Supporting Information

Highly regioselective and stereoselective cascade reductive cyclization of δ-ketoamide: practical access to oxa-bridged benzazepines

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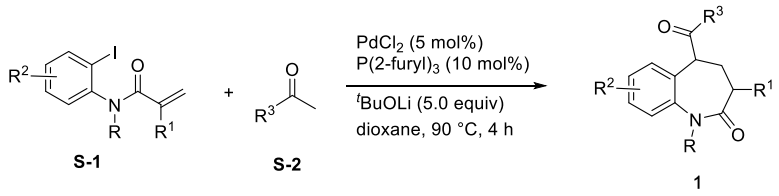
1. General considerations

All reactions were carried out under air atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. Solvents were purified and dried according to standard methods prior to use. For product purification by flash column chromatography, silica gel (200~300 mesh) and light petroleum ether (bp. 60~90) are used. ^{1}H NMR spectra were recorded on a Bruker advance III 400 MHz in $CDCl_3$ and $^{13}C\{^{1}H\}$ NMR spectra were recorded on 101 MHz in $CDCl_3$ using TMS as internal standard. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, dd = doublet of doublet, dt = triplet of doublets, ddd = doublet of doublet of doublets, coupling constant (s) in Hz, integration). Data for ^{13}C NMR is reported in terms of chemical shift (δ, ppm). High-resolution mass spectral analysis (HRMS) data were measured on a Bruker Apex II.

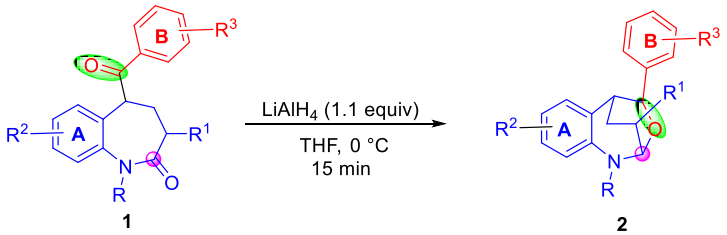
2. Preparation of substrates

Substrates **1** were synthesized according to the known literature.[1]



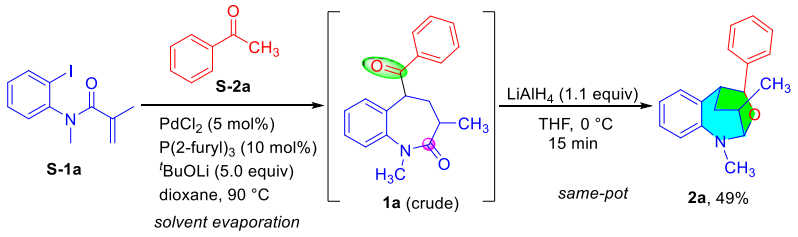
Acrylamides **S-1** (1.0 mmol, 1.0 equiv), aryl ketones **S-2** (1.5 mmol, 1.5 equiv), $PdCl_2$ (5 mol%), P(2-furyl)$_3$ (10 mol%), ^{t}BuOLi (5.0 mmol) were added to a sealed tube, dioxane (10.0 mL) were added via syringe. The mixture was flushed with N_2 and stirred at room temperature for 10 min firstly, and then was heated at 90 ℃ in an oil bath about for 4 h until completion (monitored by TLC). After cooling at room temperature, the reaction mixture was filtered through celite. The solvent in the filtrate was evaporated under reduced pressure. The residue was purified through silica gel chromatography to afford the starting material **1**.

3. Experiment procedure



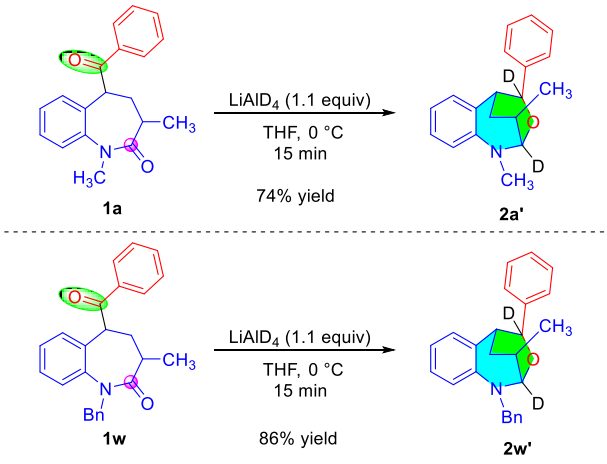
1 (0.2 mmol, 1.0 equiv) and $LiAlH_4$ (0.22 mmol, 1.1 equiv) were added to a sealed tube, THF (2.0 mL) were added via syringe. The mixture was stirred at 0 ℃ for 15 min. Upon completion of the reaction, the mixture was diluted with H_2O (0.2 mL), and the reaction mixture was filtered through celite. After evaporation of the solvent, the crude product was purified by column chromatography on silica gel to afford the coresponding product **2**.

4. One-pot synthesis of 2a



Acrylamide **S-1a** (0.2 mmol, 1.0 equiv), aryl ketone **S-2a** (0.3 mmol, 1.5 equiv), $PdCl_2$ (5 mol%), P(2-furyl)$_3$ (10 mol%), ^{t}BuOLi (1.0 mmol, 5.0 equiv) were added to a sealed tube, dioxane (2.0 mL) were added via syringe. The mixture was flushed with N_2 and stirred at room temperature for 10 min, firstly. After stirring at 90 ℃ in an oil bath about for 4 h, the solvents were removed in vacuo. Without further purification, to a solution of crude product **1a** in THF (2.0 mL) was added $LiAlH_4$ (0.22 mmol, 1.1 equiv) at 0 ℃ and stirred at the same temperature for 15 min. the resulting mixture was diluted with H_2O (0.2 mL), and then the reaction mixture was filtered through celite. After evaporation of the solvent, the crude product was purified by column chromatography on silica gel to afford the desired product **2a** in 49% yield for the two steps.

5. Deuterium labeling experiments



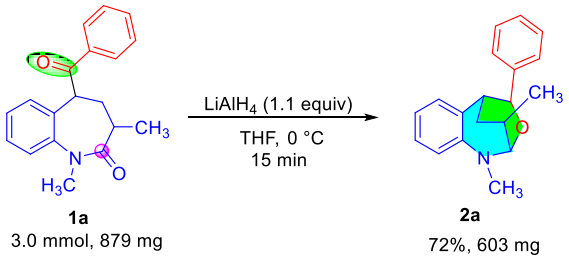
1a or **1w** (0.2 mmol, 1.0 equiv) and $LiAlD_4$ (0.22 mmol, 1.1 equiv) were added to a sealed tube, THF (2.0 mL) were added via syringe. The mixture was stirred at 0 ℃ for 15 min. Upon completion of the reaction, the mixture was diluted with D_2O (0.2 mL), and the reaction mixture was filtered through celite. After evaporation of the solvent, the crude product was purified by column chromatography on silica gel to afford the deuterium labeled products **2a'** or **2w'**.

1,3-dimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine-2,10-d$_2$ ***(2a')***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 42 mg, 74% yield, Mp = 81-83 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (m, 3H), 7.06 (dt, *J* = 7.5, 2.4 Hz, 3H), 6.54 (d, *J* = 8.2 Hz, 1H), 6.42-6.33 (m, 1H), 6.25 (dd, *J* = 7.3, 1.7 Hz, 1H), 3.08 (s, 3H), 2.74 (d, *J* = 7.5 Hz, 1H), 2.70-2.58 (m, 1H), 2.46 (ddd, *J* = 13.5, 9.7, 7.5 Hz, 1H), 1.90 (dd, *J* = 13.3, 8.5 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.8, 141.4, 130.3, 128.1, 127.7, 127.6, 127.0, 126.3,

116.7, 112.4, 94.6, 80.6, 47.8, 41.1, 35.9, 34.6, 18.1. HRMS (ESI-TOF) calcd for $C_{19}H_{19}ND_2NaO$ $[M+Na]^+$: 304.1641, found: 304.1658.

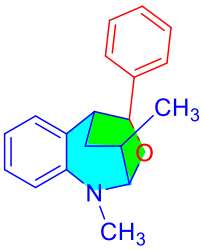
1-benzyl-3-methyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine-2,10-d_2 ***(2w')***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 61 mg, 86% yield, Mp = 95-97 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.2 Hz, 2H), 7.36 (dd, *J* = 8.4, 6.7 Hz, 2H), 7.29-7.16 (m, 6H), 6.89 (ddd, *J* = 8.7, 7.2, 1.8 Hz, 1H), 6.44 (d, *J* = 8.2 Hz, 1H), 6.36 (td, *J* = 7.3, 1.1 Hz, 1H), 6.30 (dd, *J* = 7.4, 1.8 Hz, 1H), 4.78 (d, *J* = 17.6 Hz, 1H), 4.51 (d, *J* = 17.6 Hz, 1H), 2.83 (d, *J* = 7.3 Hz, 1H), 2.69 (ddd, *J* = 9.9, 8.4, 6.7 Hz, 1H), 2.51 (ddd, *J* = 13.4, 9.7, 7.5 Hz, 1H), 2.04-1.93 (m, 1H), 1.17 (d, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.4, 141.5, 139.0, 130.5, 128.7, 128.3, 127.8, 127.6, 127.1, 126.8, 126.5, 126.3, 117.2, 114.0, 92.5, 80.7, 56.9, 47.8, 36.1, 34.6, 18.5. HRMS (ESI-TOF) calcd for $C_{25}H_{23}ND_2NaO$ $[M+Na]^+$: 380.1954, found: 380.1961.

6. Scale-up reaction



1a (3.0 mmol, 1.0 equiv) and $LiAlH_4$ (3.3 mmol, 1.1 equiv) were added to a sealed tube, THF (30.0 mL) were added via syringe. The mixture was stirred at 0 ℃ for 15 min. Upon completion of the reaction, the mixture was diluted with H_2O (3.0 mL), and the reaction mixture were extracted with EtOAc (3 times). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash column chromatography on silica gel to afford the coresponding product **2a** in 72% yield.

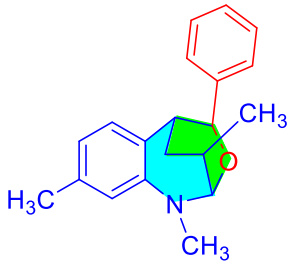
7. Spectra data



2a

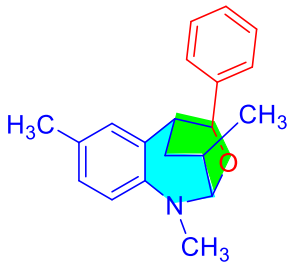
1,3-dimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2a)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 43 mg, 78% yield, Mp = 78-80 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11-7.05 (m, 3H), 7.02-6.93 (m, 3H), 6.47 (d, *J* = 8.2 Hz, 1H),

6.34-6.26 (m, 1H), 6.17 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.21-5.16 (m, 1H), 4.68 (d, *J* = 3.2 Hz, 1H), 3.00 (s, 3H), 2.69-2.64 (m, 1H), 2.56 (m, 1H), 2.38 (ddd, *J* = 13.4, 9.4, 7.6 Hz, 1H), 1.82 (dd, *J* = 13.3, 8.5 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 146.7, 141.4, 130.2, 128.1, 127.6, 127.5, 127.0, 126.2, 116.6, 112.3, 94.8, 81.0, 47.9, 41.1, 35.8, 34.6, 18.0. HRMS (ESI-TOF) calcd for $C_{19}H_{21}NNaO$ $[M+Na]^+$: 302.1515, found: 302.1518.



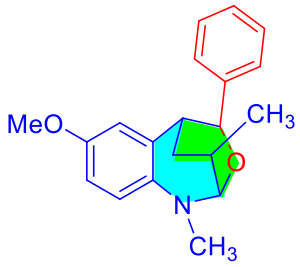
2b

1,3,8-trimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2b)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a colorless solid, 42 mg, 72% yield, Mp = 67-69 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.12 (m, 3H), 7.07 (dd, *J* = 7.7, 1.9 Hz, 2H), 6.36 (d, *J* = 1.6 Hz, 1H), 6.22-6.11 (m, 2H), 5.26-5.21 (m, 1H), 4.75 (d, *J* = 3.2 Hz, 1H), 3.08 (s, 3H), 2.75-2.69 (m, 1H), 2.63 (dddd, *J* = 9.8, 8.3, 6.6, 3.1 Hz, 1H), 2.44 (ddd, *J* = 13.4, 9.7, 7.4 Hz, 1H), 2.24 (s, 3H), 1.92-1.80 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 146.5, 141.5, 137.0, 130.2, 127.6, 126.9, 126.3, 125.3, 117.4, 113.4, 94.8, 81.0, 47.4, 41.2, 36.1, 34.6, 21.6, 18.1. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NNaO$ $[M+Na]^+$: 316.1672, found: 316.1671.



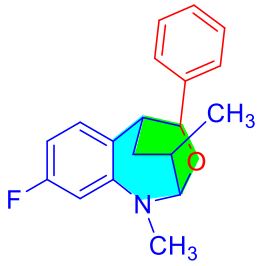
2c

1,3,7-trimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2c)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a yellow solid, 46 mg, 79% yield, Mp = 66-68 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-7.05 (m, 3H), 7.00 (dd, *J* = 7.8, 1.9 Hz, 2H), 6.77 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.38 (d, *J* = 8.2 Hz, 1H), 6.02 (d, *J* = 2.3 Hz, 1H), 5.17 (d, *J* = 1.9 Hz, 1H), 4.66 (d, *J* = 3.3 Hz, 1H), 2.99 (s, 3H), 2.66-2.60 (m, 1H), 2.60-2.50 (m, 1H), 2.37 (ddd, *J* = 13.3, 9.7, 7.4 Hz, 1H), 1.93 (s, 3H), 1.84-1.76 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 144.5, 141.6, 131.1, 128.3, 127.9, 127.7, 127.0, 126.3, 125.7, 112.6, 94.7, 81.2, 47.7, 41.5, 36.1, 34.5, 20.0, 18.2. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NNaO$ $[M+Na]^+$: 316.1672, found: 316.1679.



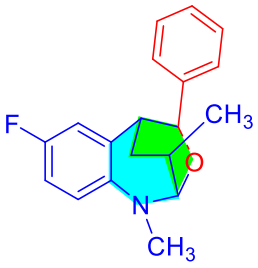
2d

7-methoxy-1,3-dimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2d)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a colorless solid, 53 mg, 87% yield, Mp = 73-75 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.12 (m, 3H), 7.10-7.05 (m, 2H), 6.61 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.48 (d, *J* = 8.8 Hz, 1H), 5.92 (d, *J* = 3.0 Hz, 1H), 5.26-5.22 (m, 1H), 4.73 (d, *J* = 3.4 Hz, 1H), 3.54 (s, 3H), 3.05 (s, 3H), 2.74-2.68 (m, 1H), 2.66-2.53 (m, 1H), 2.44 (ddd, *J* = 13.4, 9.7, 7.4 Hz, 1H), 1.93-1.82 (m, 1H), 1.11 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 151.1, 141.5, 141.0, 129.7, 127.7, 127.0, 126.1, 117.0, 113.4, 112.0, 94.6, 80.8, 55.6, 47.8, 41.8, 35.7, 34.2, 18.1. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NNaO_2$ $[M+Na]^+$: 332.1621, found: 332.1616.



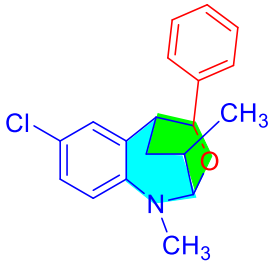
2e

8-fluoro-1,3-dimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2e)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow oil, 42 mg, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.12 (m, 3H), 7.06 (dd, *J* = 7.7, 2.0 Hz, 2H), 6.23 (dd, *J* = 12.5, 2.5 Hz, 1H), 6.14 (dd, *J* = 8.2, 6.9 Hz, 1H), 6.03 (td, *J* = 8.2, 2.5 Hz, 1H), 5.23 (d, *J* = 1.7 Hz, 1H), 4.75 (d, *J* = 3.1 Hz, 1H), 3.04 (s, 3H), 2.76-2.70 (m, 1H), 2.69-2.57 (m, 1H), 2.52-2.38 (m, 1H), 1.85 (dd, *J* = 13.4, 8.6 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.0 (d, *J* = 242.4 Hz), 148.3 (d, *J* = 10.5 Hz), 141.1, 130.9 (d, *J* = 10.1 Hz), 127.7, 127.1, 126.2, 123.8 (d, *J* = 2.6 Hz), 102.2 (d, *J* = 21.1 Hz), 99.7 (d, *J* = 26.9 Hz), 94.6, 80.8, 47.3, 41.0, 35.7, 34.7, 18.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.64. HRMS (ESI-TOF) calcd for $C_{19}H_{20}NNaFO$ $[M+Na]^+$: 320.1421, found: 320.1415.



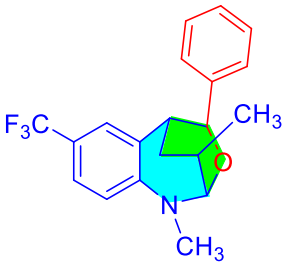
2f

7-fluoro-1,3-dimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (***2f***): Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 41 mg, 69% yield, Mp = 112-114 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (q, *J* = 6.9, 6.4 Hz, 3H), 7.07 (dd, *J* = 7.6, 2.0 Hz, 2H), 6.73 (td, *J* = 8.5, 3.0 Hz, 1H), 6.43 (dd, *J* = 8.9, 4.7 Hz, 1H), 6.03 (dd, *J* = 9.0, 3.1 Hz, 1H), 5.25 (d, *J* = 1.9 Hz, 1H), 4.74 (d, *J* = 3.3 Hz, 1H), 3.05 (s, 3H), 2.70 (dd, *J* = 7.0, 1.8 Hz, 1H), 2.66-2.56 (m, 1H), 2.45 (ddd, *J* = 13.5, 9.7, 7.5 Hz, 1H), 1.88 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.12 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.9 (d, *J* = 242.4 Hz), 143.1 (d, *J* = 2.0 Hz), 141.1, 129.8 (d, *J* = 6.4 Hz), 127.8, 127.2, 126.0, 116.8 (d, *J* = 22.4 Hz), 113.2 (d, *J* = 21.3 Hz), 112.9 (d, *J* = 7.5 Hz), 94.6, 80.7, 47.7, 41.7, 35.6, 34.4, 18.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -129.89. HRMS (ESI-TOF) calcd for $C_{19}H_{20}NNaFO$ $[M+Na]^+$: 320.1421, found: 320.1427.



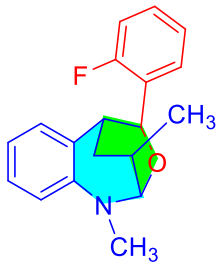
2g

7-chloro-1,3-dimethyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (***2g***): Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 42 mg, 67% yield, Mp = 113-115 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.15 (m, 3H), 7.12-7.04 (m, 2H), 6.98 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.43 (d, *J* = 8.7 Hz, 1H), 6.24 (d, *J* = 2.6 Hz, 1H), 5.24 (d, *J* = 1.8 Hz, 1H), 4.80-4.69 (m, 1H), 3.05 (s, 3H), 2.74-2.58 (m, 2H), 2.52-2.40 (m, 1H), 1.86 (ddd, *J* = 13.5, 8.4, 1.0 Hz, 1H), 1.12 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.4, 140.9, 129.9, 129.6, 127.8, 127.3, 127.1, 126.1, 121.0, 113.4, 94.6, 80.7, 47.6, 41.3, 35.7, 34.5, 18.0. HRMS (ESI-TOF) calcd for $C_{19}H_{20}NNaClO$ $[M+Na]^+$: 336.1126, found: 336.1123.



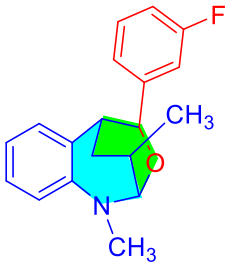
2h

*1,3-dimethyl-10-phenyl-7-(trifluoromethyl)-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (**2h**)*: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a colorless oil, 51 mg, 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 7.4, 1.9 Hz, 2H), 7.11-7.03 (m, 3H), 6.97 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 2.3 Hz, 1H), 6.27 (d, *J* = 8.5 Hz, 1H), 5.23 (d, *J* = 4.6 Hz, 1H), 4.52 (s, 1H), 3.11 (d, *J* = 4.0 Hz, 1H), 2.93 (s, 3H), 2.45 (ddd, *J* = 12.8, 9.3, 3.7 Hz, 1H), 2.35-2.19 (m, 1H), 1.72 (ddd, *J* = 12.8, 8.0, 3.3 Hz, 1H), 1.13 (d, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 149.7, 142.0, 128.8, 127.7, 126.9 (q, *J* = 3.6 Hz), 126.5, 125.2, 124.9 (q, *J* = 3.6 Hz), 124.8 (q, *J* = 271.5 Hz), 119.5 (q, *J* = 32.5 Hz), 113.6, 94.2, 81.7, 44.8, 40.7, 37.9, 34.4, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.11. HRMS (ESI-TOF) calcd for $C_{20}H_{21}NF_3O$ $[M+H]^+$: 348.1570, found: 348.1571.



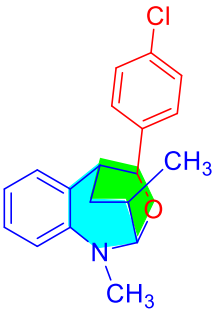
2i

*10-(2-fluorophenyl)-1,3-dimethyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (**2i**)*: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a yellow solid, 42 mg, 70% yield, Mp = 63-65 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15-7.00 (m, 3H), 6.94 (ddd, *J* = 10.7, 8.2, 1.2 Hz, 1H), 6.86 (td, *J* = 7.5, 1.2 Hz, 1H), 6.53 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.35 (td, *J* = 7.3, 1.1 Hz, 1H), 6.27 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.60 (s, 1H), 4.77 (dd, *J* = 3.2, 1.0 Hz, 1H), 3.08 (s, 3H), 2.85 (dd, *J* = 7.6, 1.7 Hz, 1H), 2.66 (dtd, *J* = 8.4, 6.7, 3.4 Hz, 1H), 2.55-2.43 (m, 1H), 1.89 (ddd, *J* = 13.3, 8.4, 1.0 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.4 (d, *J* = 245.3 Hz), 146.7, 130.1, 128.6 (d, *J* = 11.9 Hz), 128.2 (d, *J* = 2.4 Hz), 128.1 (d, *J* = 3.2 Hz), 127.6, 123.5 (d, *J* = 3.3 Hz), 116.7, 114.3 (d, *J* = 21.5 Hz), 112.3, 94.8, 74.5, 74.5, 46.1, 41.1, 35.3, 34.7, 18.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.70. HRMS (ESI-TOF) calcd for $C_{19}H_{20}NNaFO$ $[M+Na]^+$: 320.1421, found: 320.1421.



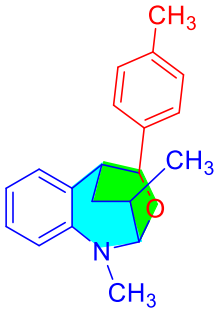
2j

10-(3-fluorophenyl)-1,3-dimethyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (***2j***): Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a colorless oil, 34 mg, 58% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.03 (m, 2H), 7.01-6.93 (m, 2H), 6.79-6.70 (m, 2H), 6.55 (td, *J* = 7.3, 1.1 Hz, 1H), 6.42 (d, *J* = 8.6 Hz, 1H), 5.26 (d, *J* = 4.9 Hz, 1H), 4.57 (s, 1H), 3.16 (q, *J* = 3.8 Hz, 1H), 2.99 (s, 3H), 2.52 (ddd, *J* = 12.8, 9.3, 3.8 Hz, 1H), 2.35 (h, *J* = 7.5 Hz, 1H), 1.75 (ddd, *J* = 12.7, 8.3, 3.1 Hz, 1H), 1.20 (d, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 245.0 Hz), 146.6, 145.7 (d, *J* = 6.7 Hz), 130.0, 128.9, 128.8 (d, *J* = 2.6 Hz), 127.7, 120.9 (d, *J* = 2.7 Hz), 118.6, 115.0, 113.0 (d, *J* = 21.4 Hz), 112.6 (d, *J* = 22.7 Hz), 94.3, 81.3 (d, *J* = 1.7 Hz), 44.3, 40.9, 38.2, 34.0, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.18. HRMS (ESI-TOF) calcd for $C_{19}H_{20}NNaFO$ $[M+Na]^+$: 320.1421, found: 320.1423.



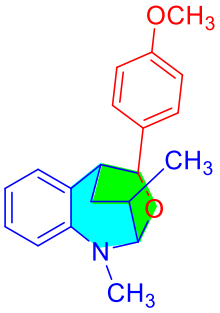
2k

10-(4-chlorophenyl)-1,3-dimethyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (***2k***): Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 38 mg, 61% yield, Mp = 105-107 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18-7.10 (m, 2H), 7.10-6.97 (m, 3H), 6.54 (d, *J* = 8.1 Hz, 1H), 6.39 (td, *J* = 7.3, 1.1 Hz, 1H), 6.24 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.23 (d, *J* = 1.8 Hz, 1H), 4.78-4.70 (m, 1H), 3.07 (s, 3H), 2.75-2.67 (m, 1H), 2.62 (dddd, *J* = 9.8, 8.5, 6.6, 3.1 Hz, 1H), 2.51-2.37 (m, 1H), 1.96-1.85 (m, 1H), 1.13 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.6, 140.1, 132.6, 130.3, 127.8, 127.7, 127.7, 127.6, 116.8, 112.4, 94.8, 80.4, 47.8, 41.1, 35.7, 34.6, 18.0. HRMS (ESI-TOF) calcd for $C_{19}H_{20}NNaClO$ $[M+Na]^+$: 336.1126, found: 336.1126.



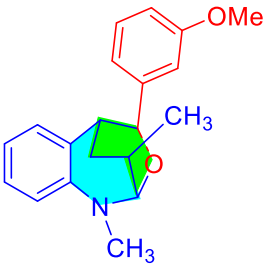
2l

1,3-dimethyl-10-(p-tolyl)-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2l)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a colorless solid, 41 mg, 69% yield, Mp = 68-70 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08-7.02 (m, 1H), 7.00-6.91 (m, 4H), 6.54 (d, *J* = 8.2 Hz, 1H), 6.39 (td, *J* = 7.3, 1.1 Hz, 1H), 6.28 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.26-5.19 (m, 1H), 4.75 (d, *J* = 3.2 Hz, 1H), 3.07 (s, 3H), 2.77-2.70 (m, 1H), 2.69-2.57 (m, 1H), 2.51-2.38 (m, 1H), 2.25 (s, 3H), 1.89 (dd, *J* = 13.3, 8.5 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.7, 138.4, 136.5, 130.3, 128.3, 128.3, 127.5, 126.2, 116.6, 112.3, 94.8, 80.9, 47.9, 41.1, 35.9, 34.6, 21.1, 18.1. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NNaO$ $[M+Na]^+$: 316.1672, found: 316.1672.



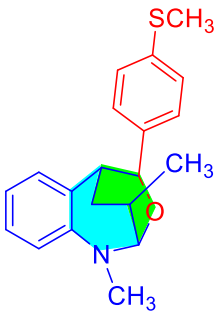
2m

10-(4-methoxyphenyl)-1,3-dimethyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2m)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 52 mg, 84% yield, Mp = 100-102 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (ddd, *J* = 8.2, 7.3, 1.7 Hz, 1H), 7.00-6.93 (m, 2H), 6.72-6.66 (m, 2H), 6.55 (d, *J* = 8.1 Hz, 1H), 6.40 (td, *J* = 7.3, 1.1 Hz, 1H), 6.28 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.21 (d, *J* = 1.6 Hz, 1H), 4.74 (d, *J* = 3.1 Hz, 1H), 3.73 (s, 3H), 3.07 (s, 3H), 2.69 (dd, *J* = 7.3, 1.7 Hz, 1H), 2.63 (tdd, *J* = 9.4, 6.5, 3.0 Hz, 1H), 2.48-2.38 (m, 1H), 1.88 (dd, *J* = 13.4, 8.6 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.6, 146.7, 133.6, 130.4, 128.2, 127.5, 127.5, 116.6, 113.0, 112.3, 94.8, 80.7, 55.1, 48.0, 41.1, 35.9, 34.6, 18.0. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NNaO_2$ $[M+Na]^+$: 332.1621, found: 332.1605.



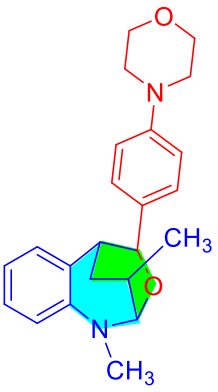
2n

10-(3-methoxyphenyl)-1,3-dimethyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2n)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow oil, 32 mg, 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 1H), 7.12-7.02 (m, 2H), 6.69 (dd, *J* = 8.2, 2.3 Hz, 2H), 6.60-6.52 (m, 2H), 6.39 (td, *J* = 7.3, 1.1 Hz, 1H), 6.28 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.23 (d, *J* = 1.7 Hz, 1H), 4.75 (dd, *J* = 3.3, 1.0 Hz, 1H), 3.57 (s, 3H), 3.08 (s, 3H), 2.73 (dt, *J* = 7.4, 1.3 Hz, 1H), 2.63 (dtd, *J* = 8.3, 6.7, 3.4 Hz, 1H), 2.51-2.40 (m, 1H), 1.91 (ddd, *J* = 13.3, 8.4, 0.9 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.0, 146.7, 143.0, 130.4, 128.5, 128.3, 127.6, 118.7, 116.8, 113.4, 112.4, 111.3, 94.7, 80.9, 54.9, 47.8, 41.2, 35.8, 34.6, 18.1. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NNaO_2$ $[M+Na]^+$: 332.1621, found: 332.1624.



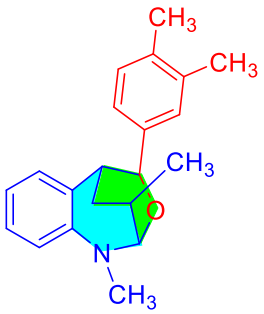
2o

1,3-dimethyl-10-(4-(methylthio)phenyl)-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepin e ***(2o)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a colorless solid, 52 mg, 80% yield, Mp = 112-114 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08-7.02 (m, 3H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.54 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.38 (td, *J* = 7.3, 1.2 Hz, 1H), 6.27 (dd, *J* = 7.3, 1.8 Hz, 1H), 5.21 (d, *J* = 1.7 Hz, 1H), 4.74 (dd, *J* = 3.2, 1.0 Hz, 1H), 3.07 (s, 3H), 2.71 (dt, *J* = 7.4, 1.2 Hz, 1H), 2.62 (dddd, *J* = 9.8, 8.4, 6.6, 3.1 Hz, 1H), 2.40 (s, 4H), 1.89 (ddd, *J* = 13.4, 8.5, 0.9 Hz, 1H), 1.12 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.6, 138.5, 136.6, 130.3, 128.0, 127.6, 126.8, 125.9, 116.7, 112.3, 94.7, 80.7, 47.8, 41.1, 35.8, 34.6, 18.0, 15.8. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NSNaO$ $[M+Na]^+$: 348.1393, found: 348.1390.



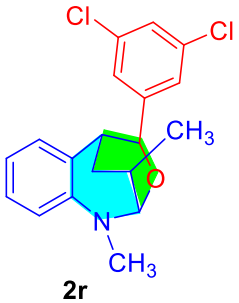
2p

1,3-dimethyl-10-(4-morpholinophenyl)-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2p)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a yellow solid, 42 mg, 58% yield, Mp = 125-127 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1H), 6.97-6.91 (m, 2H), 6.74-6.69 (m, 2H), 6.54 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.39 (td, *J* = 7.3, 1.1 Hz, 1H), 6.30 (dd, *J* = 7.3, 1.8 Hz, 1H), 5.18 (d, *J* = 1.6 Hz, 1H), 4.76-4.69 (m, 1H), 3.85-3.76 (m, 4H), 3.10-3.03 (m, 7H), 2.70 (dd, *J* = 7.2, 1.7 Hz, 1H), 2.62 (dtd, *J* = 8.6, 6.7, 3.3 Hz, 1H), 2.49-2.38 (m, 1H), 1.93-1.82 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.2, 146.7, 133.0, 130.4, 128.4, 127.5, 127.3, 116.6, 114.9, 112.3, 94.8, 80.7, 66.9, 49.4, 47.9, 41.1, 35.9, 34.6, 18.0. HRMS (ESI-TOF) calcd for $C_{23}H_{28}N_2NaO_2$ $[M+Na]^+$: 387.2043, found: 387.2044.



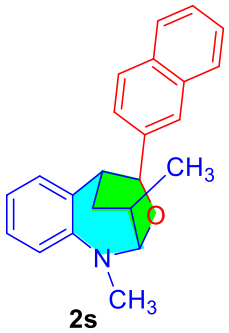
2q

10-(3,4-dimethylphenyl)-1,3-dimethyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2q)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 45 mg, 73% yield, Mp = 84-86 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (ddd, *J* = 8.5, 7.3, 1.8 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.83-6.73 (m, 2H), 6.57-6.50 (m, 1H), 6.39 (td, *J* = 7.3, 1.1 Hz, 1H), 6.30 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.18 (d, *J* = 1.7 Hz, 1H), 4.77-4.71 (m, 1H), 3.07 (s, 3H), 2.72 (dd, *J* = 7.0, 1.8 Hz, 1H), 2.68-2.56 (m, 1H), 2.49-2.36 (m, 1H), 2.15 (s, 3H), 2.11 (s, 3H), 1.93-1.83 (m, 1H), 1.12 (d, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.7, 138.7, 135.6, 135.0, 130.4, 128.9, 128.4, 127.7, 127.5, 123.7, 116.5, 112.3, 94.8, 81.0, 47.8, 41.1, 35.9, 34.6, 19.7, 19.4, 18.0. HRMS (ESI-TOF) calcd for $C_{21}H_{25}NNaO$ $[M+Na]^+$: 330.1828, found: 330.1828.



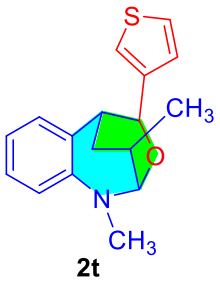
2r

10-(3,5-dichlorophenyl)-1,3-dimethyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2r)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a yellow solid, 51 mg, 73% yield, Mp = 105-107 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (t, *J* = 2.0 Hz, 1H), 7.10-7.03 (m, 1H), 6.97 (d, *J* = 1.9 Hz, 2H), 6.57-6.53 (m, 1H), 6.42 (td, *J* = 7.3, 1.1 Hz, 1H), 6.29 (dd, *J* = 7.3, 1.7 Hz, 1H), 5.18 (d, *J* = 2.0 Hz, 1H), 4.75 (d, *J* = 3.4 Hz, 1H), 3.08 (s, 3H), 2.78-2.72 (m, 1H), 2.60 (dddd, *J* = 9.9, 7.8, 6.6, 3.3 Hz, 1H), 2.49-2.37 (m, 1H), 1.92 (ddd, *J* = 13.4, 8.1, 1.1 Hz, 1H), 1.11 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.4, 145.3, 134.2, 130.1, 128.0, 127.1, 127.0, 124.8, 117.1, 112.7, 94.6, 80.0, 47.3, 41.2, 35.5, 34.6, 18.0. HRMS (ESI-TOF) calcd for $C_{19}H_{19}NCl_2NaO$ $[M+Na]^+$: 370.0736, found: 370.0733.



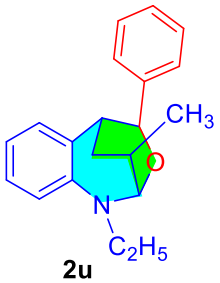
2s

1,3-dimethyl-10-(naphthalen-2-yl)-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2s)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 54 mg, 82% yield, Mp = 89-90 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (ddd, *J* = 18.2, 6.2, 3.4 Hz, 2H), 7.66-7.55 (m, 2H), 7.38 (dt, *J* = 6.7, 3.4 Hz, 2H), 7.16 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.03 (ddd, *J* = 8.5, 7.5, 1.7 Hz, 1H), 6.57 (d, *J* = 8.1 Hz, 1H), 6.30 (td, *J* = 7.2, 1.0 Hz, 1H), 6.21 (dd, *J* = 7.2, 1.7 Hz, 1H), 5.43 (d, *J* = 1.8 Hz, 1H), 4.82 (d, *J* = 3.2 Hz, 1H), 3.12 (s, 3H), 2.90-2.82 (m, 1H), 2.69 (ddt, *J* = 10.0, 6.6, 3.3 Hz, 1H), 2.50 (ddd, *J* = 13.4, 9.8, 7.6 Hz, 1H), 1.94 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.16 (d, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.7, 139.1, 133.1, 132.8, 130.3, 128.1, 128.0, 127.6, 127.5, 127.1, 125.5, 125.3, 125.1, 124.6, 116.7, 112.4, 94.8, 81.2, 47.8, 41.2, 35.9, 34.7, 18.1. HRMS (ESI-TOF) calcd for $C_{23}H_{23}NNaO$ $[M+Na]^+$: 352.1672, found: 352.1667.



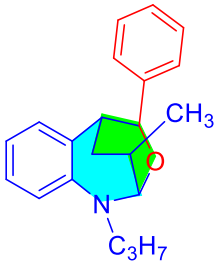
2t

1,3-dimethyl-10-(thiophen-3-yl)-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2t)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 43 mg, 76% yield, Mp = 58-60 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.03 (m, 2H), 6.95 (q, *J* = 1.2 Hz, 1H), 6.70 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.55 (d, *J* = 8.1 Hz, 1H), 6.50-6.39 (m, 2H), 5.39-5.32 (m, 1H), 4.71 (d, *J* = 3.2 Hz, 1H), 3.05 (s, 3H), 2.77 (dt, *J* = 7.6, 1.2 Hz, 1H), 2.61 (dddd, *J* = 9.9, 8.3, 6.6, 3.1 Hz, 1H), 2.42 (ddd, *J* = 13.3, 9.6, 7.3 Hz, 1H), 1.88 (ddd, *J* = 13.4, 8.3, 1.0 Hz, 1H), 1.11 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.6, 142.9, 130.2, 128.7, 127.7, 126.1, 124.7, 121.4, 116.8, 112.6, 94.6, 77.8, 47.0, 41.1, 35.6, 34.5, 18.1. HRMS (ESI-TOF) calcd for $C_{17}H_{19}NSNaO$ $[M+Na]^+$: 308.1080, found: 308.1078.



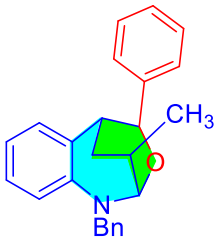
2u

1-ethyl-3-methyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2u)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a yellow solid, 49 mg, 84% yield, Mp = 71-73 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.06 (m, 5H), 7.00 (ddd, *J* = 8.6, 7.3, 1.8 Hz, 1H), 6.58 (d, *J* = 8.2 Hz, 1H), 6.37-6.29 (m, 1H), 6.24 (dd, *J* = 7.3, 1.8 Hz, 1H), 5.26 (d, *J* = 1.8 Hz, 1H), 4.75 (d, *J* = 3.3 Hz, 1H), 3.65 (m, 1H), 3.22 (m, 1H), 2.73 (dd, *J* = 7.1, 1.9 Hz, 1H), 2.68-2.55 (m, 1H), 2.45 (ddd, *J* = 13.4, 9.9, 7.3 Hz, 1H), 1.88 (dd, *J* = 13.3, 8.3 Hz, 1H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.8, 141.7, 130.6, 128.4, 127.6, 127.5, 126.9, 126.1, 116.5, 112.7, 92.9, 81.1, 48.0, 47.6, 36.0, 34.2, 18.2, 12.5. HRMS (ESI-TOF) calcd for $C_{20}H_{23}NNaO$ $[M+Na]^+$: 316.1672, found: 316.1672.



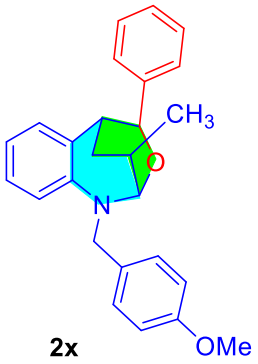
2v

3-methyl-10-phenyl-1-propyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2v)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 49 mg, 79% yield, Mp = 60-62 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.08 (m, 5H), 6.99 (ddd, *J* = 8.6, 7.4, 1.8 Hz, 1H), 6.54 (d, *J* = 8.2 Hz, 1H), 6.32 (t, *J* = 7.2 Hz, 1H), 6.25 (dd, *J* = 7.4, 1.8 Hz, 1H), 5.27 (d, *J* = 1.9 Hz, 1H), 4.76 (d, *J* = 3.5 Hz, 1H), 3.54 (ddd, *J* = 15.1, 9.2, 6.0 Hz, 1H), 3.06 (ddd, *J* = 15.6, 9.4, 7.1 Hz, 1H), 2.77-2.71 (m, 1H), 2.63 (ddt, *J* = 14.5, 7.0, 3.4 Hz, 1H), 2.45 (ddd, *J* = 13.4, 10.0, 7.2 Hz, 1H), 1.88 (dd, *J* = 13.3, 8.2 Hz, 1H), 1.76 (dddt, *J* = 13.8, 9.4, 7.0, 3.7 Hz, 2H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.2, 141.8, 130.6, 128.3, 127.6, 127.4, 126.9, 126.1, 116.5, 112.9, 92.9, 81.2, 55.5, 48.0, 36.1, 34.2, 20.4, 18.4, 11.3. HRMS (ESI-TOF) calcd for $C_{21}H_{25}NNaO$ $[M+Na]^+$: 330.1828, found: 330.1830.



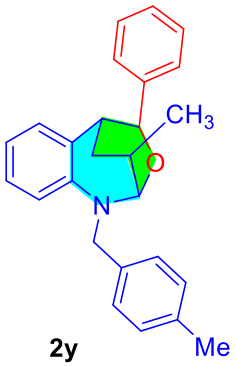
2w

1-benzyl-3-methyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2w)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 50 mg, 70% yield, Mp = 91-93 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29-7.14 (m, 6H), 6.88 (ddd, *J* = 8.6, 7.3, 1.8 Hz, 1H), 6.44 (d, *J* = 8.2 Hz, 1H), 6.36 (t, *J* = 7.2 Hz, 1H), 6.30 (dd, *J* = 7.4, 1.8 Hz, 1H), 5.33 (d, *J* = 1.8 Hz, 1H), 4.86 (d, *J* = 3.1 Hz, 1H), 4.77 (d, *J* = 17.7 Hz, 1H), 4.51 (d, *J* = 17.6 Hz, 1H), 2.83 (dd, *J* = 7.1, 1.8 Hz, 1H), 2.69 (ddtd, *J* = 16.6, 9.9, 6.9, 3.1 Hz, 1H), 2.51 (ddd, *J* = 13.3, 9.6, 7.4 Hz, 1H), 1.97 (dd, *J* = 13.3, 8.4 Hz, 1H), 1.17 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.3, 141.5, 138.9, 130.4, 128.6, 128.2, 127.7, 127.5, 127.0, 126.8, 126.4, 126.3, 117.1, 113.9, 92.9, 81.0, 56.9, 47.8, 36.0, 34.6, 18.4. HRMS (ESI-TOF) calcd for $C_{25}H_{25}NNaO$ $[M+Na]^+$: 378.1828, found: 378.1827.



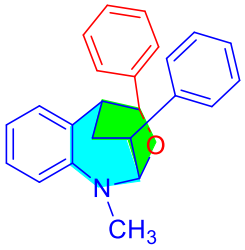
2x

*1-(4-methoxybenzyl)-3-methyl-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (**2x**)*: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a colorless solid, 64 mg, 83% yield, Mp = 101-103 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.2 Hz, 2H), 7.24-7.13 (m, 5H), 6.89 (dd, *J* = 7.6, 5.5 Hz, 3H), 6.47 (d, *J* = 8.2 Hz, 1H), 6.39-6.27 (m, 2H), 5.32 (s, 1H), 4.85 (d, *J* = 3.2 Hz, 1H), 4.72 (d, *J* = 17.3 Hz, 1H), 4.45 (d, *J* = 17.3 Hz, 1H), 3.80 (s, 3H), 2.83 (d, *J* = 7.3 Hz, 1H), 2.75-2.62 (m, 1H), 2.57-2.45 (m, 1H), 1.97 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.16 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.5, 146.3, 141.5, 130.8, 130.4, 128.3, 127.7, 127.6, 127.5, 127.0, 126.3, 117.1, 114.1, 113.9, 92.7, 81.1, 56.3, 55.3, 47.9, 36.1, 34.6, 18.4. HRMS (ESI-TOF) calcd for $C_{26}H_{27}NNaO_2$ $[M+Na]^+$: 408.1934, found: 408.1947.



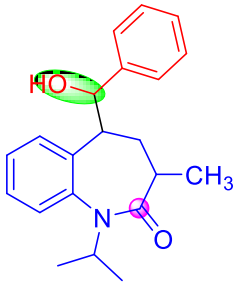
2y

*3-methyl-1-(4-methylbenzyl)-10-phenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine (**2y**)*: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a pale yellow solid, 59 mg, 80% yield, Mp = 110-112 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.7 Hz, 2H), 7.24-7.09 (m, 7H), 6.88 (td, *J* = 7.8, 7.2, 1.8 Hz, 1H), 6.45 (d, *J* = 8.2 Hz, 1H), 6.40-6.26 (m, 2H), 5.33 (d, *J* = 1.8 Hz, 1H), 4.85 (d, *J* = 3.2 Hz, 1H), 4.74 (d, *J* = 17.5 Hz, 1H), 4.47 (d, *J* = 17.5 Hz, 1H), 2.83 (d, *J* = 7.4 Hz, 1H), 2.68 (td, *J* = 9.6, 4.7 Hz, 1H), 2.57-2.45 (m, 1H), 2.35 (s, 3H), 1.97 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.17 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.4, 141.6, 136.4, 135.9, 130.4, 129.4, 128.3, 127.8, 127.6, 127.1, 126.4, 126.3, 117.1, 114.0, 92.9, 81.1, 56.7, 47.9, 36.1, 34.7, 21.1, 18.5. HRMS (ESI-TOF) calcd for $C_{26}H_{27}NNaO$ $[M+Na]^+$: 392.1985, found: 392.1985.



2aa

1-methyl-3,10-diphenyl-2,3,4,5-tetrahydro-1H-2,5-(epoxymethano)benzo[b]azepine ***(2aa)***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:1~50:1, v/v) affords the title compound as a yellow oil, 52 mg, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.44 (m, 2H), 7.37-7.31 (m, 4H), 7.28-7.24 (m, 1H), 7.17 (t, *J* = 7.7 Hz, 2H), 7.10-7.04 (m, 1H), 7.00 (ddd, *J* = 8.2, 7.3, 1.6 Hz, 1H), 6.86 (dd, *J* = 7.4, 1.6 Hz, 1H), 6.60 (td, *J* = 7.4, 1.1 Hz, 1H), 6.45 (dd, *J* = 8.2, 1.1 Hz, 1H), 5.48 (d, *J* = 4.9 Hz, 1H), 4.98 (s, 1H), 3.43 (t, *J* = 9.6 Hz, 1H), 3.35 (td, *J* = 4.5, 2.7 Hz, 1H), 2.98 (s, 3H), 2.76 (ddd, *J* = 13.3, 9.4, 4.1 Hz, 1H), 2.27 (ddd, *J* = 12.6, 9.8, 2.7 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 146.5, 145.9, 142.4, 130.3, 128.7, 128.5, 127.8, 127.5, 127.2, 126.6, 126.2, 125.4, 118.7, 115.1, 93.1, 82.1, 45.9, 44.2, 40.8, 39.7. HRMS (ESI-TOF) calcd for $C_{24}H_{23}NNaO$ $[M+Na]^+$: 364.1672, found: 364.1658.



2z'

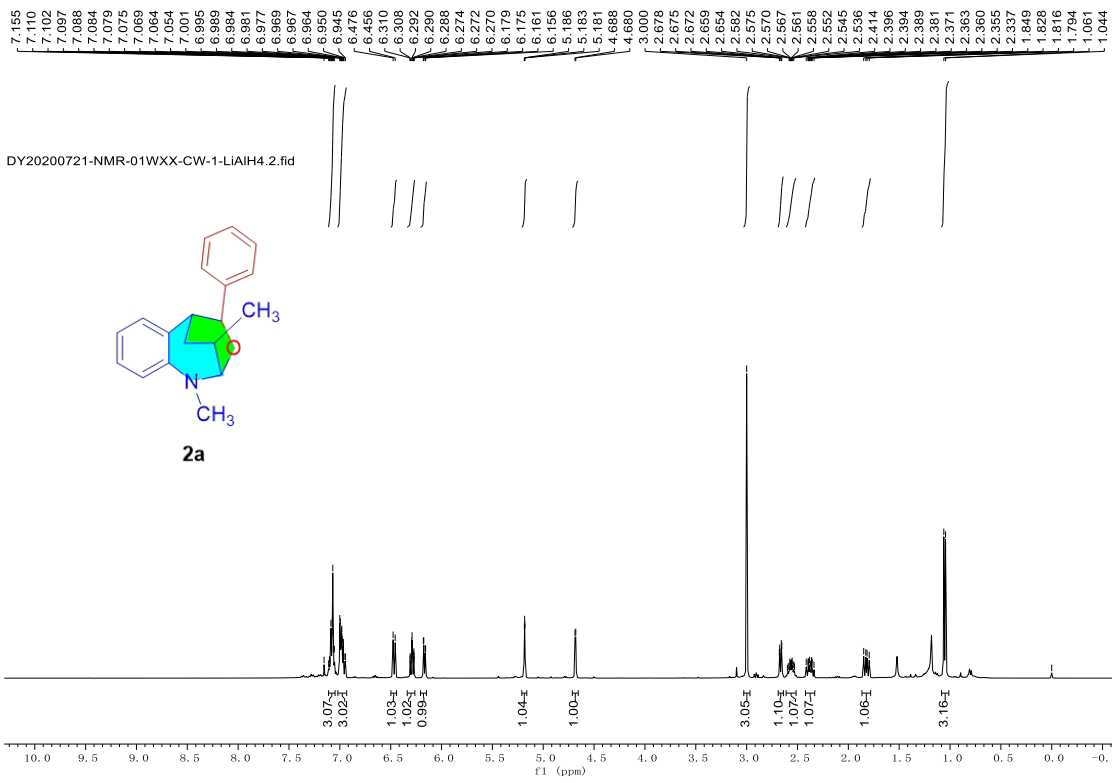
5-(hydroxy(phenyl)methyl)-1-isopropyl-3-methyl-1,3,4,5-tetrahydro-2H-benzo[b]azepin-2-one ***(2z')***: Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1~2:1, v/v) affords the title compound as a yellow oil, 33 mg, 51% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.32-7.18 (m, 7H), 7.14 (dd, *J* = 7.5, 1.8 Hz, 1H), 4.91 (d, *J* = 9.6 Hz, 1H), 4.67 (m, 1H), 3.09 (ddd, *J* = 12.9, 9.6, 6.5 Hz, 1H), 2.45 (d, *J* = 2.6 Hz, 1H), 2.02 (dt, *J* = 11.7, 6.7 Hz, 1H), 1.38 (dd, *J* = 16.7, 7.0 Hz, 4H), 1.08 (dd, *J* = 21.5, 6.8 Hz, 4H), 0.77 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.5, 142.1, 141.2, 137.5, 128.8, 128.3, 127.1, 126.9, 126.9, 125.6, 125.3, 74.7, 49.1, 45.4, 41.6, 36.0, 22.9, 20.5, 15.4. HRMS (ESI-TOF) calcd for $C_{21}H_{26}NO_2$ $[M+H]^+$: 324.1958, found: 324.1966.

8. Reference

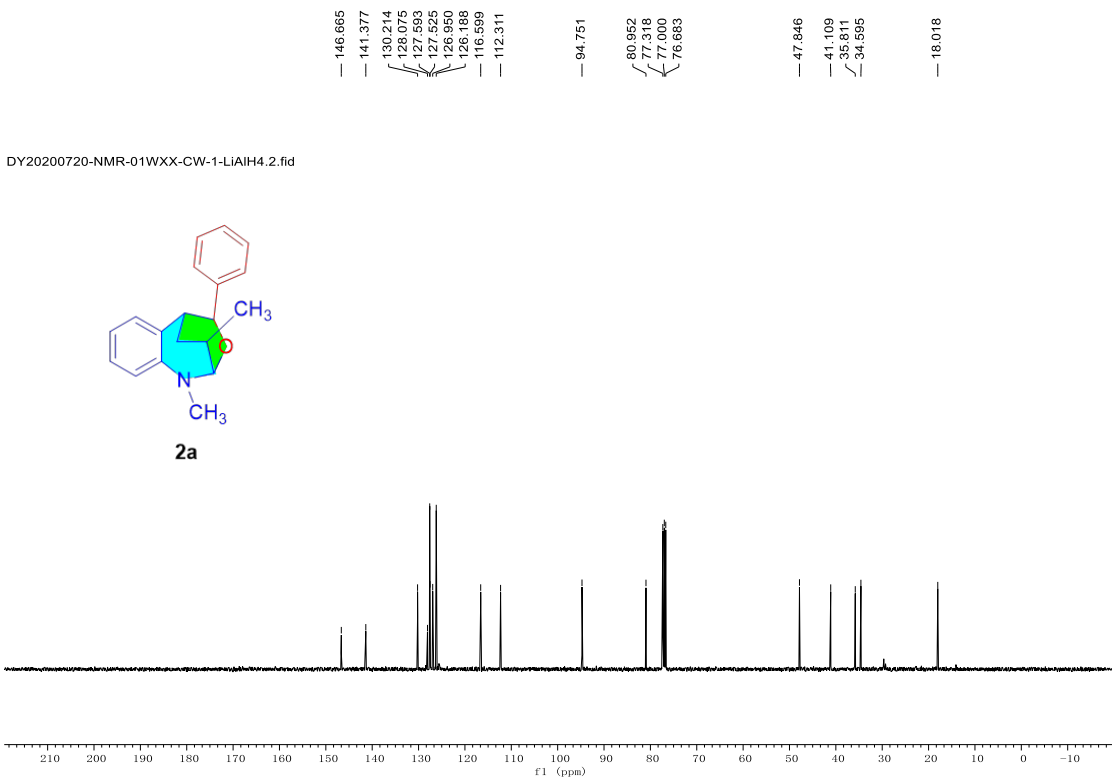
(1) Wu, X.-X.; Ye, H.; Li, M.; Qian, J.; Dai, H.; Shi, Y. *Org. Chem. Front.* **2021**, *8*, 560-565.

9. NMR spectra

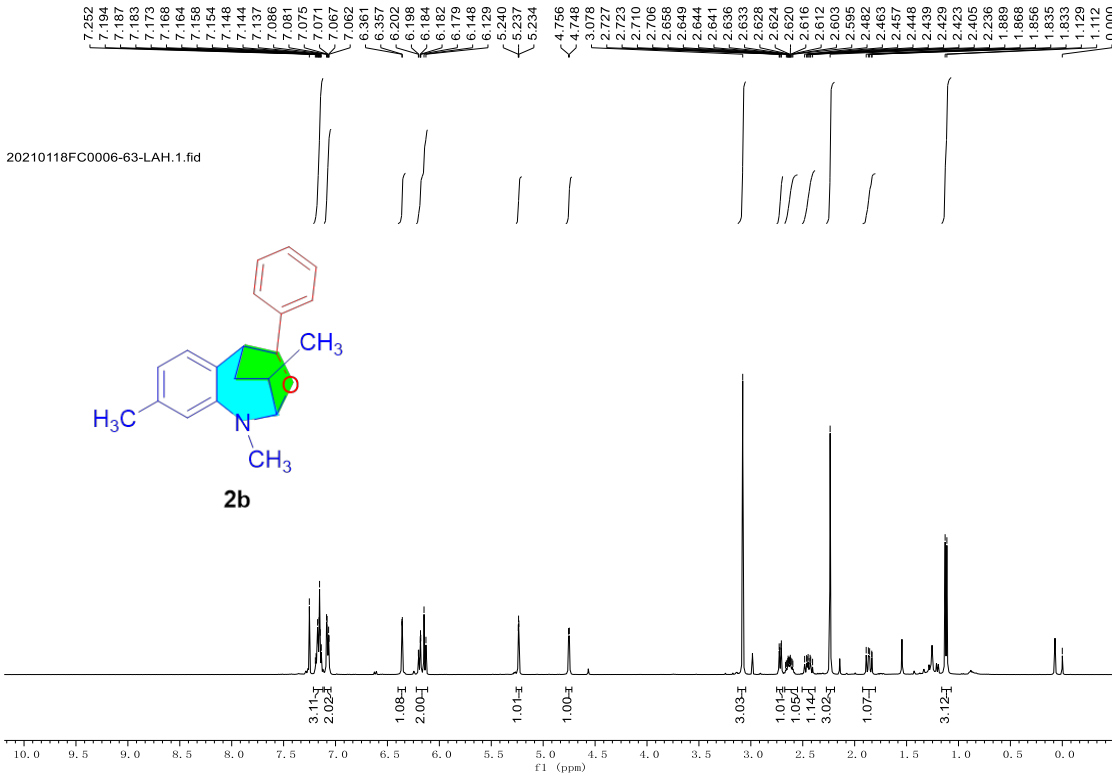
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2a**



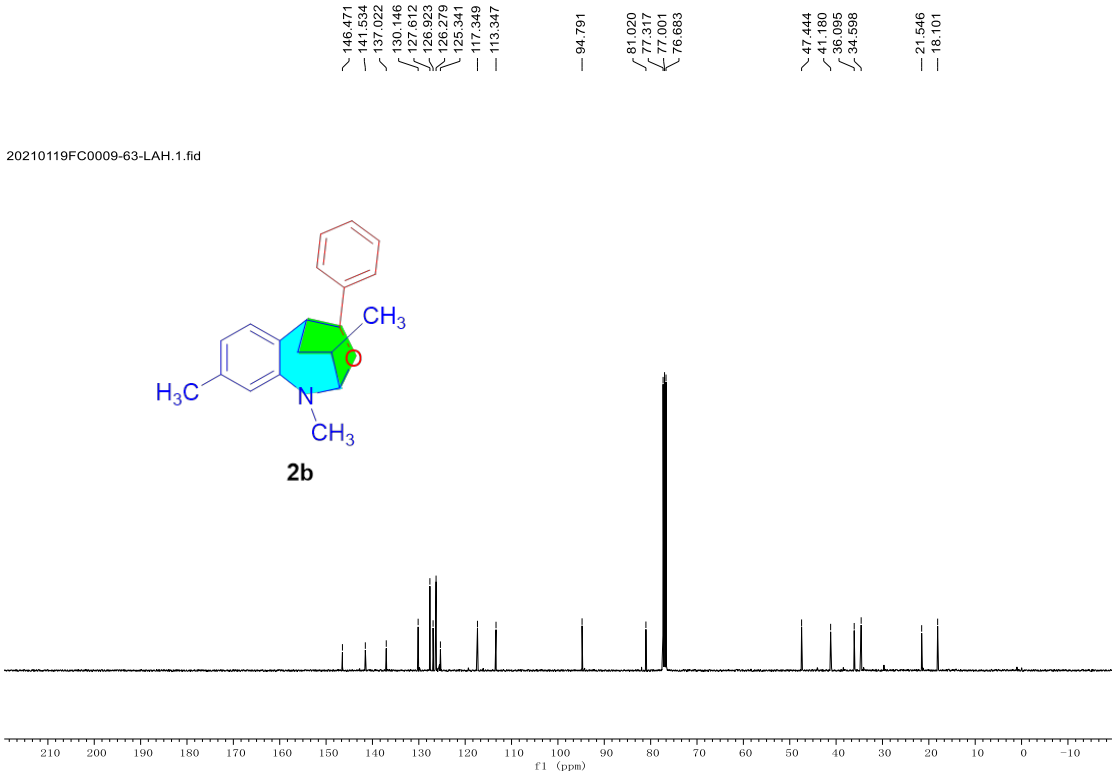
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2a**



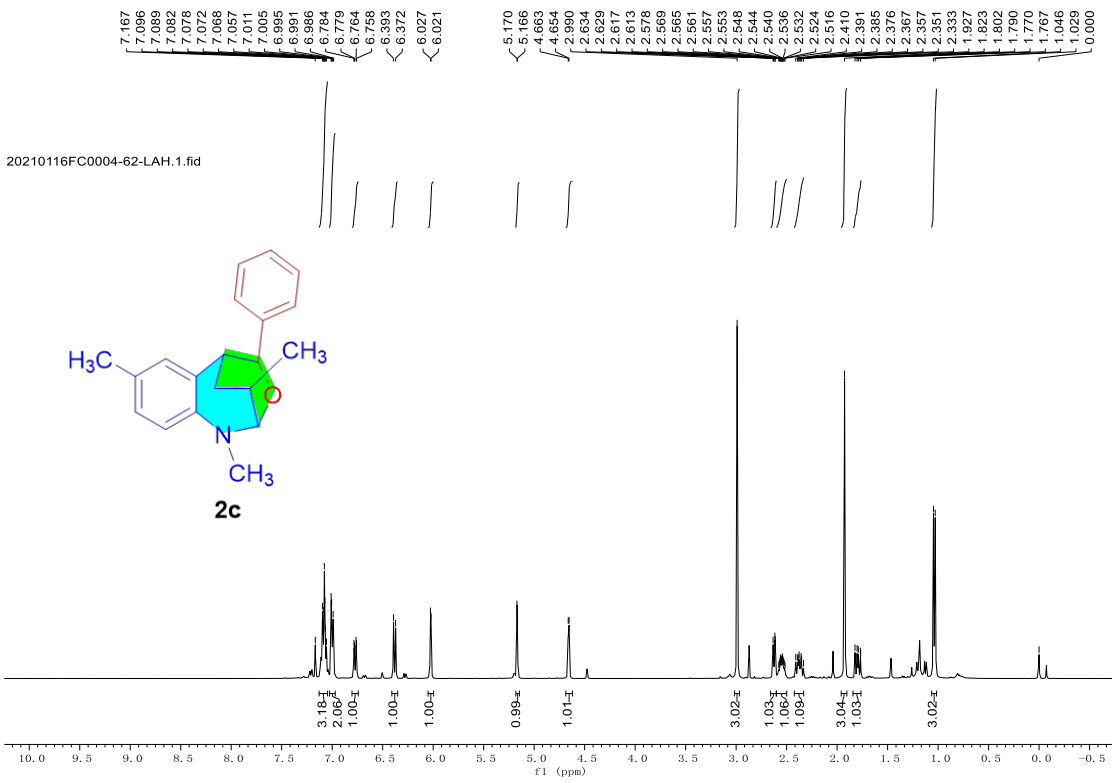
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2b**



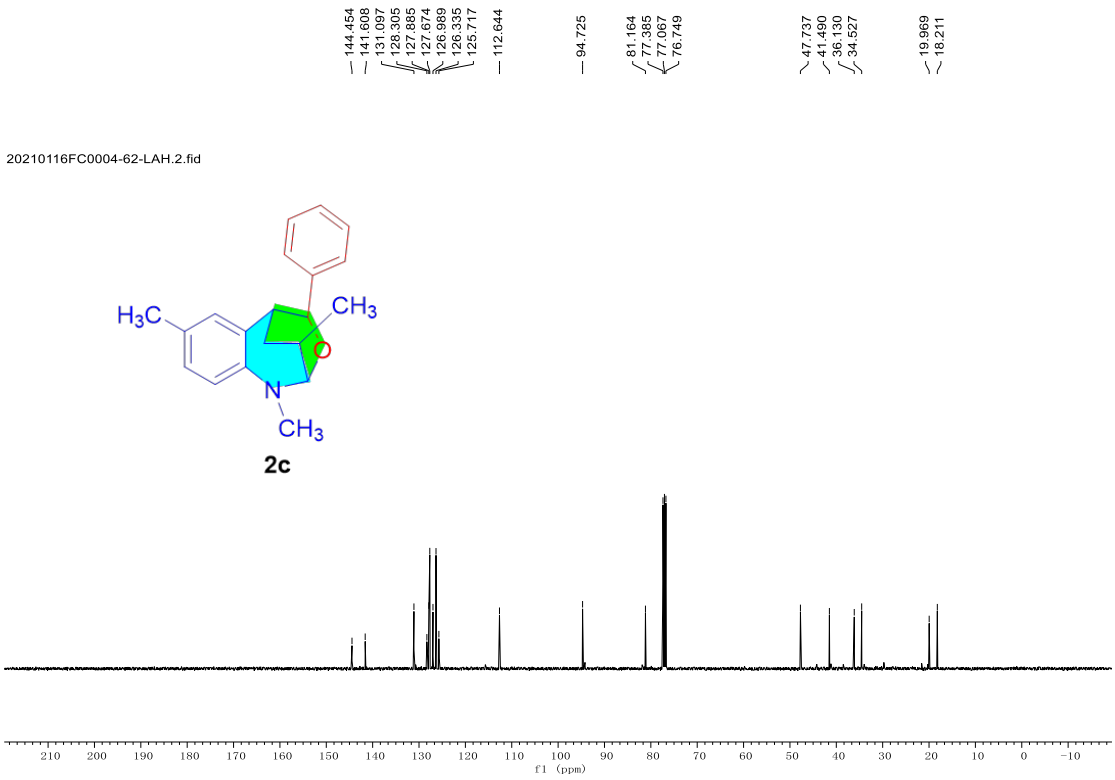
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2b**



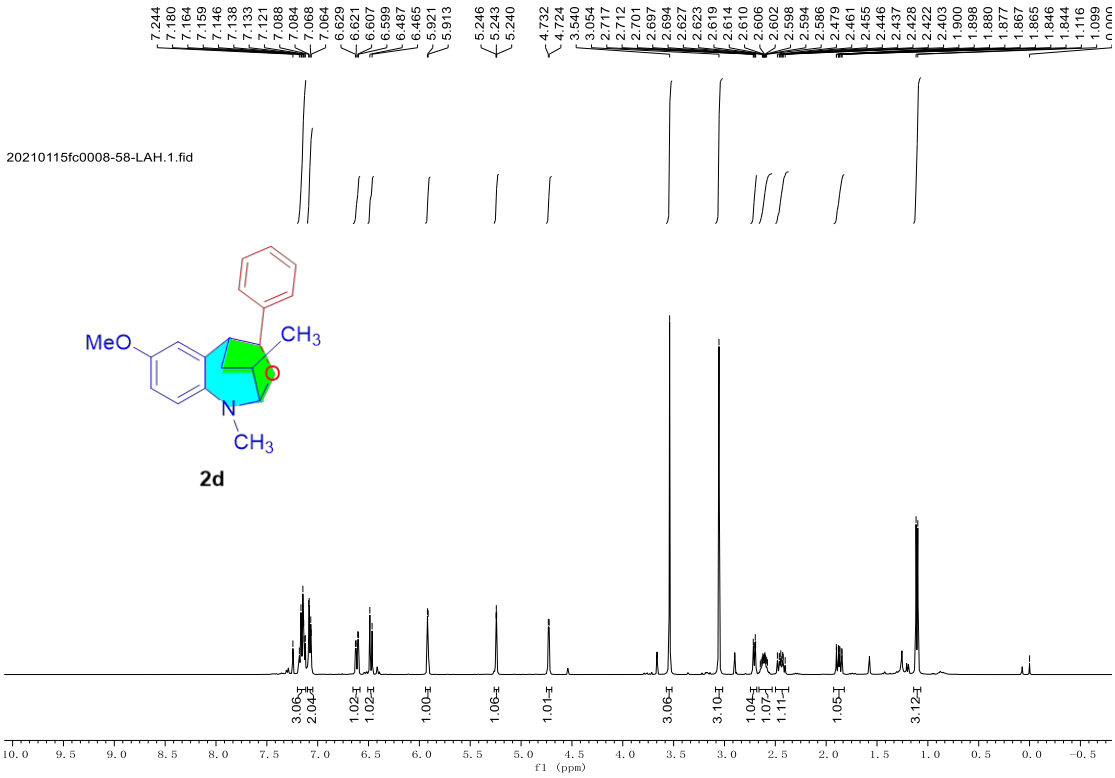
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2c**



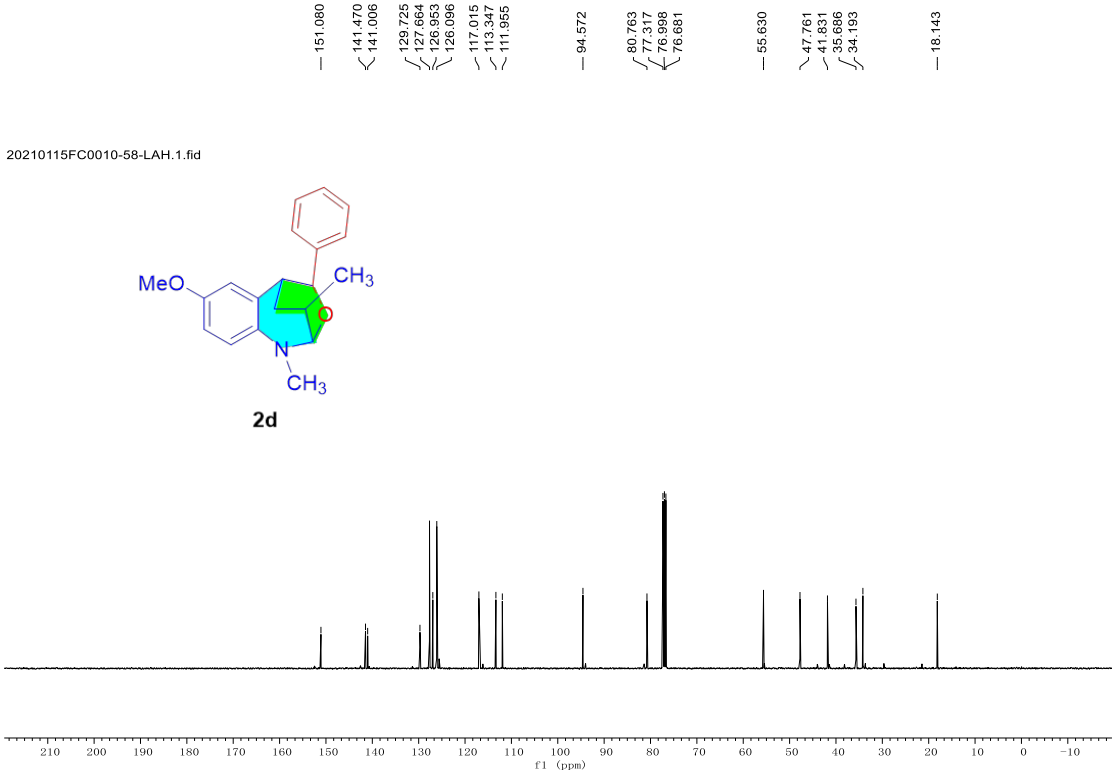
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2c**



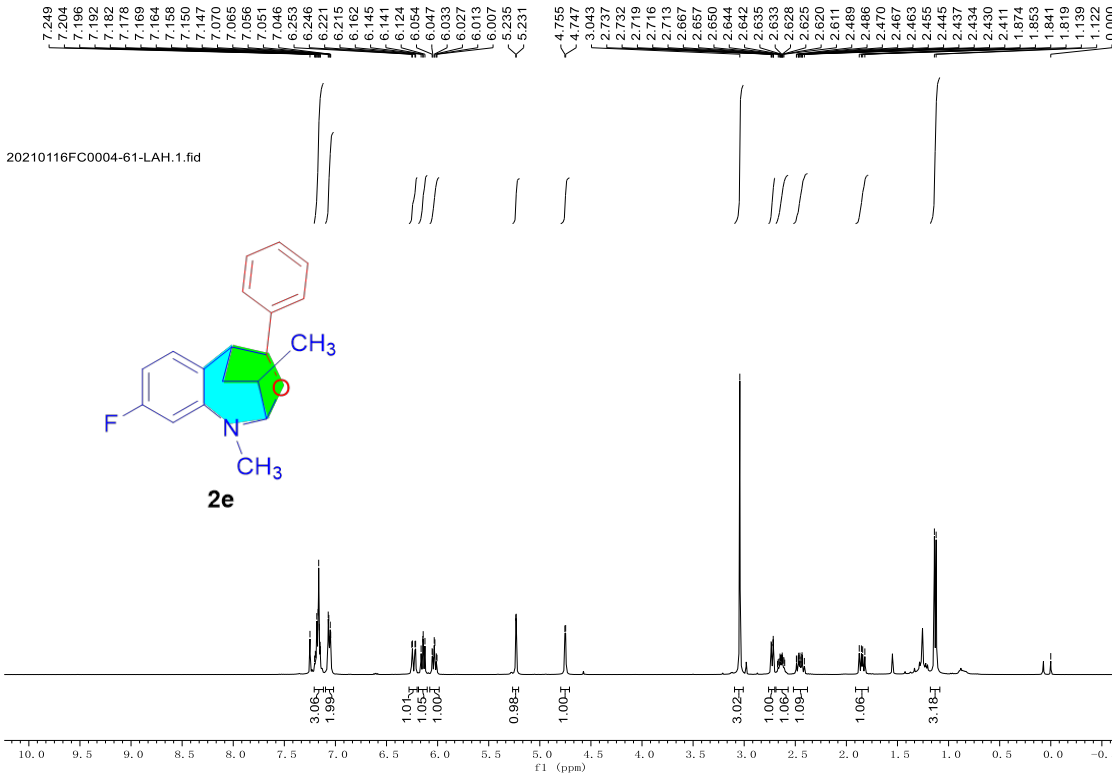
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2d**



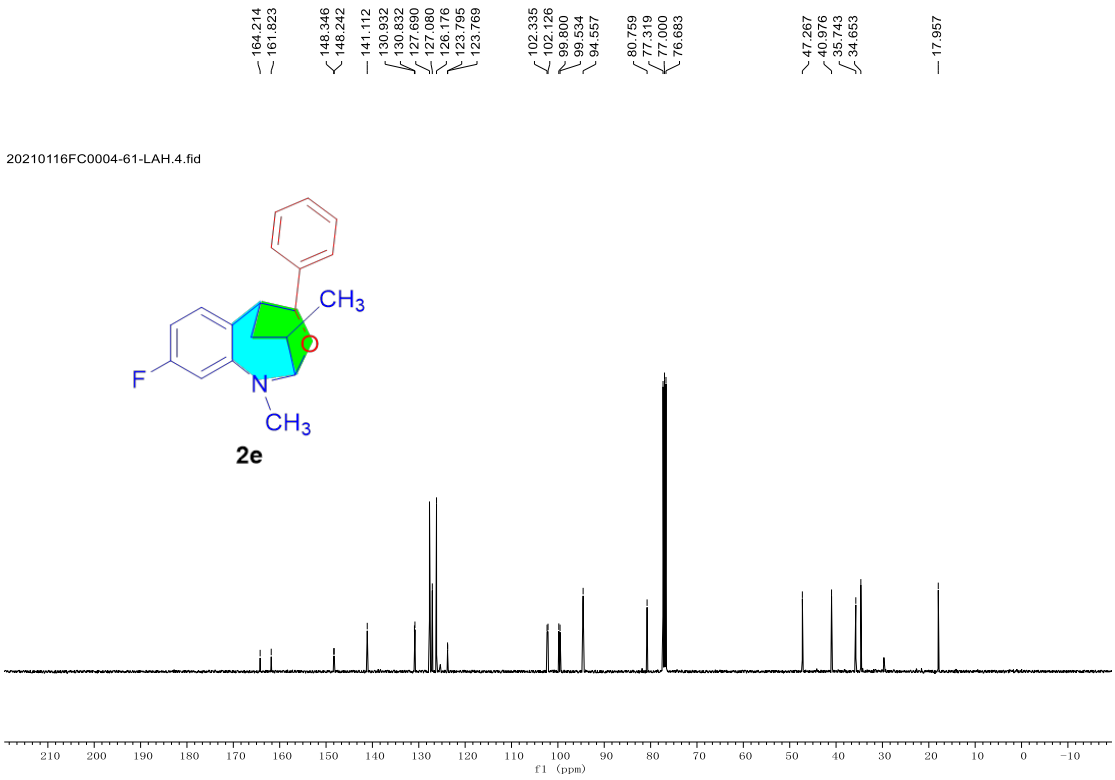
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2d**



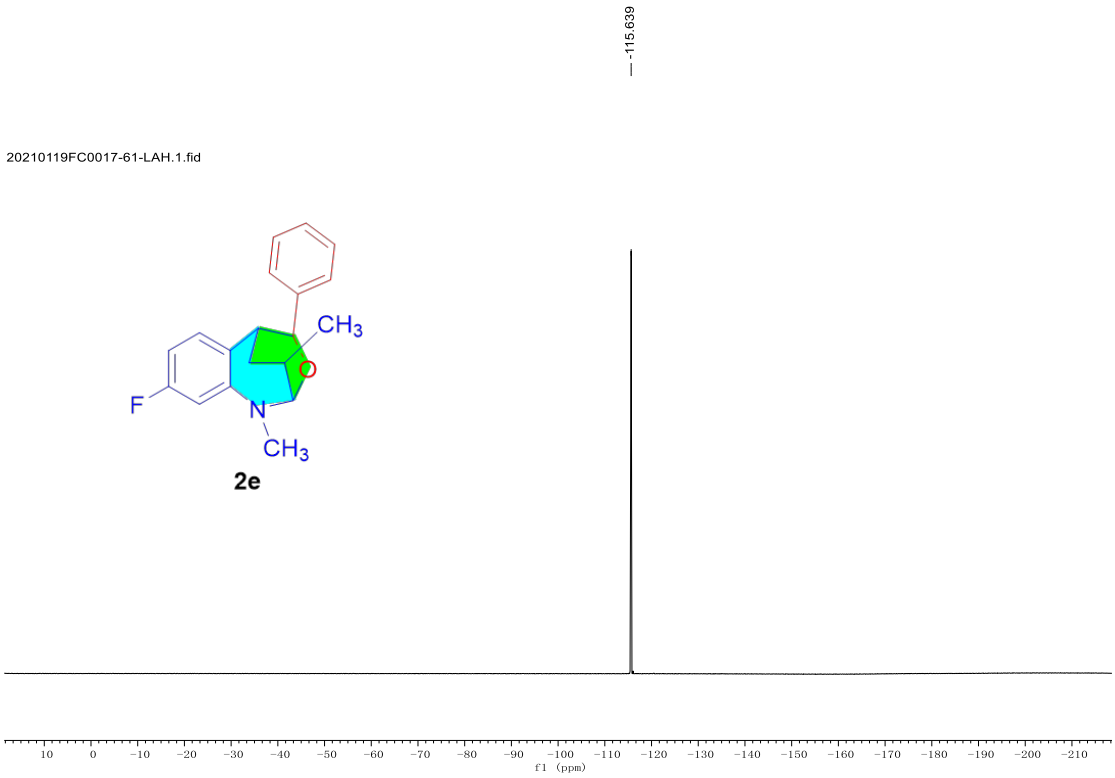
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2e**



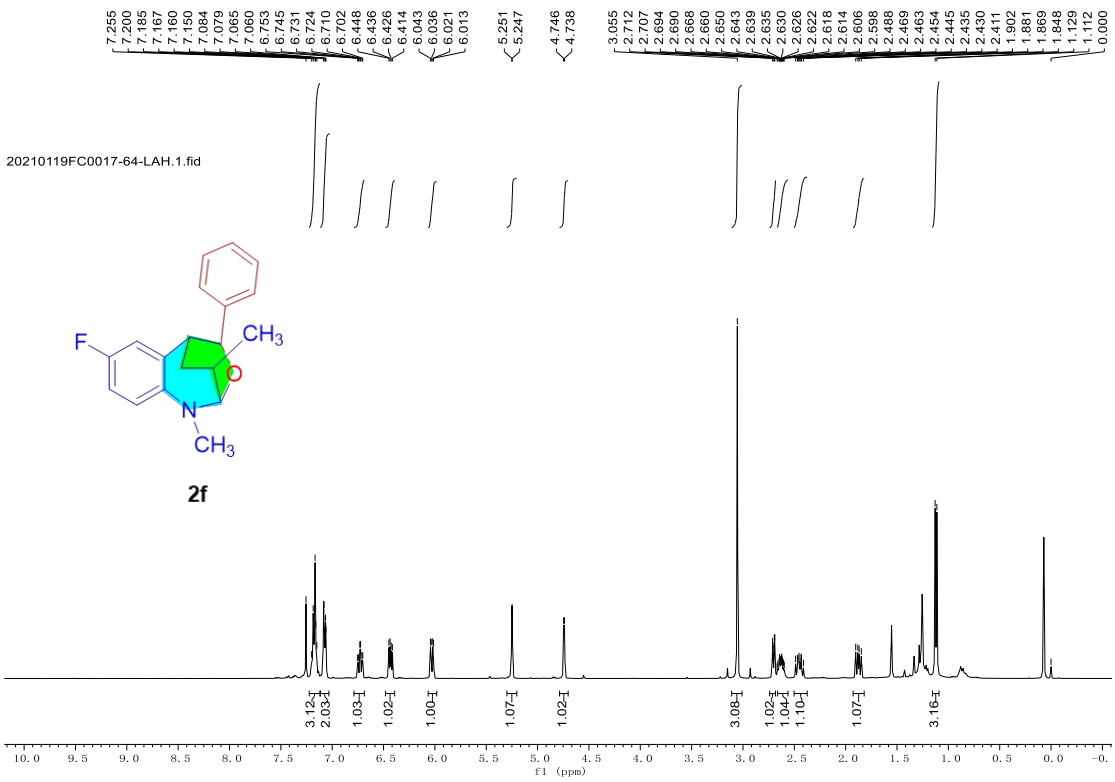
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2e**



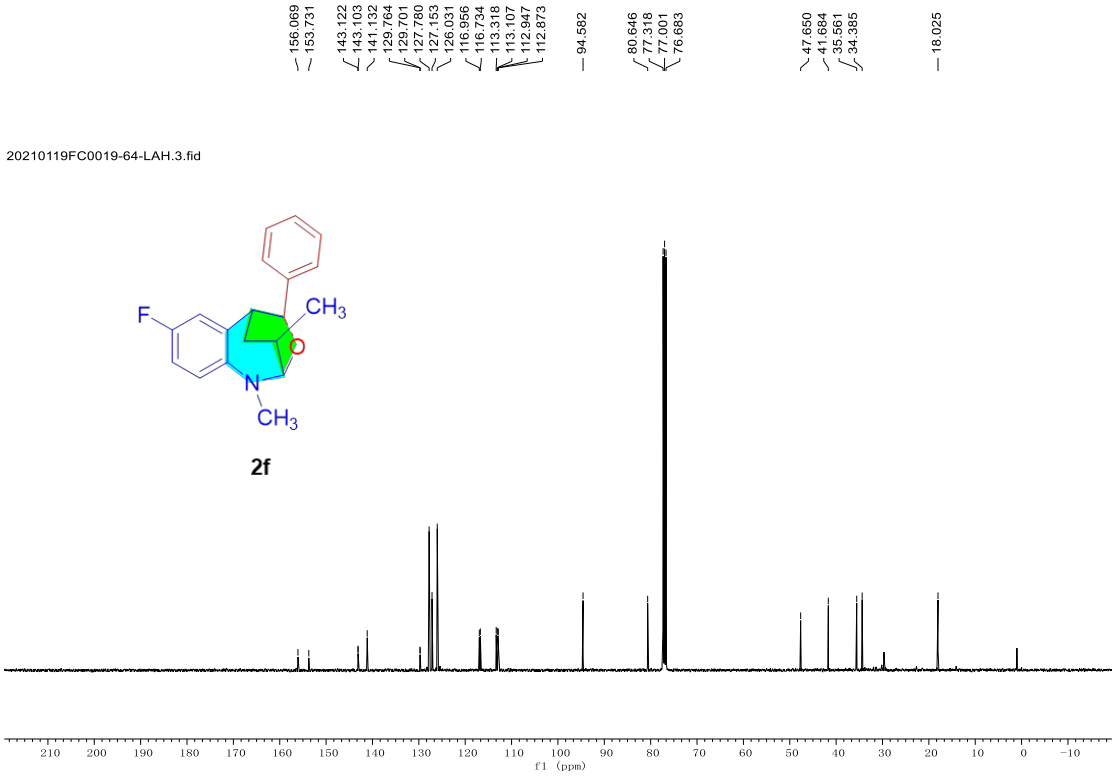
^{19}F NMR (376 MHz, $CDCl_3$) Spectrum of **2e**



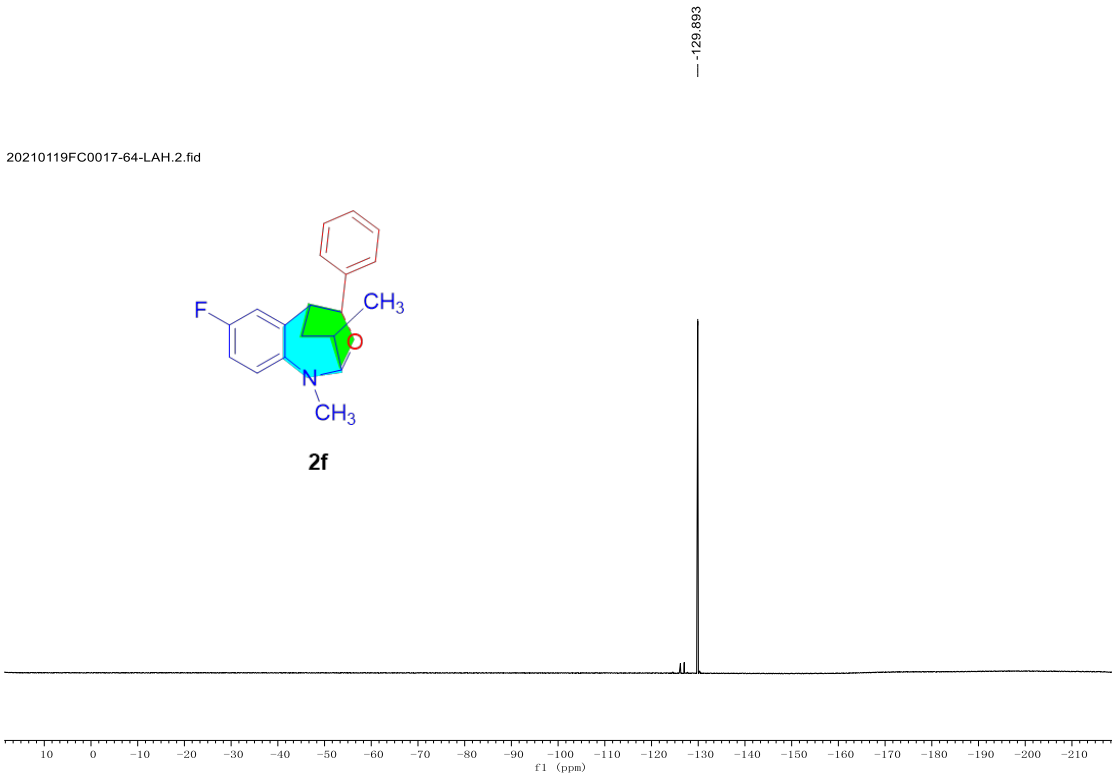
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2f**



^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2f**

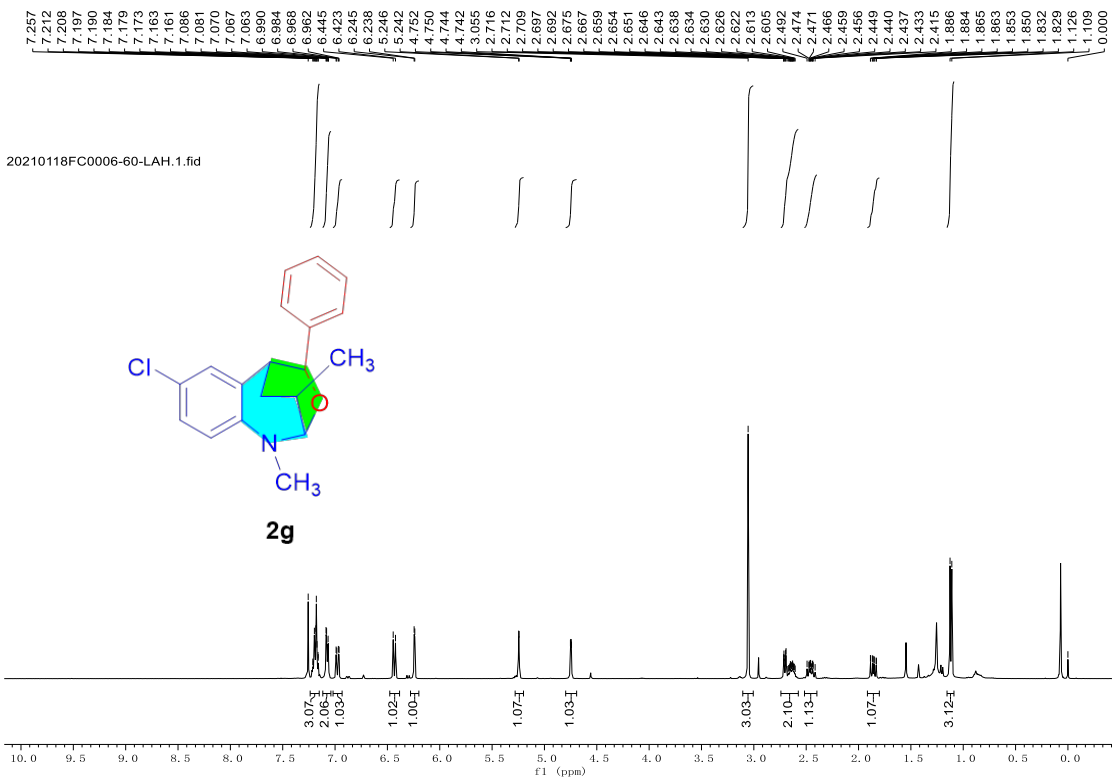


^{19}F NMR (376 MHz, $CDCl_3$) Spectrum of **2f**

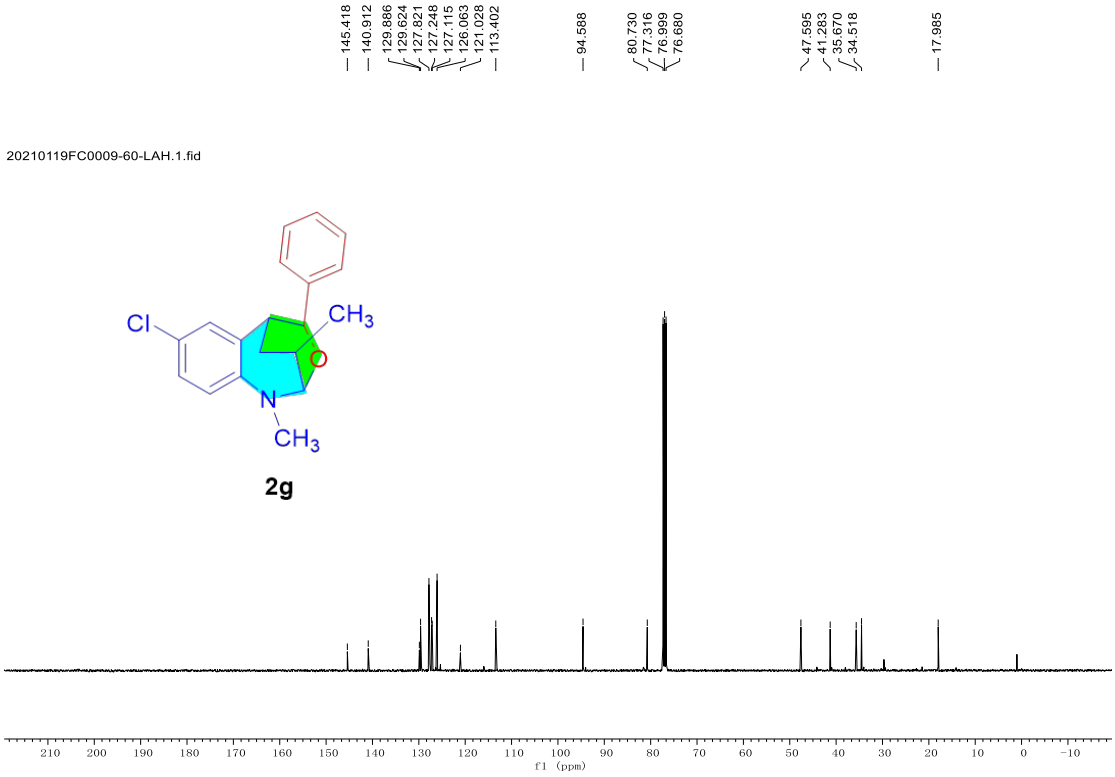


2f

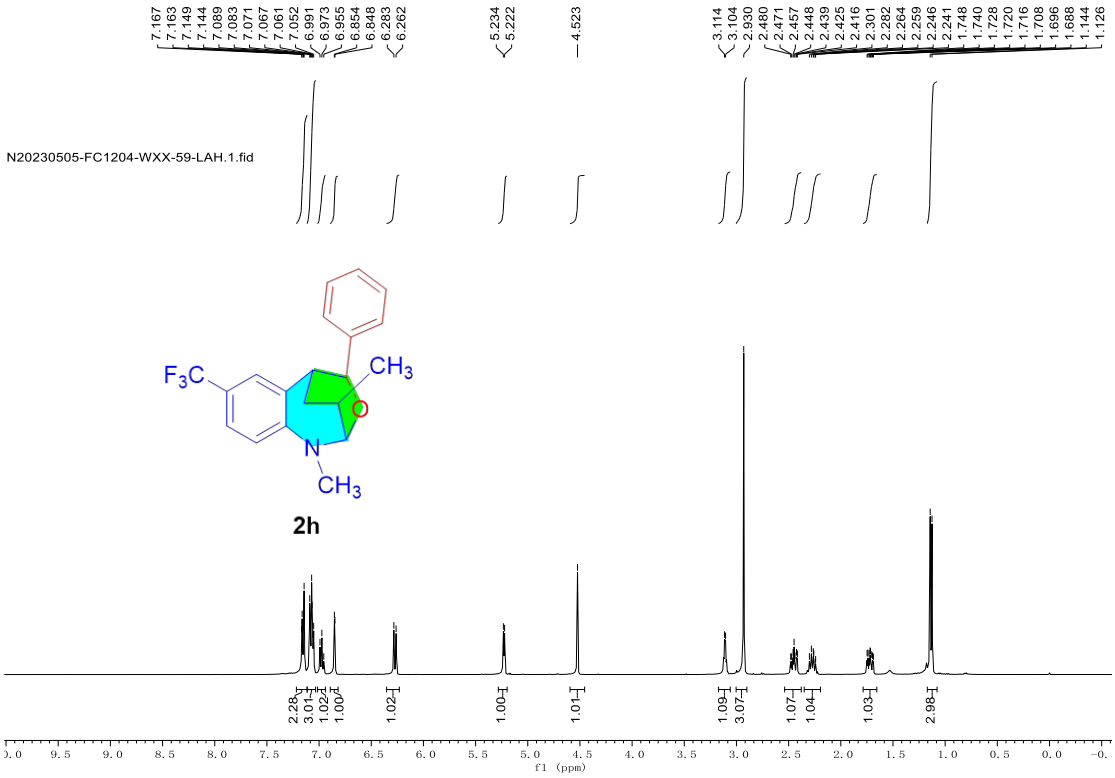
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2g**



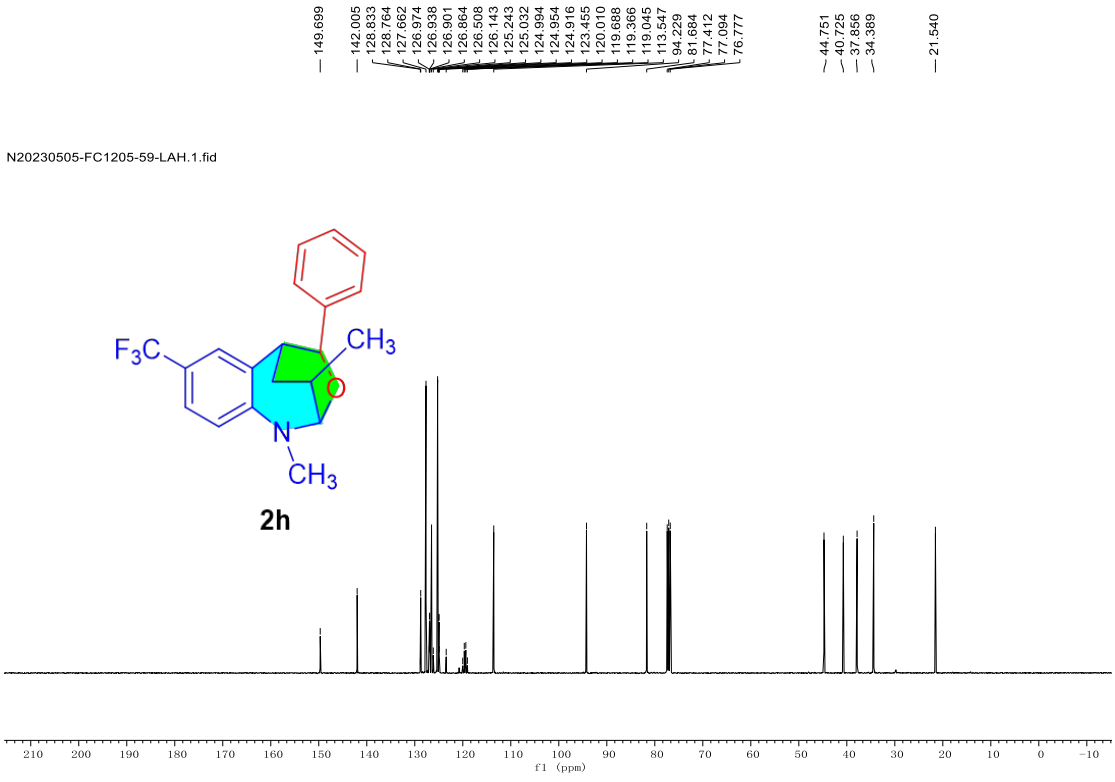
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2g**



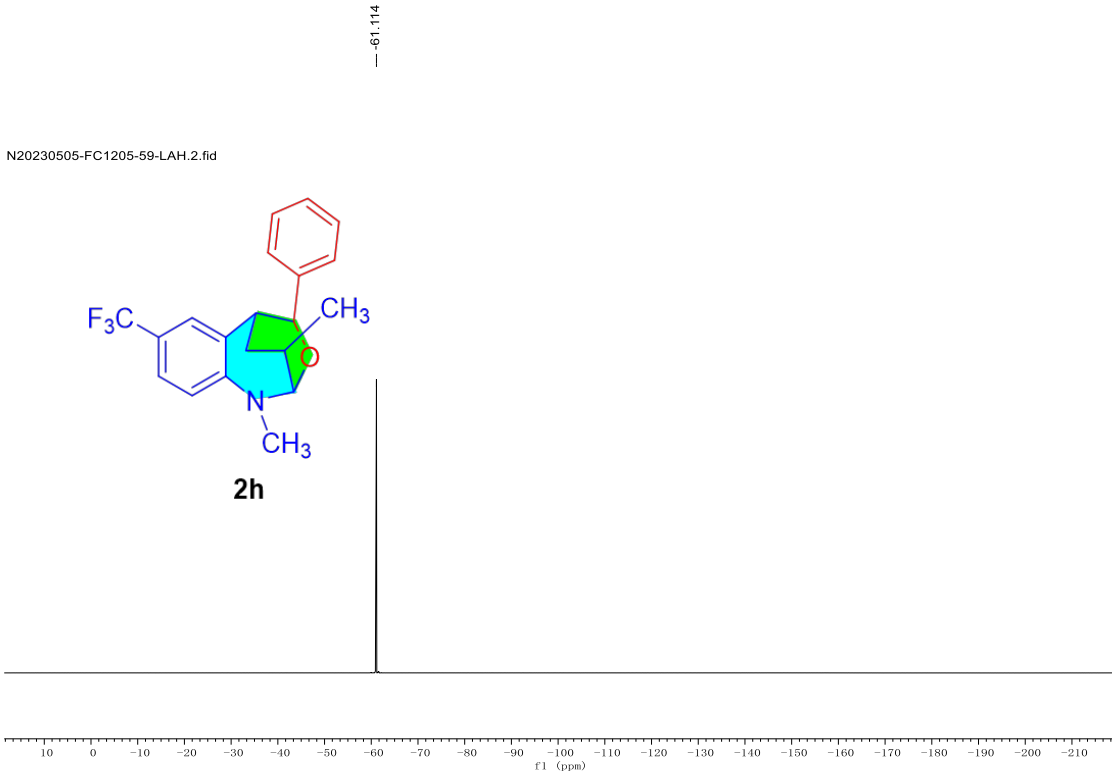
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2h**



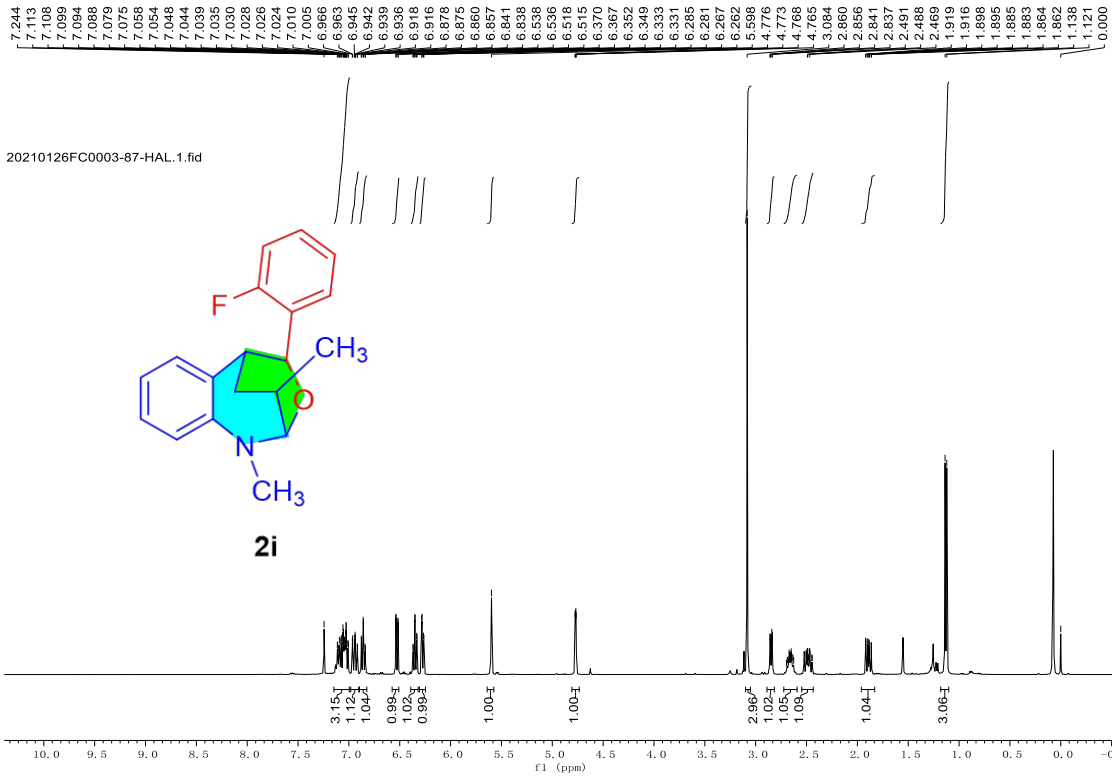
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2h**



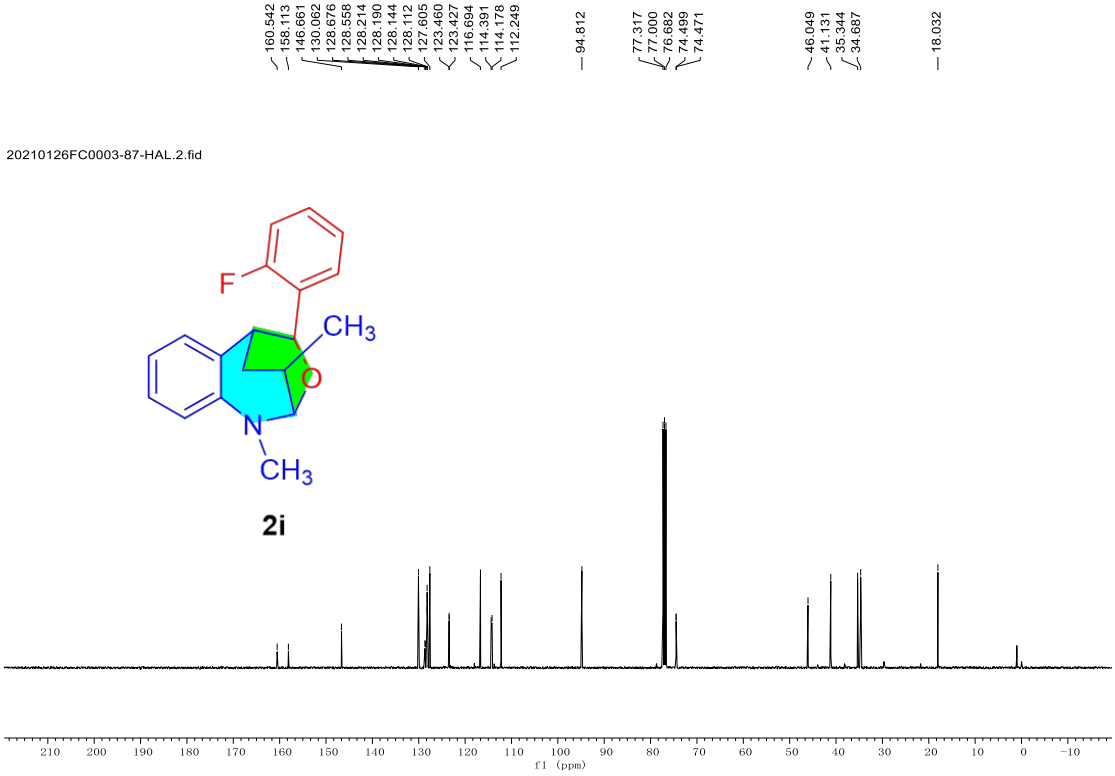
^{19}F NMR (376 MHz, $CDCl_3$) Spectrum of **2h**



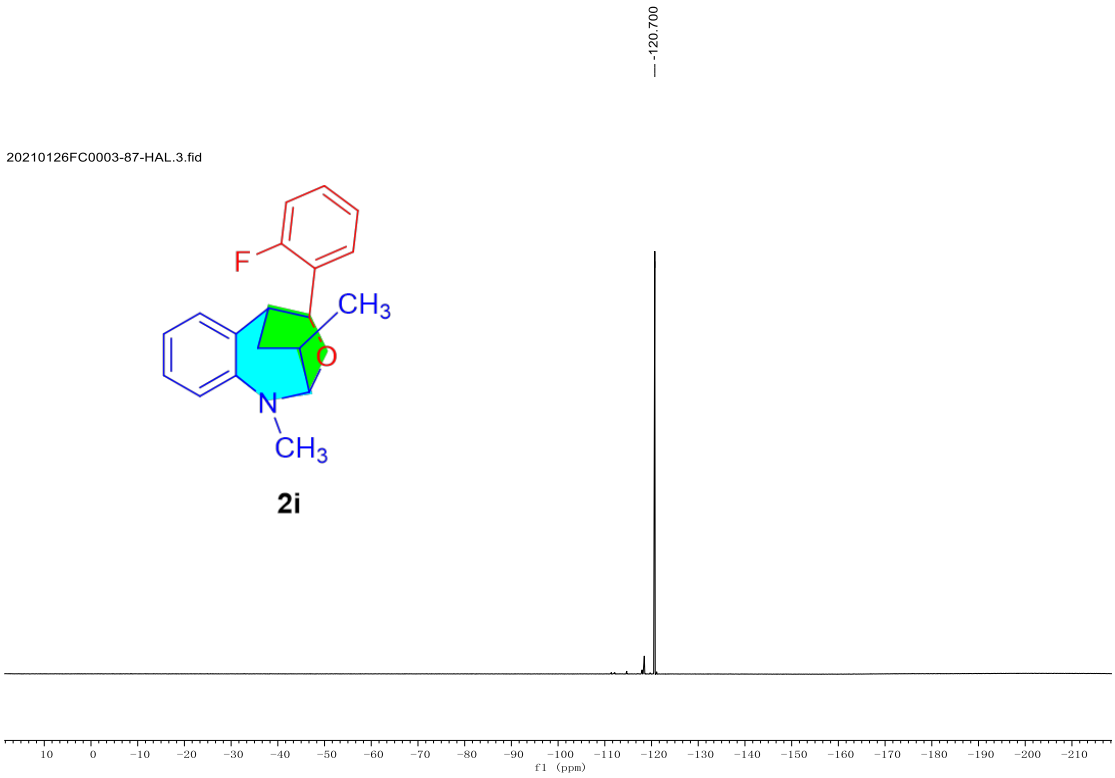
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2i**



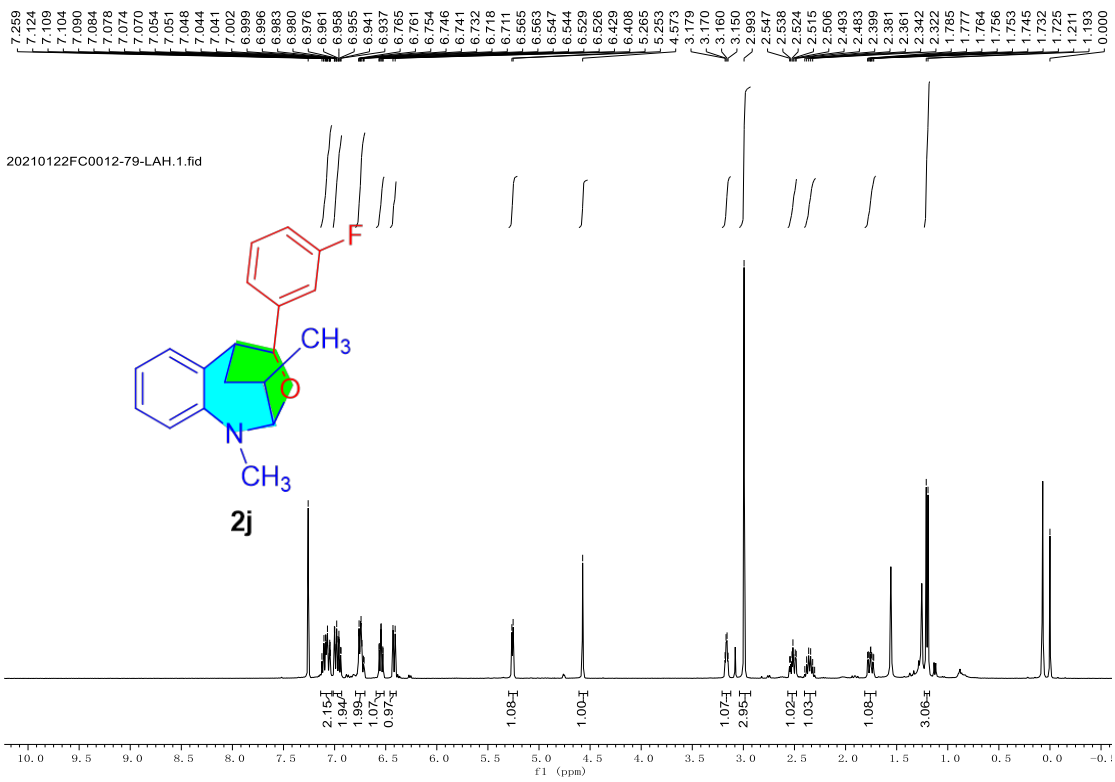
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2i**



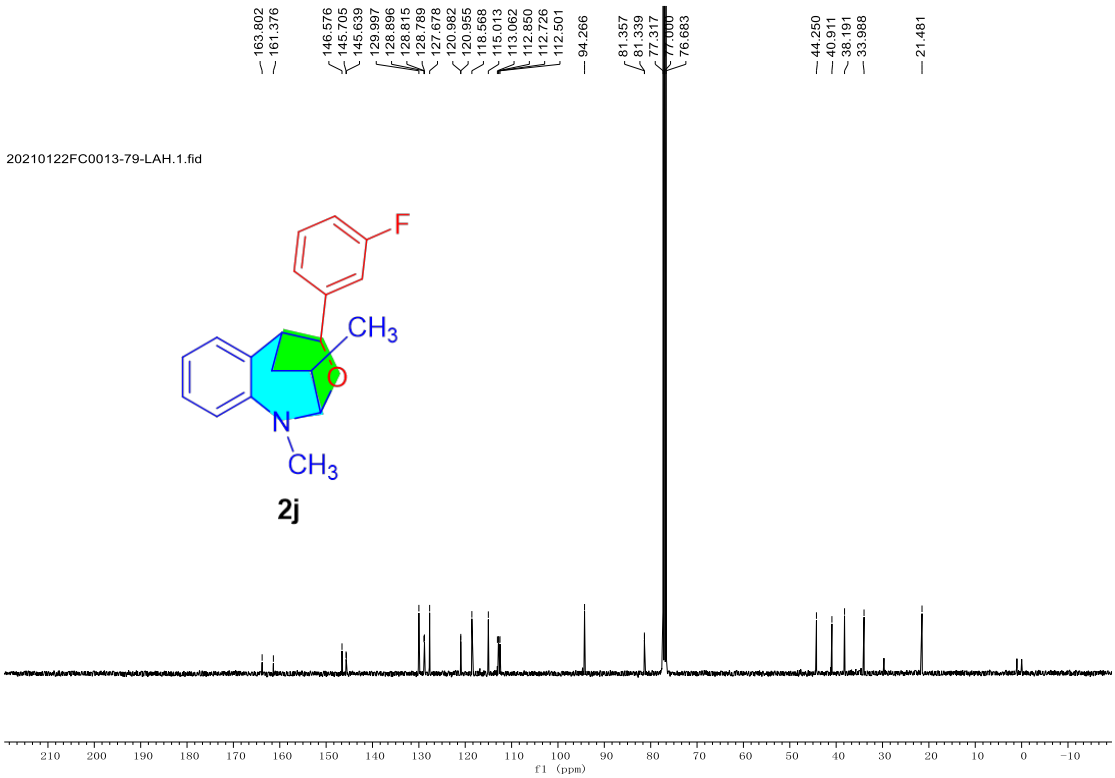
^{19}F NMR (376 MHz, $CDCl_3$) Spectrum of **2i**



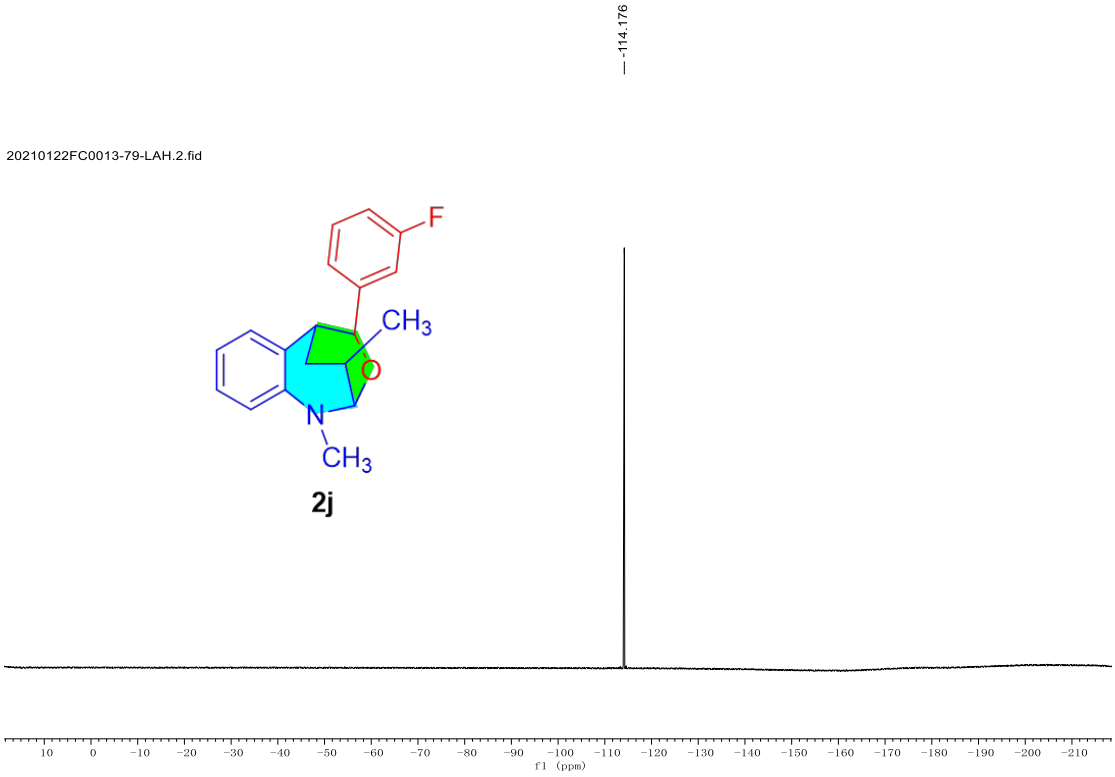
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2j**



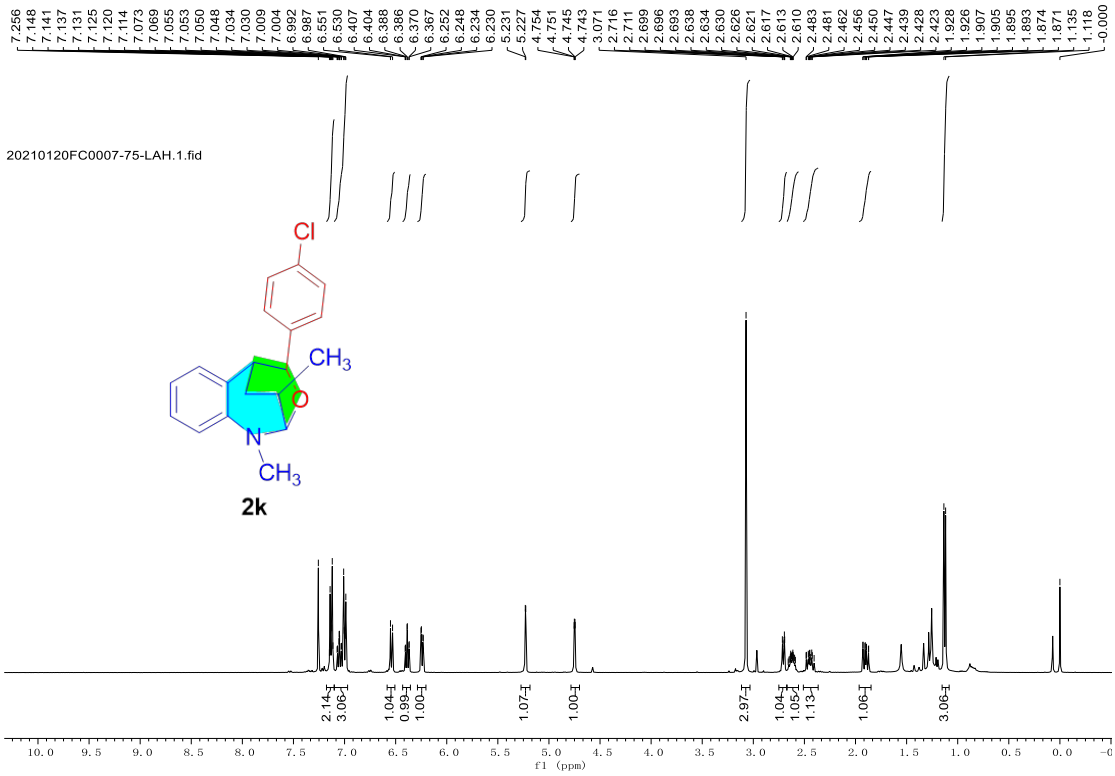
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2j**



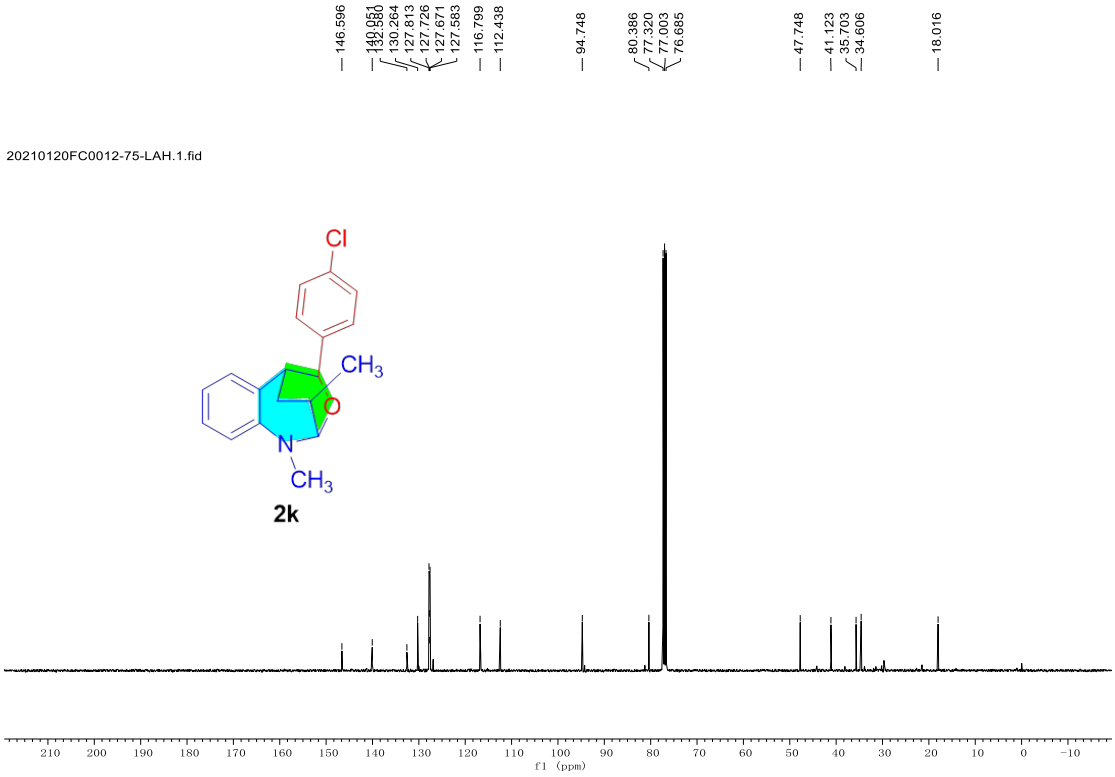
^{19}F NMR (376 MHz, $CDCl_3$) Spectrum of **2j**



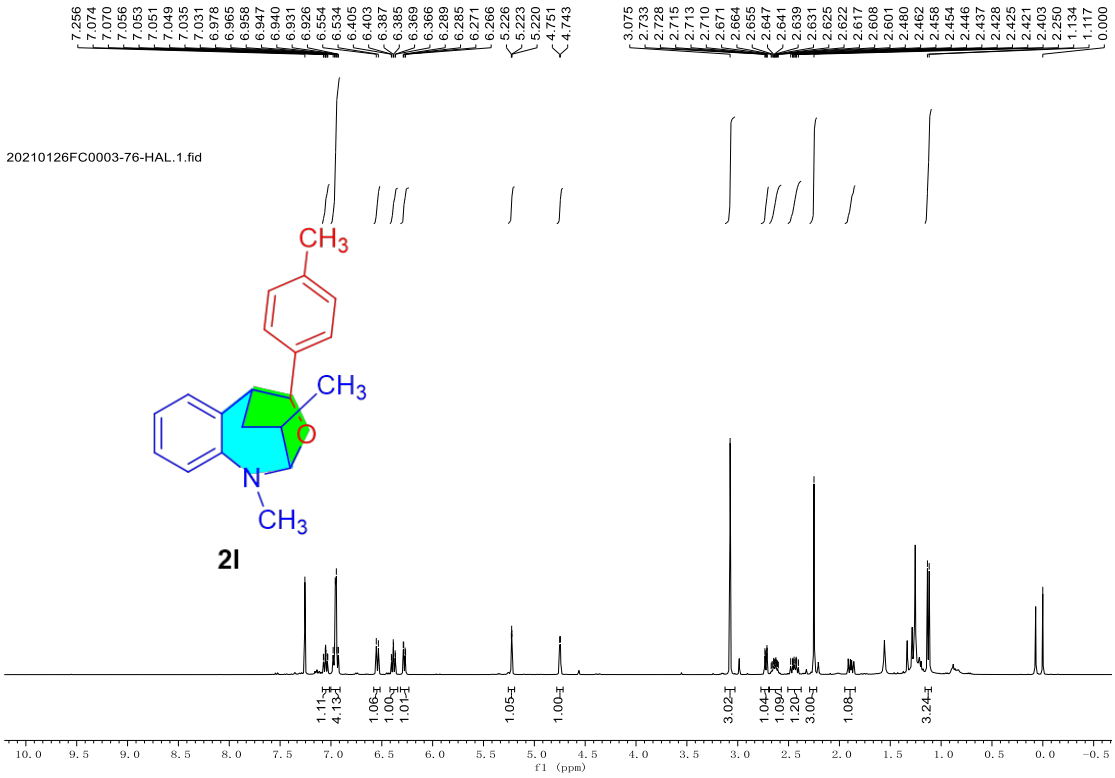
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2k**



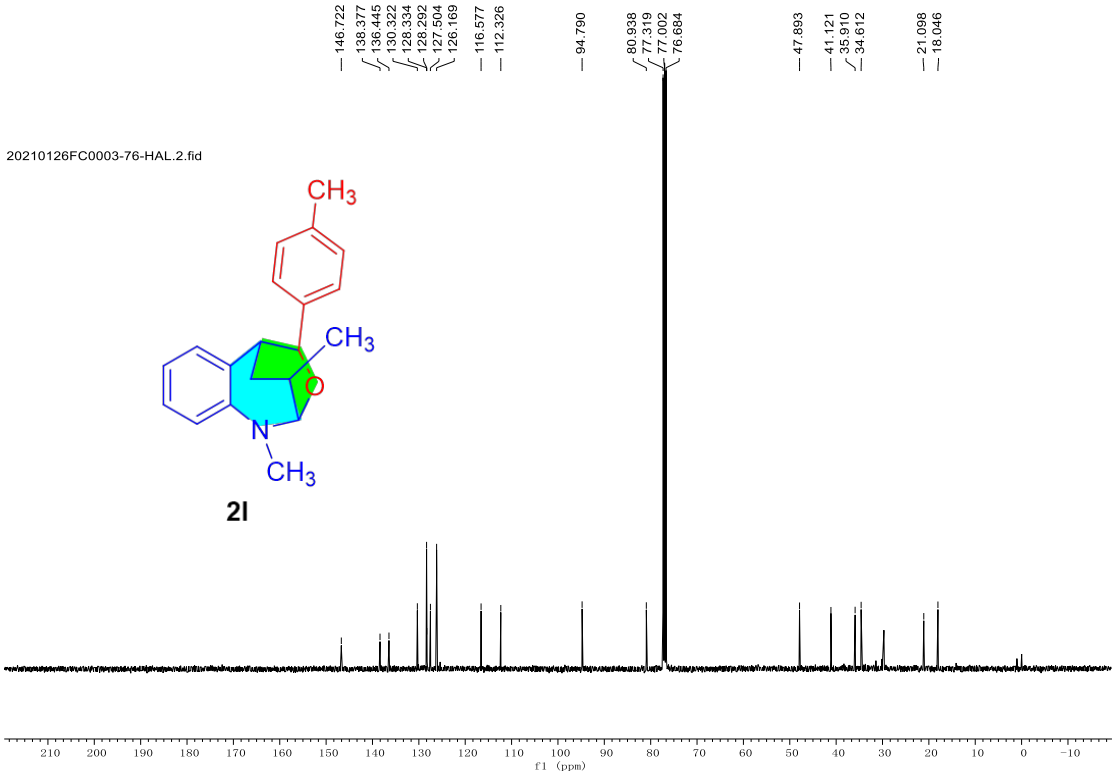
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2k**



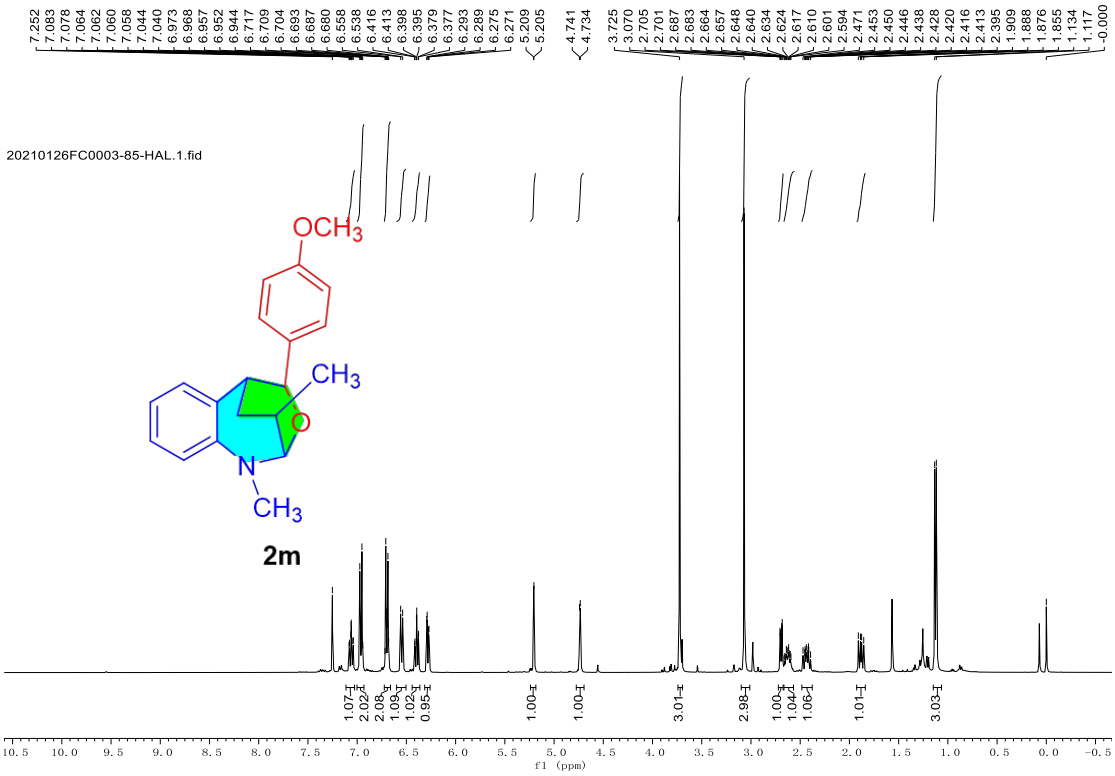
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2l**



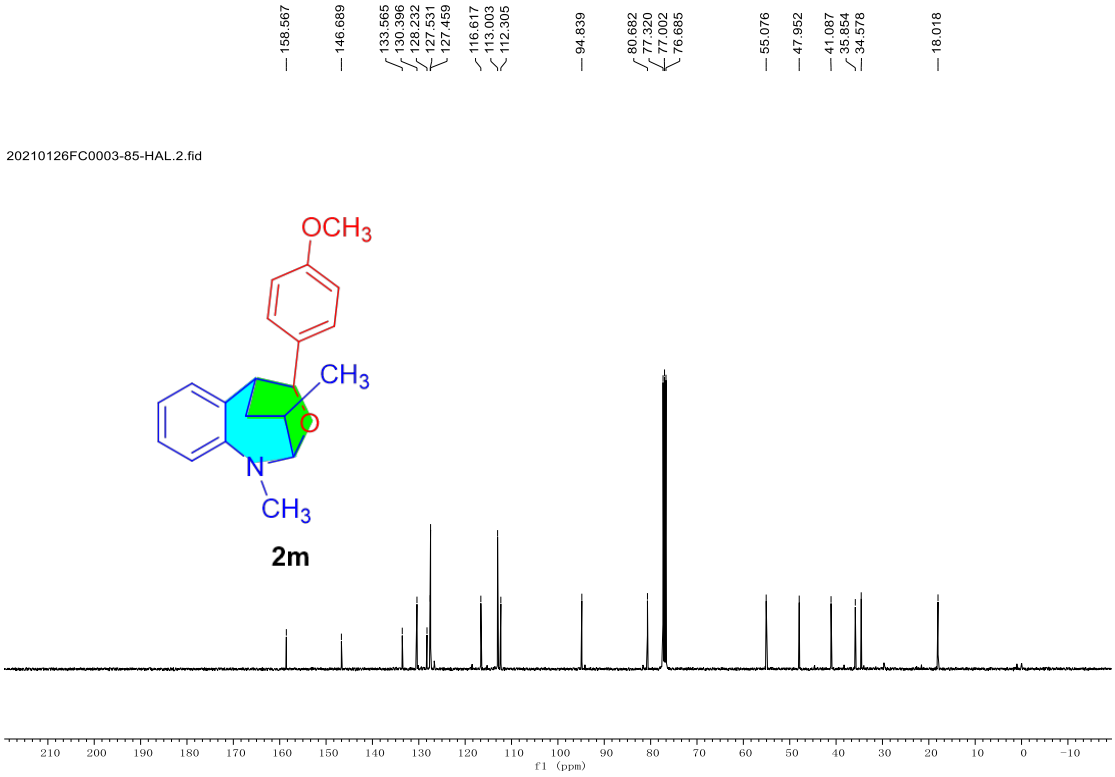
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2l**



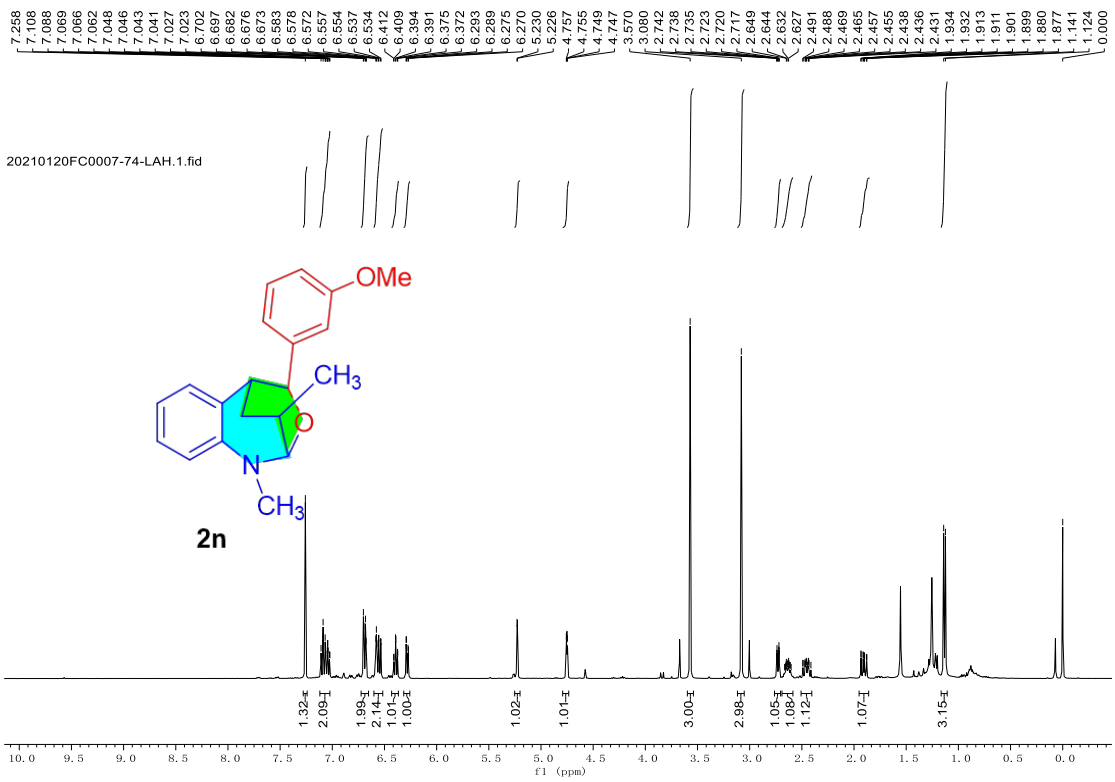
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2m**



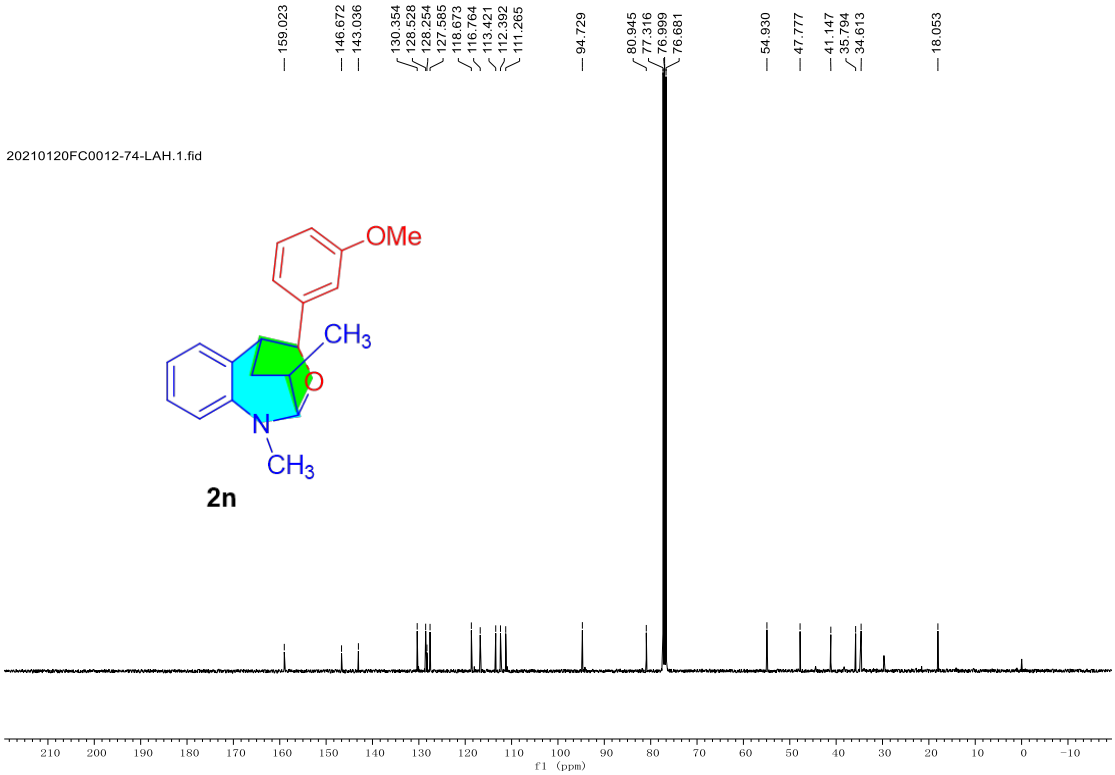
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2m**



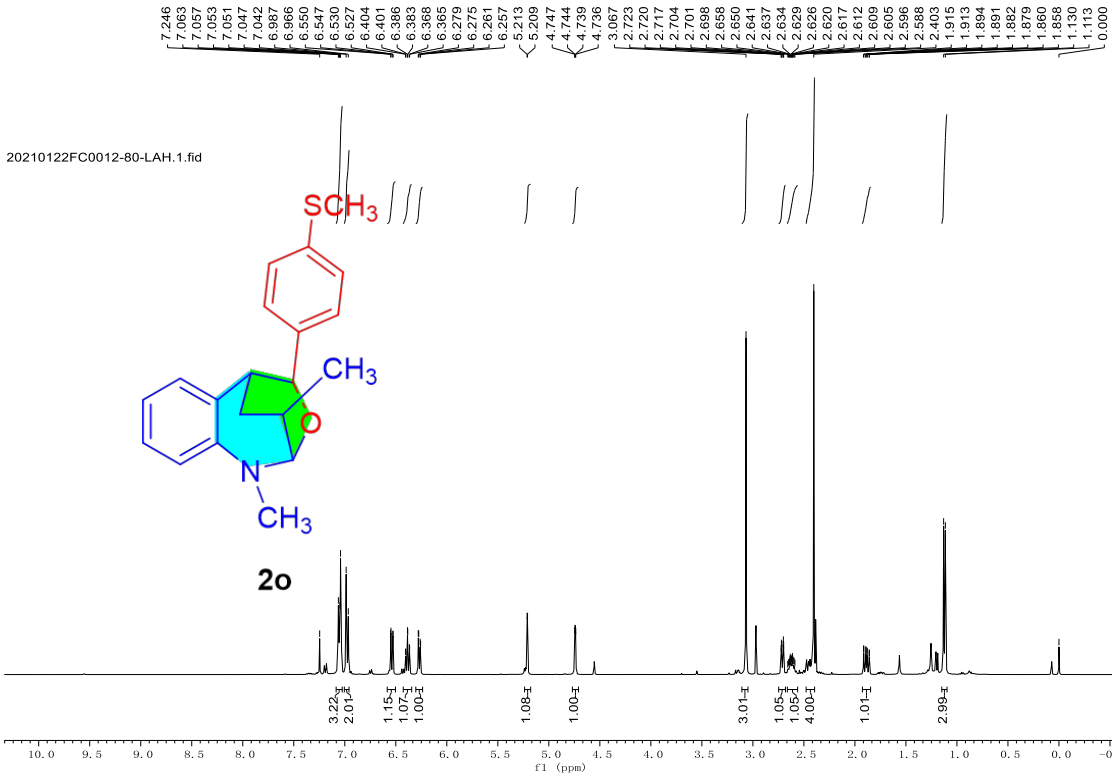
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2n**



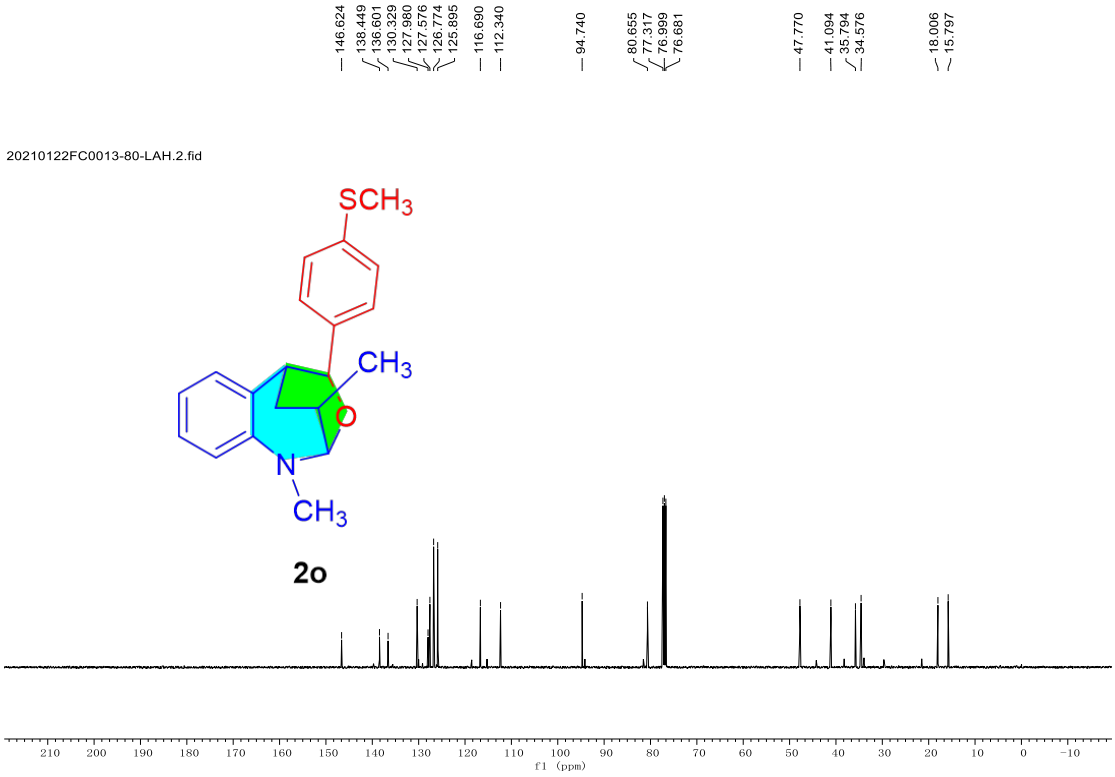
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2n**



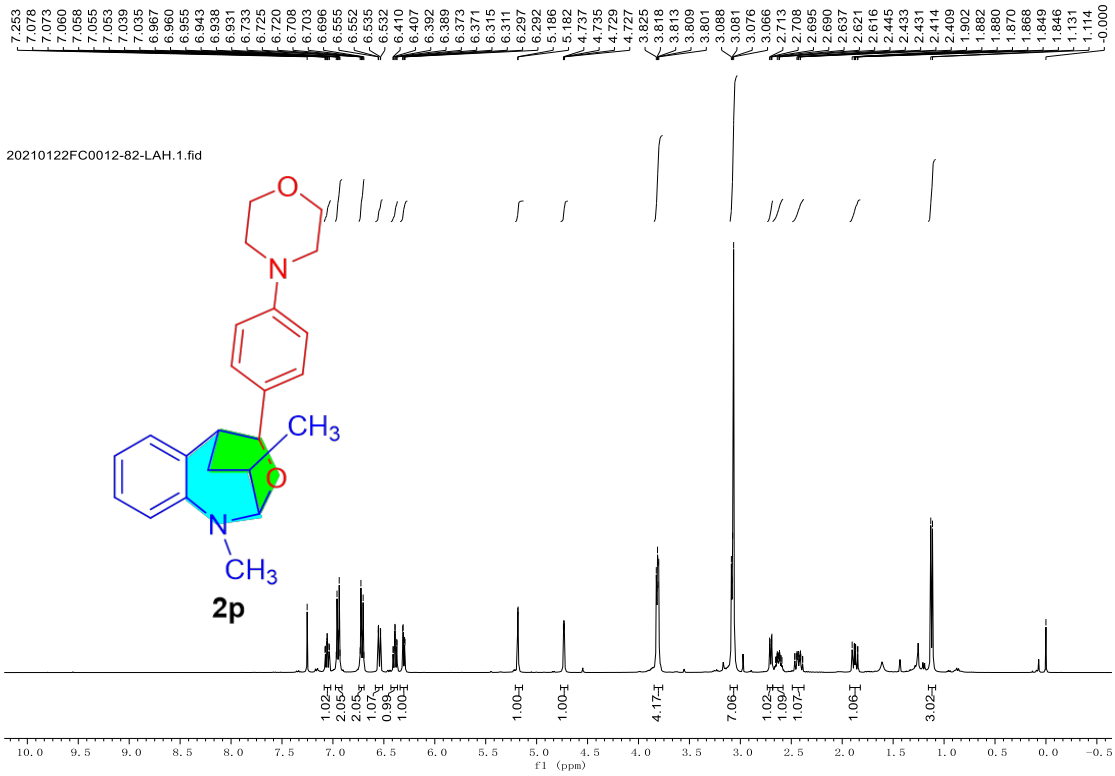
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2o**



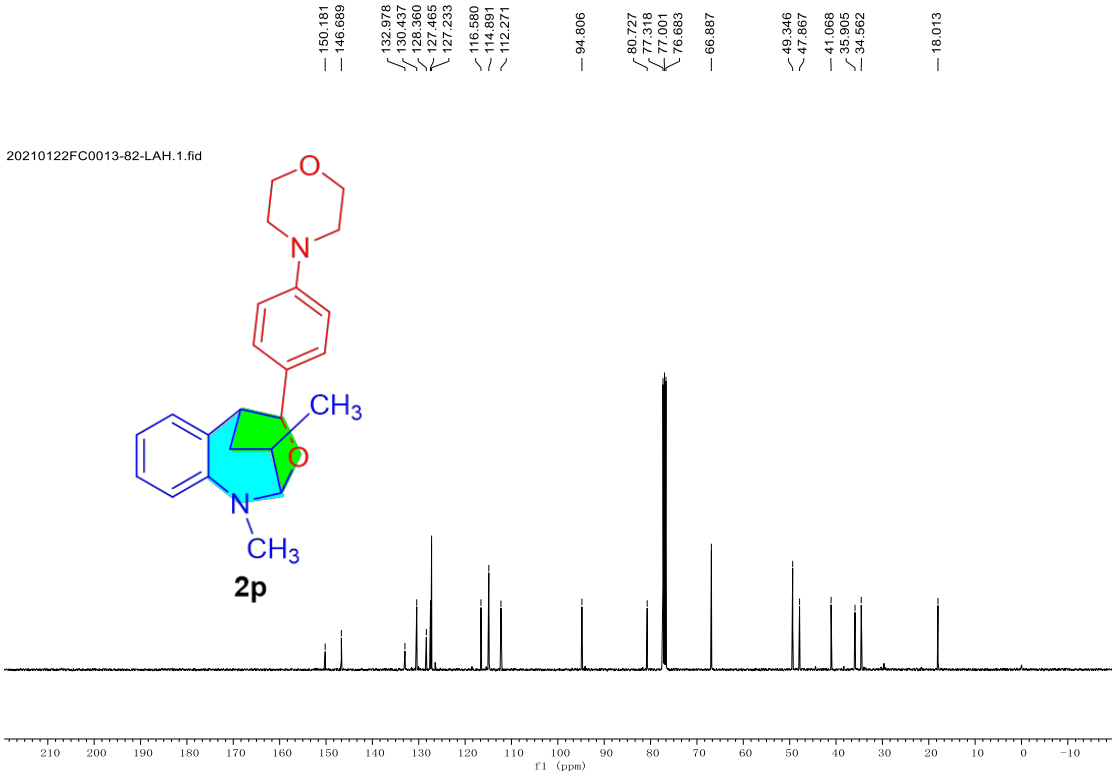
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2o**



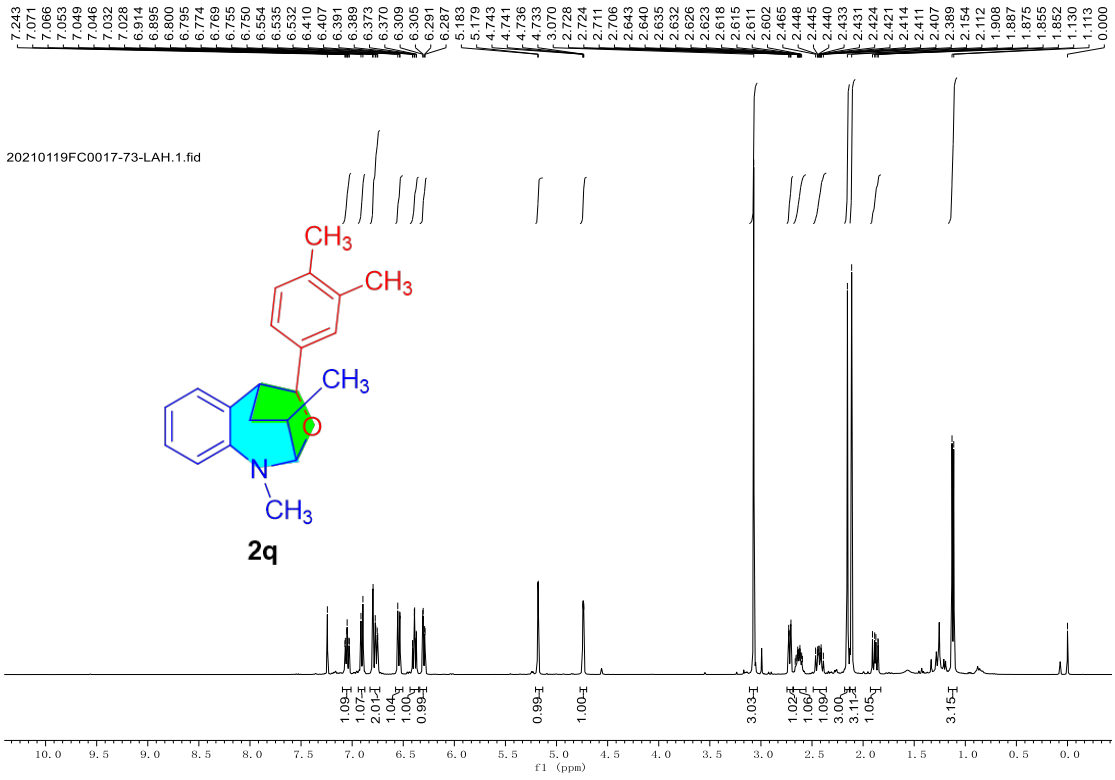
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2p**



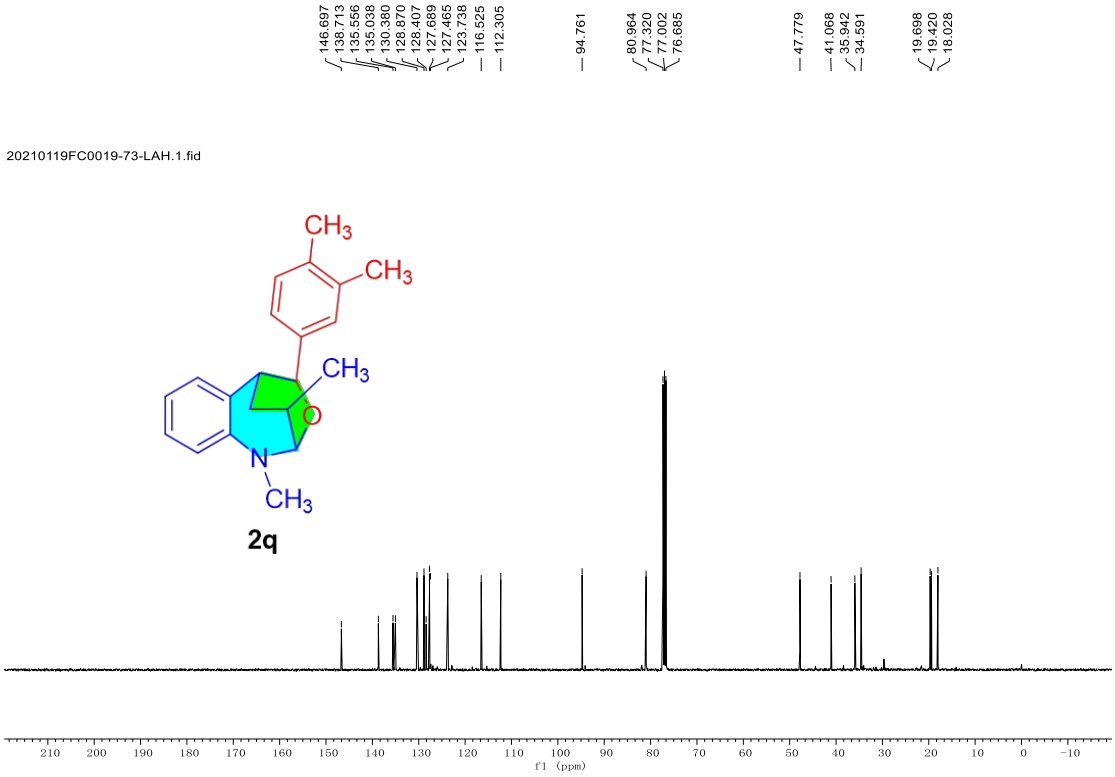
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2p**



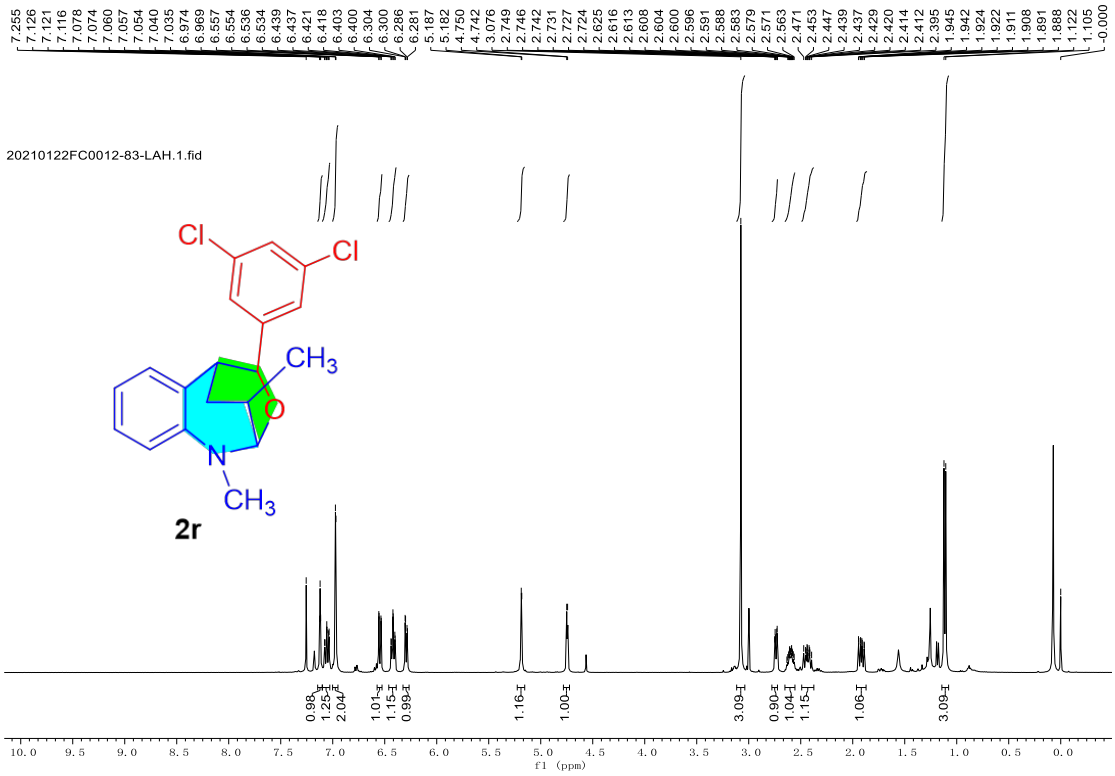
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2q**



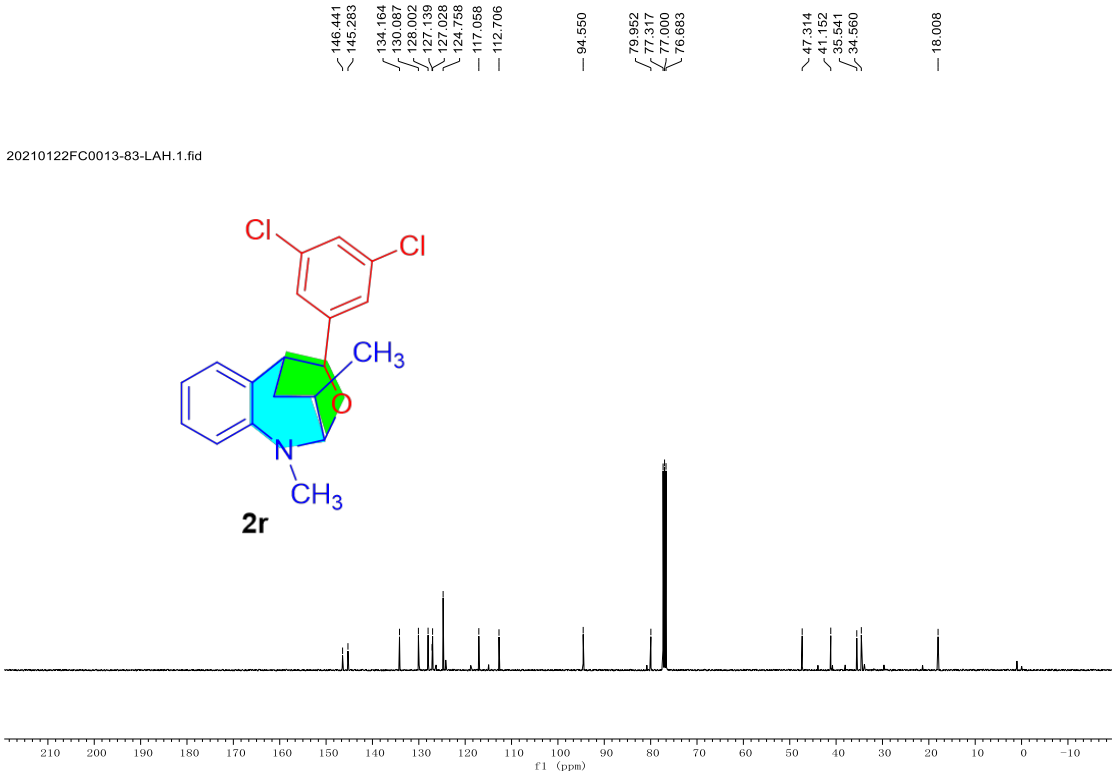
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2q**



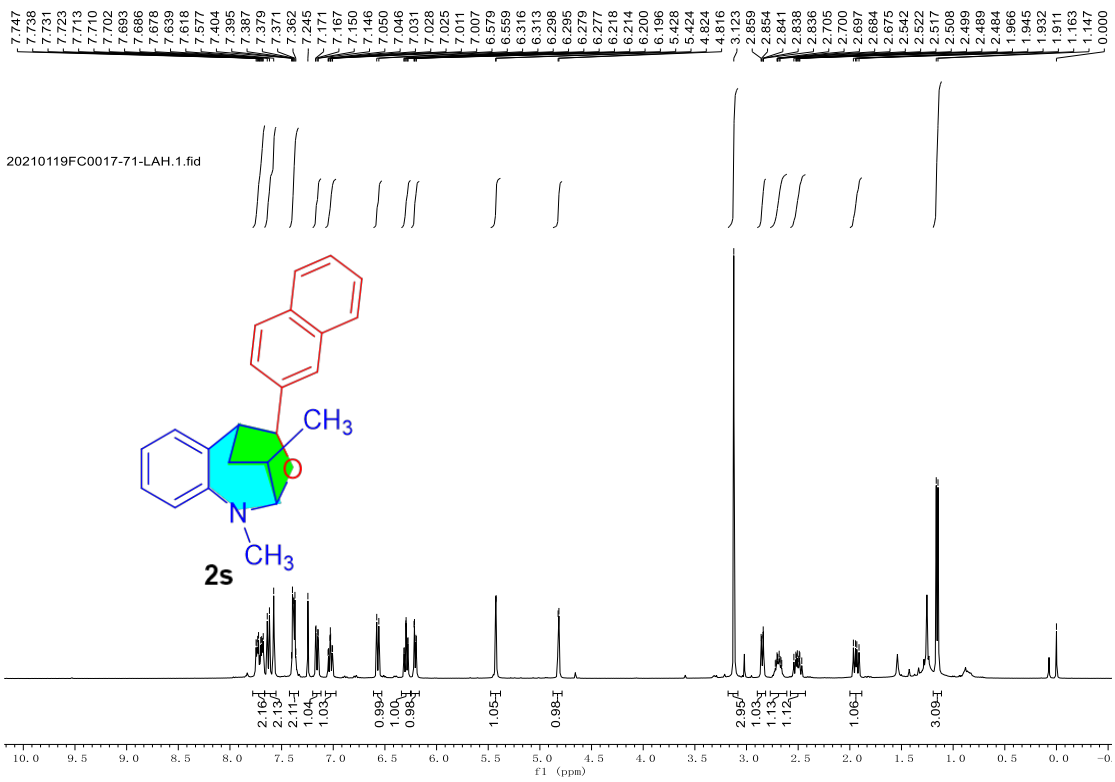
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2r**



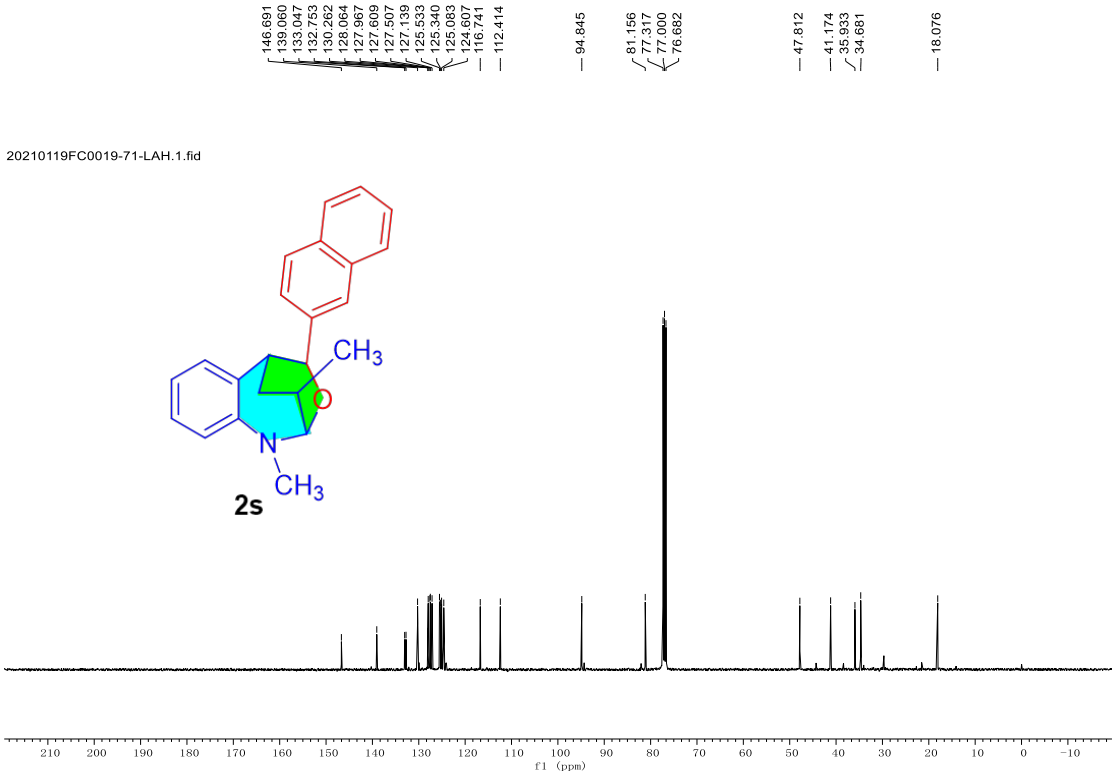
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2r**



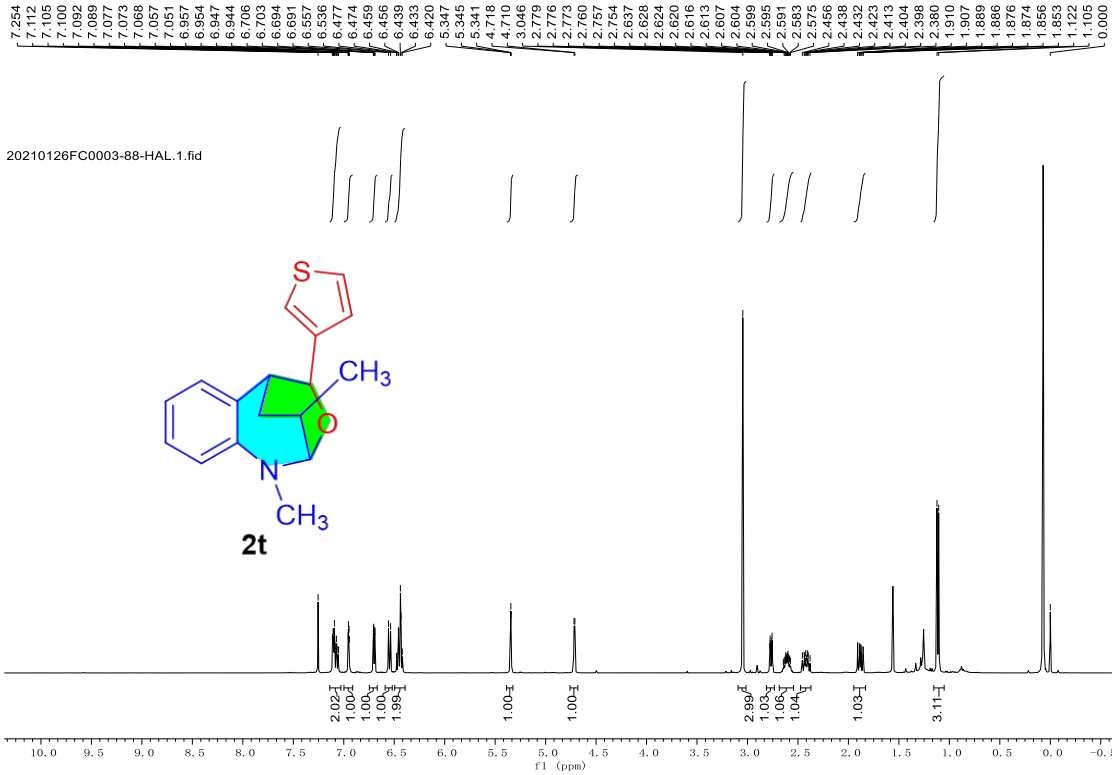
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2s**



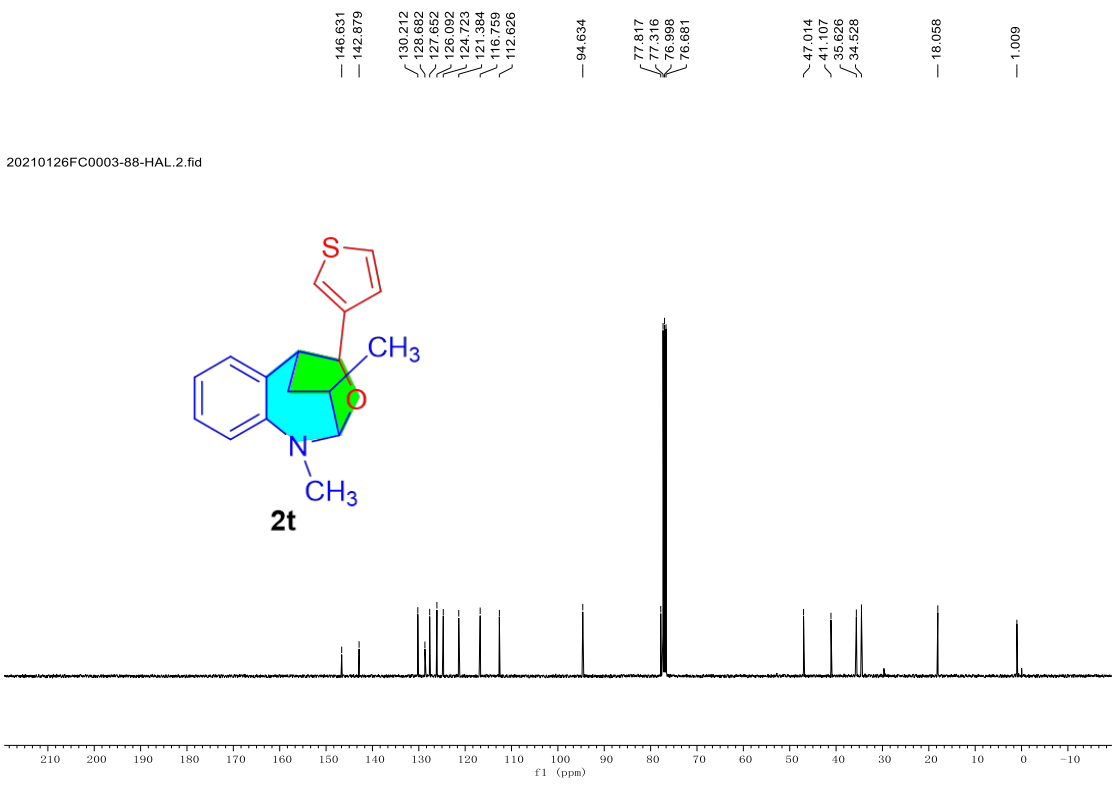
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2s**



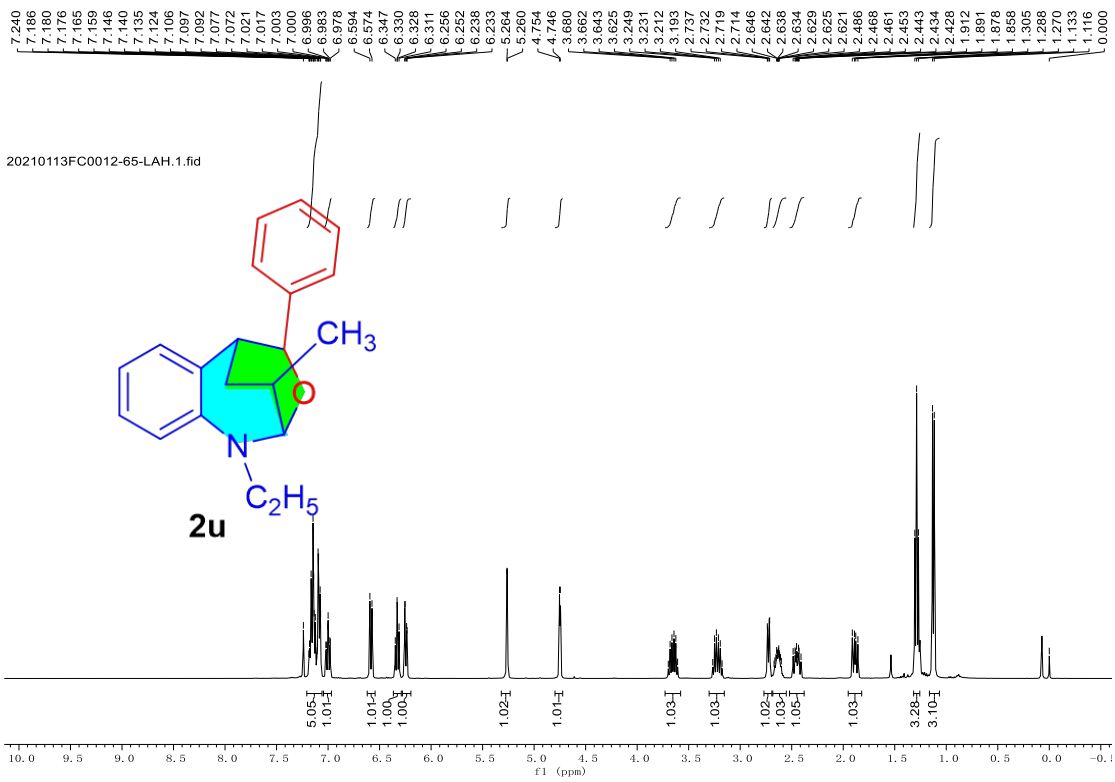
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2t**



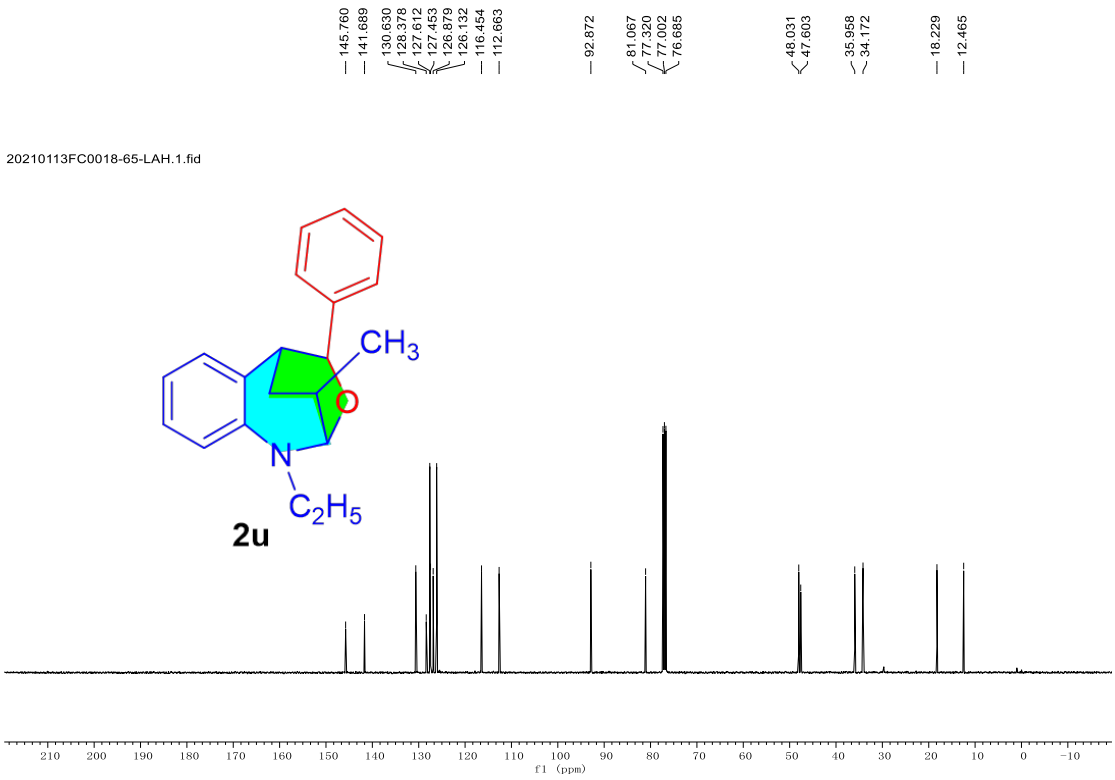
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2t**



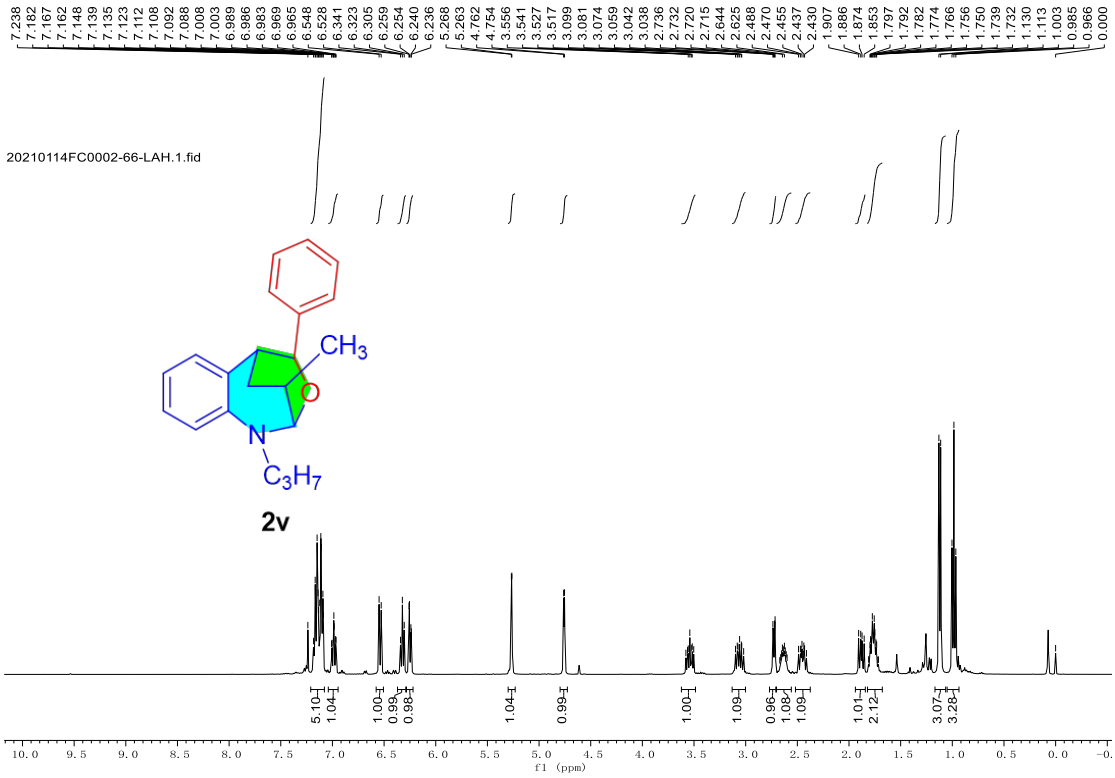
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2u**



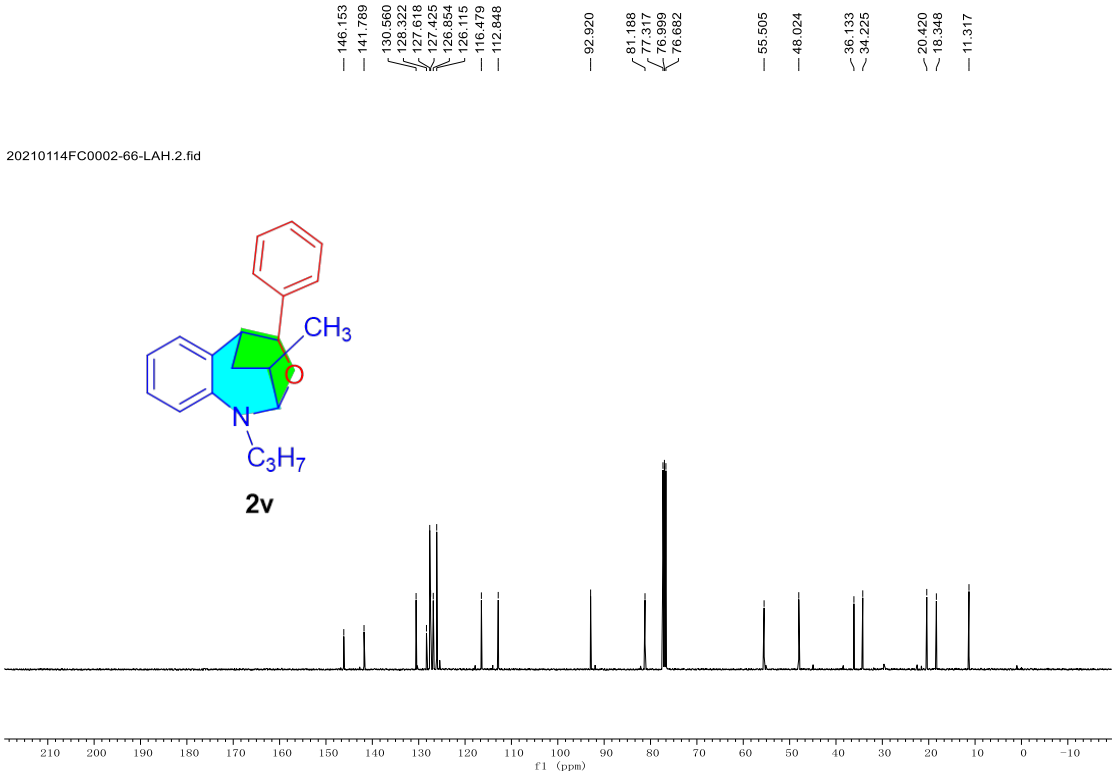
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2u**



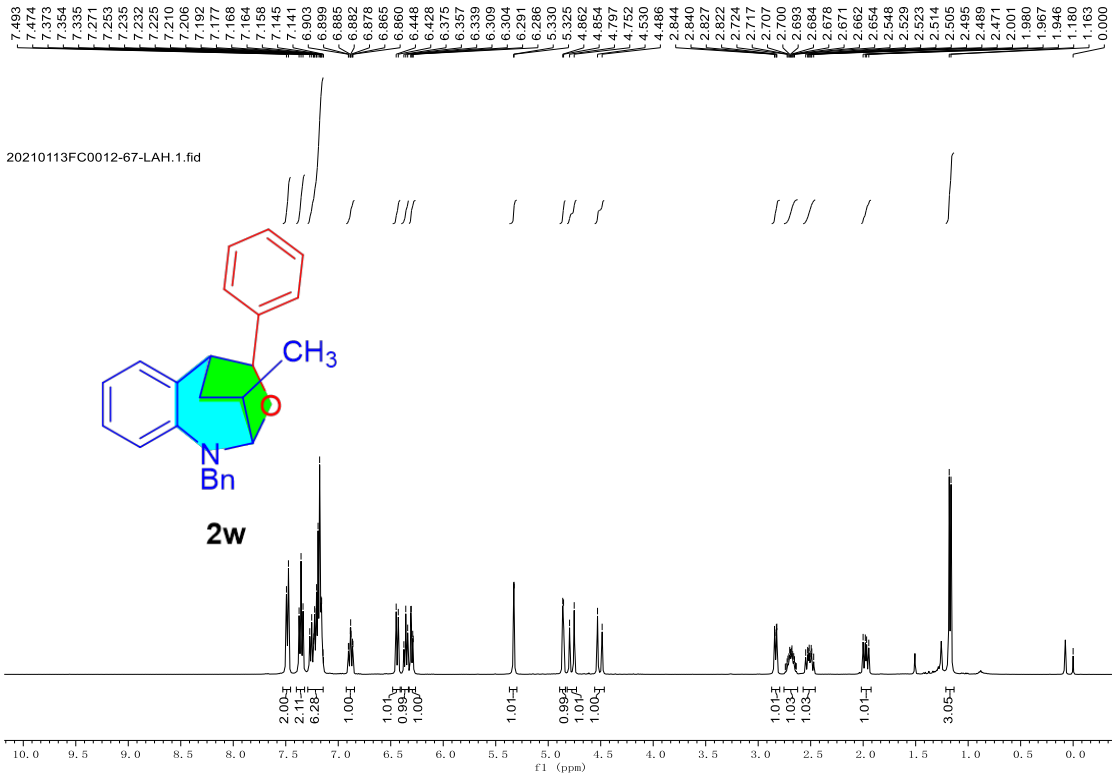
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2v**



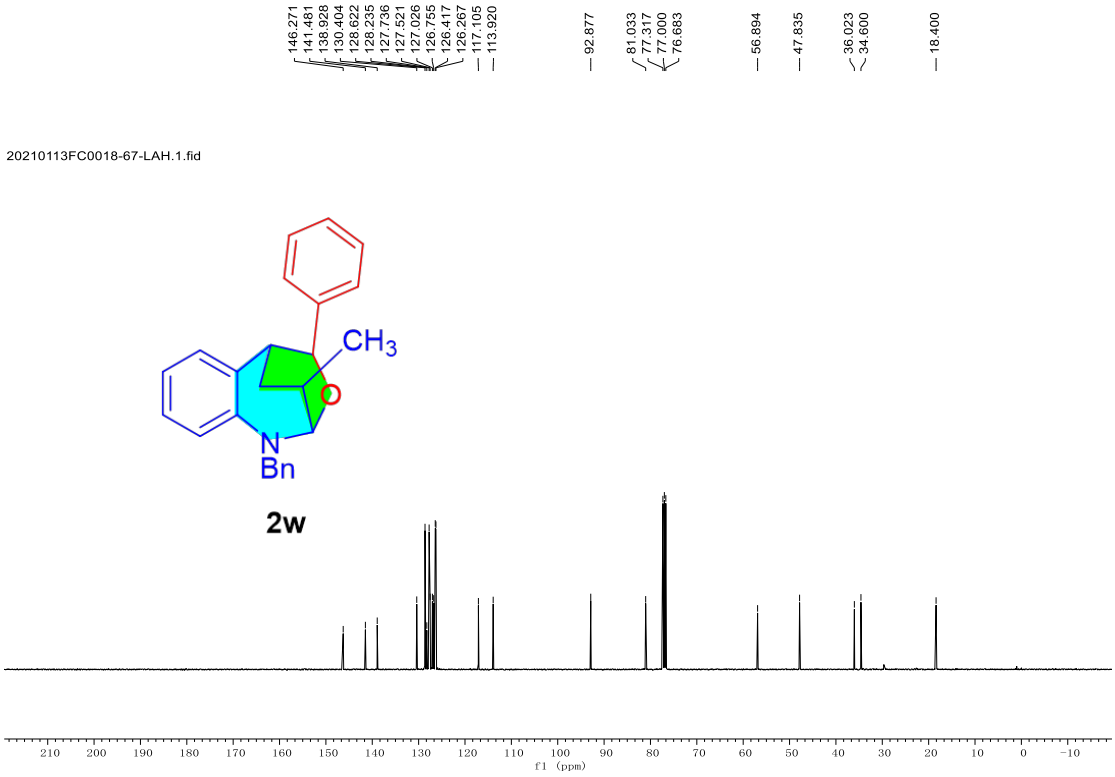
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2v**



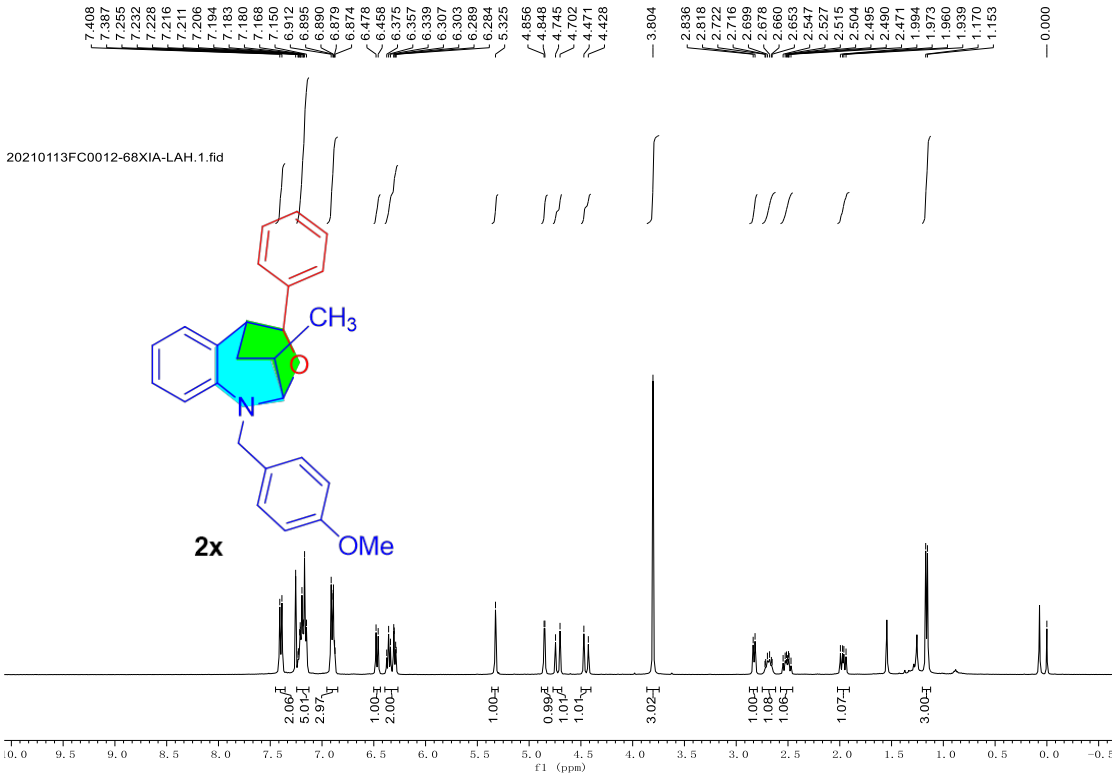
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2w**



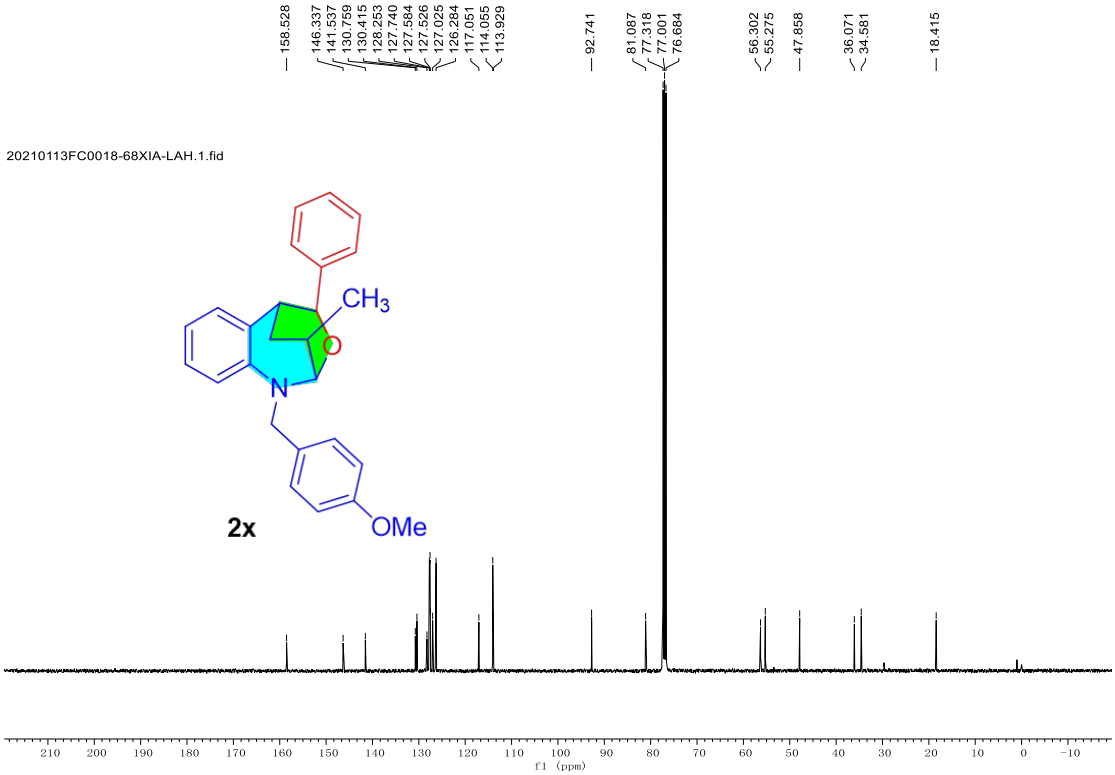
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2w**



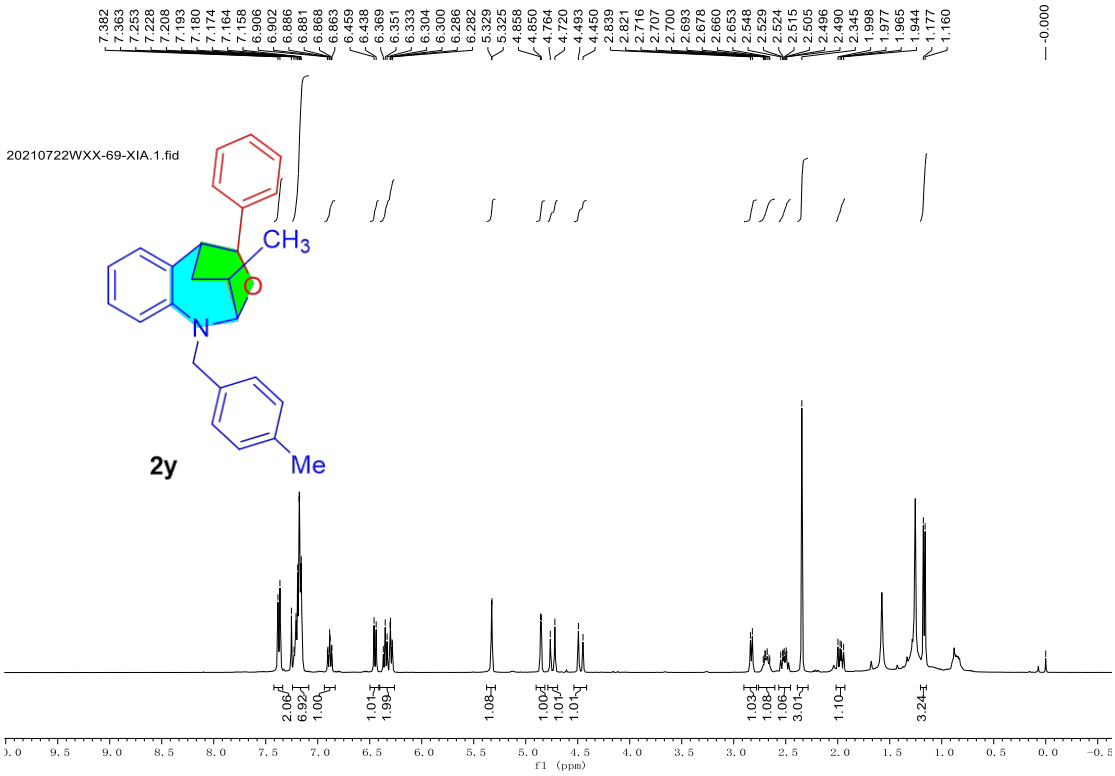
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2x**



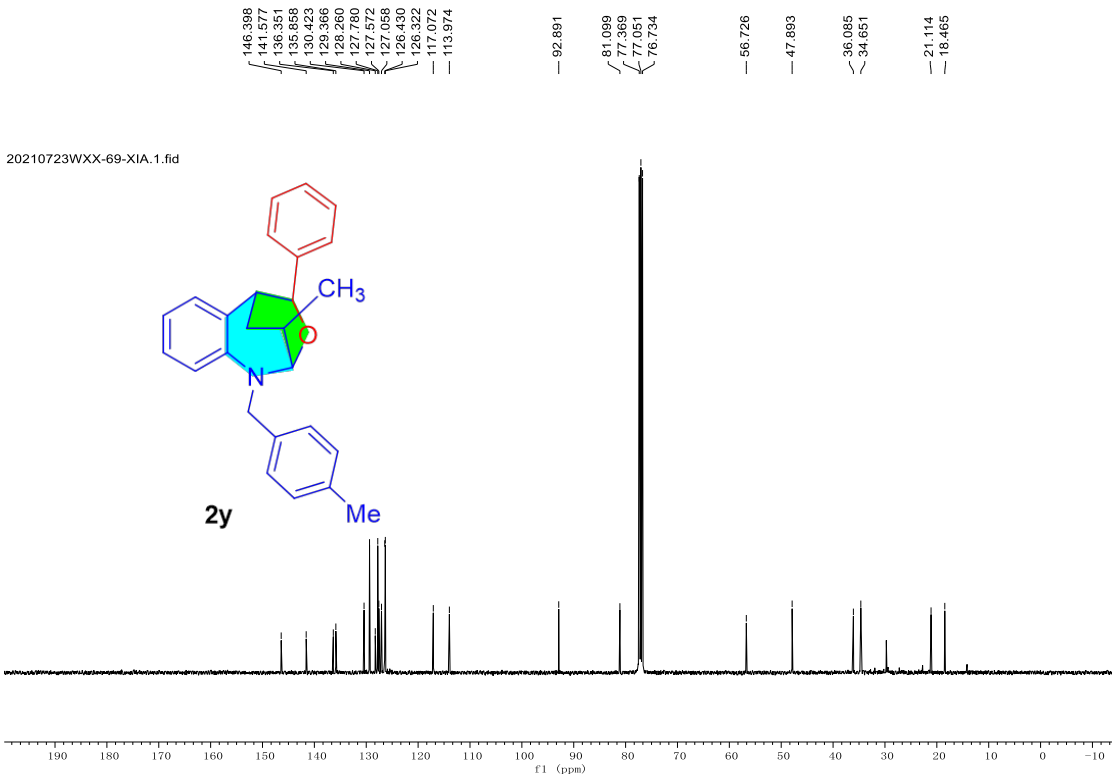
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2x**



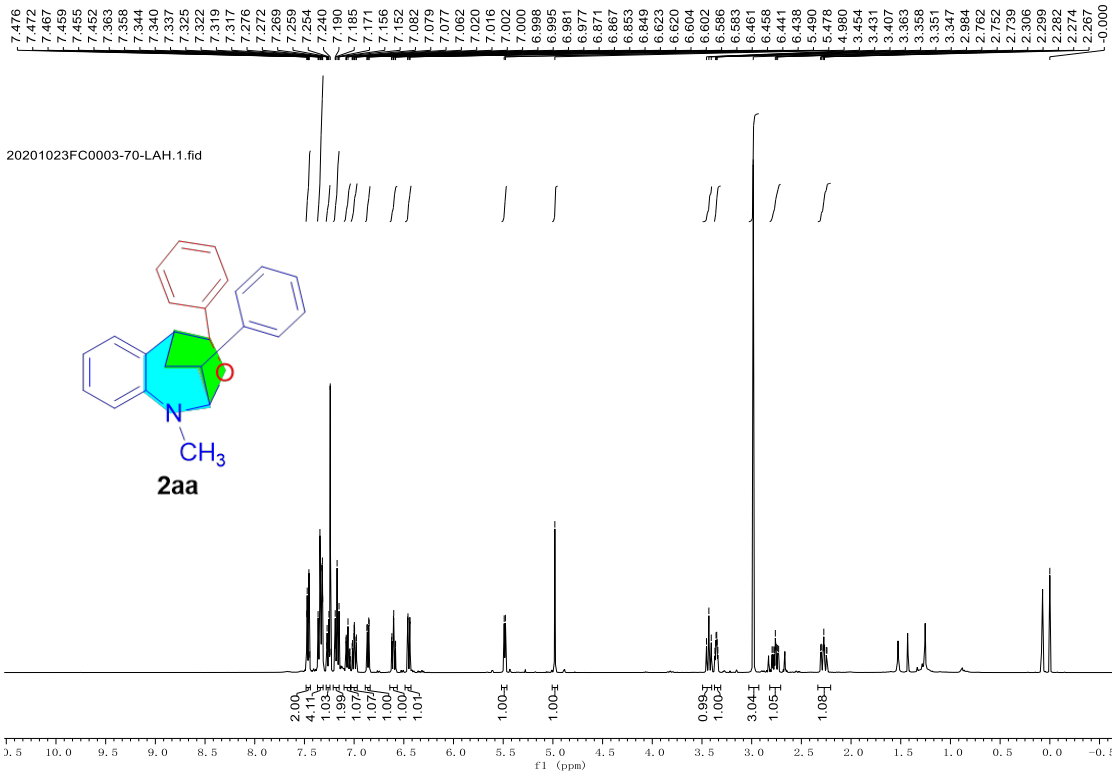
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2y**



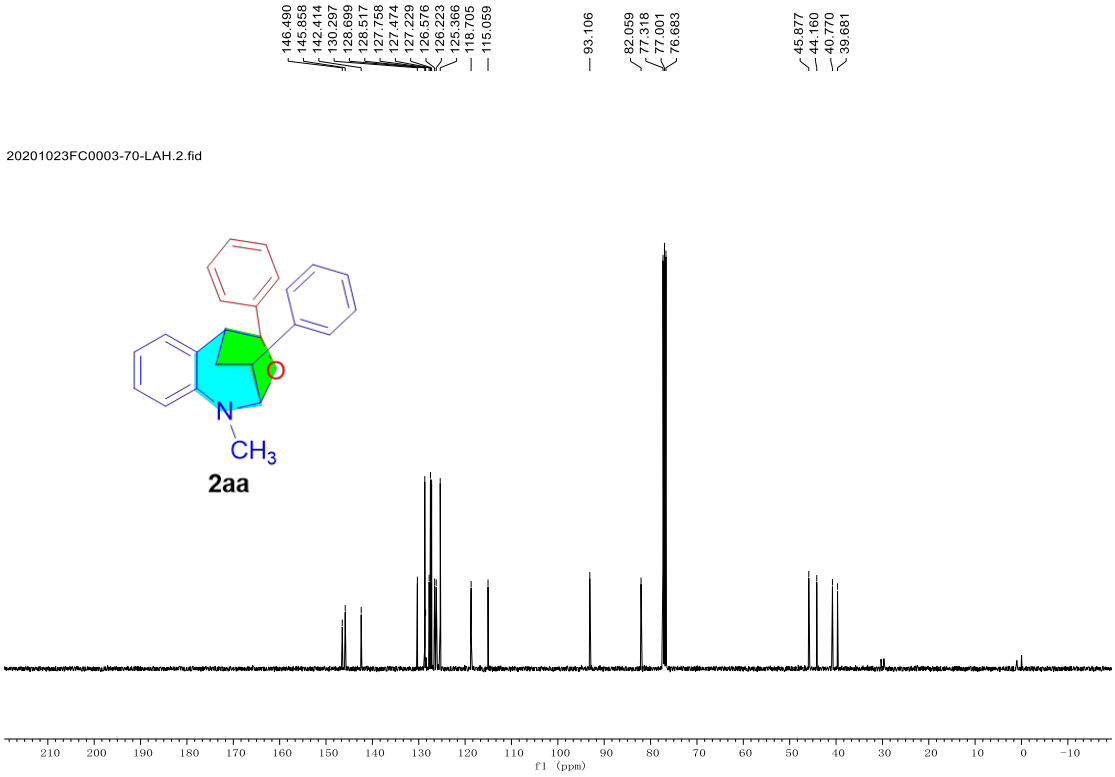
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2y**



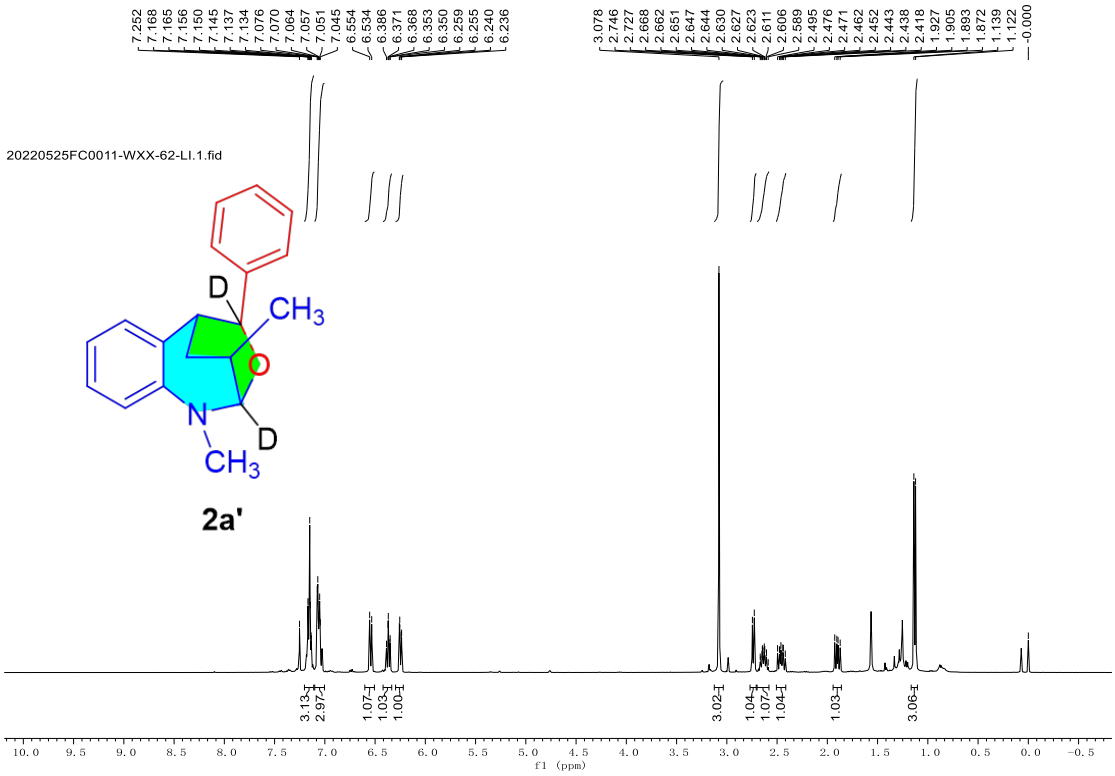
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2aa**



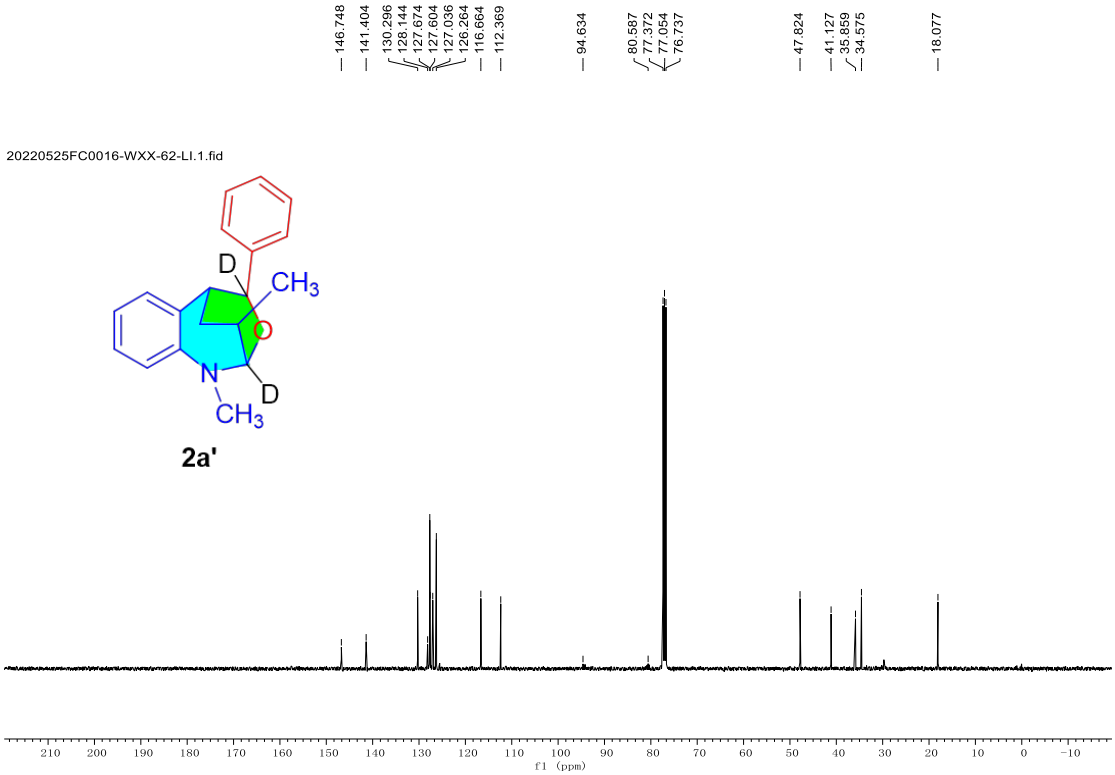
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2aa**



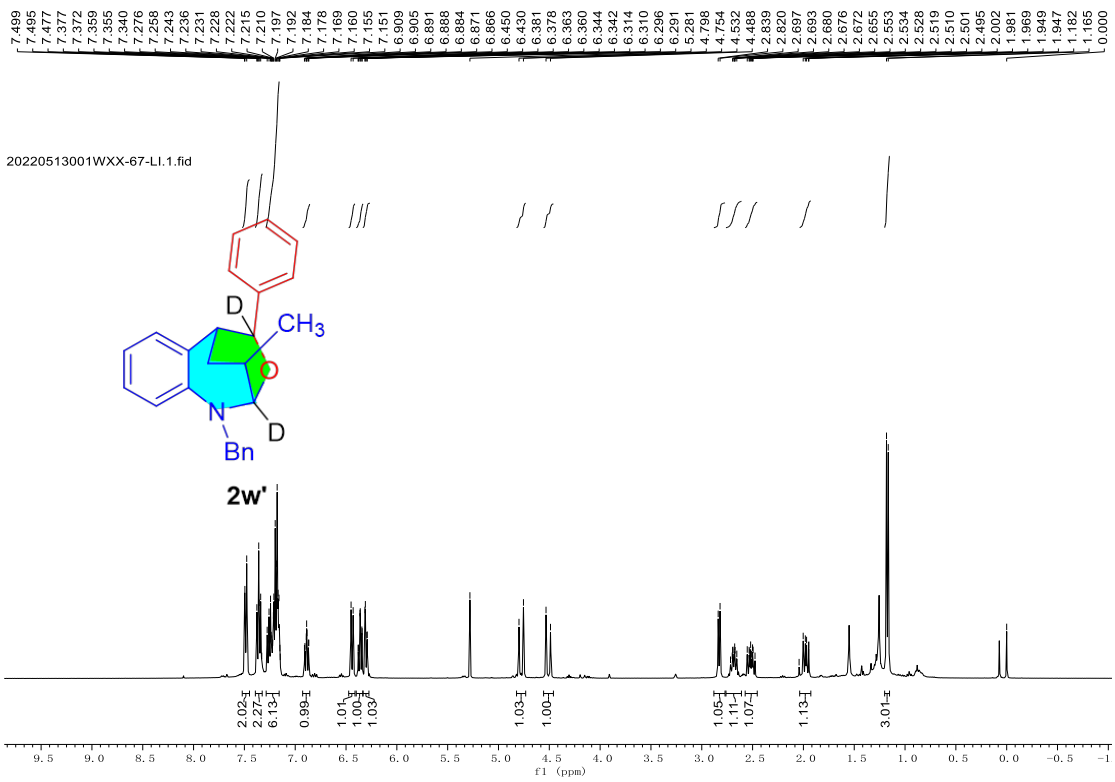
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2a'**



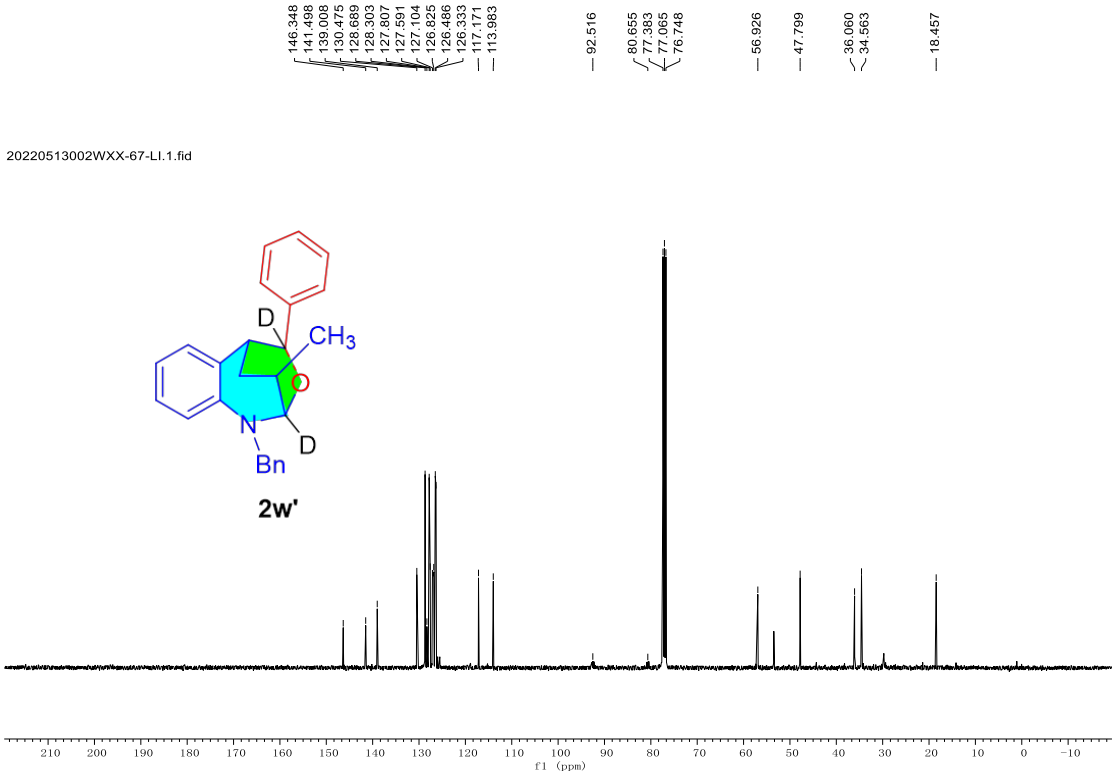
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2a'**



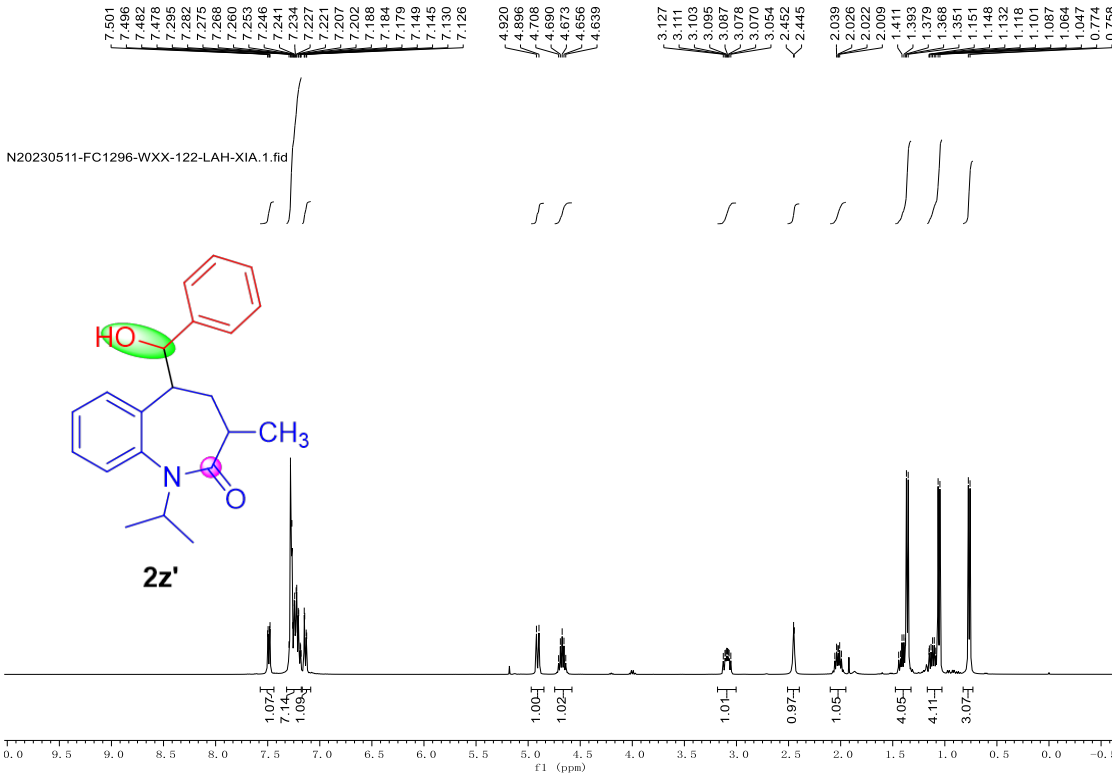
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2w'**



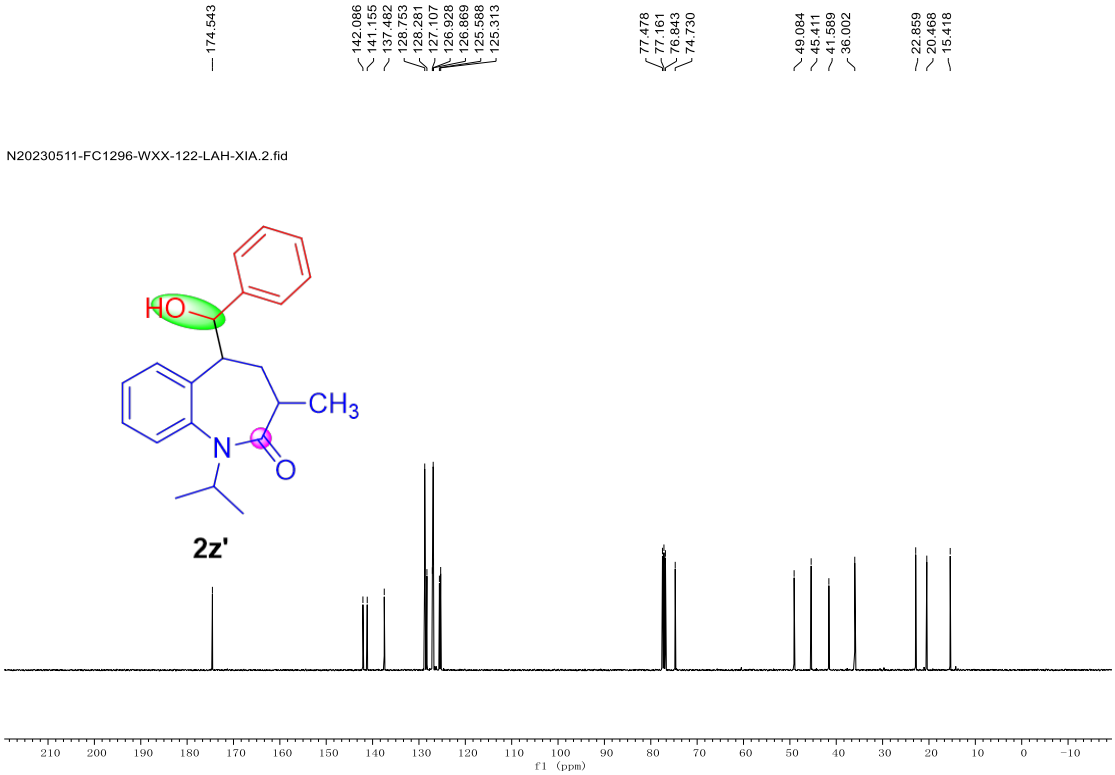
^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2w'**



^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **2z'**

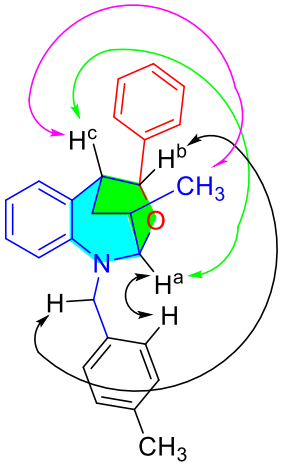


^{13}C{1H} NMR (101 MHz, $CDCl_3$) Spectrum of **2z'**



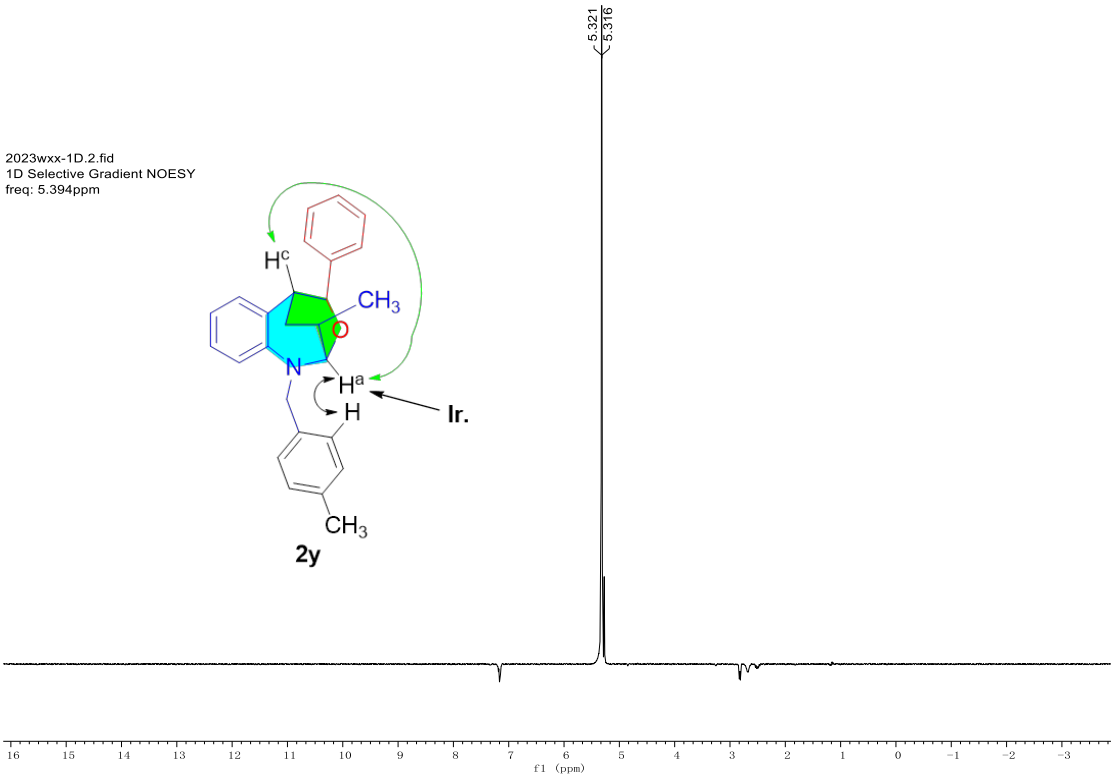
10. Description of stereochemical assignments

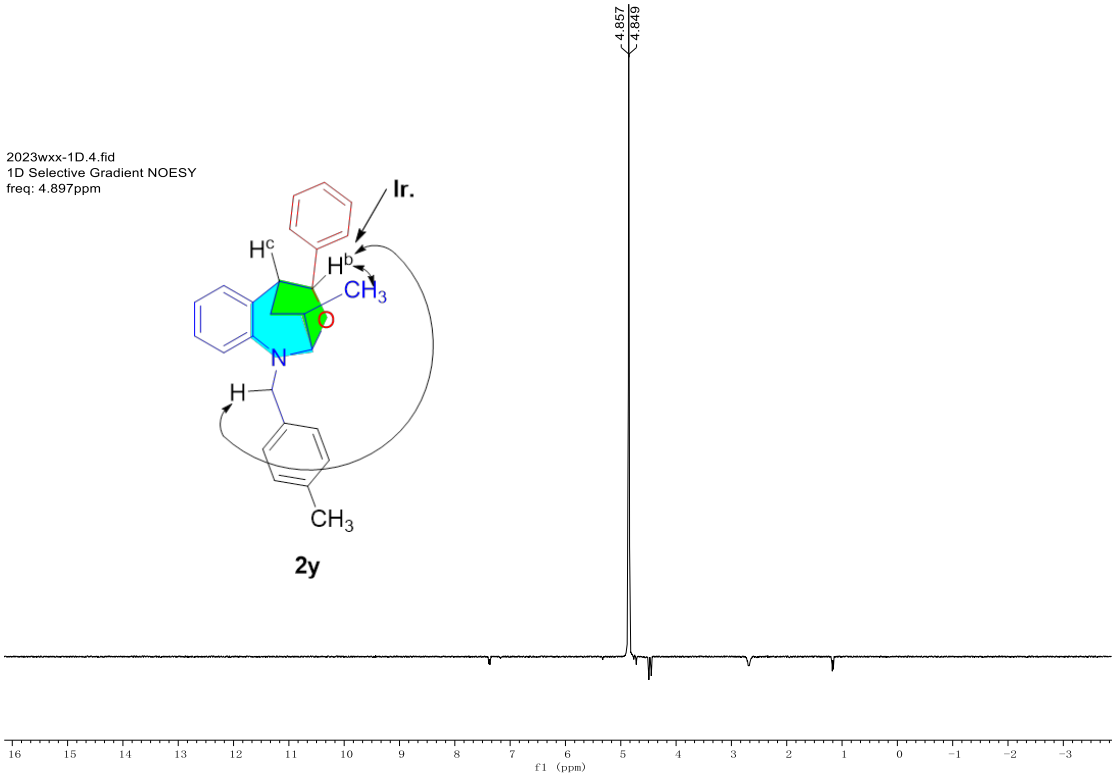
The stereochemistry of product **2y** was assigned through a combination of ^{1}H NMR and NOE experiments. Key NOE enhancements (H^a, H^b and H^c) are shown below.



2y

Proton	Chemical Shift
H^a	5.32
H^b	4.85
H^c	2.83

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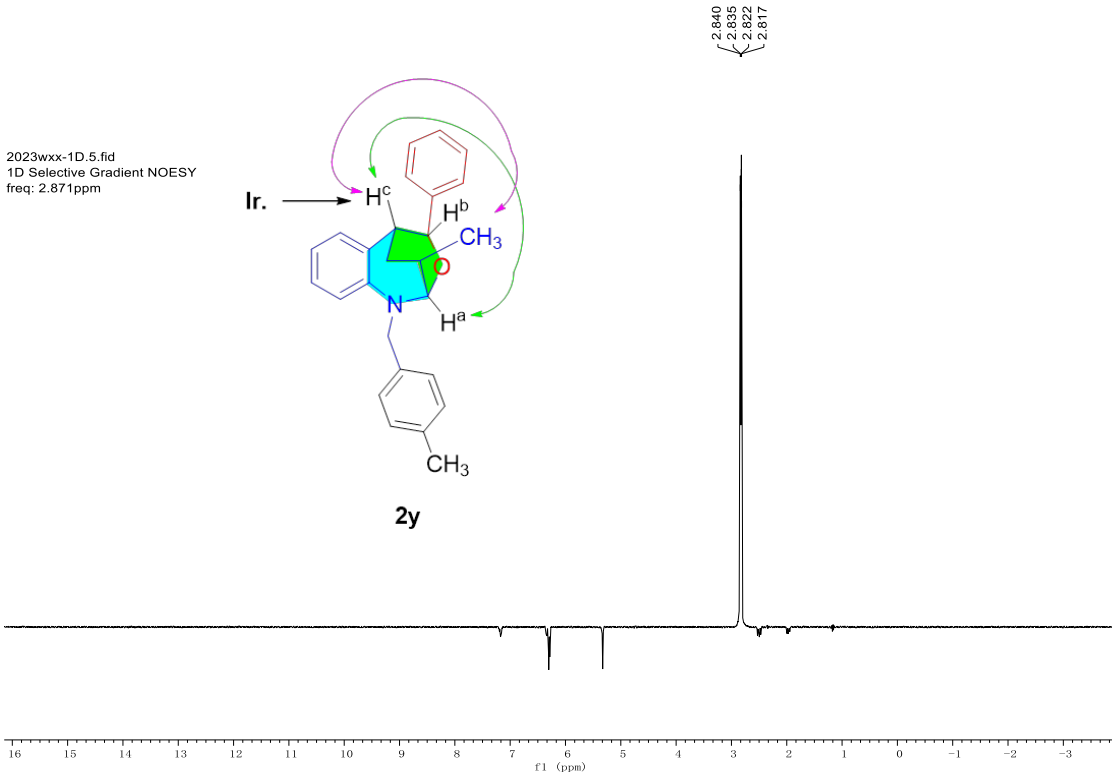
4.849
Ir.
H^c
H^b
CH_3
O
N
H
CH_3
2y
f1 (ppm)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1D Selective Gradient NOESY
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2.840
2.835
2.822
2.817
Ir.
H^c
H^b
CH_3
O
N
H^a
CH_3
2y
f1 (ppm)