Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.


# Supporting Information

## Electrochemical synthesis of pyridine carboxamides from pyridine carbohydrazides and amines in aqueous medium

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## General Information:

All products were characterized by $^{1}H$ NMR and $^{13}C$ NMR, using TMS as an internal reference ($^{1}H$ NMR: 400 MHz, $^{13}C$ NMR: 100 MHz). HRMS (ESI) data were recorded on a Q-TOF Premier. Flash column chromatography was performed using silica gel (200-300 mesh). All the compounds **1** and **2** were purchased from commercial supplies and used without purification.

## Experimental Section

**Representative Procedures for the Synthesis of Pyridine Carboxamides Except for Isonicotinamide and Picolinamide (3 as an Example):** An undivided cell was equipped with a magnet stirrer, two platinum plates (1.0 x 1.0 $cm^2$) electrodes as the working electrode and counter electrode. In the electrolytic cell, a mixture of isonicotinohydrazide **1** (0.3 mmol, 41.1 mg, 1.0 equiv), amines **2** (0.6 mmol, 2.0 equiv), KI (0.30 mmol, 49.8 mg, 1.0 equiv), EtOH/$H_2O$ (2.5/0.5 mL) was allowed to stir and electrolyze at a constant current condition (10 mA) at 40 $^{o}$C. After the reaction was completed (about 8 h), the solvent was removed with a rotary evaporator and the residue was purified by column chromatography on silica gel to afford the desired product **3**. The product was dried under high vacuum for at least 0.5 h before it was weighed and characterized by NMR spectroscopy.

**Representative Procedures for the Synthesis of Isonicotinamide and Picolinamide:** An undivided cell was equipped with a magnet stirrer, two platinum plates (1.0 x 1.0 $cm^2$) electrodes as the working electrode and counter electrode. In the electrolytic cell, a mixture of isonicotinohydrazide or picolinohydrazide (0.3 mmol, 41.1 mg, 1.0 equiv), KI (0.30 mmol, 49.8 mg, 1.0 equiv), EtOH/$NH_3{\cdot}H_2O$ (2.5/0.5 mL) was allowed to stir and electrolyze at a constant current condition (10 mA) at 40 $^{o}$C. After the reaction was completed (about 8 h), the solvent was removed with a rotary evaporator and the residue was purified by column chromatography on silica gel to afford the desired product **35** or **38.** The product was dried under high vacuum for at least 0.5 h before it was weighed and characterized by NMR spectroscopy.

**Gram-Scale Synthesis of 3:** An undivided cell was equipped with a magnet stirrer, two platinum plates (1.5 x 1.5 $cm^2$) electrodes as the working electrode and counter electrode. In the electrolytic cell, a mixture of isonicotinohydrazide **1** (6 mmol, 822.8 mg, 1.0 equiv), phenylmethanamine (12 mmol, 1285.8 mg,2.0 equiv), KI (6 mmol, 996.0 mg, 1.0 equiv),

EtOH/$H_2O$ (50/10 mL) was allowed to stir and electrolyze at a constant current condition (23 mA) at 40 $^oC$. After the reaction was completed (about 72 h), the solvent was removed with a rotary evaporator and the residue was purified by column chromatography on silica gel to afford the desired product **3**. The product was dried under high vacuum for at least 0.5 h before it was weighed and characterized by NMR spectroscopy (890 mg, 70%).

**Photographic Depiction of the Electrolysis Setup (3 as an Example):**

**Figure S1** Electrodes and electrolysis cell

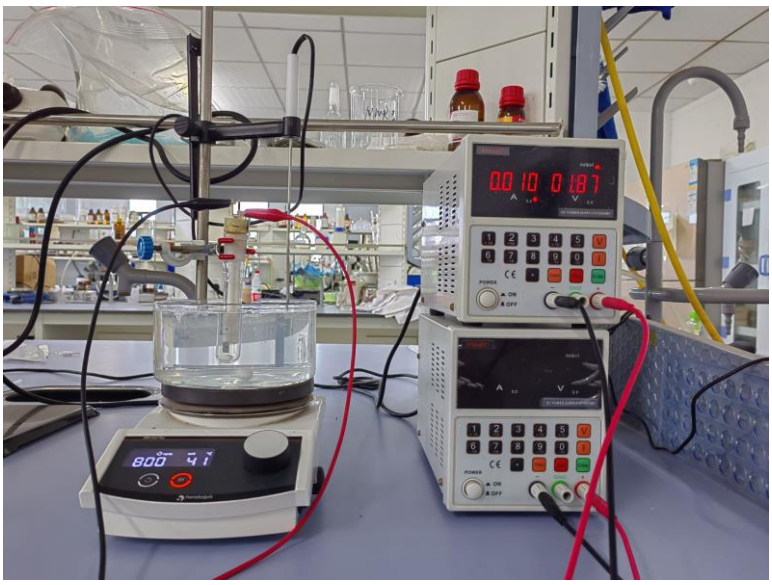
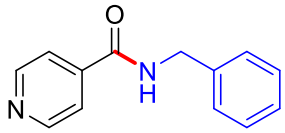


**Figure S2** Electrolysis setup

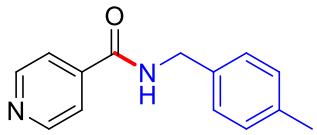
## Detail Descriptions for Products

*N-benzylisonicotinamide* (**3**) [1]



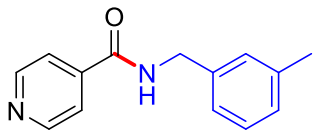
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a white solid in 80% yield (51.0 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.38 – 9.35 (m, 1H), 8.74 (d, J = 8.0 Hz, 2H), 7.82 – 7.80 (m, 2H), 7.34 – 7.33 (m, 4H), 7.28 – 7.23 (m, 1H), 4.51 (d, J = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 165.5, 150.3, 141.4, 137.5, 128.7, 127.8, 127.7, 121.0, 44.1.

*N-(4-methylbenzyl)isonicotinamide* (**4**) [2]



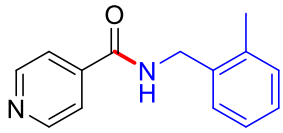
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 75% yield (50.6 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.29 – 9.26 (m, 1H), 8.73 – 8.72 (m, 2H), 7.79 – 7.78 (m, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.14 – 7.13 (m, 2H), 4.45 – 4.44 (m, 2H), 2.27 (s, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.7, 150.3, 141.4, 136.1, 136.0, 128.9, 127.4, 121.3, 42.5, 20.7.

*N-(3-methylbenzyl)isonicotinamide* (**5**)



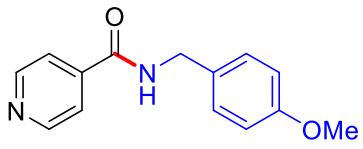
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a brown oil in 75% yield (51.2 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.32 – 9.28 (m, 1H), 8.74 – 8.73 (m, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.23 – 7.20 (m, 1H), 7.14 – 7.10 (m, 2H), 7.06 (d, J = 8.0 Hz, 1H), 4.47 – 4.46 (m, 2H), 2.29 (s, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.7, 150.3, 141.3, 139.1, 137.5, 128.3, 128.0, 127.6, 124.5, 121.3, 42.8, 21.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O$ 227.1184; Found: 227.1187.

*N-(2-methylbenzyl)isonicotinamide* (**6**)




The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a brown oil in 81% yield (55.0 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.23 – 9.20 (m, 1H), 8.75 – 8.73 (m, 2H), 7.83 – 7.81 (m, 2H), 7.28 – 7.25 (m, 1H), 7.18 – 7.14 (m, 3H), 4.49 (d, J = 8.0 Hz, 2H), 2.33 (s, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.8, 150.3, 141.4, 136.7, 135.7, 130.1, 127.6, 127.0, 125.9, 121.4, 41.0, 18.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O$ 227.1184; Found: 227.1182.

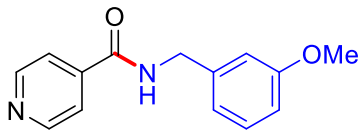
*N-(4-methoxybenzyl)isonicotinamide* (**7**)




The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 68% yield (49.5 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.30 – 9.27 (m, 1H), 8.73 – 8.71 (m, 2H), 7.79 – 7.77 (m, 2H), 7.26 – 7.24 (m, 2H), 6.90 – 6.88 (m, 2H), 4.42 (d, J = 8.0 Hz, 2H), 3.72 (s, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.7, 158.4, 150.4, 141.4, 131.2,

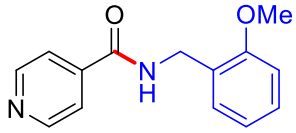
128.8, 121.4, 113.9, 55.2, 42.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_2$ 243.1134; Found: 243.1141.

*N-(3-methoxybenzyl)isonicotinamide* (**8**)



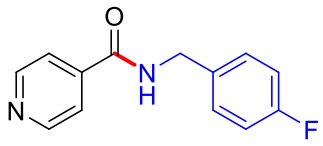

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a brown oil in 74% yield (54.1 mg); $^1$H NMR (DMSO-*d*$_6$, 400 MHz, ppm): δ = 9.35 – 9.32 (m, 1H), 8.74 – 8.73 (m, 2H), 7.81 – 7.79 (m, 2H), 7.25 (t, J = 8.0 Hz, 1H), 6.91 – 6.89 (m, 2H), 6.84 – 6.81 (m, 1H), 4.98 (d, J = 8.0 Hz, 2H), 3.73 (s, 3H); $^{13}$C NMR (DMSO-*d*$_6$, 100 MHz, ppm): δ = 164.9, 159.5, 150.4, 141.4, 140.8, 129.6, 121.4, 119.6, 113.1, 112.4, 55.1, 42.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_2$ 243.1134; Found: 243.1139.

*N-(2-methoxybenzyl)isonicotinamide* (**9**)



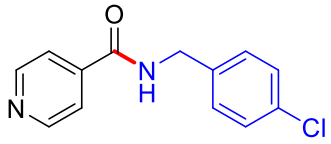

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 69% yield (50.0 mg); $^1$H NMR (DMSO-*d*$_6$, 400 MHz, ppm): δ = 9.19 – 9.16 (m, 1H), 8.74 – 8.73 (m, 2H), 7.82 – 7.81 (m, 2H), 7.25 (t, J = 8.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 6.91 (t, J = 8.0 Hz, 1H), 4.48 – 4.47 (m, 2H), 3.82 (s, 3H); $^{13}$C NMR (DMSO-*d*$_6$, 100 MHz, ppm): δ = 165.0, 156.7, 150.4, 141.4, 128.3, 127.6, 126.4, 121.5, 120.3, 110.6, 55.5, 37.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_2$ 243.1134; Found: 243.1135.

*N-(4-fluorobenzyl)isonicotinamide* (**10**)



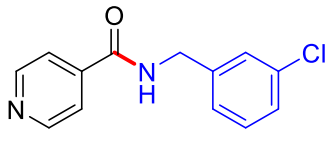
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 74% yield (50.9 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.34 – 9.31 (m, 1H), 8.74 – 8.72 (m, 2H), 7.79 – 7.78 (m, 2H), 7.38 – 7.35 (m, 2H), 7.19 – 7.13 (m, 2H), 4.48 – 4.47 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 164.8, 161.3 (d, J = 241.0 Hz), 150.3, 141.2, 135.4 (d, J = 3.0 Hz), 129.4 (d, J = 8.0 Hz), 121.3, 115.1 (d, J = 21.0 Hz), 42.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}N_2OF$ 231.0934; Found: 231.0939.

*N-(4-chlorobenzyl)isonicotinamide* (**11**)



The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 77% yield (56.9 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.37 – 9.34 (m, 1H), 8.74 – 8.73 (m, 2H), 7.79 – 7.78 (m, 2H), 7.41 – 7.34 (m, 4H), 4.48 (d, J = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 164.8, 150.4, 141.2, 138.2, 131.5, 129.2, 128.4, 121.3, 42.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}N_2OCl$ 247.0638; Found: 247.0643.

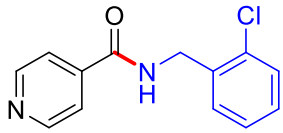
*N-(3-chlorobenzyl)isonicotinamide* (**12**)



The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 69% yield (51.0 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.40 – 9.37 (m, 1H),

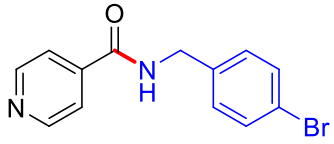
8.75 – 8.73 (m, 2H), 7.80 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 7.39 – 7.38 (m, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.33 – 7.28 (m, 2H), 4.50 (d, J = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 165.6, 150.4, 141.2, 139.6, 134.6, 130.1, 127.9, 127.8, 125.9, 121.0, 43.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}N_2OCl$ 247.0638; Found: 247.0640.

*N-(2-chlorobenzyl)isonicotinamide* (**13**)



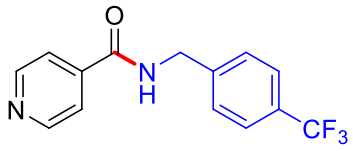

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 71% yield (52.7 mg); $^1$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.37 – 9.34 (m, 1H), 8.76 – 8.75 (m, 2H), 7.84 – 7.82 (m, 2H), 7.47 – 7.45 (m, 1H), 7.41 – 7.38 (m, 2H), 7.35 – 7.28 (m, 2H), 4.58 (d, J = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 165.1, 150.4, 141.1, 135.9, 132.2, 129.3, 128.9, 128.8, 127.3, 121.4, 40.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}N_2OCl$ 247.0638; Found: 247.0642.

*N-(4-bromobenzyl)isonicotinamide* (**14**)



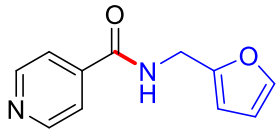

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 62% yield (53.7 mg); $^1$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.39 – 9.36 (m, 1H), 8.74 – 8.73 (m, 2H), 7.79 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 4.47 (d, J = 4.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 164.8, 150.4, 141.2, 138.7, 131.3, 129.7, 121.4, 120.0, 42.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}N_2OBr$ 291.0133; Found: 291.0138.

*N-(4-(trifluoromethyl)benzyl)isonicotinamide* (**15**) [4b]



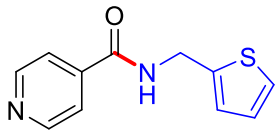
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 70% yield (59.0 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.47 – 9.44 (m, 1H), 8.76 – 8.74 (m, 2H), 7.81 – 7.80 (m, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H), 4.59 – 4.58 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 165.0, 150.5, 144.1, 141.1, 128.1, 127.7 (q, J = 31.0 Hz), 124.5 (q, J = 270.0 Hz), 125.4 (q, J = 4.0 Hz), 121.4, 42.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}N_2OF_3$ 281.0902; Found: 281.0901.

*N-(furan-2-ylmethyl)isonicotinamide* (**16**) [3]



The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 57% yield (34.6 mg); $^{1}$H NMR ($CDCl_3$, 400 MHz, ppm): δ = 8.68 – 8.67 (m, 2H), 7.63 – 7.61 (m, 2H), 7.36 – 7.35 (m, 1H), 7.03 (br, 1H), 6.34 – 6.28 (m, 2H), 4.62 (d, J = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 165.3, 150.5, 150.4, 142.4, 141.3, 121.0, 110.5, 108.0, 37.0.

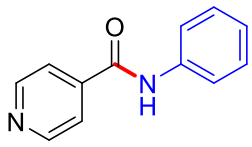
*N-(thiophen-2-ylmethyl)isonicotinamide* (**17**) [4]



The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a pale yellow solid in 59% yield (38.3 mg); $^{1}$H NMR ($CDCl_3$, 400 MHz, ppm): δ = 8.65 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 7.61 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 7.24 – 7.23 (m, 1H), 7.18 (br, 1H), 7.01 (d, J = 8.0

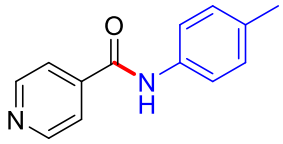
Hz, 1H), 6.95 (dd, J = 8.0 Hz, J = 4.0 Hz, 1H), 4.78 (d, J = 8.0 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 165.3, 150.4, 141.3, 140.0, 127.0, 126.5, 125.5, 121.0, 38.8.

*N-phenylisonicotinamide* (**18**) [1]



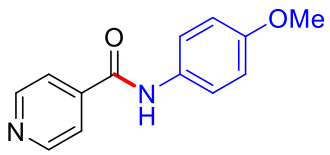
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as light brown solid in 47% yield (28.0 mg); $^1$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 10.51 (br, 1H), 8.79 (d, J = 8.0 Hz, 2H), 7.87 – 7.85 (m, 2H), 7.78 (d, J = 8.0 Hz, 2H), 7.38 (t, J = 8.0 Hz, 2H), 7.14 (t, J = 8.0 Hz, 1H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.1, 150.4, 142.1, 138.7, 128.9, 124.3, 121.7, 120.6.

*N-(p-tolyl)isonicotinamide* (**19**) [5]



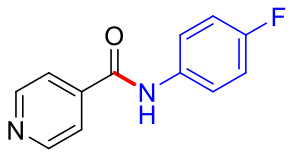
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as light brown solid in 55% yield (35.1 mg); $^1$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 10.44 (br, 1H), 8.79 – 8.77 (m, 2H), 7.86 – 7.85 (m, 2H), 7.66 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 2.28 (s, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 163.9, 150.4, 142.1, 136.2, 133.4, 129.2, 121.7, 120.6, 20.6.

*N-(4-methoxyphenyl)isonicotinamide* (**20**) [5]



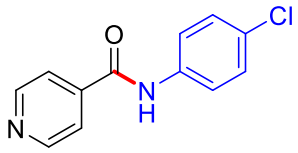
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as light brown solid in 63% yield (43.0 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 10.40 (br, 1H), 8.78 – 8.77 (m, 2H), 7.86 – 7.85 (m, 2H), 7.70 – 7.66 (m, 2H), 6.97 – 6.93 (m, 2H), 3.75 (s, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 163.6, 156.0, 150.4, 142.1, 131.7, 122.2, 121.7, 114.0, 55.3.

*N-(4-fluorophenyl)isonicotinamide* (**21**) [5]



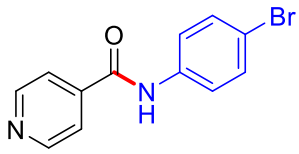

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as light brown solid in 51% yield (33.0 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 10.57 (br, 1H), 8.79 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 7.86 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 7.82 – 7.77 (m, 2H), 7.25 – 7.19 (m, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.0, 158.7 (d, J = 239.0 Hz), 150.4, 142.0, 135.1 (d, J = 3.0 Hz), 122.5 (d, J = 8.0 Hz), 121.7, 115.5 (d, J = 22.0 Hz).

*N-(4-chlorophenyl)isonicotinamide* (**22**) [5]



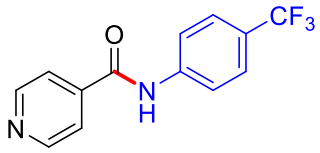

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as light brown solid in 25% yield (17.1 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 10.62 (br, 1H), 8.80 – 8.78 (m, 2H), 7.86 – 7.85 (m, 2H), 7.82 – 7.80 (m, 2H), 7.45 – 7.42 (m, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.2, 150.4, 141.8, 137.7, 128.7, 127.9, 122.1, 121.7.

*N-(4-bromophenyl)isonicotinamide* (**23**) [6]



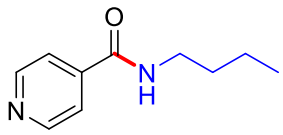

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as light brown solid in 46% yield (37.8 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 10.62 (br, 1H), 8.80 – 8.78 (m, 2H), 7.86 – 7.84 (m, 2H), 7.78 – 7.74 (m, 2H), 7.58 – 7.54 (m, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.2, 150.4, 141.8, 138.1, 131.7, 122.4, 121.7, 116.1.

*N-(4-(trifluoromethyl)phenyl)isonicotinamide* (**24**) [7]



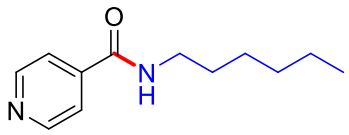

The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a yellow solid in 25% yield (20.2 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 10.83 (br, 1H), 8.81 (d, J = 8.0 Hz, 2H), 8.01 (d, J = 8.0 Hz, 2H), 7.89 – 7.87 (m, 2H), 7.75 (d, J = 8.0 Hz, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.7, 150.4, 142.4, 141.7, 126.1 (q, J = 4.0 Hz), 124.4 (q, J = 270.0 Hz), 124.3 (q, J = 32.0 Hz), 121.8, 120.4.

*N-butylisonicotinamide* (**25**) [5]



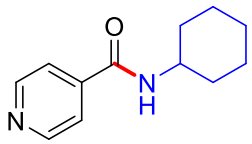

The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a brown oil in 80% yield (42.9 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 8.72 – 8.70 (m, 3H), 7.74 – 7.73 (m, 2H), 3.29 – 3.24 (m, 2H), 1.54 – 1.47 (m, 2H), 1.36 – 1.27 (m, 2H), 0.90 – 0.87 (m, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.6, 150.3, 141.7, 121.3, 39.1, 31.1, 19.7, 13.8.

*N-hexylisonicotinamide* (**26**)[5]



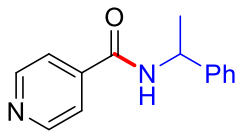
The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a brown oil in 77% yield (47.6 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 8.74 – 8.70 (m, 3H), 7.74 – 7.73 (m, 2H), 3.28 – 3.23 (m, 2H), 1.55 – 1.48 (m, 2H), 1.31 – 1.23 (m, 6H), 0.86 – 0.83 (m, 3H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.6, 150.2, 141.7, 121.3, 39.4, 31.1, 29.0, 26.2, 22.1, 14.0.

*N-cyclohexylisonicotinamide* (**27**)[5]



The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a white solid in 63% yield (38.6 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 8.70 – 8.69 (m, 2H), 8.51 (d, J = 8.0 Hz, 1H), 7.74 – 7.73 (m, 2H), 3.77 – 3.74 (m, 1H), 1.84 – 1.80 (m, 2H), 1.74 – 1.68 (m, 2H), 1.62 – 1.57 (m, 1H), 1.35 – 1.21 (m, 5H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 163.9, 150.2, 141.9, 121.5, 48.7, 32.4, 25.3, 25.0.

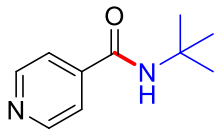
*N-(1-phenylethyl)isonicotinamide* (**28**)[8]



The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a brown oil in 68% yield (45.8 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.12 (d, J = 8.0 Hz, 1H), 8.73 – 8.72 (m, 2H), 7.80 – 7.79

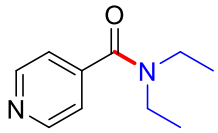
(m, 2H), 7.41 – 7.38 (m, 2H), 7.35 – 7.31 (m, 3H), 7.25 – 7.21 (m, 1H), 5.21 – 5.13 (m, 1H), 1.49 (d, J = 4.0 Hz, 1H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.1, 150.3, 144.5, 141.6, 128.4, 126.9, 126.2, 121.5, 48.8, 22.2.

*N-(tert-butyl)isonicotinamide* (**29**) [1]



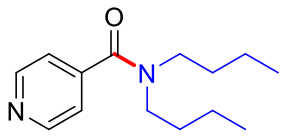
The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a brown oil in 33% yield (18.0 mg); $^1$H NMR ($CDCl_3$, 400 MHz, ppm): δ = 8.70 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 7.56 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H), 6.07 (br, 1H), 1.47 (s, 9H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 164.8, 150.4, 142.8, 120.7, 52.1, 28.7.

*N,N-diethylisonicotinamide* (**30**) [9]



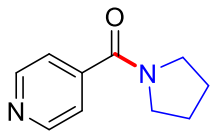
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a yellow oil in 45% yield (24.2 mg); $^1$H NMR ($CDCl_3$, 400 MHz, ppm): δ = 8.65 (d, J = 8.0 Hz, 2H), 7.25 – 7.24 (m, 2H), 3.53 (q, J = 8.0 Hz, 2H), 3.18 (q, J = 8.0 Hz, 2H), 1.23 (t, J = 8.0 Hz, 3H), 1.09 (t, J = 8.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 168.5, 150.0, 144.7, 120.6, 43.1, 39.3, 14.1, 12.7.

*N,N-dibutylisonicotinamide* (**31**) [5]



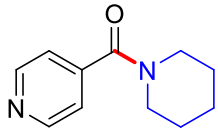
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 3:1) to give the product as a yellow oil in 46% yield (32.5 mg); $^{1}$H NMR ($CDCl_3$, 400 MHz, ppm): δ = 8.65 – 8.64 (m, 2H), 7.23 – 7.22 (m, 2H), 3.46 (t, J = 8.0 Hz, 2H), 3.10 (t, J = 8.0 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.49 – 1.42 (m, 2H), 1.40 – 1.33 (m, 2H), 1.16 – 1.07 (m, 2H), 0.95 (t, J = 8.0 Hz, 3H), 0.77 (t, J = 8.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 168.9, 150.0, 144.8, 120.8, 48.5, 44.4, 30.7, 29.5, 20.2, 19.6, 13.8, 13.5.

*Pyridin-4-yl(pyrrolidin-1-yl)methanone* (**32**) [1]



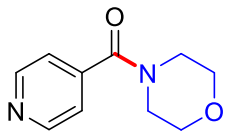

The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a yellow oil in 83% yield (44.1 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 8.67 – 8.65 (m, 2H), 7.47 – 7.46 (m, 2H), 3.46 (t, J = 8.0 Hz, 2H), 3.32 (t, J = 8.0 Hz, 2H), 1.88 – 1.78 (m, 4H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 166.2, 150.1, 144.5, 121.4, 48.7, 46.0, 26.0, 24.0.

*Piperidin-1-yl(pyridin-4-yl)methanone* (**33**) [1]



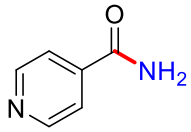

The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a yellow oil in 56% yield (31.8 mg); $^{1}$H NMR ($CDCl_3$ 400 MHz, ppm): δ = 8.65 – 8.64 (m, 2H), 7.25 – 7.24 (m, 2H), 3.69 – 3.67 (m, 2H), 3.26 – 3.23 (m, 2H), 1.66 (s, 4H), 1.52 – 1.46 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm): δ = 167.5, 150.0, 144.0, 121.0, 48.4, 42.9, 26.4, 25.4, 24.3.

*morpholino(pyridin-4-yl)methanone* (**34**) [5]



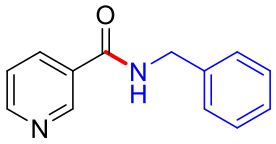
The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a yellow oil in 58% yield (32.9 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 8.67 (d, J = 8.0 Hz, 2H), 7.41 – 7.40 (m, 2H), 3.66 – 3.61 (m, 4H), 3.56 – 3.52 (m, 2H), 3.27 – 3.25 (m, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 167.0, 150.2, 143.3, 121.4, 66.1, 66.0, 47.5, 41.9.

*Isonicotinamide* (**35**) [10]



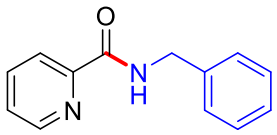
The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a white solid in 36% yield (13.2 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 8.72 – 8.71 (m, 2H), 8.25 (br, 1H), 7.77 – 7.76 (m, 2H), 7.73 (br, 1H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 166.4, 150.3, 141.4, 121.5.

*N-benzylnicotinamide* (**36**) [11]



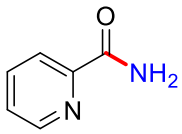
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a white solid in 22% yield (14.0 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.27 – 9.24 (m, 1H), 9.06 – 9.05 (m, 1H), 8.72 – 8.70 (m, 1H), 8.25 – 8.22 (m, 1H), 7.53 – 7.50 (m, 1H), 7.34 – 7.33 (m, 4H), 7.28 – 7.23 (m, 1H), 4.51 (d, J = 4.0 Hz, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.9, 152.0, 148.5, 139.4, 135.1, 129.9, 128.5, 127.4, 127.0, 123.6, 42.7.

*N-benzylpicolinamide* (**37**) [1]



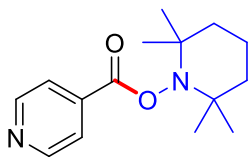
The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 1:1) to give the product as a yellow oil in 63% yield (40.3 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 9.37 – 9.34 (m, 1H), 8.66 – 8.64 (m, 1H), 8.07 – 8.05 (m, 1H), 8.02 – 7.97 (m, 1H), 7.62 – 7.58 (m, 1H), 7.34 – 7.30 (m, 4H), 7.24 – 7.21 (m, 1H), 4.51 (d, J = 4.0 Hz, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 164.1, 150.1, 148.6, 139.7, 137.9, 128.4, 127.5, 126.9, 126.7, 122.1, 42.5.

*Picolinamide* (**38**) [1]



The title compound was prepared according to the general working procedure and purified by column chromatography (ethyl acetate) to give the product as a white solid in 69% yield (25.4 mg); $^{1}$H NMR (DMSO-$d_6$, 400 MHz, ppm): δ = 8.63 – 8.61 (m, 1H), 8.13 (br, 1H), 8.05 – 8.03 (m, 1H), 8.00 – 7.95 (m, 1H), 7.66 (br, 1H), 7.60 – 7.56 (m, 1H),; $^{13}$C NMR (DMSO-$d_6$, 100 MHz, ppm): δ = 166.2, 150.4, 148.6, 137.8, 126.6, 122.0.

*2,2,6,6-Tetramethylpiperidin-1-yl isonicotinate* (**39**) [1]



The title compound was prepared according to the general working procedure and purified by column chromatography (petroleum ether / ethyl acetate = 9:1) to give the product as a white oil in 50% yield (39.7 mg); $^{1}$H NMR ($CDCl_3$, 400 MHz, ppm): δ = 8.79 (dd, J = 8.0 Hz, J = 4.0 Hz, 2H),

7.87 – 7.86 (m, 2H), 1.80 – 1.69 (m, 3H), 1.61 – 1.57 (m, 2H), 1.48 – 1.44 (m, 1H), 1.26 (s, 6H), 1.10 (s, 6H); $^{13}C$ NMR ($CDCl_3$, 100 MHz, ppm): δ = 164.9, 150.6, 136.9, 122.8, 60.6, 39.0, 31.9, 20.8, 16.9.

## Reference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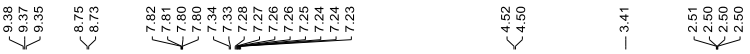
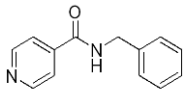
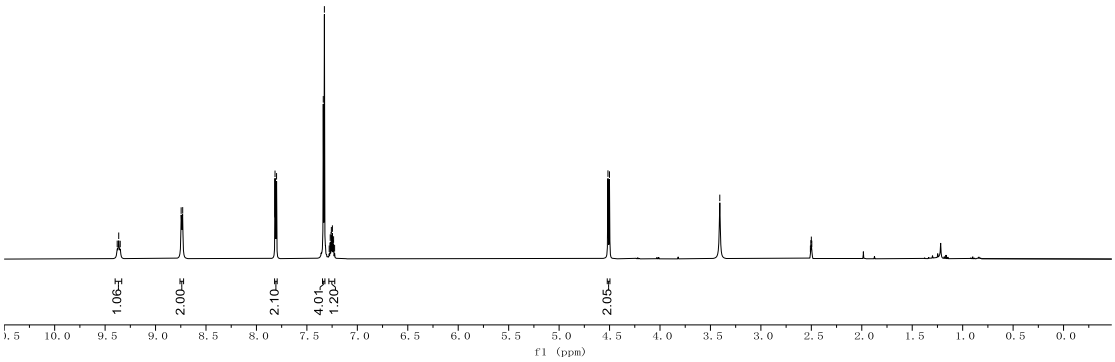
# NMR Spectra of products

## 3-$^{1}$H NMR

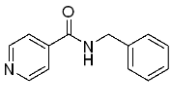


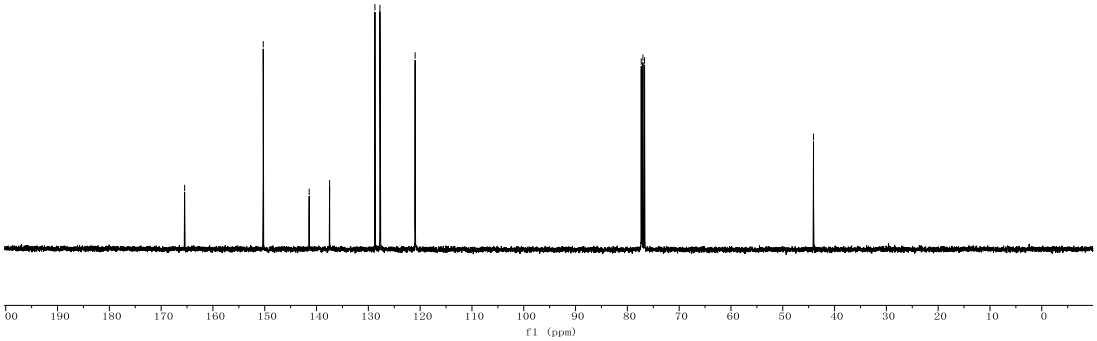

400 MHz, DMSO-$d_6$



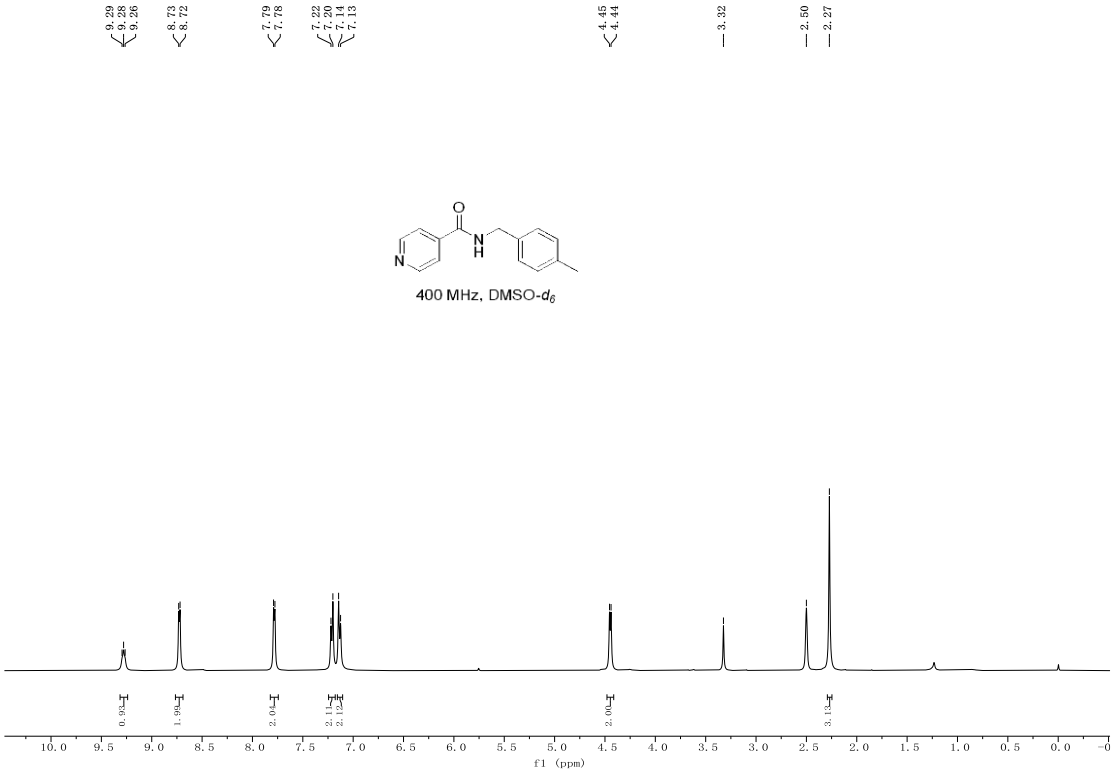

## 3-$^{13}$C NMR

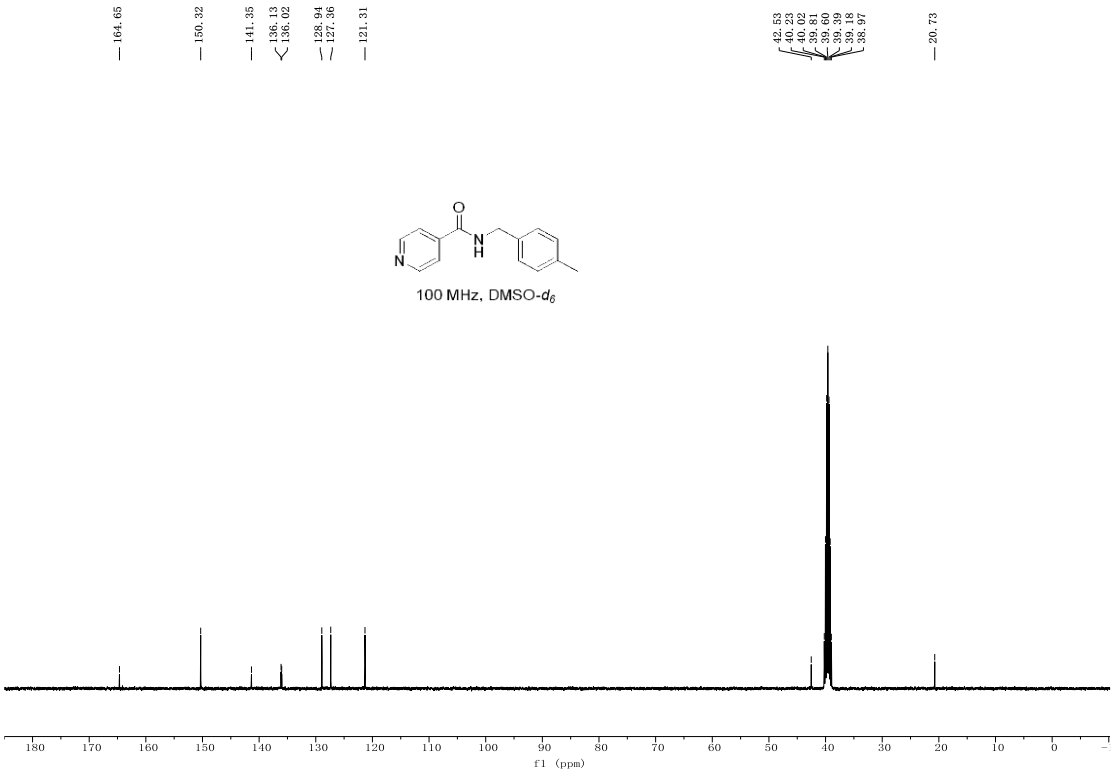

100 MHz, $CDCl_3$



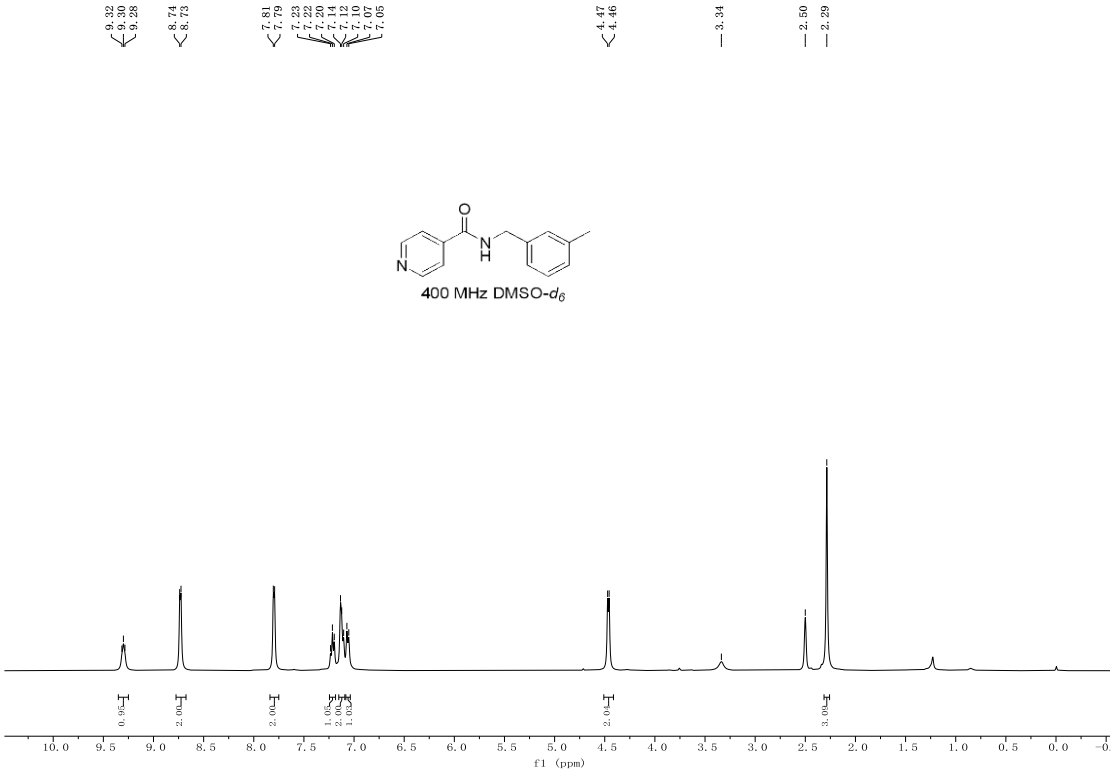
**4-$^{1}$H NMR**



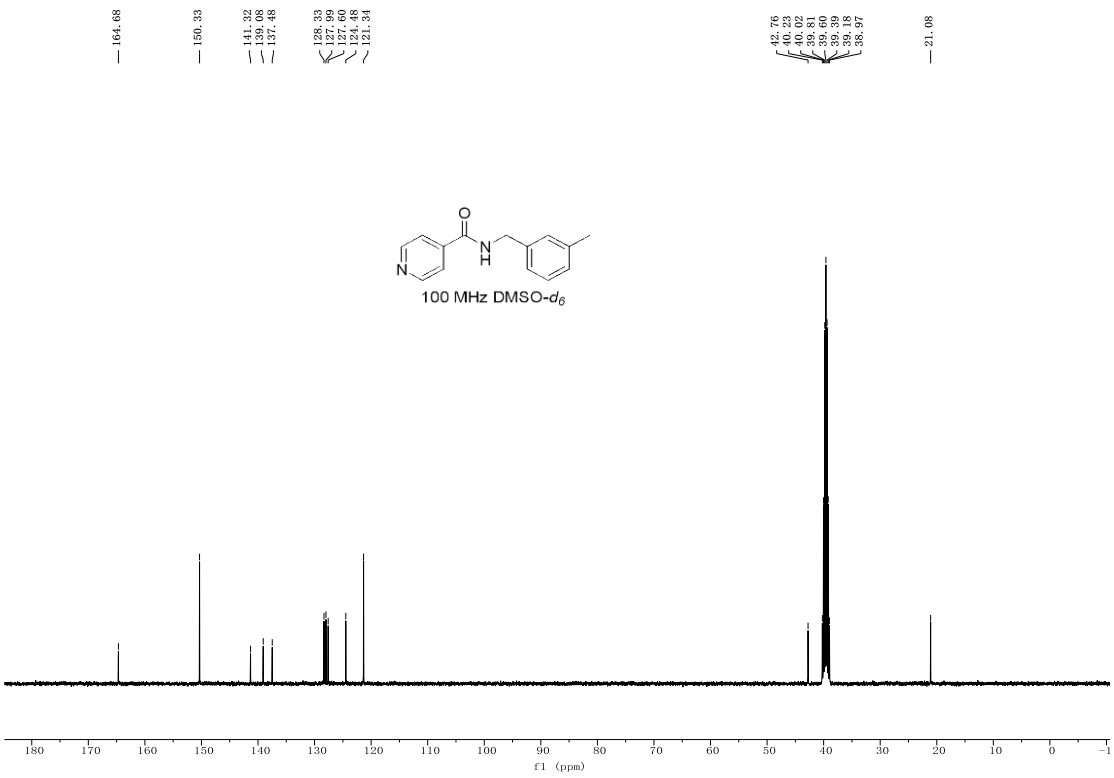

**4-$^{13}$C NMR**



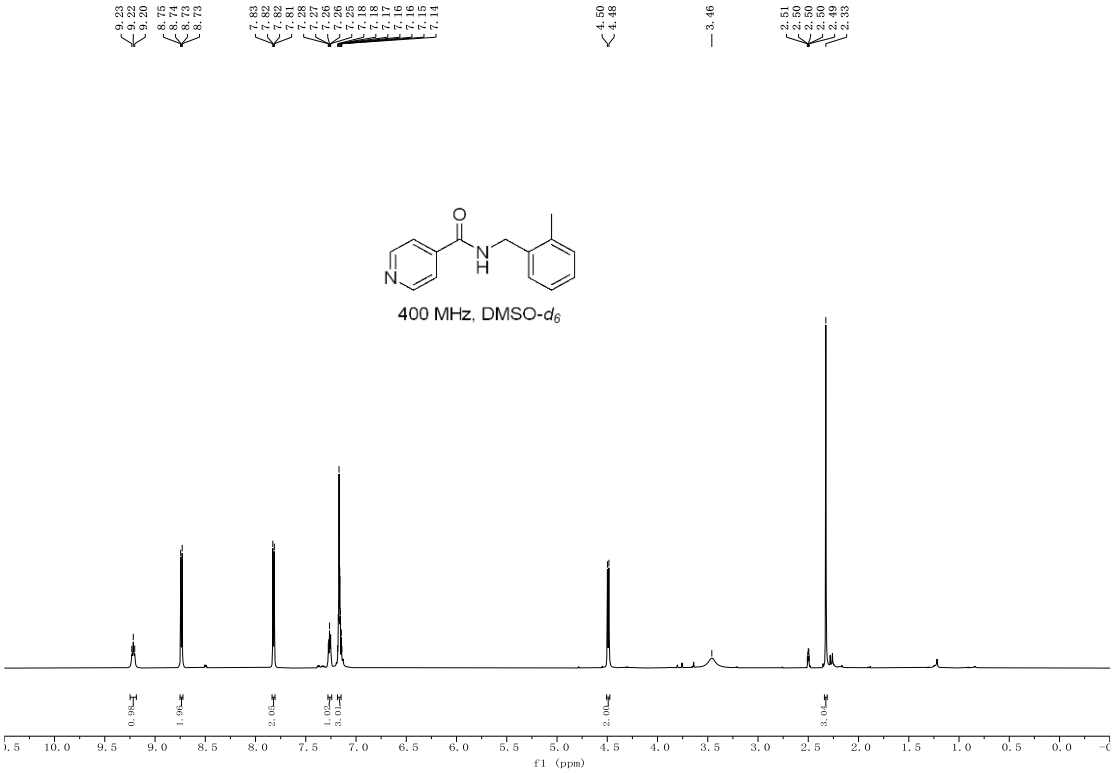
**5-$^{1}$H NMR**



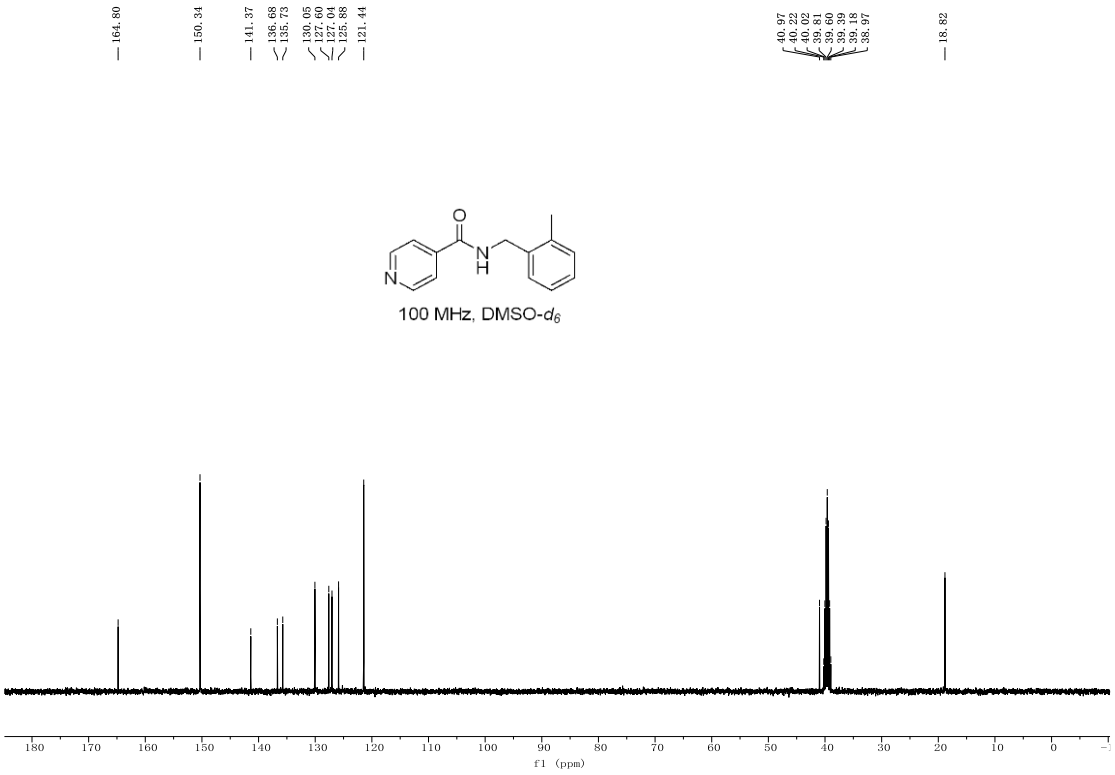

**5-$^{13}$C NMR**



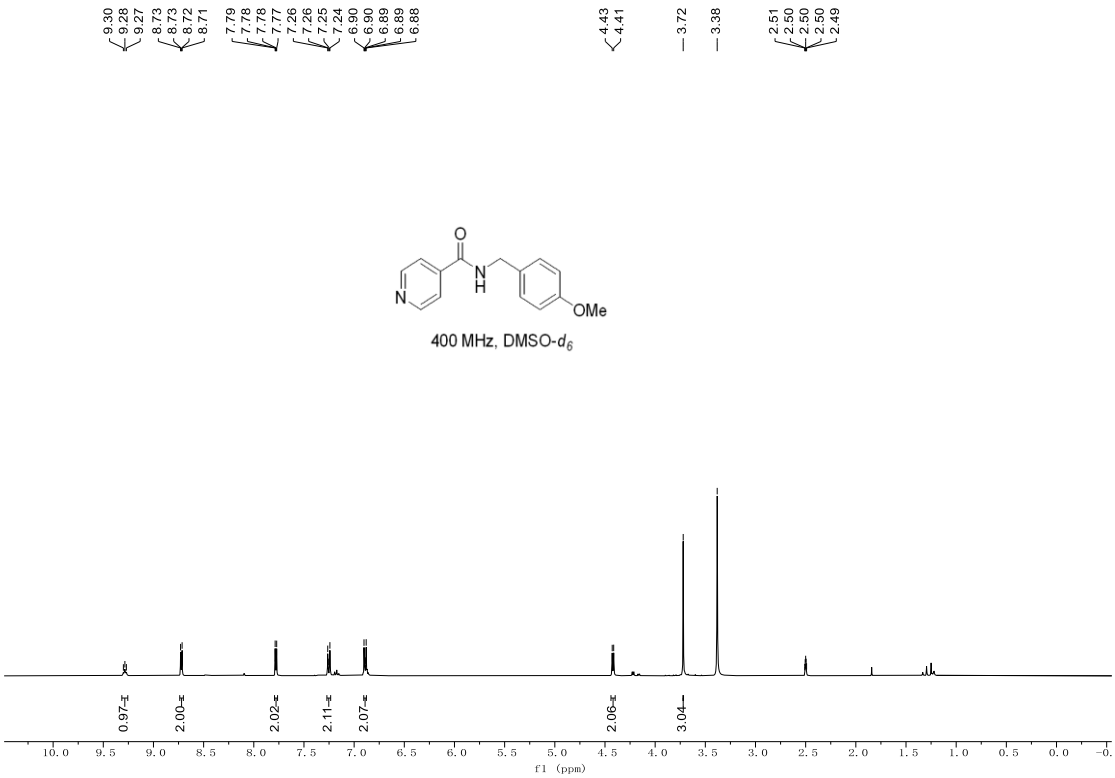
**6-$^{1}$H NMR**



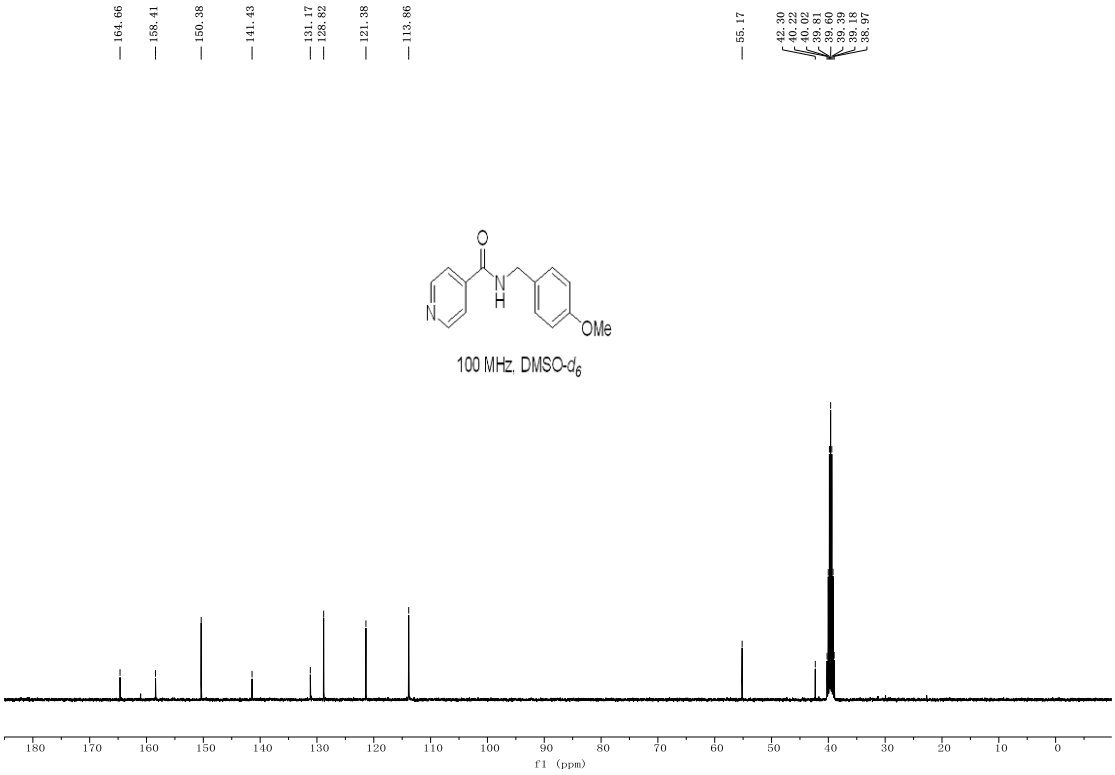

**6-$^{13}$C NMR**



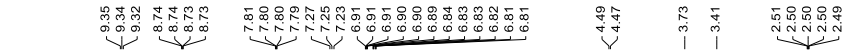
**7-$^{1}$H NMR**

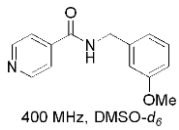



**7-$^{13}$C NMR**

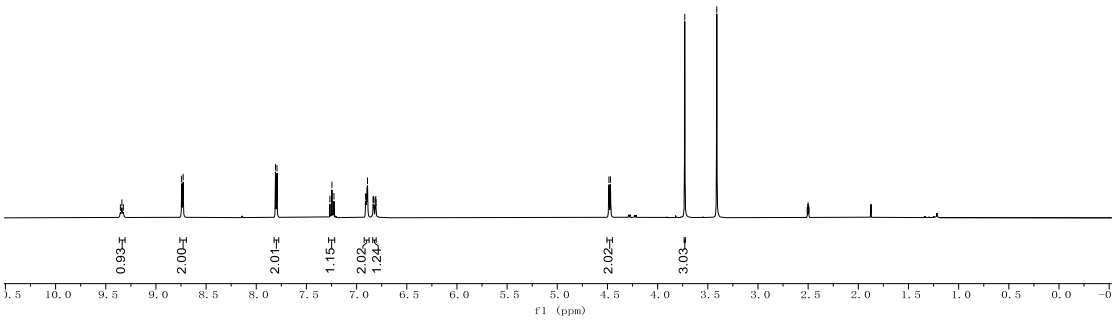


**8-$^{1}$H NMR**

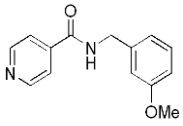


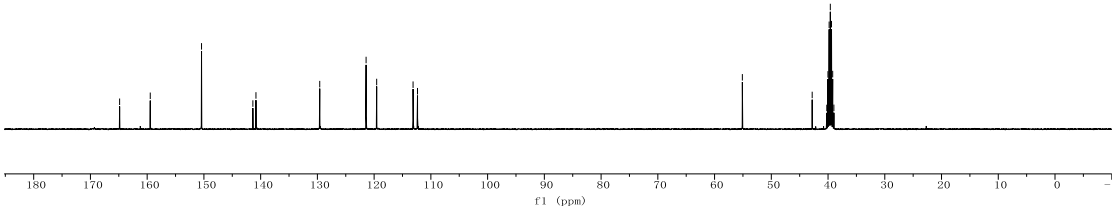

400 MHz, DMSO-$d_6$




**8-$^{13}$C NMR**

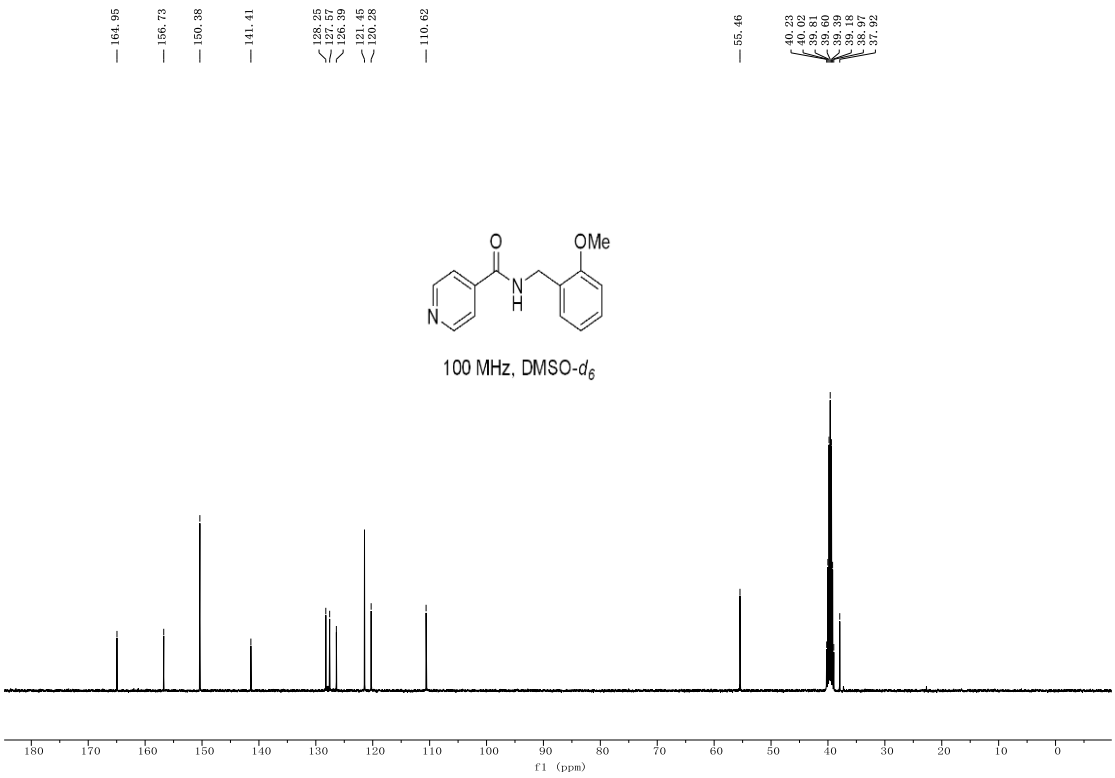




100 MHz, DMSO-$d_6$

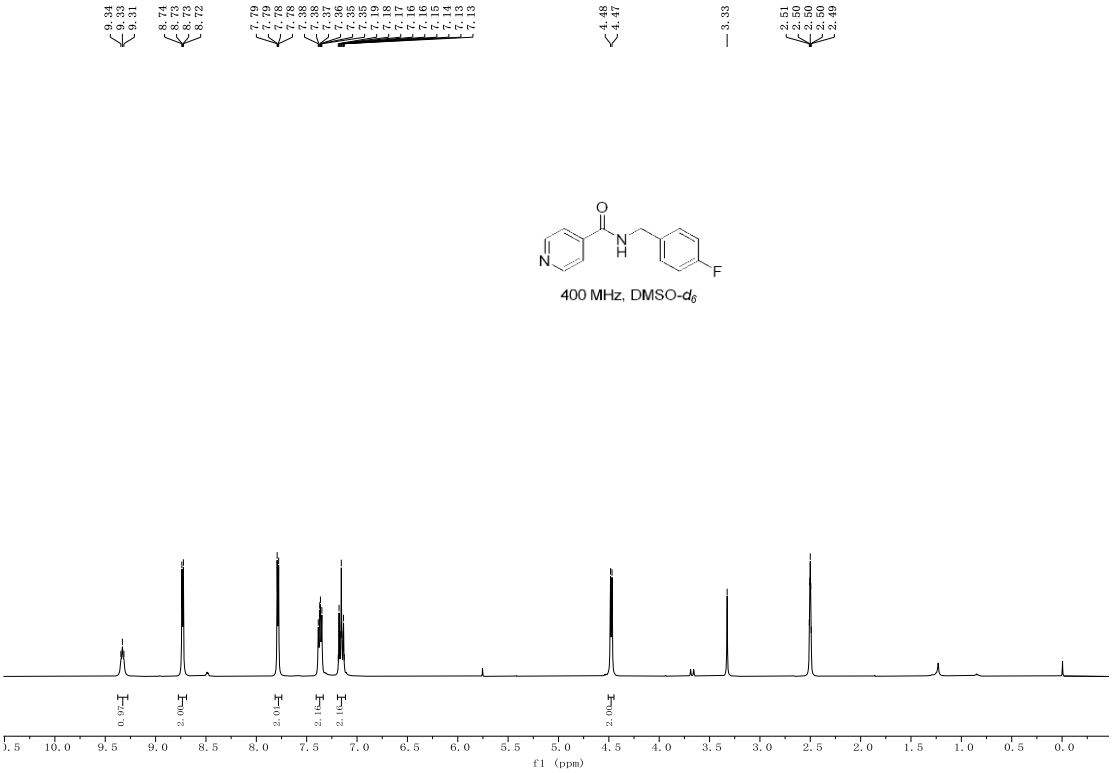


**9-$^{1}$H NMR**

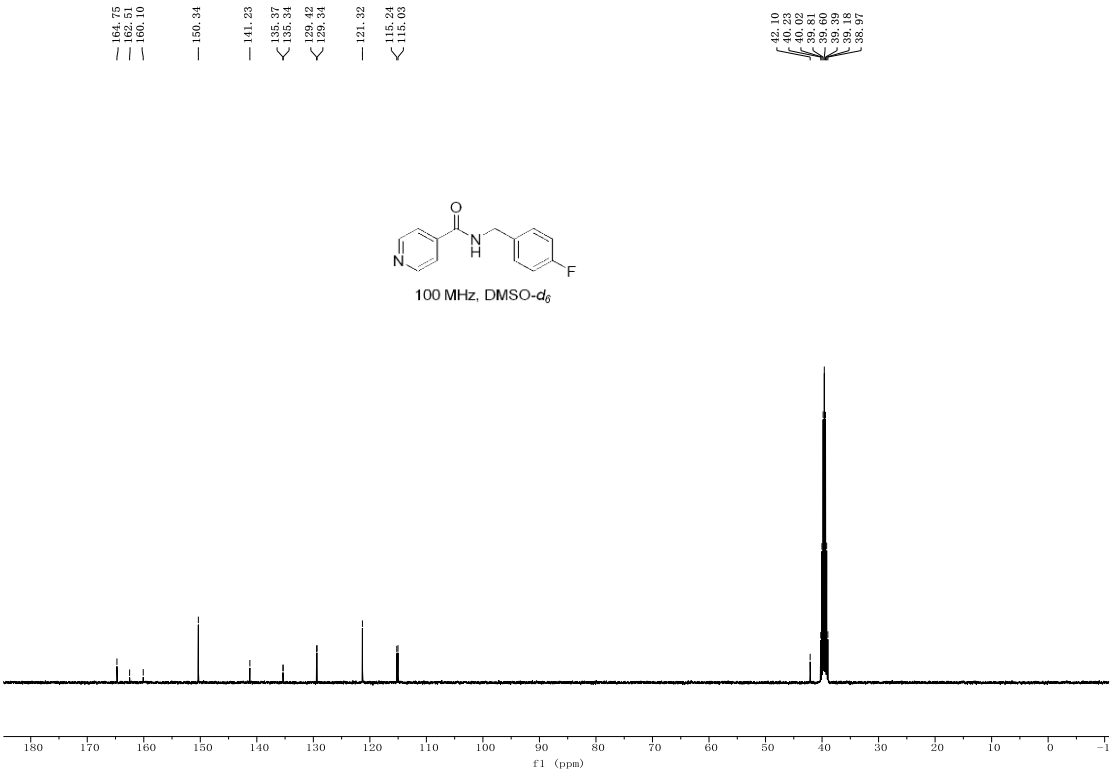

**9-$^{13}$C NMR**



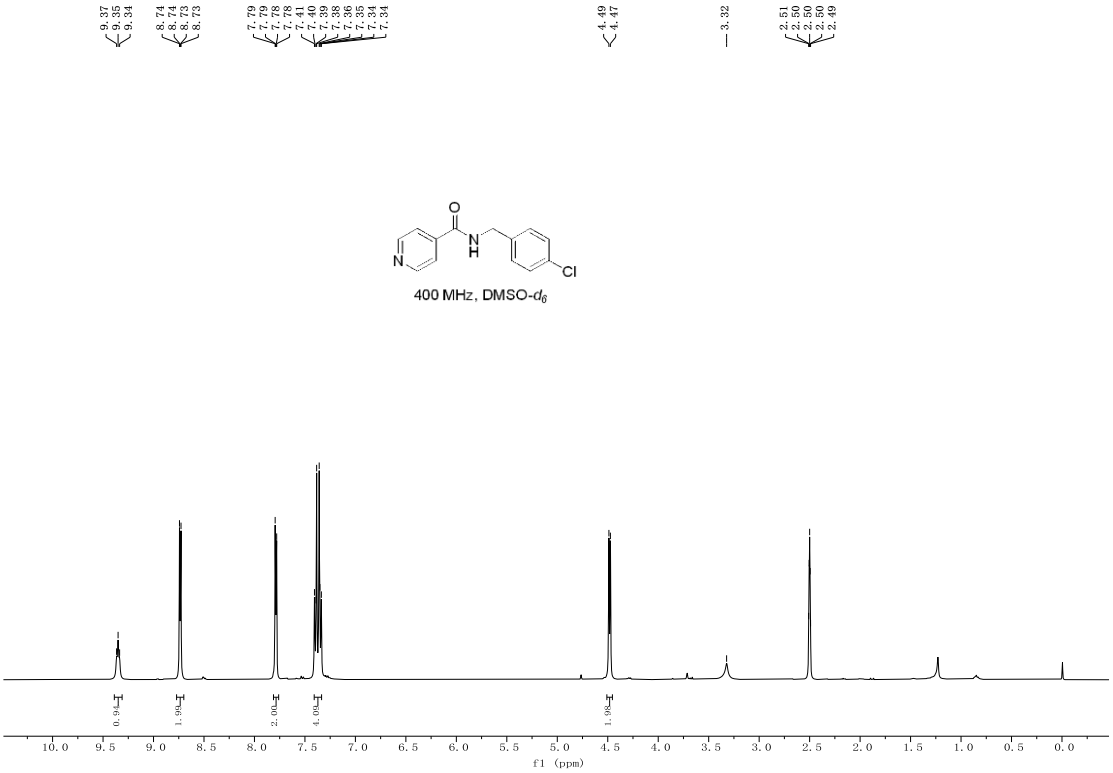
**10-$^{1}$H NMR**



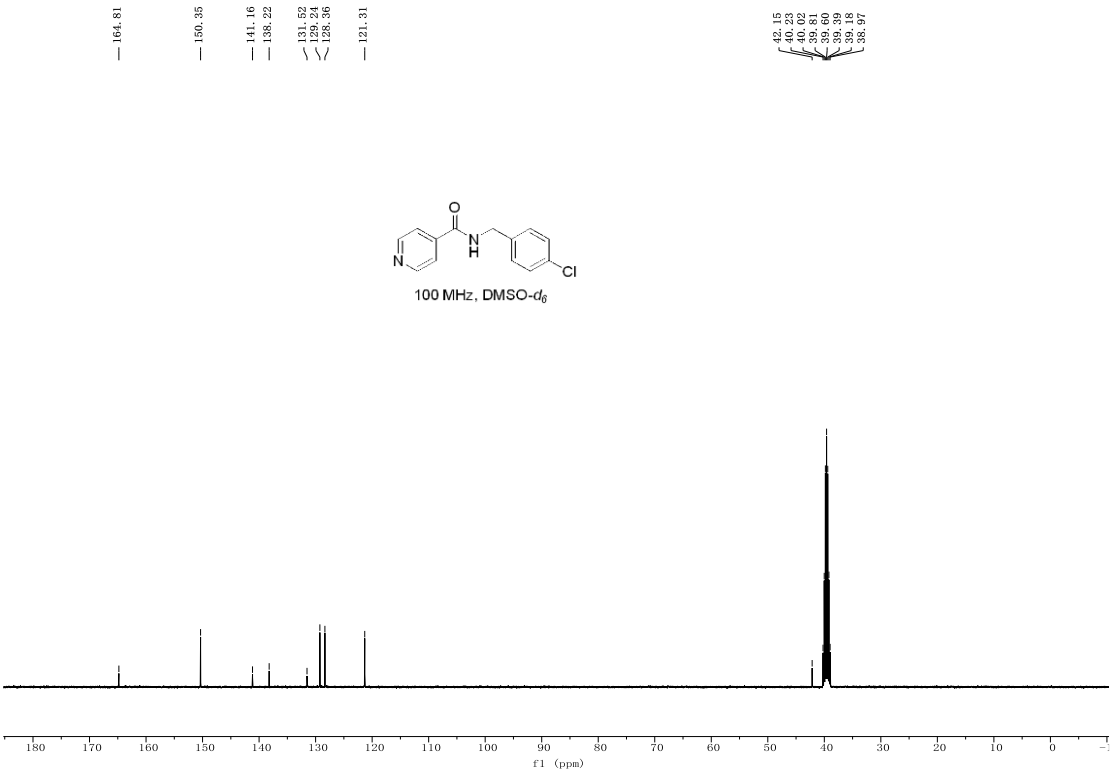

**10-$^{13}$C NMR**



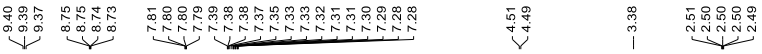
**11-$^{1}$H NMR**

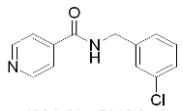



**11-$^{13}$C NMR**

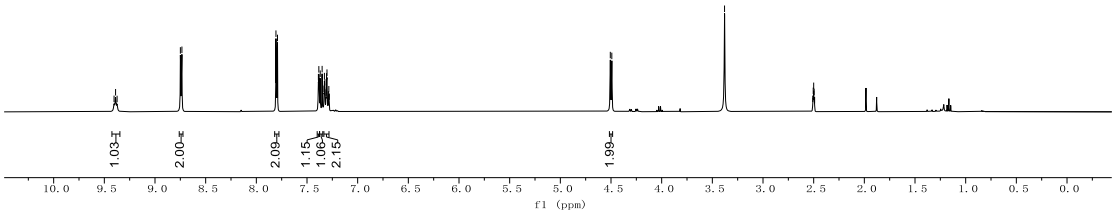


**12-$^{1}$H NMR**

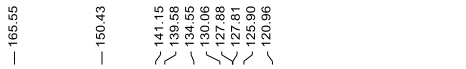


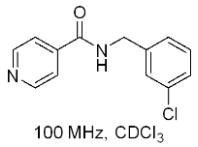




400 MHz, DMSO-$d_6$

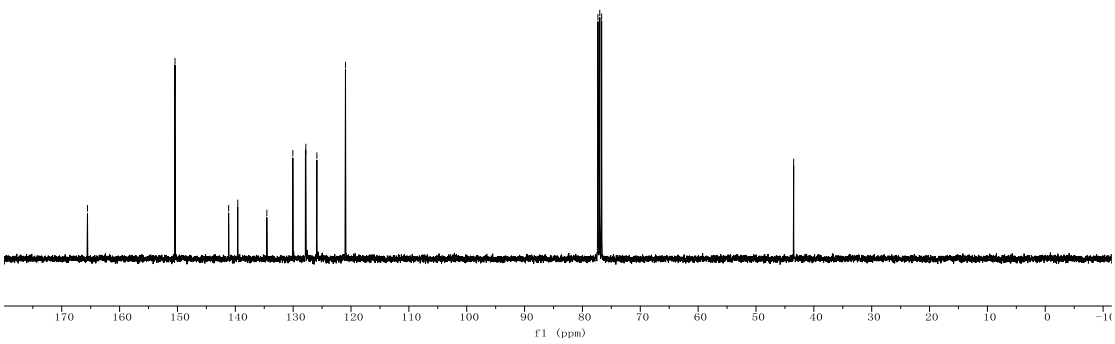



**12-$^{13}$C NMR**

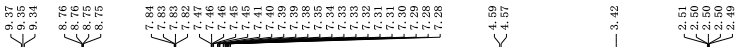


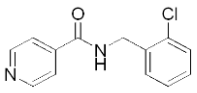




100 MHz, $CDCl_3$

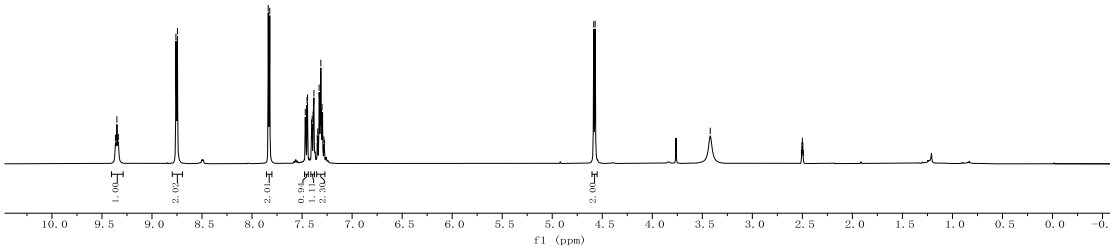


**13-$^{1}$H NMR**

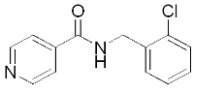


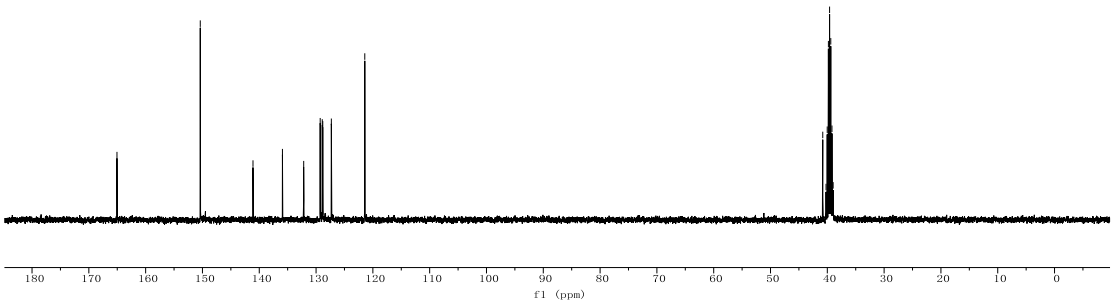

400 MHz DMSO-$d_6$



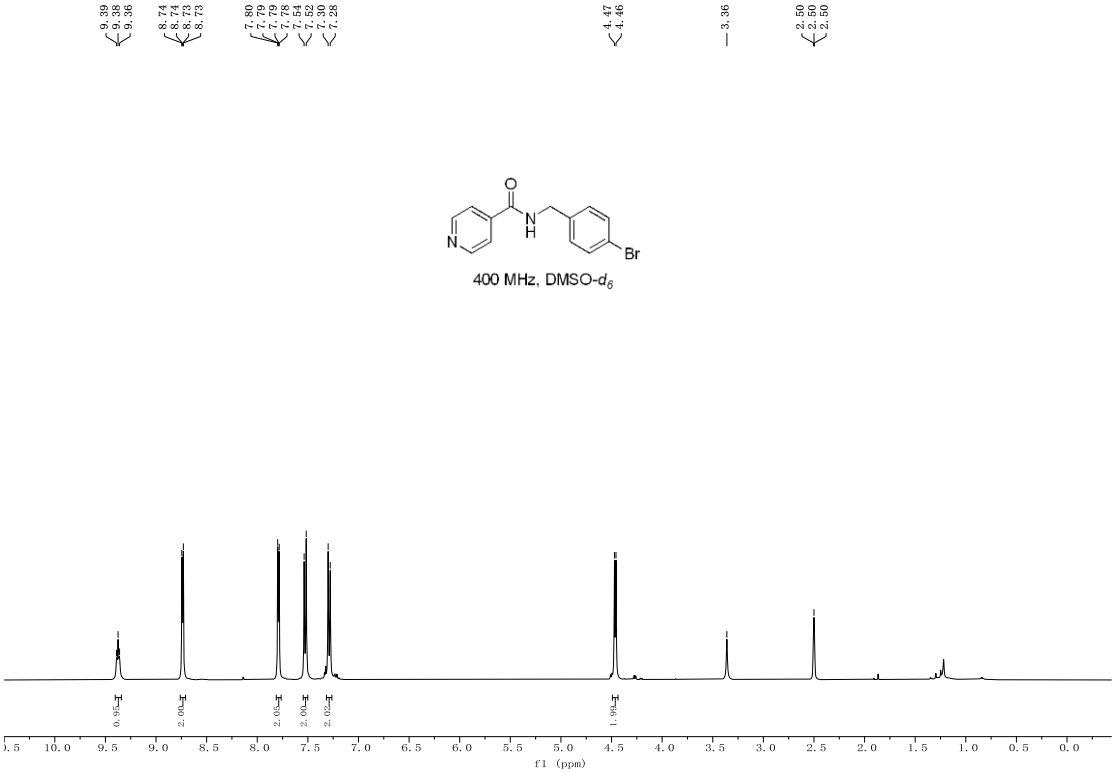

**13-$^{13}$C NMR**

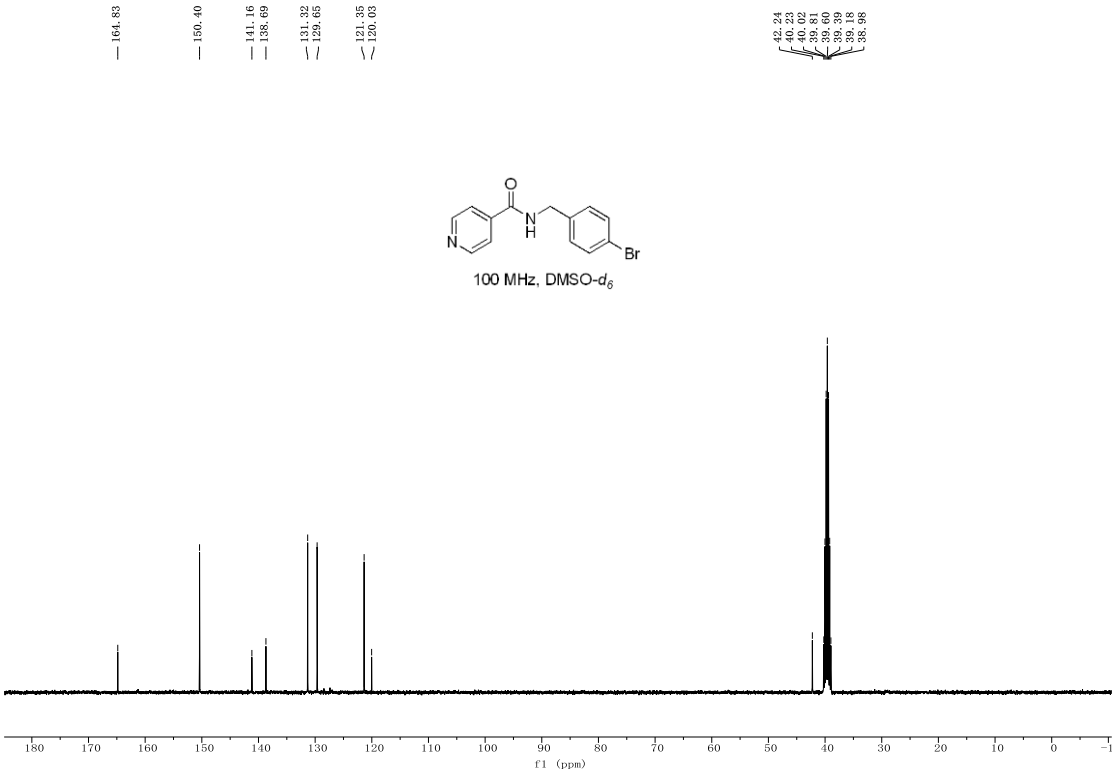

100 MHz, DMSO-$d_6$



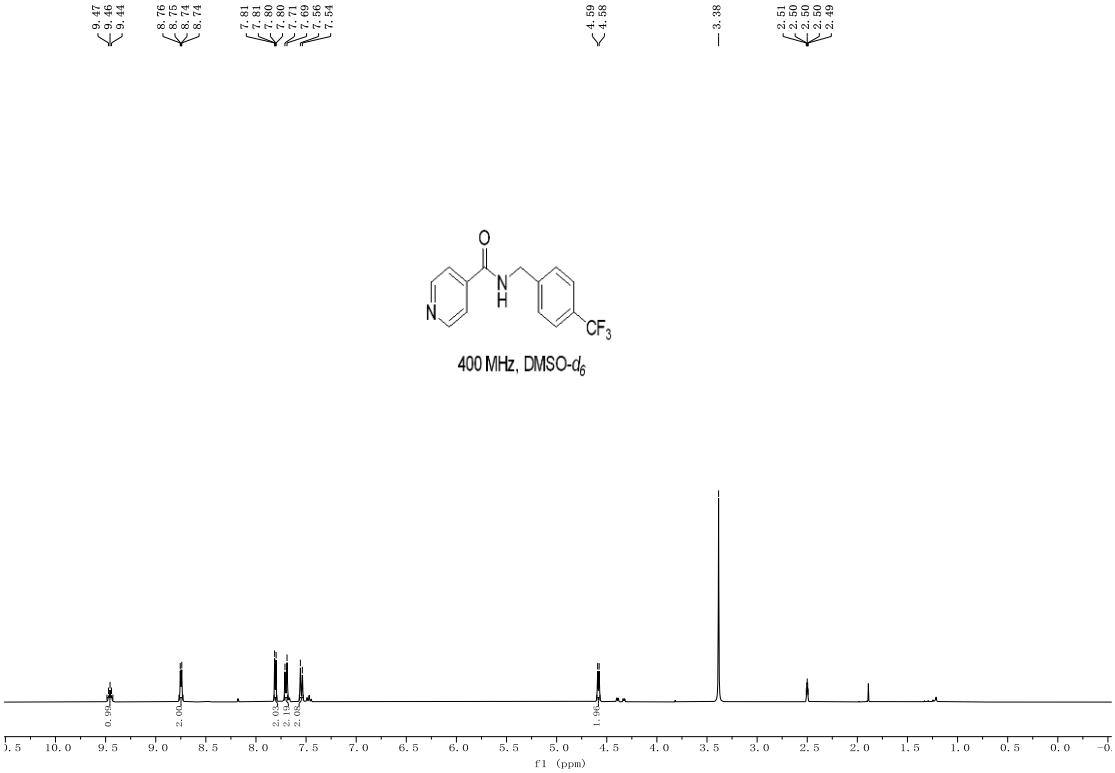
**14-$^{1}$H NMR**



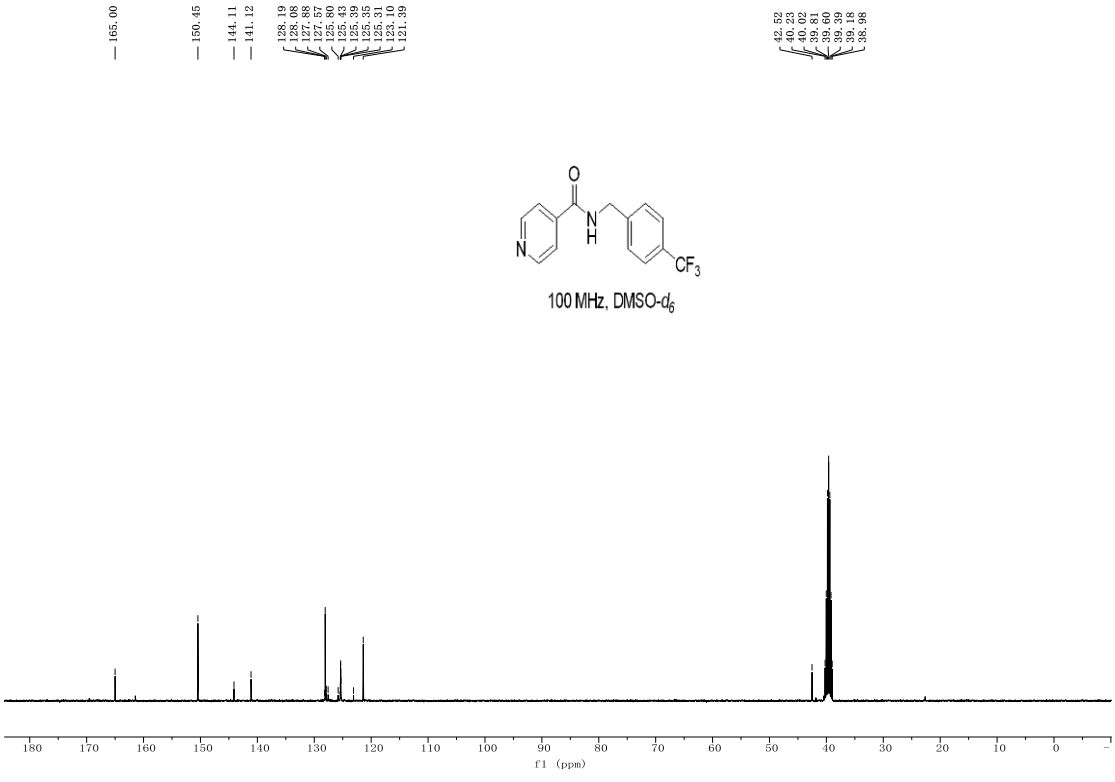

**14-$^{13}$C NMR**



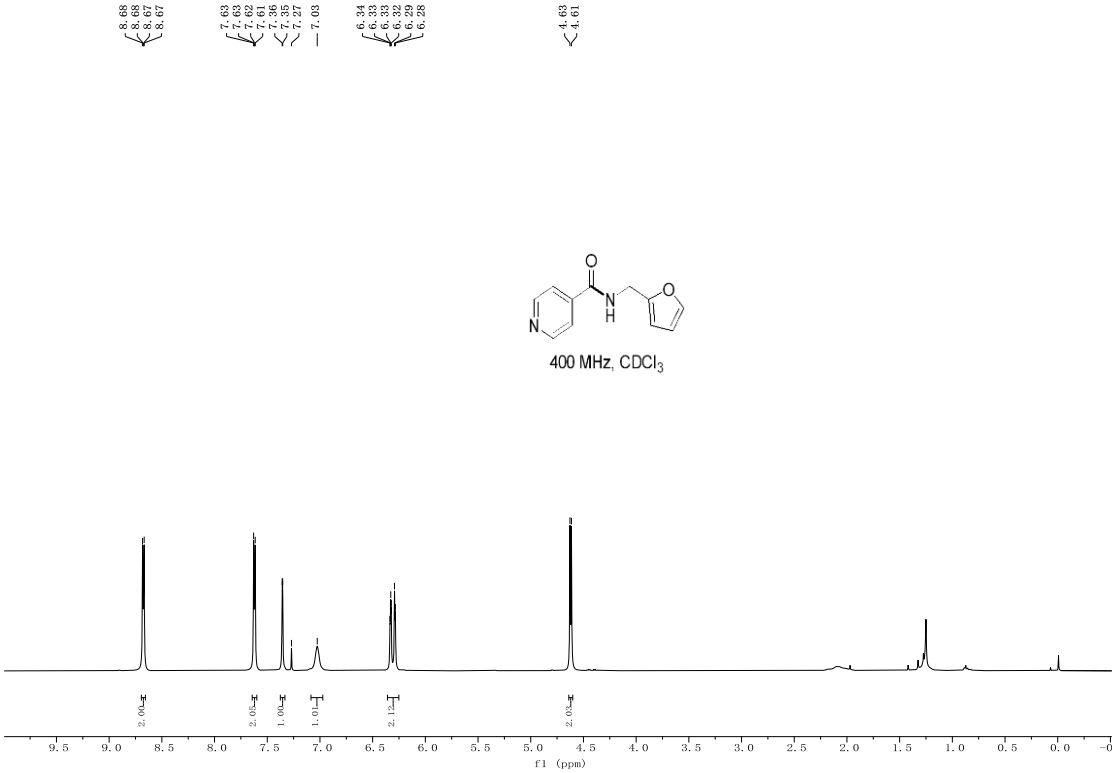
**15-$^{1}$H NMR**



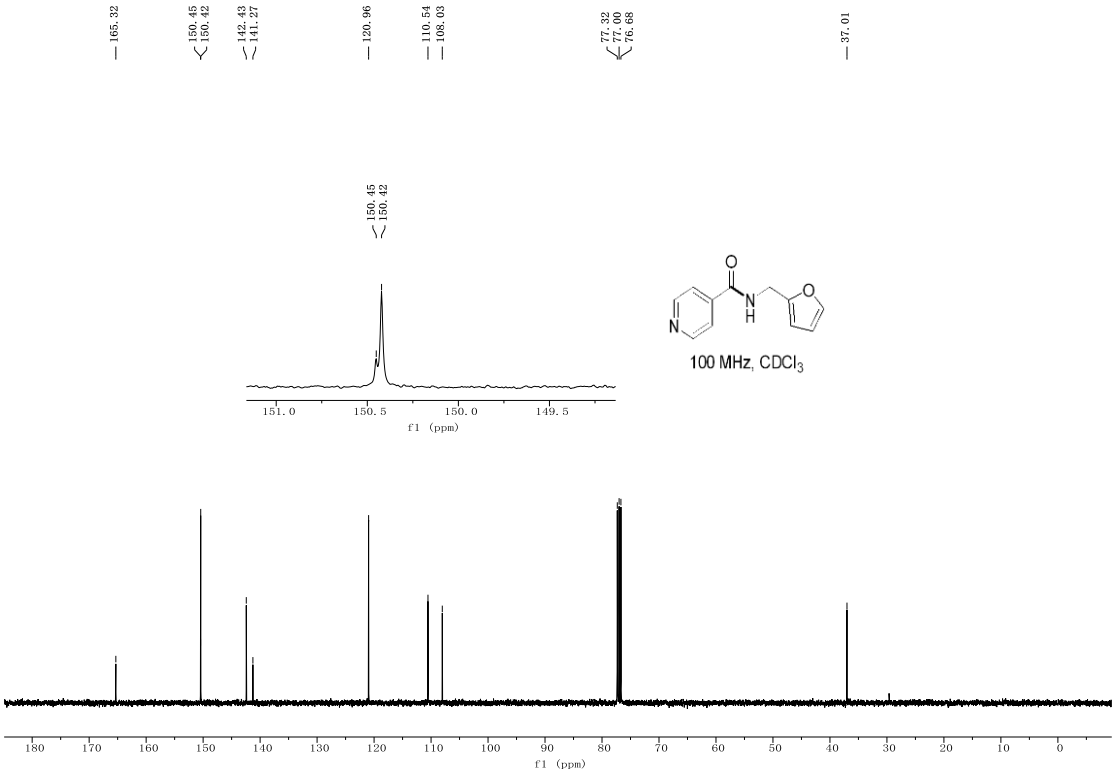

**15-$^{13}$C NMR**



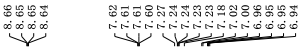
**16-$^{1}$H NMR**

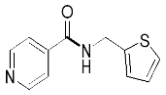



**16-$^{13}$C NMR**

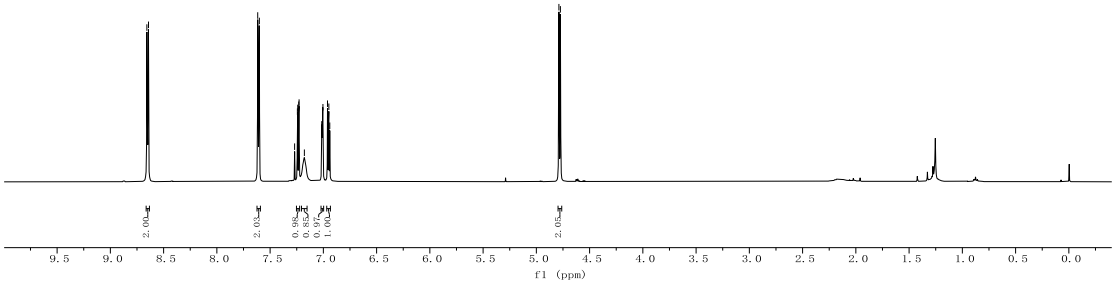


**17-$^{1}$H NMR**

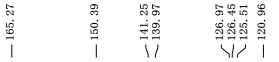


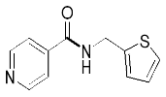




400 MHz, $CDCl_3$

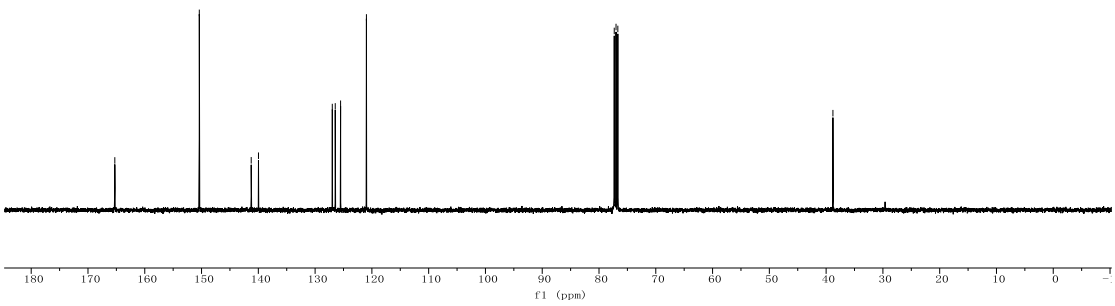



**17-$^{13}$C NMR**

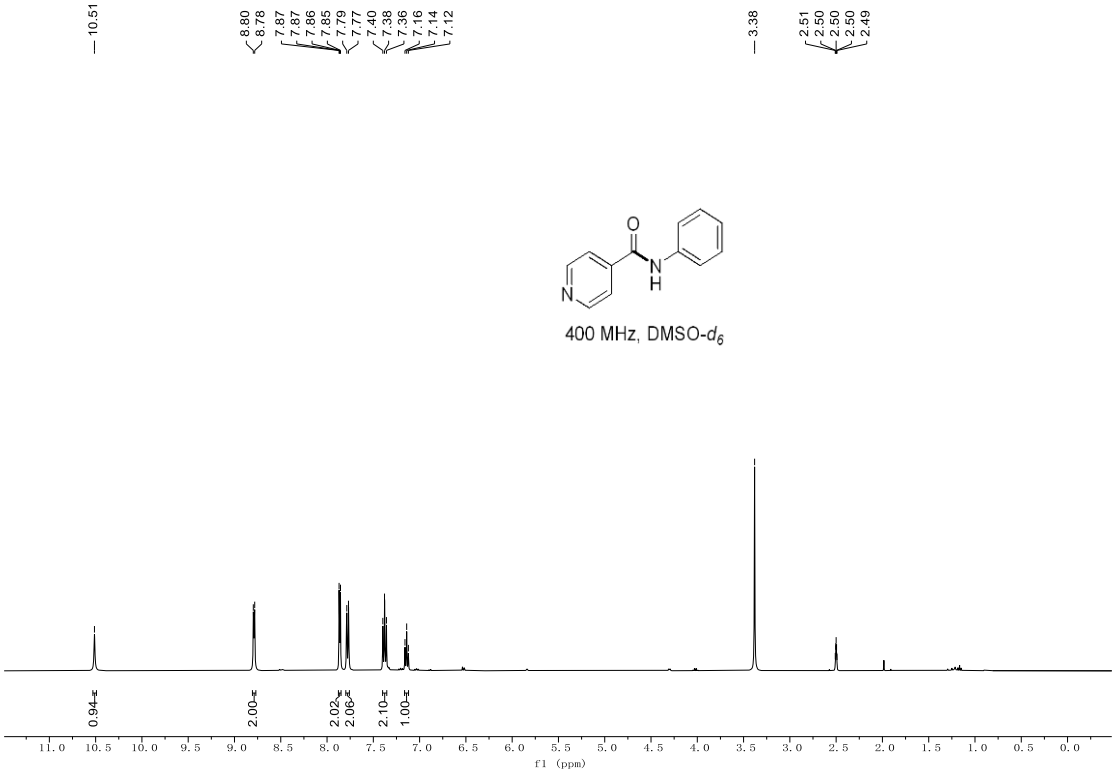


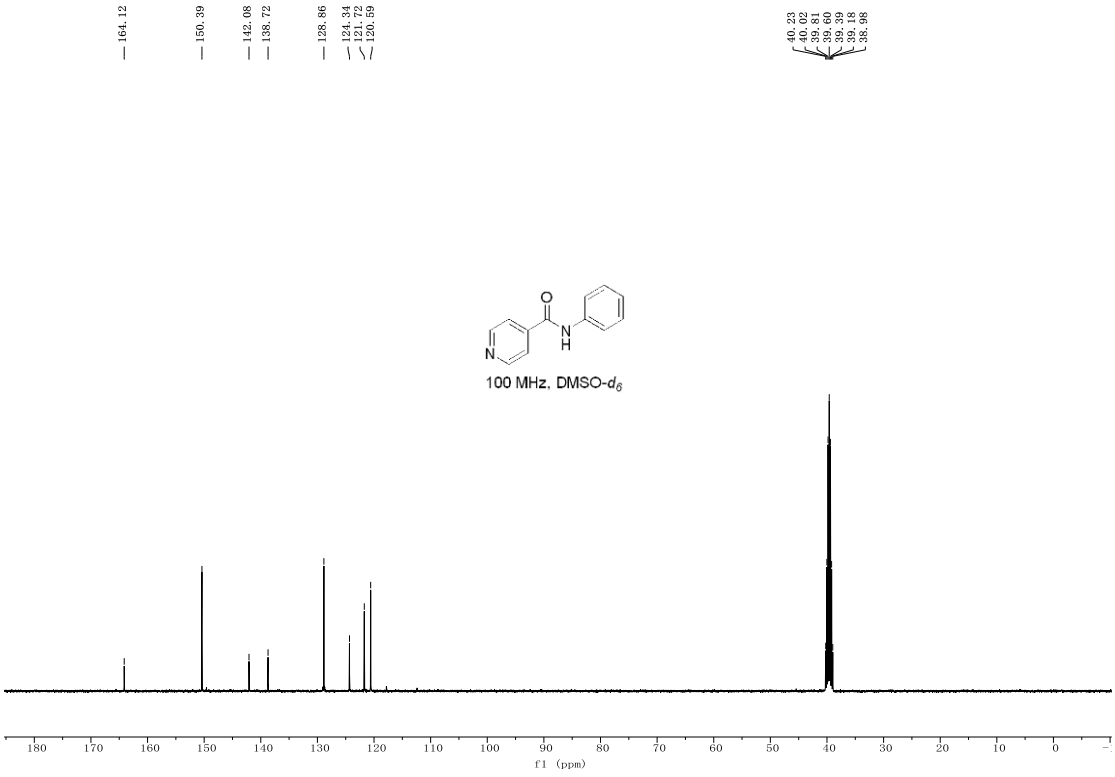

100 MHz, $CDCl_3$



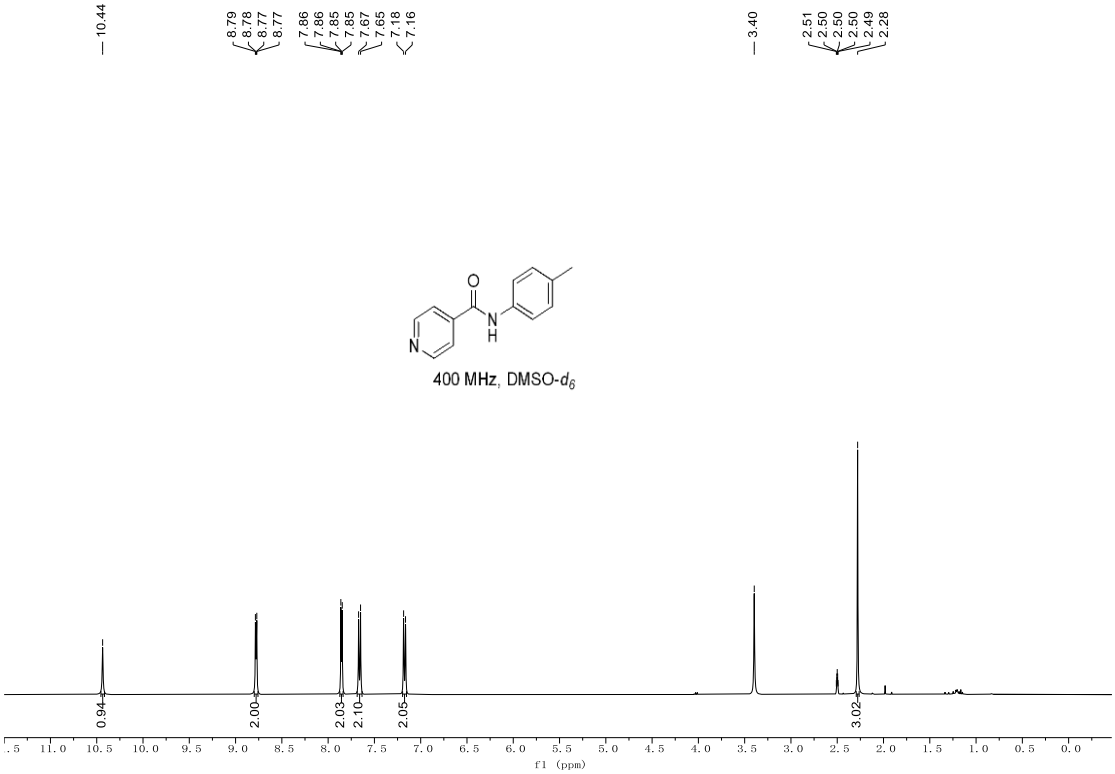
**18-$^{1}$H NMR**



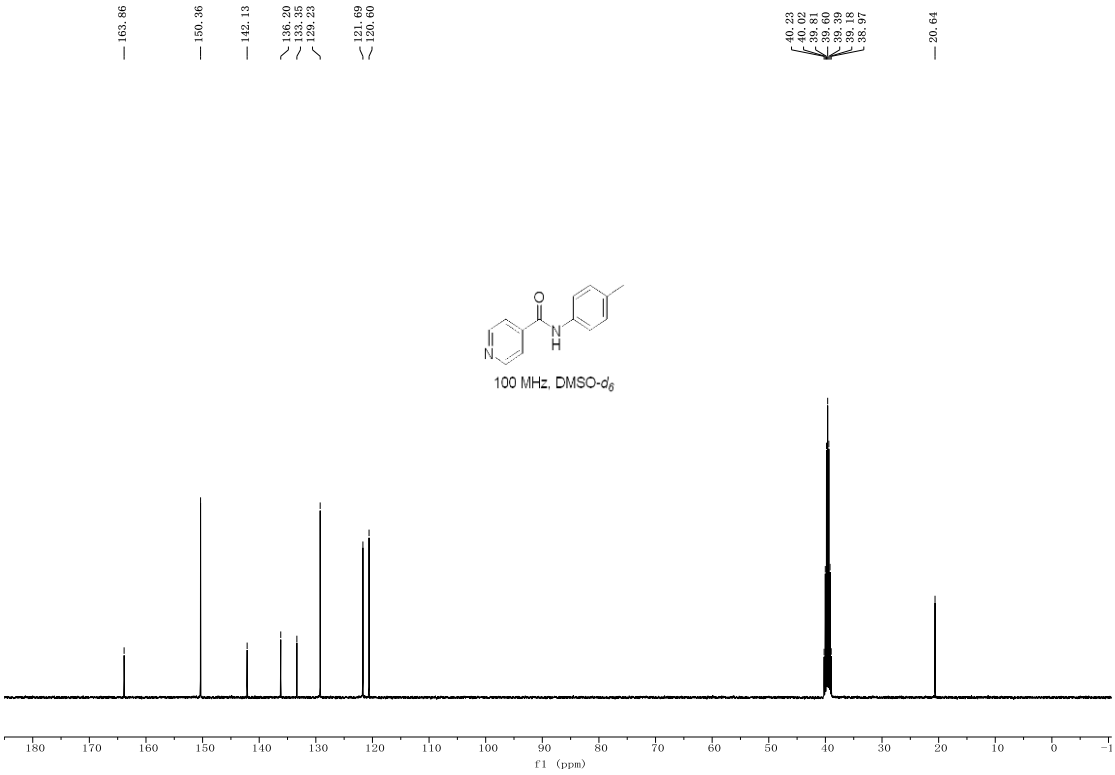

**18-$^{13}$C NMR**



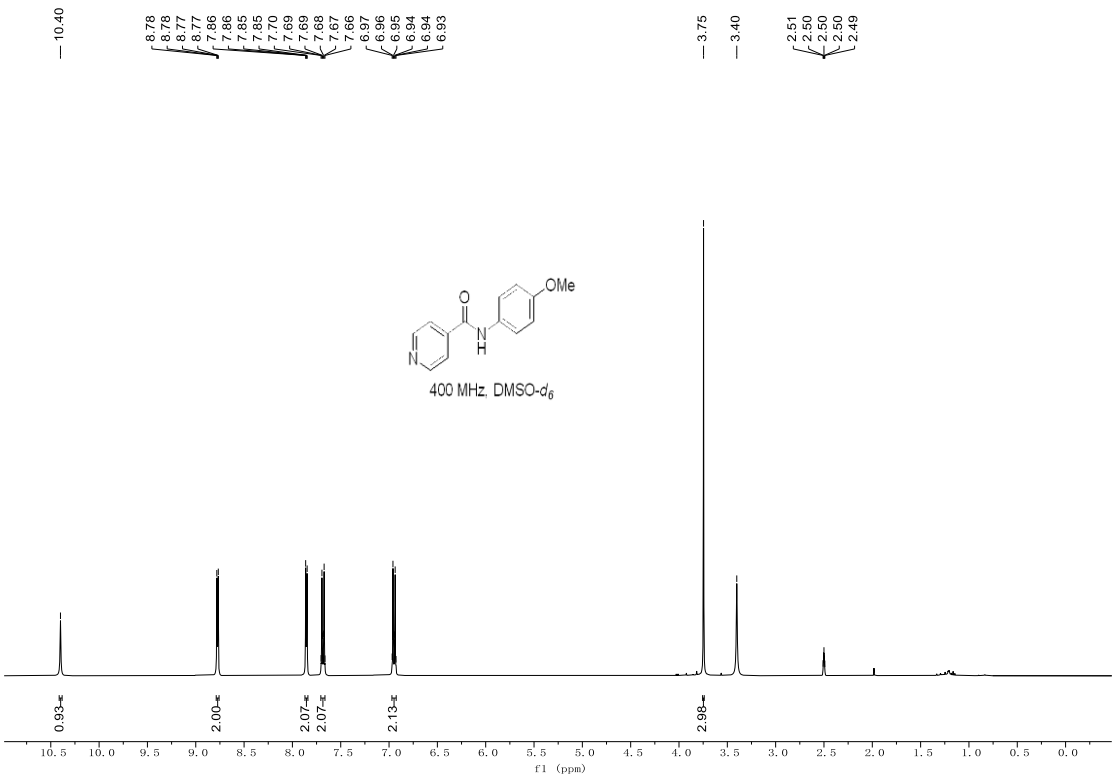
**19-$^{1}$H NMR**



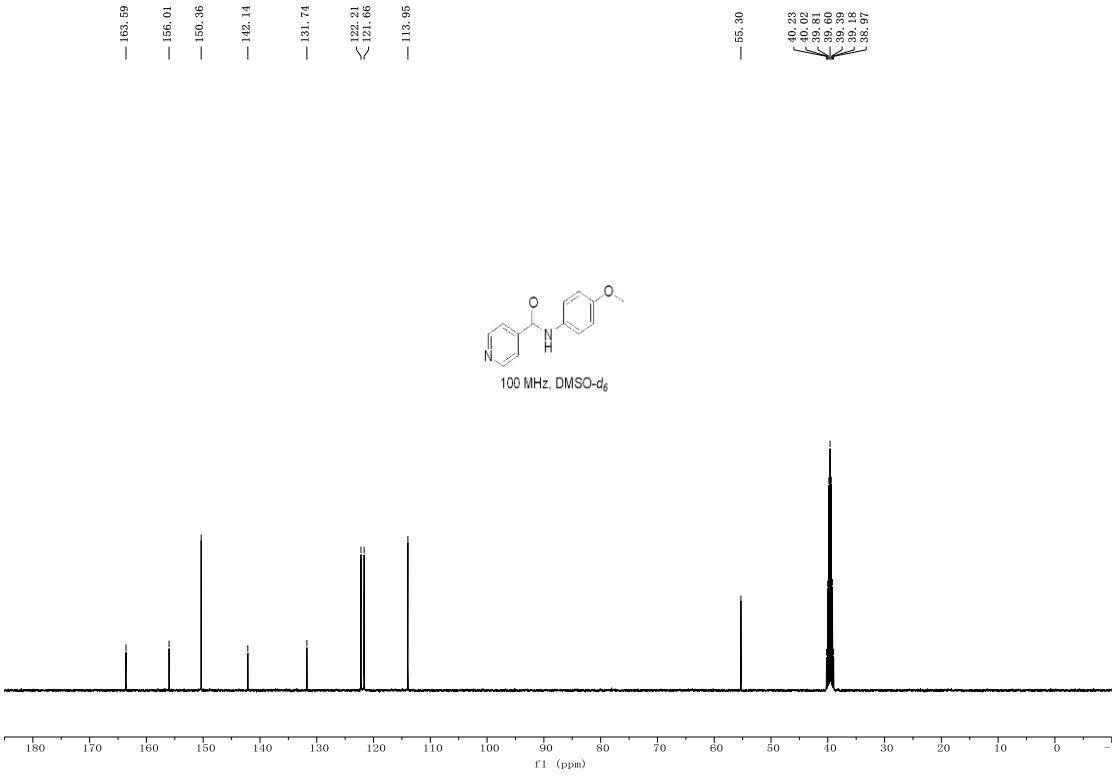

**19-$^{13}$C NMR**



**20-$^{1}$H NMR**

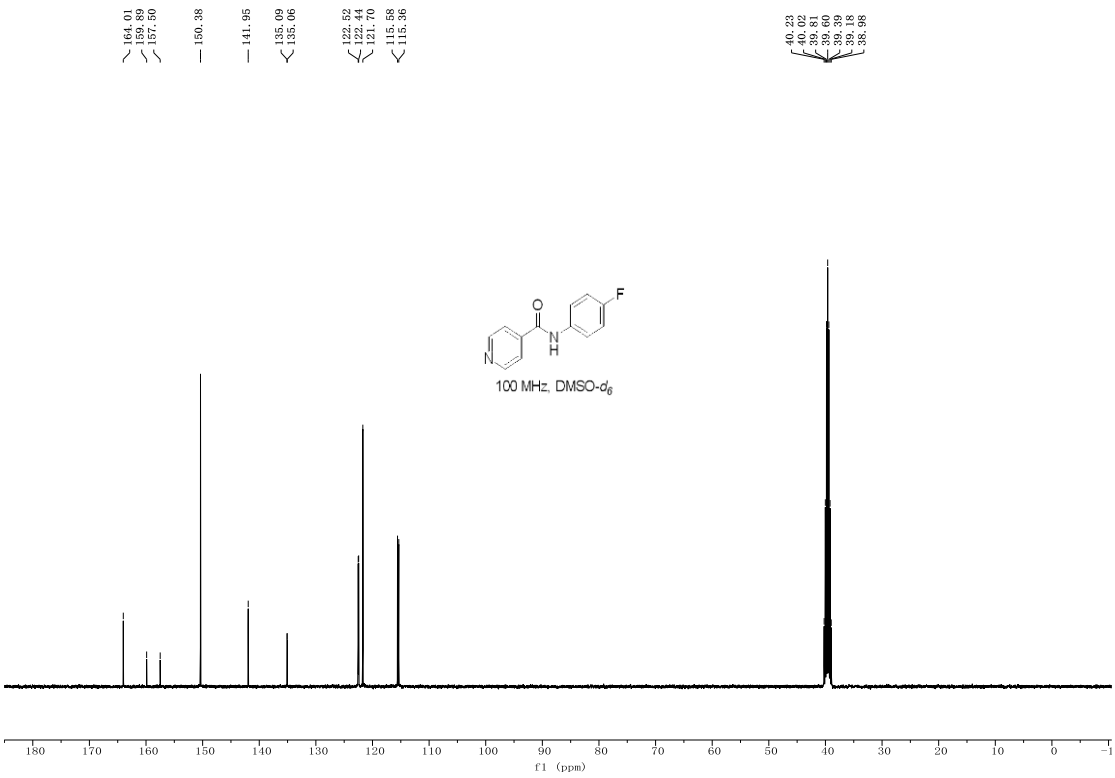



**20-$^{13}$C NMR**

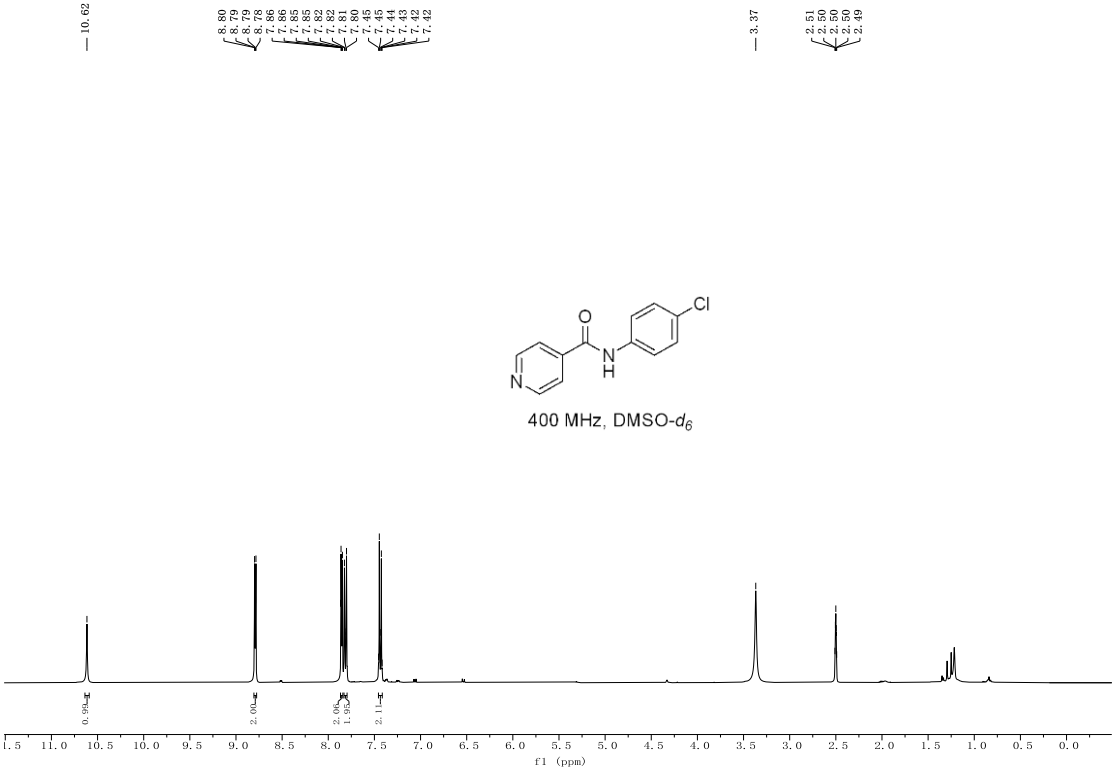


**21-$^{1}$H NMR**

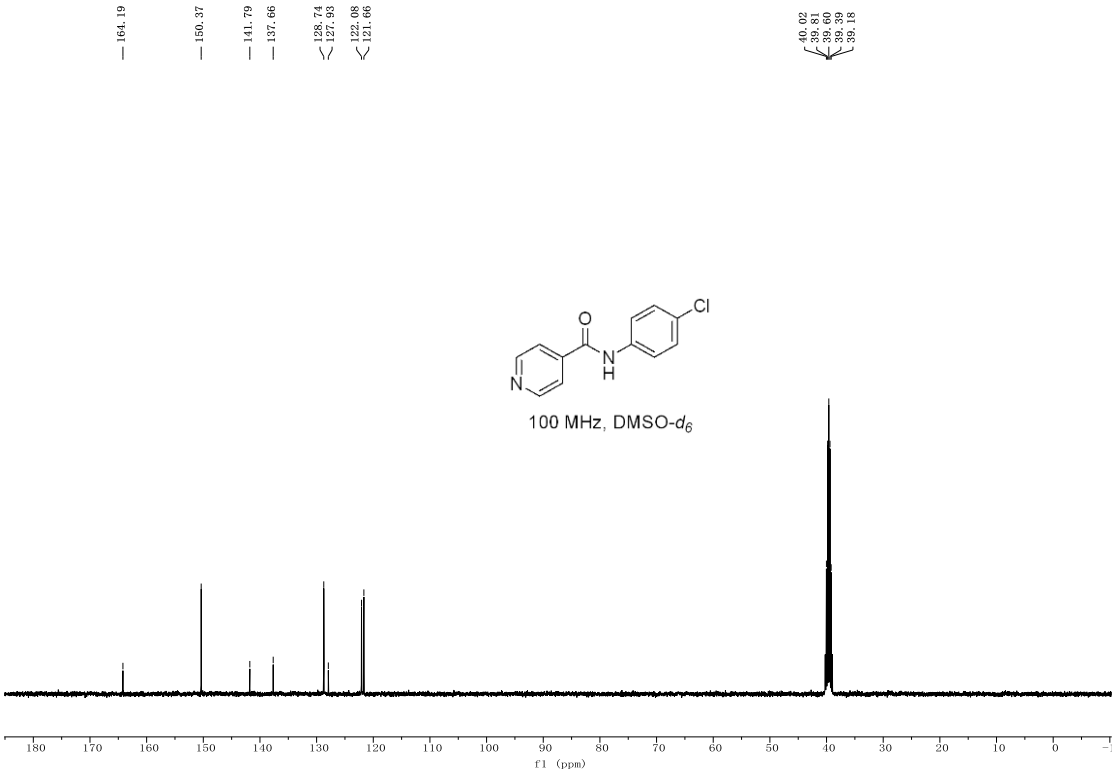

**21-$^{13}$C NMR**



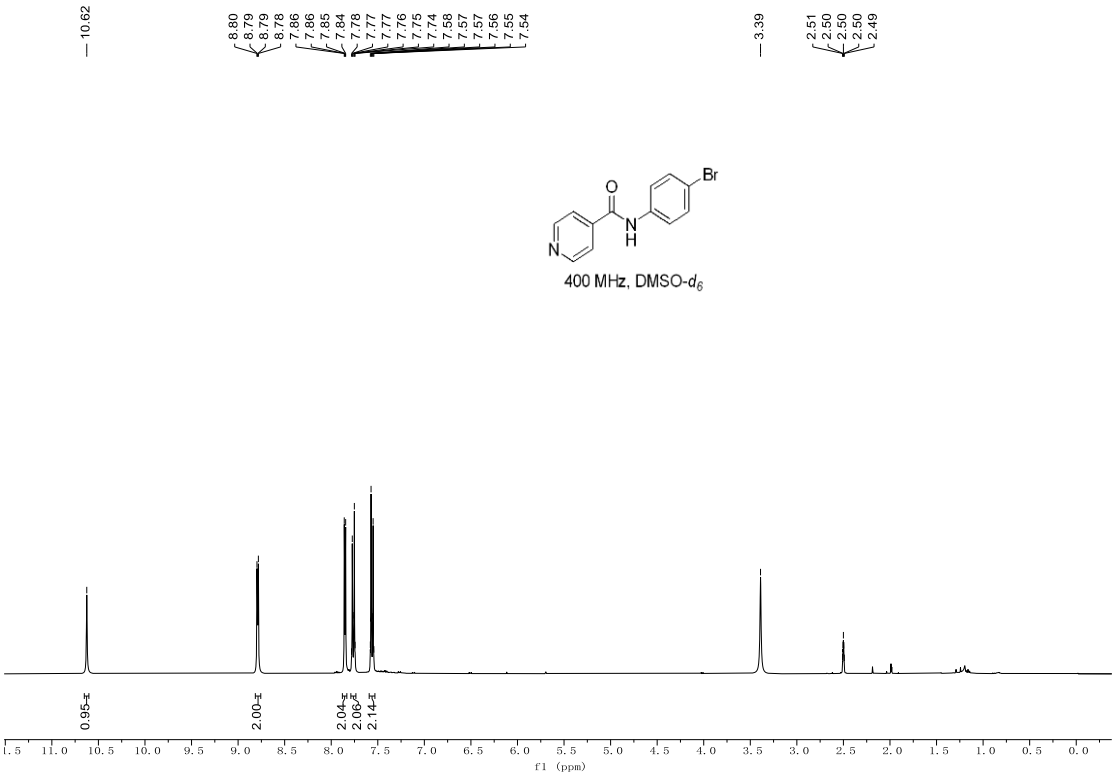
**22-$^{1}$H NMR**



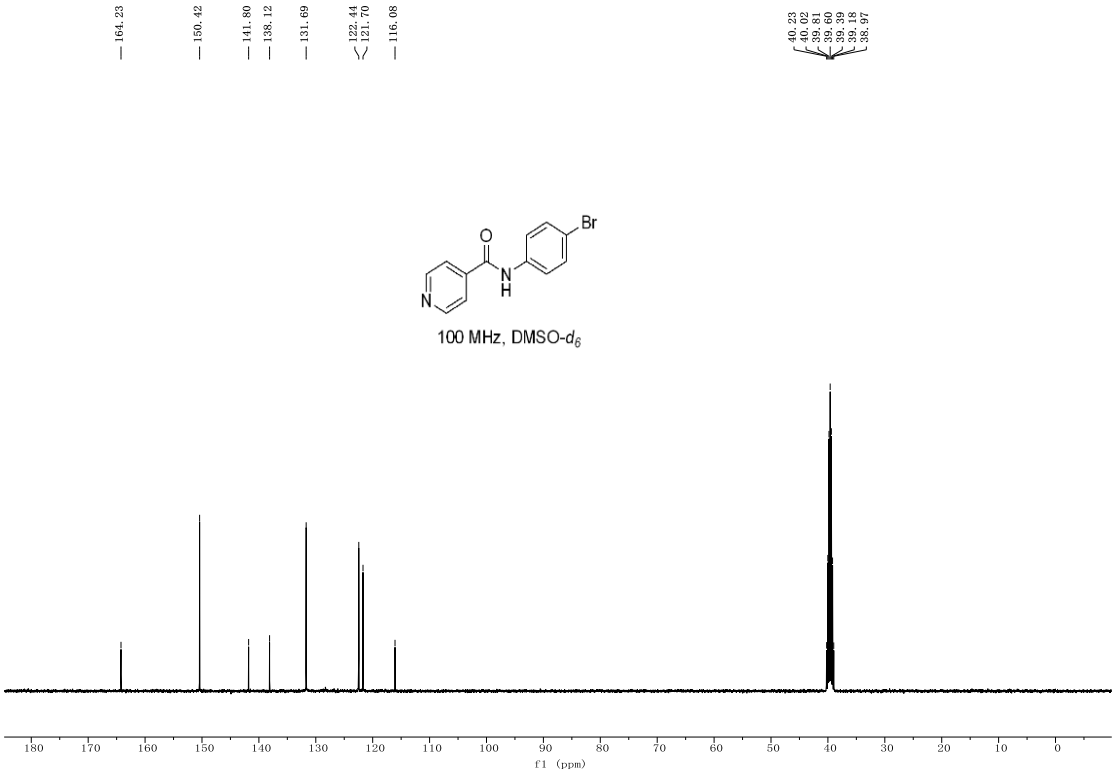

**22-$^{13}$C NMR**



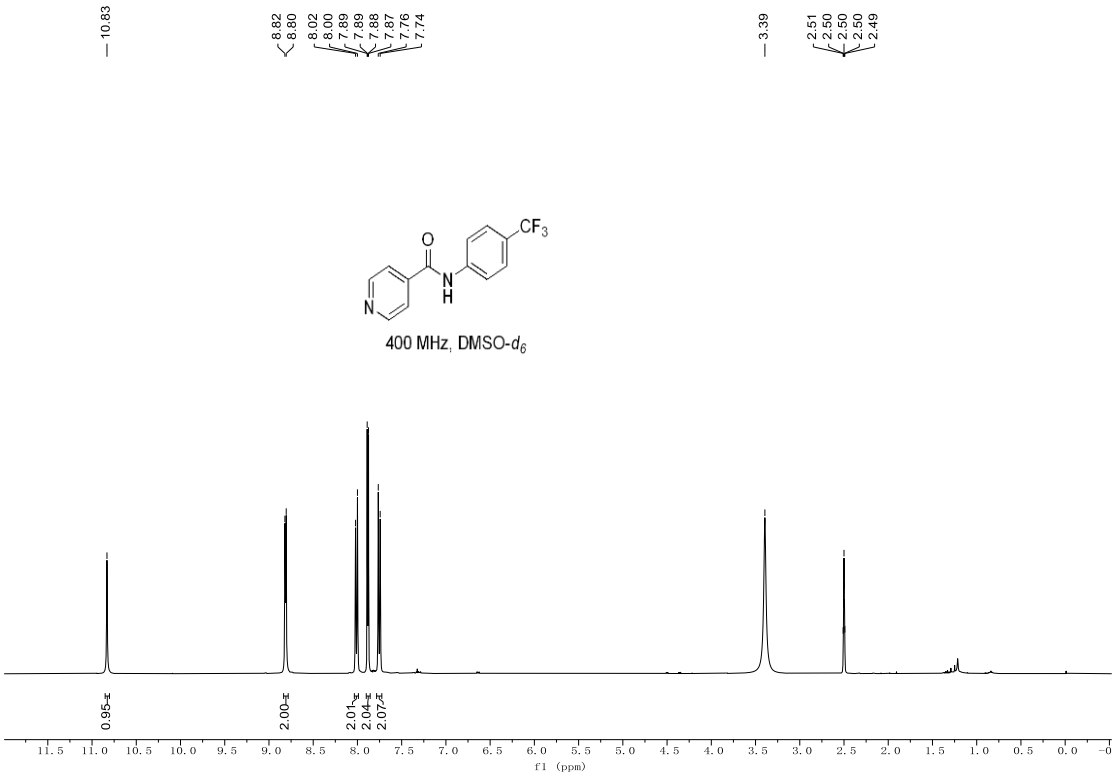
**23-$^{1}$H NMR**



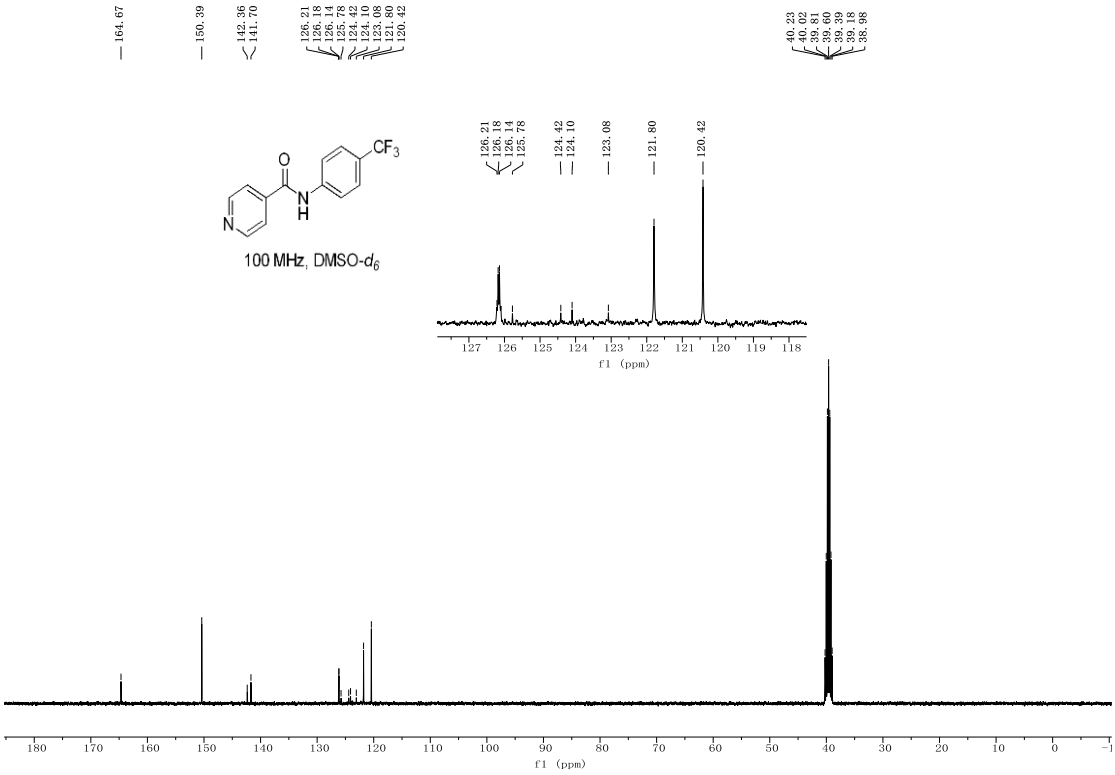

**23-$^{13}$C NMR**



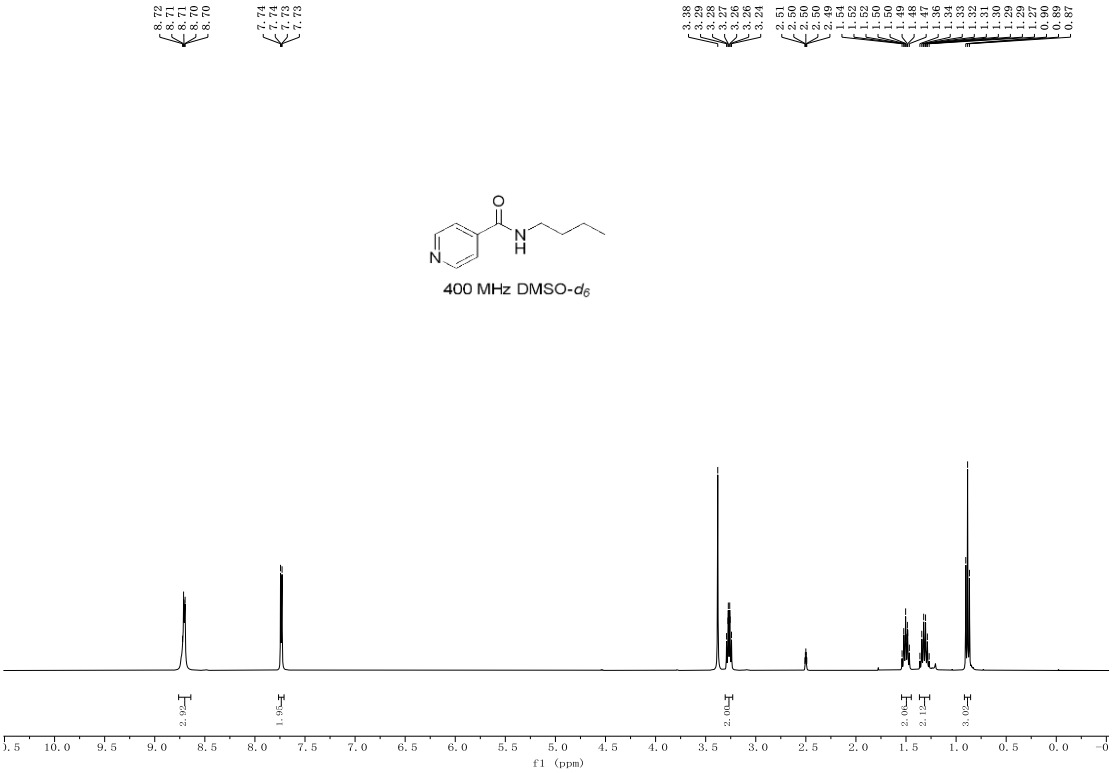
**24-$^{1}$H NMR**



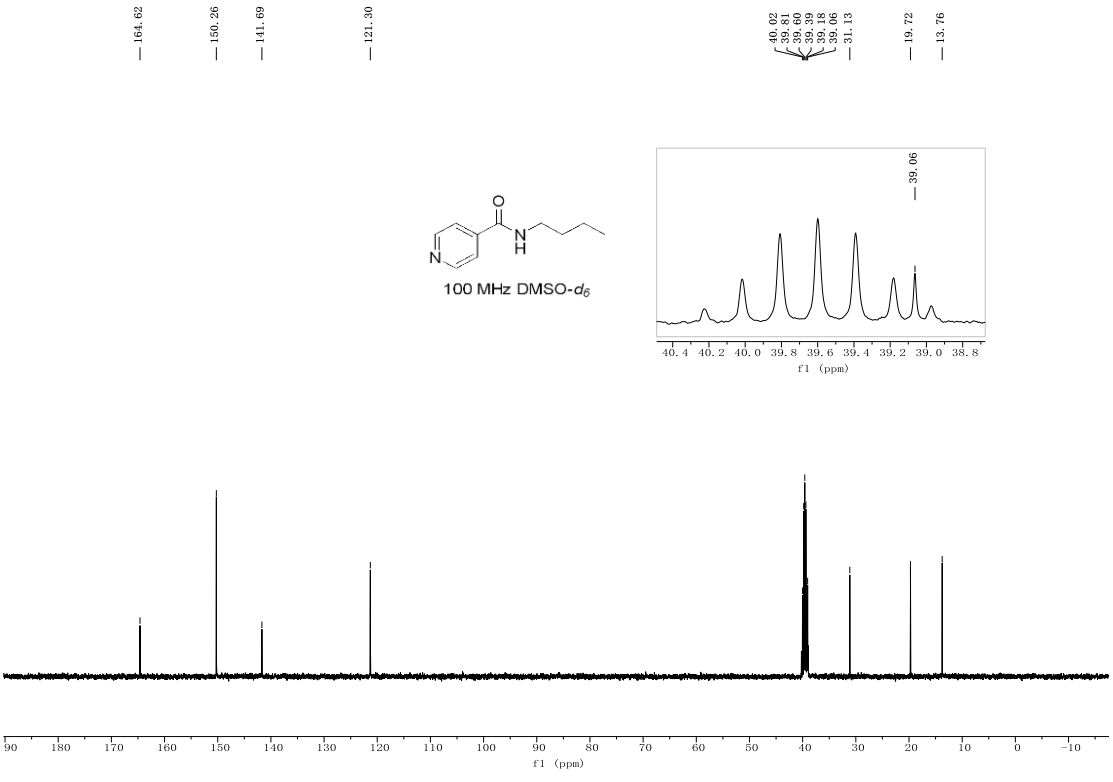

**24-$^{13}$C NMR**



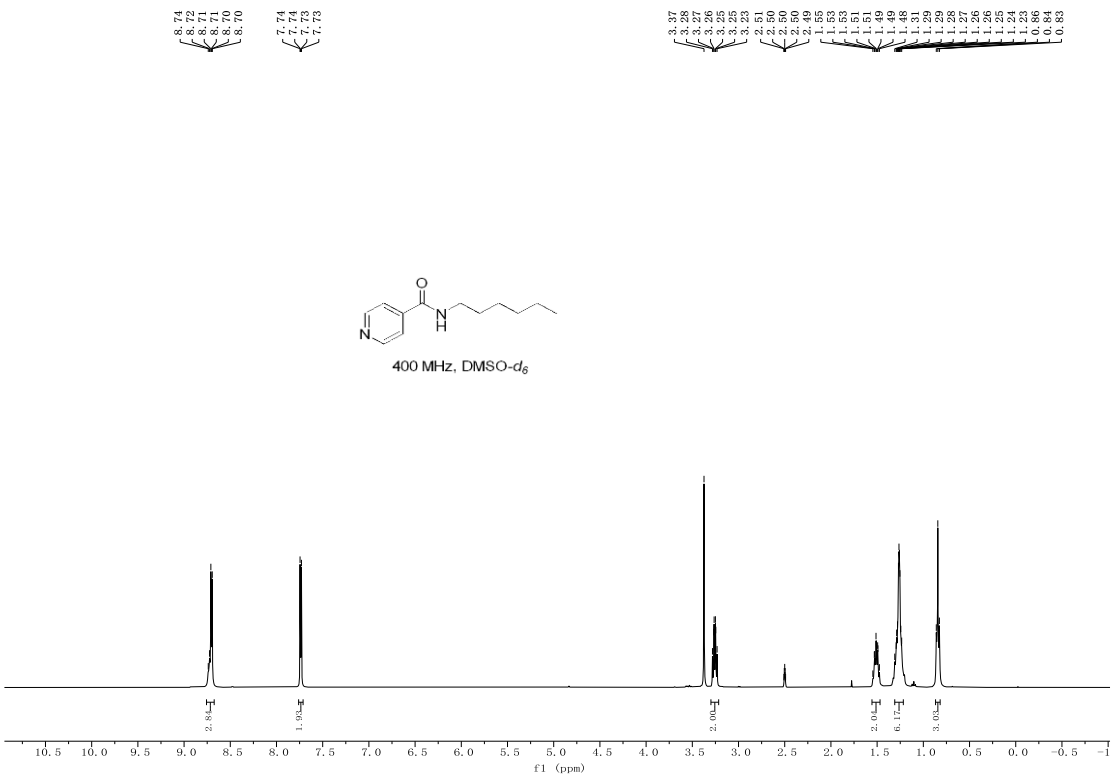
**25-$^{1}$H NMR**



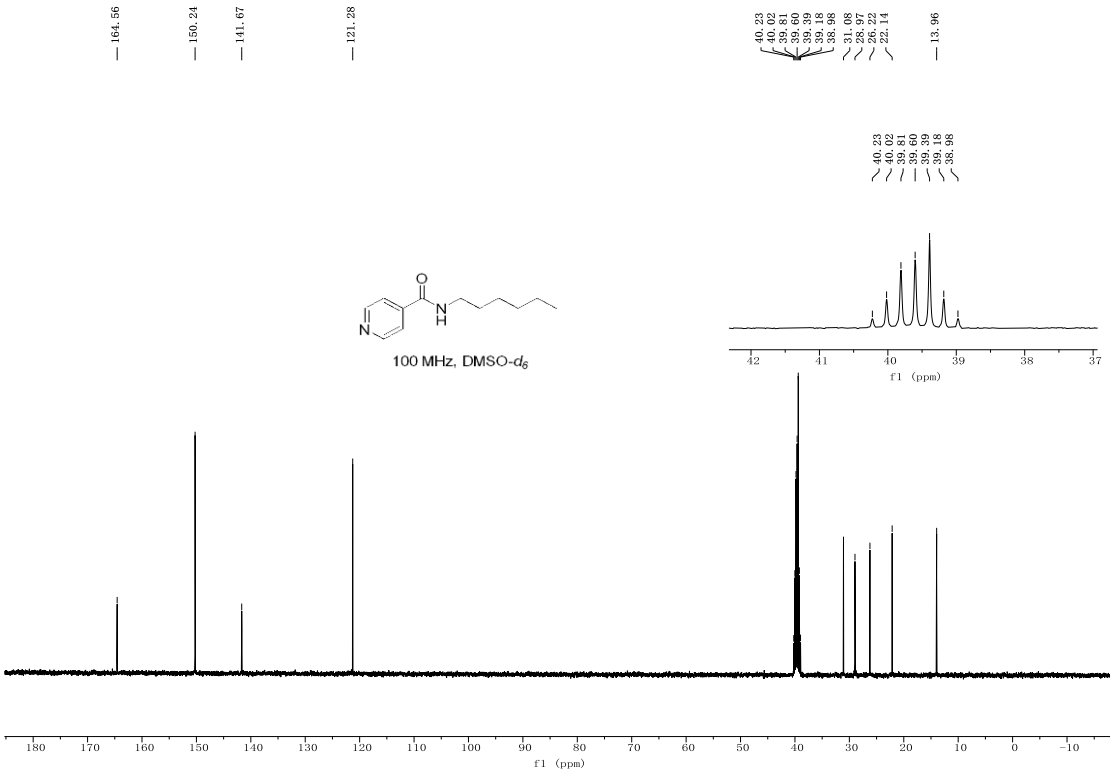

**25-$^{13}$C NMR**



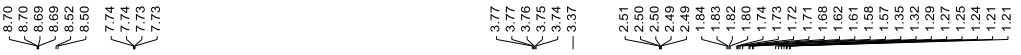
**26-$^{1}$H NMR**

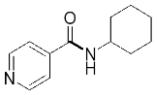



**26-$^{13}$C NMR**

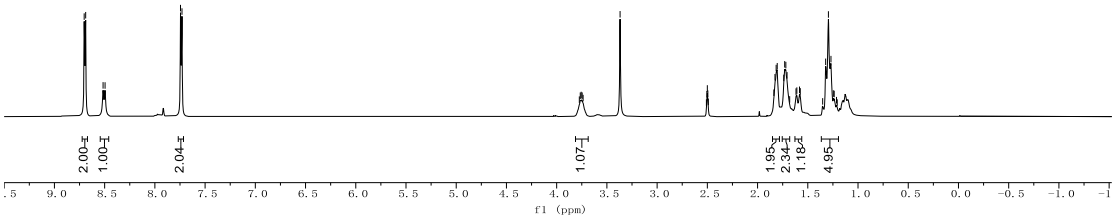


**27-$^{1}$H NMR**

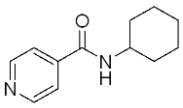


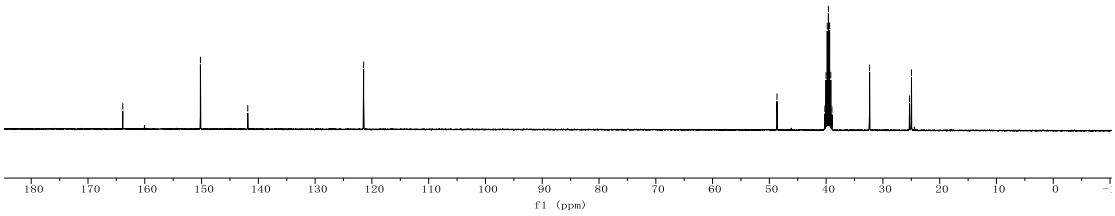

400 MHz, DMSO-$d_6$



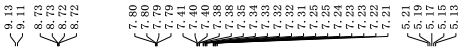

**27-$^{13}$C NMR**

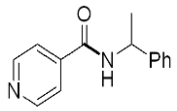




100 MHz, DMSO-$d_6$

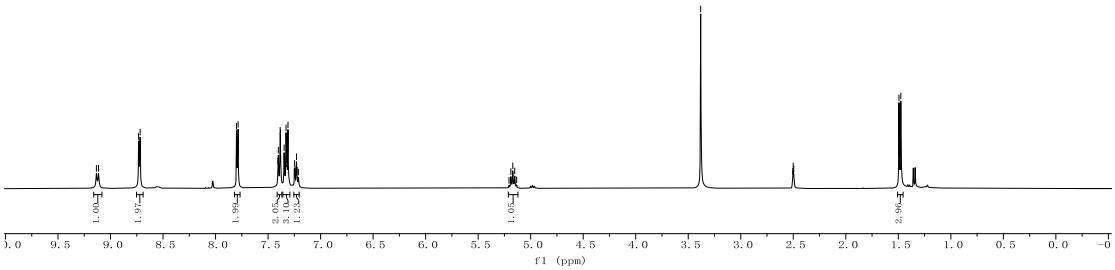


**28-$^{1}$H NMR**

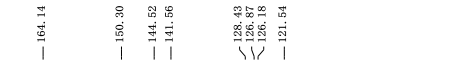


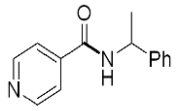




400 MHz, DMSO-$d_6$

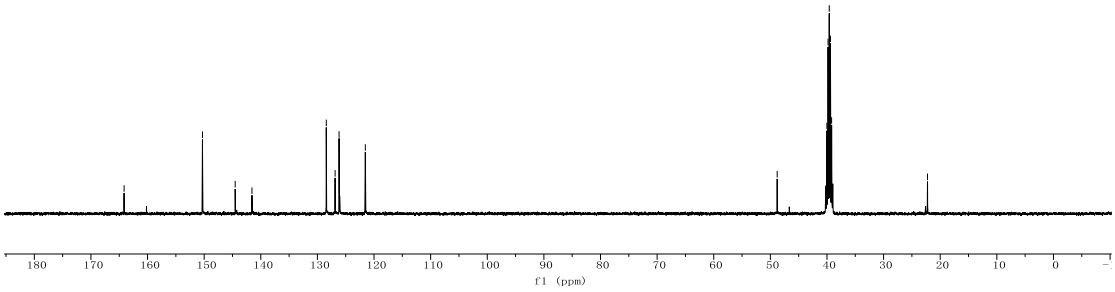



**28-$^{13}$C NMR**

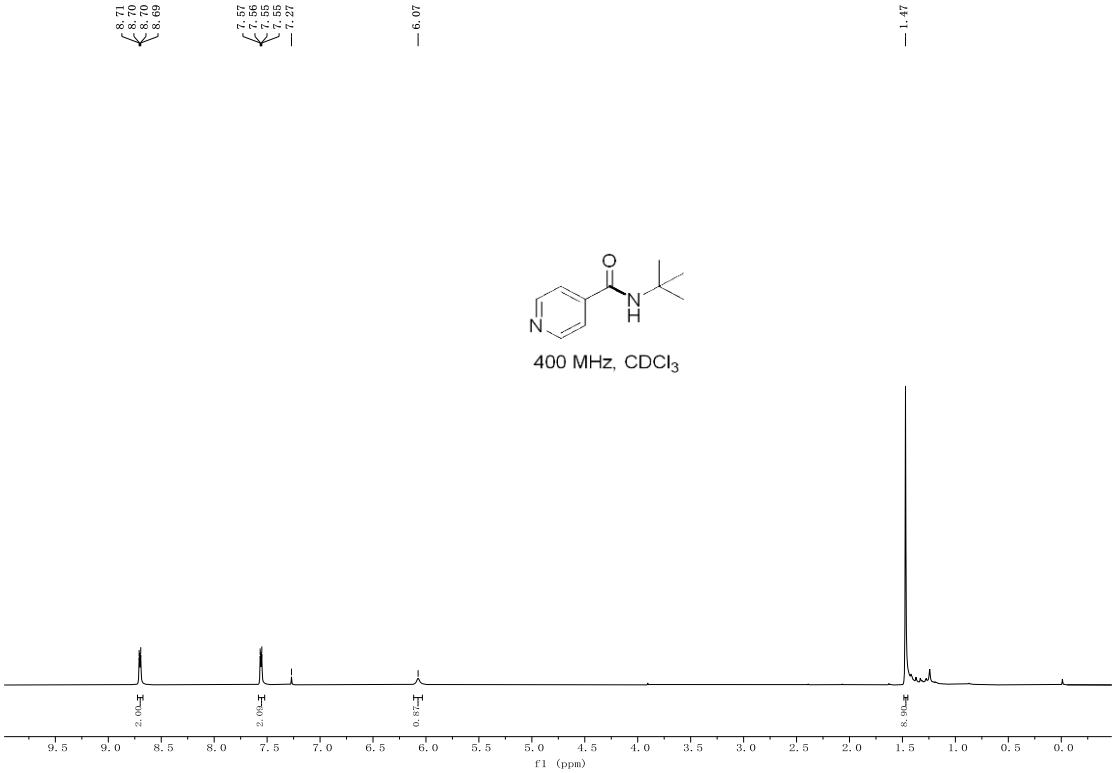


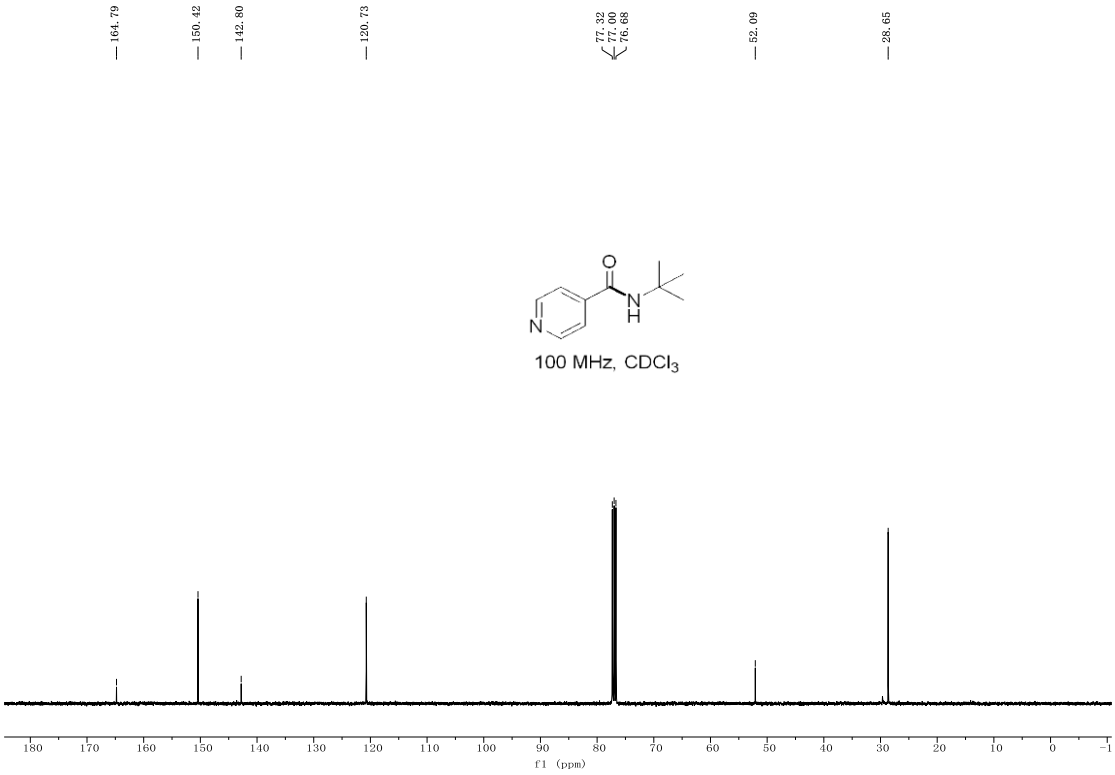

100 MHz, DMSO-$d_6$



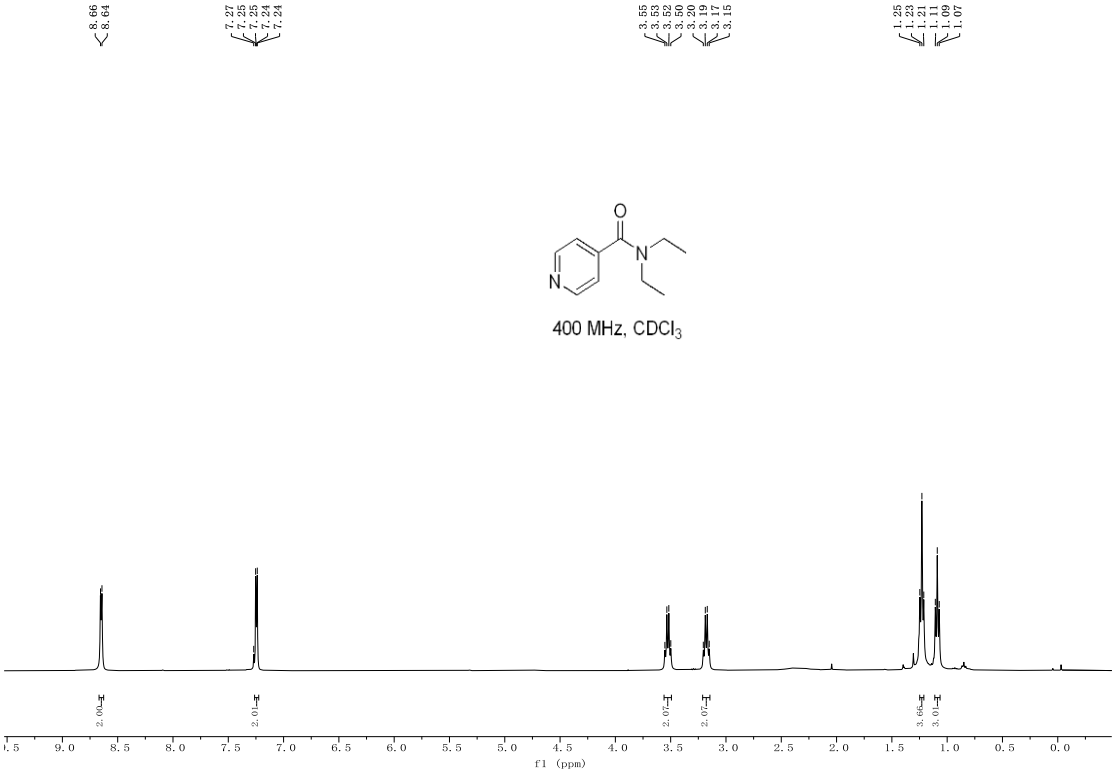
**29-$^{1}$H NMR**



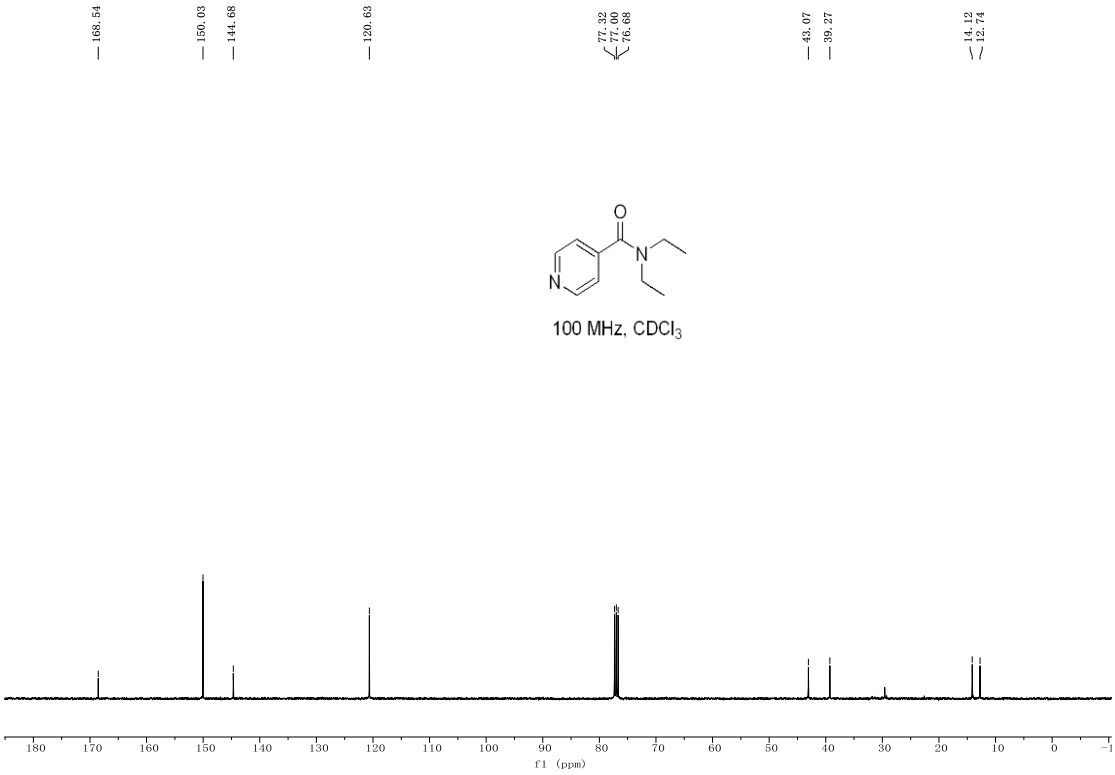

**29-$^{13}$C NMR**



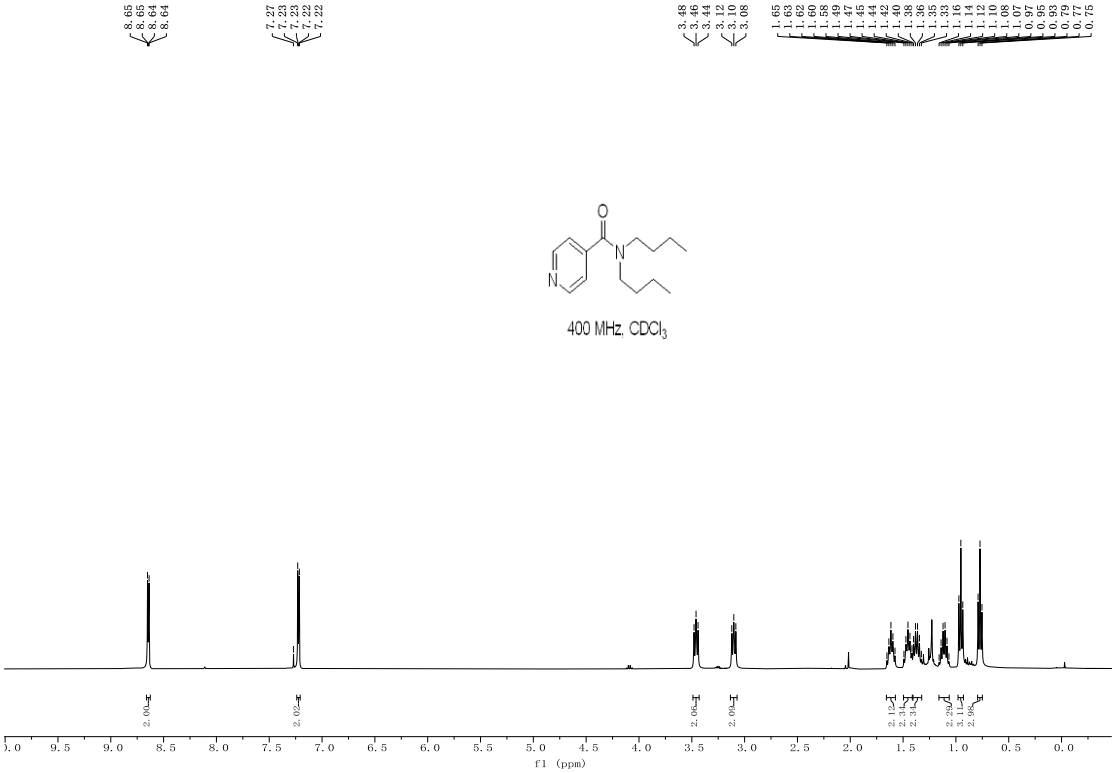
**30-$^{1}$H NMR**



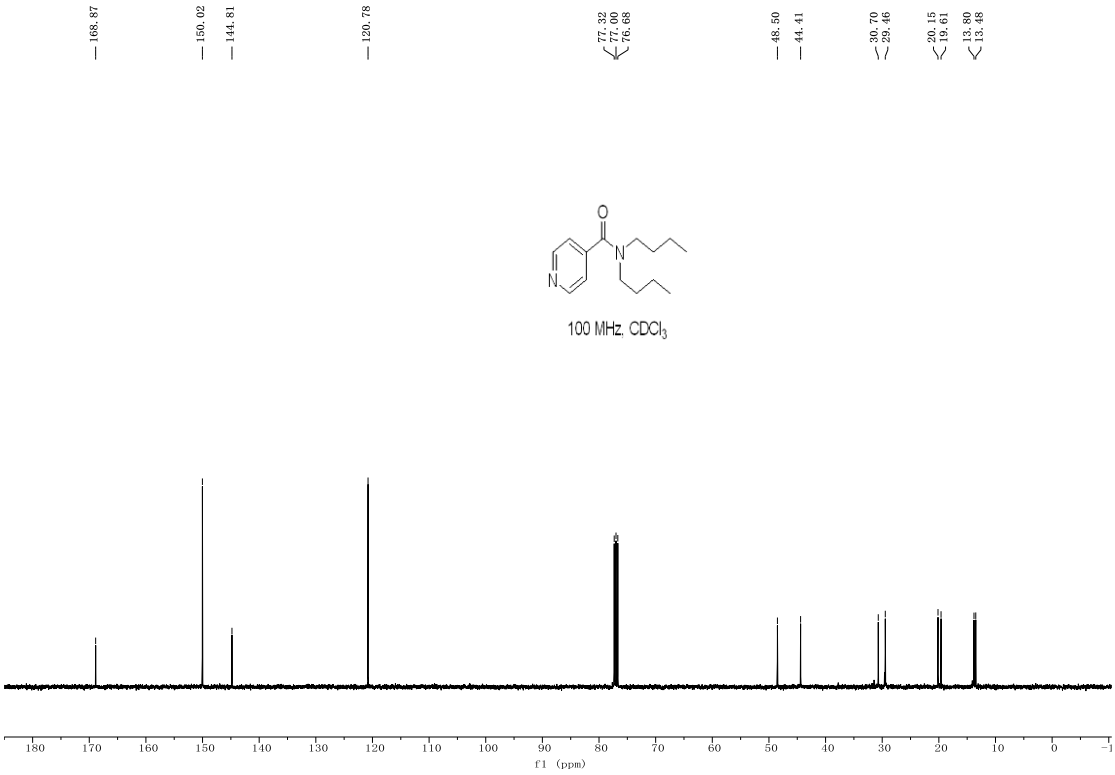

**30-$^{13}$C NMR**



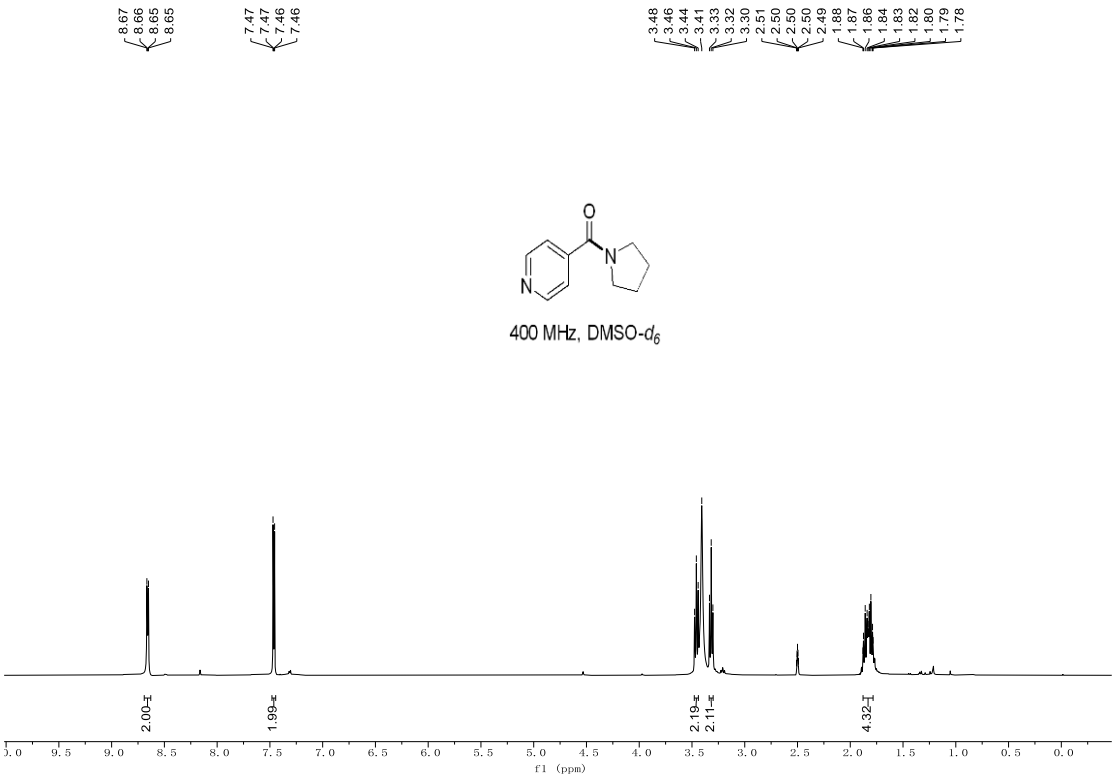
**31-$^{1}$H NMR**



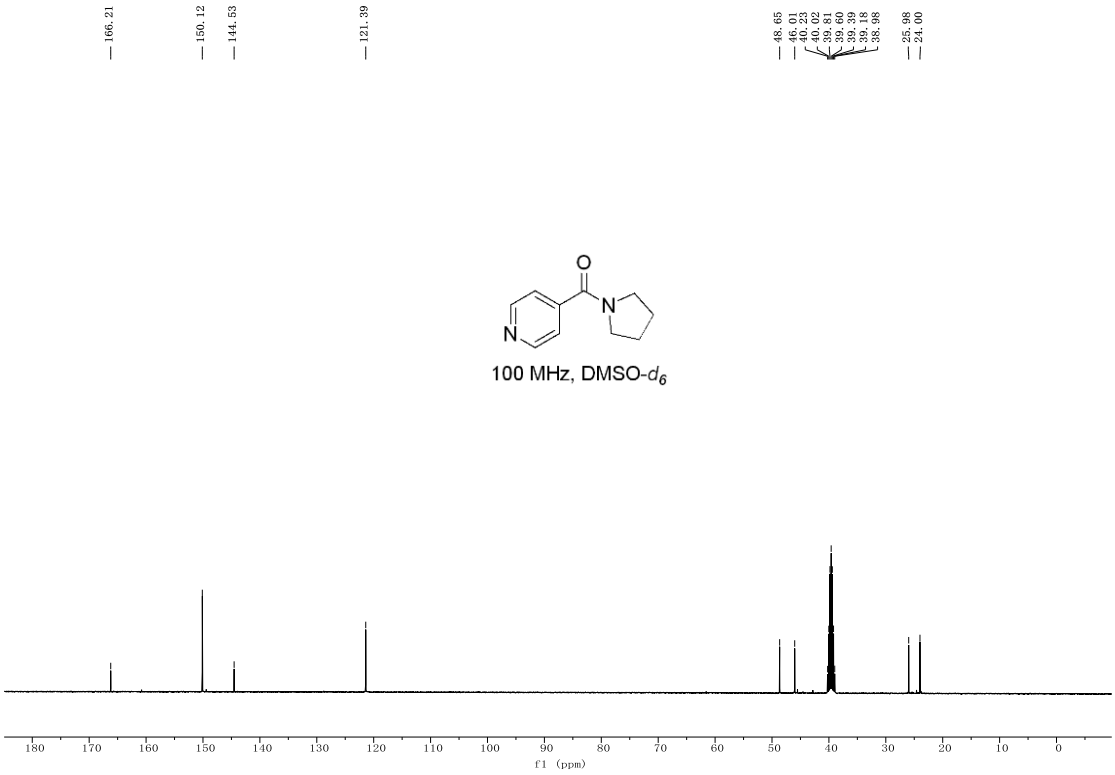

**31-$^{13}$C NMR**



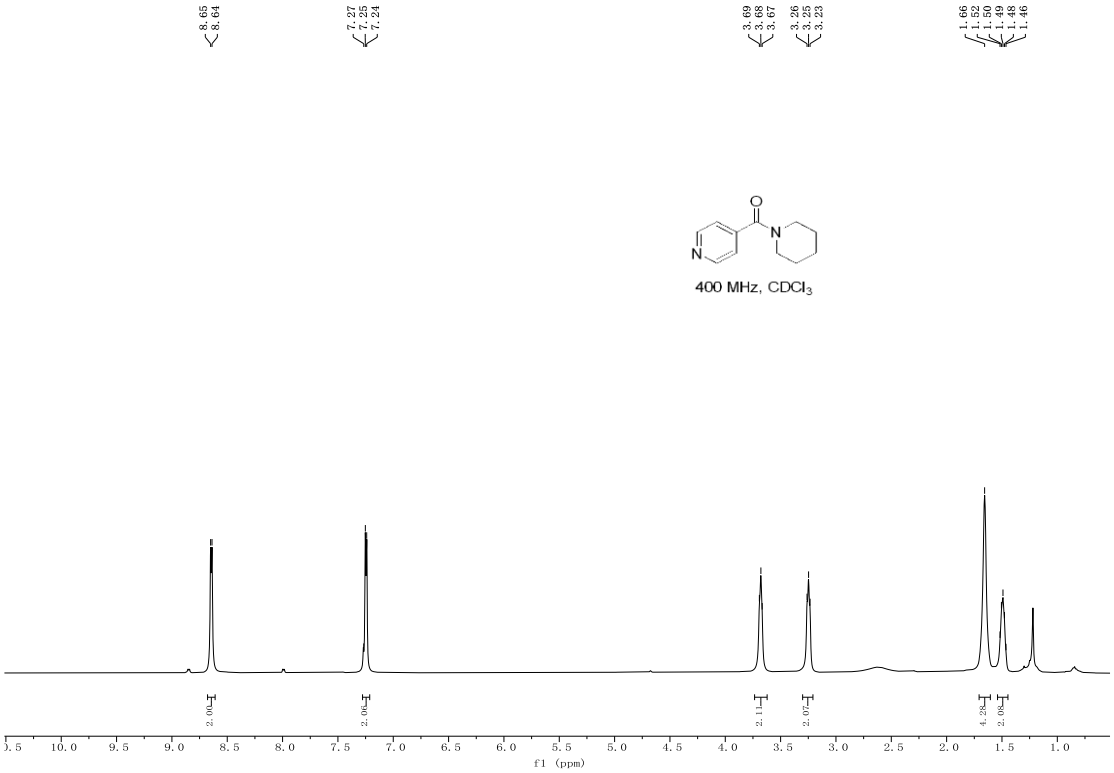
**32-$^{1}$H NMR**



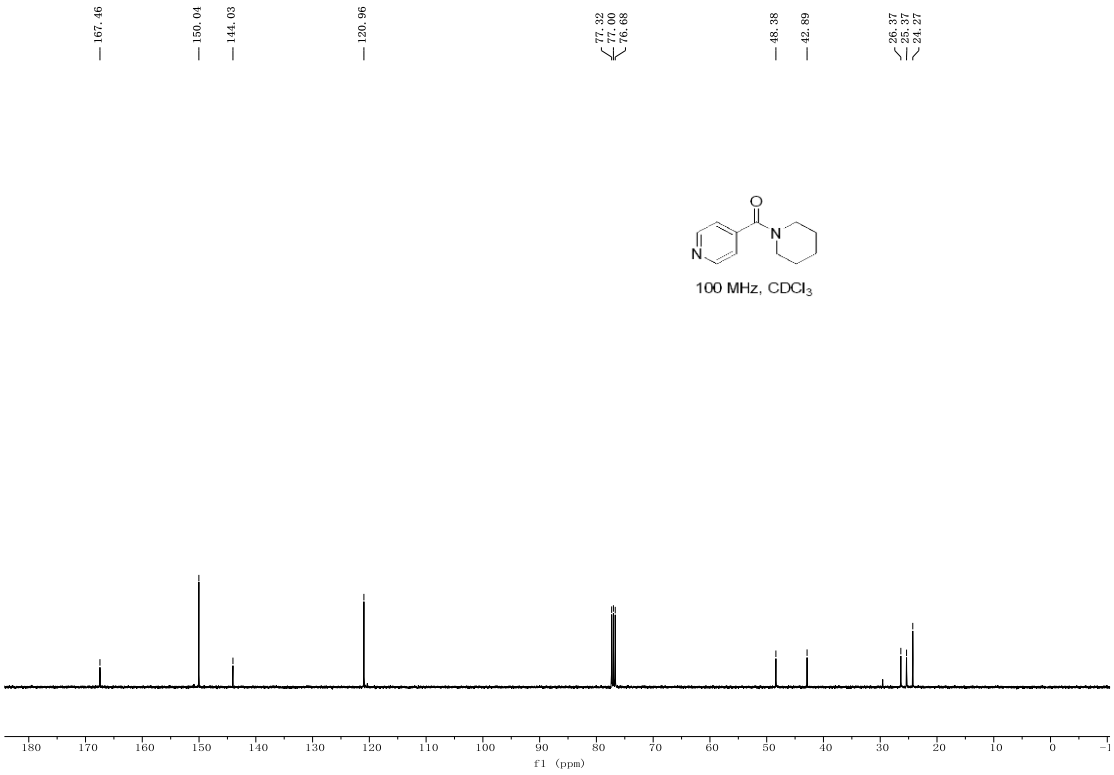

**32-$^{13}$C NMR**



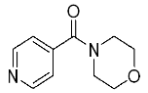
**33-$^{1}$H NMR**



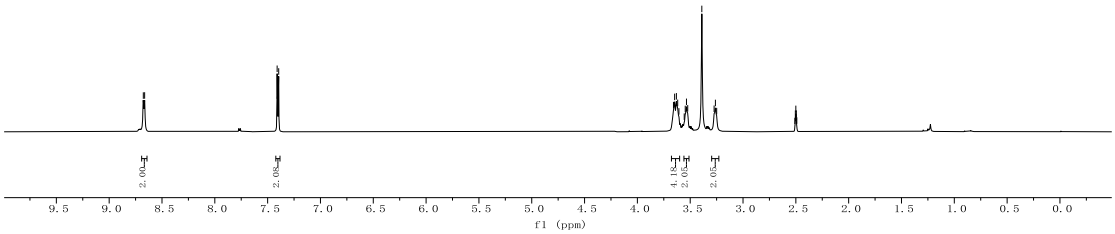

**33-$^{13}$C NMR**



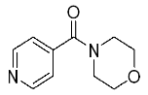
**34-$^{1}$H NMR**

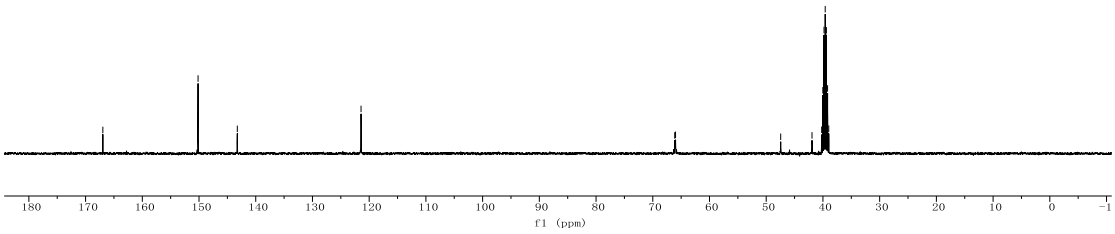
400 MHz, DMSO-$d_6$



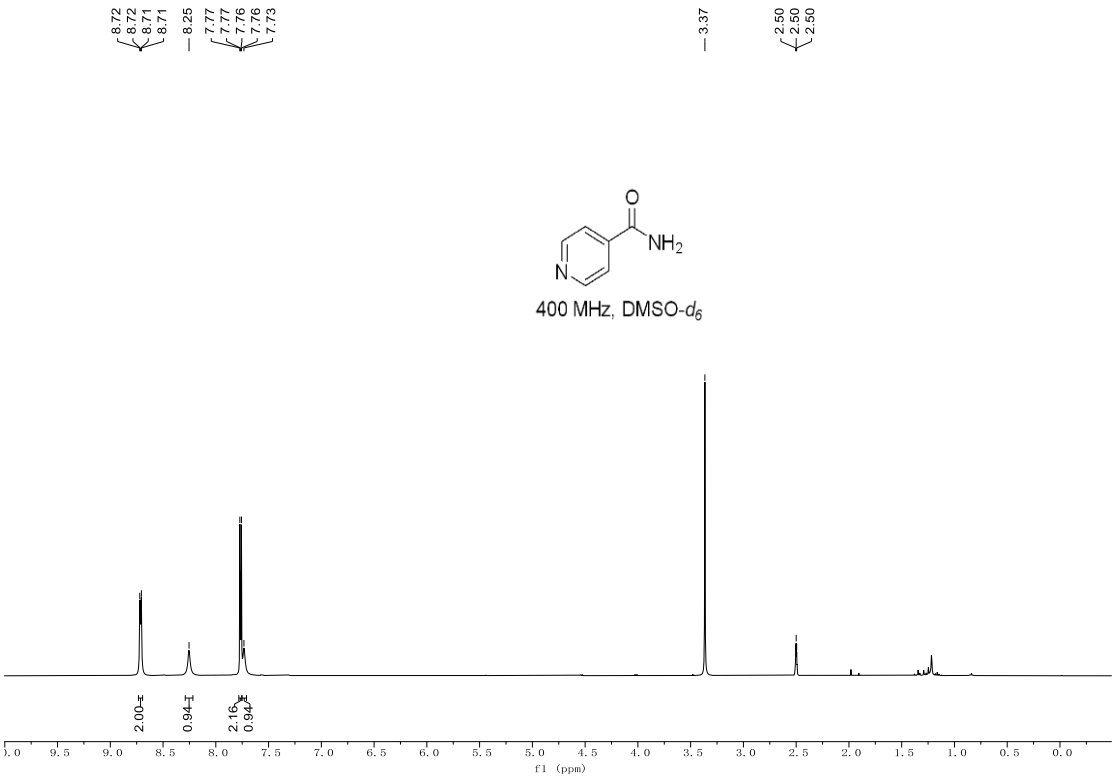

**34-$^{13}$C NMR**

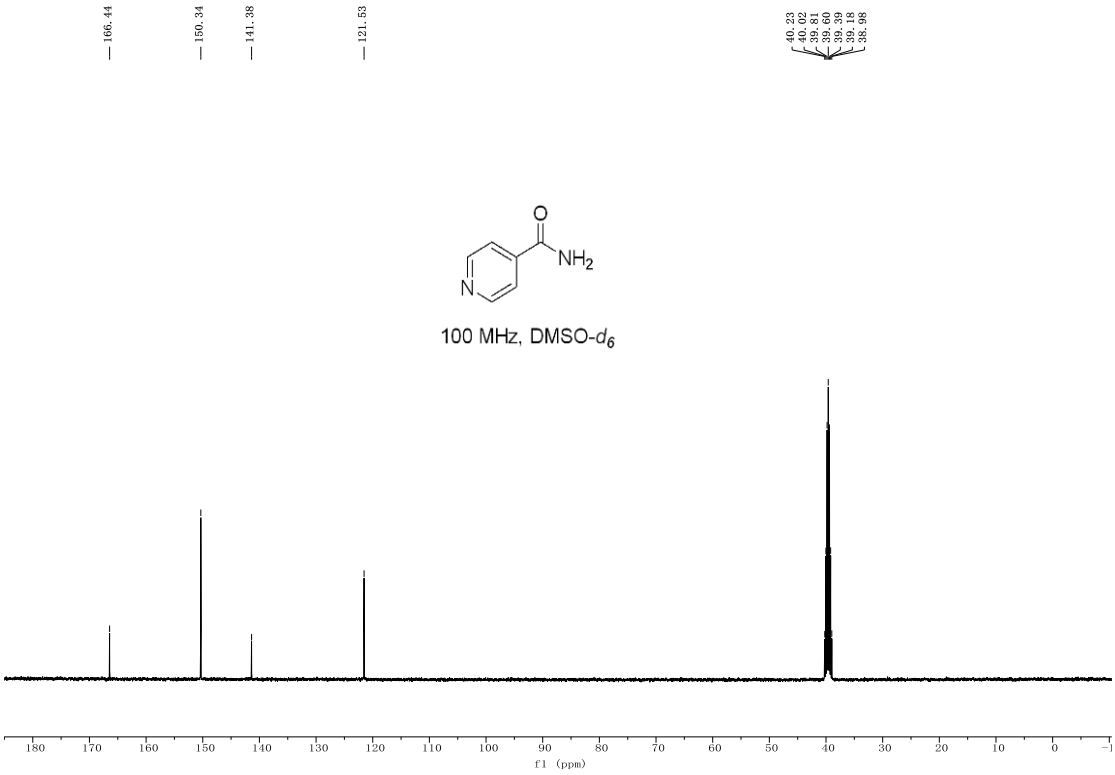
100 MHz, DMSO-$d_6$



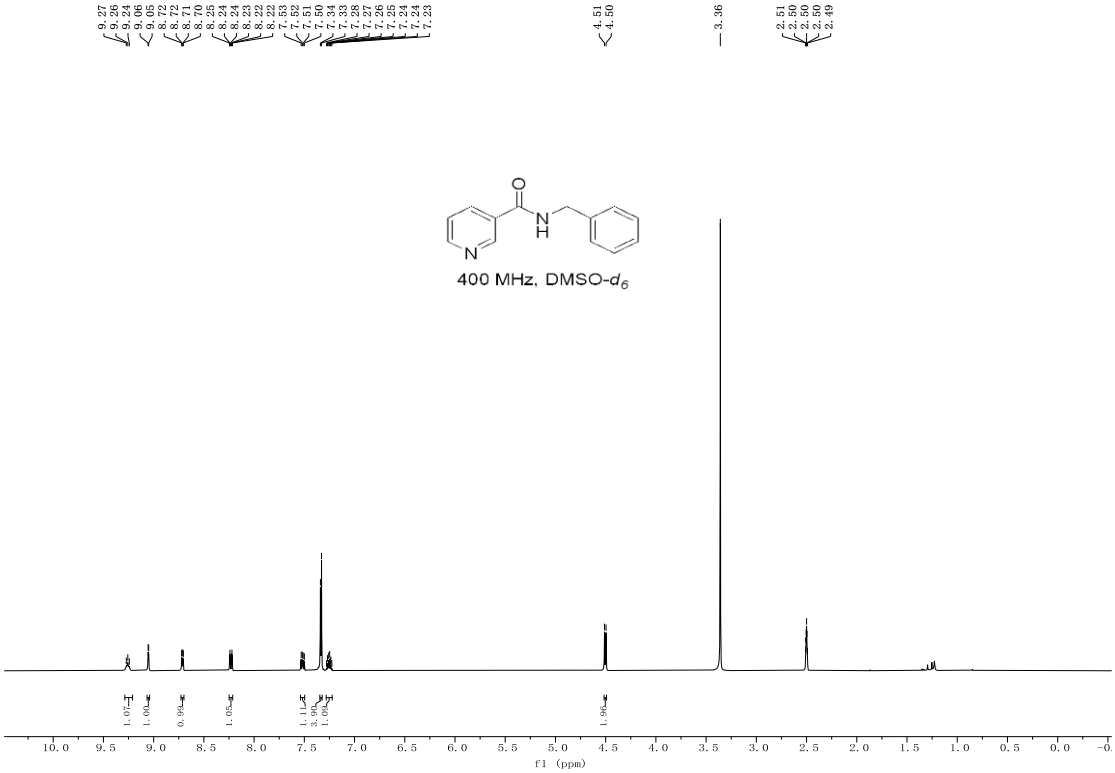
**35-$^{1}$H NMR**



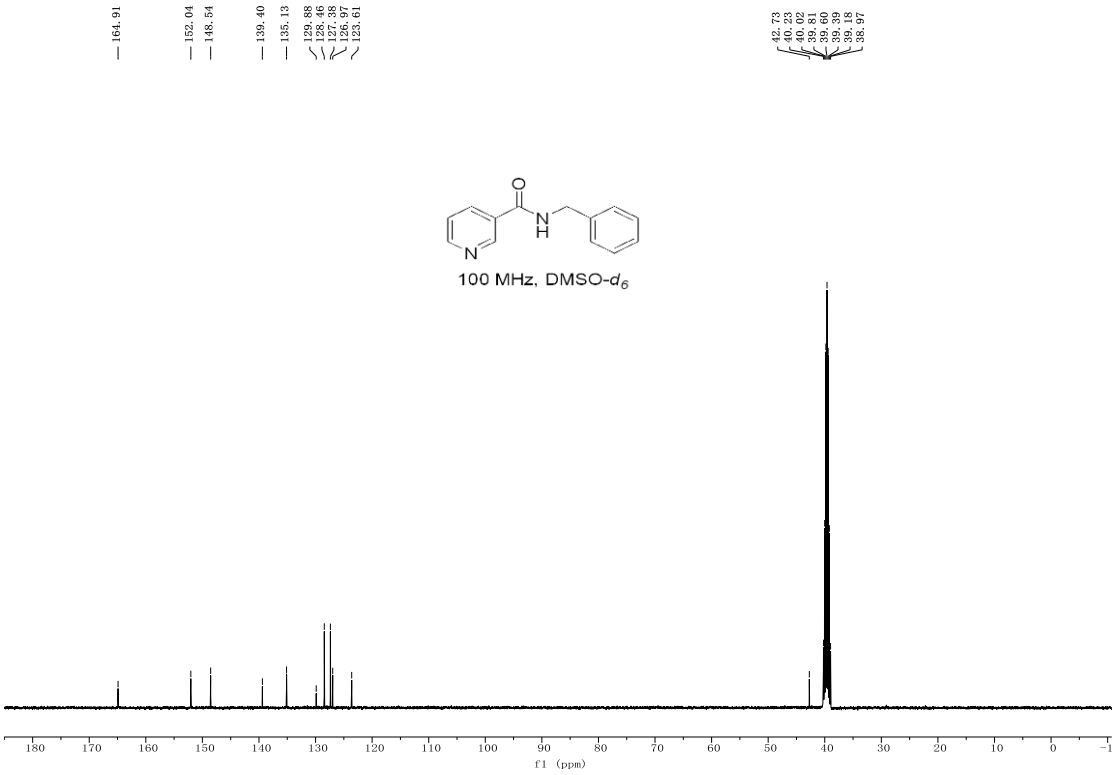

**35-$^{13}$C NMR**



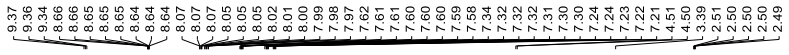
**36-$^{1}$H NMR**

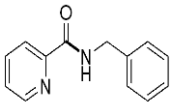



**36-$^{13}$C NMR**

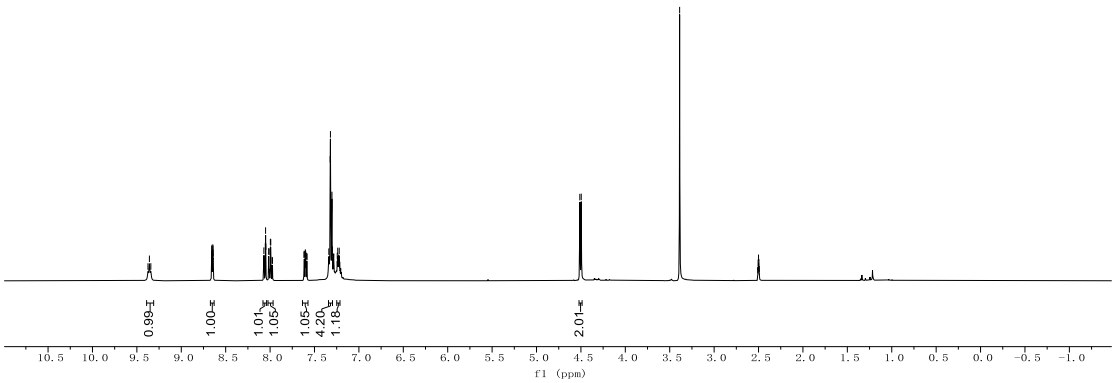


**37-$^{1}$H NMR**

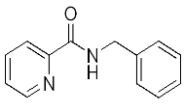


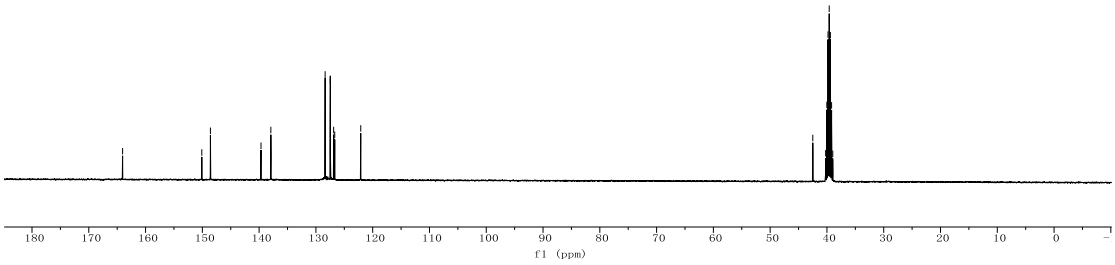

400 MHz, DMSO-$d_6$



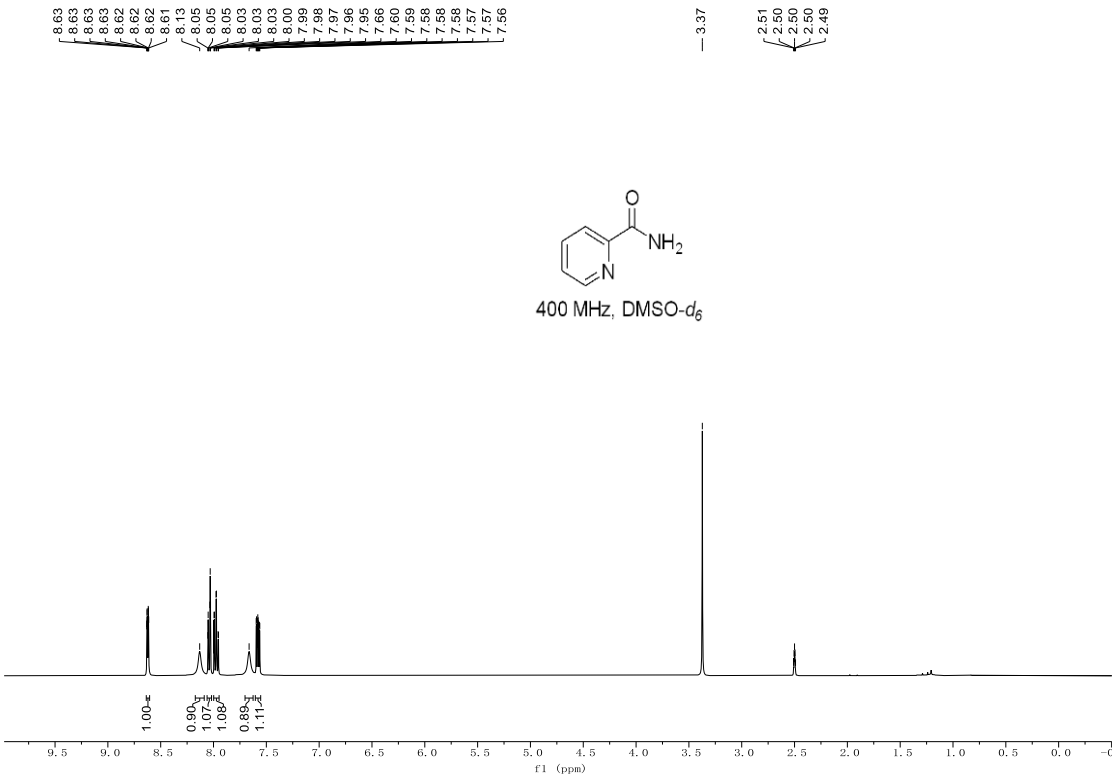

**37-$^{13}$C NMR**

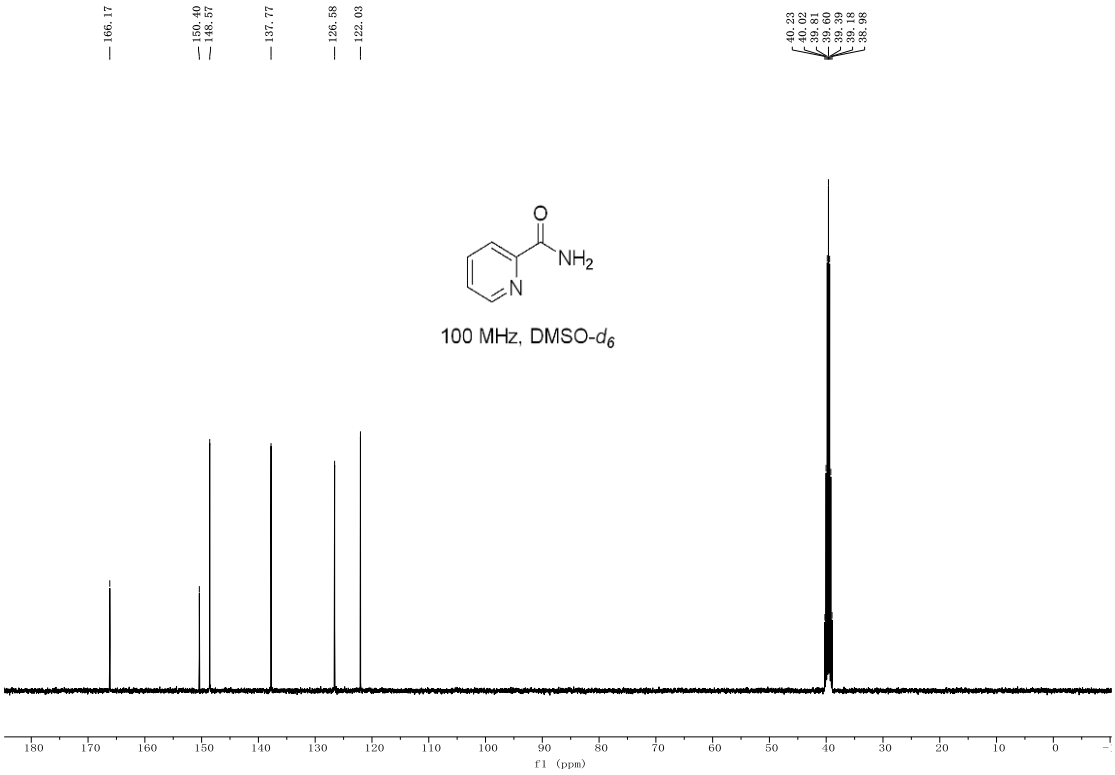

100 MHz, DMSO-$d_6$



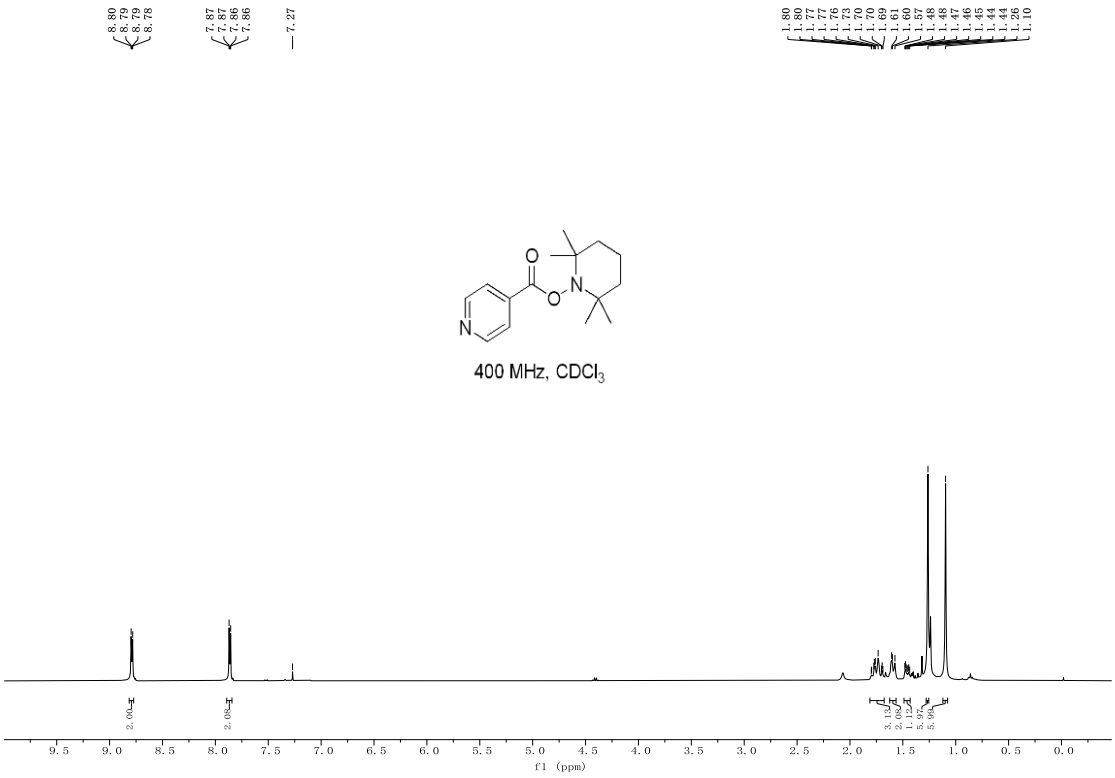
**38-$^{1}$H NMR**




**38-$^{13}$C NMR**



**39-$^{1}$H NMR**




**39-$^{13}$C NMR**