Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information for

Retro-Biosynthetic Construction of Corynanthe Alkaloid Skeletons from Rhynchophylline Alkaloids

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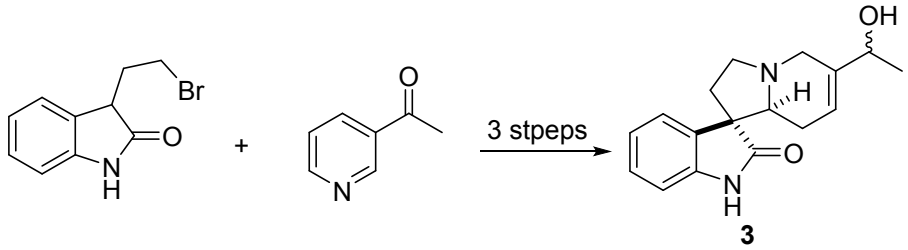
1. General Methods.

All reactions were performed under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. MeOH was distilled from magnesium and stored under an argon atmosphere. DCM was distilled over CaH_2 and rigorously degassed by freeze/pump/thaw. Reagents were purchased at the highest commercial quality and used without further purification unless indicated otherwise. Reactions were monitored by thin layer chromatography (TLC) carried out on GF254 plates (0.25 mm layer thickness) using UV light as visualizing agent and ceric ammonium molybdate as developing agent. Flash column chromatography was performed with 200-300 mesh silica gels. Yields reported were for isolated, spectroscopically pure compounds.

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AM-400 instrument and calibrated by using residual undeuterated chloroform (δ_H = 7.26 ppm and δ_C = 77.16 ppm) as internal reference. The following abbreviations were used in reporting NMR data: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets. HRMS were taken on API STAR Pulsar or Agilent 6540 Q-TOF spectrometer.

2. Experimental Procedures and Spectroscopic Data of 3-Spirooxindole Substrates.



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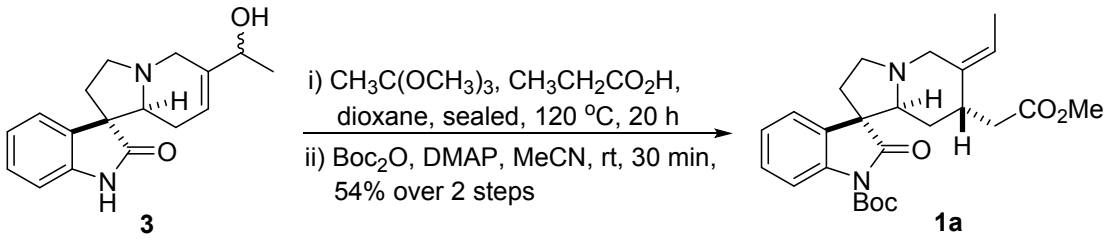
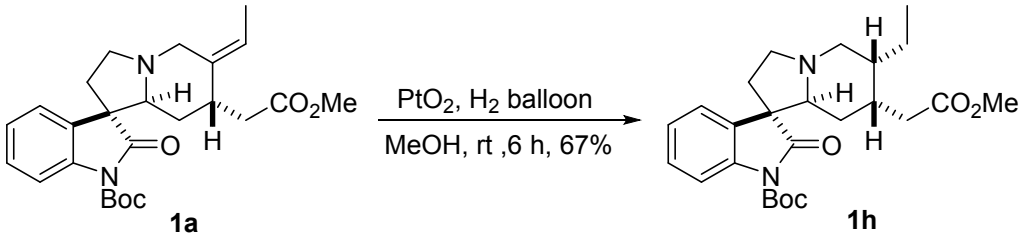
Alcohol 3: The known alcohol **3** was efficiently prepared in three steps from commercial available 3-(2-bromoethyl)indolin-2-one and 3-acetylpyridine by our reported CDC approach.[1] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H),

5.64-5.50 (s, 1H), 4.33-4.16 (q, J = 6.4 Hz, 1H), 3.77-3.53 (d, J = 15.6 Hz, 1H), 3.52-3.42 (m, 1H), 3.01-2.84 (m, 1H), 2.83-2.71 (m, 1H), 2.69-2.58 (m, 1H), 2.20-2.06 (m, 2H), 1.79-1.58 (m, 2H), 1.32-1.22 (d, J = 6.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.2, 140.4, 139.9, 133.4, 127.9, 125.3, 122.7, 119.8, 118.2, 109.7, 70.5, 69.7, 68.0, 56.6, 54.5, 53.1, 51.9, 35.4, 26.6, 22.3, 21.7.

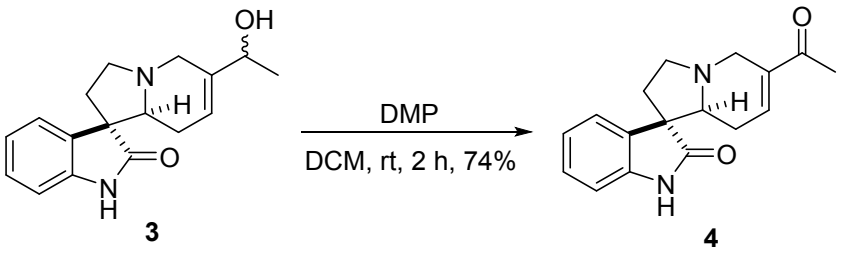


Ester 1a: The alchol **3** (1.00 g, 3.52 mmol), trimethyl orthoacetate (2.25 mL, 17.60 mmol) and propanoic acid (0.080 mL, 1.06 mmol) in 1,4-dioxane (20 mL) was charged with argon, and then the mixture was sealed and stirred at 120 °C for 20 h. After cooling to room temperature, the reaction mixture was diluted with water (30 mL), extracted with EtOAc (20 mL x 3), dried over Na_2SO_4, filtered and concentrated in *vacuo* for next step without further purification.

To a solution of above crude product in dry acetonitrile (20 mL) was added DMAP (645.1 mg, 5.28 mmol) and Boc_2O (807.0 mg, 3.70 mmol) at room temperature. After stirring for 30 min, the reaction mixture was concentrated in *vacuo*, and purified by flash column chromatography (PE/acetone = 5/1) to provide the ester **1a** (840.8 mg, 1.91 mmol, 54%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8, 1H), 7.39 (d, J = 7.8, 1H), 7.26 (t, J = 7.8, 1H), 7.12 (t, J = 7.8, 1H), 5.08 (q, J = 6.8, 1H), 4.03 (d, J = 11.8, 1H), 3.60 (s, 3H), 3.28 (td, J = 8.8, 1.5, 1H), 2.71 (dd, J = 11.8, 2.4, 1H), 2.57-2.51 (m, 2H), 2.48-2.43 (m, 2H), 2.09-2.00 (m, 2H), 1.65 (br d, 12H), 1.28-1.21 (m, 2H), 0.69 (q, J = 11.6, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 173.2, 149.4, 139.0, 136.3, 132.0, 127.8, 124.9, 124.4, 115.7, 114.6, 84.5, 72.8, 56.5, 54.0, 53.1, 51.7, 37.7, 37.3, 37.0, 33.2, 28.1, 13.2; HRMS (ESI$^+$) *m/z* calcd. for $C_{25}H_{33}N_2O_5$ $[M + H]^+$ 441.2384, found 441.2380.

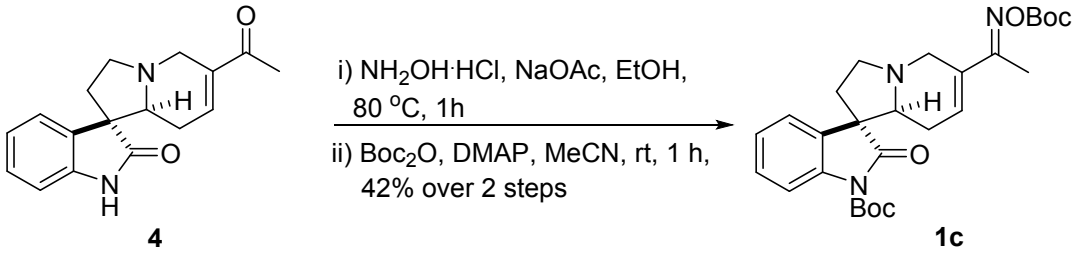


Hydrogenated product 1h: The substrate **1a** (365.8 mg, 0.831 mmol) and PtO_2 (22.7 mg, 83%, 0.083 mmol) in MeOH (8 mL) was stirred under an atmosphere of hydrogen at room temperature for 6 h. The reaction mixture was filtered through a pad of celite, and then the filtrate was concentrated. The residue was purified by silica gel column chromatography (PE/EtOAc = 4/1) to afford hydrogenated product **1h** (246.3 mg, 0.557 mmol, 67%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 3.56 (s, 3H), 3.31-3.22 (m, 2H), 2.52-2.37 (m, 4H), 2.05-1.96 (m, 1H), 1.89 (dd, *J* = 14.7, 8.6 Hz, 1H), 1.80 (t, *J* = 11.0 Hz, 1H), 1.65 (s, 9H), 1.58-1.49 (m, 2H), 1.23 (dt, *J* = 12.8, 2.2 Hz, 2H), 1.12-1.05 (m, 1H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.71 (dd, *J* = 23.6, 11.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 173.4, 149.4, 139.1, 132.2, 128.0, 124.8, 124.5, 114.8, 84.5, 72.5, 57.6, 56.8, 54.1, 51.6, 41.4, 38.4, 37.4, 37.1, 32.5, 28.3, 23.6, 11.1; HRMS (ESI$^+$) *m/z* calcd. for $C_{25}H_{35}N_2O_5$ $[M + H]^+$ 443.2540, found 443.2546.



Ketone 4: To the solution of the alcohol **3** (200.1 mg, 0.704 mmol) in DCM (10 mL) was add Dess-Martin periodinane (358.4 mg, 0.845 mmol) at room temperature. After stirring for 2 h, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and stirred for an additional 10 minutes. The reaction mixture was then separated and the aqueous layer was extracted with DCM (10 mL × 2). The combined organic fraction was dried over Na_2SO_4, filtered, concentrated in *vacuo*, and purified by a silica

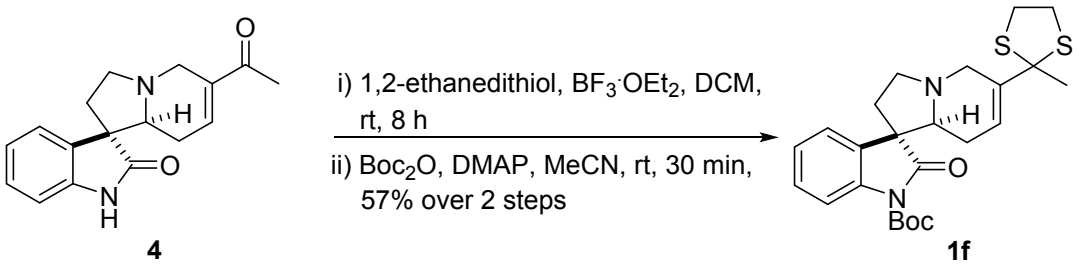
gel column chromatography (CH_2Cl_2/MeOH = 50:1) to give the ketone **4** (147.0 mg, 0.521 mmol, 74 %) as soft yellow foam. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, *J* = 27.9 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.22 (td, *J* = 7.6, 0.9 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.76 (br s, 1H), 3.98 (d, *J* = 16.0 Hz, 1H), 3.52 (td, *J* = 8.7, 3.3 Hz, 1H), 2.94 (ddd, *J* = 16.0, 3.6, 2.7 Hz, 1H), 2.77 (dd, *J* = 9.3, 5.4 Hz, 1H), 2.69 (dd, *J* = 18.6, 8.7 Hz, 1H), 2.50 (ddd, *J* = 12.9, 9.3, 3.3 Hz, 1H), 2.27 (s, 3H), 2.17-2.06 (m, 1H), 1.96-1.87 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 181.3, 140.3, 138.2, 138.1, 133.1, 128.2, 125.2, 122.9, 109.8, 66.4, 56.6, 54.0, 51.3, 35.1, 27.7, 25.4; HRMS (ESI$^+$) *m/z* calcd. for $C_{17}H_{19}N_2O_2$ $[M + H]^+$ 283.1441, found 283.1443.



Oxime 1c: To a solution of the ketone **4** (187.9 mg, 0.666 mmol) in dry ethanol (7 mL) was added hydroxylamine hydrochloride (55.5 mg, 0.799 mmol) and NaOAc (81.9 mg, 0.999 mmol) at room temperature. Then the flask was placed into an 80 ℃ oil bath and stirred for 1 h. After cooling to room temperature, the reaction mixture was diluted with water (10 mL), extracted with CH_2Cl_2 (10 mL x 3), dried over Na_2SO_4, filtered and concentrated in *vacuo* for next step without further purification.

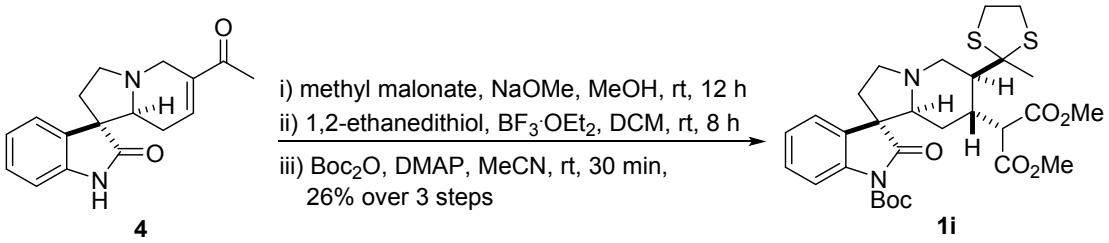
To a solution of above crude product in dry acetonitrile (7 mL) was added DMAP (244.1 mg, 1.998 mmol) and Boc_2O (305.4 mg, 1.40 mmol) at room temperature. After stirring for 1 h, the reaction mixture was concentrated in *vacuo*, and purified by flash column chromatography (PE/acetone = 5/1) to provide the oxime **1c** (139.2 mg, 0.280 mmol, 42%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.31 (td, *J* = 7.6, 1.0 Hz, 1H), 7.18 (td, *J* = 7.6, 1.0 Hz, 1H), 6.21 (t, *J* = 2.4 Hz, 1H), 4.17 (d, *J* = 16.2 Hz, 1H), 3.49 (td, *J* = 8.9, 2.9 Hz, 1H), 3.13 (ddd, *J* = 16.2, 6.9, 2.6 Hz, 1H), 2.86 (dd, *J* = 10.0, 4.4 Hz, 1H), 2.70 (q, *J* = 9.2 Hz, 1H), 2.54 (ddd, *J* = 12.5, 9.2, 2.9 Hz, 1H), 2.16-2.03 (m, 4H), 1.97-1.74 (m, 2H),

1.66 (s, 9H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 160.2, 152.2, 149.3, 139.1, 132.9, 131.7, 130.2, 128.2, 124.9, 124.7, 114.8, 84.5, 83.6, 67.7, 56.6, 54.0, 51.9, 36.7, 28.2, 27.9, 27.7, 11.9; HRMS (ESI$^+$) *m/z* calcd. for $C_{27}H_{36}N_3O_6$ $[M + H]^+$ 498.2599, found 498.2601.



Thioketal 1f: To a solution of the ketone **4** (60.4 mg, 0.214 mmol) in DCM (4 mL) at 0 ℃ was added 1,2-ethanedithiol (0.359 mL, 4.28 mmol) and boron trifluoride diethyl etherate (0.27 mL, 2.14 mmol). After stirring at room temperature for 8 h, the resultant solution was treated with saturated aqueous $NaHCO_3$ (5 mL) and extracted with DCM (5 mL x 3). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated in *vacuo* for next step without further purification.

To a solution of above crude product in dry acetonitrile (4 mL) was added DMAP (39.2 mg, 0.321 mmol) and Boc_2O (49.1 mg, 0.225 mmol) at room temperature. After stirring for 30 min, the reaction mixture was concentrated in *vacuo*, and purified by flash column chromatography (PE/acetone = 5/1) to provide the thioketal **1f** (55.8 mg, 0.122 mmol, 57%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 5.83 (s, 1H), 3.89 (d, *J* = 15.4 Hz, 1H), 3.42-3.19 (m, 7H), 3.11 (dd, *J* = 14.7, 2.0 Hz, 1H), 2.76 (dd, *J* = 8.3, 6.0 Hz, 1H), 2.64-2.60 (m, 1H), 2.53-2.47 (m, 1H), 2.12-2.02 (m, 1H), 1.91 (s, 3H), 1.64 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 149.4, 139.1, 138.2, 131.9, 128.19, 125.1, 124.6, 121.1, 114.7, 84.5, 68.6, 68.2, 56.5, 54.4, 54.1, 40.7, 40.1, 37.2, 31.5, 28.3, 26.9; HRMS (ESI$^+$) *m/z* calcd. for $C_{24}H_{31}N_2O_3S_2$ $[M + H]^+$ 459.1771, found 459.1780.

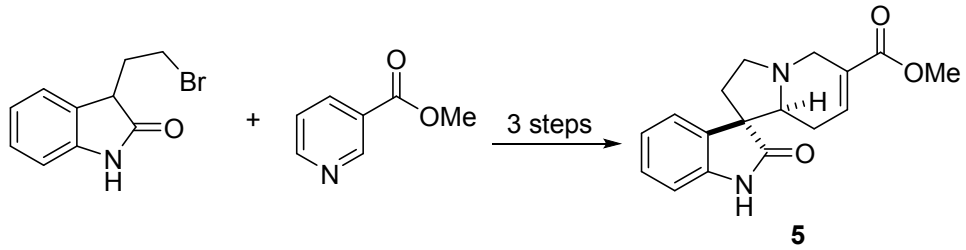


Malonic ester 1i: To the solution of the ketone **4** (100.5 mg, 0.356 mmol) in dry MeOH (7 mL) was added dimethyl malonate (0.203 mL, 1.78 mmol) and sodium methoxide (0.178 mL, 1 N in MeOH, 0.178 mmol) at 0 ℃. After stirring at room temperature for 12h, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with DCM (10 mL x 3). The combined extracts were washed with brine, dried over Na_2SO_4, and filtered by a pad of silica gel washing with 20 mL of DCM. The filtrate was then concentrated in *vacuo* for next step without further purification.

The above residue was dissolved in dry DCM (7 mL), and then was added 1,2-ethanedithiol (0.597 mL, 7.12 mmol) and boron trifluoride diethyl etherate (0.449 mL, 3.56 mmol) at 0 ℃. After stirring at room temperature for 8 h, the resultant solution was treated with saturated aqueous $NaHCO_3$ (10 mL) and extracted with DCM (10 mL x 3). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated in *vacuo* for next step without further purification.

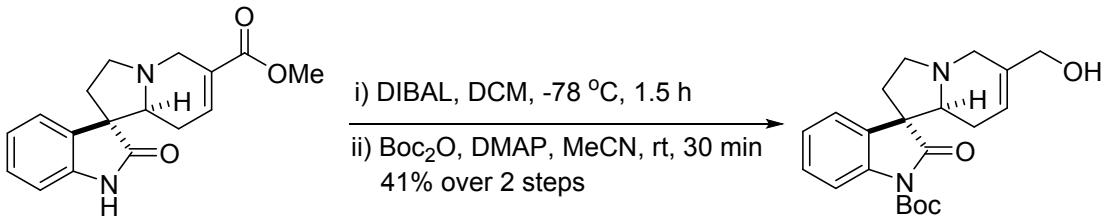
To a solution of above crude product in dry acetonitrile (7 mL) was added DMAP (65.2 mg, 0.534 mmol) and Boc_2O (81.6 mg, 0.374 mmol) at room temperature. After stirring for 30 min, the reaction mixture was concentrated in *vacuo*, and purified by flash column chromatography (PE/acetone = 4/1) to provide the malonic ester **1i** (54.9 mg, 0.093 mmol, 26%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.6 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 3.70 (s, 4H), 3.68 (s, 3H), 3.54-3.46 (m, 1H), 3.36-3.22 (m, 5H), 3.01 (dd, J = 11.0, 4.8 Hz, 1H), 2.57-2.40 (m, 4H), 2.05-1.96 (m, 2H), 1.94 (s, 3H), 1.85 (d, J = 4.6 Hz, 1H), 1.62 (s, 9H), 0.87 (d, J = 13.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.0, 169.0, 168.8, 149.1, 139.0, 131.5, 128.2, 125.0, 124.3, 114.8, 84.4, 72.7, 68.7, 57.1, 54.7, 54.6,

52.7, 52.5, 52.4, 47.1, 39.6, 39.5, 37.7, 35.3, 32.5, 28.2, 26.5; HRMS (ESI$^+$) *m/z* calcd. for $C_{29}H_{38}N_2O_7S_2Na$ $[M + Na]^+$ 613.2013, found 613.2019.



5

Unsaturated ester 5: The unsaturated ester **5** was also prepared from commercial available 3-(2-bromoethyl)indolin-2-one and methyl niconate by our reported CDC approach in three steps.[1] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 10.0 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.96-6.90 (m, 2H), 4.03 (d, *J* = 16.2 Hz, 1H), 3.73 (s, 3H), 3.64-3.56 (m, 1H), 2.96 (ddd, *J* = 16.2, 4.6, 2.4 Hz, 1H), 2.66-2.44 (m, 4H), 2.17-2.09 (m, 1H), 2.06-1.96 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.6, 166.2, 140.9, 137.3, 133.6, 128.9, 128.3, 123.2, 122.9, 109.9, 69.3, 55.8, 55.1, 52.2, 51.8, 35.2, 27.2; HRMS (ESI$^+$) *m/z* calcd. for $C_{17}H_{19}N_2O_3$ $[M + H]^+$ 299.1390, found 299.1390.

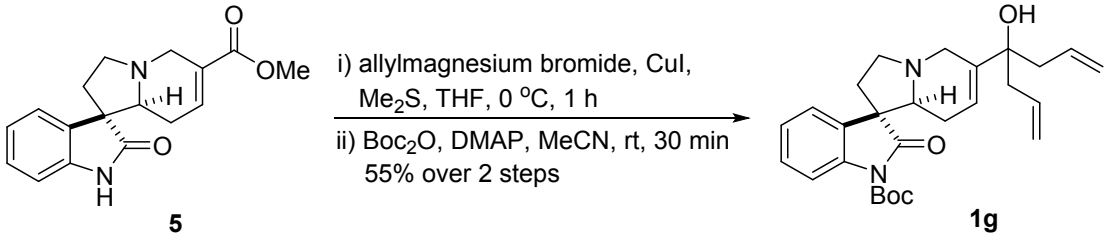


5 **1e**

Allyl alcohol 1e: To a solution of the unsaturated ester **5** (89.4 mg, 0.300 mmol) in CH_2Cl_2 (6 mL) was added diisobutylaluminum hydride (0.600 mL, 1 N in hexanes, 0.600 mmol) at -78 ℃. After stirring at this temperature for 1.5 h, the reaction mixture was quenched with saturated aqueous seignette salt (10 mL) and stirred for additional 1.5 h at room temperature. Then resultant mixture was separated, and the aqueous layer was extracted with DCM (10 mL x 3). The combined DCM extracts were washed with

brine, dried over Na_2SO_4, and concentrated in *vacuo* for next step without further purification.

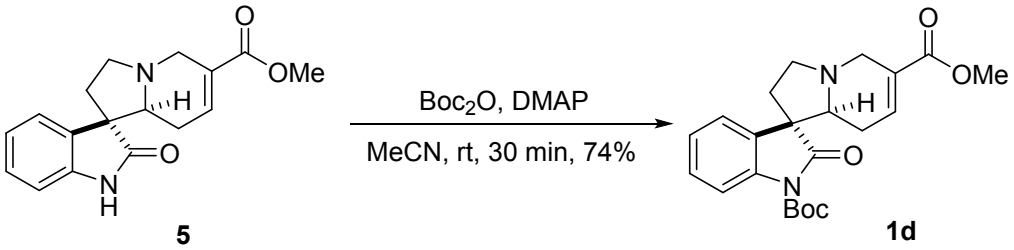
To a solution of above crude product in dry acetonitrile (6 mL) was added DMAP (55.0 mg, 0.450 mmol) and Boc_2O (68.7 mg, 0.315 mmol) at room temperature. After stirring for 30 min, the reaction mixture was concentrated in *vacuo*, and purified by flash column chromatography (DCM/MeOH = 20/1) to provide the allyl alcohol **1e** (45.5 mg, 0.123 mmol, 41%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 5.57 (s, 1H), 4.04 (d, *J* = 5.4 Hz, 2H), 3.63 (d, *J* = 15.6 Hz, 1H), 3.46 (td, *J* = 8.9, 2.4 Hz, 1H), 2.91 (dd, *J* = 15.6, 2.4 Hz, 1H), 2.82 (t, *J* = 7.3 Hz, 1H), 2.64 (dd, *J* = 17.8, 8.9 Hz, 1H), 2.56-2.47 (m, 1H), 2.14-2.04 (m, 1H), 1.92-1.76 (m, 2H), 1.64 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 149.3, 139.1, 136.1, 131.8, 128.2, 125.0, 124.7, 120.6, 114.8, 84.6, 68.7, 65.2, 56.5, 54.3, 53.7, 36.9, 28.2, 26.6; HRMS (ESI^+) *m/z* calcd. for $C_{21}H_{27}N_2O_4$ $[M + H]^+$ 371.1965, found 371.1965.



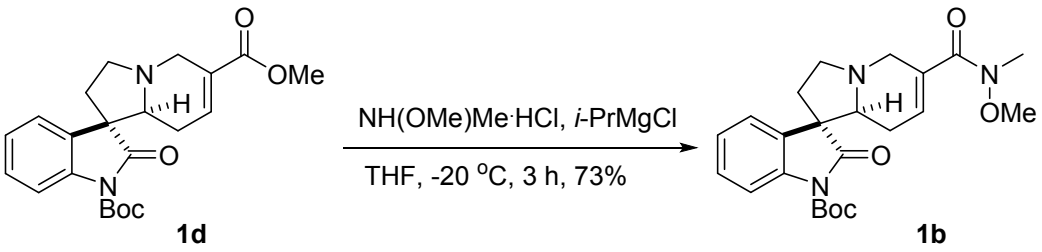
Tertiary alcohol 1g: To a stirred suspension of CuI (20.9 mg, 0.110 mmol) in THF (2 mL) was sequentially added Me_2S (22.0 μL, 0.300 mmol) and allylmagnesium bromide solution (0.500 mL, 1 N in diethyl ether, 0.500 mmol) dropwise at -78 ℃. After stirring for 30 min at the same temperature, a solution of the unsaturated ester **5** (29.8 mg, 0.100 mmol) in anhydrous THF (2 mL) was introduced, and the resulting mixture was stirred for 1h at 0 ℃. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl (10 mL) and extracted with EtOAc (3 x 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated in *vacuo* for next step without further purification.

To a solution of above crude product in dry acetonitrile (4 mL) was added DMAP

(18.3 mg, 0.150 mmol) and Boc_2O (22.9 mg, 0.105 mmol) at room temperature. After stirring for 30 min, the reaction mixture was concentrated in *vacuo*, and purified by flash column chromatography (petroleum ether/actone = 3/1) to provide the tertiary alcohol **1g** (24.8 mg, 0.055 mmol, 55%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.1 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 5.82-5.68 (m, 3H), 5.55 (s, 1H), 5.15-5.11 (m, 3H), 3.61 (d, *J* = 15.6 Hz, 1H), 3.43 (td, *J* = 8.6, 2.2 Hz, 1H), 2.86-2.70 (m, 2H), 2.62-2.36 (m, 5H), 2.34 (d, *J* = 6.4 Hz, 1H), 2.32-2.22 (m, 3H), 2.14-2.05 (m, 1H), 1.64 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 149.3, 139.1, 138.9, 133.6, 133.4, 131.9, 128.1, 125.0, 124.6, 119.4, 119.3, 119.0, 114.8, 84.5, 74.7, 68.6, 56.5, 54.6, 53.4, 44.2, 43.8, 37.1, 28.3, 26.6; HRMS (ESI$^+$) *m/z* calcd. for $C_{27}H_{35}N_2O_4$ $[M + H]^+$ 451.2591, found 451.2598.



Boc-protected amide 1d: To a solution of the unsaturated ester **5** (24.4 mg, 0.082 mmol) in dry acetonitrile (2 mL) was added DMAP (15.0 mg, 0.123 mmol) and Boc_2O (18.8 mg, 0.086 mmol) at room temperature. After stirring for 30 min, the reaction mixture was concentrated in *vacuo*, and purified by flash column chromatography (PE/EtOAc = 3/1) to provide the boc-protected amide **1d** (24.3 mg, 0.061 mmol, 74%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.30 (td, *J* = 7.6, 1.0 Hz, 1H), 7.25 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.18 (td, *J* = 7.6, 1.0 Hz, 1H), 6.95-6.87 (m, 1H), 3.99 (d, *J* = 16.2 Hz, 1H), 3.73 (s, 3H), 3.64-3.57 (m, 1H), 2.96 (ddd, *J* = 16.2, 7.2, 2.6 Hz, 1H), 2.68-2.52 (m, 3H), 2.42-2.30 (m, 1H), 2.16-2.09 (m, 1H), 2.96 (m, 1H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 166.1, 149.4, 139.5, 136.9, 131.7, 129.0, 128.5, 124.9, 122.9, 114.9, 84.5, 70.6, 55.9, 54.9, 52.0, 51.8, 35.9, 28.3, 27.0; HRMS (ESI$^+$) *m/z* calcd. for $C_{22}H_{27}N_2O_5$ $[M + H]^+$ 399.1914, found 399.1915.

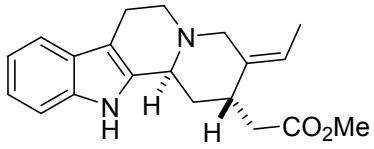


Weinreb amide 1b: To a stirred solution of compound **1d** (26.3 mg, 0.066 mmol) in THF (3 mL) at -20 °C was added *N*,*O*-dimethylhydroxylamine hydrochloride (6.73 mg, 0.069 mmol) and isopropyl magnesium chloride (99.0 μL, 2 N in THF, 0.198 mmol) dropwise. After stirring for 3 h, the reaction mixture was quenched with saturated NH_4Cl solution (10 mL), and extracted with EtOAc (10 mL x 3). The EtOAc extract was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (petroleum ether/actone = 5/1) to give Weinreb amide **1b** (20.5 mg, 0.048 mmol, 73%) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.6 Hz, 1H), 7.30-7.22 (m, 2H), 7.18 d, *J* = 7.6 Hz, 1H), 6.38-6.28 (m, 1H), 3.84 (d, *J* = 16.2 Hz, 1H), 3.62 (s, 3H), 3.58-3.52(m, 1H), 3.22 (s, 3H), 3.18-3.08 (m, 1H), 2.64-2.55 (m, 2H), 2.43-2.28 (m, 1H), 2.15-2.05 (m, 1H), 2.00-1.85 (m, 2H), 1.62 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 168.6, 149.4, 139.5, 131.9, 131.5, 129.9, 128.5, 124.9, 122.9, 114.8, 84.5, 70.9, 61.3, 56.0, 55.1, 53.4, 35.9, 34.0, 28.3, 26.5; HRMS (ESI$^+$) *m/z* calcd. for $C_{23}H_{30}N_3O_5$ $[M + H]^+$ 428.2180, found 428.2185.

3. General Procedure for the key Wagner–Meerwein Rearrangement and Spectroscopic Data of the Rearranged Products.

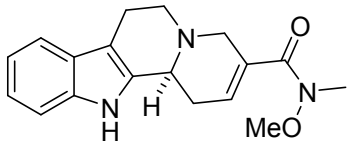
To a solution of 3-spirooxindole substrate **1** (1.0 equiv.) in anhydrous MeOH was added $NaBH_4$ (1.5 equiv.) under a nitrogen atmosphere at 0 °C. After stirring at this temperature for 1.5 h, the reaction was quenched with saturated NH_4Cl and extracted with DCM. The organic phases were combined, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford the corresponding amino-acetal intermediate, which was used in the next reaction without further purification.

To a stirred solution of the crude amino-acetal intermediate in DCM was added TFA (10.0 equiv.) at 25 ℃ under a nitrogen atmosphere. Monitoring the reaction by TLC until judged completion, the reaction mixture was quenched by addition of saturated $NaHCO_3$ and extracted with DCM. The combined extracts were washed with brine, dried over Na_2SO_4, concentrated and purified by flash chromatography to afford the rearranged product.



2a

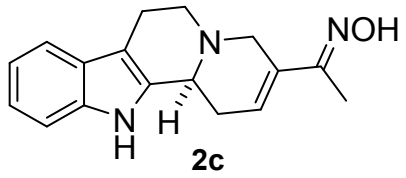
Following the general procedure, the 3-spirooxindole substrate **1a** (44.0 mg, 0.100 mmol) afforded the rearranged product **2a** (27.5 mg, 0.085 mmol, 85%) as yellow oil by silica gel chromatography (PE/acetone = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 5.41 (q, *J* = 6.8 Hz, 1H), 3.77-3.67 (m, 4H), 3.63 (d, *J* = 12.4 Hz, 1H), 3.20-3.12 (m, 1H), 3.05-2.91 (m, 3H), 2.82-2.69 (m, 2H), 2.60 (d, *J* = 7.8 Hz, 2H), 2.02-1.95 (m, 2H), 1.66 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 136.2, 135.4, 134.3, 127.5, 121.5, 120.5, 119.5, 118.2, 110.9, 108.6, 54.9, 53.0, 51.8, 51.1, 38.6, 37.9, 34.8, 21.2, 13.1; HRMS (ESI$^+$) *m/z* calcd. for $C_{20}H_{25}N_2O_2$ $[M + H]^+$ 325.1911, found 325.1908.



2b

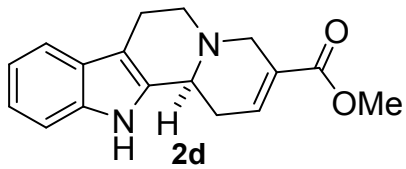
Following the general procedure, the 3-spirooxindole substrate **1b** (24.6 mg, 0.058 mmol) afforded the rearranged product **2b** (9.3 mg, 0.030 mmol, 52%) as yellow oil by silica gel chromatography (PE/EtOAc = 2/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.50 (br s, 1H), 3.70 (d, *J* = 15.6 Hz, 1H), 368 (s, 3H), 3.58 (d, *J* = 10.0 Hz, 1H), 3.38 (dd, *J* = 16.2,

2.4 Hz, 1H), 3.28 (s, 3H), 3.23 (dd, *J* = 11.4, 5.3 Hz, 1H), 3.07-2.97 (m, 1H), 2.77 (dd, *J* = 15.6, 2.0 Hz, 1H), 2.74-2.62 (m, 2H), 2.51-2.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 136.5, 134.2, 132.5, 129.7, 127.2, 121.8, 119.6, 118.4, 111.0, 108.8, 61.4, 55.0, 54.7, 52.2, 33.9, 31.4, 21.6; HRMS (ESI$^+$) *m/z* calcd. for $C_{18}H_{22}N_3O_2$ $[M + H]^+$ 312.1707, found 312.1713.



2c

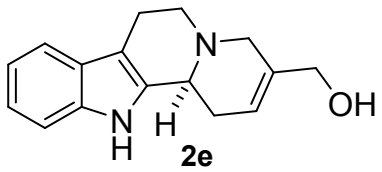
Following the general procedure, the 3-spirooxindole substrate **1c** (43.8 mg, 0.088 mmol) afforded the rearranged product **2c** (20.4 mg, 0.073 mmol, 83%) as yellow oil by silica gel chromatography (PE/acetone = 2/1). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.95 (d, *J* = 1.4 Hz, 1H), 10.82 (s, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.26 (d, *J* = 4.6 Hz, 1H), 3.76 (d, *J* = 16.0 Hz, 1H), 3.48-3.39 (m, overlapped with H_2O, 1H), 3.16-3.10 (m, 1H), 3.05 (d, *J* = 17.2 Hz, 1H), 2.89-2.77 (m, 2H), 2.65 (d, *J* = 14.0 Hz, 1H), 2.56-2.49 (m, overlapped with DMSO, 1H), 2.27-2.12 (m, 1H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 152.6, 136.2, 135.4, 134.0, 126.5, 125.2, 120.5, 118.4, 117.6, 111.0, 106.5, 55.3, 53.8, 51.9, 31.4, 21.3, 9.4; HRMS (ESI$^+$) *m/z* calcd. for $C_{17}H_{20}N_3O$ $[M + H]^+$ 282.1061, found 282.1064.



2d

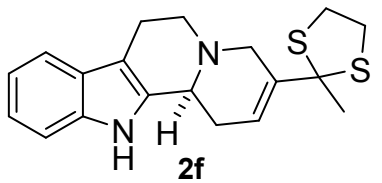
Following the general procedure, the 3-spirooxindole substrate **1d** (36.6 mg, 0.092 mmol) afforded the rearranged product **2d** (18.3 mg, 0.065 mmol, 71%) as yellow oil by silica gel chromatography (PE/EtOAc = 2/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 3.2 Hz, 1H), 3.83 (d, *J* = 16.2 Hz, 1H), 3.78 (s, 3H), 3.53 (d, *J* = 9.8 Hz, 1H), 3.30-3.17 (m, 2H), 3.07-2.96 (m, 1H), 2.83-2.63 (m, 3H), 2.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 136.5, 136.4, 133.9, 129.8, 127.2, 121.9, 119.7, 118.4, 110.9, 109.0, 54.8, 53.5, 52.3, 51.9, 32.0,

21.6; HRMS (ESI$^+$) *m/z* calcd. for $C_{17}H_{19}N_2O_2$ $[M + H]^+$ 283.1441, found 283.1444.



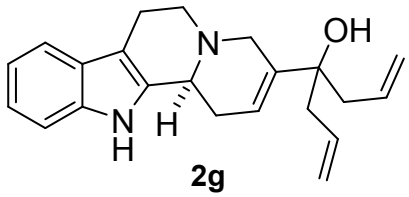
2e

Following the general procedure, the 3-spirooxindole substrate **1e** (9.3 mg, 0.025 mmol) afforded the rearranged product **2e** (4.7 mg, 0.018 mmol, 72%) as yellow oil by silica gel chromatography (PE/EtOAc = 1/1). ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 10.78 (s, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 5.71 (s, 1H), 4.79 (t, *J* = 5.4 Hz, 1H), 3.88 (d, *J* = 4.2 Hz, 2H), 3.35-3.28 (m, overlapped with H_2O, 1H), 3.11 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.94 (d, *J* = 16.0 Hz, 1H), 2.87-2.75 (m, 1H), 2.67 (t, *J* = 16.4 Hz, 2H), 2.57-2.52 (m, overlapped with DMSO, 1H), 2.11-1.97 (m, 1H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 138.0, 136.6, 136.0, 127.0, 120.9, 118.8, 118.7, 118.0, 111.4, 106.8, 63.6, 56.1, 55.1, 52.3, 30.9, 21.7; HRMS (ESI$^+$) *m/z* calcd. for $C_{16}H_{19}N_2O$ $[M + H]^+$ 255.1942, found 255.1943.



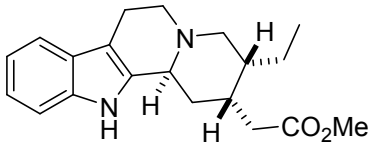
2f

Following the general procedure, the 3-spirooxindole substrate **1f** (46.3 mg, 0.101 mmol) afforded the rearranged product **2f** (26.1 mg, 0.076 mmol, 75%) as yellow oil by silica gel chromatography (PE/acetone = 2/1). Yield: 26.1 mg, 75%, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.13-6.05 (m, 1H), 3.81 (d, *J* = 15.4 Hz, 1H), 3.49 (d, *J* = 10.8, 2.0 Hz, 1H), 3.44-3.29 (m, 5H), 3.25 (dd, *J* = 11.2, 5.2 Hz, 1H), 3.10-2.98 (m, 1H), 2.78 (dd, *J* = 15.4, 2.4 Hz, 1H), 2.68 (td, *J* = 12.3, 4.2 Hz, 1H), 2.59 (d, *J* = 16.9, 4.6 Hz, 1H), 2.41-2.28 (m, 1H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 136.4, 134.7, 127.4, 121.6, 120.7, 119.6, 118.4, 110.9, 108.8, 68.2, 55.6, 55.4, 52.6, 40.7, 40.2, 31.4, 31.3, 21.6; HRMS (ESI$^+$) *m/z* calcd. for $C_{19}H_{23}N_2S_2$ $[M + H]^+$ 343.1297, found 343.1301.



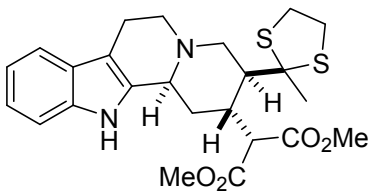
2g

Following the general procedure, the 3-spirooxindole substrate **1g** (16.2 mg, 0.036 mmol) afforded the rearranged product **2g** (8.6 mg, 0.026 mmol, 72%) as yellow oil by silica gel chromatography (PE/EtOAc = 1/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 5.90-5.77 (m, 3H), 5.18 (d, *J* = 3.8 Hz, 2H), 5.16-5.11 (m, 2H), 3.51 (d, *J* = 15.8 Hz, 1H), 3.45 (d, *J* = 18.4 Hz, 1H), 3.22 (dd, *J* = 11.4, 5.4 Hz, 1H), 3.03 (ddd, *J* = 15.8, 2.4, 1.8 Hz, 2H), 2.77 (dd, *J* = 15.6, 3.6 Hz, 1H), 2.66 (td, *J* = 11.4, 4.0 Hz, 1H), 2.57 (dt, *J* = 16.8, 5.0 Hz, 1H), 2.49 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.43 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.37-2.29 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 136.4, 134.7, 133.5, 133.5, 127.3, 121.6, 119.6, 119.3 (2C), 119.2, 118.4, 110.9, 108.6, 74.7, 55.6, 54.8, 52.8, 44.2, 43.8, 31.1, 21.6; HRMS (ESI$^+$) *m/z* calcd. for $C_{22}H_{27}N_2O$ $[M + H]^+$ 335.2118, found 335.2124.



2h

Following the general procedure, the 3-spirooxindole substrate **1h** (26.5 mg, 0.060 mmol) afforded the rearranged product **2h** (15.4 mg, 0.047 mmol, 78%) as yellow oil by silica gel chromatography (PE/acetone = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 4.08 (s, 1H), 3.73 (s, 3H), 3.26-3.13 (m, 1H), 3.11-2.94 (m, 2H), 2.72 (dd, *J* = 11.4, 3.4 Hz, 1H), 2.66-2.57 (m, 2H), 2.52 (dd, *J* = 11.4, 8.0 Hz, 1H), 2.33-2.17 (m, 2H), 1.74 (dd, *J* = 8.0, 3.4 Hz, 2H), 1.55-1.46 (m, 1H), 1.40-1.32 (m, 1H), 1.24-1.14 (m, 1H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 136.1, 133.9, 127.8, 121.5, 119.5, 118.1, 111.2, 108.1, 54.4, 52.1, 51.8, 51.6, 41.5, 37.2, 33.0, 32.5, 24.4, 18.7, 11.7; HRMS (ESI$^+$) *m/z* calcd. for $C_{20}H_{27}N_2O_2$ $[M + H]^+$ 327.2067, found 327.2071.



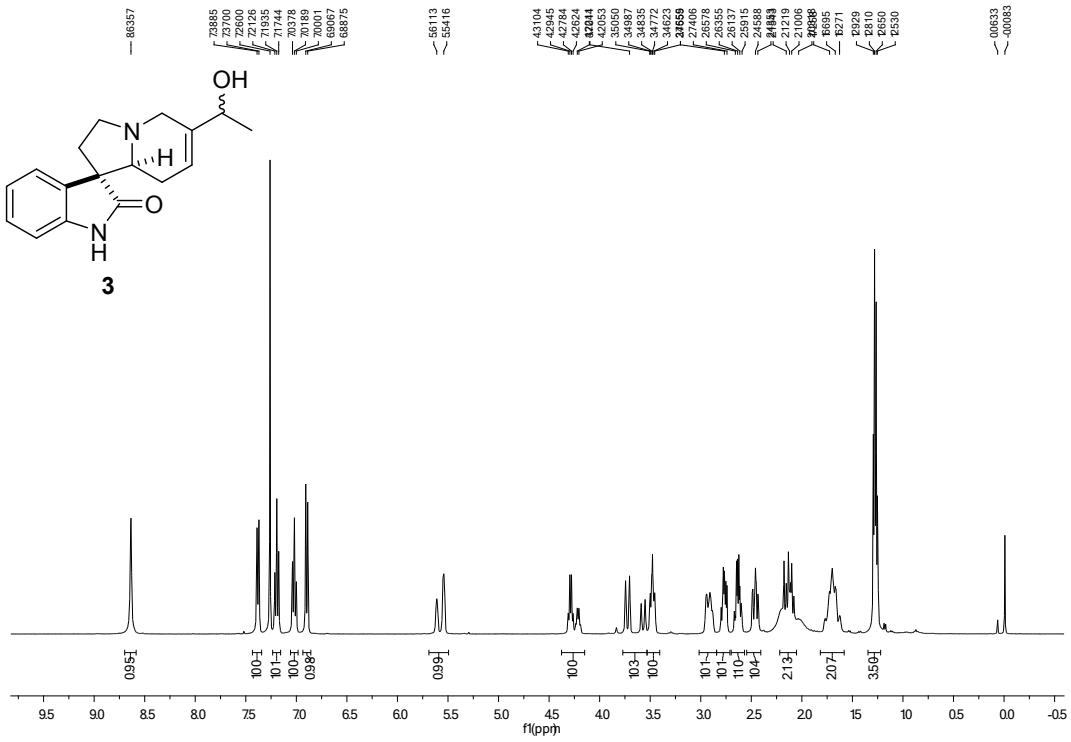
2i

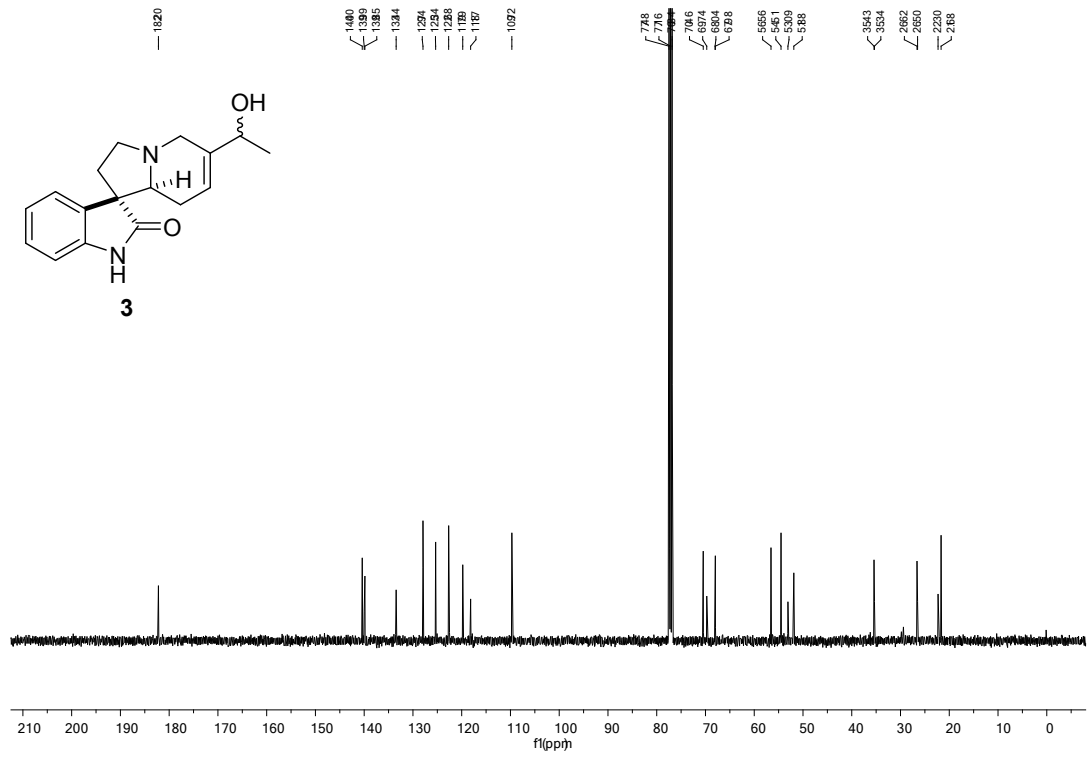
Following the general procedure, the 3-spirooxindole substrate **1i** (25.4 mg, 0.043 mmol) afforded the rearranged product **2i** (13.7 mg, 0.029 mmol, 67%) as yellow oil by silica gel chromatography (PE/acetone = 2/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 4.01 (d, *J* = 10.0 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.61 (d, *J* = 10.4 Hz, 1H), 3.33-3.20 (m, 4H), 3.17 (ddd, *J* = 16.4, 4.8, 2.4 Hz, 1H), 3.07 (dd, *J* = 10.4, 6.4 Hz, 1H), 3.02-2.88 (m, 2H), 2.81 (dd, *J* = 12.8, 4.8 Hz, 1H), 2.74-2.61 (m, 2H), 2.35-2.25 (m, 1H), 2.08 (br s, 1H), 2.00 (dt, *J* = 14.4, 2.8 Hz, 1H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 169.3, 169.2, 136.1, 134.4, 127.4, 121.5, 119.5, 118.1, 111.1, 108.7, 72.0, 55.0, 54.3, 53.3, 52.8 (2C), 52.7, 47.3, 39.6, 39.2, 35.3, 32.2, 30.3, 20.7; HRMS (ESI$^+$) *m/z* calcd. for $C_{24}H_{31}N_2O_4S_2$ $[M + H]^+$ 475.1720, found 475.1722.

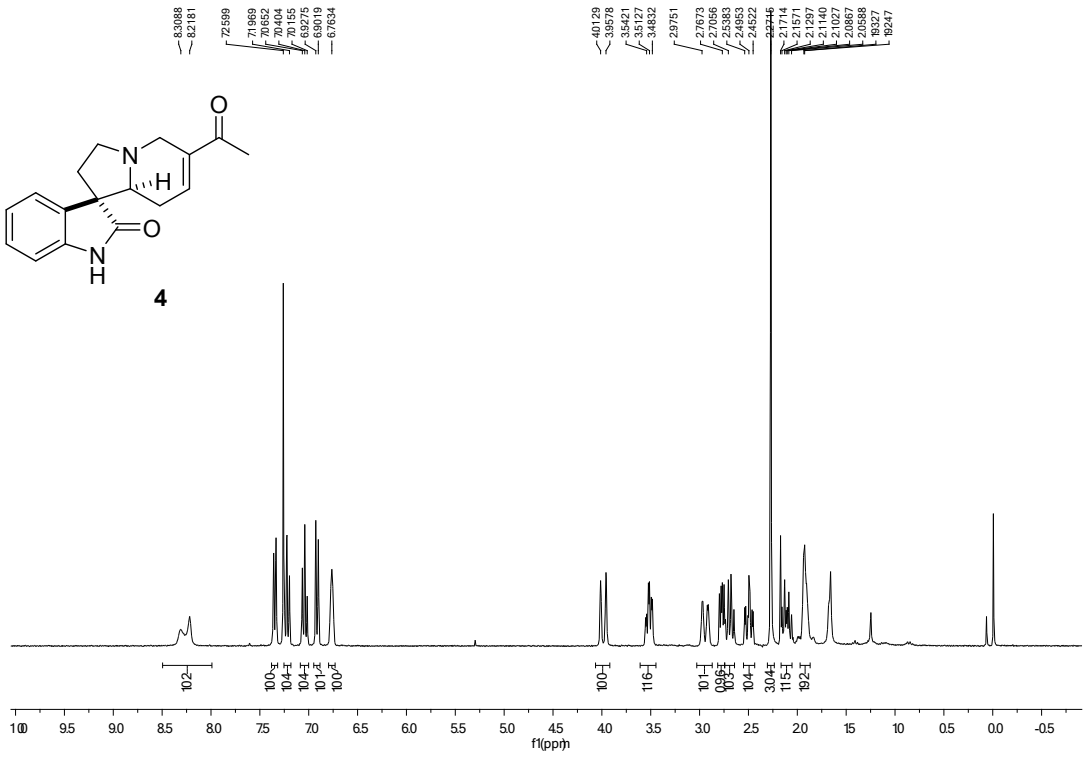
4. References.

[1] J. Xu, L.-D. Shao, D. Li, X. Deng, Y.-C. Liu, Q.-S. Zhao, C. Xia, *J. Am. Chem. Soc.* **2014**, *136*, 17962-17965;

5. Copies of ^{1}H NMR and ^{13}C NMR Spectra.



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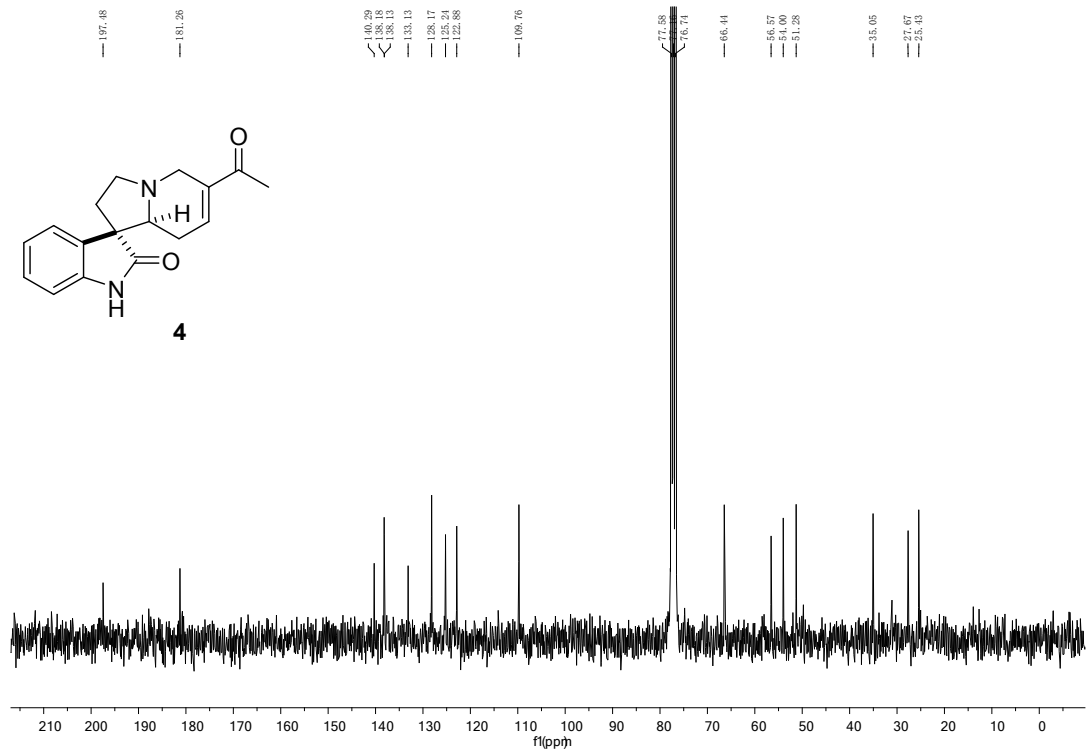
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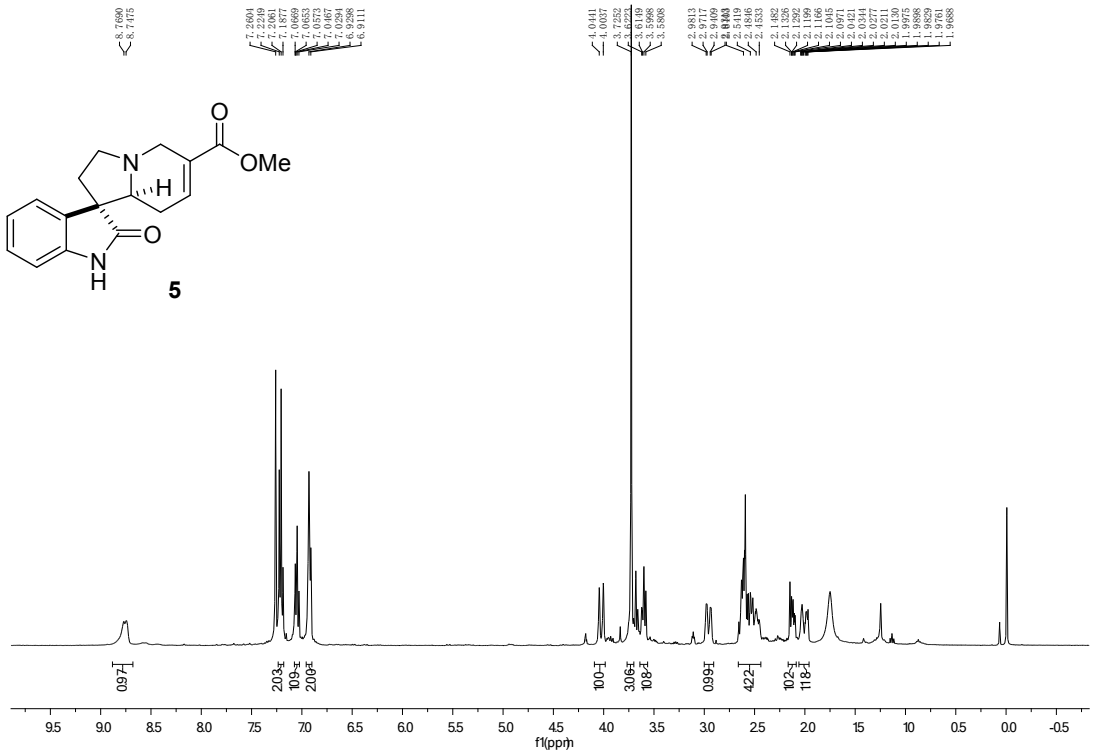
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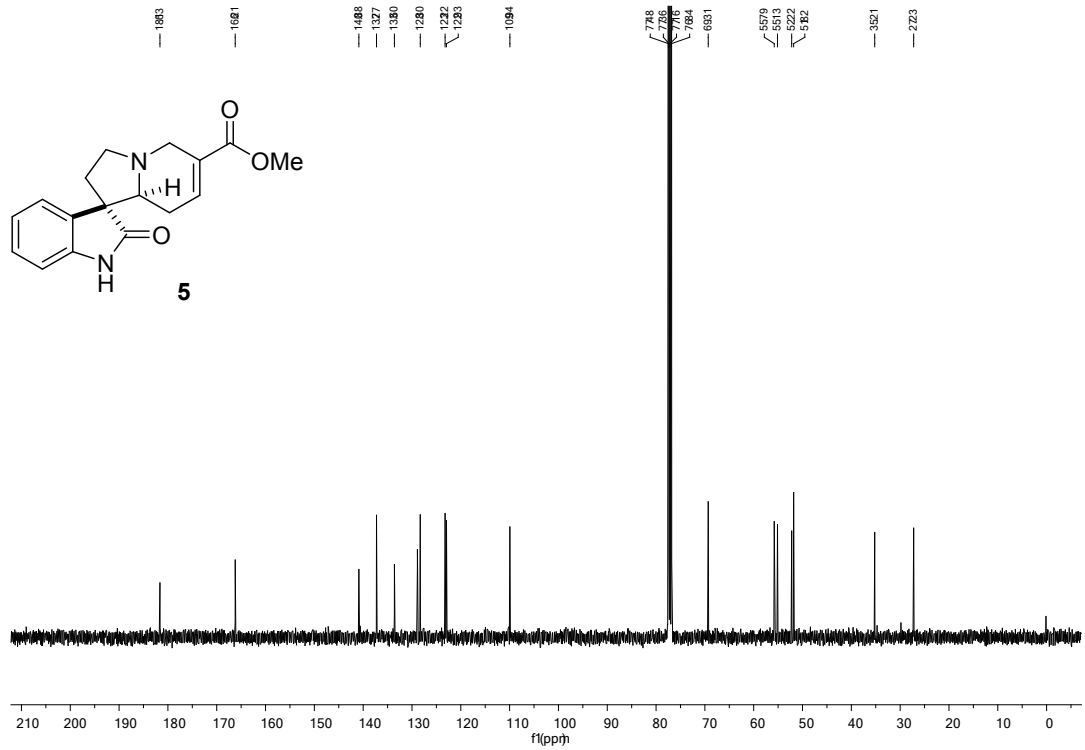
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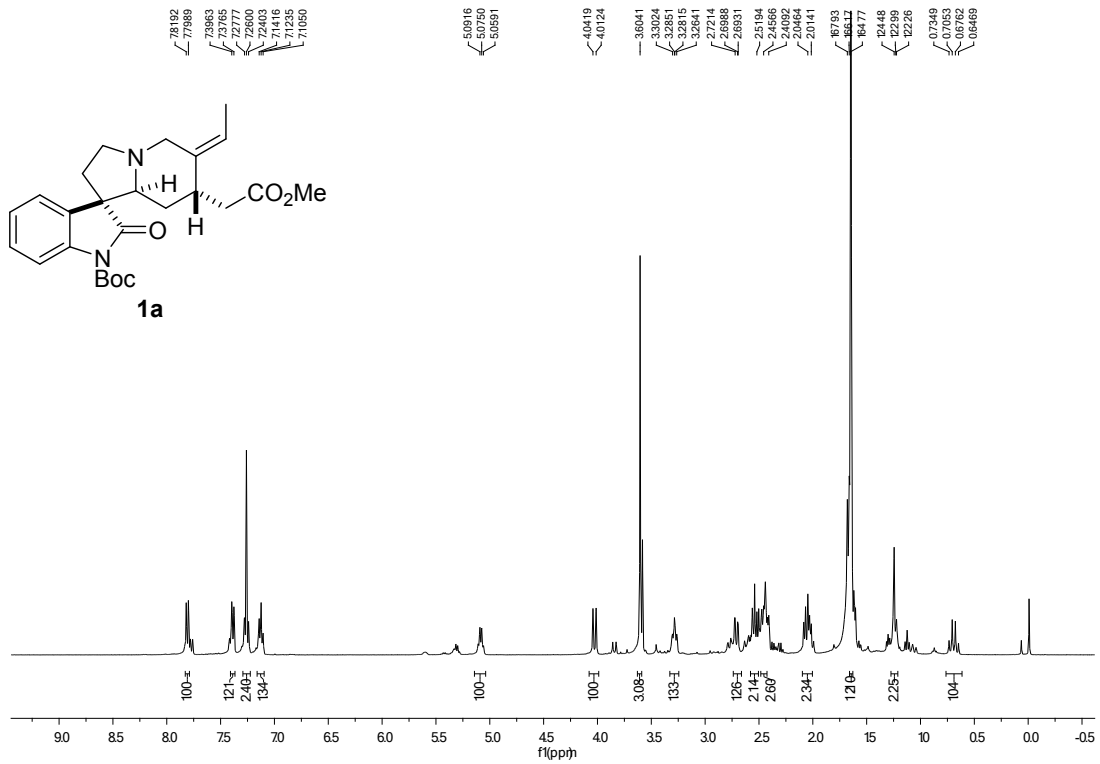
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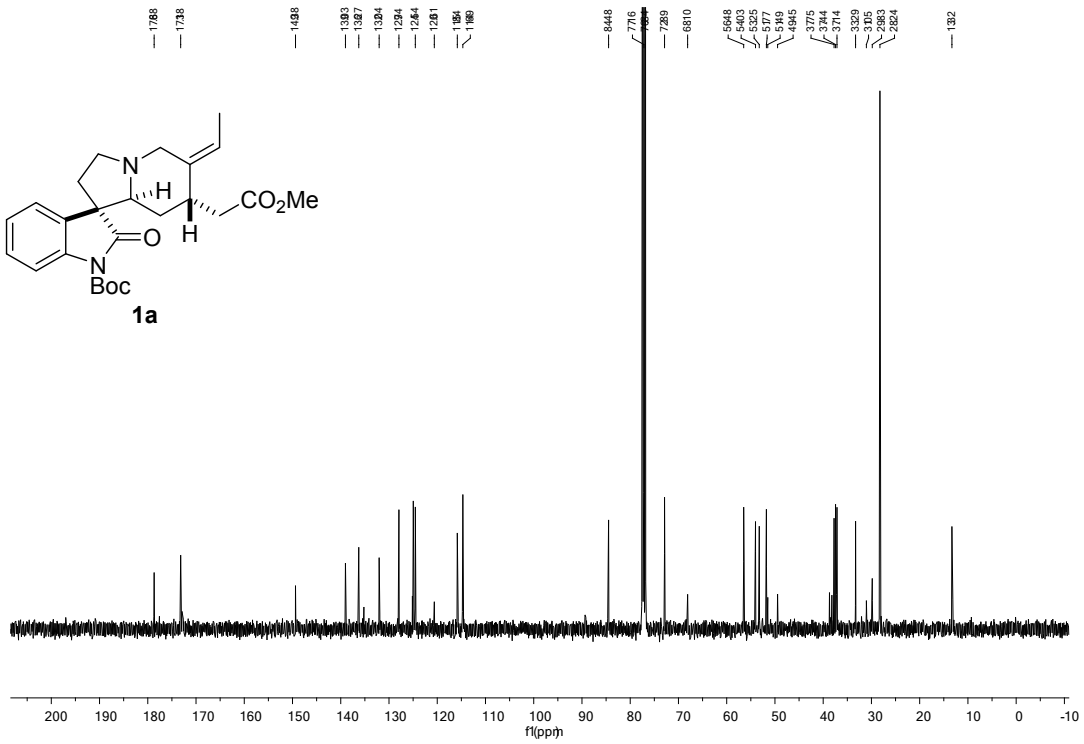
f1(ppm)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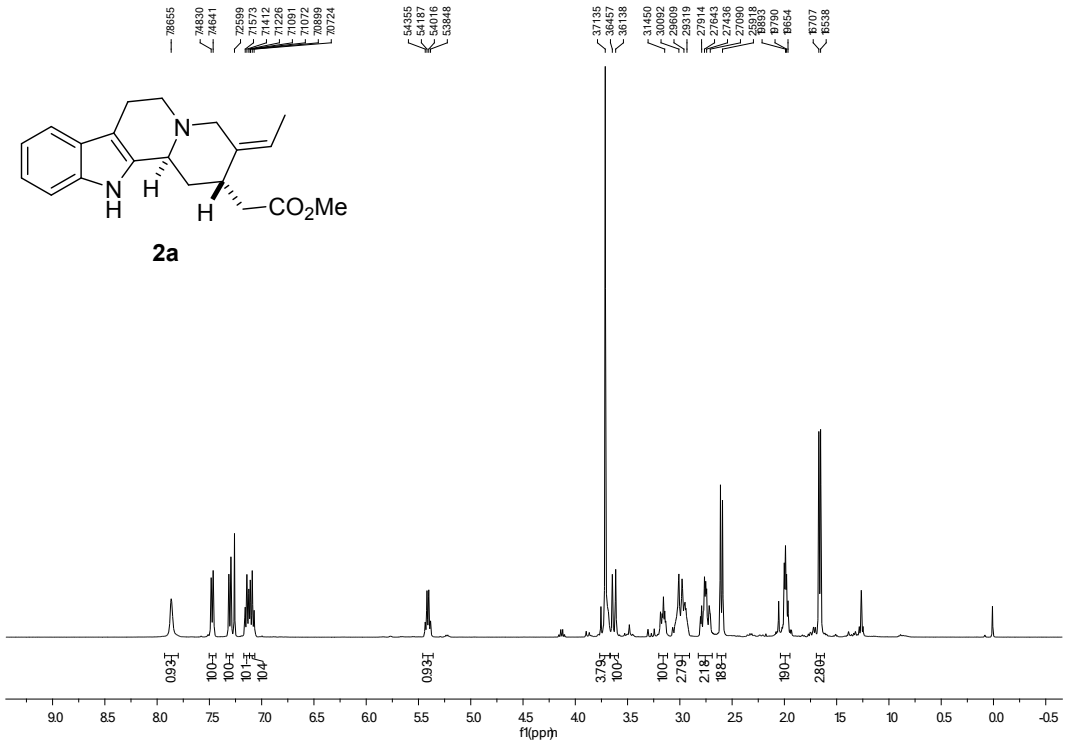
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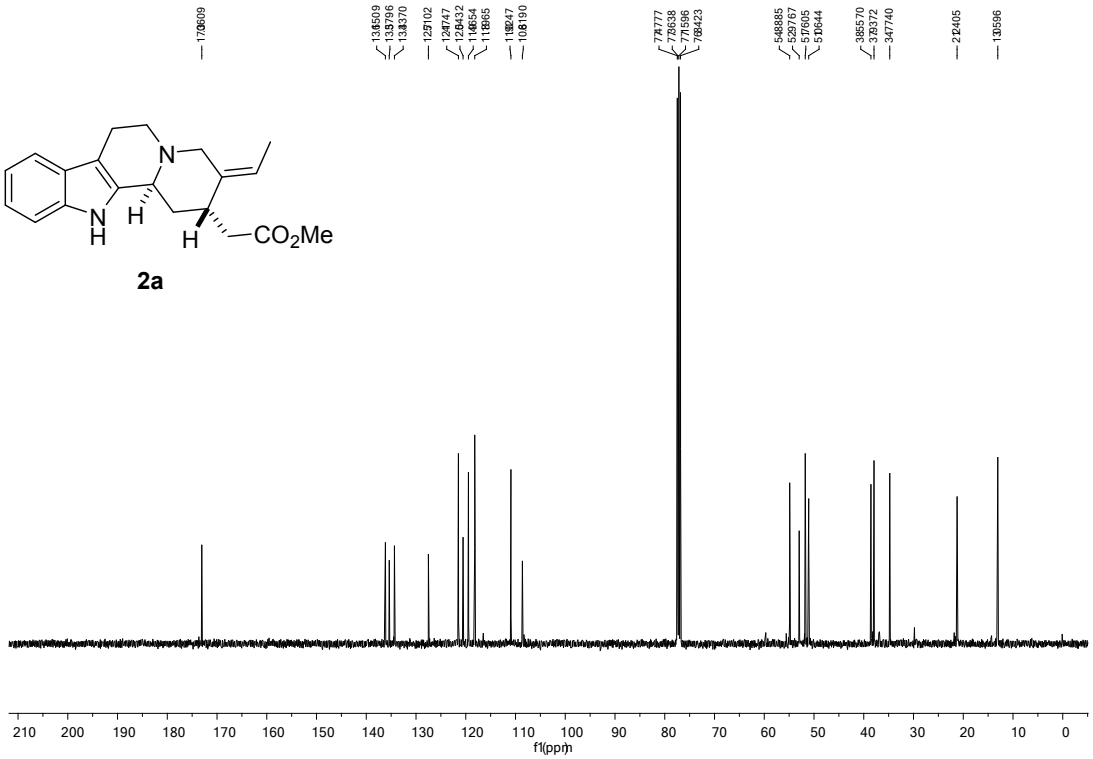
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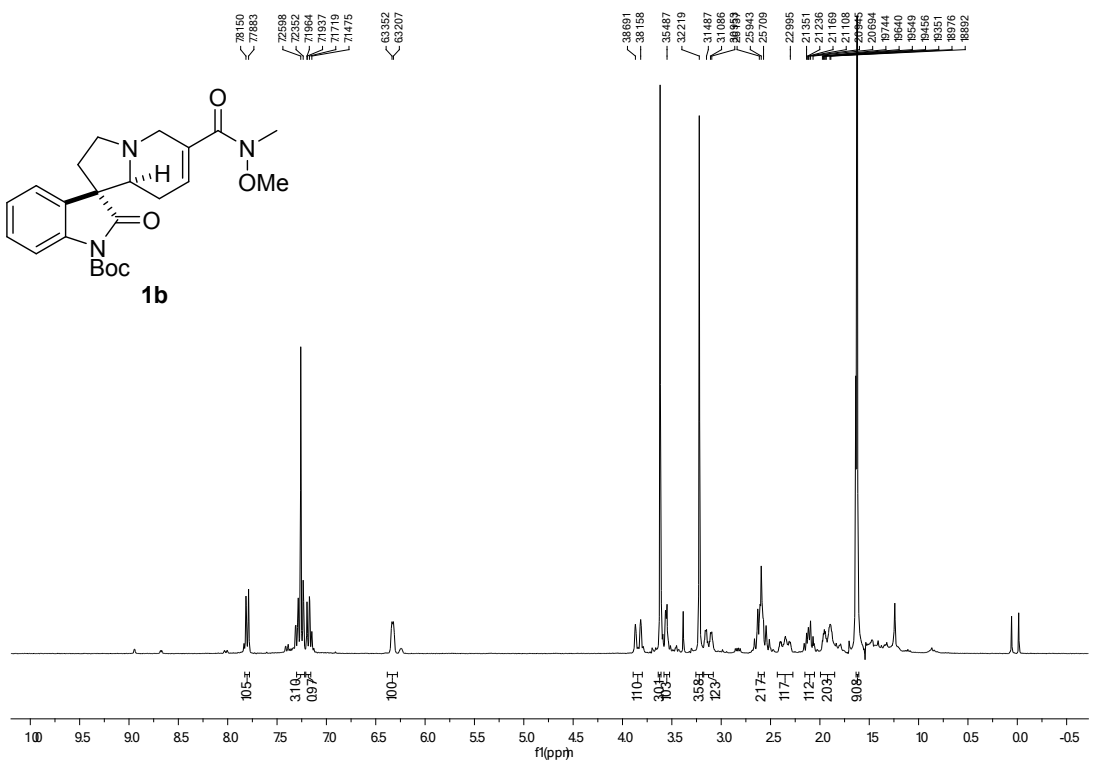
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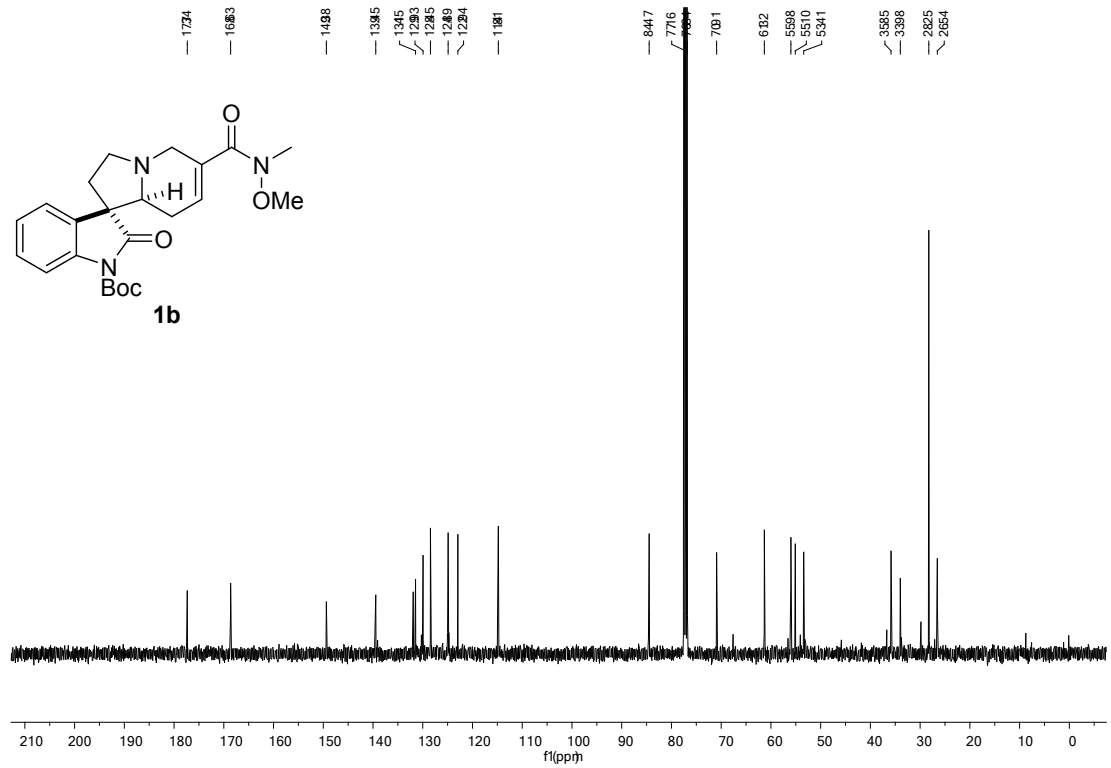
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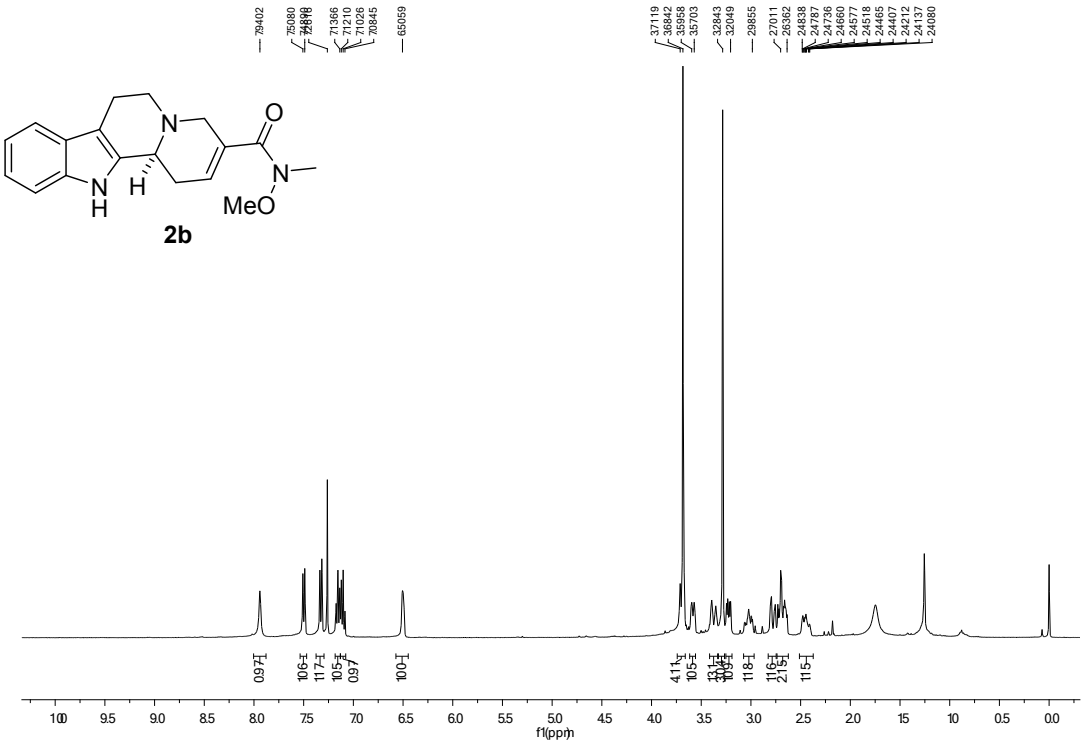
1b
f1(ppm)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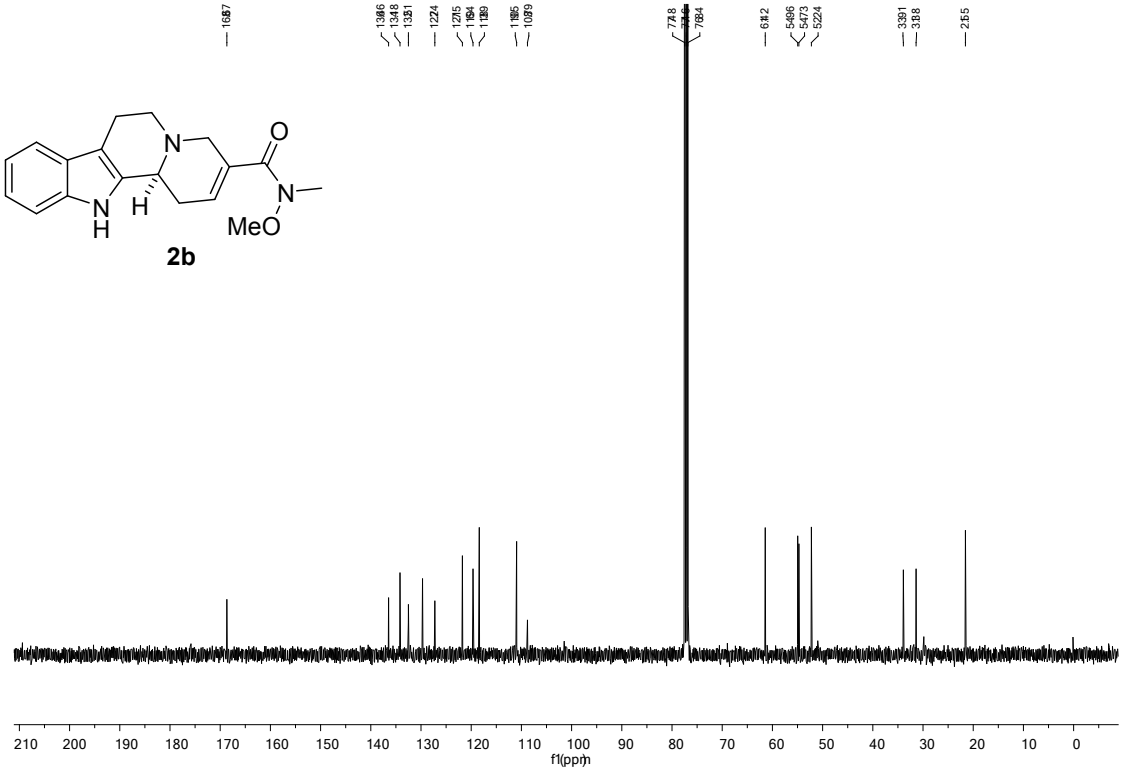
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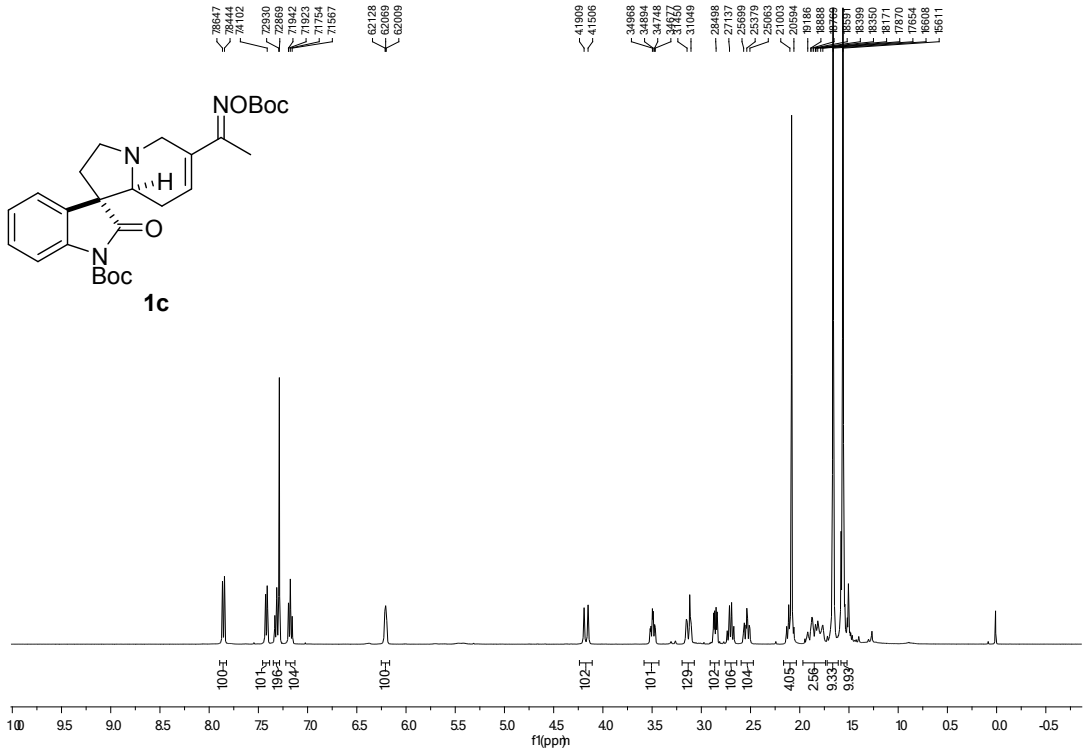
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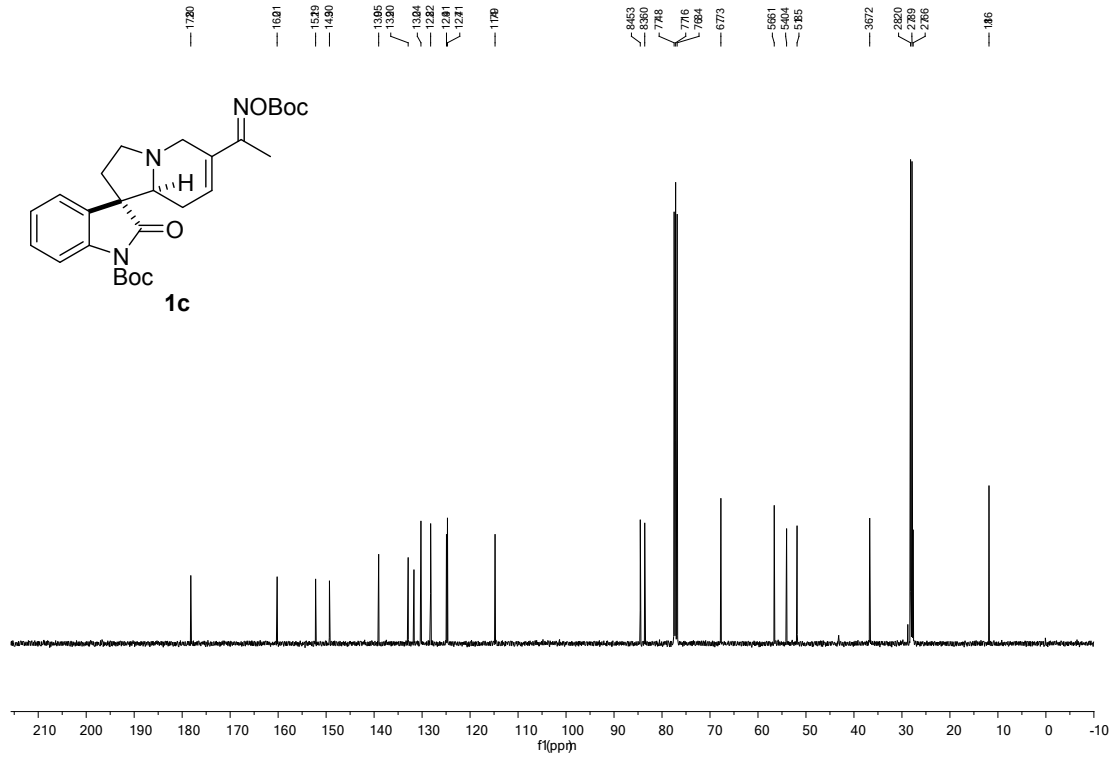
N
Boc
1c
f1(ppm)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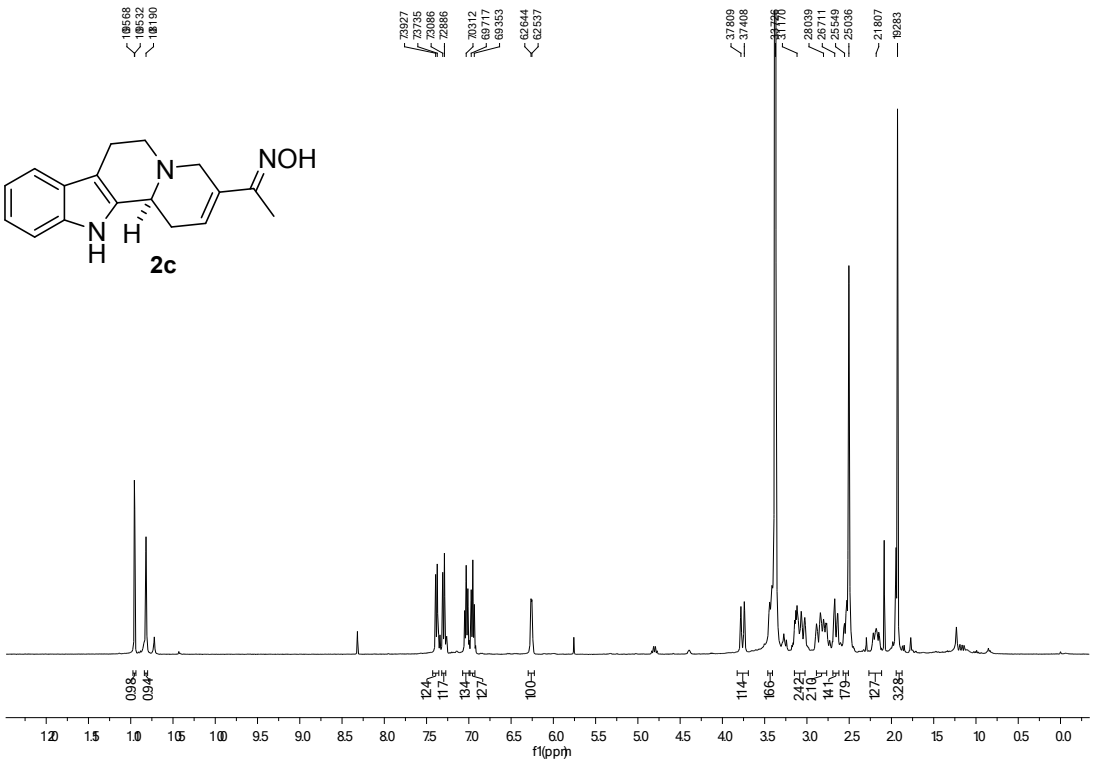
f1(ppm)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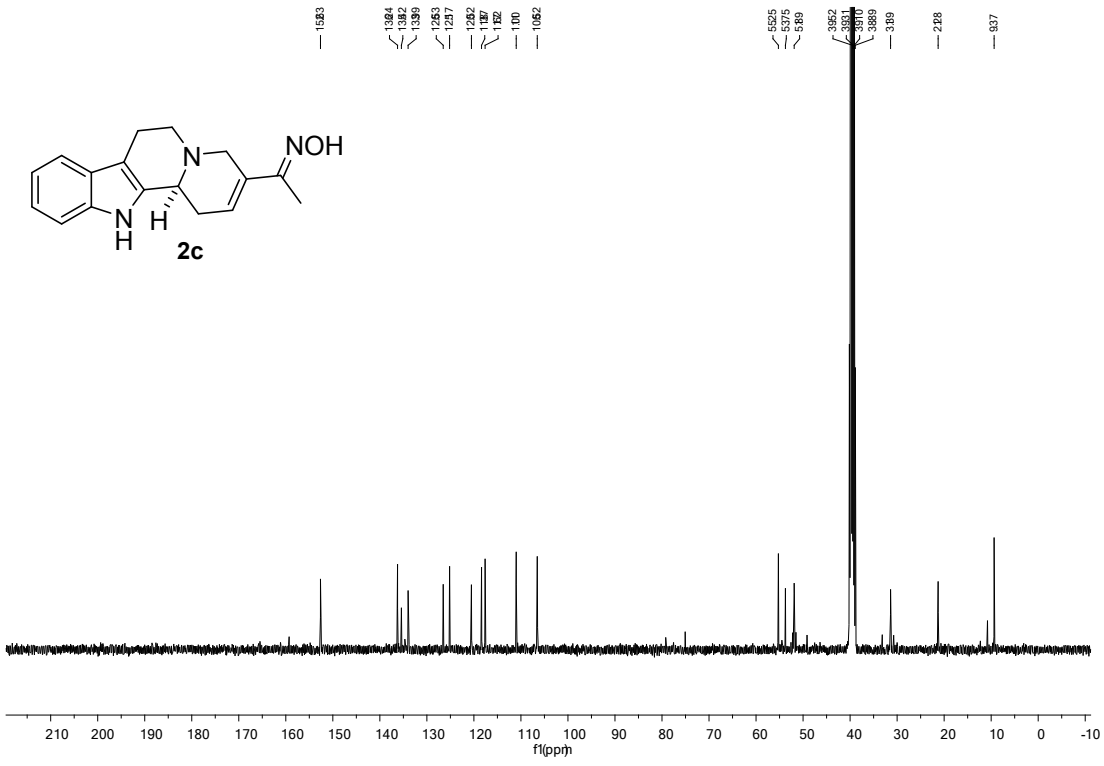
f1(ppm)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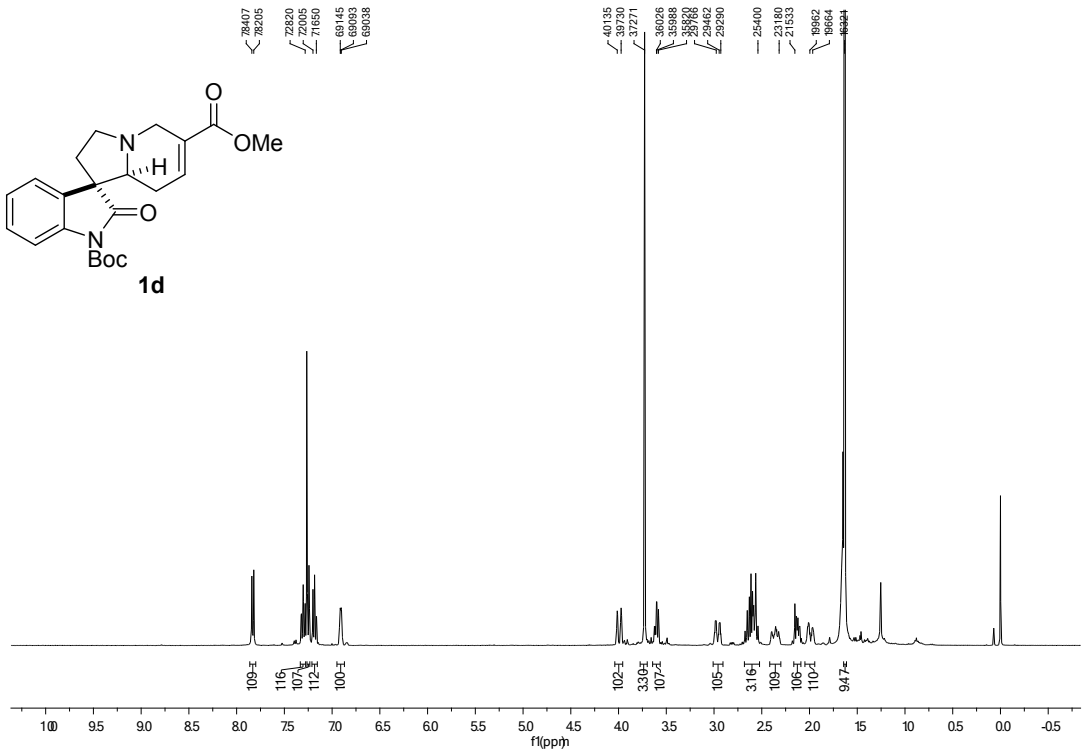
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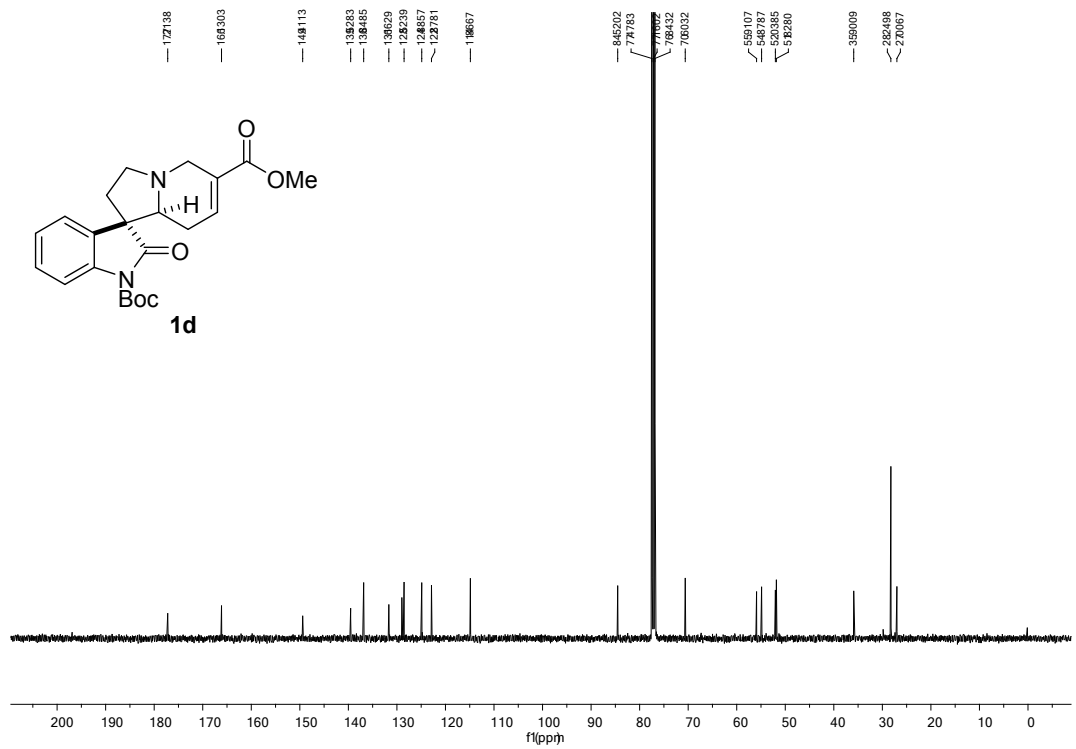
f1(ppm)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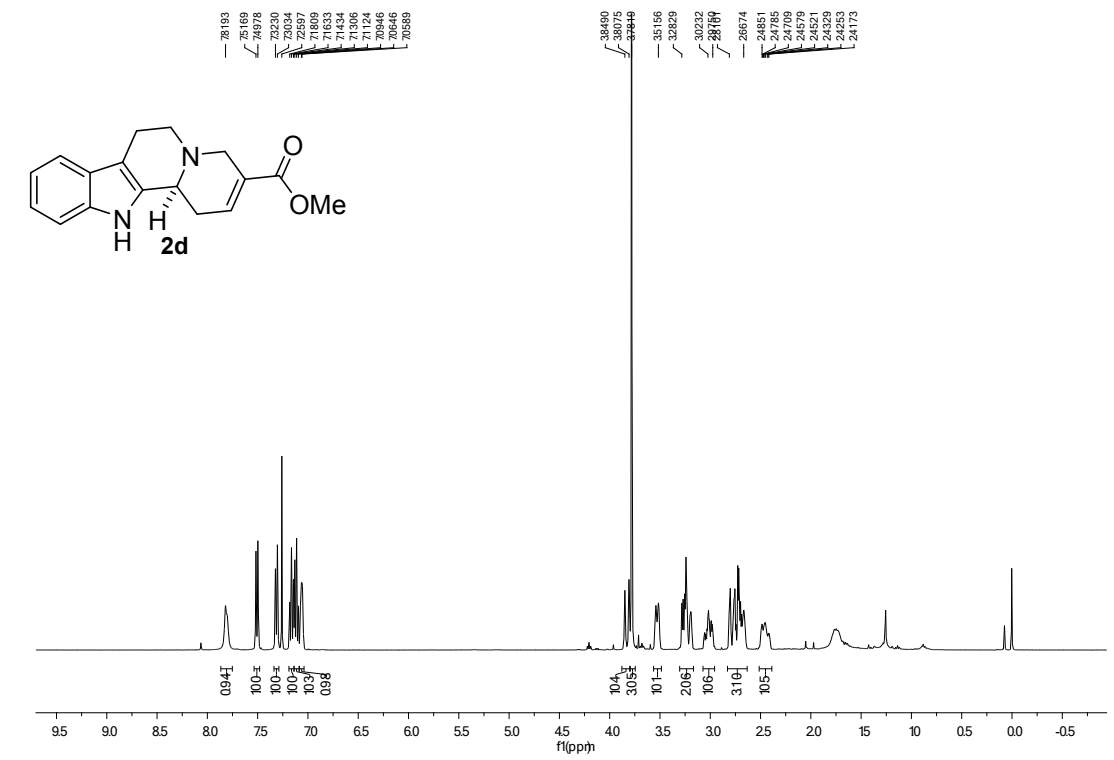
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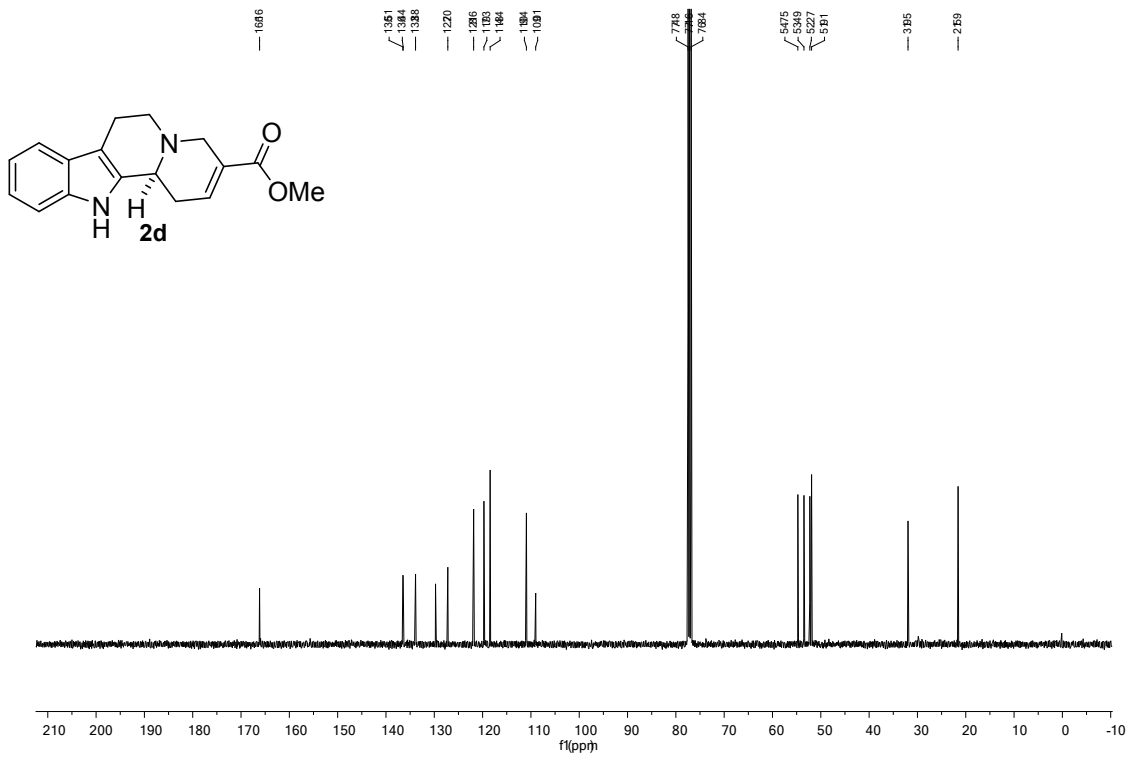
f1(ppm)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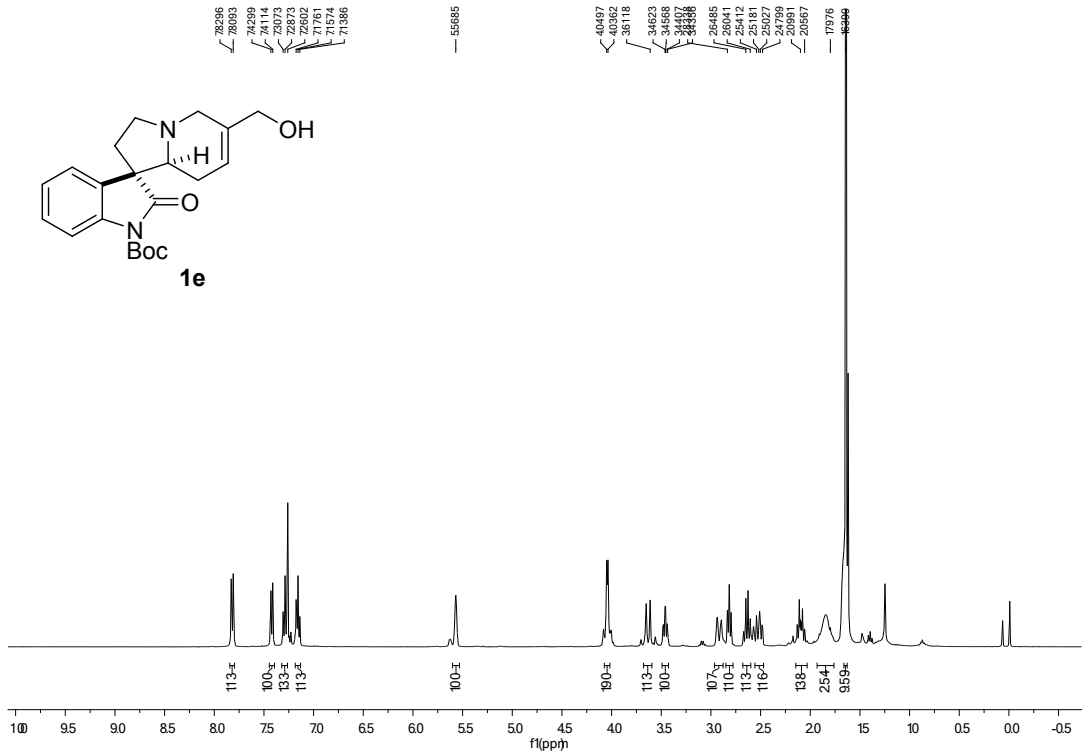
f1(ppm)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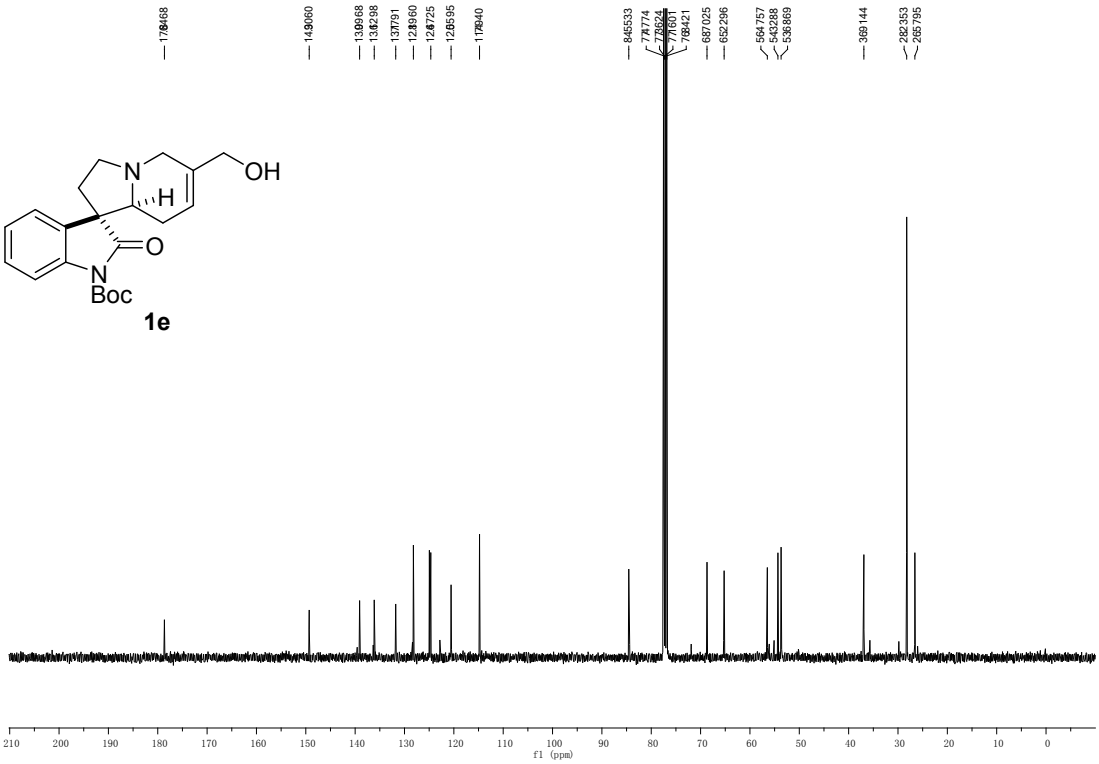
Boc
1e
f1(ppm)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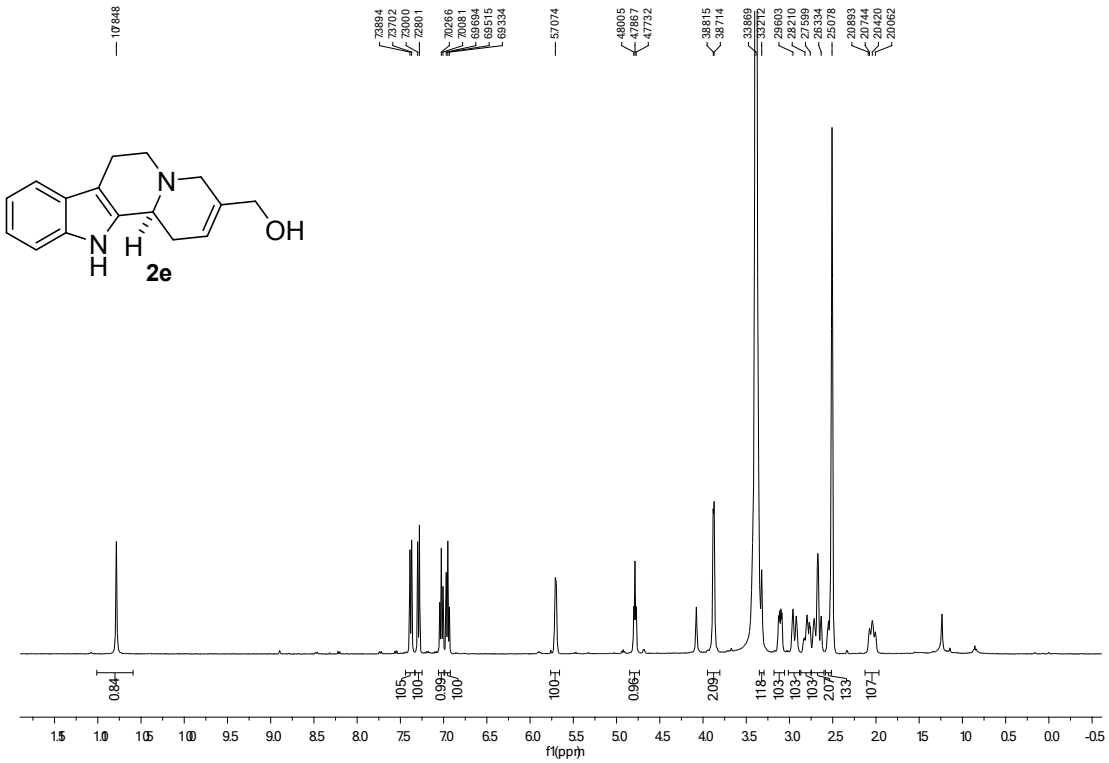
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N H
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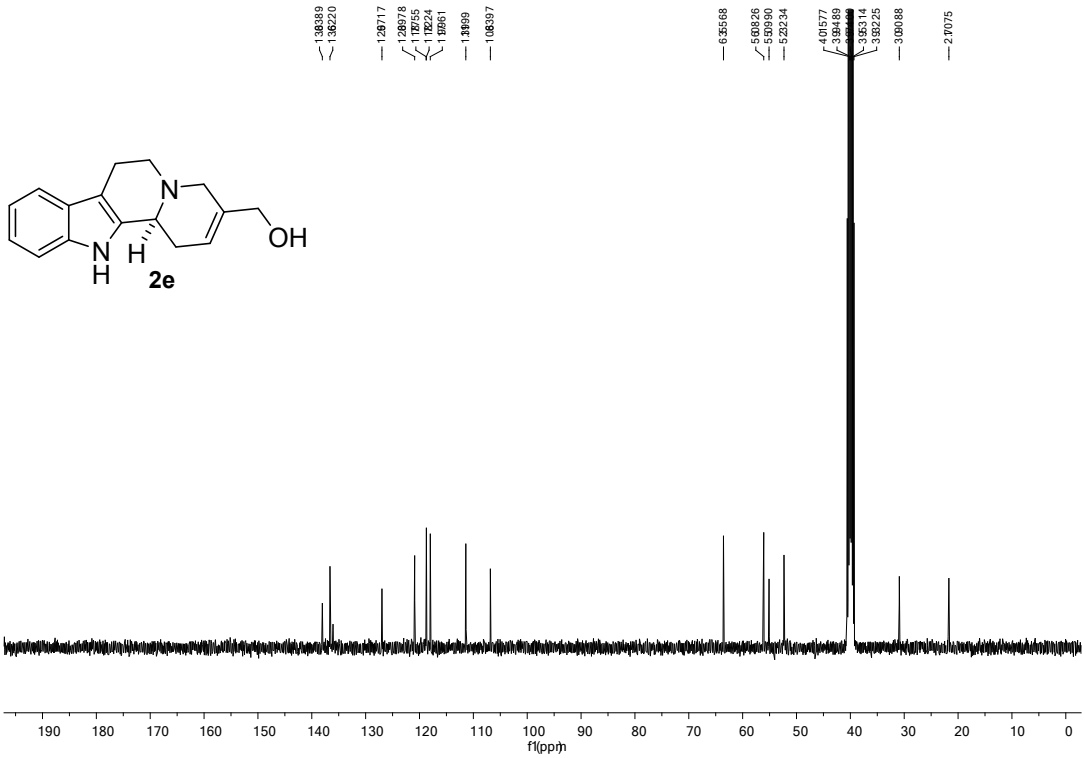
f1(ppm)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H
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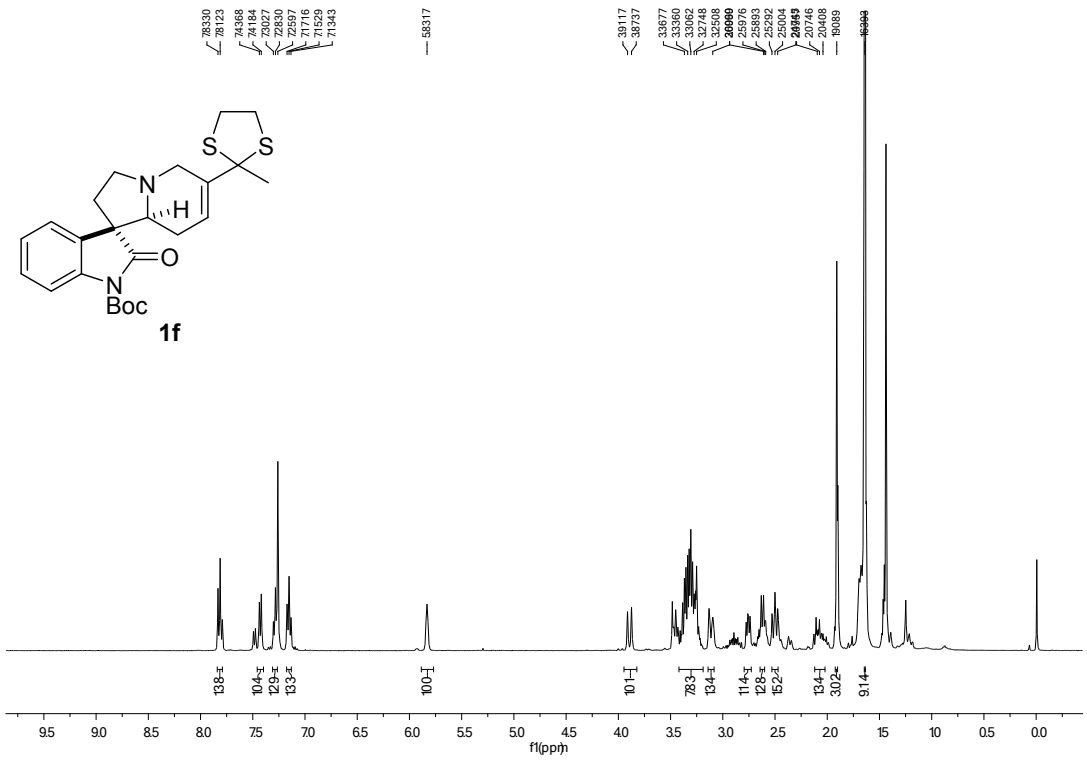
f1(ppm)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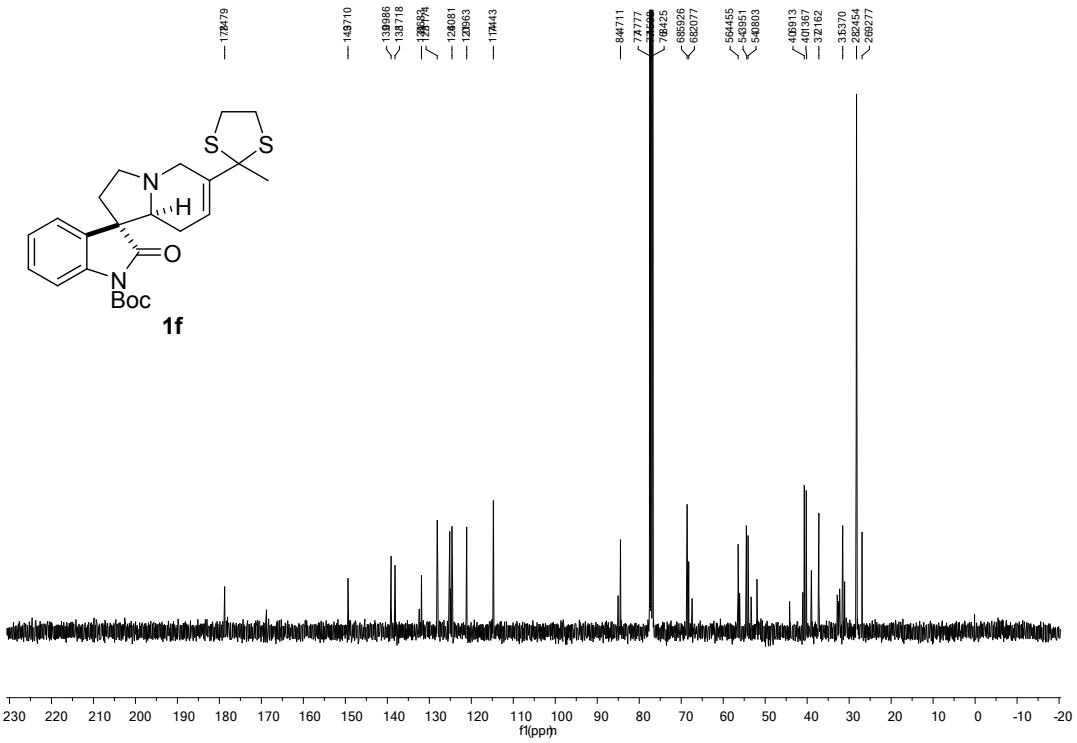
Boc
1f
f1(ppm)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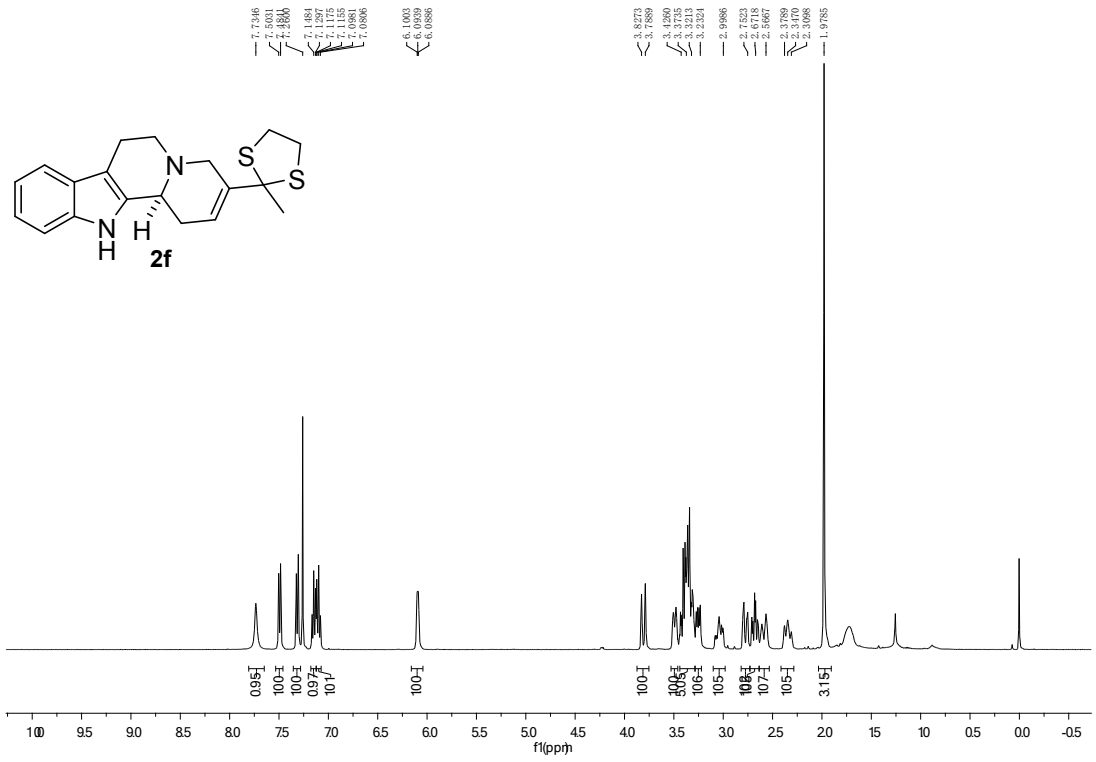
Boc
1f
f1(ppm)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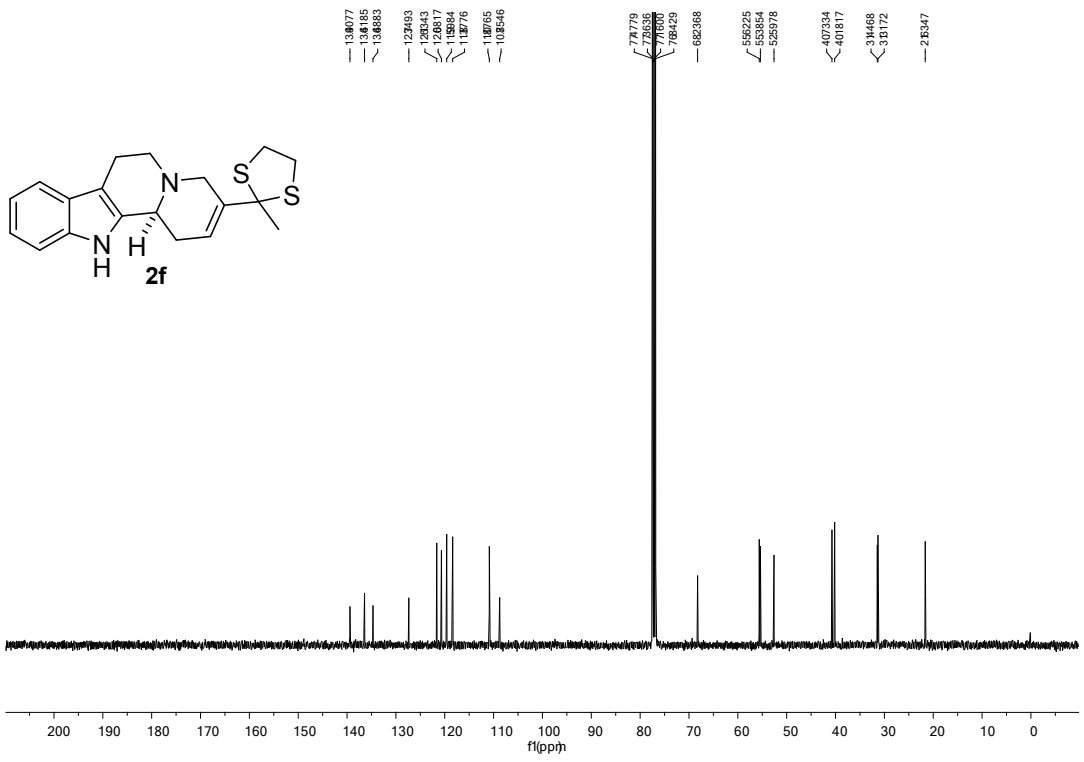
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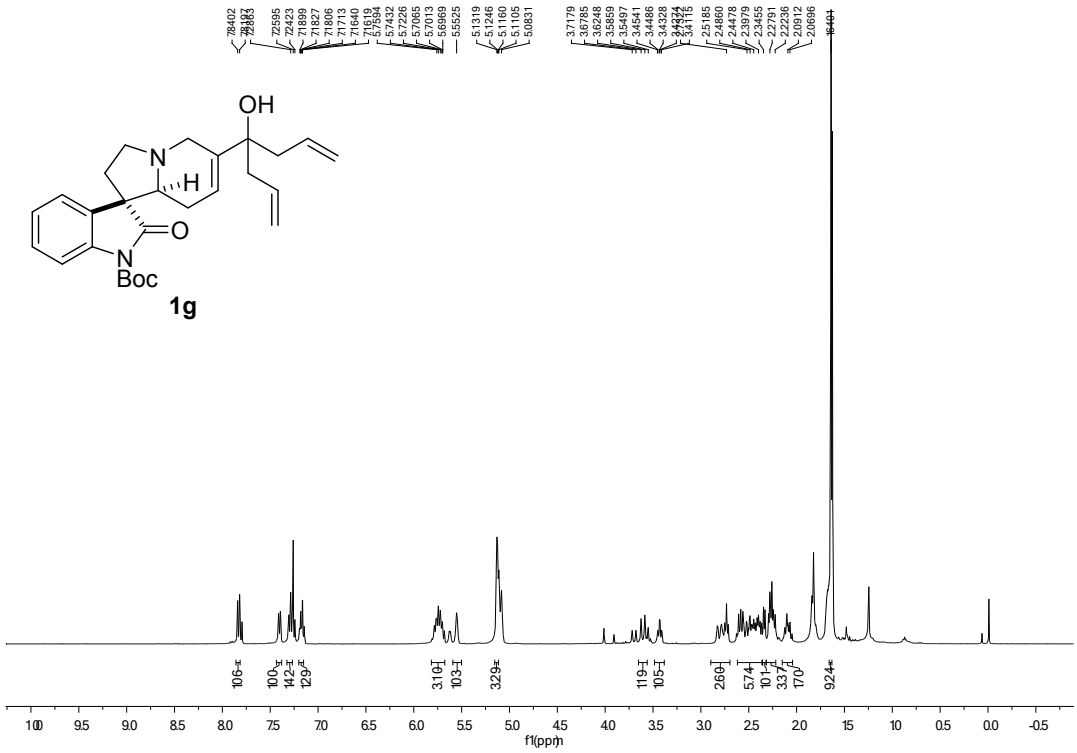
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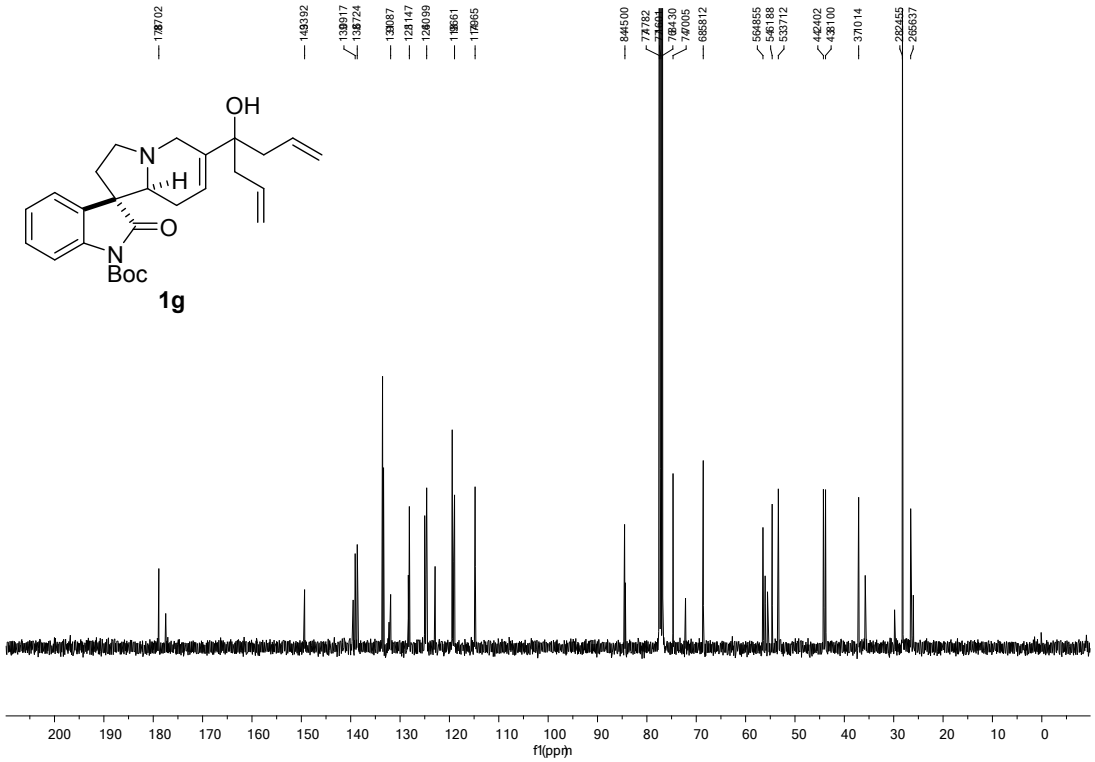
Boc
1g
f1(ppm)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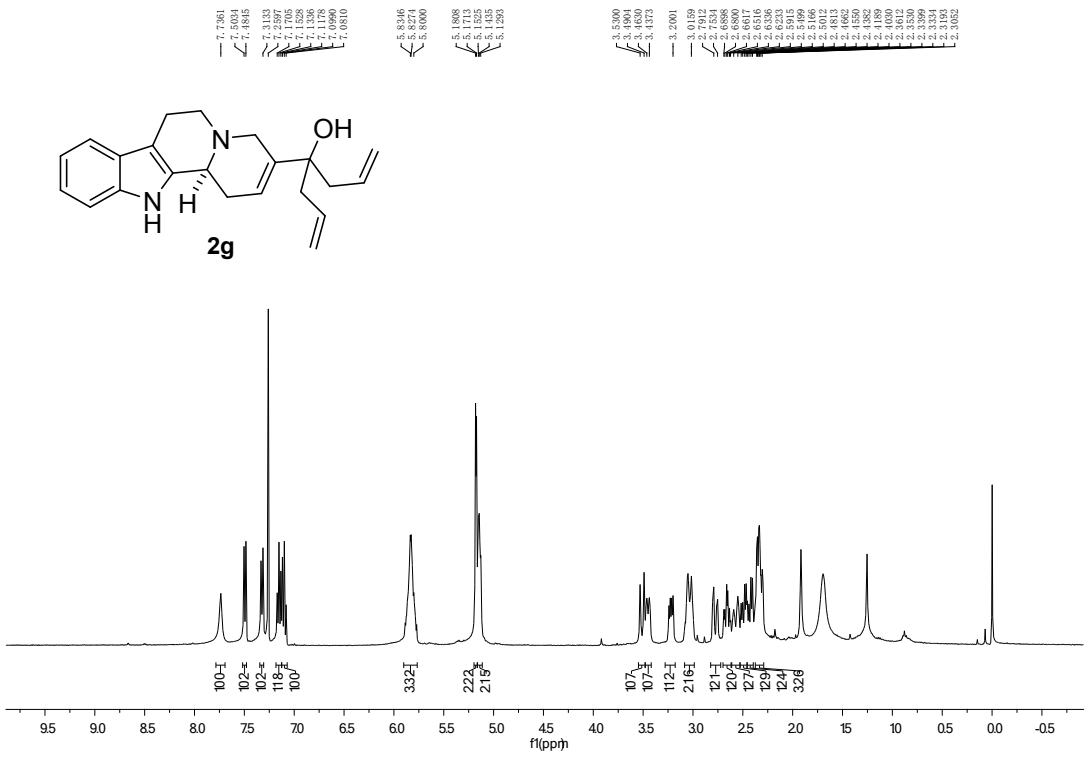
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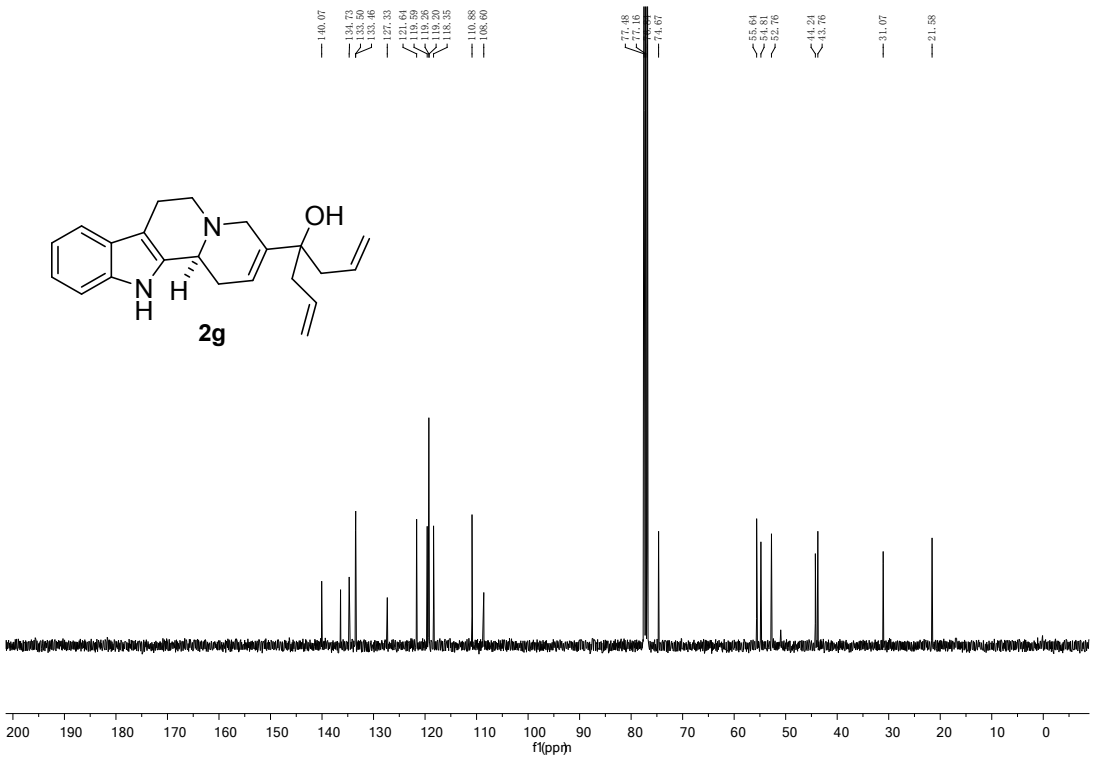
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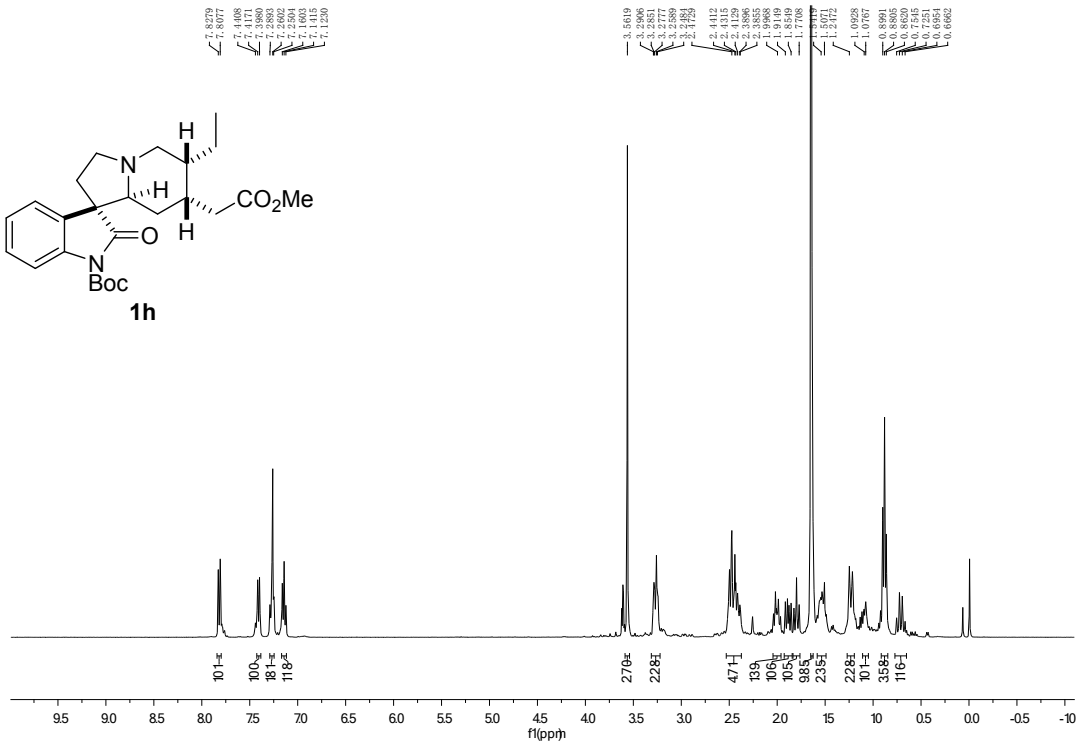
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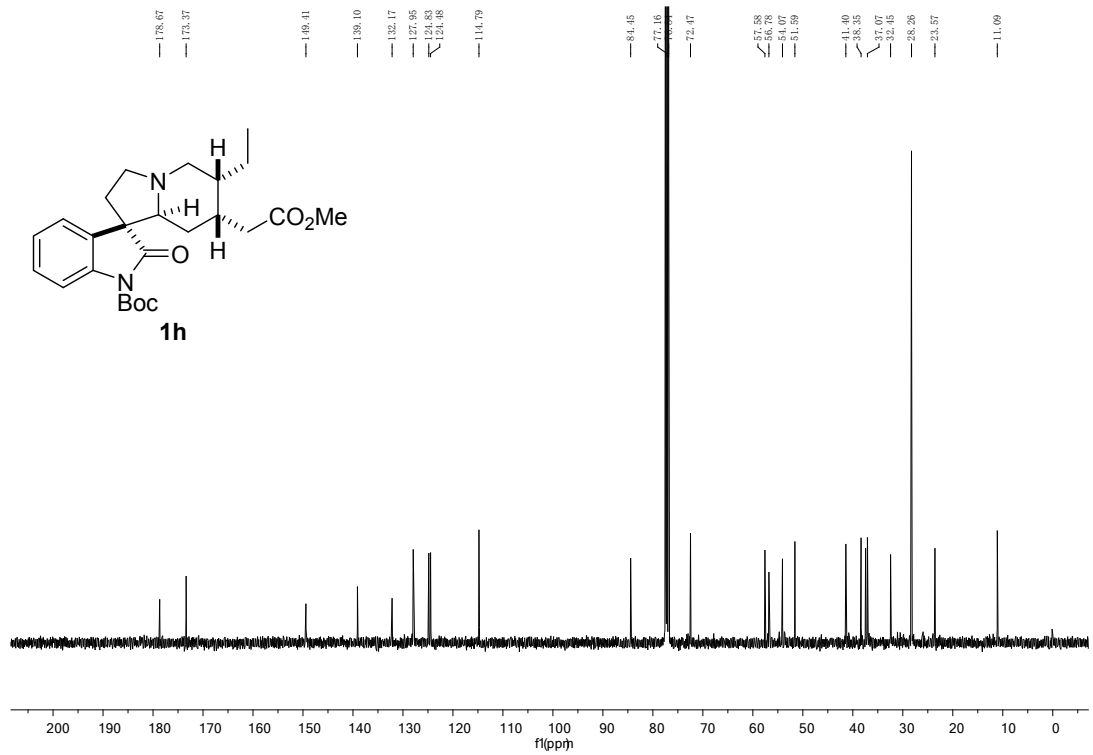
f1(ppm)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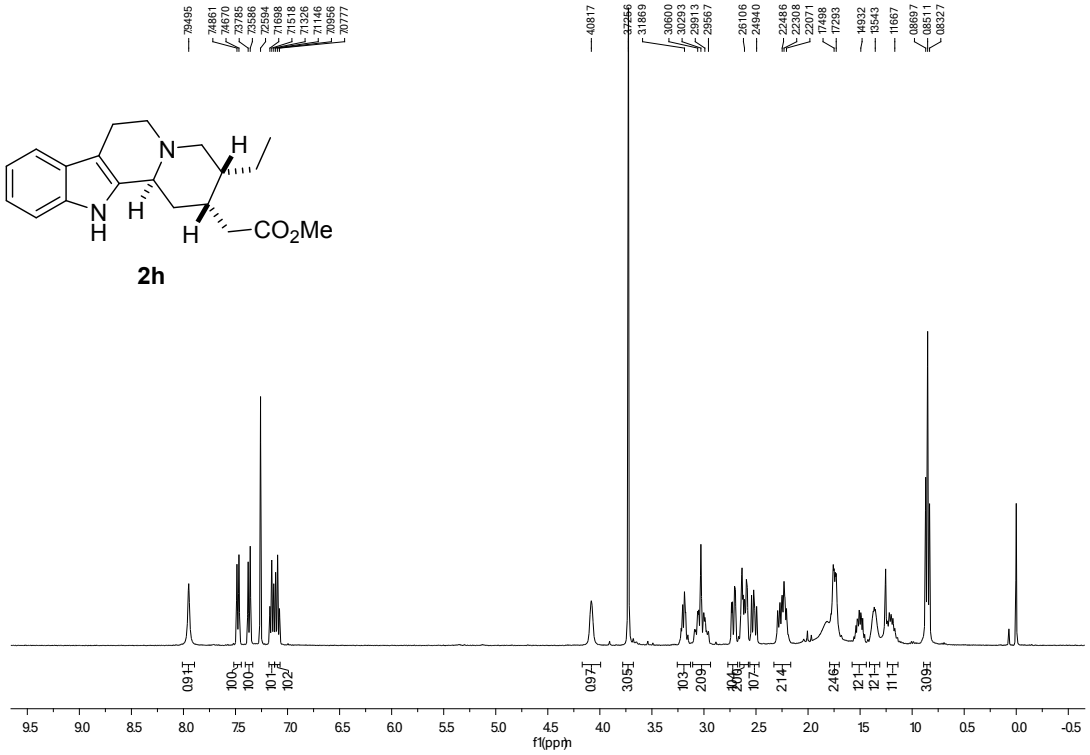
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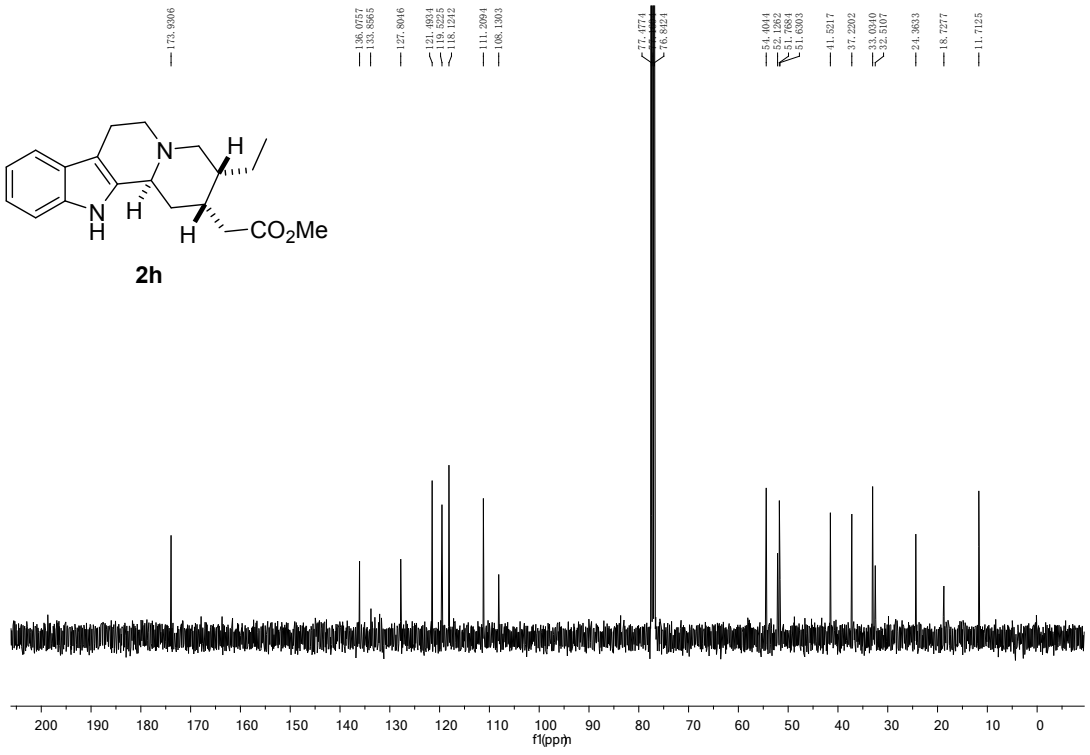
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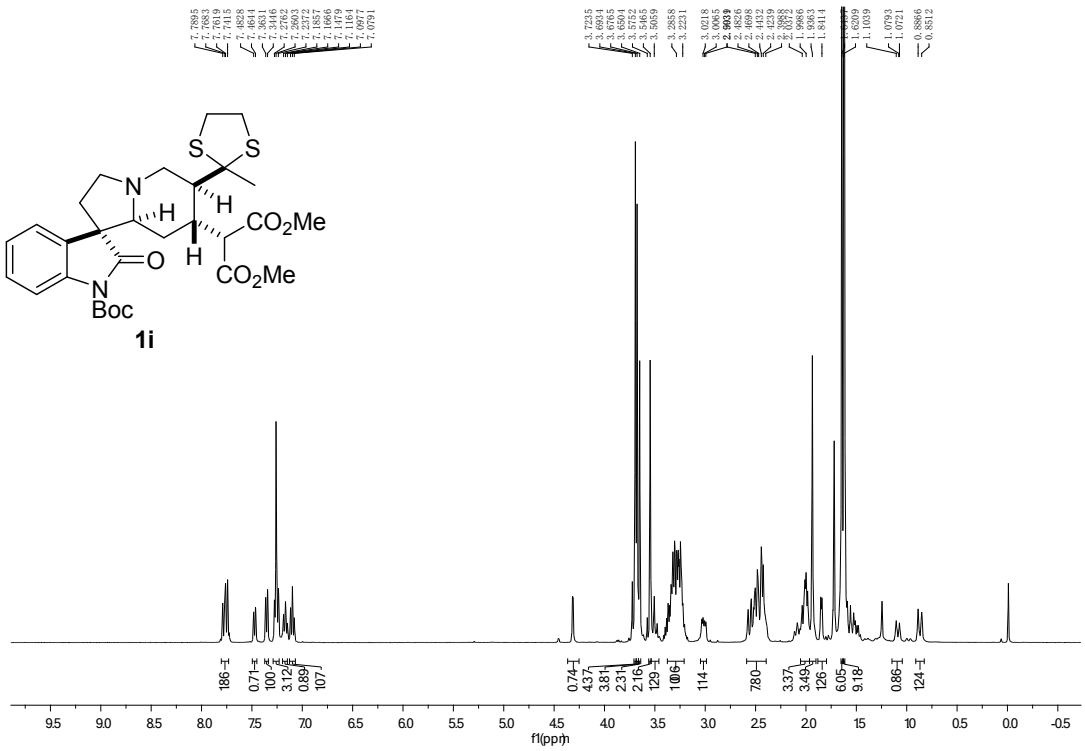
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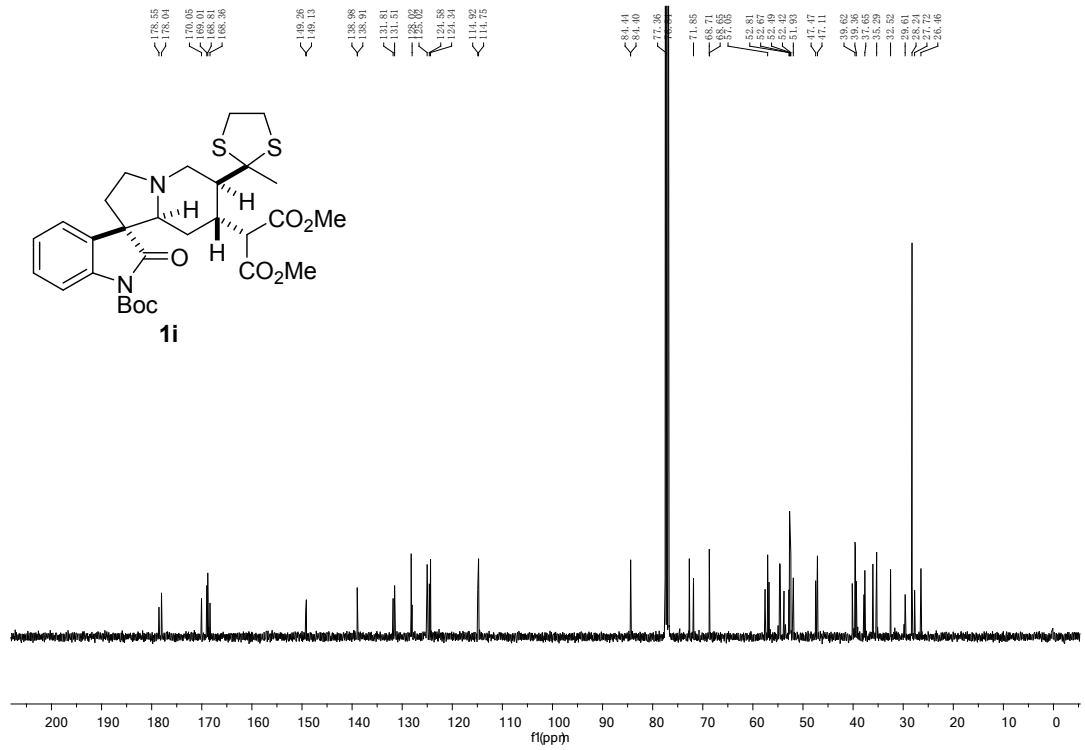
CO2Me
O
H
CO2Me
N
Boc
1i
f1(ppm)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O
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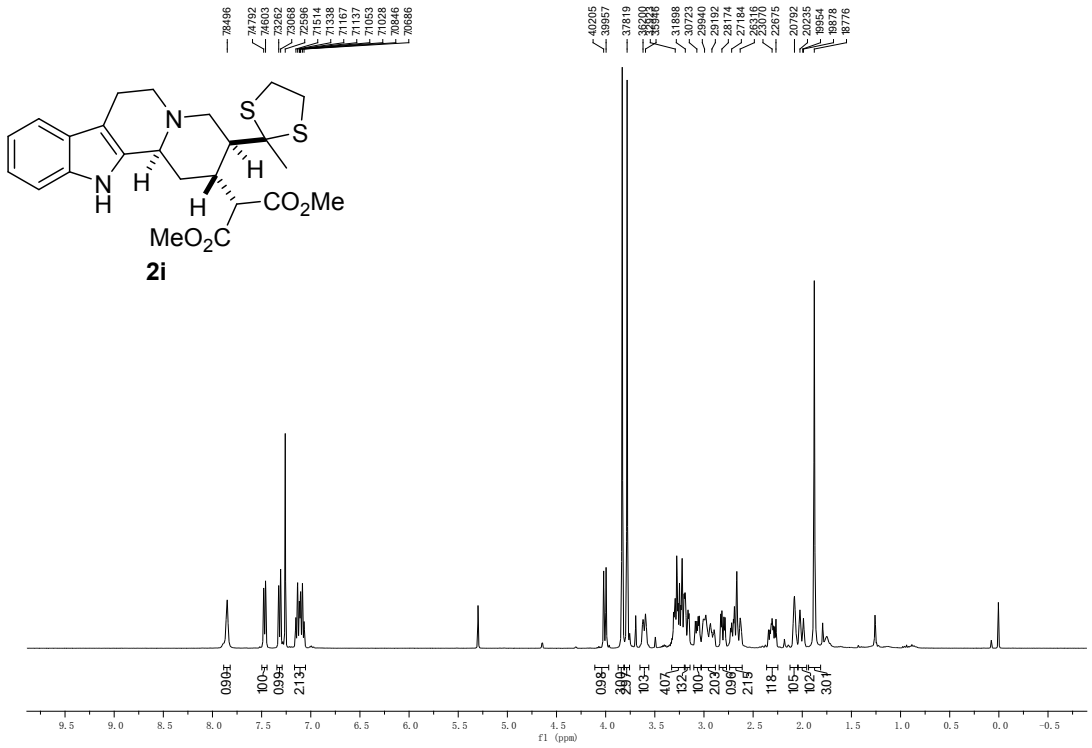
Boc
1i
f1(ppm)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H
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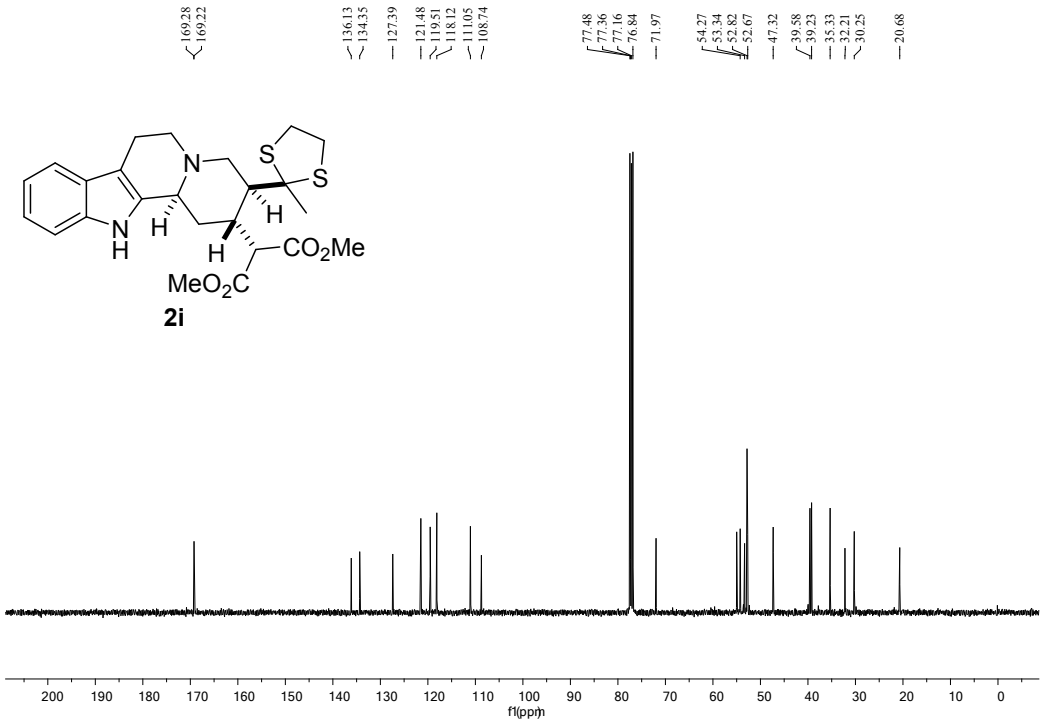
2i
f1 (ppm)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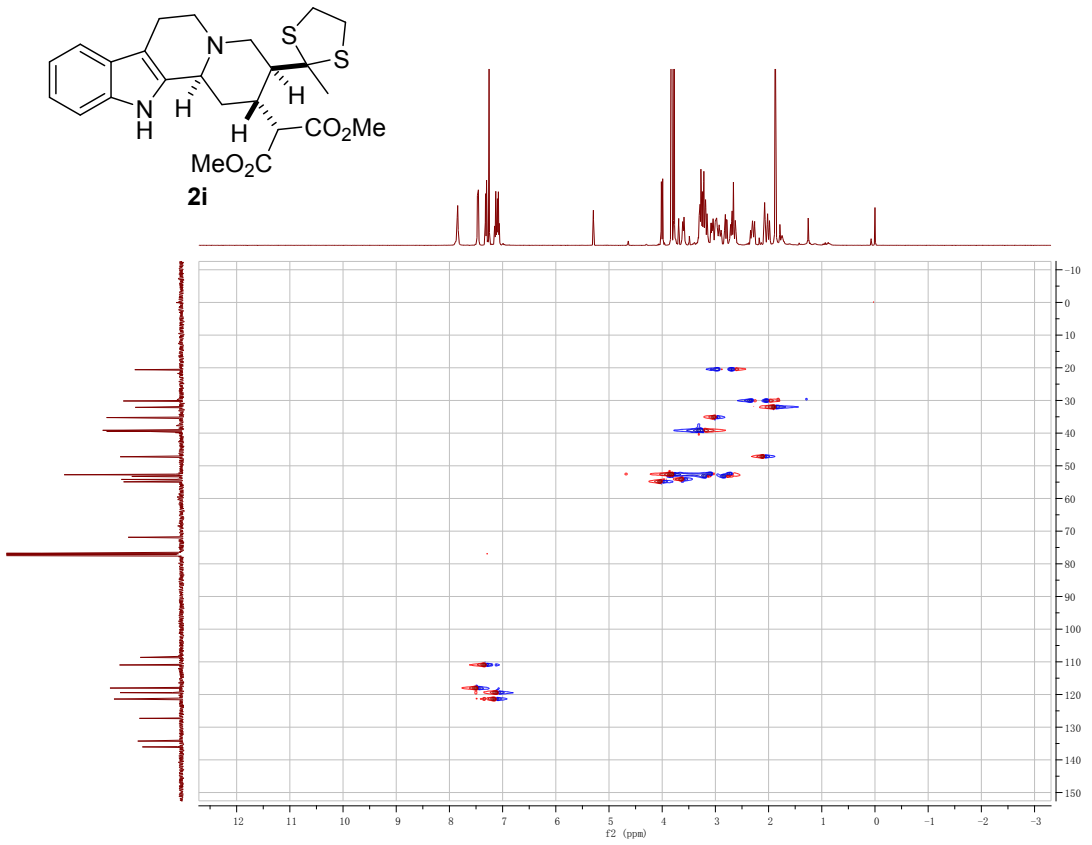
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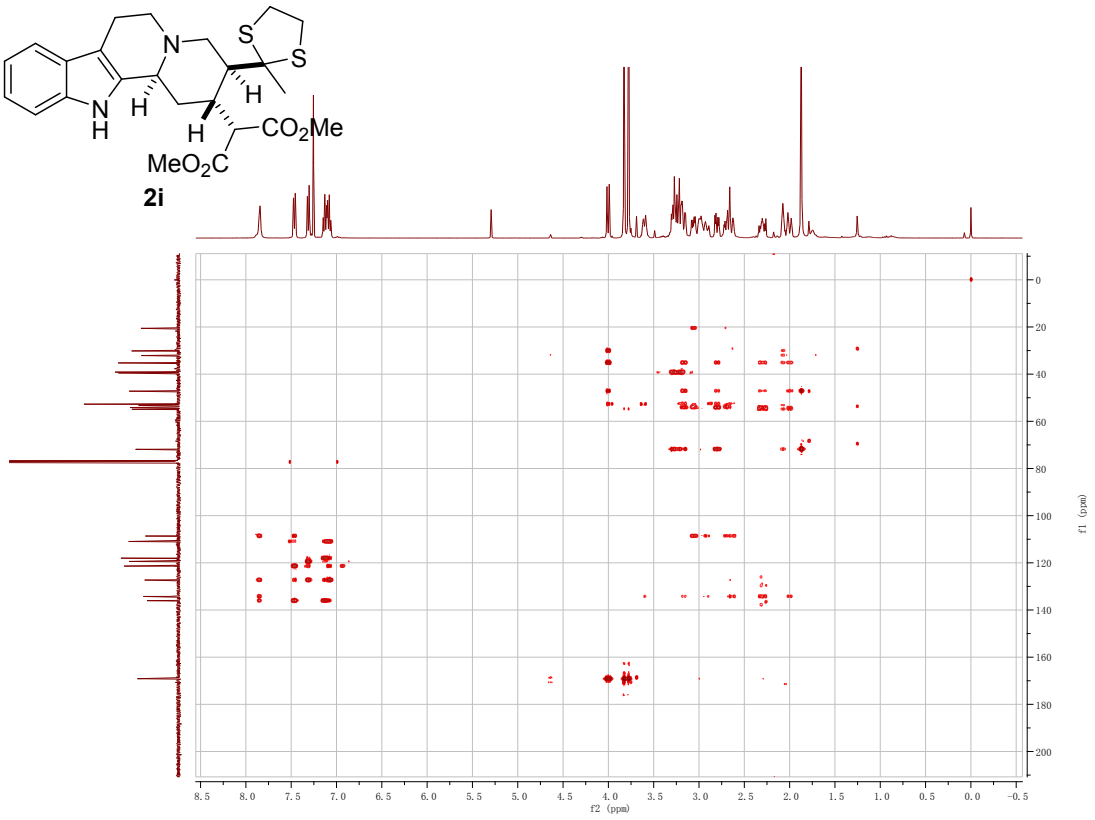
f2 (ppm)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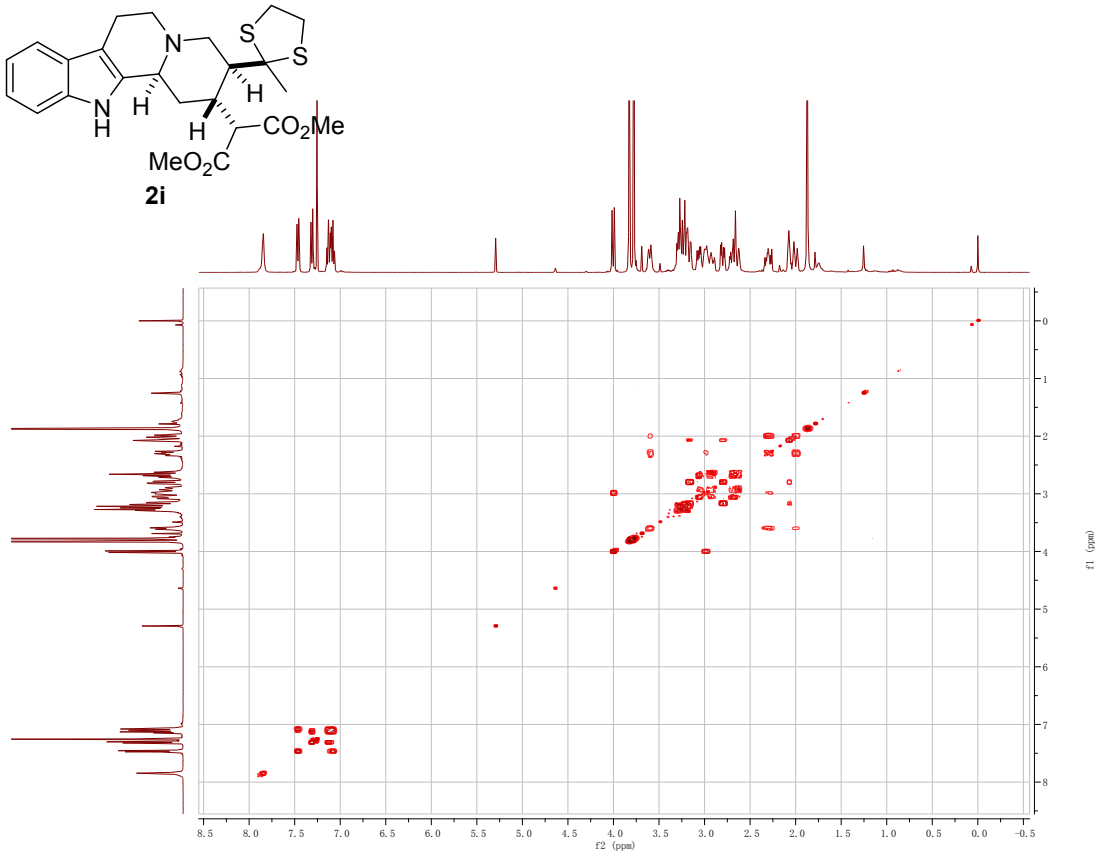
2i
f2 (ppm)
f1 (ppm)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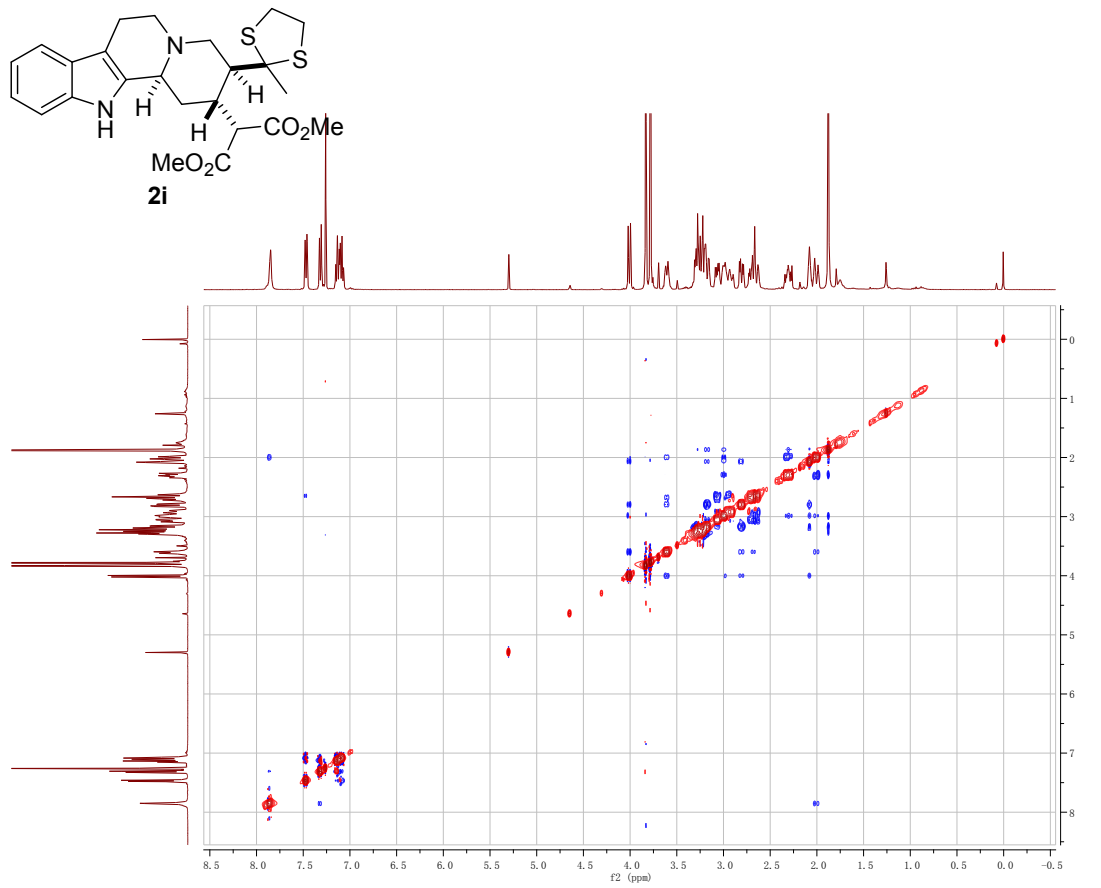
2i
f2 (ppm)
f1 (ppm)


N
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MeO2C
2i
f2 (ppm)