A novel convenient approach towards pyrrolo[1,2-*b*]pyridazines through a domino coupling-isomerization-condensation reaction

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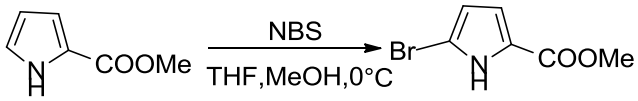
General methods:

Unless otherwise noted, all solvents and other reagents are commercially available and used without further purification. Propargyl alcohols **2** were prepared according to reported literature procedures[1] by addition of ethynyl magnesium bromide to the corresponding aldehydes. Low- and high-resolution mass spectra (ESI) were measured on an Agilent 6110 mass spectrometer and an Orbitrap mass spectrometer, respectively. ^{1}H and ^{13}C NMR spectra were determined on Bruker AM-300, Bruker AM-400, Bruker AM-500 instruments using tetramethylsilane as internal reference. Data are presented as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, br d = broad doublet, t = triplet, m = multiplet), *J* = coupling constant in hertz (Hz). Microwave reaction was performed with a CEM microwave reactor. Melting points were measured by Büchi 510 melting point apparatus without further corrected. Silica gel 60H (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China) was used for general chromatography.

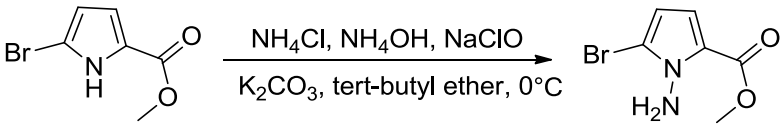
Experimental Procedures and Characterizations:

Preparation of methyl 5-bromo-1*H*-pyrrole-2-carboxylate:[2]



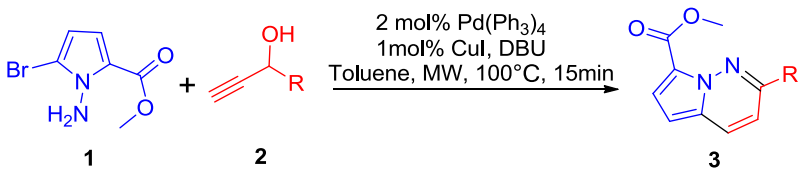
To a solution of methyl pyrrole-2-carboxylate (750 mg, 6 mmol) in THF (60 mL) and MeOH (30 mL) at 0℃ was added NBS (1.07 g, 6 mmol) in four portions in 2 h. The resulting solution was stirred for another 2 h at 0℃. Then the solvent was removed in vacuum and the crude product was purified via silica gel flash column chromatography (petroleum ether / EtOAc = 40/1) to give a white floppy solid (550 mg, 45%): ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.66 (br s, 1H), 6.82 (t, *J* = 3.2 Hz, 1H), 6.21 (dd, *J* = 3.0, 3.0 Hz, 1H), 3.87 (s, 3H); ESI m/z 204.0 $[M+1]^+$.

Preparation of methyl 1-amino-5-bromo-1*H*-pyrrole-2-carboxylate:

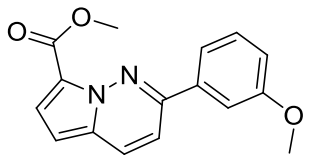


Preparation according to the literature, [3] K_2CO_3 was used here to replace NaOH. To a mixture of 5-bromo-1*H*-pyrrole-2-carboxylate (612 mg, 3 mmol), NH_4Cl (963 mg, 18 mmol), K_2CO_3 (2.07 g, 15 mmol) and aqueous solution of NH_4OH (3mL) in tert-butyl ether (50 mL), an aqueous solution of 8% NaClO (30 mL) was added slowly at 0℃ over 20 mins. The resulting reaction mixture was stirred at room temperature for 2 h. The organic layer is separated, washed with saturated aqueous $Na_2S_2O_3$ (20 mL), dried over anhydrous Na_2SO_4. The solvent was removed in vacuum and the crude product was purified via silica gel flash column chromatography (petroleum ether / EtOAc = 40/1) to give a light brown solid (460 mg, 70%): ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.82 (d, *J* = 4.5 Hz, 1H), 6.11 (d, *J* = 4.5 Hz, 1H), 5.65 (s, 2H), 3.82 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) : δ 161.40, 120.73, 115.54, 111.26, 108.62, 51.36; ESI m/z 219.0 $[M+1]^+$.

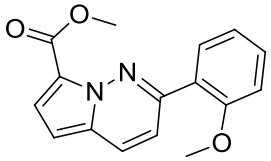
General Procedure for Preparation of pyrrolo[1,2-*b*]pyridazines 3a-t:



To the mixture of 1-amino-5-bromo-1*H*-pyrrole-2-carboxylate (0.4 mmol), arylpropargyl alcohol (0.8 mmol), $Pd(PPh_3)_4$ (9.2 mg, 0.008 mmol), CuI (0.8 mg, 0.004 mmol) in anhydrous Toulene (2 mL) was added DBU (304mg, 2 mmol) under nitrogen. Then, the reaction was performed in a microwave reactor at 100 °C. When the reaction was complete, the solvent was removed in vacuum, and the crude product was eluted on silica gel with petroleum ether/ethyl acetate to give the corresponding product.

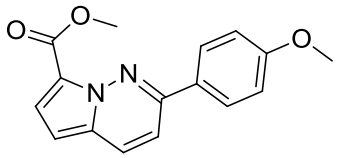


Methyl 2-(3-methoxyphenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3a : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 91% yield as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 9.4 Hz, 1H), 7.66 (t, *J* = 1.9 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 4.7 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 9.5 Hz, 1H), 7.01 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.54 (d, *J* = 4.7 Hz, 1H), 3.97 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.17, 160.09, 150.81, 137.43, 130.28, 129.93, 127.24, 120.79, 119.42, 119.06, 115.70, 112.17, 111.95, 100.79, 55.38, 51.36. HRMS (ESI) calcd. for $C_{16}H_{15}N_2O_3$ $[M+H]^+$: 283.1083. Found: 283.1072.

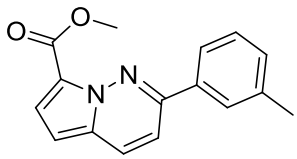


Methyl 2-(2-methoxyphenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3b : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 46% yield as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 9.3 Hz, 1H), 7.53 (d, *J* = 4.6 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 9.3 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.51 (d, *J* = 4.7 Hz, 1H), 3.93 (s, 3H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.16, 157.50, 151.11, 131.23, 130.92, 130.31, 125.92, 125.44, 121.38, 120.39, 118.72, 116.57, 111.45, 100.23, 55.67,

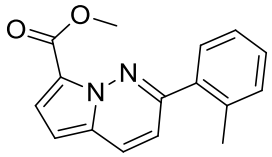
51.26. HRMS (ESI) calcd. for $C_{16}H_{15}N_2O_3$ $[M+H]^+$: 283.1083. Found: 283.1071.



Methyl 2-(4-methoxyphenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3c : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 87% yield as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 9.4 Hz, 1H), 7.51 (d, *J* = 4.7 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 1H), 6.51 (d, *J* = 4.7 Hz, 1H), 3.96 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.09, 160.23, 150.69, 130.17, 128.51, 128.33, 127.16, 120.43, 118.85, 114.34, 111.71, 100.73, 55.41, 51.36. HRMS (ESI) calcd. for $C_{16}H_{15}N_2O_3$ $[M+H]^+$: 283.1083. Found: 283.1073.

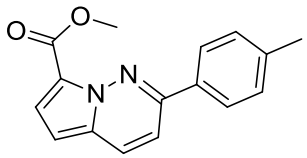


Methyl 2-(3-methylphenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3d : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 84% yield as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.81 (m, 3H), 7.56 (d, *J* = 4.7 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 9.3 Hz, 2H), 6.55 (d, *J* = 4.7 Hz, 1H), 3.98 (s, 3H), 2.47 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.21, 151.28, 138.64, 135.98, 130.64, 130.35, 128.86, 127.58, 127.24, 124.19, 120.71, 118.93, 112.16, 100.77, 51.41, 21.64. HRMS (ESI) calcd. for $C_{16}H_{15}N_2O_2$ $[M+H]^+$: 267.1134. Found: 267.1124.

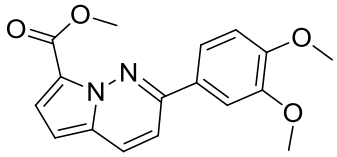


Methyl 2-(2-methylphenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3e : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 29% yield as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 9.2 Hz, 1H), 7.56 (d, *J* = 4.7 Hz, 1H), 7.49 (d,

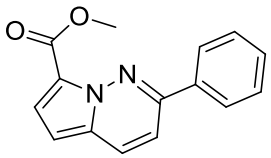
J = 7.4 Hz, 1H), 7.38 – 7.26 (m, 3H), 6.97 (d, *J* = 9.2 Hz, 1H), 6.55 (d, *J* = 4.7 Hz, 1H), 3.92 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.13, 153.26, 136.85, 136.48, 131.23, 129.87, 129.08, 126.81, 126.05, 120.63, 118.99, 115.28, 100.67, 51.37, 20.83. HRMS (ESI) calcd. for $C_{16}H_{15}N_2O_2$ $[M+H]^+$: 267.1134. Found: 267.1124.



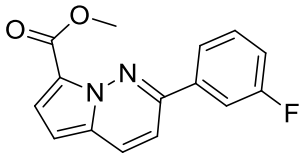
Methyl 2-(4-methylphenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3f : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 80% yield as a light brown solid (M. p. = 84−86 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 9.4 Hz, 1H), 7.54 (d, *J* = 4.7 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 9.4 Hz, 1H), 6.53 (d, *J* = 4.7 Hz, 3H), 3.98 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.23, 151.01, 140.00, 133.15, 130.30, 129.68, 127.20, 126.82, 120.58, 118.88, 111.89, 100.74, 51.38, 21.40.HRMS (ESI) calcd. for $C_{16}H_{15}N_2O_2$ $[M+H]^+$: 267.1134. Found: 267.1124.



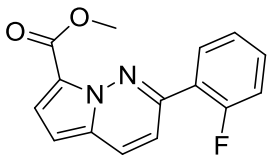
Methyl 2-(3,4-dimethoxyphenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3g : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (5:1) in a 77% yield as a white solid (M. p. = 149−151 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 9.4 Hz, 1H), 7.78 (d, *J* = 1.9 Hz, 1H), 7.53 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.51 (d, *J* = 4.7 Hz, 1H), 7.24 (d, *J* = 9.4 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.50 (d, *J* = 4.7 Hz, 1H), 4.02 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.27, 150.68, 150.57, 149.39, 130.13, 128.79, 127.13, 120.57, 119.78, 118.93, 111.65, 110.94, 109.55, 100.81, 55.99, 51.37. HRMS (ESI) calcd. for $C_{17}H_{17}N_2O_4$ $[M+H]^+$: 313.1188. Found: 313.1176.



Methyl 2-phenylpyrrolo[1,2-*b*]pyridazine-7-carboxylate 3h : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 91% yield as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.0 Hz, 2H), 7.89 (d, *J* = 9.4 Hz, 1H), 7.55 (d, *J* = 4.7 Hz, 1H), 7.53 – 7.43 (m, 4H), 7.29 (d, *J* = 9.4 Hz, 1H), 6.54 (d, *J* = 4.7 Hz, 1H), 3.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.16, 151.02, 136.00, 130.28, 129.81, 128.94, 127.29, 126.95, 120.71, 118.97, 111.90, 100.78, 51.37. HRMS (ESI) calcd. for $C_{15}H_{13}N_2O_2$ $[M+H]^+$: 253.0977. Found: 253.0968.

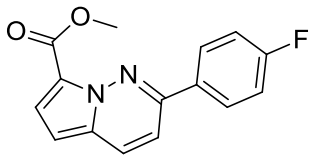


Methyl 2-(3-foluorophenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3i : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 91% yield as a light brown solid (M. p. = 90−92 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 9.4 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.83 (dt, *J* = 10.0, 2.1 Hz, 1H), 7.59 (d, *J* = 4.7 Hz, 1H), 7.49 (td, *J* = 8.0, 5.9 Hz, 1H), 7.28 (d, *J* = 4.3 Hz, 1H), 7.18 (td, *J* = 8.1, 2.3 Hz, 1H), 6.59 (d, *J* = 4.7 Hz, 1H), 4.00 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.25 (d, $^{1}J_{C\text{-}F}$= 246.1 Hz), 160.10, 149.79 (d, $^{4}J_{C\text{-}F}$= 2.8 Hz), 138.28 (d, $^{3}J_{C\text{-}F}$= 7.8 Hz), 130.51 (d, $^{3}J_{C\text{-}F}$= 8.1 Hz), 130.29, 127.53, 122.59 (d, $^{4}J_{C\text{-}F}$= 3.0 Hz), 121.02, 119.12, 116.75 (d, $^{2}J_{C\text{-}F}$= 21.3 Hz), 113.94 (d, $^{2}J_{C\text{-}F}$= 23.3 Hz), 111.56 , 101.03, 51.46. HRMS (ESI) calcd. for $C_{15}H_{12}FN_2O_2$ $[M+H]^+$: 271.0883. Found: 271.0874.

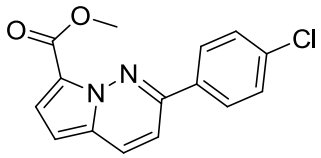


Methyl 2-(2-foluorophenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3j : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 85% yield as a yellow solid (M. p.

= 103−104 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (td, *J* = 7.8, 1.7 Hz, 1H), 7.86 (d, *J* = 9.4 Hz, 1H), 7.56 (d, *J* = 4.7 Hz, 1H), 7.48 – 7.39 (m, 1H), 7.36 – 7.25 (m, 2H), 7.21 – 7.12 (m, 1H), 6.55 (d, *J* = 4.7 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.85 (d, $^{1}J_{C\text{-}F}$ = 250.4 Hz), 160.08, 148.27, 131.43 (d, $^{3}J_{C\text{-}F}$ = 8.6 Hz), 130.95 (d, $^{4}J_{C\text{-}F}$ = 2.4 Hz), 130.27, 126.69, 124.92 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 124.37 (d, $^{2}J_{C\text{-}F}$ = 11.2 Hz), 120.87, 118.92, 116.31 (d, $^{2}J_{C\text{-}F}$ = 22.5 Hz), 115.12 (d, $^{3}J_{C\text{-}F}$ = 9.2 Hz), 100.72, 51.39. HRMS (ESI) calcd. for $C_{15}H_{12}FN_2O_2$ $[M+H]^+$: 271.0883. Found: 271.0874.

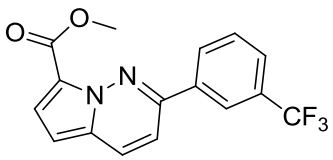


Methyl 2-(4-foluorophenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3k : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 84% yield as a yellow solid (M. p. = 108−110 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 – 8.04 (m, 2H), 7.90 (d, *J* = 9.4 Hz, 1H), 7.56 (d, *J* = 4.7 Hz, 1H), 7.25 (d, *J* = 9.4 Hz, 1H), 7.20 (ddd, *J* = 8.7, 6.9, 2.1 Hz, 2H), 6.56 (d, *J* = 4.7 Hz, 1H), 3.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.96 (d, ^{1} $J_{C\text{-}F}$= 250.7 Hz), 160.12, 150.03, 132.16 (d, ^{4} $J_{C\text{-}F}$= 2.5 Hz), 130.15, 128.88 (d, ^{3} $J_{C\text{-}F}$= 8.9 Hz), 127.44, 120.75, 118.97, 115.99(d, ^{2} $J_{C\text{-}F}$= 21.4 Hz), 111.55, 100.93, 51.41. HRMS (ESI) calcd. for $C_{15}H_{12}FN_2O_2$ $[M+H]^+$: 271.0883. Found: 271.0872.

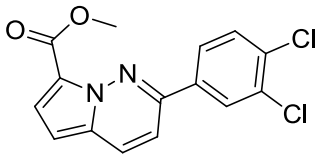


Methyl 2-(4-chlorophenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3l : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 83% yield as a yellow solid (M. p. = 122−124 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.5 Hz, 2H), 7.87 (d, *J* = 9.4 Hz, 1H), 7.54 (d, *J* = 4.7 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 9.4 Hz, 1H), 6.54 (d, *J* = 4.7 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.09, 149.83, 136.01, 134.43, 130.21, 129.17, 128.18, 127.48, 120.89, 119.02, 111.40,

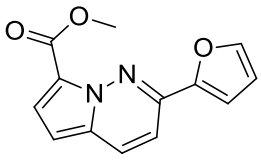
101.01, 51.42. HRMS (ESI) calcd. for $C_{15}H_{12}ClN_2O_2$ $[M+H]^+$: 287.0587. Found: 287.0581.



Methyl 2-(trifluoromethyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3m : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 44% yield as a yellow solid (M. p. = 115−117 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.8 Hz, 1H), 8.27 (s, 1H), 7.92 (d, *J* = 9.4 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.62 (t, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 4.7 Hz, 1H), 7.28 (d, *J* = 9.4 Hz, 1H), 6.57 (d, *J* = 4.7 Hz, 1H), 3.97 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.12, 149.52, 136.86, 131.33(q, $^2J_{C\text{-}F}$= 32.6 Hz), 130.28, 130.22, 129.59, 127.72, 126.41 (q, $^3J_{C\text{-}F}$= 3.4 Hz), 124.00 (q, $^1J_{C\text{-}F}$= 272.5 Hz), 123.63 (q, $^3J_{C\text{-}F}$ = 3.5 Hz) , 121.18, 119.26, 111.31, 101.18 , 51.48. HRMS (ESI) calcd. for $C_{16}H_{12}F_3N_2O_2$ $[M+H]^+$: 321.0851. Found: 287.0841.

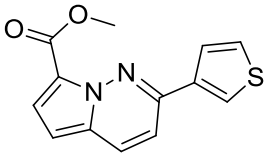


Methyl 2-(3,4-dichlorophenyl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3n : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 25% yield as a yellow solid (M. p. = 118−120 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 2.1 Hz, 1H), 7.97 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.93 (d, *J* = 9.4 Hz, 1H), 7.63 – 7.50 (m, 2H), 7.23 (d, *J* = 9.4 Hz, 1H), 6.59 (d, *J* = 4.7 Hz, 1H), 3.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.03, 148.69, 135.93, 134.08, 133.23, 130.94, 130.19, 128.65, 127.68, 126.09, 121.18, 119.17, 111.08, 101.23, 51.49. HRMS (ESI) calcd. for $C_{15}H_{11}Cl_2N_2O_2$ $[M+H]^+$: 321.0198. Found: 287.0185.

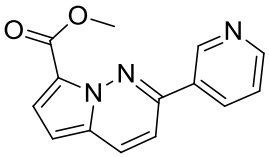


Methyl 2-(furan-2-yl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3o : following

general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 75% yield as a brown solid (M. p. = 103−105 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 9.4 Hz, 1H), 7.59 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.51 (d, *J* = 4.7 Hz, 1H), 7.23 (d, *J* = 9.4 Hz, 1H), 7.15 (dd, *J* = 3.4, 0.7 Hz, 1H), 6.55 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.51 (d, *J* = 4.7 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.59, 149.72, 143.78, 143.47, 129.74, 126.80, 120.17, 118.60, 111.75, 110.14, 109.71, 100.76, 50.99. HRMS (ESI) calcd. for $C_{13}H_{11}N_2O_3$ $[M+H]^+$: 243.0770. Found: 243.0763.

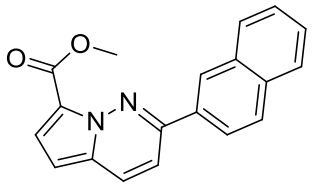


Methyl 2-(thiophen-3-yl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3p : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 90% yield as a brown solid (M. p. = 97−99 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.85 (m, 1H), 7.85 – 7.71 (m, 2H), 7.50 (d, *J* = 4.7 Hz, 1H), 7.44 – 7.33 (m, 1H), 7.15 (d, *J* = 9.3 Hz, 1H), 6.49 (d, *J* = 4.7 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.15, 147.39, 138.58, 130.16, 127.24, 126.67, 126.25, 124.47, 120.57, 118.94, 112.06, 101.00, 51.36. HRMS (ESI) calcd. for $C_{13}H_{11}N_2O_2S$ $[M+H]^+$: 259.0541. Found: 259.0530.

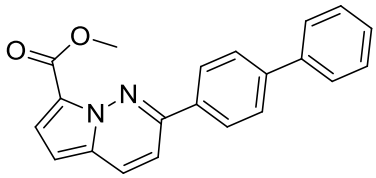


Methyl 2-(pyridin-3-yl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3q : following general procedure, this compound was purified by flash column chromatography on silica gel using EtOAc in a 79% yield as a yellow solid (M. p. = 127−129 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.69 (s, 1H), 8.45 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.93 (d, *J* = 9.4 Hz, 1H), 7.56 (d, *J* = 4.7 Hz, 1H), 7.43 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.27 (d, *J* = 9.4 Hz, 1H), 6.57 (d, *J* = 4.7 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.07, 150.77, 148.59, 148.02, 134.50, 131.89, 130.23, 127.80, 123.88, 121.10, 119.24, 111.15, 101.26, 51.48. HRMS (ESI) calcd. for $C_{14}H_{12}N_3O_2$ $[M+H]^+$:

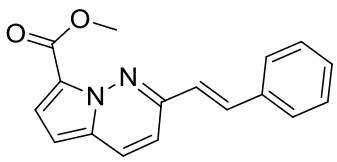
254.0930. Found: 254.0920.



Methyl 2-(naphthalen-2-yl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3r : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 96% yield as a light yellow solid (M. p. = 118−120 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.94 – 7.88 (m, 2H), 7.58 (d, *J* = 4.7 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.45 (d, *J* = 9.4 Hz, 1H), 6.56 (d, *J* = 4.6 Hz, 1H), 4.01 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.14, 150.73, 133.96, 133.28, 133.19, 130.24, 128.78, 128.65, 127.70, 127.21, 126.90, 126.51, 126.41, 124.17, 120.72, 118.96, 111.89, 100.82, 51.35. HRMS (ESI) calcd. for $C_{19}H_{15}N_2O_2$ $[M+H]^+$: 303.1134. Found: 303.1122.



Methyl 2-([1,1'-biphenyl]-4-yl)pyrrolo[1,2-*b*]pyridazine-7-carboxylate 3s : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 74% yield as a yellow solid (M. p. = 168−170 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.3 Hz, 2H), 7.89 (d, *J* = 9.4 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.70 – 7.62 (m, 2H), 7.56 (d, *J* = 4.7 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.43 – 7.36 (m, 1H), 7.33 (d, *J* = 9.4 Hz, 1H), 6.55 (d, *J* = 4.7 Hz, 1H), 3.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.19, 150.63, 142.56, 140.35, 134.87, 130.32, 128.90, 127.74, 127.64, 127.36, 127.32, 127.14, 120.76, 119.00, 111.81, 100.87, 51.42. HRMS (ESI) calcd. for $C_{21}H_{17}N_2O_2$ $[M+H]^+$: 329.1290. Found: 329.1277.



(*E*)-methyl 2-styrylpyrrolo[1,2-*b*]pyridazine-7-carboxylate 3t : following general procedure, this compound was purified by flash column chromatography on silica gel using petroleum ether : EtOAc (30:1) in a 11% yield as a yellow solid (M. p. = 129−131 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.38 (m, 2H), 7.36 – 7.31 (m, 2H), 7.30 – 7.26 (m, 1H), 6.81 (dd, *J* = 15.8, 1.4 Hz, 1H), 6.31 (dd, *J* = 15.8, 5.9 Hz, 1H), 5.15 – 5.02 (m, 1H), 2.65 (d, *J* = 2.2 Hz, 1H), 2.19 – 2.10 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.16, 150.57, 136.03, 134.39, 130.46, 128.86, 127.23, 126.78, 125.84, 120.59, 118.87, 111.29, 101.13, 51.44. HRMS (ESI) calcd. for $C_{17}H_{15}N_2O_2$ $[M+H]^+$: 279.1134. Found: 279.1123.

References:

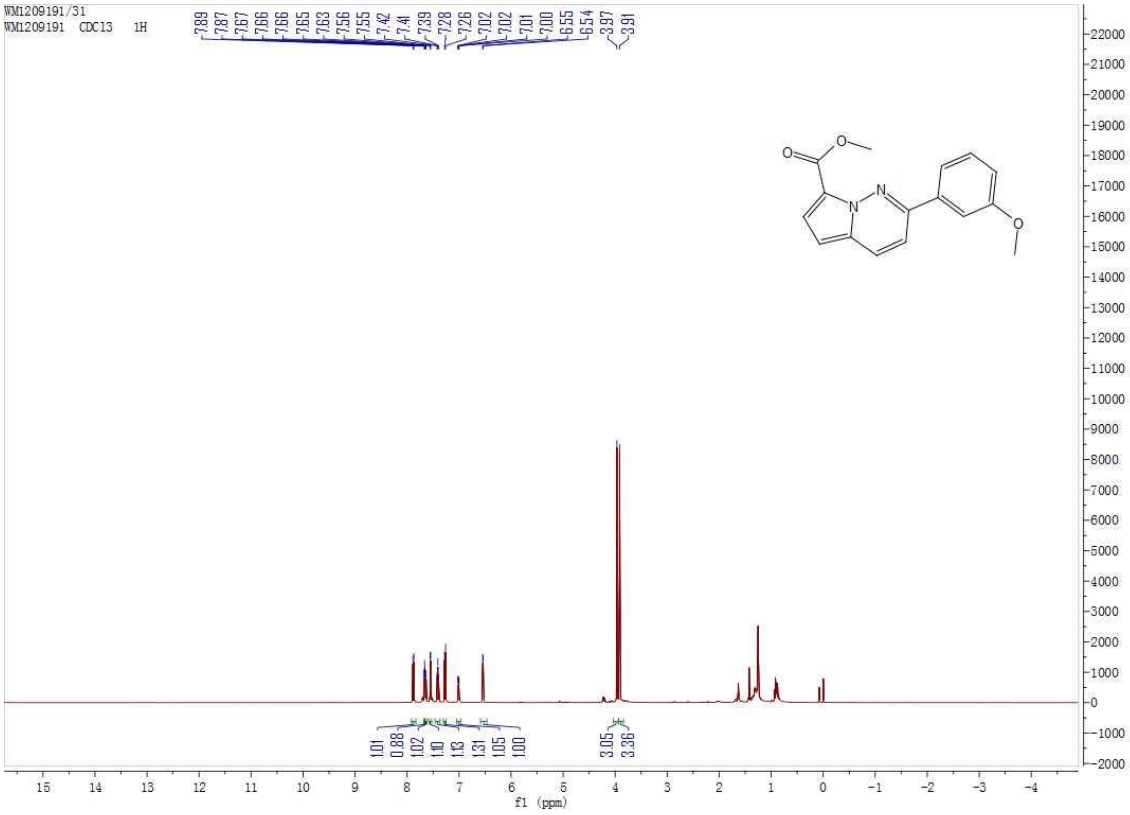
S1: N. Krause, D. Seebach, *Chem. Ber*. 1987, **120**, 1845.

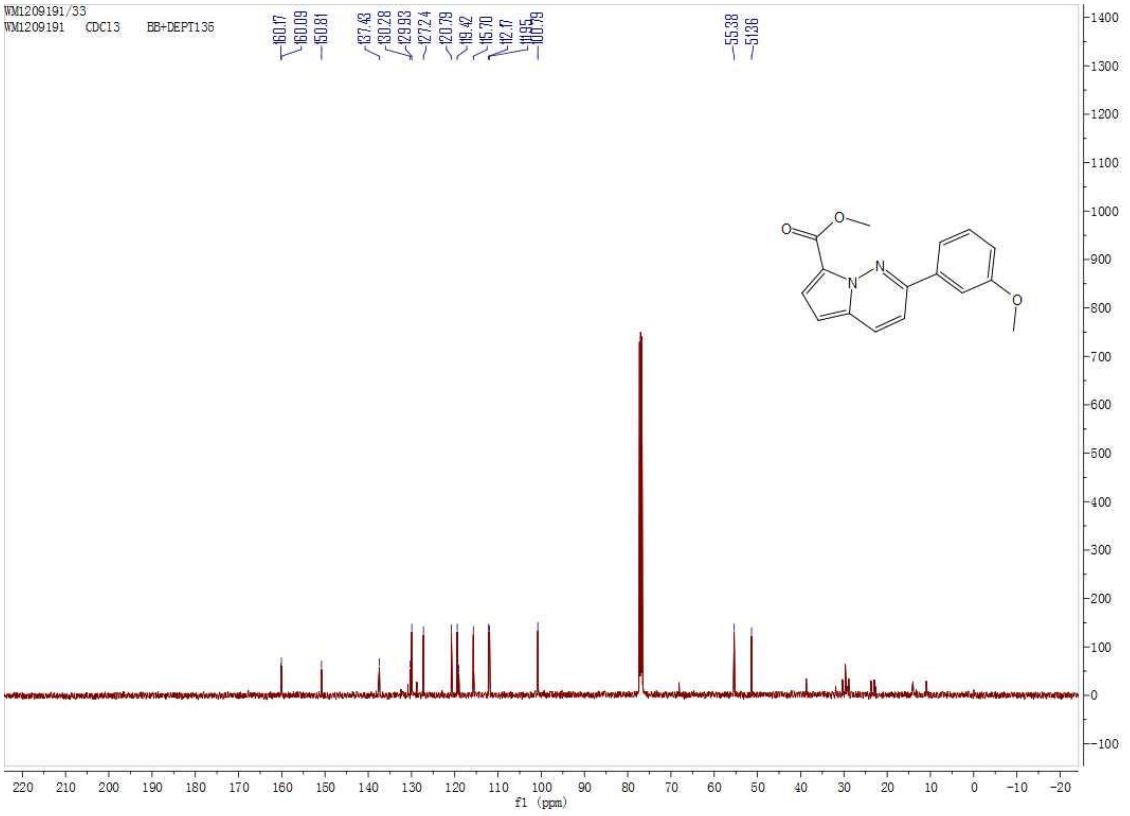
S2: B. M. Trost and G. Dong, *Chem.-Eur. J.*, 2009, **15**, 6910.

S3: US2012077814A1. 2012, pp. 25.

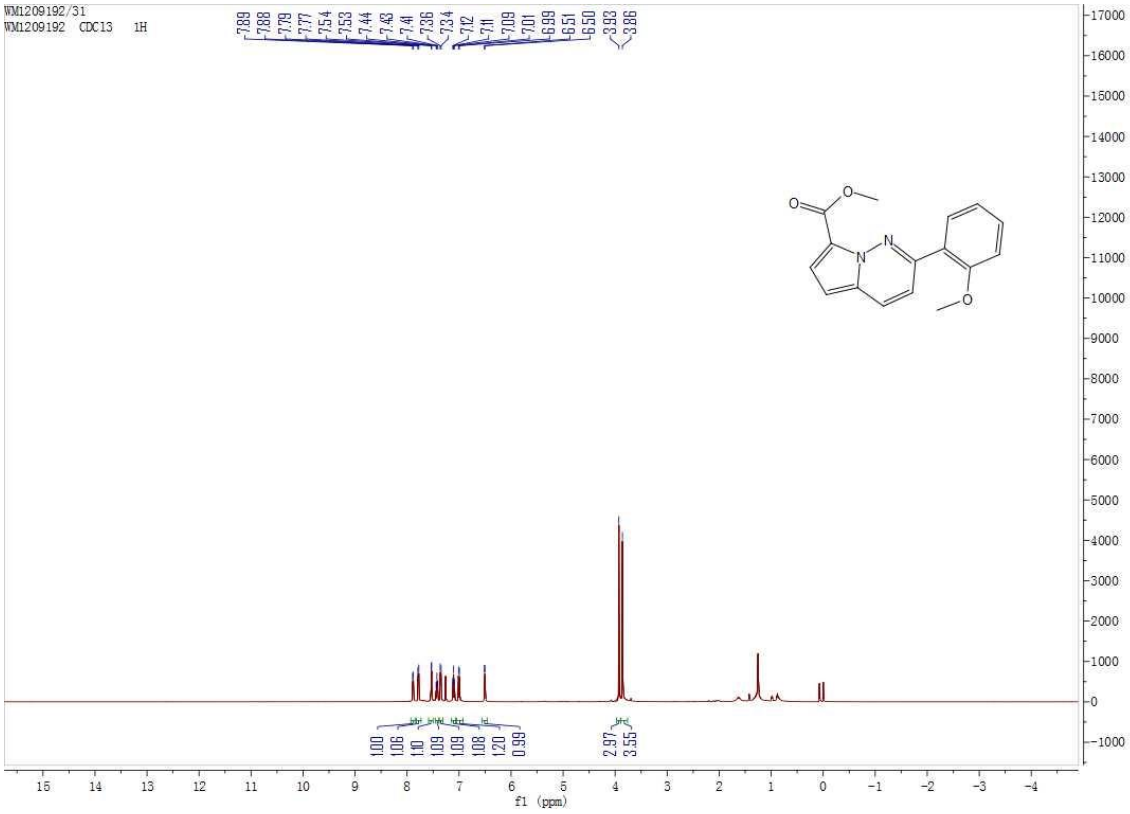
^{1}H and ^{13}C NMR Spectra of Compounds

Compound 3a





Compound 3b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7.12
7.11
7.09
7.01
6.99
6.51
6.50
3.93
3.86
1.00
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1.10
1.09
1.09
1.08
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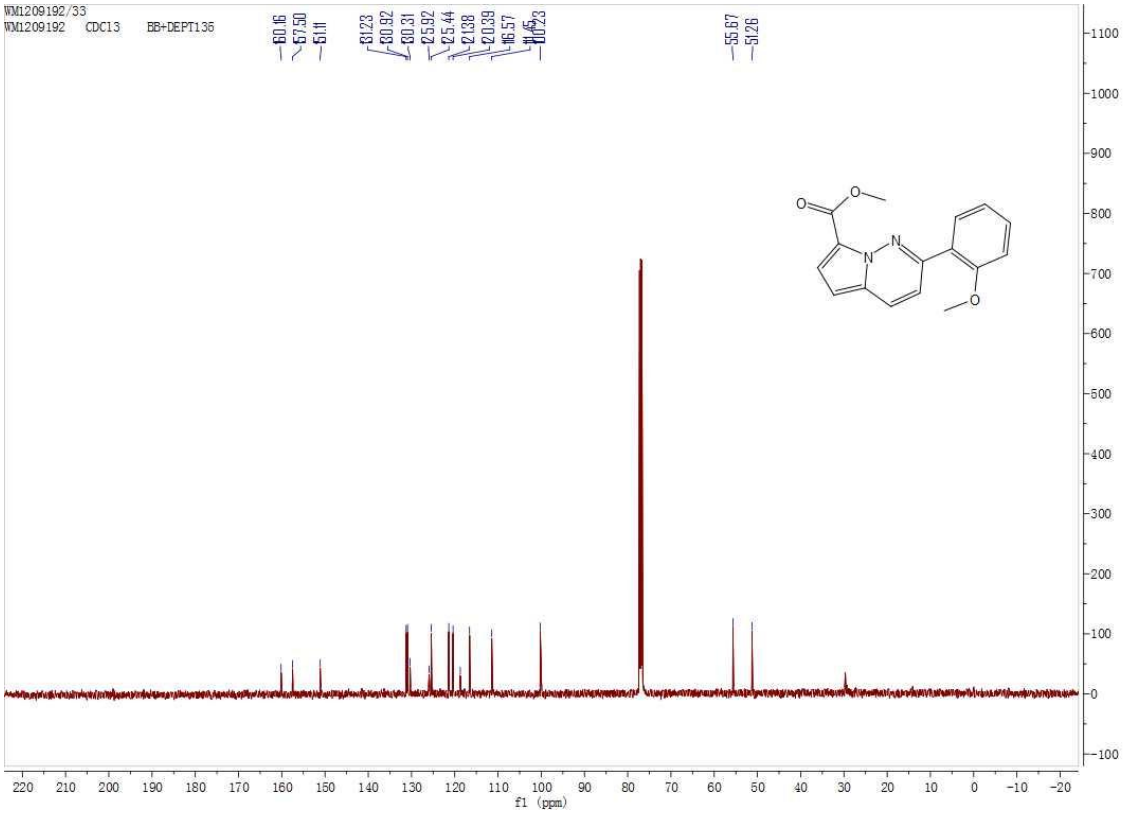
0.99
2.97
3.55
f1 (ppm)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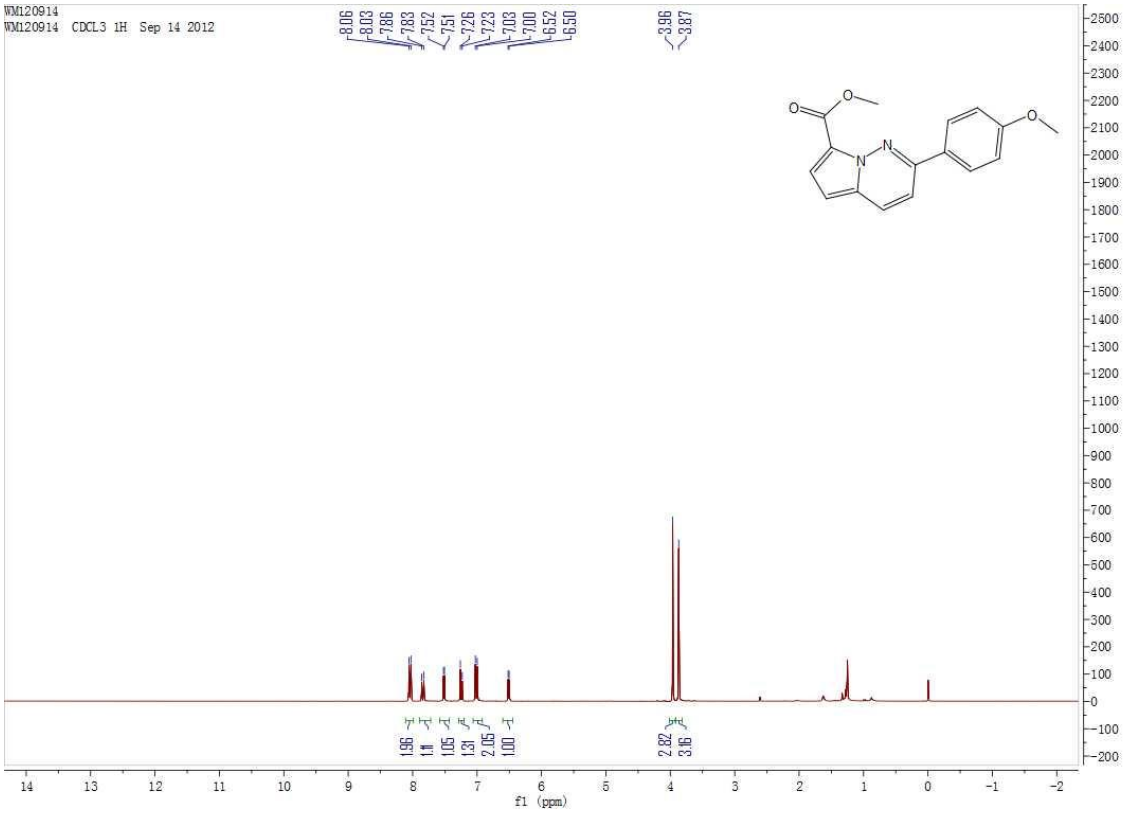
55.67
51.26
f1 (ppm)

Compound 3c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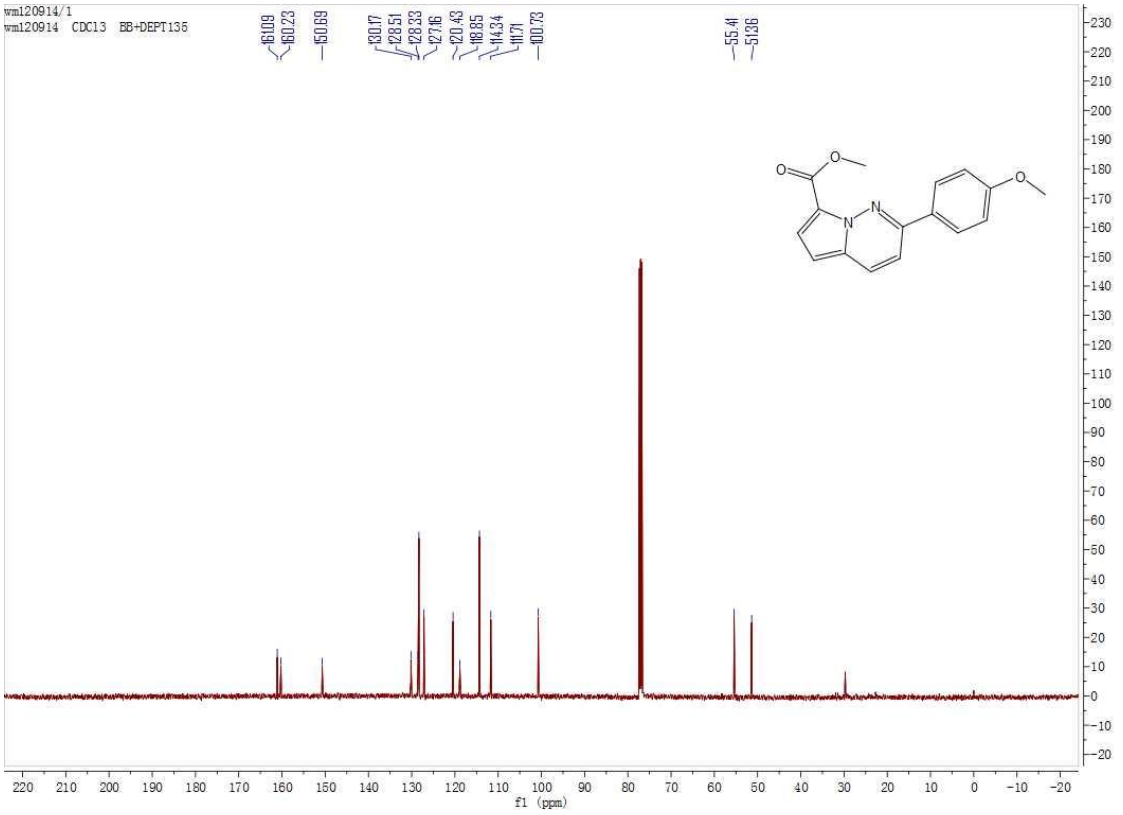
f1 (ppm)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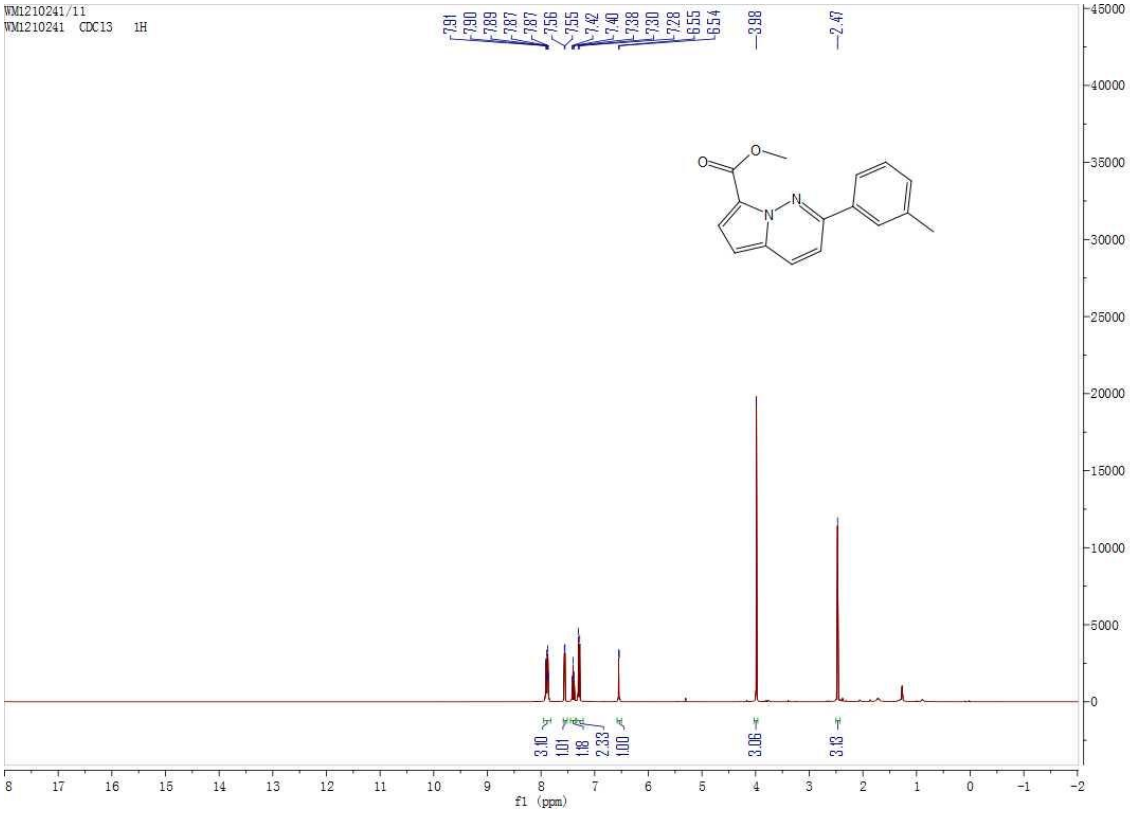
f1 (ppm)

Compound 3d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1.00
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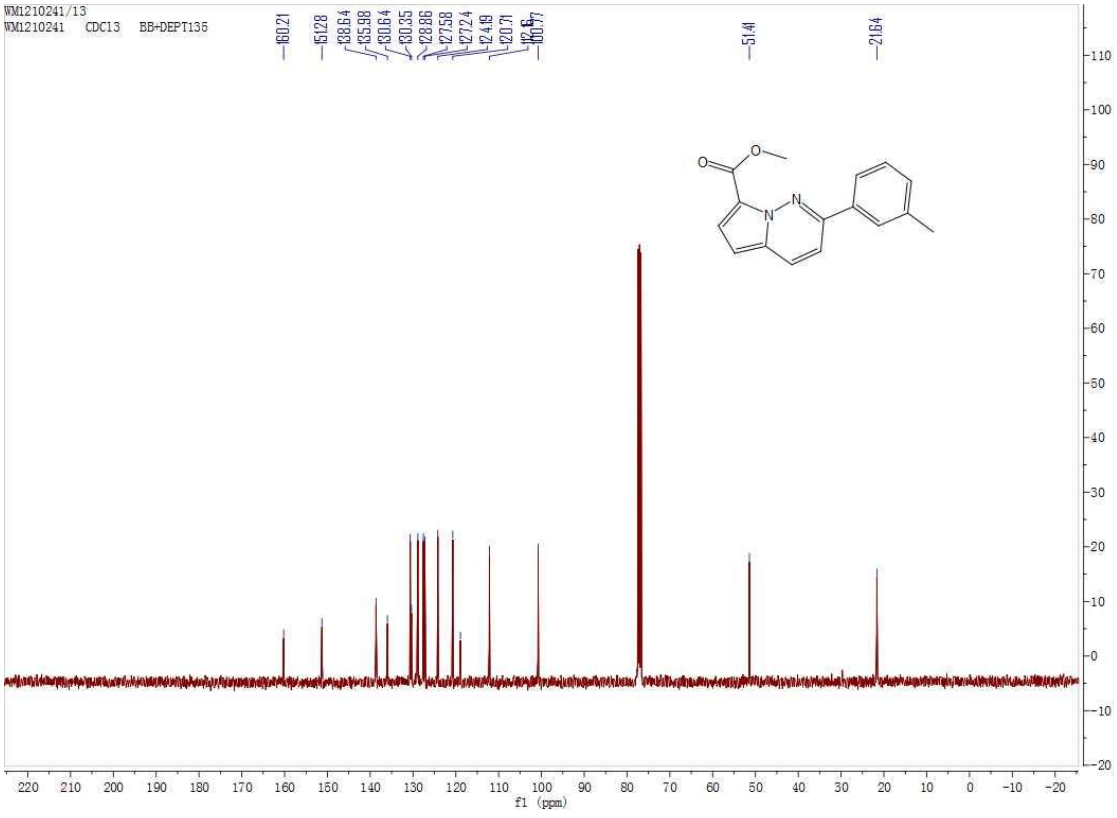
3.63
f1 (ppm)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60.77
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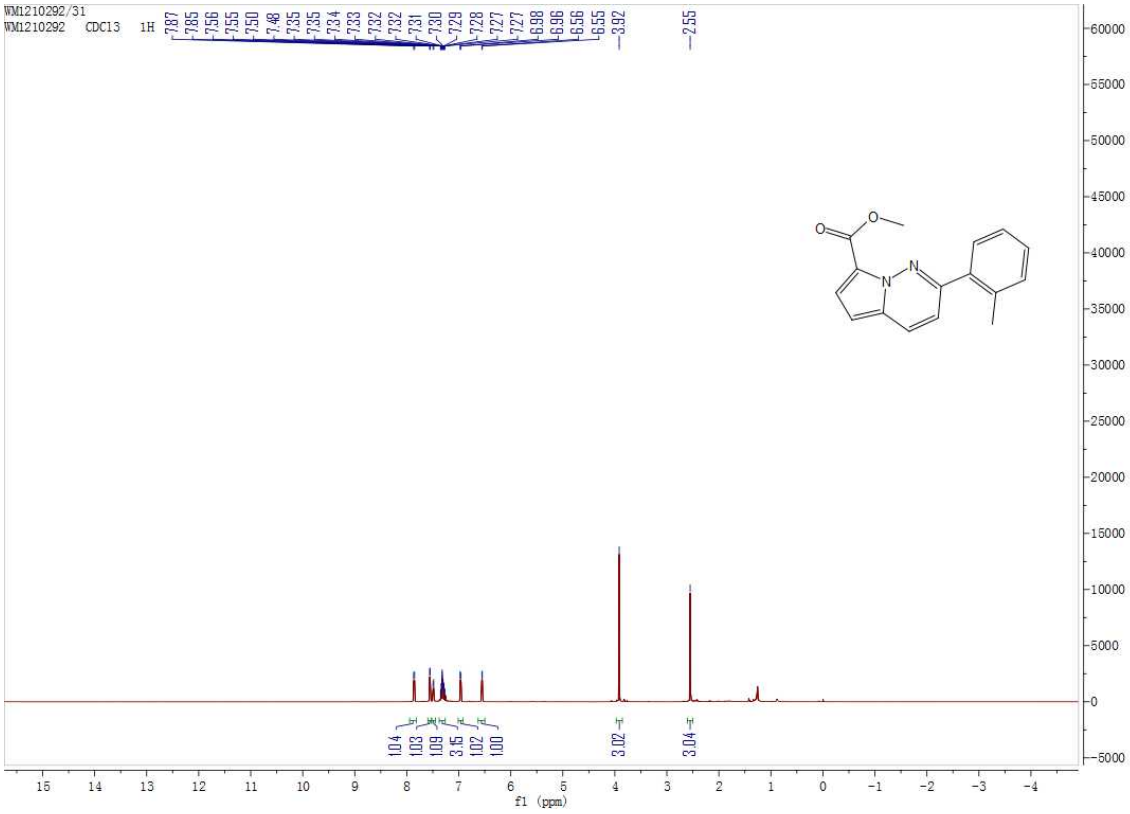
21.64
f1 (ppm)

Compound 3e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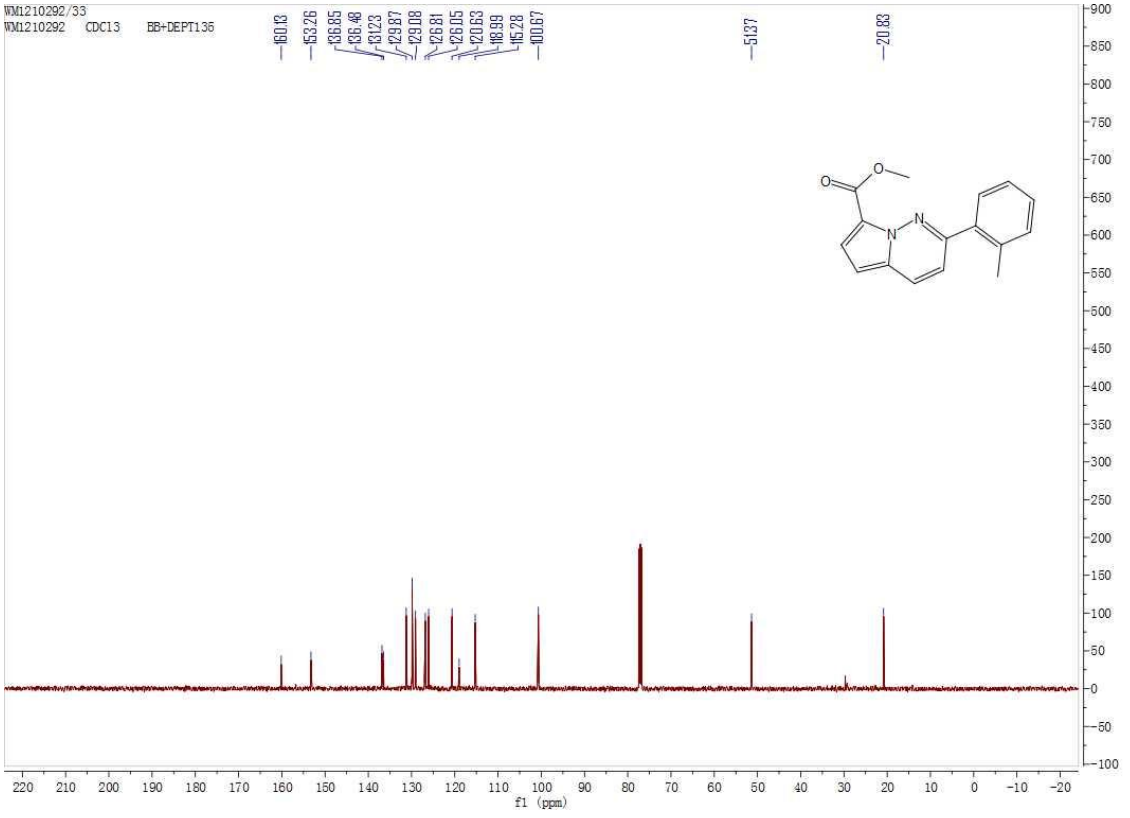
f1 (ppm)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126.05
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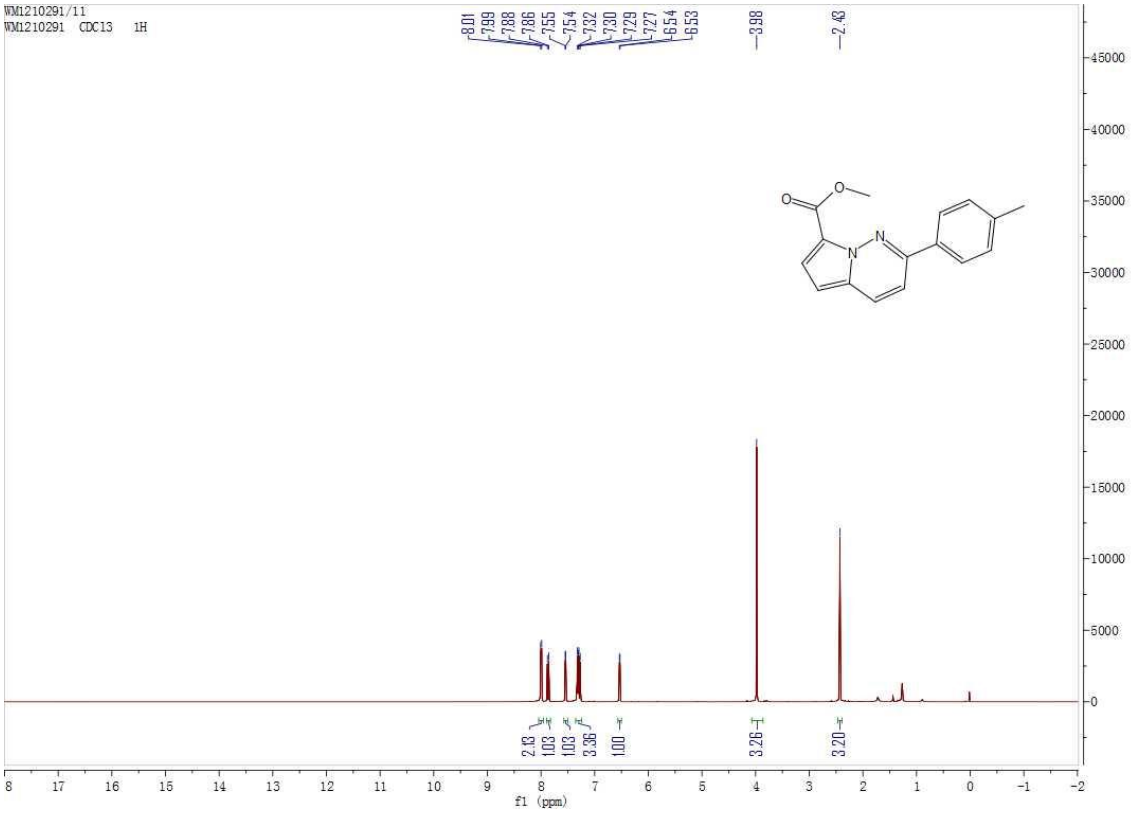
f1 (ppm)

Compound 3f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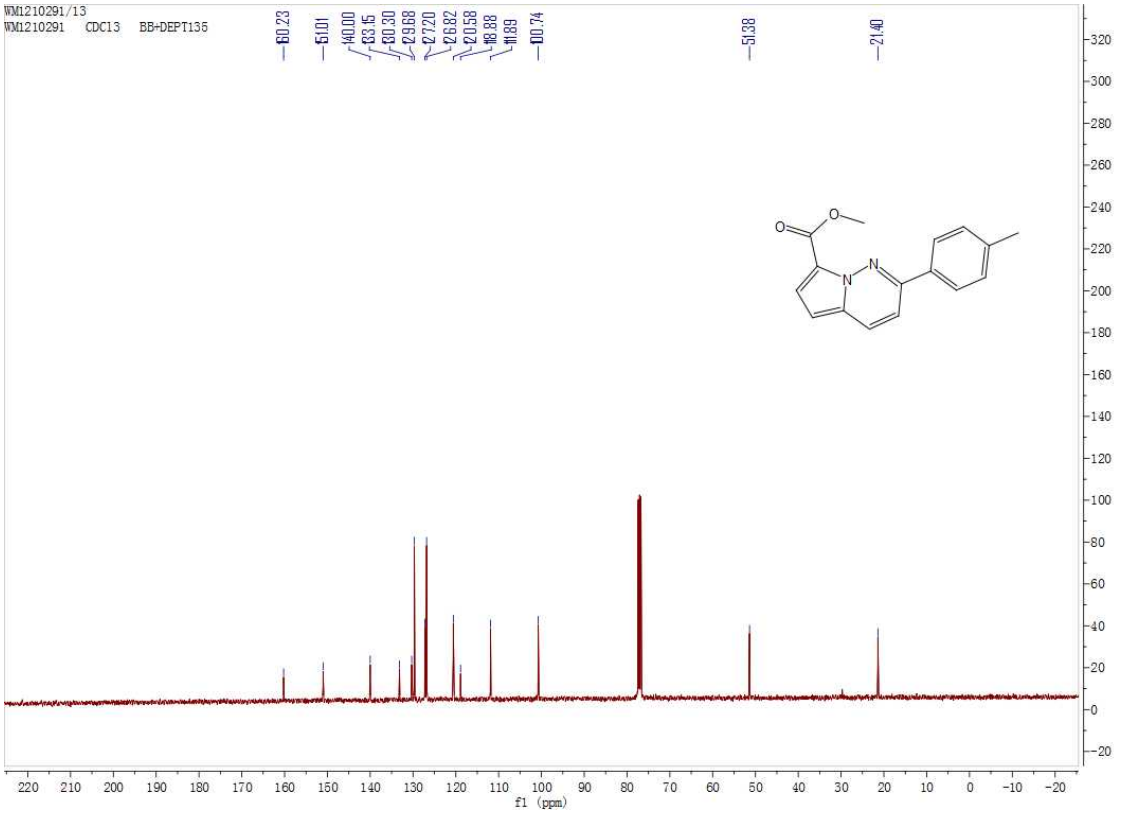
f1 (ppm)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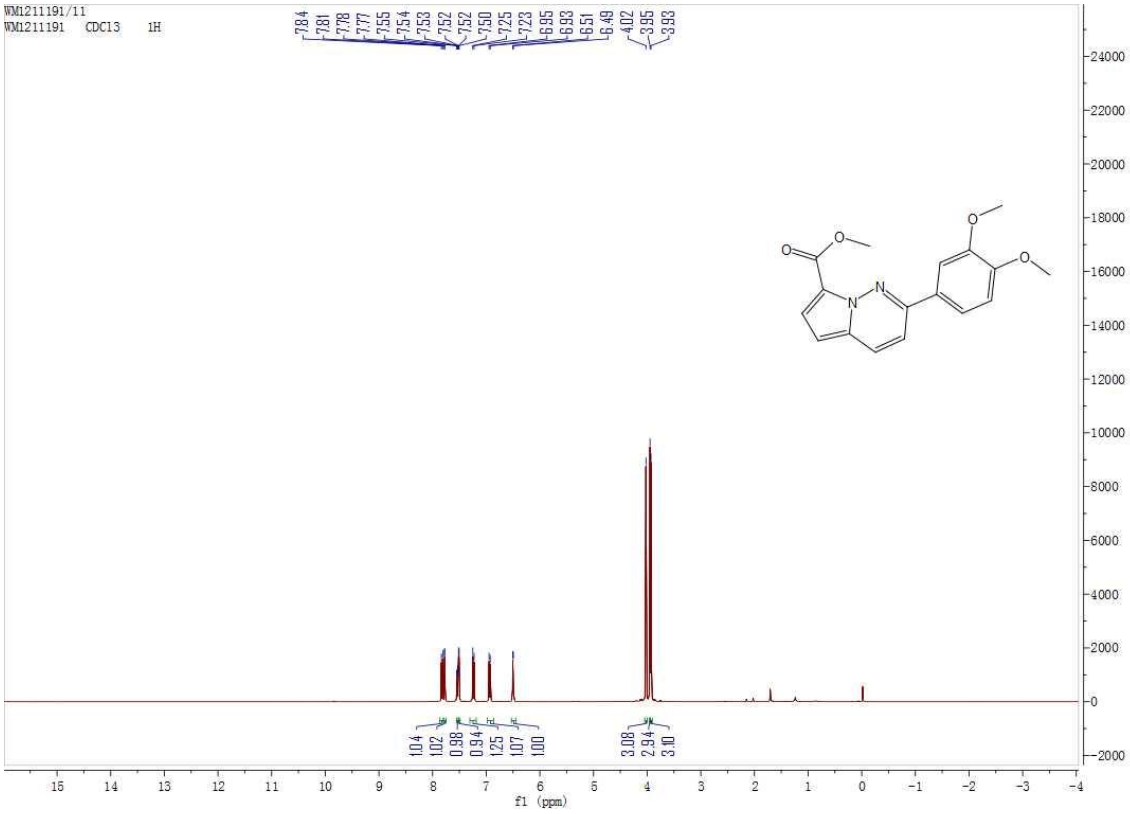
f1 (ppm)

Compound 3g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7.25
7.23
6.95
6.93
6.51
6.49
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3.95
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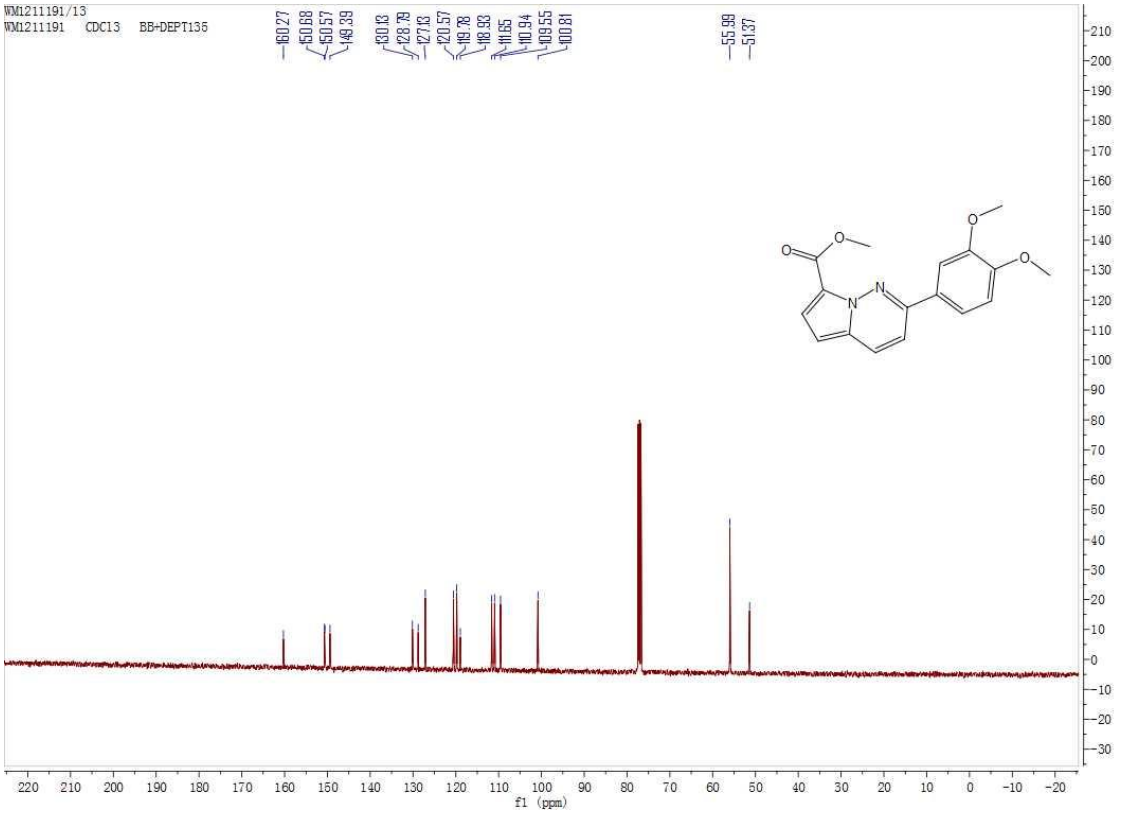
3.10
f1 (ppm)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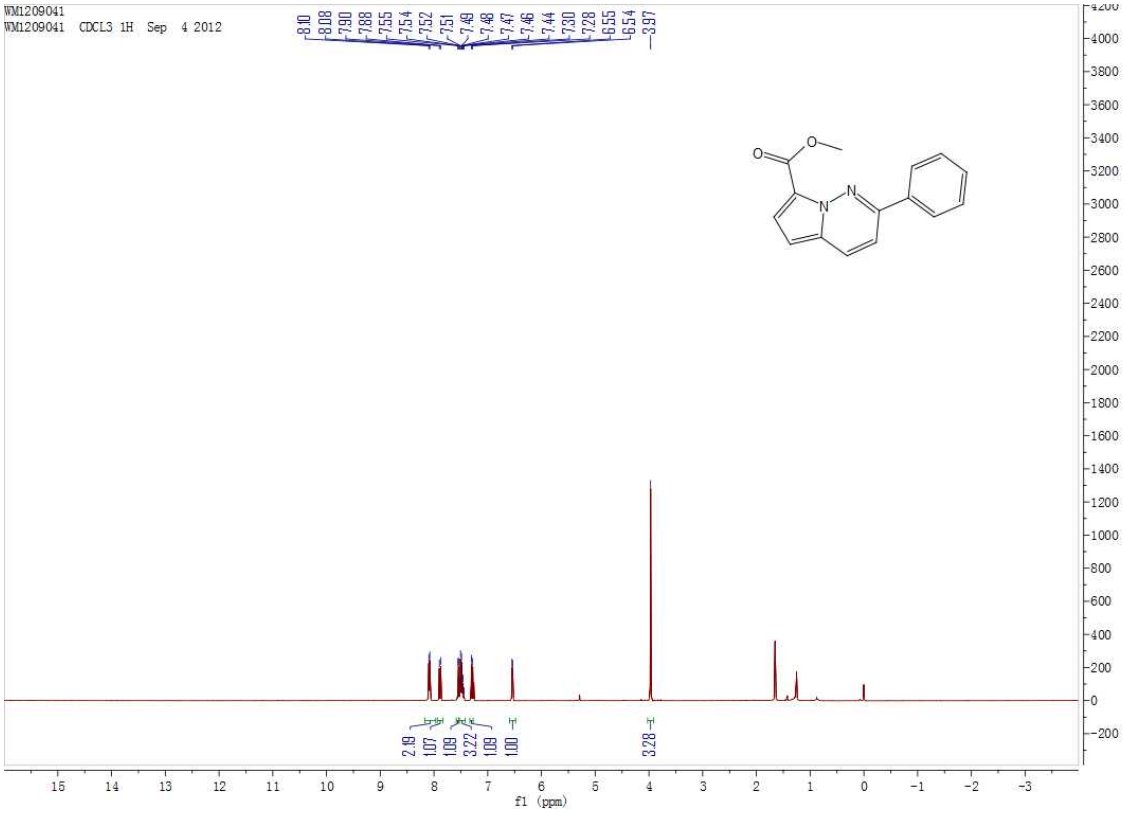
100.81
55.99
51.37
f1 (ppm)

Compound 3h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7.47
7.46
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1.09
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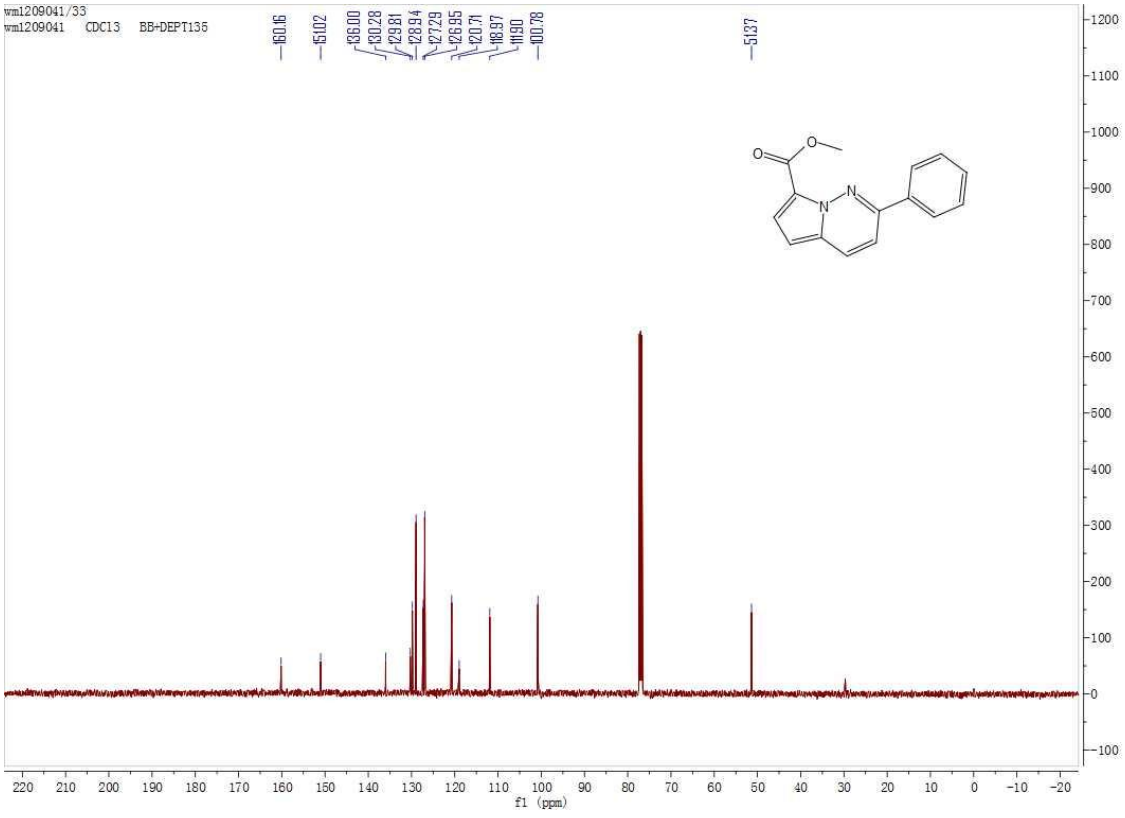
f1 (ppm)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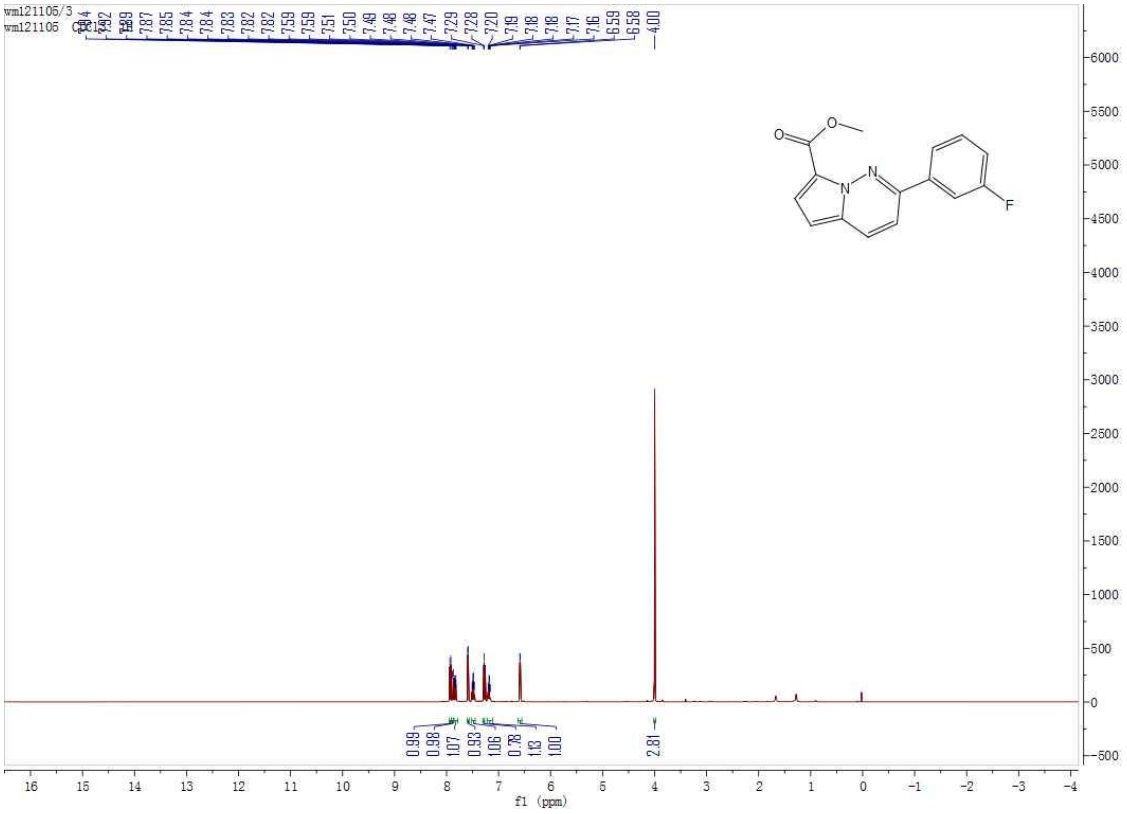
100.78
51.37
f1 (ppm)

Compound 3i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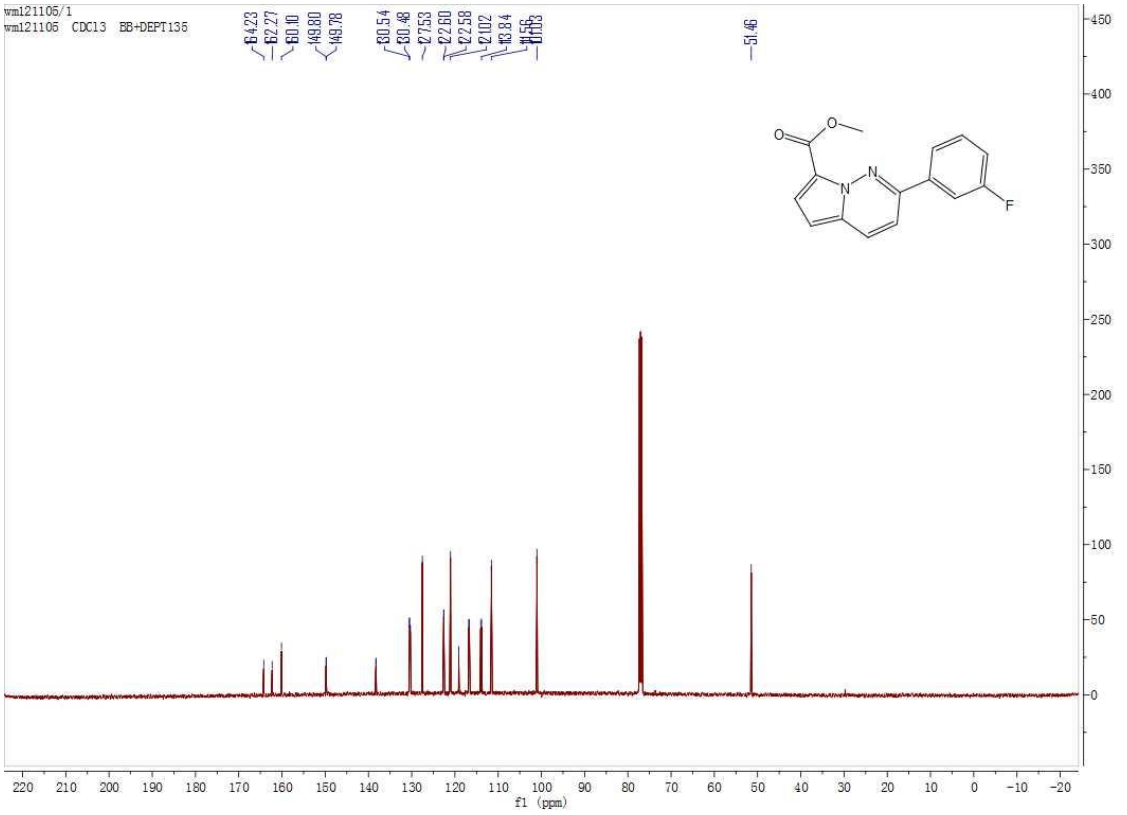
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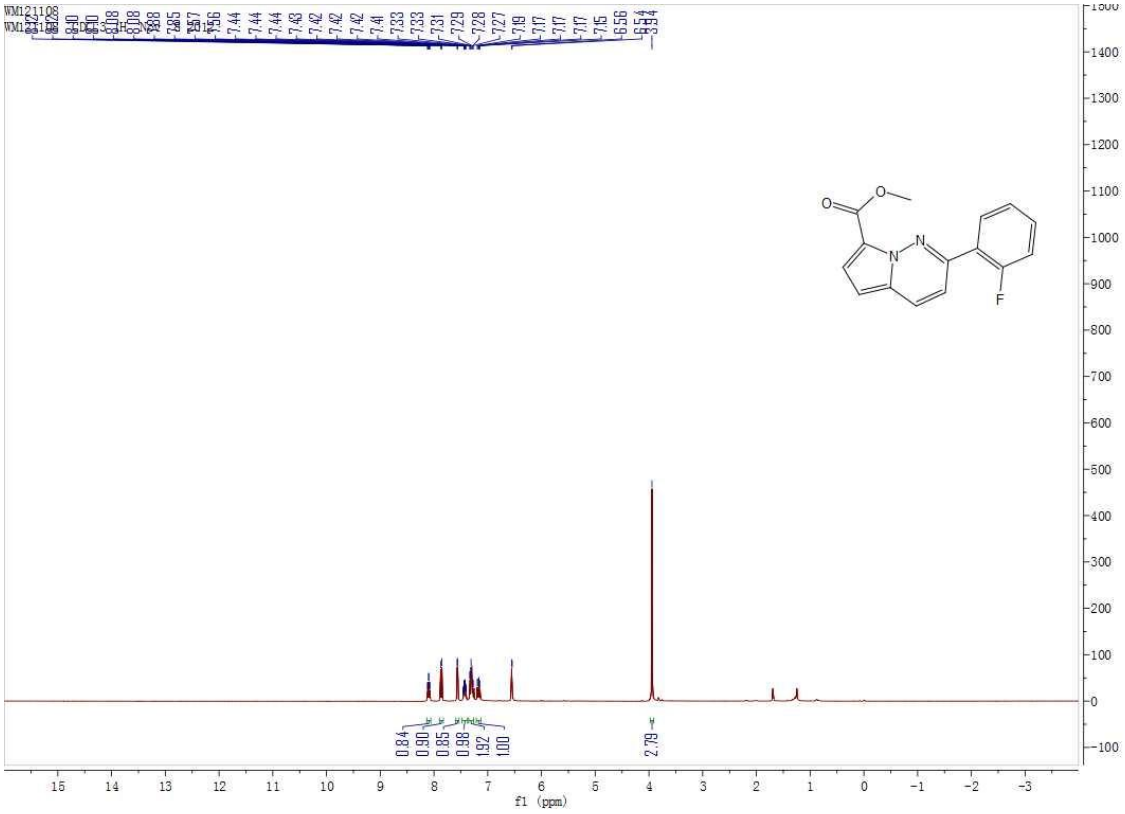
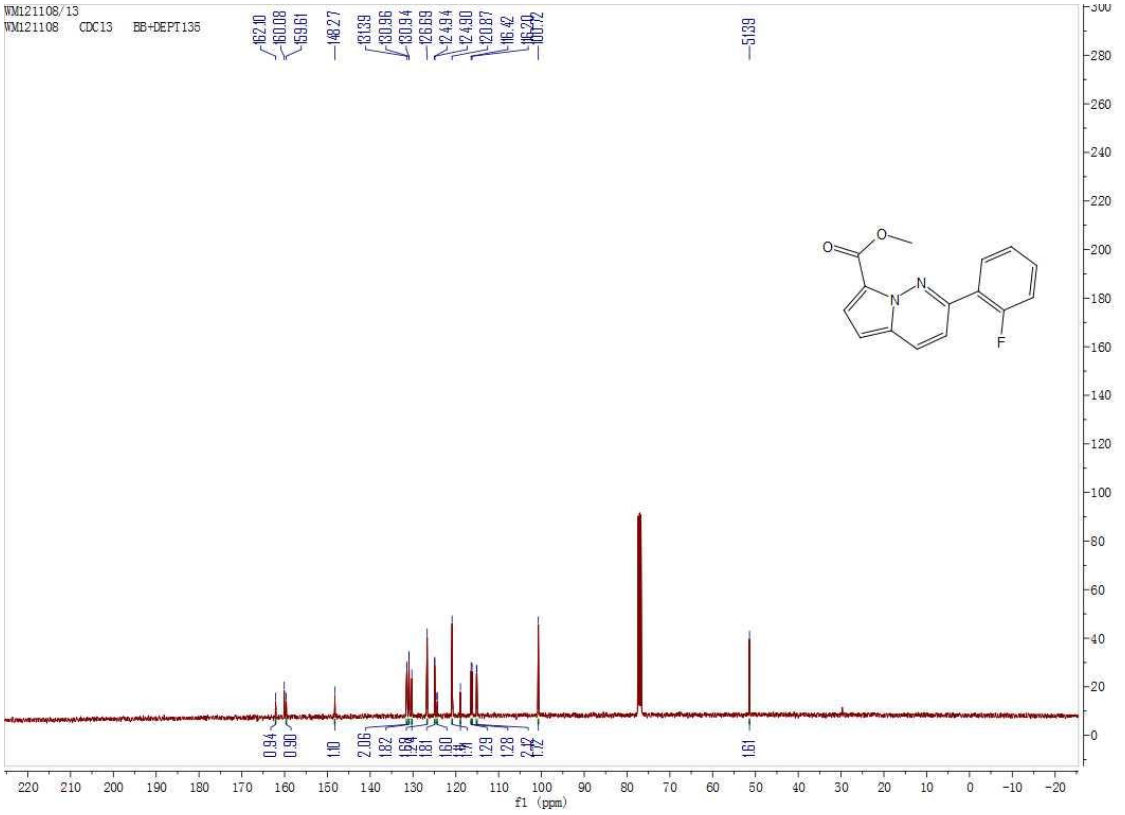
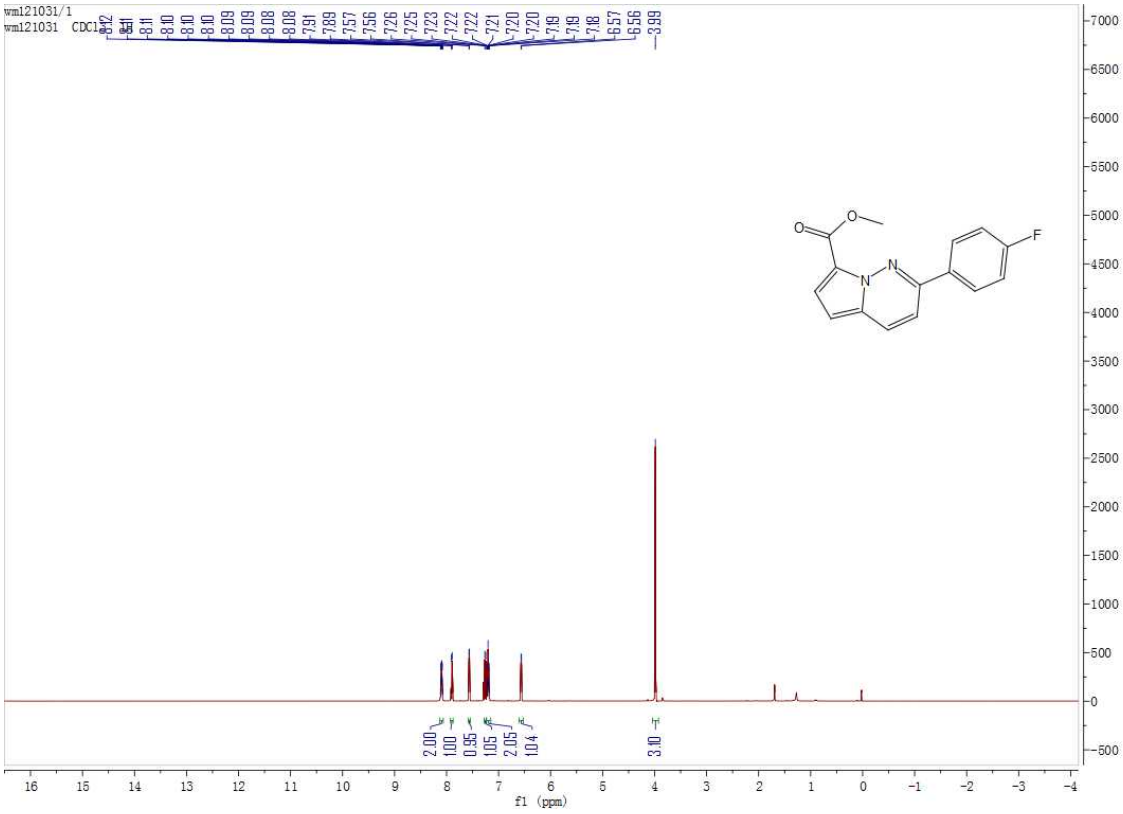
f1 (ppm)

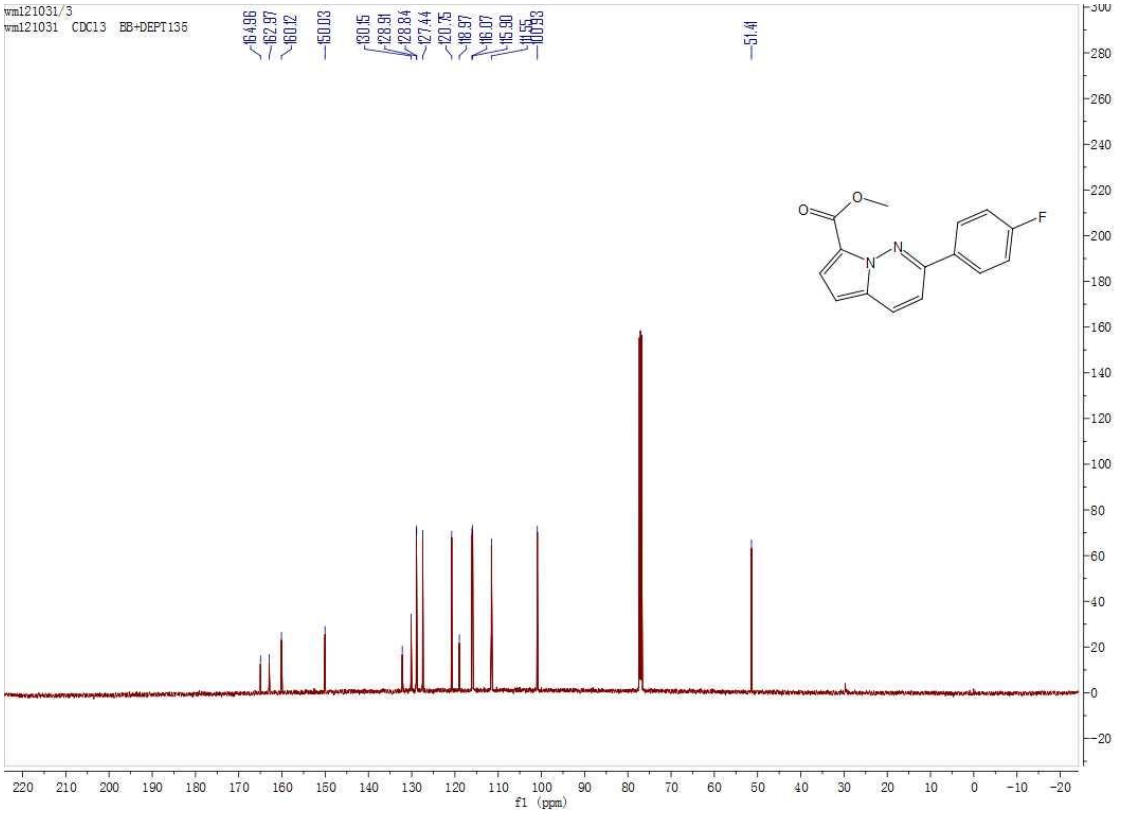
Compound 3j



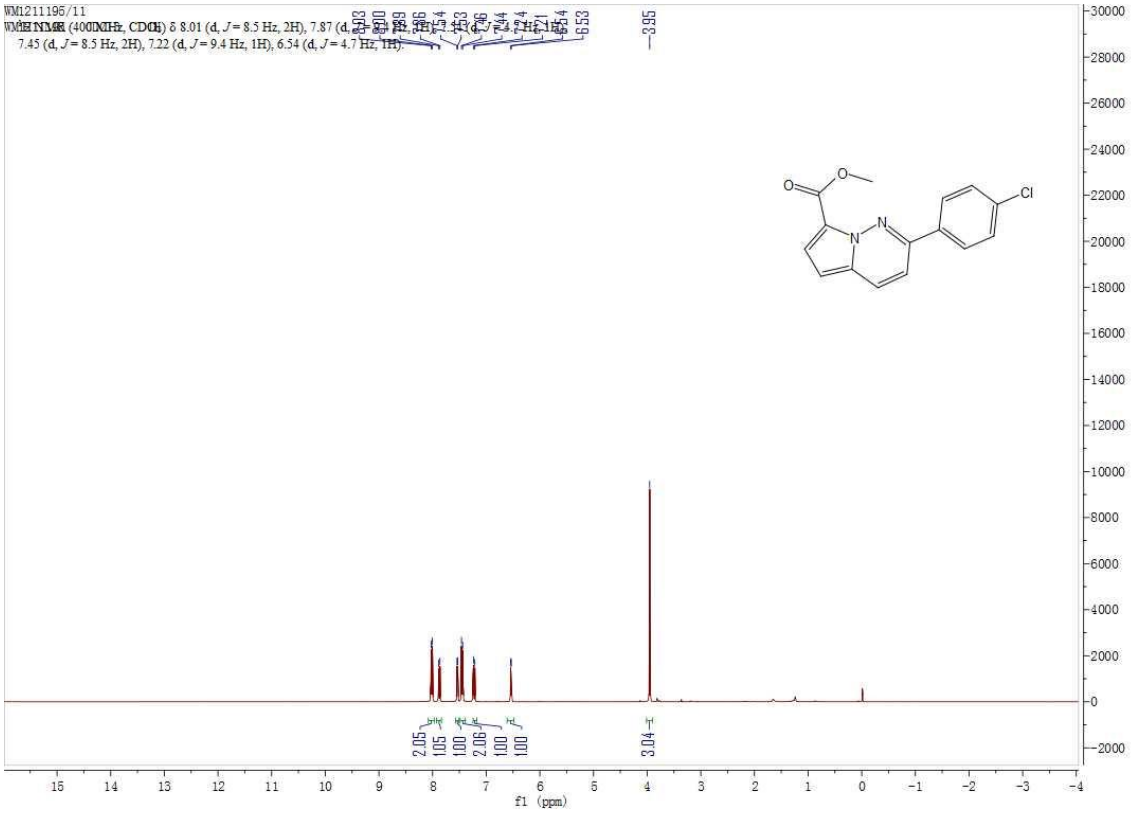


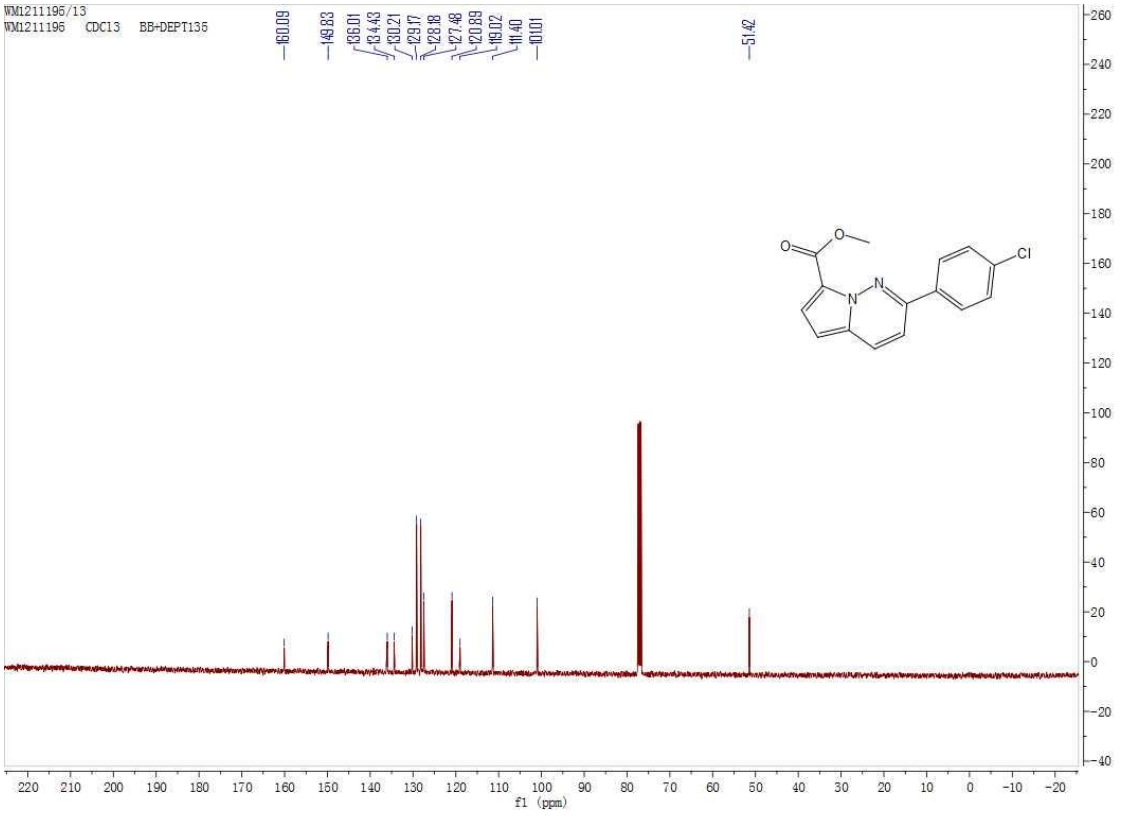
Compound 3k


wm121031/1
wm121031 CDCl3
8.12
8.11
8.10
8.10
8.10
8.09
8.09
8.08
8.08
7.91
7.89
7.57
7.56
7.26
7.25
7.23
7.22
7.22
7.21
7.20
7.20
7.19
7.19
7.18
6.57
6.56
3.99
2.00
1.00
0.95
1.05
2.05
1.04
3.10
O
O
N
N
F
f1 (ppm)

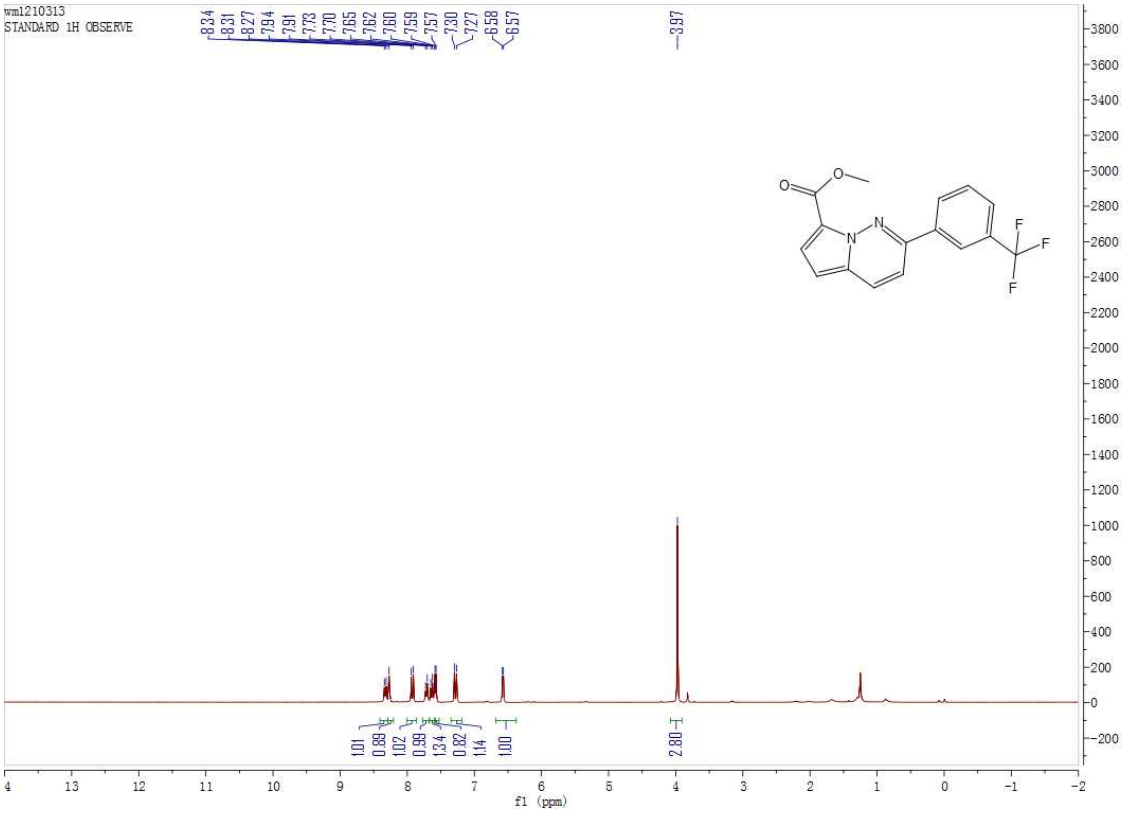

wm121031/3
wm121031 CDCl3 BB+DEPT135
164.96
162.97
160.12
150.03
130.45
128.91
128.84
127.44
120.75
118.97
116.07
115.90
101.55
100.93
51.41
O
O
N
N
F
f1 (ppm)

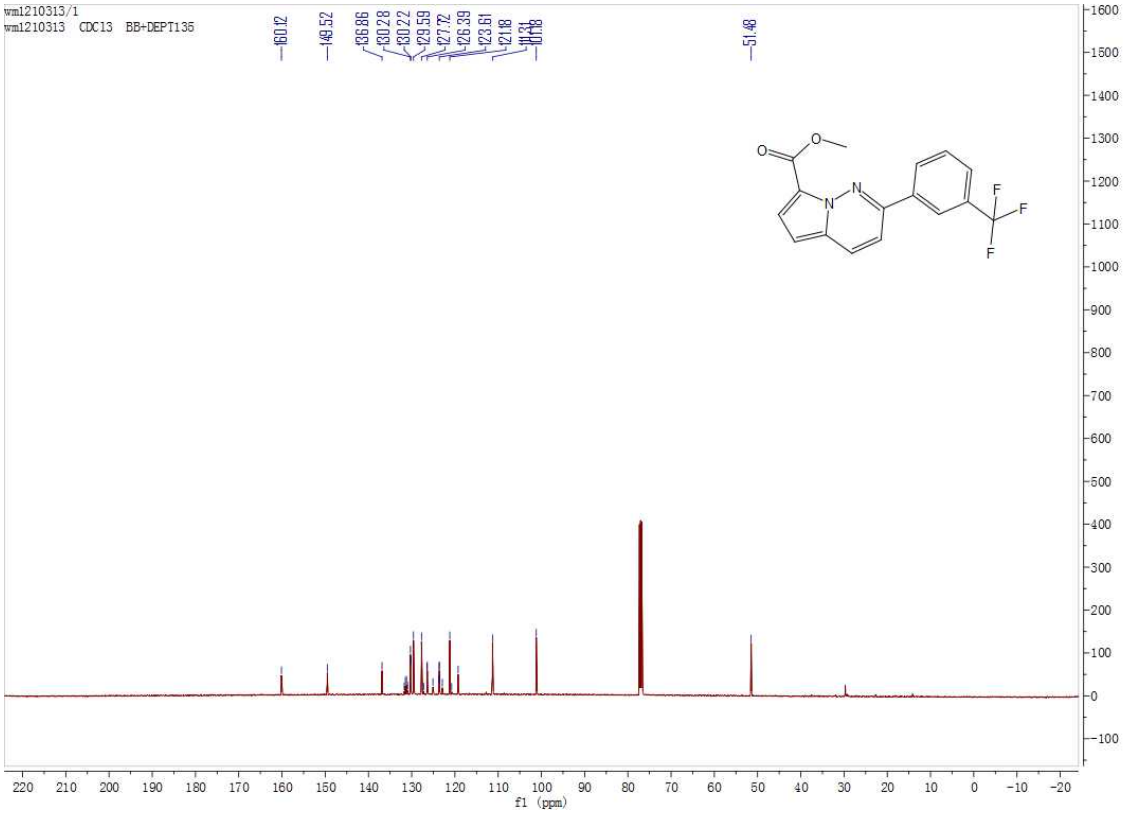
Compound 3l


WM1211195/11
7.45 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 9.4 Hz, 1H), 6.54 (d, J = 4.7 Hz, 1H).
3.95
2.05
1.05
1.00
2.06
1.00
1.00
3.04
f1 (ppm)

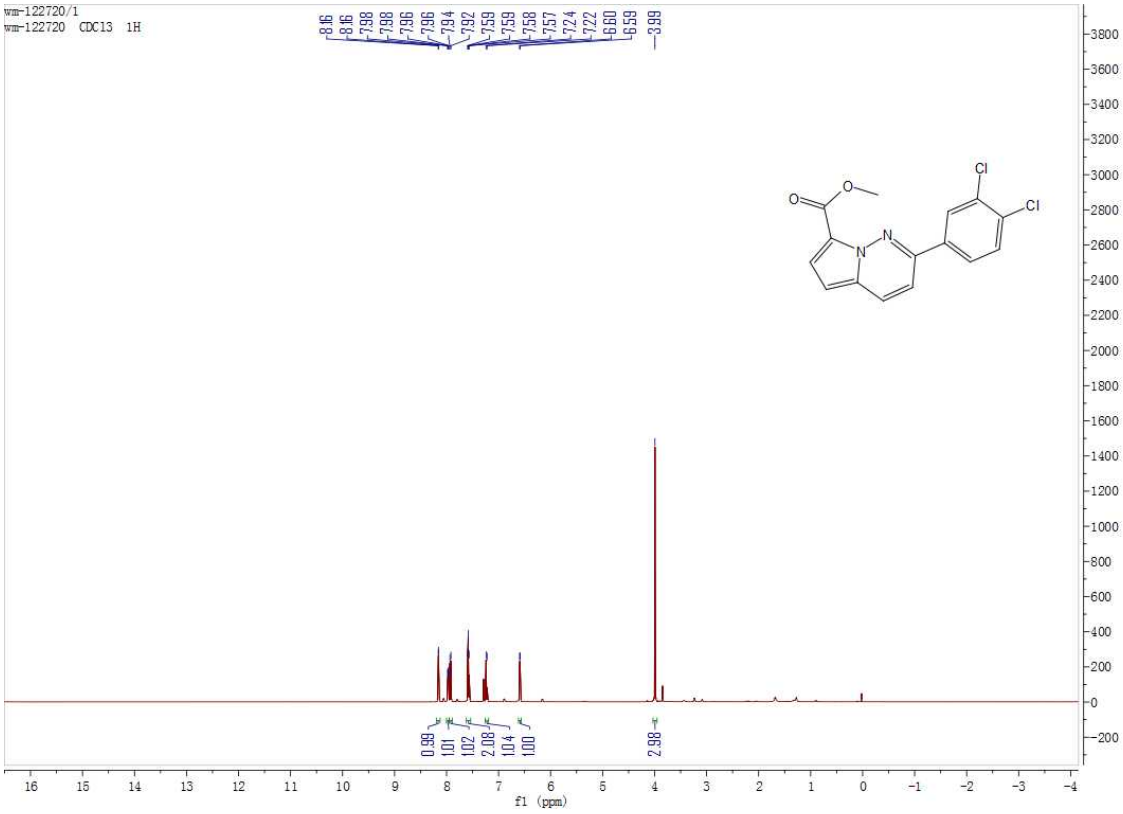

WM1211195/13
WM1211195 CDCl3 BB-DEPT135
160.09
149.83
136.01
134.43
130.21
129.17
128.18
127.48
120.89
119.02
111.40
101.01
51.42
f1 (ppm)

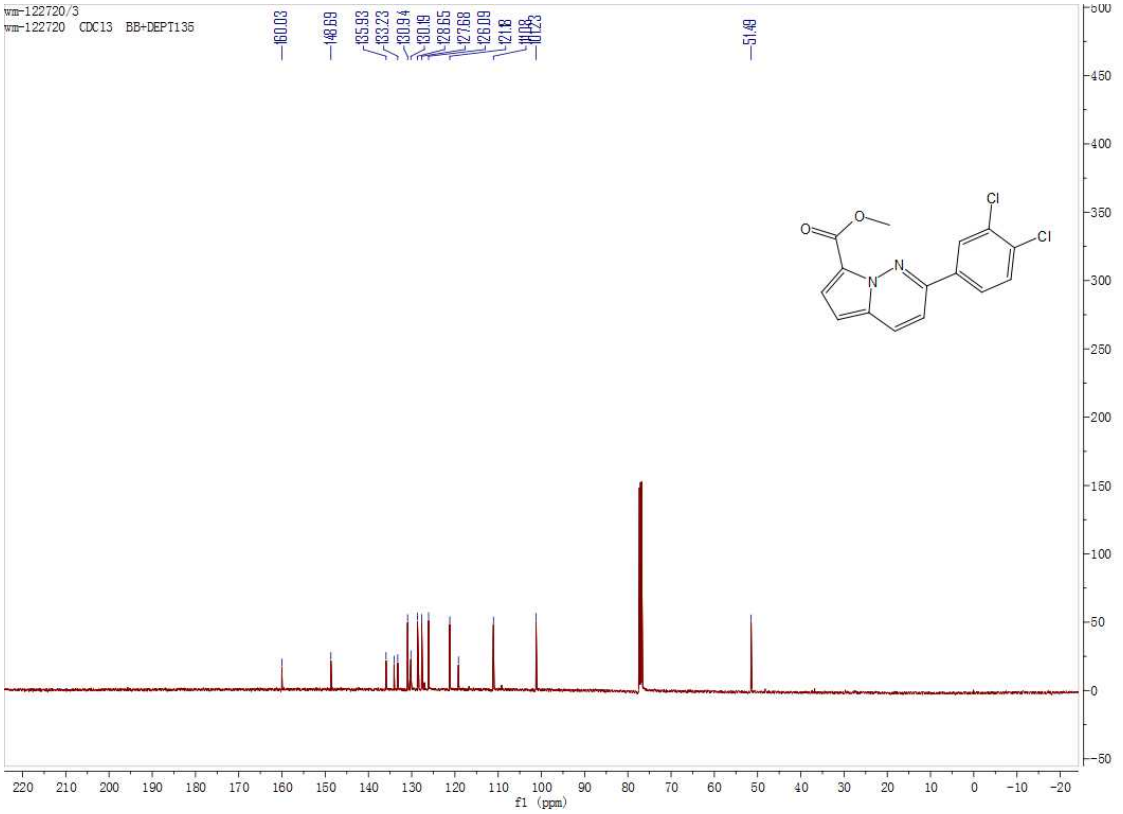
Compound 3m


wm1210313
STANDARD 1H OBSERVE
8.34
8.31
8.27
7.94
7.91
7.73
7.70
7.65
7.62
7.60
7.59
7.57
7.30
7.27
6.58
6.57
3.97
1.01
0.99
1.02
0.99
1.34
0.82
1.14
1.00
2.80
f1 (ppm)

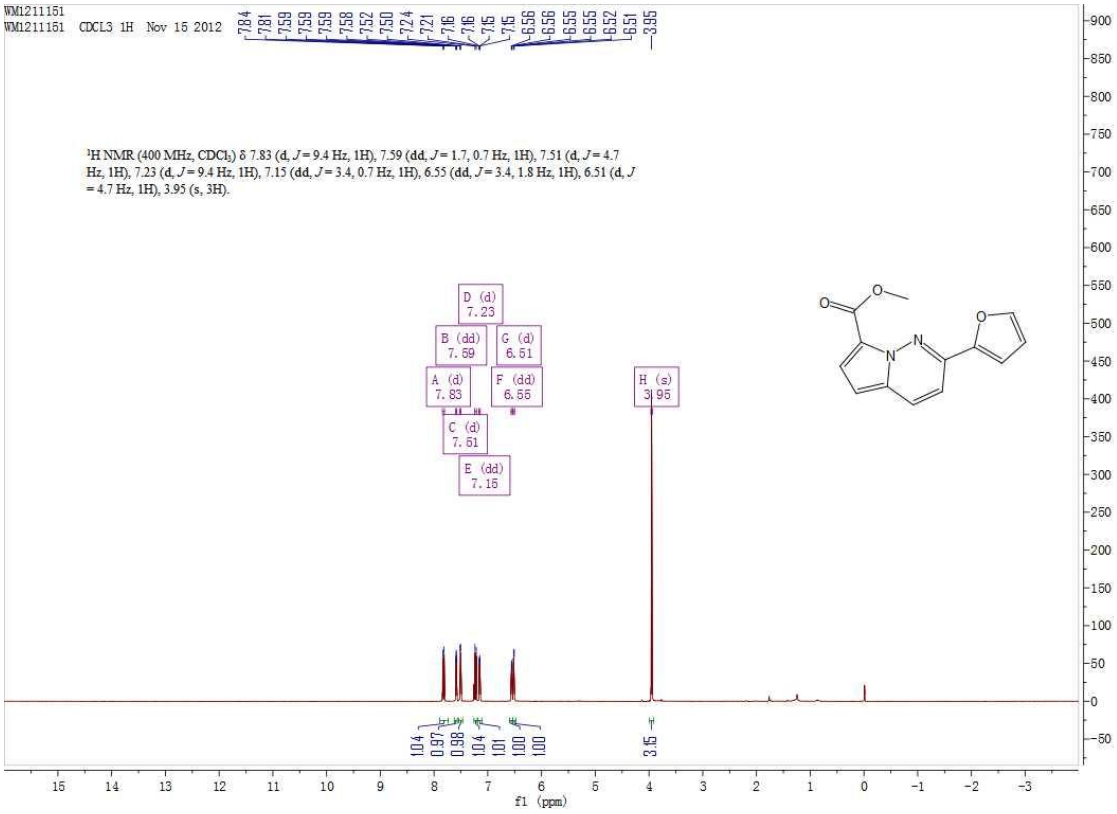

wm1210313/1
wm1210313 CDC13 BB+DEPT135
160.12
149.52
136.86
130.28
130.22
129.59
127.72
126.39
123.61
121.18
111.31
107.18
51.48
f1 (ppm)

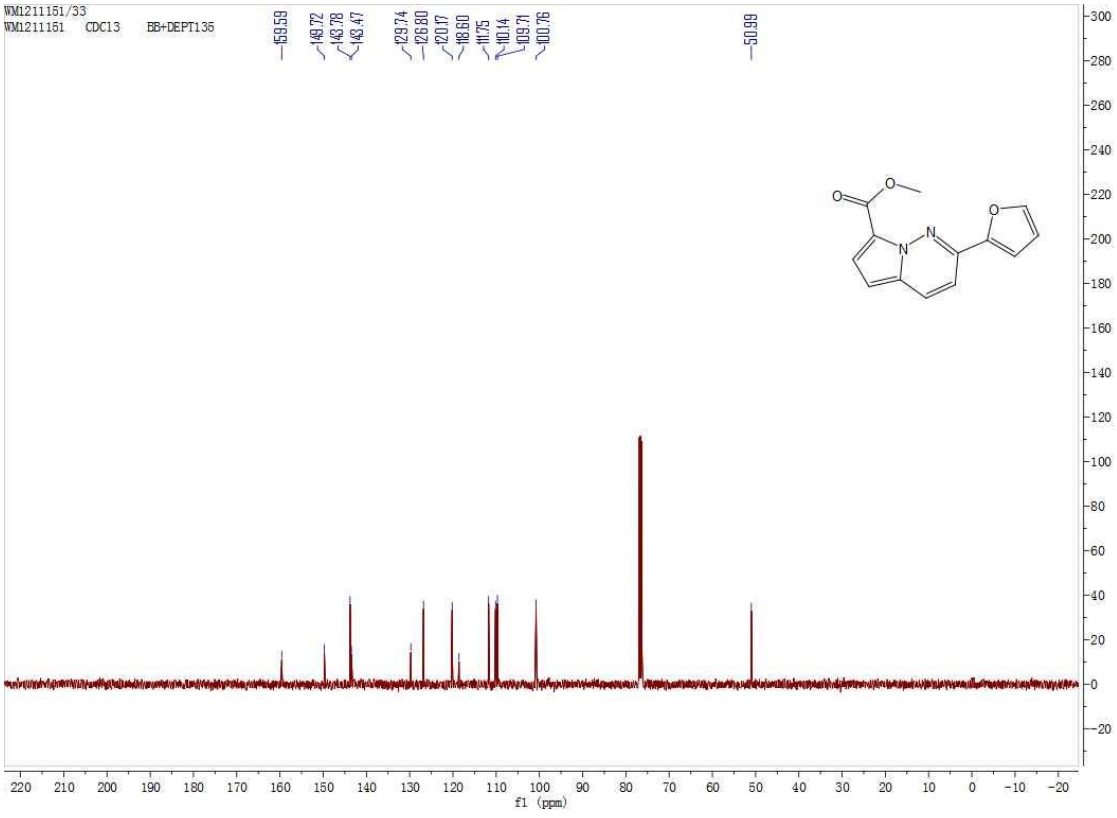
Compound 3n


wm-122720/1
wm-122720 CDC13 1H
8.16
8.16
7.98
7.98
7.96
7.96
7.94
7.92
7.59
7.59
7.58
7.57
7.24
7.22
6.60
6.59
3.99
0.99
1.01
1.02
2.08
1.04
1.00
2.98
f1 (ppm)

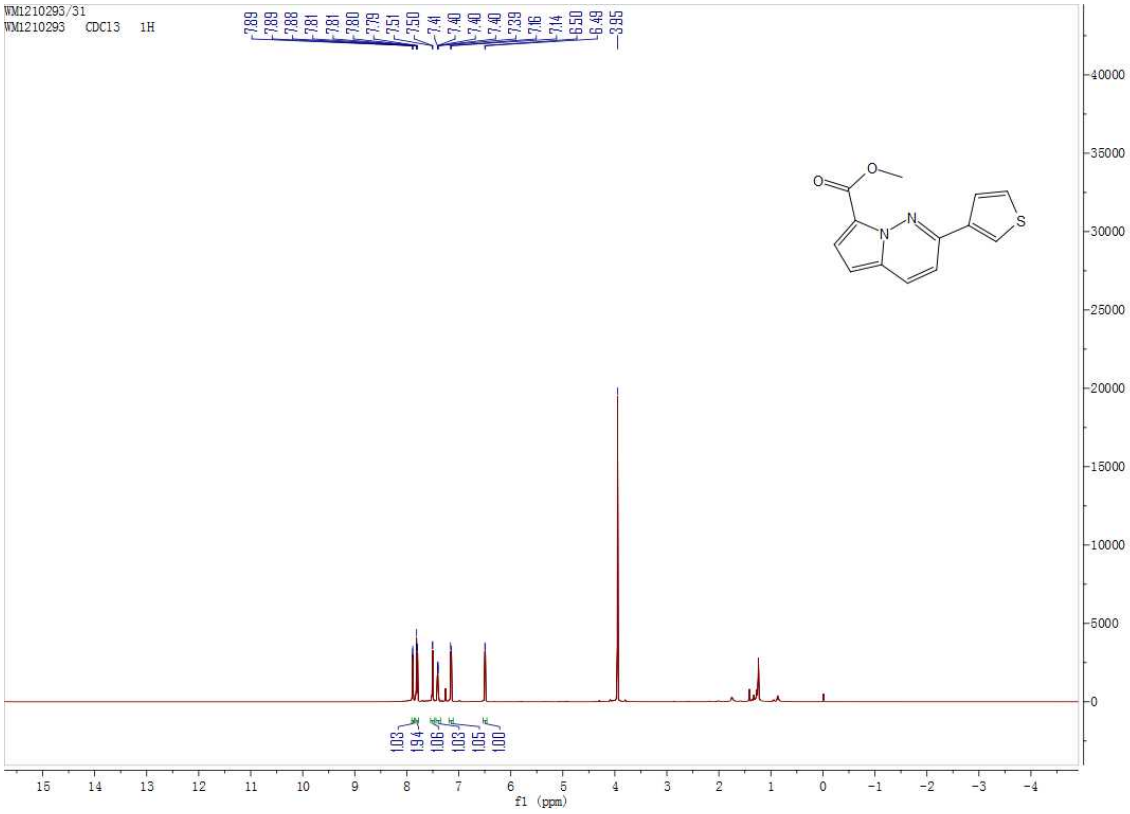

wm-122720/3
wm-122720 CDC13 BB+DEPT135
160.03
148.69
135.93
133.23
130.94
130.19
128.65
127.68
126.09
121.6
110.23
51.49
f1 (ppm)

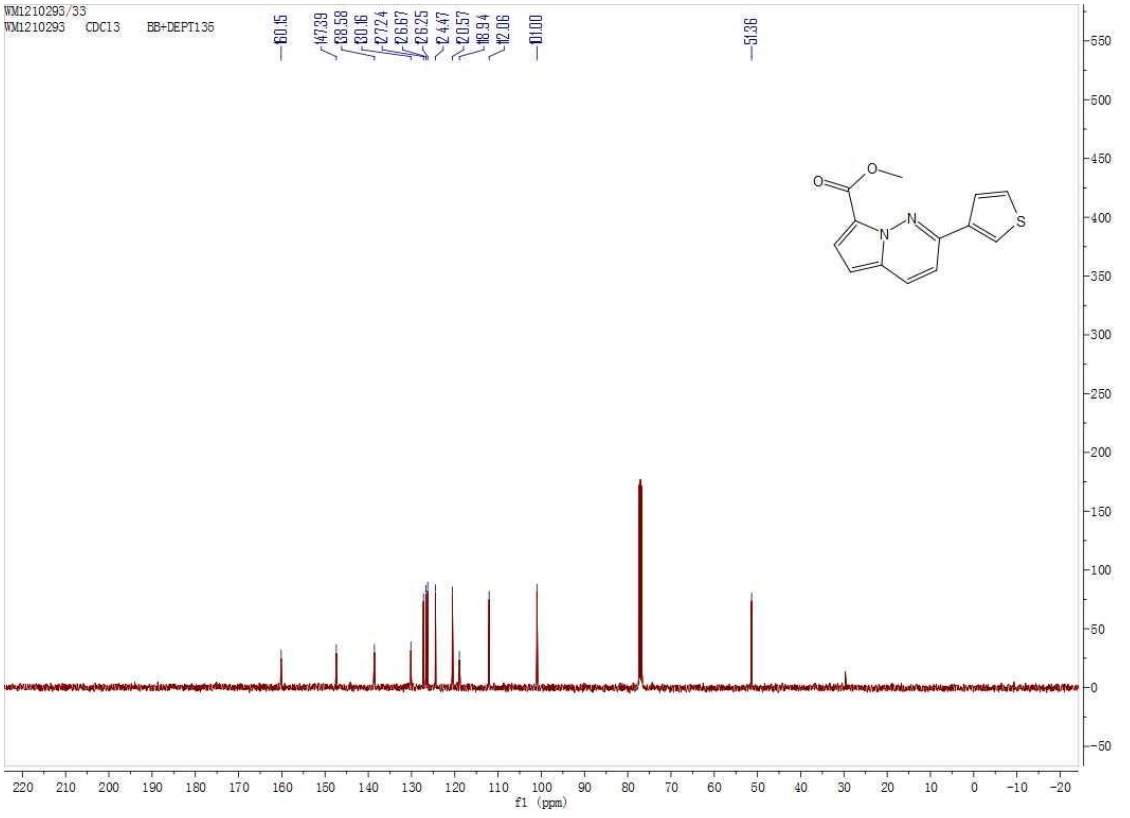
Compound 3o


WM1211151
WM1211151 CDCL3 1H Nov 15 2012
7.84 7.81 7.59 7.59 7.59 7.58 7.52 7.50 7.24 7.21 7.16 7.16 7.15 7.15 6.56 6.56 6.55 6.55 6.52 6.51 3.95
¹H NMR (400 MHz, CDCl₃) δ 7.83 (d, J = 9.4 Hz, 1H), 7.59 (dd, J = 1.7, 0.7 Hz, 1H), 7.51 (d, J = 4.7 Hz, 1H), 7.23 (d, J = 9.4 Hz, 1H), 7.15 (dd, J = 3.4, 0.7 Hz, 1H), 6.55 (dd, J = 3.4, 1.8 Hz, 1H), 6.51 (d, J = 4.7 Hz, 1H), 3.95 (s, 3H).
D (d) 7.23
B (dd) 7.59
G (d) 6.51
A (d) 7.83
F (dd) 6.55
C (d) 7.51
E (dd) 7.15
H (s) 3.95
1.04 0.97 0.98 1.04 1.01 1.00 1.00 3.15
f1 (ppm)

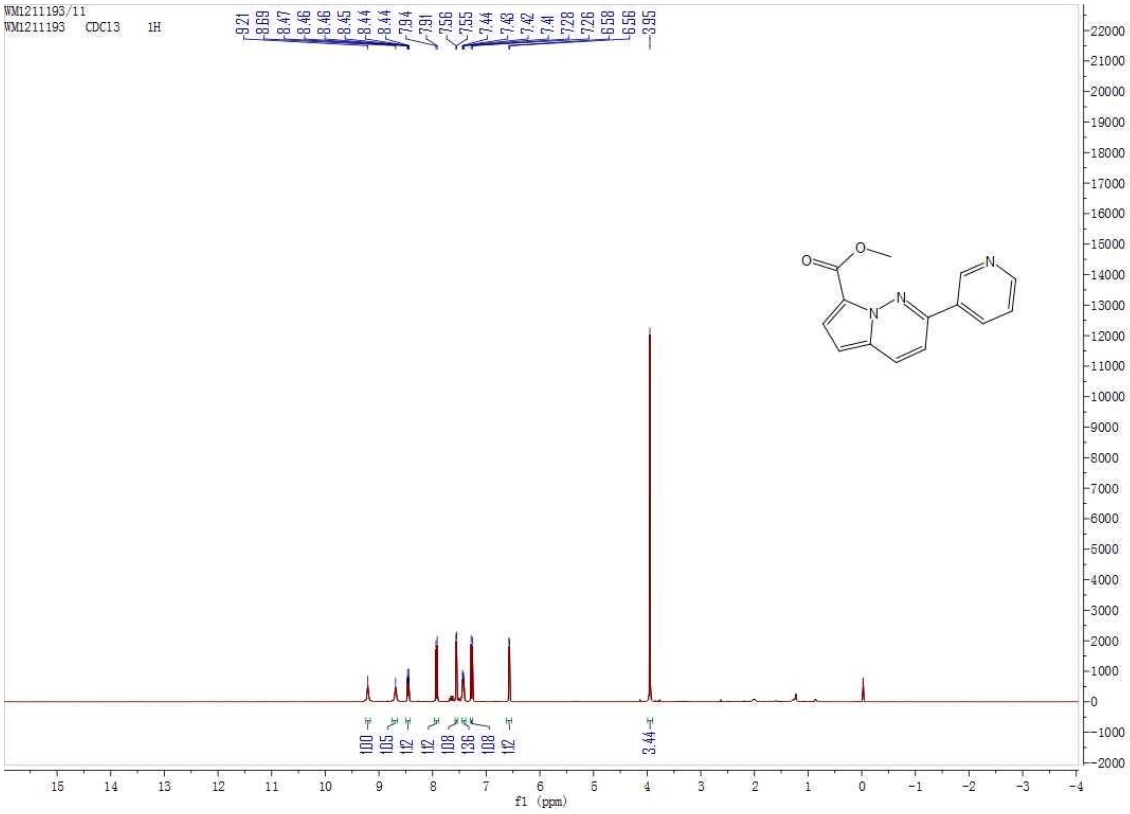

WM1211151/33
WM1211151 CDC13 BB+DEPT135
159.59 149.72 143.78 143.47 129.74 126.80 120.17 118.60 111.75 110.14 109.71 100.76 50.89
f1 (ppm)

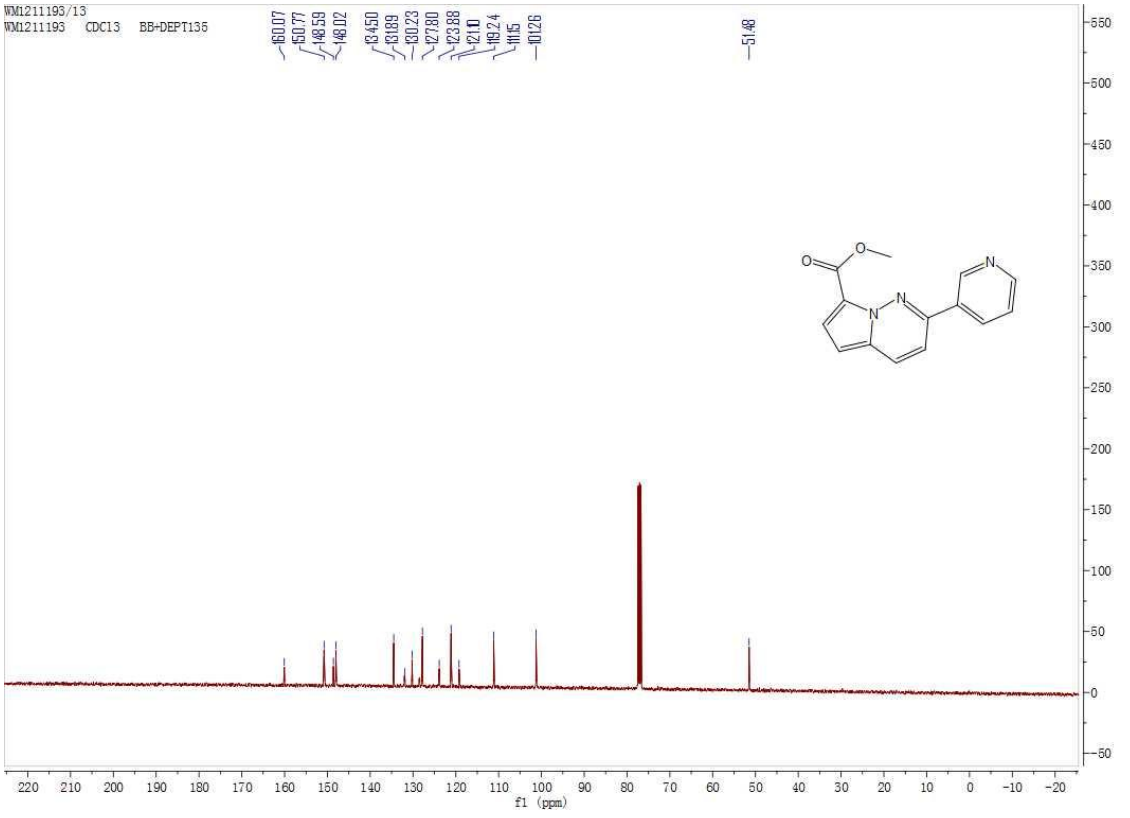
Compound 3p


WM1210293/31
WM1210293 CDC13 1H
7.89
7.89
7.88
7.81
7.81
7.80
7.79
7.51
7.50
7.41
7.40
7.40
7.40
7.39
7.16
7.14
6.50
6.49
3.95
1.03
1.94
1.06
1.03
1.05
1.00
f1 (ppm)

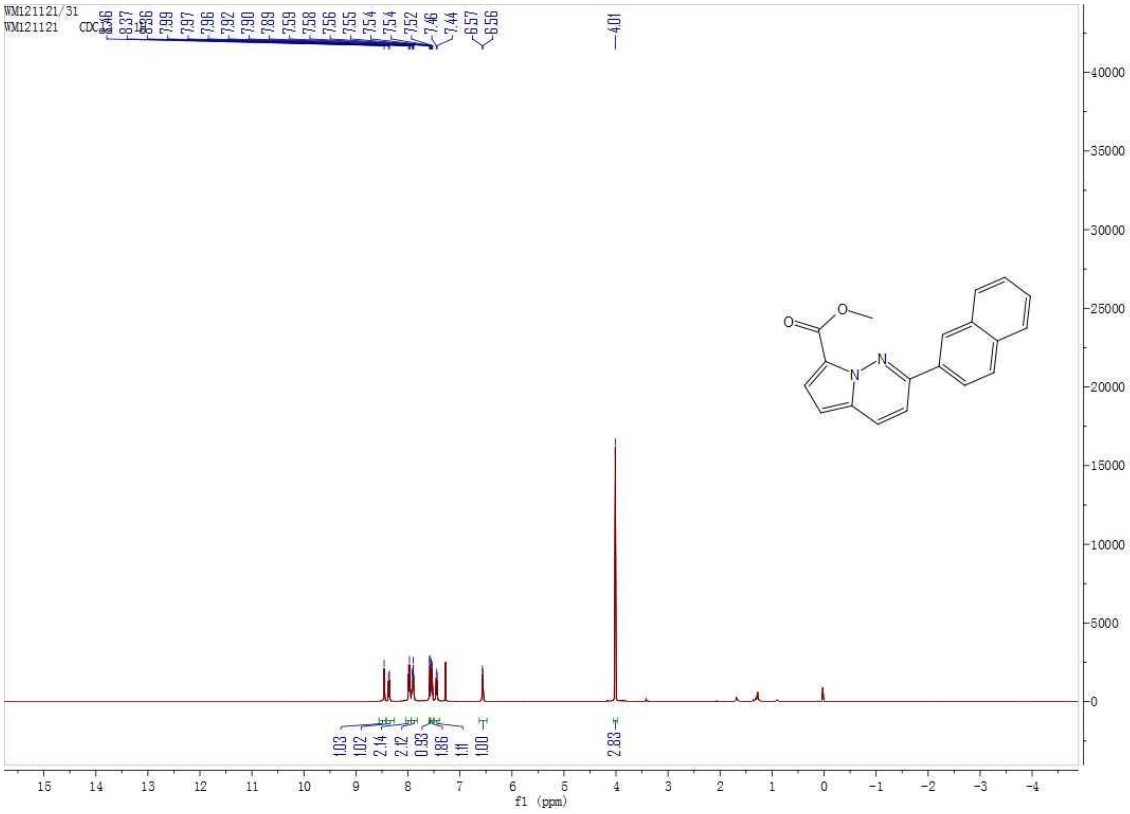

WM1210293/33
WM1210293 CDC13 BB+DEPT135
60.45
47.39
38.58
30.16
27.24
26.67
26.25
24.47
20.57
18.94
12.06
01.00
51.36
f1 (ppm)

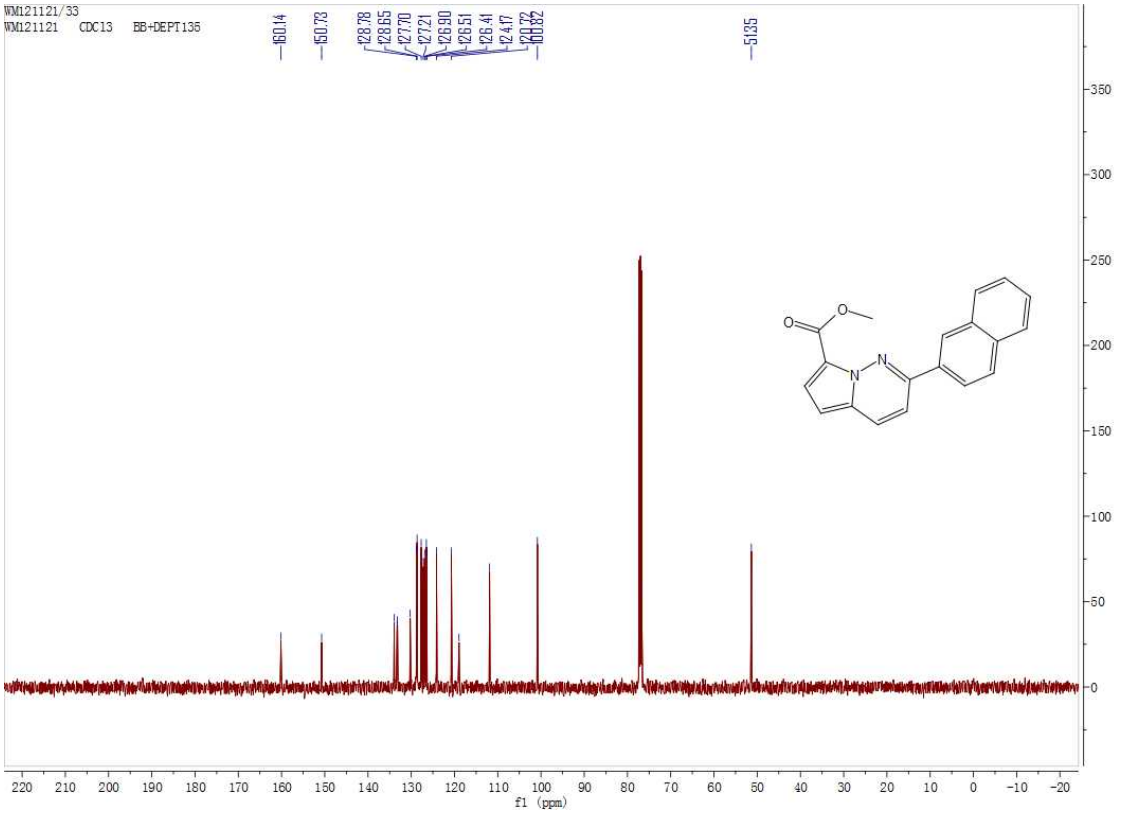
Compound 3q


WM1211193/11
WM1211193 CDCl3 1H
9.21
8.69
8.47
8.46
8.46
8.45
8.44
8.44
7.94
7.91
7.56
7.55
7.44
7.43
7.42
7.41
7.28
7.26
6.58
6.56
3.95
1.00
1.05
1.12
1.12
1.08
1.36
1.08
1.12
3.44
f1 (ppm)

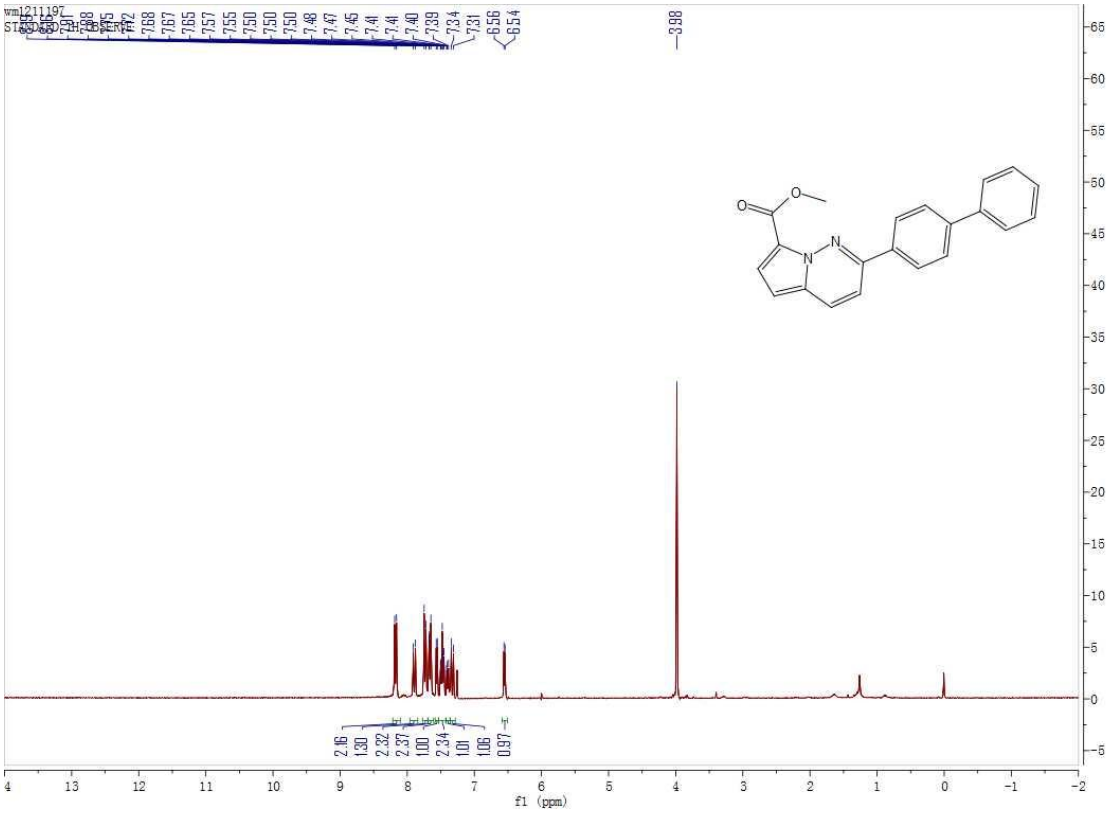

WM1211193/13
WM1211193 CDCl3 BB-DEPT135
160.07
150.77
148.59
146.02
134.50
131.89
130.23
127.80
123.88
121.10
119.24
111.15
101.26
51.48
f1 (ppm)

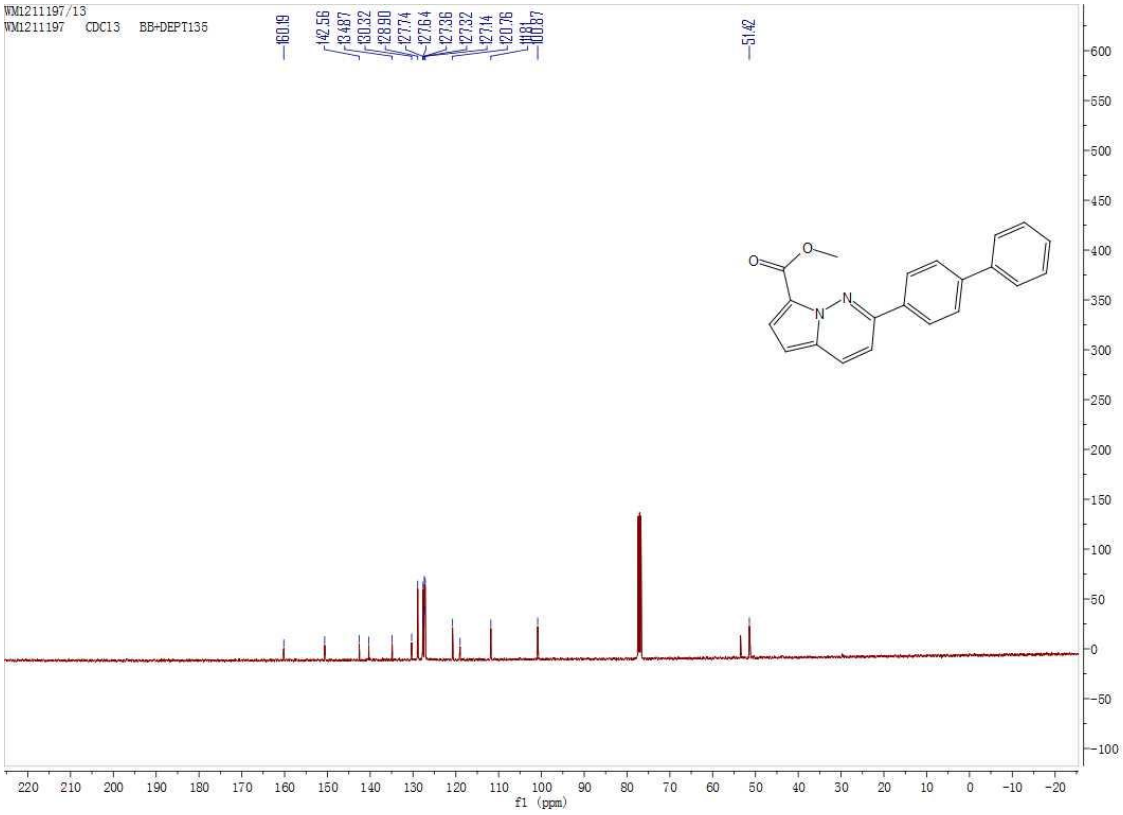
Compound 3r


WM121121/31
WM121121 CDC13
8.37
8.36
7.99
7.97
7.96
7.92
7.90
7.89
7.59
7.58
7.56
7.55
7.54
7.54
7.52
7.46
7.44
6.57
6.56
4.01
1.03
1.02
2.14
2.42
0.93
1.86
1.11
1.00
2.83
f1 (ppm)

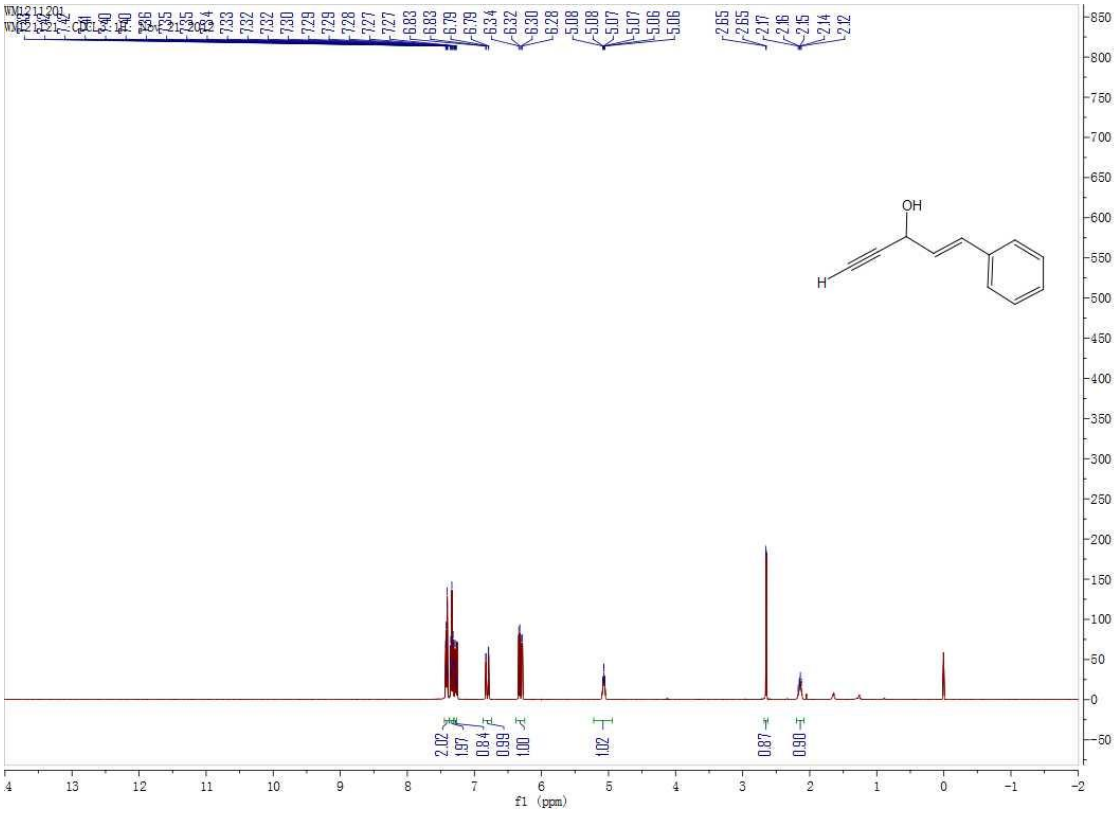

WM121121/33
WM121121 CDC13 BB+DEPT135
160.14
150.73
128.78
128.65
127.70
127.21
126.90
126.51
126.41
124.17
120.72
100.82
51.35
f1 (ppm)

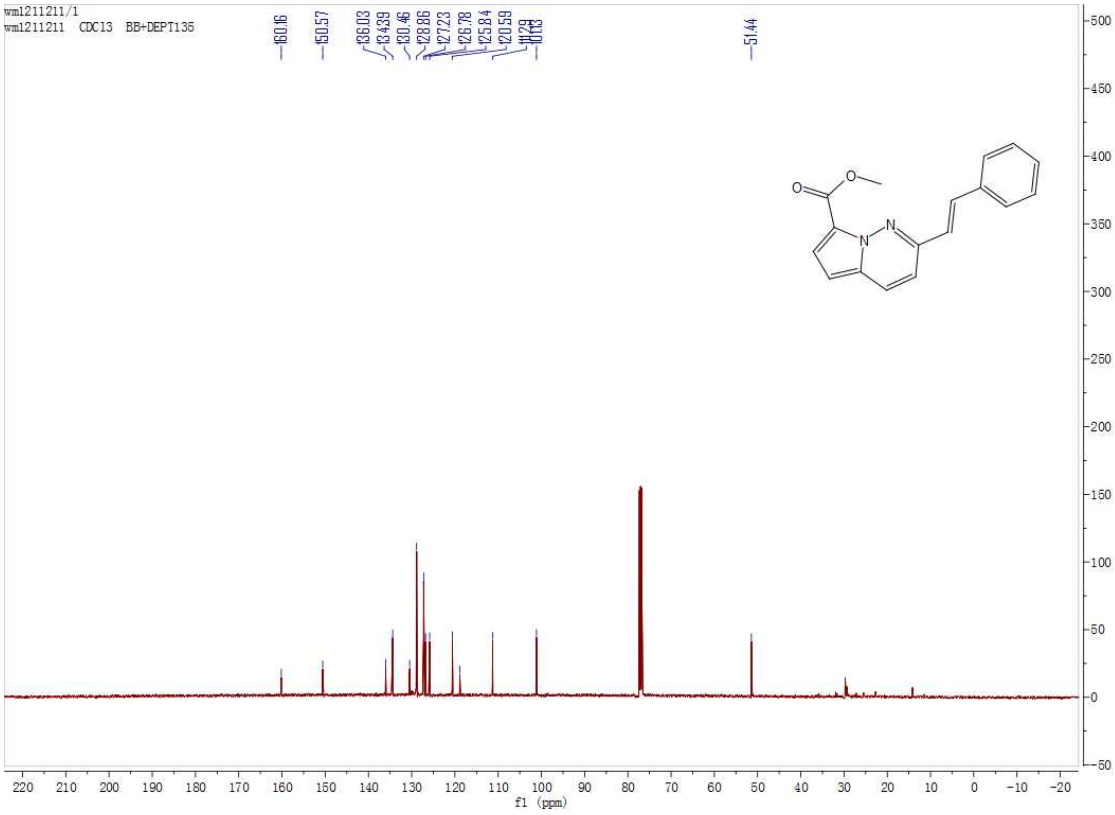
Compound 3s


wm1211197
3.98
6.56
6.54
2.16
1.30
2.32
2.37
1.00
2.34
1.01
1.06
0.97
f1 (ppm)


WM1211197/13
WM1211197 CDCl3 BB-DEPT135
160.19
142.56
134.87
130.32
128.90
127.74
127.64
127.36
127.32
127.14
120.76
100.87
51.42
f1 (ppm)

Compound 3t


OH
H
2.02
1.97
0.84
0.99
1.00
1.02
0.87
0.90
f1 (ppm)


wm1211211/1
wm1211211 CDCl3 BB+DEPT135
160.16
150.57
136.03
134.39
130.46
128.86
127.23
126.78
125.84
120.59
51.44
O
O
N
N
f1 (ppm)