Carboxylate Migration from Ethyl Cyanoformate to Methylene: Rapid Access toward Pyrrolo[1,2-*a*]pyrazines

Nithiniyal Patamajhi[1#], Sandya Tambi Dorai[1#], Surbhi Mahender Saini[1], Bikash Kumar Behera[2], Arbaz Khan[2], **Sandeep Chandrashekharappa[1]***
[1]Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research, Raebareli, Transit Campus, Bijnor-Sisendi Road, Sarojini Nagar, Near CRPF Base Camp, Lucknow (UP)-226002, India.
[2]Department of Pharmaceutical Analysis, National Institute of Pharmaceutical Education and Research, Raebareli, Transit Campus, Bijnor-Sisendi Road, Sarojini Nagar, Near CRPF Base Camp, Lucknow (UP)-226002, India.
[#]Equal contribution
[*]Corresponding author: **Dr. Sandeep Chandrashekharappa**,
E-mail: c.sandeep@niperraebareli.edu.in and c.sandeep@niperrbl.ac.in
Fax: 91-522-2975587; Tel: 91-522-2499703.

Experimental section

Chemicals were procured from Sigma-Aldrich and Spectrochem, India. Without additional purification, all the reagents were employed in the reaction. The synthesis involved two steps. The first step was carried out at a controlled temperature range of 0 °C - rt. The second step proceeded under reflux conditions using hot-air-dried glassware to ensure anhydrous conditions. Reaction progress was consistently monitored by thin-layer chromatography (TLC). Sigma-Aldrich silica gel 60 F254 aluminium-backed TLC plates were used for this purpose. The mobile phase consisted of a 3:7 mixture of ethyl acetate and hexane. Visualization of the separated components on the TLC plates was achieved using a UV-light chamber. To purify the chemicals, column chromatography was used with a borosil glass column and silica gel (100–200 mesh size). ^{1}H and ^{13}C NMR spectra were recorded using *JEOL* Nuclear Magnetic Resonance- ECZR series spectrometers operating at 500 MHz and 125 MHz, respectively. For nuclear magnetic resonance (NMR) spectroscopy, Tetramethylsilane (TMS) was used as an internal standard. Samples were analyzed in $CDCl_3$, DMSO-d_6, and Acetone-d_6 for both ^{1}H NMR and ^{13}C NMR. Mass spectra were recorded using an Agilent mass spectrometer equipped with a TOF detector.

General method for the Synthesis of 2-(2-substituted-1*H*-pyrrol-1-yl)-1-phenylethan-1-one (1a-ac)[23, 24]

To the stirred solution of pyrrolo-2-carboxaldehyde **(1a)**, (0.5 g, 5.2 mmol) and potassium carbonate (1.09 g, 7.8 mmol) in acetonitrile (15 mL), phenacyl bromide (**2a**), (1.04 g, 5.2 mmol) was added and stirred at room temperature for 24 h. The reaction completion was monitored by TLC. After completion of the reaction, the organic solvent was evaporated under reduced pressure and diluted with ethyl acetate (50 mL), wash the organic layer with water (25 mL × 2), and brine solution (25 mL × 1) and dried the organic layer over anhydrous sodium sulfate. The organic layer was concentrated under reduced pressure to get crude 1-(2-oxo-2-phenylethyl)-1*H*-pyrrole-2-carbaldehyde **1a.** The crude residue was purified *via* column chromatography using 100-200 mesh silica gel by using an ethyl acetate/hexane mixture as the

eluent, yielding 1.2 g (92%) of pure **1a** 1-(2-oxo-2-phenylethyl)-1*H*-pyrrole-2-carbaldehyde. The remaining compounds **(1b-ac)** were synthesized using the same protocol.

Method A: Two-step synthesis and purification of 3

General procedure for the synthesis of ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-phenylpropanoate (3a-e):

In a clean round-bottom flask, 4 mL of DMF was added, followed by the addition of compound **1a** (0.5 g, 2.34 mmol, 1 equiv.) at 0 °C. Sodium hydride (0.28, 7.03 mmol, 3 equiv.) was then added and stirred for 15 min. Subsequently, ethyl cyanoformate **(2)** (0.23 g, 2.34 mmol, 1 equiv.) was added, and the reaction was allowed to proceed at room temperature for 15 min. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was poured into ice, and dilution of the crude mixture with 50 mL of ethyl acetate (2 × 50 mL) and washed with water (3 × 25 mL), and brine solution (1 × 25 mL), and dried over anhydrous sodium sulphate and the organic layer was evaporated under reduced pressure to obtain the crude product. The purification was performed with column chromatography by using 100-200 mesh silica gel, whereas hexane and ethyl acetate were used as eluents.

Method B: One pot without purification of 3

General procedure for the synthesis of ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-phenylpropanoate (3f-ac):

In a clean round-bottom flask, 4 mL of DMF was added, followed by the addition of **compound 1a** (0.5 g, 2.34 mmol, 1 equiv.) at 0 °C. Sodium hydride (0.28g, 7.03 mmol, 3 equiv.) was then added and stirred for 15 min. Subsequently, ethyl cyanoformate **(2)** (0.23, 2.34 mmol, 1 equiv.) was added, and the reaction was allowed to proceed at room temperature for 15 min. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was poured into ice, and dilution of the crude mixture with 50 mL of ethyl acetate (2 × 50 mL) and washed with water (3 × 25 mL), and brine solution (1 × 25 mL), and dried over anhydrous sodium sulphate and the organic layer was evaporated under reduced pressure to obtain the crude product. and the crude product was directly taken to the next step.

General procedure for the synthesis of ethyl 3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5a-5ac):

In a clean round-bottom flask, 4 mL of toluene was added, followed by the addition of compound **3a** (0.25 g, 0.87 mmol, 1 equiv.), ammonium acetate (0.67g, 8.76 mmol, 10 equiv.), and a catalytic amount of acetic acid. The reaction mixture was refluxed for 3 h, and its progress was monitored using TLC. After reaction completion, the solvent was evaporated under a rotary evaporator, and the product was purified via column chromatography. The purification was performed with column chromatography by using 100-200 mesh silica gel, whereas hexane and ethyl acetate were used as eluents. The pale-yellow liquid compound was isolated with a yield of 73%. All the synthesized compounds were characterized by spectroscopic methods like ^{1}H, ^{13}C NMR, and HRMS.

Characterization details

1-(2-(3-bromophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde (1i): Yellow solid, 55%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.50 (s, 1H), 8.12 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.40 (t, *J* = 7.9, 7.9 Hz, 1H), 7.05 (s, 1H), 6.95 (s, 1H), 6.37 (s, 1H), 5.75 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.87, 180.00, 136.84, 132.58, 131.58, 131.20, 130.61, 129.60, 126.68, 124.96, 123.33, 110.57, 54.94; HRMS (ESI-TOF) (m/z): $[M+H]^+$ calculated for $C_{13}H_{11}BrNO_2$, 291.9974; found, 291.9977.

1-(2-(3,4-dichlorophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde (1k): Brown solid, 55%; ^{1}H NMR (500 MHz, DMSO- d_6) δ 9.44 (s, 1H), 8.22 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.25 (s, 1H), 7.10 (s, 1H), 6.32 (s, 1H), 5.89 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.51, 180.06, 137.16, 135.55, 133.58, 132.63, 131.97, 131.86, 130.31, 128.42, 124.60, 110.15, 55.61. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calculated for $C_{13}H_{10}Cl_2NO_2$, 282.0088; found, 282.0087.

2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-bromophenyl)ethan-1-one (1u): Yellow solid, 67%; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.15 (s, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 2.0 Hz, 2H), 6.23 – 6.19 (m, 1H), 5.81 (s, 2H), 2.30 (d, *J* = 2.6 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.39, 188.19, 137.56, 136.75, 132.51, 131.71, 130.91, 130.37, 127.42, 122.80, 120.77, 108.70, 56.25, 27.09; HRMS (ESI-TOF) (m/z): $[M+H]^+$ calculated for $C_{14}H_{13}Cl_2NO_2$, 306.0129; found, 308.0120

2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-methoxyphenyl)ethan-1-one (1v): Yellow solid, 60%; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.46 (m, 1H), 7.44 (s, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.11 – 7.07 (m, 2H), 6.17 (t, *J* = 2.7 Hz, 1H), 5.78 (s, 2H), 3.80 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.06, 188.12, 160.12, 137.02, 132.47, 130.61, 130.55, 120.79, 120.57, 120.01, 113.11, 108.58, 56.25, 55.99,
27.09; HRMS (ESI-TOF) (m/z): $[M+H]^+$ calculated for $C_{15}H_{16}NO_3$, 258.1130; found, 258.1137.

2-(2-benzoyl-1H-pyrrol-1-yl)-1-(4-methoxyphenyl)ethan-1-one (1y): Brown solid, 72%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.9 Hz, 2H), 7.78 (d, *J* = 7.0 Hz, 2H), 7.51 (t, *J* = 7.4, 7.4 Hz, 1H), 7.42 (t, *J* = 7.6, 7.6 Hz, 2H), 7.00 – 6.95 (m, 3H), 6.86 (dd, *J* = 4.1, 1.6 Hz, 1H), 6.30 (dd, *J* = 4.0, 2.6 Hz, 1H), 5.83 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.95, 186.53, 164.06, 139.70, 132.13, 131.53, 130.51, 130.28, 129.34, 128.15, 128.10, 123.42, 114.14, 109.03, 77.35, 55.61, 55.08; HRMS (ESI-TOF) (m/z): $[M+H]^+$ calculated for $C_{20}H_{18}NO_3$, 320.1286; found, 320.1293.

Ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-phenylpropanoate (3a): Yellowish liquid (0.230 g, 34%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.65 (s, 1H), 8.20 – 8.07 (m, 3H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 7.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.32 (d, *J* = 9.4 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 1H), 6.42 – 6.33 (m, 1H), 4.42 – 4.20 (m, 2H), 1.32 – 1.26 (m, 3H); HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{16}NO_4$, 286.1079; found, 286.1096.

Ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-(*p*-tolyl)propanoate (3b): Yellowish liquid (0.260g, 39%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.06 (s, 1H), 7.93 (d, *J* = 8.2 Hz,

2H), 7.34 – 7.31 (m, 1H), 7.25 (d, *J* = 2.0 Hz, 2H), 7.01 (d, *J* = 3.8 Hz, 1H), 6.30 (t, *J* = 3.3 Hz, 1H), 4.32 – 4.15 (m, 2H), 2.39 (s, 3H), 1.24 – 1.20 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.53, 180.45, 166.67, 145.74, 132.34, 132.01, 130.61, 129.82, 129.56, 126.66, 126.48, 111.14, 111.08, 62.63, 62.38, 29.78, 14.06; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{18}NO_4$, 300.1236; found, 300.1243.

Ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)-3-(4-methoxyphenyl)-3-oxopropanoate (3c): Yellowish liquid (0.265g, 40%); ^{1}H NMR (500 MHz, Acetone-d_6) δ 9.61 (s, 1H), 8.02 (d, *J* = 8.9 Hz, 2H), 7.97 (s, 1H), 7.31 (s, 1H), 7.14 – 7.10 (m, 1H), 7.07 (d, *J* = 8.9 Hz, 2H), 6.34 – 6.28 (m, 1H), 4.25 (q, *J* = 7.0 Hz, 2H), 3.91 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (125 MHz, ACETONE-D_6) δ 205.57, 189.00, 180.48, 166.42, 164.87, 131.93, 131.57, 131.01, 129.46, 127.47, 125.90, 114.44, 113.73, 110.58, 62.57, 62.12, 55.36, 29.49, 29.34, 29.18, 29.03, 28.87, 28.72, 28.57, 13.44; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{18}NO_5$, 316.1185; found, 316.1193.

Ethyl 3-(4-chlorophenyl)-2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxopropanoate (3e): Yellowish liquid (0.215g, 33%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.07 (s, 1H), 7.99 (d, *J* = 8.7 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.32 (d, *J* = 2.2 Hz, 1H), 7.02 (d, *J* = 4.7 Hz, 1H), 6.33 – 6.30 (m, 1H), 4.24 (dd, *J* = 7.1, 5.2 Hz, 2H), 1.22 (td, *J* = 7.2, 1.6 Hz, 3H); HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{15}ClNO_4$, 320.0689; found, 320.0711.

Ethyl 3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5a): Yellowish liquid 73%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.89 (s, 1H), 8.09 (d, *J* = 2.6 Hz, 1H), 7.51 (d, *J* = 6.8 Hz, 2H), 7.41 (q, *J* = 7.6, 7.0 Hz, 3H), 7.00 – 6.97 (m, 1H), 6.96 (d, *J* = 4.0 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.56, 145.52, 141.89, 139.37, 128.86, 128.36, 128.25, 118.55, 117.26, 116.39, 105.68, 61.91, 29.78, 13.36; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{15}N_2O_2$, 267.1133; found, 267.1135.

Ethyl 3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5b): Yellowish solid 78%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.87 (s, 1H), 8.04 (s, 1H), 7.46 (d, *J* = 8.6 Hz, 2H), 6.97 – 6.91 (m, 4H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.80, 160.00, 145.39, 145.39, 130.18, 128.26, 118.12, 117.06, 116.19, 113.75, 105.56, 61.91, 55.48, 13.61; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{16}N_2O_2$, 281.1290; found, 281.1295.

Ethyl 3-(4-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5c): Yellowish liquid 68%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.87 (s, 1H), 8.04 (s, 1H), 7.49 – 7.41 (m, 2H), 6.98 – 6.89 (m, 4H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.80, 160.01, 145.40, 141.34, 131.70, 130.18, 128.26, 118.12, 117.06, 116.19, 113.75, 105.57, 77.35, 77.10, 76.84, 61.91, 55.48, 13.61 ; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{17}N_2O_3$, 297.1239; found, 297.1238.

Ethyl 3-(4-fluorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5d): Yellowish solid 65%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.00 (s, 1H), 8.01 (s, 1H), 7.53 – 7.46 (m, 2H), 7.25 (t, *J* = 8.7 Hz, 2H), 7.05 (d, *J* = 5.7 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 0.92 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.03, 146.22, 139.59, 135.53, 131.33, 131.26, 128.22, 118.63, 117.43, 117.08, 115.63, 115.46, 106.36, 62.49, 13.74; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{13}FN_2O_2$, 285.1039: found, 285.1040.

Ethyl 3-(4-chlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5e): Yellowish liquid 65%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (s, 1H), 8.10 (s, 1H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.40

(d, *J* = 9.5 Hz, 2H), 6.98 (dd, *J* = 11.0, 3.3 Hz, 2H), 4.18 (q, *J* = 8.2 Hz, 2H), 1.00 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.26, 145.61, 140.75, 137.93, 134.49, 130.25, 128.43, 118.59, 117.50, 116.61, 105.95, 62.07, 13.49; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{14}ClN_2O_2$, 301.0744; found, 301.0745.

Ethyl 3-(4-bromophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5f): Yellowish liquid 68%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (s, 1H), 8.08 (s, 1H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 11.2 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 0.97 (t, *J* = 6.8 Hz, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.22, 145.61, 140.79, 138.41, 131.36, 130.55, 128.42, 122.67, 118.58, 117.51, 116.59, 105.94, 62.07, 29.77, 13.48; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{14}BrN_2O_2$, 345.0238; found, 345.0242.

Ethyl 3-([1,1'-biphenyl]-4-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5g): Yellowish solid 70%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.04 (s, 1H), 8.00 (s, 1H), 7.75 – 7.66 (m, 4H), 7.56 (dd, *J* = 8.1, 5.5 Hz, 2H), 7.45 (q, *J* = 7.6 Hz, 2H), 7.39 – 7.32 (m, 1H), 7.06 (d, *J* = 5.6 Hz, 2H), 4.20 (q, *J* = 7.0 Hz, 2H), 0.96 – 0.89 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.24, 146.27, 140.56, 140.10, 139.88, 138.01, 129.75, 129.57, 128.24, 127.21, 126.90, 118.73, 117.26, 117.05, 106.26, 62.59, 13.71; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{18}N_2O_2$, 343.1446; found: 343.1447.

Ethyl 3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5h): Dark yellowish solid 72%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.05 (s, 1H), 8.01 (d, *J* = 15.3 Hz, 2H), 7.94 (d, *J* = 7.6 Hz, 3H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.10 – 7.02 (m, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 0.74 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.24, 146.28, 140.25, 136.41, 133.09, 128.70, 128.27, 128.20, 128.08, 127.16, 127.02, 118.95, 117.37, 117.09, 106.33, 62.47, 13.65; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{20}H_{16}N_2O_2$, 317.1290; found, 317.1291.

Ethyl 3-(3-bromophenyl)pyrrolo[1,2-a]pyrazine-4-carboxylate (5i): Dark yellowish solid 50%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.02 (s, 1H), 8.05 (s, 1H), 7.66 – 7.57 (m, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.11 – 7.02 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.78, 146.39, 141.44, 139.11, 131.77, 131.53, 130.81, 128.30, 121.74, 118.97, 117.72, 117.31, 106.59, 62.58, 40.57, 40.40, 40.23, 40.07, 39.90, 39.73, 39.57, 13.74; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{18}N_2O_2$, 345.0238; found, 345.0244.

Ethyl 3-(3-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5j): Yellowish liquid 65%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.00 (s, 1H), 7.96 – 7.93 (m, 1H), 7.32 (t, *J* = 7.9 Hz, 1H), 7.07 – 6.95 (m, 5H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 3H), 0.94 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.18, 159.59, 146.13, 140.27, 139.79, 129.76, 128.17, 121.47, 118.90, 117.10, 117.03, 114.58, 114.50, 106.17, 62.52, 55.70, 13.71; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{16}N_2O_3$, 297.1239; found, 297.1266.

Ethyl 3-(3,4-dichlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5k); Yellowish liquid 60%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.02 (s, 1H), 8.10 (s, 1H), 7.75 – 7.65 (m, 2H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.12 – 7.04 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 0.97 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.55, 146.46, 139.91, 138.56, 131.55, 131.31, 131.07, 130.83, 129.51, 128.42, 118.98, 118.03, 117.45, 106.81, 62.64, 13.72; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{12}Cl_2N_2O_2$: 335.0356; found, 335.0373.

Ethyl 3-(2-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5l): Yellowish liquid 62%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (d, *J* = 0.9 Hz, 1H), 8.29 – 8.26 (m, 1H), 7.46 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.35 (m, 1H), 7.05 (m, 1H), 6.97 (dd, *J* = 4.3, 2.6 Hz, 1H), 6.94 (dd, *J* = 4.2, 1.3 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 4.09 (q, *J* = 7.2, 7.2, 7.2 Hz, 2H), 3.74 (s, 3H), 0.91-0.88 (t, *J* = 7.2, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.14, 156.43, 145.91, 138.71, 130.73, 129.64, 129.04, 128.64, 120.91, 119.69, 117.76, 117.73, 116.30, 105.52, 61.40, 55.51, 13.36; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{12}Cl_2N_2O_2$: 335.0356; found, 335.0373.

Ethyl 1-methyl-3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5m): Yellowish liquid 72%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.03 – 7.95 (m, 1H), 7.52 – 7.38 (m, 5H), 7.11 (d, *J* = 3.9 Hz, 1H), 7.06 – 6.96 (m, 1H), 4.15 (qd, *J* = 8.4, 7.1, 5.1 Hz, 2H), 2.68 (s, 3H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.41, 154.45, 140.38, 139.27, 129.16, 128.55, 127.33, 117.52, 117.38, 116.21, 105.63, 62.25, 22.04, 22.00, 13.66; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{16}N_2O_2$, 281.1290; found, 281.1307.

Ethyl 1-methyl-3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5n): Yellowish solid 67%); ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.91 (d, *J* = 2.4 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.05 (d, *J* = 3.9 Hz, 1H), 6.99 – 6.92 (m, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.63 (s, 3H), 2.32 (s, 3H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.54, 154.31, 139.99, 138.10, 136.25, 129.12, 129.06, 127.24, 117.32, 117.24, 116.10, 105.50, 62.31, 22.02, 21.37, 13.75; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{18}H_{18}N_2O_2$, 295.1446; found, 295.1458.

Ethyl 3-(4-methoxyphenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5o): Yellowish solid 77%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.90 (s, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.05 – 6.91 (m, 4H), 4.16 (q, *J* = 7.4 Hz, 2H), 3.77 (s, 3H), 0.97 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.67, 159.96, 154.22, 139.80, 131.39, 130.48, 127.20, 117.27, 116.89, 116.01, 114.03, 105.46, 62.27, 55.77, 22.02, 13.87; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{18}H_{18}N_2O_3$, 311.1395; found, 311.1424.

Ethyl 3-(4-fluorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5p): Yellowish liquid 65%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.56 – 7.38 (m, 3H), 7.16 – 7.05 (m, 3H), 6.93 (s, 3H), 4.13 (q, *J* = 6.3, 5.7 Hz, 2H), 2.73 (s, 3H), 0.98 – 0.93 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.60, 163.95, 154.54, 140.96, 135.84, 130.72, 130.66, 127.74, 117.66, 117.23, 115.65, 115.29, 115.12, 105.12, 77.33, 61.79, 29.81, 22.01, 13.51; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{16}FN_2O_2$: 299.1196; found: 299.1196.

Ethyl 3-(4-chlorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5q): Yellowish liquid 70%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.00 (s, 1H), 7.46 (d, *J* = 2.6 Hz, 4H), 7.08 (d, *J* = 4.2 Hz, 1H), 7.00 – 6.97 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.64 (s, 3H), 0.92 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.11, 154.65, 139.44, 138.25, 133.48, 131.00, 128.57, 127.42, 117.85, 117.45, 116.38, 105.88, 62.38, 21.99, 13.71; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{15}ClN_2O_2$: 315.0900; found, 315.0915.

Ethyl 3-(4-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5r): Yellowish solid 74%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.02 (d, *J* = 19.4 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 4.1 Hz, 1H), 7.02 – 6.97 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.65 (s, 3H), 0.94 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.10, 154.68, 139.47, 138.62, 131.50, 131.29, 130.00, 127.42, 122.06, 117.87, 116.39, 105.91, 62.40, 21.99,

13.71; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{15}BrN_2O_2$: 359.0395; found, 359.0386.

Ethyl 3-([1,1'-biphenyl]-4-yl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5s): Dark yellowish solid 71% ; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.98 (s, 1H), 7.70 (dd, *J* = 15.0, 7.8 Hz, 4H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.08 (d, *J* = 3.9 Hz, 1H), 7.00 – 6.95 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.66 (s, 3H), 0.91 (t, *J* = 7.1 Hz, 3H), ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.44, 154.51, 140.43, 140.17, 139.92, 138.29, 129.77, 129.56, 128.20, 127.36, 127.20, 126.81, 117.57, 116.25, 105.69, 62.38, 22.04, 13.69; HRMS(ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{23}H_{20}N_2O_2$: 357.1603; found, 357.1614.

Ethyl 1-methyl-3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (5t): Yellowish solid 68%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, *J* = 14.4 Hz, 1H), 7.98 (s, 1H), 7.91 – 7.83 (m, 3H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 6.2, 3.2 Hz, 2H), 6.95 (s, 2H), 4.07 (q, *J* = 7.1, 7.1, 7.1 Hz, 2H), 2.78 (s, 3H), 0.72 (t, *J* = 7.1, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CHLOROFORM-*D*): δ 164.86, 154.52, 141.81, 137.06, 133.26, 133.16, 128.37, 128.11, 127.87, 127.75, 126.91, 126.35, 126.27, 117.55, 115.59, 105.00, 61.76, 22.05, 13.36; $C_{21}H_{19}N_2O_2$; Calculated $[M+H]^+$: 331.1446; found $[M+H]^+$: 331.1447.

Ethyl 3-(3-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5u): Yellowish liquid 58%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (t, *J* = 2.0, 2.0 Hz, 1H), 8.10 (s, 1H), 7.67 (t, *J* = 1.8, 1.8 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 7.8, 7.8 Hz, 1H), 6.95 (d, *J* = 1.7 Hz, 1H), 4.17 (q, *J* = 7.2, 7.2, 7.2 Hz, 2H), 2.75 (s, 3H), 0.97 (t, *J* = 7.2, 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.30, 154.70, 141.84, 140.61, 131.99, 131.15, 129.71, 129.58, 127.62, 122.18, 117.91, 115.82, 105.25, 61.87, 21.99, 13.46; $C_{17}H_{16}BrN_2O_2$; Calculated $[M+H]^+$: 359.0395; found $[M+2+H]^+$: 361.0408.

Ethyl 3-(3-methoxyphenyl)-1-methylpyrrolo[1,2-a]pyrazine-4-carboxylate (5v): Yellowish solid 73%; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.93 (d, *J* = 2.4 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 4.1 Hz, 1H), 7.01 – 6.93 (m, 4H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 3H), 2.64 (s, 3H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.37, 159.52, 154.37, 140.57, 139.91, 129.66, 127.35, 121.53, 117.57, 117.42, 116.22, 114.63, 114.30, 105.59, 62.30, 55.71, 22.01, 13.70; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{18}H_{18}N_2O_3$: 311.1395; found, 311.1413.

Ethyl 1,3-diphenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5w): Yellowish liquid 70%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 2.5, 1.2 Hz, 1H), 8.03 (dd, *J* = 6.9, 2.7 Hz, 2H), 7.62 (d, *J* = 6.7 Hz, 2H), 7.52 (dd, *J* = 5.3, 1.9 Hz, 3H), 7.47 – 7.38 (m, 3H), 7.12 – 7.09 (m, 1H), 7.01 (dd, *J* = 4.1, 2.7 Hz, 1H), 4.17 (q, *J* = 7.1, 7.1, 7.1 Hz, 2H), 0.95 (t, *J* = 7.1, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.90, 154.23, 141.99, 139.67, 138.13, 130.18, 129.11, 129.02, 128.67, 128.63, 128.21, 126.83, 117.62, 117.41, 117.30, 116.40, 116.18, 106.86, 106.79, 106.58, 61.88, 13.41; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{19}N_2O_2$: 343.1446; found, 343.1446.

Ethyl 1-phenyl-3-(*p*-tolyl)pyrrolo[1,2-a]pyrazine-4-carboxylate (5x): yellowish liquid 76%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 1.2, 2.5 Hz, 1H), 8.06 – 8.02 (m, 2H), 7.55 – 7.50 (m, 5H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.09 (dd, *J* = 1.2, 4.2 Hz, 1H), 6.99 (dd, *J* = 2.6, 4.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, Chloroform-*d*) δ 165.06, 154.10, 141.83, 138.19, 136.69, 130.09, 129.65 – 129.55 (m), 129.07,

128.97, 128.88, 128.59, 126.77, 117.34, 117.10, 116.14, 106.52, 61.88, 21.39, 13.50; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{23}H_{21}N_2O_2$: 357.1603; found, 357.1603.

Ethyl 3-(4-methoxyphenyl)-1-phenylpyrrolo[1,2-a]pyrazine-4-carboxylate (5y): yellowish liquid 75%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.07 – 8.02 (m, 2H), 7.58 (d, *J* = 8.7 Hz, 2H), 7.53 (s, 3H), 7.09 (d, *J* = 4.2 Hz, 1H), 7.00 – 6.96 (m, 3H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.15, 160.00, 154.05, 141.45, 138.21, 132.08, 130.38, 130.10, 129.05, 128.60, 127.24, 126.72, 117.34, 116.11, 113.71, 106.54, 61.88, 55.50, 13.67; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{23}H_{21}N_2O_3$: 373.1552; found, 373.1572.

Ethyl 3-(4-fluorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5z): Yellowish liquid 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 2.5, 1.2 Hz, 1H), 8.02 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.59 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.54 – 7.50 (m, 3H), 7.16 – 7.09 (m, 3H), 7.01 (dd, *J* = 4.2, 2.7 Hz, 1H), 4.20 (q, *J* = 7.2, 7.2, 7.1 Hz, 2H), 1.02 (t, *J* = 7.2, 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CHLOROFORM-*D*) δ 164.7, 163.1 (d, *J* = 248.3 Hz), 154.3, 140.9, 138.0, 135.8, 135.8, 130.9, 130.4, 129.0 (d, *J* = 12.3 Hz), 128.7 (d, *J* = 9.2 Hz), 126.8, 117.2, 116.5, 116.3, 115.2, 107.0, 106.8, 61.9, 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{17}FN_2O_2$: 361.1352; found, 361.1374.

Ethyl 3-(4-chlorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5aa): Yellowish liquid 71%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 2.6, 1.2 Hz, 1H), 8.01 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.54 – 7.50 (m, 3H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.13 – 7.10 (m, 1H), 7.01 (dd, *J* = 4.2, 2.7 Hz, 1H), 4.21 (q, *J* = 7.2, 7.2, 7.1 Hz, 2H), 1.03 (t, *J* = 7.2, 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.60, 154.36, 140.86, 138.22, 137.95, 134.39, 130.44, 130.26, 129.02, 128.66, 128.41, 128.34, 126.84, 117.86, 117.78, 117.70, 117.29, 116.57, 107.04, 106.89, 62.03, 13.53; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{17}ClN_2O_2$: 377.1057; found, 377.1079.

Ethyl 3-(4-bromophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5ab); Yellowish liquid 70%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 2.6, 1.2 Hz, 1H), 8.01 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.54 – 7.51 (m, 3H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.11 (dd, *J* = 4.3, 1.2 Hz, 1H), 7.01 (dd, *J* = 4.2, 2.7 Hz, 1H), 4.21 (q, *J* = 7.2, 7.2, 7.1 Hz, 2H), 1.03 (t, *J* = 7.2, 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.58, 154.39, 140.92, 138.70, 137.93, 131.32, 130.74, 130.29, 129.04, 129.00, 128.67, 126.84, 122.59, 117.87, 117.74, 117.25, 116.61, 116.43, 107.09, 106.90, 62.04, 13.53; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{18}BrN_2O_2$: 421.0551; found $[M+2+H]^+$, 423.0556.

Ethyl 3-([1,1'-biphenyl]-4-yl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (5ac): Yellowish liquid 67%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 – 8.18 (m, 1H), 8.05 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.73 – 7.64 (m, 6H), 7.53 (dd, *J* = 5.1, 1.9 Hz, 3H), 7.47 (t, *J* = 7.7, 7.7 Hz, 2H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.14 – 7.11 (m, 1H), 7.03 – 7.00 (m, 1H), 4.22 (q, *J* = 7.1, 7.1, 7.1 Hz, 2H), 0.99 (t, *J* = 7.1, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.93, 154.29, 141.66, 141.21, 140.94, 138.66, 138.13, 130.18, 129.53, 129.08, 128.94, 128.64, 127.55, 127.24, 126.95, 126.86, 117.58, 117.26, 116.33, 106.75, 77.33, 61.97, 13.47; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{28}H_{22}N_2O_2$: 419.1759; found $[M+H]^+$, 419.1786.

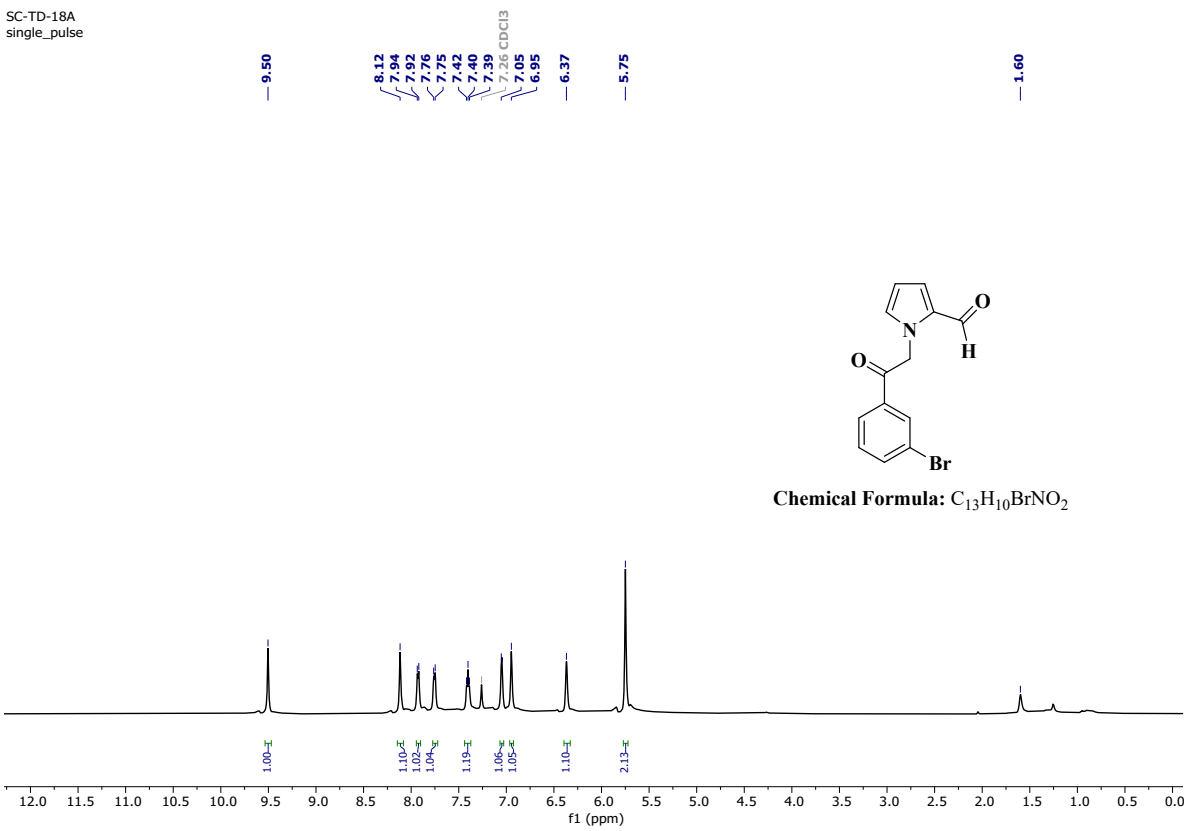


Figure S1. ^{1}H NMR spectrum of 1-(2-(3-bromophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde **(1i)**

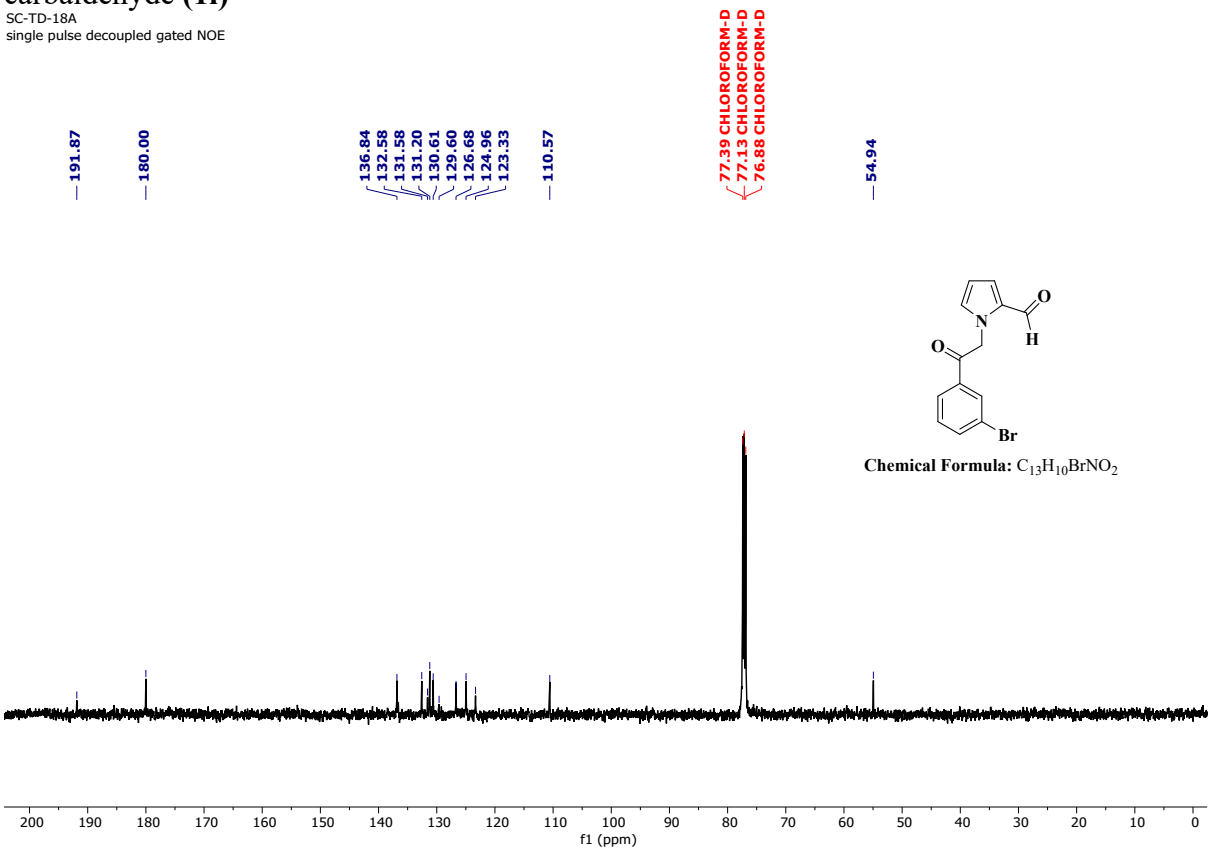


Figure S2. ^{13}C NMR spectrum of 1-(2-(3-bromophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde **(1i)**

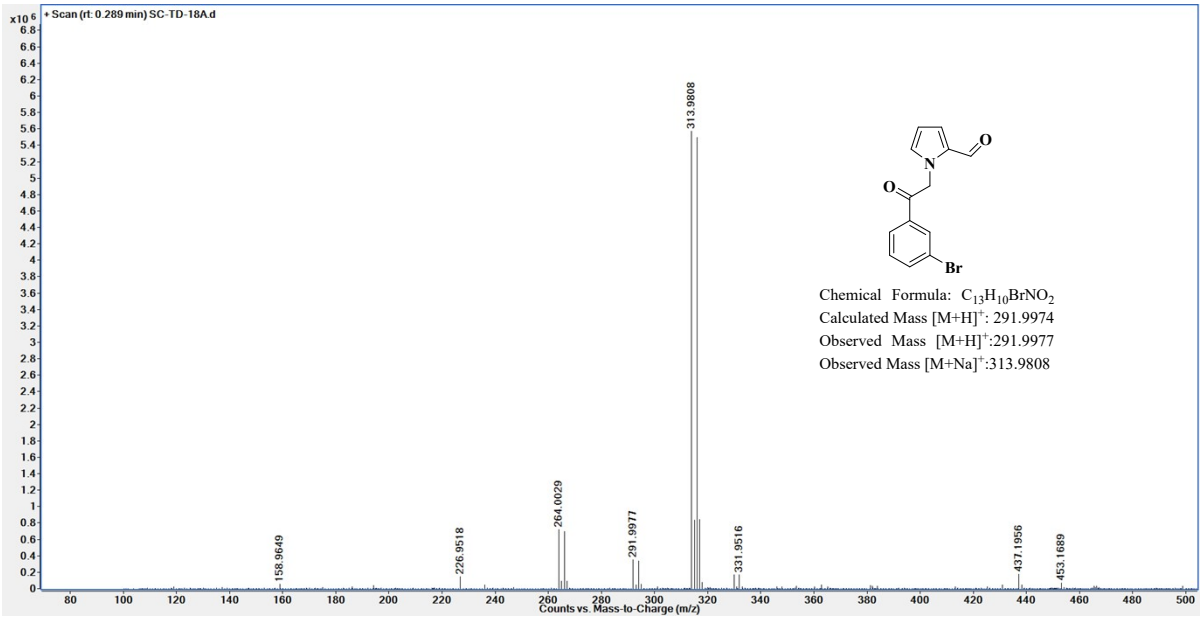


Figure S3. HRMS spectrum of 1-(2-(3-bromophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde **(1i)**

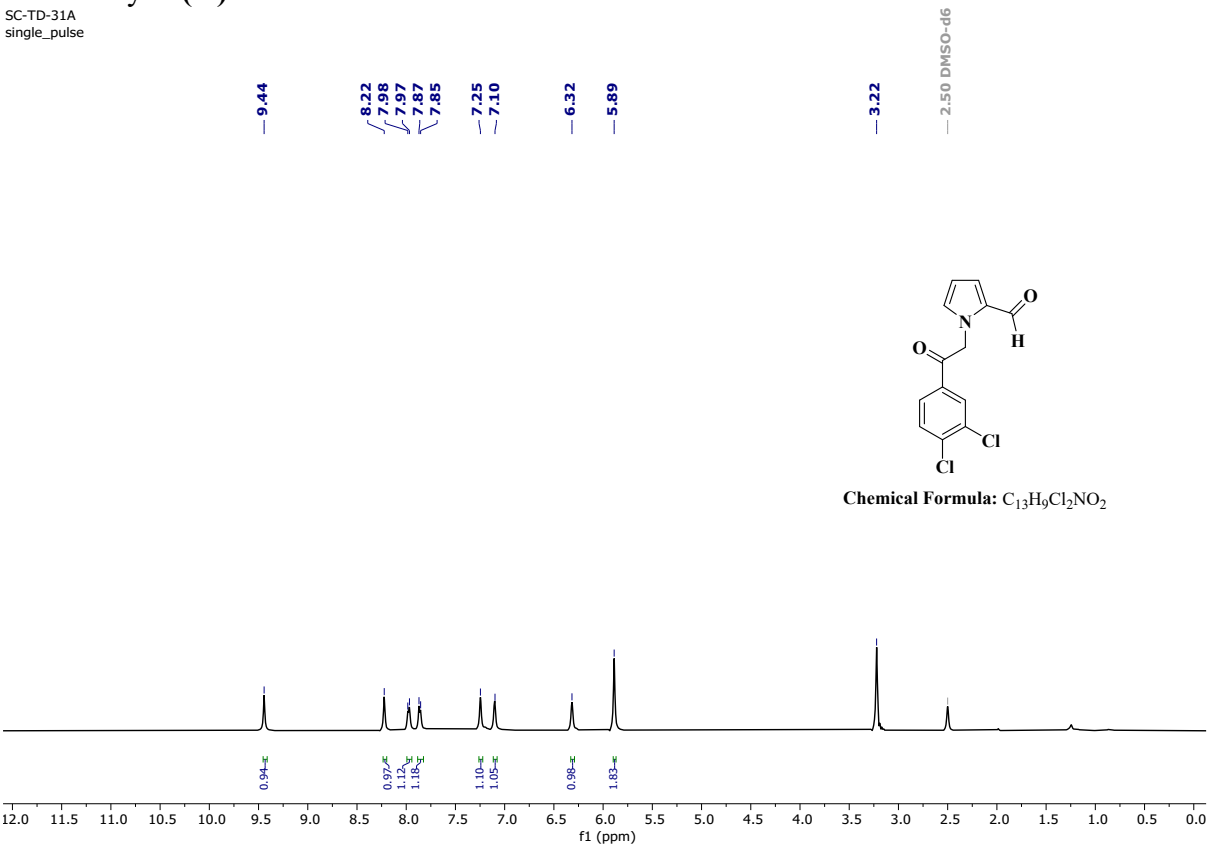


Figure S4. ^{1}H NMR spectrum of 1-(2-(3,4-dichlorophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde (**1k**)

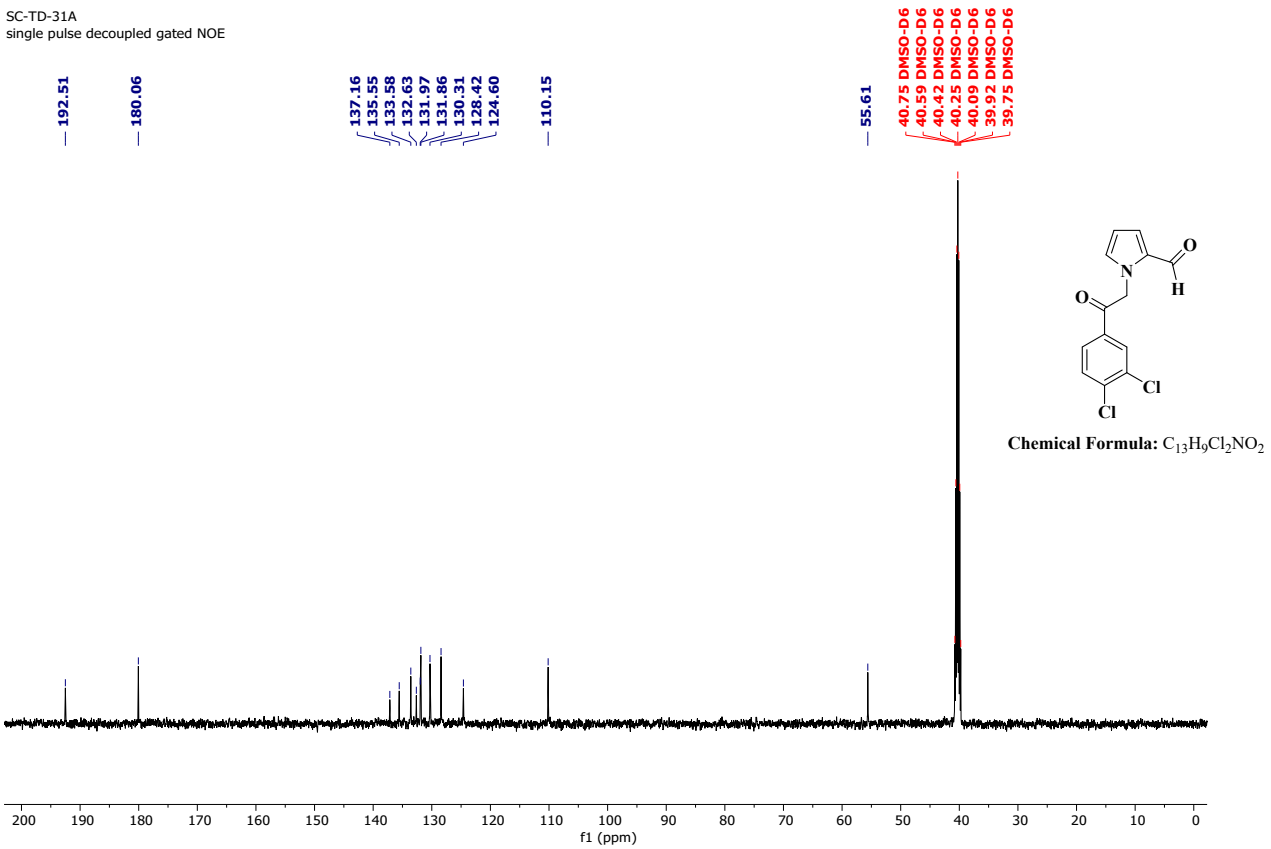


Figure S5. ^{13}C NMR spectrum of 1-(2-(3,4-dichlorophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde (**1k**)

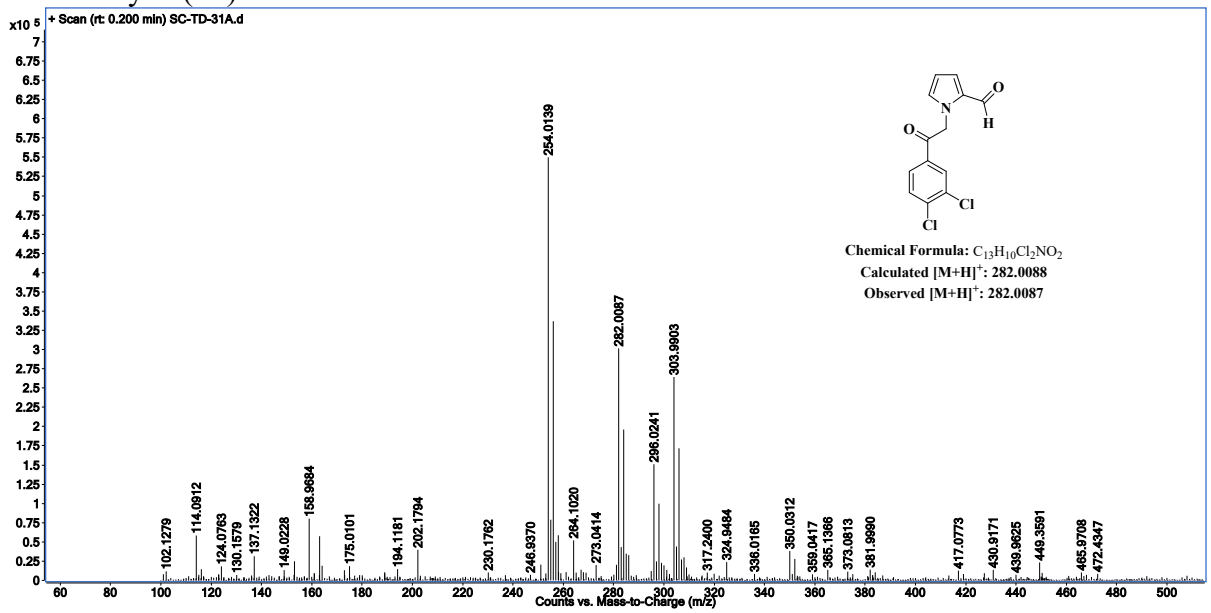
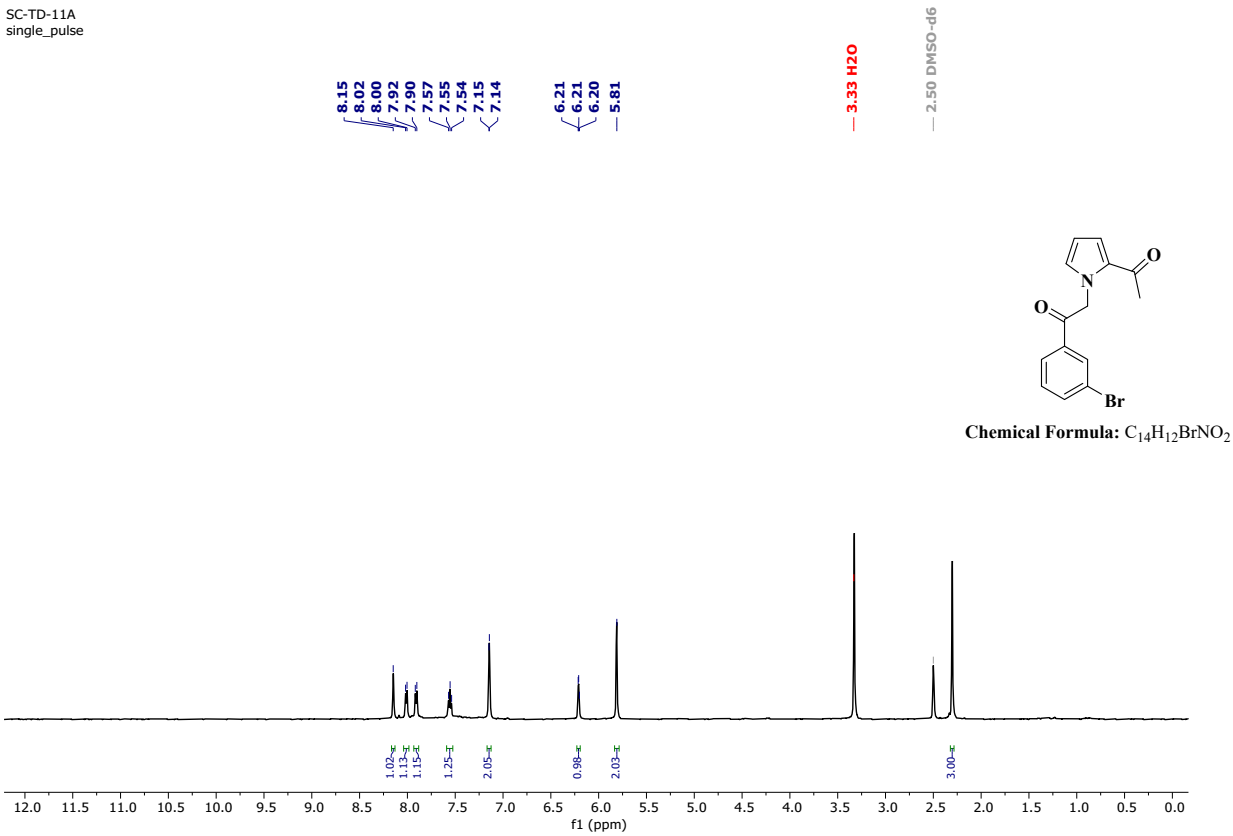
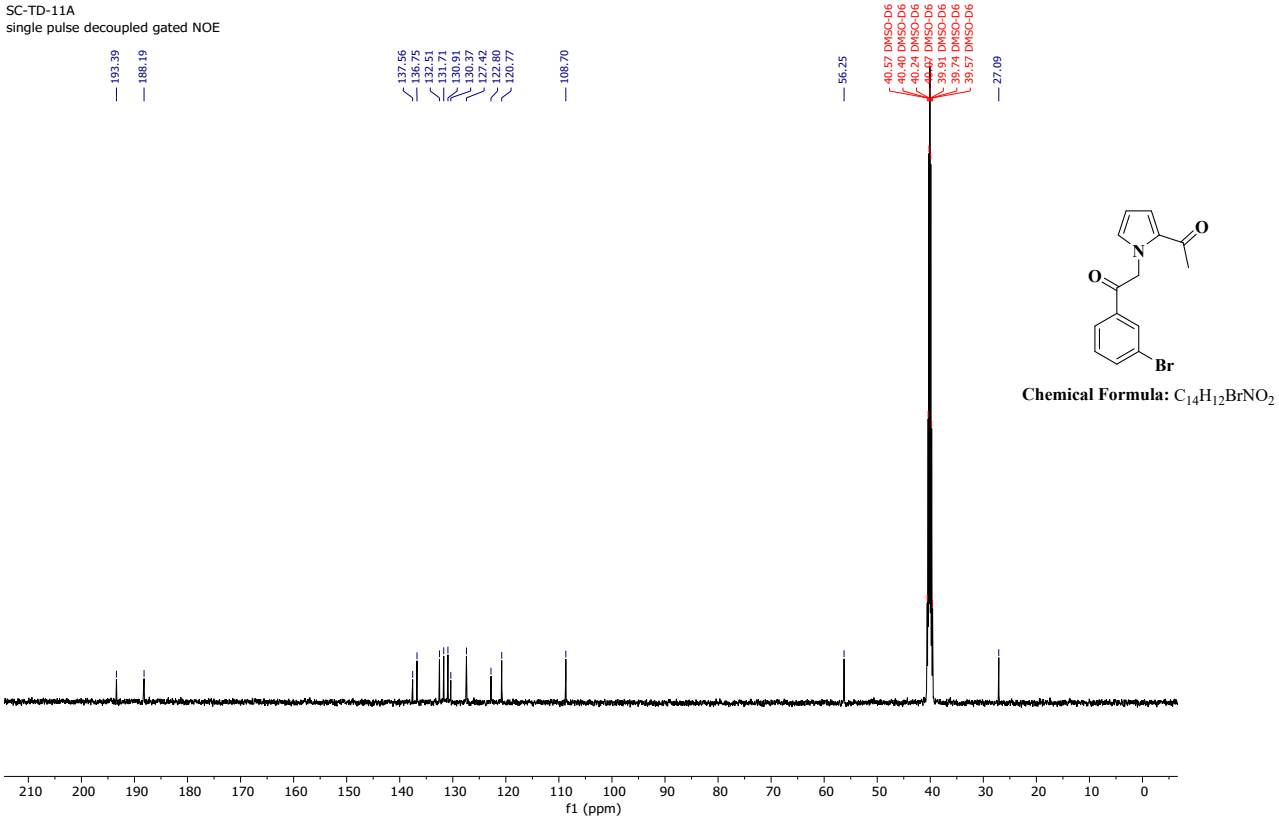


Figure S6. HRMS spectrum of 1-(2-(3,4-dichlorophenyl)-2-oxoethyl)-1*H*-pyrrole-2-carbaldehyde (**1k**)



Chemical Formula: $C_{14}H_{12}BrNO_2$

Figure S7. ^{1}H NMR spectrum of 2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-bromophenyl)ethan-1-one **(1u)**



Chemical Formula: $C_{14}H_{12}BrNO_2$

Figure S8. ^{13}C NMR spectrum of 2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-bromophenyl)ethan-1-one **(1u)**

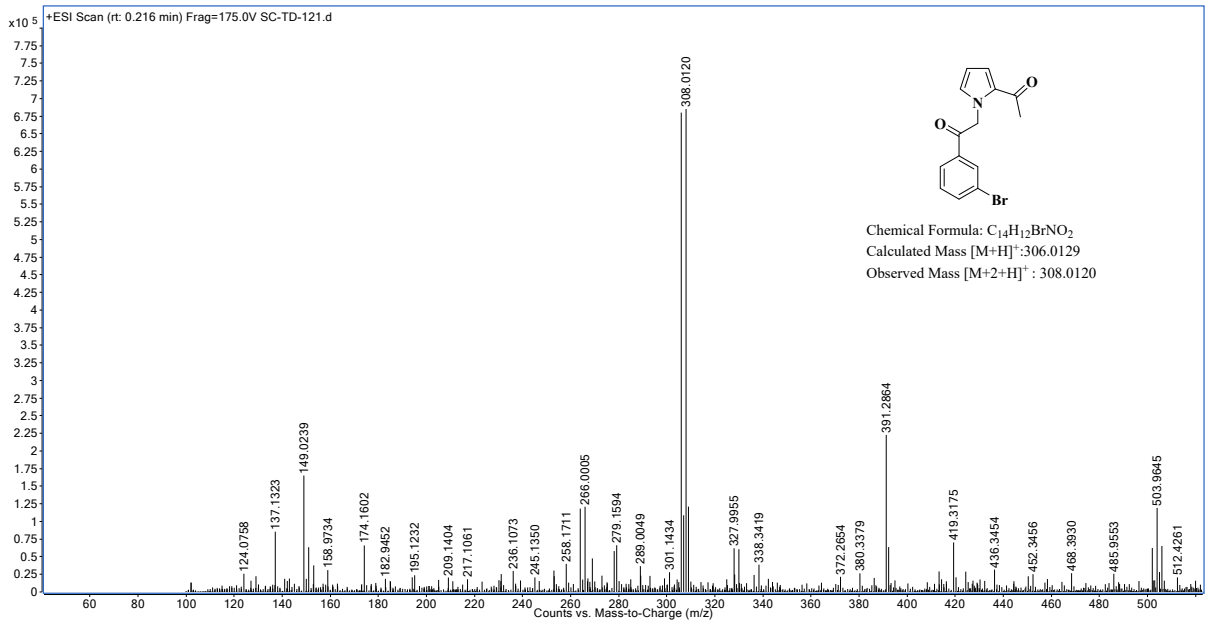


Figure S9. HRMS spectrum of 2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-bromophenyl)ethan-1-one **(1u)**

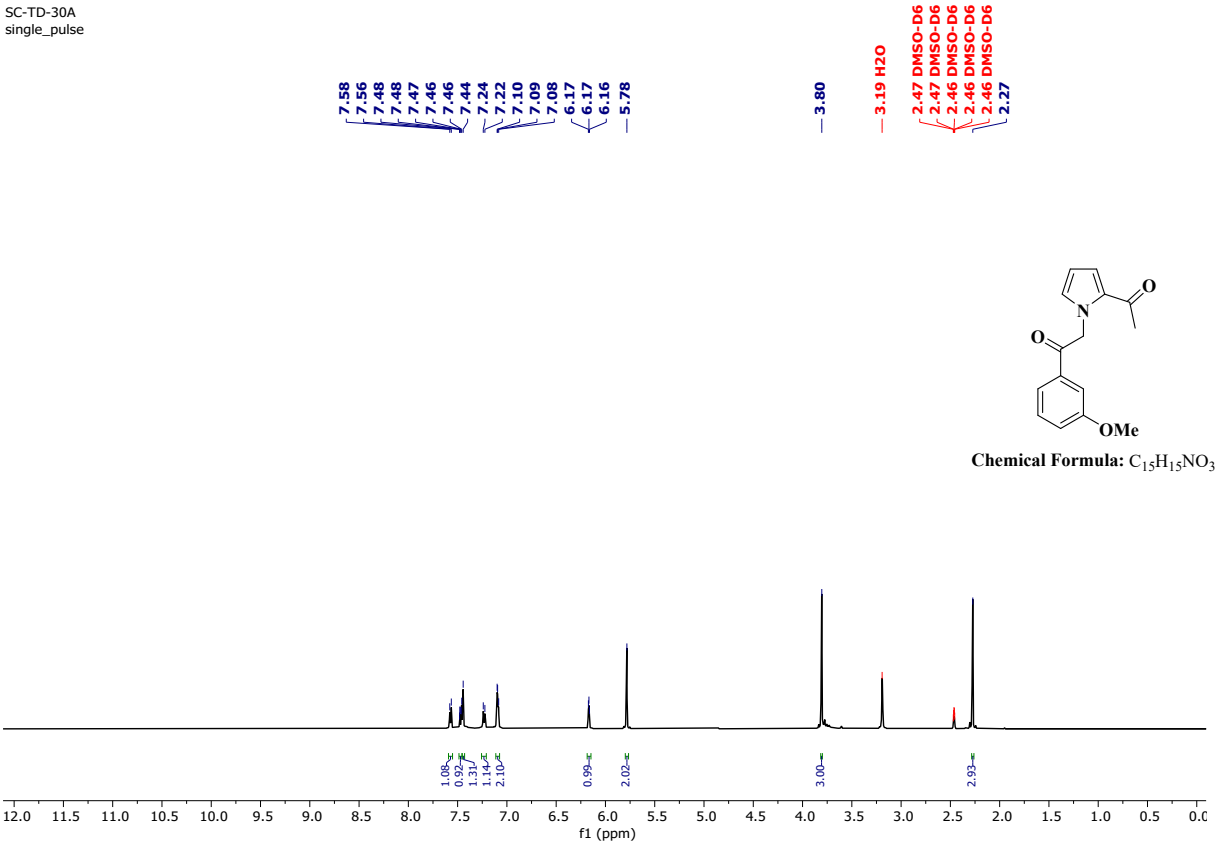


Figure S10. ^{1}H NMR spectrum of 2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-methoxyphenyl)ethan-1-one **(1v)**

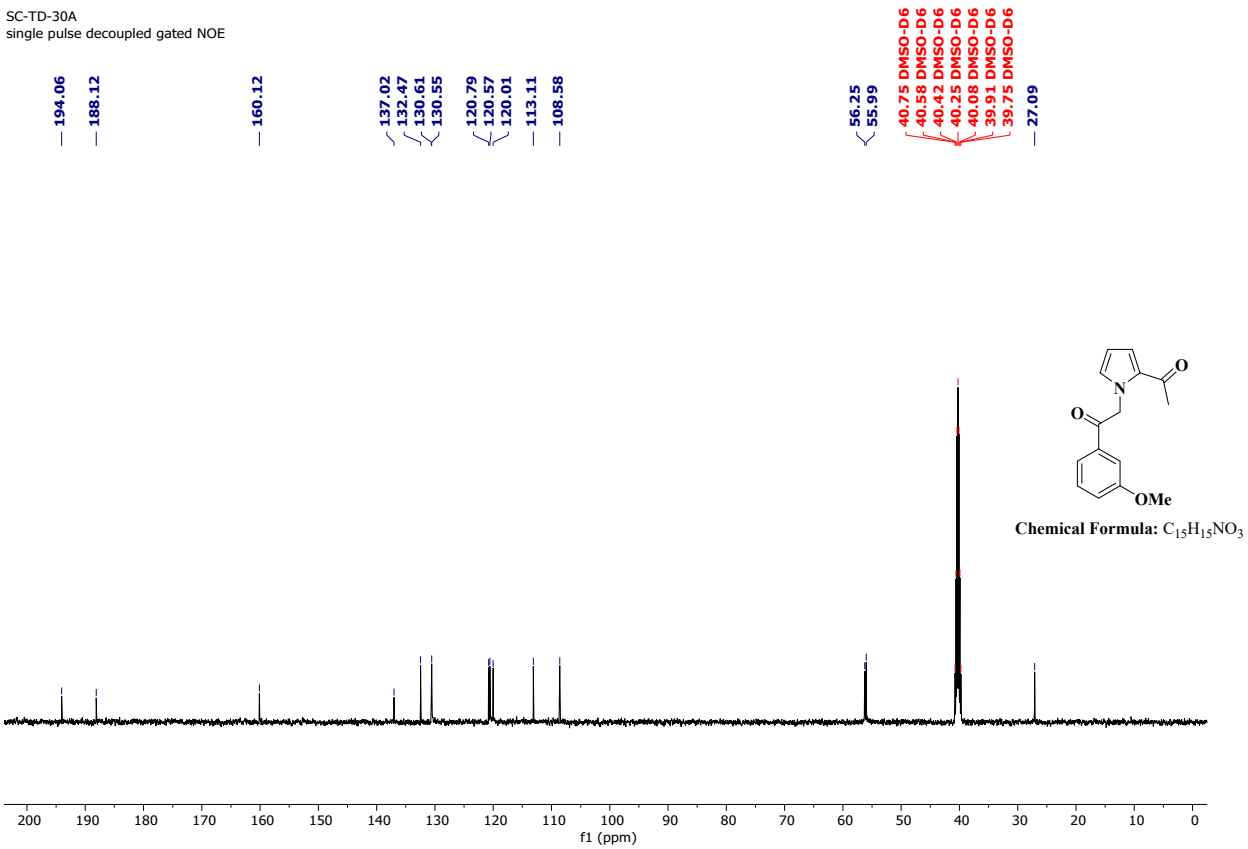


Figure S11. ^{13}C NMR spectrum of 2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-methoxyphenyl)ethan-1-one **(1v)**

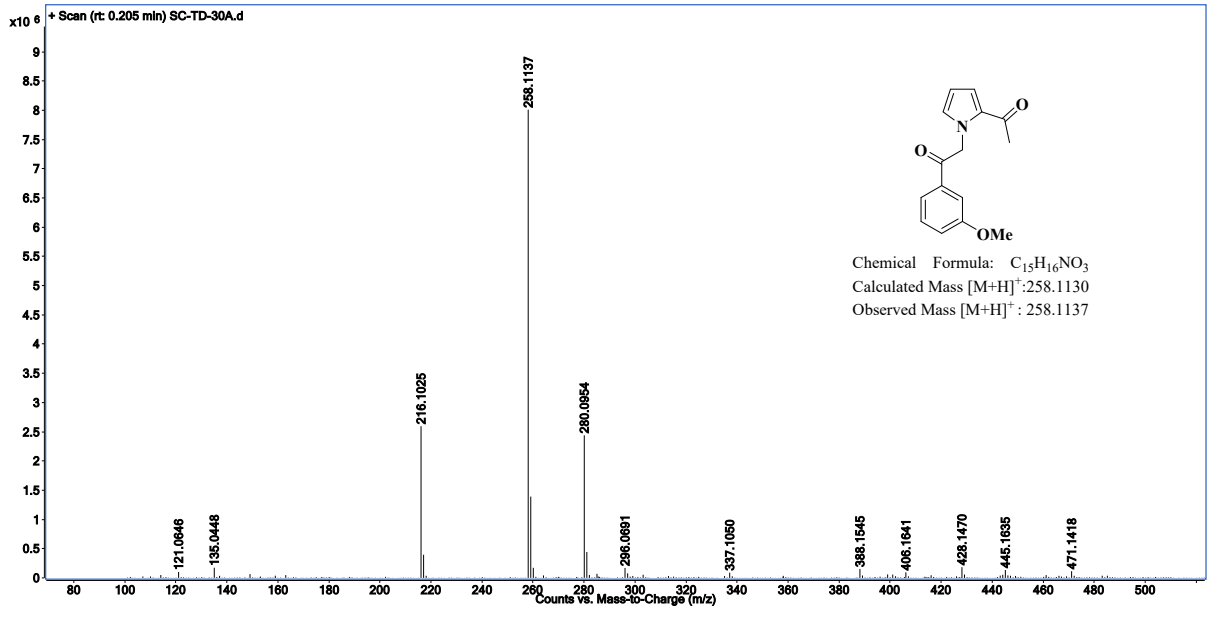


Figure S12. HRMS spectrum of 2-(2-acetyl-1*H*-pyrrol-1-yl)-1-(3-methoxyphenyl)ethan-1-one **(1v)**

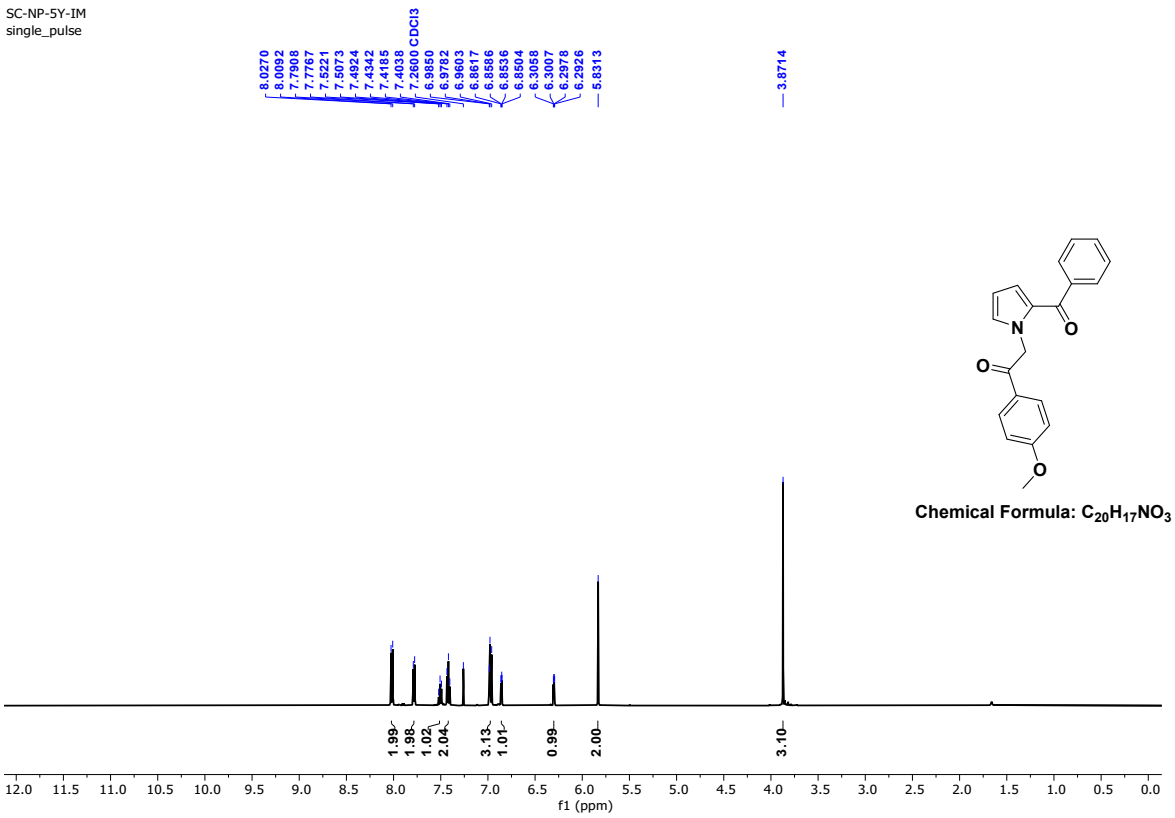


Figure S13. [1]H NMR spectrum of 2-(2-benzoyl-1*H*-pyrrol-1-yl)-1-(4-methoxyphenyl)ethan-1-one **(1y)**

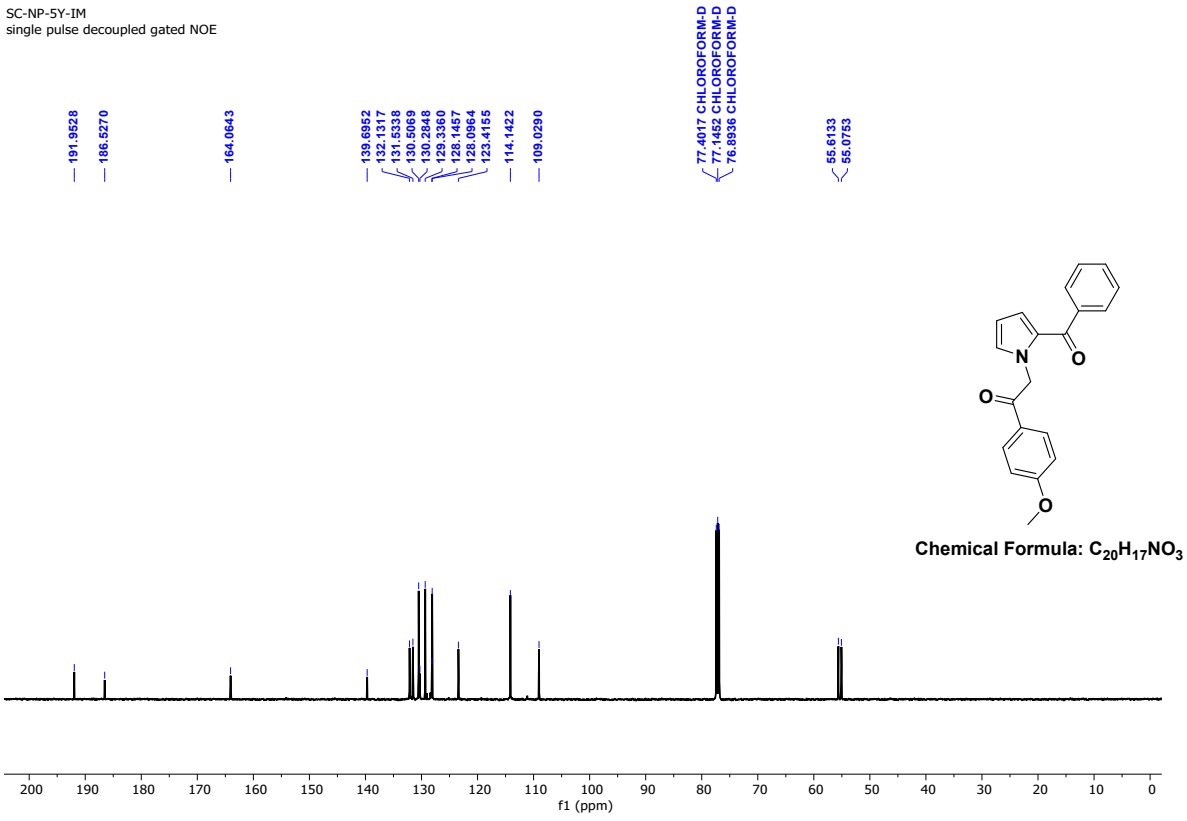


Figure S14. [13]C NMR spectrum of 2-(2-benzoyl-1*H*-pyrrol-1-yl)-1-(4-methoxyphenyl)ethan-1-one **(1y)**

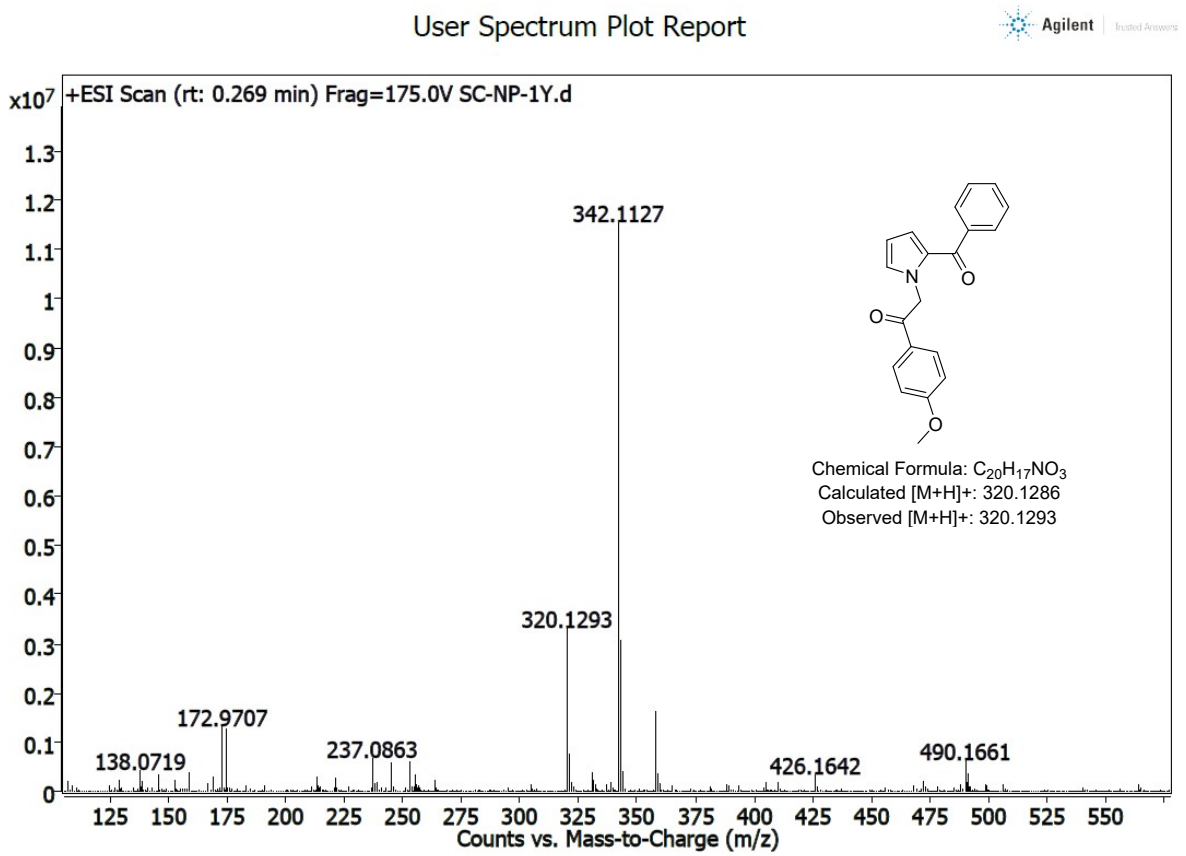


Figure S15. HRMS spectrum of 2-(2-benzoyl-1*H*-pyrrol-1-yl)-1-(4-methoxyphenyl)ethan-1-one **(1y)**

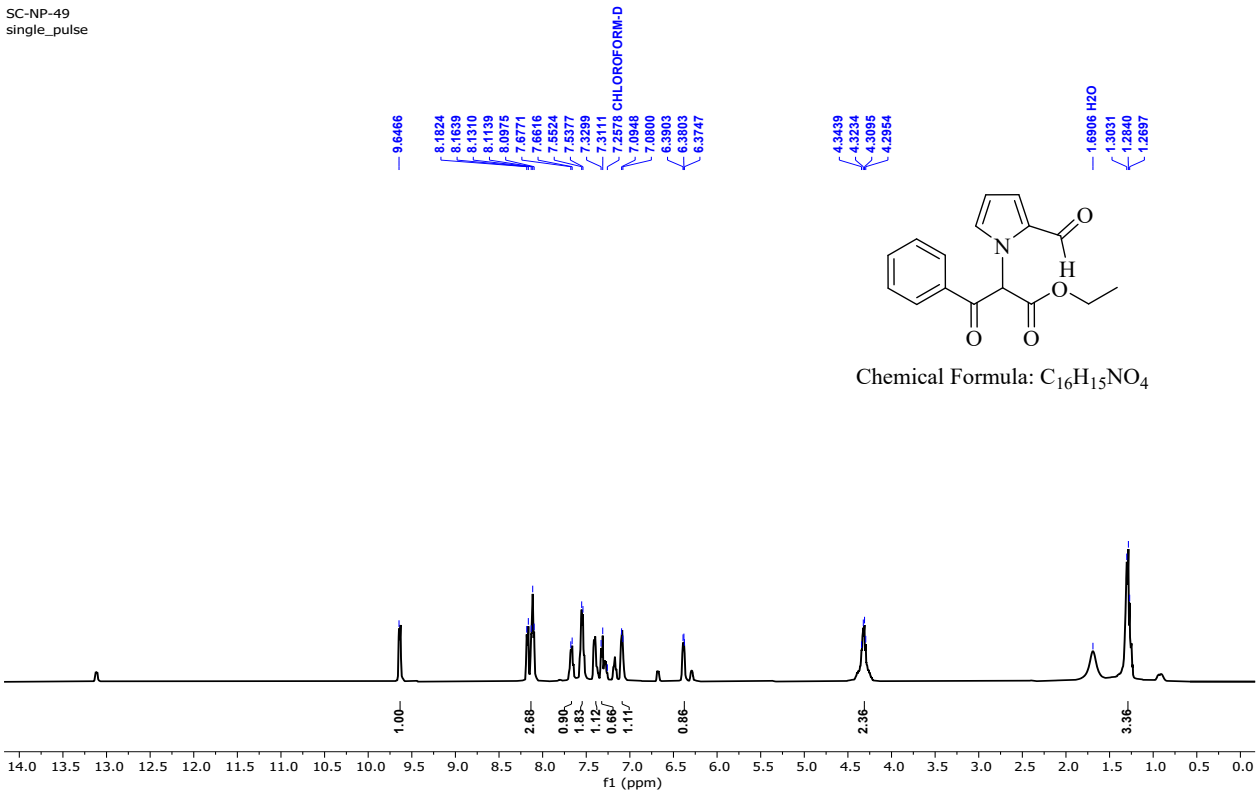


Figure S16: ^{1}H NMR spectra of **ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-phenylpropanoate (3a)**

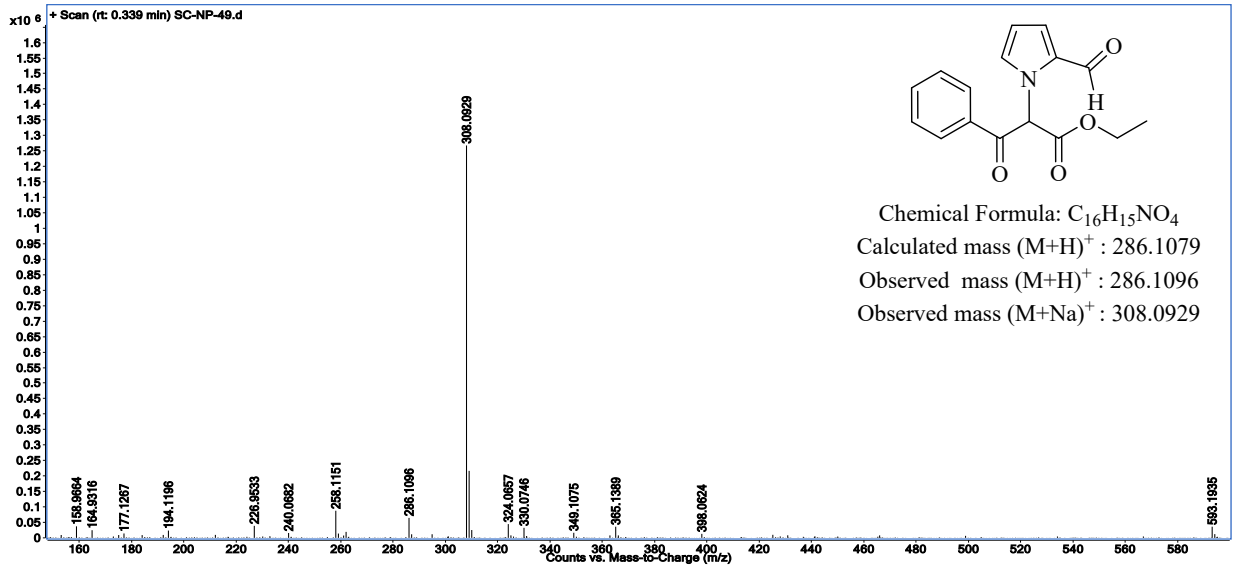


Figure S17: HRMS spectra of **ethyl 2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-phenylpropanoate (3a)**

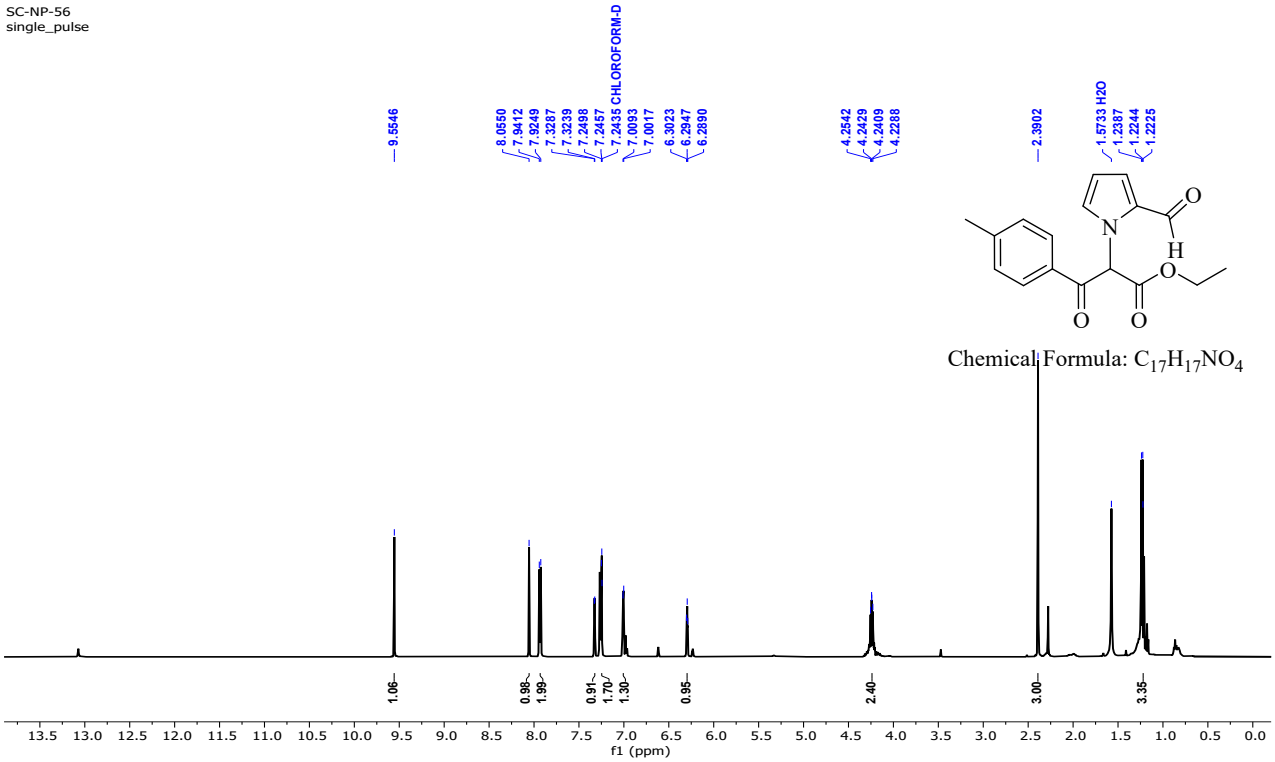


Figure S18: ^{1}H NMR spectra of ethyl-2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-(*p*-tolyl) propanoate **(3b)**

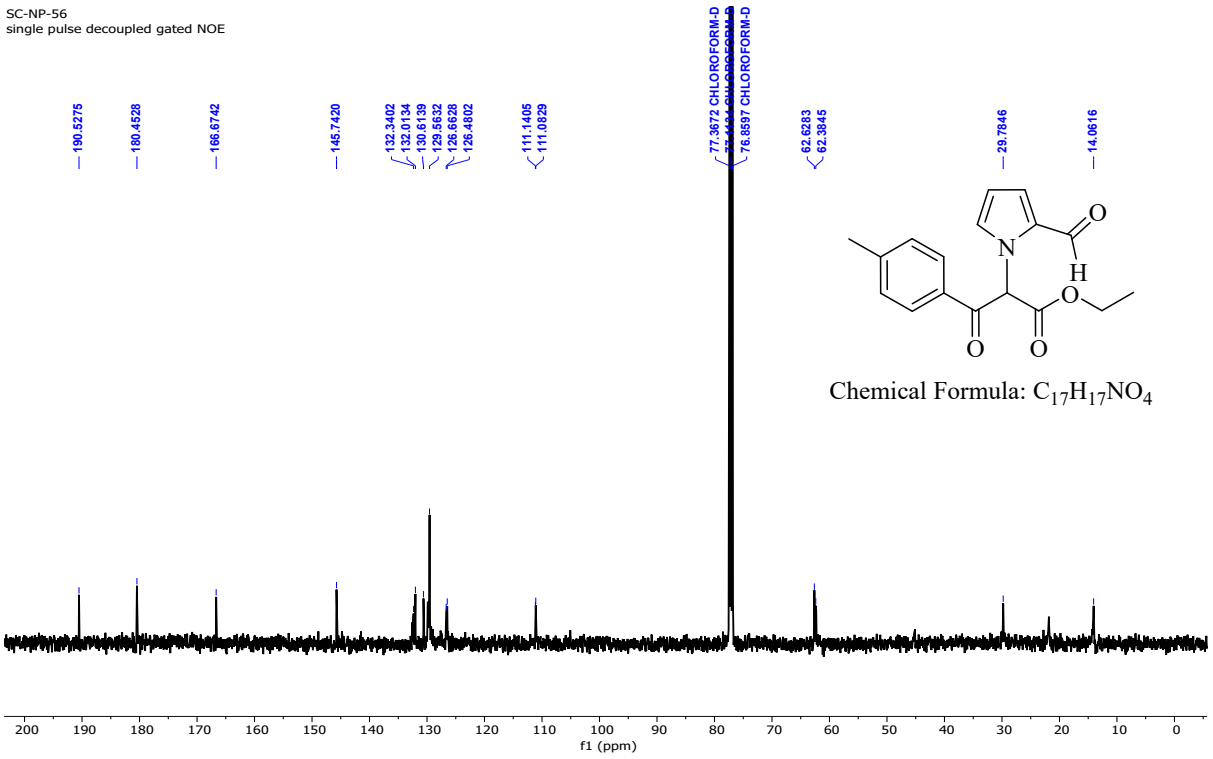


Figure S19: ^{13}C NMR spectra of ethyl-2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-(*p*-tolyl) propanoate **(3b)**

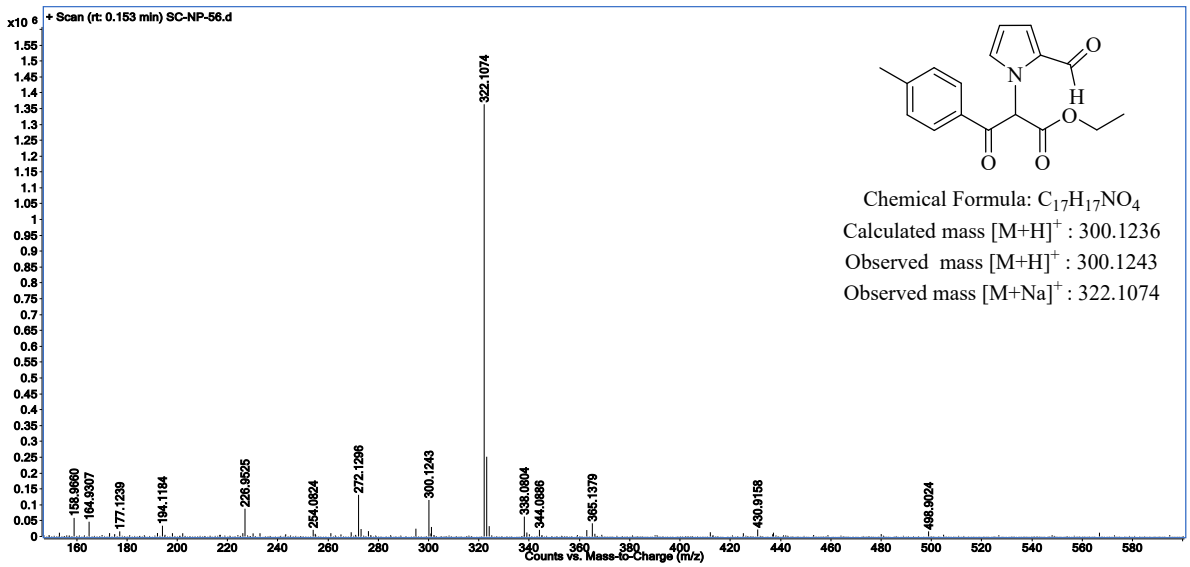


Figure S20: HRMS spectra of ethyl-2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxo-3-(*p*-tolyl)propanoate **(3b)**

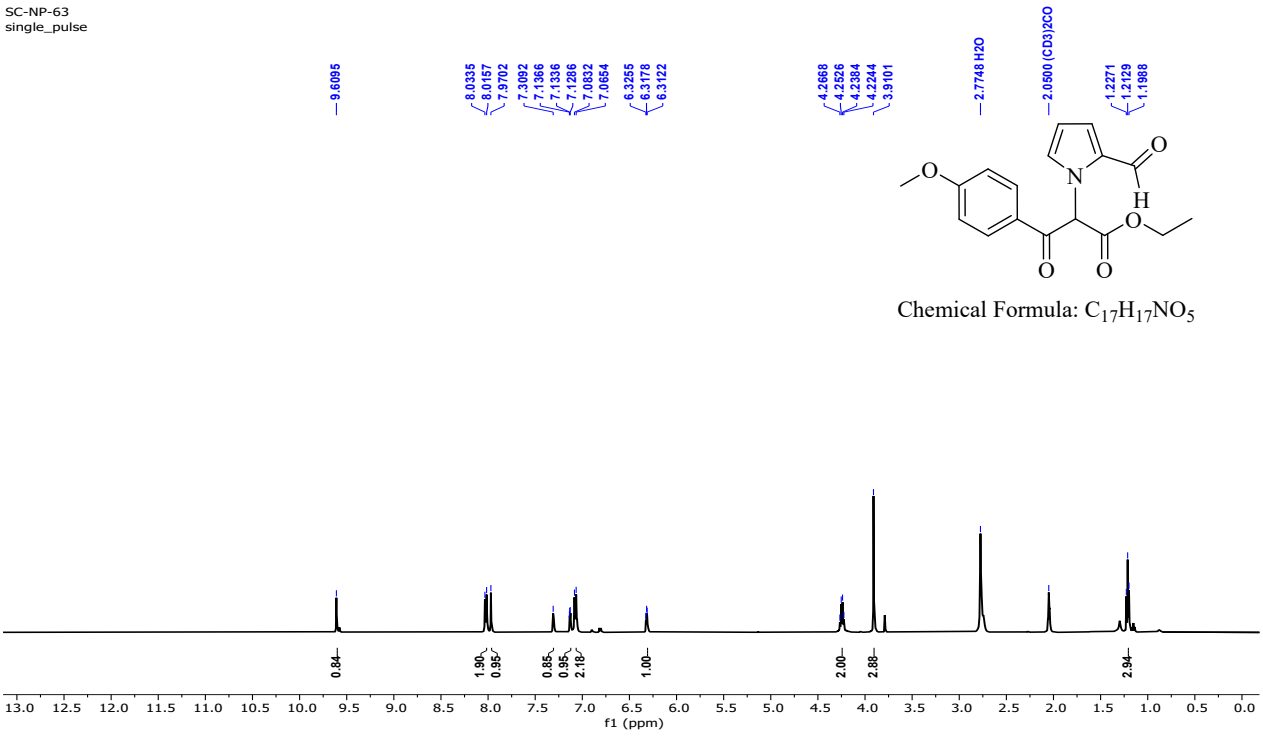


Figure S21: ^{1}H NMR spectra of ethyl-2-(2-formyl-1*H*-pyrrol-1-yl)-3-(4-methoxyphenyl)-3-oxopropanoate **(3c)**

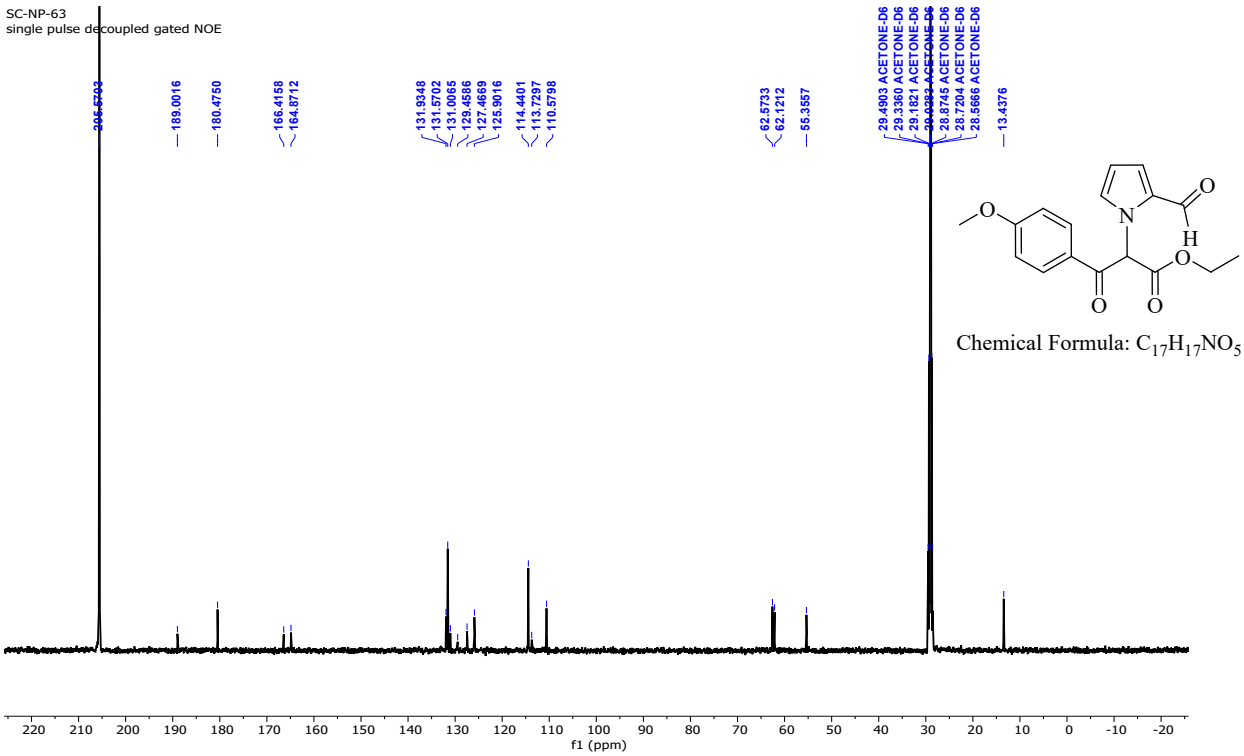


Figure S22: ^{13}C NMR spectra of ethyl-2-(2-formyl-1*H*-pyrrol-1-yl)-3-(4-methoxyphenyl)-3-oxopropanoate **(3c)**

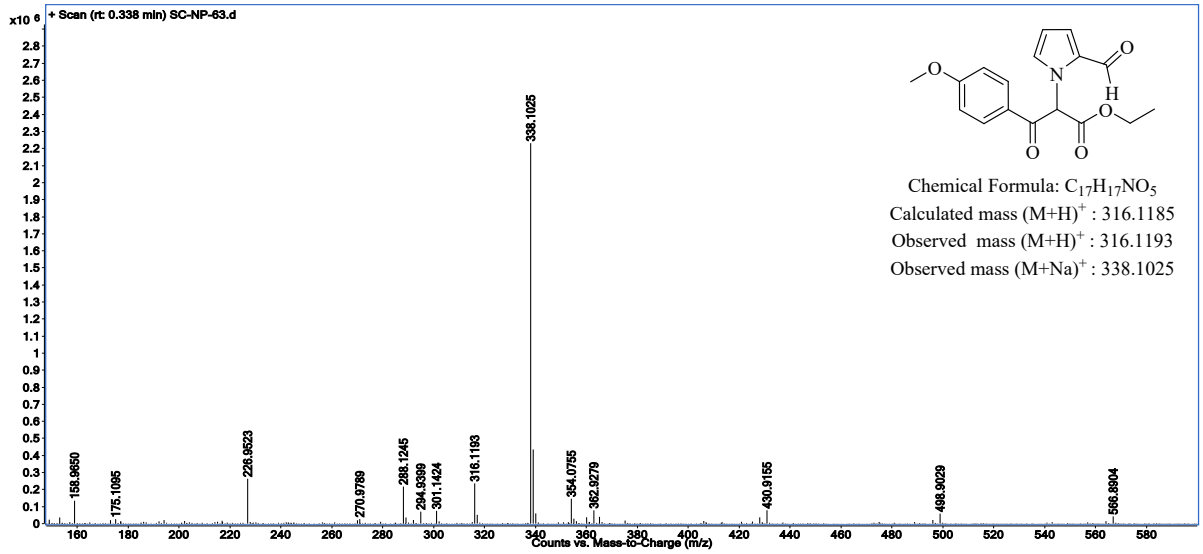


Figure S23: HRMS spectra of ethyl-2-(2-formyl-1*H*-pyrrol-1-yl)-3-(4-methoxyphenyl)-3-oxopropanoate **(3c)**

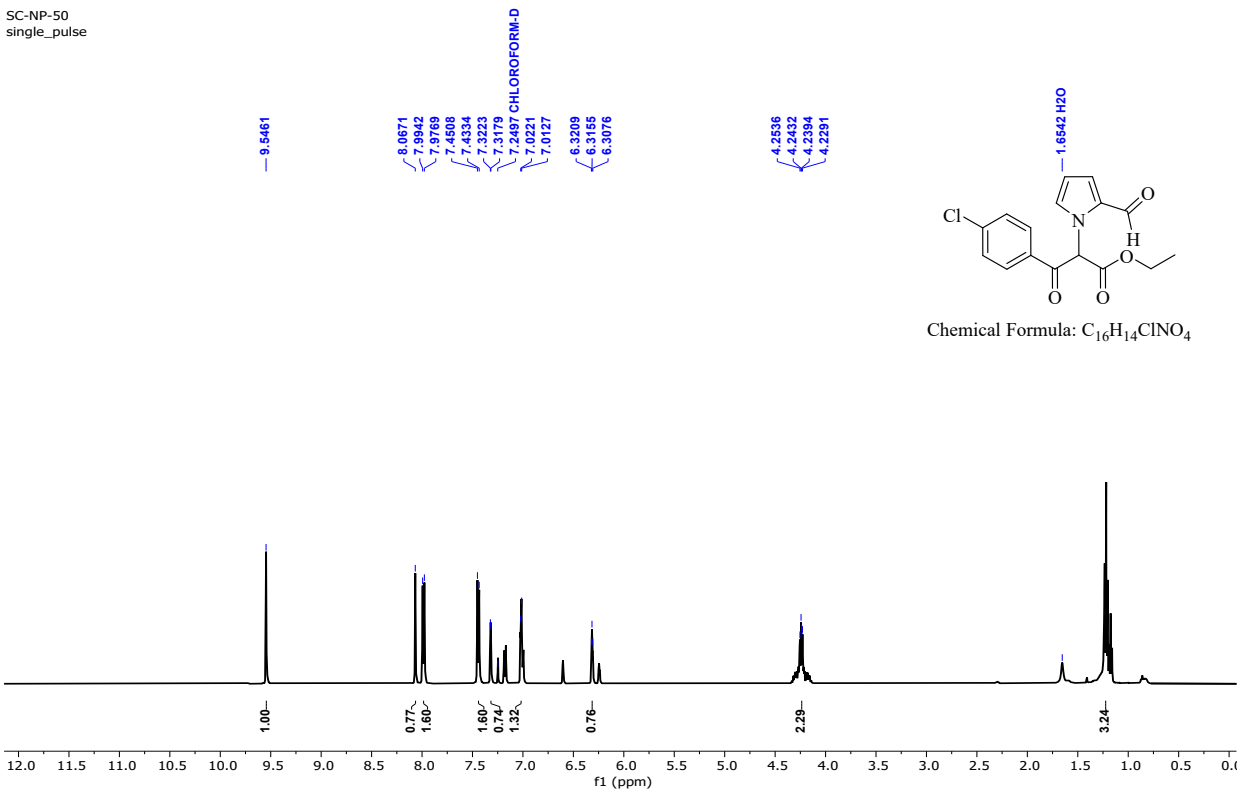


Figure S24: ^{1}H NMR spectra of ethyl-3-(4-chlorophenyl)-2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxopropanoateylate **(3e)**

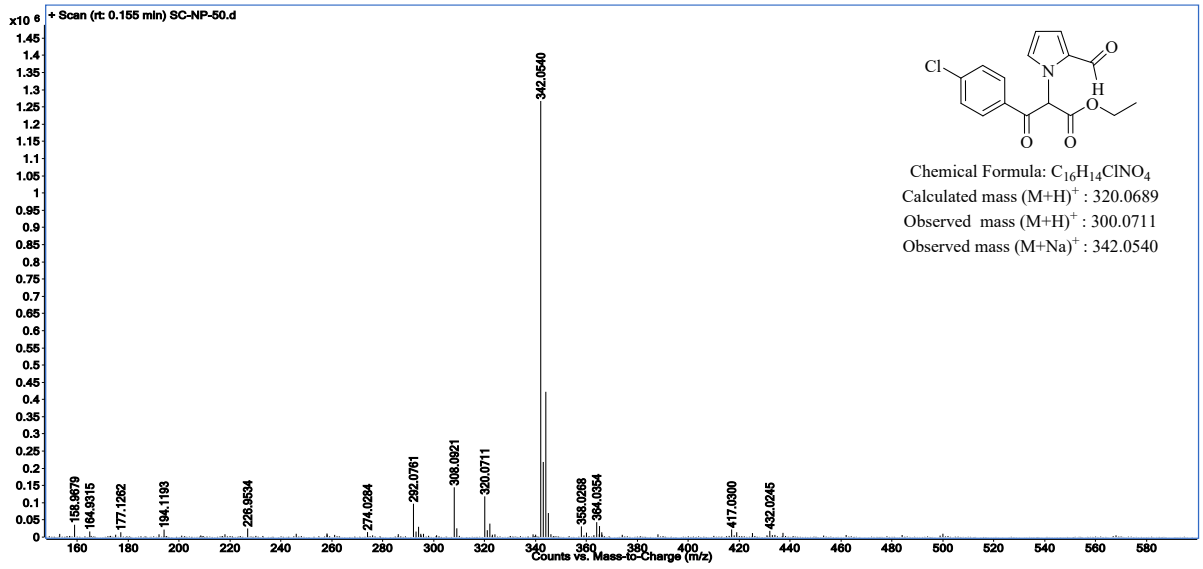
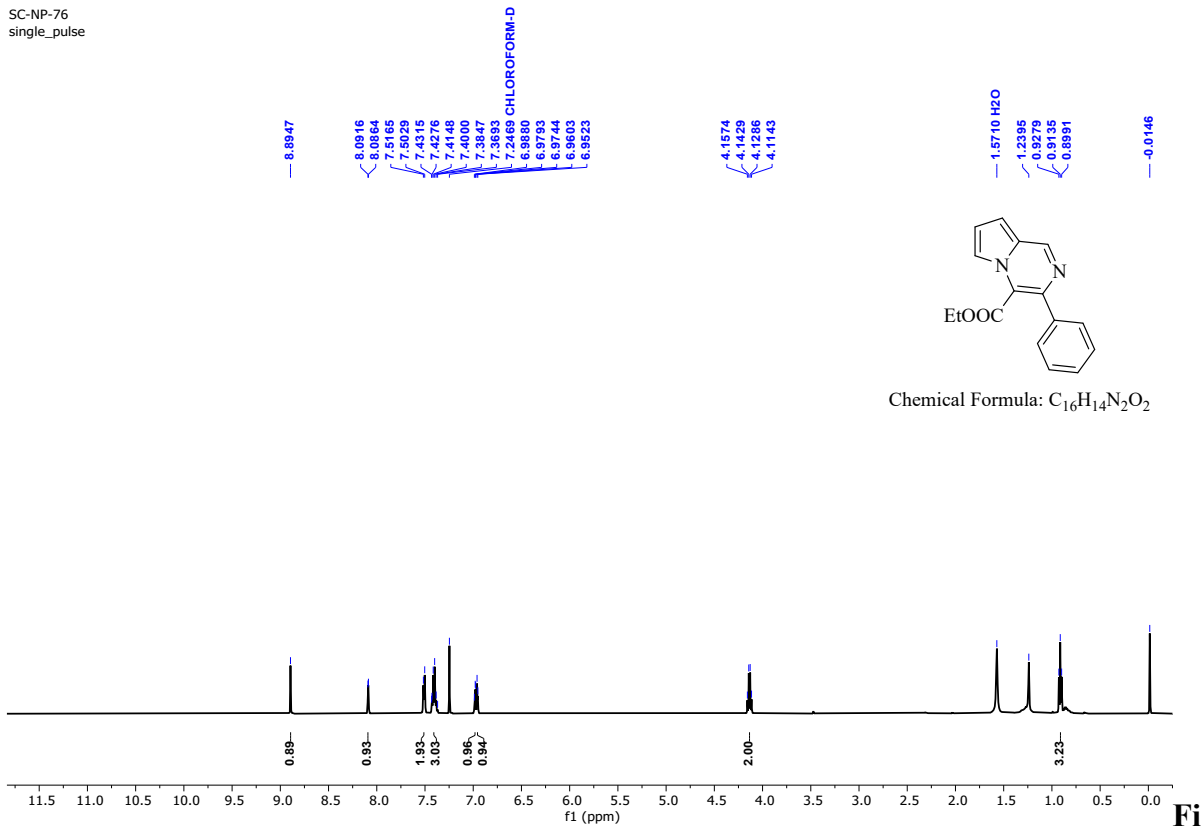
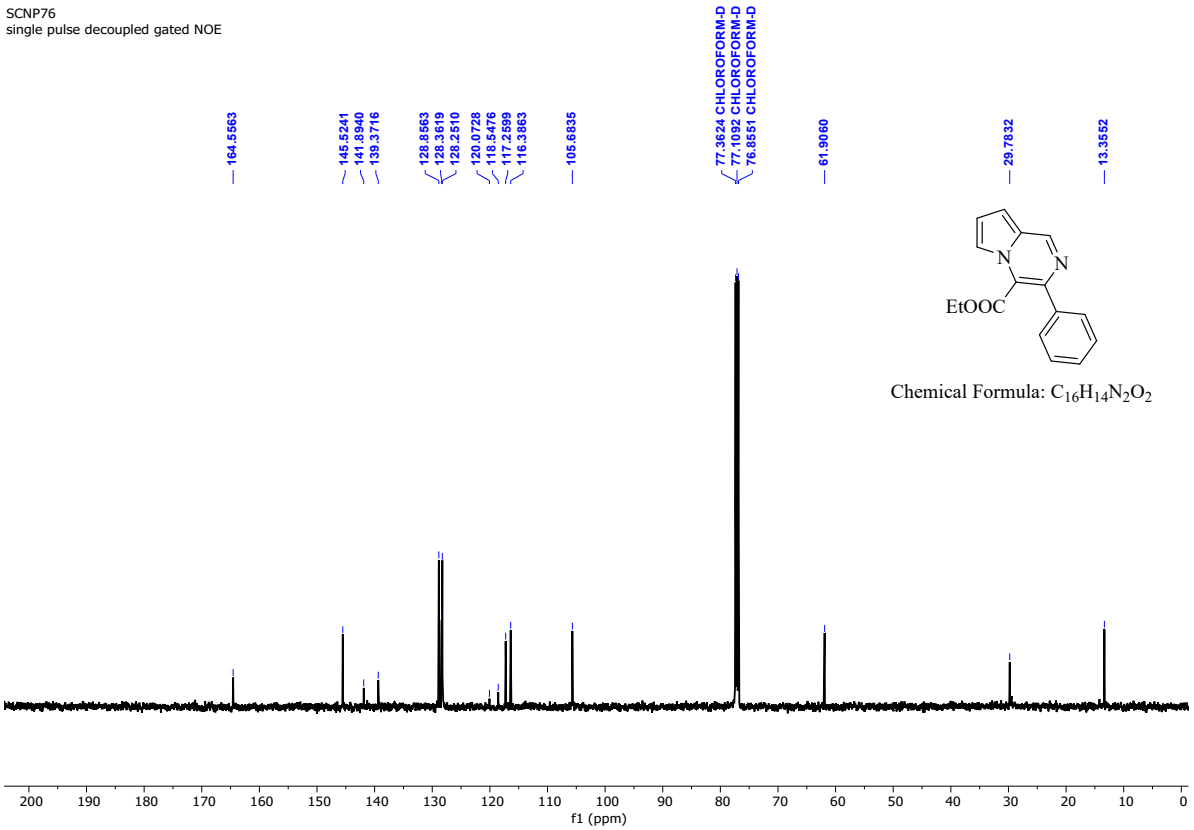


Figure S25: HRMS spectra of ethyl-3-(4-chlorophenyl)-2-(2-formyl-1*H*-pyrrol-1-yl)-3-oxopropanoateylate **(3e)**



Chemical Formula: $C_{16}H_{14}N_2O_2$

Figure S26: ^{1}H NMR spectra of ethyl-3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5a)**



Chemical Formula: $C_{16}H_{14}N_2O_2$

Figure S27: ^{13}C NMR spectra of Ethyl-3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5a)**

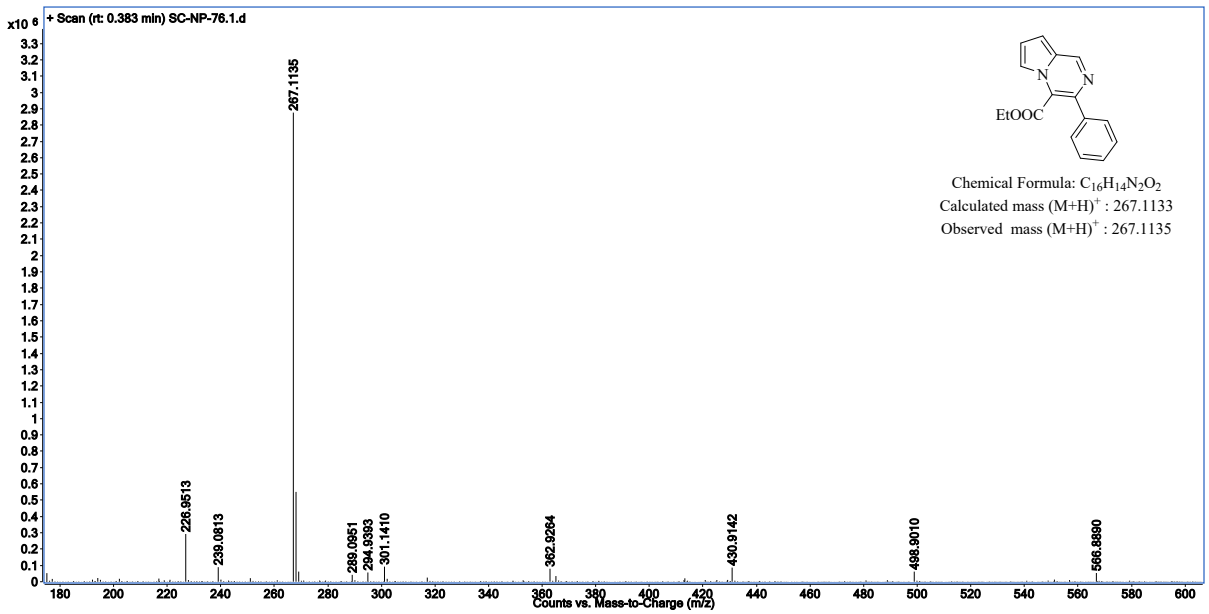


Figure S28: HRMS spectra of Ethyl-3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5a)**

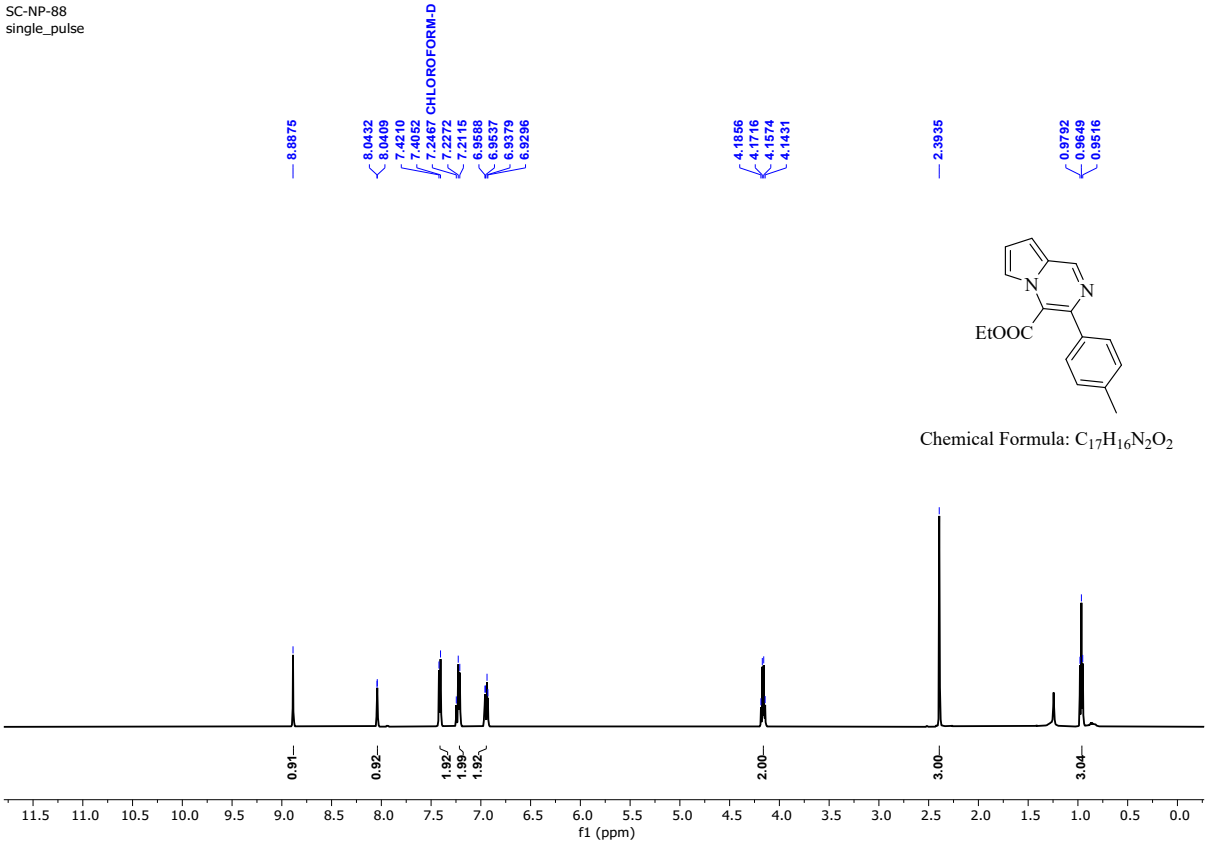


Figure S29: ^{1}H NMR spectra of ethyl 3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5b)**

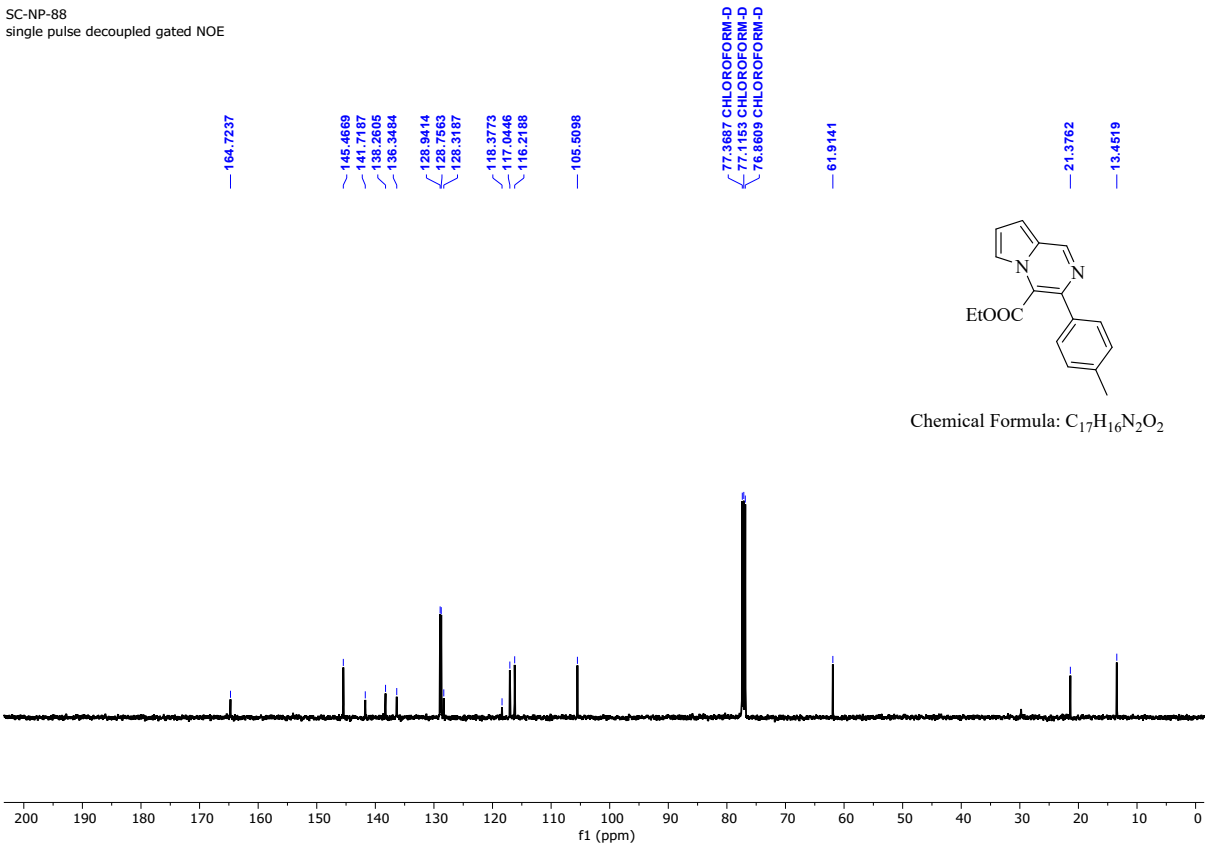


Figure S30: ^{13}C NMR spectra of ethyl 3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5b)**

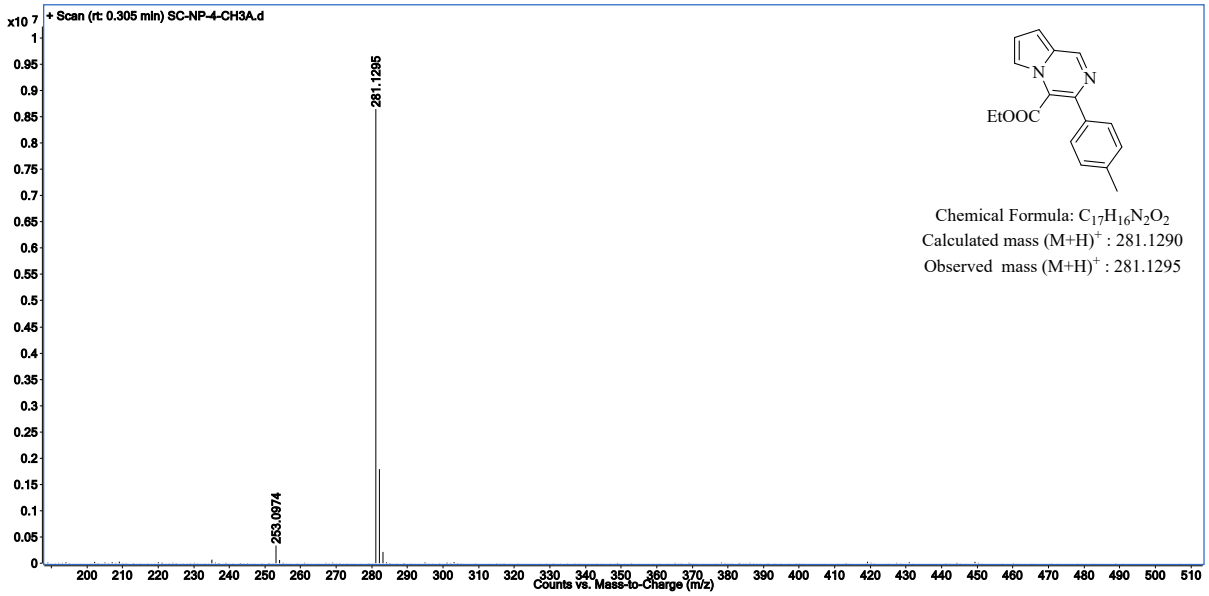
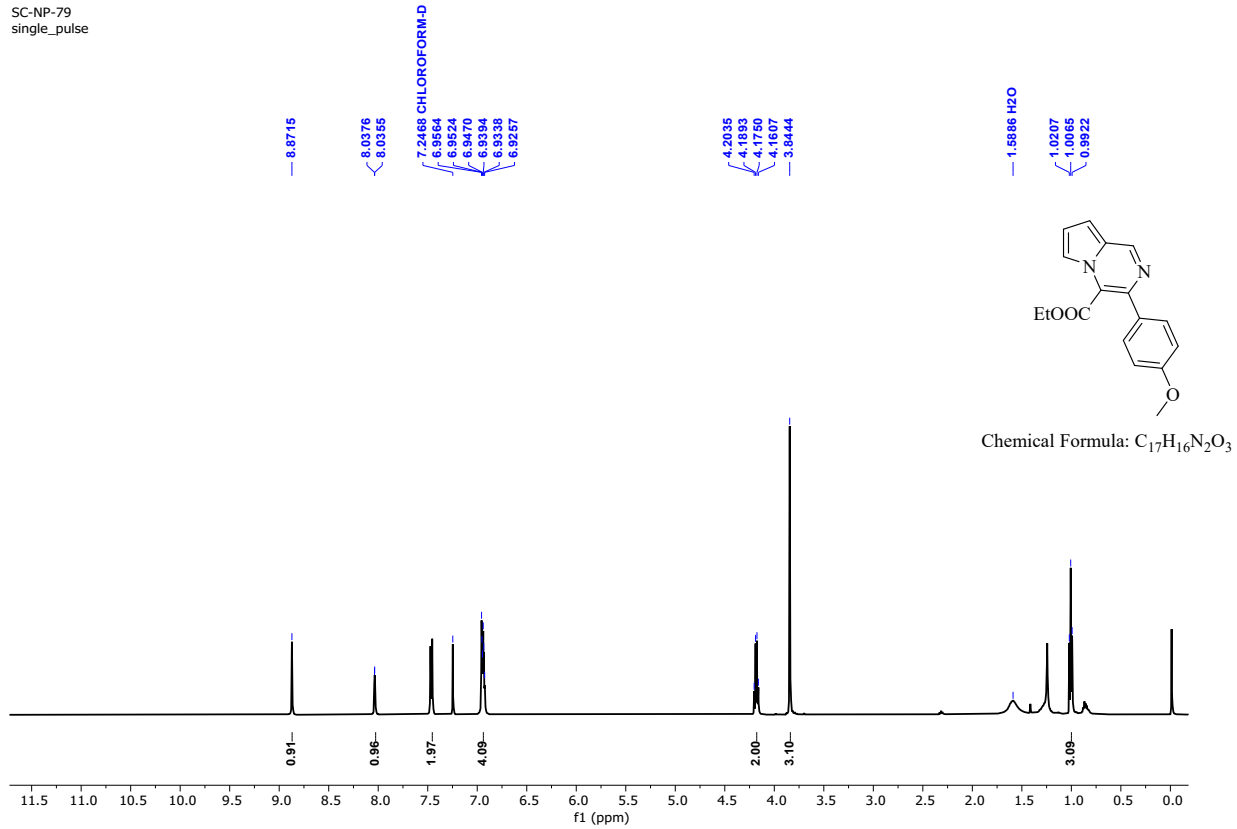
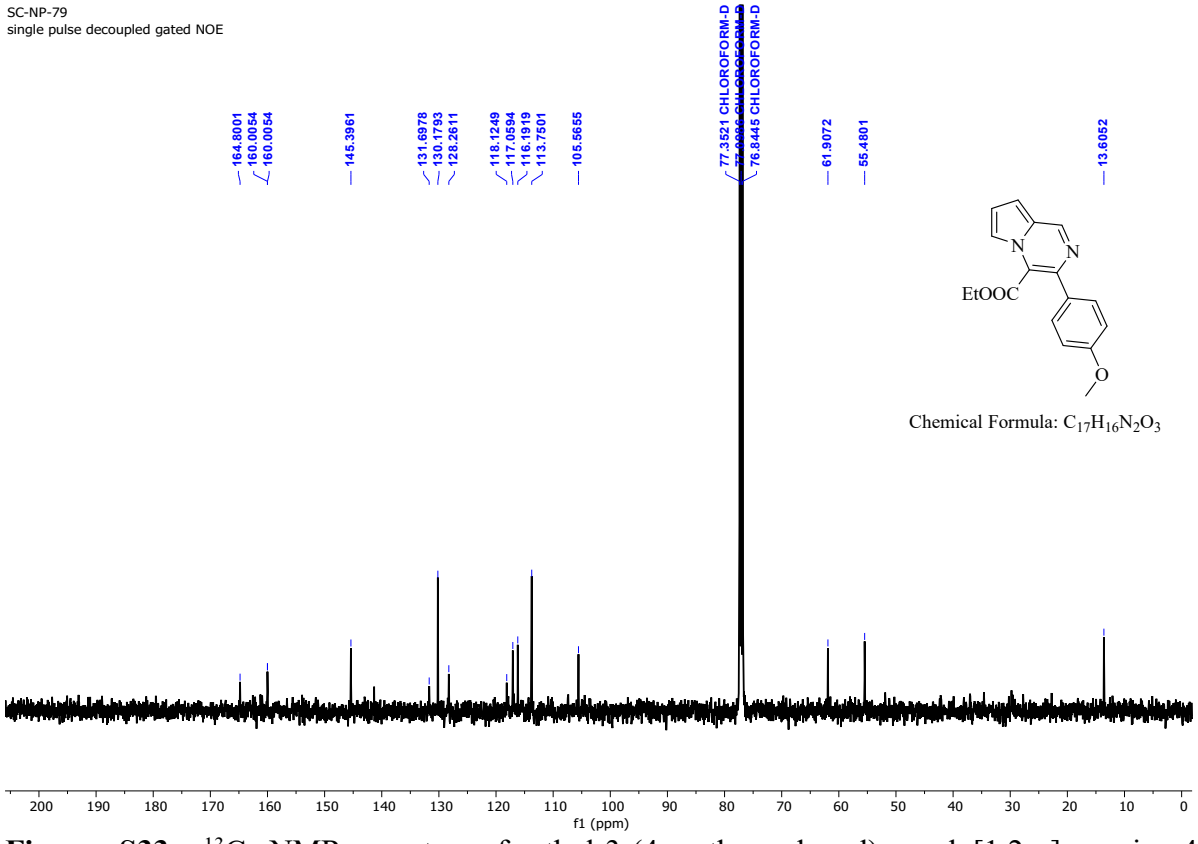


Figure S31: HRMS spectra of ethyl 3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5b)**



Chemical Formula: $C_{17}H_{16}N_2O_3$

Figure S32: ^{1}H NMR spectra of ethyl-3-(4-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5c)**



Chemical Formula: $C_{17}H_{16}N_2O_3$

Figure S33: ^{13}C NMR spectra of ethyl-3-(4-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5c)**

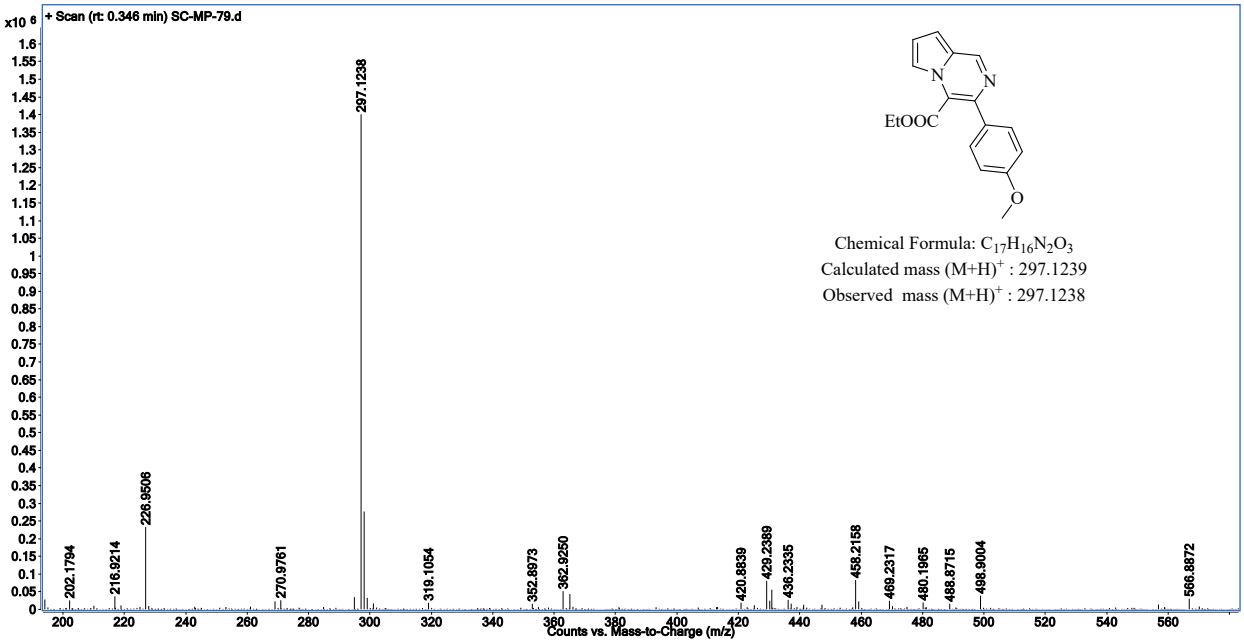


Figure S34: HRMS spectra of ethyl-3-(4-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5c)**

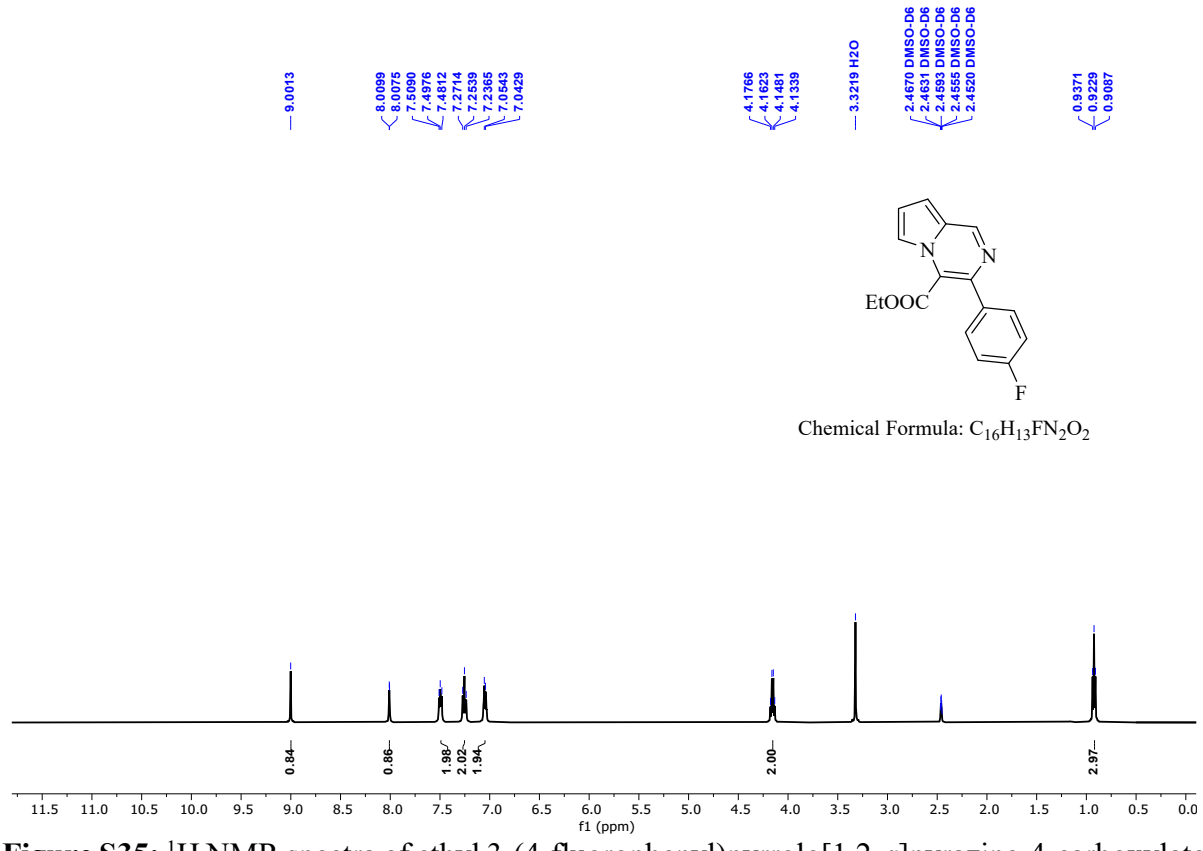


Figure S35: [1]H NMR spectra of ethyl 3-(4-fluorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5d)**

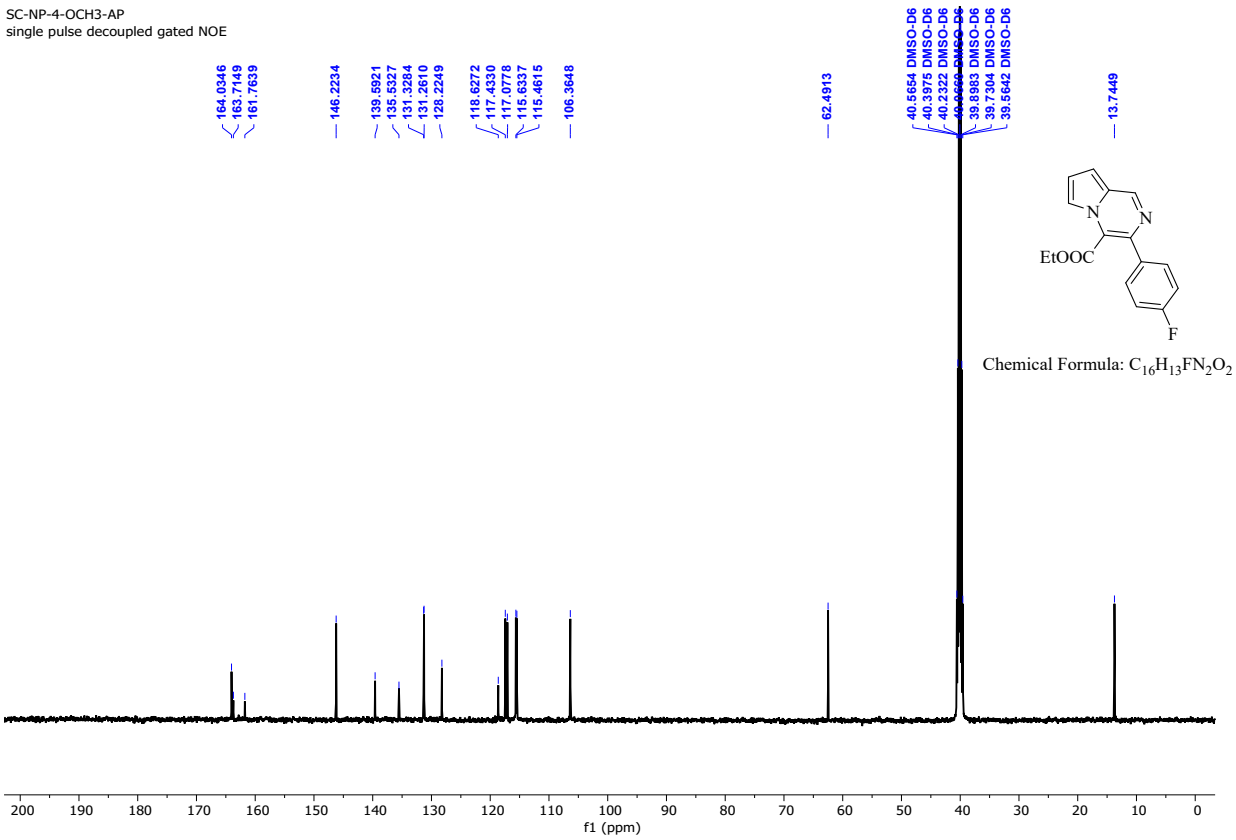


Figure S36: ^{13}C NMR spectra of ethyl 3-(4-fluorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5d)**

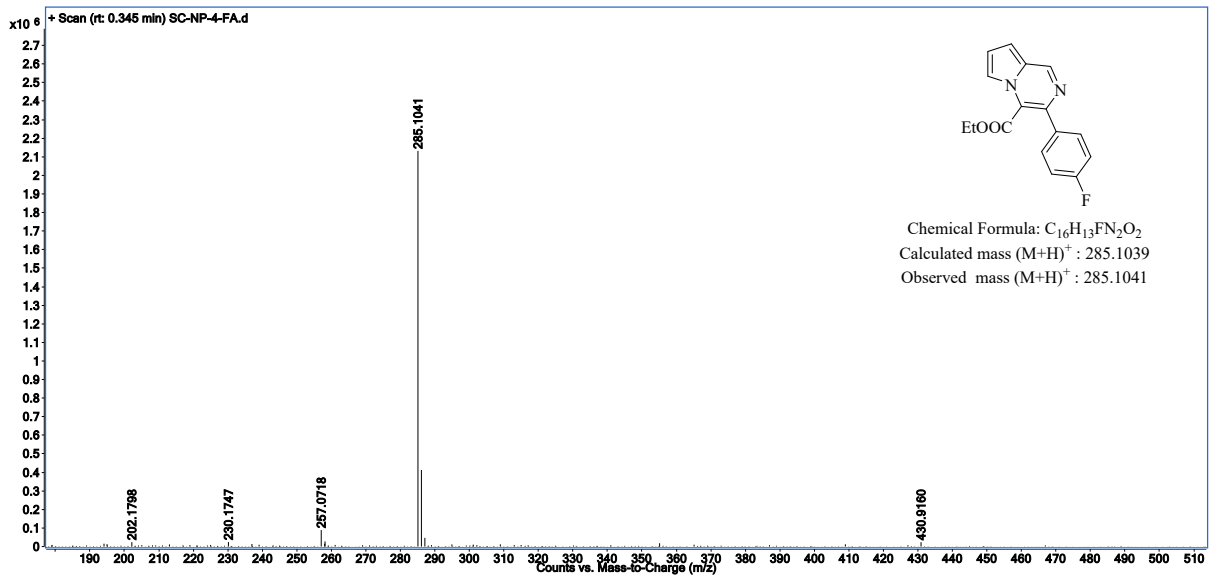


Figure S37: HRMS spectra of ethyl 3-(4-fluorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5d)**

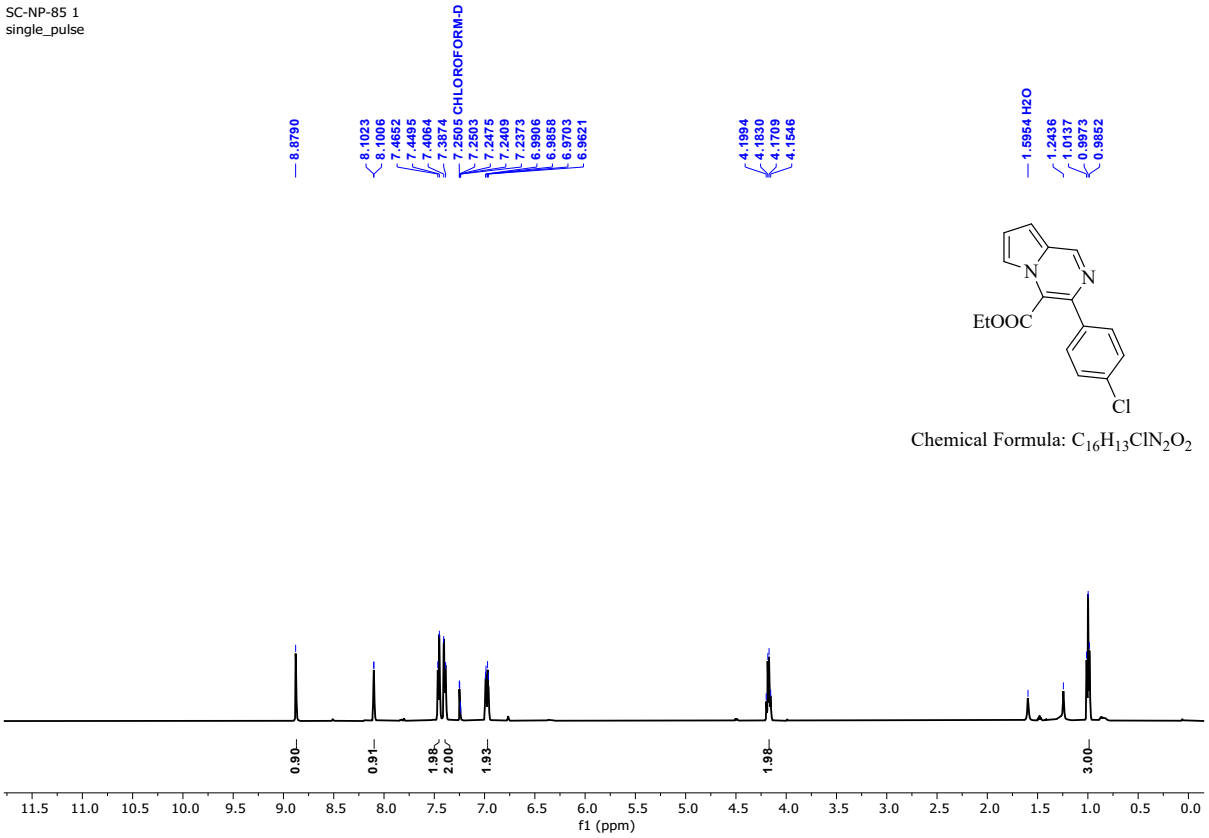


Figure S38: ^{1}H NMR spectra of ethyl-3-(4-chlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5e)**

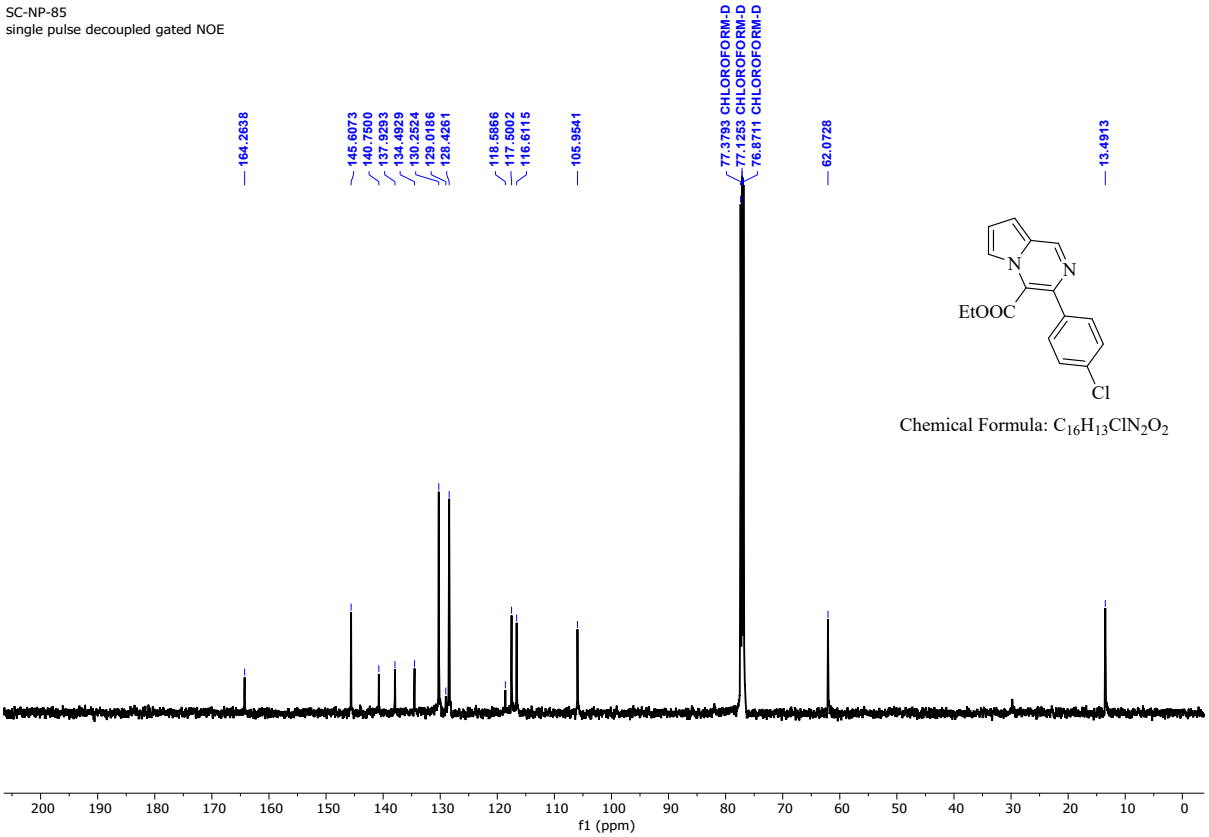


Figure S39: ^{13}C NMR spectra of ethyl-3-(4-chlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5e)**

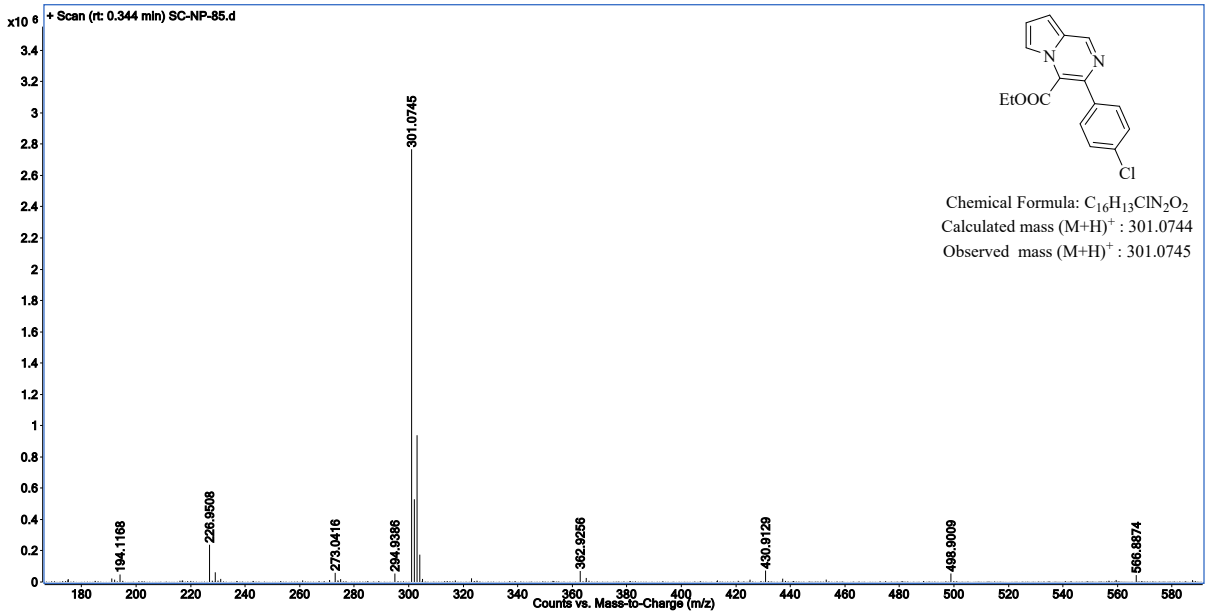


Figure S40: HRMS spectra of ethyl-3-(4-chlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5e)**

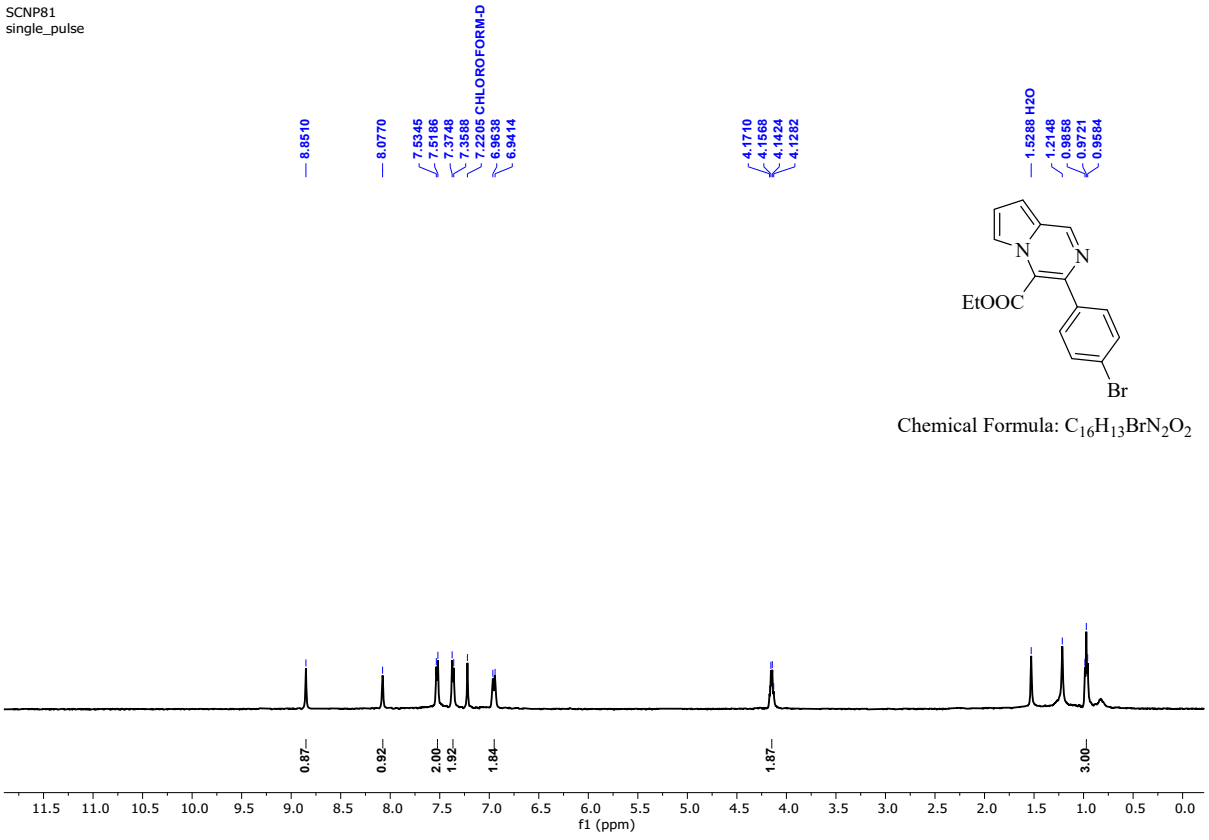


Figure S41: ^{1}H NMR spectra of ethyl-3-(4-bromophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5f)**

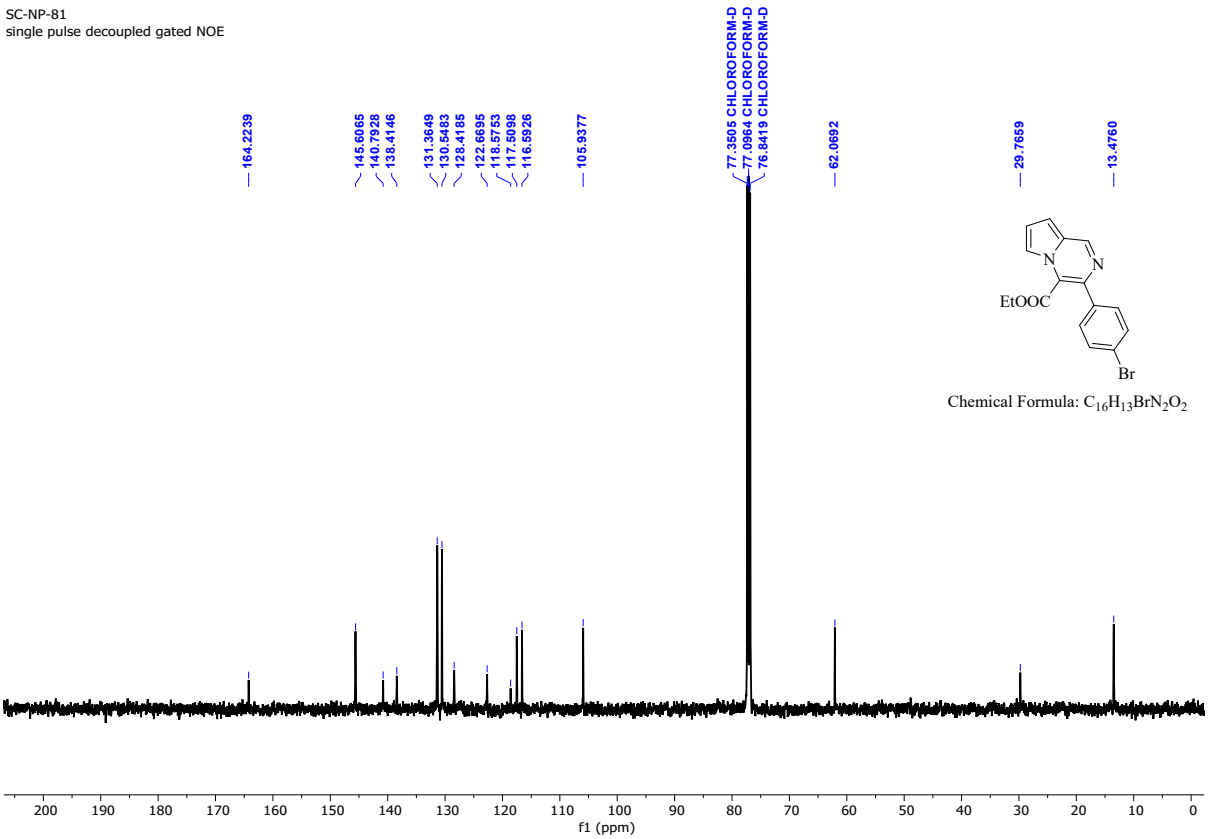


Figure S42: ^{13}C NMR spectra of ethyl-3-(4-bromophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5f)**

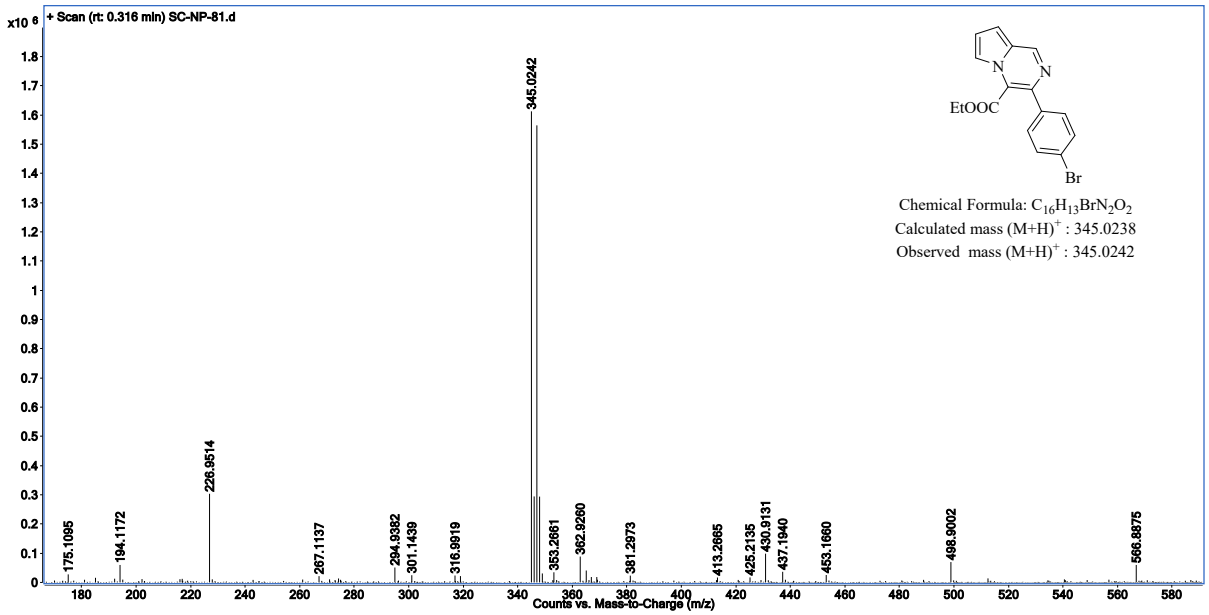


Figure S43: HRMS spectra of ethyl-3-(4-bromophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5f)**

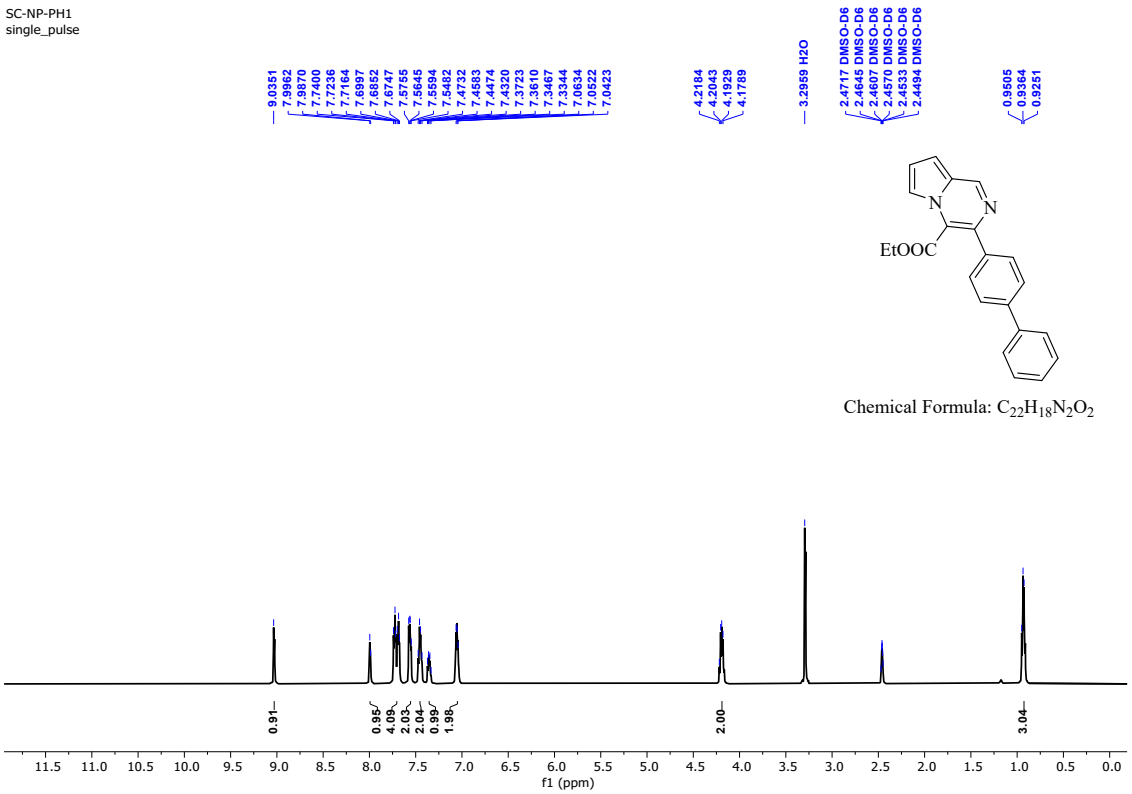


Figure S44: ^{1}H NMR spectra of ethyl 3-([1,1'-biphenyl]-4-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5g)**

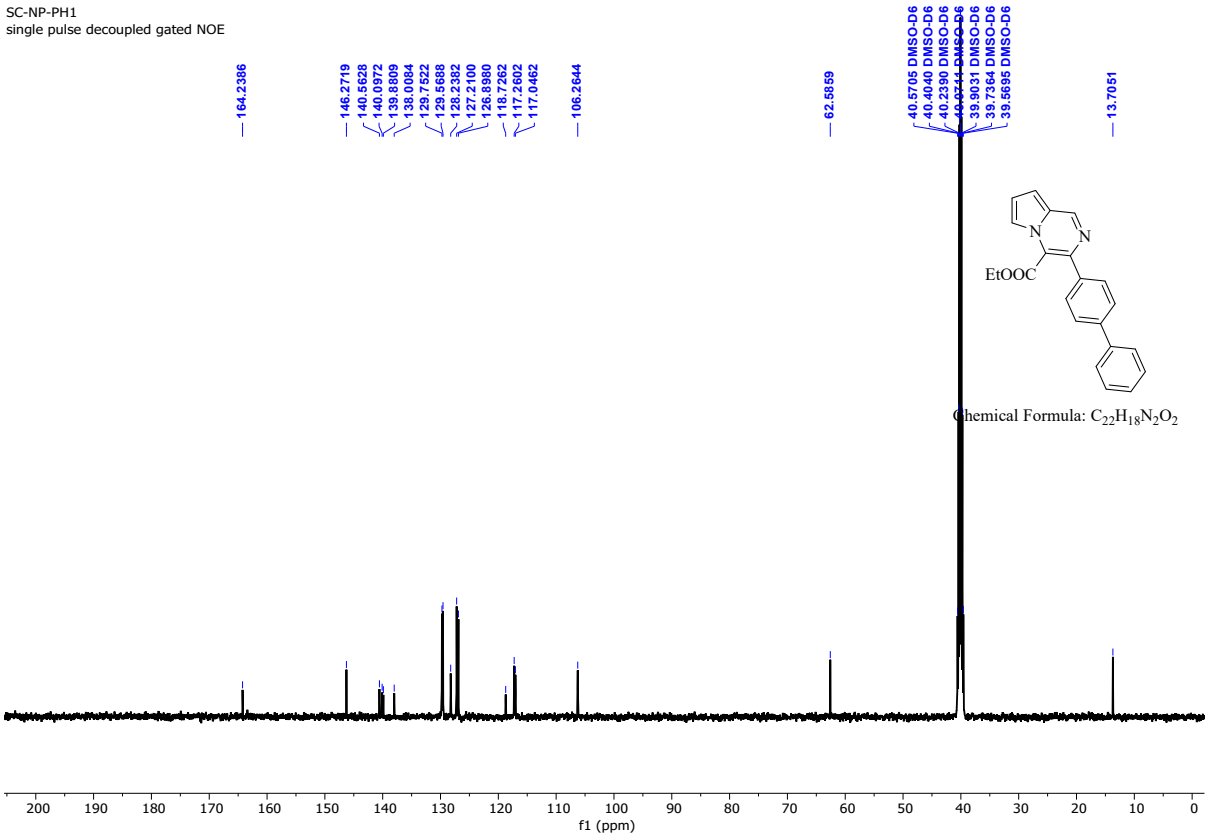


Figure S45: ^{13}C NMR spectra of ethyl 3-([1,1'-biphenyl]-4-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5g)**

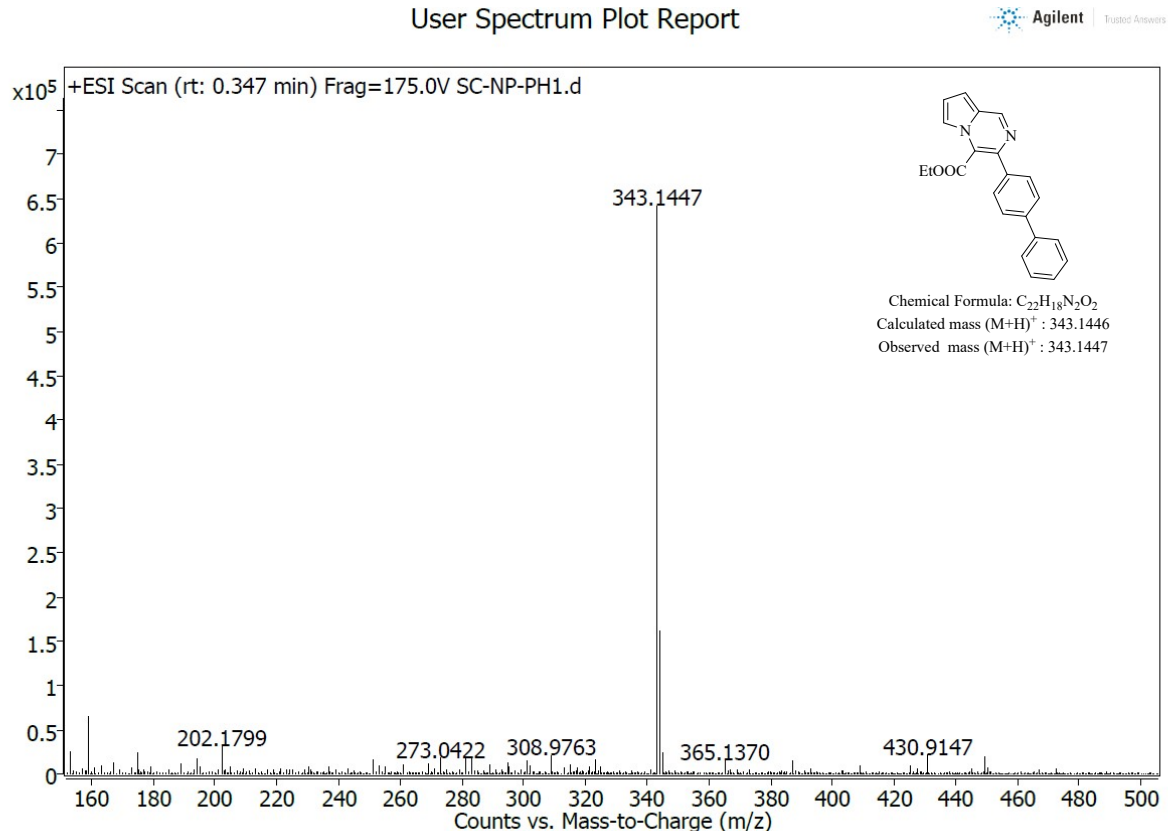


Figure S46: HRMS spectra of ethyl 3-([1,1'-biphenyl]-4-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5g)**

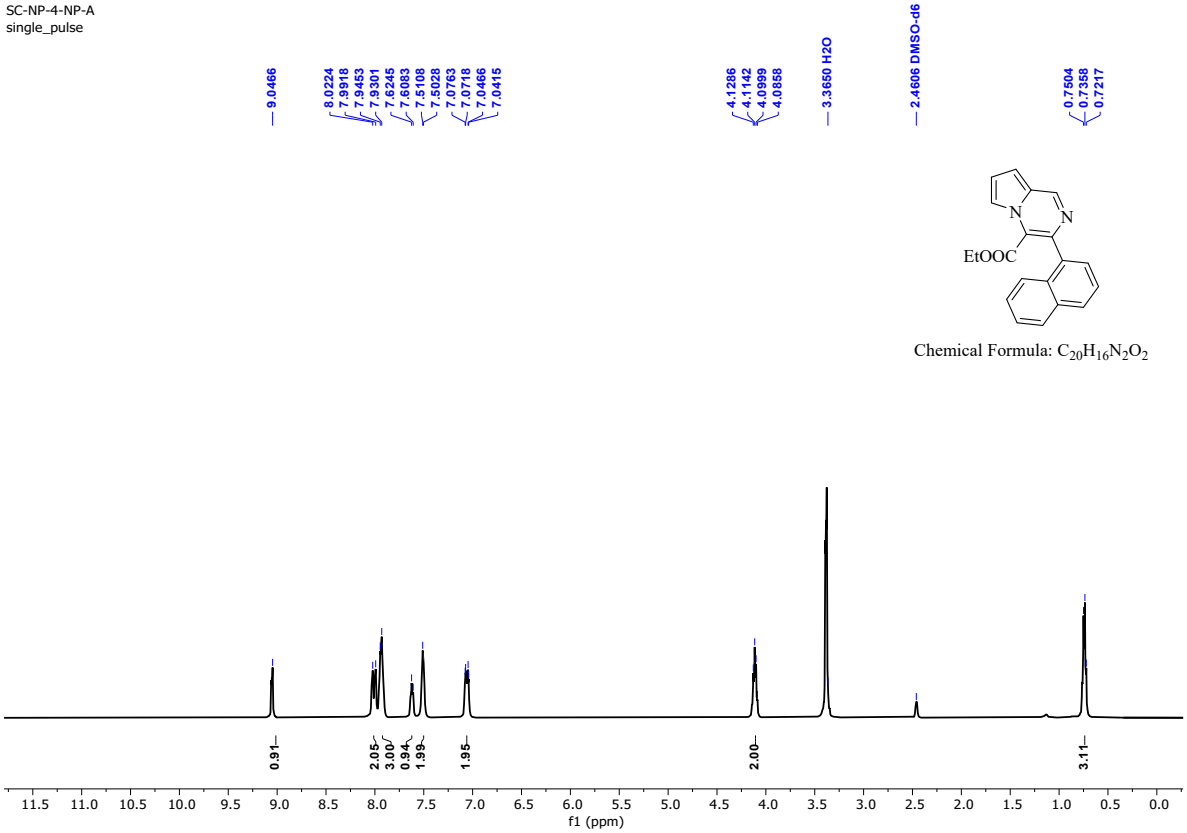


Figure S47: ^{1}H NMR spectra of ethyl 3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5h)**

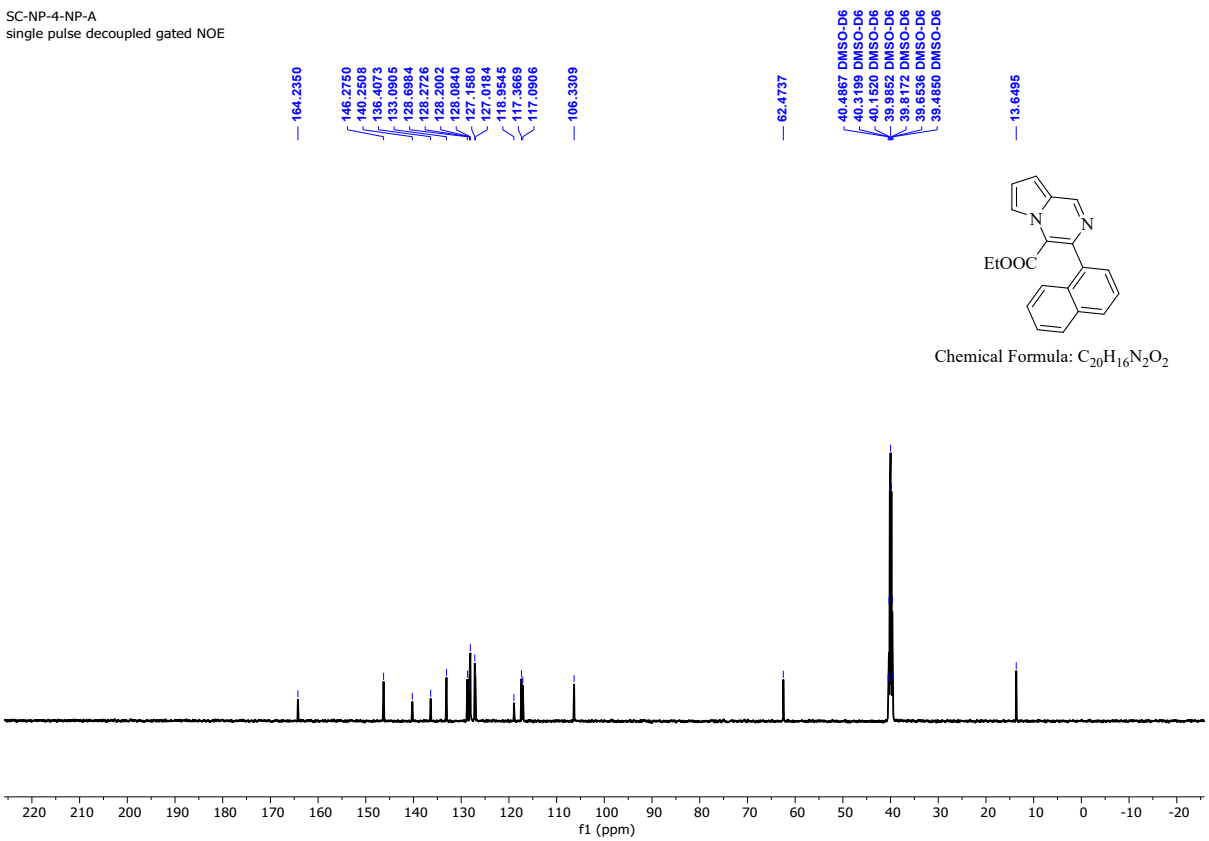


Figure S48: ^{13}C NMR Spectra of ethyl 3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5h)**

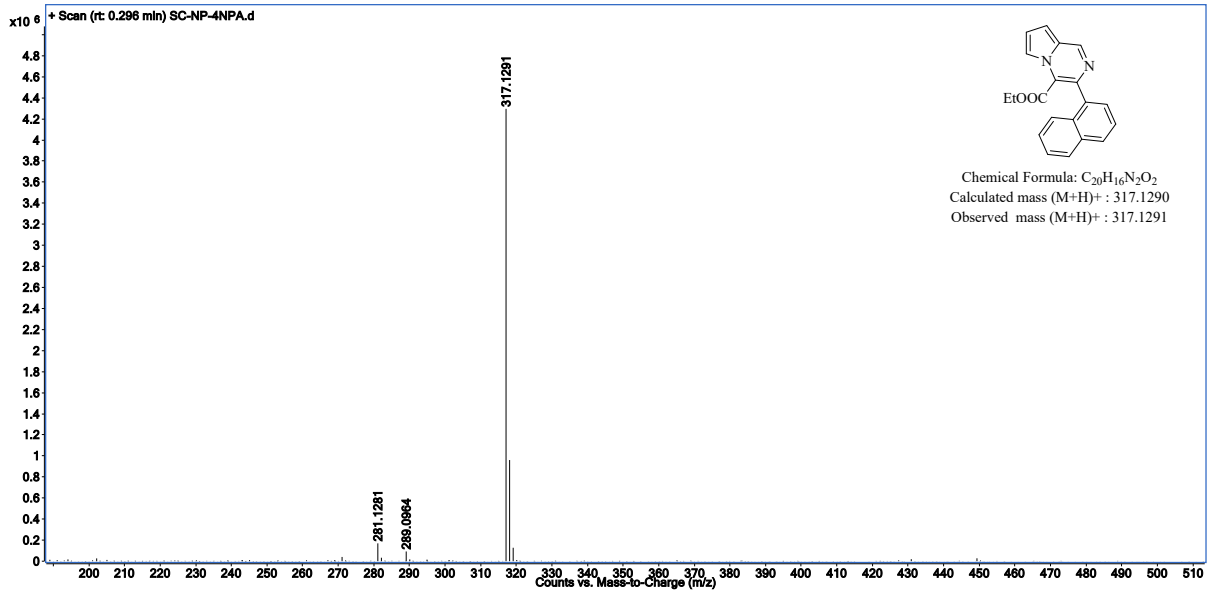


Figure S49: HRMS spectra of ethyl 3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5h)**

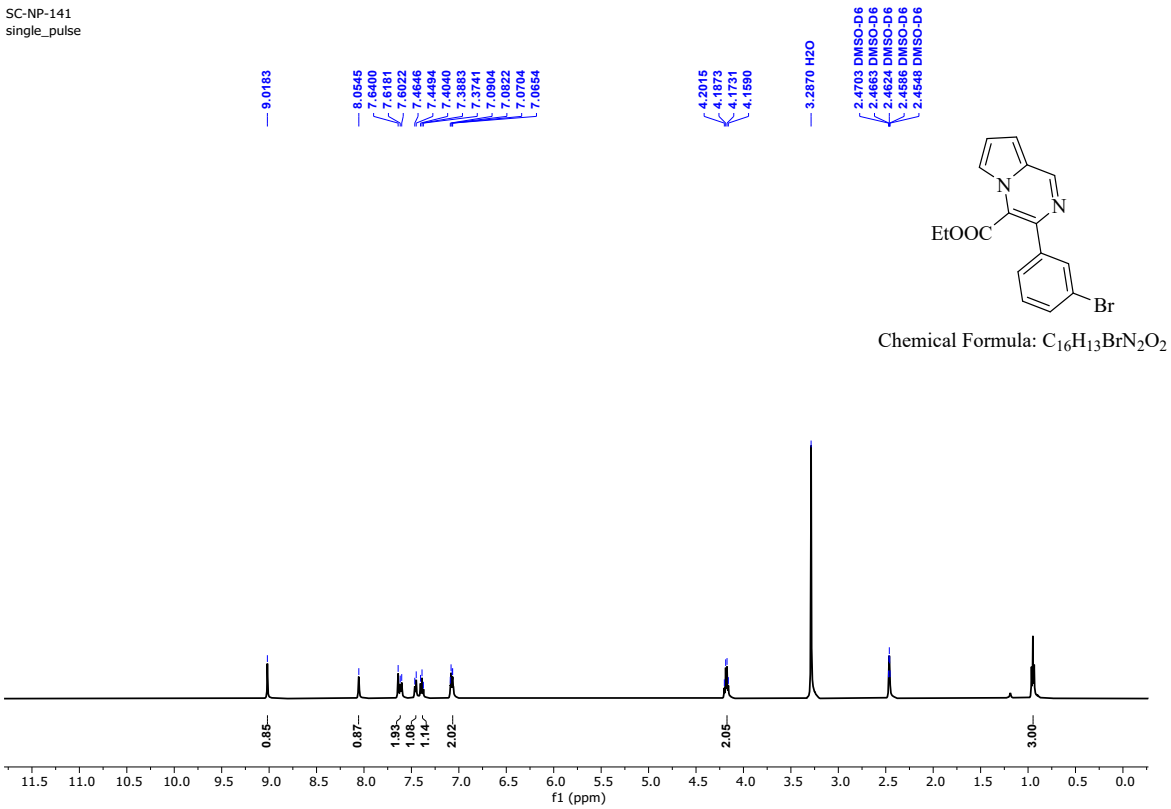


Figure S50: ^{1}H NMR spectra of ethyl 3-(3-bromophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5i)**

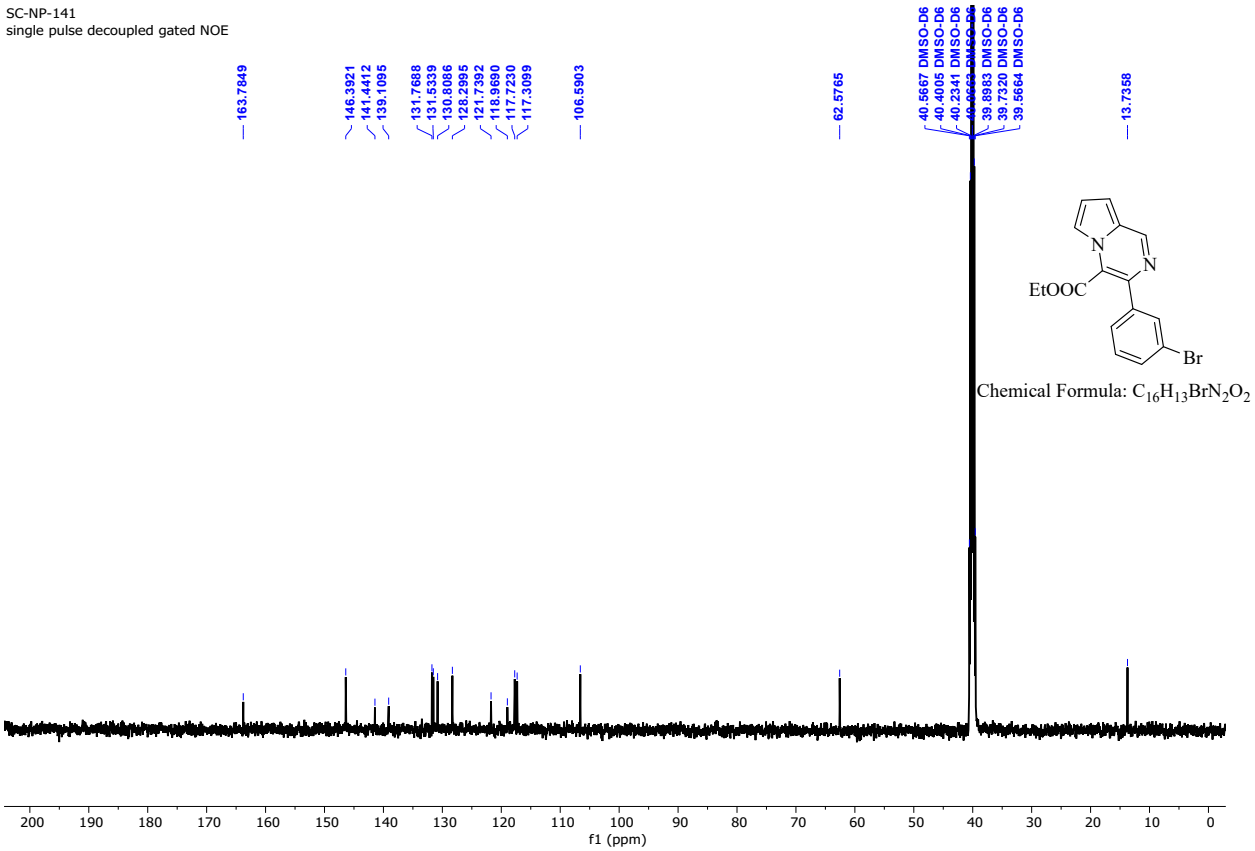


Figure S51: ^{13}C NMR Spectra of ethyl 3-(3-bromophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5i)**

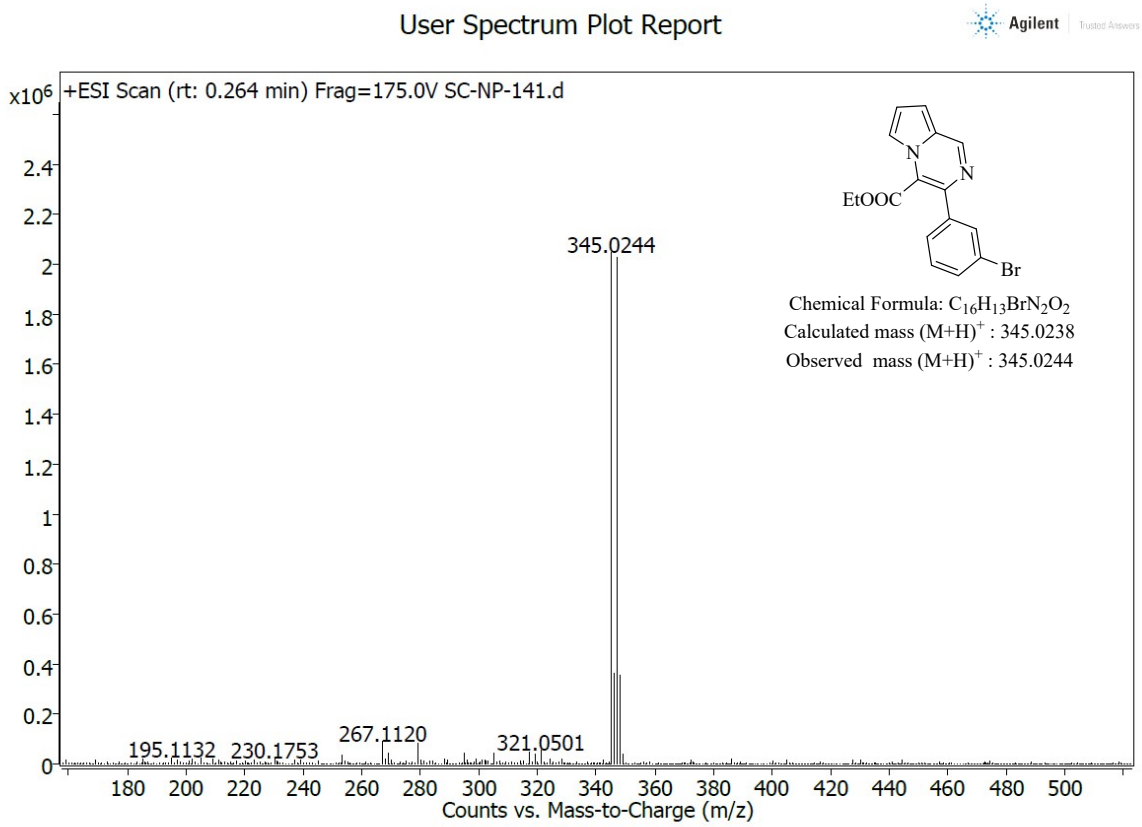


Figure S52: HRMS spectra of ethyl 3-(3-bromophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5i)**

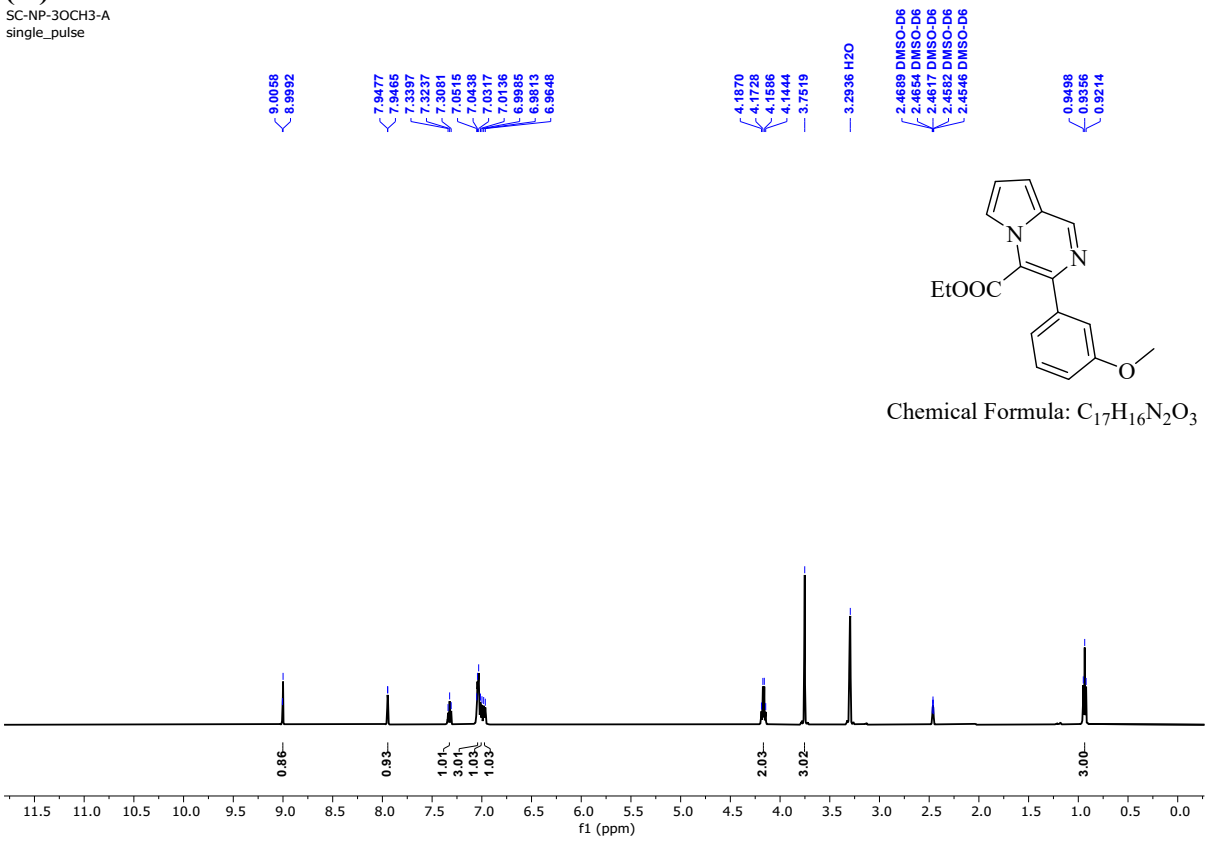


Figure S53: [1]H NMR spectra of ethyl 3-(3-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5j)**

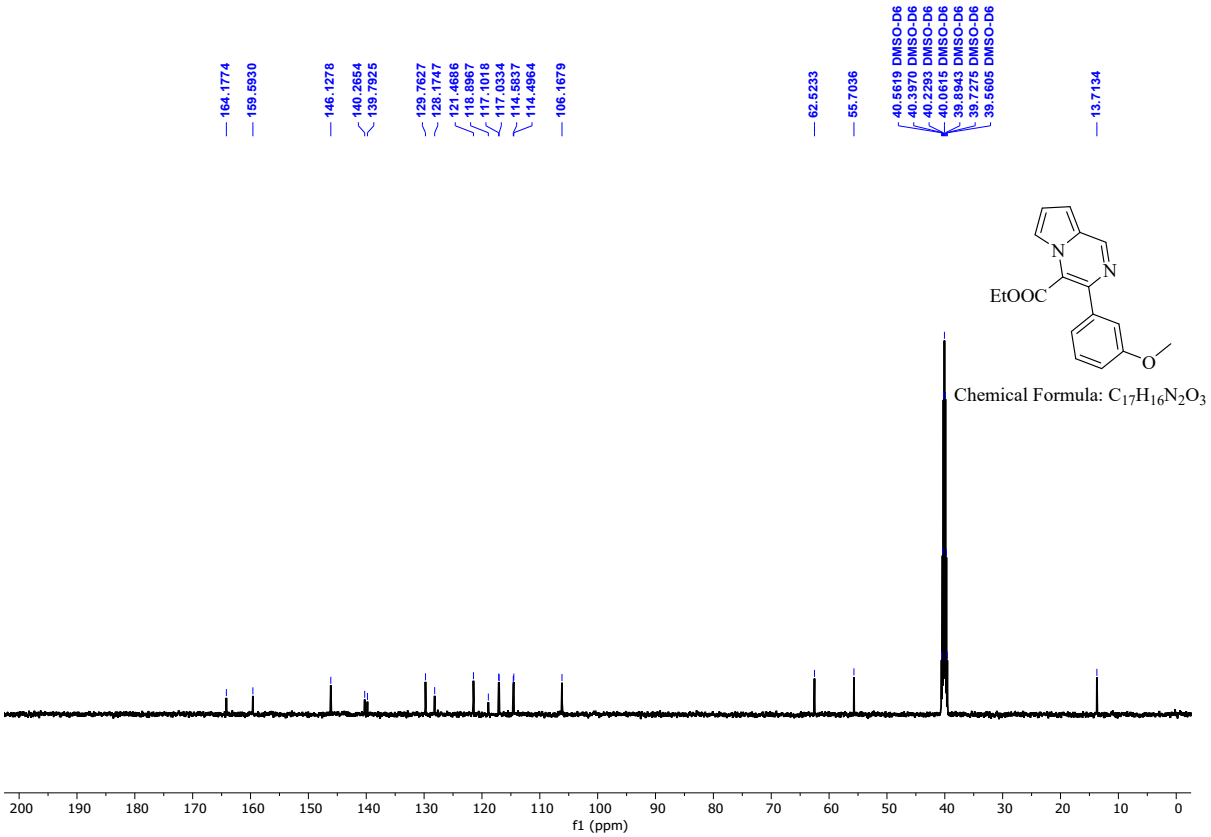


Figure S54: ^{13}C NMR spectra of ethyl 3-(3-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5j)**

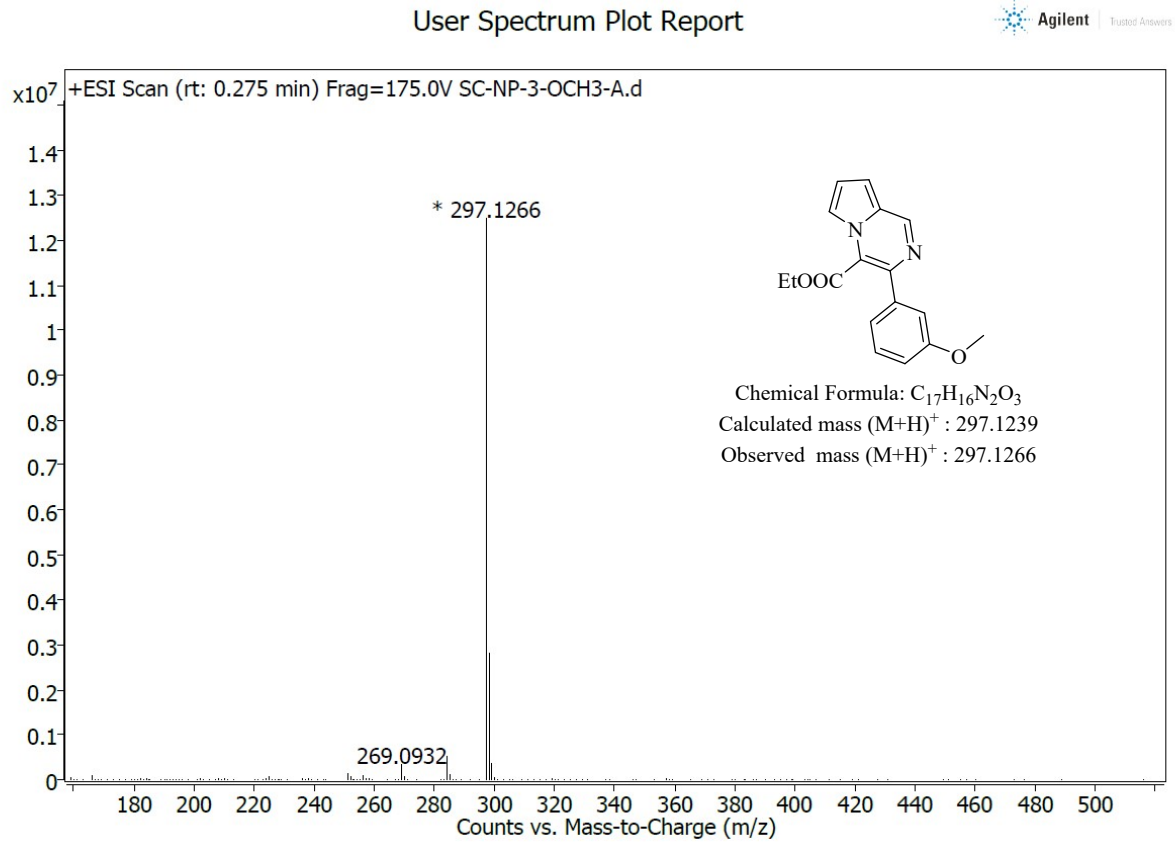


Figure S55: HRMS spectra of ethyl 3-(3-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5j)**

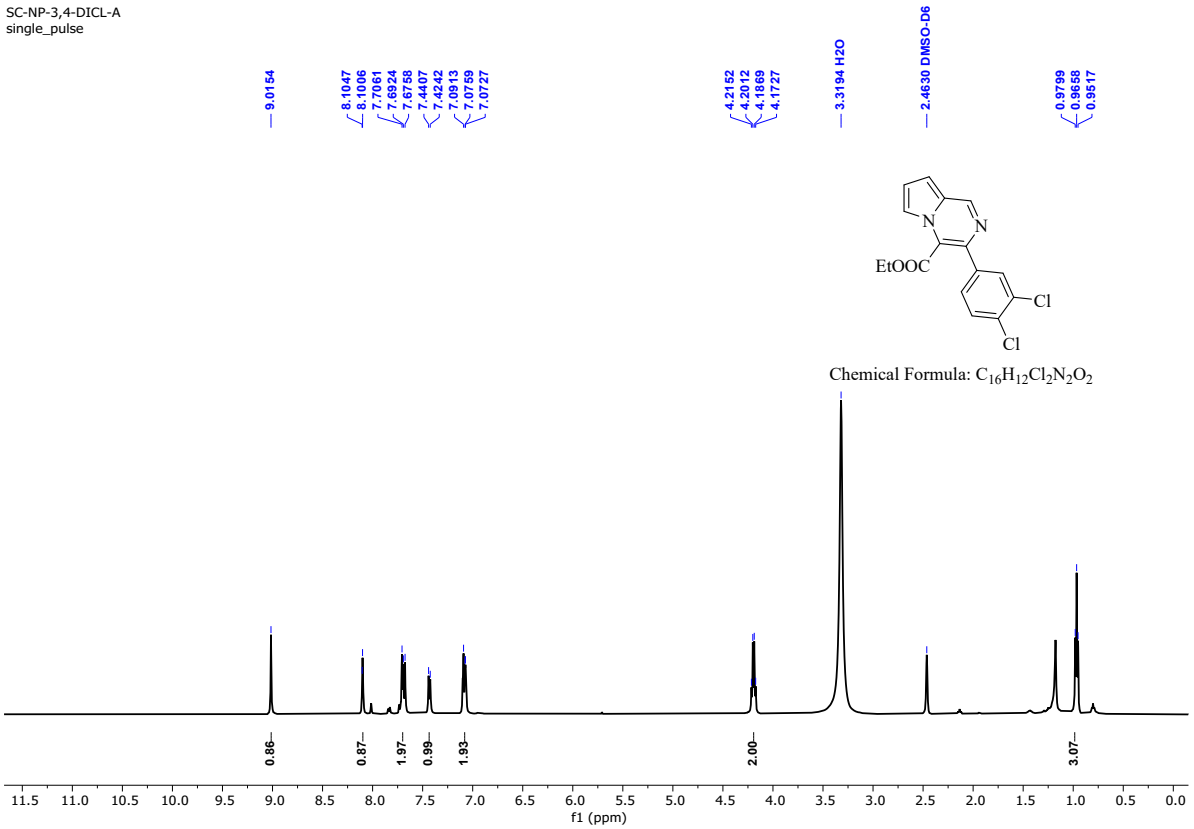


Figure S56: ^{1}H NMR spectra of ethyl 3-(3,4-dichlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5k)**

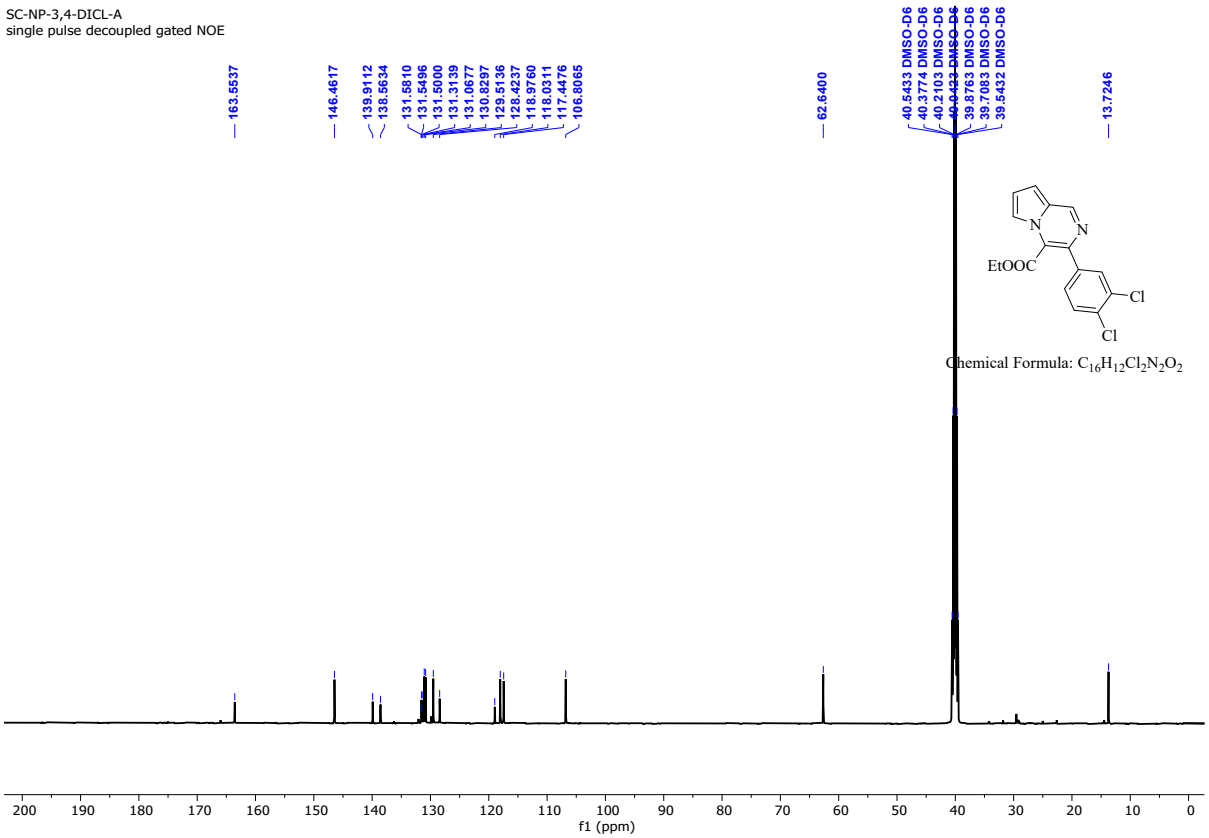


Figure S57: ^{13}C NMR spectra of ethyl 3-(3,4-dichlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5k)**

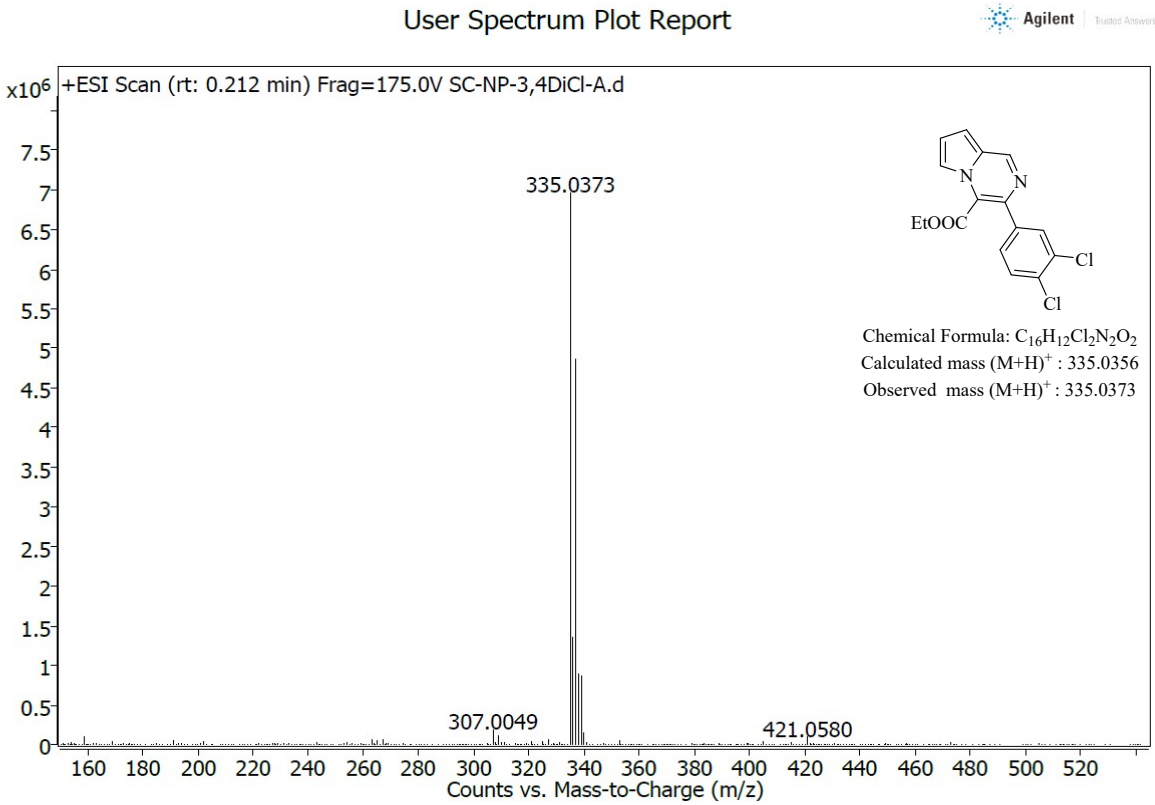


Figure S58: HRMS spectra of ethyl-3-(3,4-dichlorophenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5k)**

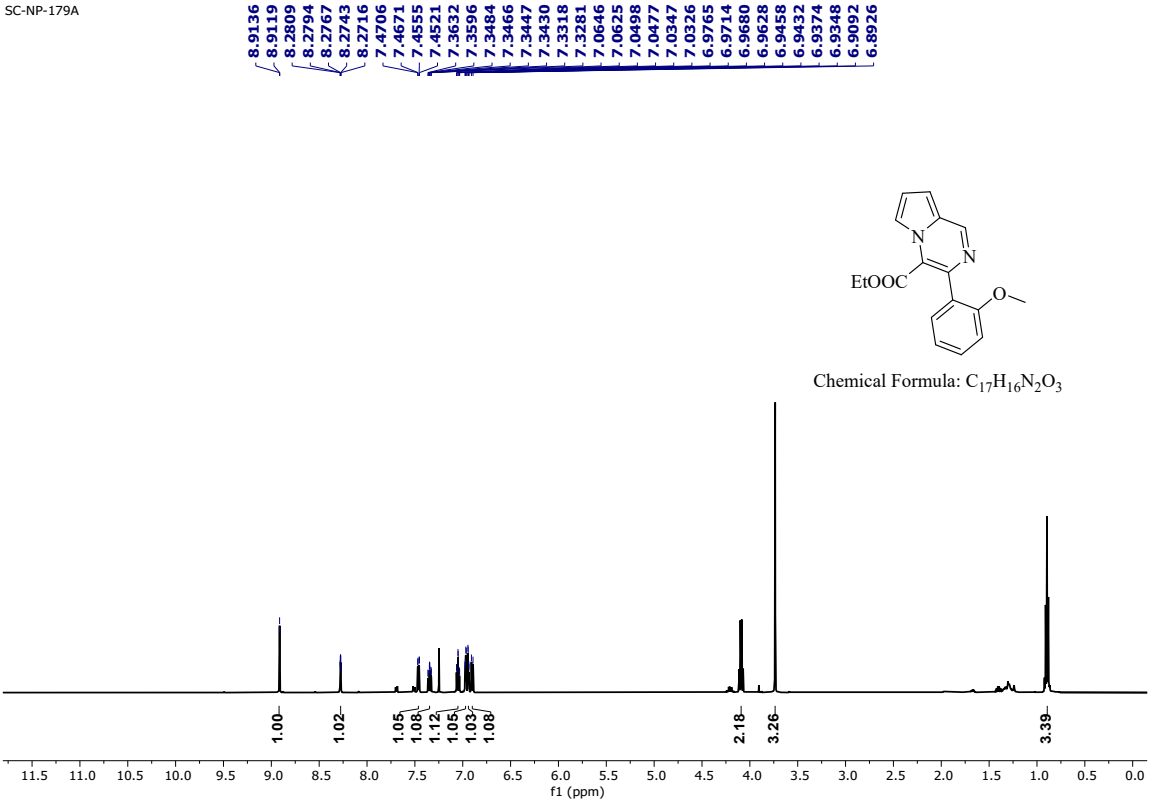


Figure S59: [1]H NMR spectra of ethyl 3-(2-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5l)**

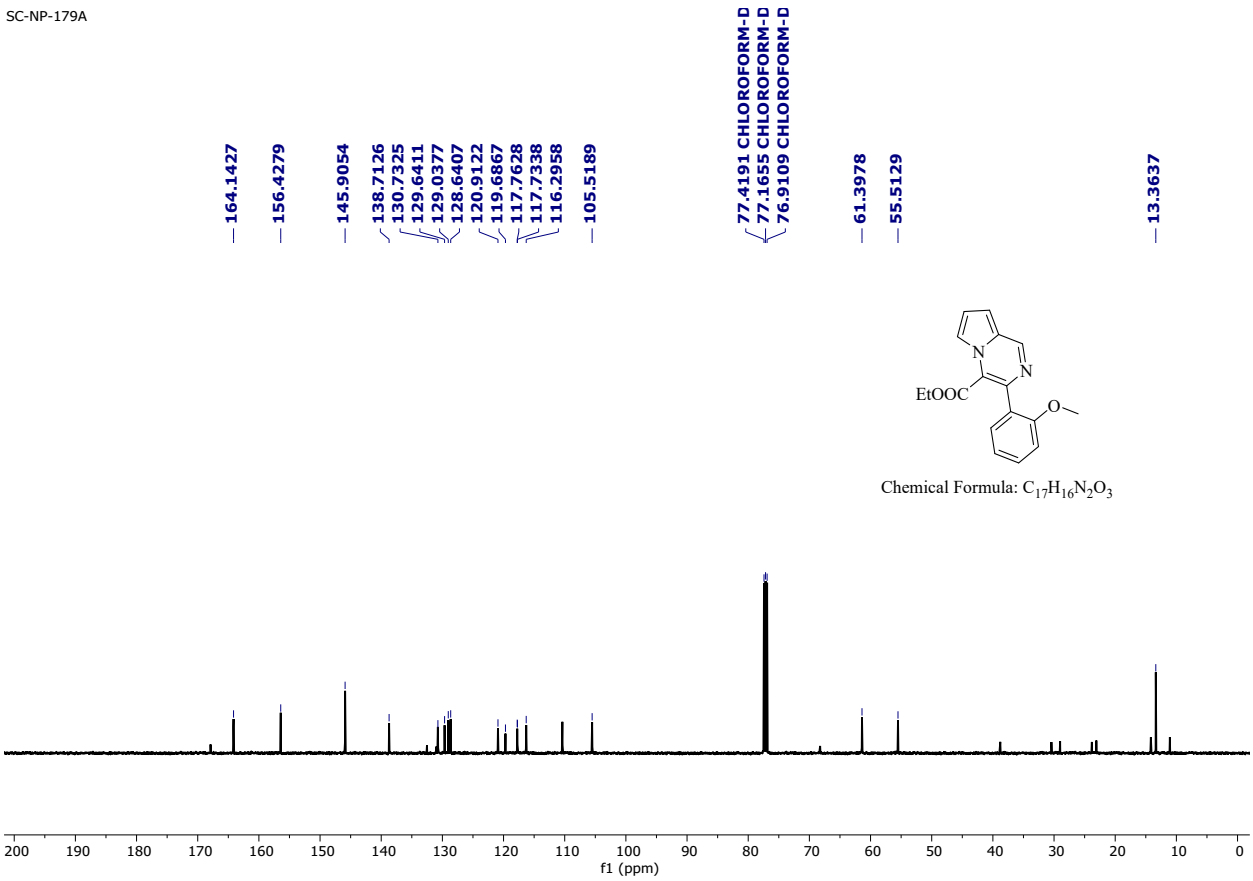


Figure S60: ^{13}C NMR spectra of ethyl 3-(2-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5l)**

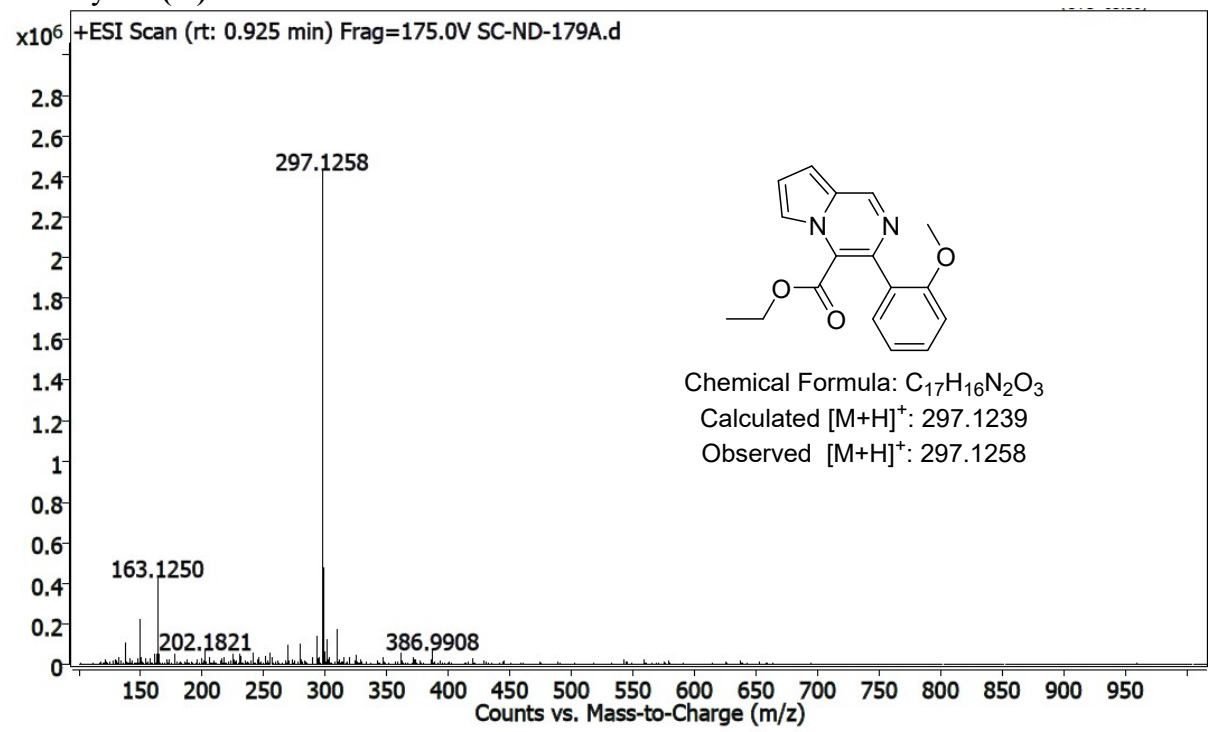


Figure S61: HRMS spectra of ethyl 3-(2-methoxyphenyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5l)**

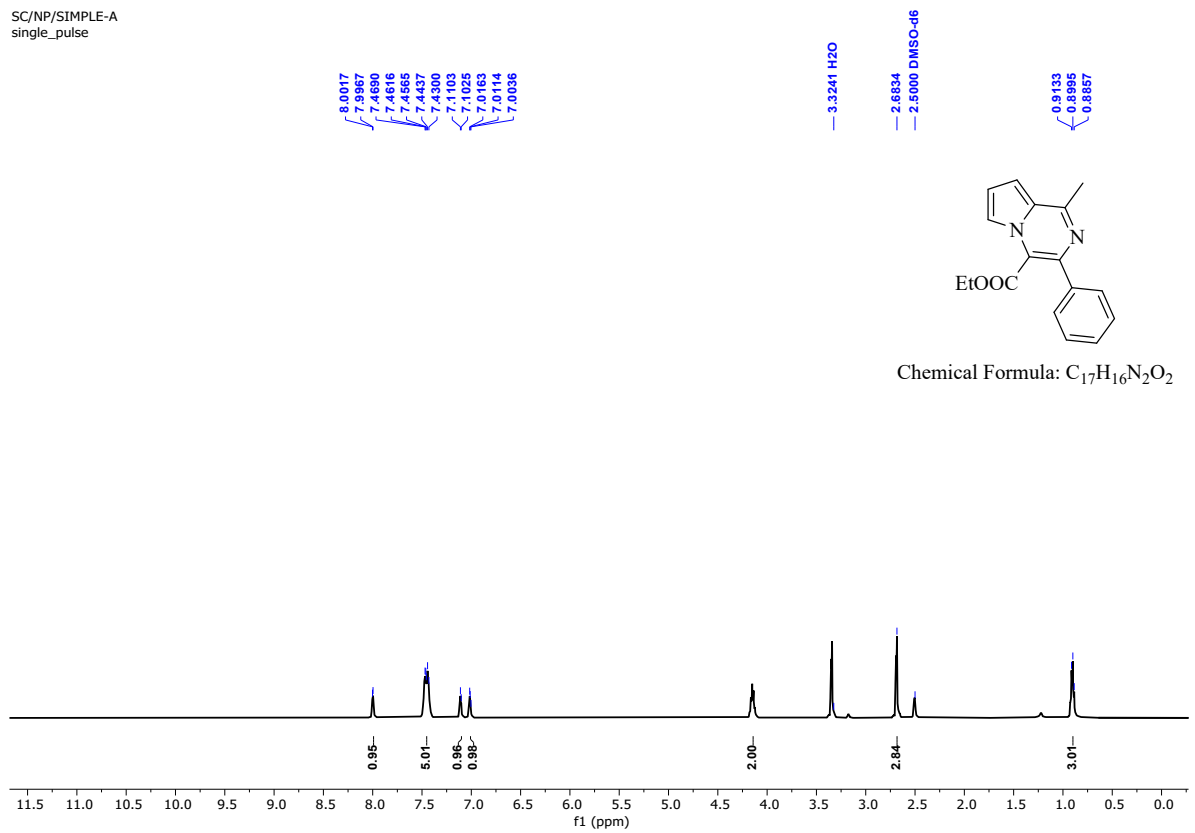


Figure S62: ^{1}H NMR spectra of ethyl 1-methyl-3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5m)**

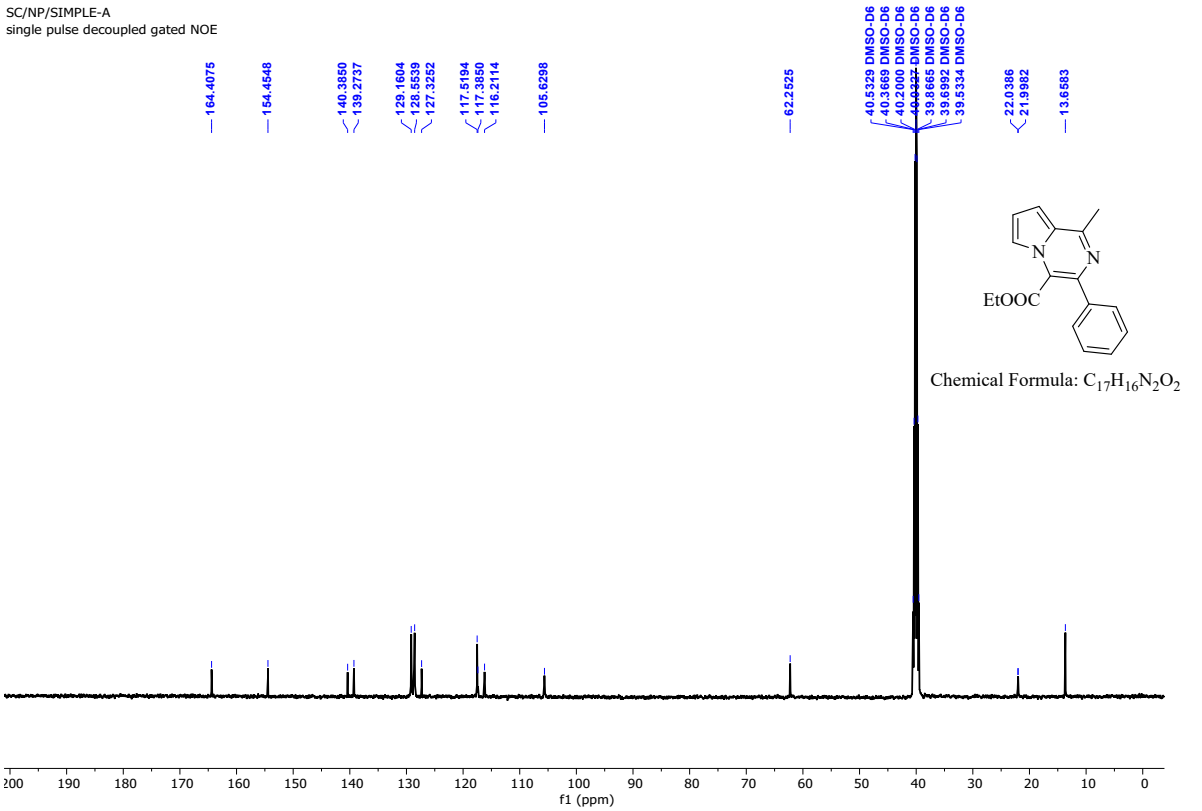


Figure S63: ^{13}C NMR spectra of ethyl 1-methyl-3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5m)**

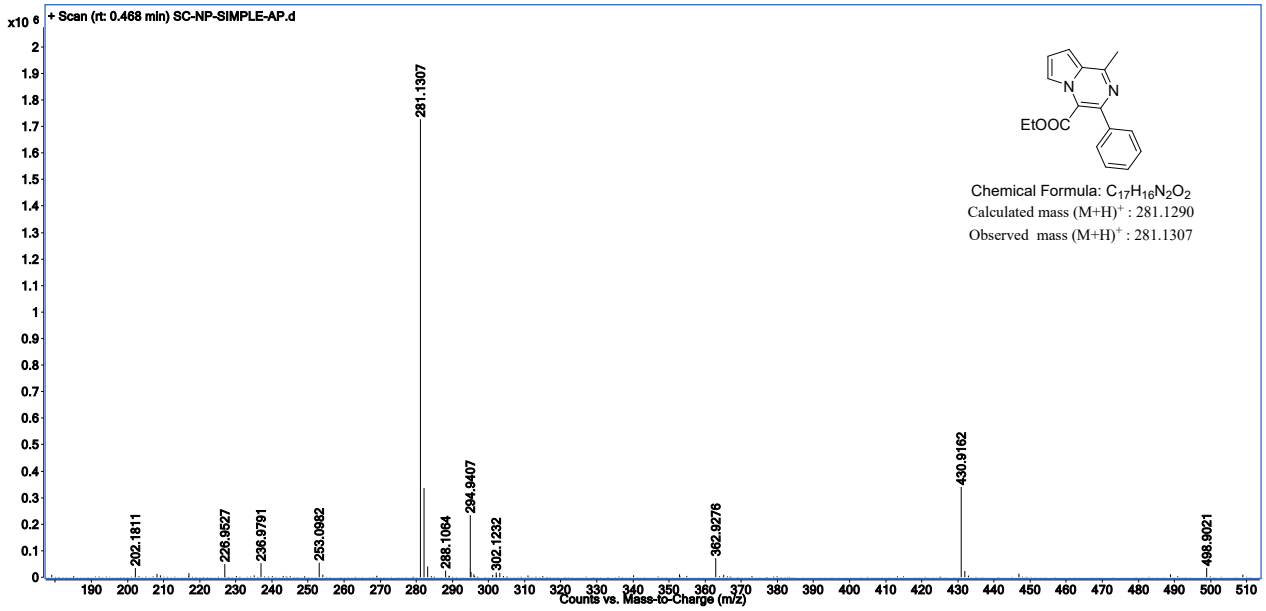


Figure S64: HRMS spectra of ethyl 1-methyl-3-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5m)**

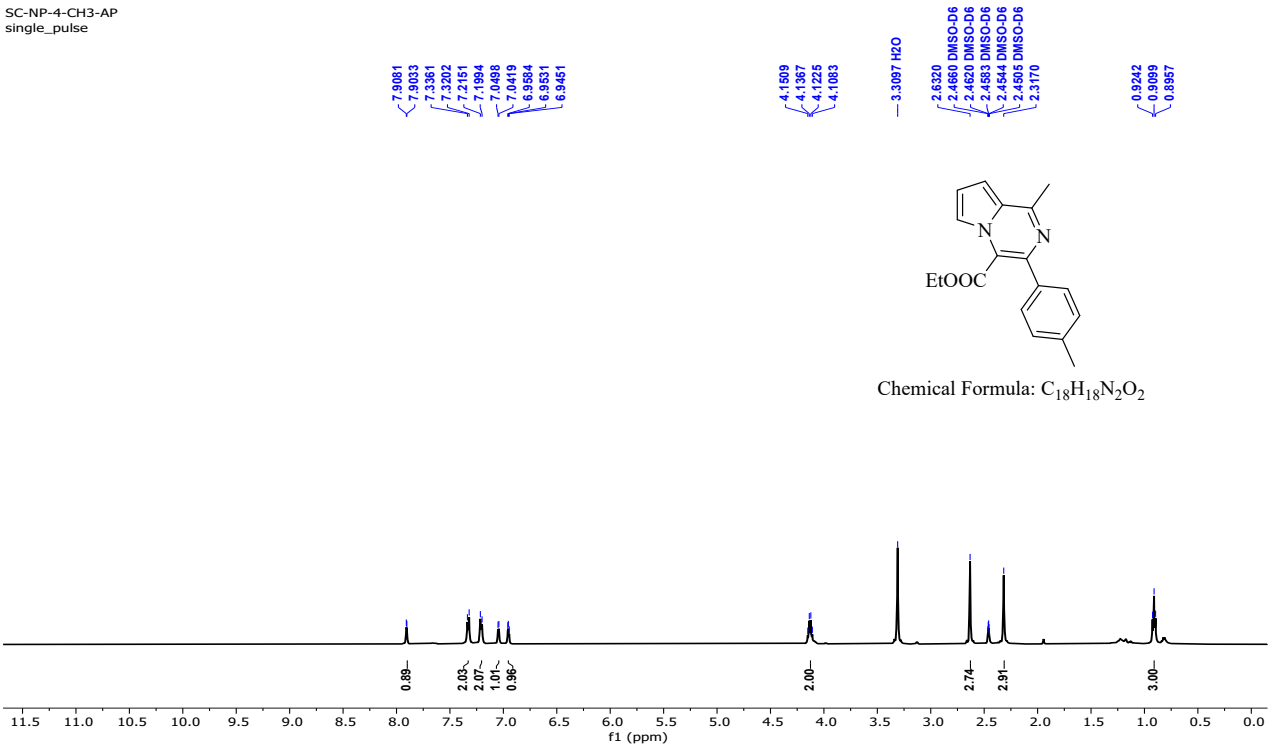


Figure S65: ^{1}H NMR spectra of ethyl 1-methyl-3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5n)**

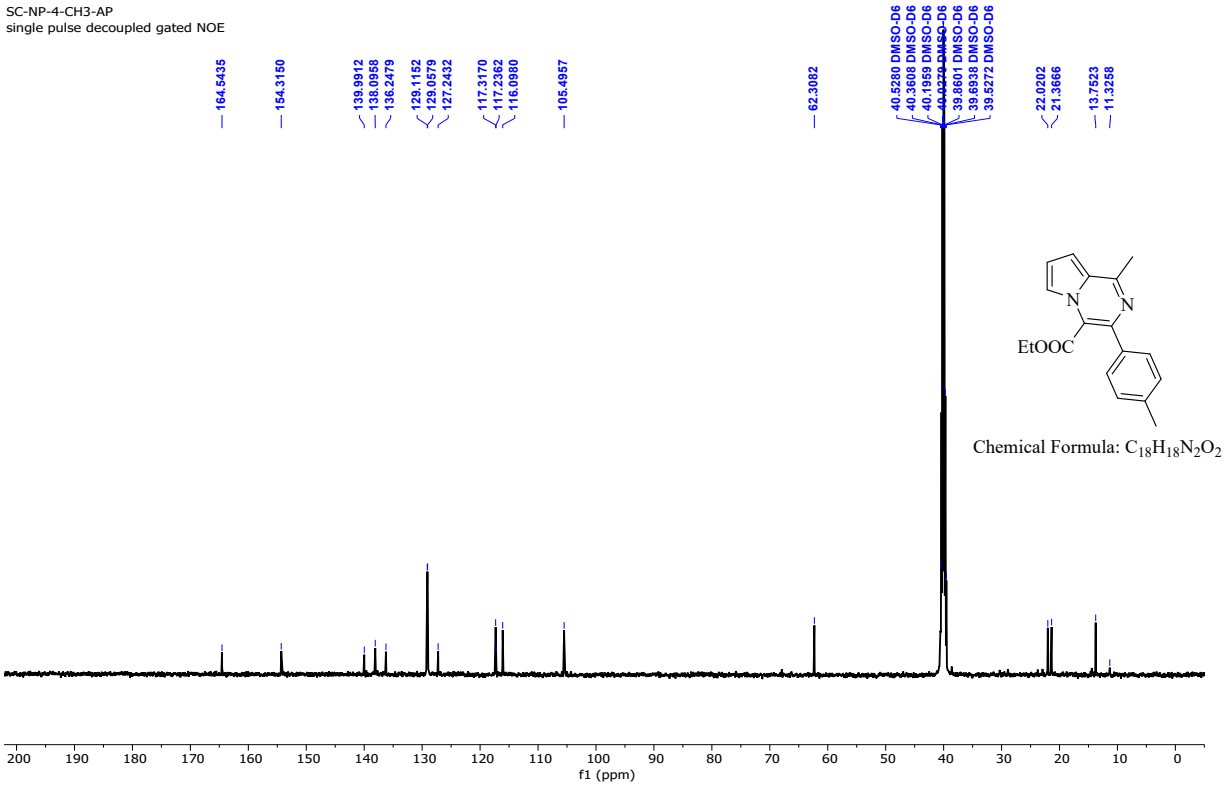


Figure S66: ^{13}C NMR spectra of ethyl 1-methyl-3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5n)**

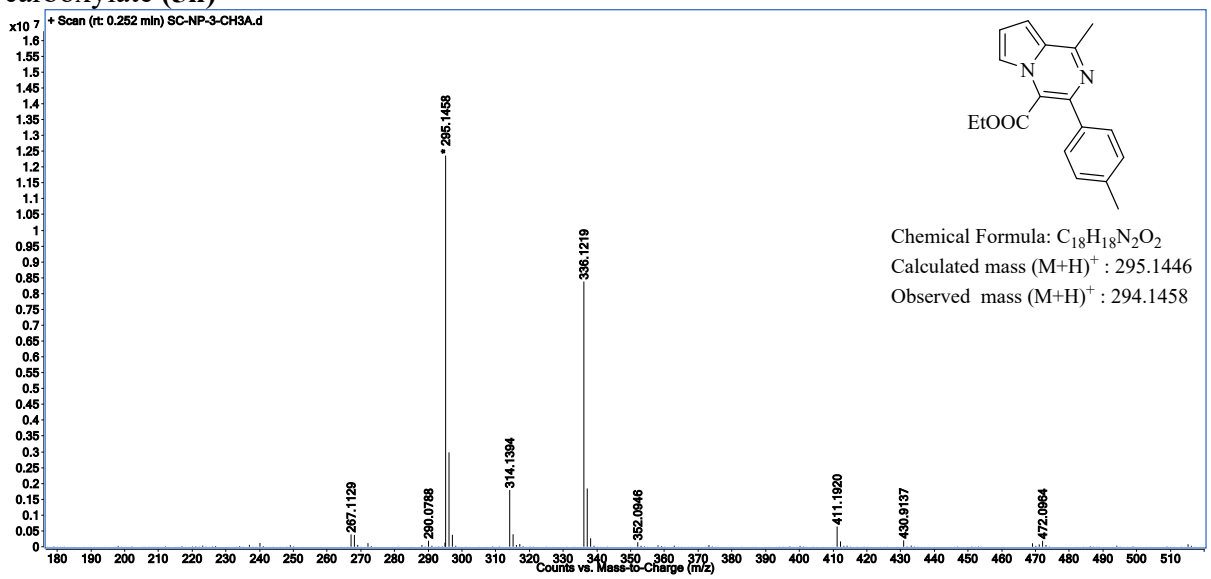


Figure S67: HRMS spectra of ethyl 1-methyl-3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5n)**

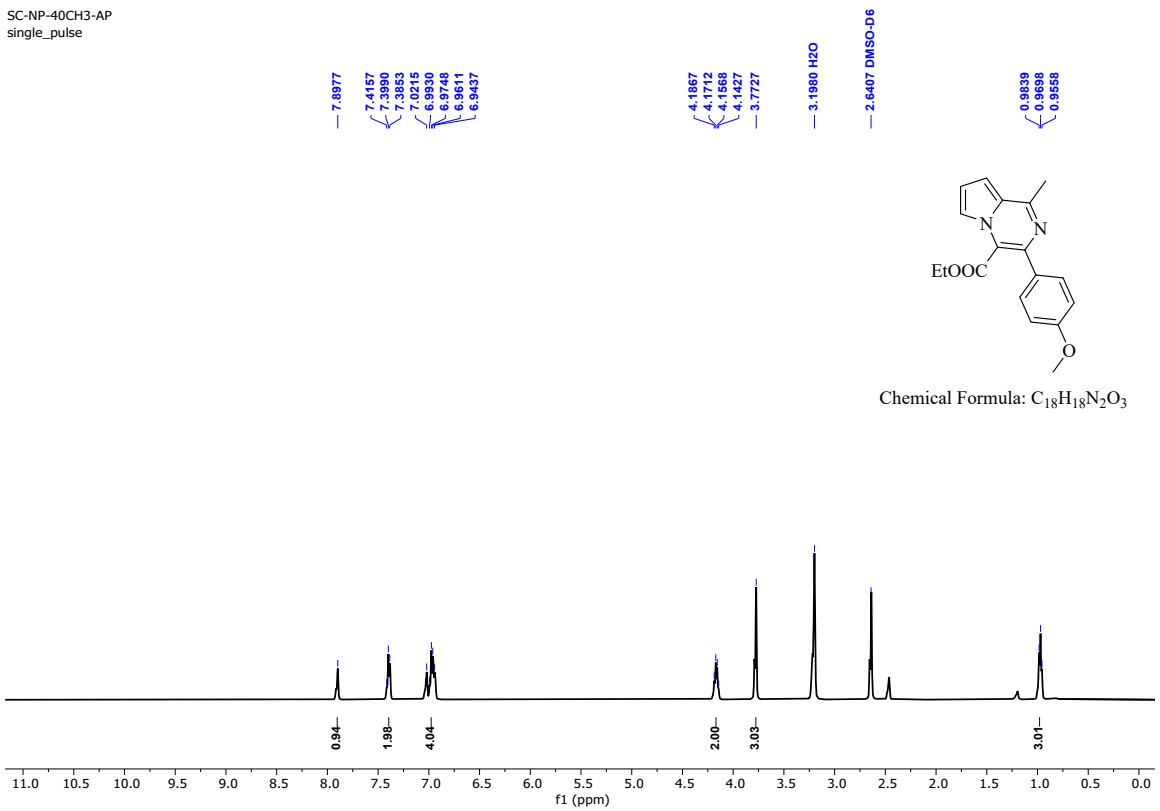


Figure S68: [1] H NMR spectra ethyl 3-(4-methoxyphenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5o)**

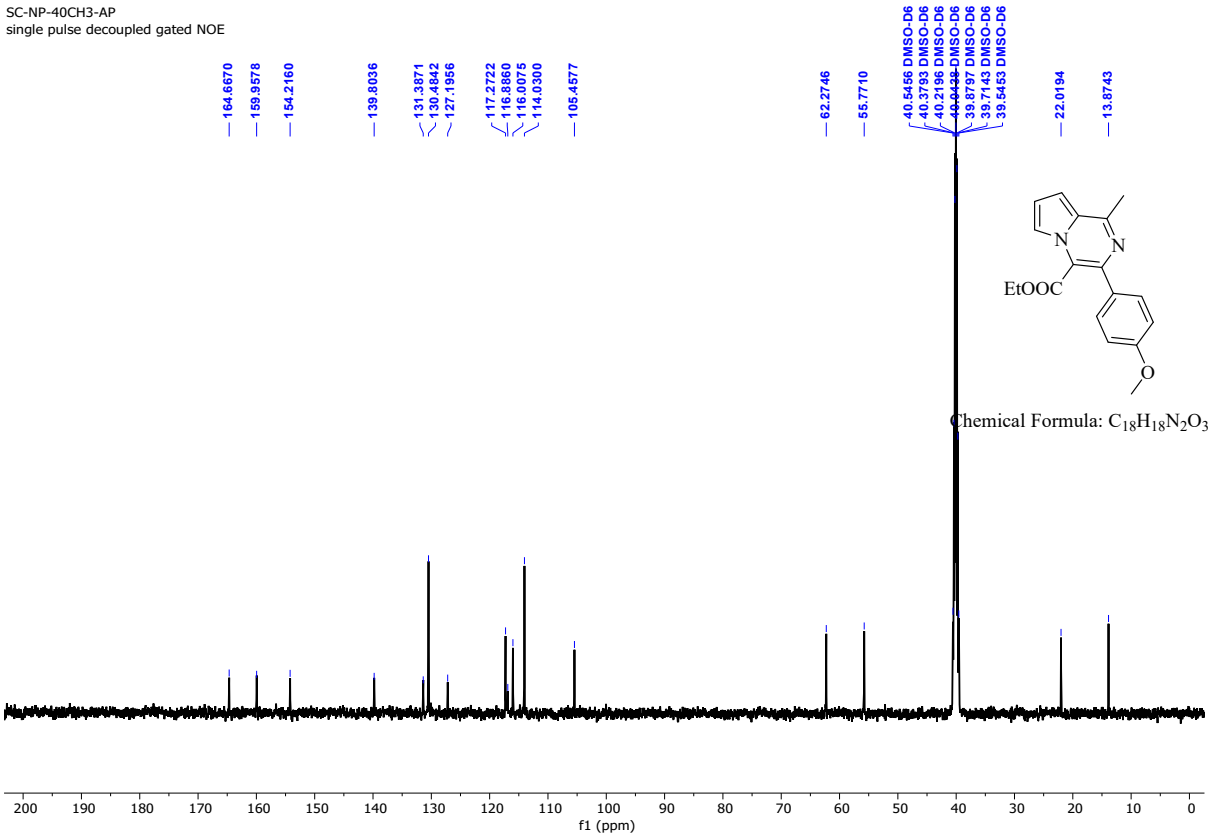


Figure S69: [13]C NMR spectra ethyl 3-(4-methoxyphenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5o)**

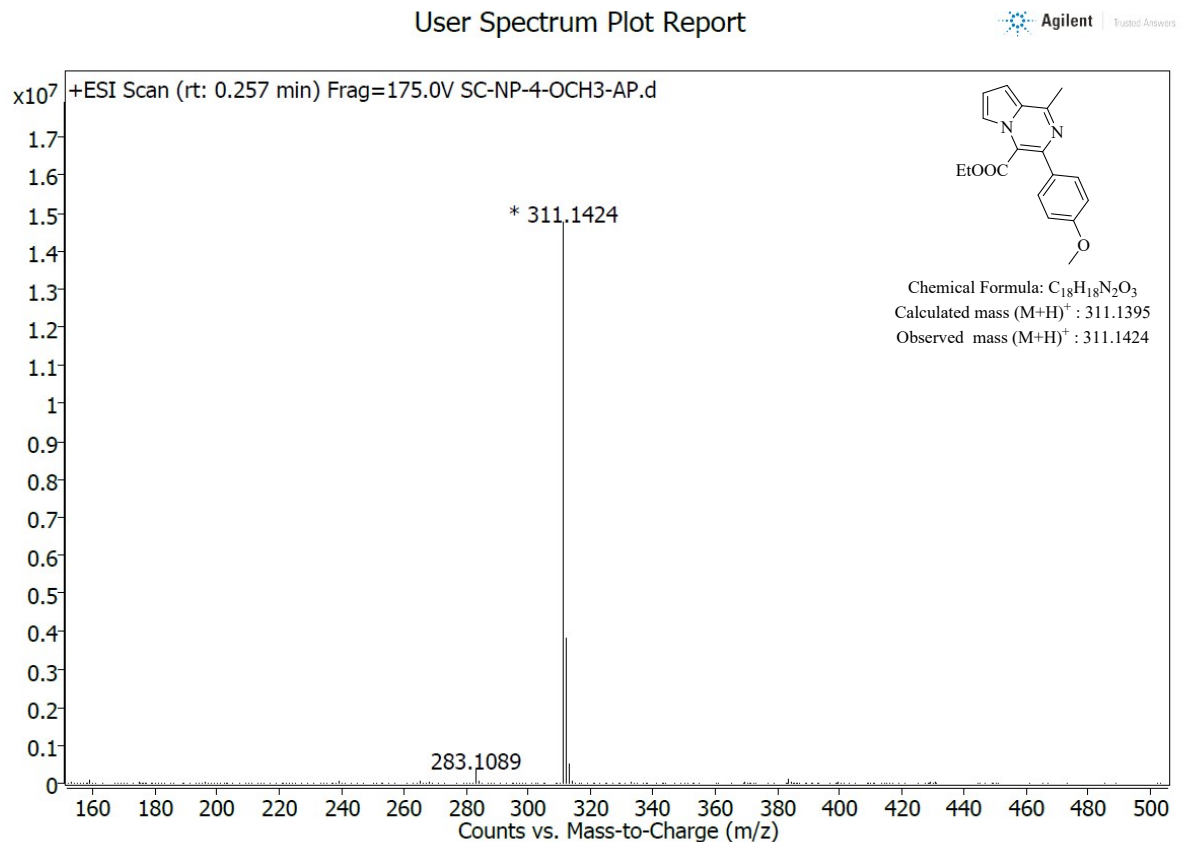


Figure S70: HRMS spectra ethyl 3-(4-methoxyphenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5o)**

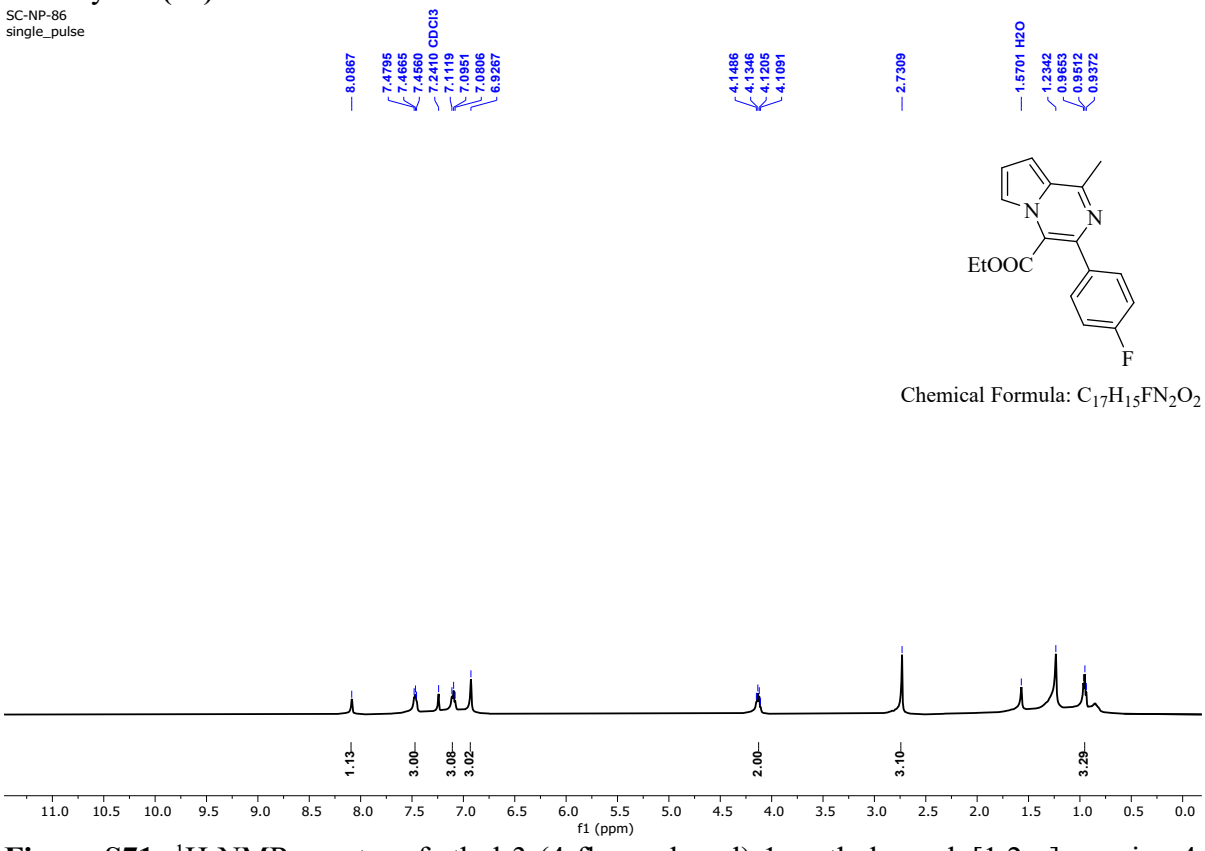


Figure S71: ^{1}H NMR spectra of ethyl-3-(4-fluorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5p)**

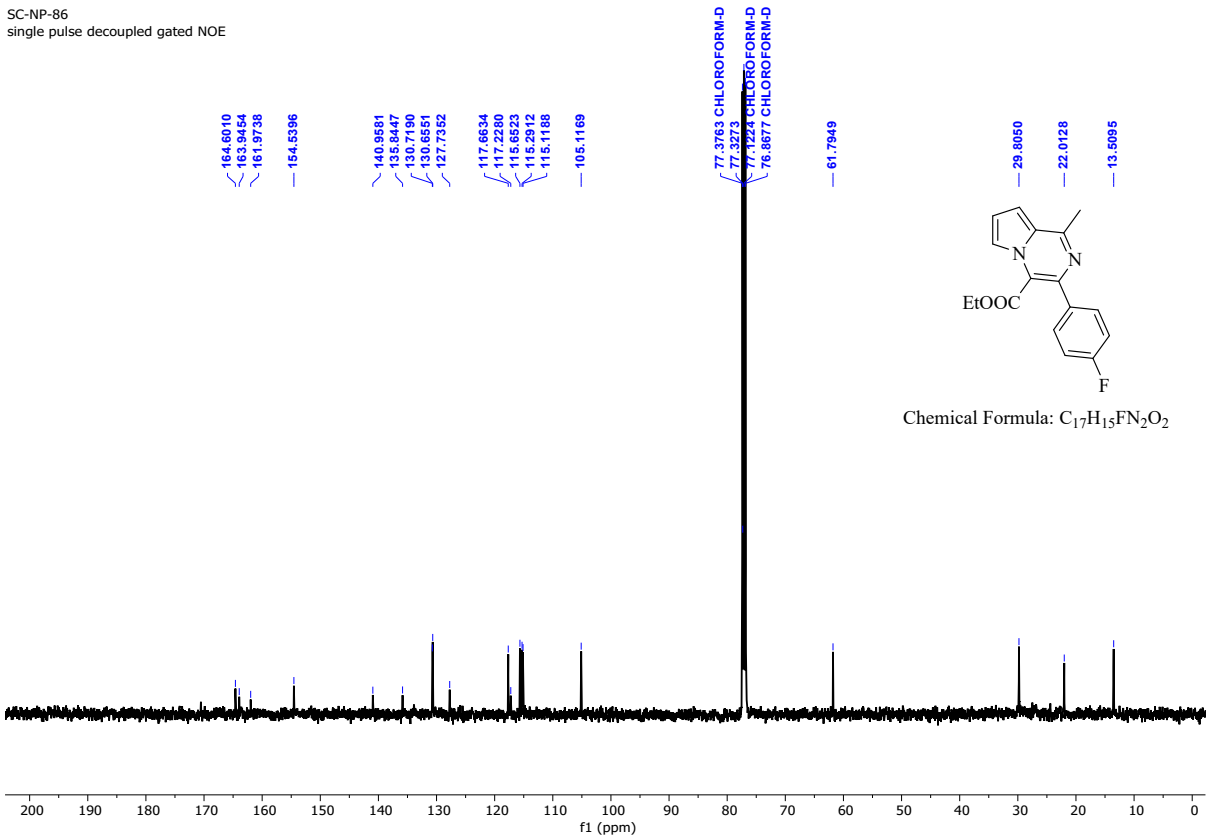


Figure S72: ^{13}C NMR spectra of ethyl-3-(4-fluorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5p)**

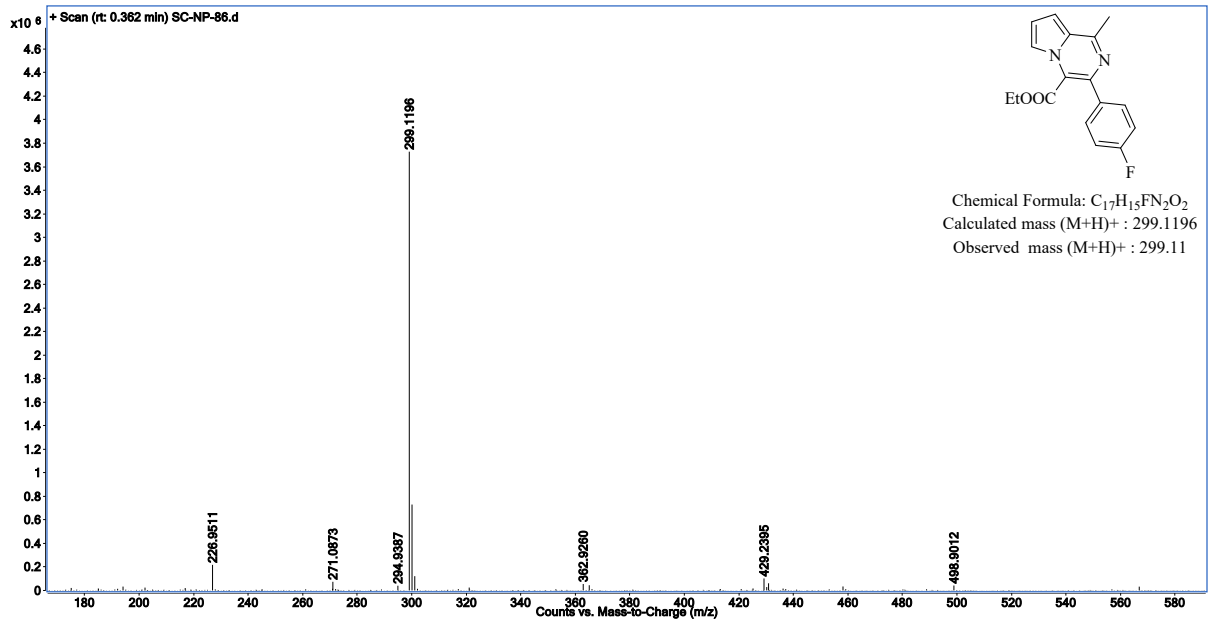


Figure S73: HRMS spectra of ethyl-3-(4-fluorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5p)**

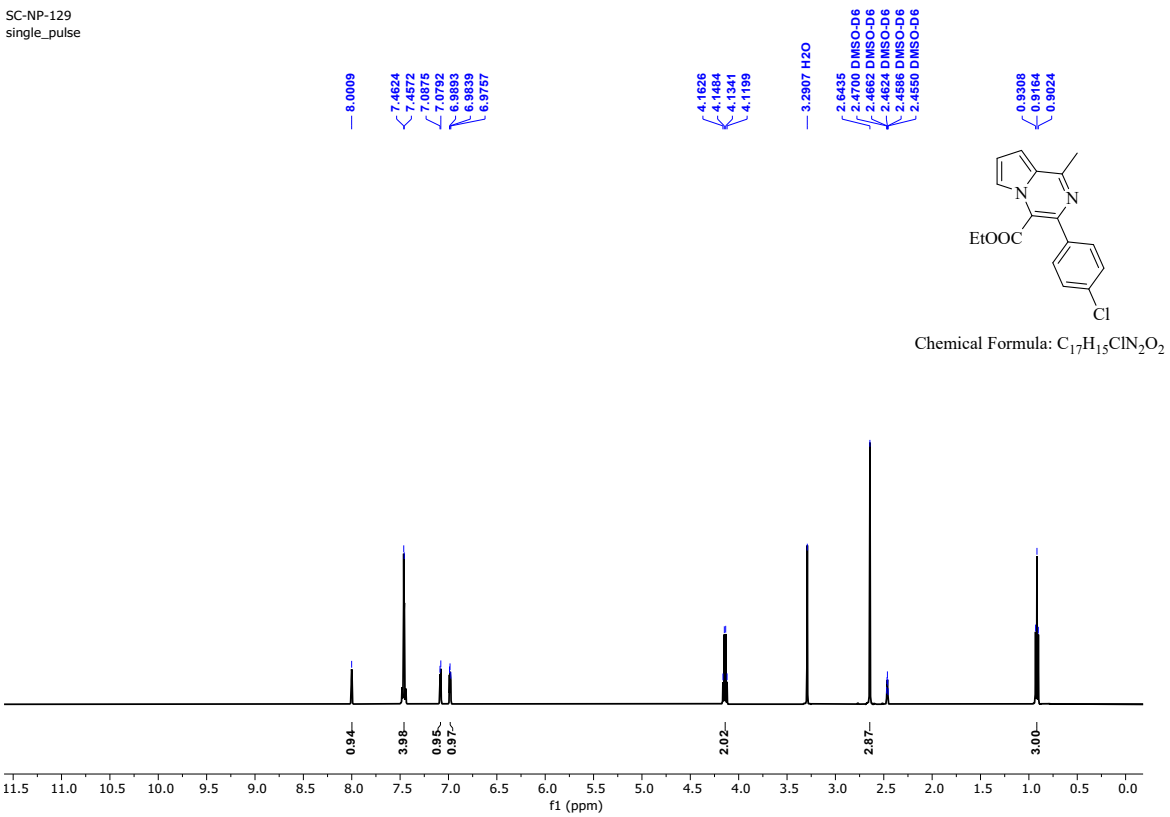


Figure S74: ^{1}H NMR spectra of ethyl 3-(4-chlorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5q)**

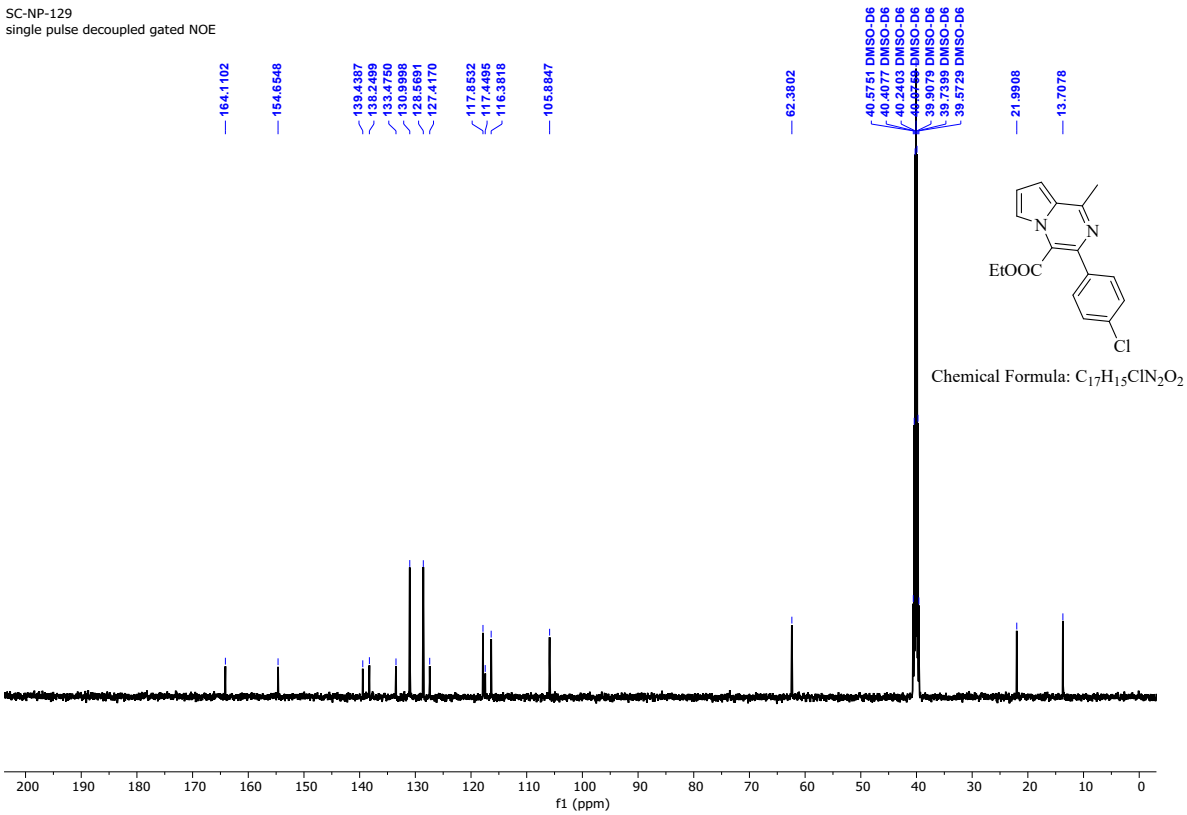


Figure S75: ^{13}C NMR spectra of ethyl 3-(4-chlorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5q)**

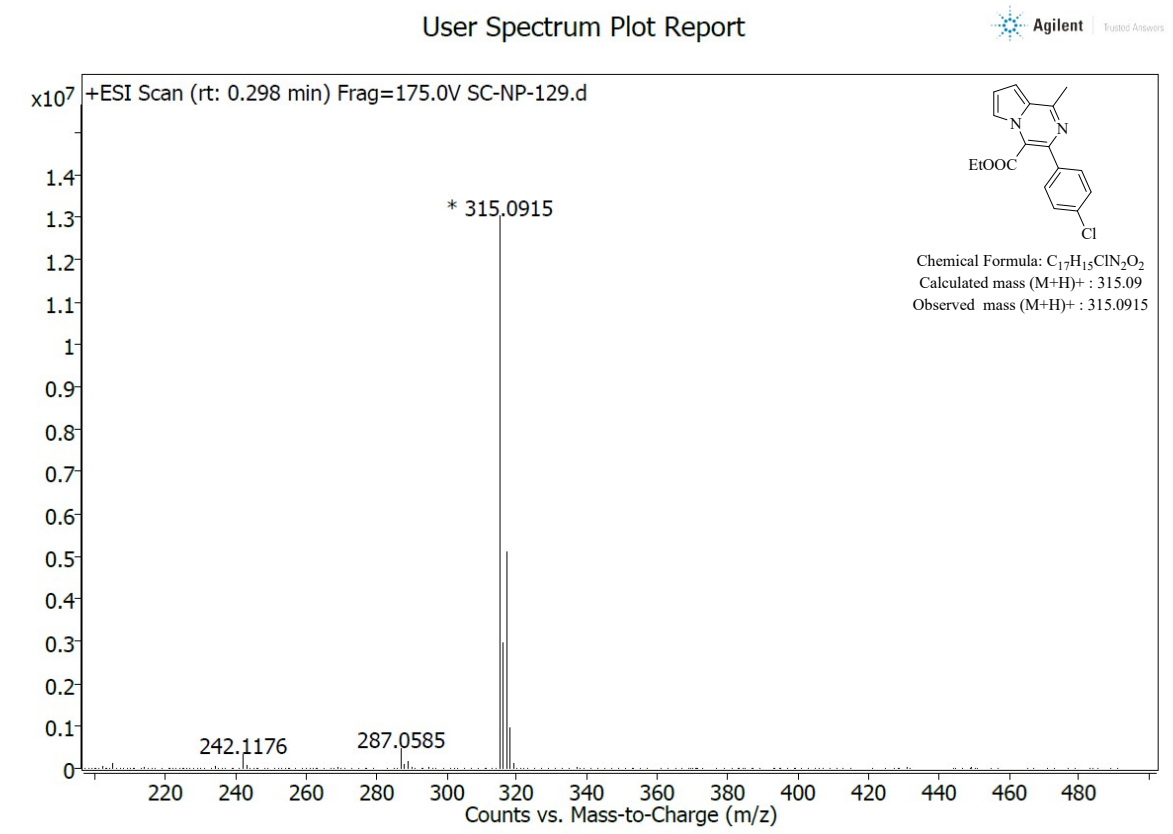


Figure S76: HRMS Spectra of ethyl 3-(4-chlorophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5q)**

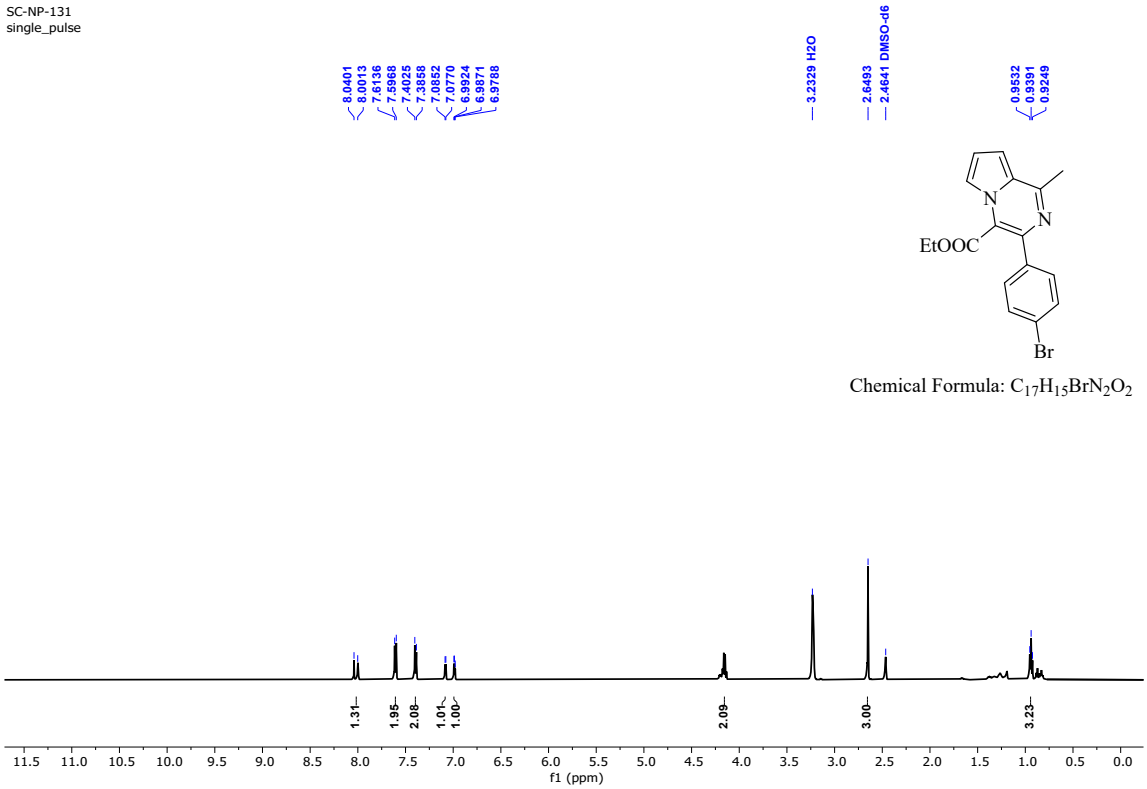


Figure S77: [1]H NMR spectra of ethyl 3-(4-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5r)**

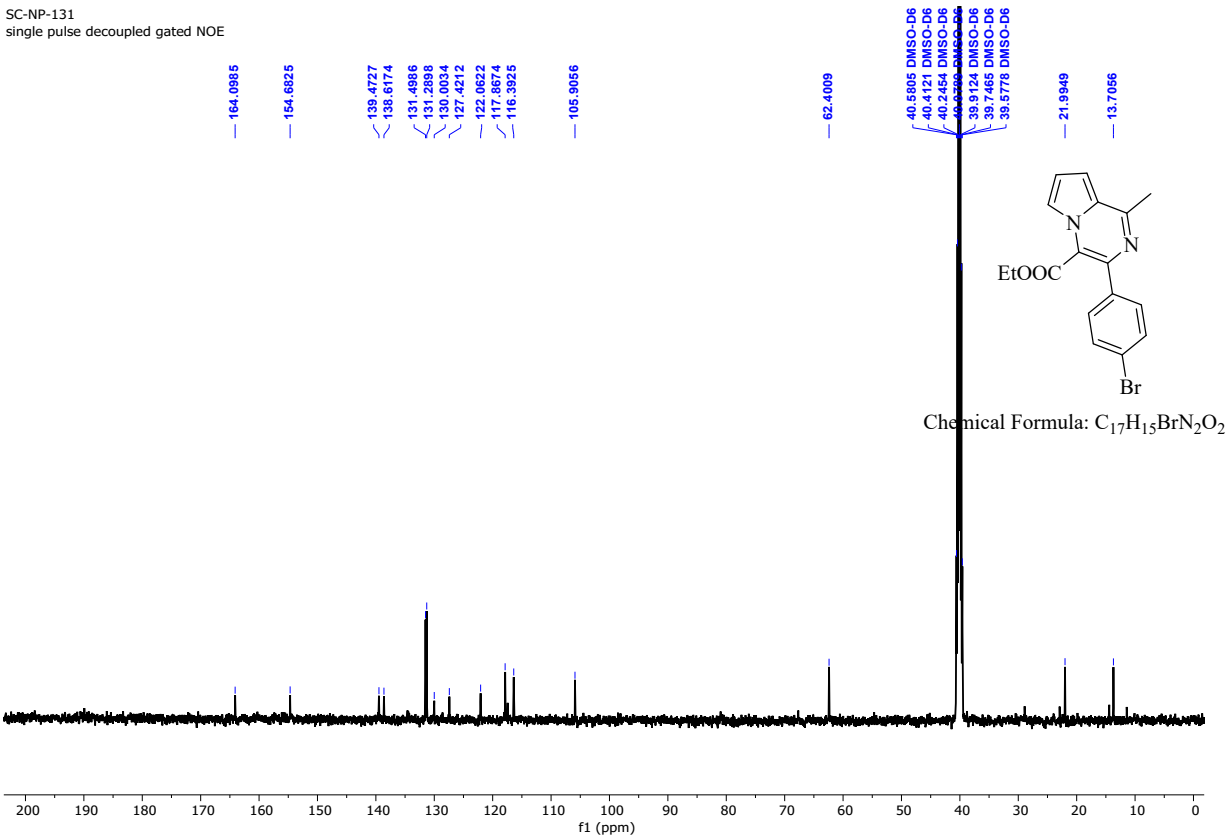


Figure S78: ^{13}C NMR spectra of ethyl 3-(4-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5r)**

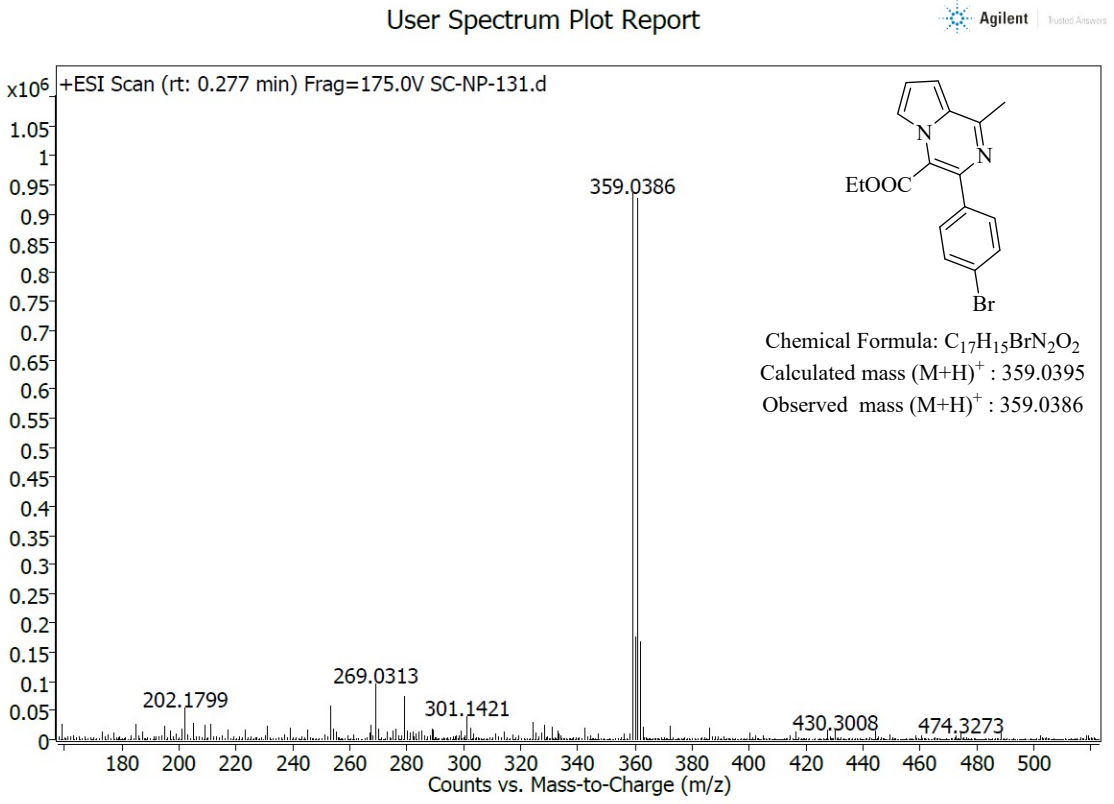


Figure S79: HRMS spectra of ethyl 3-(4-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5r)**

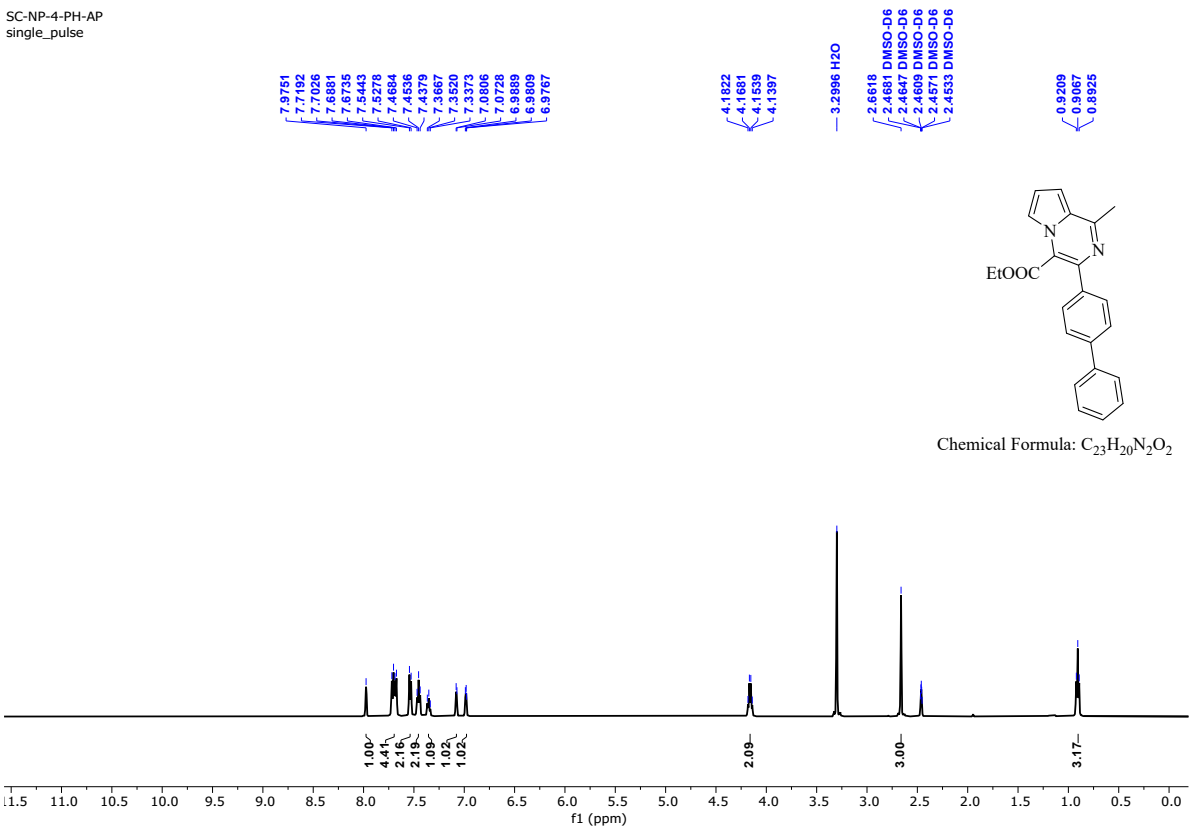


Figure S80: ^{1}H NMR spectra of ethyl 3-([1,1'-biphenyl]-4-yl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5s)**

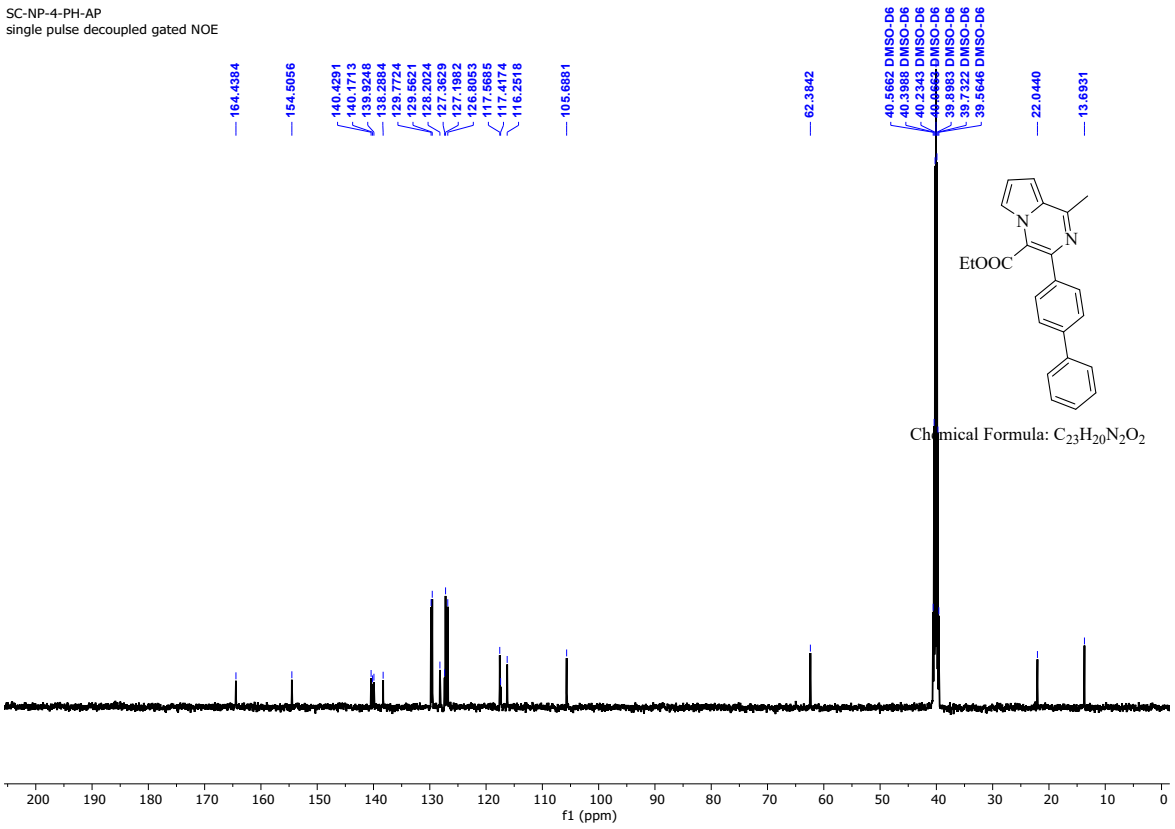


Figure S81: ^{13}C NMR spectra of ethyl 3-([1,1'-biphenyl]-4-yl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5s)**

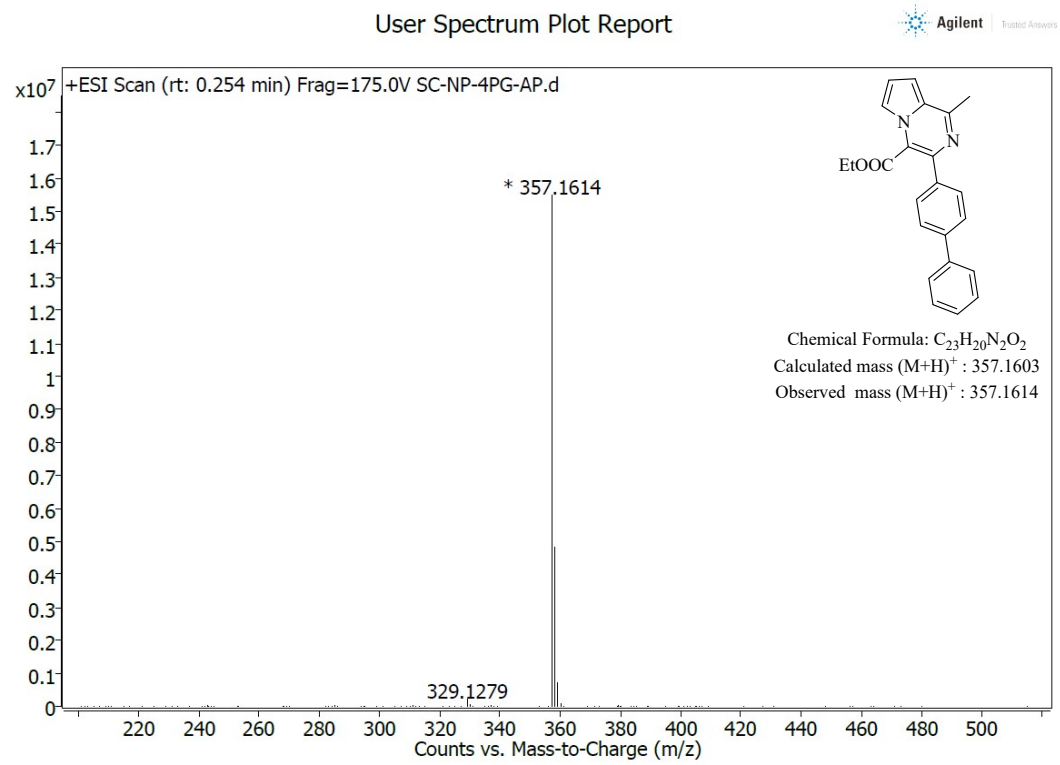


Figure S82: HRMS spectra of ethyl 3-([1,1'-biphenyl]-4-yl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5s)**

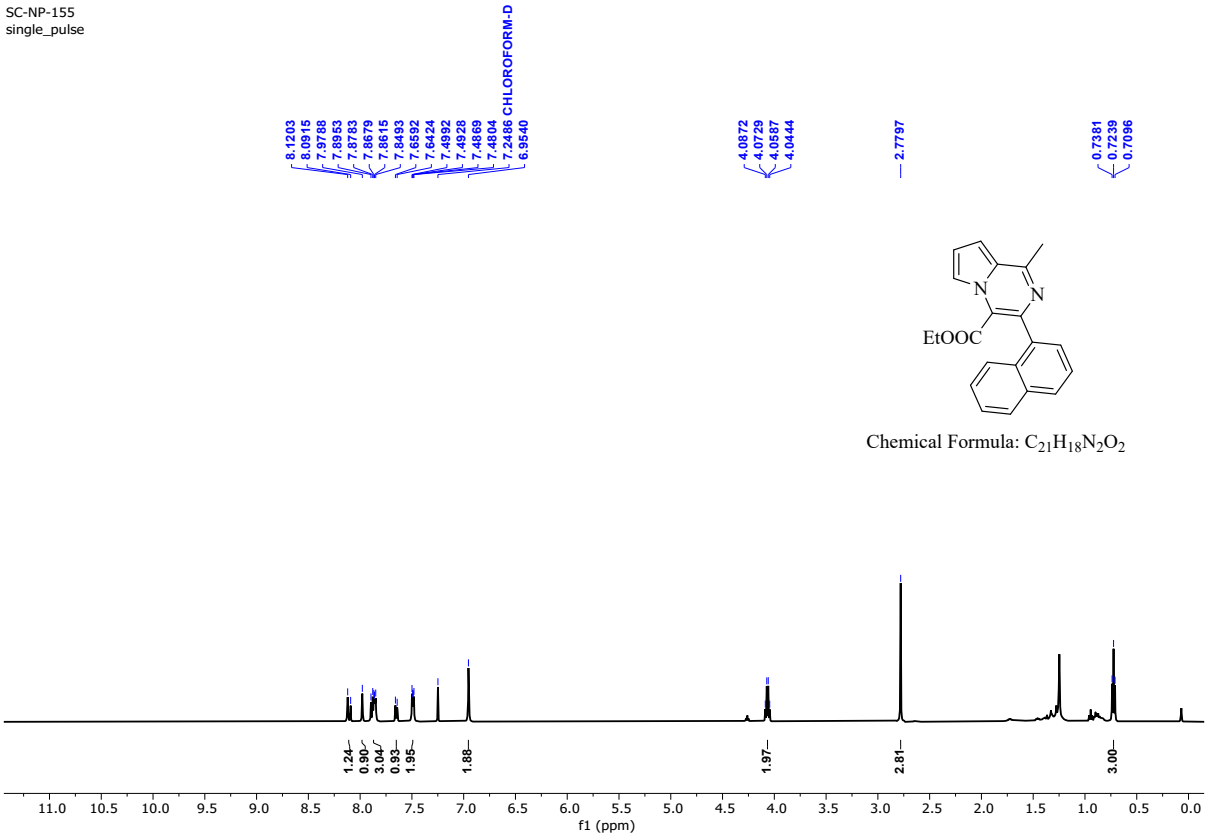


Figure S83: ^{1}H NMR spectra of ethyl 1-methyl-3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5t)**

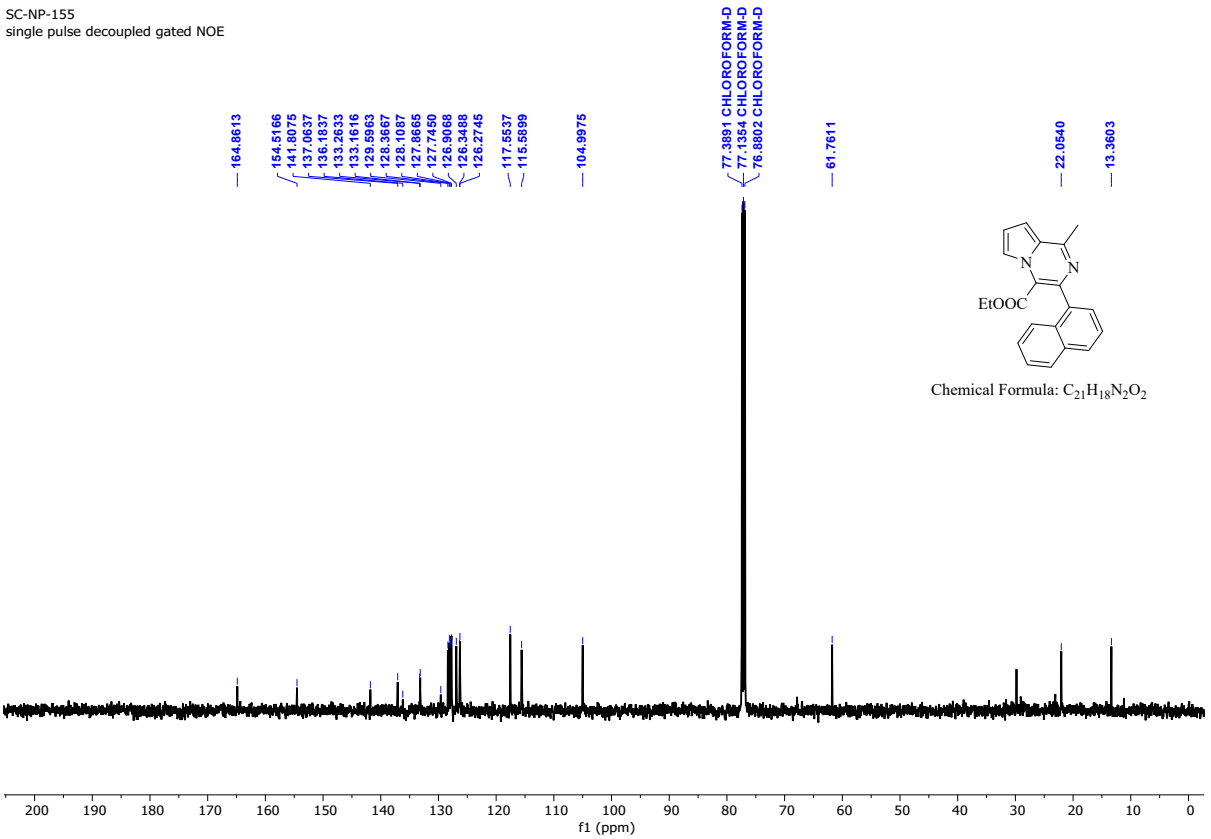


Figure S84: ^{13}C NMR spectra of ethyl 1-methyl-3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5t)**

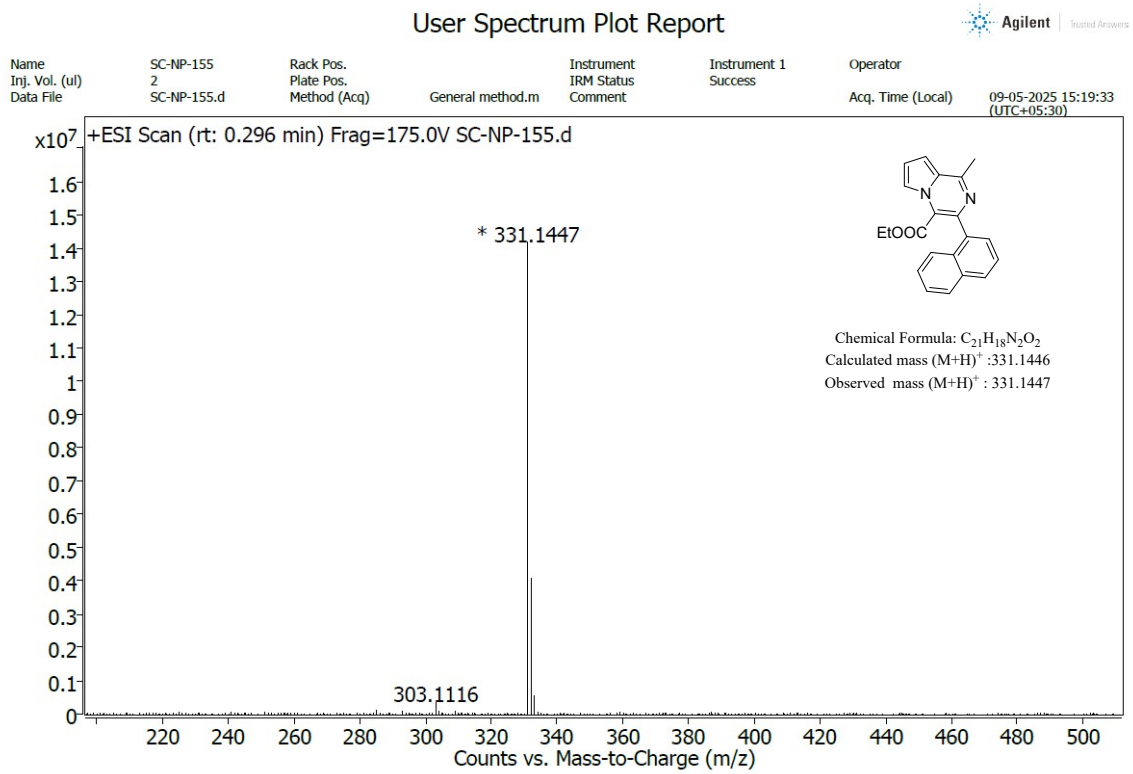


Figure S85: HRMS spectra of ethyl 1-methyl-3-(naphthalen-1-yl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5t)**

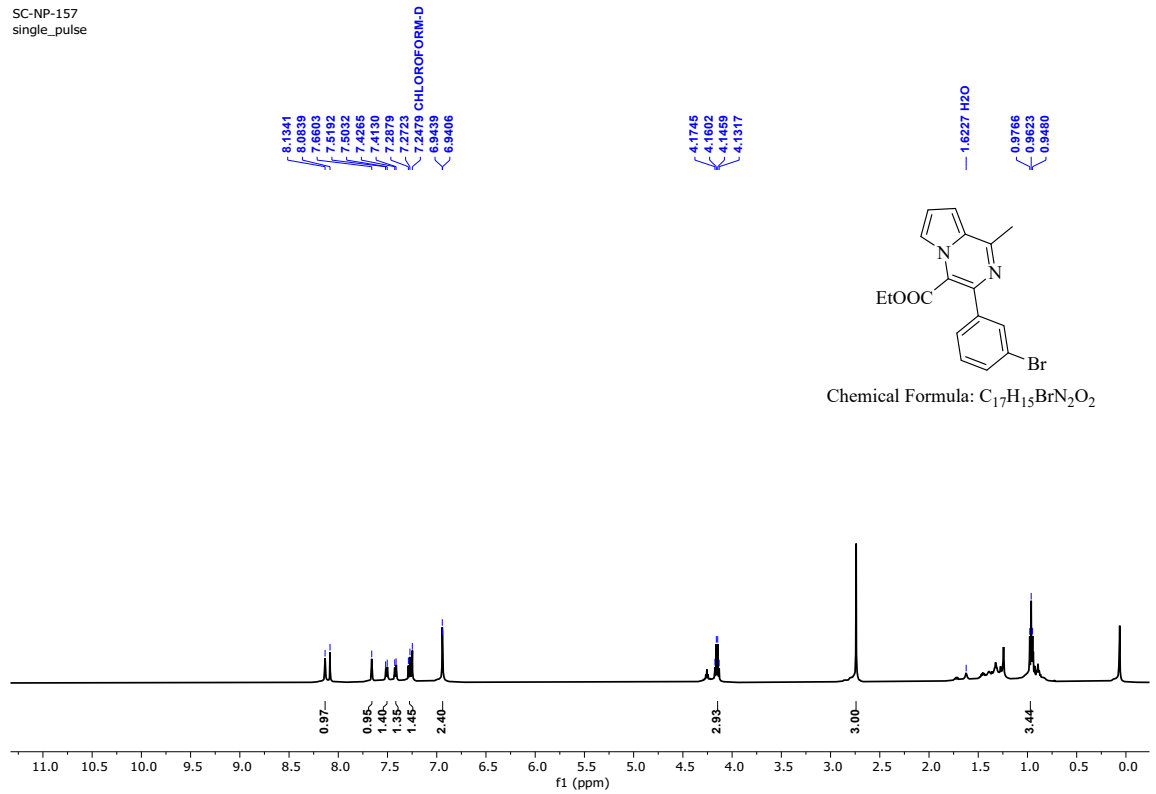


Figure S86: ^{1}H NMR spectra of ethyl 3-(3-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5u)**

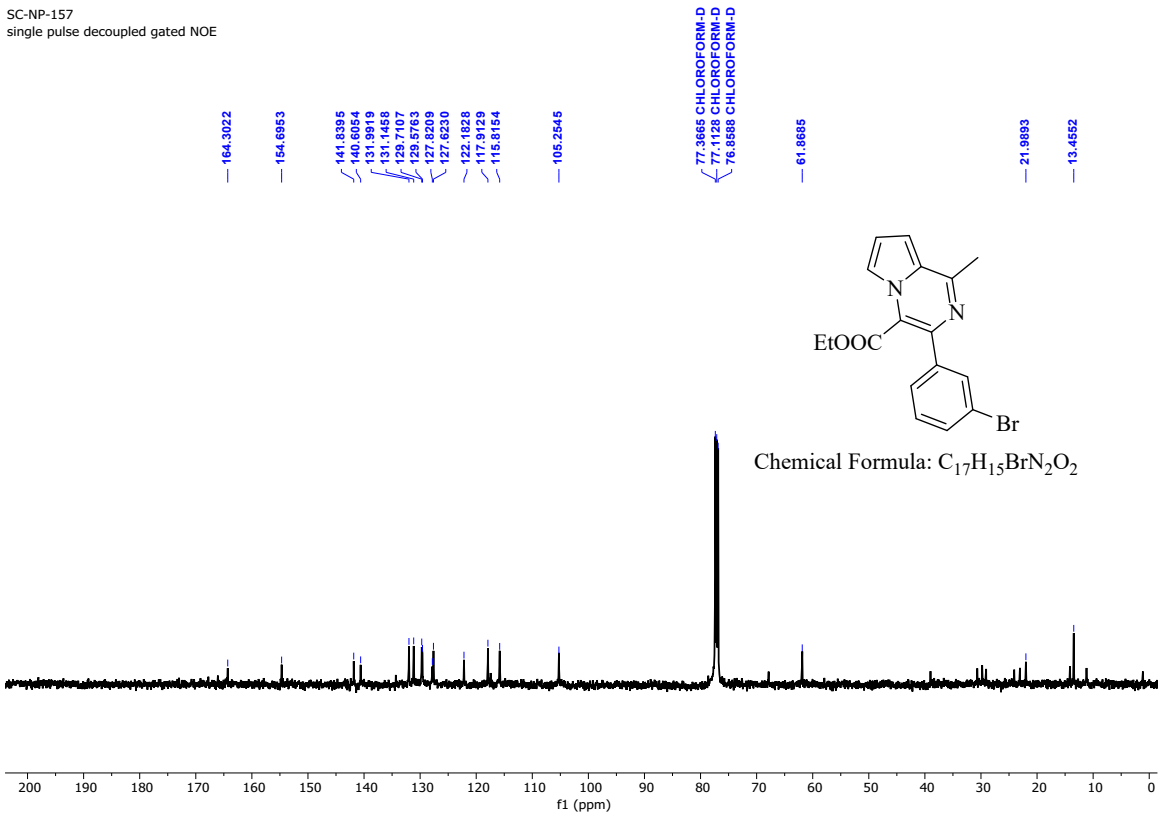


Figure S87: ^{13}C NMR spectra of ethyl 3-(3-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5u)**

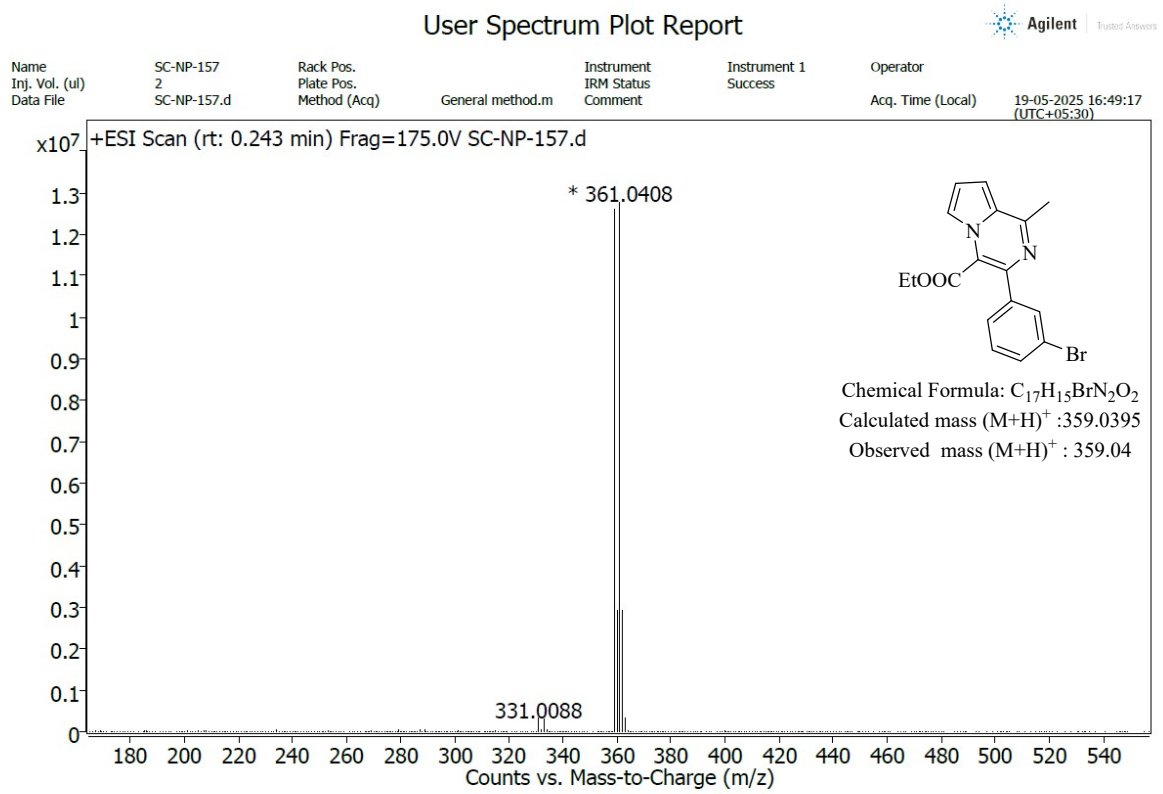


Figure S88: HRMS spectra of ethyl 3-(3-bromophenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5u)**

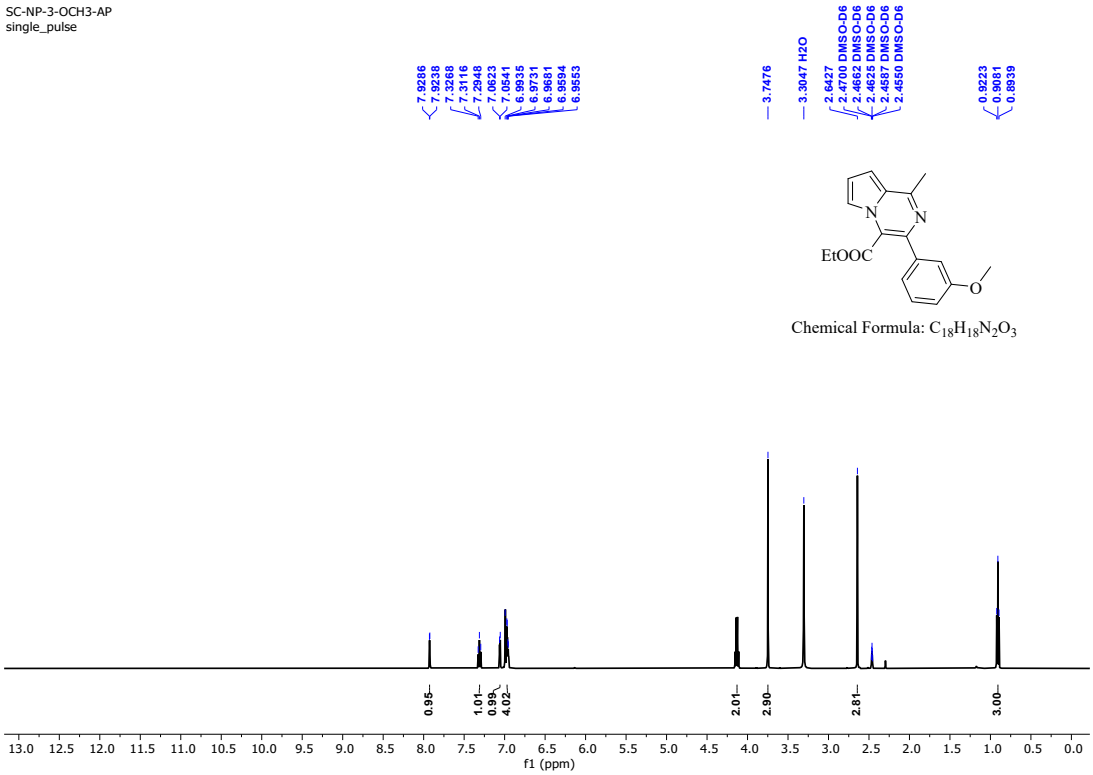


Figure S89: [1]H NMR spectra of ethyl 3-(3-methoxyphenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5v)**

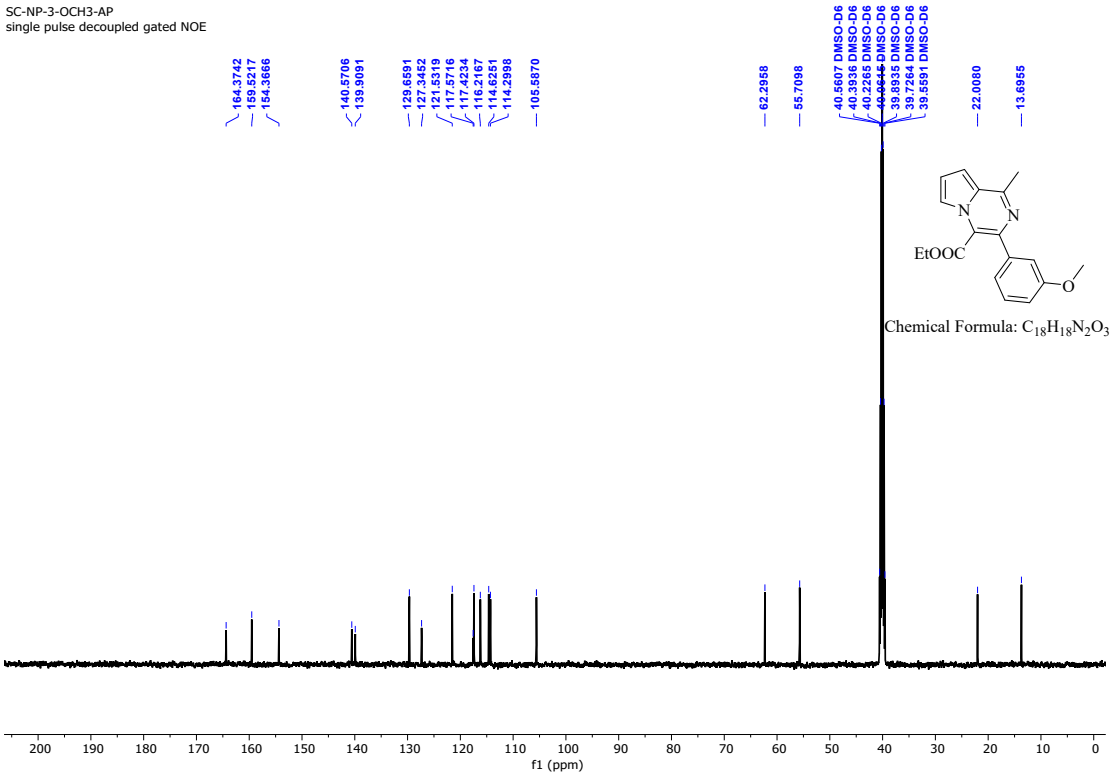


Figure S90: ^{13}C NMR spectra of ethyl 3-(3-methoxyphenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5v)**

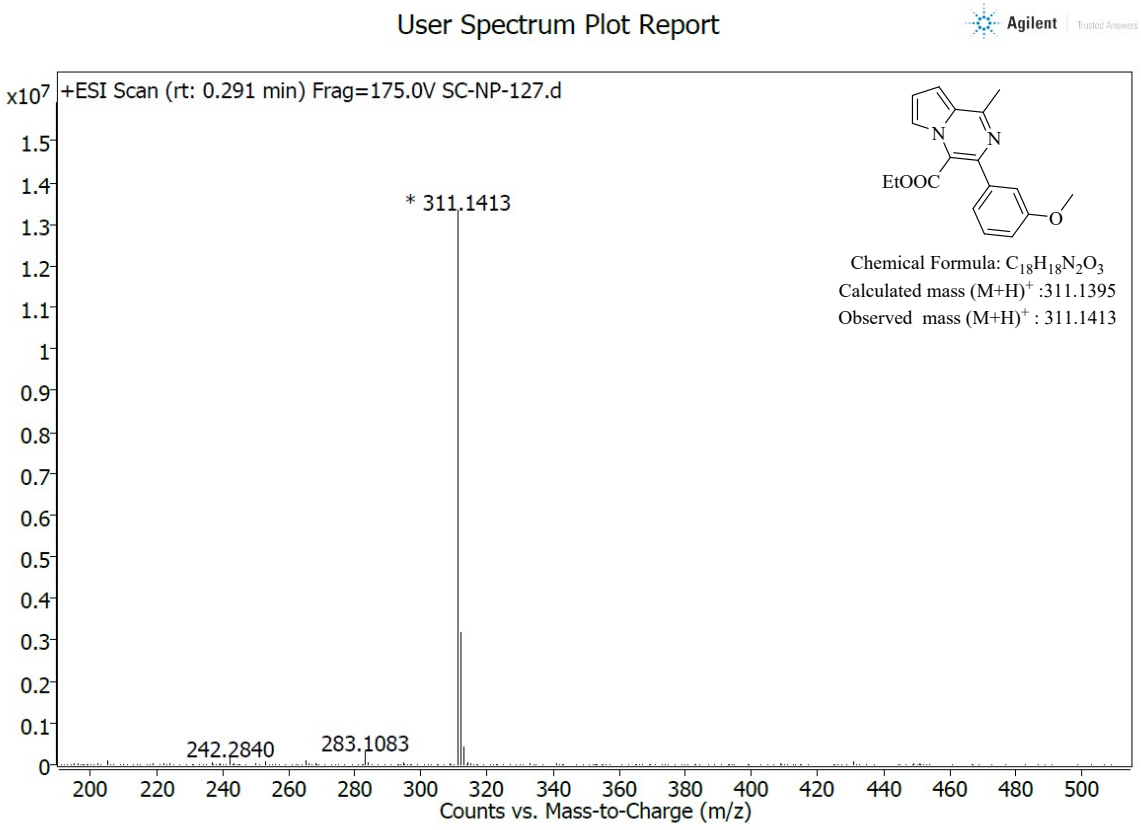


Figure S91: HRMS spectra of ethyl 3-(3-methoxyphenyl)-1-methylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5v)**

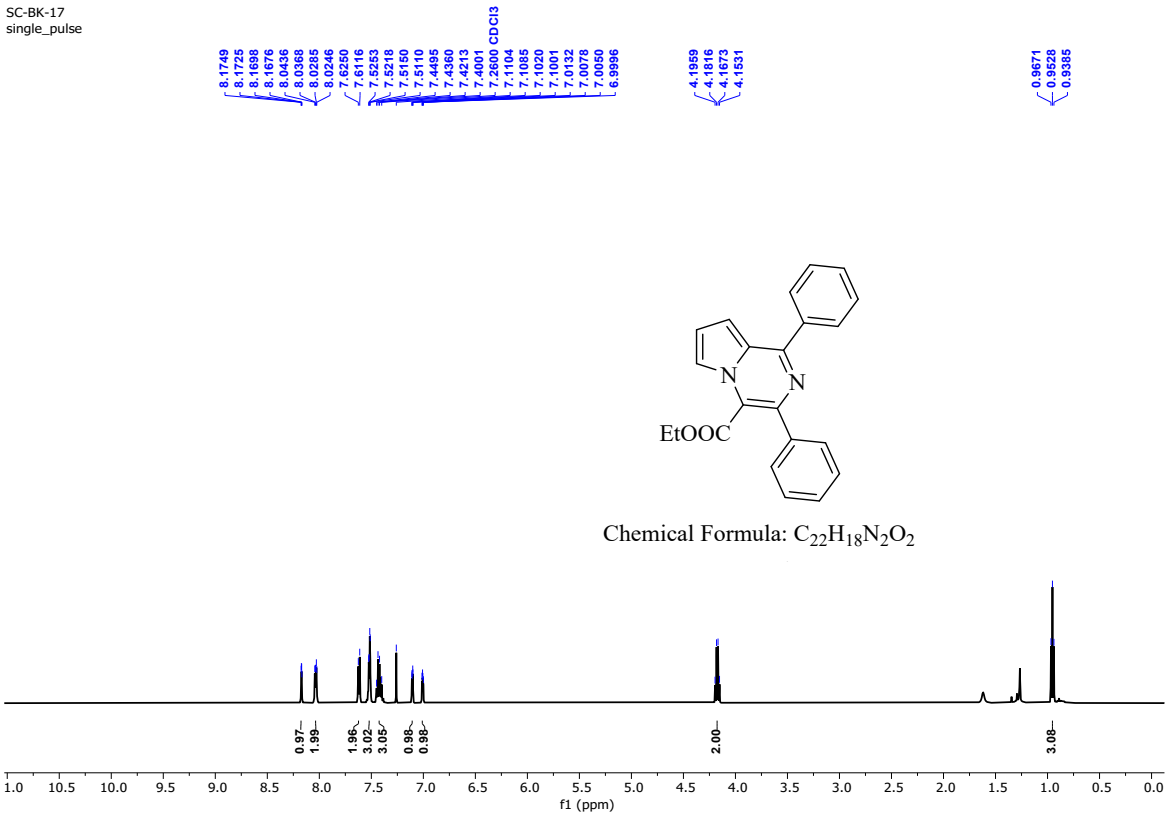


Figure S92: ^{1}H NMR spectra of ethyl 1,3-diphenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5w)**

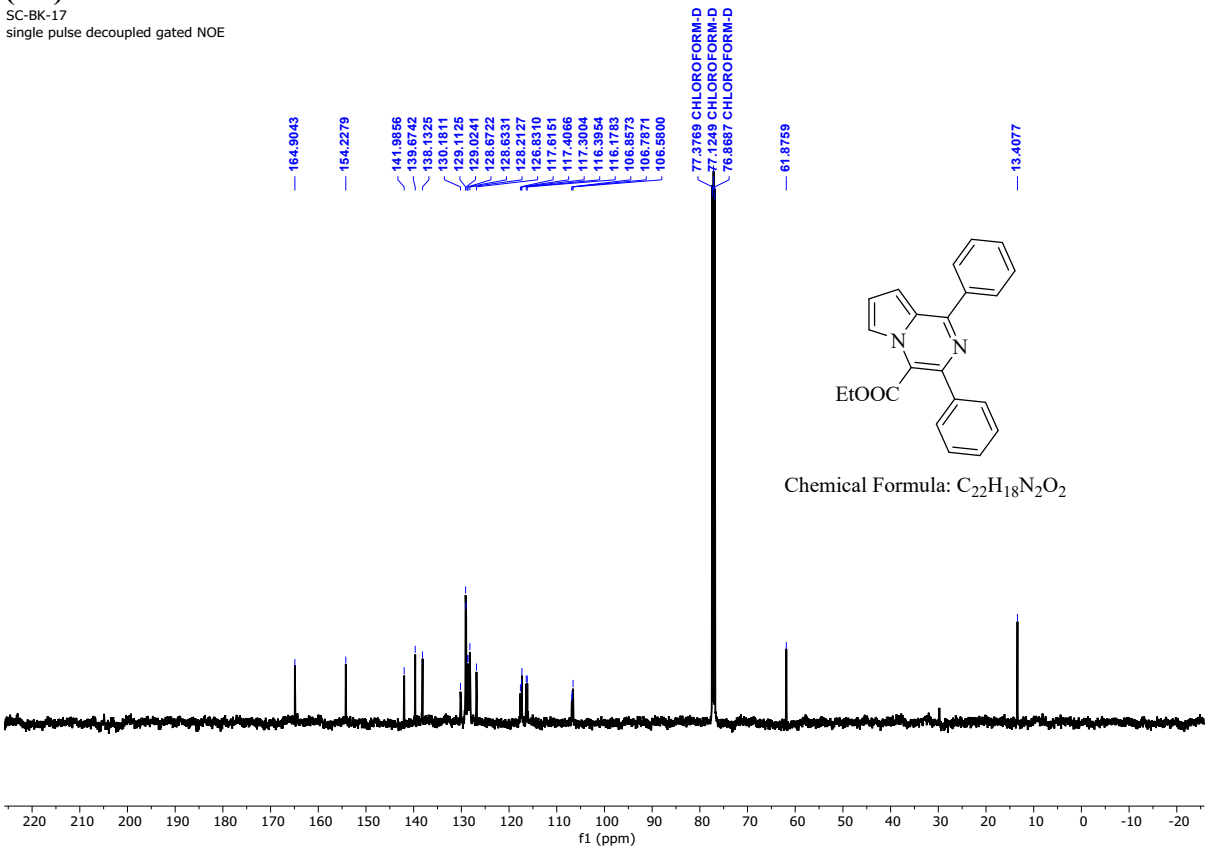


Figure S93: ^{13}C NMR spectra of ethyl 1,3-diphenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5w)**

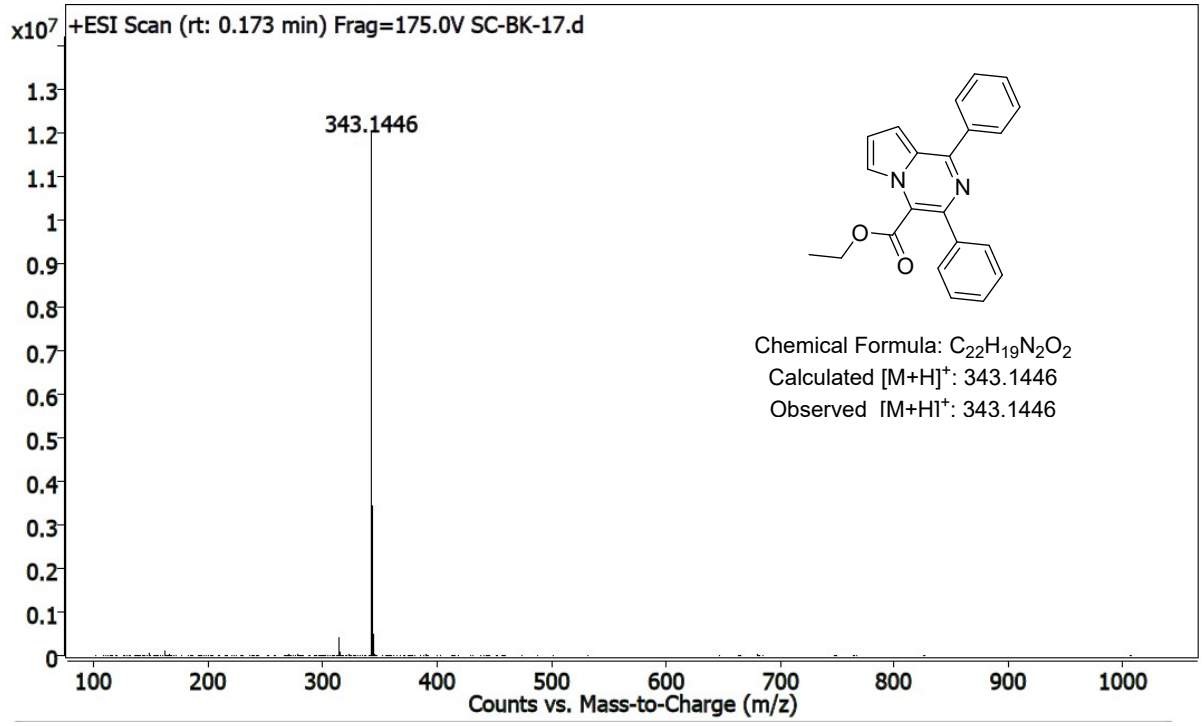


Figure S94: HRMS spectra of ethyl 1,3-diphenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5w)**

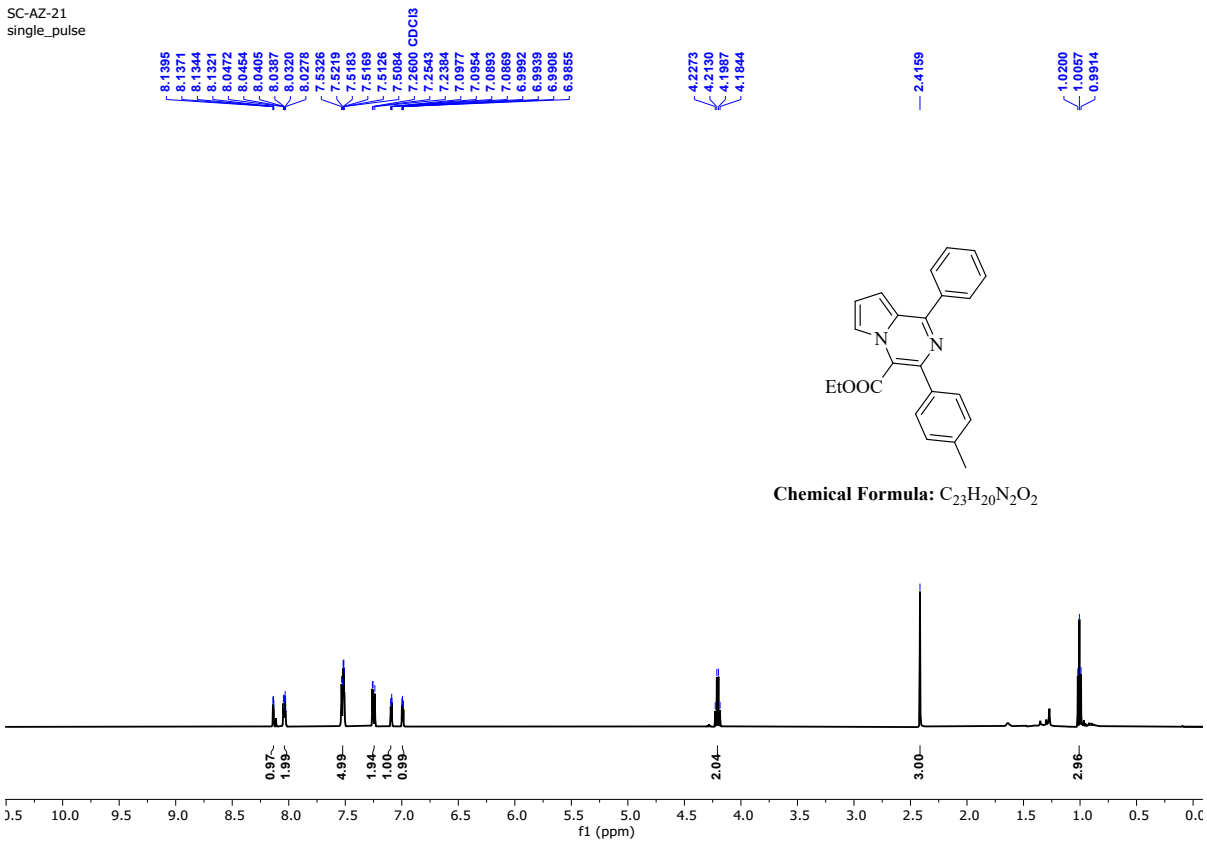


Figure S95: ^{1}H NMR spectra of ethyl 1-phenyl-3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5x**)

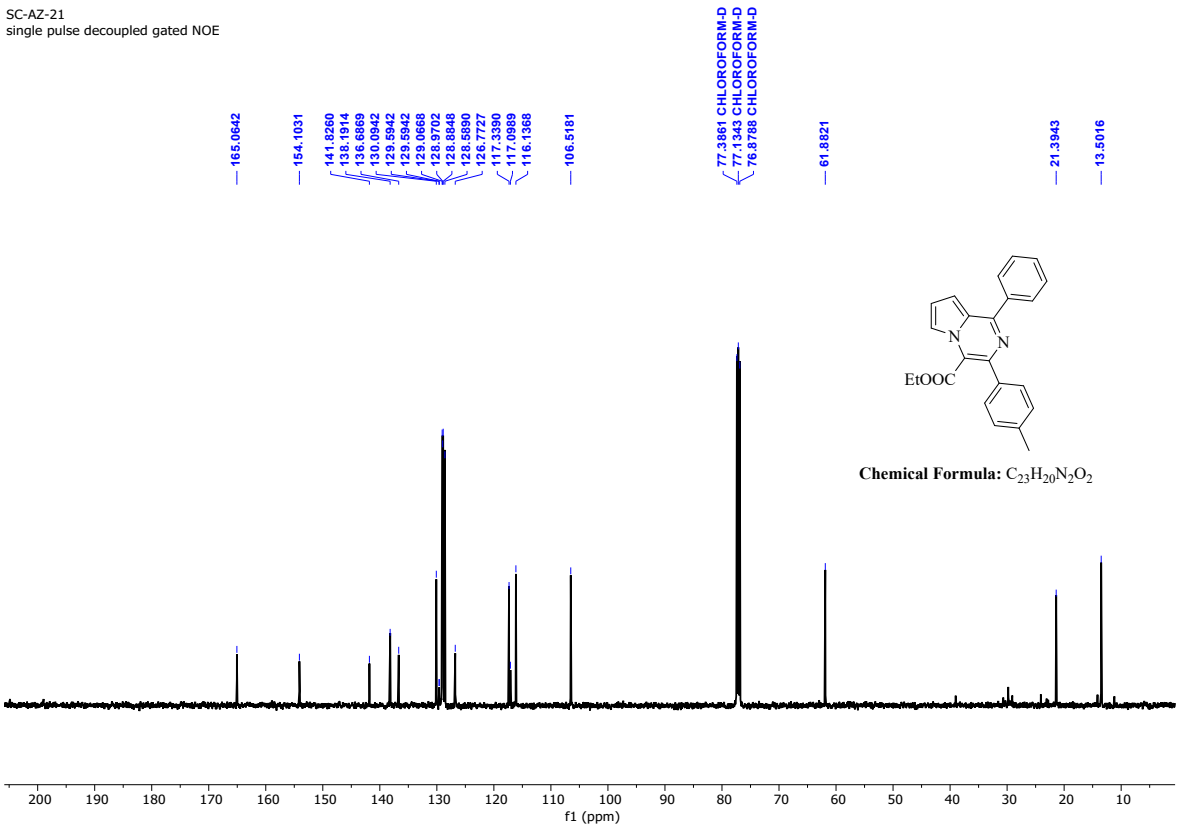


Figure S96: ^{13}C NMR spectra of ethyl 1-phenyl-3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5x**)

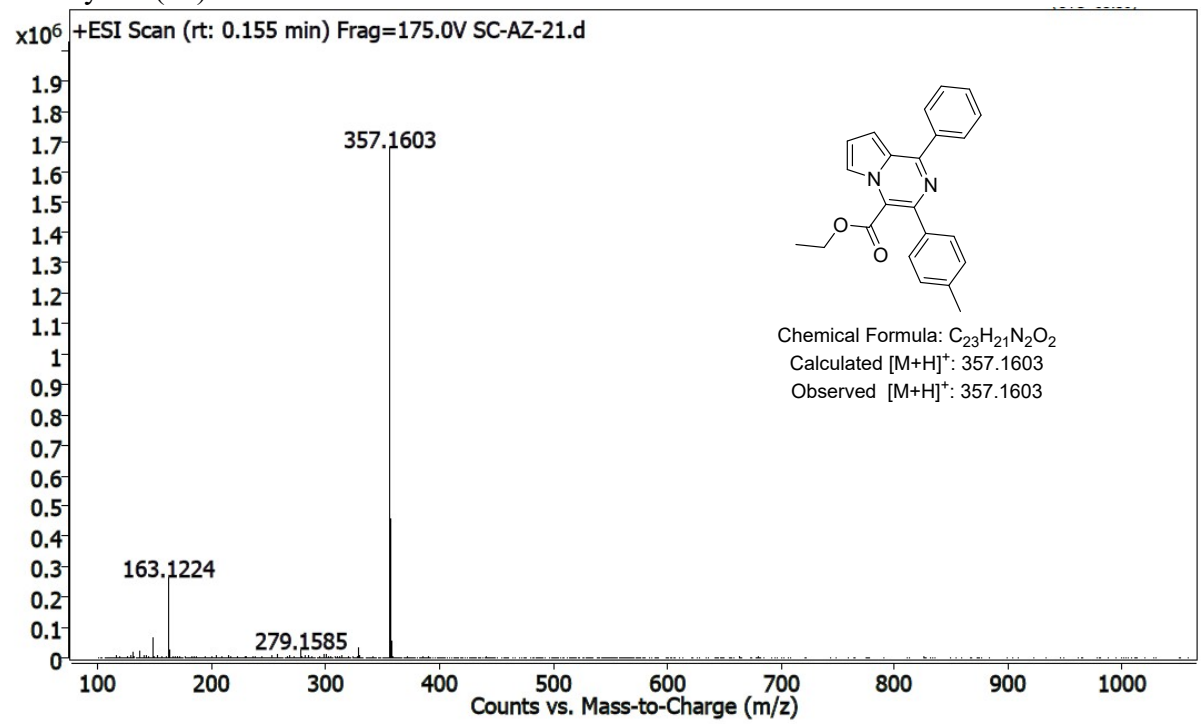


Figure S97: HRMS spectra of ethyl 1-phenyl-3-(*p*-tolyl)pyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5x**)

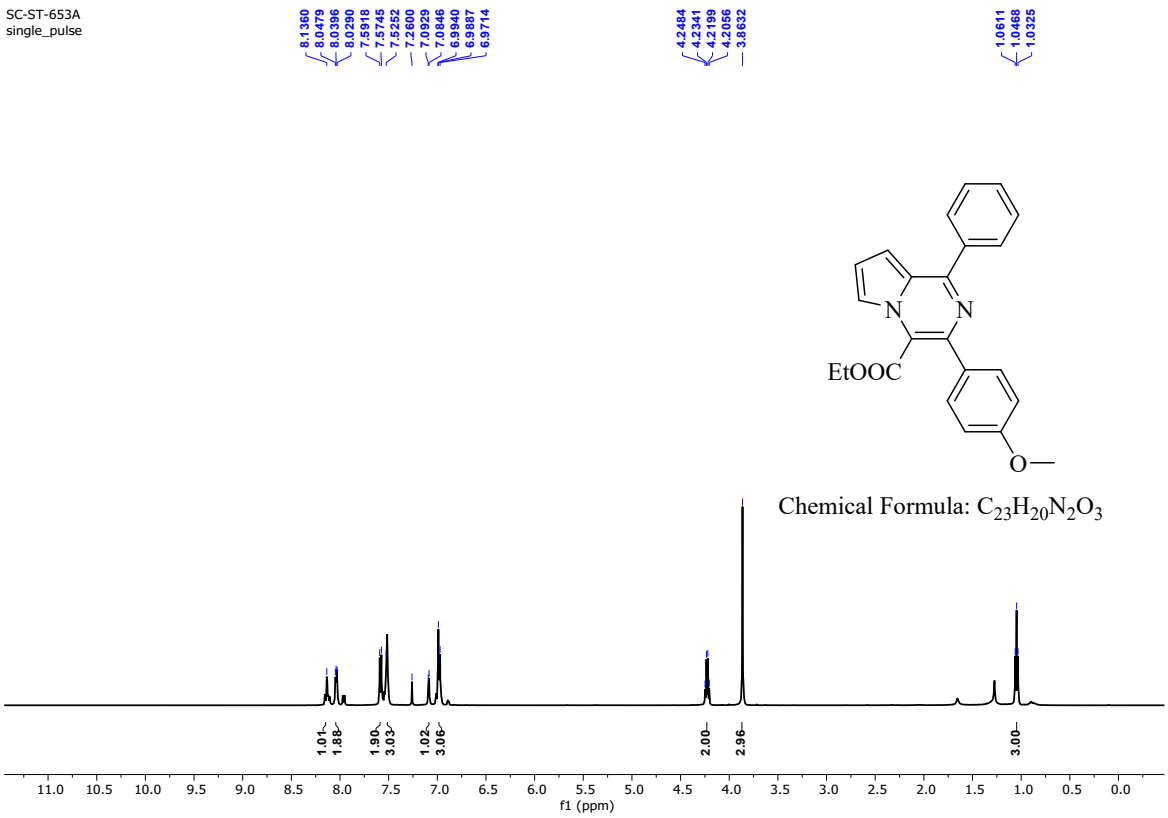


Figure S98: ^{1}H NMR spectra of ethyl 3-(4-methoxyphenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5y**)

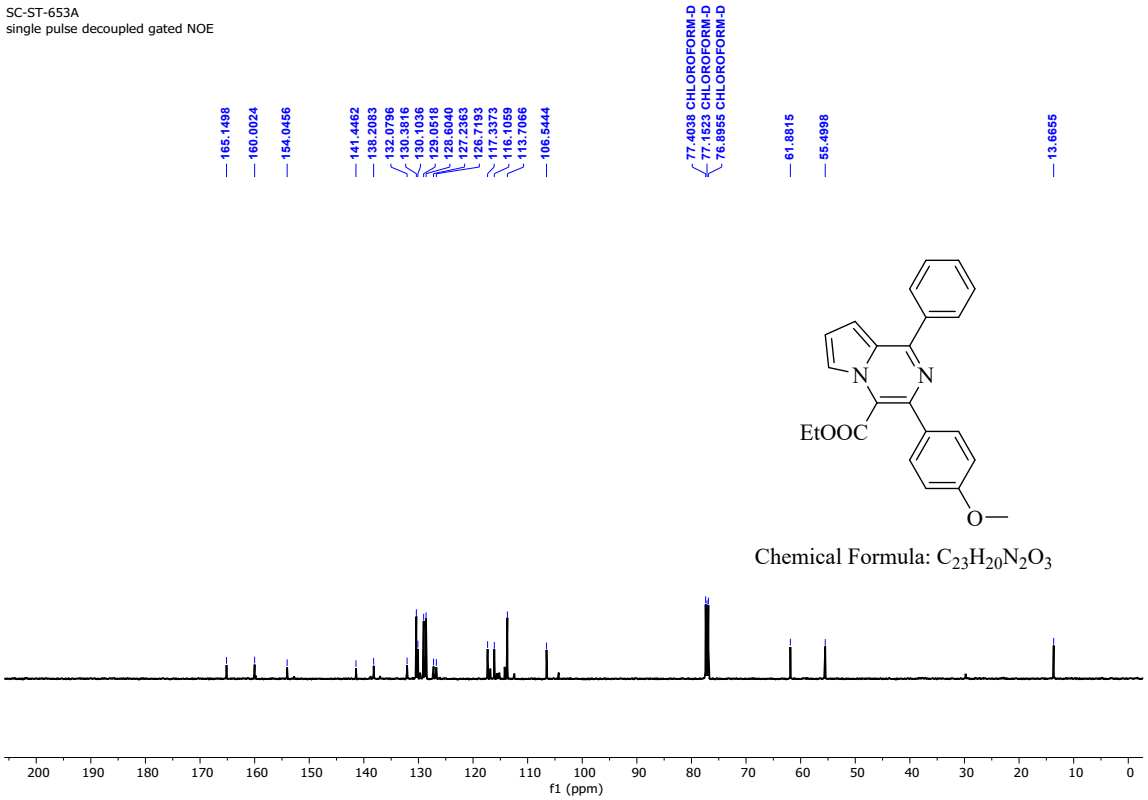


Figure S99: ^{13}C NMR spectra of ethyl 3-(4-methoxyphenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5y**)

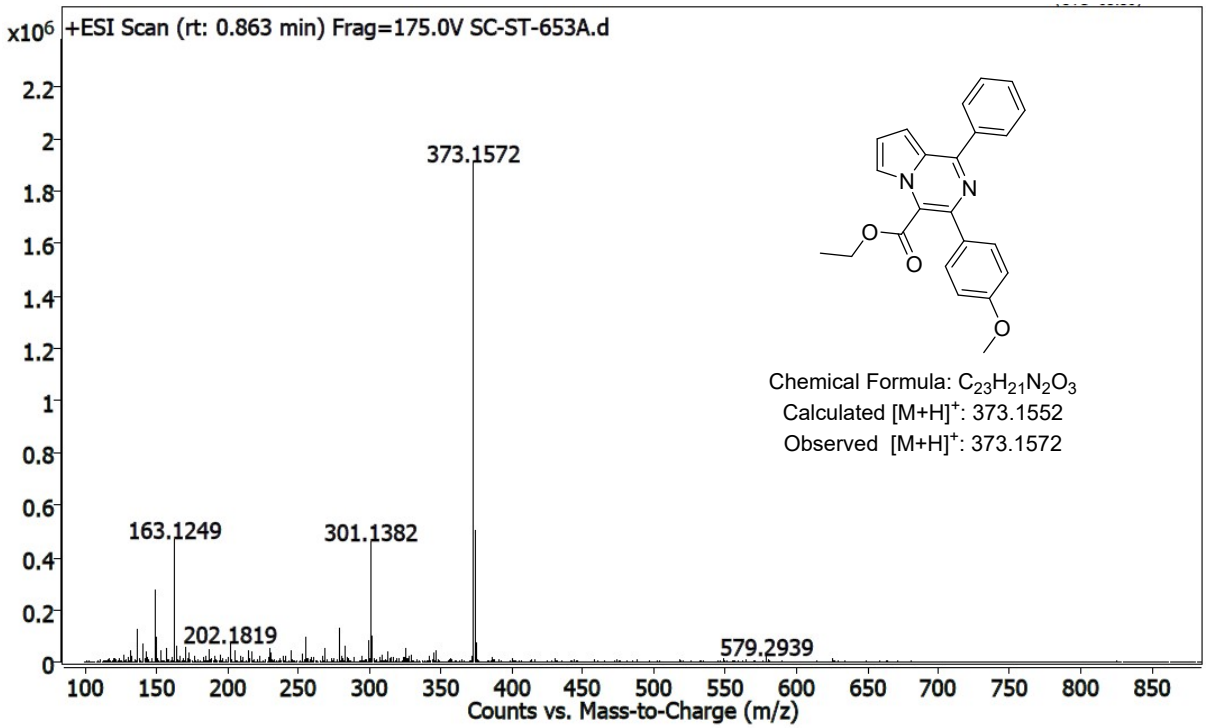


Figure S100: ^{13}C NMR spectra of ethyl 3-(4-methoxyphenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5y**)

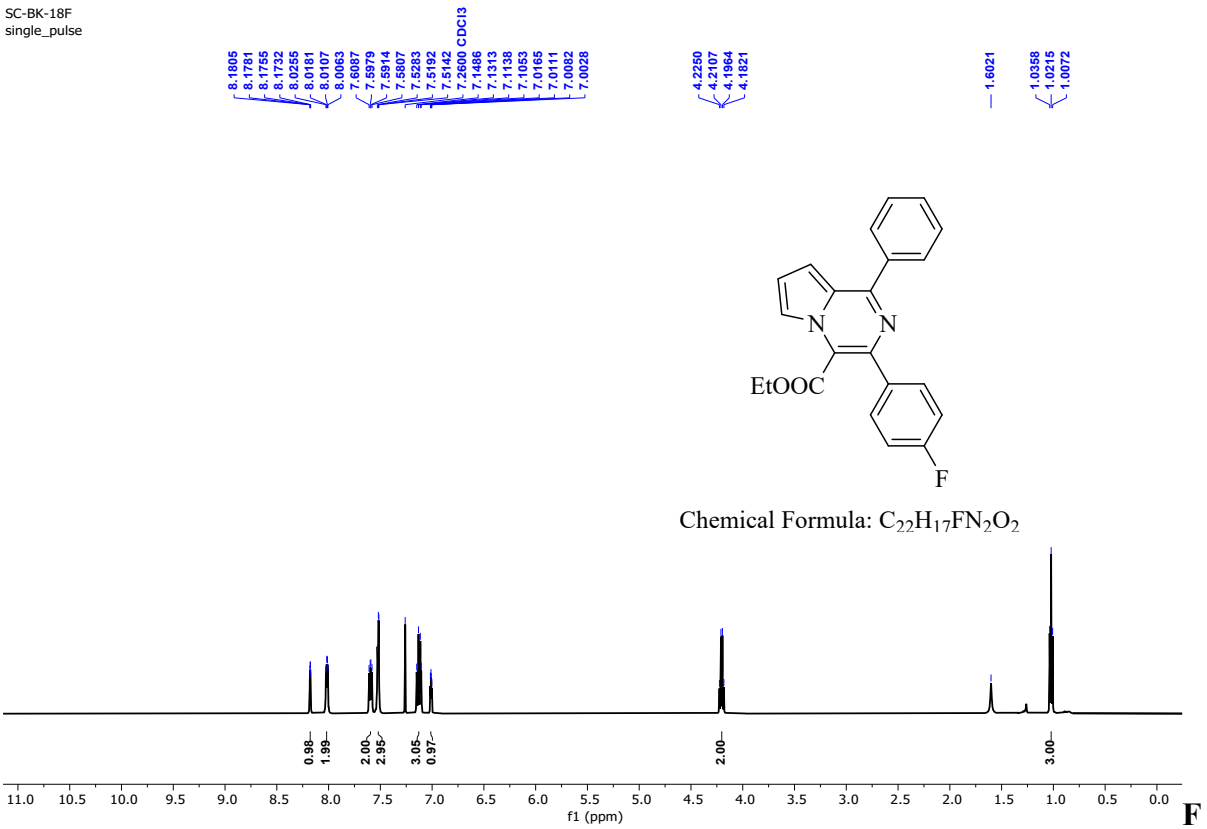


Figure S101: ^{1}H NMR spectra of ethyl 3-(4-fluorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5z**)

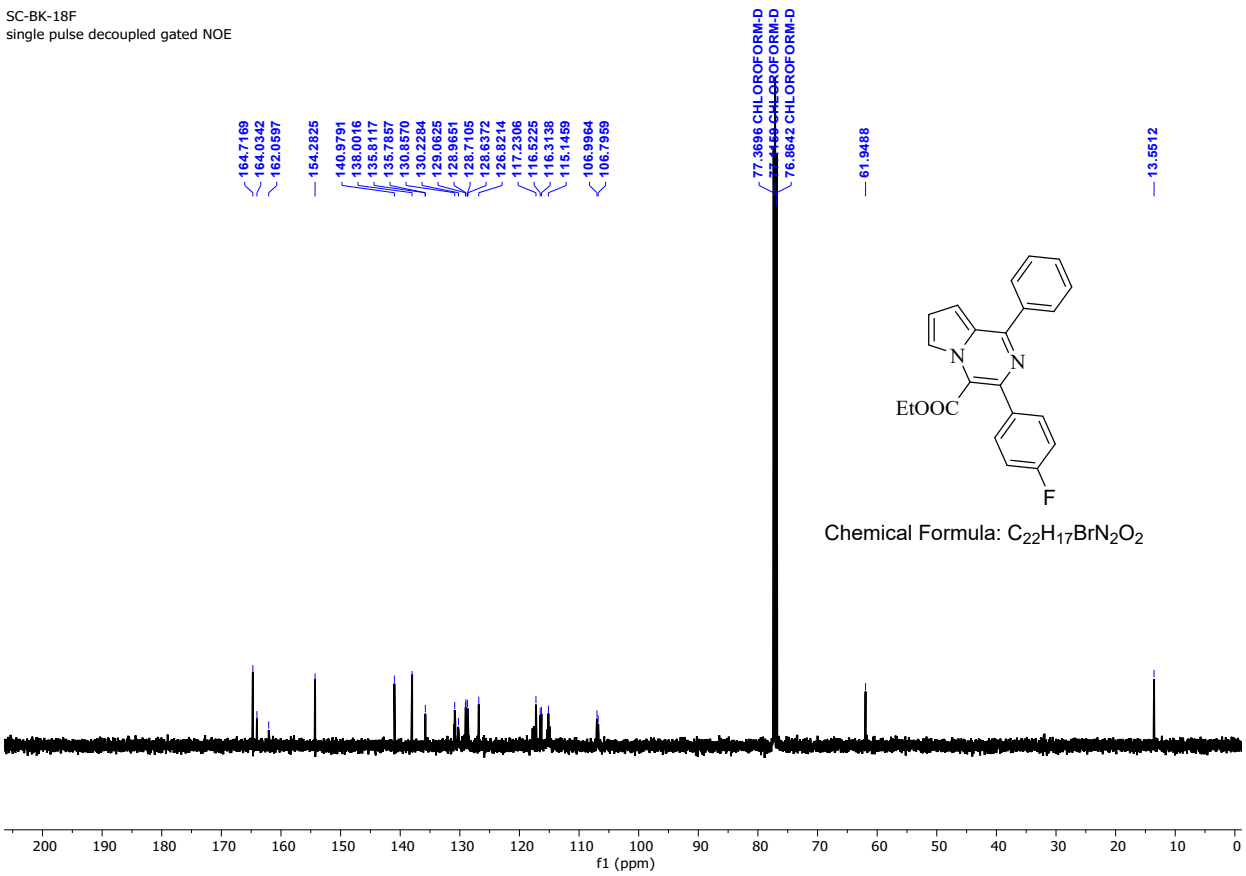


Figure S102: ^{13}C NMR spectra of ethyl 3-(4-fluorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5z**)

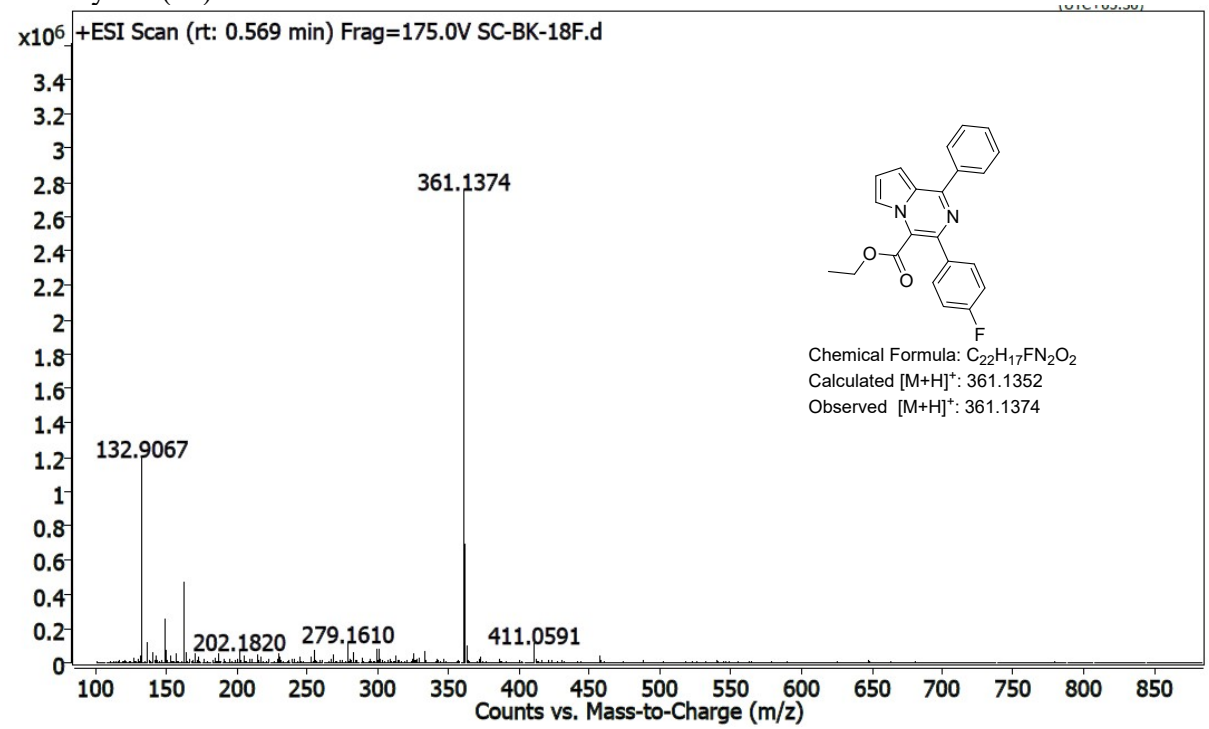


Figure S103: HRMS spectra of ethyl 3-(4-fluorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5z**)

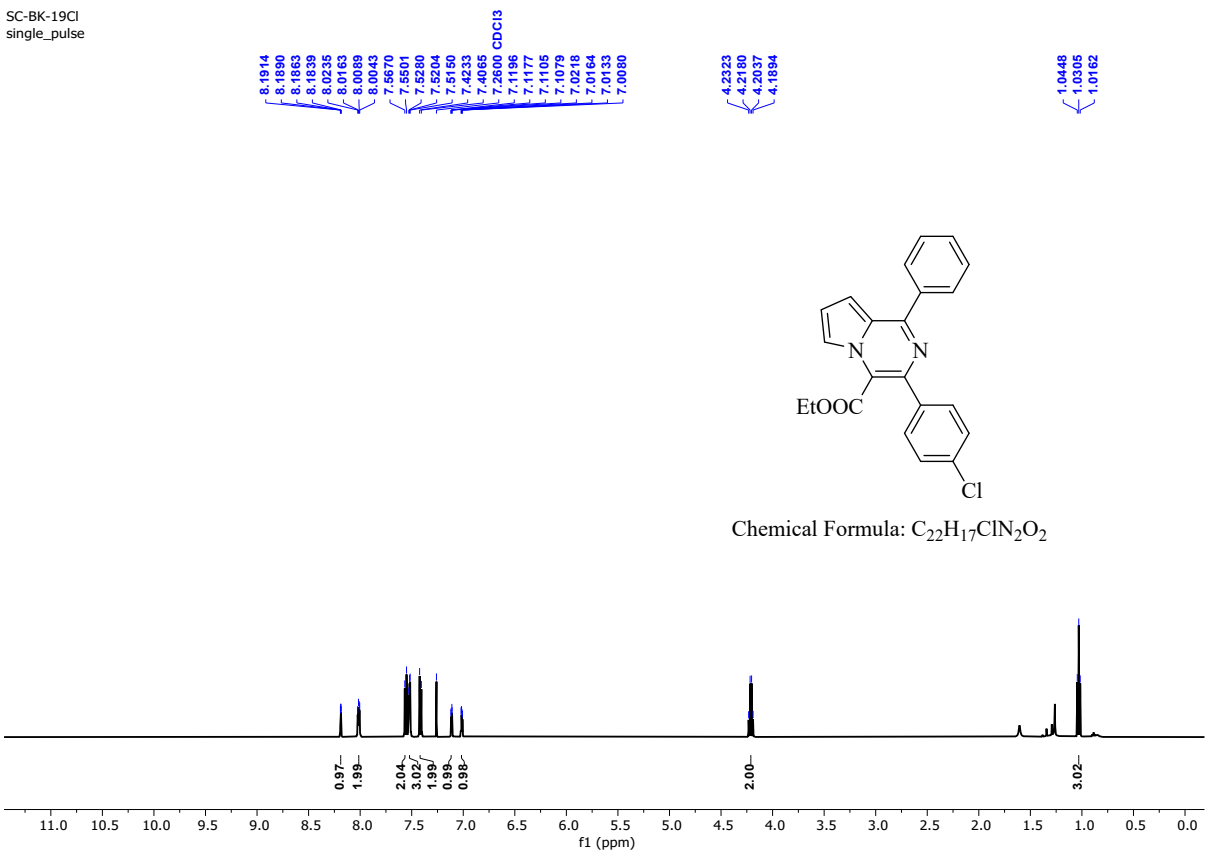


Figure S104: ^{1}H NMR spectra of ethyl 3-(4-chlorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5aa**)

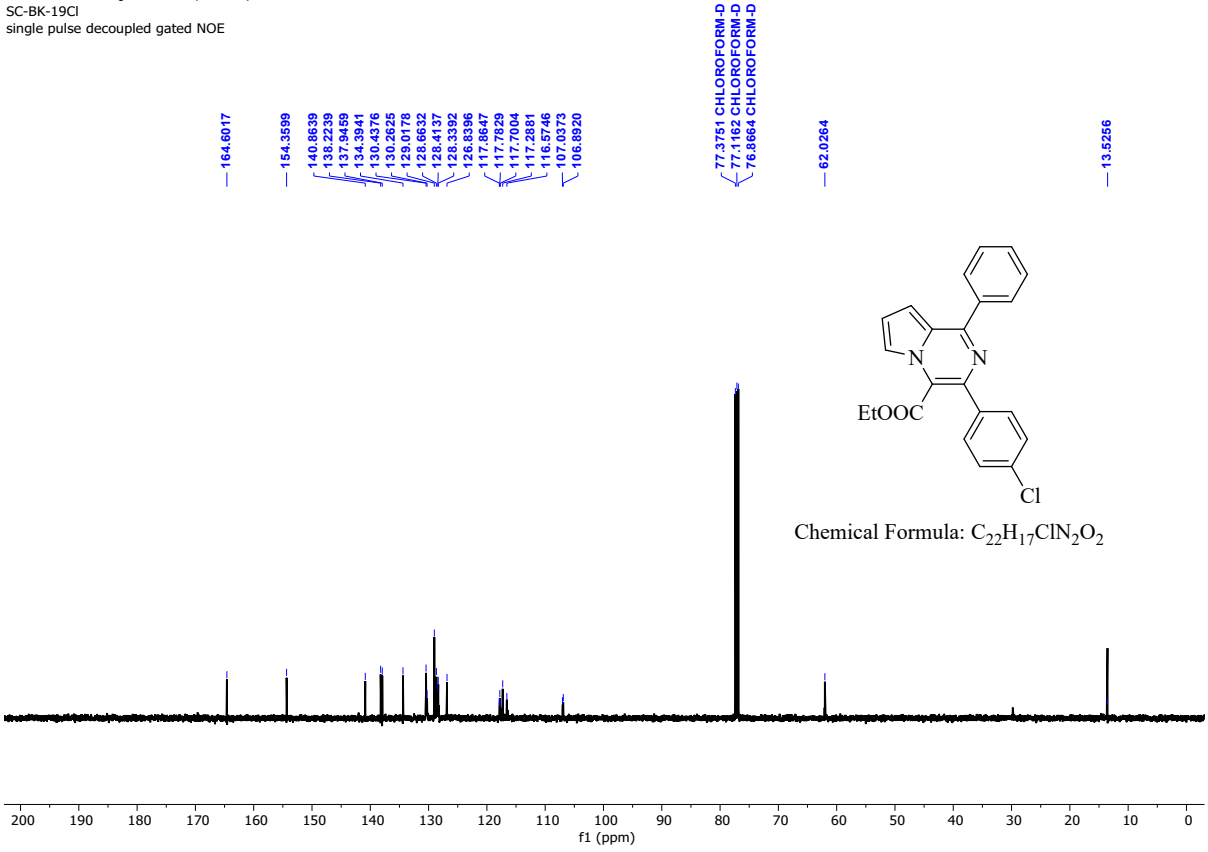


Figure S105: ^{13}C NMR spectra of ethyl 3-(4-chlorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5aa**)

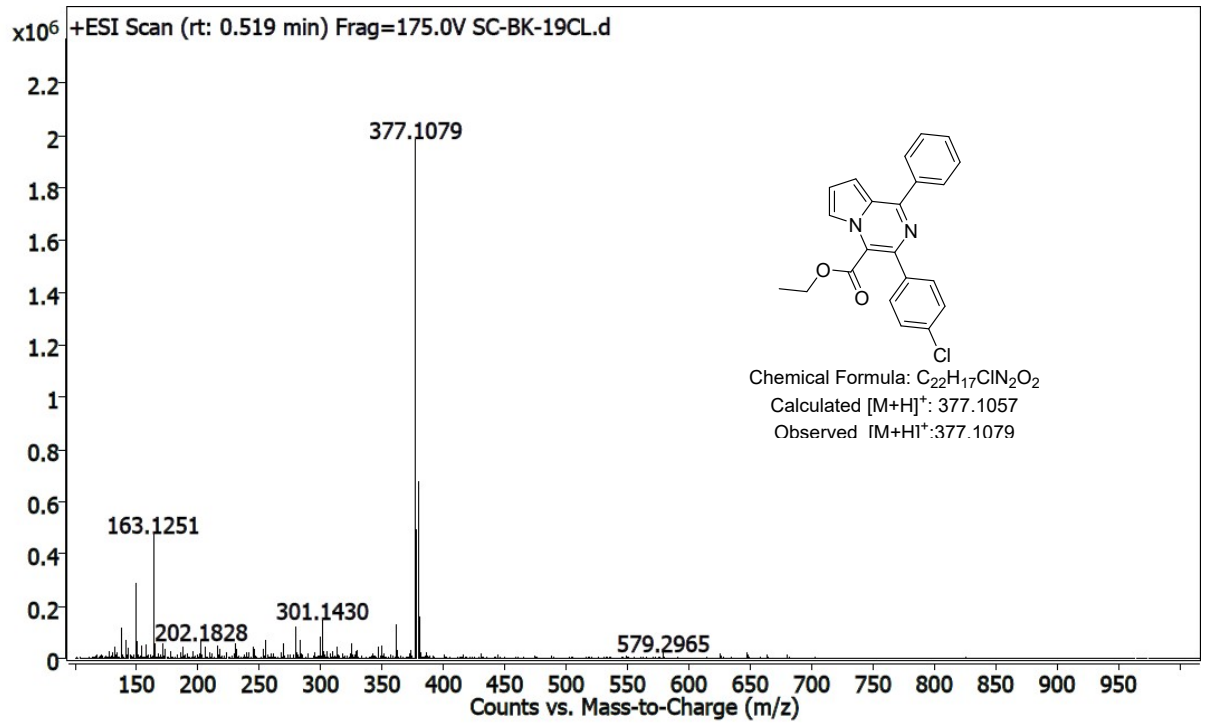


Figure S106: HRMS spectra of ethyl 3-(4-chlorophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5aa**)

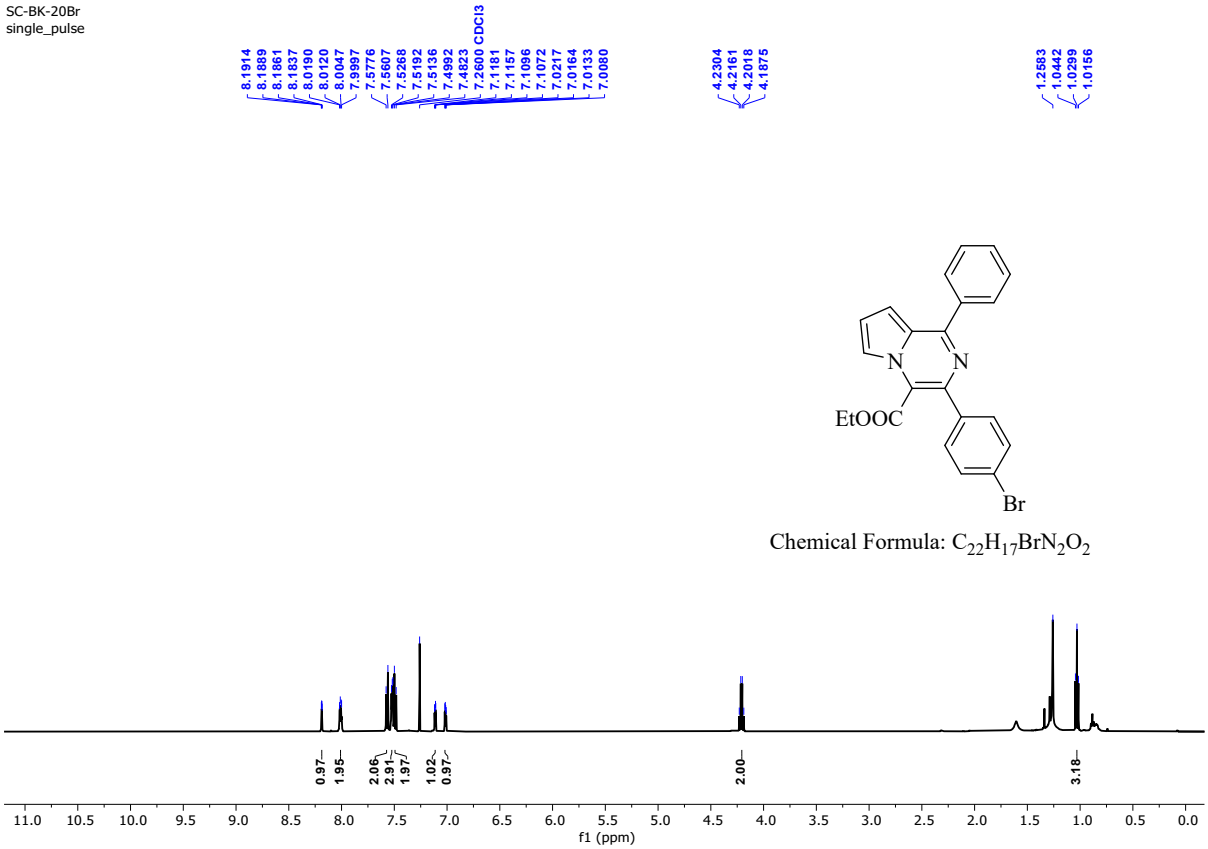


Figure S107: ^{1}H NMR spectra of ethyl 3-(4-bromophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5ab**)

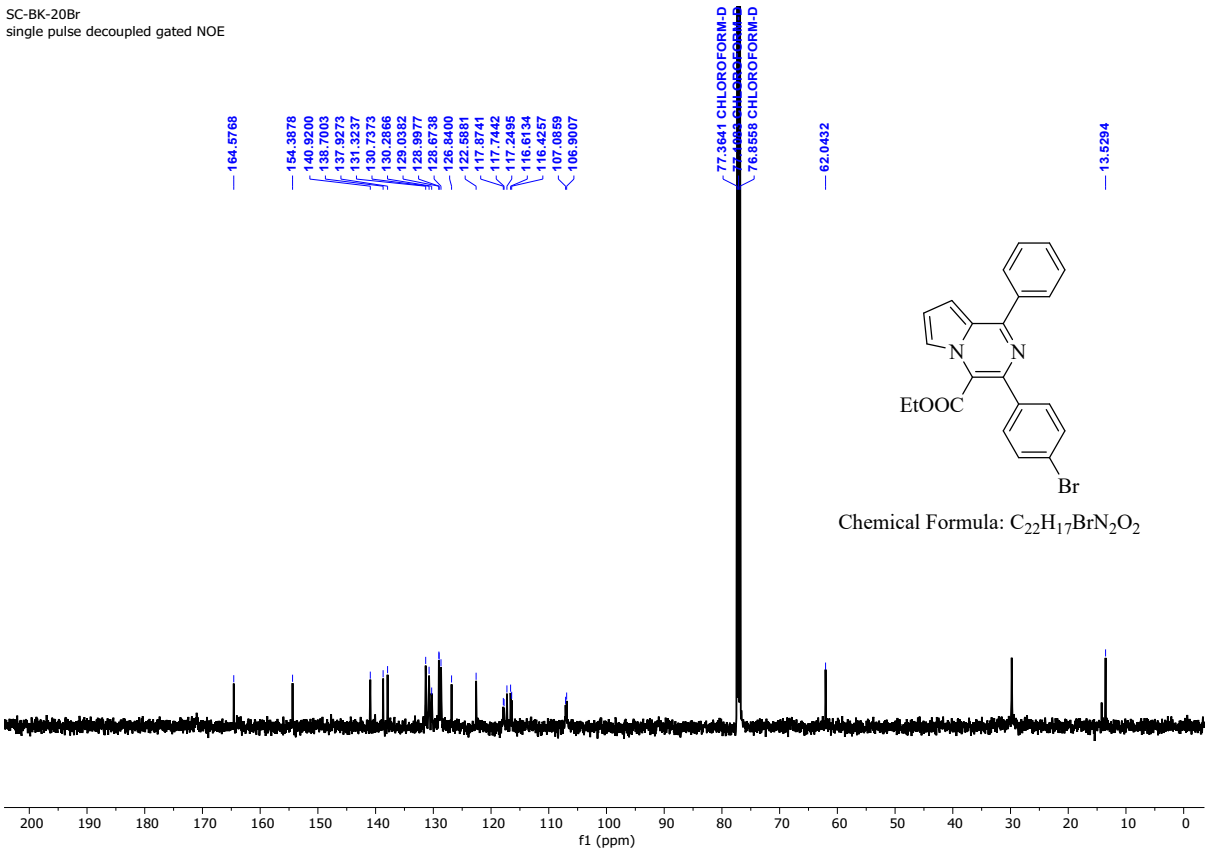


Figure S108: ^{13}C NMR spectra of ethyl 3-(4-bromophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5ab**)

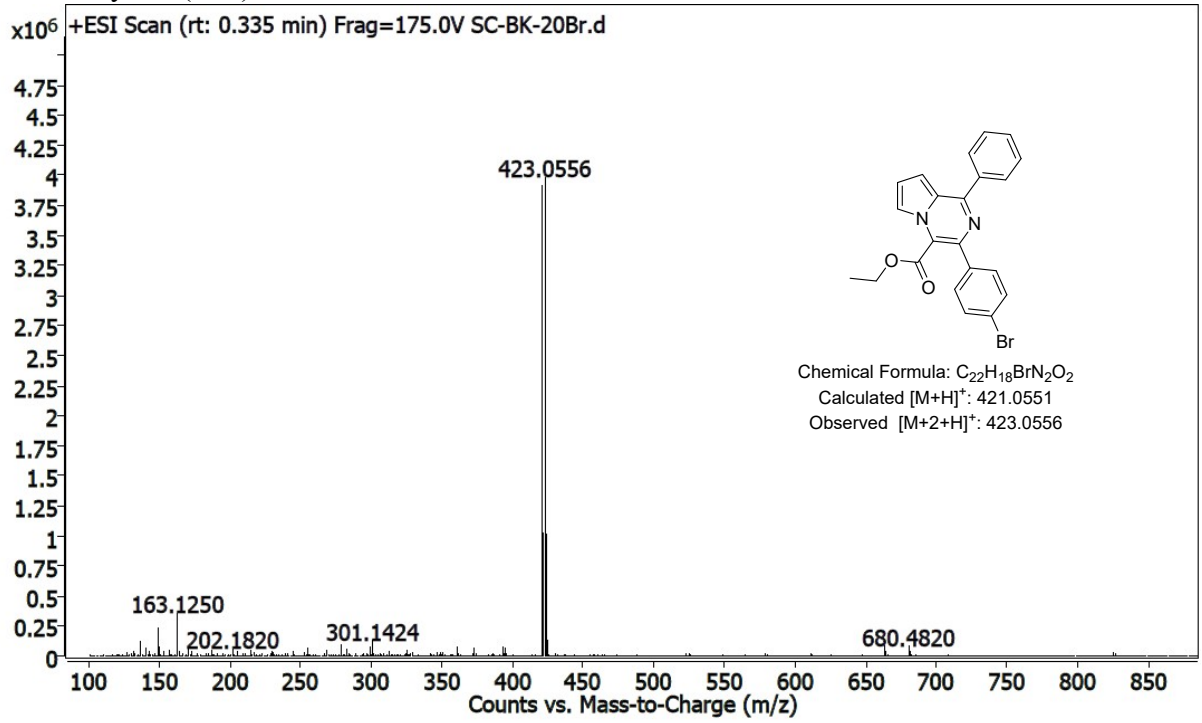


Figure S109: HRMS spectra of ethyl 3-(4-bromophenyl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate (**5ab**)

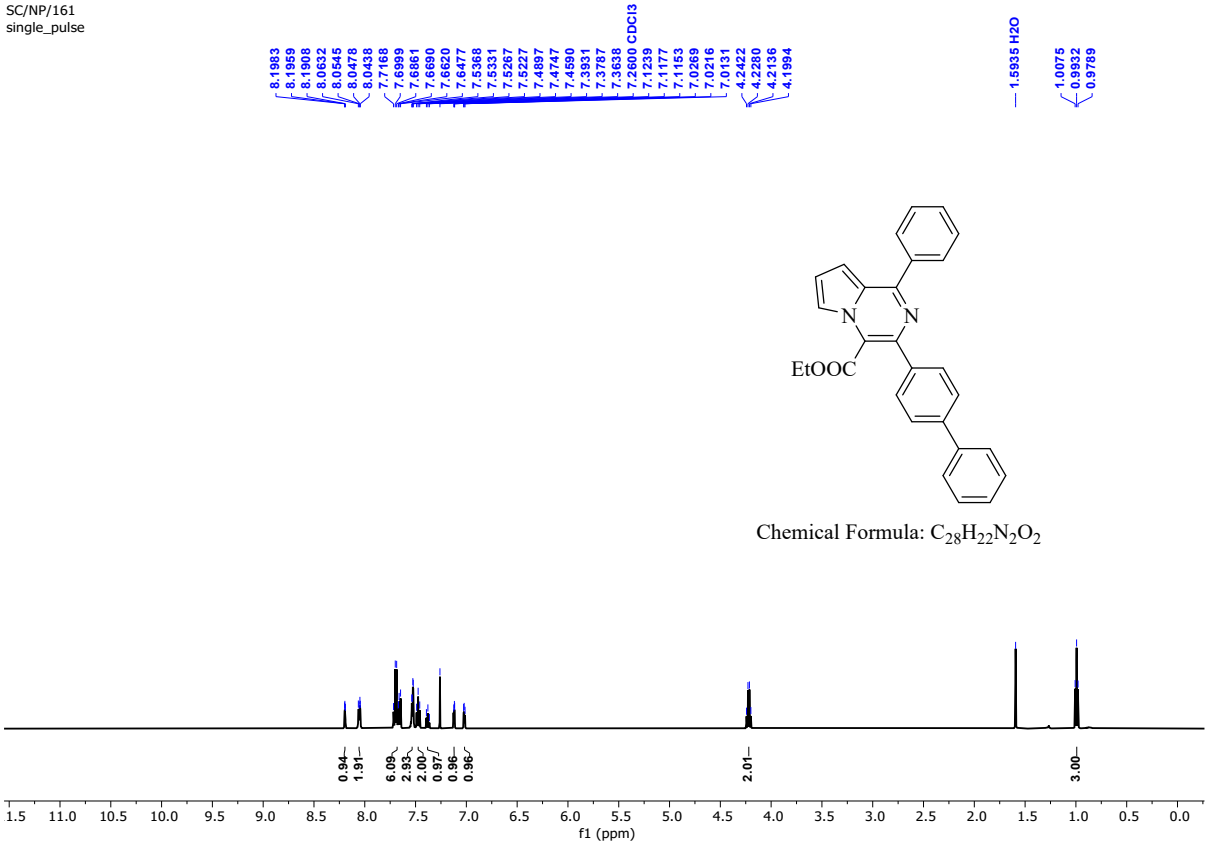


Figure S110: ^{1}H NMR spectra of ethyl 3-([1,1'-biphenyl]-4-yl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5ac)**

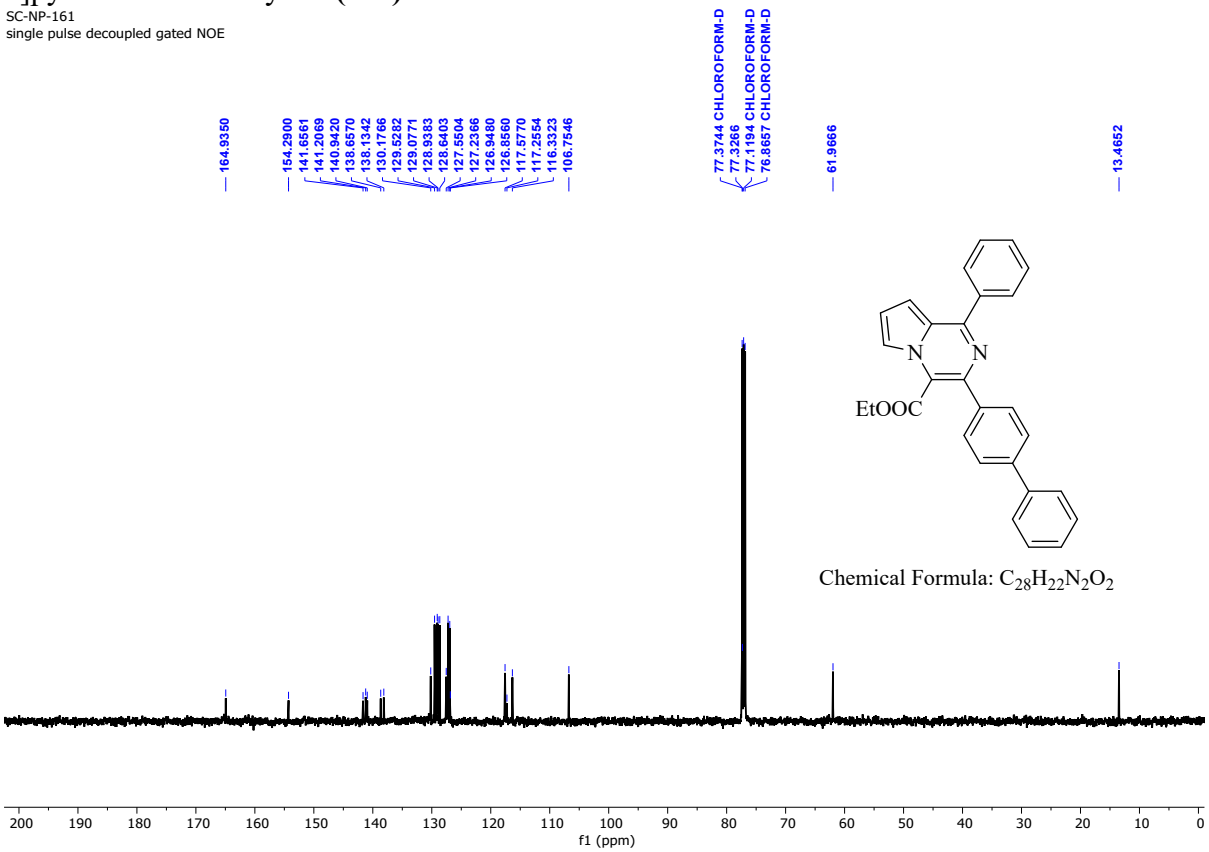


Figure S111: ^{13}C NMR spectra of ethyl 3-([1,1'-biphenyl]-4-yl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5ac)**

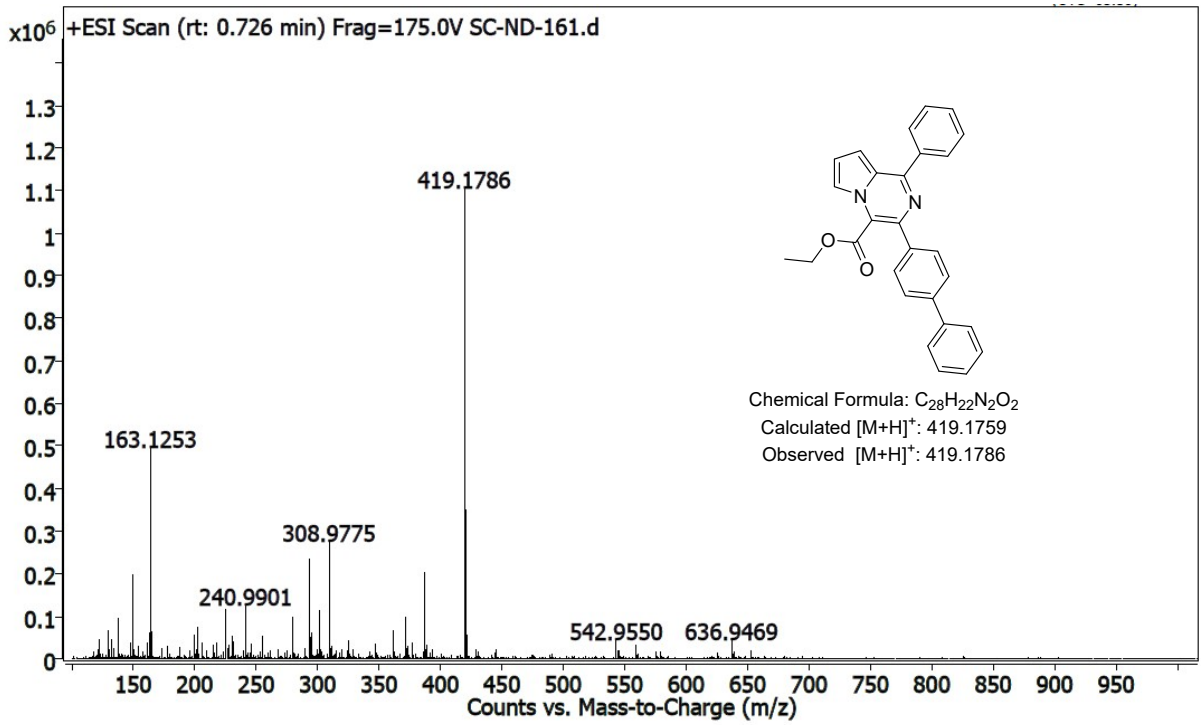


Figure S112: HRMS spectra of ethyl 3-([1,1'-biphenyl]-4-yl)-1-phenylpyrrolo[1,2-*a*]pyrazine-4-carboxylate **(5ac)**