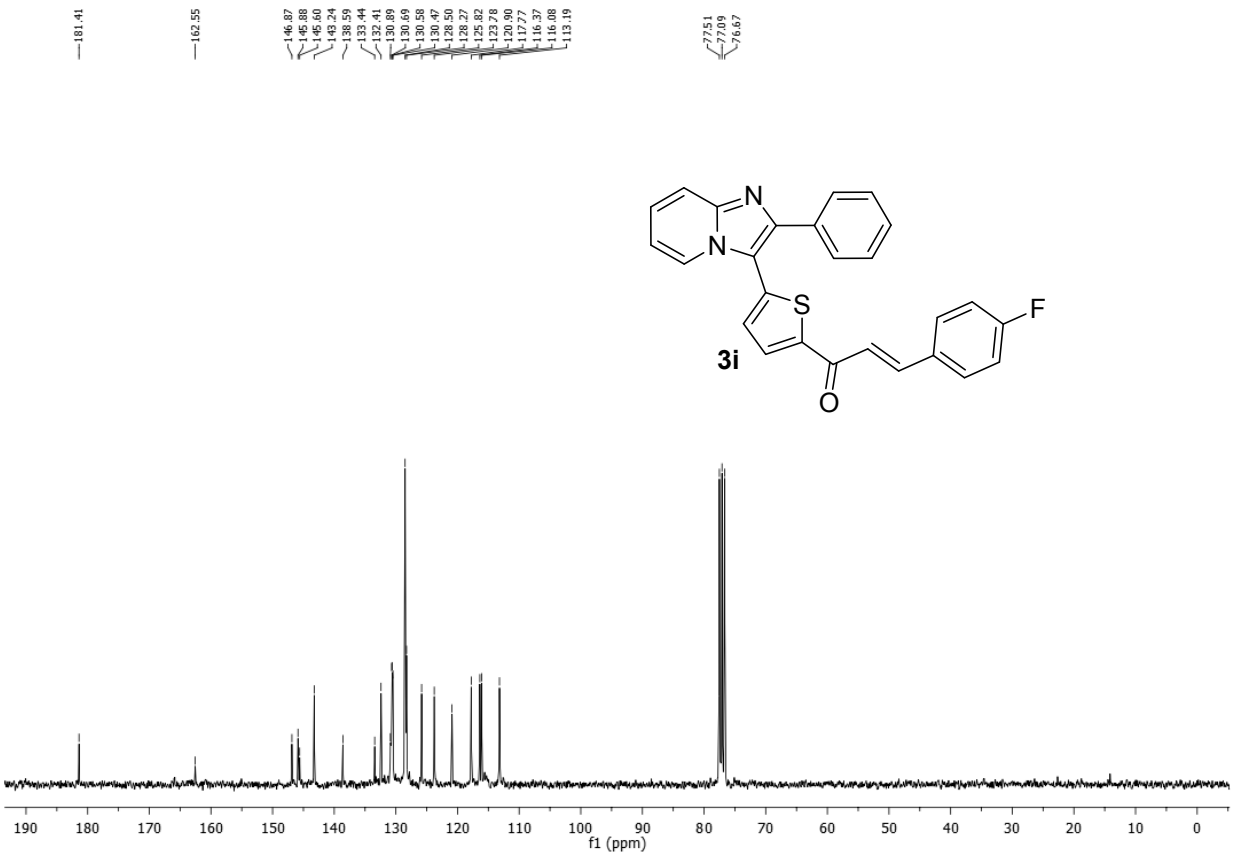
3.15
2.45
5.07
1.13
2.24
1.43
f1 (ppm)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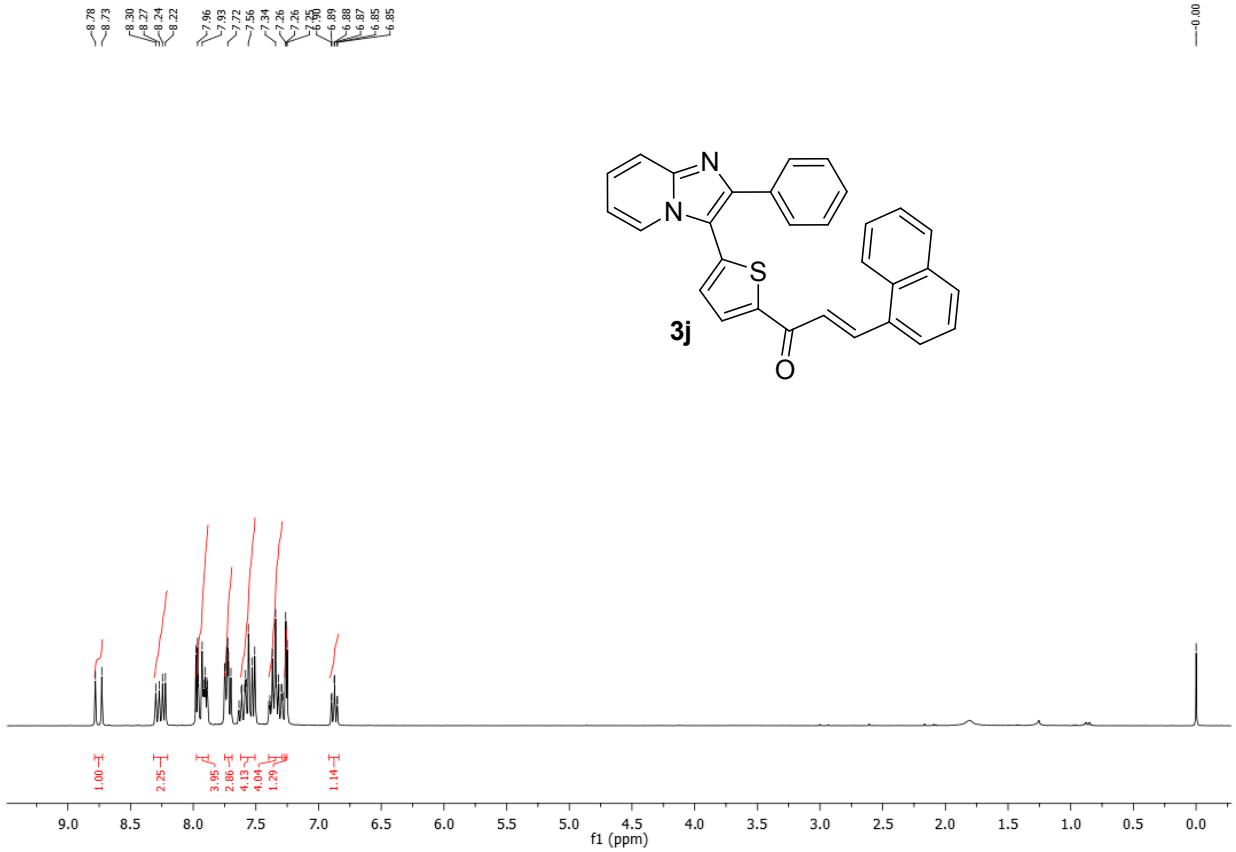
130.89
130.69
130.58
130.47
128.50
128.27
125.82
123.78
120.90
117.77
116.37
116.08
113.19
77.51
77.09
76.67
N
N
S
F
O
3i
f1 (ppm)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7.56
7.34
7.26
7.26
7.25
6.89
6.88
6.87
6.85
6.85
0.00
N
N
S
O
3j
1.00
2.25
3.95
2.86
4.13
4.04
1.29
1.14
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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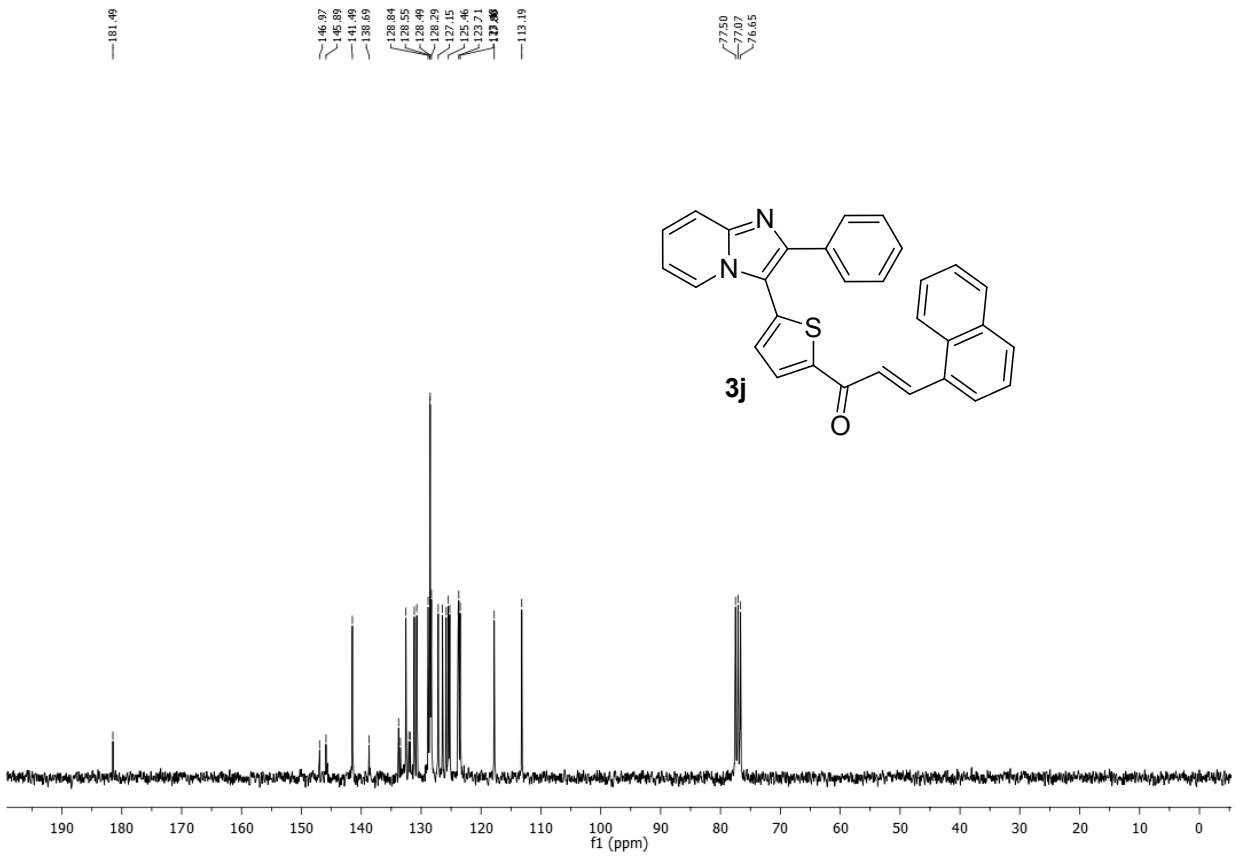
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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125.46
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113.19
77.50
77.07
76.65
N
N
S
O
3j
190
180
170
160
150
140
130
120
110
100
90
80
70
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50
40
30
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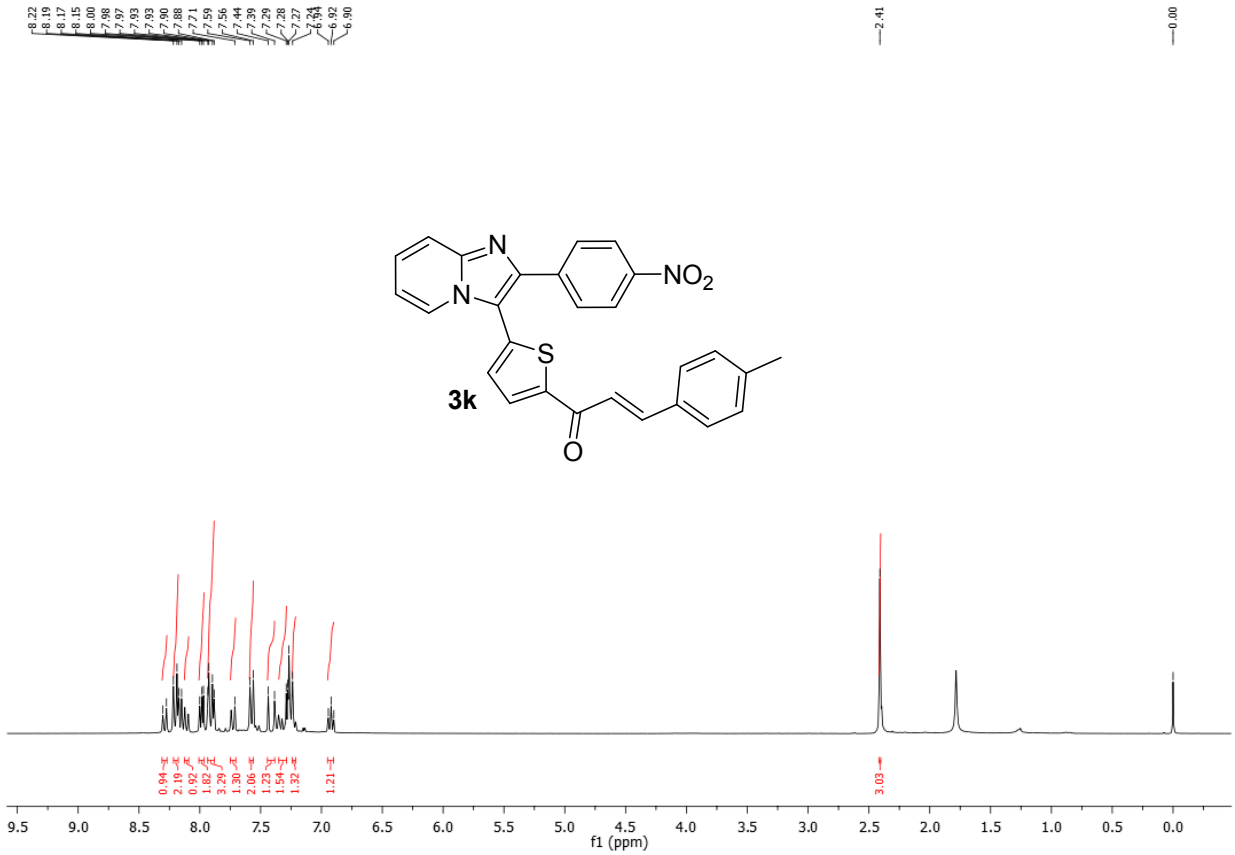
10
0
f1 (ppm)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7.71
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7.39
7.29
7.28
7.27
6.94
6.92
6.90
2.41
0.00
N
N
NO2
S
3k
O
0.94
2.19
0.92
1.82
3.29
1.30
2.06
1.23
1.54
1.32
1.21
3.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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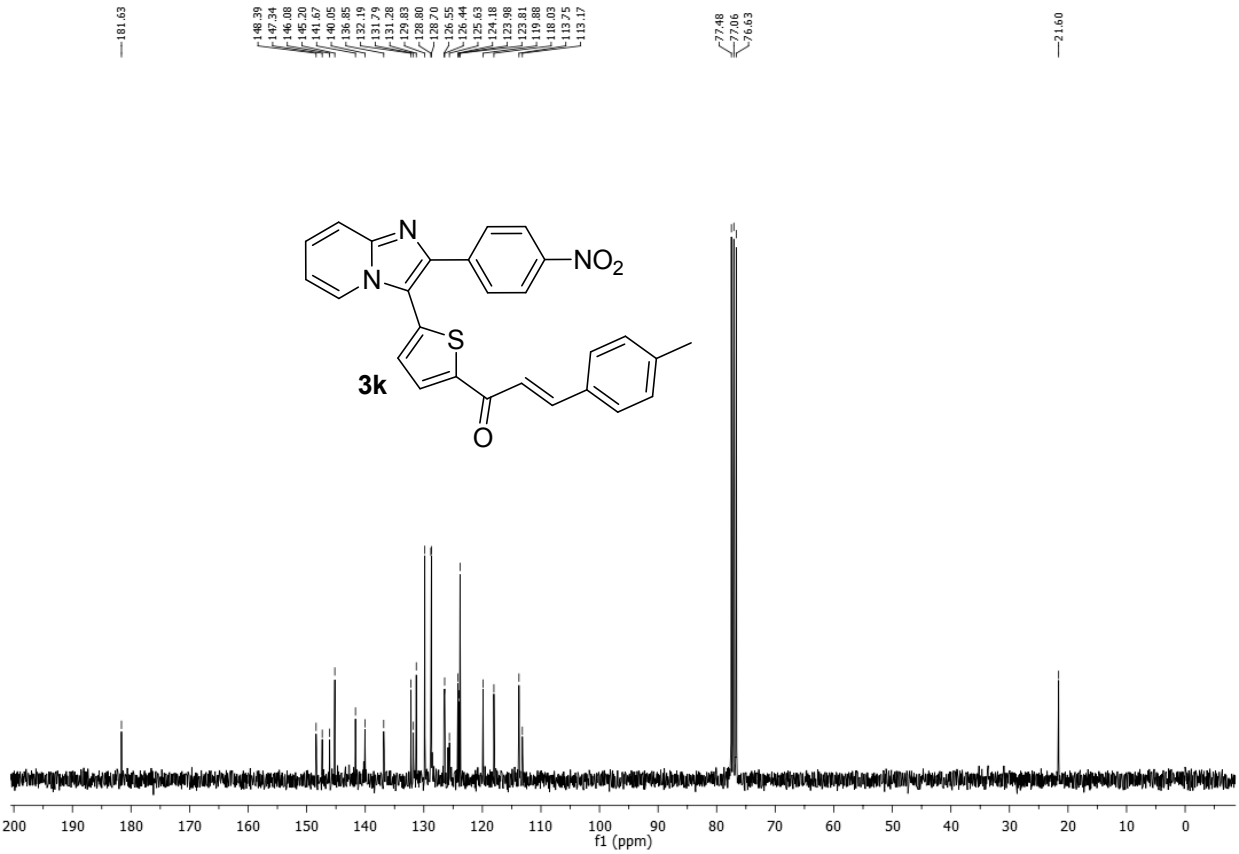
0.0
f1 (ppm)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128.70
126.55
126.44
125.63
124.18
123.98
123.81
119.88
118.03
113.75
113.17
77.48
77.06
76.63
21.60
N
N
NO2
S
3k
O
200
190
180
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120
110
100
90
80
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50
40
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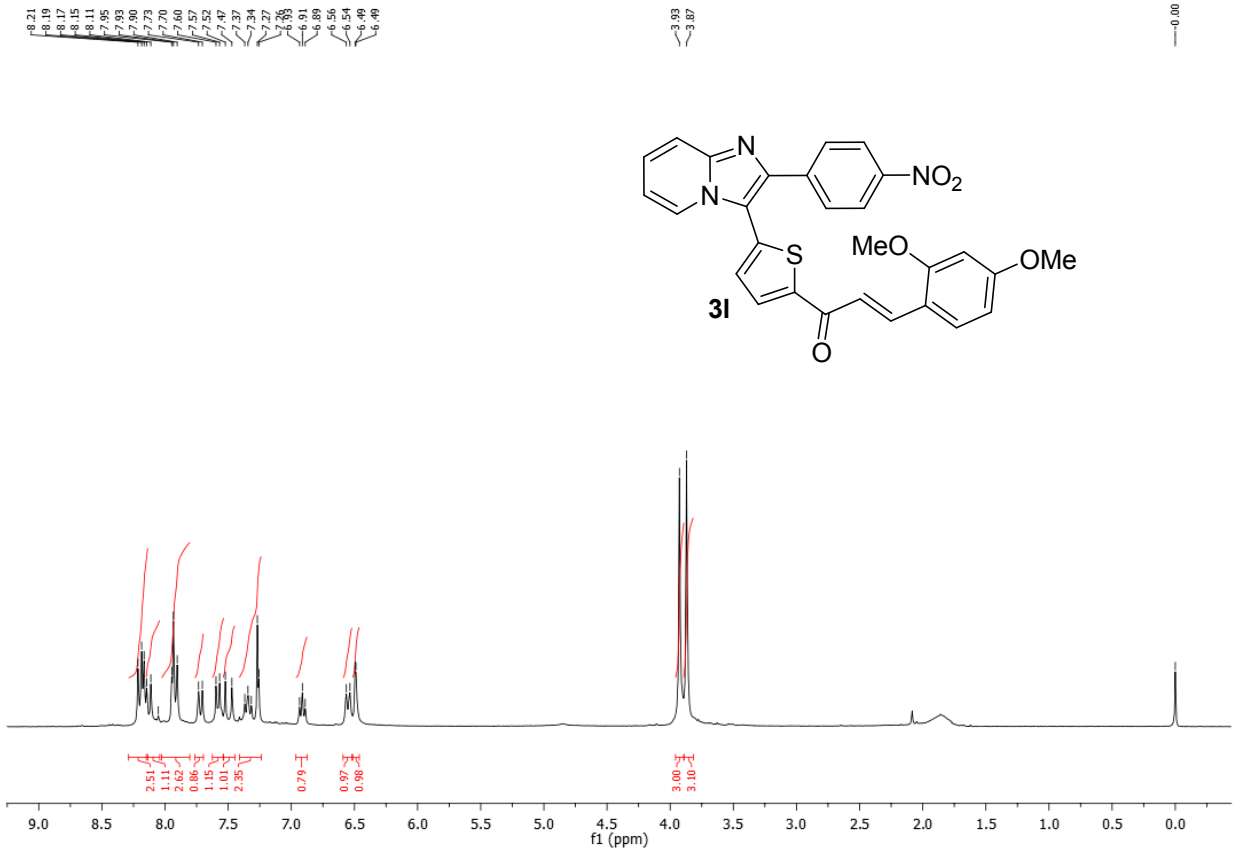
f1 (ppm)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7.52
7.47
7.37
7.34
7.27
6.91
6.89
6.56
6.54
6.49
6.49
3.93
3.87
0.00
N
N
NO2
S
MeO
OMe
O
3l
2.51
1.11
2.62
0.86
1.15
1.01
2.35
0.79
0.97
0.98
3.00
3.10
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.0
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1.0
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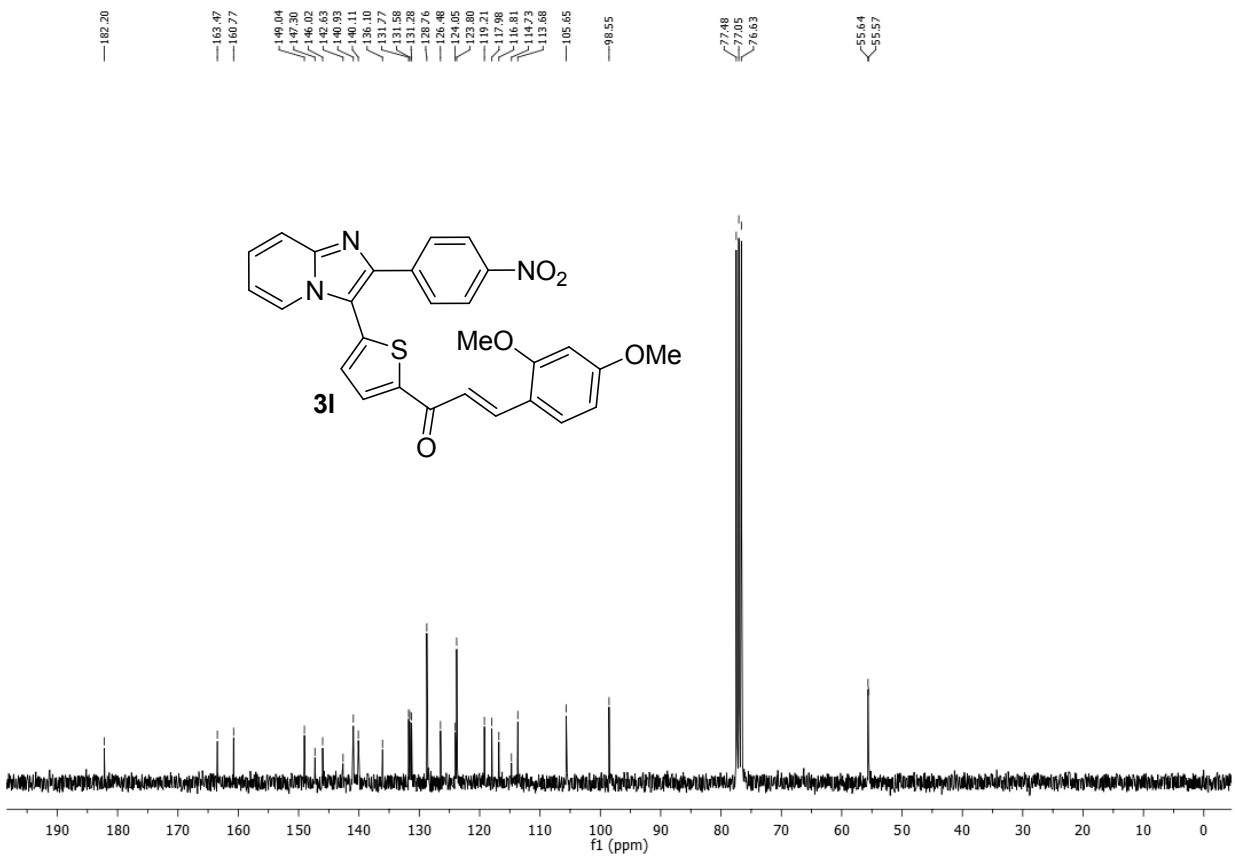
0.0
f1 (ppm)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128.76
126.48
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123.80
119.21
117.98
116.81
114.73
113.68
105.65
98.55
77.48
77.05
76.63
55.64
55.57
N
N
NO2
S
MeO
OMe
O
3l
190
180
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150
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130
120
110
100
90
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50
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30
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10
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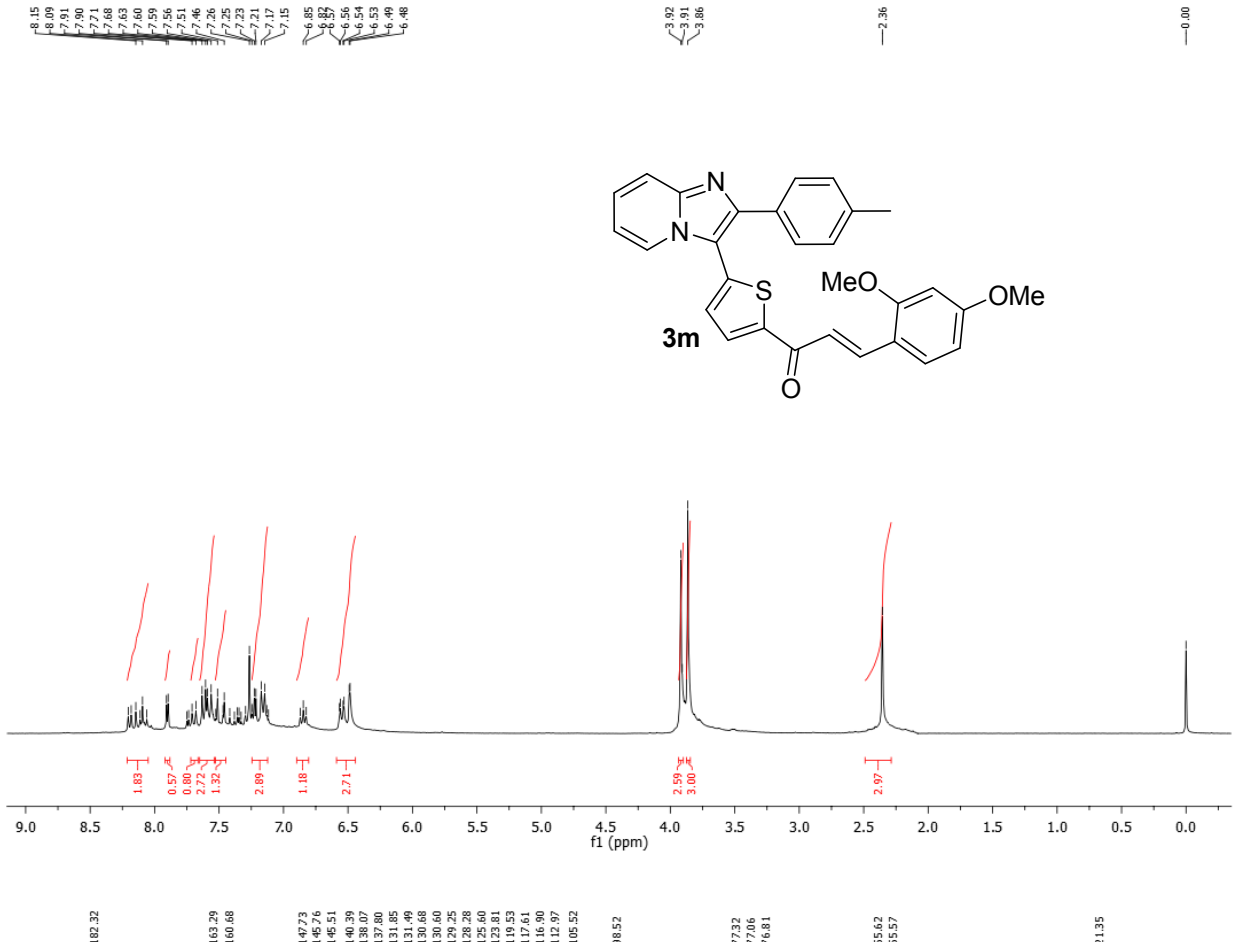
f1 (ppm)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7.46
7.26
7.25
7.23
7.21
7.17
7.15
6.85
6.82
6.56
6.54
6.53
6.49
6.48
3.92
3.91
3.86
2.36
0.00
N
N
S
MeO
OMe
3m
O
1.83
0.57
0.80
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1.32
2.89
1.18
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3.00
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8.0
7.5
7.0
6.5
6.0
5.5
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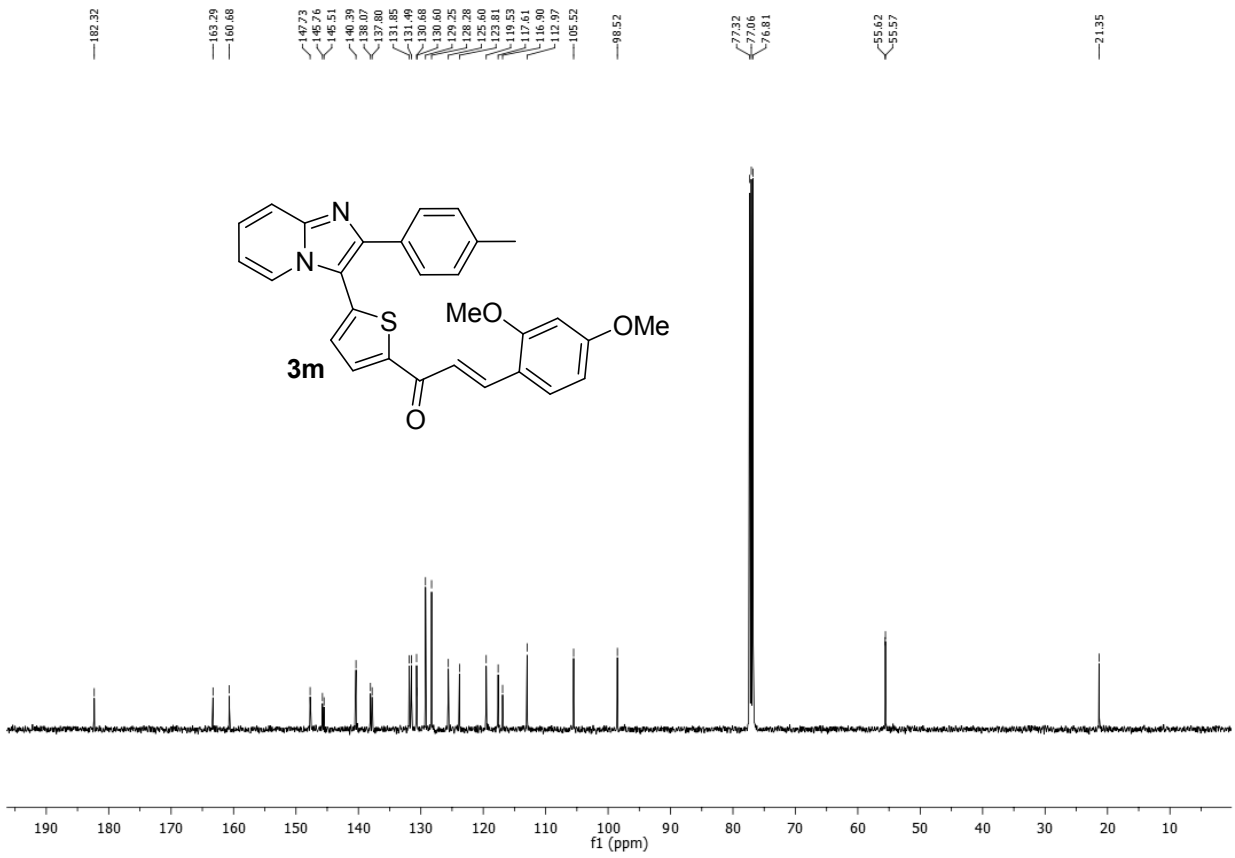
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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131.85
131.49
130.68
130.60
129.25
128.28
125.60
123.81
119.53
117.61
116.90
112.97
105.52
98.52
77.32
77.06
76.81
55.62
55.57
21.35
N
N
S
MeO
OMe
3m
O
190
180
170
160
150
140
130
120
110
100
90
80
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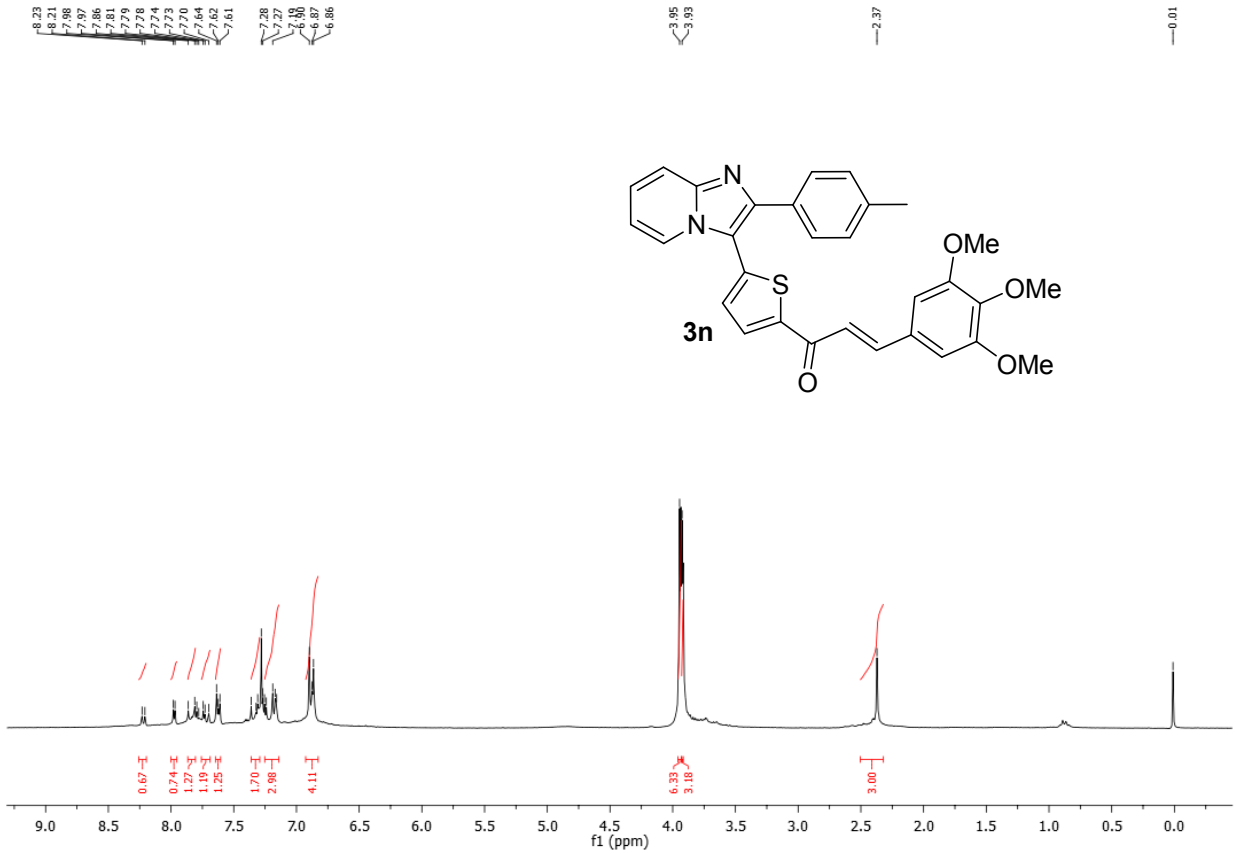
60
50
40
30
20
10
f1 (ppm)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7.78
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7.73
7.70
7.64
7.62
7.61
7.28
7.27
6.87
6.86
3.95
3.93
2.37
0.01
N
N
S
OMe
OMe
OMe
O
3n
0.67
0.74
1.27
1.19
1.25
1.70
2.98
4.11
6.33
3.18
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
2.0
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1.0
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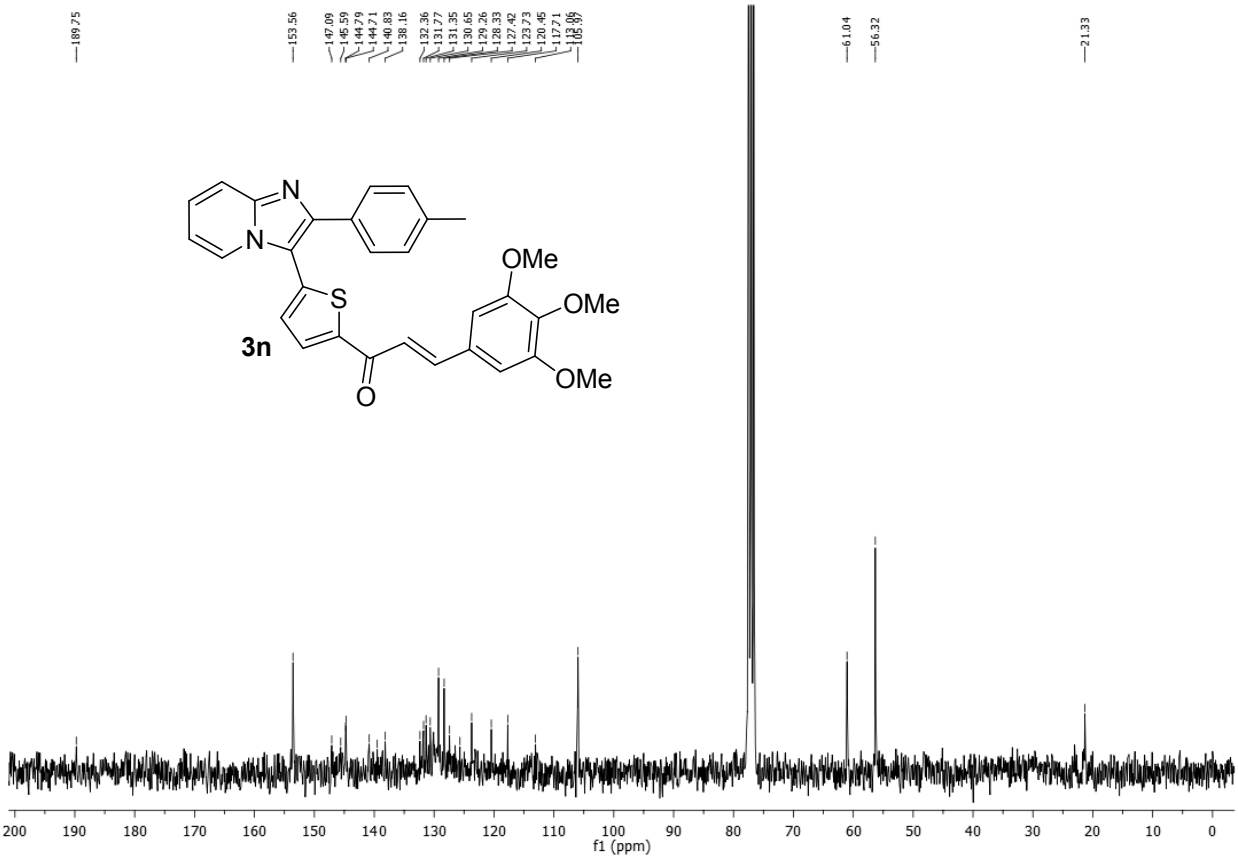
0.0
f1 (ppm)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129.26
128.33
127.42
123.73
120.45
117.71
61.04
56.32
21.33
N
N
S
OMe
OMe
OMe
O
3n
200
190
180
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130
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110
100
90
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70
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50
40
30
20
10
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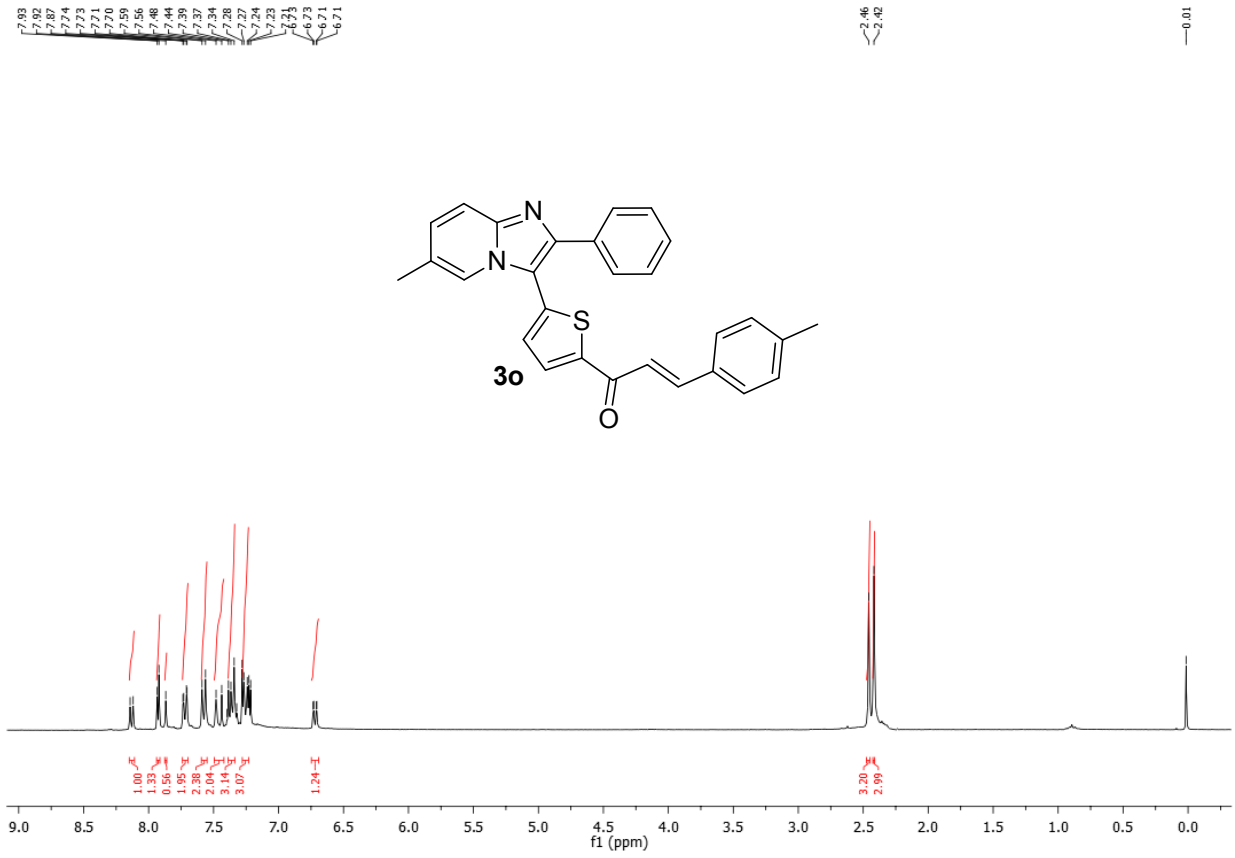
f1 (ppm)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7.37
7.34
7.28
7.27
7.24
7.23
7.21
6.73
6.71
6.71
2.46
2.42
0.01
3o
1.00
1.33
0.56
1.95
2.38
2.04
3.14
3.07
1.24
3.30
2.99
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8.5
8.0
7.5
7.0
6.5
6.0
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2.0
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1.0
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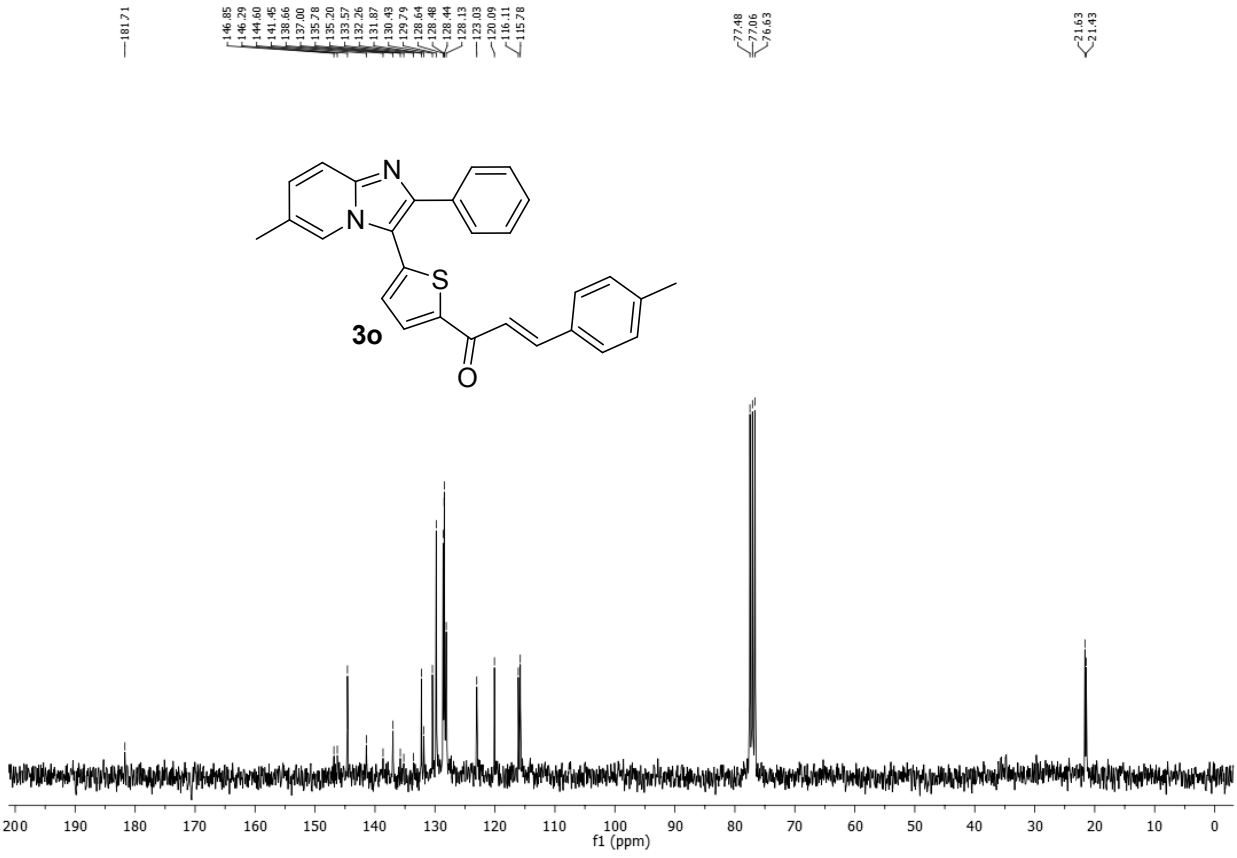
0.0
f1 (ppm)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132.26
131.87
130.43
129.79
128.64
128.48
128.44
128.13
123.03
120.09
116.11
115.78
77.48
77.06
76.63
21.63
21.43
3o
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.14
8.12
7.93
7.91
7.86
7.74
7.74
7.72
7.65
7.62
7.47
7.39
7.37
7.36
7.34
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7.23
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6.70
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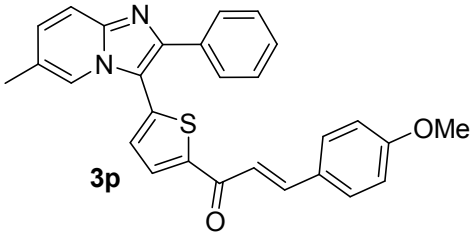
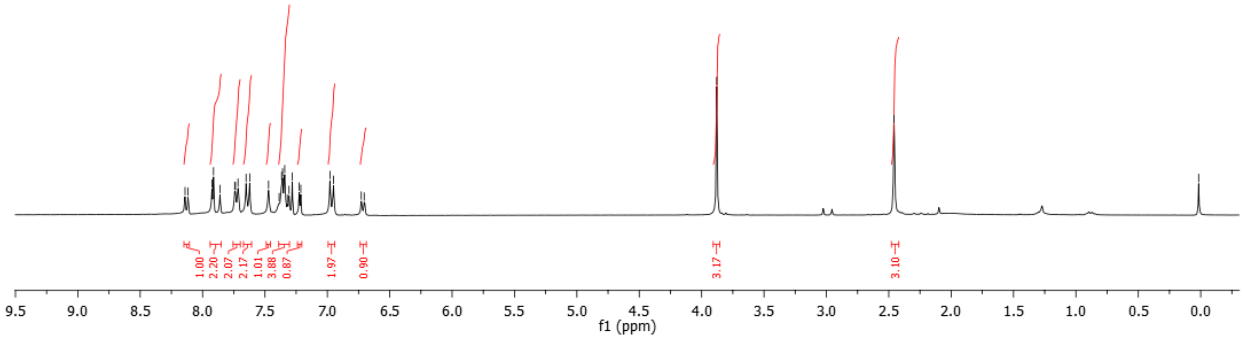
0.02


N
N
S
OMe
O

3p


1.00
2.20
2.07
2.17
1.01
3.88
0.87
1.97
0.90
3.17
3.10
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


181.64
161.90
147.01
146.29
145.29
144.33
138.45
136.91
133.65
132.05
130.42
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128.43
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127.35
123.04
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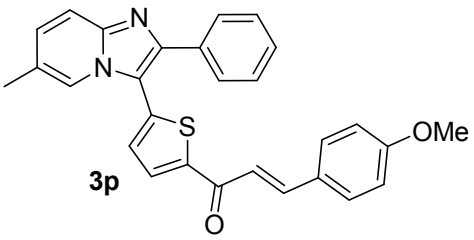
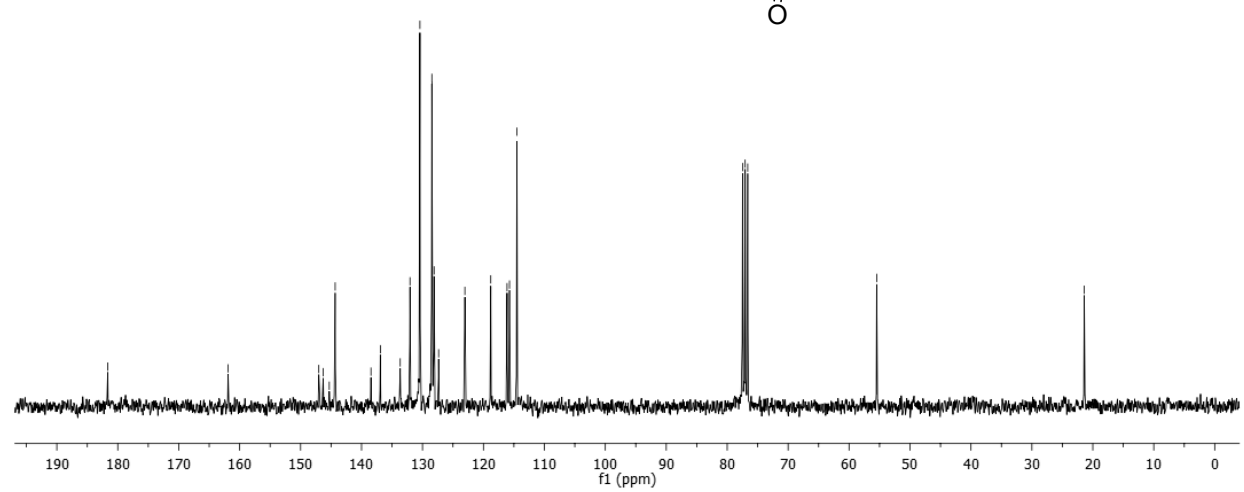
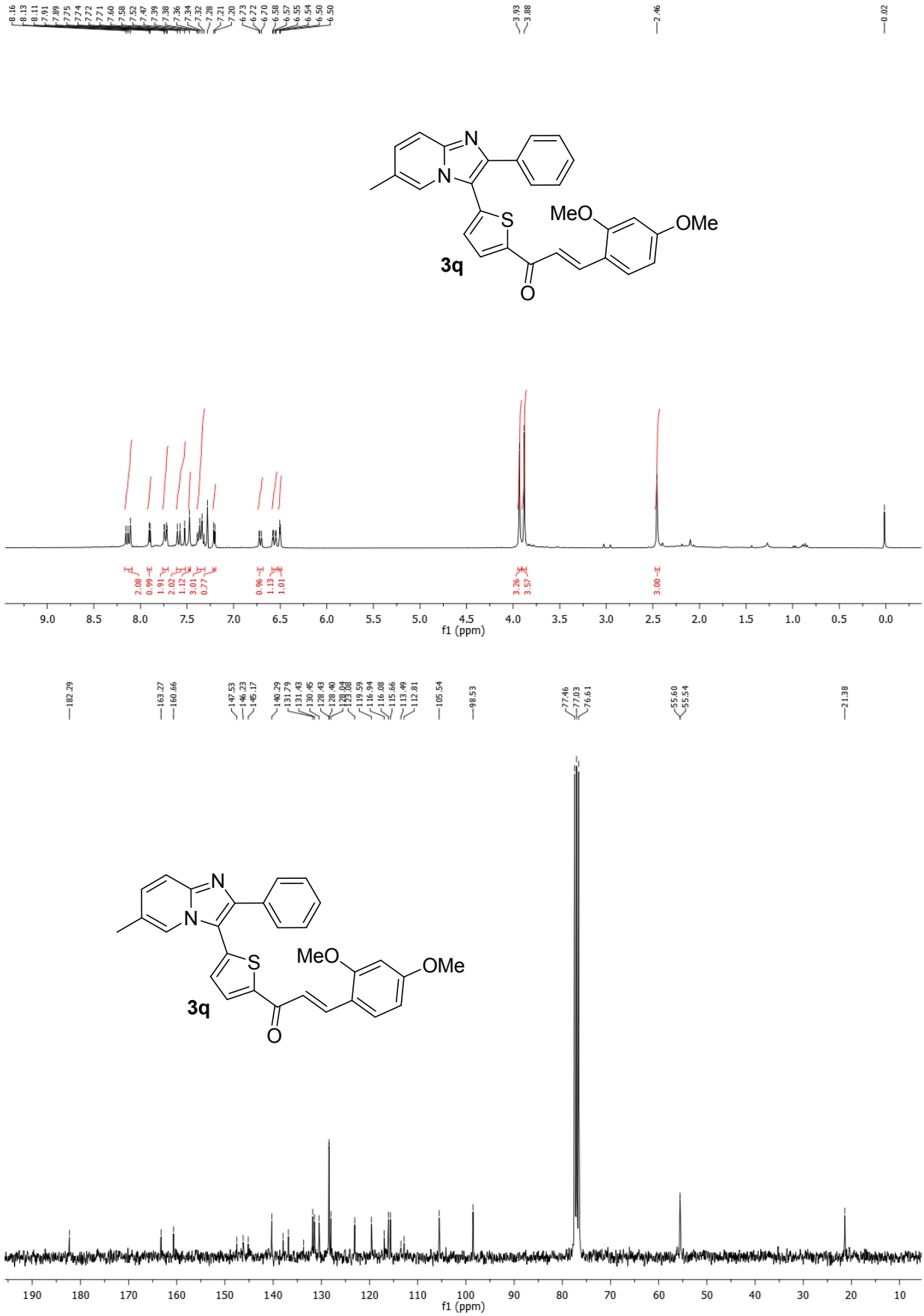
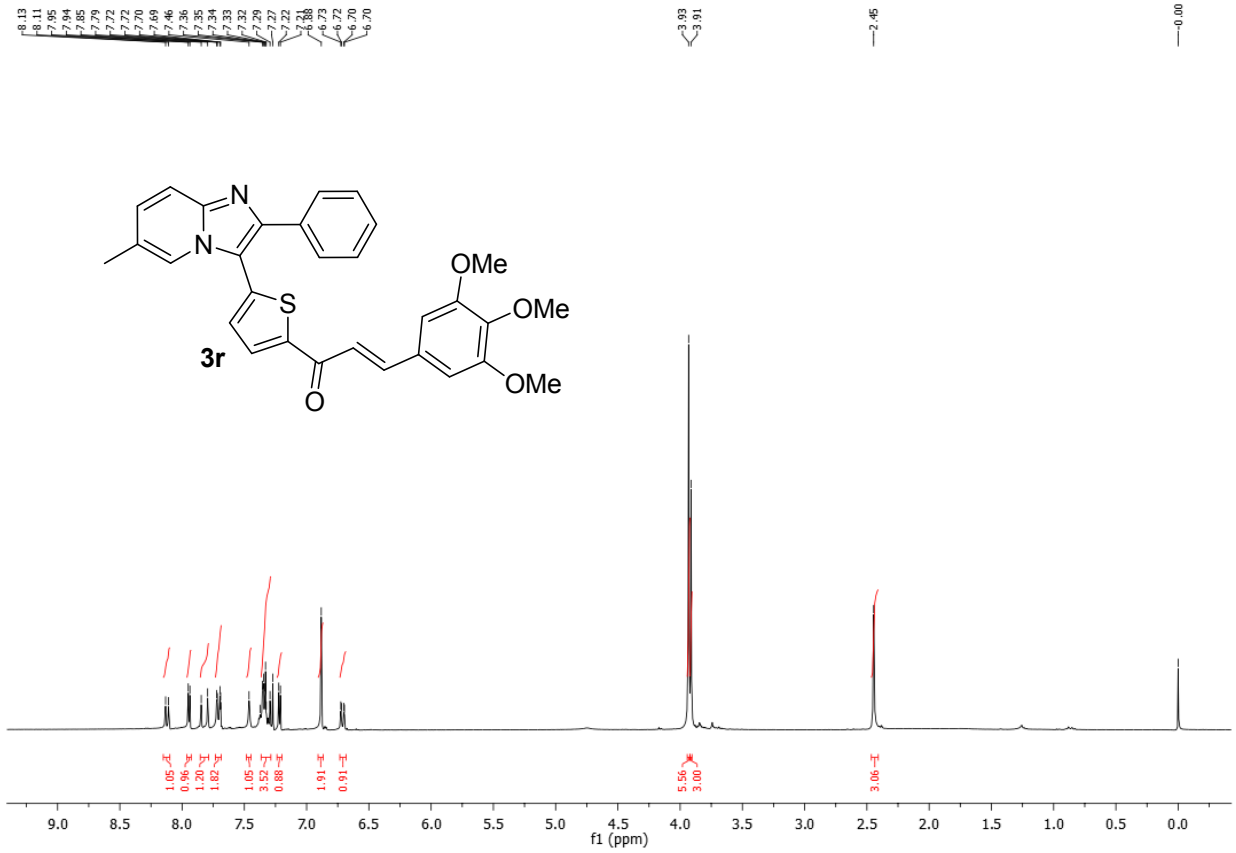
115.72
114.50
77.48
77.05
76.63
55.47
21.40

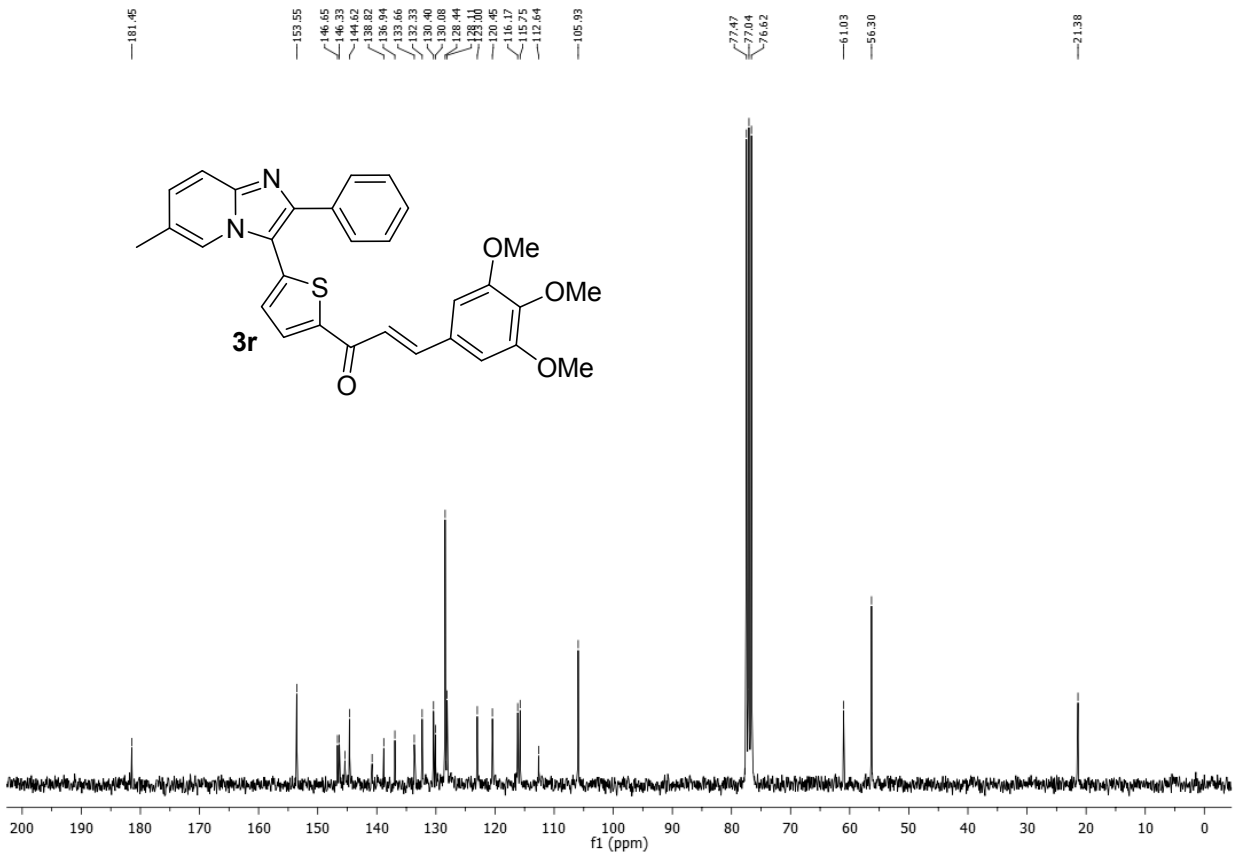

N
N
S
OMe
O

3p


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


3q
MeO
OMe
f1 (ppm)
3q
MeO
OMe
f1 (ppm)


3r
OMe
OMe
OMe
f1 (ppm)


3r
OMe
OMe
OMe
f1 (ppm)