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Supporting information

Nickel-Catalyzed Cross-Electrophile Coupling of Aryl Bromides and Cyclic Secondary Alkyl Bromides with Spiro-bidentate-pyox Ligand

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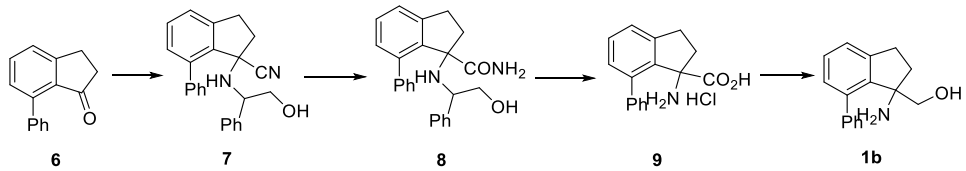
I. Experimental Section

General

All reagents were purchased from commercial suppliers and used without purification. All reactions were monitored by TLC. Chromatography refers to open column chromatography on silica gel (200-300 mesh). Melting points were uncorrected values. 1H NMR spectra were recorded at 500 MHz and 13C NMR spectra were recorded at 126 MHz by using a Bruker Avance 500M spectrometer. Mass spectra were performed on an Ultima Global spectrometer with an ESI source.

Synthesis procedure and characterization data for the spiro-bidentate-pyox and spiro-bidentate-quinox ligands L1



a. General procedures for the synthesis of 1-((2-hydroxy-1-phenylethyl)amino)-7-phenyl-2,3-dihydro-1H-indene-1-carboxamide 8

7-phenyl-1-indanone **6** was synthesized according to Levy's method[1]. To a solution of 7-phenyl-1-indanone (4.90 g, 23.5 mmol) in anhydrous toluene (78 mL) was added phenylglycine (4.2 g, 30.6 mmol). The resulting mixture was heated to reflux for 24 hours. After removal of the solvent, the residue was dissolved in anhydrous dichloromethane (60 mL), then trimethylsilyl cyanide (4.4 mL, 35.3 mmol) was added dropwise and stirred at 0 ℃ for 3 hours. Solvent was evaporated at reduced pressure and the corresponding crude **7** was dissolved in n-hexane (40 mL). To the reaction mixture was added sulfuric acid (40 mL, 90%) dropwise at 0 ℃, allowed warm to room temperature, and stirred overnight. The acidic layer was separated and poured into ice, extracted with ethyl acetate (80 mL), and basified with ammonium hydroxide to pH 8-9. The aqueous phase was extracted with ethyl acetate (3×150 mL). The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to give **8** as brown oil (8.75 g, 19% yield in three steps).

b. General procedures for the synthesis of 1-amino-7-phenyl-2,3-dihydro-1H-indene

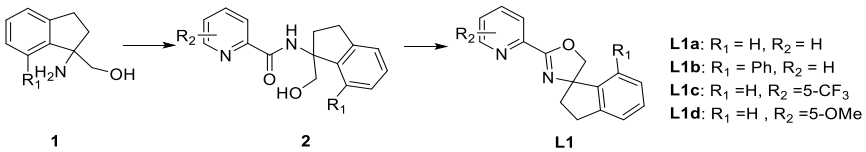
1-carboxylic acid hydrochloride 9

To a solution of **8** (0.70 g, 1.88 mmol) in a mixture of dichloromethane (11 mL) and methanol (6 mL) was added lead tetraacetate (1.25 g, 2.82 mmol) in portions at 0 ℃. The resulting mixture was stirred under argon atmosphere and allowed warm to room temperature and stirred for two hours. To the reaction mixture was added potassium dihydrogen phosphate buffer (30 mL, 0.2 mmol/L, pH = 7) and stirred at room temperature for 1 hour. The aqueous layer was separated and extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate, filtrated and concentrated. The residue was added 6N HCl (60 mL) and the mixture was heated to reflux overnight. The mixture was cooled to room temperature and extracted with dichloromethane. The aqueous layer was concentrated to give brown oil, which was used in next step without further purification.

c. General procedures for the synthesis of (1-amino-7-phenyl-2,3-dihydro-1H-inden-1-yl)methanol 1b

To a suspension of **9** (0.805 g, 2.79 mmol) in anhydrous tetrahydrofuran (15 mL) was added borane dimethyl sulfide complex (0.8 mL, 10 mmol/L) dropwise. The reaction mixture was heated to reflux for 4 hours, and then cooled to room temperature. To the reaction mixture was added sodium hydroxide solution (5 mL, 1 mol/L) dropwise. The corresponding solution was heated to reflux for 2 hours, and then cooled to room temperature. The aqueous layer was separated and extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate, filtrated and concentrated. The residue was purified by column chromatography to give **1b** as white solid (373 mg, 19% yield).

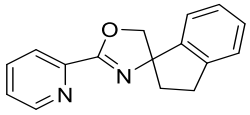
d. General procedures for the synthesis of spiro-bidentate-pyox ligands L1a-d



1 2 L1

To a solution of substituted 2-pyridine carboxylic acid (2.62 mmol) in anhydrous dichloromethane (10 mL) was added N-hydroxybenzotrizole (HOBT) (2.88 mmol), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDCI·HCl) (2.88 mol), and trietylamine (4.32 mmol) at 0 ℃ sequentially. The reaction mixture was stirred at room

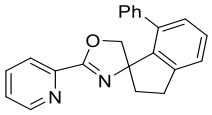
temperature for 1 hour. Then compound **1** (3.14 mmol) was added and the reaction mixture was allowed warm to room temperature and stirred for 3 hours. The solvent was evaporated to obtain the intermediate **2**. To a solution of triphenylphosphine (5.24 mmol), and 2,3-dichloro-5,6-dicyano-1,4-benzoquinon (5.24 mmol) in dichloromethane (10 mL) was added the intermediate **2** slowly at 0 ℃. The reaction mixture was warmed to room temperature and stirred for 12 hours. The reaction mixture was filtrated through celite, washed with 5% sodium hydroxide. The aqueous phase was extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate, filtrated, and concentrated under reduced pressure. The residue was purified by chromatography to give **L1a-d**.



2'-(Pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] L1a

The title compound was isolated as a light yellow oil in 49% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 4.9 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.78 (td, *J* = 7.7, 1.7 Hz, 1H), 7.41 (dd, *J* = 7.6, 4.9 Hz, 1H), 7.29 – 7.20 (m, 4H), 4.68 (d, *J* = 8.8 Hz, 1H), 4.57 (d, *J* = 8.8 Hz, 1H), 3.20 (ddd, *J* = 15.2, 8.4, 6.2 Hz, 1H), 2.97 (ddd, *J* = 15.9, 8.4, 5.5 Hz, 1H), 2.57 (ddd, *J* = 13.6, 8.4, 5.4 Hz, 1H), 2.27 (ddd, *J* = 13.8, 8.3, 6.2 Hz, 1H). 13C NMR (126 MHz, Chloroform-d) δ 162.24, 149.84, 146.90, 145.82, 143.49, 136.72, 128.37, 127.27, 125.71, 124.80, 124.27, 123.48, 81.09, 79.00, 40.26, 30.33. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{16}H_{14}N_2ONa^+$ 273.1004, found 273.1008.

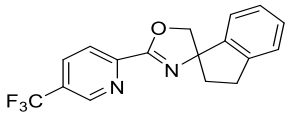


7-Phenyl-2'-(pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] L1b

The title compound was isolated as a colorless oil in 65% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.67 (d, *J* = 4.7 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 6.2 Hz, 1H), 7.29 (d, *J* = 4.7 Hz, 2H), 7.22 (d, *J* = 4.9 Hz, 2H), 7.06 (d, *J* = 4.5 Hz, 4H), 4.39 (d, *J* = 8.7 Hz, 1H), 4.26 (d, *J* = 8.7 Hz, 1H), 3.27 (dt, *J* = 15.5, 7.6 Hz, 1H), 2.98 (ddd, *J* = 15.1, 8.1, 5.2 Hz, 1H), 2.59 – 2.48 (m, 1H), 2.19

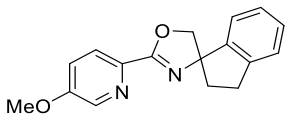
(dt, *J* = 14.0, 7.6 Hz, 1H). 13C NMR (126 MHz, Chloroform-d) δ 162.22, 149.70, 146.95, 144.83, 141.88, 140.69, 140.23, 136.42, 129.46, 129.25, 128.30, 127.71, 126.89, 125.44, 124.14, 124.08, 81.81, 77.95, 42.94, 30.23. HRMS (ESI-TOF$^+$) $[M+H]^+$ m/z calcd for $C_{22}H_{18}N_2OH^+$ 327.1497, found 327.1488.



2'-(5-(Trifluoromethyl)pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] L1c

The title compound was isolated as a white solid in 26% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.93 – 8.88 (m, 1H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.95 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.23 – 7.11 (m, 4H), 4.64 (d, *J* = 8.8 Hz, 1H), 4.53 (d, *J* = 8.9 Hz, 1H), 3.14 (ddd, *J* = 15.3, 8.4, 6.3 Hz, 1H), 2.92 (ddd, *J* = 16.0, 8.4, 5.3 Hz, 1H), 2.50 (ddd, *J* = 13.6, 8.4, 5.3 Hz, 1H), 2.20 (ddd, *J* = 13.2, 8.4, 6.3 Hz, 1H). 13C NMR (126 MHz, Chloroform-d) δ 161.12, 149.99, 146.67, 146.63, 145.35, 143.49, 134.00, 133.98, 128.52, 127.29, 124.86, 123.97, 123.34, 81.27, 79.12, 40.17, 30.28. Melting Point: 104-105℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{17}H_{13}F_3N_2ONa^+$ 341.0878, found 341.0883.

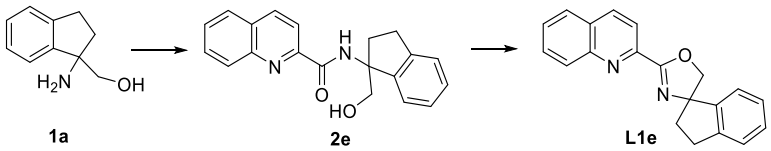


2'-(5-Methoxypyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] L1d

The title compound was isolated as a white solid in 56% yield.

1H NMR (500 MHz, Chloroform-d) δ 8.31 (d, J = 2.9 Hz, 1H), 7.99 (d, J = 8.7 Hz, 1H), 7.22 – 7.12 (m, 5H), 4.57 (d, J = 8.7 Hz, 1H), 4.47 (d, J = 8.8 Hz, 1H), 3.83 (s, 3H), 3.12 (ddd, J = 15.2, 8.5, 6.1 Hz, 1H), 2.89 (, J = ddd 15.9, 8.4, 5.5 Hz, 1H), 2.48 (ddd, J = 13.7, 8.5, 5.6 Hz, 1H), 2.18 (ddd, J = 13.1, 8.4, 6.1 Hz, 1H). 13C NMR (126 MHz, Chloroform-d) δ 162.04, 157.31, 146.03, 143.45, 139.19, 137.89, 128.28, 127.24, 125.22, 124.76, 123.48, 120.15, 80.98, 78.95, 55.83, 40.28, 30.32. Melting Point: 106-107℃. HRMS (ESI-TOF+) $[M+Na]^+$ m/z calcd for $C_{17}H_{16}N_2O_2Na^+$ 303.1109, found 303.1106; $[M+H]^+$ m/z calcd for $C_{17}H_{16}N_2O_2H^+$ 281.1290, found 281.1288.

e. General procedures for the synthesis of spiro-bidentate-quinox ligands L1e



1a 2e L1e

2'-(Quinolin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] L1e

The title compound was isolated as a white solid in 67% yield.

To a solution of substituted 2-pyridine carboxylic acid (2.62 mmol) in anhydrous dichloromethane (10 mL)was added N-hydroxybenzotrizole (HOBT) (2.88 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDCI • HCl) (2.88 mol), and triethylamine (4.32 mmol) at 0 ℃ sequentially . The reaction mixture was stirred for 1 hour at room temperature. Then **1a** (3.14 mmol) was added slowly. The reaction mixture was warmed to room temperature and stirred for 3 hours. The solvent was evaporated to obtain the intermediate **2e**. To a solution of triphenylphosphine (5.24 mmol), and 2,3-dichloro-5,6-dicyano-1,4-benzoquinon (5.24 mmol) in dichloromethane (10 mL) was added the intermediate **2e** slowly at 0 ℃. The reaction mixture was warmed to room temperature and stirred for 12 hours. The reaction mixture was filtrated through celite, washed with 5% sodium hydroxide. The aqueous phase was extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate, filtrated, and concentrated under reduced pressure. The residue was purified by chromatography to give **L1e**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.41 – 8.15 (m, 3H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.78 (t, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.33 – 7.21 (m, 4H), 4.75 (d, *J* = 8.8 Hz, 1H), 4.66 (d, *J* = 8.8 Hz, 1H), 3.22 (dt, *J* = 15.2, 7.1 Hz, 1H), 3.01 (dt, *J* = 15.5, 7.1 Hz, 1H), 2.61 (p, *J* = 6.5 Hz, 1H), 2.32 (dt, *J* = 14.0, 7.0 Hz, 1H). 13C NMR (126 MHz, Chloroform-d) δ 162.61, 147.73, 147.06, 145.84, 143.54, 136.82, 130.49, 130.18, 128.94, 128.49, 128.09, 127.67, 127.41, 124.90, 123.59, 121.25, 81.27, 79.37, 40.40, 30.41. Melting Point: 132-133℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{20}H_{16}N_2ONa^+$ 323.1160, found 323.1162.

General procedure for the cross electrophile coupling product 5

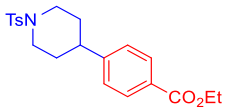
Details of Optimization and Control Experiments 5

A typical procedure for optimization and control reactions: To a dried vial equipped with

a magnetic stir bar was added metal catalyst (0.02 mmol, 10 mol%) and additive (if applicable) in glove box. The vial was moved out of the glove box, ligand and solvent were added via syringe. The reaction mixture was stirred for one hour at room temperature. Aryl halide (0.40 mmol), alkyl bromide (0.20 mmol) and reductant (0.60 mmol) were added sequentially. The reaction mixture was allowed to stir overnight under argon atmosphere at heated. The organic layer was extracted with ethyl acetate and water, then the organic layer washed with saturated salt solution, dried over with anhydrous sodium sulfate, filtrated and concentrated under reduced pressure. Through flash column chromatography (SiO_2: ethyl acetate in petroleum) to provided the cross coupling product.

General Procedure for Cross-Electronphile Coupling of Alkyl Bromides with Aryl Bromides 5

To a dried vial equipped with a magnetic stir bar was added $NiBr_2$ (4.37 mg, 0.02 mmol) and lithium chloride (8.4 mg, 0.20 mmol) in glove box. The vial was moved out of the glove box, **L1a** (5.00 mg, 0.02 mmol) and NMP (1 mL) were added via syringe. The reaction mixture was stirred for one hour at room temperature. Aryl bromide (0.40 mmol), alkyl bromide (0.20 mmol) and manganese powder (33 mg, 0.60 mmol) were added sequentially. The reaction mixture was allowed to stir overnight under argon atmosphere at 80 ℃. The organic layer was extracted with ethyl acetate and water, then the organic layer washed with saturated salt solution, dried over with anhydrous sodium sulfate, filtrated and concentrated under reduced pressure. Through flash column chromatography (SiO_2: ethyl acetate in petroleum) to provided the cross coupling product.

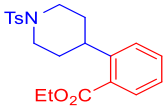


Ethyl 4-(1-tosylpiperidin-4-yl)benzoate 5a

The title compound was isolated as a white solid in 92% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 μl, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5a**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 3.94 (d, *J* = 11.9 Hz, 2H), 2.49 (dd, *J* = 11.1, 4.6 Hz, 1H), 2.45 (s, 3H), 2.35 (d, *J* = 3.7 Hz, 2H), 1.87 (dt, *J* = 7.4, 4.0 Hz, 4H), 1.38 (t, *J* = 7.2 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 166.52, 150.11, 143.70, 133.17, 130.02, 129.78, 129.03, 127.87, 126.82, 61.00, 46.79, 41.98, 32.37, 21.66, 14.44. Melting Point: 151-152℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{21}H_{25}O_3NO_4SNa^+$ 410.1402, found 410.1405.

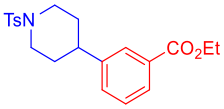


Ethyl 2-(1-tosylpiperidin-4-yl)benzoate 5b

The title compound was isolated as a white solid in 36% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), ethyl 2-bromobenzoate (64 μl, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5b**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.81 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.48 (td, *J* = 7.6, 1.5 Hz, 1H), 7.34 (dd, *J* = 8.5, 2.4 Hz, 3H), 7.28 – 7.24 (m, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.93 (d, *J* = 11.3 Hz, 2H), 3.36 (ddt, *J* = 11.8, 7.6, 3.9 Hz, 1H), 2.46 (s, 3H), 2.36 (td, *J* = 11.7, 2.9 Hz, 2H), 1.94 – 1.82 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 167.84, 146.30, 143.62, 133.12, 132.31, 130.56, 129.78, 127.89, 126.85, 126.29, 61.03, 47.18, 37.51, 32.56, 21.66, 14.36. Melting Point: 132-133℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{21}H_{25}O_3NO_4SNa^+$ 410.1402, found 410.1402.



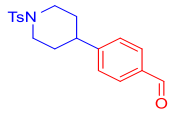
Ethyl 3-(1-tosylpiperidin-4-yl)benzoate 5c

The title compound was isolated as a white solid in 40% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), ethyl 3-bromobenzoate (64 μl, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5c**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.89 (dt, *J* = 7.4, 1.6 Hz, 1H), 7.83 (d, *J* = 1.8 Hz,

1H), 7.70 – 7.66 (m, 2H), 7.39 – 7.31 (m, 4H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.94 (d, *J* = 11.5 Hz, 2H), 2.49 (dt, *J* = 10.3, 5.3 Hz, 1H), 2.45 (s, 3H), 2.35 (td, *J* = 11.4, 4.1 Hz, 2H), 1.93 – 1.83 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 166.63, 145.25, 143.67, 133.18, 131.20, 130.87, 129.76, 128.74, 128.02, 127.93, 127.85, 61.11, 46.84, 41.76, 32.53, 21.64, 14.43. Melting Point: 138-139℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{21}H_{25}O_3NO_4SNa^+$ 410.1402, found 410.1402.

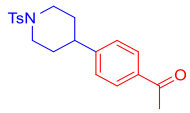


4-(1-Tosylpiperidin-4-yl)benzaldehyde 5d[2]

The title compound was isolated as a white solid in 72% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), 4-bromobenzaldehyde (74 mg, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5d**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.93 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.64 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 3.96 – 3.87 (m, 2H), 2.51 – 2.43 (m, 1H), 2.41 (s, 3H), 2.32 (td, *J* = 11.6, 3.6 Hz, 2H), 1.90 – 1.79 (m, 4H). 13C NMR (126 MHz, Chloroform-d) δ 191.93, 152.06, 143.76, 135.22, 133.17, 130.28, 129.81, 127.88, 127.57, 46.75, 42.22, 32.32, 21.68. Melting Point: 152-153℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{19}H_{21}NO_3SNa^+$ 366.1140, found 366.1142; $[M+H]^+$ m/z calcd for $C_{19}H_{21}NO_3SH^+$ 344.1320, found 344.1325.



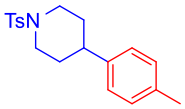
1-(4-(1-Tosylpiperidin-4-yl)phenyl)ethan-1-one 5e[3]

The title compound was isolated as a white solid in 41% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), 4-bromoacetophenone (79.6 mg, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5e**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.00 – 3.89 (m, 2H), 2.57 (s, 3H), 2.49

(dt, *J* = 10.9, 5.3 Hz, 1H), 2.45 (s, 3H), 2.35 (td, *J* = 11.6, 3.7 Hz, 2H), 1.86 (dp, *J* = 12.3, 5.0, 4.0 Hz, 4H). 13C NMR (126 MHz, Chloroform-d) δ 197.78, 150.49, 143.72, 135.83, 133.18, 129.79, 128.89, 127.88, 127.07, 46.78, 42.00, 32.36, 26.70, 21.67. Melting Point: 174-175℃. HRMS (ESI-TOF$^+$) [M+Na]$^+$ m/z calcd for $C_{20}H_{23}NO_3SNa^+$ 380.1296, found 380.1302.

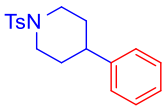


4-(p-Tolyl)-1-tosylpiperidine 5f[3]

The title compound was isolated as a white solid in 59% yield, recovered starting material 4-bromo-1-tosylpiperidine 14.2 mg.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), 1-bromo-4-methylbenzene (68.4 mg, 0.40 mmol,). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5f**.

1H NMR (500 MHz, Chloroform-d) δ 7.68 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 7.7 Hz, 2H), 7.03 (d, J = 7.7 Hz, 2H), 3.92 (d, J = 11.5 Hz, 2H), 2.45 (s, 3H), 2.43 – 2.32 (m, 3H), 2.31 (s, 3H), 1.84 (qd, J = 12.5, 3.6 Hz, 4H). 13C NMR (126 MHz, Chloroform-d) δ 143.59, 142.08, 136.28, 133.31, 129.75, 129.38, 127.91, 126.67, 47.03, 41.54, 32.77, 29.83, 21.67, 21.10. Melting Point: 146-148℃. HRMS (ESI-TOF$^+$) [M+Na]$^+$ m/z calcd for $C_{19}H_{23}NO_2SNa^+$ 352.1347, found 352.1352.



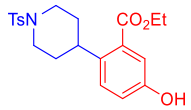
4-Phenyl-1-tosylpiperidine 5g[3]

The title compound was isolated as a white solid in 49% yield, recovered starting material 4-bromo-1-tosylpiperidine 23.7 mg.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), bromobenzene (62.8 mg, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5g**.

1H NMR (500 MHz, Chloroform-d) δ 7.68 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 7.9 Hz, 2H), 7.29 (t, J = 7.6 Hz, 2H), 7.21 (t, J = 7.3 Hz, 1H), 7.17 – 7.11 (m, 2H), 3.93 (dt, J = 12.8, 2.8 Hz, 2H), 2.45 (s, 3H), 2.41 (ddd, J = 11.5, 7.1, 3.6 Hz, 1H), 2.35 (td, J = 11.6, 3.4 Hz, 2H),

1.86 (qd, J = 12.2, 10.6, 4.8 Hz, 4H). 13C NMR (126 MHz, Chloroform-d) δ 145.04, 143.61, 133.29, 129.75, 128.72, 127.91, 126.81, 126.72, 46.99, 41.97, 32.67, 21.66. Melting Point: 146-148℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{18}H_{21}NO_2SNa^+$ 338.1191, found 338.1193; $[M+H]^+$ m/z calcd for $C_{18}H_{22}NO_2SH^+$ 316.1371, found 316.1376.

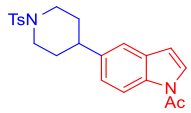


Ethyl 5-hydroxy-2-(1-tosylpiperidin-4-yl)benzoate 5h

The title compound was isolated as a white solid in 40% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), ethyl 2-bromo-5-hydroxybenzoate (97.6 mg, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5h**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.72 (s, 1H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.62 (d, *J* = 2.4 Hz, 1H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.22 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.91 (d, *J* = 8.6 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.93 (d, *J* = 11.5 Hz, 2H), 2.45 (s, 3H), 2.37 (q, *J* = 5.8, 4.5 Hz, 1H), 2.32 (td, *J* = 11.6, 3.5 Hz, 2H), 1.89 – 1.76 (m, 4H), 1.42 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 170.14, 160.43, 143.68, 135.72, 134.33, 133.14, 129.77, 127.90, 127.85, 127.55, 117.85, 112.56, 61.63, 46.92, 41.04, 32.81, 21.68, 14.36. Melting Point: 108-109℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{21}H_{25}NO_5SNa^+$ 426.1351, found 426.1337; $[M+H]^+$ m/z calcd for $C_{21}H_{25}NO_5SH^+$ 404.1532, found 404.1522.



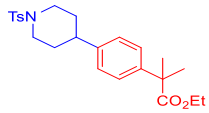
1-(5-(1-Tosylpiperidin-4-yl)-1H-indol-1-yl)ethan-1-one 5i

The title compound was isolated as a white solid in 48% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), 1-acetyl-5-bromo-1H-indole (95.2 mg, 0.40 mmol). Purified by column chromatography (SiO_2: 30% ethyl acetate in petroleum) to give **5i**.

1H NMR (500 MHz, Chloroform-d) δ 8.33 (d, J = 8.2 Hz, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 3.8 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.12 (dd, J = 8.5, 1.8 Hz, 1H), 6.59 (d, J =

3.7 Hz, 1H), 3.95 (dd, J = 9.4, 5.9 Hz, 2H), 2.62 (s, 3H), 2.51 (tt, J = 10.2, 4.9 Hz, 1H), 2.45 (s, 3H), 2.36 (td, J = 11.5, 3.7 Hz, 2H), 1.90 (dp, J = 12.4, 4.3, 3.2 Hz, 4H). 13C NMR (126 MHz, Chloroform-d) δ 168.61, 143.61, 140.61, 134.46, 133.27, 130.83, 129.75, 127.89, 125.74, 124.33, 118.45, 116.66, 109.16, 47.04, 41.87, 33.04, 23.98, 21.66. Melting Point: 204-205℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{22}H_{24}N_2O_3Na^+$ 419.1405, found 419.1411.

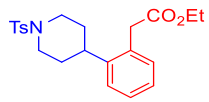


Ethyl 2-methyl-2-(4-(1-tosylpiperidin-4-yl)phenyl)propanoate 5j

The title compound was isolated as a white solid in 24% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), 2-(4-bromophenyl)-2-methylpropionic acid ethyl ester (108 mg, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5j**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.29 – 7.23 (m, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.99 – 3.87 (m, 2H), 2.45 (s, 3H), 2.43 – 2.36 (m, 1H), 2.33 (td, *J* = 11.8, 3.1 Hz, 2H), 1.92 – 1.76 (m, 4H), 1.55 (s, 6H), 1.19 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 176.81, 143.61, 143.22, 133.17, 129.74, 127.88, 126.74, 125.95, 60.91, 46.97, 46.28, 41.41, 32.59, 26.66, 21.66, 14.19. Melting Point: 118-119℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{24}H_{21}NO_4SNa^+$ 452.1871, found 452.1870.

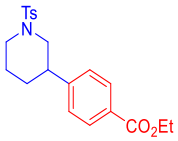


Ethyl 2-(2-(1-tosylpiperidin-4-yl)phenyl)acetate 5k

The title compound was isolated as a colorless solid in 31% yield.

This compound was prepared according to the general procedure using 4-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), 2-bromophenylacetic acid ethyl ester (96.8 mg, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5k**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.71 – 7.66 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.31 – 7.25 (m, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.21 – 7.15 (m, 2H), 4.13 – 4.02 (m, 2H), 3.99 – 3.91 (m, 2H), 3.58 (s, 2H), 2.67 (ddt, *J* = 11.8, 7.9, 4.0 Hz, 1H), 2.46 (s, 3H), 2.33 (td, *J* = 11.8, 2.8 Hz, 2H), 1.92 – 1.74 (m, 4H), 1.17 (td, *J* = 7.1, 1.4 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 171.64, 143.66, 143.59, 133.23, 131.65, 131.03, 129.80, 128.08, 127.89, 126.69, 126.49, 61.04, 47.15, 39.10, 37.56, 32.43, 21.67, 14.24. Melting Point: 88-89℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{22}H_{27}NO_4SNa^+$ 424.1558, found 424.1151.

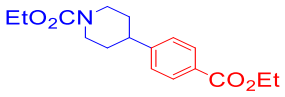


Ethyl 4-(1-tosylpiperidin-3-yl)benzoate 5n

The title compound was isolated as a white solid in 56% yield.

This compound was prepared according to the general procedure using 3-bromo-1-tosylpiperidine (63.2 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 μl, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5n**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 7.9 Hz, 2H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.85 (dt, *J* = 11.3, 5.3 Hz, 2H), 2.94 (ddt, *J* = 11.6, 7.4, 3.7 Hz, 1H), 2.43 (s, 3H), 2.33 – 2.18 (m, 2H), 2.00 – 1.90 (m, 1H), 1.89 – 1.72 (m, 2H), 1.44 (td, *J* = 12.7, 4.2 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 166.48, 147.79, 143.68, 133.27, 129.99, 129.82, 129.36, 127.79, 127.31, 61.06, 52.32, 46.49, 42.28, 30.53, 24.98, 21.67, 14.46. Melting Point: 126-127℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{21}H_{25}NO_4SNa^+$ 410.1402, found 410.1395.



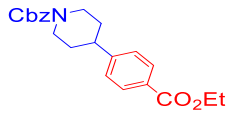
Ethyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5o

The title compound was isolated as colorless oil in 47% yield.

This compound was prepared according to the general procedure using ethyl 4-bromopiperidine-1-carboxylate (47 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 μl, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give

5o.

1H NMR (500 MHz, Chloroform-d) δ 7.94 – 7.88 (m, 2H), 7.19 (d, J = 7.8 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 4.24 (s, 1H), 4.09 (q, J = 7.0 Hz, 2H), 2.77 (d, J = 15.4 Hz, 2H), 2.66 (tt, J = 12.3, 3.7 Hz, 1H), 1.82 – 1.67 (m, 3H), 1.61 – 1.50 (m, 2H), 1.31 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 166.60, 155.66, 150.87, 129.98, 128.86, 126.88, 61.44, 60.95, 44.42, 42.84, 14.83, 14.45. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{17}H_{23}NO_4Na^+$ 328.1525, found 328.1525; $[M+H]^+$ m/z calcd for $C_{17}H_{24}NO_4H^+$ 306.1705, found 306.1706.

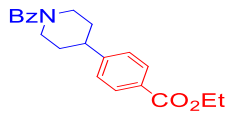


Benzyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5p[4]

The title compound was isolated as a colorless oil in 56% yield.

This compound was prepared according to the general procedure using benzyl 4-bromopiperidine-1-carboxylate (59.4 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 µl, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5p**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.00 – 7.97 (m, 2H), 7.41 – 7.35 (m, 4H), 7.33 (dq, *J* = 7.8, 2.8 Hz, 1H), 7.28 – 7.24 (m, 2H), 5.16 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 4H), 2.87 (d, *J* = 23.7 Hz, 2H), 2.74 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.84 (s, 2H), 1.63 (s, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 166.59, 155.38, 150.76, 136.93, 129.99, 128.88, 128.62, 128.13, 128.04, 126.88, 67.25, 60.96, 44.58, 42.78, 32.93, 14.46. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{22}H_{25}NO_4Na^+$ 390.1681, found 390.1674.



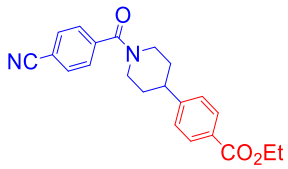
Ethyl 4-(4-benzoylcyclohexyl)benzoate 5q

The title compound was isolated as a colorless oil in 36% yield.

This compound was prepared according to the general procedure using (4-bromopiperidin-1-yl)(phenyl) methanone (53.4 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 µl, 0.40 mmol). Purified by column chromatography (SiO_2: 30% ethyl acetate in

petroleum) to give **5q**.

1H NMR (500 MHz, Chloroform-d) δ 8.02 – 7.97 (m, 2H), 7.42 (q, J = 4.2, 3.8 Hz, 5H), 7.29 (d, J = 7.9 Hz, 2H), 4.91 (s, 1H), 4.37 (q, J = 7.1 Hz, 2H), 3.90 (s, 1H), 3.13 (s, 1H), 2.85 (tt, J = 12.3, 3.7 Hz, 2H), 1.98 (s, 1H), 1.80 (s, 2H), 1.67 (s, 1H), 1.39 (t, J = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 170.58, 166.57, 150.33, 136.25, 130.05, 129.75, 129.02, 128.63, 127.04, 126.87, 61.01, 48.37, 42.98, 33.76, 32.81, 29.82, 14.47. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{22}H_{24}O_3Na^+$ 360.1576, found 360.1567; $[M+H]^+$ m/z calcd for $C_{22}H_{24}O_3H^+$ 338.1756, found 338.1745.

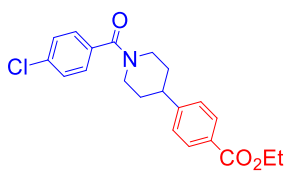


Ethyl 4-(1-(4-cyanobenzoyl)piperidin-4-yl)benzoate 5r

The title compound was isolated as a colorless oil in 27% yield, recovered starting material 4-(4-bromopiperidine-1-carbonyl) benzonitrile 19.9 mg.

This compound was prepared according to the general procedure using 4-(4-bromopiperidine-1-carbonyl) benzonitrile (58.4 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 μl, 0.40 mmol). Purified by column chromatography (SiO_2: 25% ethyl acetate in petroleum) to give **5r**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.00 (d, *J* = 8.3 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 4.89 (d, *J* = 13.4 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.75 (d, *J* = 14.0 Hz, 1H), 3.18 (s, 1H), 2.87 (t, *J* = 12.3 Hz, 2H), 2.03 (d, *J* = 15.4 Hz, 1H), 1.84 (s, 2H), 1.62 (s, 1H), 1.39 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 168.43, 166.50, 149.83, 140.56, 132.60, 130.09, 129.15, 127.74, 126.81, 118.23, 113.59, 61.06, 48.25, 42.88, 42.76, 33.70, 32.60, 14.46. Melting Point: 68-69°C. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{22}H_{22}N_2O_3H^+$ 385.1528, found 385.1519; $[M+H]^+$ m/z calcd for $C_{22}H_{22}N_2O_3H^+$ 363.1709, found 363.1702.

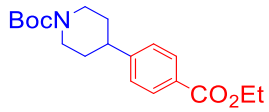


Ethyl 4-(1-(4-chlorobenzoyl)piperidin-4-yl)benzoate 5s

The title compound was isolated as a white solid in 59% yield, recovered starting material 4-bromopiperidin-1-yl) (4-chlorophenyl) methanone 10.2 mg.

This compound was prepared according to the general procedure using (4-bromopiperidin-1-yl) (4-chlorophenyl) methanone (60.2 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 µl, 0.40 mmol). Purified by column chromatography (SiO_2: 25% ethyl acetate in petroleum) to give **5s**.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.00 (dd, *J* = 8.3, 1.7 Hz, 2H), 7.46 – 7.37 (m, 4H), 7.31 – 7.25 (m, 2H), 4.88 (s, 1H), 4.42 – 4.32 (m, 2H), 3.90 (d, *J* = 6.7 Hz, 1H), 3.15 (s, 1H), 2.96 – 2.78 (m, 2H), 1.99 (s, 1H), 1.82 (s, 2H), 1.67 (s, 1H), 1.39 (td, *J* = 7.1, 1.6 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 177.43, 169.47, 166.51, 150.11, 135.81, 134.51, 130.03, 128.88, 128.59, 126.83, 60.99, 48.37, 42.86, 33.70, 32.69, 28.30, 14.44. Melting Point: 71-72°C. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{21}H_{22}ClNO_3Na^+$ 394.1186, found 394.1175; $[M+H]^+$ m/z calcd for $C_{21}H_{22}ClNO_3H^+$ 372.1366, found 372.1359.

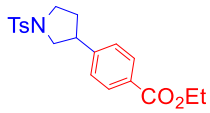


Tert-butyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5t

The title compound was isolated as a colorless oil in 61% yield.

This compound was prepared according to the general procedure using tert-butyl 4-bromopiperidine-1-carboxylate (52.6 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 µl, 0.40 mmol). Purified by column chromatography (SiO_2: 2% ethyl acetate in petroleum) to give **5t**.

1H NMR (500 MHz, Chloroform-d) δ 7.99 (d, J = 8.2 Hz, 2H), 7.32 – 7.23 (m, 2H), 4.37 (q, J = 7.1 Hz, 2H), 4.34 – 4.12 (m, 2H), 2.81 (s, 2H), 2.71 (tt, J = 12.3, 3.6 Hz, 1H), 1.83 (d, J = 13.1 Hz, 2H), 1.63 (qd, J = 12.7, 4.4 Hz, 2H), 1.49 (s, 9H), 1.39 (t, J = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 166.63, 154.92, 151.05, 129.97, 128.83, 126.90, 79.66, 60.94, 42.92, 33.02, 29.81, 28.59, 14.46. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{19}H_{27}NO_4Na^+$ 356.1838, found 356.1836.



Ethyl 4-(1-tosylpyrrolidin-3-yl)benzoate 5u

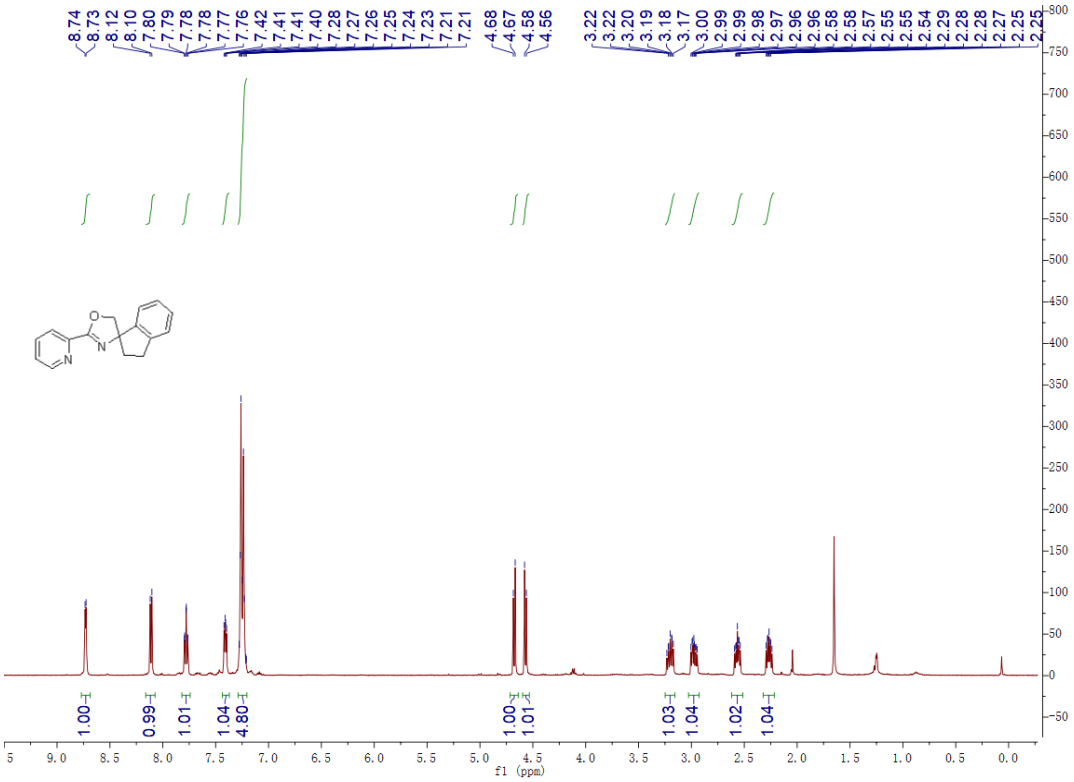
The title compound was isolated as a white solid in 87% yield.

This compound was prepared according to the general procedure using 3-bromo-1-(4-methylbenzenesulfonyl) pyrrolidine (60.6 mg, 0.20 mmol), ethyl 4-bromobenzoate (64 µl, 0.40 mmol). Purified by column chromatography (SiO_2: 5% ethyl acetate in petroleum) to give **5u**.

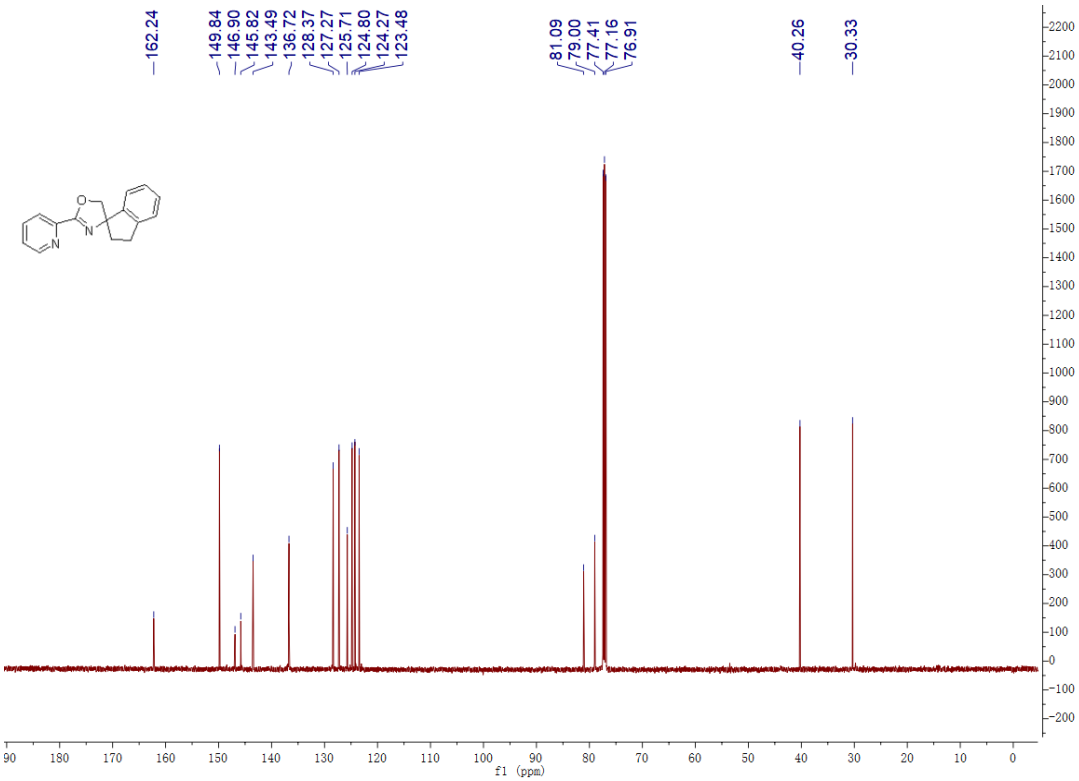
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.96 – 7.90 (m, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.72 (dd, *J* = 9.6, 7.3 Hz, 1H), 3.53 (ddd, *J* = 10.0, 8.3, 3.4 Hz, 1H), 3.36 (td, *J* = 9.5, 7.2 Hz, 1H), 3.33 – 3.25 (m, 1H), 3.25 – 3.19 (m, 1H), 2.45 (s, 3H), 2.23 (dtd, *J* = 13.4, 6.9, 3.5 Hz, 1H), 1.88 (dq, *J* = 12.5, 8.8 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-d) δ 166.37, 146.07, 143.75, 133.83, 130.01, 129.89, 129.35, 127.66, 127.05, 61.08, 53.94, 47.84, 43.85, 32.91, 21.67, 14.43. Melting Point: 130-131℃. HRMS (ESI-TOF$^+$) $[M+Na]^+$ m/z calcd for $C_{20}H_{23}NO_4SNa^+$ 396.1245, found 396.1231; $[M+H]^+$ m/z calcd for $C_{20}H_{23}NO_4SH^+$ 374.1426, found 374.1417.

II. Spectral Data for Compounds L1, 5

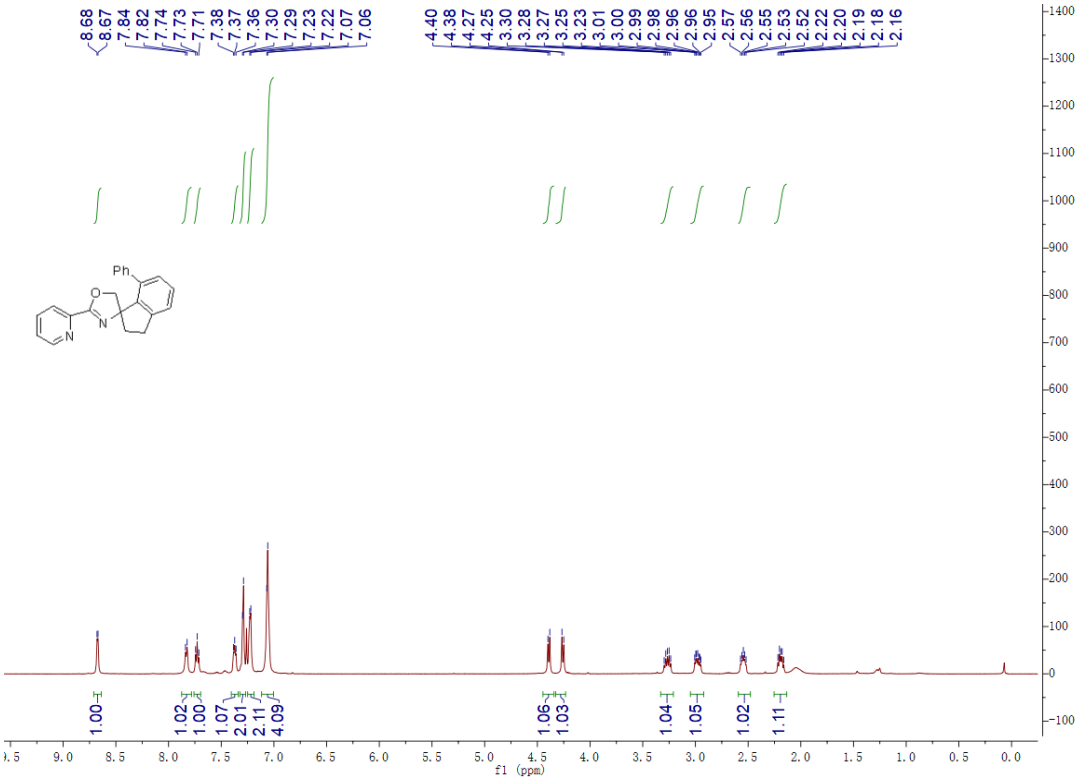
^{1}H NMR spectra of 2'-(pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1a



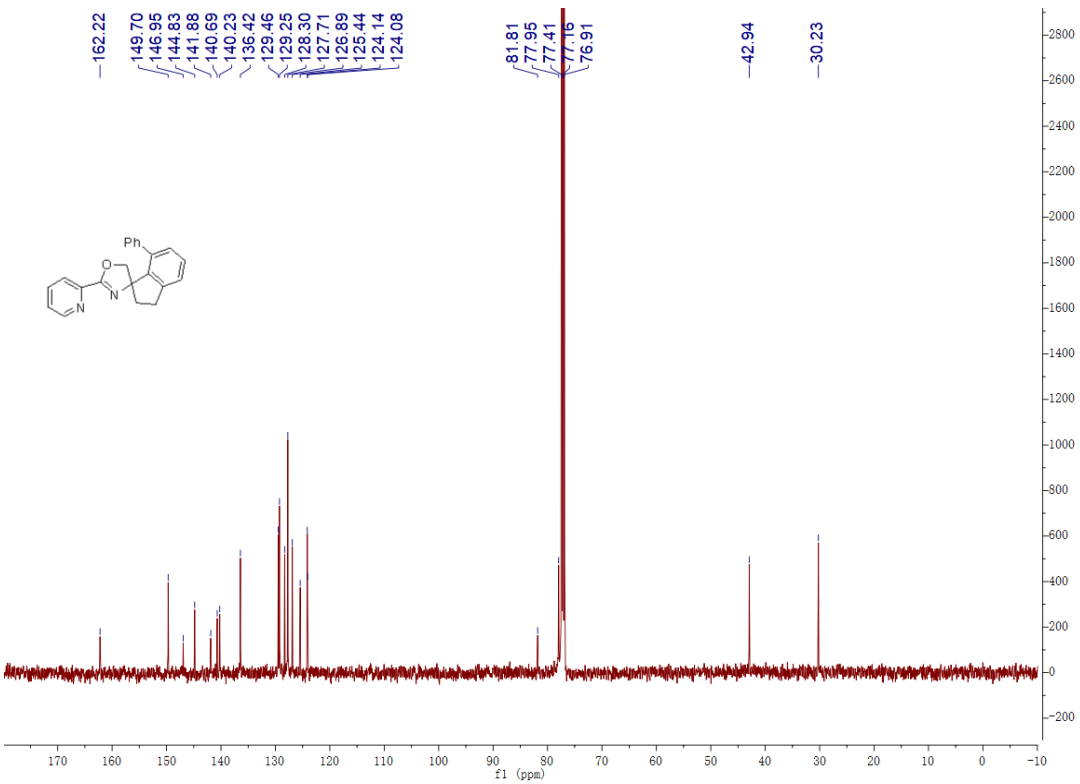
^{13}C NMR spectra of 2'-(pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1a



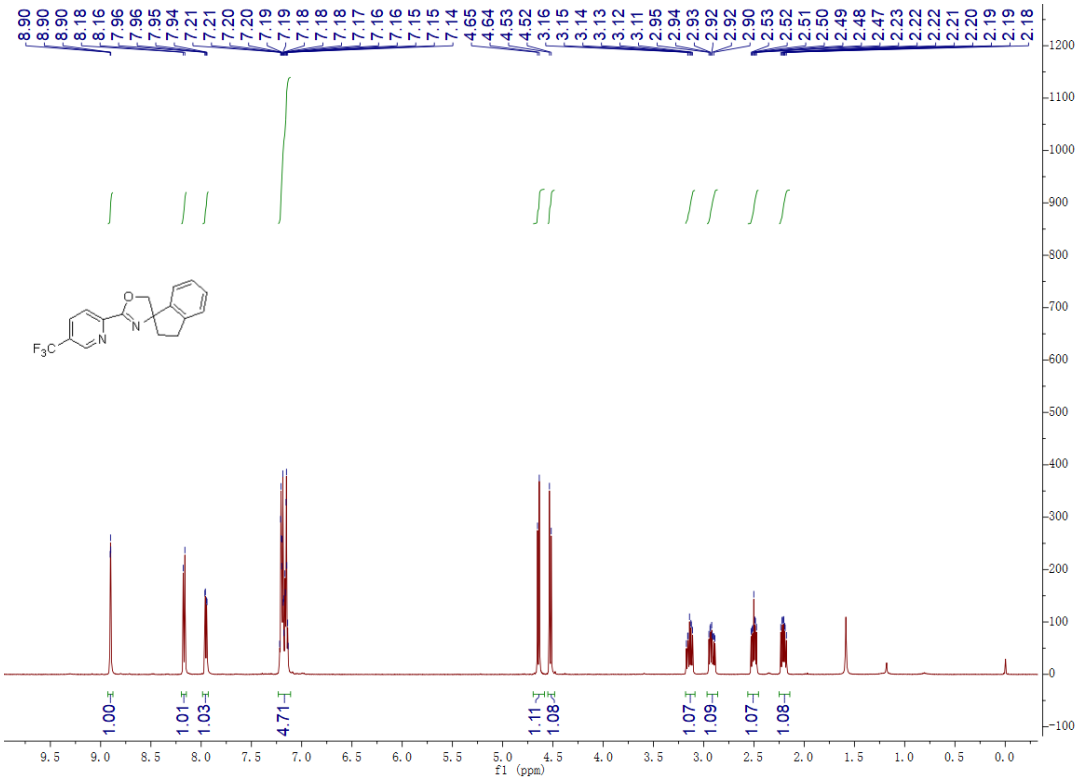
^{1}H NMR spectra of 7-phenyl-2'-(pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1b



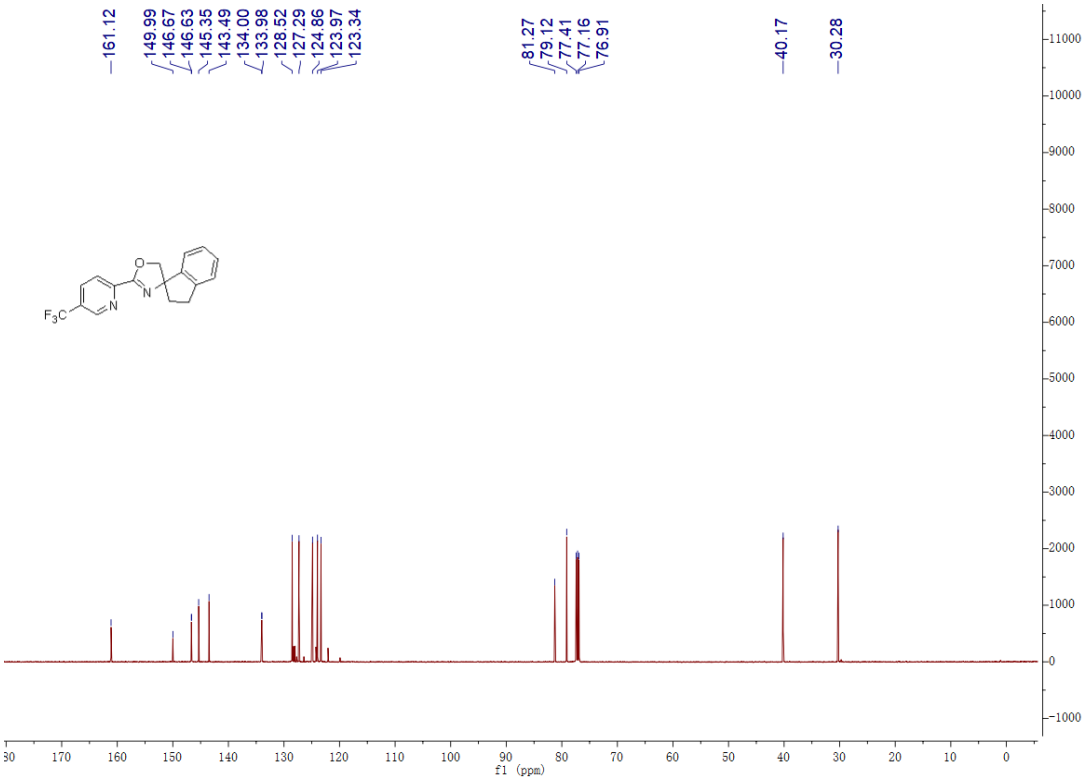
^{13}C NMR spectra of 7-phenyl-2'-(pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1b



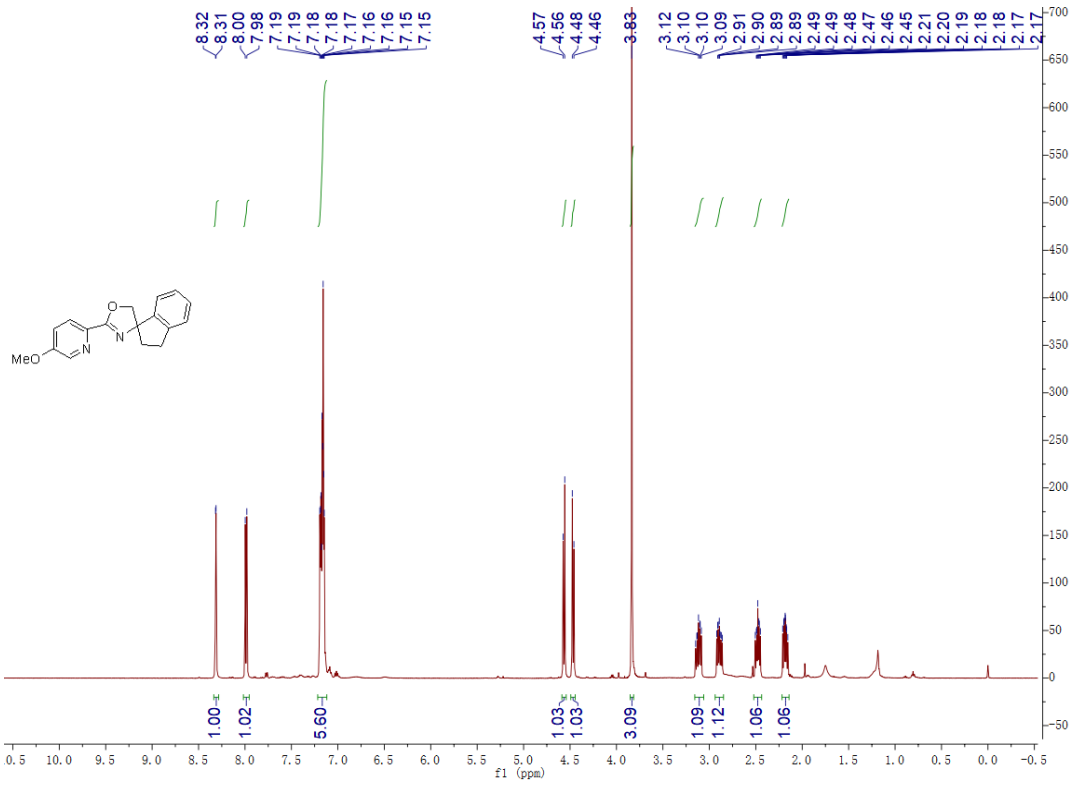
^{1}H NMR spectra of 2'-(5-(trifluoromethyl)pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1c



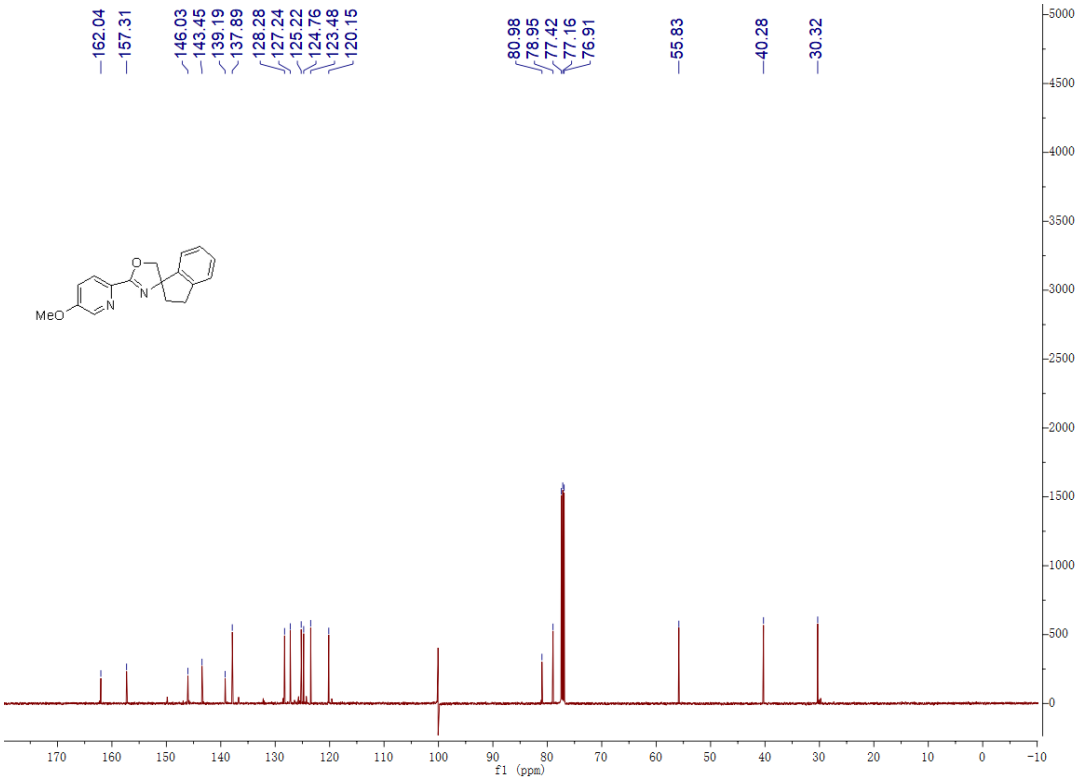
^{13}C NMR spectra of 2'-(5-(trifluoromethyl)pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1c



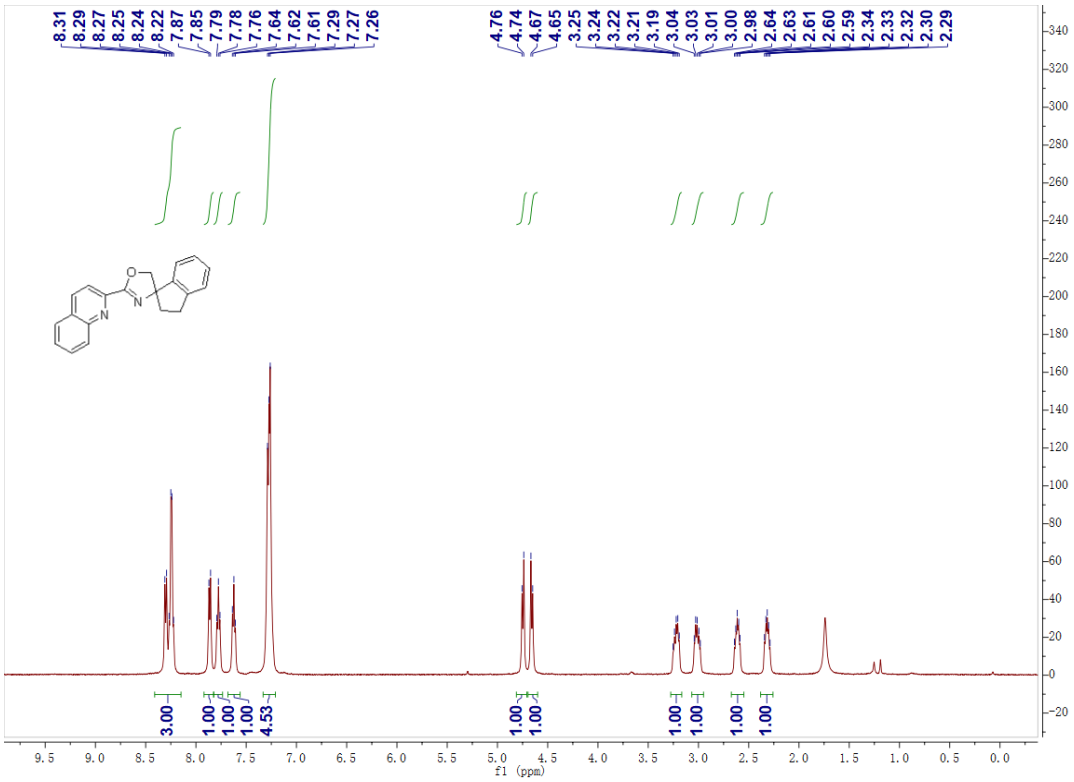
^{1}H NMR spectra of 2'-(5-methoxypyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1d



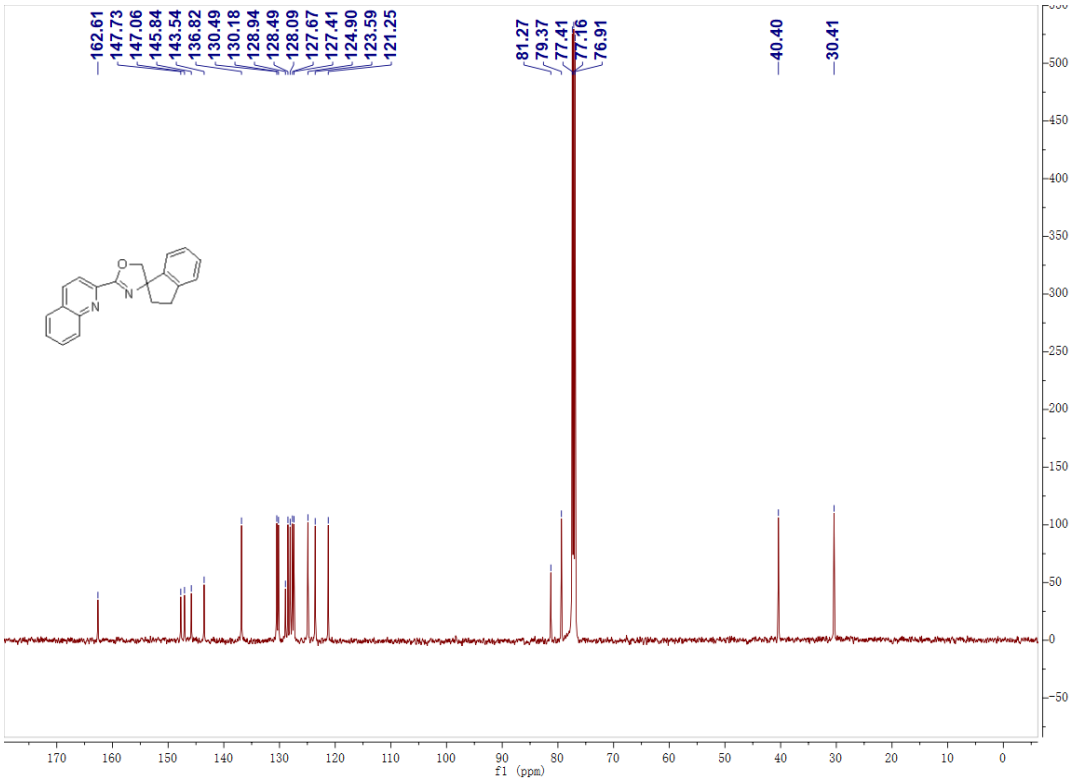
^{13}C NMR spectra of 2'-(5-methoxypyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1d



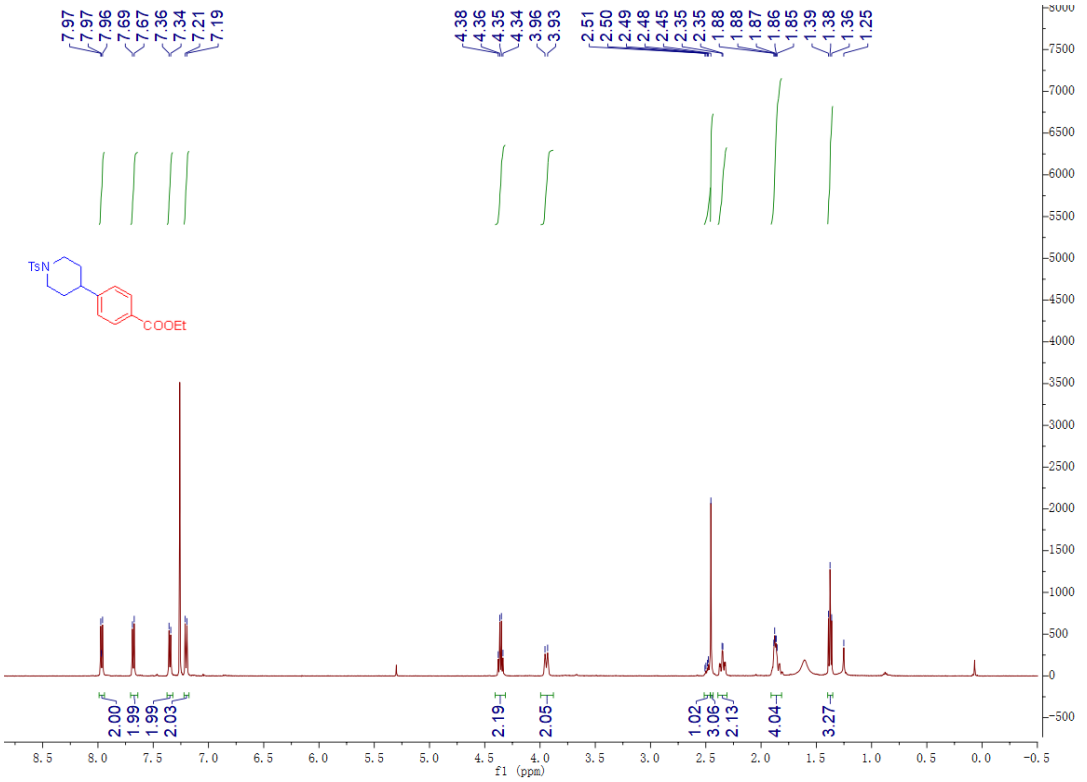
^{1}H NMR spectra of 2'-(quinolin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1e



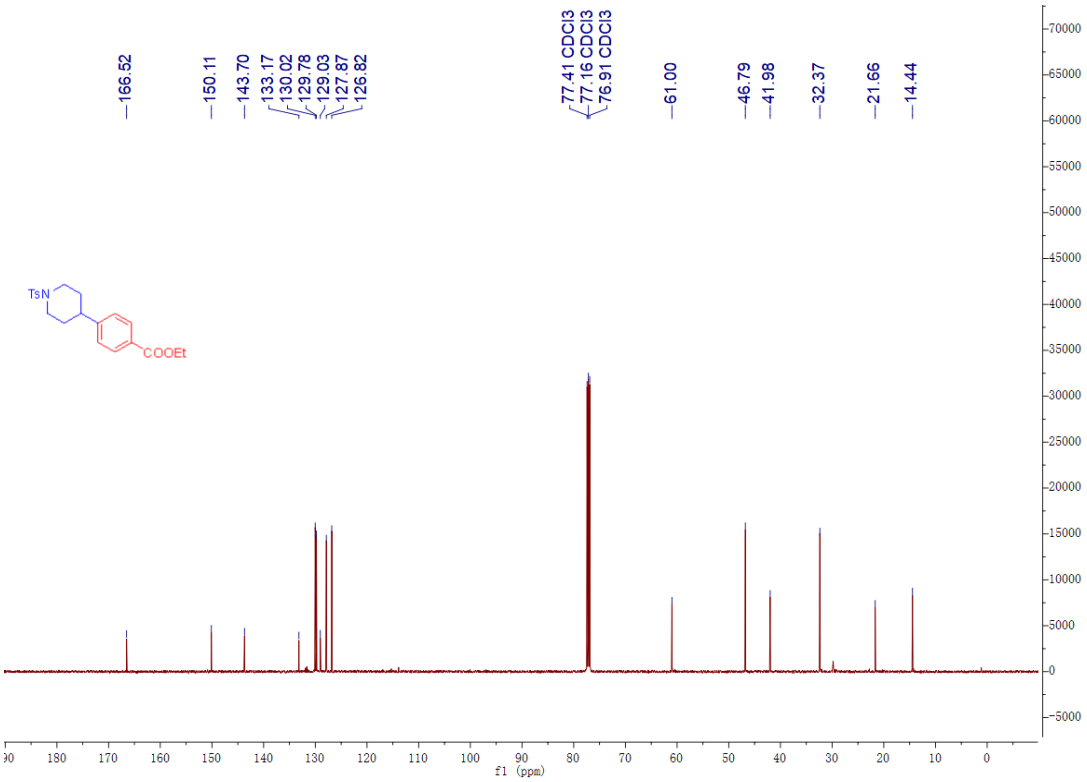
^{13}C NMR spectra of 2'-(quinolin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole L1e



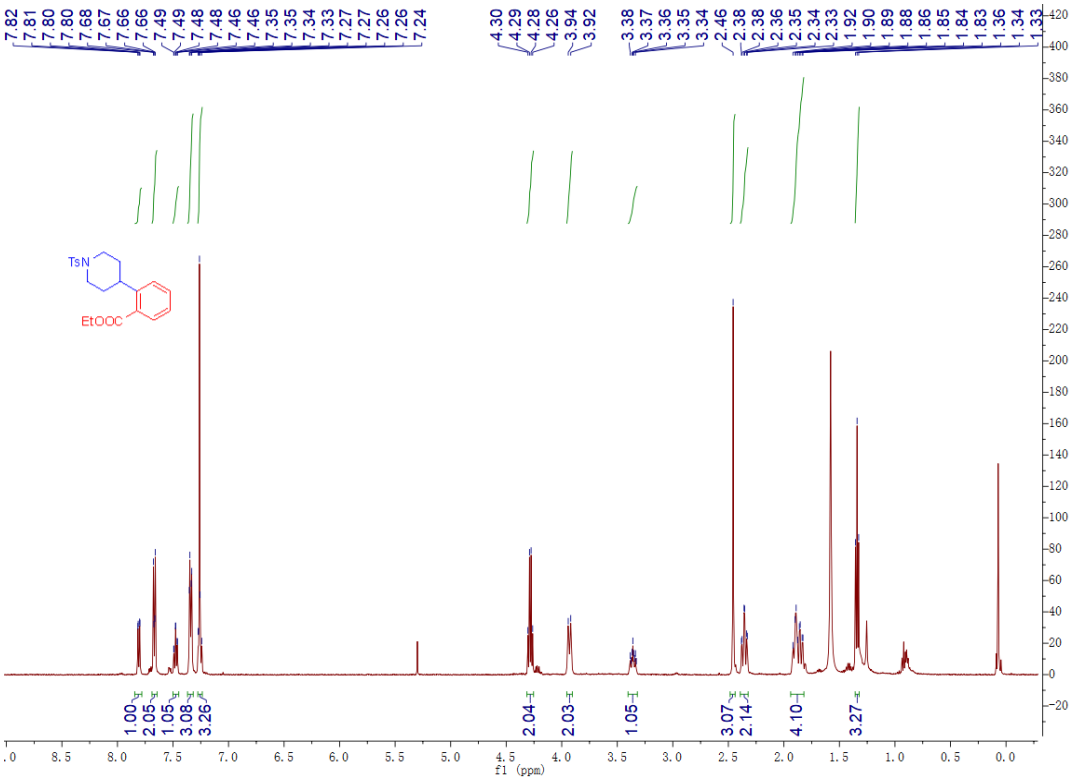
^{1}H NMR spectra of ethyl 4-(1-tosylpiperidin-4-yl)benzoate 5a



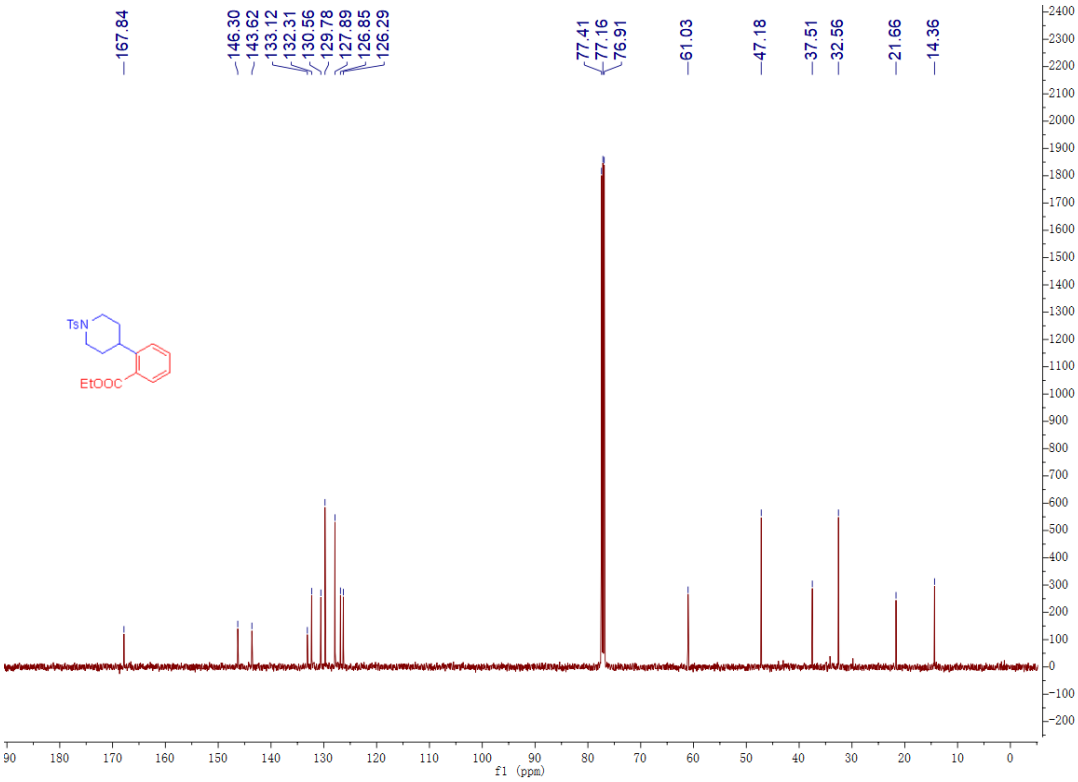
^{13}C NMR spectra of ethyl 4-(1-tosylpiperidin-4-yl)benzoate 5a



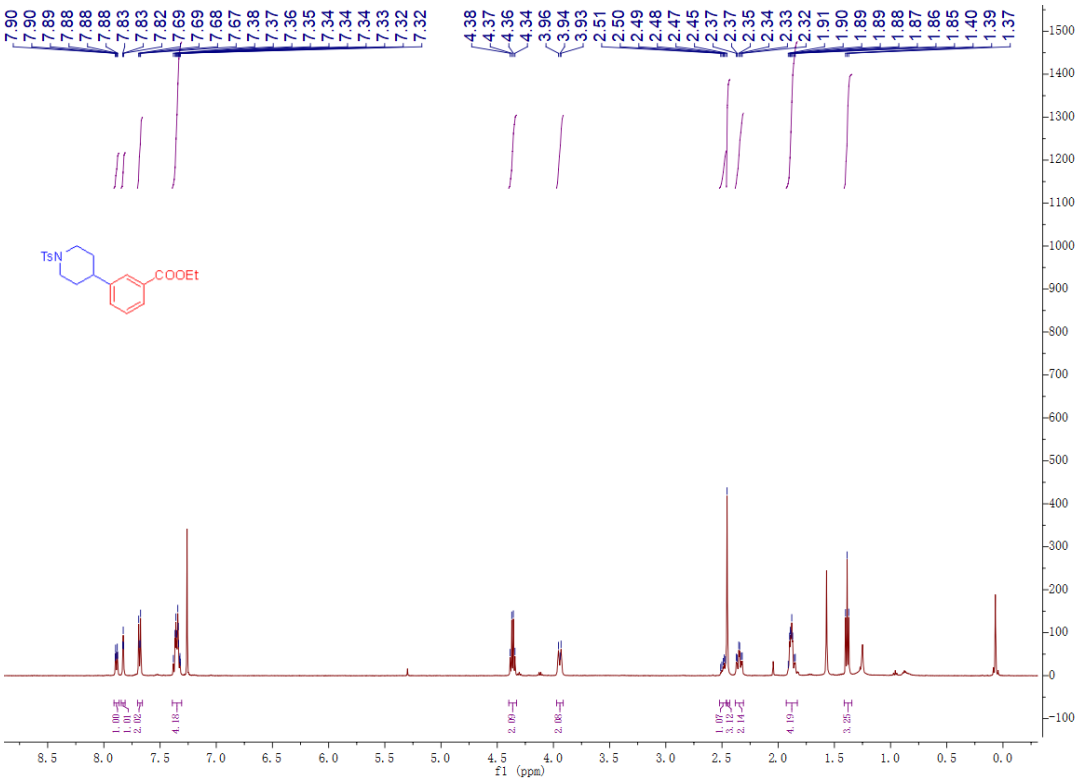
^{1}H NMR spectra of ethyl 2-(1-tosylpiperidin-4-yl)benzoate 5b



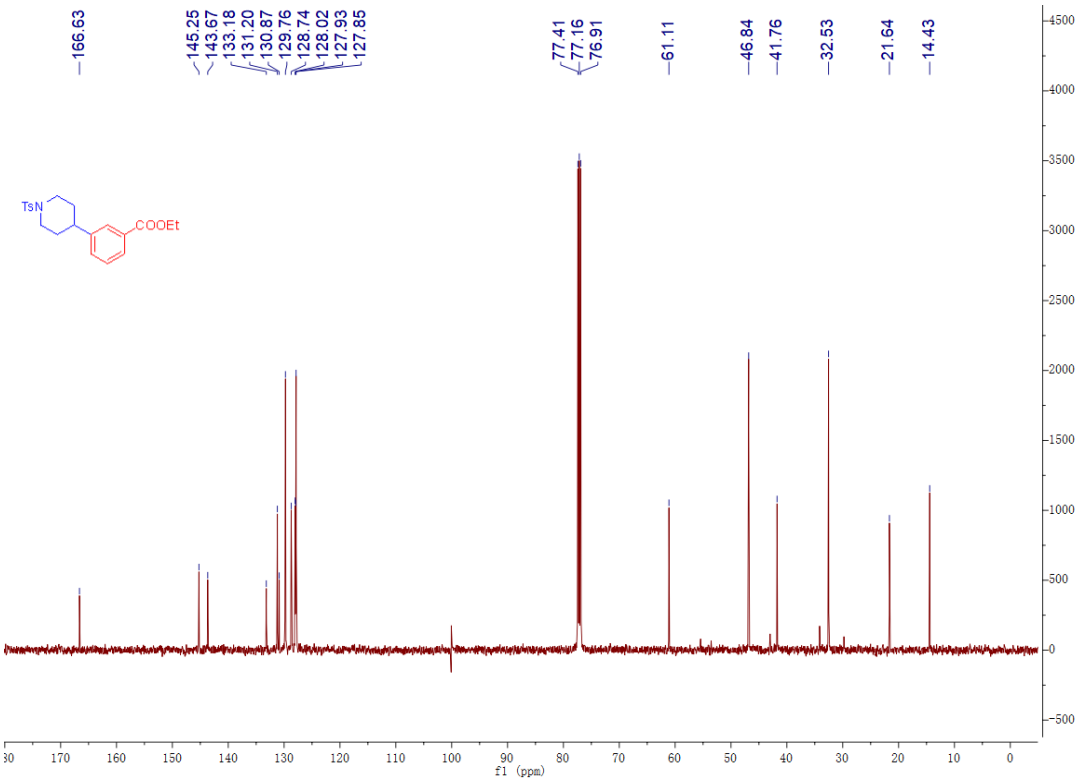
^{13}C NMR spectra of ethyl 2-(1-tosylpiperidin-4-yl)benzoate 5b



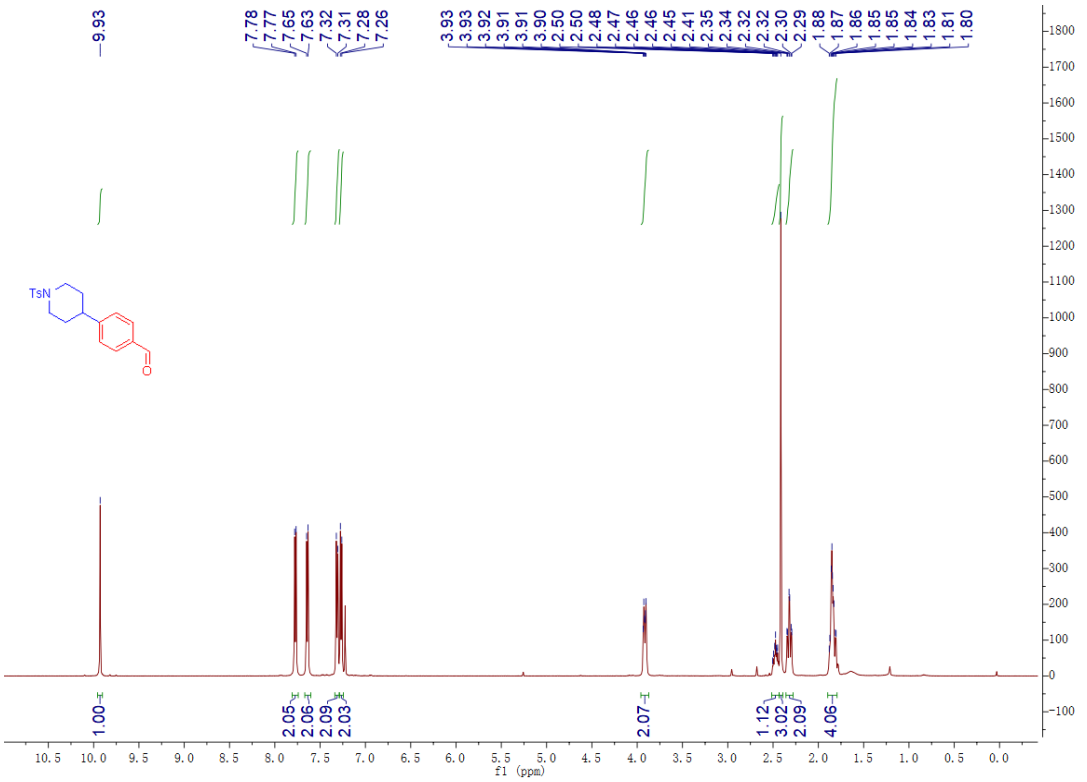
^{1}H NMR spectra of ethyl 3-(1-tosylpiperidin-4-yl)benzoate 5c



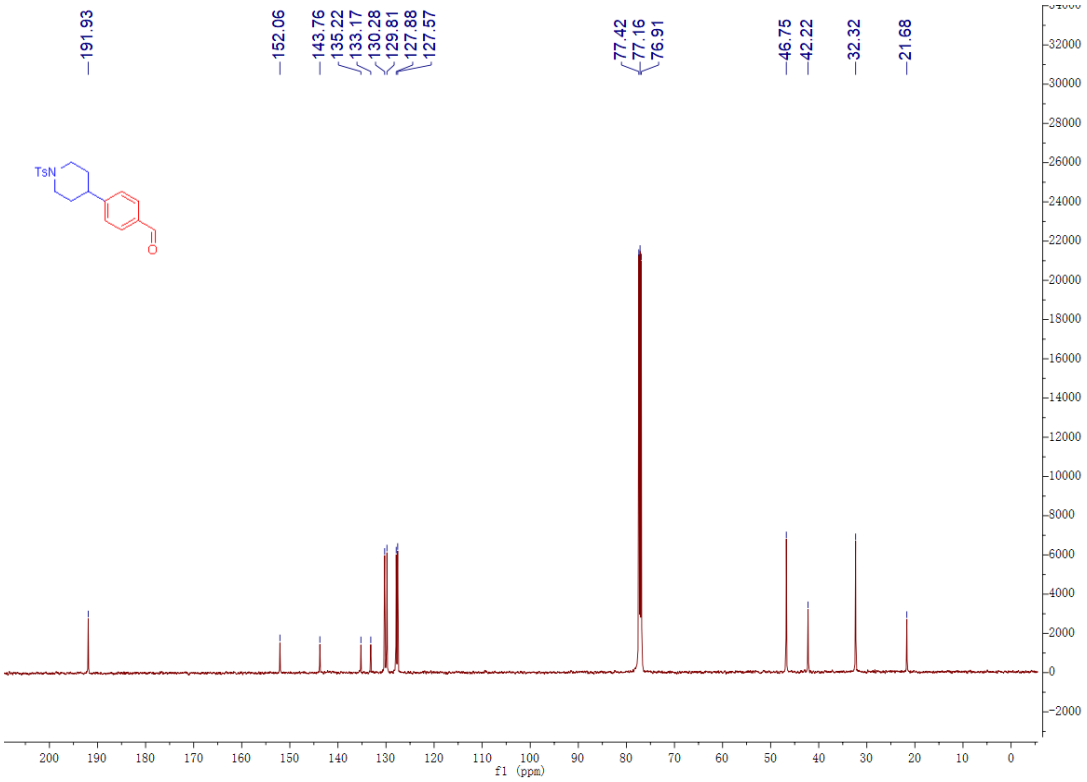
^{13}C NMR spectra of ethyl 3-(1-tosylpiperidin-4-yl)benzoate 5c



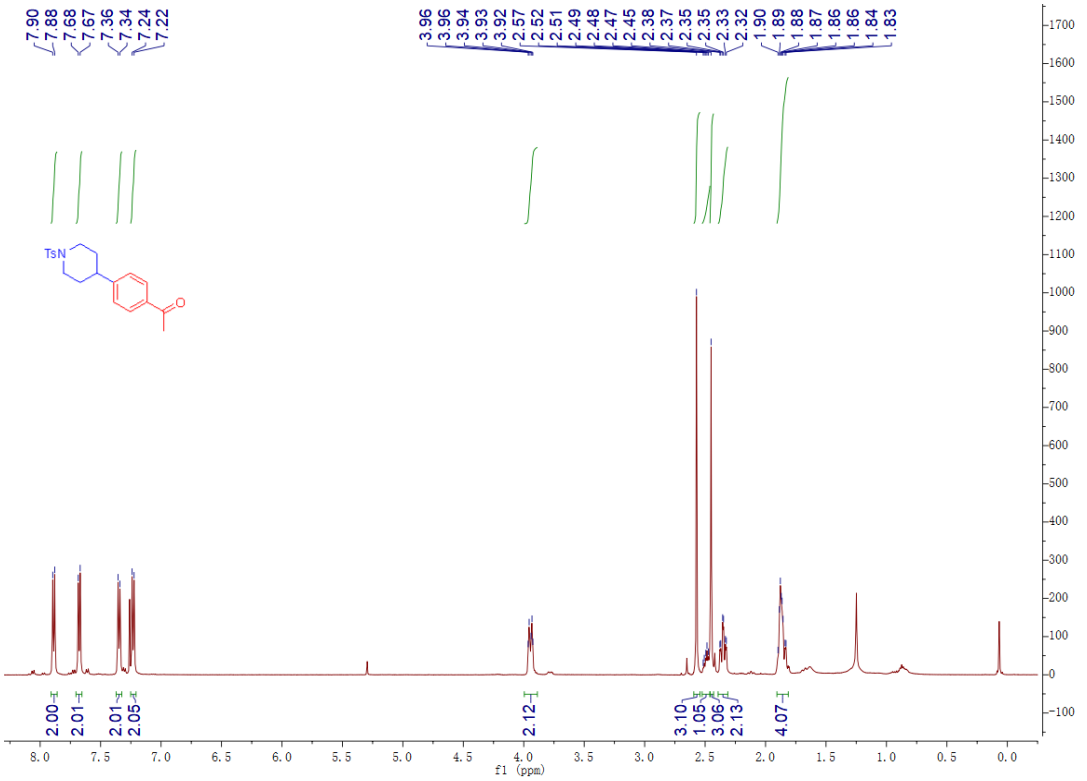
^{1}H NMR spectra of 4-(1-tosylpiperidin-4-yl)benzaldehyde 5d



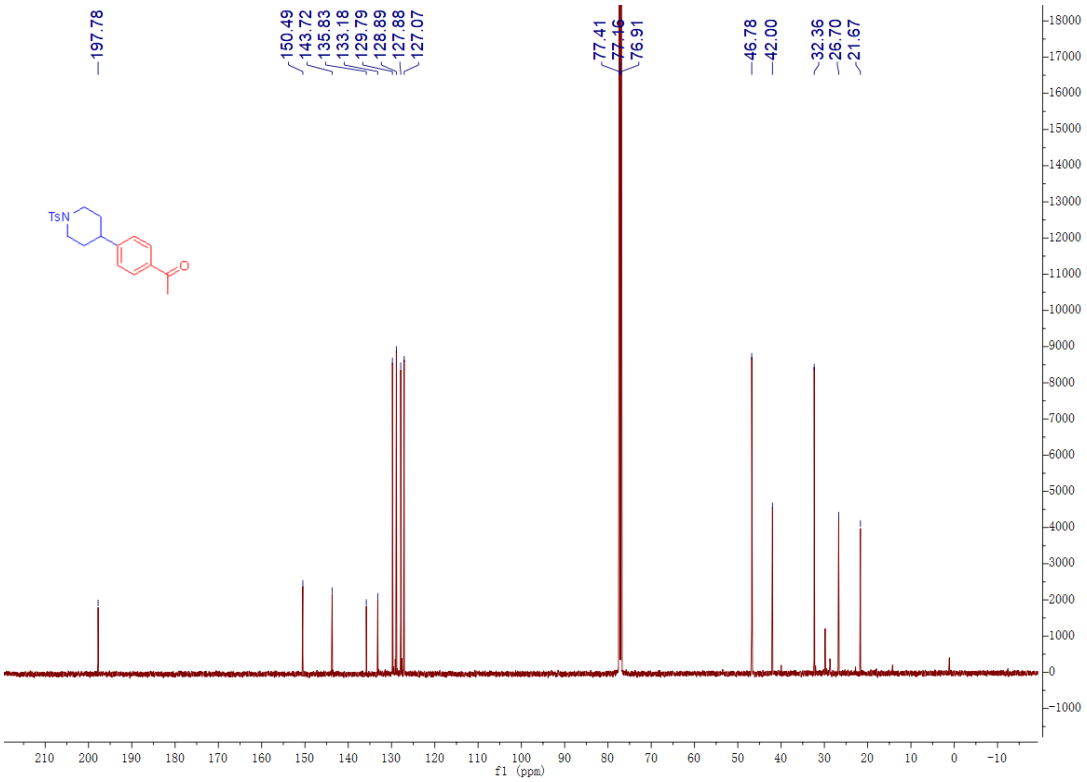
^{13}C NMR spectra of 4-(1-tosylpiperidin-4-yl)benzaldehyde 5d



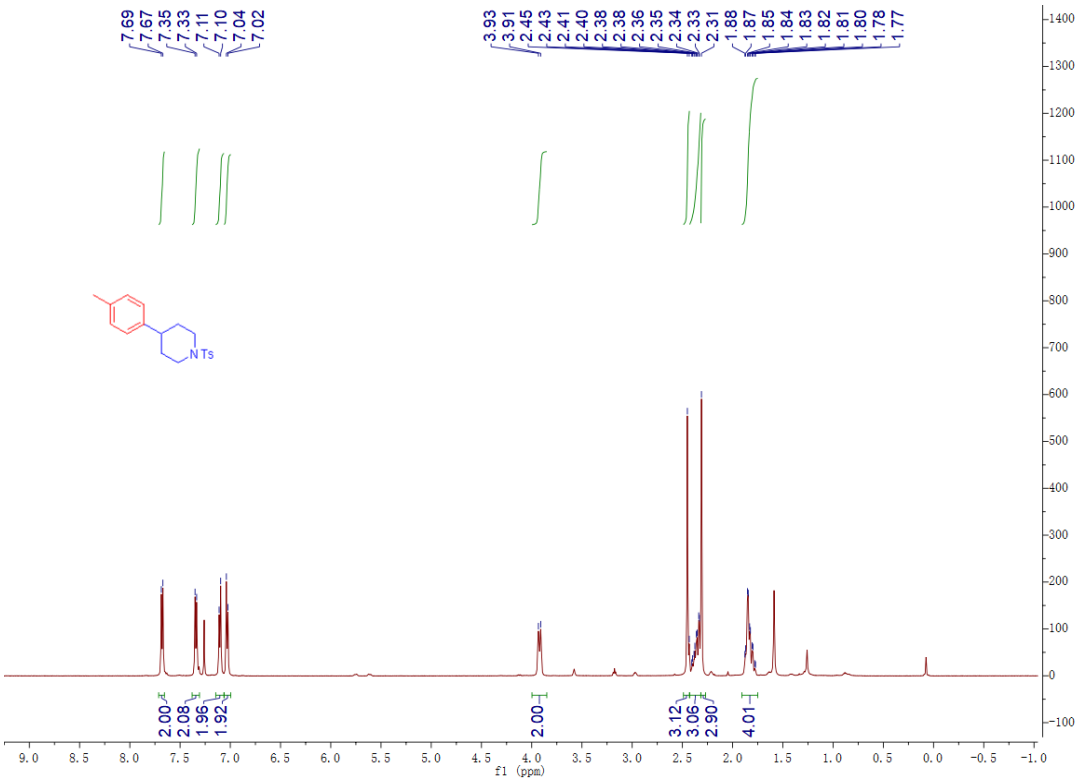
^{1}H NMR spectra of 1-(4-(1-tosylpiperidin-4-yl)phenyl)ethan-1-one 5e



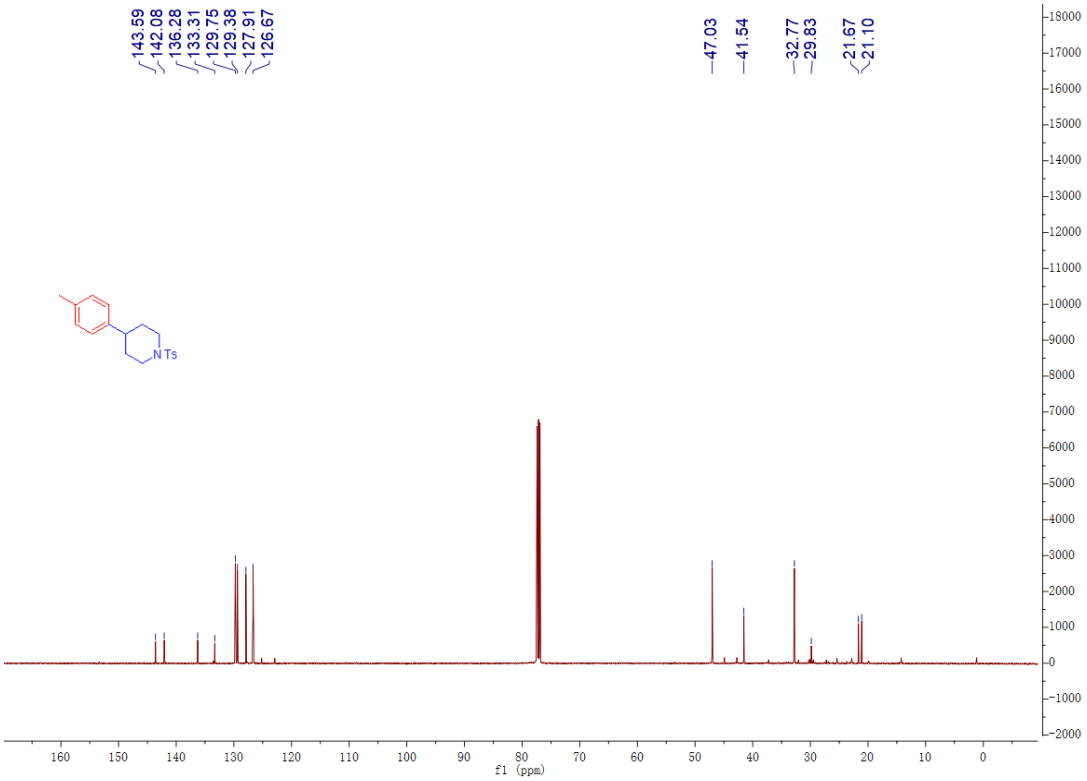
^{13}C NMR spectra of 1-(4-(1-tosylpiperidin-4-yl)phenyl)ethan-1-one 5e



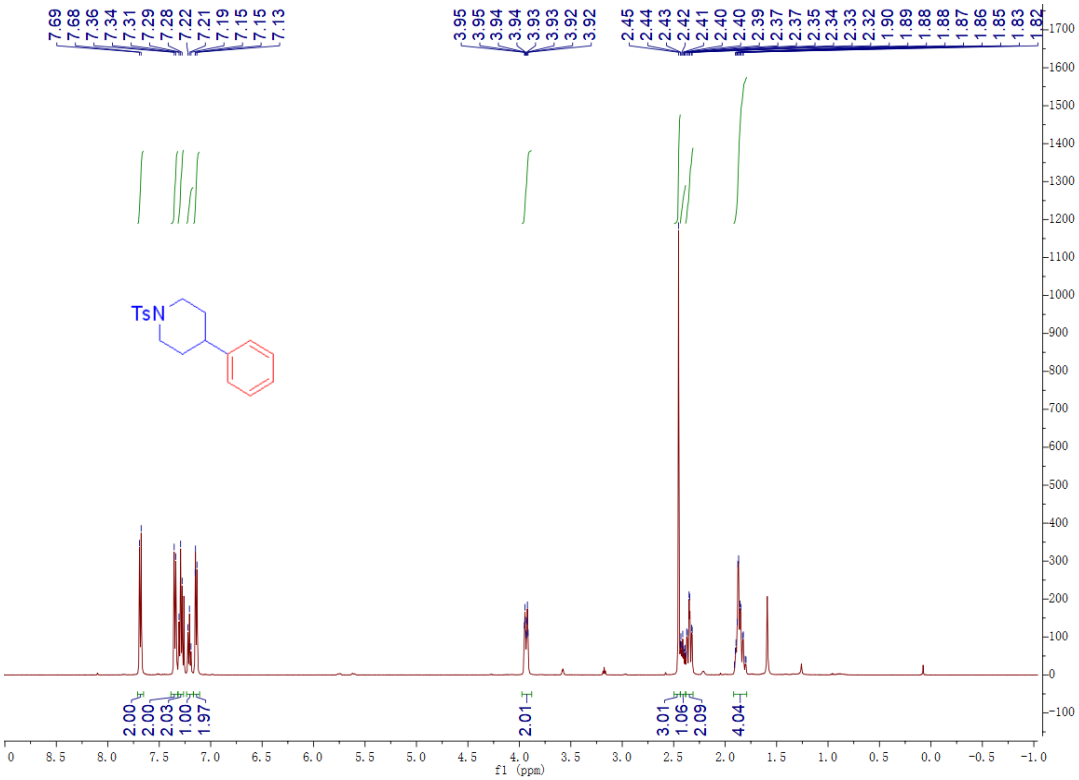
^{1}H NMR spectra of 4-(p-tolyl)-1-tosylpiperidine 5f



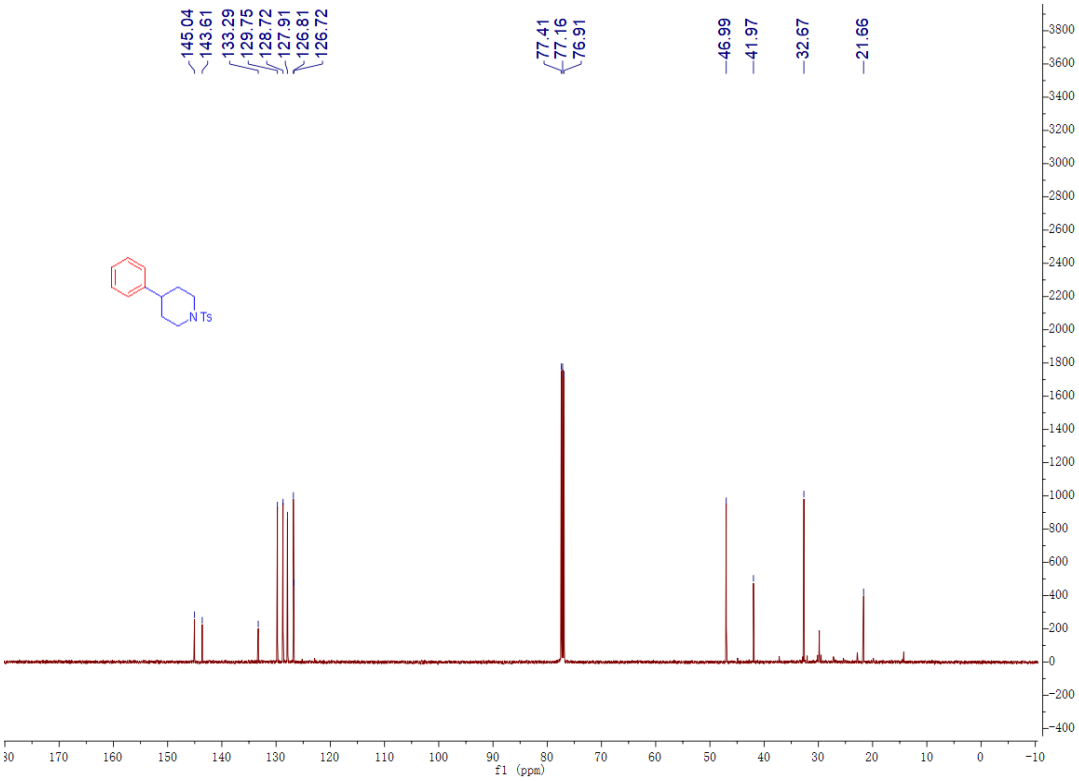
^{13}C NMR spectra of 4-(p-tolyl)-1-tosylpiperidine 5f



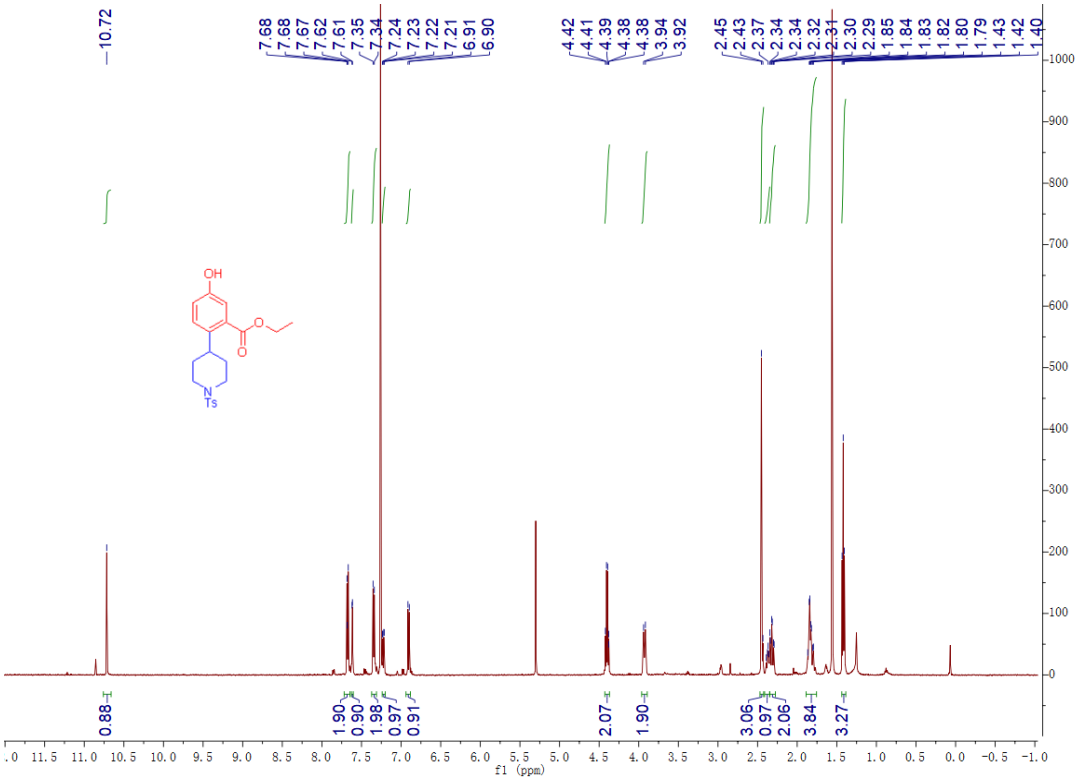
^{1}H NMR spectra of 4-phenyl-1-tosylpiperidine 5g



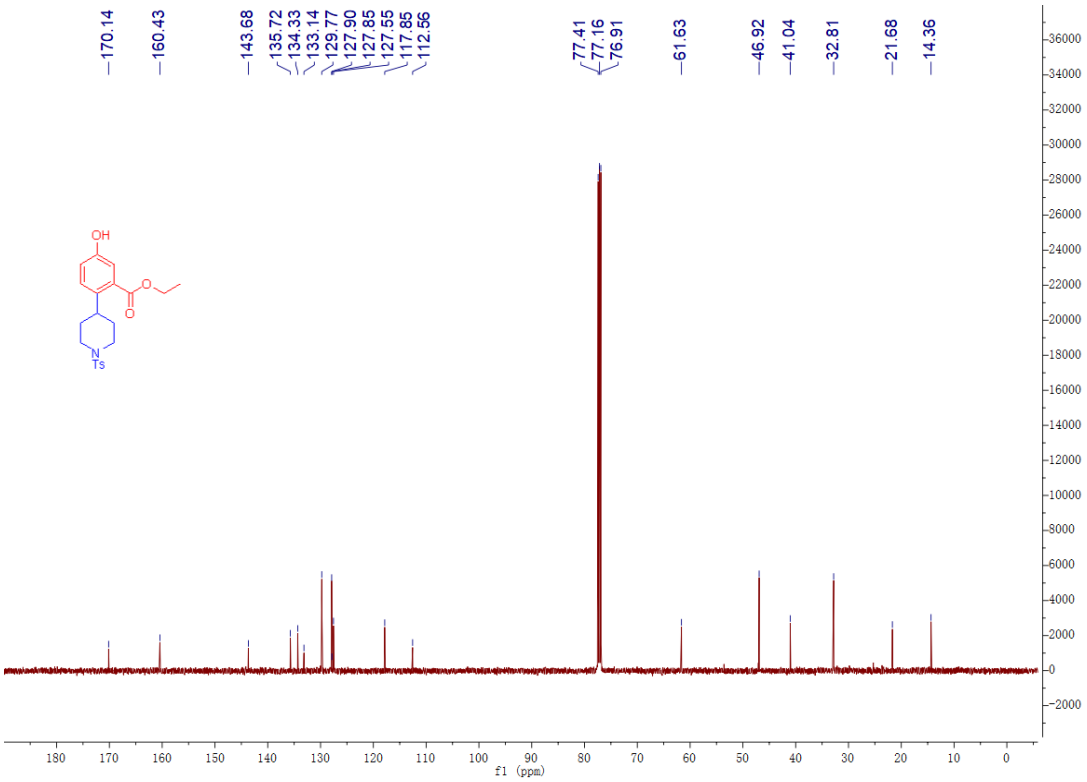
^{13}C NMR spectra of 4-phenyl-1-tosylpiperidine 5g



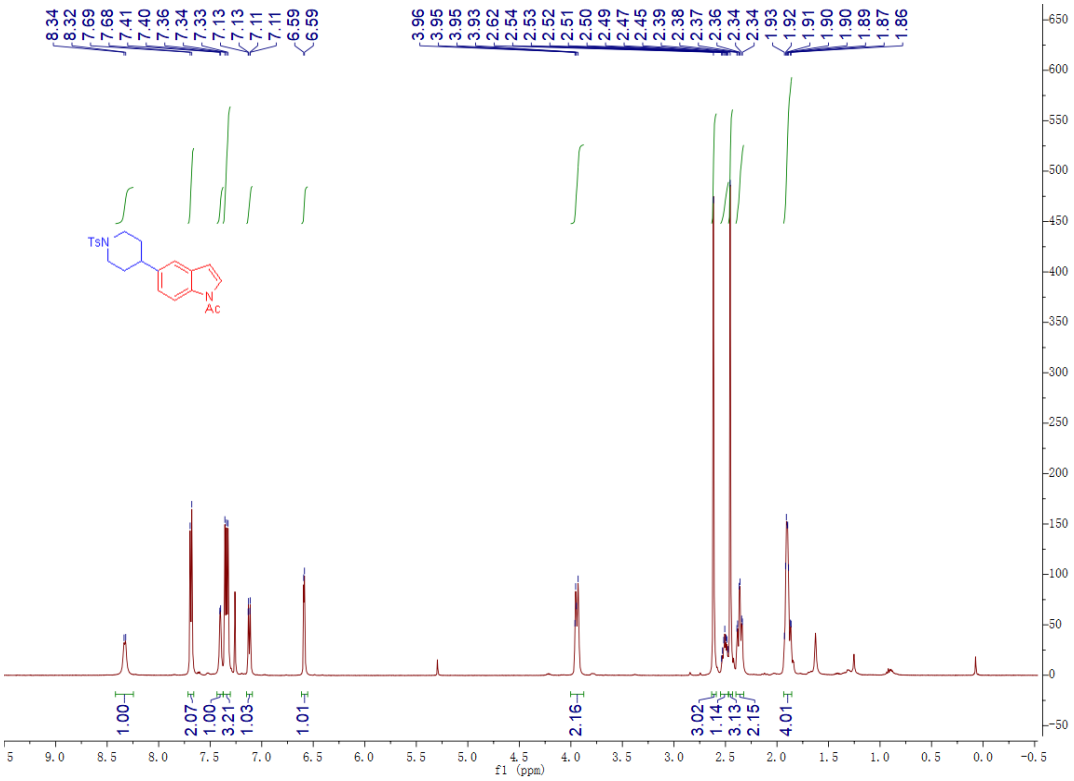
^{1}H NMR spectra of ethyl 5-hydroxy-2-(1-tosylpiperidin-4-yl)benzoate 5h



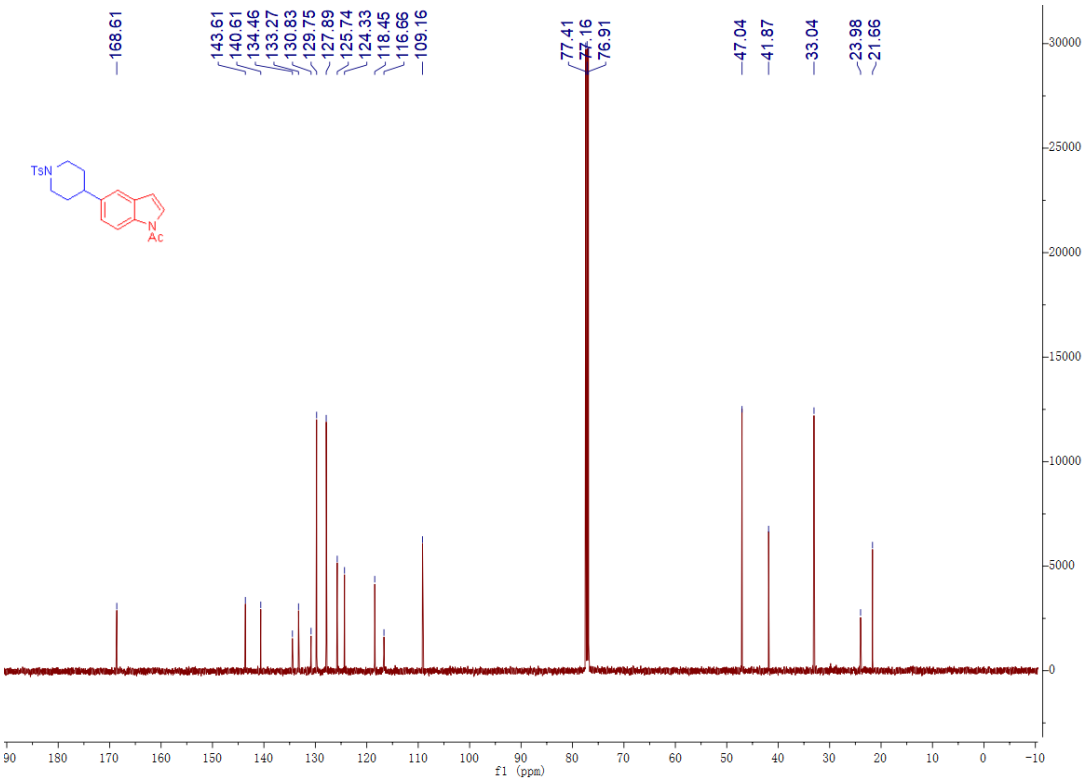
^{13}C NMR spectra of ethyl 5-hydroxy-2-(1-tosylpiperidin-4-yl)benzoate 5h



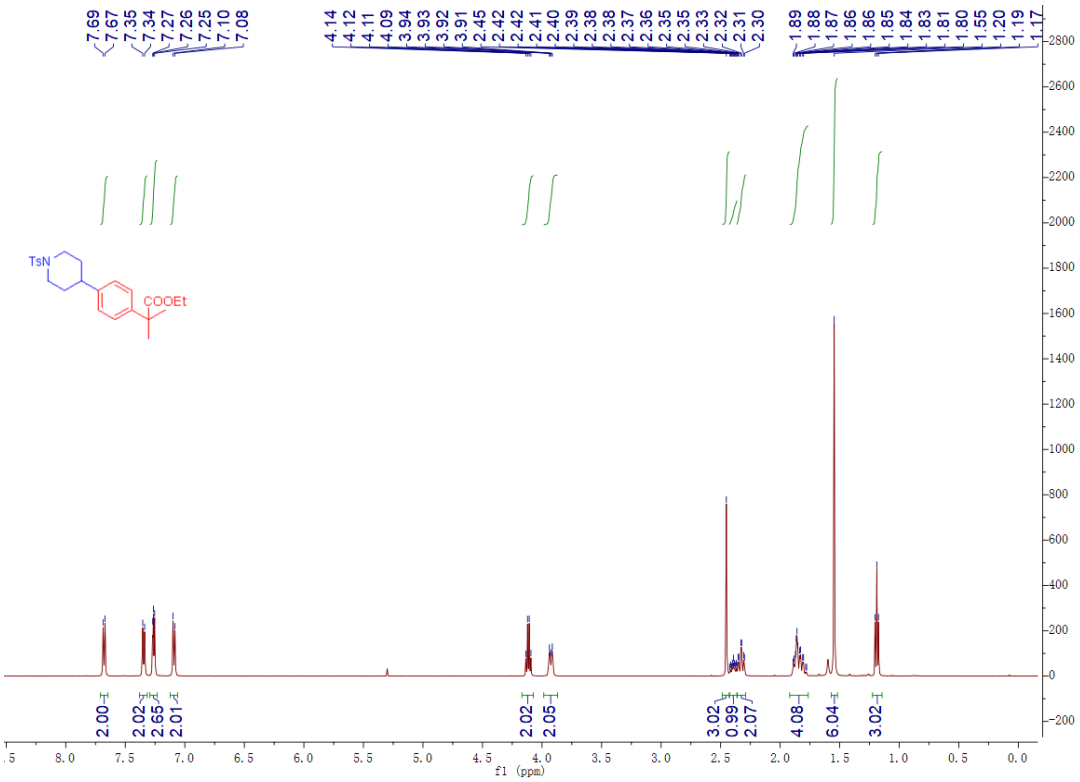
^{1}H NMR spectra of 1-(5-(1-tosylpiperidin-4-yl)-1H-indol-1-yl)ethan-1-one 5i



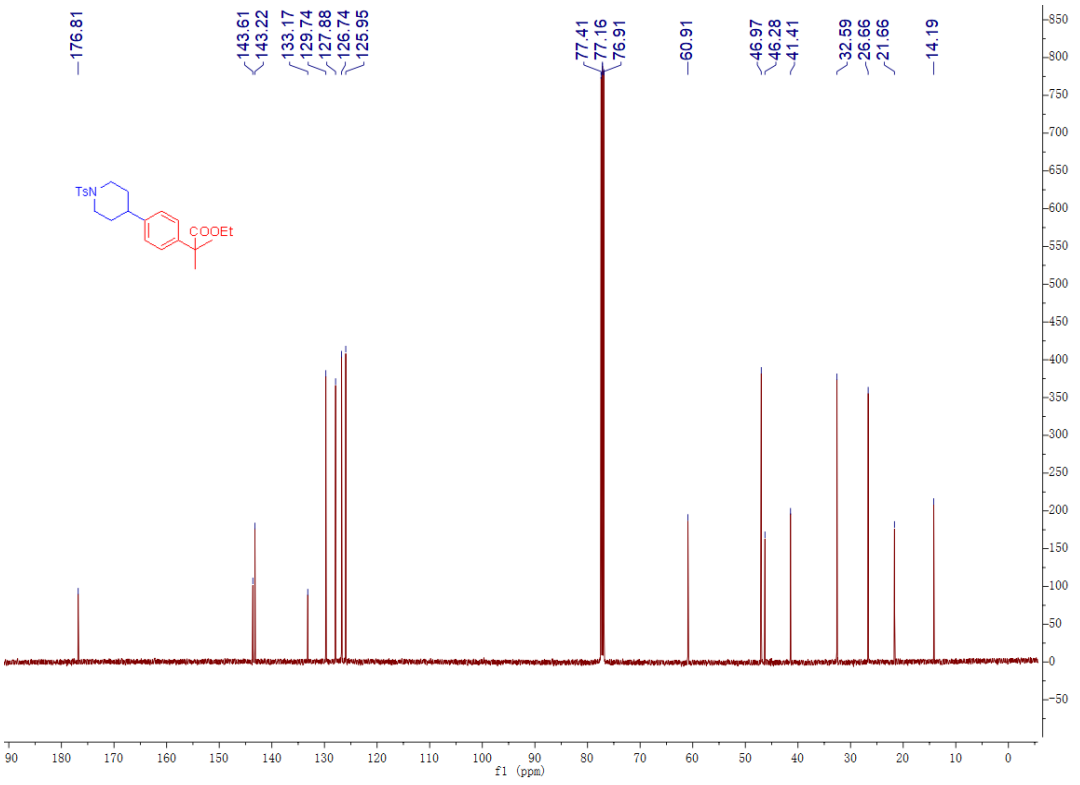
^{13}C NMR spectra of 1-(5-(1-tosylpiperidin-4-yl)-1H-indol-1-yl)ethan-1-one 5i



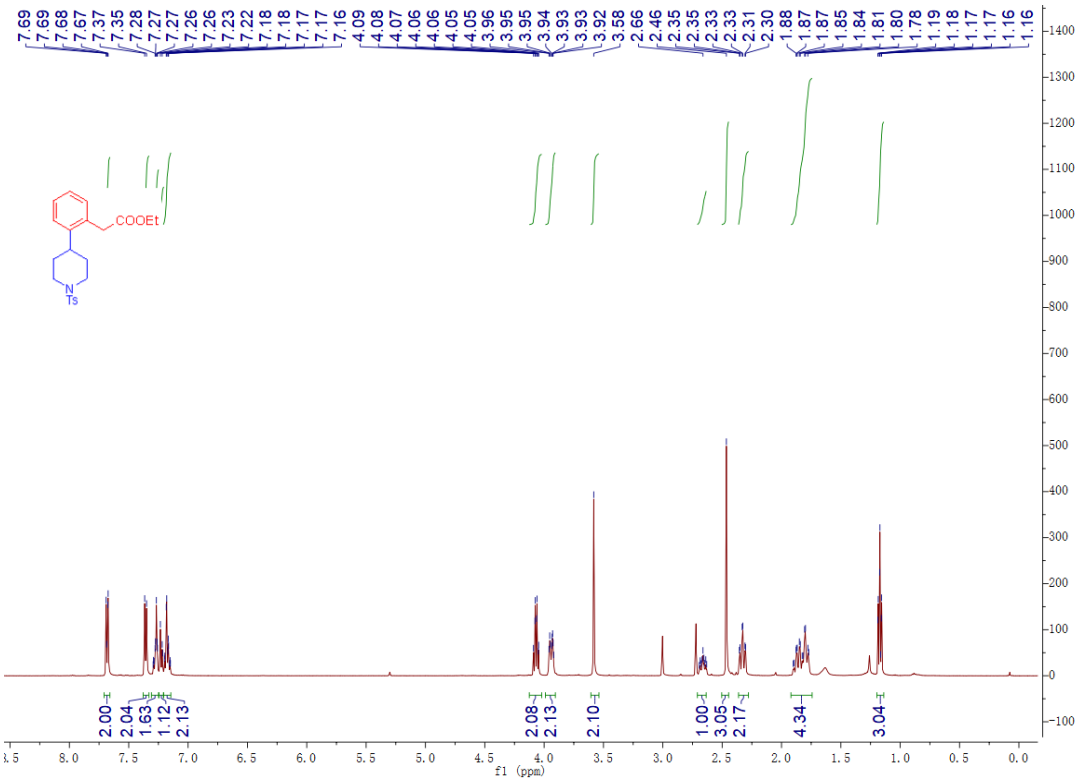
^{1}H NMR spectra of ethyl 2-methyl-2-(4-(1-tosylpiperidin-4-yl)phenyl)propanoate 5j



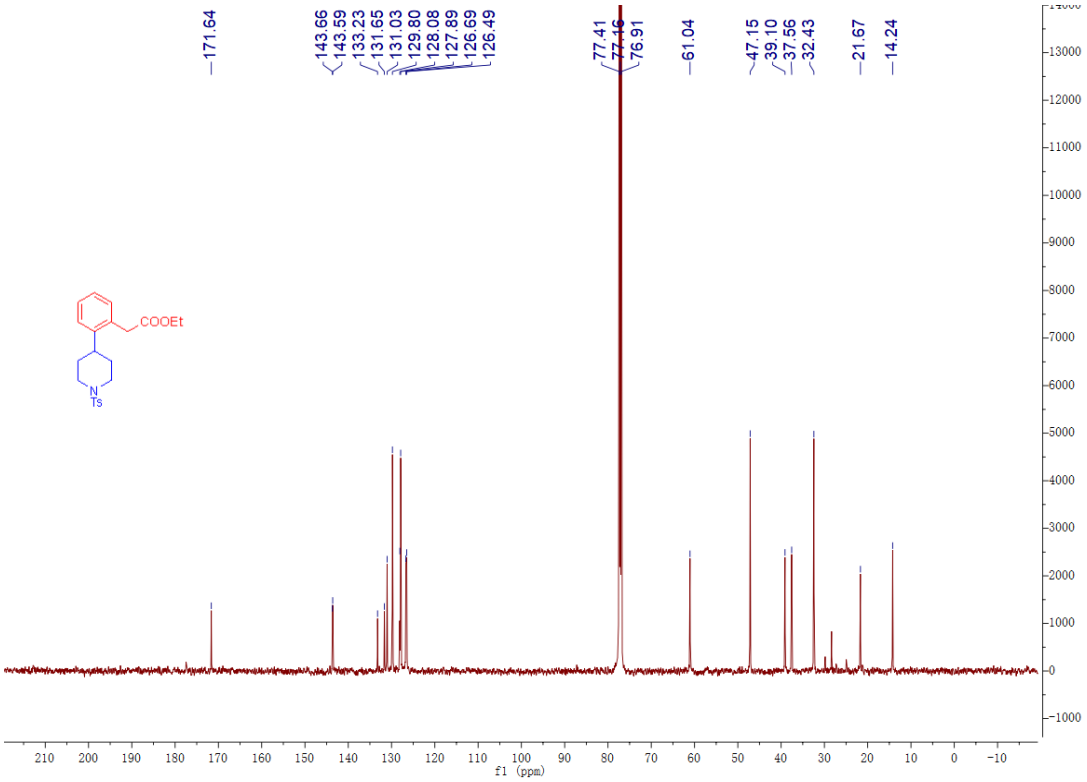
^{13}C NMR spectra of ethyl 2-methyl-2-(4-(1-tosylpiperidin-4-yl)phenyl)propanoate 5j



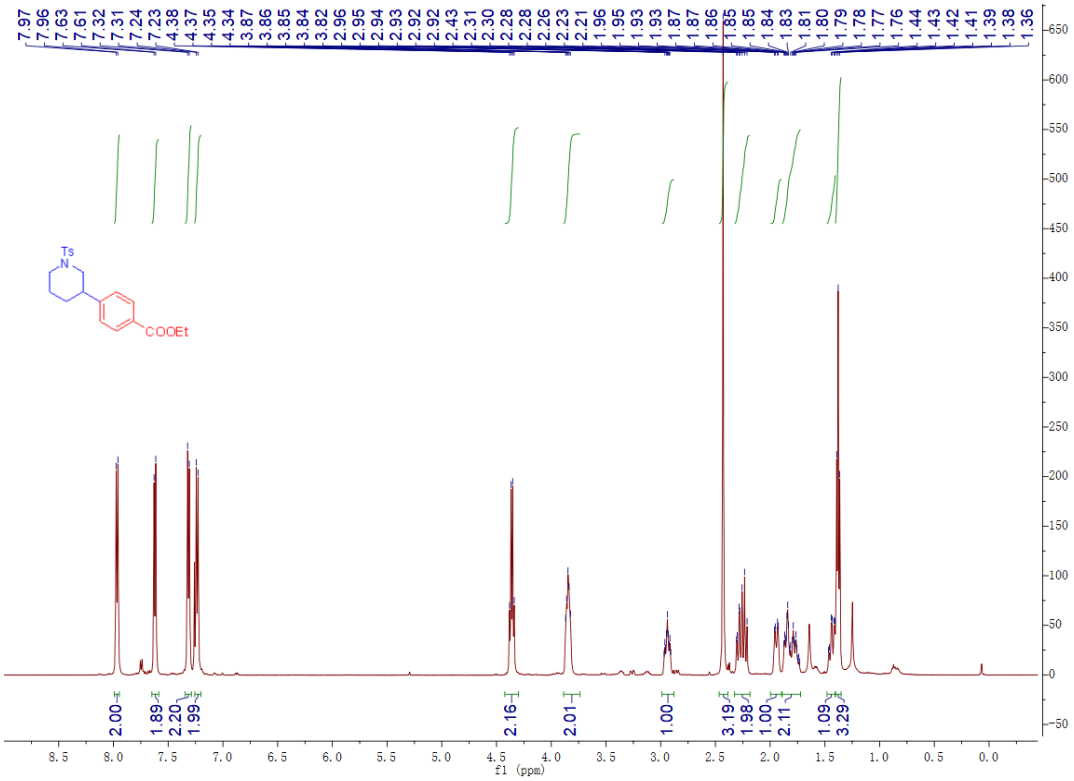
^{1}H NMR spectra of ethyl 2-(2-(1-tosylpiperidin-4-yl)phenyl)acetate 5k



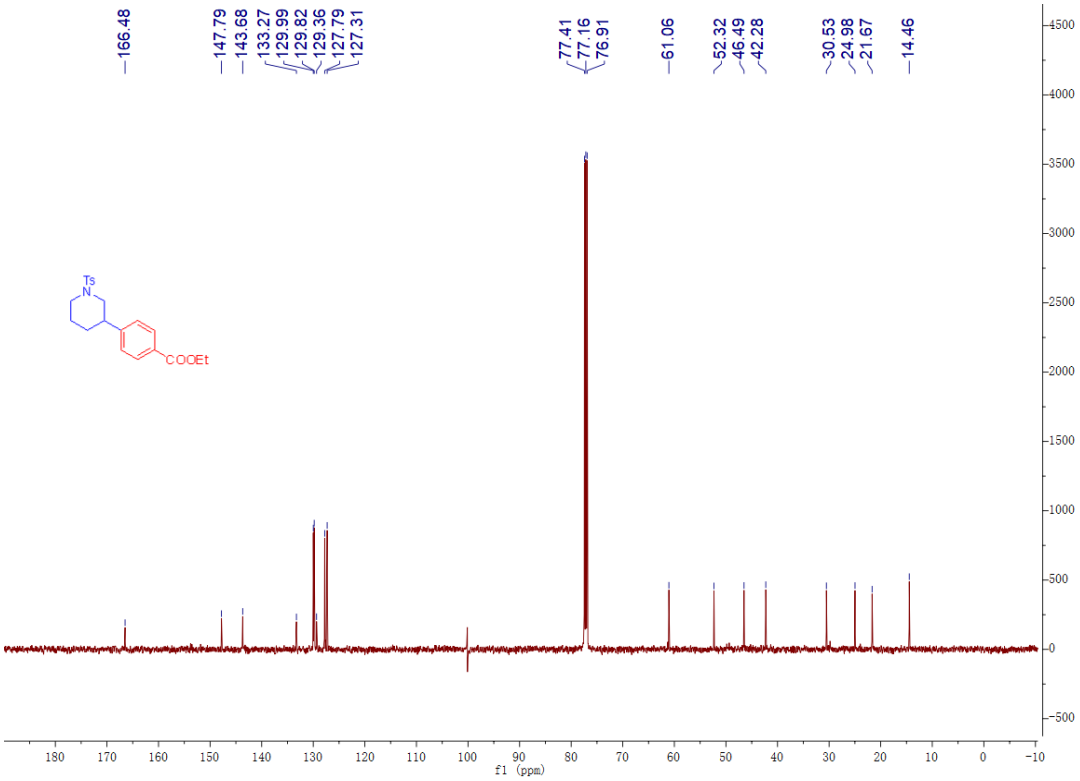
^{13}C NMR spectra of ethyl 2-(2-(1-tosylpiperidin-4-yl)phenyl)acetate 5k



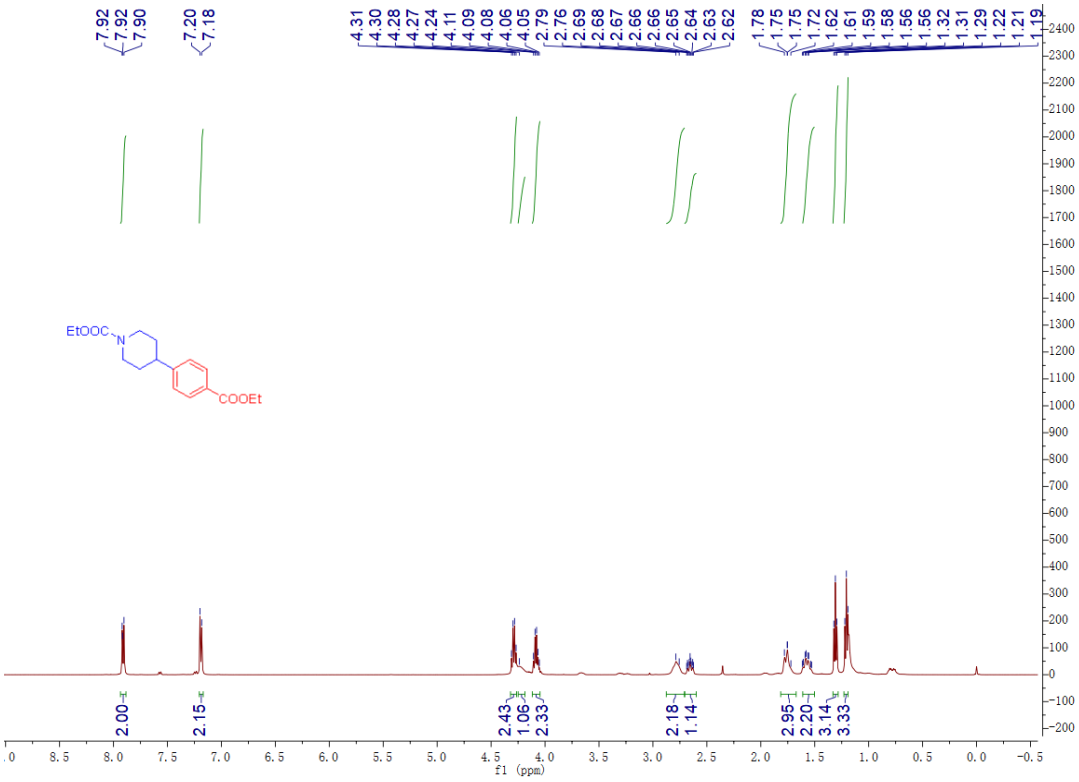
^{1}H NMR spectra of ethyl 4-(1-tosylpiperidin-3-yl)benzoate 5n



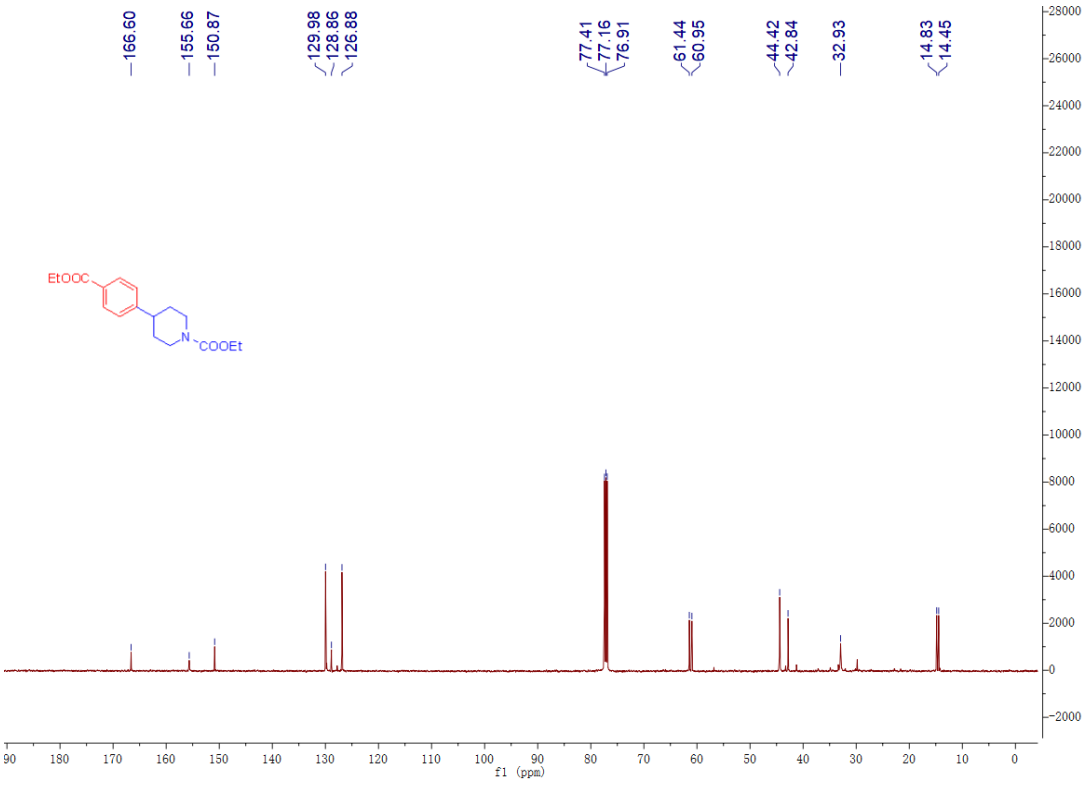
^{13}C NMR spectra of ethyl 4-(1-tosylpiperidin-3-yl)benzoate 5n



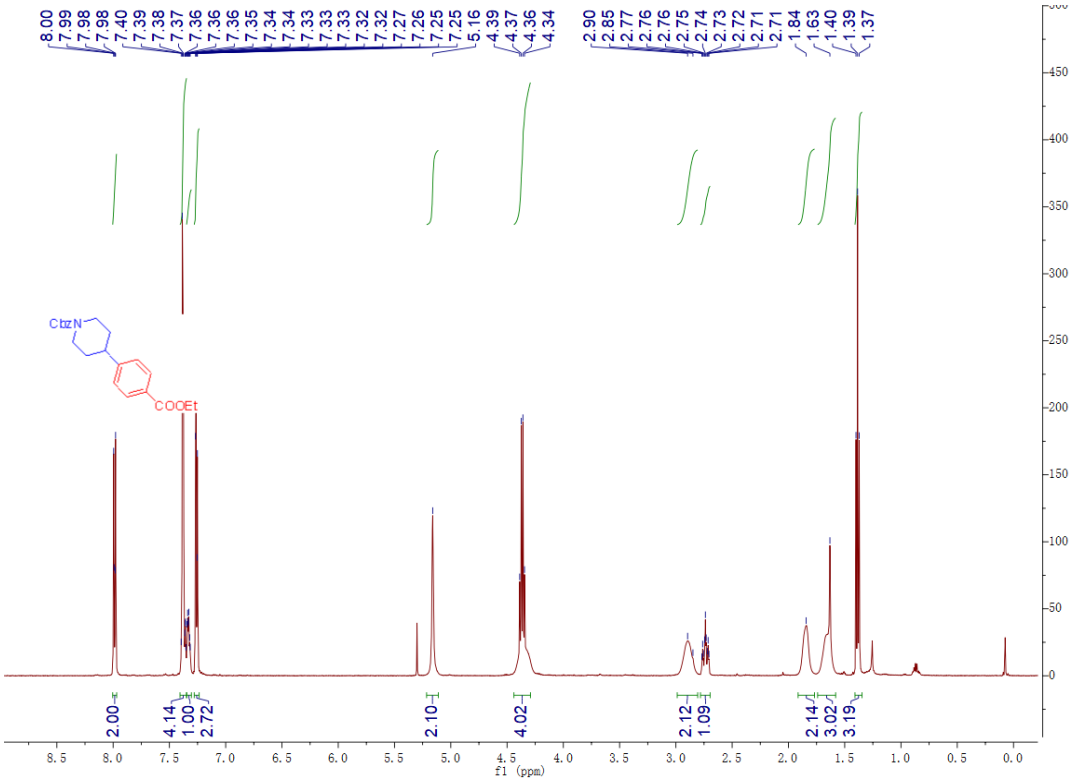
^{1}H NMR spectra of ethyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5o



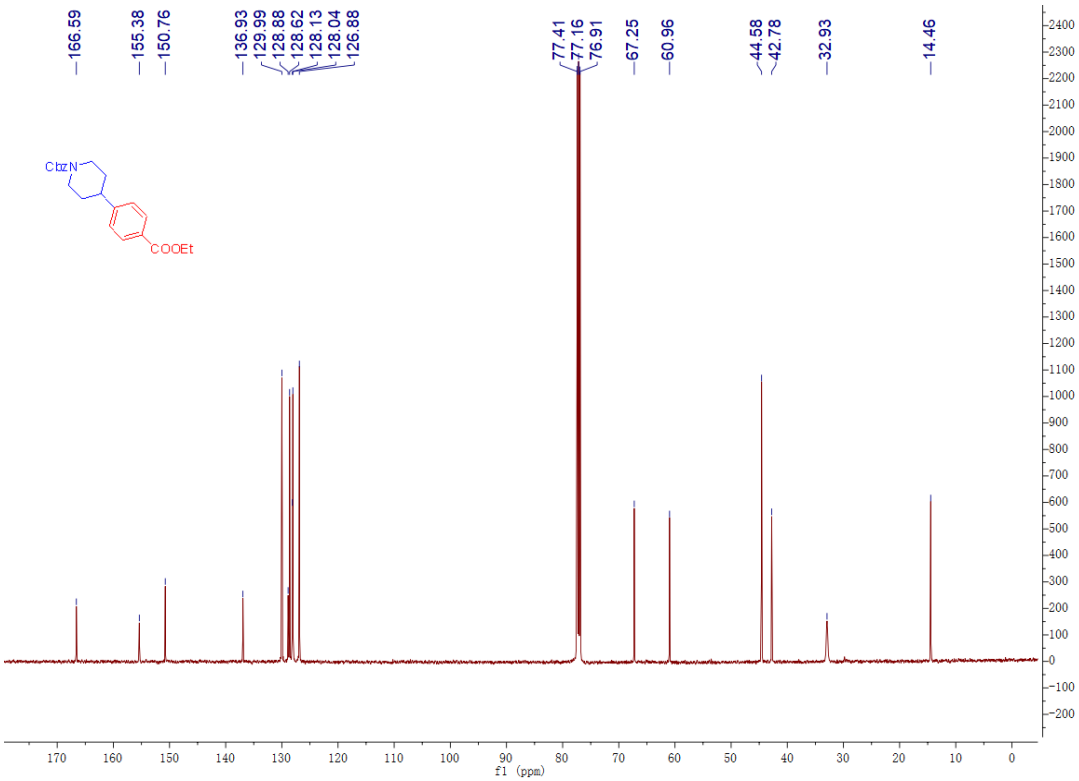
^{13}C NMR spectra of ethyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5o



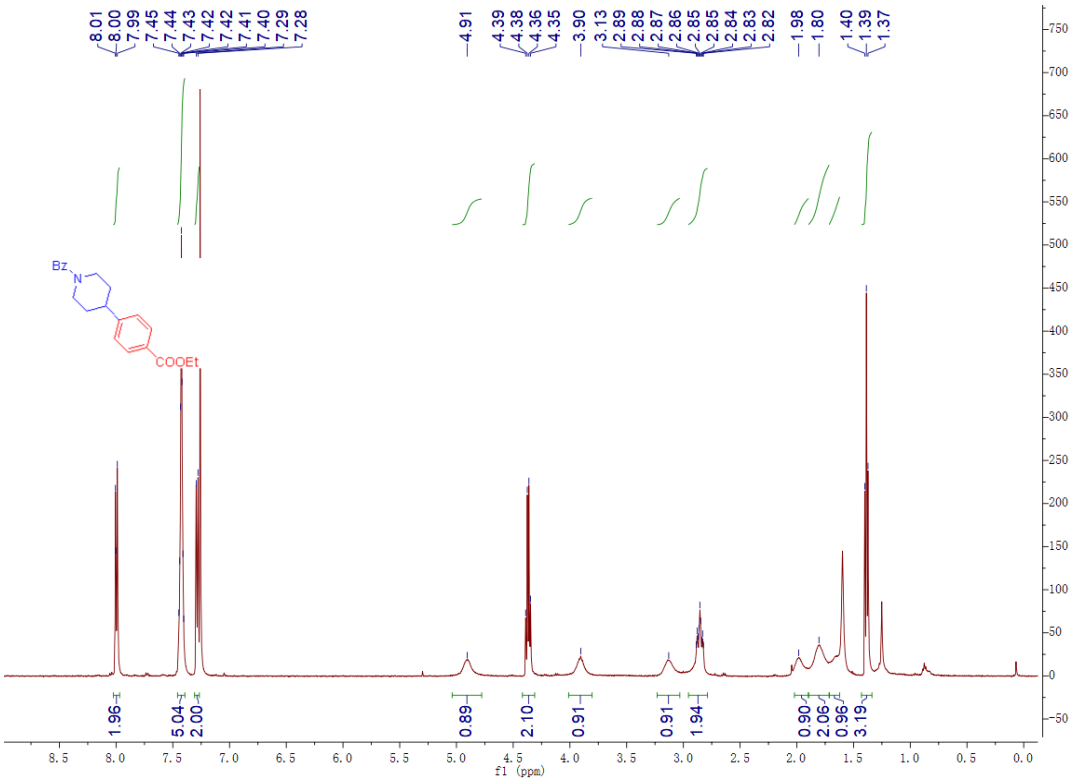
^{1}H NMR spectra of benzyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5p



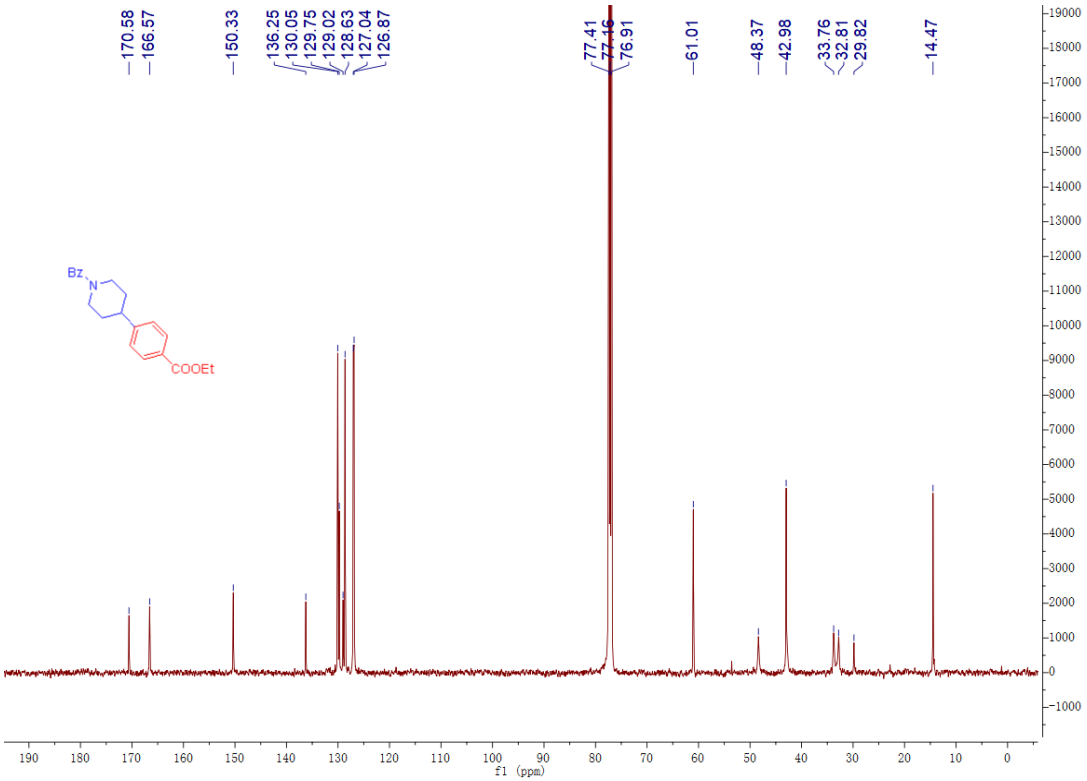
^{13}C NMR spectra of benzyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5p



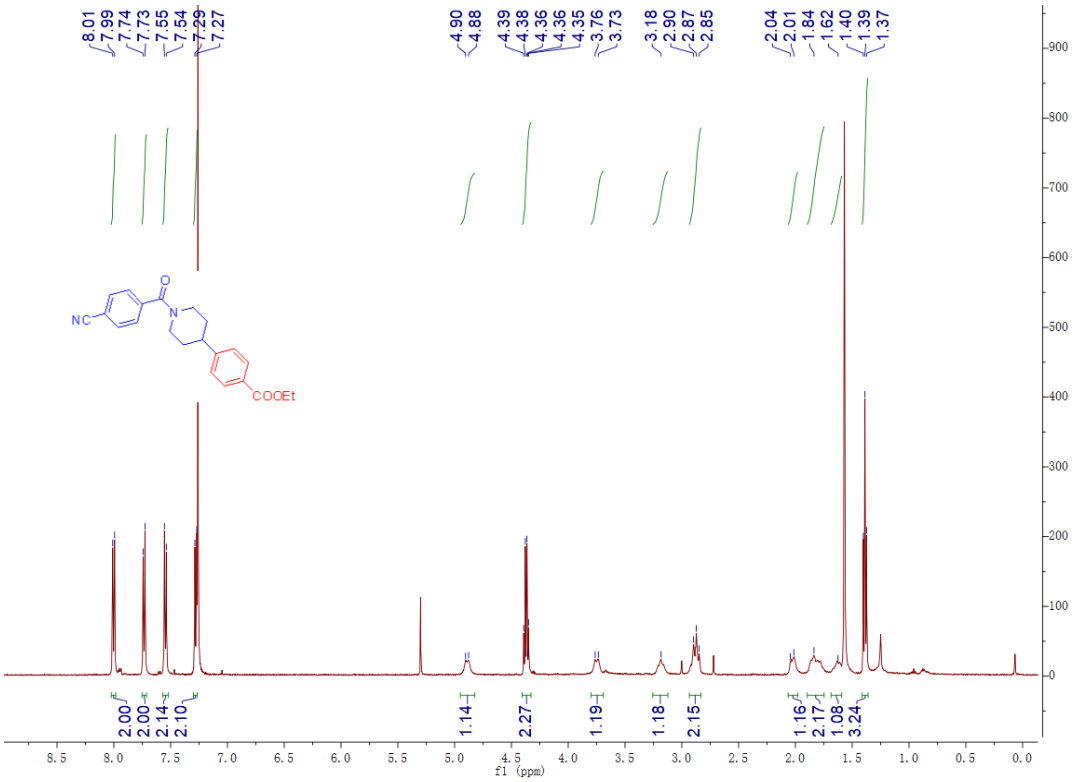
^{1}H NMR spectra of ethyl 4-(4-benzoylcyclohexyl)benzoate 5q



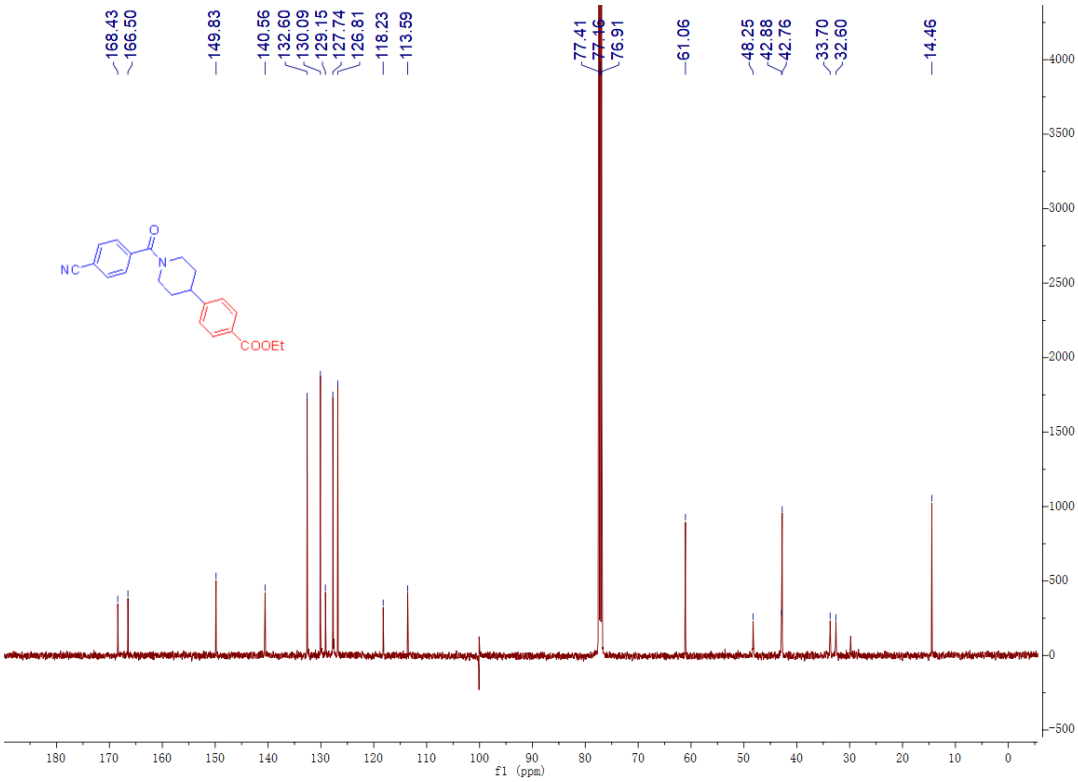
^{13}C NMR spectra of ethyl 4-(4-benzoylcyclohexyl)benzoate 5q



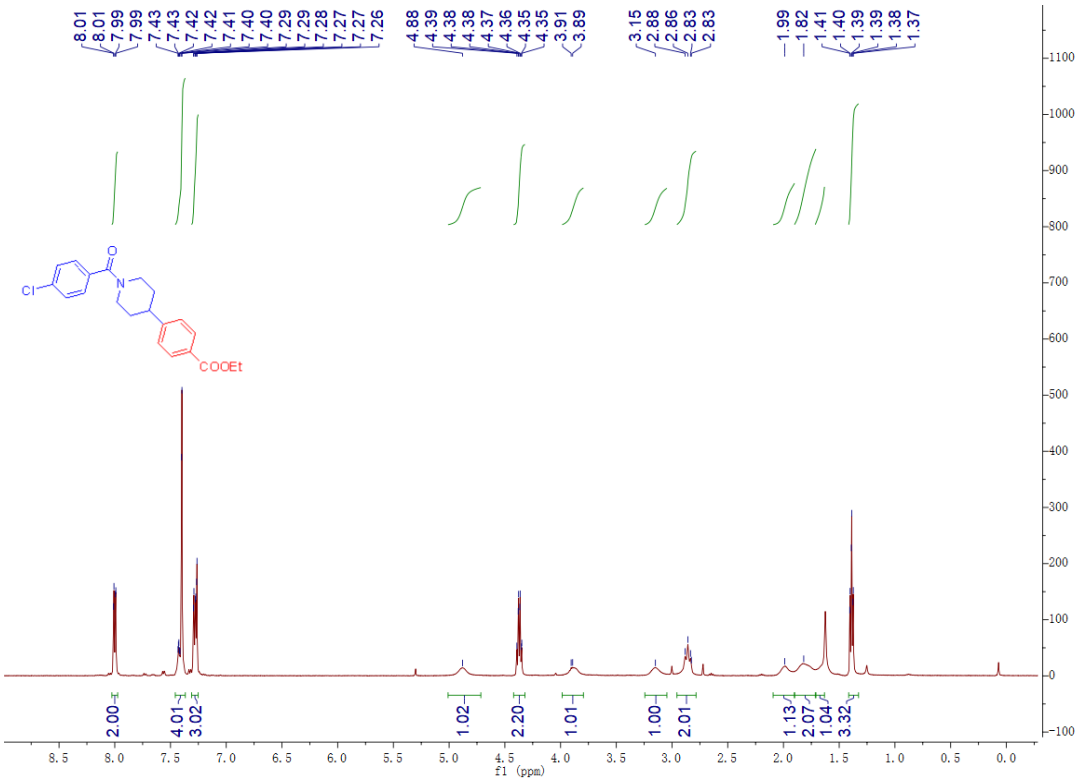
^{1}H NMR spectra of ethyl 4-(1-(4-cyanobenzoyl)piperidin-4-yl)benzoate 5r



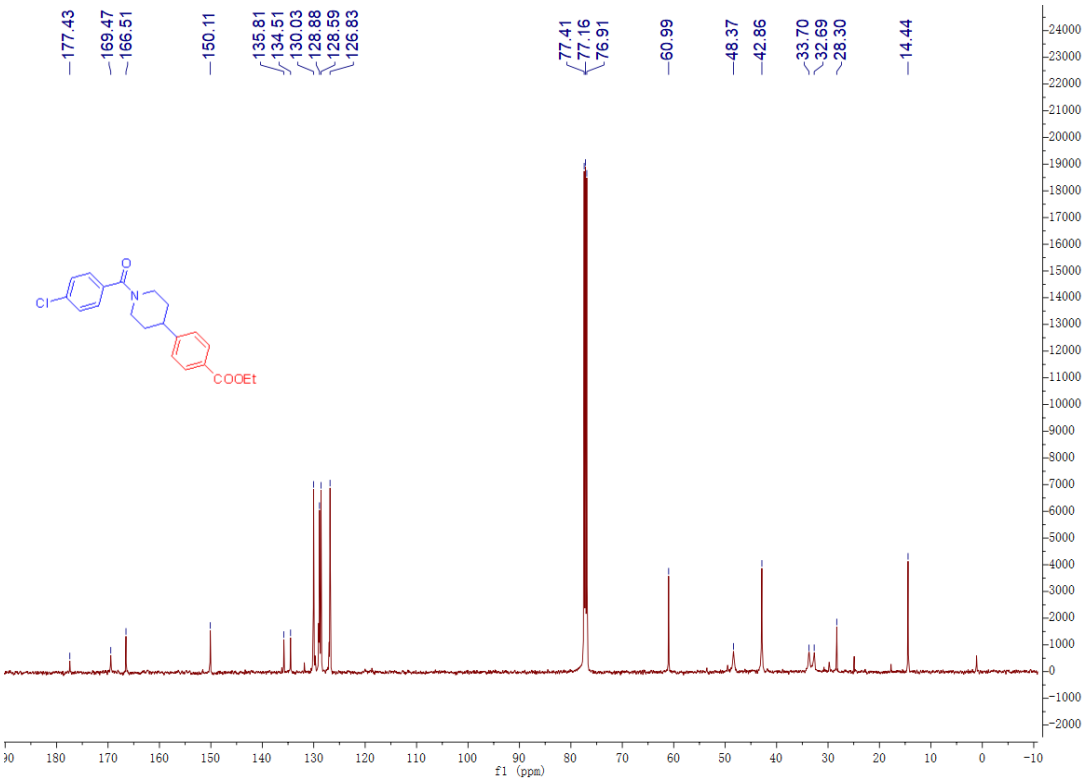
^{13}C NMR spectra of ethyl 4-(1-(4-cyanobenzoyl)piperidin-4-yl)benzoate 5r



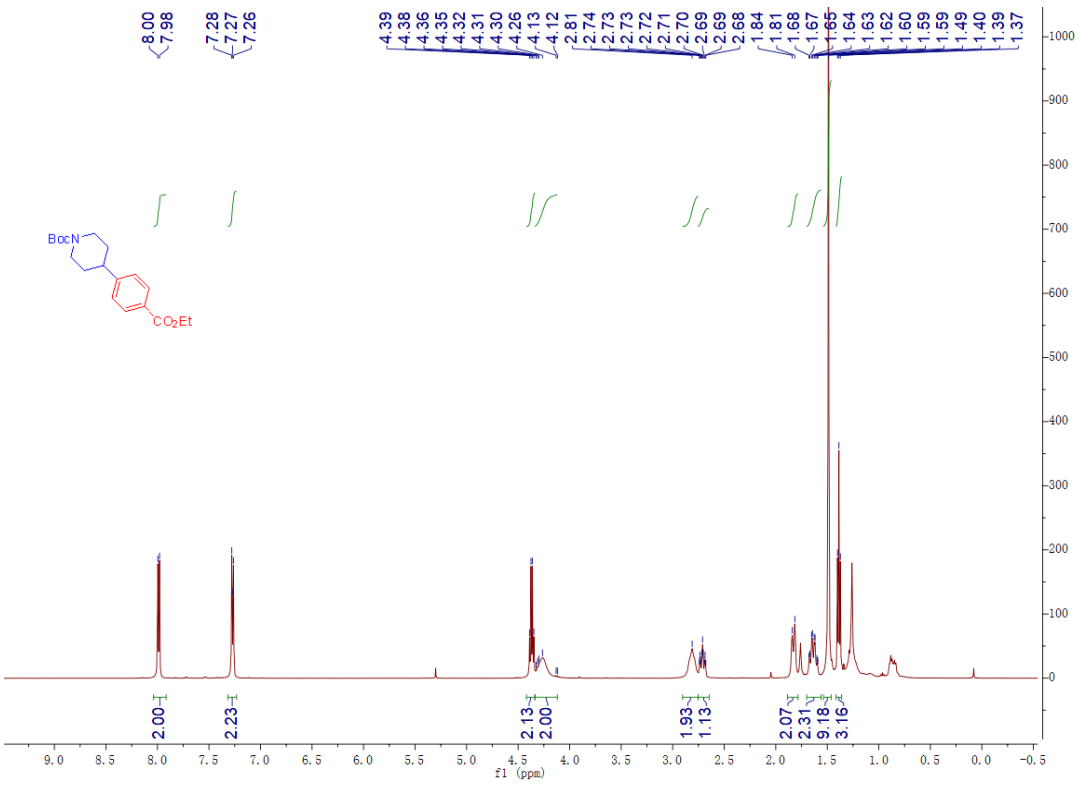
^{1}H NMR spectra of ethyl 4-(1-(4-chlorobenzoyl)piperidin-4-yl)benzoate 5s



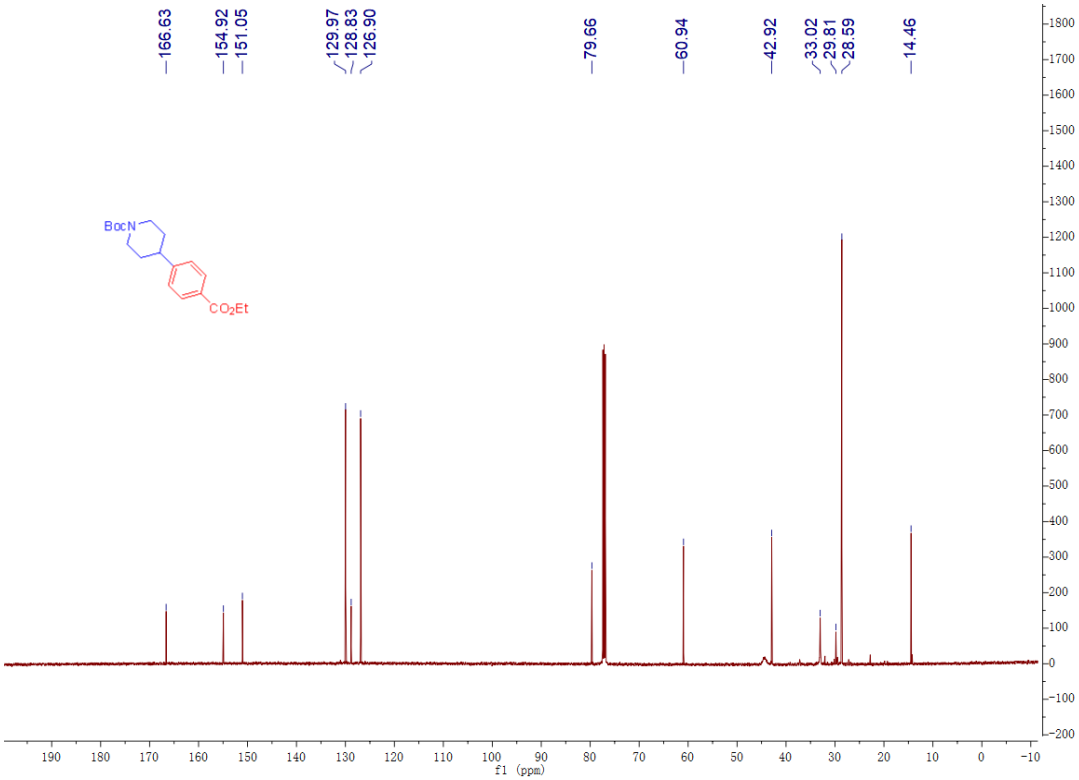
^{13}C NMR spectra of ethyl 4-(1-(4-chlorobenzoyl)piperidin-4-yl)benzoate 5s



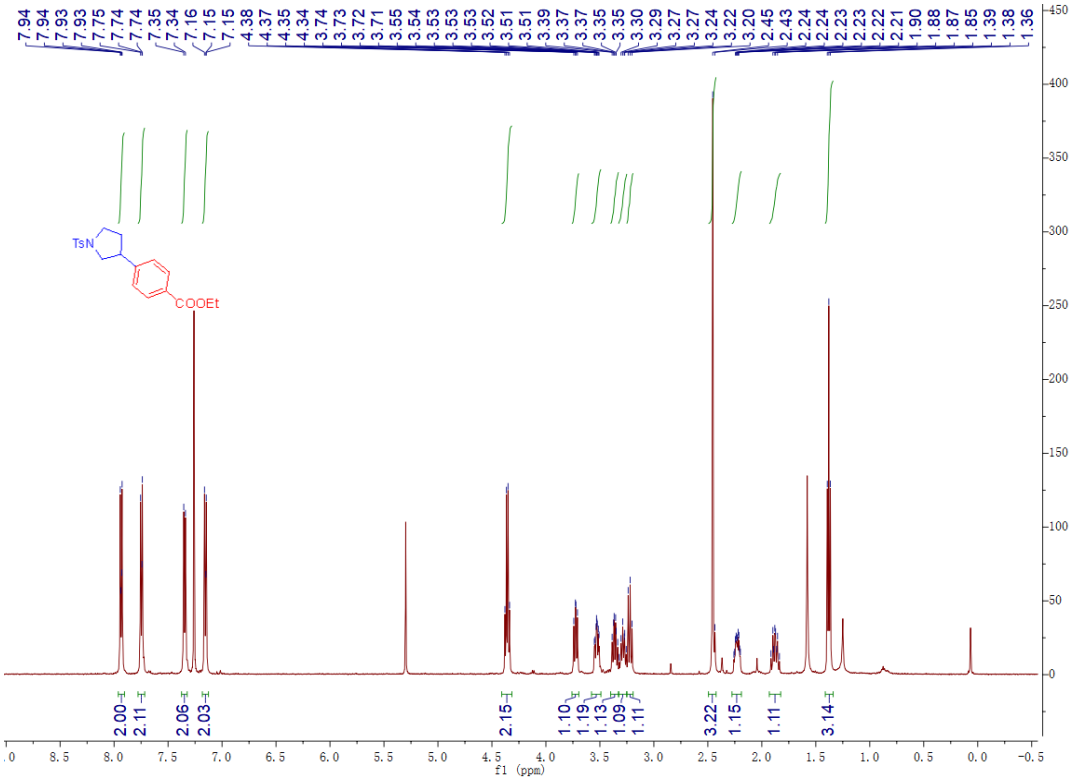
^{1}H NMR spectra of tert-butyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5t



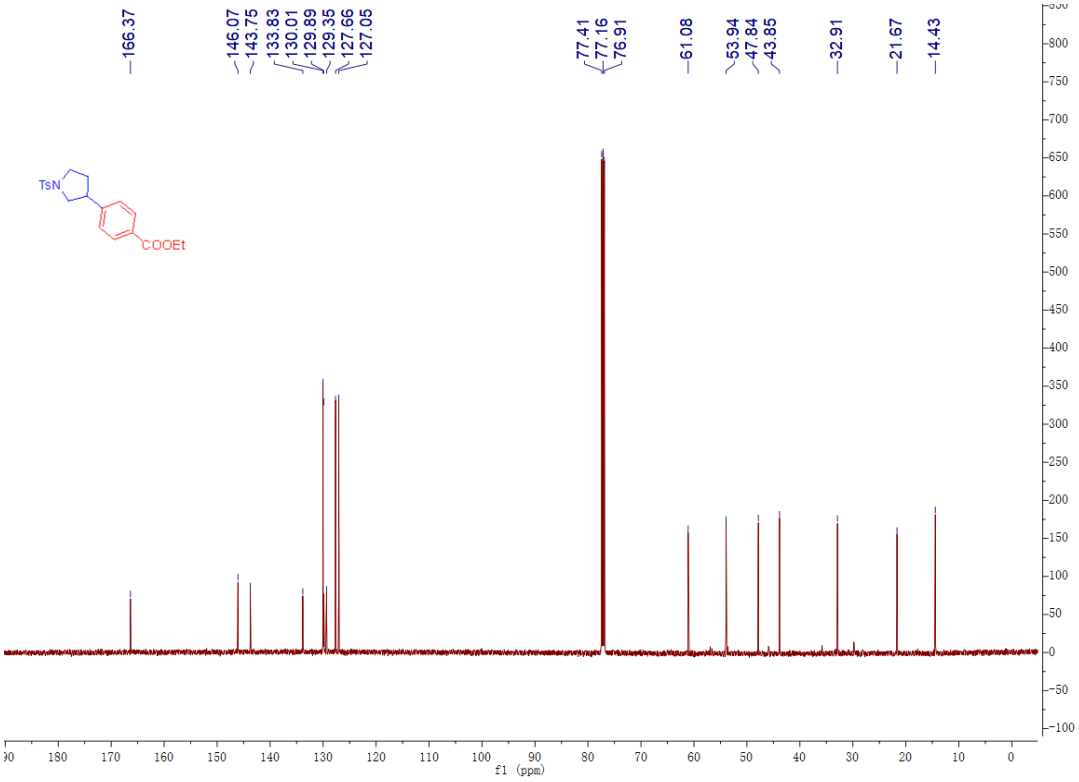
^{13}C NMR spectra of tert-butyl 4-(4-(ethoxycarbonyl)phenyl)piperidine-1-carboxylate 5t



^{1}H NMR spectra of ethyl 4-(1-tosylpyrrolidin-3-yl)benzoate 5u



^{13}C NMR spectra of ethyl 4-(1-tosylpyrrolidin-3-yl)benzoate 5u



III. References

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