Supporting Information

Access to 2-Pyridinylamide and Imidazopyridine from 2-Fluoropyridine and Amidine Hydrochloride

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A. Materials and methods

Unless otherwise noted, all commercial materials and solvents were used without further purification and all the reactions were carried out in a Schlenk tube equipped with magnetic stir bar. ^{1}H NMR spectra were recorded in $CDCl_3$ at 400 MHz (500 MHz or 600 MHz) and ^{13}C NMR NMR spectra were recorded in $CDCl_3$ at 100 MHz (125 MHz or 150 MHz) respectively, ^{1}H and ^{13}C NMR NMR were referenced to $CDCl_3$ at δ 7.26 (DMSO-d_6 at δ 2.50) and 77.0 (DMSO-d_6 at δ 39.52) respectively. GC–MS was obtained using electron ionization (Agilent Technologies 7890A/5975C). HRMS spectra were acquired using an Agilent 6210 ESI/TOF mass spectrometer and MAT 95XP (Double-focusing Magnetic Sector Analyzer), Thermo (EI, 70eV). TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF_{254}), and visualization was effected at 254 nm. All the other chemicals were purchased from Aldrich Chemicals. Commercial reagents were used without further purification.

B. General Procedure

General methods for the synthesis of N-(3-iodopyridin-2-yl)acetamide 3a: A 25 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (1.0 mmol, 223 mg), acetamidine hydrochloride **2a** (1.3 mmol, 123 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL), H_2O (3.0 mmol, 48 mg) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 ^{o}C stirring for 18h under open air. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 3:1 as eluent.

General methods for the synthesis of 3*H*-imidazo[4,5-*b*]pyridine 4a: A 25 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (1.0 mmol, 223 mg), acetamidine hydrochloride **2a** (1.3 mmol, 123 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 ^{o}C stirring for 18 h, the CuI (10 mol%, 19 mg) was add and reaction at 90 °C stirring for 10 h again. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 1:1 as eluent.

General methods for the synthesis of 1*H*-imidazo[4,5-*b*]pyridine 5a: A 25 mL Schlenk tube was

charged with 2-fluoro-3-iodopyridine **1a** (1.0 mmol, 223 mg), pivalimidamide hydrochloride **2a** (1.3 mmol, 177 mg), CuI (10 mol%, 19 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 ^oC stirring for 18h. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 1:1 as eluent.

General methods for the synthesis of imidazo[4,5-*b*]pyridine 6a: A 25 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (2.2 mmol, 491 mg), acetamidine hydrochloride **2a** (1.0 mmol, 94 mg), CuI (10 mol%, 19 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 110 ^oC stirring for 24h. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 1:1 as eluent.

Gram-scale synthesis of N-(3-iodopyridin-2-yl)acetamide 3a: A 50 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (4.48 mmol, 1 g), acetamidine hydrochloride **2a** (6.0 mmol, 1.5 equiv., 0.64 g), Cs_2CO_3 (13.5 mmol, 3.0 equiv., 4.4 g), DMSO (15 mL), H_2O (13.5 mmol, 0.24 g) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 ^oC stirring for 36 h under open air. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 3:1 as eluent, affording the N-(3-iodopyridin-2-yl)acetamide **3a** (0.97 g, 83 %) as a yellow liquid.

C. Characterization data for prepared compounds

N-(3-iodopyridin-2-yl)acetamide (3a): Yellow liquid, (243.7 mg, 93% yield); R_f = 0.34 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (500 MHz, DMSO-d_6) δ 10.12 (s, 1H), 8.42 (dd, J = 5.0, 2.0 Hz, 1H), 8.29 (dd, J = 7.5, 1.5 Hz, 1H), 7.05 (dd, J = 7.5, 4.5 Hz, 1H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 168.5, 152.5, 148.3, 148.1, 123.3, 94.0, 23.0; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_8IN_2O$ 262.9676, found 262.9670.

N-(3-iodopyridin-2-yl)propionamide (3b): Yellow solid, (223.6 mg, 81% yield); mp. 94-96 ^oC; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (600 MHz, Acetone-d_6) δ 9.01 (s, 1H), 8.40 (dd, J = 4.8, 1.8 Hz, 1H), 8.28 (dd, J = 7.8, 1.2 Hz, 1H), 7.00 (dd, J = 7.8, 4.8 Hz, 1H), 2.49 (q, J =

7.8, 15.6 Hz, 2H), 1.17 (t, J = 7.8 , 7.2 Hz, 3H); ^{13}C NMR (150 MHz, Acetone-d_6) δ 172.9, 153.4, 149.2, 148.9, 123.3, 91.7, 29.9, 9.6; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_{10}IN_2O$ 276.9832, found 276.9825.

N-(3-iodopyridin-2-yl)cyclopropanecarboxamide (3c): Yellow liquid, (175.7 mg, 61% yield); R_f = 0.35 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.15 (dd, J = 4.8, 1.8 Hz, 1H), 8.06 (dd, J = 7.8, 1.8 Hz, 1H), 6.52 (dd, J = 7.8, 4.8 Hz, 1H), 1.38-1.33 (m, 1H), 1.26 – 1.23 (m, 2H), 0.88 – 0.84 (dt, J = 7.2, 3.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.4, 160.7, 147.1, 145.8, 117.8, 94.7, 17.0, 8.9 (2C); ESI-HRMS m/z $[M+H]^+$calcd for $C_9H_{10}IN_2O$ 288.9832, found 288.9824.

N-(3-iodopyridin-2-yl)pivalamide (3d)[1]: Yellow liquid, (264.5 mg, 87% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.79 (s, 1H), 8.24 (s, 1H), 7.88 (s, 1H), 7.13 (m 1H), 1.39 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 170.0, 161.3, 147.5, 146.1, 118.3, 95.3, 38.9, 28.7; ESI-HRMS m/z $[M+H]^+$calcd for $C_{10}H_{14}IN_2O$ 305.0145, found 305.0137.

N-(3-iodopyridin-2-yl)cyclobutanecarboxamide (3e): Yellow liquid, (205.4 mg, 68% yield); R_f = 0.35 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.3 (s, 1H), 8.20 (t, J = 5.4 Hz, 1H), 8.12 (d, J = 7.8 Hz, 1H), 6.60 – 6.58 (m, 1H), 3.23 – 3.16 (m, 1H), 2.52 – 2.45 (m, 2H), 2.24 (t, J = 10.2 Hz, 2H), 2.03 – 1.90 (m, 2H); ^{13}C NMR (150 MHz, DMSO) δ 165.8, 160.9, 147.3, 146.0, 118.4, 94.6, 41.4, 26.2 (2C), 25.2, 17.9; ESI-HRMS m/z $[M+H]^+$calcd for $C_{10}H_{12}IN_2O$ 302.9989, found 302.9981.

N-(3-iodopyridin-2-yl)-2-methoxyacetamide (3f): Yellow liquid, (201 mg, 69% yield); R_f = 0.22 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.47 (s, 1H), 8.11 (d, J = 7.2 Hz, 1H), 6.86 – 6.84 (m, 1H), 4.11 (s, 2H), 3.56 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.8, 150.3, 148.5, 148.1, 121.8, 86.1, 72.6, 59.8; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_{10}IN_2O_2$ 292.9781, found 292.9775.

N-(4-methylpyridin-2-yl)acetamide (3g)[2]: Yellow liquid, (120.1 mg, 80% yield); R_f = 0.56 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.38 (s, 1H), 8.14 (dd, J = 5.0, 0.5 Hz, 1H), 7.91 (s, 1H), 6.91 (dq, J = 2.0, 1.5, 1.0 Hz, 1H), 2.29 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 152.2, 148.7, 147.5, 120.2, 113.7, 23.9, 21.0; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_{11}N_2O$ 151.0866, found 151.0861.

N-(3-fluoropyridin-2-yl)acetimidamide (3h): Yellow liquid, (137.1 mg, 89% yield); R_f = 0.24

(petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.23 (d, J = 4.8 Hz, 1H), 7.73(dd, J = 9.6, 7.8 Hz, 1H), 7.33 – 7.29 (m, 1H), 2.07 (d, J = 1.8 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.5, 152.2 (d, J = 259.1 Hz), 143.9 (d, J = 5.1 Hz), 140.2 (d, J = 12.8 Hz), 124.7 (d, J = 18.3 Hz), 122.78 (d, J = 3.6 Hz), 22.9; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_8FN_2O$ 155.0615, found 155.0608.

N-(6-fluoropyridin-2-yl)acetamide (3i): Yellow solid, (135.5 mg, 88% yield); mp. 119-121 ^{o}C; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.14 (dd, J = 7.8, 2.4 Hz, 1H), 7.09 (dd, J = 16.2, 7.8 Hz, 1H), 5.98 (dd, J = 7.2, 1.8 Hz, 1H) , 1.24 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.5, 161.3 (d, J = 236.5 Hz), 150.5 (d, J = 14.9 Hz), 143.9 (d, J = 8.0 Hz), 110.2 (d, J = 4.1 Hz), 103.3 (d, J = 35.6 Hz), 23.9; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_8FN_2O$ 155.0615, found 155.0611.

N-(5-chloropyridin-2-yl)acetamide (3j)[3]: White solid, (125.8 mg, 74% yield); mp. 172-174 ^{o}C; R_f = 0.22 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.66 (s, 1H), 8.33 (t, J = 2.9 Hz, 1H), 8.10 (d, J = 8.9 Hz, 1H), 7.85 (ddd, J = 9.0, 4.0, 2.3 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.44, 150.8, 146.3, 137.8, 124.8, 114.4, 23.9; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_8ClN_2O$ 171.0320, found 171.0314.

N-(6-chloropyridin-2-yl)acetamide (3k)[4]: White solid, (117.3 mg, 69% yield); mp. 150-152 ^{o}C; R_f = 0.22 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.77 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.81 – 7.62 (m, 1H), 7.16 – 7.11 (m, 1H), 2.08 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.6, 152.2, 148.0, 141.7, 118.9, 111.9, 23.9; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_8ClN_2O$ 171.0320, found 171.0314.

N-(6-bromopyridin-2-yl)acetamide (3l)[5]: White solid, (194.7 mg, 91% yield); mp. 155-157 ^{o}C; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.78 (s, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.28 (d, J = 7.8 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.5, 152.3, 141.3, 138.7, 122.7, 112.1, 23.9; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_8BrN_2O$ 214.9815, found 214.9808.

N-(5-bromopyridin-2-yl)acetamide (3m)[6]: White solid, (162.6 mg, 76% yield); mp. 169-171 ^{o}C; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.64 (s, 1H), 8.41 (dd, J = 2.4, 0.6 Hz, 1H), 8.06 (d, J = 9.6 Hz, 1H), 7.97 (dd, J = 9.0, 3.0 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.4, 151.1, 148.4, 140.5, 115.0, 113.2, 23.9; ESI-HRMS m/z

$[M+H]^+$calcd for $C_7H_8BrN_2O$ 214.9815, found 214.9809.

N-(3-chloro-5-fluoropyridin-2-yl)acetamide (3n): White solid, (172.0 mg, 91% yield); mp. 86-88 ^oC; R_f = 0.32 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (400 MHz, DMSO-d_6) δ 10.17 (s, 1H), 8.44 (t, J = 2.4 Hz, 1H), 8.13 (dd, J = 8.0, 2.8 Hz, 1H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.6, 156.7 (d, J = 257.95 Hz), 144.9 (d, J = 2.93 Hz), 134.7 (d, J = 23.9 Hz), 127.2 (d, J = 5.5 Hz), 126.2 (d, J = 22.5 Hz), 22.7; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_7FClN_2O$ 189.0225, found 189.0218.

N-(5-bromo-4-methylpyridin-2-yl)acetamide (3o)[1]: Brown solid, (189.2 mg, 83% yield); mp. 150-152 ^oC; R_f = 0.36 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (400 MHz, DMSO-d_6) δ 10.49 (s, 1H), 8.32 (s, 1H), 8.06 (s, 1H), 2.31 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.2, 151.4, 148.6, 147.9, 116.0, 115.1, 23.9, 22.2; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_{10}BrN_2O$ 228.9971, found 228.9965.

N-(3-iodo-5-methylpyridin-2-yl)acetamide (3p): Yellow liquid, (190.4 mg, 69% yield); R_f = 0.30 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (600 MHz, DMSO-d_6) δ 9.99 (s, 1H), 8.24 (dd, J = 1.2, 2.4 Hz, 1H), 8.13 (dd, J = 0.6, 1.8 Hz, 1H), 2.23 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.7, 150.1, 148.2, 133.1, 93.9, 40.4, 23.0, 16.7; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_{10}IN_2O$ 276.9832, found 276.9824.

N-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)acetamide (3q): Yellow liquid, (219.0 mg, 92% yield); R_f = 0.46 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 8.75 (s, 1H), 8.42 (s, 1H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.7, 151.9, 143.6 (d, J = 4.4 Hz), 136.1 (d, J = 2.4 Hz), 125.4, 123.8 (d, J = 74.44 Hz), 123.3 (d, J = 33.43 Hz), 121.5, 23.2; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_7F_3ClN_2O$ 239.0194, found 239.0191.

N-(3-bromo-5-chloropyridin-2-yl)cyclopropanecarboxamide (3r)[5]: Yellow liquid, (200.0 mg, 73% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, J = 2.4 Hz, 1H), 7.82 (d, J = 2.4 Hz, 1H), 1.44 – 1.39 (m, 1H), 1.22 – 1.19 (m, 2H), 0.90 – 0.86 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 157.9, 143.3, 140.3, 123.3 , 117.7, 17.2, 9.0.

N-(pyrazin-2-yl)acetamide (3s)[7]: White solid, (126.1 mg, 92% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 3:1); ^1H NMR (400 MHz, DMSO) δ 10.71 (s, 1H), 9.30 (s, 1H), 8.33 (d, J = 14.4 Hz, 2H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 169.5, 148.8, 142.5 , 139.4, 136.2, 23.6; ESI-HRMS m/z $[M+H]^+$calcd for $C_6H_8N_3O$ 138.0662, found 138.0666.

2-methyl-3H-imidazo[4,5-*b*]pyridine (4a)[8]: Yellow solid, (107.7mg, 81% yield); R_f = 0.23 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.22 (dd, J = 5.5 Hz, 1H), 7.85 (s, 1H), 7.14 (dd, J = 7.5, 4.5 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.6, 151.9, 142.6 131.8, 122.6, 117.2, 15.0; ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_8N_3$ 134.0713, found 134.0707.

2-ethyl-3H-imidazo[4,5-*b*]pyridine (4b)[9]: Yellow liquid, (114.7 mg, 78% yield); R_f = 0.22 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 4.8 Hz, 1H), 8.02 (dd, J = 7.9, 1.1 Hz, 1H), 7.23 (dd, J = 7.9, 4.9 Hz, 1H), 3.49 (s, 1H), 3.08 (q, J = 7.6 Hz, 2H), 1.54 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 150.0, 142.0, 134.8, 125.7, 117.8, 23.1, 12.0; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_{10}N_3$ 148.0869, found 148.0868.

2-cyclopropyl-3H-imidazo[4,5-*b*]pyridine (4c): White solid, (135.2 mg, 85% yield); mp. 173-175 ^{o}C; R_f = 0.21 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.77 (s, 1H), 8.19 (d, J = 5.0 Hz, 1H), 7.79 (dd, J = 8.0, 1.5 Hz, 1H), 7.09 (dd, J = 8.0, 5.0 Hz, 1H), 2.29 – 2.13 (m, 1H), 2.16 – 2.10 (m, 2H), 1.09 – 1.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 149.6, 141.21, 135.6, 125.6, 117.7, 10.6, 9.6; ESI-HRMS m/z $[M+H]^+$calcd for $C_9H_{10}N_3$ 160.0869, found 160.0867.

2-tert-butyl-3H-imidazo[4,5-*b*]pyridine (4d): White solid, (152.3 mg, 87% yield); mp. 155-157 ^{o}C; R_f = 0.20 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.86 (s, 1H), 8.36 (t, J = 4.8 Hz, 1H), 8.09 (d, J = 6.6 Hz, 1H), 7.25 (dd, J = 3.6, 8.4 Hz, 1H), 1.61 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.06, 149.47, 142.04, 136.05, 127.45, 117.86, 34.09, 29.50; ESI-HRMS m/z $[M+H]^+$calcd for $C_{10}H_{14}N_3$ 176.1182, found 176.1180.

2,6-dimethyl-3H-imidazo[4,5-*b*]pyridine (4e): Brown solid, (83.8 mg, 57% yield); mp. 213-215 ^{o}C; R_f = 0.22 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.50 (s, 1H), 8.07 (s, 1H), 7.64 (s, 1H), 2.49 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.5, 148.1, 142.7, 135.5, 127.5, 126.3, 18.8, 15.7; ESI-HRMS m/z $[M+H]^+$calcd for $C_8H_{10}N_3$ 148.0869, found 148.0867.

6-bromo-2-methyl-3H-imidazo[4,5-b]pyridine(4f)[8]: Brown solid, (116.1 mg, 55% yield); R_f = 0.21 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO) δ 12.90 (s, 1H), 8.30 (d, J = 2.0 Hz, 1H), 8.11 (d, J = 2.0 Hz, 1H), 2.51 (d, J = 5.3 Hz, 3H); ^{13}C NMR (125 MHz, DMSO) δ 155.9, 143.3, 112.6, 15.56.(Three carbon signals of ^{13}C NMR are missing).

6,7,8,9-tetrahydroimidazo[1,2-*a*:5,4-*b*']dipyridine (4g)[10]: Yellow liquid, (159.2 mg, 92% yield); R_f = 0.24 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.35 (dd, J = 4.8, 1.2 Hz, 1H), 7.02 (dd, J = 8.4, 1.8 Hz, 1H), 6.32 (dd, J = 7.8, 4.8 Hz, 1H), 3.24 (t, J =6.0 Hz, 2H), 2.09 (t, J =6.0 Hz, 2H), 1.17 – 1.12 (m, 2H), 1.07 – 1.02 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 153.4, 147.6, 142.1, 134.5, 125.4, 117.9, 41.2, 25.2, 21.7, 20.0; ESI-HRMS m/z $[M+H]^+$calcd for $C_{10}H_{12}N_3$ 174.1026, found 174.1016.

2-tert-butyl-1H-imidazo[4,5-*b*]pyridine (5a): White solid, (84 mg, 48% yield); mp. 247-249 ^{o}C; R_f = 0.34 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.78 (s, 1H), 8.24 (s, 1H), 7.88 (s, 1H), 7.13 (dd, J = 7.8, 3.2 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 163.8, 149.4, 142.7, 134.4, 125.7, 117.2, 33.5, 28.9 (3C); ESI-HRMS m/z $[M+H]^+$calcd for $C_{10}H_{12}N_3$ 176.1182, found 176.1174.

6,7,8,9-tetrahydroimidazo[1,2-*a*:4,5-*b*']dipyridine (5b): Yellow solid, (143.6 mg, 83% yield); mp. 95-97 ^{o}C; R_f = 0.32 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (dd, J = 4.8, 1.8 Hz, 1H), 7.78 (dd, J = 8.4, 1.8 Hz, 1H), 7.04 (dd, J = 8.4, 4.8 Hz, 1H), 4.08 (t, J = 6.0 Hz, 2H), 2.96 (t, J = 6.6 Hz, 2H), 2.00 – 1.97 (m, 2H), 1.92 – 1.87 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 147.5, 142.5, 134.8, 125.9, 118.0, 41.3, 25.5, 21.2, 20.34; ESI-HRMS m/z $[M+H]^+$calcd for $C_{10}H_{12}N_3$ 174.1026, found 174.1023.

1-(3-iodopyridin-2-yl)-2-methyl-1H-imidazo[4,5-*b*]pyridine (6a): Yellow liquid, 252 mg, 75% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (dd, J = 4.4, 1.6 Hz, 1H), 8.65 (dd, J = 8.0, 1.6 Hz, 1H), 8.43 (d, J = 3.6 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.23 (dd, J = 8.0, 4.8 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.0, 153.4, 149.8, 149.6, 149.5, 144.3, 127.1, 126.8, 118.5, 118.2, 95.2, 14.2; ESI-HRMS m/z $[M+H]^+$calcd for $C_{12}H_{10}IN_4$ 336.9945, found 336.9934.

1-(3-iodo-5-methylpyridin-2-yl)-2,6-dimethyl-1H-imidazo[4,5-*b*]pyridine (6b): White solid, (149 mg, 41% yield); mp. 152-154 ^{o}C; R_f = 0.24 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.55 (dd, J = 1.8, 0.6 Hz, 1H), 8.49 (dd, J = 1.8, 0.6 Hz, 1H), 8.26 (d, J = 2.4, 0.6 Hz, 1H), 7.27 (dd, J = 1.8, 0.6 Hz, 1H), 2.41 (s, 3H), 2.36 (d, J = 2.4 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 153.3, 152.8, 150.0, 149.3, 147.2, 144.9, 136.9, 127.5, 127.2, 118.2, 94.6, 18.0, 17.0, 14.1; ESI-HRMS m/z $[M+H]^+$calcd for $C_{14}H_{14}IN_4$ 365.0258, found 365.0254.

1-(3-bromo-5-chloropyridin-2-yl)-6-chloro-2-dimethyl-1H-imidazo[4,5-*b*]pyridine (6c): White

solid, (153 mg, 43% yield); mp. 177-179 °C; R_f = 0.20 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.82 (t, J = 2.5 Hz, 2H), 8.45 (d, J = 2.5 Hz, 1H), 8.01 (d, J = 2.5 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.3, 153.5, 147.9, 144.4, 143.0, 142.8, 133.1, 127.6, 125.3, 119.6, 118.9, 14.1; ESI-HRMS m/z [M+H]$^+$calcd for $C_{12}H_8BrCl_2N_4$ 356.9304, found 356.9304.

6-bromo-1-(3,5-dibromopyridin-2-yl)-2-methyl-1H-imidazo[4,5-*b*]pyridine (6d): Yellow liquid, (168.7 mg, 38% yield); R_f = 0.24 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 2.0 Hz, 1H), 8.80 (d, J = 2.0 Hz, 1H), 8.51 (d, J = 2.0 Hz, 1H), 8.12 (d, J = 2.0 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.1, 153.7, 150.1, 145.4, 145.0, 144.7, 128.2, 122.1, 121.6, 119.9, 113.6, 14.1; ESI-HRMS m/z [M+H]$^+$calcd for $C_{12}H_8Br_3N_4$ 444.8294, found 444.8301.

2,2,2-trifluoro-N-(3-iodopyridin-2-yl)acetimidamide (7a): Yellow liquid, (135.5 mg, 43% yield); R_f = 0.85 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.30 (dd, J = 4.8, 1.6 Hz, 1H), 8.21 (dd, J = 7.8, 1.7 Hz, 1H), 6.77 (dd, J = 7.8, 4.8 Hz, 1H), 6.02 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 148.4 (q, J = 35.5 Hz, 1C), 148.2, 146.0, 120.8, 118.0 (q, J = 276.8 Hz, 1C), 95.3. ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_6F_3IN_3$ 315.9553, found 315.9552.

N-(3-((trimethylsilyl)ethynyl)pyridin-2-yl)acetamide (8a)[11]: Yellow liquid, (197.2 mg, 85% yield); R_f = 0.48 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (dd, J =5.0, 2.0 Hz, 1H), 8.15(s, 1H), 7.71 (dd, J = 7.5, 1.5 Hz, 1H), 6.97 (dd, J = 7.5, 4.5 Hz, 1H), 0.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 147.8, 140.7, 118.5, 104.6, 98.5, 25.1, -0.09 (3C); ESI-HRMS m/z [M+H]$^+$ calcd for $C_{12}H_{17}SiON_2$ 233.1105, found 233.1097.

N-(3-phenylpyridin-2-yl)pivalamide (8b): Yellow liquid, (99.1 mg, 65% yield); R_f = 0.50 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.74 (S, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.45 (t, J = 8.0 Hz, 2H), 7.40-7.37 (m, 3H), 7.24-7.20 (m, 1H), 1.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) 175.7, 148.3, 147.4, 139.0, 137.5, 130.8, 128.8 (2C), 128.4 (2C), 128.0, 120.9, 39.6, 27.2 (3C). ESI-HRMS m/z [M+H]$^+$calcd for $C_{16}H_{19}N_2O$ 255.1492, found 255.1490.

Notes and references

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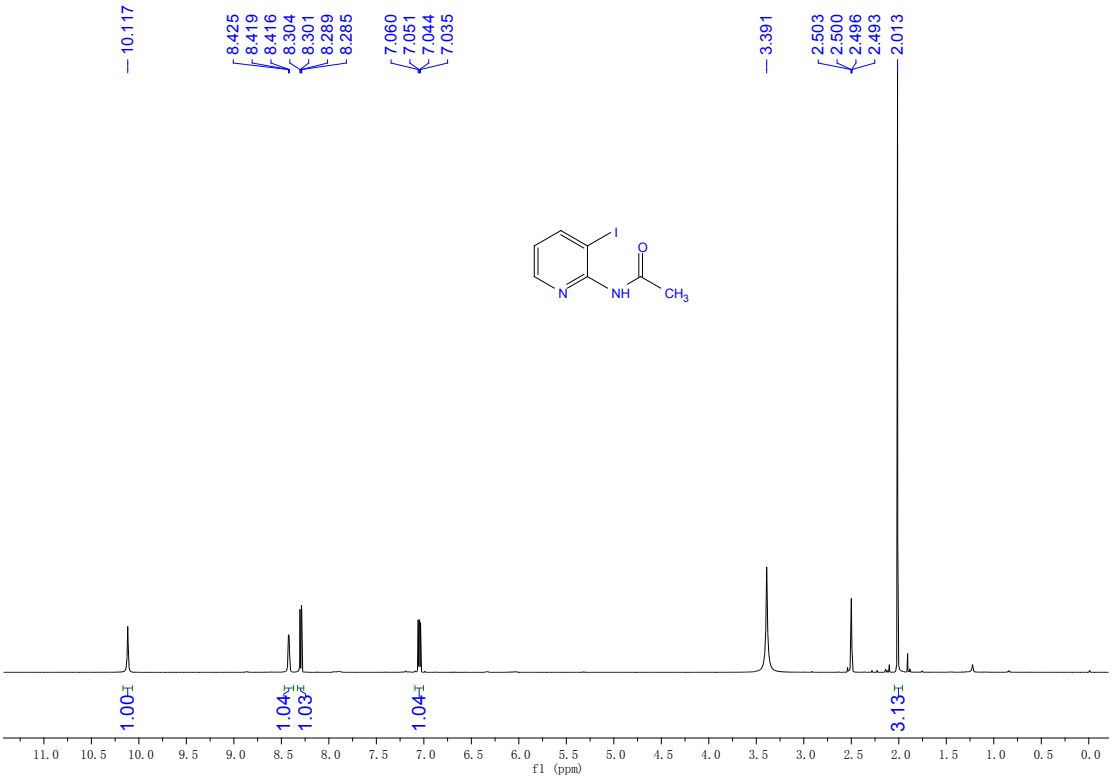
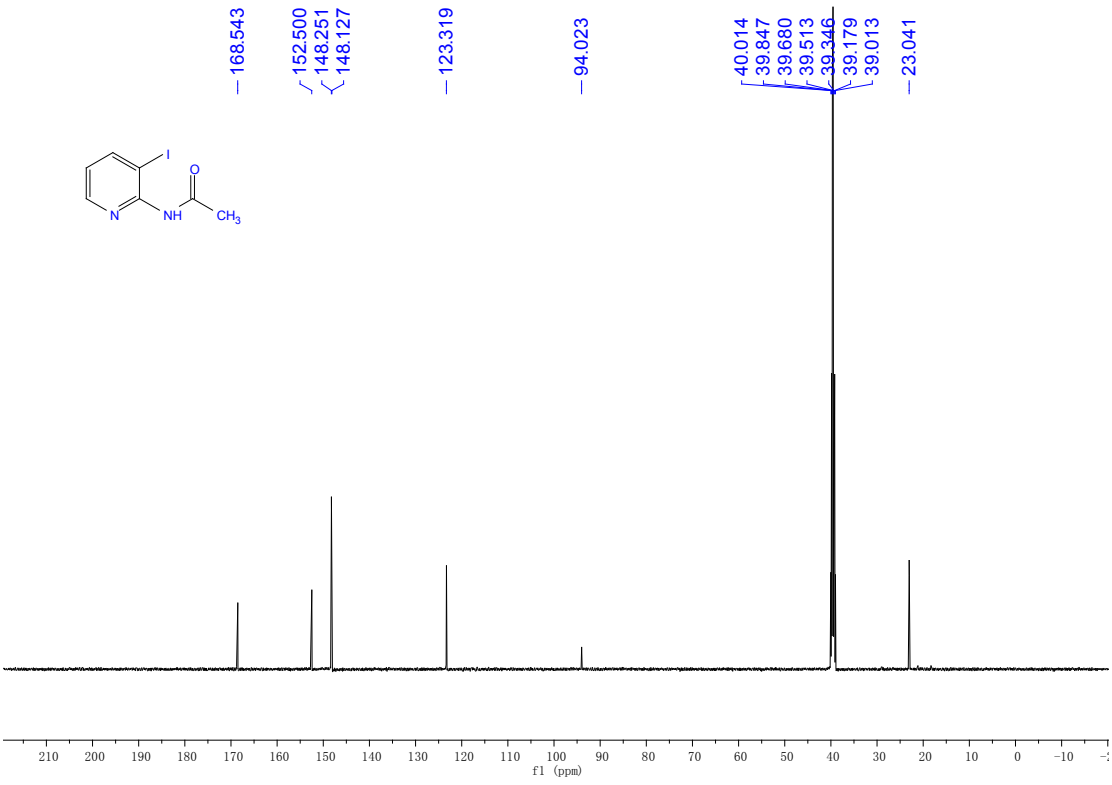
D. NMR Spectra for All Compounds

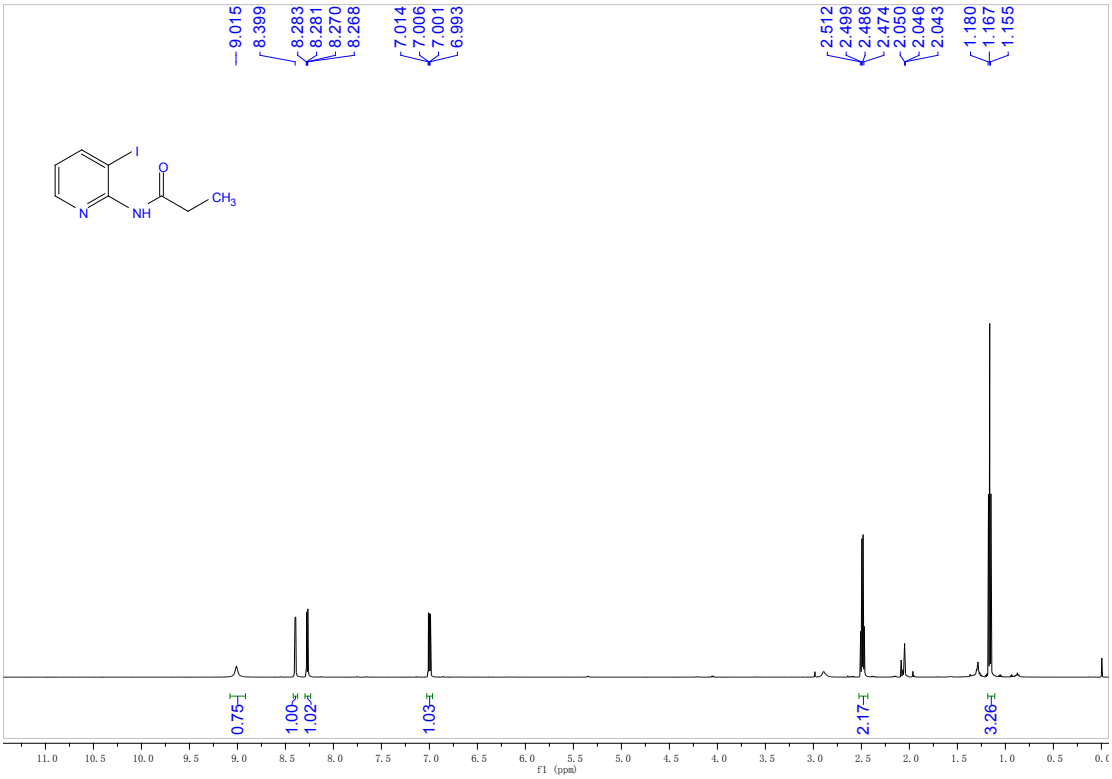
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of compound 3a



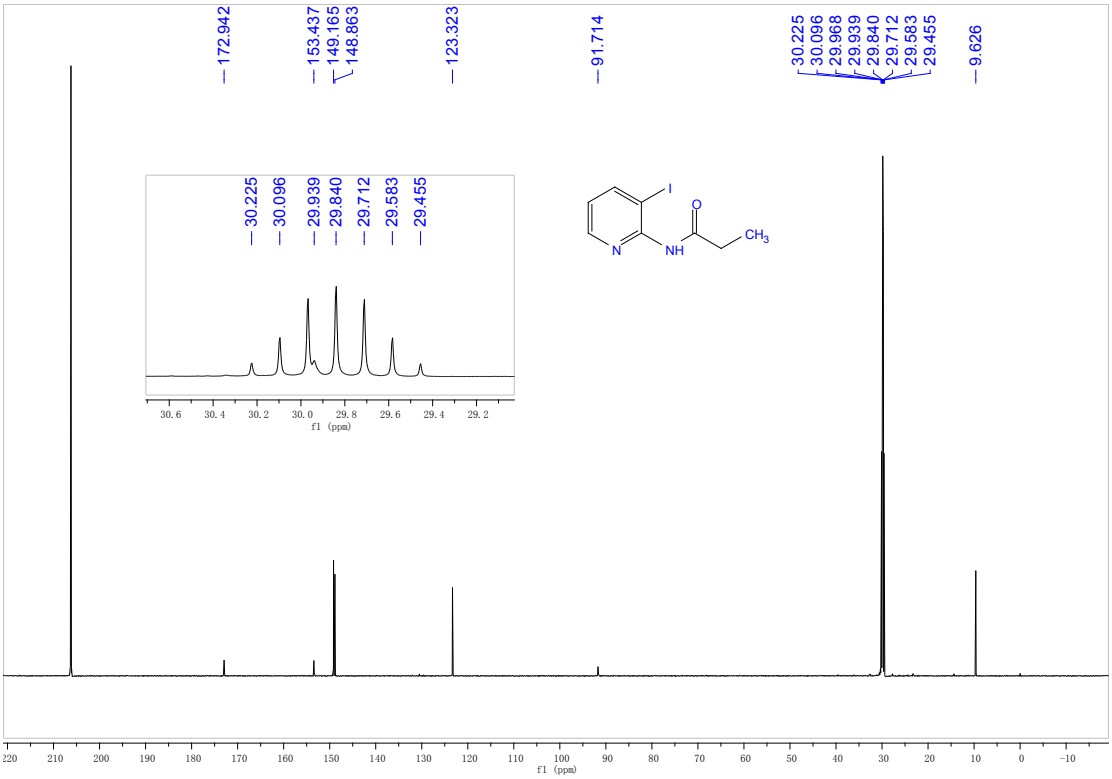
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 3a



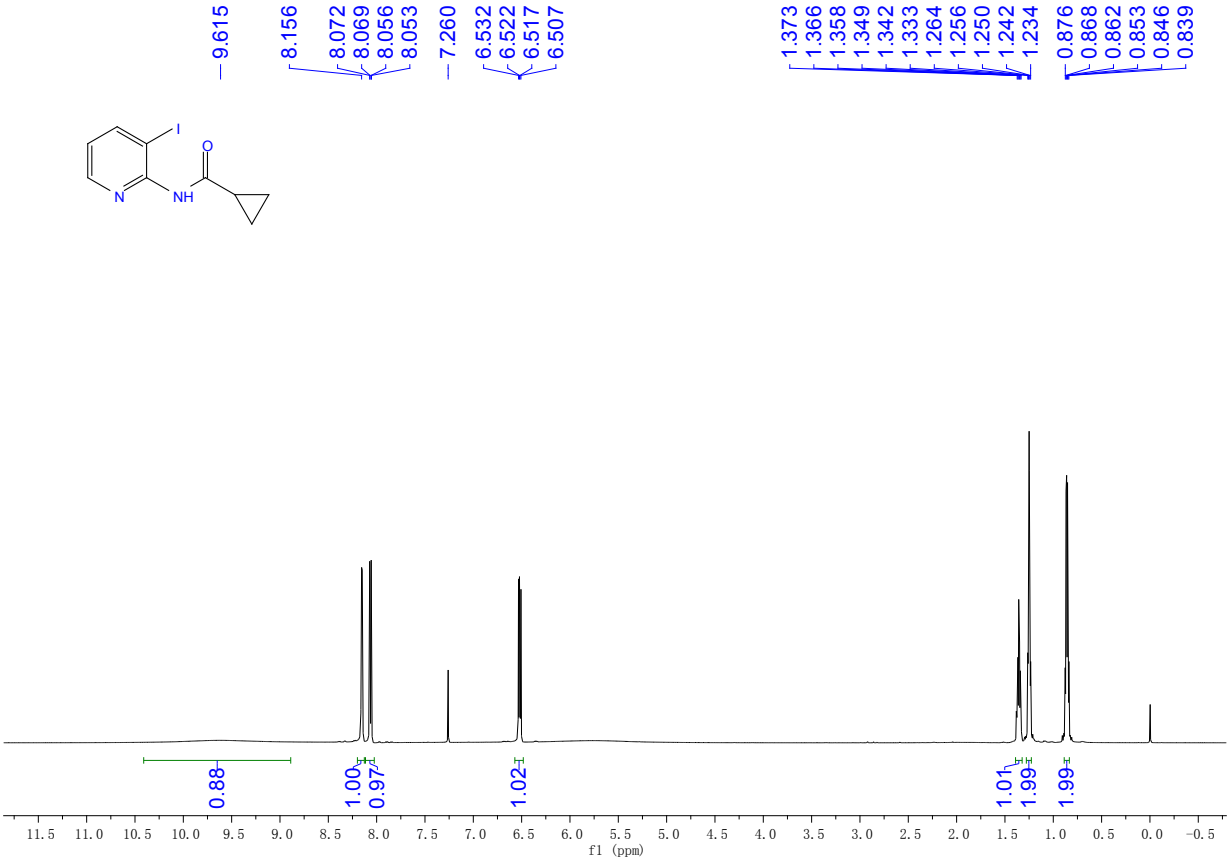
^{1}H NMR (600 MHz, Acetone-d_6) spectrum of compound 3b



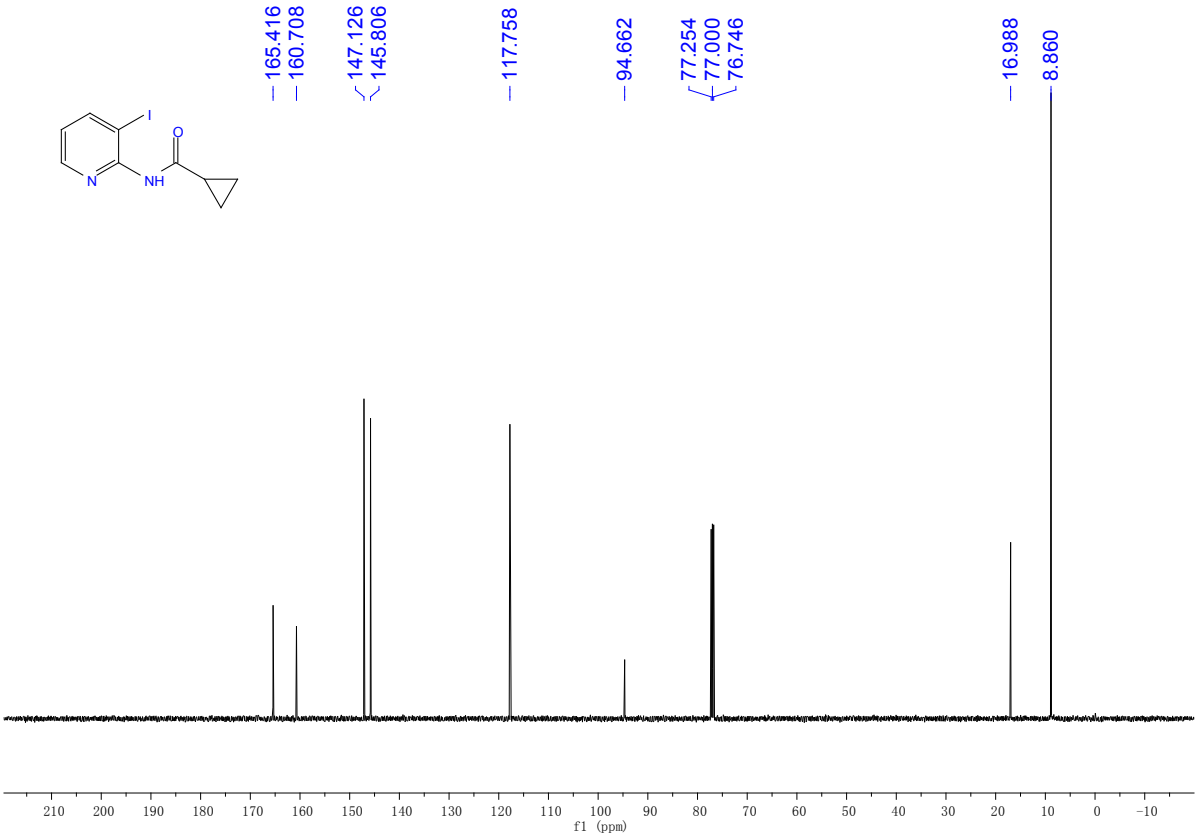
^{13}C NMR (150 MHz, Acetone-d_6) spectrum of compound 3b



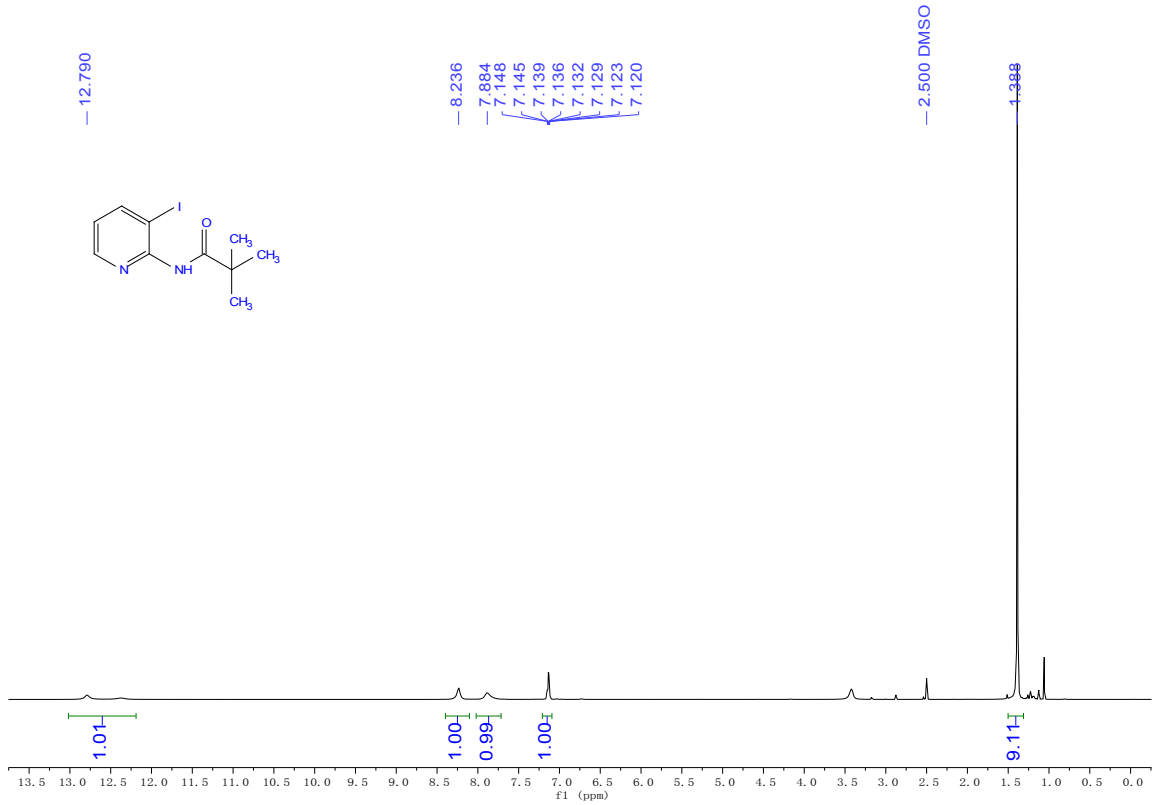
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound 3c



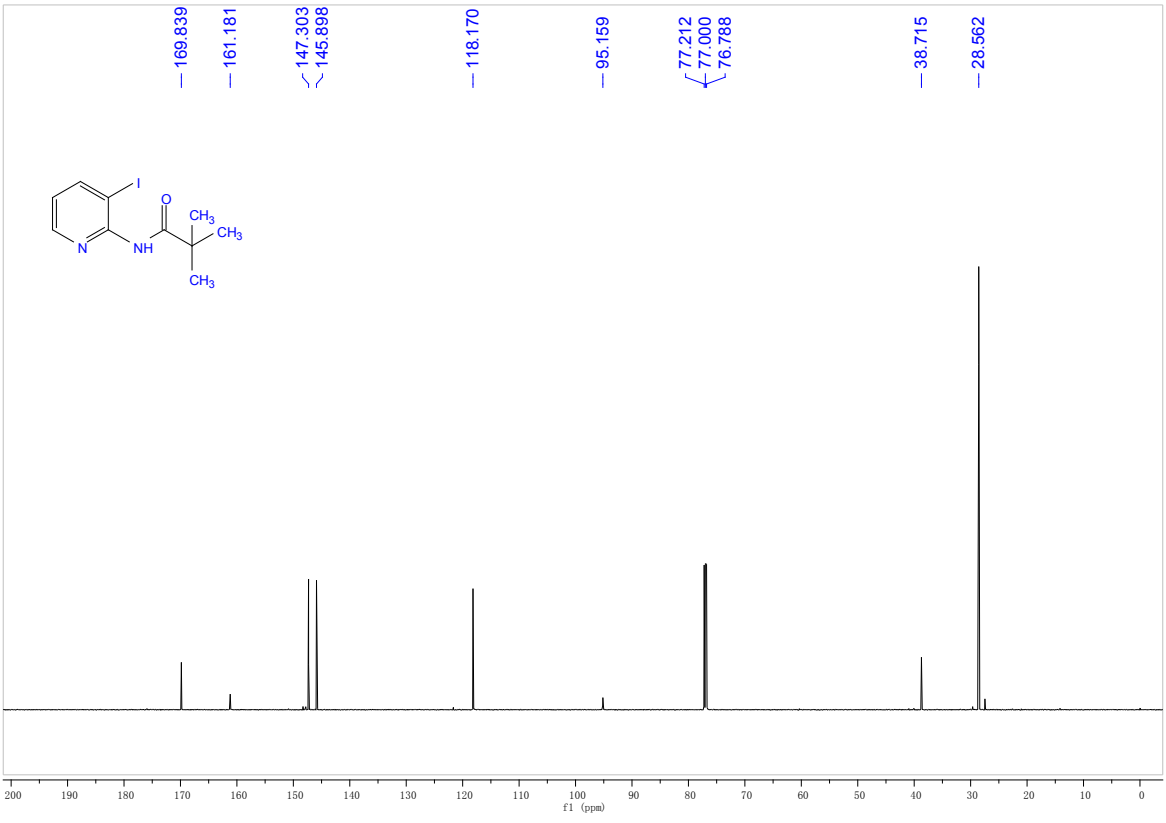
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound 3c



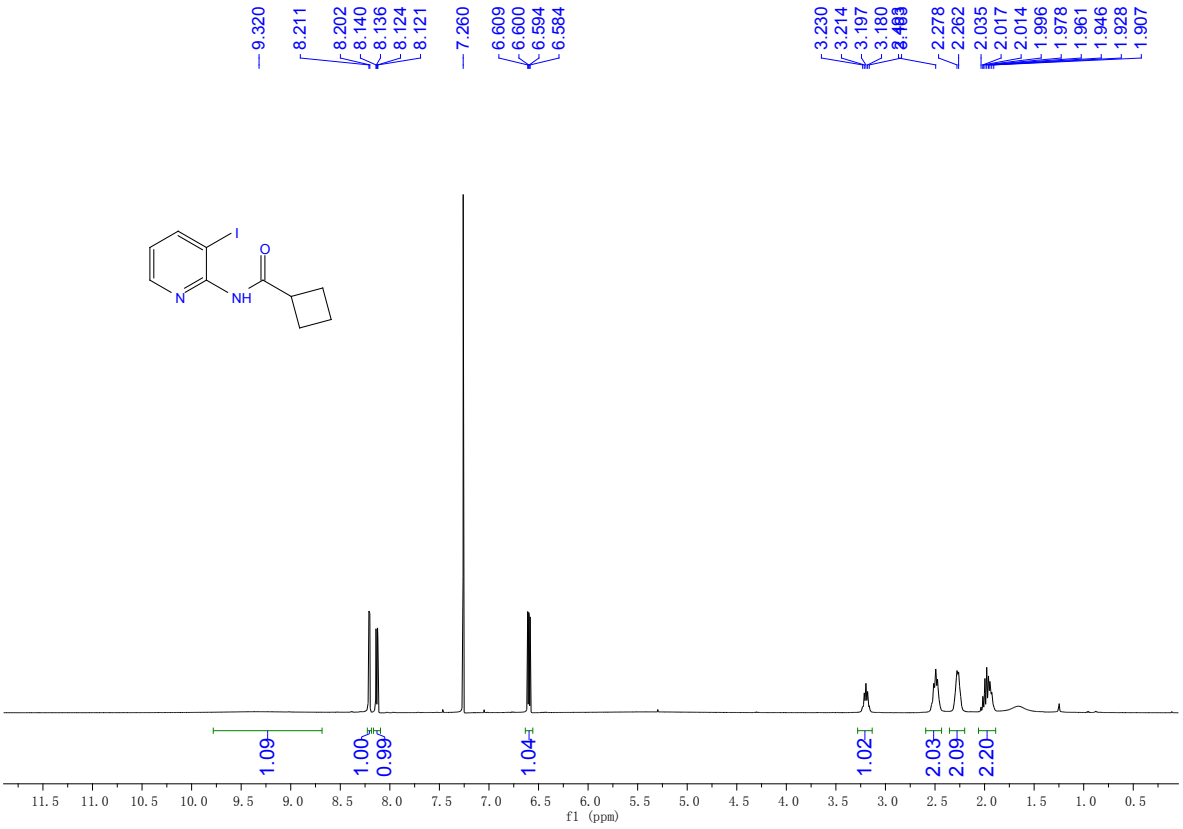
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of compound 3d



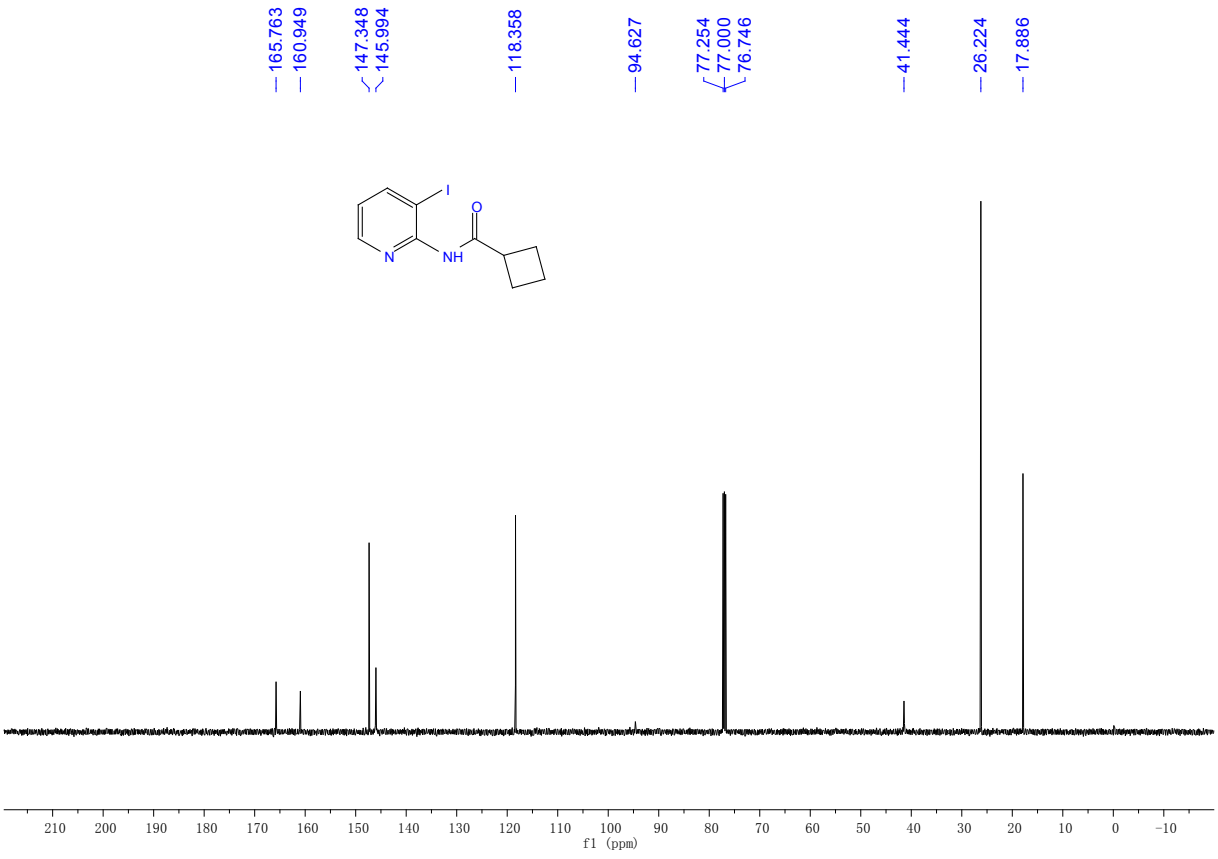
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 3d



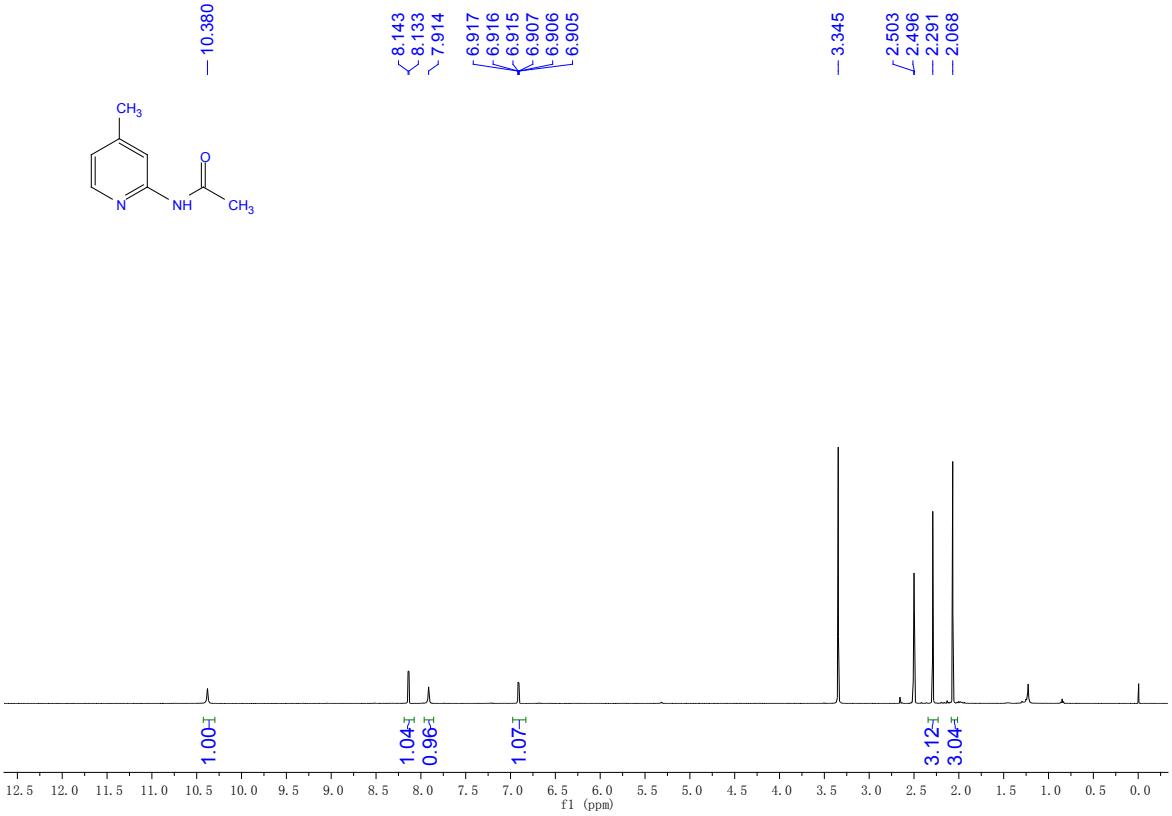
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound 3e



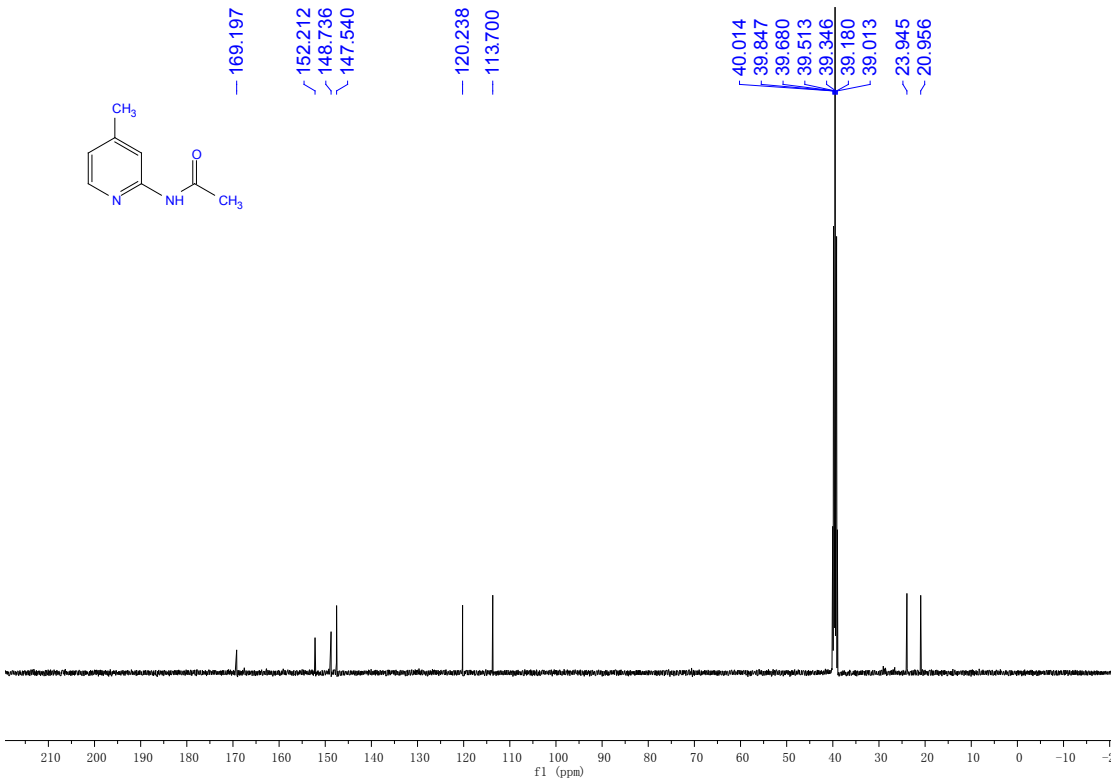
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound 3e



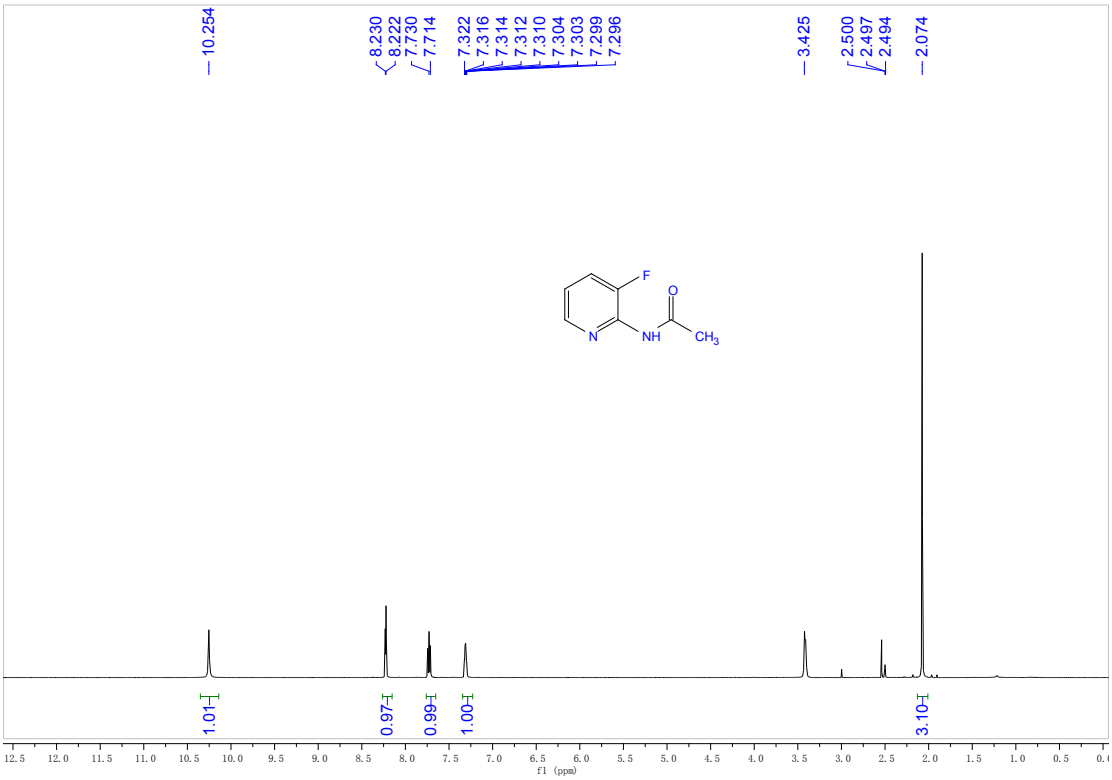
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of compound 3f



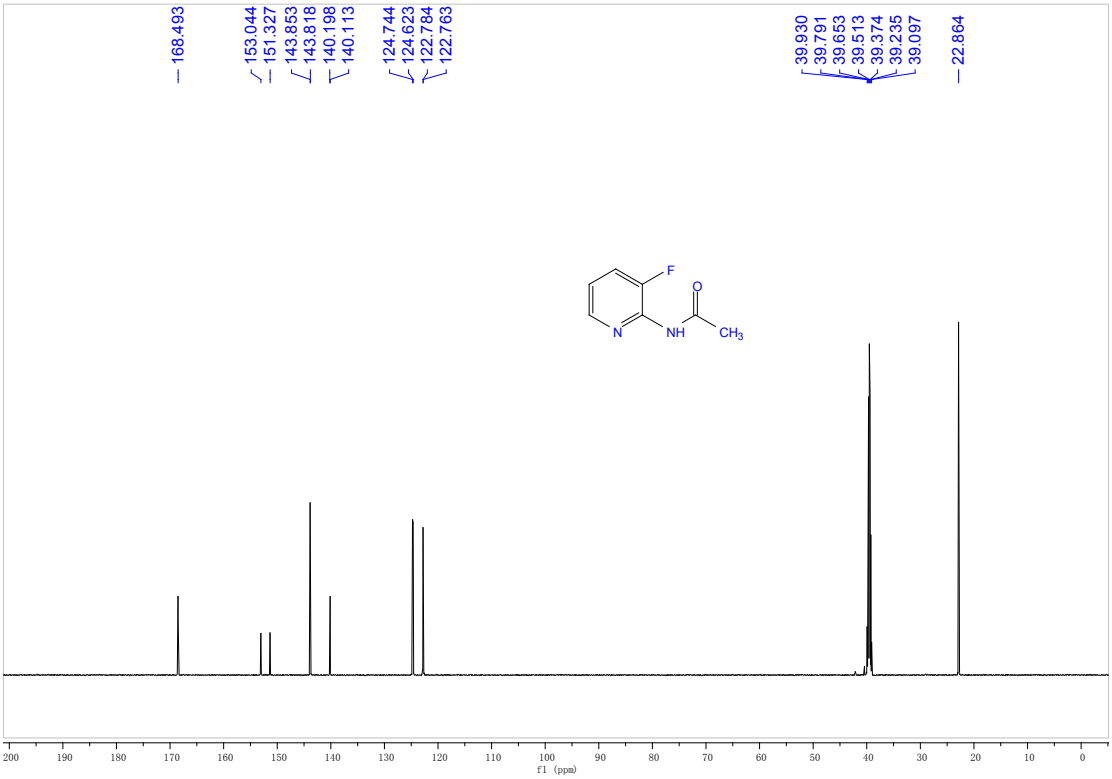
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 3f



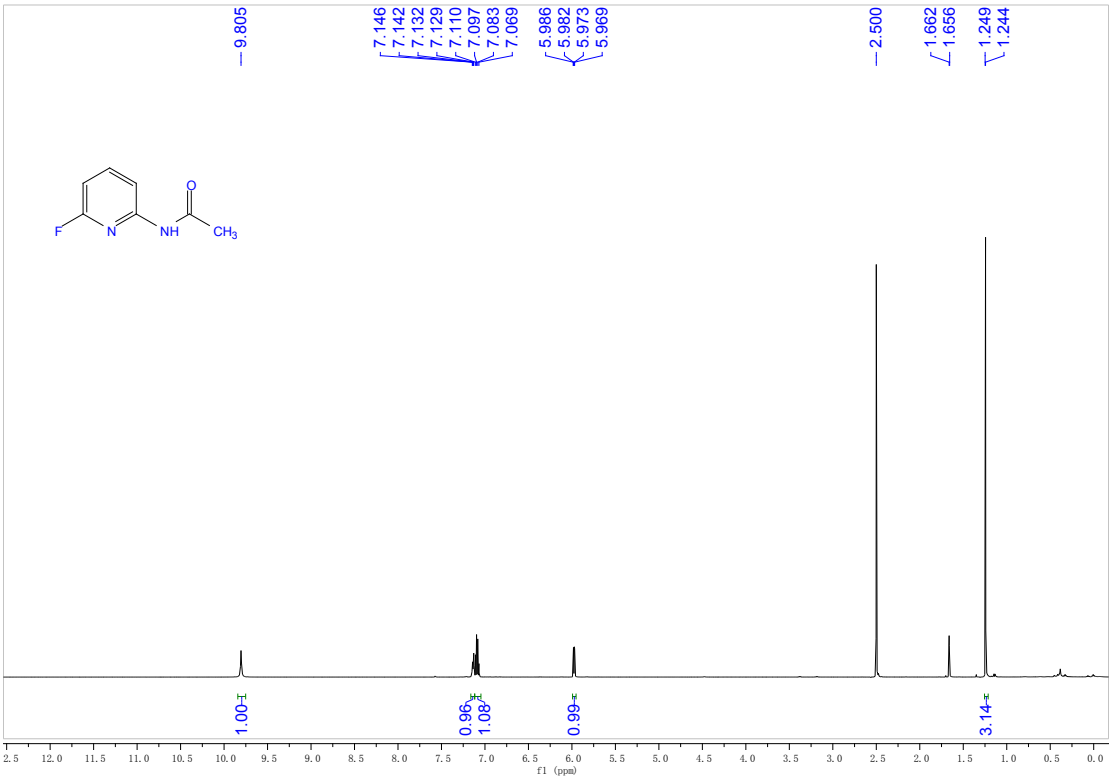
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 3g



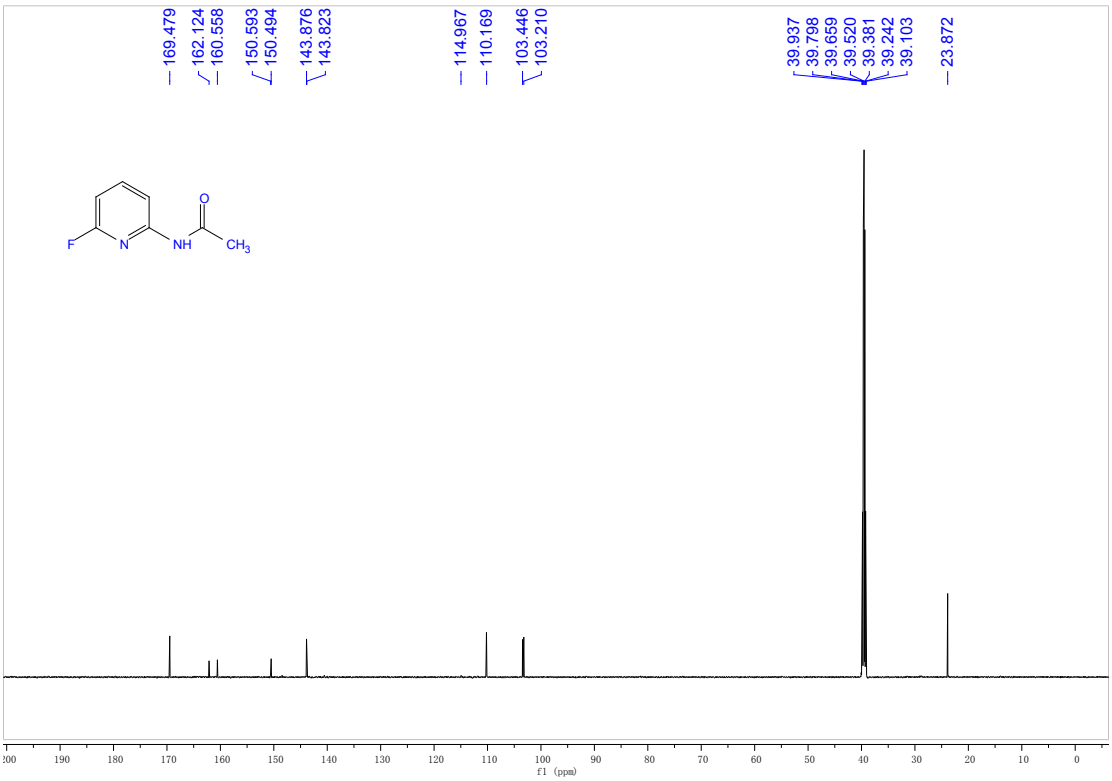
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 3g



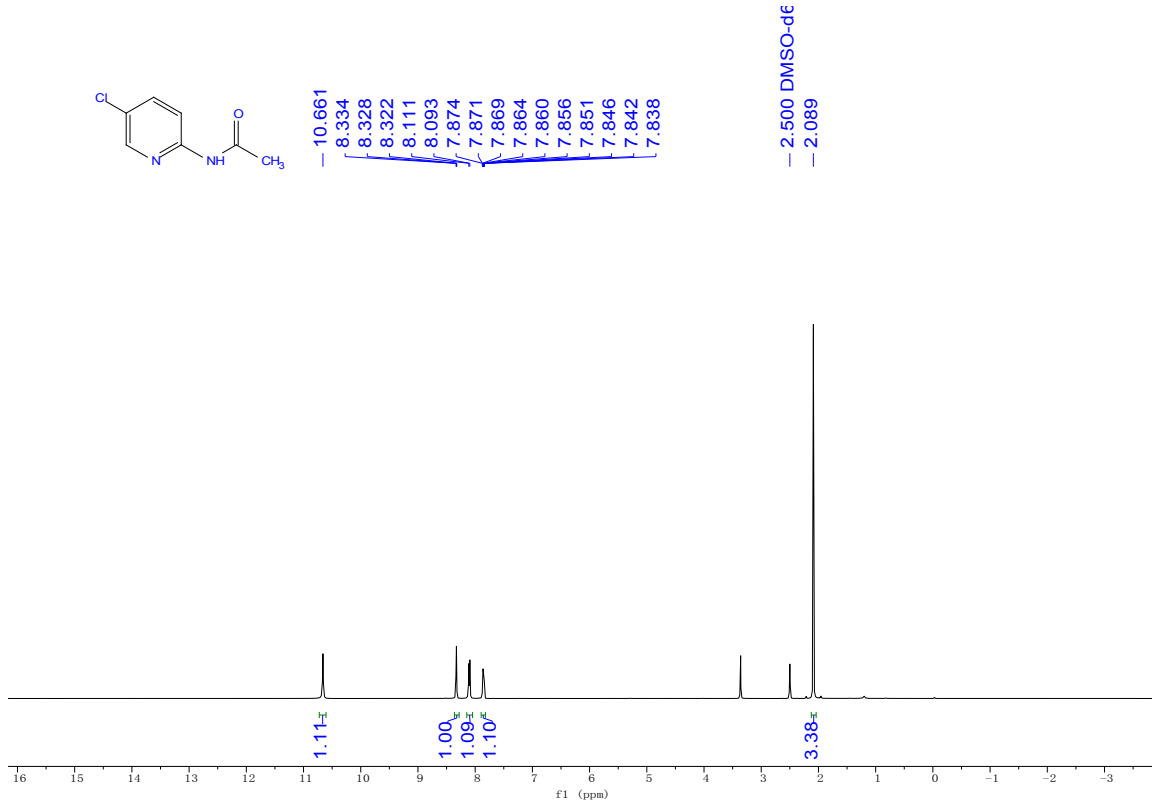
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 3h



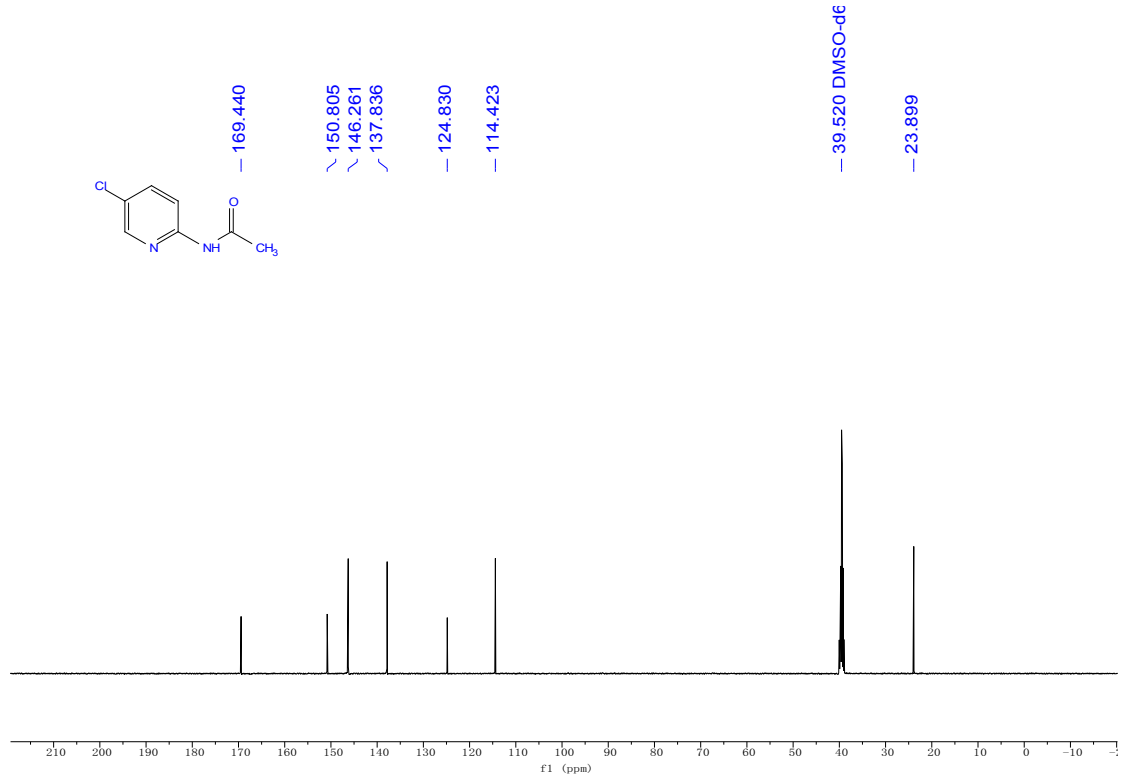
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 3h



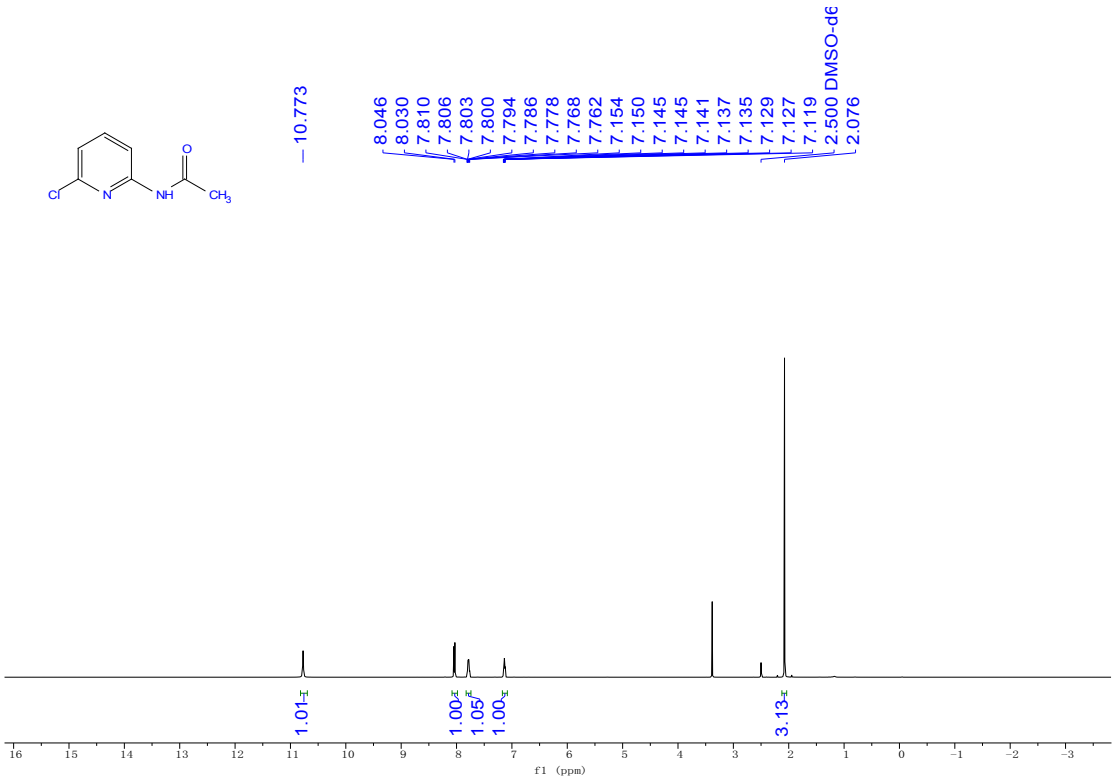
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of compound 3i



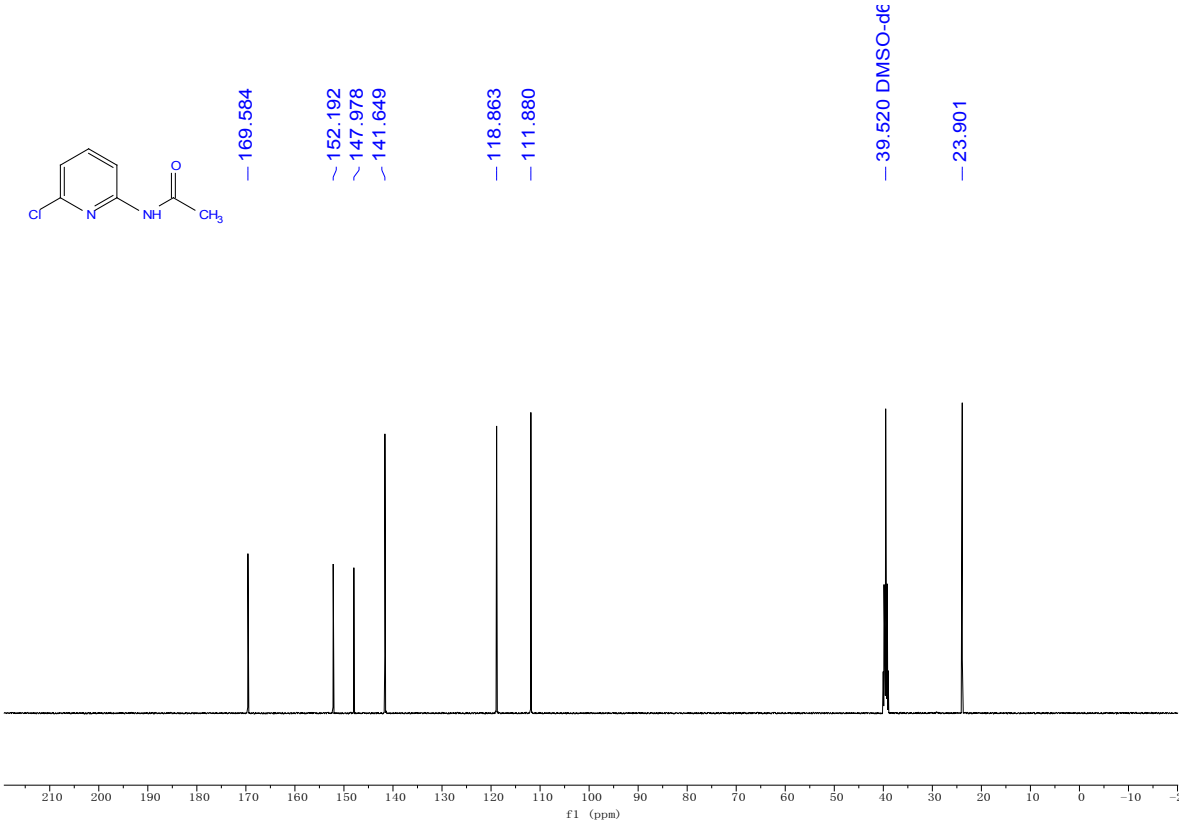
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 3i



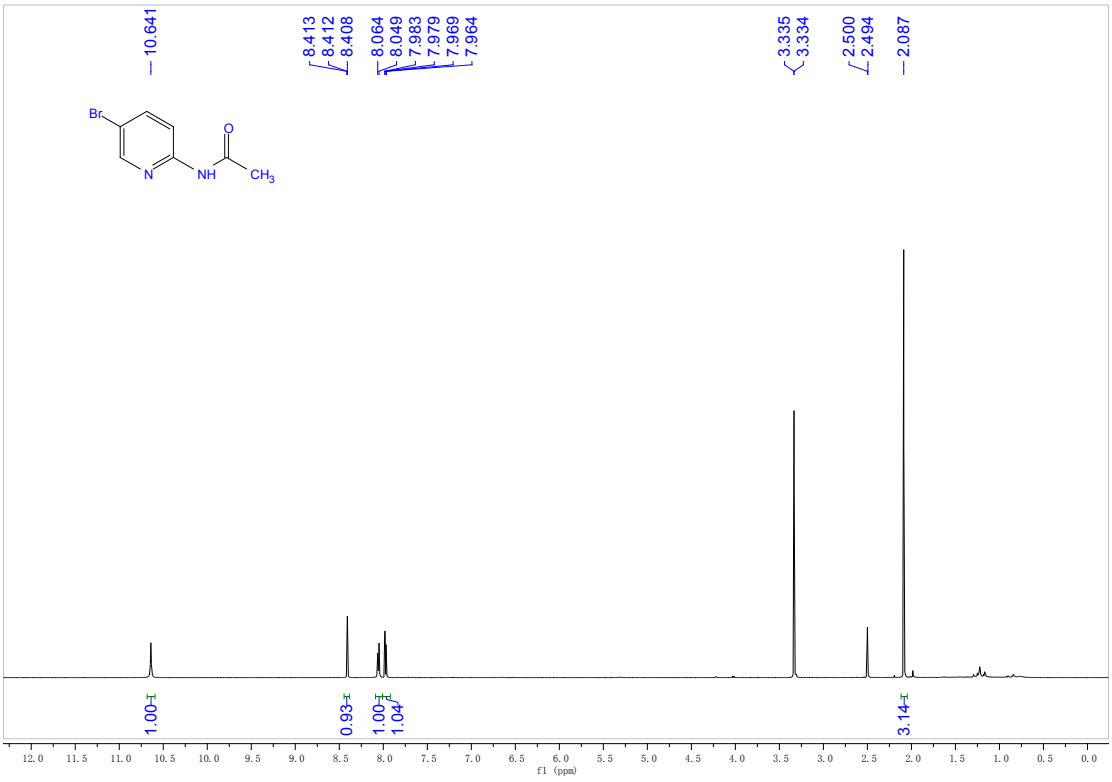
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 3j



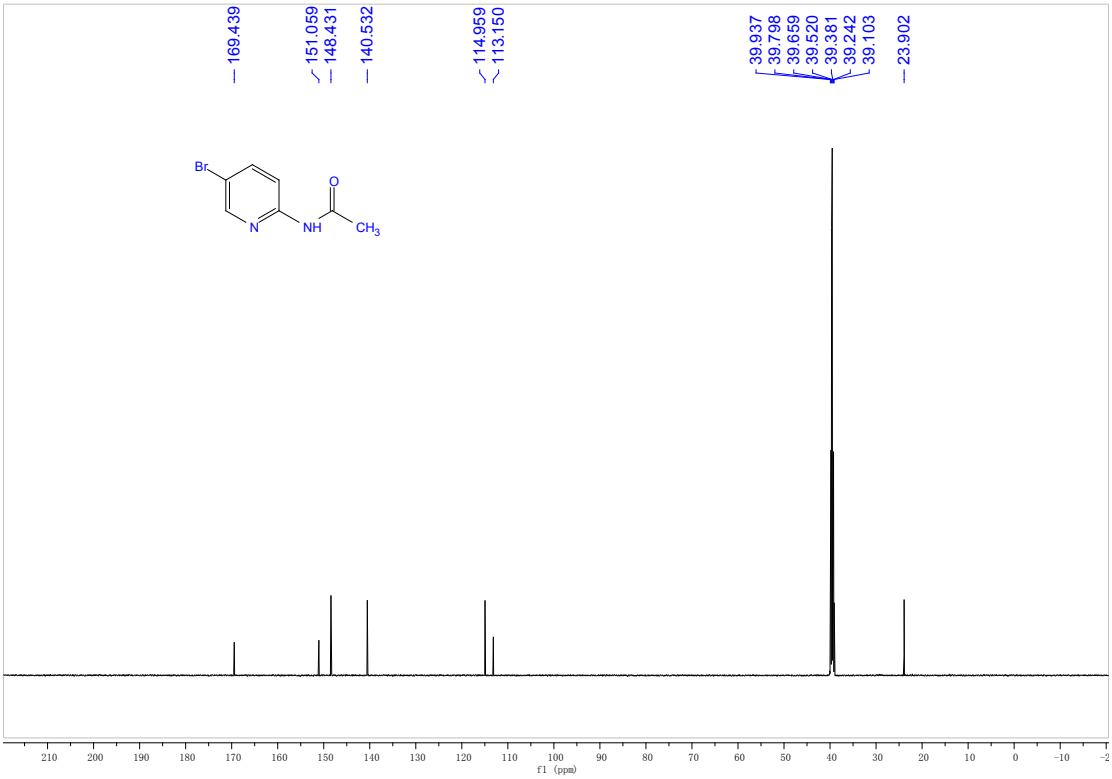
^{13}C NMR (600 MHz, DMSO-d_6) spectrum of compound 3j



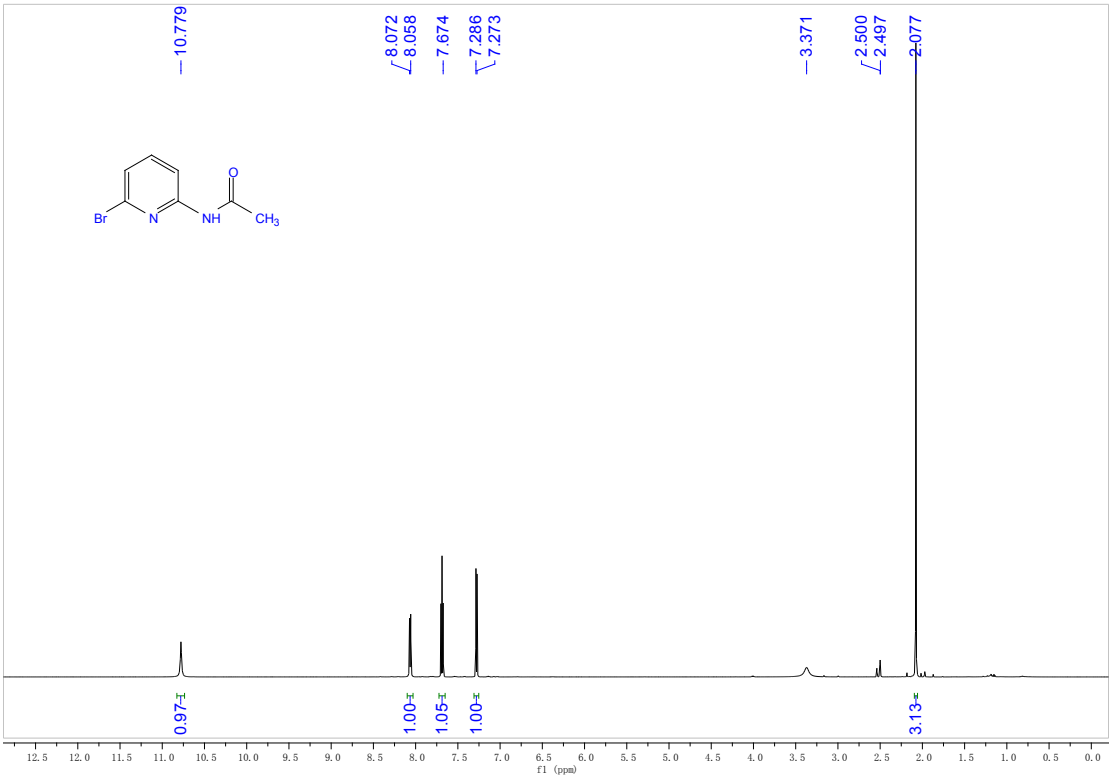
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 3k



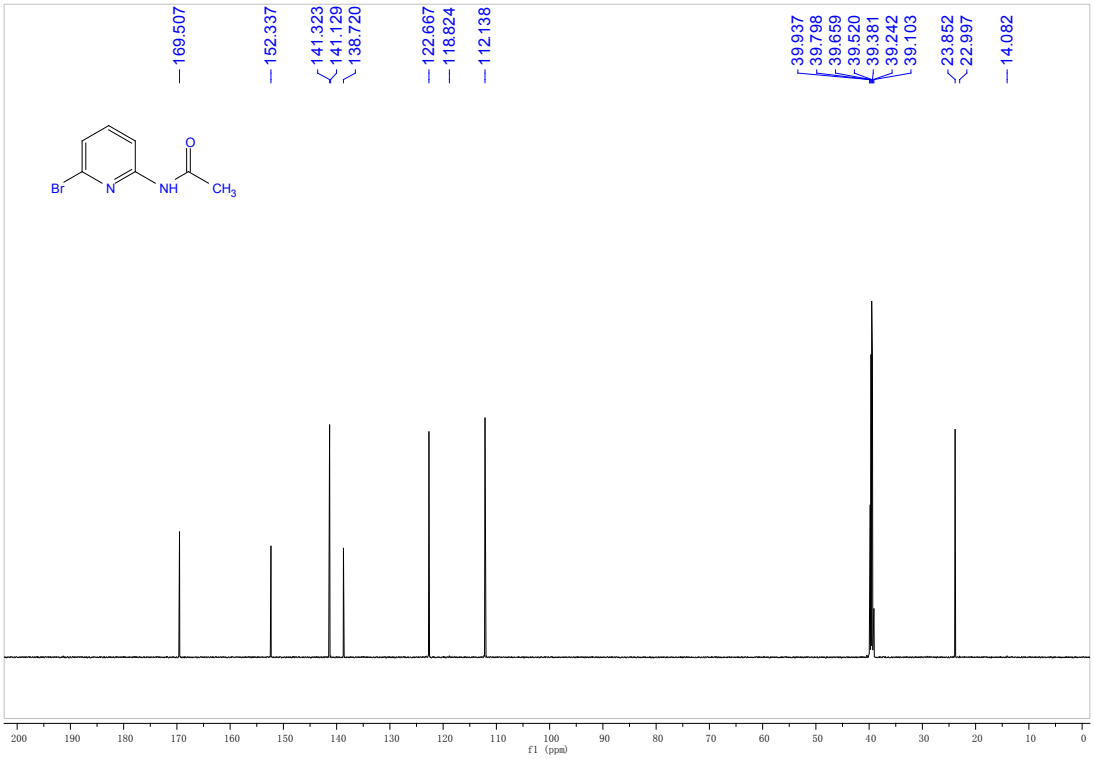
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 3k



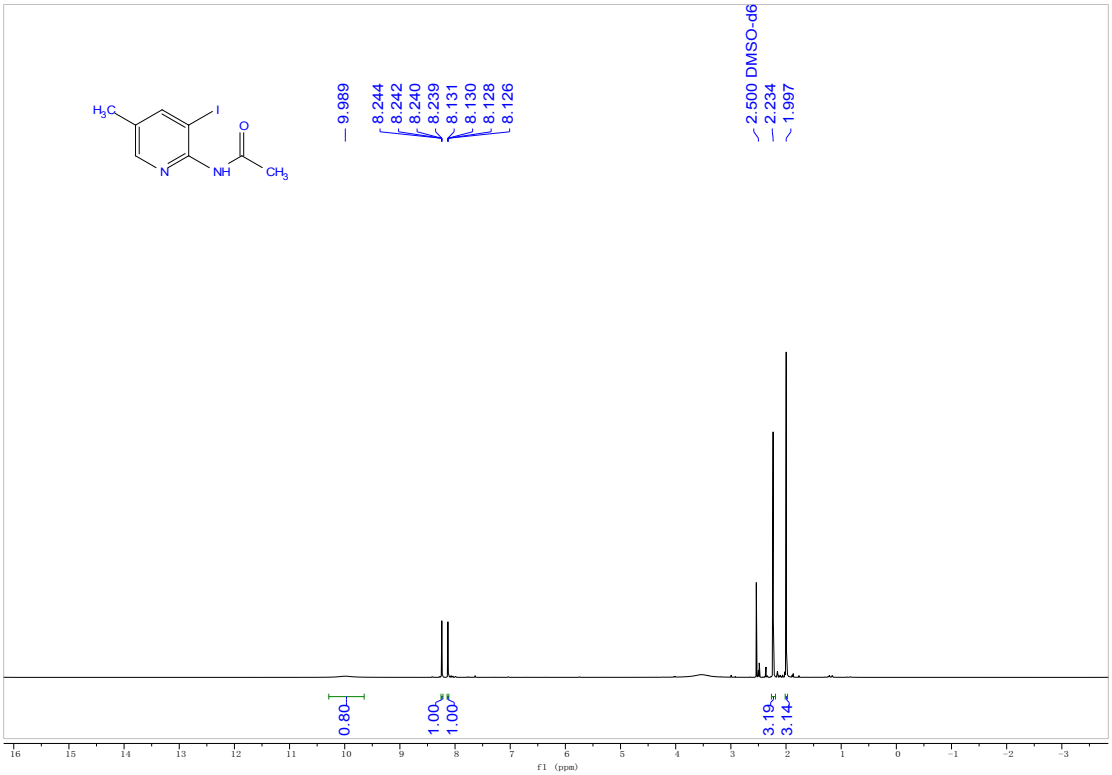
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 3l



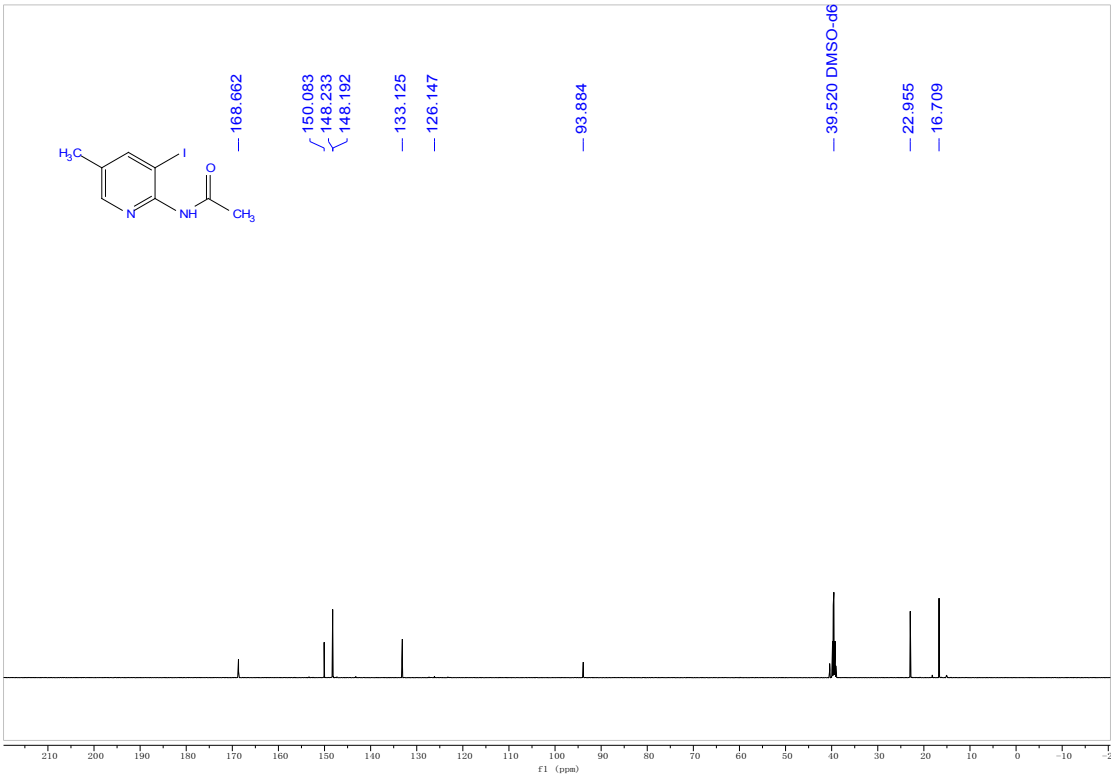
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 3l



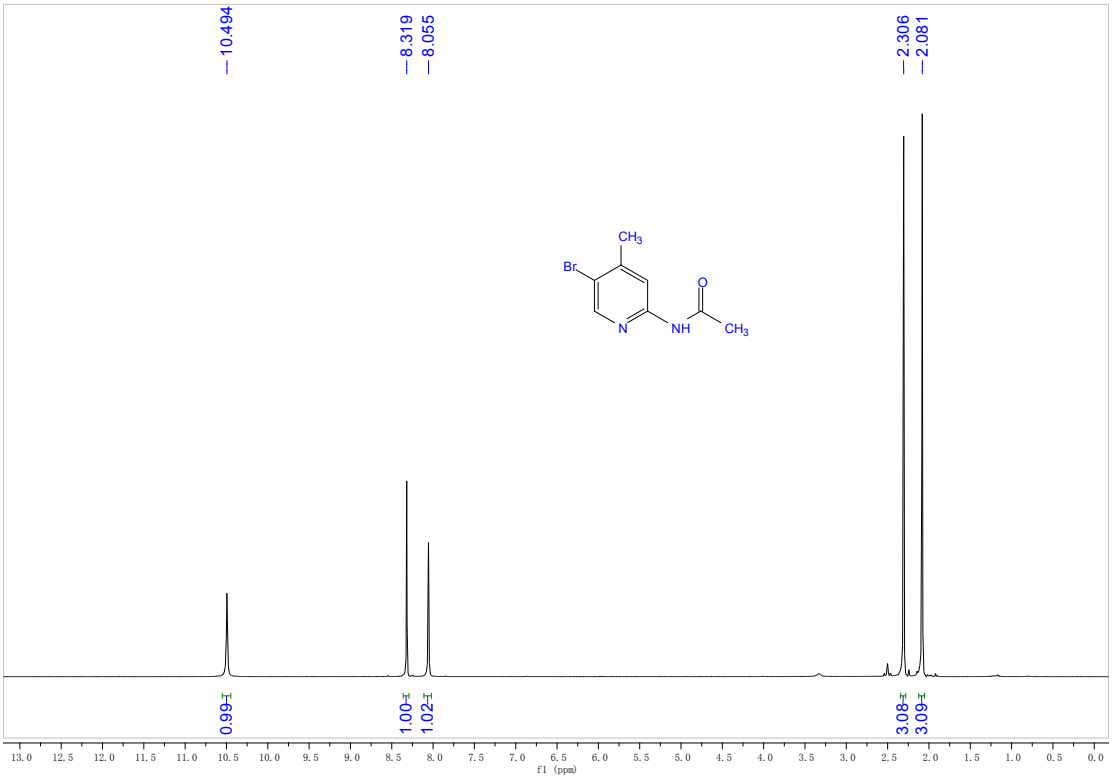
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 3m



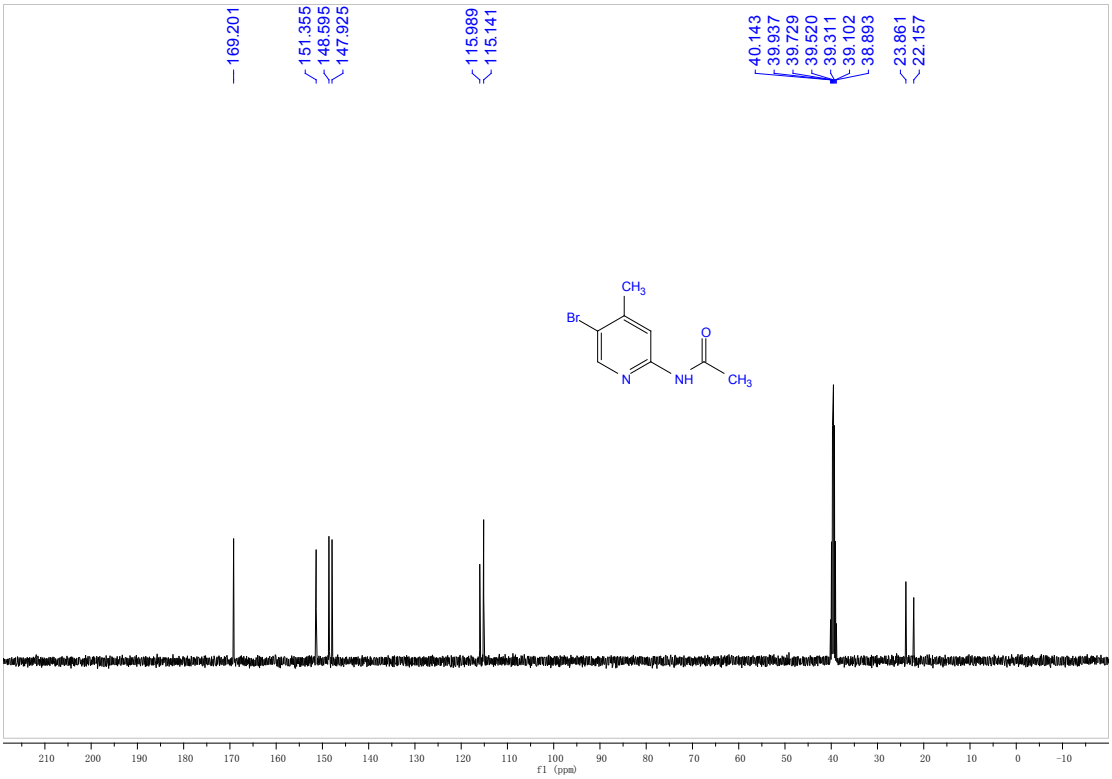
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 3m



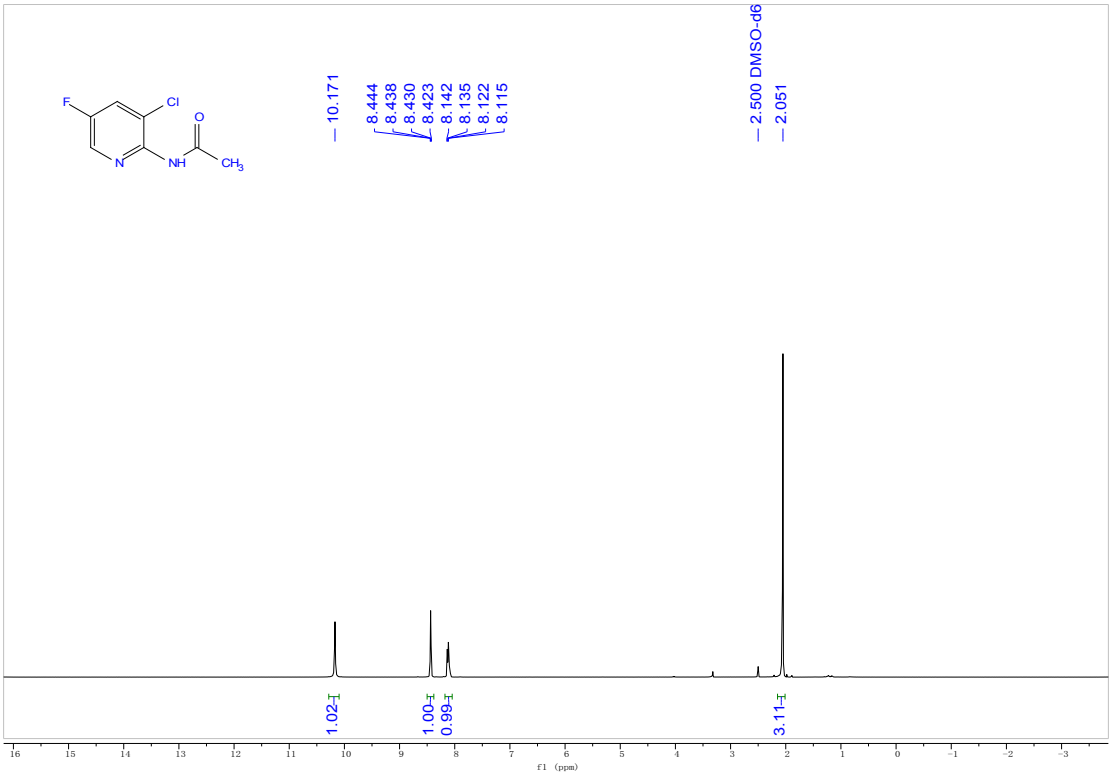
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound 3n



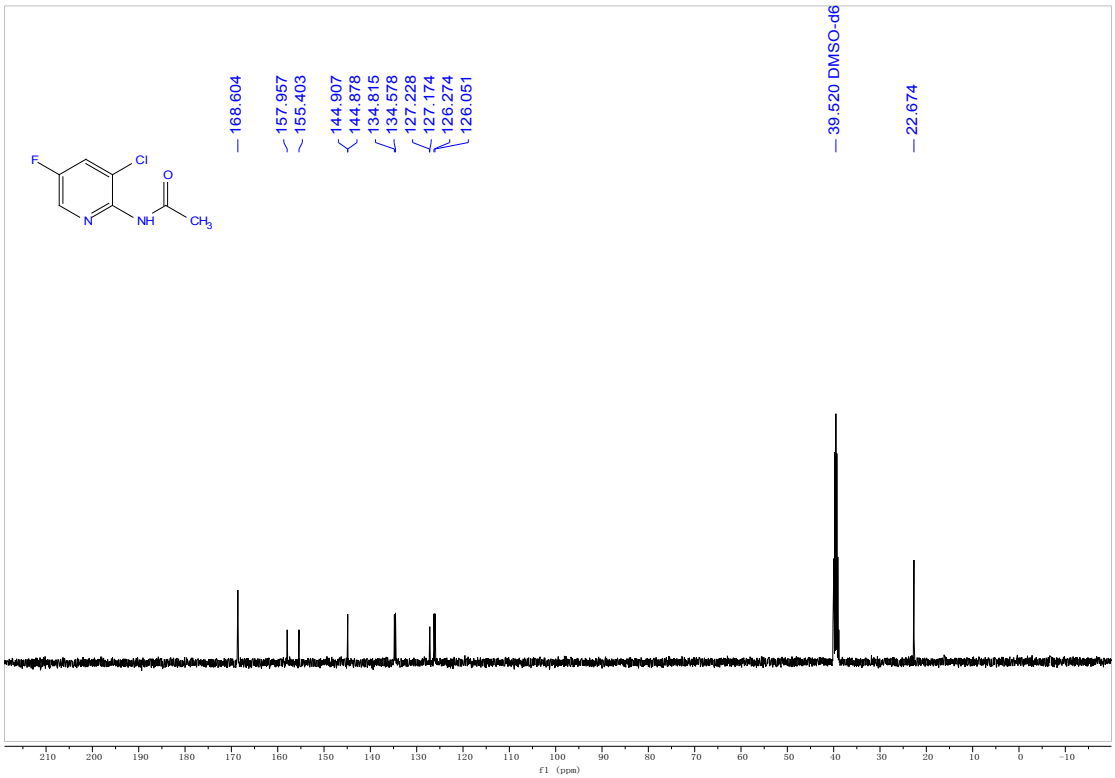
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound 3n



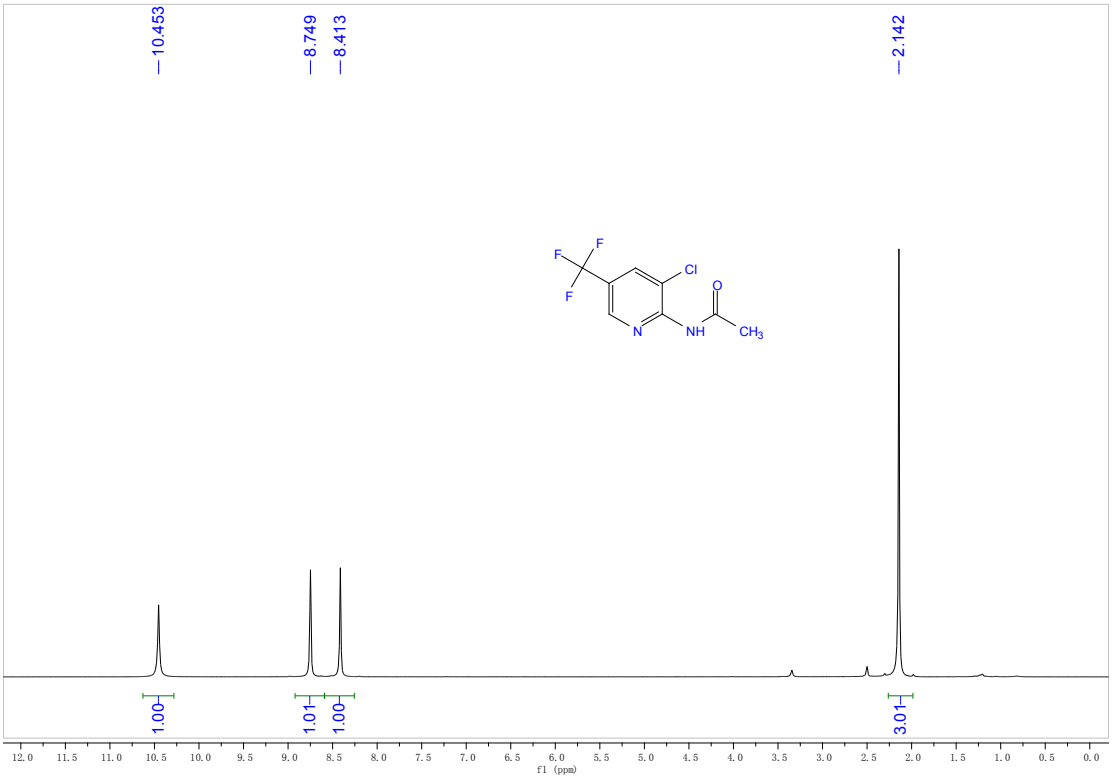
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound 3o



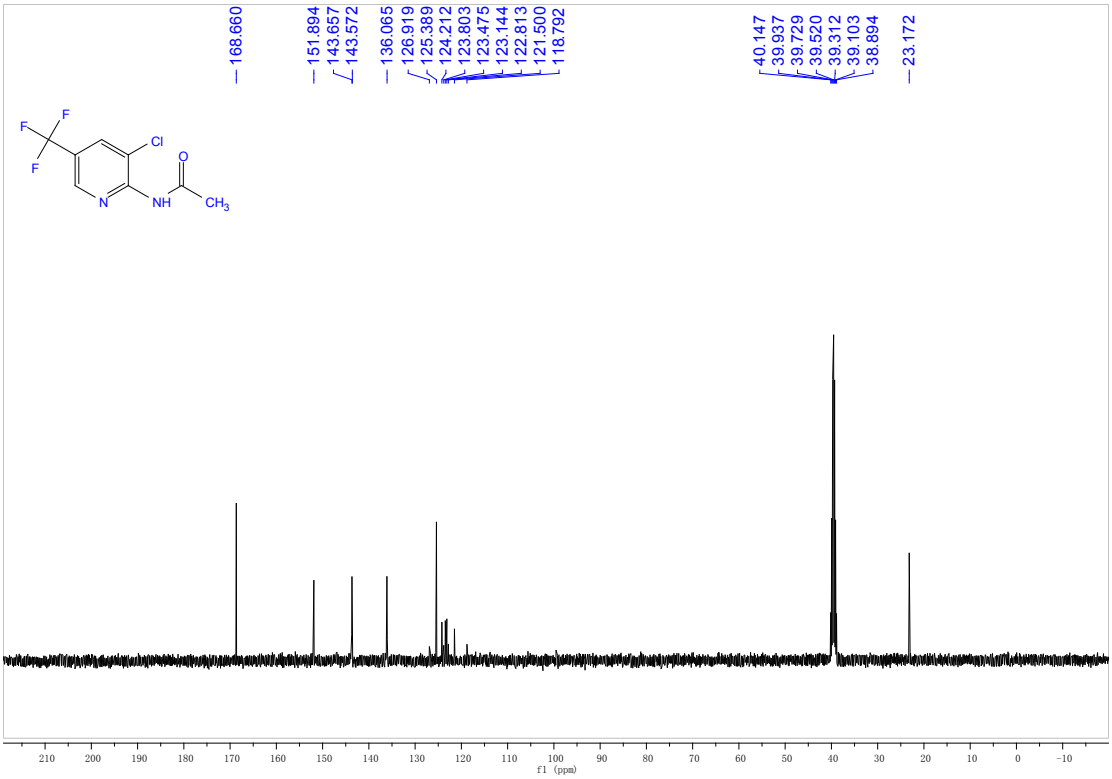
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound 3o



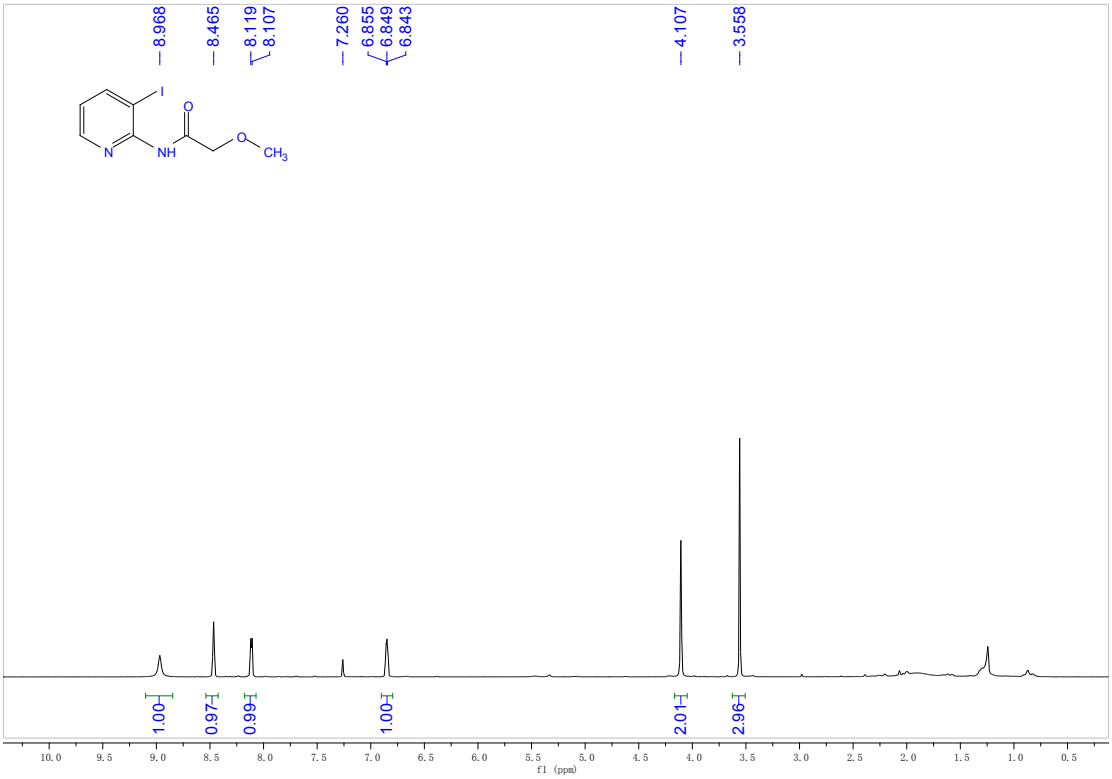
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound 3p



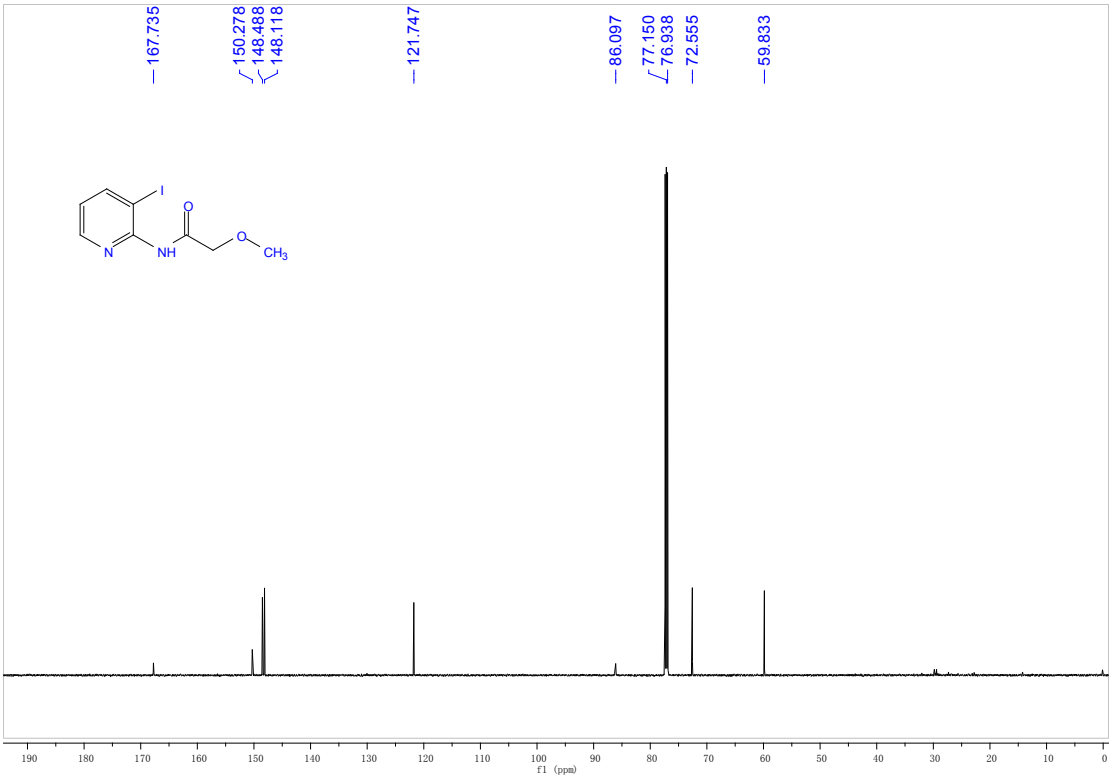
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound 3p



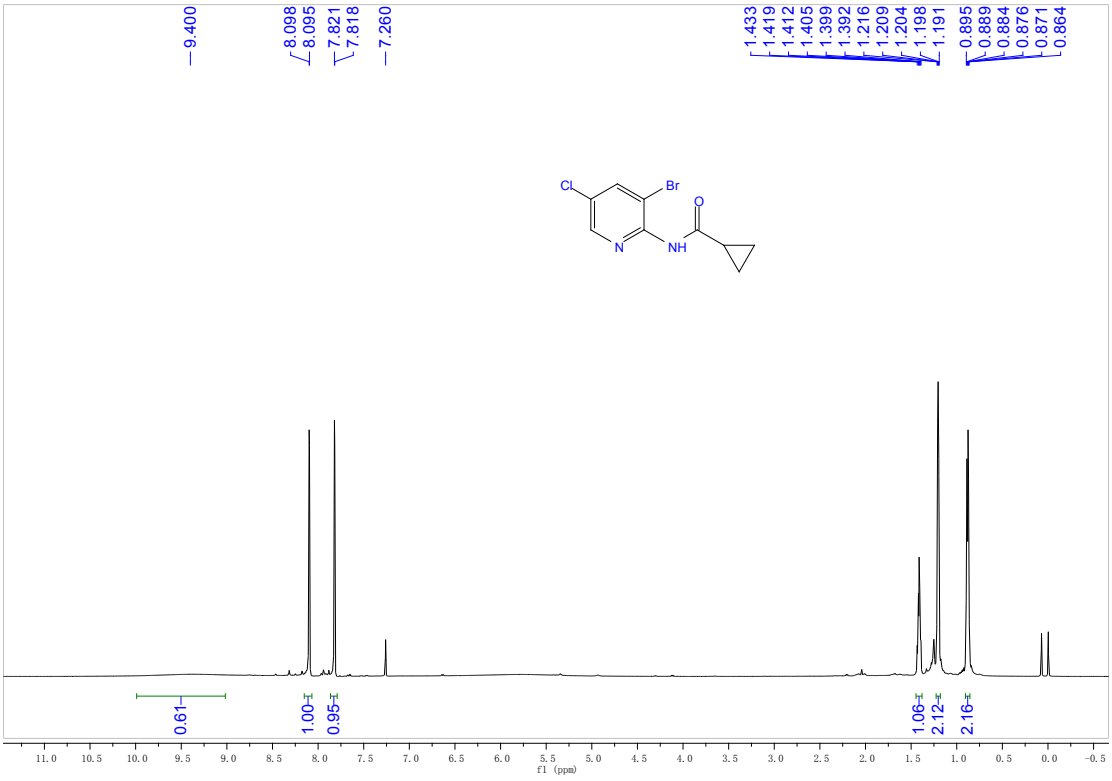
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound 3q



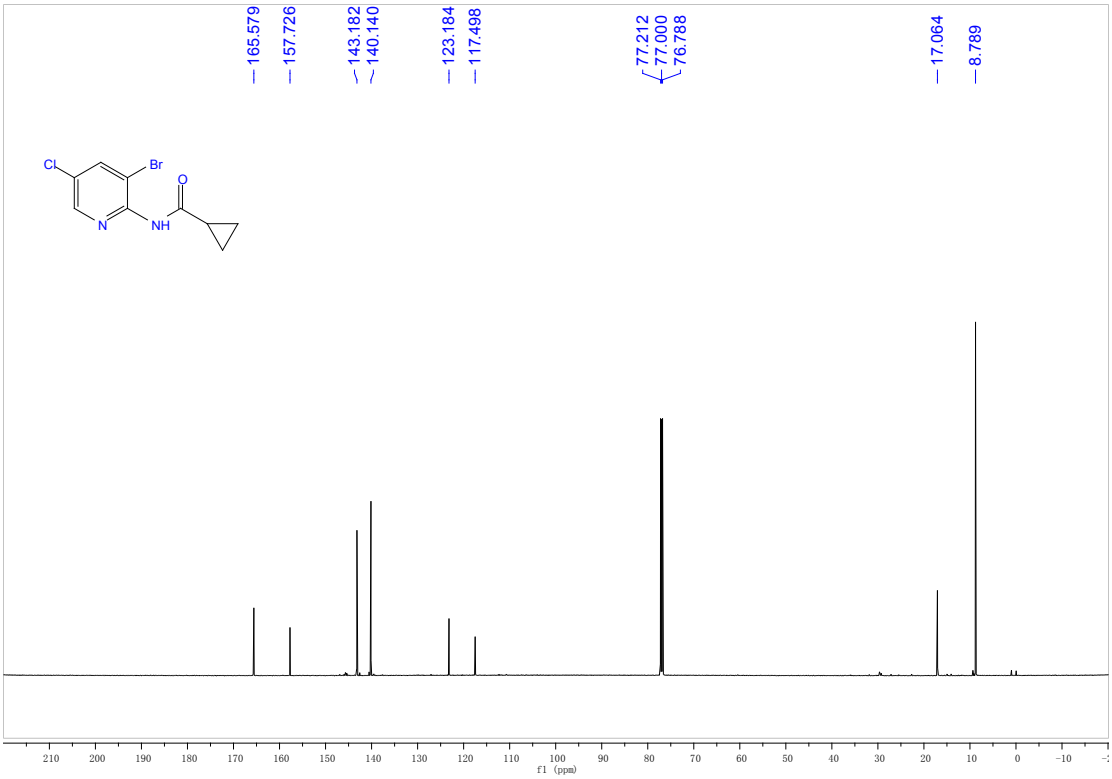
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound 3q



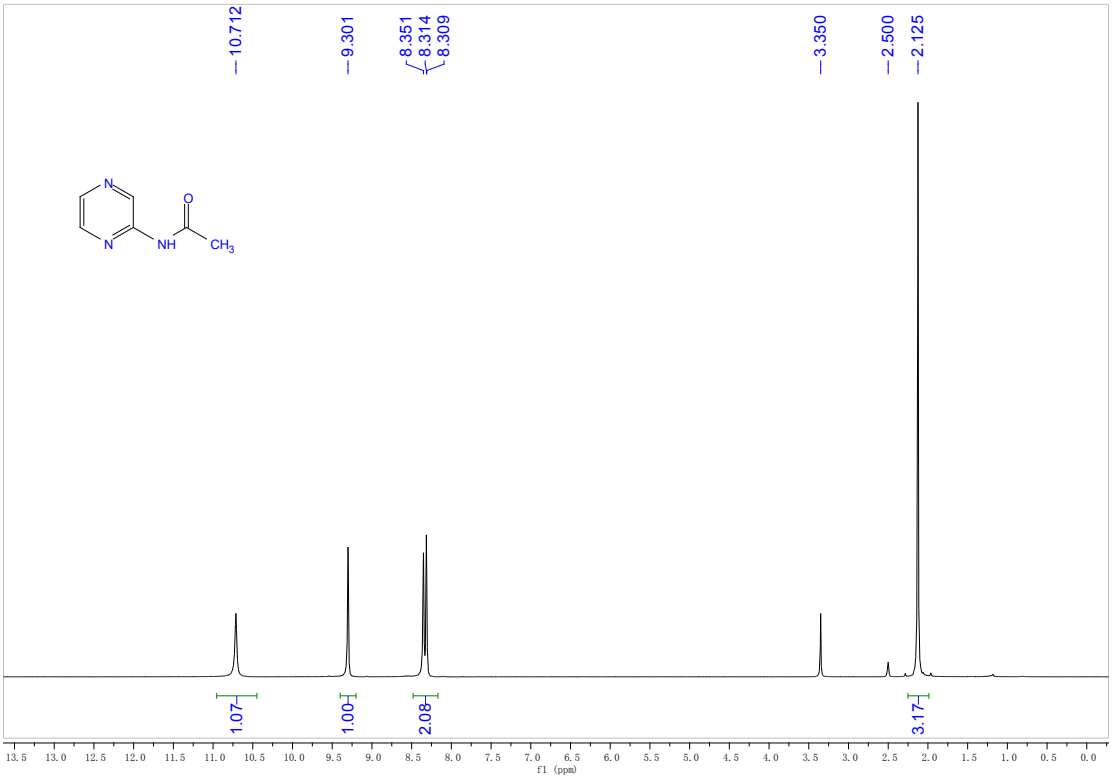
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound 3r



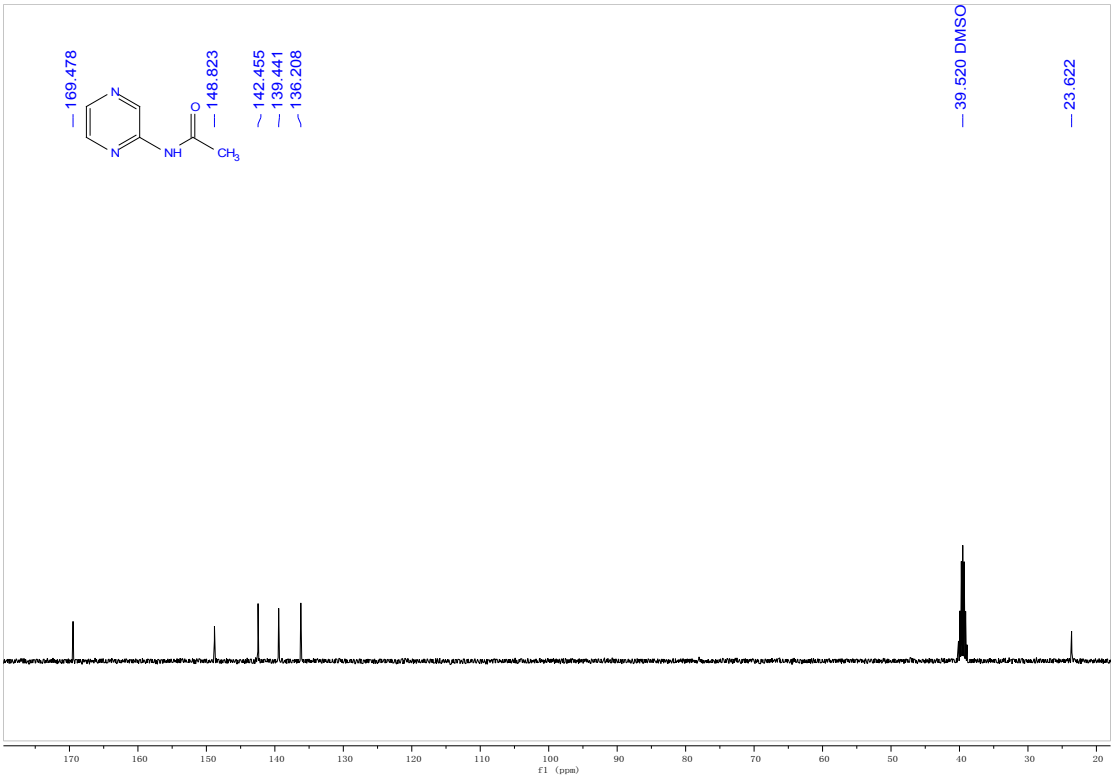
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound 3r



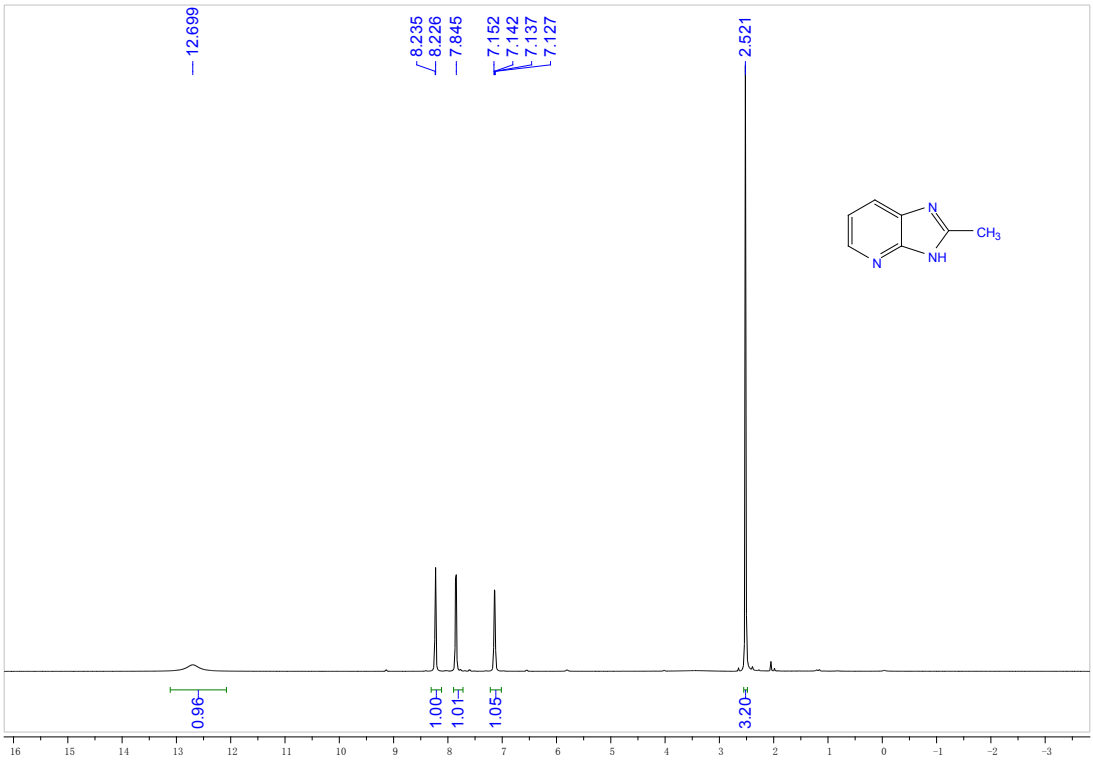
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound 3s



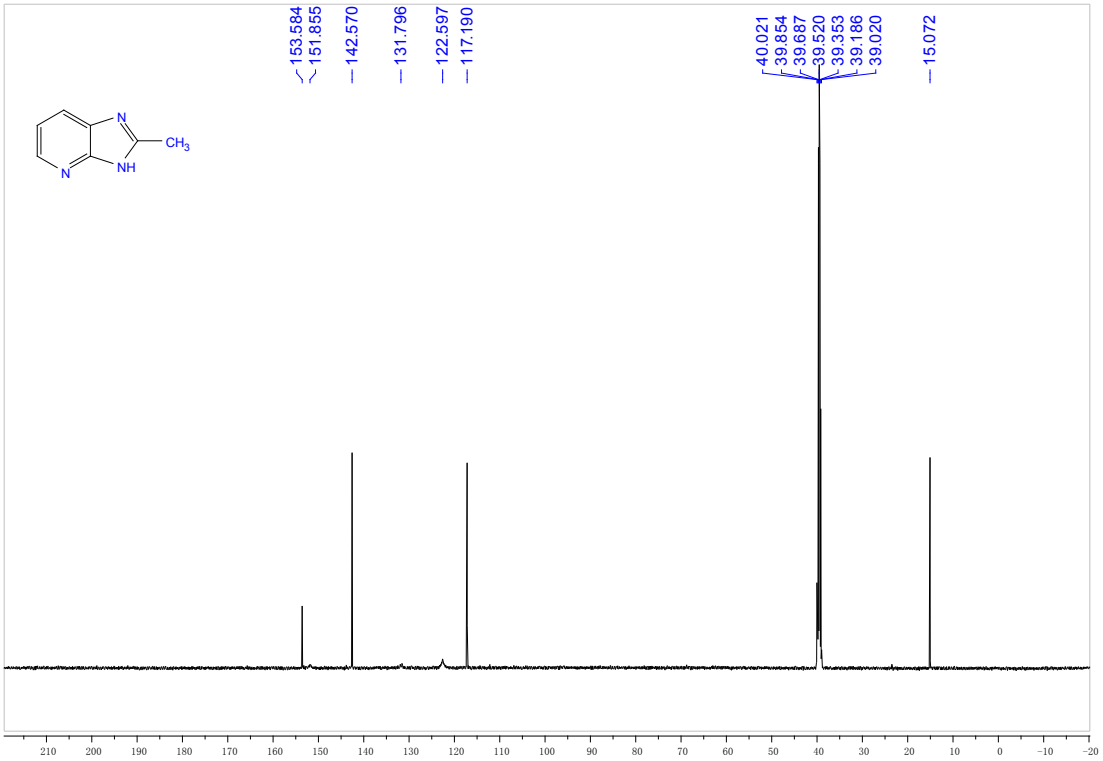
^{13}C NMR (1500 MHz, DMSO-d_6) spectrum of compound 3s



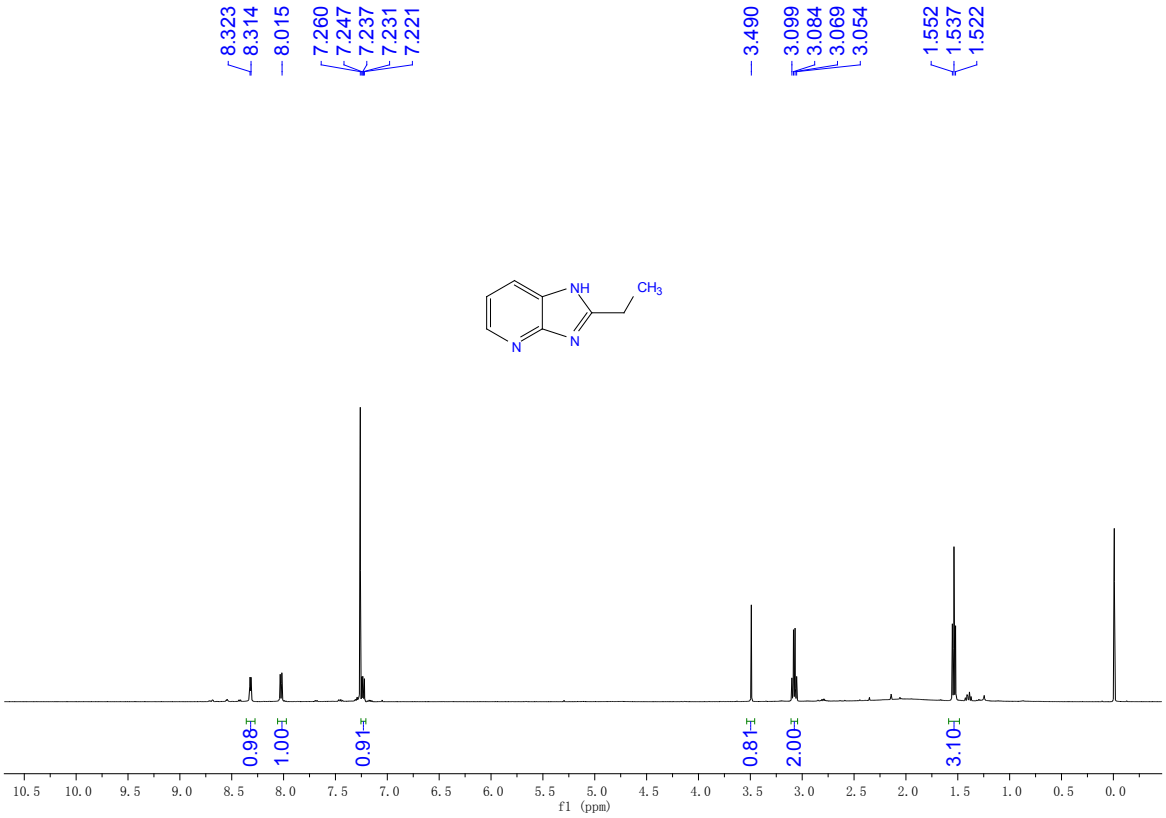
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of compound 4a



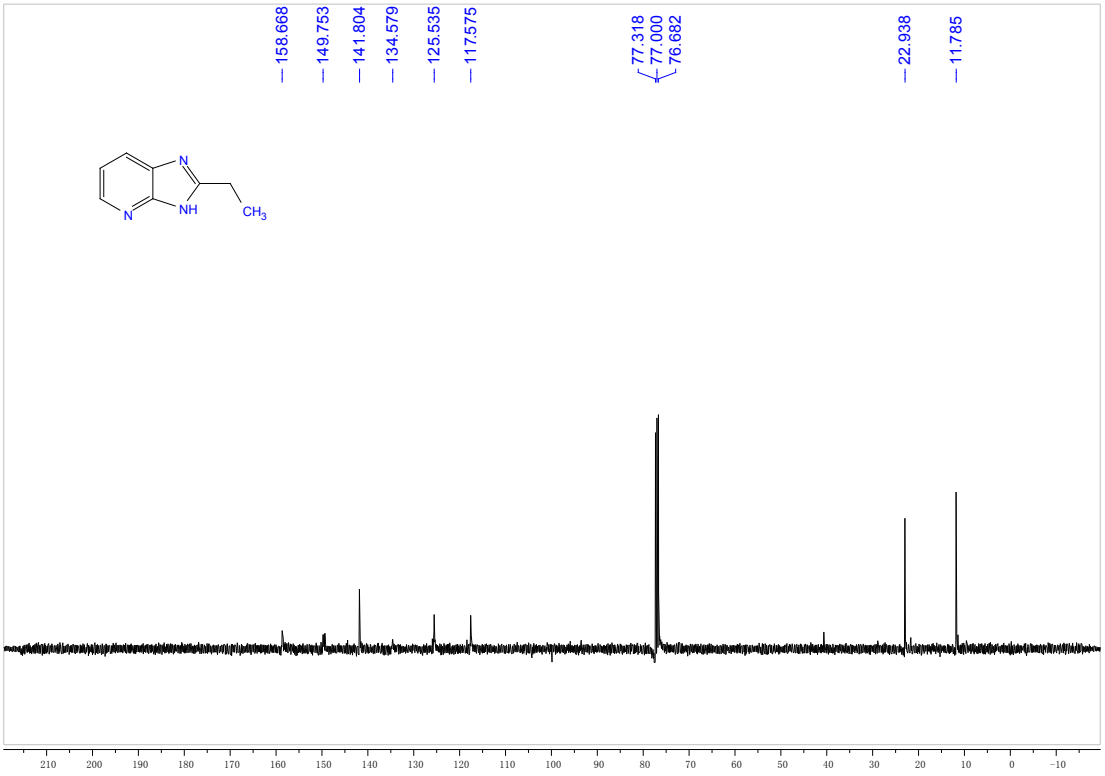
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 4a



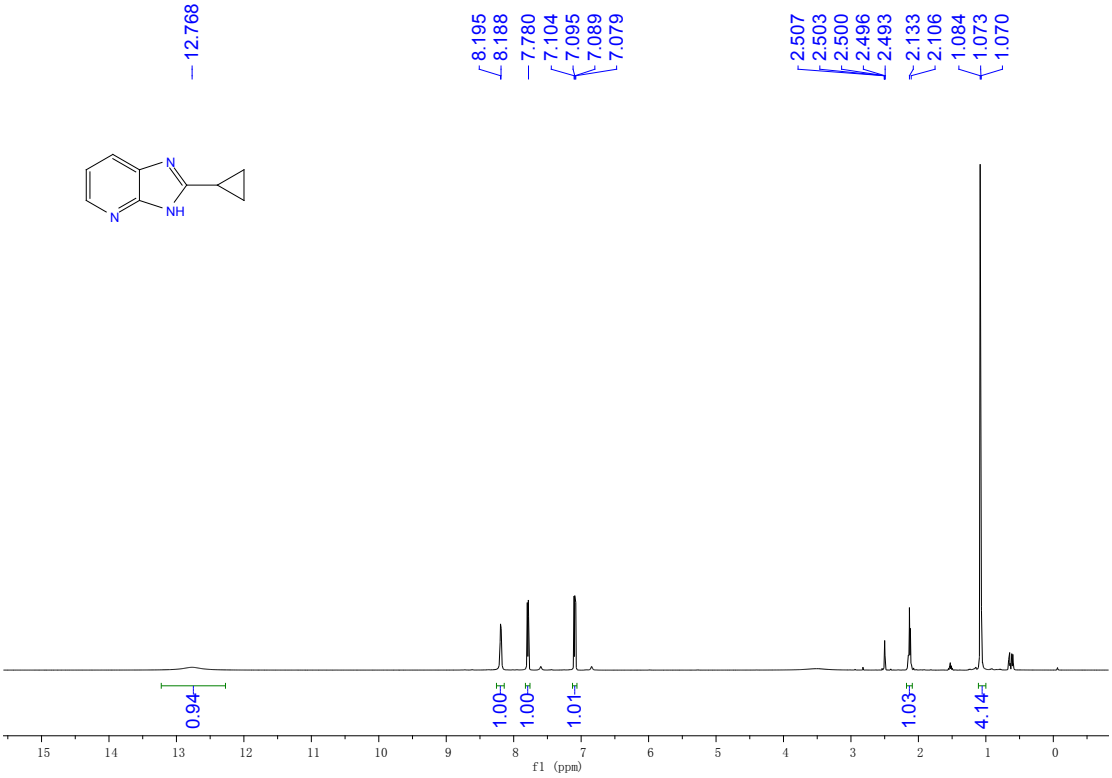
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound 4b



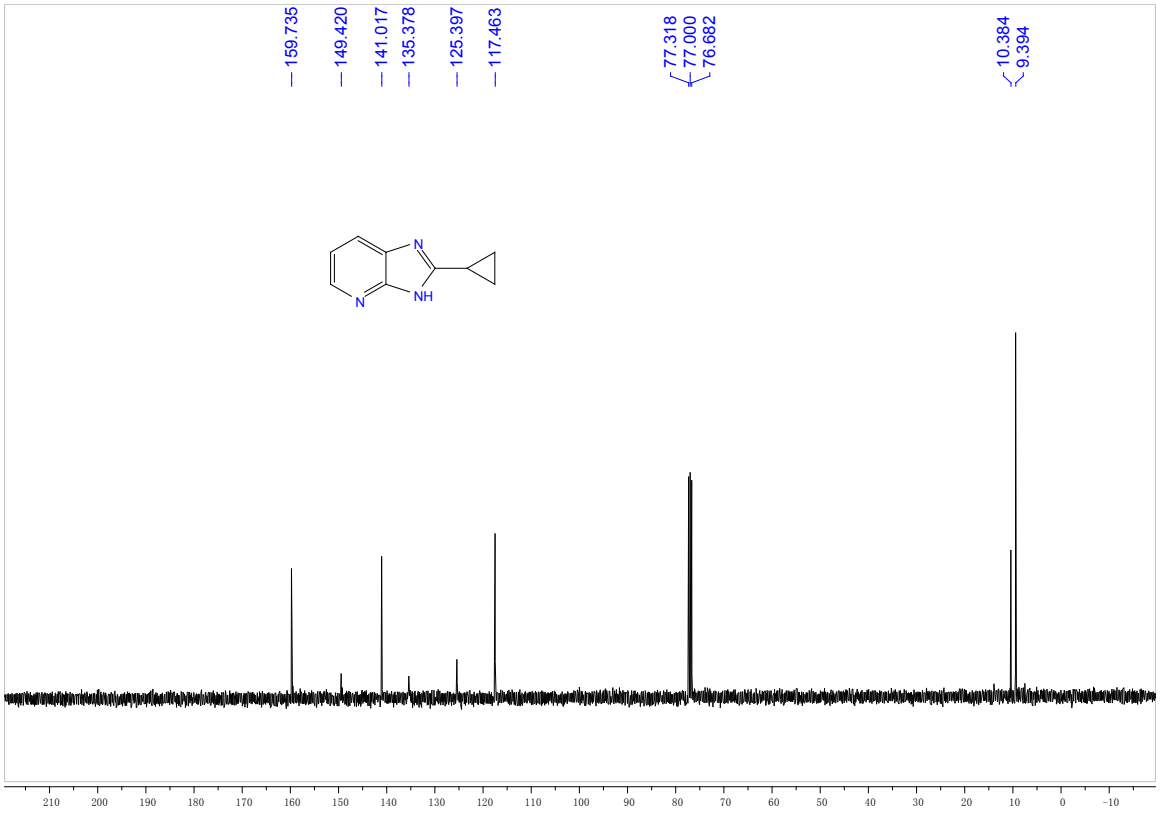
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound4b



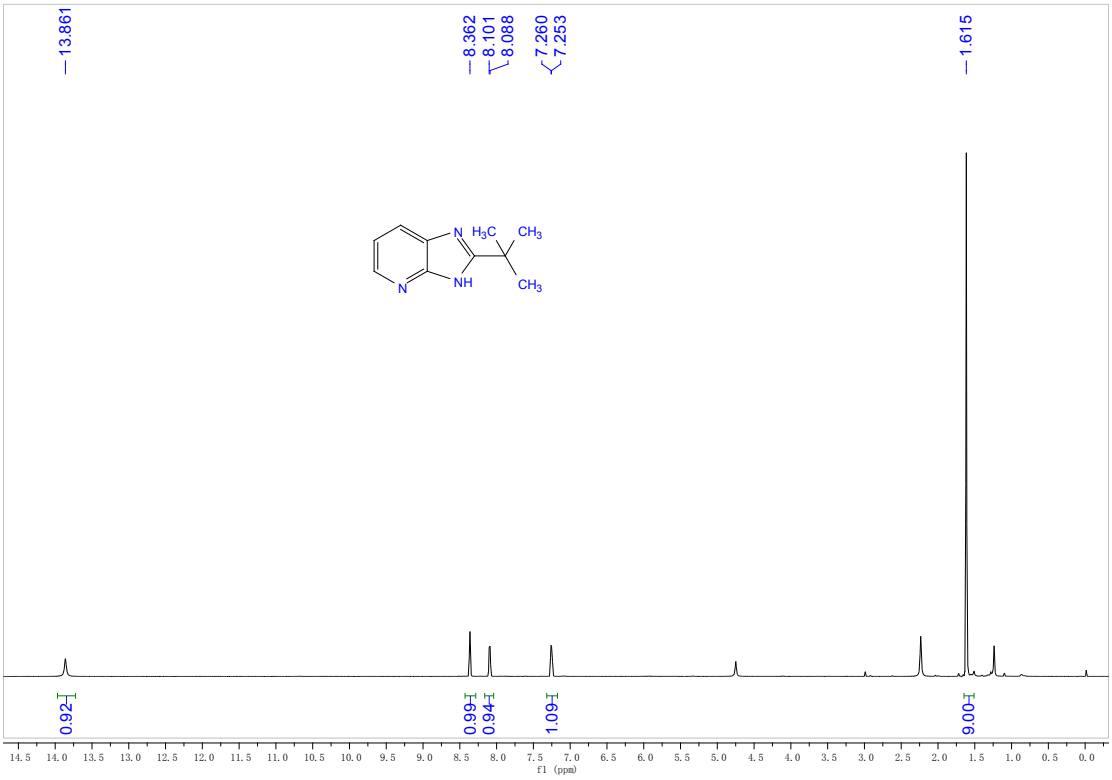
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 4c



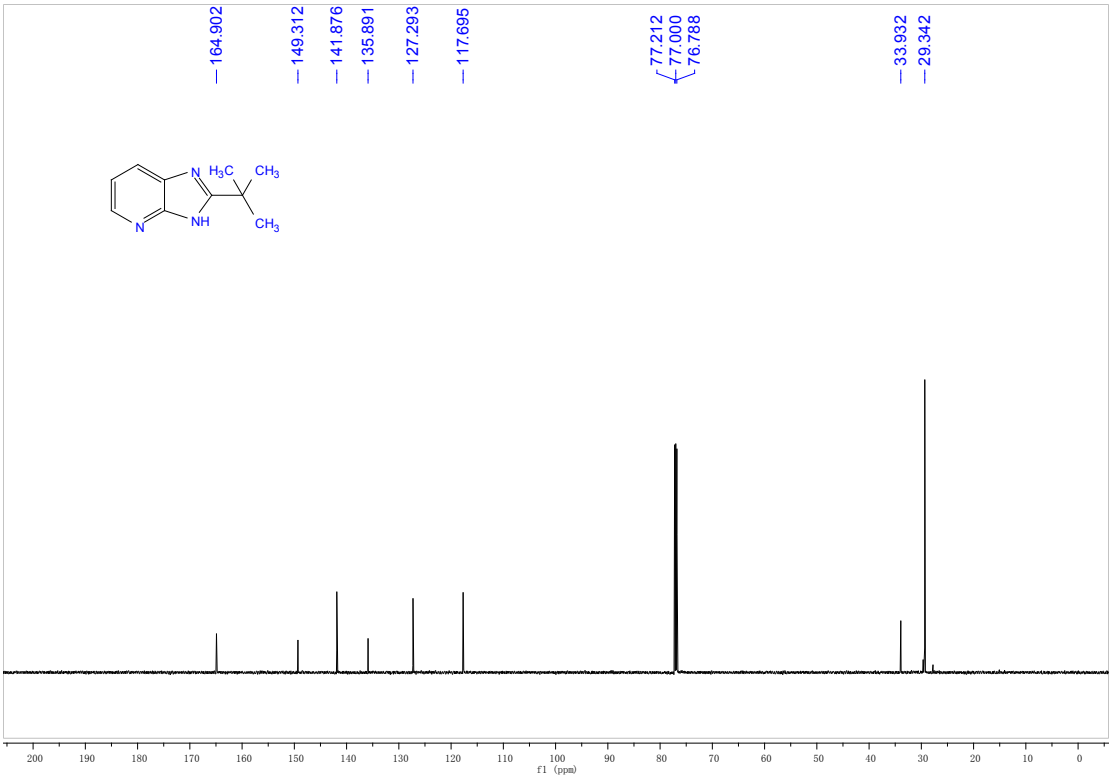
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound 4c



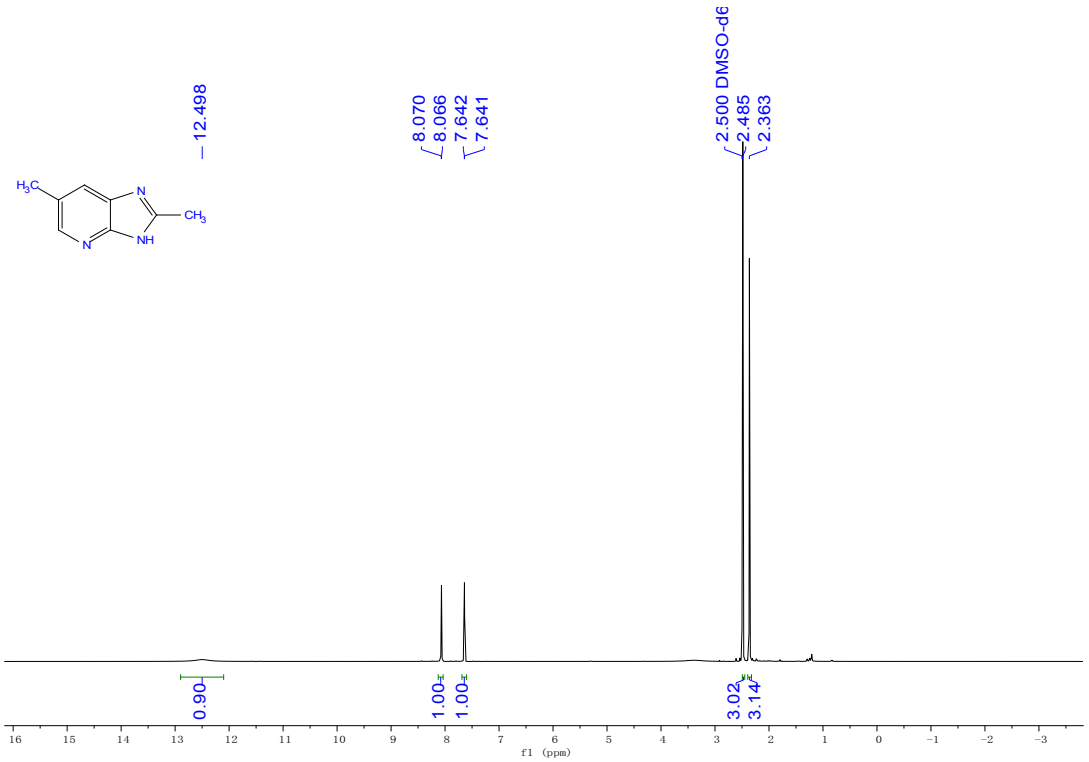
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound 4d



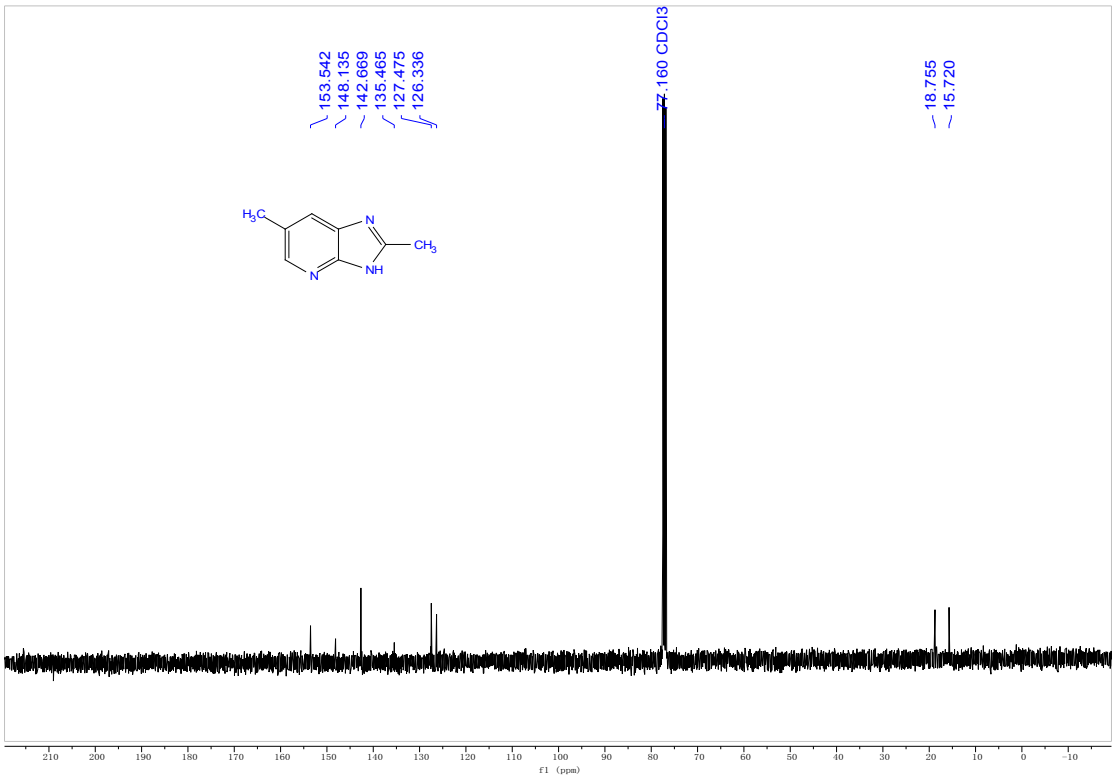
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound 4d



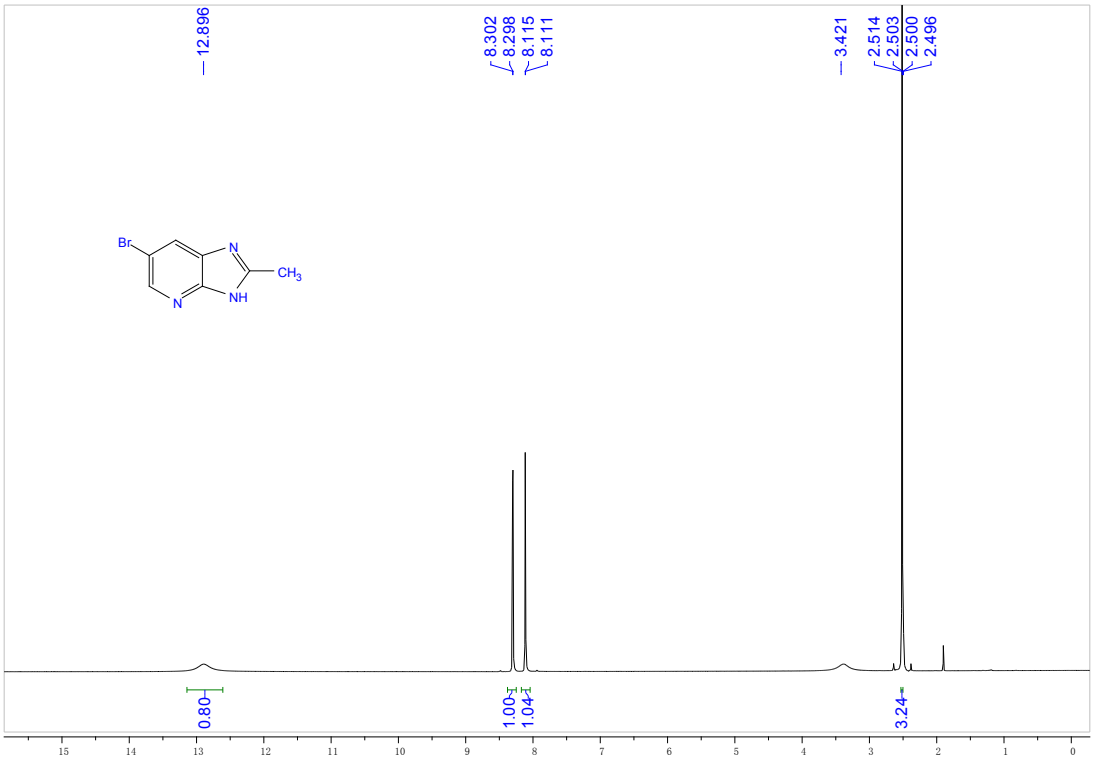
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 4e



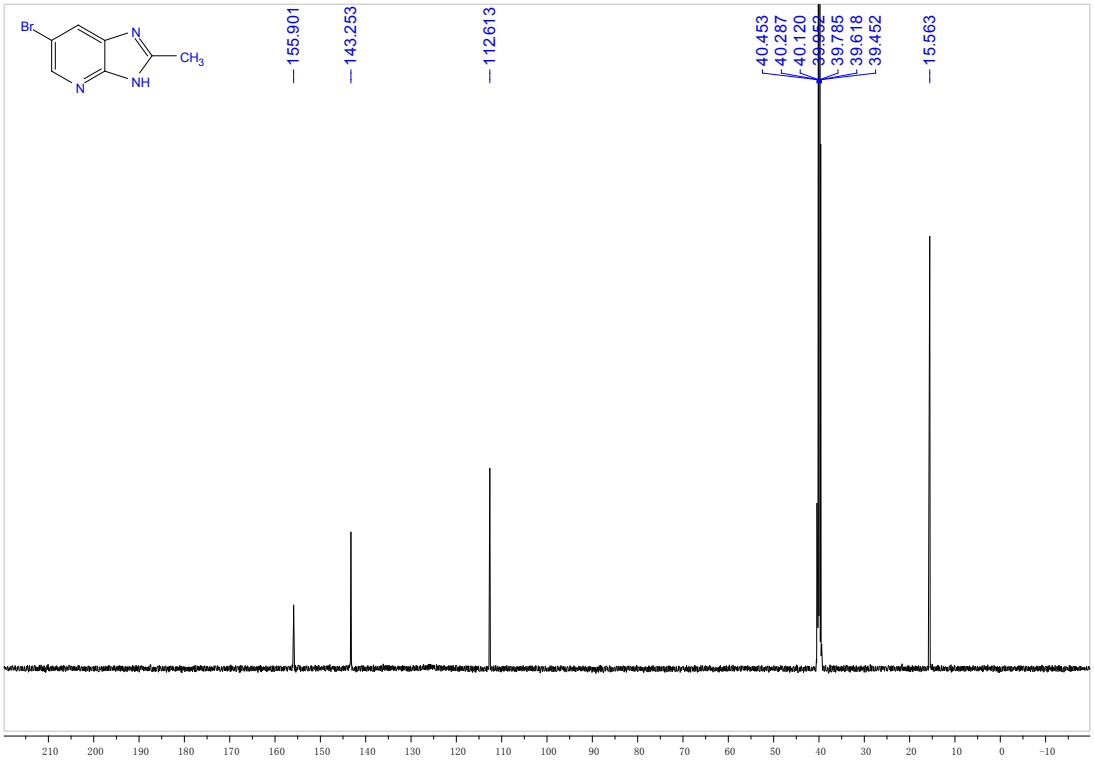
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 4e



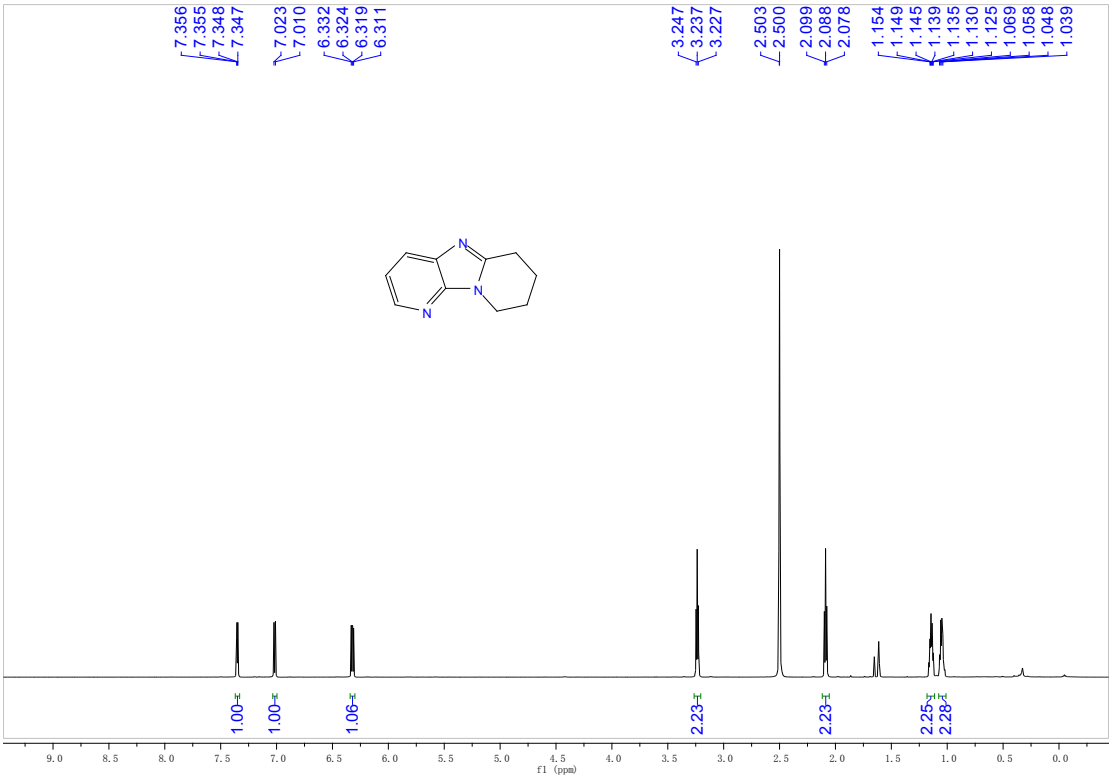
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of compound 4f



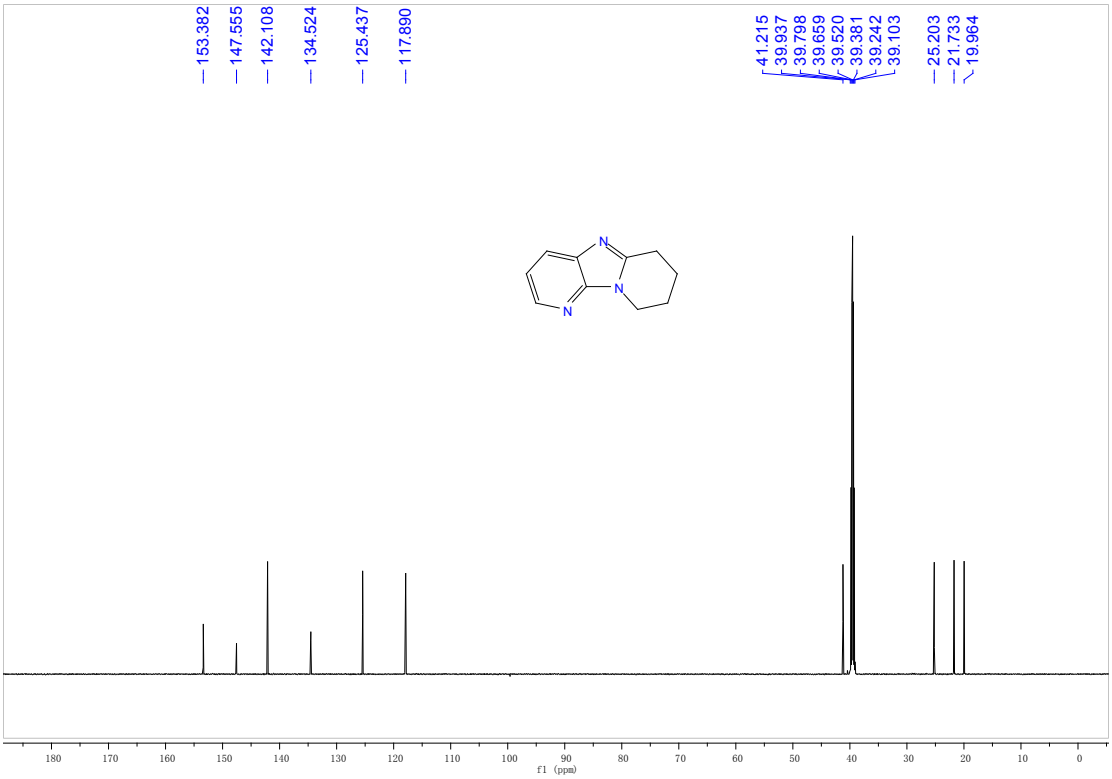
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 4f



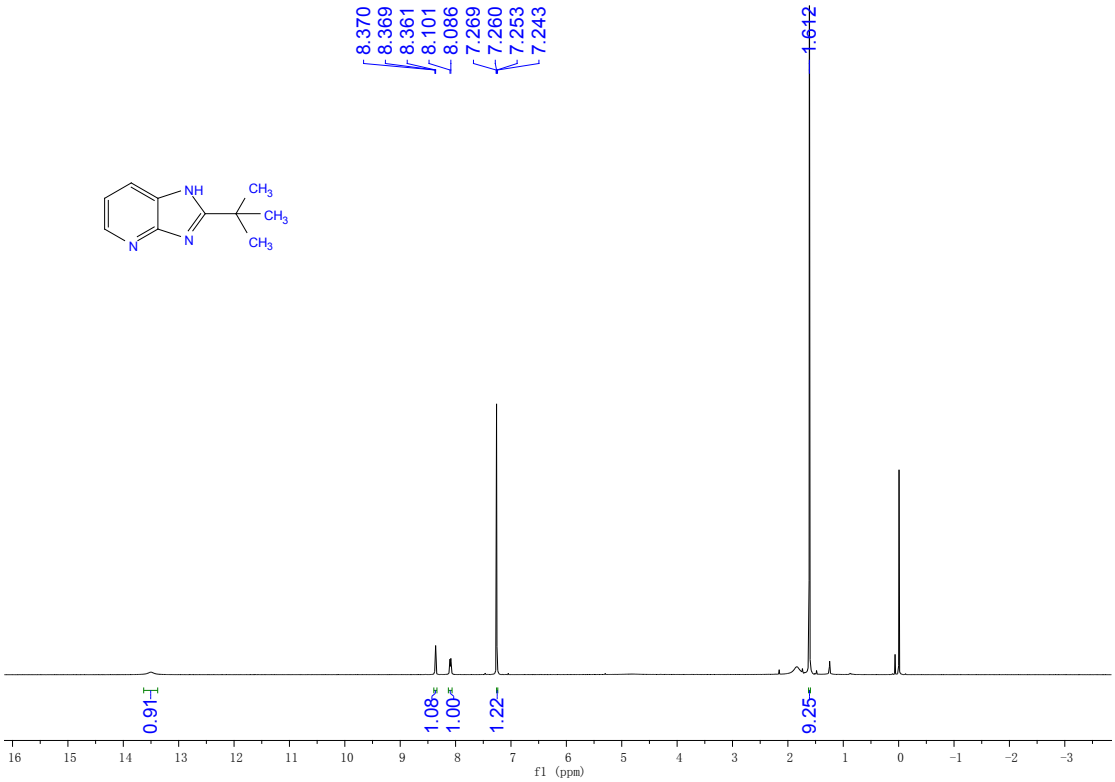
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 4g



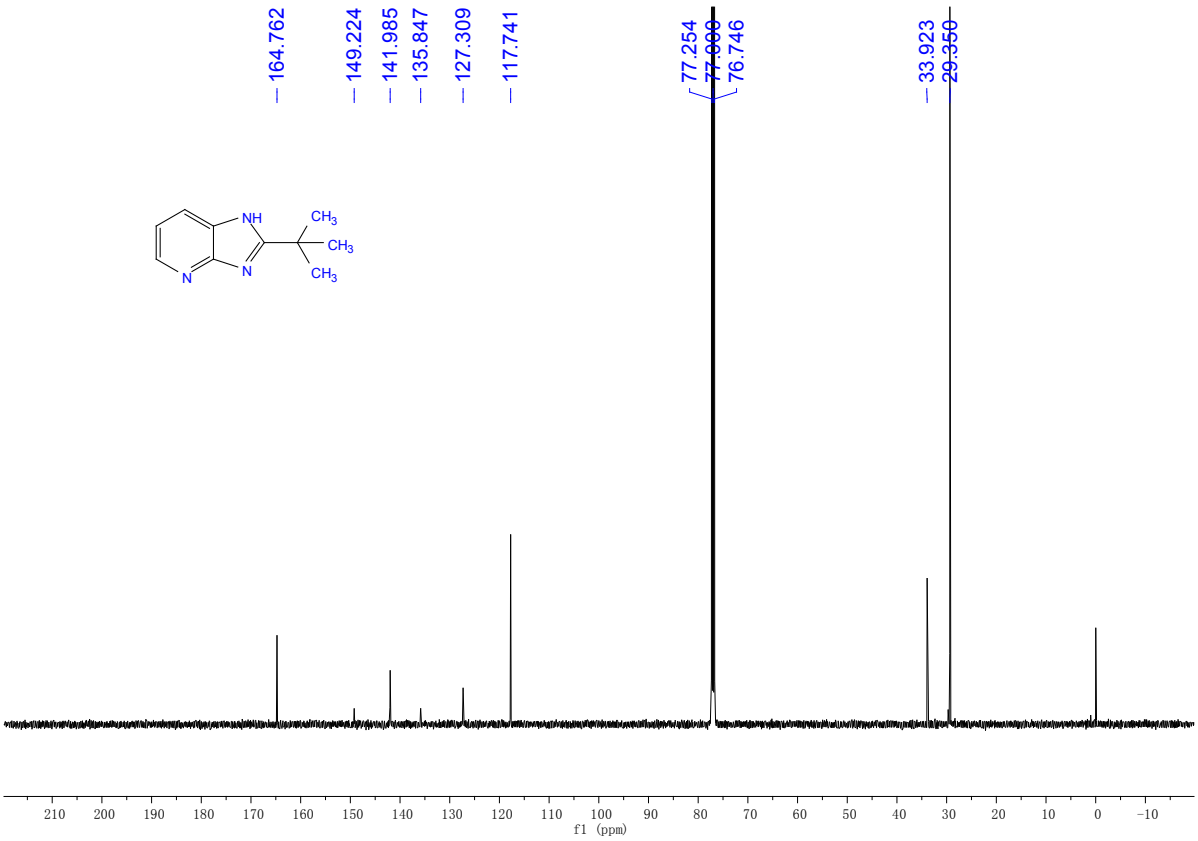
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 4g



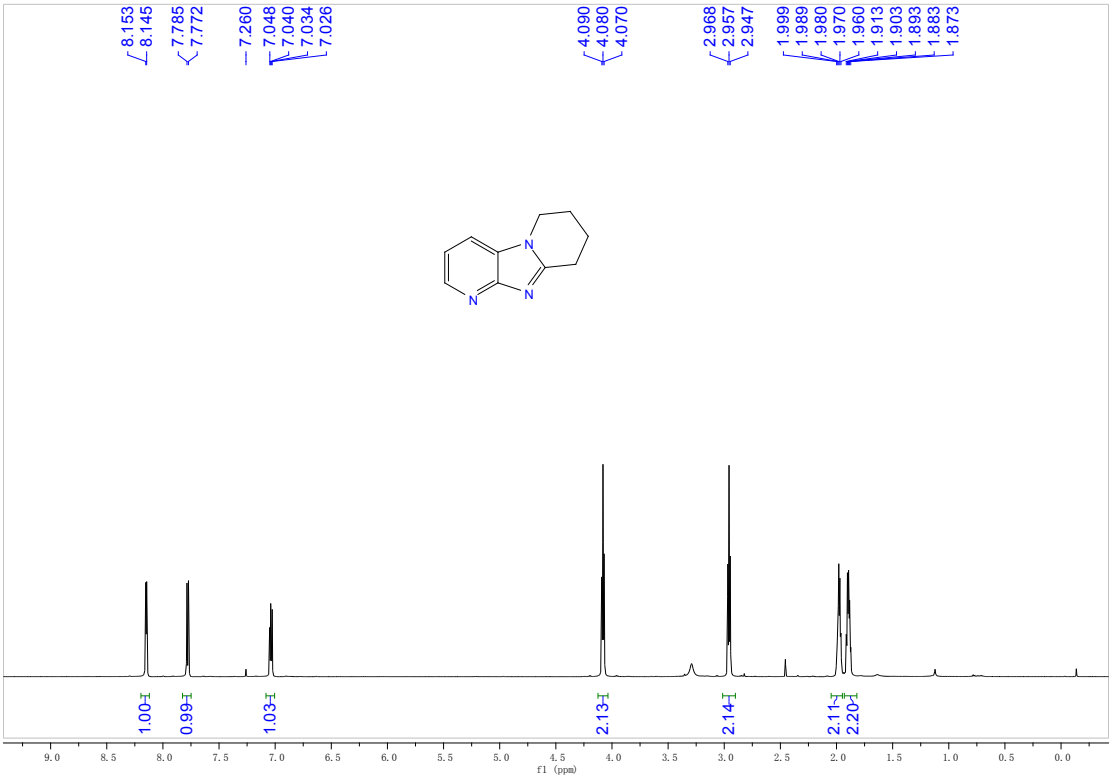
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound 5a



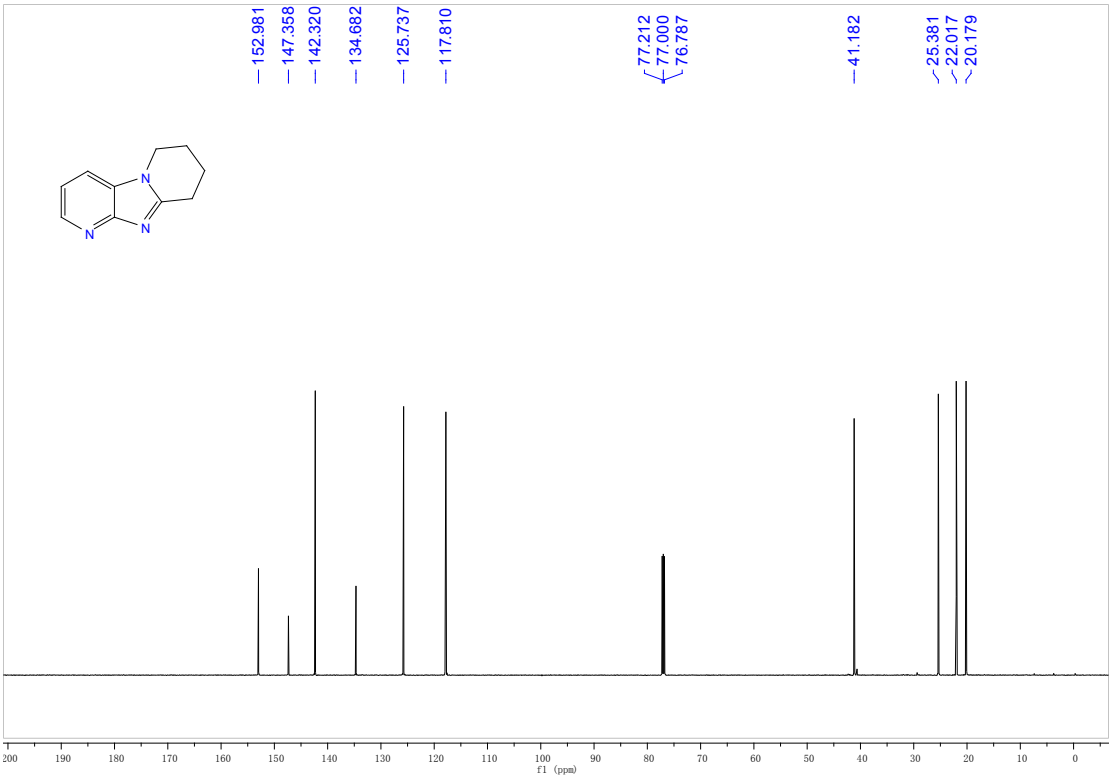
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of compound 5a



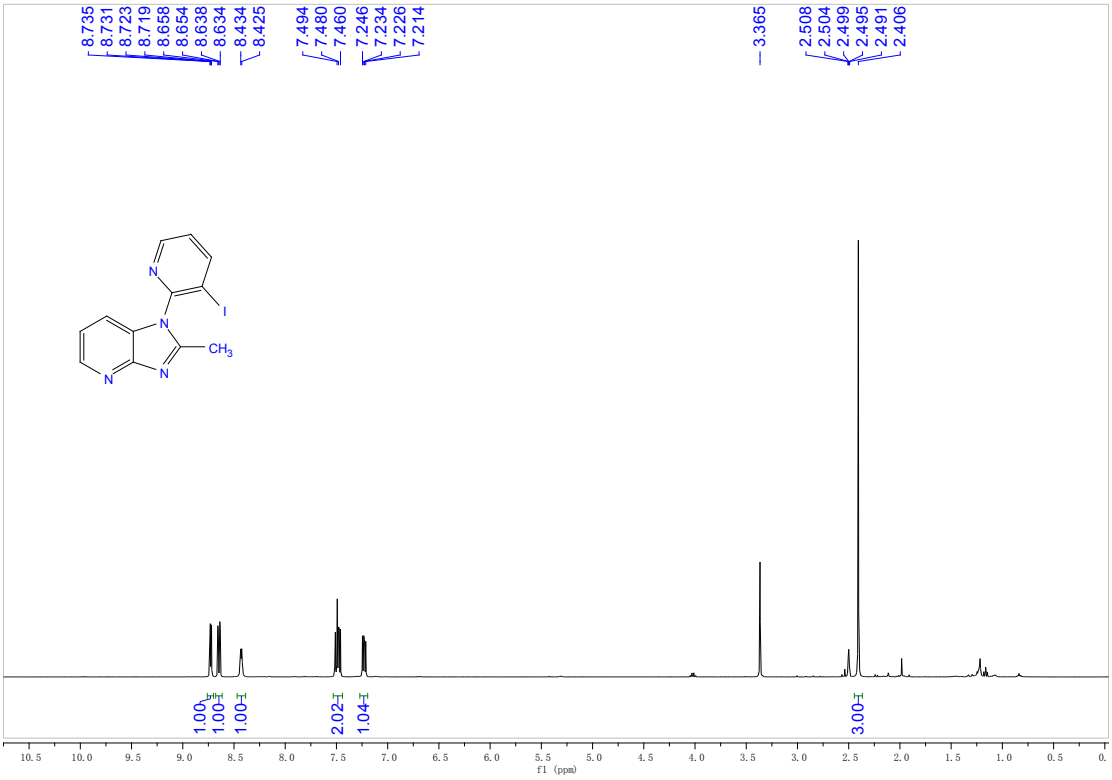
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound 5b



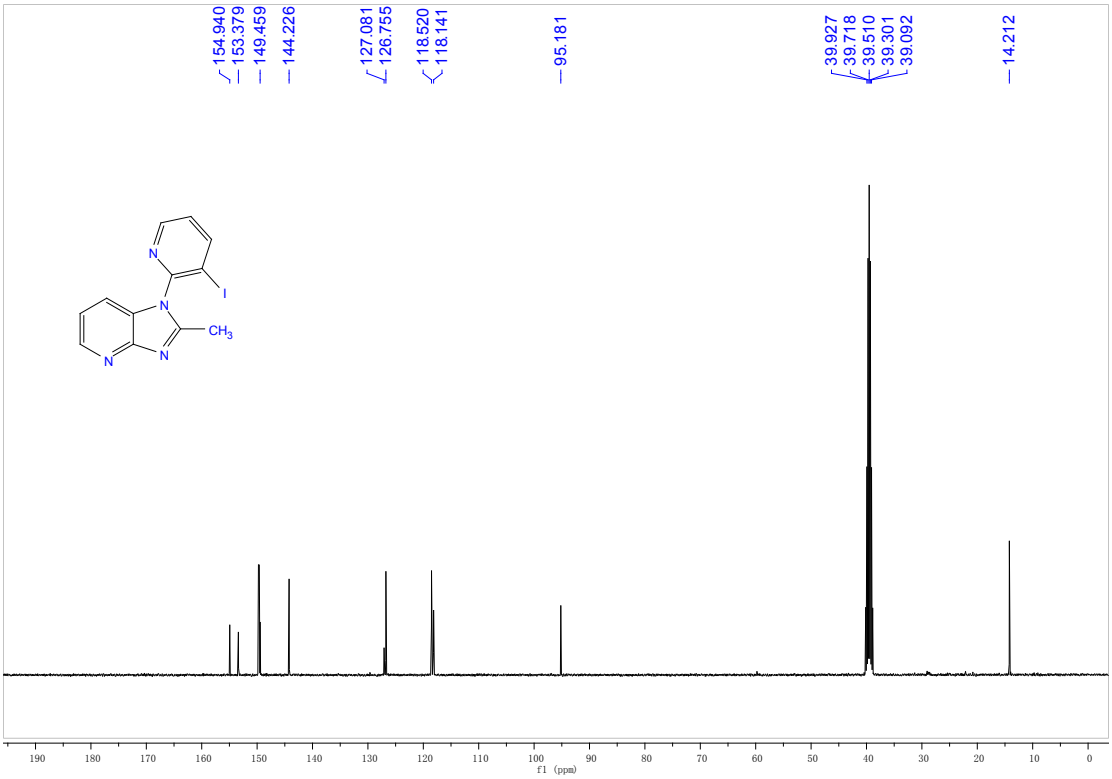
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of compound 5b



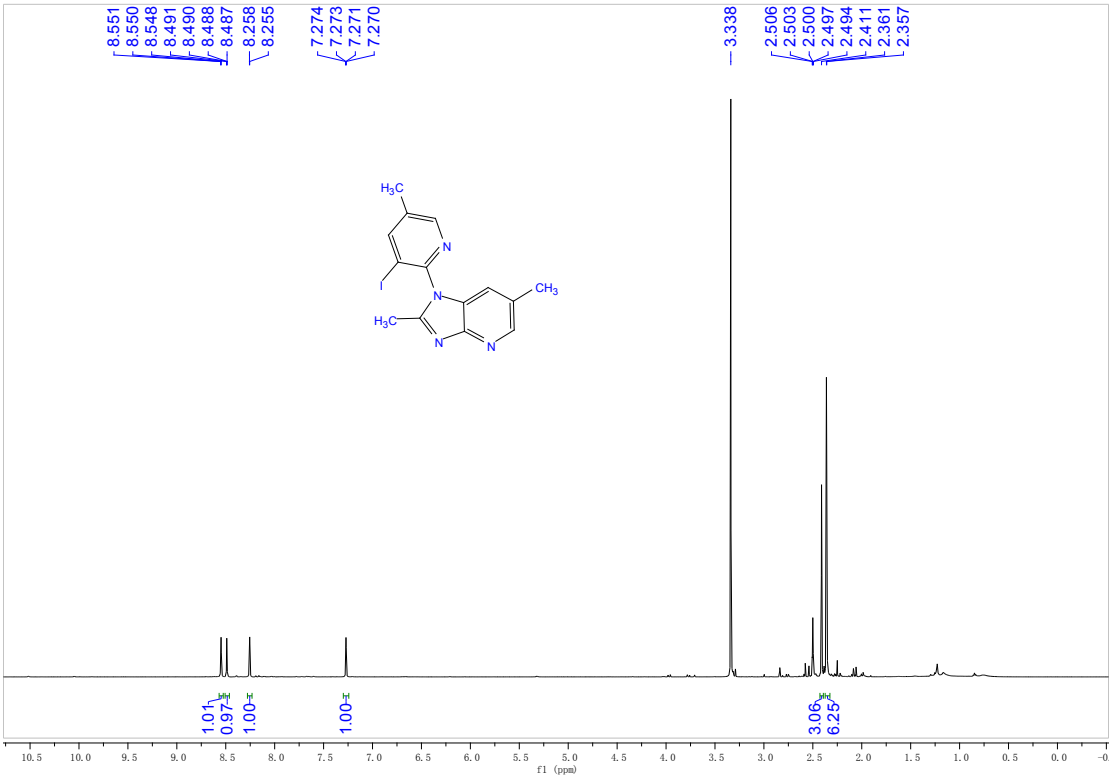
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound 6a



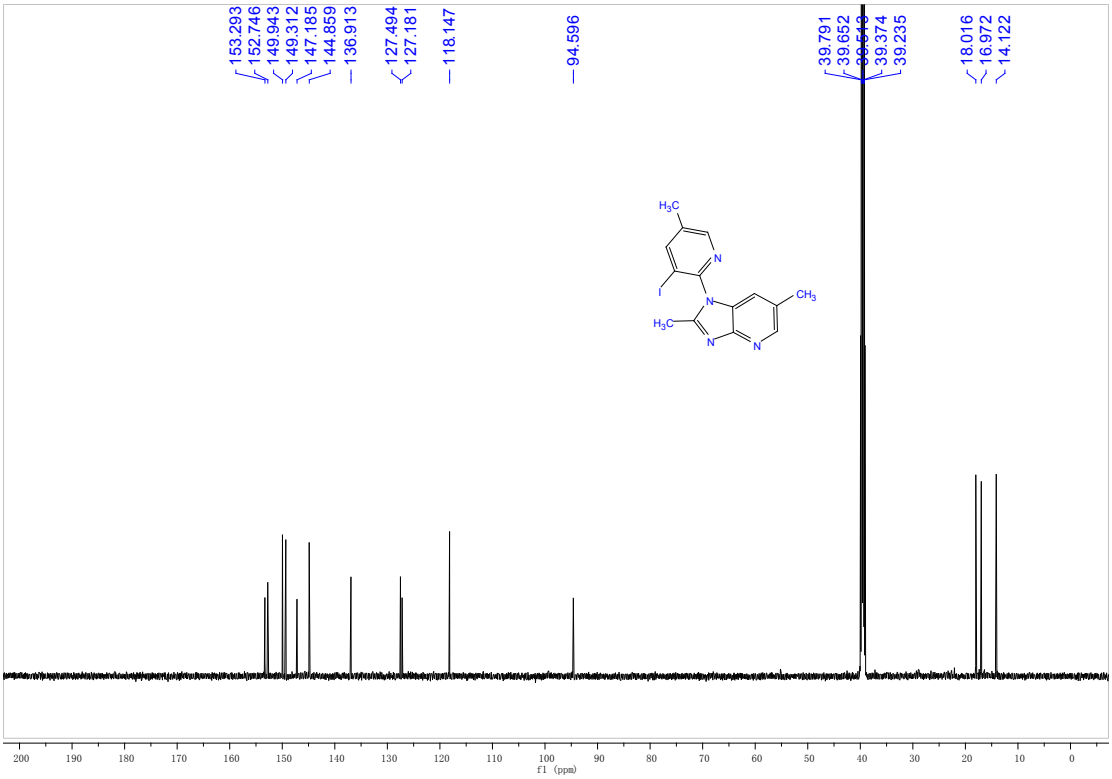
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound 6a



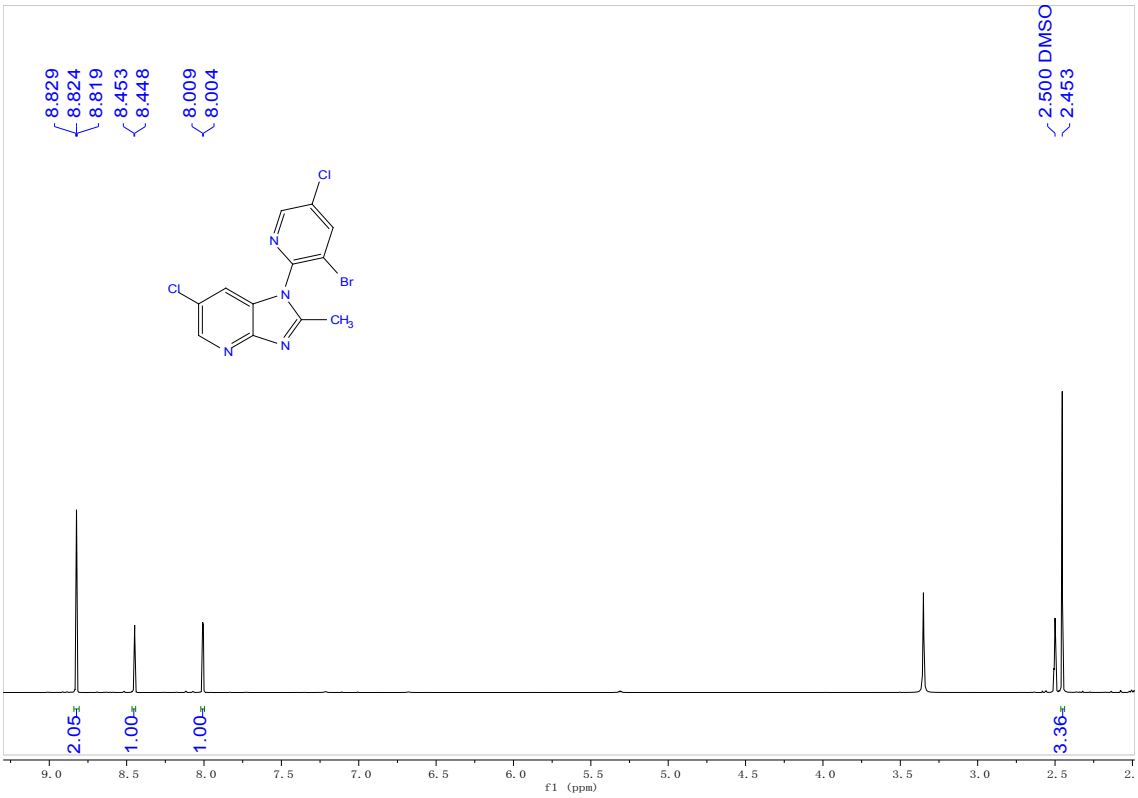
^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound 6b



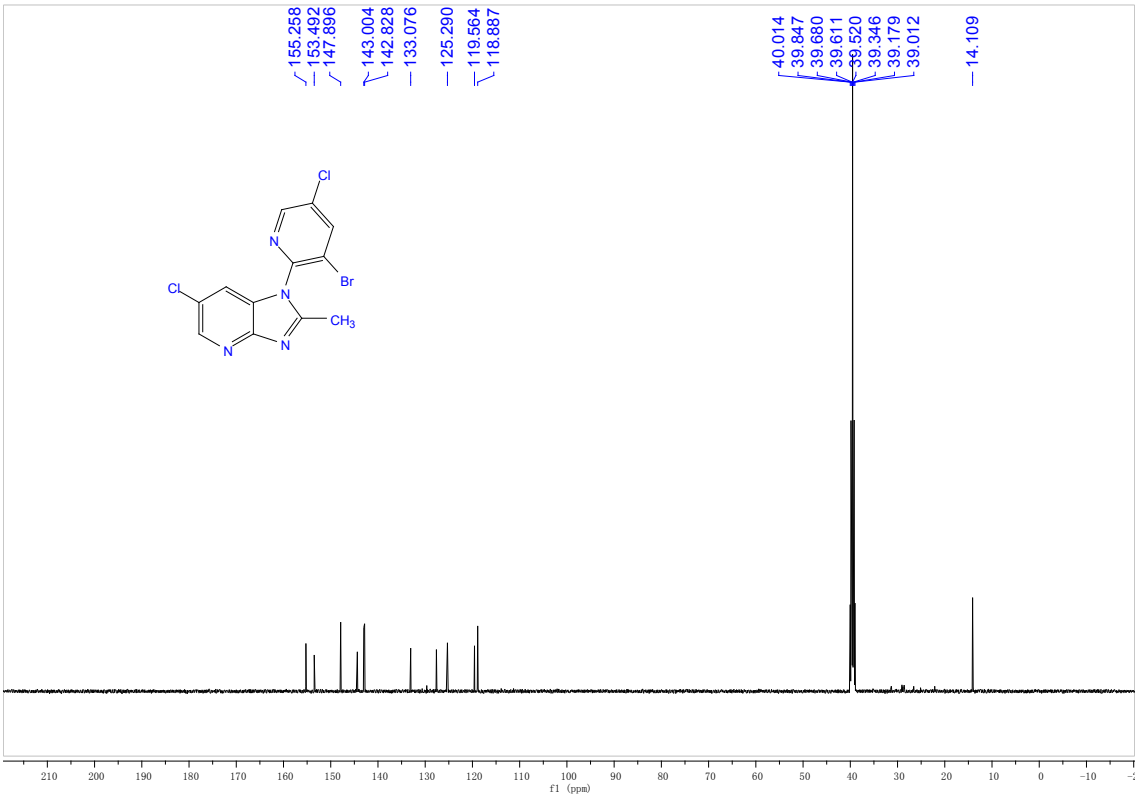
^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound 6d



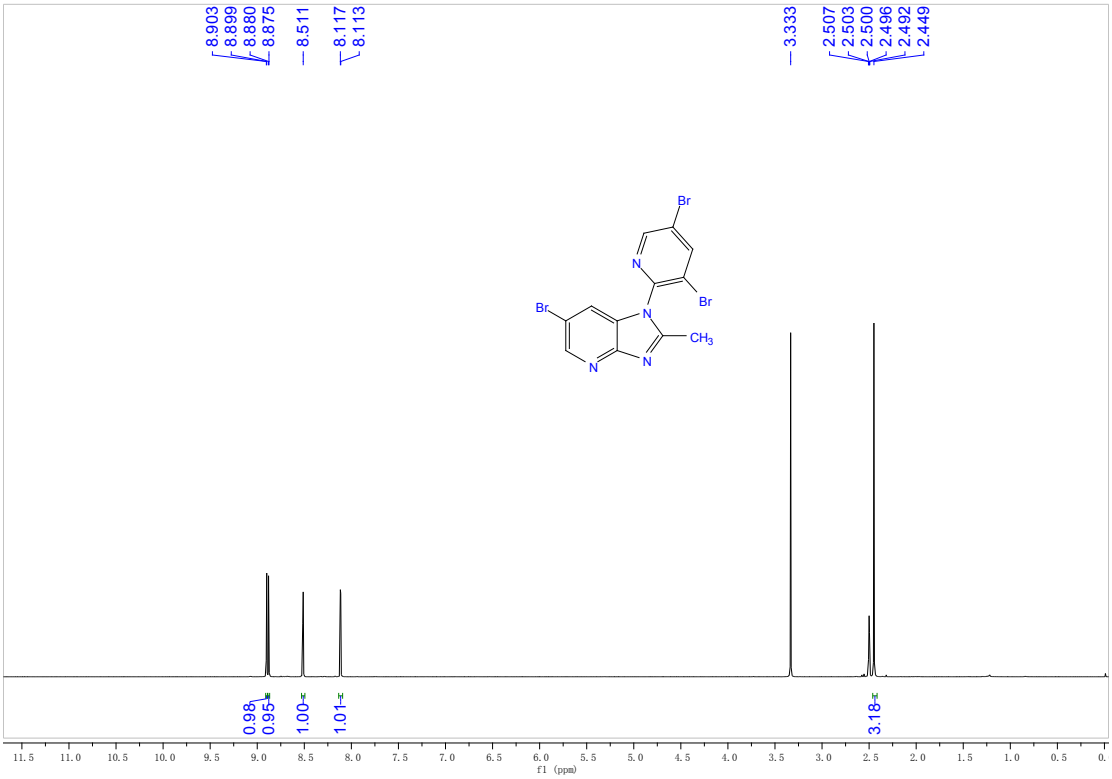
^{1}H NMR (500 MHz, DMSO-d_6) spectrum of compound 6c



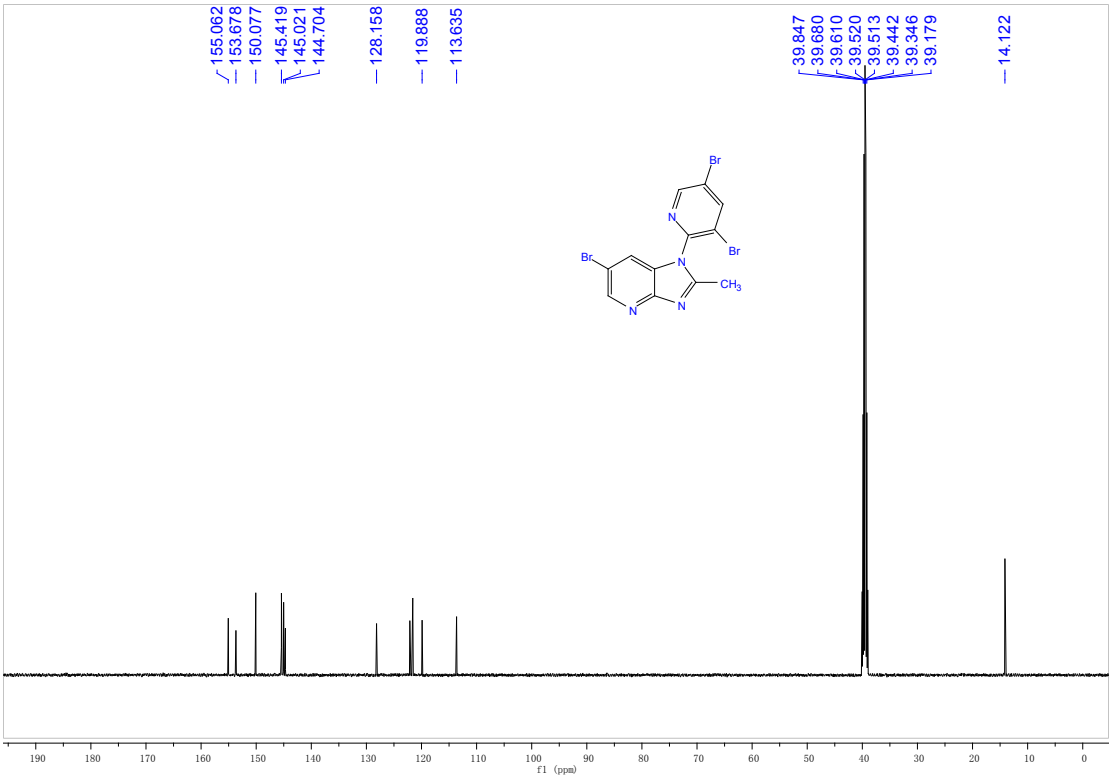
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 6c



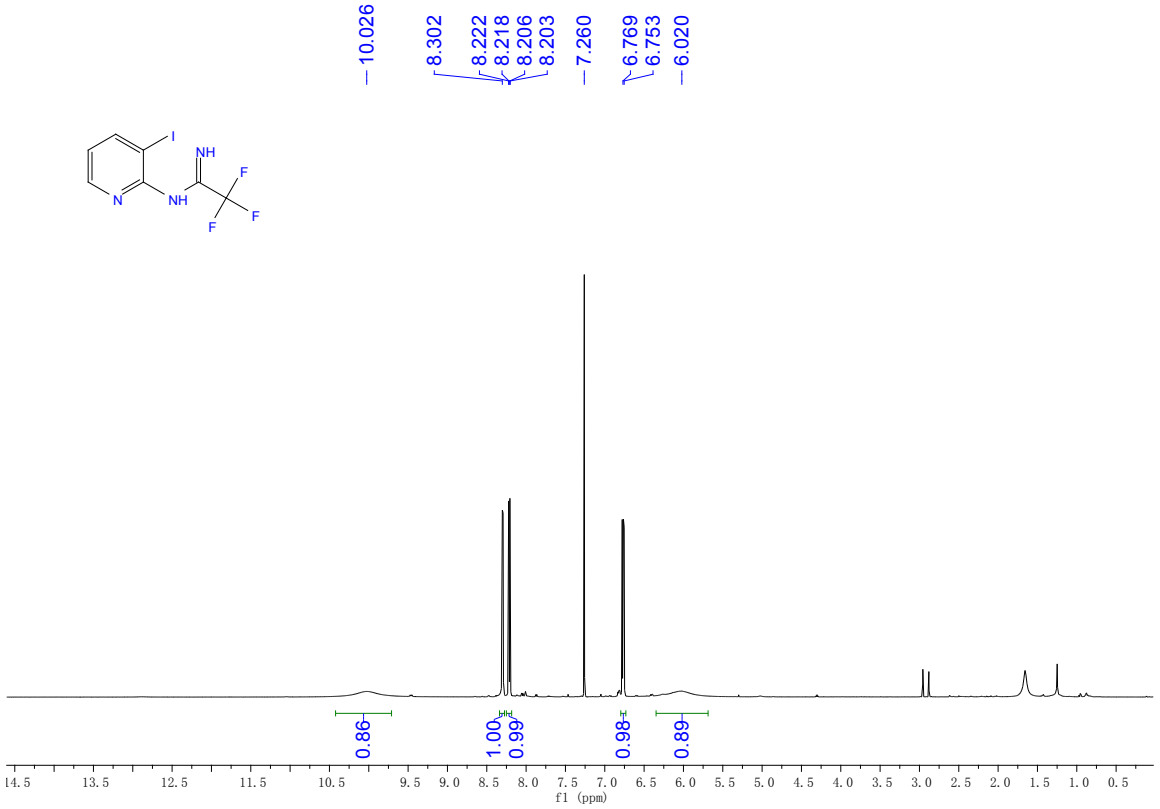
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound 6d



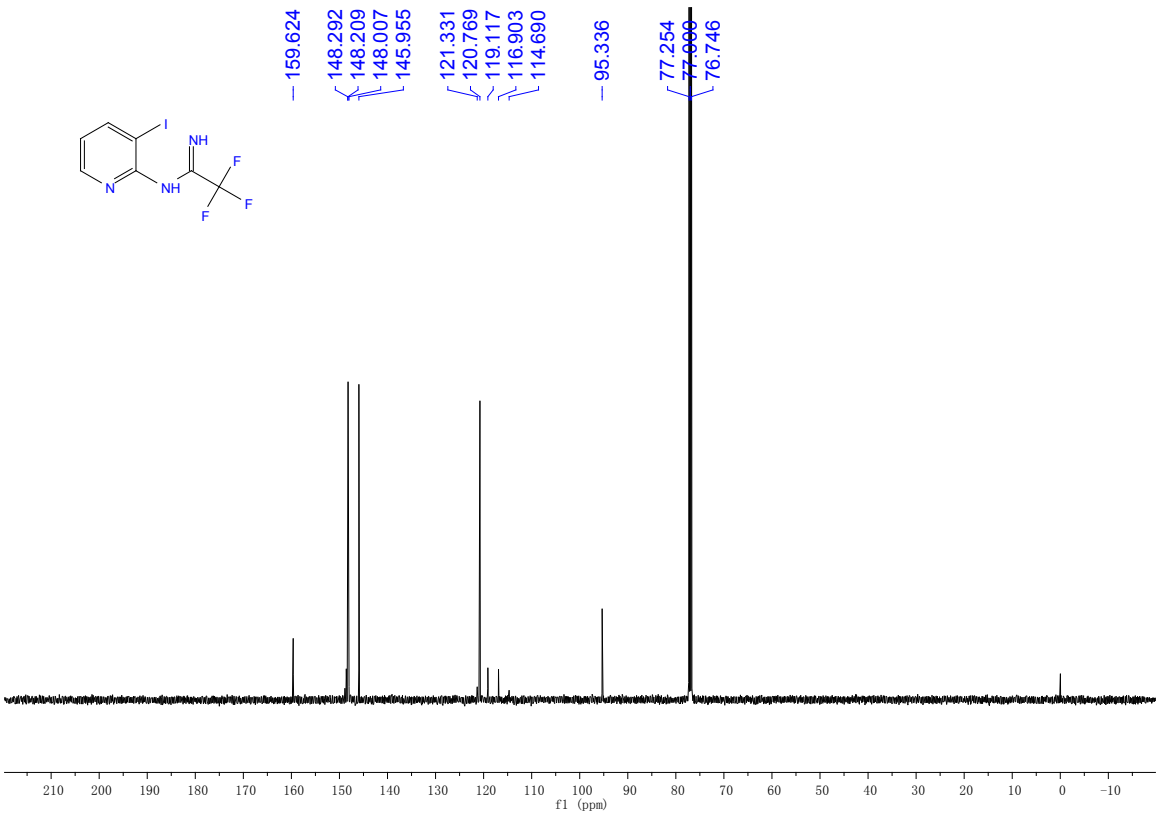
^{13}C NMR (125 MHz, DMSO-d_6) spectrum of compound 6d



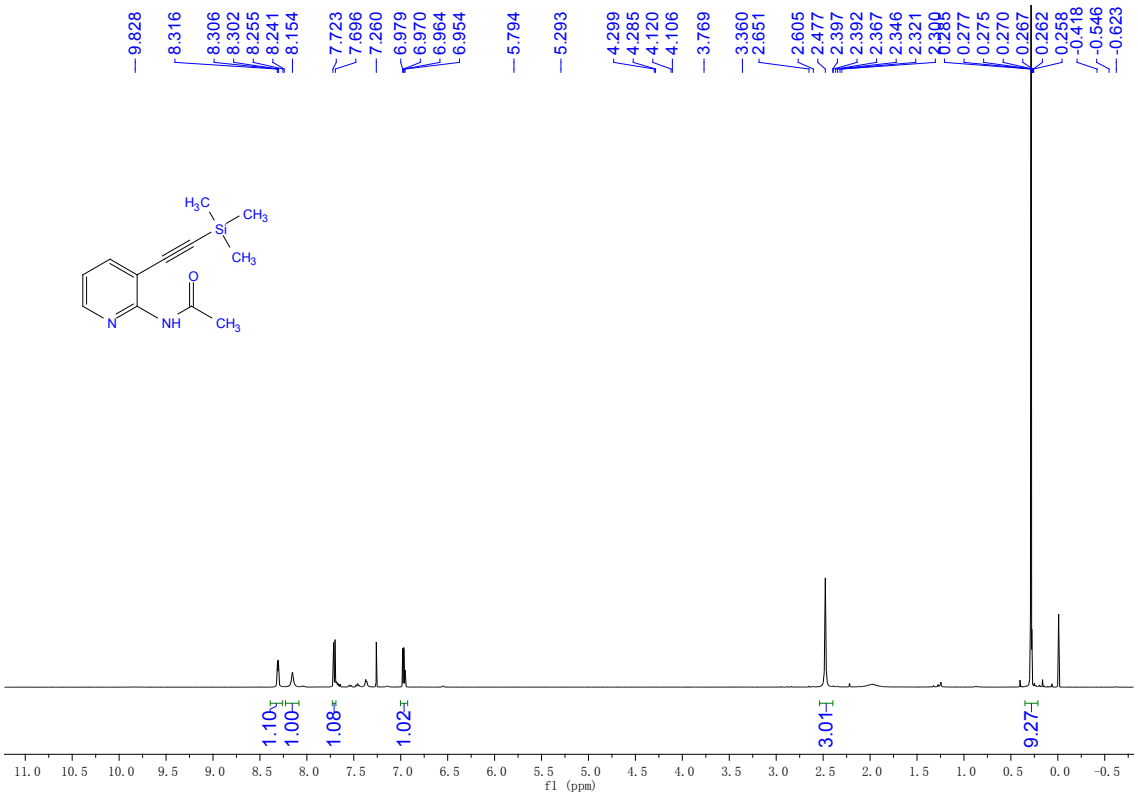
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound 7a



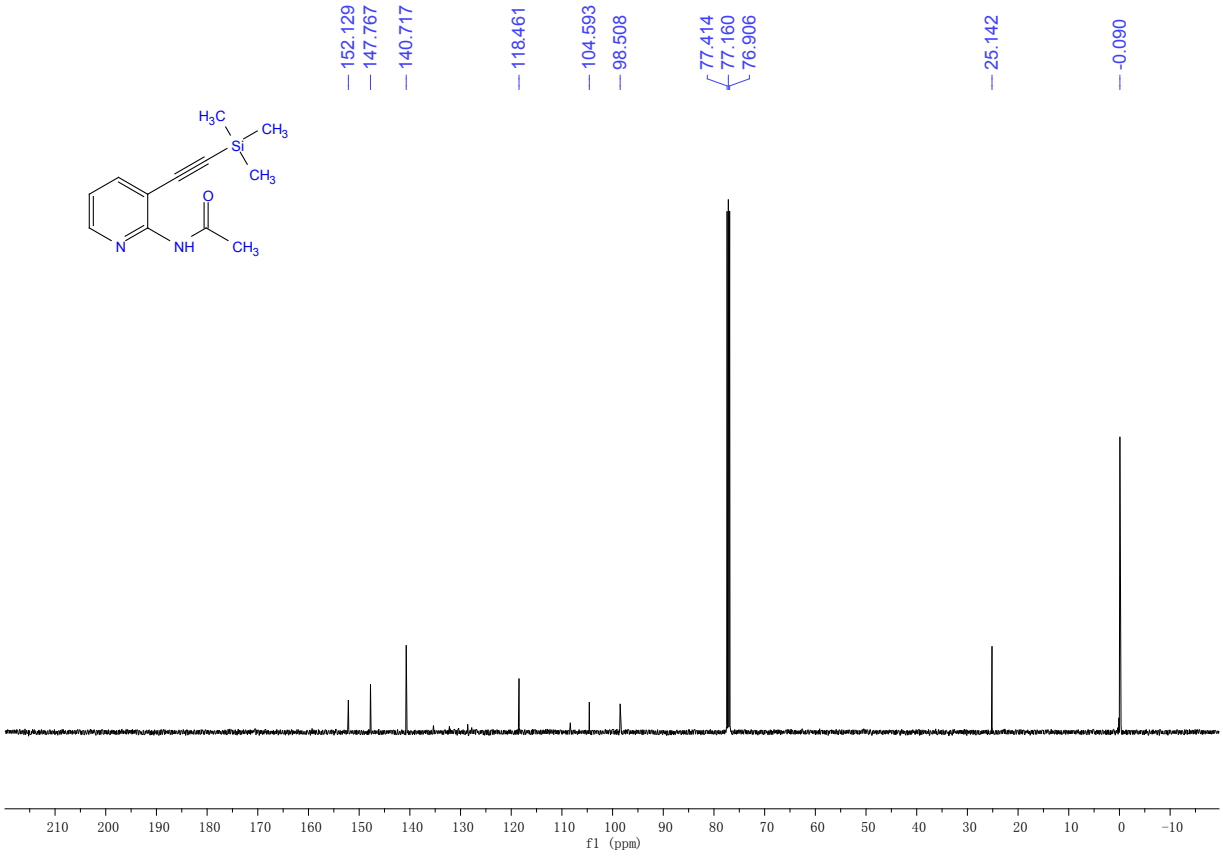
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of compound 7a



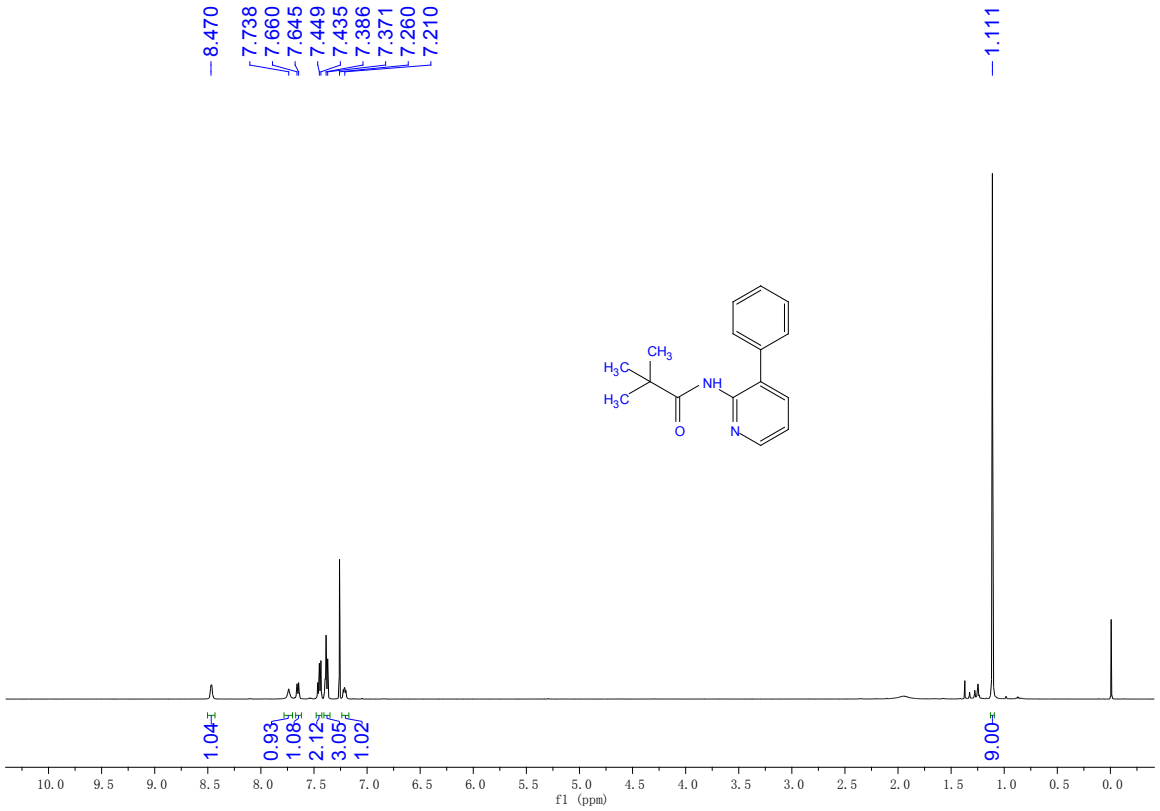
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound 8a



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



^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound 8b



^{13}C NMR (125 MHz, $CDCl_3$) spectrum of compound 8b