Supporting Information

A Concise Synthesis and Bioactivity Study of Evodiamine and Its Analogues

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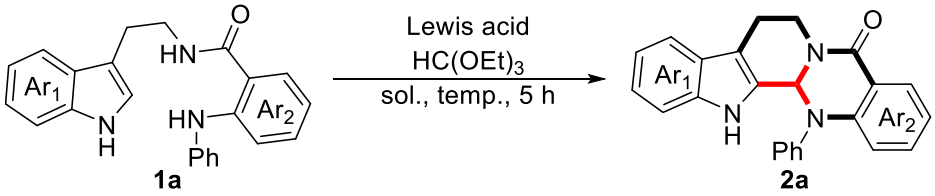
1. General information:

All reactions were carried out in a dry solvent under argon atmosphere unless otherwise noted. IR spectra were recorded as KBr pellets with absorption in cm^{-1}. NMR spectra were recorded on Bruker 400 MHz (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) spectrometers. Proton chemical shifts are reported relative to a residual solvent peak ($CDCl_3$ at 7.26 ppm, DMSO-d_6, at 2.50 ppm). Carbon chemical shifts are reported relative to a residual solvent peak ($CDCl_3$ at 77.00 ppm, DMSO-d_6 at 39.96 ppm). The following abbreviations were used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad. Fourier transform infrared spectra (FT-IR) were recorded on an Agilent Technologies Cary 630 instrument. High-resolution mass spectra (HRMS) were measured on a Brucker Daltonics Apex Ⅱ47e Specification (for HRMS). Substrates were purchased from commercial sources and used as received. Products **2a, 2g-2h, 2j-2n, 2p-2r, 2t** are known compounds.

2. Optimization of the reaction conditions:



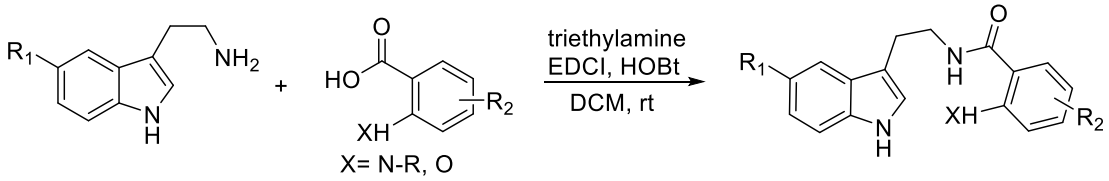
Entry	Solvent	Lewis acid	$HC(OEt)_3$ (eq)	Temp.(°C)	Yield[b] (%)
1	DMF	$AlCl_3$	3	135	**73**
2	CH_3CN	$AlCl_3$	3	135	46
3	Toluene	$AlCl_3$	3	135	28
4	DMSO	$AlCl_3$	3	135	N.R.
5	DMF	$ZnCl_2$	3	135	81
6	DMF	$ZnBr_2$	3	135	70
7	DMF	$SnCl_4$	3	135	45
8	DMF	$TiCl_4$	3	135	33
9	DMF	$BF_3•Et_2O$	3	135	93
10[c]	DMF	$BF_3•Et_2O$	3	135	91
11[d]	DMF	$BF_3•Et_2O$	3	135	75
12	DMF	/	3	135	trace
13[c]	DMF	$BF_3•Et_2O$	1	135	48
14[c]	DMF	$BF_3•Et_2O$	3	100	92
15[c]	DMF	$BF_3•Et_2O$	3	70	80
16[c]	DMF	$BF_3•Et_2O$	3	25	N.R.

Optimization of reaction conditions.[a] [a]Reaction conditions: **1a** (1 eq, 0.10 mmol), $HC(OEt)_3$ (3 eq, 0.30 mmol), Lewis acid (1 eq, 0.10 mmol), solvent (1 mL) under Ar atmosphere for 5h. [b]Isolated

yields. [c]BF_3•Et_2O was used in 0.5 eq. [d]BF_3•Et_2O was used in 0.3 eq. N.R.=no result.

3. General procedure for the synthesis:

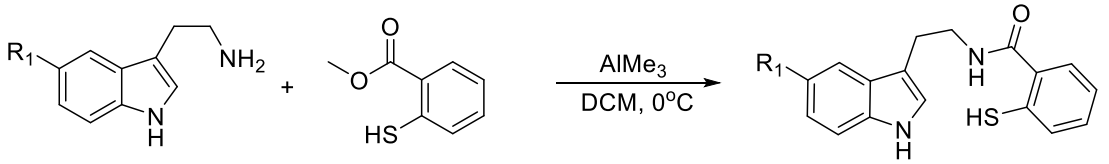
General Method A: Typical Experimental Procedure for Synthesis of N-(2-(1H-indol-3-yl)ethyl)-2-(phenylamino)benzamide[1]:



For 1 (1a as an example)

A test tube equipped with a magnetic stir bar was charged with tryptamine (1 mmol), 2-(phenylamino)benzoic acid (1 mmol), EDCl (1.2 mmol), HOBt(1.2 mmol), triethylamine (2.5 mmol) and DCM (10 mL). The resulting mixture was stirred at room temperature for 10 h, then added 25 mL water and 10 mL saturated brine solution to the mixture and extracted with DCM for 3 times (3 × 25 mL). The combined organic extracts were concentrated and the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) to give N-(2-(1H-indol-3-yl)ethyl)-2-(phenylamino)benzamide as white solid.

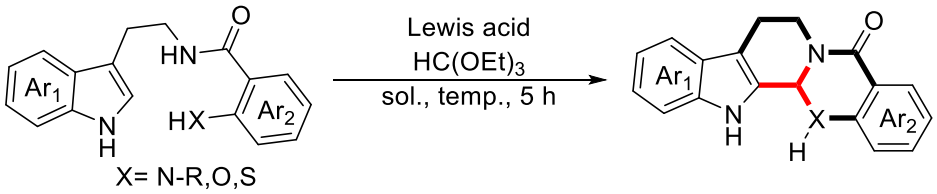
General Method B: Typical Experimental Procedure for Synthesis of N-(2-(1H-indol-3-yl)ethyl)-2-mercaptobenzamide[2]:



For 1 (1r as an example)

A test tube equipped with a magnetic stir bar was charged with tryptamine (1.2 mmol), methyl 2-mercaptobenzoate (1 mmol), $AlMe_3$ (1.2 mmol), DCM (10 mL) at 0℃. The resulting mixture was moved to room temperature and stirred for 12 h, then quenched with HCl (5 M) aqueous solution, and extracted with DCM for 3 times (3 × 25 mL), the combined organic extracts were concentrated and the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to give N-(2-(1H-indol-3-yl)ethyl)-2-mercaptobenzamide as white solid.

General Method C:



For 2 (2a as an example)

A mixture of N-(2-(1H-indol-3-yl)ethyl)-2-(phenylamino)benzamide **1a** (0.1 mmol), triethoxymethane (0.30 mmol), BF_3•Et_2O (0.05 mmol, 0.5 eq) and DMF (1.0 mL) were added and stirred at 100 ℃ for 5 h under argon atmosphere. Then, the mixture was added 25 mL water and 10 mL saturated brine solution to the mixture and extracted with ethyl acetate for 3 times (3 × 25 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/ ethyl acetate = 4/1) to afford the product **2a** as white solid.

(**2h**-**2q** was obtained at 135 ℃; **2r**-**2t** was obtained at room temperature in DCM.)

Reference:

(1) T. M. Rose, C. A. Reilly, C. E. Deering-Rice, C. Brewster and C. Brewster, *Biorg. Med. Chem. Lett.*, 2014, **24**, 5695-5698.

(2) A. Correa, I. Tellitu, E. Domínguez and R. SanMartin, *Org. Lett.*, 2006, **8**, 4811-4813.

4. General procedure for the Biological activity valuation:

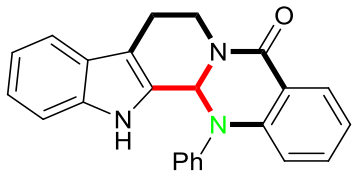
In Vitro Cytotoxicity Assay：

Cells were plated in 96-well microtiter plates at a density of 5 × 10^3/well and incubated in a humidified atmosphere with 5% CO_2 at 37 °C for 24 h. Test compounds were added onto triplicate wells with different concentrations and 0.4% DMSO for the control. After they had been incubated for 72 h, 10 μL of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) solution (5 mg/mL) was added to each well, and the plate was incubated for an additional 4 h. The formazan was dissolved in 100 μL of DMSO. The absorbance (OD) was read on a microplate reader at 490 nm. The concentration causing 50% inhibition of cell growth (IC_{50}) was determined by the Logit method. All experiments were performed three times.

DAPI staining：

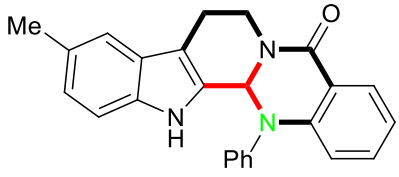
SMMC-7721 cells (1 × 10^4) were plated in 24-well plates and incubated with the test compound 2b with different concentrations for 72 h. Then the SMMC-7721 cells were washed with phosphate buffer saline (PBS) and immobilized with 4% paraformaldehyde PBS solution at room temperature for 10 min. After that, DAPI was added to reach a final concentration of 5 μg/ml and further incubated for 20 min. The immobilized cells were washed with PBS and viewed and photographed.

5. NMR Data:



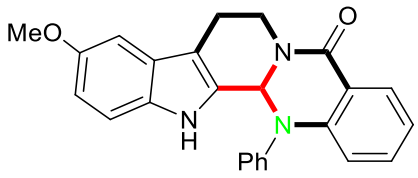
2a

14-phenyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-b]quinazolin-5(13H)-one (2a): 33.4mg, white solid , Yield 92%; ^{1}H NMR (400 MHz, DMSO) δ 11.30 (s, 1H), 7.84 (dd, J = 7.9, 1.6 Hz, 1H), 7.45 – 7.30 (m, 5H), 7.29 – 7.23 (m, 2H), 7.17 – 7.00 (m, 4H), 6.95 (t, J = 7.4 Hz, 1H), 6.61 (s, 1H), 4.59 (dd, J = 13.1, 5.8 Hz, 1H), 3.41 (d, J = 7.8 Hz, 1H), 2.90 (m, J = 17.4, 11.5, 6.1, 2.0 Hz, 1H), 2.64 (dd, J = 15.7, 4.8 Hz, 1H).^{13}C NMR (100 MHz, DMSO) δ 165.0, 146.8, 144.9, 136.5, 133.6, 132.6, 129.6, 128.4, 126.9, 124.9, 124.0, 122.6, 122.0, 121.5, 121.2, 119.3, 118.4, 112.2, 111.6, 72.3, 43.0, 19.6. IR (KBr ν/cm^{-1}) 3243, 2374, 2126, 1638, 1605, 1474, 1420, 1306, 1068, 744; HRMS (ESI^{+}) m/z calcd for $C_{24}H_{20}N_3O^{+}$ $(M+H)^{+}$ 366.1601, found 366.1603.



2b

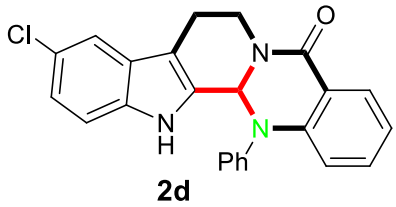
10-methyl-14-phenyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-b]quinazolin-5(13H)-one (2b) : 34.4 mg, white solid , Yield 91%; ^{1}H NMR (400 MHz, DMSO) δ 11.12 (s, 1H), 7.85 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.12 – 7.07 (m, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.59 (s, 1H), 4.58 (dd, *J* = 13.1, 5.6 Hz, 1H), 3.40 (dd, *J* = 12.4, 4.7 Hz, 1H), 2.93 – 2.81 (m, 1H), 2.61 (dd, *J* = 15.4, 4.4 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 165.0, 146.8, 144.9, 134.9, 133.6, 132.6, 129.7, 128.4, 127.8, 127.2, 124.9, 124.0, 123.7, 122.6, 121.5, 121.3, 118.1, 111.9, 111.2, 72.4, 43.0, 21.6, 19.6. IR (KBr ν/cm^{-1}) 3246, 2375, 1645, 1605, 1489, 1382, 1218, 1031, 924, 755; HRMS (ESI^{+}) m/z calcd for $C_{25}H_{22}N_3O^{+}(M+H)^{+}$ 380.1757, found 380.1755.



2c

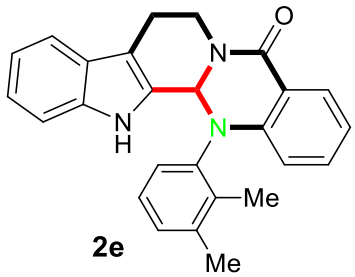
10-methoxy-14-phenyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-b]quinazolin-5(13H)-one (2c) : 36.3 mg, white solid , Yield 93%; ^{1}H NMR (400 MHz, DMSO) δ 11.09 (s, 1H), 7.84 (d, *J* = 7.2 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.34 (d, *J* = 7.2 Hz, 2H),

7.25 (d, *J* = 7.4 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 1H), 7.17 – 7.11 (m, 1H), 7.09 (d, *J* = 8.1 Hz, 1H), 7.03 (t, *J* = 7.1 Hz, 1H), 6.87 (s, 1H), 6.70 (d, *J* = 7.4 Hz, 1H), 6.58 (s, 1H), 4.58 (dd, *J* = 12.5, 5.2 Hz, 1H), 3.72 (s, 3H), 3.38 (s, 1H), 2.88 (s, 1H), 2.61 (d, *J* = 12.2 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ 165.0, 153.7, 146.8, 144.8, 133.6, 133.3, 131.6, 129.7, 128.4, 127.3, 124.9, 124.0, 122.6, 121.5, 121.2, 112.9, 112.2, 111.5, 100.3, 72.4, 55.76, 43.0, 19.7. IR (KBr ν/cm^{-1}) 3263, 2340, 1644, 1605, 1487, 1418, 1383, 1217, 1030, 917, 755; HRMS (ESI$^+$) m/z calcd for $C_{25}H_{22}N_3O_2^+$ $(M+H)^+$ 396.1707, found 396.1709.



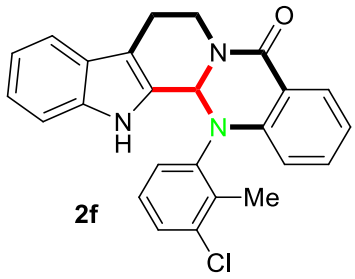
2d

10-chloro-14-phenyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-b]quinazolin-5(13H)-one (2d) : 28.1 mg, white solid , Yield 71%;^{1}H NMR (400 MHz, DMSO) δ 11.49 (s, 1H), 7.84 (dd, J = 7.8, 1.7 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.39 – 7.29 (m, 3H), 7.29 – 7.23 (m, 2H), 7.17 – 7.01 (m, 4H), 6.63 (s, 1H), 4.58 (dd, J = 13.2, 5.8 Hz, 1H), 3.49 – 3.34 (m, 1H), 2.94 – 2.80 (m, 1H), 2.64 (dd, J = 15.7, 4.9 Hz, 1H).^{13}C NMR (100 MHz, DMSO) δ 164.9, 146.7, 144.7, 134.9, 134.6, 133.7, 129.7, 128.4, 128.0, 124.9, 123.93, 123.9, 122.7, 122.0, 121.5, 121.1, 117.8, 113.6, 111.5, 72.1, 42.8, 19.4. IR (KBr ν/cm^{-1}) 3244, 2376, 2187, 1645, 1605, 1489, 1474, 1385, 1216, 1033, 927, 756; HRMS (ESI$^+$) m/z calcd for $C_{24}H_{19}ClN_3O^+$ $(M+H)^+$ 400.1211, found 400.1214.



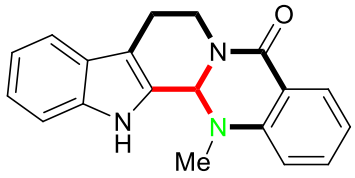
2e

14-(2,3-dimethylphenyl)-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-b]quinazolin-5(13H)-one (2e) : 36.2 mg, white solid , Yield 94%; ^{1}H NMR (400 MHz, DMSO) δ 10.78 (d, *J* = 30.5 Hz, 1H), 7.83 (dd, *J* = 31.6, 7.9 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.33 (m, *J* = 28.2, 20.7, 8.4 Hz, 3H), 7.22 – 6.84 (m, 5H), 6.54 (dd, *J* = 20.6, 8.3 Hz, 1H), 6.35 (d, *J* = 59.1 Hz, 1H), 4.33 (m, *J* = 240.7, 13.7, 6.4 Hz, 1H), 3.29 – 2.83 (m, 2H), 2.80 – 2.62 (m, 1H), 2.29 – 2.11 (m, 6H). ^{13}C NMR (100 MHz, DMSO) δ 165.6, 147.0, 143.7, 138.9, 136.5, 135.2, 133.9, 132.5, 129.3, 128.5, 127.9, 126.7, 122.1, 120.3, 119.3, 118.4, 112.0, 71.7, 60.2, 42.6, 20.7, 19.5, 15.4. IR (KBr ν/cm^{-1}) 3355, 2345, 1638, 1605, 1472, 1306, 1285, 1031, 895, 747; HRMS (ESI$^+$) m/z calcd for $C_{26}H_{24}N_3O^+$ $(M+H)^+$ 394.1914, found 394.1911.



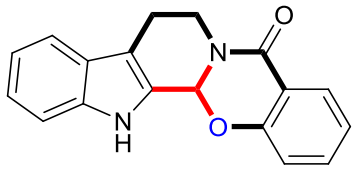
2f

14-(3-chloro-2-methylphenyl)-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-b] quinazolin-5(13H)-one (2f) : 36.9 mg, white solid , Yield 90%; ^{1}H NMR (400 MHz, DMSO) δ 10.91 (d, *J* = 19.8 Hz, 1H), 7.86 (dd, *J* = 17.9, 7.8 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.38 (p, *J* = 8.9, 8.3 Hz, 4H), 7.33 – 7.12 (m, 1H), 7.06 (d, *J* = 6.9 Hz, 1H), 6.96 (t, *J* = 7.4 Hz, 2H), 6.63 (dd, *J* = 23.4, 8.2 Hz, 1H), 6.42 (d, *J* = 67.4 Hz, 1H), 4.63 (p, *J* = 8.1, 7.0 Hz, 1H), 3.31 – 2.88 (m, 2H), 2.71 (td, *J* = 15.4, 4.5 Hz, 1H), 2.34 (d, *J* = 24.7 Hz, 3H).^{13}C NMR (100 MHz, DMSO) δ 165.3, 146.7, 135.1, 134.0, 134.0, 131.7, 129.2, 128.7, 128.1, 127.8, 126.8, 122.3, 121.3, 120.8, 119.4, 118.7, 112.2, 100.0, 71.2, 42.4, 19.5, 16.7. IR (KBr ν/cm^{-1}) 3355, 2378, 1638, 1605, 1472, 1306, 1163, 1031, 868, 747, 710; HRMS (ESI^{+}) m/z calcd for $C_{25}H_{21}ClN_3O^{+}$ $(M+H)^{+}$ 414.1368, found 414.1369.



2g
Evodiamine

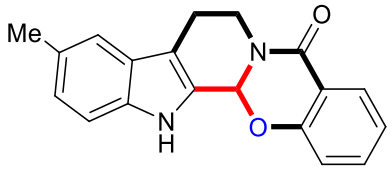
14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-b]quinazolin-5(13H)-one (2g) : 27.8 mg, white solid , Yield 92%; ^{1}H NMR (400 MHz, DMSO) δ 11.06 (s, 1H), 7.80 (dd, J = 7.8, 1.6 Hz, 1H), 7.48 (dd, J = 8.2, 5.8 Hz, 2H), 7.36 (d, J = 8.1 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 7.07 – 6.94 (m, 3H), 6.13 (s, 1H), 4.63 (dd, J = 12.9, 5.1 Hz, 1H), 3.20 (td, J = 12.1, 4.7 Hz, 1H), 2.93 (d, J = 10.0 Hz, 1H), 2.88 (s, 3H), 2.79 (dd, J = 15.5, 4.6 Hz, 1H).^{13}C NMR (100 MHz, DMSO) δ 164.7, 149.2, 136.9, 133.9, 131.0, 128.4, 126.4, 122.3, 120.7, 119.7, 119.3, 118.6, 117.9, 112.1, 111.9, 70.2, 41.3, 36.9, 19.9. IR (KBr ν/cm^{-1}) 3246, 2374, 1638, 1507, 1452, 1083, 922, 747; HRMS (ESI^{+}) m/z calcd for $C_{19}H_{18}N_3O^{+}$ $(M+H)^{+}$ 304.1444, found 304.1447.



2h

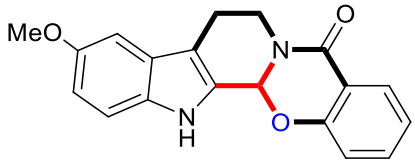
7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2h) : 19.8 mg, white solid , Yield 72%; ^{1}H NMR (400 MHz, DMSO) δ 11.52 (s, 1H), 7.91 (dd, J = 7.7, 1.7 Hz, 1H), 7.67 – 7.52 (m, 2H), 7.43 (d, J = 8.2 Hz, 1H), 7.30 – 6.97 (m, 4H), 6.68 (s, 1H), 4.73 (m, J = 12.9, 5.0, 1.9 Hz, 1H), 3.21 (td, J = 12.8, 12.4, 4.5 Hz, 1H), 2.91 (dt, J = 16.1, 12.4 Hz, 2H).^{13}C NMR (100 MHz, DMSO) δ

162.6, 157.1, 137.4, 134.8, 128.5, 128.0, 125.7, 123.2, 123.0, 119.5, 119.3, 118.8, 116.9, 112.2, 112.1, 81.6, 20.3. IR (KBr ν/cm^{-1}) 3243, 2345, 1655, 1614, 1470, 1310, 1228, 1030, 937, 751; HRMS (ESI$^+$) m/z calcd for $C_{18}H_{15}N_2O_2^+$ $(M+H)^+$ 291.1128, found 291.1126.



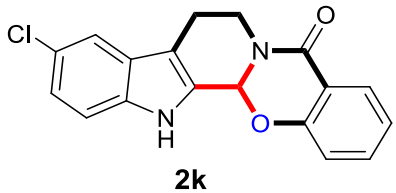
2i

10-methyl-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2i) : 22.1 mg, white solid , Yield 73%; ^{1}H NMR (400 MHz, DMSO) δ 11.36 (s, 1H), 7.90 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.36 – 7.29 (m, 2H), 7.25 – 7.19 (m, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 8.3 Hz, 1H), 6.65 (s, 1H), 4.71 (dd, *J* = 13.0, 3.3 Hz, 1H), 3.24 – 3.15 (m, 1H), 2.90 – 2.78 (m, 2H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 162.7, 157.1, 135.9, 134.8, 128.6, 128.1, 128.0, 125.9, 124.7, 123.2, 118.9, 118.9, 116.9, 112.0, 111.7, 81.7, 21.7, 20.3. IR (KBr ν/cm^{-1}) 3245, 2346, 1655, 1612, 1470, 1321, 1031, 936, 785; HRMS (ESI$^+$) m/z calcd for $C_{19}H_{17}N_2O_2^+$ $(M+H)^+$ 305.1285, found 305.1283.



2j

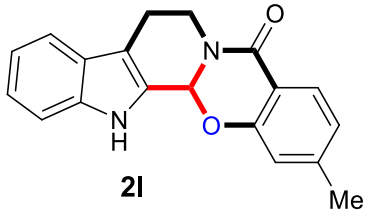
10-methoxy-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2g) : 23.5 mg, white solid , Yield 75%; ^{1}H NMR (400 MHz, DMSO) δ 11.34 (s, 1H), 7.90 (dd, J = 7.8, 1.7 Hz, 1H), 7.59 (td, J = 7.8, 1.7 Hz, 1H), 7.31 (d, J = 8.8 Hz, 1H), 7.25 – 7.18 (m, 1H), 7.16 – 7.10 (m, 1H), 7.06 (d, J = 2.5 Hz, 1H), 6.83 (dd, J = 8.8, 2.4 Hz, 1H), 6.65 (s, 1H), 4.72 (m, J = 13.0, 5.1, 1.9 Hz, 1H), 3.78 (s, 3H), 3.20 (td, J = 12.2, 4.4 Hz, 1H), 2.96 – 2.77 (m, 2H).^{13}C NMR (100 MHz, DMSO) δ 162.6, 157.0, 153.8, 134.8, 132.5, 128.5, 128.5, 125.9, 123.1, 118.8, 116.9, 113.4, 113.00, 111.9, 100.9, 81.6, 55.8, 20.4. IR (KBr ν/cm^{-1}) 3366, 2369, 1653, 1616, 1470, 1113, 1066, 1029, 980, 762; HRMS (ESI$^+$) m/z calcd for $C_{19}H_{17}N_2O_3^+$ $(M+H)^+$ 321.1234, found 321.1238.



2k

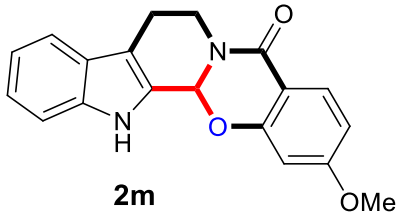
10-chloro-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2k) : 19.0 mg, white solid , Yield 60%; ^{1}H NMR (400 MHz, DMSO) δ 11.76 (s, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.64 (s, 1H), 7.62 – 7.57 (m, 2H), 7.44 (d, J = 8.7 Hz, 1H), 7.26 – 7.17 (m, 2H), 7.14 (d, J = 8.3 Hz, 1H), 6.68 (s, 1H), 4.71 (dd, J = 13.3, 5.0 Hz, 1H), 3.20 (td, J = 12.8, 12.4, 4.4 Hz, 1H), 2.94 (d, J = 15.3 Hz, 1H),

2.88 – 2.77 (m, 1H).^{13}C NMR (100 MHz, DMSO) δ 162.6, 157.0, 135.9, 134.9, 129.8, 128.6, 126.8, 124.2, 123.3, 123.1, 118.8, 116.9, 113.9, 112.1, 81.4, 20.2. IR (KBr ν/cm^{-1}) 3356, 2341, 1655, 1614, 1470, 1318, 1031, 937, 760; HRMS (ESI^{+}) m/z calcd for $C_{18}H_{14}ClN_2O_2^+$ $(M+H)^+$ 325.0738, found 325.0735.



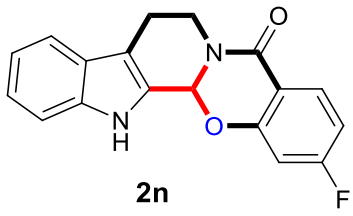
2l

2-methyl-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2l) : 21.3 mg, white solid , Yield 71%; ^{1}H NMR (400 MHz, DMSO) δ 11.49 (s, 1H), 7.78 (d, J = 7.9 Hz, 1H), 7.56 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.11 – 6.99 (m, 2H), 6.94 (s, 1H), 6.62 (s, 1H), 4.71 (dd, J = 13.0, 4.7 Hz, 1H), 3.19 (td, J = 12.2, 4.5 Hz, 1H), 2.89 (m, J = 21.8, 15.7, 7.4 Hz, 2H), 2.38 (s, 3H).^{13}C NMR (100 MHz, DMSO) δ 162.8, 157.1, 145.6, 137.4, 128.4, 128.1, 125.72, 124.2, 123.0, 119.5, 119.4, 117.0, 116.3, 112.3, 112.2, 81.6, 21.8, 20.3. IR (KBr ν/cm^{-1}) 3293, 2341, 1649, 1621, 1439, 1280, 1023, 969, 770, 692; HRMS (ESI^{+}) m/z calcd for $C_{19}H_{17}N_2O_2^+$ $(M+H)^+$ 305.1285, found 305.1287.



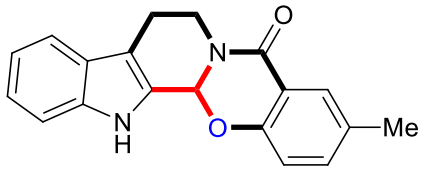
2m

2-methoxy-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2m) : 23.1 mg, white solid , Yield 73%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.50 (s, 1H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.33 – 7.25 (m, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 6.70 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.51 (d, *J* = 2.4 Hz, 1H), 6.44 (s, 1H), 4.90 (m, *J* = 13.1, 5.1, 2.3 Hz, 1H), 3.83 (s, 3H), 3.29 (m, *J* = 12.9, 10.7, 4.9 Hz, 1H), 3.12 – 2.89 (m, 2H).^{13}C NMR (100 MHz, CDCl3) δ 164.5, 163.2, 158.4, 137.1, 130.2, 127.1, 125.9, 123.6, 120.2, 119.3, 113.7, 111.6, 111.5, 109.9, 100.7, 81.4, 55.6, 39.0, 20.2. IR (KBr ν/cm^{-1}) 3364, 2345, 1664, 1618, 1448, 1279, 1027, 1008, 824, 747, 691; HRMS (ESI^{+}) m/z calcd for $C_{19}H_{17}N_2O_3^+$ $(M+H)^+$ 321.1234, found 321.1236.



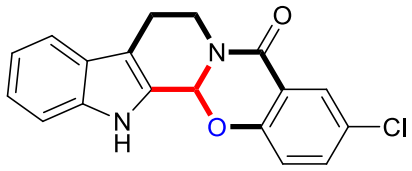
2n

2-fluoro-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2n) : 21.3 mg, white solid , Yield 70%; ^{1}H NMR (400 MHz, DMSO) δ 11.53 (s, 1H), 7.96 (dd, J = 8.7, 6.5 Hz, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.13 – 6.97 (m, 3H), 6.74 (s, 1H), 4.70 (m, J = 13.0, 5.1, 1.8 Hz, 1H), 3.21 (td, J = 12.2, 4.5 Hz, 1H), 2.91 (m, J = 24.8, 13.4, 4.5 Hz, 2H). ^{13}C NMR (100 MHz, DMSO) δ 167.0, 162.0, 158.6 (d, *J* = 13.5 Hz), 137.4, 131.1 (d, *J* = 11.1 Hz), 127.5, 125.6, 123.1, 119.5 (d, *J* = 14.0 Hz), 115.7, 112.4, 112.3, 110.9 (d, *J* = 22.5 Hz), 104.2 (d, *J* = 25.2 Hz), 82.1, 20.2. IR (KBr ν/cm^{-1}) 3278, 2376, 1655, 1618, 1448, 1310, 1131, 1034, 978, 744; HRMS (ESI^{+}) m/z calcd for $C_{18}H_{14}FN_2O_2^{+}$ $(M+H)^{+}$ 309.1034, found 309.1031.



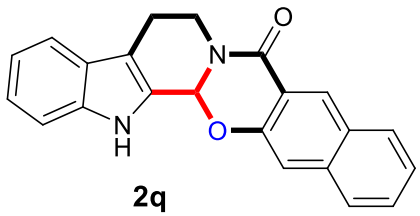
2o

3-methyl-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2o) : 22.4 mg, white solid , Yield 74%; ^{1}H NMR (400 MHz, DMSO) δ 11.50 (s, 1H), 7.70 (d, J = 2.2 Hz, 1H), 7.56 (d, J = 7.9 Hz, 1H), 7.47 – 7.33 (m, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.05 (dd, J = 12.2, 7.9 Hz, 2H), 6.61 (s, 1H), 4.72 (m, J = 12.9, 5.0, 2.0 Hz, 1H), 3.29 – 3.12 (m, 1H), 2.90 (m, J = 13.5, 11.7, 4.6 Hz, 2H), 2.34 (s, 3H).^{13}C NMR (100 MHz, DMSO) δ 162.7, 155.0, 137.4, 135.4, 132.2, 128.3, 128.1, 125.7, 123.0, 119.5, 119.3, 118.5, 116.7, 112.2, 112.0, 81.5, 20.6, 20.3. IR (KBr ν/cm^{-1}) 3357, 2375, 1657, 1493, 1439, 1308, 1081, 967, 936, 744; HRMS (ESI^{+}) m/z calcd for $C_{19}H_{17}N_2O_2^{+}$ $(M+H)^{+}$ 305.1285, found 305.1283.



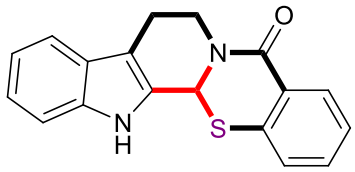
2p

3-chloro-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2p) : 19.3 mg, white solid , Yield 60%; ^{1}H NMR (400 MHz, DMSO) δ 11.54 (s, 1H), 7.84 (d, J = 2.7 Hz, 1H), 7.64 (dd, J = 8.7, 2.7 Hz, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.19 (dd, J = 8.4, 5.7 Hz, 2H), 7.06 (t, J = 7.4 Hz, 1H), 6.72 (s, 1H), 4.71 (dd, J = 13.3, 4.7 Hz, 1H), 3.23 (td, J = 12.2, 4.4 Hz, 1H), 2.92 (m, J = 24.5, 13.6, 4.0 Hz, 2H).^{13}C NMR (100 MHz, DMSO) δ 161.6, 155.8, 137.4, 134.5, 127.6, 127.5, 127.1, 125.6, 123.2, 120.3, 119.6, 119.4, 119.2, 112.3, 81.8, 55.4, 20.2. IR (KBr ν/cm^{-1}) 3275, 2374, 1642, 1472, 1444, 1272, 1232, 1180, 965, 744; HRMS (ESI^{+}) m/z calcd for $C_{18}H_{14}ClN_2O_2^{+}$ $(M+H)^{+}$ 325.0738, found 325.0736.



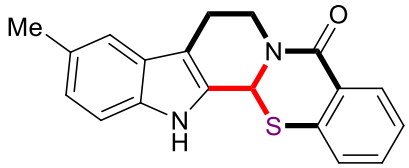
2q

15a,16-dihydro-5H-naphtho[2'',3'':5',6'][1,3]oxazino[3',2':1,2]pyrido[3,4-b]indol-8(6H)-one (2q) : 25.9 mg, white solid , Yield 76%; ^{1}H NMR (400 MHz, DMSO) δ 11.59 (s, 1H), 8.62 (s, 1H), 8.12 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.60 (q, J = 6.9, 6.5 Hz, 3H), 7.47 (dd, J = 14.6, 7.7 Hz, 2H), 7.20 (t, J = 7.6 Hz, 1H), 7.07 (t, J = 7.4 Hz, 1H), 6.78 (s, 1H), 4.84 (dd, J = 13.4, 4.4 Hz, 1H), 3.28 (td, J = 12.3, 4.9 Hz, 1H), 2.93 (d, J = 15.9 Hz, 2H).^{13}C NMR (100 MHz, DMSO) δ 162.6, 153.2, 137.5, 136.5, 130.1, 129.8, 129.4, 129.2, 128.1, 127.3, 125.7, 125.6, 123.1, 119.5, 119.5, 119.4, 112.3, 112.2, 112.2, 81.7, 20.4. IR (KBr ν/cm^{-1}) 3258, 2378, 1655, 1508, 1457, 1308, 1139, 1094, 779, 744; HRMS (ESI^{+}) m/z calcd for $C_{22}H_{17}N_2O_2^{+}$ $(M+H)^{+}$ 341.1285, found 341.1287.



2r

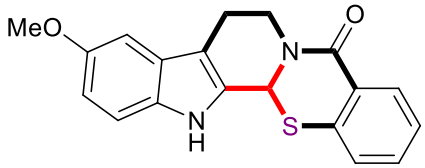
7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]thiazino[3',2':1,2]pyrido[3,4-b]indol-5-one（2r）: 22.8 mg, white solid , Yield 76%; ^{1}H NMR (400 MHz, DMSO) δ 11.34 (s, 1H), 8.08 (d, J = 7.8 Hz, 1H), 7.52 (dd, J = 14.6, 7.8 Hz, 3H), 7.43 – 7.35 (m, 2H), 7.15 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H), 6.59 (s, 1H), 4.75 (dd, J = 13.0, 4.3 Hz, 1H), 3.25 (td, J = 12.7, 12.0, 4.0 Hz, 1H), 3.00 (d, J = 15.5 Hz, 1H), 2.85 (td, J = 10.9, 5.5 Hz, 1H).^{13}C NMR (100 MHz, DMSO) δ 164.8, 137.2, 136.0, 132.5, 131.1, 129.4, 128.2, 127.5, 126.8, 126.0, 122.6, 119.5, 118.9, 112.1, 110.5, 56.8, 20.5. IR (KBr ν/cm^{-1}) 3243, 2371, 1636, 1457, 1396, 1325, 1274, 1072, 1036, 746; HRMS (ESI^{+}) m/z calcd for $C_{18}H_{15}N_2OS^{+}$ $(M+H)^{+}$ 307.0900, found 307.0903.



2s

10-methyl-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]thiazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2s) : 23.5 mg, white solid , Yield 75%, ^{1}H NMR (400 MHz, DMSO) δ 11.19 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.50 (dd, *J* = 17.4, 7.4 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.32 (s, 1H), 7.26 (d, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.56 (s, 1H), 4.79 – 4.66 (m, 1H), 3.27 – 3.11 (m, 1H), 2.97 (d, *J* = 15.4 Hz, 1H), 2.82 (td, *J* = 11.4, 6.1 Hz, 1H), 2.38 (s, 3H).^{13}C NMR (100 MHz, DMSO) δ 168.5, 164.8, 136.1, 135.6, 132.5, 131.1, 129.4, 128.2, 128.1, 127.5, 126.8, 126.2, 124.2, 118.5, 111.8,

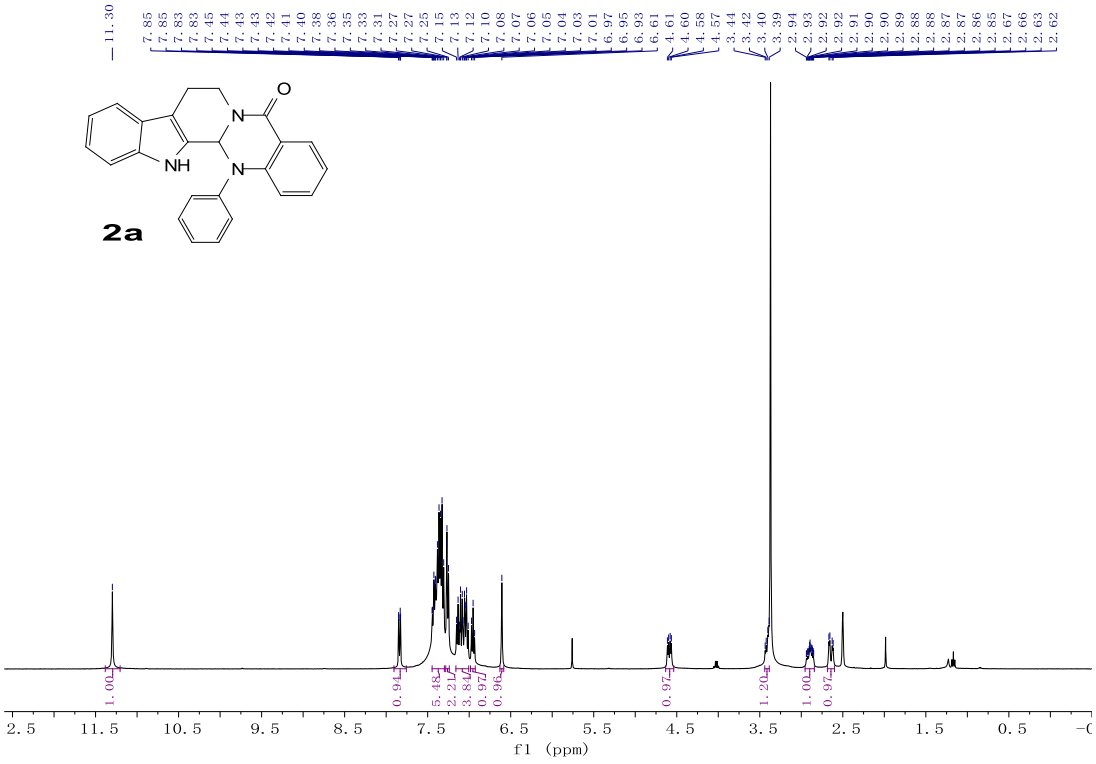
110.0, 56.9, 21.6, 20.5. IR (KBr ν/cm^{-1}) 3360, 2374, 1655, 1634, 1470, 1276, 1134, 1036, 962, 745; HRMS (ESI$^+$) m/z calcd for $C_{19}H_{17}N_2OS^+$ $(M+H)^+$ 321.1056, found 321.1054.

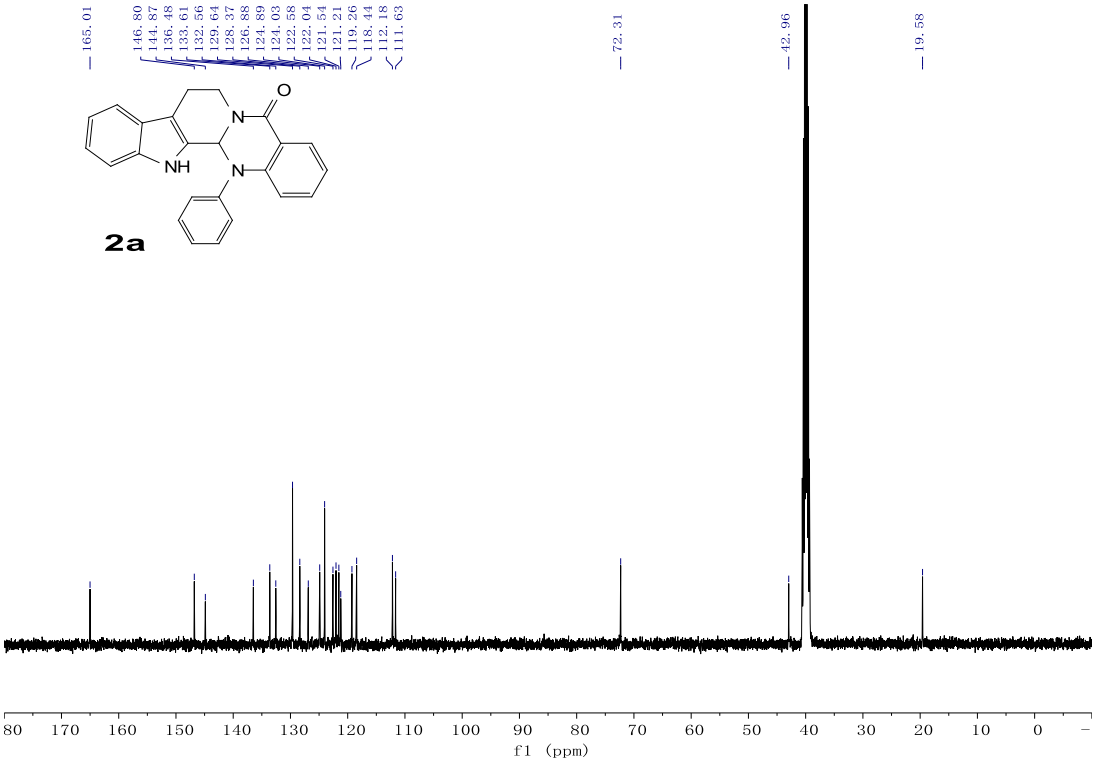


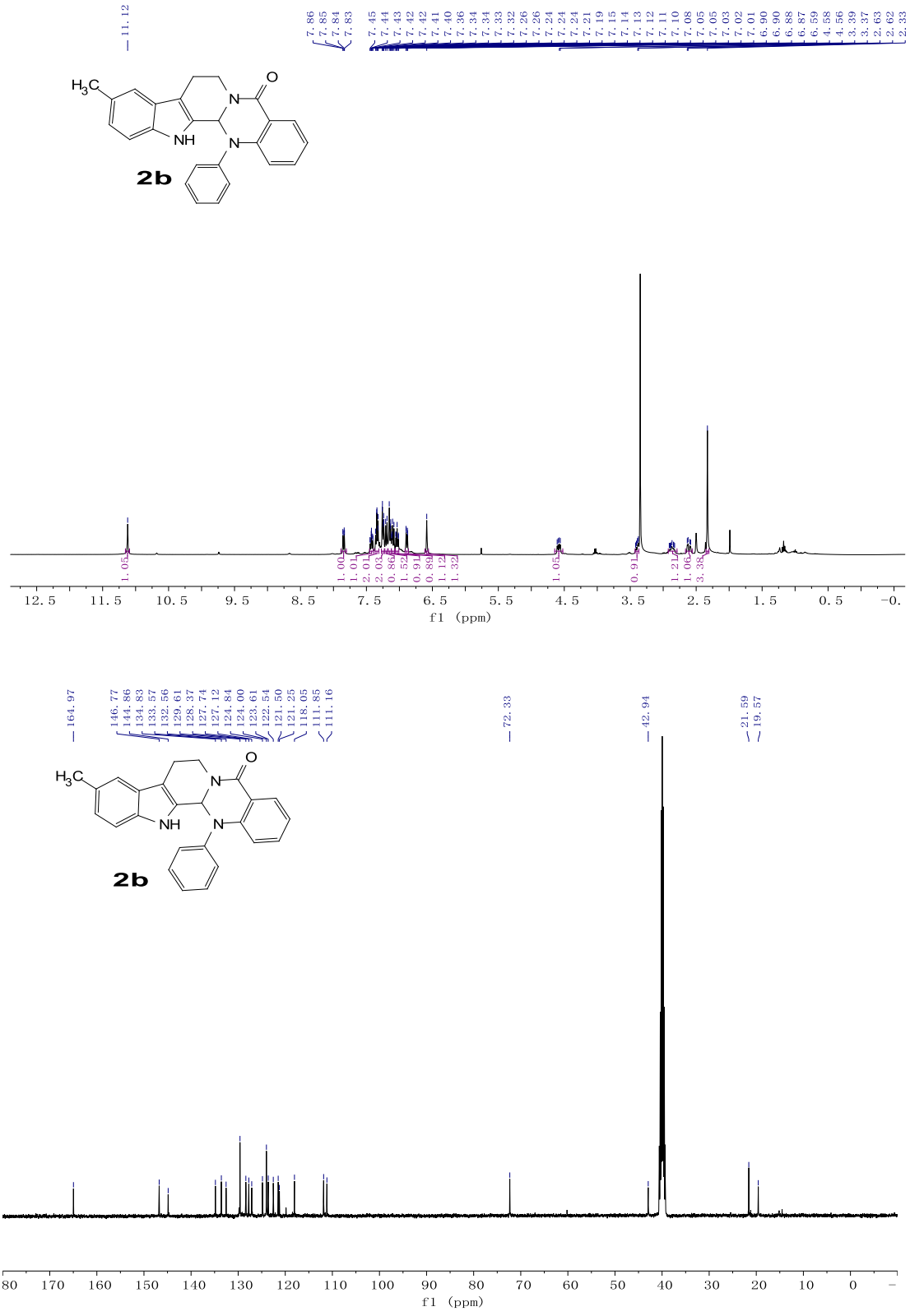
2t

10-methoxy-7,8,13,13b-tetrahydro-5H-benzo[5',6'][1,3]thiazino[3',2':1,2]pyrido[3,4-b]indol-5-one (2t) : 26.7 mg, white solid , Yield 81%; ^{1}H NMR (400 MHz, DMSO) δ 11.17 (s, 1H), 8.07 (dd, J = 8.0, 1.5 Hz, 1H), 7.50 (m, J = 17.1, 7.6, 1.5 Hz, 2H), 7.39 (td, J = 7.5, 1.5 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 7.04 (d, J = 2.4 Hz, 1H), 6.79 (dd, J = 8.8, 2.4 Hz, 1H), 6.56 (s, 1H), 4.78 – 4.69 (m, 1H), 3.77 (s, 3H), 3.23 (m, J = 12.7, 10.8, 4.1 Hz, 1H), 2.96 (s, 1H), 2.89 – 2.75 (m, 1H). ^{13}C NMR (100 MHz, DMSO) δ 164.8, 153.9, 136.1, 132.5, 132.3, 131.0, 129.4, 128.7, 127.5, 126.8, 126.3, 112.78, 112.76, 110.3, 100.7, 56.9, 55.8, 20.6. IR (KBr ν/cm^{-1}) 3334, 2374, 1655, 1507, 1456, 1398, 1278, 1075, 1033, 753; HRMS (ESI$^+$) m/z calcd for $C_{19}H_{17}N_2O_2S^+$ $(M+H)^+$ 337.1005, found 337.1003.

6. NMR Spectrums:



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O
N
NH
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2b
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170
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100
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40
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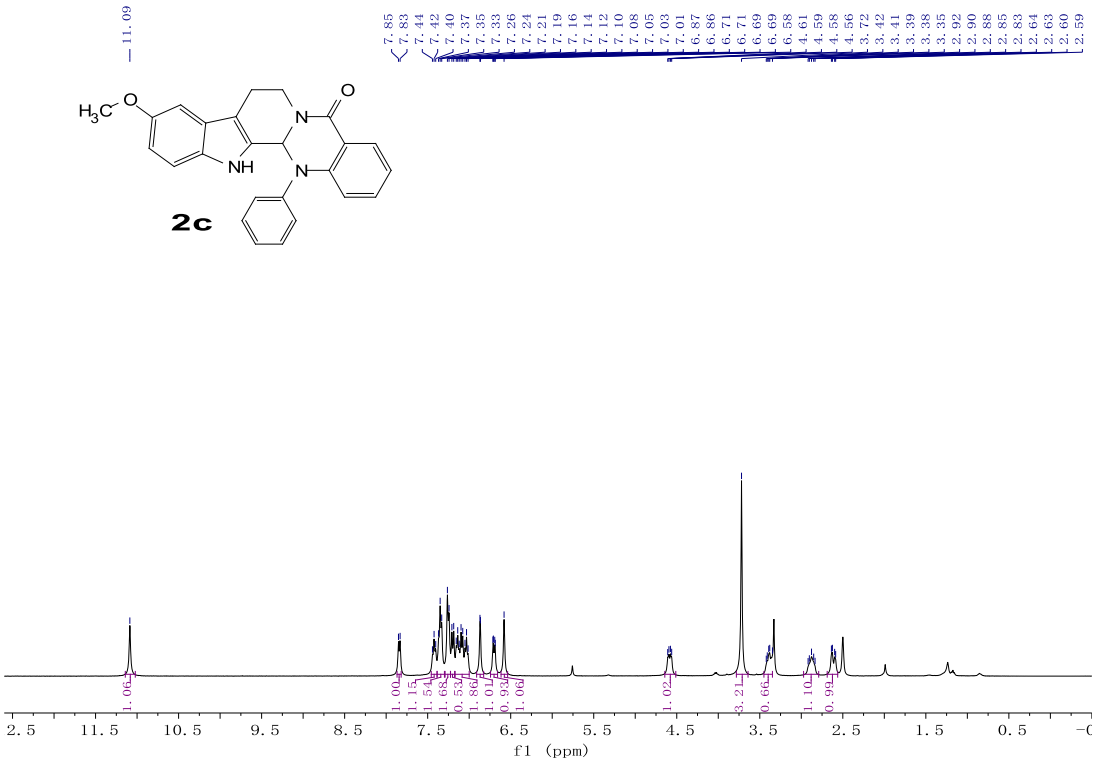
−
f1 (ppm)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2.59
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2c
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0.99
2.5
11.5
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2.5
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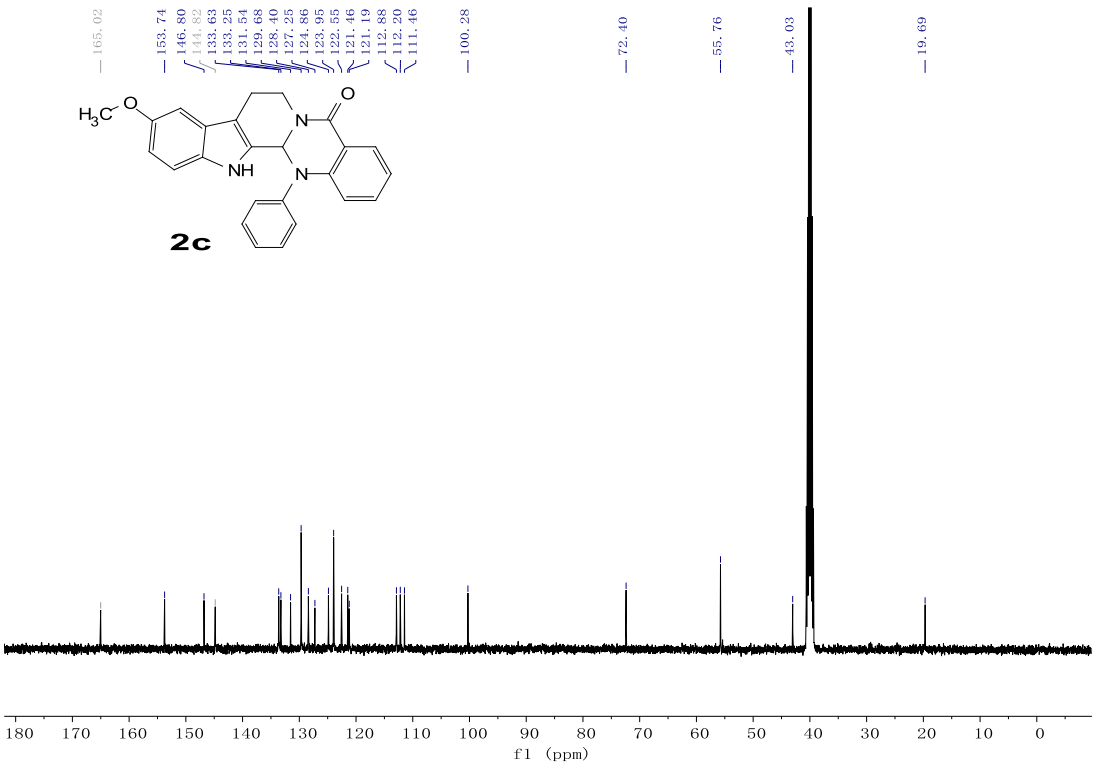
0.5
f1 (ppm)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127.25
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122.55
121.46
121.19
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112.20
111.46
100.28
72.40
55.76
43.03
19.69
H3C
O
N
O
NH
N
2c
180
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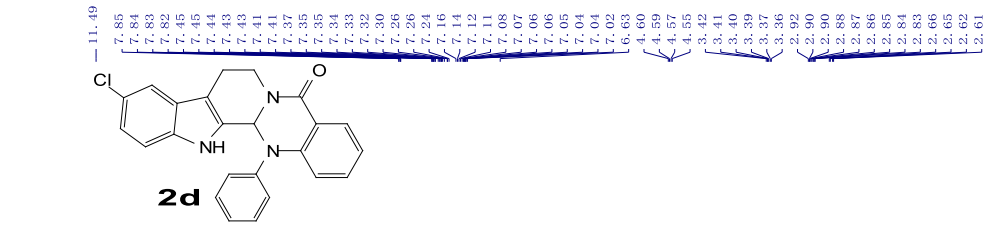
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7.35
7.34
7.33
7.32
7.30
7.26
7.24
7.16
7.14
7.12
7.11
7.08
7.07
7.06
7.05
7.04
7.04
7.02
6.63
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4.59
4.57
4.55
3.42
3.41
3.40
3.39
3.37
3.36
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2.90
2.88
2.87
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2.61
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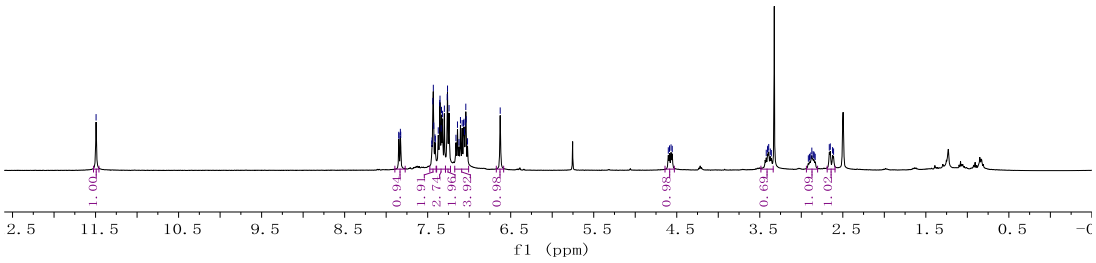
N
N
O
2d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0.98
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1.02
2.5
11.5
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7.5
6.5
5.5
4.5
3.5
2.5
1.5
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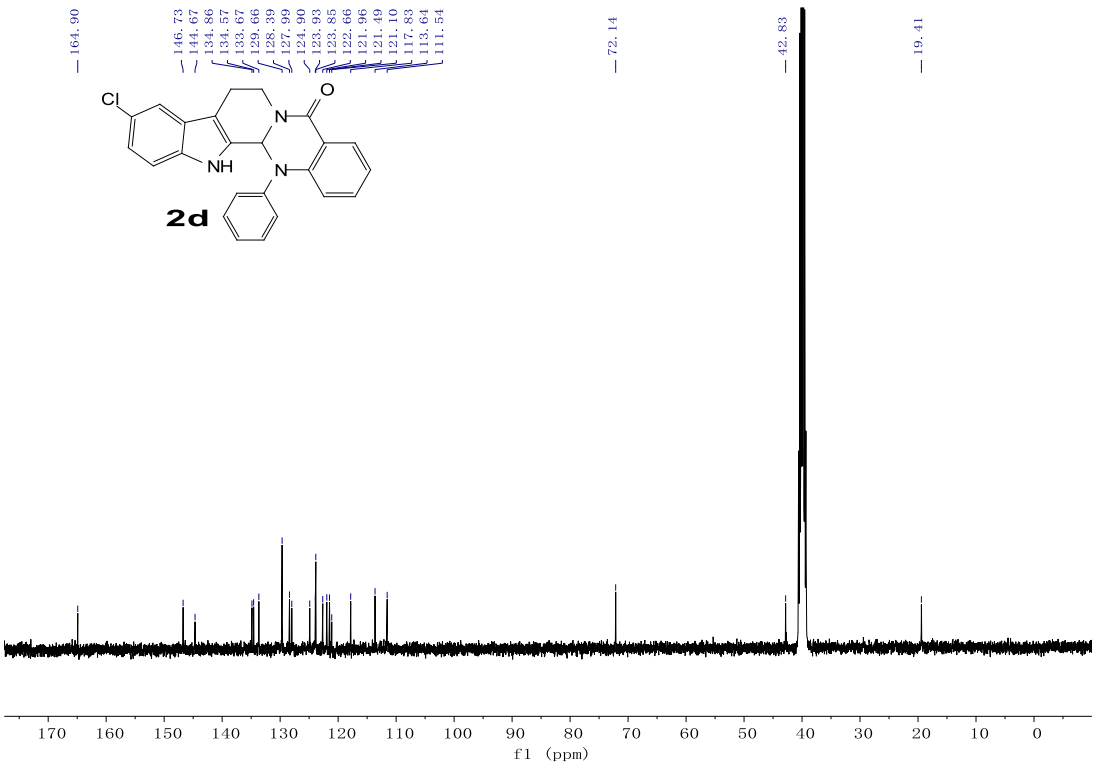
f1 (ppm)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128.39
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124.90
123.93
123.85
122.66
121.96
121.49
121.10
117.83
113.64
111.54
72.14
42.83
19.41
Cl
NH
N
N
O
2d
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100
90
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70
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50
40
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10
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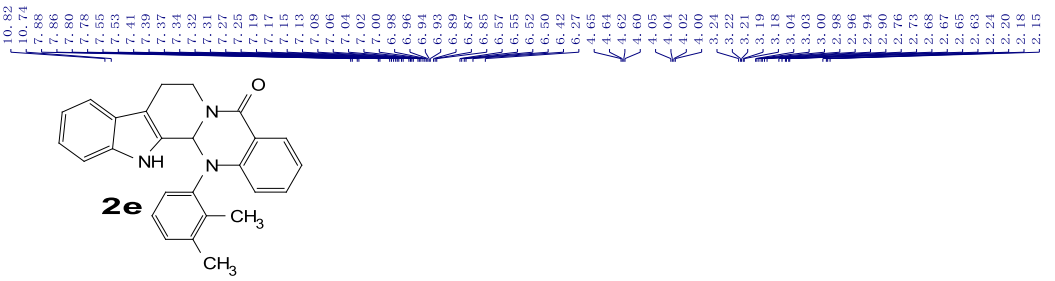
f1 (ppm)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7.32
7.31
7.27
7.25
7.19
7.17
7.15
7.13
7.08
7.06
7.04
7.02
7.00
6.98
6.96
6.94
6.93
6.89
6.87
6.85
6.57
6.55
6.52
6.50
6.42
6.27
4.65
4.64
4.62
4.60
4.05
4.04
4.02
4.00
3.24
3.22
3.21
3.19
3.18
3.04
3.03
3.00
2.98
2.96
2.94
2.90
2.76
2.73
2.68
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O
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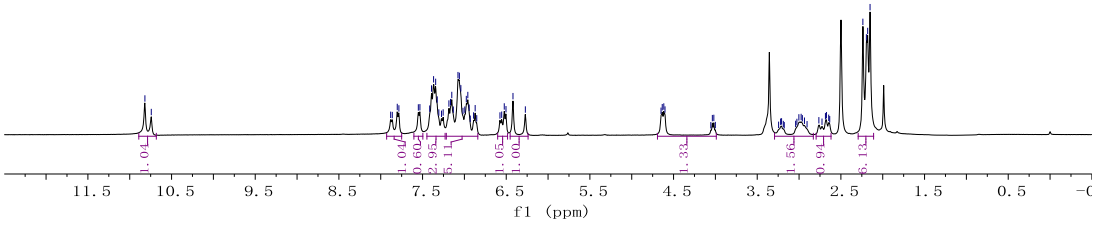
NH
N
2e
CH3
CH3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5.5
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3.5
2.5
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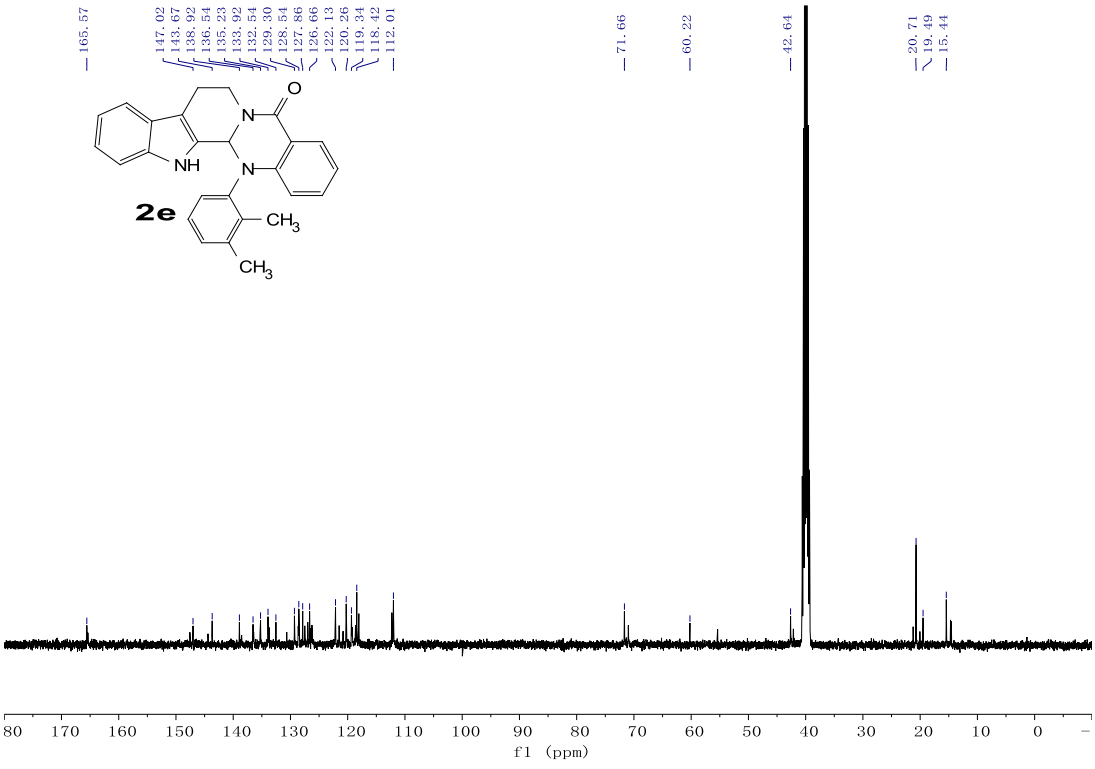
f1 (ppm)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126.66
122.13
120.26
119.34
118.42
112.01
71.66
60.22
42.64
20.71
19.49
15.44
O
N
NH
N
2e
CH3
CH3
80
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130
120
110
100
90
80
70
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50
40
30
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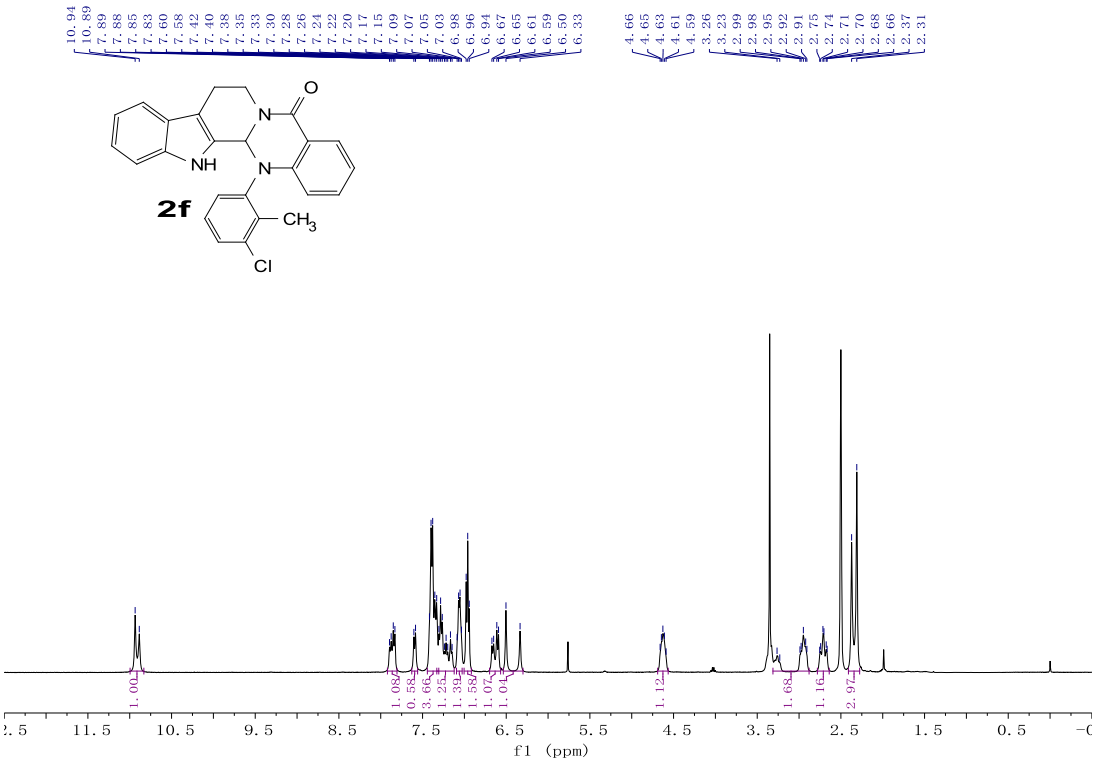
10
0
f1 (ppm)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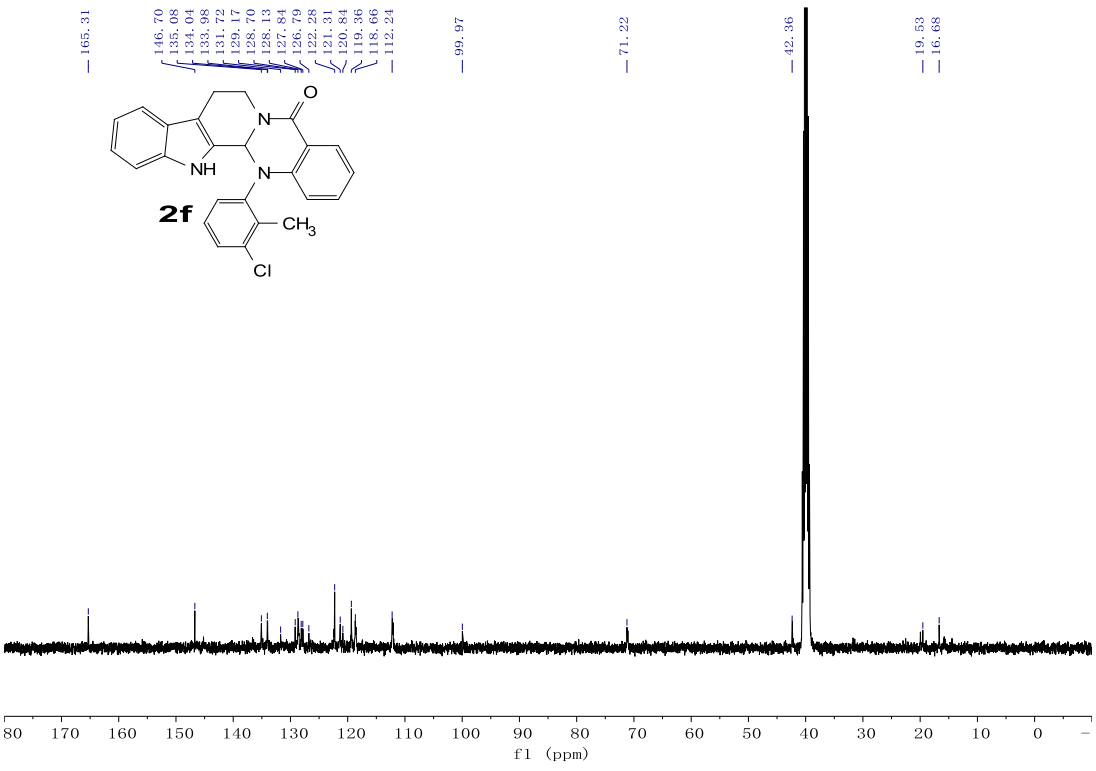
7.33
7.30
7.28
7.26
7.24
7.22
7.20
7.17
7.15
7.09
7.07
7.05
7.03
6.98
6.96
6.94
6.67
6.65
6.61
6.59
6.50
6.33
4.66
4.65
4.63
4.61
4.59
3.26
3.23
2.99
2.98
2.95
2.92
2.91
2.75
2.74
2.71
2.70
2.68
2.66
2.37
2.31
O
N
NH
N
2f
CH3
Cl
1.00
1.08
0.58
3.66
1.25
1.39
1.58
1.07
1.04
1.12
1.68
1.16
2.97
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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127.84
126.79
122.28
121.31
120.84
119.36
118.66
112.24
99.97
71.22
42.36
19.53
16.68
O
N
NH
N
2f
CH3
Cl
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130
120
110
100
90
80
70
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50
40
30
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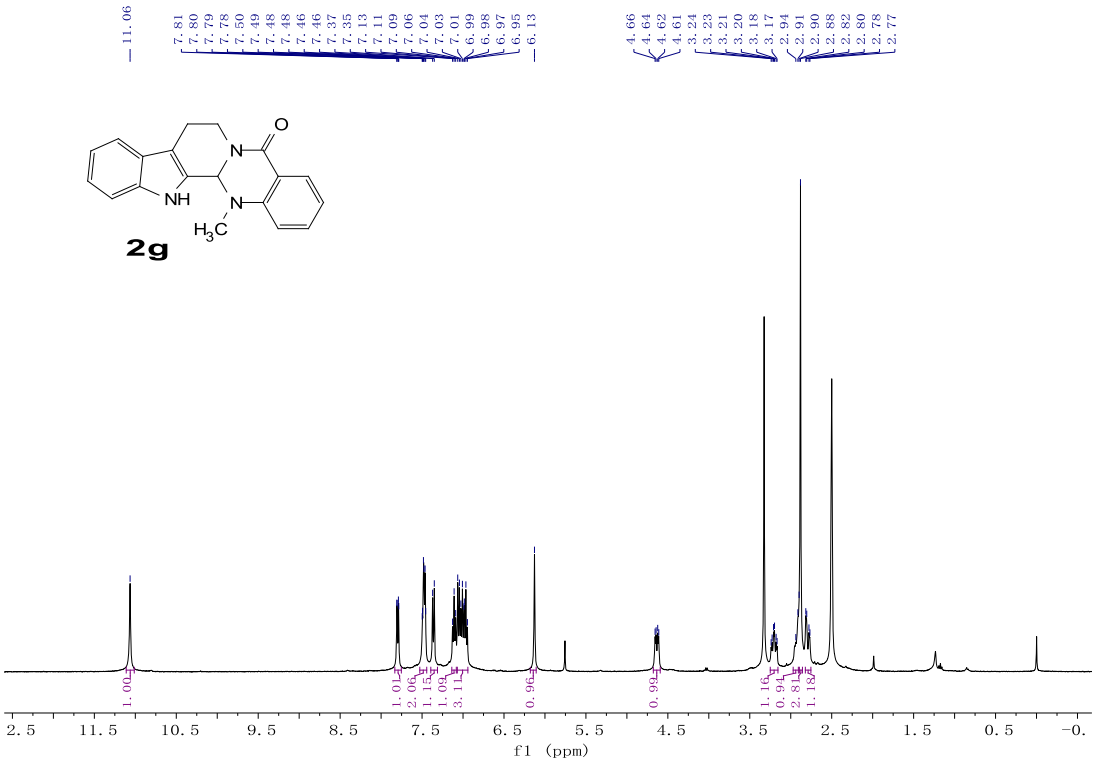
10
0
f1 (ppm)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7.48
7.48
7.46
7.46
7.37
7.35
7.13
7.11
7.09
7.06
7.04
7.03
7.01
6.99
6.98
6.97
6.95
6.13
4.66
4.64
4.62
4.61
3.24
3.23
3.21
3.20
3.18
3.17
2.94
2.91
2.90
2.88
2.82
2.80
2.78
2.77
O
N
NH
N
H3C
2g
1.00
1.01
2.06
1.15
1.09
3.11
0.96
0.99
1.16
0.94
2.81
1.18
2.5
11.5
10.5
9.5
8.5
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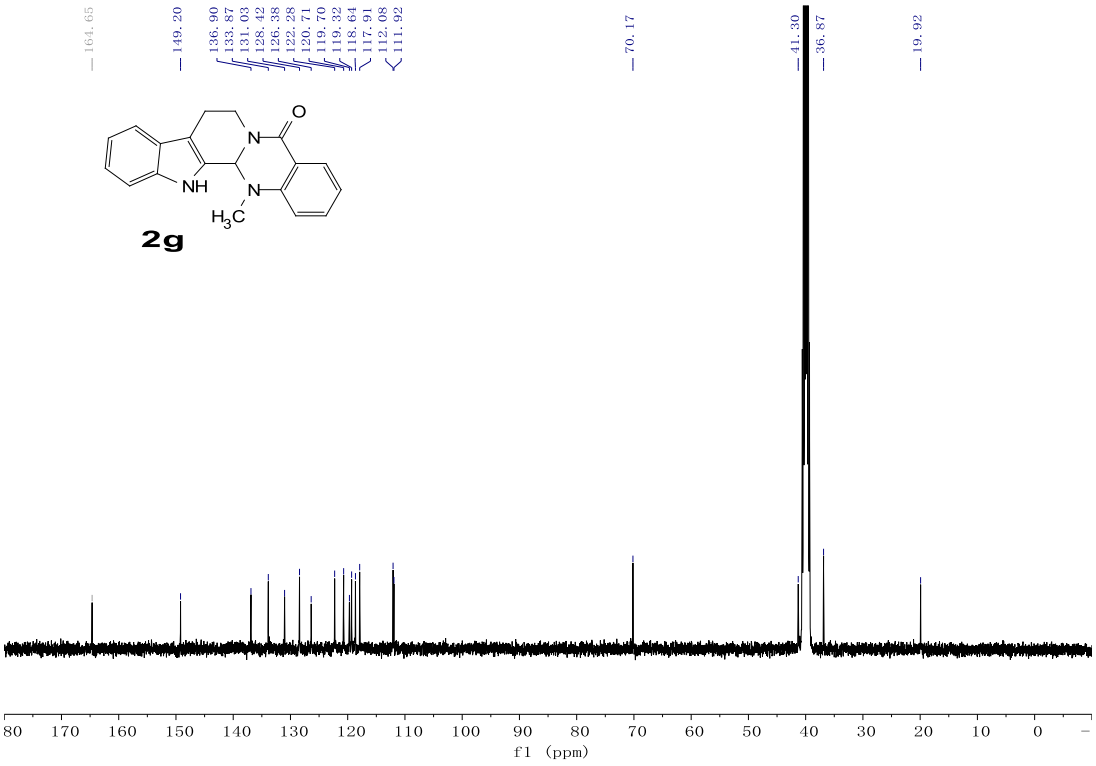
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.
f1 (ppm)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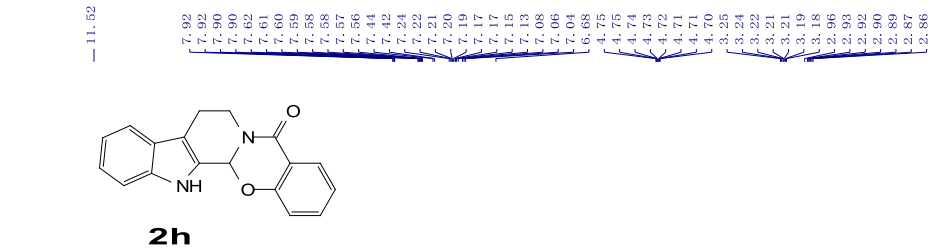
126.38
122.28
120.71
119.70
119.32
118.64
117.91
112.08
111.92
70.17
41.30
36.87
19.92
O
N
NH
N
H3C
2g
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−
f1 (ppm)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7.58
7.58
7.57
7.56
7.44
7.42
7.24
7.22
7.21
7.20
7.19
7.17
7.17
7.15
7.13
7.08
7.06
7.04
6.68
4.75
4.75
4.74
4.73
4.72
4.71
4.71
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3.25
3.24
3.22
3.21
3.21
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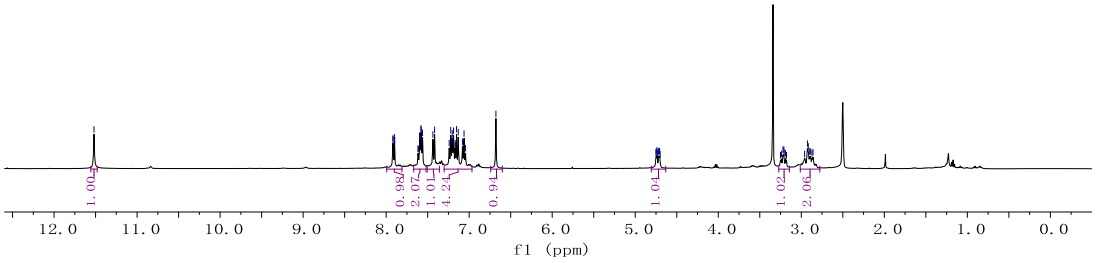
2.93
2.92
2.90
2.89
2.87
2.86

O
N
NH
O

2h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1.01
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0.94
1.04
1.02
2.06
12.0
11.0
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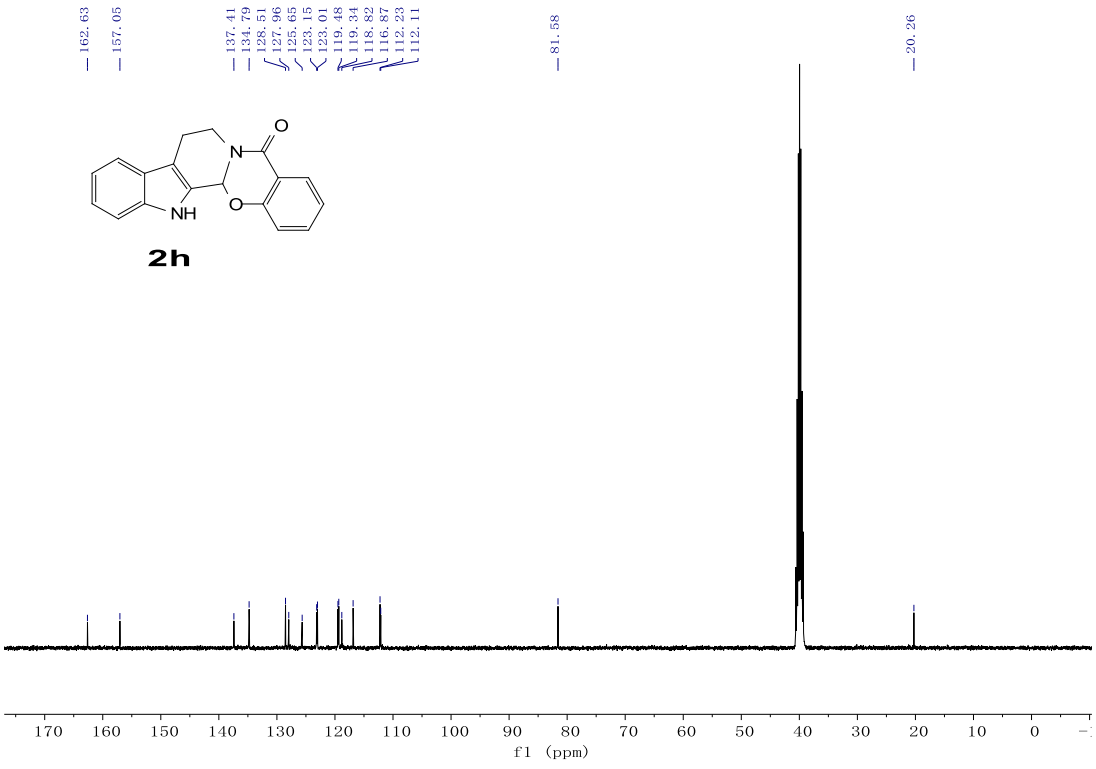
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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123.15
123.01
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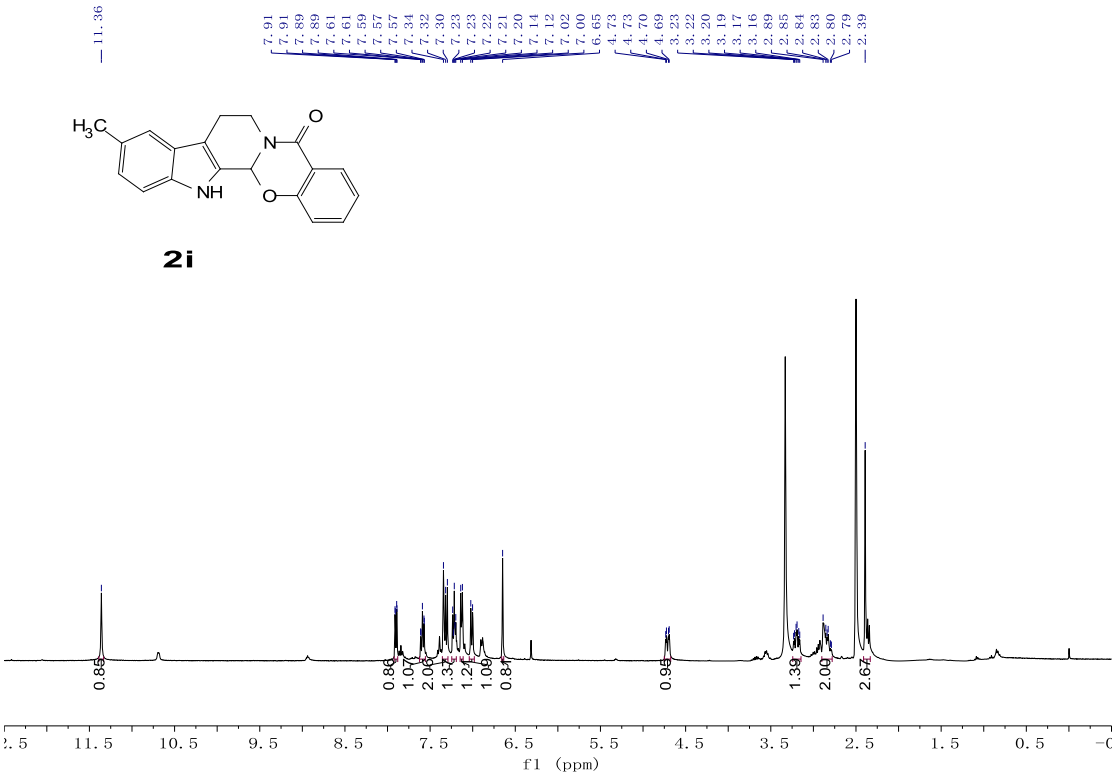
119.34
118.82
116.87
112.23
112.11
81.58
20.26
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

O
N
NH
O

2h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7.57
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7.32
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7.23
7.23
7.22
7.21
7.20
7.14
7.12
7.02
7.00
6.65
4.73
4.73
4.70
4.69
3.23
3.22
3.20
3.19
3.17
3.16
2.89
2.85
2.84
2.83
2.80
2.79
2.39
H3C
N
O
NH
O
2i
0.85
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1.39
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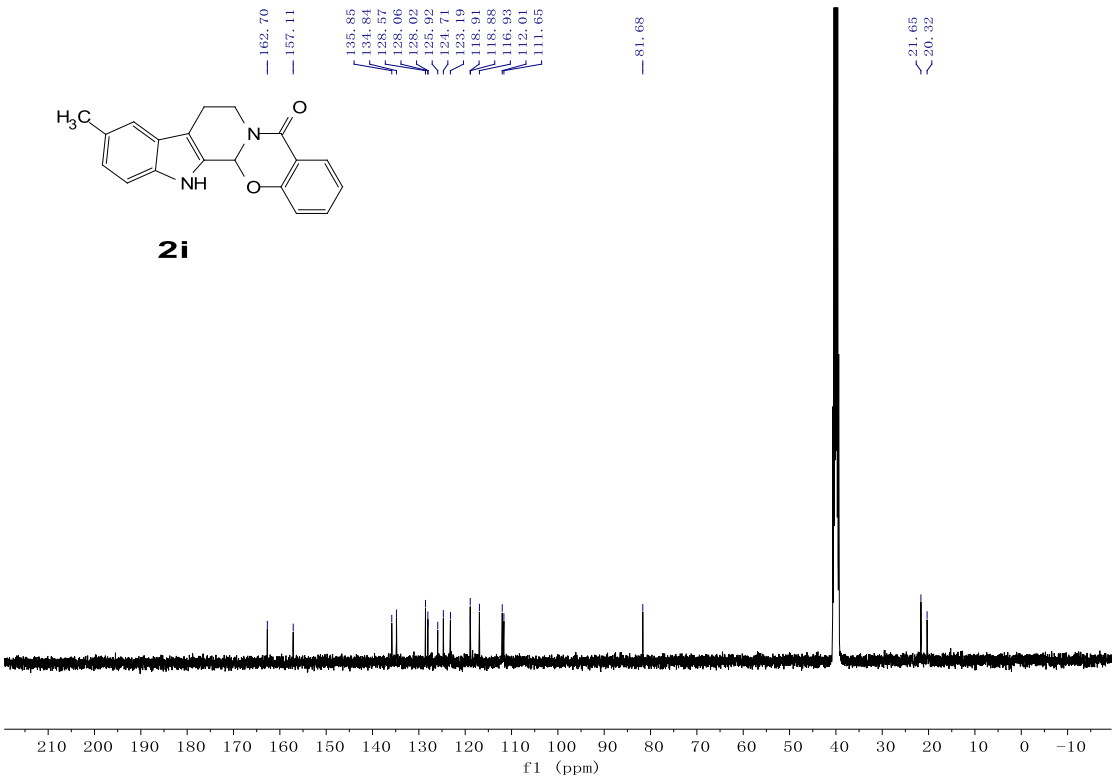
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128.02
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124.71
123.19
118.91
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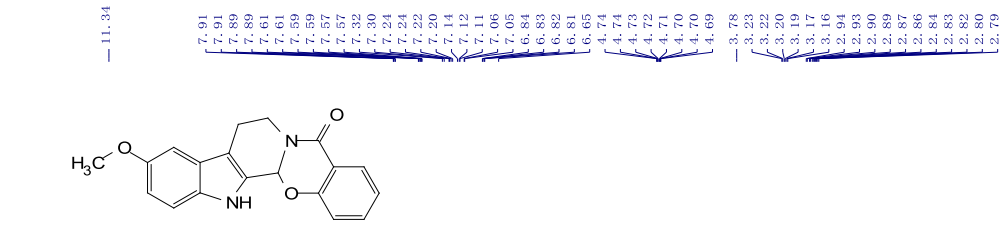
111.65
81.68
21.65
20.32
H3C
N
O
NH
O
2i
f1 (ppm)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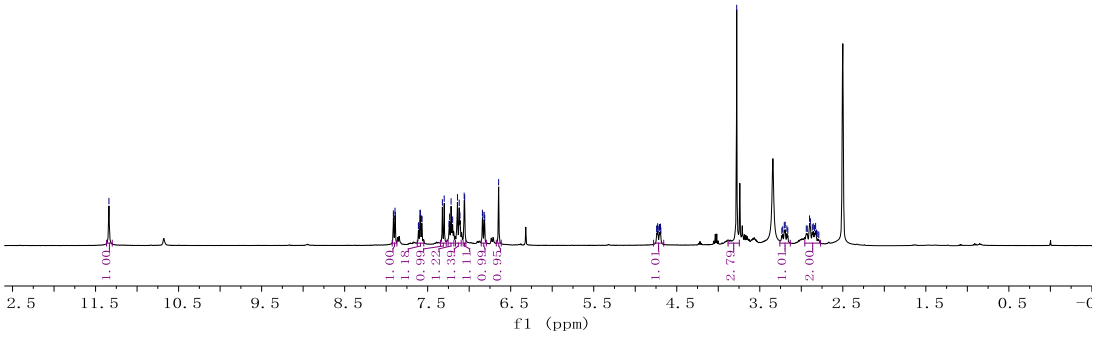
7.89
7.61
7.61
7.59
7.59
7.57
7.57
7.32
7.30
7.24
7.24
7.22
7.20
7.14
7.12
7.11
7.06
7.05
6.84
6.83
6.82
6.81
6.65
4.74
4.74
4.73
4.72
4.71
4.70
4.70
4.69
3.78
3.23
3.22
3.20
3.19
3.17
3.16
2.94
2.93
2.90
2.89
2.87
2.86
2.84
2.83
2.82
2.80
2.79

O
N
O
H_3C
O
NH

2j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1.22
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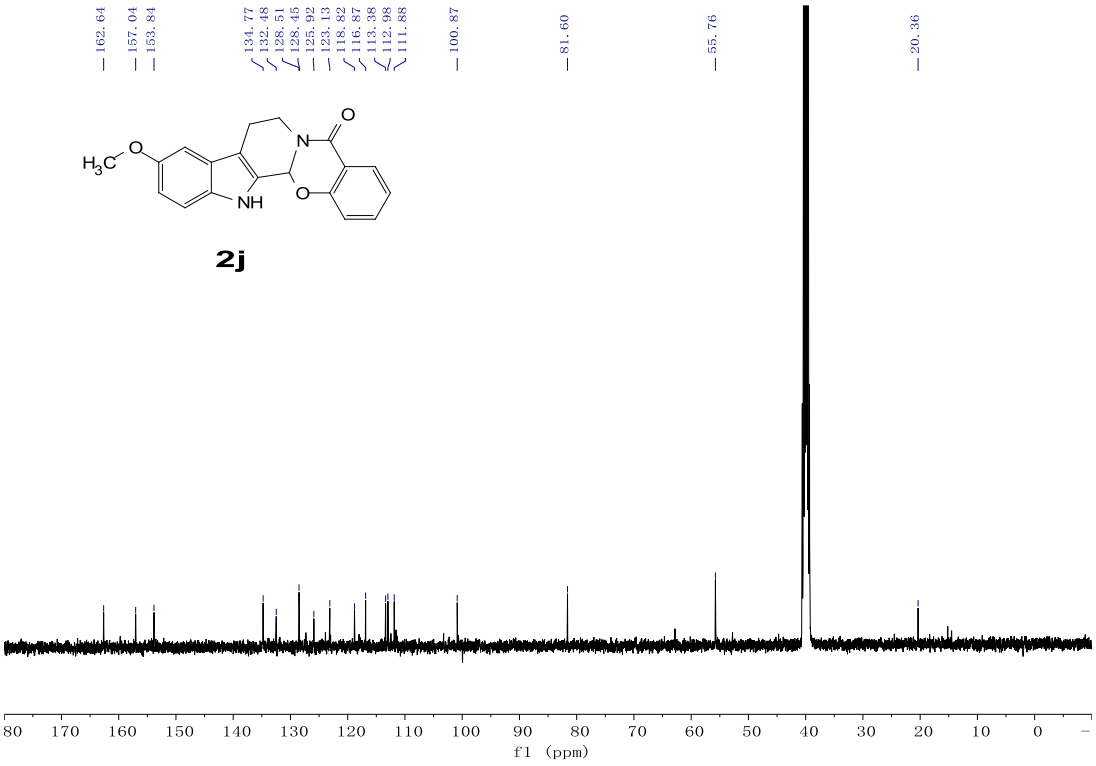
1.11
0.99
0.95
1.01
2.79
1.01
2.00
2.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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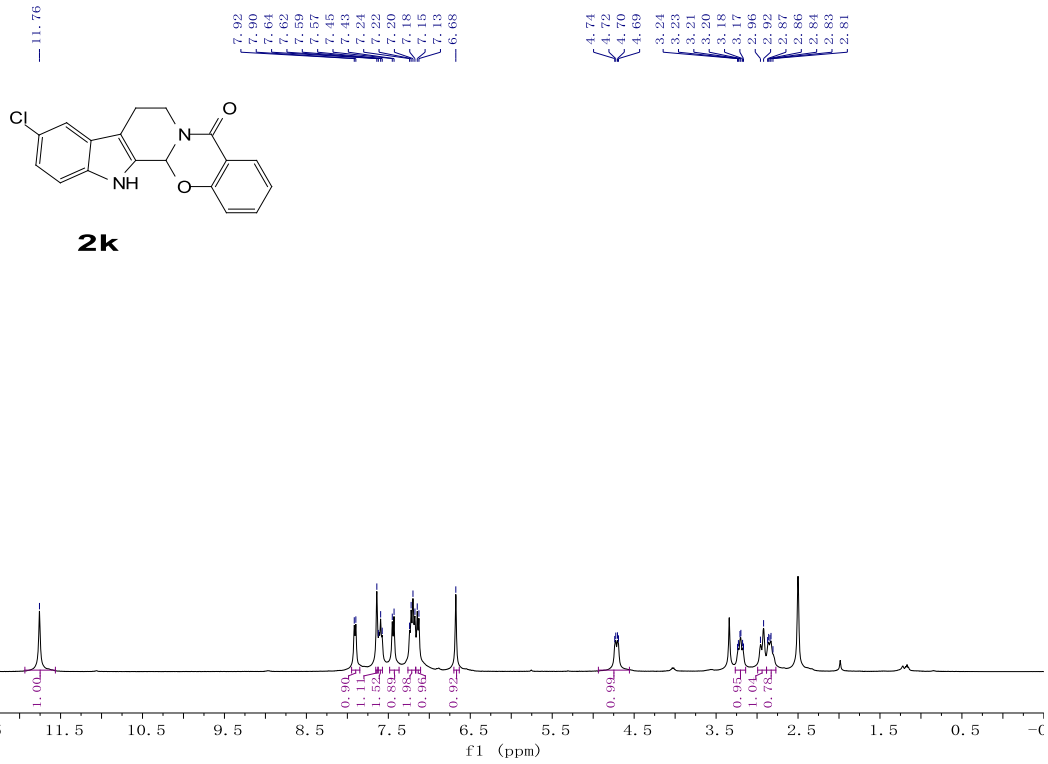
128.45
125.92
123.13
118.82
116.87
113.38
112.98
111.88
100.87
81.60
55.76
20.36
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

O
N
O
H_3C
O
NH

2j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7.57
7.45
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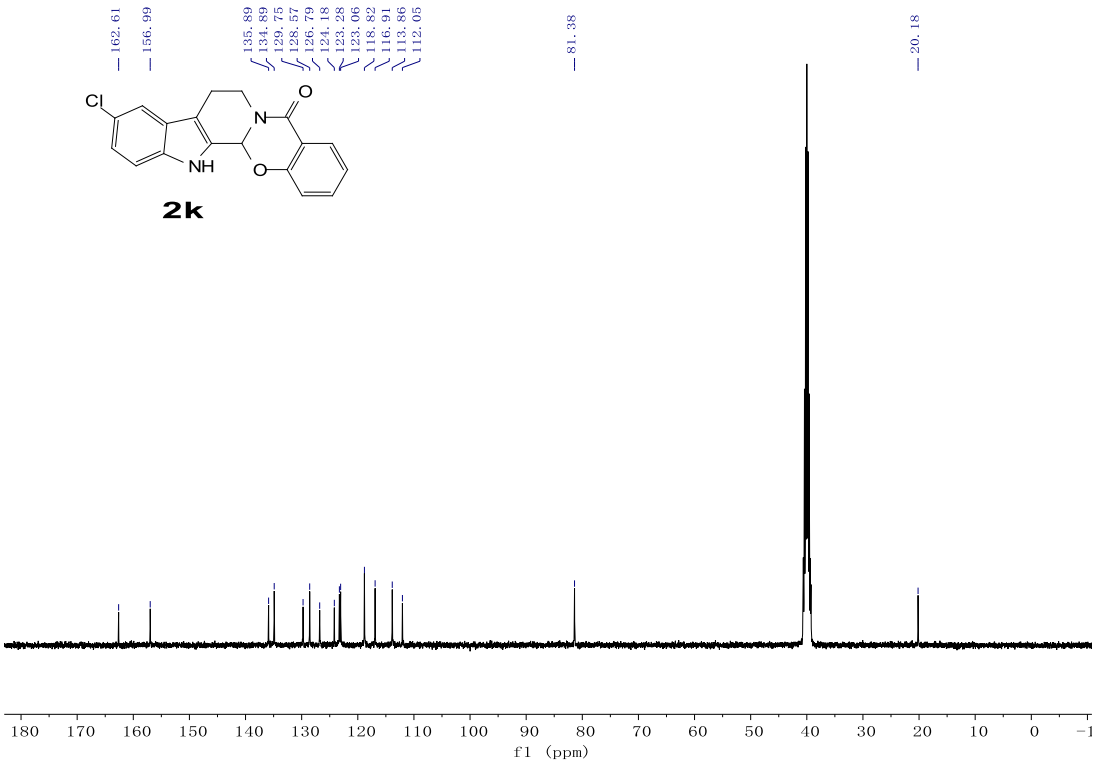
7.24
7.22
7.20
7.18
7.15
7.13
6.68
4.74
4.72
4.70
4.69
3.24
3.23
3.21
3.20
3.18
3.17
2.96
2.92
2.87
2.86
2.84
2.83
2.81
Cl
O
N
NH
O
2k
1.00
0.90
1.11
1.52
0.89
1.98
0.96
0.92
0.99
0.95
1.04
0.78
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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134.89
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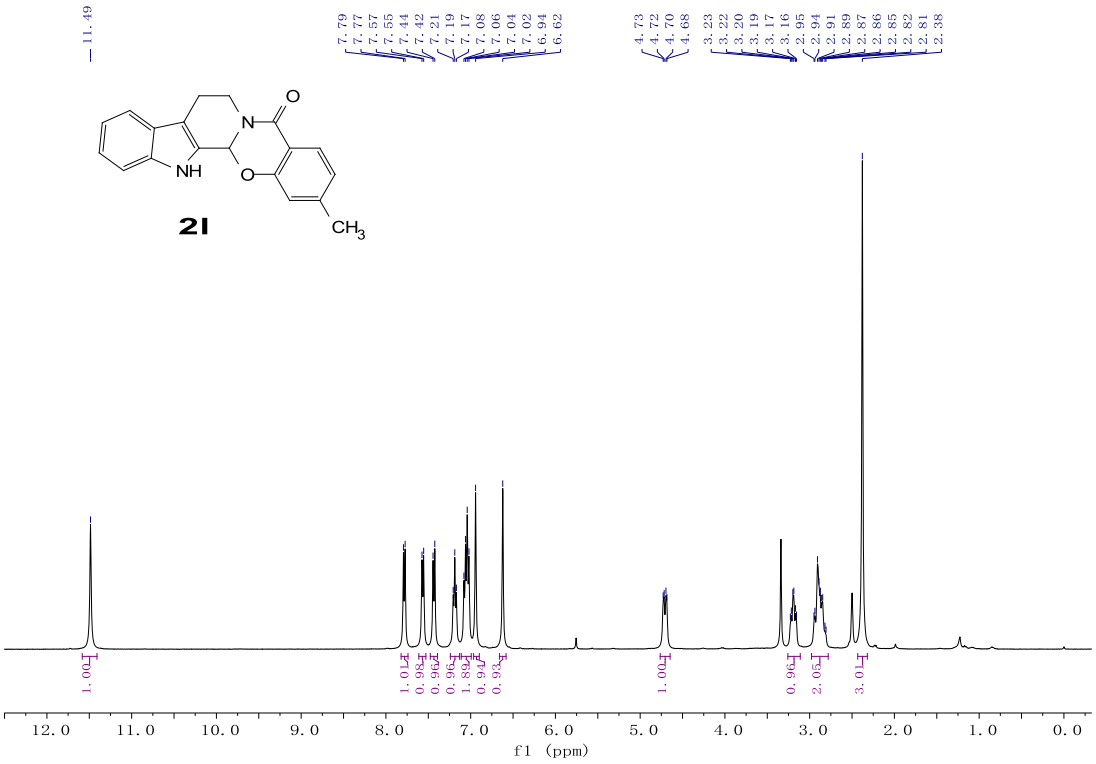
128.57
126.79
124.18
123.28
123.06
118.82
116.91
113.86
112.05
81.38
20.18
Cl
O
N
NH
O
2k
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


11.49
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7.44
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7.19
7.17
7.08
7.06
7.04
7.02
6.94
6.62
4.73
4.72
4.70
4.68
3.23
3.22
3.20
3.19
3.17
3.16
2.95
2.94
2.91
2.89
2.87
2.86
2.85
2.82
2.81
2.38
O
N
NH
O
CH3
21
1.00
1.01
0.98
0.96
0.96
1.89
0.94
0.93
1.00
0.96
2.05
3.10
12.0
11.0
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7.0
6.0
5.0
4.0
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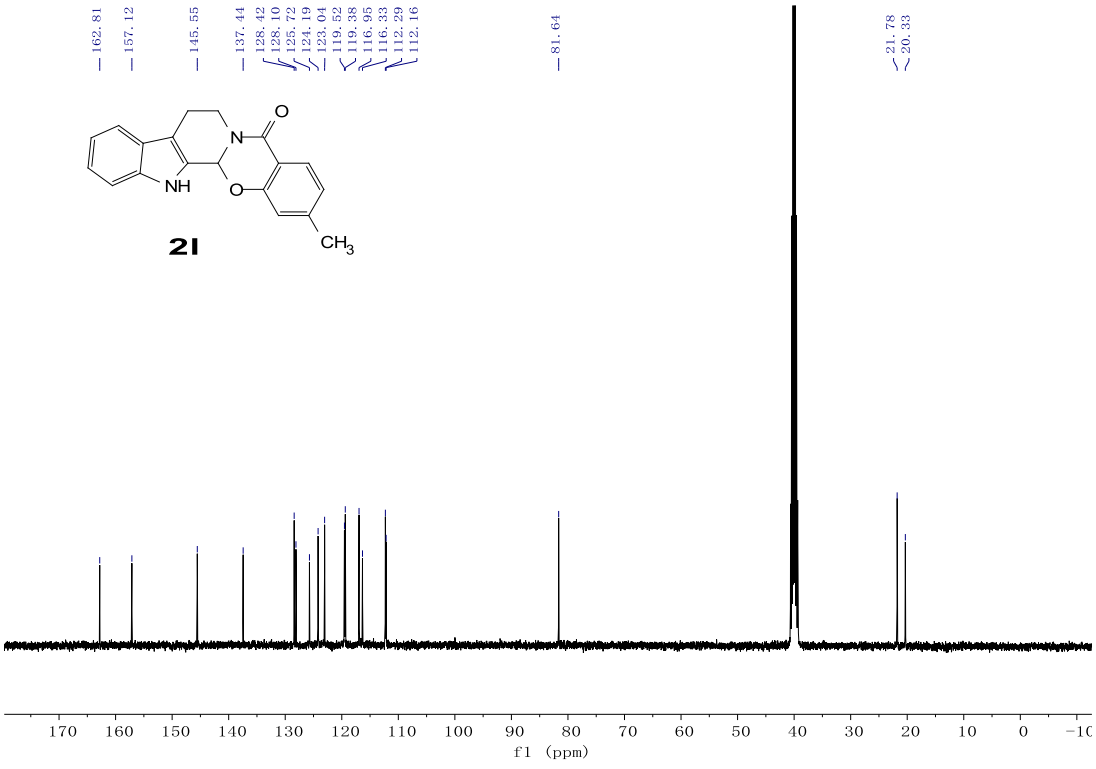
2.0
1.0
0.0
f1 (ppm)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145.55
137.44
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128.10
125.72
124.19
123.04
119.52
119.38
116.95
116.33
112.29
112.16
81.64
21.78
20.33
O
N
NH
O
CH3
21
170
160
150
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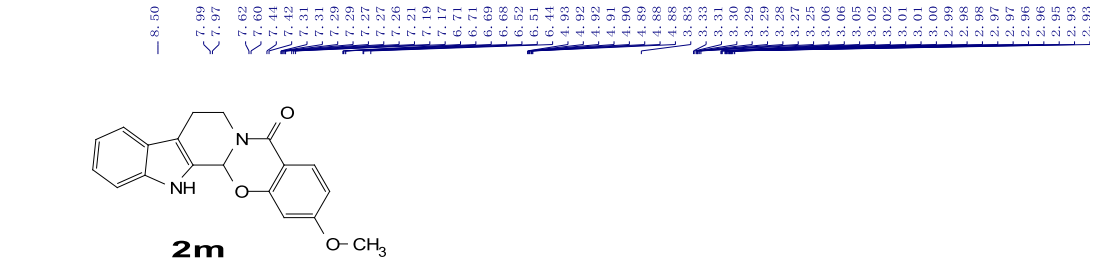
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.50
7.99
7.97
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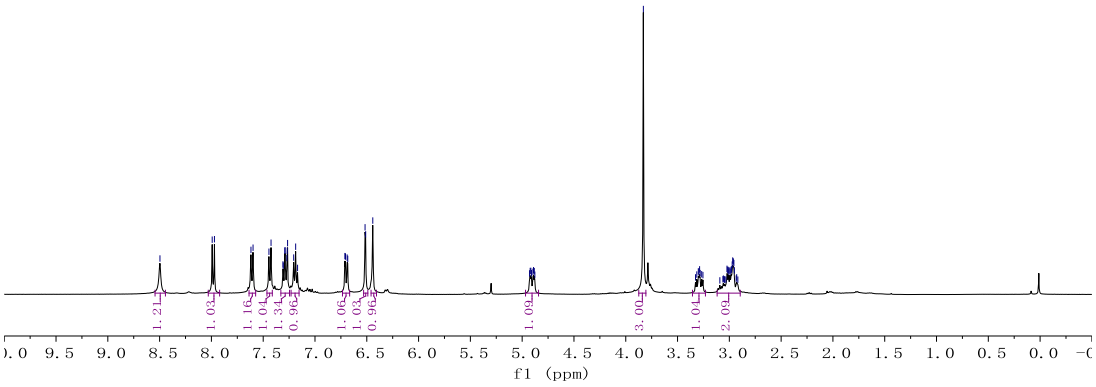
7.60
7.44
7.42
7.31
7.31
7.29
7.29
7.27
7.27
7.26
7.21
7.19
7.17
6.71
6.71
6.69
6.68
6.52
6.51
6.44
4.93
4.92
4.92
4.91
4.90
4.89
4.88
4.88
3.83
3.33
3.31
3.30
3.29
3.29
3.28
3.27
3.25
3.06
3.06
3.05
3.02
3.02
3.01
3.01
3.00
2.99
2.98
2.98
2.97
2.97
2.96
2.96
2.95
2.93
2.93

O
N
NH
O
O- CH3

2m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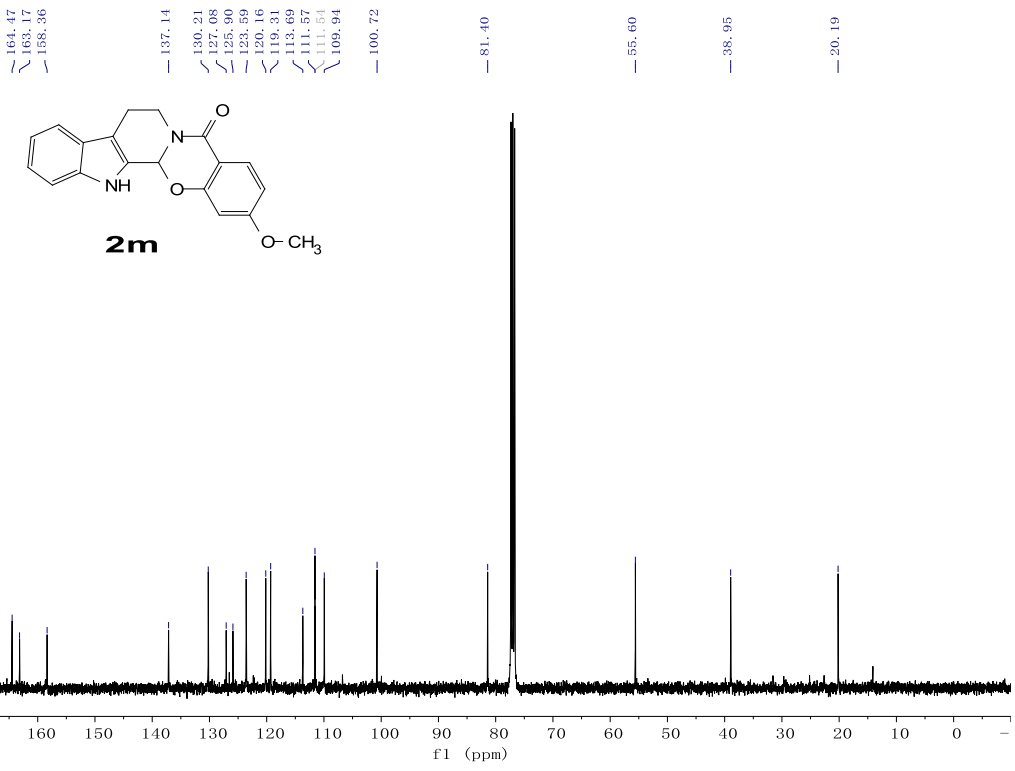
1.06
1.03
0.96
1.09
3.00
1.04
2.04
f1 (ppm)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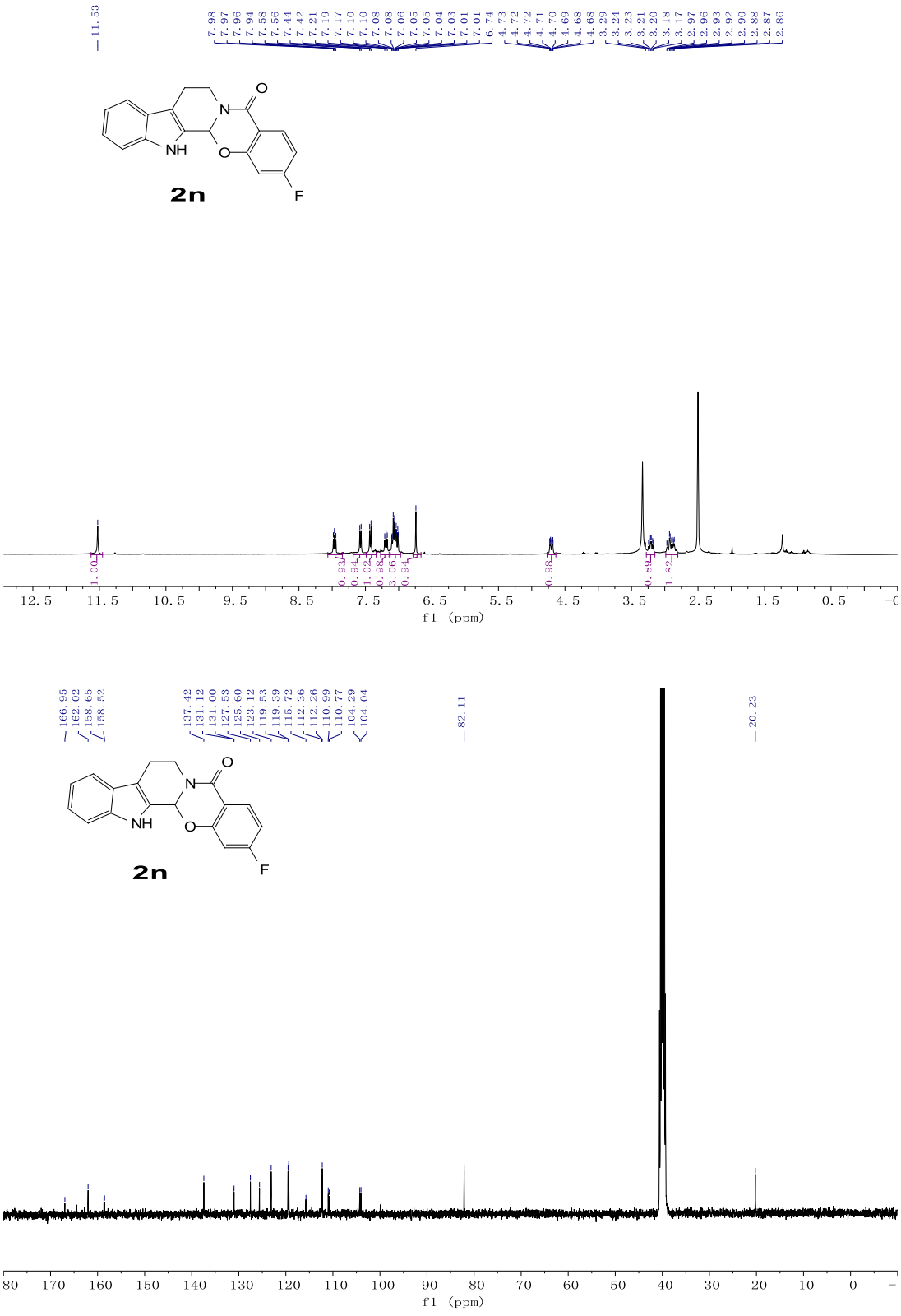
163.17
158.36
137.14
130.21
127.08
125.90
123.59
120.16
119.31
113.69
111.57
111.54
109.94
100.72
81.40
55.60
38.95
20.19
O
N
NH
O
O- CH3
f1 (ppm)

2m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7.98
7.97
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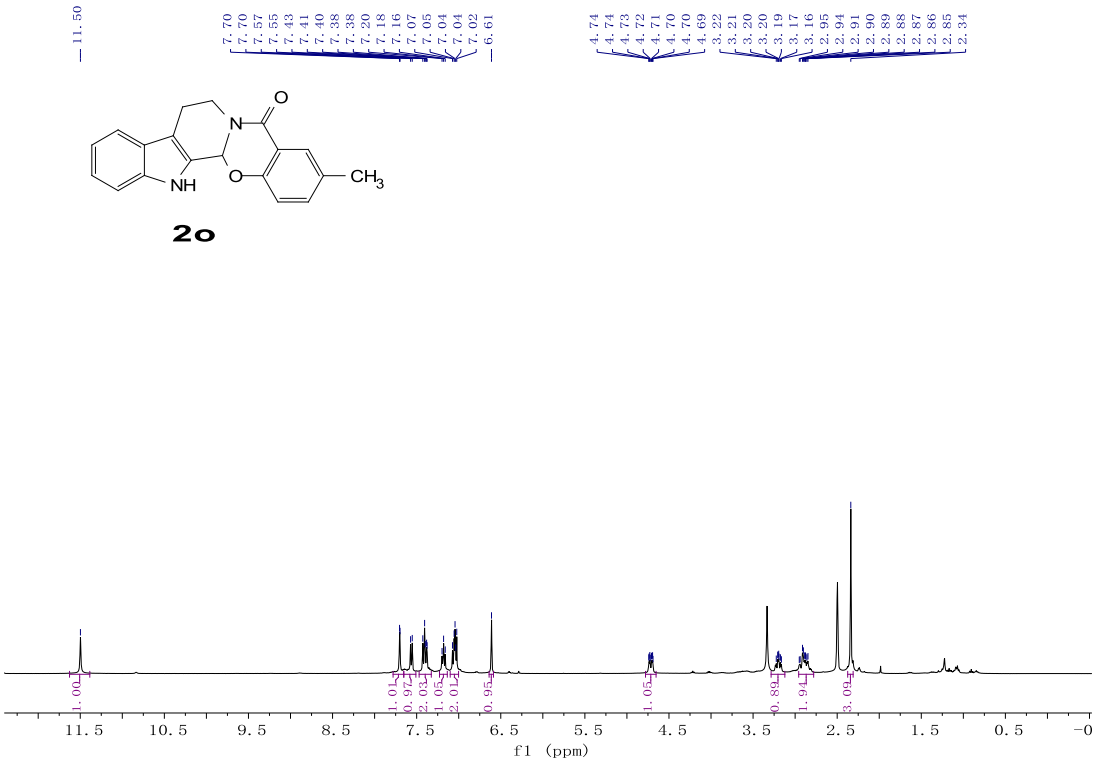
7.94
7.58
7.56
7.44
7.42
7.21
7.19
7.17
7.10
7.10
7.08
7.08
7.06
7.05
7.05
7.04
7.03
7.01
7.01
6.74
4.73
4.72
4.72
4.71
4.70
4.69
4.68
4.68
3.29
3.24
3.23
3.21
3.20
3.18
3.17
2.97
2.96
2.93
2.92
2.90
2.88
2.87
2.86
O
N
NH
O
F
2n
1.00
0.93
0.94
1.02
0.98
3.06
0.94
0.98
0.89
1.82
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)
166.95
162.02
158.65
158.52
137.42
131.12
131.00
127.53
125.60
123.12
119.53
119.39
115.72
112.36
112.26
110.99
110.77
104.29
104.04
82.11
20.23
O
N
NH
O
F
2n
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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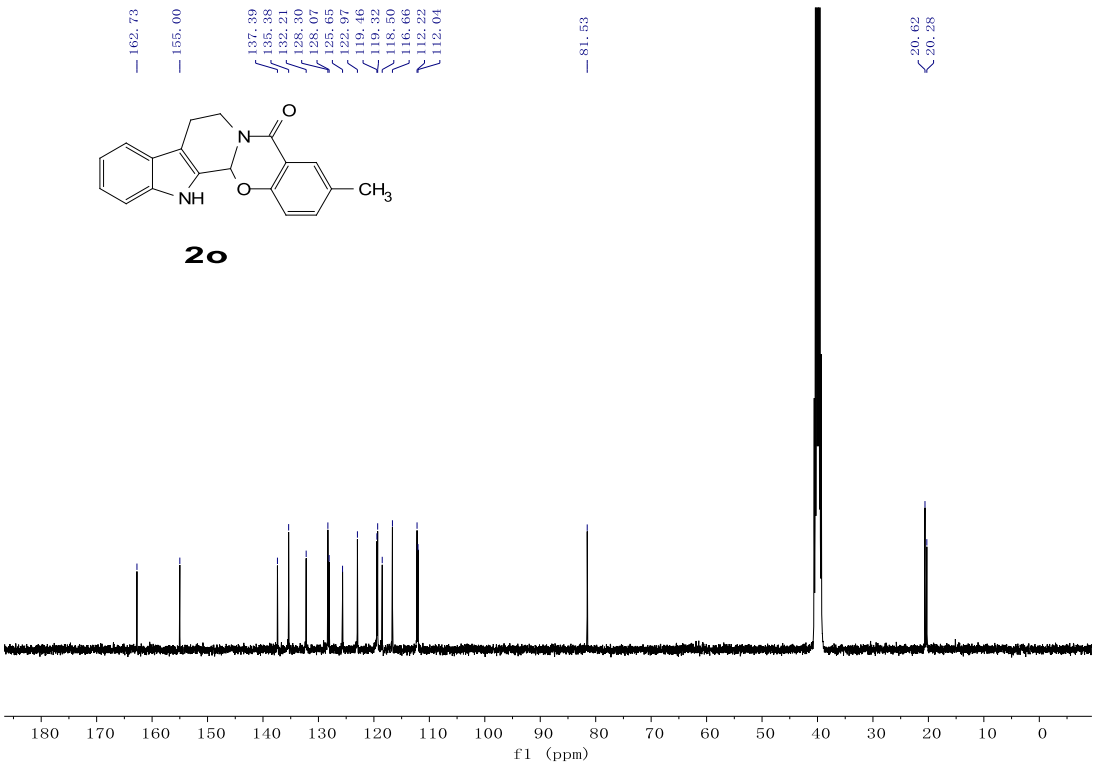
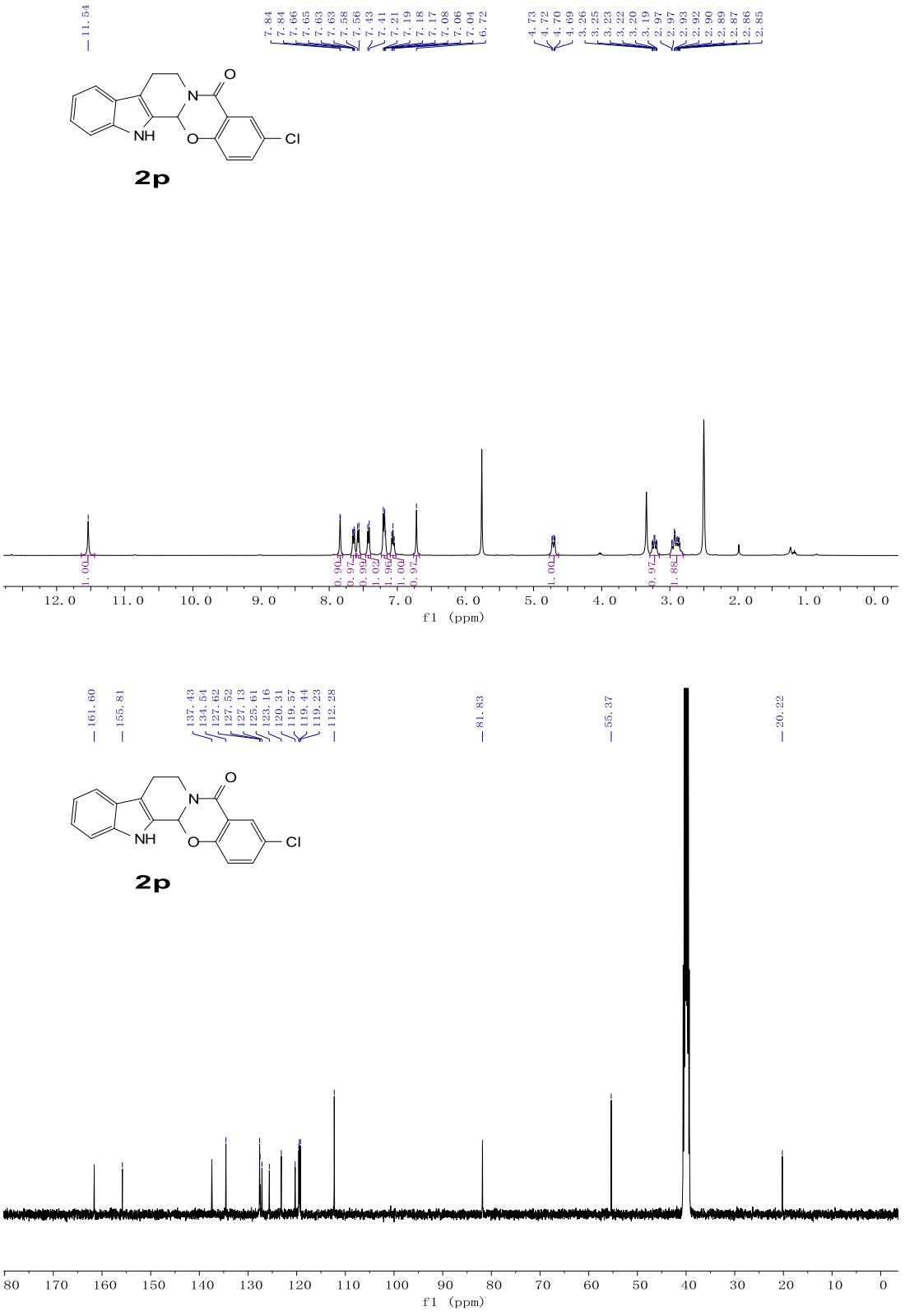
7.70
7.70
7.57
7.55
7.43
7.41
7.40
7.38
7.38
7.20
7.18
7.16
7.07
7.05
7.04
7.04
7.02
6.61
4.74
4.74
4.73
4.72
4.71
4.70
4.70
4.69
3.22
3.21
3.20
3.20
3.19
3.17
3.16
2.95
2.94
2.91
2.90
2.89
2.88
2.87
2.86
2.85
2.34
O
N
NH
O
CH3
1.00
1.01
0.97
2.03
1.05
2.01
0.95
1.05
0.89
1.94
3.09
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0
f1 (ppm)

2o


162.73
155.00
137.39
135.38
132.21
128.30
128.07
125.65
122.97
119.46
119.32
118.50
116.66
112.22
112.04
81.53
20.62
20.28
O
N
NH
O
CH3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2o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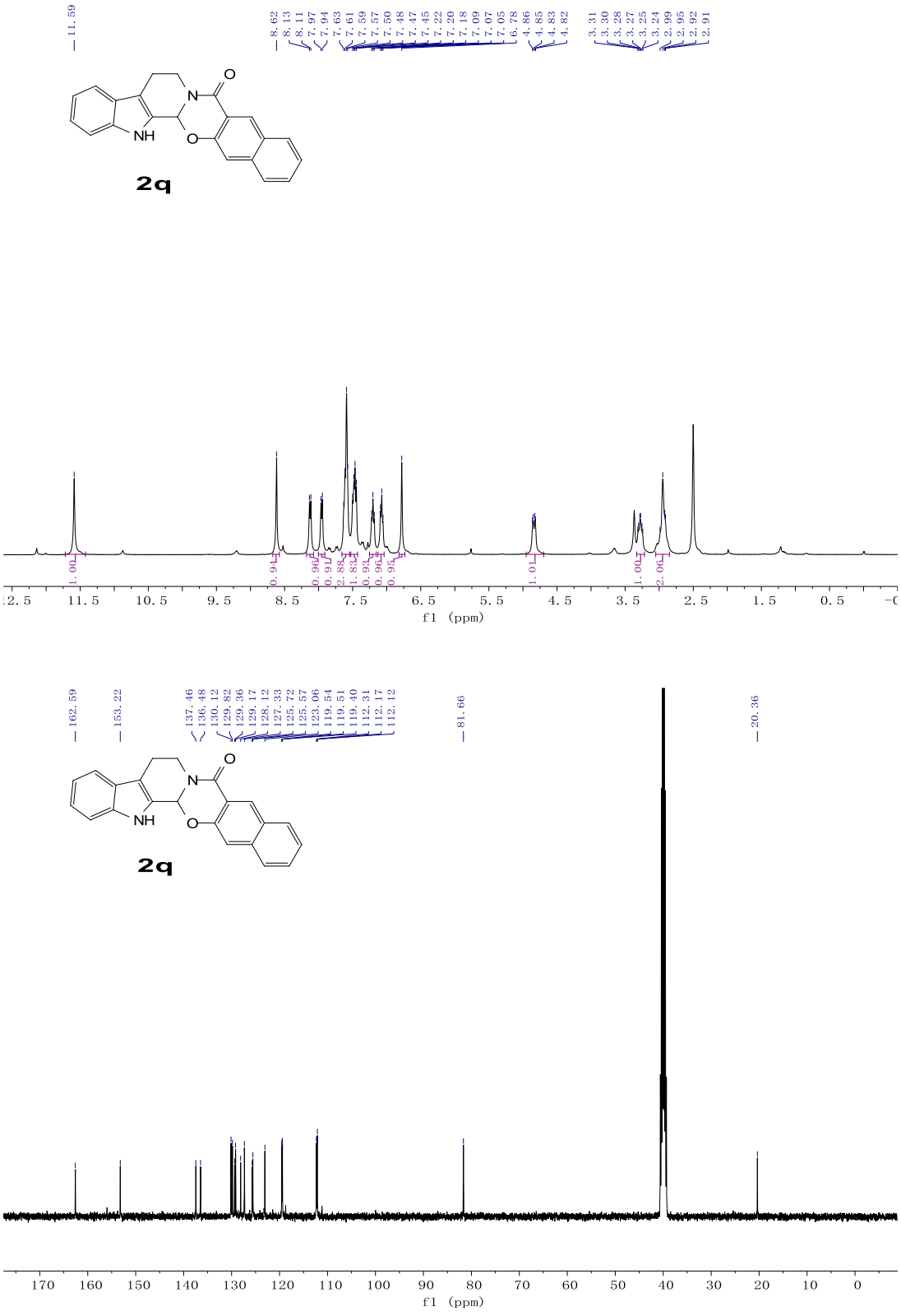
7.84
7.84
7.66
7.65
7.63
7.63
7.58
7.56
7.43
7.41
7.21
7.19
7.18
7.17
7.08
7.06
7.04
6.72
4.73
4.72
4.70
4.69
3.26
3.25
3.23
3.22
3.20
3.19
2.97
2.97
2.93
2.92
2.90
2.89
2.87
2.86
2.85
O
N
NH
O
Cl
2p
1.00
0.90
0.97
0.99
1.02
1.96
1.00
0.97
1.00
0.97
1.88
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)
161.60
155.81
137.43
134.54
127.62
127.52
127.13
125.61
123.16
120.31
119.57
119.44
119.23
112.28
81.83
55.37
20.22
O
N
NH
O
Cl
2p
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


11.59
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8.13
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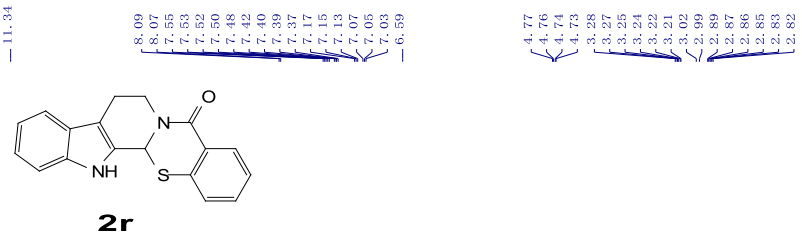
7.97
7.94
7.63
7.61
7.59
7.57
7.50
7.48
7.47
7.45
7.22
7.20
7.18
7.09
7.07
7.05
6.78
4.86
4.85
4.83
4.82
3.31
3.30
3.28
3.27
3.25
3.24
2.99
2.95
2.92
2.91
O
N
NH
O
2q
1.00
0.94
0.96
0.91
2.88
1.83
0.93
0.96
0.95
1.01
1.00
2.06
f1 (ppm)
162.59
153.22
137.46
136.48
130.12
129.82
129.36
129.17
128.12
127.33
125.72
125.57
123.06
119.54
119.51
119.40
112.31
112.17
112.12
81.66
20.36
O
N
NH
O
2q
f1 (ppm)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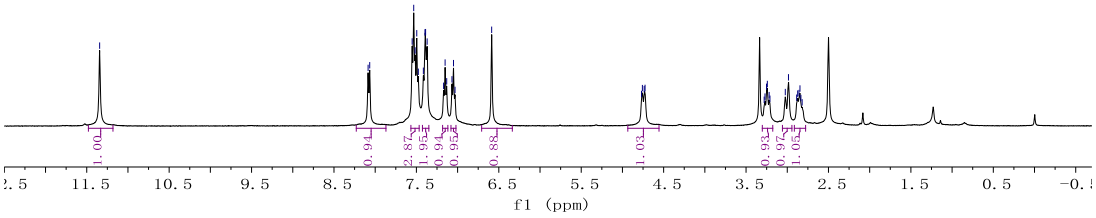
7.55
7.53
7.52
7.50
7.48
7.42
7.40
7.39
7.37
7.17
7.15
7.13
7.07
7.05
7.03
6.59
4.77
4.76
4.74
4.73
3.28
3.27
3.25
3.24
3.22
3.21
3.02
2.99
2.89
2.87
2.86
2.85
2.83
2.82
O
N
NH
S

2r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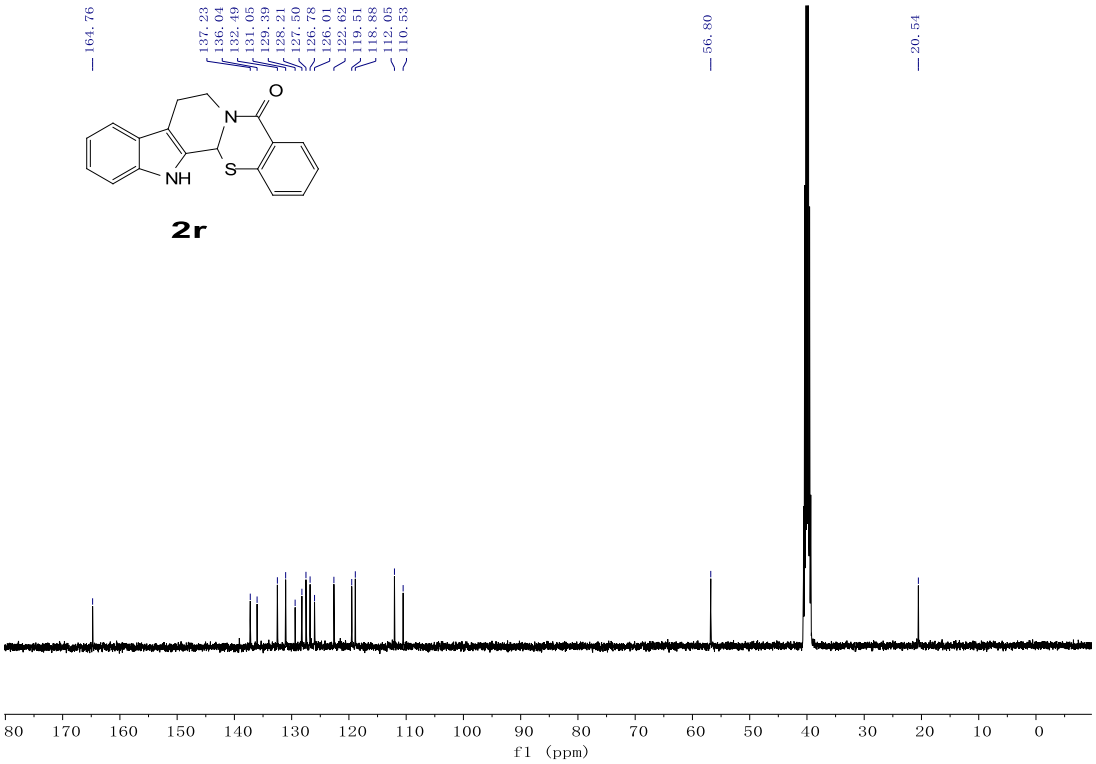
0.94
2.87
1.95
0.94
0.95
0.88
1.03
0.93
0.97
1.05
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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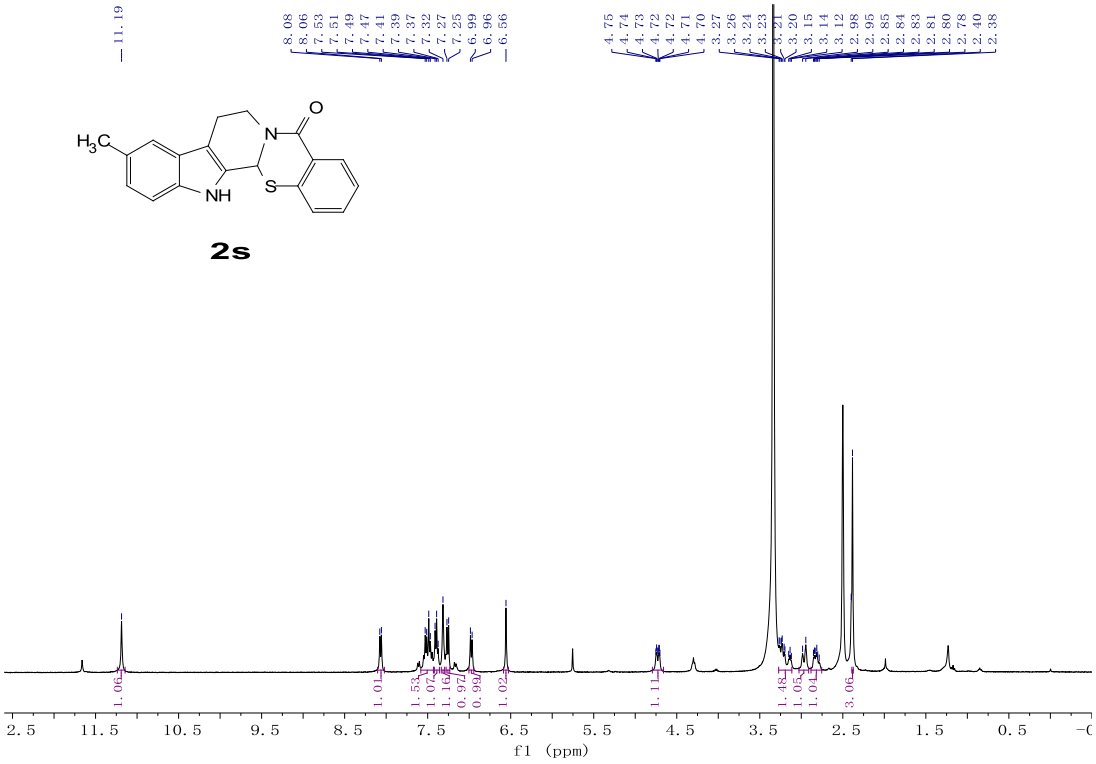
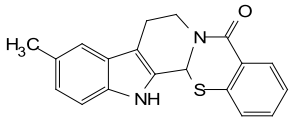
137.23
136.04
132.49
131.05
129.39
128.21
127.50
126.78
126.01
122.62
119.51
118.88
112.05
110.53
56.80
20.54
O
N
NH
S
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2r


11.19
8.08
8.06
7.53
7.51
7.49
7.47
7.41
7.39
7.37
7.32
7.27
7.25
6.99
6.96
6.56
4.75
4.74
4.73
4.72
4.72
4.71
4.70
3.27
3.26
3.24
3.23
3.21
3.20
3.15
3.14
3.12
2.98
2.95
2.85
2.84
2.83
2.81
2.80
2.78
2.40
2.38
1.06
1.01
1.53
1.07
1.16
0.97
0.99
1.02
1.11
1.48
1.05
1.04
3.06
f1 (ppm)

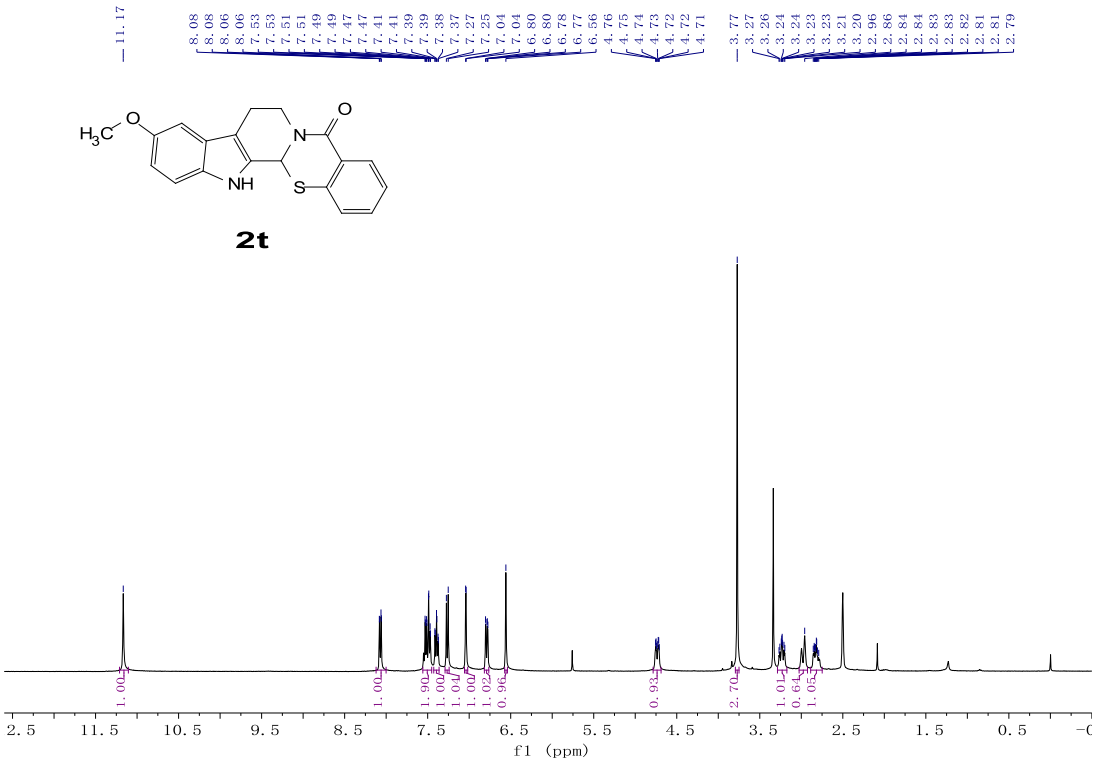

H3C
O
N
S
NH

2s

168.47
164.78
136.08
135.60
132.50
131.05
129.40
128.21
128.05
127.50
126.77
126.23
124.20
118.47
111.76
110.02
56.87
21.60
20.53
f1 (ppm)

H3C
O
N
S
NH

2s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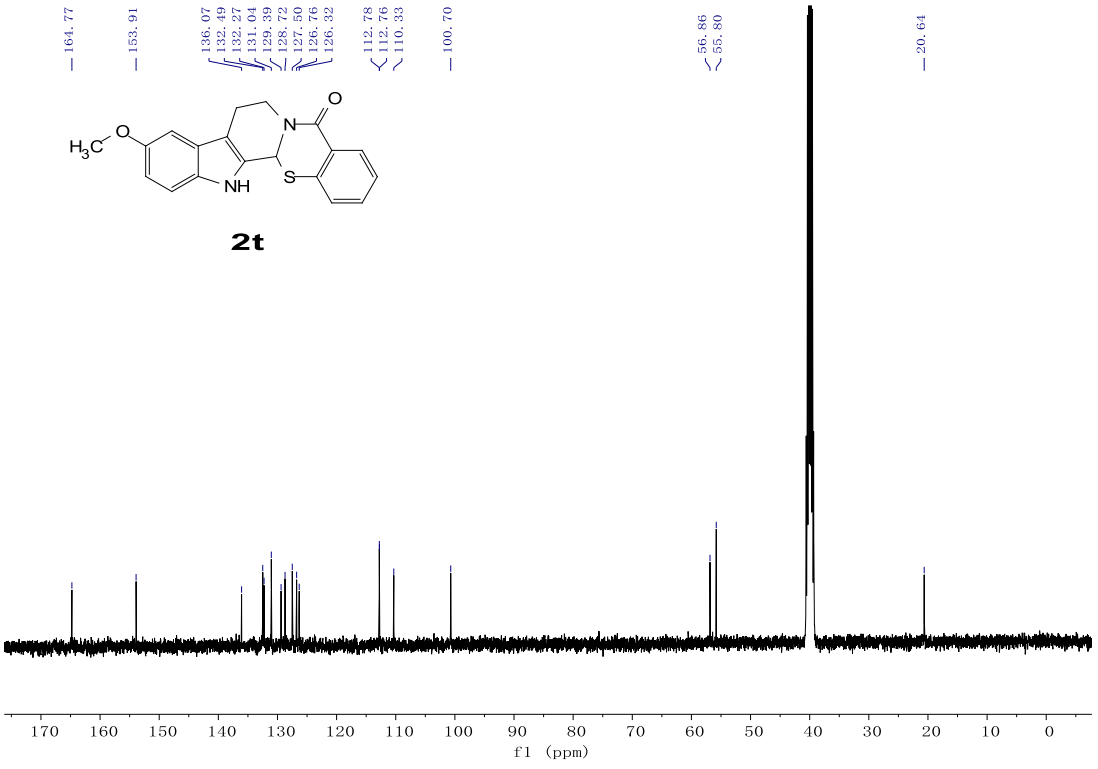
8.08
8.06
8.06
7.53
7.51
7.51
7.49
7.49
7.47
7.47
7.41
7.41
7.39
7.39
7.38
7.37
7.27
7.25
7.04
7.04
6.80
6.80
6.78
6.77
6.56
4.76
4.75
4.74
4.73
4.72
4.72
4.71
3.77
3.27
3.26
3.24
3.24
3.23
3.23
3.21
3.20
2.96
2.86
2.84
2.84
2.83
2.83
2.82
2.81
2.81
2.79
O
H3C
O
N
O
NH
S
2t
1.00
1.00
1.90
1.00
1.04
1.00
1.02
0.96
0.93
2.70
1.01
0.64
1.05
2.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)


164.77
153.91
136.07
132.49
132.27
131.04
129.39
128.72
127.50
126.76
126.32
112.78
112.76
110.33
100.70
56.86
55.80
20.64
O
H3C
O
N
O
NH
S
2t
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)