Enantioselective Synthesis of Spiroindolines via Cascade Isomerization/Spirocyclization/Dearomatization Reaction

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Supporting Information

Contents

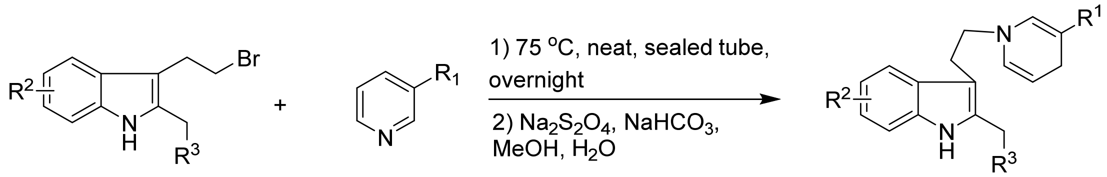
1. General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvent were treated according to general methods. Flash column chromatography was performed using 200-300 mesh silica gel. All reactions were carried out in flame-dried glassware under a dry argon atmosphere, glassware was dried in an oven at 150 °C or flame dried and cooled under a dry atmosphere. Reactions were monitored by TLC and visualized by a dual short wave/long wave UV lamp. ^{1}H NMR spectra were recorded on Bruker 400 / 600 (400 / 600 MHz) spectrophotometers. Chemical shifts (δ) are reported in ppm from the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet or unresolved, br = broad, dd = doublet of doublets, q = quartet, coupling constant (s) in Hz, integration). ^{13}C NMR spectra were recorded on Bruker 400 / 600 (101 / 151 MHz) with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm). Mass spectra were measured on a MS spectrometer.

2. Experimental section

2.1 General procedure for preparation of indolyl dihydropyridines 1a, 1b, 1c, 1h, 1i, 1j, 1s.

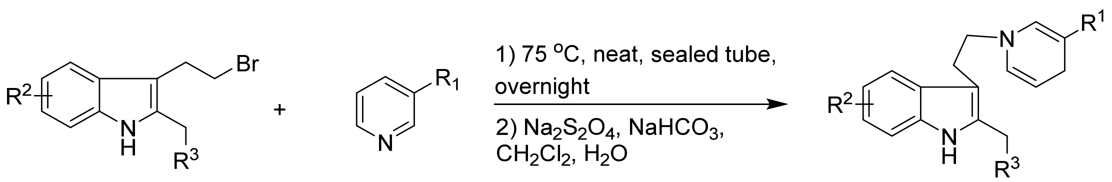
The reduction of substituted pyridinium bromide was accomplished following the reported procedures.



A mixture of substituted tryptophyl bromide (1.0 eq) and 3-substituted pyridine (1.2 eq) was heated through oil bath at 75 ºC overnight in sealed tube. The mixture was cooled to rt, crushed to grains, stirred in ethyl acetate, and filtered. The obtained pyridinium bromide was first dissolved in MeOH under argon, then added H_2O (MeOH:H_2O = 1:2). Stirred for a moment, $NaHCO_3$ (16.0 eq) was added in one portion. The mixture was degassed three times by applying vacuum, and backfilling with nitrogen while stirring vigorously. Sodium dithionite (6.2 eq) was then added in portions over in 1 hour to this stirred solution. The reaction was stirred overnight at room temperature. After the reaction was complete (by TLC analysis), the mixture was extracted by CH_2Cl_2 (3×30 mL). The combined dichloromethane layer was washed with brine, dried over Na_2SO_4 and filtrated. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/1) to afford product **1**.

2.2 General procedure for preparation of indolyl dihydropyridines 1d, 1e, 1f, 1g, 1l, 1m, 1n, 1o, 1p, 1q, 1r, 1t, 1u, 1v, 1w.

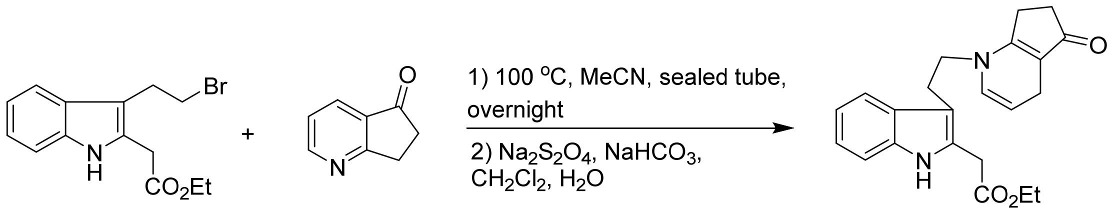
The reduction of substituted pyridinium bromide was accomplished following the reported procedures.



A mixture of substituted tryptophyl bromide (1.0 eq) and 3-substituted pyridine (1.2 eq) was heated through oil bath at 75 °C overnight in sealed tube. The mixture was cooled to rt, crushed to grains, stirred in ethyl acetate, and filtered. The obtained pyridinium bromide was first dissolved in CH_2Cl_2 under argon, then added H_2O (CH_2Cl_2:H_2O = 1:2). Stirred for a moment, $NaHCO_3$ (16.0 eq) was added in one portion. The mixture was degassed three times by applying vacuum, and backfilling with nitrogen while stirring vigorously. Sodium dithionite (6.2 eq) was then added in one portion at 0 °C. The reaction was stirred overnight at room temperature,After the reaction was complete (by TLC analysis) The mixture was extracted by CH_2Cl_2 (3×30 mL). The combined dichloromethane layer was washed with brine, dried over Na_2SO_4 and filtrated. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/1) to afford product **1**.

2.3 Procedure for preparation of indolyl dihydropyridines 1k.

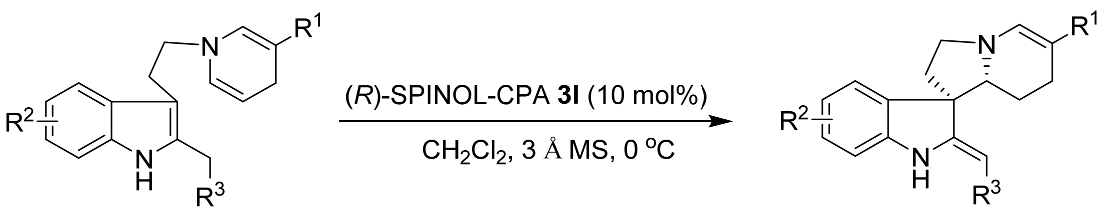
The reduction of substituted pyridinium bromide was accomplished following the reported procedures.



1k

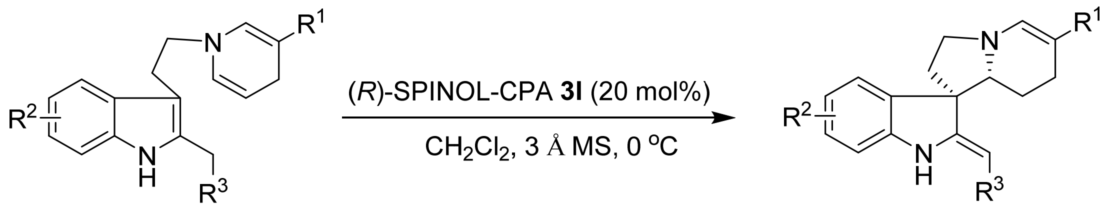
A mixture of substituted tryptophyl bromide (1.0 eq), 3-substituted pyridine (1.2 eq), and 2 mL MeCN was heated through oil bath at 100 °C overnight in sealed tube. The mixture was cooled to rt, crushed to grains, stirred in ethyl acetate, and filtered. The obtained pyridinium bromide was first dissolved in CH_2Cl_2 under argon, then added H_2O (CH_2Cl_2:H_2O = 1:2). Stirred for a moment, $NaHCO_3$ (16.0 eq) was added in one portion. The mixture was degassed three times by applying vacuum, and backfilling with nitrogen while stirring vigorously. Sodium dithionite (6.2 eq) was then added in one portion at 0 °C. The reaction was stirred overnight at room temperature,After the reaction was complete (by TLC analysis) The mixture was extracted by CH_2Cl_2 (3×30 mL). The combined dichloromethane layer was washed with brine, dried over Na_2SO_4 and filtrated. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/1) to afford product **1k**.

2.4 General procedure for catalytic asymmetric cascade spirocyclization reaction.



1b-1u **2b-2u**

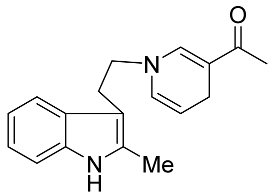
A flame-dried Schlenk tube was cooled to room temperature and filled with argon. To this flask (*R*)-SPINOL-CPA **3l** (0.005 mmol, 10 mol%), 3 Å MS (100 mg) were added. substrate **1** (0.05 mmol, 1.0 eq) was dissolved in dry CH_2Cl_2 (1.0 ml) and then added to this flask. The mixture was degassed three times by applying vacuum, and backfilling with nitrogen while stirring vigorously. The reaction was stirred at 0 °C. After the reaction was complete (by TLC analysis), the reaction mixture was quenched with Na_2CO_3 aqueous and extracted with CH_2Cl_2. The combined dichloromethane layer was washed with brine, dried over Na_2SO_4 and filtered. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/1 to ethyl acetate) to afford product **2**.



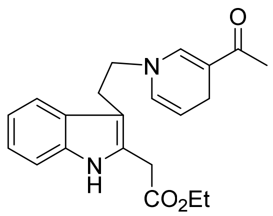
1v, 1w **2v, 2w**

A flame-dried Schlenk tube was cooled to room temperature and filled with argon. To this flask (*R*)-SPINOL-CPA **3l** (0.005 mmol, 20 mol%), 3 Å MS (100 mg) were added. substrate **1** (0.05 mmol, 1.0 eq) was dissolved in dry CH_2Cl_2 (1.0 ml) and then added to this flask. The mixture was degassed three times by applying vacuum, and backfilling with nitrogen while stirring vigorously. The reaction was stirred at 0 °C. After the reaction was complete (by TLC analysis), the reaction mixture was quenched with Na_2CO_3 aqueous and extracted with CH_2Cl_2. The combined dichloromethane layer was washed with brine, dried over Na_2SO_4 and filtered. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/1 to ethyl acetate) to afford product **2**.

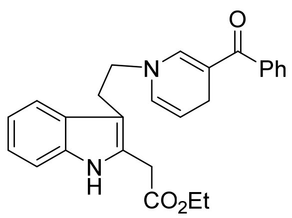
3. Identification of Compounds



1a, ethyl acetate/petroleum ether = 1/1, yellow foam, 212 mg, 85% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.27 – 7.26 (m, 1H), 7.13 – 7.08 (m, 2H), 6.24 (s, 1H), 5,70 (d, *J* = 14.4 Hz, 1H), 4.90 - 4.88 (m, 1H), 3.42 (t, *J* = 6.0 Hz, 2H), 3.04 (s, 2H), 2.94 (t, *J* = 6.0 Hz, 2H), 2.34 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.2, 144.2, 135.5, 133.5, 127.7, 121.1, 119.2, 117.2, 110.6, 107.7, 106.9, 106.7, 54.1, 25.0, 23.3, 21.3, 11.4; HRMS (ESI) calcd for $C_{18}H_{21}N_2O$ $[M+H]^+$: 281.1648, Found: 281.1644.

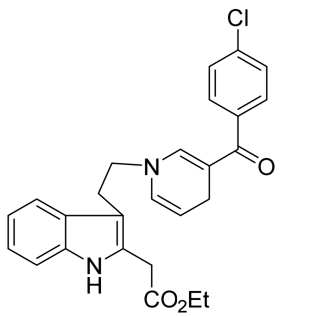


1b, ethyl acetate/petroleum ether = 1/1, yellow foam, 530 mg, 83% yield. Analytical data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.32 (s, 1H), 5.70 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.91 – 4.87 (m, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.77 (s, 2H), 3.43 (t, *J* = 6.0 Hz, 2H), 3.00 (d, *J* = 1.5 Hz, 2H), 2.96 (t, *J* = 6.2 Hz, 2H), 1.73 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$)δ195.2, 170.5, 143.8, 135.9, 128.8, 127.7, 127.3, 122.1, 119.7, 117.9, 111.2, 108.9, 108.1, 107.1, 61.6, 54.2, 31.6, 25.1, 23.5, 21.3, 14.2; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_3$ $[M+H]^+$: 353.1860, Found: 353.1862.

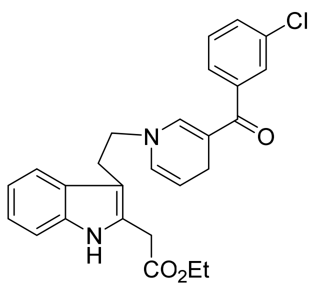


1c, ethyl acetate/petroleum ether = 1/2, yellow foam, 125 mg, 75% yield. Analytical data: ^{1}H

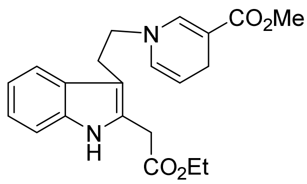
NMR (600 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.25-7.20 (m, 2H), 7.11-7.05 (m, 3H), 6.91 (d, *J* = 7.1 Hz, 2H), 6.24 (d, *J* = 1.1 Hz, 1H), 5.77 (dd, *J* = 8.0, 1.4 Hz, 1H), 5.06 –5.03 (m, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.81 (s, 2H), 3.36 (t, *J* = 5.9 Hz, 2H), 3.21 (dd, *J* = 3.4, 1.6 Hz, 2H), 2.94 (t, *J* = 6.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.3, 170.4, 147.9, 139.9, 135.9, 129.5, 128.5, 127.9, 127.8, 127. 5, 127.4, 122.3, 119.8, 117.9, 111.2, 108.8, 107.9, 107.5, 61.6, 54.6, 31.6, 24.9, 21.7, 14.1; HRMS (ESI) calcd for $C_{26}H_{26}N_2O_3Na$ $[M+Na]^+$: 437.1836, Found: 437.1839.



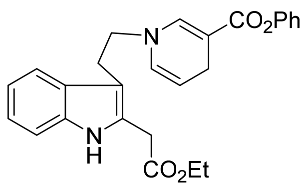
1d, ethyl acetate/petroleum ether = 1/2, orange foam, 96 mg, 52% yield. Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.25 (t, *J* = 7.3 Hz, 1H), 7.12 (t, *J* = 7.3 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.2 Hz, 2H), 6.10 (d, *J* = 1.5 Hz, 1H), 5.80 (d, *J* = 8.0 Hz, 1H), 5.08-5.06 (m, 1H), 4.19 (q, *J* = 7.1, 2H), 3.80 (s, 2H), 3.38 (t, *J* = 5.7Hz, 2H), 3.17-3.16 (m, 2H), 2.94 (t, *J* = 5.9 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.8, 170.3, 147.9, 138.1, 135.8, 135.4, 129.3, 128.6, 128.0, 127.4, 127.3, 122.4, 120.0, 117.9, 111.1, 108.8, 108.2, 107.2, 61.6, 54.6, 31.5, 24.8, 21.7, 14.1; HRMS (ESI) calcd for $C_{26}H_{26}ClN_2O_3$ $[M+H]^+$: 449.1626, Found:449.1624.



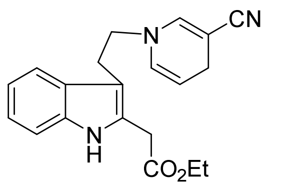
1e, ethyl acetate/petroleum ether = 1/2, orange foam, 73 mg, 46% yield. Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.22-7.17 (m, 2H), 7.14 (s, 1H), 7.09 (t, *J* = 7.8 Hz, 1H), 6.93 (t, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 6.6 Hz, 1H), 6.14 (d, J = 1.2 Hz, 1H), 5.78 (dd, J = 7.8, 1.2 Hz, 1H), 5.07 – 5.06 (m, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.79 (s, 2H), 3.37 (t, J = 6.0 Hz, 2H), 3.18 (dd, J = 3.6, 1.8 Hz, 2H), 2.93 (t, J = 6.0 Hz, 2H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.5, 170.3, 148.0, 141.6, 135.7, 134.1, 129.4, 128.9, 128.4, 127.9, 127.4, 127.3, 125.8, 122.3, 119.8, 117.8, 111.2, 108.8, 108.2, 107.4, 61.6, 54.7, 31.6, 24.8, 21.6, 14.1; HRMS (ESI) calcd for $C_{26}H_{26}ClN_2O_3$ $[M+H]^+$: 449.1626, Found:449.1624 .



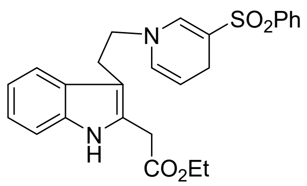
1f, ethyl acetate/petroleum ether = 1/1, yellow foam, 68 mg, 44% yield. Analytical data:^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.75 (s, 1H), 7.42 (d, J = 11.4, 1H), 7.26 (d, J = 12.0, 1H), 7.11-7.07 (m, 1H), 7.05-7.01 (m, 1H), 6.76 (s, 1H), 5.46 (dd, J = 12.0, 2.4, 1H), 4.62-4.59 (m, 1H), 4.14 (q, J = 10.8, 2H), 3.71 (s, 2H), 3.56 (s, 3H), 3.25 (t, J = 10.2, 2H), 3.01 (s, 2H), 2.85 (t, J = 10.2, 2H), 1.23 (t, J = 10.8, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.6, 168.8, 141.6, 135.8, 128.5, 128.1, 127.5, 122.0, 119.5, 117.9, 111.1, 109.1, 104.5, 96.6, 61.5, 54.3, 50.9, 31.7, 25.3, 22.0, 14.2; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_4$ $[M+H]^+$: 369.1809, Found: 369.1811.



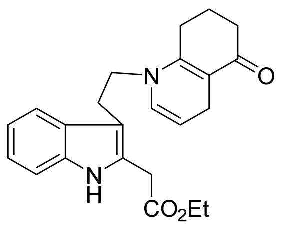
1g, ethyl acetate/petroleum ether = 1/1, yellow foam, 128 mg, 56% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.36 – 7.32 (m, 3H), 7.19 (t, J = 7.3 Hz, 2H), 7.13 (t, J = 7.1 Hz, 1H), 7.05 (d, J = 7.6 Hz, 2H), 7.00 (d, J = 1.2 Hz, 1H), 5.63 (dd, J = 8.0, 1.6 Hz, 1H), 4.82 – 4.79 (m, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.83 (s, 2H), 3.40 (t, J = 6.6 Hz, 2H), 3.20 (dd, J = 3.1, 1.4 Hz, 2H), 2.98 (t, J = 6.7 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.5, 166.5, 151.5, 143.1, 135.9, 129.1, 128.3, 128.2, 127.5, 124.9, 122.1, 121.9, 119.6, 117.9, 111.1, 109.1, 105.4, 95.7, 61.5, 54.4, 31.7, 25.3, 22.0, 14.2; HRMS (ESI) calcd for $C_{26}H_{26}N_2O_4Na$ $[M+Na]^+$: 453.1785, Found:453.1788 .



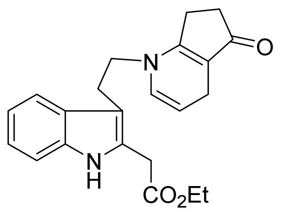
1h, ethyl acetate/petroleum ether = 1/1, yellow foam, 281 mg, 78% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.16 (s, 1H), 5.55 (d, *J* = 8.4 Hz, 1H), 4.59 – 4.56 (m, 1H), 4.25-4.21 (m, 2H), 3.80 (s, 2H), 3.29 (t, *J* = 6.6 Hz, 2H), 3.05 (s, 2H), 2.90 (t, *J* = 6.6 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.3, 143.4, 135.8, 128.6, 128.1, 127.4, 122.2, 121.6, 119.7, 117.8, 111.2, 108.9, 101.7, 61.6, 54.2, 31.7, 25.1, 23.0, 14.2; HRMS (ESI) calcd for $C_{20}H_{21}N_3O_2Na$ $[M+Na]^+$: 358.1526, Found: 358.1528.



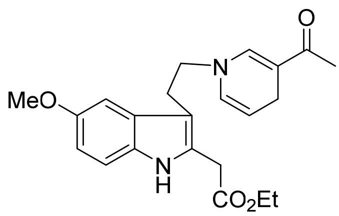
1i, ethyl acetate/petroleum ether = 1/1, yellow foam, 96 mg, 76% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 3H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.19 (t, *J* = 7.1 Hz, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 6.80 (d, *J* = 1.1 Hz, 1H), 5.55 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.61 – 4.58 (m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 2H), 3.39 (t, *J* = 6.6 Hz, 2H), 2.96 – 2.92 (m, 4H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.4, 140.3, 139.7, 135.8, 132.29, 128.9, 128.5, 128.0, 127.6, 127.4, 122.2, 119.7, 117.9, 111.1, 108.9, 104.5, 102.7, 61.5, 54.3, 31.7, 25.2, 21.3, 14.2; HRMS (ESI) calcd for $C_{25}H_{26}N_2O_4SNa$ $[M+Na]^+$: 473.1505, Found: 473.1504.



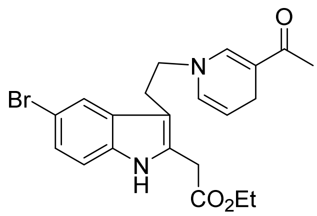
1j, acetone/petroleum ether = 1/1, yellow foam, 211 mg, 72% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 7.3 Hz, 1H), 5.73 (d, J = 8.0 Hz, 1H), 4.98 – 4.96 (m, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.80 (s, 2H), 3.51 (t, J = 6.5 Hz, 2H), 3.07 (s, 2H), 2.97 (t, J = 6.5 Hz, 2H), 2.21 (t, J = 6.5 Hz, 2H), 2.02 (t, J = 6.1 Hz, 2H), 1.62 – 1.58 (m, 2H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.0, 170.4, 155.4, 135.7, 129.4, 128.1, 127.6, 122.2, 119.8, 117.8, 111.1, 109.2, 107.2, 105.6, 61.6, 50.0, 36.1, 31.6, 25.4, 24.9, 21.4, 21.1, 14.2; HRMS (ESI) calcd for $C_{23}H_{27}N_2O_3$ $[M+H]^+$: 379.2016, Found: 379.2019.



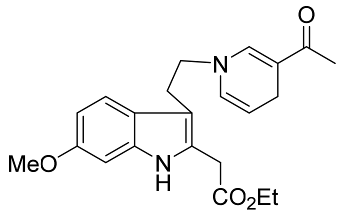
1k, acetone/petroleum ether = 1/1, orange foam, 136 mg, 45% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 7.13 (t, J = 7.1 Hz, 1H), 5.79 (dd, J = 7.9, 1.7 Hz, 1H), 4.94-4.92 (m, 1H), 4.22 – 4.18 (m, 2H), 3.77 (s, 2H), 3.49 (t, J = 6.3 Hz, 2H), 3.04 (s, 2H), 2.98 (t, J = 6.4 Hz, 2H), 2.18 (d, J = 3.9 Hz, 2H), 2.05 (d, J = 4.8 Hz, 2H), 1.30 – 1.28 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 202.4, 170.3, 168.4, 135.7, 128.9, 128.1, 127.5, 122.3, 119.8, 117.7, 111.1, 110.2, 109.2, 107.1, 61.6, 49.7, 33.0, 31.6, 24.8, 24.0, 20.1, 14.2; HRMS (ESI) calcd for $C_{22}H_{24}N_2O_3Na$ $[M+Na]^+$: 387.1679, Found:387.1679.



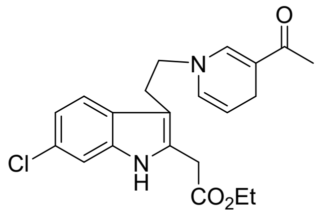
1l, ethyl acetate/petroleum ether = 1/1, yellow foam, 119 mg, 75% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.23 (d, J = 8.4 Hz, 1H), 6.94 (s, 1H), 6.84 (dd, J = 9.0, 2.4 Hz, 1H), 6.31 (s, 1H), 5.69 (d, J = 7.8 Hz, 1H), 4.90 – 4.87 (m, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 2H), 3.41 (t, J = 6.0 Hz, 2H), 2.99 (s, 2H), 2.92 (t, J = 6.0 Hz, 2H), 1.73 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.1, 170.5, 154.3, 143.7, 131.1, 129.5, 127.9, 127.8, 111.8, 111.7, 108.6, 108.2, 107.0, 100.6, 61.5, 56.0, 54.0, 31.6, 25.1, 23.5, 21.3, 14.1; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_4Na$ $[M+Na]^+$: 405.1785, Found: 405.1782.



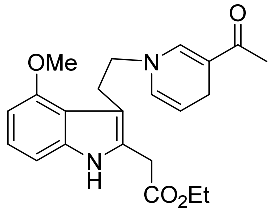
1m, ethyl acetate/petroleum ether = 1/1, yellow foam, 144 mg, 62% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.63 (d, J = 1.2 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.22 (d, J = 9.0 Hz, 1H), 6.30 (d, J = 1.2 Hz, 1H), 5.66 (dd, J = 8.4, 1.8 Hz, 1H), 4.95 – 4.83 (m, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.77 (s, 2H), 3.42 – 3.35 (t, 2H), 3.00 (d, J = 1.8 Hz, 2H), 2.92 – 2.86 (t, 2H), 1.76 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 170.3, 143.3, 134.4, 130.2, 129.1, 127.6, 125.0, 120.6, 113.0, 112.6, 108.7, 108.4, 107.1, 61.7, 54.1, 31.3, 24.9, 23.6, 21.3, 14.1; HRMS (ESI) calcd for $C_{21}H_{23}BrN_2O_3Na$ $[M+Na]^+$: 453.0784, Found: 453.0787.



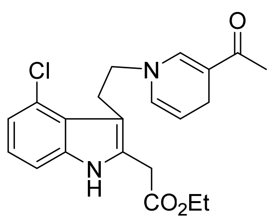
1n, ethyl acetate/petroleum ether = 1/1, yellow foam, 162 mg, 81% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.36 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 1.8 Hz, 1H), 6.78 (dd, J = 8.4, 1.8 Hz, 1H), 6.35 (d, J = 1.2 Hz, 1H), 5.67 (dd, J = 7.8, 1.8 Hz, 1H), 4.93 – 4.82 (m, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.83 (s, 3H), 3.73 (s, 2H), 3.40 (t, J = 6.0 Hz, 2H), 3.05 – 2.95 (m, 2H), 2.91 (t, J = 6 Hz, 2H), 1.77 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 170.6, 156.7, 143.6, 136.7, 127.7, 127.3, 121.7, 118.5, 109.6, 108.8, 108.2, 106.9, 94.8, 61.5, 55.7, 54.2, 31.5, 25.1, 23.5, 21.3, 14.2; HRMS (ESI) calcd for $C_{22}H_{27}N_2O_4$ $[M+H]^+$: 383.1965, Found: 383.1970.



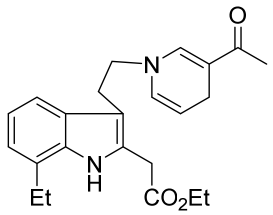
1o, ethyl acetate/petroleum ether = 1/1, yellow foam, 160 mg, 80% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.96 (d, *J* = 10.2 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.33 (d, *J* = 1.2 Hz, 1H), 7.09 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.34 (s, 1H), 5.64 (d, *J* = 7.8 Hz, 1H), 4.91 – 4.82 (m, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 2H), 3.39 (t, *J* = 6.0 Hz, 2H), 2.99 (s, 2H), 2.92 (t, *J* = 6.6 Hz, 2H), 1.78 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 170.3, 143.4, 136.2, 129.5, 128.1, 127.6, 125.9, 120.4, 118.7, 111.1, 109.1, 108.4, 107.0, 61.7, 54.2, 31.4, 25.0, 23.6, 21.3, 14.1; HRMS (ESI) calcd for $C_{21}H_{23}ClN_2O_3Na$ $[M+Na]^+$: 409.1289, Found: 409.1285.



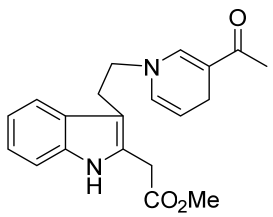
1p, ethyl acetate/petroleum ether = 1/1, yellow foam, 83 mg, 69% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.08 (t, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 6.47 (s, 1H), 5.71 (d, *J* = 7.8 Hz, 1H), 4.90 – 4.87 (m, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 3.73 (s, 2H), 3.45 (t, *J* = 6.6 Hz, 2H), 3.04 (d, *J* = 6.6 Hz, 4H), 1.82 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.9, 170.6, 154.1, 143.9, 137.5, 128.0, 127.0, 122.9, 117.2, 109.3, 108.0, 106.7, 104.5, 99.8, 61.5, 55.6, 55.1, 31.3, 26.5, 23.5, 21.4, 14.1; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_4Na$ $[M+Na]^+$: 405.1785, Found: 405.1783.



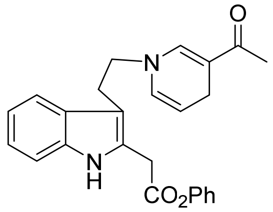
1q, ethyl acetate/petroleum ether = 1/1, yellow foam, 98 mg, 73% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.08 (s, 1H), 7.26-7.24 (m, 1H), 7.08 (d, *J* = 6.0 Hz, 2H), 6.42 (s, 1H), 5.71 (d, J = 8.4 Hz, 1H), 4.91 – 4.88 (m, 1H), 4.22 (q, J = 7.2 Hz, 2H), 3.79 (s, 2H), 3.51 (t, J = 6.6 Hz, 2H), 3.17 (t, J = 6.0 Hz, 2H), 3.02 (s, 2H), 1.80 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 170.4, 143.6, 137.3, 130.2, 127.9, 125.3, 124.0, 122.6, 120.8, 110.0, 108.9, 108.3, 106.9, 61.7, 55.8, 31.2, 25.7, 23.5, 21.3, 14.1; HRMS (ESI) calcd for $C_{21}H_{23}ClN_2O_3Na$ $[M+Na]^+$: 409.1289, Found: 409.1291.



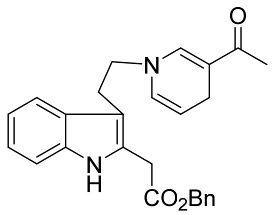
1r, ethyl acetate/petroleum ether = 1/1, yellow foam, 141 mg, 71% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.10-7.07 (m, 1H), 7.03 (d, J = 7.2 Hz, 1H), 6.31 (s, 1H), 5.70 (d, J = 7.8 Hz, 1H), 4.91 (dd, J = 7.8, 2.4 Hz, 1H), 4.21-4.18 (m, 2H), 3.79 (d, J = 1.8Hz, 2H), 3.43 (dd, J = 10.8, 6.0 Hz, 2H), 3.00 (s, 2H), 2.96 (dd, J =10.2, 4.8 Hz, 2H), 2.87 (q, J = 7.2 Hz, 2H), 1.72 (s, 3H), 1.36 (td, J = 7.8, 2.4 Hz, 3H), 1.31 (td, J = 6.6, 1.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 170.6, 143.6, 134.7, 128.3, 127.7, 127.1, 126.7, 120.9, 120.1, 115.6, 109.3, 108.2, 107.0, 61.5, 54.1, 31.5, 25.2, 24.0, 23.4, 21.3, 14.1, 13.9; HRMS (ESI) calcd for $C_{23}H_{28}N_2O_3Na$ $[M+Na]^+$: 403.1992, Found: 403.1989.



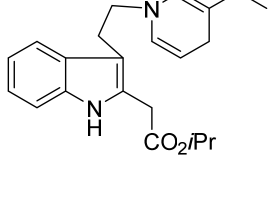
1s, ethyl acetate/petroleum ether = 1/1, yellow foam, 155 mg, 78% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 7.13 (t, J = 7.2 Hz, 1H), 6.31 (s, 1H), 5.69 (dd, J = 8.4, 1.2 Hz, 1H), 4.90 – 4.88 (m, 1H), 3.80 (s, 2H), 3.73 (s, 3H), 3.43 (t, J = 6.0 Hz, 2H), 3.00 (d, J = 1.8 Hz, 2H), 2.96 (t, J = 6.0 Hz, 2H), 1.73 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.1, 170.8, 143.6, 135.8, 128.5, 127.6, 127.2, 122.2, 119.7, 117.8, 111.1, 108.9, 108.1, 107.0, 54.1, 52.4, 31.3, 25.0, 23.4, 21.2; HRMS (ESI) calcd for $C_{20}H_{23}N_2O_3$ $[M+H]^+$: 339.1703, Found: 339.1705.



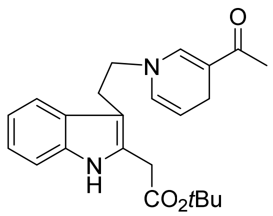
1t, ethyl acetate/petroleum ether = 2/3, yellow foam, 147 mg, 49% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.26-7.24 (m, 1H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 2H), 6.34 (s, 1H), 5.73 (d, *J* = 7.8 Hz, 1H), 4.93 – 4.91 (m, 1H), 4.05 (s, 2H), 3.47 (t, *J* = 6.0 Hz, 2H). 3.03 (d, *J* = 6.6 Hz, 4H), 1.73 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.1, 169.0, 150.3, 143.7, 135.9, 129.6, 127.9, 127.7, 127.3, 126.3, 122.4, 121.3, 119.9, 118.0, 111.2, 109.4, 108.3, 107.1, 54.2, 31.7, 25.2, 23.5, 21.3; HRMS (ESI) calcd for $C_{25}H_{24}N_2O_3Na$ $[M+Na]^+$: 423.1679, Found: 423.1677.



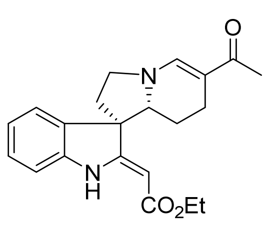
1u, ethyl acetate/petroleum ether = 2/3, yellow foam, 104 mg, 74% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.38 – 7.32 (m, 6H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 6.30 (s, 1H), 5.66-5.65 (m, 1H), 5.16 (s, 2H), 4.87-4.85 (m, 1H), 3.83 (s, 2H), 3.40 (t, *J* = 6.0 Hz, 2H), 2.99 (s, 2H), 2.94 (t, *J* = 6.0 Hz, 2H), 1.72 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.1, 170.2, 143.6, 135.9, 135.3, 128.7, 128.6, 128.5, 127.7, 127.3, 122.3, 119.8, 117.9, 111.1, 109.1, 108.2, 107.0, 67.4, 54.1, 31.6, 25.1, 23.5, 21.3; HRMS (ESI) calcd for $C_{26}H_{26}N_2O_3Na$ $[M+Na]^+$: 437.1836, Found: 437.1839.



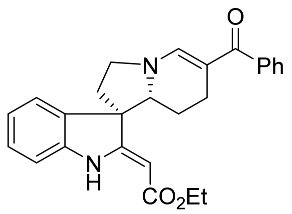
1v, ethyl acetate/petroleum ether = 1/1, yellow foam, 122 mg, 55% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 7.1 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 6.34 (s, 1H), 5.70 (dd, *J* = 7.9, 1.0 Hz, 1H), 5.07 (dt, *J* = 12.5, 6.2 Hz, 1H), 4.90 – 4.88 (m, 1H), 3.75 (s, 2H), 3.43 (t, *J* = 6.2 Hz, 2H), 3.01 (d, *J* = 1.3 Hz, 2H), 2.97 (t, *J* = 6.3 Hz, 2H), 1.74 (s, 3H), 1.27 (d, *J* = 6.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 170.0, 143.6, 135.9, 128.9, 127.7, 127.4, 122.2, 119.7, 117.9, 111.1, 108.8, 108.3, 106.9, 69.2, 54.2, 31.8, 25.1, 23.5, 21.8, 21.3; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_3Na$ $[M+Na]^+$: 389.1836, Found: 389.1839.



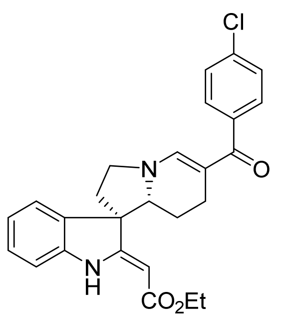
1w, ethyl acetate/petroleum ether = 1/1, orange foam, 99 mg, 68% yield. Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 7.1 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 6.35 (s, 1H), 5.69 (dd, *J* = 7.9, 1.3 Hz, 1H), 4.90 – 4.87 (m, 1H), 3.69 (s, 2H), 3.42 (t, *J* = 6.3 Hz, 2H), 3.01 (s, 2H), 2.96 (t, *J* = 6.3 Hz, 2H), 1.75 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0, 169.8, 143.6, 135.8, 129.2, 127.7, 127.4, 122.1, 119.7, 117.8, 111.1, 108.6, 108.3, 106.9, 82.2, 54.2, 32.7, 28.1, 25.1, 23.5, 21.3; HRMS (ESI) calcd for $C_{23}H_{29}N_2O_3$ $[M+H]^+$: 381.2173, Found: 381.2175.



2b, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 17.5 mg, 99% yield, > 50:1 dr, 92:8 er. $[\alpha]_D^{20}$ +138 (*c* 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.52 (s, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 6.96-6.88 (m, 3H), 4.90 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.93-3.78 (m, 2H), 3.49 (d, *J* = 8.7 Hz, 1H), 2.63 (d, *J* = 16.3 Hz, 1H), 2.33-2.23 (m, 2H), 2.16 (s, 3H), 2.06-1.97 (m, 1H), 160 (d, *J* = 12.8 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 0.97-0.87 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 169.9, 164.6, 144.1, 143.3, 130.8, 128.8, 123.8, 121.4, 109.6, 81.5, 66.7, 59.5, 58.2, 48.4, 38.9, 23.9, 21.2, 19.7, 14.5; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_3Na$ $[M+Na]^+$: 375.1679, Found: 375.1683. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 43.47 min, t_R (minor) = 58.25 min.

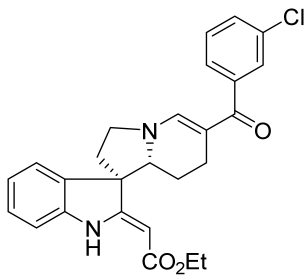


2c, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 20.1 mg, 97% yield, > 50:1 dr, 87:13 er. $[\alpha]_D^{20}$ +51.6 (*c* 1.0, $CHCl_3$); Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.50-7.49 (m, 2H), 7.43-7.39 (m, 3H), 7.26-7.21 (m, 2H), 6.92-6.89 (m, 3H), 4.92 (s, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.83 (t, *J* = 9.6 Hz, 1H), 3.73 (d, *J* = 7.8 Hz, 1H), 3.57 (dd, *J* = 11.4, 3.6 Hz, 1H), 2.86 (dd, *J* = 16.2, 3.0 Hz, 1H), 2.30-2.23 (m, 3H), 1.68 (d, *J* = 6.0 Hz, 1H), 1.33 (t, *J* = 6.6 Hz, 3H), 1.02-1.00 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.9, 169.9, 164.5, 148.3, 143.4, 141.1, 130.7, 129.3, 128.8, 128.3, 128.0, 123.8, 121.4, 109.7, 109.5, 81.6, 67.1, 59.5, 58.2, 48.5, 38.9, 29.7, 21.3, 19.9, 14.5; HRMS (ESI) calcd for $C_{26}H_{26}N_2O_3Na$ $[M+Na]^+$: 437.1836, Found: 437.1837. The enantiomeric excess was determined by Daicel Chiralpak AS-H (25 cm), Hexanes/IPA = 75/25, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 38.11 min, t_R (minor) = 76.80 min.

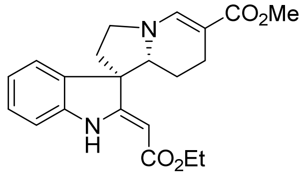


2d, ethyl acetate/petroleum ether = 1/3, pale yellow oil, 19.0 mg, 85% yield, > 50:1 dr, 90:10 er. $[\alpha]_D^{20}$ +41.5 (*c* 1.0, $CHCl_3$); Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.24 (td, *J* = 7.3, 1.3 Hz, 1H), 7.20 (s, 1H), 6.93-6.89

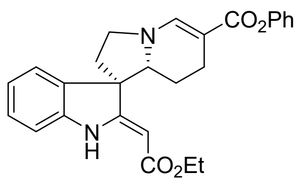
(m, 3H), 4.91 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.86 (t, J = 9.4 Hz, 1H), 3.76 (q, J = 10.6 Hz, 1H), 3.56 (dd, J = 11.2, 3.5 Hz, 1H), 2.84 (m, 1H), 2.32-2.23 (m, 2H), 2.19-2.14 (m, 1H), 1.68-1.65 (m, 1H), 1.33 (t, J = 7.1 Hz, 3H), 1.03-0.96 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.4, 169.9, 164.4, 148.2, 143.4, 139.4, 135.4, 130.6, 129.7, 128.9, 128.2, 123.7, 121.4, 109.7, 109.4, 81.6, 67.1, 59.5, 58.2, 48.6, 38.8, 21.2, 19.9 , 14.5; HRMS (ESI) calcd for $C_{26}H_{25}ClN_2O_3Na$ $[M+Na]^+$: 471.1446, Found: 471.1444. The enantiomeric excess was determined by Daicel Chiralpak AS-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 340 nm, t_R (major) = 35.87 min, t_R (minor) = 60.76 min.



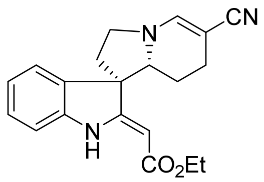
2e, ethyl acetate/petroleum ether = 1/3, pale yellow oil, 19.9 mg, 89% yield, > 50:1 dr, 85:15 er. $[\alpha]_D^{20}$ +67.2 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.47 (s, 1H), 7.41-7.39 (m, 1H), 7.37-7.32 (m, 2H), 7.25-7.20 (m, 1H), 7.20 (s, 1H), 6.94-6.90 (m, 3H), 4.92 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.88 (t, J = 9.2 Hz, 1H), 3.78 (dd, J = 18.2, 10.3 Hz, 1H), 3.57 (dd, J = 11.1, 3.5 Hz, 1H), 2.84-2.80 (m, 1H), 2.32-2.23 (m, 2H), 2.19-2.13 (m 1H), 1.69-1.67 (m, 1H), 1.33 (t, J = 7.1 Hz, 3H), 1.03-0.96 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.9, 169.9, 164.4, 148.4, 143.4, 142.9, 134.1, 130.6, 129.4, 129.3, 128.9, 128.3, 126.3, 123.7, 121.5, 109.7, 109.3, 81.6, 67.1, 59.5, 58.2, 48.7, 38.8, 21.2, 19.9, 14.5; HRMS (ESI) calcd for $C_{26}H_{25}ClN_2O_3Na$ $[M+Na]^+$: 471.1446, Found: 471.1444. The enantiomeric excess was determined by Daicel Chiralpak AS-H (25 cm), Hexanes/IPA = 70/30, 1.0 mL/min^{-1}, λ = 320 nm, t_R (major) = 38.42 min, t_R (minor) = 79.80 min.



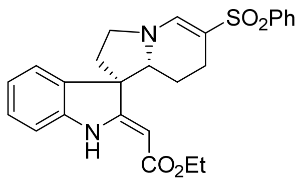
2f, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 13.1 mg, 71% yield, > 50:1 dr, 81:19 er. $[\alpha]_D^{20}$ +29.6 (c 1.0, $CHCl_3$); Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.59 (d, J = 1.1, 1H), 7.21 (td, J = 7.7, 1.1 Hz, 1H), 6.96 (d, J = 7.4 Hz, 1H), 6.92-6.87 (m, 2H), 4.90 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.86 (t, J = 9.7 Hz, 1H), 3.79-3.74 (m, 1H), 3.67 (s, 3H), 3.47 (dd, J = 11.2, 3.6 Hz, 1H), 2.46-2.43 (m, 1H), 2.29-2.19 (m, 2H), 2.14-2.09 (m, 1H), 1.56 (s, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.00-0.93 (m, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 168.6, 164.9, 143.3, 142.4, 131.1, 128.6, 124.0, 121.4, 109.5, 96.0, 81.4, 66.4, 59.4, 58.3, 50.6, 48.1, 39.0 , 21.5, 20.4, 14.5; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_4Na$ $[M+Na]^+$: 391.1628, Found: 391.1624. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 90/10, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 27.69 min, t_R (minor) = 44.88 min.



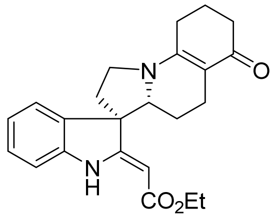
2g, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow oil, 18.9 mg, 88% yield, > 50:1 dr, 87:13 er. $[\alpha]_D^{20}$ +33.4 (c 1.0, $CHCl_3$); Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.82 (s, 1H), 7.36 (t, J = 7.4 Hz, 2H), 7.25-7.22 (m, 1H), 7.18 (t, J = 7.4 Hz, 1H), 7.11 (d, J = 8.3 Hz, 2H), 7.02 (d, J = 7.4 Hz, 1H), 6.96 (t, J = 7.4 Hz, 1H), 6.91 (d, J = 7.9 Hz, 1H), 4.92 (s, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.93 (t, J = 9.8 Hz, 1H), 3.86 (q, J =9.8 Hz, 1H), 3.53 (dd, J = 11.1, 3.2 Hz, 1H), 2.59 (dd, J = 16.4, 4.4 Hz, 1H), 2.33-2.20 (m, 3H), 1.64 (d, J = 12.8 Hz, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.08-1.01 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.0, 166.4, 164.7, 151.7, 144.0, 143.4, 130.9, 129.6, 129.1, 128.8, 124.7, 124.0, 122.0, 121.5, 115.3, 109.6, 95.2, 81.5, 66.5, 59.5, 58.3, 48.3, 39.0, 21.4 , 20.4, 14.5; HRMS (ESI) calcd for $C_{26}H_{26}N_2O_4Na$ $[M+Na]^+$: 453.1785, Found: 453.1789. The enantiomeric excess was determined by Daicel Chiralpak IE (25 cm), Hexanes/IPA = 70/30, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 30.27 min, t_R (minor) = 40.91 min.



2h, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 15.9 mg, 95% yield, > 50:1 dr, 82:18 er. $[\alpha]_D^{20}$ +31.9 (*c* 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.25-7.22 (m, 1H), 7.02 (d, *J* = 1.1 Hz, 1H), 6.95-6.94 (m, 2H), 6.89 (d, *J* = 7.8 Hz, 1H), 4.88 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.83-3.79 (m, 1H), 3.76 (dd, *J* = 18.0, 9.8 Hz, 1H), 3.43 (dd, *J* = 11.2, 3.5 Hz, 1H), 2.30-2.21 (m, 3H), 2.15-2.11 (m, 1H), 1.56-1.53 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.05-0.98 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.9, 164.5, 143.9, 143.3, 130.7, 128.9, 123.9, 122.7, 121.5, 109.6, 81.6, 65.8, 59.5, 58.3, 48.3, 38.8, 22.4, 21.2, 14.5; HRMS (ESI) calcd for $C_{20}H_{21}N_3O_2Na$ $[M+Na]^+$: 358.1526, Found: 358.1523. The enantiomeric excess was determined by Daicel Chiralpak AD-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 26.72 min, t_R (minor) = 33.20 min.

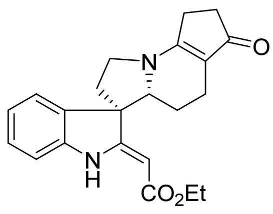


2i, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow oil, 20.9 mg, 93% yield, > 50:1 dr, 92:8 er. $[\alpha]_D^{20}$ +25.7 (*c* 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.77 (s,1H), 7.82-7.80 (m, 2H), 7.56 (s, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.23-7.20 (m, 1H), 6.95-6.91 (m, 2H), 6.87 (d, *J* = 7.9 Hz, 1H), 4.84 (s, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.90 (td, *J* = 10.8, 3.3 Hz, 1H), 3.83 (dd, *J* = 18.1, 9.1 Hz, 1H), 3.39 (dd, J = 11.2, 3.5 Hz, 1H), 2.32-2.28 (m, 1H), 2.26-2.21 (m, 2H), 2.062.00 (m, 1H), 1.56-1.54 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.00- 0.93 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.9, 164.5, 143.3, 142.7, 141.0, 131.8, 130.6, 128.9, 128.8, 126.8, 123.9, 121.5, 109.6, 102.3, 81.5, 66.1, 59.5, 58.1, 48.2, 38.9, 21.3, 20.2, 14.5; HRMS (ESI) calcd for $C_{25}H_{26}N_2O_4SNa$ $[M+Na]^+$: 473.1505, Found: 473.1500. The enantiomeric excess was determined by Daicel Chiralpak AD-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 280 nm, t_R (major) = 71.71 min, t_R (minor) = 98.01 min.



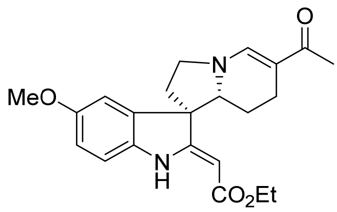
2j, acetone/petroleum ether = 1/1 to acetone, colorless oil, 18.0 mg, 95% yield, > 50:1 dr, 98:2 er. $[\alpha]_D^{20}$ +27.8 (*c* 1.0, $CHCl_3$); Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.25-7.20 (m, 1H), 6.94-6.88 (m, 3H), 4.89 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.88 (t, *J* = 7.3 Hz, 2H), 3.54 (dd, *J* = 11.3. 2.8 Hz, 1H), 2.68-2.56 (m, 3H), 2.36 (t, *J* = 6.1 Hz, 2H), 2.27 (t, *J* = 7.6 Hz, 2H), 2.04-1.97 (m, 3H), 1.59 (d, *J* = 12.8, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 0.99-0.89 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.4, 169.9, 164.4, 158.0, 143.4, 130.7, 128.8, 123.7, 121.3, 109.6, 106.3, 81.5, 67.7, 60.4, 59.5, 58.3, 46.0, 38.7, 35.9, 27.0, 21.6, 19.4, 14.5; HRMS (ESI) calcd for $C_{23}H_{26}N_2O_3Na$ $[M+Na]^+$: 401.1836, Found: 401.1830. The enantiomeric excess was determined by Daicel Chiralpak AD-H (25 cm), Hexanes/IPA = 85/15, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 44.84 min, t_R (minor) = 95.49 min.

For 1.2 mmol scale **1j**, the reaction was quenched after stirred for 96 h.The residue was purified by silica gel column chromatography (acetone/petroleum ether = 1/1 to acetone) to afford 395 mg product **2j**, 87% yield (92% brsm), > 50:1 dr, 96:4 er. $[\alpha]_D^{20}$ +27.1 (*c* 1.0, $CHCl_3$). The enantiomeric excess was determined by Daicel Chiralpak AD-H (25 cm), Hexanes/IPA = 85/15, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 41.72 min, t_R (minor) = 91.91 min.)

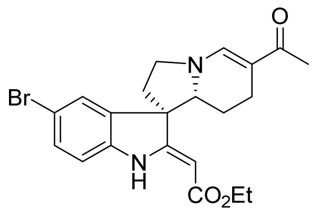


2k, acetone/petroleum ether = 1/1 to acetone, colorless oil, 16.0 mg, 88% yield, > 50:1 dr, 90:10 er. $[\alpha]_D^{20}$ +36.3 (*c* 1.0, $CHCl_3$); Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.92 – 6.87 (m, 3H), 4.91 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.91 – 3.81 (m, 2H), 3.58 (d, *J* = 9.7 Hz, 1H), 2.67 (s, 2H), 2.49 – 2.41 (m, 2H), 2.40 (dd, J = 16.2, 4.4 Hz, 1H), 2.33-2.30 (m, 2H), 2.02-1.97 (m, 1H), 1.62 (d, *J* = 13.1 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.93-0.86

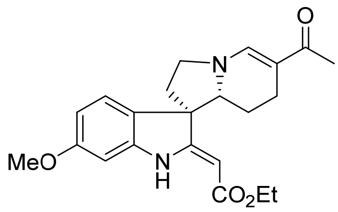
(m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.3, 170.6, 169.9, 164.3, 143.4, 130.5, 128.9, 123.6, 121.4, 109.7, 81.6, 68.0, 59.5, 58.3, 53.9, 38.9, 33.7, 24.9, 21.6, 17.5, 14.5; HRMS (ESI) calcd for $C_{22}H_{24}N_2O_3Na$ $[M+Na]^+$: 387.1679, Found: 387.1672. The enantiomeric excess was determined by Daicel Chiralpak AS-H (25 cm), Hexanes/IPA = 70/30, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 62.10 min, t_R (minor) = 106.46 min.



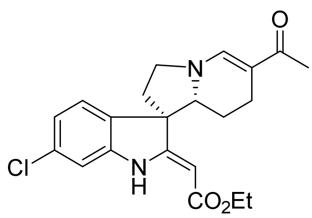
2l, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 17.0 mg, 89% yield, > 50:1 dr, 74:26 er. $[\alpha]_D^{20}$ +89.8 (*c* 1.0, $CHCl_3$); Analytical data: ^1H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.49 (s, 1H), 6.81 (d, *J* = 8.5, 1H), 6.76 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.56 (d, *J* = 2.2, 1H), 4.84 (s, 1H), 4.21(q, *J* = 7.1 Hz, 2H), 3.91 – 3.86 (m, 1H), 3.83 – 3.78 (m, 1H), 3.76 (s, 3H), 3.49 (dd, *J* = 11.2, 3.5 Hz, 1H), 2.65 (dd, *J* = 16.5, 3.3 Hz, 1H), 2.33 – 2.22 (m, 2H), 2.16 (s, 3H), 2.05 – 1.97 (m, 1H), 1.61 – 1.58 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.96 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 170.0, 165.0, 155.0, 144.1, 137.3, 132.5, 112.1, 111.9, 109.5, 80.6, 66.6, 59.4, 58.5, 56.0, 48.3, 38.7, 23.9, 21.2, 19.7, 14.5; HRMS (ESI) calcd for $C_{22}H_{27}N_2O_4$ $[M+H]^+$: 383.1965, Found: 383.1967. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 70/30, 0.8 mL/min^{-1}, λ = 310 nm, t_R (major) = 27.28 min, t_R (minor) = 40.18 min.



2m, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow solid, mp: 81 ~ 83 °C, 18.1 mg, 84% yield, 15:1 dr, 81:19 er. $[\alpha]_D^{20}$ +99.4 (*c* 1.0, $CHCl_3$); Analytical data: ^1H NMR (600 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.50 (s, 1H), 7.33 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.02 (s, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 4.91 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.90 – 3.87 (m, 1H), 3.81 (dd, *J* = 18.4, 9.1 Hz, 1H), 3.46 (dd, *J* = 11.2, 3.2 Hz, 1H), 2.65 (dd, *J* = 16.7, 3.6 Hz, 1H), 2.29 – 2.26 (m, 2H), 2.18 (s, 3H), 2.06 – 2.00 (m, 1H), 1.61 dt, J = 5.9 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H), 0.98-0.91 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.3, 169.7, 164.0, 143.8, 142.5, 133.2, 131.7, 126.8, 113.7, 110.8, 82.4, 66.8, 59.6, 58.3, 48.2, 38.9, 24.0, 21.3, 19,8, 14.4; HRMS (ESI) calcd for $C_{21}H_{23}BrN_2O_3Na$ $[M+Na]^+$: 453.0784, Found: 453.0781. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 85/15, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 64.59 min, t_R (minor) = 110.51 min.

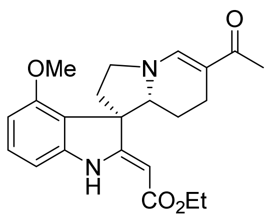


2n, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 18.0 mg, 94% yield, > 50:1 dr, 80:20 er. $[\alpha]_D^{20}$ +108.8 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, CDCl) δ 9.76 (s, 1H), 7.50 (s, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.46 (d, J = 2.2 Hz, 1H), 6.44 (dd, J = 8.2, 2.2 Hz, 1H), 4.89 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.89-3.85 (m, 1H), 3.81-3.76 (m, 4H), 3.46 (dd, J = 11.0, 3.3 Hz, 1H), 2.63 (d, J = 16.1 Hz, 1H), 2.30-2.20 (m, 2H), 2.16 (s, 3H), 2.04-1.99 (m, 1H), 1.60-1.57 (m, 1H), 1.32 (t, J = 7.1 Hz, 3H), 0.97-0.90 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.0, 169.9, 165.3, 160.7, 144.7, 144.0, 124.3, 122.9, 106.1, 96.7, 81.8, 66.7, 59.5, 57.7, 55.5, 48.4, 39.0, 24.0, 21.3, 19.7, 14.5; HRMS (ESI) calcd for $C_{22}H_{27}N_2O_4$ $[M+H]^+$: 383.1965, Found: 383.1965. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 318 nm, t_R (major) = 60.07 min, t_R (minor) = 75.98 min.

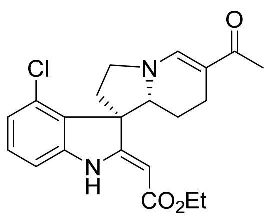


2o, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow oil, 16.0 mg, 83% yield, > 50:1 dr, 82:18 er. $[\alpha]_D^{20}$ +268.6 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.49 (s, 1H), 6.90-6.84 (m, 3H), 4.93 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.91 (t, J = 9.2 Hz, 1H), 3.80 (dd, J = 18.2, 10.2 Hz, 1H), 3.47 (dd, J = 11.2, 3.4 Hz, 1H), 2.65-2.62 (m, 1H), 2.31-

2.25 (m, 2H), 2.17 (s, 3H), 2.06-1.99 (m, 1H), 1.61 (s, 1H), 1.32 (t, J = 7.1 Hz, 3H), 0.96-0.87 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.1, 169.7, 164.3, 144.6, 143.7, 134.7, 129.4, 124.5, 121.2, 110.1, 82.8, 66.7, 59.7, 57.8, 48.2, 39.0, 24.0, 21.3, 19.7, 14.4; HRMS (ESI) calcd for $C_{21}H_{23}ClN_2O_3Na$ $[M+Na]^+$: 409.1289, Found: 409.1287. The enantiomeric excess was determined by Daicel Chiralpak As-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 34.17 min, t_R (minor) = 43.09 min.

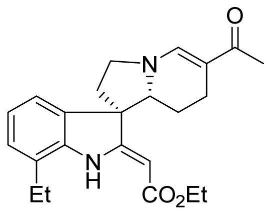


2p, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 16.1 mg, 84% yield, > 50:1 dr, 80:20 er. $[\alpha]_D^{20}$ +144 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.43 (s, 1H), 7.18 (t, J = 8.0 Hz, 1H), 6.53 (d, J = 7.8 Hz, 1H), 6.47 (d, J = 8.3 Hz, 1H), 4.92 (s, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.96 (q, J = 9.2 Hz, 1H), 3.84-3.80 (m, 1H), 3.74 (s, 3H), 3.52 (dd, J = 11.2, 3.8 Hz, 1H), 2.67-2.63 (m, 1H), 2.50-2.46 (m, 1H), 2.31-2.26 (m, 1H), 2.16 (s, 3H), 2.02-1.98 (m, 1H), 1.55 (s, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.07-1.00 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.5, 170.1, 167.6, 156.0, 145.0, 144.5, 130.4, 117.8, 104.4, 103.2, 81.4, 68.8, 59.9, 59.4, 55.3, 50.5, 39.1, 29.7, 21.8, 19.9, 14.5; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_4Na$ $[M+Na]^+$: 405.1785, Found: 405.1783. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 75/25, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 40.92 min, t_R (minor) = 35.81 min.

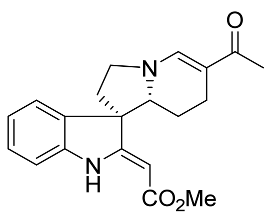


2q, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow oil, 18.0 mg, 93% yield, > 50:1 dr, 85:15 er. $[\alpha]_D^{20}$ +210.5 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.36 (s, 1H), 7.15 (t, J = 7.9 Hz, 1H), 6.89 (d, J = 8.1 Hz, 1H), 6.78 (d, J = 7.8 Hz, 1H), 4.98 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 4.03-3.98 (m, 1H), 3.86-3.82 (m, 1H), 3.53 (dd, J = 11.2, 3.6

Hz, 1H), 2.84-2.79 (m, 1H), 2.67 (dd, J = 16.4, 3.3 Hz, 1H), 2.35-2.30 (m, 1H), 2.16 (s, 3H), 2.06-2.01 (m, 1H), 1.58-1.55 (m, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.27-1.20 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.1, 169.9, 168.2, 145.4, 143.5, 130.4, 130.1, 129.3, 122.9, 108.1, 82.4, 70.2, 60.3, 59.6, 50.4, 37.6, 23.8, 21.8, 19.8, 14.4; HRMS (ESI) calcd for $C_{21}H_{23}ClN_2O_3Na$ $[M+Na]^+$: 409.1289, Found: 409.1288. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 70/30, 0.8 mL/min^{-1}, λ = 320nm, t_R (major) = 23.71 min, t_R (minor) = 33.40 min.

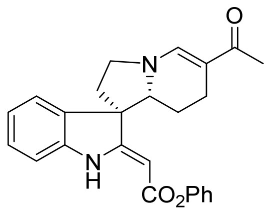


2r, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 16.0 mg, 84% yield, > 50:1 dr, 62:38 er. $[\alpha]_D^{20}$ +172.2 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.51 (s, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.90 (t, J = 7.5 Hz, 1H), 6.81 (d, J = 7.4 Hz, 1H), 4.91 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.91 (t, J = 9.8 Hz, 1H), 3.85 (dd, J = 18.2, 10.1 Hz, 1H), 3.50 (dd, J = 11.2, 3.5 Hz, 1H), 2.67 – 2.60 (m, 3H), 2.32 – 2.24 (m, 2H), 2.17 (s, 3H), 2.06-1.99 (m, 1H), 1.60-1.57 (m, 1H), 1.33 – 1.27 (m, 6H), 0.97 – 0.90 (m, 1H) ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.0, 170.1, 165.0, 144.0, 141.4, 130.5, 128.1, 125.2, 121.6, 121.3, 81.3, 66.7, 59.4, 58.5, 48.4, 39.0, 29.7, 23.8, 21.3, 19.8, 14.5, 13.6; HRMS (ESI) calcd for $C_{23}H_{29}N_2O_3$ $[M+H]^+$: 381.2173, Found: 381.2172. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 85/15, 0.8 mL/min^{-1} , λ = 320 nm, t_R (major) = 50.15 min, t_R (minor) = 63.91 min.

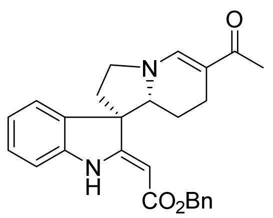


2s, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 16.1 mg, 95% yield, > 50:1 dr, 88:12 er. $[\alpha]_D^{20}$ +143.5 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.51 (s, 1H), 7.23 (td, J = 7.7, 1.1 Hz, 1H), 6.96-6.89 (m, 3H), 4.90 (s, 1H), 3.92-3.89 (m, 1H), 3.85 (dd, J = 18.2, 9.9 Hz, 1H), 3.73 (s, 3H), 3.48 (dd, J = 11.2, 3.5 Hz, 1H), 2.63 (dd, J =

15.8, 3.9 Hz, 1H), 2.31-2.24 (m, 2H), 2.16 (s, 3H), 2.05-1.99 (m, 1H), 1.60-1.57(m, 1H), 0.96-0.89 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.1, 170.2, 164.8, 144.0, 143.3, 130.9, 128.8, 123.9, 121.5, 109.6, 81.1, 66.8, 58.3, 50.8, 48.4, 38.9, 24.0, 21.3, 19.8; HRMS (ESI) calcd for $C_{20}H_{22}N_2O_3Na$ $[M+Na]^+$: 361.1523, Found: 361.1523. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 39.08 min, t_R (minor) = 49.58 min.

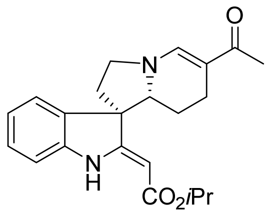


2t, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow oil, 18.0 mg, 90% yield, > 50:1 dr, 88:12 er. $[\alpha]_D^{20}$ +163.9 (*c* 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.54 (s, 1H), 7.42-7.37 (m, 2H), 7.25-7.21 (m, 2H), 7.16 (dd, *J* = 13.00, 1.7 Hz, 2H), 7.00-6.94 (m, 2H), 6.90 (d, *J* = 11.7Hz, 1H), 5.13 (s, 1H), 3.98 (t, *J* = 14.2 Hz, 1H), 3.89-3.82 (m, 1H), 3.60 (dd, *J* = 16.8, 5.3 Hz, 1H), 2.68 (dd, *J* = 24.8, 4.7 Hz, 1H), 2.43-2.28 (m, 2H), 2.19 (s, 3H), 2.11-2.03 (m, 1H), 1.67-1.61 (m, 1H), 1.00-0.90 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.2, 168.4, 166.6, 151.0, 144.0, 143.0, 131.0, 129.32 128.9, 125.4, 123.9, 121.9, 121.9, 121.4, 110.0, 80.4, 66.6, 58.6, 48.4, 38.8, 24.0, 21.3, 19.7; HRMS (ESI) calcd for $C_{25}H_{25}N_2O_3$ $[M+H]^+$: 401.1860, Found: 401.1861. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 70/30, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 28.77 min, t_R (minor) = 35.52 min.

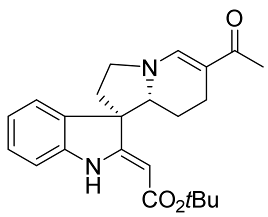


2u, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, colorless oil, 19.1 mg, 92% yield, > 50:1 dr, 88:12 er. $[\alpha]_D^{20}$ +88.3 (*c* 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.55 (s, 1H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 6.96-6.89 (m, 3H), 5.19 (s, 2H), 4.96 (s, 1H), 3.91 (t, *J* = 9.0 Hz, 1H), 3.84 (d, *J*

= 8.4 Hz, 1H), 3.50 (dd, J = 10.8, 3.0 Hz, 1H), 2.64 (d, J = 16.2 Hz, 1H), 2.30-2.26 (m, 2H), 2.18 (s, 3H), 2.05 (d, J = 16.8, 1H), 1.60 (t, J = 7.2 Hz, 1H), 0.94-0.91 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.9, 169.6, 165.0, 144.5, 143.3, 136.7, 130.8, 128.8, 128.6, 128.2, 128.1, 123.8, 121.5, 109.7, 81.2, 66.7, 65.4, 58.3, 48.5, 38.9, 23.8, 21.2, 19.7; HRMS (ESI) calcd for $C_{26}H_{26}N_2O_3Na$ $[M+Na]^+$: 437.1836, Found: 437.1834. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 35.38 min, t_R (minor) = 46.51 min.

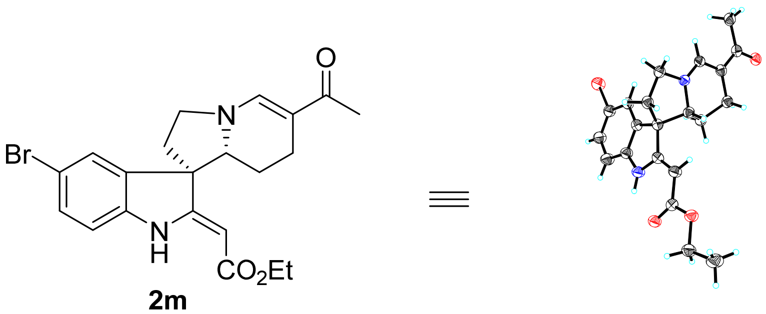


2v, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow oil, 15.0 mg, 82% yield, > 50:1 dr, 90:10 er. $[\alpha]_D^{20}$ +109.8 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.51 (s, 1H), 7.23 (t, J = 7.6 Hz, 1H), 6.95-6.87 (m, 3H), 5.09-5.05 (m, 1H), 4.87 (s, 1H), 3.91 (t, J = 9.7 Hz, 1H), 3.84 (dd, J = 18.4, 10.1 Hz, 1H), 3.49 (dd, J = 11.1, 3.1 Hz, 1H), 2.63 (d, J = 16.3 Hz, 1H), 2.32-2.23 (m, 2H), 2.17 (s, 3H), 2.05-2.00 (m, 1H), 1.61(d, J = 13.0 Hz, 1H), 1.30 (t, J = 5.3 Hz, 6H), 0.96-0.89 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.1, 169.5, 164.5, 144.0, 143.4, 130.8, 128.8, 123.8, 121.3, 109.6, 82.0, 66.7, 66.6, 58.2, 48.4, 39.0, 24.0, 22.1, 21.3, 19.7; HRMS (ESI) calcd for $C_{22}H_{26}N_2O_3Na$ $[M+Na]^+$: 389.1836, Found: 389.1835. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 27.58 min, t_R (minor) = 35.43 min.



2w, ethyl acetate/petroleum ether = 1/1 to ethyl acetate, pale yellow oil, 15.0 mg, 79% yield, > 50:1 dr, 90:10 er. $[\alpha]_D^{20}$ +135.5 (c 1.0, $CHCl_3$); Analytical data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.51 (, s, 1H), 7.21 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 7.5 Hz, 1H), 6.91 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 4.83 (s, 1H), 3.90 (t, J = 9.2 Hz, 1H), 3.83 (q, J = 9.9 Hz, 1H), 3.48 (dd, J = 11.1, 3.3 Hz, 1H), 2.64 (dd, J = 16.0, 3.7 Hz, 1H), 2.31-2.23 (m, 2H), 2.17 (s, 3H), 2.06-2.00 (m, 1H), 1.62-1.60 (m, 1H), 1.52 (s, 9H), 0.96-0.89 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.3, 169.8, 163.9, 144.0, 143.5, 130.8, 128.7, 123.8, 121.2, 109.4, 83.3, 79.5, 66.7, 58.2, 48.4, 39.1, 28.5, 21.3, 19.8; HRMS (ESI) calcd for $C_{23}H_{29}N_2O_3$ $[M+H]^+$: 381.2173, Found: 381.2175. The enantiomeric excess was determined by Daicel Chiralpak OZ-H (25 cm), Hexanes/IPA = 80/20, 0.8 mL/min^{-1}, λ = 320 nm, t_R (major) = 19.95 min, t_R (minor) = 24.57 min.

3. Crystal data and structure refinement for compound 2m.



2m

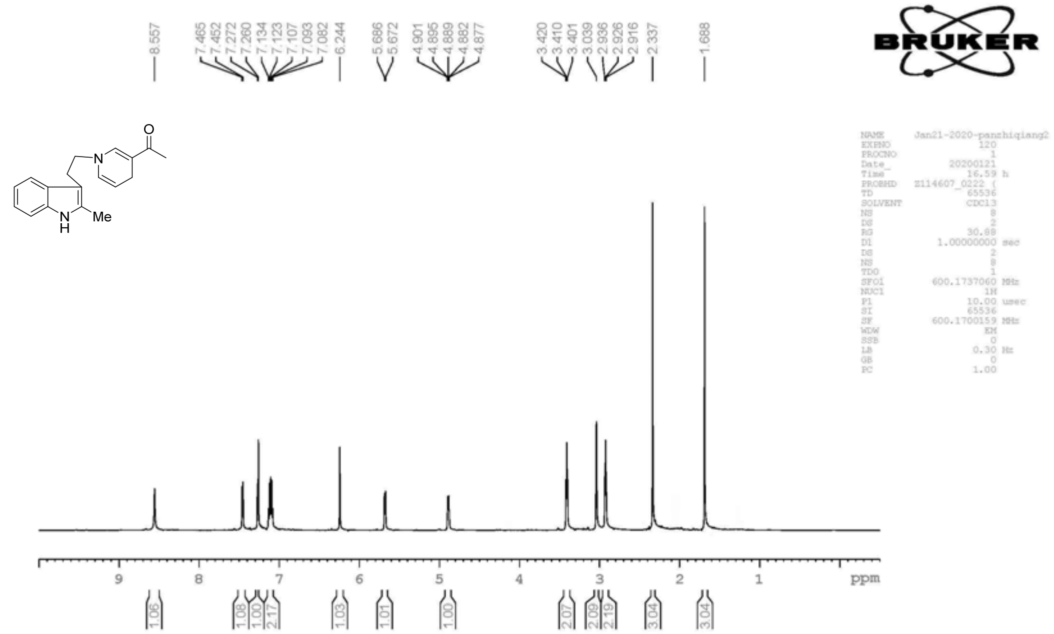
Table S2. Crystal data and structure refinement for 2m. ***CCDC1977098***

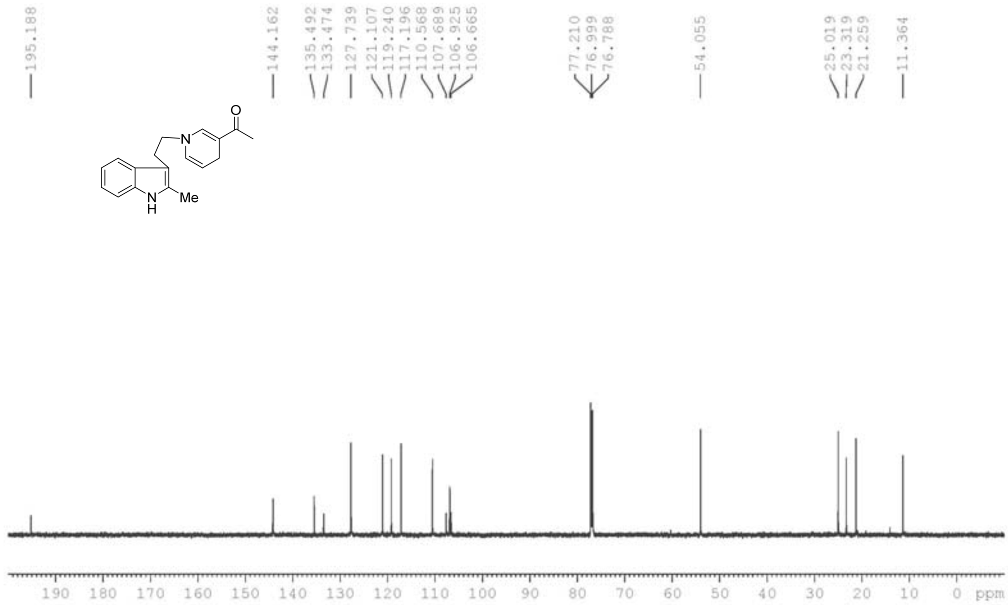
Identification code	2m
Empirical formula	$C_{22}H_{27}BrN_2O_4$
Formula weight	463.36
Temperature/K	100(2)
Crystal system	Monoclinic
Space group	P 1 21 1
a/Å	12.2117(4)
b/Å	7.7360(3)
c/Å	12.9006(4)
α/°	90
β/°	116.8450(10)
γ/°	90
Volume/Å^3	1087.38(7)
Z	2
ρ_{calc}g/cm^3	1.415
μ/mm^{-1}	2.825
F(000)	480
Crystal size/mm^3	0.510 x 0.220 x 0.180
Radiation	CuKα (λ = 2.825)
2Θ range for data collection/°	3.84 to 80.25
Index ranges	-15<=h<=15, -9<=k<=8, -16<=l<=16
Reflections collected	24312
Independent reflections	4575 [R_{int} = 0.0470]
Data/restraints/parameters	4575 / 1 / 267
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R1 = 0.0492, wR2 = 0.1350
Final R indexes [all data]	R1 = 0.0499, wR2 = 0.1359
Largest diff. peak/hole / e Å^{-3}	0.918 and -0.250

Flack parameter	0.113(9)

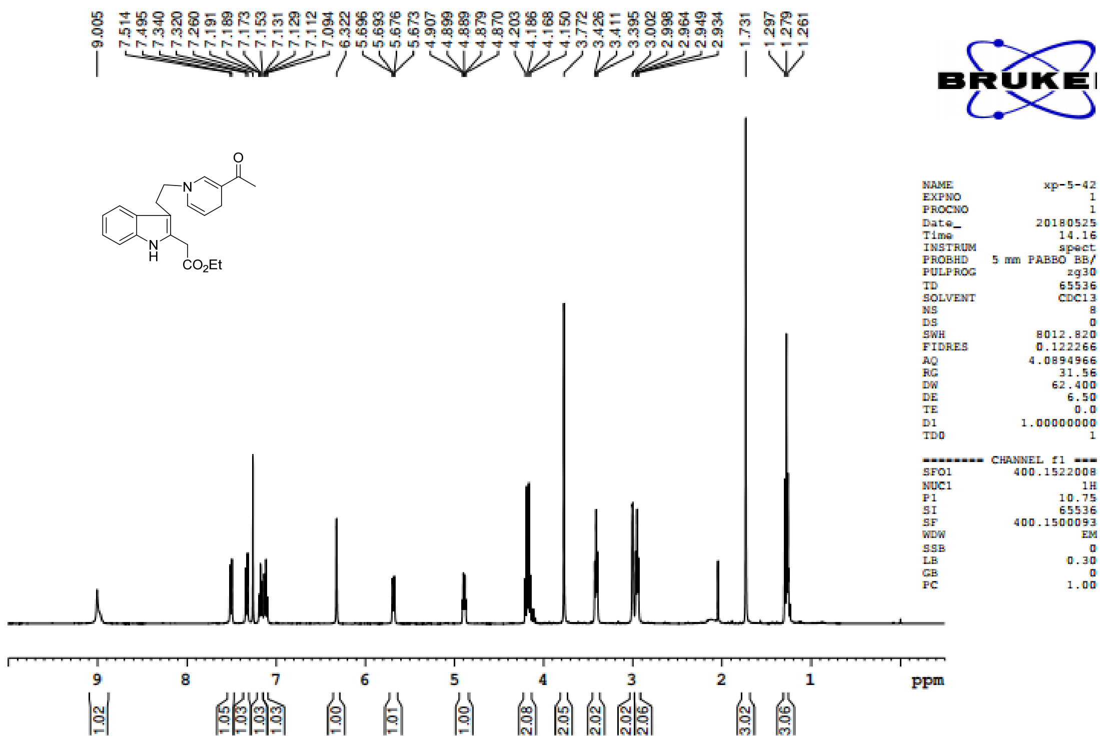
4. NMR Spectral Data

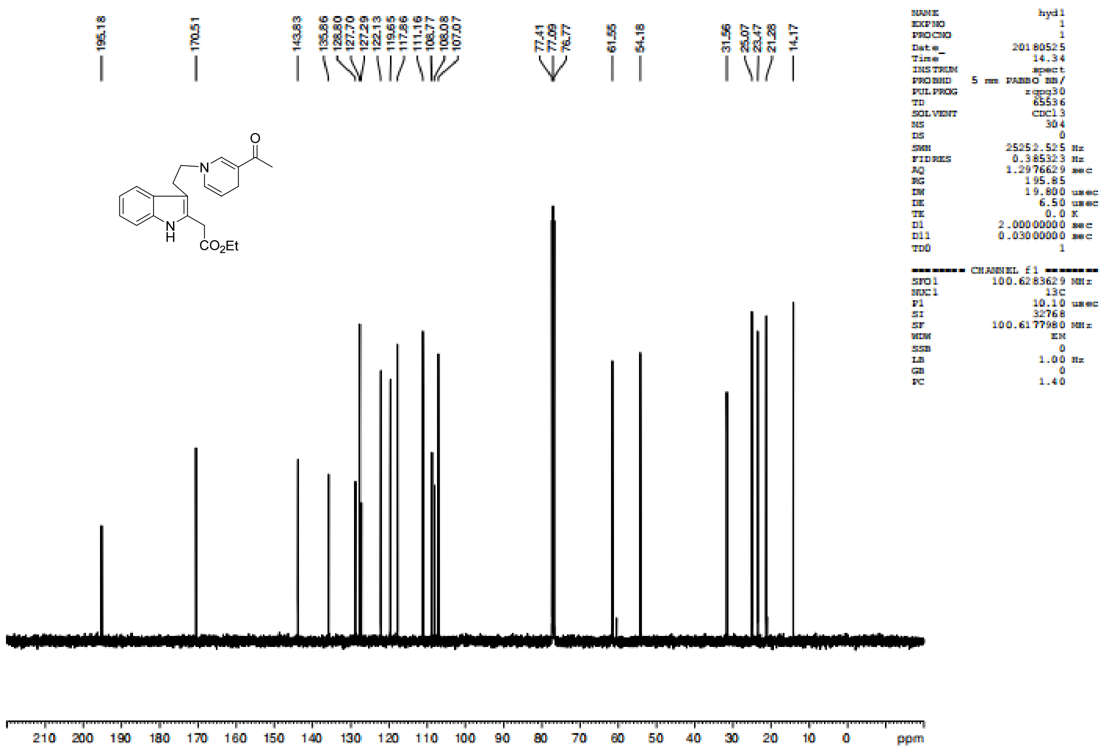
Copies of NMR spectra of **1a**



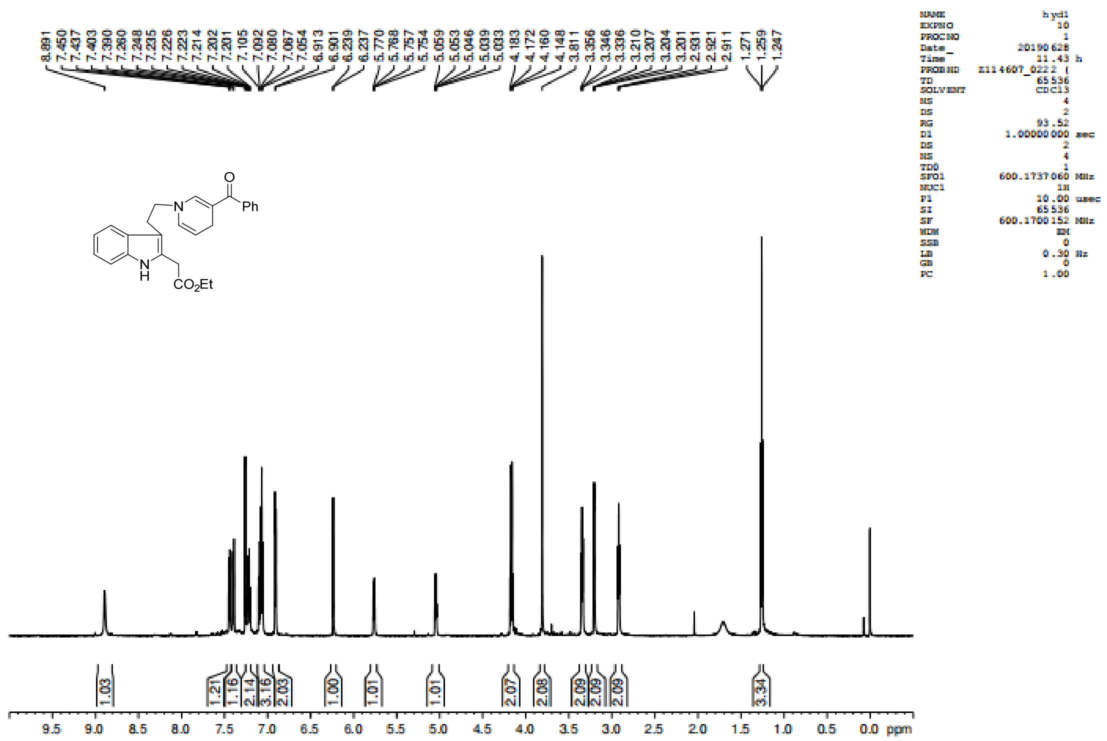


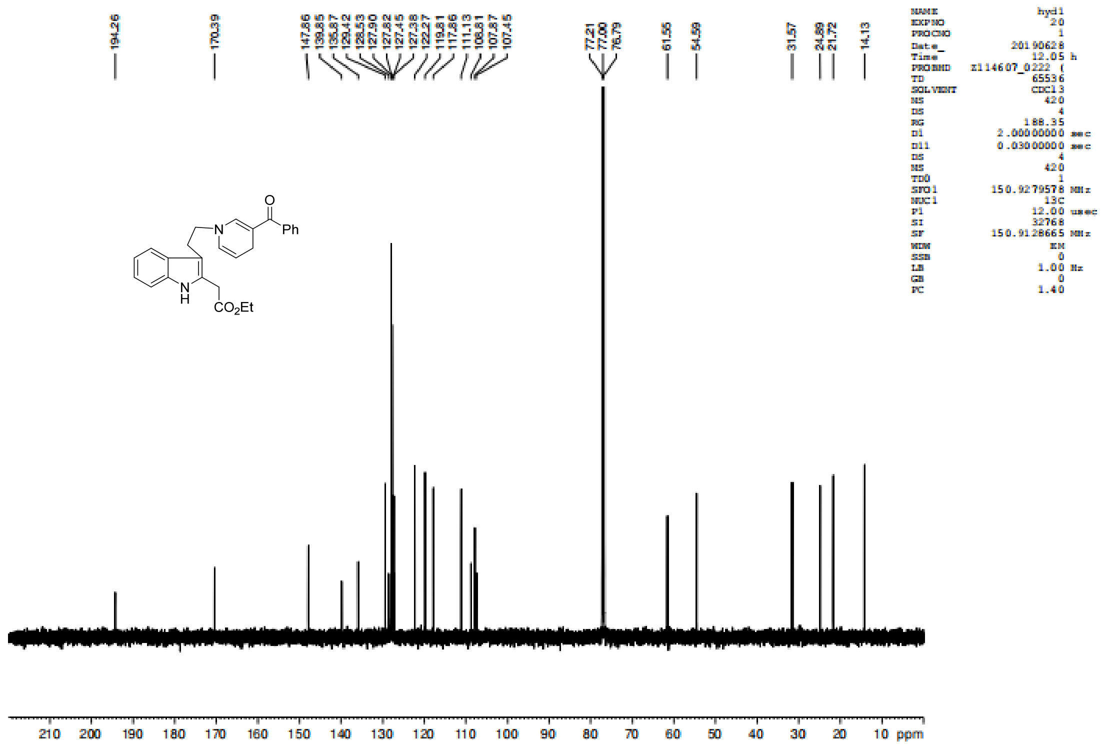
Copies of NMR spectra of **1b**



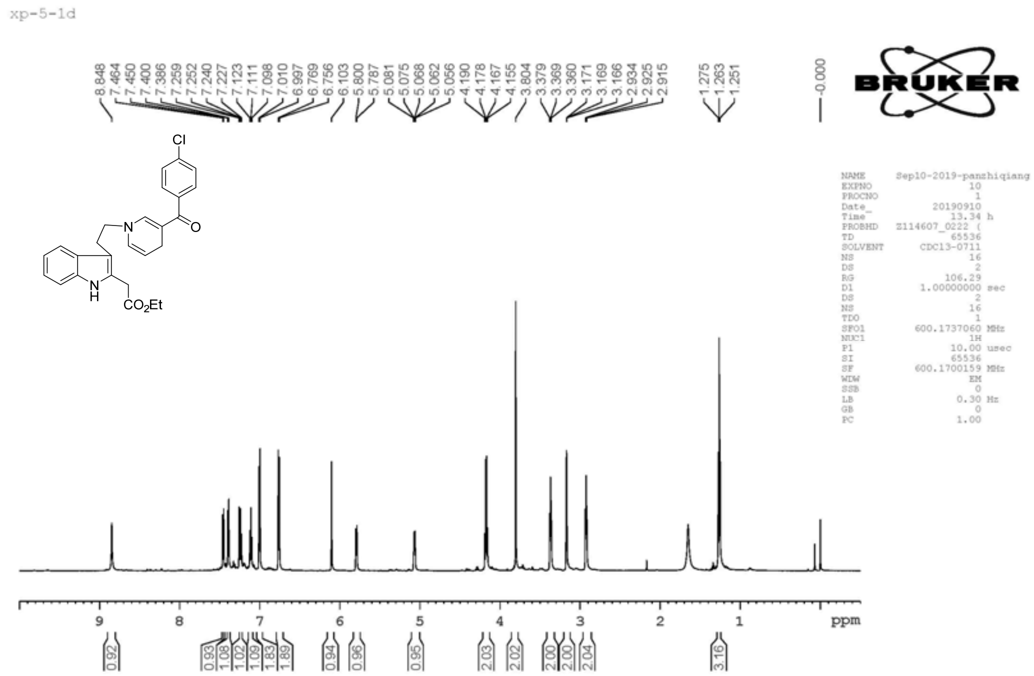


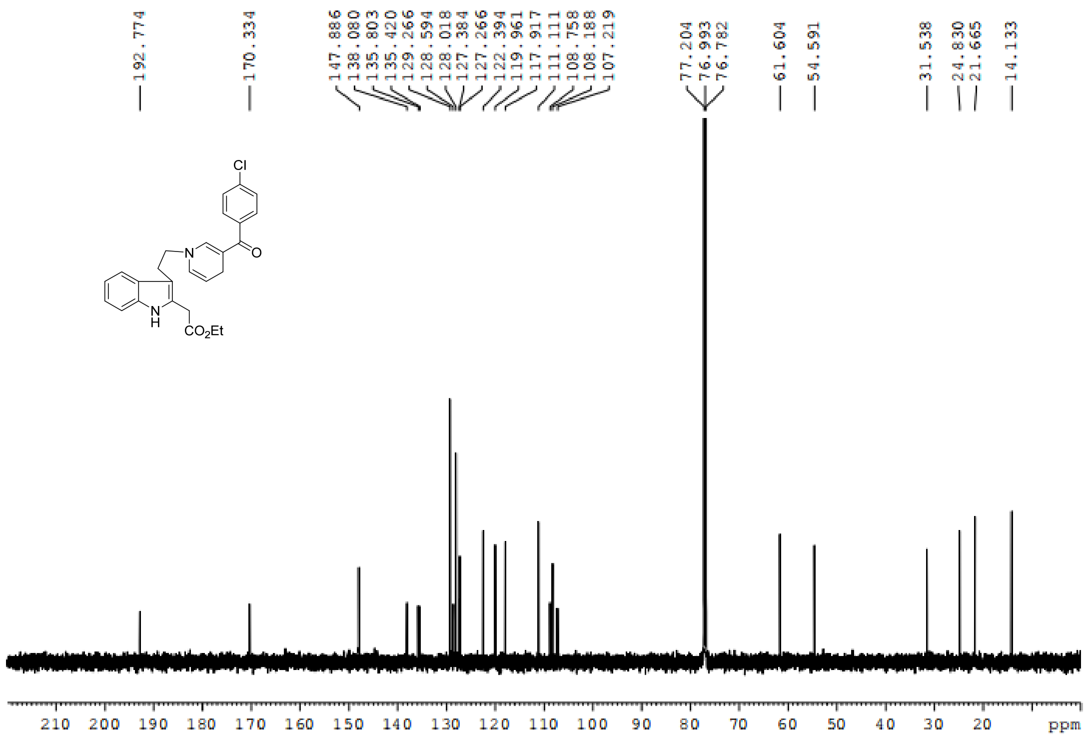
Copies of NMR spectra of **1c**



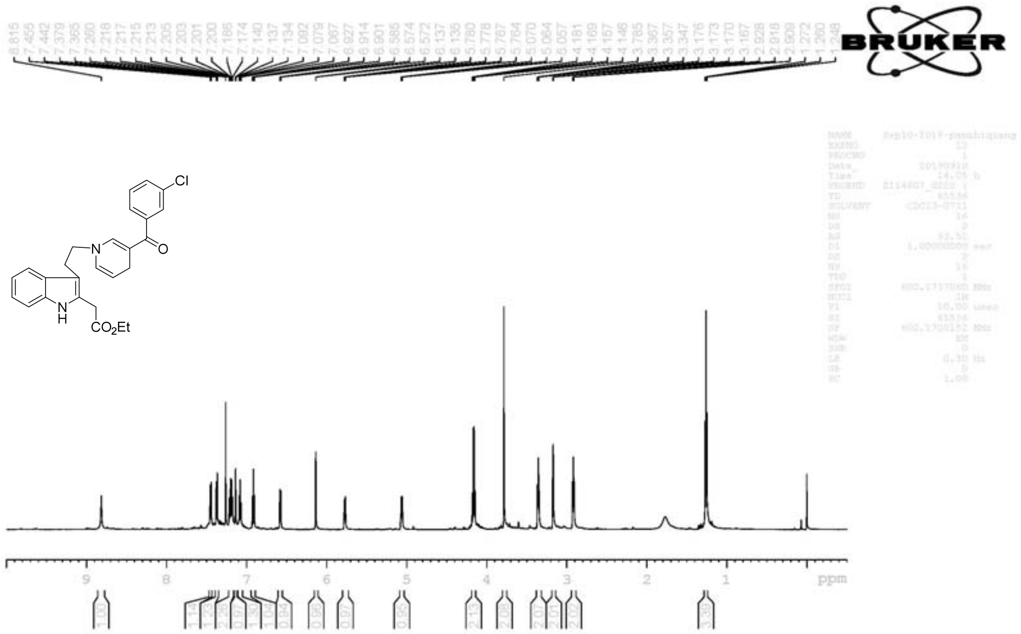


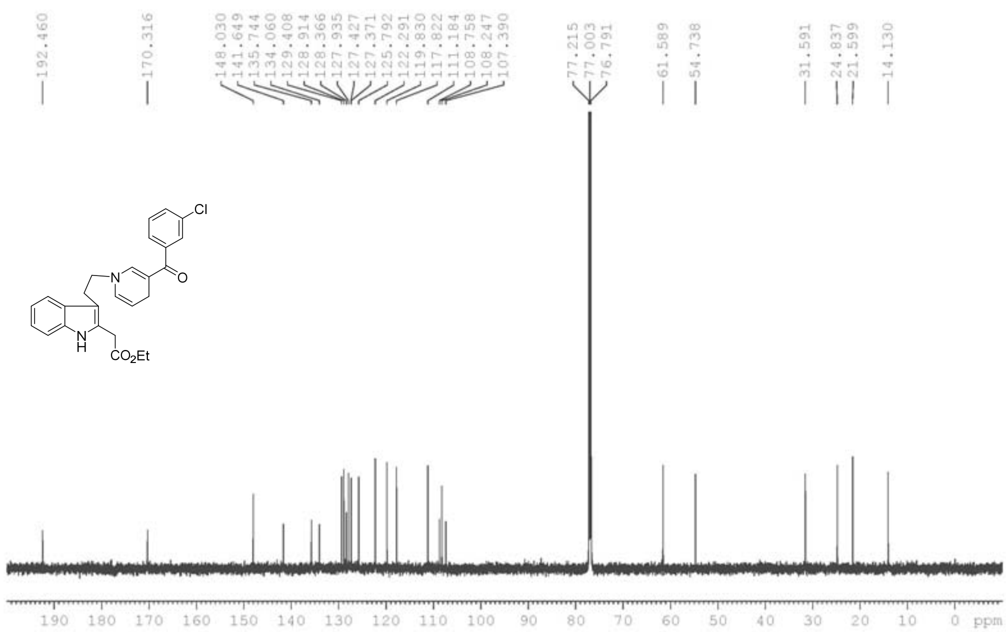
Copies of NMR spectra of **1d**



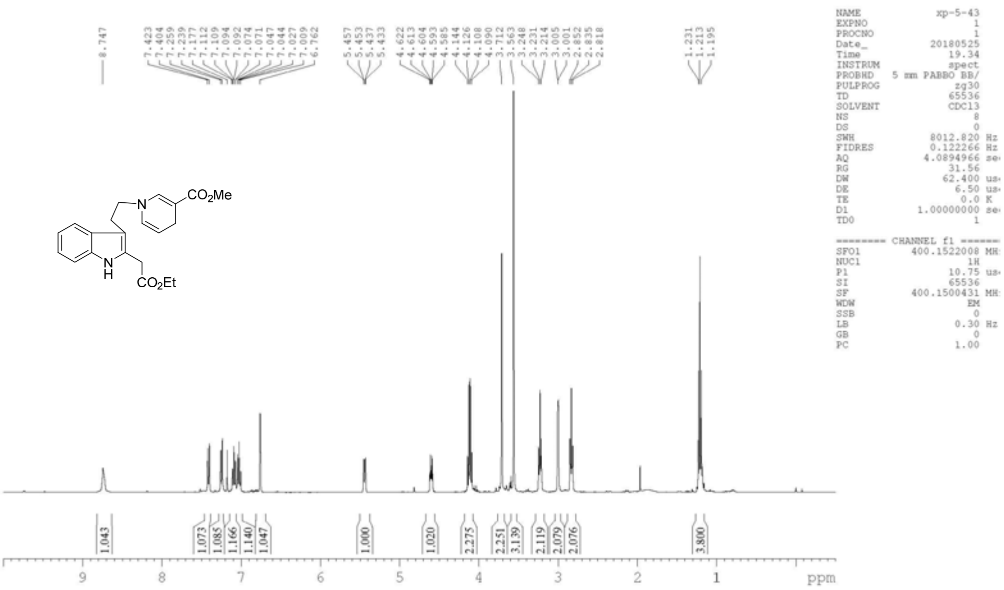


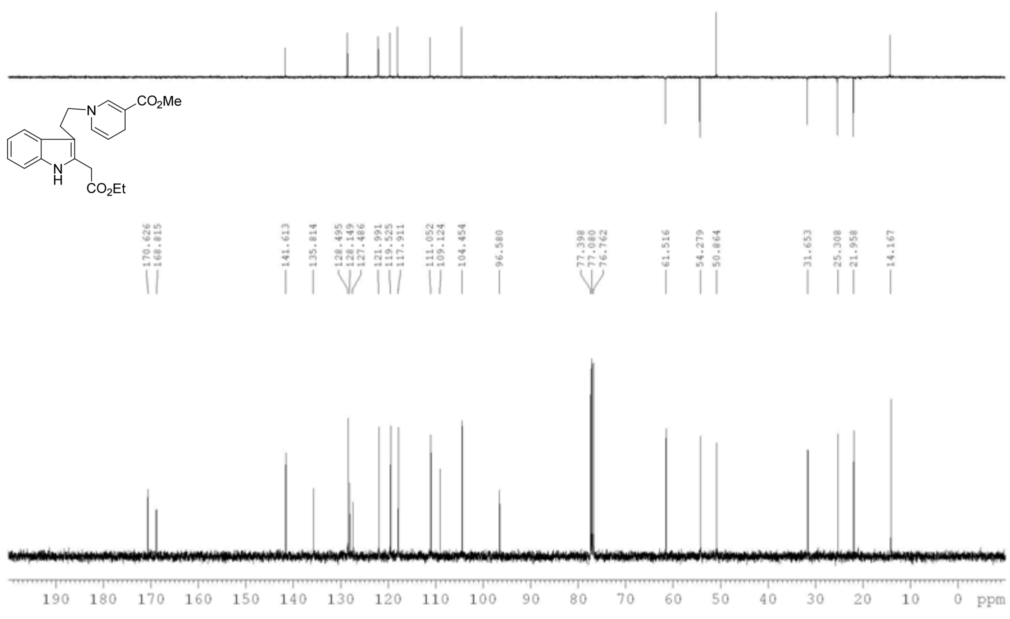
Copies of NMR spectra of **1e**



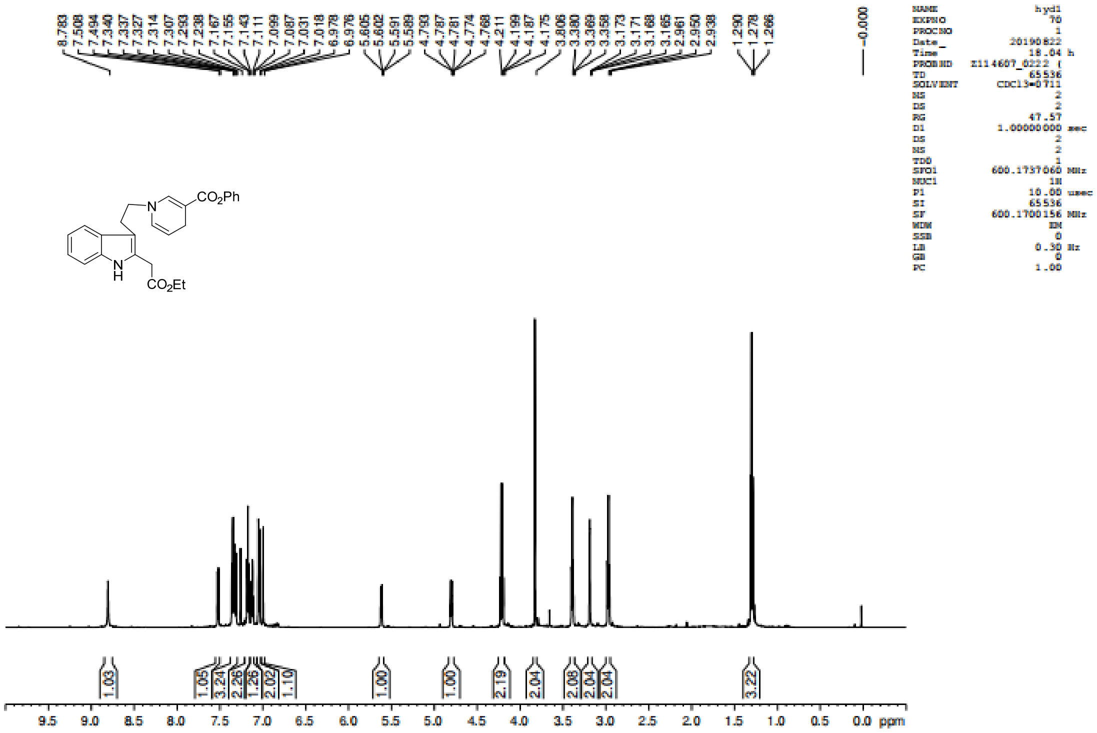


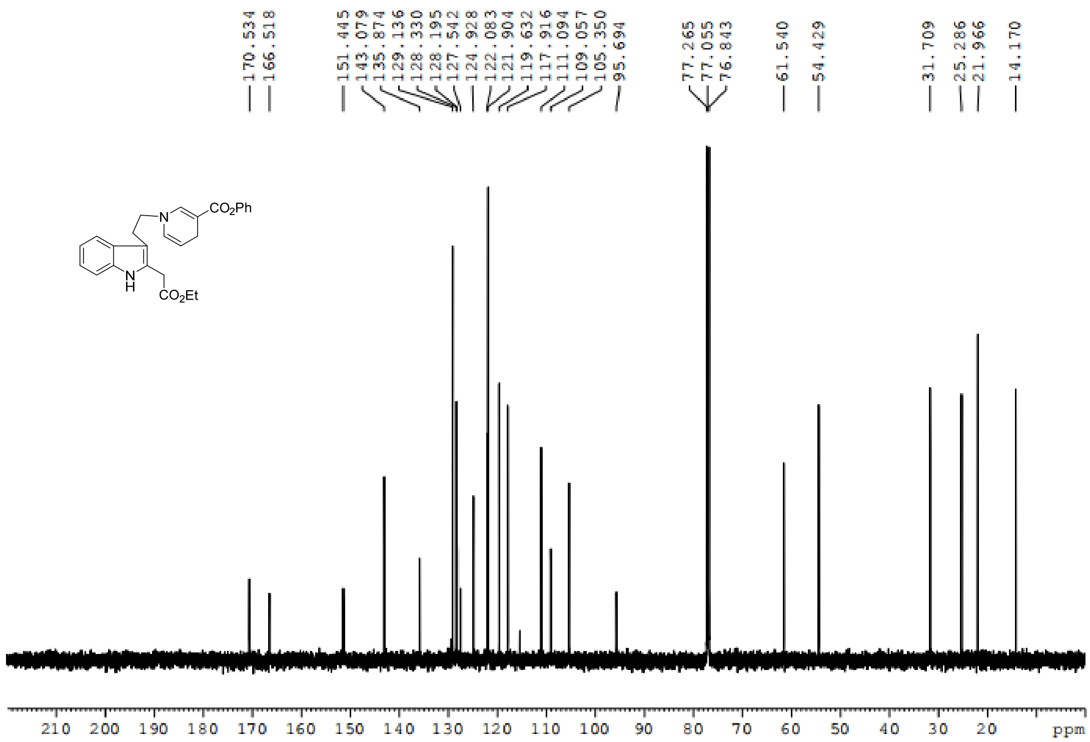
Copies of NMR spectra of **1f**



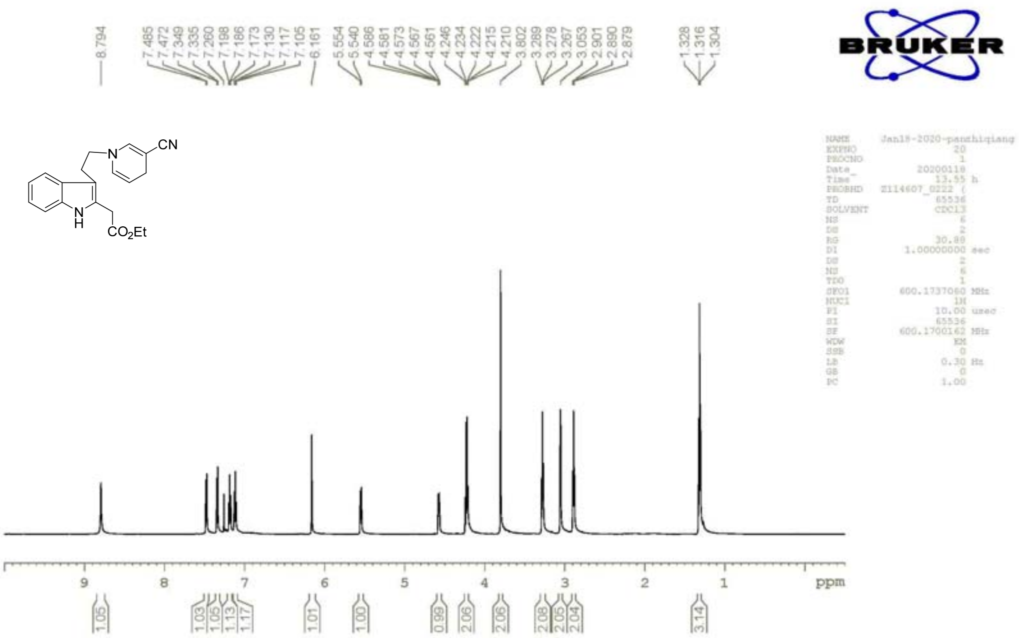


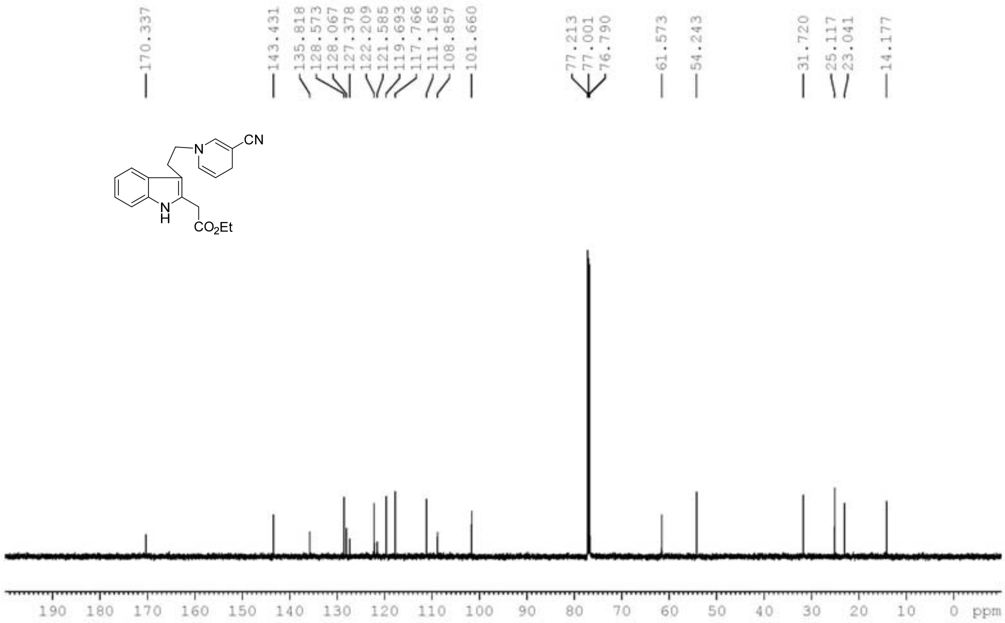
Copies of NMR spectra of **1g**



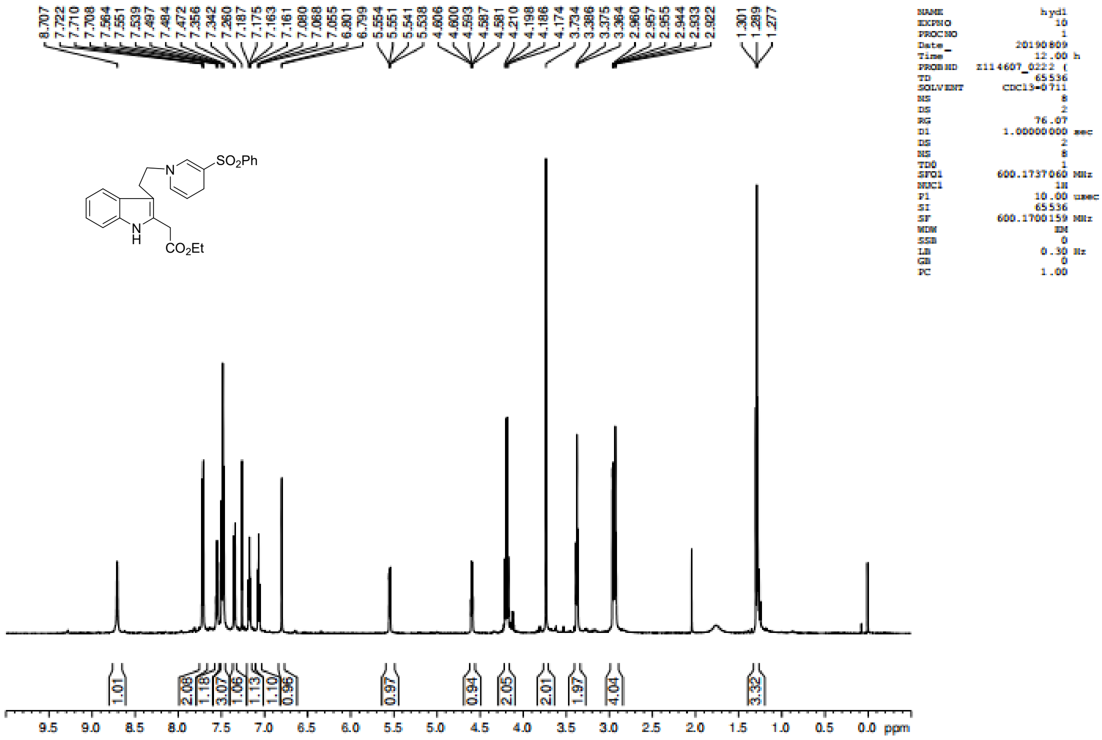


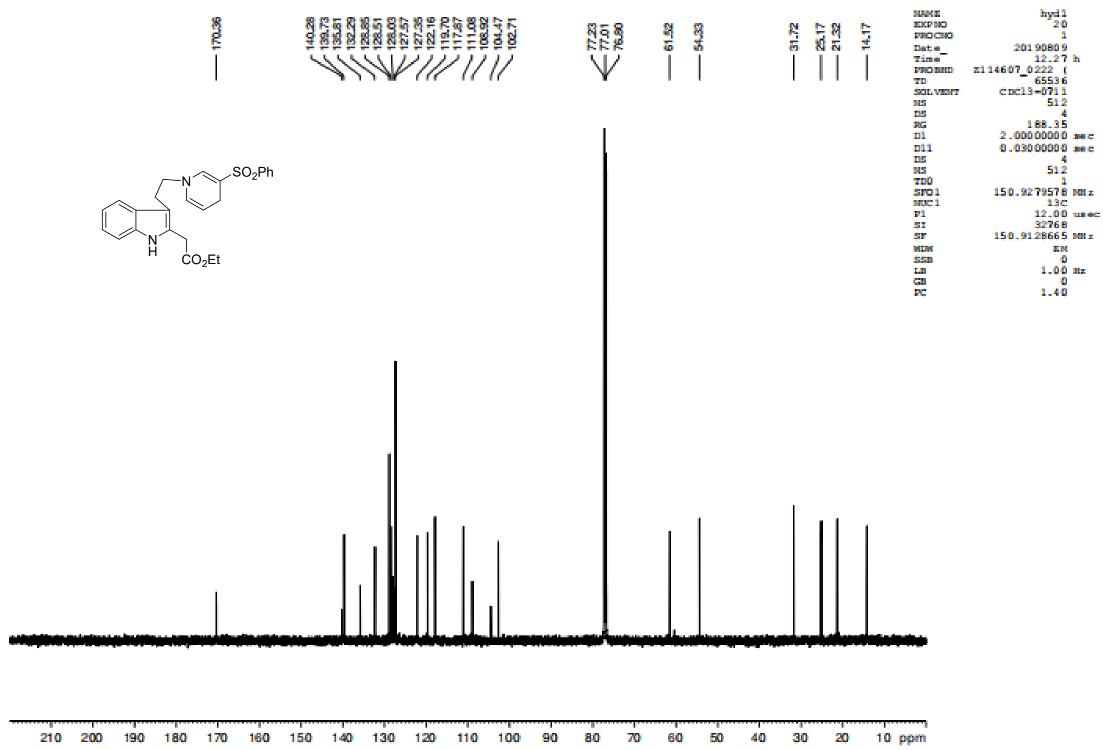
Copies of NMR spectra of **1h**



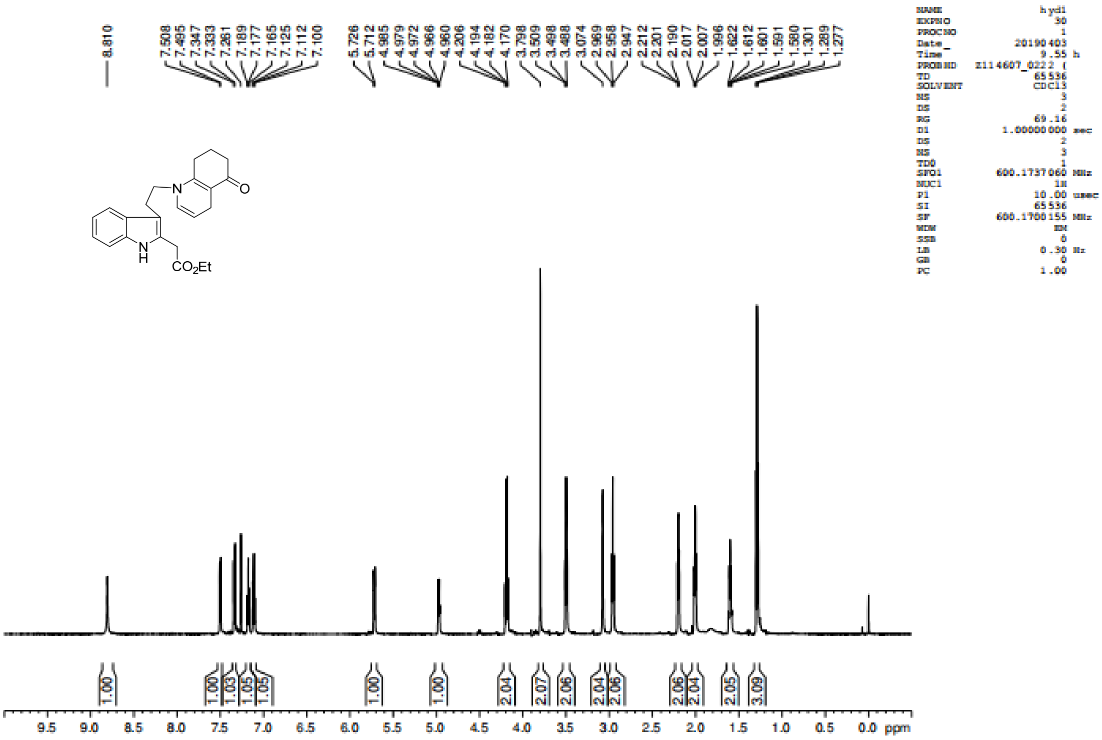


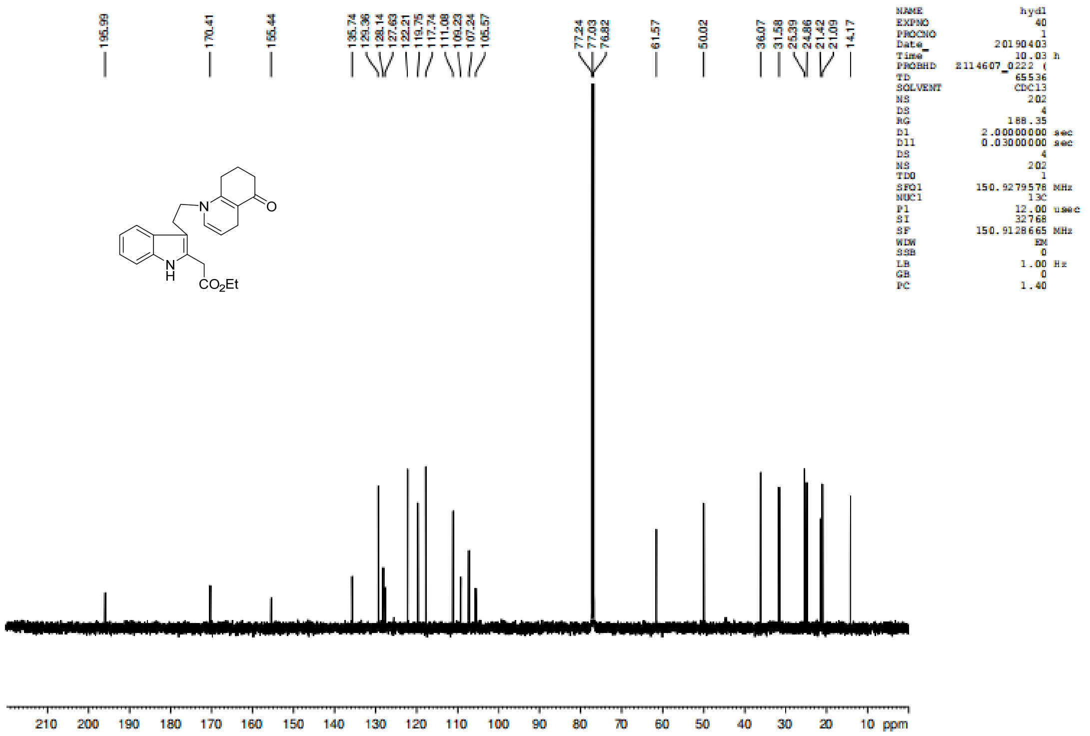
Copies of NMR spectra of **1i**



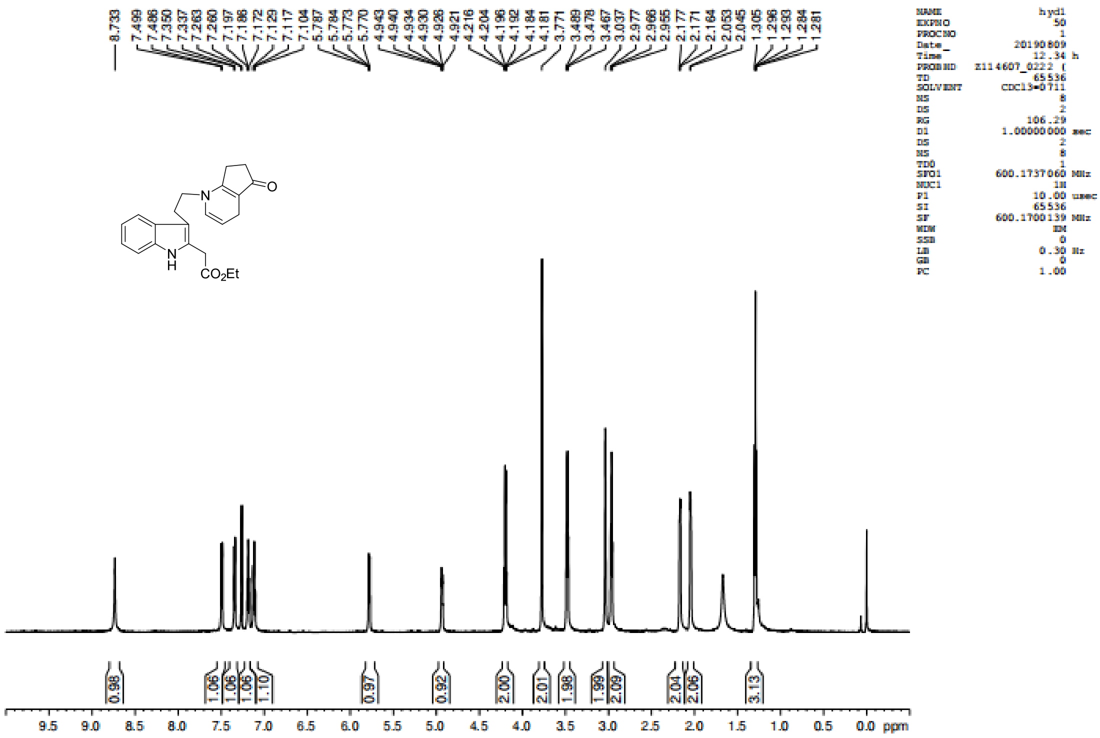


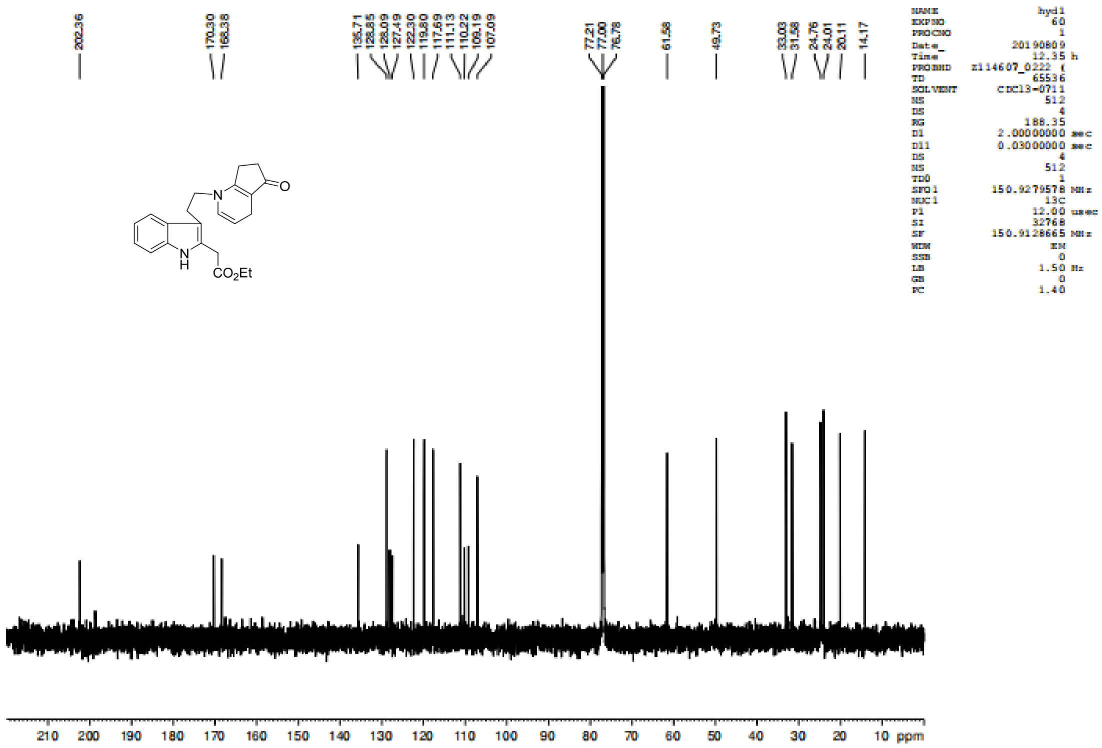
Copies of NMR spectra of **1j**



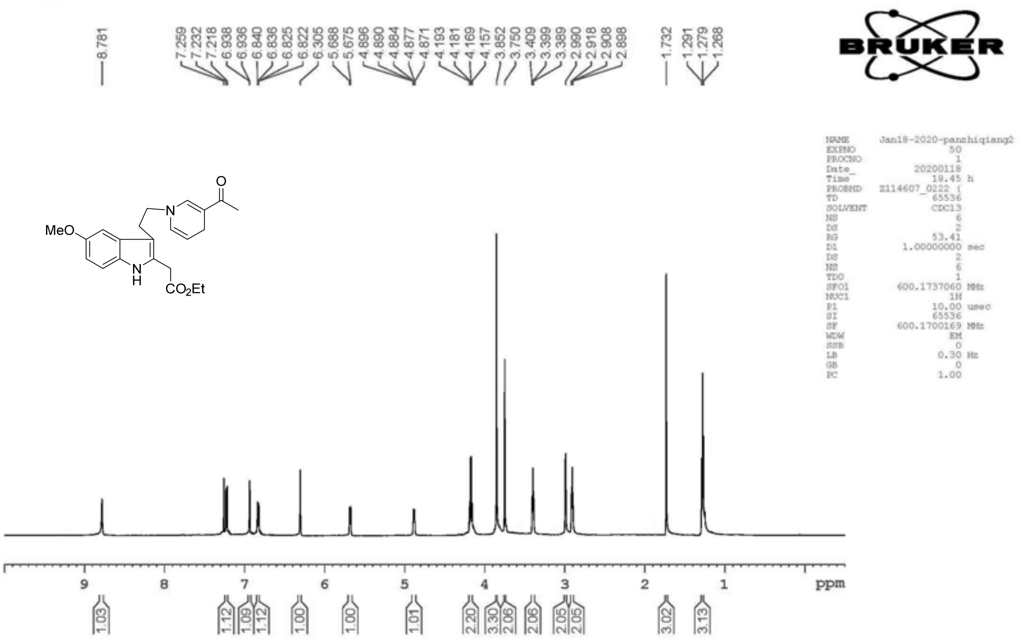


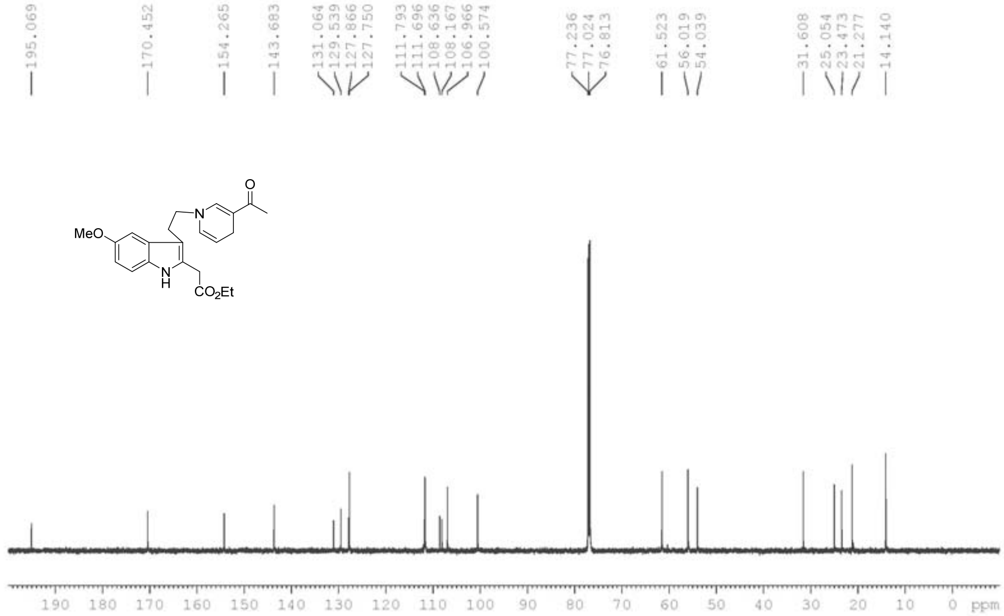
Copies of NMR spectra of **1k**



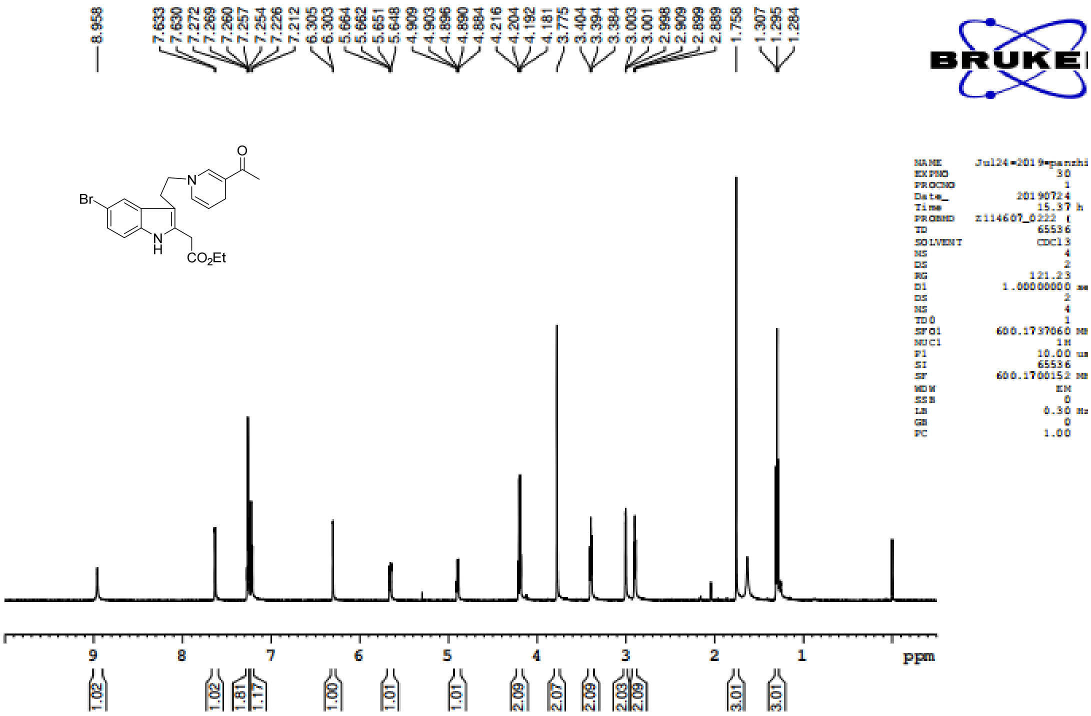


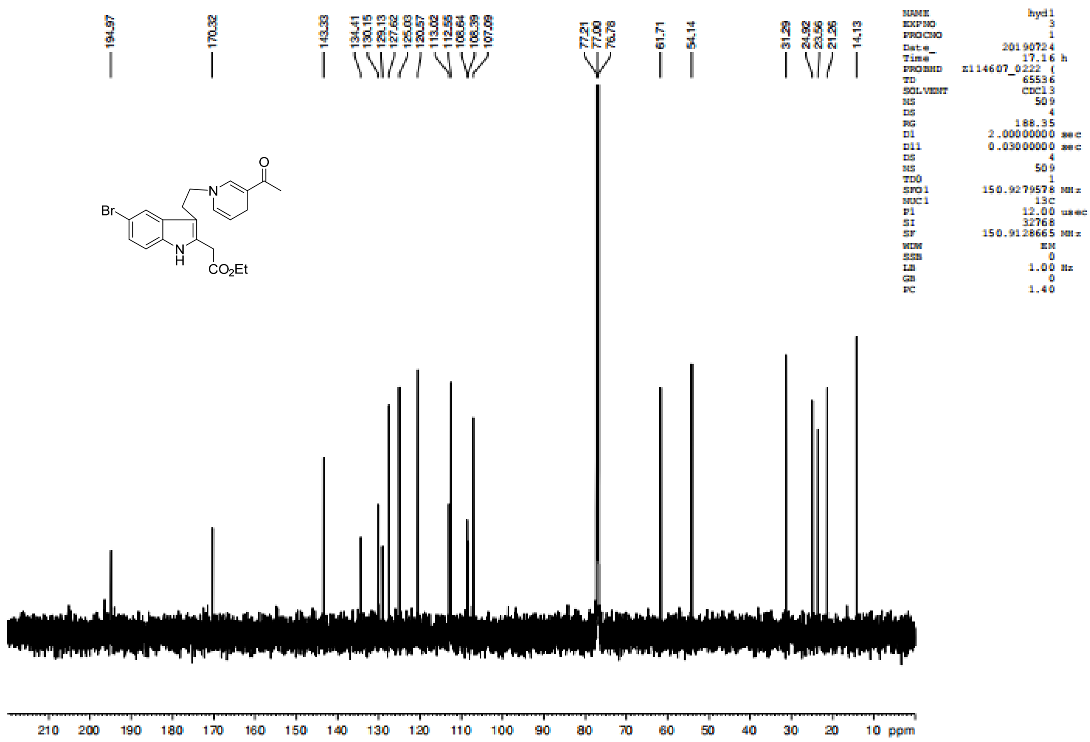
Copies of NMR spectra of **1l**



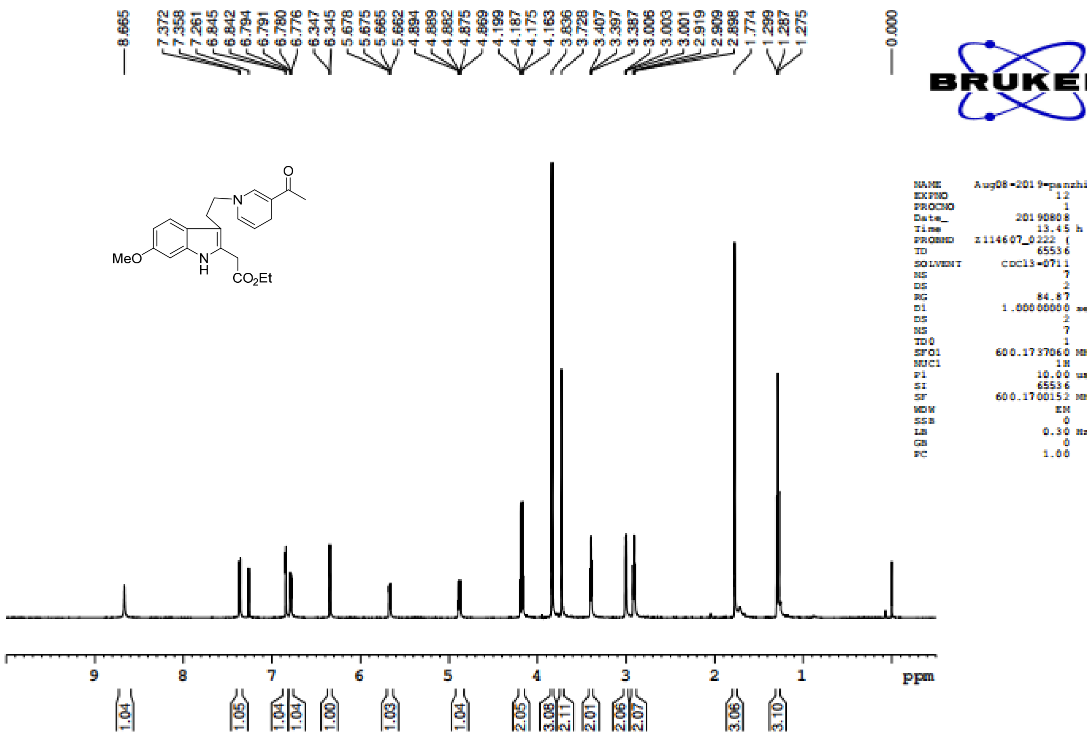


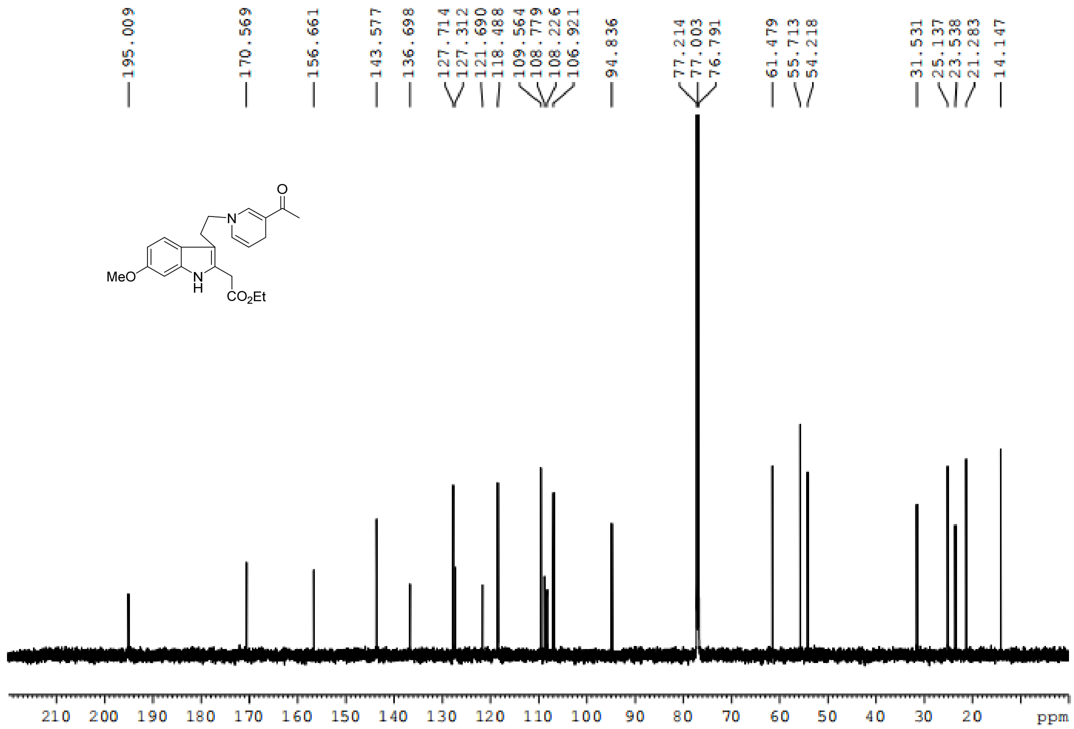
Copies of NMR spectra of **1m**



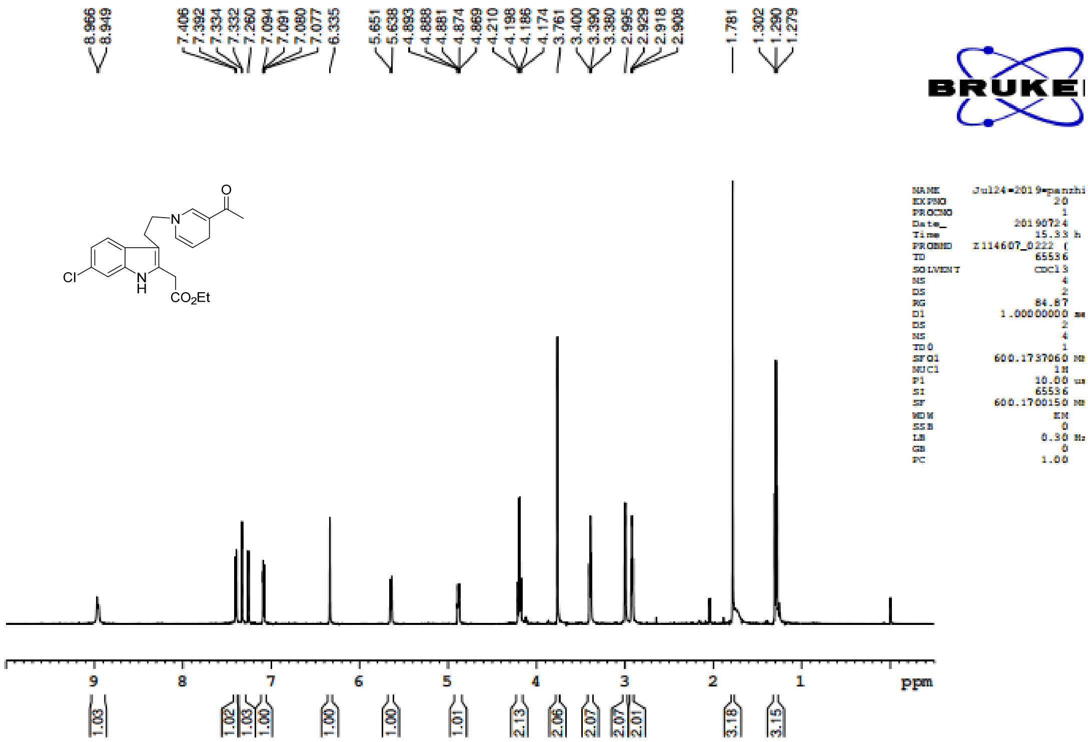


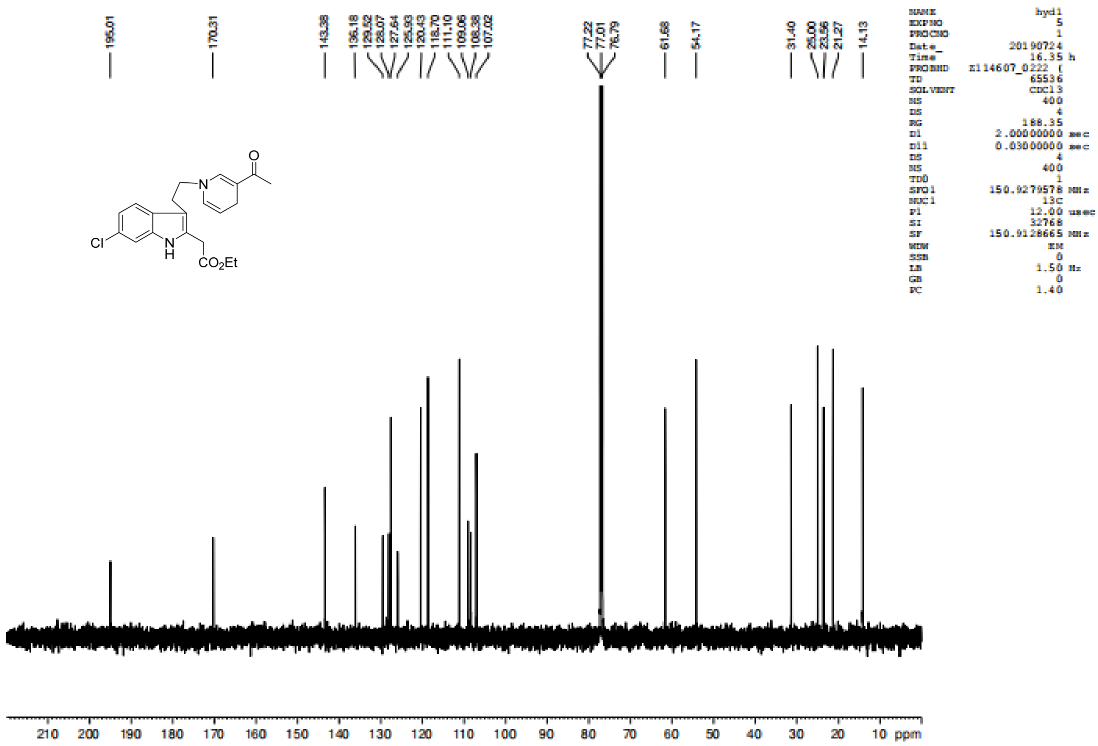
Copies of NMR spectra of **1n**



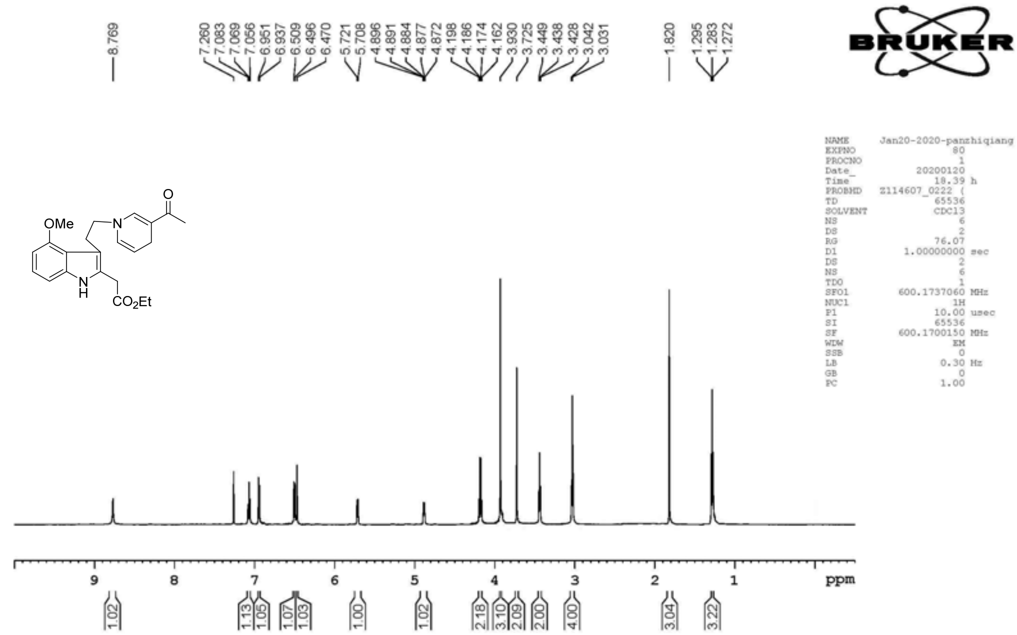


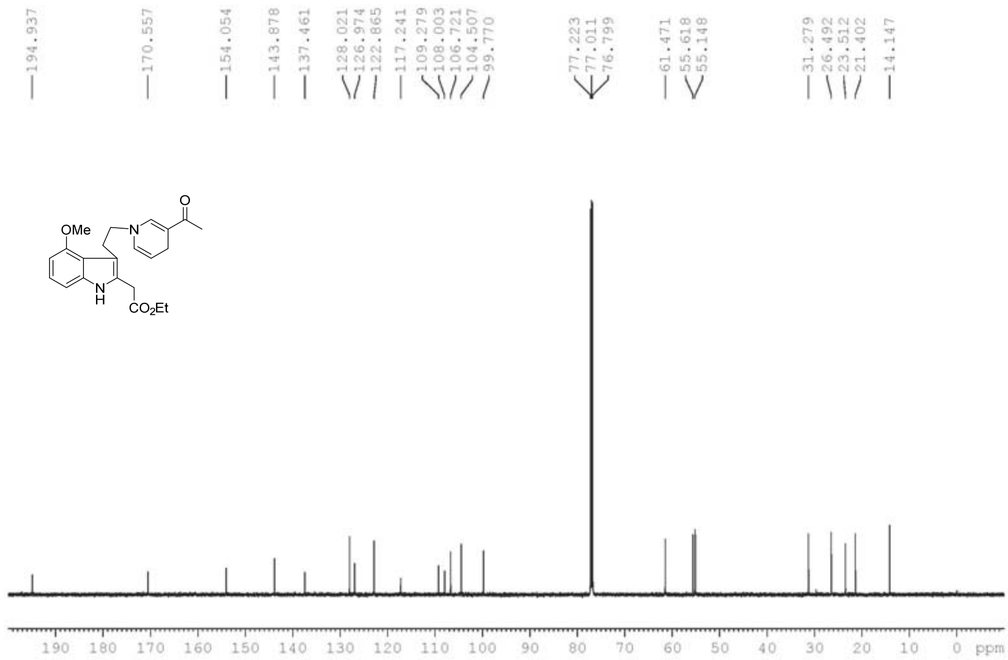
Copies of NMR spectra of **1o**



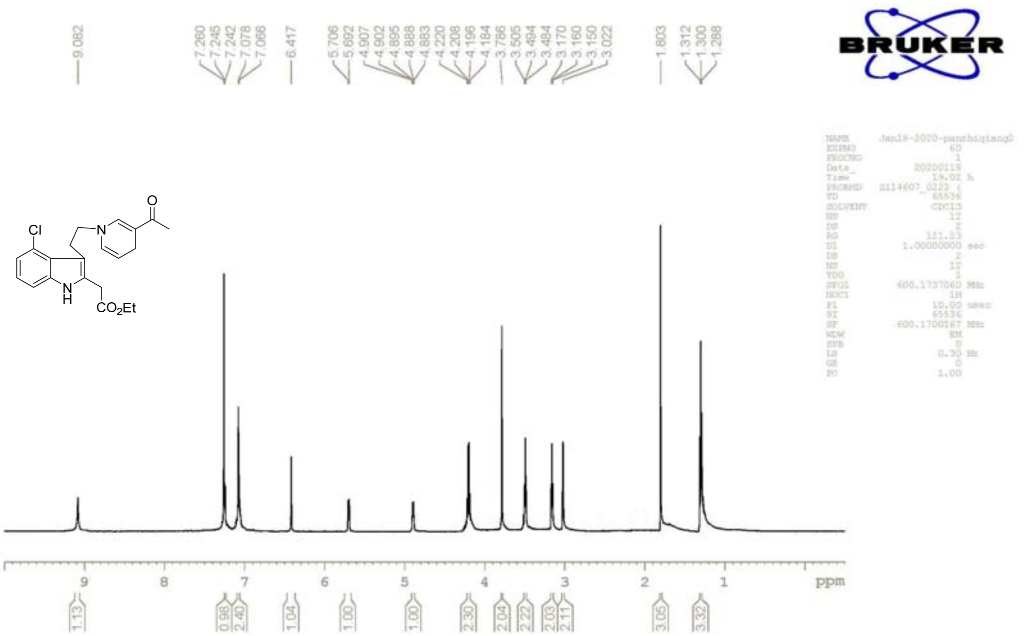


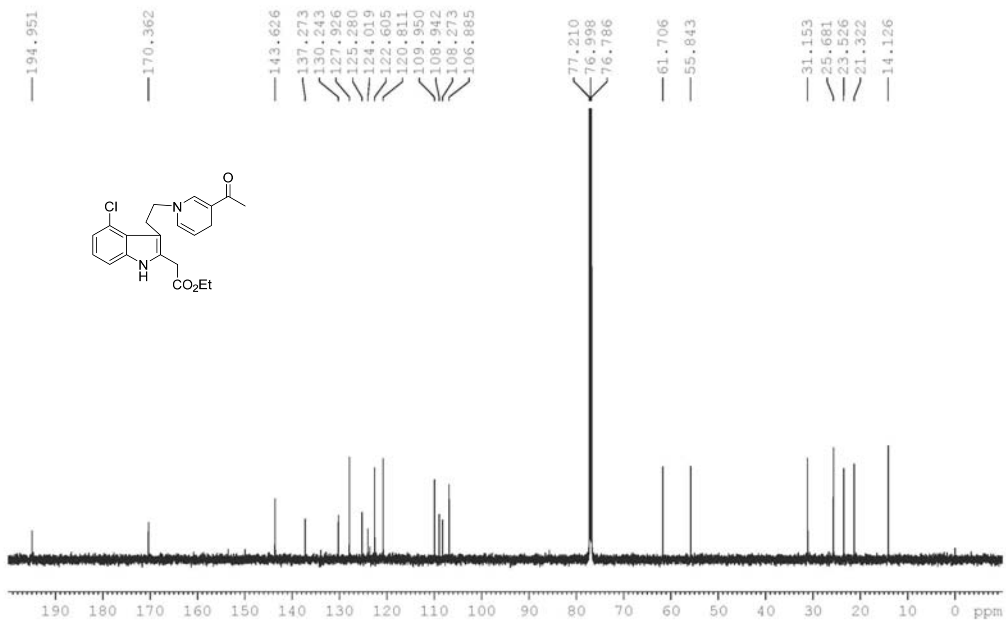
Copies of NMR spectra of **1p**



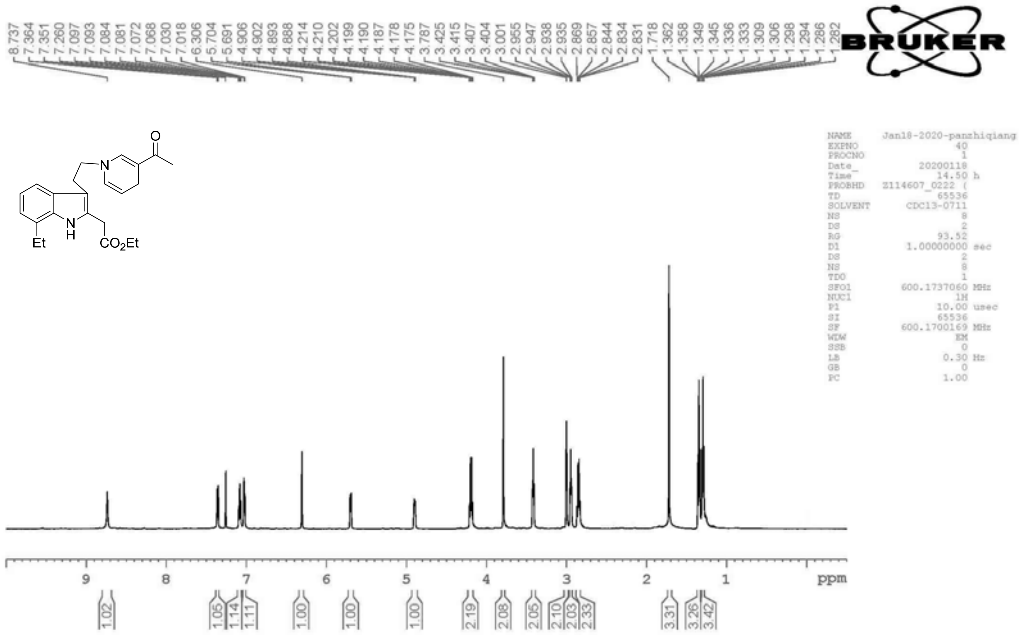


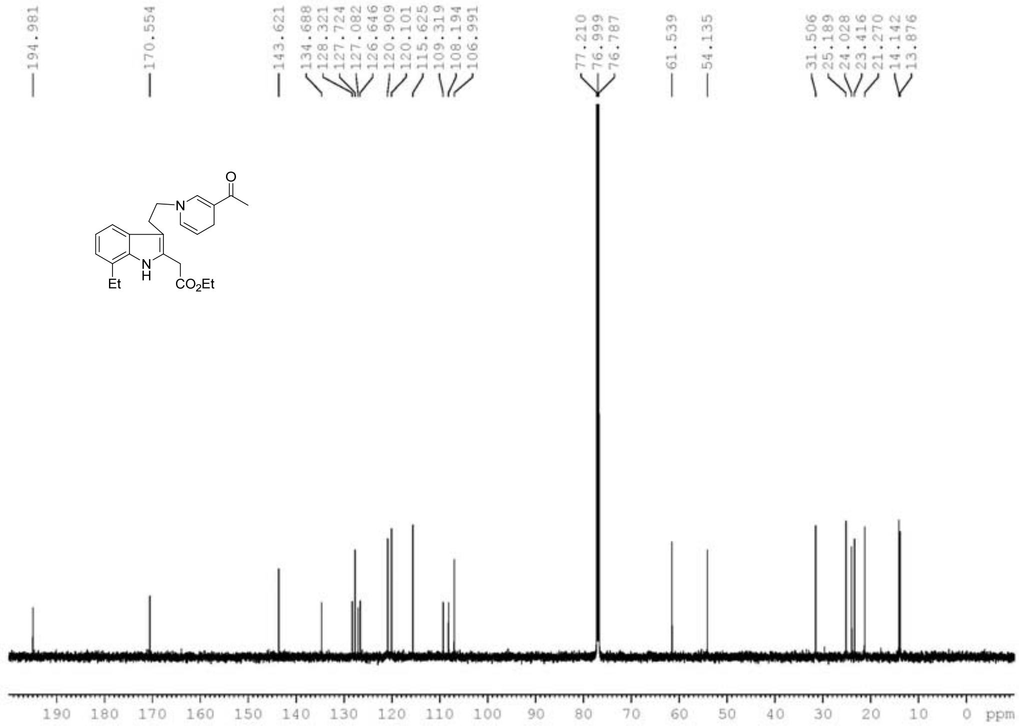
Copies of NMR spectra of **1q**



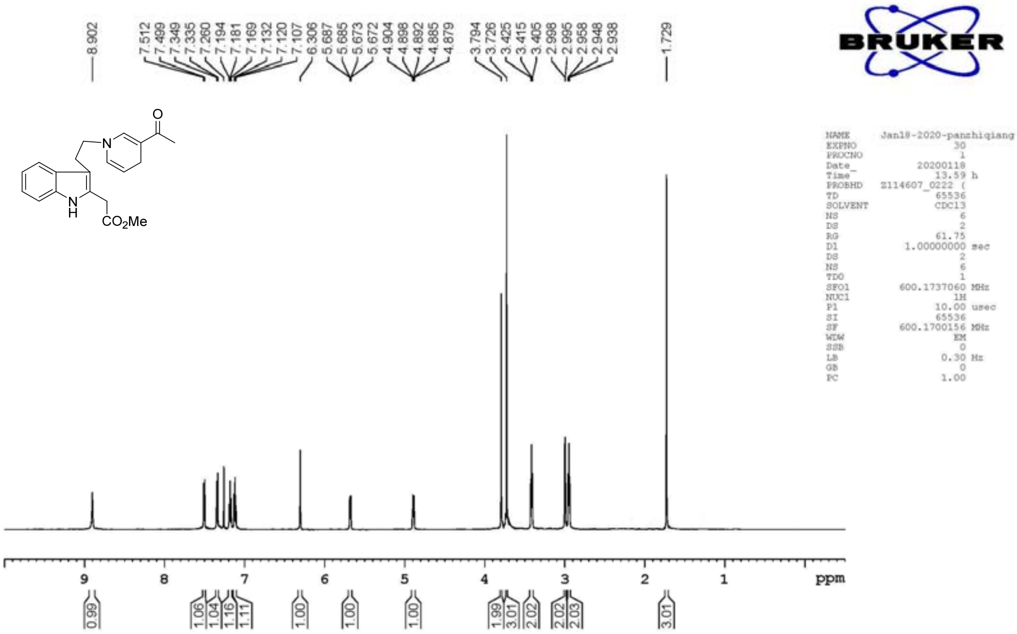


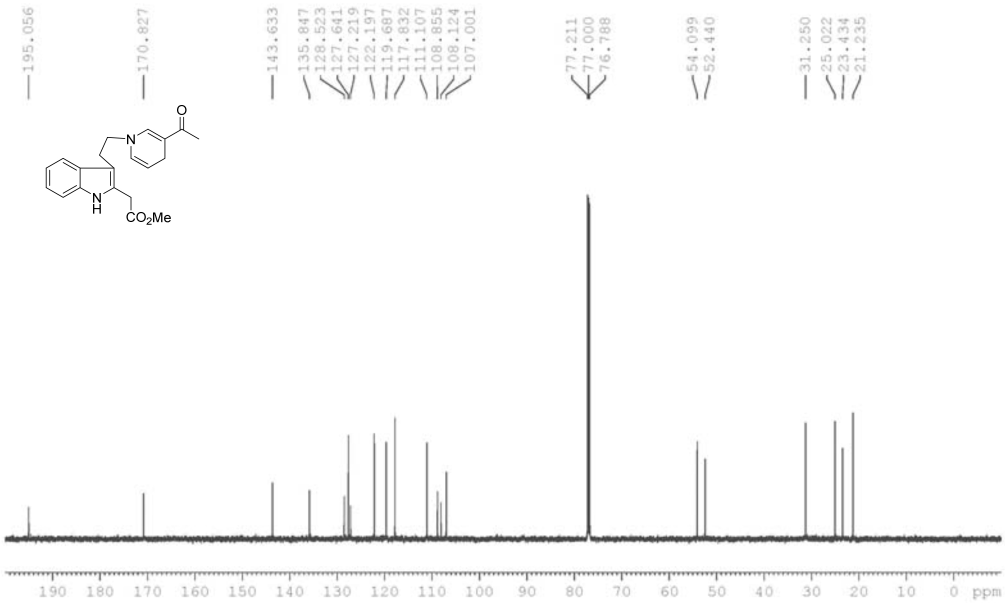
Copies of NMR spectra of **1r**



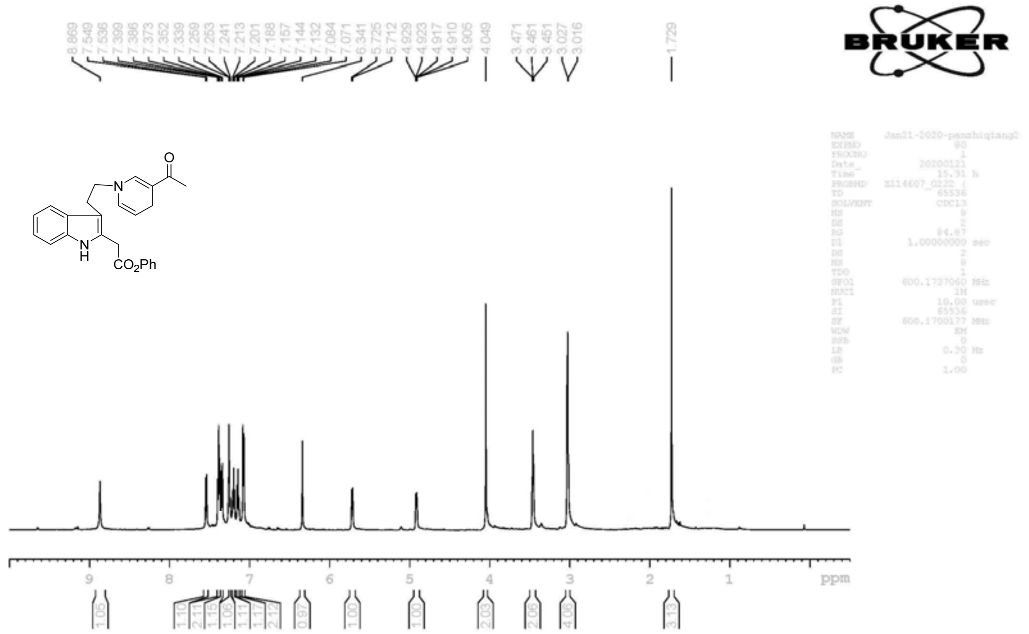


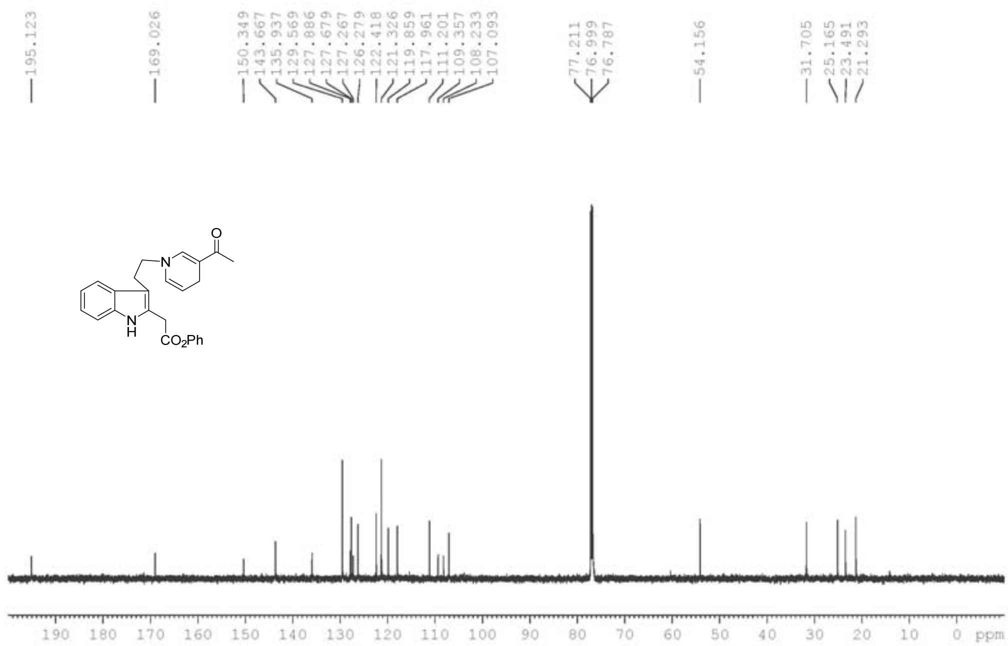
Copies of NMR spectra of **1s**



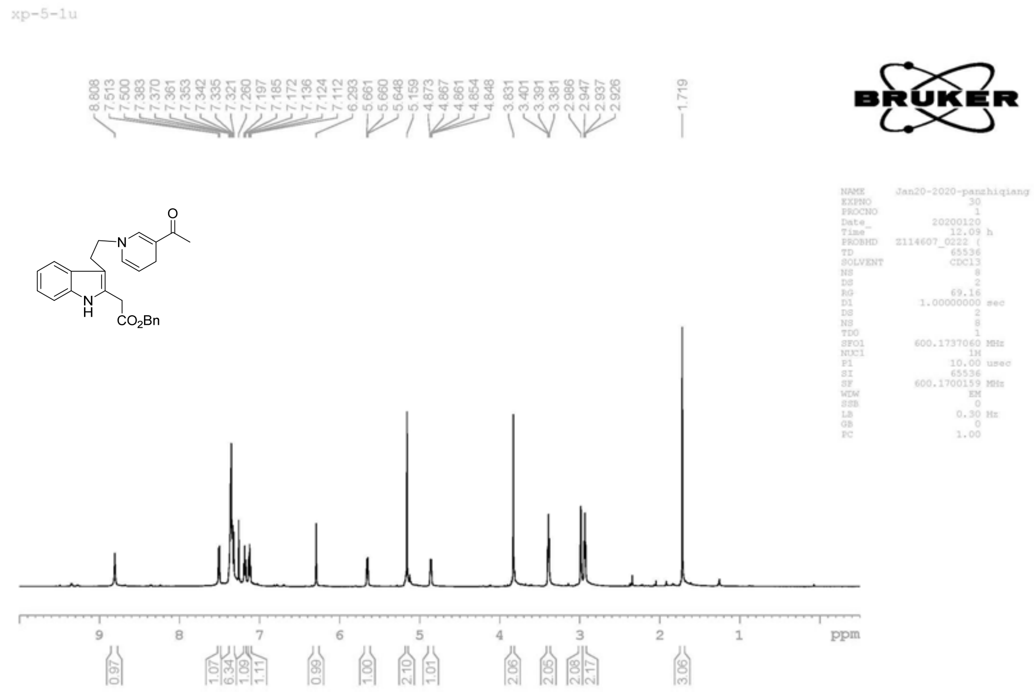


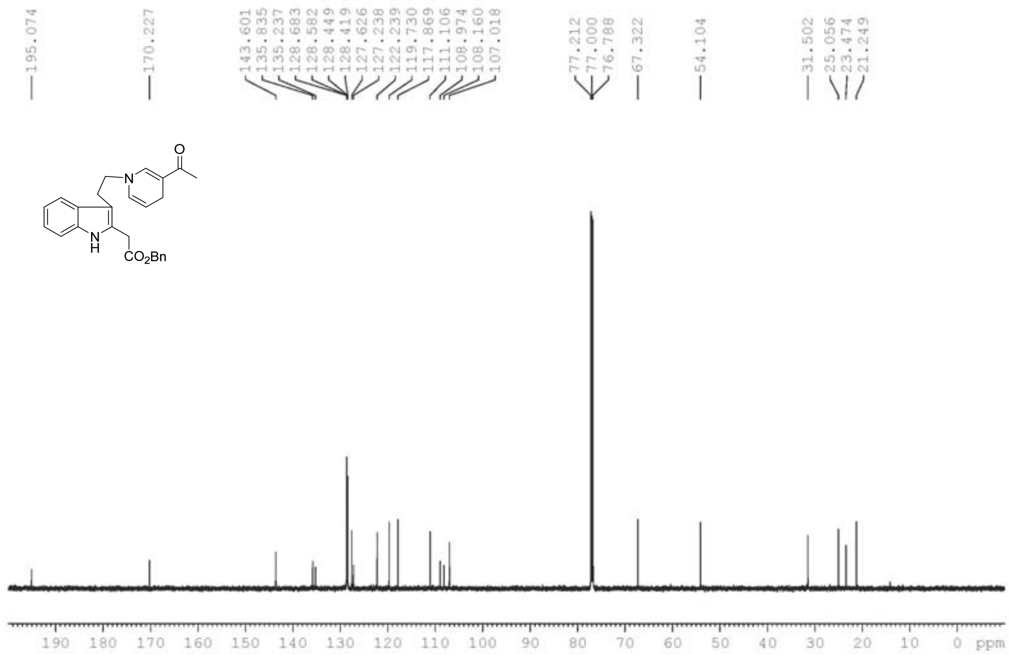
Copies of NMR spectra of **1t**



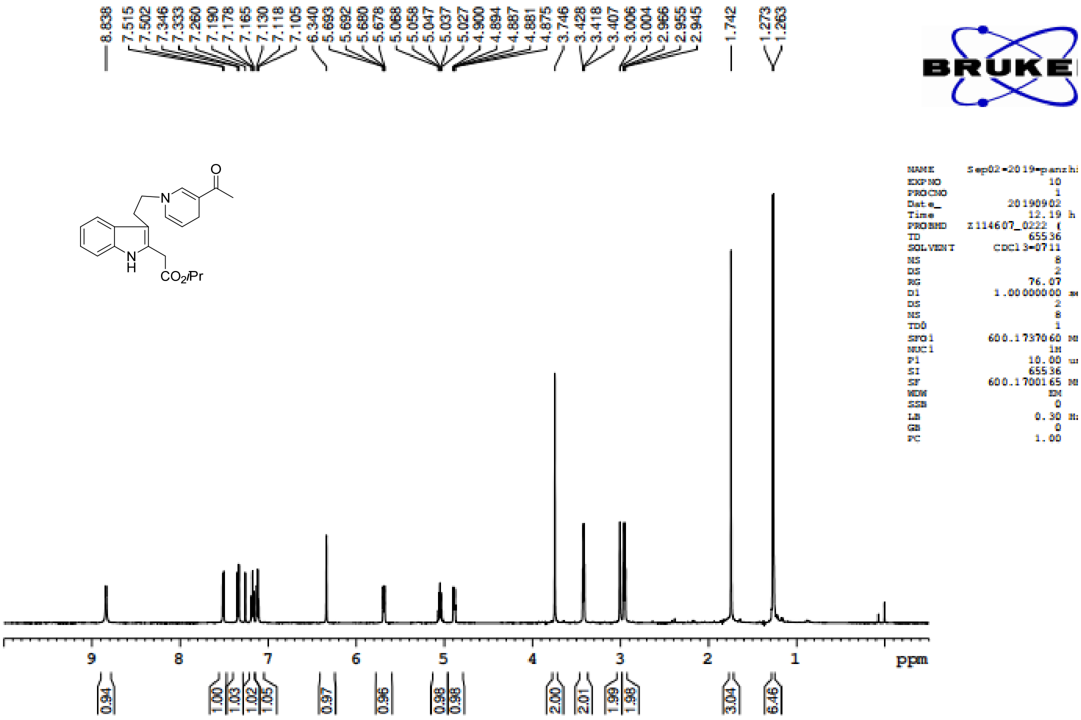


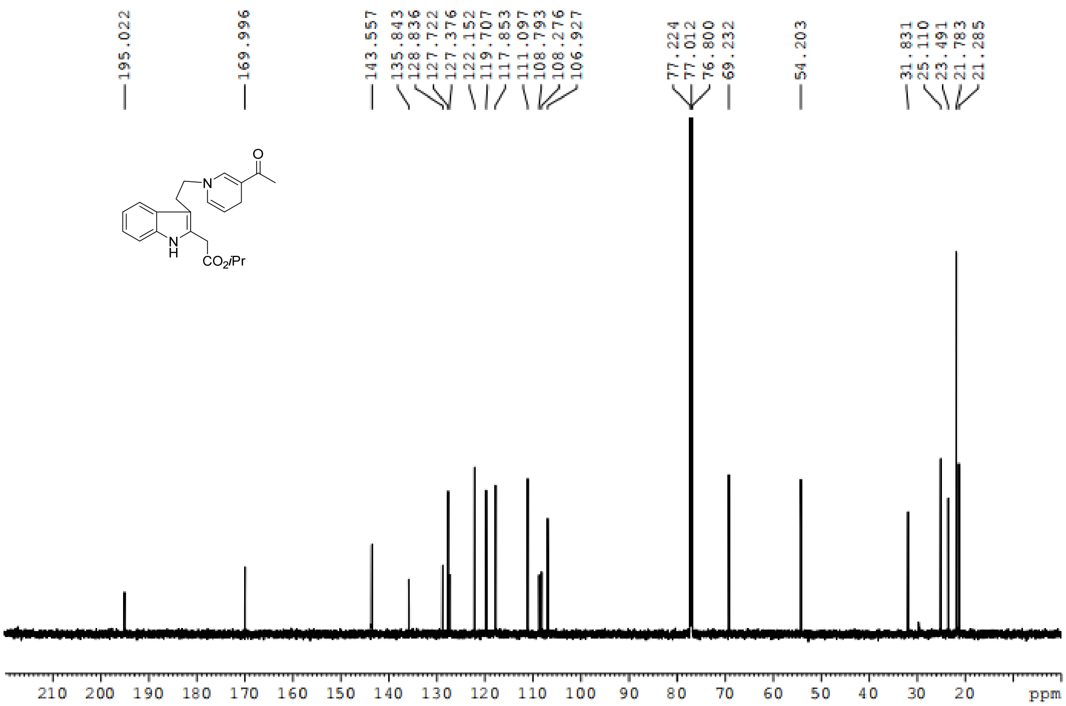
Copies of NMR spectra of **1u**



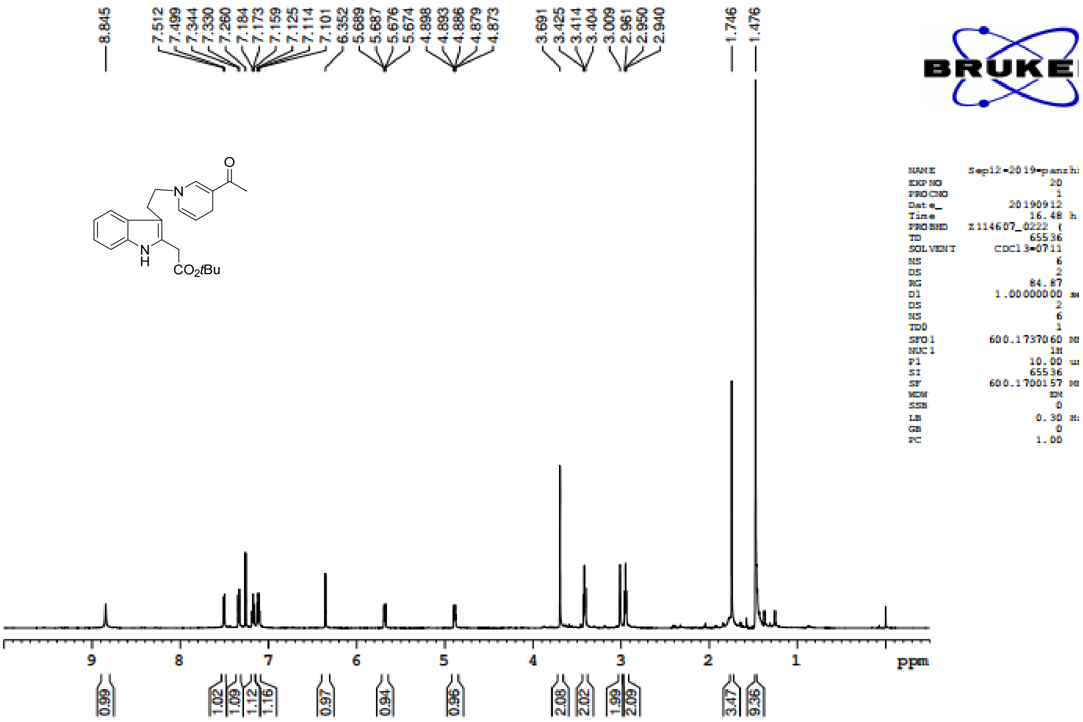


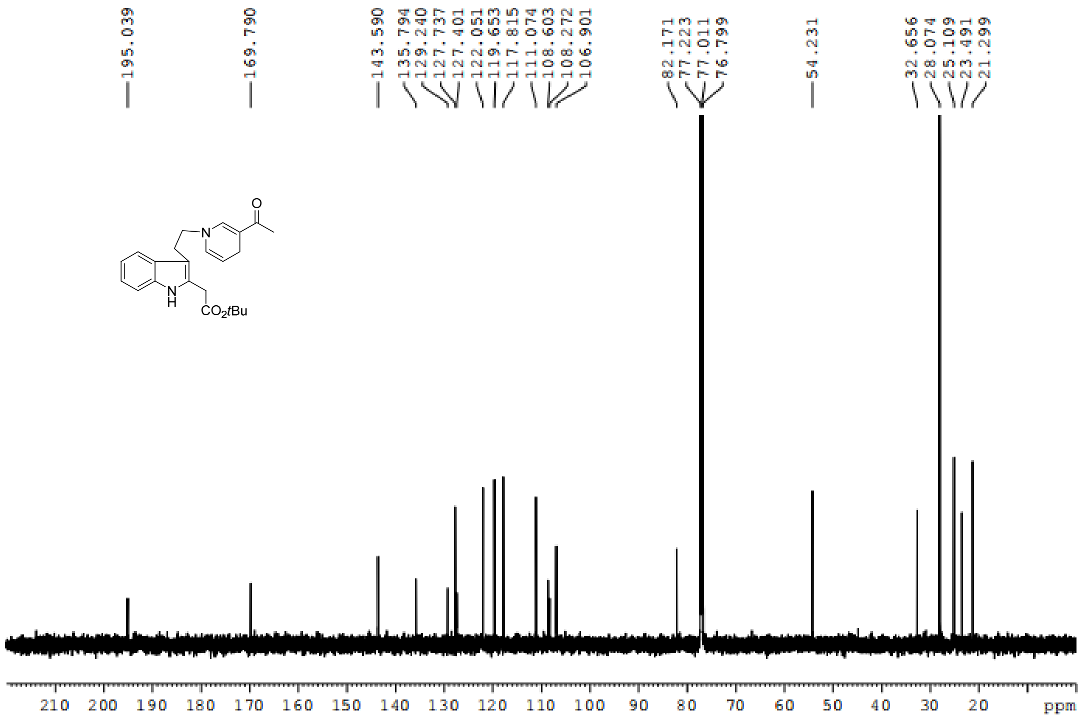
Copies of NMR spectra of **1v**



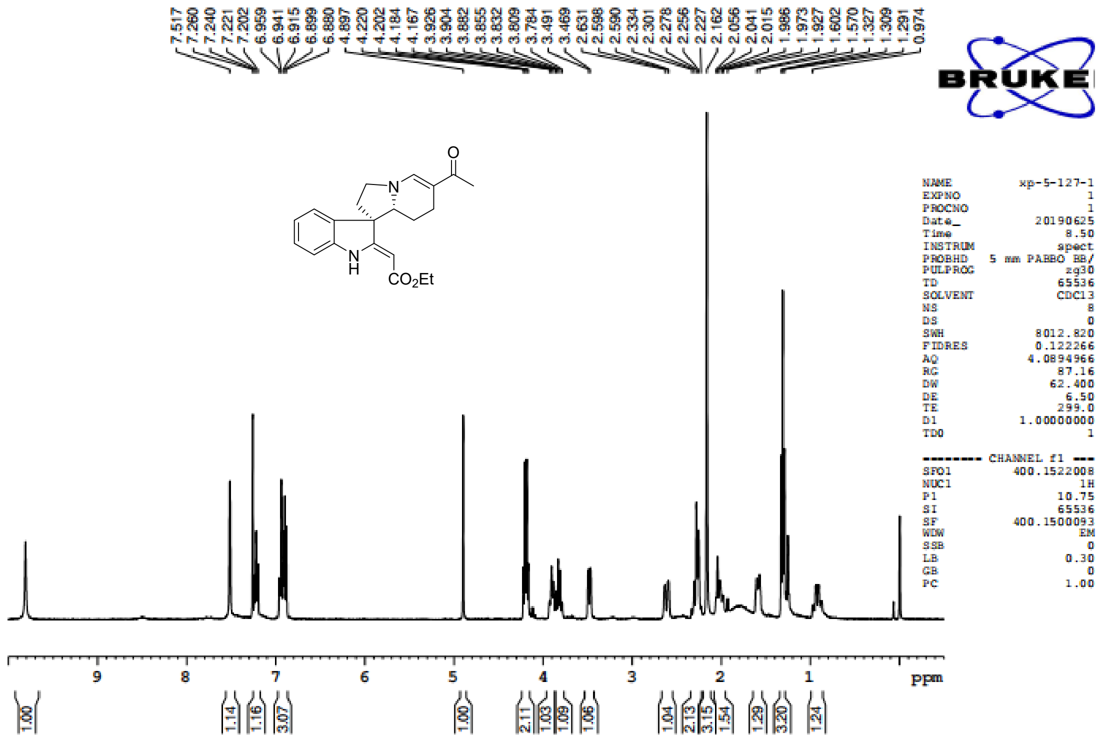


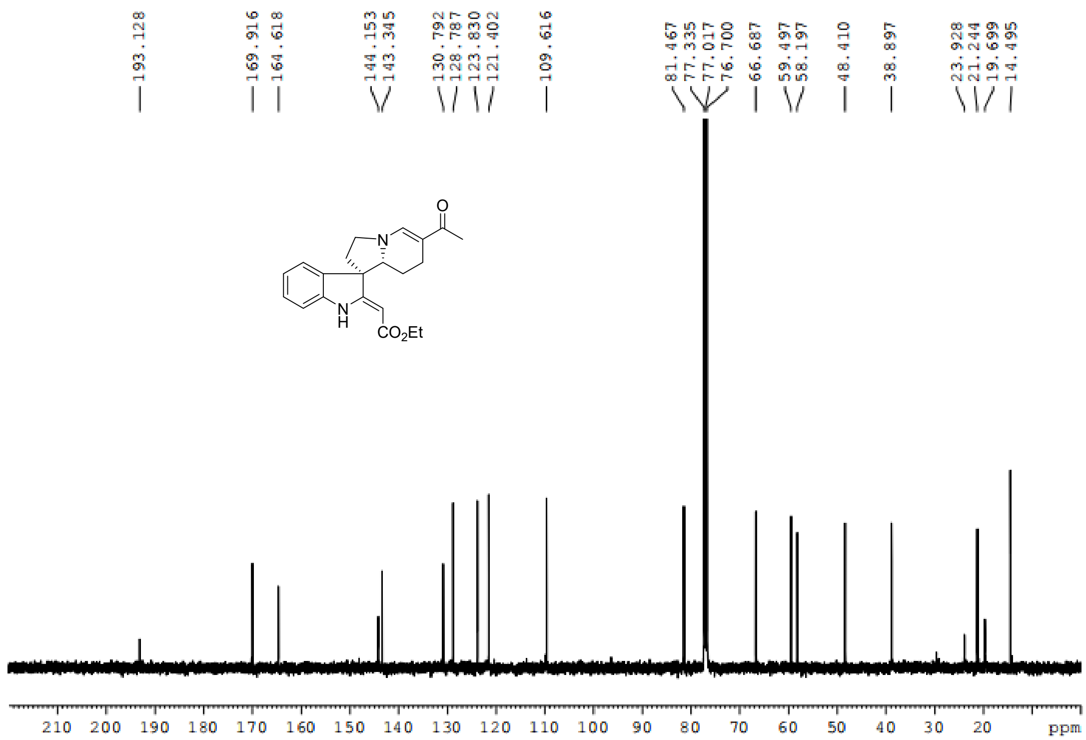
Copies of NMR spectra of **1w**



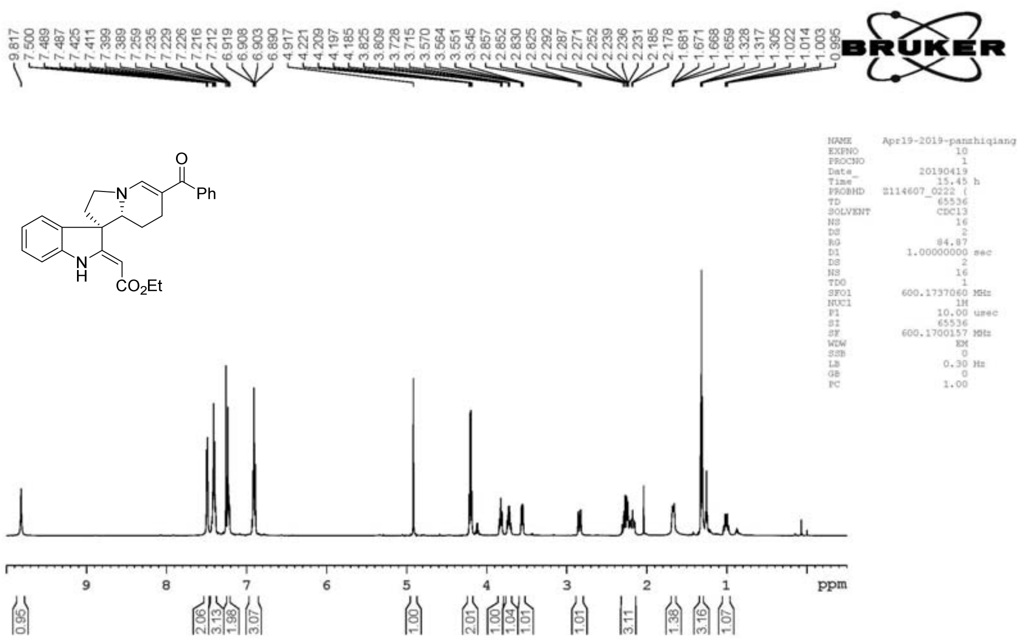


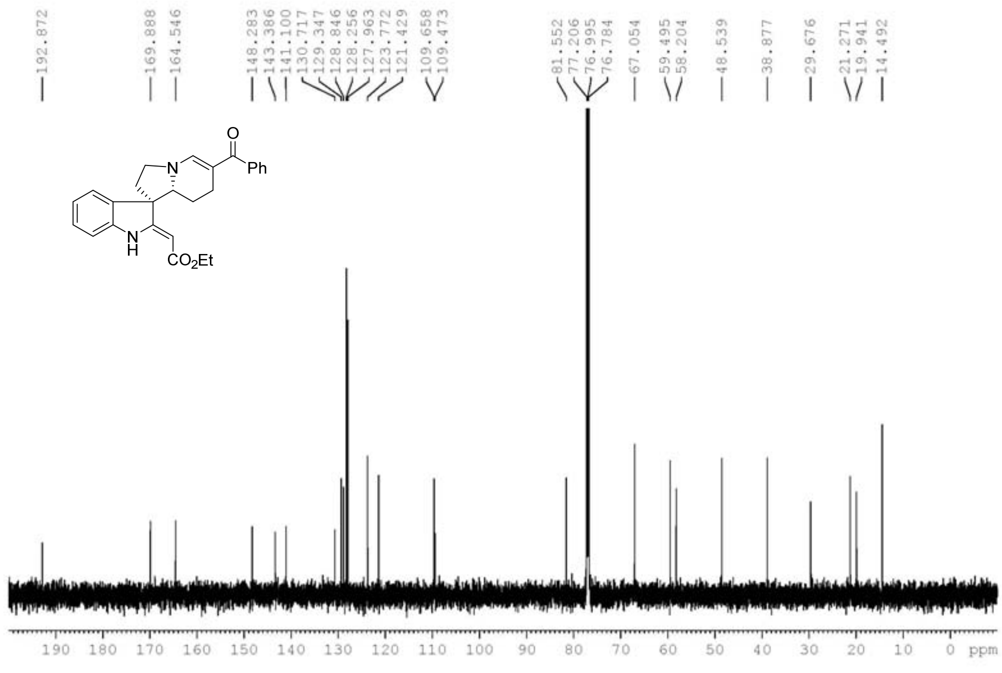
Copies of NMR spectra of **2b**



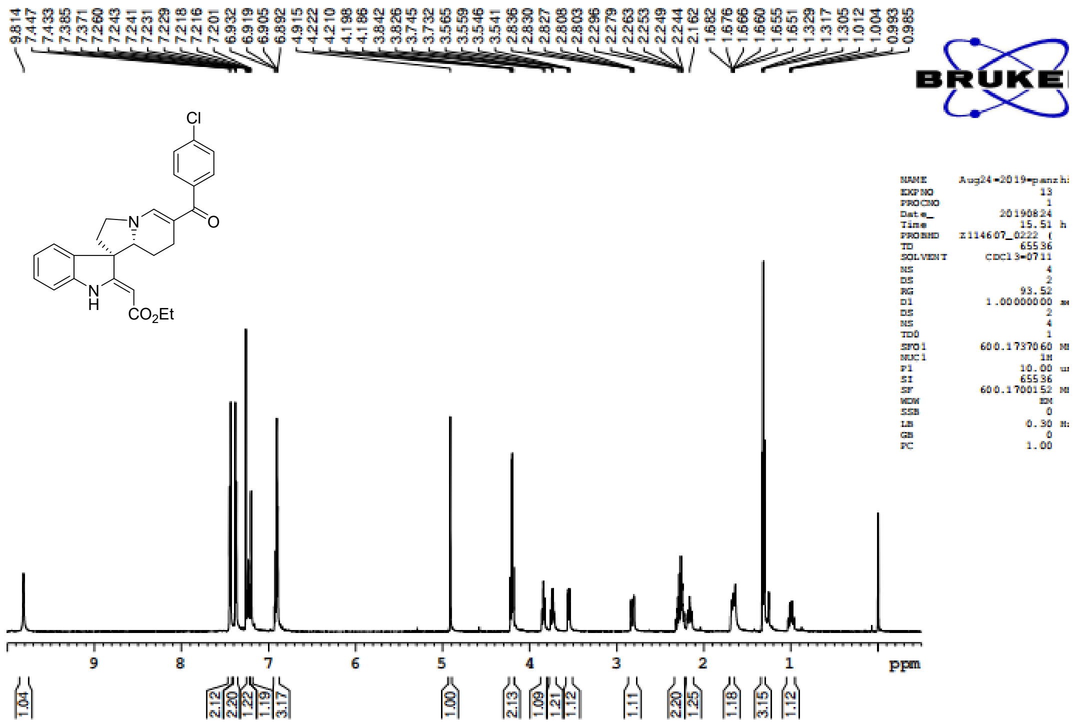


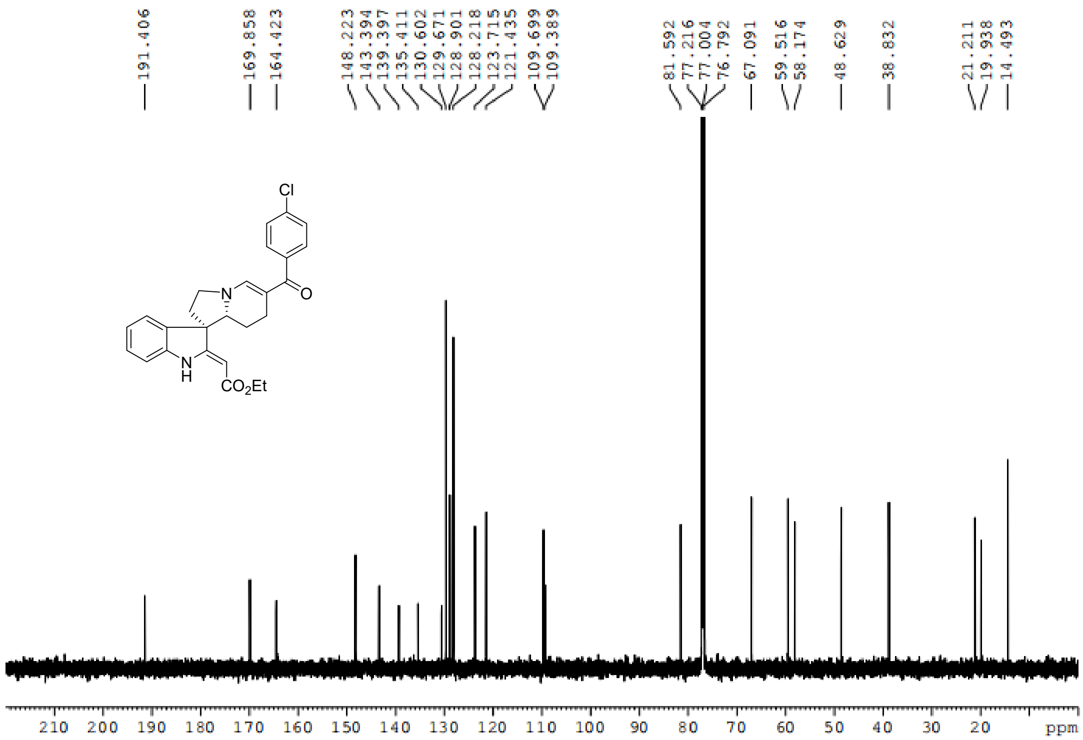
Copies of NMR spectra of **2c**



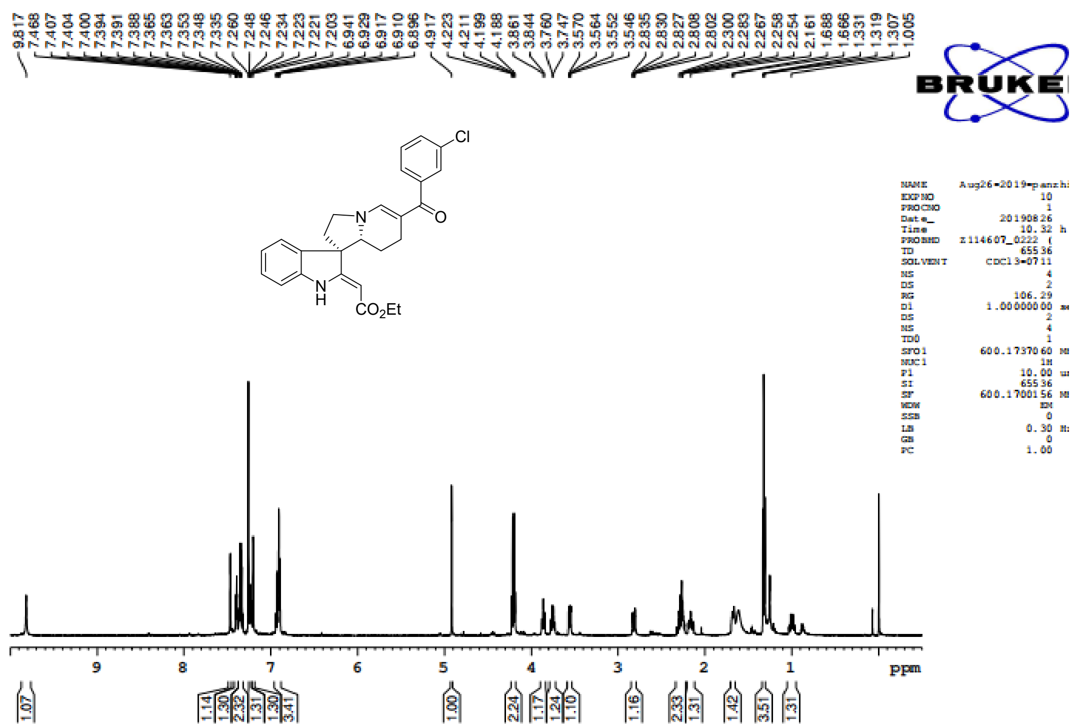


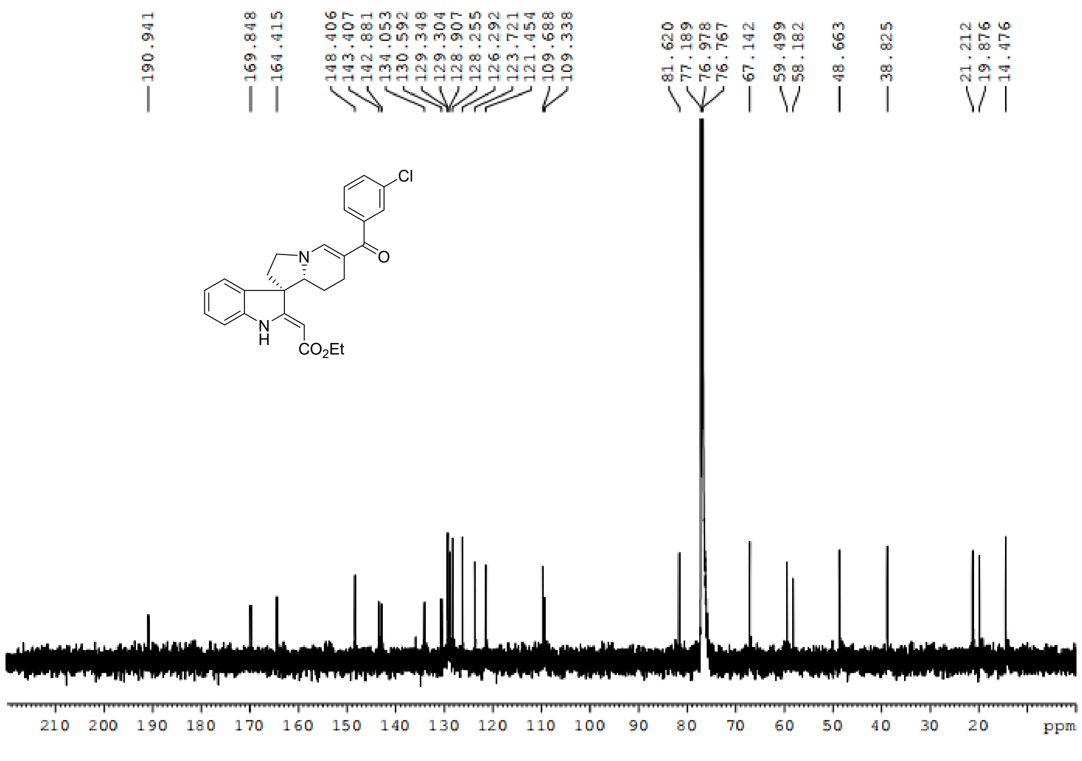
Copies of NMR spectra of **2d**



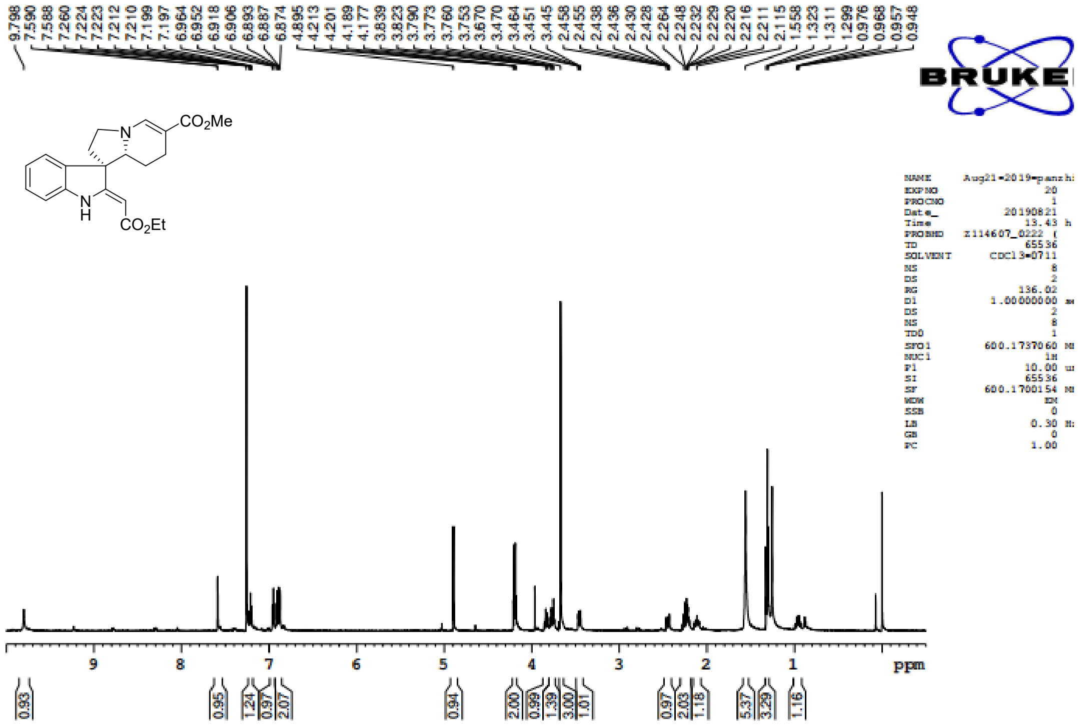


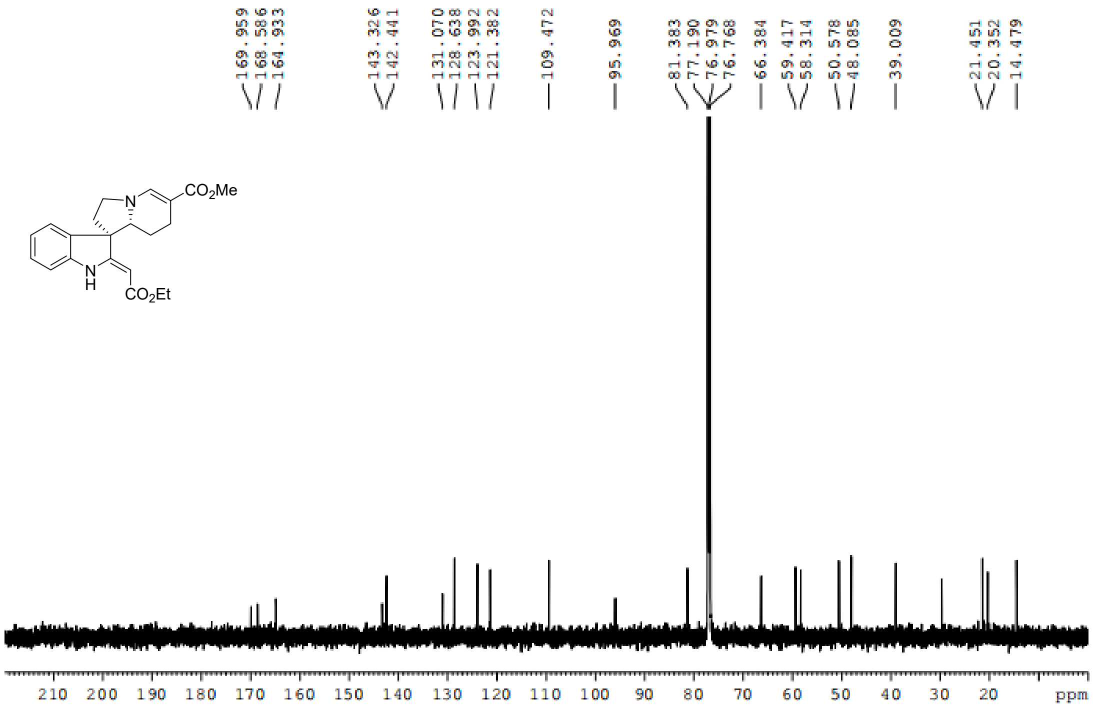
Copies of NMR spectra of **2e**



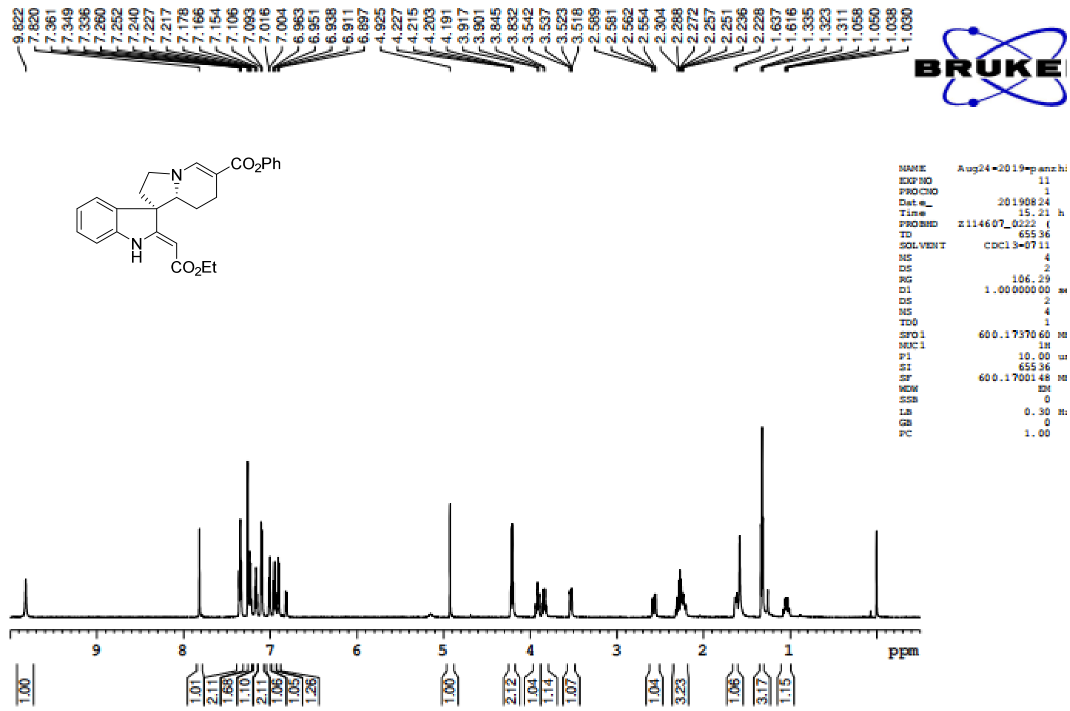


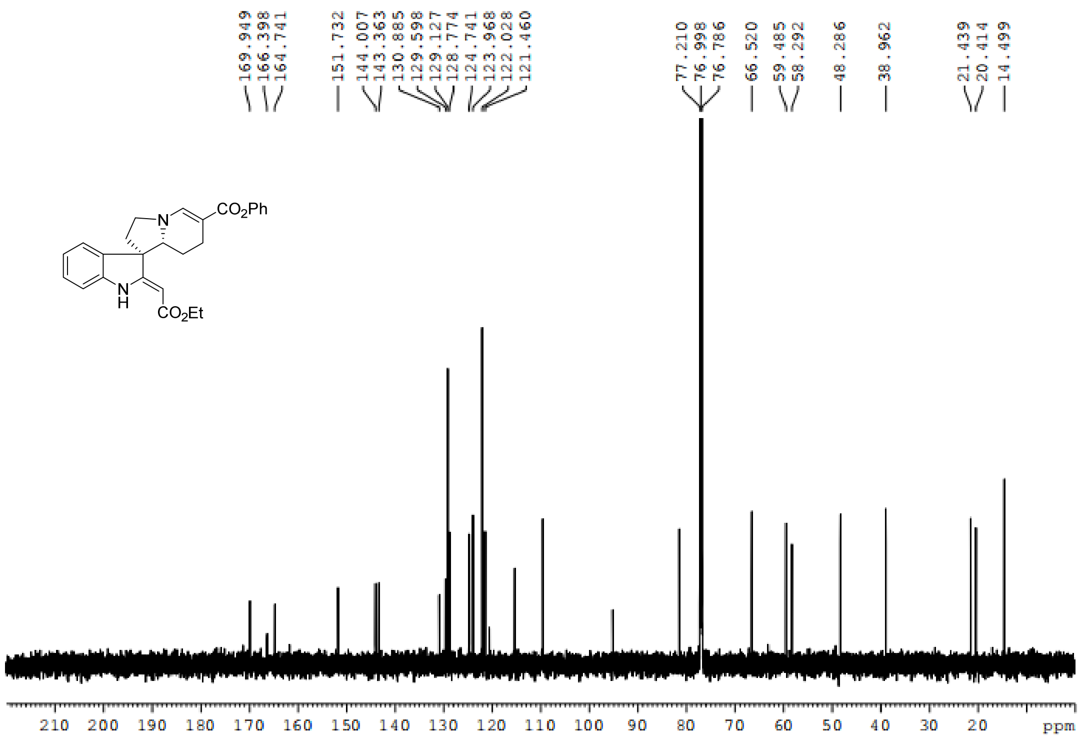
Copies of NMR spectra of **2f**



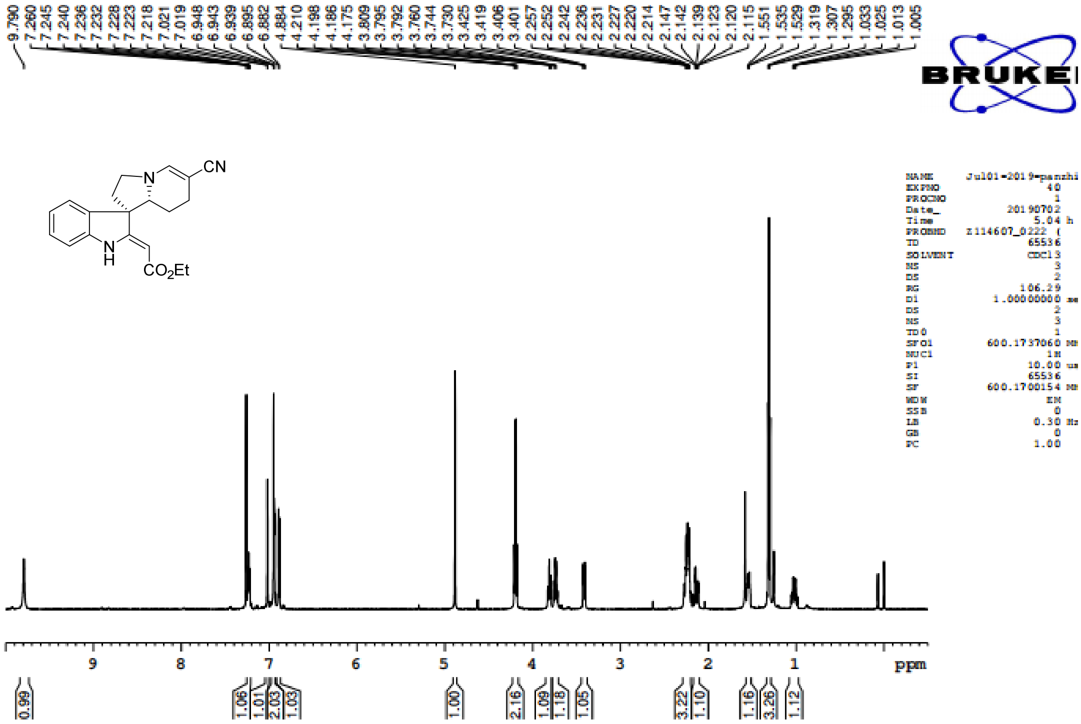


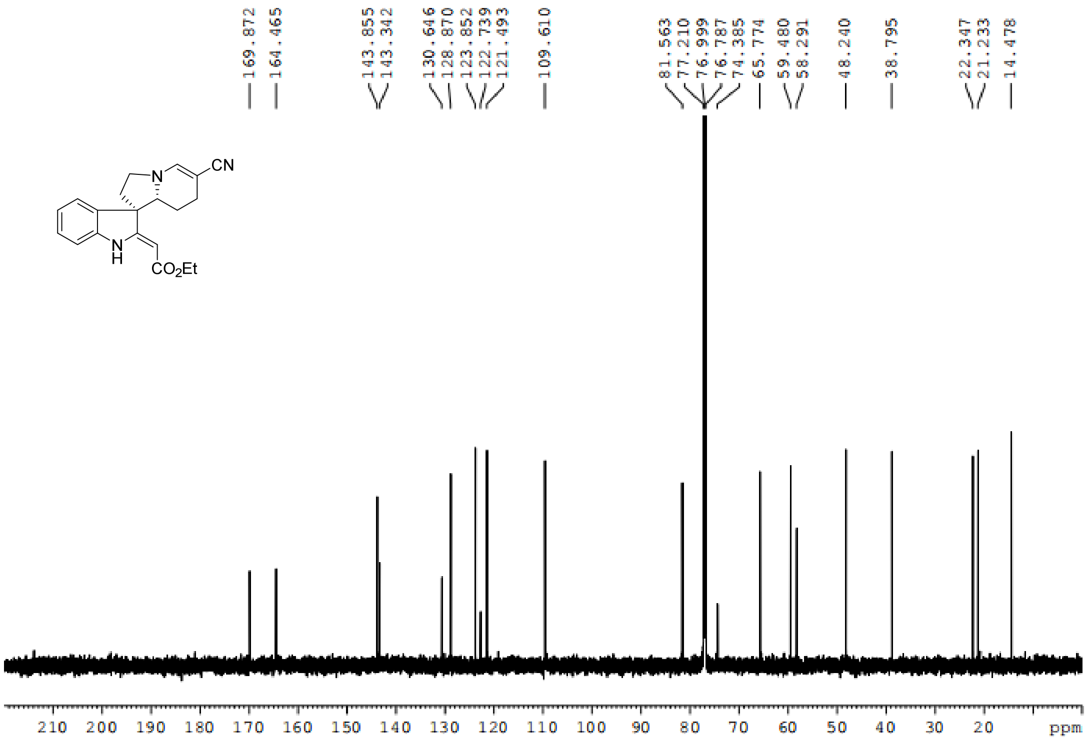
Copies of NMR spectra of **2g**



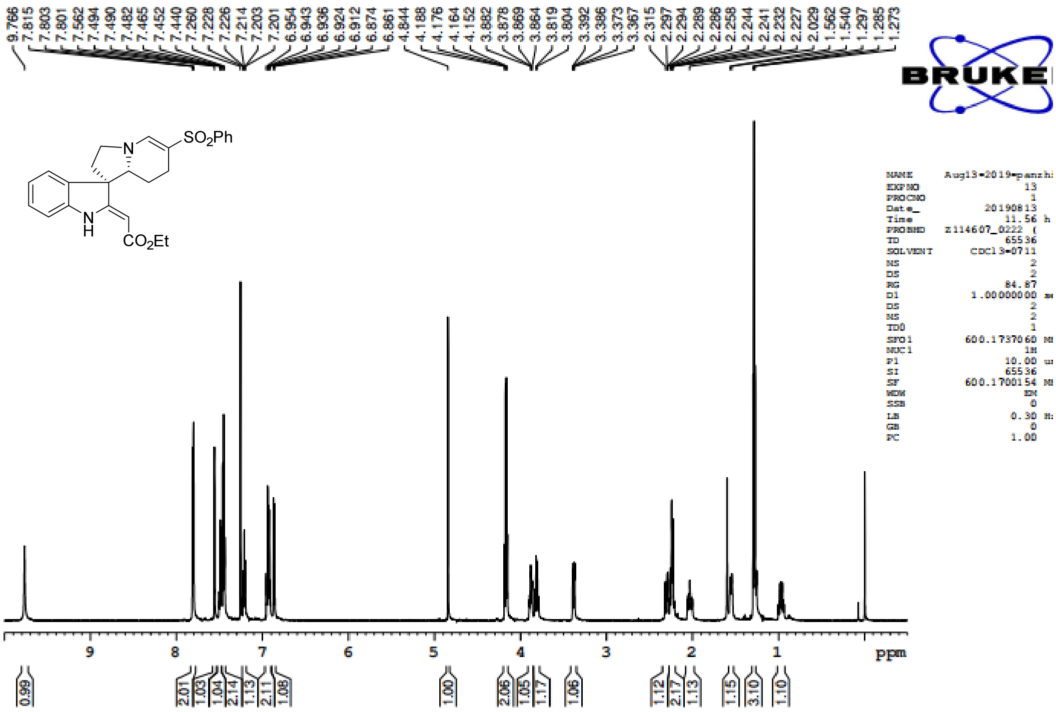


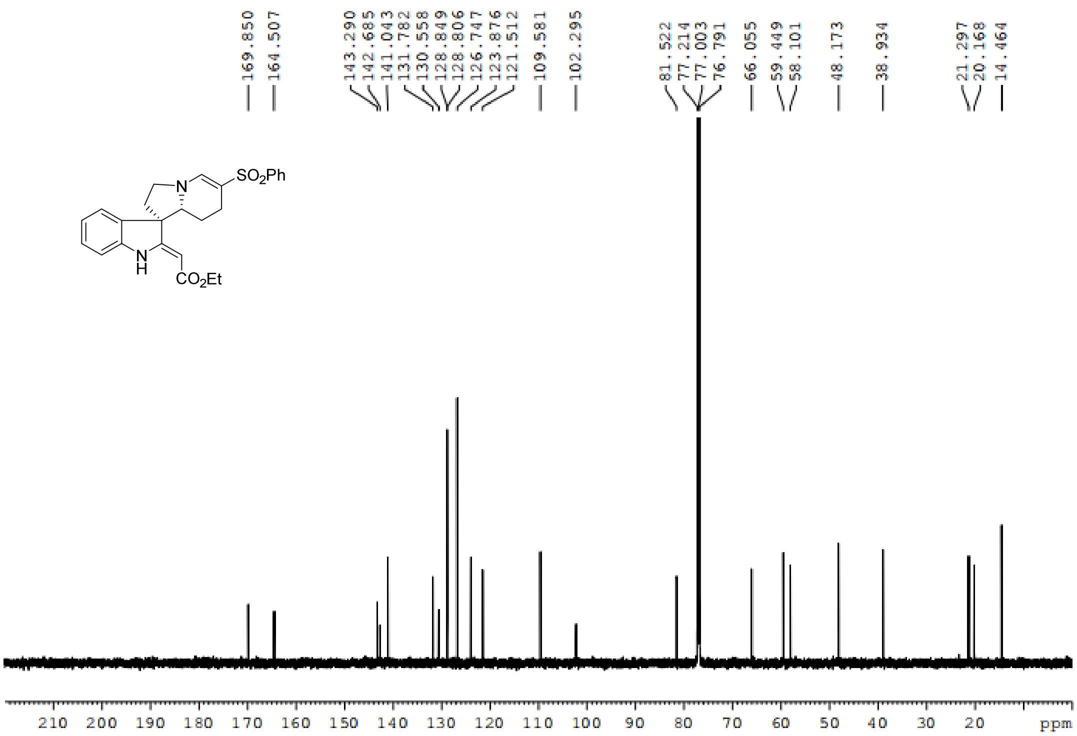
Copies of NMR spectra of **2h**



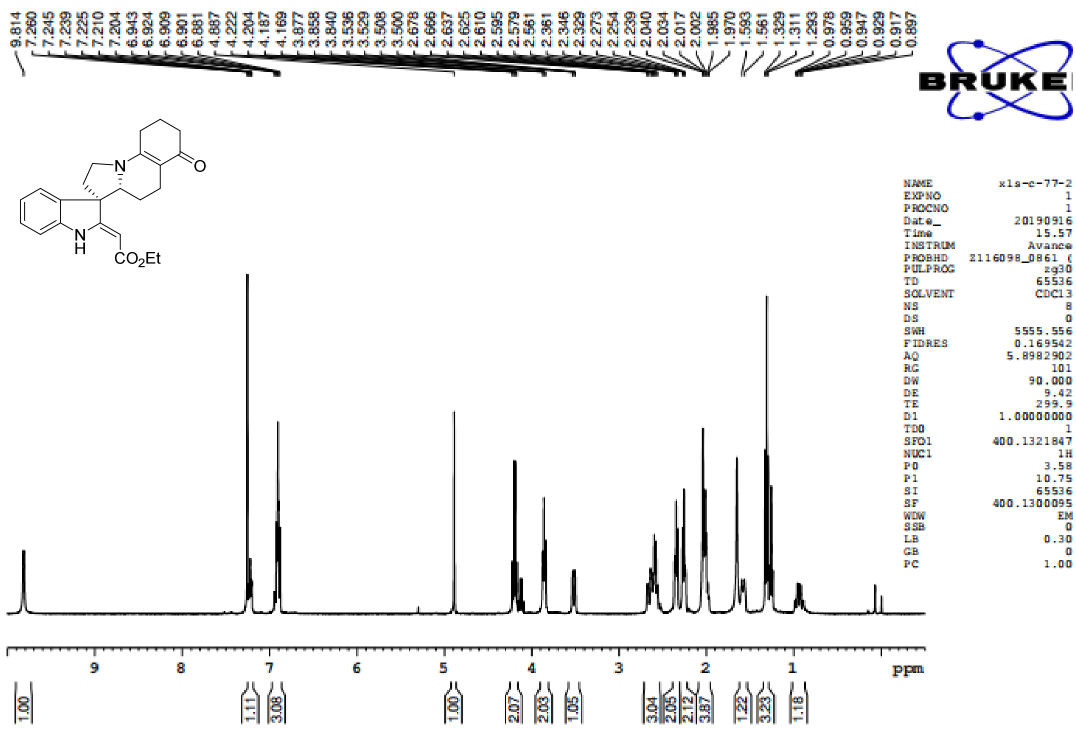


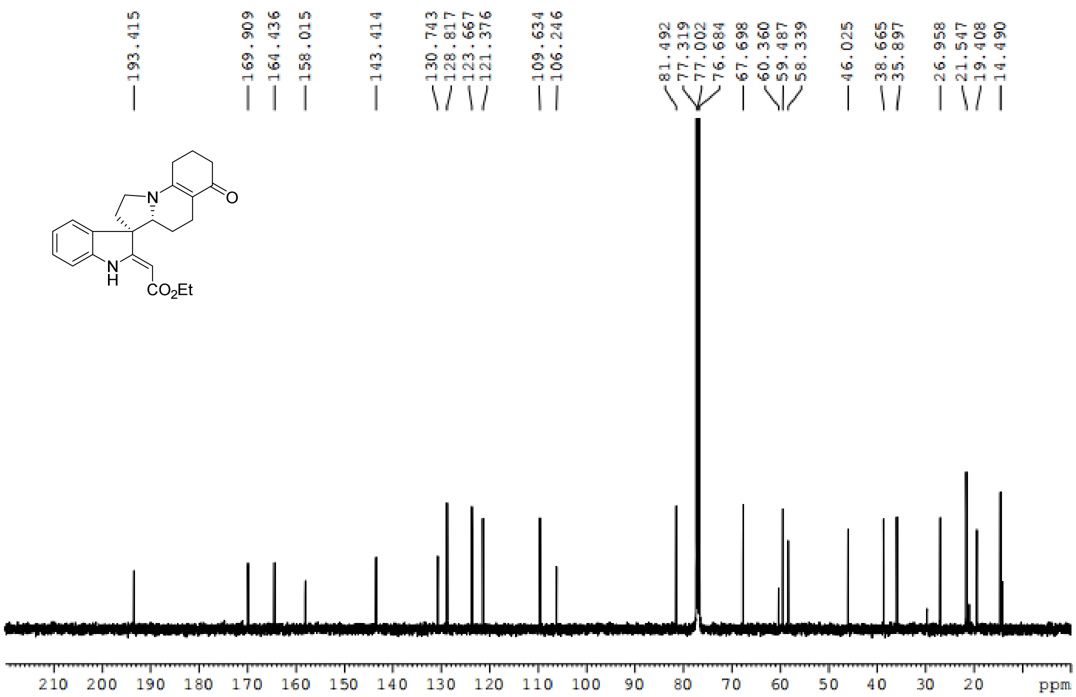
Copies of NMR spectra of **2i**



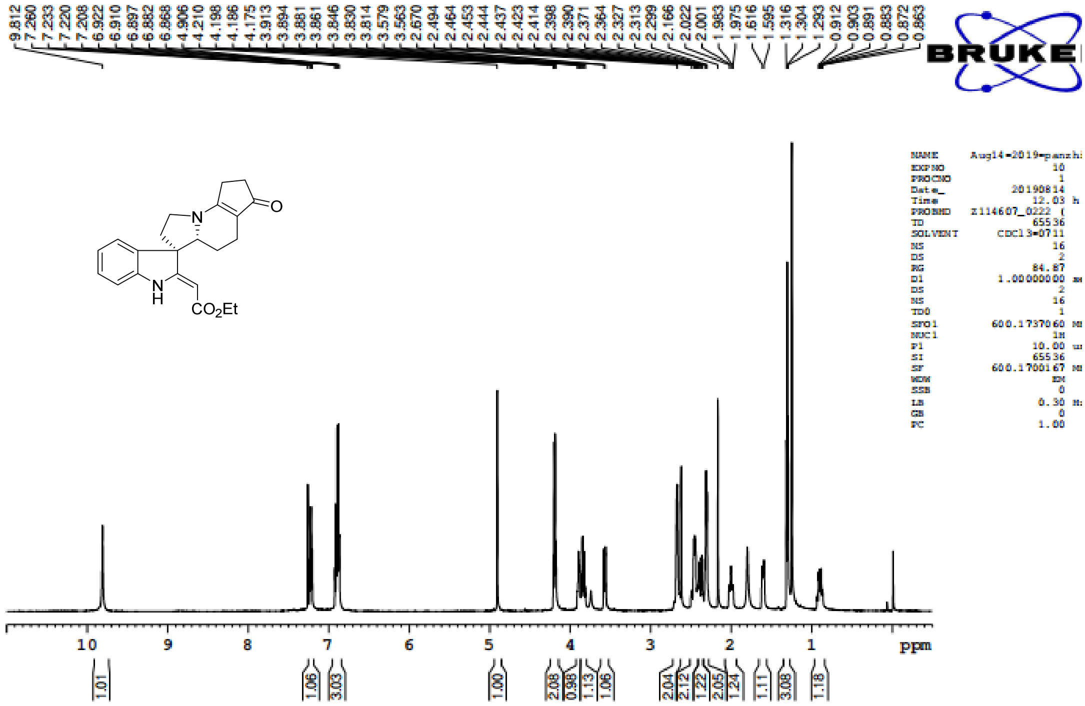


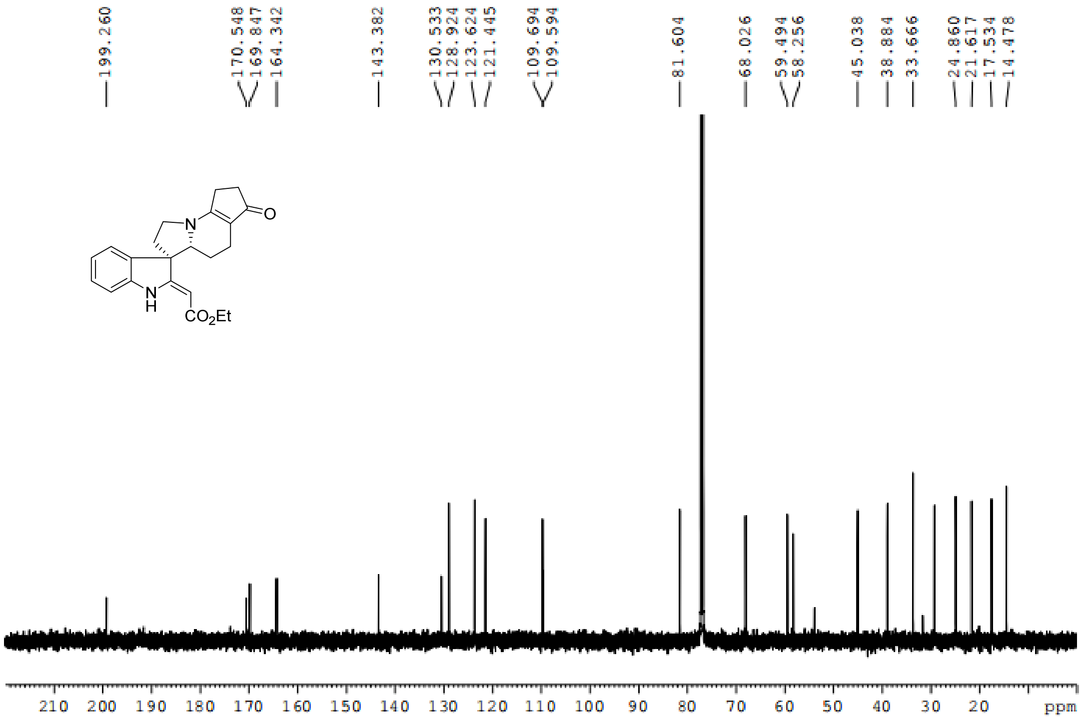
Copies of NMR spectra of **2j**



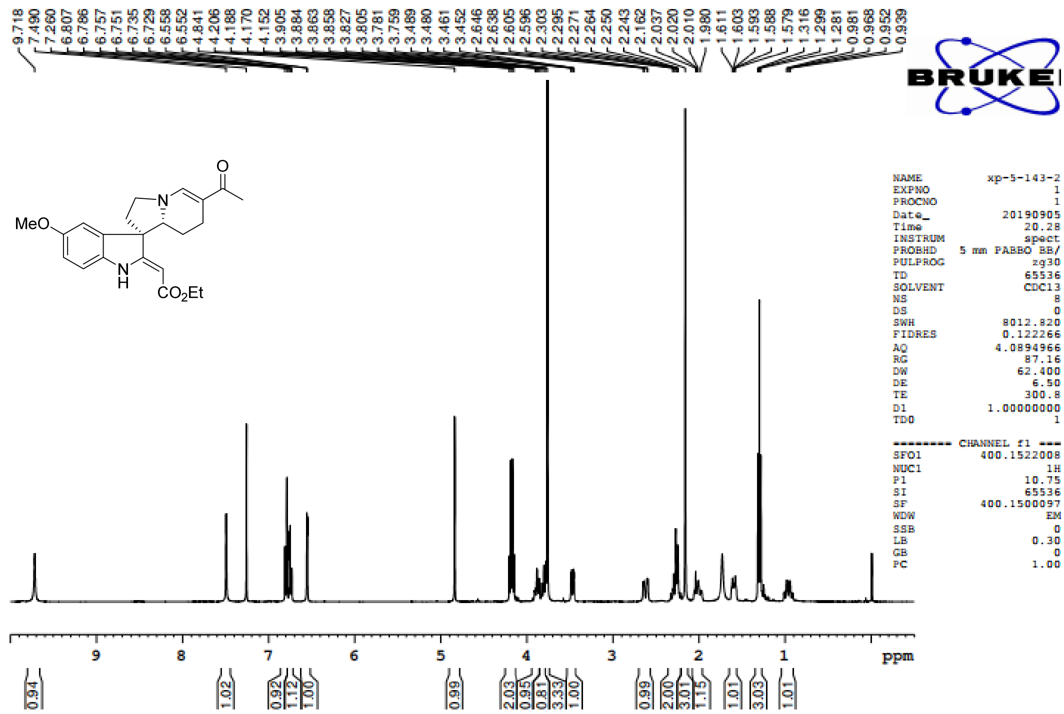


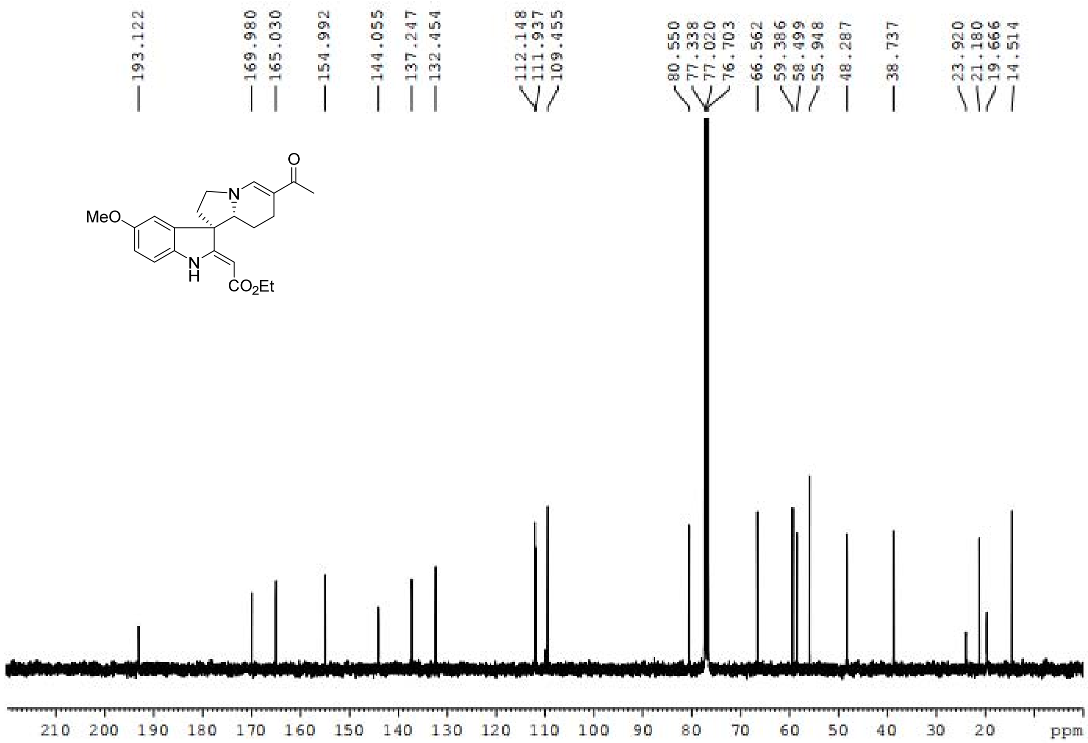
Copies of NMR spectra of **2k**



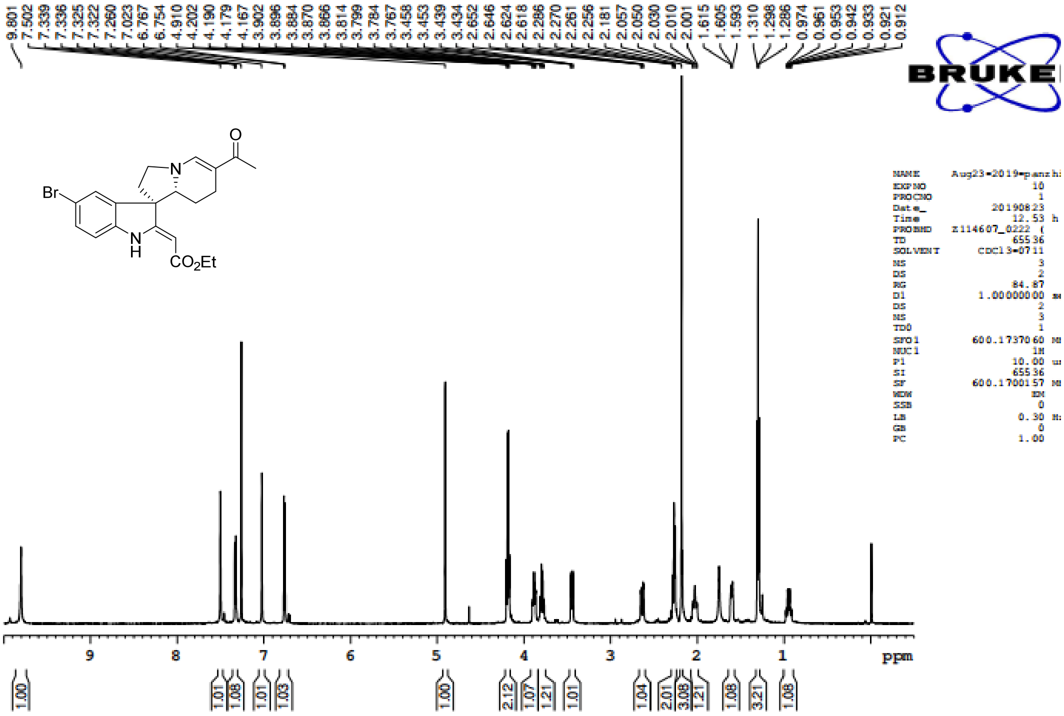


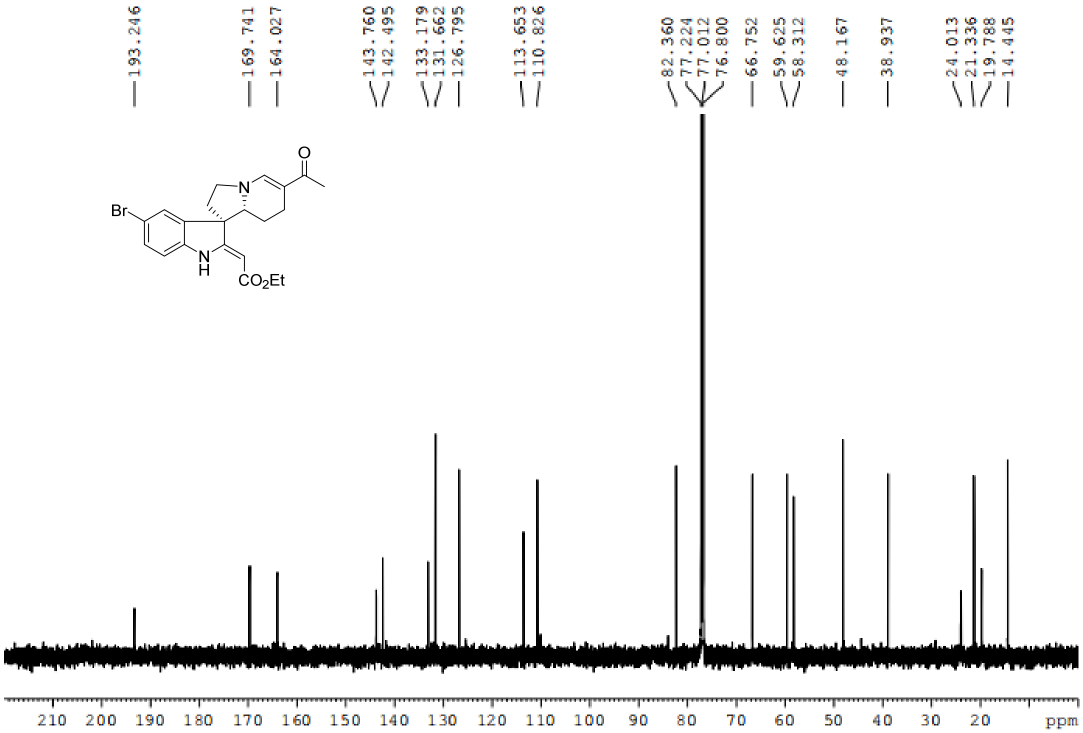
Copies of NMR spectra of **2l**



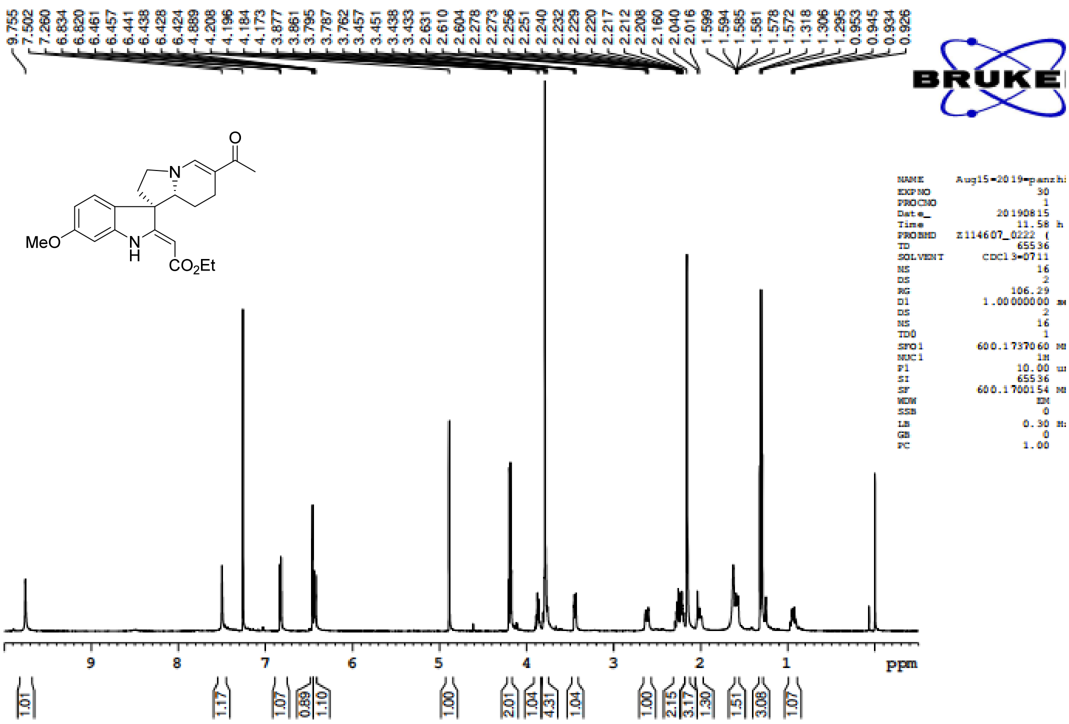


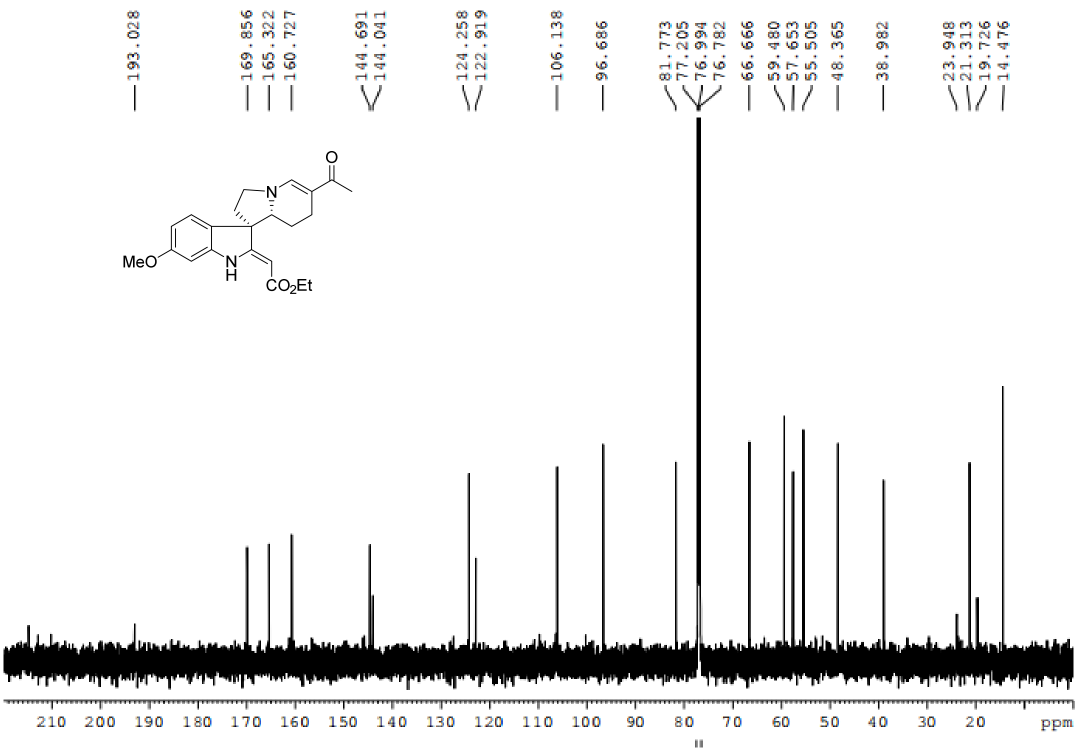
Copies of NMR spectra of **2m**



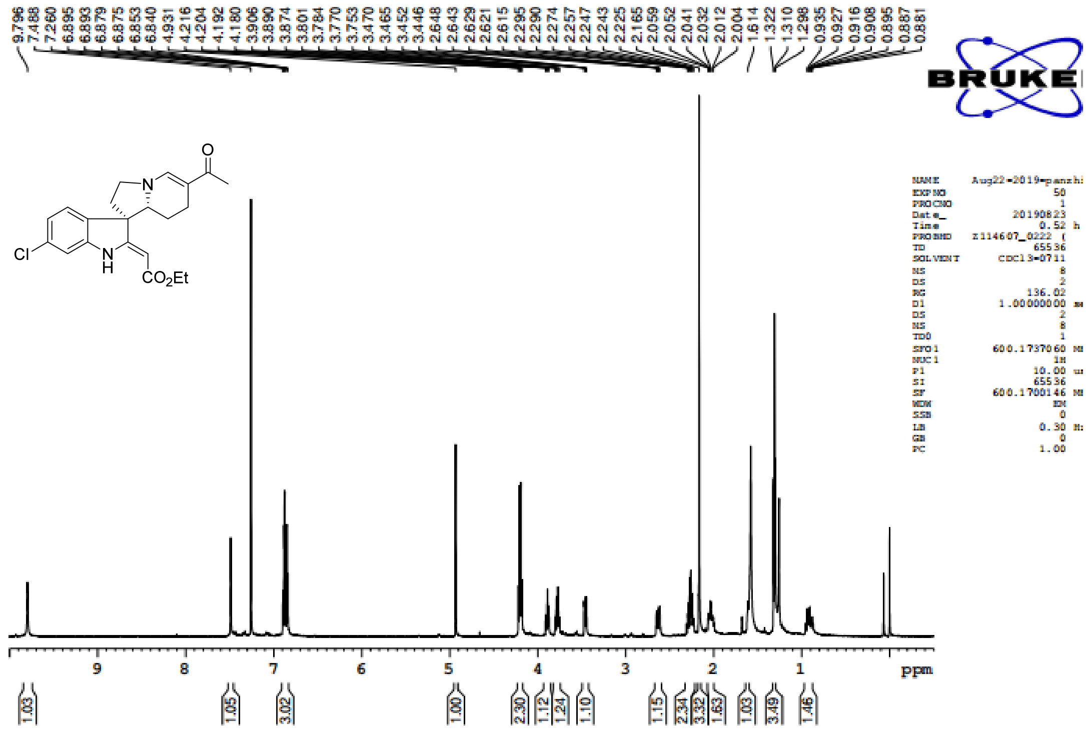


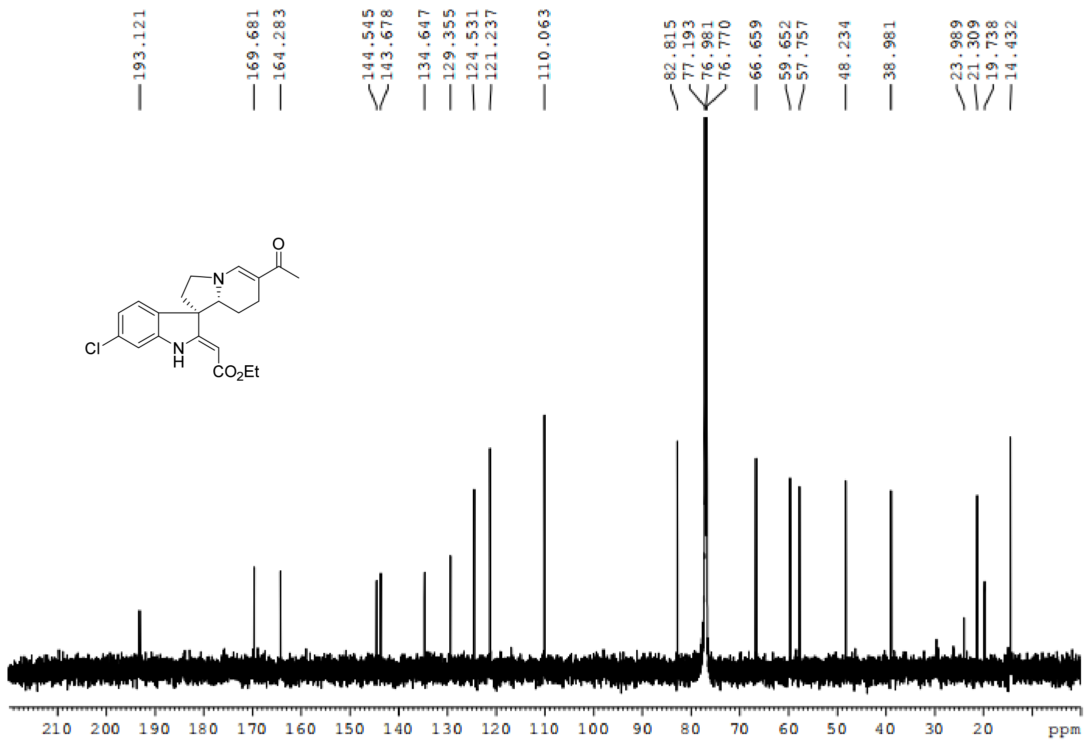
Copies of NMR spectra of **2n**



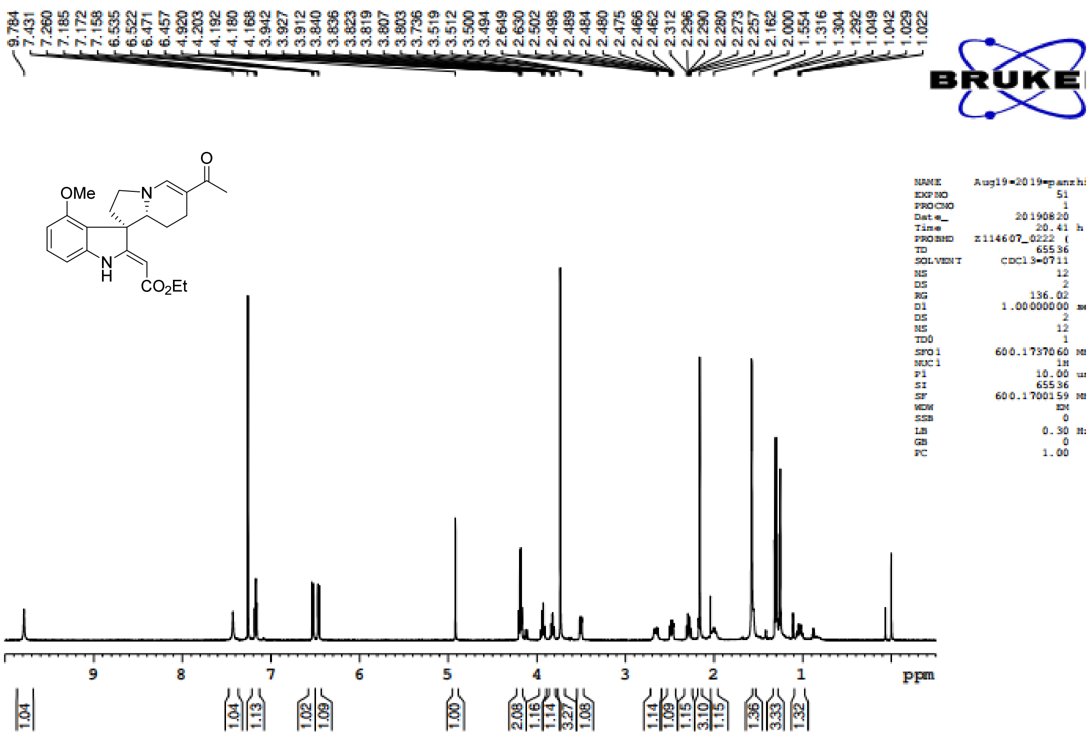


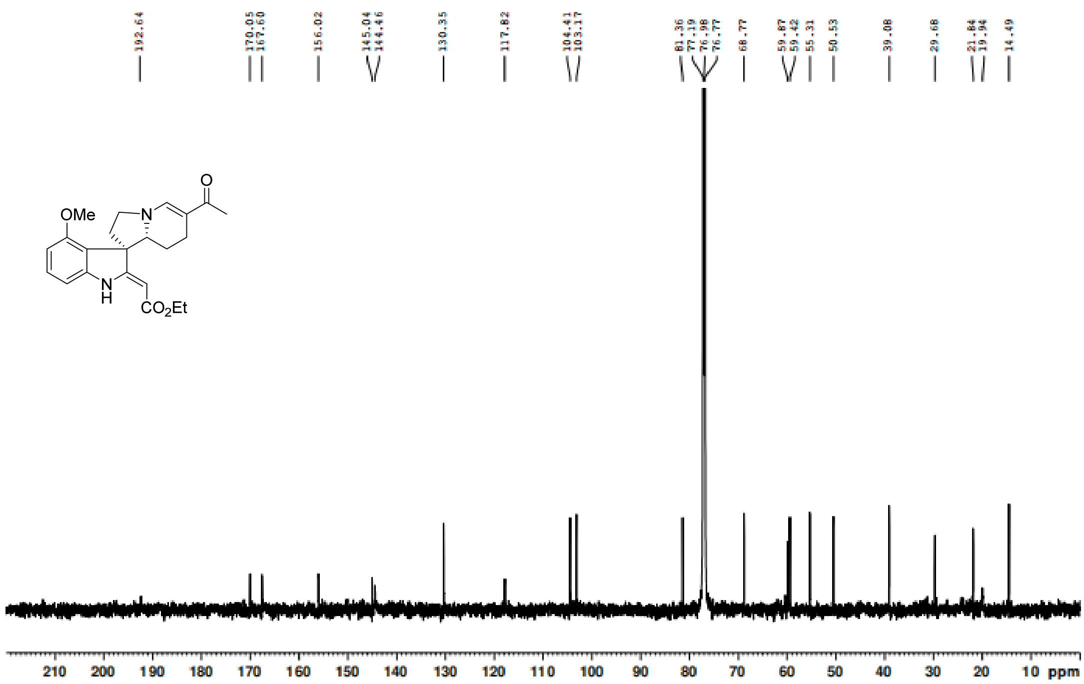
Copies of NMR spectra of **2o**



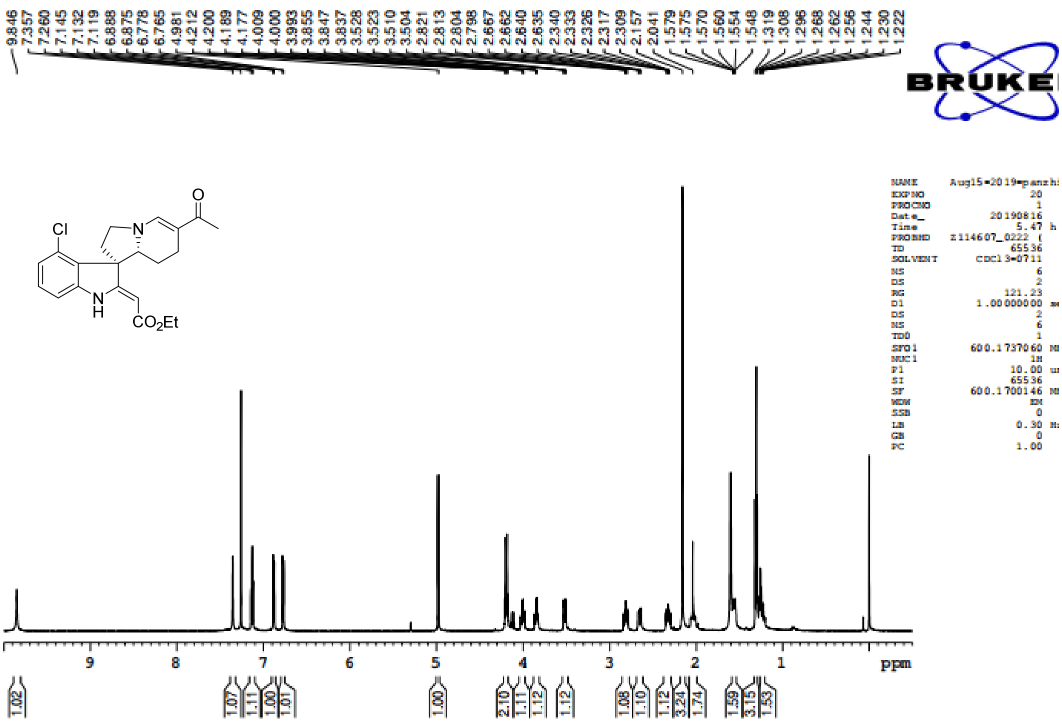


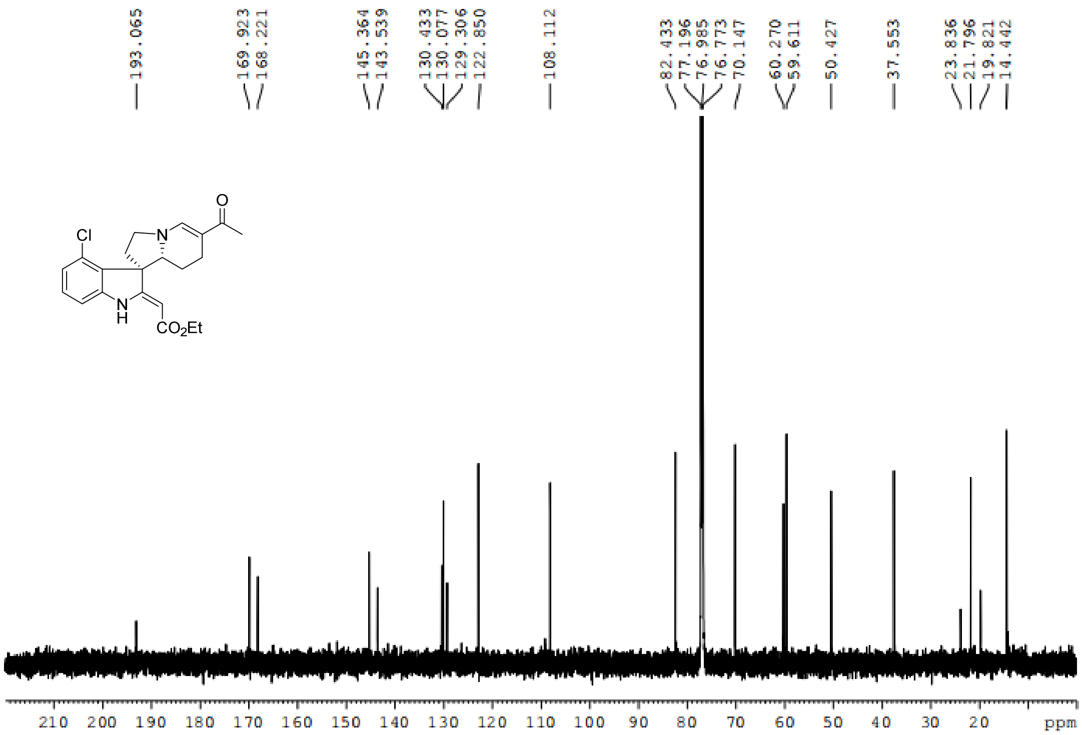
Copies of NMR spectra of **2p**



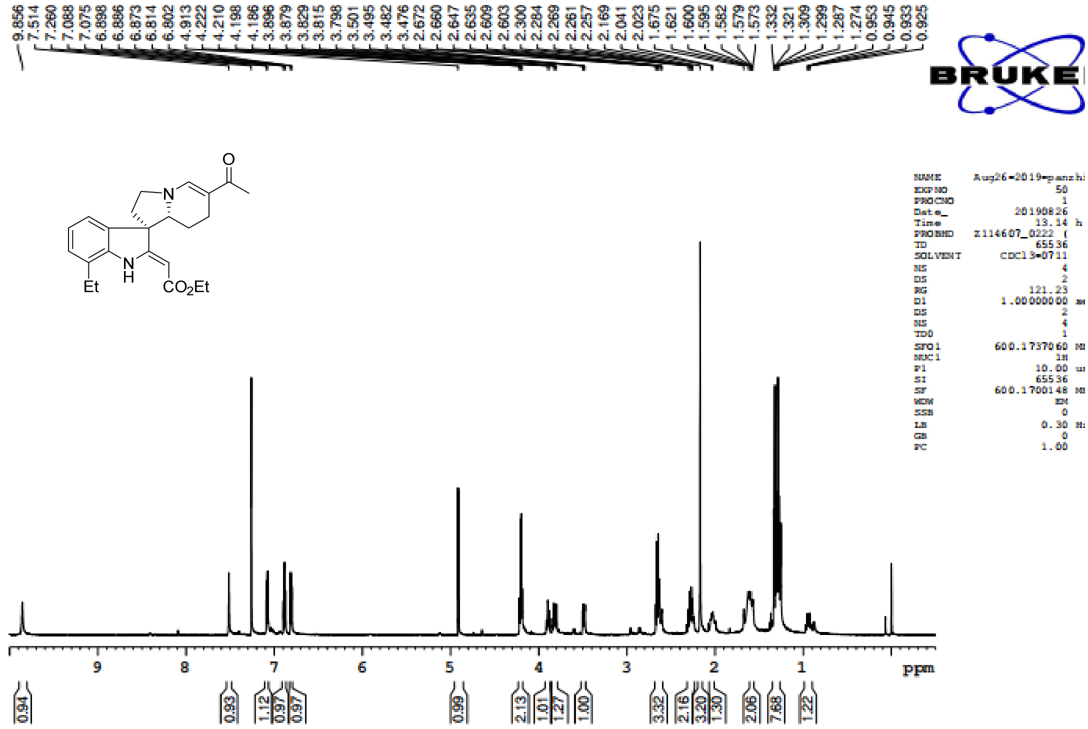


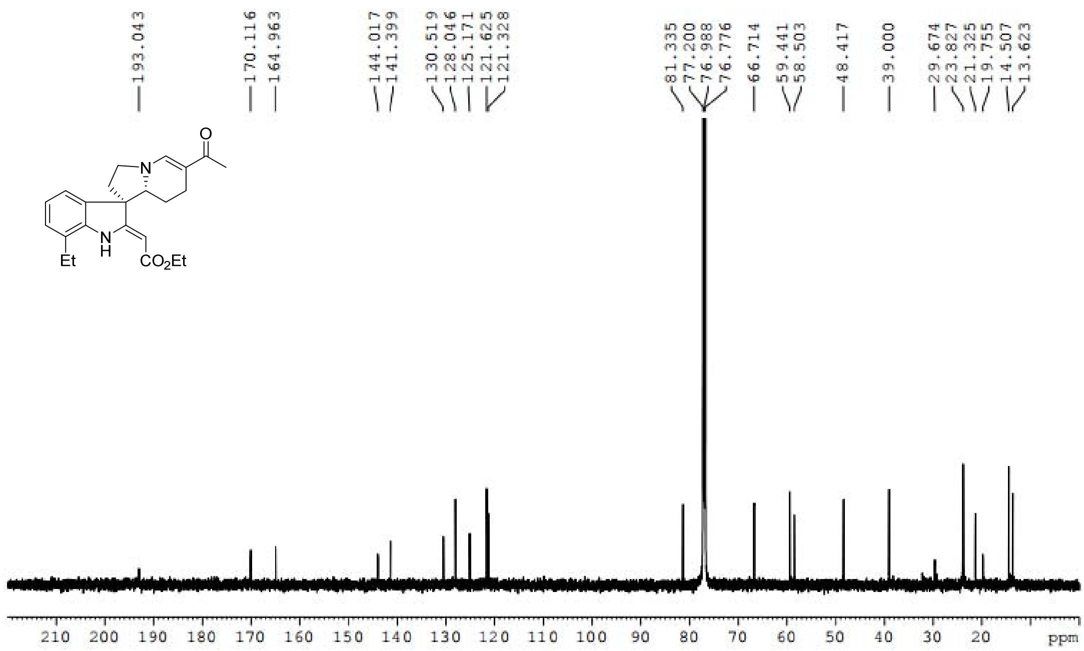
Copies of NMR spectra of **2q**



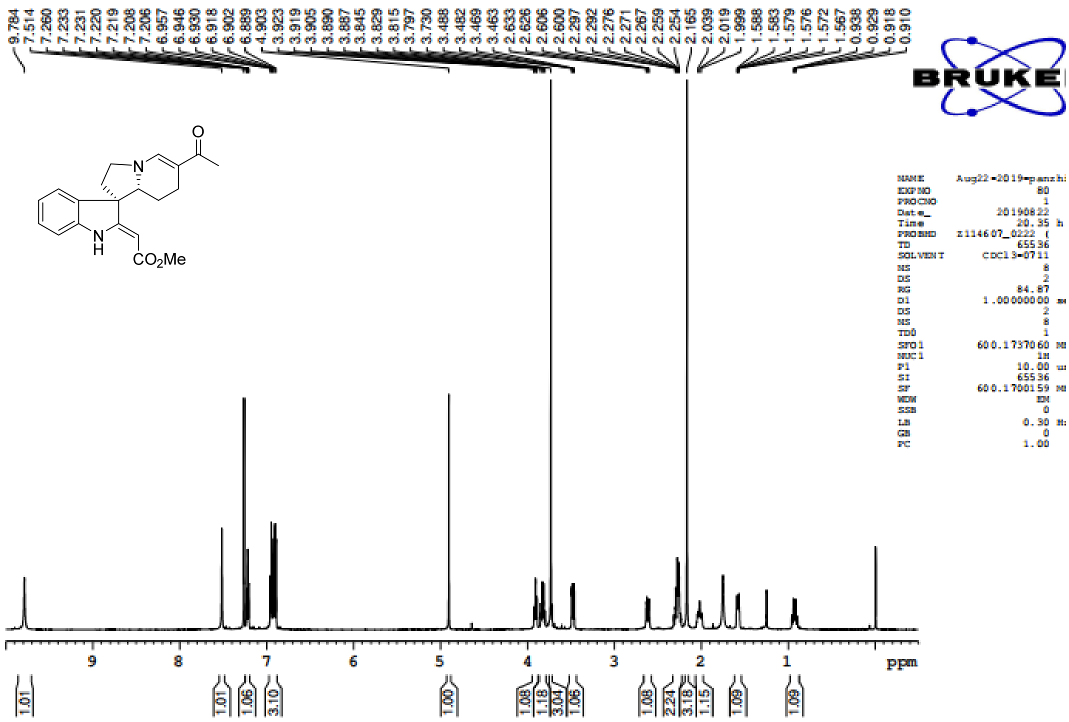


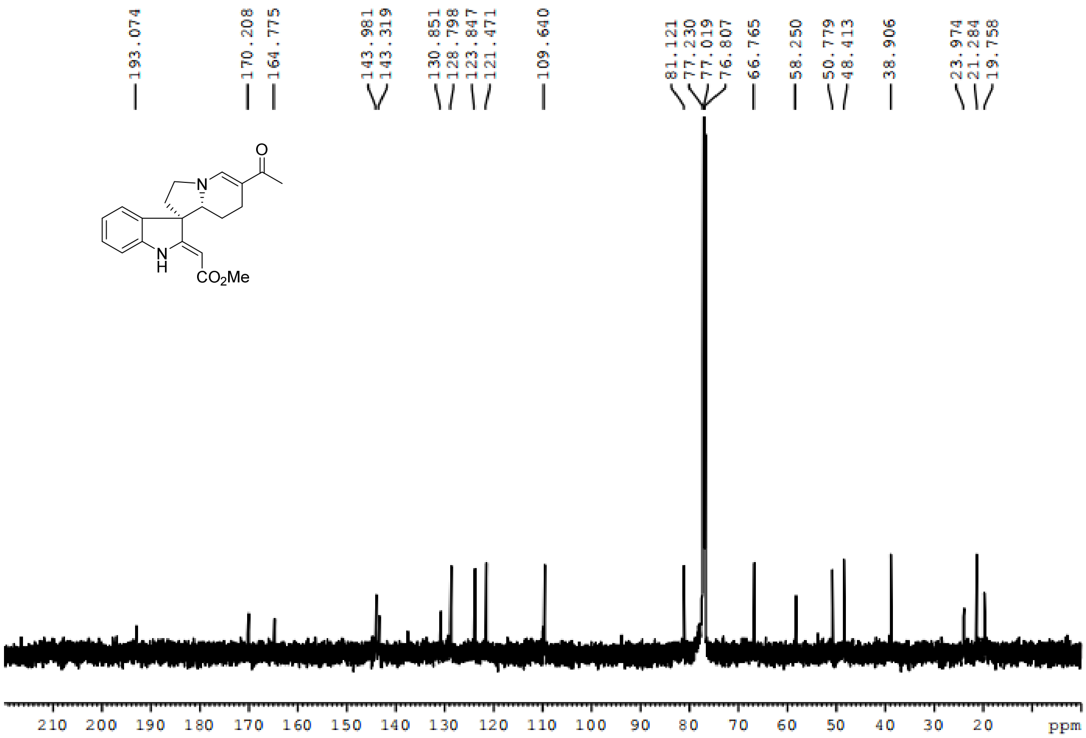
Copies of NMR spectra of **2r**



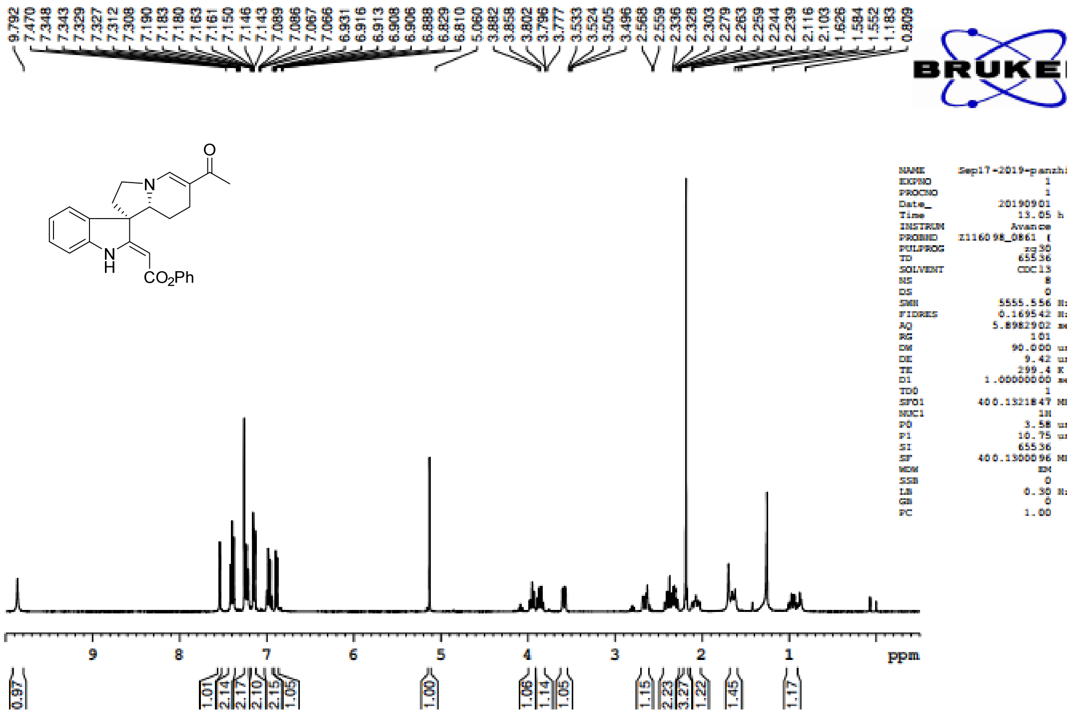


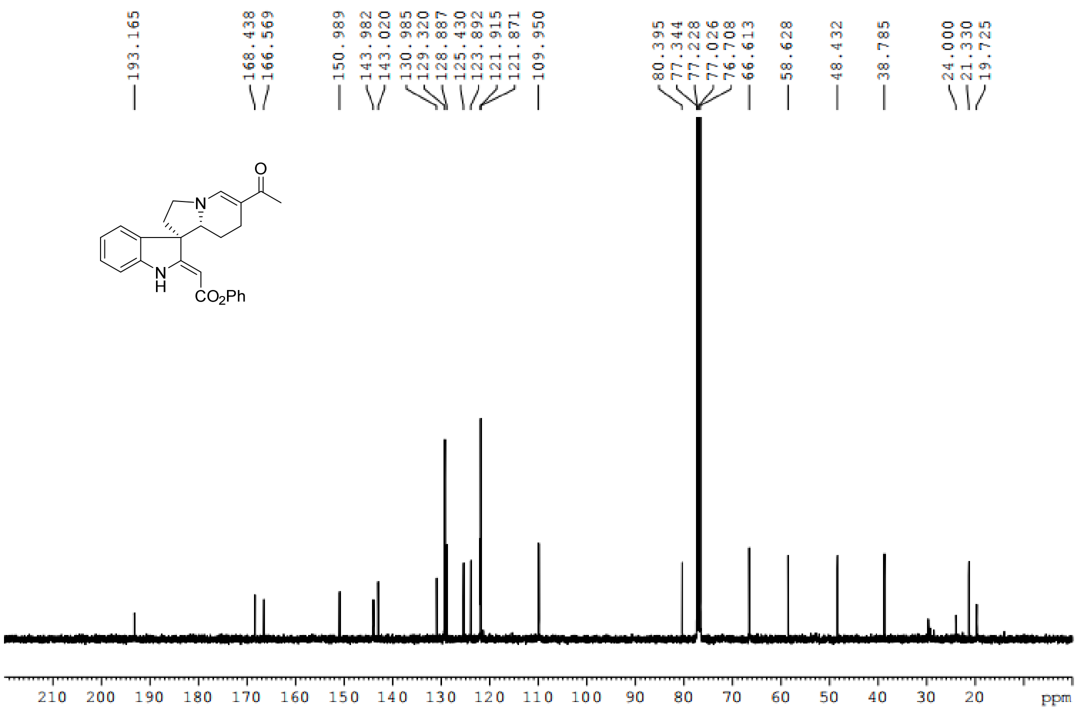
Copies of NMR spectra of **2s**



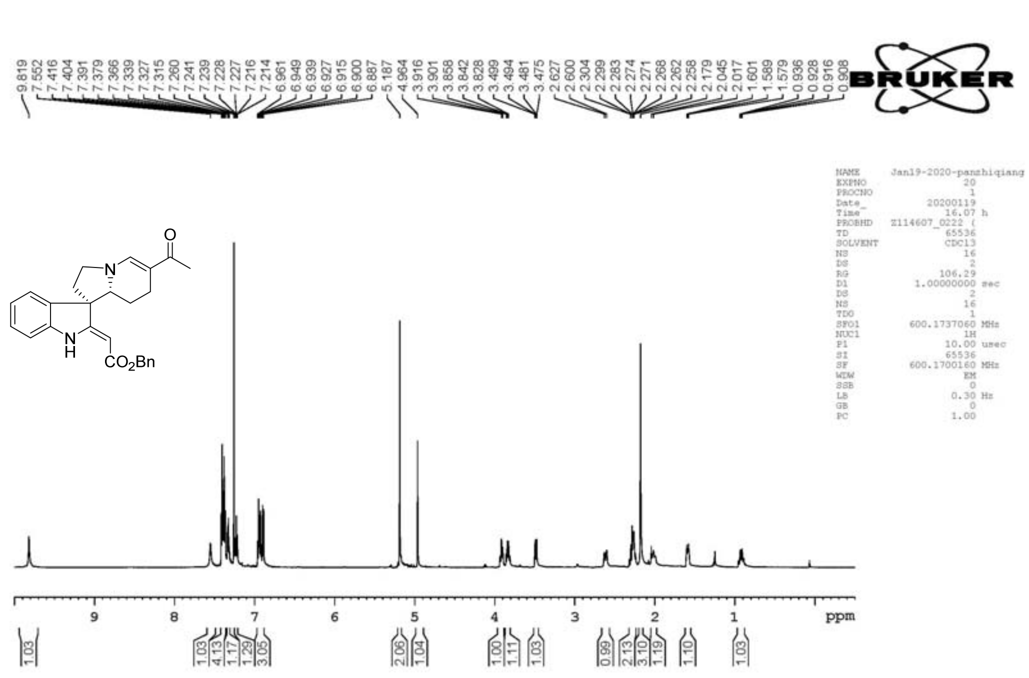


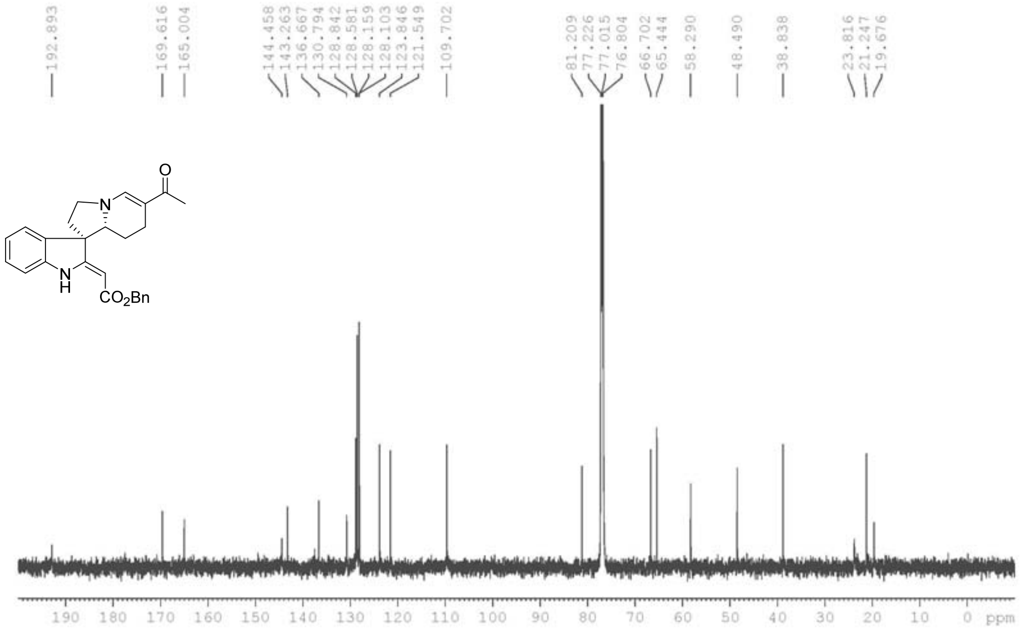
Copies of NMR spectra of **2t**



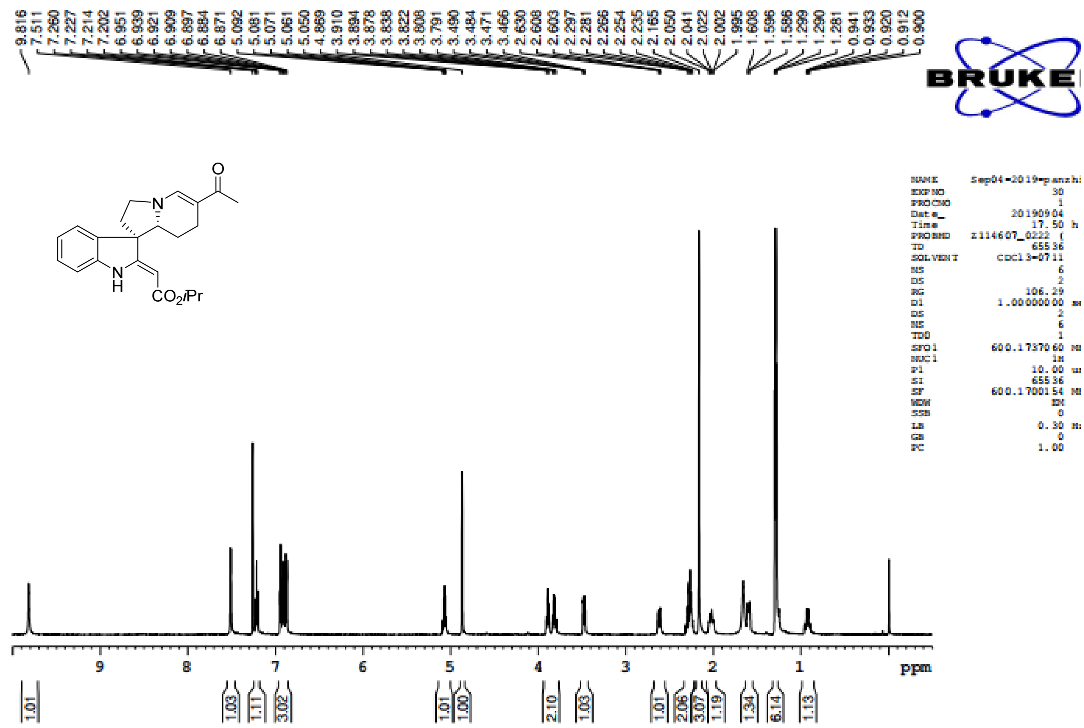


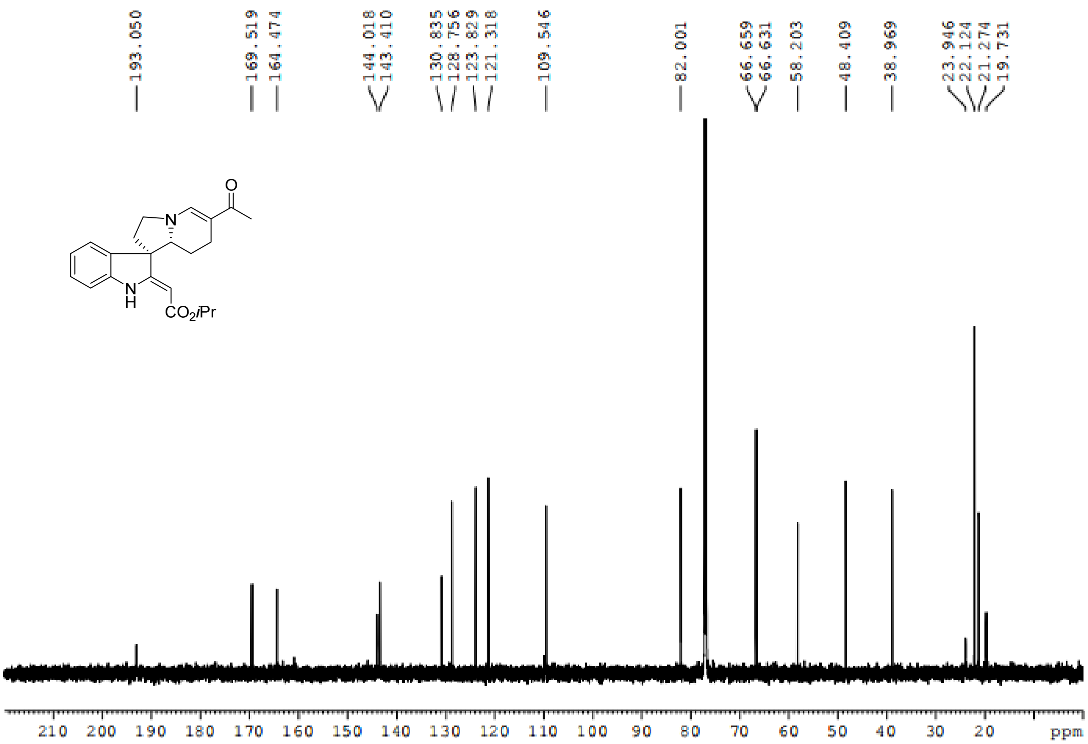
Copies of NMR spectra of **2u**



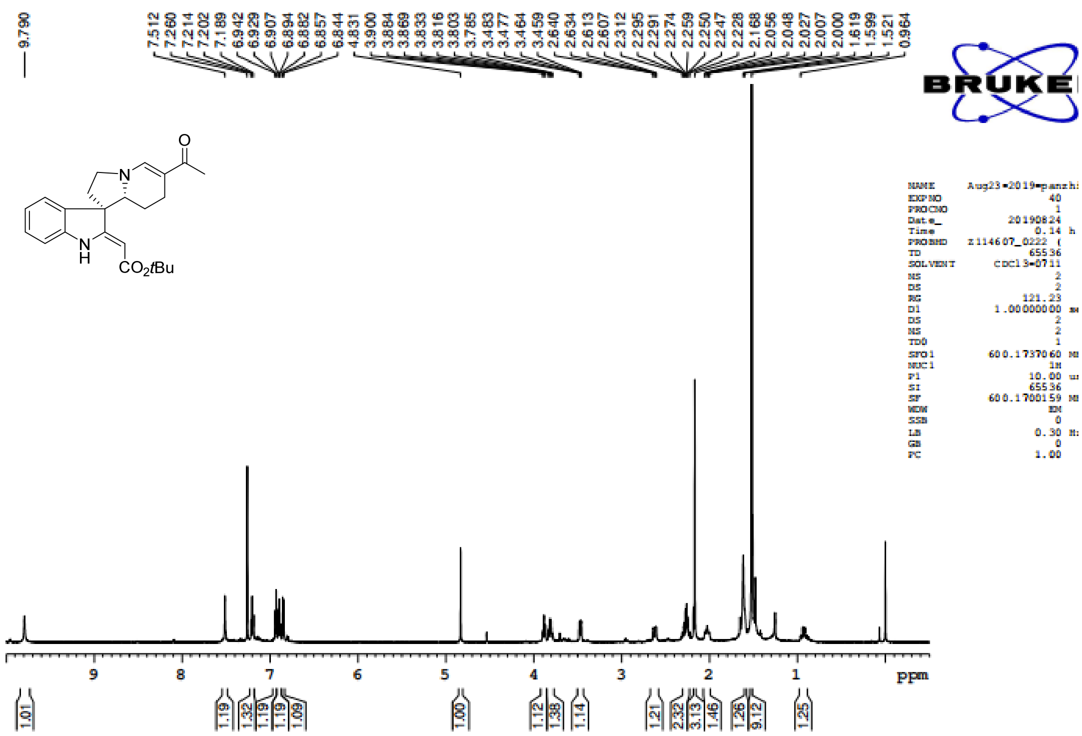


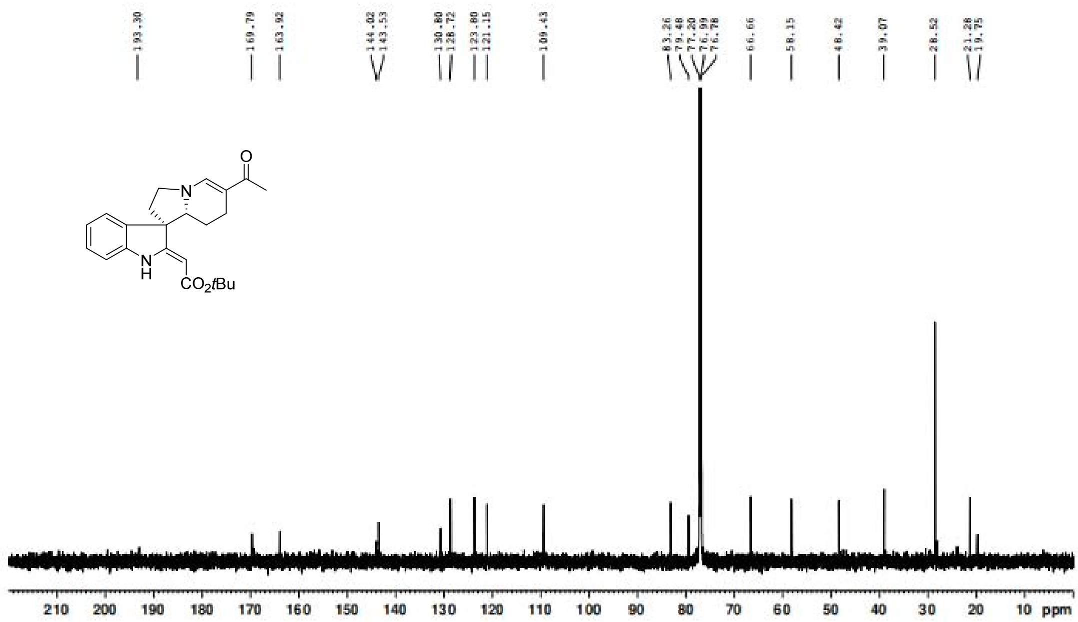
Copies of NMR spectra of **2v**





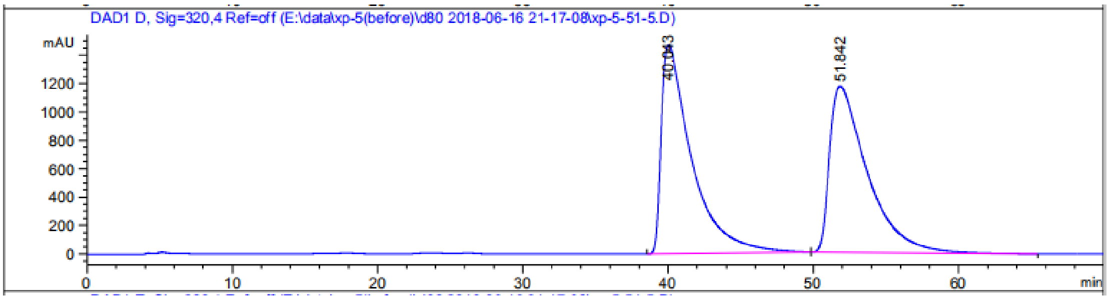
Copies of NMR spectra of **2w**



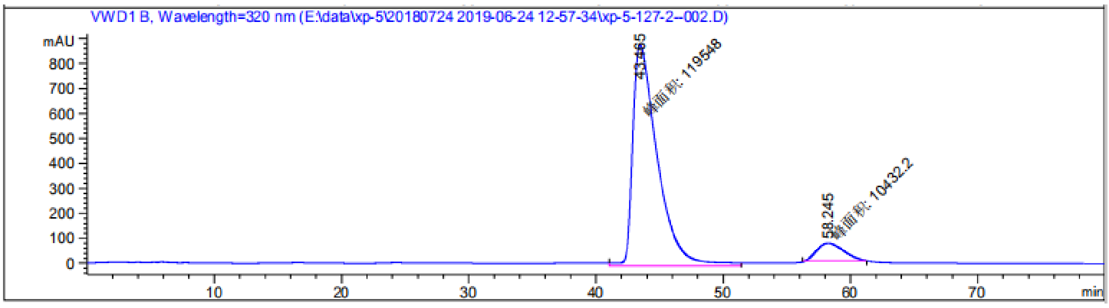


5. HPLC Traces of synthetic compounds

HPLC Chromatographs of **2b**

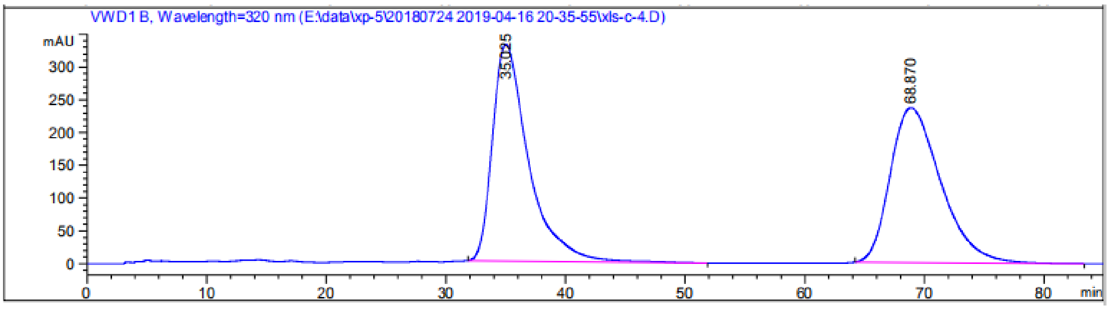


No.	Retention Time min	Area mAU*s	Height mAU	Relative Area %
1	40.043	2.13032e5	1469.23206	50.2492
2	51.842.	2.10919e5	1169.27661	49.7508

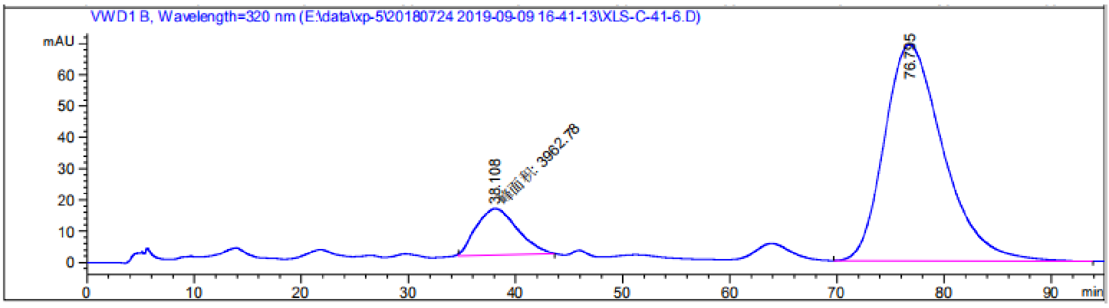


No.	Retention Time min	Area mAU*s	Height mAU	Relative Area %
1	43.465	1.19548e5	886.02887	91.9740
2	58.245	1.04322e4	70.95335	8.0260

HPLC Chromatographs of **2c**

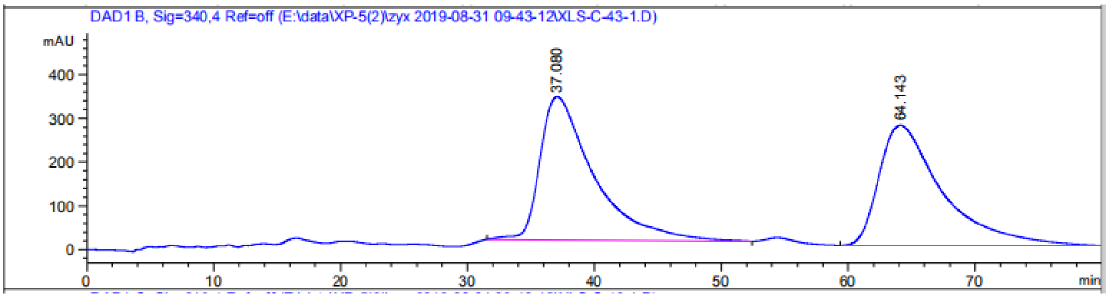


No.	RT	Area	Height	% Area
1	35.025	6.91320e4	329.98679	49.9686
2	68.870	6.92187e4	235.76665	50.0314

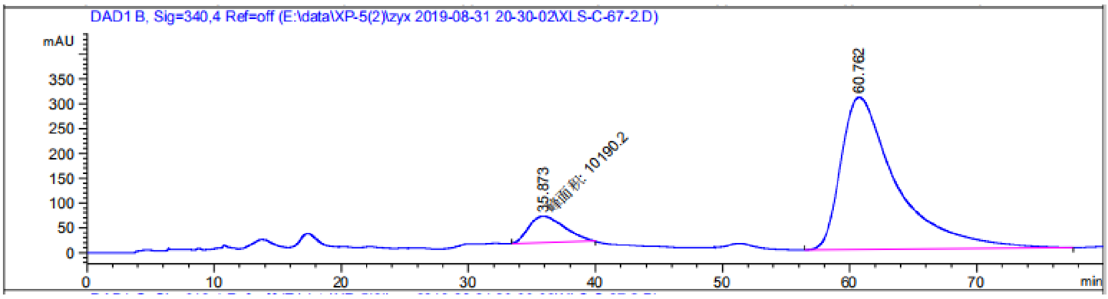


No.	RT	Area	Height	% Area
1	38.108	3962.78296	14.82190	13.0630
2	76.795	2.63731e4	69.19044	86.9370

HPLC Chromatographs of **2d**

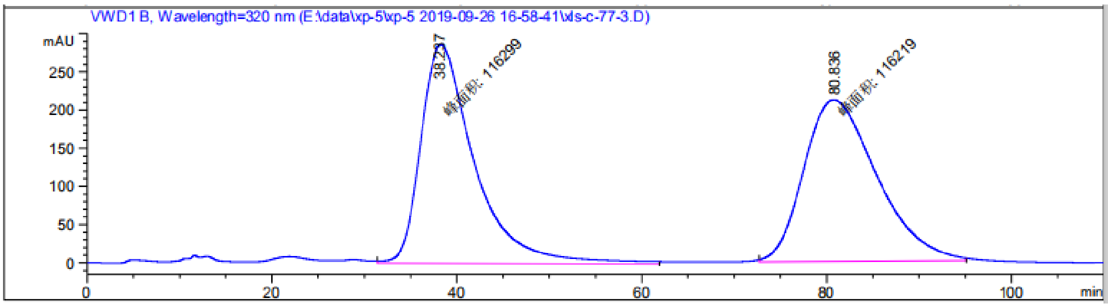


No.	RT	Area	Height	% Area
1	37.080	9.62686e4	327.08124	50.3451
2	64.143	9.49487e4	274.99734	49.6549

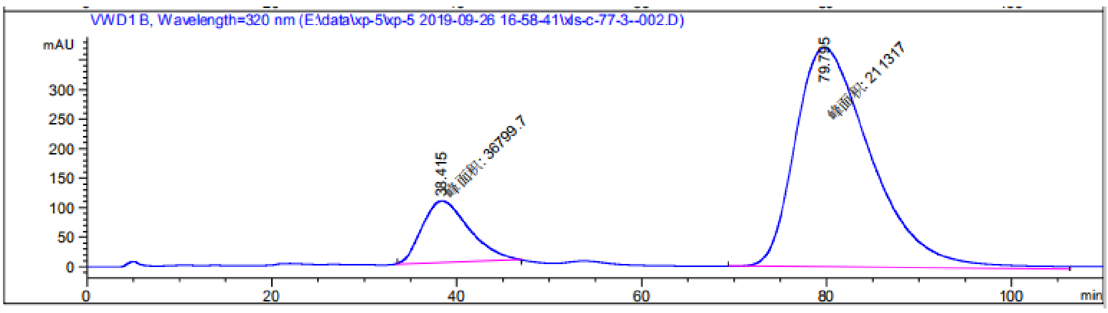


No.	RT	Area	Height	% Area
1	35.873	1.01902e4	52.73842	9.8446
2	60.762	9.33200e4	307.12946	90.1554

HPLC Chromatographs of **2e**

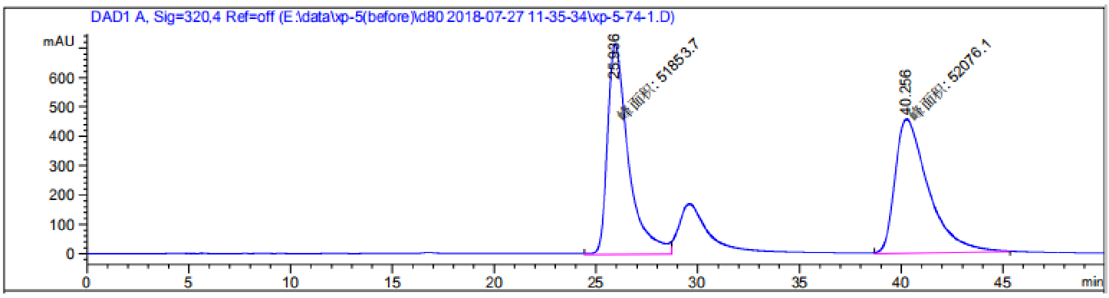


No.	RT	Area	Height	% Area
1	38.237	1.16299E5	286.91916	50.0173
2	80.836	1.16219E5	211.78023	49.9827

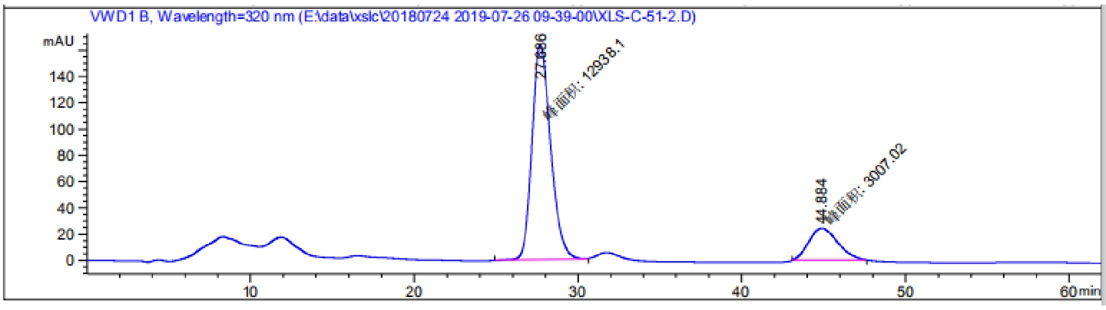


No.	RT	Area	Height	% Area
1	37.415	3.67997E4	104.25102	14.8316
2	79.795	2.11317E5	370.10733	85.1684

HPLC Chromatographs of **2f**

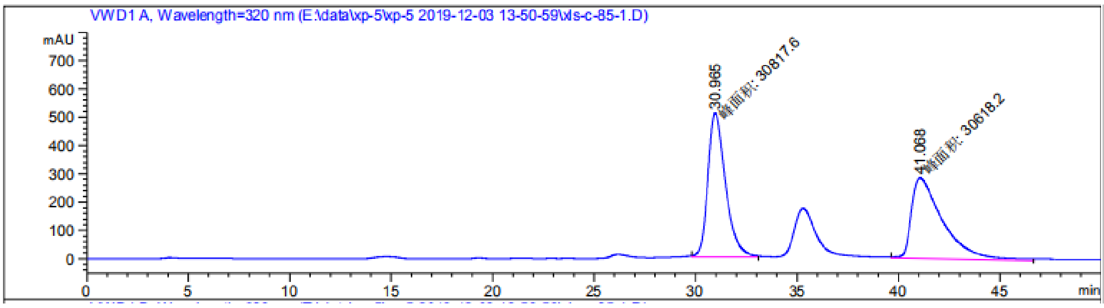


No.	RT	Area	Height	% Area
1	25.936	5.18537e4	716.78241	49.8930
2	40.256	5.20761e4	455.96027	50.1070

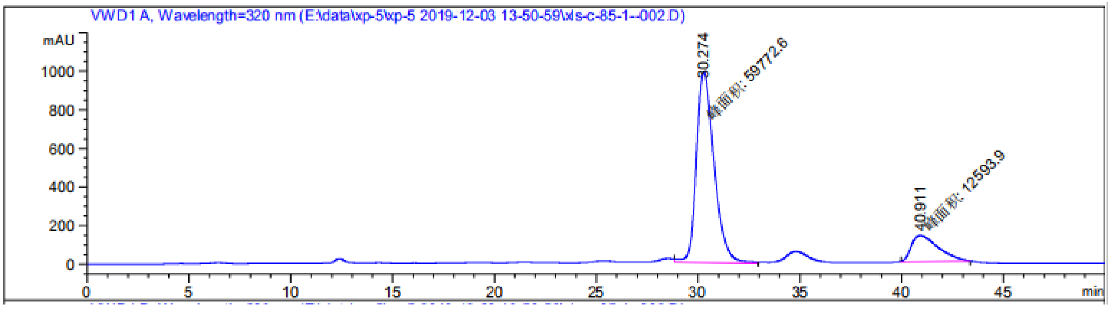


No.	RT	Area	Height	% Area
1	27.686	1.29381e4	163.82076	81.1414
2	44.884	3007.01587	24.31292	18.8586

HPLC Chromatographs of **2g**

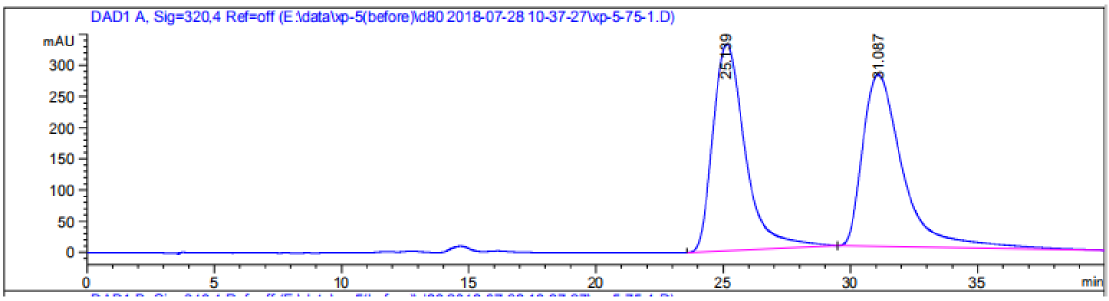


No.	RT	Area	Height	% Area
1	30.965	3.08176e4	509.28607	50.1622
2	41.068	3.06182e4	284.32397	49.8378

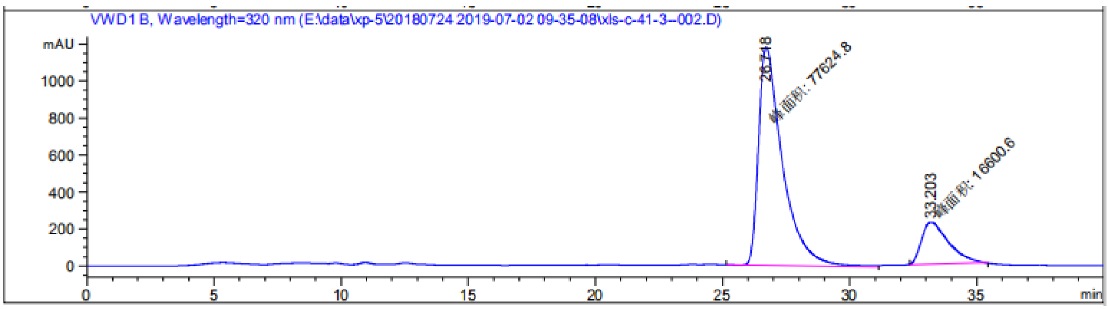


No.	RT	Area	Height	% Area
1	30.274	5.97726e4	987.68182	82.5971
2	40.911	1.25939e4	137.09364	17.4029

HPLC Chromatographs of **2h**

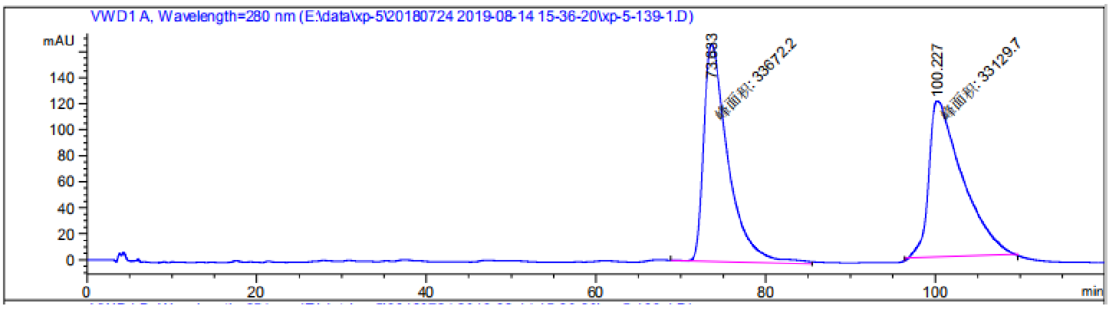


No.	RT	Area	Height	% Area
1	25.139	2.93062e4	331.52722	49.2649
2	31.087	3.01808e4	275.64615	50.7351

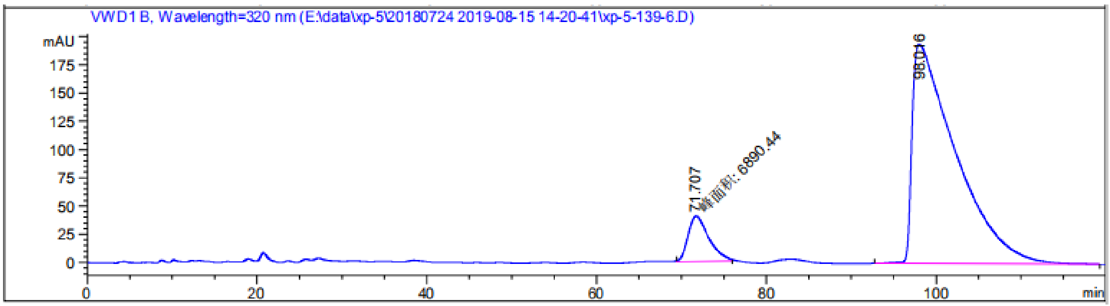


No.	RT	Area	Height	% Area
1	26.718	7.76248e4	1178.16711	82.3820
2	33.203	1.6606e4	226.29604	17.6180

HPLC Chromatographs of **2i**

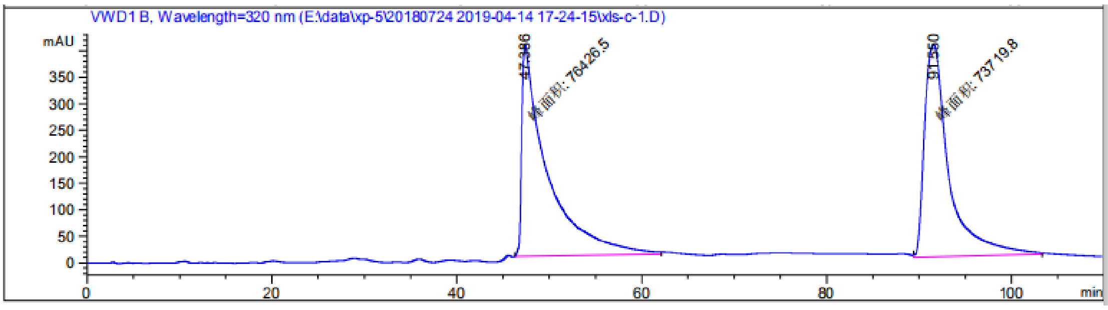


No.	RT	Area	Height	% Area
1	73.633	3.36722e4	167.16280	50.4061
2	100.227	3.31297e4	120.05046	49.5939

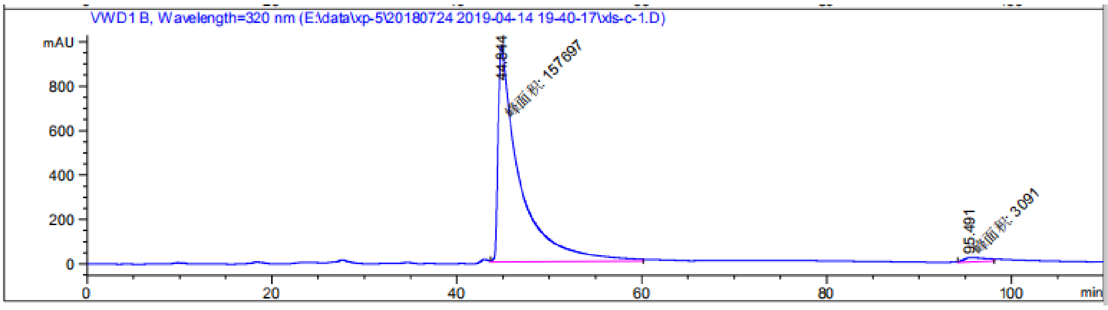


No.	RT	Area	Height	% Area
1	71.709	5236.77490	32.90313	8.0193
2	98.012	6.00655e4	163.32048	91.9807

HPLC Chromatographs of **2j**

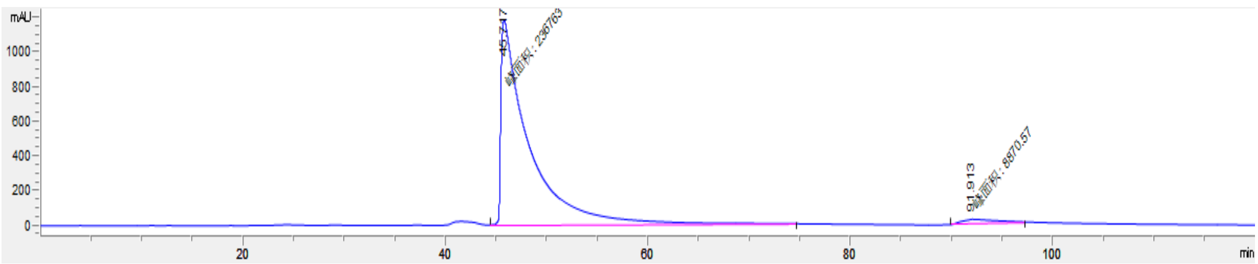


No.	RT	Area	Height	% Area
1	47.386	7.64265e4	398.95837	50.9014
2	91.550	7.37198e4	400.32397	49.0986



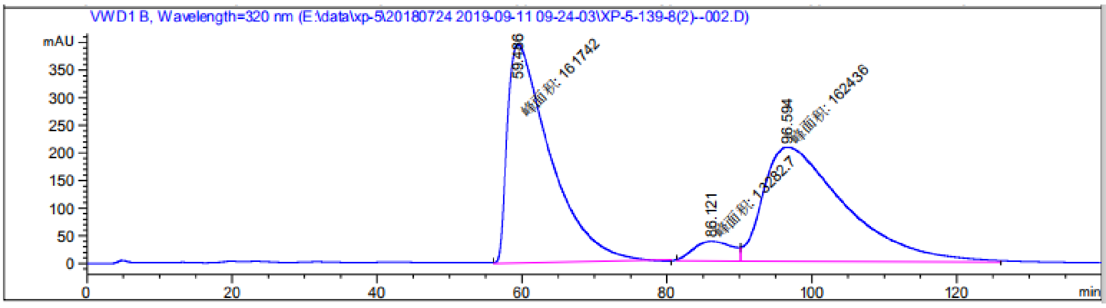
No.	RT	Area	Height	% Area
1	44.844	1.57697e5	972.56158	98.0776
2	95.491	3090.99927	19.05363	1.9224

HPLC Chromatographs of **2j** (for 1.2 mmol scale)

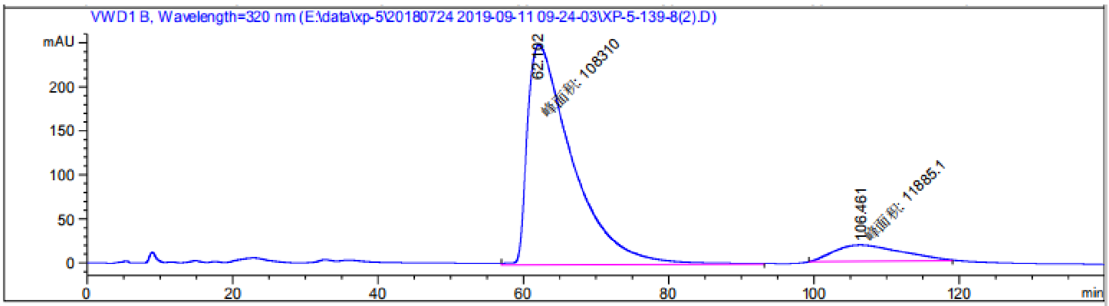


#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	45.717	236762.9	1190.6	3.3142	0.12	96.389	MM
2	91.913	8870.6	30.9	4.7792	0.361	3.611	MM

HPLC Chromatographs of **2k**

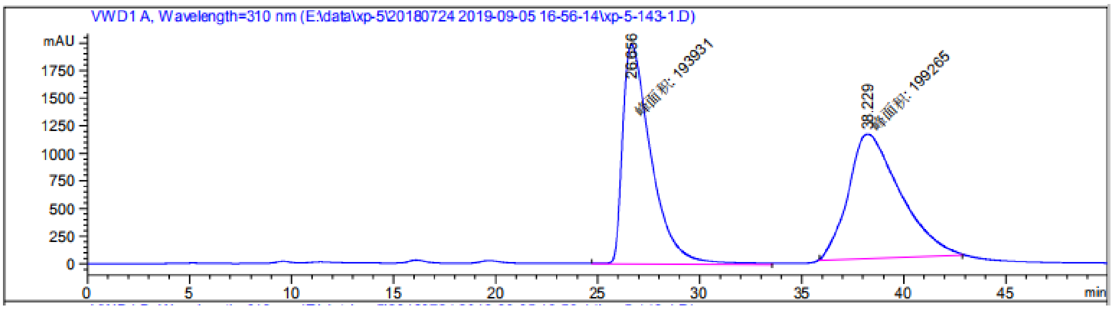


No.	RT	Area	Height	% Area
1	59.486	1.61742e5	395.57379	47.9291
2	86.121	1.32827e4	35.45404	3.9361
3	96.594	1.62436e5	206.61314	48.1248

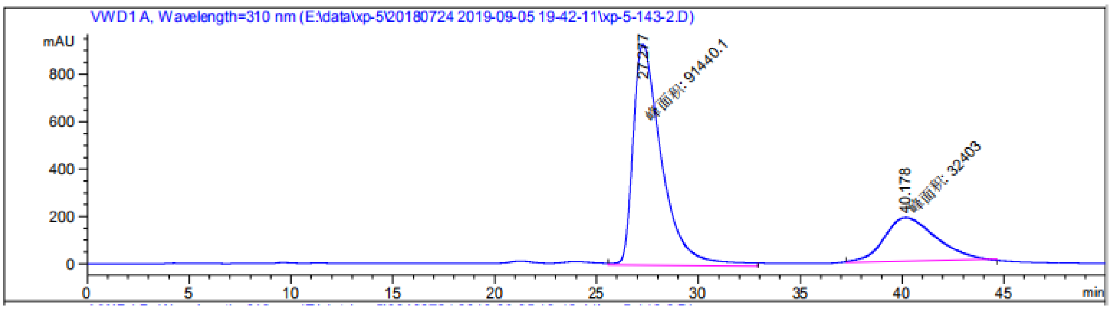


No.	RT	Area	Height	% Area
1	62.102	1.08310e5	250.56642	90.1119
2	106.461	1.18851e4	18.39356	9.8881

HPLC Chromatographs of **2l**

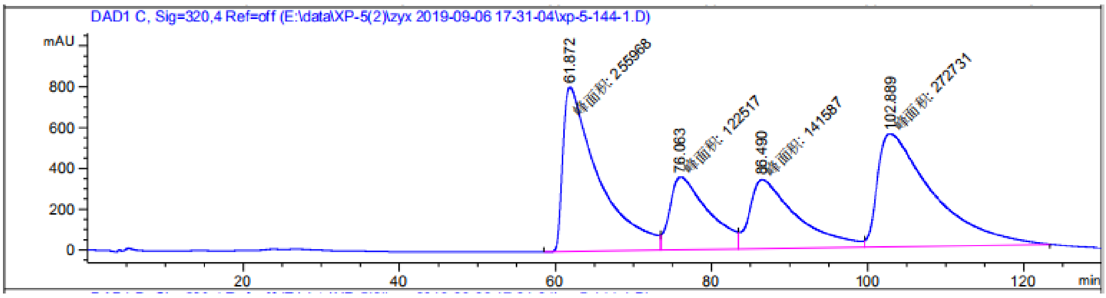


No.	RT	Area	Height	% Area
1	26.656	1.93931e5	1991.11963	49.3217
2	38.229	1.99265e5	1127.86975	50.6783

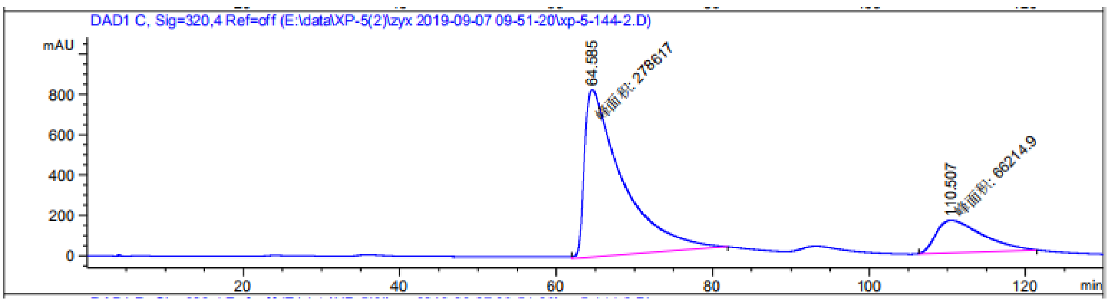


No.	RT	Area	Height	% Area
1	27.277	9.14401e4	931.90857	73.8354
2	40.178	3.24090e4	184.03590	26.1646

HPLC Chromatographs of **2m**

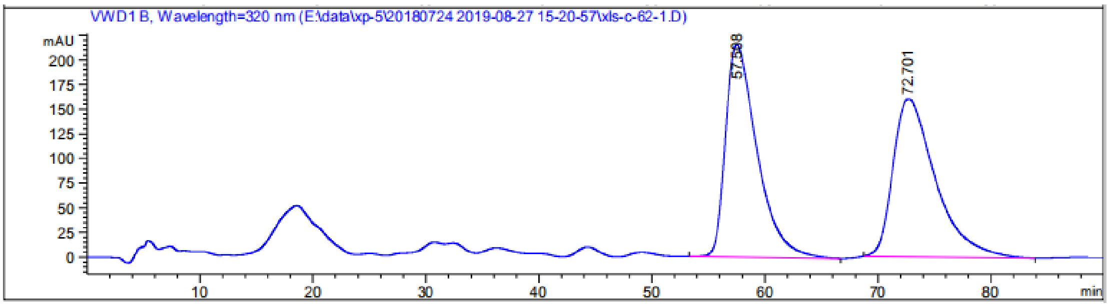


No.	RT	Area	Height	% Area
1	61.872	2.55968e5	804.04749	32.2865
2	76.063	1.22517e5	356.93442	15.4537
3	86.490	1.41587e5	338.61230	17.8590
4	102.889	2.72731e5	552.85773	34.4008

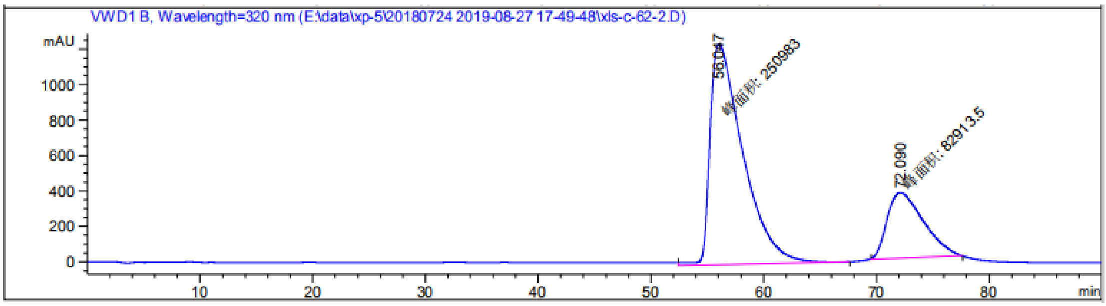


No.	RT	Area	Height	% Area
1	64.585	2.7817e5	828.94562	80.7979
2	110.507	6.62149e4	161.24443	19.2021

HPLC Chromatographs of **2n**

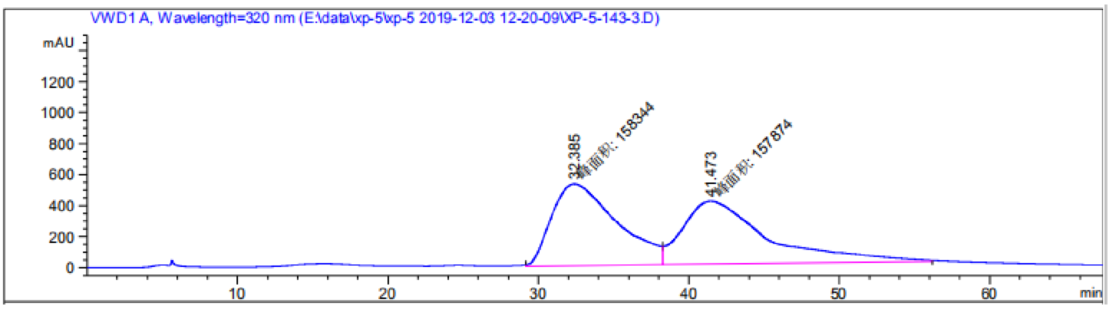


No.	RT	Area	Height	% Area
1	57.508	4.17157e4	215.41885	50.0375
2	72.701	4.16532e4	159.87820	49.9625

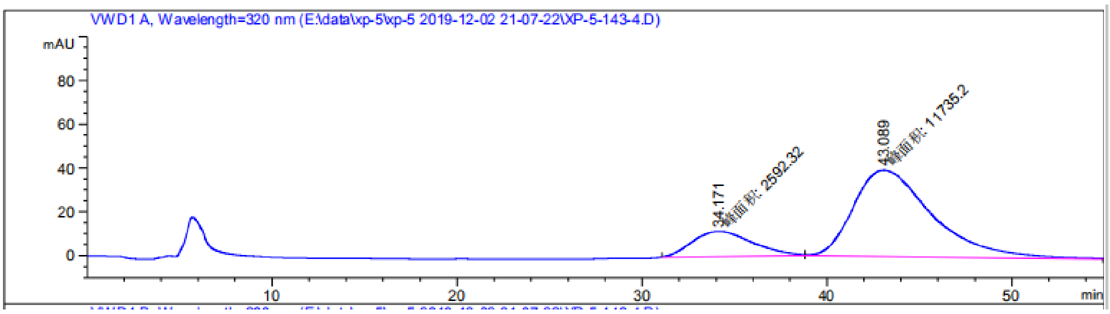


No.	RT	Area	Height	% Area
1	60.065	1.51607e5	564.05188	80.0897
2	75.978	3.76896e4	136.10732	19.9130

HPLC Chromatographs of **2o**

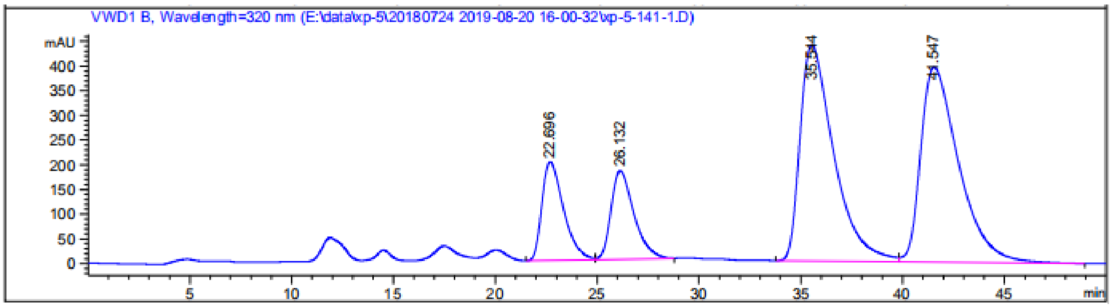


No.	RT	Area	Height	% Area
1	32.385	1.58344e5	527.92242	50.0742
2	41.473	1.57874e5	404.79361	49.9258

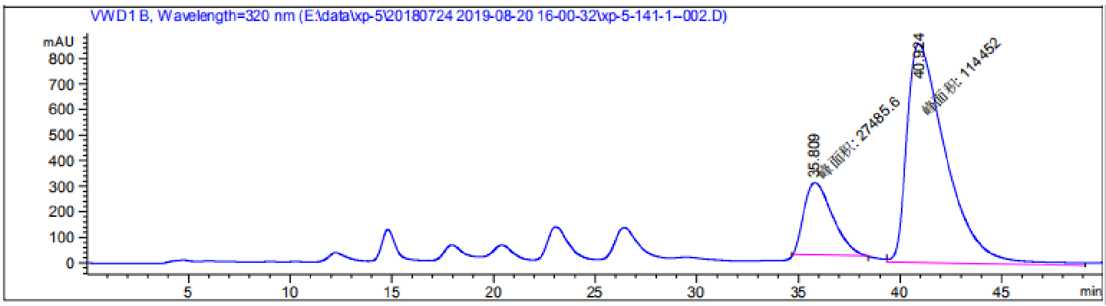


No.	RT	Area	Height	% Area
1	34.171	2592.32178	11.52236	18.0933
2	43.089	1.17352e4	39.48227	81.9067

HPLC Chromatographs of **2p**

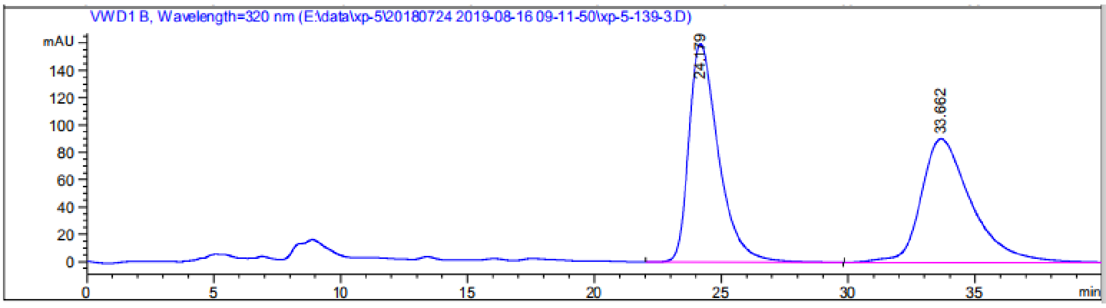


No.	RT	Area	Height	% Area
1	22.696	1.47254e4	199.50711	11.3098
2	26.132	1.39879e4	178.81096	10.7434
3	35.544	5.03571e4	437.05756	38.6767
4	41.547	5.11297e4	394.29492	39.2701

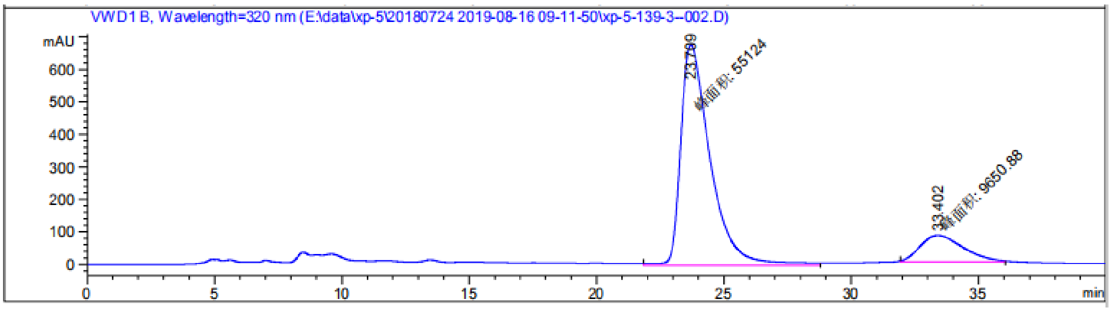


No.	RT	Area	Height	% Area
1	35.809	2.74856e4	282.36868	19.3646
2	40.924	1.14452e5	854.30878	80.6354

HPLC Chromatographs of **2q**

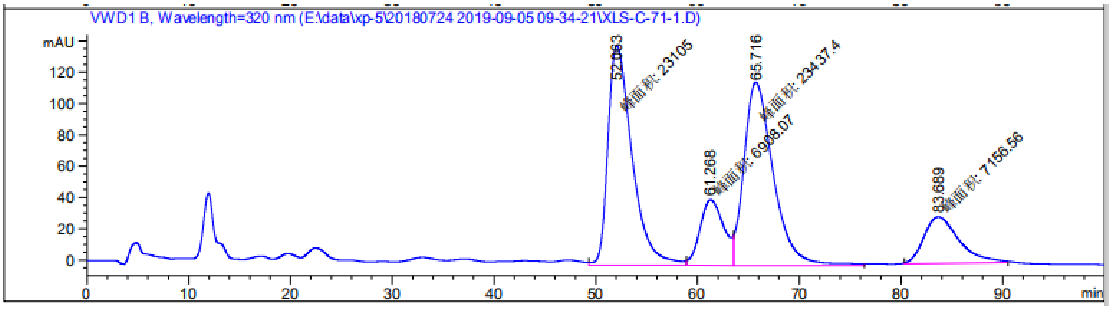


No.	RT	Area	Height	% Area
1	24.179	1.29673e4	159.39363	50.7623
2	33.662	1.25779e4	90.64059	49.2377

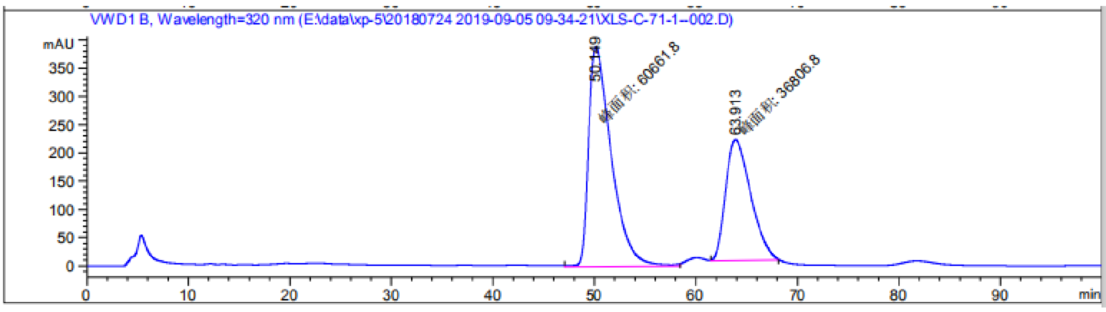


No.	RT	Area	Height	% Area
1	23.709	5.51240e4	679.70770	85.1009
2	33.402	9650.87793	81.63828	14.8991

HPLC Chromatographs of **2r**

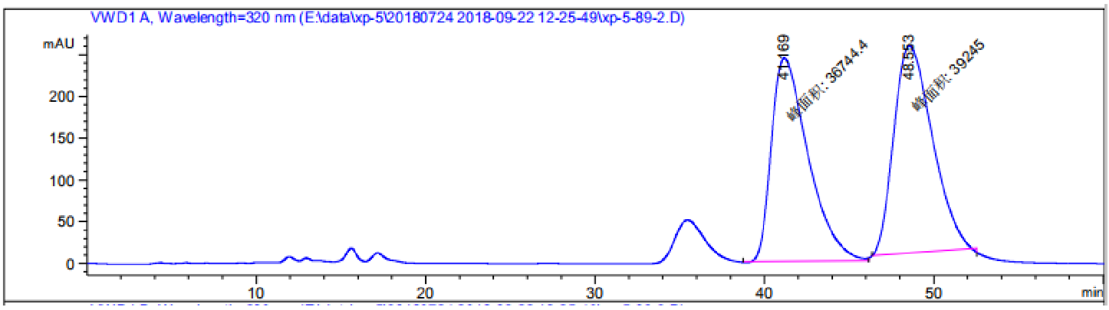


No.	RT	Area	Height	% Area
1	52.063	2.31050e4	140.14931	38.1226
2	61.268	6908.07324	41.89958	11.3982
3	65.716	2.34374e4	116.97540	38.6711
4	83.689	7156.55908	29.77675	11.8081

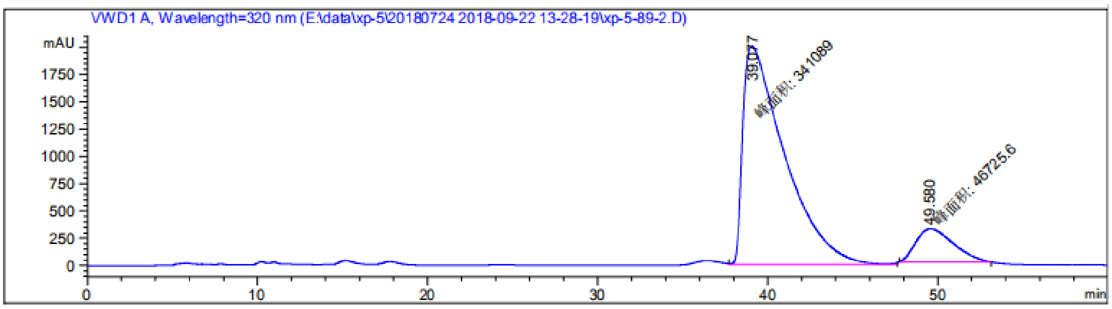


No.	RT	Area	Height	% Area
1	50.149	6.06618e4	388.43484	62.2373
2	63.913	3.68068e4	213.99442	37.7627

HPLC Chromatographs of **2s**

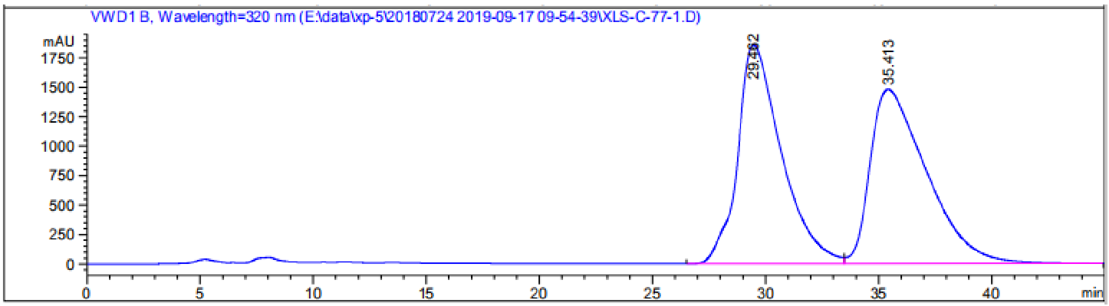


No.	RT	Area	Height	% Area
1	41.169	3.67444e4	243.64258	48.3547
2	48.553	3.92450e4	248.44824	51.6453

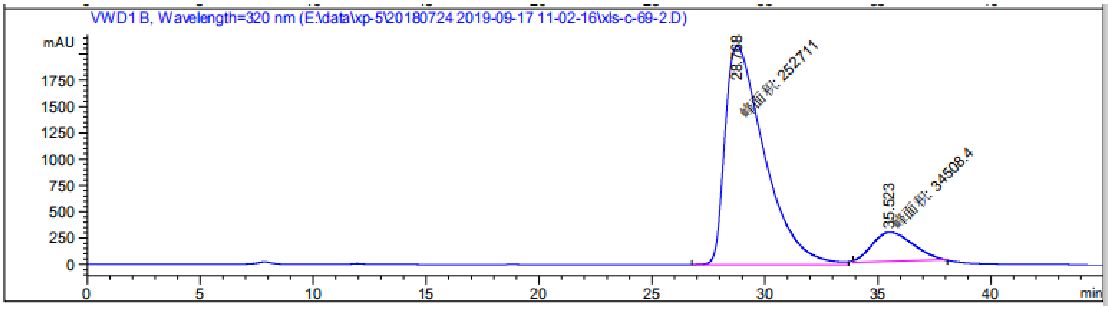


No.	RT	Area	Height	% Area
1	39.077	3.41089e5	2001.09617	87.9516
2	49.580	4.67256e4	340.69925	12.0484

HPLC Chromatographs of **2t**

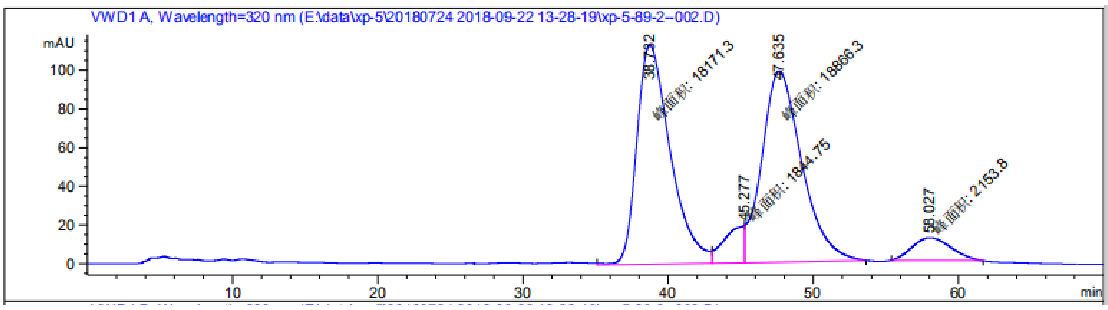


No.	RT	Area	Height	% Area
1	29.462	2.51084e5	1859.48901	49.4902
2	35.413	2.56257e5	1479.70117	50.5098

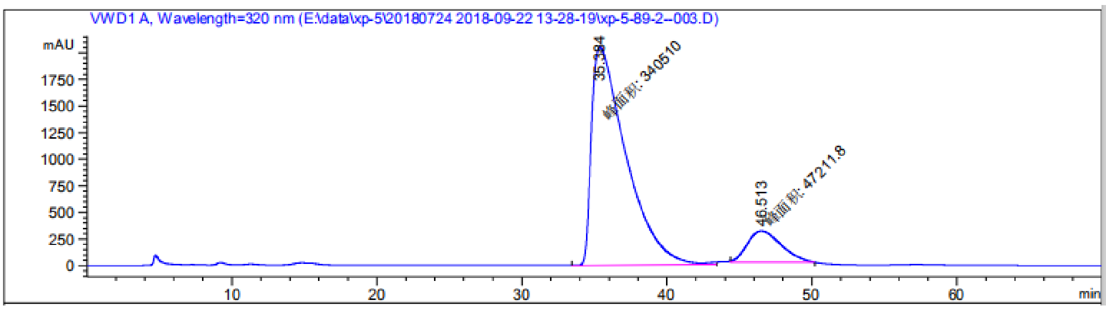


No.	RT	Area	Height	% Area
1	28.768	2.52711e5	2082.52.26	87.9854
2	35.523	3.45084e4	276.00833	12.0146

HPLC Chromatographs of **2u**

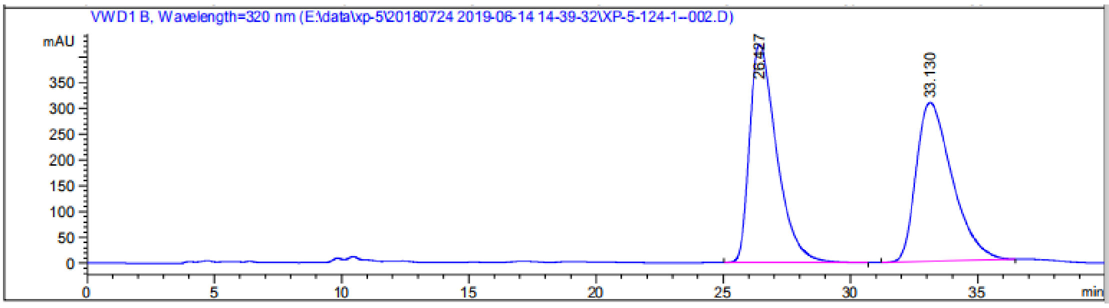


No.	RT	Area	Height	% Area
1	38.732	1.81713e4	113.14646	44.2811
2	45.277	1844.74878	19.29135	4.4954
3	47.635	1.88663e4	98.53289	45.9749
4	58.027	2153.80469	11.71779	5.2486

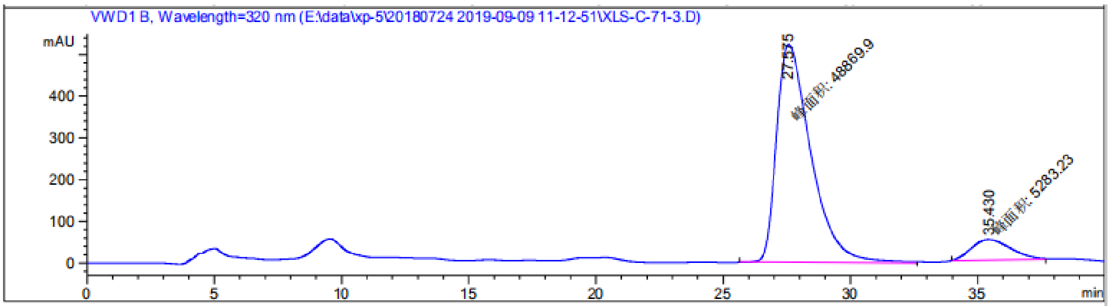


No.	RT	Area	Height	% Area
1	35.384	3.40510e5	2054.65234	87.8233
2	46.513	4.72118e4	292.32117	12.1767

HPLC Chromatographs of **2v**

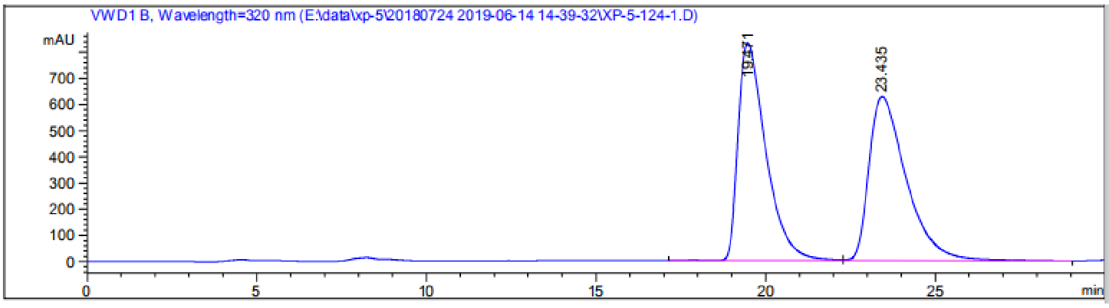


No.	RT	Area	Height	% Area
1	26.427	3.13219e4	422.33765	50.7728
2	33.130	3.03684e4	307.95016	49.2272

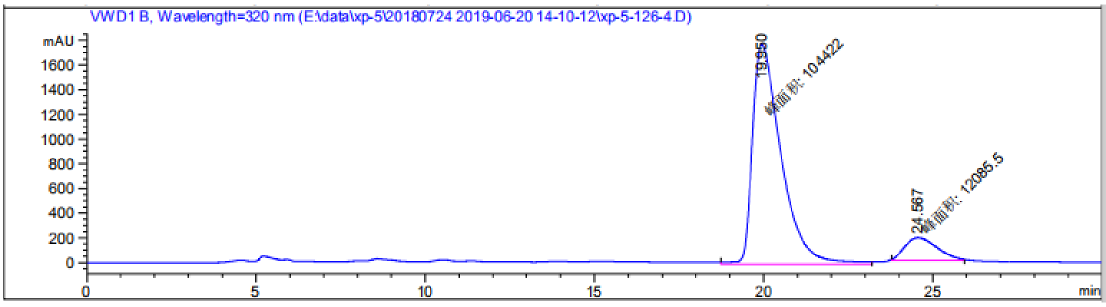


No.	RT	Area	Height	% Area
1	27.575	4.88699e4	521.21484	90.2439
2	35.430	5283.22900	49.11884	9.7561

HPLC Chromatographs of **2w**



No.	RT	Area	Height	% Area
1	19.471	4.76360e4	832.45428	49.7588
2	23.435	4.80977e4	627.02710	50.2412



No.	RT	Area	Height	% Area
1	19.950	1.04422e5	1777.11414	89.6269
2	24.567	1.20855e4	182.92143	10.3731