Supporting Information

for

Formal [3+3] Cycloaddition of Indol-2-yl Carbinol with Azadiene and the Subsequent Oxidative Ring Expansion Reaction for the Synthesis of Indole Azepinones

Xue Zhong,[a,b] You Li,[a] Wu-Xia Zhang,[a,b] Jing Zhang,[a,b] Shi-Xue Wang,[a] and Fu-She Han*[a,c]

[a] *Changchun Institute of applied Chemistry, Chinese Academy of Sciences, 5625 Renmin Street, Changchun 130022, China*

[b] *Graduate School of Chinese Academy of Sciences, Beijing 100864, China*

[c] *Key Lab of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, CAS, China*

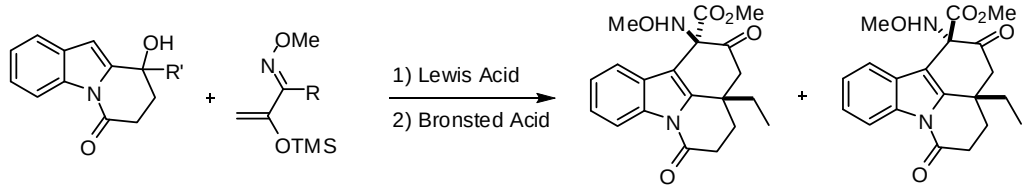
Contents:

General information

The ^{1}H-NMR spectra were recorded at 600 MHz, 400 MHz or 300MHz in $CDCl_3$ or DMSO-d6, and the ^{13}C-NMR spectra were recorded at 150 MHz in $CDCl_3$ or DMSO-d6 with TMS as internal standard. All shifts were given in ppm. All coupling constants (*J* values) were reported in Hertz (Hz). High resolution mass spectra (HRMS) were obtained on an IonSpec Ultima 7.0 T FT-ICR-MS (IonSpec, USA) with a Waters Z-spray source. Column chromatography was performed on silica gel 200-300 mesh. All reagents were commercial grades and were used without any purification unless otherwise noted. Anhydrous triethylamine, 1,2-dichloroethane, dichloromethane, and acetonitrile were obtained by distillation from calcium hydride under nitrogen. Anhydrous tetrahydrofuran was distilled according to the standard procedure. All other solvents were used without further purification.

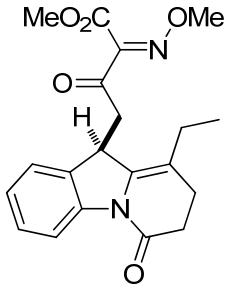
Experimental Procedures and Characterization Data

General procedures for one-pot [3+3] Cyclization:



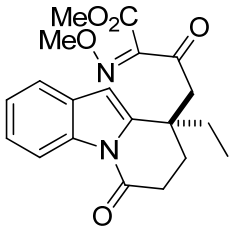
6 **7** *cis*-**3** (major) *trans*-**3** (minor)

To a solution of the tertiary alcohol **6** (0.42 mmol) and *aza*-Danishefsky's diene (**7**) (4.0 eq.) in dry MeCN (4 mL) was added $Hf(OTf)_4$ (5 mol%) at -40 ^oC. The reaction mixture was stirred at the same temperature until **6** had disappeared as monitored by TLC. Then TfOH (1.5 eq.) was recharged to the reaction vessel and the reaction mixture was stirred at 15 ^oC for 36 h. The reaction mixture was diluted with dichloromethane (50 mL) and washed sequentially with saturated aqueous Na_2CO_3 (15 mL) and $NaHCO_3$ (15 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by flash column chromatography on silica gel to give the desired products.



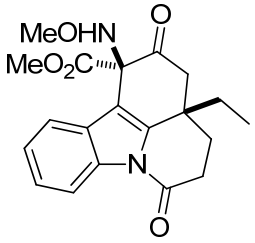
9

^{1}H-NMR (400 MHz, CD_3OD) δ: 8.08 (d, *J* = 7.6 Hz, 1H), 7.29–7.16 (m, 2H), 7.06 (t, *J* = 6.8 Hz, 1H), 4.52 (s, 1H), 4.03 (s, 3H), 3.81 (s, 3H), 3.30–3.14 (m, 2H), 2.73–2.22 (m, 6H), 1.11 (t, *J* = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, DMSO) δ: 192.47, 166.96, 160.98, 149.28, 140.69, 134.70, 131.63, 127.95, 124.32, 123.62, 115.51, 114.83, 64.52, 52.77, 43.53, 37.31, 31.71, 23.82, 23.09, 12.26.



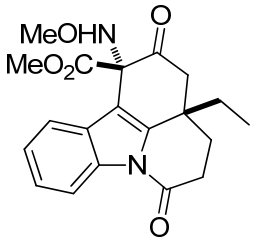
10

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.48 (d, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.41–7.17 (m, 2H), 6.30 (s, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 3.46 (d, *J* = 14.4 Hz, 1H), 3.04–2.79 (m, 3H), 2.13 (t, *J* = 6.0 Hz, 2H), 1.96 (q, *J* = 7.2 Hz, 2H), 0.97 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 193.22, 168.75, 161.36, 150.17, 142.35, 135.24, 129.45, 124.63, 124.16, 120.27, 116.55, 105.89, 64.51, 52.71, 42.69, 38.20, 30.44, 30.15, 29.90, 8.34. HRMS Calcd for $C_{20}H_{22}N_2NaO_5$ ($M+Na^+$): 393.1426; Found: 393.1439.



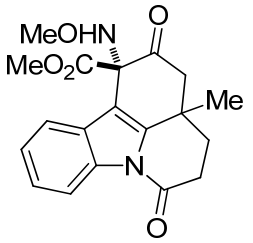
cis-**3a**

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane, and EtOAc as eluent (v/v/v = 15:1:1, then 10:1:1) to give **3a** in 85.3% yield (*cis*-**3a**/*trans*-**3a** = 2.24:1). ^{1}H-NMR of *cis*-**3a** (400 MHz, $CDCl_3$) δ: 8.47 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 3.68 (s, 3H), 3.12 (s, 3H), 3.03 (d, *J* = 14.0 Hz, 1H), 2.99–2.78 (m, 3H), 2.30–2.19 (m, 1H), 2.11–1.96 (m, 1H), 1.96–1.80 (m, 1H), 1.80–1.65 (m, 1H), 0.97 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 203.22, 168.16, 166.69, 144.16, 135.30, 127.47, 125.35, 124.66, 120.05, 116.61, 111.58, 73.17, 62.96, 53.53, 48.00, 36.53, 30.56, 30.11, 28.76, 8.35. HRMS Calcd for $C_{20}H_{22}N_2NaO_5$ ($M+Na^+$): 393.1426; Found: 393.1433.



trans-**3a**

^{1}H-NMR of *trans*-**3a** (400 MHz, $CDCl_3$) δ: 8.46 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 8.0Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 6.91–6.66 (br, 1H), 3.67 (s, 3H), 3.21 (s, 3H), 3.06 (d, *J* = 14.8 Hz,1H), 3.03–2.78 (m, 2H), 2.62 (d, *J* = 14.8 Hz, 1H), 2.32–2.20 (m, 1H), 2.13–1.82 (m, 2H), 1.81–1.64 (m, 1H), 0.98 (t, *J* = 7.6 Hz, 3H). ^{13}C-NMR of *trans*-**3a** (100 MHz, $CDCl_3$) δ: 206.68, 168.23 (2C), 143.63, 135.48, 127.41, 125.39, 124.62, 120.27, 116.64, 111.37, 71.22, 63.31, 53.28, 49.74, 36.29, 30.62, 30.34, 29.26, 8.39.



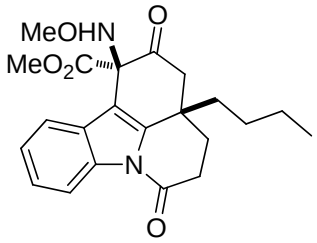
3b

The products were purified by flash column chromatography on silica gel with mixture of petroleum ether, dichloromethane, and EtOAc as eluent (v/v/v = 10:1:1) to give **3b** in 69.7% yield (*cis*/*trans* = 2.21:1).

^{1}H-NMR (400 MHz, $CDCl_3$, *cis*-**3b**) δ: 8.47 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.23–7.01 (br, 1H), 3.68 (s, 3H), 3.11 (s, 3H), 3.08–2.98 (m, 2H), 2.96–2.86 (m, 1H), 2.82 (d, *J* = 14.0 Hz, 1H), 2.31–2.15 (m, 1H), 2.08–1.97 (m, 1H), 1.44 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, *cis*-**3b**) δ: 203.12, 167.93, 166.51, 143.17, 135.17, 127.33, 125.26, 124.58, 119.79, 116.52, 111.49, 72.92, 62.81, 53.35, 52.50, 34.85, 33.34, 30.74, 24.99.

^{1}H-NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.46 (d, *J* = 8.0 Hz, 1H of both isomers), 7.71 (d, *J* = 7.6 Hz, 1H of major isomer), 7.62 (d, *J* = 7.6 Hz, 1H of major isomer), 7.36 (t, *J* = 7.6 Hz, 1H of both isomers), 7.33–7.27 (m, 1H of both isomers), 7.19–6.59 (br, 1H of both isomers), 3.68 (s, 3H of major isomer), 3.67 (s,

3H of minor isomer), 3.22 (s, 3H of minor isomer), 3.11 (s, 3H of major isomer), 3.09–2.73 (m, 4H of both isomers), 2.28–2.14 (m, 2H of both isomers), 2.11–1.99 (m, 2H of both isomers), 1.48 (s, 3H of minor isomer), 1.44 (s, 3H of major isomer). ^{13}C-NMR (100 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 206.62 (1C of minor isomer), 203.07 (1C of major isomer), 167.90 (2C of minor isomer and 1C of major isomer), 166.42 (1C of major isomer), 143.13 (1C of major isomer), 142.57 (1C of minor isomer), 135.19 (1C of major isomer), 135.05 (1C of minor isomer), 127.23 (1C of major isomer), 127.16 (1C of minor isomer), 125.14 (1C of both isomers), 124.48 (1C of major isomer), 124.36 (1C of minor isomer), 120.11 (1C of minor isomer), 119.68 (1C of major isomer), 116.40 (1C of both isomers), 111.35 (1C of major isomer), 111.11 (1C of minor isomer), 72.81 (1C of major isomer), 70.99 (1C of minor isomer), 63.02 (1C of minor isomer), 62.70 (1C of major isomer), 53.96 (1C of major isomer), 53.27 (1C of minor isomer), 53.00 (1C of minor isomer), 52.38 (1C of major isomer), 34.77 (1C of major isomer), 34.71 (1C of minor isomer), 30.65(1C of both isomers), 25.29 (1C of minor isomer), 24.88 (1C of major isomer). HRMS Calcd for $C_{19}H_{20}N_2NaO_5$ ($M+Na^+$): 379.1270; Found: 379.1262.

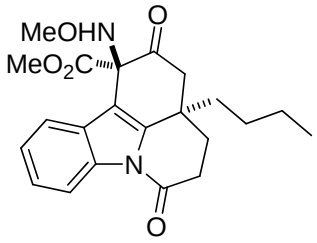


cis-**3c**

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 15:1:1) to give **3c** in 73.6% yield (*cis*/*trans* = 2.24:1). HRMS Calcd for $C_{22}H_{26}N_2NaO_5$ ($M+Na^+$): 421.1739; Found: 421.1744.

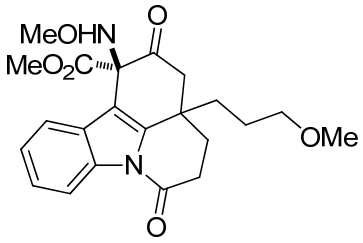
^{1}H-NMR (400 MHz, $CDCl_3$, *cis*-**3c**) δ: 8.46 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 3.68 (s, 3H), 3.12 (s, 3H), 3.08–2.79 (m, 4H), 2.31–2.18 (m, 1H), 2.11–1.97 (m, 1H), 1.86–1.73 (m, 1H), 1.73–1.60 (m, 1H), 1.47–1.19 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, *cis*-**3c**) δ: 202.03, 167.02, 165.55, 143.01, 134.10, 126.29, 124.15, 123.48, 118.84, 115.44, 110.30, 71.91, 61.74, 52.35, 47.52, 35.23, 34.67, 29.60, 29.51, 24.86,

21.84, 12.83.



trans-**3c**

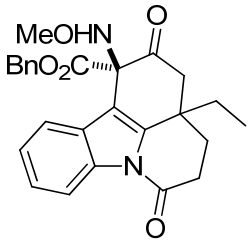
^{1}H-NMR (300 MHz, $CDCl_3$, *trans*-**3c**) δ: 8.46 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.36 (m, 1H), 7.29 (m, 1H), 6.76 (br, 1H), 3.67 (s, 3H), 3.21 (s, 3H), 3.07 (d, *J* = 14.7 Hz, 1H), 3.02–2.79 (m, 2H), 2.63 (d, *J* = 14.7 Hz, 1H), 2.31–2.20 (m, 1H), 2.09–1.93 (m, 1H), 1.91–1.78 (m, 1H), 1.74–1.60 (m, 1H), 1.43–1.25 (m, 4H), 0.90 (t, *J* = 6.6 Hz, 3H). ^{13}C-NMR **(**150 MHz, $CDCl_3$, *trans*-**3c**) δ: 206.64, 168.17 (2C), 143.56, 135.38, 127.33, 125.29, 124.53, 120.20, 116.56, 111.17, 71.37, 63.22, 53.11, 50.37, 36.32, 36.08, 30.95, 30.66, 25.96, 23.00, 13.93.



3d

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 5:1:1) to give **3d** in 47.4% yield (*cis/trans* = 2.84:1). ^{1}H-NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.46 (d, *J* = 8.0 Hz, 1H of both isomers), 7.65 (d, *J* = 7.6 Hz, 1H of both isomers), 7.36 (t, *J* = 7.6 Hz, 1H of both isomers), 7.32 (t, *J* = 7.6 Hz, 1H of both isomers), 3.68 (s, 3H of both isomers), 3.46-3.33 (m, 1H of both isomers), 3.33–3.25 (m, 4H of both isomers), 3.21 (s, 3H of minor isomer), 3.13 (s, 3H of major isomer), 3.07–2.79 (m, 4H of major isomer and 3H of minor isomer), 2.66 (d, *J* = 16.4 Hz, 1H of minor isomer), 2.31–2.19 (m, 1H of both isomers), 2.14–1.87 (m, 2H of both isomers), 1.76–1.63 (m, 2H of both isomers), 1.63–1.49 (m, 1H of both isomers). ^{13}C-NMR (100 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 206.25 (1C of minor isomer), 203.04 (1C of major isomer), 168.11 (1C of major isomer and 2C of minor

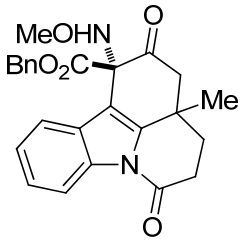
isomer), 166.58 (1C of major isomer), 143.74 (1C of major isomer), 142.97 (1C of minor isomer), 135.22 (1C of both isomers), 127.31 (1C of both isomers), 125.32 (1C of both isomers), 124.58 (1C of both isomers), 120.15 (1C of minor isomer), 119.97 (1C of major isomer), 116.55 (1C of both isomers), 111.53 (1C of major isomer), 111.27 (1C of minor isomer), 73.07 (1C of minor isomer), 72.21 (1C of major isomer), 63.20 (1C of minor isomer), 62.88 (1C of major isomer), 58.68 (1C of both isomers), 53.46 (1C of major isomer), 53.10 (1C of minor isomer), 50.26 (1C of minor isomer), 48.58 (1C of major isomer), 36.20 (1C of major isomer), 35.90 (1C of minor isomer), 33.11 (1C of minor isomer), 32.58 (1C of major isomer), 31.00 (1C of minor isomer), 30.80 (1C of major isomer), 30.51 (1C of both isomers), 24.22 (1C of both isomers). HRMS Calcd for $C_{22}H_{26}N_2NaO_6$ ($M+Na^+$): 437.1689; Found: 437.1699.



3e

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 15:1:1, 10:1:1) to give **3e** in 90.0% yield (*cis*/*trans* = 2.44:1). ^{1}H-NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.45 (d, *J* = 8.0 Hz, 1H of both isomers), 7.64 (d, *J* = 7.6 Hz, 1H of minor isomer), 7.57 (d, *J* = 7.6 Hz, 1H of major isomer), 7.35 (t, *J* = 7.6 Hz, 8.0 Hz, 1H of both isomers), 7.31–7.19 (m, 5H of both isomers), 7.15–7.06 (m, 2H of both isomers), 6.91–6.69 (br, 1H of minor isomer), 5.23–5.13 (m, 1H of both isomers), 5.10–4.97 (m, 1H of both isomers), 3.21 (s, 3H of minor isomer), 3.11 (s, 3H of major isomer), 3.07–2.96 (m, 1H of both isomers), 2.96–2.76 (m, 3H of major isomer, 2H of minor isomer), 2.58 (d, *J* = 14.8 Hz, 1H of minor isomer), 2.27–2.15 (m, 1H of both isomers), 2.05–1.91 (m, 1H of both isomers), 1.91-1.53 (m, 4H of both isomers), 0.95 (t, *J* = 7.6 Hz, 1H of major isomer), 0.82 (t, *J* = 7.6 Hz, 1H of minor isomer). ^{13}C-NMR (100 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 206.55 (1C of both isomers), 202.88 (1C of both isomers), 167.98 (2C of minor isomer), 167.32 (1C of major isomer), 165.81 (1C of major isomer), 143.85 (1C of major isomer), 143.40 (1C of minor isomer), 135.18 (1C of minor isomer), 135.04 (1C of major isomer),

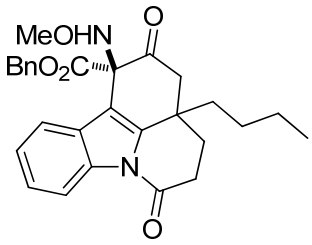
134.49 (1C of both isomers), 128.50 (3C of major isomer), 128.33 (3C of minor isomer), 128.07 (2C of minor isomer), 127.97 (2C of major isomer), 127.18 (1C of major isomer), 127.10 (1C of minor isomer), 125.10 (1C of both isomers), 124.35 (1C of major isomer), 124.32 (1C of minor isomer), 120.17 (1C of minor isomer), 120.02 (1C of major isomer), 116.30 (1C of both isomers), 111.42 (1C of major isomer), 111.08 (1C of minor isomer), 73.20 (1C of major isomer), 71.07 (1C of minor isomer), 67.96 (1C of major isomer), 67.77 (1C of minor isomer), 63.06 (1C of minor isomer), 62.72 (1C of major isomer), 49.54 (1C of minor isomer), 47.79 (1C of major isomer), 36.28 (1C of major isomer), 35.96 (1C of minor isomer), 30.33 (1C of both isomers), 30.01 (1C of minor isomer), 29.90 (1C of major isomer), 28.91 (1C of minor isomer), 28.57 (1C of major isomer), 8.11 (1C of major isomer), 7.98 (1C of minor isomer). HRMS Calcd for $C_{26}H_{26}N_2NaO_5$ ($M+Na^+$): 469.1739; Found: 469.1732.



3f

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 10:1:1) to give **3f** in 67.0% yield (*cis*/*trans* = 1.86:1). ^{1}H-NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.45 (d, *J* = 8.0 Hz, 1H of both isomers), 7.67 (d, *J* = 7.6 Hz, 1H of minor isomer), 7.53 (d, *J* = 7.6 Hz, 1H of major isomer), 7.35 (t, *J* = 7.6 Hz, 1H of both isomers), 7.31–7.18 (m, 4H of both isomers), 7.15–7.04 (m, 2H of both isomers), 5.25–5.11 (m, 1H of both isomers), 5.11–4.95 (m, 1H of both isomers), 3.22 (s, 3H of minor isomer), 3.10 (s, 3H of major isomer), 3.08–2.72 (m, 4H of both isomers), 2.25–2.11 (m, 1H of both isomers), 2.08–1.96 (m, 1H of both isomers), 1.43 (s, 3H of major isomer), 1.34 (m, 3H of minor isomer). ^{13}C-NMR (100 MHz, $CDCl_3$, mixture of diastereomers) δ: 206.52 (1C of minor isomer), 202.88 (1C of major isomer), 167.86 (2C of minor isomer), 167.28 (1C of major isomer), 165.74 (1C of major isomer), 143.04 (1C of major isomer), 142.56 (1C of minor isomer), 135.13 (1C of minor isomer), 134.96 (1C of major isomer), 134.51 (1C of minor isomer), 134.44

(1C of minor isomer), 128.44 ((3C of major isomer), 128.28 (3C of minor isomer), 127.93 (2C of major isomer), 127.87 (1C of minor isomer), 127.13 (1C of major isomer), 127.06 (1C of minor isomer), 125.06 (1C of both isomers), 124.33 (1C of major isomer), 124.28 (1C of minor isomer), 120.16 (1C of minor isomer), 119.84 (1C of major isomer), 116.27 (1C of bothr isomers), 111.35 (1C of major isomer), 111.07 (1C of minor isomer), 73.02 (1C of major isomer), 71.08 (1C of minor isomer), 67.88 (1C of major isomer), 67.64 (1C of minor isomer),62.98 (1C of minor isomer), 62.65 (1C of major isomer), 53.88 (1C of minor isomer), 52.36 (1C of major isomer), 34.64 (1C of both isomers), 33.17 (1C of major isomer), 32.86 (1C of minor isomer), 30.58 (1C of both isomers), 25.14 (1C of minor isomer), 24.87 (1C of major isomer). HRMS Calcd for $C_{25}H_{24}N_2NaO_5$ ($M+Na^+$): 455.1583; Found: 455.1574.



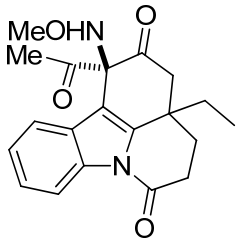
3g

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 20:1:1, then 15:1:1) to give **3g** in 86.3% yield (*cis*/*trans* = 2.12:1).

^{1}H-NMR (400 MHz, $CDCl_3$, *cis*-**3g**) δ: 8.45 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.30–7.06 (m, 6H), 5.11 (dd, J_1 = 41.6 Hz, J_2 = 12.0 Hz, 2H), 3.12 (s, 3H), 3.06–2.76 (m, 4H), 2.26–2.10 (m, 1H), 2.07–1.88 (m, 1H), 1.88–1.73 (m, 1H), 1.73–1.60 (m, 1H), 1.44–1.15 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, *cis*-**3g**) δ: 202.84, 167.99, 165.85, 143.93, 135.02, 134.55, 128.47, 127.94, 127.20, 125.04, 124.32, 120.01, 116.30, 111.30, 73.15, 67.91, 62.65, 48.50, 36.17, 35.65, 30.54, 30.44, 25.80, 22.79, 13.81.

^{1}H-NMR (400 MHz, $CDCl_3$, *trans*-**3g**) δ: 8.45 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.30–7.04 (m, 6H), 6.99–6.57 (br, 1H), 5.25–4.93 (m, 2H), 3.21 (s, 3H), 3.09–3.00 (d, *J* = 14.8 Hz, 1H), 3.00–2.77 (m, 2H), 2.67–2.56 (d, *J*

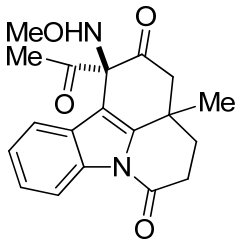
= 14.8 Hz, 1H), 2.29-2.13 (m, 1H), 2.06–1.91 (m, 1H), 1.82–1.64 (m, 1H), 1.56–1.44 (m, 1H), 1.36–0.94 (m, 4H), 0.76 (t, *J* = 7.6 Hz, 3H). ^{13}C-NMR (150 MHz, $CDCl_3$, *trans*-**3g**) δ: 206.41, 168.03, 167.41, 143.52, 135.19, 134.60, 128.35, 128.29, 128.05, 127.13, 125.04, 124.32, 120.14, 116.30, 110.90, 71.01, 67.66, 63.04, 50.07, 35.94, 35.88, 30.51, 30.44, 25.70, 22.55, 13.80. HRMS Calcd for $C_{28}H_{30}N_2NaO_5$ ($M+Na^+$): 497.2052; Found: 497.2043.



3h

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 10:1:1) to give **3h** in 78.9% yield (*cis*/*trans* = 2.73:1). ^{1}H-NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.48 (d, *J* = 8.0 Hz, 1H of both isomers), 7.53 (d, *J* = 7.6 Hz, 1H of both isomers), 7.37 (t, *J* = 7.6 Hz, 1H of both isomers), 7.29 (t, *J* = 7.6 Hz, 1H of both isomers), 3.22 (s, 3H of minor isomer), 3.14 (s, 3H of major isomer), 3.04 (d, *J* = 14.4 Hz, 1H of both isomers), 3.00–2.80 (m, 2H of both isomers), 2.72 (d, *J* = 14.4 Hz, 1H of both isomers), 2.31–2.17 (m, 4H of major isomer and 1H of minor isomer), 2.12–1.97 (m, 1H of major isomer and 4H of minor isomer), 1.93–1.78 (m, 1H of both isomers), 1.78–1.65 (m, 1H of both isomers), 0.86 (t, *J* = 7.6 Hz, 3H of both isomers). ^{13}C-NMR (100 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 203.30 (1C of major isomer), 200.15 (1C of major isomer), 167.91 (1C of major isomer), 143.91 (1C of major isomer), 135.39 (1C of minor isomer), 135.19 (1C of major isomer), 127.08 (1C of major isomer), 126.19 (1C of minor isomer), 125.61 (1C of minor isomer), 125.20 (1C of major isomer), 124.78 (1C of minor isomer), 124.44 (1C of major isomer), 119.83 (1C of both isomers), 116.52 (1C of major isomer), 116.12 (1C of minor isomer), 112.00 (1C of major isomer), 109.5 (1C of minor isomer), 80.28 (1C of both isomers), 63.46 (1C of minor isomer), 62.59 (1C of major isomer), 48.94 (1C of minor isomer), 48.06 (1C of major isomer), 36.33 (1C of major isomer), 35.61 (1C of minor isomer), 30.31 (1C of minor isomer), 30.59 (1C of minor isomer), 30.31 (1C

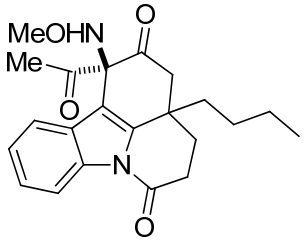
of major isomer), 30.17 (1C of minor isomer),30.06 (1C of major isomer), 28.70 (1C of both isomers), 27.01 (1C of both isomers), 8.45 (1C of minor isomer), 8.11 (1C of major isomer). HRMS Calcd for $C_{20}H_{22}N_2NaO_4$ ($M+Na^+$): 377.1477; Found: 377.1489.



3i

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 8:1:1) to give **3i** in 77.6% yield (*cis/trans* = 1.64:1). ^{1}H-NMR (300 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.48 (d, *J* = 7.8 Hz, 1H of both isomers), 7.56 (d, *J* = 7.5 Hz, 1H of minor isomer), 7.50 (d, *J* = 7.5 Hz, 1H of major isomer), 7.38 (t, *J* = 7.2 Hz, 1H of both isomers), 7.33–7.28 (m, 2H of both isomers and 1H of major isomer), 6.84 (br, 1H of minor isomer), 3.23 (s, 3H of minor isomer), 3.12 (s, 3H of major isomer), 3.09–2.80 (m, 4H of both isomers), 2.31–2.15 (m, 1H of both isomers and 3H of major isomer), 2.15–2.01 (m, 1H of both isomers and 3H of minor isomer), 1.50 (s, 3H of minor isomer), 1.44 (s, 3H of major isomer). ^{13}C-NMR **(**150 MHz, $CDCl_3$, mixture of isomers) δ: 207.35 (1C of minor isomer), 203.51 (1C of major isomer), 201.98 (1C of minor isomer), 200.09 (1C of major isomer), 168.07 (1C of minor isomer), 167.97 (1C of major isomer), 143.38 (1C of major isomer), 142.67 (1C of minor isomer), 135.61 (1C of minor isomer), 135.38 (1C of major isomer), 127.27 (1C of major isomer), 127.02 (1C of minor isomer), 125.62 (1C of minor isomer), 125.45 (1C of major isomer), 124.77 (1C of minor isomer), 124.70 (1C of major isomer), 120.14 (1C of minor isomer), 119.90 (1C of major isomer), 116.76 (1C of major isomer), 116.71 (1C of minor isomer), 112.15 (1C of major isomer), 111.36 (1C of minor isomer), 80.38 (1C of major isomer), 76.51 (1C of minor isomer), 63.01 (1C of minor isomer), 62.78 (1C of major isomer), 53.76 (1C of minor isomer), 52.85 (1C of major isomer), 35.44 (1C of minor isomer), 35.01 (1C of major isomer), 33.56 (1C of minor isomer), 33.49 (1C of major isomer), 30.88 (1C of minor isomer), 30.83 (1C of major isomer), 27.42 (1C of minor isomer), 27.19 (1C of major isomer), 25.86 (1C

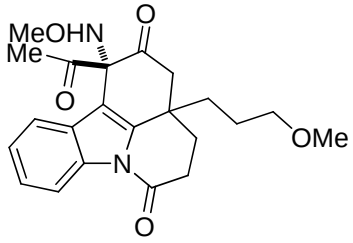
of minor isomer), 25.20 (1C of major isomer). HRMS Calcd for $C_{22}H_{20}N_2NaO$ ($M+Na^+$): 363.1321; Found: 363.1320 (major isomer). HRMS Calcd for $C_{19}H_{20}N_2NaO_4$ ($M+Na^+$): 363.1321; Found: 363.1310 (minor isomer).



3j

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 15:1:1) to give **3j** in 86.3% yield (*cis*/*trans* = 2.10:1). ^{1}H-NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.48 (d, *J* = 8.0 Hz, 1H of both isomers), 7.53 (d, *J* = 7.6 Hz, 1H of both isomers), 7.37 (t, *J* = 7.6 Hz, 1H of both isomers), 7.29 (t, *J* = 7.6 Hz, 1H of both isomers), 6.82 (br, 1H of minor isomer), 3.21 (s, 3H of minor isomer), 3.14 (s, 3H of major isomer), 3.04 (d, *J* = 14.8 Hz, 1H of both isomers), 3.01–2.81 (m, 2H of both isomers), 2.81–2.67 (m, 1H of both isomers), 2.34–1.99 (m, 5H of both isomers), 1.99–1.89 (m, 1H of minor isomer), 1.85–1.74 (m, 1H of major isomer), 1.71–1.61 (m, 1H of major isomer), 1.57–1.47 (m, 1H of minor isomer), 1.45–1.18 (m, 4H of both isomers), 0.97–0.82 (m, 3H of both isomers). ^{13}C-NMR (100 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 207.20 (1C of minor isomer), 203.44 (1C of major isomer), 202.09 (1C of minor isomer), 200.31 (1C of major isomer), 168.21 (1C of minor isomer), 168.10 (1C of major isomer), 144.08 (1C of major isomer), 143.61 (1C of minor isomer), 135.55 (1C of minor isomer), 135.36 (1C of major isomer), 127.27 (1C of major isomer), 127.00 (1C of minor isomer), 125.53 (1C of minor isomer), 125.35 (1C of major isomer), 124.71 (1C of minor isomer), 124.61 (1C of major isomer), 119.99 (1C of both isomers), 116.69 (1C of major isomer), 116.29 (1C of minor isomer), 112.10 (1C of major isomer), 111.10 (1C of minor isomer), 80.39 (1C of major isomer), 76.32 (1C of minor isomer), 62.98 (1C of minor isomer), 62.70 (1C of major isomer), 49.76 (1C of minor isomer), 48.94 (1C of major isomer), 36.63 (1C of major isomer), 36.57 (1C of minor isomer), 36.39 (1C of minor isomer), 35.94 (1C of major isomer), 30.93 (1C of both isomers), 30.61 (1C of both isomers), 27.45 (1C of minor isomer), 27.15 (1C of major isomer), 25.97 (1C of both isomers), 22.91 (1C

of both isomers), 13.92 (1C of both isomers). HRMS Calcd for $C_{22}H_{26}N_2NaO_4$ ($M+Na^+$): 405.1790; Found: 405.1800.

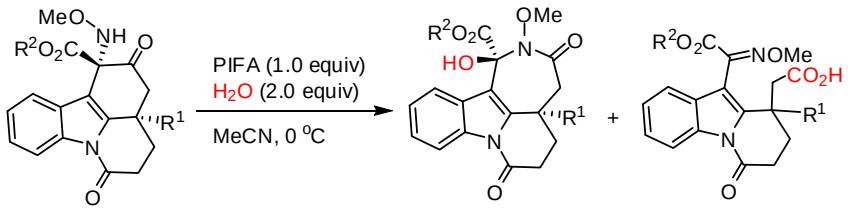


3k

The products were purified by flash column chromatography on silica gel with a mixture of petroleum ether, dichloromethane and EtOAc as eluent (v/v/v = 4:1:1) to give **3k** in 41.8% yield (*cis*/*trans* = 3.93:1). ^{1}H-NMR (300 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 8.48 (d, *J* = 7.8 Hz, 1H of both isomers), 7.53 (d, *J* = 7.8 Hz, 1H of both isomers), 7.37 (t, *J* = 8.3 Hz, 1H of both isomers), 7.33–7.25 (m, 1H of both isomers and 1H of major isomer), 6.83 (br, 1H of minor isomer), 3.47–3.34 (m, 1H of both isomers), 3.34–3.23 (m, 4H of both isomers), 3.22 (s, 3H of minor isomer), 3.15 (s, 3H of major isomer), 3.07–2.92 (m, 2H of both isomers), 2.92–2.72 (m, 2H of both isomers), 2.33–2.19 (m, 1H of both isomers and 3H of major isomer), 2.15–2.02 (m, 1H of both isomers and 3H of minor isomer), 2.02–1.86 (m, 1H of both isomers), 1.75–1.52 (m, 3H of both isomers). ^{13}C-NMR (150 MHz, $CDCl_3$, mixture of diastereoisomers) δ: 206.73 (1C of minor isomer), 202.93 (1C of major isomer), 201.81 (1C of minor isomer), 199.97 (1C of major isomer), 167.86 (1C of minor isomer), 167.77 (1C of major isomer), 143.56 (1C of major isomer), 143.17 (1C of minor isomer), 135.19 (1C of minor isomer), 135.02 (1C of major isomer), 126.93 (1C of major isomer), 126.67 (1C of minor isomer), 125.07 (1C of minor isomer), 124.91 (1C of major isomer), 124.24 (1C of minor isomer), 124.16 (1C of major isomer), 119.69 (1C of both isomers), 116.29 (1C of major isomer), 116.25 (1C of minor isomer), 111.81 (1C of major isomer), 110.79 (1C of minor isomer), 80.03 (1C of major isomer), 75.97 (1C of minor isomer), 71.86 (1C of major isomer), 71.66 (1C of minor isomer), 62.55 (1C of minor isomer), 62.31 (1C of major isomer), 58.28 (1C of minor isomer), 58.23 (1C of major isomer), 49.30 (1C of minor isomer), 48.56 (1C of major isomer), 36.04 (1C of minor isomer), 35.88 (1C of major isomer), 33.07 (1C of minor isomer), 32.44 (1C of major isomer), 30.60 (1C of major isomer), 30.54 (1C of minor isomer), 30.15 (1C of both isomers), 27.17 (1C of minor isomer), 26.81 (1C

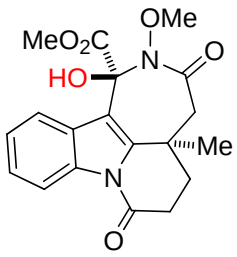
of major isomer), 23.83 (1C of both isomers). HRMS Calcd for $C_{22}H_{26}N_2NaO_5$ (M+Na+): 421.1739; Found: 421.1761.

General Experimental Procedures for Ring Expansion Reaction of 3:



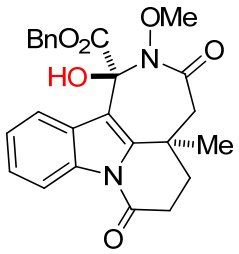
3 **11** **12**

To a solution of **3** (0.1 mmol) in MeCN (1 mL) was added H_2O (2.0 eq.) and PIFA (1.0 eq.) at 0 °C and the resultant solution was stirred at the same temperature for 2 h (monitored by TLC). The reaction was diluted with dichloromethane (20 mL) and washed with brine (10 mL×2). The organic phase was dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by flash column chromatography with a mixed petroleum ether, dichloromethane, and EtOAc as eluent (v/v/v = 5:1:1 to 3:1:1) on silica gel to give the desired product.



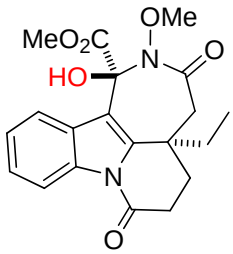
11a

^{1}H-NMR (300 MHz, $CDCl_3$, only major isomer is shown) δ: 8.53 (d, J = 8.1 Hz, 1H), 7.40–7.31 (m, 2H), 7.30–7.22 (m, 1H), 5.24 (br, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.18 (d, J = 15.3 Hz, 1H), 3.11–2.97 (m, 1H), 2.92–2.77 (m, 2H), 2.21–2.02 (m, 1H), 1.95–1.83 (m, 1H), 1.59 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, only major isomer is shown) δ: 171.31, 169.22, 168.52, 142.45, 134.27, 126.56, 125.68, 124.82, 118.26, 116.76, 112.74, 88.58, 63.51, 54.23, 49.60, 35.39, 32.19, 30.33, 21.41. HRMS Calcd for $C_{19}H_{21}N_2O_6$ ($M+H^+$): 373.1399; Found: 373.1381.



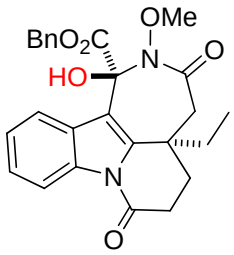
11b

^{1}H-NMR (300 MHz, $CDCl_3$, only major isomer is shown) δ: 8.50 (d, *J* = 8.4 Hz, 1H), 7.36–7.06 (m, 8H), 5.30 (d, *J* = 12.0 Hz, 1H), 5.21 (br, 1H), 5.17 (d, *J* = 12.0 Hz, 1H), 3.66 (s, 3H), 3.15 (d, *J* = 15.2 Hz, 1H), 3.21–2.95 (m, 2H), 2.91–2.71 (m, 2H), 2.16–1.99 (m, 1H), 1.93–1.80 (m, 1H), 1.54 (s, 3H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 171.28, 168.54 (2C), 142.42, 134.26, 133.95, 128.98, 128.92, 128.69, 126.48, 125.64, 124.75, 118.53, 116.66, 112.78, 88.87, 69.56, 63.55, 49.76, 35.45, 32.21, 30.36, 21.39. HRMS Calcd for $C_{25}H_{24}N_2NaO_6$ ($M+Na^+$): 471.1532; Found: 471.1529.



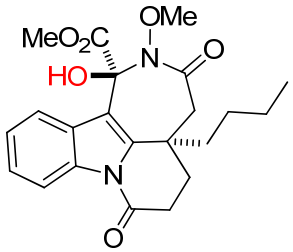
11c

^{1}H-NMR (400 MHz, $CDCl_3$, only major isomer is shown) δ: 8.51 (d, *J* = 8.4 Hz, 1H), 7.40–7.30 (m, 2H), 7.30–7.24 (m, 1H), 5.46–5.17 (br, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.10–2.75 (m, 4H), 2.20–2.03 (m, 2H), 1.98–1.80 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, only major isomer is shown) δ: 170.92, 169.25, 168.57, 143.51, 134.24, 126.59, 125.60, 124.76, 118.26, 116.71, 112.43, 88.56, 63.52, 54.23, 45.83, 35.30, 29.95, 25.86, 8.34. HRMS Calcd for $C_{20}H_{22}N_2NaO_6$ ($M+Na^+$): 409.1376; Found: 409.1381.



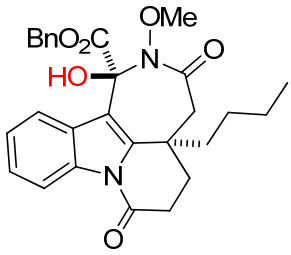
11d

^{1}H-NMR (400 MHz, $CDCl_3$, only major isomer is shown) δ: 8.49 (d, *J* = 8.4 Hz, 1H), 7.38–7.13 (m, 6H), 7.07 (d, *J* = 7.2 Hz, 2H), 5.36–5.14 (m, 3H), 3.66 (s, 3H), 3.03 (d, *J* = 15.6 Hz, 1H), 2.97–2.74 (m, 3H), 2.18–1.98 (m, 2H), 1.93–1.78 (m, 2H), 1.00 (t, *J* = 7.6 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, only major isomer is shown) δ: 170.92, 168.63, 168.46, 143.40, 134.18, 133.94, 128.87, 128.80, 128.61, 126.50, 125.53, 124.66, 118.53, 116.56, 112.51, 88.88, 69.44, 63.51, 45.94, 35.26, 29.99, 25.79, 8.35. HRMS Calcd for $C_{26}H_{26}N_2NaO_6$ ($M+Na^+$): 485.1688; Found: 485.1657. $C_{26}H_{26}KN_2O_6$ ($M+K^+$): 501.1428; Found: 501.1398.



11e

^{1}H-NMR (400 MHz, $CDCl_3$, only major isomer is shown) δ: 8.51 (d, *J* = 8.0 Hz, 1H), 7.40–7.30 (m, 2H), 7.30–7.19 (m, 1H), 5.31–5.17 (br, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.06 (d, *J* = 15.6 Hz, 1H), 3.00–2.72 (m, 3H), 2.19–1.98 (m, 2H), 1.95–1.81 (m, 2H), 1.56–1.29 (m, 4H), 0.93 (t, *J* = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, only major isomer is shown) δ: 171.21, 169.31, 168.62, 143.65, 134.27, 126.61, 125.66, 124.83, 118.21, 116.78, 112.40, 88.57, 63.46, 54.28, 46.33, 35.24, 32.77, 30.74, 30.12, 26.01, 23.14, 13.96. HRMS Calcd for $C_{22}H_{26}N_2NaO_6$ ($M+Na^+$): 437.1689; Found: 437.1700.



11f

^{1}H-NMR (400 MHz, $CDCl_3$, only major isomer is shown) δ: 8.49 (d, J = 8.0 Hz, 1H), 7.38–7.12 (m, 6H), 7.12–7.04 (d, J = 7.2 Hz, 2H), 5.42–5.33 (br, 1H), 5.22 (dd, J_1 = 61.6 Hz, J_2 = 12.0 Hz, 2H), 3.64 (s, 3H), 2.94 (dd, J_1 = 57.6 Hz, J_2 = 15.6 Hz, 2H), 2.80 (m, 3H), 2.15–1.92 (m, 2H), 1.92–1.71 (m, 2H), 1.50–1.16 (m, 4H), 0.86 (t, J = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, only major isomer is shown) δ: 170.97, 168.64, 168.36, 143.38, 134.11, 128.82, 128.73, 128.57, 126.49, 125.46, 124.61, 118.58, 116.52, 112.33, 88.88, 69.32, 63.32, 46.42, 35.05, 32.62, 30.67, 30.00, 25.93, 22.96, 13.82. HRMS Calcd for $C_{28}H_{30}N_2NaO_6$ ($M+Na^+$): 513.2002; Found: 513.2001.

Copies of ^{1}H- and ^{13}C-NMR Spectra

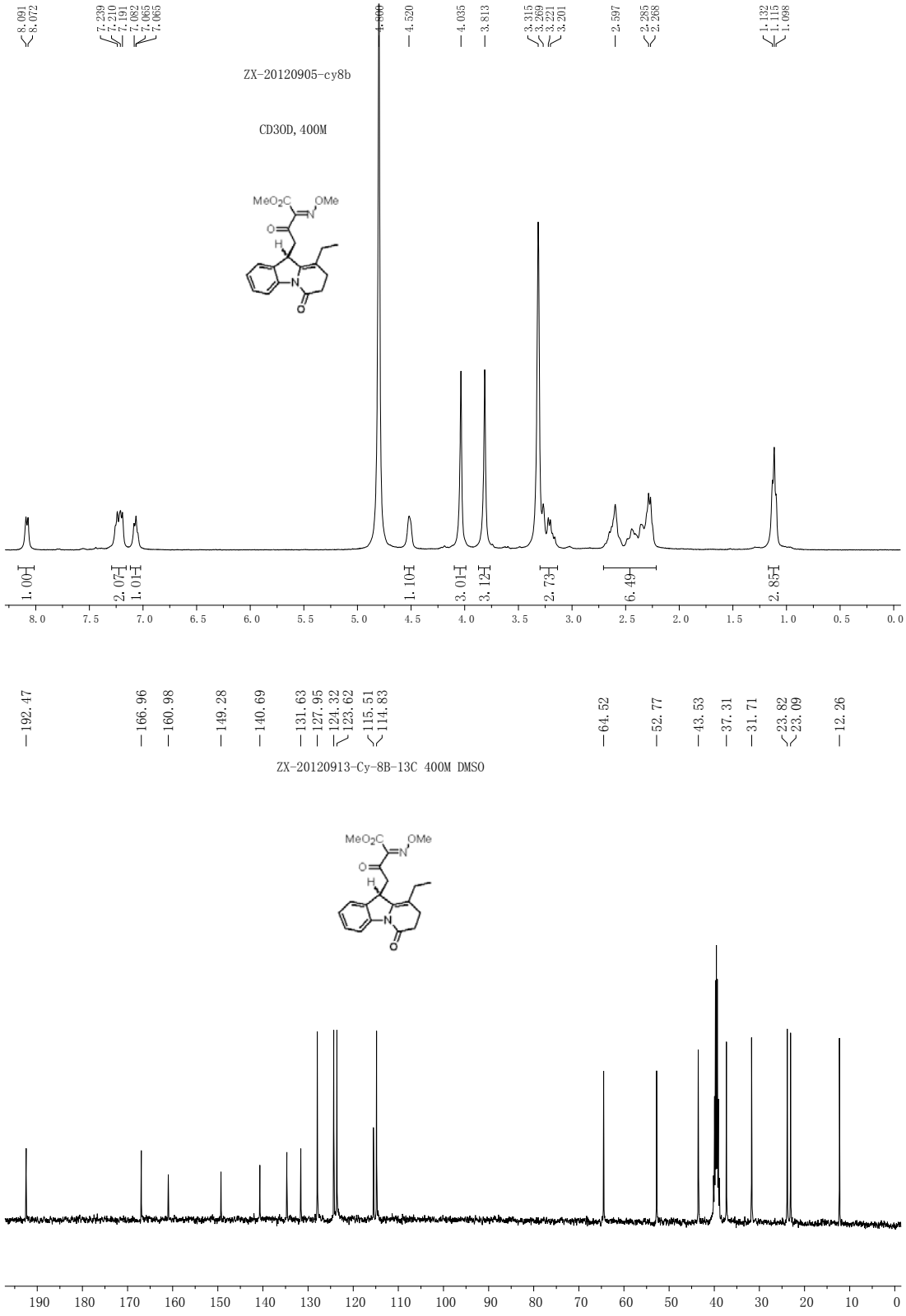


Figure S1. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of Compound **9**

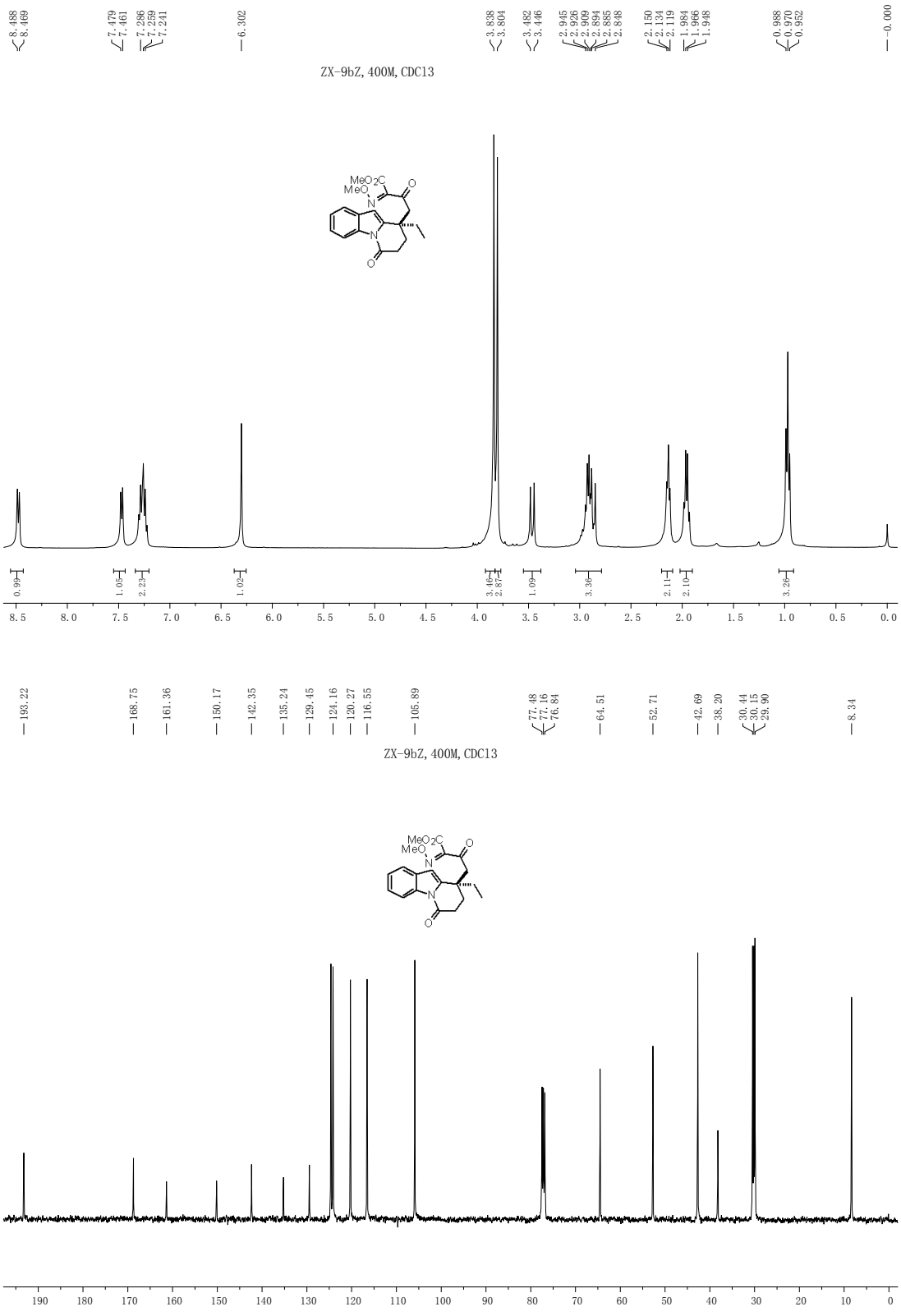


Figure S2. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of Compound **10**

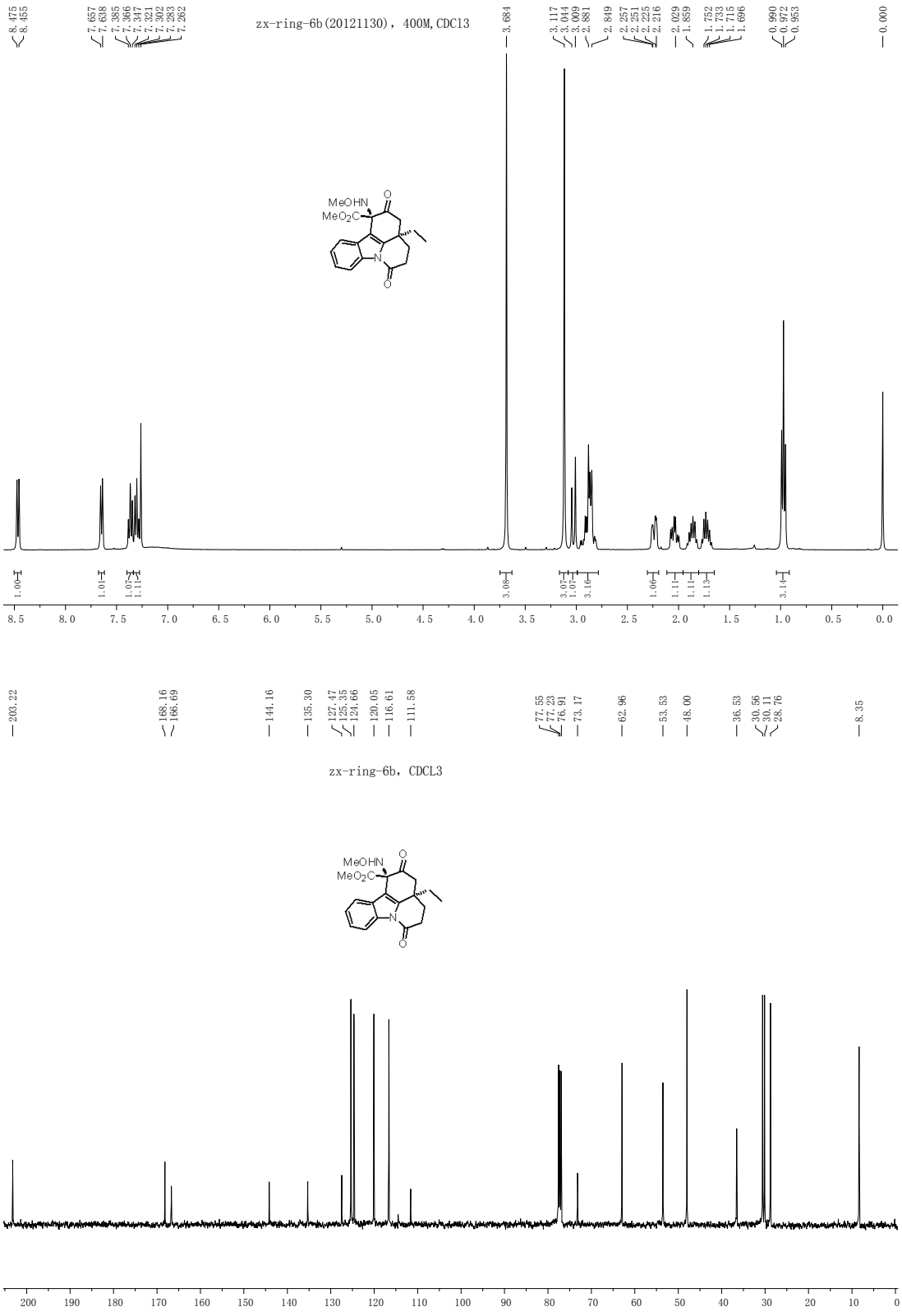


Figure S3. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of Compound *cis*-**3a**

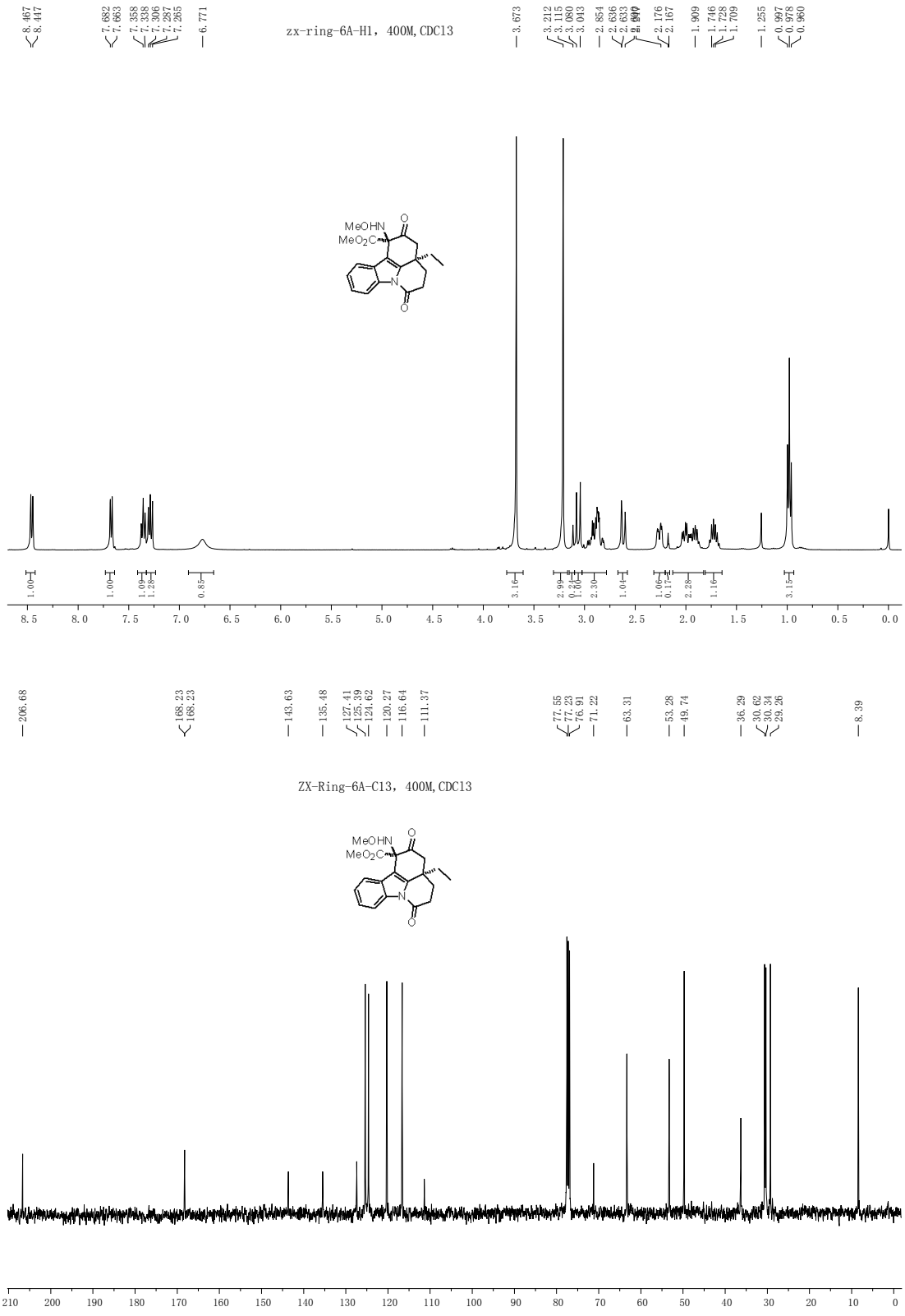


Figure S4. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of Compound *trans*-**3a**

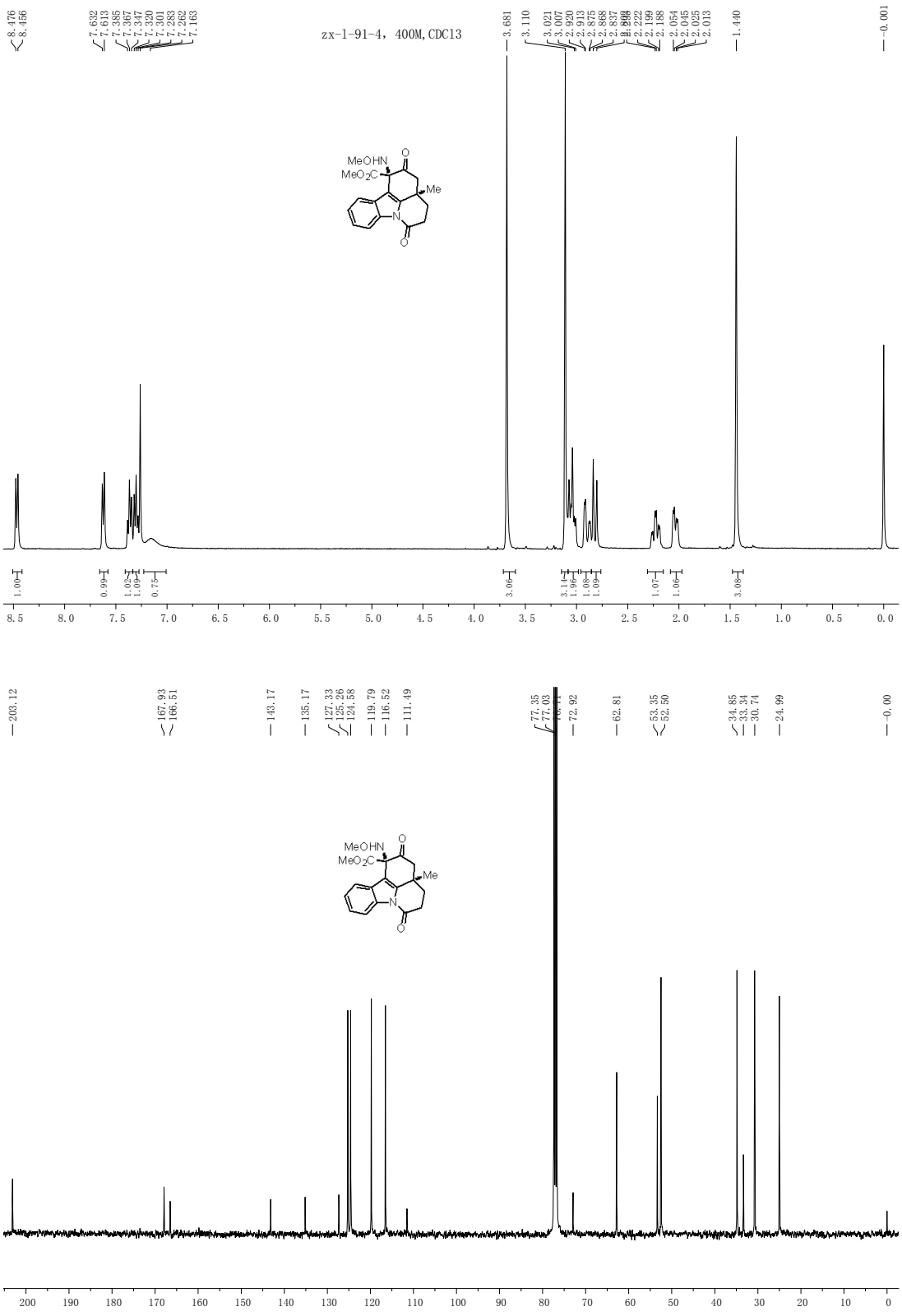


Figure S5. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of *cis*-**3b**

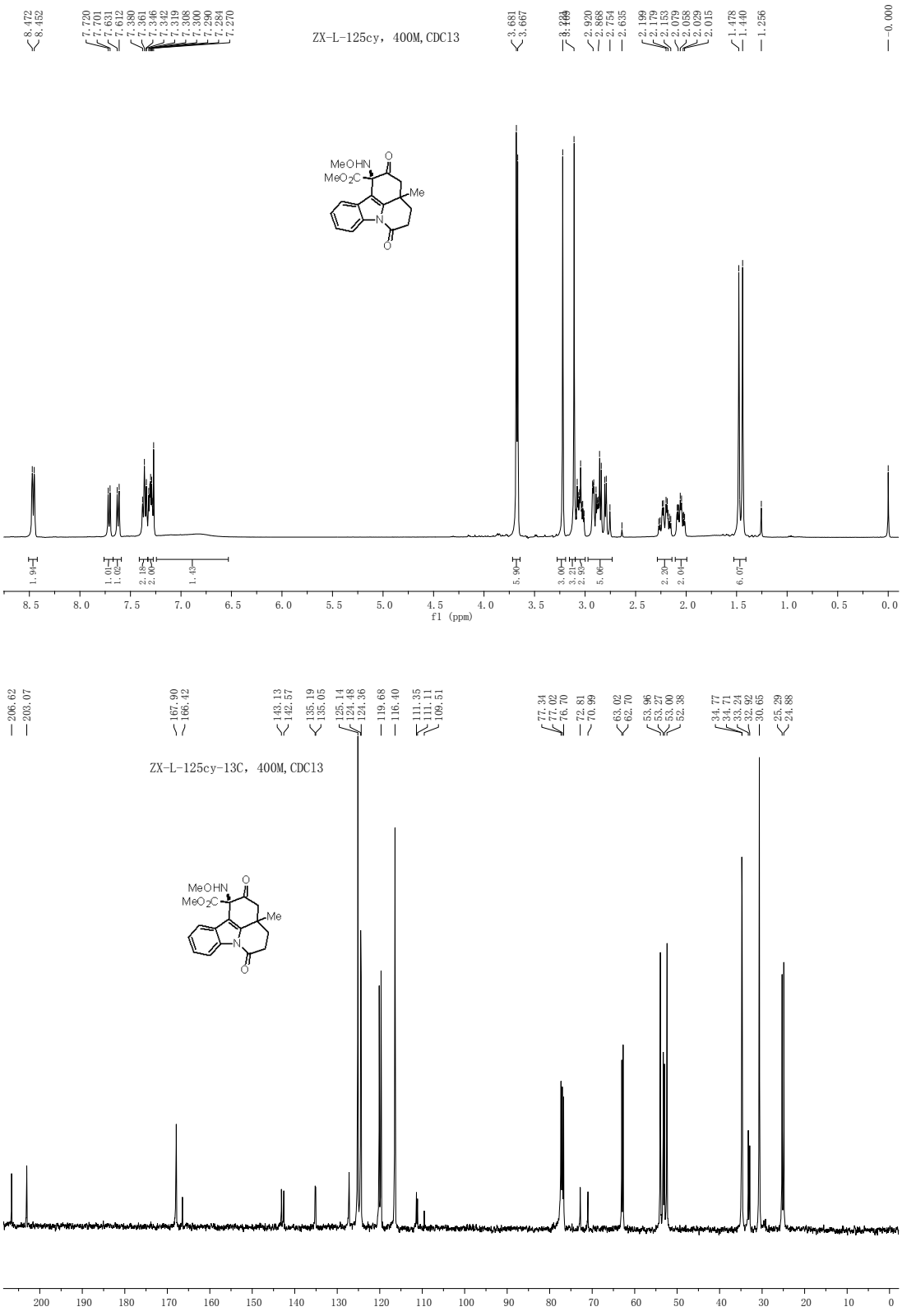


Figure S6. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis*-/*trans*-**3b**

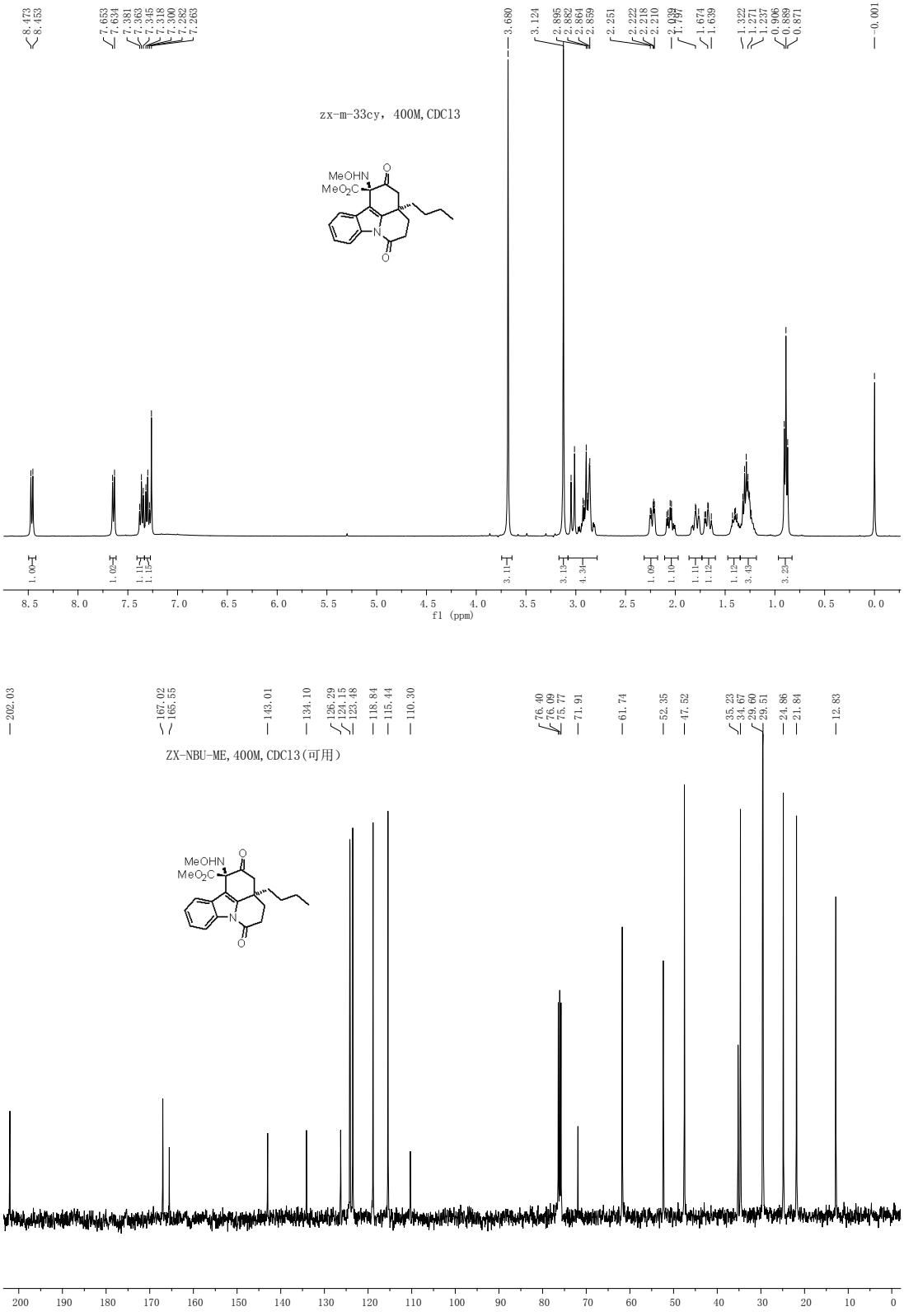


Figure S7. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of *cis*-**3c**

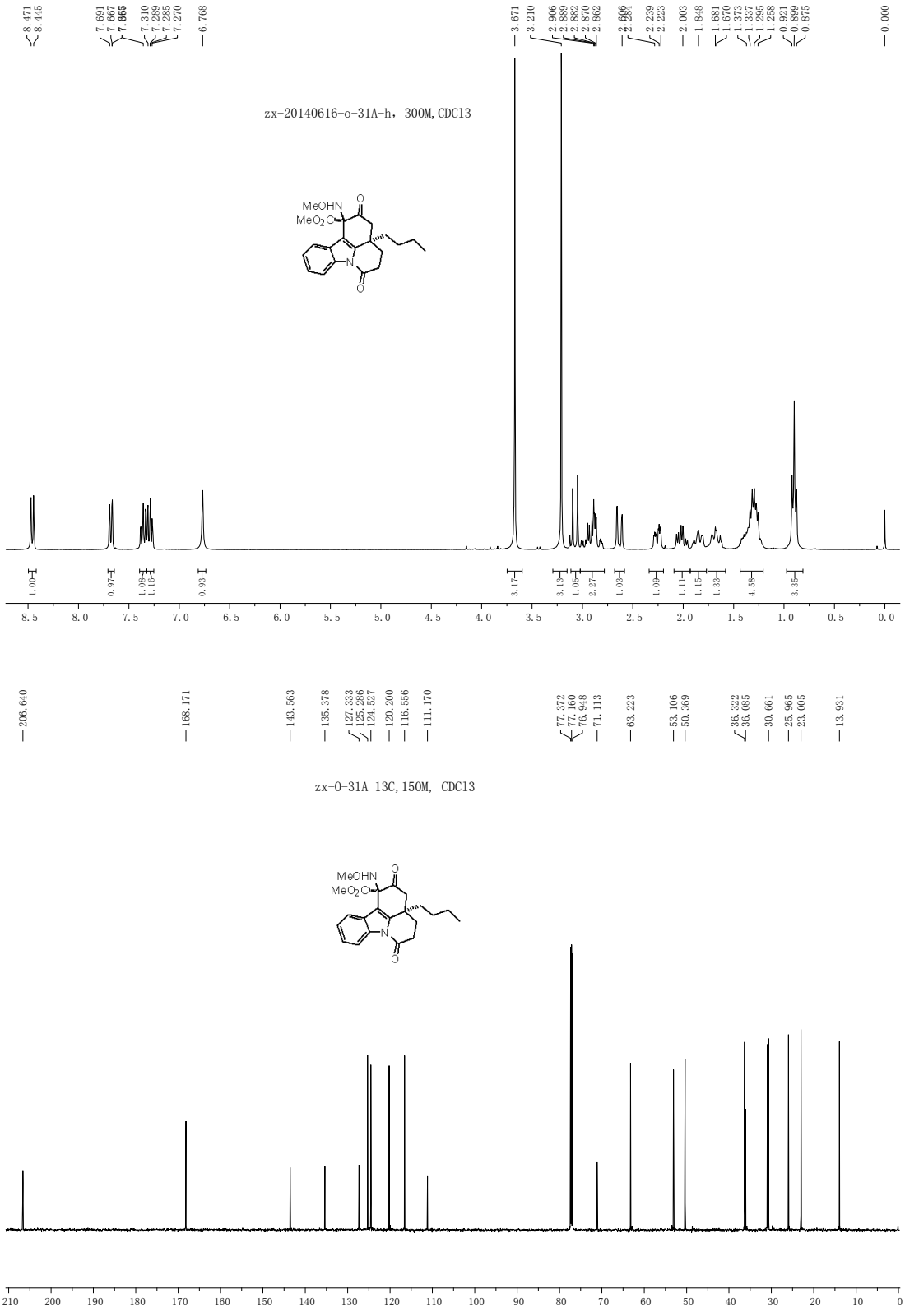


Figure S8. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of *trans*-**3c**

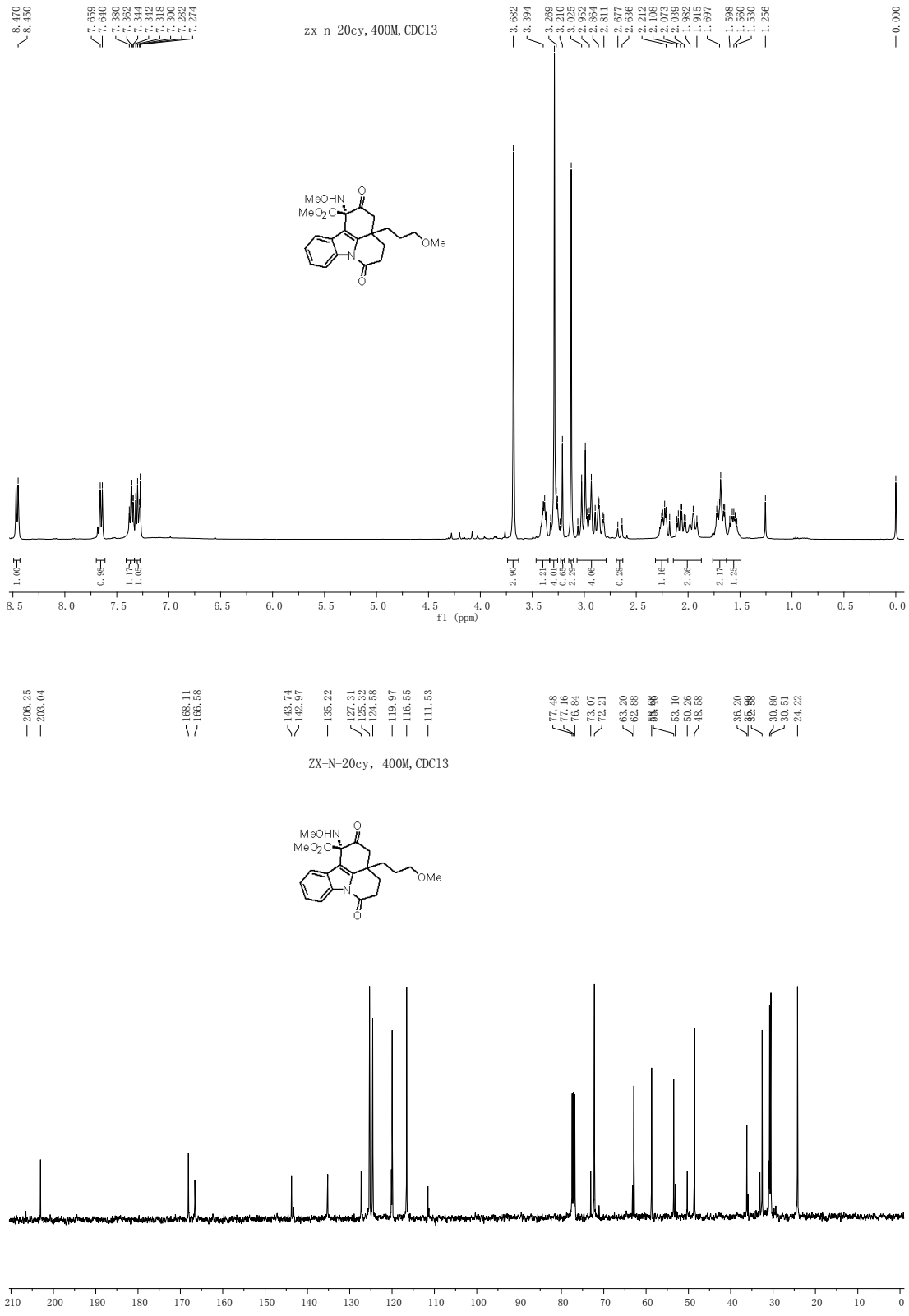


Figure S9. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis-/trans*-**3d**

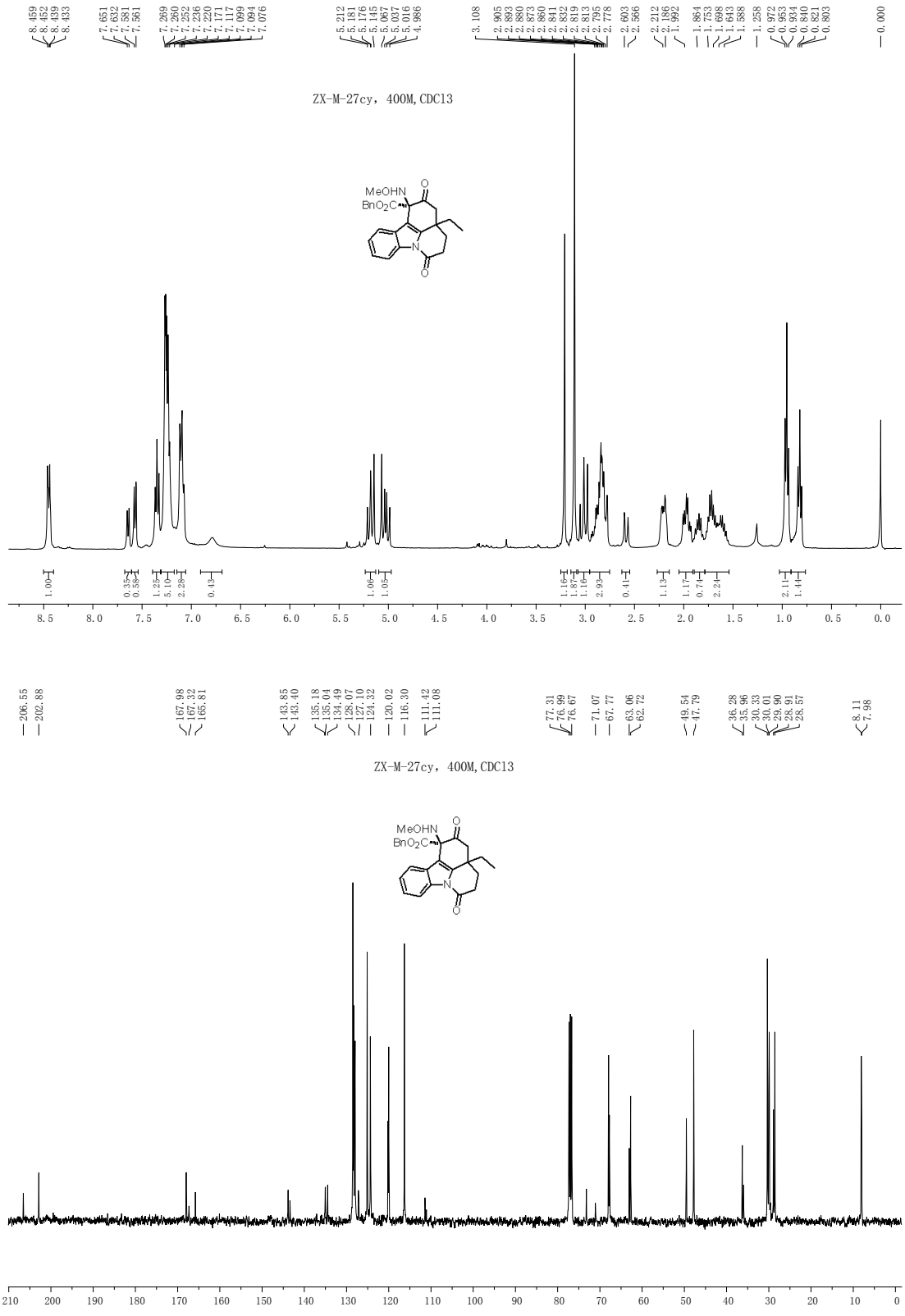


Figure S10. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis-/trans*-**3e**

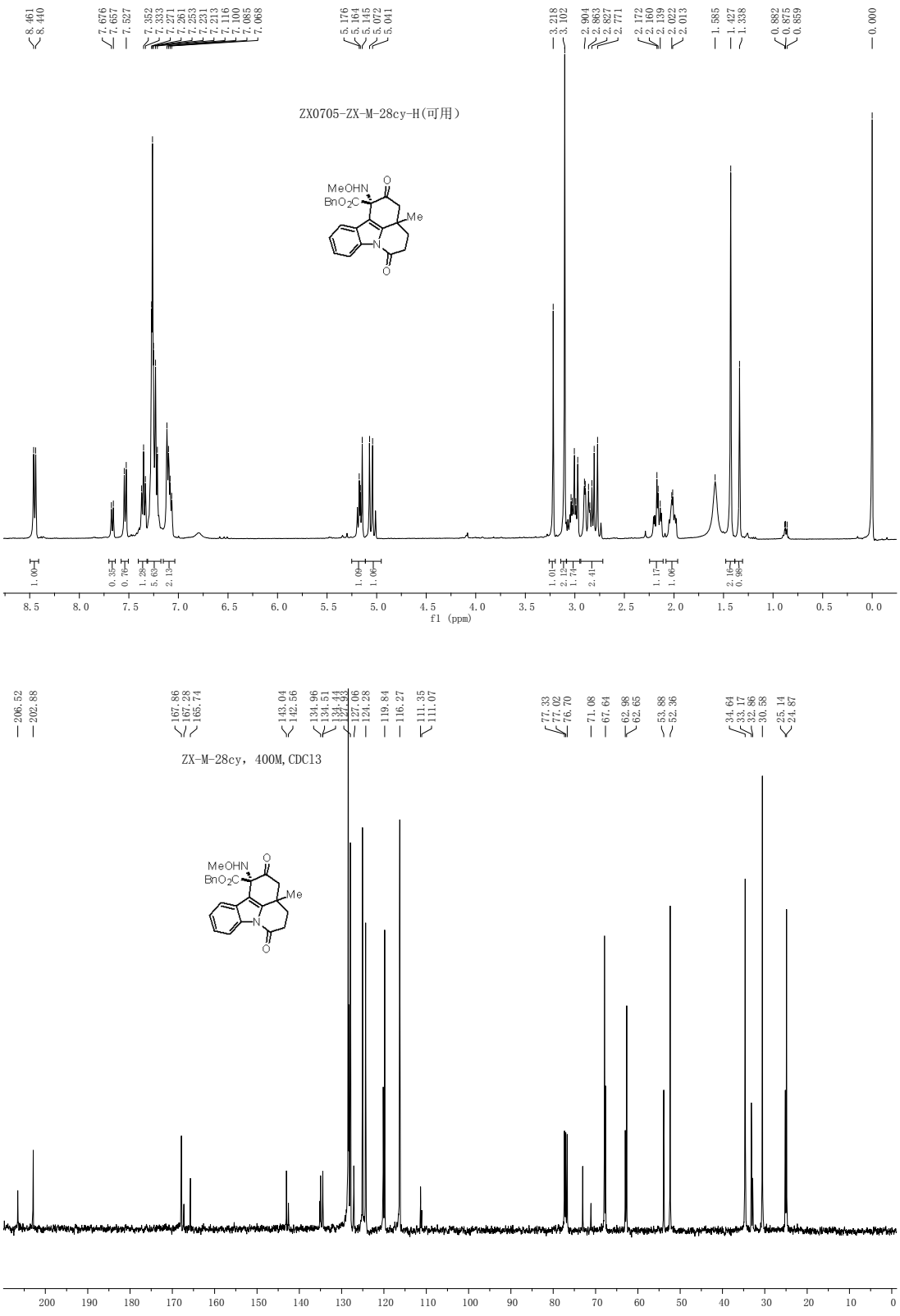


Figure S11. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis-/trans*-**3f**

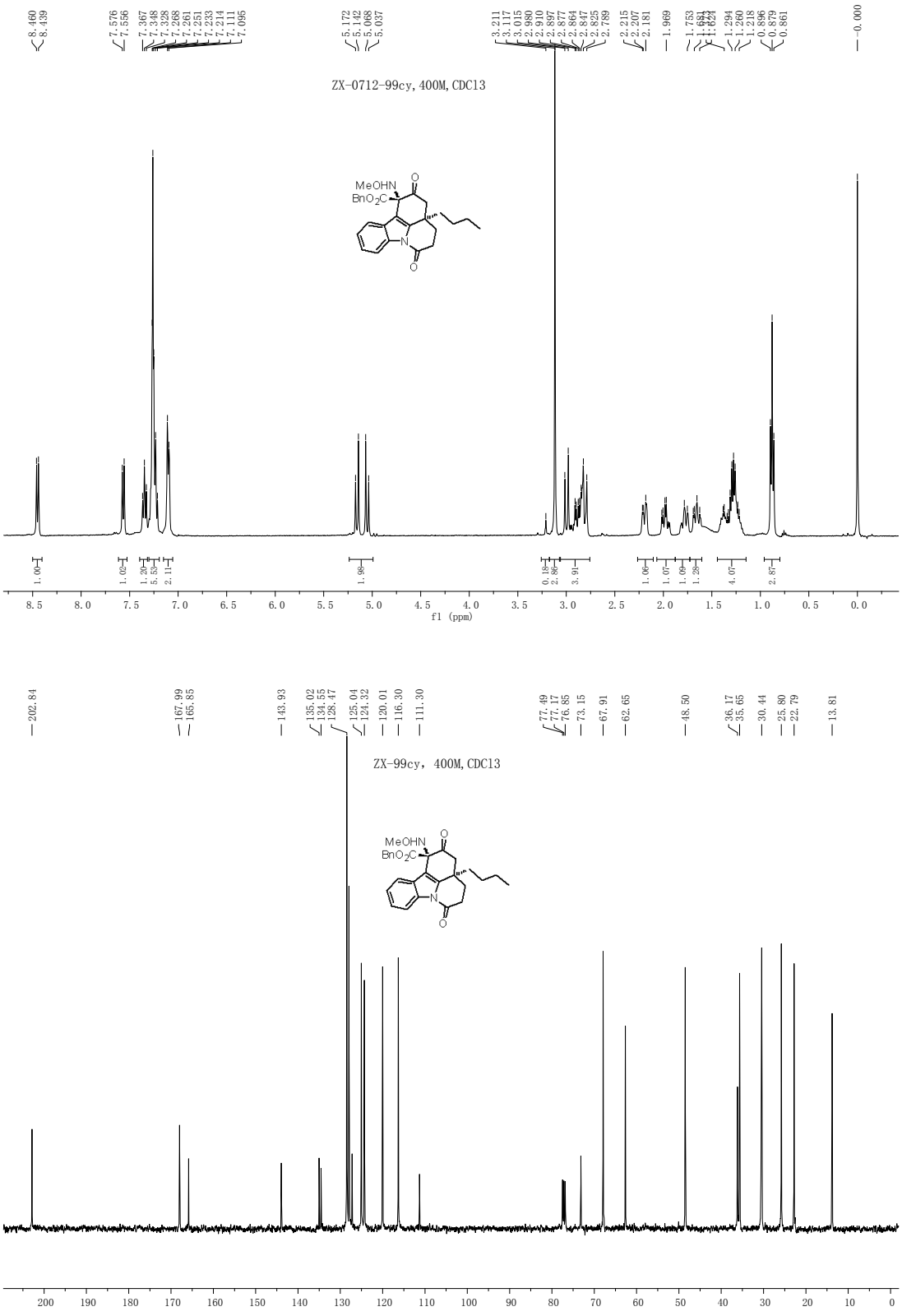


Figure S12. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis*-**3g**

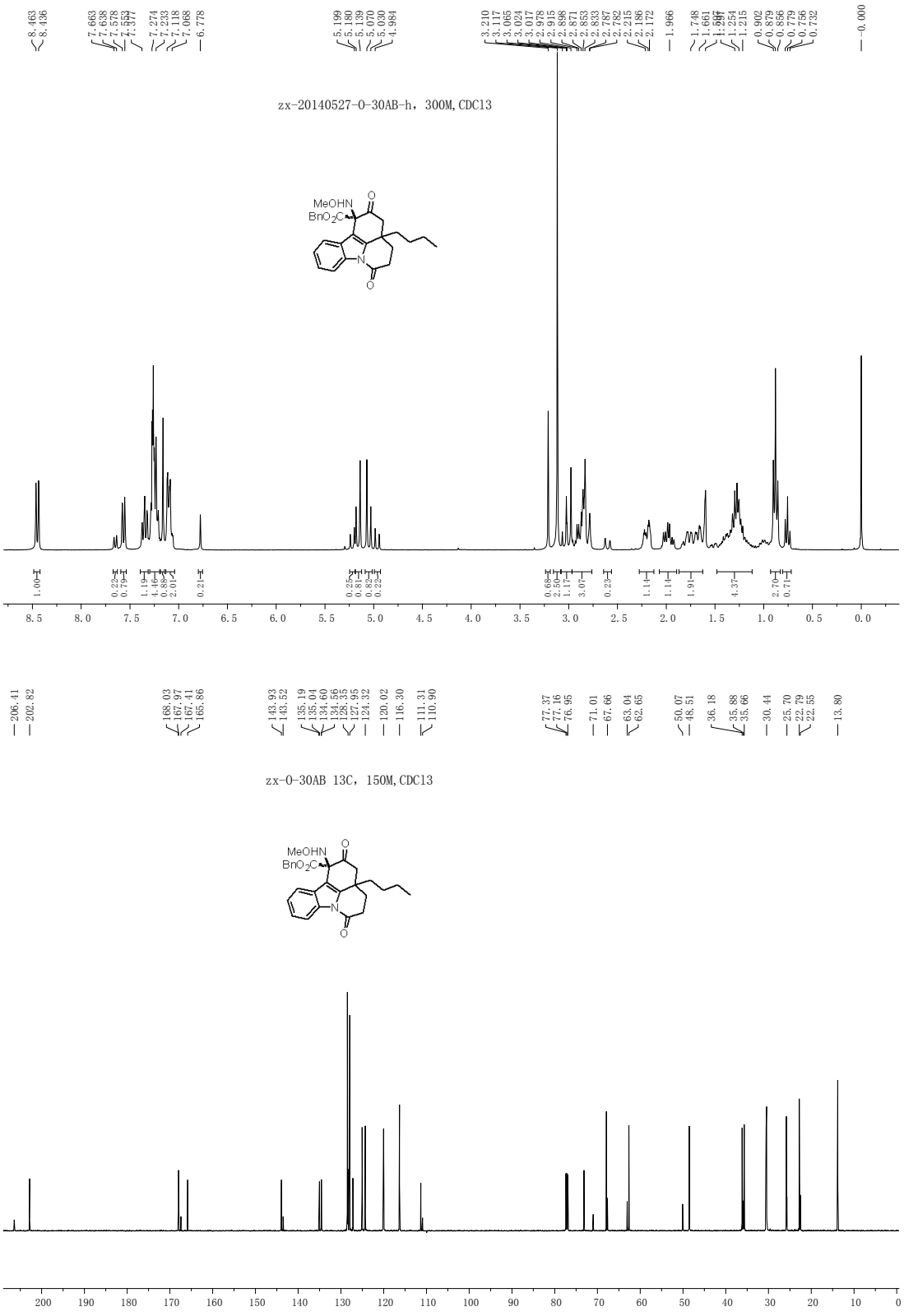


Figure S13 ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of *cis-/trans*-**3g**

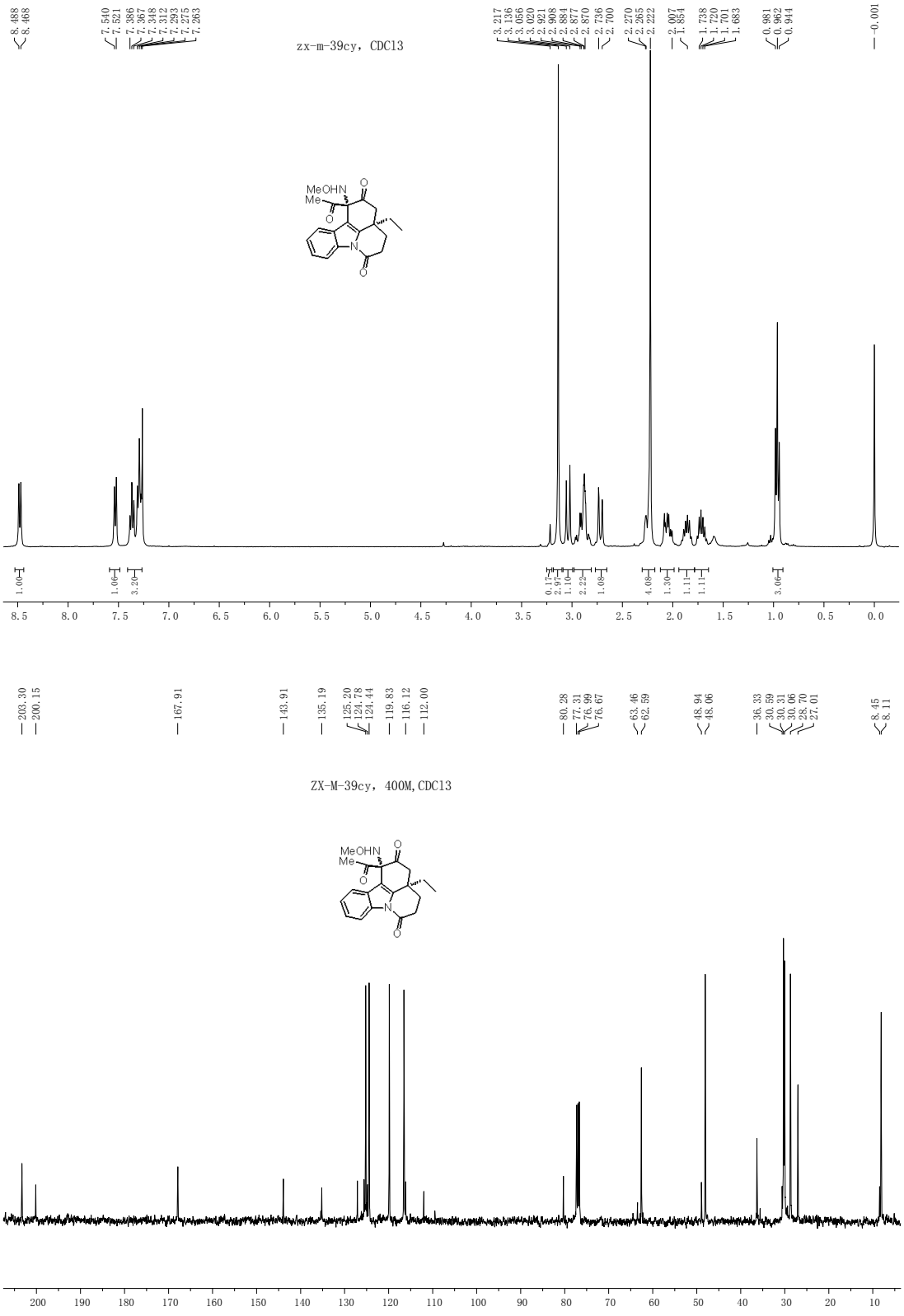


Figure S14. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis-/trans*-**3h**

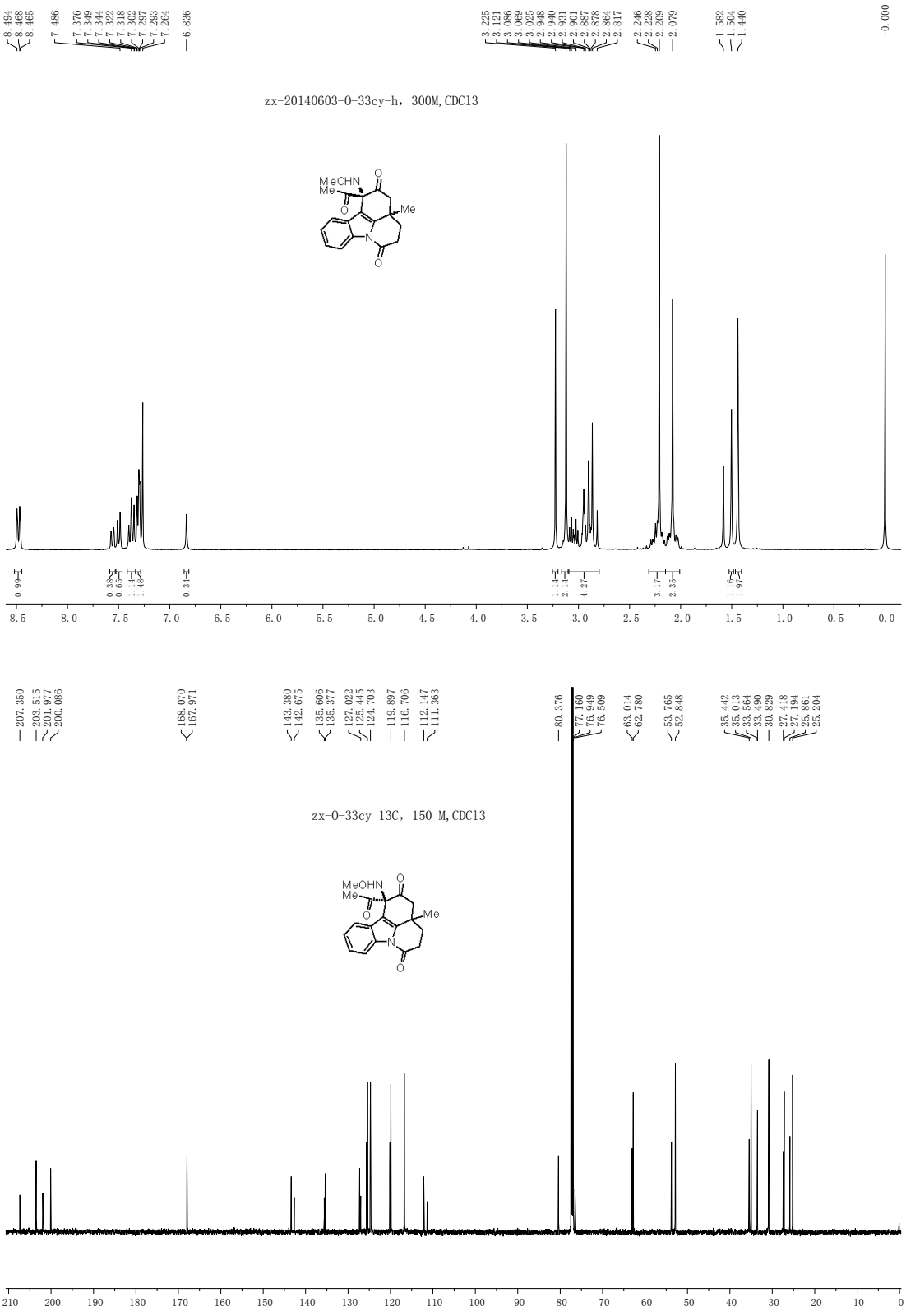


Figure S15. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis-/trans*-**3i**

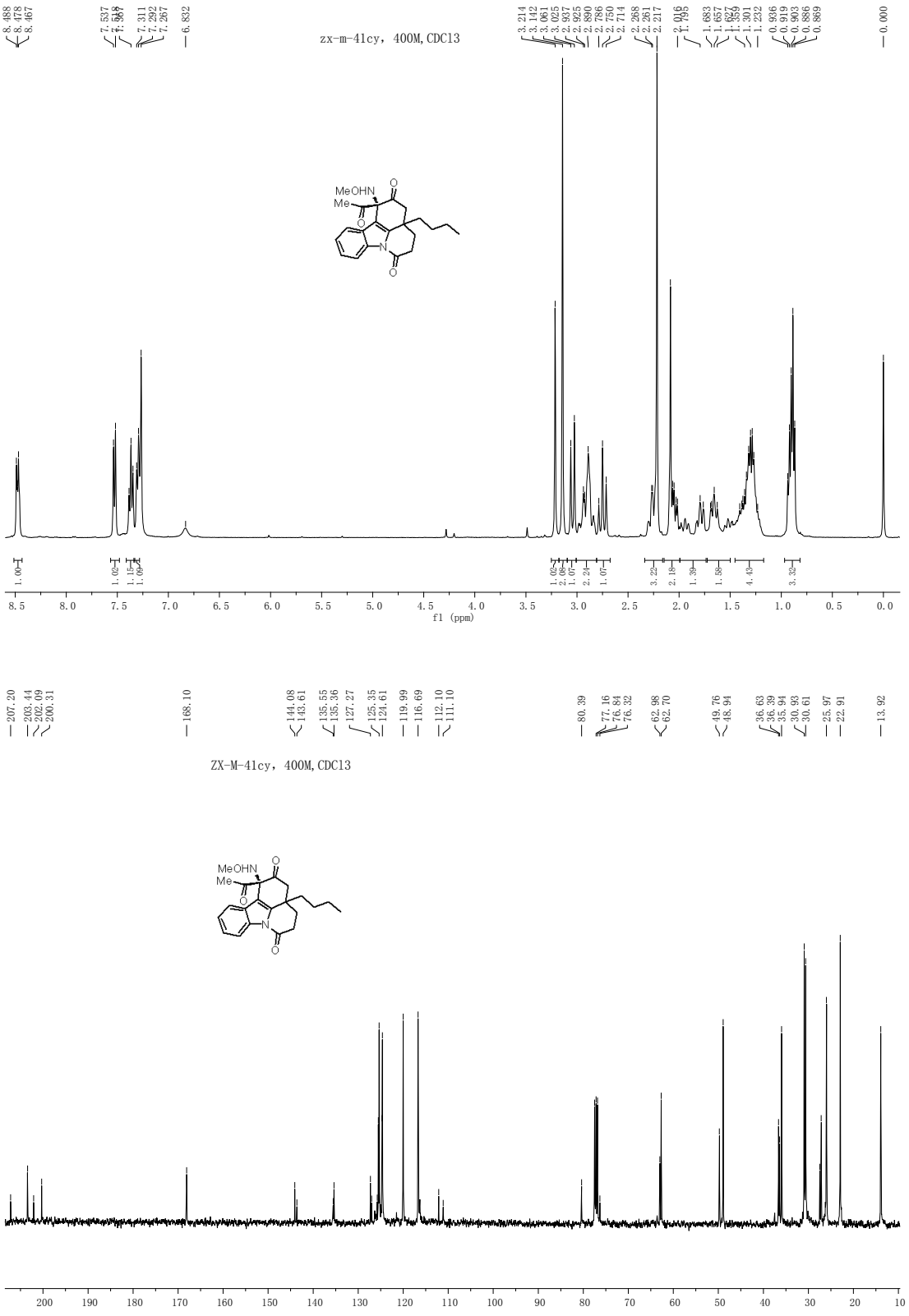


Figure S16. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis-/trans*-**3j**

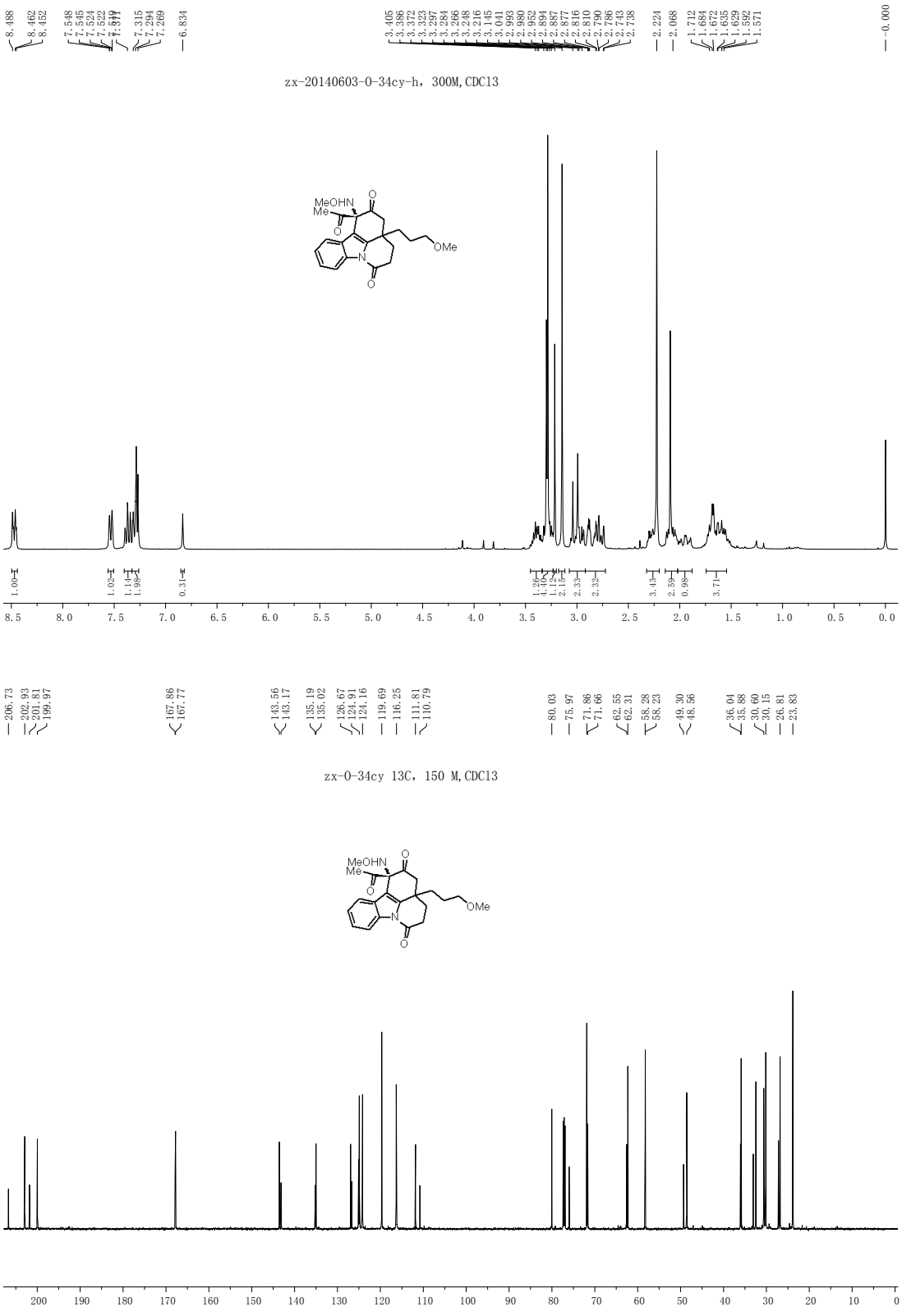


Figure S17. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of mixture of *cis-/trans*-**3k**

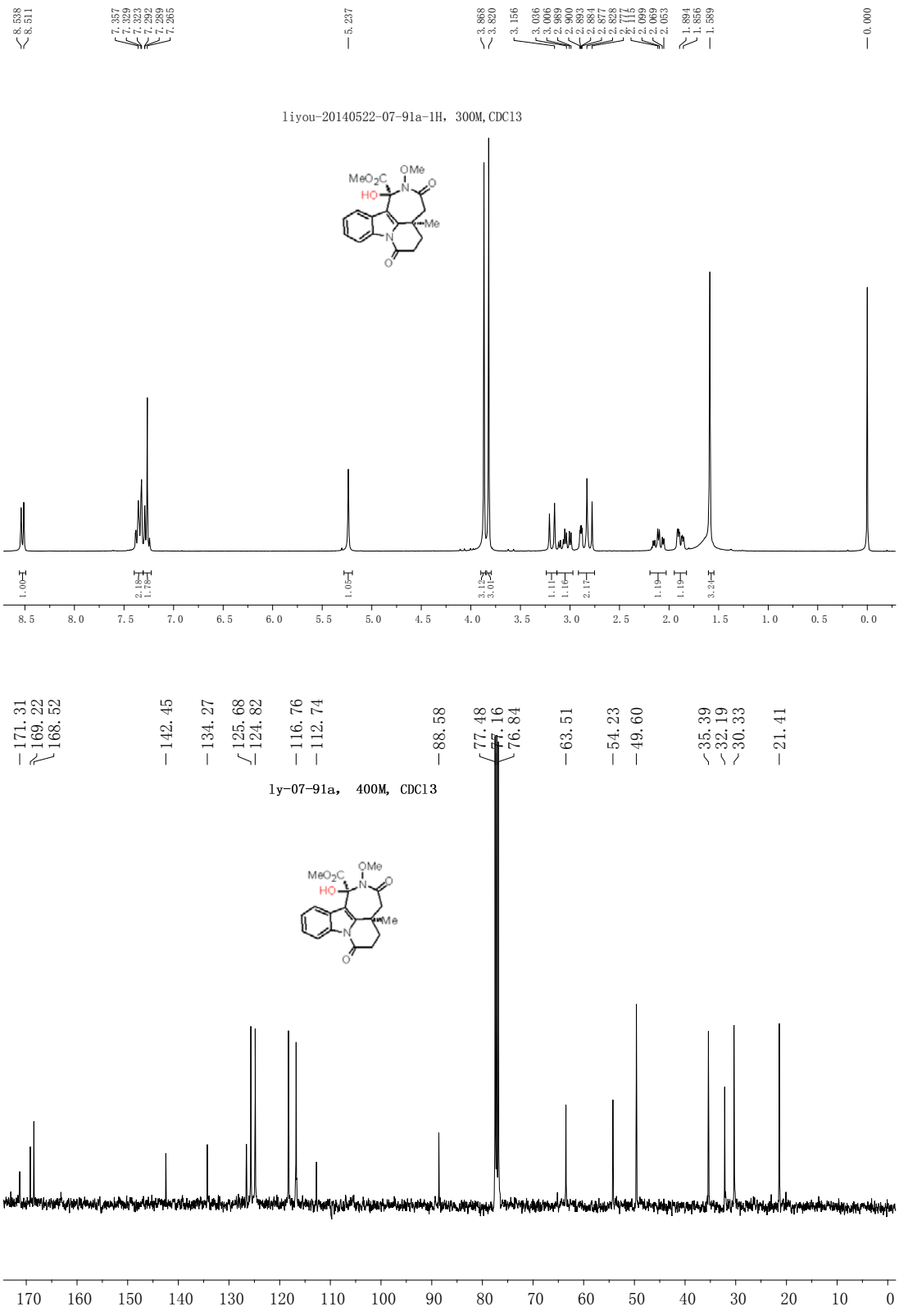


Figure S18. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **11a**

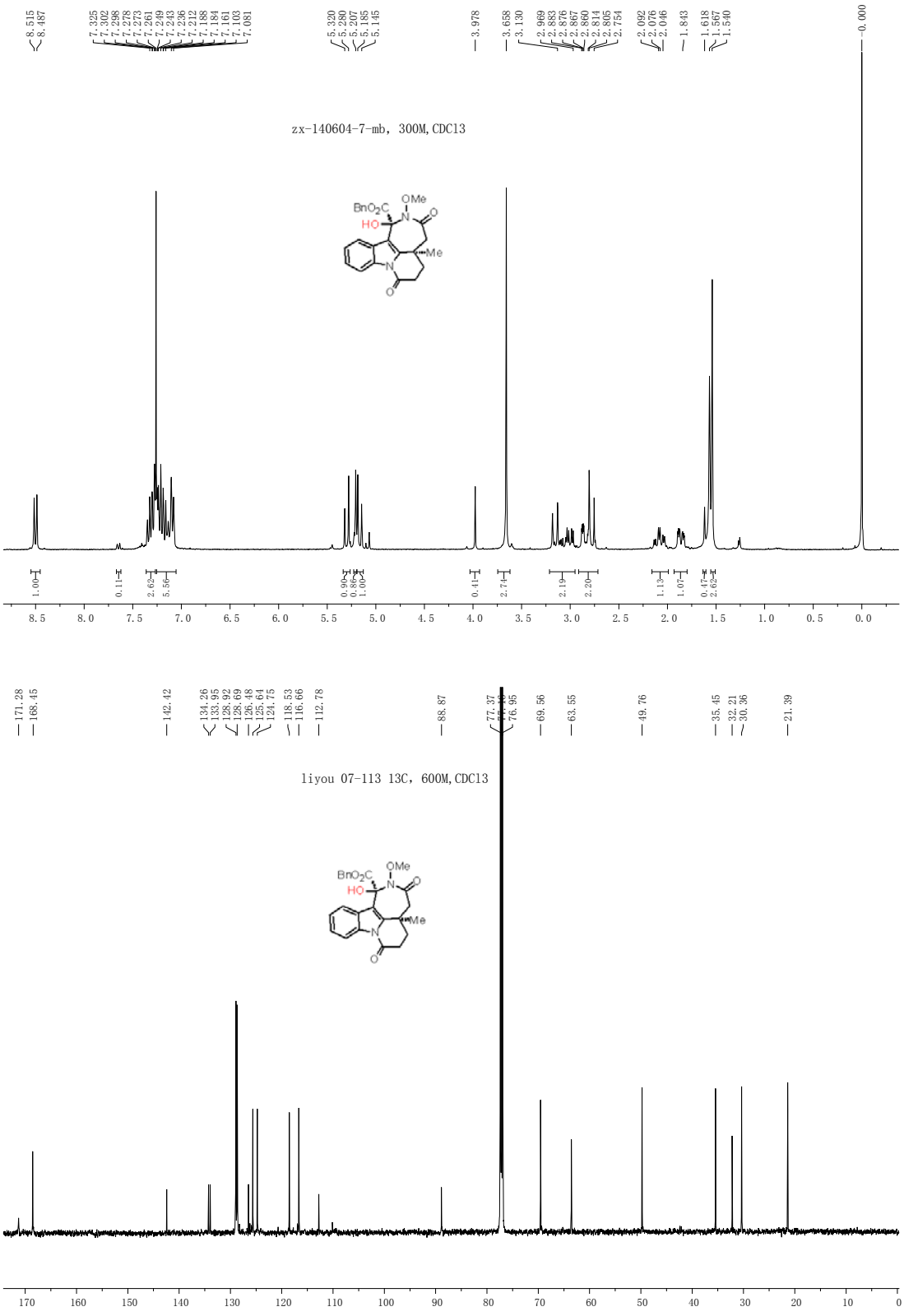


Figure S19. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **11b**

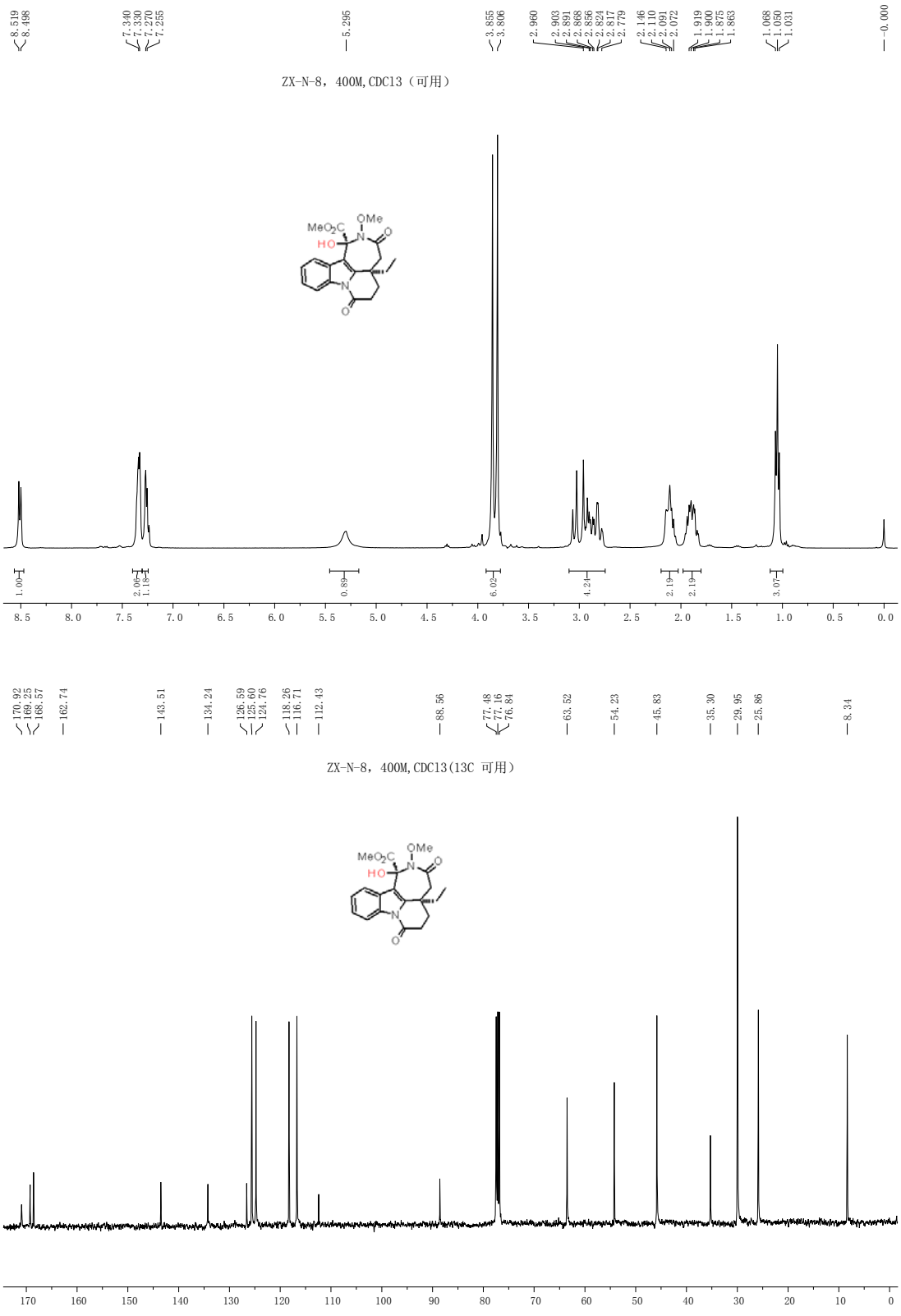


Figure S20 ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **11c**

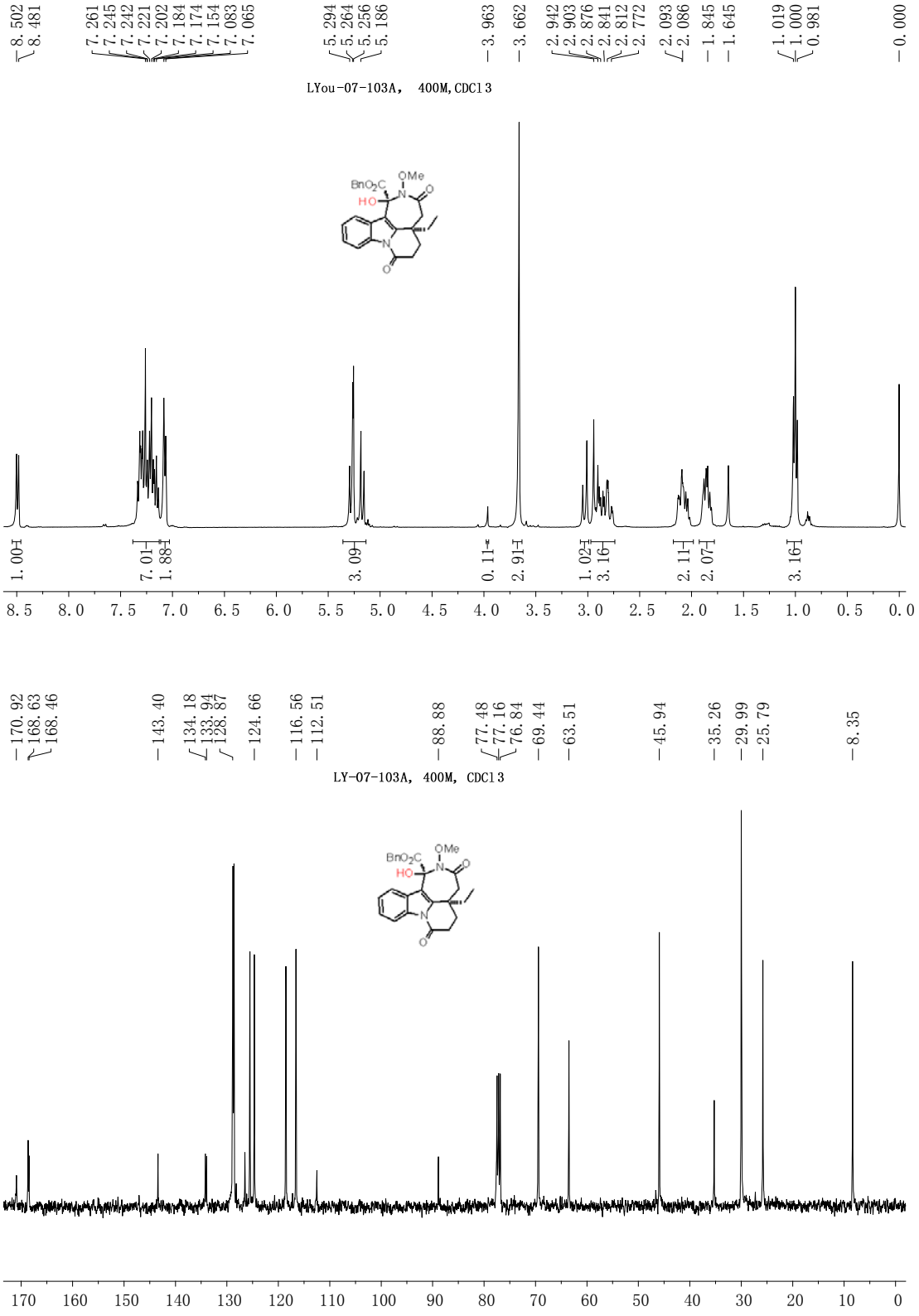


Figure S21. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **11d**

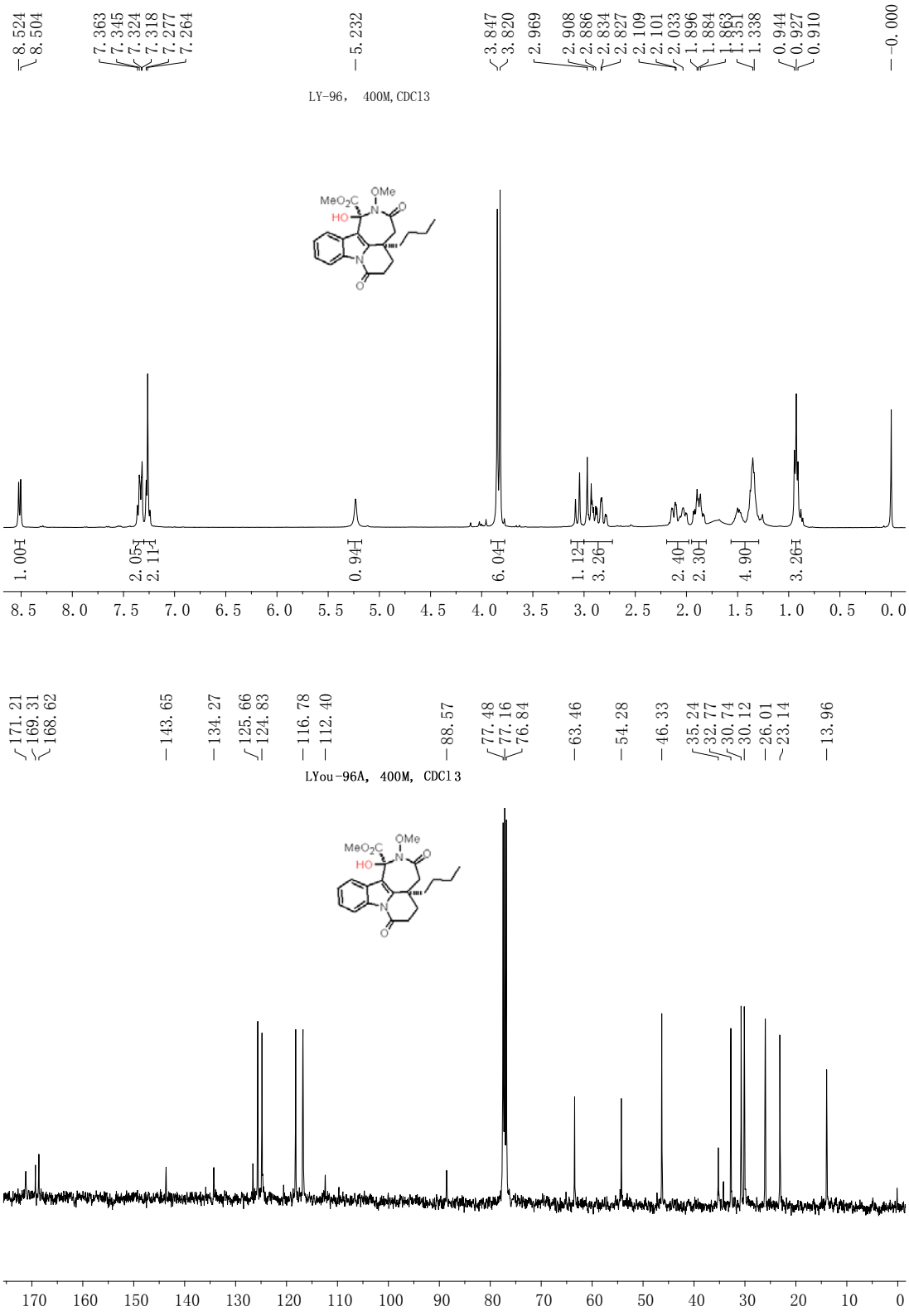


Figure S22. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **11e**

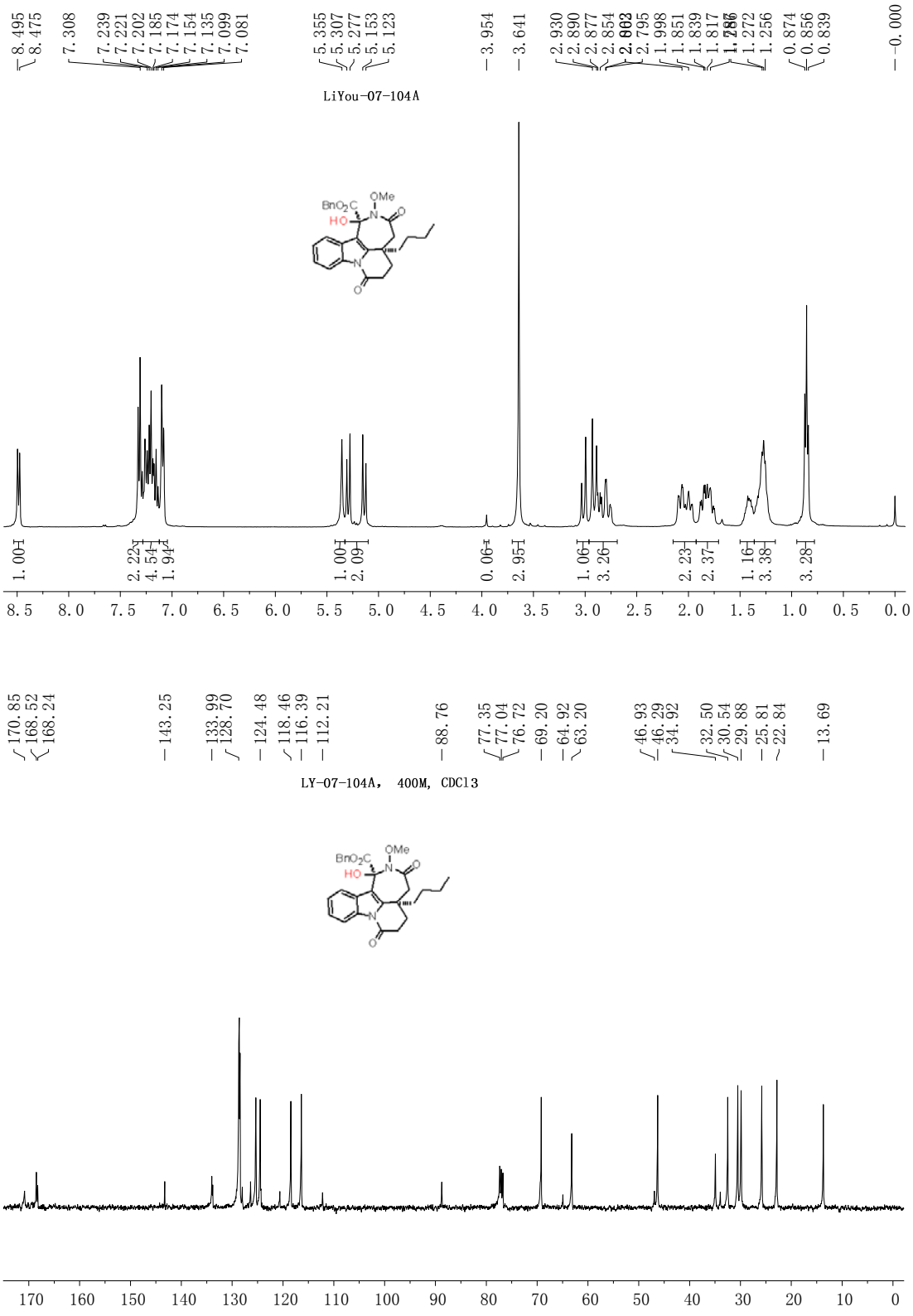


Figure S23. ^{1}H- (upper) and ^{13}C-NMR (lower) spectra of compound **11f**