Supporting Information

A Facile Semi-Synthetic Approach towards Halogen-Substituted Aminobenzoic Acid Analogues of Platensimycin

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Figure S1. The CD spectra of **PTM** and synthetic **PTMA**.

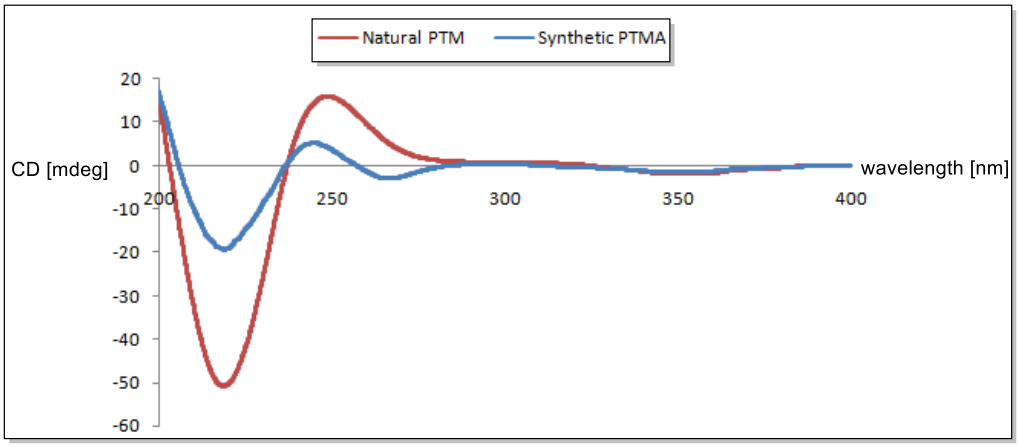
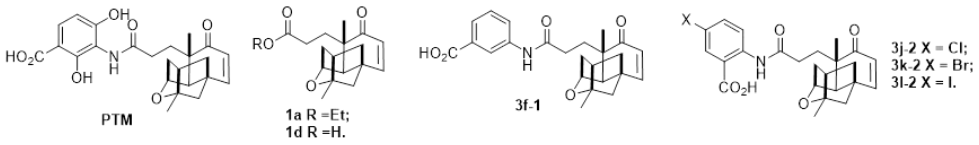
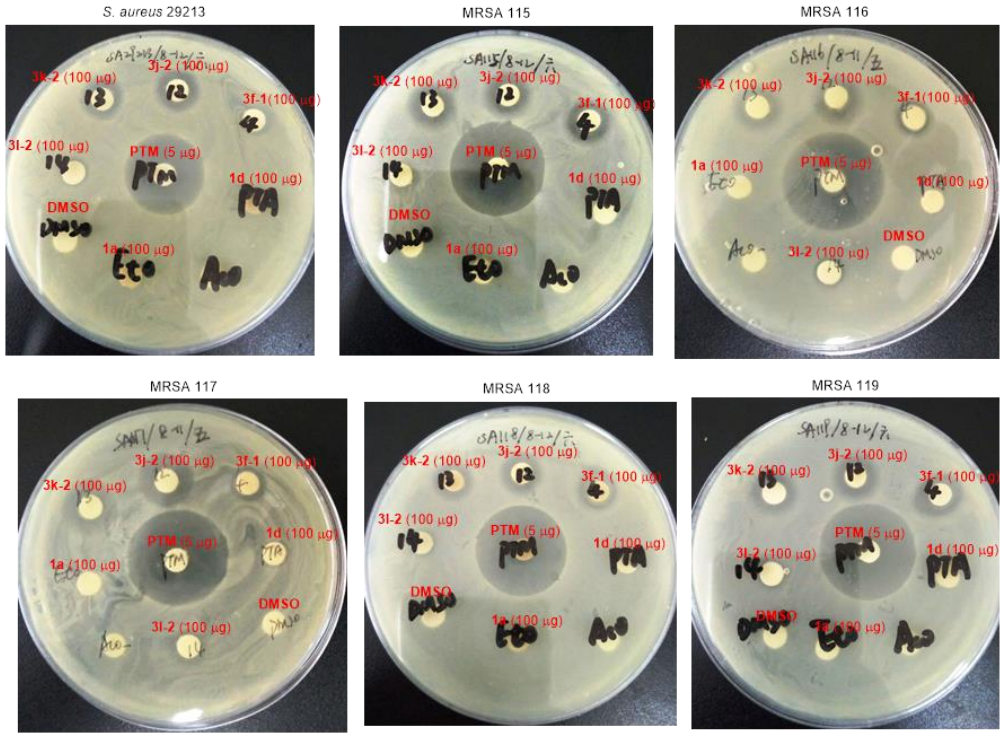


Figure S2. Agar diffusion assay. (A) Structures of the tested compounds in agar diffusion assay; (B) A few PTM aminobenzoates (**3f-1**, **3j-2**, **3k-2**, **3l-2**) showed clear zone of inhibition against *S. aureus* strains when tested in 100 μg/disk, using PTM (5 μg/disk) as a positive control and DMSO as a negative control. The experiment was repeated at least for three times and only the results from one experiment were presented.

A

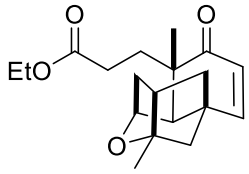


B



Characterization Data of Products

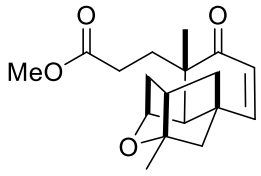
Ethyl 3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanoate (1a)



Yield: 95%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (d, J = 10.1 Hz, 1H), 5.84 (d, J = 10.1 Hz, 1H), 4.35 (s, 1H), 4.10 – 4.05 (m, 2H), 2.37 (t, J = 6.5 Hz, 1H), 2.32 (s, 1H), 2.30 – 2.11 (m, 3H), 2.03 (dd, J = 6.3, 5.3 Hz, 1H), 1.99 – 1.94 (m, 2H), 1.81 (dd, J = 11.1, 3.6 Hz, 1H), 1.77 – 1.64 (m, 2H), 1.61 – 1.54 (m, 1H), 1.40 (s, 3H), 1.19 (s, 3H), 1.19 (dd, J = 6.3, 3.2 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 203.25, 173.31, 153.51, 127.22, 86.96, 76.44, 60.35, 54.90, 46.27, 45.94, 44.62, 43.13, 40.55, 30.70, 29.32, 24.50, 23.00, 14.18;
HRMS (ESI) *m/z* calcd for $C_{19}H_{27}O_4$, $[M+H]^+$ 319.1909; Found: 319.1912.

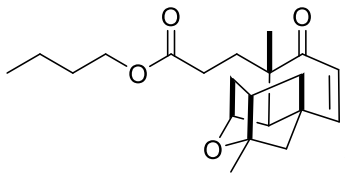
Methyl 2-(1'-benzyl-8-bromo-3a-nitro-2'-oxo-3-phenyl-3a,9b-dihydro-3H,4H-spiro[furo[3,2-c]chromene-2,3'-indolin]-4-yl)acetate (1b)



Yield: 94%;

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.43 (d, J = 10.1 Hz, 1H), 5.83 (d, J = 10.1 Hz, 1H), 4.34 (s, 1H), 3.60 (s, 3H), 2.36 (t, J = 6.5 Hz, 1H), 2.32 – 2.13 (m, 5H), 2.03 (d, J = 5.3 Hz, 1H), 2.00 – 1.91 (m, 3H), 1.81 (dd, J = 11.1, 3.4 Hz, 1H), 1.70 (ddd, J = 19.0, 12.8, 8.2 Hz, 3H), 1.57 (d, J = 11.1 Hz, 1H), 1.39 (s, 3H), 1.18 (s, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 203.21, 173.74, 153.55, 127.18, 86.96, 76.41, 54.87, 51.60, 46.27, 45.93, 45.91, 44.60, 43.11, 40.53, 30.72, 29.09, 24.47, 22.98;
HRMS (ESI) *m/z* calcd for $C_{18}H_{25}O_4$, $[M+H]^+$ 305.1753; Found: 305.1753.

Butyl 3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanoate (1c)

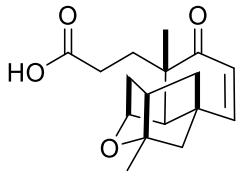


Yield: 95%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (d, J = 10.1 Hz, 1H), 5.85 (d, J = 10.1 Hz, 1H), 4.36 (s, 1H), 4.02 (td, J = 6.6, 3.0 Hz, 3H), 2.38 (t, J = 6.5 Hz, 1H), 2.27 (ddd, J = 13.0, 11.8, 8.9 Hz, 4H), 2.22 – 2.12 (m, 1H), 2.08 – 1.94 (m, 5H), 1.82 (dd, J = 11.1,

3.6 Hz, 2H), 1.77 – 1.64 (m, 3H), 1.62 – 1.50 (m, 5H), 1.41 (s, 3H), 1.35 (dd, *J* = 12.9, 5.2 Hz, 4H), 1.20 (s, 3H), 0.90 (dd, *J* = 8.6, 6.2 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) *δ* 203.25, 173.40, 153.49, 127.24, 86.96, 76.46, 64.29, 54.91, 46.27, 45.95, 44.63, 43.14, 40.56, 30.71, 30.63, 29.28, 24.50, 23.01, 19.12, 13.71;
HRMS (ESI) *m/z* calcd for $C_{21}H_{30}NaO_4$, $[M+Na]^+$ 369.2041; Found: 369.2042.

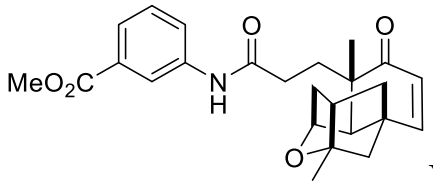
1'-benzyl-5-(4-methoxyphenyl)-4-nitro-3-phenyl-4, 5-dihydro-3H-spiro[furan-2, 3'-indolin]-2'-one (1d)



Yield: 90%;

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 6.46 (d, *J* = 10.1 Hz, 1H), 5.88 (d, *J* = 10.1 Hz, 1H), 4.42 (s, 1H), 2.41 (t, *J* = 6.5 Hz, 1H), 2.38 – 2.31 (m, 2H), 2.31 – 2.21 (m, 2H), 2.13 – 2.05 (m, 1H), 2.05 – 1.96 (m, 2H), 1.87 (dd, *J* = 11.2, 3.5 Hz, 1H), 1.81 – 1.68 (m, 2H), 1.60 (d, *J* = 11.2 Hz, 1H), 1.44 (s, 3H), 1.22 (s, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) *δ* 203.30, 177.62, 153.57, 127.23, 87.15, 76.46, 54.84, 46.31, 45.94, 45.92, 44.63, 43.14, 40.49, 30.48, 28.89, 24.43, 22.93;
HRMS (ESI) *m/z* calcd for $C_{17}H_{23}O_4$, $[M+H]^+$ 291.1596; Found: 291.1597.

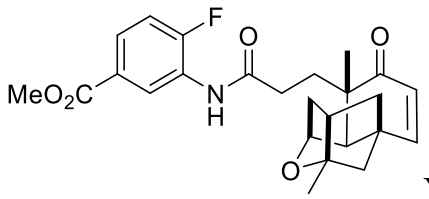
Methyl 3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoate (3a-1)



Yield: 87%;

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 8.33 (s, 1H), 8.04 (s, 1H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 6.48 (d, *J* = 10.1 Hz, 1H), 5.88 (d, *J* = 10.1 Hz, 1H), 4.44 (s, 1H), 3.87 (s, 3H), 2.41 (t, *J* = 6.5 Hz, 1H), 2.37 – 2.14 (m, 5H), 2.03 (ddd, *J* = 25.9, 20.4, 8.3 Hz, 4H), 1.89 (ddd, *J* = 13.3, 10.9, 5.6 Hz, 1H), 1.84 – 1.71 (m, 2H), 1.60 (d, *J* = 11.2 Hz, 1H), 1.42 (s, 3H), 1.23 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 204.49, 171.40, 166.84, 154.31, 138.63, 130.72, 129.04, 127.08, 124.90, 124.18, 120.47, 87.12, 76.46, 54.90, 52.17, 46.95, 46.14, 46.11, 44.68, 43.06, 40.56, 32.84, 31.40, 24.29, 22.99;
HRMS (ESI) *m/z* calcd for $C_{25}H_{29}NNaO_5$, $[M+Na]^+$ 446.1943; Found: 446.1943.

Methyl 3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-4-fluoro benzoate (3b-1)



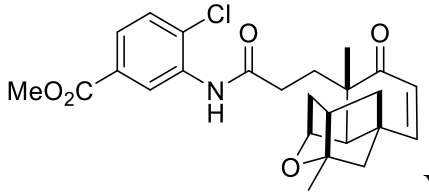
Yield: 42%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, J = 6.8 Hz, 1H), 7.87 (s, 1H), 7.82 – 7.71 (m, 1H), 7.20 – 7.07 (m, 1H), 6.51 (d, J = 10.1 Hz, 1H), 5.92 (d, J = 10.1 Hz, 1H), 4.44 (s, 1H), 3.89 (s, 3H), 2.43 (t, J = 6.5 Hz, 2H), 2.35 (d, J = 7.0 Hz, 1H), 2.33 – 2.24 (m, 2H), 2.09 (d, J = 9.6 Hz, 2H), 2.03 (dd, J = 16.4, 7.7 Hz, 3H), 1.86 (dd, J = 11.4, 3.1 Hz, 2H), 1.76 (s, 2H), 1.71 (s, 3H), 1.63 (d, J = 11.1 Hz, 2H), 1.45 (s, 3H), 1.26 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.24, 170.97, 165.78, 154.02, 127.15, 126.80, 126.13, 123.31, 115.03, 114.83, 87.17, 76.47, 54.88, 52.26, 46.96, 46.16, 46.13, 44.66, 43.11, 40.58, 33.02, 31.38, 24.23, 23.01;

HRMS (ESI) *m/z* calcd for $C_{25}H_{28}FNNaO_5$, $[M+Na]^+$ 464.1849; Found: 464.1846.

Methyl 4-chloro-3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoate (3c-1)



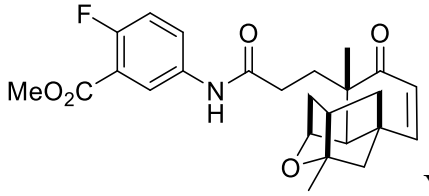
Yield: 34%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.94 (s, 1H), 7.74 (dd, J = 8.4, 2.0 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 10.1 Hz, 1H), 5.95 (d, J = 10.1 Hz, 1H), 4.47 (s, 1H), 3.92 (s, 3H), 2.45 (t, J = 6.4 Hz, 2H), 2.35 (ddd, J = 12.8, 11.9, 6.7 Hz, 4H), 2.19 – 2.01 (m, 5H), 1.91 (ddd, J = 14.5, 8.7, 3.1 Hz, 3H), 1.86 – 1.76 (m, 2H), 1.65 (d, J = 11.2 Hz, 3H), 1.47 (s, 3H), 1.29 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.07, 171.20, 166.21, 154.00, 134.82, 129.95, 129.70, 129.09, 127.15, 125.59, 122.74, 87.06, 76.49, 54.88, 52.34, 46.83, 46.18, 46.12, 44.67, 43.12, 40.58, 33.07, 30.30, 24.25, 23.01;

HRMS (ESI) *m/z* calcd for $C_{25}H_{28}ClNNaO_5$, $[M+Na]^+$ 480.1553; Found: 480.1554.

Methyl 5-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-2-fluoro benzoate (3d-1)



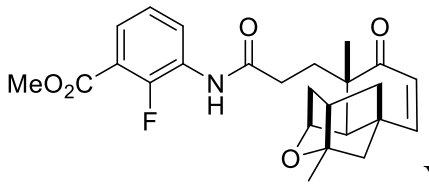
Yield: 34%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 20.0 Hz, 1H), 7.96 (dd, J = 6.1, 2.7 Hz, 1H), 7.93 – 7.83 (m, 1H), 7.10 (t, J = 9.6 Hz, 1H), 6.54 (d, J = 10.1 Hz, 1H), 5.93 (d, J = 10.0 Hz, 1H), 4.46 (s, 1H), 3.93 (s, 3H), 2.45 (t, J = 6.5 Hz, 1H), 2.35 (d, J = 7.6 Hz, 2H), 2.30 (dd, J = 13.9, 2.9 Hz, 1H), 2.22 (dd, J = 17.1, 5.9 Hz, 1H), 2.18 – 2.08 (m, 2H), 2.04 (dd, J = 17.3, 7.3 Hz, 2H), 1.98 – 1.86 (m, 3H), 1.82 (dd, J = 13.4, 6.6 Hz, 2H), 1.65 (d, J = 11.2 Hz, 1H), 1.47 (s, 3H), 1.27 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.65, 171.37, 164.60, 154.45, 134.40, 134.37, 127.14, 126.03, 122.69, 118.58, 118.47, 117.48, 117.25, 87.14, 76.46, 54.88, 52.41, 47.07, 46.13, 46.10, 44.67, 43.07, 40.57, 32.89, 31.53, 24.28, 22.99;

HRMS (ESI) *m/z* calcd for $C_{25}H_{28}FNNaO_5$, $[M+Na]^+$ 464.1849; Found: 464.1848.

Methyl 3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-2-fluoro benzoate (3e-1)



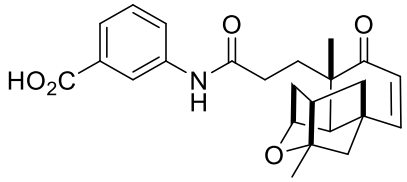
Yield: 43%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.02 (s, 1H), 7.59 (d, J = 6.9 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 6.50 (d, J = 10.1 Hz, 1H), 5.92 (d, J = 10.0 Hz, 1H), 4.43 (s, 1H), 3.92 (s, 3H), 2.41 (dd, J = 12.0, 5.2 Hz, 2H), 2.38 – 2.32 (m, 2H), 2.32 – 2.19 (m, 2H), 2.13 – 1.95 (m, 4H), 1.95 – 1.73 (m, 5H), 1.62 (d, J = 11.2 Hz, 2H), 1.44 (s, 3H), 1.25 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.27, 171.65, 164.77, 154.24, 127.78, 127.16, 125.94, 125.82, 124.02, 123.98, 118.33, 87.17, 76.48, 54.87, 52.41, 46.97, 46.12, 44.66, 43.11, 40.57, 33.08, 31.40, 24.24, 23.00.

HRMS (ESI) *m/z* calcd for $C_{25}H_{28}FNNaO_5$, $[M+Na]^+$ 464.1849; Found: 464.1850.

3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoic acid (3f-1)



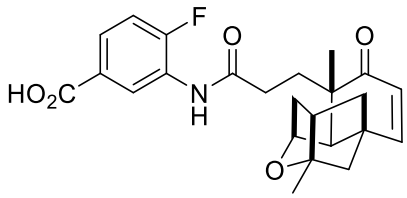
Yield: 73%;

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.53 (d, J = 8.2 Hz, 1H), 7.98 (s, 1H), 7.79 (d, J = 7.7 Hz, 1H), 7.41 (t, J = 7.9 Hz, 2H), 6.55 (d, J = 10.1 Hz, 1H), 5.96 (d, J = 10.0 Hz, 1H), 4.68 (s, 1H), 2.52 – 2.42 (m, 3H), 2.27 (dd, J = 18.5, 5.9 Hz, 1H), 2.20 – 2.12 (m, 1H), 2.12 – 1.97 (m, 3H), 1.94 (dd, J = 11.4, 3.1 Hz, 1H), 1.86 – 1.73 (m, 2H), 1.69 (d, J = 11.4 Hz, 1H), 1.51 (s, 3H), 1.28 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 204.29, 171.78, 169.00, 154.15, 139.27, 130.25, 129.25, 127.32, 125.06, 124.93, 120.55, 87.93, 76.48, 54.82, 46.49, 46.12, 46.00, 44.83, 42.96, 40.33, 32.66, 32.21, 29.69, 24.44, 22.75;

HRMS (ESI) *m/z* calcd for $C_{24}H_{28}NO_5$, $[M+H]^+$ 410.1967; Found: 410.1969.

3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-4-fluorobenzoic acid (3g-1)



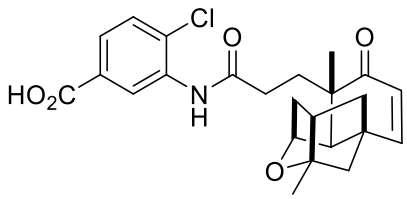
Yield: 78%;

^{1}H NMR (400 MHz, MeOD) δ 8.60 (d, J = 6.3 Hz, 1H), 7.84 (dd, J = 6.7, 5.1 Hz, 1H), 7.24 (dd, J = 10.3, 8.6 Hz, 1H), 6.67 (d, J = 10.1 Hz, 1H), 5.91 (d, J = 10.1 Hz, 1H), 4.51 (s, 1H), 2.53 – 2.38 (m, 4H), 2.36 – 2.25 (m, 2H), 2.18 – 2.03 (m, 4H), 1.87 (ddd, J = 13.2, 6.4, 3.9 Hz, 3H), 1.79 (dd, J = 21.6, 7.3 Hz, 2H), 1.45 (d, J = 2.3 Hz, 3H), 1.28 (s, 3H);

^{13}C NMR (126 MHz, MeOD) δ 204.32, 172.98, 154.67, 127.14, 126.47, 126.15, 115.00, 114.84, 87.35, 76.63, 54.45, 46.45, 45.94, 45.90, 44.70, 42.52, 40.09, 31.21, 31.03, 23.72, 21.79;

HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FNO_5$, $[M+H]^+$ 428.1873; Found: 428.1872.

4-Chloro-3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoic acid (3h-1)

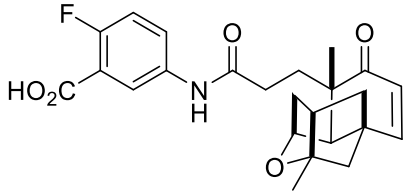


Yield: 46%;

^{1}H NMR (400 MHz, MeOD) δ 8.43 (s, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.54 (d, J = 8.3

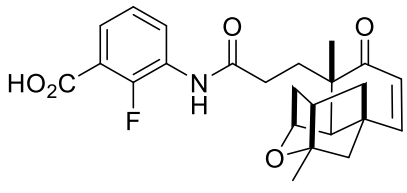
Hz, 1H), 6.68 (d, *J* = 10.2 Hz, 1H), 5.92 (d, *J* = 10.1 Hz, 1H), 4.52 (s, 1H), 2.46 (t, *J* = 5.6 Hz, 3H), 2.41 – 2.26 (m, 3H), 2.10 (dd, *J* = 11.7, 5.9 Hz, 5H), 1.88 (ddd, *J* = 13.1, 9.7, 5.0 Hz, 3H), 1.83 – 1.73 (m, 3H), 1.45 (d, *J* = 4.0 Hz, 3H), 1.29 (s, 3H);
^{13}C NMR (101 MHz, MeOD) *δ* 204.32, 173.01, 154.69, 134.48, 129.12, 127.06, 126.47, 87.38, 76.64, 54.45, 46.48, 45.93, 45.91, 44.70, 42.51, 40.10, 31.09, 23.71, 21.80;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}ClNO_5$, $[M+H]^+$ 444.1578; Found: 444.1575.

5-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-2-fluorobenzoic acid (3i-1)



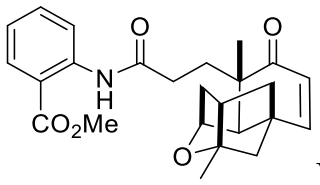
Yield: 80%;
^{1}H NMR (400 MHz, MeOD) *δ* 8.08 (dd, *J* = 6.4, 2.6 Hz, 1H), 7.86 (d, *J* = 4.4 Hz, 1H), 7.72 (dd, *J* = 4.9, 2.7 Hz, 1H), 7.21 (d, *J* = 9.3 Hz, 1H), 7.17 – 7.08 (m, 1H), 6.67 (d, *J* = 10.1 Hz, 1H), 5.91 (d, *J* = 10.1 Hz, 1H), 4.51 (s, 1H), 2.49 – 2.34 (m, 4H), 2.26 (ddd, *J* = 14.3, 11.8, 6.9 Hz, 3H), 2.17 – 2.00 (m, 5H), 1.88 (dd, *J* = 11.1, 6.9 Hz, 3H), 1.77 (dd, *J* = 16.0, 6.9 Hz, 2H), 1.44 (d, *J* = 4.2 Hz, 3H), 1.27 (s, 3H);
^{13}C NMR (101 MHz, MeOD) *δ* 204.26, 172.56, 154.67, 134.51, 129.45, 127.04, 126.48, 123.58, 123.05, 116.48, 116.25, 87.34, 76.61, 54.48, 46.44, 45.95, 45.89, 44.71, 42.52, 40.10, 31.58, 31.15, 23.74, 21.80;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FNO_5$, $[M+H]^+$ 428.1873; Found: 428.1873.

3-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-2-fluorobenzoic acid (3j-1)



Yield: 77%;
^{1}H NMR (400 MHz, MeOD) *δ* 8.06 (t, *J* = 6.8 Hz, 1H), 7.65 (dd, *J* = 10.5, 3.8 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 10.1 Hz, 1H), 5.92 (s, 1H), 4.51 (s, 1H), 2.54 – 2.39 (m, 4H), 2.39 – 2.24 (m, 3H), 2.17 – 1.99 (m, 5H), 1.88 (dd, *J* = 8.9, 3.9 Hz, 3H), 1.77 (dd, *J* = 20.9, 7.2 Hz, 2H), 1.44 (s, 3H), 1.27 (s, 3H);
^{13}C NMR (126 MHz, MeOD) δ 204.35, 173.05, 154.71, 127.88, 127.03, 126.48, 124.30, 123.16, 117.44, 87.35, 76.63, 54.45, 48.48, 48.15, 47.98, 47.81, 47.64, 47.46, 47.29, 47.12, 46.49, 45.93, 45.89, 44.70, 42.52, 40.10, 31.26, 31.05, 23.74, 21.81;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FNO_5$, $[M+H]^+$ 428.1873; Found: 428.1875.

Methyl 2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoate (3a-2)



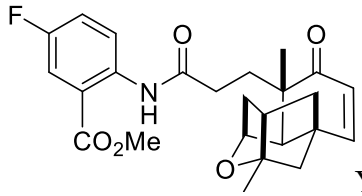
Yield: 63%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.99 (s, 1H), 8.68 (dd, J = 8.5, 0.9 Hz, 1H), 8.00 (dd, J = 8.0, 1.5 Hz, 1H), 7.52 (ddd, J = 8.7, 7.4, 1.6 Hz, 1H), 7.05 (ddd, J = 8.3, 7.4, 1.2 Hz, 1H), 6.47 (d, J = 10.1 Hz, 1H), 5.90 (d, J = 10.1 Hz, 1H), 4.46 (s, 1H), 3.92 (s, 3H), 2.49 – 2.37 (m, 3H), 2.37 – 2.27 (m, 2H), 2.15 – 1.95 (m, 4H), 1.95 – 1.81 (m, 2H), 1.81 – 1.65 (m, 3H), 1.61 (d, J = 11.2 Hz, 2H), 1.44 (s, 3H), 1.26 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.45, 171.51, 168.65, 153.54, 141.59, 134.61, 130.77, 127.31, 122.30, 120.46, 114.90, 86.98, 76.53, 54.91, 52.36, 46.45, 46.10, 46.06, 44.71, 43.19, 40.60, 33.16, 30.98, 24.55, 23.06;

HRMS (ESI) *m/z* calcd for $C_{25}H_{29}NNaO_5$, $[M+Na]^+$ 446.1943; Found: 446.1944.

Methyl 2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-5-fluoro benzoate (3b-2)



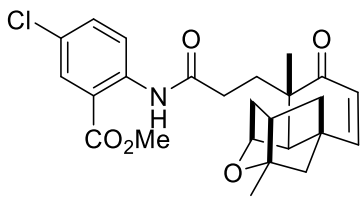
Yield: 52%;

^{1}H NMR(400 MHz,$CDCl_3$): δ 10.84 (s, 1H), 8.69 (dd, J = 9.3, 5.1 Hz, 1H), 7.69 (dd, J = 9.3, 3.1 Hz, 1H), 7.26 – 7.21 (m, 1H), 6.48 (d, J = 10.1 Hz, 1H), 5.91 (d, J = 10.1 Hz, 1H), 4.46 (s, 1H), 3.94 (s, 3H), 2.51 – 2.37 (m, 3H), 2.37 – 2.26 (m, 2H), 2.15 – 2.06 (m, 2H), 2.02 (d, J = 11.4 Hz, 2H), 1.92 – 1.82 (m, 2H), 1.77 (dd, J = 11.9, 6.8 Hz, 1H), 1.62 (d, J = 11.2 Hz, 5H), 1.45 (s, 3H), 1.27 (s, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 203.52, 171.37, 167.57, 153.62, 127.40, 122.45, 122.32, 121.76, 121.55, 116.90, 116.70, 87.04, 76.57, 54.96, 52.70, 46.53, 46.11, 44.77, 43.19, 40.58, 33.06, 30.96, 24.54, 23.04;

HRMS (ESI) *m/z* calcd for $C_{25}H_{28}FNNaO_5$, $[M+Na]^+$ 464.1849; Found: 464.1853.

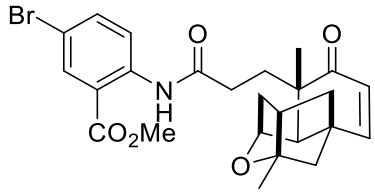
Methyl 5-chloro-2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoate (3c-2)



Yield: 27%;

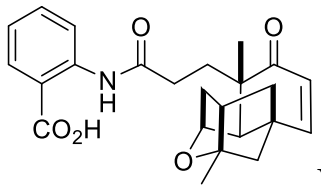
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.94 (s, 1H), 8.70 (d, J = 9.1 Hz, 1H), 8.00 (d, J = 2.6 Hz, 1H), 7.49 (dd, J = 9.1, 2.6 Hz, 1H), 6.50 (d, J = 10.1 Hz, 1H), 5.93 (d, J = 10.1 Hz, 1H), 4.48 (s, 1H), 3.96 (s, 3H), 2.44 (dd, J = 12.5, 5.0 Hz, 4H), 2.39 – 2.30 (m, 4H), 2.07 (d, J = 14.4 Hz, 5H), 1.92 (s, 4H), 1.64 (d, J = 11.2 Hz, 4H), 1.47 (s, 3H), 1.31 (s, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 203.45, 171.63, 167.61, 153.60, 140.14, 134.41, 130.33, 127.26, 121.89, 116.13, 87.03, 76.50, 54.88, 52.66, 46.43, 46.04, 44.68, 43.16, 40.58, 31.94, 30.89, 24.50, 23.02;
HRMS (ESI) *m/z* calcd for $C_{25}H_{28}ClNNaO_5$, $[M+Na]^+$ 480.1553; Found: 480.1552.

Methyl 5-bromo-2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoate (3d-2)



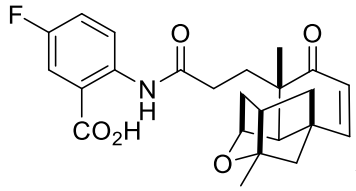
Yield: 10%;
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.94 (s, 1H), 8.64 (d, J = 9.1 Hz, 1H), 8.15 (d, J = 2.4 Hz, 1H), 7.70 – 7.58 (m, 1H), 6.50 (d, J = 10.1 Hz, 1H), 5.93 (d, J = 10.1 Hz, 1H), 4.48 (s, 1H), 3.96 (s, 3H), 2.52 – 2.39 (m, 4H), 2.39 – 2.28 (m, 3H), 2.10 – 2.00 (m, 5H), 1.90 (dd, J = 11.2, 3.2 Hz, 3H), 1.64 (d, J = 11.2 Hz, 4H), 1.47 (s, 3H), 1.30 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 203.42, 171.54, 167.48, 153.57, 140.58, 137.29, 133.28, 127.26, 122.16, 116.46, 114.63, 87.00, 76.50, 54.90, 52.65, 46.43, 46.10, 46.05, 44.69, 43.17, 40.58, 31.93, 30.89, 24.49, 23.03;
HRMS (ESI) *m/z* calcd for $C_{25}H_{28}BrNNaO_5$, $[M+Na]^+$ 524.1048; Found: 524.1051.

2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoic acid (3h-2)



Yield: 51%;
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.09 (d, J = 10.8 Hz, 1H), 8.63 (d, J = 8.5 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.53 (d, J = 10.1 Hz, 1H), 5.96 (d, J = 10.1 Hz, 1H), 4.57 (s, 1H), 2.47 (dd, J = 20.1, 13.8 Hz, 3H), 2.41 – 2.24 (m, 3H), 2.18 – 2.01 (m, 4H), 1.97 (dd, J = 16.2, 13.1 Hz, 2H), 1.80 (dd, J = 11.7, 7.0 Hz, 1H), 1.65 (d, J = 11.3 Hz, 2H), 1.48 (s, 3H), 1.28 (s, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 203.72, 171.48, 170.92, 153.95, 141.75, 134.76, 131.53, 127.31, 122.29, 120.26, 87.46, 77.23, 54.67, 46.57, 46.02, 45.70, 44.75, 43.11, 40.47, 33.16, 31.08, 24.58, 22.92;
HRMS (ESI) *m/z* calcd for $C_{24}H_{28}NO_5$, $[M+H]^+$ 410.1967; Found: 410.1969.

2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-5-fluorobenzoic acid (3i-2)



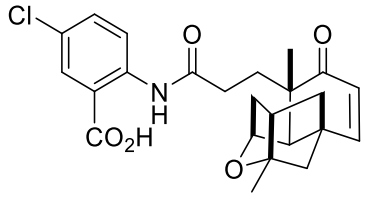
Yield: 61%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.92 (s, 1H), 8.58 (dd, J = 9.3, 5.1 Hz, 1H), 7.66 (dd, J = 9.2, 3.1 Hz, 1H), 7.16 (ddd, J = 9.4, 7.7, 3.1 Hz, 1H), 6.53 (d, J = 10.1 Hz, 1H), 5.94 (d, J = 10.1 Hz, 1H), 4.58 (s, 2H), 3.84 – 3.62 (m, 1H), 2.52 (s, 1H), 2.48 – 2.38 (m, 2H), 2.30 (ddd, J = 13.9, 10.7, 8.1 Hz, 2H), 2.09 (dd, J = 12.0, 2.6 Hz, 2H), 2.04 (s, 1H), 2.03 – 1.95 (m, 2H), 1.91 (s, 1H), 1.79 (dd, J = 11.9, 6.8 Hz, 1H), 1.64 (d, J = 11.3 Hz, 1H), 1.46 (s, 3H), 1.26 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 203.96, 171.63, 169.17, 153.95, 138.07, 127.32, 122.11, 121.64, 121.46, 117.45, 117.26, 87.73, 54.70, 46.60, 46.06, 45.62, 44.78, 43.11, 40.44, 32.98, 30.93, 24.57, 22.85;

HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FNO_5$, $[M+H]^+$ 428.1873; Found: 428.1872.

5-chloro-2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoic acid (3j-2)



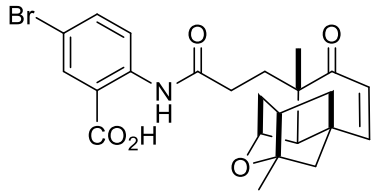
Yield: 45%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.34 – 8.24 (m, 2H), 8.19 (d, J = 8.4 Hz, 2H), 7.75 – 7.64 (m, 2H), 7.09 – 6.97 (m, 2H), 6.50 (d, J = 10.1 Hz, 1H), 5.92 (d, J = 10.1 Hz, 1H), 4.46 (s, 1H), 2.42 (s, 2H), 2.37 (d, J = 2.8 Hz, 4H), 2.23 (s, 3H), 2.16 – 1.97 (m, 7H), 1.97 – 1.83 (m, 3H), 1.83 – 1.71 (m, 2H), 1.64 (s, 2H), 1.45 (s, 4H), 1.26 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.91, 171.50, 153.91, 151.55, 147.80, 138.28, 127.19, 119.53, 113.97, 87.00, 76.46, 54.87, 46.77, 46.12, 46.06, 44.67, 43.13, 40.56, 32.92, 31.29, 24.30, 23.02;

HRMS (ESI) *m/z* calcd for $C_{24}H_{27}ClNO_5$, $[M+H]^+$ 444.1578; Found: 444.1581.

5-Bromo-2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzoic acid (3k-2)



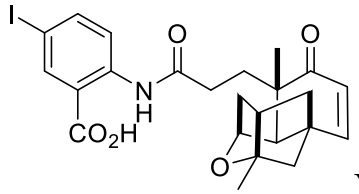
Yield: 40%;

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.04 (d, J = 21.1 Hz, 1H), 8.54 (dd, J = 9.0, 5.4 Hz, 1H), 7.65 (t, J = 2.7 Hz, 1H), 7.56 (dd, J = 9.0, 2.1 Hz, 1H), 6.48 (d, J = 10.1 Hz, 1H), 6.21 (s, 2H), 5.91 (d, J = 10.1 Hz, 1H), 4.41 (d, J = 36.6 Hz, 1H), 2.46 – 2.37 (m, 2H), 2.37 – 2.17 (m, 3H), 2.15 – 2.04 (m, 2H), 2.04 – 1.96 (m, 3H), 1.86 (ddd, J = 10.7, 8.0, 3.3 Hz, 2H), 1.77 (dd, J = 11.9, 6.9 Hz, 1H), 1.64 (ddd, J = 17.2, 11.3, 4.9 Hz, 4H), 1.45 (s, 3H), 1.25 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 203.42, 171.48, 170.07, 153.60, 139.21, 135.88, 129.97, 127.31, 123.30, 120.53, 114.77, 87.08, 76.51, 54.93, 46.47, 46.13, 46.05, 44.72, 43.21, 40.62, 33.26, 31.16, 24.48, 23.07;

HRMS (ESI) *m/z* calcd for $C_{24}H_{27}BrNO_5$, $[M+H]^+$ 488.1072; Found: 488.1080.

2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-5-iodobenzoic acid (3l-2)



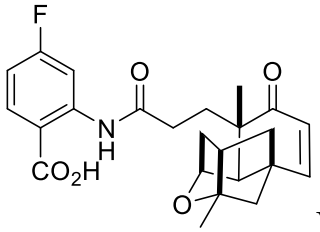
Yield: 10%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.99 (s, 1H), 8.36 (d, J = 9.0 Hz, 1H), 8.29 (d, J = 2.2 Hz, 1H), 7.75 – 7.65 (m, 1H), 6.56 (d, J = 10.1 Hz, 1H), 5.99 (d, J = 10.1 Hz, 1H), 4.65 (s, 1H), 2.58 (s, 1H), 2.48 (t, J = 6.4 Hz, 1H), 2.39 (dd, J = 14.4, 8.9 Hz, 2H), 2.30 (ddd, J = 16.8, 12.4, 6.0 Hz, 2H), 2.12 (dd, J = 15.3, 4.9 Hz, 2H), 2.06 (dd, J = 13.0, 3.3 Hz, 3H), 1.98 (dd, J = 9.8, 4.9 Hz, 1H), 1.82 (dd, J = 11.5, 6.6 Hz, 1H), 1.68 (s, 2H), 1.50 (s, 3H), 1.28 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.17, 171.64, 169.16, 154.05, 143.07, 141.35, 139.81, 127.41, 121.98, 116.32, 100.09, 87.92, 76.84, 54.63, 46.67, 46.05, 45.41, 44.79, 43.13, 40.42, 32.90, 30.44, 24.62, 22.87;

HRMS (ESI) *m/z* calcd for $C_{24}H_{27}INO_5$, $[M+H]^+$ 536.0934; Found: 536.0941.

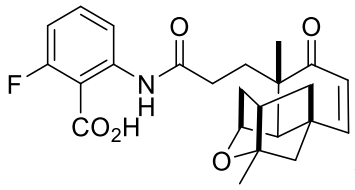
2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-5-iodobenzoic acid (3m-2)



Yield: 28%;

^{1}H NMR (400 MHz, Acetone) δ 11.39 (s, 1H), 8.56 (dd, J = 12.5, 2.7 Hz, 1H), 8.17 (dd, J = 8.9, 6.7 Hz, 1H), 6.99 – 6.82 (m, 1H), 6.61 (d, J = 10.1 Hz, 1H), 5.83 (d, J = 10.1 Hz, 1H), 4.45 (s, 1H), 2.77 (s, 1H), 2.48 (ddd, J = 14.1, 11.9, 5.0 Hz, 1H), 2.43 – 2.36 (m, 2H), 2.36 – 2.20 (m, 2H), 2.07 – 2.04 (m, 3H), 1.91 – 1.81 (m, 2H), 1.78 (dd, J = 10.9, 3.5 Hz, 1H), 1.71 (d, J = 10.9 Hz, 1H), 1.38 (s, 3H), 1.25 (s, 3H);
^{13}C NMR (101 MHz, Acetone) δ 202.50, 171.54, 168.77, 153.74, 144.43, 144.29, 133.99, 133.88, 126.68, 111.33, 109.19, 108.96, 106.55, 106.27, 86.55, 76.11, 54.57, 46.19, 46.09, 45.95, 44.74, 42.69, 40.38, 33.15, 30.87, 23.98, 22.48;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FNO_5$, $[M+H]^+$ 428.1873; Found: 428.1872.

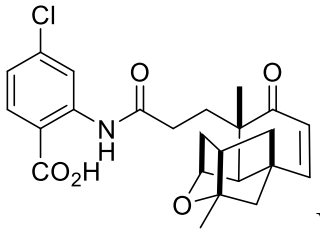
2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-5-iodobenzoic acid (3o-2)



Yield: 43%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.99 (s, 1H), 8.56 (d, J = 9.1 Hz, 1H), 7.96 (d, J = 2.6 Hz, 1H), 7.39 (dd, J = 9.1, 2.6 Hz, 1H), 6.56 (d, J = 10.1 Hz, 1H), 5.98 (d, J = 10.1 Hz, 1H), 4.63 (s, 1H), 2.57 (s, 1H), 2.47 (dd, J = 13.3, 6.8 Hz, 2H), 2.39 – 2.23 (m, 2H), 2.21 – 2.00 (m, 4H), 1.94 (ddd, J = 29.9, 15.1, 10.8 Hz, 1H), 1.82 (dd, J = 11.7, 6.8 Hz, 1H), 1.67 (d, J = 11.1 Hz, 1H), 1.50 (s, 3H), 1.29 (s, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 204.02, 171.67, 169.15, 154.00, 140.28, 134.35, 130.95, 127.37, 127.30, 121.59, 115.87, 87.87, 76.82, 54.65, 46.64, 46.06, 45.46, 44.78, 43.12, 40.43, 32.90, 30.60, 24.62, 22.86;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FNO_5$, $[M+H]^+$ 428.1873; Found: 428.1876.

2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-5-iodobenzoic acid (3p-2)

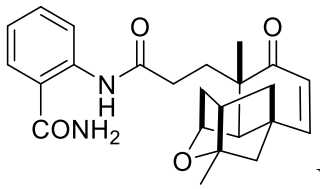


Yield: 51%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 8.47 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 7.2

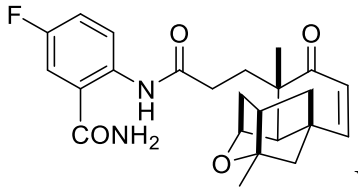
Hz, 1H), 6.93 – 6.72 (m, 2H), 6.47 (d, *J* = 10.0 Hz, 1H), 6.36 (s, 1H), 5.89 (d, *J* = 10.0 Hz, 1H), 4.44 (s, 1H), 2.42 (dd, *J* = 22.9, 8.8 Hz, 3H), 2.35 – 2.25 (m, 2H), 2.22 (dd, *J* = 14.3, 5.2 Hz, 1H), 2.01 (s, 2H), 1.99 (s, 1H), 1.93 – 1.80 (m, 2H), 1.80 – 1.72 (m, 1H), 1.60 (d, *J* = 11.1 Hz, 2H), 1.43 (s, 3H), 1.26 (s, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) *δ* 203.41, 171.63, 167.80, 153.59, 142.12, 133.68, 127.27, 117.38, 110.07, 109.84, 87.03, 76.48, 54.86, 46.44, 46.00, 45.98, 44.66, 43.15, 40.58, 33.29, 31.02, 24.53, 23.03;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}ClNO_5$, $[M+H]^+$ 444.1578; Found: 444.1576.

2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzamide (3q-2)



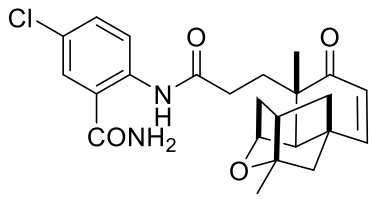
Yield: 68%;
^{1}H NMR (400 MHz, MeOD) *δ* 8.64 (dd, *J* = 8.4, 0.7 Hz, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 7.84 (dd, *J* = 3.3, 1.4 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.23 – 7.18 (m, 1H), 6.62 (d, *J* = 10.1 Hz, 1H), 5.87 (d, *J* = 10.1 Hz, 1H), 4.47 (s, 1H), 2.46 – 2.38 (m, 3H), 2.33 (dd, *J* = 12.2, 5.7 Hz, 1H), 2.30 – 2.19 (m, 2H), 2.11 – 2.01 (m, 4H), 1.89 – 1.76 (m, 3H), 1.70 (d, *J* = 11.2 Hz, 1H), 1.42 (s, 3H), 1.21 (s, 3H).
^{13}C NMR (101 MHz, MeOD) *δ* 204.25, 172.49, 167.23, 154.72, 139.18, 138.11, 132.36, 132.00, 126.37, 121.16, 120.36, 87.34, 76.54, 54.36, 46.99, 46.34, 45.87, 45.84, 44.67, 42.45, 40.08, 32.55, 31.19, 23.74, 21.78;
HRMS (ESI) *m/z* calcd for $C_{24}H_{28}N_2NaO_4$, $[M+Na]^+$ 431.1946; Found: 431.1946.

2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-5-fluorobenzamide (3r-2)



Yield: 52%;
^{1}H NMR (400 MHz, $CDCl_3$) *δ* 11.13 (s, 1H), 8.57 (dd, *J* = 8.9, 5.1 Hz, 1H), 7.55 (t, *J* = 4.9 Hz, 1H), 7.42 (dd, *J* = 6.2, 2.6 Hz, 1H), 6.79 (d, *J* = 59.0 Hz, 2H), 6.50 (dd, *J* = 9.9, 4.1 Hz, 1H), 5.92 (dd, *J* = 10.0, 4.6 Hz, 1H), 4.46 (s, 1H), 2.41 (d, *J* = 12.6 Hz, 3H), 2.35 – 2.17 (m, 2H), 2.17 – 1.96 (m, 4H), 1.88 (s, 4H), 1.64 (d, *J* = 10.9 Hz, 2H), 1.47 (d, *J* = 4.1 Hz, 3H), 1.26 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 203.55, 171.50, 170.52, 153.75, 138.66, 132.81, 127.41, 127.25, 122.89, 120.30, 87.16, 76.47, 54.89, 46.46, 46.09, 46.03, 44.69, 43.16, 40.61, 33.38, 31.36, 24.44, 23.06;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FN_2NaO_4$, $[M+Na]^+$ 449.1852; Found: 449.1851.

5-Chloro-2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzamide (3s-2)



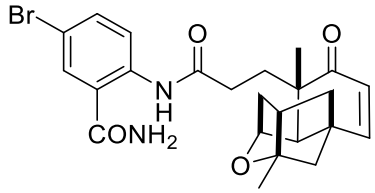
Yield: 46%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.96 (s, 1H), 8.55 (dd, *J* = 9.1, 5.2 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.23 – 7.13 (m, 1H), 6.81 – 6.53 (m, 2H), 6.49 (d, *J* = 10.1 Hz, 1H), 5.91 (d, *J* = 10.1 Hz, 1H), 4.46 (s, 1H), 2.48 – 2.31 (m, 5H), 2.25 (s, 2H), 2.15 – 1.95 (m, 5H), 1.85 (ddd, *J* = 25.0, 16.0, 5.0 Hz, 5H), 1.62 (d, *J* = 11.0 Hz, 2H), 1.45 (s, 3H), 1.25 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 203.56, 171.41, 170.51, 153.73, 136.23, 127.27, 123.55, 119.89, 119.72, 114.00, 113.81, 87.15, 76.51, 54.92, 46.50, 46.13, 46.05, 44.72, 43.18, 40.61, 33.26, 31.38, 24.45, 23.05;

HRMS (ESI) *m/z* calcd for $C_{24}H_{27}ClN_2NaO_4$, $[M+Na]^+$ 465.1556; Found: 465.1556.

5-Bromo-2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)benzamide (3t-2)



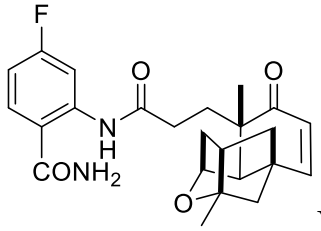
Yield: 18%;

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.95 (s, 1H), 8.49 (d, *J* = 9.1 Hz, 1H), 8.09 (d, *J* = 2.4 Hz, 1H), 7.50 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.54 (d, *J* = 10.1 Hz, 1H), 5.96 (d, *J* = 10.1 Hz, 1H), 4.61 (s, 1H), 2.46 (t, *J* = 6.1 Hz, 1H), 2.40 (dd, *J* = 11.4, 4.7 Hz, 1H), 2.30 (ddd, *J* = 20.2, 11.7, 4.3 Hz, 3H), 2.16 – 2.09 (m, 1H), 2.06 – 1.97 (m, 3H), 1.97 – 1.87 (m, 1H), 1.80 (dd, *J* = 11.4, 6.3 Hz, 1H), 1.66 (s, 1H), 1.47 (s, 3H), 1.26 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 203.96, 171.65, 169.00, 153.90, 140.82, 137.28, 133.91, 127.43, 121.85, 116.17, 114.59, 87.88, 76.85, 54.67, 46.66, 46.08, 45.50, 44.83, 43.15, 40.43, 32.82, 30.49, 24.63, 22.88;

HRMS (ESI) *m/z* calcd for C24H28BrN2O4, $[M+H]^+$ 487.1232; Found: 487.1237.

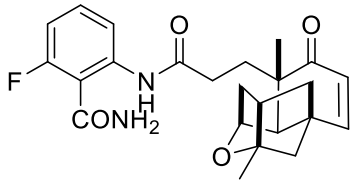
2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-4-fluorobenzamide (3u-2)



Yield: 16%;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.52 (s, 1H), 8.45 (dd, *J* = 11.8, 2.6 Hz, 1H), 7.58 (dd, *J* = 8.8, 6.0 Hz, 1H), 6.84 – 6.69 (m, 1H), 6.61 (d, *J* = 27.9 Hz, 2H), 6.50 (d, *J* = 10.1 Hz, 1H), 5.91 (d, *J* = 10.1 Hz, 1H), 4.47 (s, 1H), 2.50 – 2.36 (m, 4H), 2.30 (ddd, *J* = 17.3, 14.7, 8.9 Hz, 3H), 2.07 (s, 3H), 2.03 (dd, *J* = 7.7, 3.5 Hz, 3H), 1.94 – 1.83 (m, 2H), 1.83 – 1.73 (m, 2H), 1.65 (s, 2H), 1.46 (s, 3H), 1.26 (s, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 203.42, 171.49, 170.89, 153.65, 142.50, 129.45, 127.23, 114.27, 109.84, 108.33, 107.95, 87.11, 76.48, 54.87, 46.44, 46.07, 46.03, 44.68, 43.15, 40.59, 33.40, 31.20, 24.45, 23.06;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FN_2NaO4$, $[M+Na]^+$ 449.1852; Found: 449.1853.

2-(3-((4S,4aR,5S,7R,8S,9aS)-4,8-dimethyl-3-oxo-3,4,4a,5,6,7,8,9-octahydro-5,8-epoxy-7,9a-methanobenzo[7]annulen-4-yl)propanamido)-6-fluorobenzamide (3w-2)



Yield: 42%;
^{1}H NMR (400 MHz, MeOD) δ 8.01 (d, *J* = 8.3 Hz, 1H), 7.46 (td, *J* = 8.4, 6.4 Hz, 1H), 6.98 (dd, *J* = 10.5, 8.5 Hz, 1H), 6.67 (d, *J* = 10.1 Hz, 1H), 5.90 (d, *J* = 10.1 Hz, 1H), 4.49 (s, 1H), 2.49 – 2.34 (m, 4H), 2.34 – 2.25 (m, 2H), 2.25 – 2.17 (m, 1H), 2.15 – 2.01 (m, 4H), 1.93 – 1.78 (m, 4H), 1.75 (d, *J* = 11.2 Hz, 1H), 1.44 (s, 3H), 1.27 (s, 3H);
^{13}C NMR (101 MHz, MeOD) δ 204.38, 172.51, 167.19, 161.31, 158.85, 154.88, 138.80, 132.00, 131.91, 126.40, 118.22, 111.14, 110.90, 87.42, 76.60, 54.39, 47.04, 46.44, 45.89, 44.67, 42.48, 40.11, 32.42, 31.02, 23.71, 21.81;
HRMS (ESI) *m/z* calcd for $C_{24}H_{27}FN_2NaO4$, $[M+Na]^+$ 449.1852; Found: 449.1854.

Figure S3. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **1a** in $CDCl_3$.

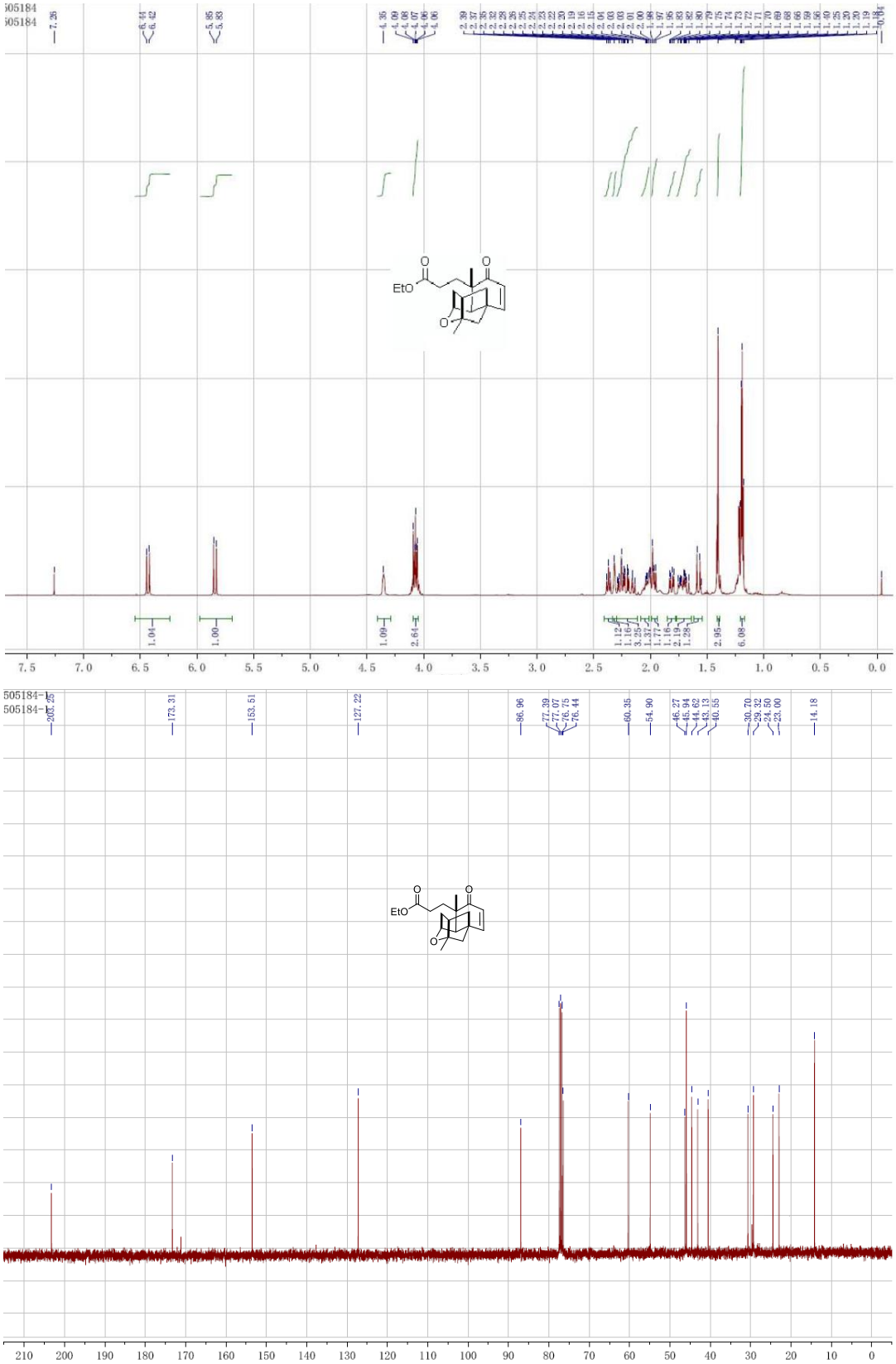


Figure S4. ^{1}H NMR (500 MHz) and ^{13}C NMR (101 MHz) spectrum of **1b** in $CDCl_3$.

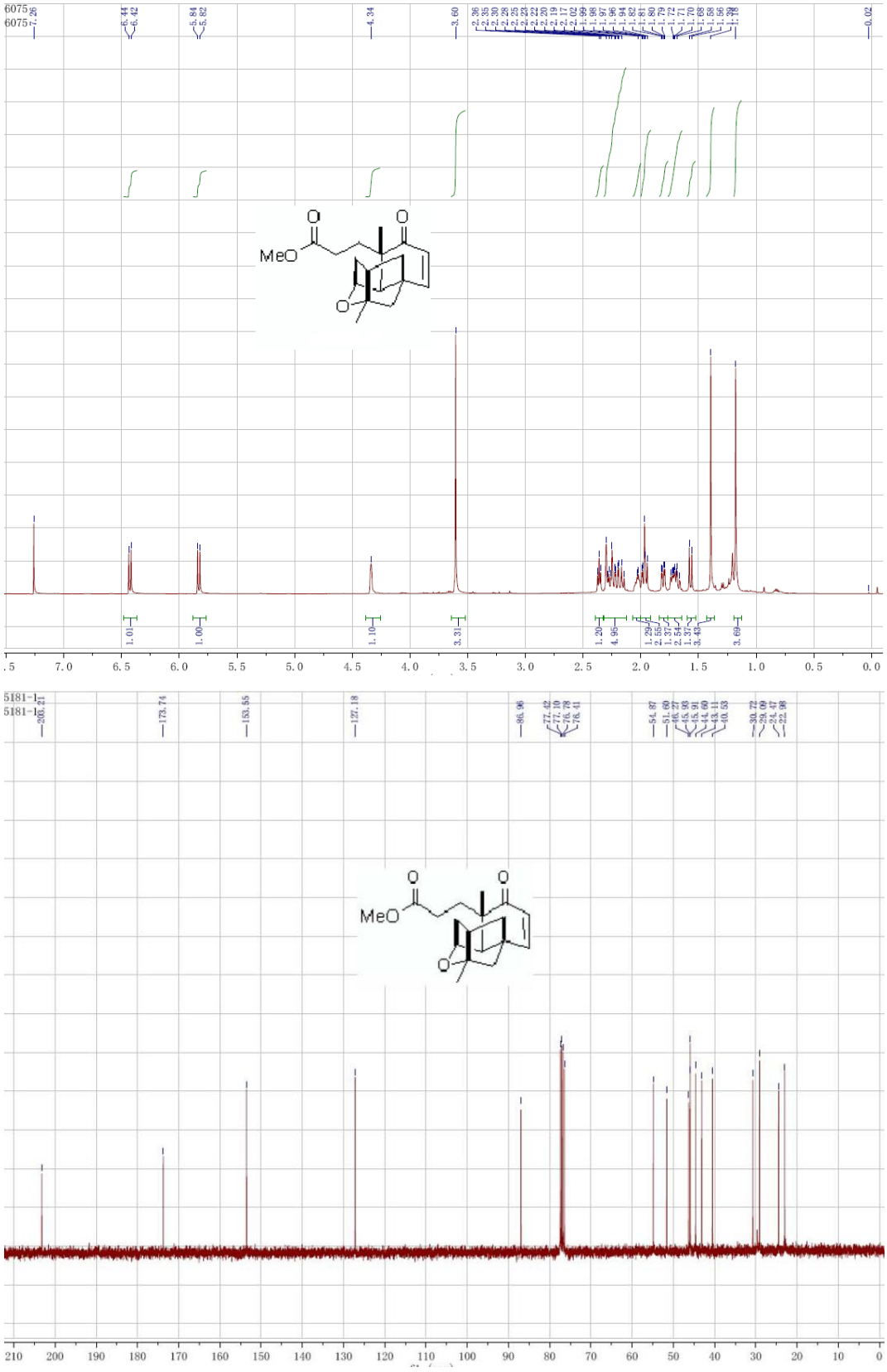


Figure S5. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **1c** in $CDCl_3$.

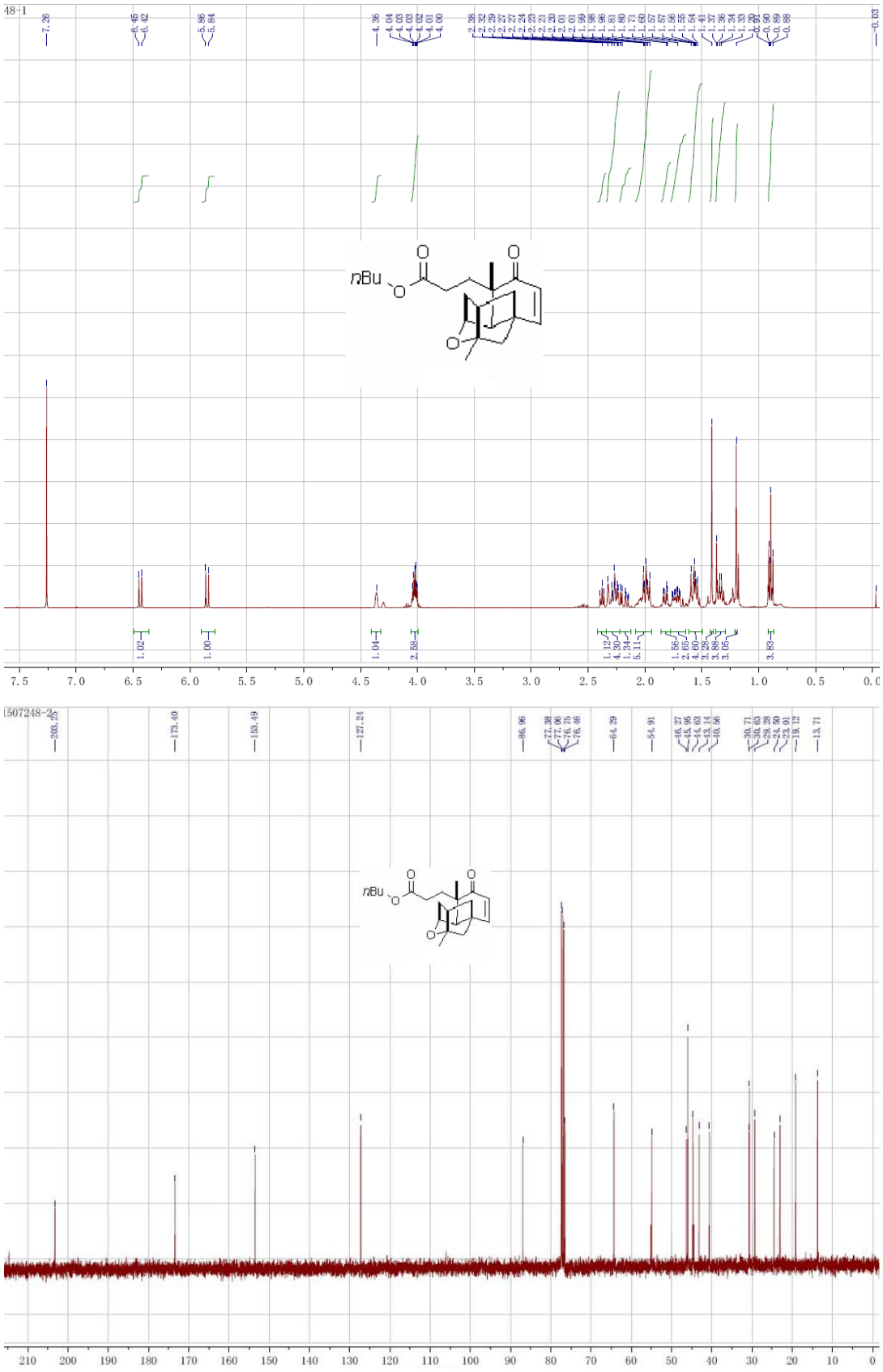


Figure S6. ^{1}H NMR (500 MHz) and ^{13}C NMR (101 MHz) spectrum of **1d** in $CDCl_3$.

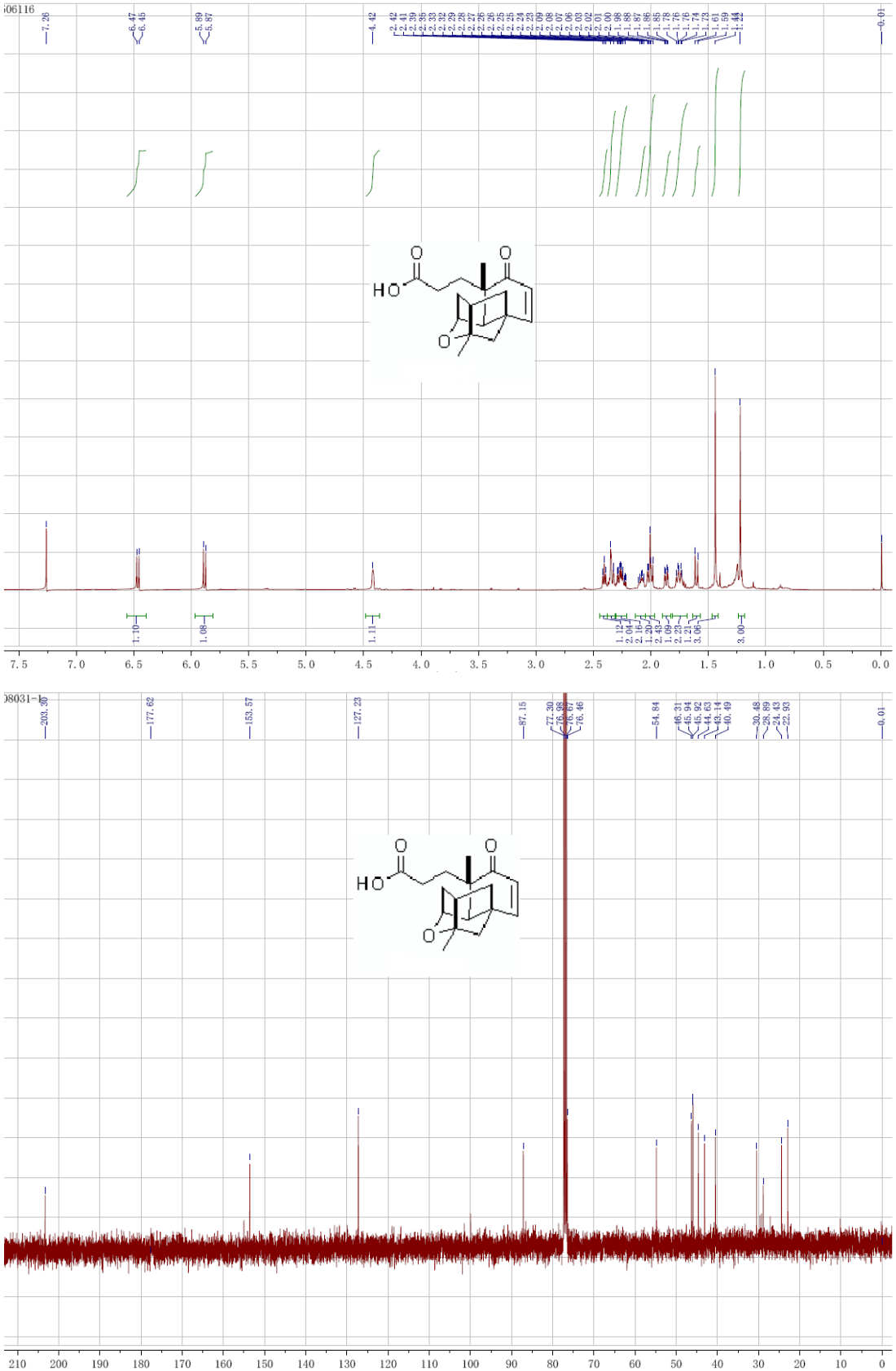


Figure S7. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3a-1** in $CDCl_3$.

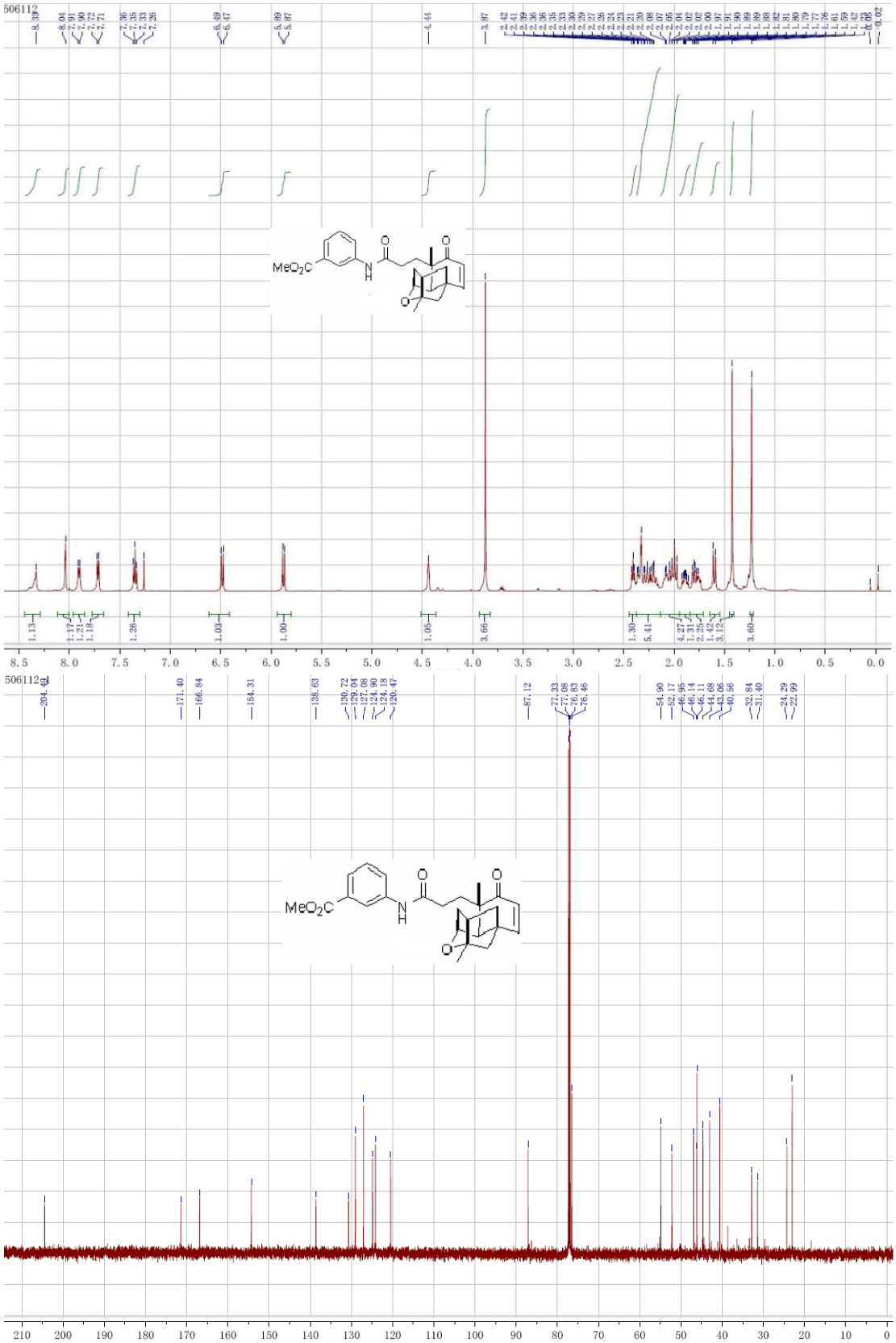


Figure S8. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3b-1** in $CDCl_3$.

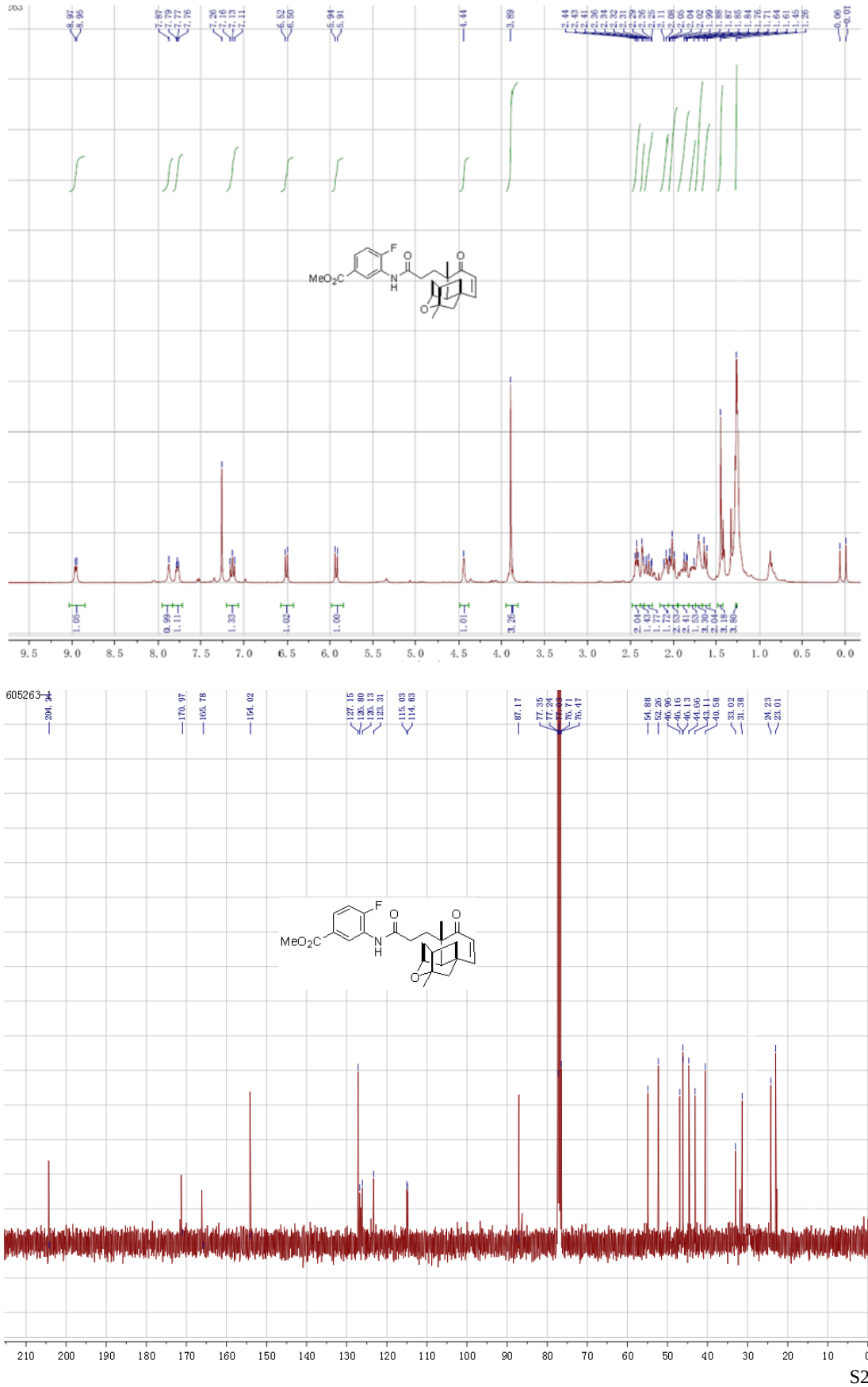
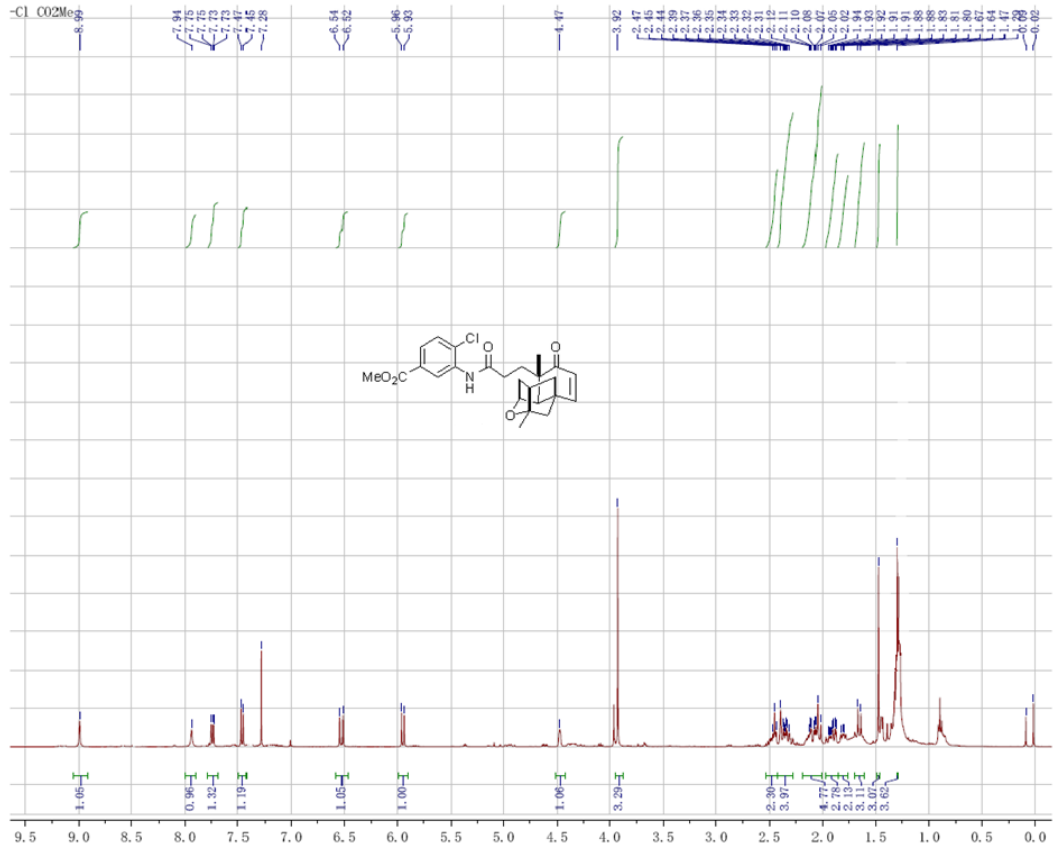


Figure S9. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3c-1** in $CDCl_3$.



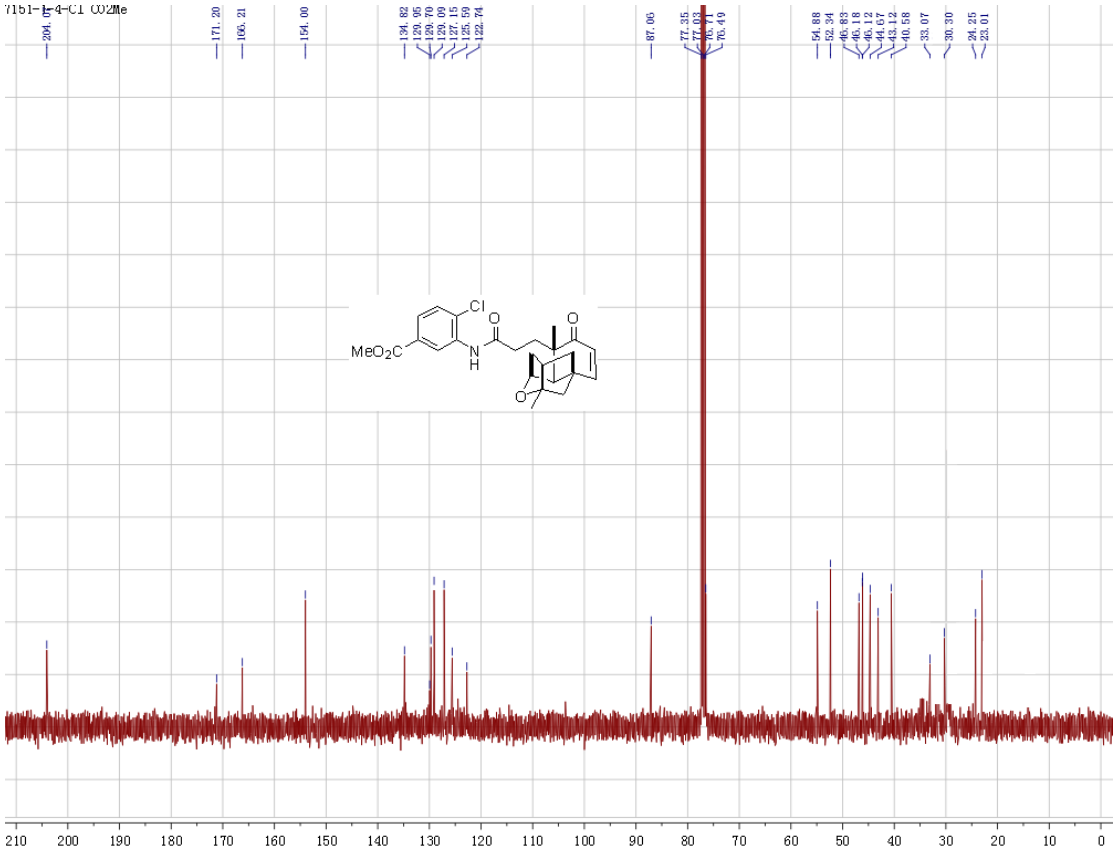


Figure S10. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3d-1** in $CDCl_3$.

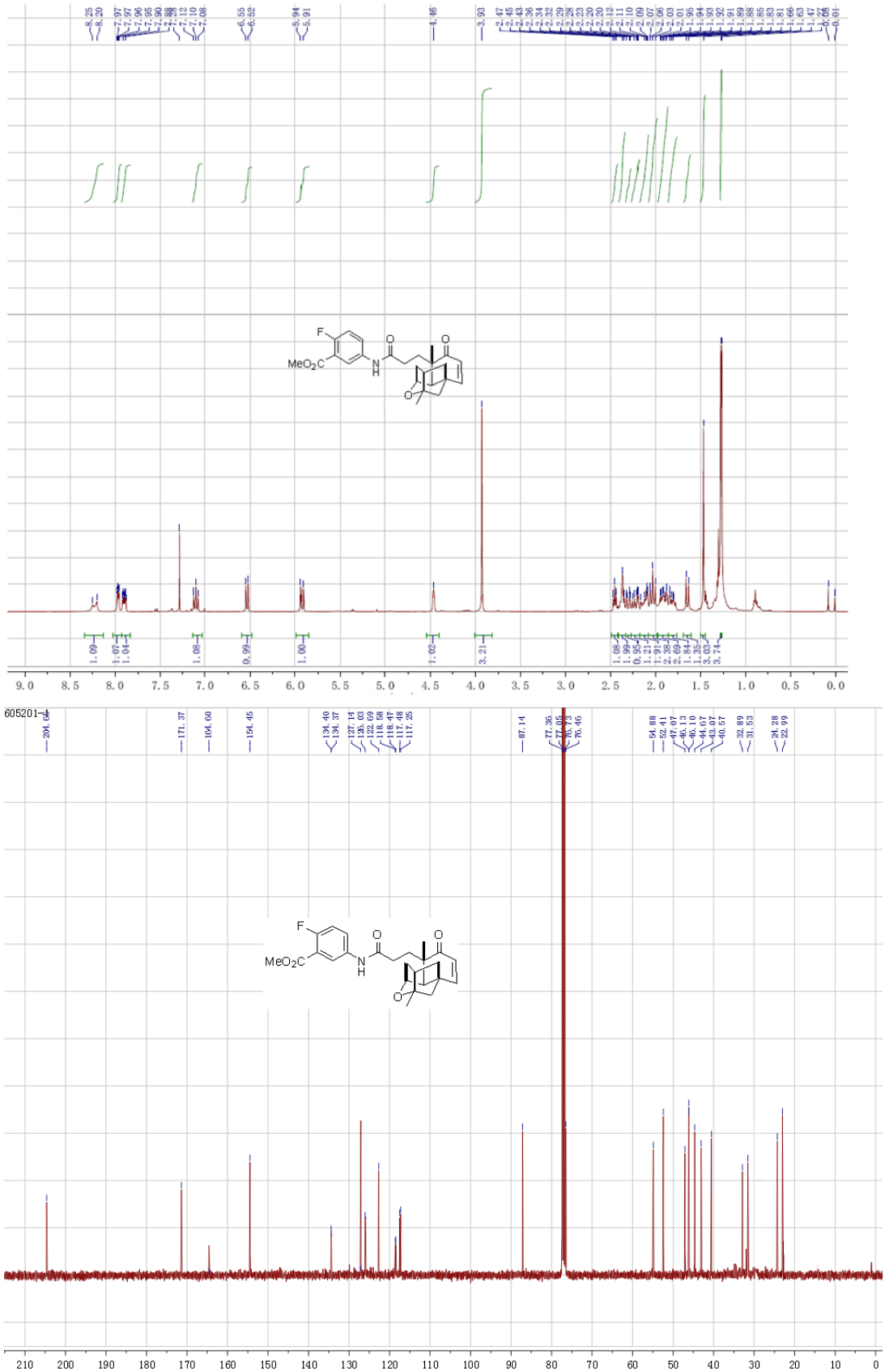


Figure S11. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3e-1** in $CDCl_3$.

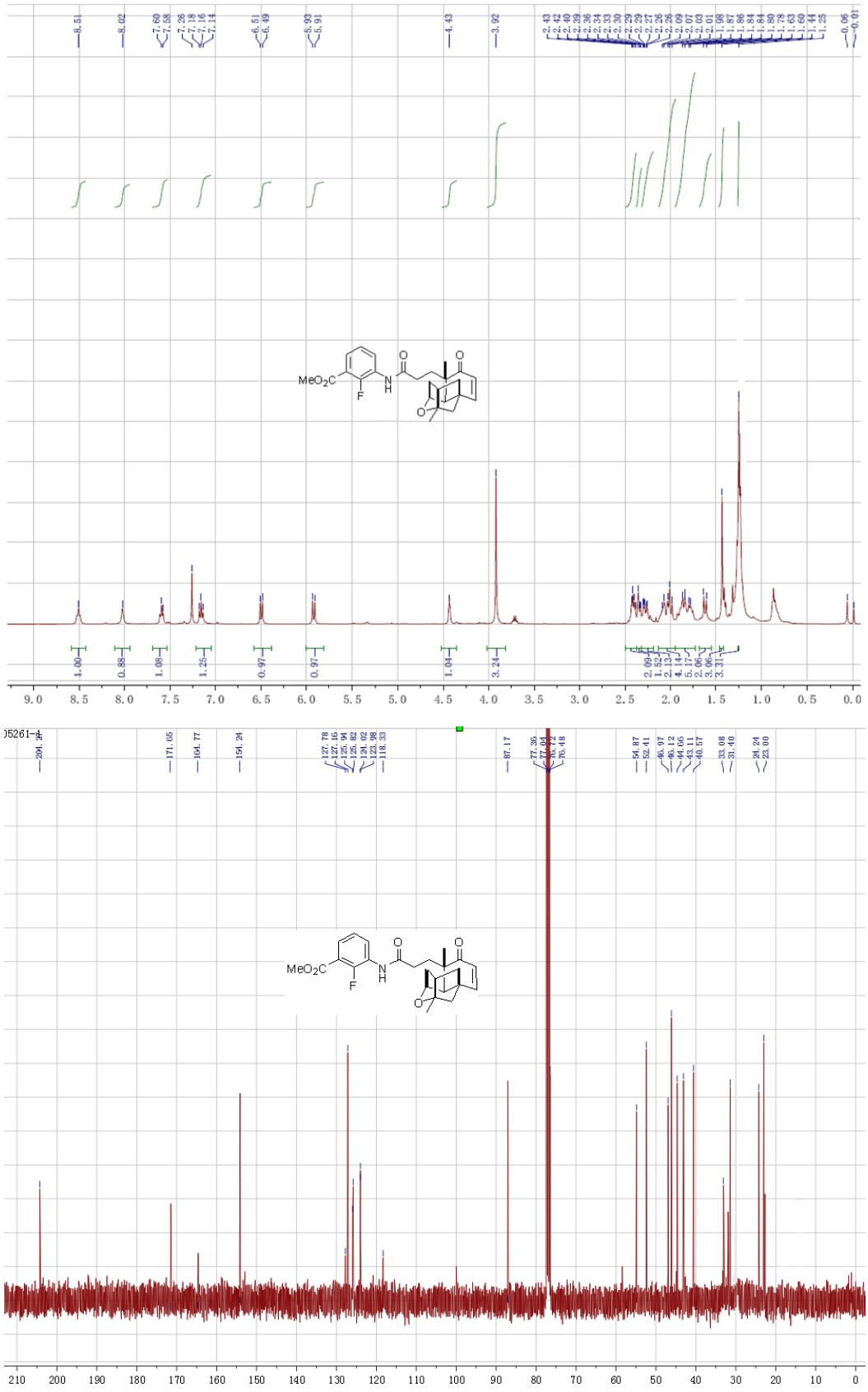


Figure S12. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3f-1** in $CDCl_3$.

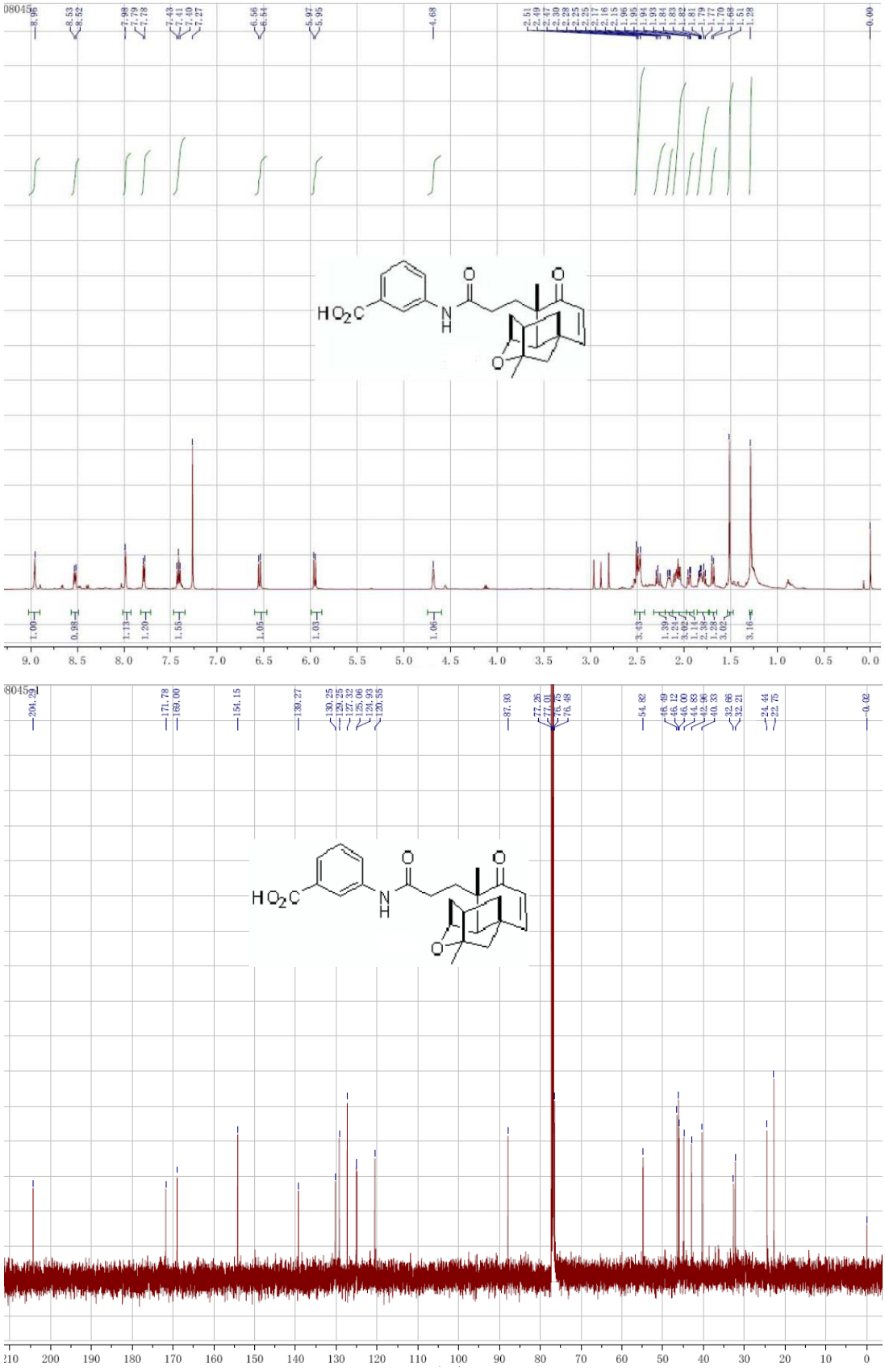


Figure S13. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3g-1** in MeOD.

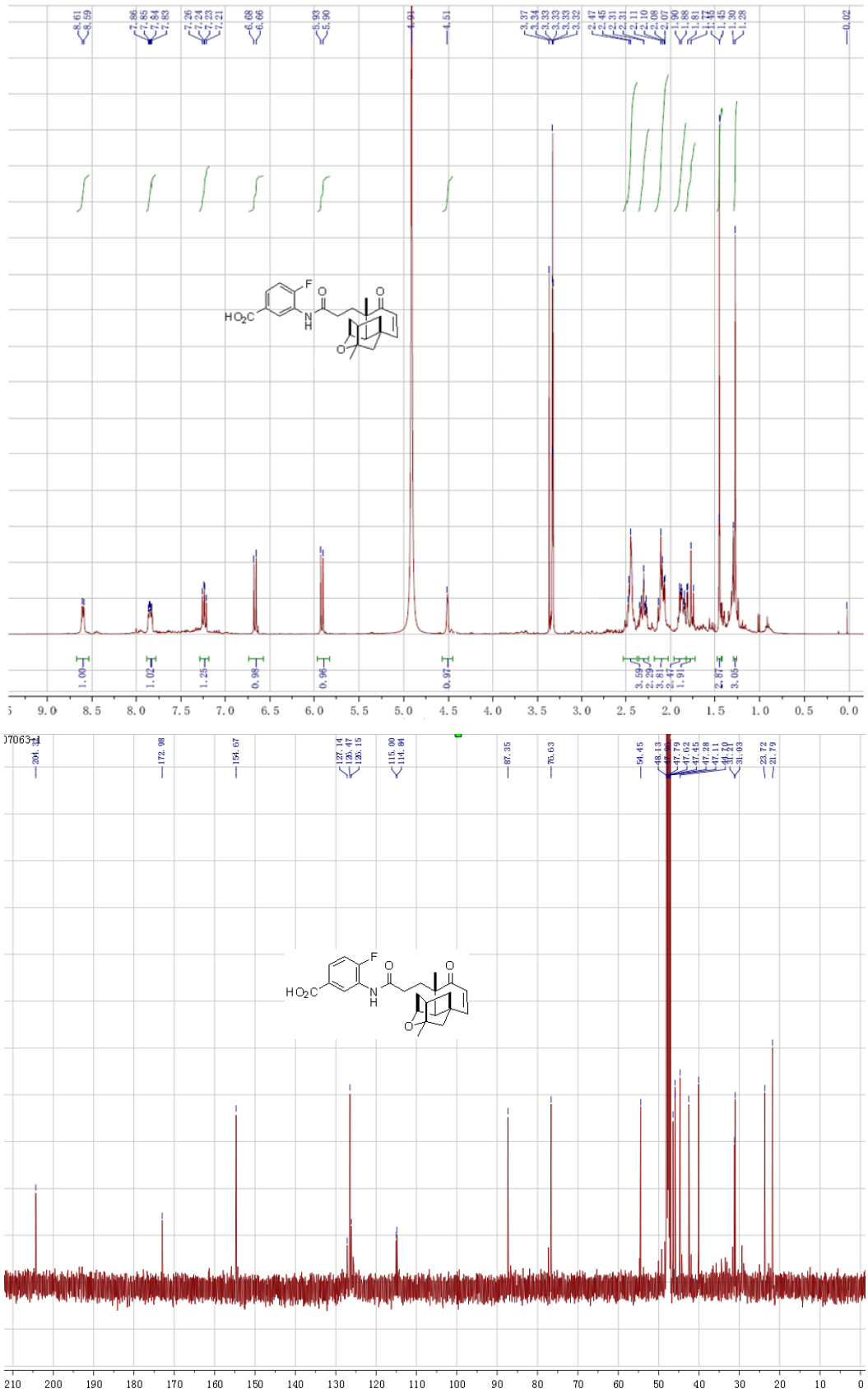


Figure S14. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3h**-1 in MeOD.

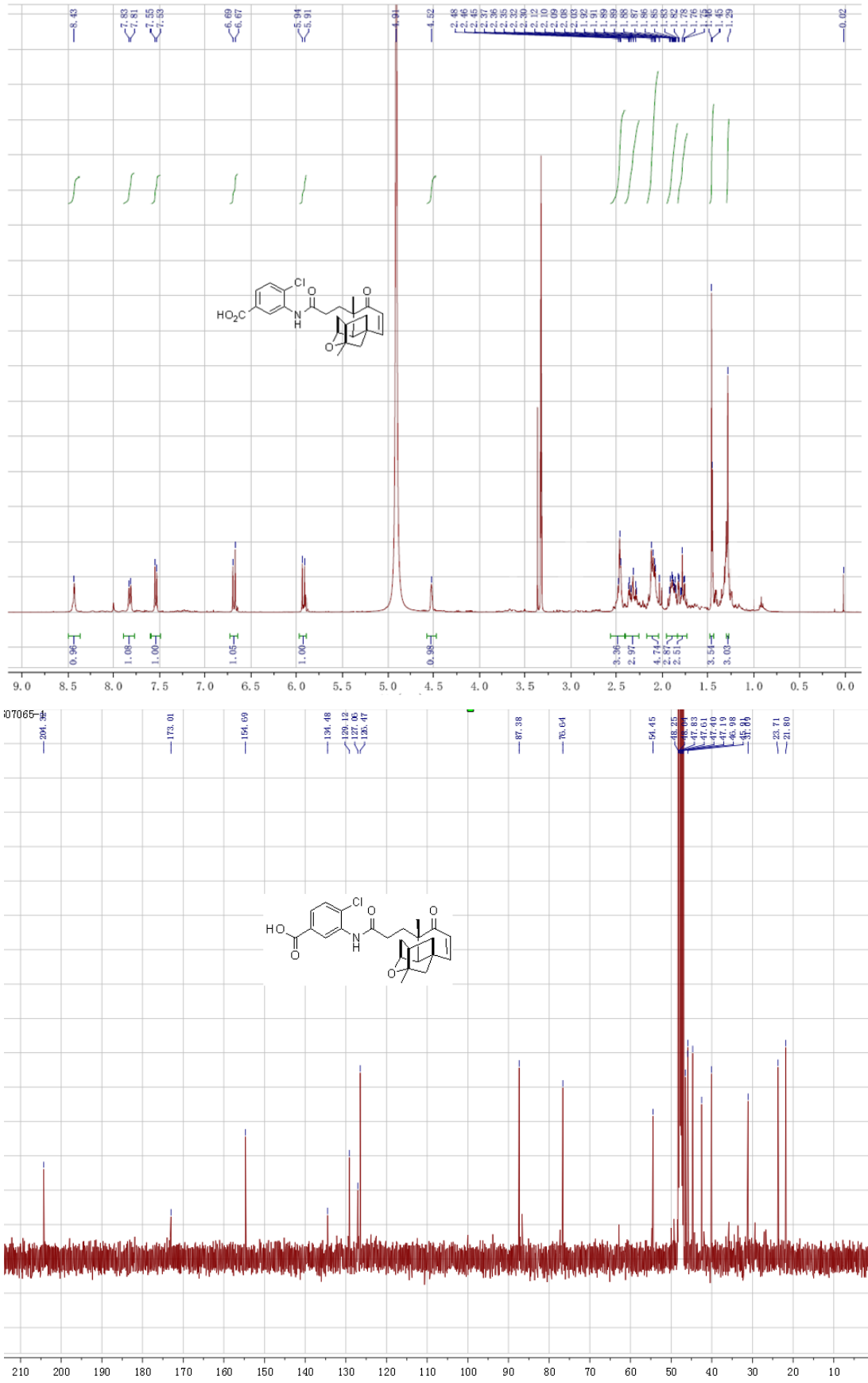


Figure S15. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3i-1** in MeOD.

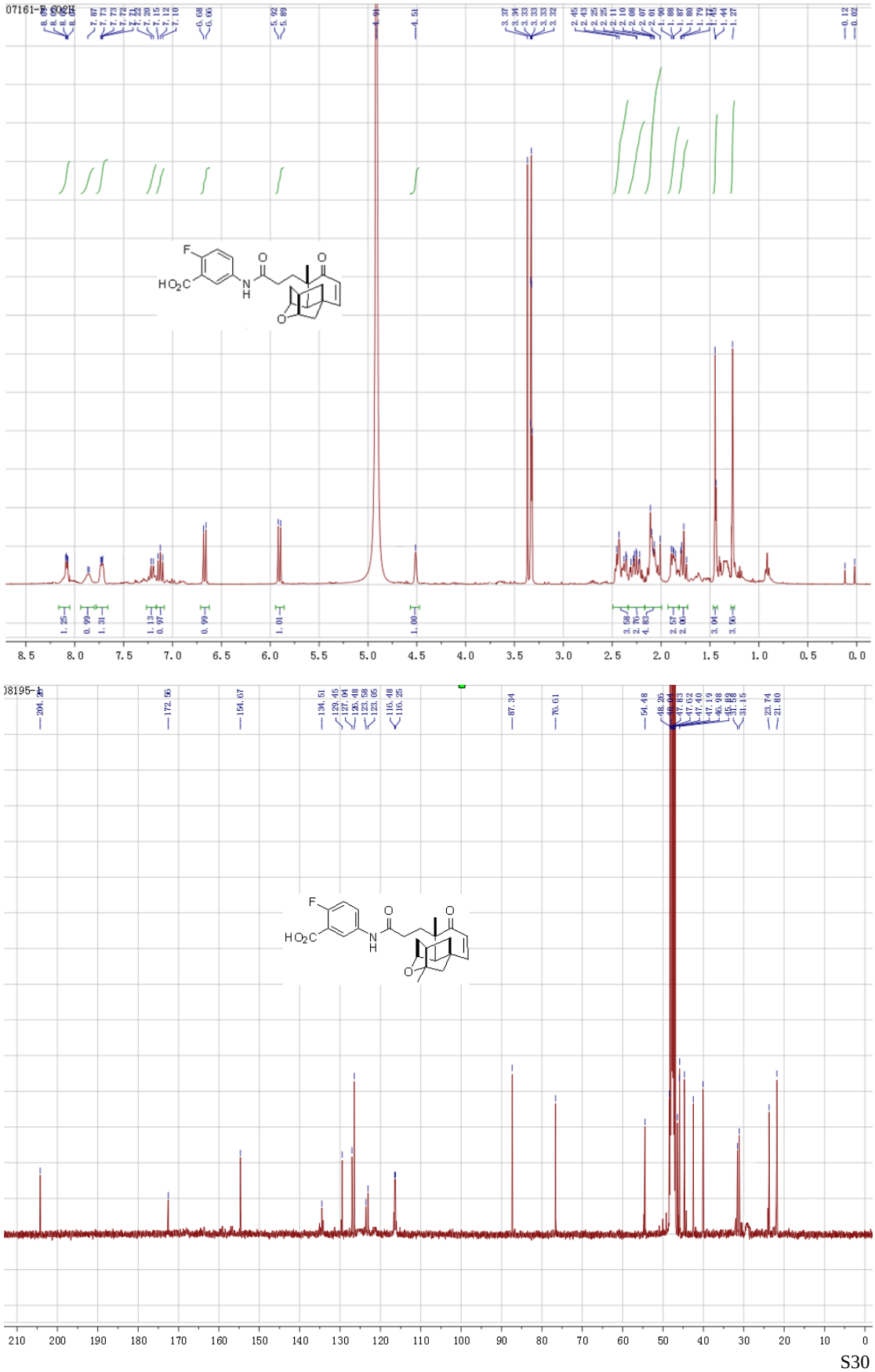


Figure S16. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3j-1** in MeOD.

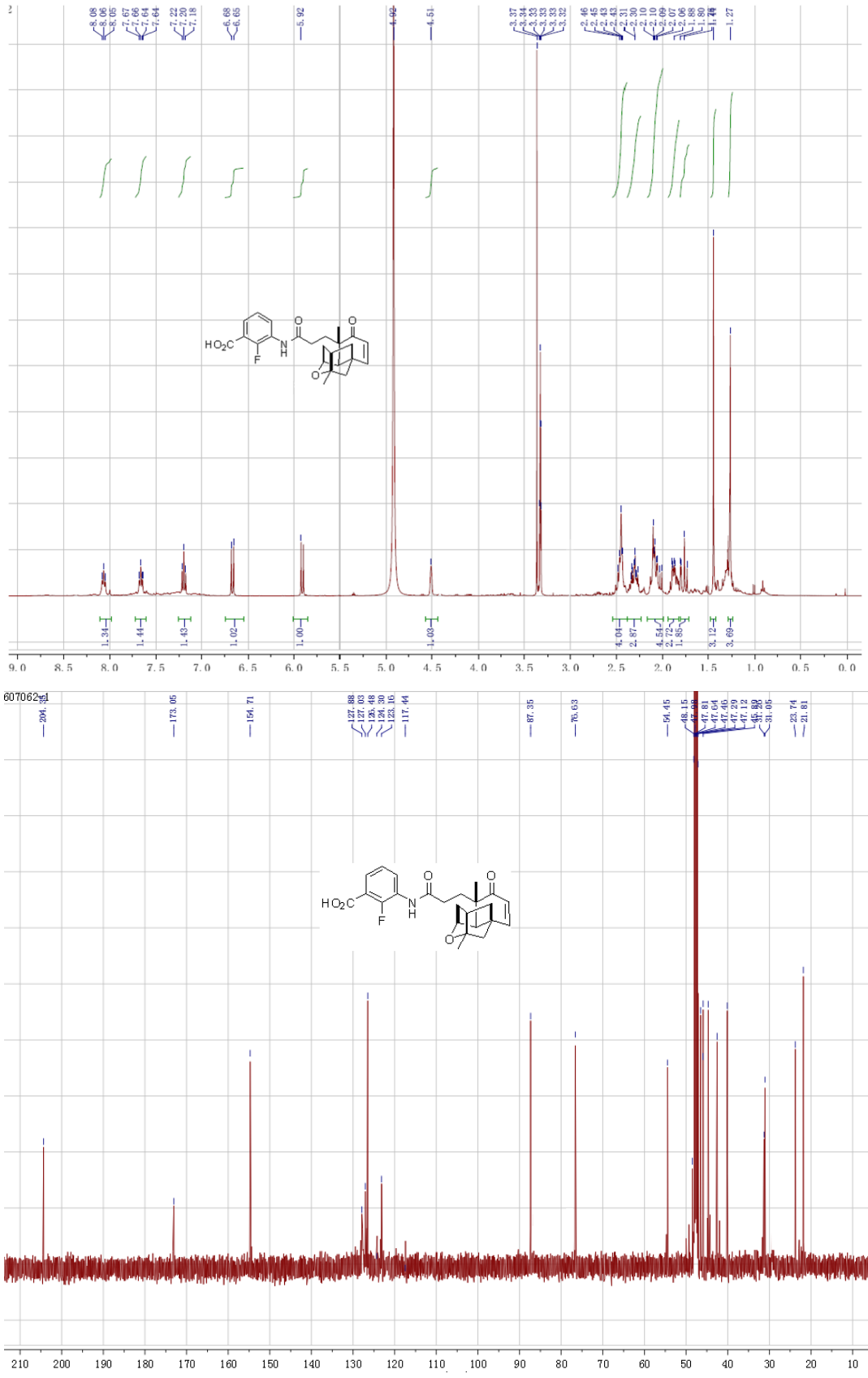


Figure S17. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3a-2** in $CDCl_3$.

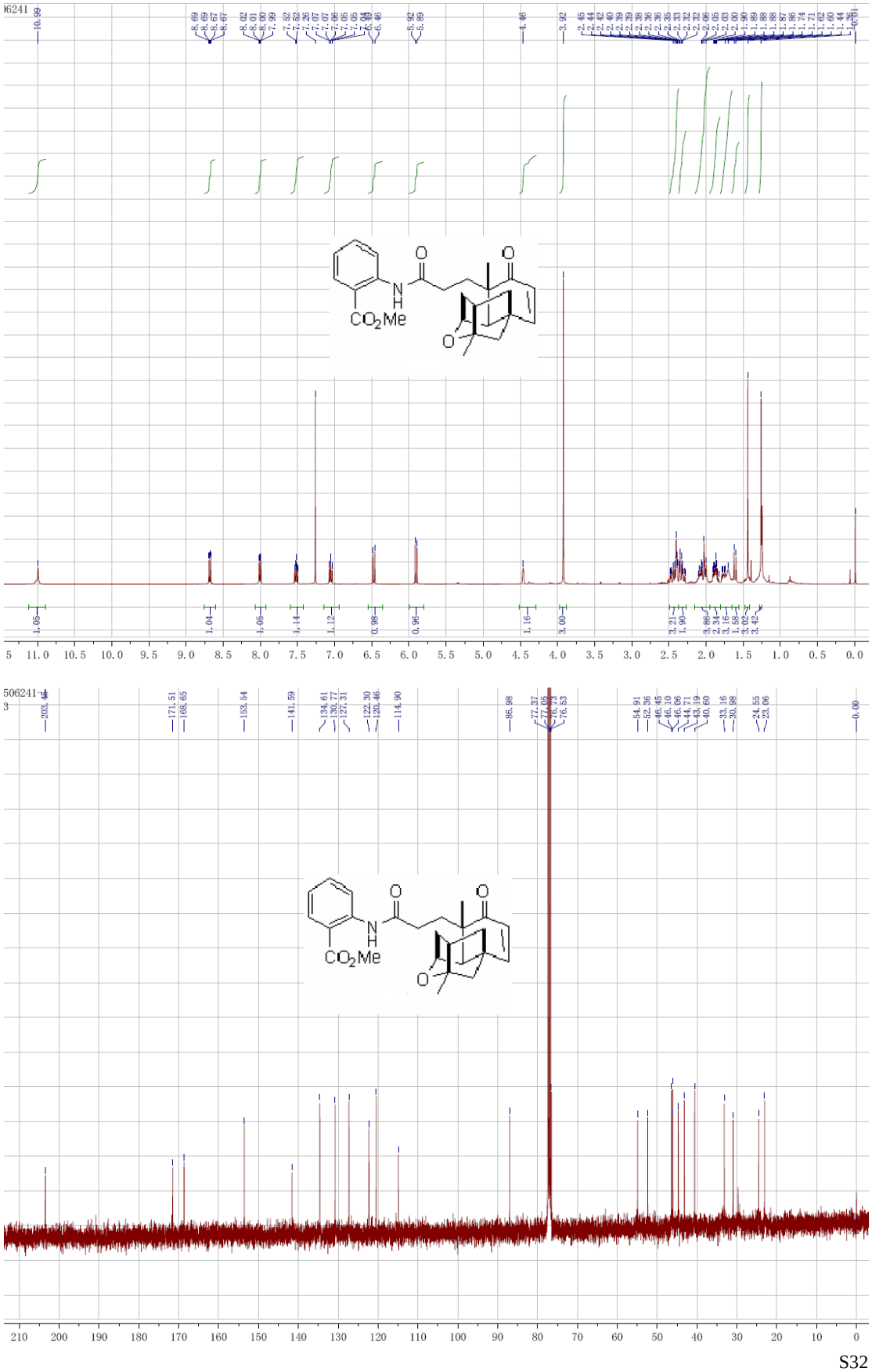


Figure S18. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3b-2** in $CDCl_3$.

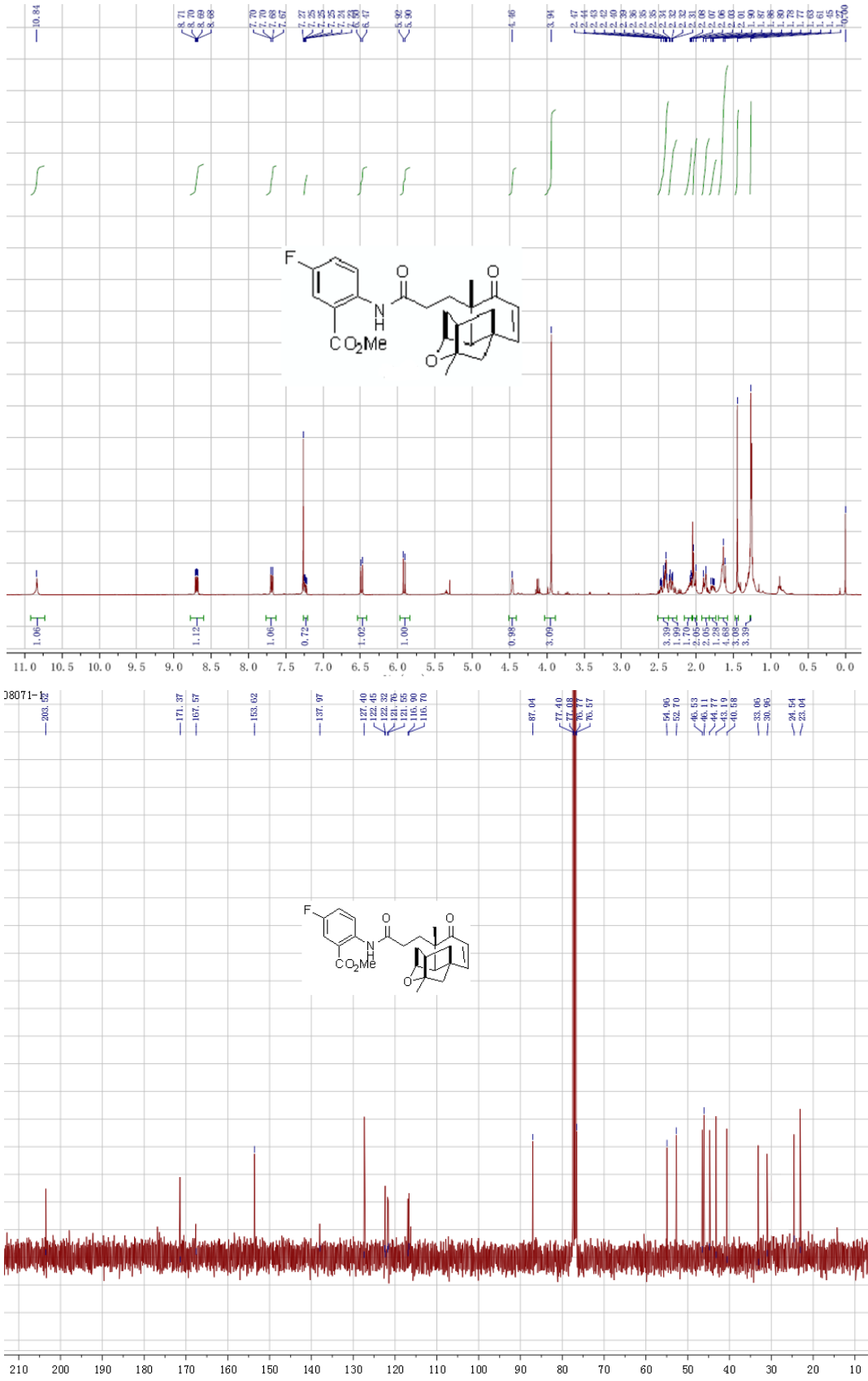
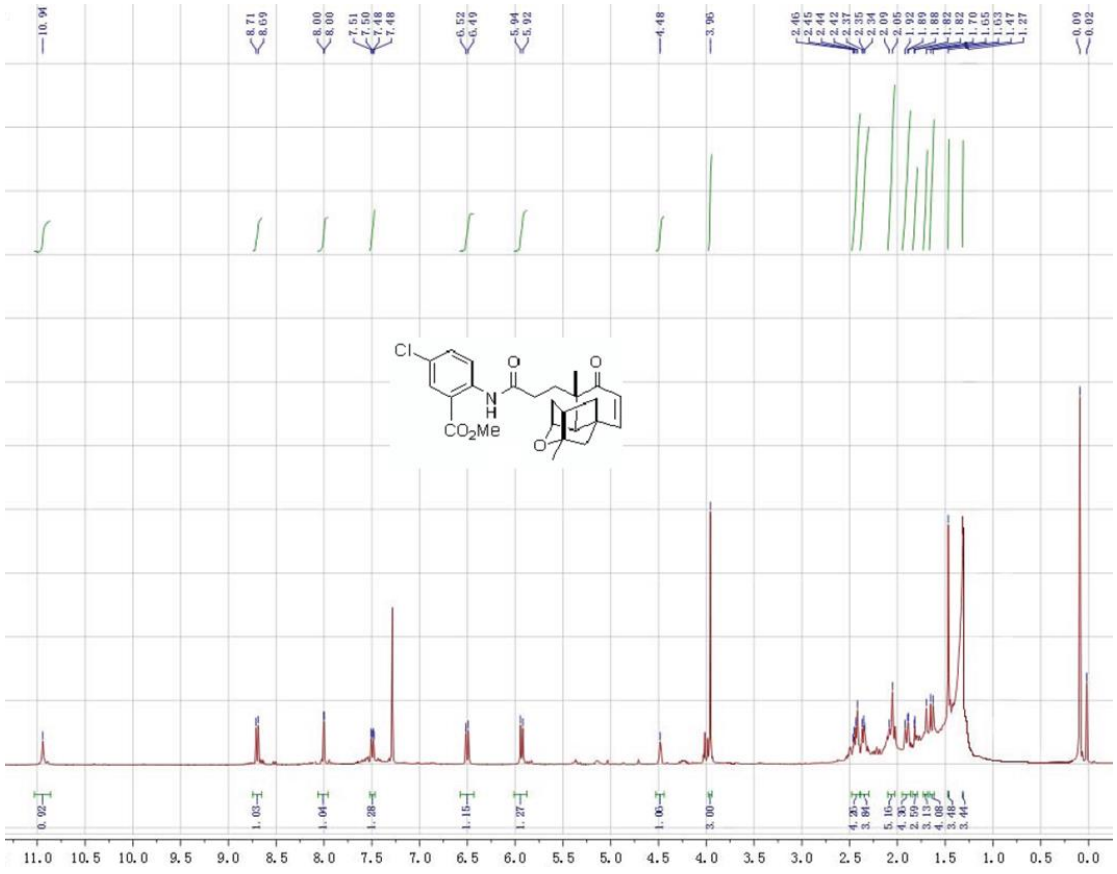


Figure S19. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3c-2** in $CDCl_3$.



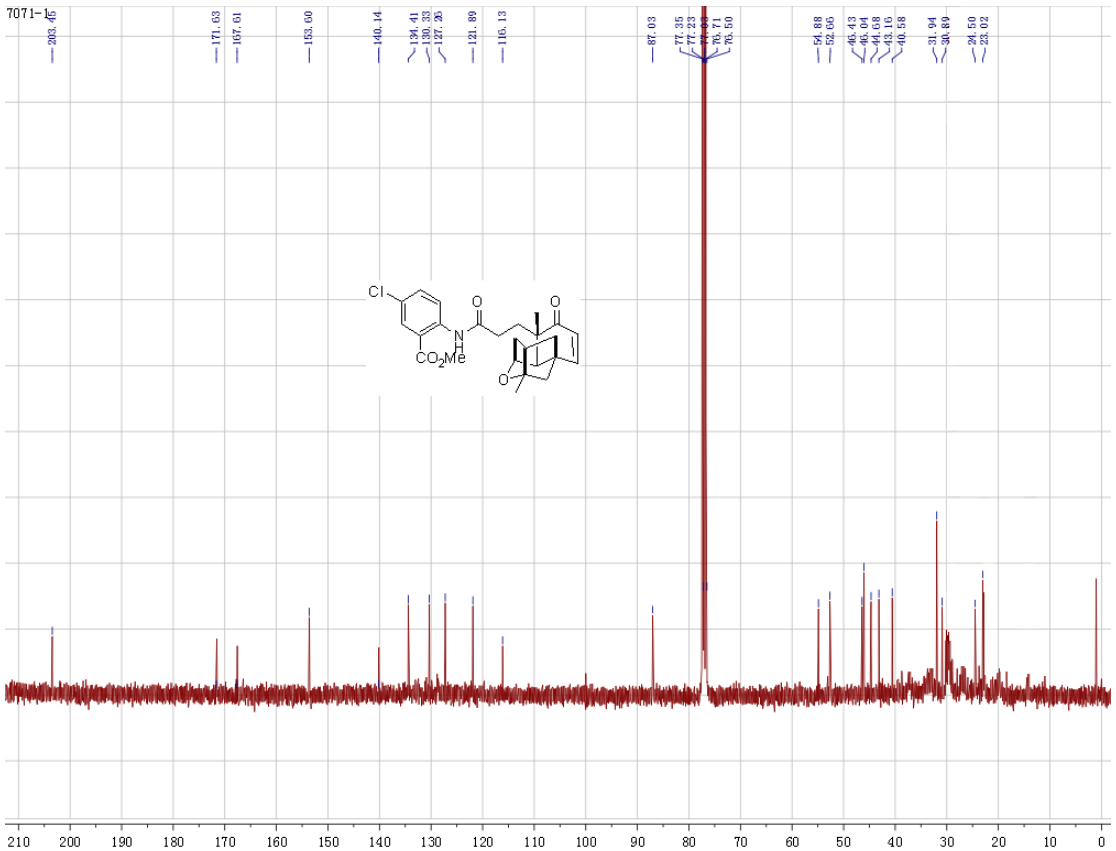


Figure S20. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3d-2** in $CDCl_3$.

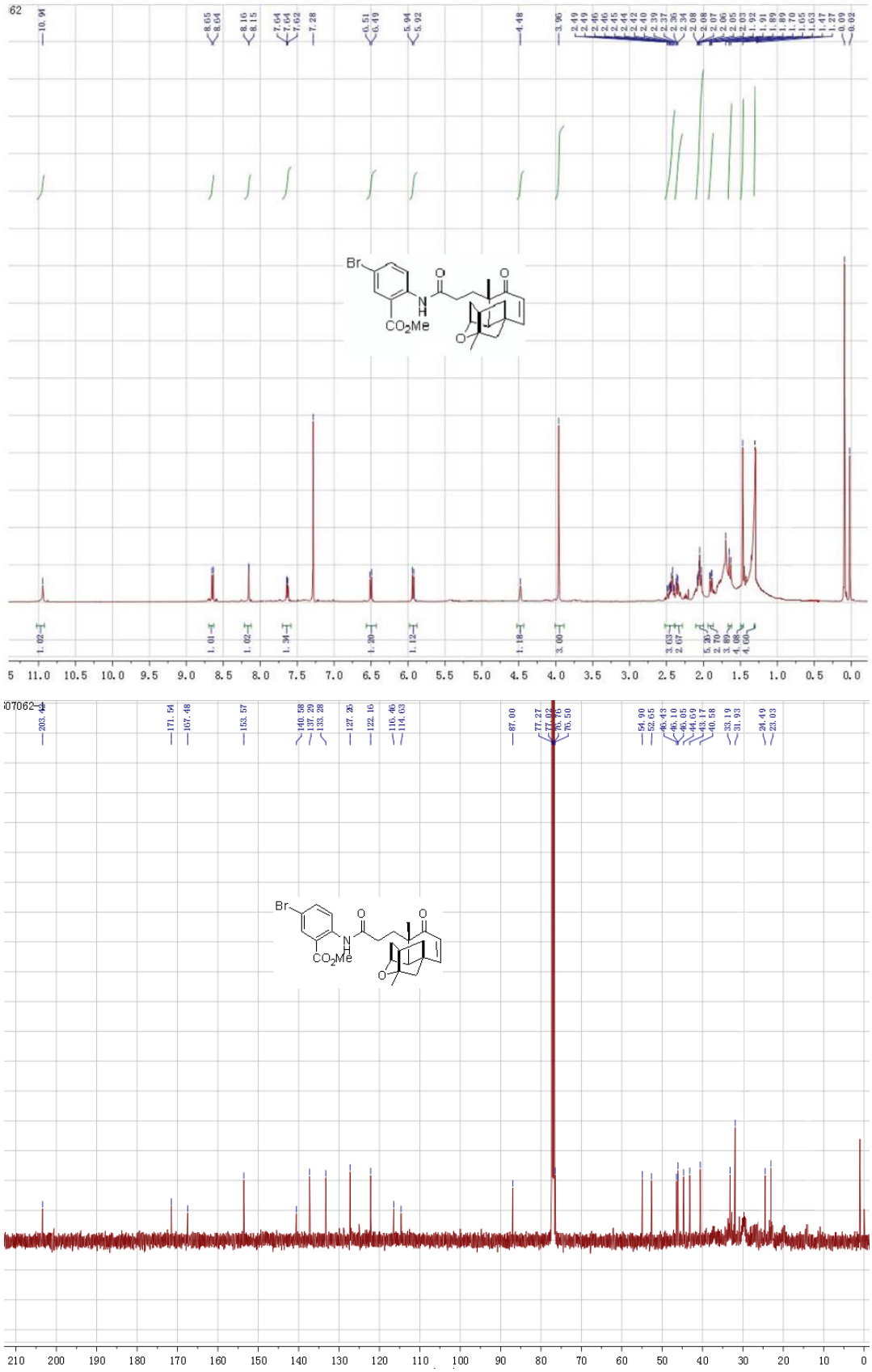


Figure S21. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3h-2** in $CDCl_3$.

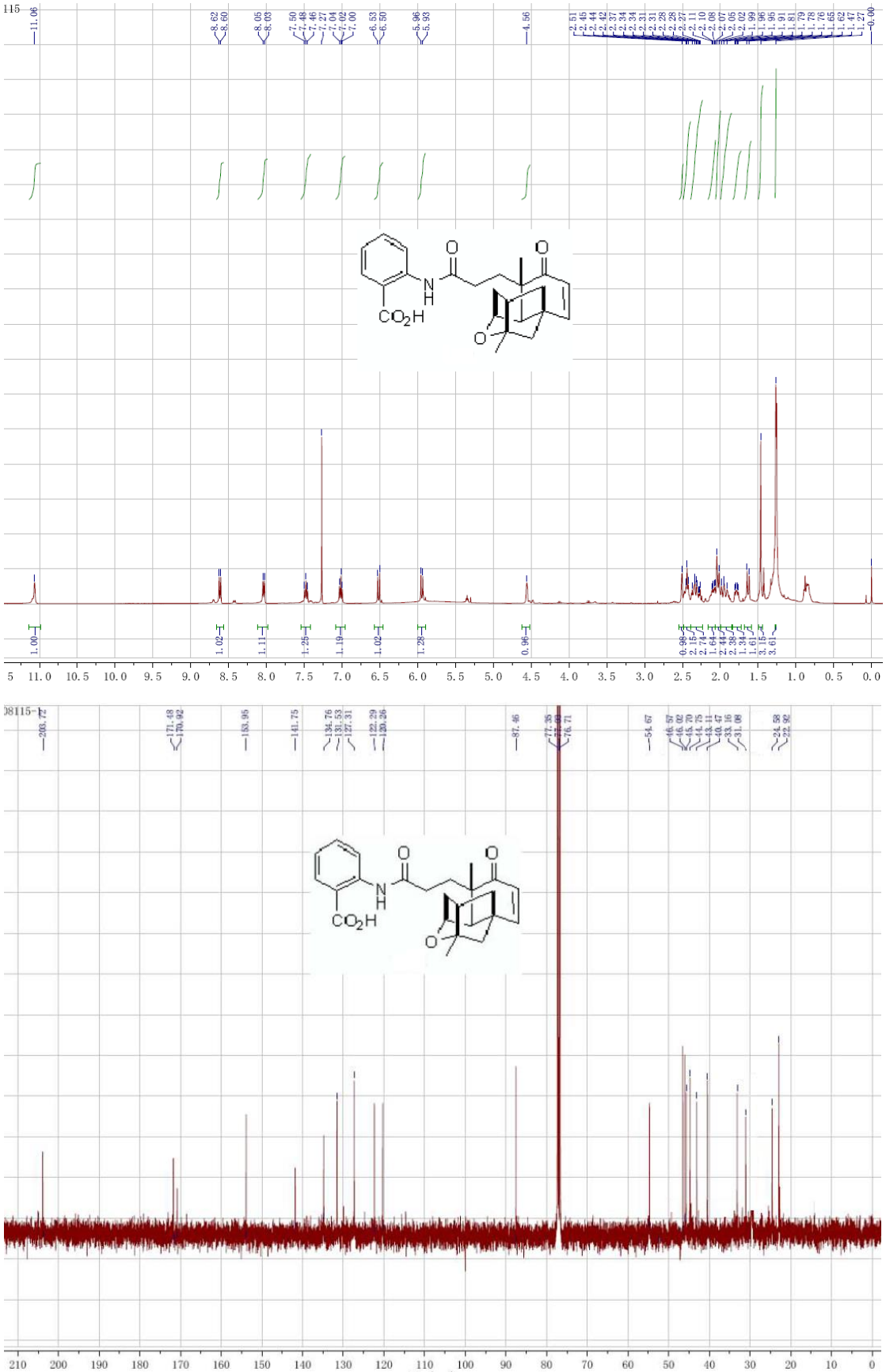


Figure S22. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3i-**2 in $CDCl_3$.

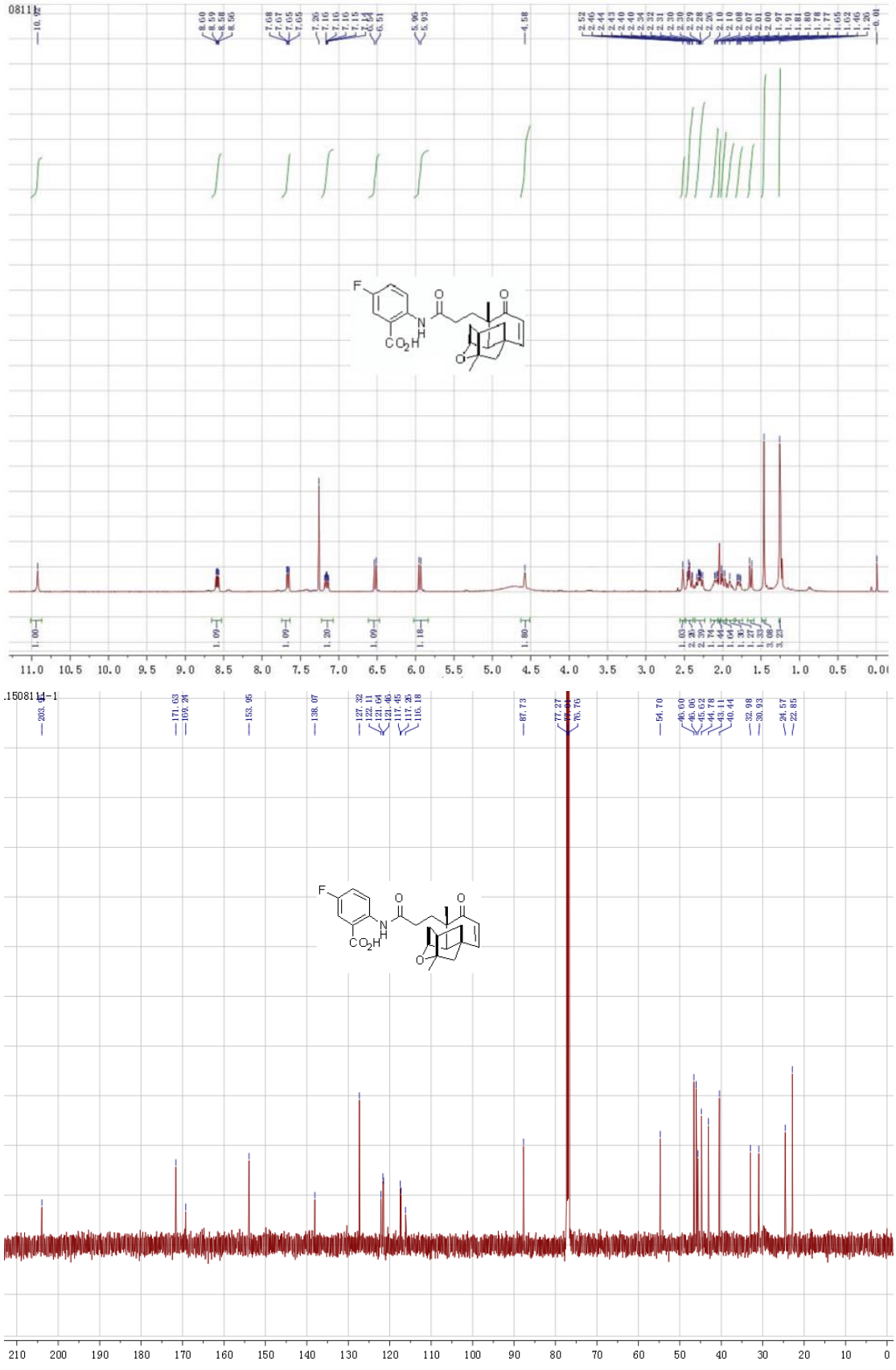


Figure S23. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3j-2** in $CDCl_3$.

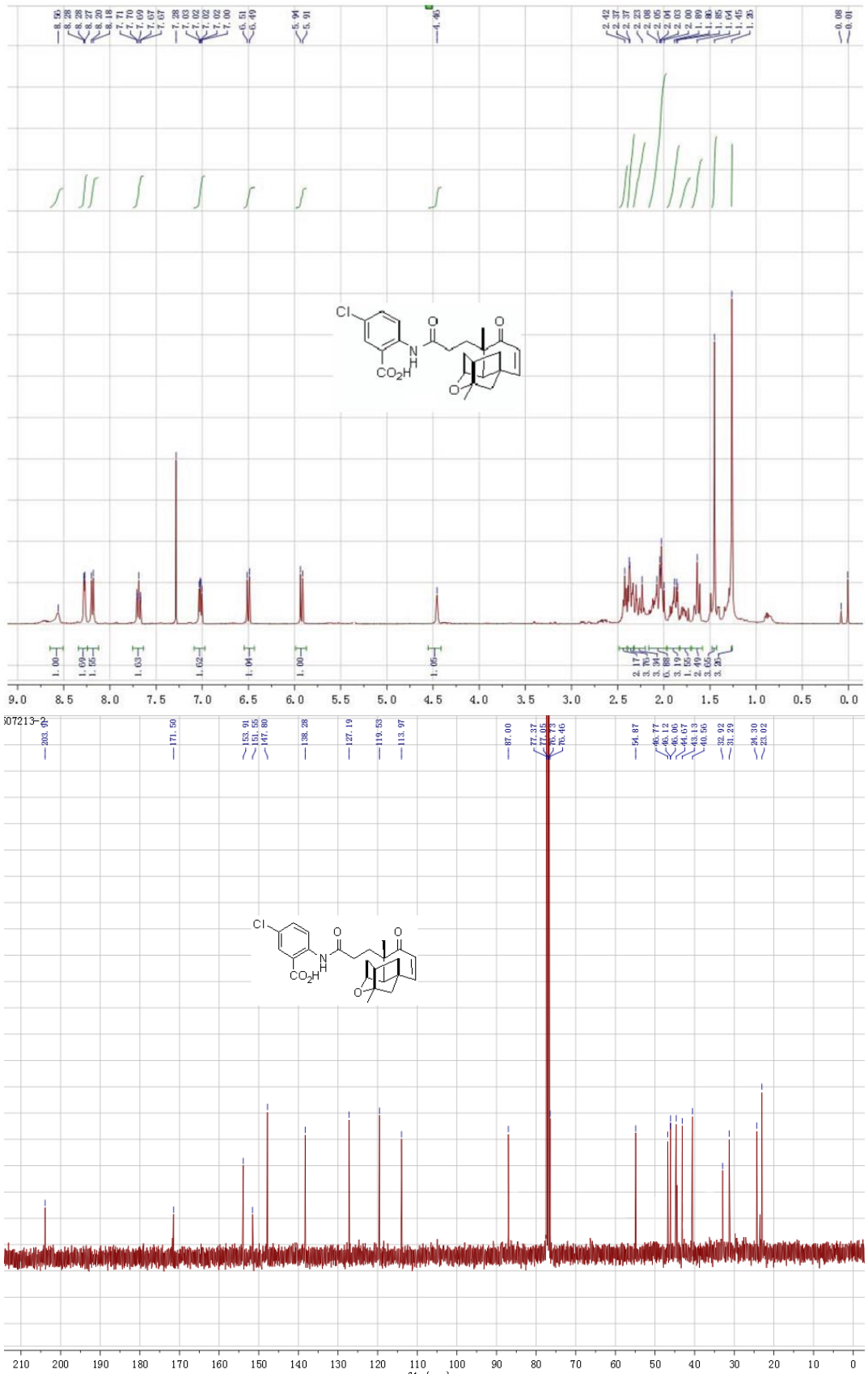


Figure S24. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3k**-2 in $CDCl_3$.

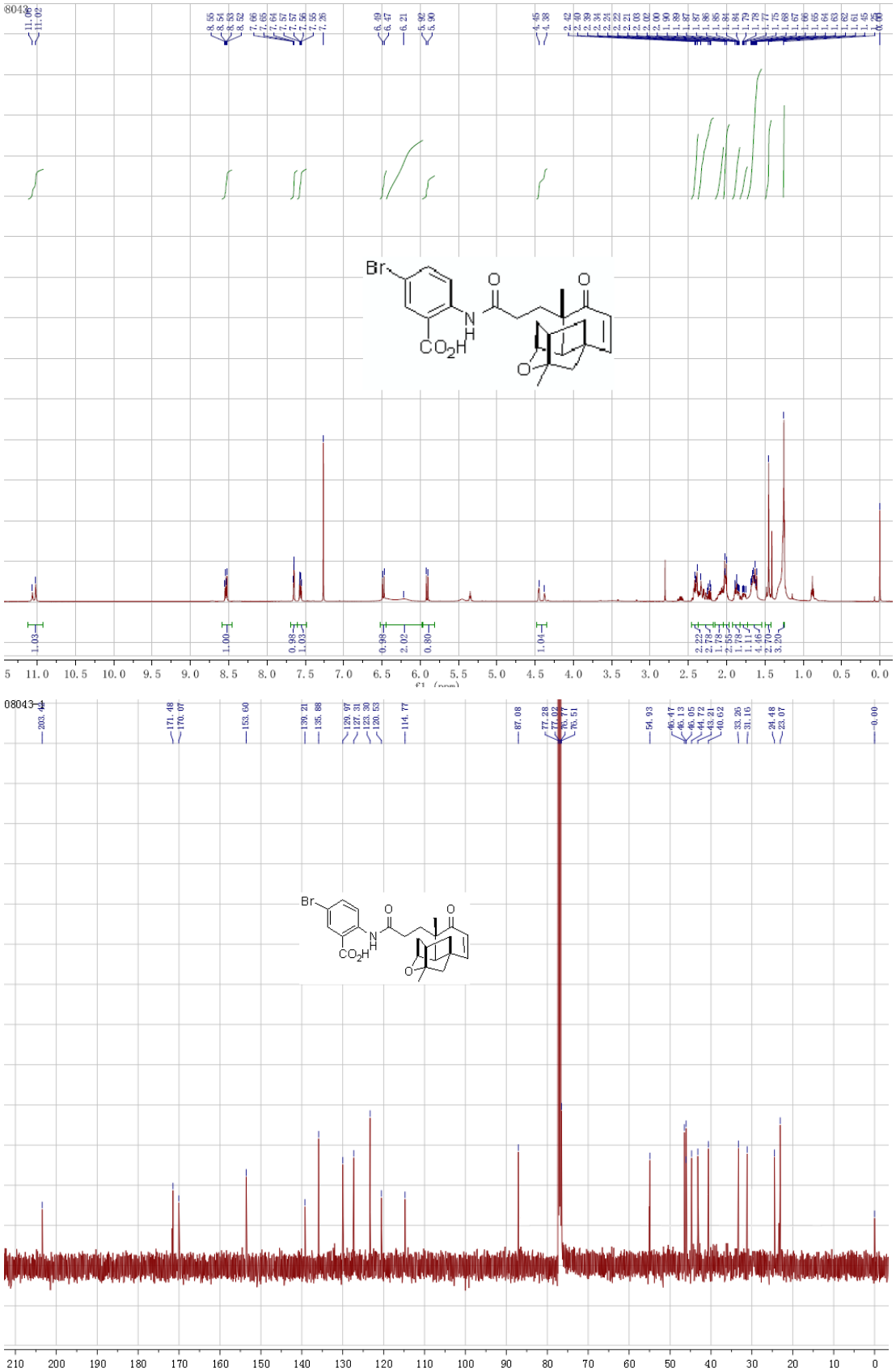


Figure S25. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3l-2** in $CDCl_3$.

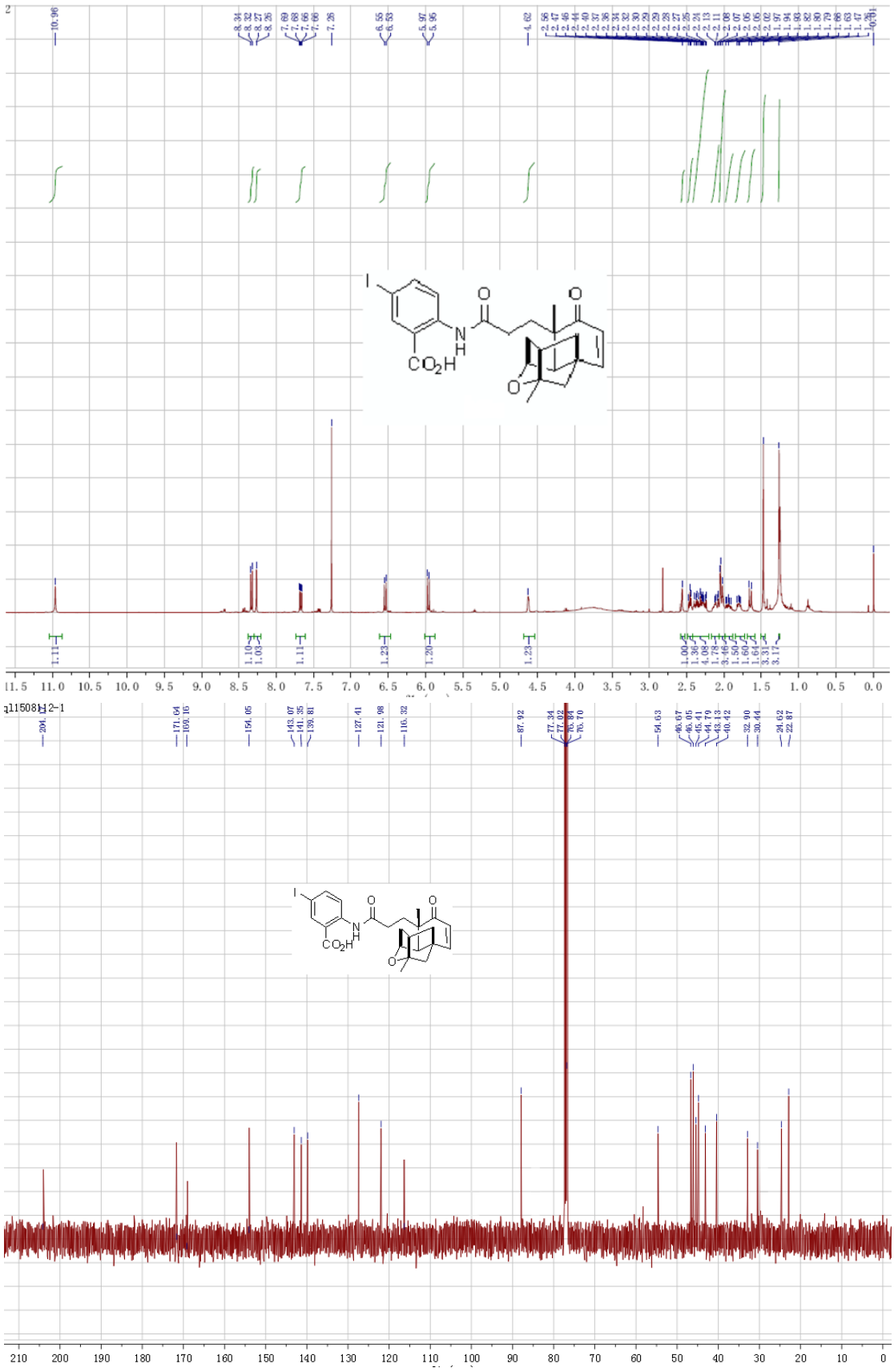


Figure S26. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3m-2** in Acetone.

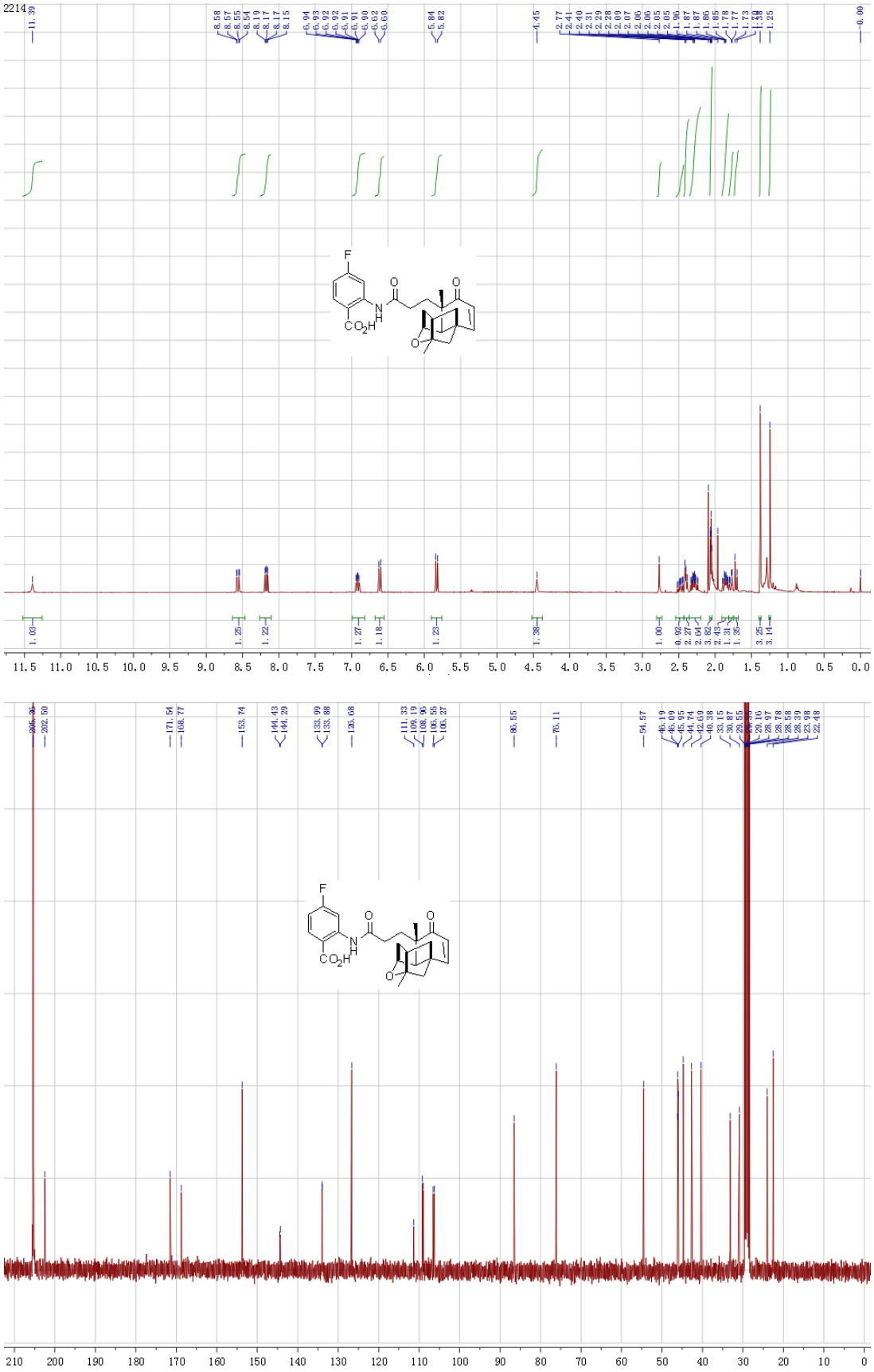


Figure S27. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3o-2** in $CDCl_3$.

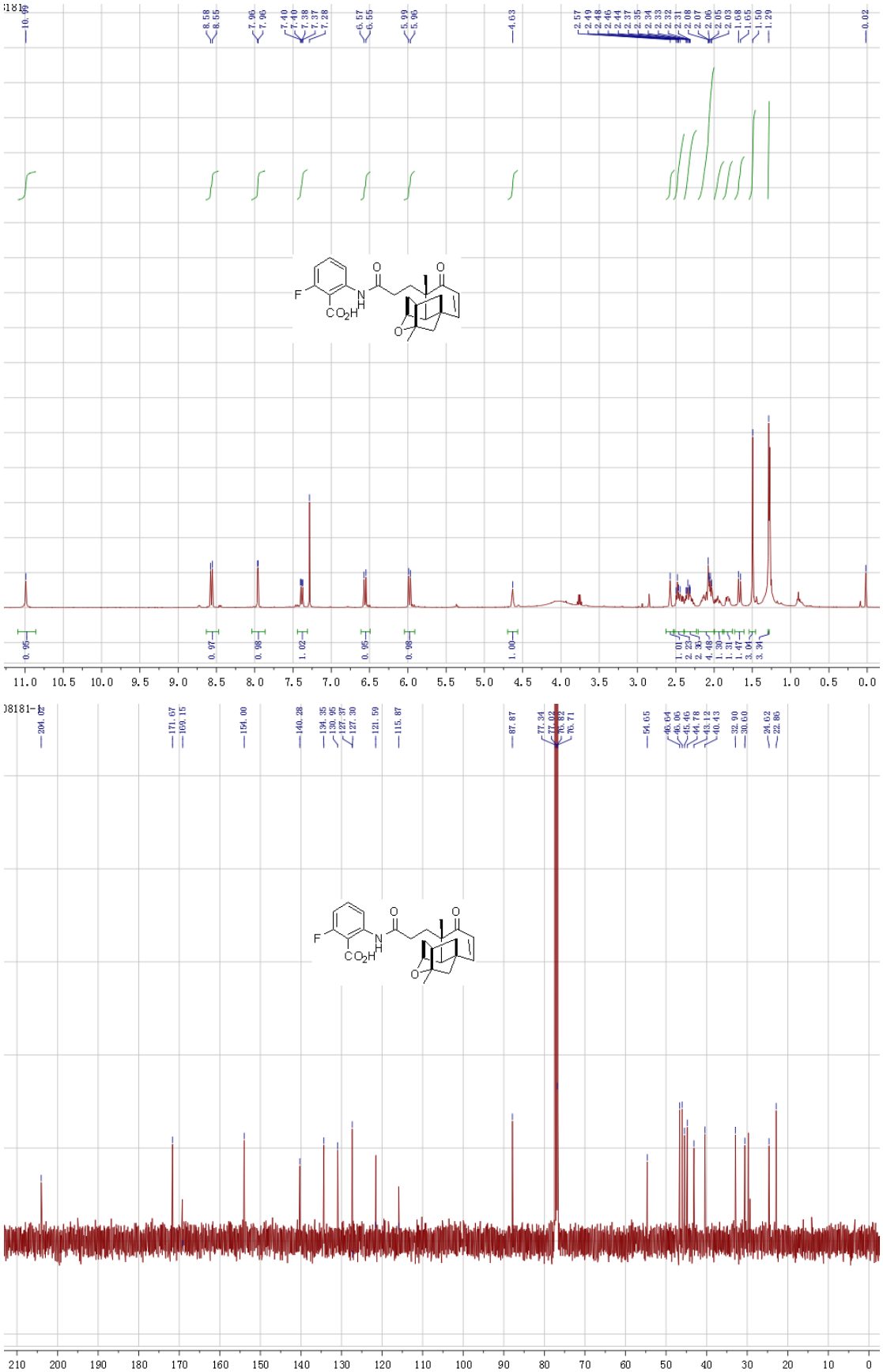


Figure S28. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3p-2** in $CDCl_3$.

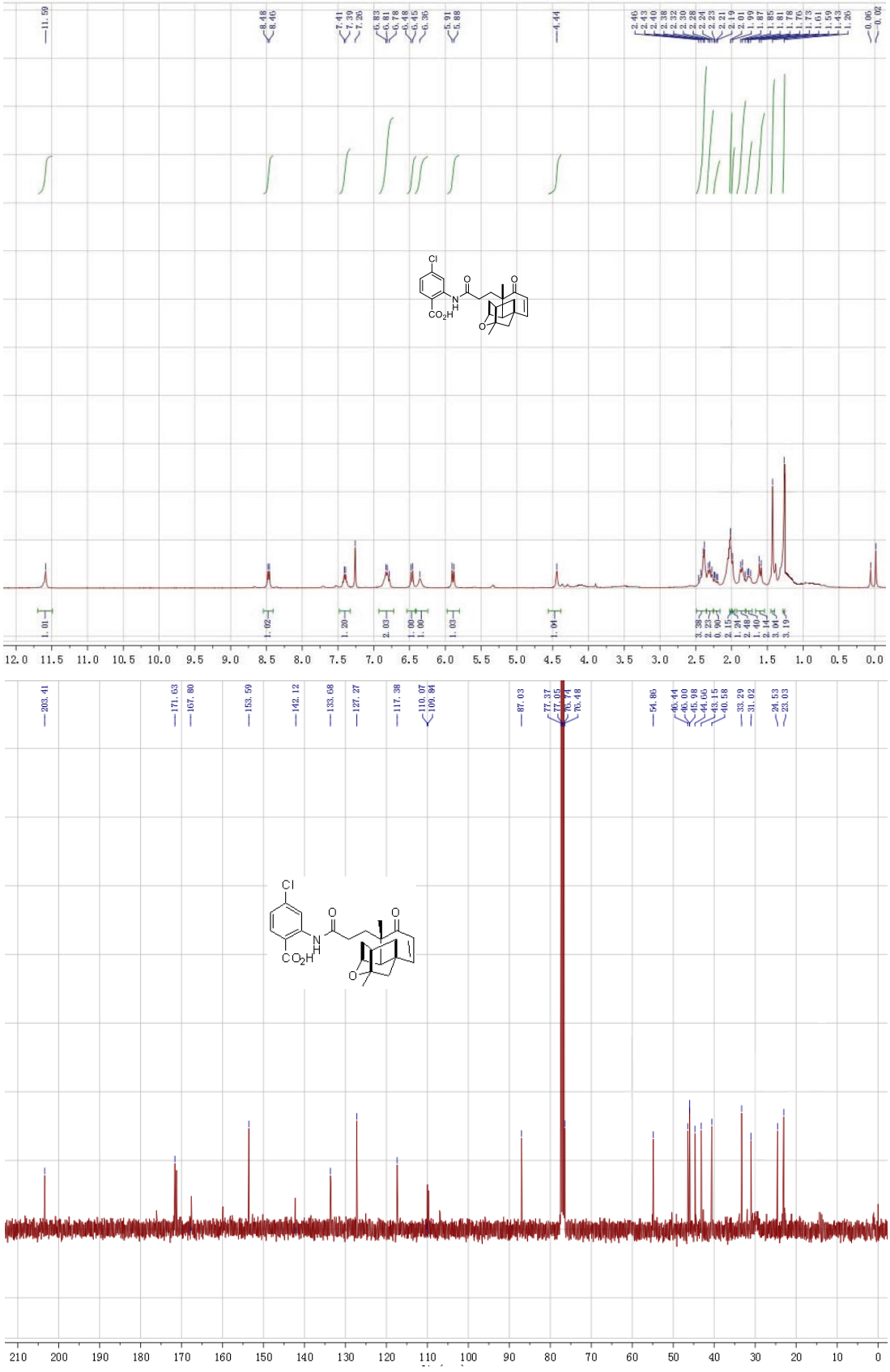


Figure S29. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3q-2** in MeOD.

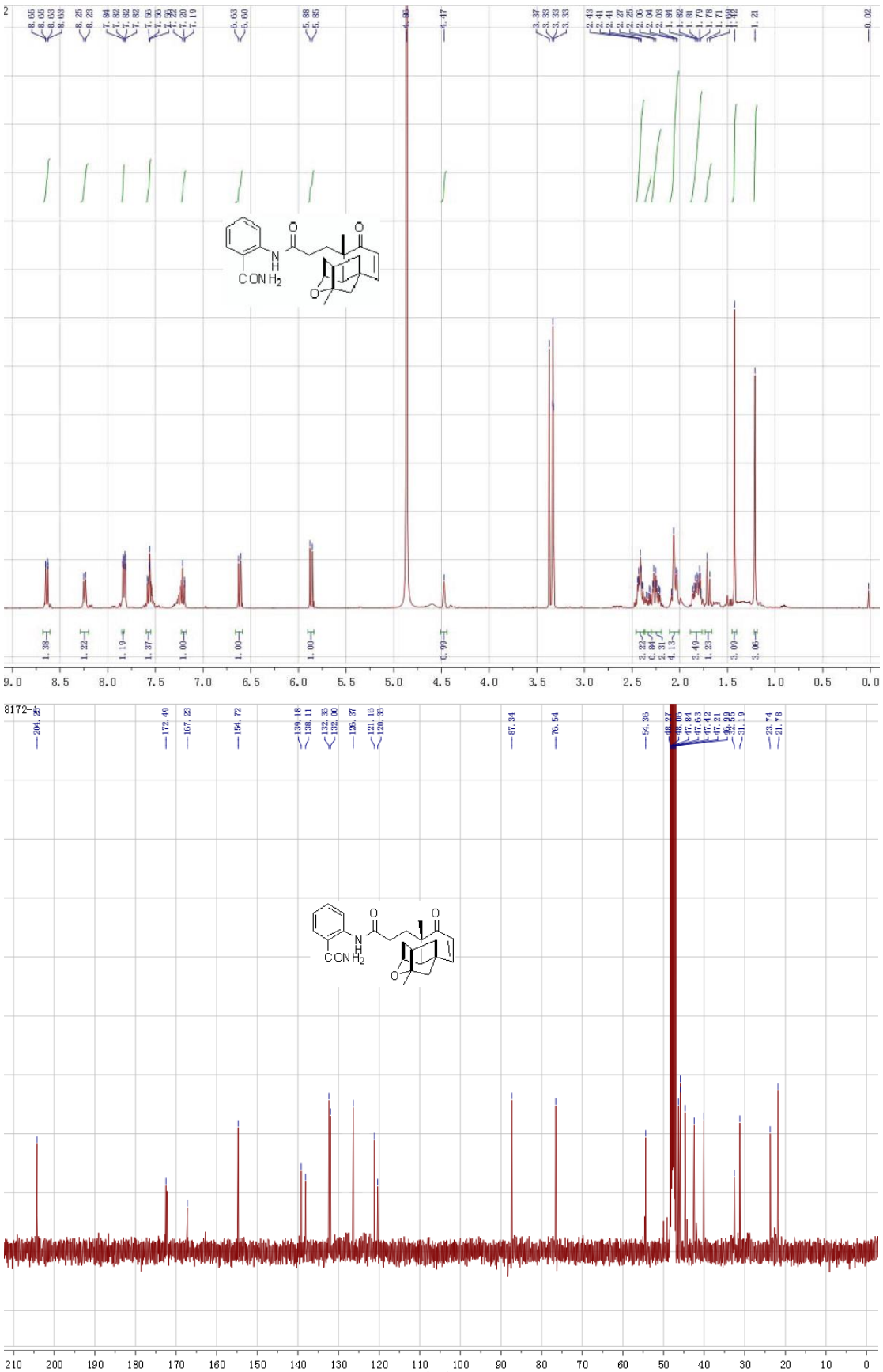


Figure S30. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3r-2** in $CDCl_3$.

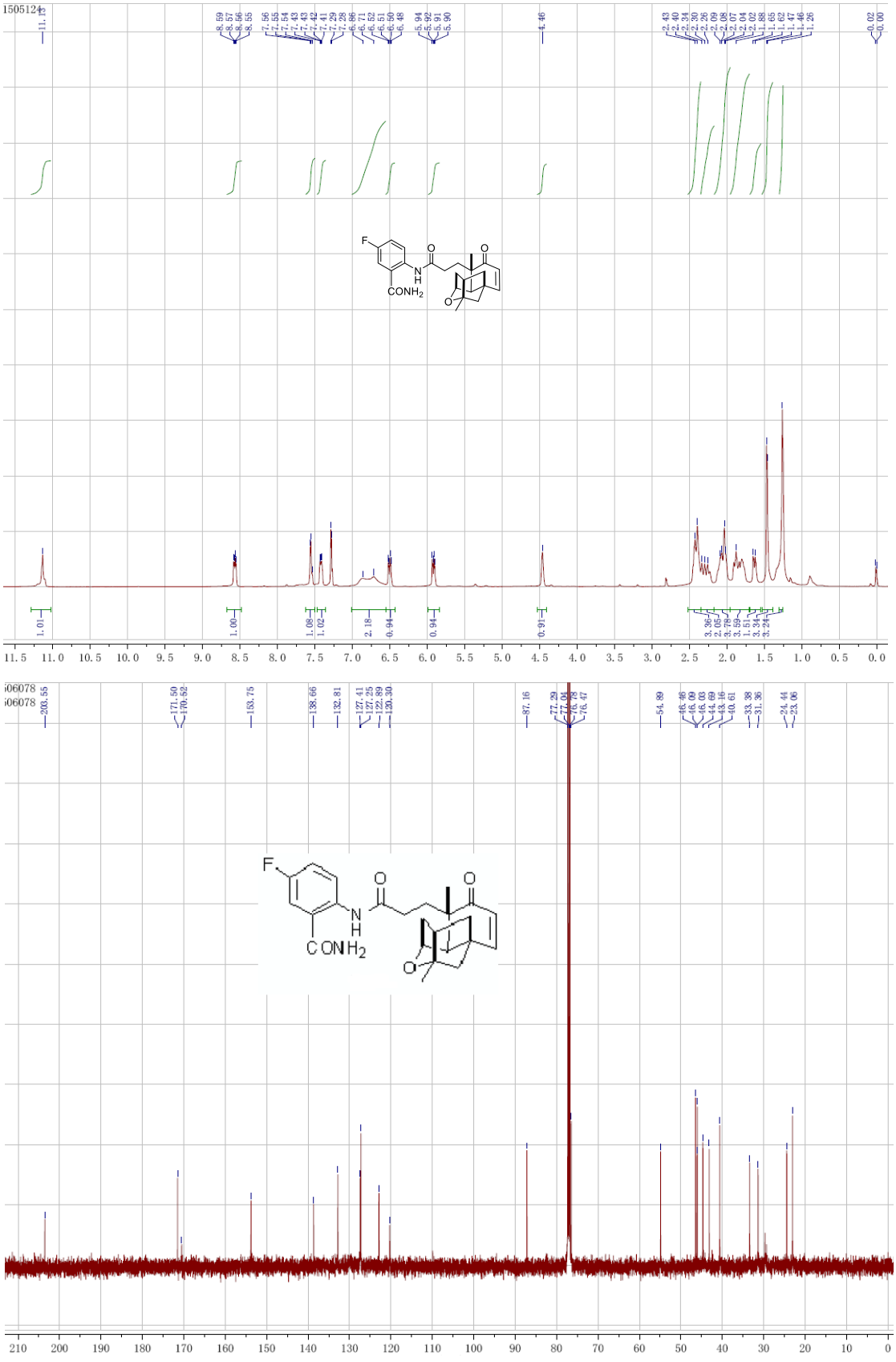


Figure S31. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3s-2** in $CDCl_3$.

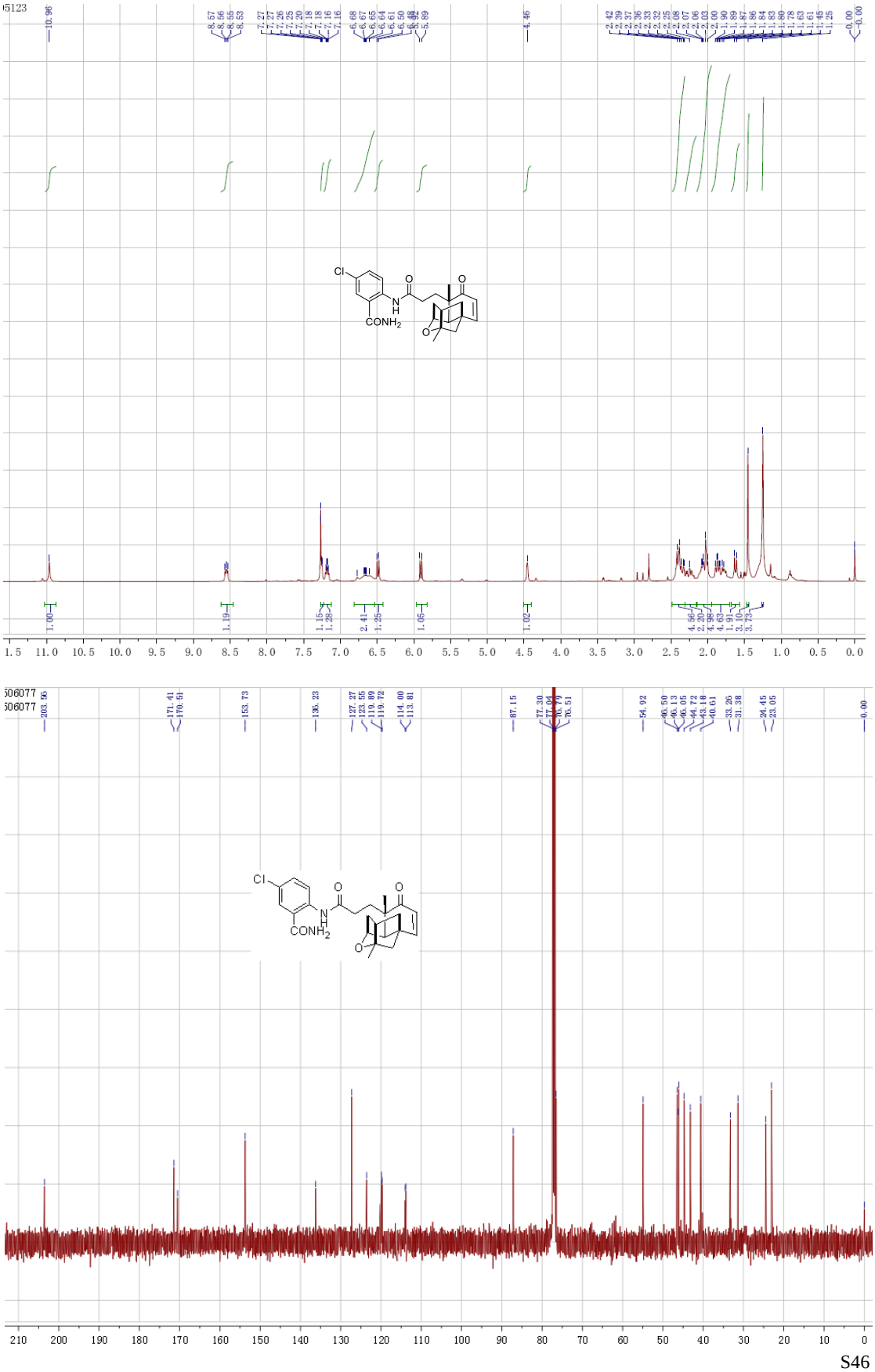
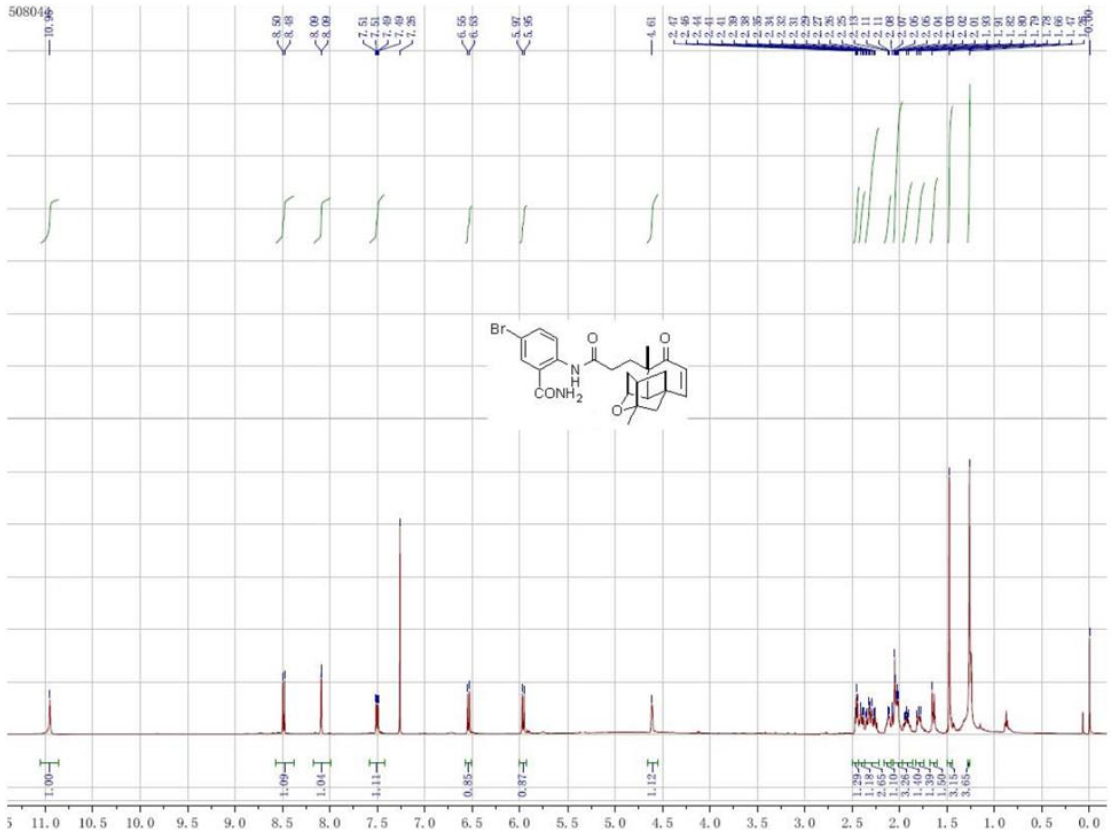


Figure S32. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3t-2** in $CDCl_3$.



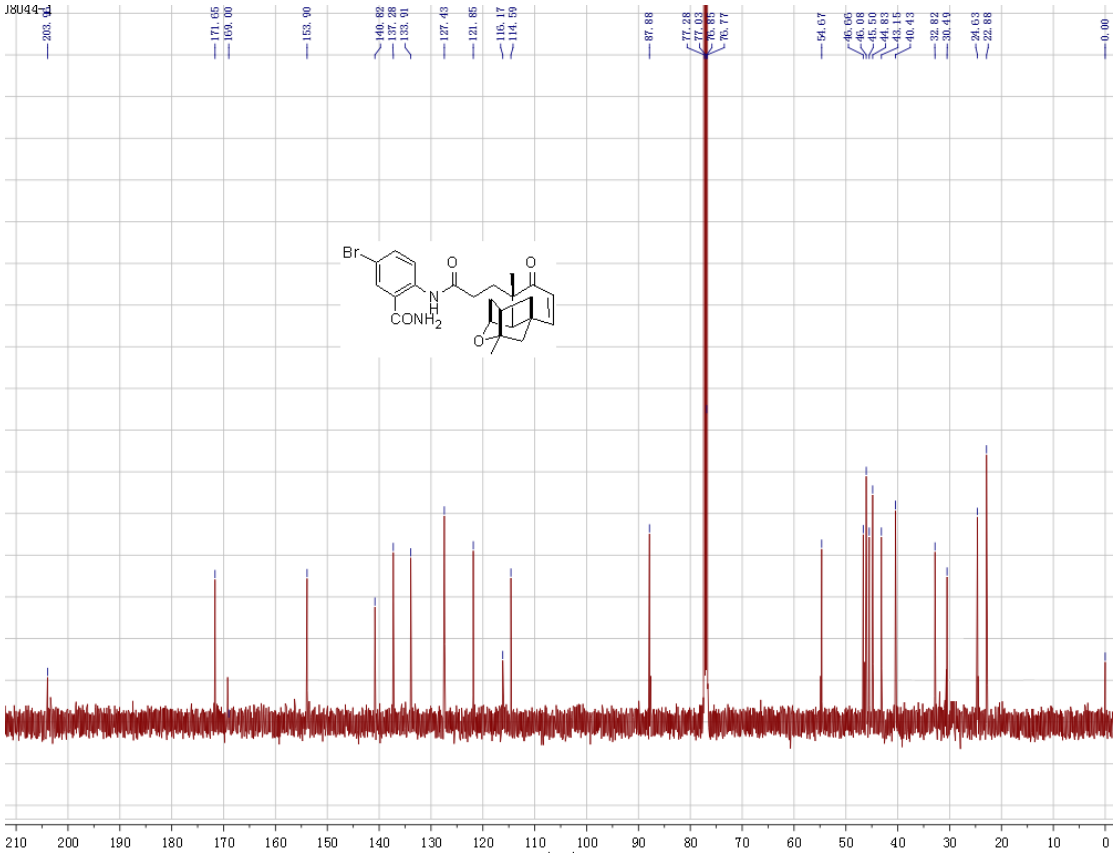


Figure S33. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3u-2** in $CDCl_3$.

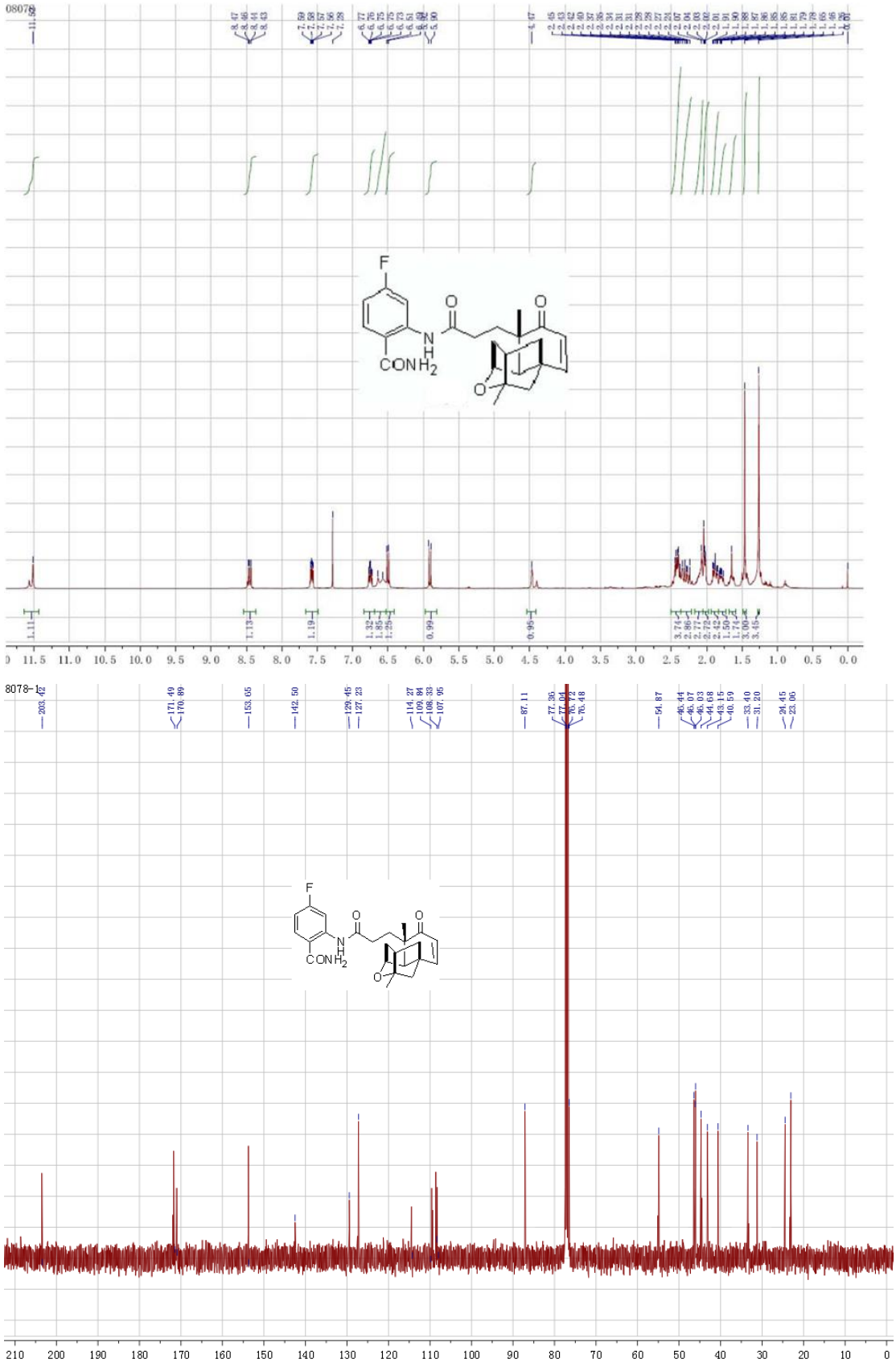


Figure S34. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectrum of **3w-2** in MeOD.

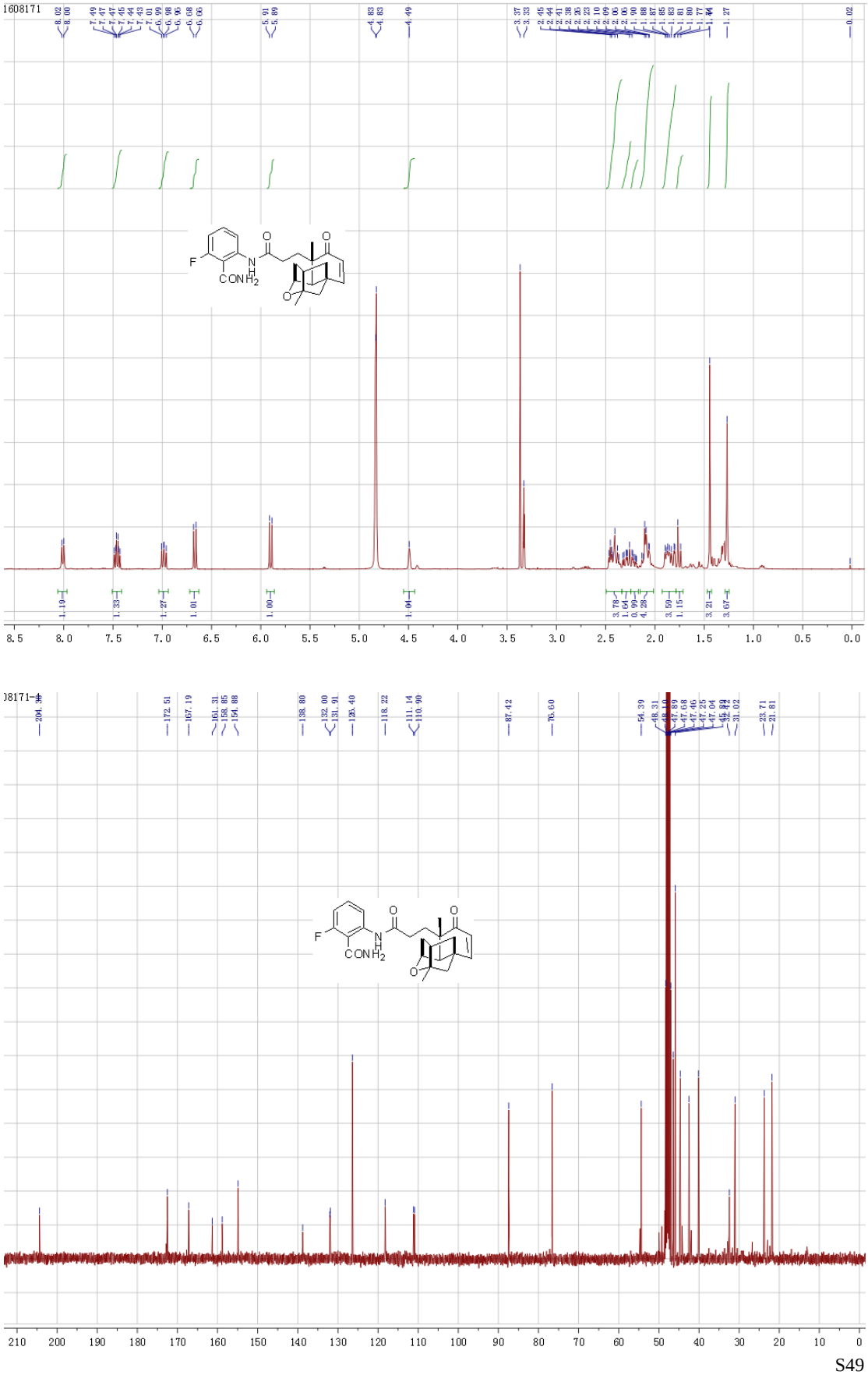
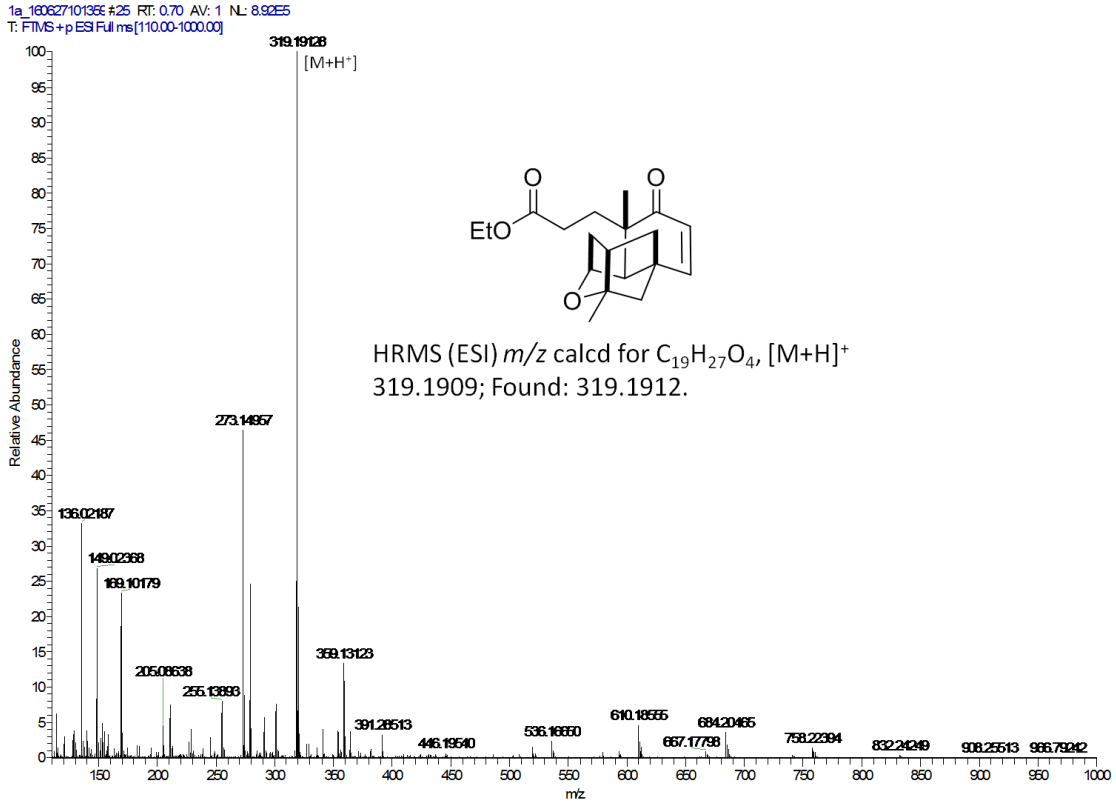


Figure S35. HRMS spectrum of **1a** and **1b**.



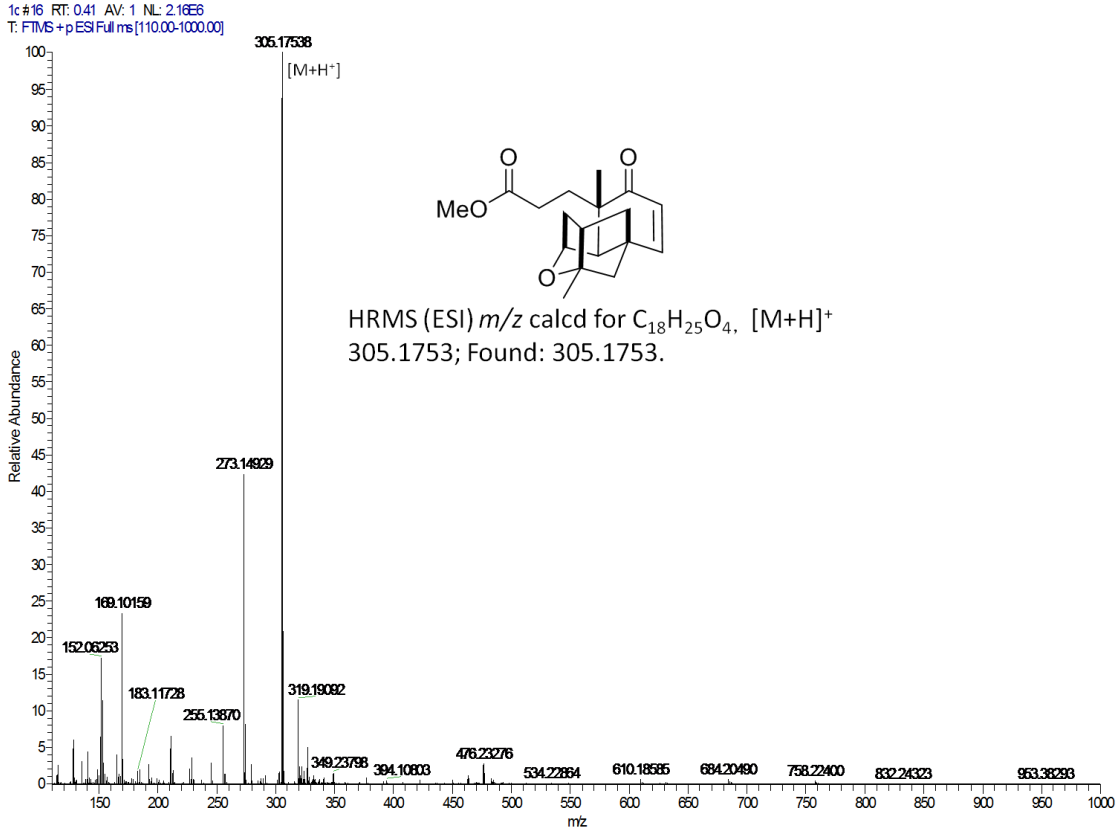
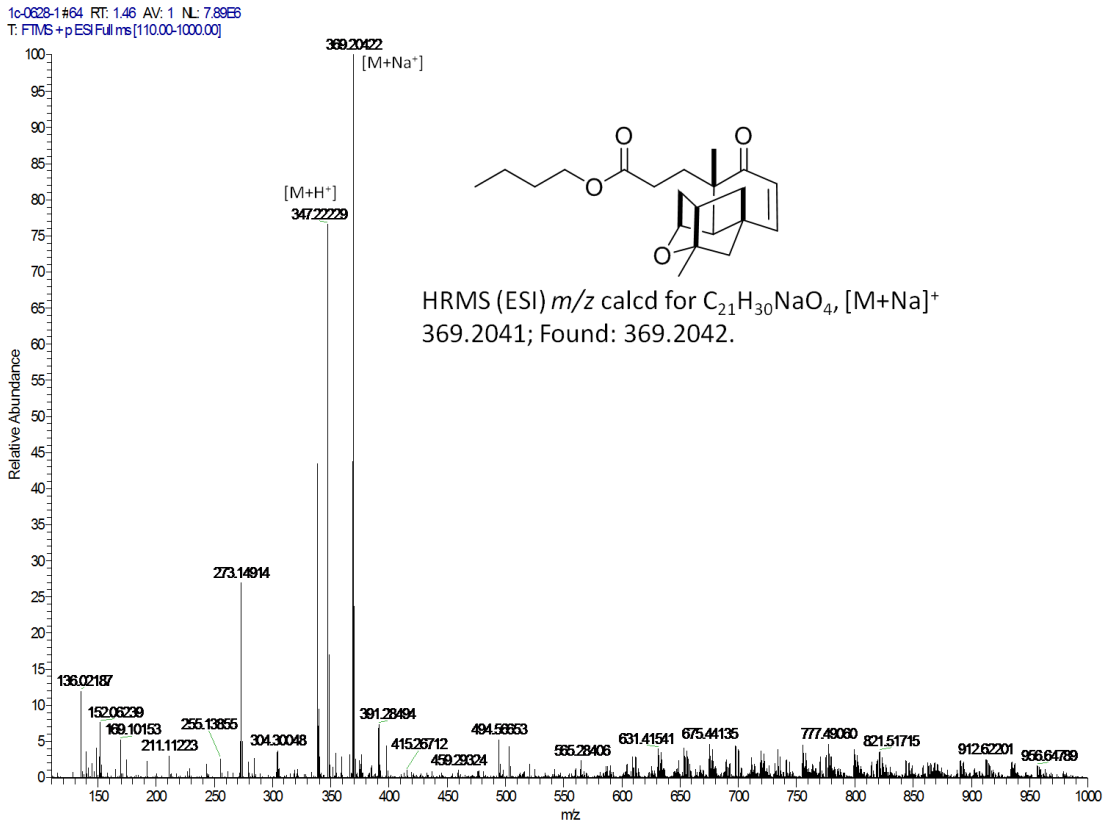


Figure S36. HRMS spectrum of **1c** and **1d**.



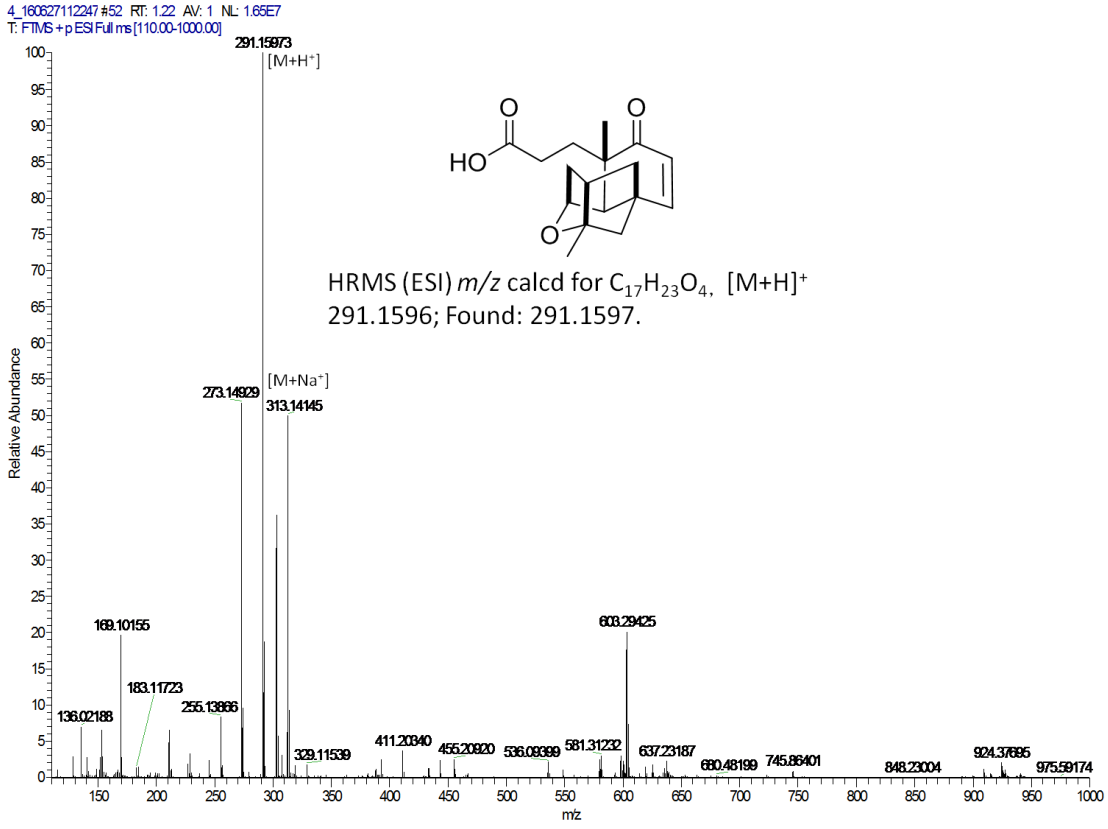
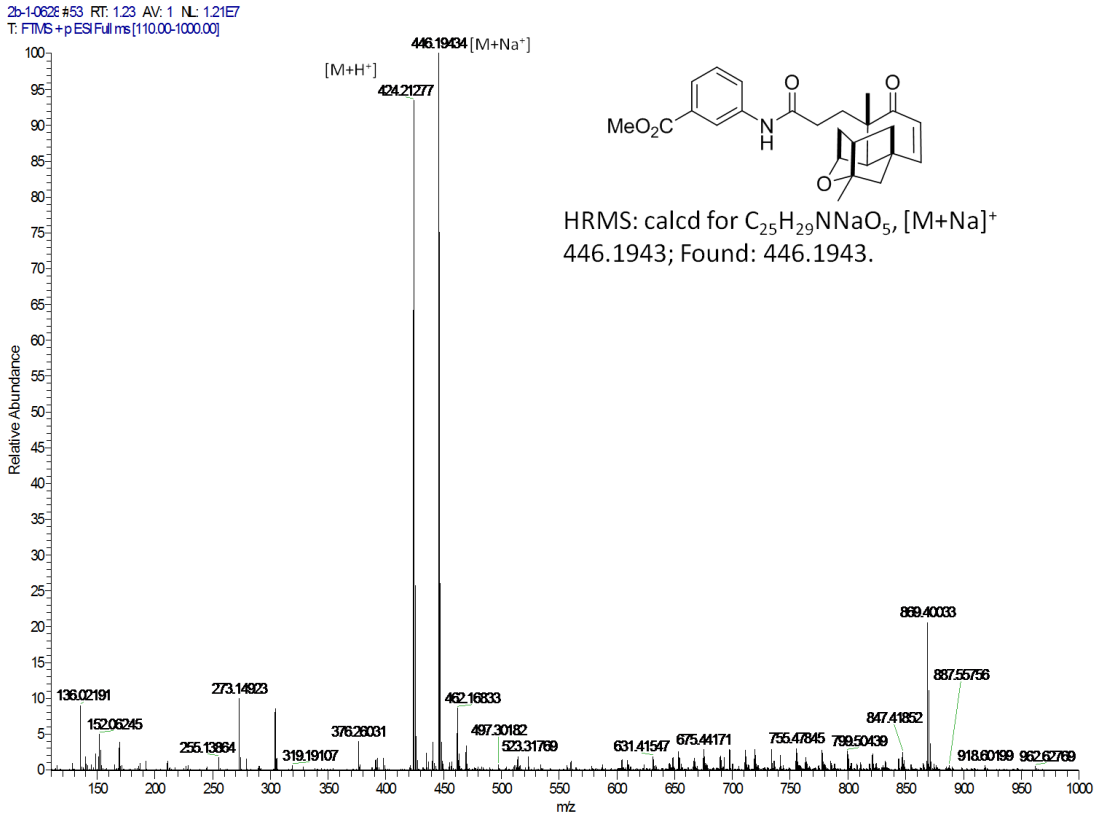


Figure S37. HRMS spectrum of **3a-1** and **3b-1**.



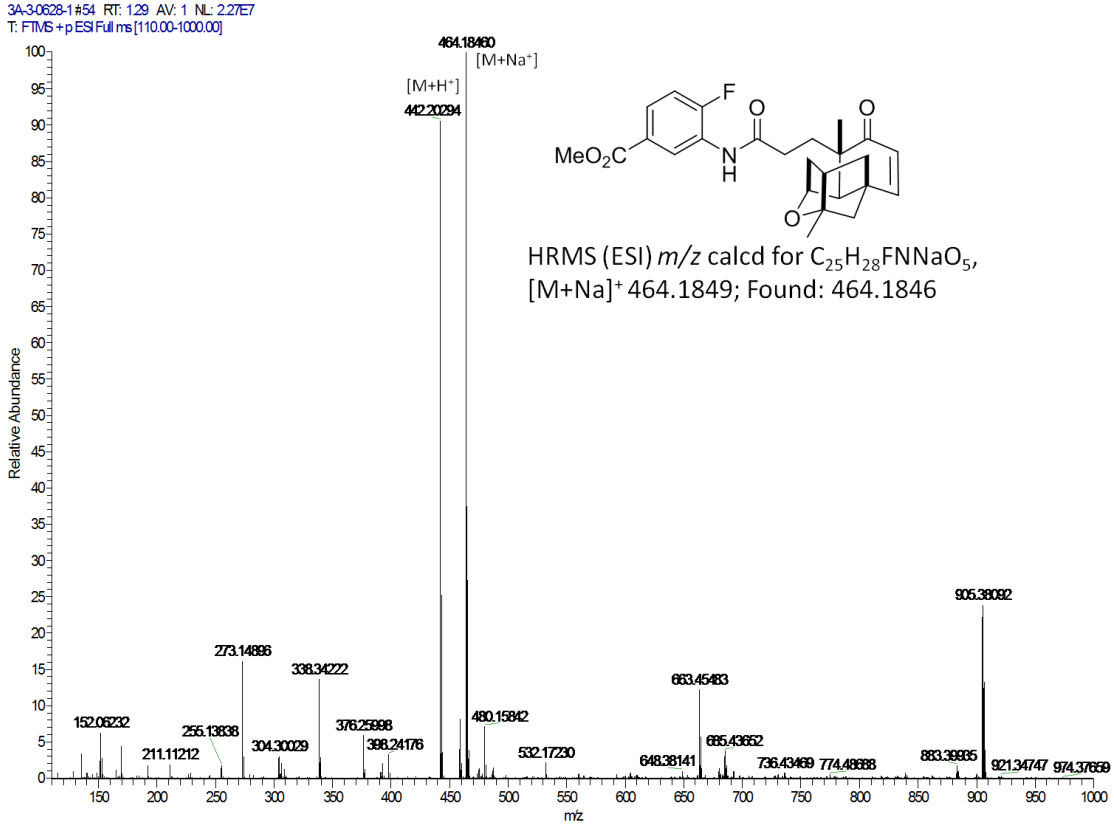
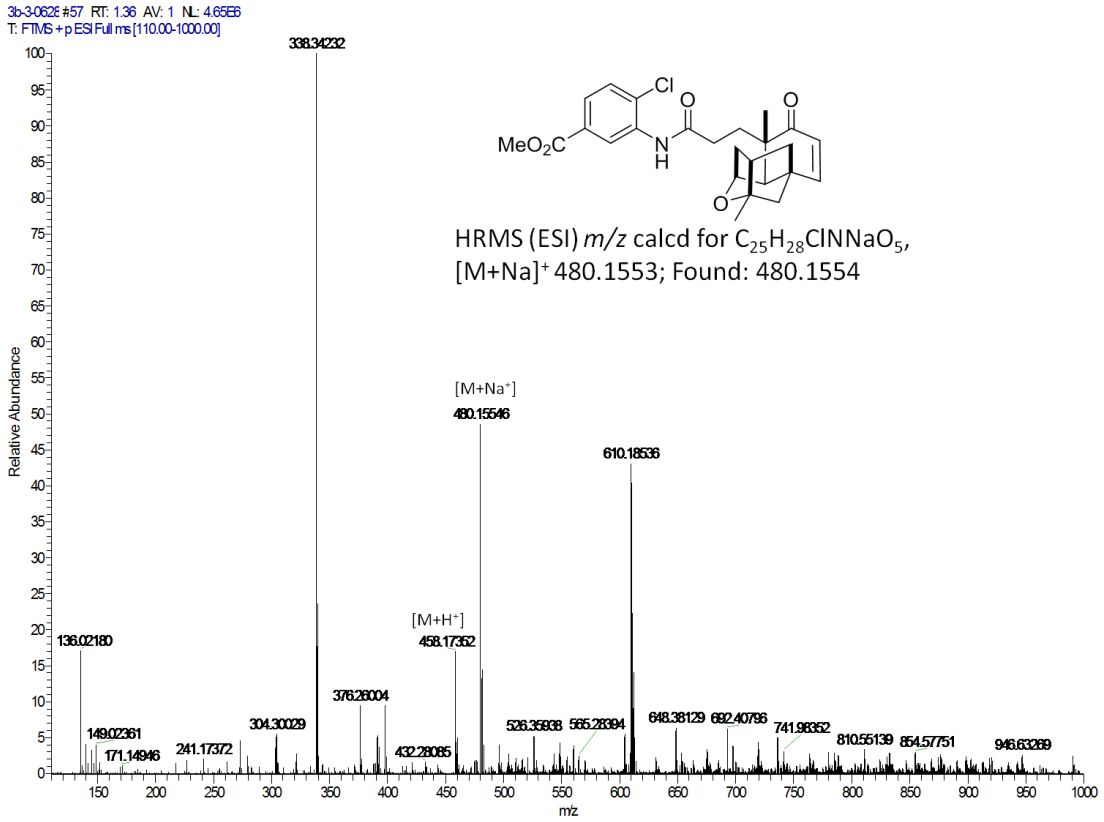


Figure S38. HRMS spectrum of **3c-1** and **3d-1**.



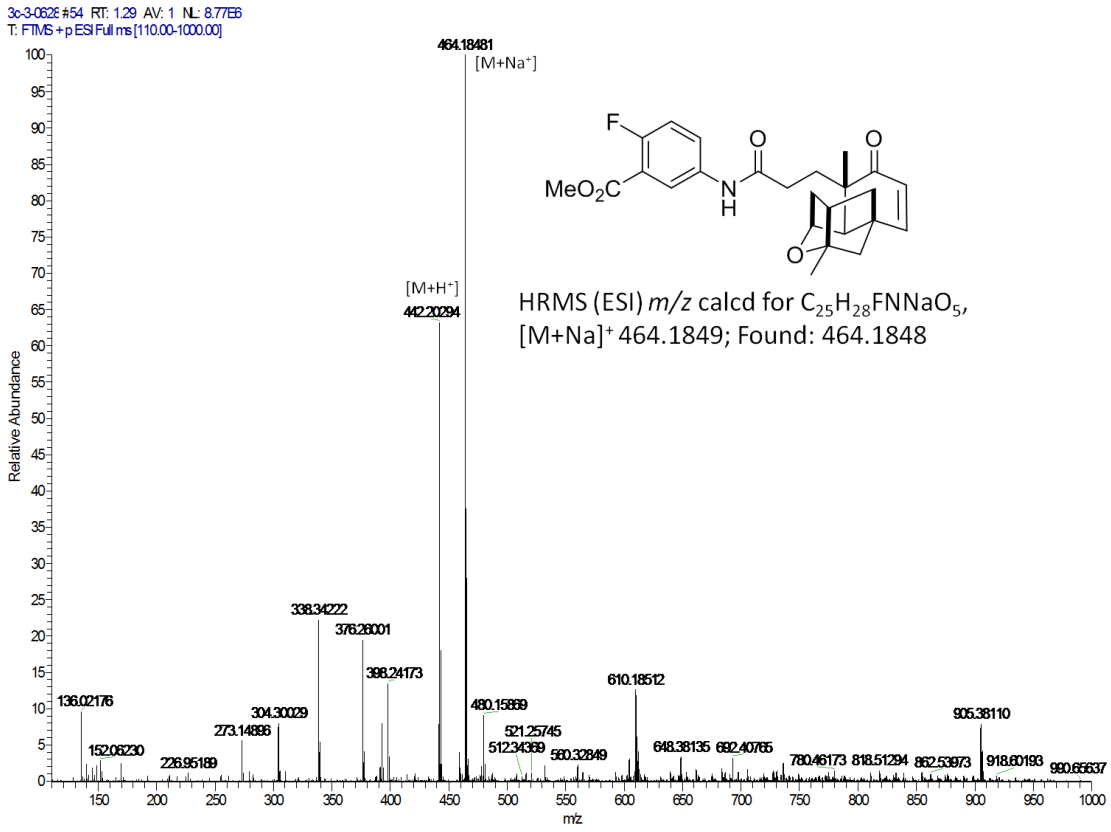


Figure S39. HRMS spectrum of **3e-1** and **3f-1**.

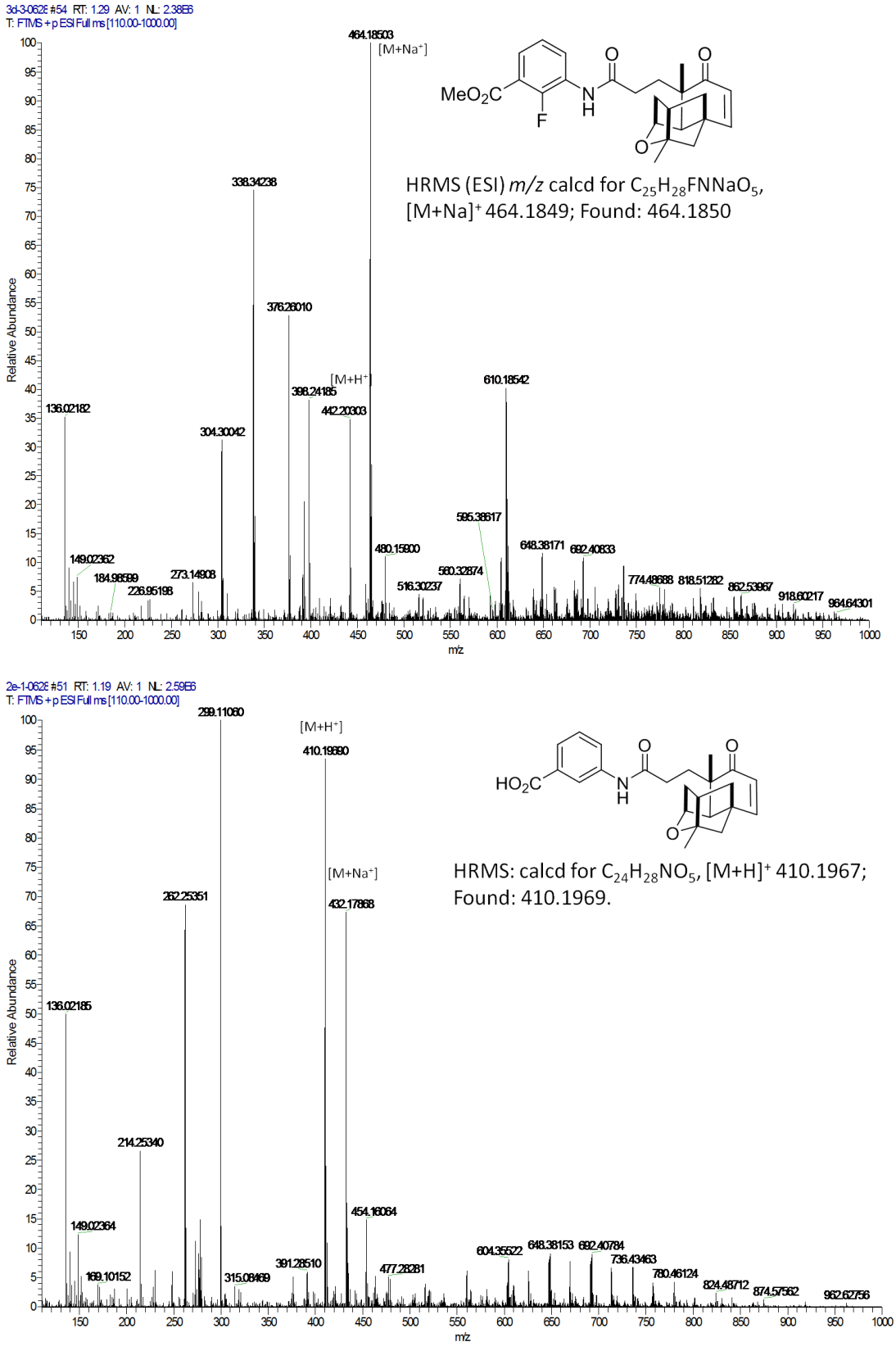
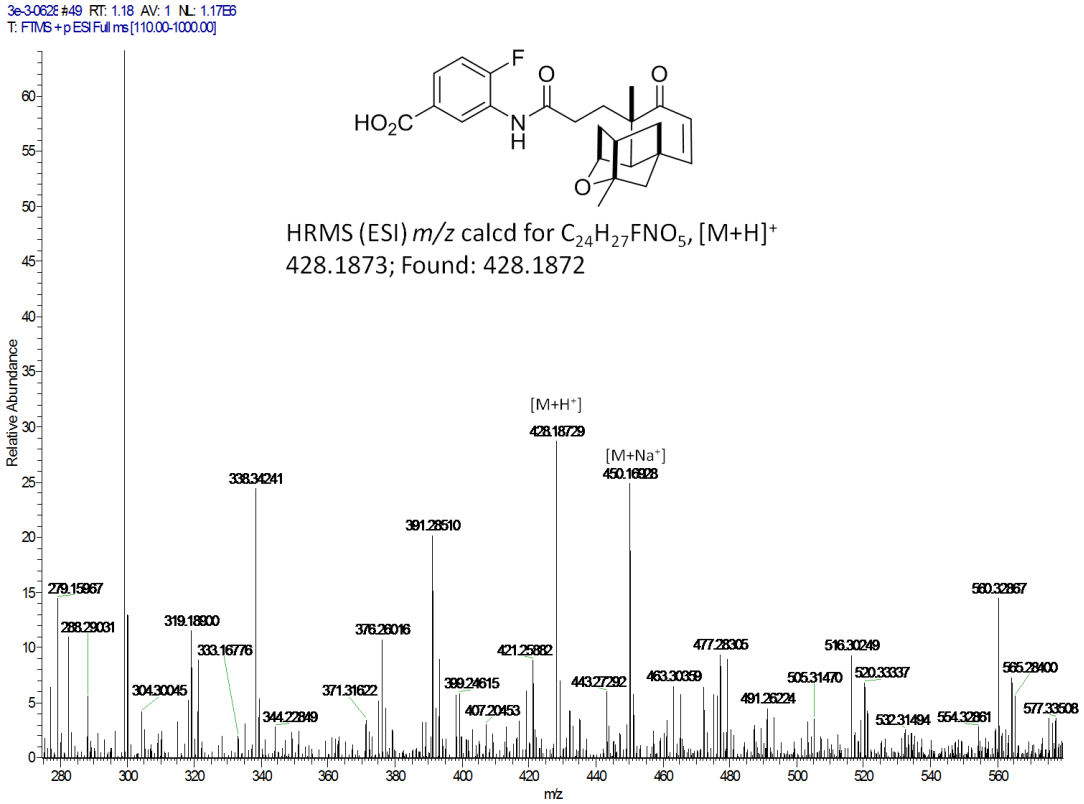


Figure S40. HRMS spectrum of **3g-1** and **3h-1**.



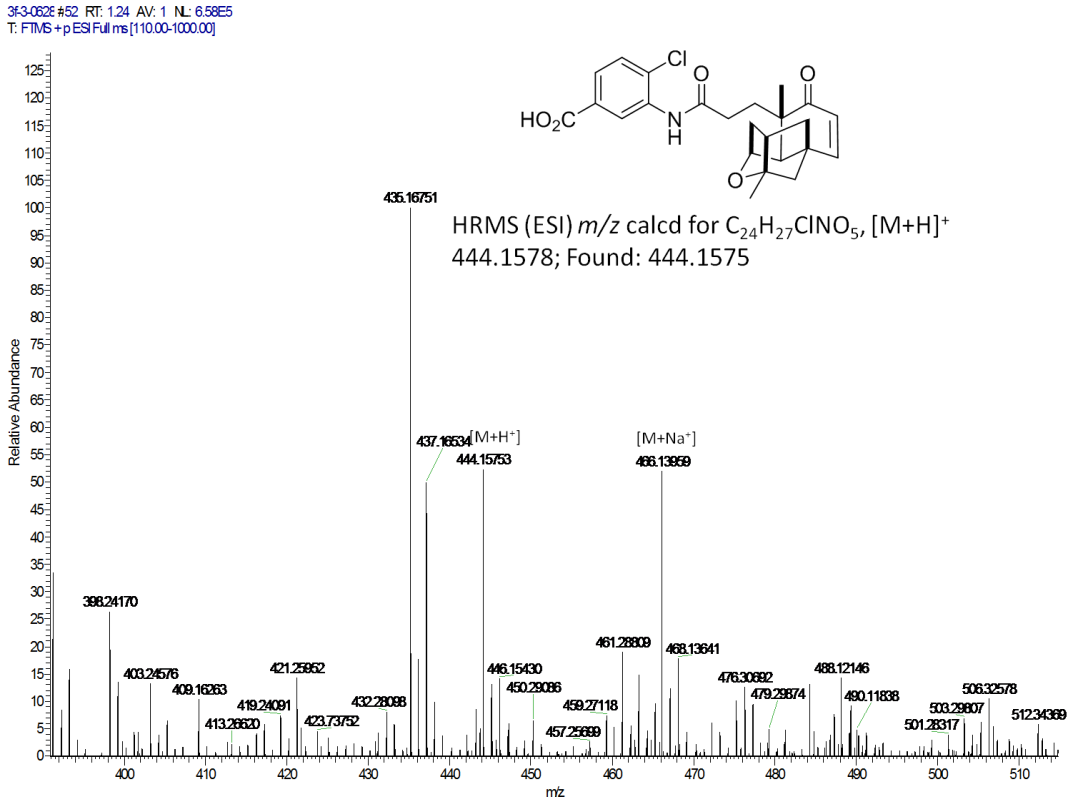
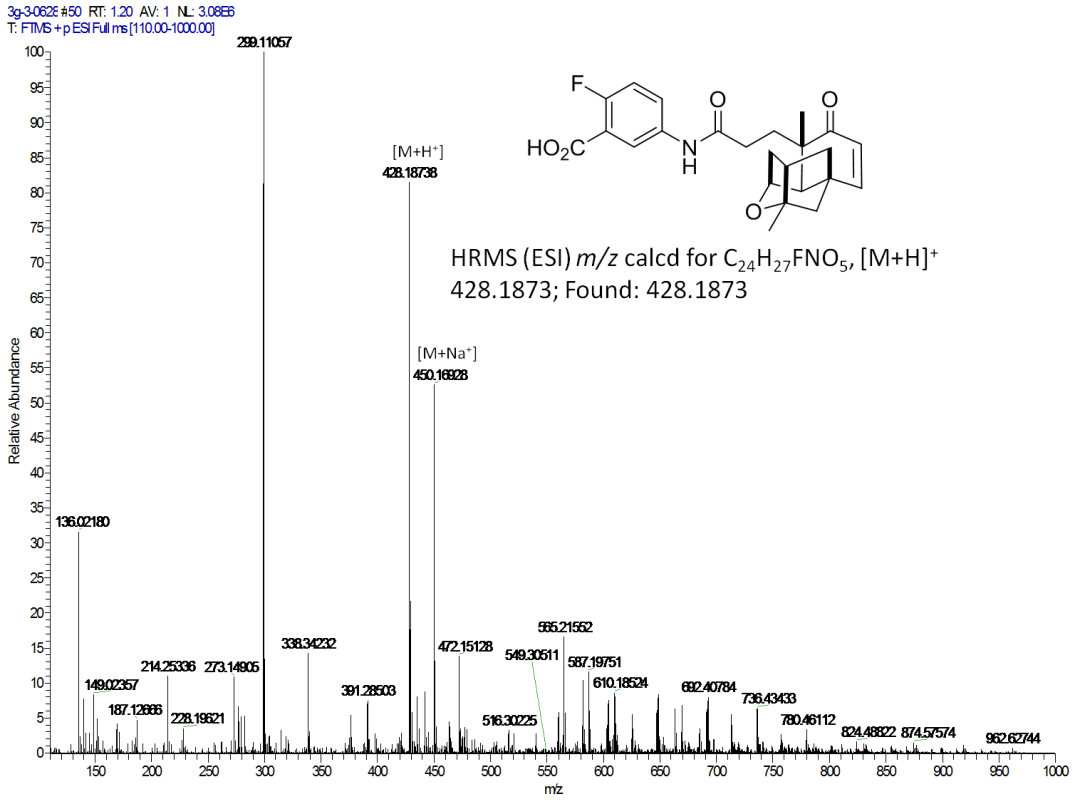


Figure S41. HRMS spectrum of **3i-1** and **3j-1**.



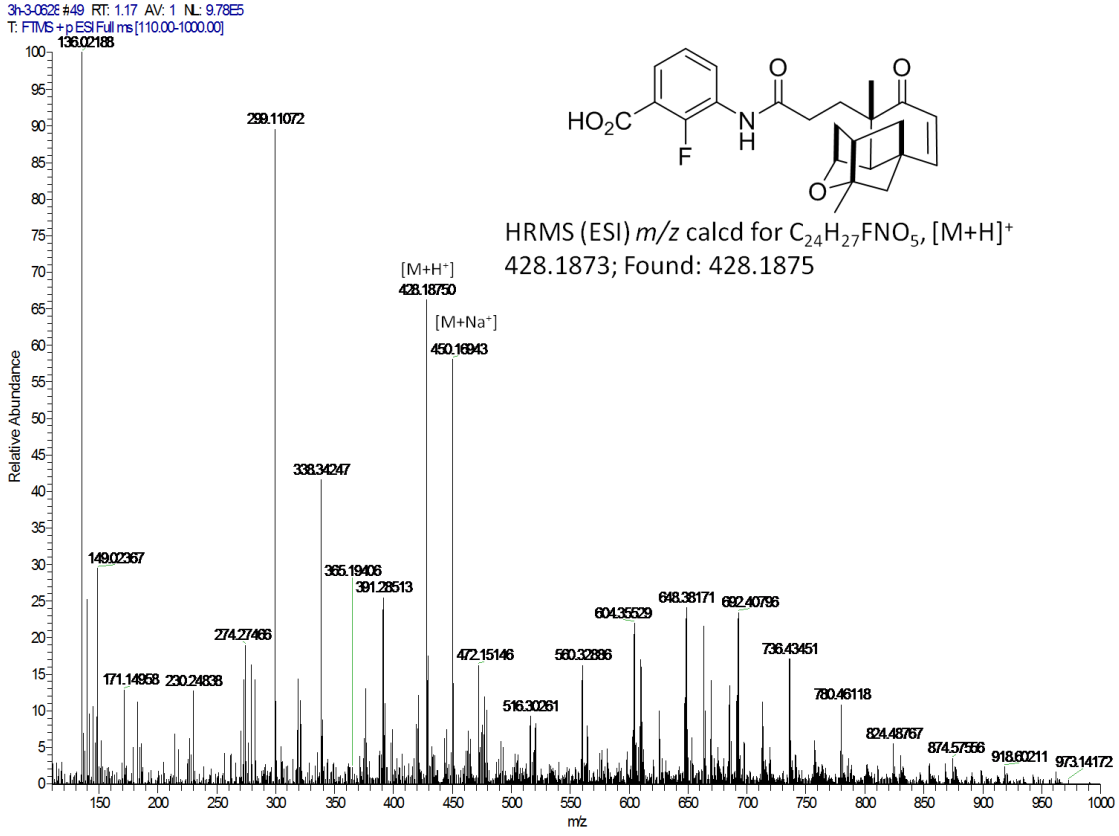
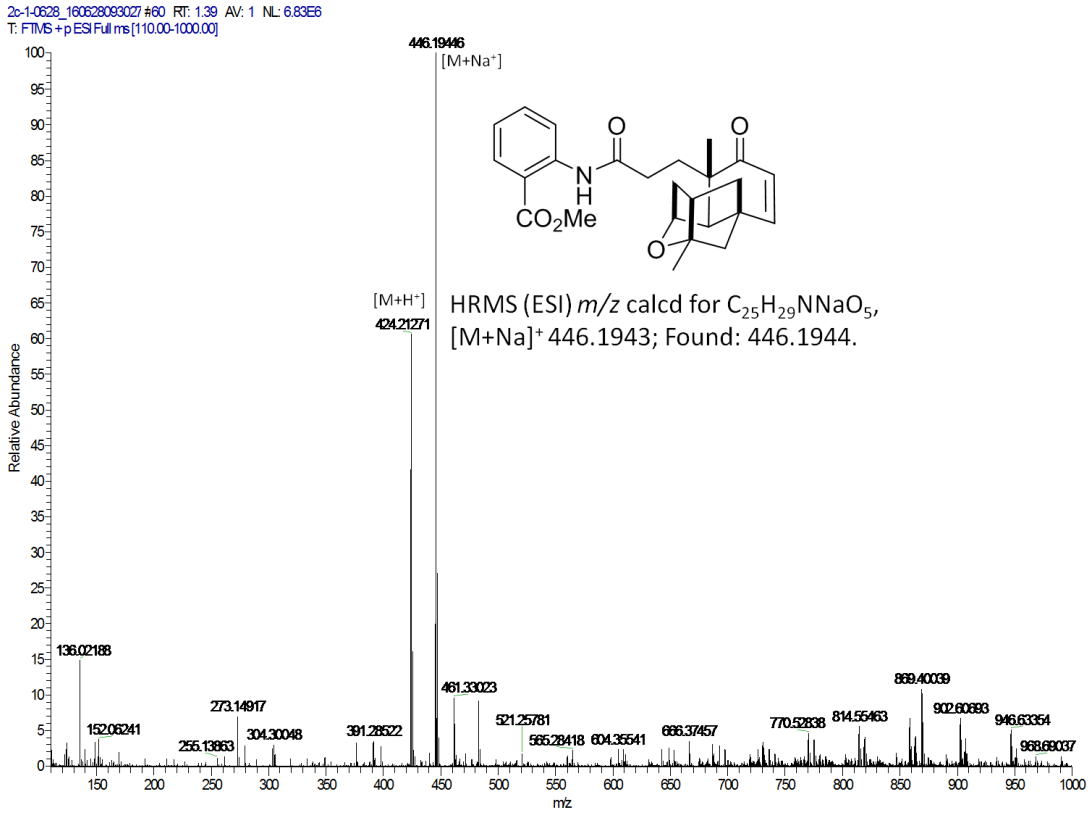


Figure S42. HRMS spectrum of **3a-2** and **3b-2**.



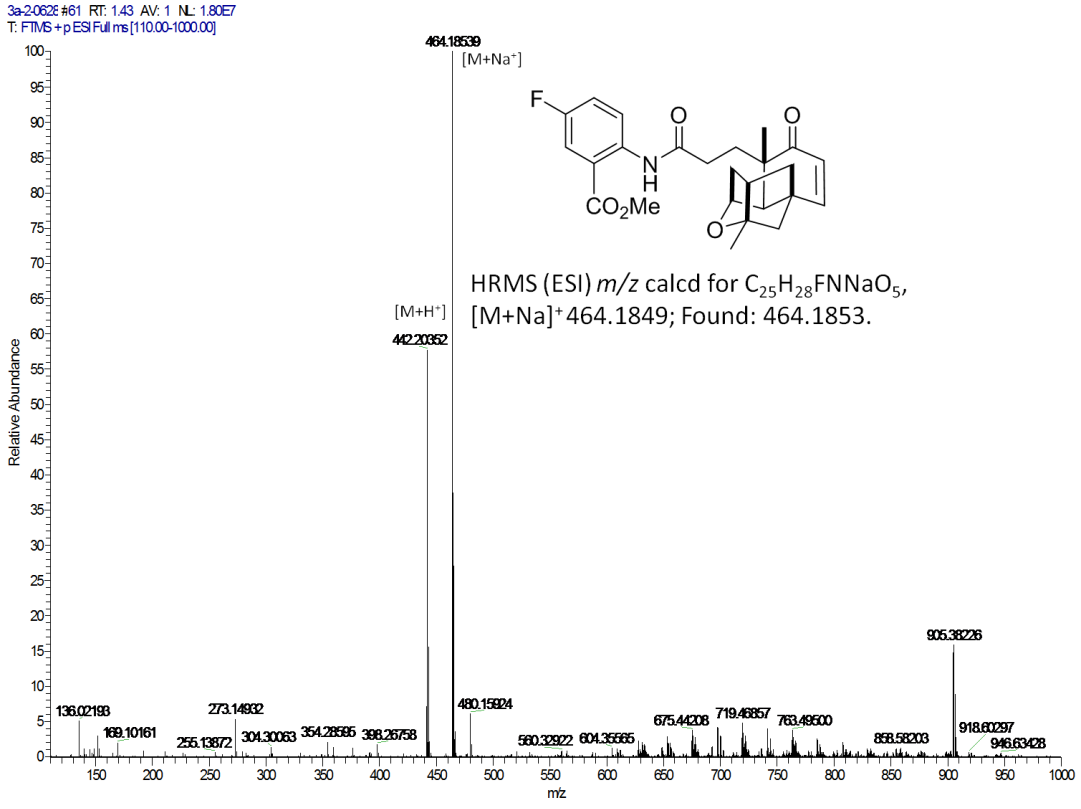
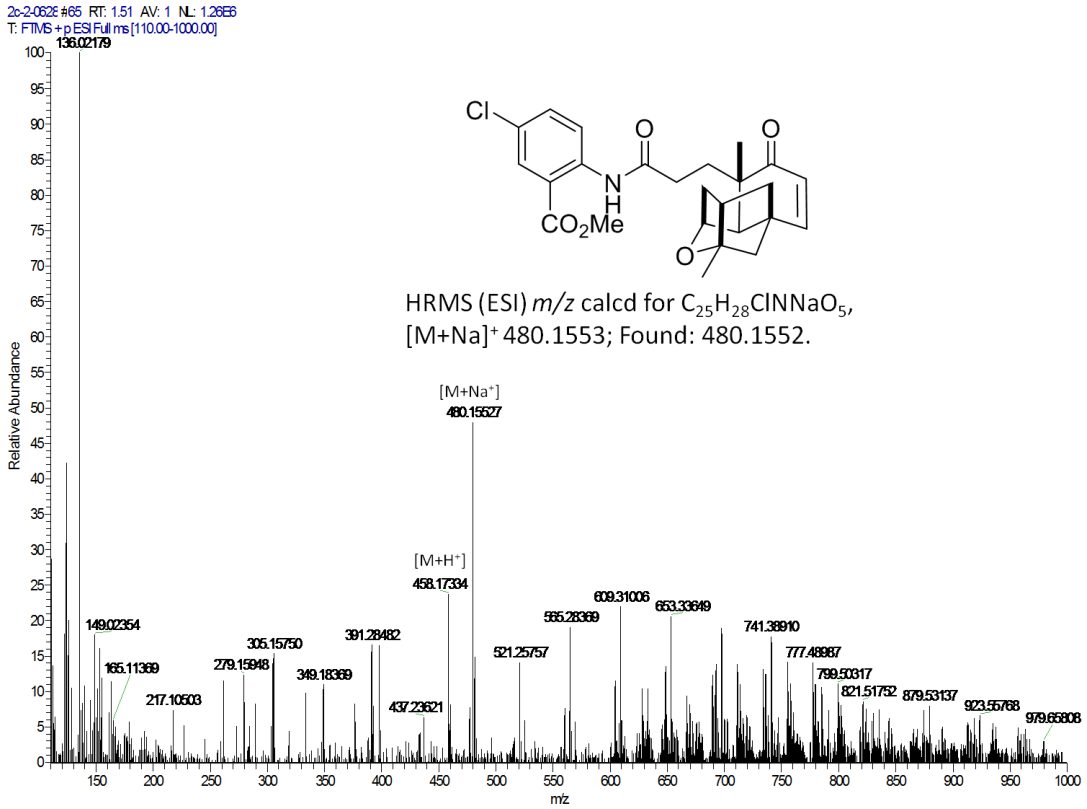


Figure S43. HRMS spectrum of **3c-2** and **3d-2**.



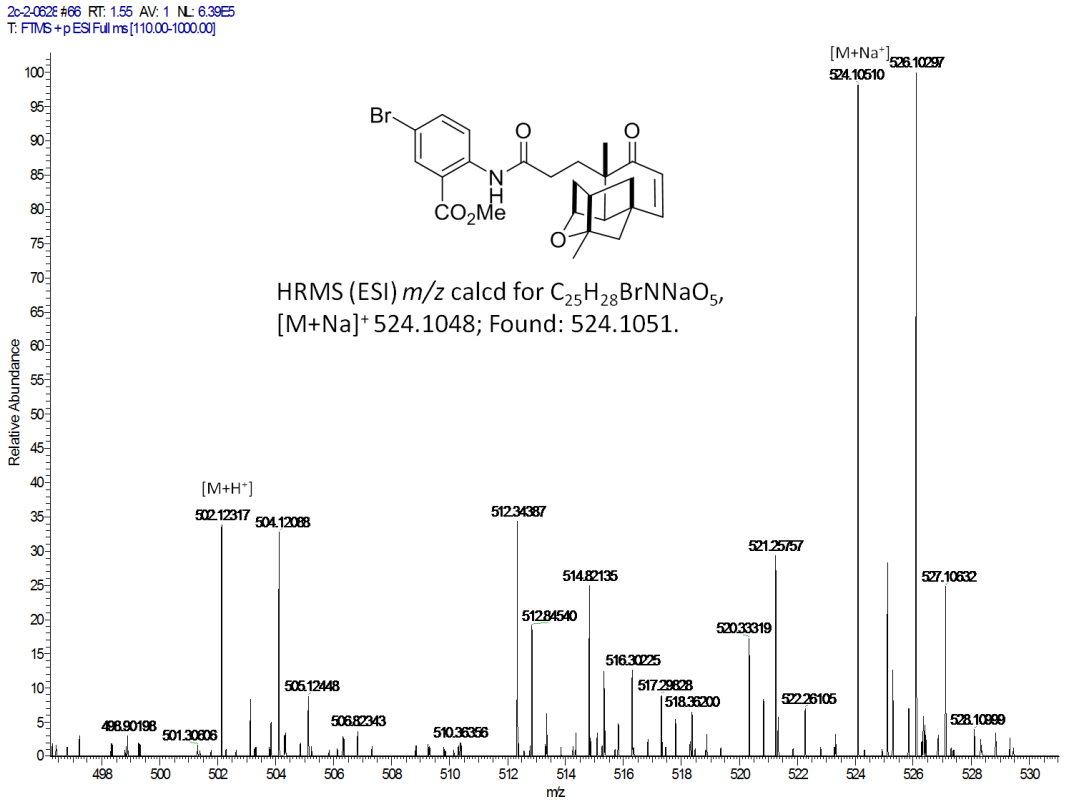
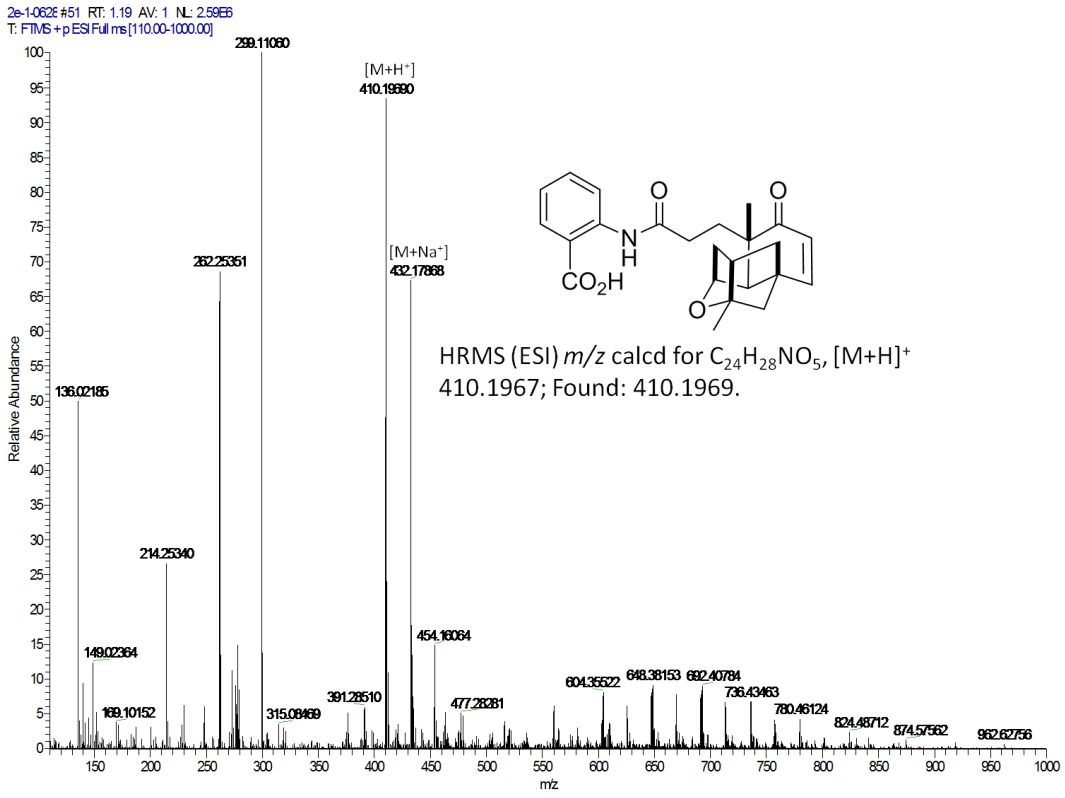


Figure S44. HRMS spectrum of **3h-2** and **3i-2**.



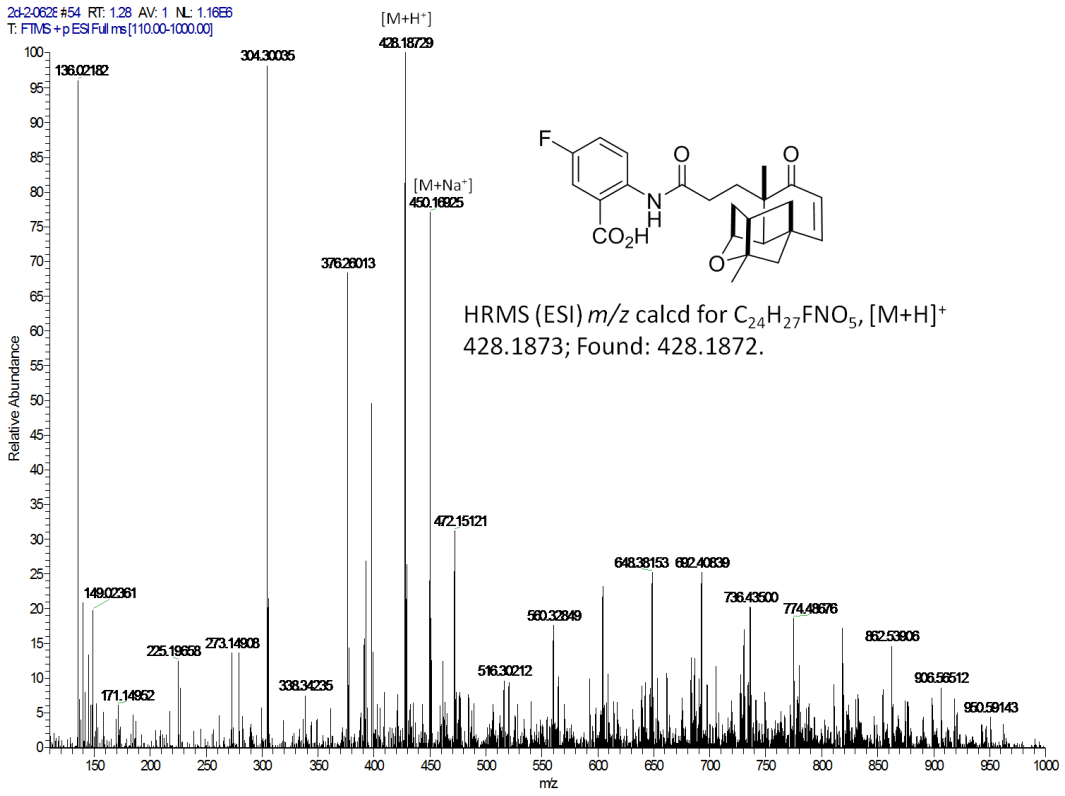
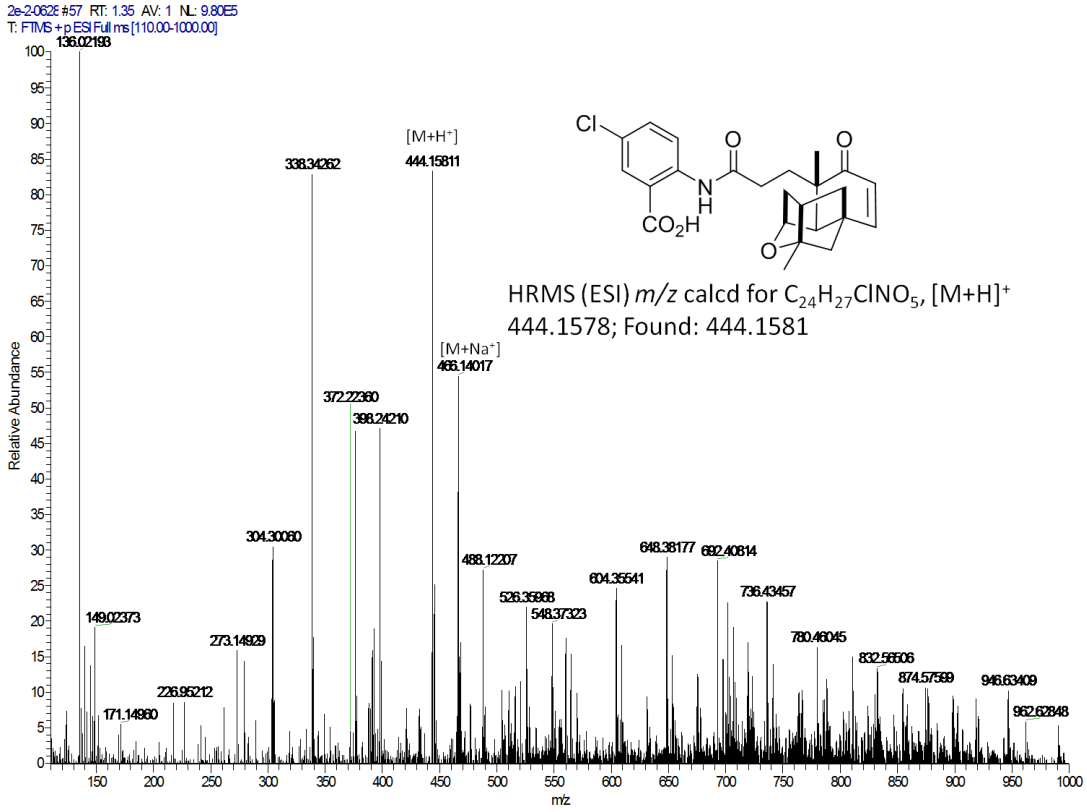


Figure S45. HRMS spectrum of **3j-2** and **3k-2**.



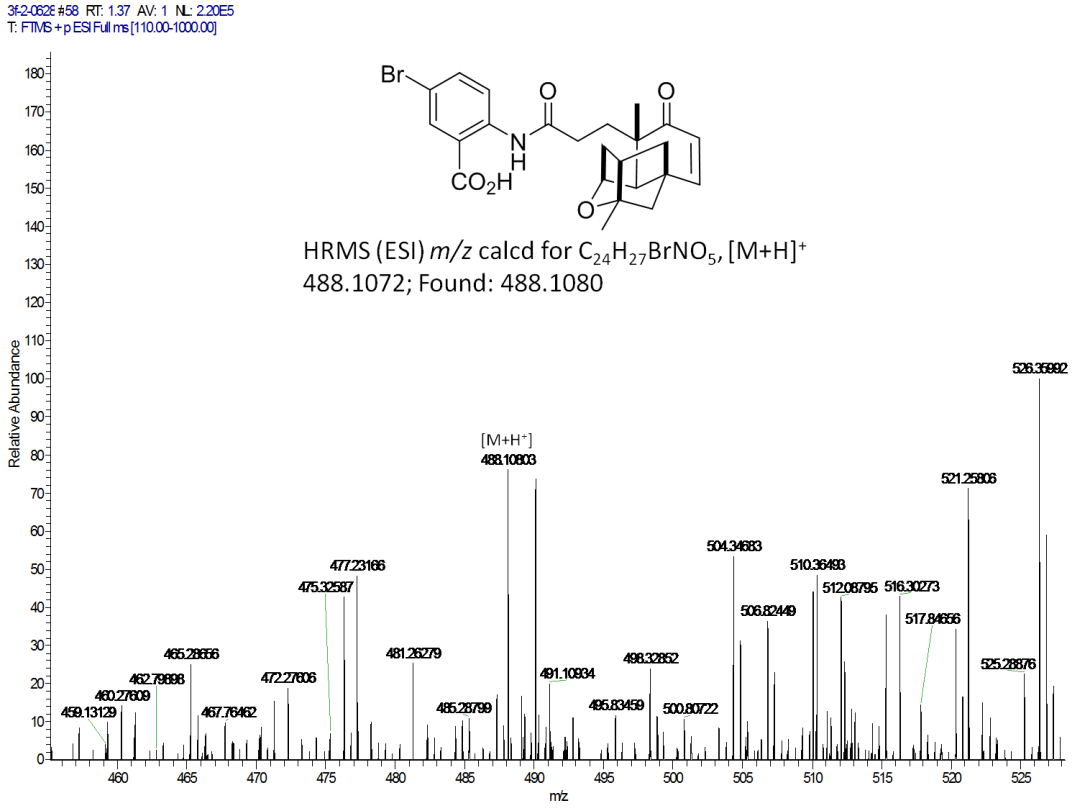
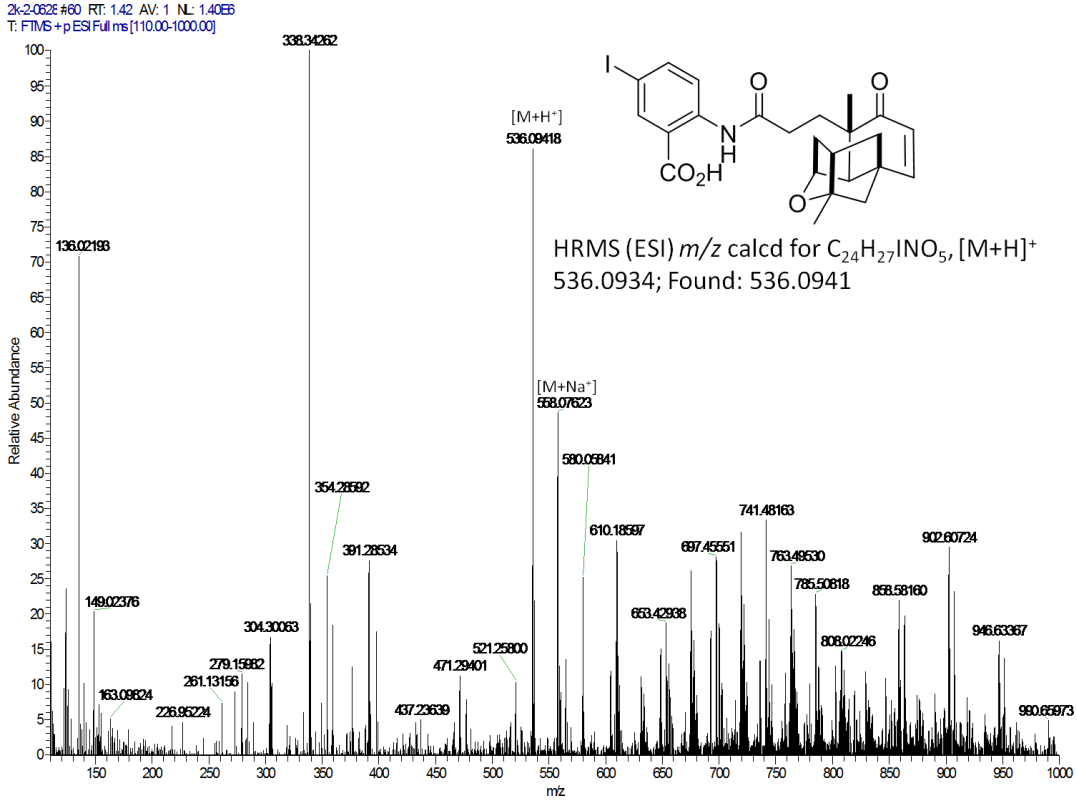


Figure S46. HRMS spectrum of **3l-2** and **3m-2**.



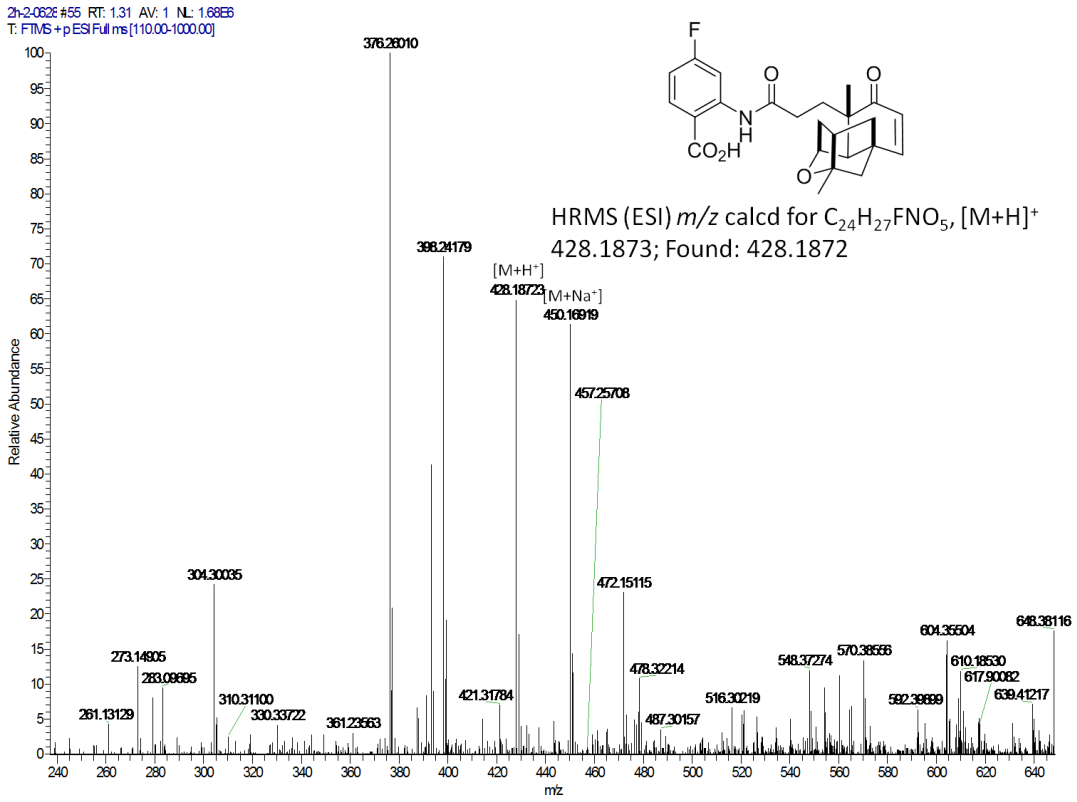
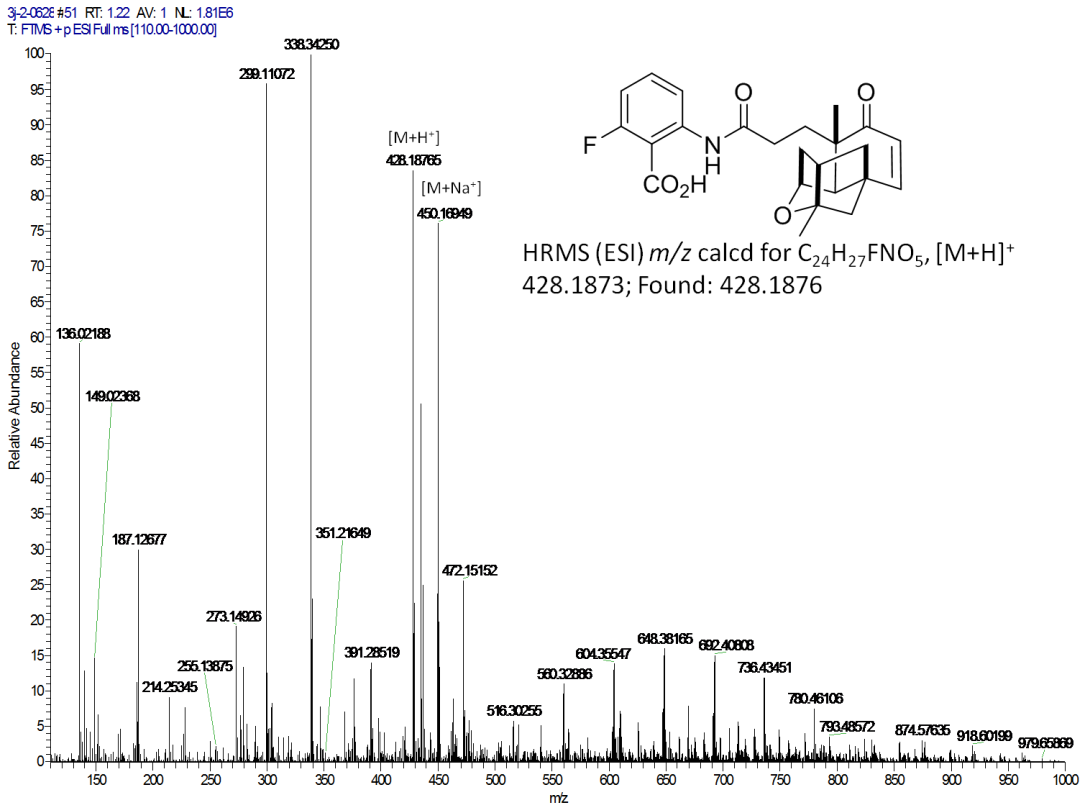


Figure S47. HRMS spectrum of **3o-2** and **3p-2**.



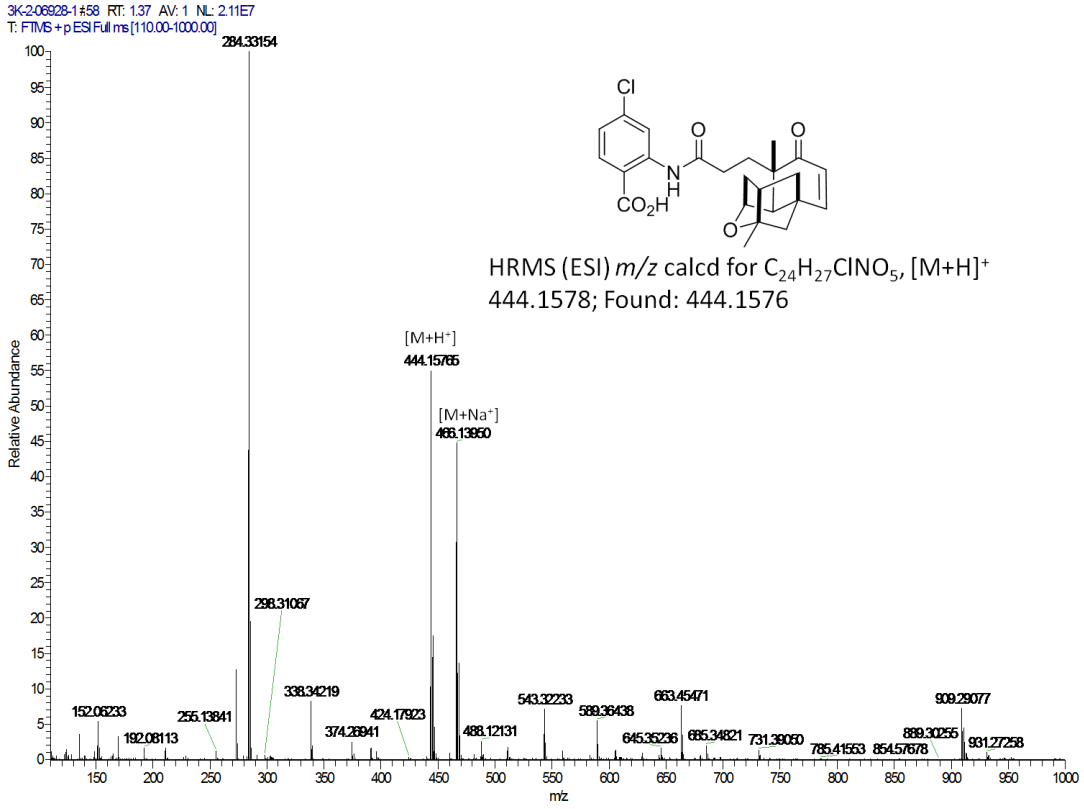
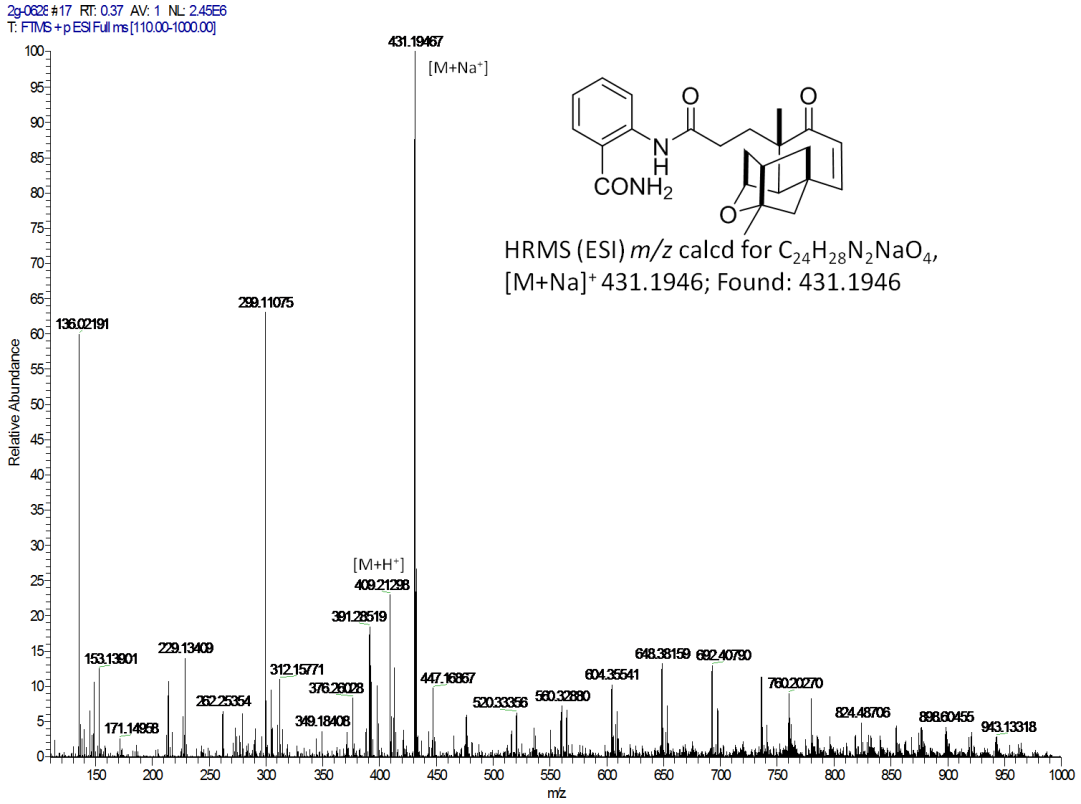


Figure S48. HRMS spectrum of **3q-2** and **3r-2**.



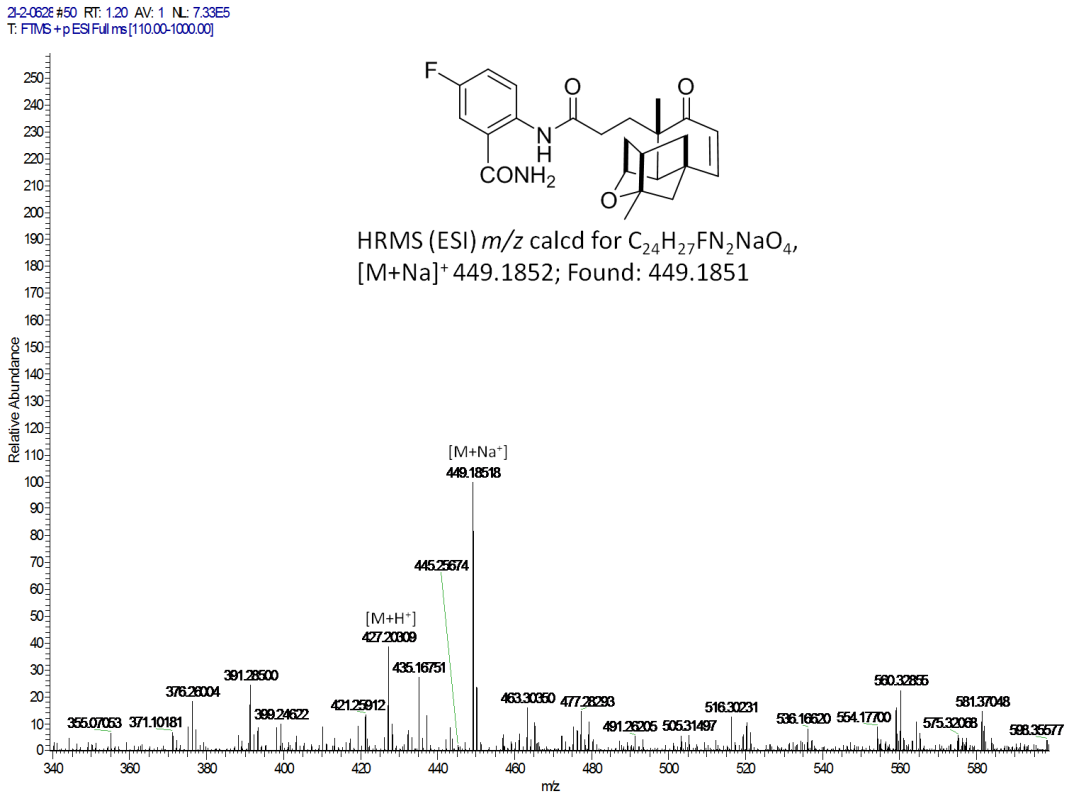
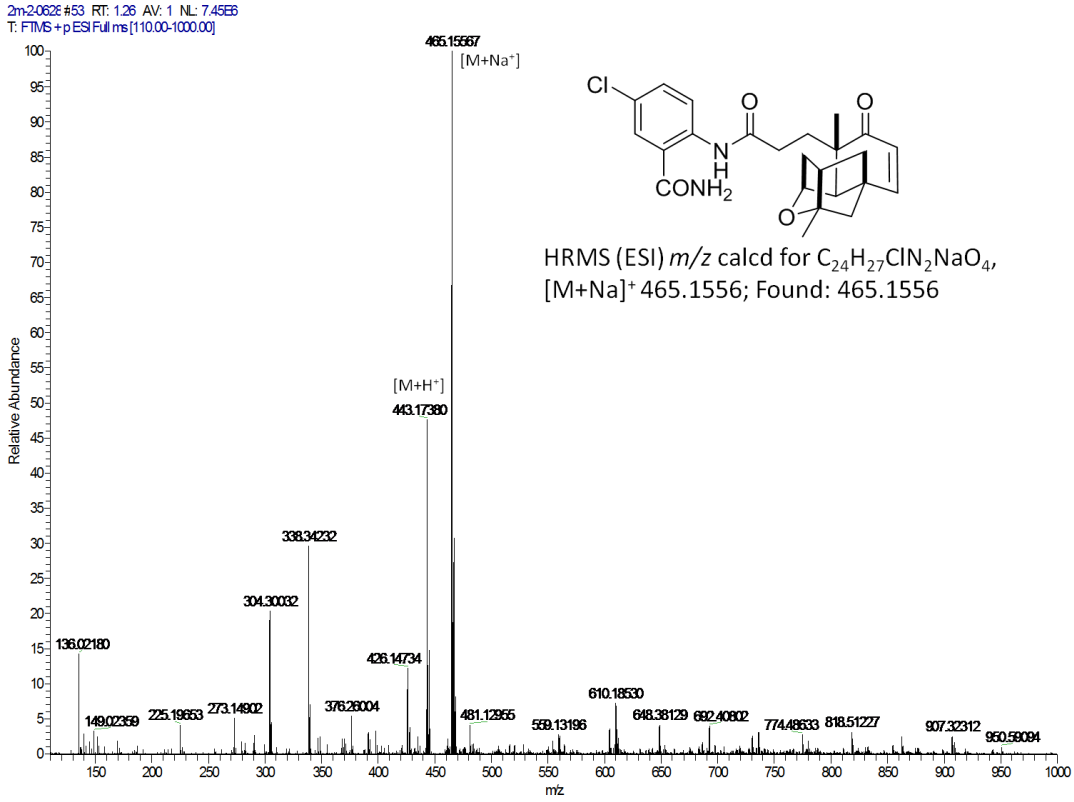


Figure S49. HRMS spectrum of **3s-2** and **3t-2**.



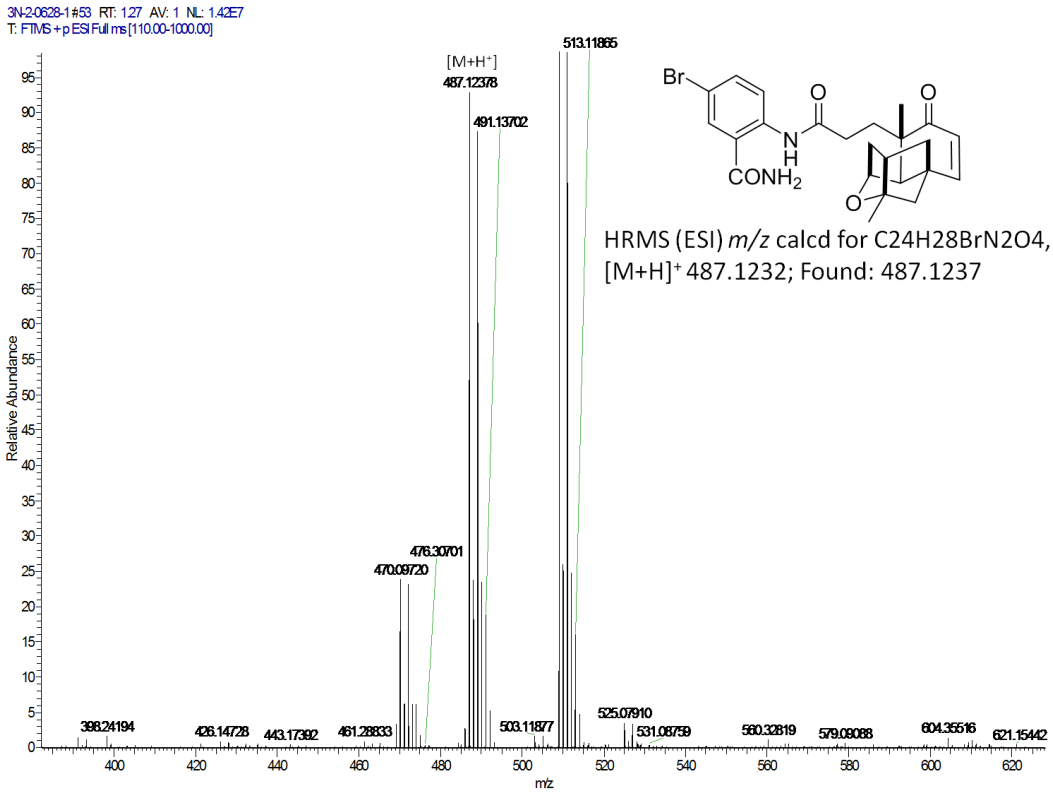


Figure S50. HRMS spectrum of **3u-2** and **3w-2**.