Condensation of Anthranilic Acids with Pyridines to Pyridoquinazolones via Pyridines Dearomatization

Yajun Yang [a,‡], Cuiju Zhu [b,‡], Min Zhang [b], Shijun Huang [b], Jingjing Lin [a], Xiandao Pan [a,*], and Weiping Su [b,*]

[a] State Key Laboratory of Bioactive Substances and Functions of Natural Medicines, and Beijing Key Laboratory of Active Substances Discovery and Druggability Evaluation, Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100050, China

[b] State Key Laboratory of Structural Chemistry, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Yangqiao West Road 155, Fuzhou, Fujian 350002, China

*Corresponding authors
Prof. Xiandao Pan, e-mail: xdp@imm.ac.cn
Prof. Weiping Su, e-mail: wpsu@fjirsm.ac.cn

‡These two authors contributed equally.

Contents

General Comments

All reactions were carried out under dry O_2 or dry air with dry solvents under anhydrous conditions unless otherwise noted. 4-Aminobenzo[d][1,3]dioxole-5-carboxylic acid,[1] 2-amino-4-benzyloxy -5-methoxybenzoic acid,[1] substituted carboline [2] and substituted 3,4-dihydro-β-carboline [3] were prepared according to the reported procedures. All other reagents used for experiments were purchased from Alfa Aesar, TCI, Sigma-Aldrich Co. CH_2Cl_2 was distilled from CaH_2 under nitrogen and stored under nitrogen. NMR spectra were obtained on a Bruker AVANCE 400 (400 MHz for ^1H NMR; 100 MHz for ^{13}C NMR; 377 MHz for ^{19}F NMR) spectrometer. HRMS were obtained on an Agilent Technologies 6224 TOF LC/MS equipped with an ESI source or HEXIN 10000 TOF-MS equipped with an API source.

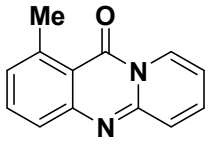
General Experimental Procedure

For compounds 3a-n and 4a-u: A 25 mL of Schlenk tube equipped with a stir bar was charged with 2-amino-6-methyl-benzoic acid (60.5 mg, 0.4 mmol, 1.0 equiv), EDCl (153.4 mg, 0.8 mmol, 2.0 equiv), pyridine (0.29 mL, 3.6 mmol, 9.0 equiv), CH_2Cl_2 (2.0 mL), was added in turn to the Schlenk tube through the rubber septum using syringes, Then, the tube was evacuated and refilled with O_2 for three times. Finally, the septum was replaced with a Teflon screwcap under O_2 flow. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

For compounds 5a-r: A 25 mL of Schlenk tube equipped with a stir bar was charged with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (60.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml) was added in turn to the Schlenk tube through the rubber septum using syringes. Then, the tube was stirred at 80^{o}C under air. After 4 hours, the

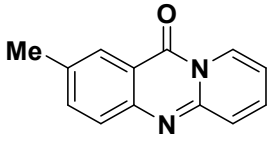
reaction mixture was concentrated under reduced pressure., The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

The Characterization of Products



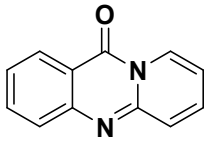
(**3a**)

1-Methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3a)：Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (73.9 mg, 88% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.78 (d, *J* = 8.0 Hz, 1H), 7.63-7.53 (m, 2H), 7.45-7.37 (m, 2H), 7.15 (d, *J* = 4.0 Hz, 1H), 6.78-6.75 (m, 1H), 2.92 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.90, 150.00, 147.54, 141.53, 134.10, 134.04, 127.45, 126.52, 125.98, 125.00, 115.03, 112.11, 23.63; HRMS (ESI) m/z calcd.for $C_{13}H_{11}N_2O$ $[M+H]^+$ 211.08659, found 211.08626.



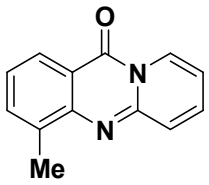
(**3b**)

2-Methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3b)：Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (77.3 mg, 92% yield). ^{1}H NMR(400MHz, $CDCl_3$) : δ 8.87 (d, *J* = 8.0 Hz, 1H), 8.23 (s, 1H), 7.72-7.66 (m, 2H), 7.50-7.48 (m, 2H), 6.86-6.82 (m, 1H), 2.54 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 158.89, 147.12, 146.68, 136.92, 135.38, 133.51, 126.72, 126.63, 126.32, 126.22, 116.04, 112.31, 21.37; HRMS (ESI) m/z calcd. for $C_{13}H_{11}N_2O$ $[M+H]^+$ 211.08659, found 211.08620.



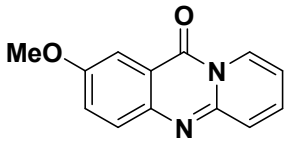
（**3c**）

11*H*-pyrido[2,1-*b*]quinazolin-11-one (3c)：Following the general procedure with 2-Amino-5-methylbenzoic acid (54.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at 80°C under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (55.7 mg, 71% yield). ^{1}H NMR (400MHz, $CDCl_3$) : δ 8.89 (d, *J* = 8.0 Hz, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 7.87-7.78 (m, 2H), 7.52-7.49 (m, 2H), 6.88-6.86 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.99, 148.57, 147.69, 135.05, 134.07, 127.29, 126.89, 126.69, 126.34, 125.20, 116.28, 112.47; HRMS (ESI) m/z calcd. for $C_{12}H_9N_2O$ $[M+H]^+$197.07094, found 197.07043.



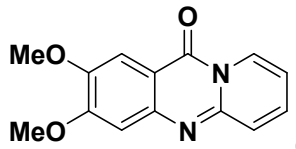
(**3d**)

4-Methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3d): Following the general procedure with 2-Amino-3-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (50.4 mg, 60% yield). ^{1}H NMR (400MHz, $CDCl_3$) : δ 8.83 (d, *J* = 7.3 Hz, 1H), 8.28 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.0 Hz, 1H), 7.51 (d, *J* = 9.1 Hz, 1H), 7.44 (dd, *J* = 8.2 and7.2 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 6.81 (t, *J* = 6.8 Hz, 1H), 2.68 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 159.30, 147.3, 146.64, 135.35, 135.03, 133.35, 126.88, 125.50, 124.89, 124.74, 116.19, 112.35, 17.66; HRMS (ESI) m/z calcd.for $C_{13}H_{11}N_2O$ $[M+H]^+$ 211.08659, found 211.08624.



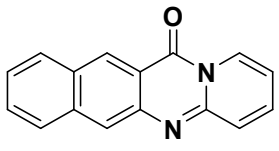
(**3e**)

2-Methoxy-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3e): Following the general procedure with 2-Amino-3-methoxylbenzoic acid (66.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (65.1 mg, 72% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.82 (d, *J* = 8.0 Hz, 1H), 7.70 (s, 1H), 7.67 (s, 1H), 7.45-7.41 (m, 3H), 6.83-6.79 (m, 1H), 3.93 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.57, 157.29, 145.98, 143.63, 132.74, 128.62, 126.70, 126.35, 126.33, 116.80, 112.50, 105.07, 55.80; HRMS (ESI) m/z calcd.for $C_{13}H_{11}N_2O_2$ $[M+H]^+$ 227.08150, found 227.08104.



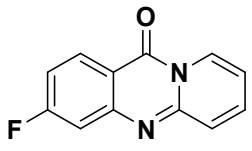
(**3f**)

2,3-Dimethoxy-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3f): Following the general procedure with 2-Amino-4,5-dimethylbenzoic acid (78.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (82.9 mg, 81% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.91(d, *J* = 8.0 Hz, 1H), 7.73 (s, 1H), 7.48 (s, 2H), 7.17 (s, 1H), 6.89-6.86 (m, 1H), 4.05 (s, 6H); ^{13}C NMR(100MHz, $CDCl_3$): δ 157.82, 156.24, 148.60, 146.86, 145.54, 133.19, 126.58, 125.87, 112.35, 109.81, 106.46, 105.16, 56.34, 56.31; HRMS (ESI) m/z calcd.for $C_{14}H_{13}N_2O_3$ $[M+H]^+$ 257.09207, found: 257.09161.



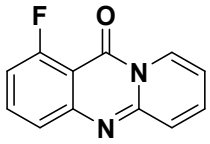
(**3g**)

12*H*-Benzo[g]pyrido[2,1-*b*]quinazolin-12-one (3g): Following the general procedure with 3-amino-2-naphthoic acid (74.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (73.8 mg, 75% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 9.11 (s, 1H), 8.78 (d, *J* = 8.0 Hz, 1H), 8.28 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.01(d, *J* = 8.0 Hz, 1H), 7.64-7.60 (m, 1H), 7.54-7.50 (m, 1H), 7.42 (m, 2H), 6.73 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$): δ 159.86, 147.13, 143.49, 137.34, 133.65, 130.62, 129.37, 129.00, 128.59, 127.77, 126.52, 126.34, 125.64, 123.89, 116.28, 111.32; HRMS (ESI) m/z calcd.for $C_{16}H_{11}N_2O$ $[M+H]^+$ 247.08659, found 247.08618.



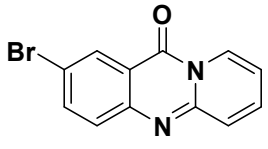
(**3h**)

3-Fluoro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3h): Following the general procedure with 2-Amino-4-fluorobenzoic acid (62.0 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (40.2 mg, 47% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.83 (d, *J* = 8.0 Hz, 1H), 8.04 (dd, *J* = 8.0 and 4.0 Hz, 1H), 7.78 (dd, *J* = 8.0 and 4.0 Hz, 1H), 7.60-7.47 (m, 3H), 6.90-6.86 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$): δ 160.89, 158.36, 147.03, 145.40, 133.83, 129.48, 126.39, 124.53, 124.29, 116.98, 112.82, 111.29, 111.06; HRMS (ESI) m/z calcd.for $C_{12}H_8N_2OF$ $[M+H]^+$ 215. 06152, found 215.06108.



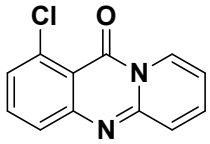
(**3i**)

1-Fluoro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3i): Following the general procedure with 2-Amino-6-fluorobenzoic acid (62.0 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (59.9 mg, 70% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.90 (d, *J* = 8.0 Hz, 1H), 7.78-7.73 (m, 1H), 7.59-7.47 (m, 3H), 7.12-7.08 (m, 1H), 6.92-6.88 (m, 1H); ^{13}C NMR(100MHz, $CDCl_3$): δ 162.96, 160.31, 150.41, 148.41, 135.19, 135.09, 126.58, 126.11, 122.75, 112.79, 110.87, 110.67; HRMS (ESI) m/z calcd.for $C_{12}H_8N_2OF$ $[M+H]^+$ 215.06152, found 215.06111.



(**3j**)

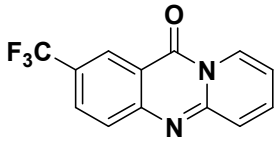
2-Bromo-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3j): Following the general procedure with 2-Amino-5-bromobenzoic acid (86.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (60.3 mg, 55% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.87 (d, *J* = 8.0 Hz, 1H), 8.57 (d, *J* = 4.0 Hz, 1H), 7.89 (dd, *J* = 8.0 and 4.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.58-7.49 (m, 2H), 6.92-6.89 (m, 1H); ^{13}C NMR(100MHz, $CDCl_3$): δ 157.82, 147.79, 147.26, 138.17, 134.47, 129.45, 128.74, 126.70, 126.36, 118.25, 117.34, 112.96; HRMS (ESI) m/z calcd.for $C_{12}H_8N_2OBr$ $[M+H]^+$ 274.98145, found 274.98114.



(**3k**)

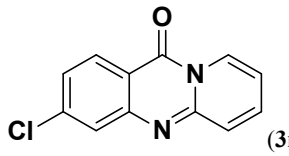
1-Chloro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3k): Following the general procedure with 2-Amino-6-chlorobenzoic acid (68.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (55.2 mg, 60% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.90 (d, *J* = 4.0 Hz, 1H), 7.68-7.67 (m, 2H), 7.58-7.54 (m, 1H), 7.48-7.46 (m, 2H), 6.92-6.88 (m, 1H); ^{13}C NMR(100MHz, $CDCl_3$): δ 156.87, 150.82, 148.10, 135.03, 134.39, 134.10, 127.51, 126.47, 126.20, 126.02, 113.41, 112.86; HRMS (ESI) m/z calcd.for $C_{12}H_8N_2OCl$

$[M+H]^+$ 231.03197, found: 231.03163.



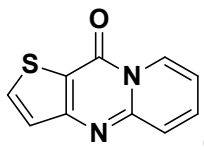
(**3l**)

2-Trifluoromethyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3l): Following the general procedure with 2-Amino-5-trifluoromethylbenzoic acid (82.0 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (52.8 mg, 50% yield). ^{1}H NMR (400MHz, DMSO-d_6): δ 8.30 (s, 1H), 8.21 (d, J = 4.0 Hz, 1H), 8.04-8.03 (m, 3H), 7.54 (d, J = 8.0 Hz, 1H), 7.01(d, J = 8.0 Hz, 1H); ^{13}C NMR (100MHz, DMSO-d_6): δ 157.90, 157.61, 153.69, 148.79, 132.74, 132.72, 128.01, 126.42, 126.39, 124.98, 124.95, 117.57, 106.83; HRMS (ESI) m/z calcd.for $C_{13}H_8N_2OF_3$ $[M+H]^+$ 265.05832, found 265.05780.



(**3m**)

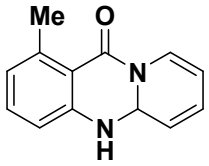
3-Chloro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3m): Following the general procedure with 2-Amino-4-chlorobenzoic acid (68.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (40.5 mg, 44% yield). ^{1}H NMR (400MHz, DMSO-d_6): δ 8.78 (dd, J = 4.0 and 8.0 Hz, 1H), 8.28 (d, J = 8.0 Hz, 1H), 7.78-7.74 (m, 2H), 7.52-7.48 (m, 2H), 7.11-7.08 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.37, 149.10, 148.58, 141.51 135.11, 128.73, 126.71, 125.99, 125.85, 114.40, 113.04; HRMS (ESI) m/z calcd.for $C_{12}H_8N_2OCl$ $[M+H]^+$ 231.03197, found: 231.03171.



(**3n**)

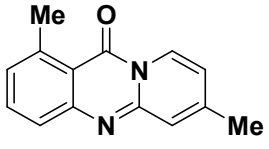
10-Oxo-10*H*-pyrido[1,2-*a*]thieno[3,2-*d*]pyrimidine (3n**)**: Following the general procedure with 3-Amino-2-thiopheneacetic acid (57.2 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (34.8 mg, 43% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 9.5 (d, J = 8.0 Hz, 1H), 7.7.98 (d, J = 4.0 Hz,

1H), 7.43(d, *J* = 8.0 Hz, 2H), 7.06(d, *J* = 4.0 Hz, 2H); ^{13}C NMR(100MHz, $CDCl_3$): δ 157.90, 154.43, 149.09, 136.62, 134.29, 126.39, 126.11, 124.89, 115.49, 113.66; HRMS (ESI) m/z calcd.for $C_{10}H_7N_2OS$ $[M+H]^+$ 203.02736, found: 203.02678.



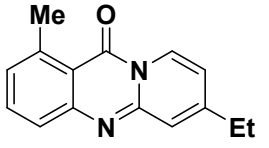
(3aa)

1-methyl-5*H*-pyrido[2,1-b]quinazolin-11(5a*H*)-one (3aa)**:** Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under argon gas. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:20) to afford a yellow solid (61.9 mg, 73% yield). ^{1}H NMR(500MHz, DMSO-d_6): δ 7.25-7.21(m, 2H), 7.15(d, *J* = 5.0 Hz, 1H), 6.71(d, *J* = 10.0 Hz, 1H), 6.63(d, *J* = 5.0 Hz, 1H), 6.10-6.06(m, 1H), 6.56-6.51(m, 2H), 6.30-6.27(m, 1H), 2.54(s, 3H); ^{13}C NMR(125MHz, DMSO-d_6): δ 161.40, 148.07, 141.87, 133.87, 123.66, 123.46, 122.42, 119.04, 114.02, 113.82, 103.66, 66.19, 22.67; HRMS (ESI) m/z calcd.for $C_{13}H_{13}N_2O$ $[M+H]^+$ 213.10224, found 213.10167.



(4a)

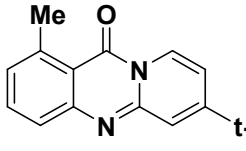
1,7-Dimethyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4a): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-methylpyridine (111.6 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure.The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2 = 100:10) to afford a yellow solid (65.4 mg, 73% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.68 (d, *J* = 8.0 Hz, 1H), 7.61-7.57 (m, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.16-7.12 (m, 2H), 6.61 (dd, *J* = 4.0 and 8.0 Hz, 1H), 2.92 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.98, 150.37, 147.68, 145.79, 141.53, 134.08, 127.01, 125.79, 124.82, 123.34, 115.21, 114.77, 23.66, 21.35; HRMS (ESI) m/z calcd.for $C_{14}H_{13}N_2O$ $[M+H]^+$ 225.10224, found 225.10188.



(4b)

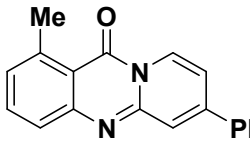
1-Methyl-7-ethyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4b): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-ethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O

(20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (68.5 mg, 72% yield). ^{1}H NMR(400MHz, $CDCl_3$): δ 8.71 (d, *J* = 8.0 Hz, 1H), 7.62-7.58 (m, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.18 (s, 1H), 7.14 (d, *J* = 4.0 Hz, 1H), 6.64 (dd, *J* = 4.0 and 8.0Hz, 1H), 2.93 (s, 3H), 2.67(q, *J* = 8.0 Hz, 2H), 1.29 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 159.01, 151.25, 150.46, 147.91, 141.50, 134.01, 126.96, 125.88, 124.85, 121.77, 114.81, 114.25, 28.17, 23.60, 12.87; HRMS (ESI) m/z calcd.for $C_{15}H_{15}N_2O$ $[M+H]^+$ 239.11789, found 239.11739.



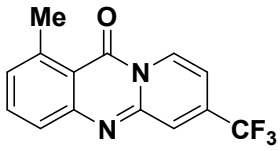
(4c)

1-Methyl-7-tert-Butyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4c): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-tert-butylpyridine (0.2 mL, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (60.6 mg, 57% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.75 (d, *J* = 8.0 Hz, 1H), 7.63-7.54 (m, 2H), 7.32 (d, *J* = 0.8 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 6.8 (dd, *J* = 8.0 Hz, 1H), 2.94 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.95, 158.02, 150.52, 148.04, 141.50, 134.04, 126.99, 125.89, 124.78, 119.80, 114.8, 111.94, 35.11, 29.66, 29.45, 23.72, 23.54; HRMS (ESI) m/z calcd.for $C_{17}H_{19}N_2O$ $[M+H]^+$ 267.14919, found 267.14862.



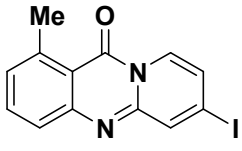
(4d)

1-Methyl-7-phenyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4d): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-phenylpyridine (186.3 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (62.9 mg, 55% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.89 (dd, *J* = 8.0 and 0.8 Hz, 1H), 7.74-7.72 (m, 2H), 7.66-7.61 (m, 3H), 7.52-7.47 (m, 3H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.12 (dd, *J* = 8.0 and 2.0 Hz, 1H), 2.98 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.95, 150.53, 147.91, 146.04, 141.68, 136.42, 134.25, 129.83, 129.28, 127.40, 126.84 126.78, 125.01, 121.68, 115.03, 111.98, 23.65; HRMS(ESI) m/z calcd.for $C_{19}H_{15}N_2O$ $[M+H]^+$ 287.11789, found 287.11728.



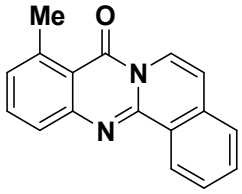
(4e)

1-Methyl-7-trifluoromethyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4e): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-trifluoromethylpyridine (0.2 mL, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (55.6 mg, 50% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.84 (d, *J* = 8.0 Hz, 1H), 7.71-7.67 (m, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.28-7.26 (m, 1H), 6.84 (dd, *J* = 8.0 Hz, 1H), 2.94 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 158.34, 149.56, 145.87, 141.84, 134.60, 128.84, 128.46, 125.53, 124.69, 124.64, 115.63, 106.86, 106.83, 23.52; HRMS (ESI) m/z calcd.for $C_{14}H_{10}N_2OF_3$ $[M+H]^+$ 279.07397, found 279.07339.



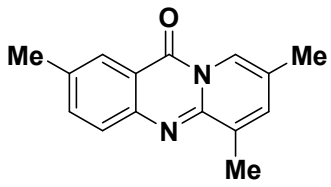
(4f)

1-Methyl-7-iodo-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4f): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-iodopyridine (164.0 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (84.7 mg, 63% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.46 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 4.0 Hz, 1H), 7.67-7.63 (m, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.99 (dd, *J* = 8.0 Hz, 1H), 2.93 (s, 1H); ^{13}C NMR(100MHz, $CDCl_3$): δ 158.70, 149.78, 146.76, 141.82, 134.68, 134.53, 128.06, 126.47, 125.28, 120.93, 115.24, 102.64, 23.55; HRMS(ESI) m/z calcd.for $C_{13}H_{10}N_2OI$ $[M+H]^+$ 336.98323, found 336.98248.



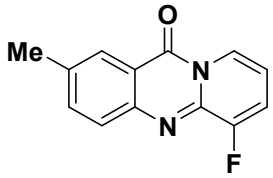
(4g)

1-Methyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (4g): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), isoqiunoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH_2Cl_2=100:10) to afford a yellow solid (57.2 mg, 55% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.95 (d, *J* = 8.0 Hz, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 7.68-7.54 (m, 5H), 7.20 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 2.96 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 159.49, 148.92, 145.80, 141.48, 133.80, 132.87, 131.94, 128.22, 128.13, 127.28, 127.01, 126.22, 125.71, 121.72, 116.37, 112.69, 23.56; HRMS (ESI) m/z calcd.for $C_{17}H_{13}N_2O$ $[M+H]^+$ 261.10224, found 261.10190.



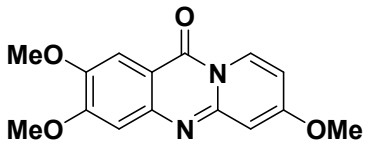
(**4h**)

2,6,8-Trimethyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4h): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), 3,5-dimethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (67.6 mg, 71% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.21 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.22 (s, 1H), 2.57 (s, 3H), 2.52 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 159.20, 146.30, 146.23, 136.32, 135.17, 134.92, 133.73, 127.19, 126.04, 121.69, 121.51, 115.79, 21.36, 18.41, 18.32; HRMS (ESI) m/z calcd.for $[M+H]^+$ 239.11789 $C_{15}H_{15}N_2O$, found 239.11736.



(**4i**)

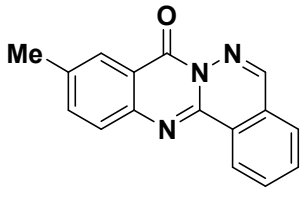
2-Methyl-6-fluoro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4i): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), 3-fluoropyridine (349.2 mg, 3.6 mmol), and EDCI (153.4 mg, 0.8 mmol). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (50.2 mg, 55% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.67 (d, *J* = 8.0 Hz, 1H), 8.22 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 6.78-6.73 (m, 1H), 2.54 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 158.36, 155.31, 152.75, 145.60, 137.19, 136.49, 126.92, 126.32, 122.77, 116.40, 114.40, 109.85, 21.41; HRMS (ESI) m/z calcd.for $C_{13}H_{10}N_2OF$ $[M+H]^+$ 229.07717, found: 229.07687.



(**4j**)

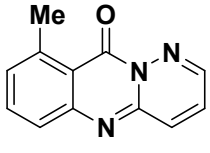
2,3,7-Trimethoxy-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4o): Following the general procedure with 2-Amino-4,5-dimethoxylbenzoic acid (78.8 mg, 0.4 mmol), 4-methoxylpyridine (87.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (52.6 mg, 46% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.80 (d, *J* = 8.0 Hz, 1H), 7.65 (s, 1H), 7.05 (s, 1H), 6.67 (d, *J* = 4.0 Hz, 1H), 7.60-7.58 (m, 1H), 4.03 (s, 3H), 4.02 (s, 3H), 3.94 (s, 3H);

^{13}C NMR (100MHz, $CDCl_3$): δ 163.11, 157.89, 156.31, 148.87, 147.78, 146.36, 126.79, 108.78, 108.72, 105.92, 105.35, 100.01, 56.26, 56.26, 56.01; HRMS (ESI) m/z calcd.for $C_{15}H_{15}N_2O_4$ $[M+H]^+$ 287.10263, found 287.10205.



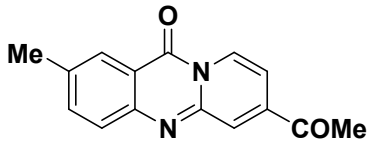
(4k)

9-methyl-8*H*-phthalazino[1,2-b]quinazolin-8-one (4q): Following the general procedure with 2-amino-6-methyl-benzoic acid (60.4 mg, 0.4 mmol), phthalazine (104.0mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL).. The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: ethyl acetate=100:40) to afford a yellow solid (55.3 mg, 53% yield). ^{1}H NMR (500MHz, $CDCl_3$) : δ 8.92 (d, *J* = 5.0 Hz, 1H), 8.66 (s, 1H), 8.32 (s, 1H), 7.88 (t, *J* = 5.0 Hz, 1H), 7.83 (t, *J* = 5.0 Hz, 1H), 7.76 (t, *J* = 10.0 Hz, 2H), 7.66 (d, *J* = 10.0 Hz, 1H), 2.54 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) : δ159.08, 145.31, 144.59, 142.57, 136.77, 136.51, 133.34, 132.74, 129.13, 127.30, 127.12, 127.07, 126.01, 124.96, 120.00, 21.41; HRMS (ESI) m/z calcd.for $C_{16}H_{12}N_3O$ $[M+H]^+$ 262.09804, found 262.09598.



(4l)

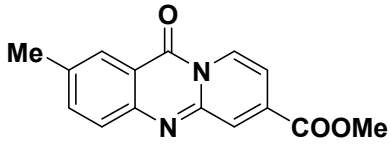
9-methyl-10*H*-pyridazino[6,1-b]quinazolin-10-one (4r): Following the general procedure with 2-amino-6-methyl-benzoic acid (60.4 mg, 0.4 mmol), pyridazine (64.0 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL).. The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: ethyl acetate=100:40) to afford a yellow solid (38.8 mg, 46% yield). ^{1}H NMR (500MHz, $CDCl_3$) : δ 8.45 (s, 1H), 8.35 (s, 1H), 7.72(s, 3H), 7.25 (s, 1H), 2.56 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) : δ 158.61, 145.37, 144.44, 143.55, 137.13, 137.00, 135.30, 127.11, 127.01, 124.80, 119.32, 21.48; HRMS (ESI) m/z calcd.for $C_{12}H_{10}N_3O$ $[M+H]^+$ 212.08184, found 212.08124.



(4m)

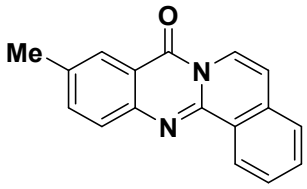
7-acetyl-2-methyl-11*H*-pyrido[2,1-b]quinazolin-11-one (4t): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-acetylpyridine (96.8 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced

pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (48.4 mg, 48% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.88-8.86 (m, 1H), 8.29-8.28 (m, 1H), 8.03-8.02 (m, 1H), 7.77-7.76 (m, 2H), 7.30-7.28 (m, 1H), 2.69-2.68 (m, 3H), 2.58(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 196.43, 158.55, 146.72, 146.52, 140.01, 137.25, 137.07, 129.13, 127.31, 127.26, 126.55, 116.94, 108.71, 29.73, 21.56; HRMS (ESI) m/z calcd.for $[M+H]^+$ 253.09715 $C_{15}H_{13}N_2O_2$, found 253.09636.



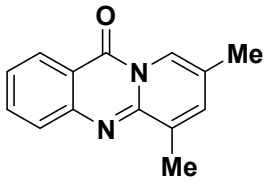
(**4n**)

methyl 2-methyl-11-oxo-11*H*-pyrido[2,1-b]quinazoline-7-carboxylate (4u): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), Methyl isonicotinate (109.6 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (45.0 mg, 42% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.85 (dd, *J* = 8.0 and 4.0 Hz, 1H), 8.27-8.26 (s, 1H), 8.17-8.16 (m, 1H), 7.77-7.72 (m, 2H), 7.25 (dd, *J* = 8.0 and 4.0 Hz, 1H), 4.00 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 164.39, 158.59, 146.55, 146.36, 137.16, 136.84, 134.52, 129.83, 127.35, 127.20, 126.41, 116.77, 110.28, 53.07, 21.54; HRMS (ESI) m/z calcd.for $[M+H]^+$ 269.09207 $C_{15}H_{13}N_2O_3$, found 269.09128.



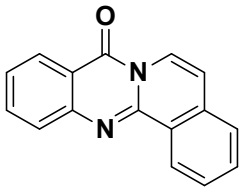
(**4o**)

2-Methyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (4j): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), isoquinoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (62.4 mg, 60% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 9.07 (d, *J* = 8.0 Hz, 1H), 8.66 (d, *J* = 8.0 Hz, 1H), 8.25 (s, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.72-7.64 (m, 4H), 7.02 (d, *J* = 8.0 Hz, 1H), 2.55 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 159.38, 145.55, 145.46, 136.48, 135.91, 132.68, 131.90, 128.37, 127.53, 127.31, 127.02, 126.37, 121.96, 117.46, 112.98, 21.39; HRMS (ESI) m/z calcd.for $C_{17}H_{13}N_2O$ $[M+H]^+$ 261.10224, found 261.10178.



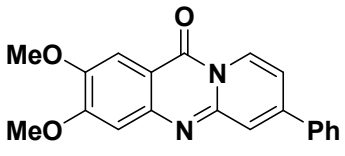
(**4p**)

6,8-Dimethyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4k): Following the general procedure with 2-Aminobenzoic acid (54.8 mg, 0.4 mmol), 3,5-dimethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (60.9 mg, 68% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.43(d, *J* = 8.0 Hz, 1H), 7.82-7.78 (m, 2H), 7.46-7.43 (m, 1H), 7.26 (s, 1H)), 2.58 (s, 3H), 2.32 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 159.28, 148.14, 146.74, 135.38, 133.78, 133.32, 127.34, 127.10, 123.40, 121.72, 121.69, 116.02, 18.41, 18.31; HRMS(ESI) m/z calcd.for $C_{14}H_{13}N_2O$ $[M+H]^+$ 225.10224, found 225.10176.



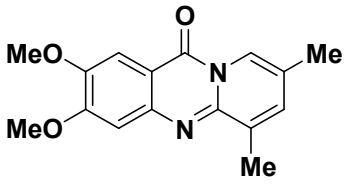
(**4q**)

8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (4l): Following the general procedure with 2-Aminobenzoic acid (60.4 mg, 0.4 mmol), isoquinoline (103.2 mg, 2.0 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (59.0 mg, 60% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 9.10 (d, *J* = 8.0 Hz, 1H), 8.67 (d, *J* = 8.0 Hz, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 7.90-7.87 (m, 2H), 7.75-7.66 (m, 3H), 7.54-7.51 (m, 1H), 7.05 (d, *J* = 8.0Hz, 1H); ^{13}C NMR(100MHz, $CDCl_3$): δ 159.43, 147.49, 146.10, 134.75, 132.82, 132.12, 128.43, 127.49, 127.41, 127.23, 127.18, 126.40, 125.71, 121.87, 117.72, 113.12; HRMS (ESI) m/z calcd.for $C_{16}H_{11}N_2O$ $[M+H]^+$ 247.08659, found 247.08607.



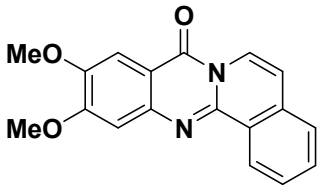
(**4r**)

2,3-Dimethoxy-7-phenyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4m): Following the general procedure with 2-Amino-4,5-dimethoxylbenzoic acid (78.8, 0.4 mmol), 4-phenylpyridine (124.0 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (110.2 mg, 83% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.94 (d, *J* = 8.0 Hz, 1H), 7.73-7.67 (m, 4H), 7.54-7.46 (m, 3H), 7.17-7.14 (m, 2H), 4.04 (s, 3H), 4.04 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 157.70, 156.28, 148.52, 147.14, 145.98, 145.16, 136.53, 129.35, 129.35, 129.33 126.81, 126.77, 126.77, 112.15, 109.70, 106.42, 105.25, 56.33, 56.33; HRMS(ESI) m/z calcd.for $C_{20}H_{17}N_2O_3$ $[M+H]^+$ 333.12337, found 333.12259.



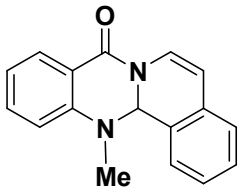
(**4s**)

2,3-Dimethoxy-6,8-dimethyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (4n): Following the general procedure with 2-Amino-4,5-dimethoxylbenzoic acid (78.8 mg, 0.4 mmol), 3,5-dimethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (79.5 mg, 70% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.62 (s, 1H), 7.69 (s, 1H), 7.22 (s, 1H), 7.18 (s, 1H), 4.05 (s, 3H), 4.03 (s, 3H), 2.57 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 158.14, 155.82, 148.38, 145.95, 145.11, 134.95, 133.24, 121.72, 121.53, 109.64, 106.85, 105.04, 56.32, 56.27, 18.38, 18.32; HRMS (ESI) m/z calcd.for $C_{16}H_{17}N_2O_3$ $[M+H]^+$ 285.12337, found 285.12277.



(**4t**)

2,3-Dimethoxy-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (4p): Following the general procedure with 2-Amino-4,5-dimethoxylbenzoic acid (78.8 mg, 0.4 mmol), isoquinoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL).. The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (79.6 mg, 65% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 9.02 (d, J = 8.0 Hz, 1H), 8.67 (d, J = 8.0 Hz, 1H), 7.74-7.62 (m, 4H), 7.27 (s, 1H), 7.03 (d, J = 8.0 Hz, 1H), 4.08 (s, 3H), 4.04 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$): δ 158.45, 155.78, 148.75, 145.16, 144.22, 132.56, 131.74, 128.32, 127.38, 126.93, 126.70, 126.41, 121.97, 112.91, 111.15, 107.36, 105.55, 56.34, 56.32; HRMS (ESI) m/z calcd.for $C_{18}H_{15}N_2O_3$ $[M+H]^+$ 307.10772, found 307.10712.

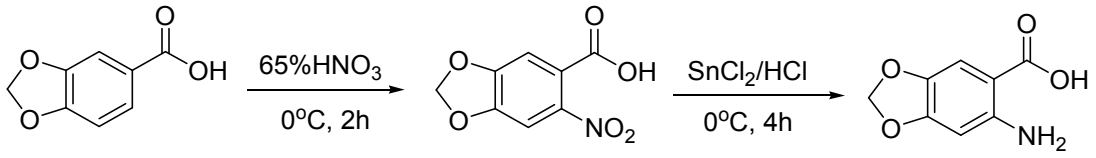


(4u)

13,13a-dihydro-13-methylisoquinolino[1,2-b]quinazolin-8-one (4s): Following the general procedure with 2-(*N*-methylamino)benzoic acid (60.4 mg, 0.4 mmol), isoquinoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL).. The reaction mixture was stirred at room temperature under 1 atm O_2. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: ethyl acetate=100:40) to

afford a yellow solid (67.1 mg, 64% yield). ^{1}H NMR(500MHz, $CDCl_3$) : δ 8.09 (d, *J* = 5.0 Hz, 1H), 7.54(t, *J* = 5.0 Hz, 1H), 7.46 (d, *J* = 5.0 Hz, 1H), 7.41 (d, *J* = 10.0 Hz, 1H), 7.28-7.20 (m, 4H), 7.06 (d, *J* = 10.0 Hz, 1H), 6.46 (s, 1H), 5.72 (d, *J* = 10.0 Hz, 1H), 2.64 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) : δ 162.09, 150.59, 134.34, 131.76, 129.36, 129.33, 127.92, 127.39, 126.84, 125.84, 124.20, 123.44, 122.96, 106.09, 72.24, 36.80; HRMS (ESI) m/z calcd.for $C_{17}H_{15}N_2O$ $[M+H]^+$ 263.11844, found 263.11652.

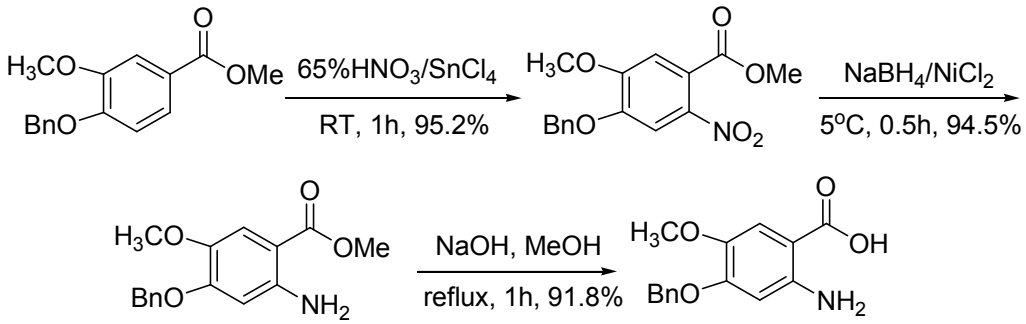
The synthesis of substituted anthranilic Acids:



4-Aminobenzo[d][1,3]dioxole-5-carboxylic acid

To a solution of 65% HNO_3 (10 mL, 102 mmol) at 0°C (ice-salt bath) was added benzo[d][1,3]dioxole-5-carboxylic acid (1.0 g, 6.0 mmol). After the resulting mixture was kept at 0°C for 1 h, then the solution was generally raised to room temperature for 1 h. Ice water (50g) was added to the solution. The solid was filtered, washed by water, and dried to afford a yellow solid (1.136g, 89.7%). ^{1}H NMR (500MHz, $CDCl_3$): δ 7.31 (s, 2H), 6.27 (s, 2H).

To a solution of concentration HCl (10 mL, 140 mmol) at 0°C (ice-salt bath) was added 4-nitrobenzo[d][1,3]dioxole-5-carboxylic acid (1.0 g, 4.7 mmol) and $SnCl_2 \cdot 2H_2O$ (3.17, 14.1 mmol). After the resulting mixture was kept at 0°C for 4 h, then ice water (50g) was added to the solution. The solution was adjusted to pH=5 with NaOH, and concentrated under vacuum. The residue was re-dissolved in methanol (100 ml). The solid was filtered, washed by methanol. The filtrate was dried and concentrated to afford a brown solid (619 mg, 72.8%). ^{1}H NMR (400MHz, CD_3OD): δ 7.17 (s, 1H), 6.27 (s, 1H), 5.86 (s, 2H).



2-Amino-4-(benzyloxy)-5-methoxybenzoic acid

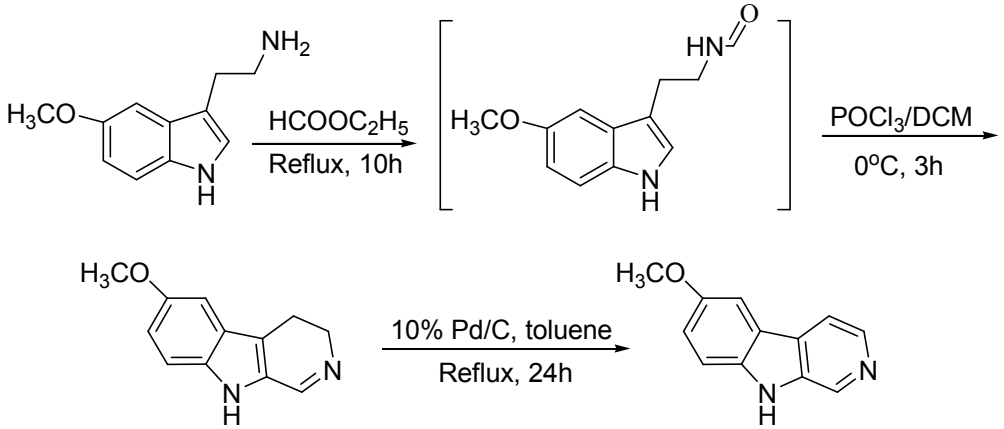
To a solution of methyl 4-(benzyloxy)-3-methoxybenzoate (8.76 g, 32.17 mmol) in CH_2Cl_2 at -20 °C was added a fresh prepared mixture consisting of tin (Ⅳ) chloride (40 ml of 1M in CH_2Cl_2, 40 mmol) and fuming nitric acid (2.14 ml, 51 mmol) in 10 min. The mixture was kept at -20 °C for 50 min, Water (100 ml) was added to the reaction and separated. The aqueous phase was extracted by ethyl acetate (3 × 60 mL) and the combined organic phases were washed with brine and dried under sodium sulfate. Concentration under vacuum then gave a residue that was triturated with methanol to generate a product (9.72 g, 95.2%).

To a solution of methyl 4-(benzyloxy)-5-methoxy-2-nitrobenzoate (6.34 g, 19.98 mmol) in CH_2Cl_2 (100 ml) and MeOH (50 ml) was added nickel (Ⅱ) chloride hexahydrate (1.5 g, 6.3 mmol). Sodium borohydride (2.5 g, 66 mmol) was then added in portions to the reaction at 0-5 °C in 30 min. The solvents were evaporated under vacuum and to the resulting residue was added cold 2N HCl (100 ml). The mixture was extracted with ethyl acetate (3 × 60 mL). After washing with brine and drying, the organic layer was evaporated under vacuum. Recrystallization of

the residue gave a product (5.43 g, 94.5%).

A solution of methyl 2-amino-4-(benzyloxy)-5-methoxybenzoate (4.88 g, 16.98 mmol) in 2N NaOH (60 ml) and methanol (60 ml) was heated at reflux for 1h. Methanol was removed by a rotary evaporator and the aqueous residue was acidified to PH 2 with cold concentrated HCl. Filtration and washing with water then gave the target compound (4.26, 91.8%). ^{1}H NMR (500MHz, DMSO-d_6): δ 7.43-7.34 (m, 5H), 7.15 (s, 1H), 6.42 (s, 1H),5.42 (s, 2H), 3.63 (s, 3H).

The synthesis of substituted carboline:

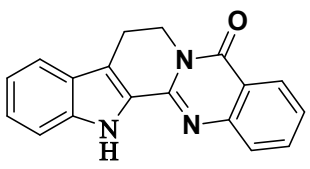


4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole

A solution of 5-methoxyltryptamine (1.90 g, 10 mmol) in 10 mL ethyl formate was heated at reflux for 10 h. Evaporation under vacuum gave a product (2.18 g, 100% yield). To the cooled solution of *N*-formyltryptamine (0.96 g, 5 mmol) in 3 mL of CH_2Cl_2 was added $POCl_3$ (1.25 mL) drop wise at 0~5 °C. After the addition, the reaction mixture was stirred at r.t. for another 2 hrs. Then it was concentrated in *vacuo* to remove unconsumed $POCl_3$ and CH_2Cl_2. The dark solid residue was suspended in ethyl acetate (50 mL) and extracted with 10% AcOH/water (4 × 30 mL). The combined AcOH extracts were basified with conc. aquous ammonia until pH 9. The precipitated solid was extracted with CH_2Cl_2 (3× 30 mL) to give the product as yellow foam (793 mg, 92.8%). ESI-MS: 201.1061[M+H].

6-methoxy-9H-pyrido[3,4-b]indole

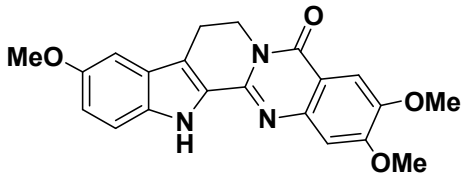
A solution of 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (0.40 g, 2 mmol) and 10% palladium on carbon (100 mg) in 20 mL toluene was heated at reflux for 24 h. The reaction was cooled, filtrated through celite, washed with CH_2Cl_2, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford a yellow solid (0.25 g, 64%). ^{1}H NMR (500MHz, DMSO-d_6): δ 11.38 (s, 1H), 8.84 (s, 1H), 8.27(d, J = 5.0 Hz, 1H), 8.07(d, J = 5.0 Hz, 1H), 7.77 (s, 1H), 7.50-7.49 (m, 1H), 7.18-7.17 (m, 1H), 3.85 (s, 3H).



(5a)

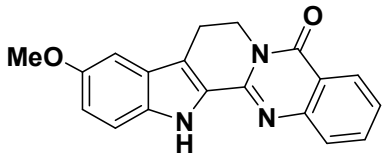
Rutaecarpine (5a): Following the general procedure with 2-Aminobenzoic acid (1.13 g, 8.23 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (1.40g, 8.23 mmol), EDCI (2.20 g, 11.5 mmol), and DMF (20 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The

residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (2.0 g, 85% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 9.41 (s, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.72-7.69 (m, 1H), 7.66-7.62 (m, 2H), 7.44-7.37 (m, 2H), 7.32-7.30 (m, 1H), 7.19-7.16 (m, 1H), 4.59 (t, *J* = 8.0 Hz, 2H), 3.23 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ 161.62, 147.49, 145.07, 138.35, 134.36, 127.27, 127.16, 126.57, 126.23, 125.63, 125.60, 121.18, 120.63, 120.09, 118.43, 112.12, 41.16, 19.68; HRMS (API) m/z calcd.for $C_{18}H_{14}N_3O$ $[M+H]^+$ 288.1123, found 288.1131.



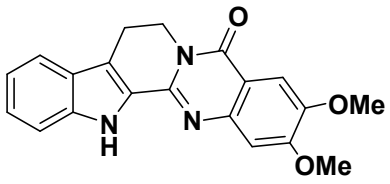
(5b)

Euxylophoricine D (5b): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (60.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (61.2 mg, 54% yield). ^{1}H NMR (500MHz, DMSO-d_6): δ 11.61 (s, 1H), 7.47 (s, 1H), 7.35 (d, *J* = 10.0 Hz, 1H), 7.10 (s, 1H), 7.05 (s, 1H), 6.89 (d, *J* = 10.0 Hz, 1H), 4.42 (t, *J* = 5.0 Hz, 2H), 3.92 (s, 3H), 3.88 (s, 3H), 3.79 (s, 3H), 3.13 (t, *J* = 5.0 Hz, 2H); ^{13}C NMR(125MHz, DMSO-d_6): δ 159.94, 154.56, 153.78, 148.15, 144.17, 143.39, 133.79, 127.70, 125.21, 116.55, 115.61, 113.63, 113.36, 107.06, 105.87, 100.43, 55.83, 55.78, 55.36, 40.83, 19.09; HRMS (ESI) m/z calcd.for $C_{21}H_{20}N_3O_4$ $[M+H]^+$ 378.14483, found 378.14331.



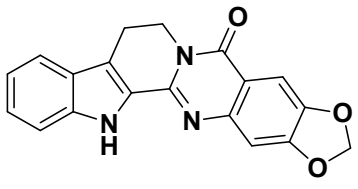
(5c)

Hortiacine (5c): Following the general procedure with 2-Aminobenzoic acid (49.3 mg, 0.36 mmol), 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (60.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (75.4 mg, 79% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 9.14 (s, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 7.71-7.65 (m, 2H), 7.42-7.31 (m, 2H), 7.01 (s, 2H), 4.58 (t, *J* = 8.0 Hz, 2H), 3.88 (s, 3H), 3.20 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR(125MHz, $CDCl_3$): δ 161.65, 154.68, 147.57, 144.92, 134.34, 133.50, 127.67, 127.22, 126.61, 126.14, 125.88, 121.09, 117.83, 116.72, 112.95, 100.61, 55.78, 41.12, 19.73; HRMS (ESI) m/z calcd.for $C_{19}H_{16}N_3O_2$ $[M+H]^+$ 318.12370, found 318.12216.



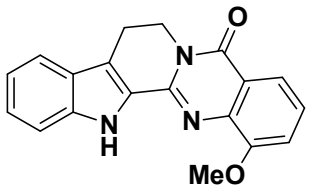
(5d)

Euxylophoricine A (5d): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (90.8 mg, 87% yield). ^{1}H NMR (500MHz, DMSO-d_6): δ 11.72 (s, 1H), 7.58 (s, 1H), 7.42 (d, J = 10.0 Hz, 2H), 7.21 (s, 1H), 7.02 (d, J = 10.0 Hz, 2H), 4.39 (s, 2H), 3.88 (s, 3H)), 3.84 (s, 3H), 3.11 (s, 2H); ^{13}C NMR(125MHz, DMSO-d_6): δ 159.93, 154.57, 148.22, 144.13, 143.34, 138.54, 127.38, 125.04, 124.52, 119.88, 119.74, 116.96, 113.72, 112.53, 107.11, 105.88, 55.85, 55.79, 40.80, 19.03; HRMS (API) m/z calcd.for $C_{21}H_{20}N_3O_4$ $[M+H]^+$ 348.1348, found 348.1343.



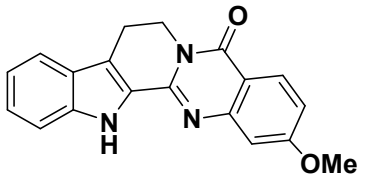
(5e)

Euxylophoricine C (5e): Following the general procedure with 6-aminobenzo[d][1,3]dioxole-5-carboxylic acid (65.2 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (41.8 mg, 42% yield). ^{1}H NMR (500MHz, DMSO-d_6): δ 7.63 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 4.0 Hz, 2H), 7.08 (d, J = 4.0 Hz, 2H), 6.21 (s, 2H), 4.42 (t, J = 8.0 Hz, 2H), 3.15 (t, J = 4.0 Hz, 2H); ^{13}C NMR (125MHz, DMSO-d_6): δ 159.90, 153.17, 146.76, 145.07, 144.27, 138.62, 127.16, 124.98, 124.61, 119.93, 119.77, 117.27, 115.39, 112.60, 104.66, 103.28, 102.53, 40.86, 19.01; HRMS (ESI) m/z calcd.for $C_{19}H_{14}N_3O_3$ $[M+H]^+$ 332.10297, found 332.10165



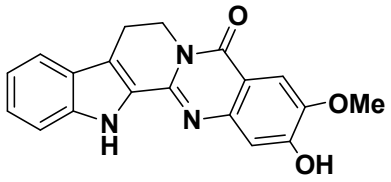
(5f)

1-Methoxyrutaecarpine (5f): Following the general procedure with 2-Amino-3-methoxybenzoic acid (60.1 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (45.8 mg, 48% yield). ^{1}H NMR (400MHz, Acetone-d_6+$CDCl_3$): δ 9.95 (s, 1H), 7.90 (d, J = 4.0 Hz, 1H), 7.61 (d, J = 4.0 Hz, 1H), 7.42-7.30 (m, 3H), 7.16 (d, J = 8.0 Hz, 2H), 4.57 (t, J = 8.0 Hz, 2H), 4.01 (s, 3H), 3.21 (t, J = 8.0 Hz, 2H); ^{13}C NMR (125MHz, Acetone-d_6+$CDCl_3$): δ 161.40, 153.96, 144.44, 138.33, 138.16, 127.30, 126.36, 125.48, 125.46, 122.18, 120.49, 120.01, 118.75, 118.12, 114.07, 112.18, 56.20, 41.23, 19.65; HRMS (ESI) m/z calcd.for $C_{19}H_{16}N_3O_2$ $[M+H]^+$ 318.12370, found 318.12268.



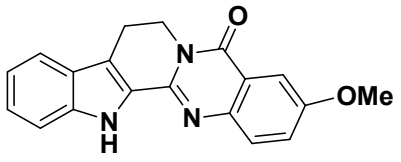
(5g)

2-Methoxyrutaecarpine (5g): Following the general procedure with 2-Amino-4-methoxybenzoic acid (60.1 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (61.1 mg, 64% yield). ^{1}H NMR (500MHz, DMSO-d_6): δ 11.85 (s, 1H), 8.09 (d, J = 10.0 Hz, 1H), 7.67 (d, J = 10.0 Hz, 1H), 7.51 (d, J = 5.0 Hz, 1H), 7.30 (s, 1H), 7.13-7.09 (m, 3H), 4.45 (t, J = 5.0 Hz, 2H), 3.94 (s, 5H); 3.20 (t, J = 5.0 Hz, 3H); ^{13}C NMR(125MHz, DMSO-d_6): δ 164.05, 160.27, 149.53, 145.95, 138.71, 128.39, 127.18, 124.97, 124.87, 120.08, 119.86, 118.01, 115.40, 114.27, 112.64, 107.65, 55.67, 40.68, 19.04; HRMS (ESI) m/z calcd.for $C_{19}H_{16}N_3O_2$ $[M+H]^+$ 318.12370, found 318.12274.



(5h)

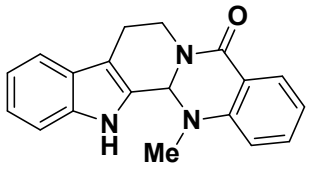
Euxylophoricine F (5h): Following the general procedure with 2-Amino-4-benzyloxy-5-methoxybenzoic acid (98.3 mg, 0.36 mmol), 4,9-dihydro-3*H*-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in methanol (5 ml). After addition of 10% palladium on carbon (10 mg) and ammonium formate (0.3 g), the mixture was heated to reflux for 1 hour. The reaction was cooled, filtrated through celite, washed with methanol, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (31.1 mg, 31% yield). ^{1}H NMR (500MHz , $CDCl_3$ +CD_3OD): δ 7.63（m, 2H）, 7.47 (d, J = 8.0Hz, 1H), 7.34 (m, 1H), 7.17 (m, 1H), 7.05 (s, 1H), 4.56 (t, J = 8Hz, 2H), 4.01 (s, 3H), 3.22 (t, J = 8Hz, 2H); ^{13}C NMR(125MHz, $CDCl_3$+CD_3OD): δ 161.19, 153.12, 147.81, 144.37, 143.24, 138.41, 126.55, 125.37, 125.17, 120.36, 119.84, 118.22, 113.42, 112.17, 109.70, 106.37, 56.10, 41.19, 19.55; HRMS (ESI) m/z calcd.for $C_{19}H_{16}N_3O_3$ $[M+H]^+$ 334.11862, found 334.11771.



(5i)

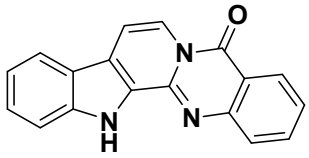
3-Methoxyrutaecarpine (5i): Following the general procedure with 2-Amino-5-methoxybenzoic acid (60.1 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (54.4 mg, 57% yield). ^{1}H NMR (400MHz, DMSO-d_6): δ 11.81 (s, 1H), 7.62 (d, J = 8.0 Hz,

2H), 7.55 (s, 1H), 7.47-7.41 (m, 2H), 7.24 (t, *J* = 4.0 Hz, 1H), 7.07 (t, *J* = 4.0 Hz, 1H), 4.43 (t, *J* = 8.0 Hz, 2H)), 3.88 (s, 3H), 3.16 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR(125MHz, DMSO-d_6): δ 164.73, 149.22, 136.92, 133.95, 131.09, 128.46, 126.42, 122.34, 120.75, 119.69, 119.37, 118.70, 117.92, 112.13, 111.96, 70.23, 41.36, 36.91, 19.95; HRMS (ESI) m/z calcd.for $C_{19}H_{16}N_3O_2$ $[M+H]^+$ 318.12370, found 318.12225.



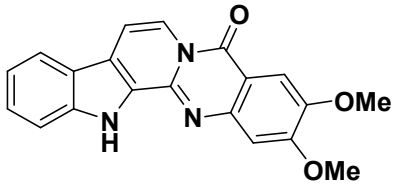
(5j)

Evodiamine (5j): Following the general procedure with 2-Methylaminobenzoic acid (49.2 mg, 0.33 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH_2Cl_2 (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH_2Cl_2, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (75.4 mg, 83% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.22 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.51-7.47 (m, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.28-7.13 (m, 4H), 5.92 (s, 1H), 4.89-4.85 (m, 1H), 3.33-3.26 (m, 1H), 2.98 (s, 2H), 2.50 (s, 3H); ^{13}C NMR(100MHz, DMSO-d_6): δ 164.73, 149.22, 136.92, 133.95, 131.10, 128.46, 126.42, 122.34, 120.75, 119.69, 119.37, 118.70, 117.92, 112.13, 111.96, 70.22, 41.36, 36.91, 19.95. HRMS (ESI) m/z calcd.for $C_{19}H_{18}N_3O$ $[M+H]^+$ 304.14444, found 304.14343.



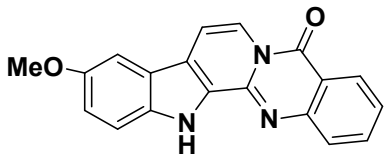
(5k)

7,8-Dehydrorutaecarpine (5k): Following the general procedure with 2-Amino-benzoic acid (49.3 mg, 0.36 mmol), 9*H*-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH_2Cl_2 (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH_2Cl_2, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a white solid (57.5 mg, 67% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 10.23 (s, 1H), 8.76 (d, *J* = 8.0 Hz, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 4.0 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.49-7.46 (m, 3H), 7.35-7.31 (m，1H) ; ^{13}C NMR(125MHz, $CDCl_3$): δ.159.38, 147.81, 140.33, 139.44, 134.92, 129.48, 127.78, 127.25, 126.19, 124.81, 122.57, 121.21, 120.90, 118.73, 116.57, 112.24, 107.67; HRMS (ESI) m/z calcd.for $C_{18}H_{12}N_3O$ $[M+H]^+$ 286.09749, found 286.09665.



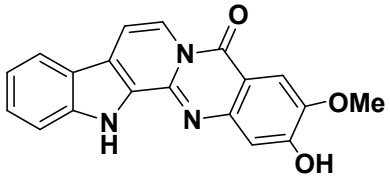
(5l)

Euxylophoricine B (5l): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 9*H*-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (89.0 mg, 86% yield). ^{1}H NMR(400MHz, $CDCl_3$+CD_3OD): δ 8.73 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.72 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.59-7.50 (m, 2H), 7.36-7.31 (m, 2H), 7.11 (s, 1H), 4.07 (s, 3H), 4.04 (s, 3H); ^{13}C NMR(100MHz, $CDCl_3$ and CD_3OD): δ 162.28, 160.14, 158.31, 152.19, 148.24, 143.60, 131.04, 126.10, 124.88, 124.55, 122.99, 122.13, 117.46, 116.24, 113.45, 111.69, 109.55, 109.17, 60.10. HRMS (ESI) m/z calcd.for $C_{20}H_{16}N_3O_3$ $[M+H]^+$ 346.11862, found 346.11746.



(5m)

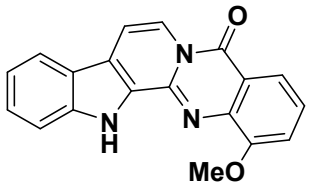
Euxylophoricine E (5m): Following the general procedure with 2-Amino-benzoic acid (49.3 mg, 0.36 mmol), 9*H*-6-methoxy-pyrido[3,4-b]indole (59.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH_2Cl_2 (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH_2Cl_2, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (84.4 mg, 89% yield). ^{1}H NMR (400MHz, DMSO-d_6): δ 12.54 (s, 1H), 8.57 (d, *J* = 4.0 Hz, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 7.89（d, *J* = 8.0 Hz, 1H), 7.81 (t, *J* = 4.0 Hz, 2H), 7.68 (s, 1H), 7.56 (d, *J* = 12.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 12.0 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR(125MHz, DMSO-d_6): δ 159.13, 154.74, 148.07, 140.65, 135.51, 135.33, 130.05, 127.55, 126.66, 124.98, 122.62, 120.11, 118.05, 117.61, 116.42, 114.10, 108.74, 102.22, 55.97; HRMS (ESI) m/z calcd.for $C_{19}H_{14}N_3O_2$ $[M+H]^+$ 316.10805, found 316.10706.



(5n)

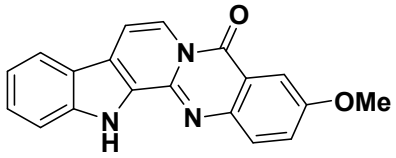
2-Hydroxy-3-Methoxy-7,8-Dehydrorutaecarpine (5n): Following the general procedure with 2-Amino-4-benzyloxy-5-methoxybenzoic acid (98.3 mg, 0.36 mmol), 9*H*-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in methanol (5 ml). after addition of 10% palladium on carbon (10 mg) and ammonium formate (0.3 g), the mixture was heated to reflux for 1 hour. The reaction was cooled, filtrated through celite, washed with methanol, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (45.8 mg, 46% yield). ^{1}H NMR (400MHz, DMSO-d_6): δ 12.55 (s, 1H), 8.58 (d, *J* = 4.0 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.74（d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 2H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.19 (s, 1H), 3.93 (s, 3H); ^{13}C NMR (125MHz, DMSO-d_6): δ 157.92, 154.93, 148.03, 144.83, 140.21, 139.50, 129.91, 126.83, 122.39, 121.25, 120.89, 119.51, 118.07, 113.14, 109.98, 109.00, 107.94, 106.31, 56.24; HRMS

(ESI) m/z calcd.for $C_{19}H_{14}N_3O_3$ $[M+H]^+$ 332.10297, found 332.10129.



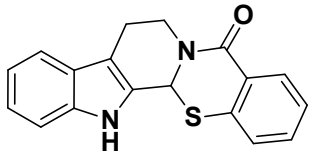
(5o)

1-Methoxy-7,8-dehydrorutaecarpine (5o): Following the general procedure with 2-Amino-3-methoxybenzoic acid (60.1 mg, 0.36 mmol), 9*H*-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH_2Cl_2 (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH_2Cl_2, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (51.2 mg, 54% yield). ^{1}H NMR (400MHz, DMSO-d_6): δ 12.53 (s, 1H), 8.62 (d, J = 4.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.91（d, J = 4.0 Hz, 1H), 7.85 (d, J = 4.0 Hz, 1H), 7.74 (d, J = 4.0 Hz, 1H), 7.49 (t, J = 4.0 Hz, 1H), 7.44 (d, J = 4.0 Hz, 2H), 7.29 (t, J = 4.0 Hz, 1H), 4.02 (s, 3H); ^{13}C NMR (125MHz, DMSO-d_6): δ 158.94, 154.36, 140.46, 139.55, 139.24, 130.12, 127.08, 125.20, 122.27, 121.29, 121.04, 120.25, 118.44, 118.15, 117.27, 114.69, 113.49, 108.83, 56.34; HRMS (ESI) m/z calcd.for $C_{19}H_{14}N_3O_2$ $[M+H]^+$ 316.10805, found 316.10696.



(**5p**)

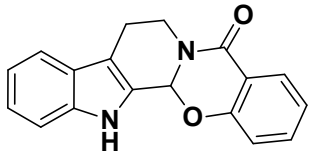
3-Methoxy-7,8-dehydrorutaecarpine (5p): Following the general procedure with 2-Amino-5-methoxybenzoic acid (60.1 mg, 0.36 mmol), 9*H*-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3.0 ml). The reaction mixture was stirred at 80^{o}C under dry air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (82.2 mg, 87% yield). ^{1}H NMR (400MHz, DMSO-d_6): δ 12.62 (s, 1H), 8.59 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.80-7.78 (m, 2H), 7.68-7.66 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.49-7.45 (m, 1H), 7.29-7.25 (m, 1H), 3.91 (s, 3H); ^{13}C NMR (100MHz, DMSO-d_6): δ 158.66, 156.84, 142.96, 140.25, 139.04, 130.02, 128.55, 126.84, 126.21, 122.39, 121.20, 120.93, 119.46, 117.99, 116.95, 113.18, 108.59, 106.12, 56.10. HRMS (ESI) m/z calcd.for $C_{19}H_{14}N_3O_2$ $[M+H]^+$ 316.10805, found 316.10706.



(**5q**)

7,8,13,13*b*-Tetrahydro-5*H*-benzo[5',6']|[1,3]thiazino[3',2':1,2]-pyrido[3,4-*b*]indol-5-one (5q): Following the general procedure with 2-Mercaptobenzoic acid (184.8 mg, 1.2 mmol), 4,9-dihydro-3*H*-pyrido[3,4-b]indole (170.0 mg, 1.0 mmol), EDCI (268.4 mg, 1.4 mmol), and CH_2Cl_2 (3.0 ml). The reaction mixture was stirred at room

temperature. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (198.9 mg, 65% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 8.22 (d, *J* = 8.0 Hz, 1H), 8.10 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.44-7.34 (m, 2H), 7.34 (m, 2H), 7.28-7.26 (m, 1H), 7.19-7.17 (m, 1H), 6.35 (s, 1H), 4.85-4.82 (m, 1H), 3.49-3.47 (m, 1H), 3.04 (s, 2H); ^{13}C NMR(100MHz, $CDCl_3$): δ 164.83, 137.25, 136.07, 132.58, 131.12, 129.42, 128.25, 127.57, 126.86, 126.04, 122.70, 119.59, 118.96, 112.11, 110.57, 56.82, 40.43, 20.58. HRMS (API) m/z calcd.for $C_{18}H_{15}N_2OS$ $[M+H]^+$ 307.0900, found 307.0910.



(**5r**)

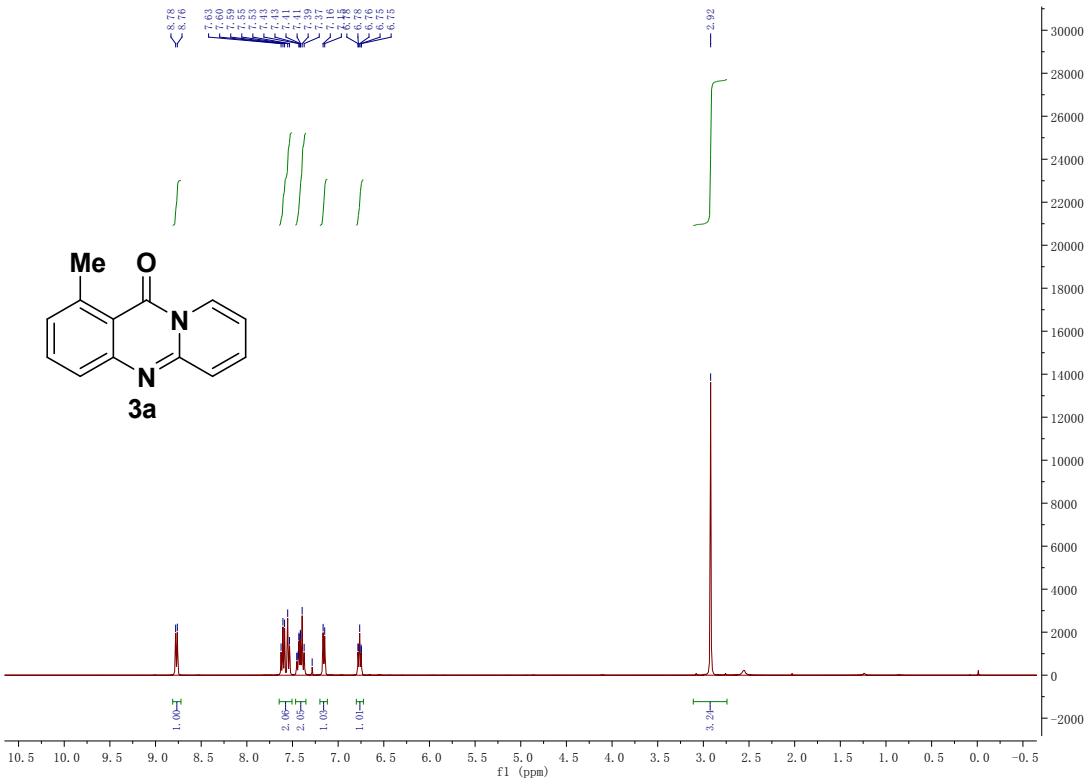
7,8,13,13*b*-Tetrahydro-5*H*-benzo[5',6']|[1,3]oxazino[3',2':1,2]-pyrido[3,4-*b*]indol-5-one (5r): Following the general procedure with 2-Hydroxybenzoic acid (164.4 mg, 1.2 mmol), 4,9-dihydro-3*H*-pyrido[3,4-b]indole (170.0 mg, 1.0 mmol), EDCI (268.4 mg, 1.4 mmol), and CH_2Cl_2 (3.0 ml). The reaction mixture was stirred at room temperature. After 4 hours, the reaction mixture was diluted with 30 mL of CH_2Cl_2. Then it was washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2: MeOH=100:1) to afford a yellow solid (168.2 mg, 58% yield). ^{1}H NMR (400MHz, $CDCl_3$ and CD_3OD): δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 4.0 Hz, 1H), 7.51-7.43 (m, 2H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.18-7.12 (m, 2H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.47 (s, 1H), 4.90-4.87 (m, 1H), 3.31-3.26 (m, 1H), 3.06-2.94 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$ and CD_3OD): δ 167.51, 160.90, 141.28, 138.30, 132.39, 130.80, 129.55, 127.12, 126.84, 123.58, 122.96, 122.27,120.31, 116.68, 115.64, 85.21, 43.26, 24.06. HRMS (API) m/z calcd.for $C_{18}H_{15}N_2O_2$ $[M+H]^+$291.1128, found291.1123.

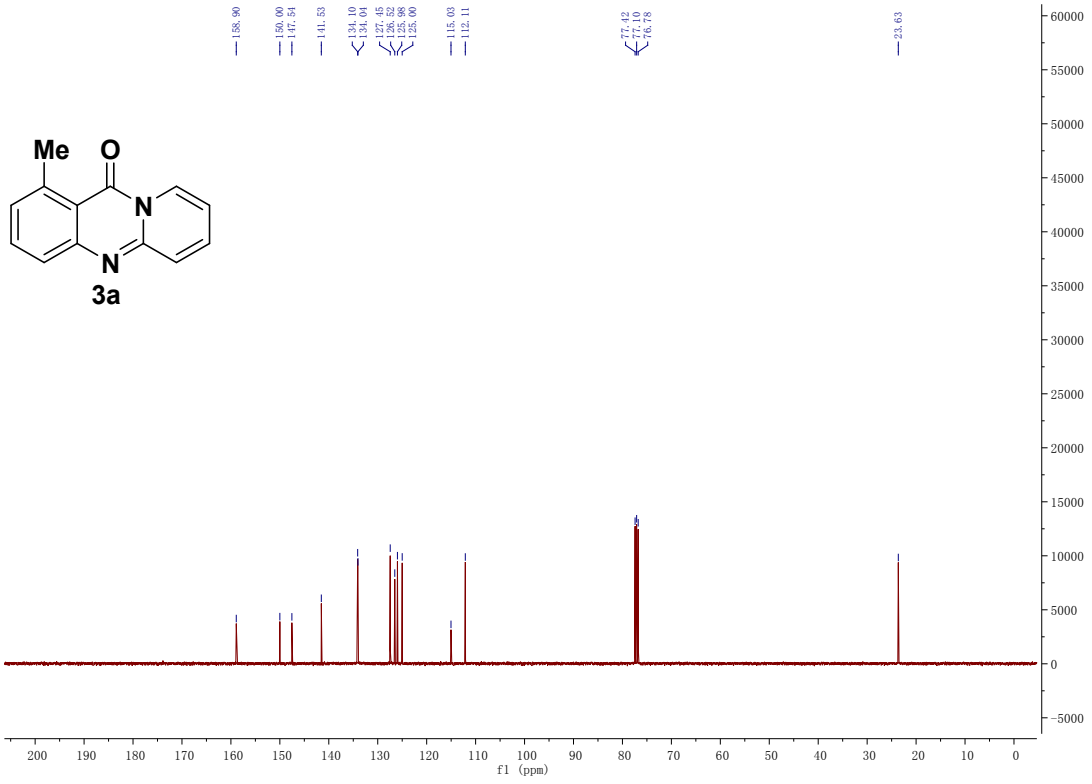
Reference:

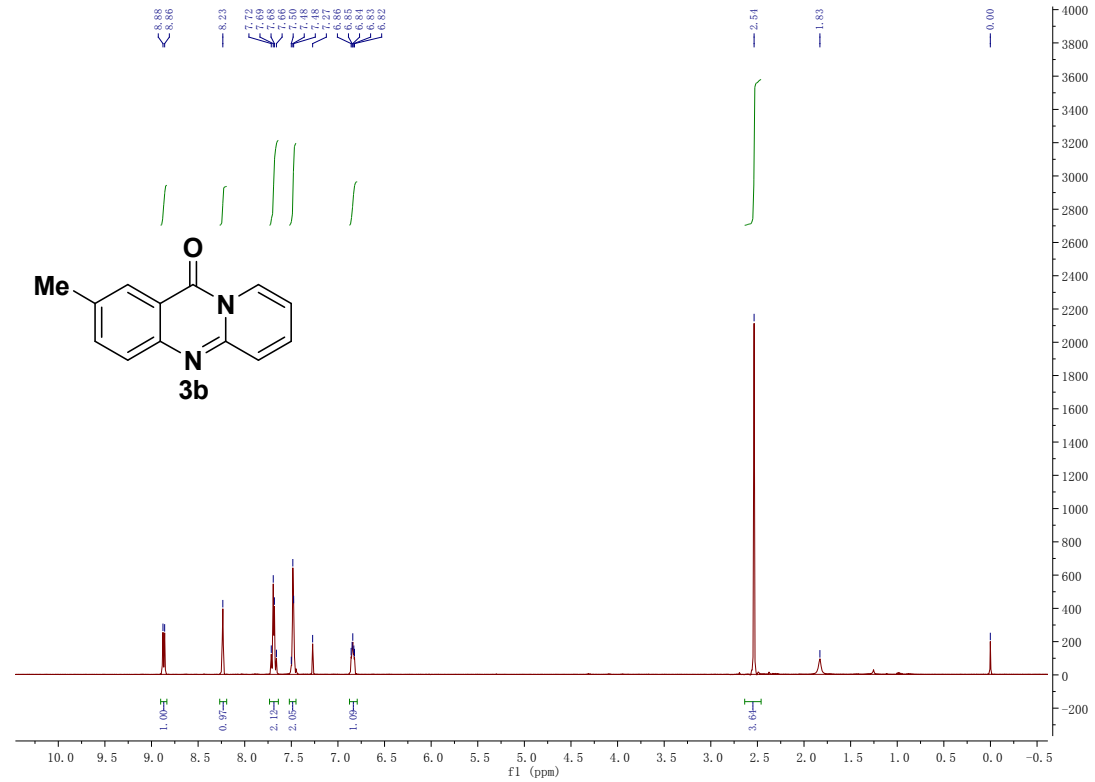
(1) T. Wang, A. Lui, and I. Cloudsdale, *Org. Lett*., 1999, **1**, 1835.

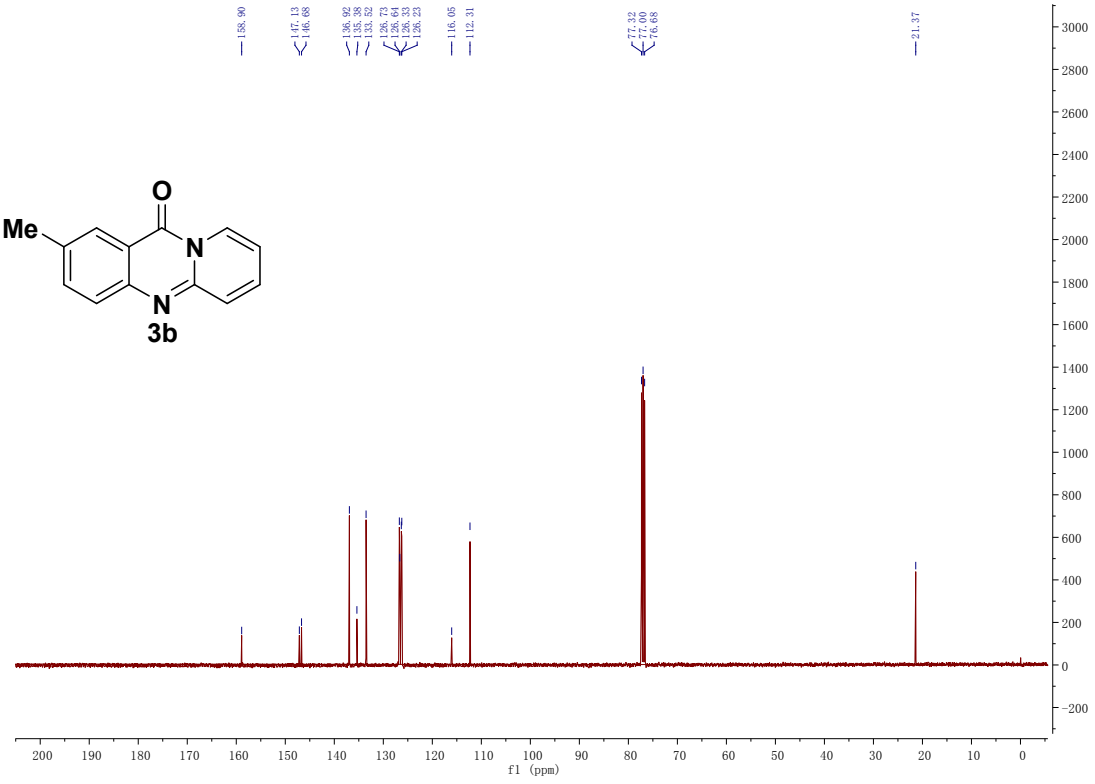
(2) U. Huan, B. Klin, F. H. Darras, J. Heilmann, and M. Decker, *Eur. J. Med. Chem*., 2014, **81**, 15.

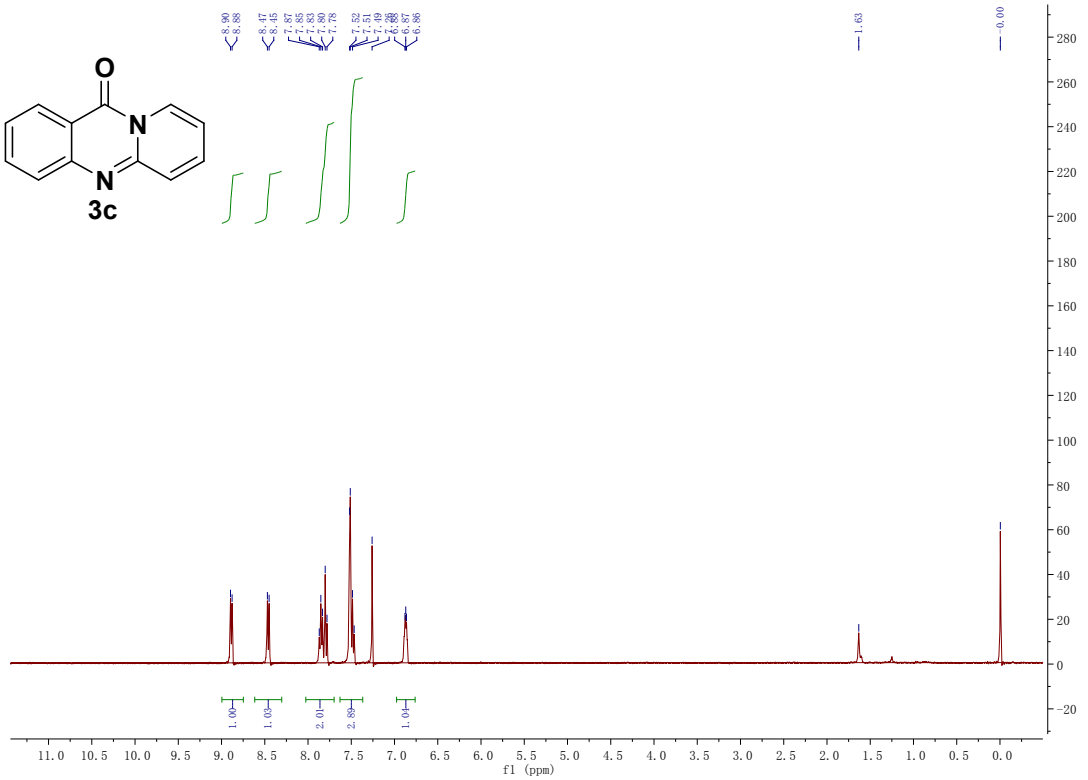
(3) R. Otto, R. Penzis, F. Gaube, T. Winckler, D. Appenroth, C. Fleck, C. Tränkle, J. Lehmann, and C. Enzensperger, *Eur J. Med. Chem*., 2014, **87**, 63.

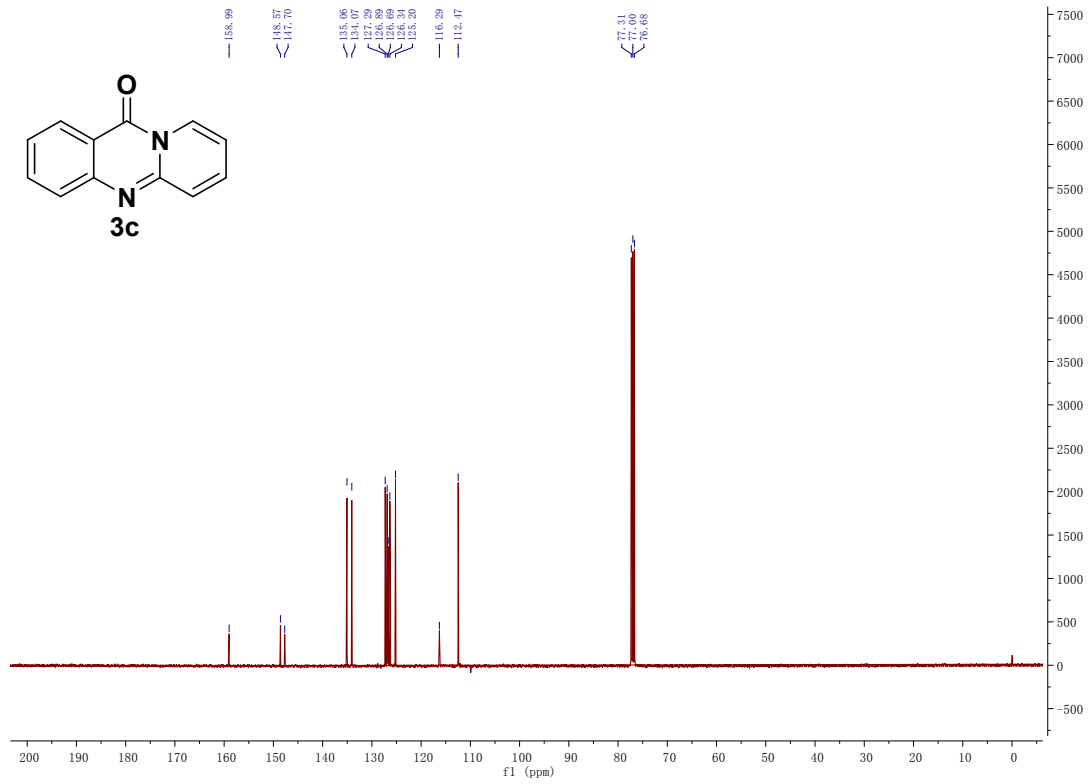

Me
O
N
N
3a
8.78
8.76
7.63
7.60
7.59
7.55
7.53
7.43
7.41
7.41
7.39
7.37
7.16
6.78
6.76
6.75
2.92
1.00
2.06
2.05
1.03
1.01
3.21
f1 (ppm)

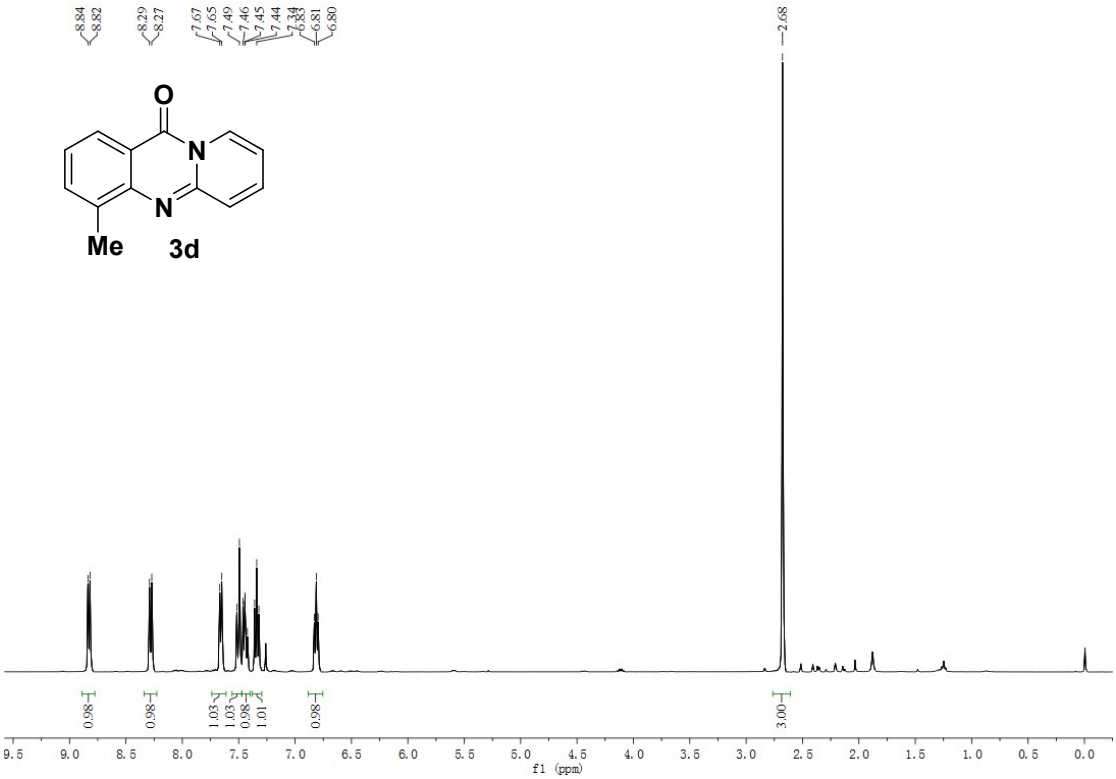

Me
O
N
N
3a
158.90
150.00
147.54
141.53
134.10
131.04
127.45
126.52
125.98
125.00
115.03
112.11
77.42
77.10
76.78
23.63
f1 (ppm)

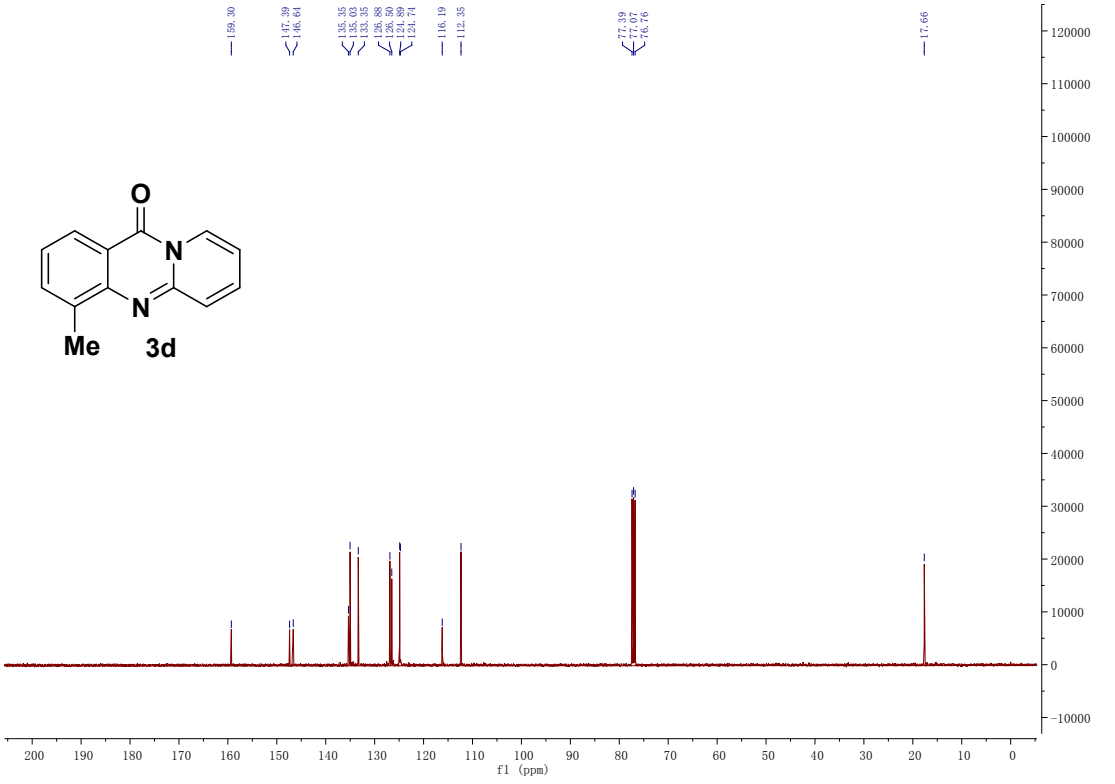

8.88
8.86
8.23
7.72
7.69
7.68
7.66
7.50
7.48
7.27
6.86
6.85
6.84
6.83
6.82
2.54
1.83
0.00
Me
O
N
N
3b
1.00
0.97
2.12
2.05
1.00
3.61
f1 (ppm)

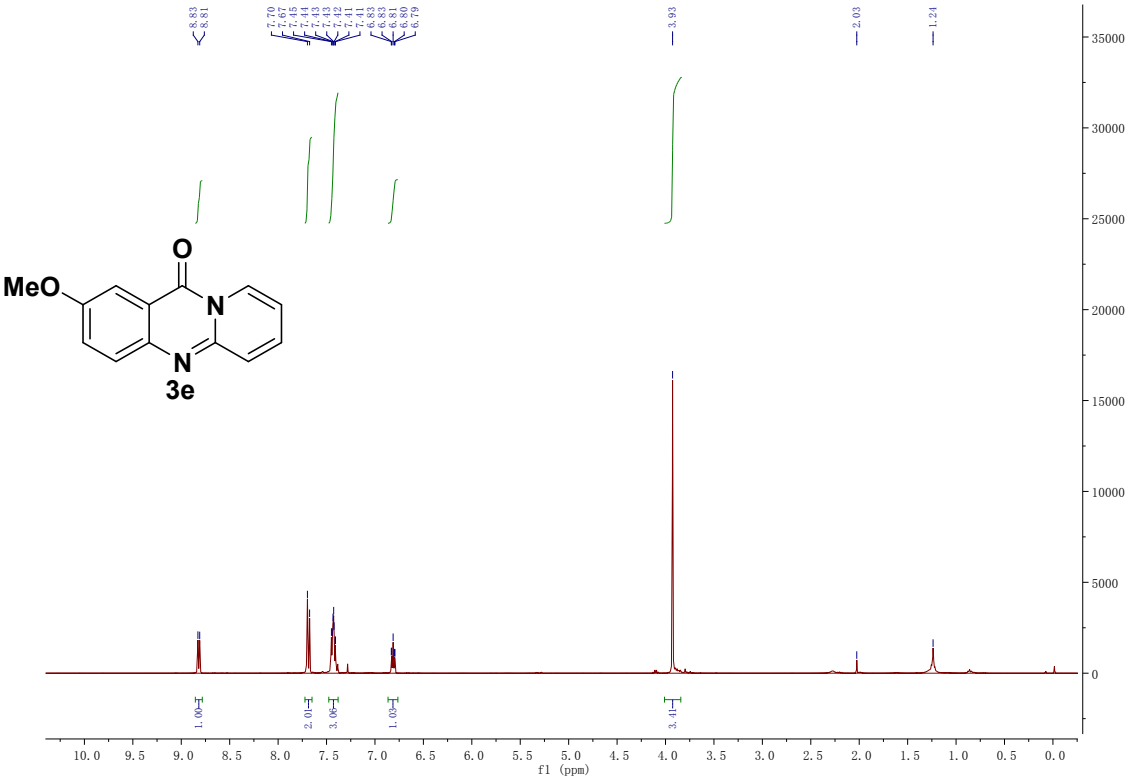

158.90
147.13
146.68
136.92
135.38
133.52
126.73
126.64
126.33
126.23
116.05
112.31
77.32
77.00
76.68
21.37
Me
O
N
N
3b
f1 (ppm)

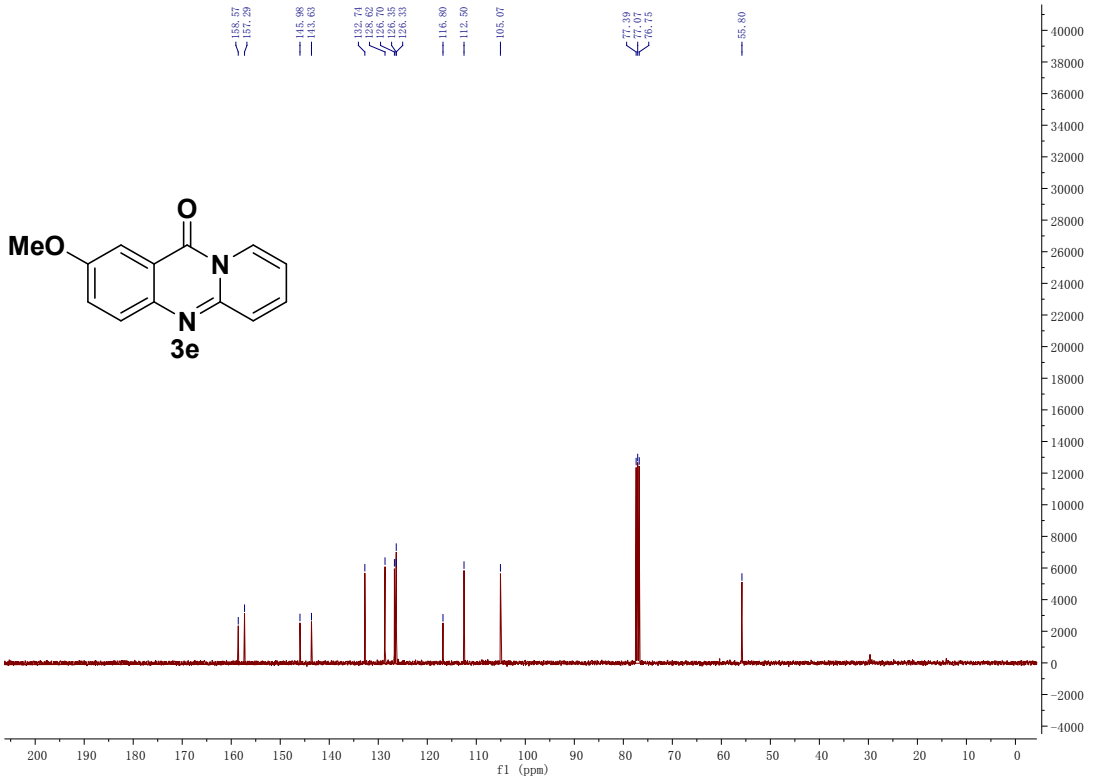

O
N
N
3c
8.90
8.88
8.47
8.45
7.85
7.83
7.80
7.78
7.52
7.51
7.49
6.87
6.86
1.63
0.00
1.00
1.00
2.01
2.89
1.04
f1 (ppm)

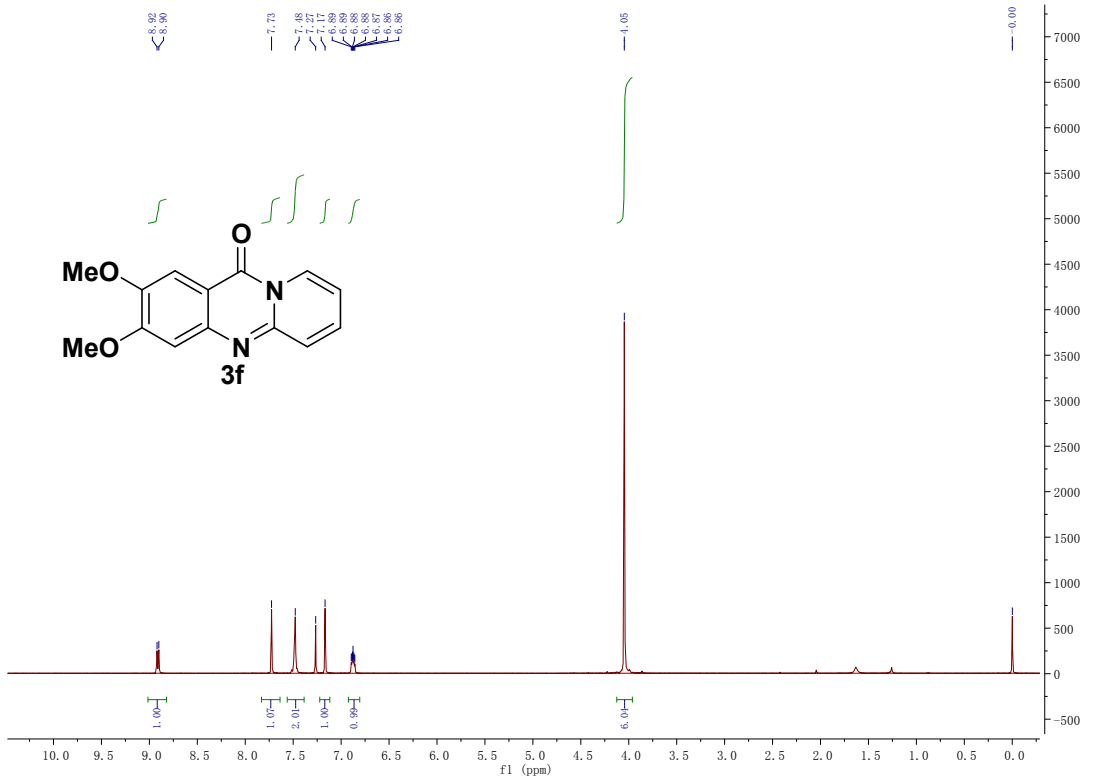

O
N
N
3c
158.99
148.57
147.70
135.06
134.07
127.29
126.89
126.69
126.34
125.20
116.29
112.47
77.31
77.00
76.68
f1 (ppm)

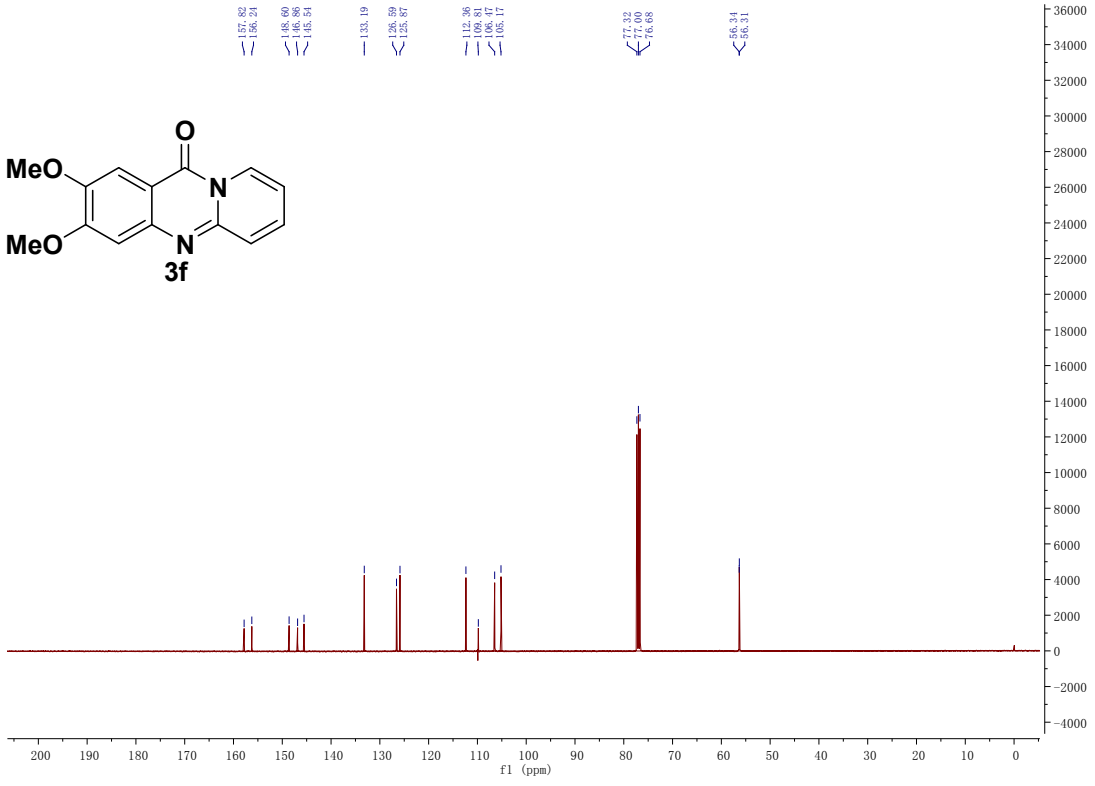

8.84
8.82
8.29
8.27
7.67
7.65
7.49
7.46
7.45
7.44
7.34
6.83
6.81
6.80
2.68
O
N
N
Me
3d
0.98
0.98
1.03
1.03
0.98
1.01
0.98
3.00
f1 (ppm)

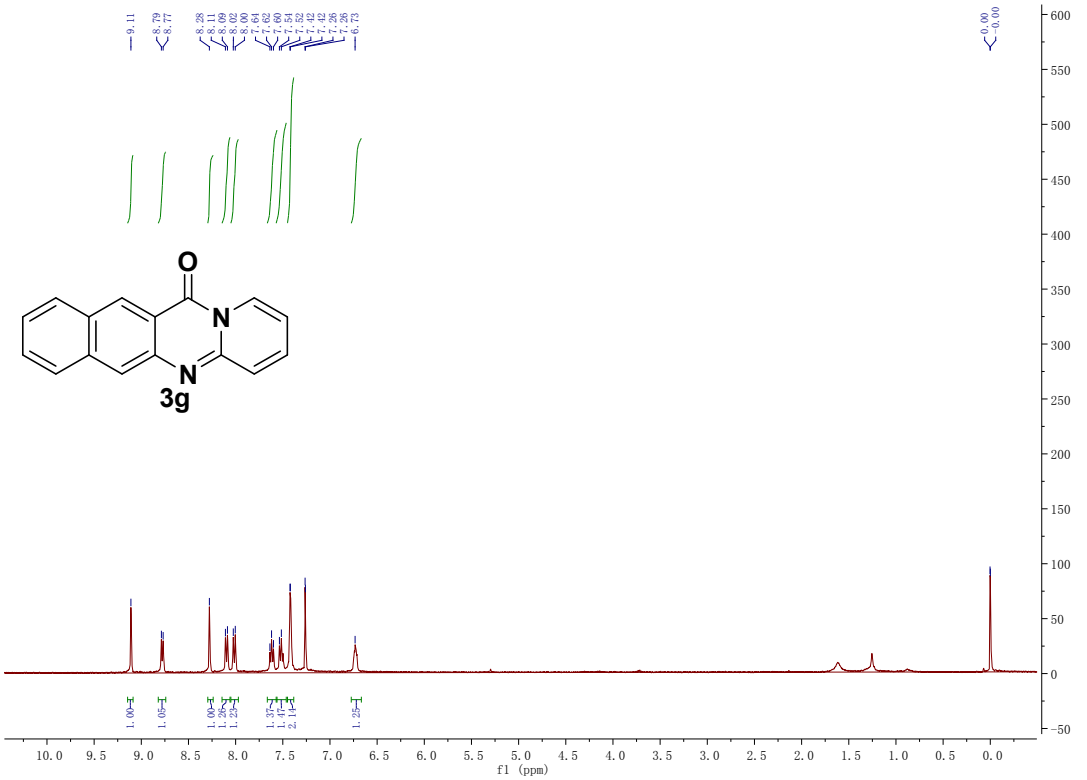

159.30
147.39
146.64
135.35
135.03
133.35
126.88
126.50
124.89
124.74
116.19
112.35
77.39
77.07
76.76
17.66
O
N
N
Me
3d
f1 (ppm)

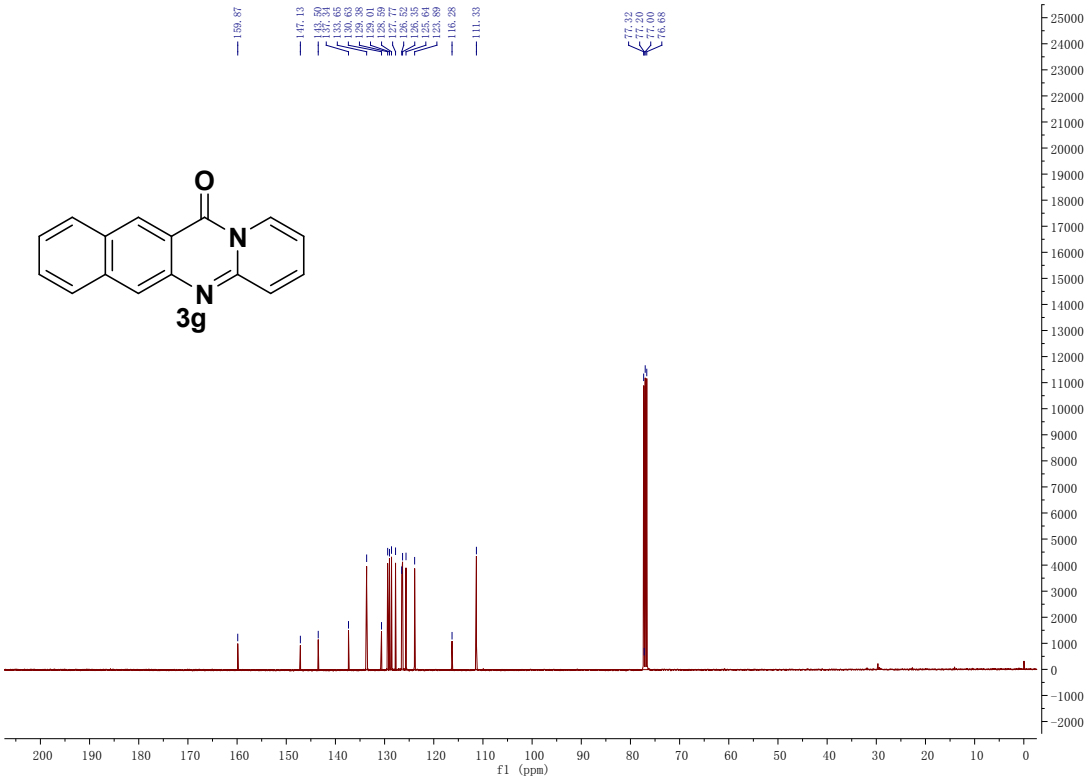

8.83
8.81
7.70
7.67
7.45
7.44
7.43
7.42
7.41
6.83
6.81
6.80
6.79
3.93
2.03
1.24
MeO
O
N
N
3e
1.00
2.01
3.06
1.03
3.41
f1 (ppm)

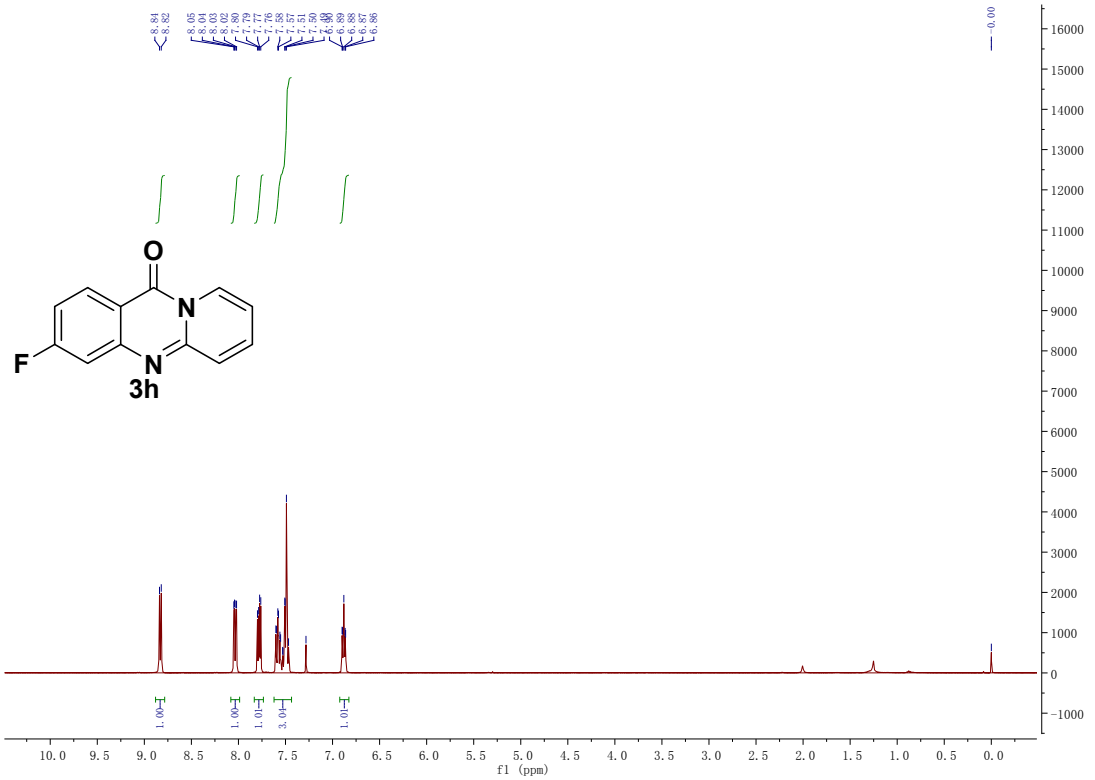

158.57
157.29
145.98
143.63
132.74
128.62
128.70
126.35
126.33
116.80
112.50
105.07
77.39
77.07
76.75
55.80
MeO
O
N
N
3e
f1 (ppm)

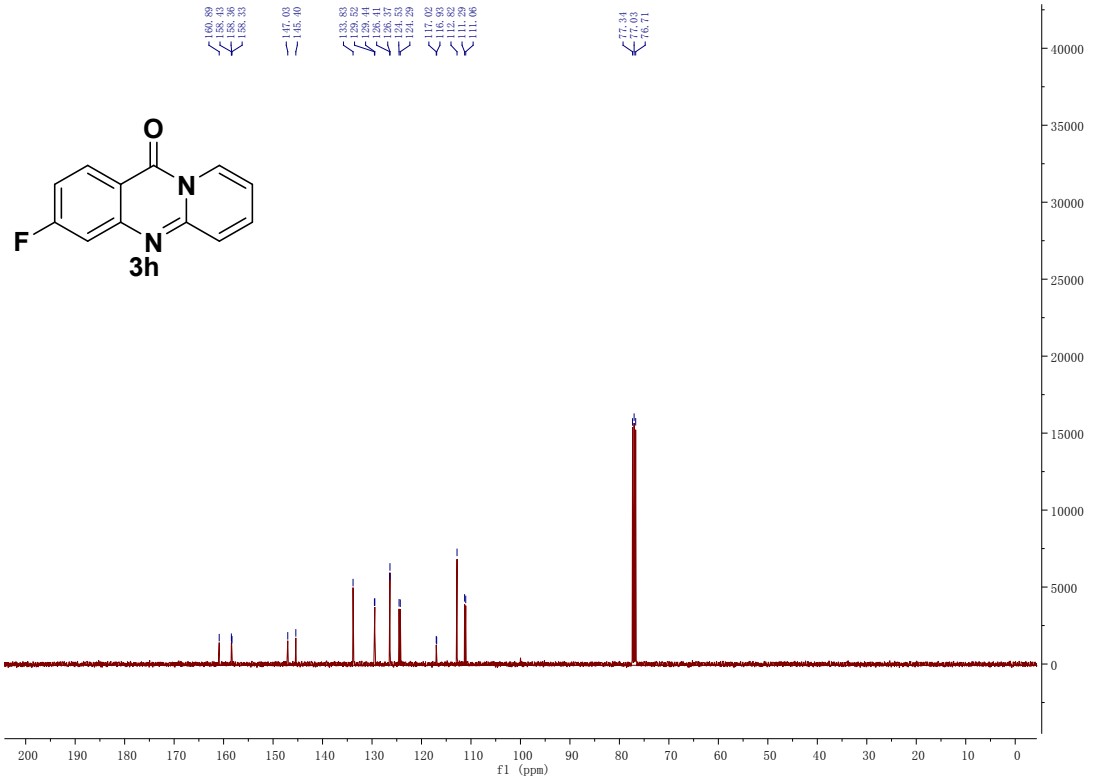

8.92
8.90
7.73
7.48
7.27
7.17
6.89
6.88
6.88
6.87
6.86
6.86
4.05
0.00
MeO
MeO
O
N
N
3f
1.00
1.07
2.01
1.00
0.98
6.04
f1 (ppm)

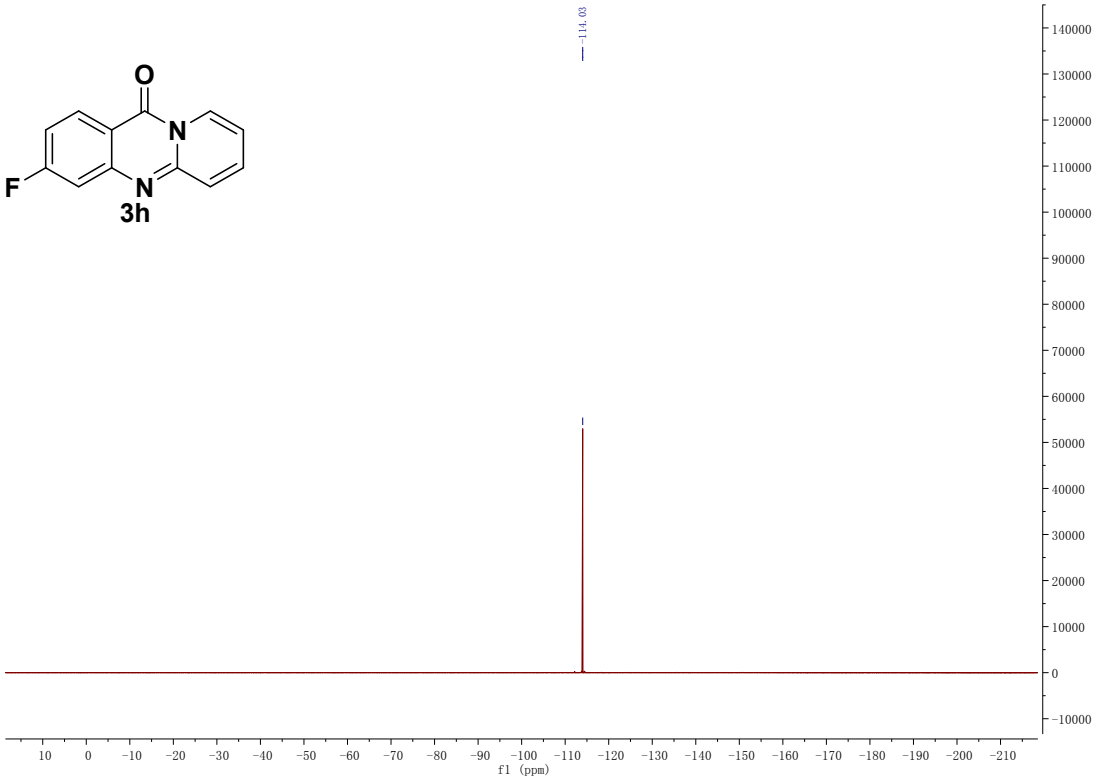

157.82
156.24
148.69
146.86
145.54
133.19
126.59
125.87
112.36
109.81
106.47
105.17
77.32
77.00
76.68
56.34
56.31
MeO
MeO
O
N
N
3f
f1 (ppm)

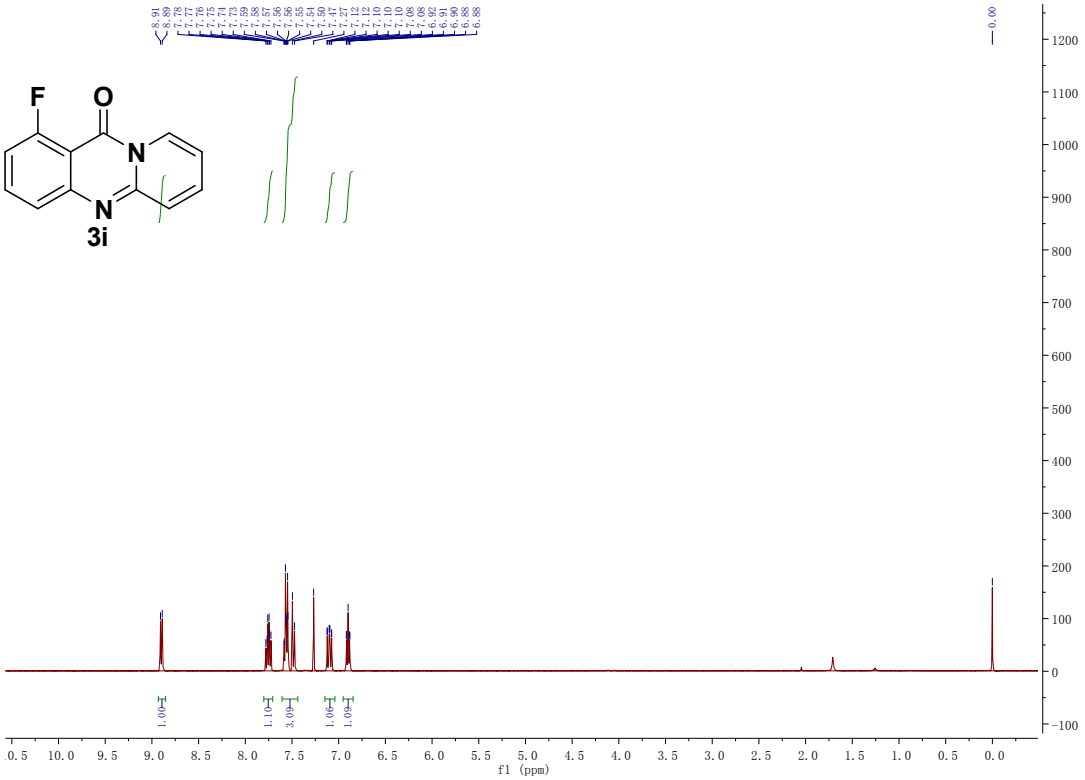

9.11
8.79
8.77
8.28
8.11
8.09
8.02
8.00
7.64
7.62
7.60
7.54
7.52
7.42
7.42
7.26
7.26
6.73
0.00
0.00
O
N
N
3g
f1 (ppm)

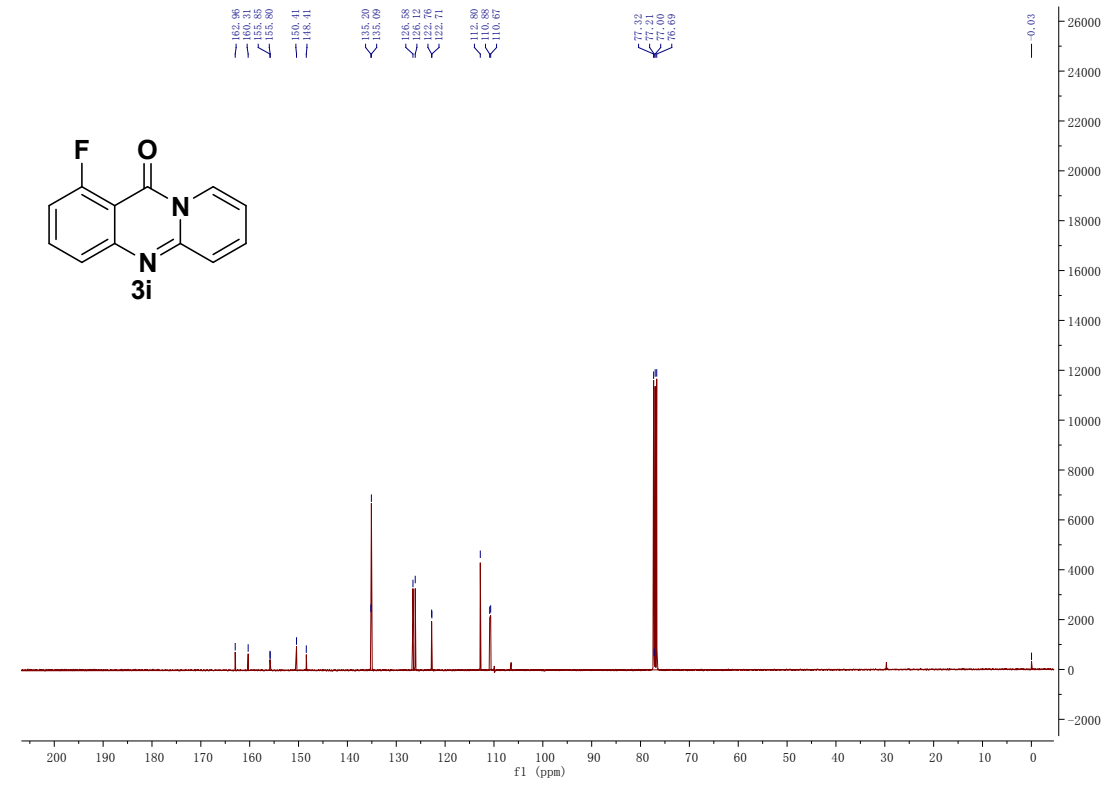

159.87
147.13
143.50
137.34
133.65
130.63
129.38
129.01
128.89
127.77
126.52
126.35
125.64
123.89
116.26
111.33
77.32
77.20
77.00
76.68
O
N
N
3g
f1 (ppm)

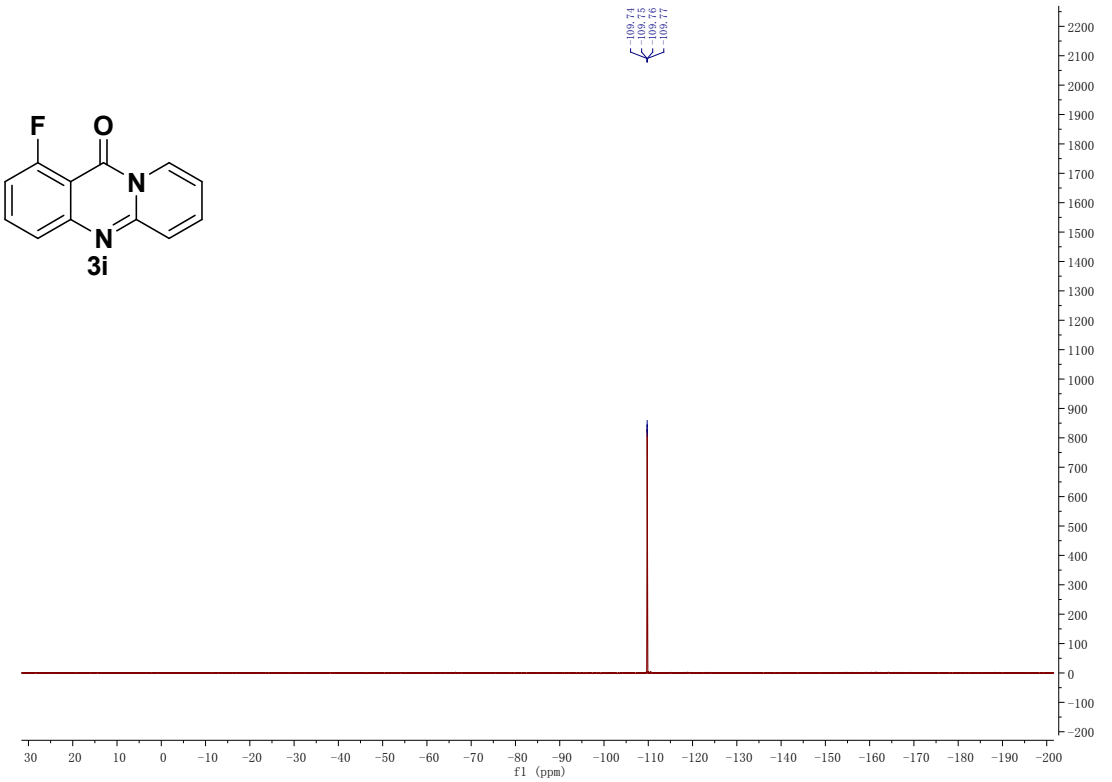

8.84
8.82
8.05
8.04
8.03
8.02
7.80
7.79
7.77
7.76
7.58
7.57
7.51
7.50
6.89
6.88
6.87
6.86
-0.00
O
N
F
N
3h
1.00
1.00
1.01
3.04
1.01
f1 (ppm)

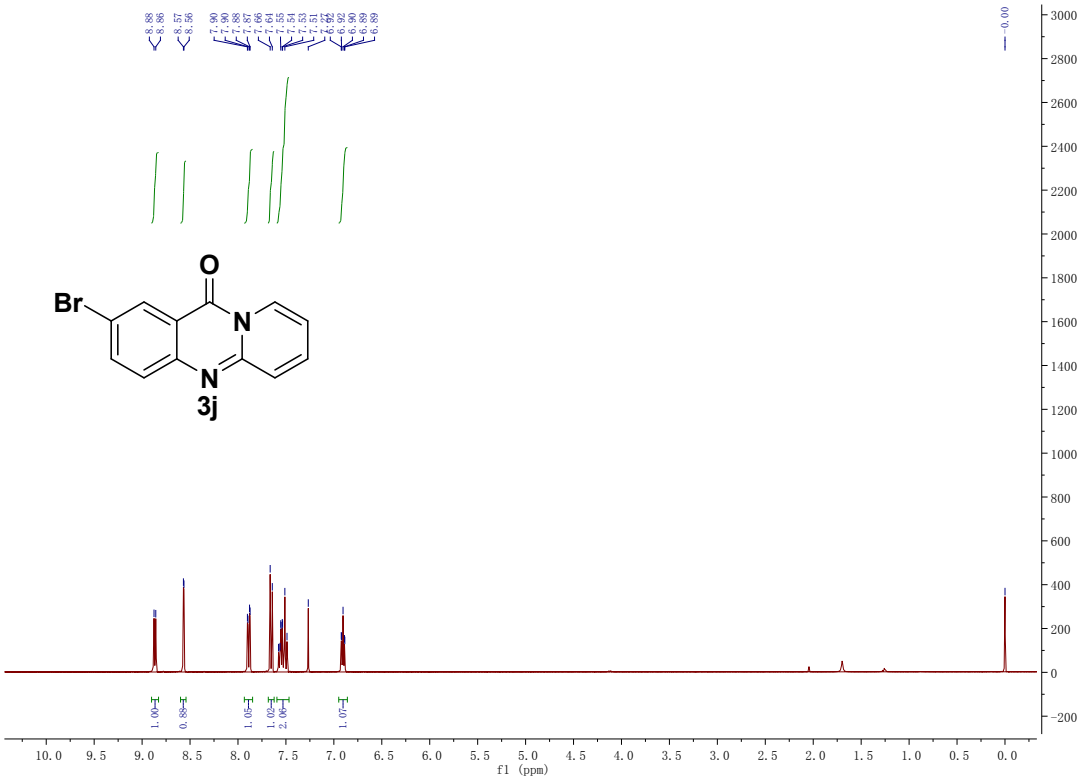

160.89
158.43
158.36
158.33
147.03
145.40
133.83
129.52
129.44
126.41
126.37
124.53
124.29
117.02
116.93
112.02
112.00
111.06
77.34
77.03
76.71
O
N
F
N
3h
f1 (ppm)

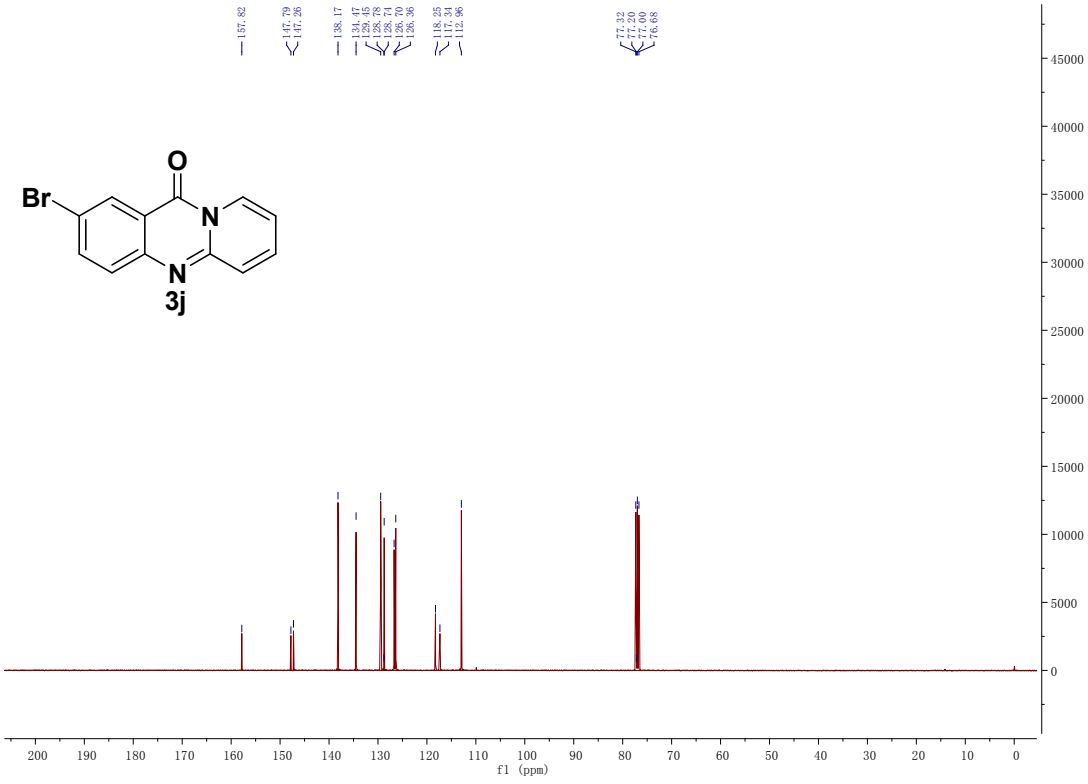

O
N
F
N
3h
-114.03
f1 (ppm)

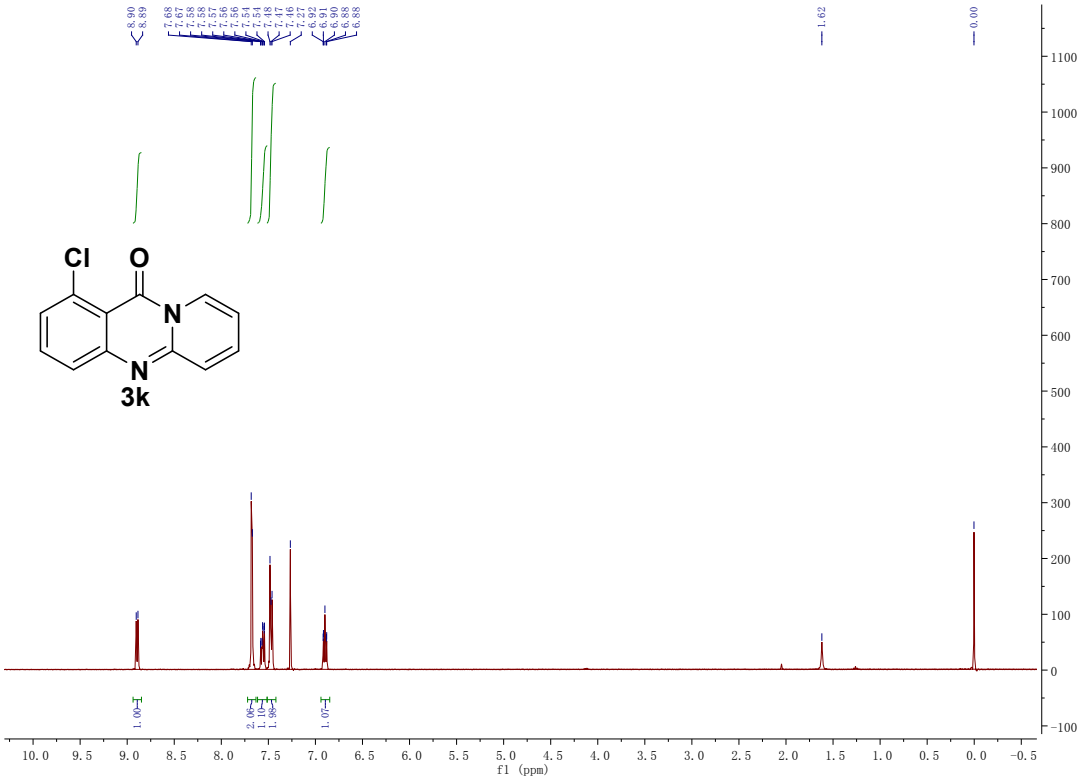

F
O
N
N
3i
8.91
8.89
7.78
7.77
7.76
7.75
7.74
7.73
7.59
7.58
7.57
7.56
7.55
7.54
7.50
7.47
7.27
7.12
7.11
7.10
7.10
7.08
7.08
6.92
6.91
6.90
6.88
6.88
0.00
1.00
1.10
3.09
1.06
1.09
f1 (ppm)

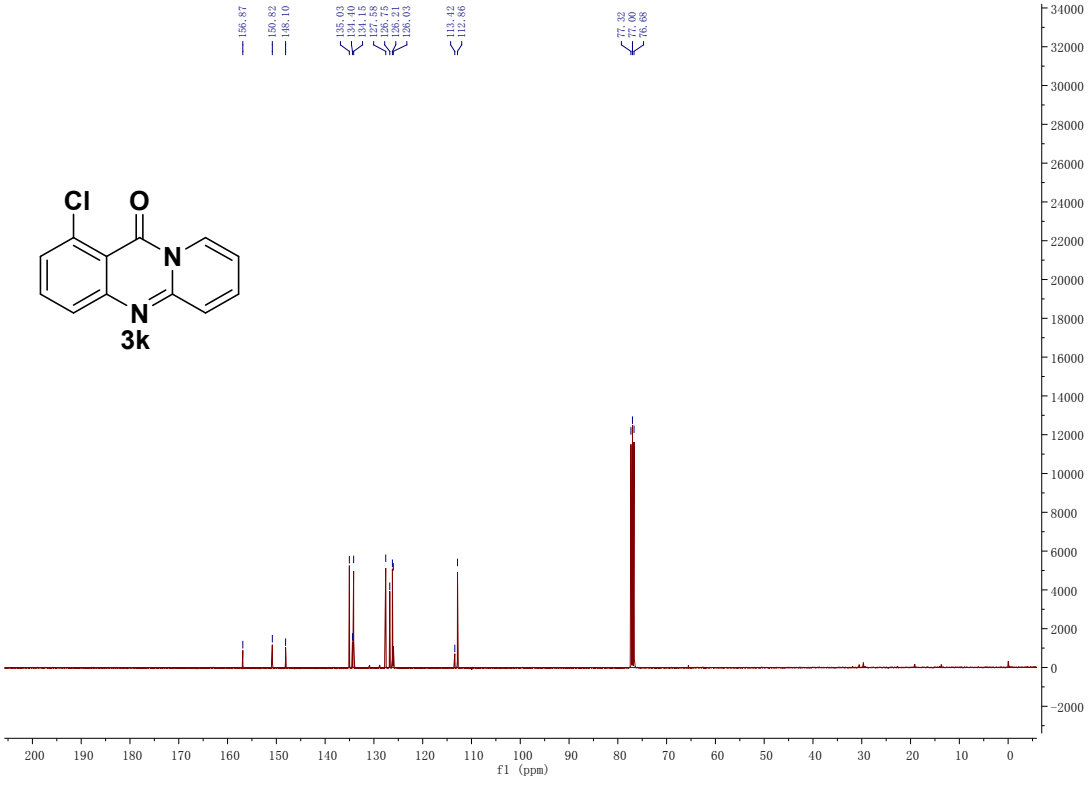

162.96
160.31
155.85
155.80
150.41
148.41
135.20
135.09
126.58
126.12
122.76
122.71
112.80
110.88
110.67
77.32
77.11
77.00
76.69
-0.03
F
O
N
N
3i
f1 (ppm)

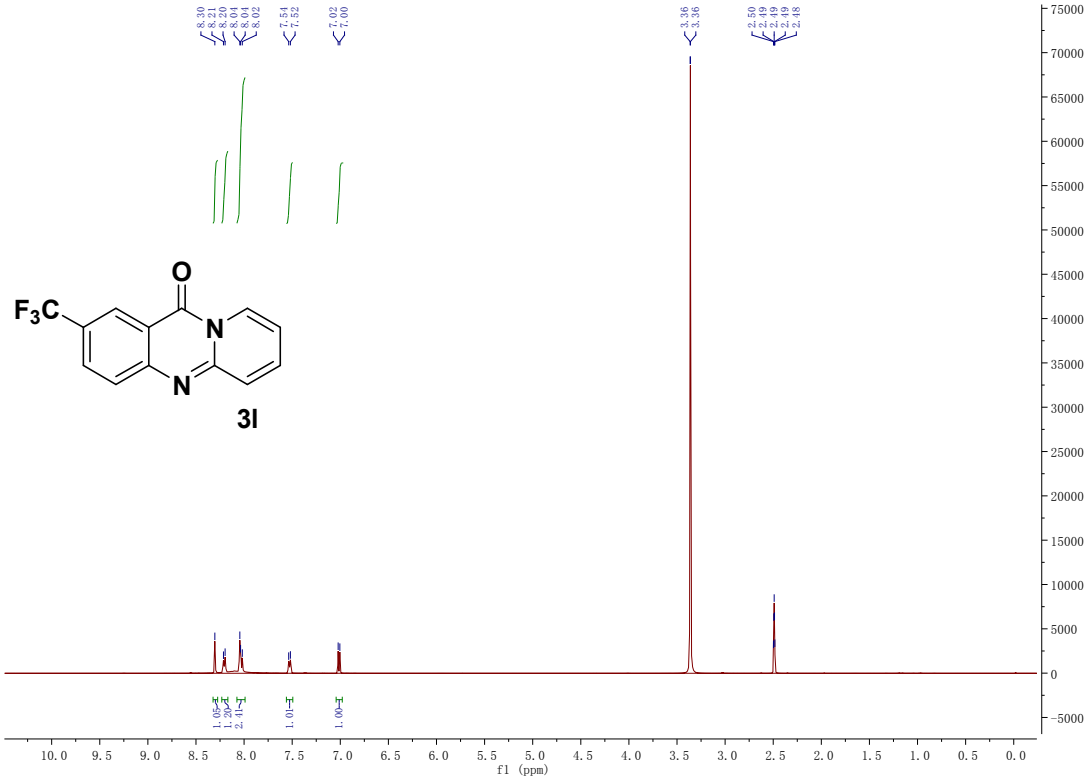

-109.74
-109.75
-109.76
-109.77
F
O
N
N
3i
f1 (ppm)

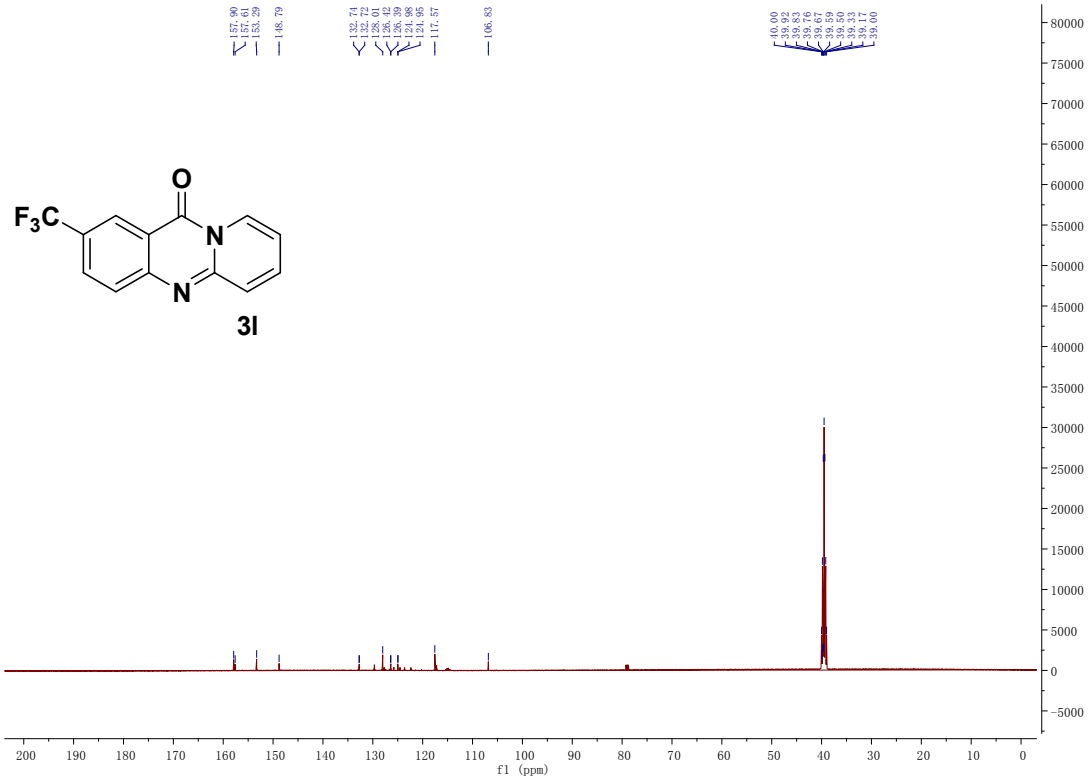

8.88
8.86
8.57
8.56
7.90
7.88
7.87
7.66
7.64
7.55
7.54
7.53
7.51
6.92
6.90
6.89
6.89
-0.00
Br
O
N
N
3j
1.00
0.88
1.05
1.02
2.06
1.07
f1 (ppm)

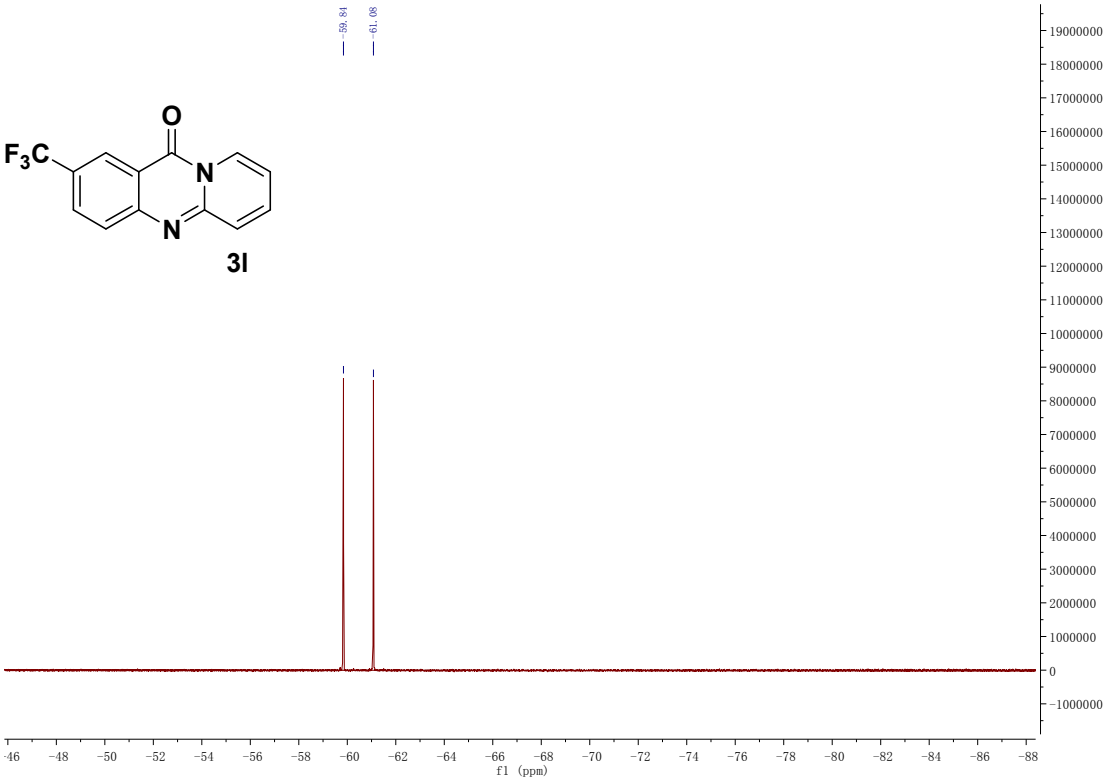

157.82
147.79
147.26
138.17
134.47
129.45
128.78
128.74
126.70
126.36
118.25
117.34
112.96
77.32
77.00
76.68
Br
O
N
N
3j
f1 (ppm)

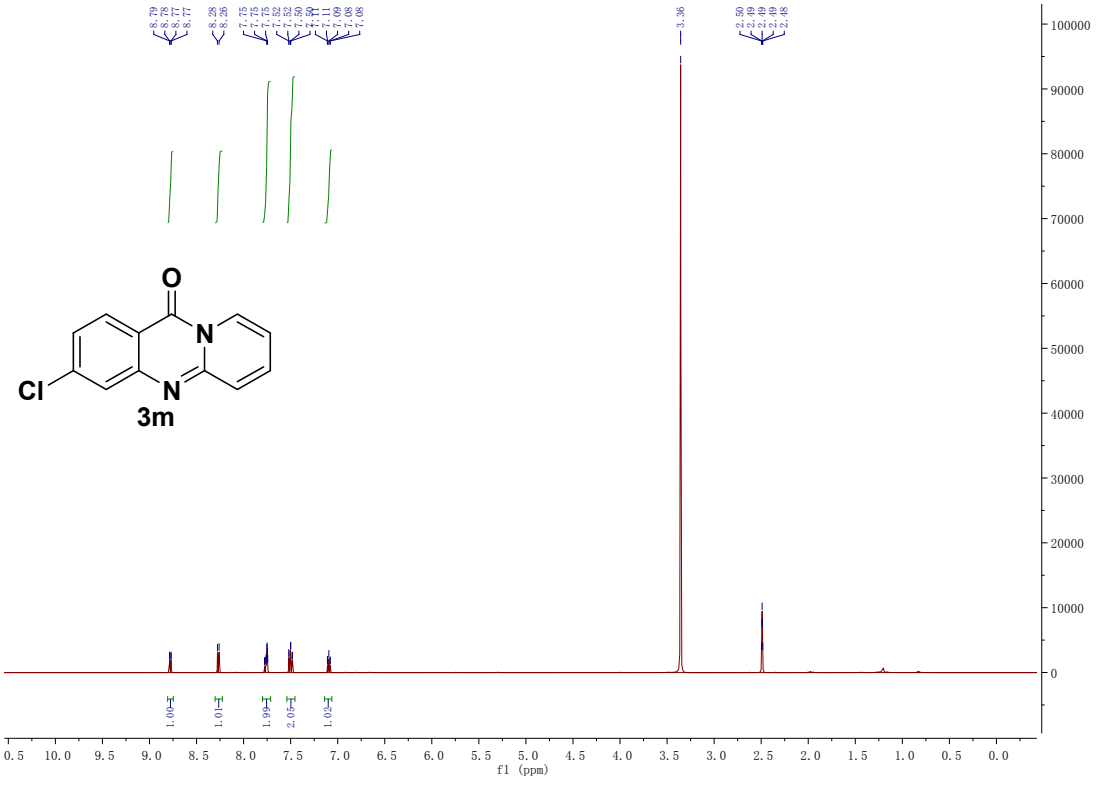

8.90
8.89
7.68
7.67
7.58
7.58
7.57
7.56
7.56
7.54
7.54
7.48
7.47
7.46
7.27
6.92
6.91
6.90
6.88
6.88
1.62
0.00
Cl
O
N
N
3k
1.00
2.06
1.10
1.98
1.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

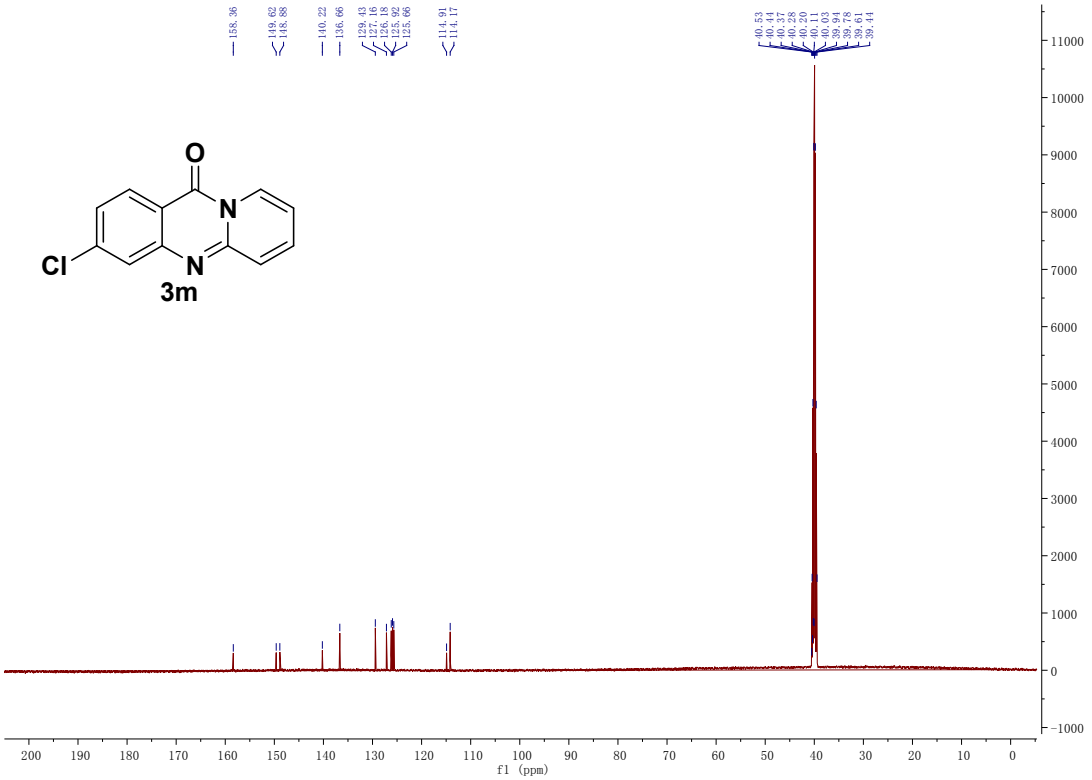

156.87
150.82
148.10
135.03
134.40
134.15
127.58
126.75
126.21
126.03
113.42
112.86
77.32
77.00
76.68
Cl
O
N
N
3k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000

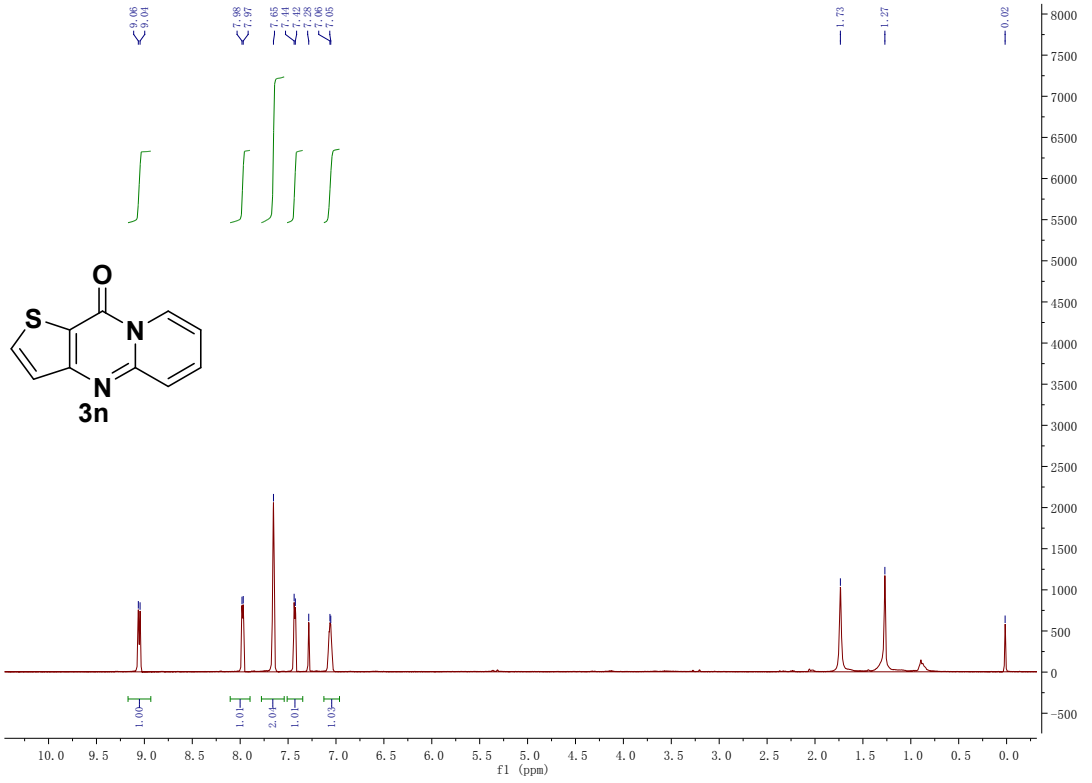

8.30
8.21
8.20
8.04
8.04
8.02
7.54
7.52
7.02
7.00
3.36
3.36
2.50
2.19
2.19
2.19
2.18
1.05
2.20
2.41
1.01
1.00
F3C
O
N
N
3l
f1 (ppm)

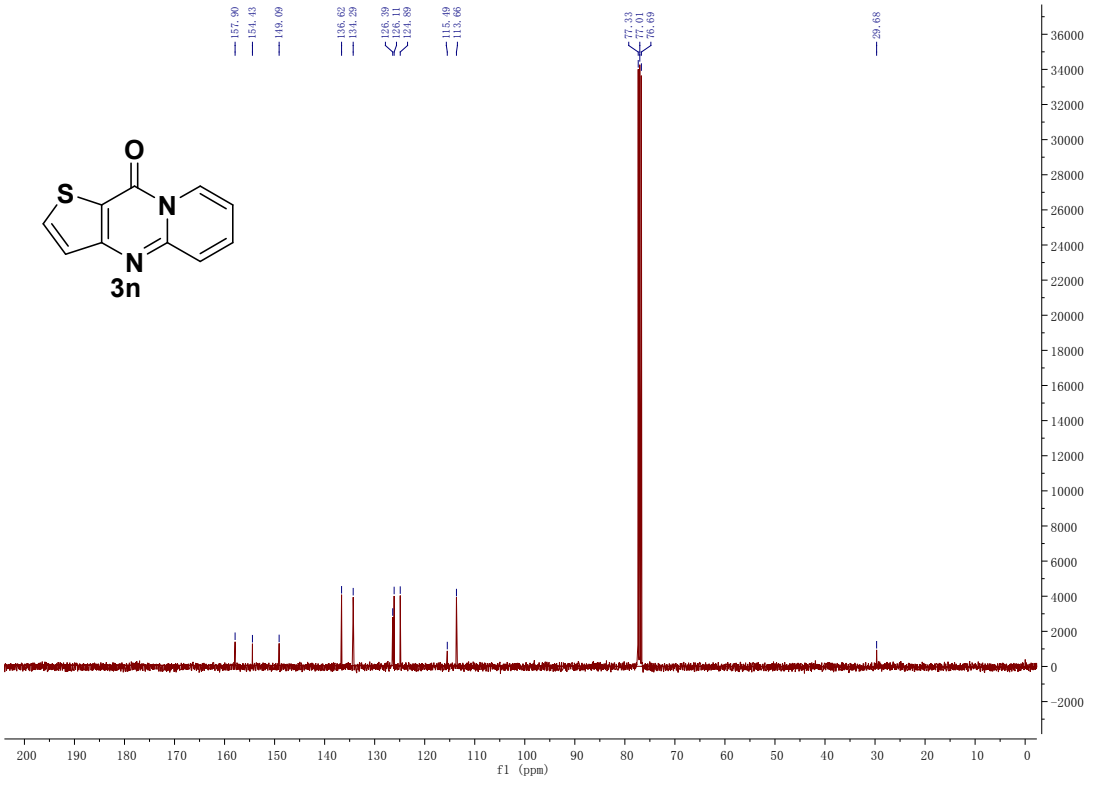

157.90
157.61
153.29
148.79
132.74
132.72
128.01
126.42
126.39
124.98
124.95
117.57
106.83
40.00
39.92
39.83
39.76
39.67
39.59
39.50
39.33
39.17
39.00
F3C
O
N
N
3l
f1 (ppm)

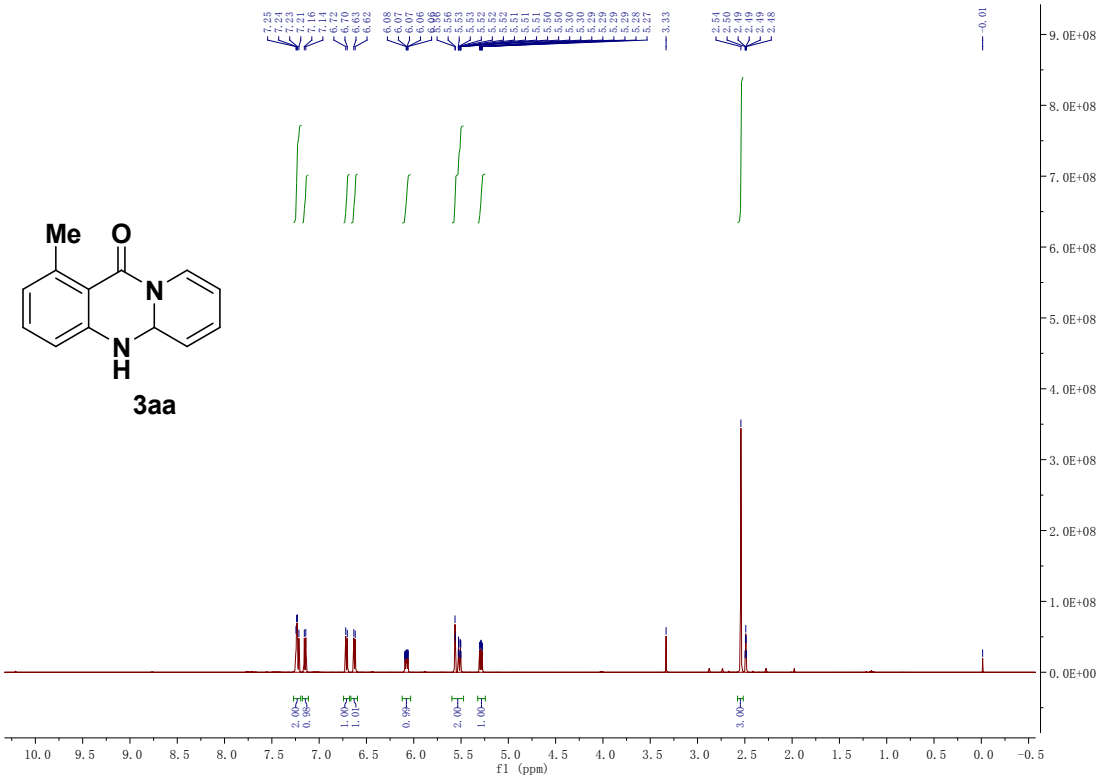

-59.84
-61.08
F3C
O
N
N
3l
f1 (ppm)

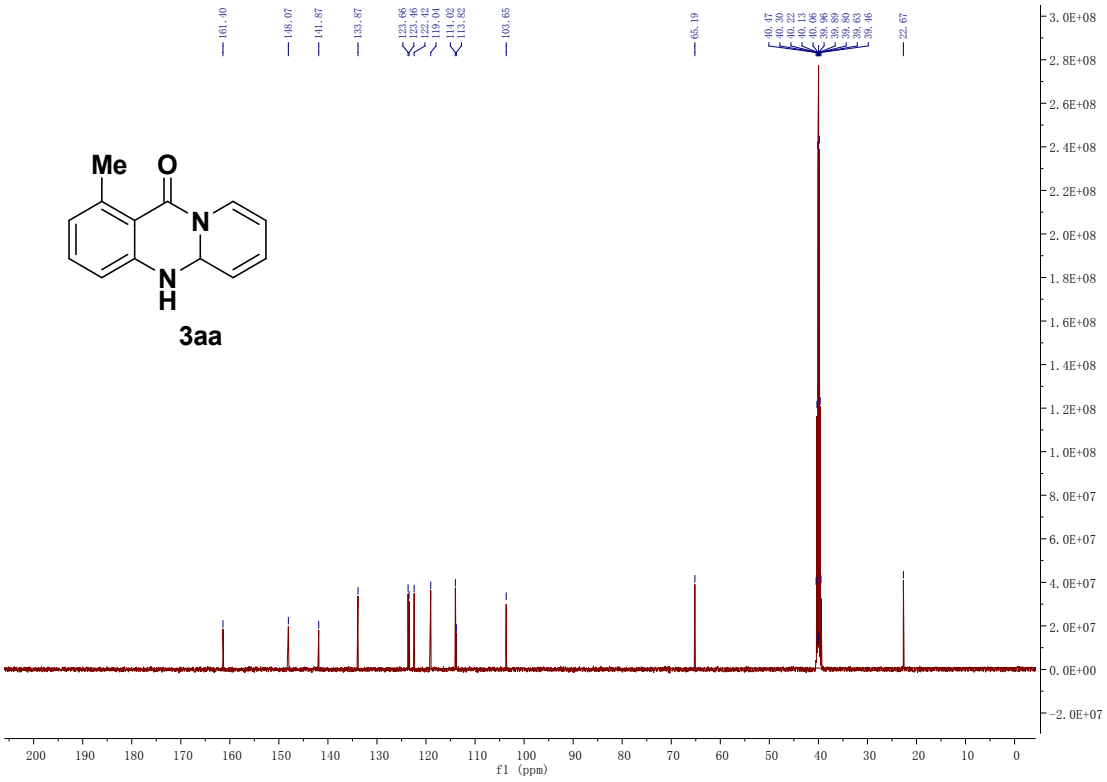

8.79
8.78
8.77
8.77
8.28
8.26
7.75
7.75
7.75
7.52
7.50
7.11
7.09
7.08
7.08
3.36
2.50
2.49
2.49
2.48
Cl
O
N
N
3m
1.00
1.01
1.99
2.05
1.02
f1 (ppm)

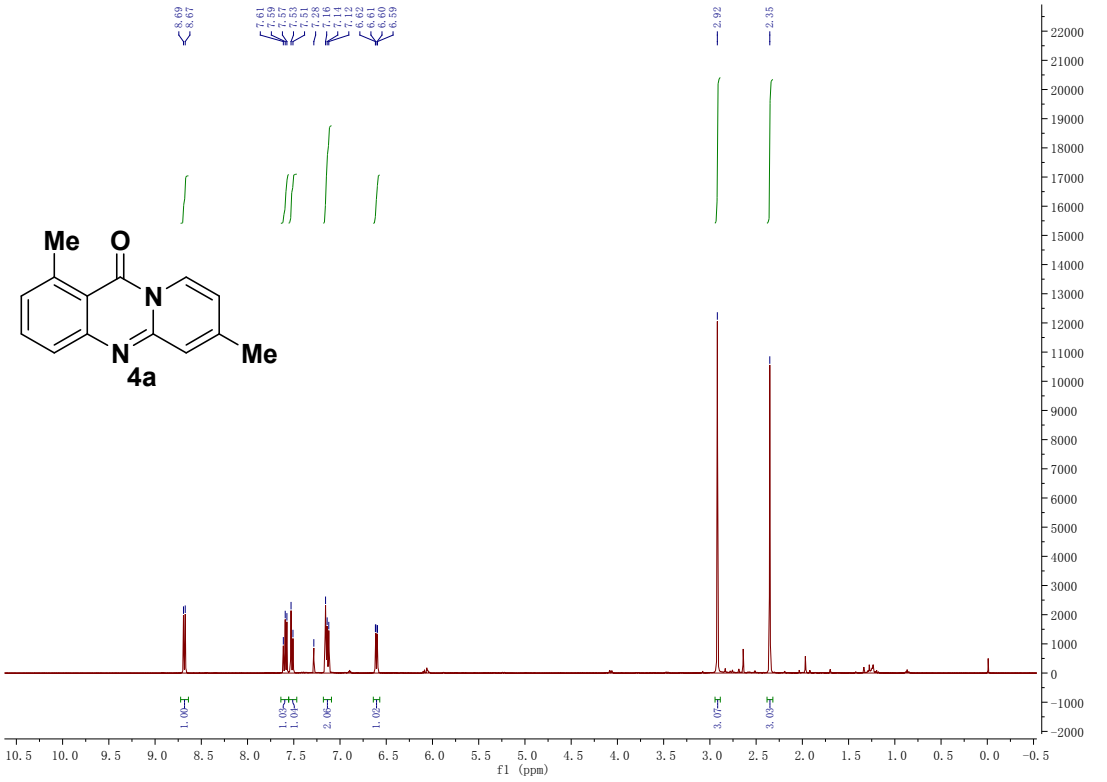

158.36
149.62
148.88
140.22
136.66
129.43
127.16
126.18
125.92
125.66
114.91
114.17
40.53
40.44
40.37
40.28
40.20
40.11
40.03
39.94
39.78
39.61
39.44
O
N
Cl
N
3m
f1 (ppm)

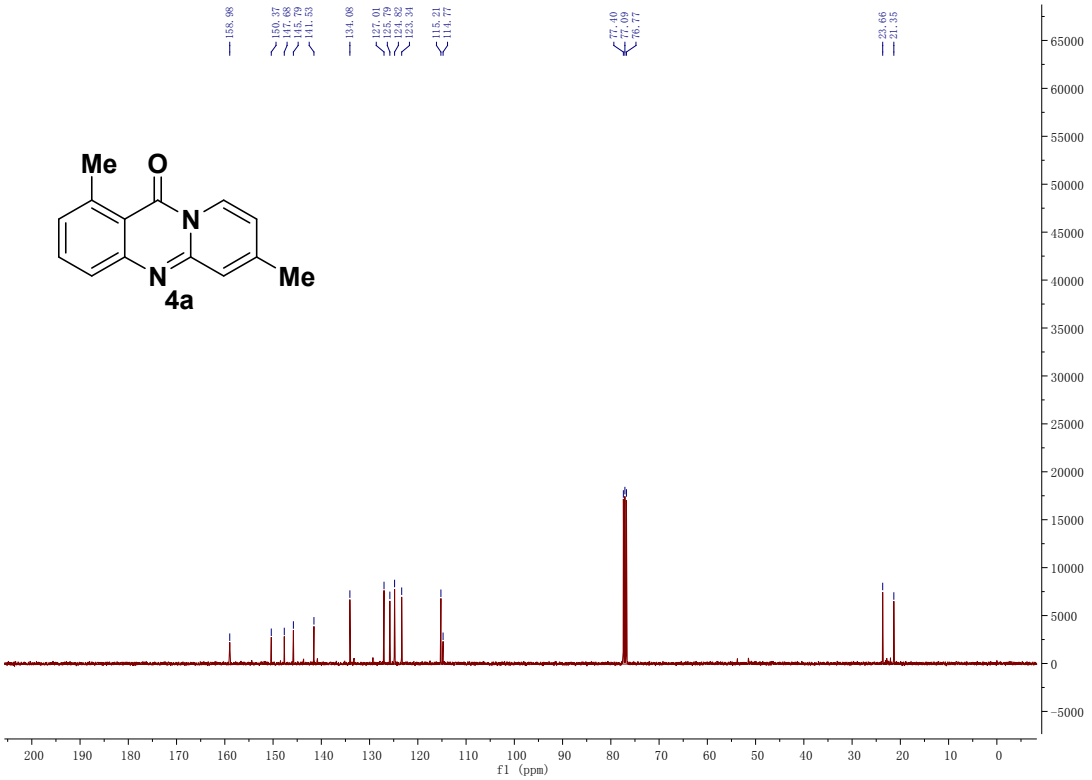

9.06
9.04
7.98
7.97
7.65
7.44
7.42
7.38
7.06
7.05
1.73
1.27
0.02
1.00
1.01
2.04
1.01
1.03
O
S
N
N
3n
f1 (ppm)

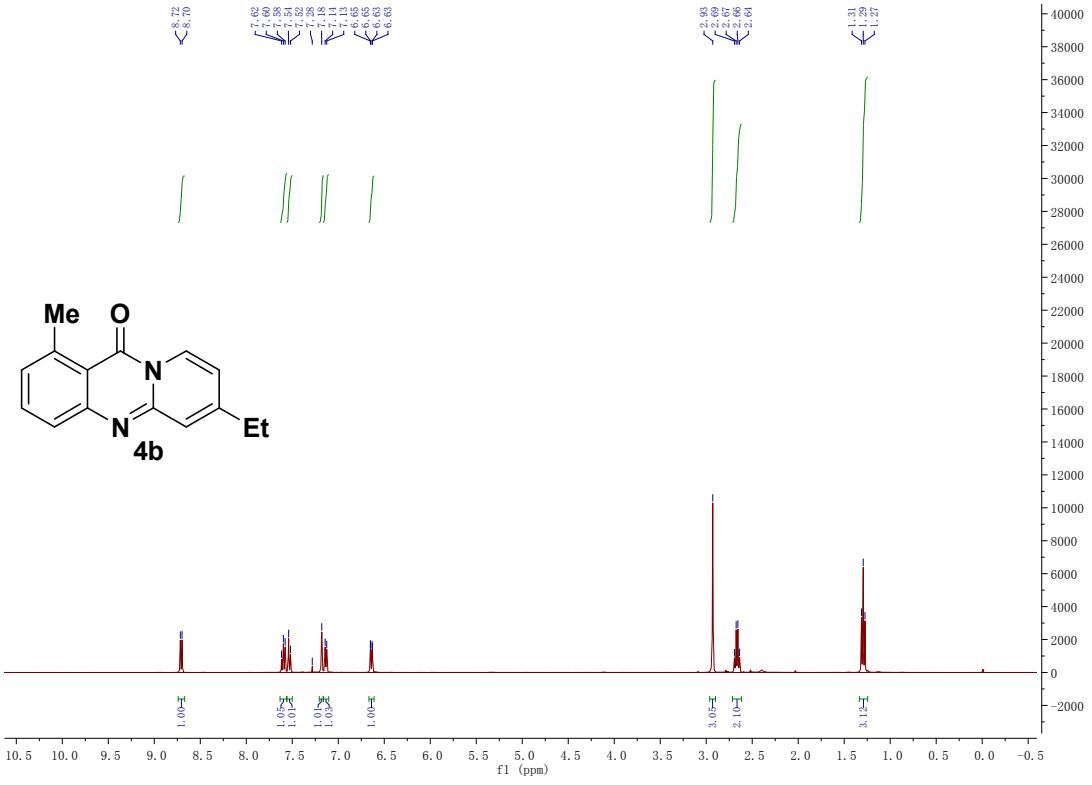

157.90
154.43
149.09
136.62
134.29
126.39
126.11
124.69
115.49
113.66
77.33
77.01
76.69
29.68
O
S
N
N
3n
f1 (ppm)

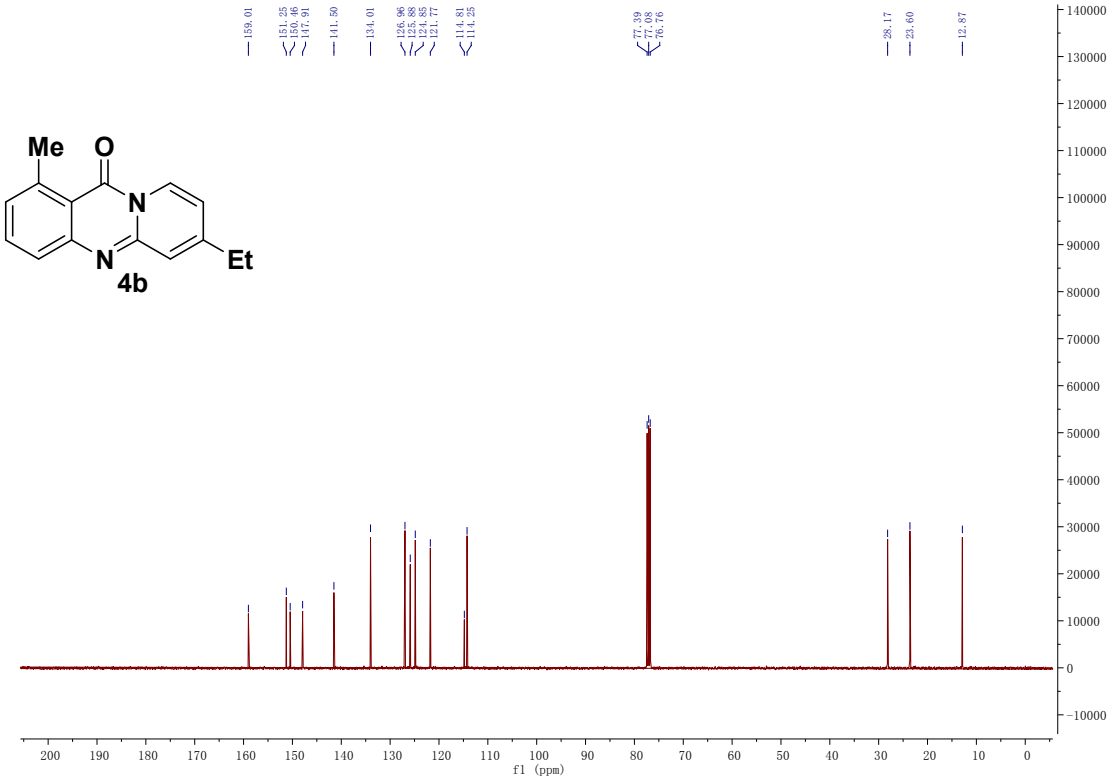

7.25
7.24
7.23
7.21
7.16
7.14
7.11
6.72
6.70
6.63
6.62
6.08
6.07
6.07
6.06
6.06
5.56
5.53
5.52
5.52
5.51
5.51
5.51
5.50
5.50
5.30
5.30
5.29
5.29
5.29
5.29
5.28
5.27
3.33
2.54
2.50
2.49
2.49
2.49
2.48
0.01
Me
O
N
N
H
3aa
2.00
0.99
1.00
1.01
0.99
2.00
1.00
3.00
f1 (ppm)

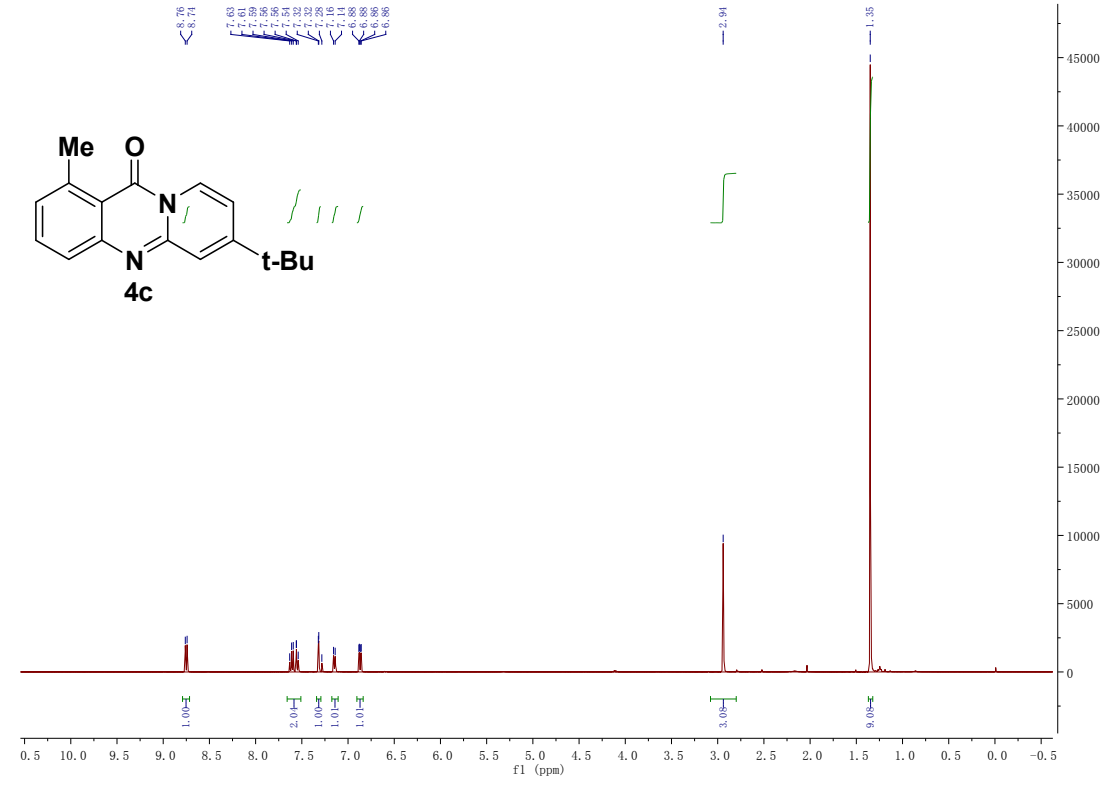

161.40
148.07
141.87
133.87
123.66
123.46
122.42
114.04
114.02
113.82
103.65
65.19
40.47
40.30
40.22
40.13
40.06
39.96
39.89
39.80
39.63
39.46
22.67
Me
O
N
N
H
3aa
f1 (ppm)

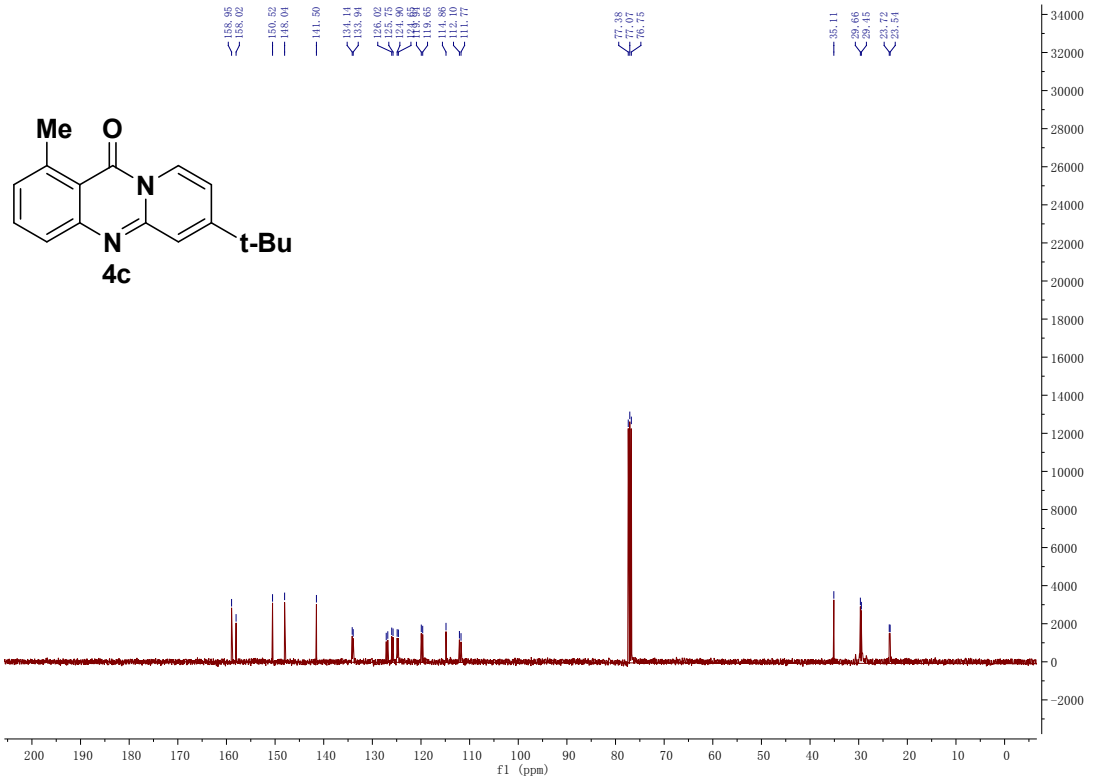

8.69
8.67
7.61
7.59
7.57
7.53
7.51
7.28
7.16
7.11
7.12
6.62
6.61
6.60
6.59
2.92
2.35
Me
O
N
N
Me
4a
1.00
1.03
1.04
2.06
1.02
3.07
3.03
f1 (ppm)

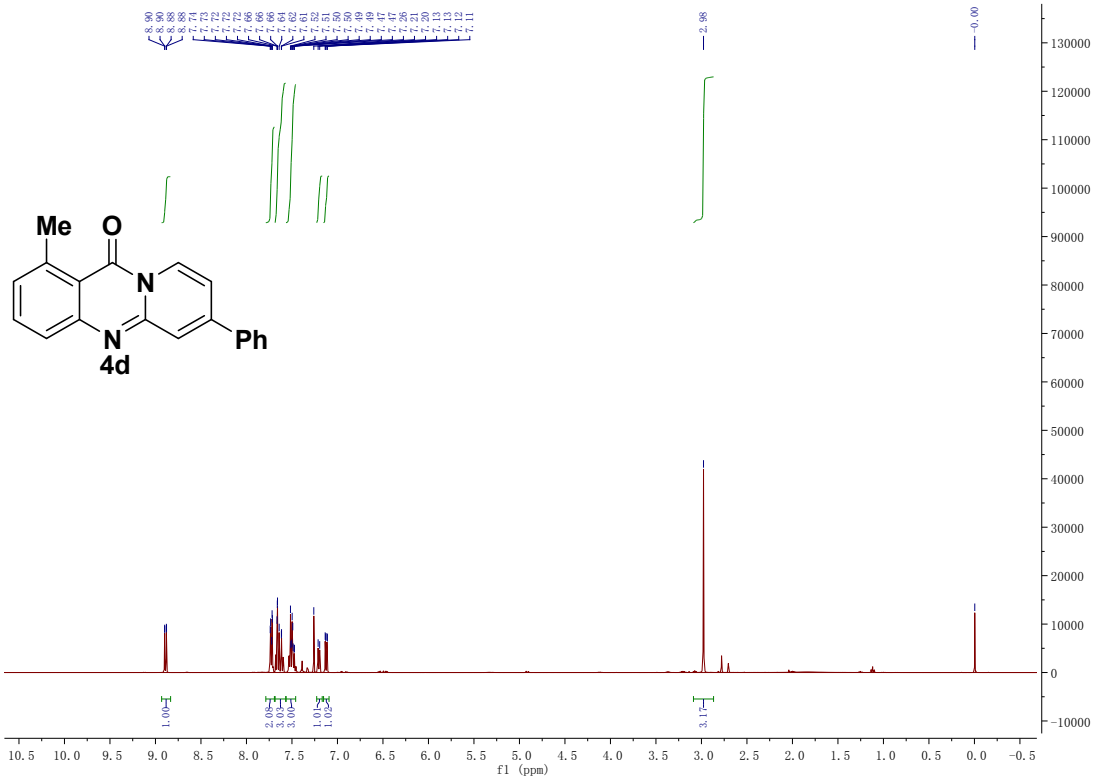

158.98
150.37
147.68
145.79
141.53
134.08
127.01
125.79
124.82
123.94
115.21
114.77
77.40
77.09
76.77
23.66
21.35
Me
O
N
N
Me
4a
f1 (ppm)

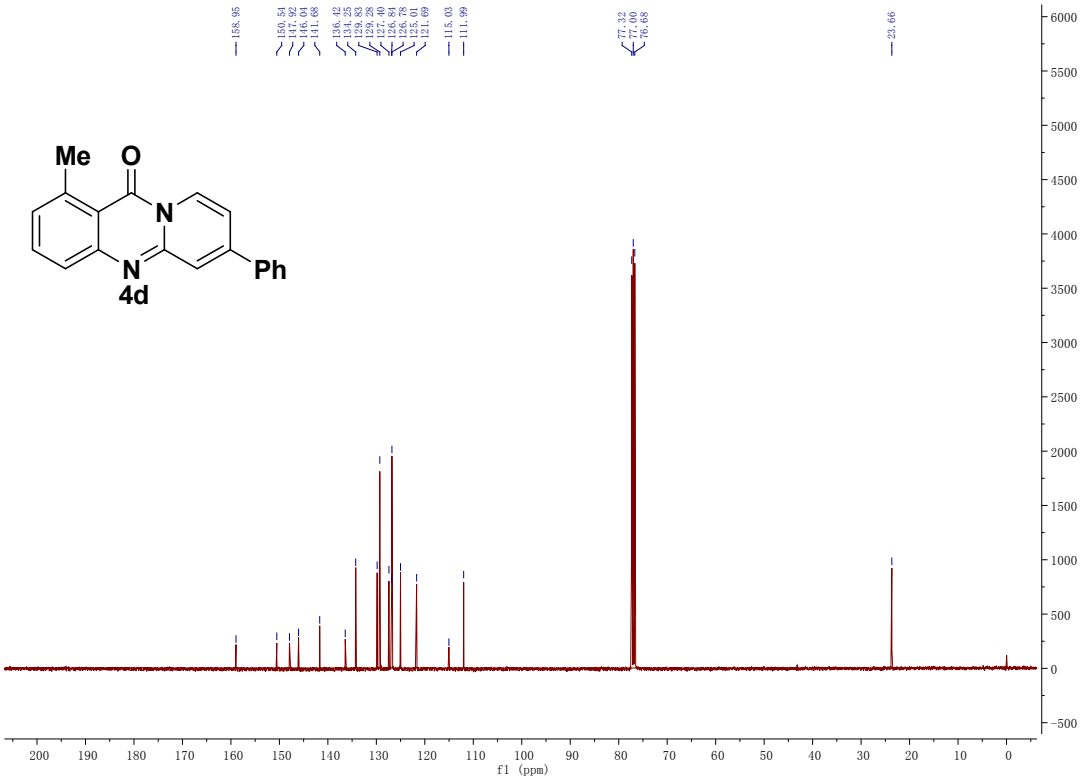

8.72
8.70
7.62
7.60
7.58
7.54
7.52
7.28
7.15
7.13
6.65
6.65
6.63
6.63
2.93
2.89
2.67
2.66
2.64
1.31
1.29
1.27
Me
O
N
N
Et
4b
1.00
1.05
1.01
1.03
1.00
3.05
2.10
3.12
f1 (ppm)

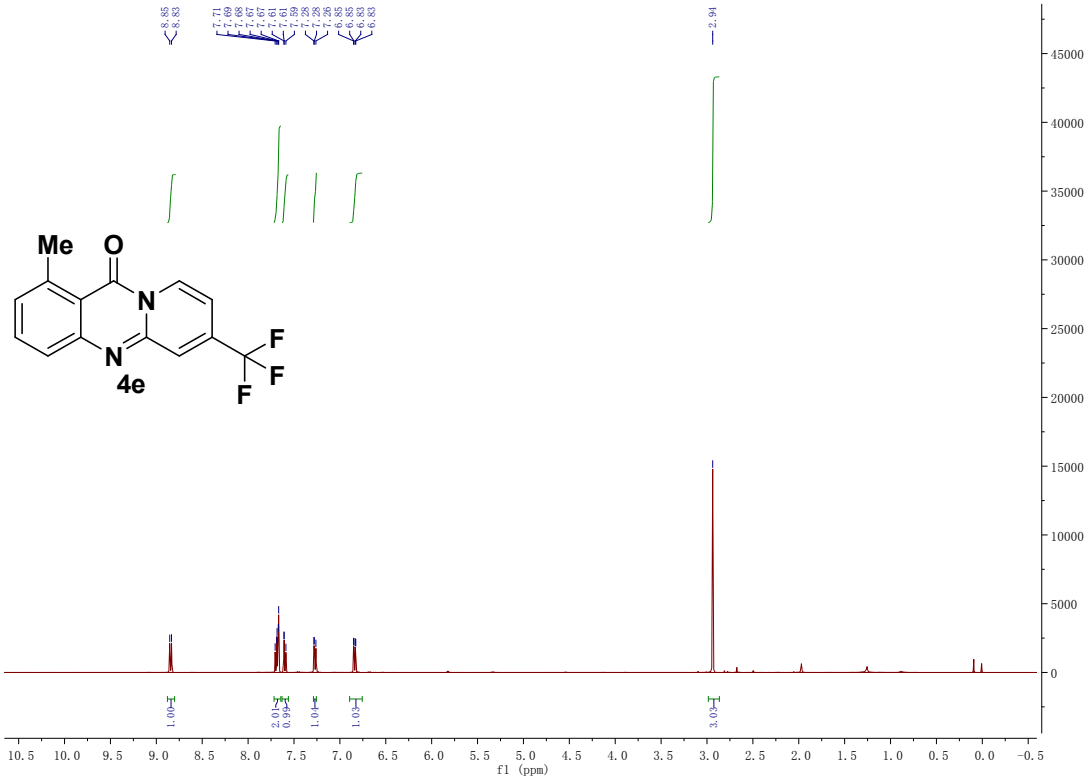

Me
O
N
N
Et
4b
159.01
151.25
150.46
147.91
141.50
134.01
126.96
125.88
123.85
121.77
114.81
114.25
77.39
77.08
76.76
28.17
23.60
12.87
f1 (ppm)

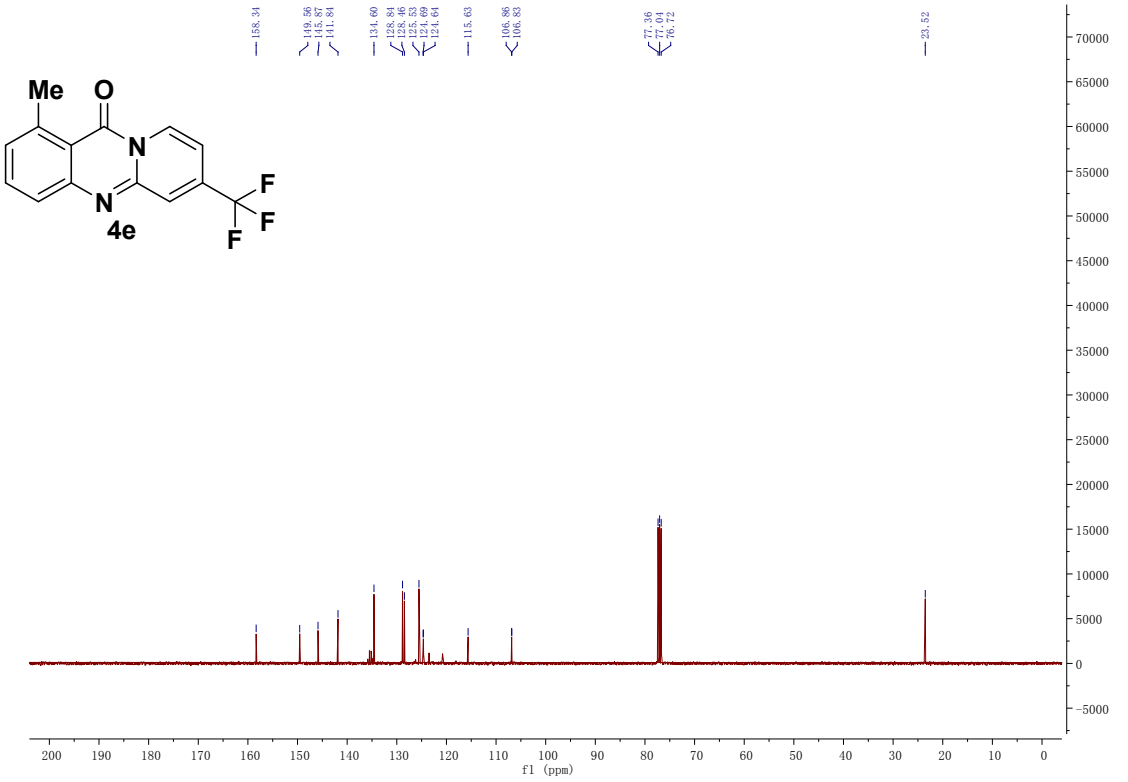

Me
O
N
N
t-Bu
4c
8.76
8.74
7.63
7.61
7.59
7.56
7.54
7.32
7.28
7.16
7.14
6.88
6.86
6.86
2.94
1.35
1.00
2.04
1.00
1.01
1.01
3.09
9.09
f1 (ppm)

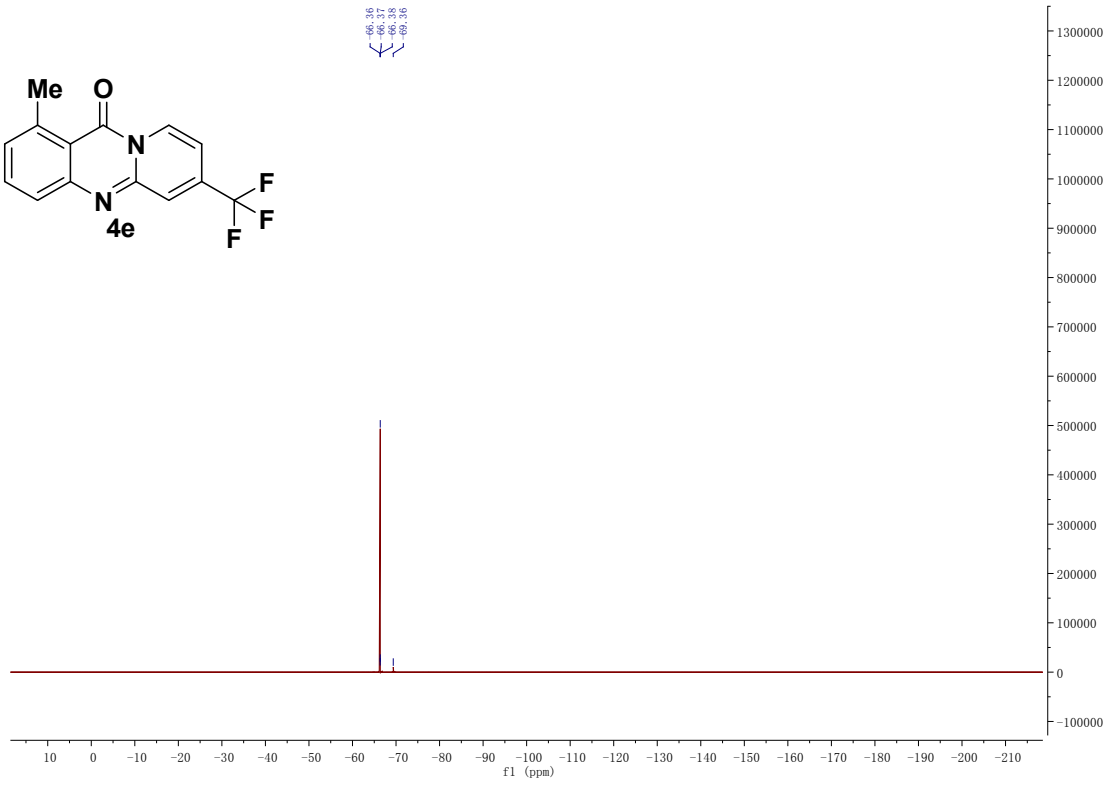

Me
O
N
N
t-Bu
4c
f1 (ppm)

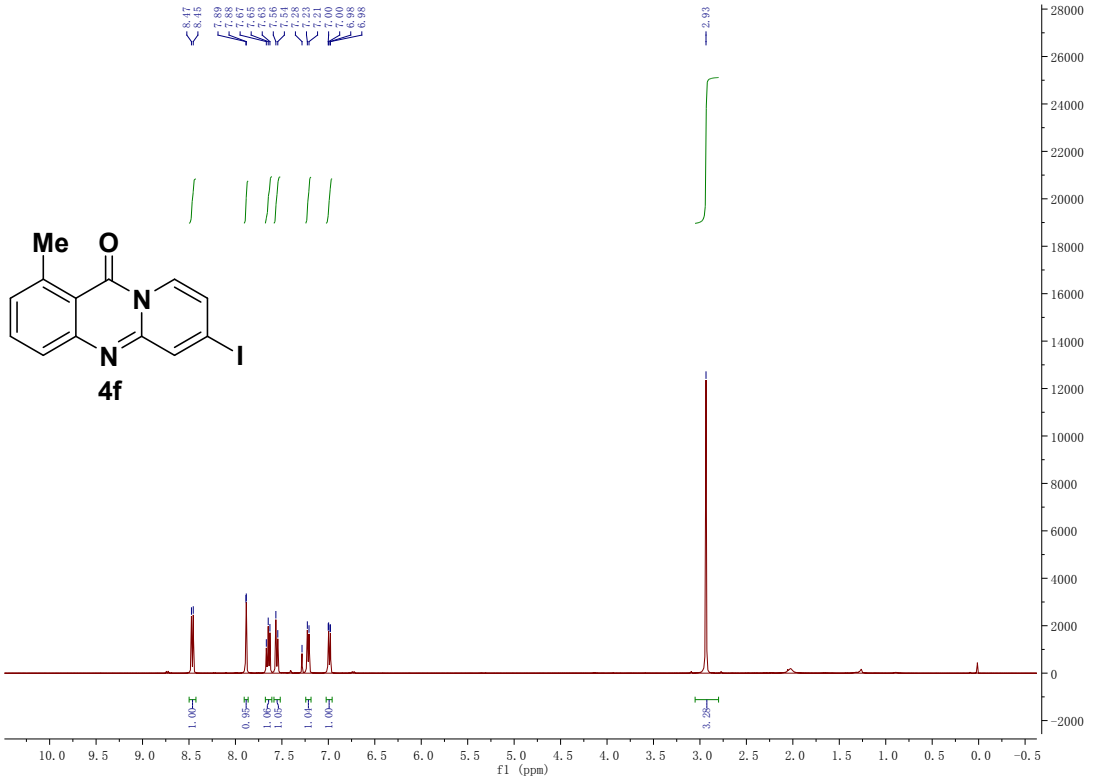

Me
O
N
N
Ph
4d
f1 (ppm)

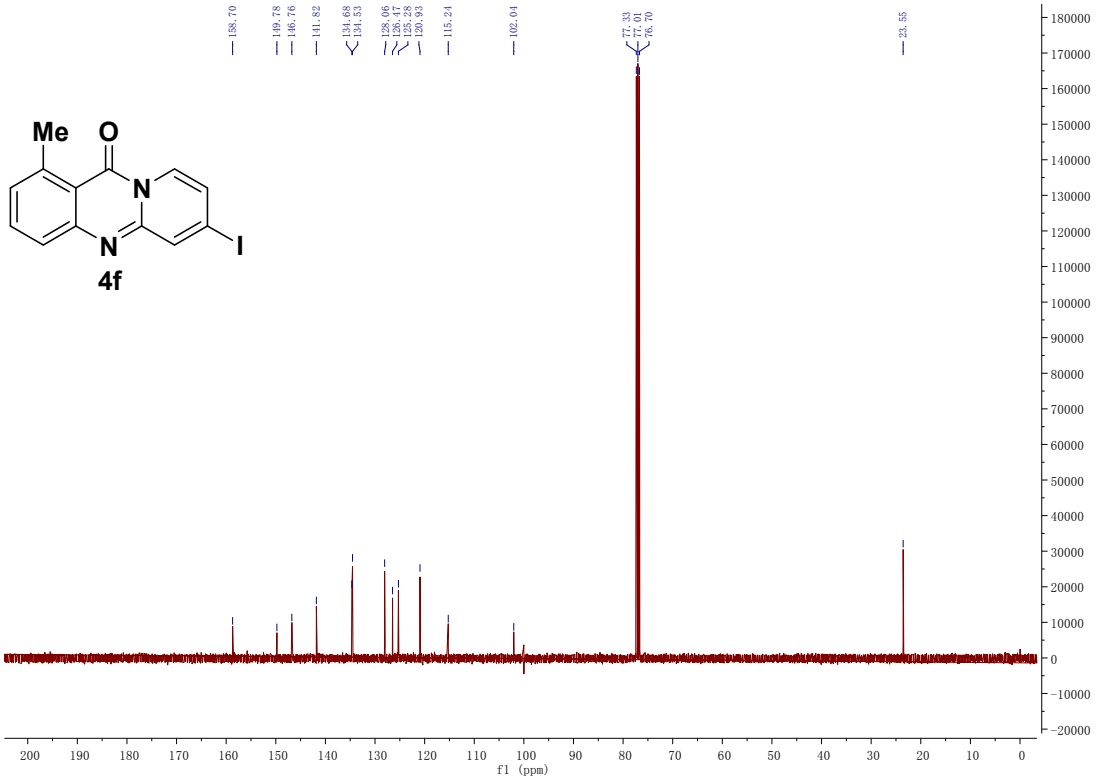

158.95
150.54
147.92
146.04
141.68
136.42
131.25
129.83
129.28
127.40
127.04
126.78
125.01
121.69
115.03
111.99
77.32
77.00
76.68
23.66
Me
O
N
N
Ph
4d
f1 (ppm)

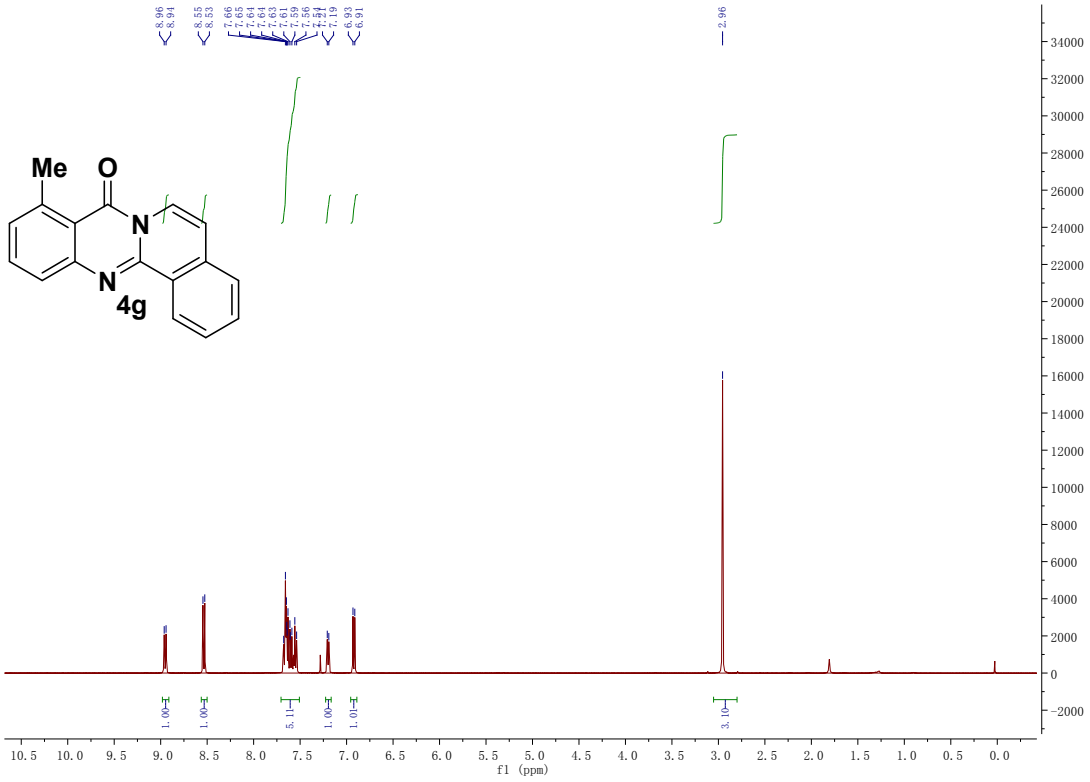

8.85
8.83
7.71
7.69
7.68
7.67
7.67
7.61
7.61
7.59
7.28
7.26
6.85
6.85
6.83
6.83
2.94
Me
O
N
N
F
F
F
4e
1.00
2.01
0.99
1.04
1.03
3.03
f1 (ppm)

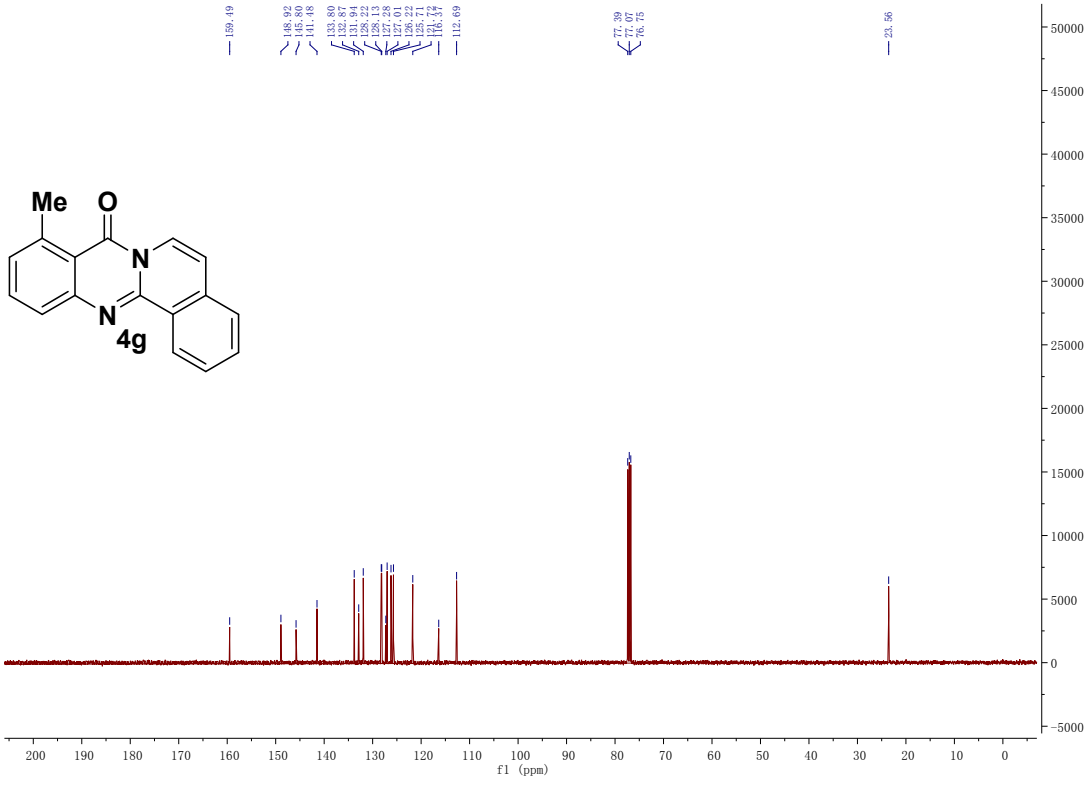

158.34
149.56
145.87
141.84
134.60
128.84
128.46
125.53
124.69
124.64
115.63
106.86
106.83
77.36
77.04
76.72
23.52
Me
O
N
N
F
F
F
4e
f1 (ppm)

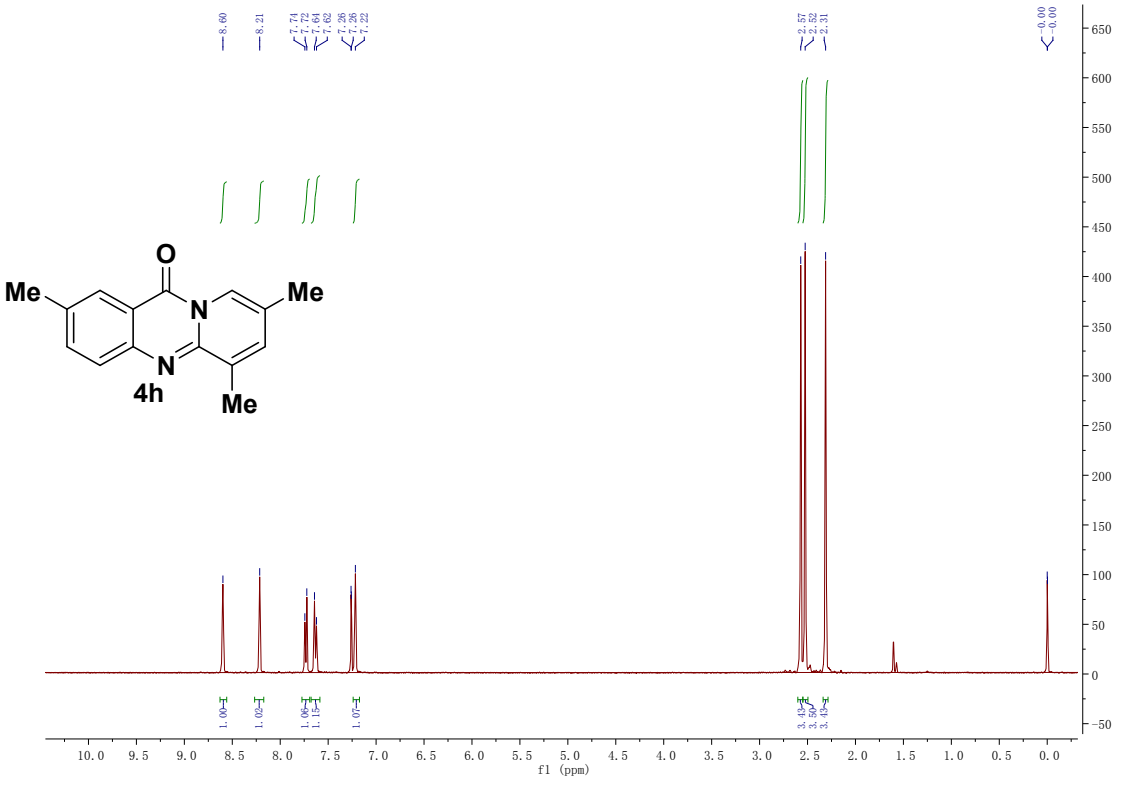

66.36
66.37
66.38
69.36
Me
O
N
N
F
F
F
4e
f1 (ppm)

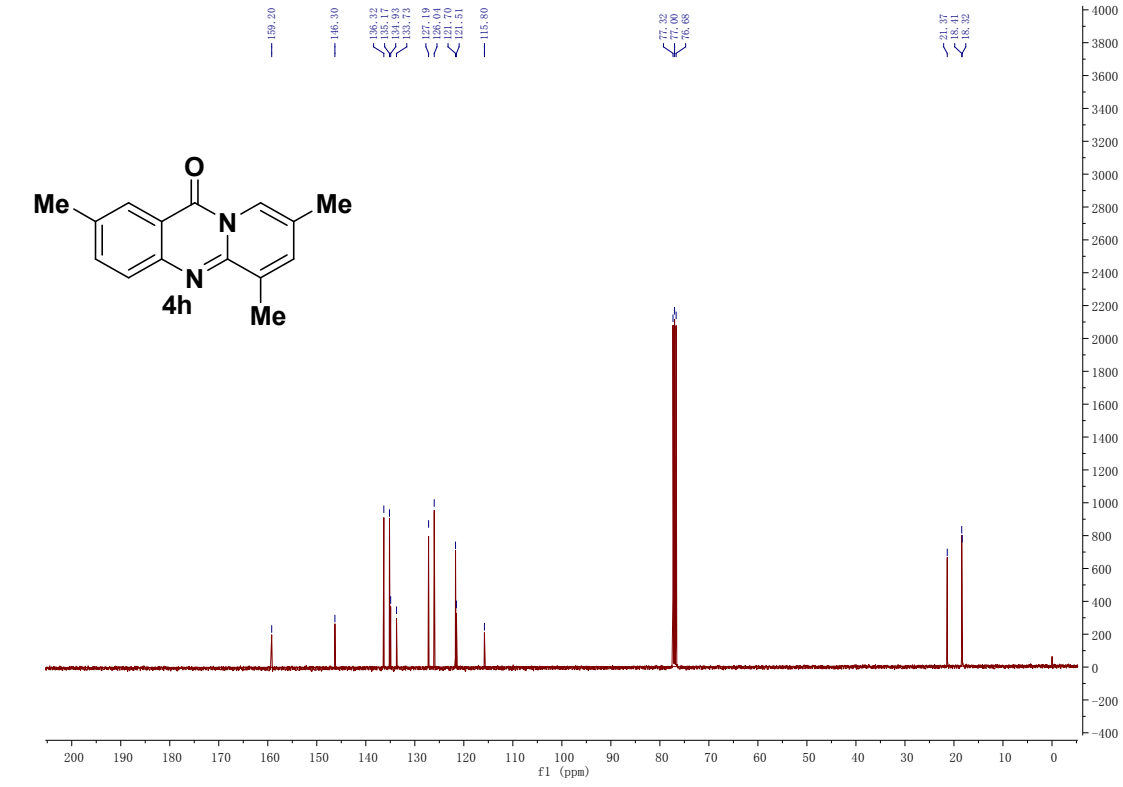

8.47
8.45
7.89
7.88
7.67
7.65
7.63
7.56
7.54
7.28
7.23
7.21
7.00
6.98
6.98
2.93
Me
O
N
N
I
4f
1.00
0.95
1.06
1.05
1.04
1.00
3.28
f1 (ppm)

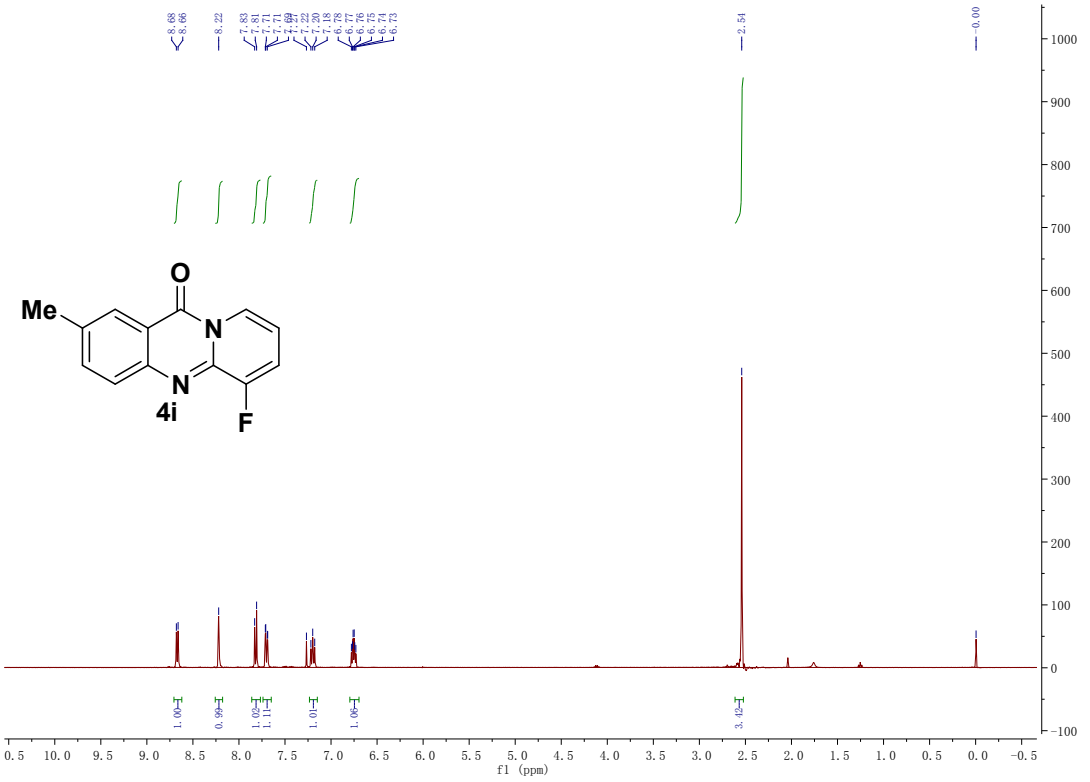

158.70
149.78
146.76
141.82
134.68
134.53
128.06
126.47
125.98
120.93
115.24
102.04
77.33
77.01
76.70
23.55
Me
O
N
N
I
4f
f1 (ppm)

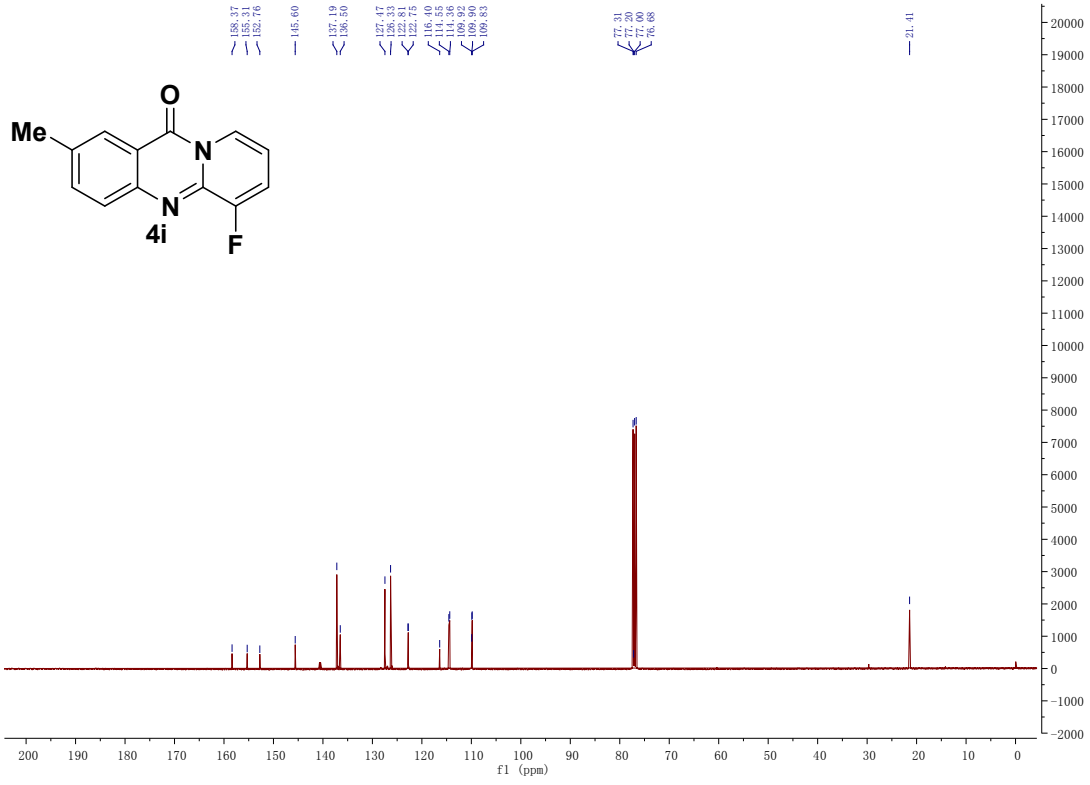

8.96
8.94
8.55
8.53
7.66
7.65
7.64
7.64
7.63
7.61
7.59
7.56
7.54
7.51
7.19
6.93
6.91
2.96
Me
O
N
N
4g
1.00
1.00
5.11
1.06
1.01
3.10
f1 (ppm)

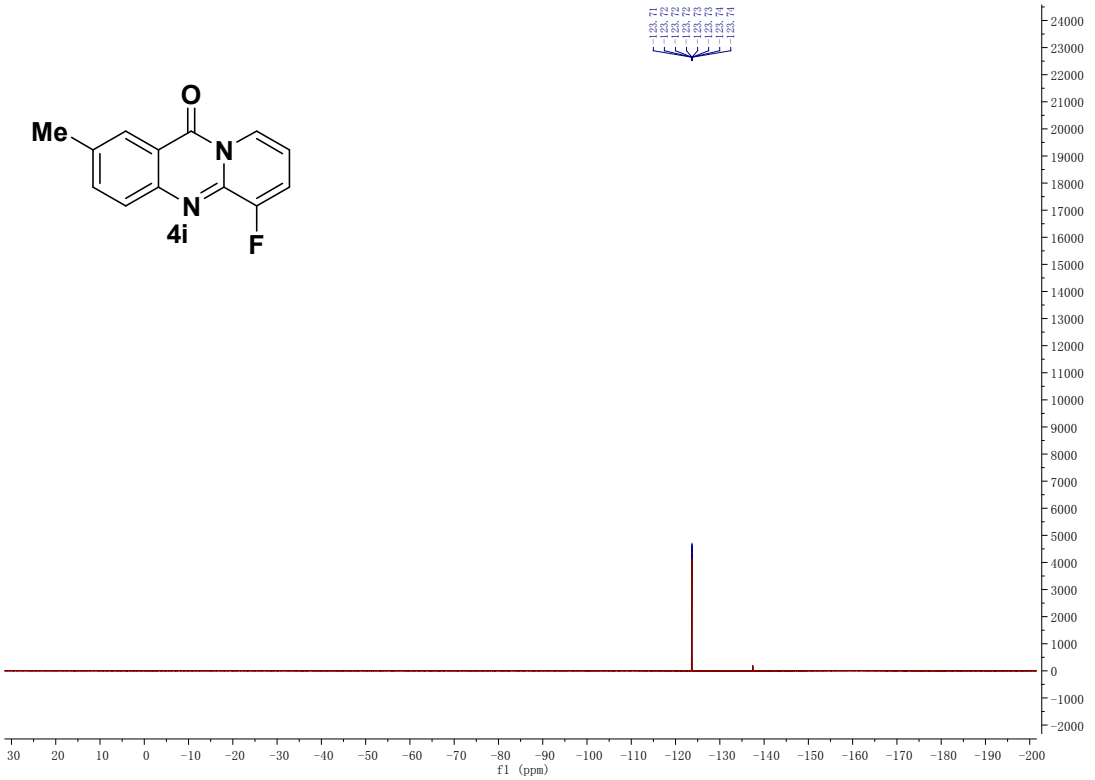

159.49
148.92
145.80
141.48
133.80
132.87
131.94
129.22
128.13
127.28
127.01
126.22
125.71
121.74
116.37
112.69
77.39
77.07
76.75
23.56
Me
O
N
N
4g
f1 (ppm)

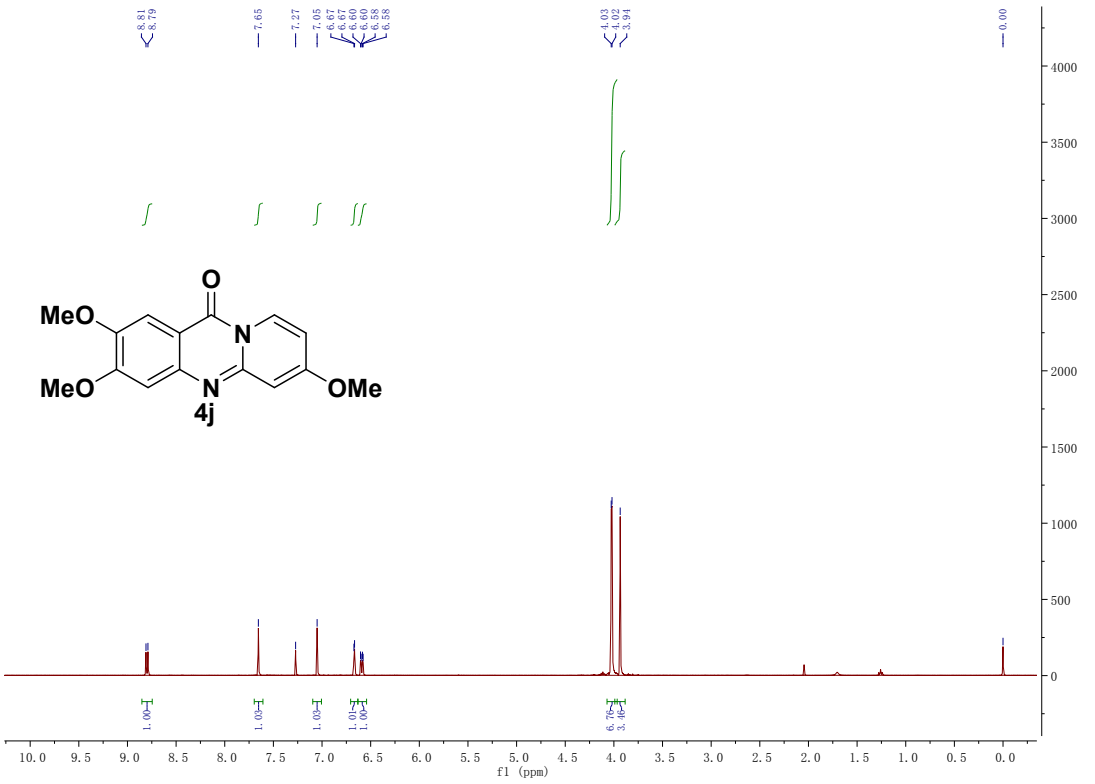

8.60
8.21
7.74
7.72
7.64
7.62
7.26
7.26
7.22
2.57
2.52
2.31
0.00
0.00
Me
Me
Me
O
N
N
4h
f1 (ppm)

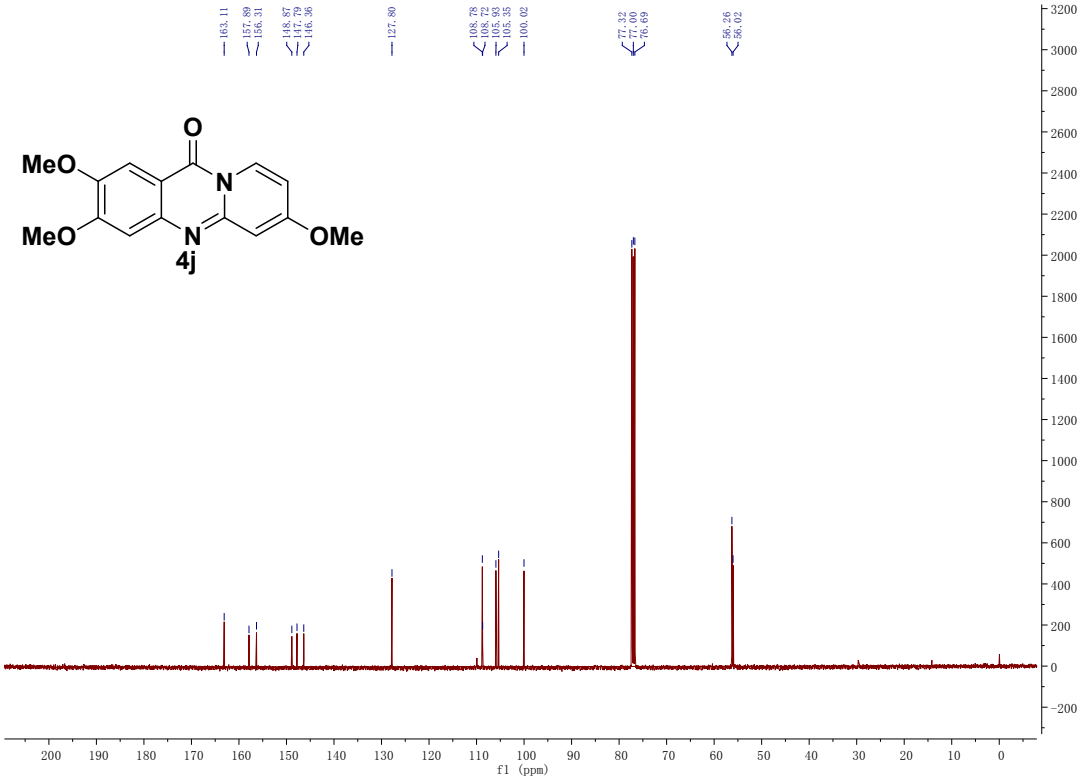

159.20
146.30
136.32
135.17
134.93
133.73
127.19
126.04
123.70
121.51
115.80
77.32
77.00
76.68
21.37
18.41
18.32
Me
Me
Me
O
N
N
4h
f1 (ppm)

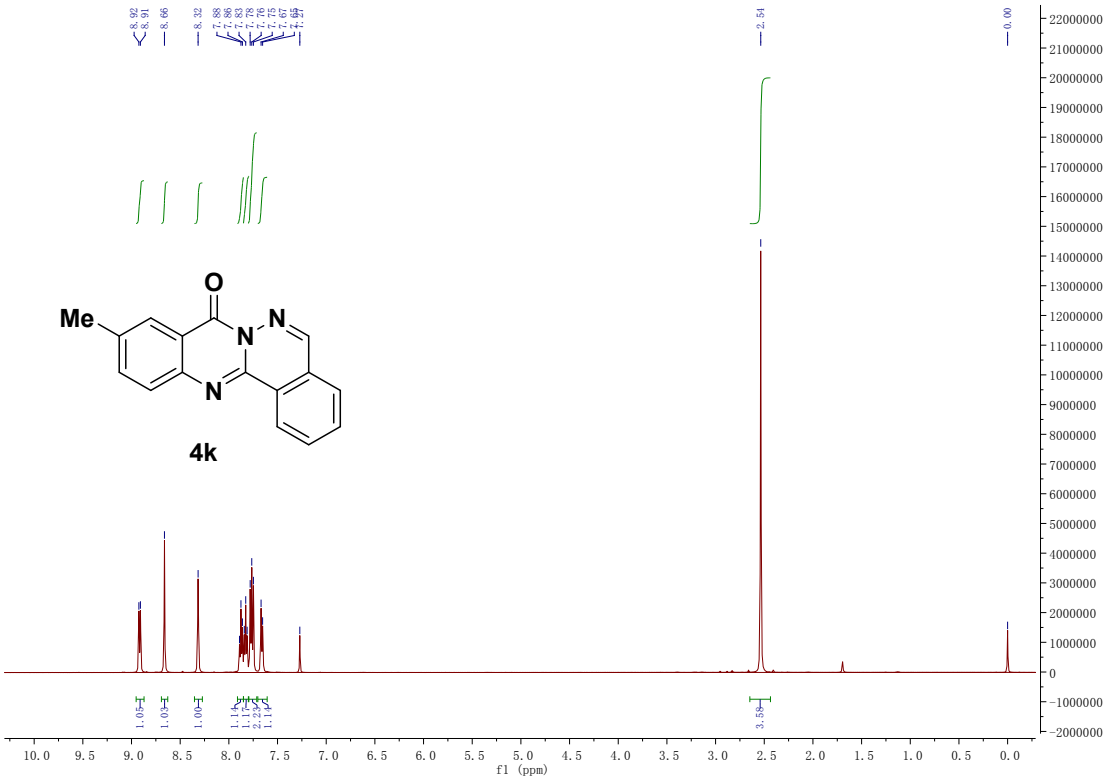

8.68
8.66
8.22
7.83
7.81
7.71
7.71
7.69
7.41
7.22
7.20
7.18
6.78
6.77
6.76
6.75
6.74
6.73
2.54
0.00
Me
O
N
N
4i
F
1.00
0.99
1.02
1.11
1.01
1.00
3.42
f1 (ppm)

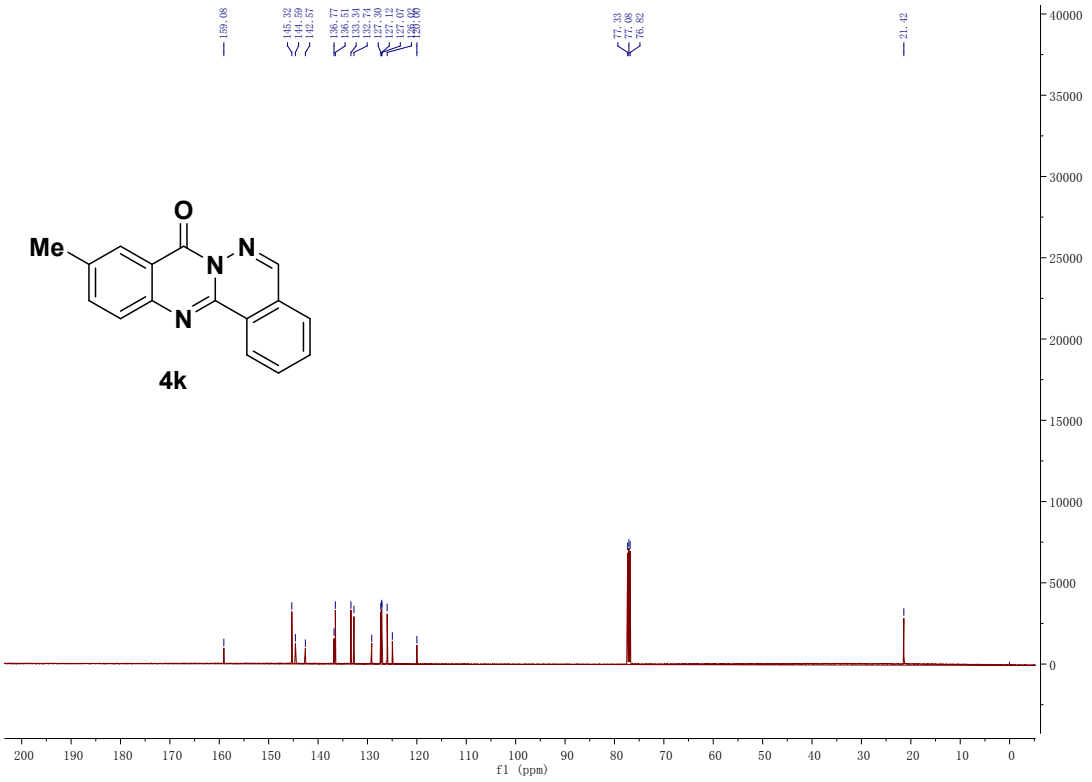

158.37
155.31
152.76
145.60
137.19
136.50
127.47
126.33
122.81
122.75
116.40
114.55
114.36
109.92
109.90
109.83
77.31
77.20
77.00
76.68
21.41
Me
O
N
N
4i
F
f1 (ppm)

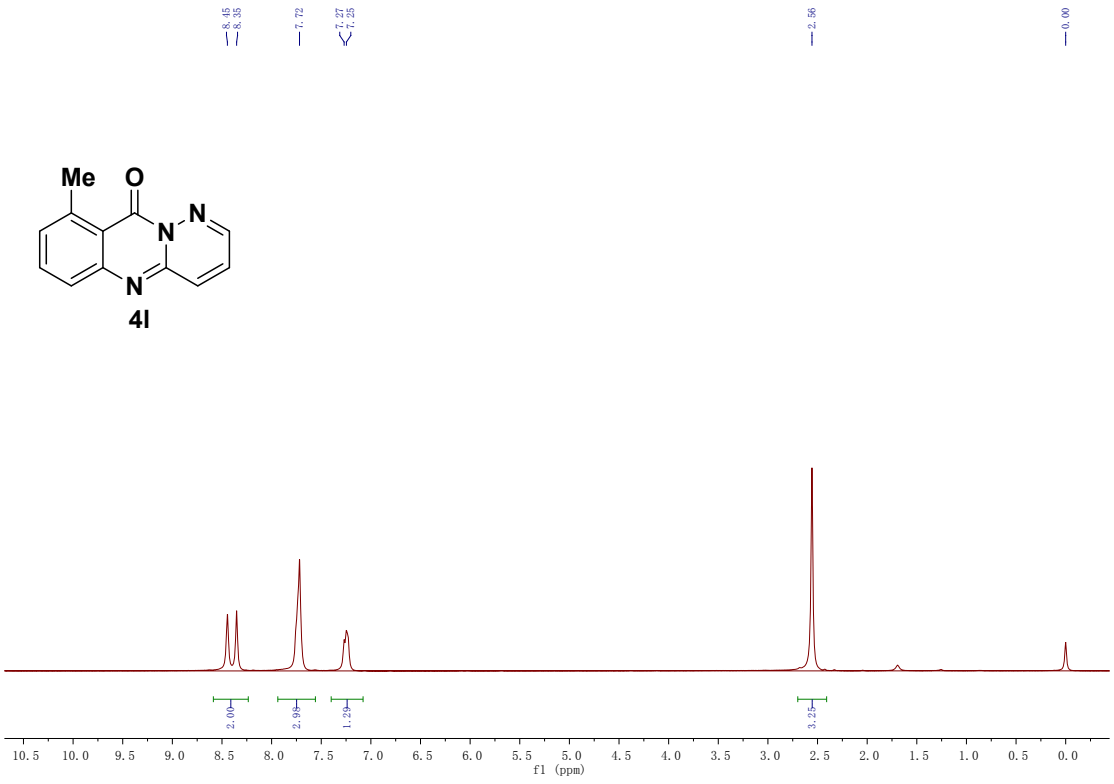

Me
O
N
N
4i
F
f1 (ppm)

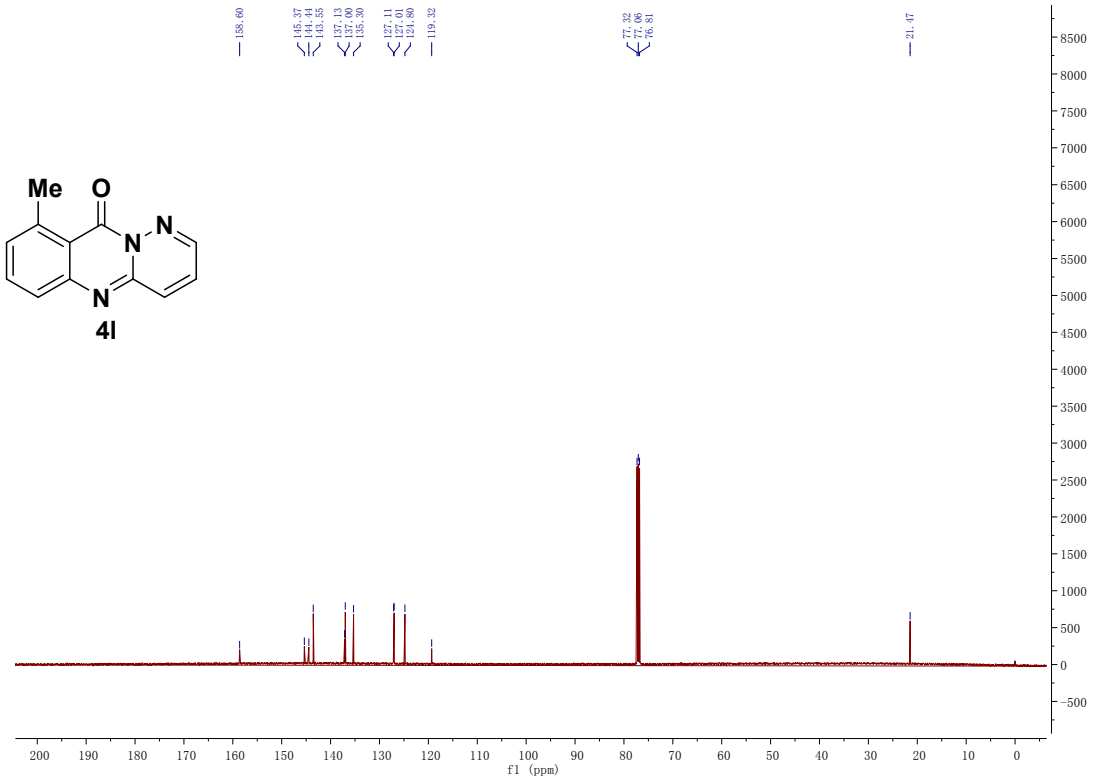

MeO
MeO
O
N
N
OMe
4j
f1 (ppm)

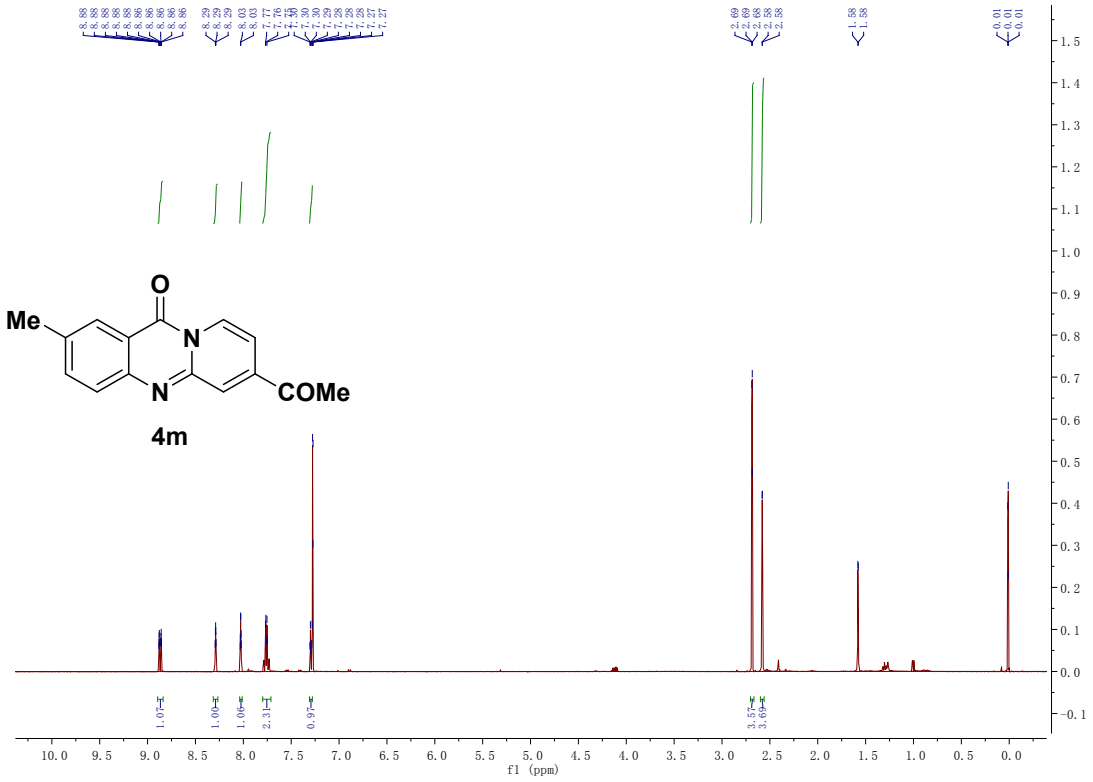

163.11
157.89
156.31
148.87
147.79
146.96
127.80
108.78
108.72
105.93
105.35
100.02
77.32
77.00
76.69
56.26
56.02
MeO
MeO
N
N
O
OMe
4j
f1 (ppm)

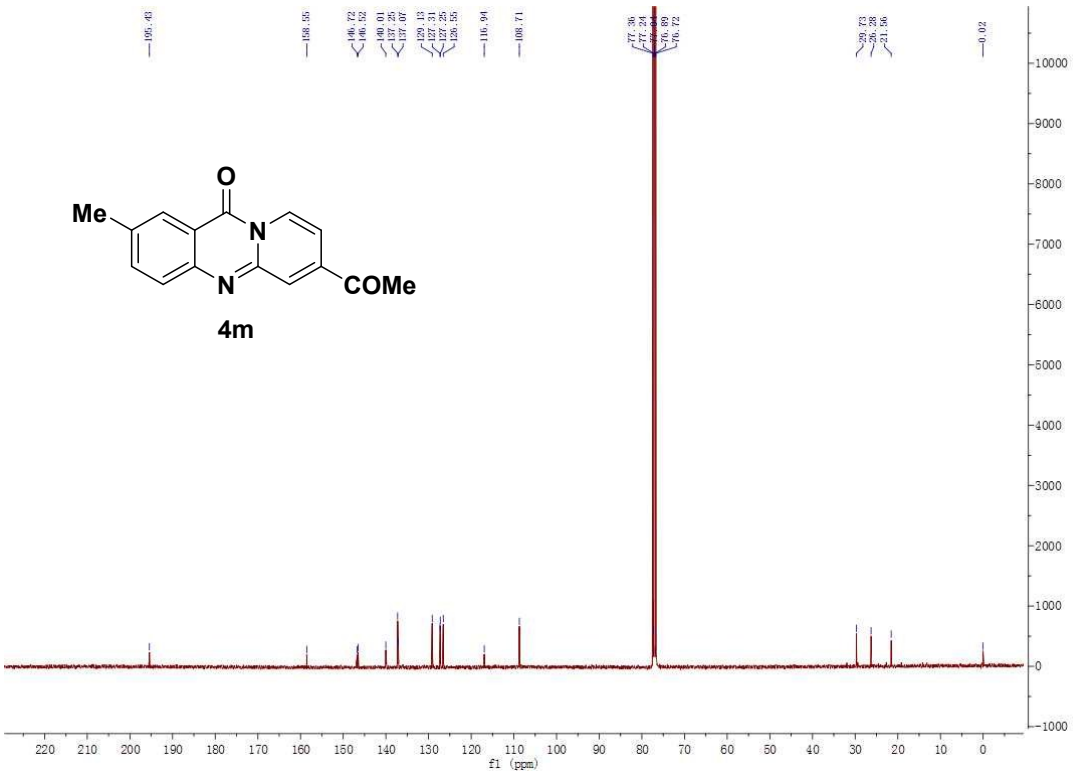

8.92
8.91
8.66
8.32
7.88
7.86
7.83
7.78
7.76
7.75
7.67
7.49
7.47
2.54
0.00
Me
N
N
N
O
4k
1.05
1.03
1.00
1.14
1.17
2.29
1.14
3.59
f1 (ppm)

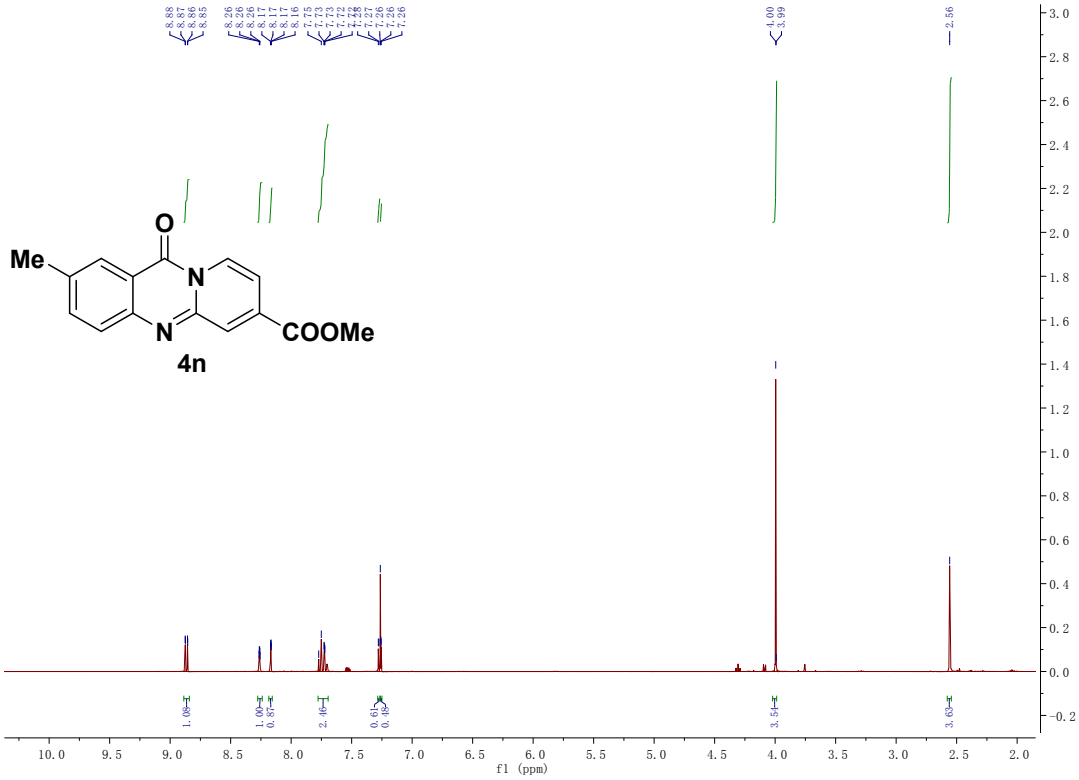

159.08
145.32
144.59
142.57
136.77
136.51
133.34
132.71
132.30
127.12
127.07
77.33
77.08
76.82
21.42
Me
O
N
N
N
4k
f1 (ppm)

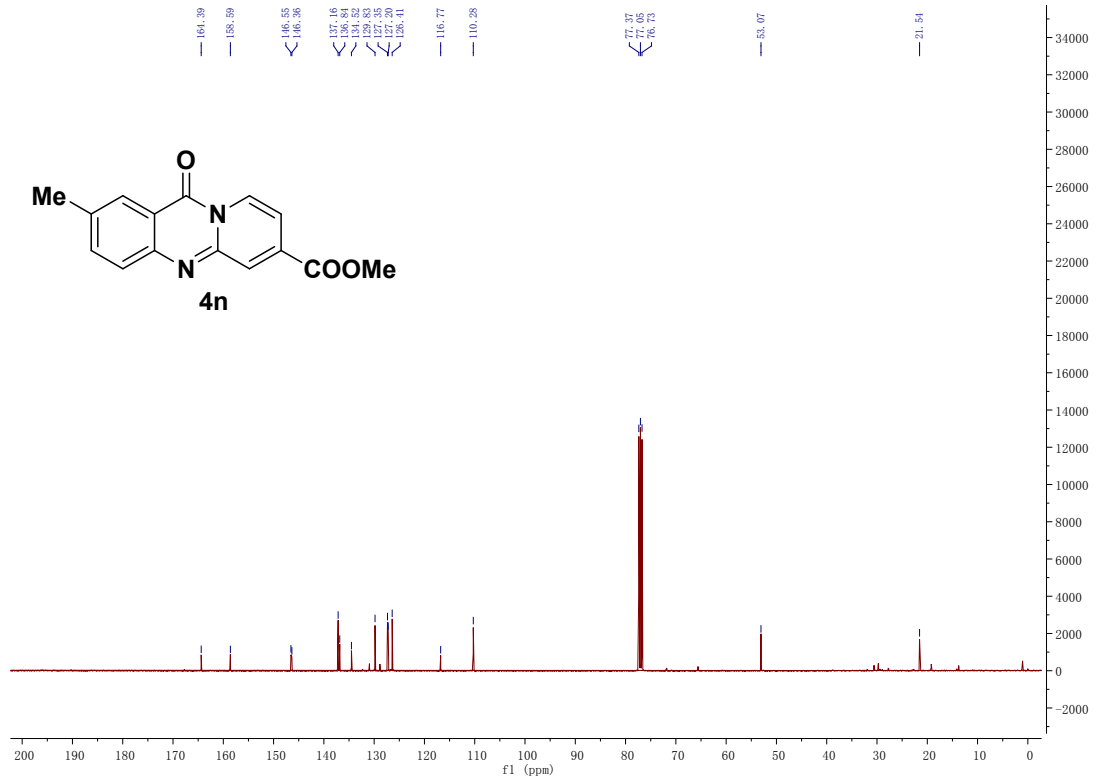

8.45
8.35
7.72
7.27
7.25
2.56
0.00
Me
O
N
N
N
4l
2.00
2.99
1.29
3.25
f1 (ppm)

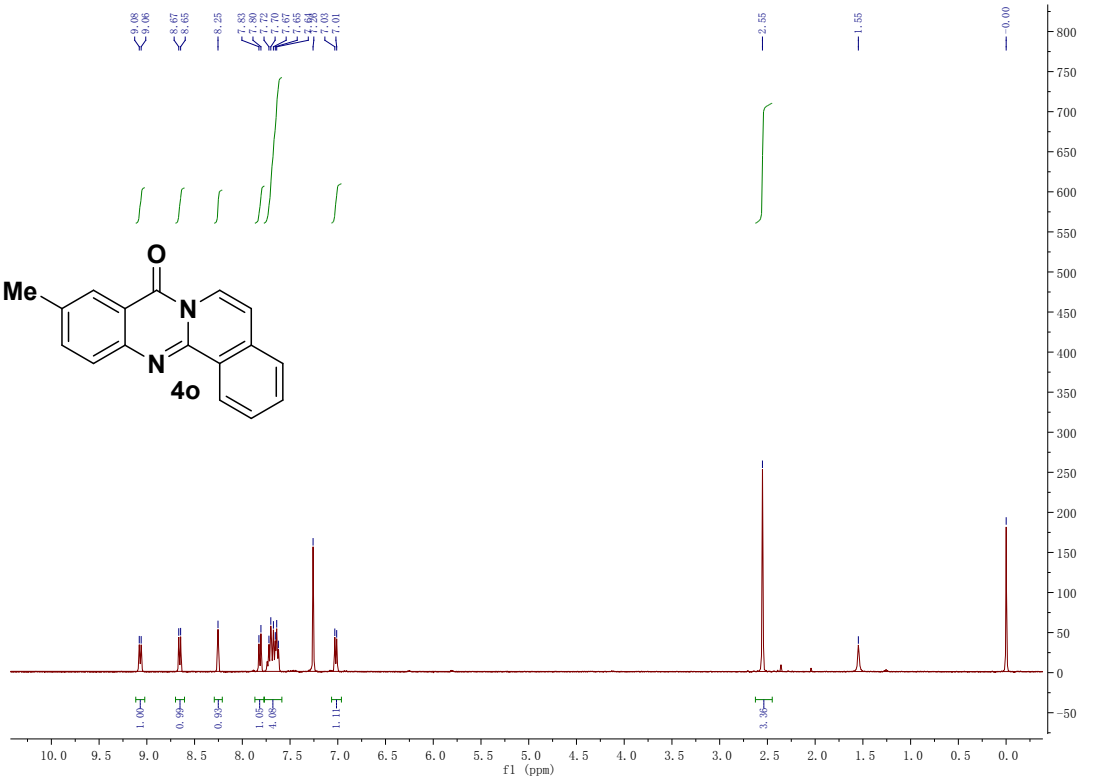

Me
O
N
N
N
4l
f1 (ppm)

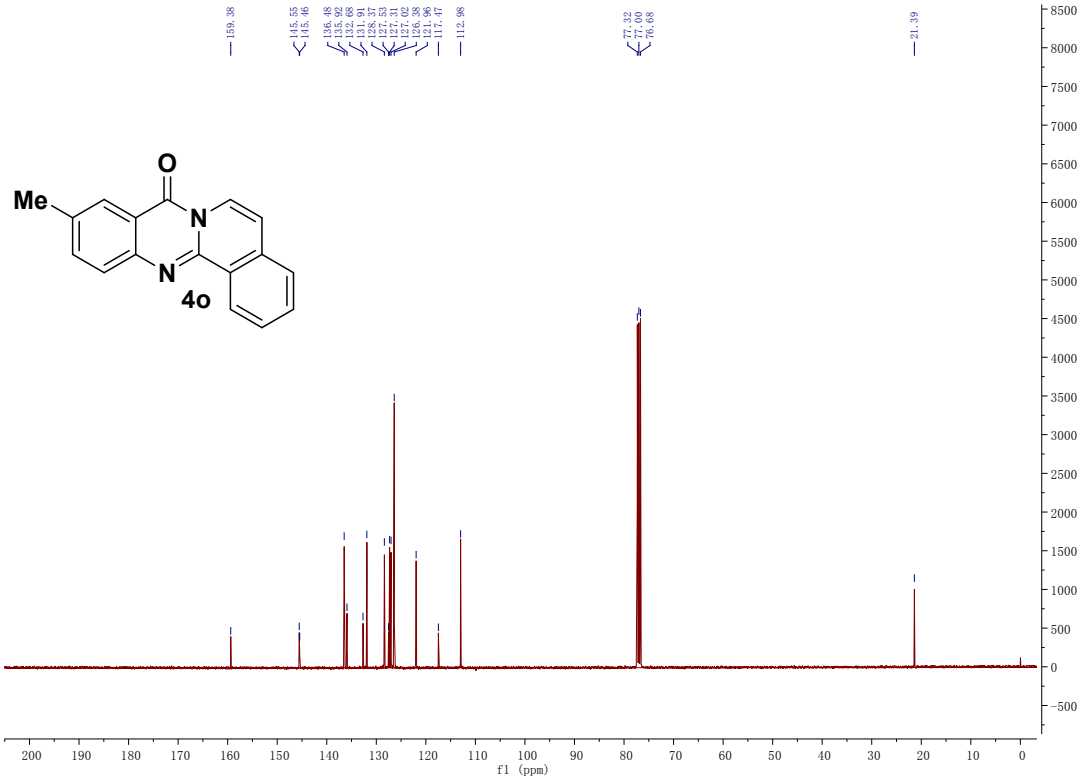

O
Me
N
N
COMe
4m
f1 (ppm)

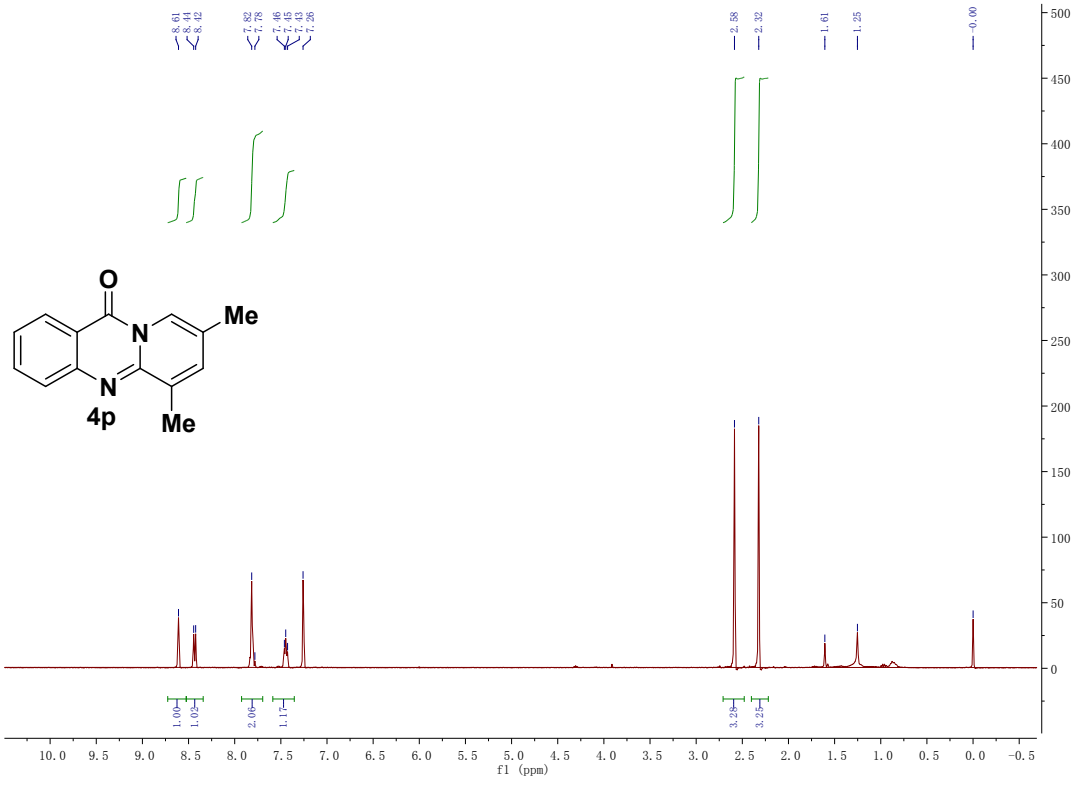

O
Me
N
N
COMe
4m
f1 (ppm)

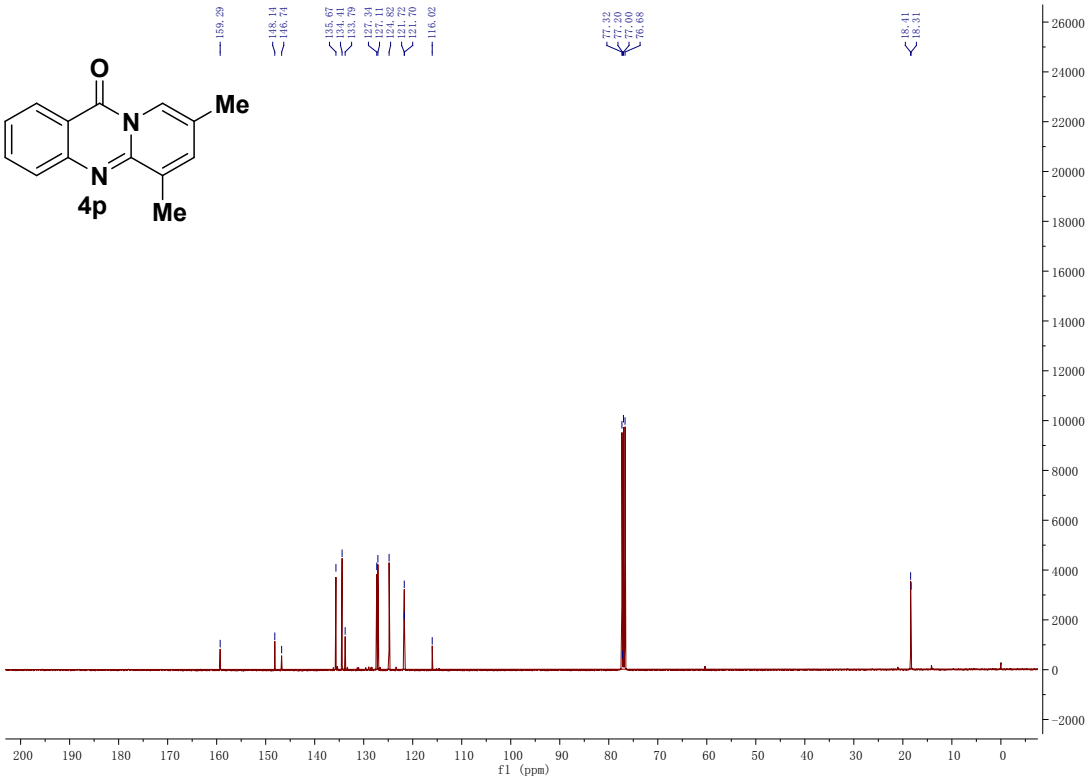

O
Me
N
N
COOMe
4n
f1 (ppm)

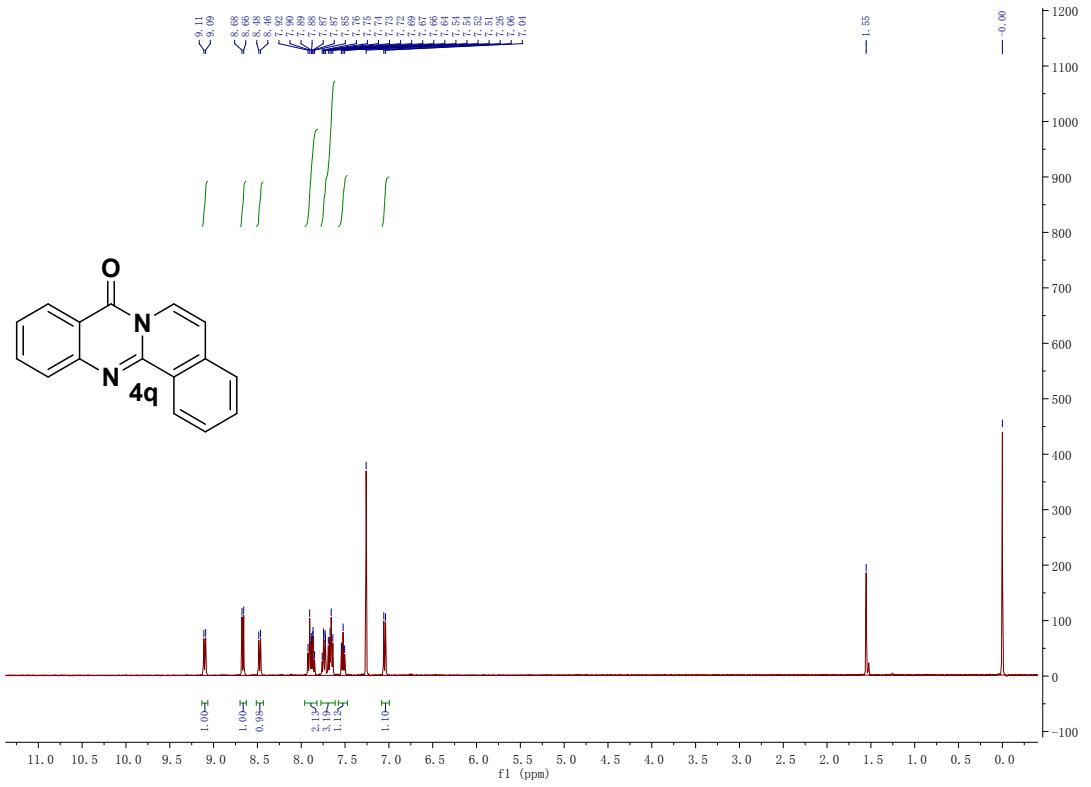

164.39
158.59
146.55
146.36
137.16
136.84
134.52
129.83
127.35
127.20
126.41
116.77
110.28
77.37
77.05
76.73
53.07
21.54
O
Me
N
N
COOMe
4n
f1 (ppm)

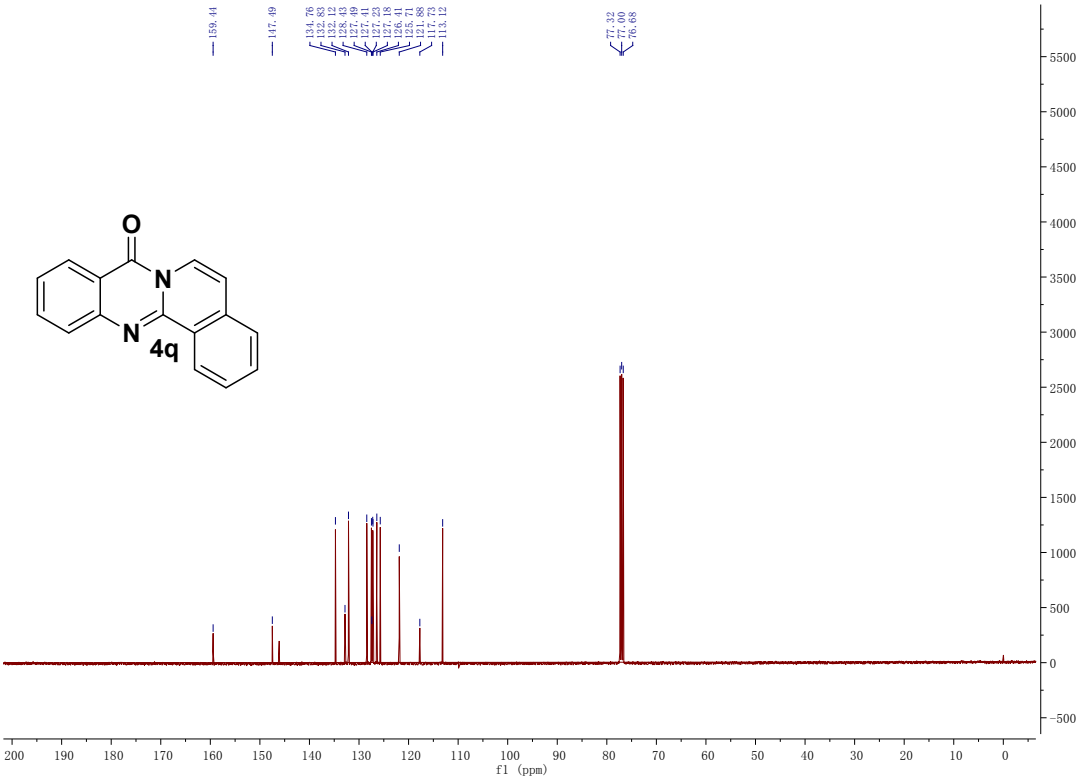

9.08
9.06
8.67
8.65
8.25
7.83
7.80
7.72
7.70
7.67
7.65
7.04
7.03
7.01
2.55
1.55
0.00
1.00
0.99
0.93
1.05
4.09
1.11
3.36
O
Me
N
N
4o
f1 (ppm)

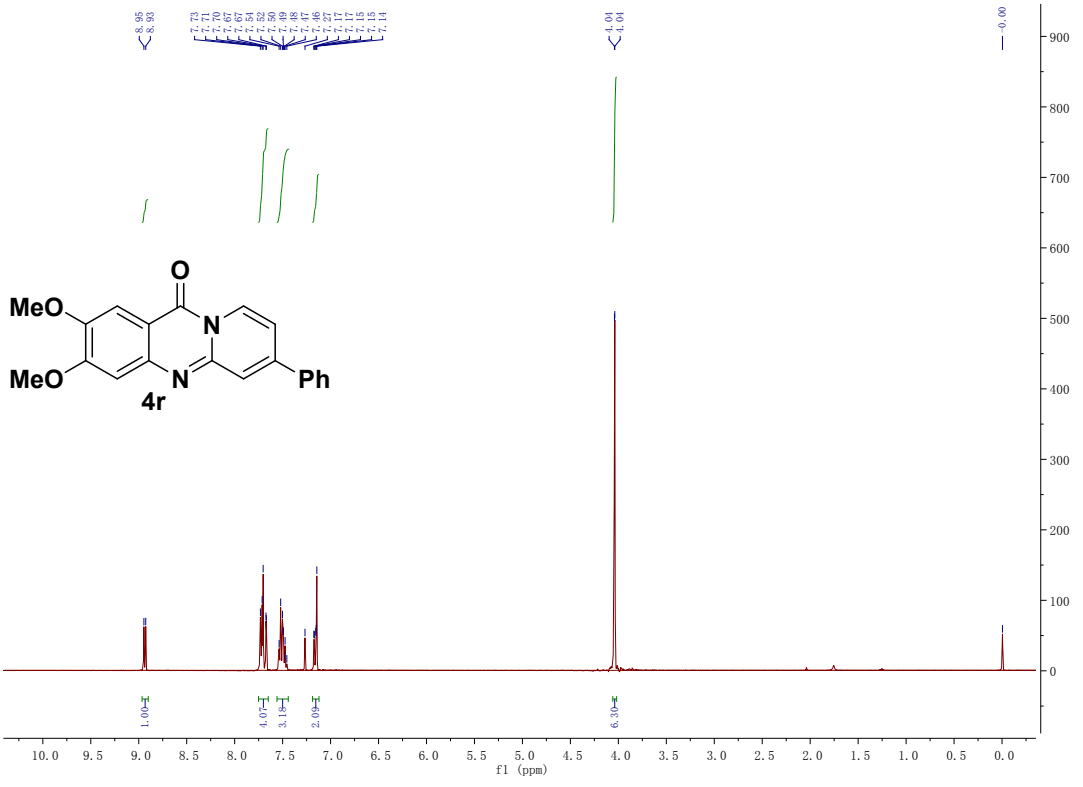

159.38
145.55
145.46
136.48
135.92
133.66
131.91
128.37
127.53
127.31
127.02
126.38
121.96
117.47
112.98
77.32
77.00
76.68
21.39
Me
O
N
N
4o
f1 (ppm)

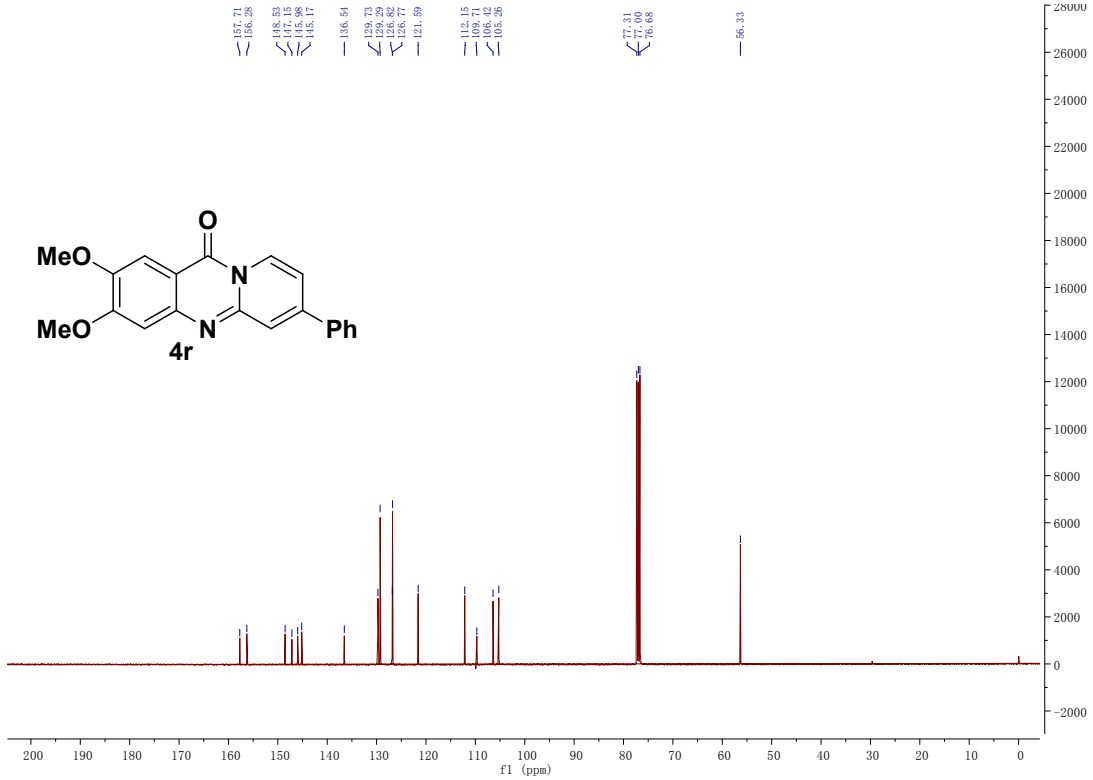

8.61
8.44
8.42
7.82
7.78
7.46
7.45
7.43
7.26
2.88
2.32
1.61
1.25
0.00
O
N
Me
N
4p
Me
1.00
1.02
2.06
1.17
3.28
3.25
f1 (ppm)

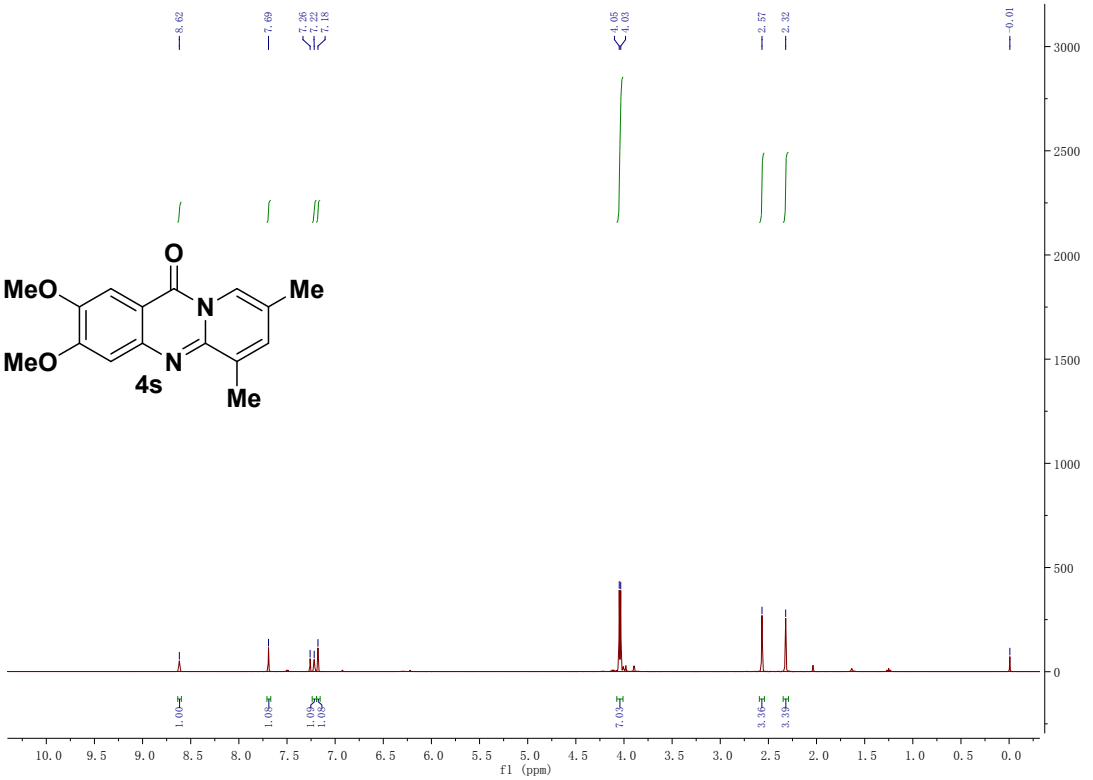

O
N
Me
N
4p
Me
159.29
148.14
146.74
135.67
134.41
133.79
127.34
127.11
124.82
121.72
121.70
116.02
77.32
77.00
76.68
18.41
18.31
f1 (ppm)

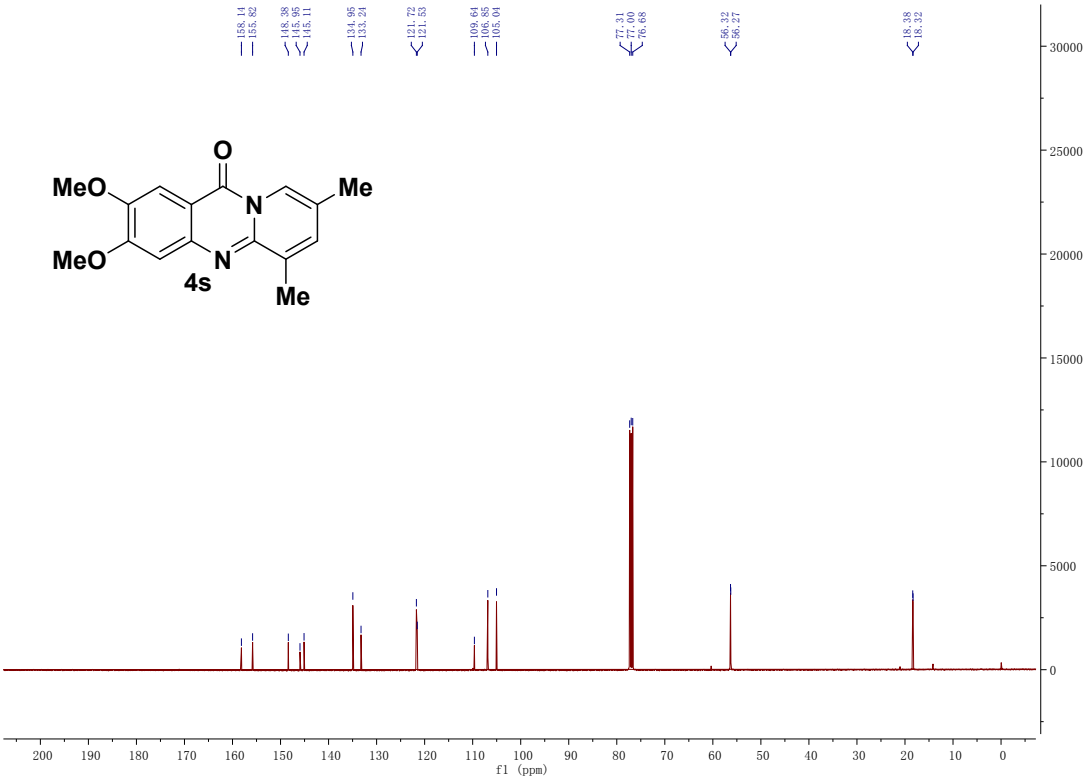

9.11
9.09
8.68
8.66
8.48
8.46
7.92
7.90
7.89
7.88
7.87
7.85
7.76
7.75
7.74
7.73
7.72
7.69
7.67
7.66
7.64
7.54
7.54
7.52
7.51
7.26
7.06
7.04
1.55
-0.00
O
N
N
4q
1.00
1.00
0.99
2.19
3.19
1.25
1.10
f1 (ppm)

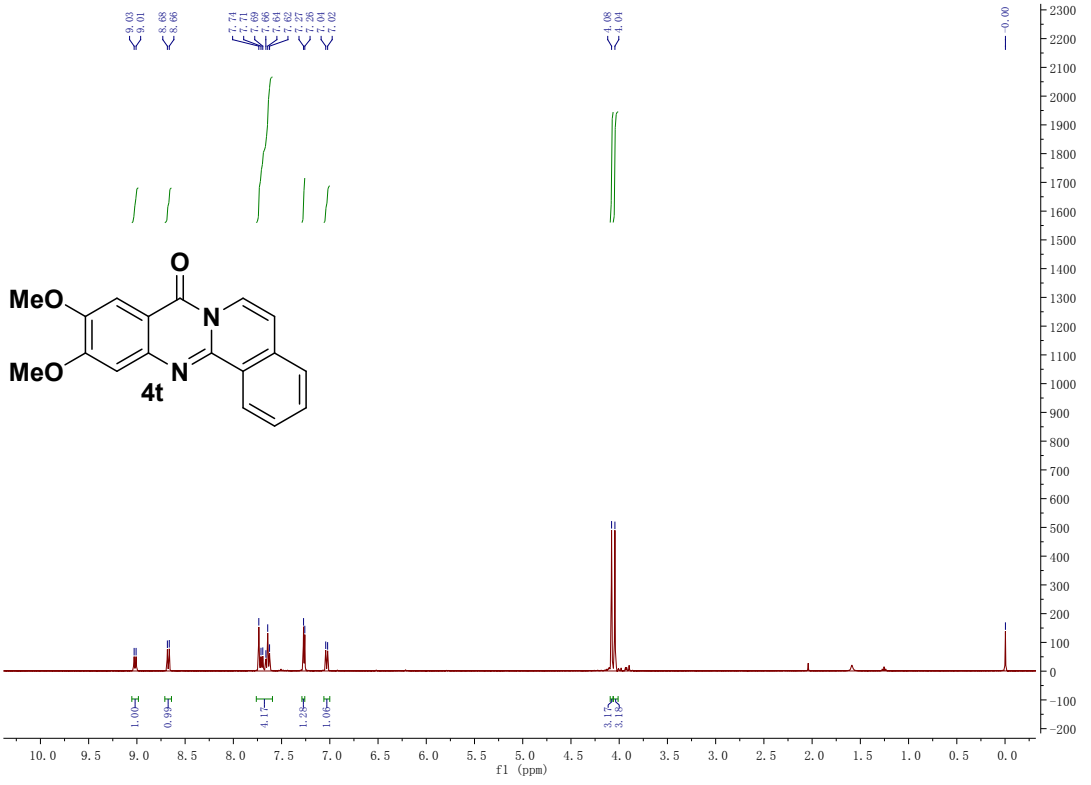

159.44
147.49
134.76
133.65
132.12
128.43
127.49
127.11
127.03
127.18
126.41
125.71
121.98
117.73
113.12
77.32
77.00
76.68
O
N
N
4q
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

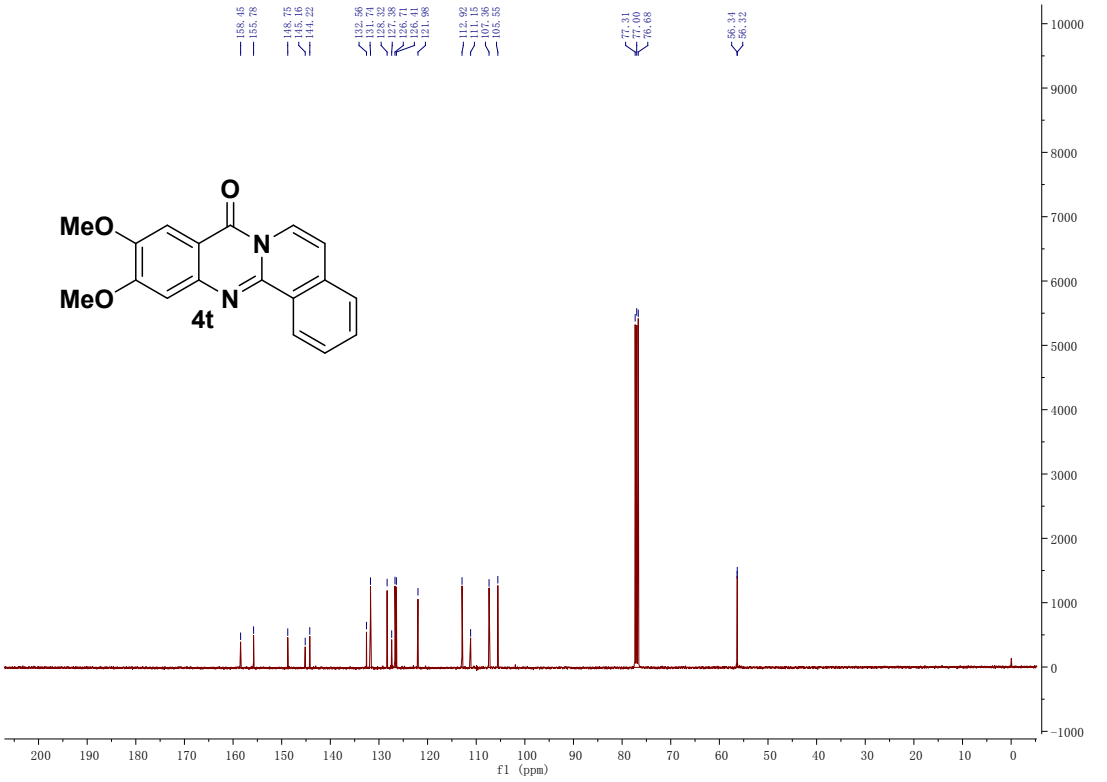

8.95
8.93
7.73
7.71
7.70
7.67
7.67
7.54
7.52
7.50
7.49
7.48
7.47
7.46
7.27
7.17
7.17
7.15
7.15
7.14
4.04
4.01
-0.00
O
MeO
MeO
N
N
Ph
4r
1.00
4.07
3.19
2.09
6.30
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

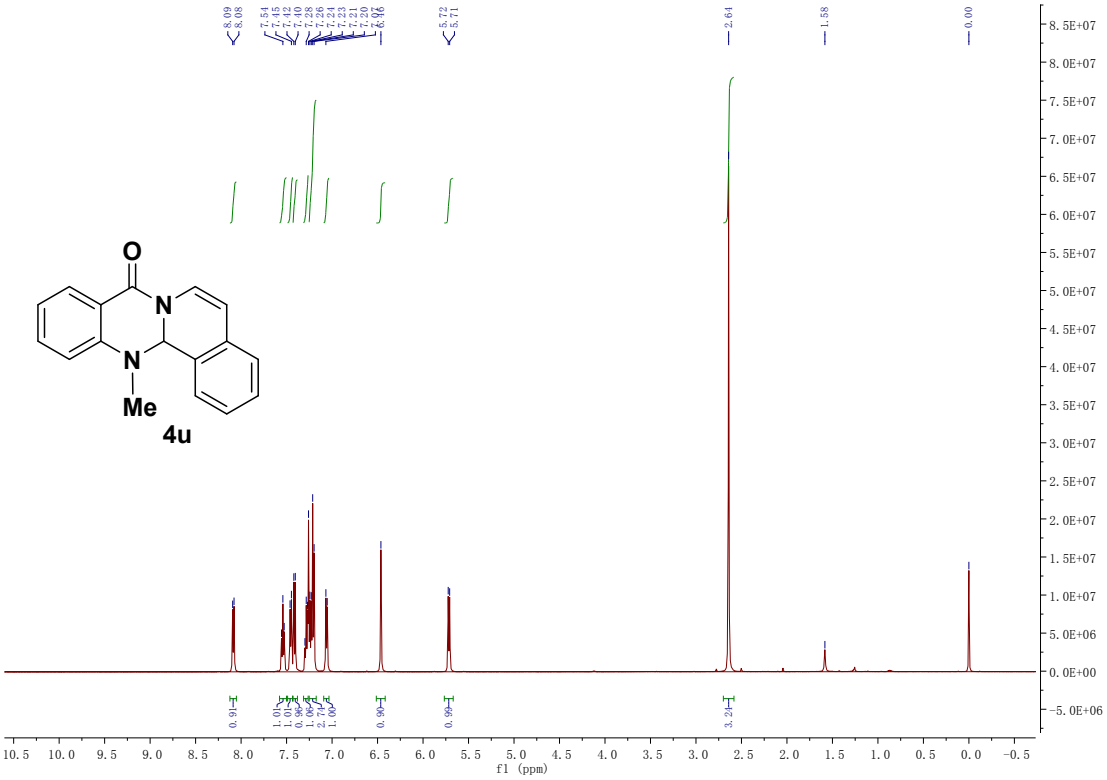

157.71
156.28
148.53
147.15
145.98
145.17
136.54
129.73
129.29
126.82
126.77
121.89
112.15
109.71
106.42
105.26
77.31
77.00
76.68
56.33
MeO
MeO
O
N
N
Ph
4r
f1 (ppm)

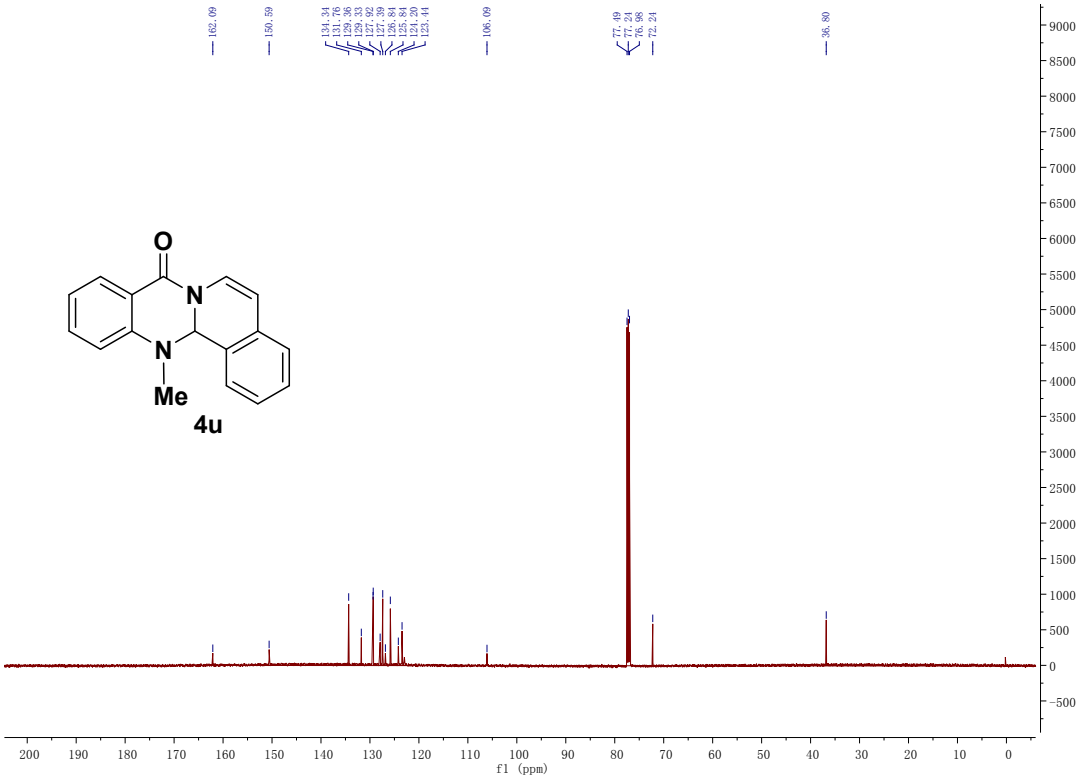

8.62
7.69
7.26
7.22
7.18
4.05
4.03
2.57
2.32
0.01
MeO
MeO
O
N
N
Me
Me
4s
1.00
1.03
1.09
1.09
7.03
3.36
3.39
f1 (ppm)

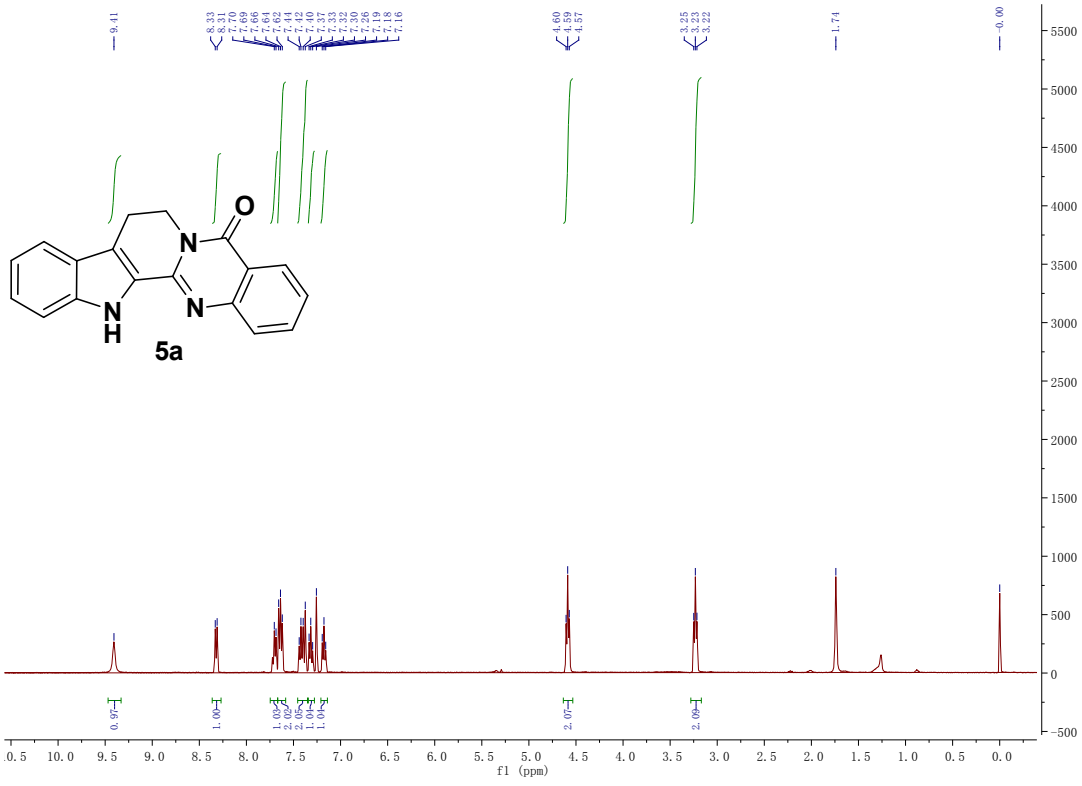

158.14
155.82
148.38
145.95
145.11
134.95
133.24
121.72
121.53
109.64
106.85
105.04
77.31
77.00
76.68
56.32
56.27
18.38
18.32
MeO
MeO
N
N
Me
Me
O
4s
f1 (ppm)

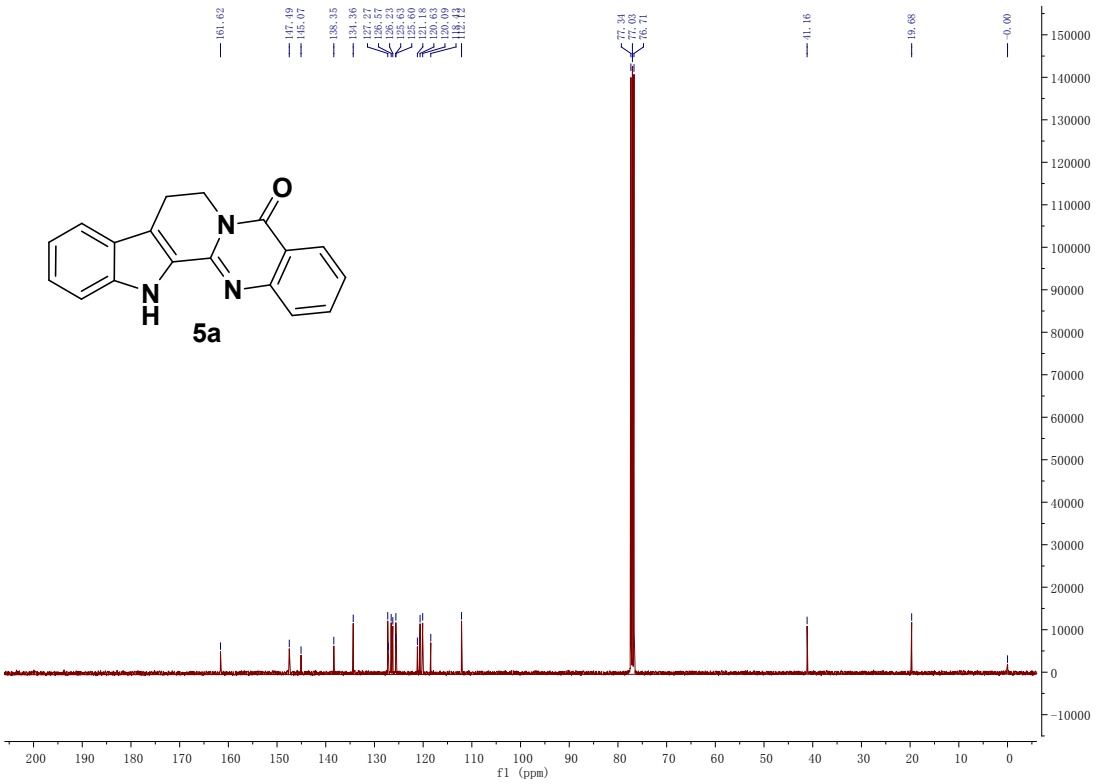

9.03
9.01
8.68
8.66
7.74
7.71
7.69
7.68
7.66
7.64
7.62
7.27
7.26
7.04
7.02
4.08
4.04
-0.00
MeO
MeO
N
N
O
4t
1.00
0.99
4.17
1.28
1.06
3.17
3.13
f1 (ppm)

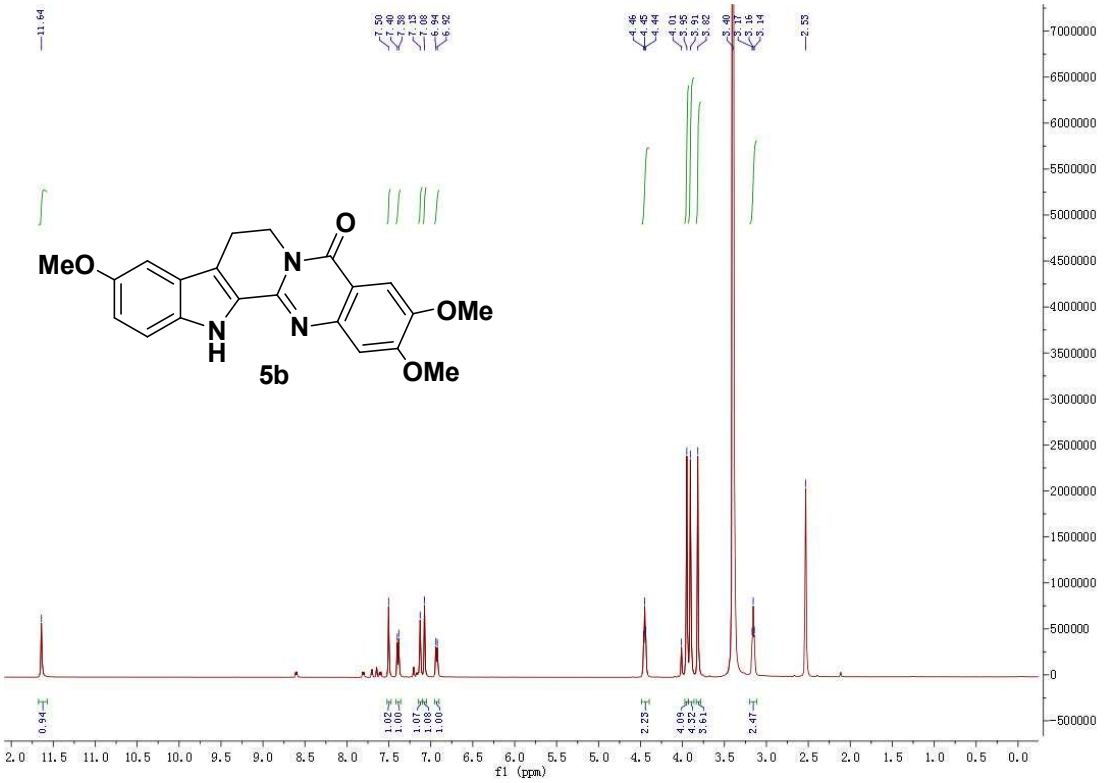

158.45
155.78
148.75
145.16
144.22
132.66
131.74
129.32
128.36
126.71
126.41
121.98
112.92
111.15
107.36
105.55
77.31
77.00
76.68
56.34
56.32
MeO
MeO
O
N
N
4t
f1 (ppm)

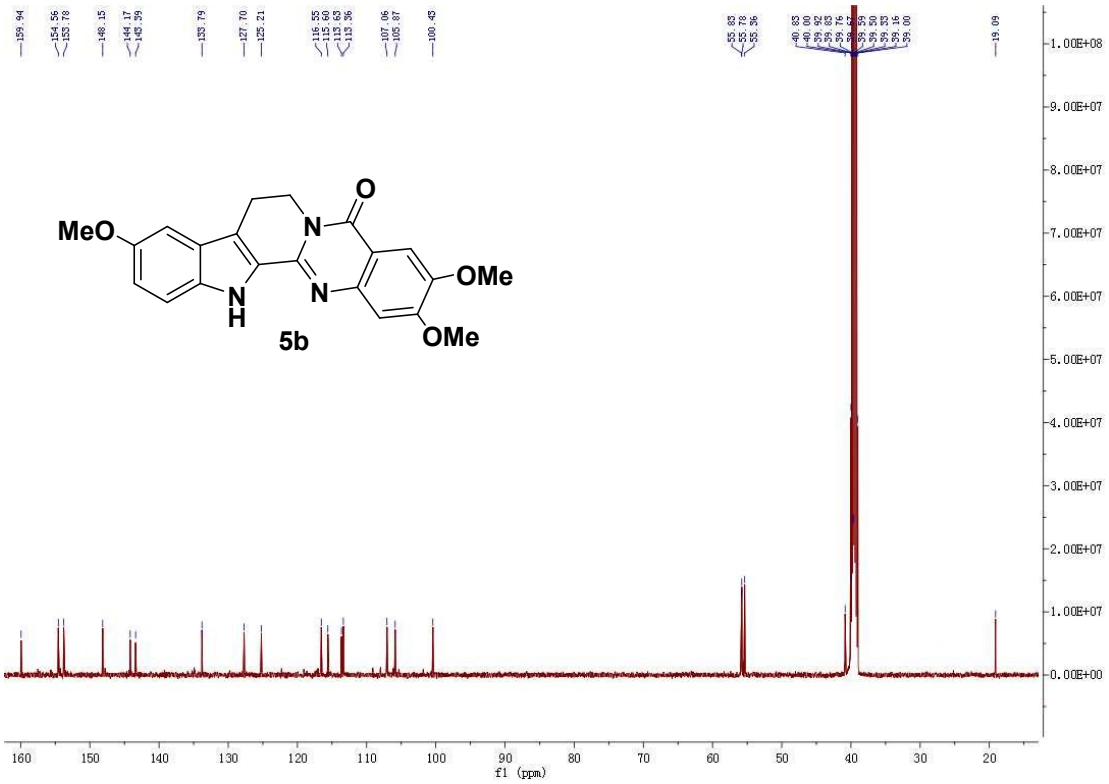

8.09
8.08
7.54
7.45
7.42
7.40
7.28
7.26
7.24
7.23
7.21
7.20
6.48
6.46
5.72
5.71
2.64
1.58
0.00
O
N
N
Me
4u
0.91
1.01
1.01
0.96
2.74
1.00
0.90
0.99
3.24
f1 (ppm)

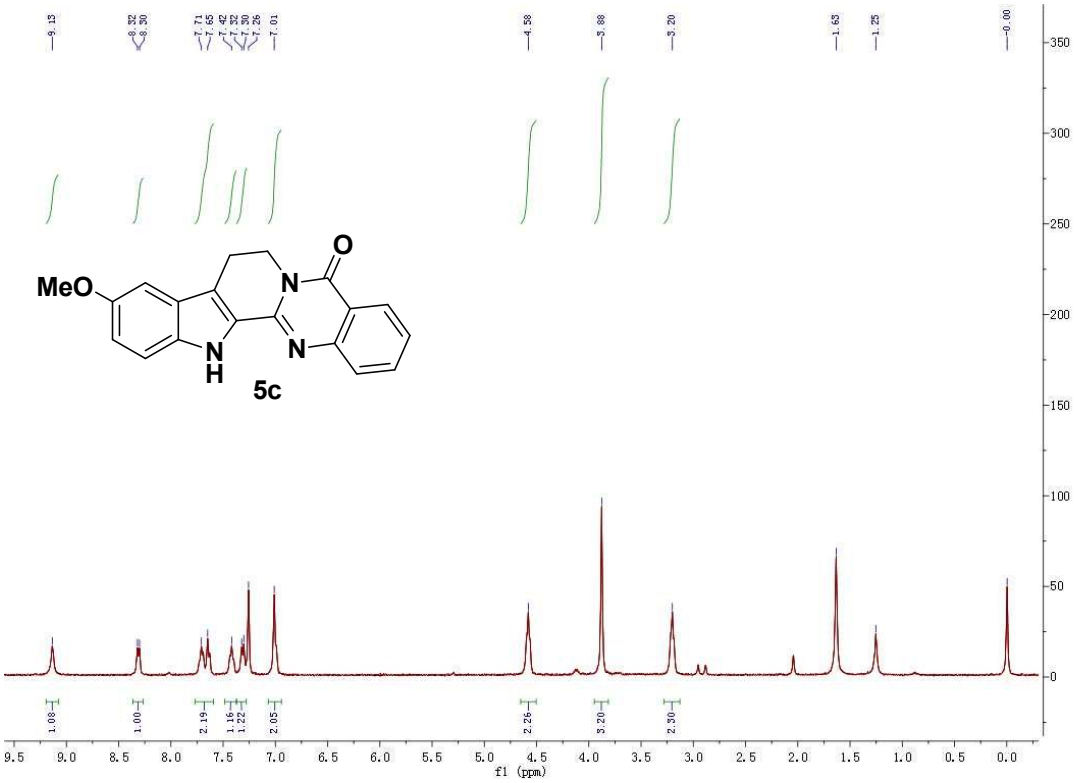

162.09
150.59
131.34
131.26
129.36
129.33
127.92
127.39
126.84
125.84
124.20
123.44
106.09
77.49
77.24
76.98
72.24
36.80
O
N
N
Me
4u
f1 (ppm)

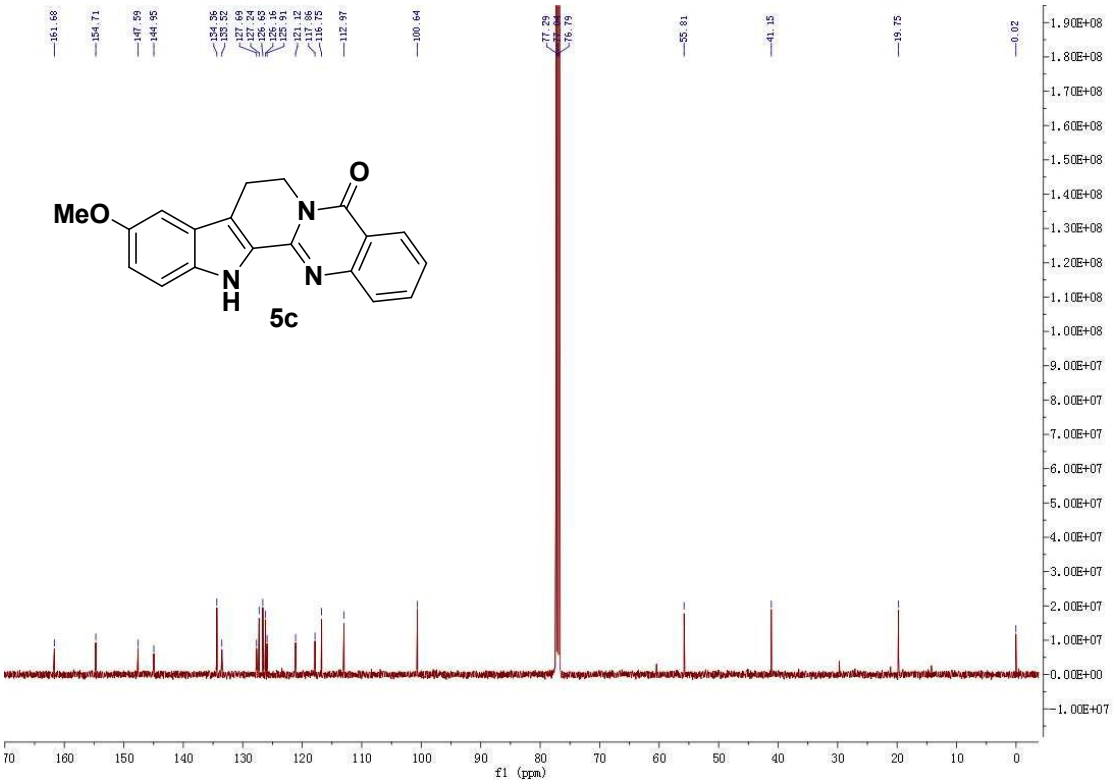

9.41
8.33
8.31
7.70
7.69
7.66
7.64
7.62
7.44
7.42
7.40
7.37
7.33
7.32
7.30
7.26
7.19
7.18
7.16
4.60
4.59
4.57
3.25
3.23
3.22
1.74
0.00
O
N
N
N
H
5a
0.97
1.00
1.03
2.02
2.05
1.04
1.04
2.07
2.09
f1 (ppm)

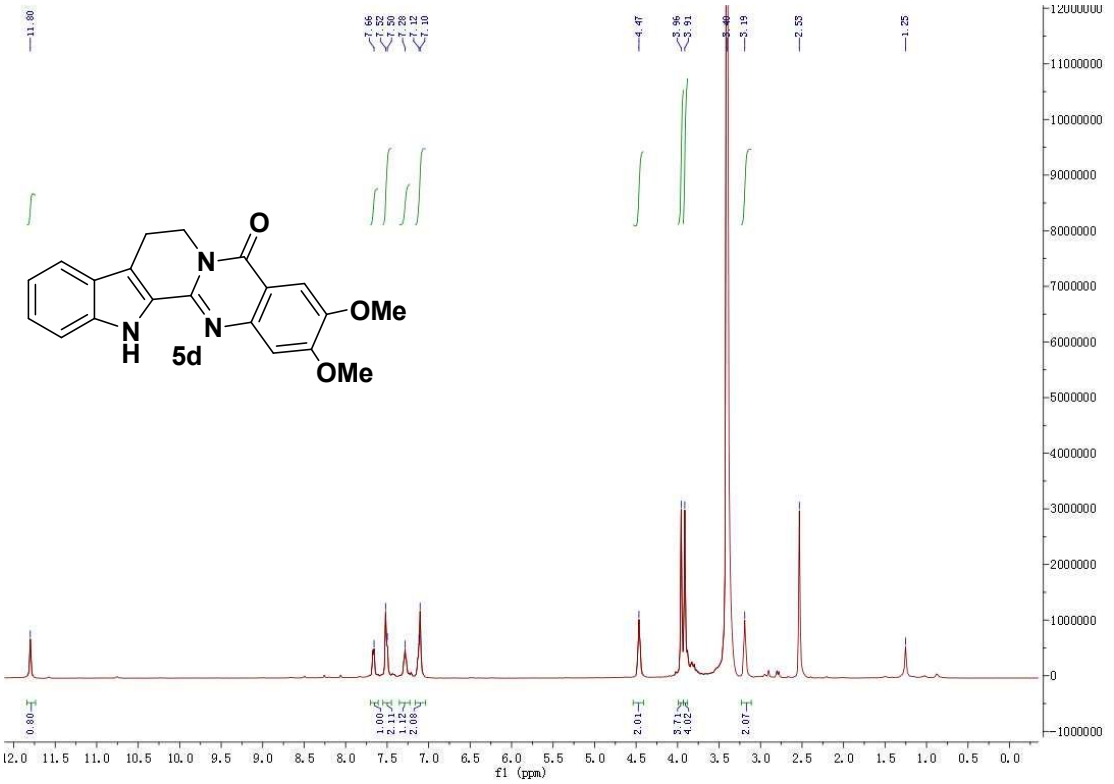

161.62
147.49
145.07
138.35
134.36
127.27
126.57
126.23
125.63
125.60
121.18
120.65
120.09
118.43
112.72
77.34
77.03
76.71
41.16
19.68
-0.00
O
N
N
N
H
5a
f1 (ppm)

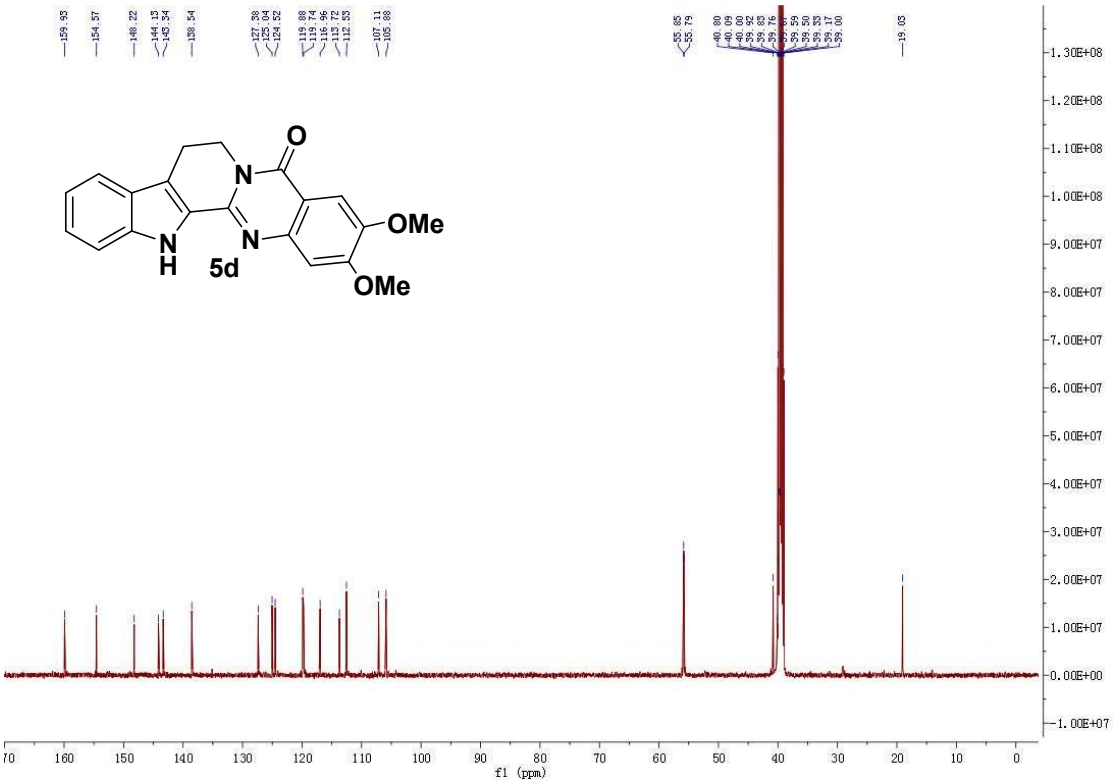

11.64
7.50
7.40
7.38
7.13
7.08
6.94
6.92
4.46
4.45
4.44
4.01
3.95
3.91
3.82
3.40
3.17
3.16
3.14
2.53
MeO
O
N
N
N
H
OMe
OMe
5b
0.84
1.02
1.00
1.07
1.08
1.00
2.23
4.09
4.32
3.61
2.47
f1 (ppm)

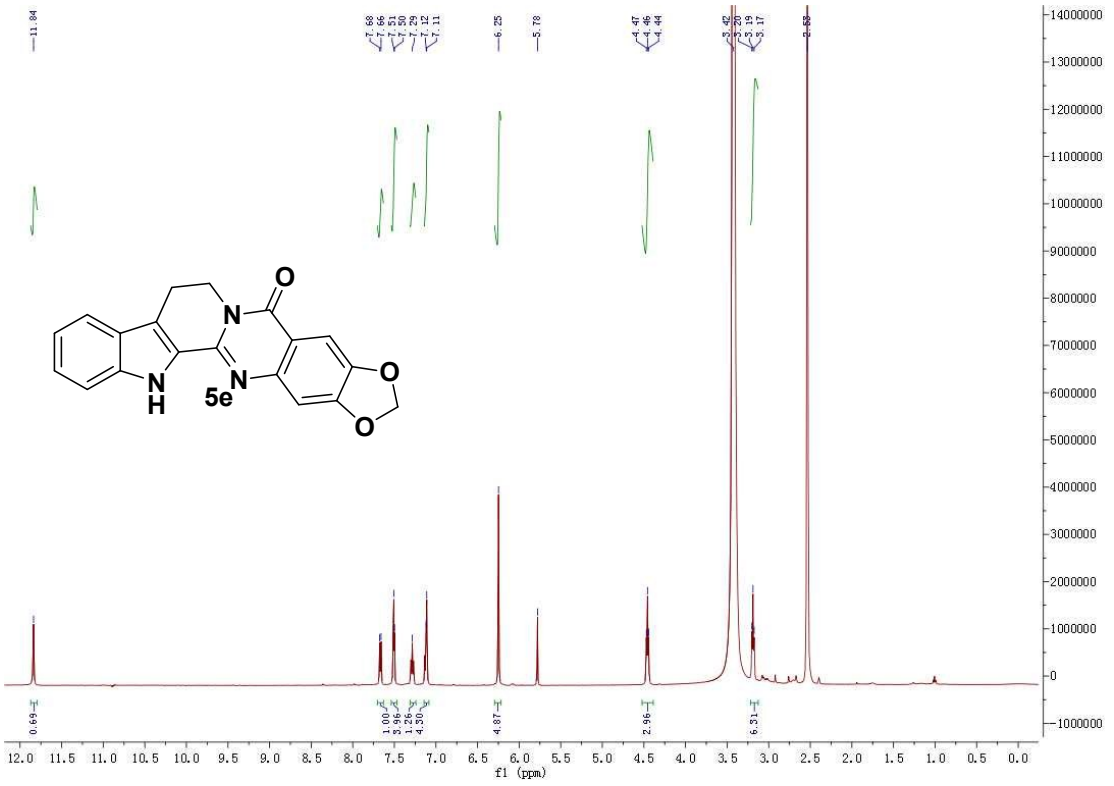

MeO
O
N
N
H
N
OMe
OMe
5b
f1 (ppm)

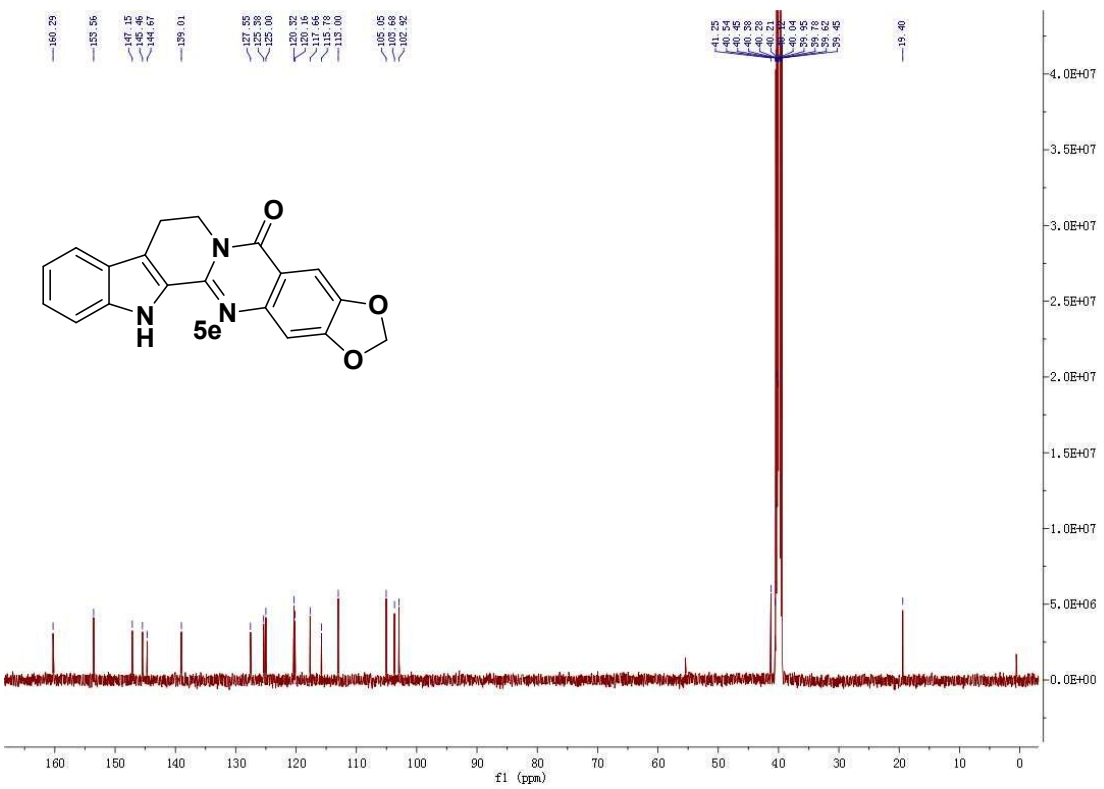

MeO
O
N
N
H
N
5c
f1 (ppm)

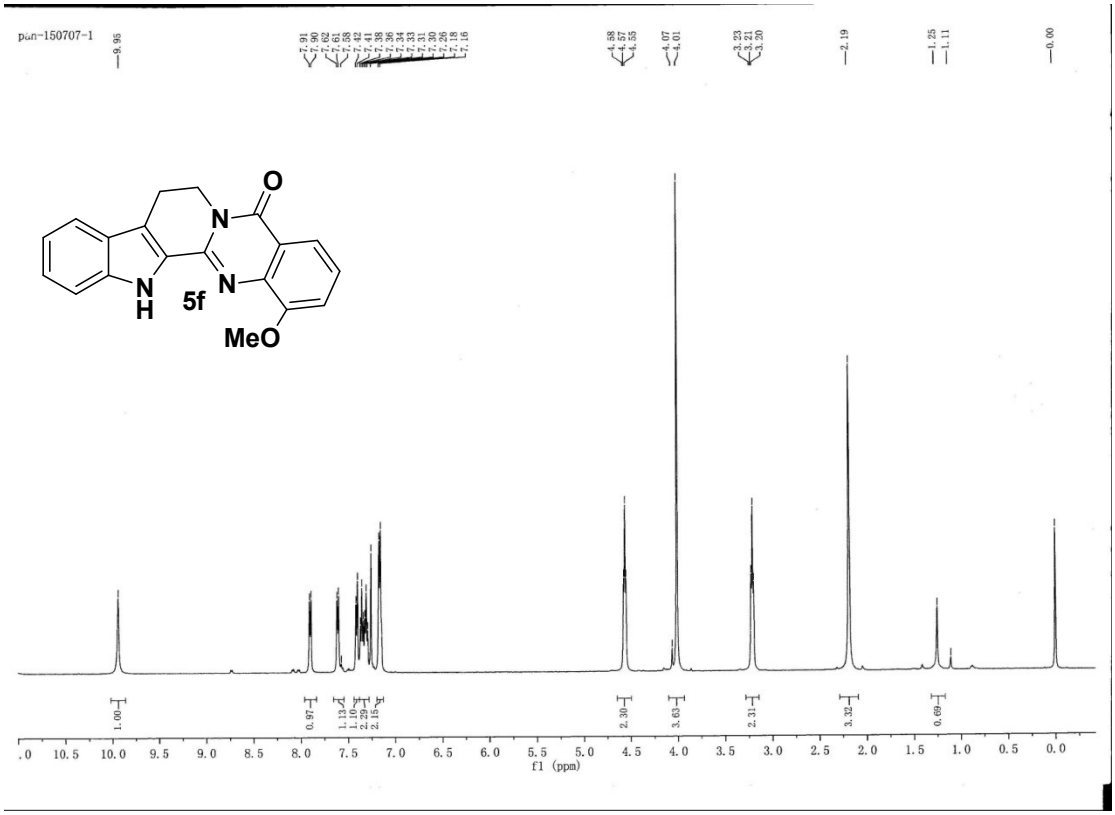

MeO
O
N
N
H
5c
f1 (ppm)

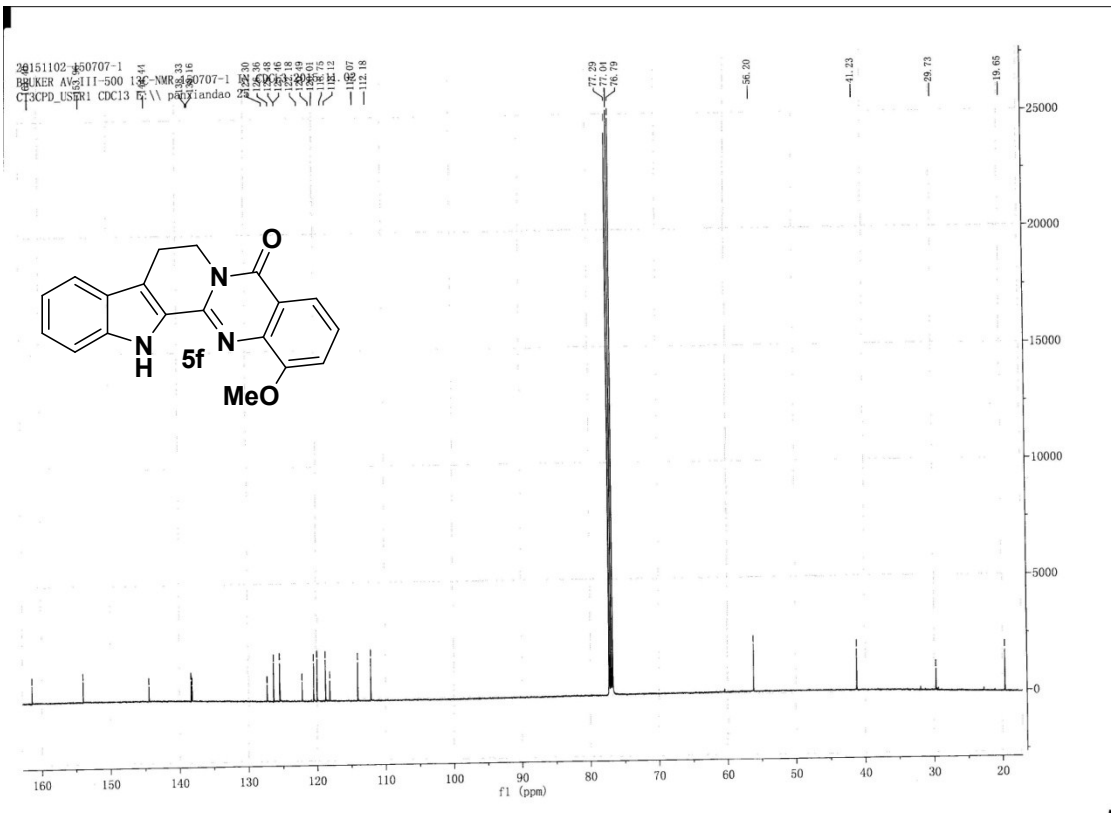

OMe
OMe
O
N
N
H
5d
f1 (ppm)

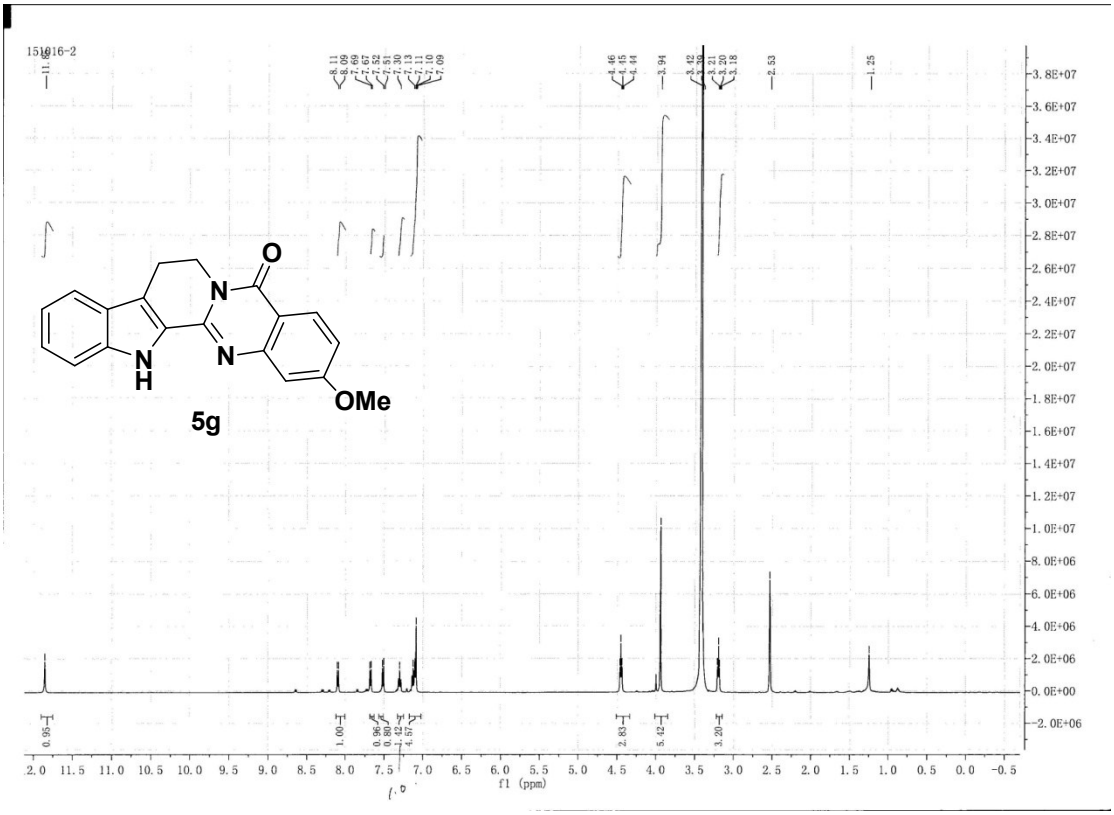

O
N
OMe
N
H
5d
OMe
f1 (ppm)

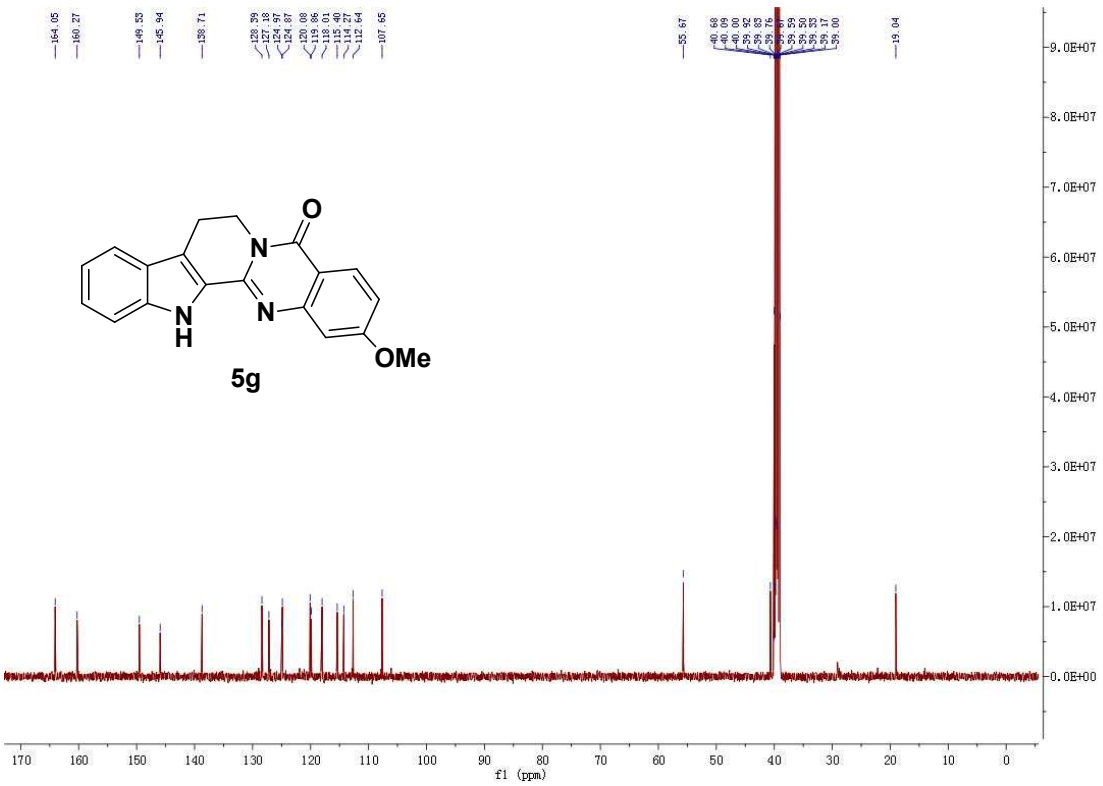

O
N
O
N
H
5e
O
f1 (ppm)

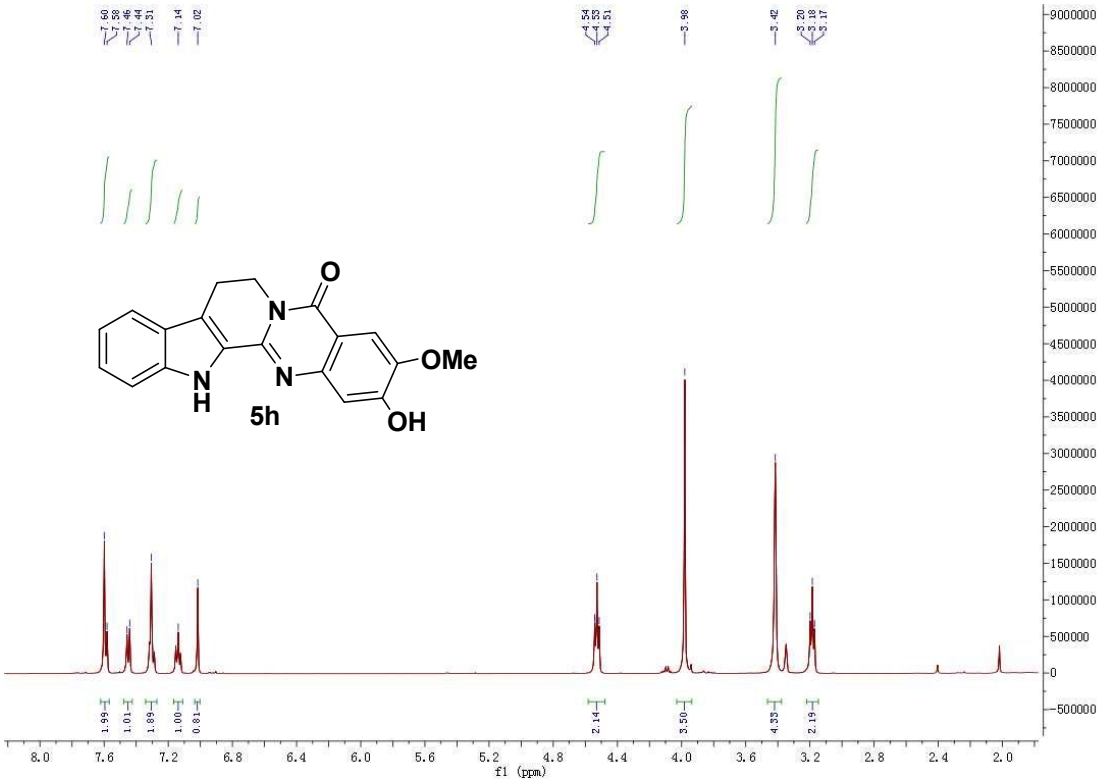

160.29
153.56
147.15
145.46
144.67
139.01
127.55
125.38
125.00
120.32
120.16
117.66
115.78
115.00
105.05
103.69
102.92
41.25
40.54
40.45
40.38
40.29
40.21
40.04
39.95
39.78
39.62
39.45
19.40
O
N
N
H
5e
N
O
O
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

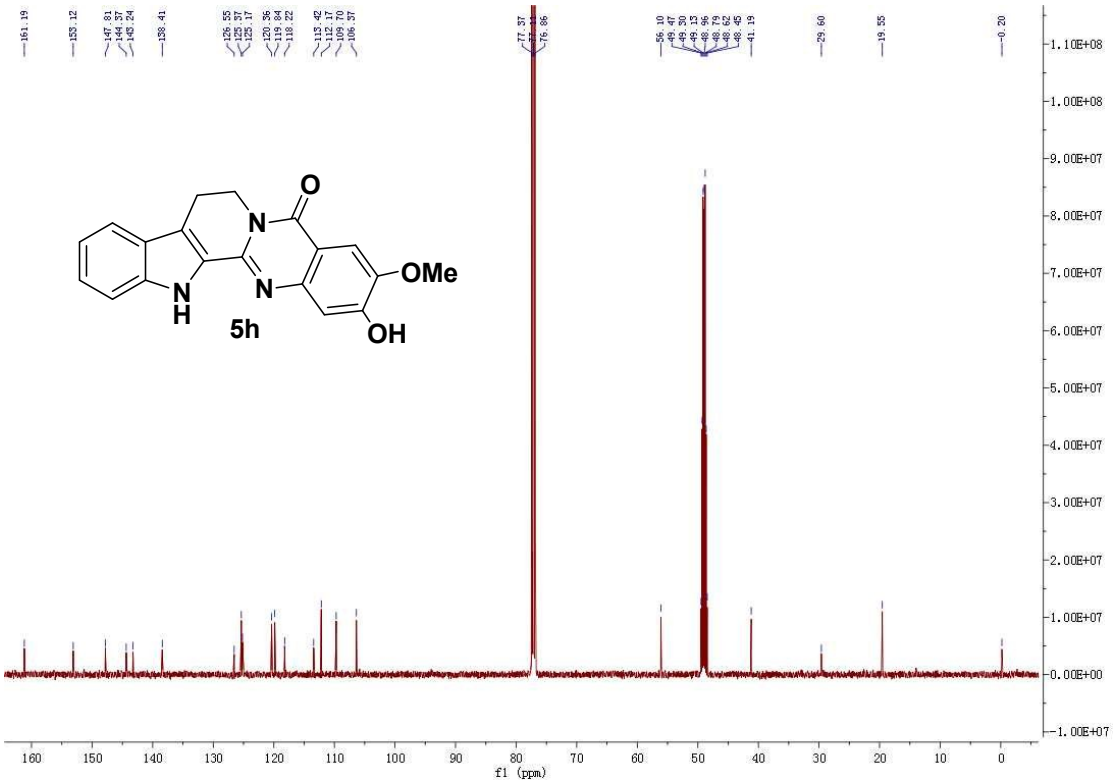

pan-150707-1
9.95
7.91
7.90
7.62
7.61
7.58
7.42
7.41
7.38
7.36
7.34
7.33
7.31
7.30
7.26
7.18
7.16
4.68
4.67
4.55
4.07
4.01
3.23
3.21
3.20
2.19
1.25
1.11
0.00
O
N
N
H
5f
N
MeO
1.00
0.97
1.13
1.10
1.29
2.15
2.30
3.63
2.31
3.32
0.69
.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

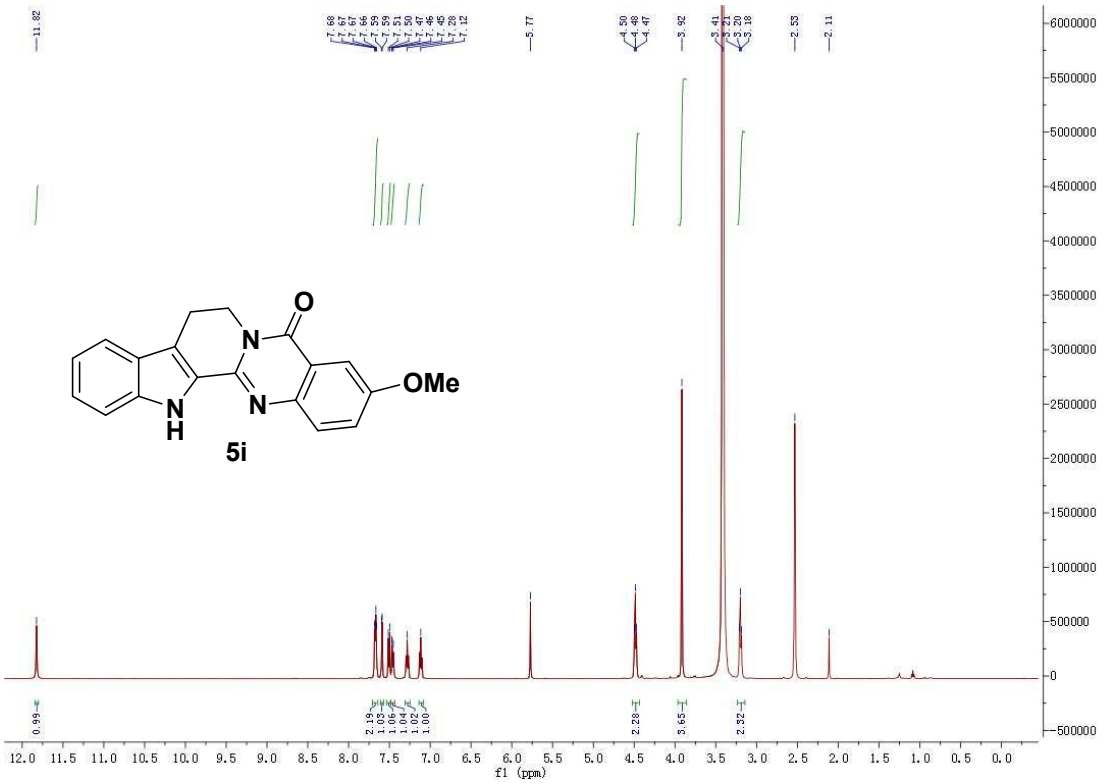

5f
MeO

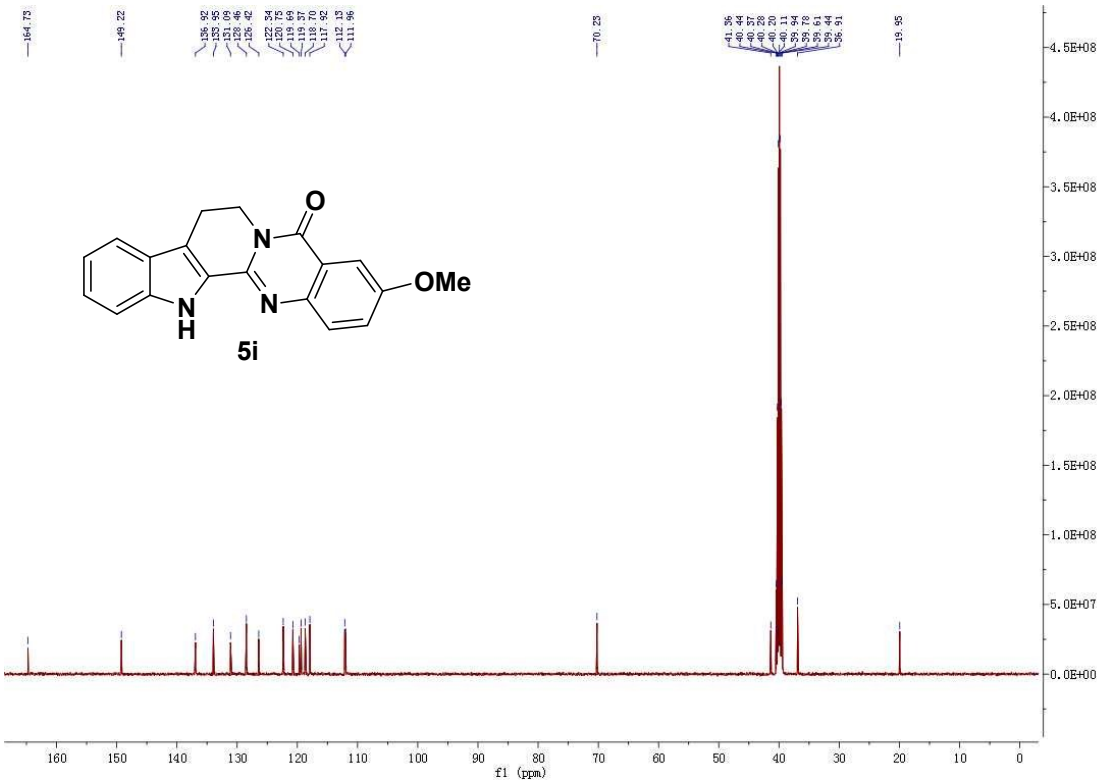

5g
OMe

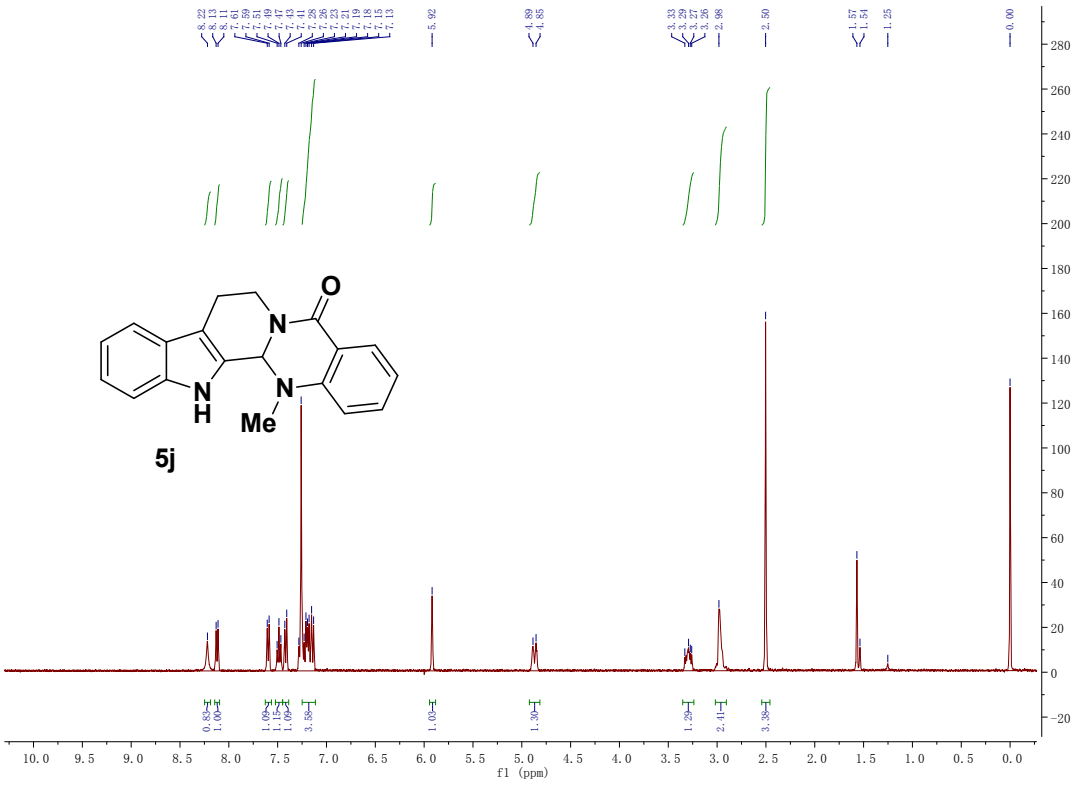

164.05
160.27
149.53
145.94
138.71
128.39
127.18
124.97
124.87
120.08
119.86
118.01
115.40
114.27
112.64
107.65
55.67
40.66
40.09
40.00
39.92
39.85
39.76
39.67
39.59
39.50
39.33
39.17
39.00
19.04
O
N
N
N
H
OMe
5g
9.0E+07
8.0E+07
7.0E+07
6.0E+07
5.0E+07
4.0E+07
3.0E+07
2.0E+07
1.0E+07
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

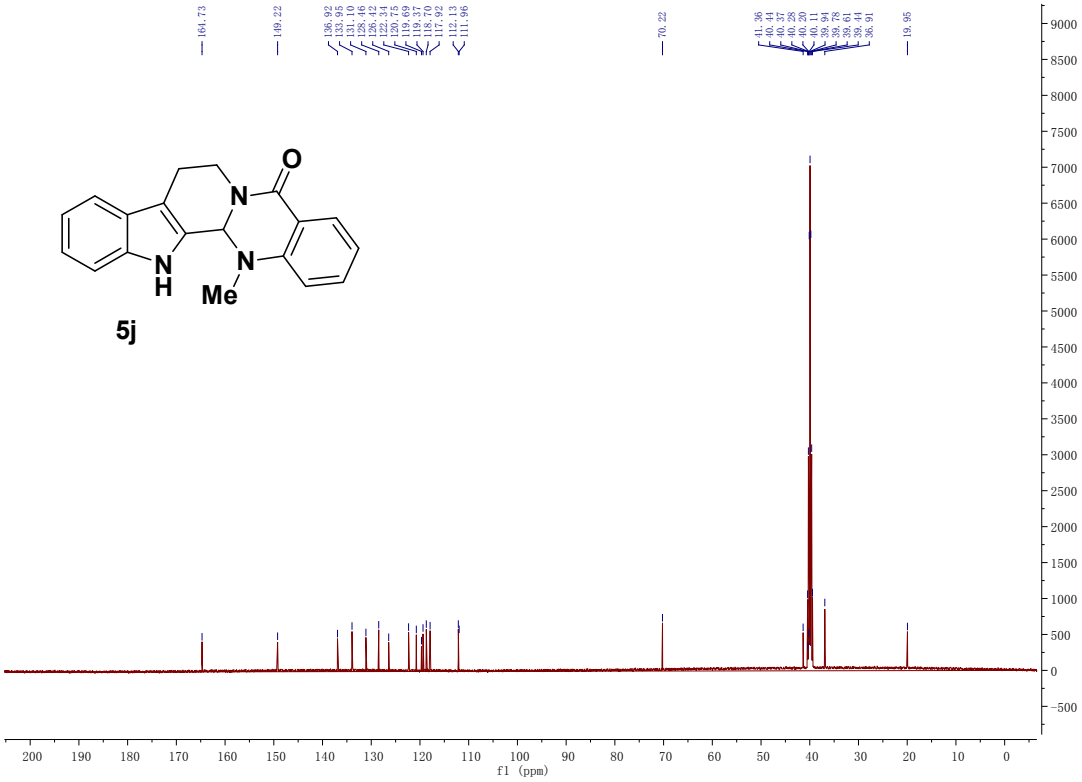

7.60
7.58
7.46
7.44
7.31
7.14
7.02
4.54
4.53
4.51
3.98
3.42
3.20
3.19
3.17
O
N
N
N
H
OMe
OH
5h
9000000
8500000
8000000
7500000
7000000
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
1.99
1.01
1.89
1.00
0.81
2.14
3.50
4.35
2.19
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
f1 (ppm)


O
N
OMe
N
H
OH
5h
fl (ppm)

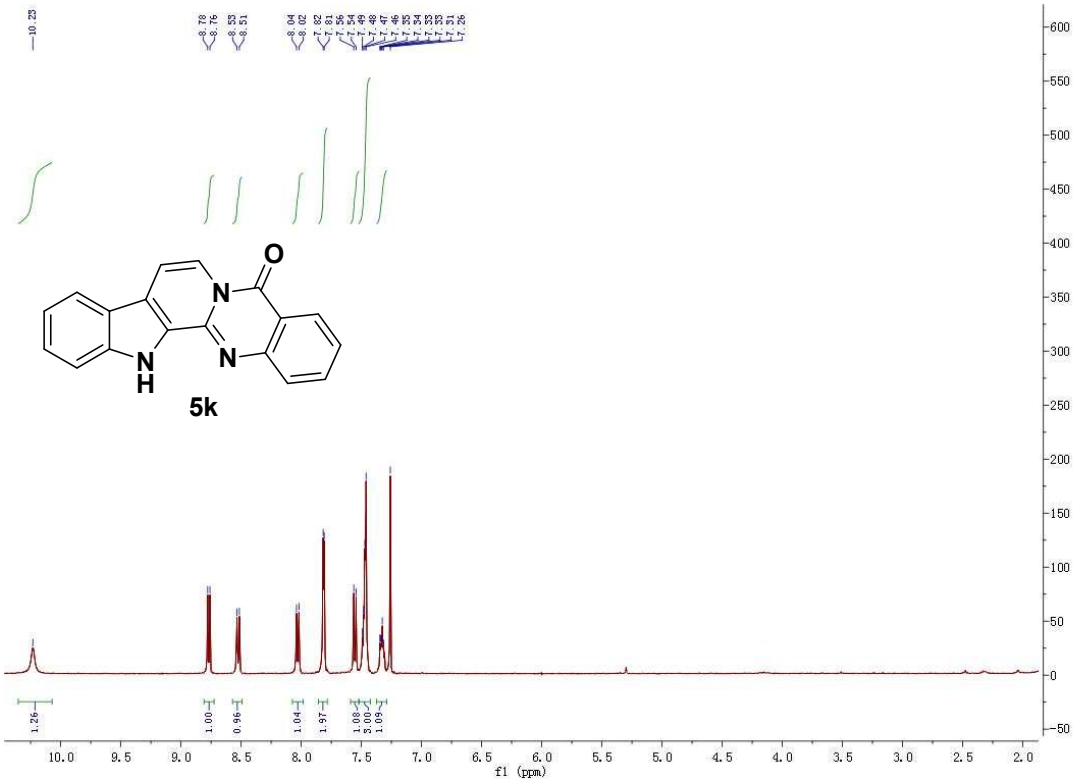

O
N
OMe
N
H
5i
fl (ppm)


164.73
149.22
136.92
133.95
131.69
131.46
126.42
122.34
120.75
119.69
119.57
118.70
117.92
112.15
111.96
70.23
41.95
40.44
40.37
40.28
40.20
40.11
39.94
39.78
39.61
39.44
39.27
39.11
38.94
38.91
19.95
O
N
N
N
H
OMe
5i
f1 (ppm)

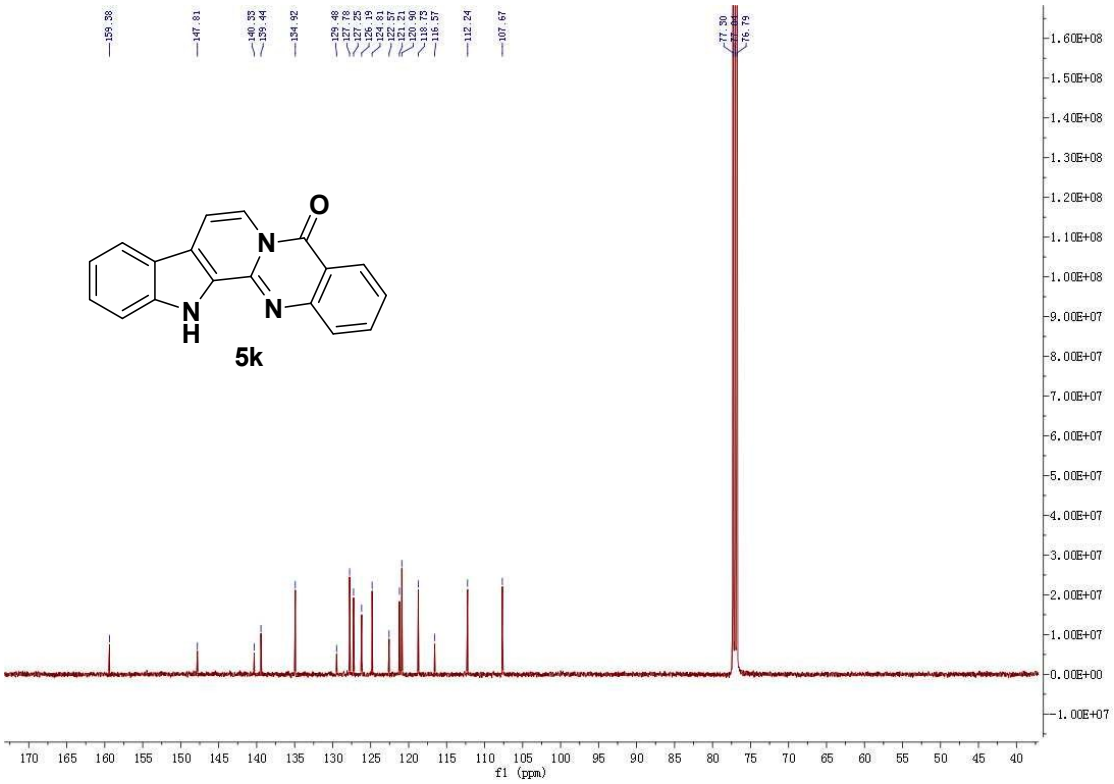

8.22
8.13
8.11
7.61
7.59
7.51
7.49
7.47
7.43
7.41
7.28
7.25
7.23
7.21
7.19
7.18
7.15
7.13
5.92
4.89
4.85
3.33
3.29
3.27
3.26
2.98
2.50
1.57
1.54
1.25
0.00
O
N
N
N
H
Me
5j
f1 (ppm)

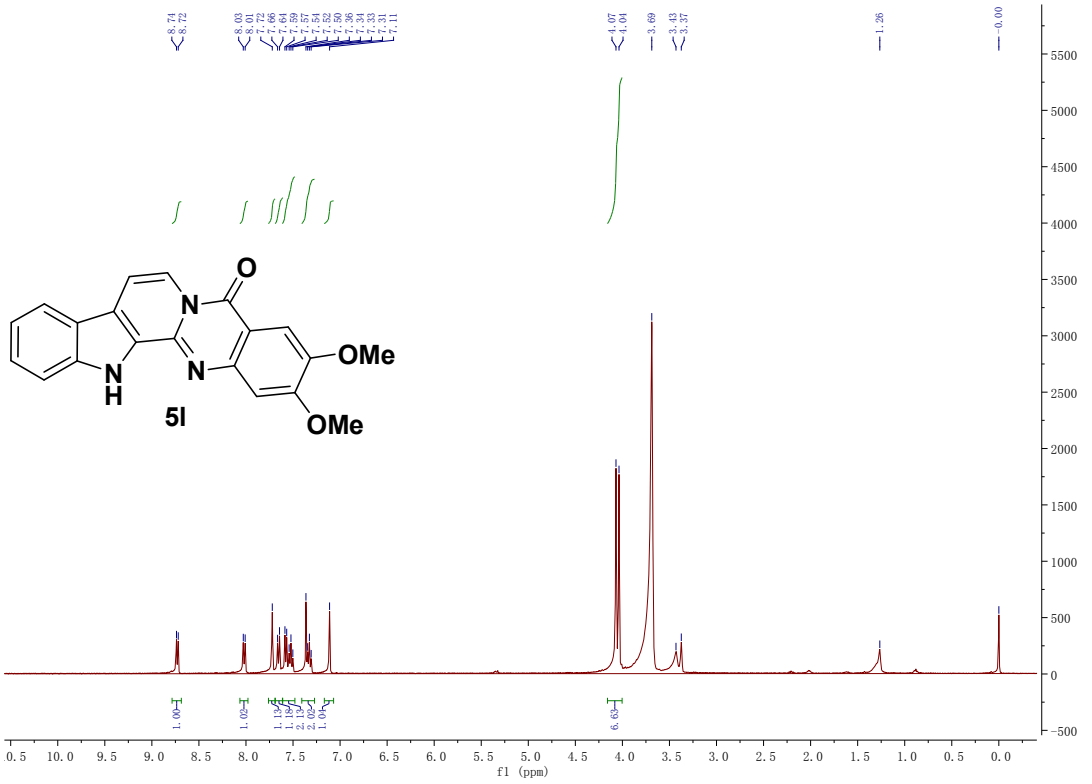

164.73
149.22
136.92
133.95
131.10
128.46
126.42
122.34
120.75
119.69
119.37
118.70
117.92
112.13
111.96
70.22
41.36
40.44
40.37
40.28
40.20
40.11
39.94
39.78
39.61
39.44
36.91
19.95
O
N
N
N
H
Me
f1 (ppm)

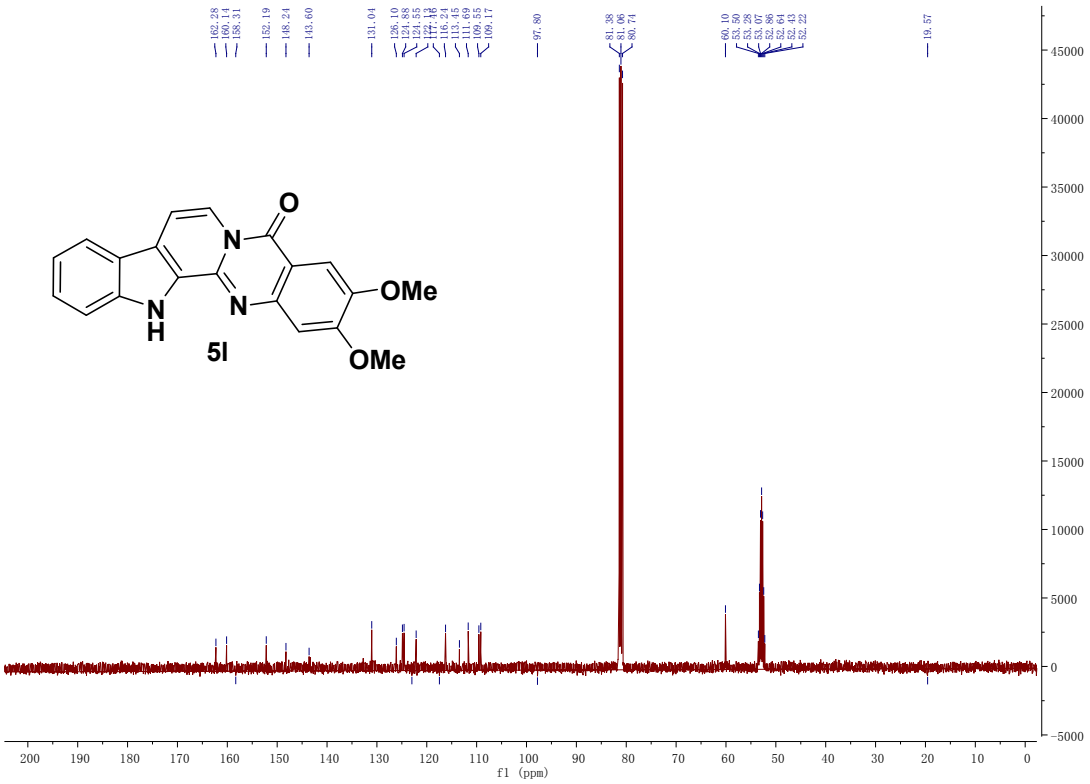
5j

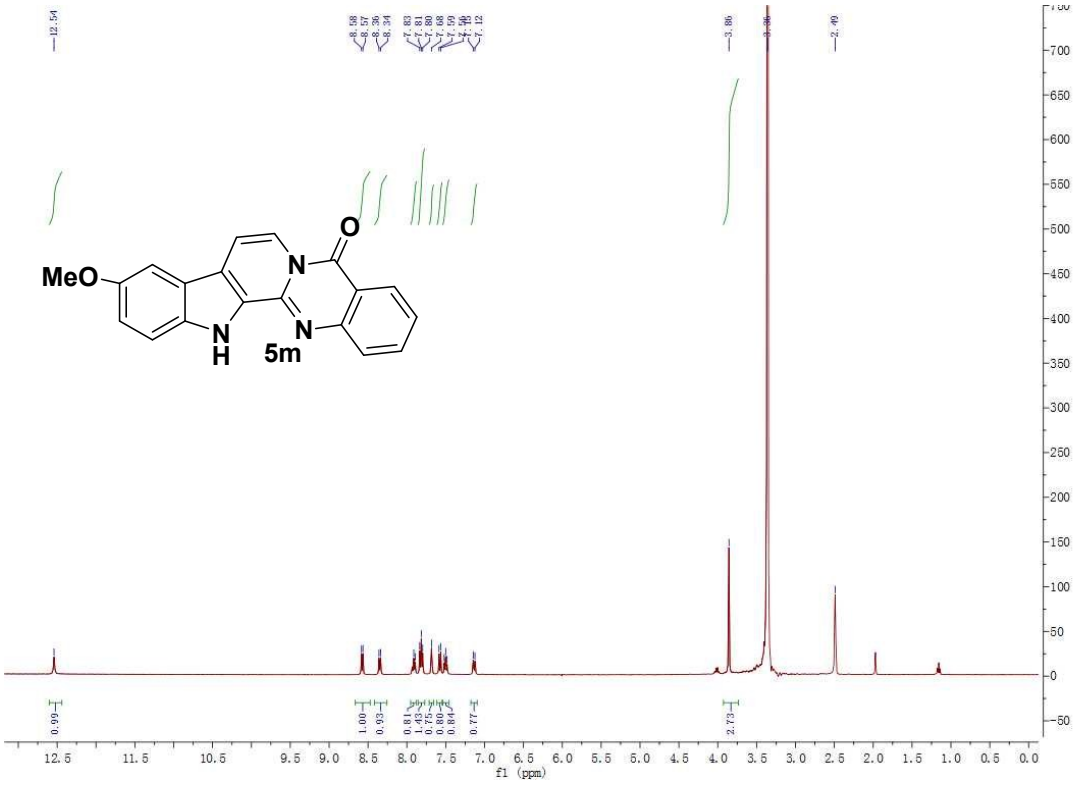

10.23
8.78
8.76
8.53
8.51
8.04
8.02
7.82
7.81
7.56
7.54
7.49
7.48
7.47
7.46
7.35
7.34
7.33
7.33
7.31
7.31
7.26
O
N
N
N
H
1.26
1.00
0.96
1.04
1.97
1.08
3.00
1.09
f1 (ppm)

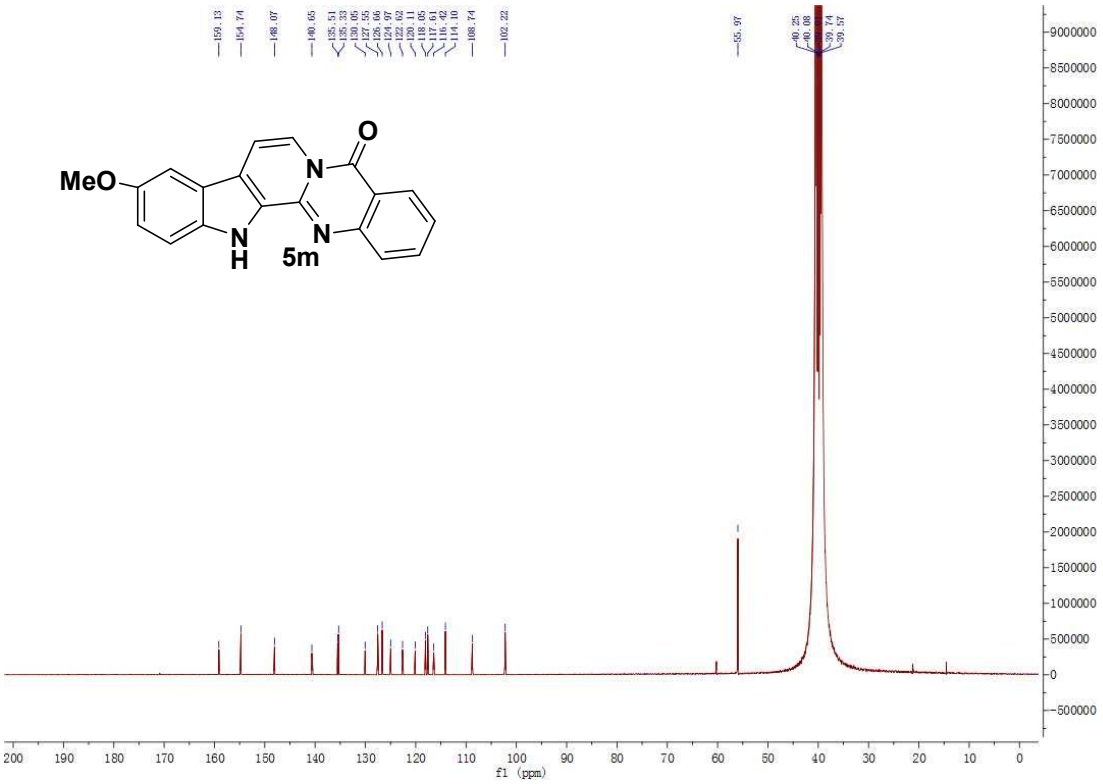
5k

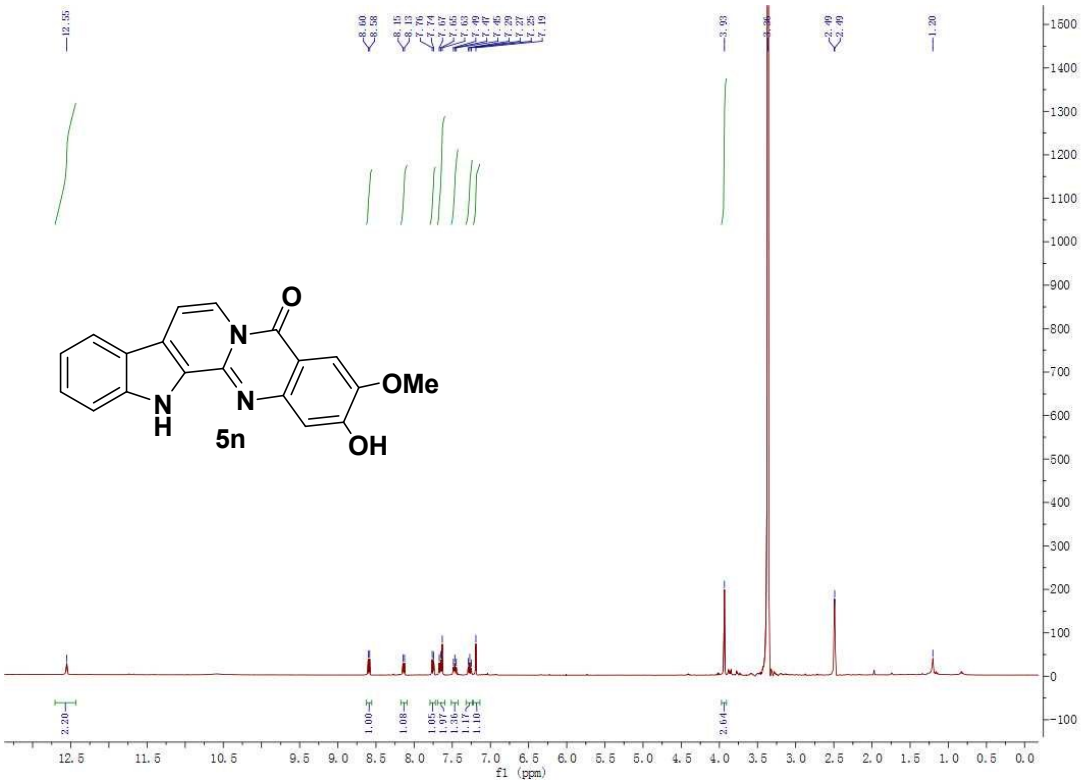

159.38
147.81
140.33
139.44
134.92
129.48
127.78
127.25
126.19
125.81
122.57
121.21
120.90
118.73
116.57
112.24
107.67
77.30
76.79
O
N
N
N
H
5k
fl (ppm)

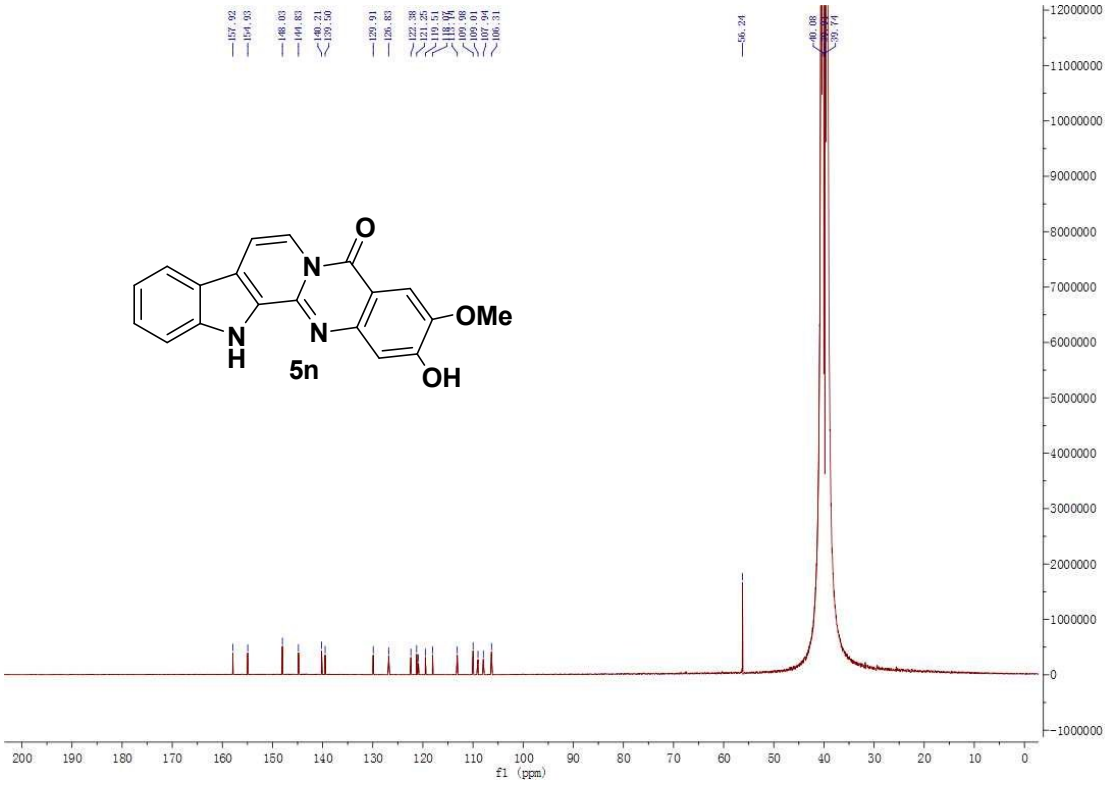

8.71
8.72
8.03
8.01
7.72
7.66
7.64
7.59
7.57
7.54
7.52
7.50
7.36
7.34
7.33
7.31
7.11
4.07
4.04
3.69
3.43
3.37
1.26
0.00
O
N
N
N
H
OMe
OMe
5l
fl (ppm)

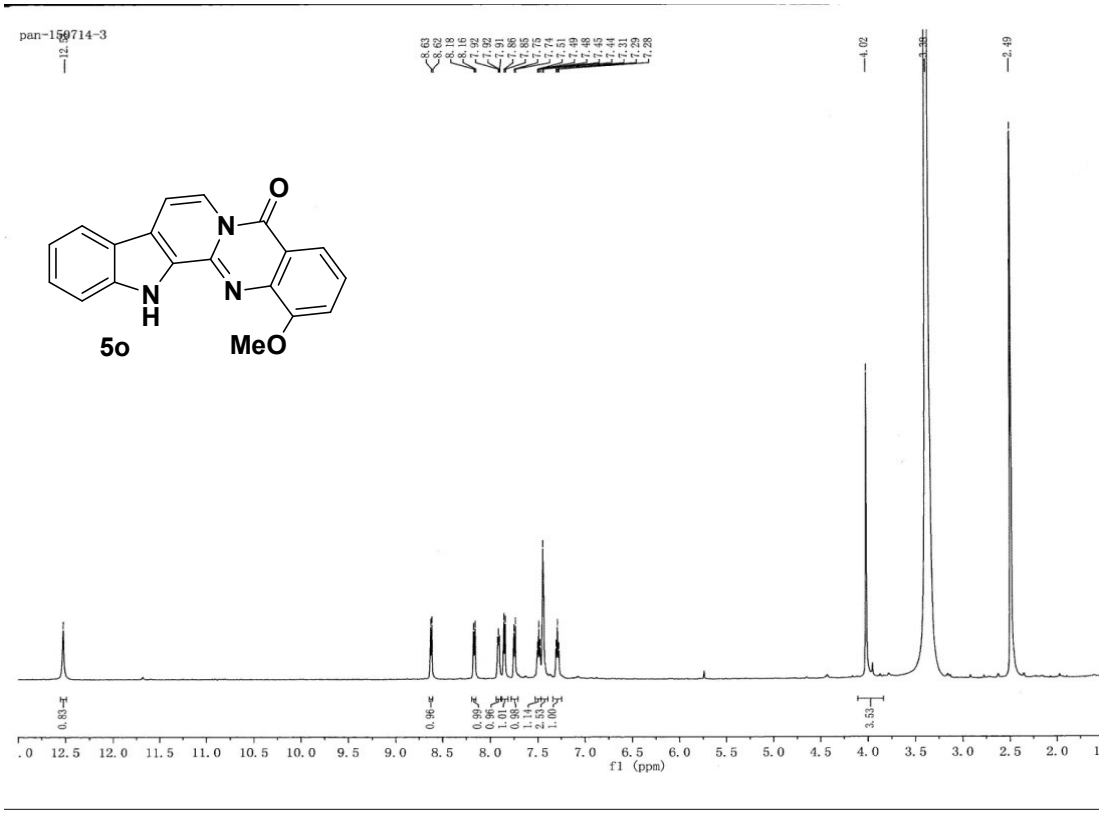

162.28
160.14
138.31
152.19
148.24
143.60
131.04
126.10
124.88
124.55
97.80
81.38
81.06
80.71
60.10
53.50
53.28
53.07
52.86
52.64
52.43
52.22
19.57
OMe
OMe
5l
f1 (ppm)

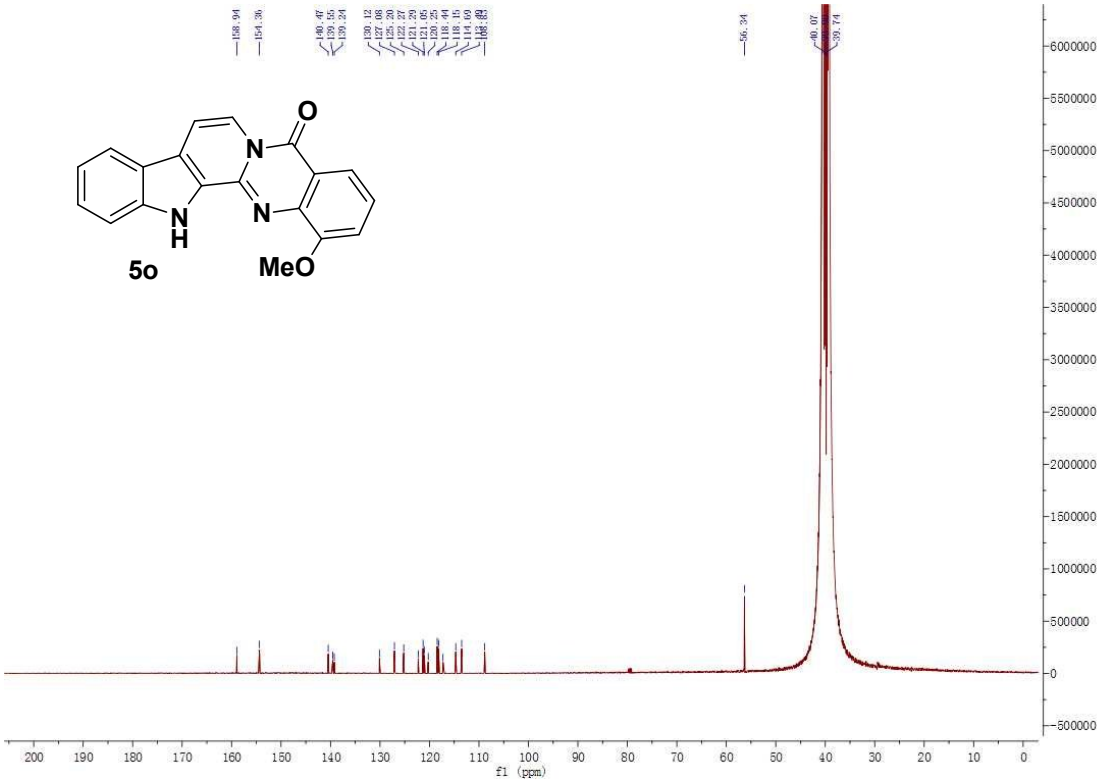

12.54
8.58
8.57
8.36
8.34
7.83
7.81
7.80
7.68
7.66
7.12
3.86
2.49
MeO
5m
0.99
1.00
0.93
0.81
1.43
0.75
0.80
0.64
0.77
2.73
f1 (ppm)

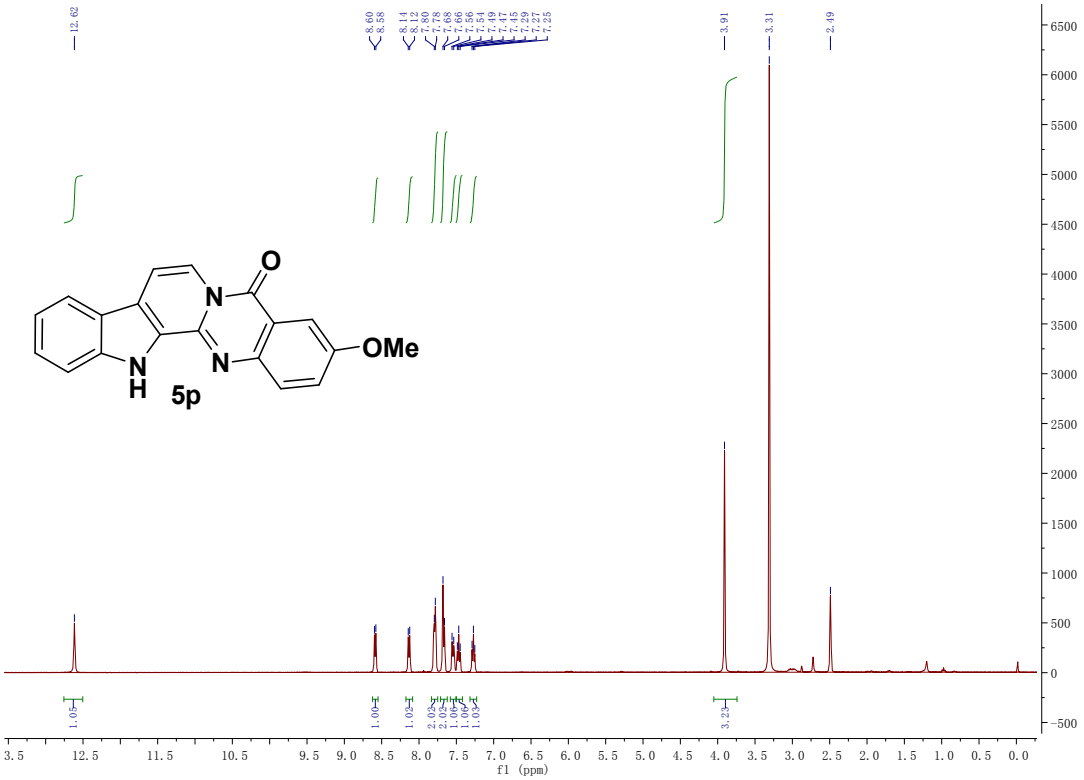

MeO
O
N
N
H
N
5m
f1 (ppm)

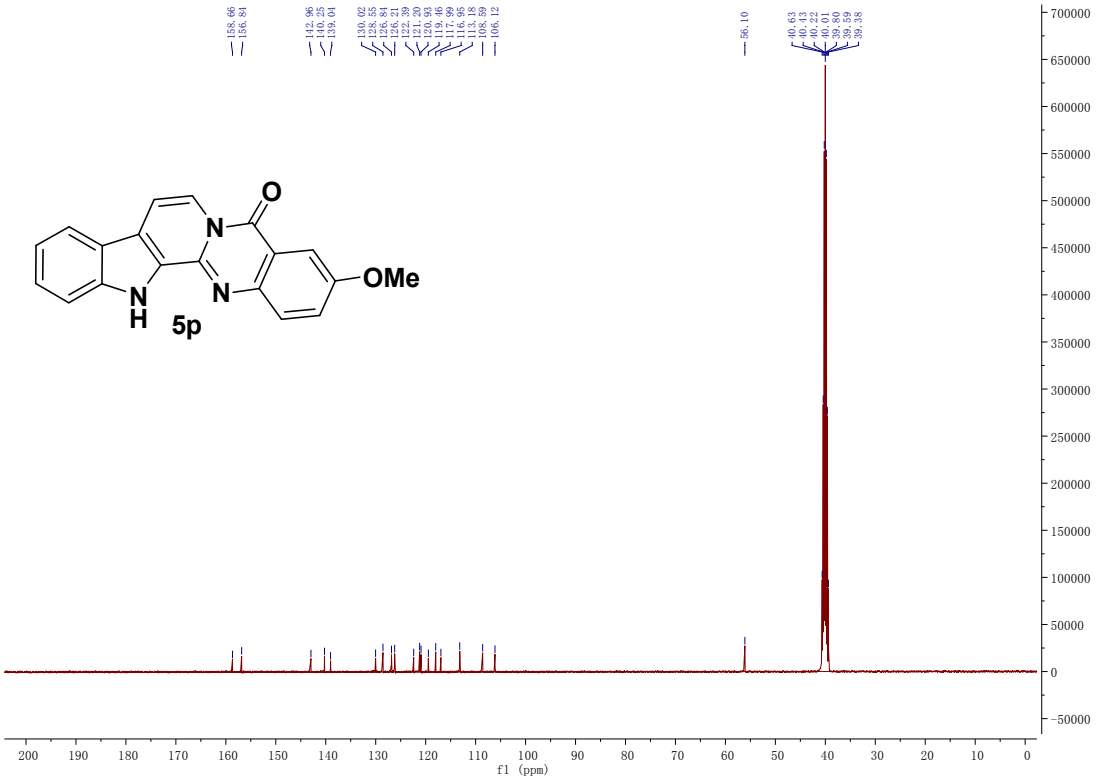

OMe
O
N
N
H
N
5n
OH
f1 (ppm)

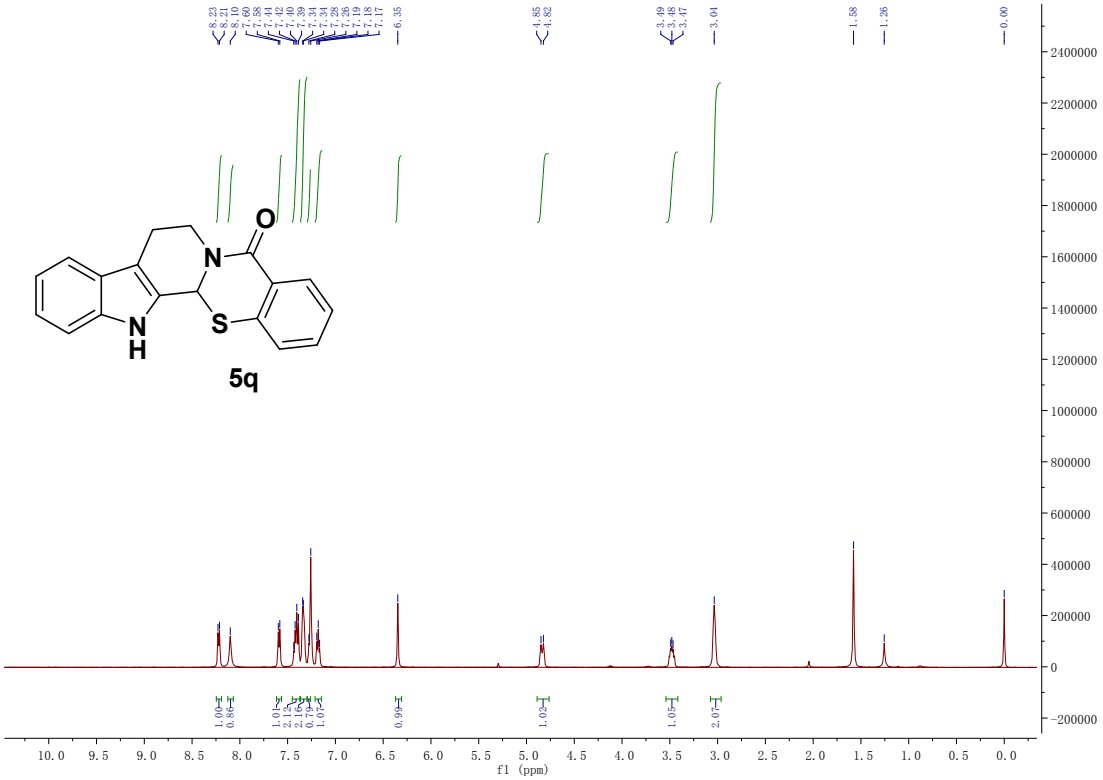

157.92
154.93
148.03
144.83
140.21
139.50
129.91
126.83
122.38
121.25
119.51
118.04
111.74
109.98
109.01
107.94
106.31
56.24
40.08
39.74
O
N
N
H
OMe
OH
5n
f1 (ppm)

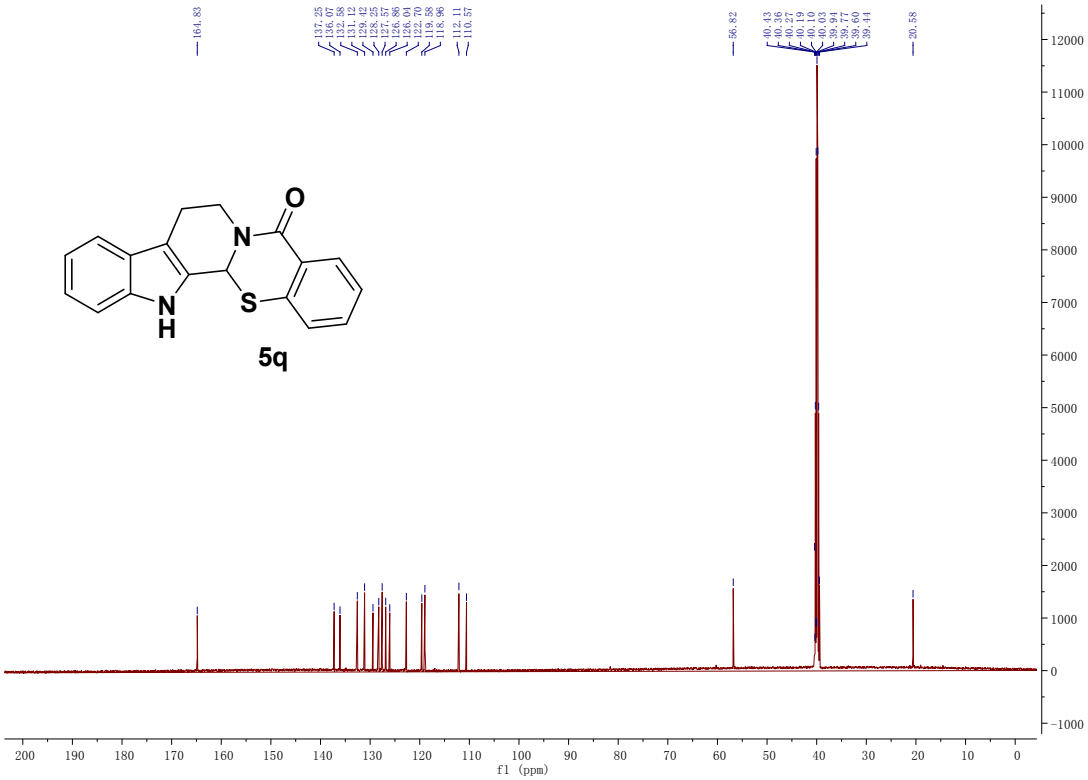

pan-150714-3
12.49
8.63
8.62
8.18
8.15
7.92
7.91
7.86
7.75
7.74
7.51
7.49
7.48
7.45
7.44
7.31
7.29
7.28
4.02
3.39
2.49
O
N
N
H
5o
MeO
f1 (ppm)

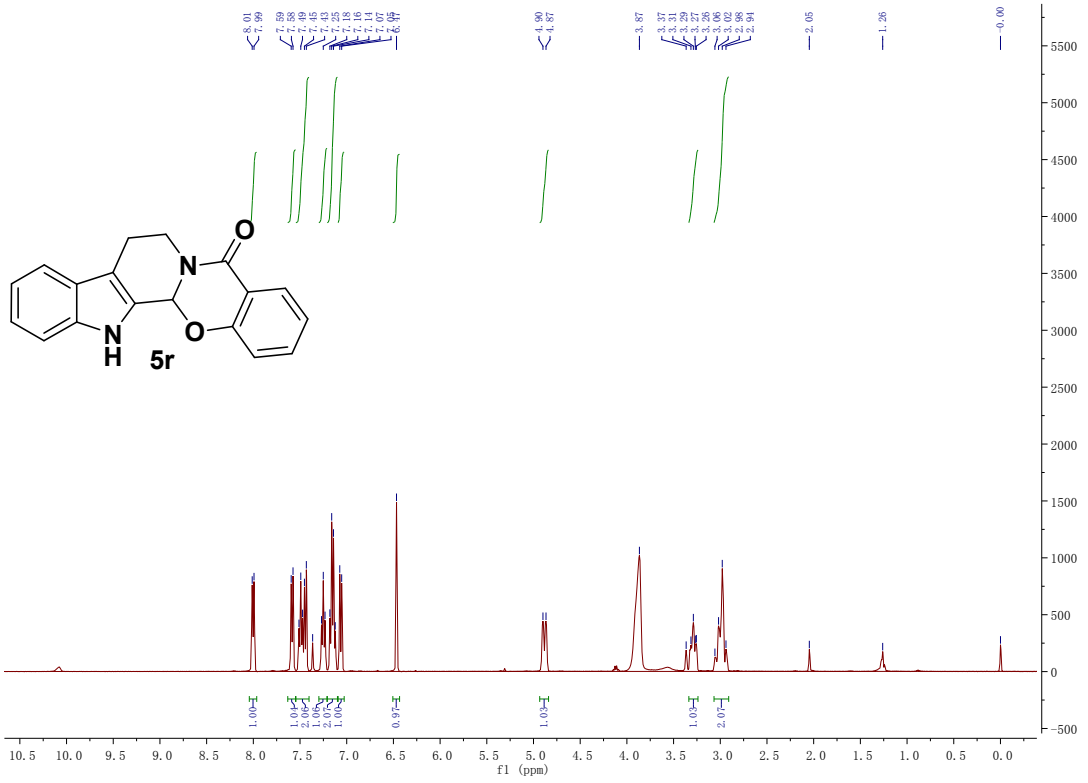

O
N
N
N
H
5o
MeO
f1 (ppm)

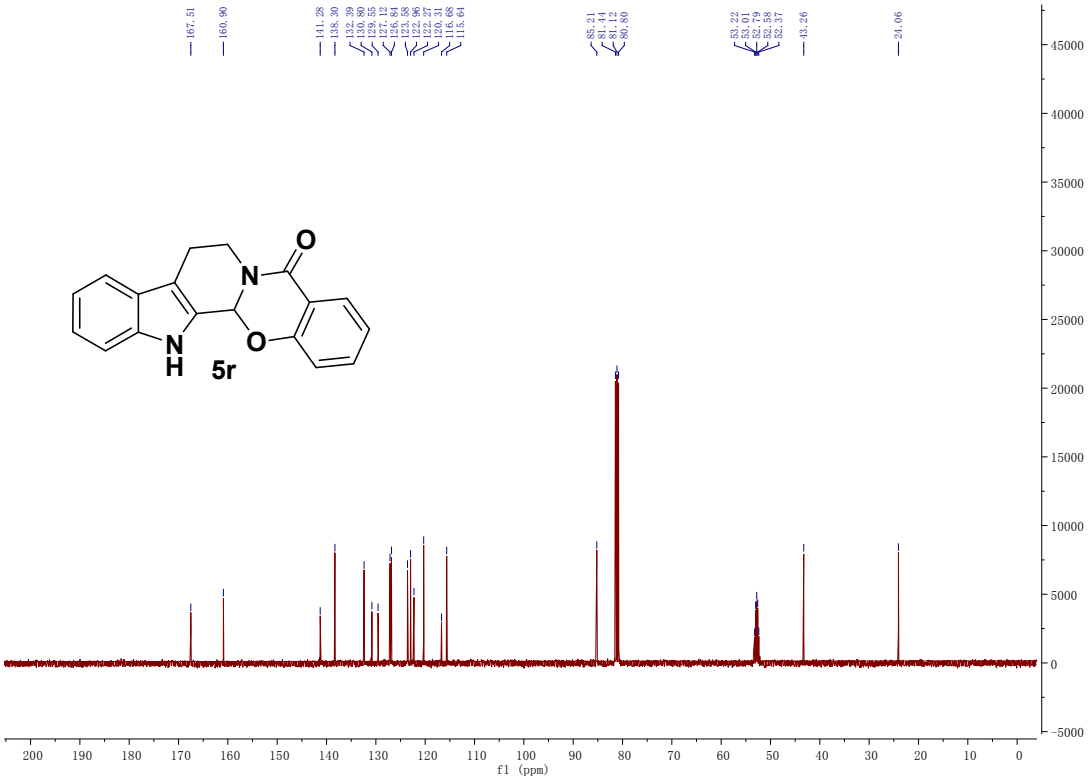

O
N
N
N
H
5p
OMe
f1 (ppm)


158.66
156.84
142.96
140.25
139.04
130.02
128.55
126.84
125.21
122.39
121.20
120.93
119.46
117.89
116.95
113.18
108.59
106.12
56.10
40.63
40.43
40.22
40.01
39.80
39.59
39.38
O
N
N
N
H
OMe
5p
fl (ppm)


8.23
8.21
8.10
7.60
7.58
7.44
7.42
7.40
7.39
7.34
7.34
7.28
7.26
7.19
7.18
7.17
6.35
4.85
4.82
3.49
3.48
3.47
3.04
1.58
1.26
0.00
1.00
0.86
1.01
2.12
2.16
1.04
1.07
0.99
1.02
1.05
2.07
O
N
S
N
H
5q
fl (ppm)


164.83
137.25
136.07
132.88
131.12
129.42
128.25
127.57
126.86
125.64
122.70
119.58
118.96
112.11
110.57
56.82
40.43
40.36
40.27
40.19
40.10
40.03
39.94
39.77
39.60
39.44
20.58
O
N
S
N
H
5q
f1 (ppm)


8.01
7.99
7.59
7.58
7.49
7.45
7.43
7.35
7.18
7.16
7.14
7.07
7.05
6.47
4.90
4.87
3.87
3.37
3.31
3.29
3.27
3.26
3.06
3.02
2.98
2.94
2.05
1.26
-0.00
O
N
O
N
H
5r
f1 (ppm)


167.51
160.90
141.28
138.30
132.39
130.80
129.55
127.12
125.84
123.58
122.96
122.27
120.31
116.68
115.64
85.21
81.44
81.12
80.80
53.22
53.01
52.79
52.58
52.37
43.26
24.06
O
N
O
N
H
5r
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)