Supporting Information

Gold-Catalyzed Tandem Synthesis of Complex Bioactive Spiro-dipyrroloquinolines and Its Application in the One-step Synthesis of Incargranine B Aglycone and Seneciobipyrrolidine (I)

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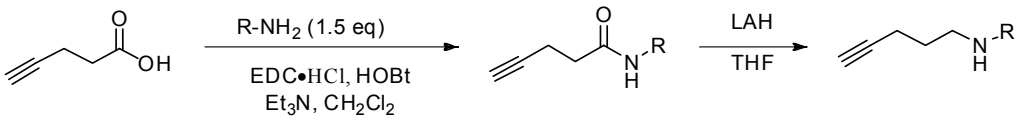
Experimental section

General methods. All manipulations with air-sensitive reagents were carried out under a dry argon atmosphere. Unless otherwise stated, all commercial reagents were used without additional purification. Solvents were dried using standard methods and distilled before use. The Au[P(*t*-Bu)$_2$(o-biphenyl)]Cl[S1] catalyst were prepared following literature procedures. Analytical thin layer chromatography (TLC) was performed on percolated silica gel 60 F254 plates. Visualization on TLC was achieved by use of UV light (254 nm) or iodine. NMR spectra were recorded on a Bruker DPX-300/400 spectrometer at 300/400 MHz for ^{1}H NMR, 75/100 MHz for ^{13}C NMR in and 282 MHz for ^{19}F NMR in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; m, multiplet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Mass spectra were determined on a Finnigan MAT 95 mass spectrometer.

Synthesis of starting materials

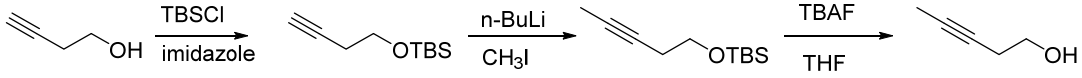
Typical experimental procedures for the syntheses of aminoalkyne substrates (1a-1i and 1m) *[S2]*



To a solution of EDC·HCl (2.30 g, 12.0 mmol) and HOBt (1.50 g, 11.2 mmol) in DCM (20 mL) was added a solution of 4-pentynoic acid (0.78 g, 8.0 mmol) in DCM (10 mL) followed by addition of a solution of amines (12.0 mmol) in DCM (10 mL). The mixture was cooled to 0 ^{o}C and Et_3N (1.2 mL, 12.0 mmol) was added dropwise. After being slowly warmed to room temperature and stirred overnight, the reaction mixture was diluted with DCM, washed successively with water, aqueous HCl 5%, saturated $NaHCO_3$, and brine, and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography on silica gel with EtOAc/Petroleum ether (1/2) as eluent afforded substituted 4-pentynoylamides in good to excellent yields.

To a solution of substituted 4-pentynoylamide (4.0 mmol) in THF (30 mL) was slowly added lithium aluminum hydride (0.62 g, 16.0 mmol) at 0 ^{o}C. The reaction mixture was slowly warmed to room temperature and stirred for 24-30 h, and then quenched with Baechströms reagent ($Na_2SO_4·10H_2O$) and stirred for 30 min. After filtration, the filtrate was evaporated and chromatographed on silica gel column with EtOAc/Petroleum ether (1/20) as eluent to afford substituted aminoalkynes in good to excellent yields.

The experimental procedures for the syntheses of pent-3-yn-1-ol:



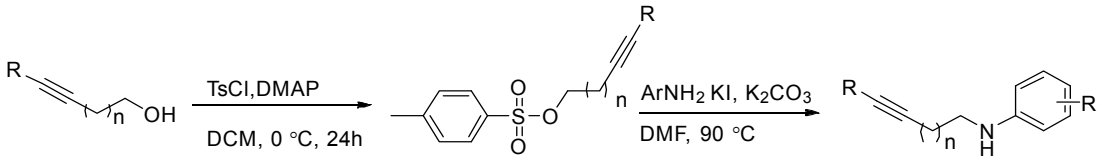
To a solution of 3-butyn-1-ol (9.26 g, 132.1 mmol) and imidazole (21.59 g, 317.1 mmol) in DCM (200 mL) was added tert-butyl-dimethyl-silyl chloride (TBSCl) (23.90 g, 158.5 mmol). After stirring at ambient temperature for 3 h, the reaction mixture was filtered through a pad of silica and concentrated under reduced pressure.

Purification by flash column chromatography afforded the desired compounds afforded the alkyne (24.62 g, 100%) as a clear colorless oil.

A solution of the silyl ether prepared above (8.8 g, 48 mmol) in 200 ml tetrahydrofuran was cooled under an inert atmosphere to -78°C. and a solution of n-BuLi (20 ml, 50 mmol, 2.5 M in hexanes) was added over 15 minutes by syringe. The solution was stirred at -78°C for 1.5 hours, at which time iodomethane (20.31g, 144 mmol) was added dropwise and the solution allowed to warm to room temperature overnight. Then, 1 N aqueous ammonium chloride solution (20 mL) was added, the tetrahydrofuran removed in vacuo, and the aqueous extracted twice with diethylether. The ether solution was washed twice with water, then brine, and dried over magnesium sulfate. The solvent was removed in vacuo to give the product, which was used without further purification.

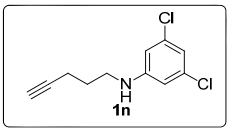
To the above obtained product (1.98 g, 10 mmol) in wet THF (30mL) at room temperature was added TBAF·$3H_2O$ (3.15g, 10mmol). The reaction was stirred until TLC analysis showed that desilylation had taken place. AcOEt (50 mL) and sat. aq NH_4Cl were added. The organic phase was separated, washed with sat. aq NaCl, and dried over $MgSO_4$. Purification by flash column chromatography afforded the desired compounds afforded the **pent-3-yn-1-ol** as a clear colorless oil.

The experimental procedures for the syntheses of aminoalkynes (1n, 1o, 1p, 3, 5 and 7): *[S3] [S4]*



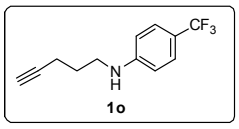
To a solution of alcohol (15.8 mmol), triethylamine (2.70 mL, 19.0 mmol), and 4-(dimethylamino) pyridine (39 mg, 0.3 mmol) in DCM (53 mL) at 0 ^oC was added *p*-toluenesulfonyl chloride (3.16 g, 16.6 mmol) in three portions. The reaction mixture was brought to rt and stirred for 15 h. Aq. NaOH (1 N, 30 mL) was added, and the mixture was vigorously stirred for 15 min at rt. The usual workup (DCM, brine) gave *p*-toluenesulfonate derivatives in excellent yields as yellowish oil.

To a solution of aniline (3.0 mmol, 1.5 eq), the above obtained *p*-toluenesulfonate derivatives (2.0 mmol, 1 eq) and KI (33 mg, 0.2 mmol, 0.1 eq.) in DMF (4 mL) was added K_2CO_3 (0.82 g, 6.0 mmol, 3 eq.). The mixture was heated to 90 °C. After the complete consumption of the *p*-toluenesulfonate derivatives (TLC), the reaction mixture was cooled to room temperature, quenched with a saturated solution of NH_4Cl, extracted with AcOEt, washed with small amounts of water, dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography afforded the desired compounds in moderate yields as a yellow oil.



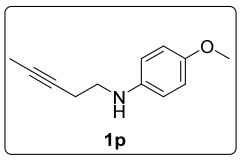
1n

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (t, *J* = 1.6 Hz, 1H), 6.46 (d, *J* = 1.6 Hz, 2H), 3.94 (s, 1H), 3.24 (q, *J* = 6.4 Hz, 2H), 2.31 (td, *J* = 6.8 and 2.4 Hz, 2H), 2.03 (t, *J* = 2.4 Hz, 1H), 1.82 (p, *J* = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-d) δ 149.6, 135.4, 116.9, 110.7, 83.2, 69.4, 42.4, 27.4, 16.0.



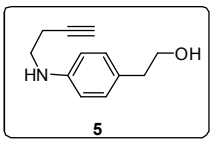
1o

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.4 and 1.2 Hz, 2H), 6.61 (dd, *J* = 8.4 and 1.2 Hz, 2H), 4.10 (s, 1H), 3.31 (t, *J* = 6.8 Hz, 2H), 2.32 (td, *J* = 6.8 and 2.8 Hz, 2H), 2.02 (t, *J* = 2.8 Hz, 1H), 1.85 (p, *J* = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.5, 126.5 (q, *J* = 3.7 Hz), 125.0 (q, *J* = 268.7 Hz), 118.5 (q, *J* = 32.6 Hz), 111.7, 83.3, 69.2, 42.2, 27.5, 16.0.



1p

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, *J* = 8.5 Hz, 2H), 6.63 (d, *J* = 8.5 Hz, 2H), 3.75 (s, 3H), 3.20 (t, *J* = 6.5 Hz, 2H), 2.46 – 2.39 (m, 2H), 1.81 (t, *J* = 2.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.44, 141.99, 114.93, 114.70, 77.43, 76.48, 55.81, 44.07, 19.48, 3.54.



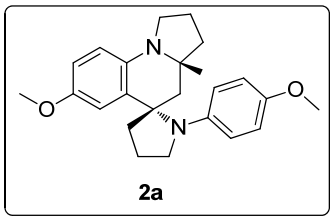
5

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.4 Hz, 2H), 6.60 (d, *J* = 8.4 Hz, 2H), 3.93 (br s, 1H), 3.75 (t, *J* = 6.8 Hz, 2H), 3.28 (t, *J* = 6.8 Hz, 2H), 2.73 (t, *J* = 6.8 Hz, 2H), 2.47 (td, *J* = 6.8 Hz and 2.6 Hz, 2H), 2.26 (br s, 1H), 2.06 (t, *J* = 2.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9, 129.7, 127.5, 113.3, 81.7, 70.0, 63.6, 42.5, 38.0, 18.9. HRMS (ESI) [M+H] calculated for $[C_{12}H_{16}NO]^+$ 190.1232, found 190.1228.

Aminoalkynes 1j-1L were prepared following literature procedures. *[S2]*

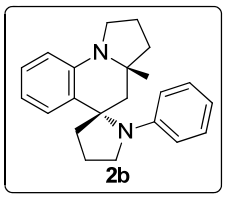
General procedure for gold(III)-catalyzed synthesis of azaspiro polycycles:

To a 25 mL Schlenk tube equipped with a magnetic stir bar was added 100 mg ultra-dried 4Å molecular sieve. Then potassium tetrachloroaurate (III) (38 mg, 0.1 mmol) was added under argon atmosphere followed by addition of anhydrous ethanol (1 mL) under argon atmosphere. Finally aminoalkyne (1.0 mmol) was added to the reaction mixture and then stirred at the corresponding temperature as shown in Scheme 2. After reaction completion (monitored by TLC), the reaction mixture was filtered through celite. Then the solvent was removed in *vacuo*, and the residue was purified by silica gel column chromatography (EtOAc/Petroleum ether = 1/20 – 1/40) to give the desired products. (Compounds **2a-2g** and **2i-2l).** For compound **2h**, the reaction mixture was filtered through powdered activated carbon without further purification to obtain pure product **2h**.



2a

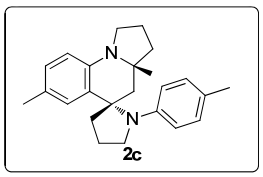
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 - 6.67 (m, 2H), 6.66 - 6.62 (m, 1H), 6.39 (d, *J* = 8.4 Hz, 1H), 6.31 - 6.29 (m, 2H), 3.68 (s, 3H), 3.64 (s, 3H), 3.66 - 3.58 (m, 1H), 3.51 - 3.37 (m, 1H), 3.27 (q, *J* = 7.8 Hz, 1H), 2.53 - 2.49 (m, 1H), 2.42 - 2.28 (m, 2H), 2.24 - 2.15 (m, 1H), 2.13 - 2.03 (m, 3H), 1.92 - 1.78 (m, 2H), 1.68 - 1.66 (m, 1H), 1.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 150.5, 139.8, 138.7, 129.2, 114.7, 114.5, 114.0, 113.0, 112.4, 63.3, 59.8, 55.8, 49.7, 46.3, 46.2, 41.9, 40.8, 29.9, 22.8, 21.8, 21.5. HRMS (ESI) [M+H] calculated for $[C_{24}H_{31}N_2O_2]^+$ 379.2386, found 379.2380.



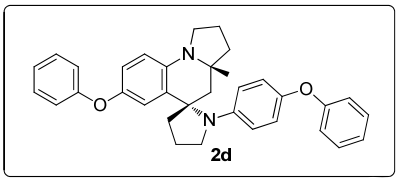
2b

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (t, *J* = 8.0 Hz, 1H), 6.95 - 6.91 (m, 3H), 6.46 - 6.42 (m, 2H), 6.44 (d, *J* = 8.0 Hz, 1H), 6.32 (d, *J*=8.0 Hz, 2H), 3.59 - 3.54 (m, 1H), 3.48 - 3.44 (m, 1H), 3.41 - 3.35 (m, 1H), 3.28 - 3.23 (m, 1H), 2.48 - 2.44 (m, 1H), 2.37 (d, *J* = 13.6 Hz, 1H), 2.28 - 2.24 (m, 1H), 2.24 - 2.20 (m, 1H), 2.12 - 1.99 (m, 4H), 1.83 - 1.76 (m, 2H), 1.64 - 1.59 (m, 1H), 1.08(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 143.6, 128.4, 127.6, 127.2, 126.8, 116.2, 115.0, 113.6, 111.5, 63.1, 59.6, 49.3, 46.0, 45.6, 41.4, 40.8, 22.37,

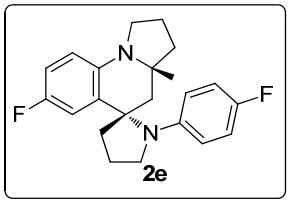
22.2, 21.4. HRMS (ESI) [M+H] calculated for $[C_{22}H_{27}N_2]^+$ 319.2169, found 319.2164.



^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 - 6.81 (m, 4H), 6.37 (d, *J* = 8.4 Hz, 1H), 6.28 (d, *J* = 8.4 Hz, 2H), 3.66 - 3.62 (m, 1H), 3.52 - 3.47 (m, 1H), 3.46 - 3.38 (m, 1H), 3.32 - 3.28 (m, 1H), 2.52-2.47 (m, 1H), 2.43 (d, *J* = 13.6 Hz, 1H), 2.39 - 2.30 (m, 1H), 2.26 - 2.17 (m, 1H), 2.16 (s, 3H), 2.12 (s, 3H), 2.11 - 2.04 (m, 3H), 1.88 - 1.84 (m, 1H), 1.79 (d, *J* = 13.6 Hz, 1H), 1.70 - 1.65 (m, 1H), 1.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 141.4, 129.0, 128.2, 127.6, 127.2, 125.0, 123.8, 113.7, 111.6, 62.8, 59.5, 49.3, 46.1, 45.7, 41.2, 40.7, 22.4, 21.8, 21.4, 20.7, 20.1. HRMS (ESI) [M+H] calculated for $[C_{24}H_{31}N_2]^+$ 347.2487, found 347.2482.

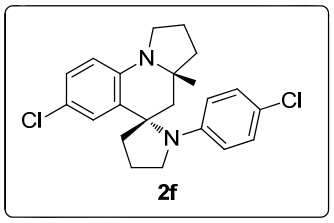


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 8.8, 7.6 Hz, 2H), 7.13 (dd, *J* = 8.8, 7.6 Hz, 2H), 6.99 - 6.95 (m, 1H), 6.91 - 6.88 (m, 3H), 6.82 - 6.75 (m, 3H), 6.74 (d, *J* = 2.8 Hz, 1H), 6.58 (dt, *J* = 8.8 and 0.8 Hz, 2H), 6.40 (d, *J* = 8.8 Hz, 1H), 6.31 (d, *J* = 8.8 Hz, 2H), 3.56 - 3.41 (m, 3H), 3.32 - 3.30 (m, 1H), 2.63 - 2.54 (m, 1H), 2.40 (d, *J* = 13.6 Hz, 1H), 2.34 - 2.24 (m, 1H), 2.15 - 2.08 (m, 4H), 2.00 - 1.87 (m, 2H), 1.75 - 1.72 (m, 1H), 1.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 159.4, 146.2, 146.1, 141.7, 141.4, 129.5, 128.3, 121.8, 121.4, 120.5, 120.3, 117.3, 116.2, 114.5, 112.6, 63.5, 59.9, 49.7, 45.9, 45.8, 42.5, 40.9, 22.5, 21.8, 21.4. HRMS (ESI) [M+H] calculated for $[C_{34}H_{35}N_2O_2]^+$ 503.2693, found 503.2693.



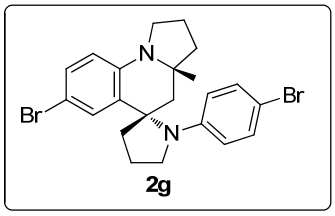
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 - 6.69 (m, 4H), 6.34 (dd, *J* = 8.8 and 4.8 Hz, 1H), 6.27 - 6.20 (m, 2H), 3.62 - 3.60 (m, 1H), 3.51 - 3.38 (m, 2H), 3.31 - 3.23 (m, 1H), 2.53 - 2.51 (m, 1H), 2.37 - 2.25 (m, 2H), 2.18 - 2.16 (m, 1H), 2.13 - 2.04 (m, 3H), 1.93 -1.86 (m, 1H), 1.84 (d, *J* = 13.6 Hz, 1H), 1.73 - 1.62 (m, 1H), 1.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5 (d, J_{CF} = 232.1 Hz), 154.8 (d, J_{CF} = 232.6 Hz), 141.4, 140.5, 128.7 (d, J_{CF} = 5.5 Hz), 115.1 (d, J_{CF} = 21.5 Hz), 114.3 (d, J_{CF} = 22.2 Hz), 114.3 (d, J_{CF} = 7.1 Hz), 113.8 (d, J_{CF}= 22.6 Hz), 112.4 (d, J_{CF} = 7.1 Hz), 63.3,

59.9, 49.8, 46.2, 46.0, 41.7, 40.8, 22.6, 21.7, 21.4. ^{19}F NMR (375 MHz, $CDCl_3$) δ -128.6, -130.9. HRMS (ESI) [M+H] calculated for $[C_{22}H_{25}N_2F_2]^+$ 355.1980, found 355.1973.



2f

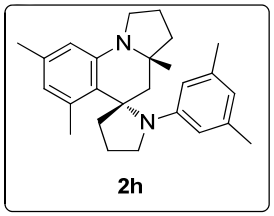
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 - 6.92 (m, 3H), 6.36 (d, *J* = 8.8 Hz, 1H), 6.24 (d, *J* = 8.8 Hz, 2H), 3.57 - 3.52 (m, 1H), 3.53 - 3.37 (m, 2H), 3.29 (dt, *J* = 9.6 and 6.8 Hz, 1H), 2.54 (ddd, *J* = 12.3, 6.6 and 5.0 Hz, 1H), 2.38 - 2.26 (m, 2H), 2.23 - 2.16 (m, 1H), 2.16 - 2.04 (m, 3H), 1.95 - 1.87 (m, 1H), 1.83 (d, *J* = 13.5 Hz, 1H), 1.67 (q, *J* = 10.6 Hz, 1H), 1.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 142.19, 128.3, 128.2, 127.7, 126.7, 121.0, 120.3, 114.7, 112.8, 63.0, 59.8, 49.4, 46.0, 45.6, 41.1, 40.6, 22.3, 21.9, 21.2. HRMS (ESI) [M+H] calculated for $[C_{22}H_{25}N_2Cl_2]^+$ 387.1389, found 387.1385.



2g

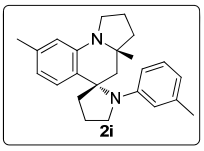
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 7.07 (d, *J* = 2.4 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 1H), 6.18 (d, *J* = 8.8 Hz, 1H), 3.62-3.60 (m, 1H), 3.49 - 3.43 (m, 1H), 3.43 - 3.37 (m, 1H), 3.29 - 3.28 (m, 1H), 2.52 - 2.50 (m, 1H), 2.36 - 2.26 (m, 2H), 2.20 - 2.07 (m, 4H), 1.88 - 1.87 (m, 1H), 1.81 (d, *J* = 13.6 Hz), 1.67 - 1.65 (m, 1H), 1.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 142.6, 131.2, 130.6, 129.5, 128.6, 115.4, 113.4, 108.3, 107.6, 63.0, 59.7, 49.4, 46.0, 45.6, 40.9, 40.6, 22.3, 22.0, 21.2.

HRMS (ESI) [M+H] calculated for $[C_{22}H_{25}N_2Br_2]^+$ 475.0379, found 475.0379.

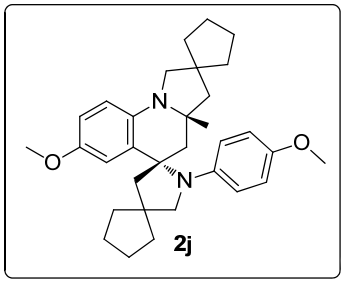


2h

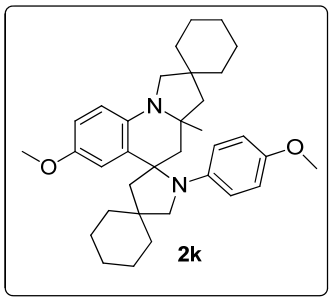
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (s, 3H), 6.00 (s, 2H), 3.58 - 3.32 (m, 4H), 2.57 - 2.39 (m, 3H), 2.28 (d, *J* = 14.4 Hz, 2H), 2.21 (s, 3H), 2.19 - 2.13 (m, 2H), 2.13 - 2.06 (m, 6H), 2.02 (s, 3H), 1.95 - 1.85 (m, 2H), 1.76 - 1.66 (m, 1H), 1.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 144.4, 137.8, 137.0, 136.4, 122.9, 120.6, 116.9, 111.4, 110.6, 112.0, 63.5, 58.9, 48.2, 46.6, 42.8, 41.2, 39.7, 21.9, 21.9, 21.8, 21.7, 21.5, 21.3. HRMS (ESI) [M+H] calculated for $[C_{26}H_{35}N_2]^+$ 375.2800, found 375.2794.



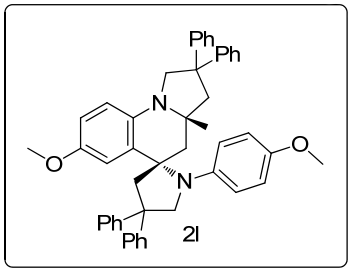
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 - 7.04 (m, 1H), 7.02 - 7.00 (m, 1H), 6.54 - 6.50 (m, 2H), 6.42 (s, 2H), 6.25 - 6.233 (m, 1H), 3.79 - 3.75 (m, 1H),3.68 - 3.65 (m, 1H),3.60 - 3.57 (m, 1H), 3.52 - 3.47 (m, 1H), 2.68 - 2.63 (m, 1H), 2.60 (d, *J* = 13.6 Hz, 1H), 2.49 - 2.41 (m, 2H), 2.41 (s, 3H), 2.33 (s, 3H), 2.30 - 2.19 (m, 3H), 2.03 - 1.96 (m, 2H), 1.87 - 1.82 (m, 2H), 1.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 143.4, 137.7, 137.0, 128.1, 126.9, 124.0, 117.2, 115.7, 114.2, 112.0, 111.8, 62.7, 59.4, 49.1, 45.8, 45.5, 41.4, 40.7, 22.2, 22.0, 21.8, 21.4, 21.3. HRMS (ESI) [M+H] calculated for $[C_{24}H_{31}N_2]^+$ 347.2482, found 347.2481.



^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (d, *J* = 2.8 Hz, 1H), 6.64 - 6.60 (m, 3H), 6.39 (d, *J* = 8.8 Hz, 2H), 6.31 (d, *J* = 8.8 Hz, 1H), 3.67 (s, 3H), 3.62 (s, 3H), 3.34 (dd, *J* = 12.8 and 8.8 Hz, 2H), 3.28 (d, *J* = 9.2 Hz, 1H), 3.28 (d, *J* = 9.6 Hz, 1H). 2.55 (d, *J* = 13.2 Hz, 1H), 1.76 (m, 19H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 150.5, 140.0, 139.1, 130.8, 114.7, 114.3, 114.2, 112.7, 112.5, 64.3, 62.1, 60.5, 59.1, 58.8, 55.7, 55.6, 54.1, 48.3, 47.6, 43.1, 42.1, 40.0, 39.7, 39.4, 25.1, 24.5, 24.2, 23.9, 22.0. HRMS (ESI) [M+H] calculated for $[C_{32}H_{43}N_2O_2]^+$ 487.3319, found 487.3319.



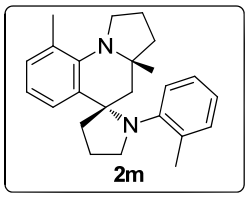
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (d, *J* = 2.8 Hz, 1H), 6.63 (d, *J* = 9.2 Hz, 3H), 6.45 (d, *J* = 9.2 Hz, 2H), 6.32 (d, *J* = 8.4 Hz, 1H), 3.67 (s, 3H), 3.62 (s, 3H), 3.42 (s, 1H), 3.37 (d, *J* = 9.2 Hz, 1H), 3.33 (d, *J* = 9.2 Hz, 1H), 2.56 (d, *J* = 13.6 Hz, 1H), 2.46 (d, *J* = 14.4 Hz, 1H), 2.21 (d, *J* = 13.6 Hz, 1H), 1.94 (d, *J* = 13.6 Hz, 1H), 1.73 - 1.36 (m, 26H), 1.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 150.6, 140.3, 139.3, 131.4, 115.1, 114.4, 114.2, 112.5, 112.4, 64.3, 61.3, 60.4, 59.3, 57.5, 55.7, 55.5, 44.6, 40.9, 40.1, 40.0, 39.3, 39.0, 38.5, 26.9, 26.0, 25.8, 24.1, 24.0, 23.6, 23.5, 21.5. HRMS (ESI) [M+H] calculated for $[C_{34}H_{47}N_2O_2]^+$ 515.3632, found 515.3630.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.30 (m, 10H), 7.25 - 7.21 (m, 4H), 7.20 - 7.21 (m, 7H), 6.69 - 6.63 (m, 3H), 6.58 - 6.56 (m, 2H), 6.54 - 6.52 (m, 1H), 6.45 (d, *J* = 2.4 Hz, 1H), 4.42 (d, *J* = 10.4 Hz, 1H), 4.11 - 4.06 (m, 2H), 3.93 (d, *J* = 10 Hz, 1H), 3.72 (s, 3H), 3.43 (d, *J* = 13.2 Hz, 1H), 3.41 (s, 3H), 3.29 (d, *J* = 13.2 Hz, 1H), 2.71 (d, *J* = 13.2 Hz, 1H), 2.35 - 2.30 (m, 2H),1.48 - 1.44 (m, 1H), 1.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152. 2, 151.4, 151.2, 147.8, 147.6, 147.5, 139.4, 138.7, 130.7, 128.6, 128.4, 128.3, 128.2, 127.7, 127.1, 126.9, 126.5, 126.2, 126.2, 126.1, 125.7, 115.4, 114.4, 114.0, 113.9, 113.8, 64.7, 60.9, 59.4, 58.7, 58.3, 55.6, 55.5, 54.6, 53.1, 51.6, 42.9, 22.2. HRMS (ESI) [M+H] calculated for $[C_{48}H_{47}N_2O_2]^+$ 683.3638, found 683.3630.

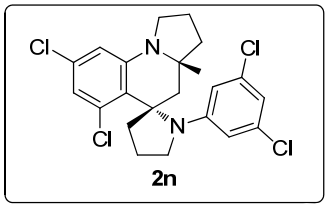
General procedure for gold(I)-catalyzed synthesis of azaspiro polycycles:

To a 25 mL Schlenk tube equipped with a magnetic stir bar was added 100 mg ultra-dried dry 4 Å molecular sieve. Then (*t*Bu)$_2$(*o*-diphenyl)PAuCl (5 mol%) and $AgN(Tf)_2$ (5 mol%) were added under argon atmosphere followed by addition of ultra-dried DCE (2.5 mL) under argon atmosphere. The mixture was stirred for about 1 hour. Next the aminoalkyne (1.0 mmol) was added to the reaction mixture and then stirred at 75 ^{o}C. After reaction completion (monitored by TLC), the reaction mixture was filtered through celite. Then the solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (EtOAc/Petroleum ether = 1/20 – 1/40) to give the desired products. (Compounds **2m-2o**).



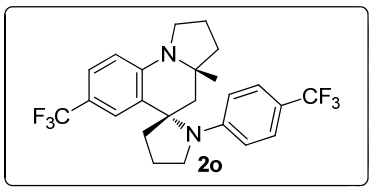
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (d, *J* = 7.8 Hz, 1H), 6.92 (t, *J* = 8.0 Hz, 1H), 6.43 - 6.39 (m, 2H), 6.31 (s, 2H), 6.12 (dd, *J* = 8.4 and 2.4 Hz, 1H), 3.71 - 3.65 (m, 1H), 3.61 - 3.54 (m, 1H), 3.53 - 3.46 (m, 1H), 3.42 - 3.36 (m, 1H), 2.59 - 2.53 (m, 1H), 2.48 (d, *J* = 13.6 Hz, 1H), 2.42 - 2.35 (m, 1H), 2.30 (s, 3H), 2.23 (s, 3H), 2.20 - 2.09 (m, 4H), 1.95 - 1.86 (m, 2H), 1.78 - 1.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 143.5, 137.9, 137.1, 128.2, 127.0, 124.0, 117.3, 115.8, 114.2, 112.1, 110.8, 62.8, 59.5, 49.2, 45.9,

45.6, 41.4, 40.7, 22.3, 22.1, 21.9, 21.5, 21.4. HRMS (ESI) [M+H] calculated for $[C_{24}H_{31}N_2]^+$ 347.2482, found 347.2482.



2n

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (d, *J* = 2.0 Hz, 1H), 6.49(t, *J* = 2.0 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 6.13(d, *J* = 2.0 Hz, 2H), 6.30 (d, *J* = 8.4 Hz, 2H), 3.57 - 3.52 (m, 1H), 3.47 - 3.44 (m, 1H), 3.39 - 3.34 (m, 2H), 2.83 - 2.80 (m, 1H), 2.35 - 2.27 (m, 1H), 2.22 (d, *J* = 12.4 Hz, 1H), 2.19 - 2.04 (m, 4H), 1.98 (d, *J* = 12.4 Hz, 1H), 1.95 - 1.92 (m, 1H), 1.78 - 1.75 (m, 1H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 150.0, 134.4, 134.0, 133.3, 118.8, 118.5, 114.7, 110.8, 110.4, 63.4, 59.3, 48.7, 46.4, 43.0, 40.7, 38.7, 21.9, 21.6, 21.1. HRMS (ESI) [M+H] calculated for $[C_{22}H_{23}N_2Cl_4]^+$ 457.0610, found 457.0575.



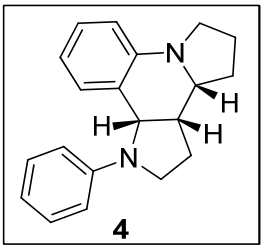
2o

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 8.4 and 2.0 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 2.4 Hz, 1H), 3.75 - 3.68 (m, 1H), 3.60 - 3.57 (m, 1H), 3.56 - 3.45 (m, 1H), 3.44 - 3.40 (m, 1H), 2.63 - 2.57 (m, 1H), 2.45 - 2.30 (m, 2H), 2.28 - 2.08 (m, 4H), 2.02 - 1.84 (m, 2H), 1.79 - 1.65 (m, 1H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 145.7, 125.7 (q, J_{CF} = 3.7 Hz), 125.1 (q, J_{CF} = 275.9 Hz), 125.0 (q, J_{CF} = 275.9 Hz), 125.3 (q, J_{CF} = 3.7 Hz), 123.9 (q, J_{CF} = 3.7 Hz), 113.0, 111.2, 117.7 (q, J_{CF} = 32.5 Hz), 116.7 (q, J_{CF} = 32.5 Hz), 63.2, 59.8, 49.5, 45.9, 45.7, 40.7, 40.7, 22.7, 22.2, 21.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ -60.7 (s, 3F), -60.8 (s, 3F). HRMS (ESI) [M+H] calculated for $[C_{24}H_{25}N_2F_6]^+$ 455.1916, found 455.1917.

General procedure for gold(I)-catalyzed synthesis of dipyrroloquinoline ring framework:

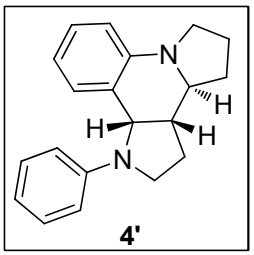
To a 25 mL Schlenk tube equipped with a magnetic stir bar were added $(PhO)_2P(O)OH$ (10 mol%), (*t*Bu)$_2$(*o*-diphenyl)PAu(CH_3CN)SbF_6 (5 mol%) under argon atmosphere followed by addition of ultra-dried DCM (2.0 mL) under argon atmosphere. Then the 1,3-aminoalkyne was added to the reaction mixture and then stirred at ambient temperature for 12 h. Then the solvent was removed in vacuo, and

the residue was purified by silica gel column chromatography (EtOAc/Petroleum ether = 1/9 or 1/1) to give the desired products.



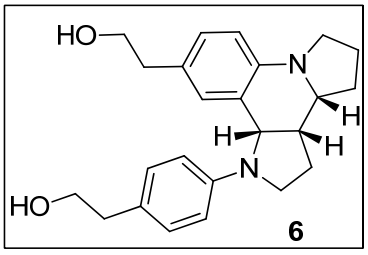
4

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 - 7.23 (m, 3H), 7.13 - 7.03 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 2H), 6.69 (t, *J* = 7.2 Hz, 1H), 6.51 (td, *J* = 7.6 and 1.0 Hz, 1H), 6.39 (dd, *J* = 8.0, 0.8 Hz, 1H), 5.11 (d, *J* = 6.8 Hz, 1H), 3.77 - 3.68 (m, 1H), 3.43 (t, *J* = 8.8 Hz, 1H), 3.39 - 3.18 (m, 3H), 2.54 - 2.46 (m, 1H), 2.14 - 2.06 (m, 1H), 2.07 - 1.90 (m, 3H), 1.90 - 1.76 (m, 1H), 1.73 - 1.63 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 143.1, 129.3, 128.8, 128.0, 122.9, 115.7, 115.4, 111.2, 110.2, 57.4, 56.4, 47.3, 46.5, 40.0, 30.2, 23.3, 23.2. HRMS (ESI) [M-H] calculated for $[C_{20}H_{21}N_2]^-$ 289.1705, found 289.1674.



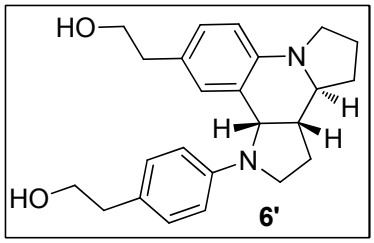
4'

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 - 7.15 (m, 3H), 7.11 (dt, *J* = 7.6, 1.6 Hz, 1H), 6.79 - 6.66 (m, 5H), 4.44 (d, *J* = 9.2 Hz, 1H), 3.66 (t, *J* = 8.0 Hz, 1H), 3.46 (td, *J* = 8.8, 2.8 Hz, 1H), 3.33 - 3.29 (m, 1H), 2.85 - 2.77 (m, 1H), 2.76 - 2.72 (m, 1H), 2.45 - 2.38 (m, 1H), 2.29 - 2.08 (m, 3H), 2.02 - 1.92 (m, 1H), 1.84 - 1.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 147.1, 129.0, 128.3, 127.1, 126.9, 118.9, 116.4, 112.6, 112.1, 64.6, 59.4, 49.1, 48.2, 47.2, 31.9, 30.5, 22.3. HRMS (ESI) [M-H] calculated for $[C_{20}H_{23}N_2]^-$ 291.1861, found 291.1875.



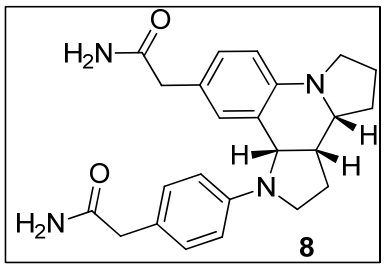
6

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 - 7.10 (m, 3H), 6.94 (dd, *J* = 8.2 Hz and 2.0 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 2H), 6.37 (d, *J* = 8.2 Hz, 1H), 5.07 (d, *J* = 7.0 Hz, 1H), 3.84 (t, *J* = 6.4 Hz, 2H), 3.73 - 3.61 (m, 3H), 3.45 (m, 2H), 3.28 - 3.18 (m, 2H), 2.80 (t, *J* = 6.4 Hz, 2H), 2.62 (t, *J* = 6.6 Hz, 2H), 2.57 - 2.47 (m, 1H), 2.15 - 1.80 (m, 5H), 1.78 - 1.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 142.1, 129.9, 129.1, 128.5, 125.2, 125.1, 123.4, 111.8, 110.6, 63.9, 63.8, 58.0, 56.7, 47.6, 46.6, 40.2, 38.18, 38.15, 30.0, 23.2, 23.1. HRMS (ESI) [M+H] calculated for $[C_{24}H_{31}N_2O_2]^+$ 379.2386, found 379.2380

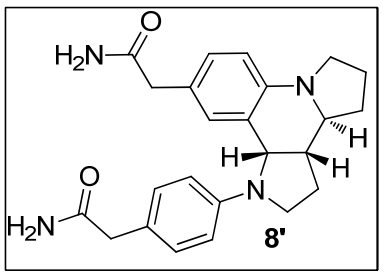


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.5 Hz, 2H), 7.02 (dd, *J* = 8.0 Hz and 1.6 Hz, 1H), 6.88 (s, 1H), 6.73 - 6.60 (m, 3H), 4.33 (d, *J* = 8.8 Hz, 1H), 3.81 (t, *J* = 6.4 Hz, 2H), 3.68 (t, *J* = 6.5 Hz, 2H), 3.62 (t, *J* = 8.0 Hz, 1H), 3.50 - 3.40 (td, *J* = 8.8 Hz and 3.4 Hz, 1H), 3.35 - 3.24 (m, 1H), 2.87 (q, *J* = 9.2 Hz, 1H), 2.78 (t, *J* = 6.0 Hz, 2H), 2.72 - 2.60 (m, 3H), 2.55 - 2.46 (m, 1H), 2.30 - 2.07 (m, 3H), 2.05 - 1.84 (m, 2H), 1.85 - 1.66 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 145.5, 129.6, 128.0, 127.9, 127.8, 127.7, 127.0, 114.0, 112.1, 64.3, 63.9, 63.8, 60.3, 49.6, 47.4, 47.3, 38.4, 38.2, 31.8, 30.1, 22.4. HRMS (ESI) [M+H] calculated for $[C_{24}H_{31}N_2O_2]^+$ 379.2386, found 379.2379.

The two diastereomers **8** and **8'** were not separated by simple flash chromatography. So they were purified directly by preparative HPLC (reverse phase, XB-C 18 5 250 mm x 22 mm column, 70:30 MeOH: H_2O, 10 mL/min) to give the desired products.



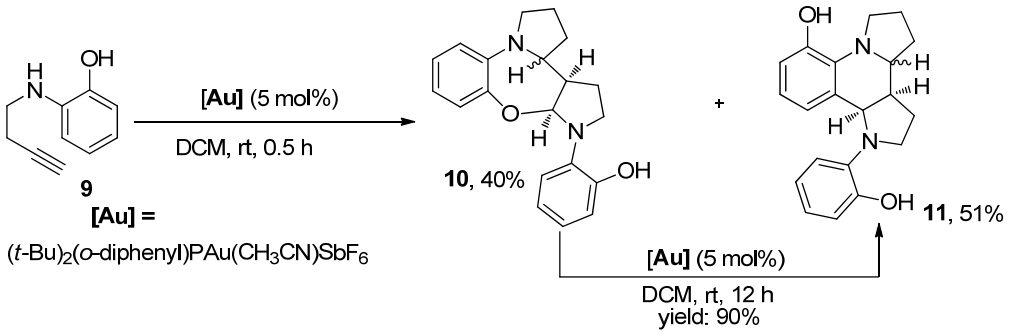
^{1}H NMR (400 MHz, DMSO) δ 7.35 (s, 1H), 7.24 (s, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 7.00 - 6.90 (m, 2H), 6.80 (s, 1H), 6.76 - 6.66 (m, 3H), 6.34 (d, *J* = 8.4 Hz, 1H), 5.02 (d, *J* = 7.2 Hz, 1H), 3.66 - 3.56 (m, 1H), 3.35 - 3.27 (m, 2H), 3.25 (s, 2H), 3.20 - 3.10 (m, 2H), 3.06 (s, 2H), 2.49 - 2.39 (m, 1H), 2.09 - 1.83 (m, 4H), 1.71 - 1.57 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ 173.6, 173.3, 148.2, 142.2, 130.2, 129.4, 128.9, 123.6, 123.55, 123.52, 111.5, 110.9, 57.9, 56.5, 48.5, 47.0, 42.0, 41.9, 40.4, 30.0, 23.4, 23.1. HRMS (ESI) [M+H] calculated for $[C_{24}H_{29}N_4O_2]^+$ 405.2291, found 405.2293.



^{1}H NMR (400 MHz, DMSO) δ 7.36 (s, 1H), 7.28 (s, 1H), 7.10 - 7.00 (m, 3H), 6.81 (s, 1H), 6.78 (s, 1H), 6.70 (s, 1H), 6.61 (d, *J* = 6.0 Hz, 1H), 6.54 (d, *J* = 6.4 Hz, 2H), 4.21 (d, *J* = 9.2 Hz, 1H), 3.59 (t, *J* = 8.0 Hz, 1H), 3.23 (s, 2H), 3.22 - 3.09 (m, 3H), 2.75 (q, *J* = 9.0 Hz, 1H), 2.73 - 2.64 (m, 1H), 2.40 - 2.31 (m, 1H), 2.26 - 2.13 (m, 2H), 2.06 - 2.00 (m, 1H), 1.98 - 1.90 (m, 1H), 1.73 - 1.57 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ 173.0,

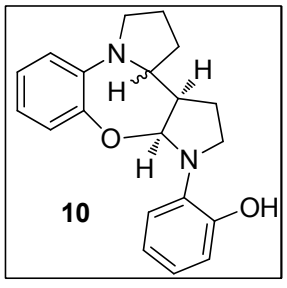
172.7, 148.1, 145.6, 129.5, 127.8, 127.6, 127.2, 126.1, 124.4, 112.7, 112.0, 64.1, 59.8, 49.6, 47.4, 47.1, 41.8, 41.5, 31.4, 30.0, 21.9. HRMS (ESI) [M+H] calculated for $[C_{24}H_{29}N_4O_2]^+$ 405.2291, found 405.2286.

Experiments for mechanistic studies:



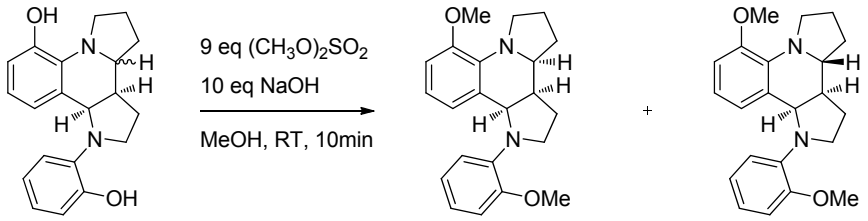
To a 25 mL Schlenk tube equipped with a magnetic stir bar was added (tBu)$_2$(o-diphenyl)PAu(CH_3CN)SbF_6 (5 mol%) under argon atmosphere followed by addition of ultra-dried DCM (2.0 mL) under argon atmosphere. Then the aminoalkyne **9** was added to the reaction mixture. The sealed tube was stirred at ambient temperature for 0.5 h and the reaction mixture was filtered through celite. Then the solvent was removed in vacuo without further purification. Compounds **10** and **11** were obtained in 40% and 51% yields as determined by ^{1}H-NMR, respectively.

To a 25 mL Schlenk tube equipped with a magnetic stir bar was added (tBu)$_2$(o-diphenyl)PAu(CH_3CN)SbF_6 (5 mol%) under argon atmosphere followed by addition of ultra-dried DCM (2.0 mL) under argon atmosphere. Then compound **10** was added to the reaction mixture and then stirred at ambient temperature for 12 h. Then the solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (EtOAc/Petroleum ether = 1/9) to give **11** (90% yield), which was very difficult to purify and did not obtain pure NMR spectra.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.11 (dd, J = 7.6, 1.2 Hz, 1H), 7.03 - 6.93 (m, 4H), 6.84 - 6.77 (m, 1H), 6.68 (m, 1H), 6.54 (dd, J = 8.0, 1.2 Hz, 1H), 5.15 (d, J = 5.6 Hz, 1H), 4.05 - 3.97 (m, 1H), 3.65 - 3.59 (m, 1H), 3.49 - 3.41 (m, 1H), 3.35 - 3.28 (m, 1H), 3.03 (q, J = 8.4 Hz, 1H), 2.54 - 2.42 (m,

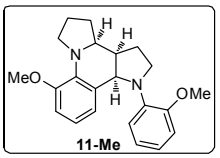
1H), 2.11 - 1.96 (m, 5H), 1.90 - 1.82 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 143.7, 140.7, 133.7, 125.3, 124.1, 121.8, 120.5, 119.4, 117.8, 116.0, 113.6, 99.5, 60.7, 52.7, 50.8, 49.1, 29.9, 27.0, 23.3. HRMS (ESI) [M+Na] calculated for $[C_{20}H_{22}N_2O_2Na]^+$ 345.1573, found 345.1570.



11 **11-Me** **11′-Me**

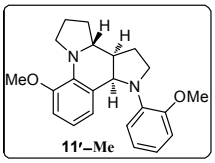
51% **26%**

To further confirm structure **11**, it was protected by methyl group to obtain pure two diastereomers **11-Me** and **11'-Me**. To a 25 mL Schlenk tube equipped with a magnetic stir bar were added **11** (87 mg, 0.27 mmol) and NaOH (108 mg, 2.70 mmol) in acetone (10 mL) followed by addition of dimethylsulfate (230 μl, 2.40 mmol) under argon atmosphere. The sealed tube was then stirred at ambient temperature for 10 min. Then the solvent was removed in *vacuo*, and the residue was purified by silica gel column chromatography (EtOAc/Hx = 1:20) to give **11-Me** and **11′-Me** in 51% and 26% yields**.**



11-Me

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 - 6.80 (m, 3H), 6.70 - 6.60 (m, 2H), 6.50 - 6.40 (m, 2H), 5.63 (d, *J* = 7.6 Hz, 1H), 3.92 (s, 3H), 3.90 - 3.80 (m, 1H), 3.77 (s, 3H), 3.60 - 3.50 (m, 2H), 3.25 - 3.10 (m, 2H), 2.87 - 2.77 (m ,1H), 2.08 - 1.80 (m, 5H), 1.80 - 1.67 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 148.1, 138.5, 137.3, 126.5, 121.7, 121.2, 119.8, 118.2, 117.5, 111.2, 110.8, 59.6, 59.5, 55.8, 55.4, 51.6, 47.7, 41.1, 28.7, 23.6, 22.3. HRMS (ESI) [M+H] calculated for $[C_{22}H_{27}N_2O_2]^+$ 351.2073, found 351.2068.



11′–Me

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 - 7.00 (m, 2H), 6.94 - 6.80 (m, 2H), 6.67 (dd, *J* = 7.8 Hz and 1.2 Hz, 1H), 6.50 (t, *J* = 7.8 Hz, 1H), 6.23 (dd, *J* = 7.8 Hz and 0.8 Hz, 1H), 4.33 (d, 5.2 Hz, 1H), 4.02 -

3.91 (m, 1H), 3.82 (s, 3H), 3.60 (s, 3H), 3.58 - 3.50 (m, 1H), 3.40 - 3.31 (m, 1H), 3.30 - 3.22 (m ,1H), 3.14 - 3.05 (m, 1H), 2.30 - 2.13 (m, 2H), 2.08 - 1.87 (m, 3H), 1.87 - 1.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 150.4, 138.6, 136.1, 127.0, 125.0, 124.3, 122.9, 120.6, 118.1, 112.1, 109.8, 60.5, 58.4, 55.5, 55.2, 52.2, 50.4, 37.7, 29.2, 27.1, 23.5. HRMS (ESI) [M+H] calculated for $[C_{22}H_{27}N_2O_2]^+$ 351.2073, found 351.2068.

Cytotoxicity Studies (MTT Assay)

The anti-proliferative activities of compound **2j** against **A549** (Lung Adenocarcinoma), **MGC80-3** (Gasteric Adenocarcarcinoma) cancer cell lines were measured using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, a tetrazole) method. Cells were seeded in 96-well microtiter plates (at a density of 4000 cells per well) for overnight attachment and exposed to each of the compound (1.0 ~ 50.0 μM) for 72 h. The MTT solution (5.0 mg/mL in RPIM 1640 medium; SigmaAldrich) was added (20.0μl/well), and plates were incubated for a further 4 h at 37 ^{o}C. The purple formazan crystals were dissolved in 100.0 μL of DMSO. After 5 min, the plates were read on an automated micro-plate spectrophotometer (Bio-Tek Instruments, Winooski, VT) at 570 nm. Assays were performed in triplicate on three independent experiments. The concentration of drug inhibiting 50% of cells (IC_{50}) was calculated using the software of dose-effect analysis with microcomputers.

References：

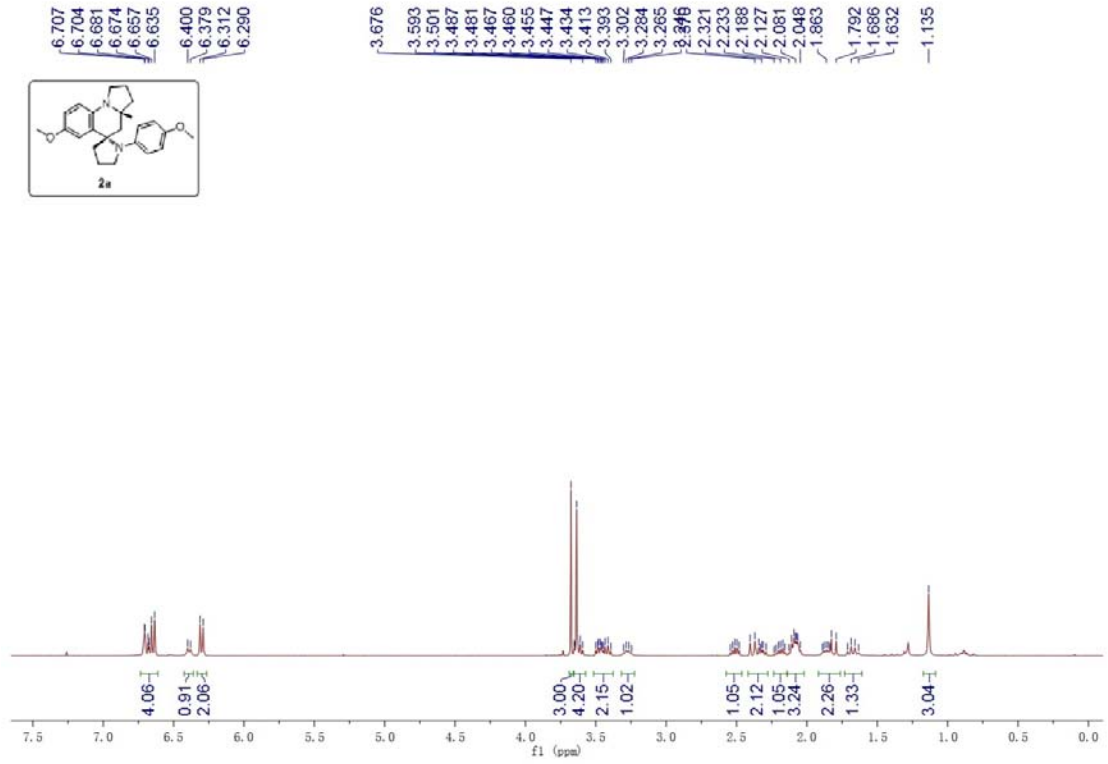
[S1] C. Nieto-Oberhuber, S. López, A. M. Echavarren, *J. Am. Chem. Soc.* **2005**, *127*, 6178.

[S2] X.-Y. Liu, C.-M. Che, *Angew. Chem.* **2008**, *120,* 3865-3870; *Angew. Chem. Int. Ed.* **2008**, *47*, 3805.

[S3] F. Fang, M. Vogel, J. V. Hines, S. C. Bergmeier, *Org. Biomol. Chem*. **2012**, *10*, 3080.

[S4] C. Gronnier, Y. Odabachian, F. Gagosz, *Chem. Commun.* **2011**, *47*, 218.

Spectra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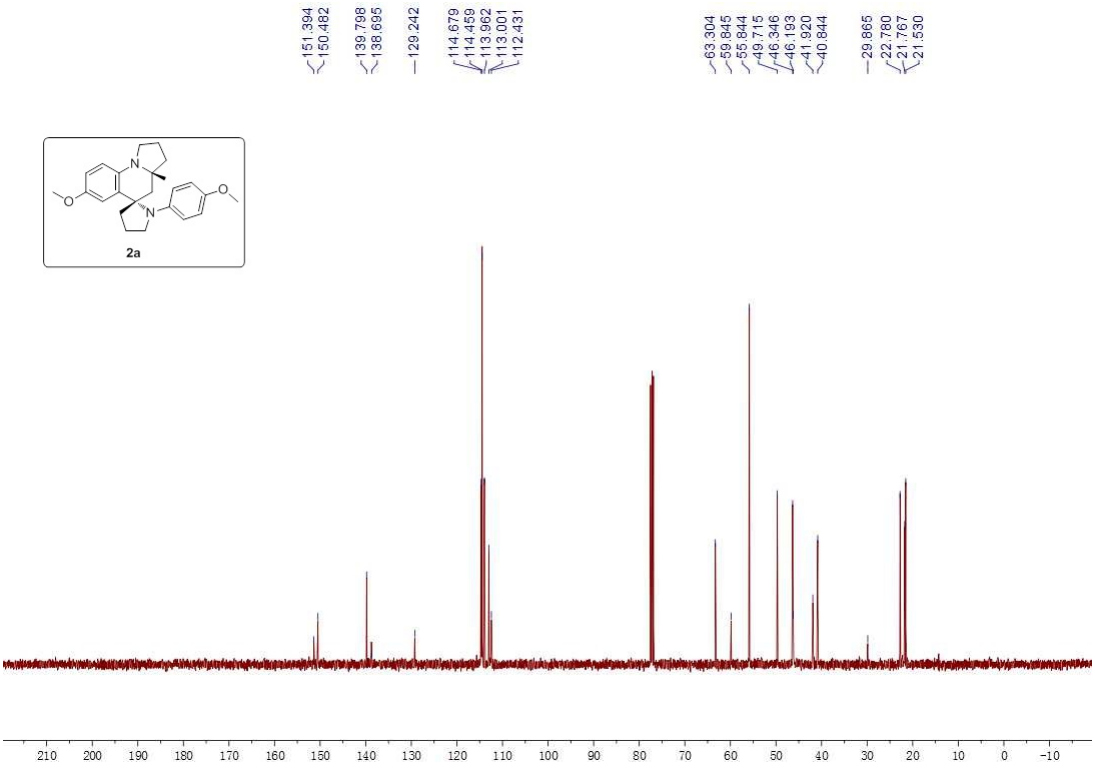
3.487
3.481
3.467
3.460
3.455
3.447
3.434
3.413
3.393
3.302
3.284
3.265
2.321
2.233
2.188
2.127
2.081
2.048
1.863
1.792
1.686
1.632
1.135
2a
4.06
0.91
2.06
3.00
4.20
2.15
1.02
1.05
2.12
1.05
3.24
2.26
1.33
3.04
f1 (ppm)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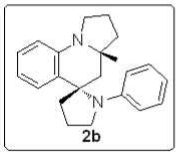
21.767
21.530
2a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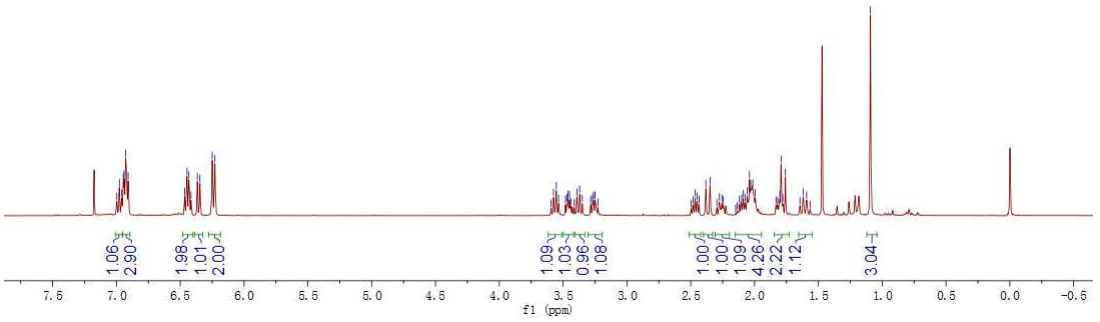
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1.00
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2.22
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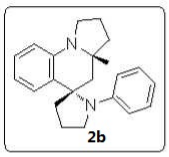
3.04
f1 (ppm)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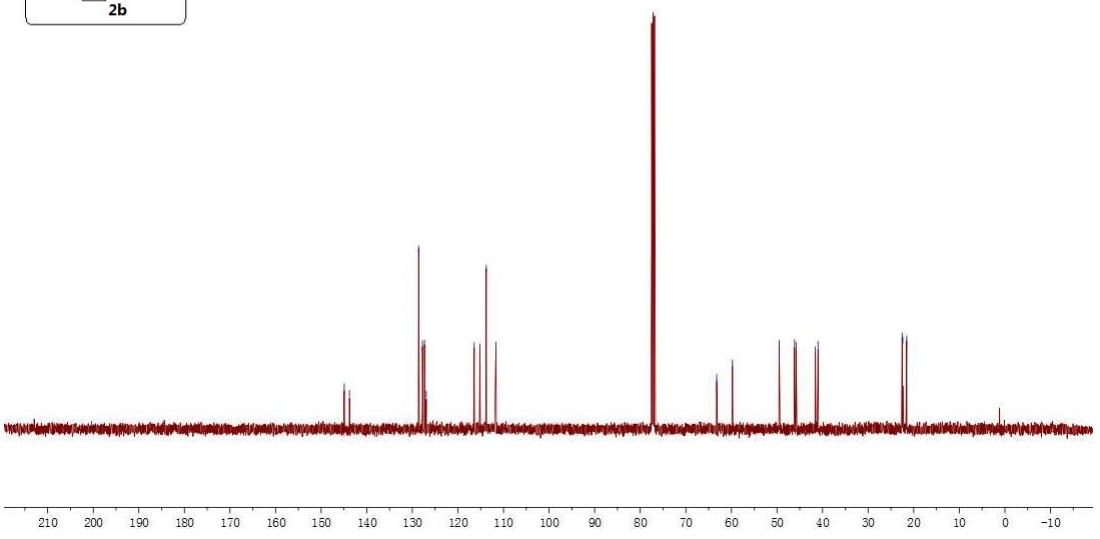

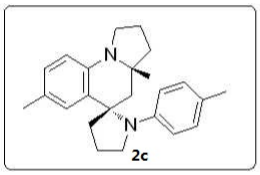
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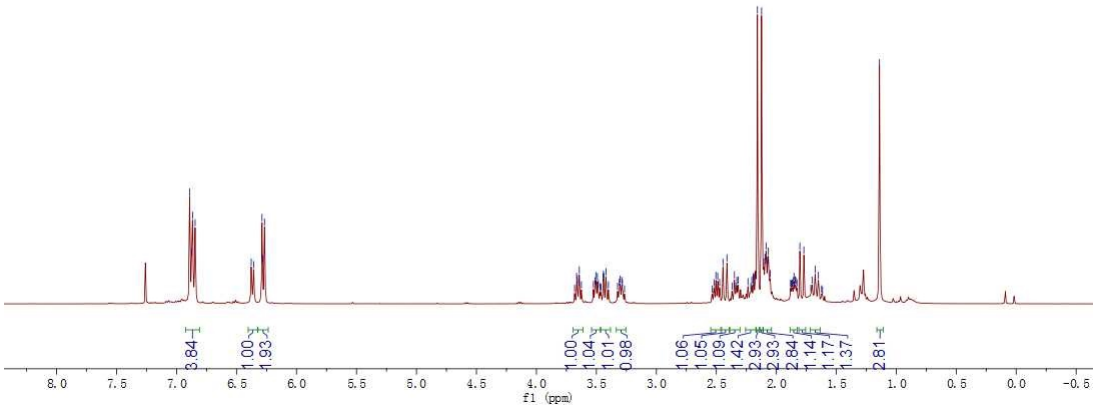
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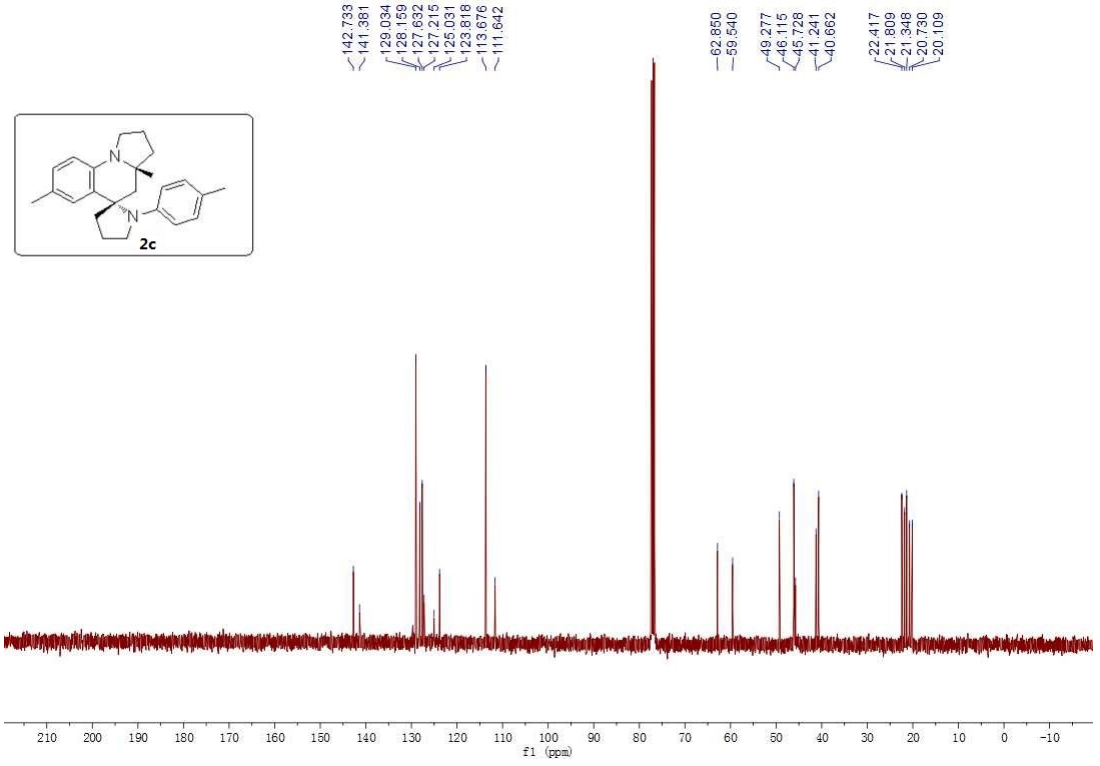
f1 (ppm)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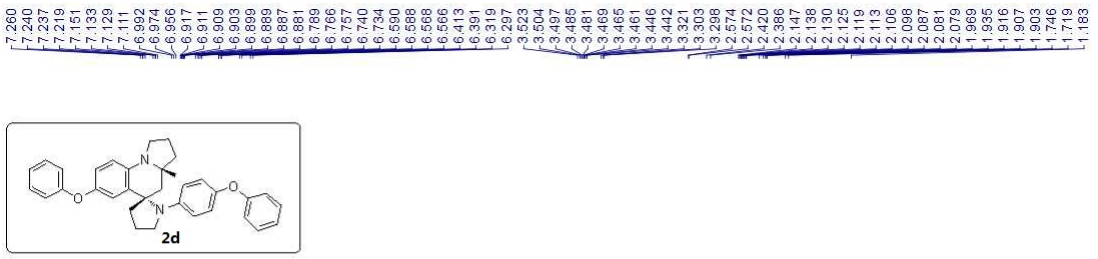
20.109
2c
f1 (ppm)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6.766
6.757
6.740
6.734
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6.566
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3.523
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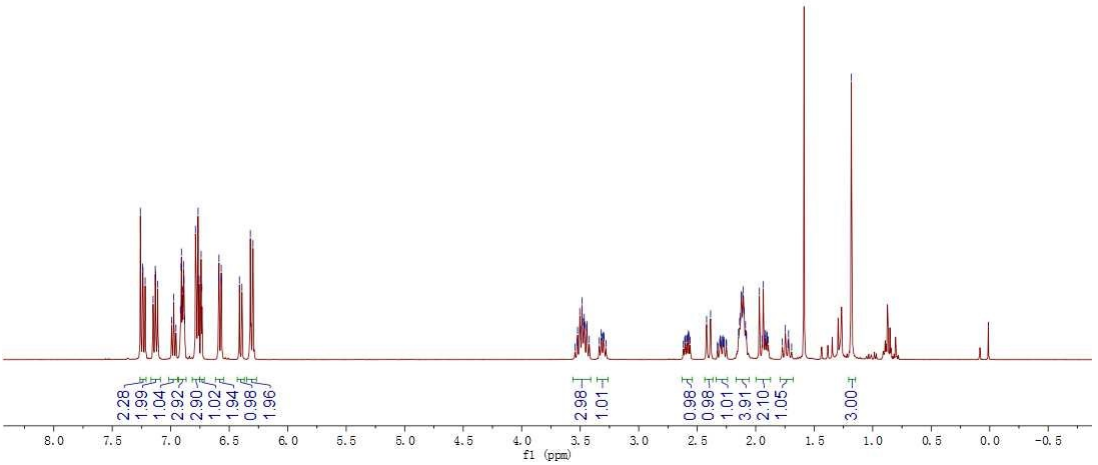
2d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7.0
6.5
6.0
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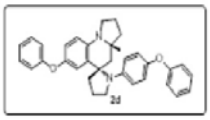
f1 (ppm)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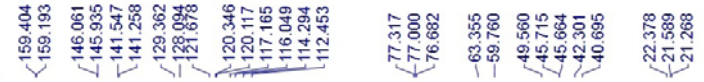
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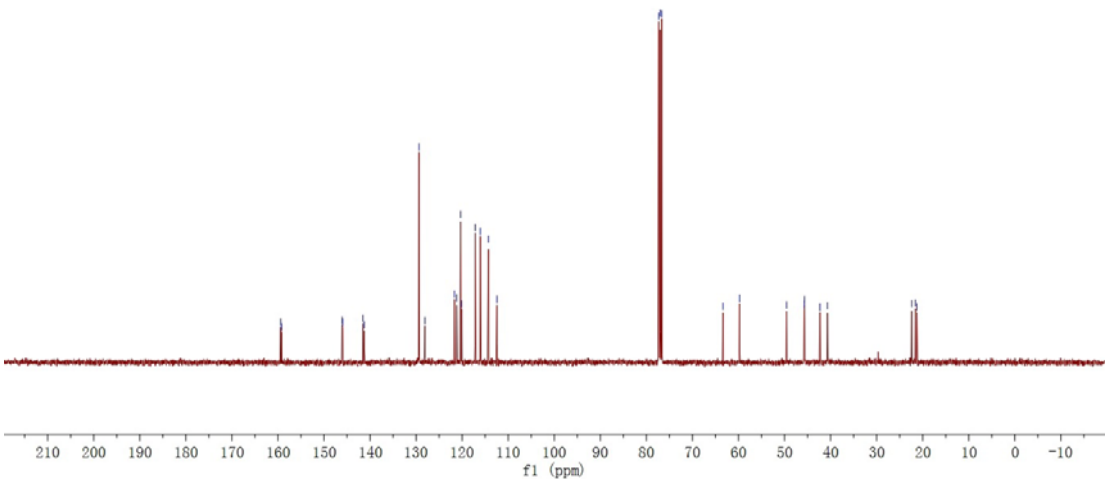
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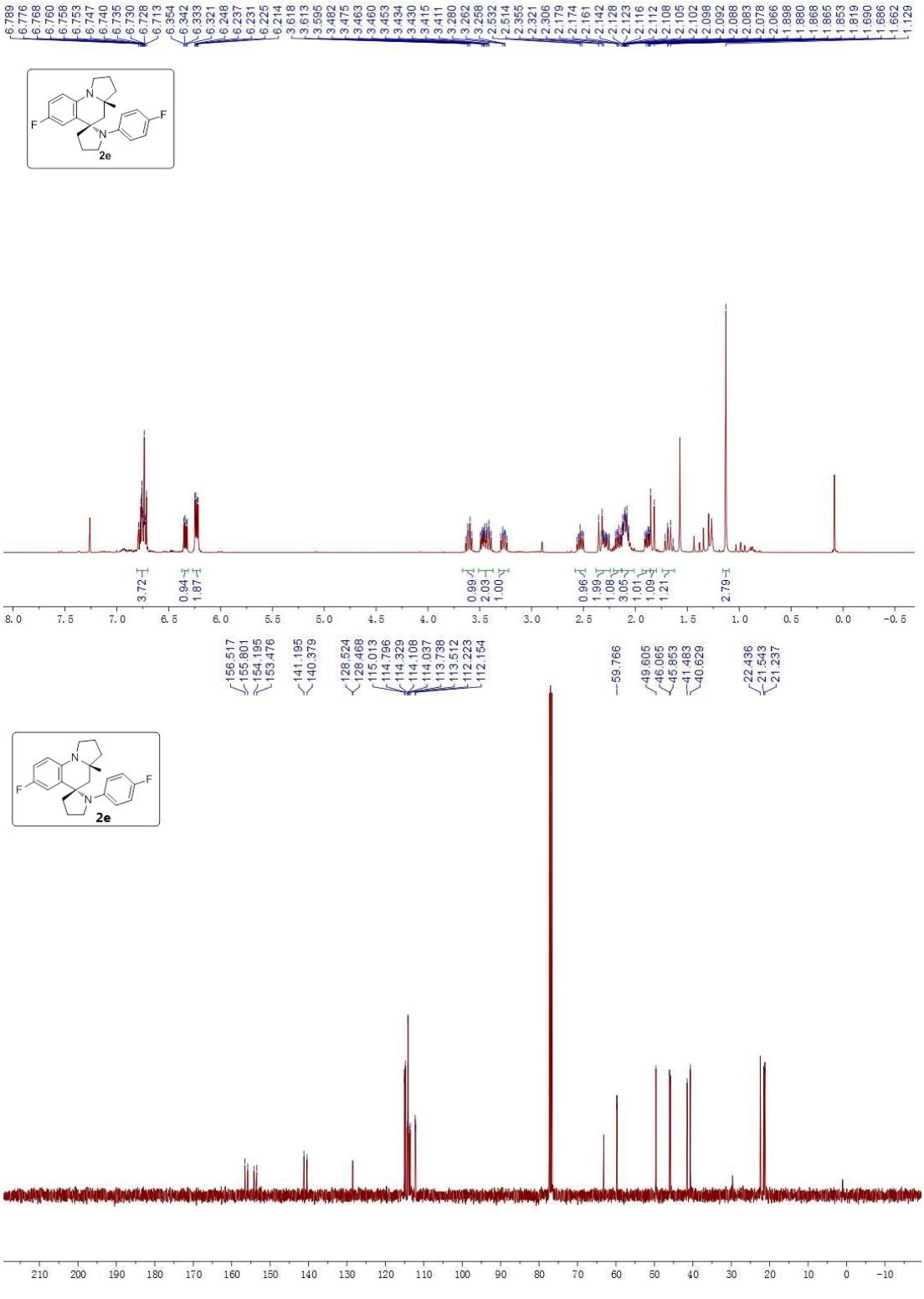
f1 (ppm)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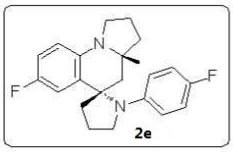
2e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N
F
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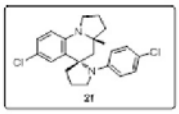
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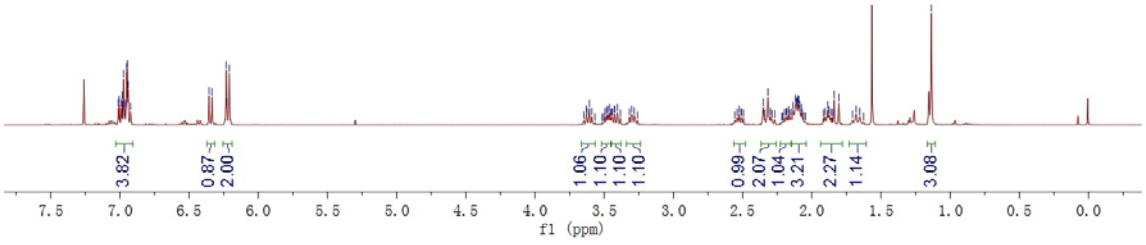
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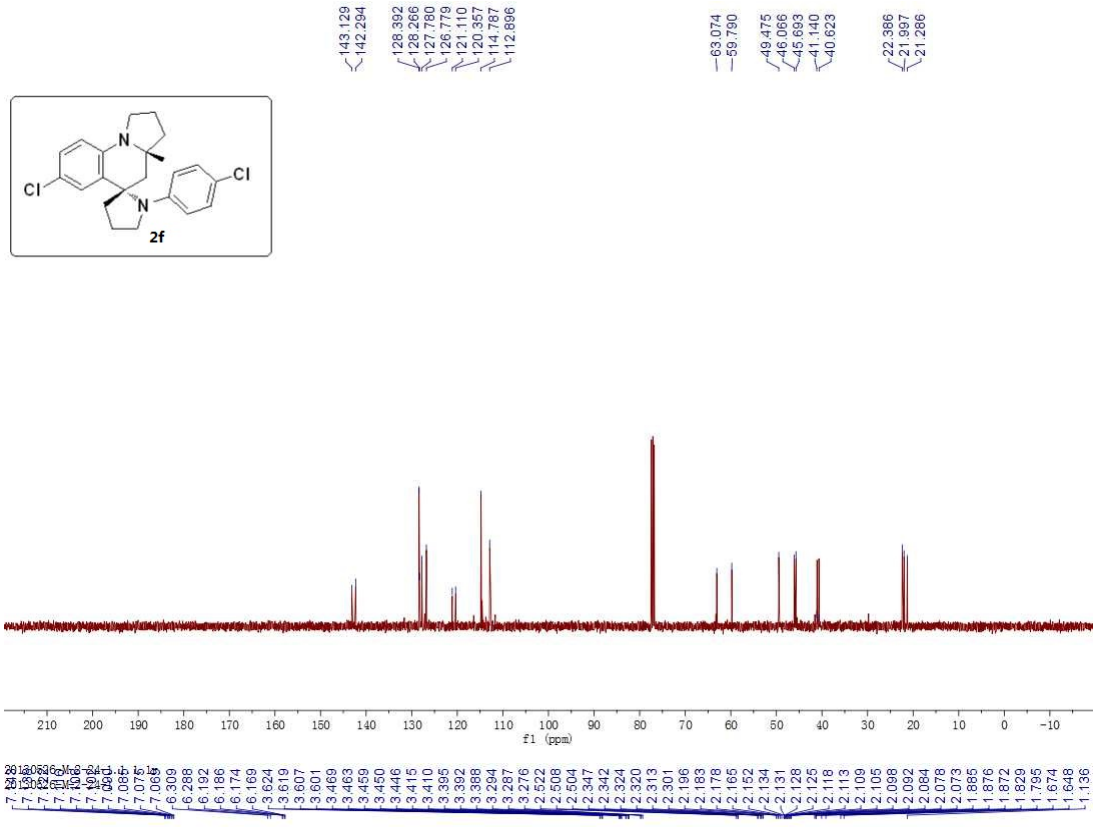
f1 (ppm)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N
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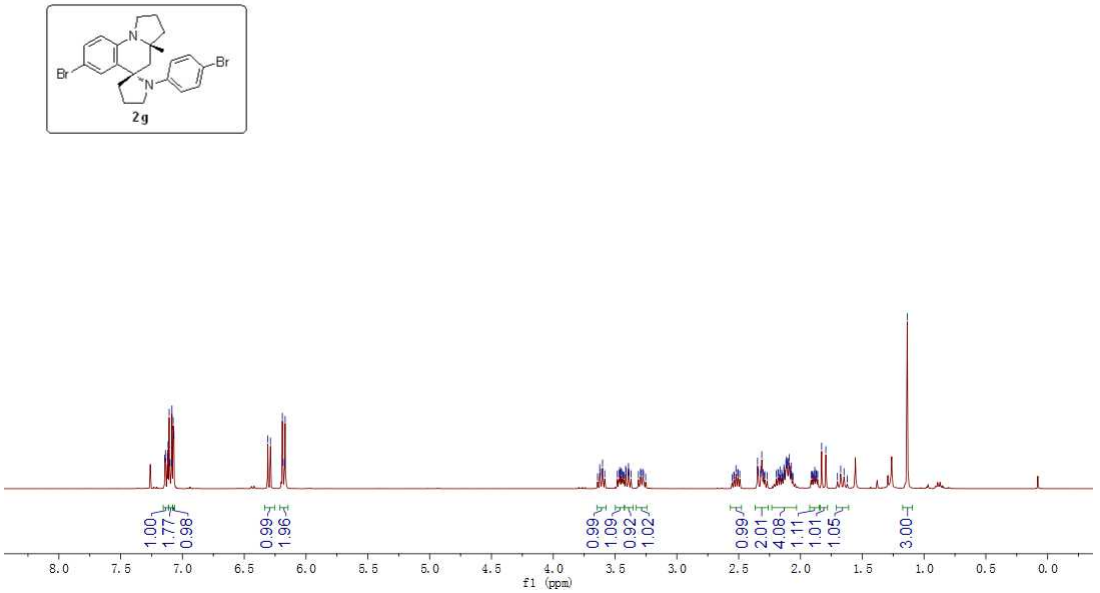
f1 (ppm)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1.01
1.05
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f1 (ppm)

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Solvent CDCl3

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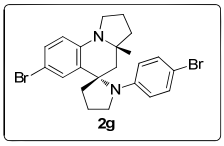

2g

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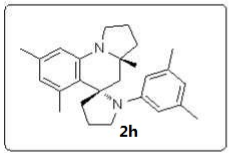

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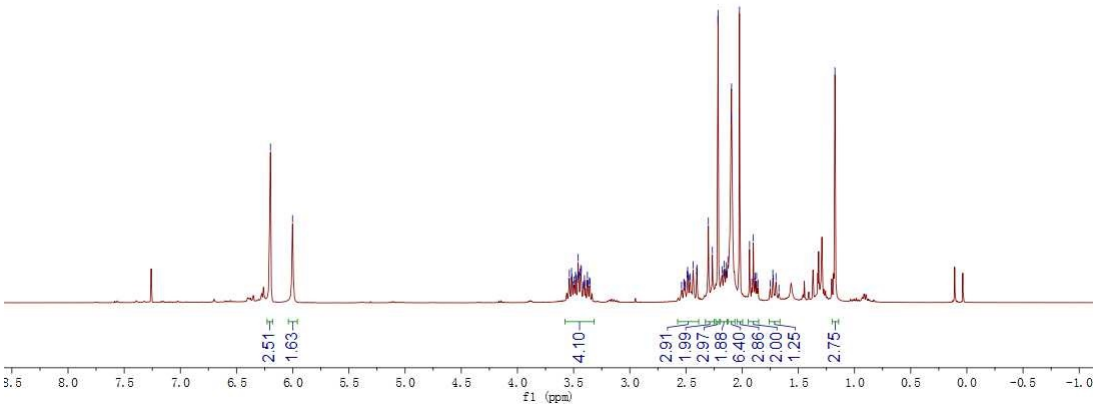

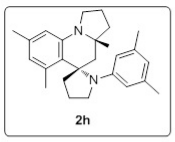
2h

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116.918
111.444
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63.546
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41.170
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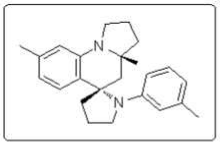
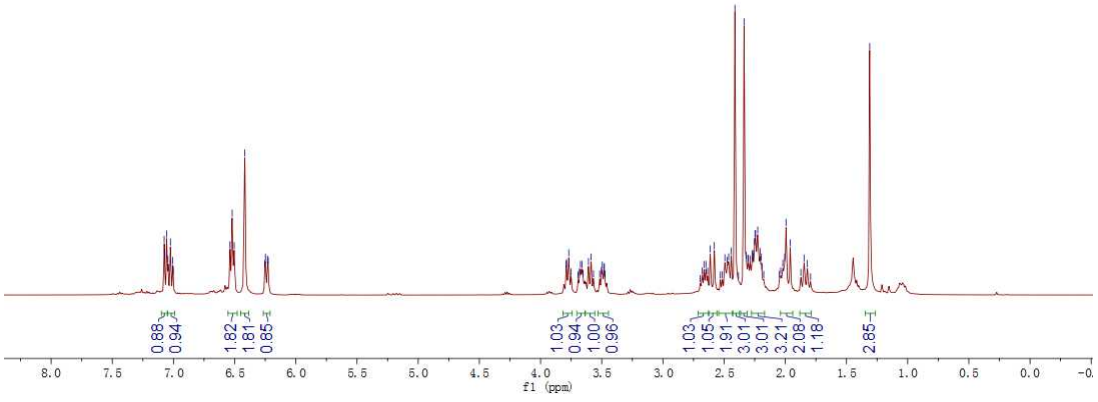
21.787
21.660
21.494
21.341
f1 (ppm)

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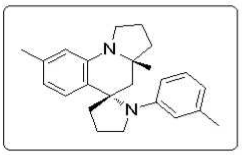
2.85
f1 (ppm)



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21.819
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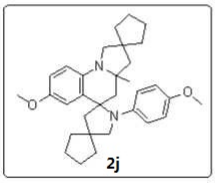
21.307
f1 (ppm)


2j

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6.29
3.67
3.62
3.39
3.37
3.34
3.32
3.29
3.27
3.07
3.04
2.56
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2.49
2.46
2.43
2.17
1.98
1.82
1.70
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1.64
1.63
1.54
1.45
1.01
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1.00
1.00
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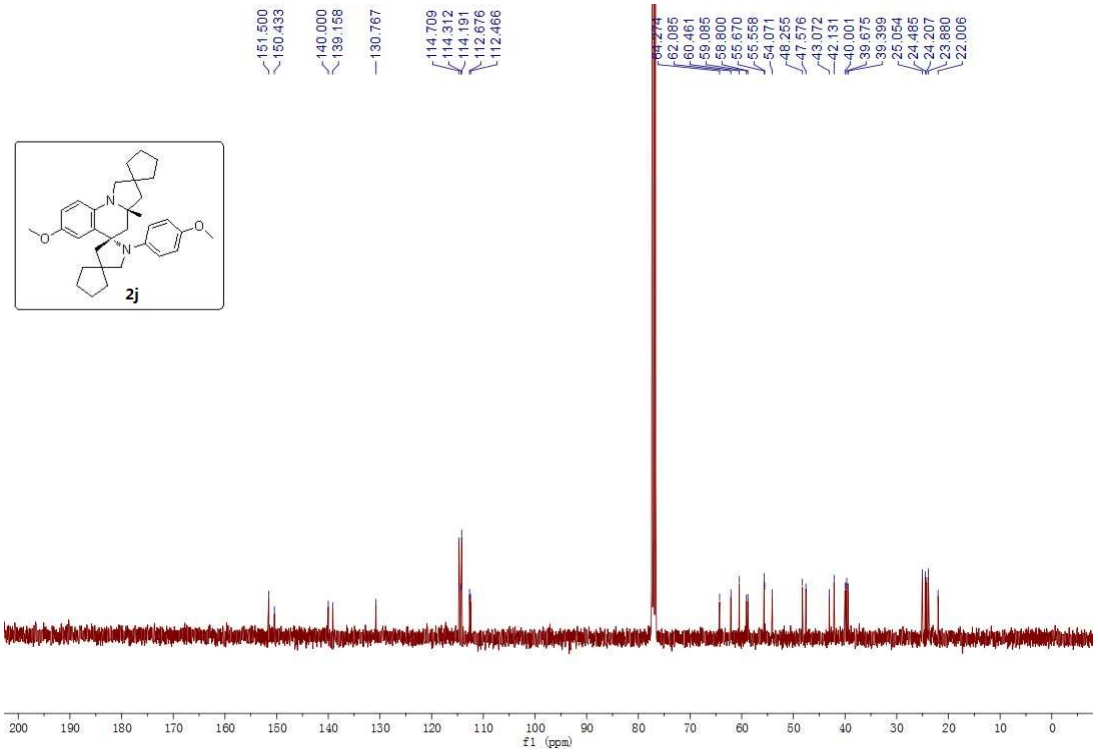
2.05
19.03
8.04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114.191
112.676
112.466
65.274
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60.461
59.085
58.800
55.670
55.558
54.071
48.255
47.576
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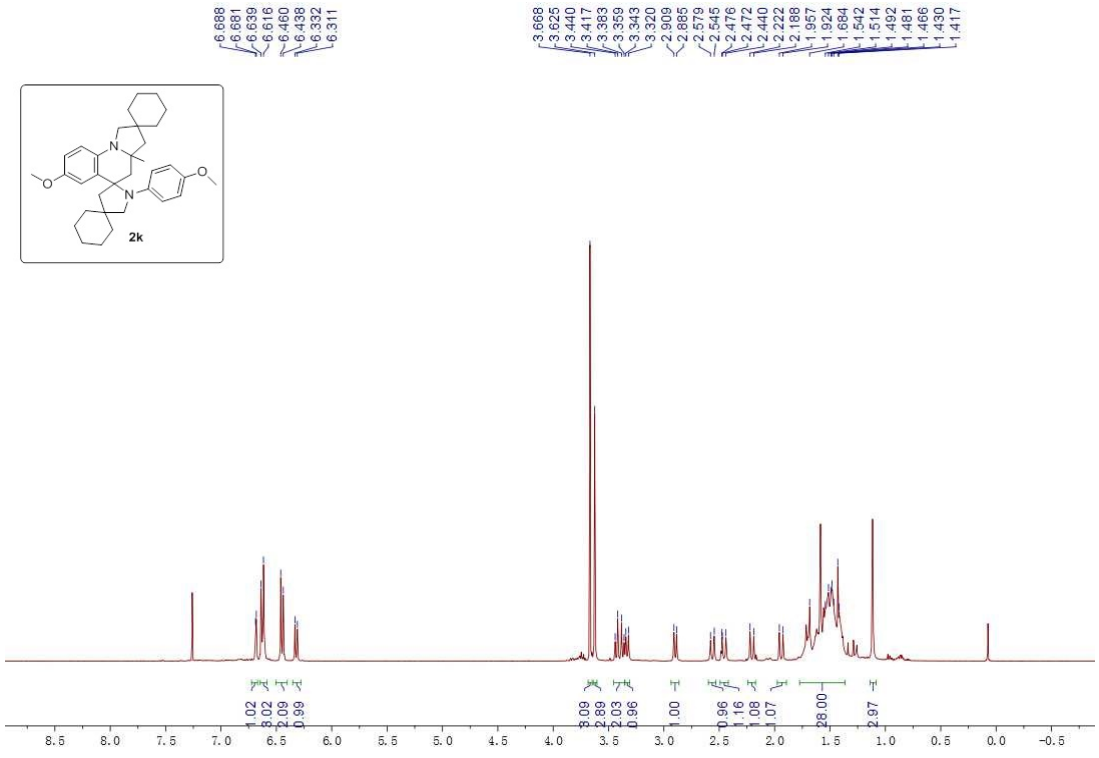
f1 (ppm)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3.417
3.383
3.359
3.343
3.320
2.909
2.885
2.579
2.545
2.476
2.472
2.440
2.222
2.188
1.957
1.924
1.684
1.542
1.514
1.492
1.481
1.466
1.430
1.417
2k
1.02
8.02
2.09
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2.03
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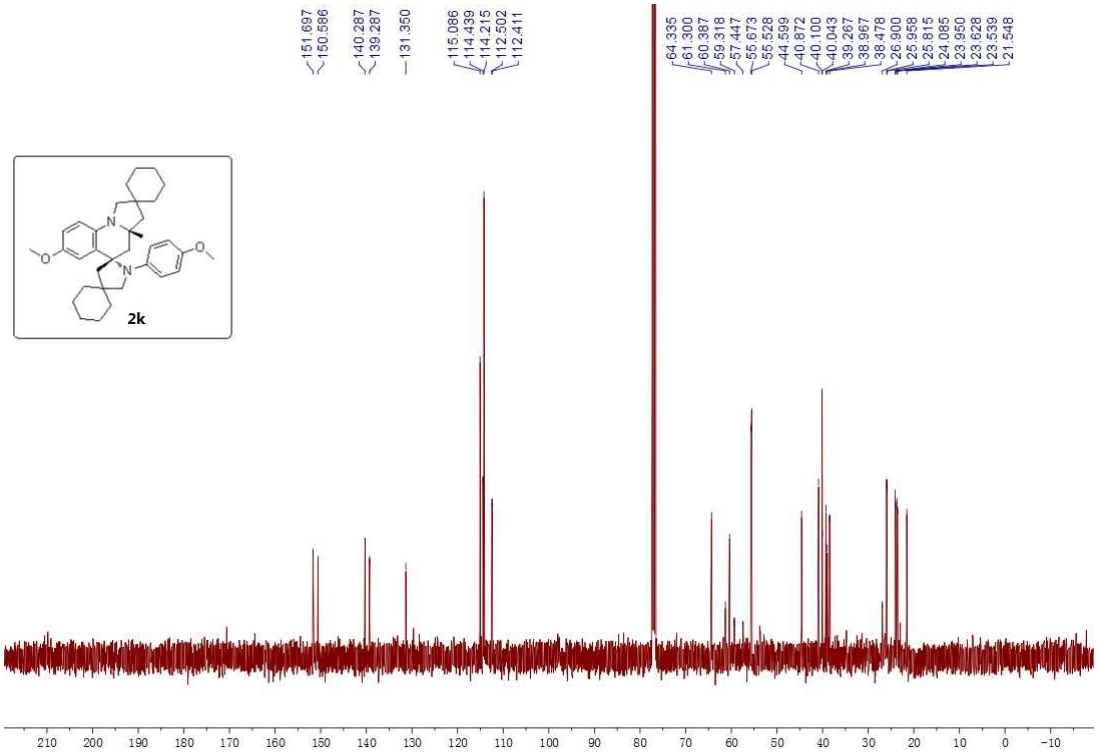
1.07
28.00
2.97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139.287
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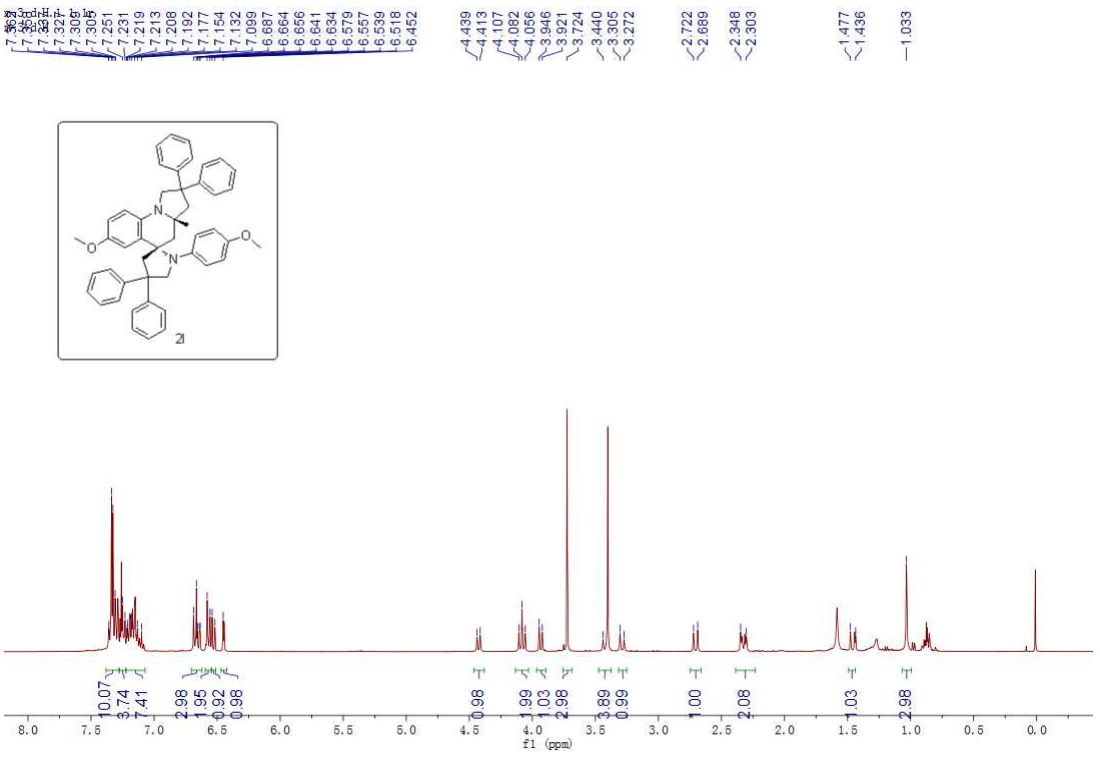
114.439
114.215
112.502
112.411
64.335
61.300
60.387
59.318
57.447
55.673
55.528
44.599
40.872
40.100
40.043
39.267
38.967
38.478
26.900
25.958
25.815
24.085
23.950
23.628
23.539
21.548
2k
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10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7.177
7.154
7.132
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6.656
6.641
6.634
6.579
6.557
6.539
6.518
6.452
4.439
4.413
4.107
4.082
4.056
3.946
3.921
3.724
3.440
3.305
3.272
2.722
2.689
2.348
2.303
1.477
1.436
1.033
2l
10.07
3.74
7.41
2.98
1.95
0.92
0.98
0.98
1.99
1.03
2.98
3.89
0.99
1.00
2.08
1.03
2.98
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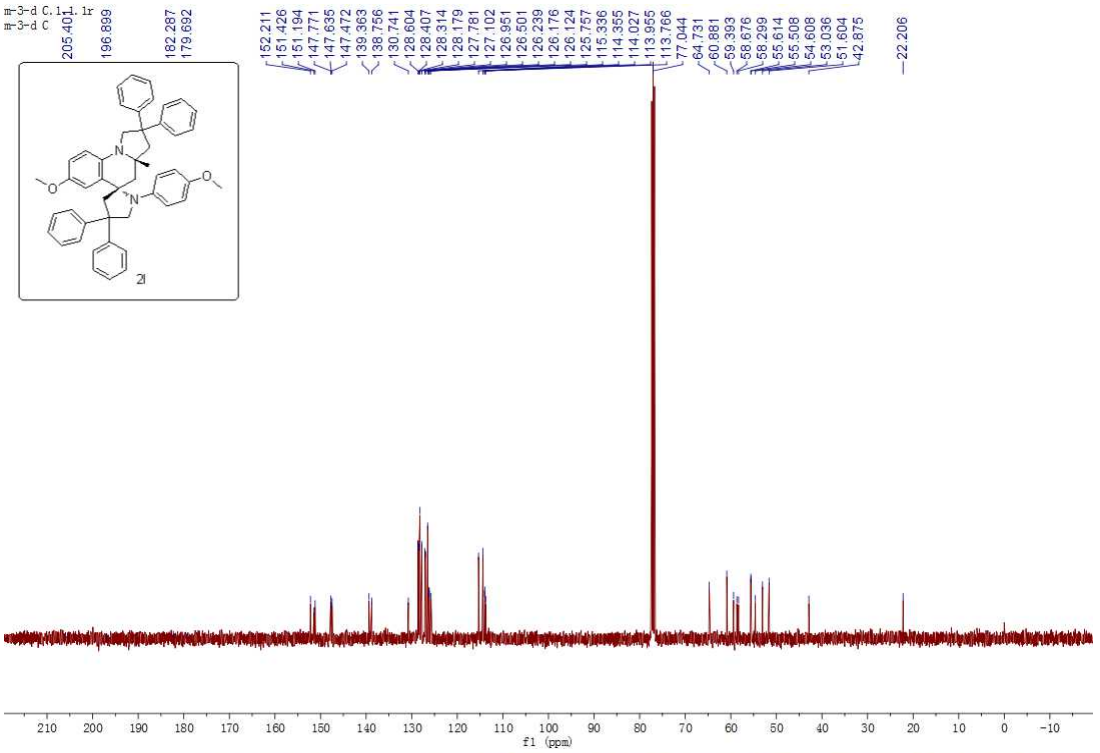
f1 (ppm)


m-3-d C.1.1r
m-3-d C
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179.692
152.211
151.426
151.194
147.771
147.635
147.472
139.363
138.756
130.741
128.604
128.407
128.314
128.179
127.781
127.102
126.951
126.501
126.239
126.176
126.124
125.757
115.336
114.355
114.027
113.955
113.766
77.044
64.731
60.881
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54.608
53.036
51.604
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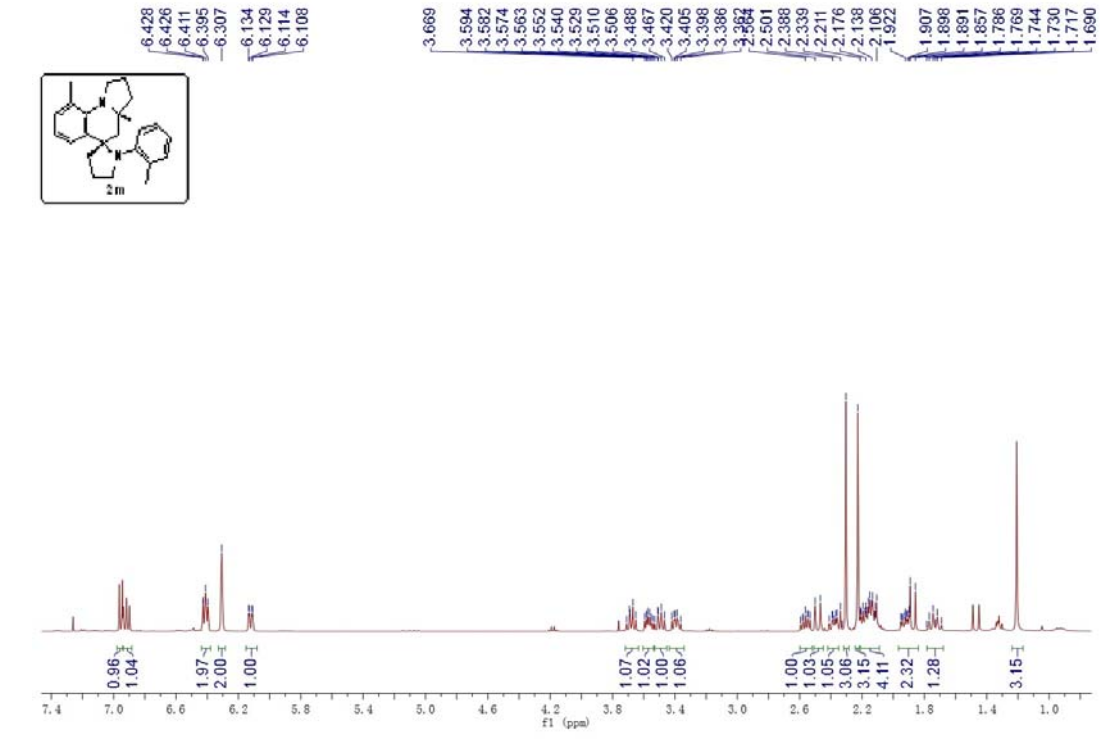
2l
f1 (ppm)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6.114
6.108
3.669
3.594
3.582
3.574
3.563
3.552
3.540
3.529
3.510
3.506
3.488
3.467
3.420
3.405
3.398
3.386
2.501
2.388
2.339
2.211
2.176
2.138
2.106
1.922
1.907
1.898
1.891
1.857
1.786
1.769
1.744
1.730
1.717
1.690
2m
0.96
1.04
1.97
2.00
1.00
1.07
1.02
1.00
1.06
1.00
1.03
1.05
3.06
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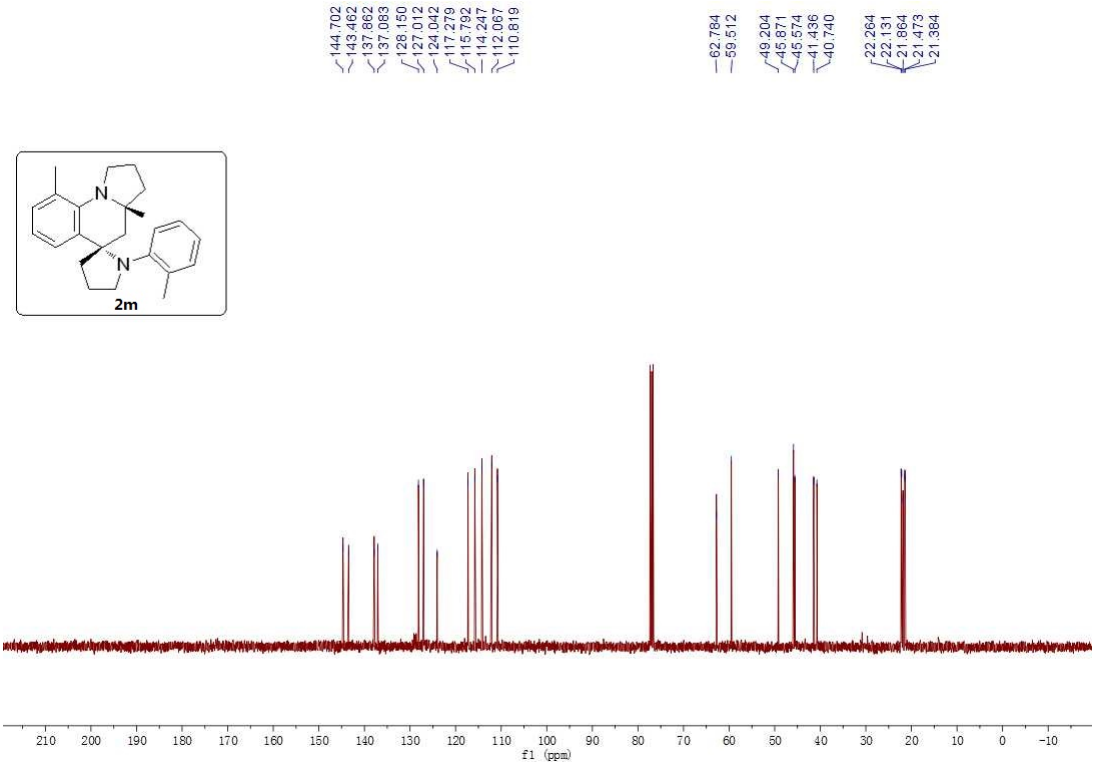
2.32
1.28
3.15
f1 (ppm)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110.819
62.784
59.512
49.204
45.871
45.574
41.436
40.740
22.264
22.131
21.864
21.473
21.384
2m
f1 (ppm)


6.556
6.551
6.499
6.494
6.490
6.394
6.388
6.138
6.133
3.566
3.563
3.543
3.521
3.475
3.472
3.468
3.453
3.448
3.429
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3.366
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3.349
3.346
3.338
2.826
2.821
2.800
2.796
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2.353
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2.267
2.237
2.232
2.201
2.189
2.183
2.179
2.175
2.167
2.163
2.160
2.155
2.151
2.146
2.143
2.140
2.131
2.129
2.125
2.120
2.117
2.038
2.003
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1.943
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1.926
1.918
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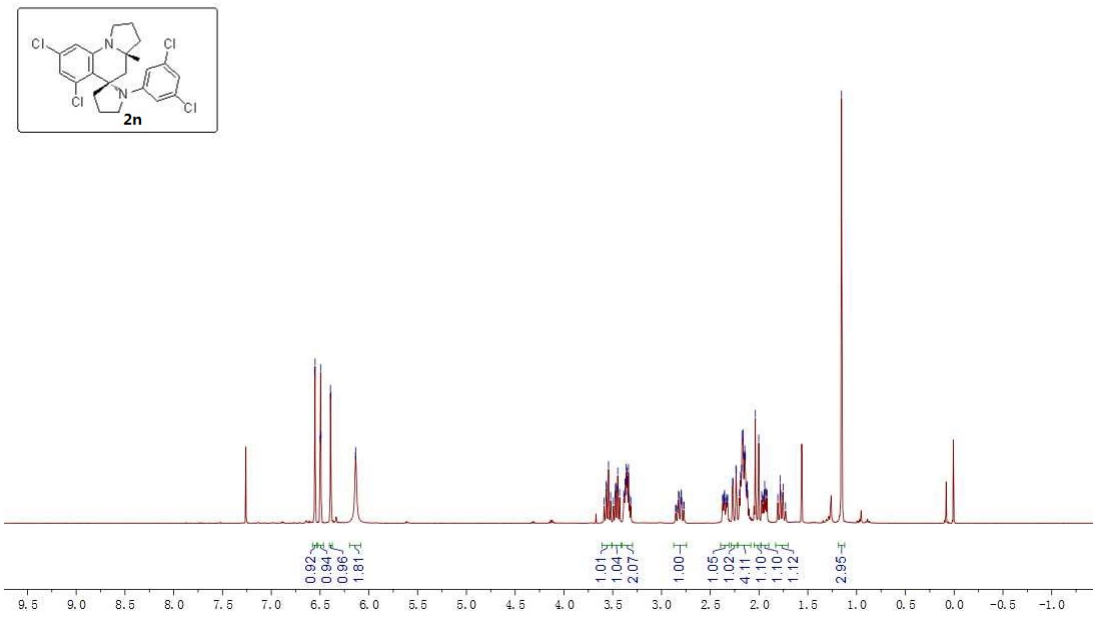
1.753
1.154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1.05
1.02
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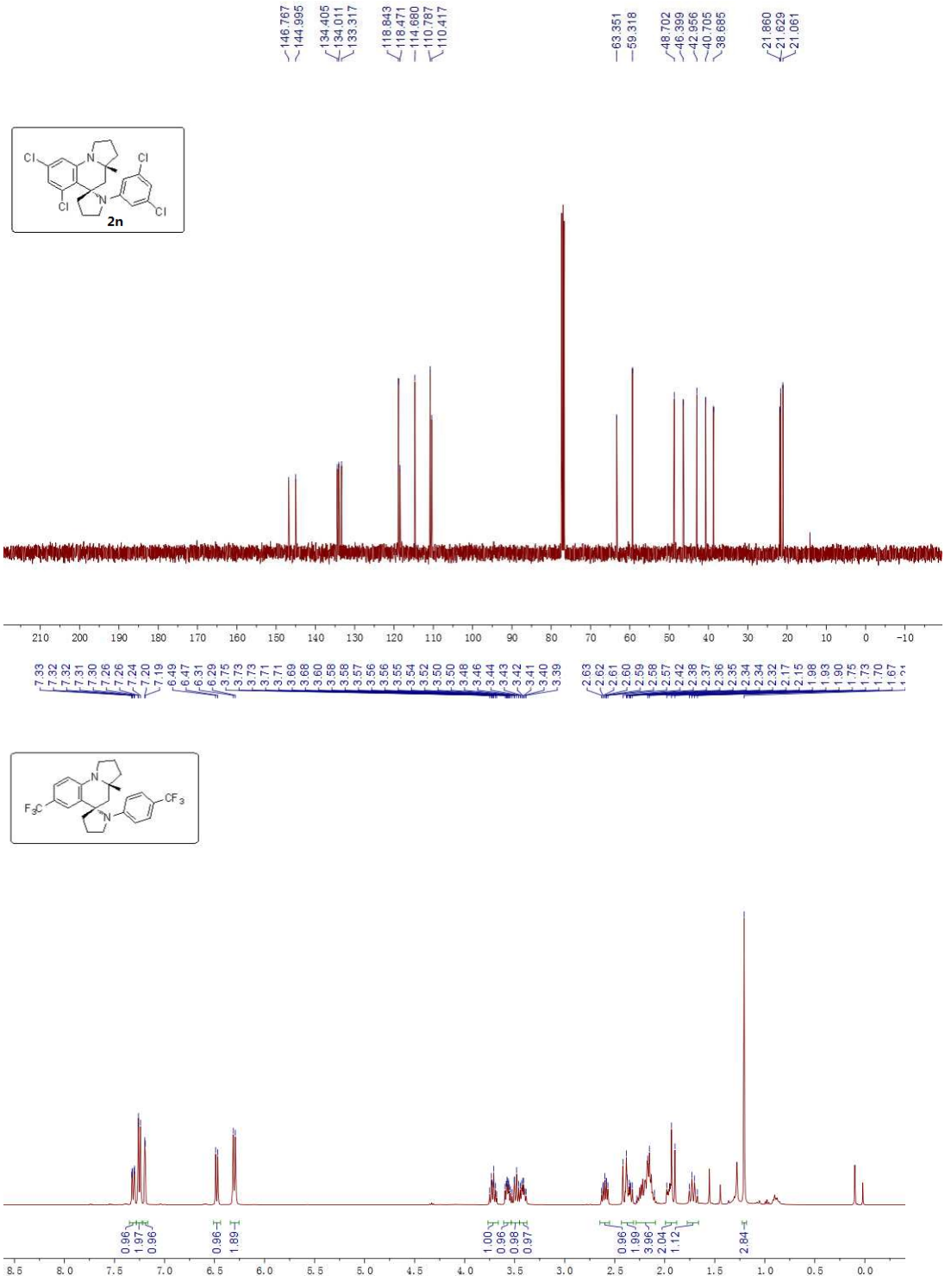
1.10
1.12
2.95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110.417
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48.702
46.399
42.956
40.705
38.685
21.860
21.629
21.061
2n
7.33
7.32
7.32
7.31
7.30
7.26
7.26
7.24
7.20
7.19
6.49
6.47
6.31
6.29
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3.73
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3.71
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3.58
3.57
3.56
3.56
3.55
3.54
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3.50
3.48
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3.43
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3.41
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3.39
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2.62
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2.60
2.59
2.58
2.57
2.42
2.38
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1.90
1.75
1.73
1.70
1.67
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1.97
0.96
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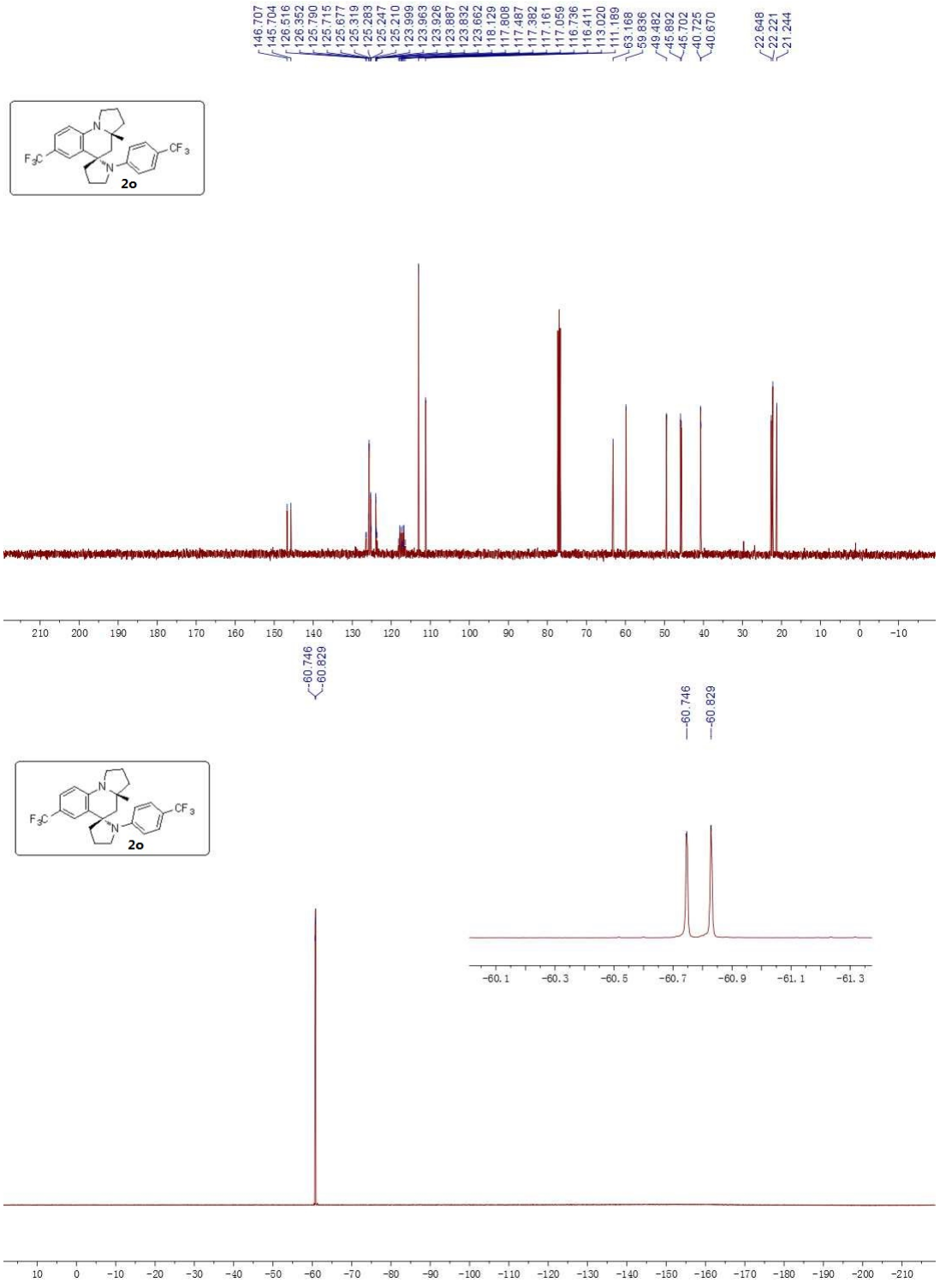
2.84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123.963
123.926
123.887
123.832
123.662
118.129
117.808
117.487
117.382
117.161
117.059
116.736
116.411
113.020
111.189
63.168
59.836
49.482
45.892
45.702
40.725
40.670
22.648
22.221
21.244
2o
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
-60.746
-60.829
-60.746
-60.829
2o
-60.1 -60.3 -60.5 -60.7 -60.9 -61.1 -61.3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210


7.312
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7.285
7.111
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6.719
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6.536
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6.449
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6.429
5.165
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3.319
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2.024
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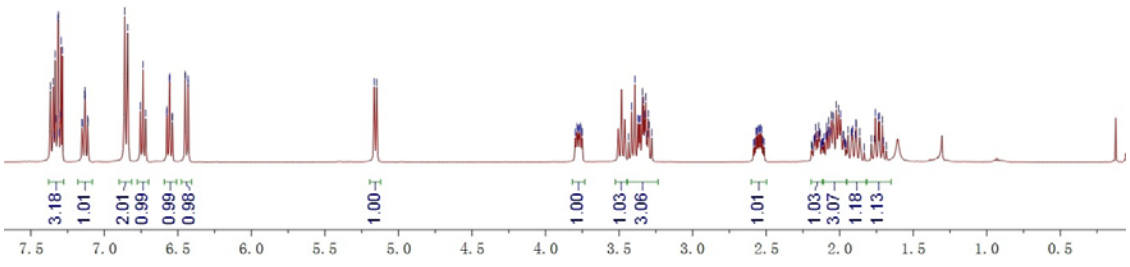
1.710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1.03
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


148.775
143.102
129.285
128.748
127.990
122.898
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111.177
110.193
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56.373
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46.539
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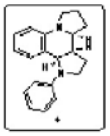
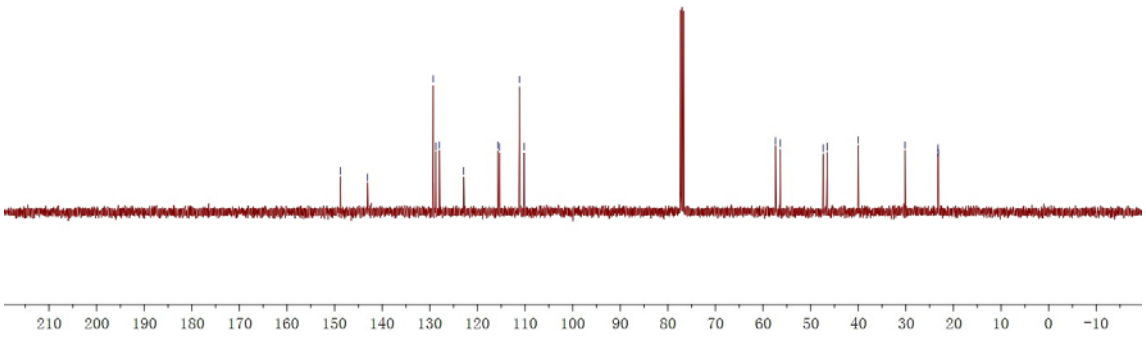
23.165

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200
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140
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120
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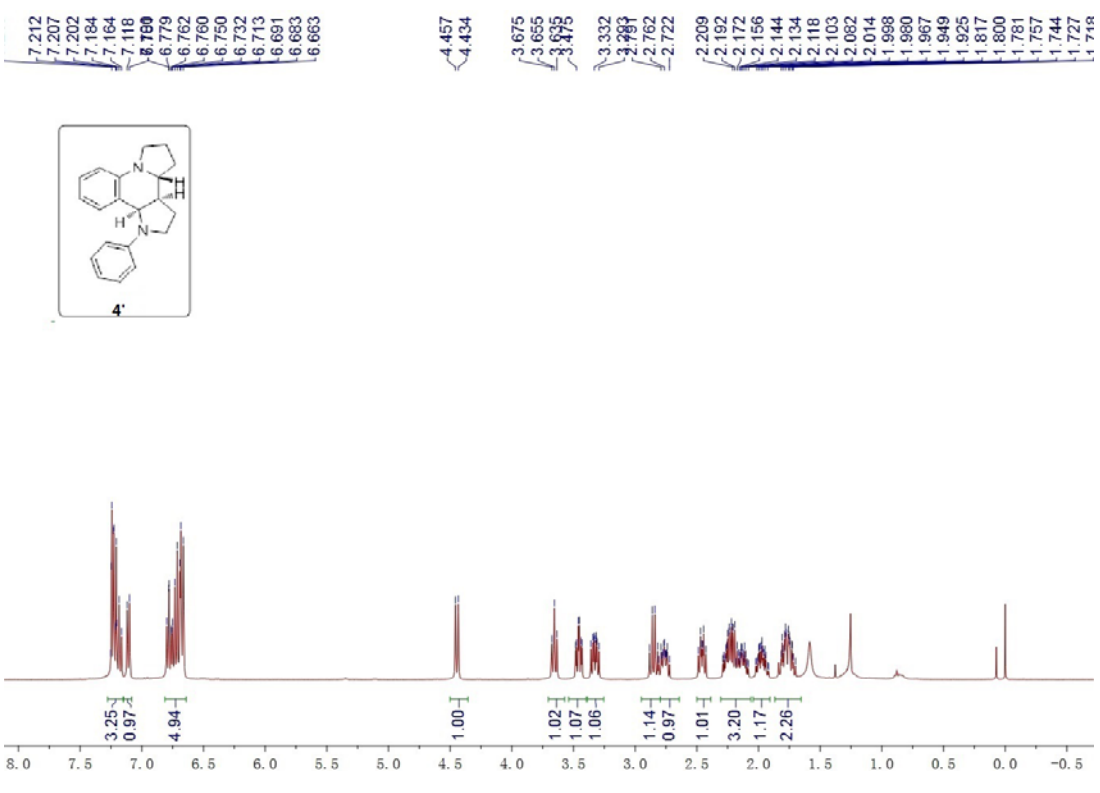
100
90
80
70
60
50
40
30
20
10
0
-10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6.683
6.663
4.457
4.434
3.675
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3.475
3.332
2.762
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1.925
1.817
1.800
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1.757
1.744
1.727
4'
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0.97
4.94
1.00
1.02
1.07
1.06
1.14
0.97
1.01
3.20
1.17
2.26
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7.5
7.0
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6.0
5.5
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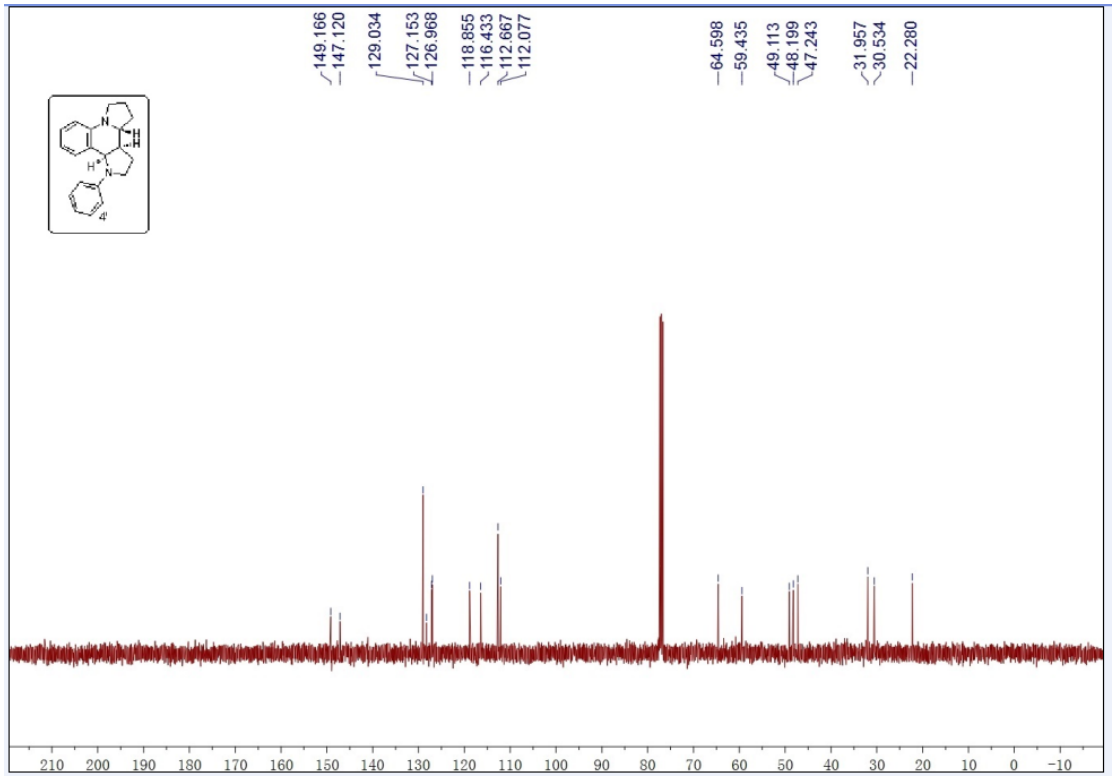
-0.5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112.667
112.077
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59.435
49.113
48.199
47.243
31.957
30.534
22.280
4'
210
200
190
180
170
160
150
140
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120
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100
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50
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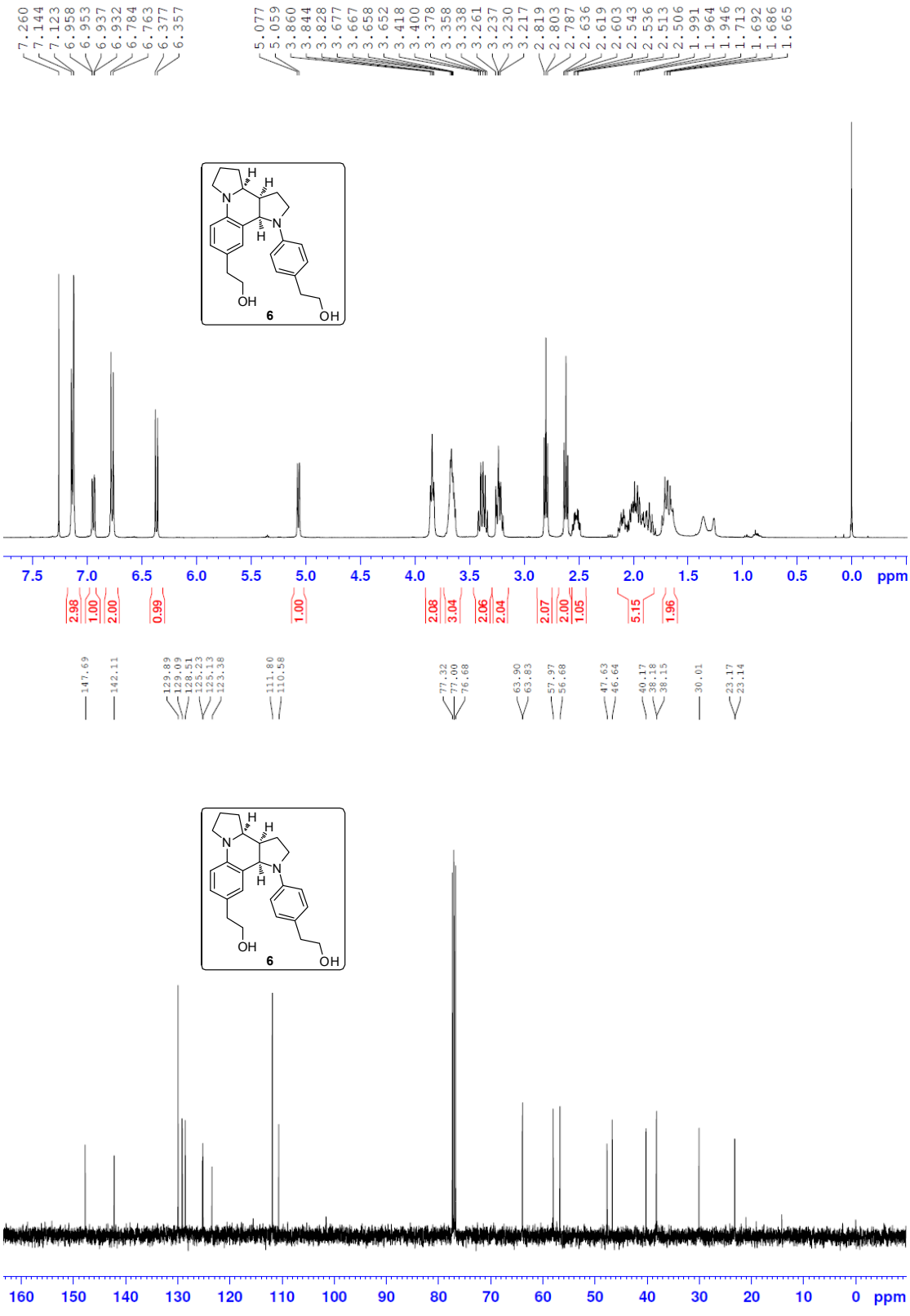
0
-10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2.536
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1.692
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OH
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OH
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6.5
6.0
5.5
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4.5
4.0
3.5
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2.0
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1.0
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ppm
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2.06
2.04
2.07
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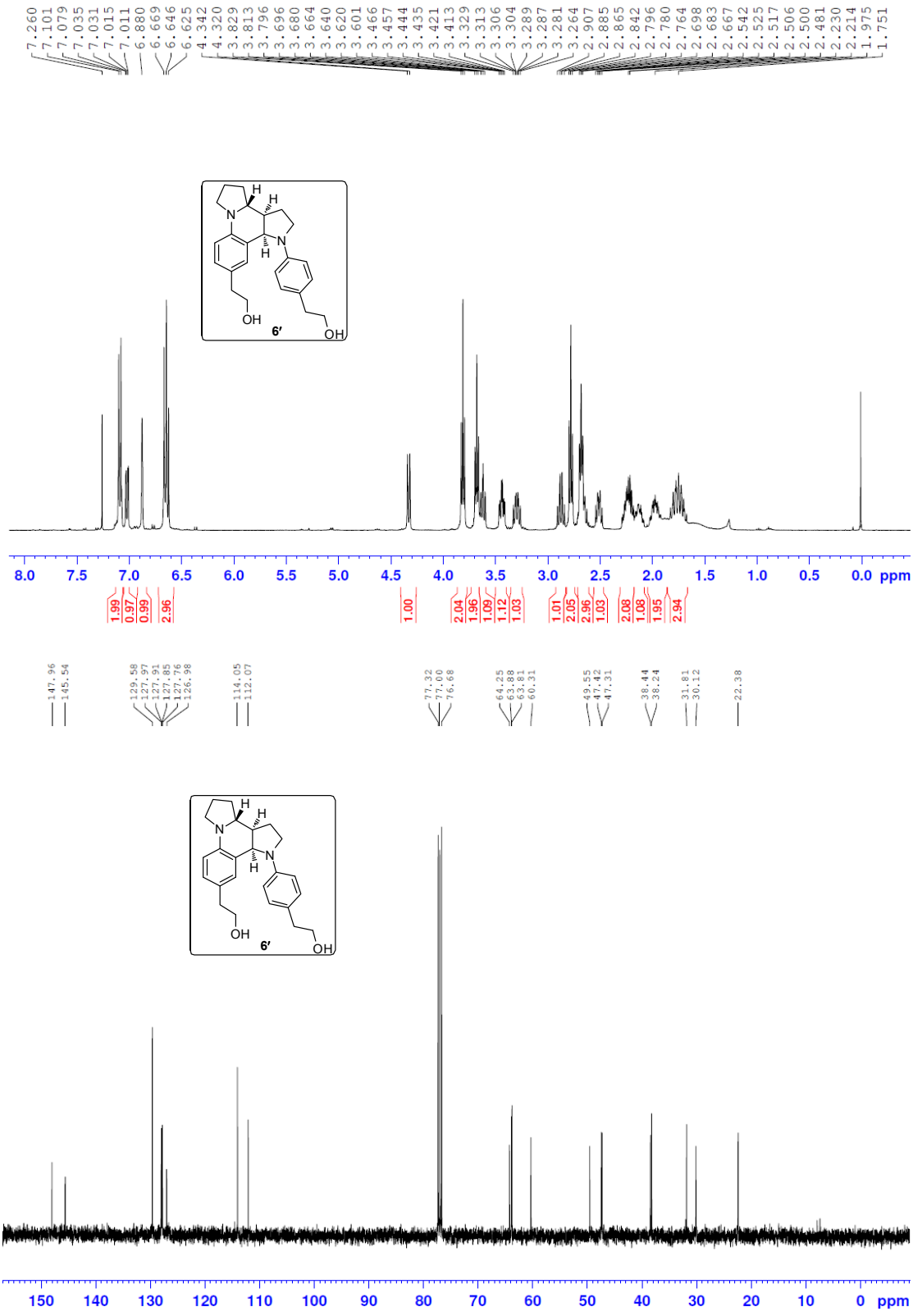
63.90
63.83
57.97
56.68
47.63
46.64
40.17
38.18
38.15
30.01
23.17
23.14
OH
6
OH
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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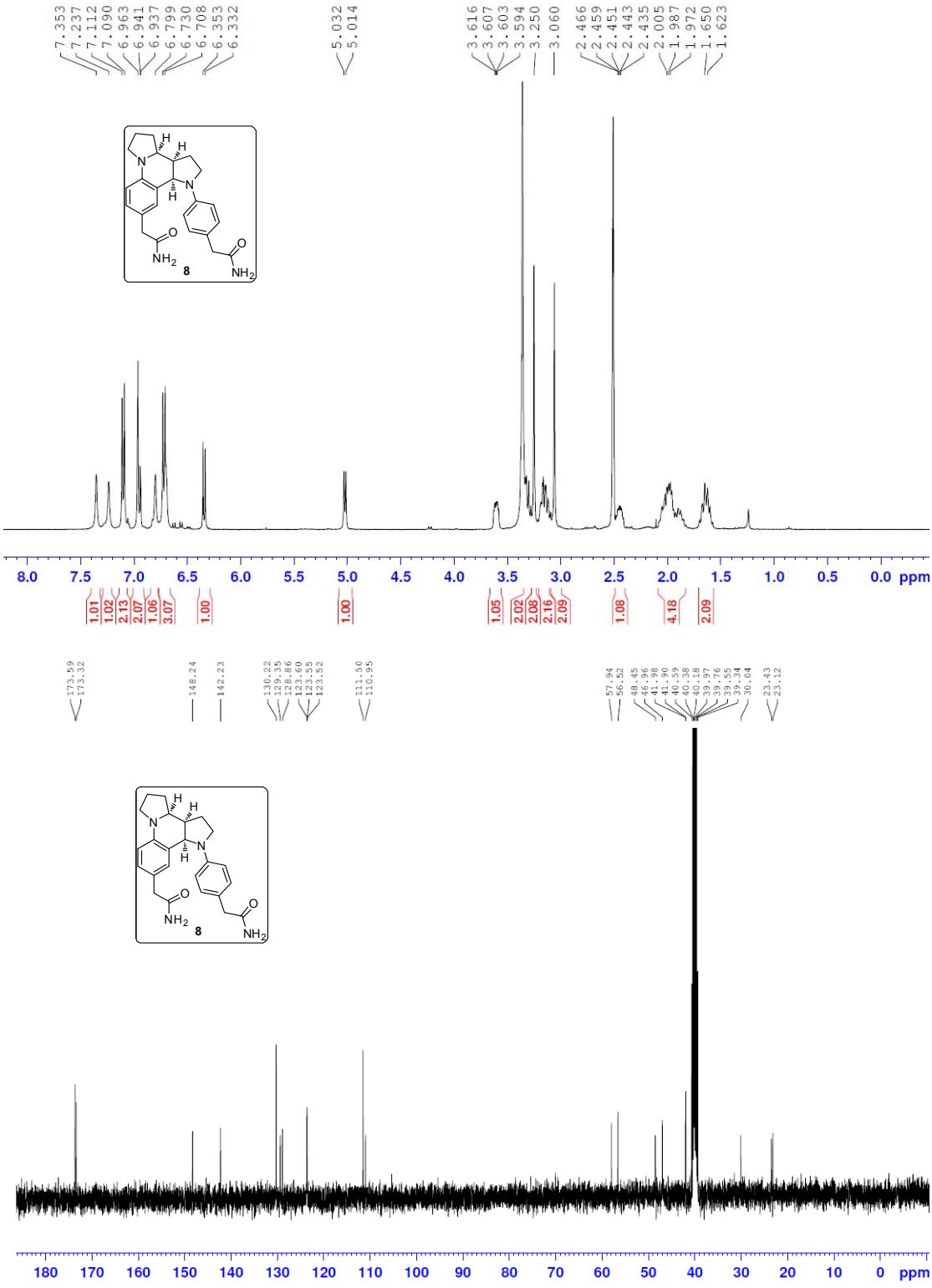
7.101
7.079
7.035
7.031
7.015
7.011
6.880
6.669
6.646
6.625
4.342
4.320
3.829
3.813
3.796
3.696
3.680
3.664
3.640
3.620
3.601
3.466
3.457
3.444
3.435
3.421
3.413
3.329
3.313
3.306
3.304
3.289
3.287
3.281
3.264
2.907
2.885
2.865
2.842
2.796
2.780
2.764
2.698
2.683
2.667
2.542
2.525
2.517
2.506
2.500
2.481
2.230
2.214
1.975
1.751
OH
6′
OH
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.99
0.97
0.99
2.96
1.00
2.04
1.96
1.09
1.12
1.03
1.01
2.05
2.96
1.03
2.08
1.08
1.95
2.94
147.96
145.54
129.58
127.97
127.91
127.85
127.76
126.98
114.05
112.07
77.32
77.00
76.68
64.25
63.88
63.81
60.31
49.55
47.42
47.31
38.44
38.24
31.81
30.12
22.38
OH
6′
OH
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm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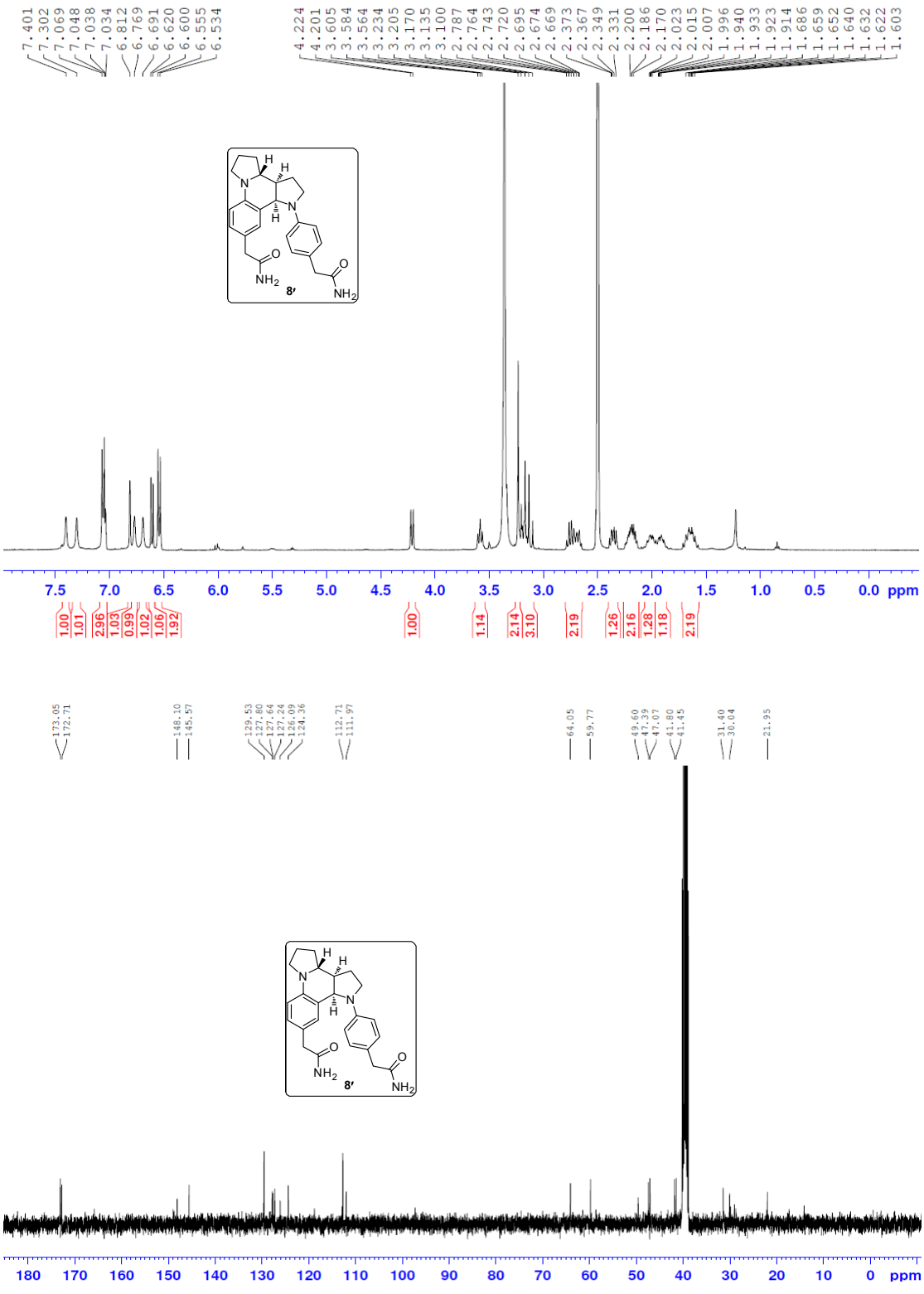
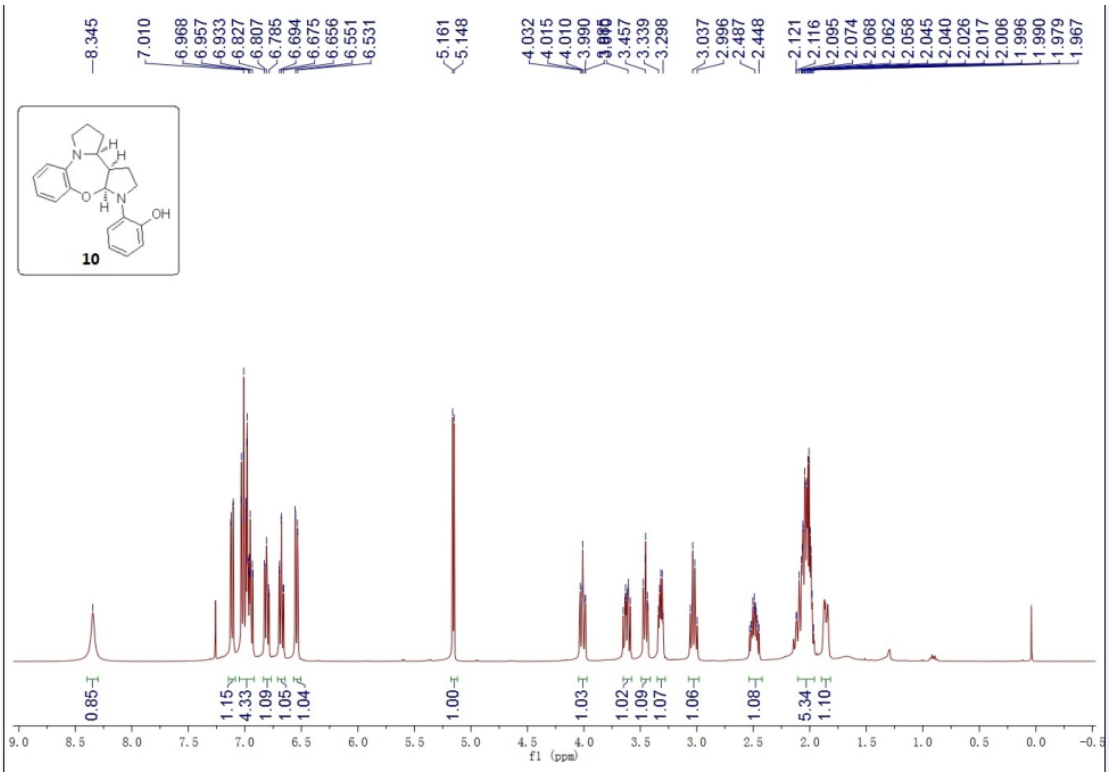
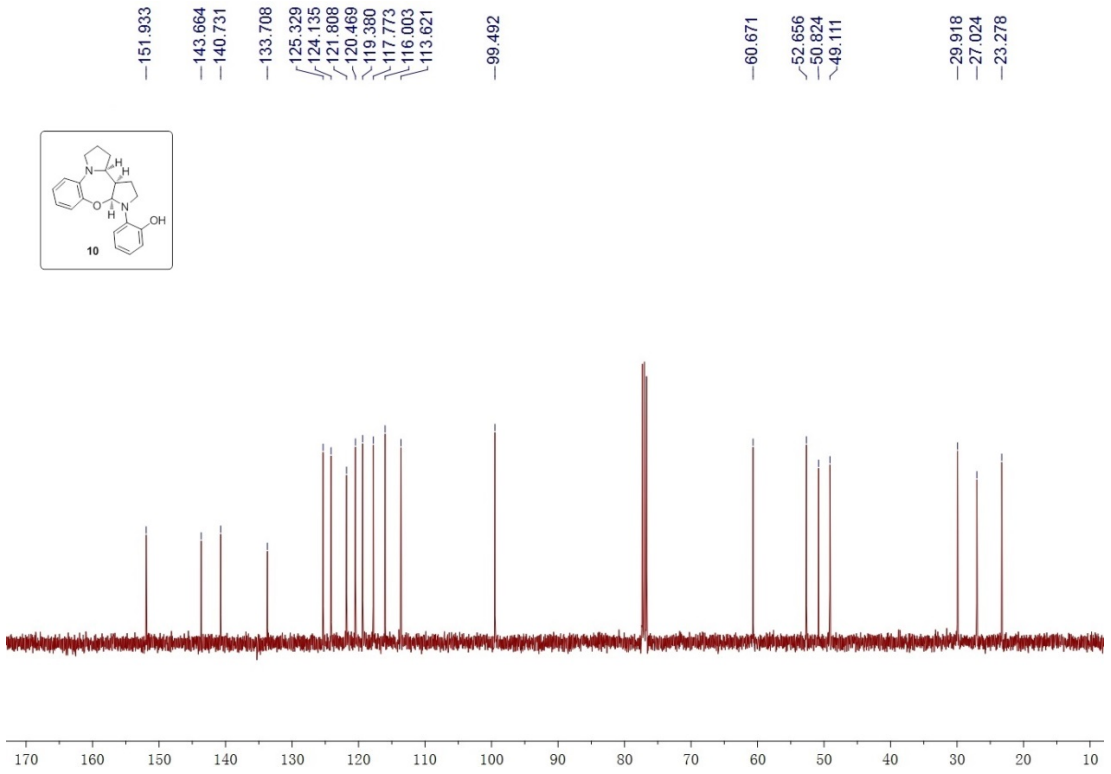
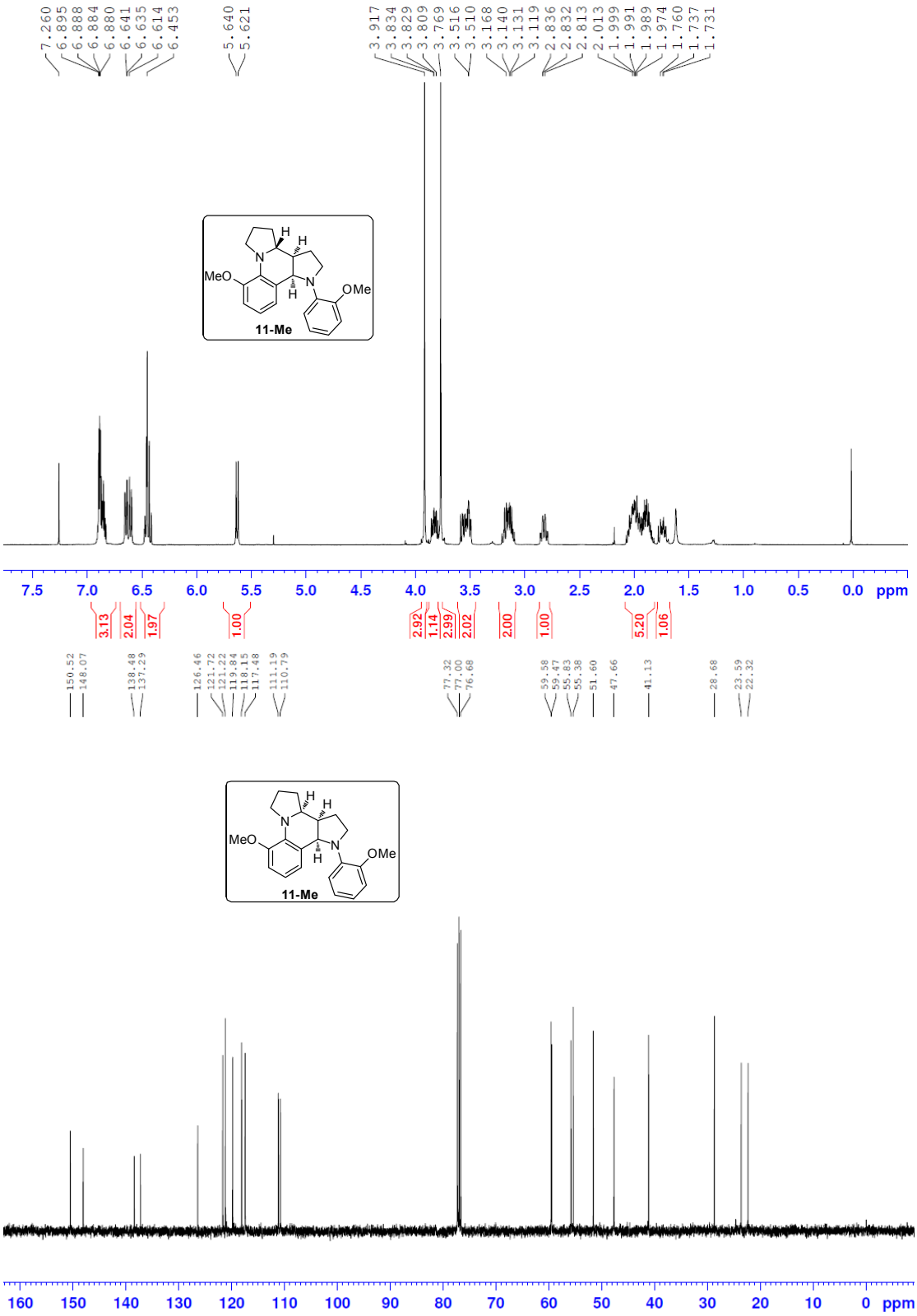
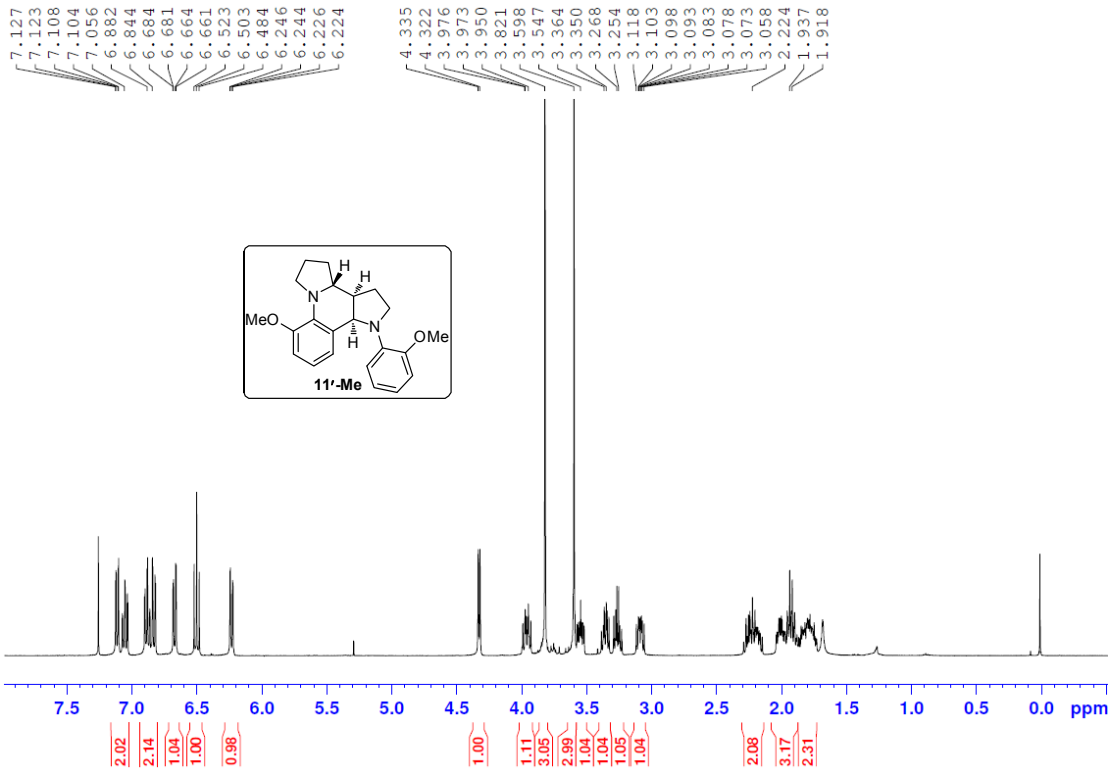
7.237
7.112
7.090
6.963
6.941
6.937
6.799
6.730
6.708
6.353
6.332
5.032
5.014
3.616
3.607
3.603
3.594
3.250
3.060
2.466
2.459
2.451
2.443
2.435
2.005
1.987
1.972
1.650
1.623
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.01 1.02 2.13 2.07 1.06 3.07 1.00 1.00 1.05 2.02 2.08 2.16 2.09 1.08 4.18 2.09
173.59
173.32
148.24
142.23
130.22
129.35
128.86
123.60
123.55
123.52
111.50
110.95
57.94
56.52
48.45
46.66
41.98
41.90
40.59
40.38
40.18
39.97
39.76
39.55
39.34
30.04
23.43
23.12
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

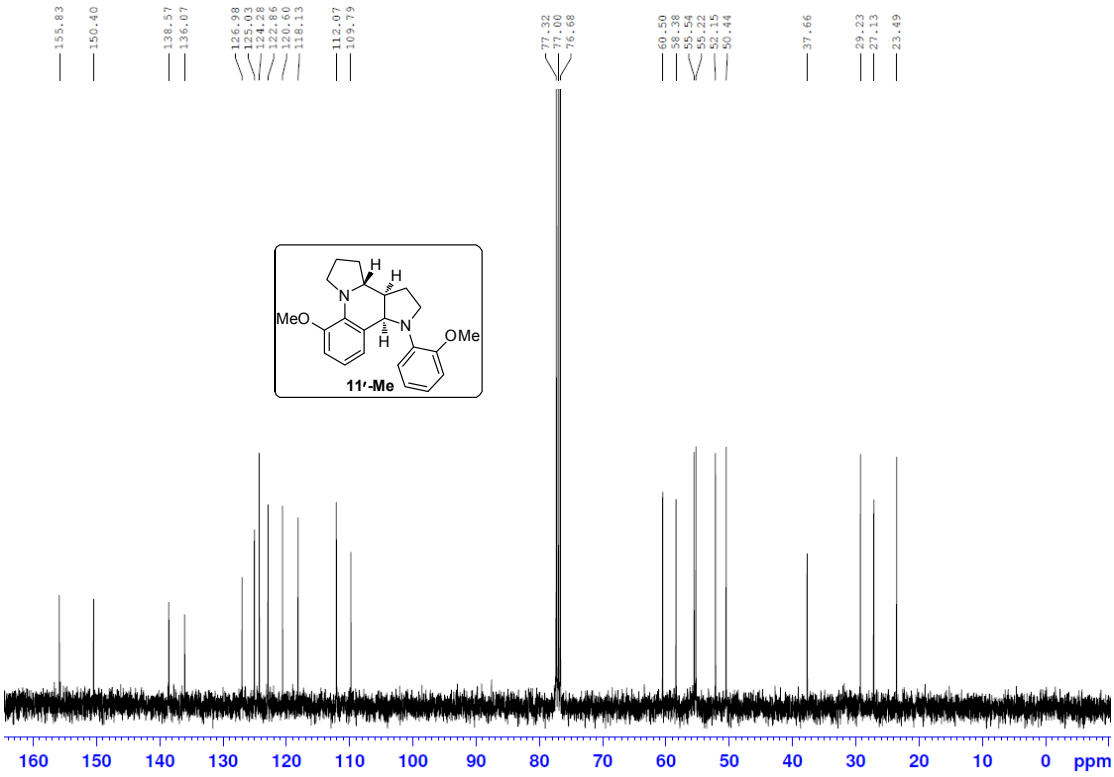

7.401
7.302
7.069
7.048
7.038
7.034
6.812
6.769
6.691
6.620
6.600
6.555
6.534
4.224
4.201
3.605
3.584
3.564
3.234
3.205
3.170
3.135
3.100
2.787
2.764
2.743
2.720
2.695
2.674
2.669
2.373
2.367
2.349
2.331
2.200
2.186
2.170
2.023
2.015
2.007
1.996
1.940
1.933
1.923
1.914
1.686
1.659
1.652
1.640
1.632
1.622
1.603
8′
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.00
1.01
2.96
1.03
0.99
1.02
1.06
1.92
1.00
1.14
2.14
3.10
2.19
1.26
2.16
1.28
1.18
2.19
173.05
172.71
148.10
145.57
129.53
127.80
127.64
127.44
126.09
124.36
112.71
111.97
64.05
59.77
49.60
47.39
47.07
41.80
41.45
31.40
30.04
21.95
8′
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


8.345
7.010
6.968
6.957
6.933
6.827
6.807
6.785
6.694
6.675
6.656
6.551
6.531
5.161
5.148
4.032
4.015
4.010
3.990
3.457
3.339
3.298
3.037
2.996
2.487
2.448
2.121
2.116
2.095
2.074
2.068
2.062
2.058
2.045
2.040
2.026
2.017
2.006
1.996
1.990
1.979
1.967
10
0.85
1.15
4.33
1.09
1.05
1.04
1.00
1.03
1.02
1.09
1.07
1.06
1.08
5.34
1.10
f1 (ppm)


151.933
143.664
140.731
133.708
125.329
124.135
121.808
120.469
119.380
117.773
116.003
113.621
99.492
60.671
52.656
50.824
49.111
29.918
27.024
23.278
10


7.260
6.895
6.888
6.884
6.880
6.641
6.635
6.614
6.453
5.640
5.621
3.917
3.834
3.829
3.809
3.769
3.516
3.510
3.168
3.140
3.131
3.119
2.836
2.832
2.813
2.013
1.999
1.991
1.989
1.974
1.760
1.737
1.731
MeO
OMe
11-Me
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
3.13 2.04 1.97 1.00 2.92 1.14 2.99 2.02 2.00 1.00 5.20 1.06
150.52
148.07
138.48
137.29
126.46
121.72
121.22
119.84
118.15
117.48
111.19
110.79
77.32
77.00
76.68
59.58
59.47
55.83
55.38
51.60
47.66
41.13
28.68
23.59
22.32
MeO
OMe
11-Me
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.127
7.123
7.108
7.104
7.056
6.882
6.844
6.684
6.681
6.664
6.661
6.523
6.503
6.484
6.246
6.244
6.226
6.224
4.335
4.322
3.976
3.973
3.950
3.821
3.598
3.547
3.364
3.350
3.268
3.254
3.118
3.103
3.098
3.093
3.083
3.078
3.073
3.058
2.224
1.937
1.918
MeO
OMe
11′-Me
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.02
2.14
1.04
1.00
0.98
1.00
1.11
3.05
2.99
1.04
1.04
1.05
1.04
2.08
3.17
2.31


155.83
150.40
138.57
136.07
126.98
125.03
124.28
122.86
120.60
118.13
112.07
109.79
77.32
77.00
76.68
60.50
58.38
55.54
55.22
52.15
50.44
37.66
29.23
27.13
23.49
MeO
OMe
11′-Me
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm