Supporting Information

Eco-Friendly α,β-C(sp^3)-H Difunctionalization of Tertiary Amines via Sequential [1,5]-Hydride Transfer and Hetero-Diels-Alder Cyclization

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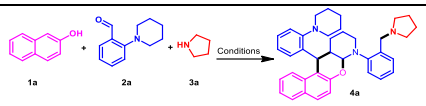
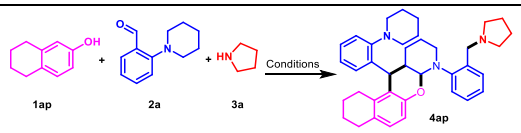
Table S1 Optimization of reaction conditions[a,b]



Entry	Solvent	Temp. (°C)	Ratio of 1a:2a:3a	Yield (%)
1	CH_3CN	80	1:2:1	54
2	DMSO	80	1:2:1	7
3	DMF	80	1:2:1	trace
4	$PhCH_3$	80	1:2:1	0
5	CCl_4	80	1:2:1	14
6	EtOH	80	1:2:1	trace
7	^{n}BuOH	80	1:2:1	10
8	^{t}BuOH	80	1:2:1	trace
9	Dibutylether	80	1:2:1	0
10	1,4-Dioxane	80	1:2:1	0
11	NMP	80	1:2:1	0
12	DMEA	80	1:2:1	25
13	2-Butanone	80	1:2:1	trace
14	DCE	80	1:2:1	64
15	DCE	80	1.5:2:1	48
16	DCE	80	1:3:1	56
17	DCE	80	1:2:1.5	68
18	**DCE**	**1 00**	**1:2:1.5**	**78**
19	DCE	120	1:2:1.5	70

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1 mmol), **3a** (0.5 mmol) at 80 °C in solvent (2 mL) for 26 h unless indicated; [b]isolated yield.

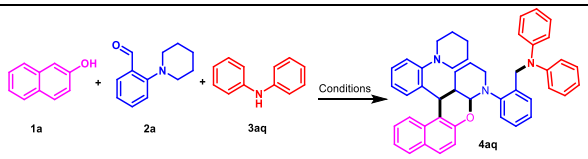
Table S2 Optimization of reaction conditions with 5,6,7,8-tetrahydronaphthalen-2-ol [a]



Entry	Solvent	Temp. (°C)	Additive	Yield (%)
1	DCE	100	HCl	0
2	DCE	100	HOAc	trace
3	DCE	100	TFA	0
4	DCE	100	TsOH	0

[a]Reaction conditions: **1ap** (0.5 mmol), **2a** (1 mmol), **3a** (0.5 mmol) at 100 °C in solvent (2 mL) for 26 h.

Table S3 Optimization of reaction conditions with diphenylamine[a]



Entry	Solvent	Temp. (°C)	Additive	Yield (%)
1	DCE	100	HCl	0
2	DCE	100	HOAc	trace
3	DCE	100	TFA	0
4	DCE	100	TsOH	0

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1 mmol), **3aq** (0.5 mmol) at 100 °C in solvent (2 mL) for 26 h.

General methods. Various aryl 2-(piperidin-1-yl)benzaldehydes, 2-(diethylamino)benzaldehyde and 2-(azepan-1-yl)benzaldehyde were prepared according to the previously reported literature.[1] Their analysis data were identical with the reported data. Other starting materials, reagents and solvents were purchased commercial sources and used as received. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 101 MHz, respectively. High-resolution mass spectra (HRMS) were performed with a Q-TOF-Premier mass spectrometer. HPLC analyses were carried out on an Agilent 1260 Infinity II instrument. Melting points were determined using a X-4 digital micro melting point apparatus. Diffraction data were collected on a Bruker Smart Apex II CCD diffractometer with graphite-monochromated Mo Kα (λ = 0.71073 Å). All reactions were monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F_{254}).

General Procedure for the synthesis of o-amino benzaldehydes 2 (2b as an example) An oven-dried round-bottom flask was charged with 5-bromo-2-fluorobenzaldehyde (10 mmol, 1.0 equiv.), piperidine (12 mmol, 1.2 equiv.), K_2CO_3 (20 mmol, 2.0 equiv.) and DMF (50 mL). The reaction mixture was stirred vigorously, refluxed in an oil bath for 12 h, and monitored by TLC. Upon consumption, the mixture was cooled to room temperature, diluted with water (100 mL), and extracted with EtOAc (3 x 100 mL). The combined extracts were washed with brine (3 × 50 mL), dried by anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure, and the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford **2b**.

4-Bromo-2-(piperidin-1-yl)benzaldehyde (*2b*). Petroleum ether/ethyl acetate (50:1) as eluent; Yellow oil (2.4 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.23 – 7.15 (m, 2H), 3.10 – 2.99 (m, 4H), 1.80 – 1.70 (m, 4H), 1.65 – 1.55 (m, 2H).

4-Chloro-2-(piperidin-1-yl)benzaldehyde (*2c*).[2] Petroleum ether/ethyl acetate (50:1) as eluent; Yellow oil (2.2 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.07 – 6.99 (m, 2H), 3.10 – 3.01 (m, 4H), 1.80 – 1.71 (m, 4H), 1.65 – 1.55 (m, 2H).

4-Methyl-2-(piperidin-1-yl)benzaldehyde (*2d*). Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.0 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 6.85 – 6.91 (m, 2H), 3.10 – 2.98 (m, 4H), 2.38 (s, 3H), 1.80 – 1.71 (m, 4H), 1.64 – 1.55 (m, 2H).

4-Formyl-3-(piperidin-1-yl)benzonitrile (*2e*).[3] Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.1 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.37 – 7.24 (m, 2H), 3.15 – 3.04 (m, 4H), 1.83 – 1.74 (m, 4H), 1.68 – 1.60 (m, 2H).

Methyl 4-formyl-3-(piperidin-1-yl)benzoate (*2f*). Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.3 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (s, 1H), 7.86 – 7.66 (m, 3H), 3.94 (s, 3H), 3.13 – 2.82 (m, 6H), 1.83 – 1.73 (m, 4H), 1.67 – 1.56 (m, 2H).

5-Bromo-2-(piperidin-1-yl)benzaldehyde (*2g*).[2] Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.6 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.88 (d, *J* = 2.6 Hz, 1H), 7.57 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.98 (d, *J* = 8.6 Hz, 1H), 3.06 – 2.97 (m, 4H), 1.81 – 1.71 (m, 4H), 1.64 – 1.56 (m, 2H).

5-Chloro-2-(piperidin-1-yl)benzaldehyde (*2h*). Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.2 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 7.74 (d, *J* = 2.6 Hz, 1H), 7.43 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.04 (d, *J* = 8.7 Hz, 1H), 3.07 – 2.98 (m, 4H), 1.82 – 1.71 (m, 4H), 1.65 – 1.56 (m, 2H).

5-Methyl-2-(piperidin-1-yl)benzaldehyde (*2i*). Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (1.9 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.25 – 7.10 (m, 2H), 3.10 – 2.84 (m, 7H), 1.82 – 1.71 (m, 4H), 1.65 – 1.56 (m, 2H).

2-(Diethylamino)benzaldehyde (*2j*).[4] Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (1.7 g, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 7.81 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.53 – 7.46 (m, 1H), 7.16 (d, *J* = 8.3 Hz, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 3.19 (q, *J* = 7.1 Hz, 4H), 1.07 (t, *J* = 7.0 Hz, 6H).

2-(Azepan-1-yl)benzaldehyde (*2k*).[1] Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (1.9 g, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.74 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.44 – 7.38 (m, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.93 (t, *J* = 7.4 Hz, 1H), 3.44 – 3.35 (m, 4H), 1.86 – 1.78 (m, 4H), 1.73 – 1.65 (m, 4H).

2-Chloro-6-(piperidin-1-yl)benzaldehyde (*2l*). Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.1 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.35 (t, *J* = 8.1 Hz, 1H), 7.06 – 6.97 (m, 2H), 3.08 – 2.98 (m, 4H), 1.82 – 1.70 (m, 4H), 1.65 – 1.59 (m, 2H).

2-Methoxy-6-(piperidin-1-yl)benzaldehyde (*2m*).[5] Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.1 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.40 (t, *J* = 8.3 Hz, 1H), 6.66 (d, *J* = 8.2 Hz, 1H), 6.56 (d, *J* = 8.3 Hz, 1H), 3.88 (s, 3H), 3.14 – 2.93 (m, 4H), 1.82 – 1.65 (m, 4H), 1.63 – 1.51 (m, 2H).

3-Bromo-2-(piperidin-1-yl)benzaldehyde (*2n*). Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.6 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 7.75 (d, *J* = 7.8 Hz, 2H), 7.08 (t, *J* = 7.8 Hz, 1H), 3.74 – 2.85 (m, 4H), 1.82 – 1.62 (m, 6H).

3-Chloro-2-(piperidin-1-yl)benzaldehyde (*2o*).[6] Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.2 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 7.70 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.54 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 3.56 – 2.95 (m, 4H), 1.78 – 1.60 (m, 6H).

2-(Azocan-1-yl)benzaldehyde (*2p*).[7] Petroleum ether/ethyl acetate (30:1) as eluent; Yellow oil (2.1 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.74 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.13 (d, *J* = 8.5 Hz, 1H), 6.93 (t, *J* = 7.4 Hz, 1H), 3.51 – 3.34 (m, 4H), 1.79 – 1.64 (m, 10H).

General Procedure for the synthesis of N,O-acetals 4 (4a as an example). A sealed tube was charged with naphthalen-2-ol **1a** (0.5 mmol, 1 equiv.), 2-(piperidin-1-yl)benzaldehyde **2a** (1 mmol, 2 equiv.), pyrrolidine **3a** (0.75 mmol, 1.5 equiv.) and dichloroethane (2 mL). The reaction was carried at 100 °C for 26 hours until almost completed conversion of the substrates by TLC analysis. After completion of the reaction, the reaction solvent was evaporated and the residue was added in petroleum ether/ethyl acetate (8:1) solution. The precipitate was filtered by a Buchner funnel and washed with petroleum ether/ethyl acetate (8:1) twice. Drying the filter cake under vacuo afforded the pure product **4a**.

Gram-scale preparation of N,O-acetal 4a. A solution of naphthalen-2-ol **1a** (5 mmol, 1 equiv.), 2-(piperidin-1-yl)benzaldehyde **2a** (10 mmol, 2 equiv.), pyrrolidine **3a** (7.5 mmol, 1.5 equiv.) in dichloroethane (20 mL) was heated at 100 °C for 26 hours. After completion of the reaction, the reaction solvent was evaporated and the residue was added in petroleum ether/ethyl acetate (8:1) solution. The precipitate was filtered by a Buchner funnel and washed with petroleum ether/ethyl acetate (8:1) twice (10 mL × 2). Drying the filter cake under vacuo afforded yellow product **4a** (1.95 g, 70%).

12-(2-(Piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4a*). Yellow solid (217.3 mg, 78%), mp 175 - 176 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.61 (m, 3H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 6.8 Hz, 1H), 7.35 – 7.07 (m, 7H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 4.94 (s, 1H), 4.80 (s, 1H), 3.71 – 2.76 (m, 8H), 2.50 – 2.27 (m, 5H), 2.00 – 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 151.9, 149.9, 141.9, 133.3, 130.5, 129.6, 129.4, 128.6, 128.5, 127.9, 127.3, 126.2, 124.9, 124.7, 124.5, 123.2, 122.8, 122.1, 119.2, 113.1, 85.5, 55.0, 54.3, 53.7, 45.7, 41.3, 40.8, 27.4, 26.0, 25.7, 24.4, 23.3. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{44}N_3O$ 558.3479; found 558.3488.

2-Methyl-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4b*). Yellow solid (188.5 mg, 66%), mp 135 - 136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.55 (m, 3H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.33 – 7.20 (m, 3H), 7.18 – 7.07 (m, 3H), 7.05 (d, *J* = 8.2 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 5.09 (s, 1H), 4.87 (s, 1H),3.67 – 2.77 (m, 8H), 2.45 – 2.17 (m, 8H), 1.99 – 1.57 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 151.7, 149.9, 142.0, 135.6, 133.5, 130.1, 129.5, 128.2, 128.2, 127.5, 127.4, 127.1, 124.9, 124.5, 124.4, 122.7, 121.8, 118.2, 113.0, 85.3, 55.0, 55.0 (2), 54.0, 45.5, 41.0, 40.1, 27.3, 26.0, 25.9, 24.5, 23.4, 22.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{46}N_3O$ 572.3635; found 572.3626.

2-Methoxy-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4c*). Yellow solid (182.0 mg, 62%), mp 159 - 160 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.53 (m, 3H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.30 – 7.19 (m, 2H), 7.14 – 7.07 (m, 2H), 7.02 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.87 (dt, *J* = 8.8, 2.5 Hz, 1H), 6 .75 (t, *J* = 7.4 Hz, 1H), 6.68 (s, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 4.97 (s, 1H), 4.70 (s, 1H), 3.66 – 2.82 (m, 11H), 2.46 – 2.21 (m, 5H), 1.97 – 1.50 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 153.8, 152.0, 149.9, 141.5, 134.6, 134.0, 130.2, 129.9, 129.6, 128.2, 127.4, 127.2, 124.6, 124.5, 124.5, 124.5, 121.9, 116.7, 114.7, 112.4, 102.9, 85.4, 55.1, 55.0, 54.0, 45.6, 41.4, 41.0, 29.8, 27.4, 26.1, 25.9, 24.4, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{46}N_3O_2$ 588.3585; found 588.3580.

2-Ethoxy-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4d*). Yellow solid (207.4 mg, 69%), mp 126 – 127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.56 (m, 2H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.32 – 7.23 (m, 2H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.89 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.78 (t, *J* = 7.4 Hz, 1H), 6.67 (d, *J* = 2.4 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 4.78 (s, 1H), 4.72 (s, 1H), 3.99 – 3.49 (m, 6H), 3.33 – 2.64 (m, 8H), 2.30 – 1.62 (m, 15H), 1.24 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 153.1, 151.9, 150.4, 141.5, 134.4, 131.9, 130.4, 123.0, 129.4, 128.5, 127.5, 126.5, 126.1, 124.7, 124.5, 121.9, 116.3, 115.5, 112.0, 103.5, 85.2, 63.0, 55.1, 52.6, 52.1, 46.4, 42.5, 40.8, 27.3, 26.0, 25.3, 24.3 22.9, 14.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O_2$ 602.3741; found 602.3745.

2-Bromo-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4e*). Yellow solid (222.3 mg, 70%), mp 89 - 90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 6.1 Hz, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.9 Hz, 1H), 7.50 (d, *J* = 8.6 Hz, 1H), 7.42 (t, *J* = 6.8 Hz, 1H), 7.33 – 7.20 (m, 3H), 7.19 – 7.04 (m, 3H), 6.80 – 6.65 (m, 2H), 5.29 (s, 1H), 4.89 (s, 1H), 3.66 – 2.80 (m, 8H), 2.41 – 2.17 (m, 5H), 2.04 – 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 151.6, 149.9, 141.5, 134.9, 134.7, 130.2, 129.9, 129.3, 128.2, 127.8, 127.4, 127.3, 126.1, 126.0, 124.7, 124.6, 124.3, 121.7, 120.8, 119.6, 113.6, 85.7, 55.4, 55.0, 54.1, 45.5, 40.6, 39.4, 27.4, 26.2, 26.0, 24.5, 23.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{79}BrN_3O$ 636.2584; found 636.2587; $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{81}BrN_3O$ 638.2564; found 638.2576.

3-Methyl-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4f*). Yellow solid (199.9 mg, 70%), mp 105 - 106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (t, *J* = 9.3 Hz, 2H), 7.50 (s, 1H), 7.45 (s, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.17 – 7.05 (m, 4H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 4.95 (s, 1H), 4.78 (s, 1H), 3.70 – 2.79 (m, 8H), 2.56 – 2.21 (m, 8H), 1.97 – 1.59 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.6, 151.9, 149.9, 142.0, 132.1, 131.4, 130.2, 129.6, 128.3, 127.9, 127.2, 124.5, 123.1, 122.0, 119.2, 113.1, 85.4, 54.8, 53.9, 45.5, 41.2, 40.8, 27.4, 26.0, 25.8, 24.5, 23.4, 21.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{46}N_3O$ 572.3635; found 572.3632.

3-Ethyl-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4g*). Yellow solid (213.6 mg, 73%), mp 76 - 77 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 9.1 Hz, 2H), 7.50 (s, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 7.29 – 7.19 (m, 2H), 7.16 - 7.06 (m, 4H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 1H), 4.96 (s, 1H), 4.78 (s, 1H), 3.64 – 2.81 (m , 8H), 3.37 (q, *J* = 19.2 Hz, 2H), 2.48 – 2.20 (m, 5H), 1.96 – 1.56 (m, 14H), 1.24 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.6, 152.0, 149.9, 142.1, 138.5, 133.9, 131.7, 130.2, 129.7, 129.6, 128.1, 127.5, 127.3, 127.2, 126.4, 124.5, 124.5, 123.3, 122.1, 119.2, 113.1, 85.4, 55.0, 54.9, 54.0, 45.6, 41.2, 40.8, 29.8, 28.6, 27.4, 26.1, 25.9, 24.5, 23.5, 15.6. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O$ 586.3792; found 586.3788.

3-Methoxy-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4h*). Purified by column chromatography using petroleum ether/ethyl acetate/Et_3N (35:1:0.04) as eluent, yellow solid (196.7 mg, 67%), mp 74 - 75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 10.2 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 9.2 Hz, 1H), 7.30 – 7.22 (m, 2H), 7.18 – 7.06 (m, 4H), 6.92 (dd, *J* = 9.2, 2.7 Hz, 1H), 6.75 (t, *J* = 8.0 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 4.93 (s, 1H), 4.76 (s, 1H), 3.84 (s, 3H), 3.66 – 2.76 (m, 8H), 2.50 – 2.19 (m, 5H), 1.96 – 1.56 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 151.9, 151.5, 149.9, 142.0, 130.2, 130.1, 129.6, 128.4, 127.4, 127.3, 127.2, 124.8, 124.5, 124.5, 124.4, 122.1, 119.7, 118.2, 113.5, 107.2, 85.3, 55.3, 55.0, 54.8, 53.9, 45.5, 41.2, 40.8, 27.4, 26.0, 25.8, 24.4, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{46}N_3O_2$ 588.3585; found 588.3592.

3-Bromo-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4i*). Yellow solid (235.0 mg, 74%), mp 103 - 104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.9 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.23 (m, 4H), 7.21 – 7.09 (m, 3H), 6.76 (t, *J* = 7.4 Hz, 1H), 6.54 (d, *J* = 7.5 Hz, 1H), 5.00 (s, 1H), 4.77 (s, 1H), 3.64 – 2.79 (m, 8H), 2.48 – 2.27 (m, 5H), 1.97 – 1.50 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 151.8, 149.8, 141.6, 133.4, 131.9, 130.6, 130.3, 129.4, 129.4, 127.7, 127.6, 127.4, 125.1, 124.8, 124.7, 124.5, 122.2, 120.4, 116.4, 113.6, 85.7, 55.0, 54.7, 53.8, 45.6, 41.1, 40.5, 27.4, 26.0, 25.8, 24.4, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{79}BrN_3O$ 636.2584; found 636.2584; $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{81}BrN_3O$ 638.2564; found 638.2577.

12-(2-(Piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine-3-carbonitrile (*4j*). Yellow solid (203.7 mg, 80%), mp 177 - 178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 1.7 Hz, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.37 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.33 – 7.23 (m, 3H), 7.17- 7.10 (m, 2H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.50 (d, *J* = 7.8 Hz, 1H), 5.08 (s, 1H), 4.80 (s, 1H), 3.66 – 2.83 (m, 8H), 2.52 – 2.21 (m, 5H), 2.00 – 1.52 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 151.8, 149.6, 141.1, 135.3, 134.3, 130.7, 129.3, 129.0, 128.3, 127.7, 127.1, 125.3, 125.0, 124.6, 124.3, 122.4, 121.1, 119.6, 114.0, 106.0, 86.2, 55.1, 54.2, 53.6, 45.7, 41.0, 40.4, 29.7, 27.3, 25.9, 25.7, 24.3, 23.3. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{43}N_4O$ 583.3431; found 583.3429.

12-(2-(Piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine-3-carboxylic acid (*4k*). Yellow solid (96.2 mg, 32%), mp 160 - 161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.89 – 7.75 (m, 3H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.34 – 7.20 (m, 3H), 7.16 (t, *J* = 7.6 Hz, 1H), 6.77 (t, *J* = 7.4 Hz, 1H), 6.52 (d, *J* = 7.6 Hz, 1H), 4.89 (s, 1H), 4.84 (s, 1H), 4.57 (t, *J* = 5.8 Hz, 2H), 3.86 – 3.46 (m, 4H), 3.33- 2.18 (m, 9H), 2.11 – 1.66 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 154.8, 151.9, 150.0, 141.4, 136.0, 131.8, 131.5, 130.2, 129.7, 129.3, 128.6, 127.7, 126.2, 126.0, 125.7, 124.6, 124.0, 123.4,

122.3, 120.0, 113.5, 85.9, 64.4, 55.1, 53.0, 52.7, 46.1, 41.8, 41.7, 40.5, 27.4, 25.9, 25.4, 24.3, 23.1. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{44}N_3O_3$ 602.3377; found 602.3380.

5-Bromo-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4l*). Yellow solid (257.2 mg, 81%), mp 124 - 125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.66 –7.52 (m, 3H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.37 – 7.23 (m, 4H), 7.21 – 7.10 (m, 2H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.55 (dd, *J* = 7.7, 1.6 Hz, 1H), 4.93 (s, 1H), 4.78 (s, 1H), 3.63 – 2.74 (m, 8H), 2.55 – 2.31 (m, 5H), 1.98- 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 151.8, 149.7, 141.4, 134.1, 130.7, 129.4, 128.4, 127.9, 127.7, 127.5, 127.1, 125.3, 125.0, 124.6, 124.1, 123.6, 123.1, 122.4, 122.3, 113.4, 86.0, 55.0, 54.0, 53.5, 45.8, 41.2, 40.7, 27.4, 25.9, 25.6, 24.4, 23.3. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{79}BrN_3O$ 636.2584; found 636.2591; $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{81}BrN_3O$ 638.2564; found 638.2582.

6-Methyl-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4m*). Yellow solid (182.7 mg, 64%), mp 193-194 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (t, *J* = 7.9 Hz, 2H), 7.52 (s, 1H), 7.44 – 7.30 (m, 2H), 7.34 – 7.06 (m, 6H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 7.6 Hz, 1H), 4.97 (s, 1H), 4.79 (s, 1H), 3.68 – 2.81 (m, 8H), 2.57 – 2.17 (m, 8H), 2.06 – 1.50 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.1, 151.9, 149.9, 141.9, 134.8, 132.2, 130.1, 129.7, 129.0, 128.1, 127.9, 127.6, 127.2, 127.1, 125.2, 124.7, 124.5, 124.5, 123.0, 122.6, 122.1, 112.4, 85.6, 55.0, 54.0, 45.6, 40.8, 40.7, 27.4, 26.0, 25.8, 24.5, 23.4, 17.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{46}N_3O$ 572.3635; found 572.3625..

6-Methoxy-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4n*). Yellow solid (182.0 mg, 62%), mp 145 - 146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.43 – 7.32 (m, 2H), 7.32 – 7.16 (m, 3H), 7.16 – 7.06 (m, 3H), 7.06 (s, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 5.03 (s, 1H), 4.83 (s, 1H), 4.00 (s, 3H), 3.68 – 2.75 (m, 8H), 2.48 – 2.16 (m, 5H), 1.99 – 1.52 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.1, 151.9, 149.9, 141.9, 134.8, 132.2, 130.1, 129.7, 129.0, 128.1, 127.9, 127.6, 127.2, 127.1, 125.2, 124.7, 124.5, 124.5, 123.0, 122.6, 122.1, 112.4, 85.6, 55.0, 54.0, 45.6, 40.8, 40.7, 27.4, 26.0, 25.8, 24.5, 23.4, 17.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{46}N_3O_2$ 588.3585; found 588.3584.

6-Bromo-12-(2-(piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4o*). Yellow solid (231.8 mg, 73%), mp 188 - 189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.69 – 7.61 (m, 1H), 7.48 – 7.40 (m, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.33 – 7.19 (m, 4H), 7.13 (q, *J* = 7.7 Hz, 2H), 6.76 (t, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 5.10 (s, 1H), 4.86 (s, 1H), 3.65- 2.84 (m, 8H), 2.57 – 2.11 (m, 5H), 1.99- 1.50 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 149.6, 149.1, 141.3, 135.2, 132.4, 131.2, 130.1, 129.6, 129.5, 127.6, 127.5, 127.4, 126.4, 126.1, 125.0, 124.6, 123.5, 123.3, 122.2, 115.2, 113.8, 87.0, 55.1, 55.0, 54.0, 46.0, 41.1, 40.6, 27.4, 25.9, 24.4, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{79}BrN_3O$ 636.2584; found 636.2590; $[M + H]^+$ Calcd for $C_{38}H_{43}{}^{81}BrN_3O$ 638.2564; found 638.2582.

14-(2-(Piperidin-1-yl)phenyl)-10-(2-(pyrrolidin-1-ylmethyl)phenyl)-9a,10,12,13,13a,14-hexahydro-11*H*-dibenzo[5,6:7,8]chromeno[2,3-*b*]pyridine (*4p*). Yellow solid (215.5 mg, 71%), mp 194 - 195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 – 8.55 (m, 2H), 8.44 (t, *J* = 4.1 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.61 (m, 2H), 7.60 – 7.47 (m, 2H), 7.44 – 7.26 (m, 4H), 7.22 – 7.09 (m, 2H), 6.80 – 6.68 (m, 2H), 5.12 (s, 1H), 4.83 (s, 1H), 3.80 - 2.76 (m, 8H), 2.58 – 2.31 (m, 5H), 2.07 – 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0, 150.0, 148.2, 141.6, 132.5, 131.0, 130.6, 129.6, 128.1, 127.4, 126.8, 126.8, 126.5, 126.2, 124.9, 124.6, 124.4, 123.9, 123.5, 122.8, 122.7, 122.4, 122.3, 109.3, 86.0,

55.0, 54.5, 53.8, 45.8, 41.2, 41.2 (2), 29.7, 27.4, 26.0, 25.8, 24.5, 23.4, 14.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{42}H_{46}N_3O$ 608.3635; found 608.3639.

12-(2-(Piperidin-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-pyrido[3',2':5,6]pyrano[3,2-f]quinoline (*4q*). Yellow solid (47.4 mg, 17%), mp 185 - 186 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.61 (m, 4H), 7.46 – 7.40 (m, 1H), 7.38 – 7.09 (m, 6H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.57 (dd, *J* = 7.7, 1.6 Hz, 1H), 4.88 (s, 1H), 4.80 (s, 1H), 3.67 – 3.53 (m, 3H), 3.30 – 2.32 (m, 10H), 1.96 – 1.60 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.87, 151.90, 150.02, 141.89, 133.28, 130.84, 129.56, 129.48, 128.68, 128.62, 128.50, 127.35, 126.29, 125.33, 125.10, 124.49, 123.22, 122.90, 122.13, 119.14, 113.02, 85.47, 55.00, 53.68, 53.40, 45.86, 41.54, 40.74, 29.73, 27.38, 26.03, 25.59, 24.40, 23.22. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{37}H_{43}N_4O$ 559.3431; found 559.3433.

12-(4-Bromo-2-(piperidin-1-yl)phenyl)-8-(5-bromo-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4r*). Yellow solid (256.7 mg, 72%), mp 215 - 216 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.62 (m, 3H), 7.42 – 7.10 (m, 7H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.45 (d, *J* = 8.2 Hz, 1H), 4.89 (s, 1H), 4.68 (s, 1H), 3.62 – 2.74 (m, 8H), 2.49 – 2.09 (m, 5H), 2.00 – 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 152.9, 150.9, 140.9, 133.4, 133.1, 131.4, 131.2, 129.5, 128.9, 128.6, 127.6, 127.5, 127.5, 126.4, 125.8, 123.0, 122.9, 120.8, 120.6, 119.2, 112.3, 85.0, 54.9, 54.8, 54.1, 45.4, 40.8, 40.5, 27.2, 25.9, 25.6, 24.3, 23.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{79}Br_2N_3O$ 714.1689; found 714.1688; $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{79}Br^{81}BrN_3O$ 716.1669; found 716.1670.

12-(4-Chloro-2-(piperidin-1-yl)phenyl)-8-(5-chloro-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4s*). Yellow solid (212.5 mg, 68%), mp 227 - 228 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.64 (m, 2H), 7.58 (s, 1H), 7.48 (d, *J* = 8.3 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.31 – 7.21 (m, 3H), 7.17 (d, *J* = 8.9 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.74 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.51 (d, *J* = 8.3 Hz, 1H), 4.86 (s, 1H), 4.70 (s, 1H), 3.62 – 2.75 (m, 8H), 2.54 – 2.19 (m, 5H), 1.99 – 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 152.7, 150.8, 140.3, 133.6, 133.0, 132.8, 131.6, 130.7, 129.6, 129.0, 128.6, 126.5, 125.3, 125.1, 124.5, 123.1, 123.0, 122.9, 119.1, 112.4, 85.0, 54.9, 53.8, 53.7, 45.7, 41.2, 40.4, 27.2, 25.9, 25.5, 24.3, 23.3. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{35}Cl_2N_3O$ 626.2699; found 626.2701; $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{35}Cl^{37}ClN_3O$ 628.2670; found 628.2678.

12-(4-Methyl-2-(piperidin-1-yl)phenyl)-8-(5-methyl-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4t*). Yellow solid (204.8 mg, 70%), mp 218 - 219 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.63 (m, 2H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.50 (s, 1H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.31 – 7.12 (m, 3H), 6.99 – 7.09 (m, 2H), 6.55 (d, *J* = 7.9 Hz, 1H), 6.43 (d, *J* = 7.8 Hz, 1H), 4.84 (s, 1H), 4.74 (s, 1H), 3.78 – 3.51 (m, 3H), 3.30 – 2.28 (m, 13H), 2.22 (s, 3H), 1.96 – 1.55 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 151.7, 150.0, 139.1, 138.7, 136.9, 133.3, 131.0, 129.5, 129.4, 128.6, 128.5, 126.4, 126.3, 126.1, 125.1, 123.3, 122.9, 122.9, 119.1, 113.2, 85.5, 55.0, 53.1, 53.0, 46.0, 41.7, 40.5, 27.4, 26.1, 25.5, 24.4, 23.1, 21.5, 21.1. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O$ 586.3792; found 586.3795.

12-(4-Methoxy-2-(piperidin-1-yl)phenyl)-8-(5-methoxy-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4u*). Yellow solid (179.0 mg, 58%), mp 163 - 164 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.59 (m, 2H), 7.57 – 7.36 (m, 2H), 7.36 – 7.18 (m, 3H), 7.16 (d, *J* = 8.9 Hz, 1H), 6.81 (s, 1H), 6.72 (d, *J* = 9.4 Hz, 1H), 6.47 (d, *J* = 8.5 Hz, 1H), 6.28 (d, *J* = 7.0 Hz, 1H), 4.92 (s, 1H), 4.67 (s, 1H), 3.85 (s, 3H), 3.68 (s, 3H), 3.62 – 2.74 (m, 8H), 2.60 – 2.29 (m, 5H), 2.02 – 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 158.9, 153.0, 152.8, 151.3,

133.9, 133.3, 131.6, 130.3, 129.5, 128.6, 128.5, 126.2, 123.3, 122.9, 119.2, 113.3, 111.3, 109.9, 109.0, 108.3, 85.5, 55.3, 55.1, 54.9, 53.6, 53.3, 45.9, 41.5, 40.2, 27.3, 26.0, 25.6,24.4, 23.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O$ 618.3690; found 618.3685.

3-(12-(4-Cyano-2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)-4-(pyrrolidin-1-ylmethyl)benzonitrile (*4v*). Purified by column chromatography using petroleum ether/ethyl acetate/Et_3N (35:1:0.04) as eluent, yellow solid (170.0 mg, 56%), mp 112 - 113 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.81 – 7.71 (m, 2H), 7.65 (s, 1H), 7.54 (s, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.24 (m, 3H), 7.18 (d, *J* = 8.9 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 4.82 (s, 1H), 4.79 (s, 1H), 3.63 – 2.74 (m, 8H), 2.53 – 2.24 (m, 5H), 1.94 – 1.54 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 152.6, 150.0, 147.6, 132.8, 131.1, 130.5, 129.7, 129.5, 128.8, 128.2, 126.7, 126.1, 123.3, 122.6, 119.1, 111.5, 111.3, 84.6, 54.8, 54.7, 54.1, 45.5, 40.9, 40.8, 27.1, 25.7, 25.6, 24.1, 23.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{42}N_5O$ 608.3384; found 608.3377.

12-(5-Bromo-2-(piperidin-1-yl)phenyl)-8-(4-bromo-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4w*). Yellow solid (253.1 mg, 71%), mp 196 - 197 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.72 (m, 1H), 7.69 (d, *J* = 8.9 Hz, 1H), 7.64 (d, *J* = 2.4 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.32 – 7.21 (m, 3H), 7.14 (d, *J* = 8.7 Hz, 2H), 6.67 (d, *J* = 2.4 Hz, 1H), 4.90 (s, 1H), 4.74 (s, 1H), 3.64 – 2.70 (m, 8H), 2.49 – 2.15 (m, 5H), 1.98 – 1.45 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8,151.1, 148.8, 144.5, 134.7, 133.2, 133.1, 132.0, 131.2, 130.6, 129.6, 129.1, 128.7, 126.7, 126.5, 124.2, 123.1, 122.9, 119.1, 118.6, 118.1, 112.0, 85.0, 54.9, 54.0, 53.7, 45.7, 41.2, 40.6, 27.3, 25.9, 25.6, 24.3, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{79}Br_2N_3O$ 714.1689; found 714.1691; $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{79}Br^{81}BrN_3O$ 716.1669; found 714.1675.

12-(5-Chloro-2-(piperidin-1-yl)phenyl)-8-(4-chloro-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4x*). Yellow solid (221.9 mg, 71%), mp 192 - 193 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.64 (m, 2H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.48 (d, *J* = 2.6 Hz, 1H), 7.36 (d, *J* = 6.9 Hz, 1H), 7.31 – 7.06 (m, 6H), 6.53 (d, *J* = 2.5 Hz, 1H), 4.91 (s, 1H), 4.75 (s, 1H), 3.62 – 2.69 (m, 8H), 2.45 – 2.20 (m, 5H), 1.96 – 1.49 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.9, 150.6, 148.1, 144.1, 135.8, 133.1, 130.3, 130.0, 130.0 (2), 129.5, 129.3, 129.0, 128.6, 127.6, 127.5, 126.4, 126.0, 123.7, 123.0, 122.9, 119.2, 112.1, 85.1, 55.0, 54.6, 53.9, 45.5, 41.0, 40.6, 27.3, 25.9, 25.7, 24.3, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{35}Cl_2N_3O$ 626.2699; found 626.2701; $[M + H]^+$ Calcd for $C_{38}H_{42}{}^{35}Cl^{37}ClN_3O$ 628.2670; found 628.2686.

12-(5-Methyl-2-(piperidin-1-yl)phenyl)-8-(4-methyl-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4y*). Yellow solid (201.9 mg, 69%), mp 91 - 92 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.62 (m 2H), 7.68 (d, *J* = 8.8 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.31 – 7.05 (m, 5H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.33 (s, 1H), 4.88 (s, 1H), 4.77 (s, 1H), 3.67 – 2.67 (m, 8H), 2.58 – 2.19 (m, 8H), 2.08 – 1.51 (m, 17H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 149.4, 147.5, 141.8, 135.0, 133.8, 133.4, 131.2, 130.0, 129.4, 129.0, 128.5, 128.4, 127.9, 126.2, 125.2, 123.3, 122.8, 122.0, 119.2, 113.1, 85.7, 55.1, 54.0, 53.6, 45.9, 41.5, 40.7, 29.7, 27.4, 26.1, 25.6, 24.4, 23.3, 21.1, 21.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O$ 586.3792; found 586.3790.

12-(5-Methoxy-2-(piperidin-1-yl)phenyl)-8-(4-methoxy-2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4z*). Purified by column chromatography using petroleum ether/ethyl acetate/Et_3N (35:1:0.04) as eluent, yellow solid (172.8 mg, 56%), mp 65 - 66 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.57 (m, 3H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.30

– 7.11 (m, 4H), 7.06 (s, 1H), 6.83 (dd, *J* = 8.8, 3.1 Hz, 1H), 6.63 (dd, *J* = 8.6, 3.0 Hz, 1H), 6.12 (d, *J* = 3.0 Hz, 1H), 4.92 (s, 1H), 4.79 (s, 1H), 3.79 (s, 3H), 3.62 – 2.69 (m, 11H), 2.45– 2.25 (m, 5H), 1.93 – 1.44 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 156.2, 153.2, 145.2, 143.8, 143.0, 135.2, 133.4, 129.4, 128.6, 128.5, 126.5, 126.2, 123.2, 123.1, 122.7, 119.3, 116.4, 115.0, 113.2, 112.9, 110.6, 85.8, 55.6, 55.0, 54.8, 53.8, 46.1, 41.3, 40.8, 29.8, 27.5, 26.1, 25.7, 24.4, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O_3$ 618.3690; found 618.3685.

4-(12-(5-Cyano-2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)-3-(pyrrolidin-1-ylmethyl)benzonitrile (*4aa*). Yellow solid (188.2 mg, 62%), mp 152 - 154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.70 (m, 3H), 7.62 – 7.54 (m, 2H), 7.46 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.36 – 7.26 (m, 4H), 7.16 (d, *J* = 8.9 Hz, 1H), 6.89 (d, *J* = 2.0 Hz, 1H), 4.90 (s, 1H), 4.70 (s, 1H), 3.64 – 2.90 (m, 8H), 2.51 – 2.18 (m, 5H), 1.99 – 1.59 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 153.6, 152.6, 142.5, 134.5, 134.2, 133.3, 132.8, 131.8, 131.6, 129.7, 129.6, 128.9, 126.7, 123.9, 123.4, 122.7, 122.5, 119.4, 119.0, 111.4, 107.5, 107.3, 84.4, 54.6, 54.5, 54.1, 45.2, 40.6, 40.3, 27.0, 25.7, 25.6, 24.2, 23.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{42}N_5O$ 608.3384; found 608.3378.

13-(2-(Azepan-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-7a,8,9,10,11,12,12a,13-octahydrobenzo[5,6]chromeno[2,3-*b*]azepine (*4ab*). Purified by column chromatography using petroleum ether/ethyl acetate/Et_3N (35:1:0.04) as eluent, yellow solid (117.2 mg, 40%), mp 59 - 60 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (t, *J* = 8.0 Hz, 2H), 7.52 (s, 1H), 7.40 (d, *J* = 7.4 Hz, 2H), 7.32 – 7.16 (m, 5H), 7.11 (t, *J* = 7.6 Hz, 2H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 4.98 (s, 1H), 4.80 (s, 1H), 3.51 – 2.81 (m, 8H), 2.60 – 2.18 (m, 9H), 2.18– 1.48 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 152.5, 148.6, 148.5, 141.5, 133.4, 131.2, 129.6, 128.5, 128.4, 127.5, 126.3, 124.5, 124.3, 123.8, 123.1, 123.0, 118.9, 115.7, 115.5, 114.1, 109.8, 91.4, 58.6, 58.2, 53.4, 53.3, 50.6, 43.6, 41.8, 38.5, 30.6, 29.8, 29.0, 27.6, 27.2, 26.3, 23.7, 23.6, 23.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O$ 586.3792; found 586.3788.

14-(2-(Azocan-1-yl)phenyl)-8-(2-(pyrrolidin-1-ylmethyl)phenyl)-8,9,10,11,12,13,13a,14-octahydro-7a*H*-benzo[5,6]chromeno[2,3-*b*]azocine (*4ac*). Purified by column chromatography using petroleum ether/ethyl acetate/Et_3N (35:1:0.04) as eluent, yellow oil (89.0 mg, 29%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.74 (m, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.45-7.44 (m, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.23–7.12 (m, 4H), 6.97 (d, *J* = 7.2 Hz, 1H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 1H), 6.58 (t, *J* = 7.6 Hz, 3H), 5.08 (s, 1H), 4.29 (s, 1H), 3.58 (d, *J* = 11.2 Hz, 2H), 3.50–3.39 (m, 2H), 3.30–3.22 (m, 2H), 3.08 (t, *J* = 6.8 Hz, 2H), 2.76-2.75 (m, 2H), 2.56 (d, *J* = 5.2 Hz, 2H), 2.43-2.37 (m, 6H), 1.92-1.79 (m, 17H).^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 152.4, 148.5, 141.6, 133.3, 131.2, 129.5, 129.1, 128.43, 128.42, 128.2, 127.2, 126.2, 125.8, 124.1, 123.0, 122.8, 118.8, 115.4, 115.3, 114.1, 109.5, 91.3, 59.7, 57.9, 55.5, 53.4, 53.3, 50.6, 43.1, 41.3, 38.9, 29.4, 28.3, 28.0, 27.9, 27.5, 26.8, 26.5, 23.63, 23.57, 23.3. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{42}H_{52}N_3O$ 614.4105; found 614.4102.

12-(2-(Piperidin-1-yl)phenyl)-8-(2-(piperidin-1-ylmethyl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4ad*). Yellow solid (228.4 mg, 80%), mp 150 - 151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.60 (m, 3H), 7.65 (t, *J* = 8.0 Hz, 2H), 7.42 (t, *J* = 8.2 Hz, 2H), 7.31 – 7.14 (m, 5H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 1H), 4.95 (s, 1H), 4.81 (s, 1H), 3.62 – 2.76 (m, 8H), 2.57 – 1.59 (m, 15H), 1.39 – 1.26 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 151.9, 150.4, 141.9, 134.0, 133.4, 130.4, 129.6, 129.4, 128.5, 128.4, 127.3, 127.2, 126.2, 124.8, 124.5, 124.5, 123.2, 122.7, 122.2, 119.3, 113.2, 85.5, 58.2, 55.0, 54.4, 45.7, 41.0, 40.7, 29.7, 27.4, 26.0, 25.9, 25.8, 24.5, 24.3. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{46}N_3O$ 572.3635; found 572.3627.

8-(2-(Azepan-1-ylmethyl)phenyl)-12-(2-(piperidin-1-yl)phenyl)-7a,8,10,11,11a,12-hexahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridine (*4ae*). Yellow solid (222.3 mg, 76%), mp 108 - 109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.51 (m, 4H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.33 – 7.18 (m, 4H), 7.18 – 7.07 (m, 3H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 4.93 (s, 1H), 4.81 (s, 1H), 3.69 – 2.76 (m, 8H), 2.55 – 2.32 (m, 5H), 1.99 - 1.50 (m, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 151.9, 150.2, 142.0, 133.3, 130.6, 129.5, 129.4, 128.6, 128.5, 127.7, 127.2, 126.2, 124.7, 124.6, 124.5, 123.3, 122.8, 122.2, 119.2, 113.1, 85.5, 55.9, 55.1, 45.7, 41.3, 40.7, 29.7, 27.4, 27.1, 26.9, 26.1, 25.8, 24.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{48}N_3O$ 586.3792; found 586.3796.

***N*,*N*-Dimethyl-1-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)phenyl)methanamine (*4af*).** Yellow solid (228.4 mg, 86%), mp 72 - 73 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.57 (m, 3H), 7.48 – 7.34 (m, 2H), 7.35 – 7.07 (m, 7H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 4.81 (s, 1H), 3.79 – 2.28 (m, 9H), 2.00 – 1.58 (m, 16H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 151.9, 150.5, 141.9, 133.4, 130.7, 129.7, 129.4, 128.5, 128.5 (2), 127.9, 127.2, 126.2, 124.8, 124.6, 124.4, 123.3, 122.7, 122.1, 119.3, 113.2, 85.7, 58.7, 55.0, 45.4, 44.8, 41.1, 40.7, 32.0, 29.8, 27.4, 26.1, 25.79, 24.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{36}H_{42}N_3O$ 532.3322; found 532.3319.

***N*-Ethyl-*N*-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)benzyl)ethanamine (*4ag*).** Yellow solid (246.0 mg, 88%), mp 224-225 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* = 8.9 Hz, 1H), 7.54 (t, *J* = 9.8 Hz, 2H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.30 – 7.19 (m, 4H), 7.18 – 7.05 (m, 3H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.55 (d, *J* = 7.6 Hz, 1H), 4.91 (s, 1H), 4.79 (s, 1H), 3.71 – 2.71 (m, 8H), 2.54 – 1.60 (m, 15H), 0.83 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 151.9, 150.1, 141.9, 133.3, 130.5, 129.6, 129.4, 128.6, 128.5, 127.3, 126.2, 124.8, 124.5, 124.2, 123.2, 122.8, 122.2, 119.2, 113.0, 85.5, 77.3, 55.0, 51.2, 46.5, 45.6, 41.3, 40.8, 27.4, 26.0, 25.6, 24.4, 10.6. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{46}N_3O$ 560.3635; found 560.3626.

***N*-(2-(12-(2-(Piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)benzyl)-*N*-propylpropan-1-amine (*4ah*).** Yellow solid (258.3 mg, 88%), mp 140 - 141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.68 (m, 1H), 7.66 (d, *J* = 8.9 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.43 (d, *J* = 9.3 Hz, 1H), 7.30 – 7.16 (m, 4H), 7.17 – 7.06 (m, 3H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 4.90 (s, 1H), 4.79 (s, 1H), 3.69 – 2.75 (m, 8H), 2.52- 1.53 (m, 14H), 1.41 – 1.15 (m, 5H), 0.75 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 151.9, 149.9, 141.9, 133.4, 129.8, 129.6, 129.4, 128.5, 128.4, 127.2, 126.7, 126.2, 124.5, 124.1, 123.4, 123.2, 122.7, 122.2, 119.3, 113.1, 85.5, 56.0, 55.0, 52.9, 45.1, 41.0, 40.8, 27.4, 26.0, 25.7, 24.5, 19.8, 11.9. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{50}N_3O$ 588.3948; found 588.3951.

***N*-Isopropyl-*N*-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)benzyl)propan-2-amine (*4ai*).** Yellow solid (229.0 mg, 78%), mp 174-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.8 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.37 (m, 2H), 7.30 – 7.16 (m, 4H), 7.30 – 7.04 (m, 3H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 7.2 Hz, 1H), 4.88 (s, 1H), 4.80 (s, 1H), 3.78 – 2.40 (m, 11H), 2.01 – 1.63 (m, 10H), 0.83 (d, *J* = 6.5 Hz, 6H), 0.75 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 151.9, 149.2, 141.9, 137.9, 133.3, 129.5, 129.4, 129.3, 128.4, 127.3, 126.1, 126.0, 124.5, 124.0, 123.2, 123.1, 122.7, 122.4, 119.3, 113.0, 85.4, 48.3, 45.0, 42.9, 41.0, 40.8, 27.4, 26.1, 25.9, 24.5, 21.1, 20.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{50}N_3O$ 588.3948; found 588.3942.

***N*-Methyl-*N*-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)benzyl)ethanamine (*4aj*).** Yellow solid (188.4 mg, 69%), mp 124 - 125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.64 (m, 2H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.48 – 7.39 (m, 1H), 7.35 – 7.18 (m, 4H), 7.19 – 7.08 (m, 3H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.56 (dd, *J* = 7.7, 1.6 Hz, 1H), 4.92 (s, 1H), 4.80 (s, 1H), 3.69 – 2.73 (m, 8H), 2.5 – 2.16 (m, 3H), 2.01 (s, 3H), 1.94 – 1.59 (m, 10H), 0.93 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 151.9, 150.3, 141.9, 133.3, 130.7, 129.6, 129.4, 128.6, 128.5, 128.1, 127.3, 126.3, 125.0, 124.8, 124.5, 123.2, 122.8, 122.1, 119.2, 113.1, 85.6, 55.3, 55.0, 50.7, 45.6, 41.3, 40.8, 27.4, 26.0, 25.7, 24.4, 11.1. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{37}H_{44}N_3O$ 546.3479; found 546.3483.

***N*-Ethyl-*N*-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)benzyl)propan-1-amine (*4ak*).** Purified by column chromatography using petroleum ether/ethyl acetate/Et_3N (35:1:0.04) as eluent, yellow solid (212.0 mg, 74%), mp 57 - 58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 6.9 Hz, 1H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.58– 7.17 (m, 2H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.17 (m, 4H), 7.17 – 7.07 (m, 3H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.56 (d, *J* = 7.7 Hz, 1H), 4.91 (s, 1H), 4.79 (s, 1H), 3.68 – 2.69 (m, 8H), 2.59 – 2.03 (m, 5H), 2.01 – 1.16 (m, 12H), 0.86 – 0.71 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 152.0, 150.0, 142.0, 134.6, 133.4, 130.0, 129.7, 129.5, 128.6, 128.5, 127.3, 127.0, 126.3, 124.5, 124.3, 123.7, 123.3, 122.8, 122.2, 119.3, 113.1, 85.6, 55.4, 55.0, 52.3, 47.4, 45.3, 41.1, 40.9, 27.5, 26.1, 25.8, 24.5, 19.7, 12.0, 11.3. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{48}N_3O$ 574.3792; found 574.3786.

***N*-Methyl-*N*-(2-(14-(2-(piperidin-1-yl)phenyl)-12,13,13a,14-tetrahydro-11*H*-dibenzo[5,6:7,8]chromeno[2,3-*b*]pyridin-10(9a*H*)-yl)benzyl)propan-2-amine (*4al*).** Yellow solid (231.4 mg, 76%), mp 150 - 151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 77.77 – 7.54 (m, 4H), 7.42 (d, *J* = 9.0 Hz, 1H), 7.33 – 7.06 (m, 7H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 8.1 Hz, 1H), 4.89 (s, 1H), 4.80 (s, 1H), 3.69 – 2.30 (m, 10H), 2.09 – 1.46 (m, 13H), 1.05 – 0.69 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 151.9, 150.1, 142.0, 133.3, 130.3, 129.5, 129.4, 128.6, 128.5, 127.6, 127.3, 126.2, 124.8, 124.5, 124.2, 123.3, 122.8, 122.2, 119.3, 113.0, 85.5, 55.0, 53.2, 51.3, 45.5, 41.4, 40.8, 36.2, 27.4, 26.0, 25.7, 24.5, 17.9, 16.7. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{46}N_3$ 560.3635; found 560.3630.

***N*-Ethyl-*N*-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)benzyl)propan-2-amine (*4am*).** Yellow solid (180.5 mg, 63%), mp 140 - 141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 6.9 Hz, 2H), 7.66 (d, *J* = 8.9 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.33 – 7.06 (m, 7H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 8.1 Hz, 1H), 4.89 (s, 1H), 4.80 (s, 1H), 3.74 – 2.65 (m, 10H), 2.50 – 1.56 (m, 13H), 1.05 – 0.69 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 151.9, 149.8, 142.0, 133.3, 129.5, 129.5, 128.6, 128.5, 127.4, 126.3, 124.5, 123.2, 122.8, 122.3, 119.2, 112.9, 85.5, 55.0, 47.0, 45.4, 43.8, 41.4, 40.8, 27.4, 26.1, 25.6, 24.4, 16.7. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{48}N_3O$ 574.3792; found 574.3790.

***N*-Methyl-*N*-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)benzyl)butan-1-amine (*4an*).** Yellow solid (226.4 mg, 79%), mp 136 - 137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.61 (m, 2H), 7.59 – 7.51 (m, 1H), 7.48 – 7.37 (m, 2H), 7.30 – 7.16 (m, 4H), 7.16 – 7.04 (m, 3H), 6.74 (t, *J* = 7.6 Hz, 1H), 6.60 – 6.53 (m, 1H), 4.98 (s, 1H), 4.80 (s, 1H), 3.71 – 2.71 (m, 8H), 2.54 – 1.53 (m, 16H), 1.38 – 1.12 (m, 4H), 0.87 – 0.77 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 152.0, 150.2, 142.0, 133.8, 133.4, 130.3, 129.7, 129.4, 128.6, 128.5, 127.4, 127.3, 126.2, 124.5, 124.4, 124.1, 123.3, 122.8, 122.2, 119.3, 113.2, 85.65, 57.3, 56.6, 55.0, 45.4, 42.0, 41.1, 40.8, 28.9, 27.4, 26.1, 25.8, 24.5, 20.7, 14.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{48}N_3O$ 574.3792; found 574.3784.

***N*-Benzyl-*N*-methyl-1-(2-(12-(2-(piperidin-1-yl)phenyl)-10,11,11a,12-tetrahydro-9*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-8(7a*H*)-yl)phenyl)methanamine (*4ao*).** Yellow solid (282.3 mg, 93%), mp 62 - 63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77– 7.62 (m, 2H), 7.61– 7.50 (m, 2H), 7.48– 7.40 (m, 1H), 7.36 – 7.05 (m, 12H), 6.70 (s, 1H), 6.56 (s, 1H), 4.98 (s, 1H), 4.80 (s, 1H), 3.68 – 2.79 (m, 11H), 2.50 – 2.30 (m, 1H), 1.99 – 1.61 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 151.9, 149.9, 141.9, 133.3, 130.5, 129.6, 129.4, 128.6, 128.5, 127.9, 127.3, 126.2, 124.9, 124.7, 124.5, 123.2, 122.8, 122.1, 119.2, 113.1, 85.5, 62.3, 61.3, 58.6, 56.2, 55.0, 45.3, 42.4, 42.1, 41.7, 41.1, 40.8, 27.5, 26.0, 25.8, 24.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{42}H_{46}N_3O$ 608.3635; found 608.3634.

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Figure S1 High resolution mass spectrum of intermediate **A or B or C**

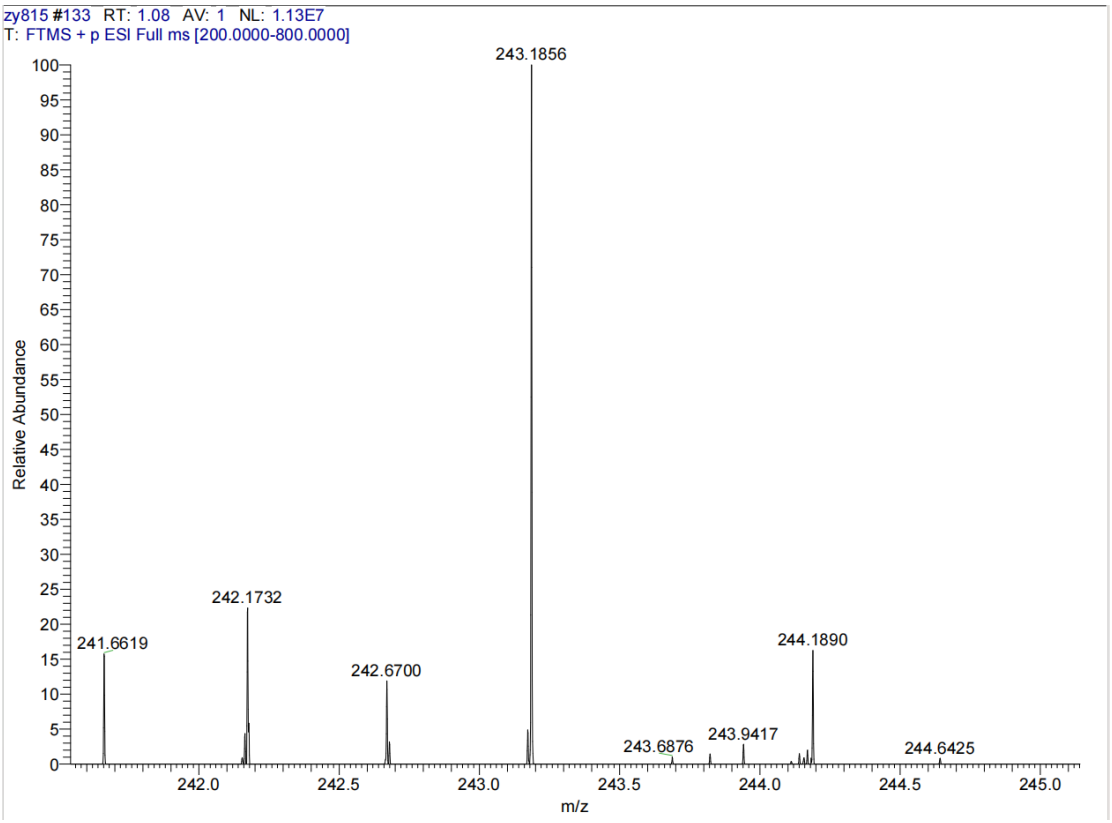


Figure S2 High resolution mass spectrum of intermediate **D**

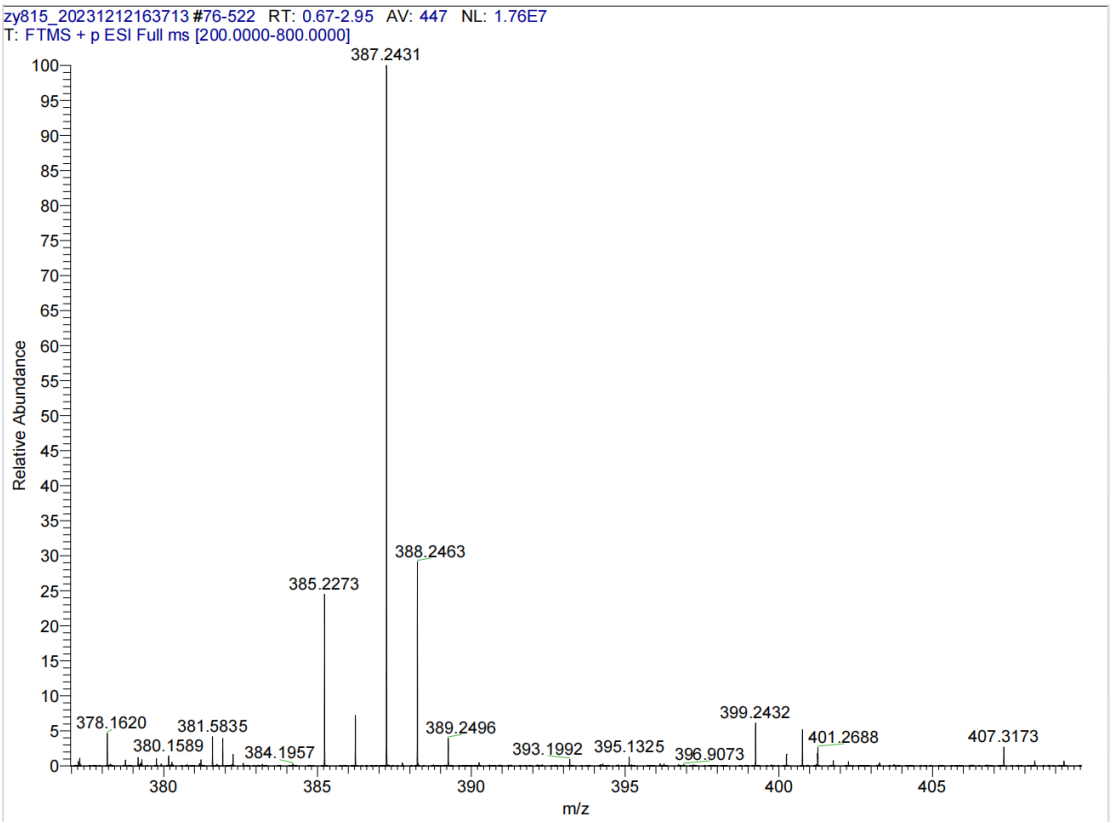
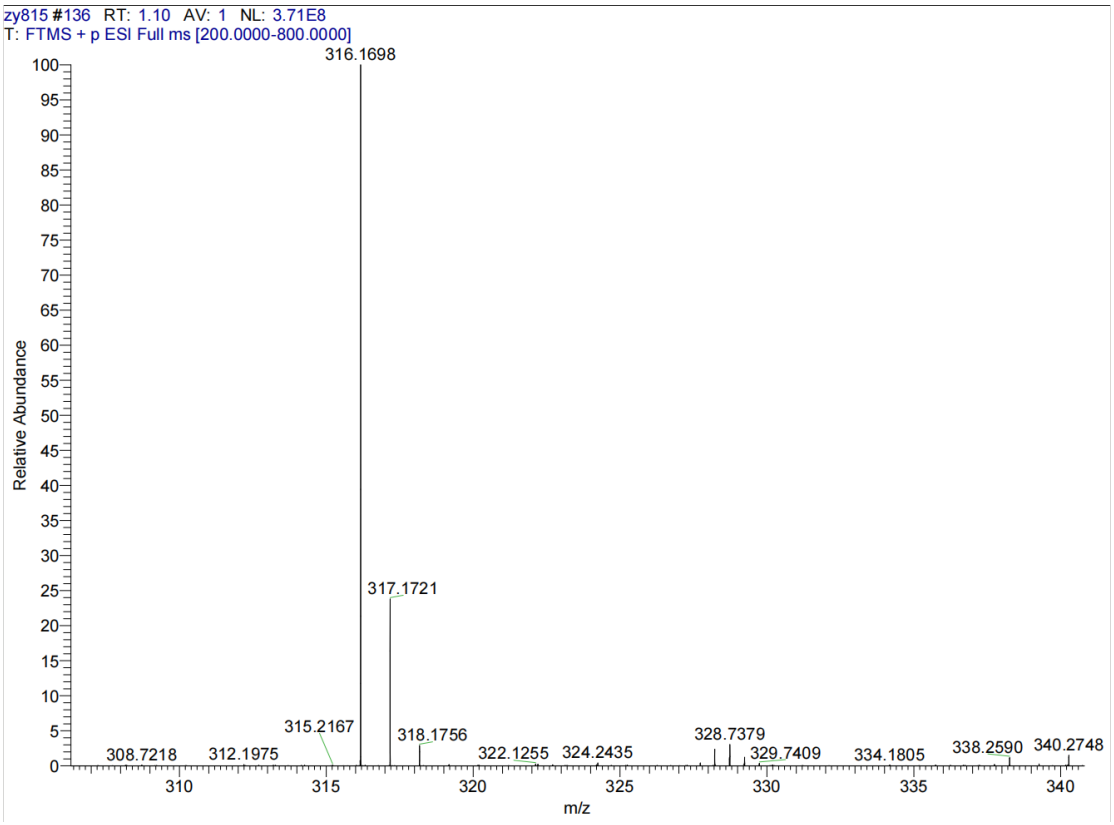
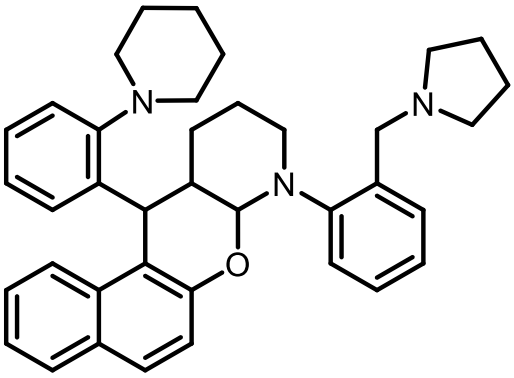


Figure S3 High resolution mass spectrum of intermediate **E**



Crystal Data

The crystal of **4a** was obtained from ethyl acetate/petroleum ether at room temperature The structure of compound **4a** was assigned by single crystal X-ray analysis. Diffraction data were collected on a Bruker Smart Apex II CCD diffractometer with graphite-monochromated Mo Kα (λ = 0.71073 Å). The crystal date of compound **4a** have been deposited in CCDC with number 2306808.



4a

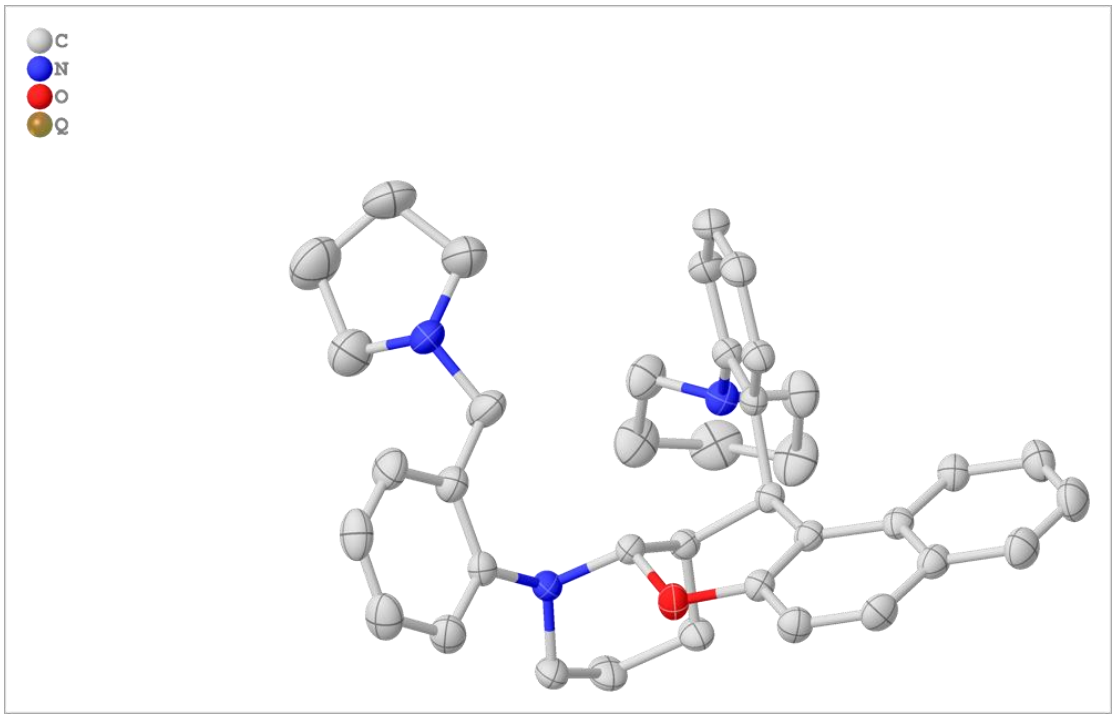


Figure S1 X-ray structure of compound **4a** (CCDC 2306808**)** (Thermal ellipsoids are drawn at the 50% probability level).

Table S1 Crystal data and structure refinement for 4a.

Identification code	**4a**
Empirical formula	$C_{38}H_{43}N_3O$
Formula weight	557.785
Temperature/K	296.15
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	13.2032(10)
b/Å	16.3569(13)
c/Å	14.4981(11)
α/°	90
β/°	93.013(2)
γ/°	90
Volume/Å^3	3126.7(4)
Z	4
ρ_{calc}g/cm^3	1.185
μ/mm^{-1}	0.071
F(000)	1000.0
Crystal size/mm^3	0.15 × 0.15 × 0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	1.88 to 28.37
Index ranges	-17≤h≤17, -21≤k≤21, -19≤l≤19
Reflections collected	59745
Independent reflections	7800 [R_{int} = 0.0743, R_{sigma} = 0.0464]
Data/restraints/parameters	7800/42/405
Goodness-of-fit on F^2	0.9940
Final R indexes [I>=2σ (I)]	R_1 = 0.0490, wR_2 = 0.1092
Final R indexes [all data]	R_1 = 0.1050, wR_2 = 0.1377
Largest diff. peak/hole / e Å^{-3}	0.3412/-0.2527

Table S2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **4a**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
O(1)	3250.0(11)	4208.0(10)	5677.9(10)	47.2(4)
N(1)	1471.9(14)	4283.9(11)	5490.5(12)	42.8(4)
N(2)	1582.9(14)	5439.5(11)	8648.9(13)	44.9(5)
N(3)	-132.5(17)	2556.6(15)	7084.9(15)	63.9(6)
C(1)	1482(2)	4980.7(15)	4856.1(17)	53.7(6)
C(2)	1523(2)	5777.2(15)	5389.0(18)	60.0(7)
C(3)	2397(2)	5799.2(14)	6114.7(17)	50.6(6)
C(4)	2331.3(16)	5052.3(13)	6730.8(14)	39.0(5)
C(5)	3188.3(16)	4986.9(13)	7489.1(14)	37.1(5)
C(6)	4159.5(16)	4712.8(13)	7063.5(15)	38.8(5)
C(7)	5125.3(17)	4825.5(13)	7534.9(16)	41.4(5)
C(8)	5237.2(18)	5170.1(14)	8426.5(17)	48.6(6)
C(9)	6162(2)	5273.2(17)	8870.4(19)	60.7(7)
C(10)	7046(2)	5028.9(19)	8440(2)	66.3(8)
C(11)	6974(2)	4692.7(17)	7586(2)	60.5(7)
C(12)	6025.4(17)	4578.4(15)	7108.9(17)	46.9(5)
C(13)	5932.8(18)	4228.2(16)	6215.8(18)	53.0(6)
C(14)	5018.2(18)	4128.7(16)	5767.2(17)	51.1(6)
C(15)	4125.4(16)	4359.5(13)	6198.3(15)	40.2(5)
C(16)	2309.3(15)	4287.5(13)	6157.7(14)	39.0(5)
C(17)	2856.4(16)	4425.1(13)	8262.3(14)	38.6(5)
C(18)	3288.0(18)	3666.2(13)	8415.6(16)	45.4(5)
C(19)	2947(2)	3132.2(15)	9075.0(17)	53.9(6)
C(20)	2143(2)	3350.1(17)	9586.7(18)	59.4(7)
C(21)	1701(2)	4108.9(16)	9448.0(17)	54.4(6)
C(22)	2044.9(17)	4655.0(14)	8800.6(14)	41.9(5)
C(23)	2016(2)	6085.7(17)	9228(2)	67.2(8)
C(24)	1657(3)	6915.3(19)	8870(3)	87.3(10)
C(25)	511(3)	6961(2)	8796(3)	87.9(10)
C(26)	78(2)	6246.5(19)	8256(3)	82.6(10)
C(27)	479(2)	5444.3(18)	8639(2)	67.9(8)
C(28)	1201.3(16)	3500.5(14)	5119.4(15)	42.8(5)
C(29)	1319.3(19)	3310.7(18)	4199.9(18)	59.0(7)
C(30)	1039(2)	2553(2)	3852(2)	70.1(8)
C(31)	667(2)	1975.8(19)	4410(2)	69.3(8)
C(32)	542(2)	2152.4(17)	5322(2)	66.2(8)
C(33)	791.2(19)	2908.0(16)	5691.3(17)	54.9(6)
C(34)	633(3)	3069(2)	6704(2)	79.5(10)
C(35)	-118(4)	2522(3)	8071(3)	126.4(18)
C(36)	-1084(3)	2116(3)	8286(3)	114.4(15)
C(37)	-1809(3)	2309(3)	7437(3)	119.0(15)
C(38)	-1152(3)	2718(3)	6744(3)	93.0(11)

Table S3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **4a**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
O(1)	39.6(8)	57.6(10)	44.4(8)	-9.3(7)	2.3(7)	-3.6(7)
N(1)	43.4(10)	43.7(10)	40.6(10)	6.1(8)	-4.5(8)	-6.3(8)
N(2)	41.6(10)	43.9(11)	49.6(11)	-4.2(9)	5.6(8)	1.4(8)
N(3)	60.4(14)	70.7(15)	60.3(14)	13.5(11)	1.3(11)	-25.3(11)
C(1)	56.5(15)	53.4(14)	49.7(14)	13.8(11)	-11.2(11)	-8.4(12)
C(2)	72.0(18)	46.1(14)	60.3(16)	16.3(12)	-12.0(13)	1.9(12)
C(3)	60.9(15)	37.1(12)	53.2(14)	5.4(10)	-4.4(11)	-1.3(11)
C(4)	37.3(11)	38.5(11)	41.1(11)	2.3(9)	2.8(9)	-0.3(9)
C(5)	38.2(11)	33.1(10)	39.9(11)	-1.2(9)	1.8(9)	-1.7(8)
C(6)	37.9(11)	33.7(11)	44.8(12)	2.3(9)	2.7(9)	-2.4(9)
C(7)	41.3(12)	35.0(11)	47.5(12)	3.8(9)	-0.2(9)	-1.7(9)
C(8)	44.8(13)	46.1(13)	54.4(14)	-3.3(11)	-1.3(10)	-0.1(10)
C(9)	59.3(16)	60.6(17)	60.6(16)	-7.1(13)	-12.7(13)	-3.3(13)
C(10)	45.5(15)	77(2)	74.6(19)	0.6(16)	-13.9(13)	-2.3(13)
C(11)	40.5(13)	68.4(18)	72.4(18)	0.6(14)	1.1(12)	1.4(12)
C(12)	38.5(12)	45.6(13)	56.6(14)	5.3(11)	3.1(10)	0.3(10)
C(13)	40.5(13)	59.7(15)	60.2(15)	-2.0(12)	15.6(11)	2.3(11)
C(14)	48.8(14)	57.0(15)	48.2(13)	-6.3(11)	9.2(11)	-1.9(11)
C(15)	38.2(11)	39.0(11)	43.4(11)	0.0(9)	2.5(9)	-2.6(9)
C(16)	36.4(11)	40.4(11)	40.2(11)	3.5(9)	1.0(9)	-4.0(9)
C(17)	39.1(11)	37.5(11)	38.7(11)	-0.6(9)	-2.5(9)	-4.5(9)
C(18)	48.6(13)	41.2(12)	46.0(12)	0.0(10)	-1.8(10)	1.4(10)
C(19)	62.3(16)	42.1(13)	56.3(14)	8.2(11)	-7.3(12)	-0.9(11)
C(20)	63.8(16)	60.4(16)	53.5(15)	16.9(13)	-1.8(12)	-12.6(13)
C(21)	51.5(14)	62.5(16)	49.5(14)	5.4(12)	5.7(11)	-5.8(12)
C(22)	42.6(12)	44.5(12)	38.4(11)	-0.9(9)	0.9(9)	-3.2(10)
C(23)	68.9(18)	55.7(16)	76.2(19)	-18.7(14)	-4.1(15)	1.1(14)
C(24)	88(2)	49.2(17)	124(3)	-15.0(18)	3(2)	0.8(16)
C(25)	94(3)	61(2)	111(3)	-4.4(19)	19(2)	25.1(17)
C(26)	57.8(18)	74(2)	116(3)	5.8(19)	2.2(17)	18.3(15)
C(27)	46.2(15)	64.8(18)	93(2)	1.6(16)	6.8(14)	5.8(13)
C(28)	36.2(11)	46.8(13)	44.8(12)	-1.4(10)	-2.8(9)	-1.8(9)
C(29)	54.3(15)	71.1(18)	52.0(14)	-7.2(13)	5.9(12)	-5.4(13)
C(30)	63.1(17)	84(2)	63.5(17)	-25.8(16)	5.1(14)	-1.6(15)
C(31)	58.2(17)	58.6(17)	89(2)	-26.5(16)	-11.7(15)	-0.3(13)
C(32)	68.6(18)	53.5(16)	75.7(19)	-3.5(14)	-3.5(15)	-16.3(13)
C(33)	55.6(15)	54.7(15)	54.2(14)	-1.6(12)	0.9(12)	-13.8(12)
C(34)	93(2)	83(2)	63.7(18)	-3.0(16)	14.7(16)	-44.8(18)
C(35)	136(4)	169(5)	73(2)	16(3)	-1(2)	-76(3)
C(36)	118(3)	145(4)	83(3)	25(3)	32(2)	-40(3)
C(37)	88(3)	148(4)	124(4)	-4(3)	38(3)	-25(3)
C(38)	71(2)	112(3)	97(3)	6(2)	11.4(19)	-7(2)

Table S4 Bond Lengths for **4a.**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O(1)	C(15)	1.369(3)	C(11)	C(12)	1.411(4)
O(1)	C(16)	1.461(2)	C(12)	C(13)	1.415(3)
N(1)	C(1)	1.465(3)	C(13)	C(14)	1.351(3)
N(1)	C(16)	1.430(3)	C(14)	C(15)	1.414(3)
N(1)	C(28)	1.428(3)	C(17)	C(18)	1.379(3)
N(2)	C(22)	1.433(3)	C(17)	C(22)	1.409(3)
N(2)	C(23)	1.449(3)	C(18)	C(19)	1.387(3)
N(2)	C(27)	1.456(3)	C(19)	C(20)	1.374(4)
N(3)	C(34)	1.445(3)	C(20)	C(21)	1.382(4)
N(3)	C(35)	1.430(4)	C(21)	C(22)	1.389(3)
N(3)	C(38)	1.434(4)	C(23)	C(24)	1.520(4)
C(1)	C(2)	1.514(4)	C(24)	C(25)	1.512(5)
C(2)	C(3)	1.520(3)	C(25)	C(26)	1.502(5)
C(3)	C(4)	1.519(3)	C(26)	C(27)	1.509(4)
C(4)	C(5)	1.539(3)	C(28)	C(29)	1.386(3)
C(4)	C(16)	1.501(3)	C(28)	C(33)	1.402(3)
C(5)	C(6)	1.520(3)	C(29)	C(30)	1.381(4)
C(5)	C(17)	1.531(3)	C(30)	C(31)	1.353(4)
C(6)	C(7)	1.427(3)	C(31)	C(32)	1.373(4)
C(6)	C(15)	1.380(3)	C(32)	C(33)	1.380(4)
C(7)	C(8)	1.411(3)	C(33)	C(34)	1.517(4)
C(7)	C(12)	1.426(3)	C(35)	C(36)	1.485(5)
C(8)	C(9)	1.360(3)	C(36)	C(37)	1.551(6)
C(9)	C(10)	1.410(4)	C(37)	C(38)	1.517(5)
C(10)	C(11)	1.353(4)			

Table S5 Bond Angles for **4a.**

Atom	Atom	Atom	Angle/°		Atom	Atom	Atom	Angle/°
C(15)	O(1)	C(16)	115.83(16)		O(1)	C(15)	C(14)	114.03(19)
C(16)	N(1)	C(1)	112.90(17)		C(6)	C(15)	C(14)	121.7(2)
C(28)	N(1)	C(1)	118.16(18)		O(1)	C(16)	C(4)	110.21(16)
C(28)	N(1)	C(16)	115.32(18)		N(1)	C(16)	O(1)	108.91(16)
C(22)	N(2)	C(23)	114.4(2)		N(1)	C(16)	C(4)	111.69(18)
C(22)	N(2)	C(27)	115.09(19)		C(18)	C(17)	C(5)	121.77(19)
C(23)	N(2)	C(27)	111.5(2)		C(18)	C(17)	C(22)	118.1(2)
C(35)	N(3)	C(34)	115.6(3)		C(22)	C(17)	C(5)	120.02(19)
C(35)	N(3)	C(38)	108.4(3)		C(17)	C(18)	C(19)	122.1(2)
C(38)	N(3)	C(34)	115.1(3)		C(20)	C(19)	C(18)	119.8(2)
N(1)	C(1)	C(2)	110.5(2)		C(19)	C(20)	C(21)	119.2(2)
C(1)	C(2)	C(3)	112.3(2)		C(20)	C(21)	C(22)	121.7(2)
C(4)	C(3)	C(2)	108.86(19)		C(17)	C(22)	N(2)	118.94(19)
C(3)	C(4)	C(5)	114.41(18)		C(21)	C(22)	N(2)	121.9(2)
C(16)	C(4)	C(3)	110.17(18)		C(21)	C(22)	C(17)	119.2(2)
C(16)	C(4)	C(5)	109.24(17)		N(2)	C(23)	C(24)	110.3(2)
C(6)	C(5)	C(4)	109.55(17)		C(25)	C(24)	C(23)	111.2(3)
C(6)	C(5)	C(17)	113.59(17)		C(26)	C(25)	C(24)	110.5(3)
C(17)	C(5)	C(4)	109.67(16)		C(25)	C(26)	C(27)	111.6(3)
C(7)	C(6)	C(5)	121.29(19)		N(2)	C(27)	C(26)	109.9(2)
C(15)	C(6)	C(5)	120.32(19)		C(29)	C(28)	N(1)	121.7(2)
C(15)	C(6)	C(7)	118.38(19)		C(29)	C(28)	C(33)	118.7(2)
C(8)	C(7)	C(6)	122.6(2)		C(33)	C(28)	N(1)	119.6(2)
C(8)	C(7)	C(12)	117.4(2)		C(30)	C(29)	C(28)	120.7(3)
C(12)	C(7)	C(6)	120.0(2)		C(31)	C(30)	C(29)	120.4(3)
C(9)	C(8)	C(7)	122.1(2)		C(30)	C(31)	C(32)	119.7(3)
C(8)	C(9)	C(10)	119.9(3)		C(31)	C(32)	C(33)	121.6(3)
C(11)	C(10)	C(9)	120.0(3)		C(28)	C(33)	C(34)	122.0(2)
C(10)	C(11)	C(12)	121.3(2)		C(32)	C(33)	C(28)	118.8(2)
C(11)	C(12)	C(7)	119.2(2)		C(32)	C(33)	C(34)	119.2(2)
C(11)	C(12)	C(13)	122.3(2)		N(3)	C(34)	C(33)	113.8(2)
C(13)	C(12)	C(7)	118.5(2)		N(3)	C(35)	C(36)	105.1(3)
C(14)	C(13)	C(12)	121.4(2)		C(35)	C(36)	C(37)	104.1(3)
C(13)	C(14)	C(15)	120.0(2)		C(38)	C(37)	C(36)	105.3(3)
O(1)	C(15)	C(6)	124.27(19)		N(3)	C(38)	C(37)	104.4(3)

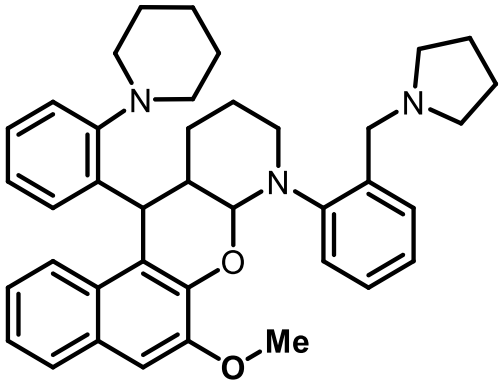
Table S6 Torsion Angles for **4a.**

A	B	C	D	Angle/°	A	B	C	D	Angle/°
N(1)	C(1)	C(2)	C(3)	53.3(3)	C(15)	C(6)	C(7)	C(8)	-179.1(2)
N(1)	C(28)	C(29)	C(30)	-179.0(2)	C(15)	C(6)	C(7)	C(12)	0.3(3)
N(1)	C(28)	C(33)	C(32)	-179.5(2)	C(16)	O(1)	C(15)	C(6)	-12.0(3)
N(1)	C(28)	C(33)	C(34)	-0.6(4)	C(16)	O(1)	C(15)	C(14)	168.65(19)
N(2)	C(23)	C(24)	C(25)	55.6(4)	C(16)	N(1)	C(1)	C(2)	-55.3(3)
N(3)	C(35)	C(36)	C(37)	-26.2(5)	C(16)	N(1)	C(28)	C(29)	-113.4(2)
C(1)	N(1)	C(16)	O(1)	-63.3(2)	C(16)	N(1)	C(28)	C(33)	67.6(3)
C(1)	N(1)	C(16)	C(4)	58.7(2)	C(16)	C(4)	C(5)	C(6)	48.6(2)
C(1)	N(1)	C(28)	C(29)	24.5(3)	C(16)	C(4)	C(5)	C(17)	-76.7(2)
C(1)	N(1)	C(28)	C(33)	-154.5(2)	C(17)	C(5)	C(6)	C(7)	-75.4(2)
C(1)	C(2)	C(3)	C(4)	-53.9(3)	C(17)	C(5)	C(6)	C(15)	105.8(2)
C(2)	C(3)	C(4)	C(5)	178.8(2)	C(17)	C(18)	C(19)	C(20)	1.2(4)
C(2)	C(3)	C(4)	C(16)	55.3(3)	C(18)	C(17)	C(22)	N(2)	-179.7(2)
C(3)	C(4)	C(5)	C(6)	-75.5(2)	C(18)	C(17)	C(22)	C(21)	-1.1(3)
C(3)	C(4)	C(5)	C(17)	159.23(19)	C(18)	C(19)	C(20)	C(21)	-1.4(4)
C(3)	C(4)	C(16)	O(1)	62.7(2)	C(19)	C(20)	C(21)	C(22)	0.4(4)
C(3)	C(4)	C(16)	N(1)	-58.5(2)	C(20)	C(21)	C(22)	N(2)	179.5(2)
C(4)	C(5)	C(6)	C(7)	161.62(18)	C(20)	C(21)	C(22)	C(17)	0.9(4)
C(4)	C(5)	C(6)	C(15)	-17.2(3)	C(22)	N(2)	C(23)	C(24)	166.8(2)
C(4)	C(5)	C(17)	C(18)	110.7(2)	C(22)	N(2)	C(27)	C(26)	-166.7(2)
C(4)	C(5)	C(17)	C(22)	-65.1(2)	C(22)	C(17)	C(18)	C(19)	0.1(3)
C(5)	C(4)	C(16)	O(1)	-63.8(2)	C(23)	N(2)	C(22)	C(17)	-92.0(3)
C(5)	C(4)	C(16)	N(1)	175.02(16)	C(23)	N(2)	C(22)	C(21)	89.5(3)
C(5)	C(6)	C(7)	C(8)	2.1(3)	C(23)	N(2)	C(27)	C(26)	60.9(3)
C(5)	C(6)	C(7)	C(12)	-178.60(19)	C(23)	C(24)	C(25)	C(26)	-51.8(4)
C(5)	C(6)	C(15)	O(1)	-1.9(3)	C(24)	C(25)	C(26)	C(27)	52.6(4)
C(5)	C(6)	C(15)	C(14)	177.4(2)	C(25)	C(26)	C(27)	N(2)	-56.7(4)
C(5)	C(17)	C(18)	C(19)	-175.8(2)	C(27)	N(2)	C(22)	C(17)	137.0(2)
C(5)	C(17)	C(22)	N(2)	-3.8(3)	C(27)	N(2)	C(22)	C(21)	-41.5(3)
C(5)	C(17)	C(22)	C(21)	174.8(2)	C(27)	N(2)	C(23)	C(24)	-60.5(3)
C(6)	C(5)	C(17)	C(18)	-12.3(3)	C(28)	N(1)	C(1)	C(2)	165.8(2)
C(6)	C(5)	C(17)	C(22)	171.93(19)	C(28)	N(1)	C(16)	O(1)	76.8(2)
C(6)	C(7)	C(8)	C(9)	179.9(2)	C(28)	N(1)	C(16)	C(4)	-161.28(18)
C(6)	C(7)	C(12)	C(11)	-179.8(2)	C(28)	C(29)	C(30)	C(31)	-1.6(4)
C(6)	C(7)	C(12)	C(13)	0.4(3)	C(28)	C(33)	C(34)	N(3)	156.6(3)
C(7)	C(6)	C(15)	O(1)	179.17(19)	C(29)	C(28)	C(33)	C(32)	1.4(4)
C(7)	C(6)	C(15)	C(14)	-1.5(3)	C(29)	C(28)	C(33)	C(34)	-179.7(3)
C(7)	C(8)	C(9)	C(10)	-0.3(4)	C(29)	C(30)	C(31)	C(32)	1.8(5)
C(7)	C(12)	C(13)	C(14)	0.2(4)	C(30)	C(31)	C(32)	C(33)	-0.3(5)
C(8)	C(7)	C(12)	C(11)	-0.5(3)	C(31)	C(32)	C(33)	C(28)	-1.3(4)
C(8)	C(7)	C(12)	C(13)	179.8(2)	C(31)	C(32)	C(33)	C(34)	179.8(3)
C(8)	C(9)	C(10)	C(11)	0.0(4)	C(32)	C(33)	C(34)	N(3)	-24.5(4)
C(9)	C(10)	C(11)	C(12)	0.0(4)	C(33)	C(28)	C(29)	C(30)	0.0(4)
C(10)	C(11)	C(12)	C(7)	0.2(4)	C(34)	N(3)	C(35)	C(36)	168.3(4)
C(10)	C(11)	C(12)	C(13)	180.0(3)	C(34)	N(3)	C(38)	C(37)	-163.1(3)
C(11)	C(12)	C(13)	C(14)	-179.6(2)	C(35)	N(3)	C(34)	C(33)	163.5(4)
C(12)	C(7)	C(8)	C(9)	0.5(3)	C(35)	N(3)	C(38)	C(37)	-31.9(4)
C(12)	C(13)	C(14)	C(15)	-1.4(4)	C(35)	C(36)	C(37)	C(38)	7.3(5)
C(13)	C(14)	C(15)	O(1)	-178.5(2)	C(36)	C(37)	C(38)	N(3)	14.1(5)
C(13)	C(14)	C(15)	C(6)	2.2(4)	C(38)	N(3)	C(34)	C(33)	-68.9(4)
C(15)	O(1)	C(16)	N(1)	167.81(17)	C(38)	N(3)	C(35)	C(36)	37.3(5)
C(15)	O(1)	C(16)	C(4)	45.0(2)					

Table S7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for **4a.**

Atom	***x***	***y***	***z***	**U(eq)**
H(3)	17	2000	6883	77
H(1A)	876	4970	4447	64
H(1B)	2067	4942	4481	64
H(2A)	890	5852	5688	72
H(2B)	1596	6227	4961	72
H(3A)	3038	5800	5817	61
H(3B)	2359	6293	6482	61
H(4)	1688	5084	7037	47
H(5)	3305	5533	7751	44
H(8)	4661	5332	8720	58
H(9)	6211	5505	9457	73
H(10)	7678	5099	8743	80
H(11)	7562	4534	7309	73
H(13)	6514	4063	5932	64
H(14)	4976	3908	5175	61
H(16)	2246	3816	6568	47
H(18)	3825	3507	8066	54
H(19)	3262	2628	9170	65
H(20)	1900	2991	10021	71
H(21)	1159	4258	9797	65
H(23A)	2750	6059	9232	81
H(23B)	1815	6012	9857	81
H(24A)	1919	7339	9285	105
H(24B)	1920	7012	8268	105
H(25A)	252	6961	9409	106
H(25B)	302	7466	8492	106
H(26A)	250	6297	7616	99
H(26B)	-655	6253	8275	99
H(27A)	260	5368	9261	82
H(27B)	211	4997	8260	82
H(29)	1590	3698	3813	71
H(30)	1106	2440	3229	84
H(31)	496	1462	4176	83
H(32)	283	1753	5701	79
H(34A)	1271	2984	7054	95
H(34B)	442	3637	6777	95
H(35A)	-82	3067	8334	152
H(35B)	459	2208	8315	152
H(36A)	-1346	2337	8847	137
H(36B)	-989	1531	8359	137
H(37A)	-2107	1810	7182	143
H(37B)	-2349	2671	7608	143
H(38A)	-1278	2487	6133	112
H(38B)	-1282	3301	6716	112

The crystal of **4n** was obtained from ethyl acetate/petroleum ether at room temperature The structure of compound **4n** was assigned by single crystal X-ray analysis. Diffraction data were collected on a Bruker Smart Apex II CCD diffractometer with graphite-monochromated Mo Kα (λ = 0.71073 Å). The crystal date of compound **4n** have been deposited in CCDC with number 2375645.



4n

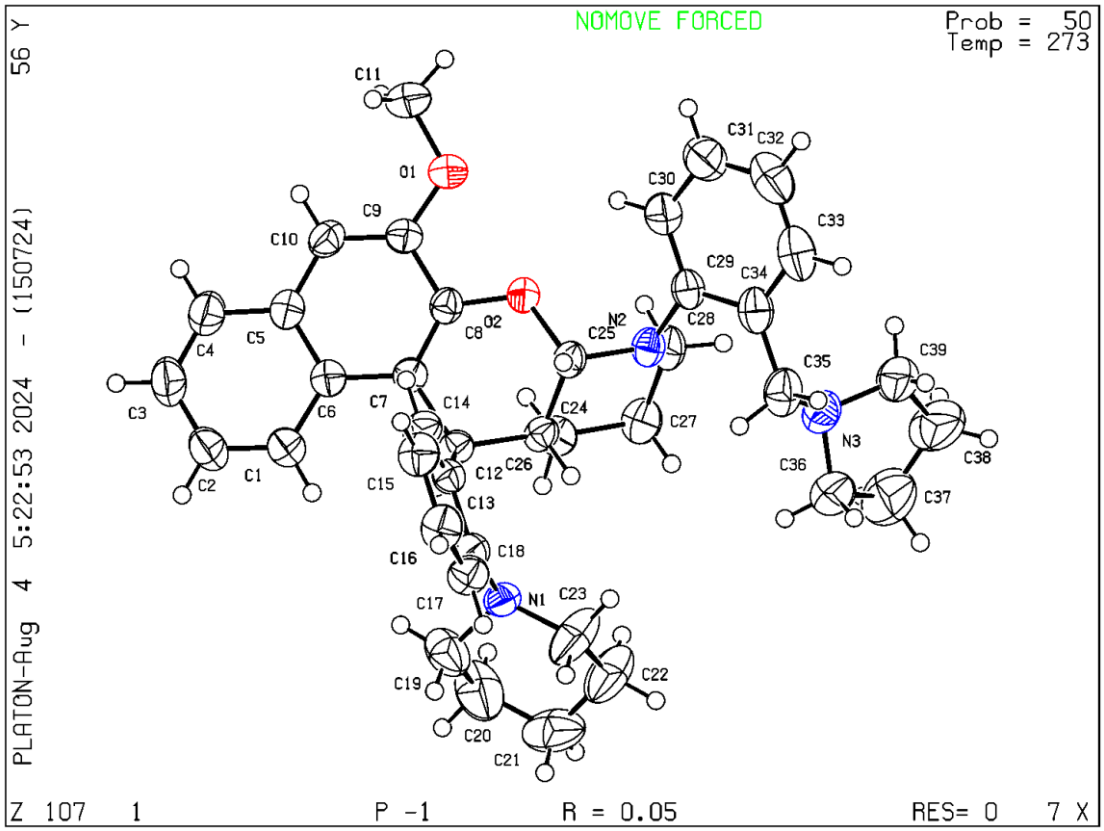


Figure S1 X-ray structure of compound **4n** (CCDC 2375645**)** (Thermal ellipsoids are drawn at the 50% probability level).

Table S1 Crystal data and structure refinement for 4n.

Identification code	**4n**
Empirical formula	$C_{39}H_{45}N_3O_2$
Formula weight	587.78
Temperature/K	273.15
Crystal system	triclinic
Space group	P-1
a/Å	9.5701(5)
b/Å	12.7196(8)
c/Å	14.9523(9)
α/°	105.788(2)
β/°	92.153(2)
γ/°	109.699(2)
Volume/Å^3	1632.07(17)
Z	2
ρ_{calc}g/cm^3	1.196
μ/mm^{-1}	0.074
F(000)	632.0
Crystal size/mm^3	0.23 × 0.22 × 0.18
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.568 to 56.604
Index ranges	-12 ≤ h ≤ 11, -16 ≤ k ≤ 16, -19 ≤ l ≤ 19
Reflections collected	35820
Independent reflections	8087 [R_{int} = 0.0711, R_{sigma} = 0.0512]
Data/restraints/parameters	8087/0/398
Goodness-of-fit on F^2	1.033
Final R indexes [I>=2σ (I)]	R_1 = 0.0547, wR_2 = 0.1314
Final R indexes [all data]	R_1 = 0.0943, wR_2 = 0.1655
Largest diff. peak/hole / e Å^{-3}	0.27/-0.25

Table S2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **4n**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
O2	5523.9(13)	6508.5(10)	3411.8(8)	44.4(3)
O1	3679.7(15)	5079.8(11)	4100.4(9)	54.0(4)
N2	6757.1(15)	8521.3(12)	3565.3(10)	40.4(3)
N1	9421.9(16)	6936.2(12)	890.0(10)	42.1(3)
N3	8244.4(18)	11280.4(14)	3783.6(12)	54.3(4)
C8	5231.7(17)	5363.7(14)	2940.4(12)	37.6(4)
C13	8629.6(18)	5929.6(14)	2066.1(11)	36.8(4)
C6	5432.5(19)	3739.2(15)	1730.6(12)	40.2(4)
C7	5870.7(17)	4976.9(14)	2176.9(11)	37.5(4)
C18	9782.4(18)	6477.3(14)	1610.5(12)	38.7(4)
C12	7027.5(17)	5852.2(14)	1816.5(12)	36.9(4)
C9	4159.0(19)	4560.0(15)	3314.1(12)	41.9(4)
C25	6838.6(18)	7390.7(14)	3218.6(12)	38.0(4)
C24	6906.3(18)	7068.7(14)	2171.5(12)	38.6(4)
C5	4326(2)	2949.2(15)	2083.1(13)	44.2(4)
C14	8999(2)	5520.2(16)	2777.3(13)	45.5(4)
C29	7024.3(19)	9062.0(15)	4560.2(13)	42.7(4)
C10	3717(2)	3388.1(15)	2883.6(13)	46.2(4)
C28	5513(2)	8691.7(16)	3092.2(14)	47.7(4)
C1	6050(2)	3265.3(17)	947.9(13)	51.0(5)
C17	11244.4(19)	6581.2(16)	1879.8(14)	49.3(4)
C26	5588(2)	7171.1(16)	1641.8(13)	46.7(4)
C34	8124(2)	10184.0(16)	4916.3(14)	48.6(4)
C27	5534(2)	8390.7(17)	2048.3(14)	53.0(5)
C16	11585(2)	6171.2(17)	2587.1(15)	53.3(5)
C15	10463(2)	5641.8(17)	3040.0(14)	51.2(5)
C4	3856(2)	1731.1(17)	1617.7(15)	57.7(5)
C30	6197(2)	8529.3(17)	5161.6(14)	56.7(5)
C35	9041(2)	10769.7(17)	4273.1(16)	57.6(5)
C2	5576(3)	2080.7(18)	519.7(15)	63.0(6)
C3	4459(3)	1310.9(18)	850.6(16)	67.8(6)
C33	8329(3)	10739.9(19)	5876.4(16)	63.7(6)
C11	2813(3)	4331(2)	4590.6(16)	70.6(7)
C31	6425(3)	9100(2)	6111.4(16)	70.6(6)
C32	7484(3)	10208(2)	6466.7(16)	70.5(6)
C19	9211(3)	6171(2)	-55.3(15)	73.5(7)
C39	8100(3)	12340(2)	4367.2(18)	73.2(7)
C36	8916(3)	11605(2)	2995.9(18)	74.1(7)
C22	9773(4)	8620(2)	323(2)	90.4(9)
C20	8569(4)	6622(2)	-749.0(17)	95.4(10)
C21	9553(3)	7856(3)	-675(2)	90.4(9)
C23	10393(3)	8129(2)	991(2)	85.6(8)
C38	7728(4)	12937(3)	3699(2)	103.6(10)
C37	8099(5)	12350(3)	2765(2)	110.1(11)

Table S3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **4n**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
O2	49.2(7)	33.4(6)	51.1(7)	12.3(5)	17.5(6)	14.8(5)
O1	58.0(8)	48.4(7)	56.6(8)	17.7(6)	26.5(6)	16.9(6)
N2	40.3(7)	35.6(7)	48.1(8)	13.6(6)	3.5(6)	16.8(6)
N1	45.1(8)	43.2(8)	42.3(8)	18.5(6)	11.0(6)	16.3(6)
N3	48.7(9)	45.4(9)	67.8(11)	20.1(8)	10.3(8)	13.3(7)
C8	35.4(8)	34.4(8)	43.7(9)	12.0(7)	4.5(7)	13.3(7)
C13	38.1(8)	35.5(8)	38.6(9)	10.4(7)	6.5(7)	15.8(7)
C6	40.6(9)	40.2(9)	40.0(9)	11.8(7)	2.7(7)	15.5(7)
C7	34.8(8)	37.8(8)	40.4(9)	12.6(7)	5.2(7)	13.2(7)
C18	38.3(8)	38.9(9)	41.6(9)	12.6(7)	7.0(7)	16.7(7)
C12	34.9(8)	38.5(8)	39.6(9)	14.0(7)	6.4(7)	14.0(7)
C9	40.4(9)	43.2(9)	43.4(9)	14.1(8)	10.6(7)	15.5(7)
C25	34.5(8)	34.9(8)	47.4(10)	14.6(7)	5.8(7)	14.5(7)
C24	35.2(8)	38.4(9)	48.4(10)	19.2(7)	9.0(7)	15.8(7)
C5	46.4(9)	37.3(9)	46.8(10)	12.4(8)	2.7(8)	13.2(7)
C14	46.2(9)	49.1(10)	50.1(10)	23.7(8)	10.1(8)	20.7(8)
C29	45.7(9)	38.0(9)	48.8(10)	11.5(8)	5.5(8)	21.9(7)
C10	42.0(9)	39.3(9)	55.0(11)	17.8(8)	11.0(8)	8.5(7)
C28	44.0(9)	40.4(9)	63.1(12)	15.5(8)	3.3(8)	21.3(8)
C1	58.3(11)	47.6(10)	47.0(10)	12.1(8)	10.3(9)	20.6(9)
C17	37.1(9)	53.0(11)	60.8(12)	20.1(9)	10.4(8)	17.2(8)
C26	47.2(10)	53.9(11)	46.3(10)	17.7(8)	3.6(8)	25.6(8)
C34	46.1(10)	42.0(10)	59.1(12)	10.5(9)	-2.7(8)	22.4(8)
C27	54.3(11)	54.6(11)	61.4(12)	24.9(10)	1.0(9)	28.7(9)
C16	39.7(9)	53.9(11)	69.4(13)	19.3(10)	0.6(9)	21.2(8)
C15	53.0(11)	54.8(11)	53.2(11)	21.1(9)	-0.5(9)	25.6(9)
C4	65.1(12)	40.8(10)	60.4(12)	13.8(9)	6.7(10)	12.1(9)
C30	71.2(13)	46.3(11)	55.0(12)	14.4(9)	13.9(10)	24.3(10)
C35	40.3(10)	45.5(10)	81.2(15)	13.7(10)	3.9(9)	12.9(8)
C2	83.9(15)	53.8(12)	50.0(11)	6.4(10)	14.2(11)	30.3(11)
C3	90.4(17)	39.8(11)	63.0(14)	4.1(10)	7.1(12)	20.1(11)
C33	64.6(13)	50.9(12)	67.3(14)	0.5(10)	-12.3(11)	26.3(10)
C11	76.0(15)	63.3(13)	69.6(14)	24.3(11)	37.9(12)	15.2(11)
C31	101.8(19)	67.3(15)	57.3(13)	22.6(11)	21.2(13)	44.5(14)
C32	95.0(18)	72.8(15)	50.4(12)	6.0(11)	-1.5(12)	50.0(14)
C19	118(2)	75.9(15)	46.1(12)	17.7(11)	11.8(12)	59.5(15)
C39	90.9(17)	61.1(14)	87.7(17)	36.0(13)	34.0(14)	39.6(13)
C36	76.1(15)	60.8(14)	74.2(15)	20.0(12)	21.4(13)	10.2(12)
C22	108(2)	67.3(16)	92(2)	49.0(15)	-9.6(16)	9.4(14)
C20	161(3)	87.0(19)	47.4(13)	13.6(13)	-10.9(16)	65(2)
C21	102(2)	130(3)	83.3(19)	72.7(19)	34.0(16)	62.8(19)
C23	87.6(18)	64.4(15)	92.5(19)	48.5(14)	-16.3(14)	-4.2(13)
C38	125(3)	105(2)	133(3)	78(2)	57(2)	69(2)
C37	156(3)	97(2)	99(2)	54.9(19)	22(2)	52(2)

Table S4 Bond Lengths for **4n.**

Atom	Atom	Length/Å		Atom	Atom	Length/Å
O2	C8	1.3591(19)		C24	C26	1.526(2)
O2	C25	1.4757(19)		C5	C10	1.412(3)
O1	C9	1.361(2)		C5	C4	1.417(3)
O1	C11	1.423(2)		C14	C15	1.386(3)
N2	C25	1.420(2)		C29	C34	1.400(2)
N2	C29	1.431(2)		C29	C30	1.385(3)
N2	C28	1.469(2)		C28	C27	1.505(3)
N1	C18	1.439(2)		C1	C2	1.371(3)
N1	C19	1.443(3)		C17	C16	1.373(3)
N1	C23	1.450(3)		C26	C27	1.524(3)
N3	C35	1.446(3)		C34	C35	1.504(3)
N3	C39	1.446(3)		C34	C33	1.390(3)
N3	C36	1.453(3)		C16	C15	1.371(3)
C8	C7	1.367(2)		C4	C3	1.363(3)
C8	C9	1.434(2)		C30	C31	1.379(3)
C13	C18	1.401(2)		C2	C3	1.394(3)
C13	C12	1.528(2)		C33	C32	1.378(3)
C13	C14	1.387(2)		C31	C32	1.373(3)
C6	C7	1.436(2)		C19	C20	1.515(3)
C6	C5	1.422(2)		C39	C38	1.506(3)
C6	C1	1.411(2)		C36	C37	1.512(4)
C7	C12	1.515(2)		C22	C21	1.505(4)
C18	C17	1.393(2)		C22	C23	1.512(3)
C12	C24	1.539(2)		C20	C21	1.505(4)
C9	C10	1.359(2)		C38	C37	1.510(4)
C25	C24	1.516(2)				

Table S5 Bond Angles for **4n.**

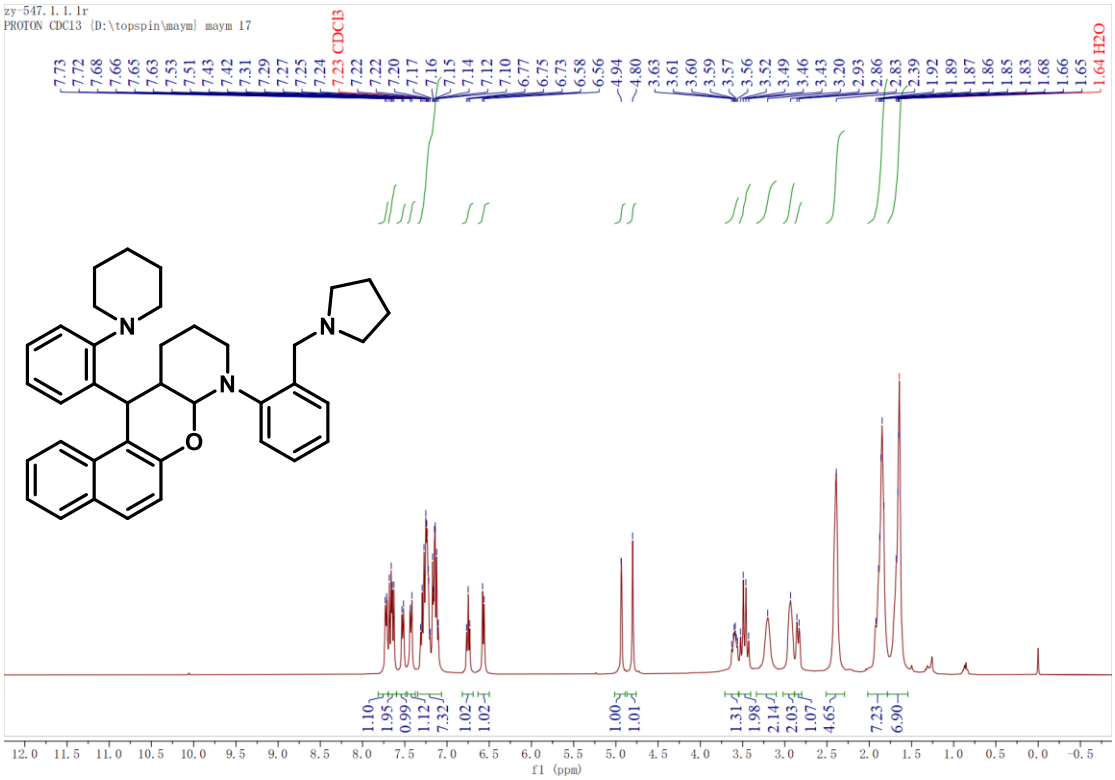
Atom	Atom	Atom	Angle/°		Atom	Atom	Atom	Angle/°
C8	O2	C25	117.56(12)		C26	C24	C12	113.25(14)
C9	O1	C11	116.77(15)		C10	C5	C6	119.73(15)
C25	N2	C29	118.02(14)		C10	C5	C4	121.33(17)
C25	N2	C28	115.19(14)		C4	C5	C6	118.94(17)
C29	N2	C28	113.32(13)		C15	C14	C13	121.68(17)
C18	N1	C19	114.57(15)		C34	C29	N2	117.81(16)
C18	N1	C23	114.23(15)		C30	C29	N2	122.09(16)
C19	N1	C23	112.35(18)		C30	C29	C34	120.05(18)
C35	N3	C39	114.11(18)		C9	C10	C5	120.76(16)
C35	N3	C36	114.75(18)		N2	C28	C27	110.97(15)
C39	N3	C36	104.50(17)		C2	C1	C6	121.36(18)
O2	C8	C7	124.83(14)		C16	C17	C18	121.62(17)
O2	C8	C9	113.76(14)		C27	C26	C24	109.81(15)
C7	C8	C9	121.40(15)		C29	C34	C35	120.68(18)
C18	C13	C12	120.31(14)		C33	C34	C29	118.02(19)
C14	C13	C18	118.24(15)		C33	C34	C35	121.30(18)
C14	C13	C12	121.36(15)		C28	C27	C26	111.54(15)
C5	C6	C7	119.18(15)		C15	C16	C17	119.50(17)
C1	C6	C7	122.75(15)		C16	C15	C14	119.81(18)
C1	C6	C5	118.06(16)		C3	C4	C5	121.10(19)
C8	C7	C6	119.08(15)		C31	C30	C29	120.7(2)
C8	C7	C12	119.88(14)		N3	C35	C34	112.51(15)
C6	C7	C12	121.04(14)		C1	C2	C3	120.38(19)
C13	C18	N1	118.83(14)		C4	C3	C2	120.11(19)
C17	C18	N1	122.01(15)		C32	C33	C34	121.4(2)
C17	C18	C13	119.15(16)		C32	C31	C30	119.7(2)
C13	C12	C24	110.50(13)		C31	C32	C33	120.0(2)
C7	C12	C13	113.16(13)		N1	C19	C20	110.76(18)
C7	C12	C24	110.48(13)		N3	C39	C38	105.7(2)
O1	C9	C8	114.33(14)		N3	C36	C37	103.5(2)
C10	C9	O1	125.89(15)		C21	C22	C23	110.7(3)
C10	C9	C8	119.78(15)		C21	C20	C19	110.9(2)
O2	C25	C24	109.42(13)		C20	C21	C22	109.4(2)
N2	C25	O2	109.95(12)		N1	C23	C22	110.8(2)
N2	C25	C24	111.33(13)		C39	C38	C37	105.3(2)
C25	C24	C12	110.36(13)		C38	C37	C36	104.2(2)
C25	C24	C26	110.83(12)					

Table S6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for **4n.**

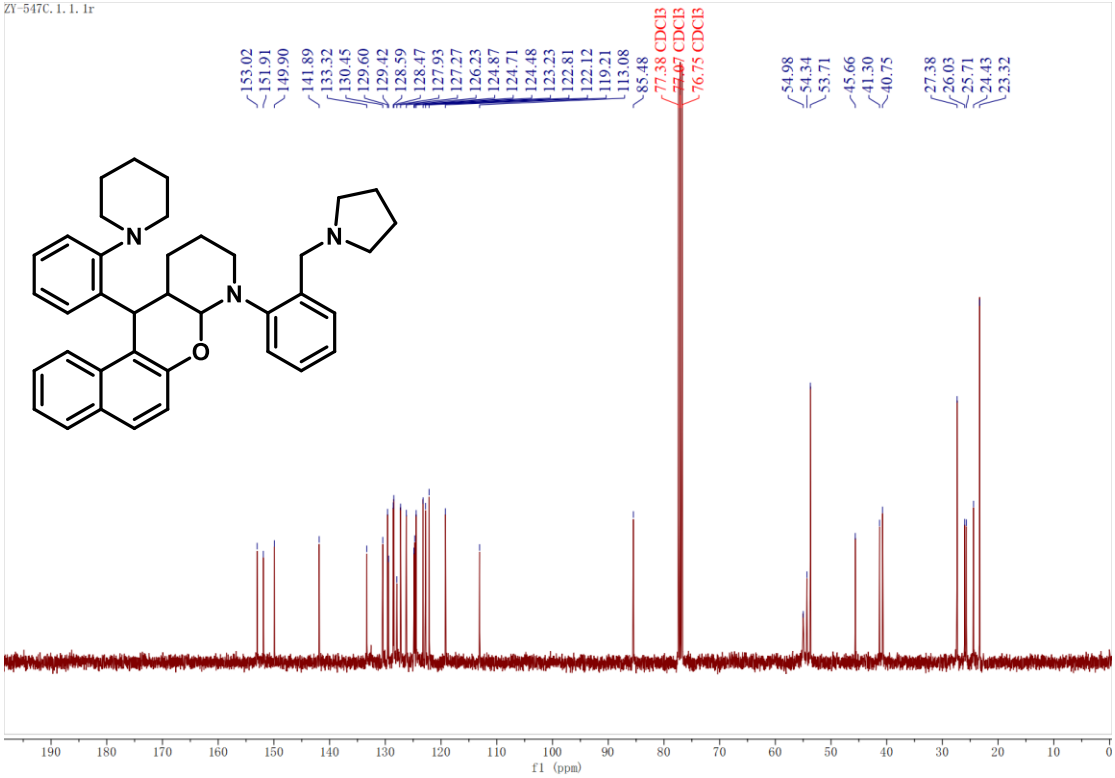
Atom	***x***	***y***	***z***	**U(eq)**
H12	6797.87	5590.3	1130.03	44
H25	7747.64	7389.28	3541.85	46
H24	7825.2	7638.82	2071.64	46
H14	8245.09	5154.83	3085.77	55
H10	3005.22	2869.51	3119.2	55
H28A	5592.38	9501.38	3339.09	57
H28B	4568.37	8199.91	3219.16	57
H1	6795.34	3767.16	717.97	61
H17	12008.32	6936.87	1572.97	59
H26A	5696.5	7030.5	981.84	56
H26B	4659.04	6586.11	1694.39	56
H27A	6401.71	8963.3	1917.48	64
H27B	4643.03	8426.76	1746.35	64
H16	12568.94	6251.99	2757.64	64
H15	10684.45	5365.14	3522.06	61
H4	3123.49	1209.34	1839.22	69
H30	5479.72	7778.48	4922.19	68
H35A	9955.79	11378.69	4638.09	69
H35B	9320.58	10197.89	3816.74	69
H2	6000.75	1788.74	5.32	76
H3	4124.56	509.39	547.44	81
H33	9051.21	11486.91	6125.81	76
H11A	1872.17	3827.79	4207.83	106
H11B	2634.57	4796.65	5165.82	106
H11C	3347.97	3864.14	4728.9	106
H31	5862.94	8736.31	6510.02	85
H32	7631.58	10600.2	7105.82	85
H19A	8535.08	5390.25	-94.01	88
H19B	10165.08	6122.09	-214.23	88
H39A	9031.08	12839.97	4778.87	88
H39B	7307.33	12155.04	4748.28	88
H36A	8760.25	10916.62	2466.63	89
H36B	9983.15	12047.3	3170.8	89
H22A	8821.2	8671.27	485.83	109
H22B	10459.95	9404.65	381.41	109
H20A	8480.66	6117.08	-1381.55	114
H20B	7573.14	6600.92	-626.09	114
H21A	9089.57	8150.36	-1090.1	108
H21B	10516.36	7868.15	-862.46	108
H23A	11384.71	8144.02	863.91	103
H23B	10484.38	8614.12	1631.44	103
H38A	8322.39	13768.05	3909.02	124
H38B	6673.97	12835.79	3652.04	124
H37A	8733.91	12926.85	2499.91	132
H37B	7193.54	11869.52	2323.53	132

NMR Spectra

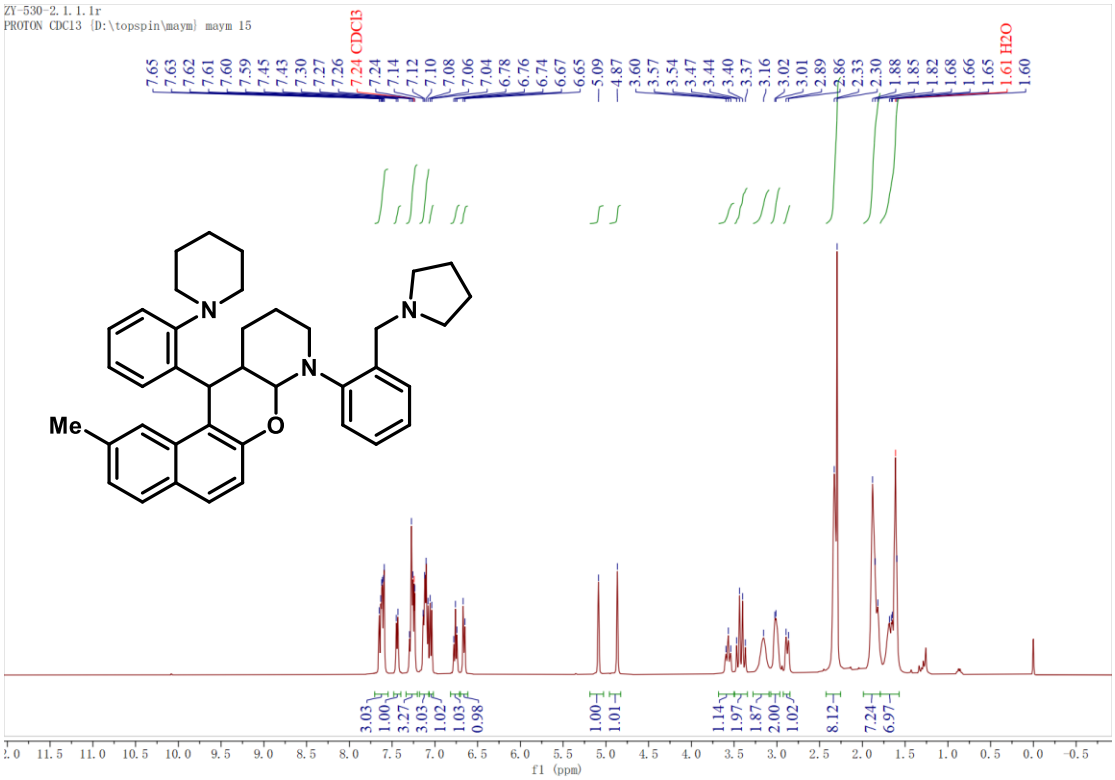
^{1}H NMR of Compound **4a** (400 MHz, $CDCl_3$)



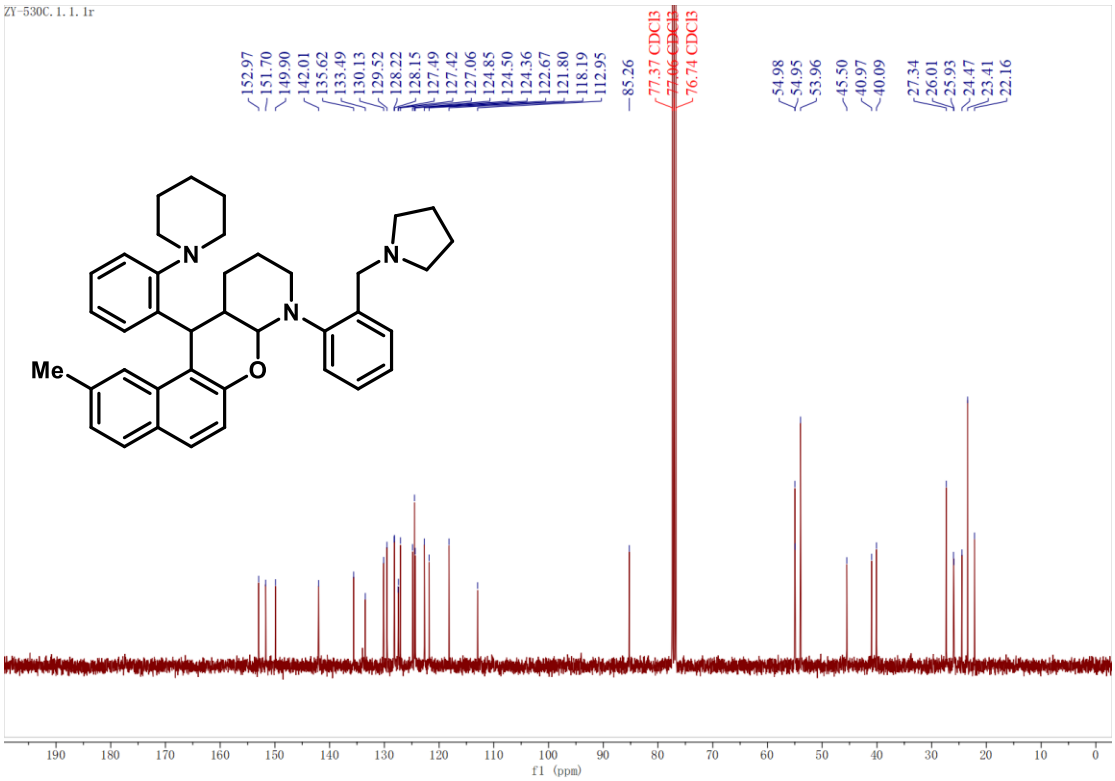
^{13}C NMR of Compound **4a** (101 MHz, $CDCl_3$)



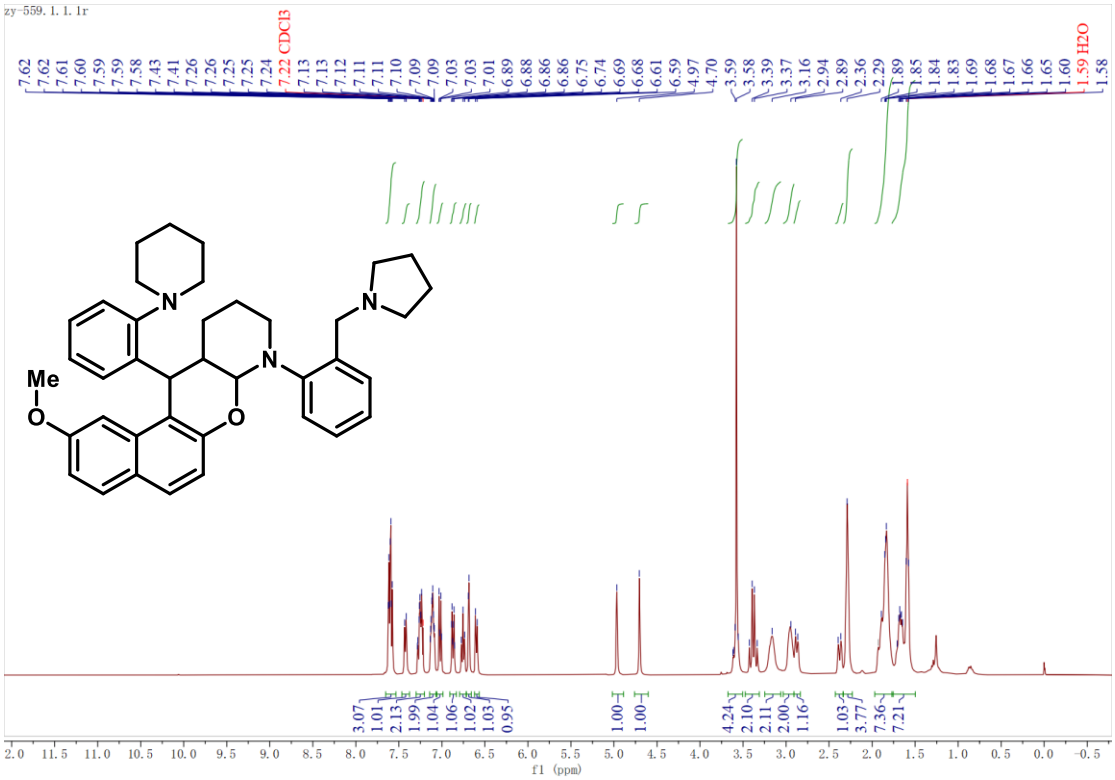
^{1}H NMR of Compound **4b** (400 MHz, $CDCl_3$)



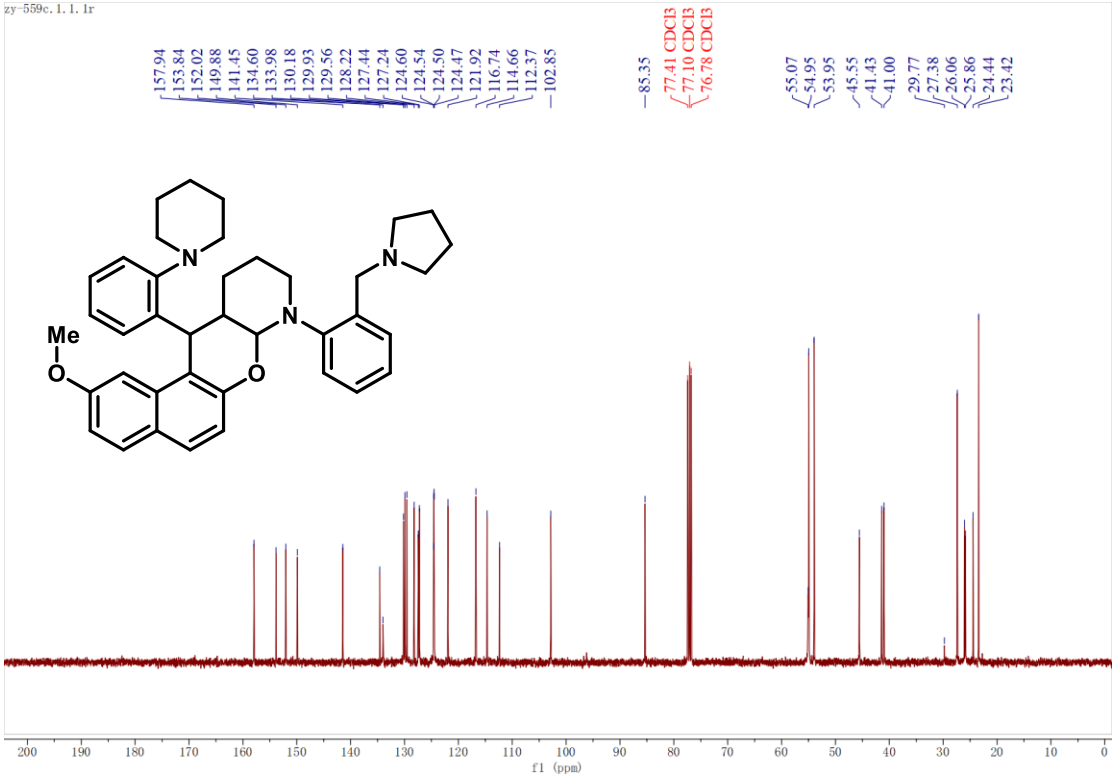
^{13}C NMR of Compound **4b** (101 MHz, $CDCl_3$)



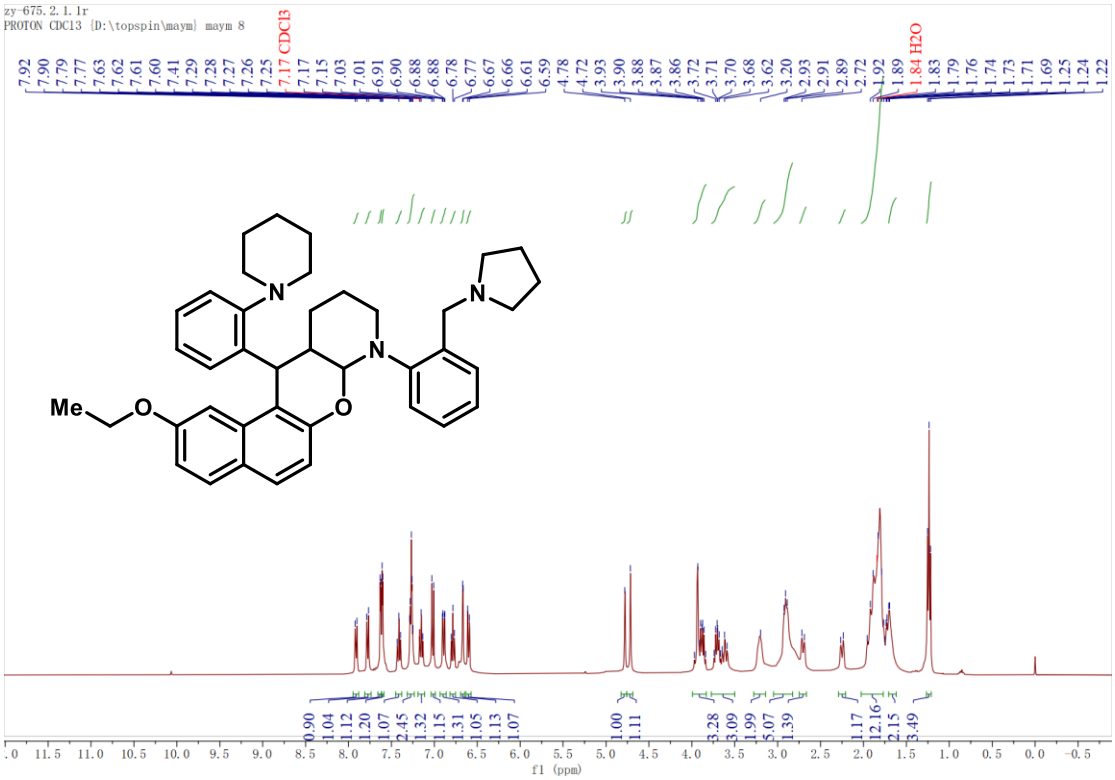
^{1}H NMR of Compound **4c** (400 MHz, $CDCl_3$)



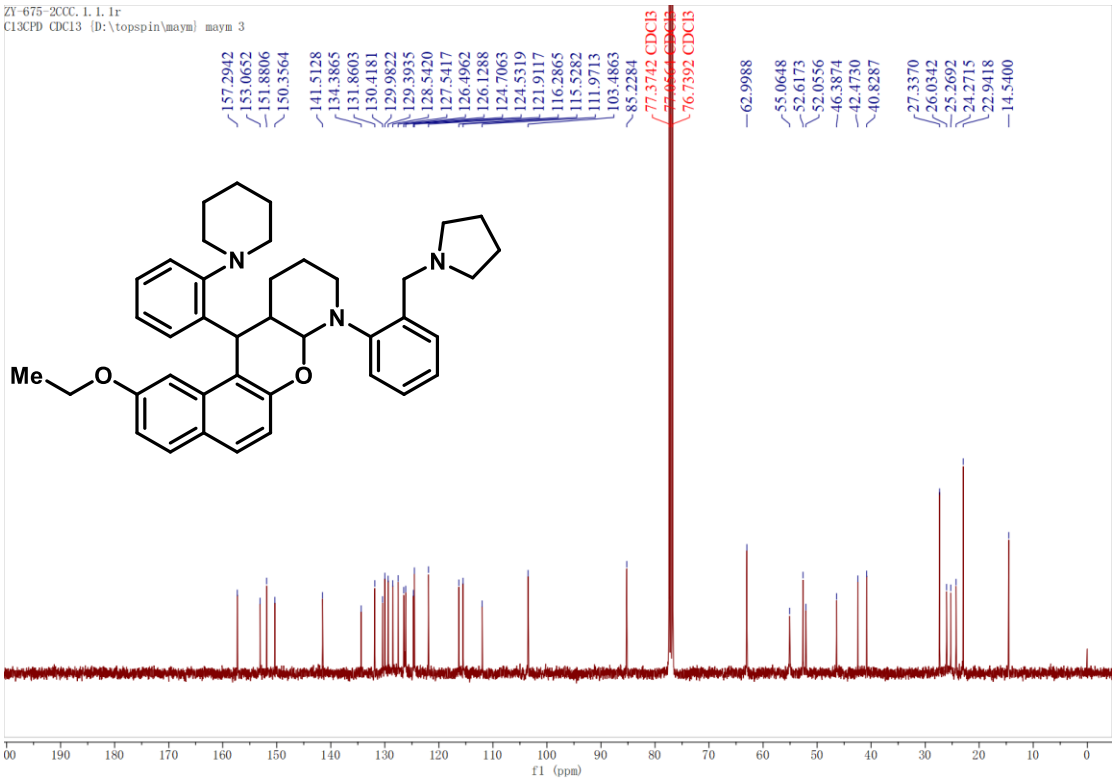
^{13}C NMR of Compound **4c** (101 MHz, $CDCl_3$)



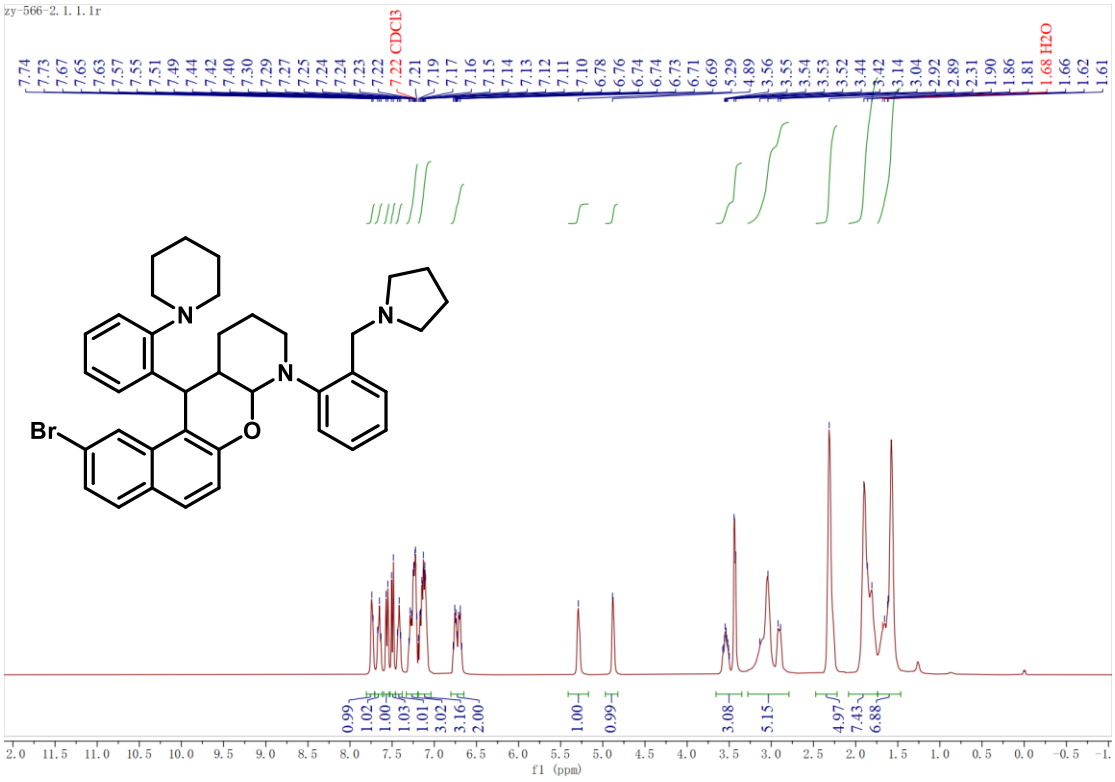
^{1}H NMR of Compound **4d** (400 MHz, $CDCl_3$)



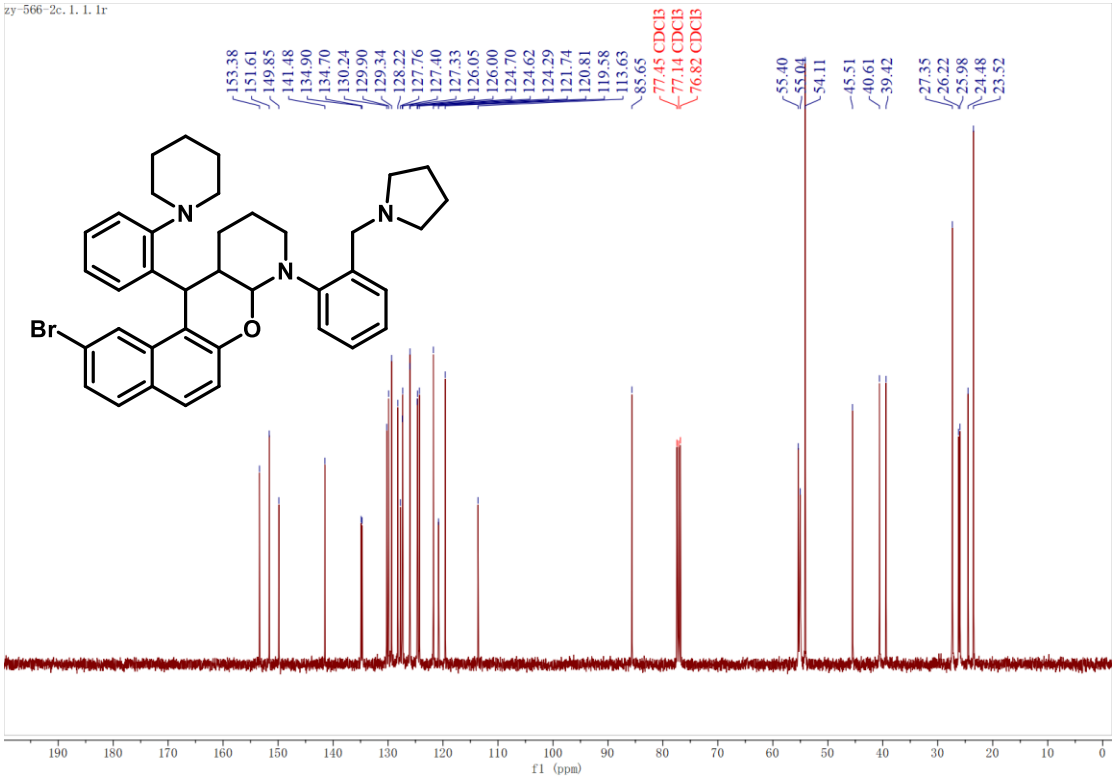
^{13}C NMR of Compound **4d** (101 MHz, $CDCl_3$)



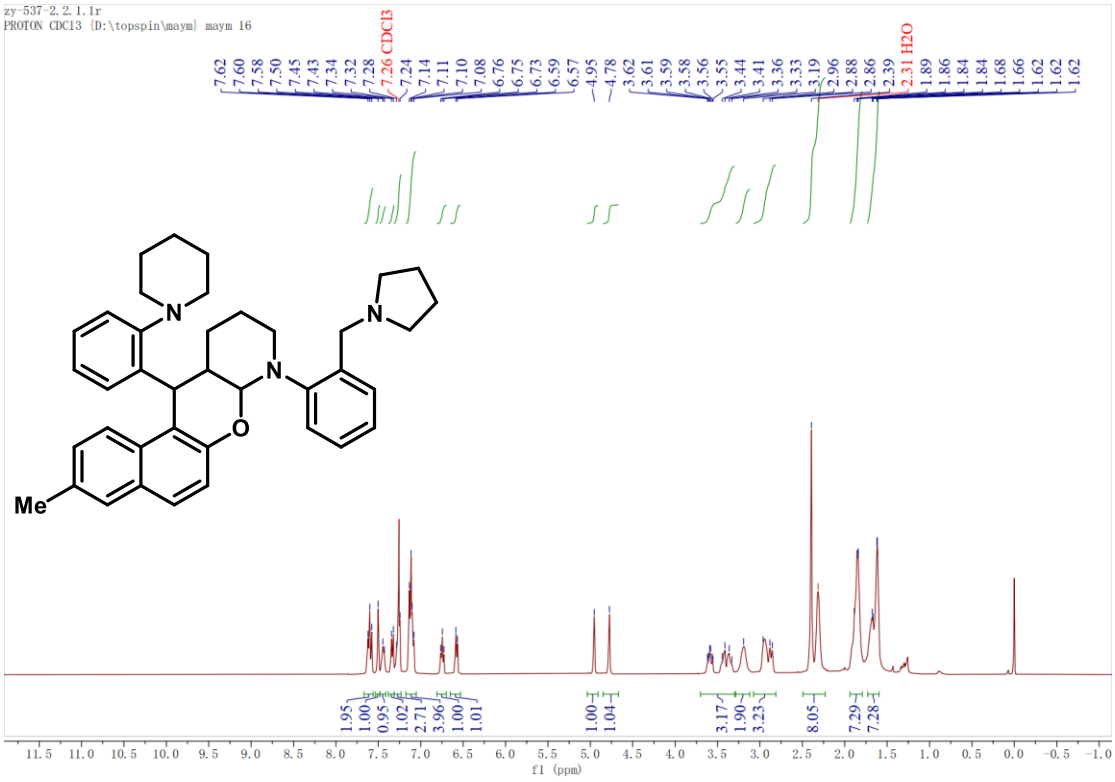
^{1}H NMR of Compound **4e** (400 MHz, $CDCl_3$)



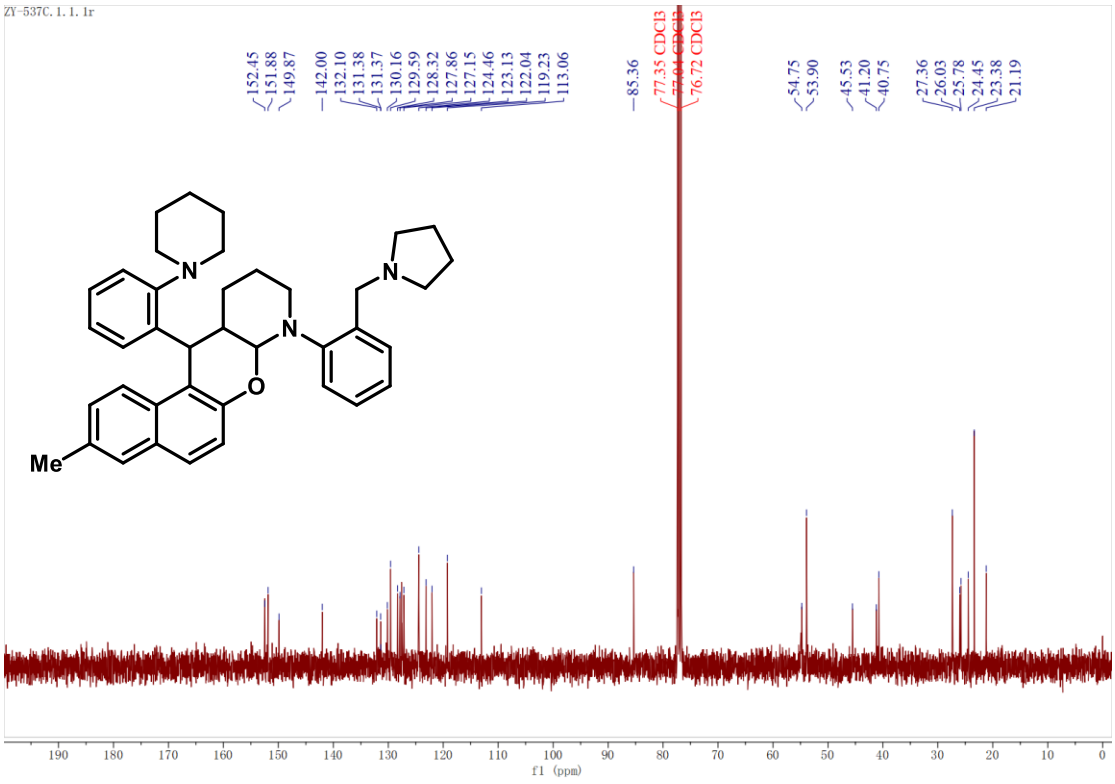
^{13}C NMR of Compound **4e** (101 MHz, $CDCl_3$)



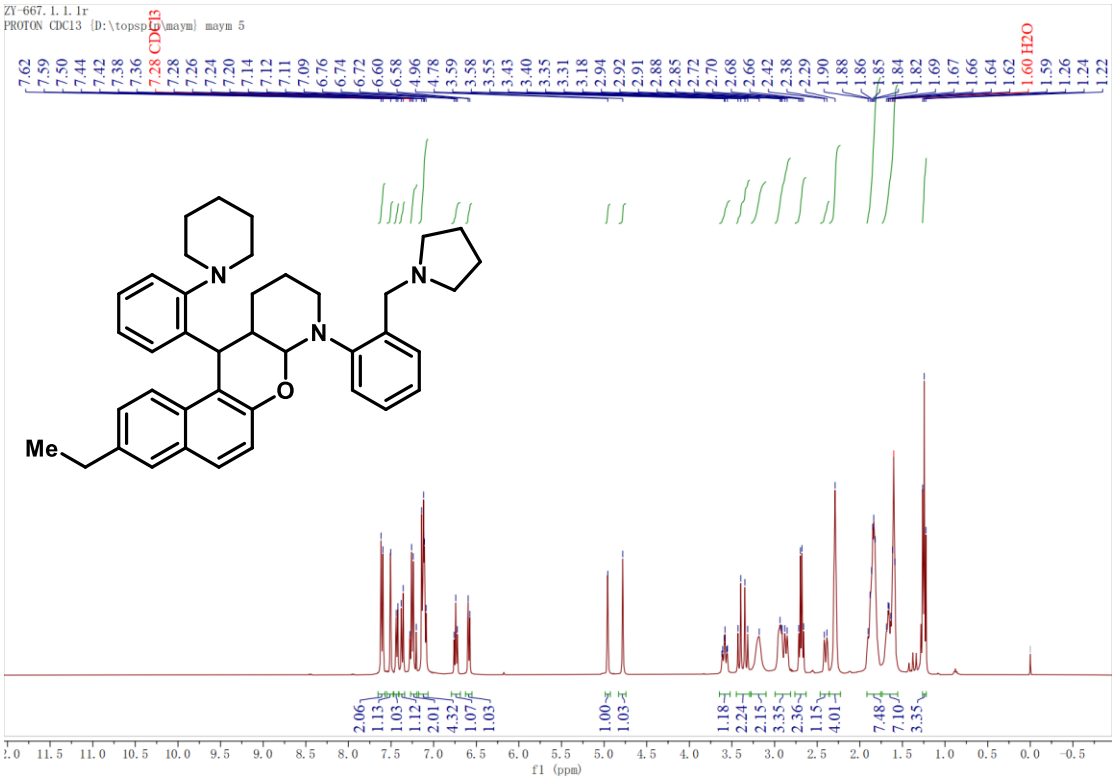
^{1}H NMR of Compound **4f** (400 MHz, $CDCl_3$)



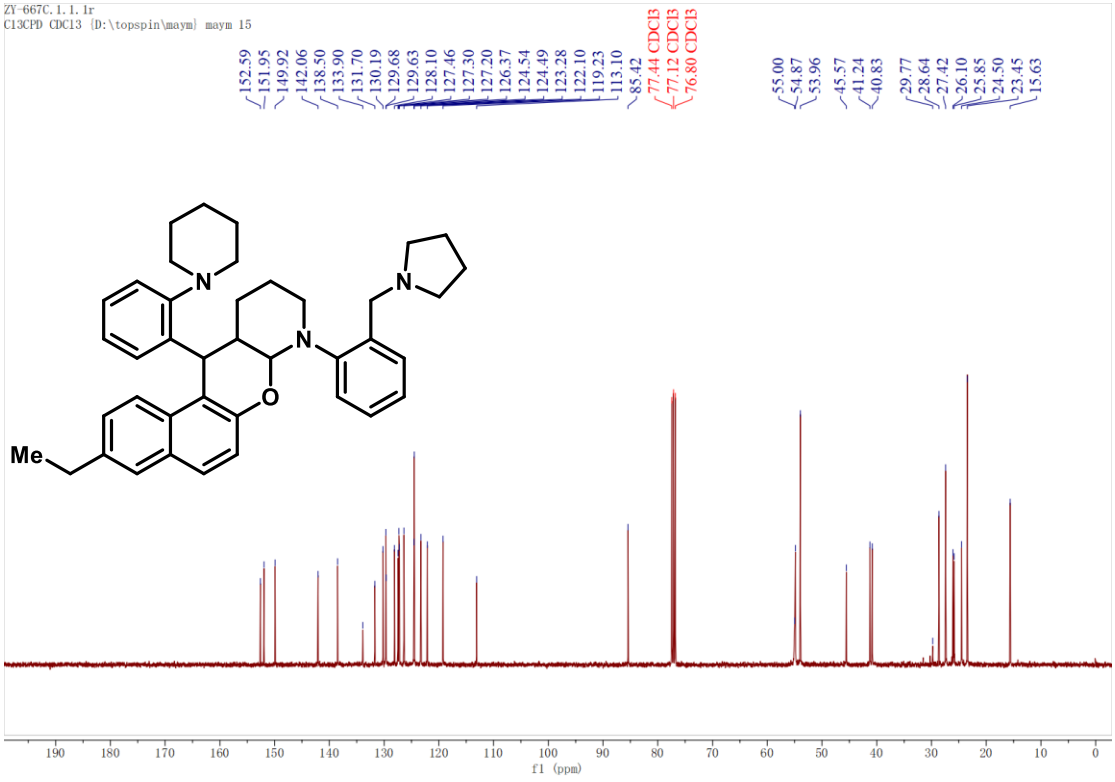
^{13}C NMR of Compound **4f** (101 MHz, $CDCl_3$)



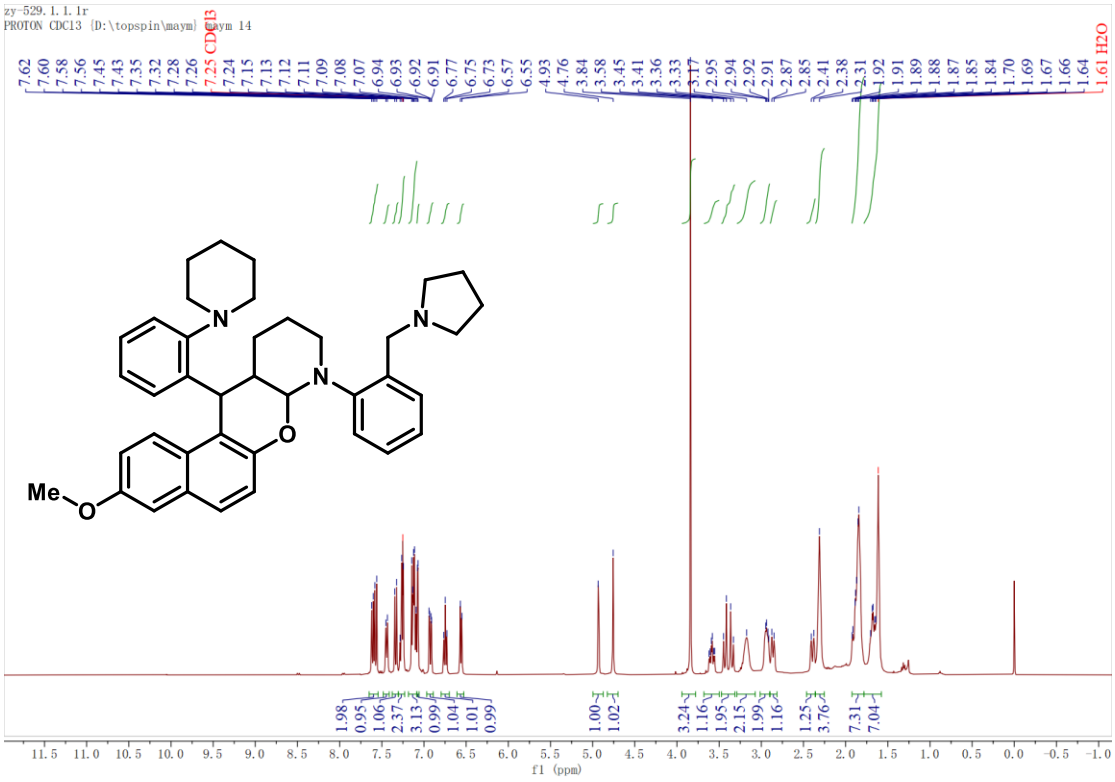
^{1}H NMR of Compound **4g** (400 MHz, $CDCl_3$)



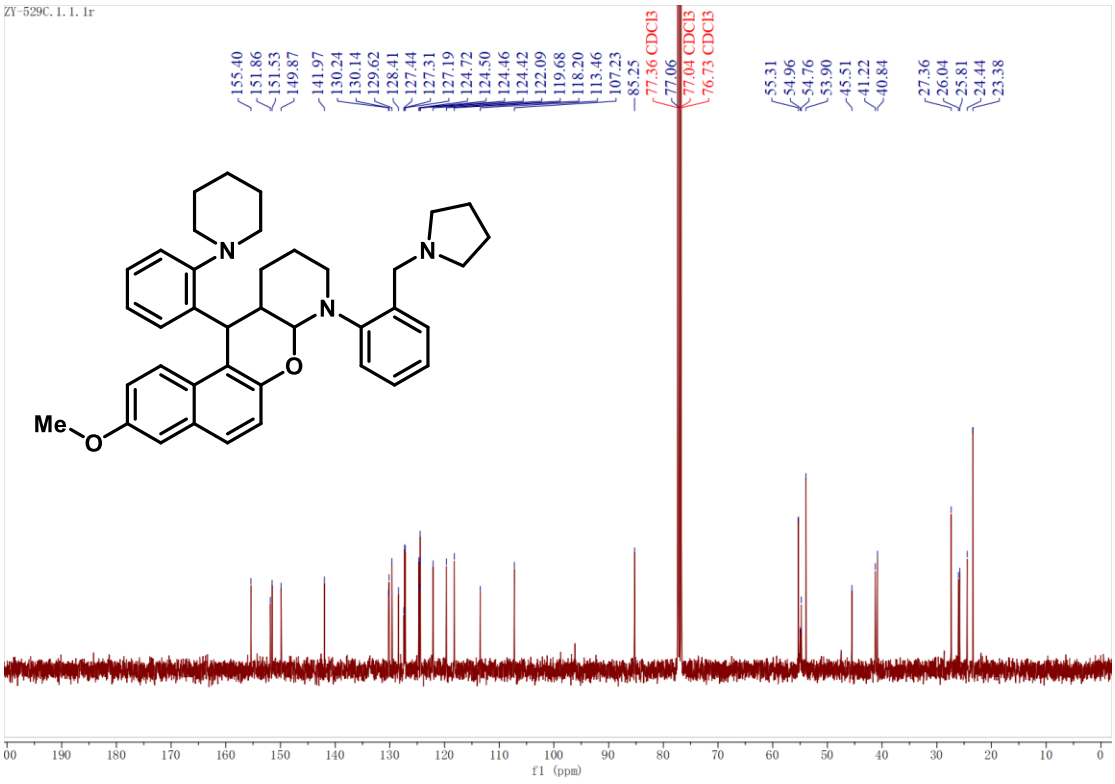
^{13}C NMR of Compound **4g** (101 MHz, $CDCl_3$)



^{1}H NMR of Compound **4h** (400 MHz, $CDCl_3$)



^{13}C NMR of Compound **4h** (101 MHz, $CDCl_3$)



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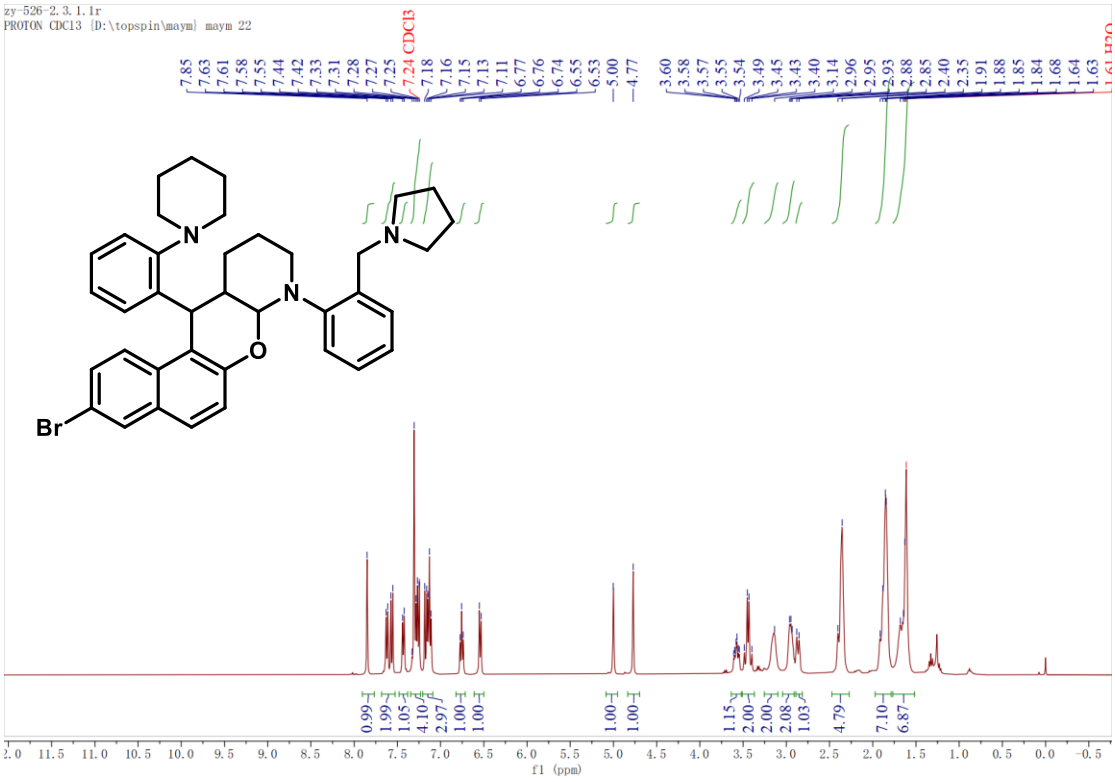
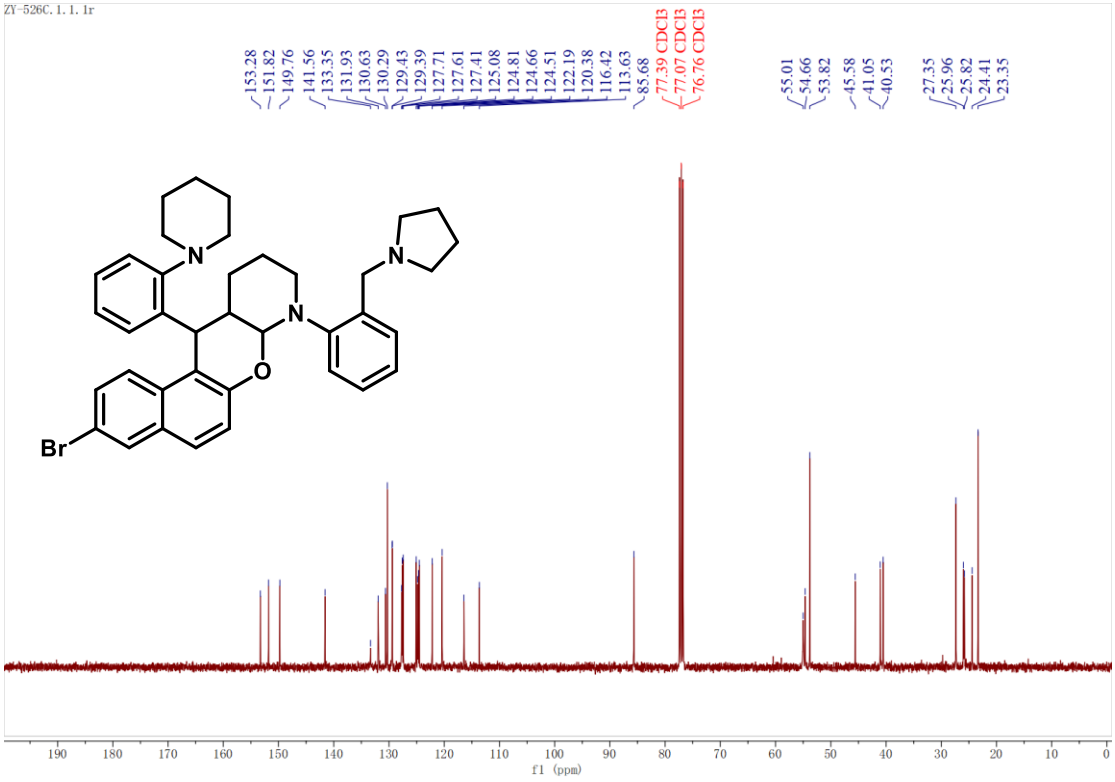
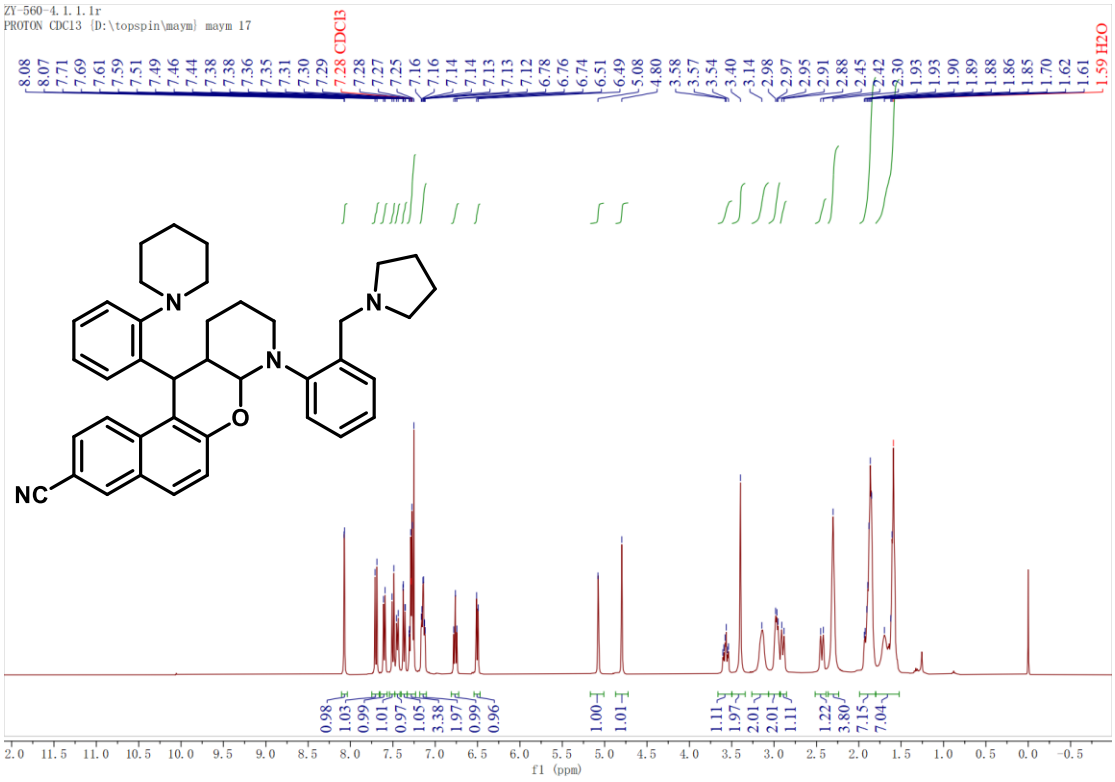
^{1}H NMR of Compound **4i** (400 MHz, $CDCl_3$)



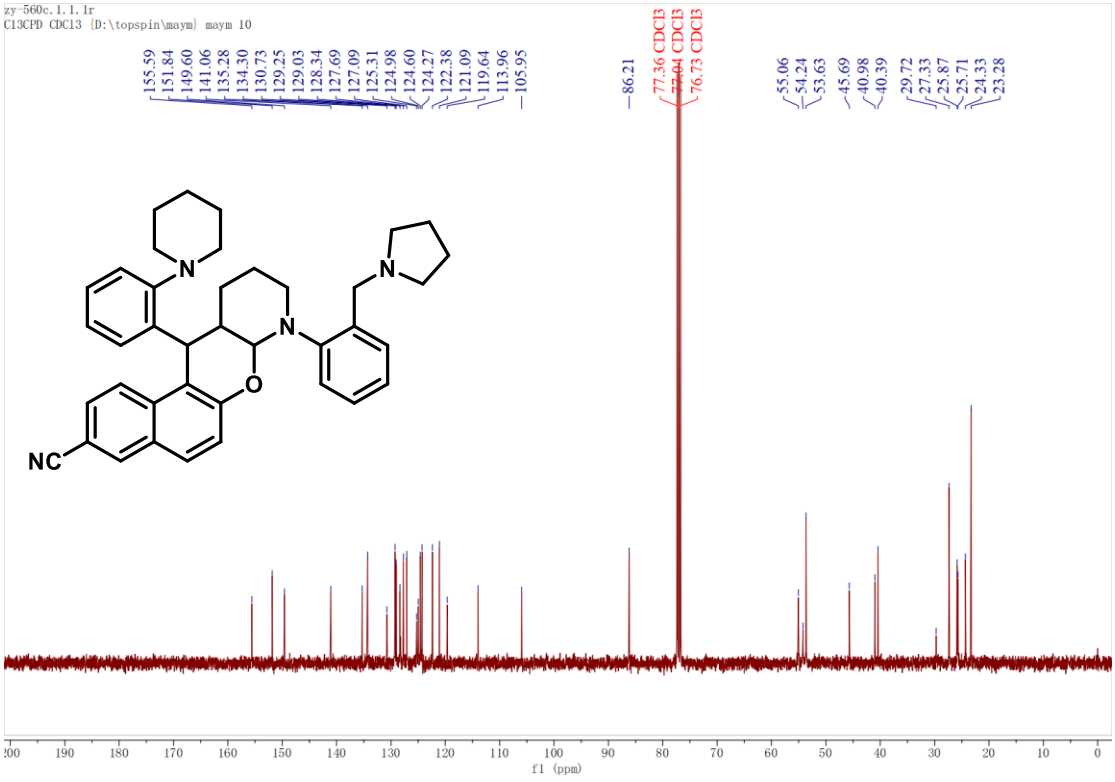
^{13}C NMR of Compound **4i** (101 MHz, $CDCl_3$)



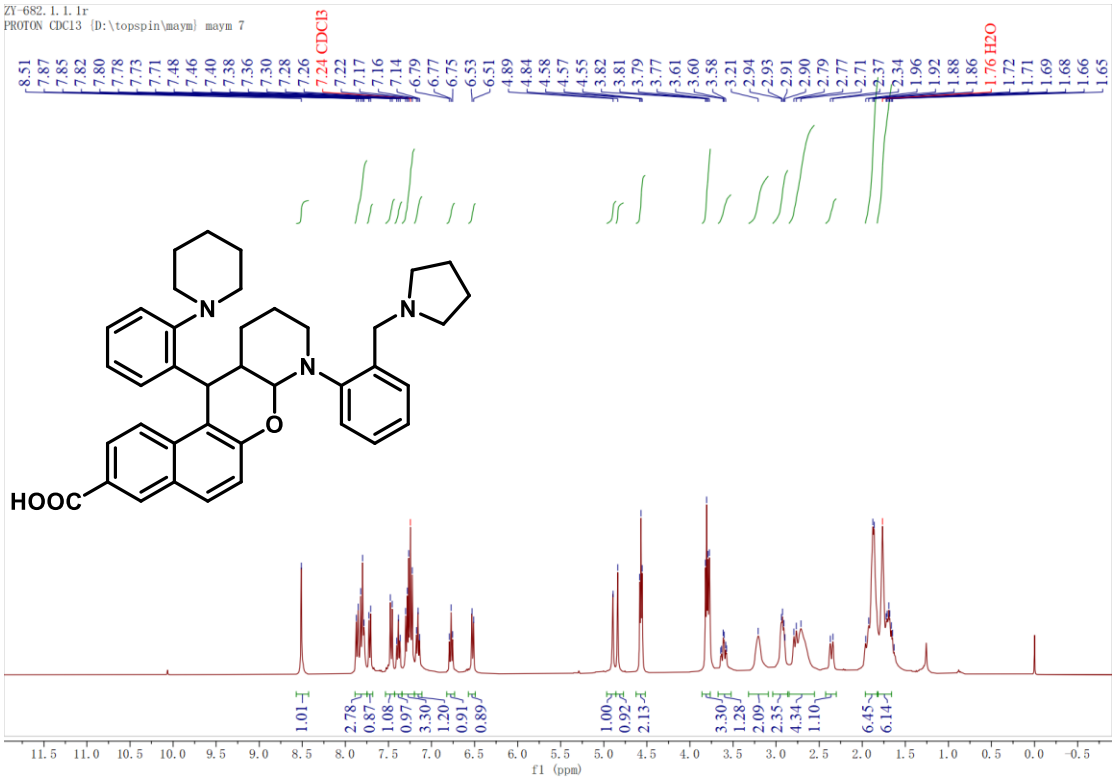
^{1}H NMR of Compound **4j** (400 MHz, $CDCl_3$)



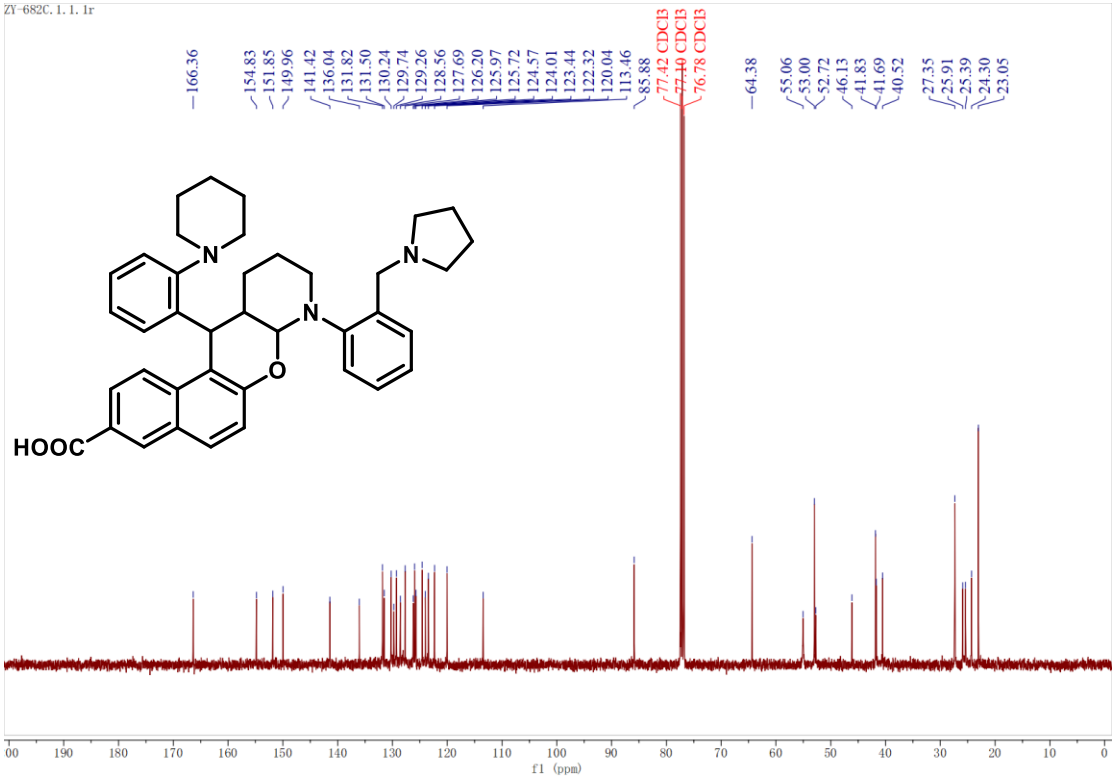
^{13}C NMR of Compound **4j** (101 MHz, $CDCl_3$)



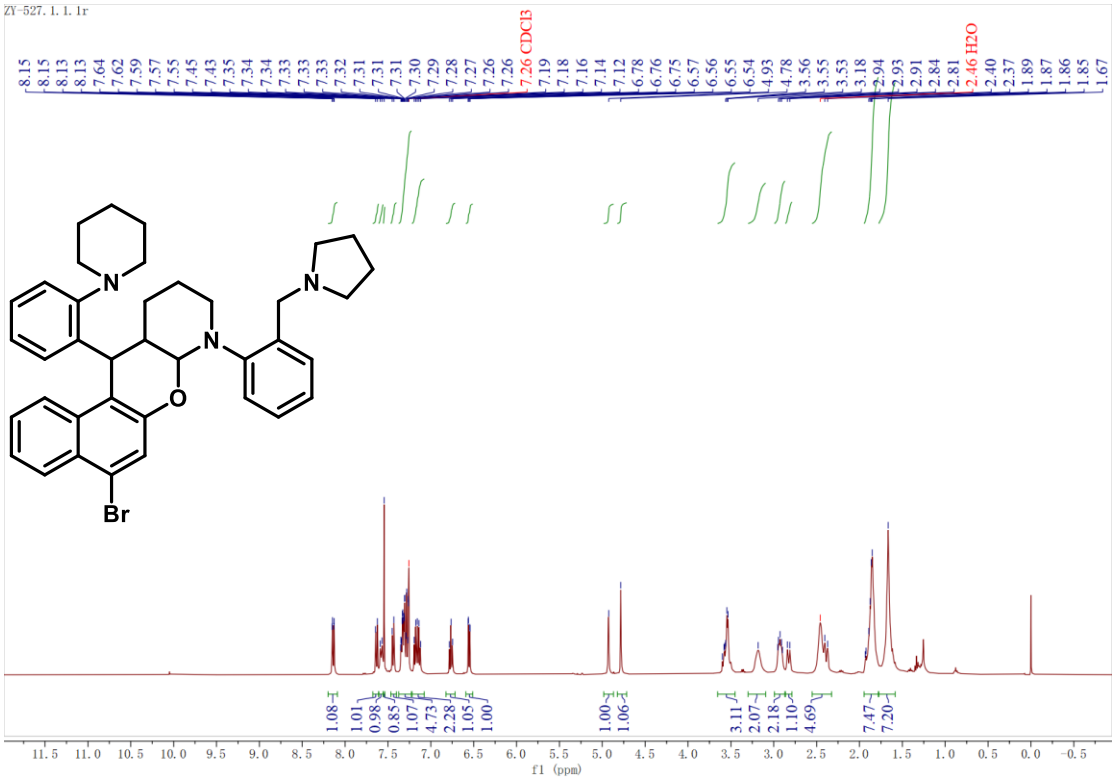
^{1}H NMR of Compound **4k** (400 MHz, $CDCl_3$)



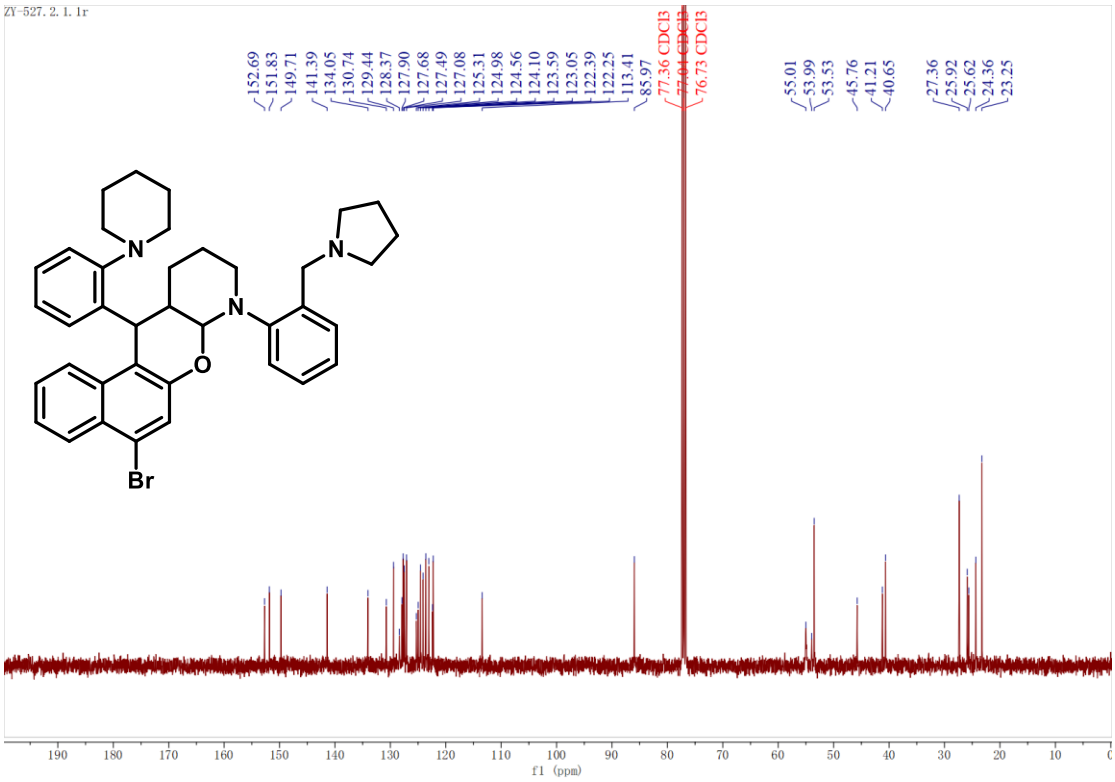
^{13}C NMR of Compound **4k** (101 MHz, $CDCl_3$)



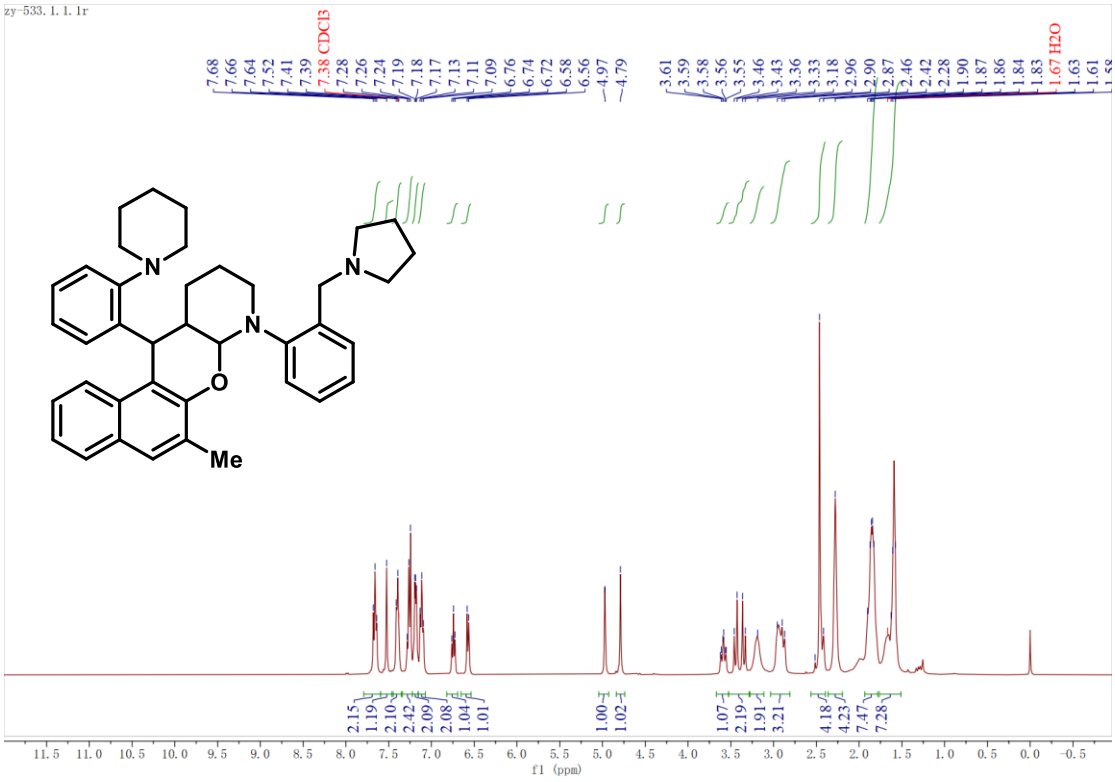
^{1}H NMR of Compound **4l** (400 MHz, $CDCl_3$)



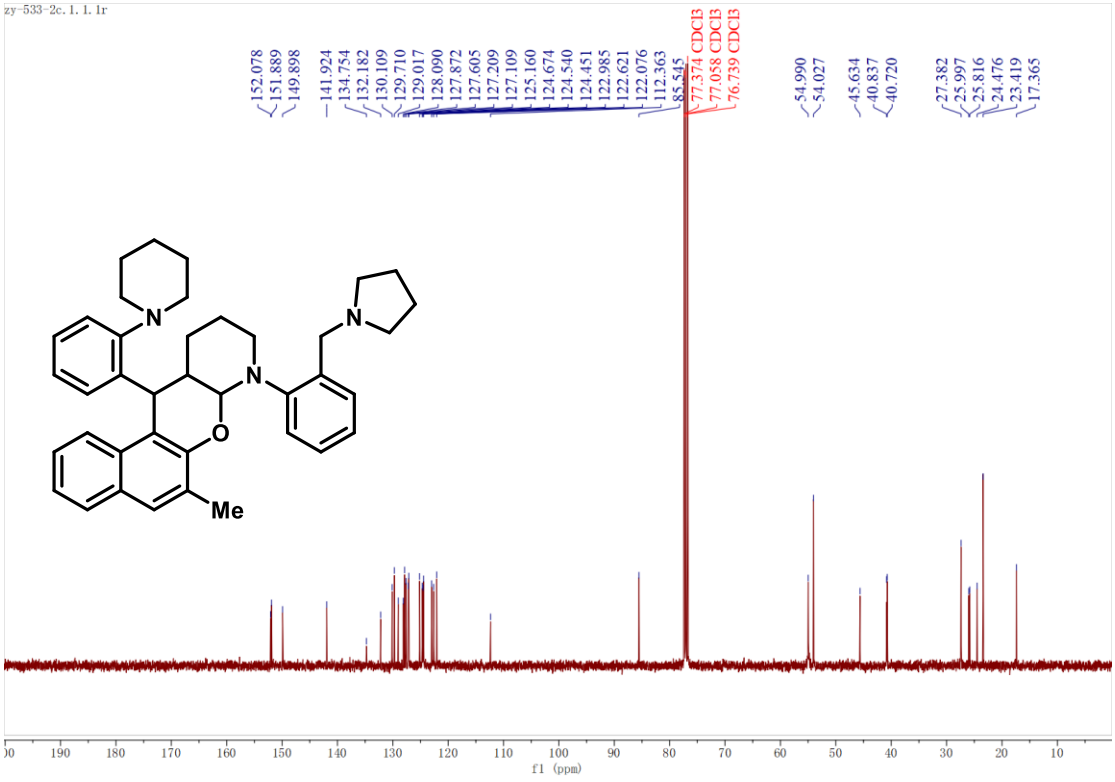
^{13}C NMR of Compound **4l** (101 MHz, $CDCl_3$)



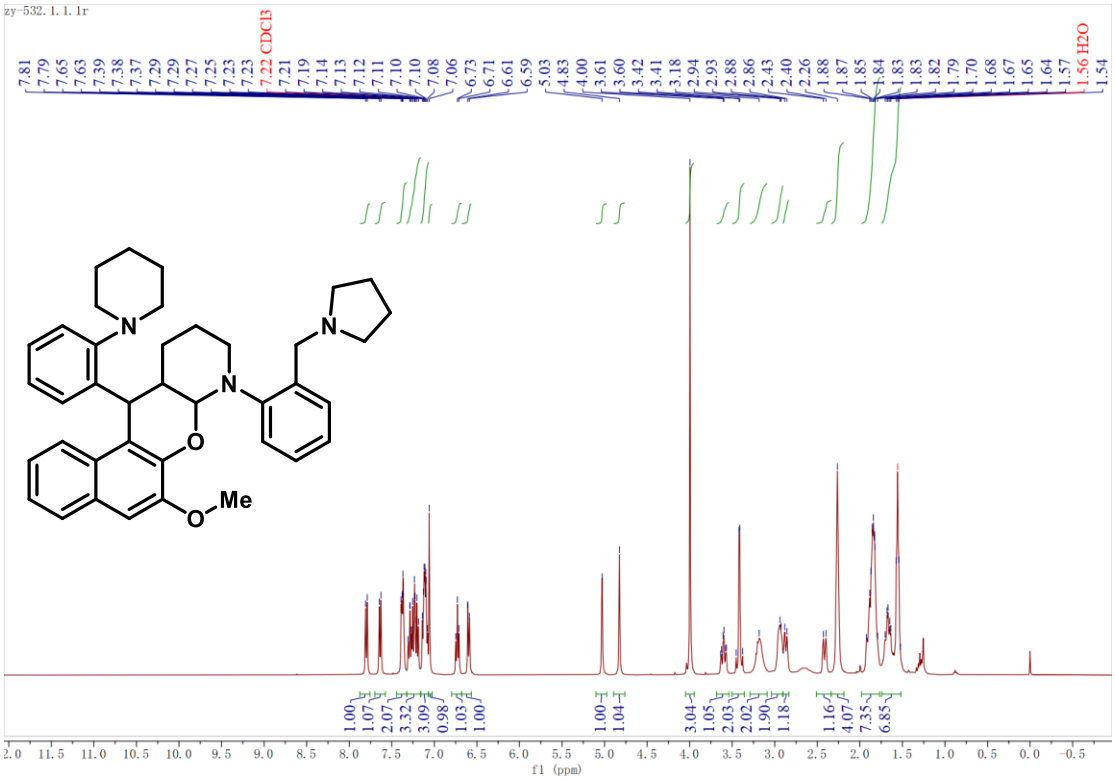
^{1}H NMR of Compound **4m** (400 MHz, $CDCl_3$)



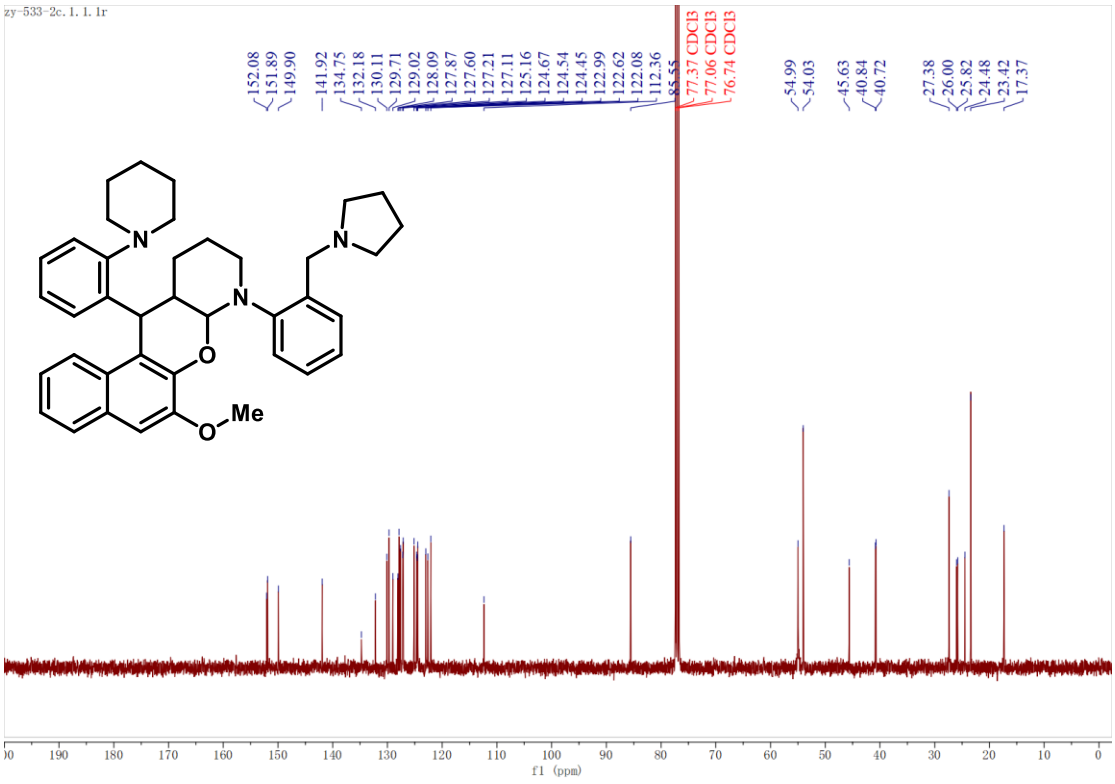
^{13}C NMR of Compound **4m** (101 MHz, $CDCl_3$)



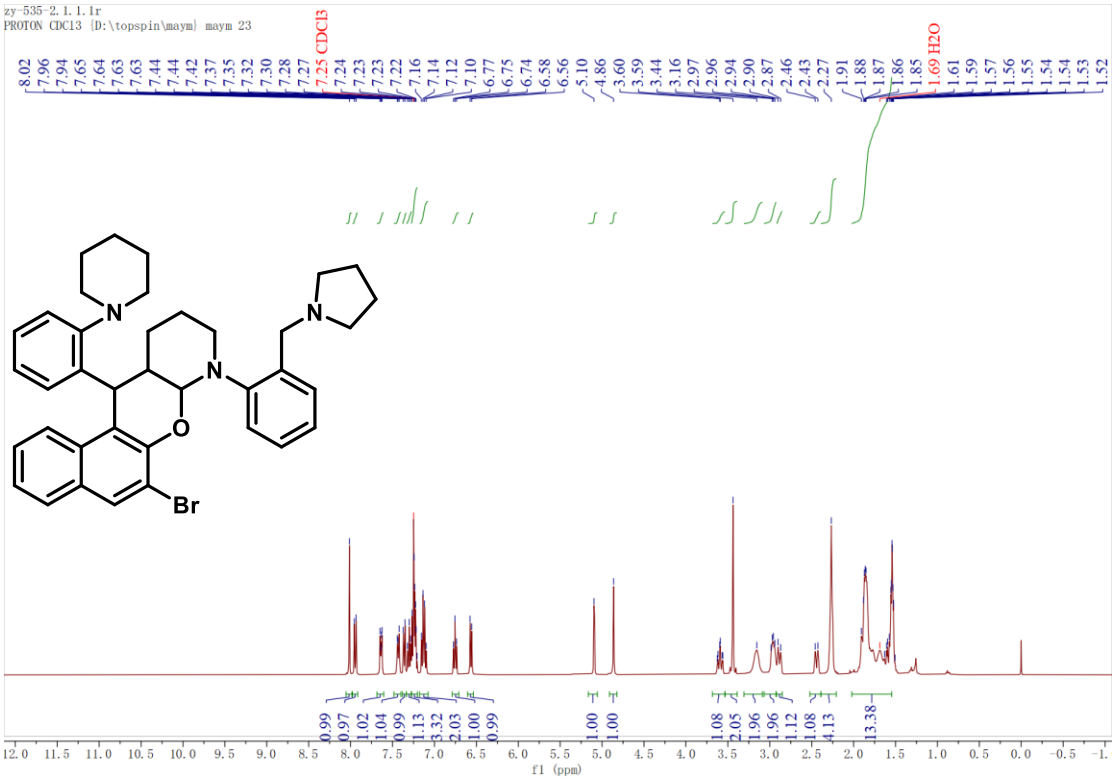
^{1}H NMR of Compound **4n** (400 MHz, $CDCl_3$)



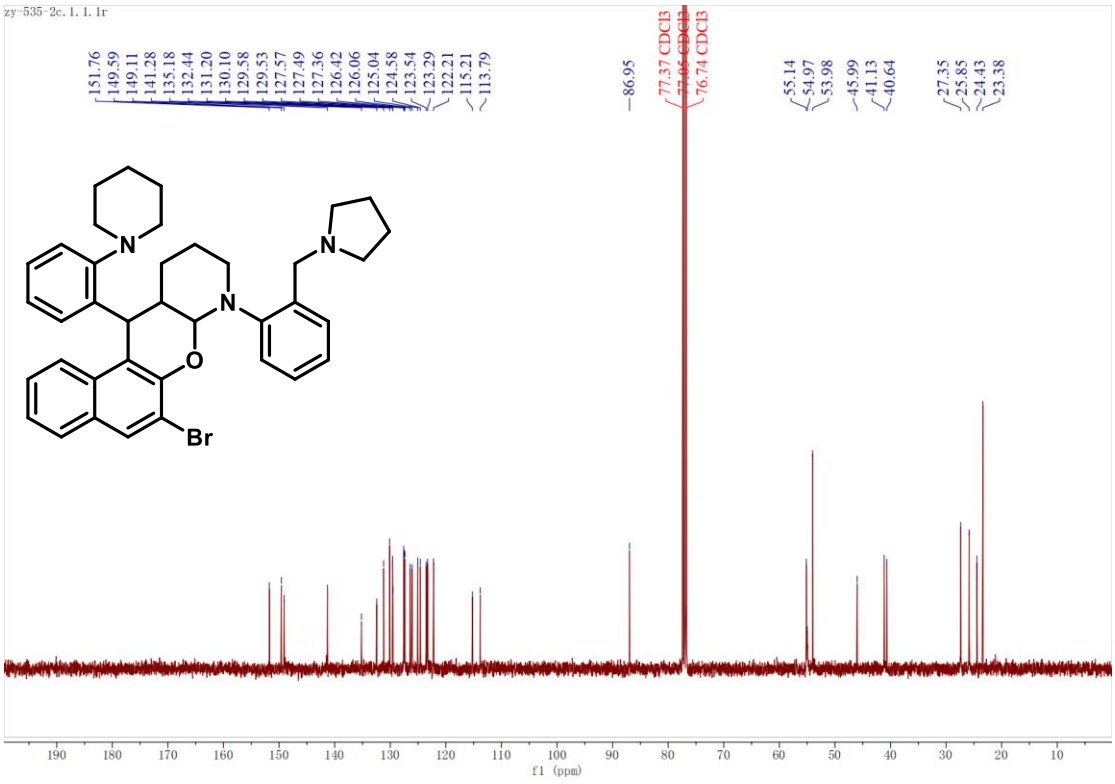
^{13}C NMR of Compound **4n** (101 MHz, $CDCl_3$)



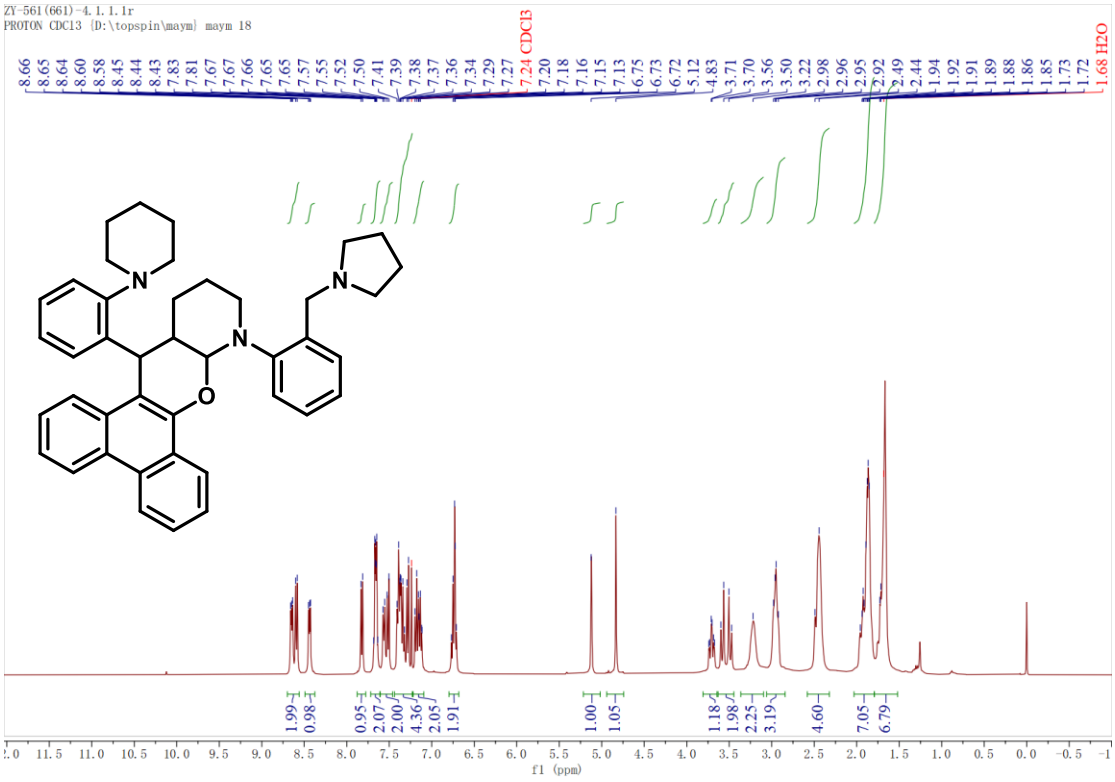
^{1}H NMR of Compound **4o** (400 MHz, $CDCl_3$)



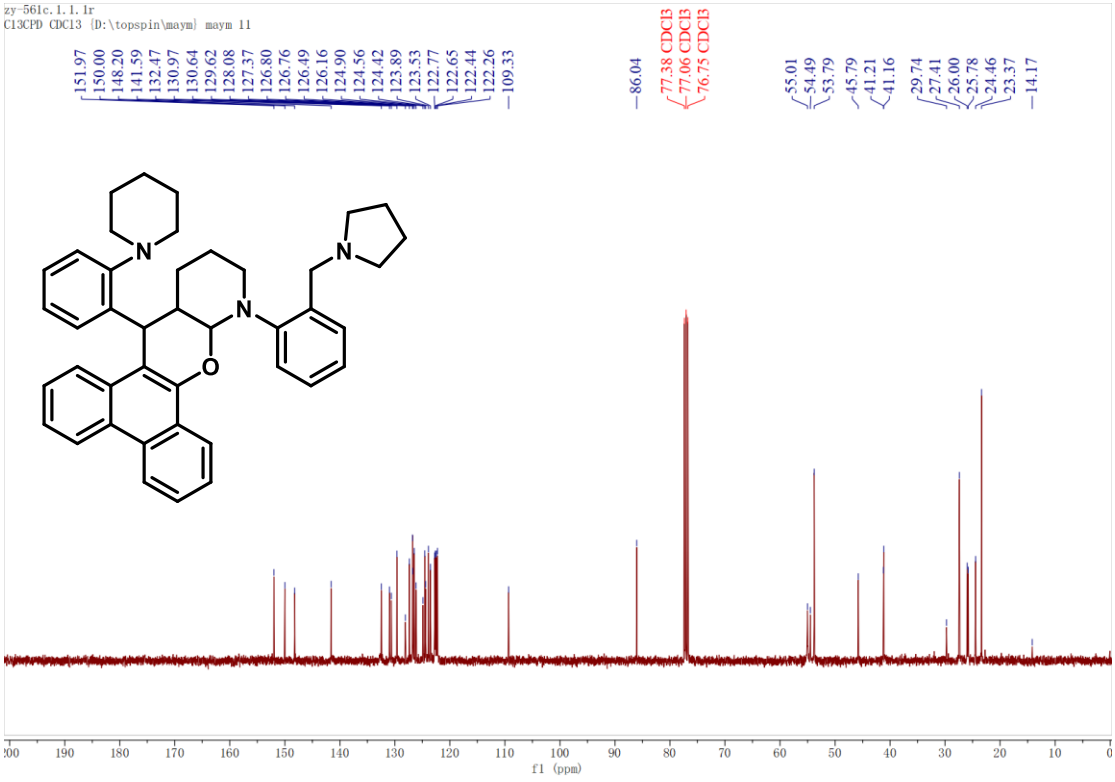
^{13}C NMR of Compound **4o** (101 MHz, $CDCl_3$)



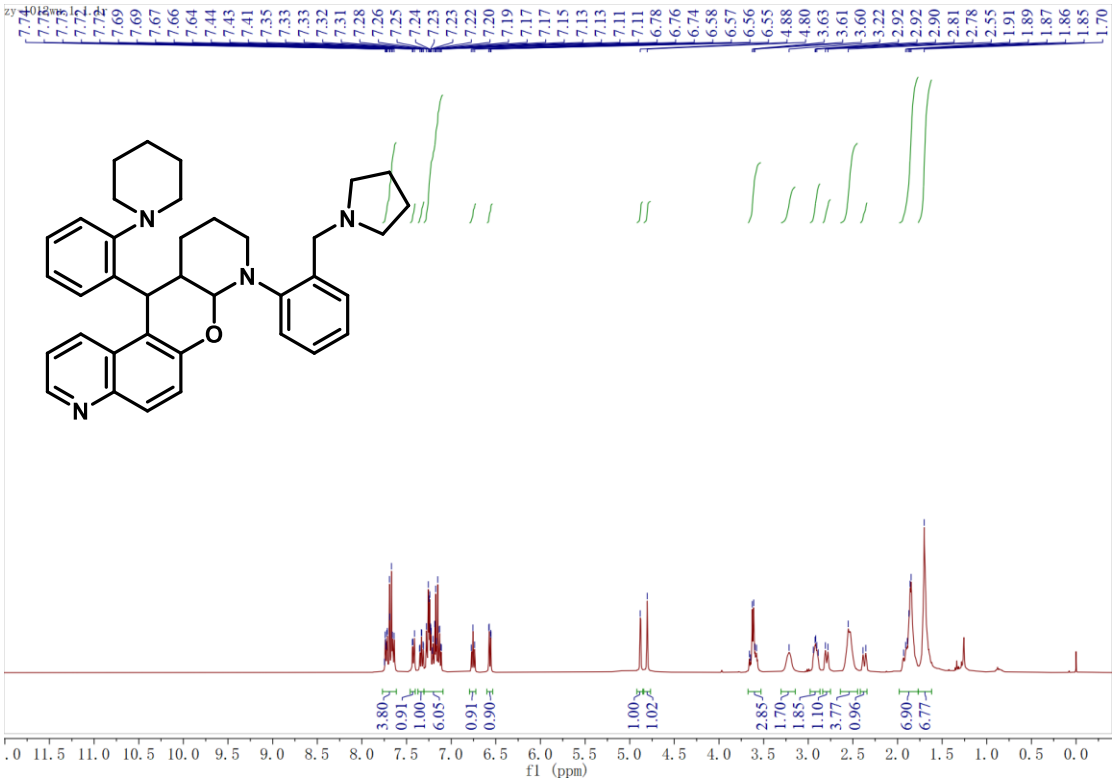
^{1}H NMR of Compound **4p** (400 MHz, $CDCl_3$)



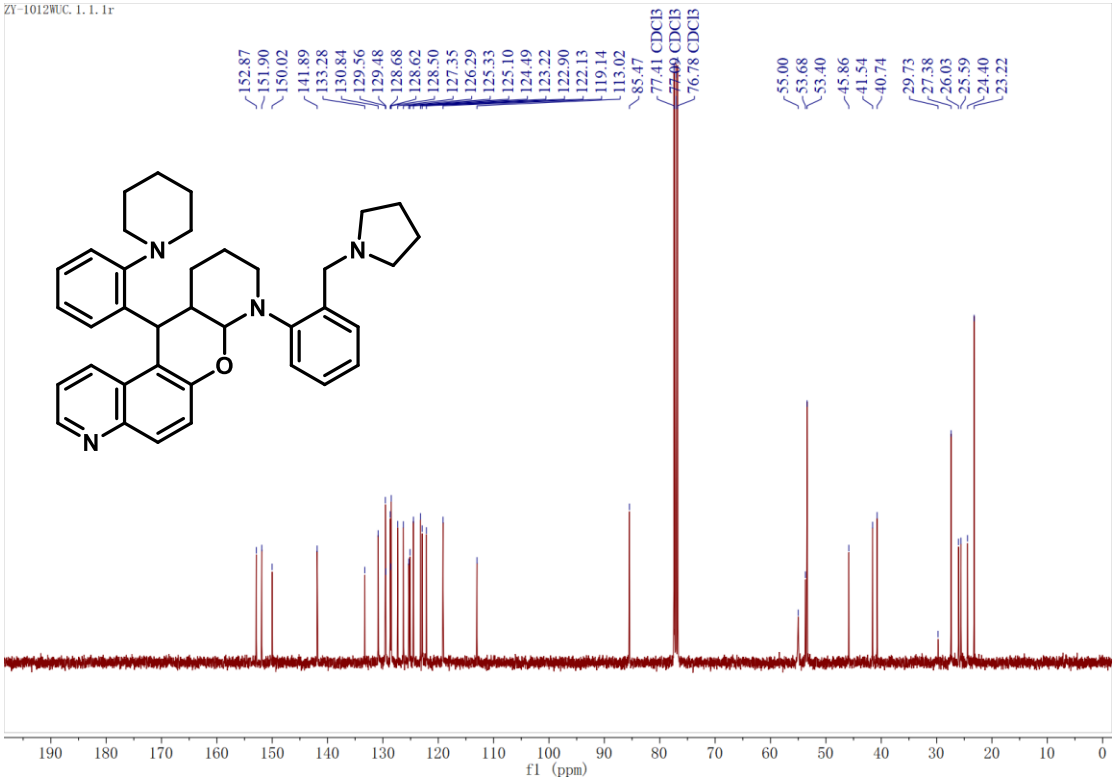
^{13}C NMR of Compound **4p** (101 MHz, $CDCl_3$)



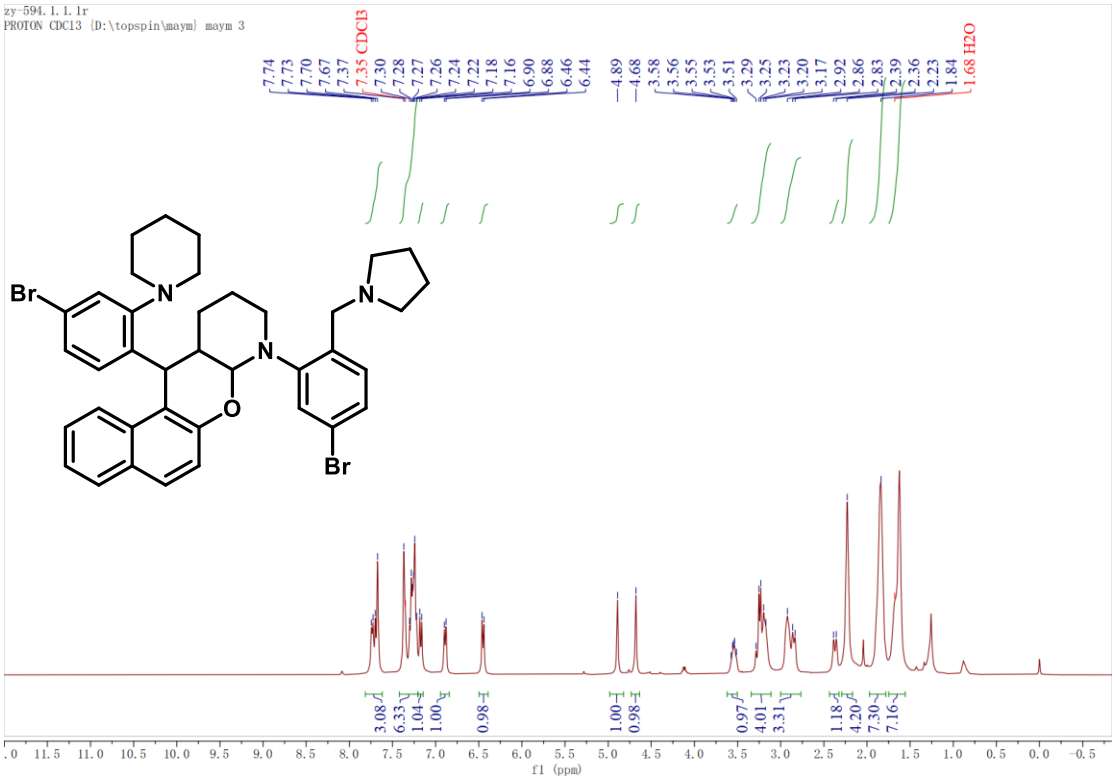
^{1}H NMR of Compound **4q** (400 MHz, $CDCl_3$)



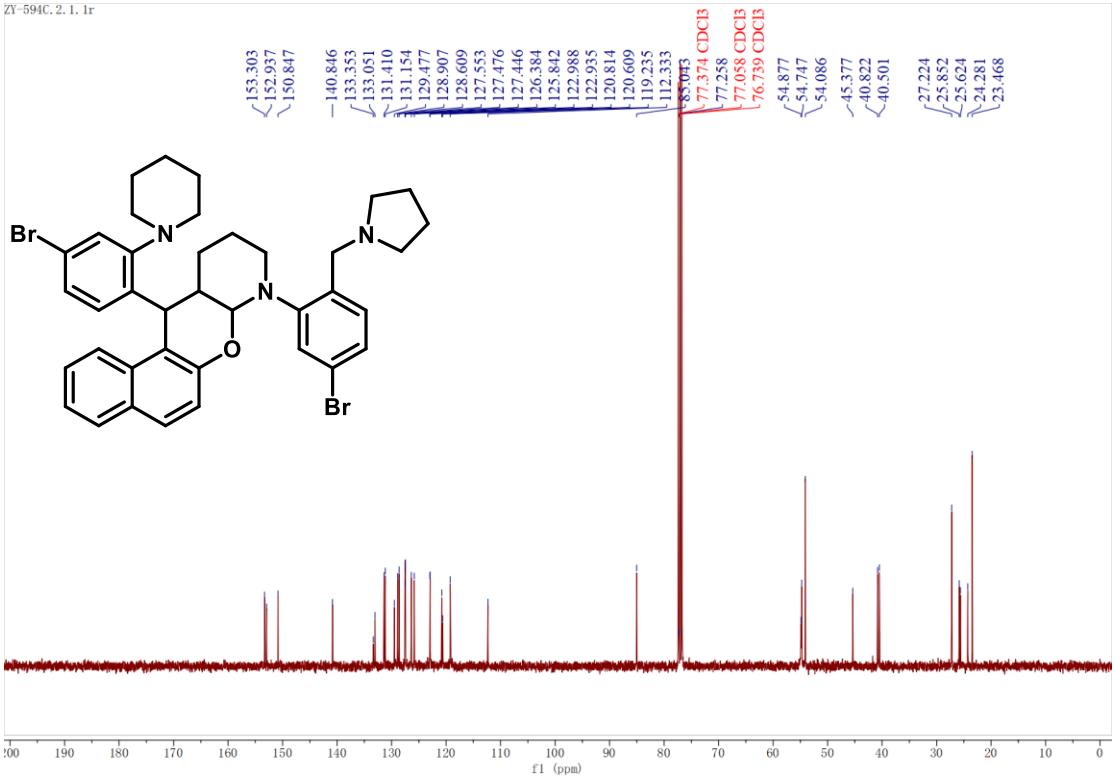
^{13}C NMR of Compound **4q** (101 MHz, $CDCl_3$)



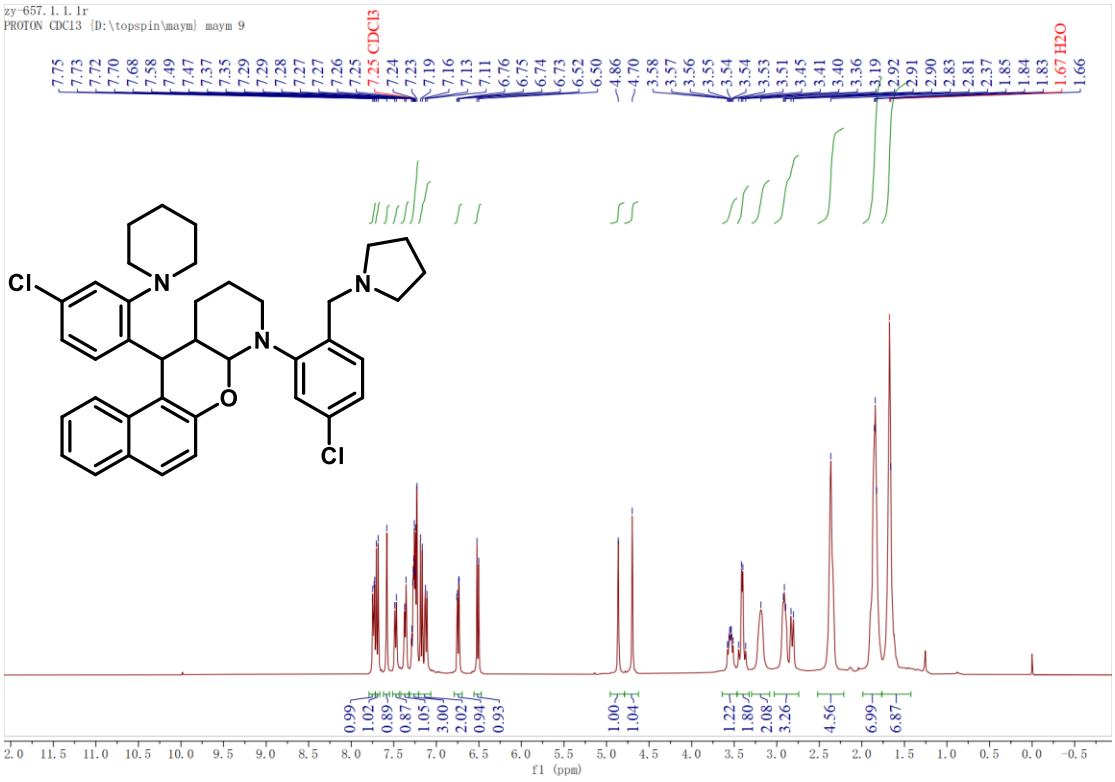
^{1}H NMR of Compound **4r** (400 MHz, $CDCl_3$)



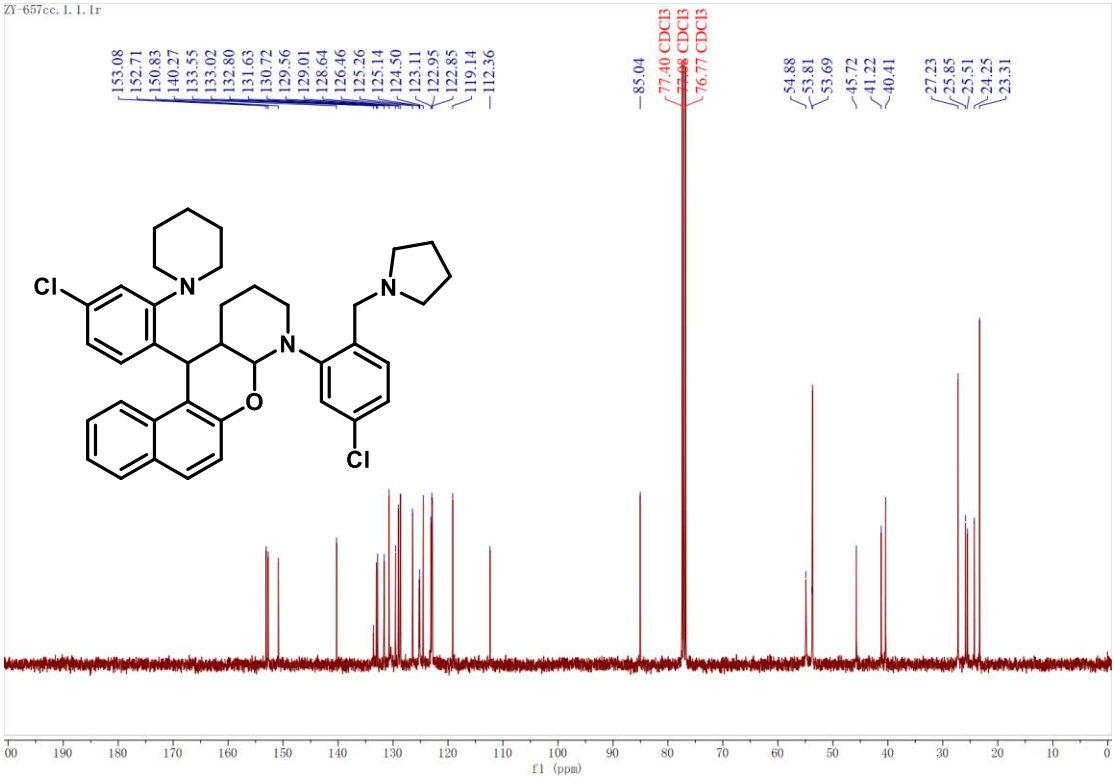
^{13}C NMR of Compound **4r** (101 MHz, $CDCl_3$)



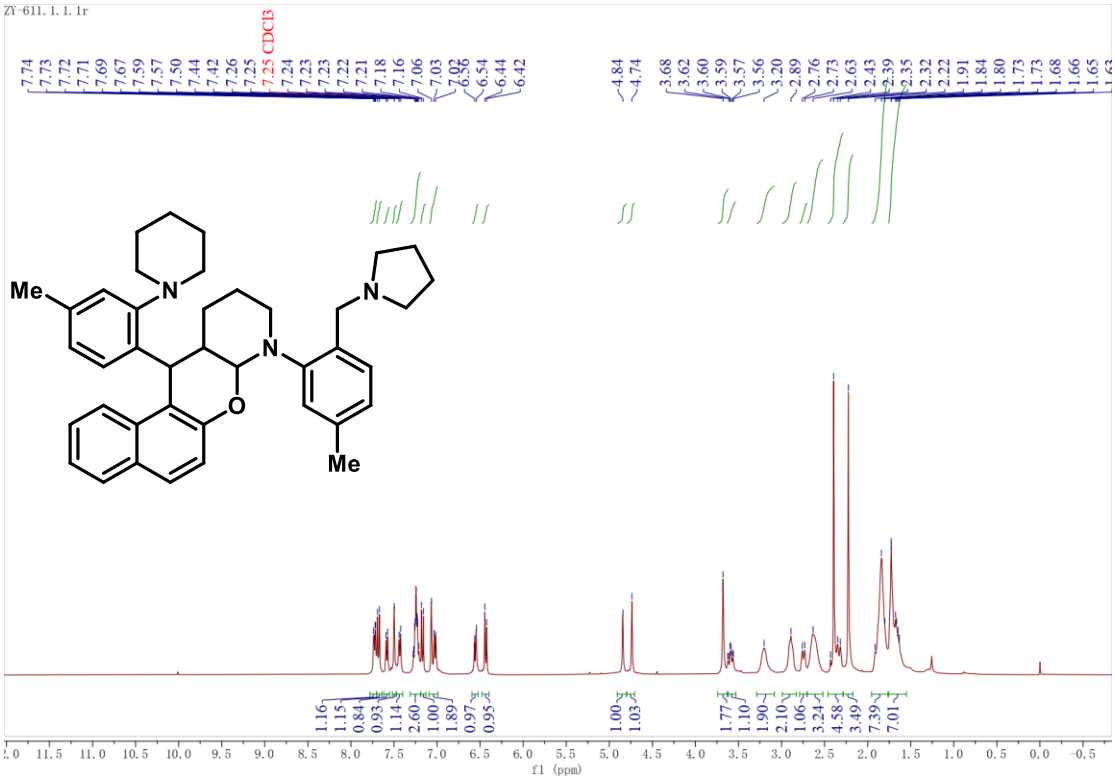
^{1}H NMR of Compound **4s** (400 MHz, $CDCl_3$)



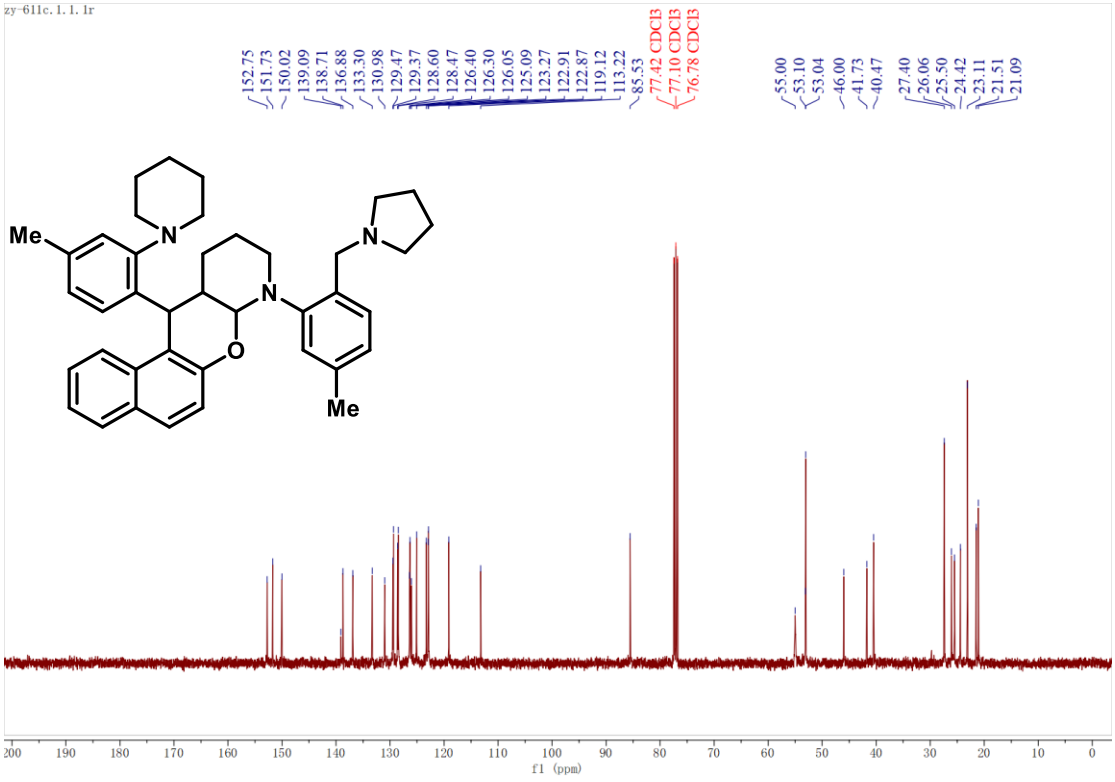
^{13}C NMR of Compound **4s** (101 MHz, $CDCl_3$)



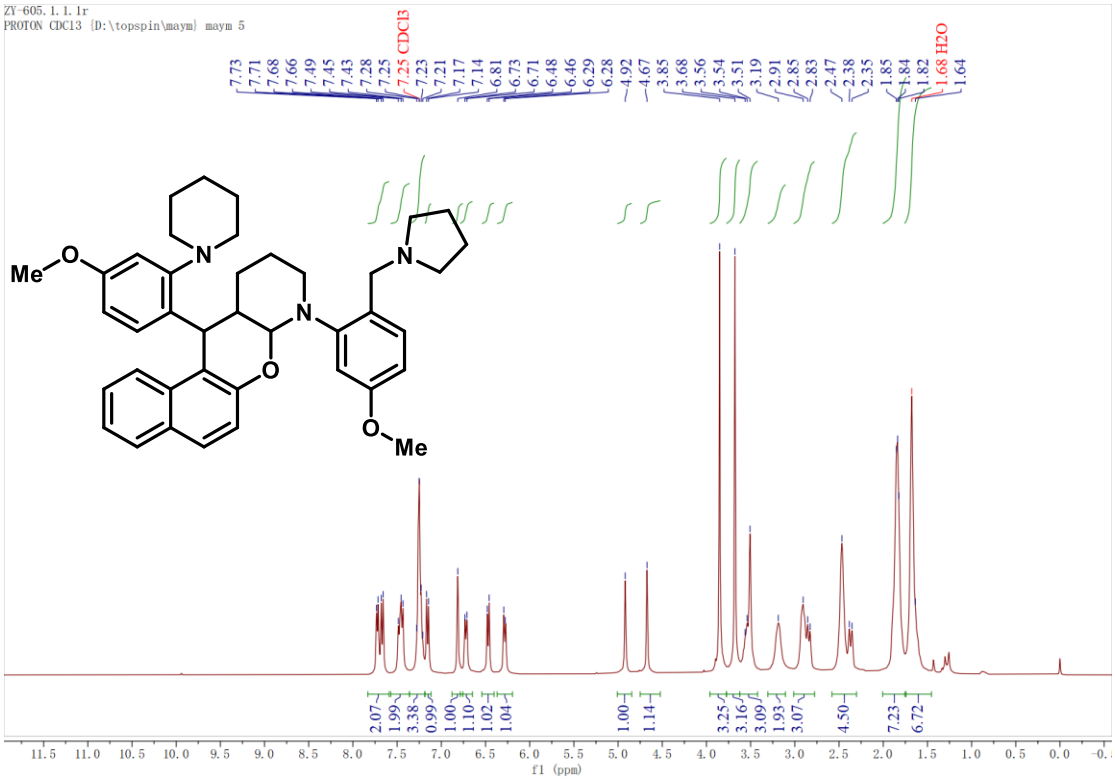
^{1}H NMR of Compound **4t** (400 MHz, $CDCl_3$)



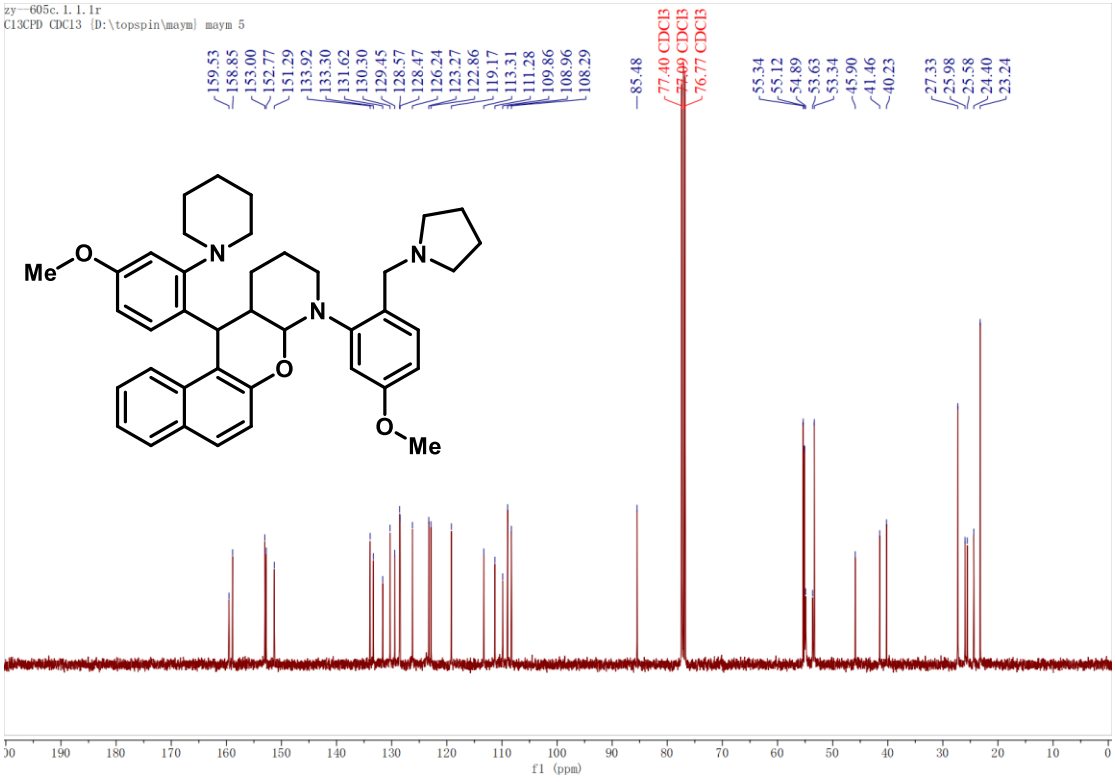
^{13}C NMR of Compound **4t** (101 MHz, $CDCl_3$)



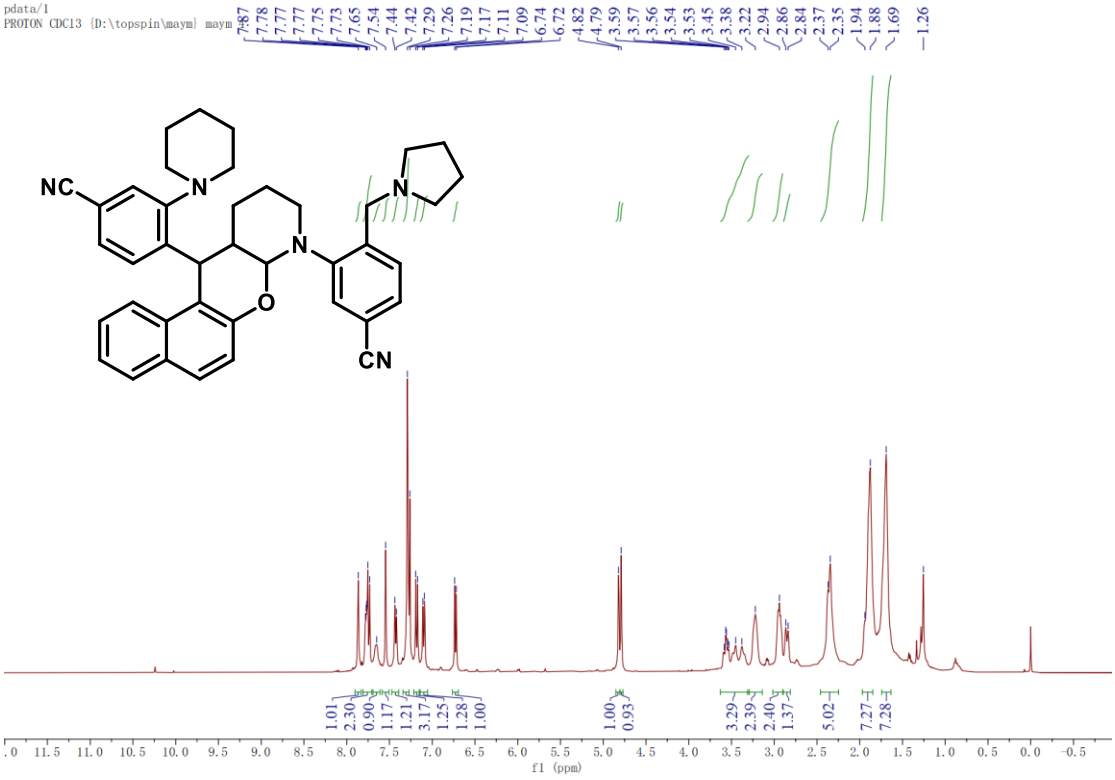
^{1}H NMR of Compound **4u** (400 MHz, $CDCl_3$)



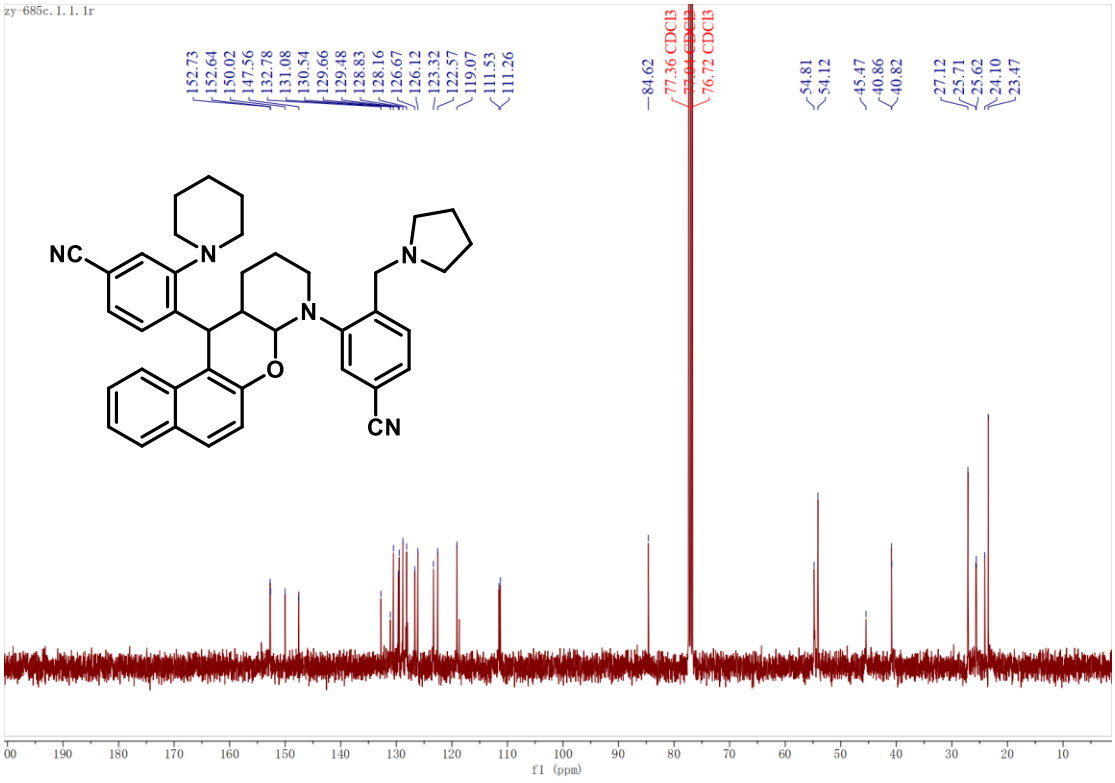
^{13}C NMR of Compound **4u** (101 MHz, $CDCl_3$)



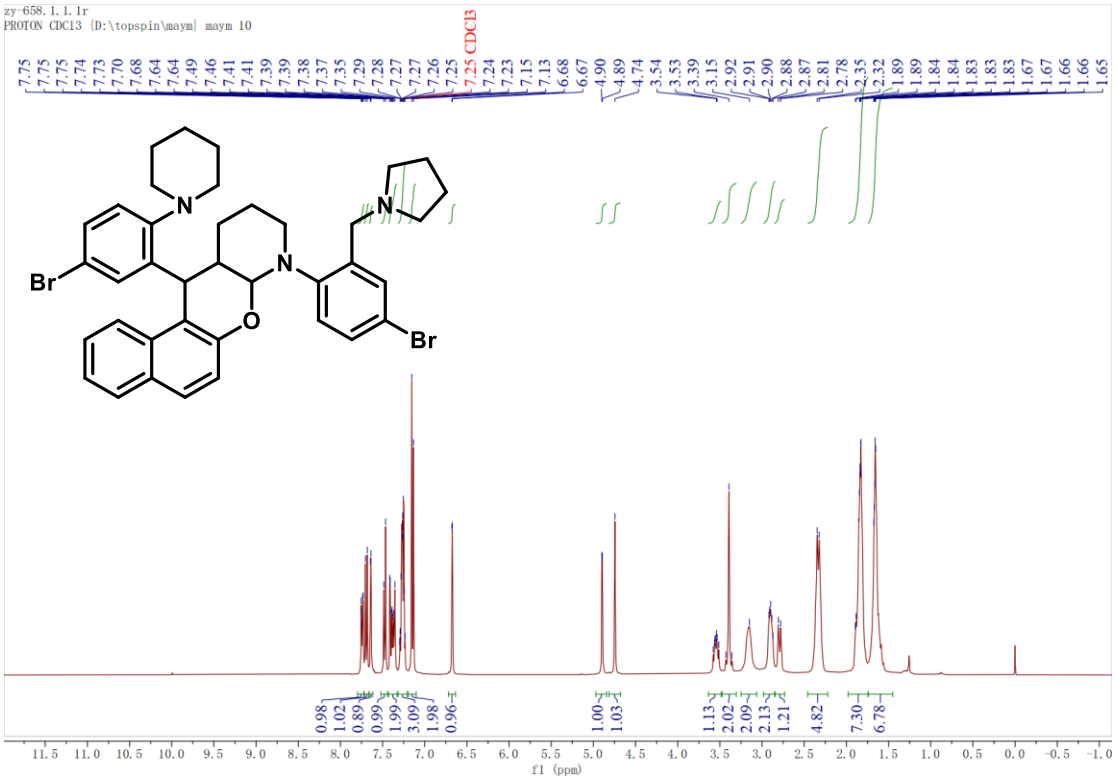
^{1}H NMR of Compound **4v** (400 MHz, $CDCl_3$)



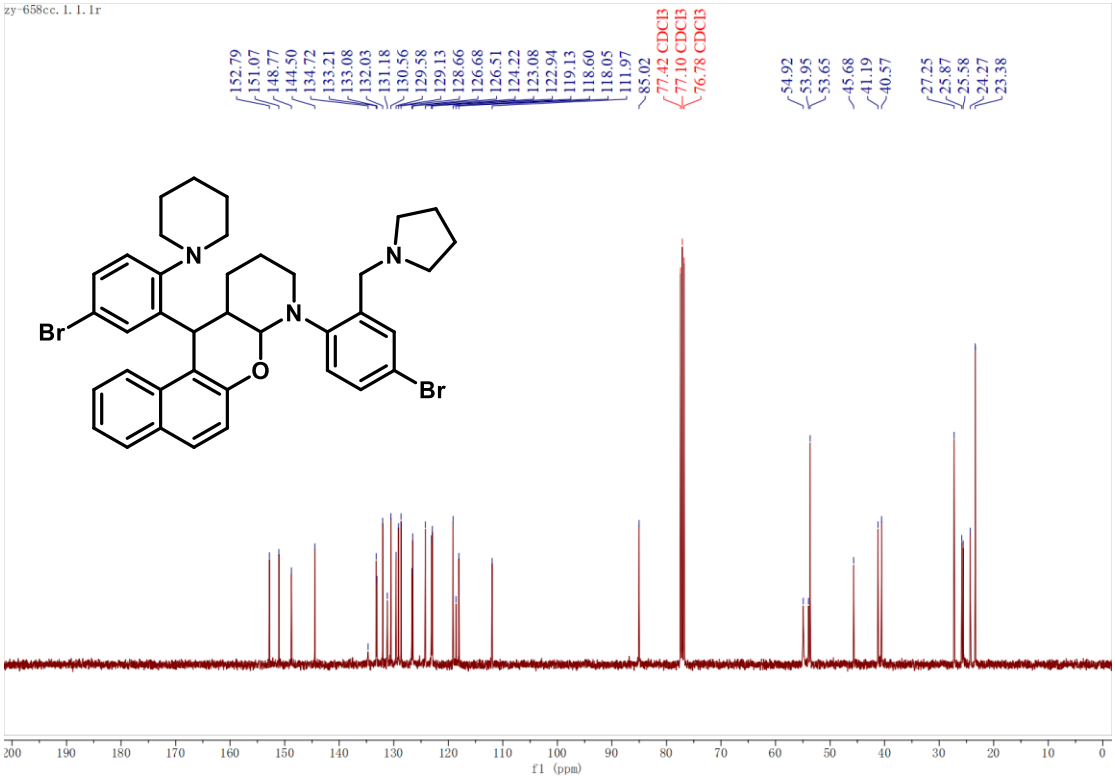
^{13}C NMR of Compound **4v** (101 MHz, $CDCl_3$)



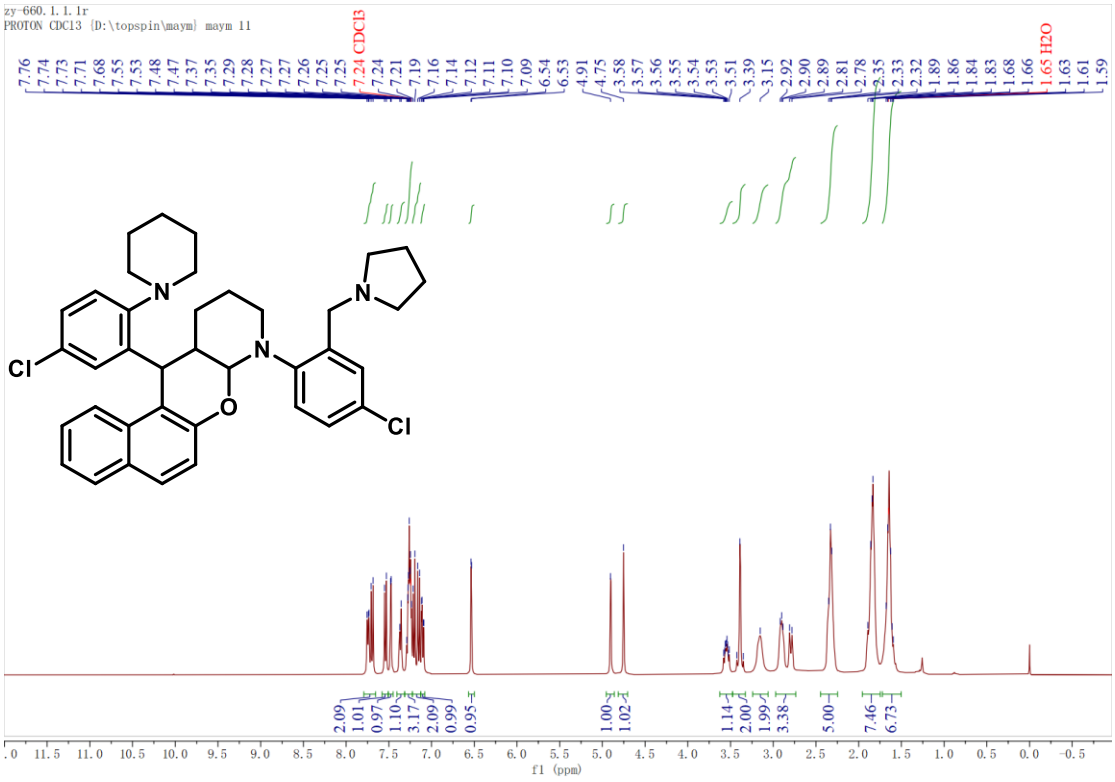
^{1}H NMR of Compound **4w** (400 MHz, $CDCl_3$)



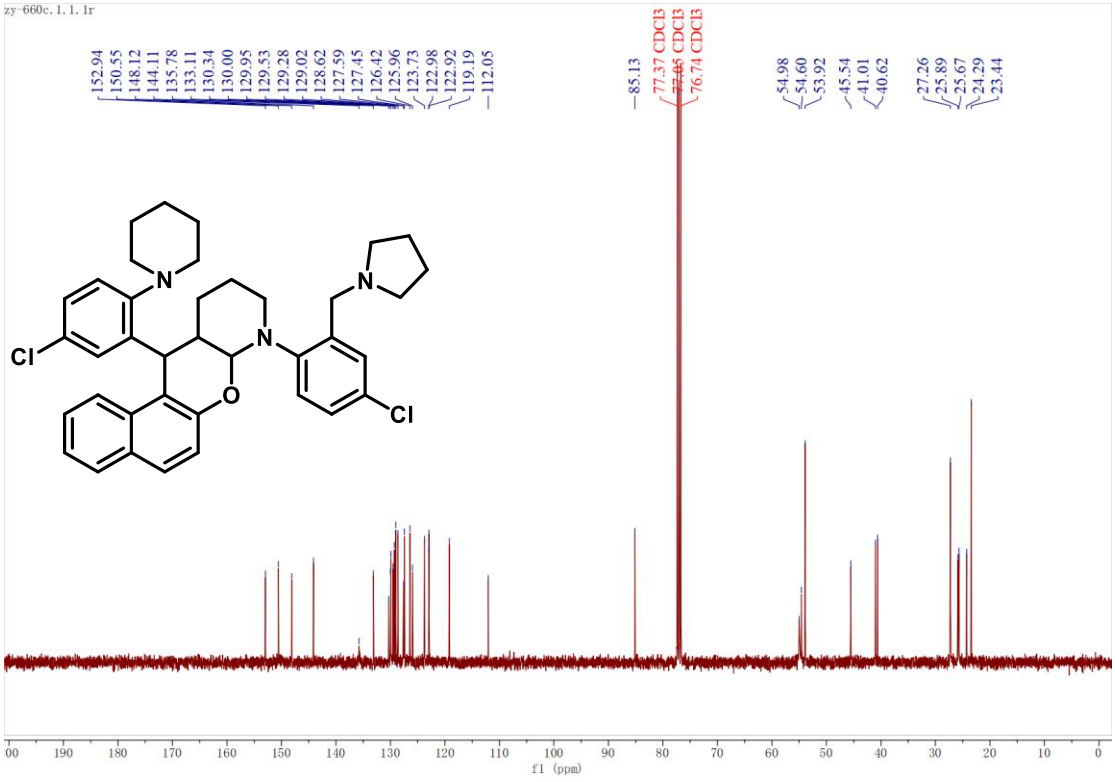
^{13}C NMR of Compound **4w** (101 MHz, $CDCl_3$)



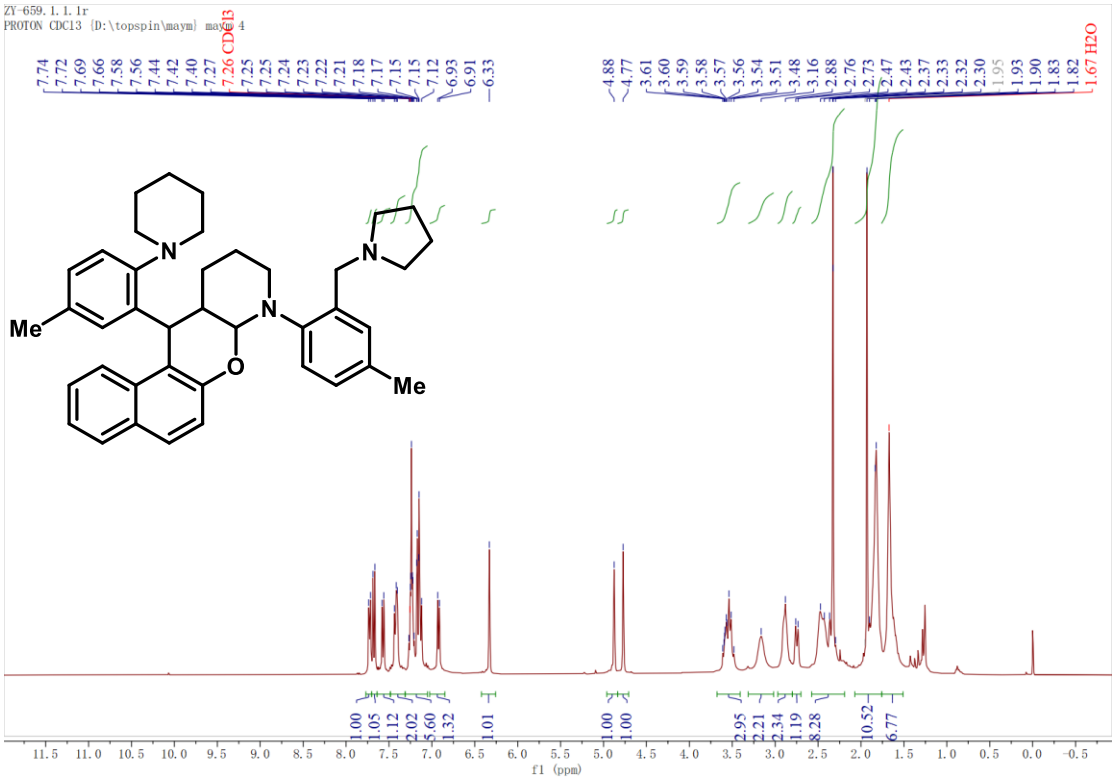
^{1}H NMR of Compound **4x** (400 MHz, $CDCl_3$)



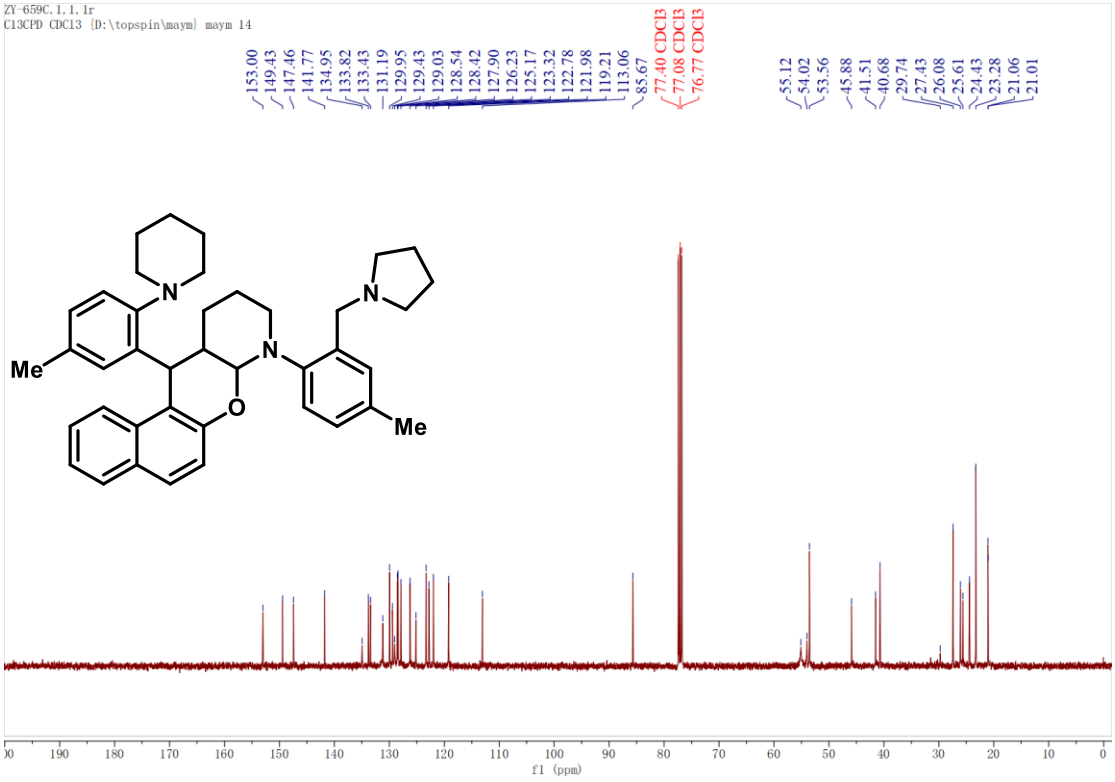
^{13}C NMR of Compound **4x** (101 MHz, $CDCl_3$)



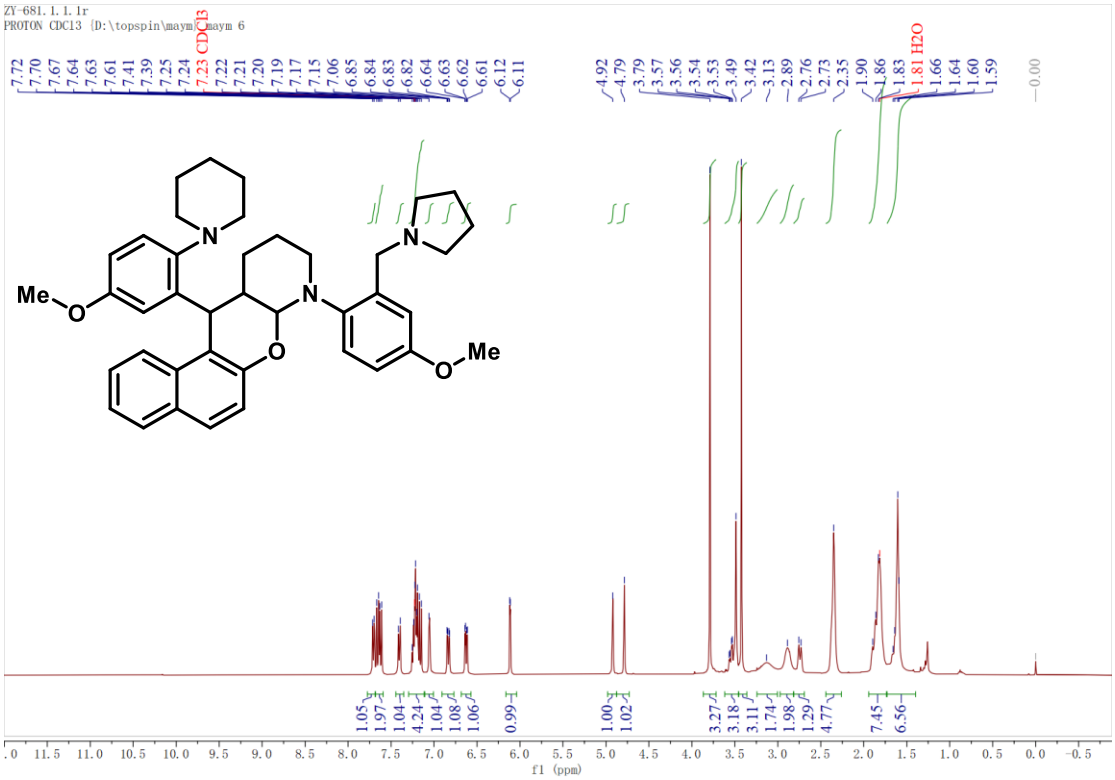
^{1}H NMR of Compound **4y** (400 MHz, $CDCl_3$)



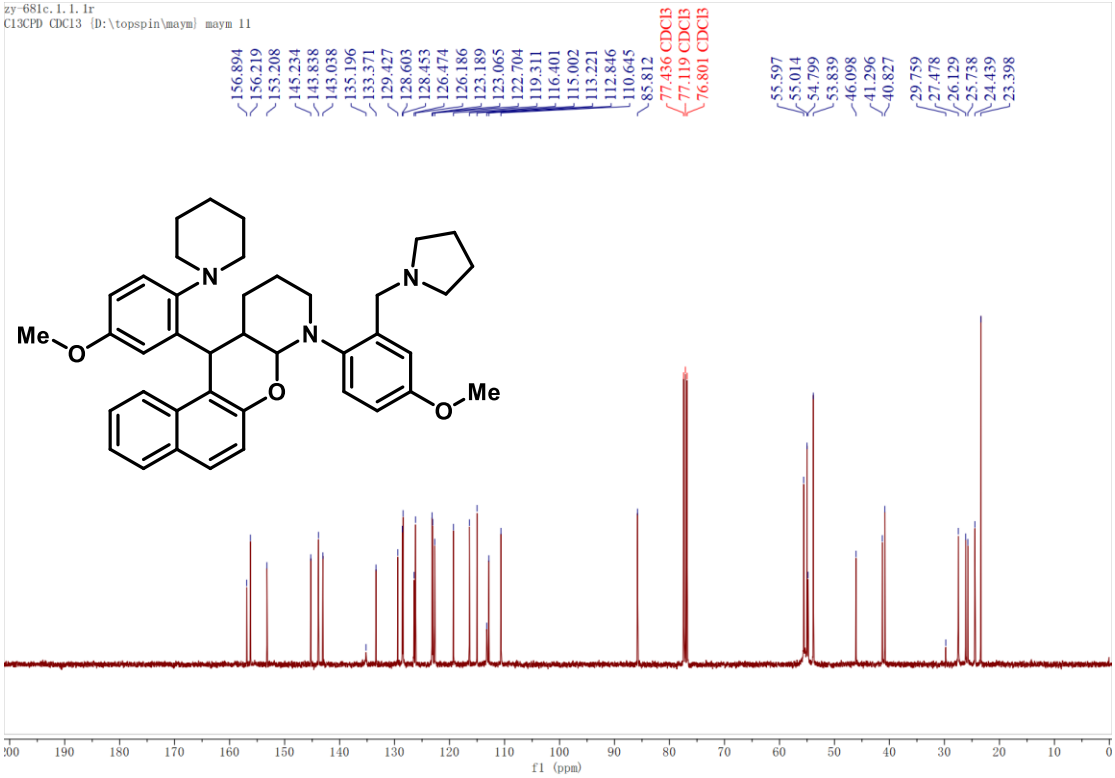
^{13}C NMR of Compound **4y** (101 MHz, $CDCl_3$)



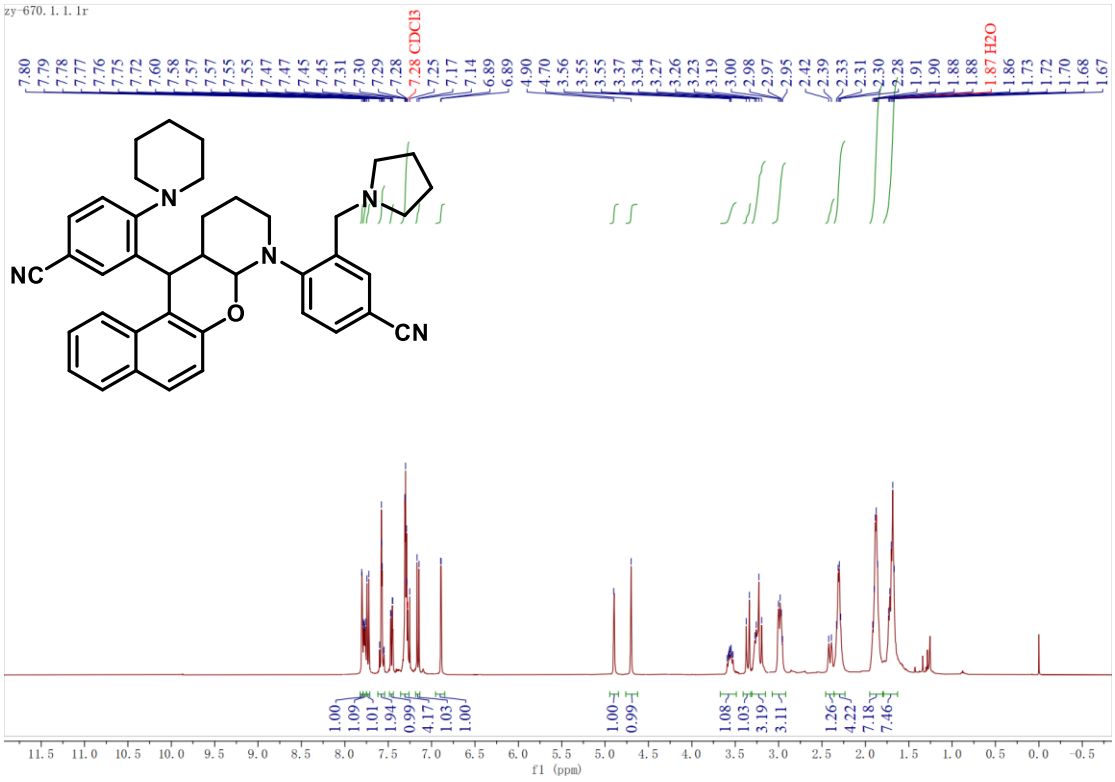
^{1}H NMR of Compound **4z** (400 MHz, $CDCl_3$)



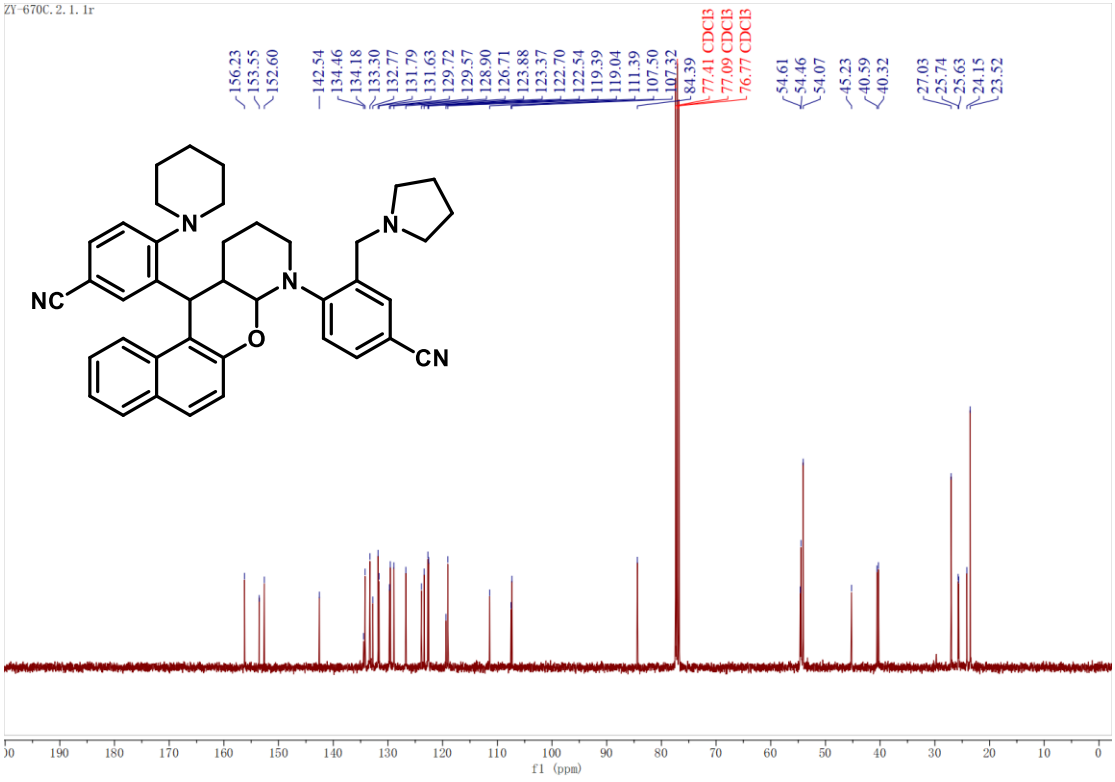
^{13}C NMR of Compound **4z** (101 MHz, $CDCl_3$)



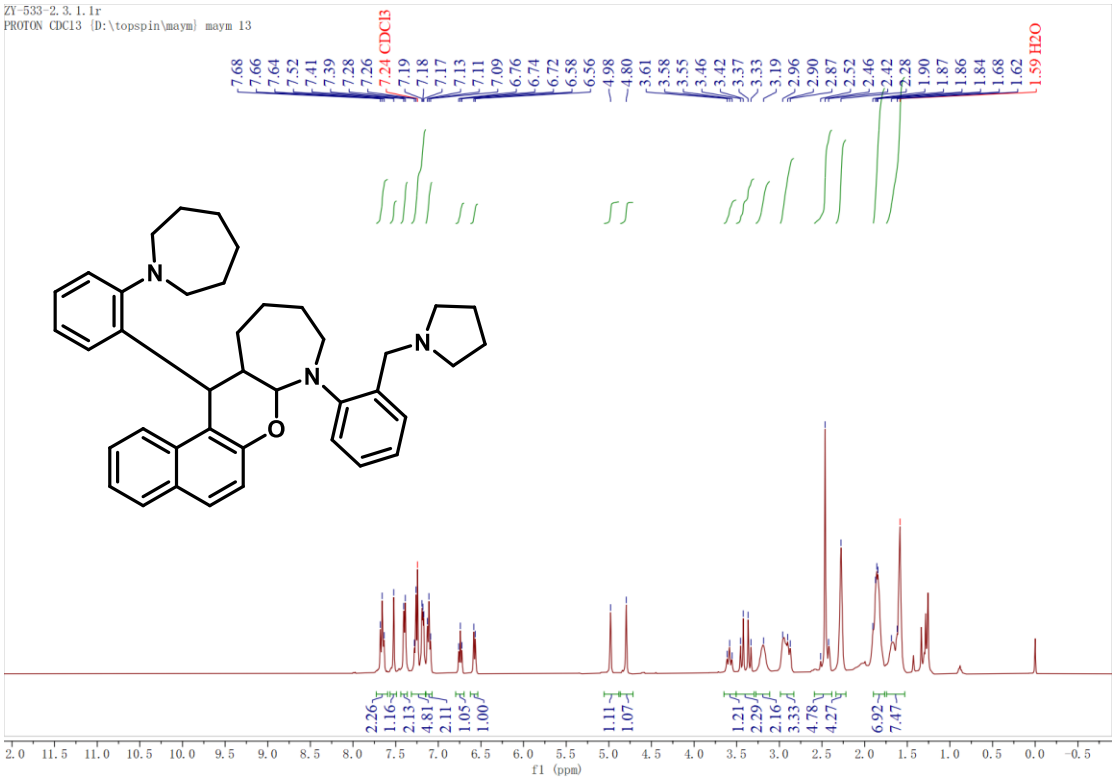
^{1}H NMR of Compound **4aa** (400 MHz, $CDCl_3$)



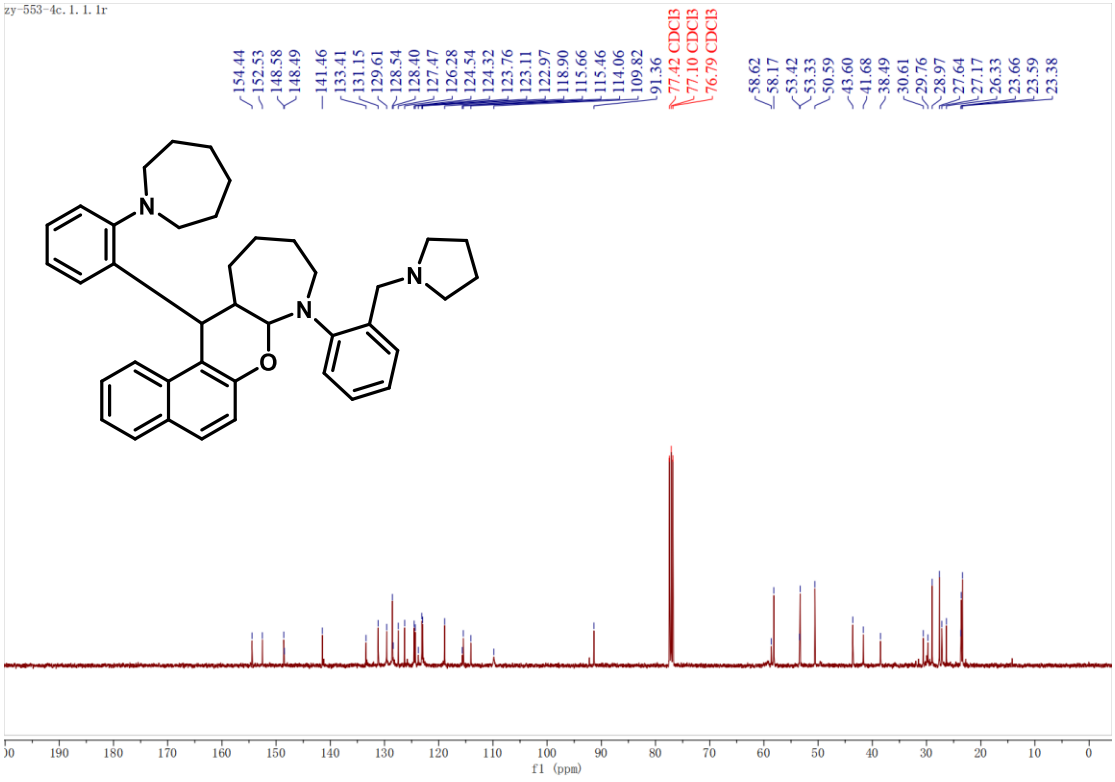
^{13}C NMR of Compound **4aa** (101 MHz, $CDCl_3$)



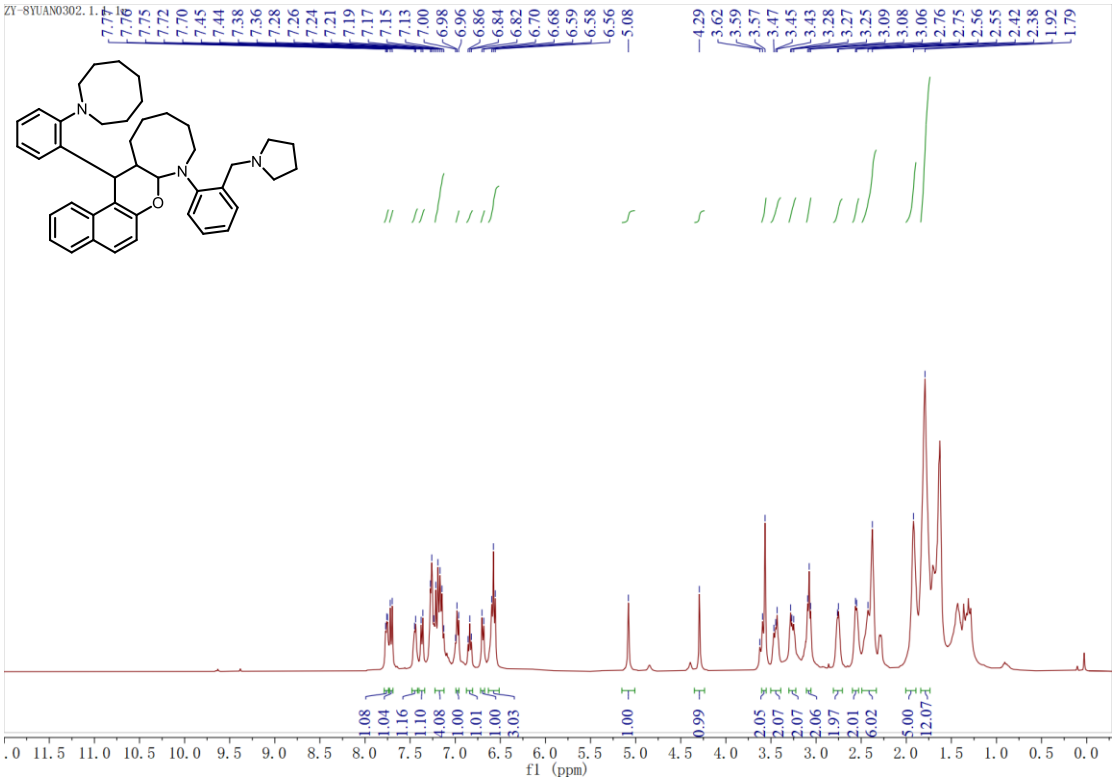
^{1}H NMR of Compound **4ab** (400 MHz, $CDCl_3$)



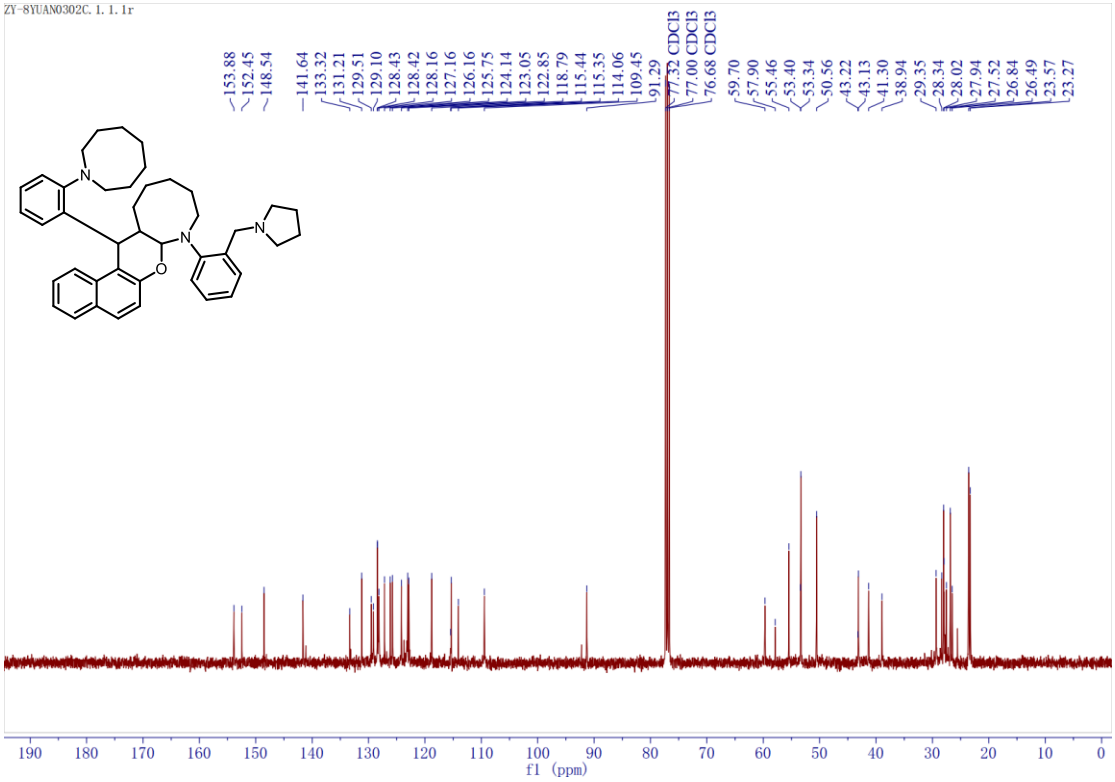
^{13}C NMR of Compound **4ab** (101 MHz, $CDCl_3$)



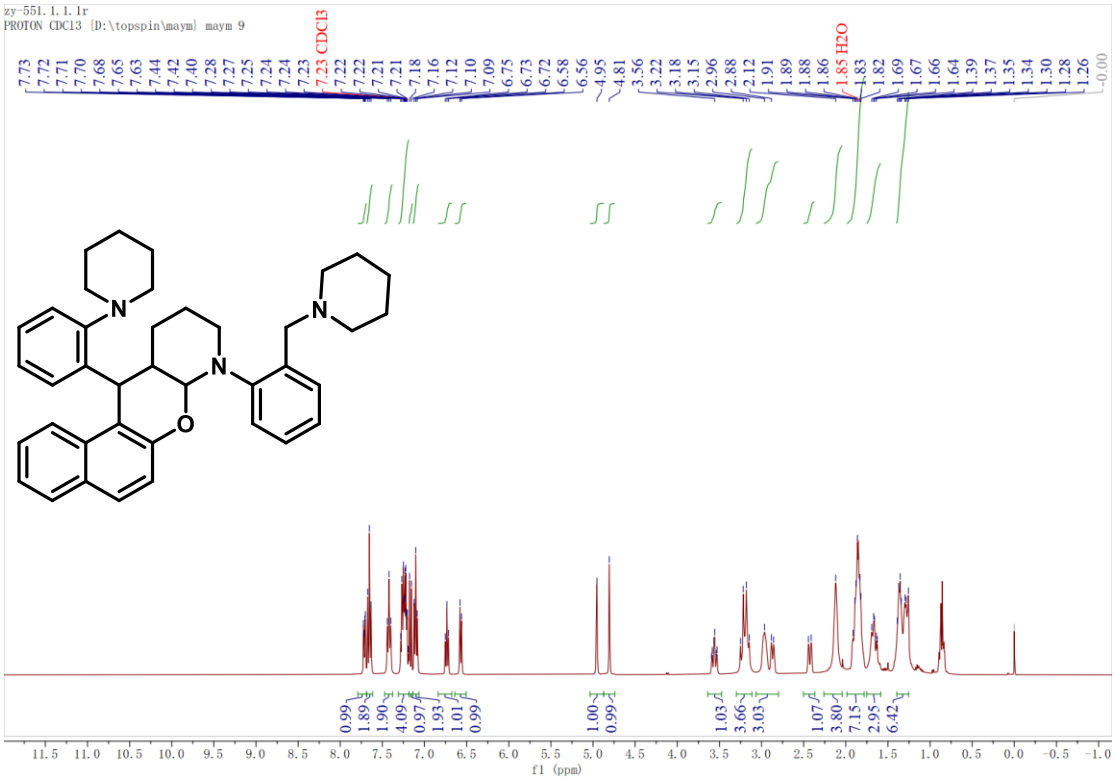
^{1}H NMR of Compound **4ac** (400 MHz, $CDCl_3$)



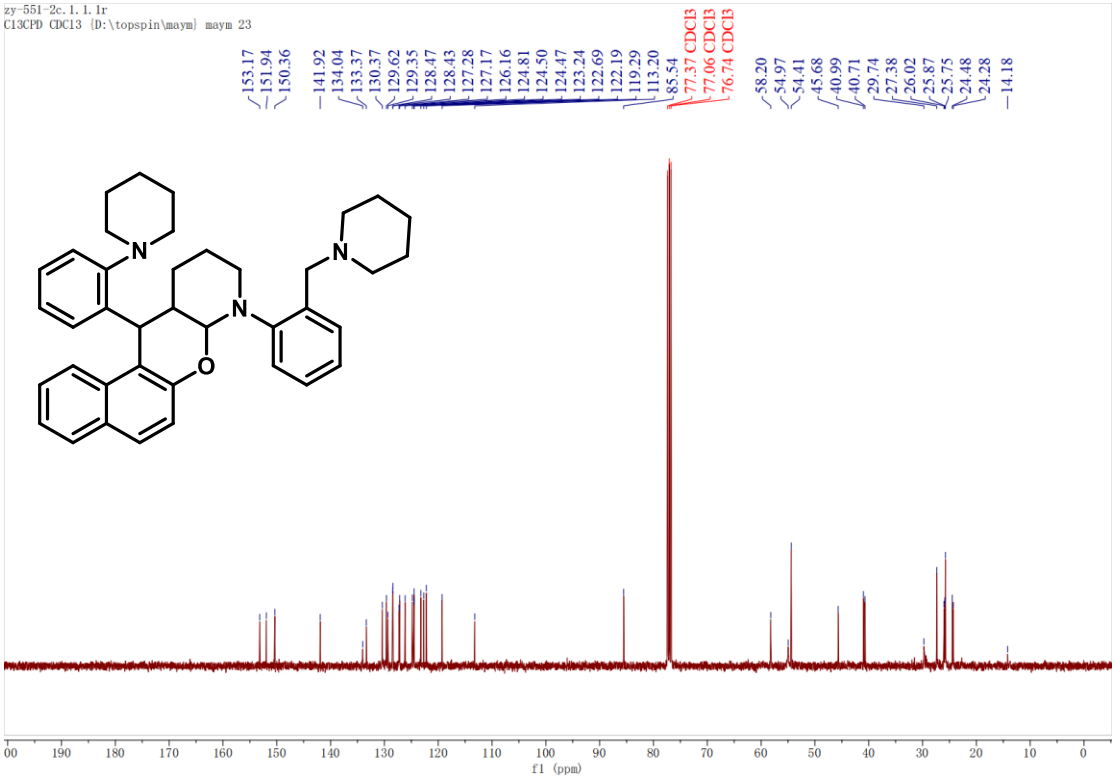
^{13}C NMR of Compound **4ac** (101 MHz, $CDCl_3$)



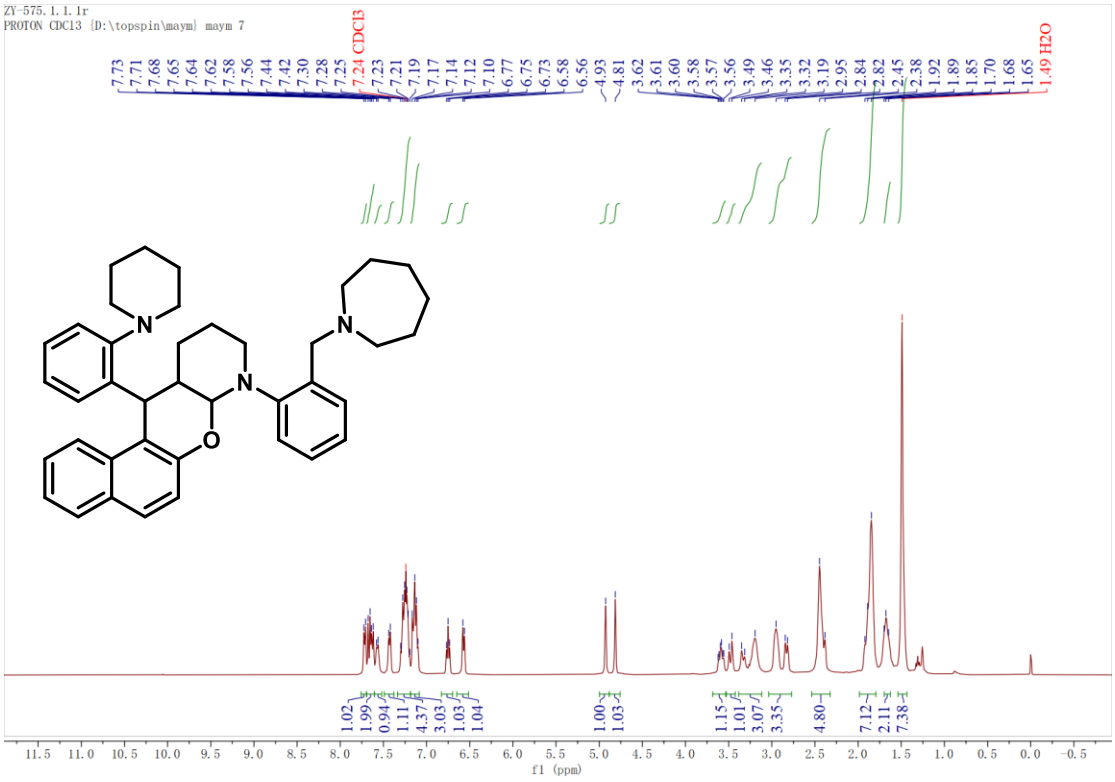
^{1}H NMR of Compound **4ad** (400 MHz, $CDCl_3$)



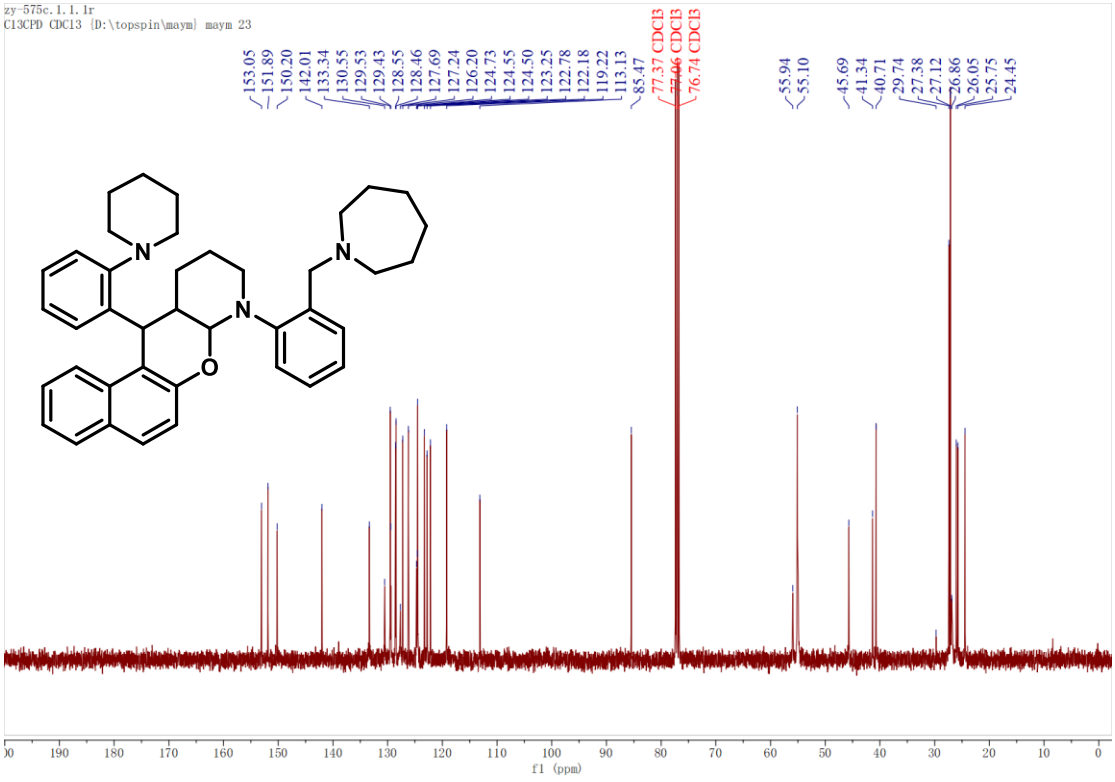
^{13}C NMR of Compound **4ad** (101 MHz, $CDCl_3$)



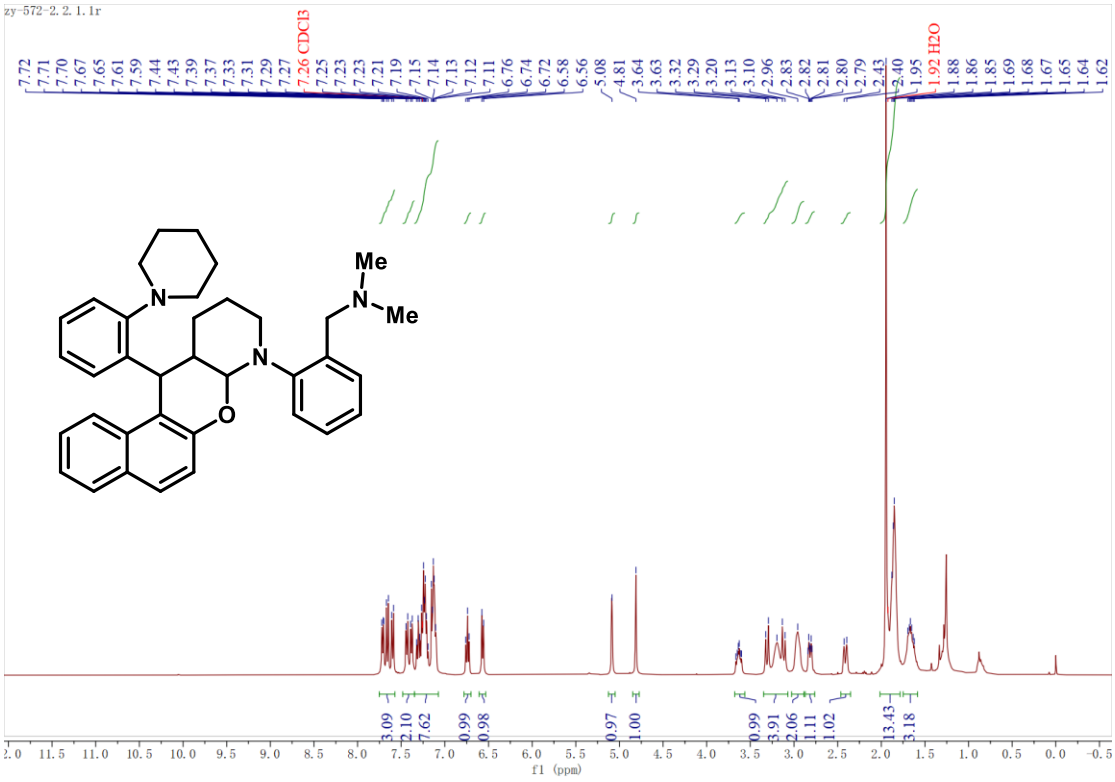
^{1}H NMR of Compound **4ae** (400 MHz, $CDCl_3$)



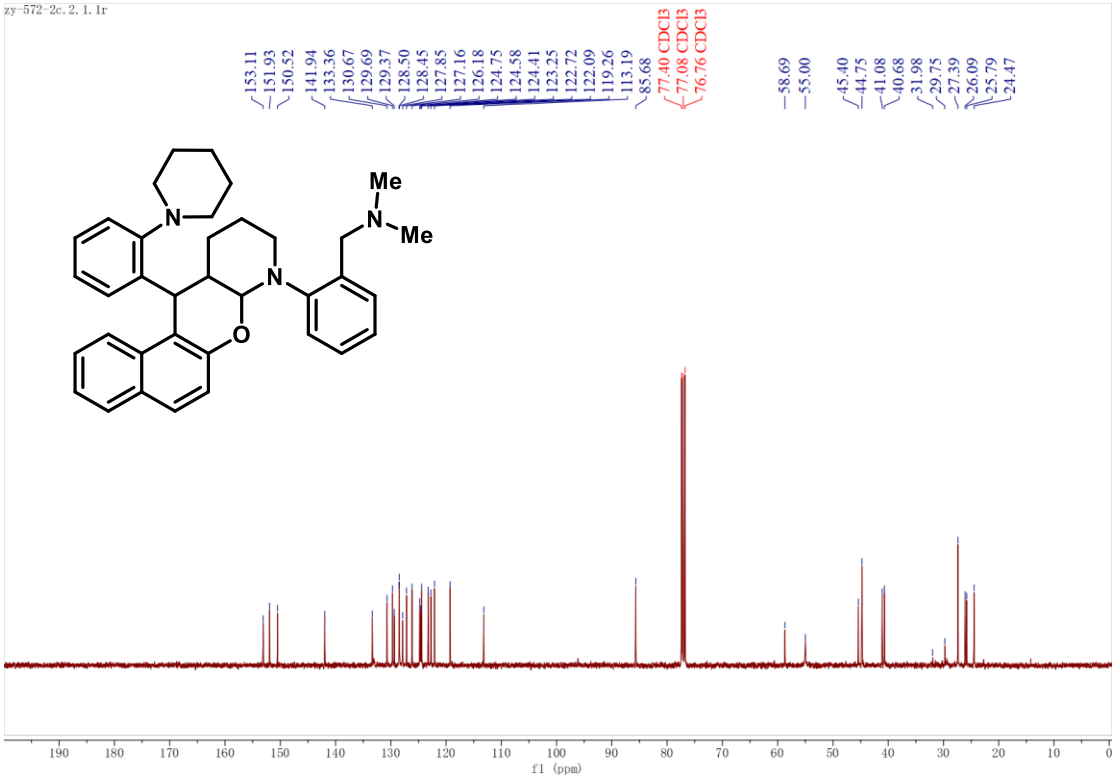
^{13}C NMR of Compound **4ae** (101 MHz, $CDCl_3$)



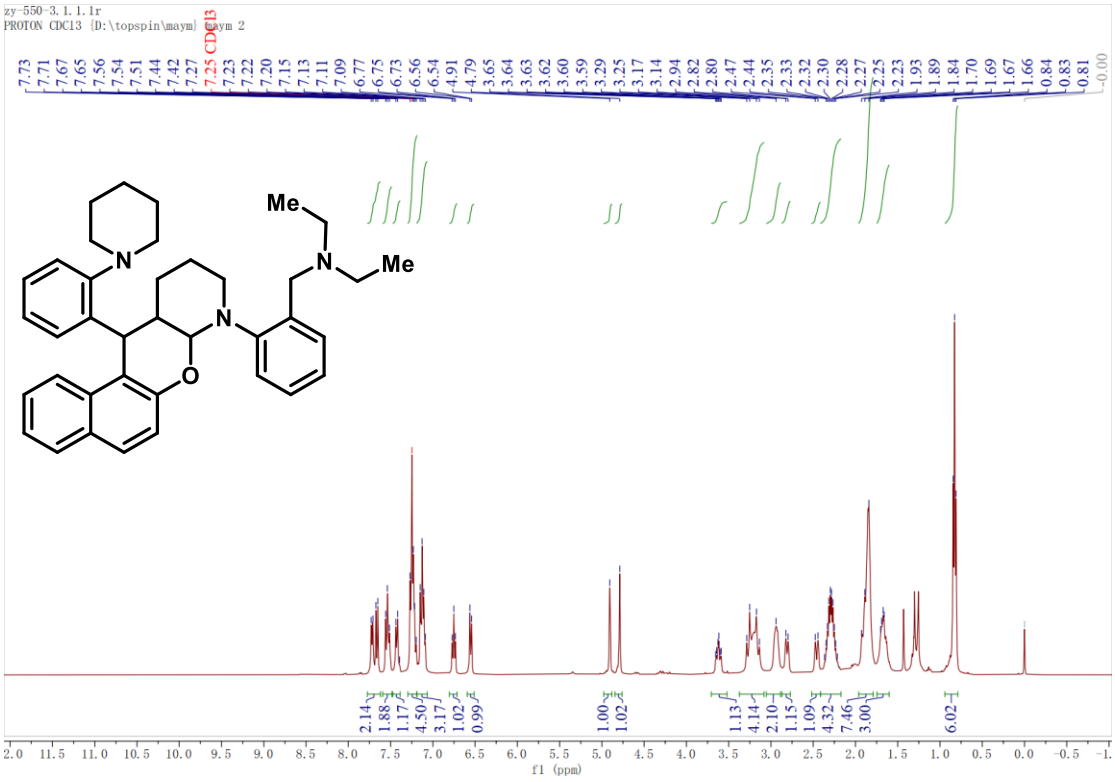
^{1}H NMR of Compound **4af** (400 MHz, $CDCl_3$)



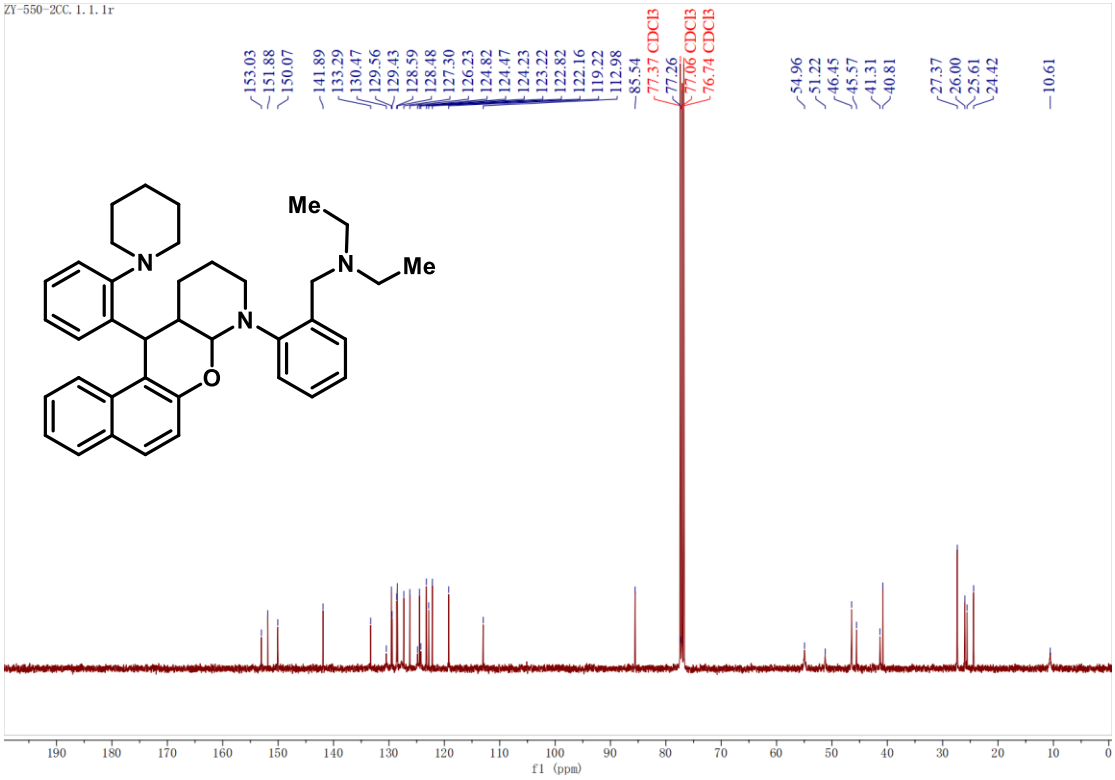
^{13}C NMR of Compound **4af** (101 MHz, $CDCl_3$)



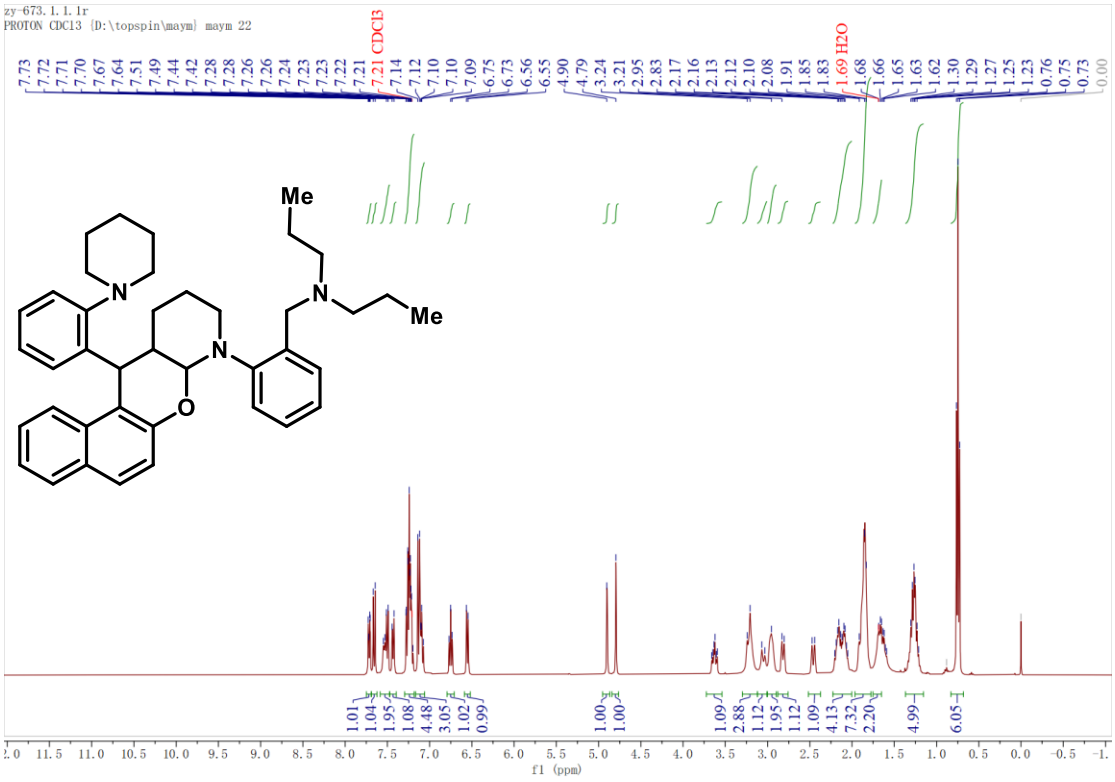
^{1}H NMR of Compound **4ag** (400 MHz, $CDCl_3$)



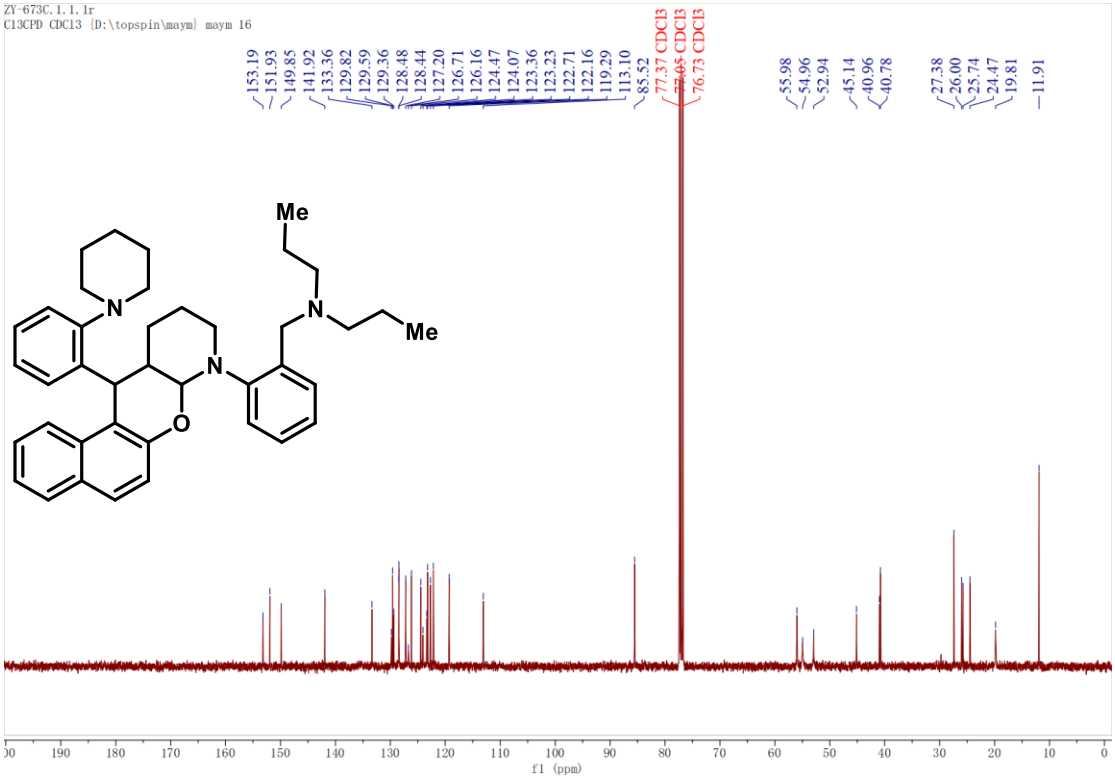
^{13}C NMR of Compound **4ag** (101 MHz, $CDCl_3$)



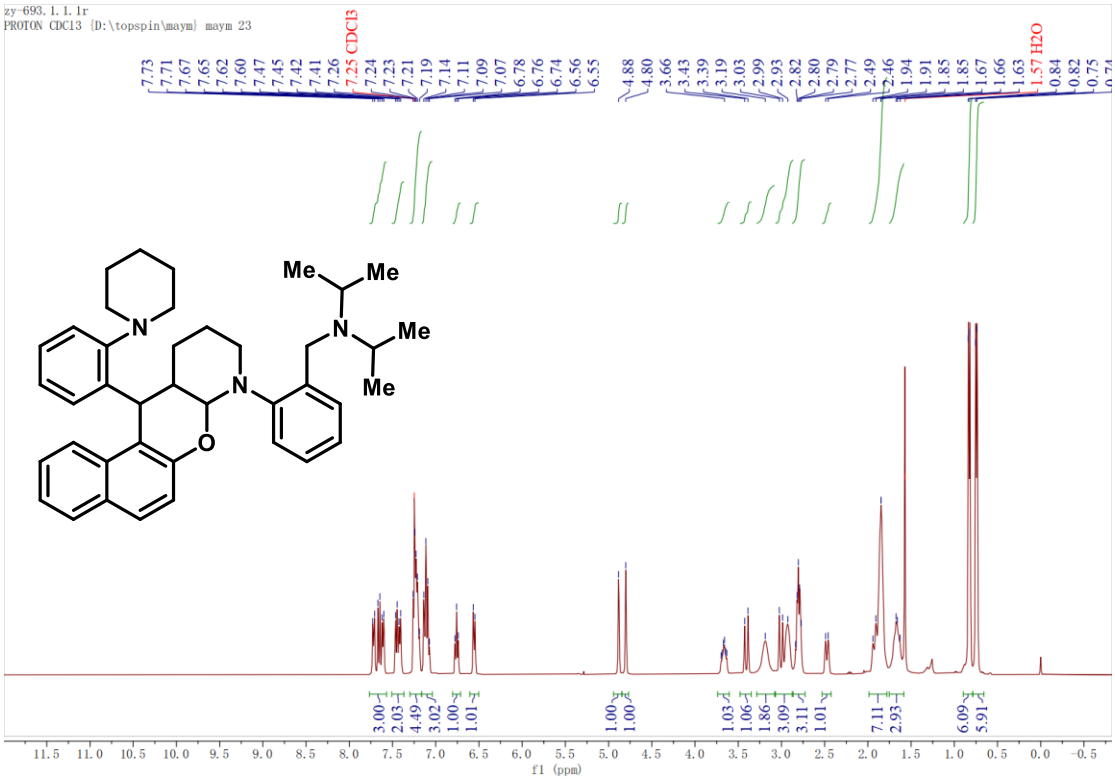
^{1}H NMR of Compound **4ah** (400 MHz, $CDCl_3$)



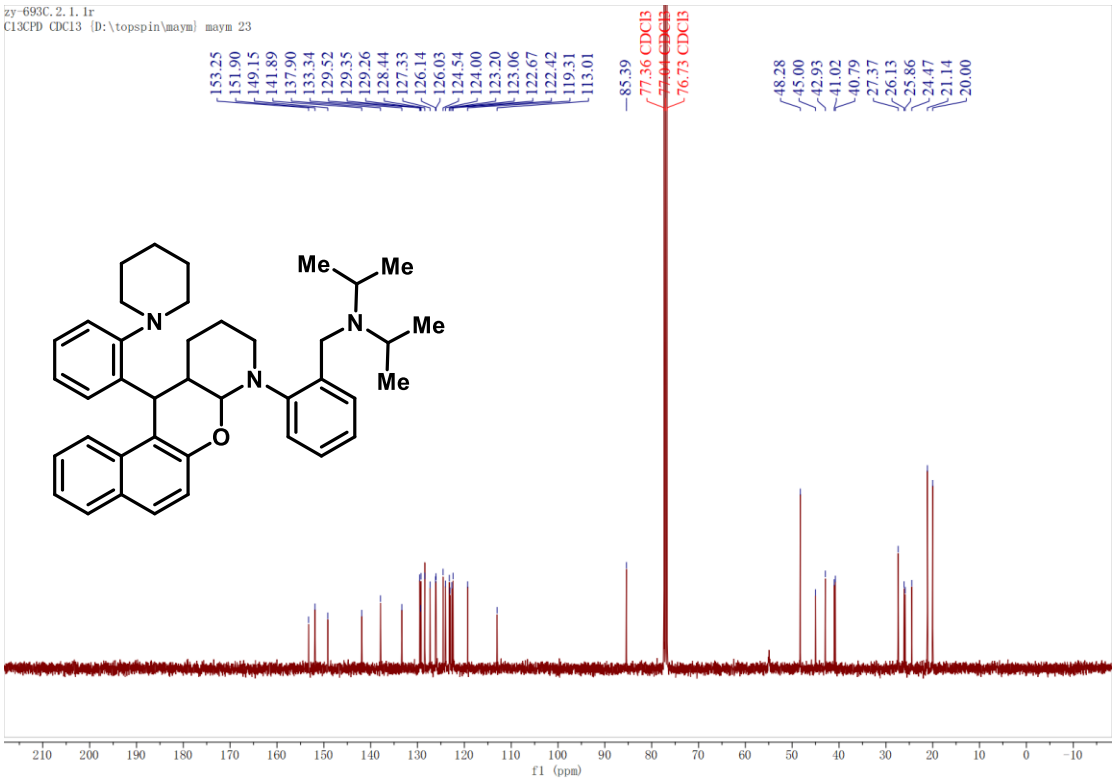
^{13}C NMR of Compound **4ah** (101 MHz, $CDCl_3$)



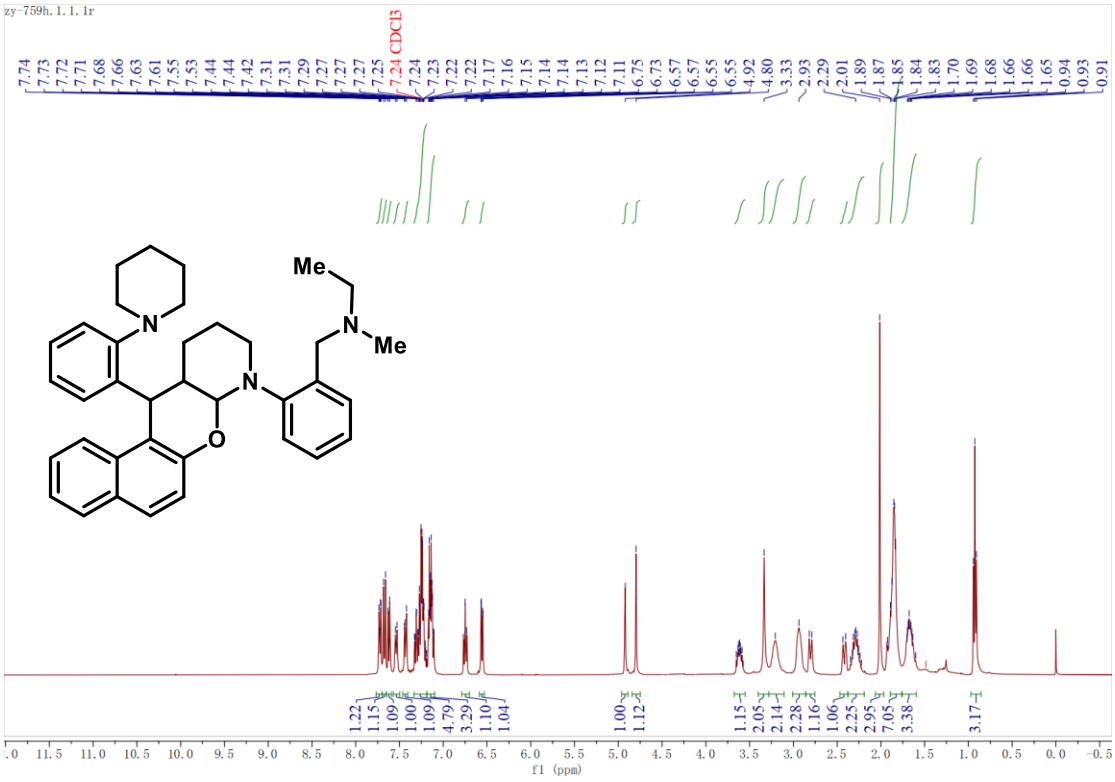
^{1}H NMR of Compound **4ai** (400 MHz, $CDCl_3$)



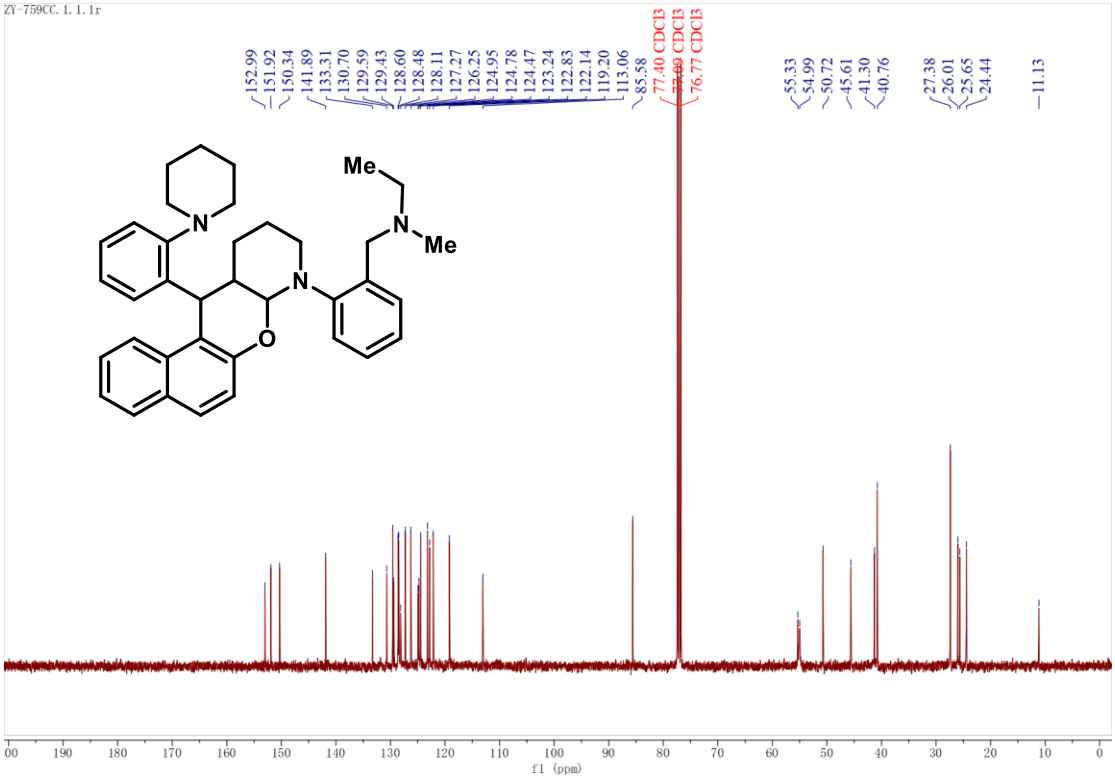
^{13}C NMR of Compound **4ai** (101 MHz, $CDCl_3$)



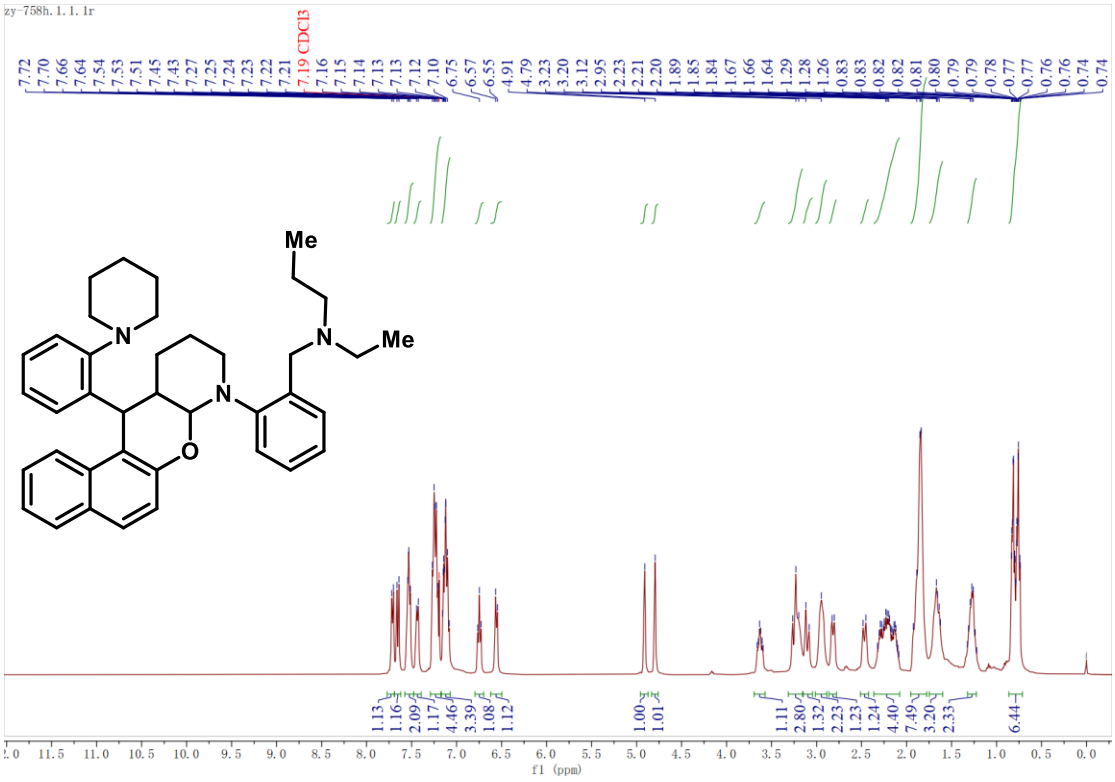
^{1}H NMR of Compound **4aj** (400 MHz, $CDCl_3$)



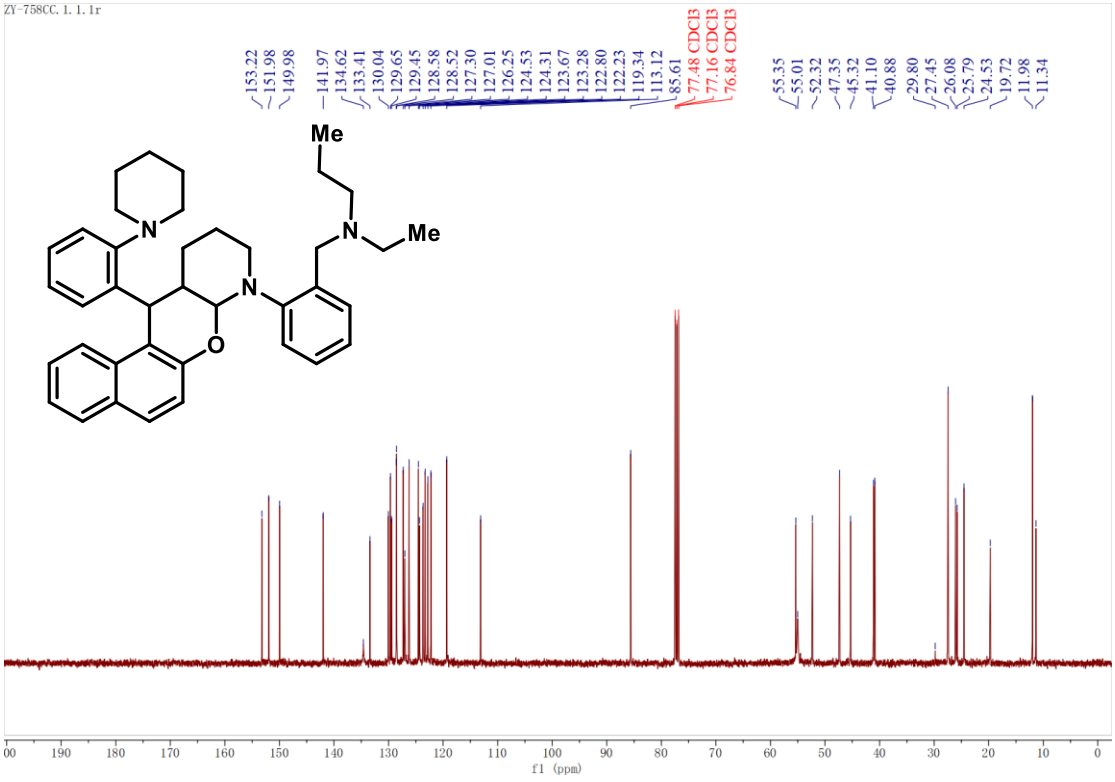
^{13}C NMR of Compound **4aj** (101 MHz, $CDCl_3$)



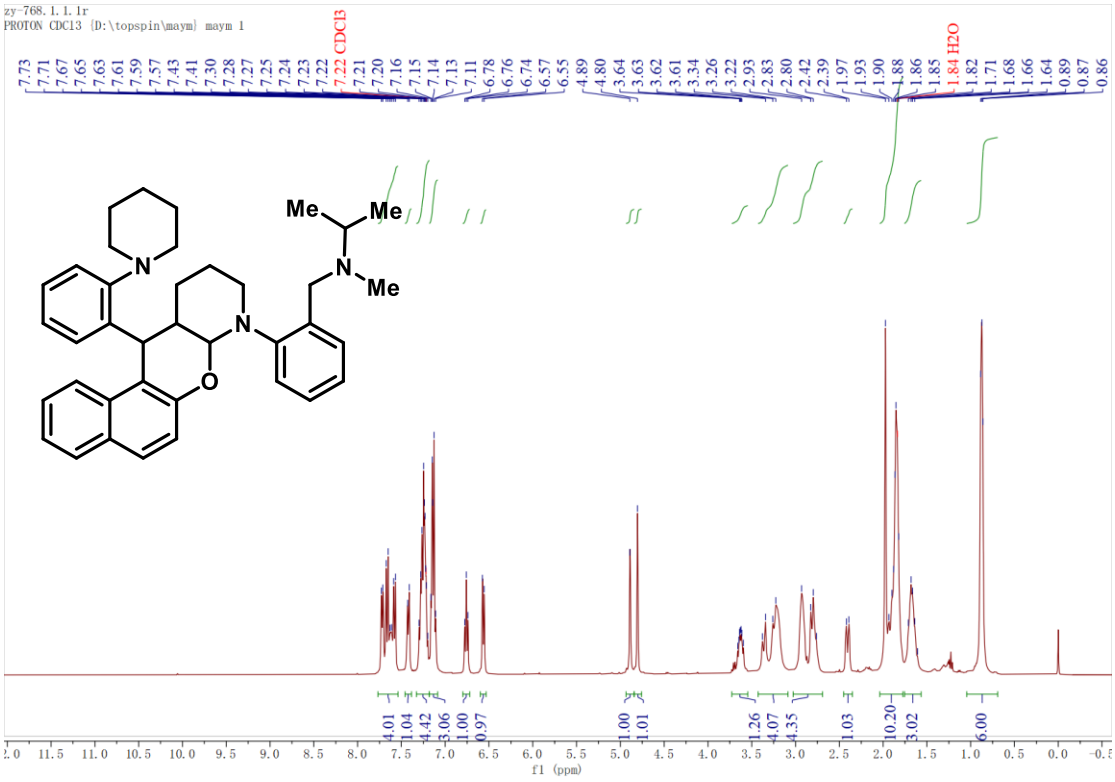
^{1}H NMR of Compound **4ak** (400 MHz, $CDCl_3$)



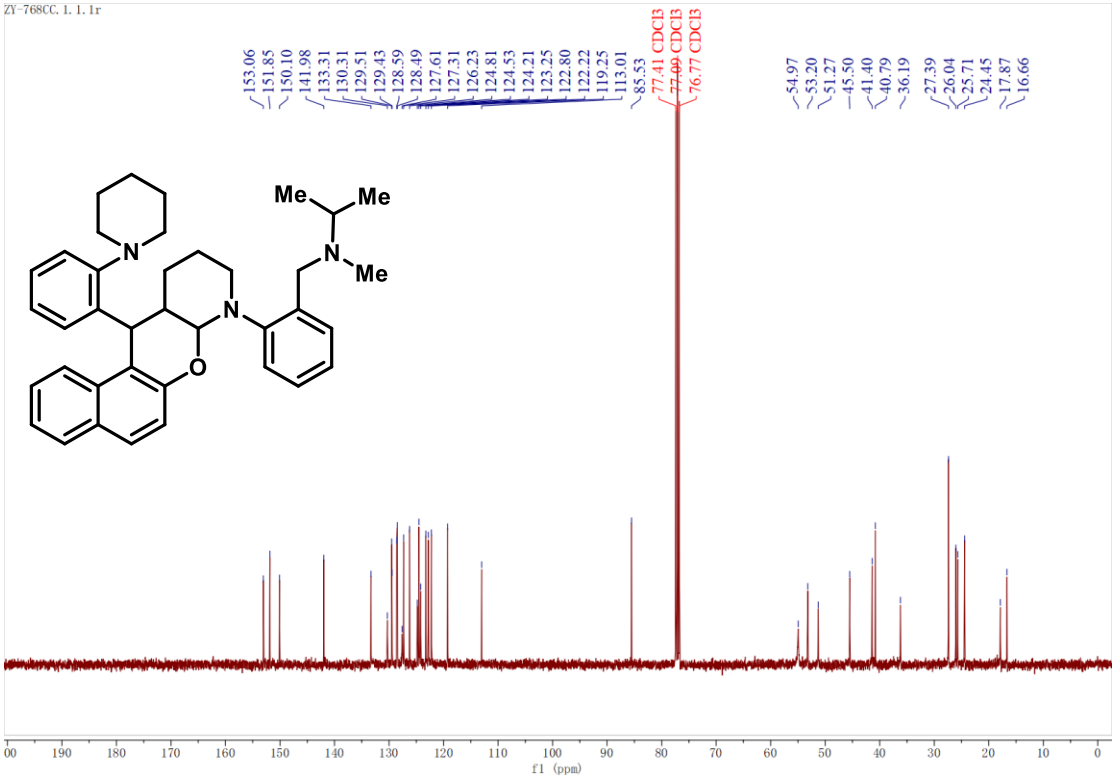
^{13}C NMR of Compound **4ak** (101 MHz, $CDCl_3$)



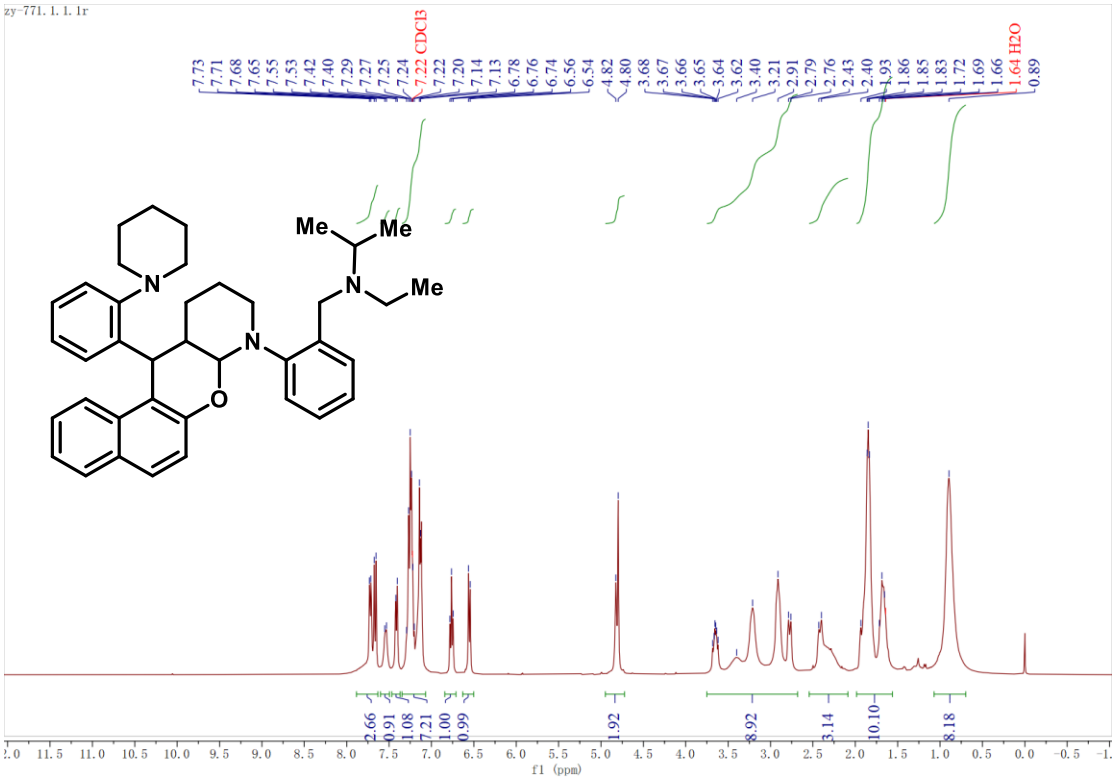
^{1}H NMR of Compound **4al** (400 MHz, $CDCl_3$)



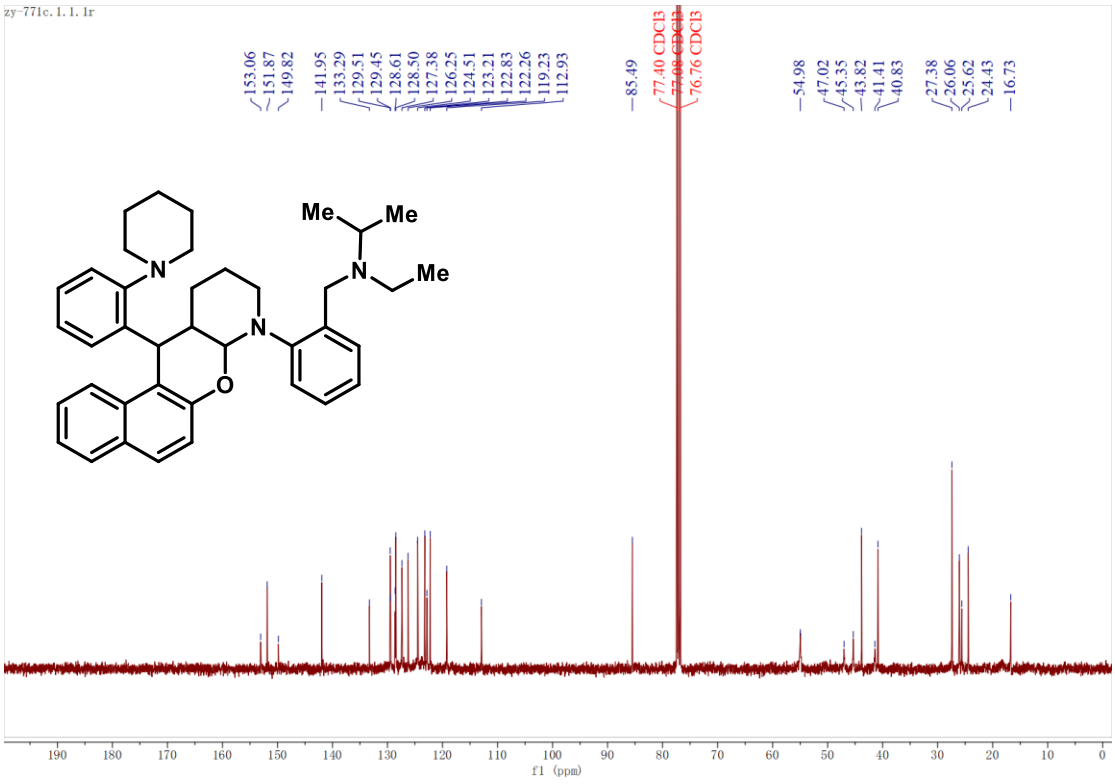
^{13}C NMR of Compound **4al** (101 MHz, $CDCl_3$)



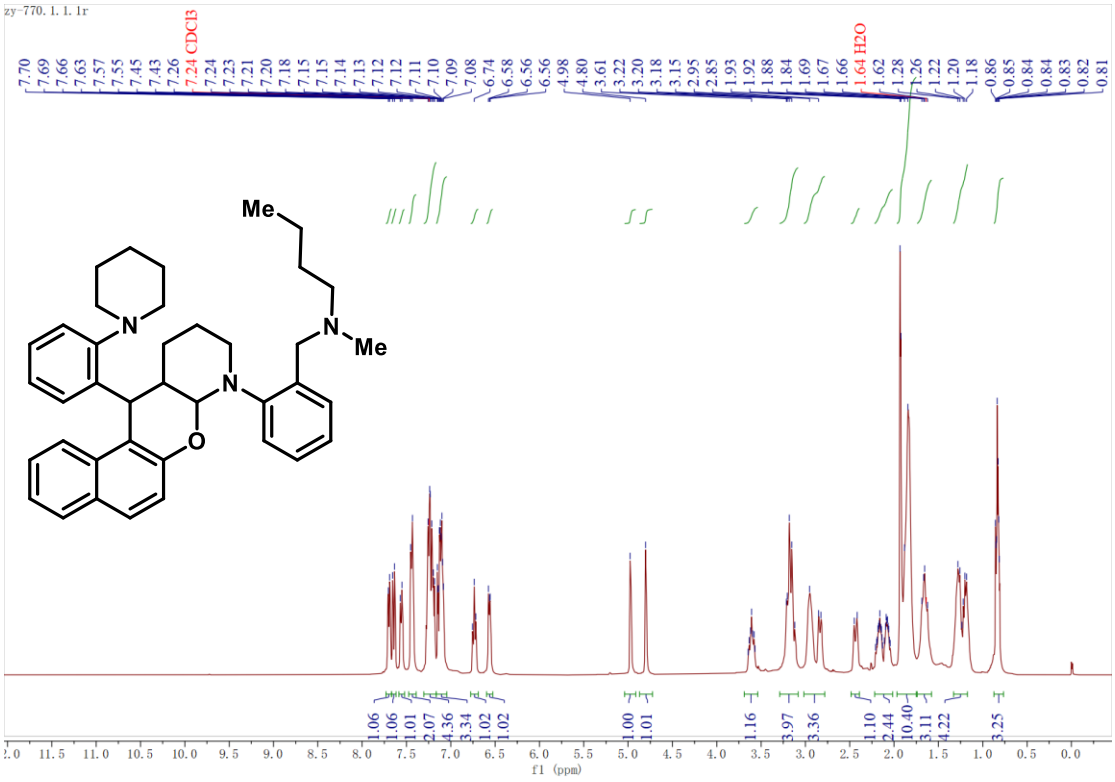
^{1}H NMR of Compound **4am** (400 MHz, $CDCl_3$)



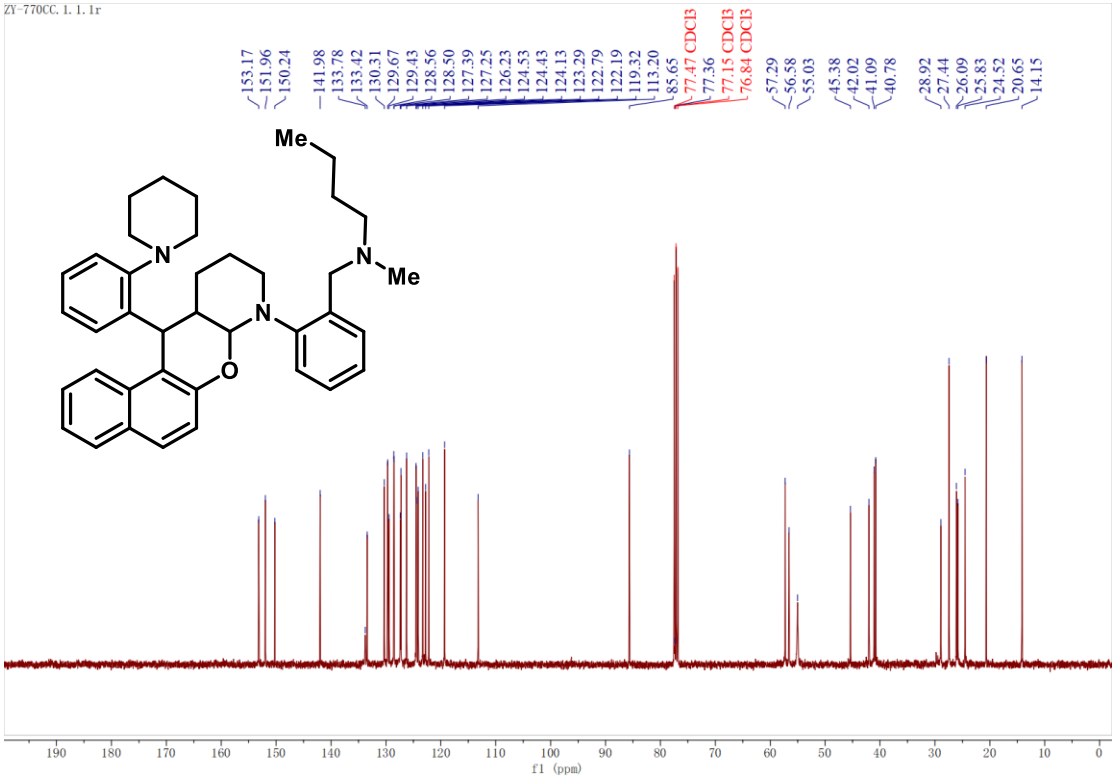
^{13}C NMR of Compound **4am** (101 MHz, $CDCl_3$)



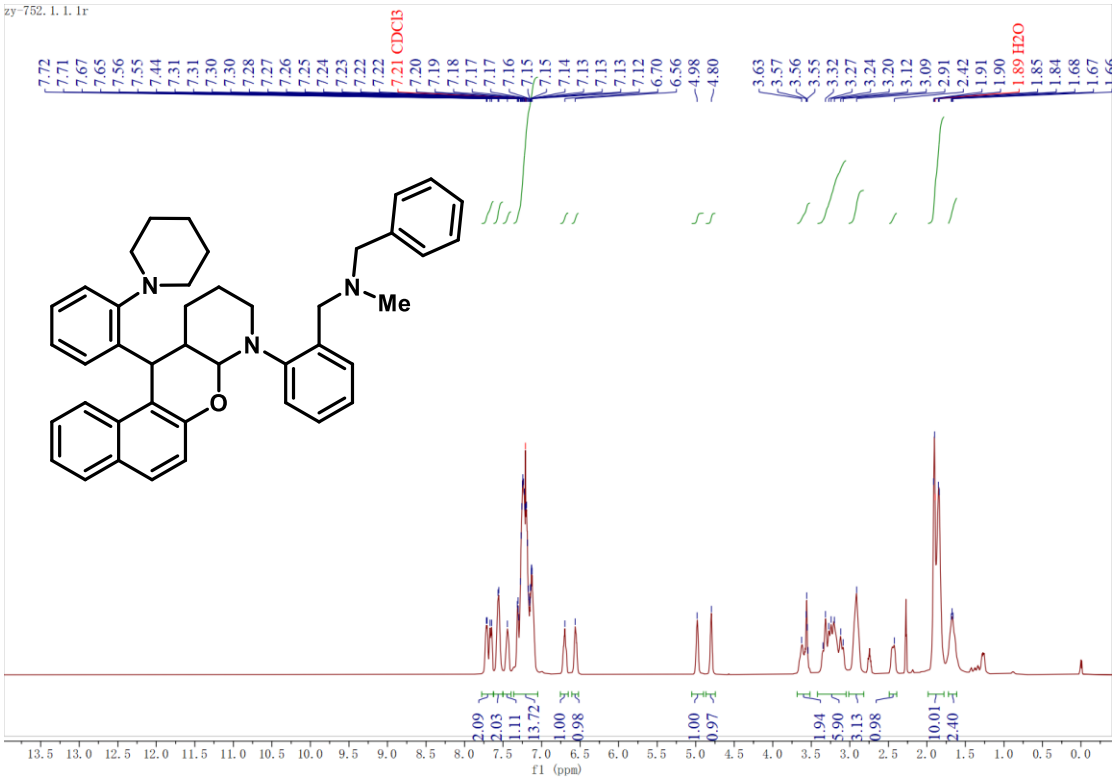
^{1}H NMR of Compound **4an** (400 MHz, $CDCl_3$)



^{13}C NMR of Compound **4an** (101 MHz, $CDCl_3$)



^{1}H NMR of Compound **4ao** (400 MHz, $CDCl_3$)



^{13}C NMR of Compound **4ao** (101 MHz, $CDCl_3$)