*Supporting Information for*

# Total Synthesis of Linoxepin Facilitated by Ni-Catalyzed Tandem Reductive Cyclization

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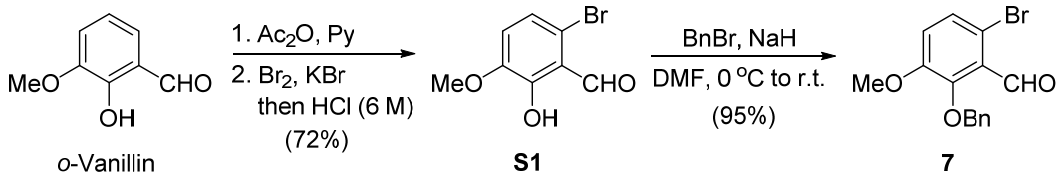
## General Procedure

For product purification by flash column chromatography, SiliaFlash P60 (particle size: 40~63 μm, pore size 60A) and petroleum ether (bp. 60~90 °C) were used. All solvents were purified and dried by standard techniques and distilled prior to use. All experiments were conducted under an argon or nitrogen atmosphere in oven-dried or flame-dried glassware with magnetic stirring, unless otherwise specified. Organic extracts were dried over $Na_2SO_4$, unless otherwise noted. IR spectra were recorded on a *Nicolet* FT-170SX spectrometer. $^{1}H$ and $^{13}C$ NMR spectra were taken on a *Bruker* AM-400, AM-600, Ascend-400, Ascend-600 spectrometer with TMS as an internal standard and $CDCl_3$ as solvent unless otherwise noted. HRMS were determined on a *Bruker Daltonics* APEXII 47e FT-ICR spectrometer with ESI positive ion mode. The X-ray diffraction studies were carried out on a Bruker SMART Apex CCD area detector diffractometer equipped with graphite-monochromated Mo-Kα radiation source. Melting points were measured on X-4 series microscope melting point apparatus.

The following chemicals were purchased and used as received: Zn (99.9%, dust), $NiCl_2$•DME (97%), crotonic acid (98%), pyridine (99.5%, SuperDry, with molecular sieves), DMA (99.5%, Extra Dry, with molecular sieves), DMF (99.8%, Extra Dry, with molecular sieves), 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TBCD, 97%).

**Preparation of *o*-Bromobenzaldehyde 7**




*o*-bromobenzaldehyde **S1** was prepared according to a general protocol described by Fuchs and co-workers.[1] In a 200 mL round-bottom flask, *o*-vanillin (20.0 g, 131 mmol) was dissolved in anhydrous pyridine (35 mL). Acetic anhydride (13.6 mL, 144 mmol, 1.1 equiv) was then added dropwise, and the whole mixture was stirred at room temperature for 24 hours. The resultant mixture was then poured into icy HCl (6 M, 120 mL). The mixture was stirred at 0 $^{o}$C for 20 minutes with glass rod, filtered, and the resulting 2-acetoxybenzaldehyde as a white powder was washed with icy HCl (6 M, 60 mL) and water (20 mL). This crude product could be used directly for the next reaction without further purification.

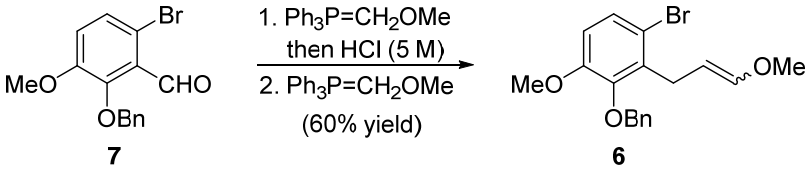
In a 1000 mL round-bottom flask, KBr (51.44 g, 432 mmol, 3.3 equiv) was dissolved in water (450 mL). $Br_2$ (7.9 mL, 157 mmol, 1.2 equiv) was then added dropwise at room temperature, and stirring was continued for 10 minutes. The generated bromination reagent was ready to use.

Meanwhile, the above 2-acetoxybenzaldehyde was placed in another 1000 mL round-bottom flask, followed by the addition of the freshly made bromination reagent dropwise. The mixture was stirred at room temperature for 2 hours, and filtered. The resulting pink powder was transfered into a 500 mL round-bottom flask, HCl (6 M, 275 mL) was then added dropwise. The mixture was stirred for 3 hours, filtered, and a yellow solid was obtained. The desired **S1** (21.69 g, 72% yield) as yellow acicular crystals were collected after recrystallization in anhydrous MeOH (220 mL). $R_f$ = 0.51 (petroleum ether/EtOAc = 2 : 1); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 12.29 (s, 1H), 10.30 (s, 1H), 7.10 (d, $J$ = 8.4 Hz, 1H), 6.92 (d, $J$ = 8.7 Hz, 1H), 3.90 (s, 3H) ppm; $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 198.3, 154.4, 148.3, 123.3, 118.1, 117.1, 116.3, 56.2 ppm.

[1] Toth, J. E.; Hamann, P. R.; Fuchs, P. L. *J. Org. Chem*. **1988**, *53*, 4694.

In a 250 mL round-bottom flask, **S1** (10.0 g, 43.5 mmol) was dissolved in anhydrous DMF (80 mL), and the resulting solution was cooled to 0 °C, followed by the addition of NaH (60%, 1.91 g, 47.9 mmol, 1.1 equiv). After stirring for 30 minutes at this temperature, BnBr (24.8 mL, 209 mmol, 4.8 equiv) and TBAI (2.09 g, 5.66 mmol, 0.13 equiv) was added, and the resulting mixture was gradually warmed to room temperature and stirred for 6 hours further. The reaction was carefully quenched by the addition of water (10 mL). The resultant mixture was extracted with $CH_2Cl_2$ (3 × 100 mL), and the combined organic layers were washed with water (6 × 40 mL) and brine (50 mL) respectively, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/EtOAc = 100 : 1 → petroleum ether/EtOAc = 20 : 1) on silica gel to afford *o*-bromobenzaldehyde **7** (13.22 g, 95% yield) as a yellow oil. $R_f$ = 0.37 (petroleum ether/EtOAc = 4 : 1); IR (film): $\nu_{max}$ = 1703, 1537, 1469, 1439, 1398, 1367, 1297, 1264, 1226, 1067, 970, 811, 698 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 10.23 (s, 1H), 7.43 (d, $J$ = 8.0 Hz, 1H), 7.42 (d, $J$ = 8.0 Hz, 1H), 7.38–7.32 (m, 4H), 6.96 (d, $J$ = 8.8 Hz, 1H), 5.10 (s, 2H), 3.88 (s, 3H) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 190.3, 152.8, 150.7, 136.3, 129.5, 129.0, 128.6 (2C), 128.5 (2C), 128.4, 117.4, 112.4, 76.4, 56.2 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{14}{}^{79}BrO_3$ $[M+H]^+$: 321.0121, found: 321.0118.

**Preparation Enol Methylether 6**



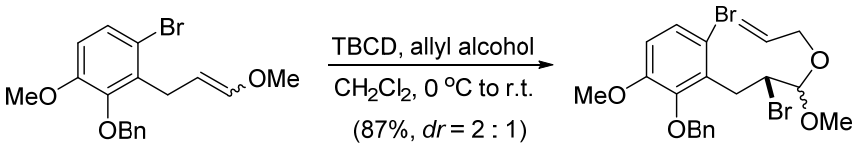

*t*-BuOK (98%, 7.15 g, 62.6 mmol, 2.0 equiv) was added in portions to a suspension of (methoxymethyl)triphenylphosphonium chloride (22.54 g, 65.7 mmol, 2.1 equiv) in THF (80 mL) at 0 ºC. After stirring for 40 minutes at 0 ºC, a solution of *o*-bromobenzaldehyde **7** (10.0 g, 31.3 mmol) in THF (20 mL) was added dropwise and the resulting mixture was gradually warmed to room temperature, and stirred for 5

hours. The reaction was then quenched by the addition of saturated aqueous $NH_4Cl$ solution (8 mL). The mixture was extracted with EtOAc (2 × 150 mL), and the combined organic layers were washed with water (2 × 40 mL) and brine (30 mL) respectively, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 40 : 1 → petroleum ether/EtOAc = 10 : 1) on silica gel. The resulting enol ether was dissolved in acetone (40 mL) followed by the addition of HCl (5 M, 7 mL) at room temperature. The mixture was heated to 60 $^oC$ and stirred for 4 hours, and then cooled to room temperature. The solvent was evaporated in vacuo, and the residue was extracted with EtOAc (2 × 80 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (2 × 20 mL), water (20 mL) and brine (20 mL) respectively, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The resulting *o*-bromo phenylacetaldehyde could be used directly for the next reaction without further purification.

*t*-BuOK (98%, 3.93 g, 34.4 mmol, 1.1 equiv) was added in portions to a suspension of (methoxymethyl)triphenylphosphonium chloride (12.9 g, 37.6 mmol, 1.2 equiv) in THF (60 mL) at 0 ºC. After stirring for 40 minutes at 0 ºC, a solution of the above *o*-bromophenylacetaldehyde in THF (20 mL) was added dropwise and the resulting mixture was gradually warmed to room temperature, and stirred for 6 hours. The reaction was quenched by the addition of saturated aqueous $NH_4Cl$ solution (5 mL). The mixture was extracted with EtOAc (2 × 80 mL), and the combined organic layers were washed with water (2 × 30 mL) and brine (20 mL) respectively, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 80 : 1 → petroleum ether/EtOAc = 20 : 1) on silica gel to afford the corresponding enol methylether **6** (6.79 g, 60% yield) as a pale yellow oil. $R_f$ = 0.63 (petroleum ether/EtOAc = 4 : 1); (*Z isomer*) $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.52 (d, $J$ = 7.2 Hz, 1H), 7.47 (d, $J$ = 7.2 Hz, 1H), 7.39–7.25 (m, 4H), 6.69 (d, $J$ = 8.7 Hz, 1H), 5.90 (d, $J$ = 6.0 Hz, 1H, =C*H*$OCH_3$), 4.96 (s, 2H), 4.41 (q, $J$ = 6.6 Hz, 1H, -C*H*=$CHOCH_3$), 3.84 (s, 3H), 3.65 (d, $J$ = 6.6 Hz, 1H), 3.55 (s, 3H), 3.40 (d, $J$ = 7.2 Hz, 1H) ppm; $^{13}C$ NMR (100 MHz,

$CDCl_3$): $\delta$ = 152.5, 148.5, 146.8, 146.2, 137.7, 135.3, 128.3, 128.1, 127.9 (2C), 115.4, 111.5, 103.9, 99.8, 74.8, 59.5, 55.9, 28.8 ppm; HRMS (ESI): *m/z* calcd for $C_{18}H_{19}{}^{79}BrO_3Na$ $[M+Na]^+$: 385.0410, found: 385.0401.

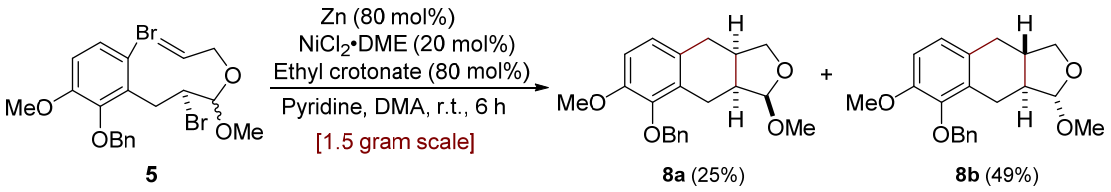
**Preparation of *β*-Bromo Acetal 5**




**6** **5**

In a 250 mL round-bottom flask, enol methylether **6** (4.2 g, 11.6 mmol) was dissolved in anhydrous $CH_2Cl_2$ (50 mL) and cooled to 0 °C. To this solution was added TBCD (5.87 g, 13.9 mmol, 1.2 equiv) portionwise, and the mixture was stirred for 35 minutes at 0 °C. A solution of allyl alcohol (15.8 mL, 232 mmol, 20 equiv) in $CH_2Cl_2$ (10 mL) was then added dropwise, and the resulting mixture was gradually warmed to room temperature and stirred further for 9 hours. The reaction was quenched with 5% aqueous $NaHCO_3$ (5 mL), $Na_2SO_3$ (5 mL) and stirred further for 30 minutes. The resulting mixture was then extracted with $CH_2Cl_2$ (2 × 100 mL), and the combined organic layers were washed with water (3 × 20 mL) and brine (20 mL) respectively, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/EtOAc = 50 : 1 → petroleum ether/EtOAc = 10 : 1) on silica gel to afford **5** (5.03 g, 87% yield, dr = 2 : 1) as a colorless oil. $R_f$ = 0.56 (petroleum ether/EtOAc = 4 : 1); IR (film): $\nu_{max}$ = 1638, 1385, 913, 745, 544 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.53–7.46 (m, 2H), 7.43–7.32 (m, 3H), 7.28 (d, *J* = 8.7 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 1H), 5.94–5.80 (m, 1H), 5.27 (dd, *J* = 17.1, 13.8 Hz, 1H), 5.14 (dd, *J* = 17.1, 9.3 Hz, 1H), 5.06–4.98 (m, 2H), 4.59–4.47 (m, 2H), 4.18–4.10 (m, 1H), 4.08–3.95 (m, 1H), 3.87 (s, 3H), 3.40–3.33 (m, 2H), 3.34 (s, 3H) ppm; (*slightly major isomer*) $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 152.0, 147.2, 137.2, 133.9, 132.4, 128.5, 128.3 (2C), 128.2 (2C), 127.9, 117.1, 115.8, 112.1, 104.2, 74.6, 68.4, 55.7, 55.0, 52.3, 33.6 ppm; HRMS (ESI): *m/z* calcd for $C_{21}H_{24}{}^{79}Br_2O_4Na$ $[M+Na]^+$: 520.9934, found: 520.9926.

## Stereoselective Synthesis of Tricyclic Acetals 8a and 8b



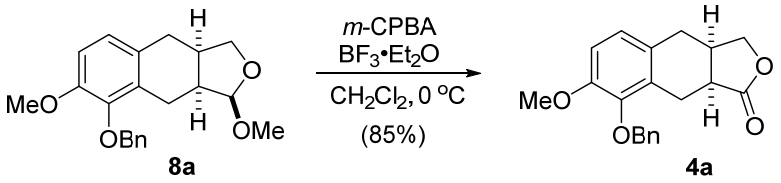

To a 50 mL round-bottom flask were added $NiCl_2$•DME (135 mg, 0.6 mmol, 20 mol%) and Zn (156 mg, 2.4 mmol, 80 mol%). The flask was evacuated and then backfilled with argon. This process was repeated 4 times. The pyridine (3 mL) and ethyl crotonate (0.3 mL, 2.4 mmol, 80 mol%) were then added successively at room temperature. The temperature then rose to 55 °C, and stirring (350 r/min) was continued for 15 minutes. The resulting red-brown Ni(0) complex was cooled to room temperature, and a solution of *β*-bromo acetal **5** (1.5 g, 3.0 mmol) in DMA (10 mL) was added dropwise. After stiring for 6 hours, the mixture was diluted and extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with water (3 × 20 mL) and brine (10 mL) respectively, dried over $Na_2SO_4$, filtered and concentrated. The resulting crude products were purified by flash column chromatography (petroleum ether/EtOAc = 50 : 1 → petroleum ether/EtOAc = 20 : 1) on silica gel to afford **8a** (252 mg, 25% yield) as a pale yellow oil and **8b** (495 mg, 49% yield) as a yellow oil.

Data for **8a**: $R_f$ = 0.50 (petroleum ether/EtOAc = 4 : 1); IR (film): $\nu_{max}$ = 1645, 1456, 1383, 769, 571 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.48 (d, $J$ = 6.6 Hz, 2H), 7.40–7.32 (m, 3H), 6.82 (d, $J$ = 8.1 Hz, 1H), 6.71 (d, $J$ = 8.1 Hz, 1H), 5.00 (d, $J$ = 11.1 Hz, 1H), 4.95 (d, $J$ = 11.1 Hz, 1H), 4.91 (d, $J$ = 5.1 Hz, 1H), 4.06 (t, $J$ = 7.5 Hz, 1H), 3.86 (s, 3H), 3.55 (t, $J$ = 7.2 Hz, 1H), 3.34 (s, 3H), 2.97 (dd, $J$ = 15.3, 7.2 Hz, 1H), 2.71–2.63 (m, 1H), 2.57 (dd, $J$ = 15.0, 9.0 Hz, 1H), 2.46–2.27 (m, 3H) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 150.8, 146.0, 138.0, 130.8, 128.8, 128.3 (2C), 128.0 (2C), 127.8, 124.7, 110.6, 110.0, 73.9, 71.6, 56.5, 55.9, 47.8, 41.5, 31.4, 26.1 ppm; HRMS (ESI): *m/z* calcd for $C_{21}H_{24}O_4$ Na $[M+Na]^+$: 363.1567, found: 363.1561.

Data for **8b**: $R_f$ = 0.37 (petroleum ether/EtOAc = 4 : 1); IR (film): $\nu_{max}$ = 1645,

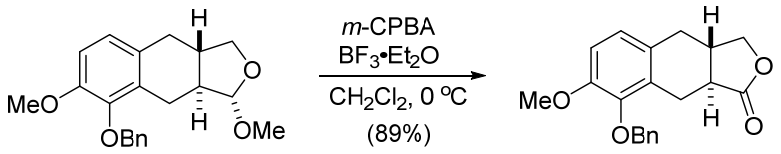
913, 745, 655 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.49 (d, $J$ = 6.9 Hz, 2H), 7.41–7.33 (m, 3H), 6.86 (d, $J$ = 8.1 Hz, 1H), 6.79 (d, $J$ = 8.4 Hz, 1H), 5.04 (d, $J$ = 11.1 Hz, 1H), 4.96 (d, $J$ = 10.8 Hz, 1H), 4.84 (d, $J$ = 6.0 Hz, 1H), 4.11 (t, $J$ = 6.9 Hz, 1H), 3.87 (s, 3H), 3.67 (dd, $J$ = 10.5, 8.1 Hz, 1H), 3.48 (s, 3H), 3.29 (dd, $J$ = 16.8, 4.8 Hz, 1H), 2.88 (dd, $J$ = 15.3, 4.2 Hz, 1H), 2.62 (dd, $J$ = 15.0, 12.3 Hz, 1H), 2.41 (dd, $J$ = 16.2, 12.6 Hz, 1H), 2.12–1.97 (m, 1H), 1.87 (ddd, $J$ = 18.3, 12.3, 6.3 Hz, 1H) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 151.2, 144.7, 138.0, 133.2, 131.7, 128.33 (2C), 128.28 (2C), 127.8, 122.4, 109.2, 105.5, 74.7, 70.7, 55.9, 54.7, 42.4, 38.4, 32.1, 20.1 ppm; HRMS (ESI): *m/z* calcd for $C_{21}H_{24}O_4$ Na $[M+Na]^+$: 363.1567, found: 363.1558.

**Synthesis of Lactones 4a and 4b**




To a stirred solution of acetal **8a** (1.2 g, 3.53 mmol) in $CH_2Cl_2$ (20 mL) was added *m*-CPBA (77%, 1.577 g, 7.06 mmol, 2.0 equiv) at 0 °C, followed by the addition of $BF_3$•$Et_2O$ (0.67 mL, 5.3 mmol, 1.5 equiv) dropwise. After 20 minutes, the reaction mixture was quenched by saturated aqueous $Na_2SO_3$ (1 mL) and extracted with $CH_2Cl_2$ (3 × 20 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (3 × 10 mL), water (10 mL) and brine (10 mL), then dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The resulting crude products were purified by flash column chromatography (petroleum ether/EtOAc = 10 : 1 → petroleum ether/EtOAc = 4 : 1) on silica gel to afford **4a** (964 mg, 85% yield) as a white solid. $R_f$ = 0.43 (petroleum ether/EtOAc = 2 : 1); Mp. 119–121 °C; IR (film): $\nu_{max}$ = 1763, 1646, 1488, 1385, 1270, 913, 745, 655 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 7.51 (d, $J$ = 6.8 Hz, 2H), 7.40–7.30 (m, 3H), 6.86 (d, $J$ = 8.0 Hz, 1H), 6.76 (d, $J$ = 8.4 Hz, 1H), 5.05 (d, $J$ = 10.8 Hz, 1H), 4.88 (d, $J$ = 10.4 Hz, 1H), 4.44 (dd, $J$ = 9.2, 7.6 Hz, 1H), 3.88 (dd, $J$ = 9.2, 4.0 Hz, 1H), 3.85 (s, 3H), 3.17 (dd,

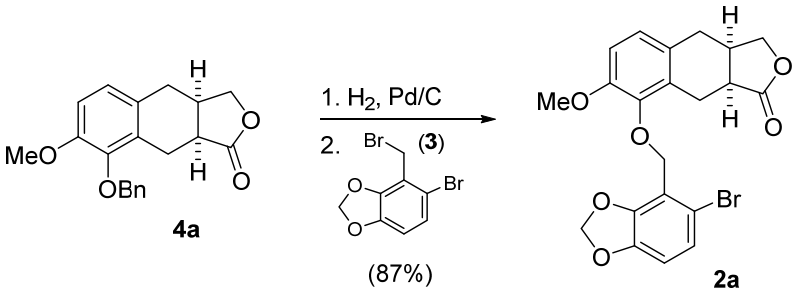
*J* = 15.2, 3.2 Hz, 1H), 3.00–2.89 (m, 2H), 2.84 (dd, *J* = 15.2, 6.8 Hz, 1H), 2.74 (dd, *J* = 14.8, 5.2 Hz, 1H), 2.49 (dd, *J* = 14.8, 5.6 Hz, 1H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 179.6, 151.7, 145.2, 137.7, 129.9, 128.6, 128.5 (2C), 128.3 (2C), 127.9, 123.4, 110.4, 74.9, 72.3, 55.8, 38.5, 33.6, 31.8, 22.4 ppm; ESI–MS: *m/z*: 347.1 $[M+Na]^+$.




**8b** **4b**

**4b** was prepared as a white solid (1.18 g, 89% yield) from **8b** in a similar way to that of lactone **4a**. $R_f$ = 0.38 (petroleum ether/EtOAc = 2 : 1); Mp. 131–133 °C; IR (film): $\nu_{max}$ = 1779, 1645, 1487, 1275, 993, 913, 745 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.46 (d, *J* = 6.8 Hz, 2H), 7.39–7.30 (m, 3H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 1H), 5.03 (d, *J* = 10.8 Hz, 1H), 5.00 (d, *J* = 11.2 Hz, 1H), 4.56 (dd, *J* = 8.4, 6.8 Hz, 1H), 4.00 (dd, *J* = 10.4, 8.4 Hz, 1H), 3.87 (s, 3H), 3.41 (dd, *J* = 16.8, 5.2 Hz, 1H), 3.00 (dd, *J* = 15.2, 4.4 Hz, 1H), 2.75 (dd, *J* = 14.8, 12.0 Hz, 1H), 2.53 (dd, *J* = 16.8, 12.0 Hz, 1H), 2.43–2.23 (m, 2H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 177.0, 151.1, 146.1, 137.6, 129.6, 128.4 (2C), 128.2 (2C), 128.0, 127.3, 124.8, 111.1, 74.1, 72.3, 55.9, 41.8, 39.7, 32.3, 23.9 ppm; ESI–MS: *m/z* 347.1 $[M+Na]^+$.

**Synthesis of Tetracyclic Compounds 2a, 2b and 10a-c**




In a 50 mL round-bottom flask, lactone **4a** (301 mg, 0.93 mmol) was dissolved in anhydrous MeOH (20 mL) followed by the addition of Pd/C (10% wt/wt, 297 mg). The flask was evacuated and then backfilled with hydrogen. This process was repeated 3 times. The flask was hydrogenated under 1 atm for 30 minutes. The

mixture was filtered and concentrated under reduced pressure. The resulting phenol could be used directly for the next reaction without further purification. In a 50 mL round-bottom flask, the above phenol and **3**[2] (300 mg, 1.02 mmol, 1.1 equiv) was dissolved in anhydrous MeCN (15 mL) followed by the addition of $K_2CO_3$ (257 mg, 1.86 mmol, 2.0 equiv). The resulting mixture was gradually warmed to 80 °C and stirred further for 2.5 hours. After filtration and concentration under reduced pressure, the crude product was purified by flash column chromatography (petroleum ether/EtOAc = 4 : 1 → petroleum ether/EtOAc = 1 : 1) on silica gel to afford **2a** (361 mg, 87% yield) as a white solid. $R_f$ = 0.38 (petroleum ether/EtOAc = 2 : 1); Mp. 173–174 °C; IR (film): $\nu_{max}$ = 1635, 1488, 1455, 1260, 913, 744, 545 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 7.04 (d, $J$ = 8.4 Hz, 1H), 6.85 (d, $J$ = 8.0 Hz, 1H), 6.74 (d, $J$ = 8.0 Hz, 1H), 6.66 (d, $J$ = 8.4 Hz, 1H), 6.04 (d, $J$ = 1.2 Hz, 1H), 5.99 (d, $J$ = 1.2 Hz, 1H), 5.17 (d, $J$ = 10.8 Hz, 1H), 5.14 (d, $J$ = 11.2 Hz, 1H), 4.45 (dd, $J$ = 8.8, 6.8 Hz, 1H), 3.96 (dd, $J$ = 8.0, 3.2 Hz, 1H), 3.85 (s, 3H), 3.15 (dd, $J$ = 15.6, 7.2 Hz, 1H), 2.90 (dd, $J$ = 15.6, 5.2 Hz, 1H), 2.83–2.75 (m, 3H), 2.47 (t, $J$ = 6.8 Hz, 1H) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 179.4, 151.8, 148.5, 147.1, 144.9, 130.2, 128.9, 125.1, 123.3, 119.0, 116.5, 110.4, 109.5, 102.0, 72.3, 68.3, 56.0, 38.4, 34.3, 31.8, 22.0 ppm; ESI–MS: *m/z* 447.1 $[M+H]^+$.

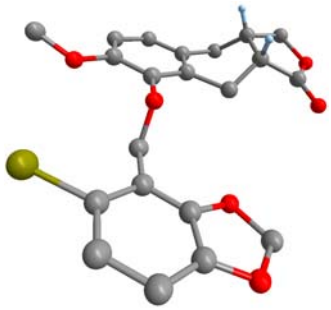
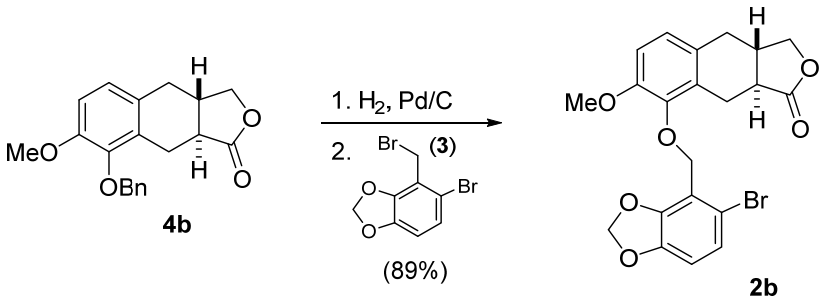


**Table S1**: X-ray crystal data of **2a** (selected H atoms have been omitted for clarity)

| | |
|---|---|
| Empirical formula | $C_{21}H_{19}BrO_6$ |
| Temperature (K) | 293(2) |
| Crystal color | colorless |
| Formula weight | 447.27 |

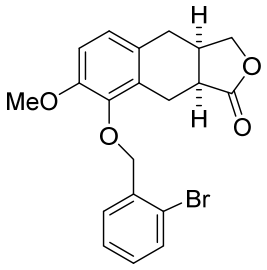
[2] Weinstabl, H.; Suhartono, M.; Qureshi, Z.; Lautens, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 5305.

| | |
|---|---|
| Crystal system | triclinic |
| Space group | *P*-1 |
| *a* (Å) | 7.6456(9) |
| *b* (Å) | 8.944(3) |
| *c* (Å) | 13.8908(19) |
| *α* (°) | 98.172(17) |
| *β* (°) | 100.703(11) |
| *γ* (°) | 94.856(16) |
| *V* (Å $^3$) | 917.9(3) |
| *Z* | 2 |
| Density (calculated) (g/cm$^3$) | 1.618 |
| *F* (000) | 456 |
| *λ* (Å) | 0.71073 |
| Reflections collected | 5735 |
| Independent reflections | 3599 |
| 2θ range for data collection (°) | 6.74—52.04 |
| Index range | $-8 \le h \le 9$<br>$-11 \le k \le 10$<br>$-16 \le l \le 17$ |
| Final *R* indices [I>2σ(*I*)] | $R_1 = 0.0698$, $wR_2 = 0.1270$ |
| Largest difference peak and hole [e Å $^{-3}$] | 0.525, –0.659 |



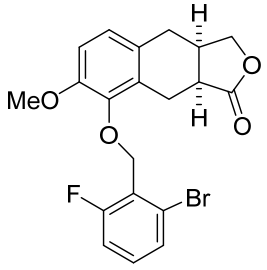

**2b** was prepared as a white solid (171 mg, 89% yield) from **4b** in a similar way to that of lactone **2a**. $R_f$ = 0.3 (petroleum ether/EtOAc = 2 : 1); Mp. 186–187 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.05 (d, $J$ = 8.4 Hz, 1H), 6.86 (d, $J$ = 8.4 Hz, 1H), 6.79 (d, $J$ = 8.4 Hz, 1H), 6.68 (d, $J$ = 8.4 Hz, 1H), 6.05 (s, 2H), 5.17 (d, $J$ = 10.5 Hz, 1H), 5.13 (s, $J$ = 10.5 Hz, 1H), 4.55 (dd, $J$ = 8.7, 6.6 Hz, 1H), 3.99 (dd, $J$ = 10.2, 8.7 Hz,

1H), 3.87 (s, 3H), 3.49 (dd, $J$ = 17.4, 5.1 Hz, 1H), 2.99 (dd, $J$ = 15.3, 4.5 Hz, 1H), 2.74 (dd, $J$ = 15.0, 11.7 Hz, 1H), 2.54 (dd, $J$ = 16.8, 12.0 Hz, 1H), 2.45–2.33 (m, 1H), 2.27 (dd, $J$ = 11.7, 5.1 Hz, 1H) ppm; $^{13}$C NMR (100MHz, $CDCl_3$): $\delta$ = 177.0, 151.3, 148.4, 147.1, 146.0, 129.8, 127.2, 125.2, 124.9, 119.0, 116.3, 111.0, 109.7, 102.0, 72.2, 67.8, 56.1, 41.7, 39.8, 32.2, 23.8 ppm; HRMS (ESI): $m/z$ calcd for $C_{21}H_{20}{}^{79}BrO_6^+$ $[M+H]^+$: 447.0438, found: 447.0436.




**10a**

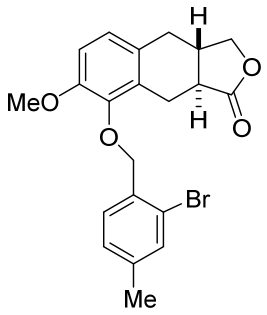
**10a** was prepared as a white solid (123 mg, 90% yield) in a similar way to that of lactone **2a**. $R_f$ = 0.61 (petroleum ether/EtOAc = 2 : 1); Mp. 143–144 °C; $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 7.74 (dd, $J$ = 7.8, 1.8 Hz, 1H), 7.57 (dd, $J$ = 7.8, 1.2 Hz, 1H), 7.37 (td, $J$ = 7.8, 1.2 Hz, 1H), 7.18 (td, $J$ = 7.8, 1.8 Hz, 1H), 6.88 (d, $J$ = 8.4 Hz, 1H), 6.77 (d, $J$ = 7.8 Hz, 1H), 5.11 (d, $J$ = 12.6 Hz, 1H), 5.03 (d, $J$ = 12.0 Hz, 1H), 4.46 (dd, $J$ = 9.0, 7.8 Hz, 1H), 3.92 (dd, $J$ = 9.6, 4.2 Hz, 1H), 3.84 (s, 3H), 3.16 (dd, $J$ = 15.0, 3.6 Hz, 1H), 3.01–2.90 (m, 3H), 2.78 (dd, $J$ = 15.0, 6.0 Hz, 1H), 2.52 (dd, $J$ = 15.0, 6.6 Hz, 1H) ppm; $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 179.4, 151.7, 145.1, 137.4, 132.4, 129.8, 129.7, 129.1, 128.7, 127.5, 123.6, 122.7, 110.5, 73.8, 72.3, 55.9, 38.5, 33.8, 31.8, 22.3 ppm; HRMS (ESI): $m/z$ calcd for $C_{20}H_{20}{}^{79}BrO_4^+$ $[M+H]^+$: 403.0539, found: 403.0539.




**10b**

**10b** was prepared as a white solid (133 mg, 93% yield) in a similar way to that of

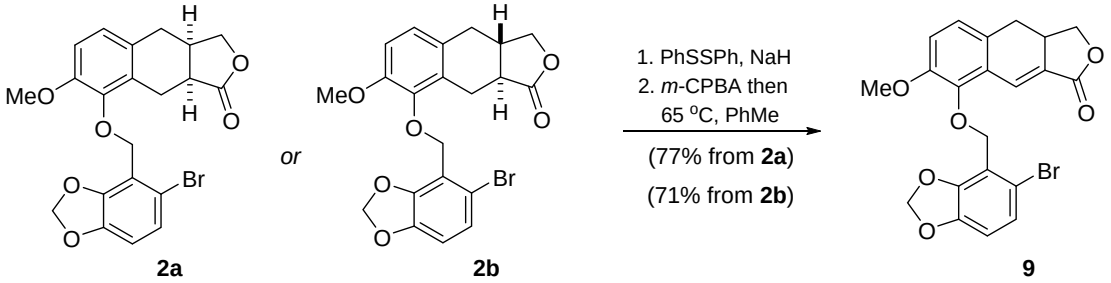
lactone **2a**. $R_f$ = 0.45 (petroleum ether/EtOAc = 2 : 1); Mp. 122–123 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.41 (d, $J$ = 8.1 Hz, 1H), 7.19 (dt, $J$ = 5.7, 8.1 Hz, 1H), 7.05 (t, $J$ = 9.0 Hz, 1H), 6.87 (d, $J$ = 8.4 Hz, 1H), 6.74 (d, $J$ = 8.1 Hz, 1H), 5.27–5.18 (m, 2H), 4.45 (dd, $J$ = 8.7, 7.2 Hz, 1H), 3.93 (dd, $J$ = 9.3, 3.3 Hz, 1H), 3.85 (s, 3H), 3.02–3.00 (m, 2H), 2.94–2.82 (m, 2H), 2.75 (dd, $J$ = 14.7, 5.1 Hz, 1H), 2.47 (dd, $J$ = 14.4, 6.6 Hz, 1H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 179.3, 162.2 (d, $J_{C-F}$ = 251.0 Hz), 151.7, 144.8, 130.9 (d, $J_{C-F}$ = 9.0 Hz), 130.1, 128.7, 128.6 (d, $J_{C-F}$ = 3.0 Hz), 126.5 (d, $J_{C-F}$ = 5.0 Hz), 125.1 (d, $J_{C-F}$ = 17.0 Hz), 123.5, 114.8 (d, $J_{C-F}$ = 23.0 Hz), 110.3, 72.1, 67.5 (d, $J_{C-F}$ = 3.0 Hz), 55.9, 38.3, 34.1, 31.8, 22.0 ppm; $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –111.18 ppm; HRMS (ESI): $m/z$ calcd for $C_{20}H_{18}{}^{79}BrFO_4Na^+$ $[M+Na]^+$: 443.0265, found: 443.0259.




**10c**

**10c** was prepared as a white solid (70 mg, 89% yield) in a similar way to that of lactone **2b**. $R_f$ = 0.60 (petroleum ether/EtOAc = 2 : 1); Mp. 178–180 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.57 (d, $J$ = 7.6 Hz, 1H), 7.39 (s, 1H), 7.17 (d, $J$ = 7.6 Hz, 1H), 6.89 (d, $J$ = 8.4 Hz, 1H), 6.82 (d, $J$ = 8.4 Hz, 1H), 5.07 (d, $J$ = 12.4 Hz, 1H), 5.03 (d, $J$ = 12.0 Hz, 1H), 4.57 (dd, $J$ = 8.4, 6.8 Hz, 1H), 4.01 (dd, $J$ = 10.0, 8.4 Hz, 1H), 3.85 (s, 3H), 3.43 (dd, $J$ = 17.2, 5.2 Hz, 1H), 3.01 (dd, $J$ = 15.2, 4.4 Hz, 1H), 2.77 (dd, $J$ = 15.2, 11.6 Hz, 1H), 2.60 (dd, $J$ = 16.8, 12.0 Hz, 1H), 2.44–2.37 (m, 1H), 2.34 (s, 3H), 2.29 (dd, $J$ = 13.2, 5.2 Hz, 1H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 177.1, 151.0, 146.0, 139.2, 134.1, 132.8, 129.4, 129.0, 128.3, 127.3, 124.9, 122.0, 110.9, 73.0, 72.3, 55.9, 41.7, 39.7, 32.2, 23.8, 20.8 ppm; HRMS (ESI): $m/z$ calcd for $C_{21}H_{21}{}^{79}BrO_4Na^+$ $[M+Na]^+$: 439.0515, found: 439.0511.

**Synthesis of Tetracyclic Compounds 9 and 11a-c**



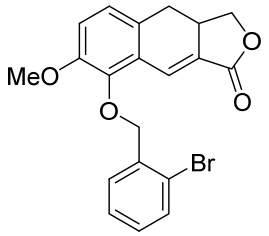

**2a** **2b** **9**

To a 25 mL round-bottom flask containing NaH (60%, 36 mg, 0.9 mmol, 1.5 equiv) was added DMF (2 mL), and the mixture was cooled to 0 °C followed by the addition a solution of **2b** (268 mg, 0.6 mmol) in DMF (4 mL). 10 minutes later, a solution of PhSSPh (99%, 265 mg, 1.2 mmol, 2.0 equiv) in DMF (2 mL) was added dropwise, and the whole mixture was stirred for 3 hours at 0 °C. The reaction was quenched by ice water (1 mL) and extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with water (2 × 8 mL) and brine (8 mL) respectively, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The resulting $\alpha$-phenyl sulfide could be used directly for the next reaction without further purification.

To a stirred solution of above $\alpha$-phenyl sulfide in $CH_2Cl_2$ (8 mL) was added $NaHCO_3$ (101 mg, 1.2 mmol, 2.0 equiv) at 0 °C, followed by the addition of *m*-CPBA (75%, 151 mg, 0.66 mmol, 1.1 equiv). After stirring for 10 minutes, the reaction mixture was quenched by saturated aqueous $NaHCO_3$ (1 mL) and extracted with $CH_2Cl_2$ (3 × 30 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (2 × 8 mL), water (8 mL) and brine (8 mL) respectively, then dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The resulting sulfoxide could be used directly for the next reaction without further purification.

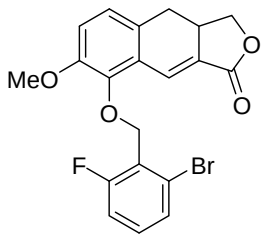
An oven-dried 10 mL round-bottom flask was charged with 4Å molecular sieve (300 mg) at room temperature under argon, followed by the addition of a solution of the above sulfoxide in anhydrous toluene (3 mL). After stirring for 40 minutes at 65 ºC, the mixture was cooled to room temperature, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 8 : 1 → petroleum ether/EtOAc = 2 : 1) on silica gel to afford **9** as a white solid (189 mg, 71% yield). $R_f$ = 0.35 (petroleum ether/EtOAc = 2 :

1); Mp. 202–203 °C; $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.84 (d, $J$ = 3.2 Hz, 1H), 6.99 (d, $J$ = 8.0 Hz, 1H), 6.93 (d, $J$ = 8.4 Hz, 1H), 6.85 (d, $J$ = 8.0 Hz, 1H), 6.65 (d, $J$ = 8.4 Hz, 1H), 6.14 (d, $J$ = 0.8 Hz, 1H), 6.07 (s, 1H), 5.22 (s, 2H), 4.71 (t, $J$ = 8.8 Hz, 1H), 3.98 (t, $J$ = 8.8 Hz, 1H), 3.91 (s, 3H), 3.12 (dddd, $J$ = 15.6, 12.4, 8.8, 3.2 Hz, 1H), 2.95 (dd, $J$ = 15.2, 7.2 Hz, 1H), 2.60 (t, $J$ = 15.6 Hz, 1H) ppm; $^{13}$C NMR (100MHz, $CDCl_3$): $\delta$ = 169.7, 152.2, 148.5, 147.1, 145.5, 128.6, 127.6, 127.2, 127.1, 125.1, 123.7, 118.0, 116.3, 113.3, 109.8, 102.3, 72.5, 68.8, 56.1, 34.4, 32.2 ppm; HRMS (ESI): $m/z$ calcd for $C_{21}H_{18}{}^{79}BrO_6^+$ $[M+H]^+$: 445.0281, found: 445.0278.



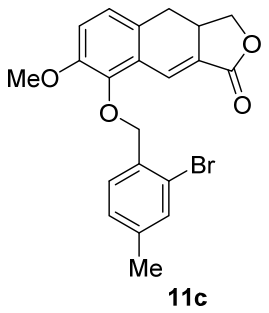

**11a**

**11a** was prepared as a white solid (40 mg, 75% yield) in a similar way to that of lactone **9**. $R_f$ = 0.55 (petroleum ether/EtOAc = 2 : 1); Mp. 150–151 °C; $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.75 (d, $J$ = 3.2 Hz, 1H), 7.64 (d, $J$ = 6.8 Hz, 1H), 7.56 (d, $J$ = 8.0 Hz, 1H), 7.36 (t, $J$ = 6.8 Hz, 1H), 7.19 (t, $J$ = 8.0 Hz, 1H), 6.96 (d, $J$ = 8.4 Hz, 1H), 6.89 (d, $J$ = 8.4 Hz, 1H), 5.15 (d, $J$ = 12.4 Hz, 1H), 5.10 (d, $J$ = 12.4 Hz, 1H), 4.74 (t, $J$ = 8.8 Hz, 1H), 4.01 (t, $J$ = 8.8 Hz, 1H), 3.87 (s, 3H), 3.23 (dddd, $J$ = 16.0, 12.0, 8.8, 3.6 Hz, 1H), 2.99 (dd, $J$ = 15.2, 7.2 Hz, 1H), 2.65 (t, $J$ = 15.2 Hz, 1H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 169.7, 151.8, 146.0, 136.5, 132.5, 129.5, 129.3, 128.1, 128.0, 127.6, 127.3, 127.1, 123.7, 122.6, 113.4, 74.5, 72.5, 56.0, 34.5, 32.3 ppm; HRMS (ESI): $m/z$ calcd for $C_{20}H_{18}O_4{}^{79}Br^+$ $[M+H]^+$: 401.0383, found: 401.0384.




**11b**

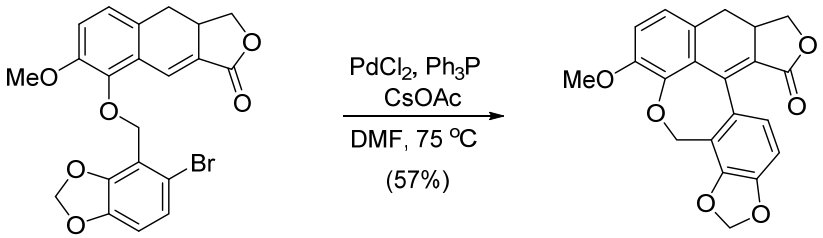
**11b** was prepared as a white solid (53 mg, 68% yield) in a similar way to that of lactone **9**. $R_f$ = 0.35 (petroleum ether/EtOAc = 2 : 1); Mp. 135–137 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.69 (d, $J$ = 3.2 Hz, 1H), 7.39 (d, $J$ = 8.0 Hz, 1H), 7.18 (dt, $J$ = 8.0, 6.0 Hz, 1H), 7.03 (t, $J$ = 8.0 Hz, 1H), 6.93 (d, $J$ = 8.0 Hz, 1H), 6.86 (d, $J$ = 8.4 Hz, 1H), 5.30 (s, 1H), 5.29 (s, 1H), 4.69 (t, $J$ = 8.8 Hz, 1H), 3.96 (t, $J$ = 8.8 Hz, 1H), 3.89 (s, 3H), 3.12 (dddd, $J$ = 15.6, 12.0, 8.8, 3.2 Hz, 1H), 2.94 (dd, $J$ = 15.2, 7.2 Hz, 1H), 2.59 (t, $J$ = 15.2 Hz, 1H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 169.5, 162.1 (d, $J_{C-F}$ = 251.0 Hz), 152.0, 145.8, 131.2 (d, $J_{C-F}$ = 10.0 Hz), 128.7 (d, $J_{C-F}$ = 4.0 Hz), 128.2, 127.6, 127.4, 127.2, 126.6 (d, $J_{C-F}$ = 4.0 Hz), 124.3 (d, $J_{C-F}$ = 18.0 Hz), 123.7, 114.8 (d, $J_{C-F}$ = 23.0 Hz), 113.4, 72.4, 68.1 (d, $J_{C-F}$ = 3.0 Hz), 56.1, 34.5, 32.3 ppm; $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –111.18 ppm; HRMS (ESI): $m/z$ calcd for $C_{20}H_{17}O_4F^{79}Br^+$ $[M+H]^+$: 419.0289, found: 419.0283.




**11c**

**11c** was prepared as a white solid (34 mg, 79% yield) in a similar way to that of lactone **9**. $R_f$ = 0.50 (petroleum ether/EtOAc = 2 : 1); Mp. 185–186 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.73 (d, $J$ = 3.2 Hz, 1H), 7.47 (d, $J$ = 8.0 Hz, 1H), 7.39 (s, 1H), 7.15 (d, $J$ = 7.6 Hz, 1H), 6.94 (d, $J$ = 8.4 Hz, 1H), 6.88 (d, $J$ = 8.4 Hz, 1H), 5.12 (d, $J$ = 12.0 Hz, 1H), 5.07 (d, $J$ = 12.0 Hz, 1H), 4.73 (t, $J$ = 8.8 Hz, 1H), 4.00 (t, $J$ = 8.8 Hz, 1H), 3.87 (s, 3H), 3.21 (dddd, $J$ = 16.0, 12.4, 9.2, 3.6 Hz, 1H), 2.98 (dd, $J$ = 15.2, 6.8 Hz, 1H), 2.63 (t, $J$ = 15.2 Hz, 1H), 2.33 (s, 3H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 169.7, 151.8, 146.1, 139.7, 133.4, 133.0, 129.6, 128.3, 128.2, 127.8, 127.3, 127.1, 123.6, 122.7, 113.4, 74.4, 72.5, 56.0, 34.5, 32.3, 20.8 ppm; HRMS (ESI): $m/z$ calcd for $C_{21}H_{20}O_4{}^{79}Br^+$ $[M+H]^+$: 415.0539, found: 415.0537.

**Synthesis of Linoxepin (1)**




**9** (±)-Linoxepin (**1**)

An oven-dried 5 mL round-bottom flask was charged with **9** (10 mg, 0.023 mmol), $PdCl_2$ (0.8 mg, 0.0046 mmol, 0.2 equiv), $PPh_3$ (2.6 mg, 0.01 mmol, 0.44 equiv) and CsOAc (44 mg, 0.23 mmol, 10 equiv), and was evacuated then backfilled argon. This process was repeated 3 times, followed by the addition of deoxygenated DMF (1 mL). After stirring for 5 minutes at room temperature, this suspension was heated to 75 °C and stirred further for 4 hours. The reaction was quenched by saturated aqueous $NH_4Cl$ (0.5 mL) and extracted with 1/1 mixture of EtOAc / hexanes (2 × 10 mL). The organic layers were washed with water (2 × 2 mL) and brine (2 mL), then dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The resulting crude products were purified by flash column chromatography (petroleum ether/EtOAc = 4 : 1 → petroleum ether/EtOAc = 2 : 1) on silica gel to afford racemic linoxepin (**1**, 4.8 mg, 57% yield) as a yellow solid. $R_f$ = 0.2 (petroleum ether/EtOAc = 2 : 1); Mp. 206–208 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 6.87 (d, $J$ = 8.4 Hz, 1H), 6.82 (d, $J$ = 8.8 Hz, 1H), 6.80 (d, $J$ = 8.0 Hz, 1H), 6.74 (d, $J$ = 8.0 Hz, 1H), 6.03 (s, 2H), 5.40 (d, $J$ = 12.4 Hz, 1H), 5.14 (d, $J$ = 12.4 Hz, 1H), 4.68 (t, $J$ = 8.8 Hz, 1H), 4.03 (t, $J$ = 8.8 Hz, 1H), 3.85 (s, 3H), 3.28 (ddt, $J$ = 14.4, 8.8, 6.0 Hz, 1H), 3.00 (dd, $J$ = 14.4, 5.6 Hz, 1H), 2.66 (t, $J$ = 14.4 Hz, 1H) ppm; $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 168.8, 149.5, 149.1, 148.6, 145.7, 144.8, 129.5, 128.2, 124.4, 124.2, 122.3, 119.8, 116.5, 111.9, 108.1, 101.9, 70.0, 64.7, 56.2, 36.9, 34.5 ppm; HRMS (ESI): $m/z$ calcd for $C_{21}H_{17}O_6^+$ $[M+H]^+$: 365.1020, found: 365.1016. This product was dissolved in EtOAc (1 mL) and hexane (2 mL). After 4 days, colorless single crystals were obtained by slow evaporation of solvents at room temperature.

**Table S2**: NMR Data Comparison of Synthetic Linoxepin

| **$^{1}$H NMR [$\delta$ H (ppm), *J* (Hz)]** | | **$^{13}$C NMR [$\delta$ C (ppm)]** | |
|---|---|---|---|
| Gao' report[3] ($CDCl_3$, 400 MHz) | Our synthetic sample ($CDCl_3$, 400 MHz) | Gao' report[3] ($CDCl_3$, 100 MHz) | Our synthetic sample ($CDCl_3$, 150 MHz) |
| 6.89–6.79 *m* | 6.87 *d* (8.4) | 168.94 | 168.80 |
| | 6.82 *d* (8.8) | 149.62 | 149.48 |
| | 6.80 *d* (8.0) | 149.20 | 149.06 |
| 6.74 *d* (8.1) | 6.74 *d* (8.0) | 148.72 | 148.58 |
| 6.03 *s* | 6.03 *s* | 145.84 | 145.70 |
| 5.39 *d* (12.5) | 5.40 *d* (12.4) | 144.95 | 144.82 |
| 5.14 *d* (12.5) | 5.14 *d* (12.4) | 129.61 | 129.47 |
| 4.68 *t* (8.9) | 4.68 *t* (8.8) | 128.33 | 128.19 |
| 4.03 *t* (8.7) | 4.03 *t* (8.4) | 124.52 | 124.38 |
| 3.85 *s* | 3.85 *s* | 124.31 | 124.16 |
| 3.36–3.22 *m* | 3.28 *ddt* (14.4, 8.8, 6.0) | 122.40 | 122.26 |
| 2.99 *dd* (14.6, 5.7) | 3.00 *dd* (14.4, 5.6) | 119.97 | 119.83 |
| 2.66 *t* (14.6) | 2.66 *t* (14.4) | 116.67 | 116.53 |
| | | 112.04 | 111.89 |
| | | 108.27 | 108.13 |
| | | 102.00 | 101.86 |
| | | 70.14 | 69.99 |
| | | 64.81 | 64.67 |
| | | 56.35 | 56.20 |
| | | 37.01 | 36.86 |
| | | 34.62 | 34.48 |

[3] Xu, M.; Hou, M.; He, H.; Gao, S. *Angew. Chem., Int. Ed*. **2021**, *60*, 16655.

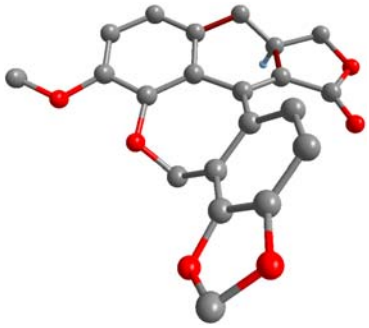
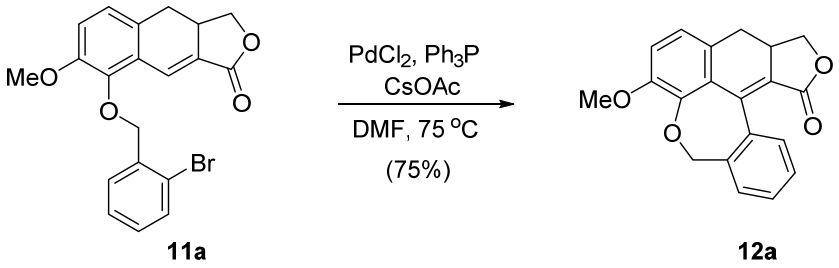


**Table S3**: X-ray crystal data of Linoxepin (**1**) (selected H atoms have been omitted for clarity)

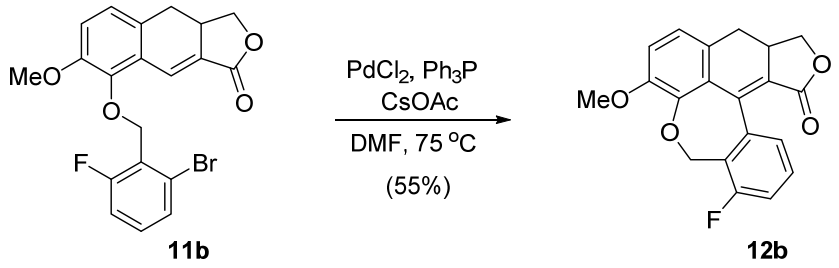
| | |
|---|---|
| Empirical formula | $C_{21}H_{16}O_6$ |
| Temperature (K) | 293.02(10) |
| Crystal color | light yellow |
| Formula weight | 364.34 |
| Crystal system | Monoclinic |
| Space group | $P2_1/n$ |
| $a$ (Å) | 11.52(17) |
| $b$ (Å) | 8.28(2) |
| $c$ (Å) | 17.87(11) |
| $\alpha$ (°) | 90.00 |
| $\beta$ (°) | 106.8(8) |
| $\gamma$ (°) | 90.00 |
| $V$ (Å $^3$) | 1633(26) |
| $Z$ | 4 |
| Density (calculated) (g/cm$^3$) | 1.482 |
| $F$ (000) | 760 |
| $\lambda$ (Å) | 0.71073 |
| Reflections collected | 5663 |
| Independent reflections | 3177 |
| 2$\theta$ Range for data collection (°) | 6.84—52.04 |
| Index range | $-6 \leq h \leq 14$<br>$-10 \leq k \leq 5$<br>$-22 \leq l \leq 16$ |
| Final $R$ indices [I>2σ($I$)] | $R_1 = 0.0752$, $wR_2 = 0.1575$ |
| Largest difference peak and hole [e Å $^{-3}$] | 0.182, –0.181 |

**Synthesis of Linoxepin Analogues 12a-c**




**11a** **12a**

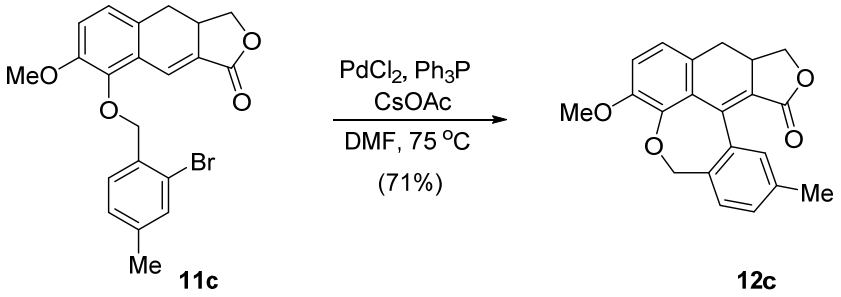
**12a** was prepared as a yellow solid (18 mg, 75% yield) in a similar way to that of Linoxepin. $R_f$ = 0.46 (petroleum ether/EtOAc = 2 : 1); Mp. 171–172 °C; $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 7.43–7.38 (m, 3H), 7.33 (td, $J$ = 7.2, 1.8 Hz, 1H), 6.85 (dd, $J$ = 8.4, 1.2 Hz, 1H), 6.81 (d, $J$ = 7.8 Hz, 1H), 5.43 (d, $J$ = 12.6 Hz, 1H), 5.08 (d, $J$ = 12.0 Hz, 1H), 4.71 (t, $J$ = 9.0 Hz, 1H), 4.07 (t, $J$ = 9.0 Hz, 1H), 3.84 (s, 3H), 3.35–3.28 (m, 1H), 3.02 (dd, $J$ = 15.0, 6.0 Hz, 1H), 2.65 (dt, $J$ = 15.0, 1.8 Hz, 1H) ppm; $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 168.5, 149.4, 148.8, 146.2, 135.4, 134.7, 130.6, 130.1, 128.4, 128.1, 127.8, 124.3, 122.0, 119.7, 111.9, 72.1, 70.1, 56.2, 36.7, 34.4 ppm; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{17}O_4$ $[M+H]^+$: 321.1121, found: 321.1120.




**11b** **12b**

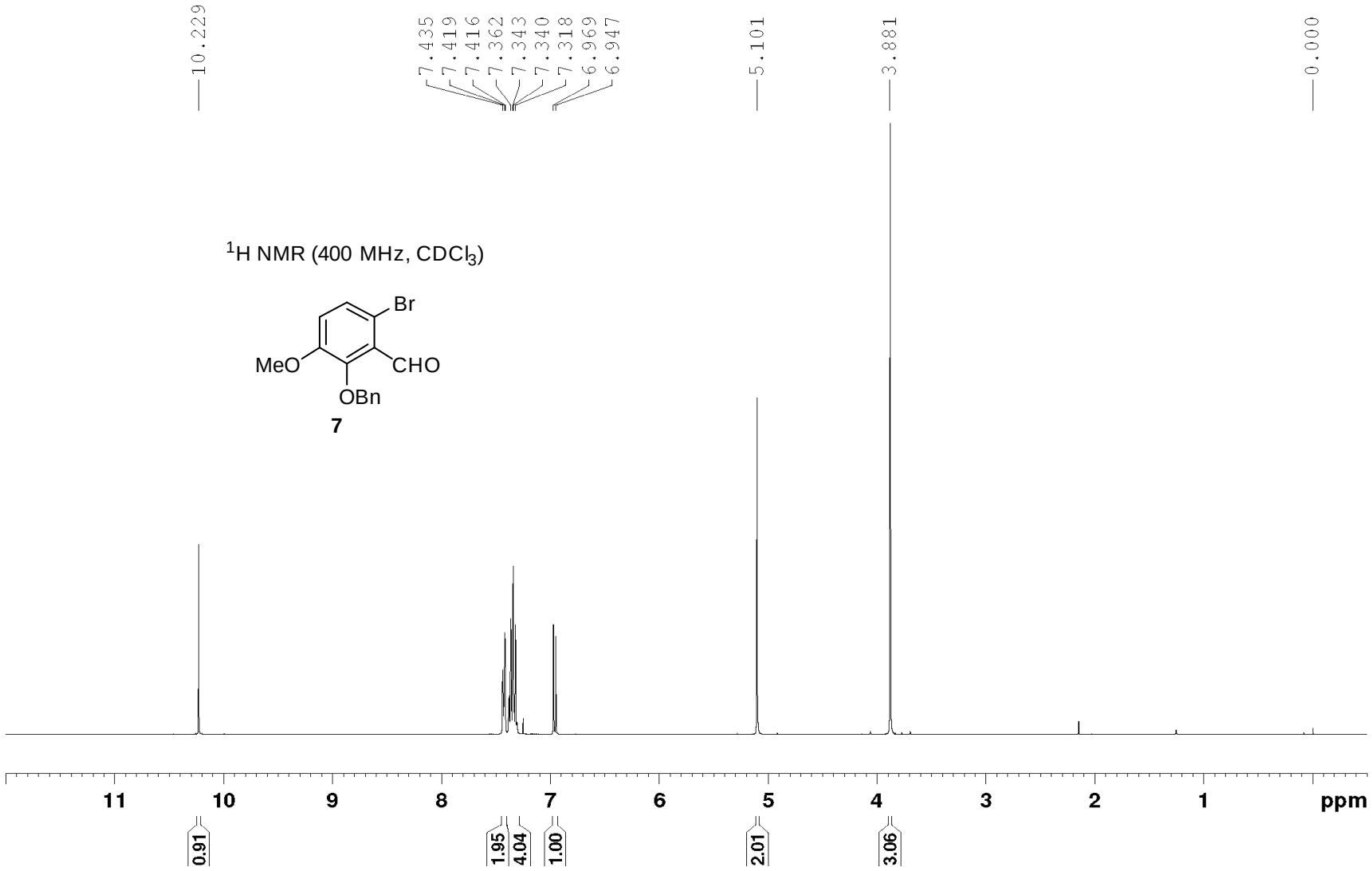
**12b** was prepared as a yellow solid (9.0 mg, 55% yield) in a similar way to that of Linoxepin; $R_f$ = 0.26 (petroleum ether/EtOAc = 2 : 1); Mp. 139–140 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.30–7.25 (m, 1H), 7.16 (dd, $J$ = 8.0, 1.2 Hz, 1H), 7.14 (td, $J$ = 8.0, 1.2 Hz, 1H), 6.86 (dd, $J$ = 8.0, 0.8 Hz, 1H), 6.82 (d, $J$ = 8.0 Hz, 1H), 5.58 (d, $J$ = 12.4 Hz, 1H), 5.16 (dd, $J$ = 12.4, 2.0 Hz, 1H), 4.72 (t, $J$ = 8.8 Hz, 1H), 4.07 (t, $J$ = 8.8 Hz, 1H), 3.85 (s, 3H), 3.37–3.27 (m, 1H), 3.02 (dd, $J$ = 14.8, 6.0 Hz, 1H), 2.69 (td, $J$ = 14.8, 1.2 Hz, 1H) ppm; $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 168.3, 159.2 (d, $J_{C-F}$ = 247.5 Hz), 149.5, 148.9, 144.8, 137.7 (d, $J_{C-F}$ = 3.0 Hz), 129.6 (d, $J_{C-F}$ = 9.0 Hz), 128.0, 126.2 (d, $J_{C-F}$ = 3.0 Hz), 125.3, 122.4 (d, $J_{C-F}$ = 16.5 Hz), 121.5, 119.9, 116.8

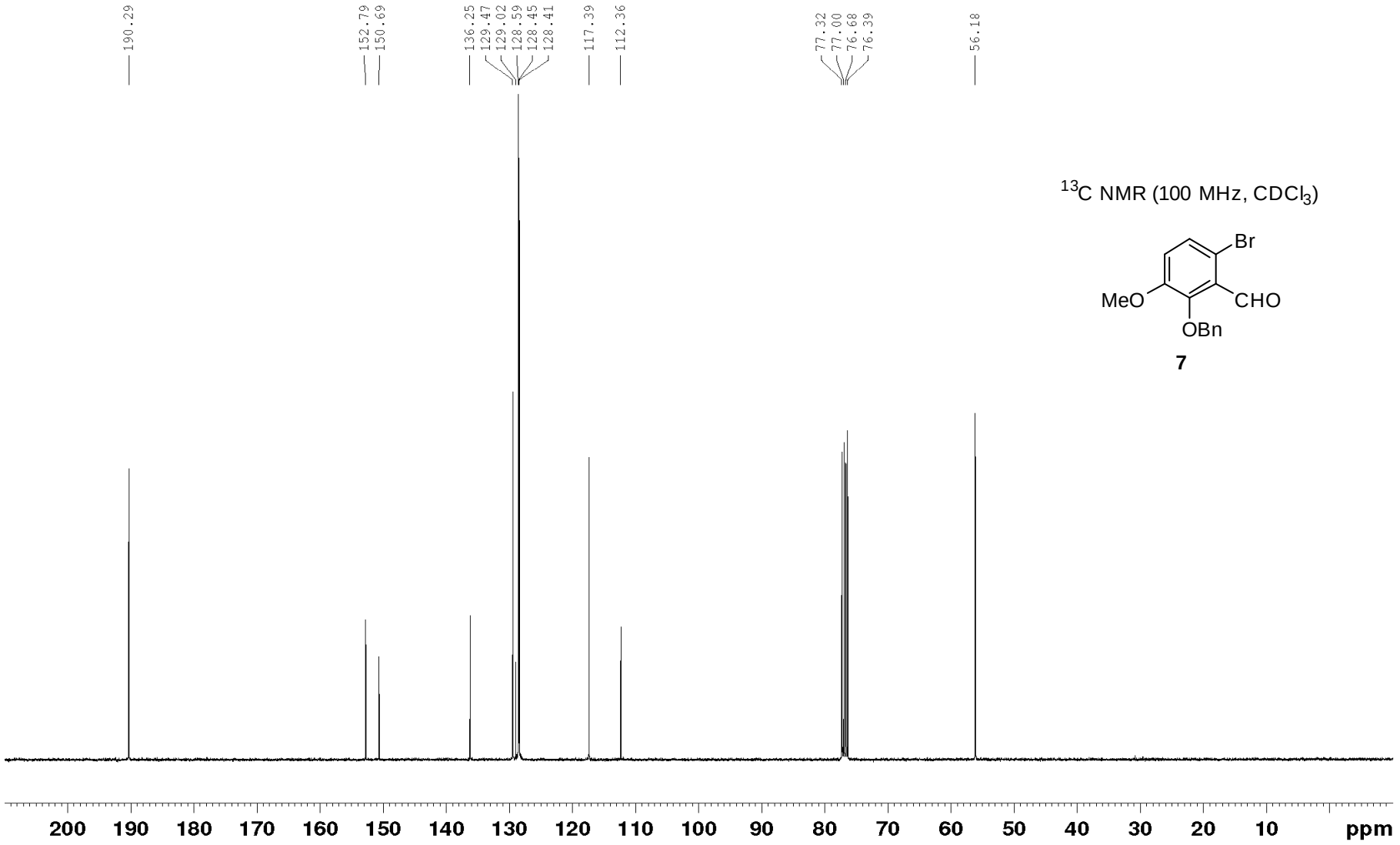
(d, $J_{C-F}$ = 21.0 Hz), 112.2, 70.2, 63.8 (d, $J_{C-F}$ = 4.5 Hz), 56.2, 36.7, 34.3 ppm; $^{19}$F NMR (565 MHz, $CDCl_3$): $\delta$ = –121.30 ppm; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{16}O_4F^+$ $[M+H]^+$: 339.1027, found: 339.1022.




**11c** **12c**

**12c** was prepared as a white solid (8.5 mg, 71% yield) in a similar way to that of Linoxepin; $R_f$ = 0.4 (petroleum ether / EtOAc = 2 : 1); Mp. 182–183 °C; $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 7.28 (d, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.19 (s, 1H), 6.83 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.39 (d, *J* = 12.0 Hz, 1H), 5.05 (d, *J* = 12.0 Hz, 1H), 4.71 (t, *J* = 9.0 Hz, 1H), 4.07 (t, *J* = 9.0 Hz, 1H), 3.84 (s, 3H), 3.34–3.27 (m, 1H), 3.01 (dd, *J* = 15.0, 6.0 Hz, 1H), 2.68 (td, *J* = 15.0, 1.8 Hz, 1H), 2.34 (s, 3H) ppm; $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 168.5, 149.4, 148.8, 146.5, 138.2, 135.4, 131.9, 131.2, 130.7, 128.1, 127.8, 124.1, 122.0, 119.6, 111.9, 71.8, 70.1, 56.2, 36.7, 34.5, 21.2 ppm; HRMS (ESI): *m*/*z* calcd for $C_{21}H_{19}O_4$ $[M+H]^+$: 335.1278, found: 335.1275.

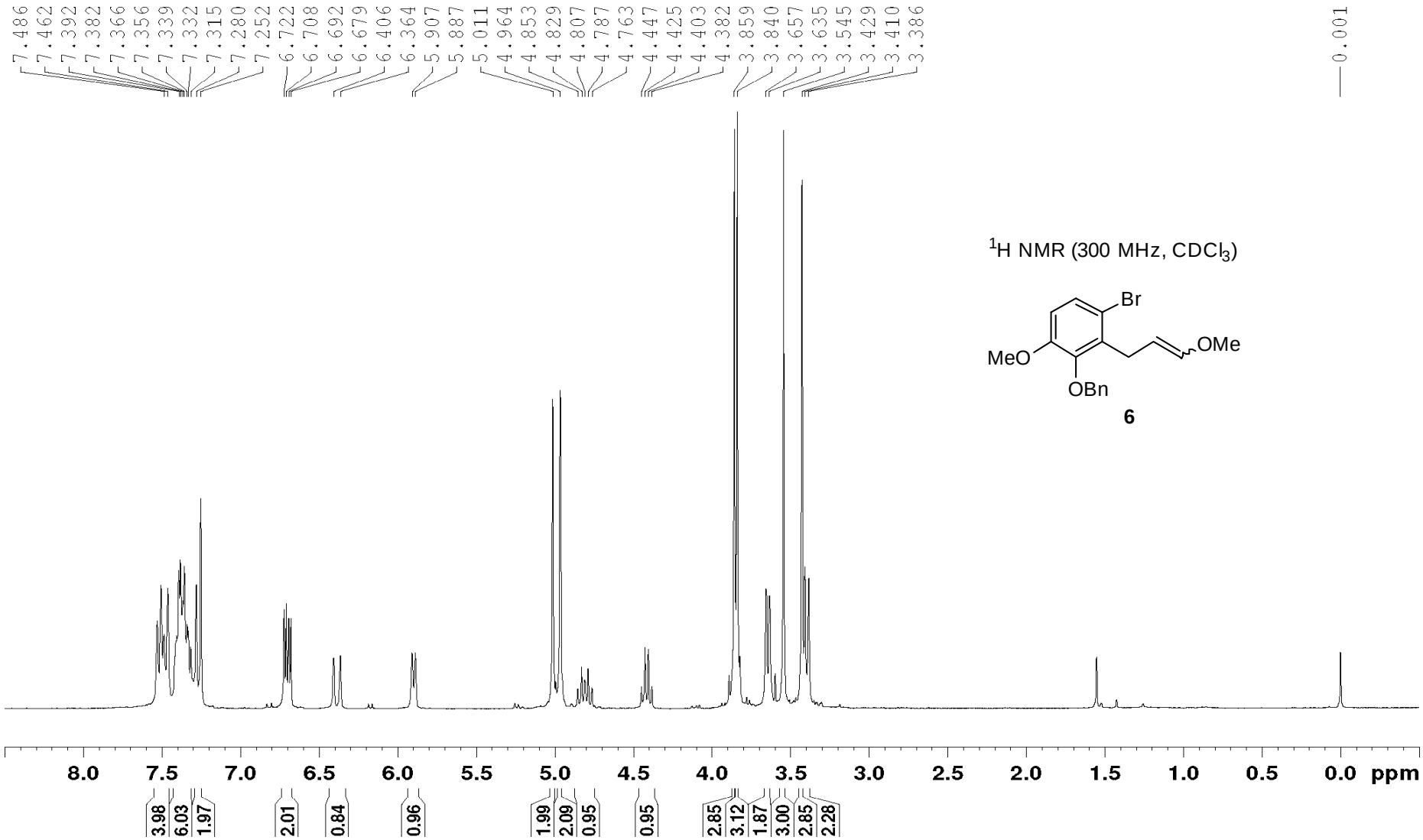

10.229
7.435
7.419
7.416
7.362
7.343
7.340
7.318
6.969
6.947
5.101
3.881
0.000
$^1$H NMR (400 MHz, $CDCl_3$)
Br
MeO
CHO
OBn
7
11
10
9
8
7
6
5
4
3
2
1
ppm
0.91
1.95
4.04
1.00
2.01
3.06

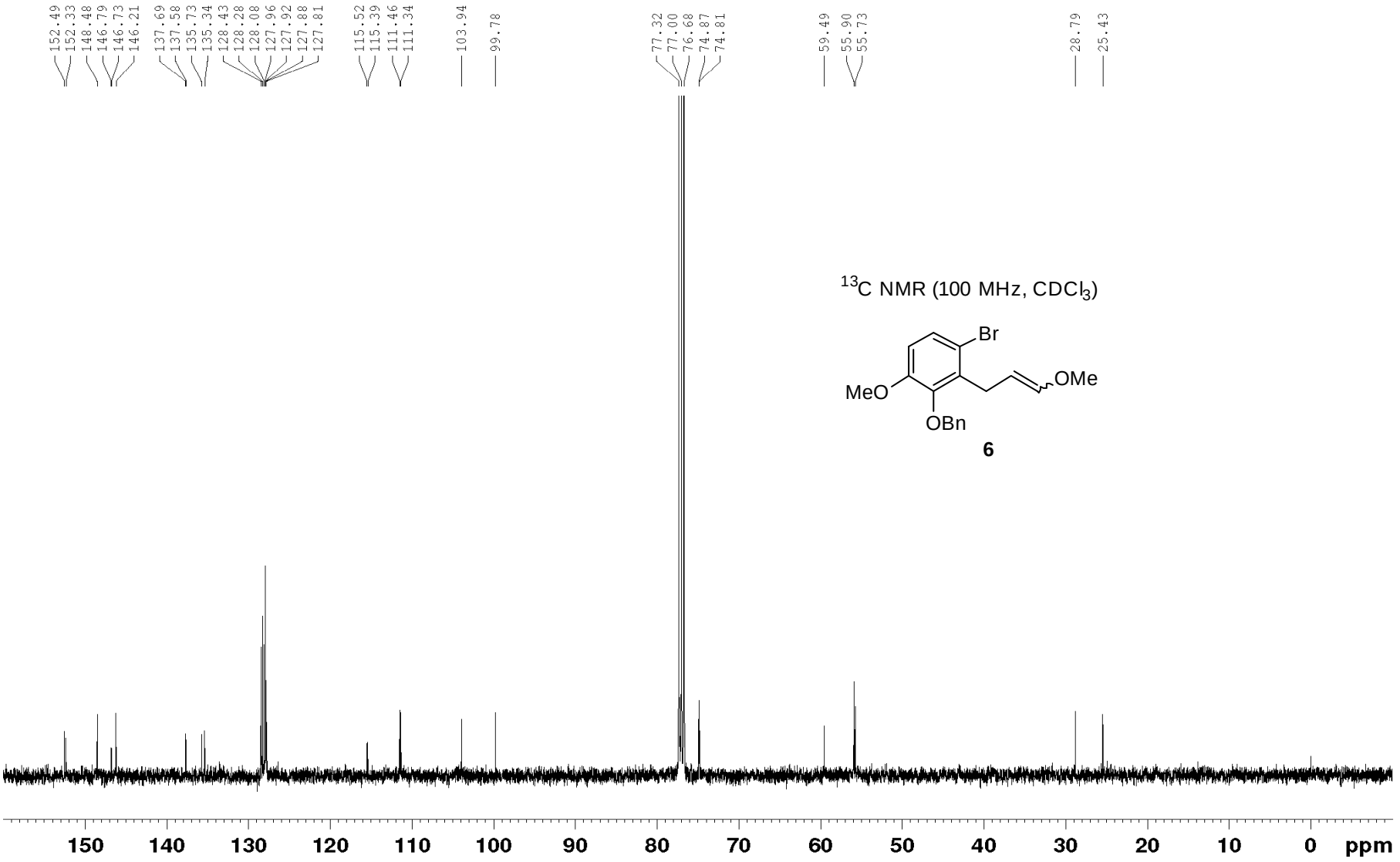



$^{13}C$ NMR (100 MHz, $CDCl_3$)




**7**

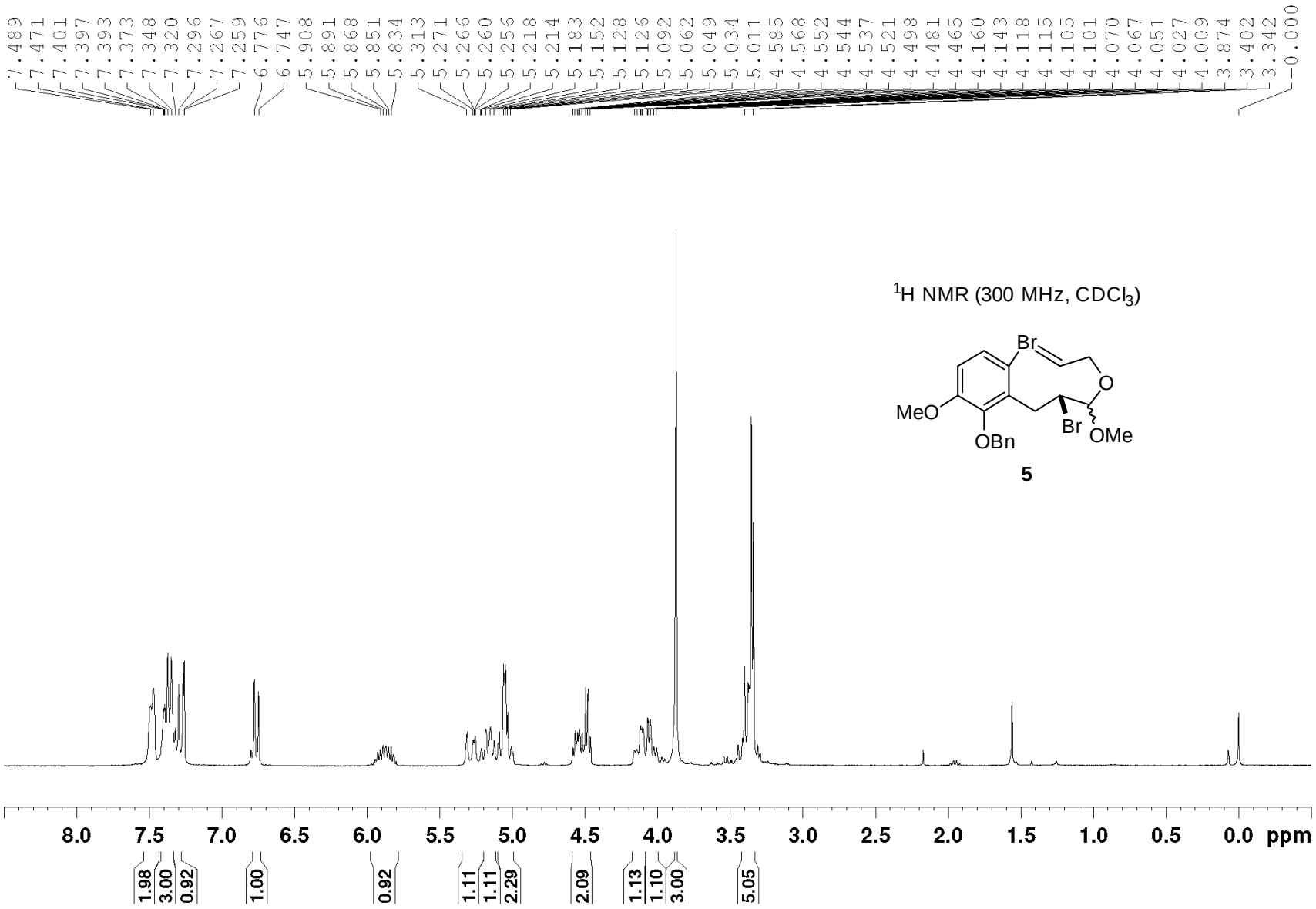

7.486
7.462
7.392
7.382
7.366
7.356
7.339
7.332
7.315
7.280
7.252
6.722
6.708
6.692
6.679
6.406
6.364
5.907
5.887
5.011
4.964
4.853
4.829
4.807
4.787
4.763
4.447
4.425
4.403
4.382
3.859
3.840
3.657
3.635
3.545
3.429
3.410
3.386
0.001
$^1$H NMR (300 MHz, $CDCl_3$)
Br
MeO
OMe
OBn
6
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.98
6.03
1.97
2.01
0.84
0.96
1.99
2.09
0.95
0.95
2.85
3.12
1.87
3.00
2.85
2.28

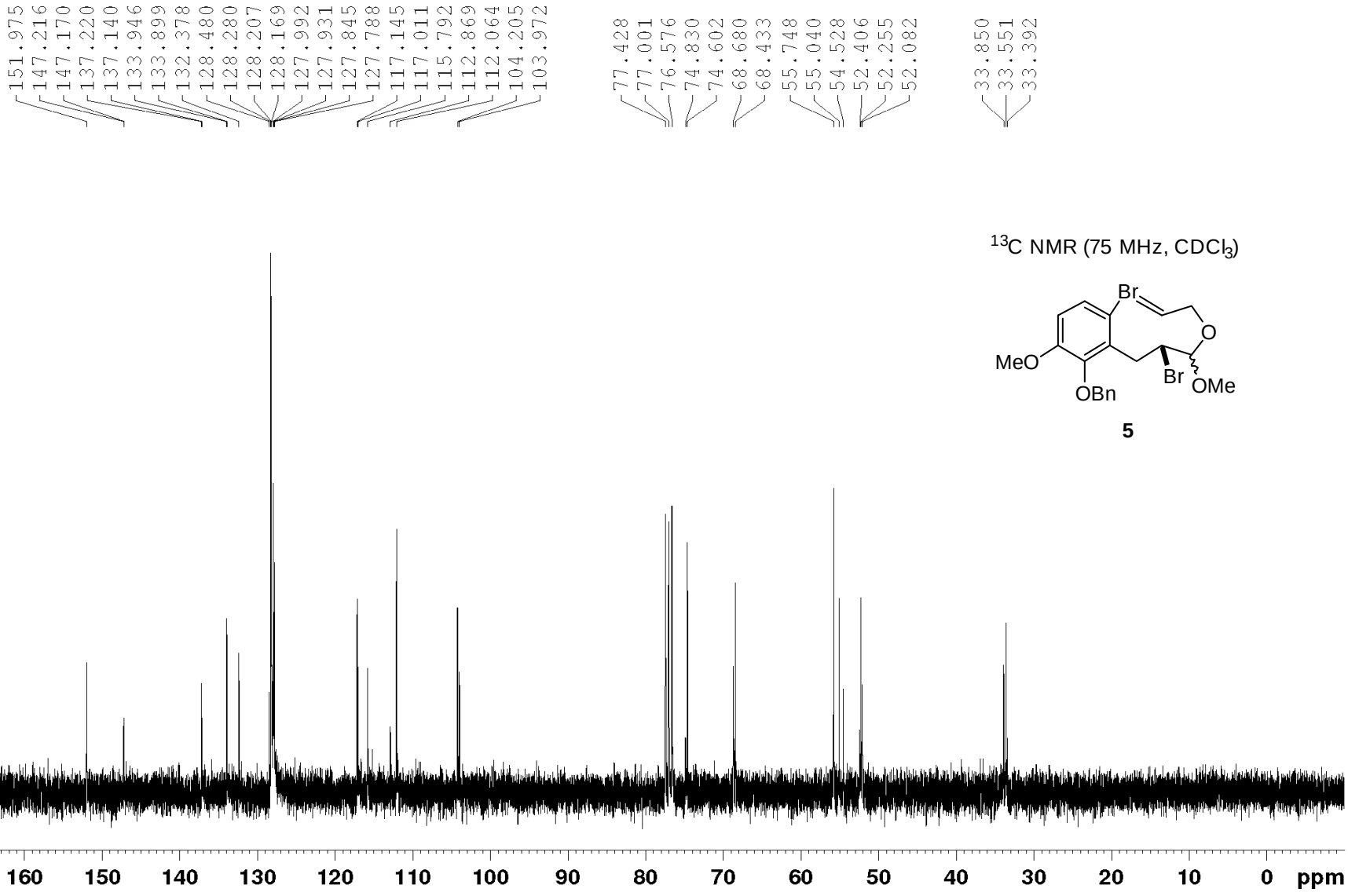



$^{13}C$ NMR (100 MHz, $CDCl_3$)




**6**

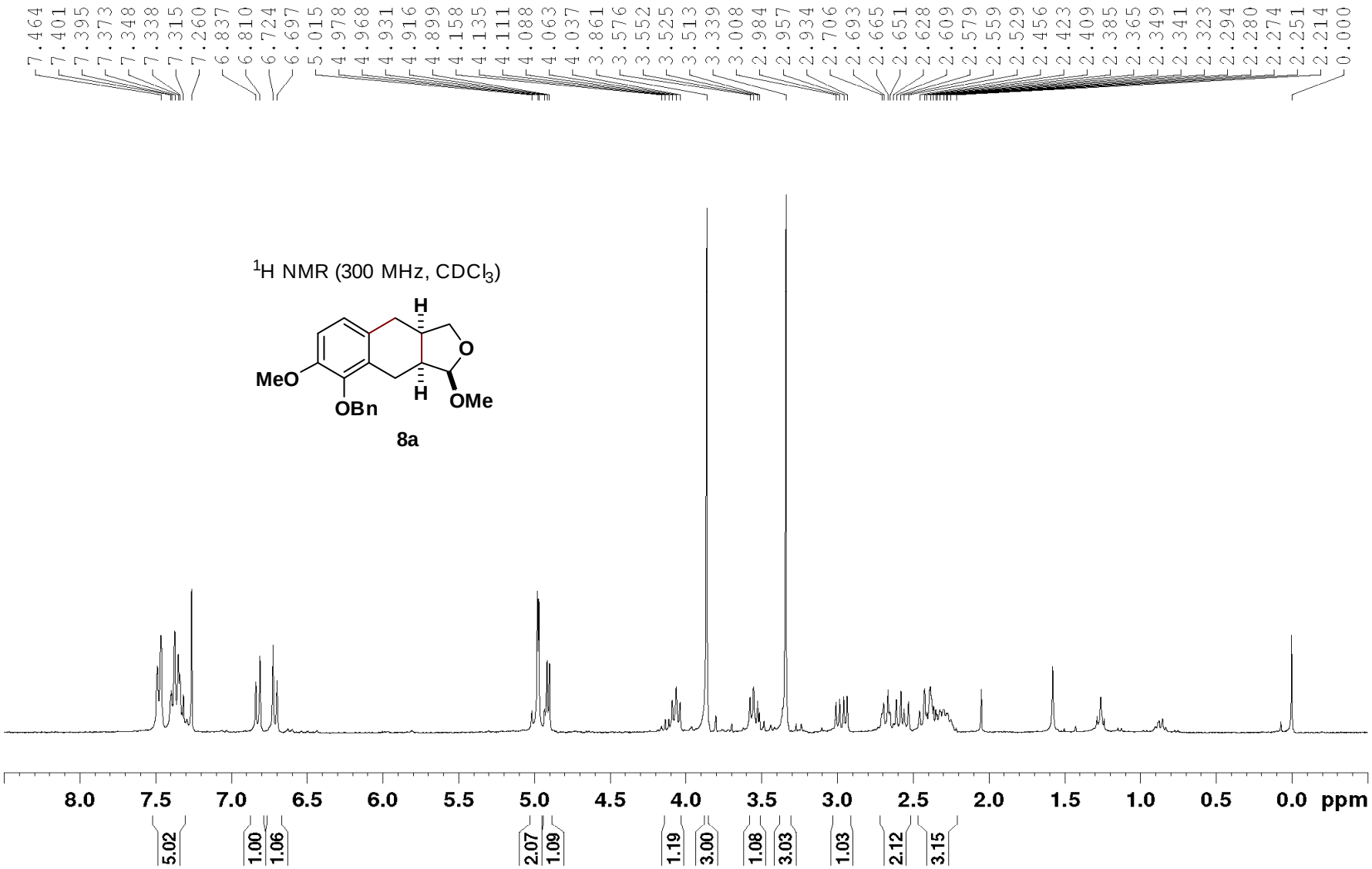

7.489
7.471
7.401
7.397
7.393
7.373
7.348
7.320
7.296
7.267
7.259
6.776
6.747
5.908
5.891
5.868
5.851
5.834
5.313
5.271
5.266
5.260
5.256
5.218
5.214
5.183
5.152
5.128
5.126
5.092
5.062
5.049
5.034
5.011
4.585
4.568
4.552
4.544
4.537
4.521
4.498
4.481
4.465
4.160
4.143
4.118
4.115
4.105
4.101
4.070
4.067
4.051
4.027
4.009
3.874
3.402
3.342
0.000
1H NMR (300 MHz, CDCl3)
Br
O
MeO
Br
OMe
OBn
5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.98
3.00
0.92
1.00
0.92
1.11
1.11
2.29
2.09
1.13
1.10
3.00
5.05

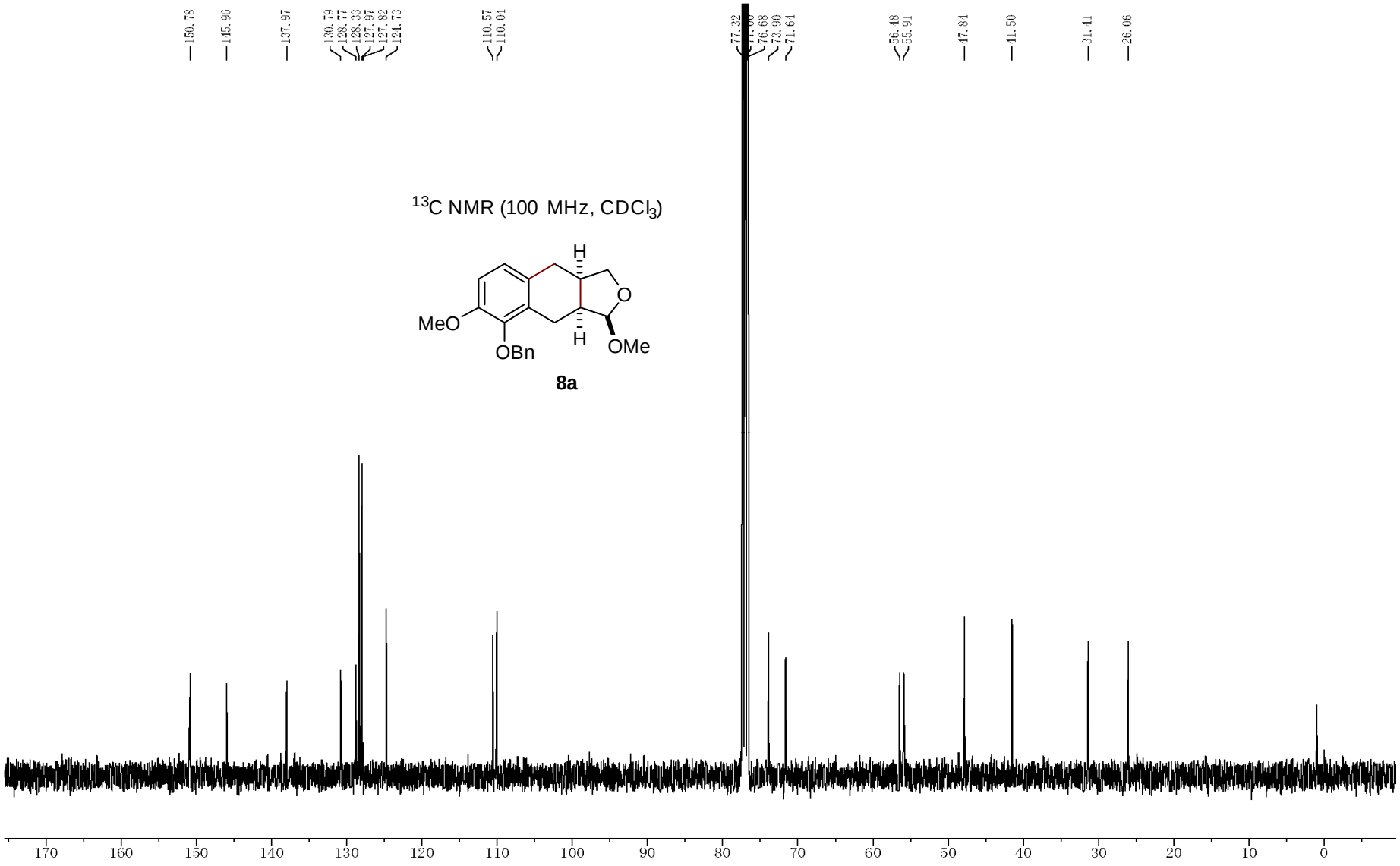



$^{13}C$ NMR (75 MHz, $CDCl_3$)




**5**

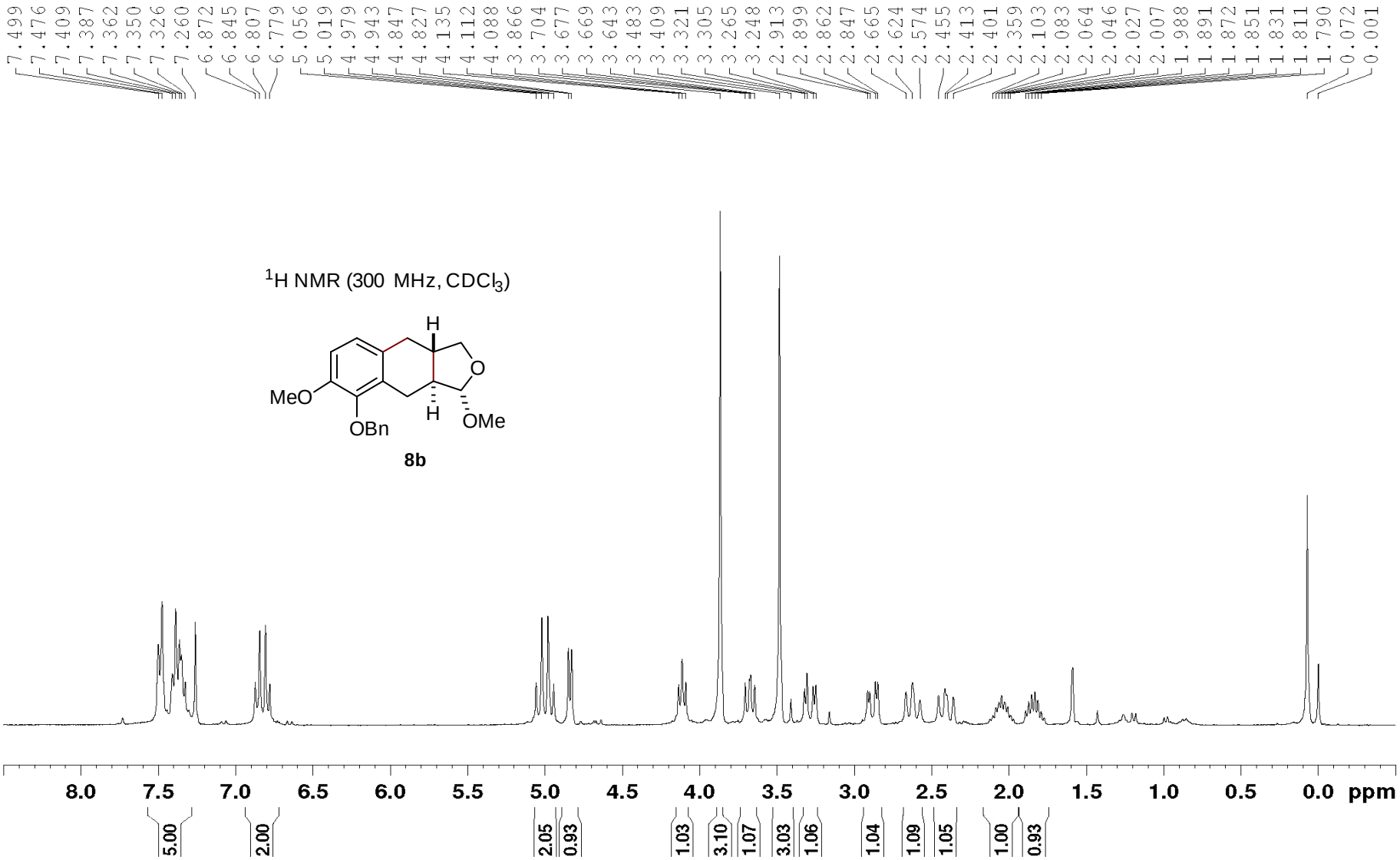

7.464
7.401
7.395
7.373
7.348
7.338
7.315
7.260
6.837
6.810
6.724
6.697
5.015
4.978
4.968
4.931
4.916
4.899
4.158
4.135
4.111
4.088
4.063
4.037
3.861
3.576
3.552
3.525
3.513
3.339
3.008
2.984
2.957
2.934
2.706
2.693
2.665
2.651
2.628
2.609
2.579
2.559
2.529
2.456
2.423
2.409
2.385
2.365
2.349
2.341
2.323
2.294
2.280
2.274
2.251
2.214
0.000
1H NMR (300 MHz, CDCl3)
H
O
MeO
H
OMe
OBn
8a
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
5.02
1.00
1.06
2.07
1.09
1.19
3.00
1.08
3.03
1.03
2.12
3.15

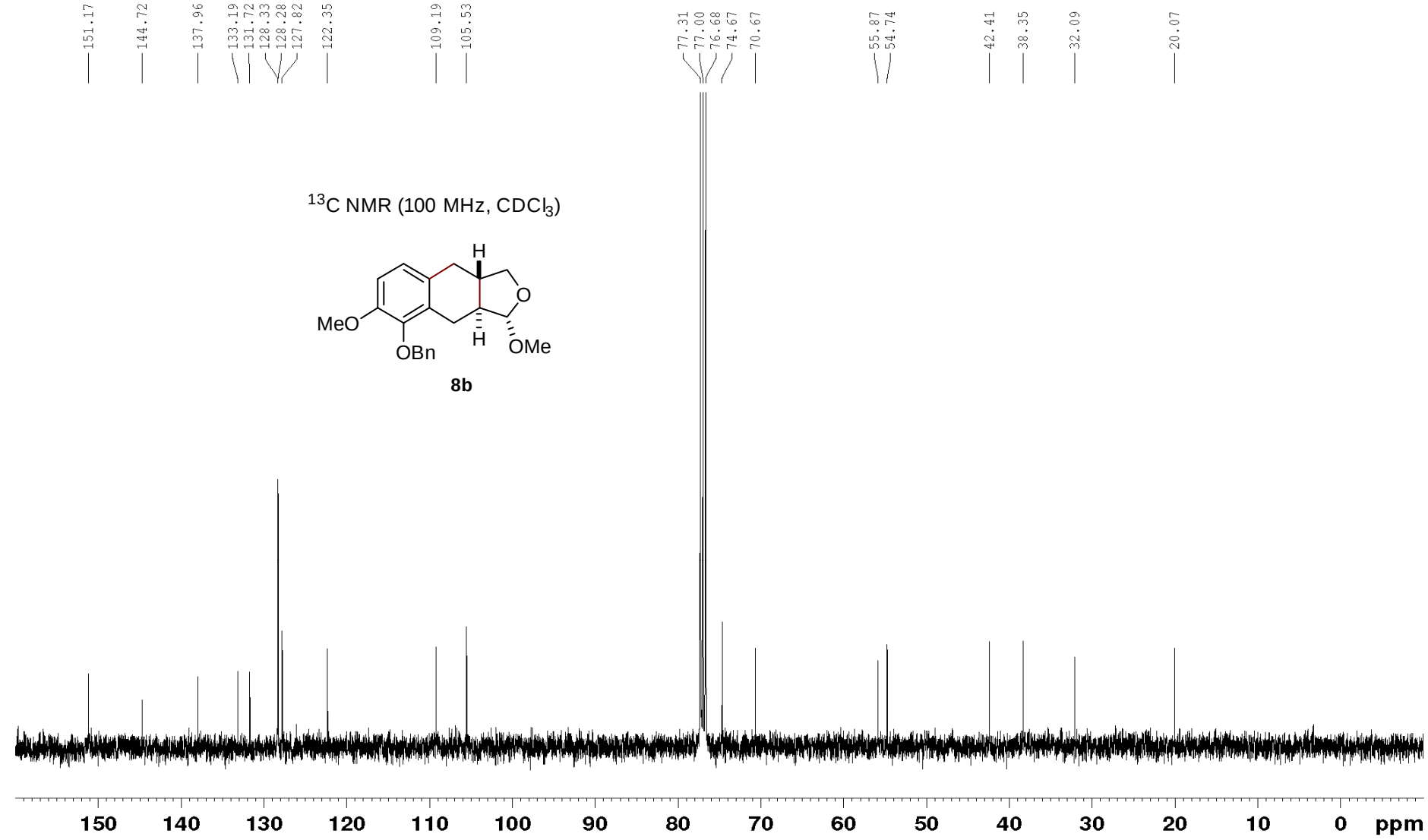



$^{13}$C NMR (100 MHz, $CDCl_3$)




**8a**


7.499
7.476
7.409
7.387
7.362
7.350
7.326
7.260
6.872
6.845
6.807
6.779
5.056
5.019
4.979
4.943
4.847
4.827
4.135
4.112
4.088
3.866
3.704
3.677
3.669
3.643
3.483
3.409
3.321
3.305
3.265
3.248
2.913
2.899
2.862
2.847
2.665
2.624
2.574
2.455
2.413
2.401
2.359
2.103
2.083
2.064
2.046
2.027
2.007
1.988
1.891
1.872
1.851
1.831
1.811
1.790
0.072
0.001
1H NMR (300 MHz, CDCl3)
H
O
MeO
H
OMe
OBn
8b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
5.00
2.00
2.05
0.93
1.03
3.10
1.07
3.03
1.06
1.04
1.09
1.05
1.00
0.93

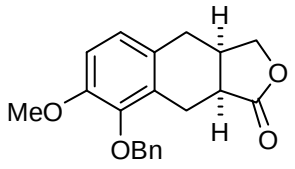



$^{13}$C NMR (100 MHz, $CDCl_3$)

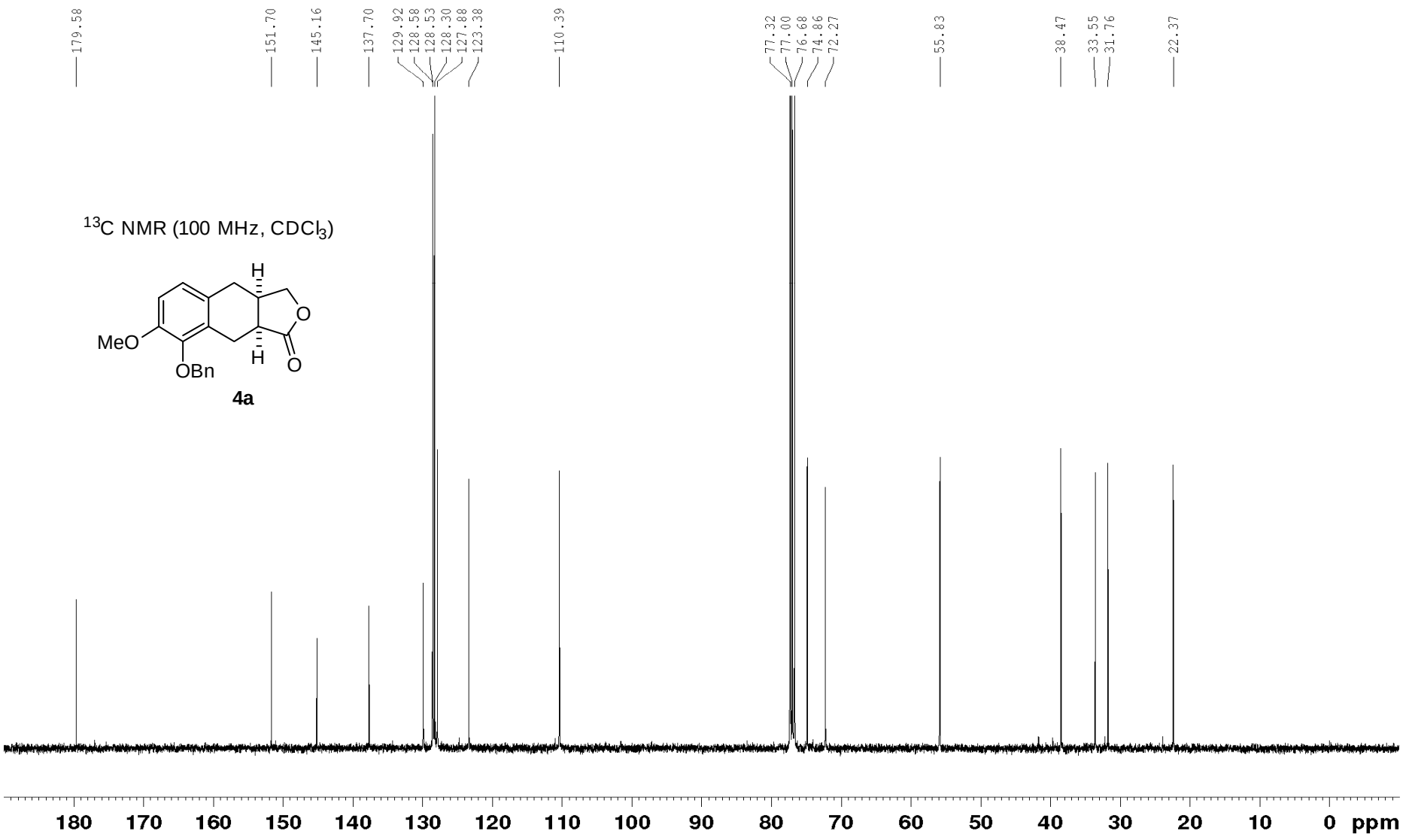


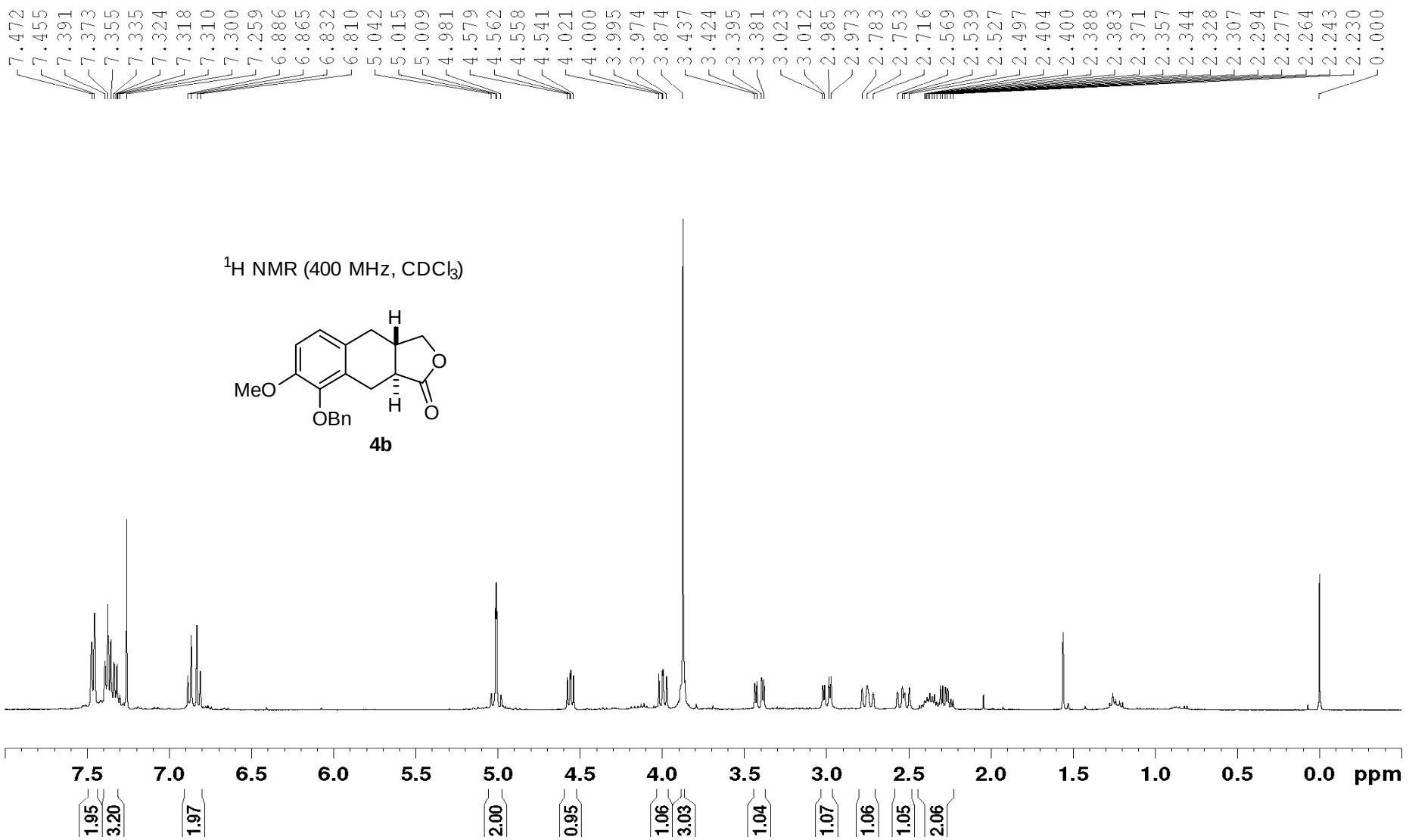

**8b**

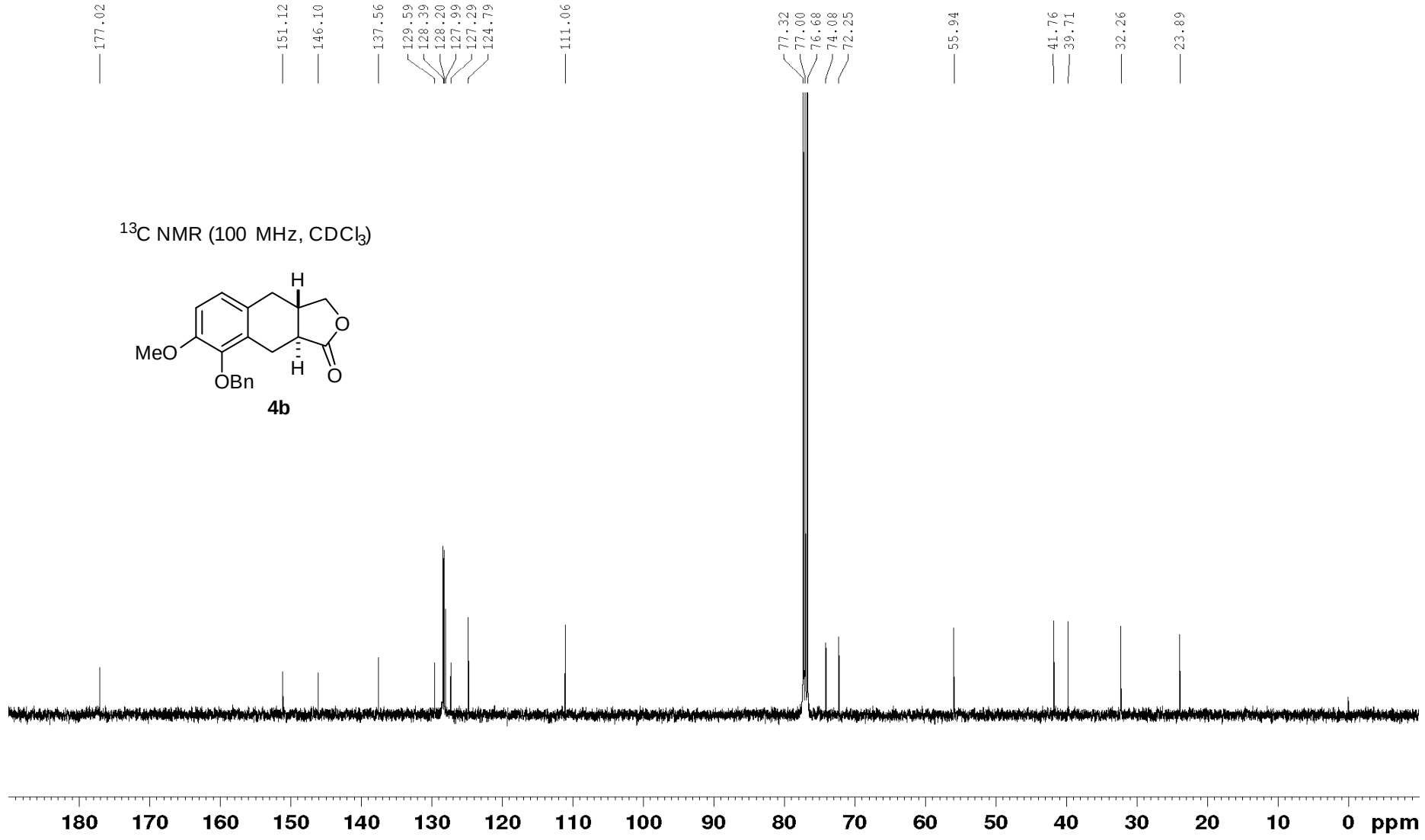
$^1$H NMR (400 MHz, $CDCl_3$)



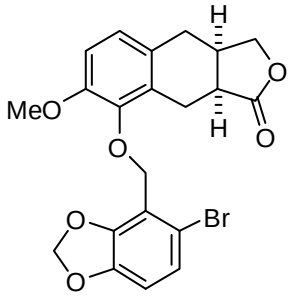

**4a**


179.58
151.70
145.16
137.70
129.92
128.58
128.53
128.30
127.88
123.38
110.39
77.32
77.00
76.68
74.86
72.27
55.83
38.47
33.55
31.76
22.37
$^{13}$C NMR (100 MHz, $CDCl_3$)
MeO
OBn
H
H
O
O
**4a**
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

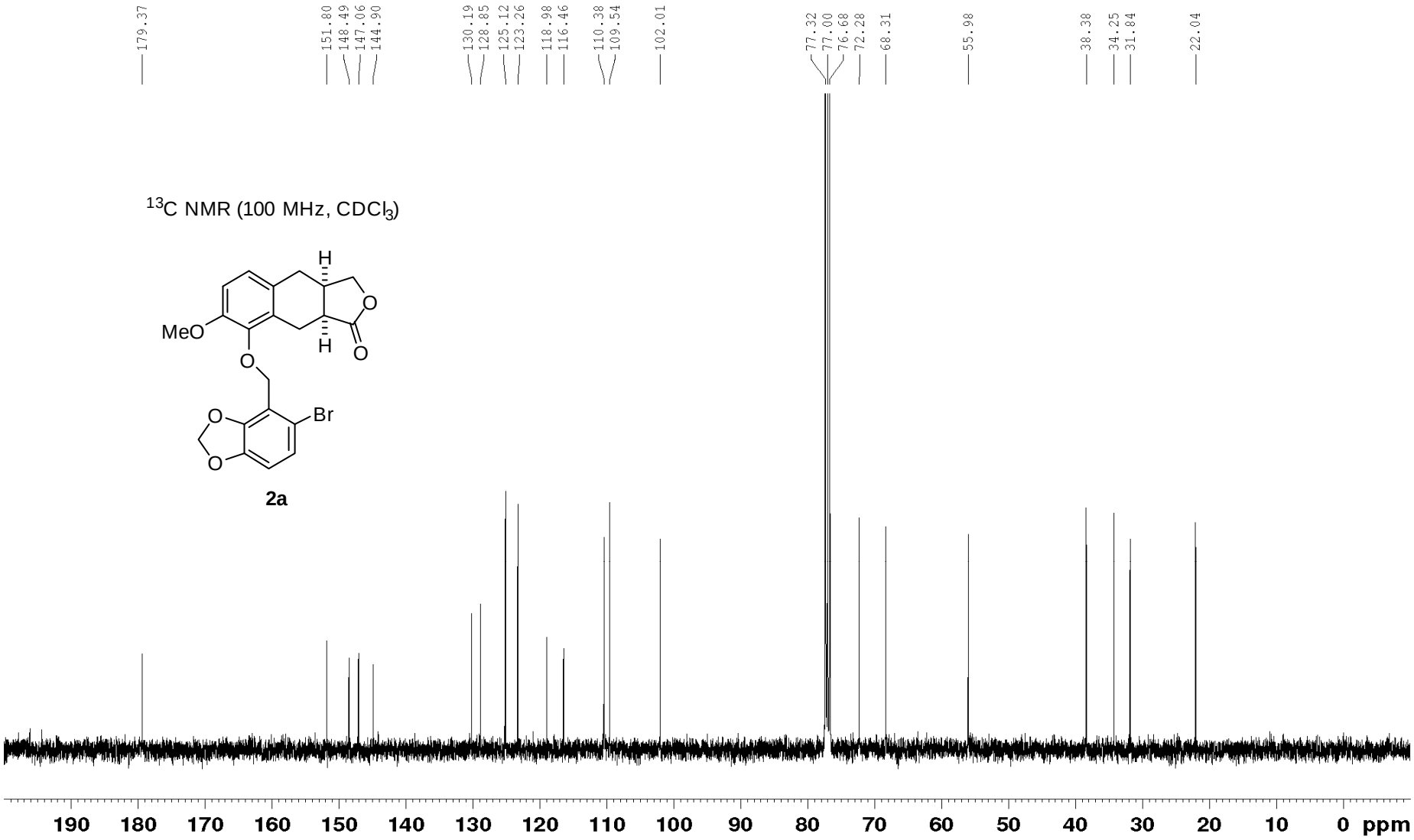

7.472
7.455
7.391
7.373
7.355
7.335
7.324
7.318
7.310
7.300
7.259
6.886
6.865
6.832
6.810
5.042
5.015
5.009
4.981
4.579
4.562
4.558
4.541
4.021
4.000
3.995
3.974
3.874
3.437
3.424
3.395
3.381
3.023
3.012
2.985
2.973
2.783
2.753
2.716
2.569
2.539
2.527
2.497
2.404
2.400
2.388
2.383
2.371
2.357
2.344
2.328
2.307
2.294
2.277
2.264
2.243
2.230
0.000
$^1$H NMR (400 MHz, $CDCl_3$)
H
O
MeO
OBn
H
O
**4b**
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.95
3.20
1.97
2.00
0.95
1.06
3.03
1.04
1.07
1.06
1.05
2.06

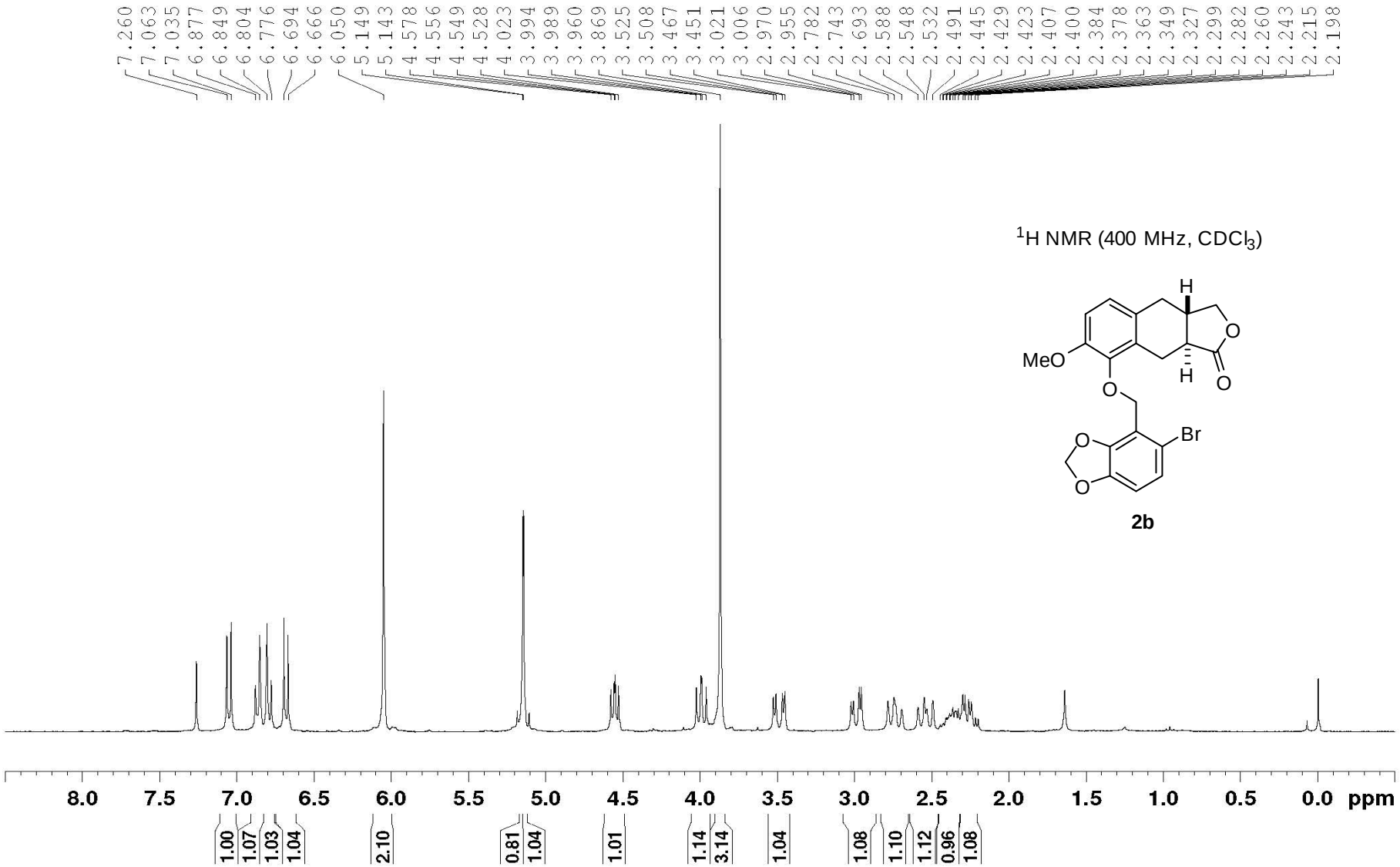

177.02
151.12
146.10
137.56
129.59
128.39
128.20
127.99
127.29
124.79
111.06
77.32
77.00
76.68
74.08
72.25
55.94
41.76
39.71
32.26
23.89
$^{13}$C NMR (100 MHz, $CDCl_3$)
MeO
OBn
H
H
O
O
4b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

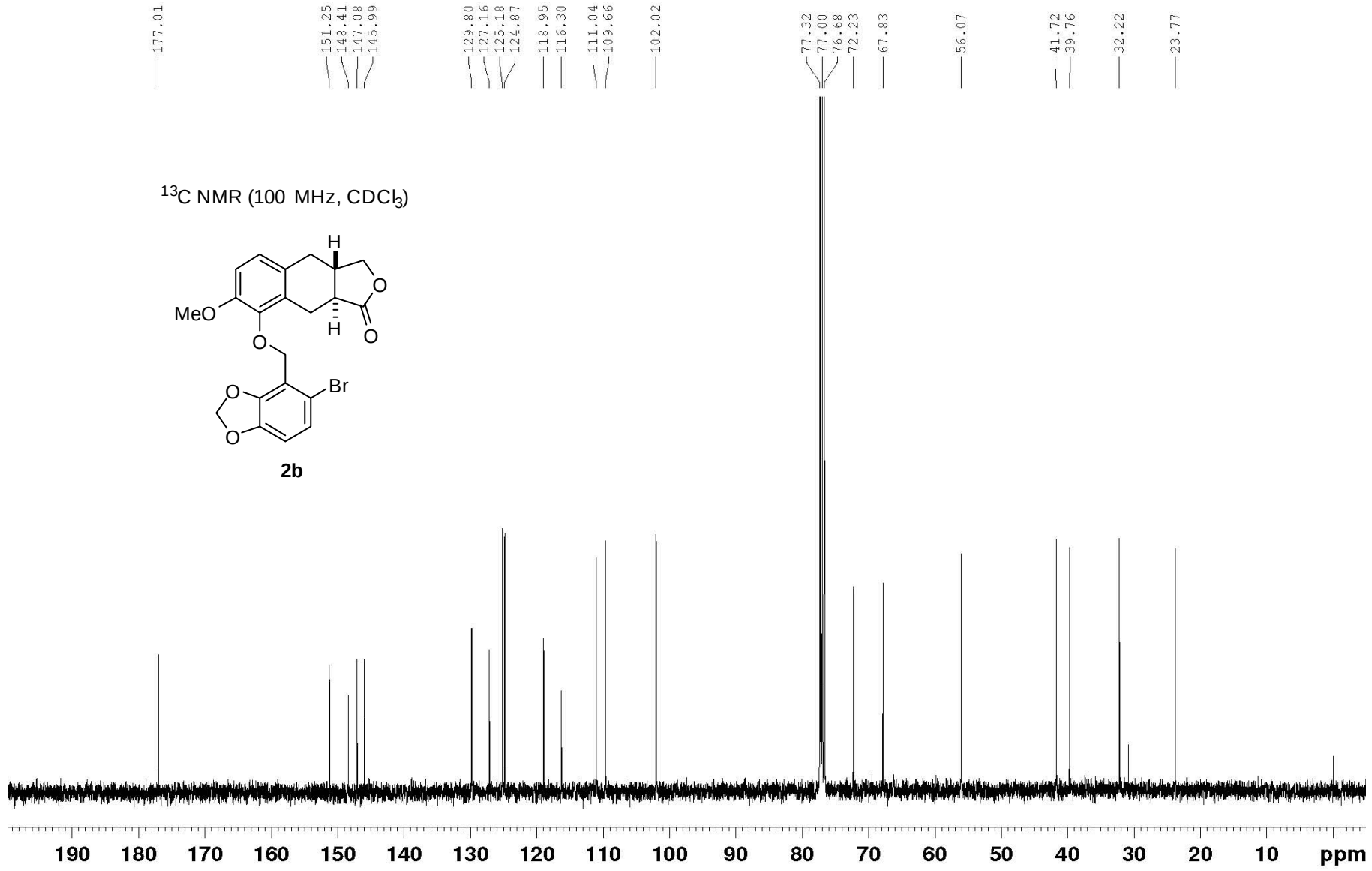
$^1$H NMR (400 MHz, $CDCl_3$)

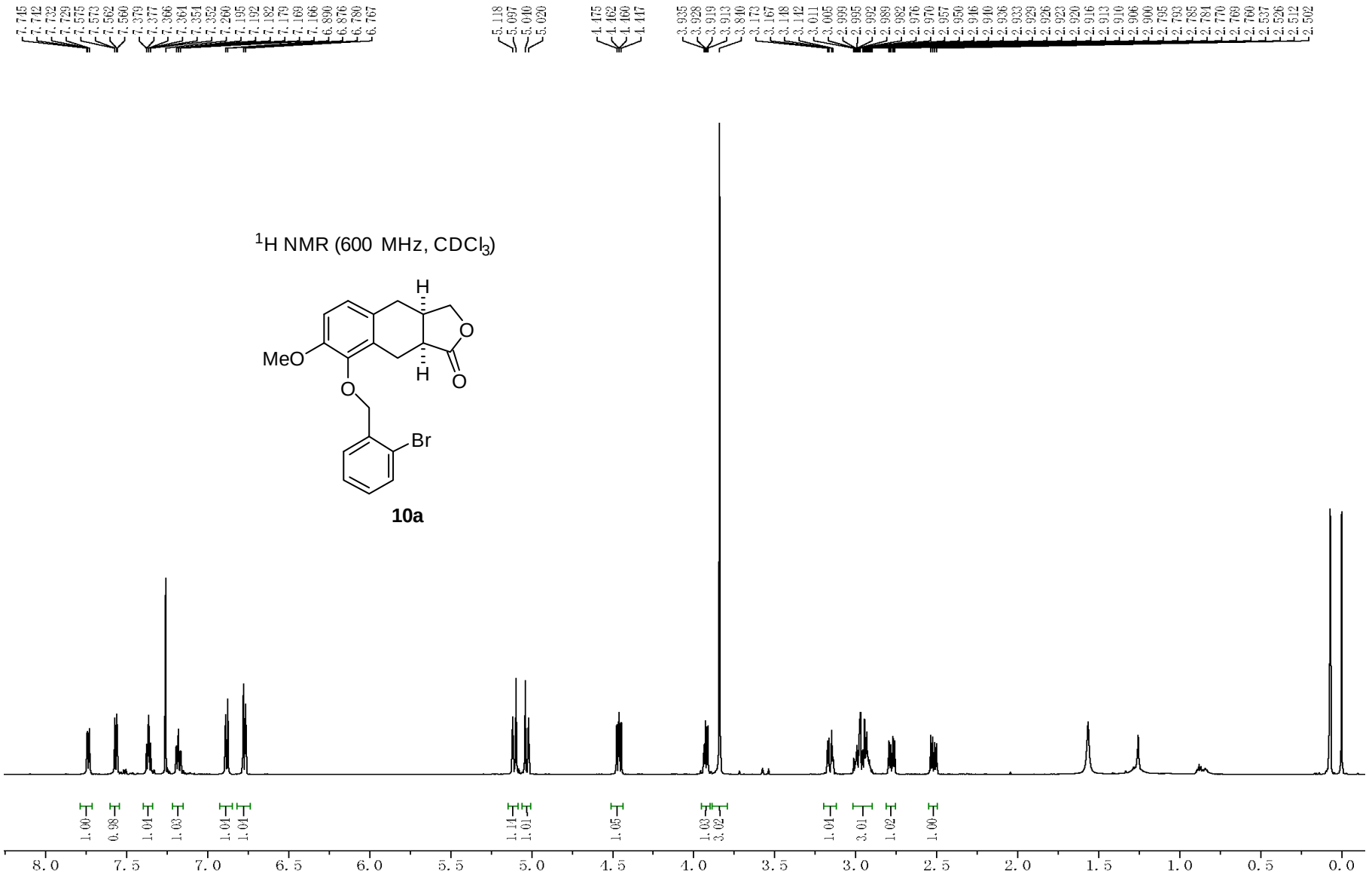


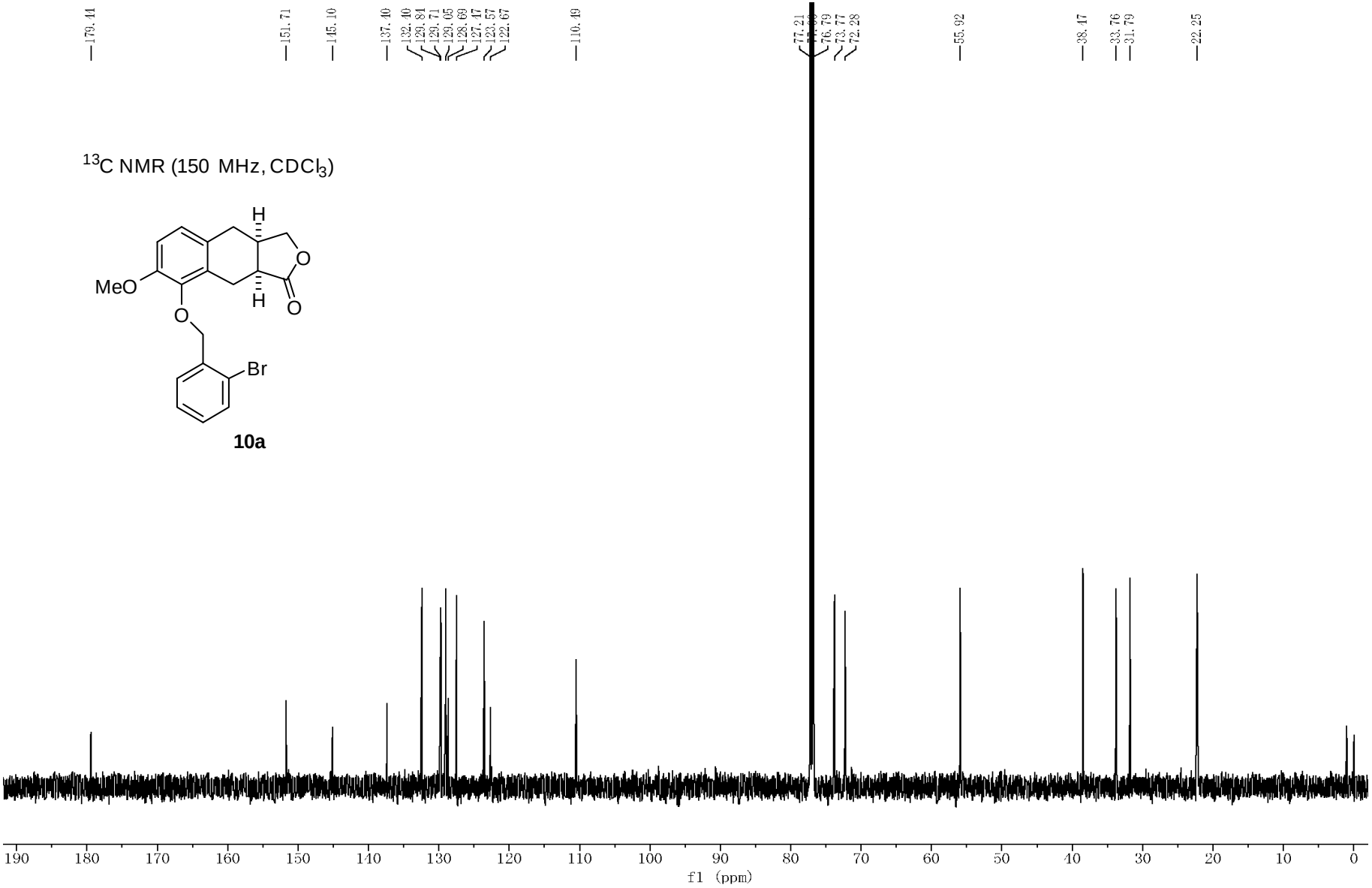

**2a**

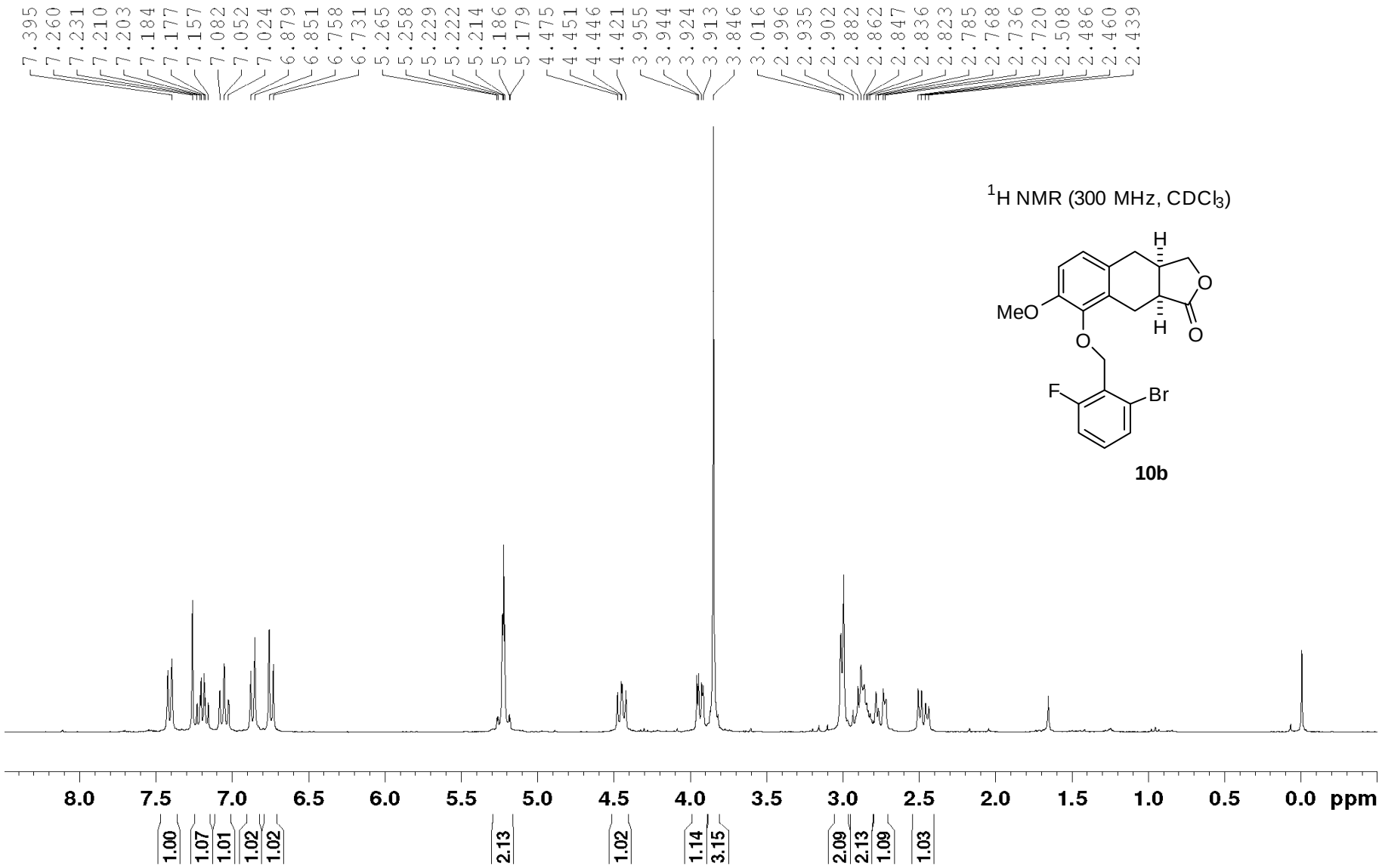

179.37
151.80
148.49
147.06
144.90
130.19
128.85
125.12
123.26
118.98
116.46
110.38
109.54
102.01
77.32
77.00
76.68
72.28
68.31
55.98
38.38
34.25
31.84
22.04
$^{13}$C NMR (100 MHz, $CDCl_3$)
MeO
O
H
H
O
O
O
O
Br
**2a**
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

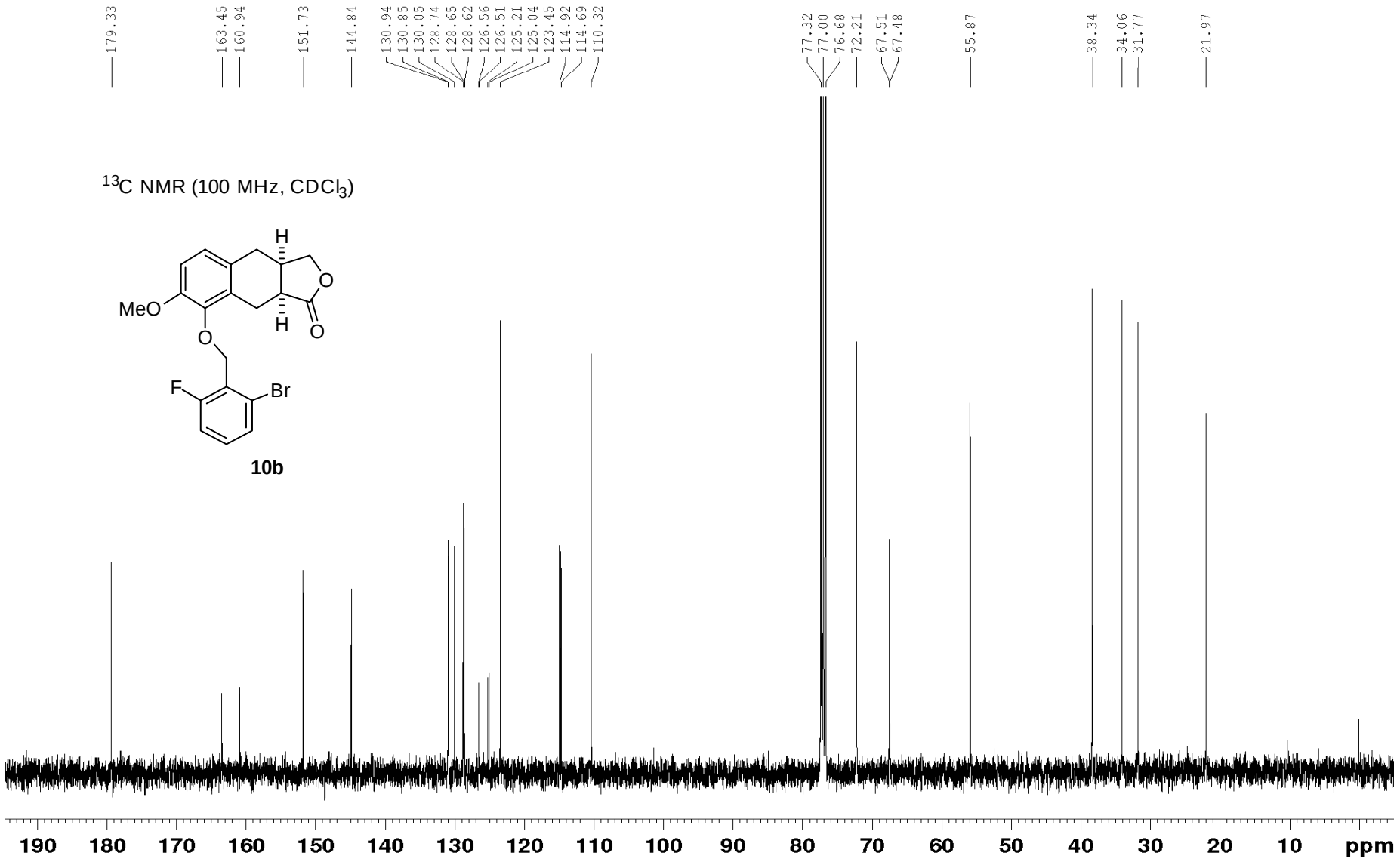

7.260
7.063
7.035
6.877
6.849
6.804
6.776
6.694
6.666
6.050
5.149
5.143
4.578
4.556
4.549
4.528
4.023
3.994
3.989
3.960
3.869
3.525
3.508
3.467
3.451
3.021
3.006
2.970
2.955
2.782
2.743
2.693
2.588
2.548
2.532
2.491
2.445
2.429
2.423
2.407
2.400
2.384
2.378
2.363
2.349
2.327
2.299
2.282
2.260
2.243
2.215
2.198
1H NMR (400 MHz, CDCl3)
MeO
O
H
H
O
O
O
O
Br
2b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.07
1.03
1.04
2.10
0.81
1.04
1.01
1.14
3.14
1.04
1.08
1.10
1.12
0.96
1.08


177.01
151.25
148.41
147.08
145.99
129.80
127.16
125.18
124.87
118.95
116.30
111.04
109.66
102.02
77.32
77.00
76.68
72.23
67.83
56.07
41.72
39.76
32.22
23.77
$^{13}$C NMR (100 MHz, $CDCl_3$)
MeO
O
H
H
O
O
O
O
Br
2b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

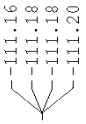

7.745
7.742
7.732
7.729
7.575
7.573
7.562
7.560
7.379
7.377
7.366
7.364
7.354
7.352
7.260
7.195
7.192
7.182
7.179
7.169
7.166
6.890
6.876
6.780
6.767
5.118
5.097
5.040
5.020
4.475
4.462
4.460
4.447
3.935
3.928
3.919
3.913
3.840
3.173
3.167
3.148
3.142
3.011
3.005
2.999
2.995
2.992
2.989
2.982
2.976
2.970
2.957
2.950
2.946
2.940
2.936
2.933
2.929
2.926
2.923
2.920
2.916
2.913
2.910
2.906
2.900
2.795
2.793
2.785
2.784
2.770
2.769
2.760
2.537
2.526
2.512
2.502
$^1$H NMR (600 MHz, CDCl$_3$)
MeO
O
H
H
O
O
Br
**10a**
1.00
0.98
1.04
1.03
1.04
1.04
1.14
1.01
1.05
1.03
3.02
1.04
3.01
1.02
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


179.44
151.71
145.10
137.40
132.40
129.84
129.71
129.05
128.69
127.47
123.57
122.67
110.49
77.21
76.79
73.77
72.28
55.92
38.47
33.76
31.79
22.25
$^{13}$C NMR (150 MHz, $CDCl_3$)
MeO
O
H
H
O
O
Br
**10a**
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

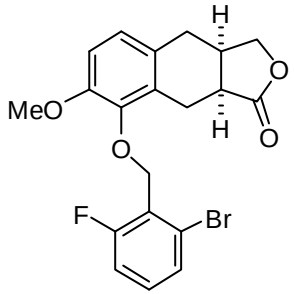

7.395
7.260
7.231
7.210
7.203
7.184
7.177
7.157
7.082
7.052
7.024
6.879
6.851
6.758
6.731
5.265
5.258
5.229
5.222
5.214
5.186
5.179
4.475
4.451
4.446
4.421
3.955
3.944
3.924
3.913
3.846
3.016
2.996
2.935
2.902
2.882
2.862
2.847
2.836
2.823
2.785
2.768
2.736
2.720
2.508
2.486
2.460
2.439
$^1$H NMR (300 MHz, CDCl$_3$)
H
O
MeO
H
O
O
F
Br
10b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.07
1.01
1.02
1.02
2.13
1.02
1.14
3.15
2.09
2.13
1.09
1.03


179.33
163.45
160.94
151.73
144.84
130.94
130.85
130.05
128.74
128.65
128.62
126.56
126.51
125.21
125.04
123.45
114.92
114.69
110.32
77.32
77.00
76.68
72.21
67.51
67.48
55.87
38.34
34.06
31.77
21.97
$^{13}$C NMR (100 MHz, $CDCl_3$)
MeO
O
H
H
O
O
F
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

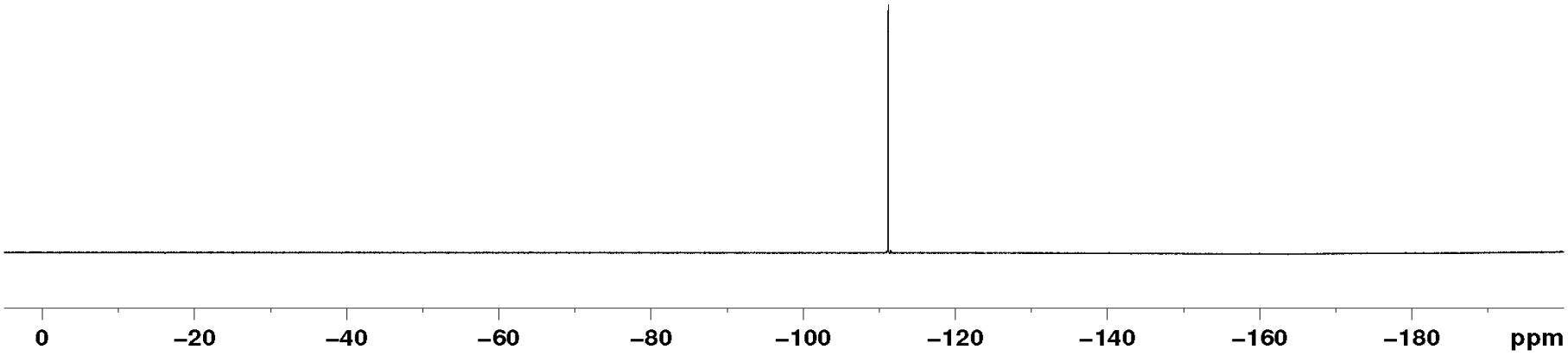
**10b**

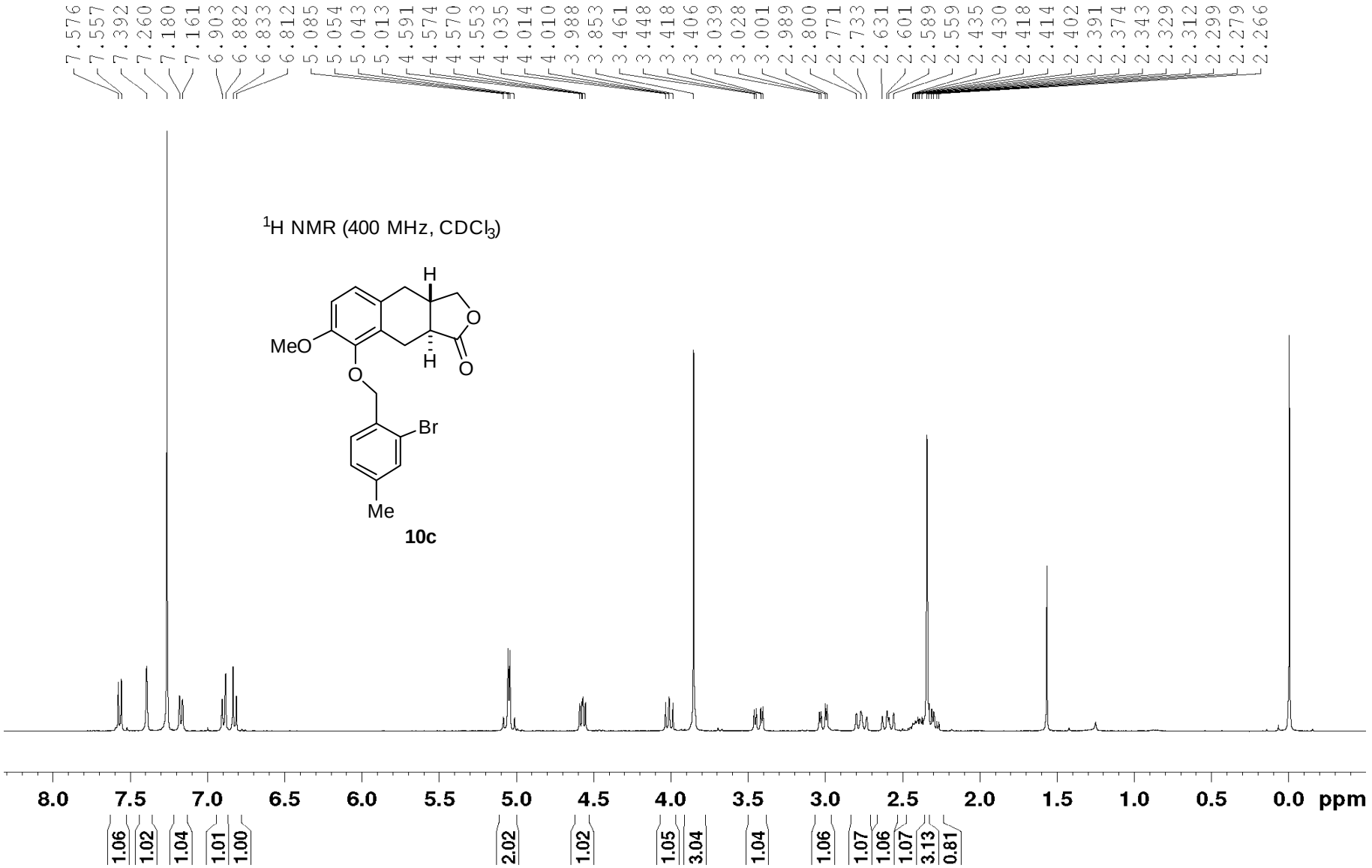


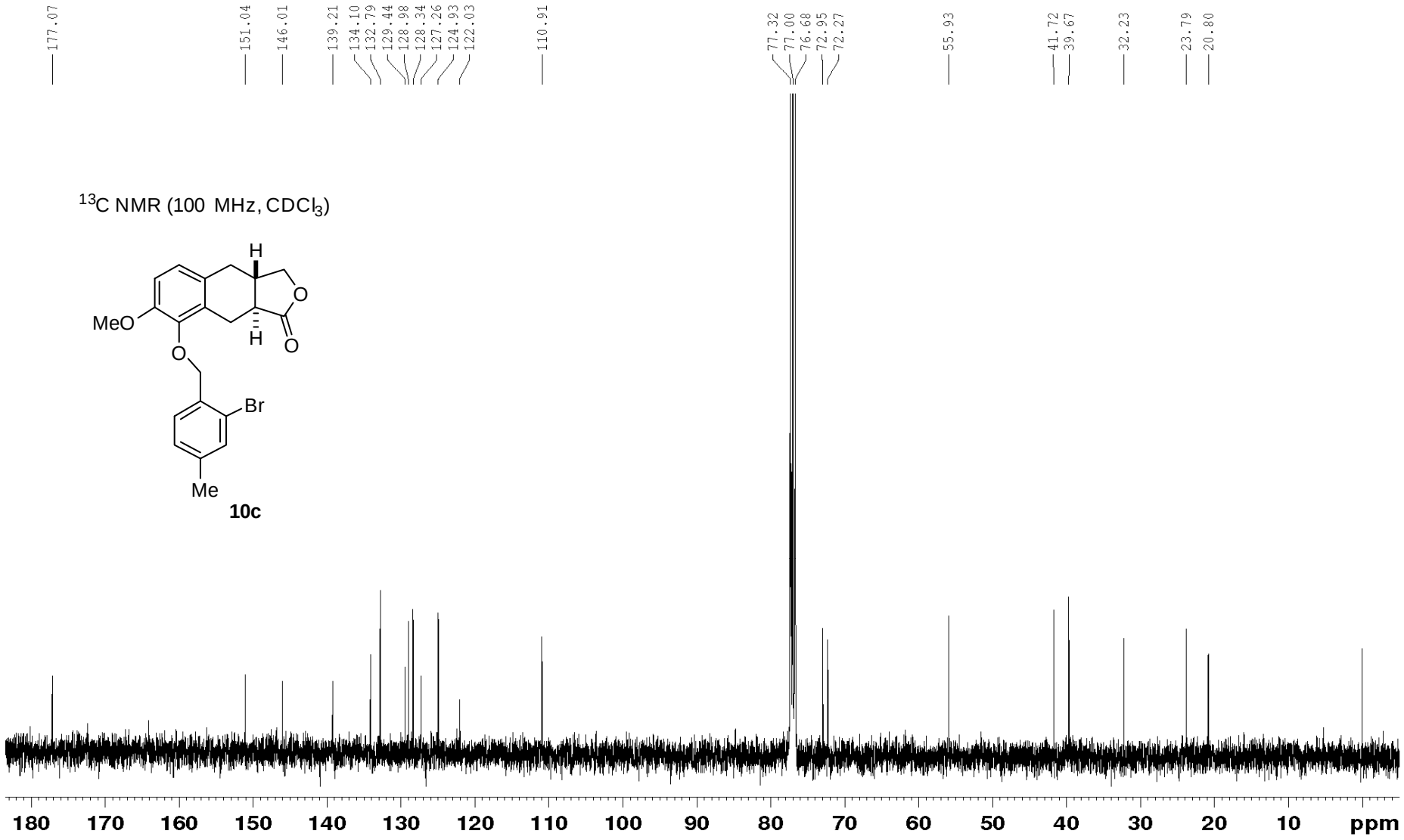

$^{19}F$ NMR (376 MHz, $CDCl_3$)




**10b**



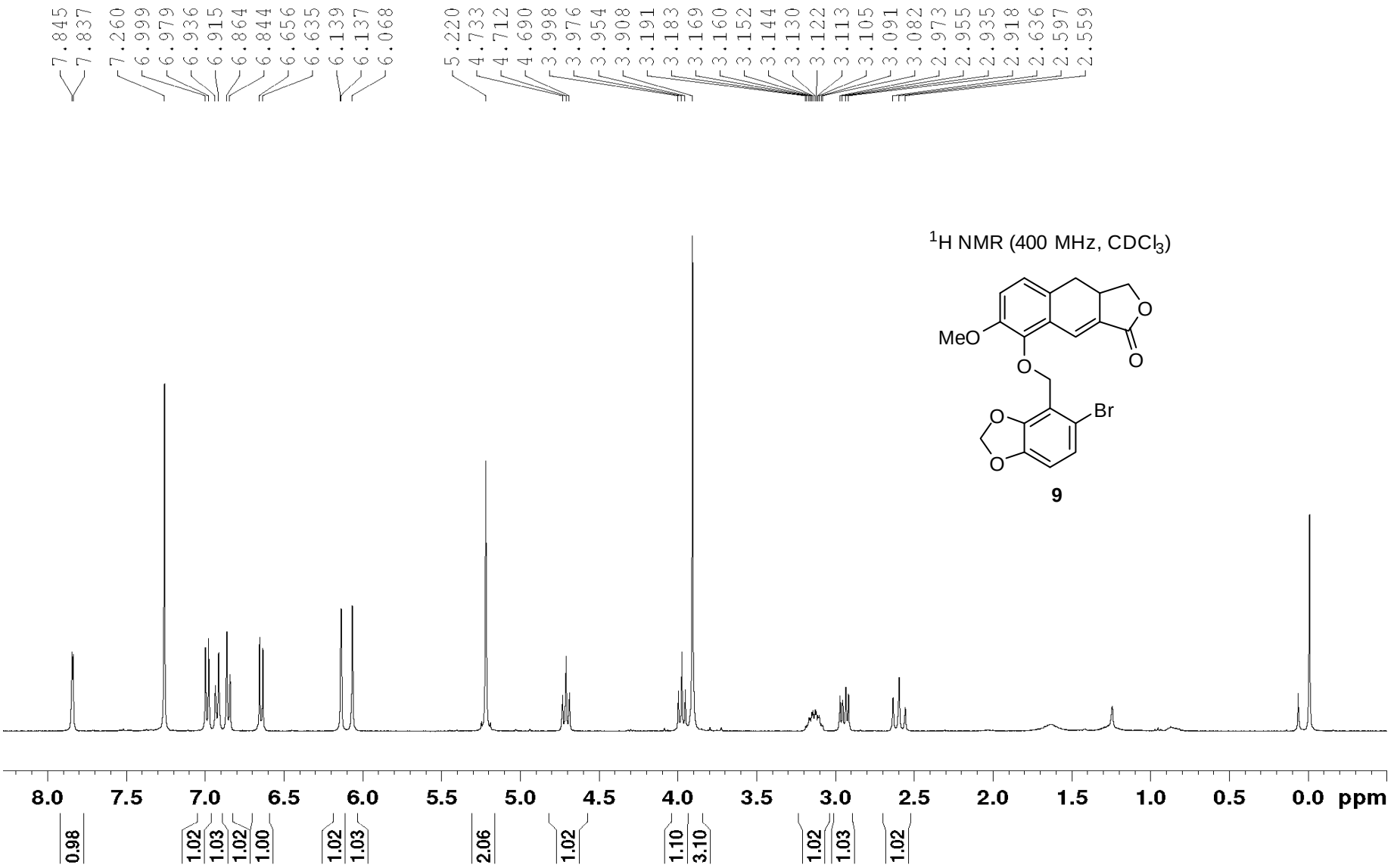

7.576
7.557
7.392
7.260
7.180
7.161
6.903
6.882
6.833
6.812
5.085
5.054
5.043
5.013
4.591
4.574
4.570
4.553
4.035
4.014
4.010
3.988
3.853
3.461
3.448
3.418
3.406
3.039
3.028
3.001
2.989
2.800
2.771
2.733
2.631
2.601
2.589
2.559
2.435
2.430
2.418
2.414
2.402
2.391
2.374
2.343
2.329
2.312
2.299
2.279
2.266
$^1$H NMR (400 MHz, CDCl$_3$)
H
O
MeO
H
O
O
Br
Me
10c
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.06
1.02
1.04
1.01
1.00
2.02
1.02
1.05
3.04
1.04
1.06
1.07
1.06
1.07
3.13
0.81

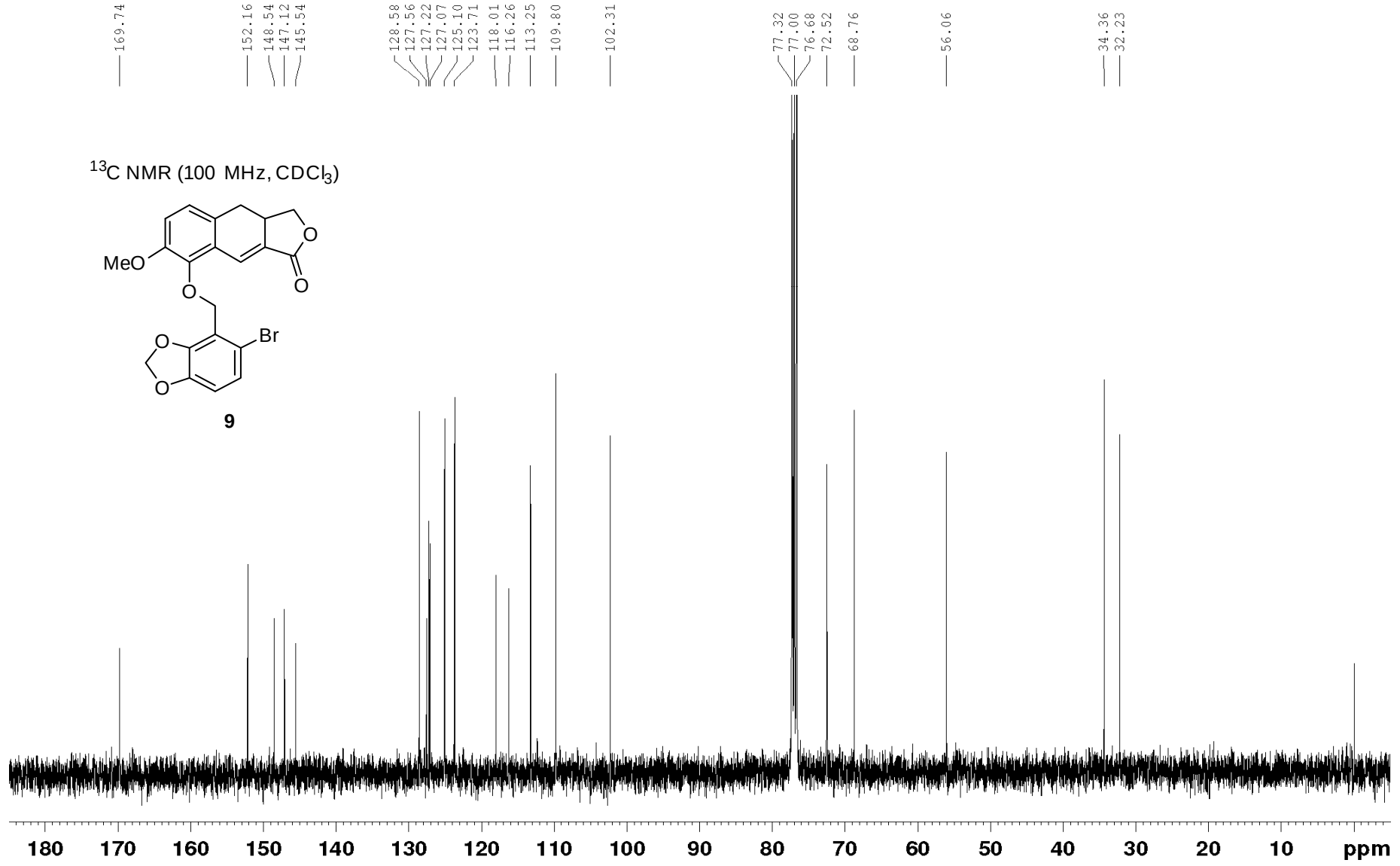


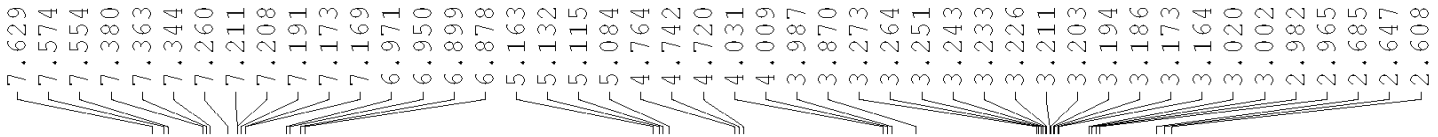

$^{13}$C NMR (100 MHz, $CDCl_3$)



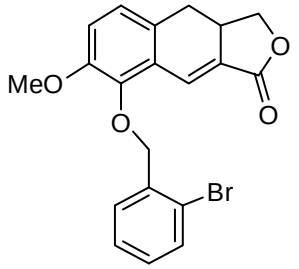

**10c**


7.845
7.837
7.260
6.999
6.979
6.936
6.915
6.864
6.844
6.656
6.635
6.139
6.137
6.068
5.220
4.733
4.712
4.690
3.998
3.976
3.954
3.908
3.191
3.183
3.169
3.160
3.152
3.144
3.130
3.122
3.113
3.105
3.091
3.082
2.973
2.955
2.935
2.918
2.636
2.597
2.559
$^1$H NMR (400 MHz, $CDCl_3$)
MeO
O
O
O
O
O
Br
9
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.98
1.02
1.03
1.02
1.00
1.02
1.03
2.06
1.02
1.10
3.10
1.02
1.03
1.02

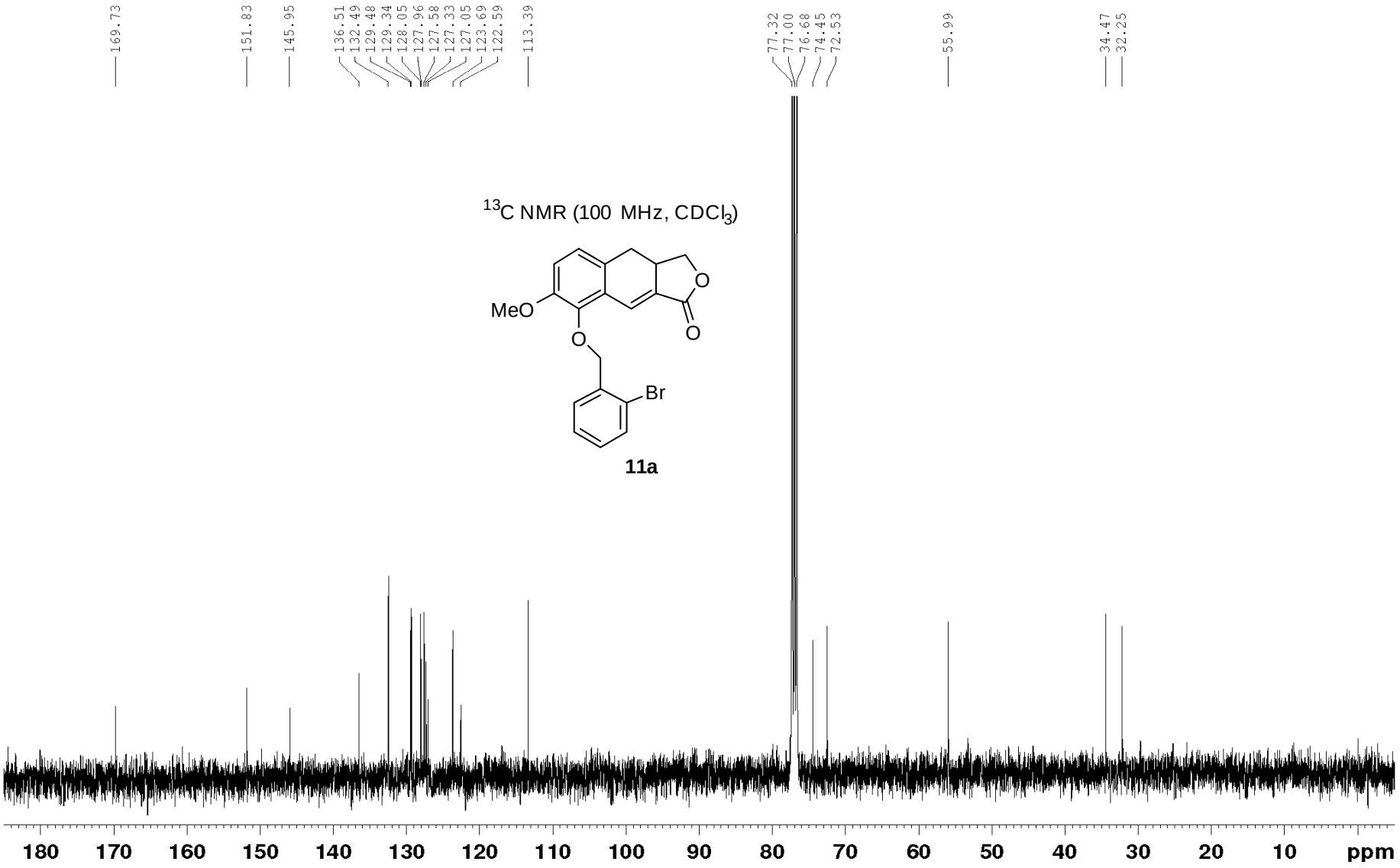

169.74
152.16
148.54
147.12
145.54
128.58
127.56
127.22
127.07
125.10
123.71
118.01
116.26
113.25
109.80
102.31
77.32
77.00
76.68
72.52
68.76
56.06
34.36
32.23
$^{13}$C NMR (100 MHz, $CDCl_3$)
MeO
O
O
O
O
O
Br
9
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm




$^1$H NMR (400 MHz, $CDCl_3$)



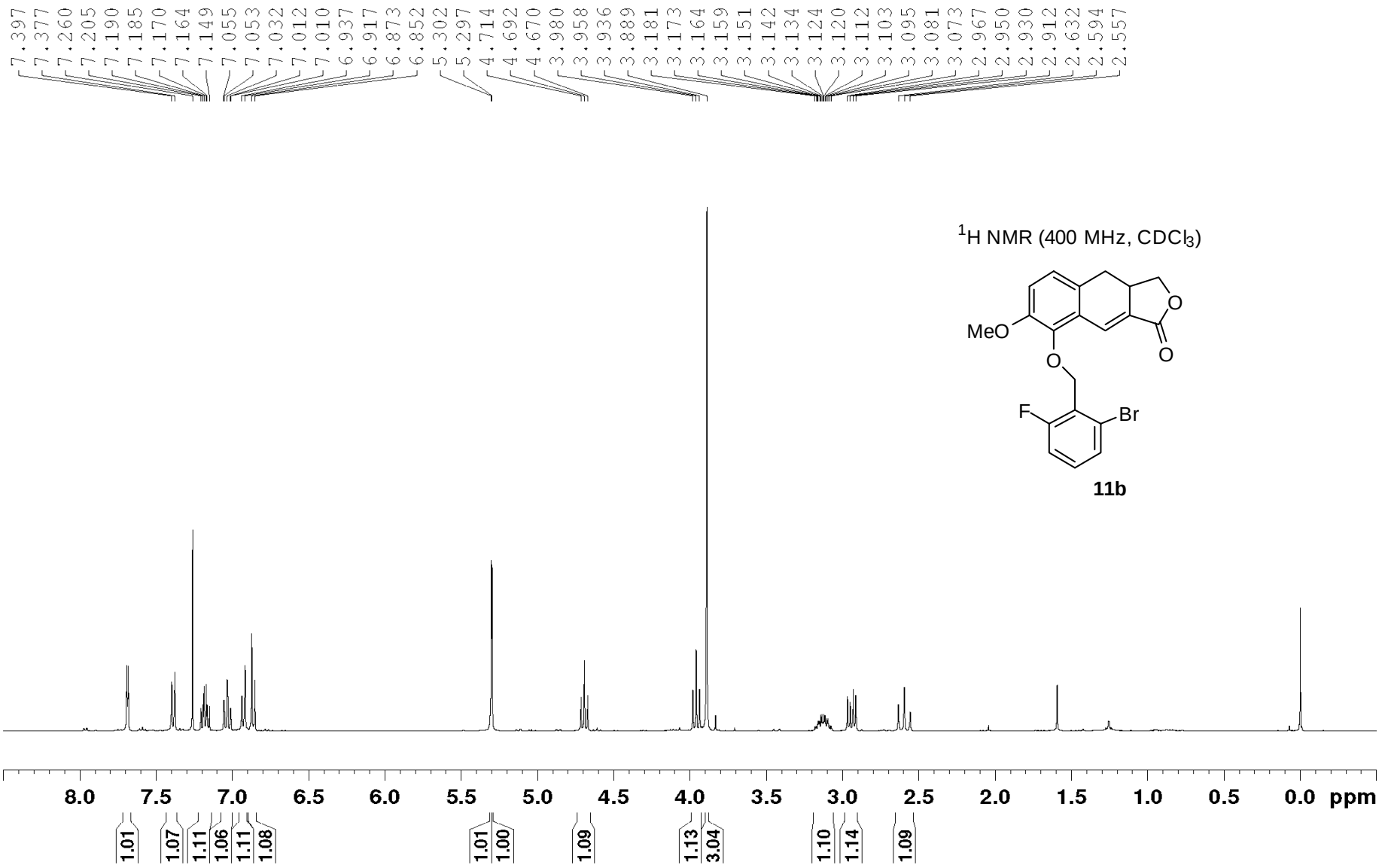

**11a**

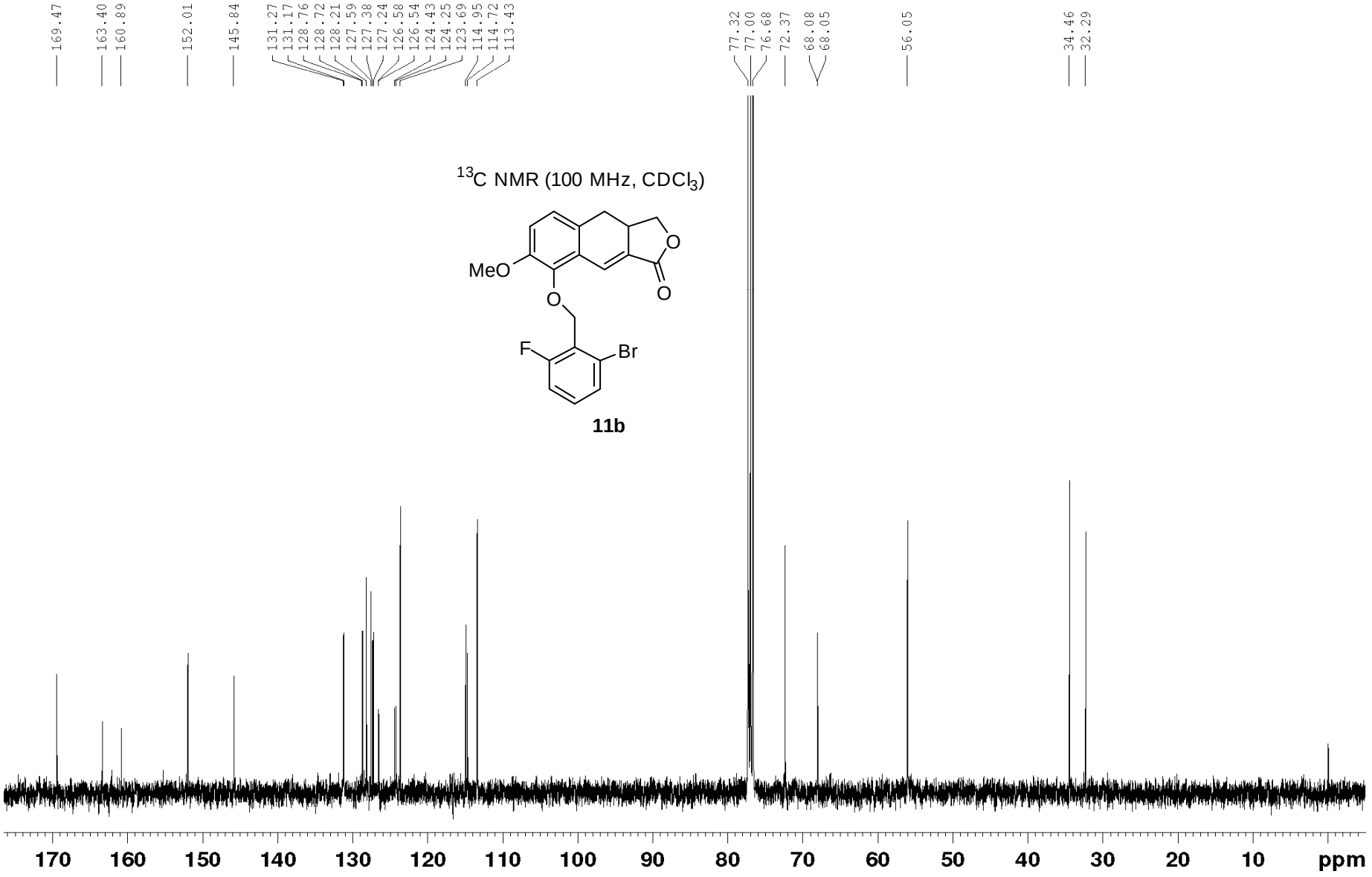



$^{13}$C NMR (100 MHz, $CDCl_3$)

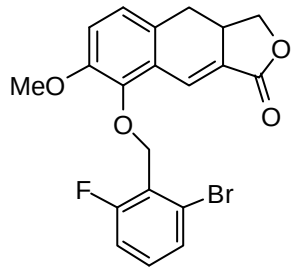



**11a**

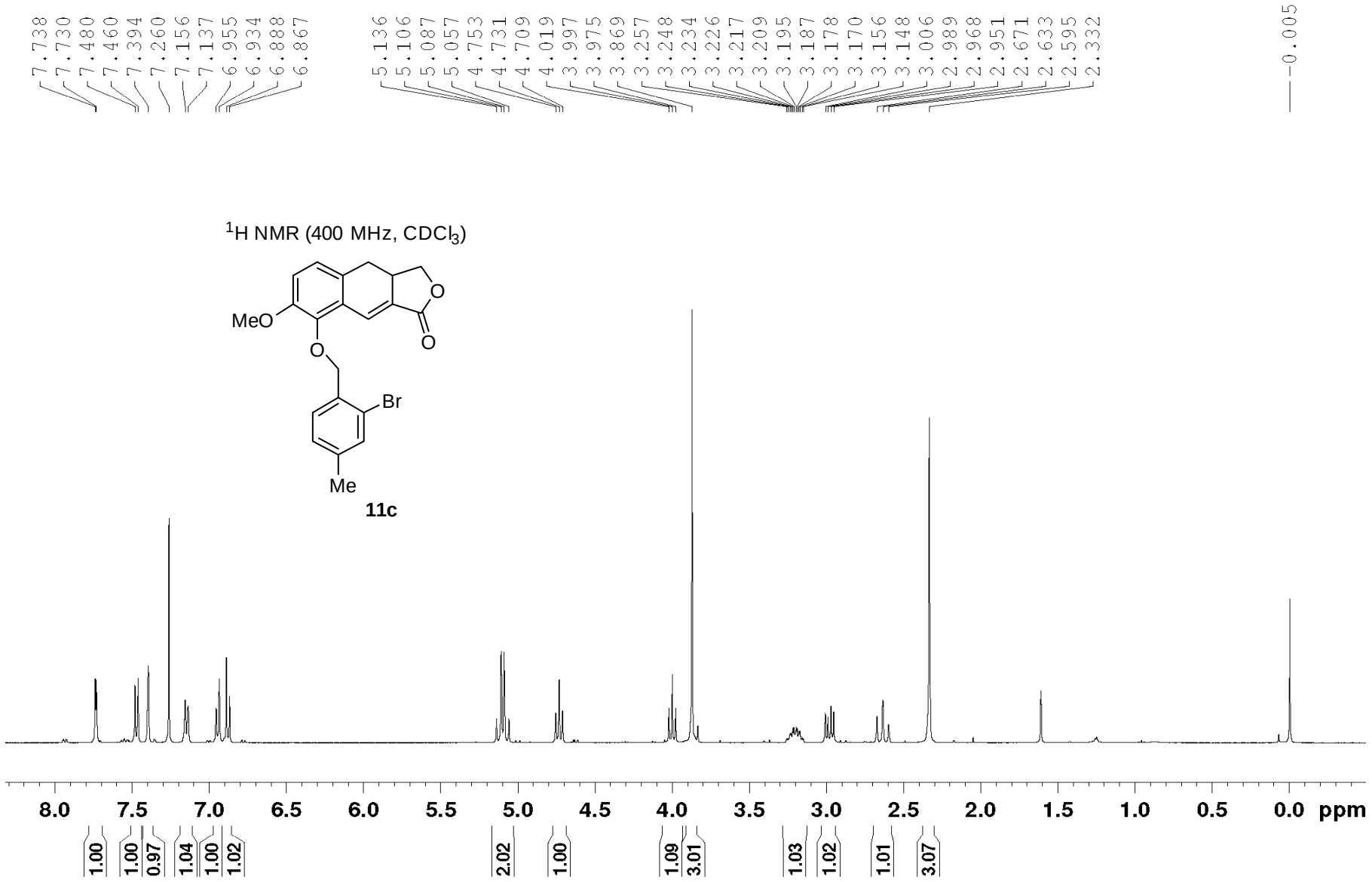

7.397
7.377
7.260
7.205
7.190
7.185
7.170
7.164
7.149
7.055
7.053
7.032
7.012
7.010
6.937
6.917
6.873
6.852
5.302
5.297
4.714
4.692
4.670
3.980
3.958
3.936
3.889
3.181
3.173
3.164
3.159
3.151
3.142
3.134
3.124
3.120
3.112
3.103
3.095
3.081
3.073
2.967
2.950
2.930
2.912
2.632
2.594
2.557
$^1$H NMR (400 MHz, CDCl$_3$)
MeO
O
O
O
F
Br
11b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.01
1.07
1.11
1.06
1.11
1.08
1.01
1.00
1.09
1.13
3.04
1.10
1.14
1.09

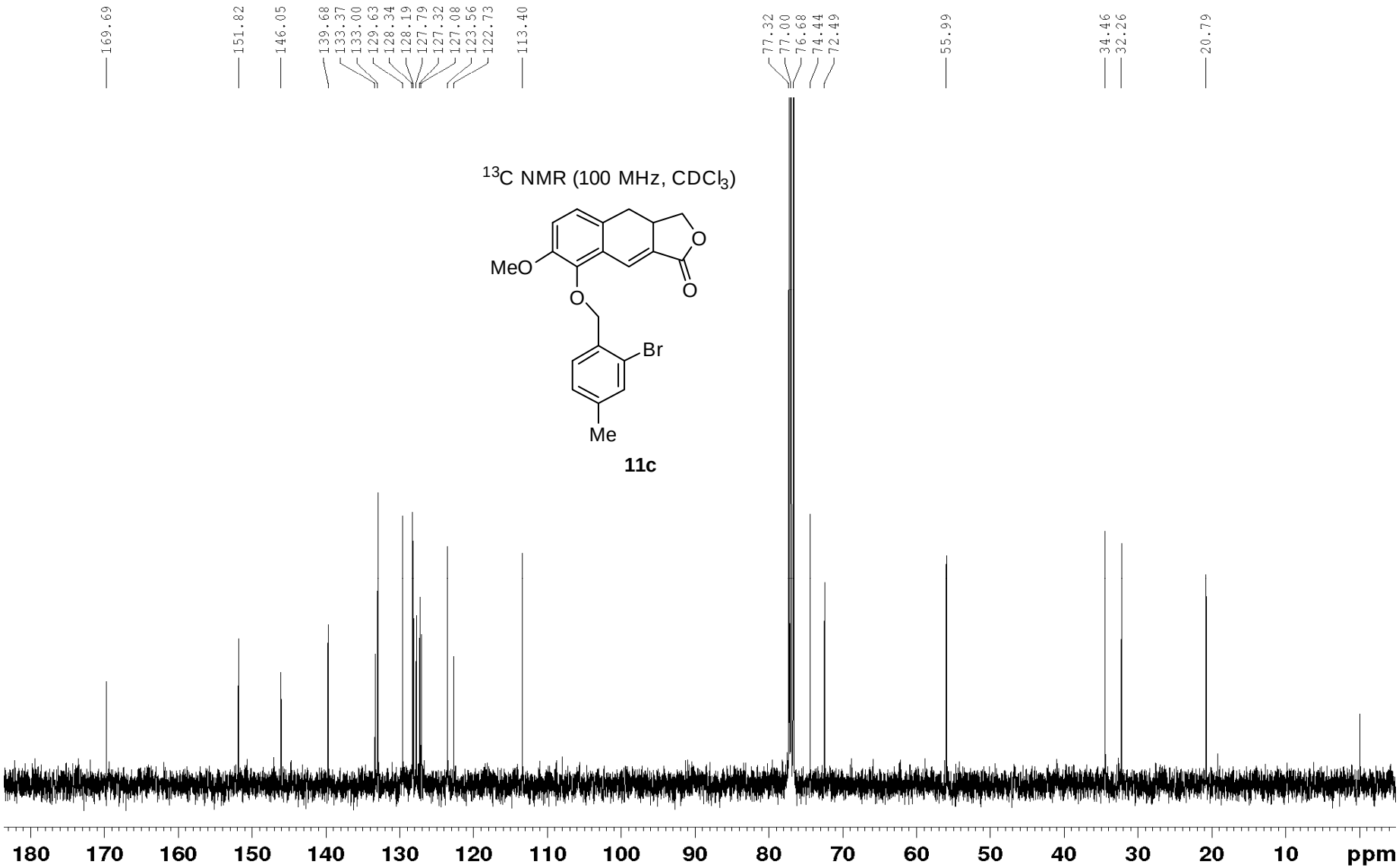

169.47
163.40
160.89
152.01
145.84
131.27
131.17
128.76
128.72
128.21
127.59
127.38
127.24
126.58
126.54
124.43
124.25
123.69
114.95
114.72
113.43
77.32
77.00
76.68
72.37
68.08
68.05
56.05
34.46
32.29
$^{13}$C NMR (100 MHz, $CDCl_3$)
MeO
O
O
O
F
Br
11b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

$^{19}$F NMR (376 MHz, $CDCl_3$)




**11b**

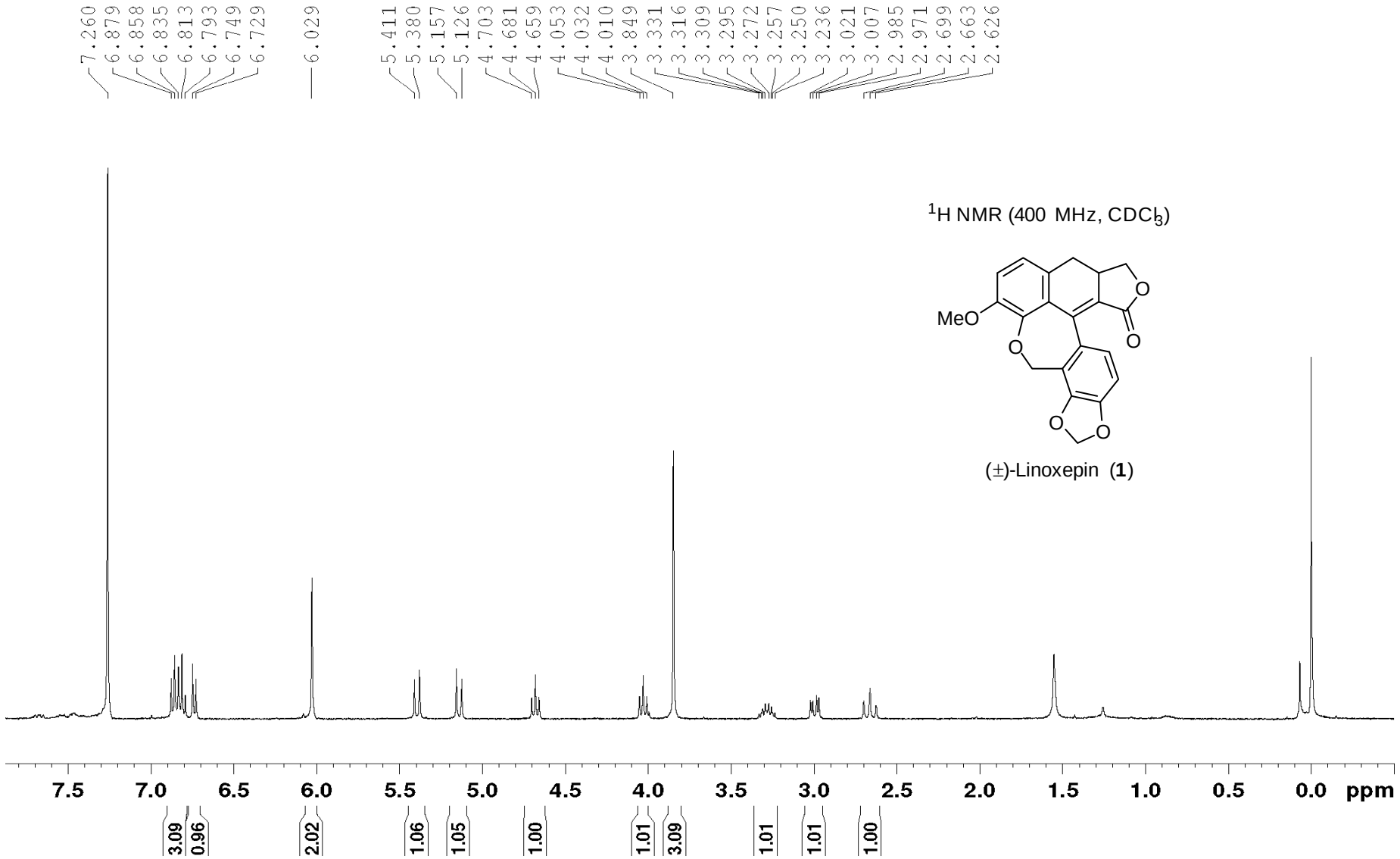

7.738
7.730
7.480
7.460
7.394
7.260
7.156
7.137
6.955
6.934
6.888
6.867
5.136
5.106
5.087
5.057
4.753
4.731
4.709
4.019
3.997
3.975
3.869
3.257
3.248
3.234
3.226
3.217
3.209
3.195
3.187
3.178
3.170
3.156
3.148
3.006
2.989
2.968
2.951
2.671
2.633
2.595
2.332
0.005
$^1$H NMR (400 MHz, $CDCl_3$)
MeO
O
O
O
Br
Me
**11c**
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.00
0.97
1.04
1.00
1.02
2.02
1.00
1.09
3.01
1.03
1.02
1.01
3.07

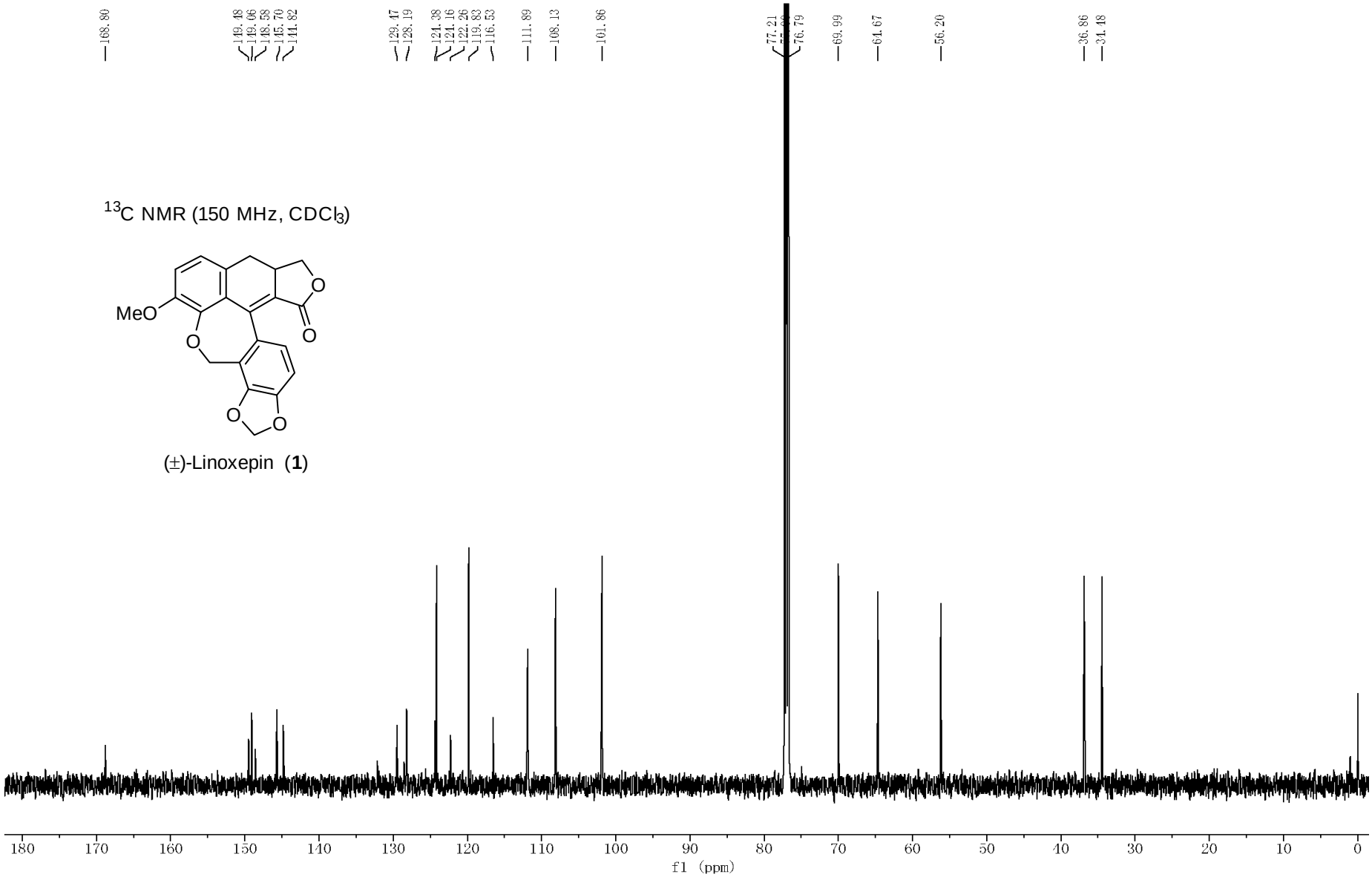



$^{13}$C NMR (100 MHz, $CDCl_3$)




**11c**

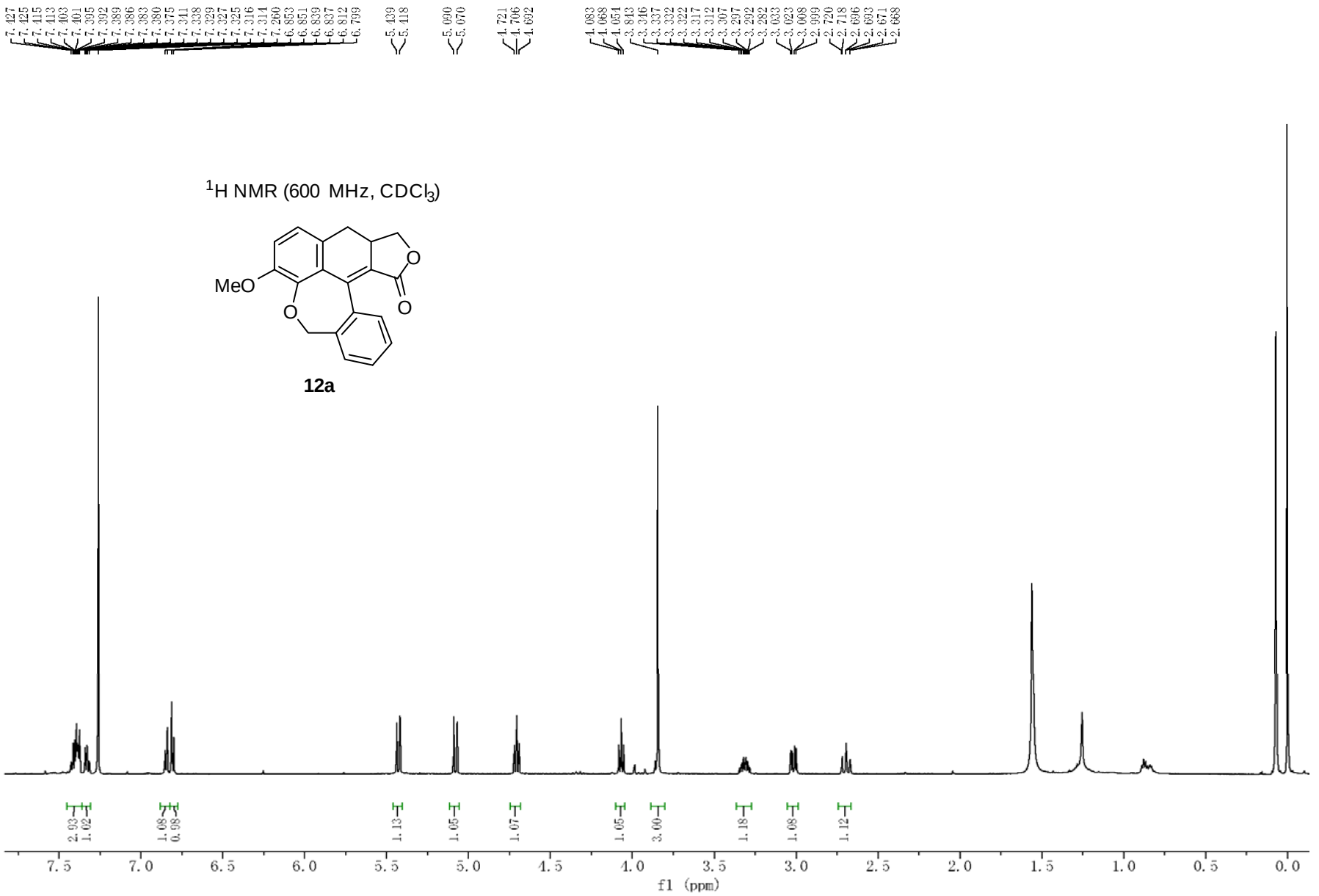

7.260
6.879
6.858
6.835
6.813
6.793
6.749
6.729
6.029
5.411
5.380
5.157
5.126
4.703
4.681
4.659
4.053
4.032
4.010
3.849
3.331
3.316
3.309
3.295
3.272
3.257
3.250
3.236
3.021
3.007
2.985
2.971
2.699
2.663
2.626
$^1$H NMR (400 MHz, CDCl$_3$)
MeO
O
O
O
O
O
(±)-Linoxepin (**1**)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.09
0.96
2.02
1.06
1.05
1.00
1.01
3.09
1.01
1.01
1.00

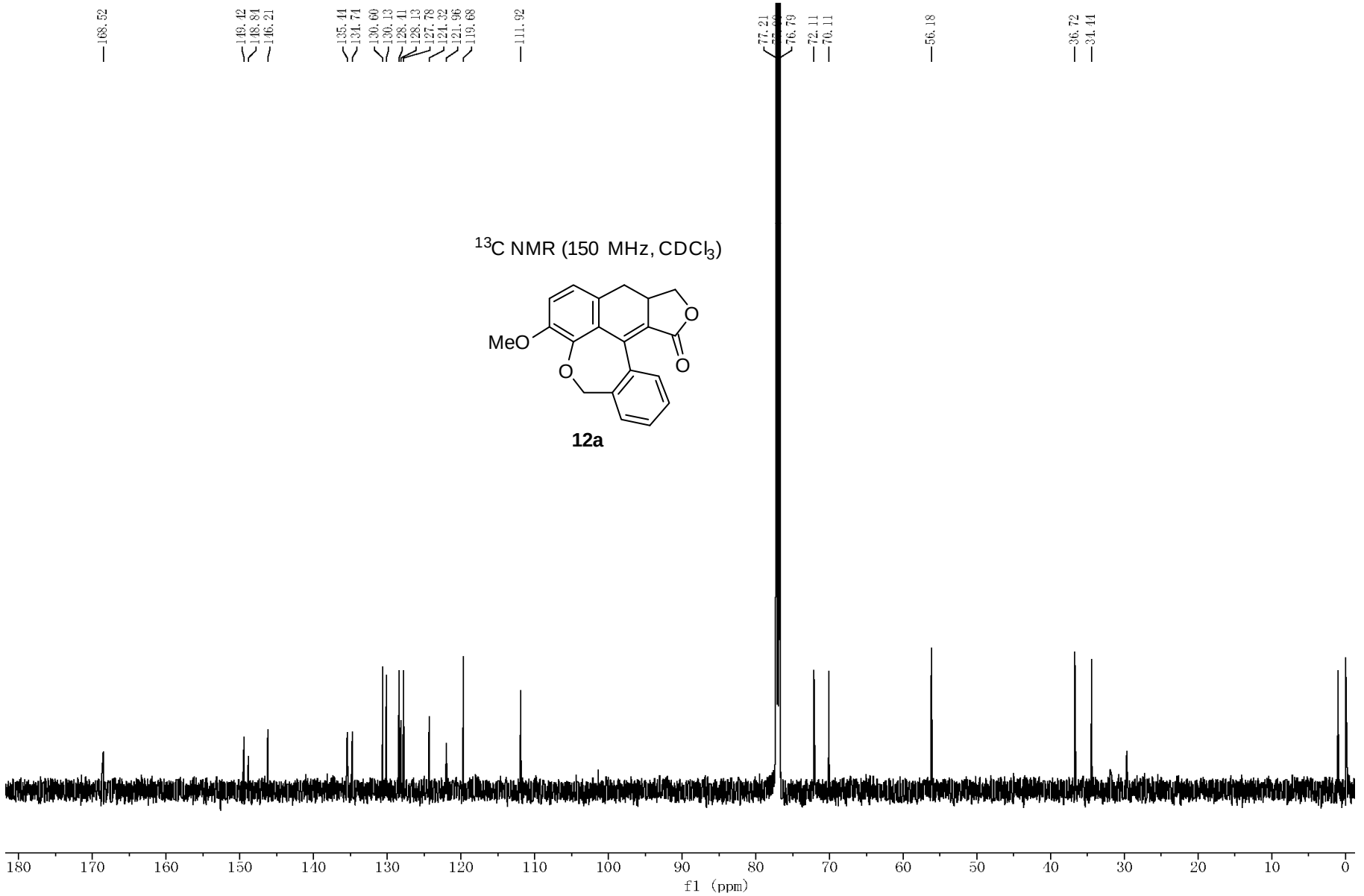


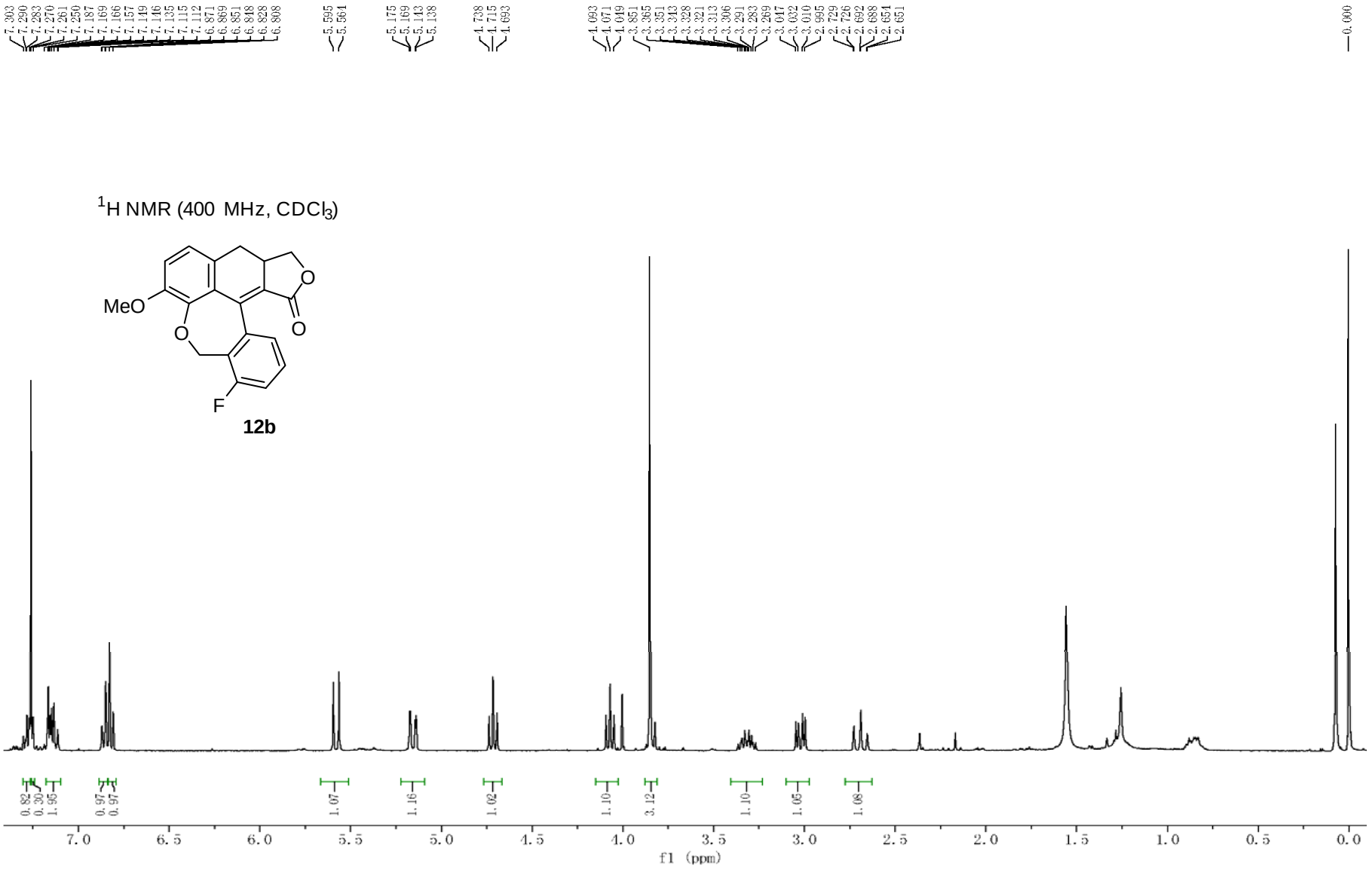

$^{13}$C NMR (150 MHz, $CDCl_3$)

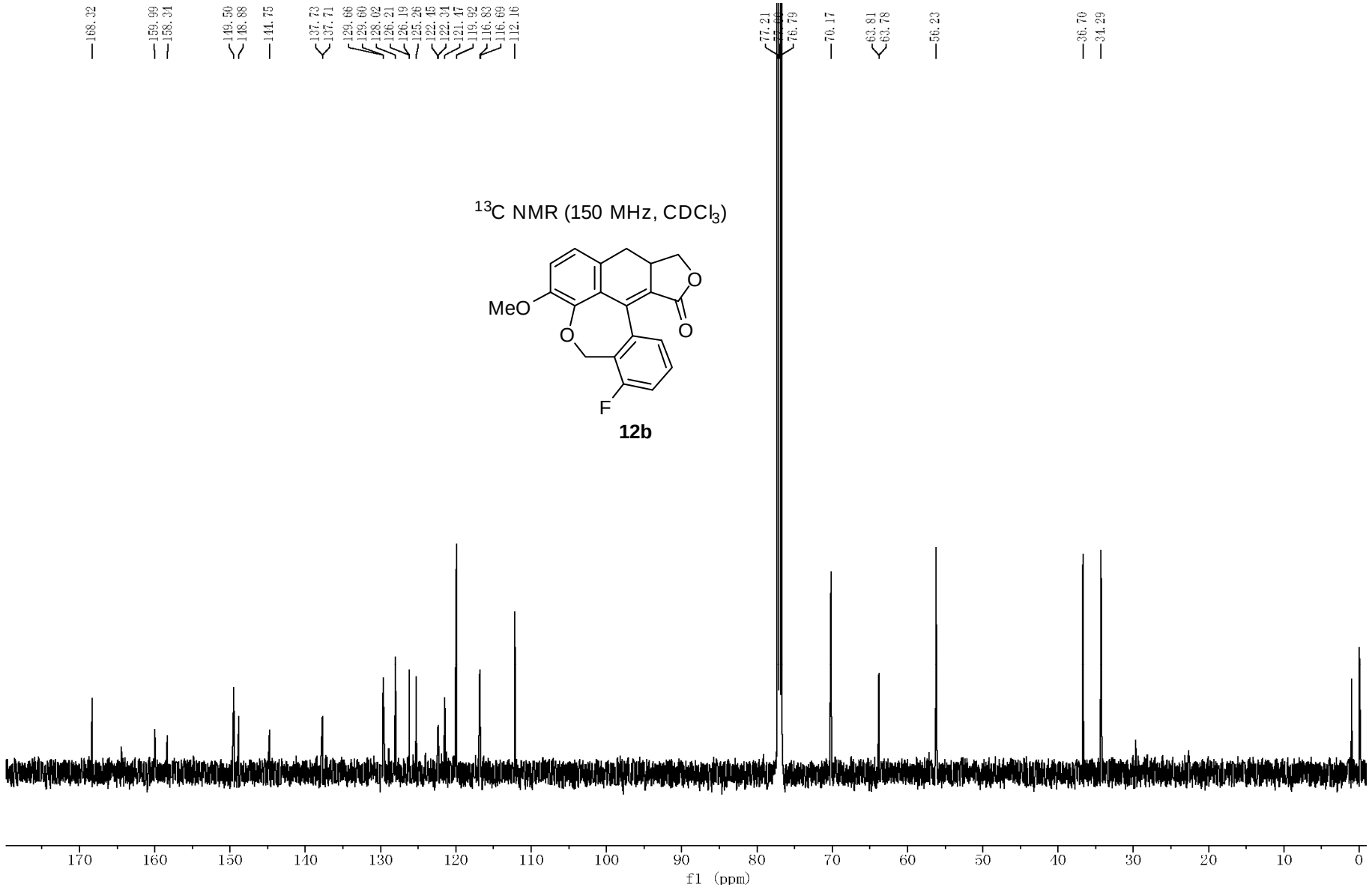



(±)-Linoxepin (**1**)

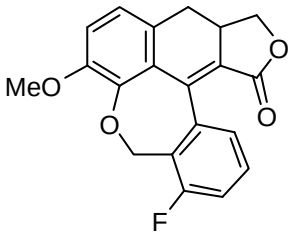

7.427
7.425
7.415
7.413
7.403
7.401
7.395
7.392
7.389
7.386
7.383
7.380
7.375
7.341
7.338
7.329
7.327
7.325
7.316
7.314
7.260
6.853
6.851
6.839
6.837
6.812
6.799
5.439
5.418
5.090
5.070
4.721
4.706
4.692
4.083
4.068
4.051
3.843
3.346
3.337
3.332
3.322
3.317
3.312
3.307
3.297
3.292
3.282
3.033
3.023
3.008
2.999
2.720
2.718
2.696
2.693
2.671
2.668
$^1$H NMR (600 MHz, $CDCl_3$)
MeO
O
O
O
**12a**
2.93
1.02
1.08
0.98
1.13
1.05
1.07
1.05
3.00
1.18
1.08
1.12
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


168.52
149.42
148.84
146.21
135.44
134.74
130.60
130.13
128.41
128.13
127.78
124.32
121.96
119.68
111.92
77.21
76.79
72.11
70.11
56.18
36.72
34.44
$^{13}$C NMR (150 MHz, $CDCl_3$)
MeO
O
O
O
12a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

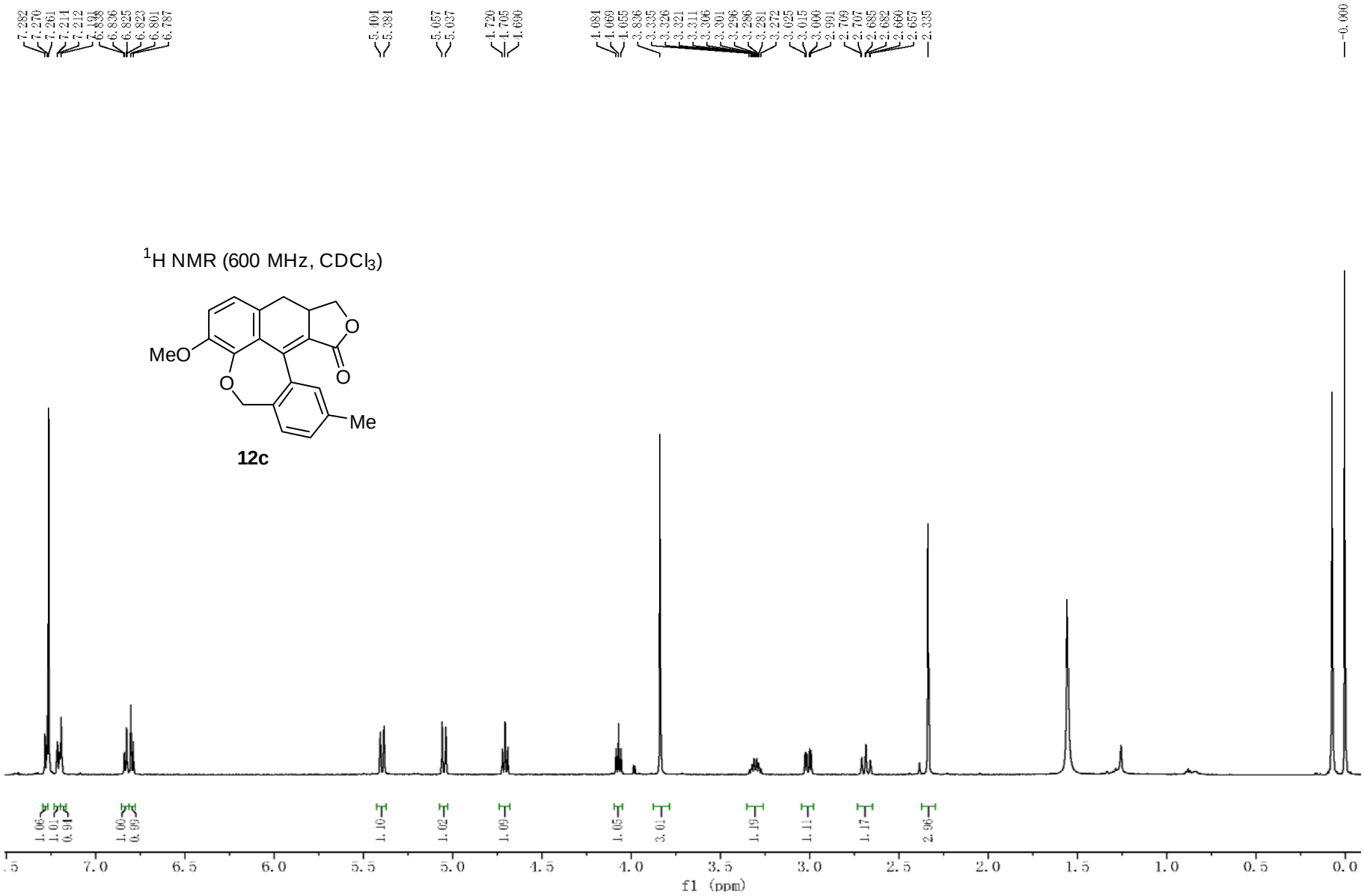

7.303
7.290
7.283
7.270
7.261
7.250
7.187
7.169
7.166
7.157
7.149
7.146
7.135
7.115
7.112
6.871
6.869
6.851
6.848
6.828
6.808
5.595
5.564
5.175
5.169
5.143
5.138
4.738
4.715
4.693
4.093
4.071
4.049
3.851
3.365
3.351
3.343
3.328
3.321
3.313
3.306
3.291
3.283
3.269
3.047
3.032
3.010
2.995
2.729
2.726
2.692
2.688
2.654
2.651
0.000
1H NMR (400 MHz, CDCl3)
MeO
O
O
O
F
12b
0.82
0.30
1.95
0.97
0.97
1.07
1.16
1.02
1.10
3.12
1.10
1.05
1.08
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

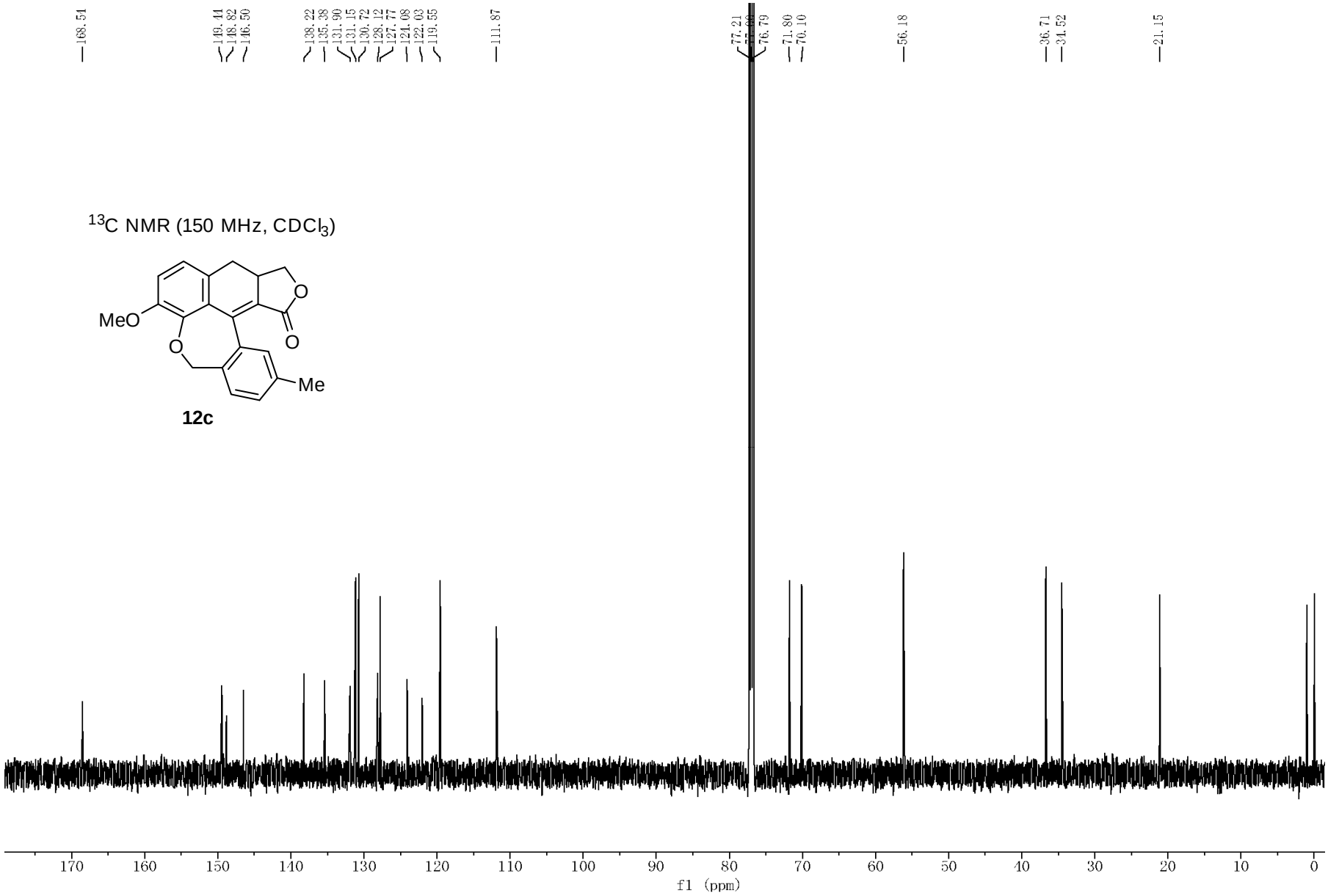

168.32
159.99
158.34
149.50
148.88
144.75
137.73
137.71
129.66
129.60
128.02
126.21
126.19
125.26
122.45
122.34
121.47
119.92
116.83
116.69
112.16
77.21
76.79
70.17
63.81
63.78
56.23
36.70
34.29
$^{13}$C NMR (150 MHz, $CDCl_3$)
MeO
O
O
O
F
12b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{19}$F NMR (565 MHz, $CDCl_3$)




**12b**


7.282
7.270
7.261
7.214
7.212
6.838
6.836
6.825
6.823
6.801
6.787
5.404
5.384
5.057
5.037
4.720
4.705
4.690
4.084
4.069
4.055
3.836
3.335
3.326
3.321
3.311
3.306
3.301
3.296
3.286
3.281
3.272
3.025
3.015
3.000
2.991
2.709
2.707
2.685
2.682
2.660
2.657
2.335
0.000
$^1$H NMR (600 MHz, CDCl$_3$)
MeO
O
O
O
Me
12c
1.06
1.01
0.94
1.00
0.99
1.10
1.02
1.09
1.05
3.01
1.19
1.11
1.17
2.96
f1 (ppm)




$^{13}$C NMR (150 MHz, $CDCl_3$)




**12c**