Supporting Information for

Intramolecular Ni-catalyzed Reductive Coupling Enables Enantiodivergent Synthesis of Linoxepin

Zi-Hao Liu[†], Jian Xiao[†,*], Qian-Qian Zhai[†], Xi Tang[†], Li-Jun Xu[‡], Zhi-Yuan Zhuang[‡], Ya-Wen Wang[†] and Yu Peng[†,*]

[†] *School of Chemistry, Key Laboratory of Advanced Technologies of Materials (Ministry of Education), Southwest Jiaotong University, Chengdu 610031, P. R. China*
[‡] *State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, P. R. China*

pengyu@swjtu.edu.cn

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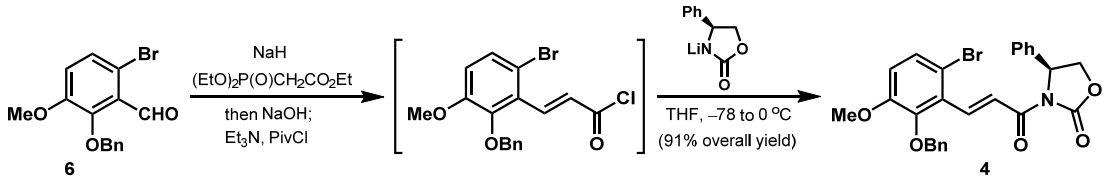
General Procedure

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 of 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. ^{1}H and ^{13}C NMR spectra were taken on a *Bruker* AM-400, AM-600, Ascend-400, Ascend-600 and Varian mercury 300 MHz 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 or Cu-Kα radiation source. Melting points were measured on X-4 series microscope melting point apparatus. The $[\alpha]_D$ was recorded using APII 36050 Automatic Polarimeter.

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), triethyl phosphonoacetate (98%), (*S*)-4-phenyl-2-oxazolidinone (98%), CuBr (98%), TMSOTf (99%), 2,4,4,6-tetrabromo-2,5-cyclohexadienone (97%).

Synthesis of Unsaturated Amide 4



NaH (60%, 10.54 g, 263.5 mmol, 1.7 equiv) was added to anhydrous THF (200 mL) in a 500 mL round-bottom flask, and the resulting slurry was cooled to 0 °C, followed by the addition of triethyl phosphonoacetate (60.28 g, 263.5 mmol, 1.7 equiv) dropwise over a 10 min period. After stirring for 30 min at this temperature, a solution of *o*-bromobenzaldehyde **6**[1] (49.60 g, 155 mmol) in THF (150 mL) was added dropwise. The resultant mixture was gradually warmed to room temperature, and stirred further for 4 h. The reaction was cooled to 0 °C again, then quenched by the addition of water (15 mL) carefully. The resulting mixture was extracted with EtOAc (3 × 250 mL), and the combined organic layers were washed with water (2 × 40 mL) and brine (40 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting *α*, *β*-unsaturated ethyl ester could be used directly for the next reaction without further purification.

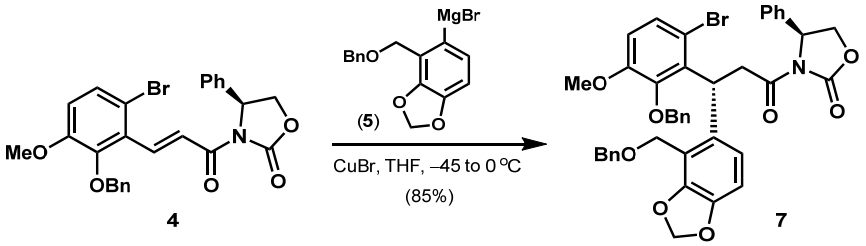
The above ester (155 mmol) was dissolved in MeOH (300 mL) was added NaOH (4*N*, 30 mL). The resulting mixture was stirred for 5 h at 70 °C and then cooled to room temperature. The solvent was removed, and HCl (6*N*, 250 mL) was added dropwise at 0 ºC. After stirring for 20 min, the mixture was filtered and the resulting *α, β*-unsaturated acid could be used directly for the next reaction without further purification.

In a 2 L round-bottom flask, (*S*)-4-phenyl-2-oxazolidinone (27.82 g, 170.5 mmol, 1.1 equiv) was dissolved in anhydrous THF (400 mL) and the resulting solution was cooled to −78 °C. A solution of freshly prepared LDA (170.5 mmol, 1.1 equiv) was then added dropwise, with stirring for 1 h at the same temperature. The generated lithium amide was ready to use.

(1) (a) Toth, J. E.; Hamann, P. R.; Fuchs, P. L. *J. Org. Chem*. **1988**, *53*, 4694. (b) Zhang, J.-J.; Yan, C.-S.; Peng, Y.; Luo, Z.-B.; Xu, X.-B.; Wang, Y.-W. *Org. Biomol. Chem.* **2013**, *11*, 2498.

Meanwhile, triethylamine (25.9 mL, 186 mmol, 1.2 equiv) was added to a precooled THF (0 °C, 150 mL) solution of the above acid in a 500 mL round-bottom flask, followed by the slow addition of pivaloyl chloride (20.9 mL, 170.5 mmol, 1.1 equiv). The mixture was stirred for 30 min at 0 °C, and the generated acyl chloride was then added to the above lithium amide slowly. The resulting mixture was gradually warmed to 0 °C, and stirred further for 3 h. The reaction was carefully quenched by the addition of saturated aqueous NH_4Cl solution (25 mL). The resultant mixture was extracted with EtOAc (3 × 300 mL), and the combined organic layers were washed with water (2 × 40 mL) and brine (40 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 = 5 : 1 → petroleum ether/EtOAc = 1 : 1) on silica gel to afford **4** (71.51 g, 91% overall yield) as a white solid. R_f = 0.6 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = +38.50 (c = 2.00, $CHCl_3$); Mp. 111–113 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (d, J = 15.9 Hz, 1H), 7.86 (d, J = 15.9 Hz, 1H), 7.42–7.23 (m, 11H), 6.77 (d, J = 8.7 Hz, 1H), 5.47 (dd, J = 8.7, 3.9 Hz, 1H), 5.05 (d, J = 10.8 Hz, 1H), 4.99 (d, J = 11.1 Hz, 1H), 4.65 (t, J = 8.7 Hz, 1H), 4.23 (dd, J = 9.0, 3.9 Hz, 1H), 3.81 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.8, 153.3, 152.5, 148.2, 141.0, 139.0, 136.9, 129.2, 129.1 (2C), 128.5, 128.4 (2C), 128.3, 128.1 (2C), 127.9, 125.9 (2C), 123.5, 115.8, 114.3, 75.0, 69.9, 57.7, 56.0 ppm; HRMS (ESI): calcd. for $C_{26}H_{22}NO_5{}^{79}BrNa^+$ $[M+Na]^+$: 530.0574, found: 530.0591.

Asymmetric Synthesis of Amide 7 by Conjugated Addition



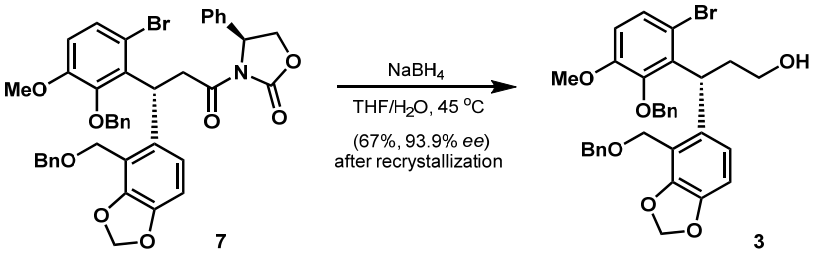
In a 250 mL round-bottom flask, 4-(benzyloxymethyl)-5-iodobenzo[*d*][1,3]dioxole

[2] (7.546 g, 20.5 mmol, 2.0 equiv) was dissolved in anhydrous THF (20 mL) and the resulting solution was cooled to –20 °C. A solution of *i*-PrMgBr (21.53 mmol, 2.1 equiv) was then added dropwise, with stirring for 30 min at the same temperature. The generated Grignard reagent **5** was ready to use.

Meanwhile, to a slurry of CuBr (2.251 g, 15.38 mmol, 1.5 equiv) in THF (30 mL) at –45 °C were added dimethylsulfide (30 mL) and freshly prepared Grignard reagent **5**. The generated organocopper reagent was stirred further for 40 min at the same temperature, a solution of **4** (5.21 g, 10.25 mmol) in THF (30 mL) was then added dropwise. The resulting mixture was gradually warmed to 0 ºC over a 30 min period, and stirred further for 4 h at 0 ºC. The reaction was carefully quenched by the addition of saturated aqueous NH_4Cl solution (10 mL). The resulting mixture was extracted with EtOAc (3 × 200 mL), and the combined organic layers were washed with 10% aqueous $NH_3•H_2O$ (40 mL), water (40 mL) and brine (30 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 = 10 : 1 → petroleum ether/EtOAc = 2 : 1) on silica gel to afford **7** (6.534 g, 85% yield) as a white solid. R_f = 0.35 (petroleum ether/EtOAc = 4 : 1); $[\alpha]_D^{22}$ = +13.00 (*c* = 1.00, $CHCl_3$); Mp. 62–63 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.30 (m, 5H), 7.24–7.17 (m, 9H), 7.08–7.06 (m, 2H), 6.62 (d, *J* = 8.8 Hz, 1H), 6.46 (d, *J* = 8.4 Hz, 1H), 6.41 (d, *J* = 8.4 Hz, 1H), 5.91 (d, *J* = 1.2 Hz, 1H), 5.88 (d, *J* = 1.2 Hz, 1H), 5.23 (dd, *J* = 8.8, 3.6 Hz, 1H), 5.19 (t, *J* = 8.0 Hz, 1H), 4.87 (d, *J* = 10.8 Hz, 1H), 4.58 (d, *J* = 11.2 Hz, 1H), 4.51 (d, *J* = 11.2 Hz, 1H), 4.34 (s, 2H), 4.31 (dd, *J* = 16.4, 11.2 Hz, 1H), 4.06 (dd, *J* = 6.4, 2.4 Hz, 1H), 4.03 (dd, *J* = 20.4, 8.4 Hz, 1H), 3.75 (s, 3H), 3.58 (dd, *J* = 18.8, 7.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 153.5, 152.6, 148.4, 147.3, 145.3, 139.1, 138.5, 137.9, 136.2, 135.7, 128.9 (2C), 128.32, 128.27, 128.2 (2C), 128.0 (2C), 127.9 (2C), 127.6, 127.5 (2C), 127.1, 125.6 (2C), 121.2, 118.3, 115.8, 111.8, 107.7, 100.9, 74.2, 72.1, 69.9, 63.8, 57.4, 55.6, 41.1, 40.1 ppm; HRMS (ESI): calcd. for $C_{41}H_{36}NO_8{}^{79}BrNa^+$ $[M+Na]^+$: 772.1517, found: 772.1539.

(2) Tietze, L. F.; Duefert, S. C.; Clerc, J.; Bischoff, M.; Maass, C.; Stalke, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 3191.

Synthesis of Alcohol 3



To a solution of **7** (4.58 g, 6.12 mmol) in THF (120 mL) was added water (3 mL) followed by the addition of $NaBH_4$ (98%, 3.543 g, 91.8 mmol, 15.0 equiv) portionwise. The reaction temperature was raised to 45 ^{o}C. 12 h later, THF was evaporated in vacuo. The resulting mixture was extracted with EtOAc (3 × 150 mL), and the combined organic layers were washed with water (2 × 25 mL) and brine (25 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 = 2 : 1) on silica gel. One day later, colorless single crystals were obtained by slow evaporation of solvents at room temperature to afford alcohol **3** (2.423 g, 67% yield). R_f = 0.65 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = +36.00 (c = 1.00, $CHCl_3$); Mp. 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 11H), 7.04 (d, J = 8.0 Hz, 1H), 6.63 (d, J = 8.4 Hz, 1H), 6.58 (d, J = 8.4 Hz, 1H), 5.92 (s, 2H), 4.90 (t, J = 8.0 Hz, 1H), 4.75 (d, J = 10.8 Hz, 1H), 4.59 (d, J = 10.4 Hz, 1H), 4.52 (d, J = 10.8 Hz, 1H), 4.50 (d, J = 11.6 Hz, 1H), 4.41 (d, J = 11.6 Hz, 1H), 3.91–3.89 (m, 1H), 3.73 (s, 3H), 3.62–3.54 (m, 2H), 2.49–2.41 (m, 1H), 2.38–2.30 (m, 1H), 1.86 (brs, 1H, -O*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 148.2, 147.3, 145.3, 138.5, 138.0, 137.5, 135.5, 128.10 (3C), 128.07 (2C), 127.54 (2C), 127.51 (3C), 127.3, 122.3, 119.0, 116.0, 111.8, 107.8, 100.9, 73.7, 72.3, 63.7, 60.7, 55.6, 41.0, 36.8 ppm; HRMS (ESI): calcd. for $C_{32}H_{31}O_6{}^{79}BrNa^+$ $[M+Na]^+$: 613.1196, found: 613.1214; HPLC (Chiralpak OD column *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 13.61 min, t_{minor} = 19.85 min, 93.9% *ee*).

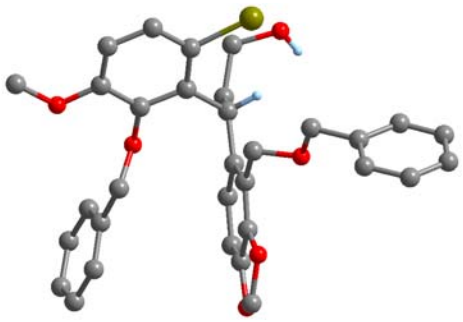
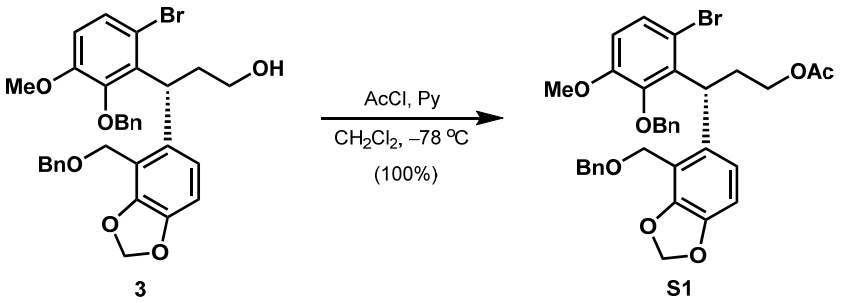


Table S1: X-ray crystal data of alcohol **3** (selected H atoms have been omitted for clarity)

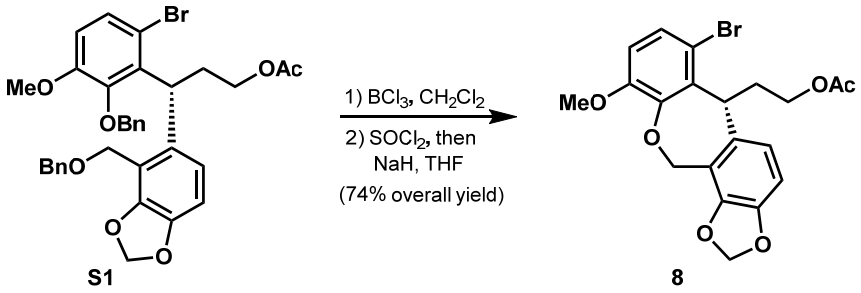
Empirical formula	$C_{32}H_{31}O_6Br$
Temperature (K)	293.00(2)
Crystal color	colorless
Formula weight	591.48
Crystal system	monoclinic
Space group	$P2_1$
a (Å)	10.8450(5)
b (Å)	11.7874(6)
c (Å)	11.0385(5)
α (°)	90.00
β (°)	97.286(5)
γ (°)	90.00
V (Å ^{3})	1399.71(11)
Z	2
Density (calculated) (g/cm^3)	1.403
F (000)	612.0
λ (Å)	0.71073
Reflections collected	5394
Independent reflections	3860
2θ Range for data collection (°)	6.62—52.04
Index range	$-12 \le h \le 13$ $-14 \le k \le 8$ $-13 \le l \le 13$
Final *R* indices [I>2σ(*I*)]	$R_1 = 0.0432$, $wR_2 = 0.0773$
Largest difference peak and hole [e Å $^{-3}$]	0.272, –0.437

Synthesis of Acetate S1



In a 250 mL round-bottom flask, alcohol **3** (2.488 g, 4.21 mmol) was dissolved in anhydrous CH_2Cl_2 (50 mL) and the resulting solution was cooled to −78 °C, followed by the addition of pyridine (0.85 mL, 10.53 mmol, 2.5 equiv). After 10 min, AcCl (0.6 mL, 8.42 mmol, 2.0 equiv) was added dropwise, with stirring for 2 h at the same temperature. The resultant mixture was then extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layers were washed with water (2 × 10 mL) and brine (10 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give acetate **S1** (2.665 g, 100% yield) as a colorless oil, which could be used directly for the next reaction without further purification. R_f = 0.65 (petroleum ether/EtOAc = 4 : 1); $[\alpha]_D^{26}$ = +51.01 (c = 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.18 (m, 11H), 6.97 (d, J = 8.4 Hz, 1H), 6.62 (d, J = 9.0 Hz, 1H), 6.59 (d, J = 8.4 Hz, 1H), 5.93 (s, 2H), 4.88 (t, J = 7.5 Hz, 1H), 4.72 (d, J = 10.8 Hz, 1H), 4.53 (s, 2H), 4.50 (d, J = 13.2 Hz, 1H), 4.40 (d, J = 11.7 Hz, 1H), 4.15 (dt, J = 11.1, 6.6 Hz, 1H), 3.99 (dt, J = 11.1, 6.3 Hz, 1H), 3.80–3.72 (m, 1H), 3.72 (s, 3H), 2.59–2.37 (m, 2H), 1.96 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0, 152.8, 148.2, 147.4, 145.4, 138.6, 138.1, 137.1, 135.1, 128.1 (2C), 128.0 (2C), 127.5 (4C), 127.4 (2C), 127.1, 121.9, 119.1, 116.1, 111.9, 107.7, 100.9, 73.5, 72.2, 63.6, 62.8, 55.5, 41.5, 32.4, 21.0 ppm. HRMS (ESI): calcd. for $C_{34}H_{33}O_7{}^{79}BrNa^+$ $[M+Na]^+$: 655.1302, found: 655.1302.

Synthesis of Benzooxepine 8



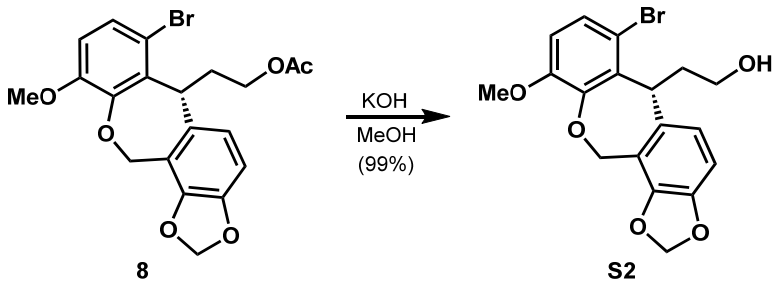
In a 250 mL round-bottom flask, compounds **S1** (5.962 g, 9.41 mmol) was dissolved in anhydrous CH_2Cl_2 (50 mL) and the resulting solution was cooled to −78 ^oC, followed by the addition of BCl_3 (37.64 mL, 37.64 mmol, 4.0 equiv, 1.0 M in CH_2Cl_2) dropwise. The resulting mixture was gradually warmed to 0 ºC over a 30 min period, and stirred further for 1.5 h at 0 ºC. The reaction was carefully quenched by the addition of saturated aqueous $NaHCO_3$ (8 ml). The resultant mixture was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layers were washed with water (2 × 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 = 5 : 1 → petroleum ether/EtOAc = 2 : 1) on silica gel to afford benzyl alcohol intermediate (4.18 g, 98% yield) as a brown oil.

In a 100 mL round-bottom flask, the above benzyl alcohol (9.22 mmol) was dissolved in ether (30 mL) at room temperature, followed by the addition of $SOCl_2$ (1.34 mL, 18.44 mmol, 2.0 eq) dropwise at 0 ºC. The reaction mixture was warmed to room temperature, and stirred for 8 h. The reaction was quenched with saturated $NaHCO_3$ (10 ml) at 0 ºC. The resulting mixture was extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with water (2 × 10 mL) and brine (10 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting benzyl chloride intermediate could be used directly for the next reaction without further purification.

In a 100 mL round-bottom flask, the above benzyl chloride was dissolved in THF

(30 mL) and the resulting solution was cooled to 0 °C, followed by the addition of NaH (60%, 738 mg, 18.44 mmol, 2.0 equiv) portionwise. The reaction mixture was warmed to room temperature, and stirred for 5 h. After the reaction is completed, it was quenched with ice water (5 mL). The resulting mixture was extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with water (2 × 8 mL) and brine (10 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 = 10 : 1) on silica gel to afford **8** (2.968 g, 74% overall yield) as a colorless oil. R_f = 0.7 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = –110.00 (*c* = 0.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.7 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.71 (d, *J* = 8.7 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 1H), 5.92 (d, *J* = 0.9 Hz, 1H), 5.87 (d, *J* = 0.9 Hz, 1H), 5.43 (d, *J* = 16.2 Hz, 1H), 4.90 (d, *J* = 15.9 Hz, 1H), 4.51 (t, *J* = 7.8 Hz, 1H), 3.98 (t, *J* = 6.0 Hz, 2H), 3.86 (s, 3H), 2.60 (ddd, *J* = 14.1, 7.8, 6.0 Hz, 1H), 2.40 (ddd, *J* = 13.2, 7.5, 6.6 Hz, 1H), 2.06 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 152.0, 146.7, 146.0, 143.9, 138.1, 131.7, 128.7, 123.5, 118.1, 114.1, 112.0, 106.7, 101.4, 67.7, 62.6, 56.0, 46.4, 35.4, 21.0 ppm; HRMS (ESI): calcd. for $C_{20}H_{19}O_6{}^{79}BrNa^+$ $[M+Na]^+$: 457.0257, found: 457.0271.

Synthesis of Alcohol S2

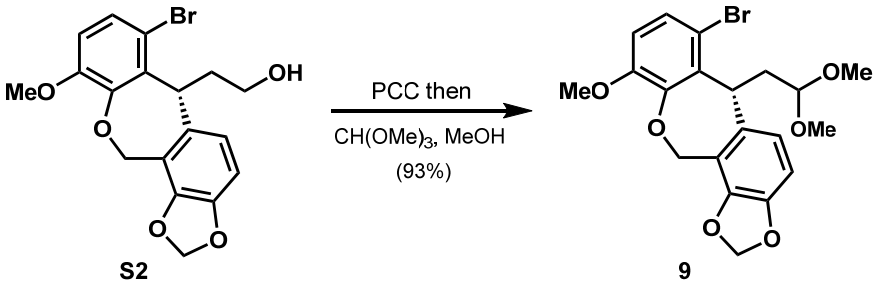


8 S2

In a 250 mL round-bottom flask, compounds **8** (1.38 g, 3.17 mmol) was dissolved in anhydrous MeOH (60 mL), followed by the addition of KOH (85%, 251 mg, 3.8 mmol, 1.2 equiv) portionwise at room temperature. The reaction mixture was then stirred for 1.5 h at room temperature. After the reaction is completed, it was quenched with saturated $NaHCO_3$ (8 mL) at 0 °C. The resultant mixture was extracted with

DCM (3 × 50 mL), and the combined organic layers were washed with water (2 × 10 mL) and brine (10 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 = 10 : 1) on silica gel to afford alcohol **S2** (1.24 g, 99% yield) as a white solid. R_f = 0.6 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = –96.00 (c = 0.1, $CHCl_3$); Mp. 51–52 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, J = 8.8 Hz, 1H), 6.81 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 9.2 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 5.93 (d, J = 1.6 Hz, 1H), 5.88 (d, J = 1.2 Hz, 1H), 5.43 (d, J = 16.0 Hz, 1H), 4.90 (d, J = 16.0 Hz, 1H), 4.56 (t, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.56(t, J = 5.6 Hz, 2H), 2.51(dddd, J = 14.0, 11.6, 8.4, 5.6 Hz, 1H), 2.33 (ddd, J = 20.4, 13.6, 7.2 Hz, 1H), 1.52 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.0, 146.8, 145.8, 143.9, 138.4, 132.1, 128.6, 123.6, 118.2, 114.1, 111.9, 106.8, 101.4, 67.7, 61.0, 56.0, 46.3, 39.7 ppm. HRMS (ESI): calcd. for $C_{18}H_{18}O_5{}^{79}Br^+$ $[M+H]^+$: 393.0332, found: 393.0335.

Synthesis of Acetal 9

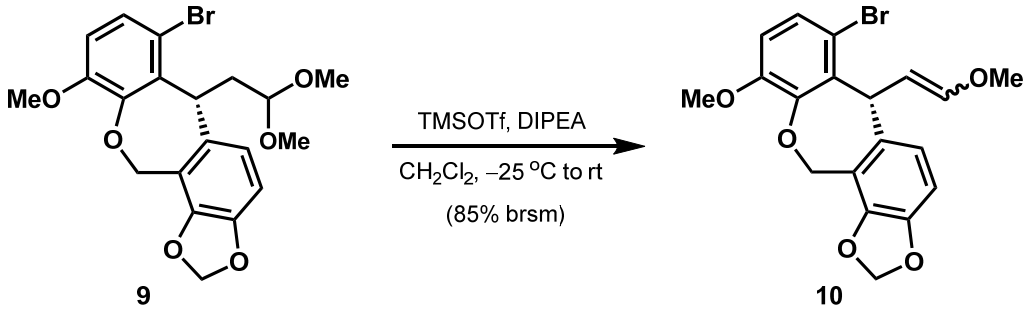


In a 100 mL round-bottom flask, alcohol **S2** (2.44 g, 6.21 mmol) was dissolved in anhydrous CH_2Cl_2 (40 mL) followed by the addition of PCC (99%, 2.029 g, 9.32 mmol, 1.5 equiv) portionwise at 0 °C. The resulting mixture was allowed to slowly warmed to room temperature, and stirred further for 5 h. The reaction mixture was then filtered by a short plug of silica gel, and the filtrate was concentrated under reduced pressure to give the aldehyde, which could be used directly for the next reaction without further purification.

The above aldehyde (6.21 mmol) was dissolved in anhydrous MeOH (20 mL)

followed by the addition of trimethyl orthoformate (3 mL) dropwise and (±)-camphorsulfonic acid (99%, 145 mg, 0.62 mmol, 0.1 equiv). The reaction mixture was stirred for 35 min at 45 °C, and cooled to room temperature, then concentrated under reduced pressure. The resulting crude product was purified by flash column chromatography (petroleum ether/EtOAc = 4 : 1) on silica gel to afford acetal **9** (2.524 g, 93% overall yield) as a white solid. R_f = 0.55 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = –64.00 (c = 1.00, $CHCl_3$); Mp. 46–47 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, J = 8.7 Hz, 1H), 6.81 (d, J = 8.1 Hz, 1H), 6.70 (d, J = 8.7 Hz, 1H), 6.64 (d, J = 8.1 Hz, 1H), 5.92 (s, 1H), 5.86 (s, 1H), 5.44 (d, J = 16.2 Hz, 1H), 4.90 (d, J = 15.9 Hz, 1H), 4.51 (t, J = 7.5 Hz, 1H), 4.18 (t, J = 6.0 Hz, 1H), 3.86 (s, 3H), 3.29 (s, 3H), 3.26 (s, 3H), 2.59 (ddd, J = 13.8, 8.1, 6.0 Hz, 1H), 2.39 (ddd, J = 13.8, 6.9, 6.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.0, 146.6, 145.9, 143.8, 138.7, 131.9, 128.7, 123.5, 118.1, 113.9, 111.9, 106.7, 102.5, 101.4, 67.6, 56.0, 53.1, 51.5, 45.6, 38.8 ppm; HRMS (ESI): calcd. for $C_{20}H_{21}O_6{}^{79}BrNa^+$ $[M+Na]^+$: 459.0414, found: 459.0427.

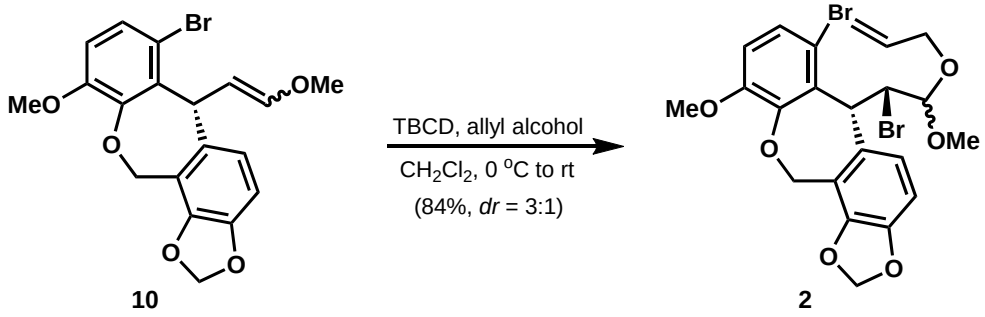
Synthesis of Enol Ether 10



The acetal **9** (1.0 g, 2.29 mmol) and *N*-ethyl diisopropylamine (1.20 mL, 6.87 mmol, 3.0 equiv) were dissolved in CH_2Cl_2 (45 mL). After the resulting solution was cooled to –25 °C, TMSOTf (0.84 mL, 4.58 mmol, 2.0 equiv) was then added dropwise through a syringe with stirring. The pale yellow mixture was stirred for 25 min at this temperature. The reaction was quenched by the addition of a saturated aqueous $NaHCO_3$ solution (10 mL). The resultant mixture was extracted with CH_2Cl_2

(3 × 50 mL), and the combined organic layers were washed with water (2 × 20 mL) and brine (20 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude product was purified by flash column chromatography (petroleum ether/EtOAc = 20 : 1 → petroleum ether/EtOAc = 10 : 1) on silica gel to afford **10** (610 mg, 66% yield, *Z*:*E* = 1:1.4) as a colorless oil and recover the aldehyde (230 mg, 25% yield). R_f = 0.65 (petroleum ether/EtOAc = 4 : 1); $[\alpha]_D^{20}$ = −154.00 (*c* = 1.00, $CHCl_3$); (*major isomer*) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 9.0 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.65 (d, *J* = 7.5 Hz, 1H), 6.52 (d, *J* = 12.6 Hz, 1H), 5.88 (d, *J* = 0.9 Hz, 1H), 5.86 (s, 1H), 5.57 (dd, *J* = 9.0, 6.9 Hz, 1H), 5.45 (d, *J* = 12.9 Hz, 1H), 4.95 (d, *J* = 9.3 Hz, 1H), 4.90 (d, *J* = 9.9 Hz, 1H), 3.85 (s, 3H), 3.46 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.8, 147.6, 146.5, 145.7, 144.0, 137.9, 132.8, 128.4, 123.1, 117.8, 113.4, 111.7, 108.2, 107.2, 101.4, 67.3, 59.7, 56.0, 49.0 ppm; HRMS (ESI): calcd. for $C_{19}H_{17}O_5{}^{79}BrNa^+$ $[M+Na]^+$: 427.0152, found: 427.0160.

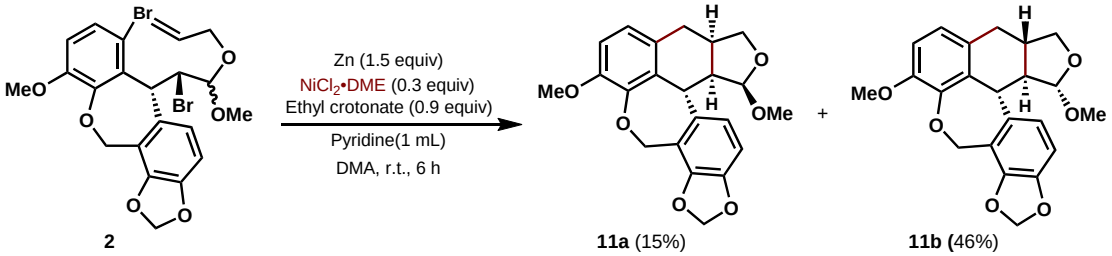
Preparation of Cyclization Precursor 2



In a 100 mL round-bottom flask, enol ether **10** (500 mg, 1.24 mmol) was dissolved in anhydrous CH_2Cl_2 (30 mL) and cooled to 0 °C. To this solution was added TBCD (97%, 625 mg, 1.49 mmol, 1.2 equiv) portionwise, and the mixture was stirred for 40 min at 0 °C. A solution of allyl alcohol (98.5%，1.7 mL, 24.8mmol, 20 equiv) in CH_2Cl_2 (2 mL) was then added dropwise, and the resulting mixture was gradually warmed to room temperature and stirred for 9 h further. The reaction was quenched with saturate aqueous $NaHCO_3$ (5 mL), Na_2SO_3 (5 mL) and stirred further for 30 min.

The resulting mixture was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were washed with water (2 × 10 mL) and brine (10 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 = 20 : 1) on silica gel to afford **2** (560 mg, 84% yield) as a colorless oil. R_f = 0.5 (petroleum ether/EtOAc = 4 : 1); $[\alpha]_D^{22}$ = –95.00 (*c* = 1.00, $CHCl_3$); (*major isomer*) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 9.0 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 8.7 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 6.04–5.90 (m, 1H), 5.97 (d, *J* = 1.2 Hz, 1H), 5.88 (d, *J* = 0.9 Hz, 1H), 5.46 (dd, *J* = 11.1, 2.1 Hz, 1H), 5.41 (d, *J* = 16.5 Hz, 1H), 5.21 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.96 (dd, *J* = 14.7, 3.6 Hz, 2H), 4.91 (d, *J* = 16.2 Hz, 1H), 4.32 (dt, *J* = 4.8, 1.2 Hz, 1H), 4.06 (d, *J* = 2.1 Hz, 2H), 3.87 (s, 3H), 3.33 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 146.7, 145.5, 144.0, 138.2, 134.0, 128.9, 128.2, 124.9, 118.0, 116.8, 114.9, 112.3, 106.6, 102.1, 101.6, 68.9, 67.6, 56.0, 55.7, 55.3, 52.6 ppm; HRMS (ESI): calcd. for $C_{22}H_{22}O_6{}^{79}Br_2Na^+$ $[M+Na]^+$: 562.9675, found: 562.9684.

Diastereodivergent Syntheses of Pentacyclic Skeleton 11a and 11b



2 **11a** (15%) **11b** (46%)

To a 25 mL round-bottom flask were added $NiCl_2$•DME (28 mg, 0.13 mmol, 0.3 equiv) and Zn (41 mg, 1.27 mmol, 1.5 equiv). The flask was evacuated and then backfilled argon. This process was repeated 4 times. The pyridine (1 mL) and ethyl crotonate (47 μL, 0.38 mmol, 0.9 equiv) were then added successively at room temperature. The temperature then rose to 57 °C, and stirring (300 r/min) was continued for 15 min. The resulting red-brown Ni(0) complex was cooled to room temperature, and a solution of *β*-bromo acetal **2** (230 mg, 0.42 mmol) in DMA (8 mL)

was added dropwise. After stirring for 6 h, the mixture was diluted and extracted with EtOAc (2 × 50 mL), and the combined organic layers were washed with water (2 × 15 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 = 15 : 1 → petroleum ether/EtOAc = 10 : 1) on silica gel to afford **11a** (25 mg, 15% yield) as a white solid and **11b** (77 mg, 46% yield) as a white solid.

Data for **11a**: R_f = 0.65 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = +58.23 (*c* = 1.00, $CHCl_3$); Mp. 70–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 5.97 (d, *J* = 1.2 Hz, 1H), 5.95 (d, *J* = 1.2 Hz, 1H), 5.45 (d, *J* = 12.8 Hz, 1H), 4.93 (d, *J* = 13.2 Hz, 1H), 4.62 (d, *J* = 4.4 Hz, 1H), 4.46 (d, *J* = 10.8 Hz, 1H), 4.18 (t, *J* = 8.4 Hz, 1H), 3.83 (s, 3H), 3.76 (dd, *J* = 8.4, 6.4 Hz, 1H), 3.40 (s, 3H), 2.81 (dd, *J* = 13.6, 12.4 Hz, 1H), 2.67–2.61 (m, 2H), 2.39–2.28 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.3, 149.1, 145.9, 145.2, 134.0, 133.8, 128.4, 122.9, 119.9, 118.9, 108.2, 107.6, 104.4, 101.2, 71.0, 67.3, 56.1, 54.0, 53.1, 41.2, 39.4, 34.1 ppm; HRMS (ESI): calcd for $C_{22}H_{22}O_6Na^+$ $[M+Na]^+$: 405.1309, found: 405.1307.

Data for **11b**: R_f = 0.60 (petroleum ether/EtOAc = 1 : 1); $[\alpha]_D^{22}$ = –56.77 (*c* = 1.00, $CHCl_3$); Mp. 62–63 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.67–6.64 (m, 2H), 5.97 (d, *J* = 1.2 Hz, 1H), 5.95 (d, *J* = 1.5 Hz, 1H), 5.64 (d, *J* = 13.5 Hz, 1H), 5.31 (d, *J* = 13.5 Hz, 1H), 5.00 (d, *J* = 11.4 Hz, 1H), 4.77 (d, *J* = 5.1 Hz, 1H), 4.08 (dd, *J* = 8.1, 6.3 Hz, 1H), 3.79 (s, 3H), 3.77 (dd, *J* = 10.8, 8.1 Hz, 1H), 3.38 (s, 3H), 2.84–2.72 (m, 2H), 2.54 (td, *J* = 11.7, 5.1 Hz, 1H), 2.27–2.12 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.8, 146.4, 146.1, 144.8, 133.9, 129.3, 127.7, 122.2, 119.9, 117.7, 110.2, 109.6, 107.1, 101.3, 70.3, 62.7, 56.2, 56.0, 52.0, 43.3, 41.7, 32.8 ppm; HRMS (ESI): calcd. for $C_{22}H_{22}O_6Na^+$ $[M+Na]^+$: 405.1309, found: 405.1301. This product (5 mg) was dissolved in EtOAc (1 mL) and hexane (3 mL). After 4 days, colorless single crystals were obtained by slow evaporation of solvents at room temperature.

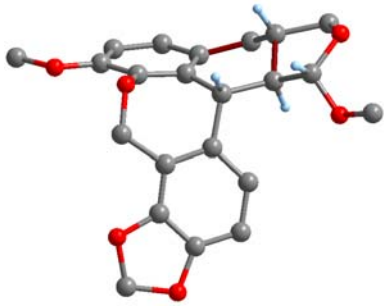
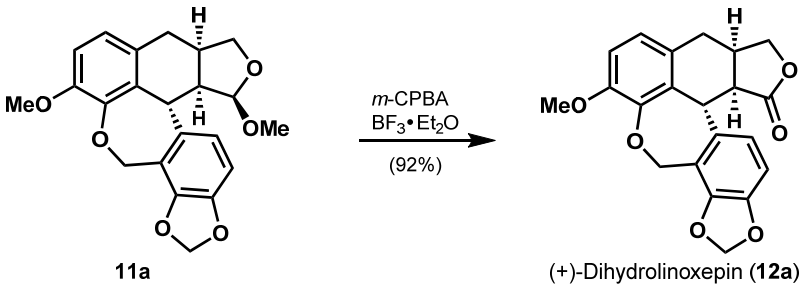


Table S2: X-ray crystal data of **11b** (selected H atoms have been omitted for clarity)

Empirical formula	$C_{22}H_{22}O_6$
Temperature (K)	149.99(10)
Crystal color	colorless
Formula weight	382.39
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a (Å)	8.41567(15)
b (Å)	11.8302(3)
c (Å)	18.4063(3)
α (°)	90.00
β (°)	90.00
γ (°)	90.00
V (Å ^{3})	1832.52(6)
Z	4
Density (calculated) (g/cm^3)	1.386
F (000)	808.0
λ (Å)	1.54184
Reflections collected	7110
Independent reflections	3323
2θ Range for data collection (°)	8.84—154.05
Index range	$-10 \leq h \leq 10$ $-14 \leq k \leq 14$ $-14 \leq l \leq 22$
Final *R* indices [I>2σ(*I*)]	$R_1 = 0.0339$, $wR_2 = 0.0850$
Largest difference peak and hole [e Å $^{-3}$]	0.223, –0.170

Synthesis of (+)-Dihydrolinoxepin (12a)



To a stirred solution of acetal **11a** (20 mg, 0.052 mmol) in CH_2Cl_2 (3 mL) was added *m*-CPBA (75%, 23 mg, 0.1 mmol, 2.0 equiv) at 0 °C, followed by the addition of BF_3•Et_2O (78 μL, 0.078 mmol, 1.5 equiv, 1.0 M in CH_2Cl_2) dropwise. After 15 minutes, the reaction mixture was quenched by saturated aqueous Na_2SO_3 (1 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (3 × 5 mL), water (5 mL) and brine (5 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 = 5 : 1) on silica gel to afford **12a** (17.5 mg, 92% yield) as a white solid. R_f = 0.45 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{21}$ = +30.00 (*c* = 0.1, $CHCl_3$); Mp. 229–231 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.72 (s, 2H), 6.63 (s, 2H), 5.96 (d, *J* = 1.2 Hz, 1H), 5.88 (d, *J* = 0.9 Hz, 1H), 5.61 (d, *J* = 15.0 Hz, 1H), 5.38 (s, 1H), 5.17 (d, *J* = 15.0 Hz, 1H), 4.54 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.15 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.83 (s, 3H), 3.44 (dd, *J* = 8.1, 1.5 Hz, 1H), 3.26–3.15 (m, 1H), 2.96 (dd, *J* = 16.8, 7.8 Hz, 1H), 2.64 (dd, *J* = 16.8, 7.5 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 150.1, 146.4, 145.1, 143.9, 134.0, 131.8, 124.2, 123.3, 117.1, 116.0, 111.3, 106.3, 101.5, 73.1, 67.0, 56.1, 41.0, 34.6, 31.9, 29.1 ppm; HRMS (ESI): calcd. for $C_{21}H_{18}O_6Na^+$ $[M+Na]^+$: 389.0996, found: 389.1008. This product (2 mg) was dissolved in $CDCl_3$ (0.6 mL). After 6 days, colorless single crystals were obtained by slow evaporation of solvents at room temperature.

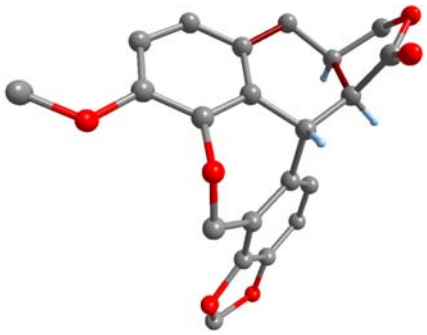
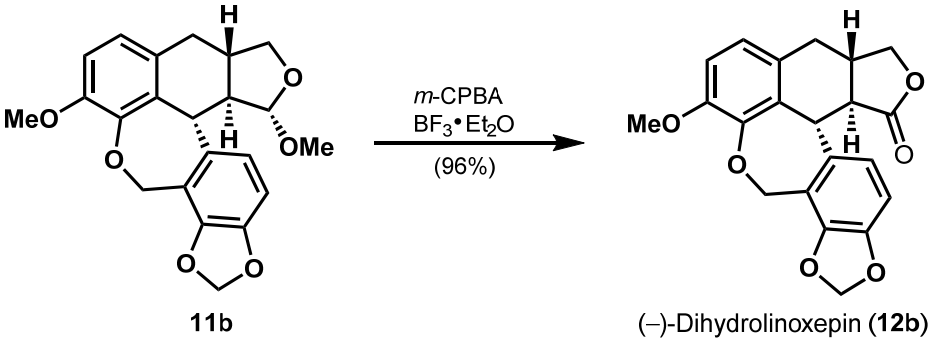


Table S3: X-ray crystal data of **12a** (selected H atoms have been omitted for clarity)

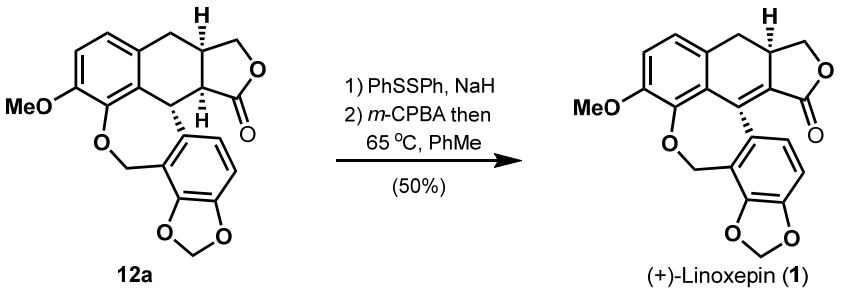
Empirical formula	$C_{21}H_{18}O_6$
Temperature (K)	293.00(2)
Crystal color	colorless
Formula weight	366.35
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a (Å)	7.60702(16)
b (Å)	8.8987(2)
c (Å)	25.6270(6)
α (°)	90.00
β (°)	90.00
γ (°)	90.00
V (Å ^{3})	1734.75(7)
Z	4
Density (calculated) (g/cm^3)	1.403
F (000)	768.0
λ (Å)	1.54184
Reflections collected	5783
Independent reflections	2905
2θ Range for data collection (°)	10.52—133.18
Index range	$-8 \leq h \leq 9$ $-10 \leq k \leq 10$ $-21 \leq l \leq 30$
Final *R* indices [I>2σ(*I*)]	$R_1 = 0.0311$, $wR_2 = 0.0812$
Largest difference peak and hole [e Å $^{-3}$]	0.182, –0.151

Synthesis of (–)-Dihydrolinoxepin (12b)



To a stirred solution of acetal **11b** (25 mg, 0.065 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (75%, 30 mg, 0.13 mmol, 2.0 equiv) at 0 °C, followed by the addition of BF_3•Et_2O (98 μL, 0.098 mmol, 1.5 equiv, 1.0 M in CH_2Cl_2) dropwise. After 15 minutes, the reaction mixture was quenched by saturated aqueous Na_2SO_3 (1 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (3 × 5 mL), water (5 mL) and brine (5 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 = 5 : 1) on silica gel to afford **12b** (23 mg, 96% yield) as a white solid. R_f = 0.45 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{21}$ = –127.00 (*c* = 1.00, $CHCl_3$); Mp. 201–203 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.77 (d, *J* = 8.4 Hz, 1H), 6.74 (s, 2H), 6.71 (d, *J* = 8.4 Hz, 1H), 5.96 (d, *J* = 1.2 Hz, 1H), 5.94 (d, *J* = 1.2 Hz, 1H), 5.60 (d, *J* = 14.0 Hz, 1H), 5.25 (d, *J* = 14.4 Hz, 1H), 5.15 (d, *J* = 11.2 Hz, 1H), 4.58 (dd, *J* = 8.8, 6.8 Hz, 1H), 4.13 (dd, *J* = 10.4, 8.8 Hz, 1H), 3.82 (s, 3H), 3.03 (dd, *J* = 13.6, 11.6 Hz, 1H), 2.92 (dd, *J* = 14.8, 4.0 Hz, 1H), 2.83 (dd, *J* = 14.4, 11.6 Hz, 1H), 2.65–2.53 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9, 149.8, 146.5, 146.0, 144.9, 132.0, 129.3, 127.2, 123.3, 118.3, 118.1, 110.6, 107.0, 101.5, 71.2, 64.3, 56.0, 45.4, 40.0, 37.3, 33.8 ppm; HRMS (ESI): calcd. for $C_{21}H_{18}O_6Na^+$ $[M+Na]^+$: 389.0996, found: 389.1006.

Synthesis of (+)-Linoxepin (1)



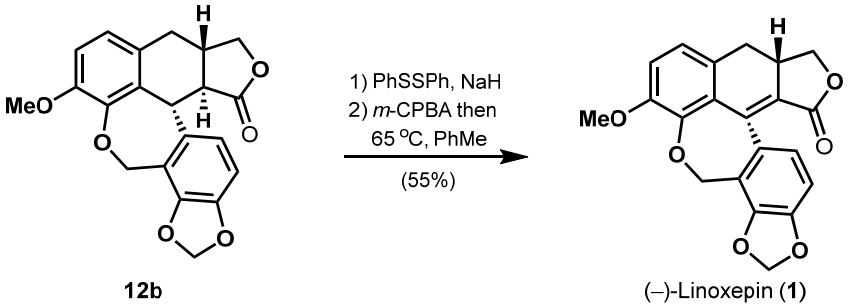
To a 25 mL round-bottom flask containing NaH (60%, 1.6 mg, 0.041 mmol, 1.5 equiv) was added DMF (1 mL), and the mixture was cooled to 0 °C followed by the addition a solution of **12a** (10 mg, 0.027 mmol) in DMF (1 mL). 10 minutes later, a solution of PhSSPh (12 mg, 0.54 mmol, 2.0 equiv) in DMF (1 mL) 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 × 10 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 α-phenyl sulfide could be used directly for the next reaction without further purification.

To a stirred solution of the above α-phenyl sulfide in CH_2Cl_2 (2 mL) was added $NaHCO_3$ (4.6 mg, 0.054 mmol, 2.0 equiv) at 0 °C, followed by the addition of *m*-CPBA (85%, 6.0 mg, 0.03 mmol, 1.1 equiv) in CH_2Cl_2 (1 mL). After stirring for 10 minutes, the reaction mixture was quenched by saturated aqueous $NaHCO_3$ (1 mL) and extracted with CH_2Cl_2 (3 × 20 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 (25 mg) at room temperature under argon, followed by the addition of a solution of the above sulfoxide in anhydrous toluene (2 mL). After stirring for 1 h at 65 ºC, the

mixture was cooled to room temperature, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (petroleum ether/EtOAc = 5 : 1 → petroleum ether/EtOAc = 2 : 1) on silica gel to afford (+)-Linoxepin (**1**) as a yellow solid (5.0 mg, 50% yield). R_f = 0.3 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = +18.00 (*c* = 0.05, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 6.88–6.79 (m, 3H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.03 (s, 2H), 5.40 (d, *J* = 12.6 Hz, 1H), 5.14(d, *J* = 12.6 Hz, 1H), 4.69 (t, *J* = 8.8 Hz, 1H), 4.04 (t, *J* = 8.7 Hz, 1H), 3.85 (s, 3H), 3.35–3.22(m, 1H), 3.00 (dd, *J* = 14.7, 5.7 Hz, 1H), 2.66 (t, *J* = 14.7 Hz, 1H) ppm. HRMS (ESI): calcd. for $C_{21}H_{17}O_6^+$ $[M+H]^+$: 365.1020, found: 365.1019.

Synthesis of (–)-Linoxepin (1)



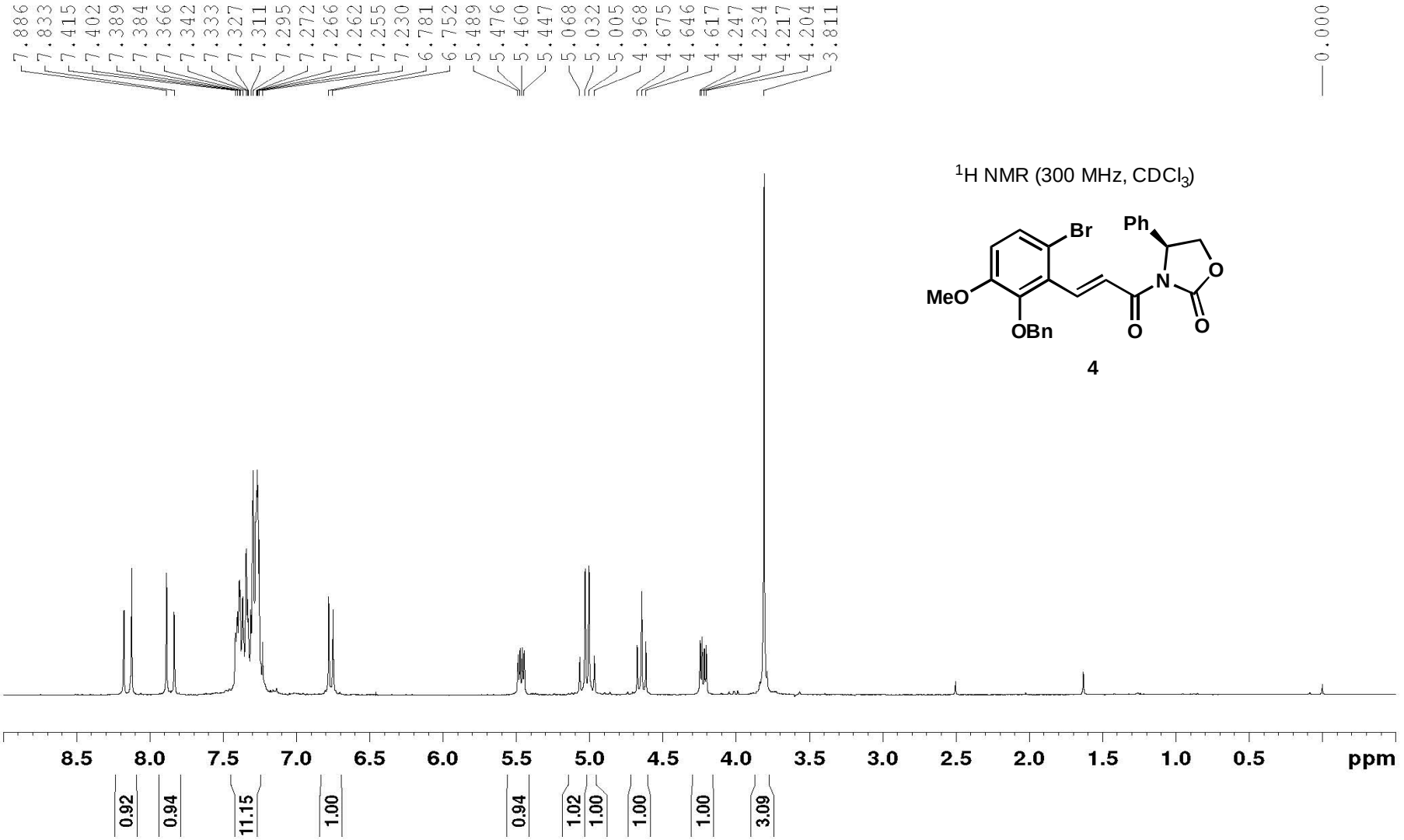
12b (–)-Linoxepin (**1**)

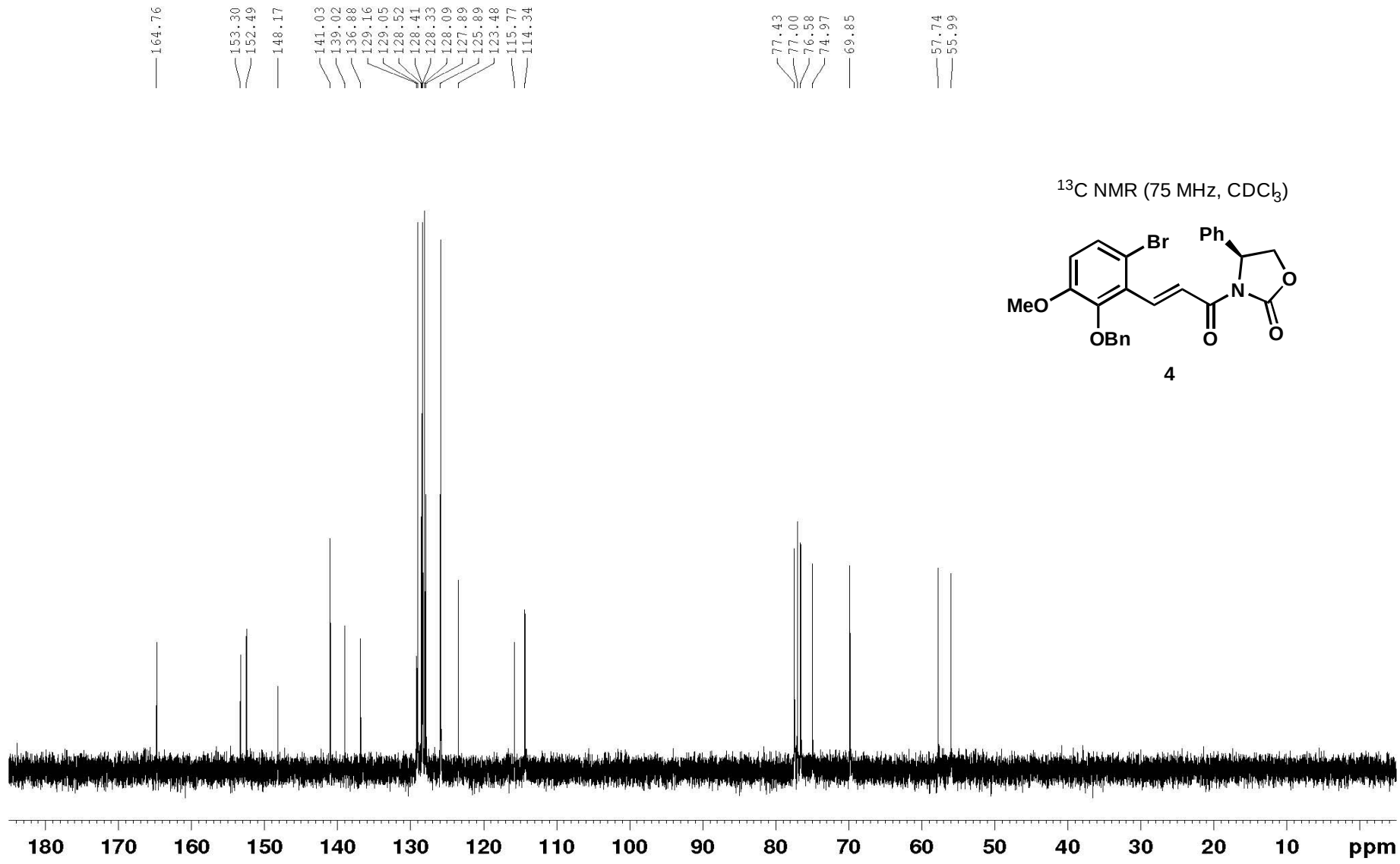
To a 25 mL round-bottom flask containing NaH (60%, 3.3 mg, 0.083 mmol, 1.5 equiv) was added DMF (1 mL), and the mixture was cooled to 0 °C followed by the addition a solution of **12b** (20 mg, 0.055 mmol) in DMF (2 mL). 10 minutes later, a solution of PhSSPh (24 mg, 0.11 mmol, 2.0 equiv) in DMF (1 mL) 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 × 10 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 α-phenyl sulfide could be used directly for the next reaction without further purification.

To a stirred solution of above α-phenyl sulfide in CH_2Cl_2 (3 mL) was added

$NaHCO_3$ (9.2 mg, 0.11 mmol, 2.0 equiv) at 0 °C, followed by the addition of *m*-CPBA (85%, 12.4 mg, 0.061 mmol, 1.1 equiv) in CH_2Cl_2 (2 mL). After stirring for 10 minutes, the reaction mixture was quenched by saturated aqueous $NaHCO_3$ (1 mL) and extracted with CH_2Cl_2 (3 × 20 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.

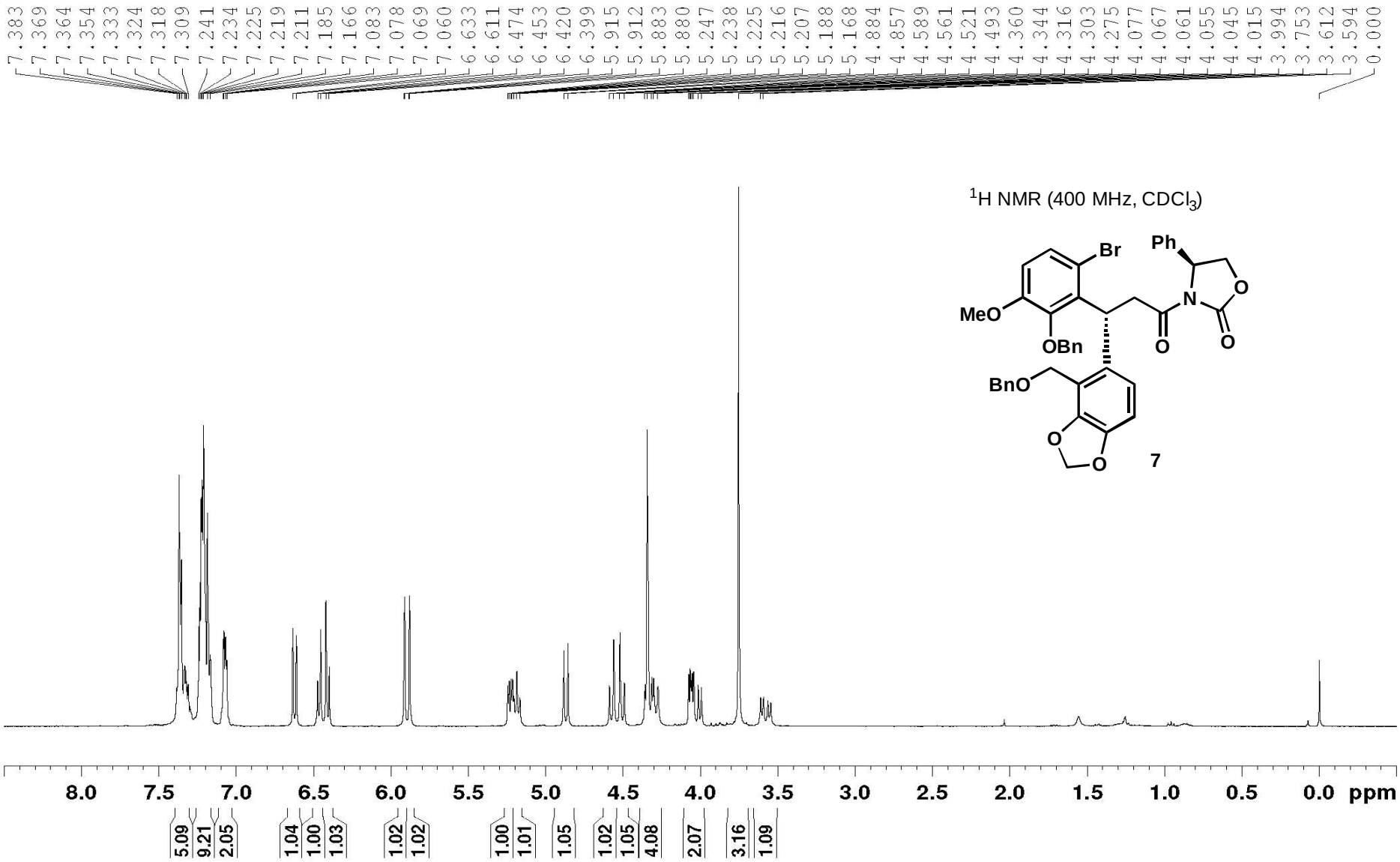
An oven-dried 10 mL round-bottom flask was charged with 4Å molecular sieve (35 mg) at room temperature under argon, followed by the addition of a solution of the above sulfoxide in anhydrous toluene (4 mL). After stirring for 1 h at 65 ºC, the mixture was cooled to room temperature, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 5 : 1 → petroleum ether/EtOAc = 2 : 1) on silica gel to afford (–)-Linoxepin (**1**) as a yellow solid (11.0 mg, 55% yield). R_f = 0.3 (petroleum ether/EtOAc = 2 : 1); $[\alpha]_D^{22}$ = –16.00 (*c* = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88–6.79 (m, 3H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.03 (s, 2H), 5.40 (d, *J* = 12.4 Hz, 1H), 5.14 (d, *J* = 12.6 Hz, 1H), 4.69 (t, *J* = 8.8 Hz, 1H), 4.04 (t, *J* = 8.8 Hz, 1H), 3.85 (s, 3H), 3.34–3.24 (m, 1H), 3.00 (dd, *J* = 14.4, 5.6 Hz, 1H), 2.66 (t, *J* = 14.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 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): calcd. for $C_{21}H_{17}O_6^+$ $[M+H]^+$: 365.1020, found: 365.1020.

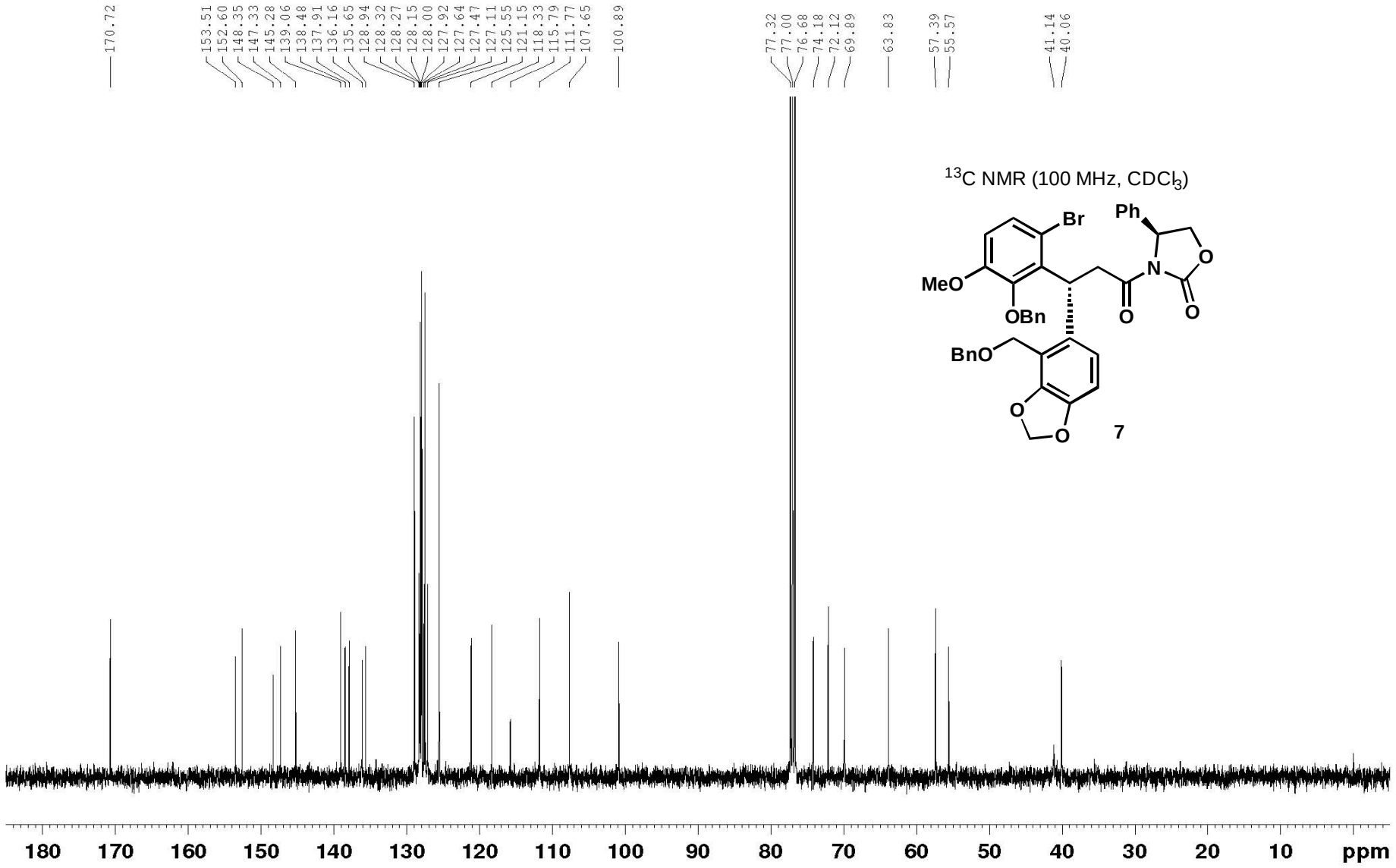

7.886
7.833
7.415
7.402
7.389
7.384
7.366
7.342
7.333
7.327
7.311
7.295
7.272
7.266
7.262
7.255
7.230
6.781
6.752
5.489
5.476
5.460
5.447
5.068
5.032
5.005
4.968
4.675
4.646
4.617
4.247
4.234
4.217
4.204
3.811
0.000
^{1}H NMR (300 MHz, $CDCl_3$)
Br
Ph
MeO
OBn
N
O
O
O
4
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.92
0.94
11.15
1.00
0.94
1.02
1.00
1.00
1.00
3.09



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

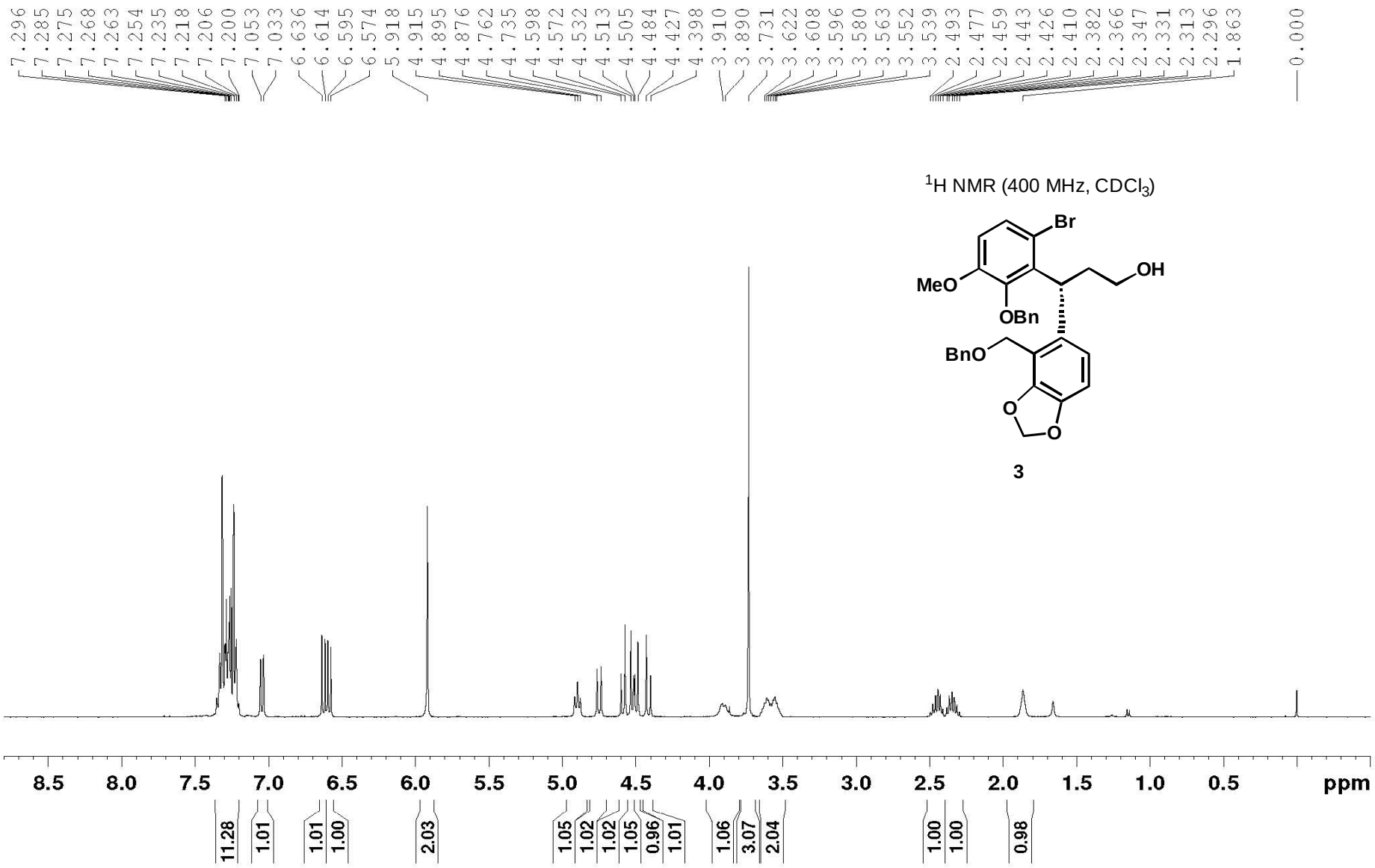
4

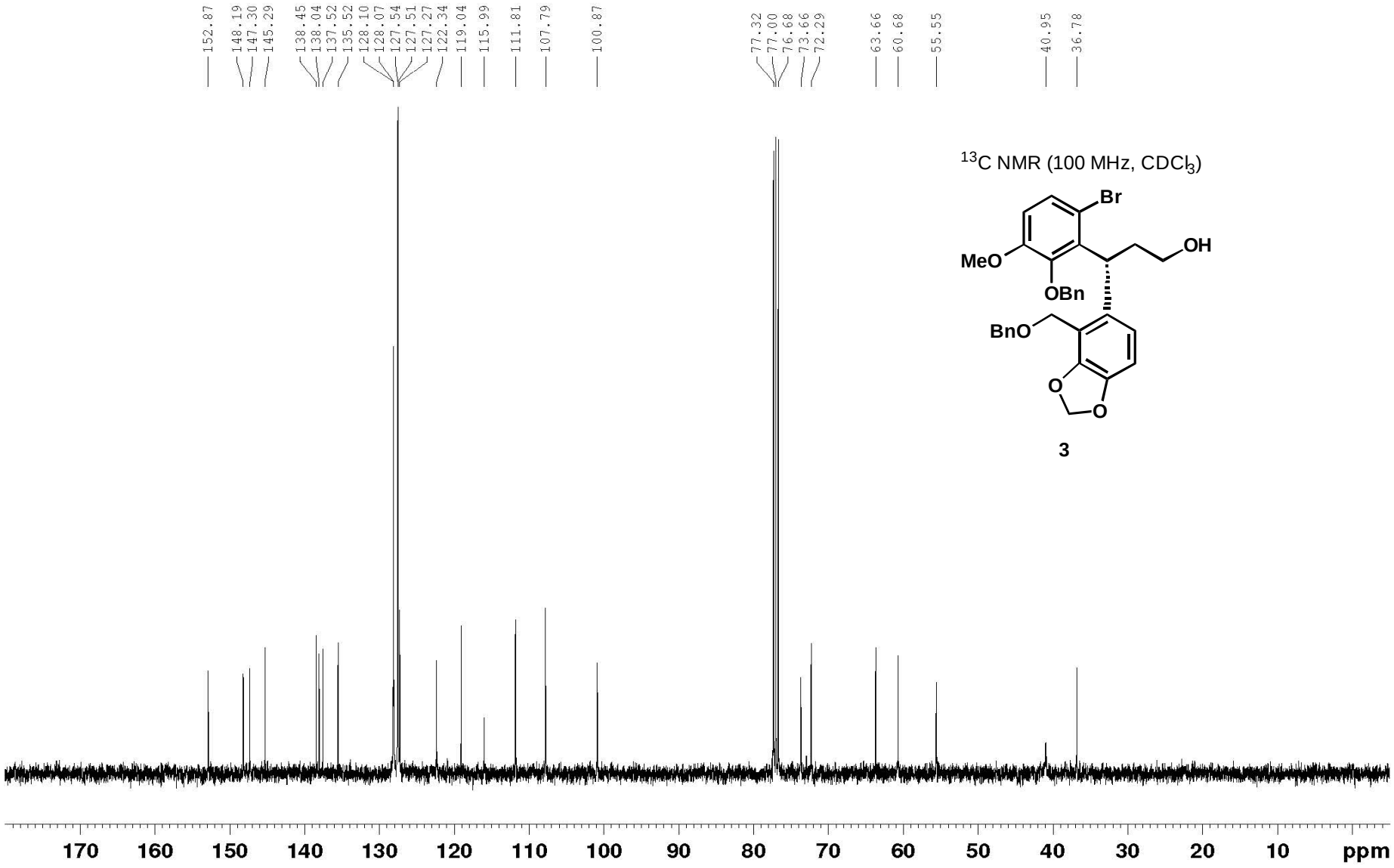

7.383
7.369
7.364
7.354
7.333
7.324
7.318
7.309
7.241
7.234
7.225
7.219
7.211
7.185
7.166
7.083
7.078
7.069
7.060
6.633
6.611
6.474
6.453
6.420
6.399
5.915
5.912
5.883
5.880
5.247
5.238
5.225
5.216
5.207
5.188
5.168
4.884
4.857
4.589
4.561
4.521
4.493
4.360
4.344
4.316
4.303
4.275
4.077
4.067
4.061
4.055
4.045
4.015
3.994
3.753
3.612
3.594
0.000
^{1}H NMR (400 MHz, CDCl$_3$)
Br
Ph
MeO
OBn
BnO
N
O
O
O
O
O
7
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
5.09
9.21
2.05
1.04
1.00
1.03
1.02
1.02
1.00
1.01
1.05
1.02
1.05
4.08
2.07
3.16
1.09



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

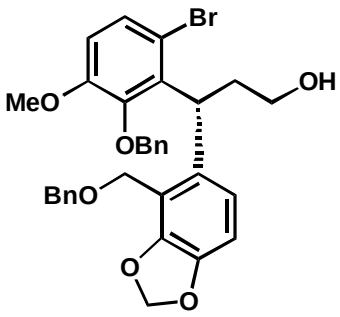
7


7.296
7.285
7.275
7.268
7.263
7.254
7.235
7.218
7.206
7.200
7.053
7.033
6.636
6.614
6.595
6.574
5.918
4.915
4.895
4.876
4.762
4.735
4.598
4.572
4.532
4.513
4.505
4.484
4.427
4.398
3.910
3.890
3.731
3.622
3.608
3.596
3.580
3.563
3.552
3.539
2.493
2.477
2.459
2.443
2.426
2.410
2.382
2.366
2.347
2.331
2.313
2.296
1.863
0.000
^{1}H NMR (400 MHz, CDCl$_3$)
Br
MeO
OH
OBn
BnO
O
O
3
8.5
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
ppm
11.28
1.01
1.01
1.00
2.03
1.05
1.02
1.02
1.05
0.96
1.01
1.06
3.07
2.04
1.00
1.00
0.98

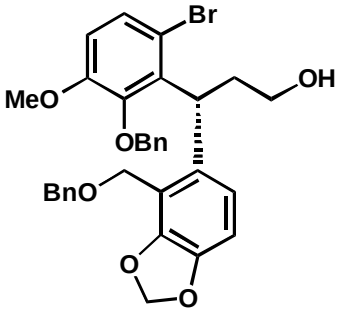


^{13}C NMR (100 MHz, $CDCl_3$)

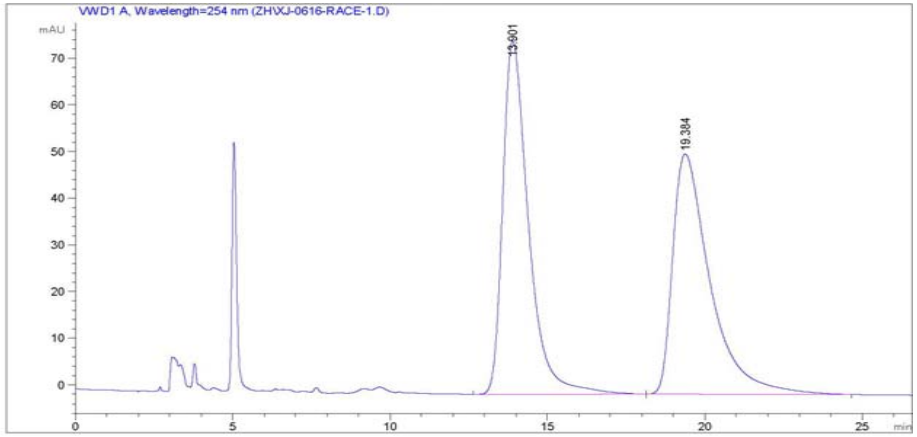
3



rac-**3**



(+)-**3**

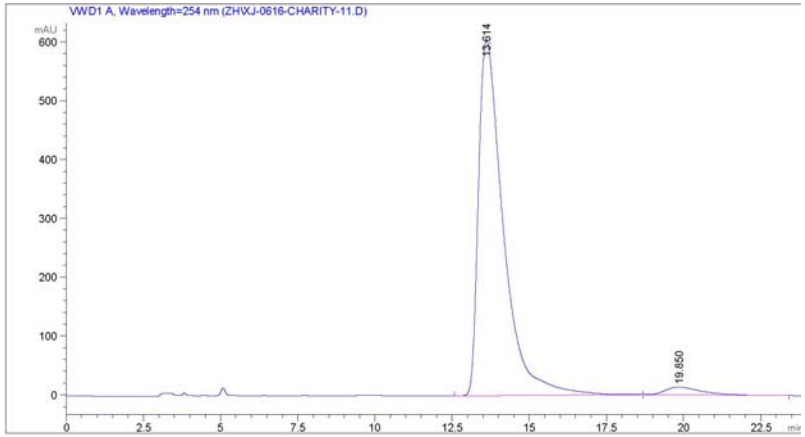


面积百分比报告

排序 : 信号
乘积因子: : 1.0000
稀释因子: : 1.0000
内标使用乘积因子和稀释因子

信号 1: VWD1 A, Wavelength=254 nm

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	13.901	BB	0.8588	4309.73975	75.74882	50.4230
2	19.384	BB	1.2163	4237.42529	51.48107	49.5770

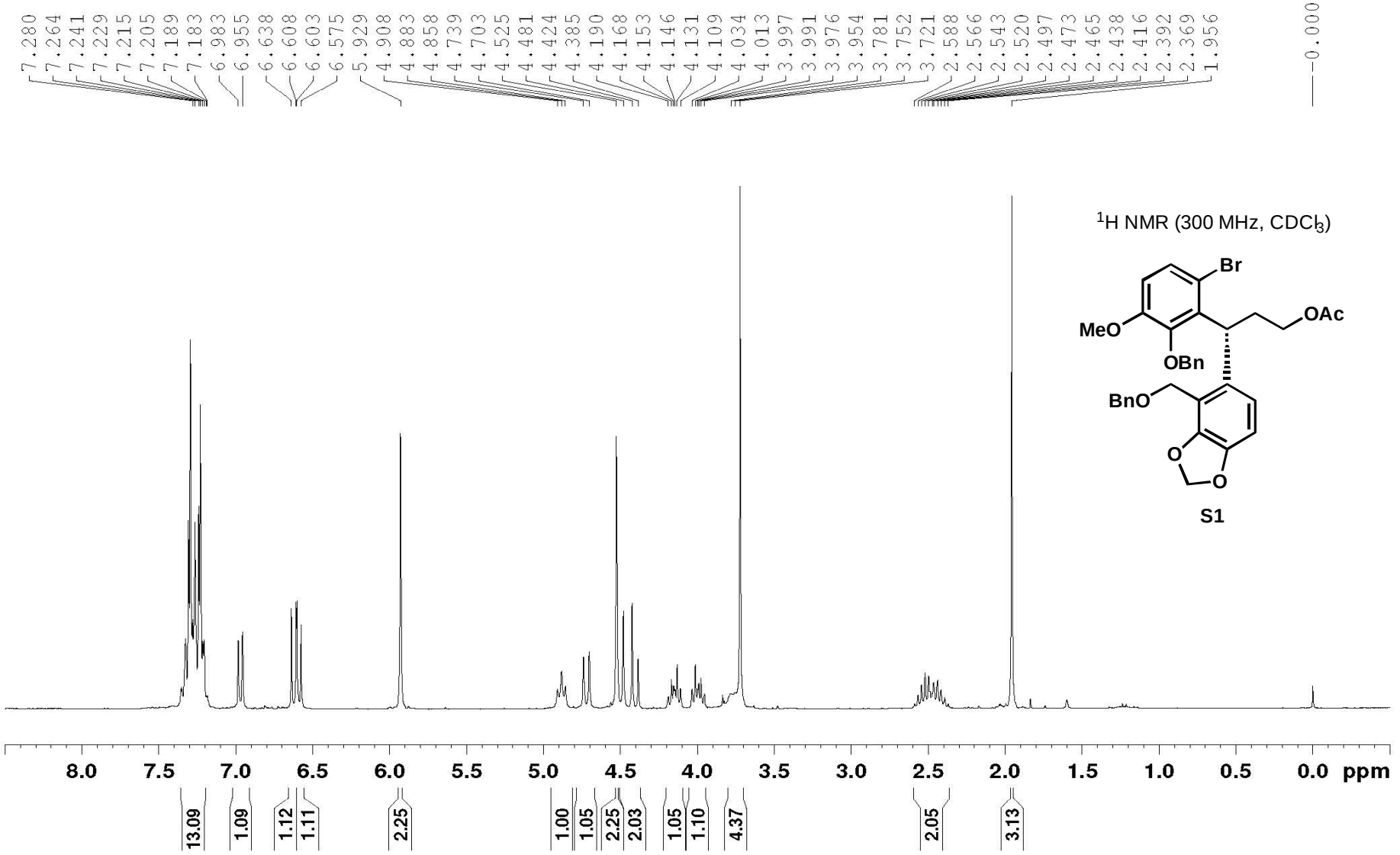


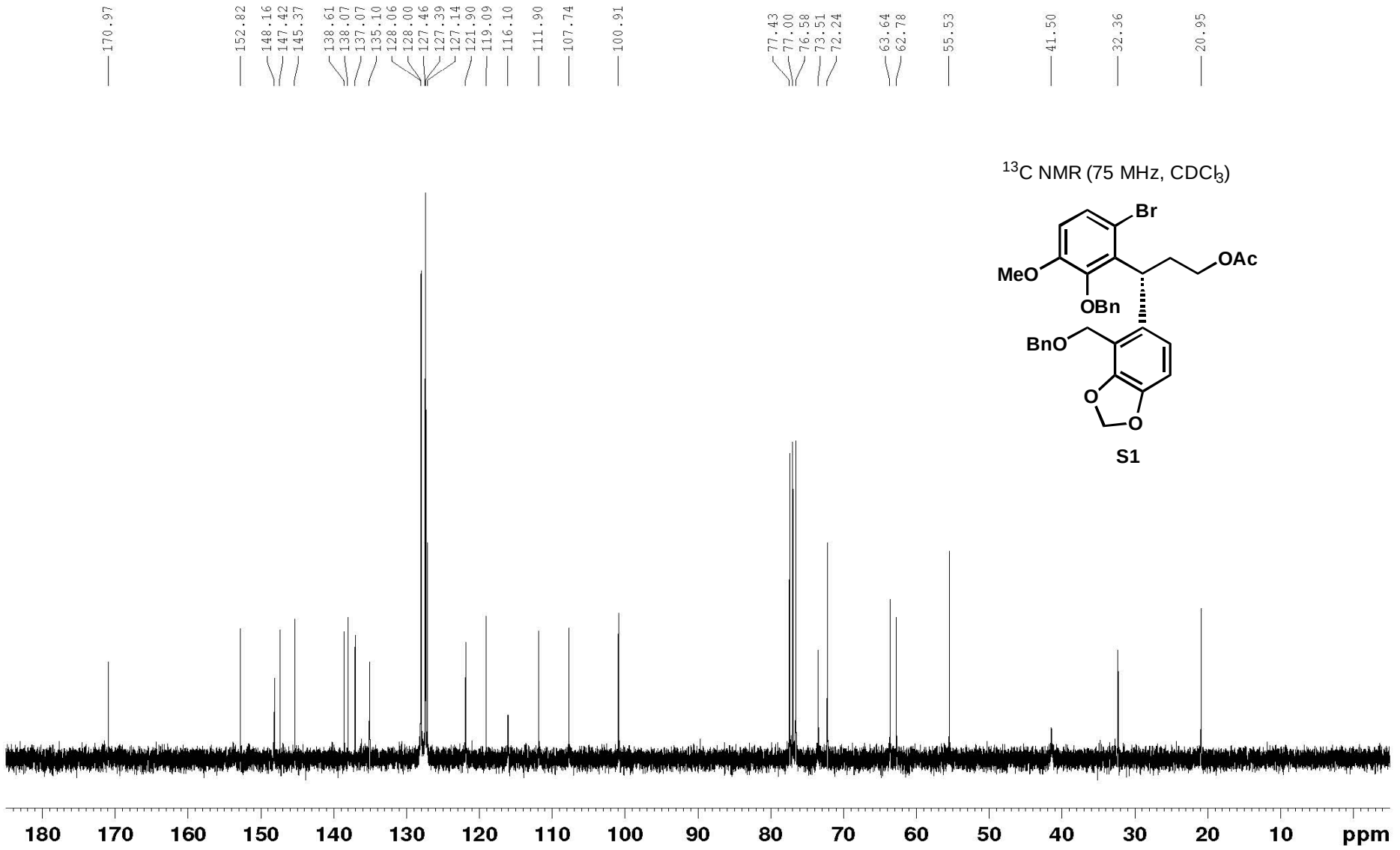
面积百分比报告

排序 : 信号
乘积因子: : 1.0000
稀释因子: : 1.0000
内标使用乘积因子和稀释因子

信号 1: VWD1 A, Wavelength=254 nm

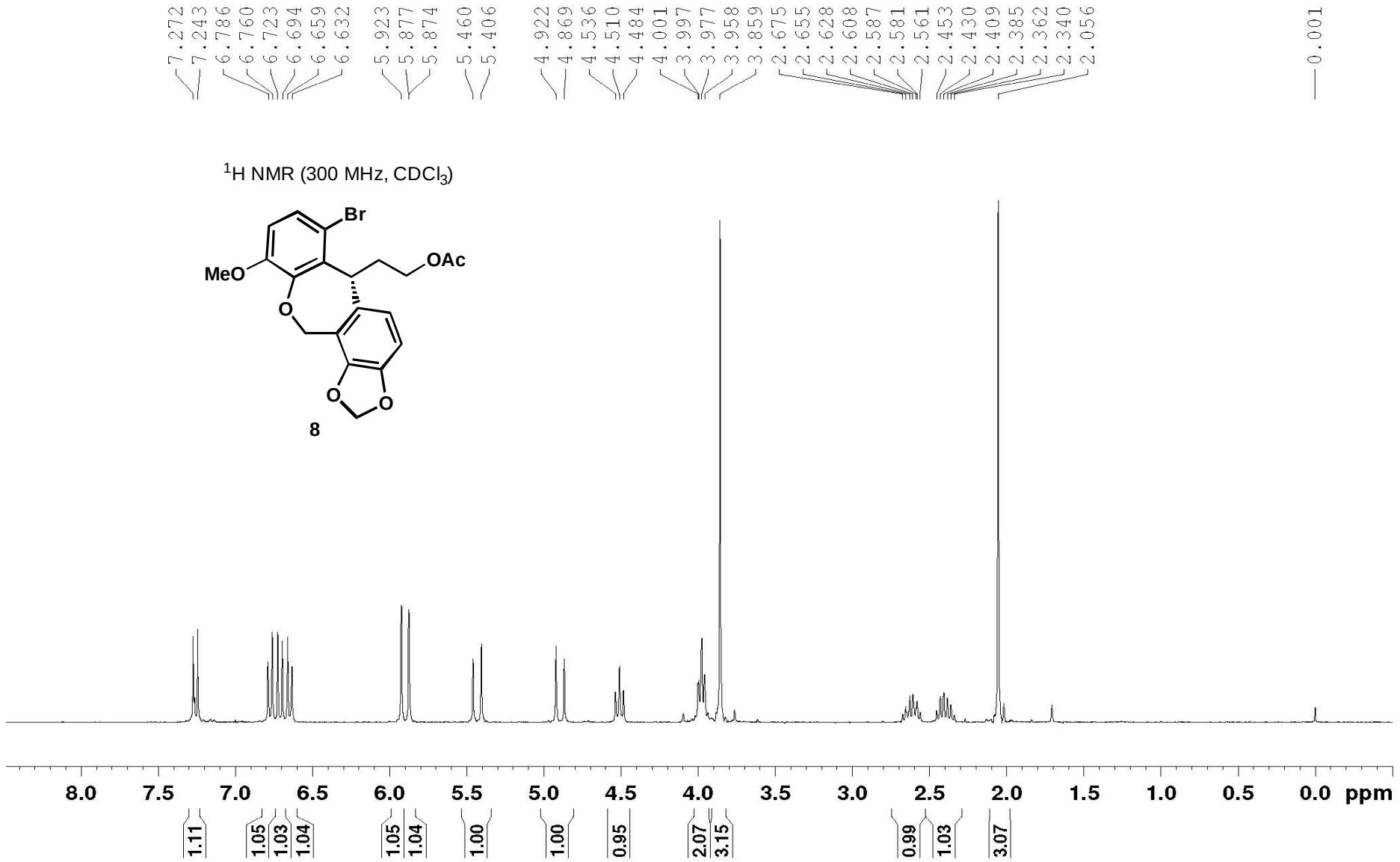
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	13.614	BB	0.8399	3.37929e4	602.90515	96.9351
2	19.850	BB	1.1850	1068.47925	13.06707	3.0649

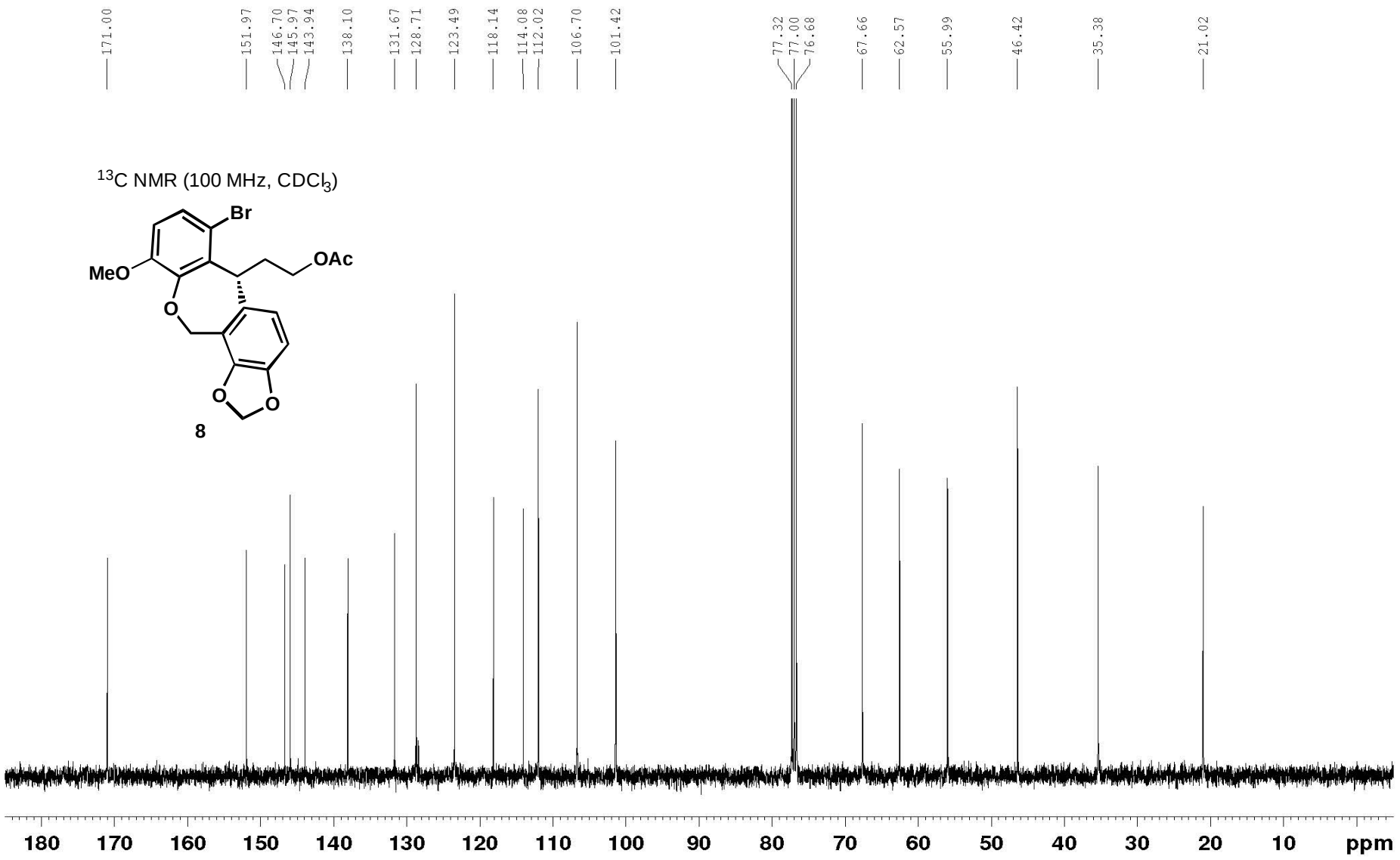

7.280
7.264
7.241
7.229
7.215
7.205
7.189
7.183
6.983
6.955
6.638
6.608
6.603
6.575
5.929
4.908
4.883
4.858
4.739
4.703
4.525
4.481
4.424
4.385
4.190
4.168
4.153
4.146
4.131
4.109
4.034
4.013
3.997
3.991
3.976
3.954
3.781
3.752
3.721
2.588
2.566
2.543
2.520
2.497
2.473
2.465
2.438
2.416
2.392
2.369
1.956
0.000
1H NMR (300 MHz, CDCl3)
Br
OAc
MeO
OBn
BnO
O
O
S1
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
13.09
1.09
1.12
1.11
2.25
1.00
1.05
2.25
2.03
1.05
1.10
4.37
2.05
3.13

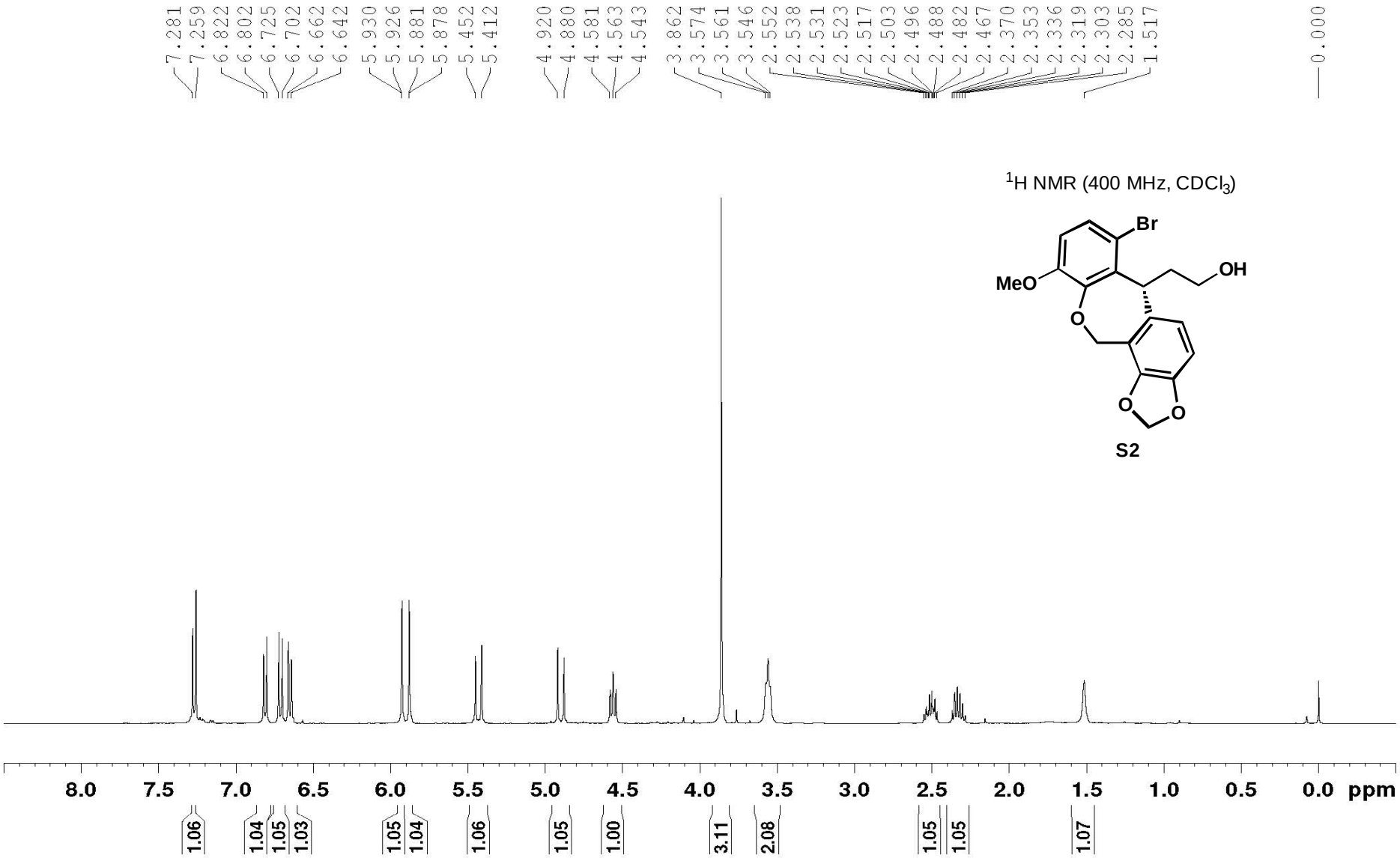


^{13}C NMR (75 MHz, $CDCl_3$)

S1

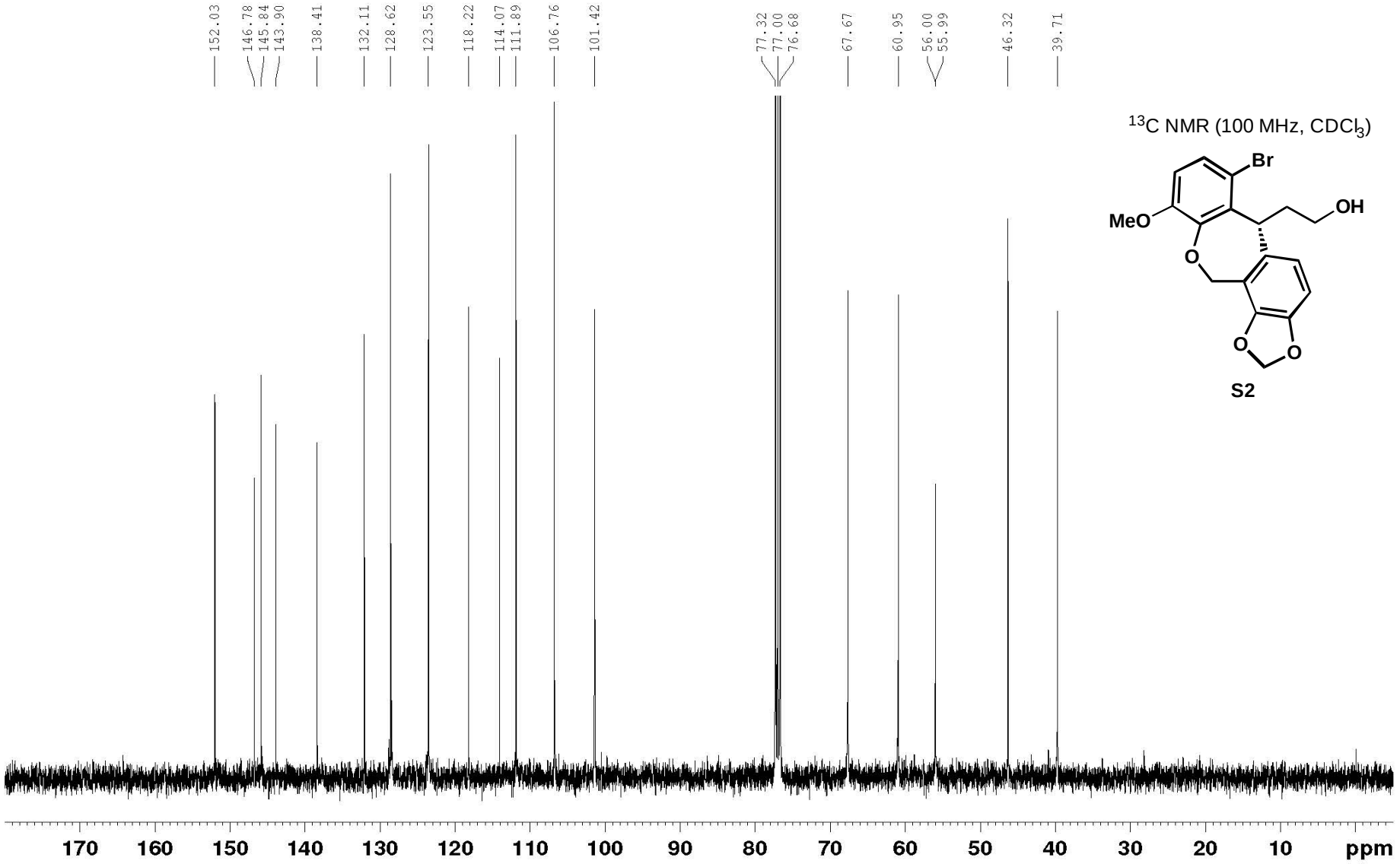

7.272
7.243
6.786
6.760
6.723
6.694
6.659
6.632
5.923
5.877
5.874
5.460
5.406
4.922
4.869
4.536
4.510
4.484
4.001
3.997
3.977
3.958
3.859
2.675
2.655
2.628
2.608
2.587
2.581
2.561
2.453
2.430
2.409
2.385
2.362
2.340
2.056
0.001
1H NMR (300 MHz, CDCl3)
Br
MeO
OAc
O
O
O
8
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.11
1.05
1.03
1.04
1.05
1.04
1.00
1.00
0.95
2.07
3.15
0.99
1.03
3.07


171.00
151.97
146.70
145.97
143.94
138.10
131.67
128.71
123.49
118.14
114.08
112.02
106.70
101.42
77.32
77.00
76.68
67.66
62.57
55.99
46.42
35.38
21.02
^{13}C NMR (100 MHz, $CDCl_3$)
Br
MeO
OAc
O
O
O
8
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



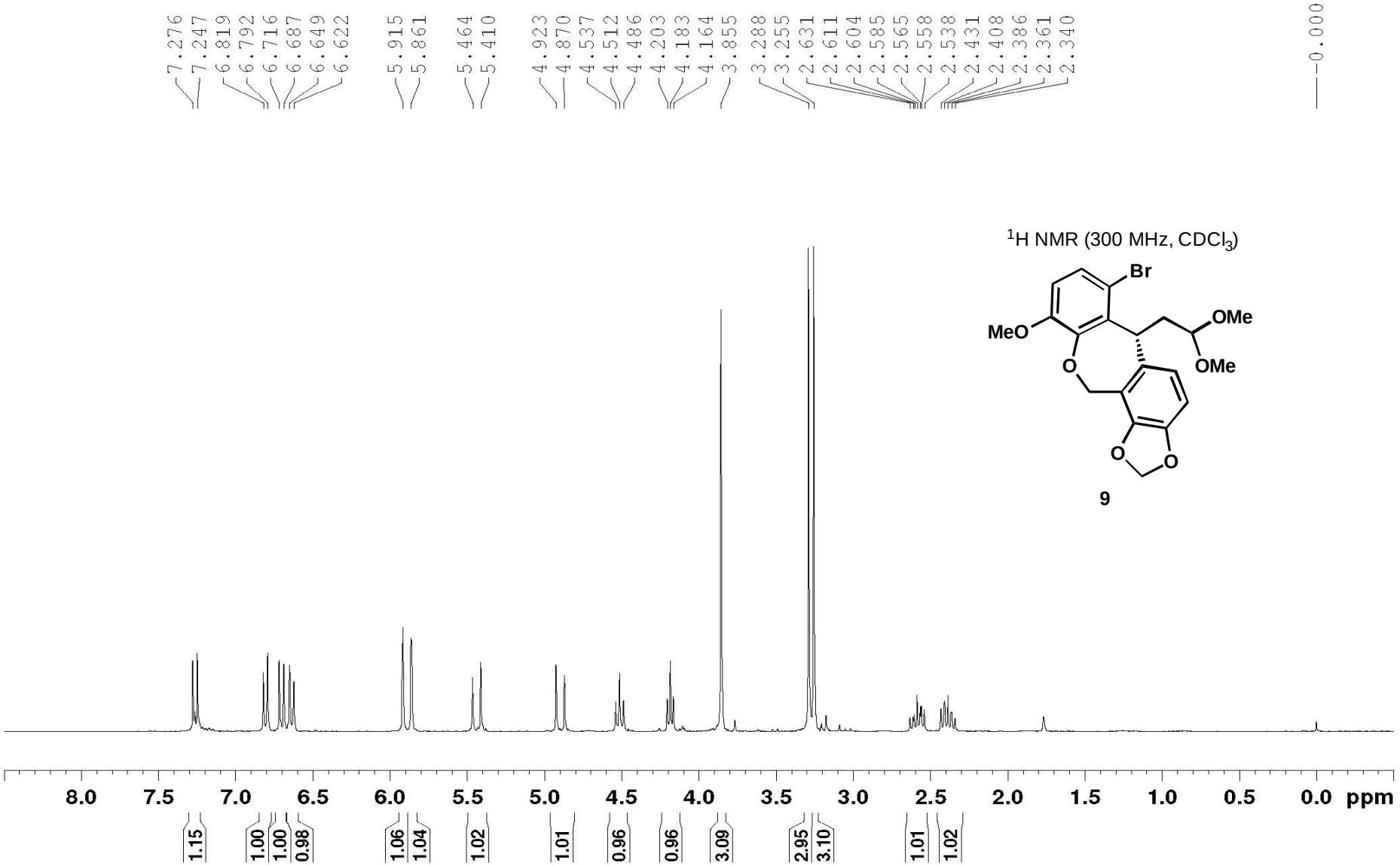
^{1}H NMR (400 MHz, $CDCl_3$)

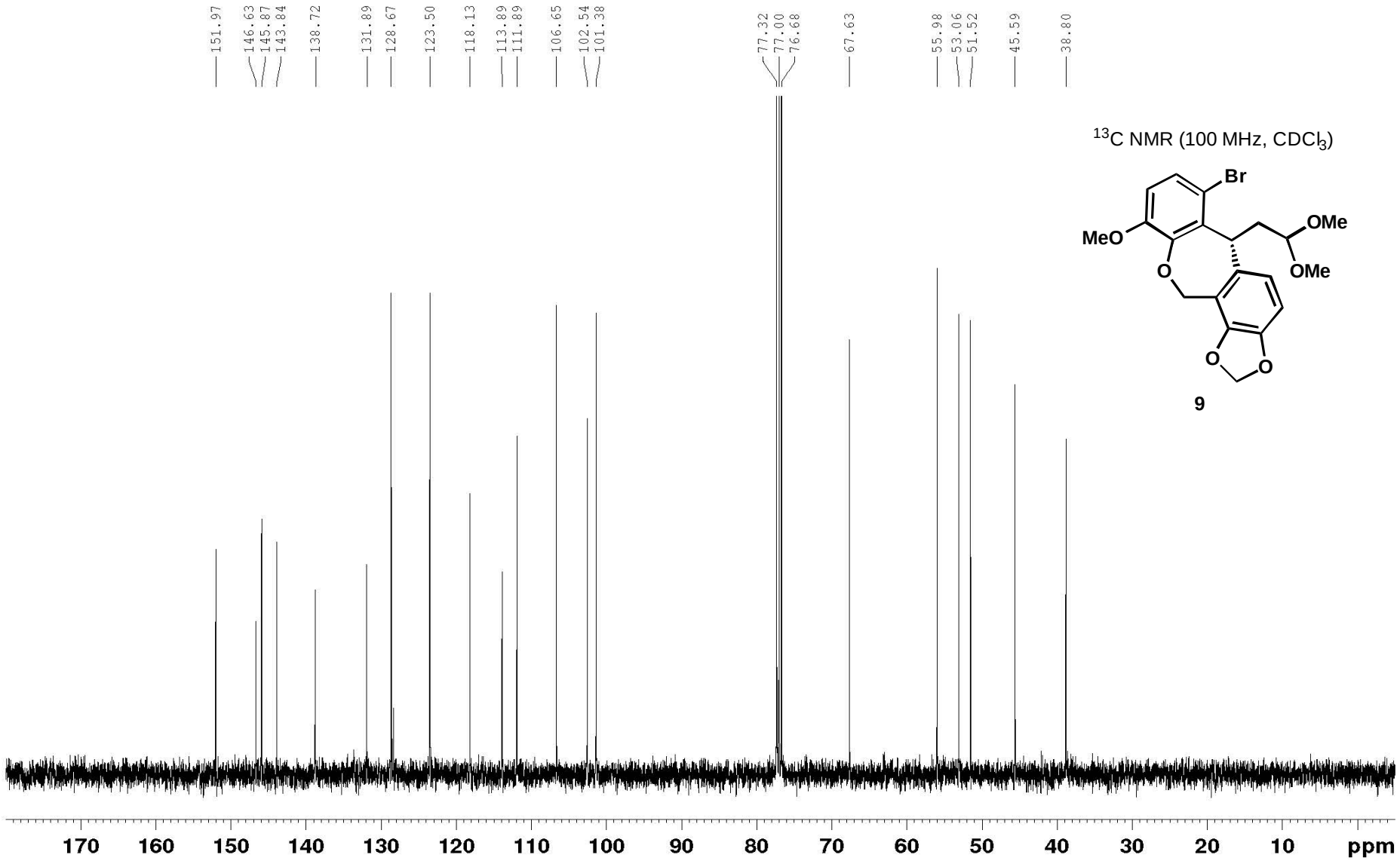
S2



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

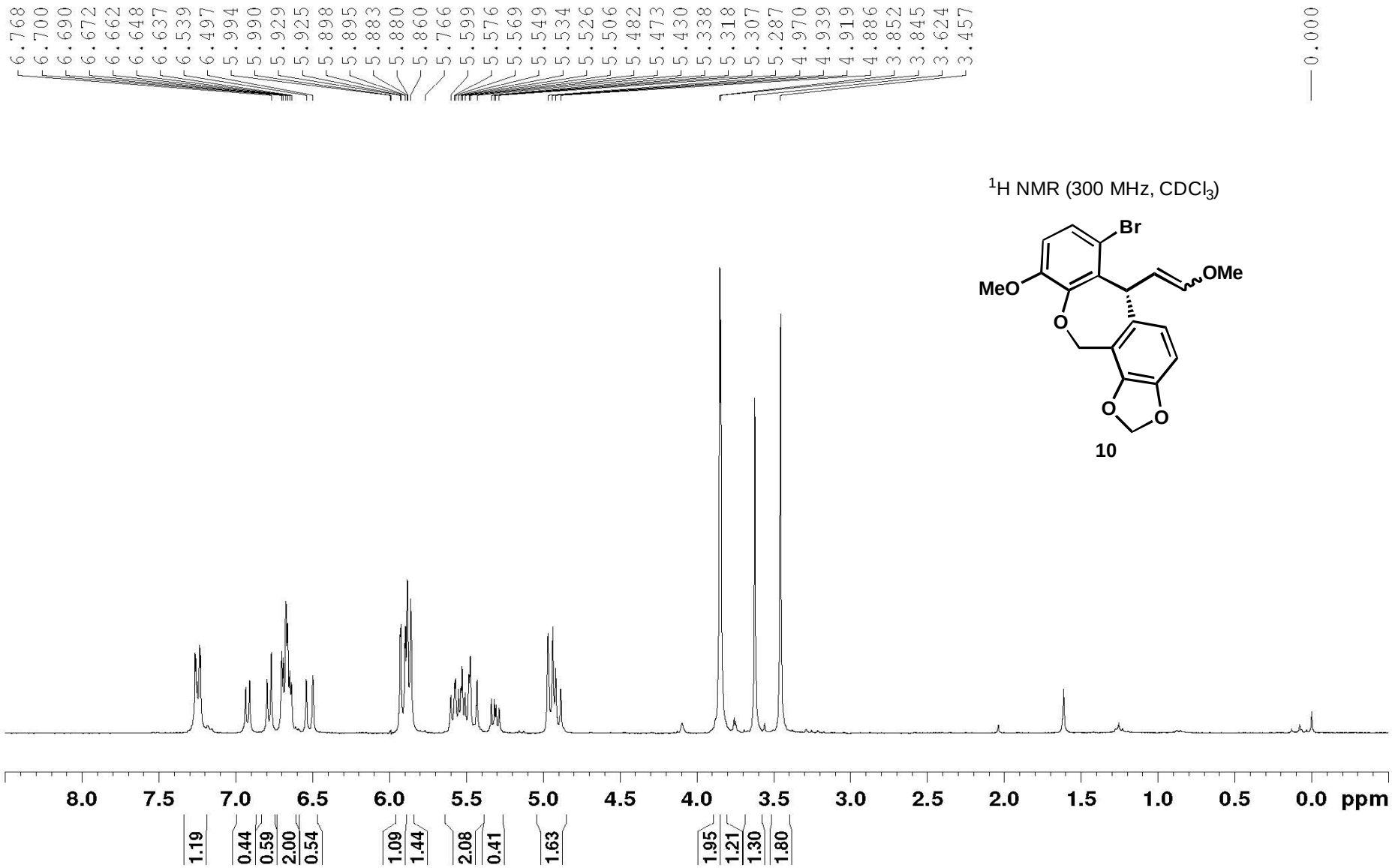
S2

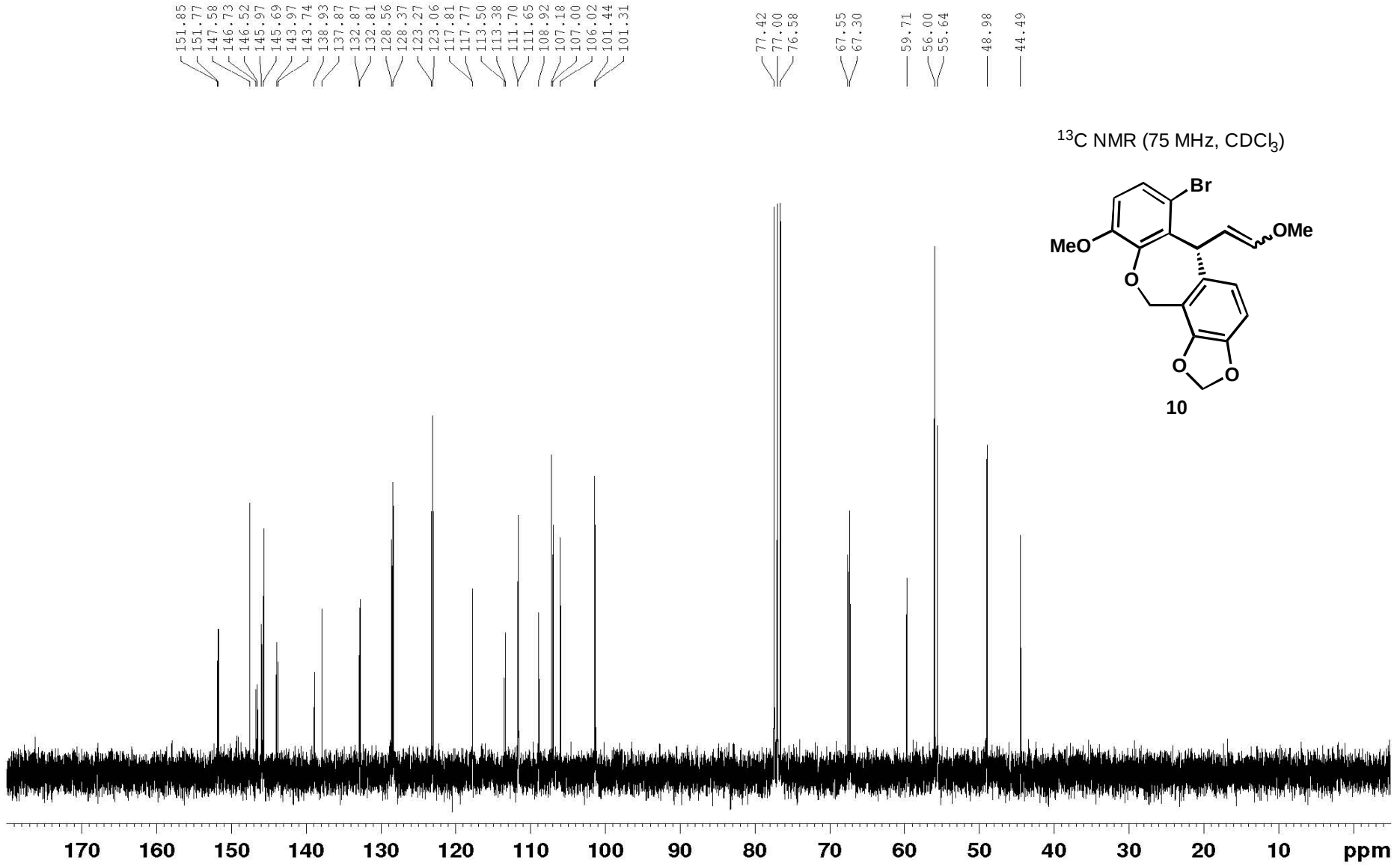

7.276
7.247
6.819
6.792
6.716
6.687
6.649
6.622
5.915
5.861
5.464
5.410
4.923
4.870
4.537
4.512
4.486
4.203
4.183
4.164
3.855
3.288
3.255
2.631
2.611
2.604
2.585
2.565
2.558
2.538
2.431
2.408
2.386
2.361
2.340
0.000
^{1}H NMR (300 MHz, $CDCl_3$)
Br
MeO
OMe
OMe
O
O
O
O
9
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.15
1.00
1.00
0.98
1.06
1.04
1.02
1.01
0.96
0.96
3.09
2.95
3.10
1.01
1.02



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

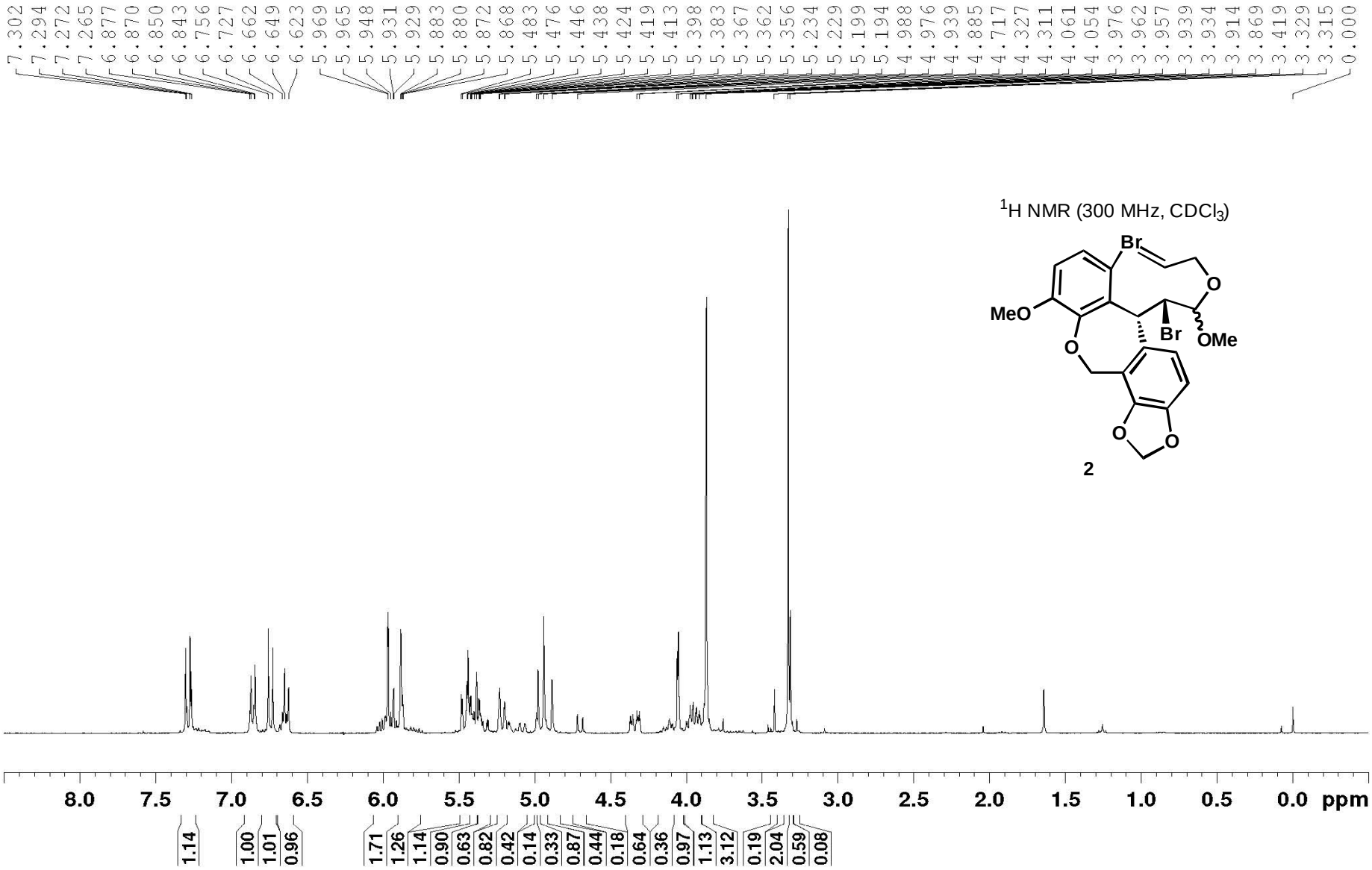
9

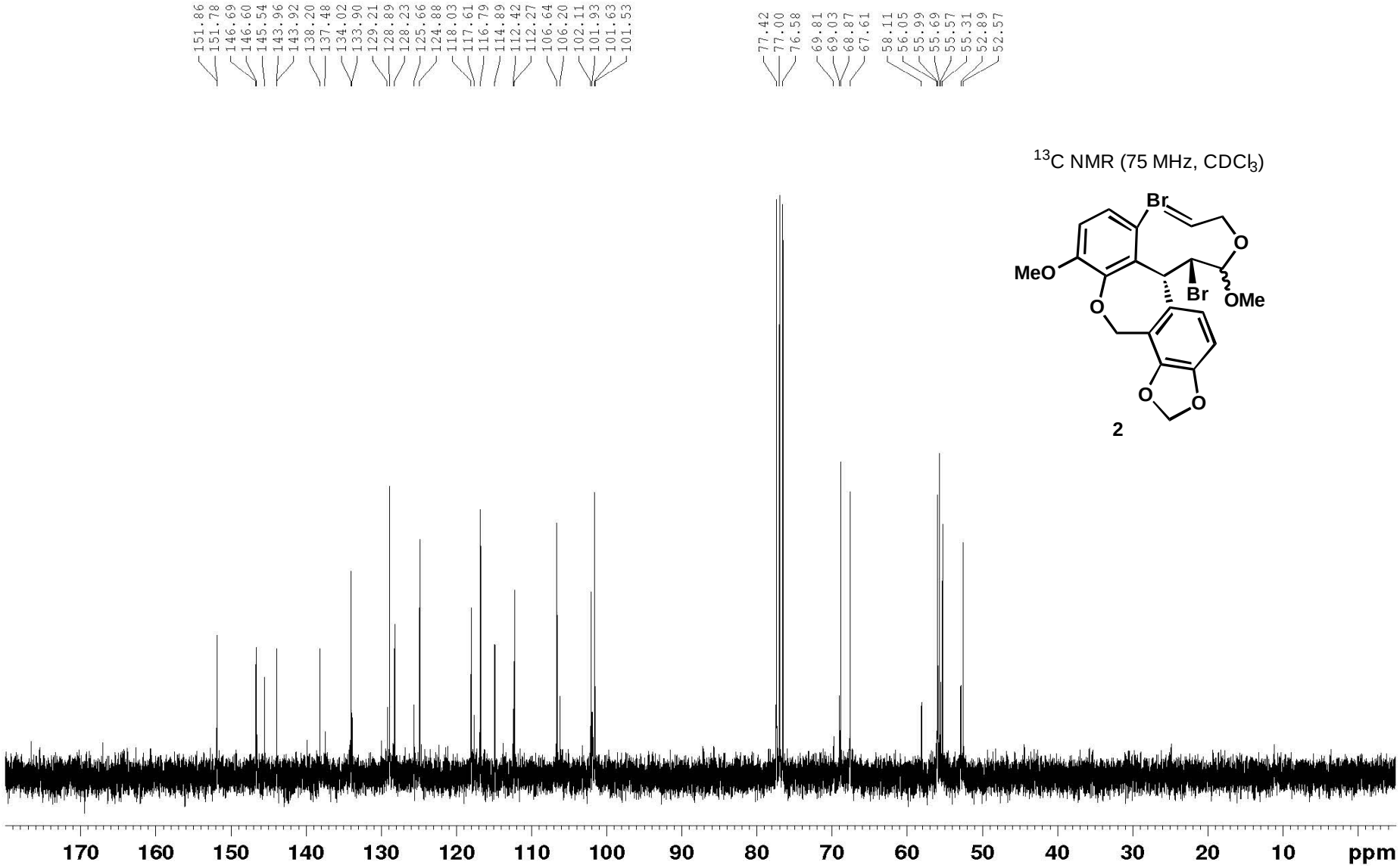

6.768
6.700
6.690
6.672
6.662
6.648
6.637
6.539
6.497
5.994
5.990
5.929
5.925
5.898
5.895
5.883
5.880
5.860
5.766
5.599
5.576
5.569
5.549
5.534
5.526
5.506
5.482
5.473
5.430
5.338
5.318
5.307
5.287
4.970
4.939
4.919
4.886
3.852
3.845
3.624
3.457
0.000
1H NMR (300 MHz, CDCl3)
Br
MeO
OMe
O
O
O
10
8.0
7.5
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
1.19
0.44
0.59
2.00
0.54
1.09
1.44
2.08
0.41
1.63
1.95
1.21
1.30
1.80

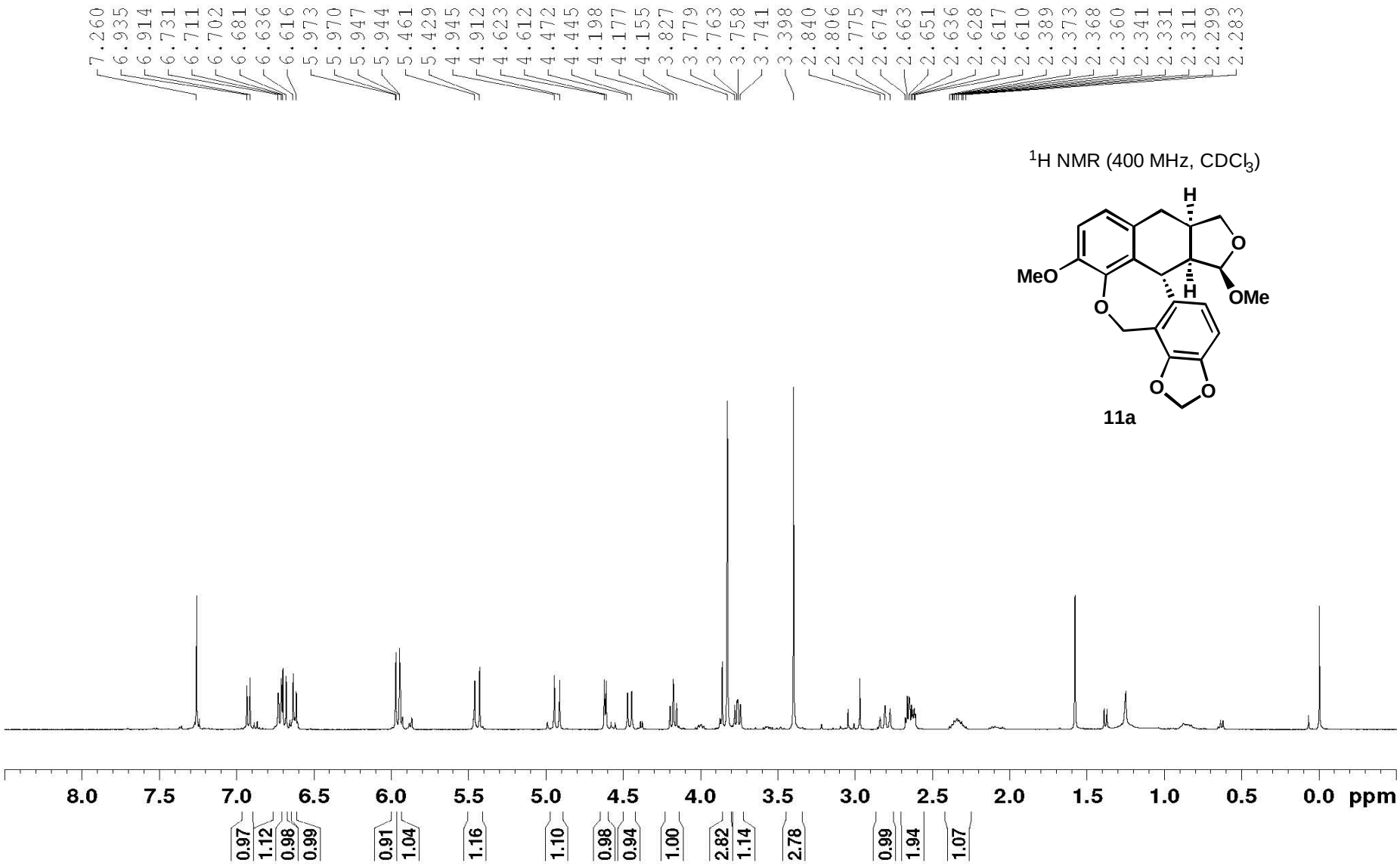


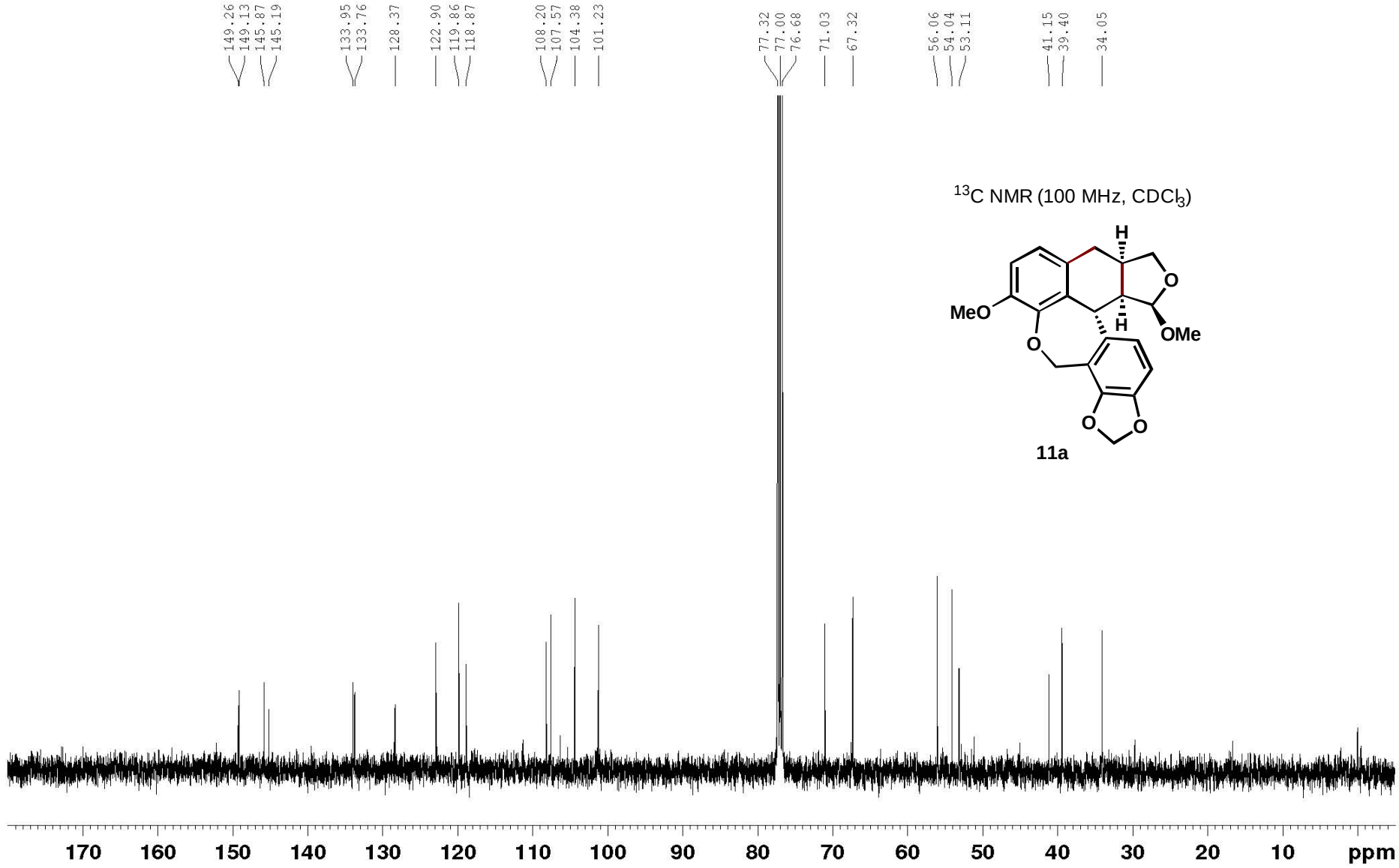
^{13}C NMR (75 MHz, $CDCl_3$)

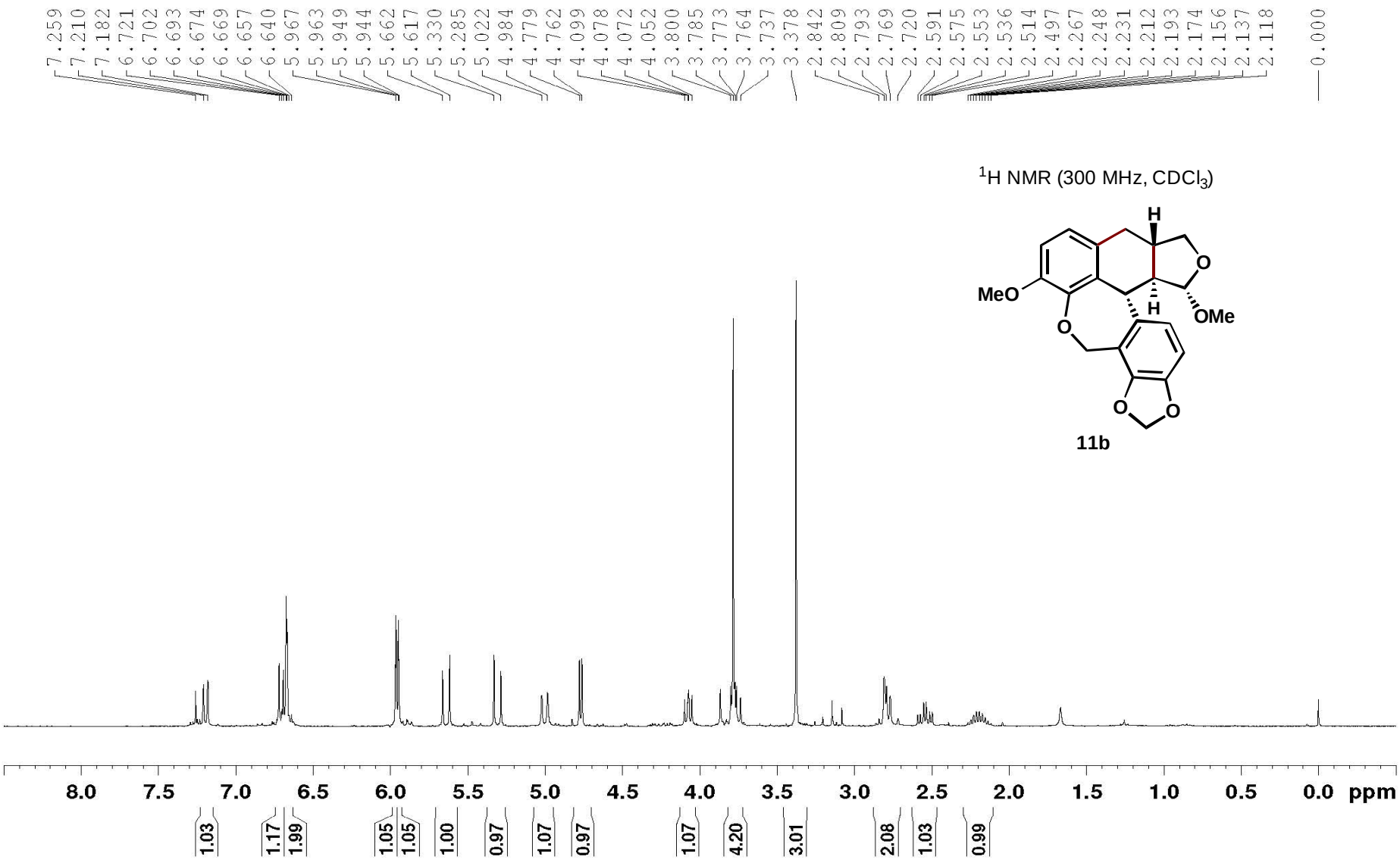
10

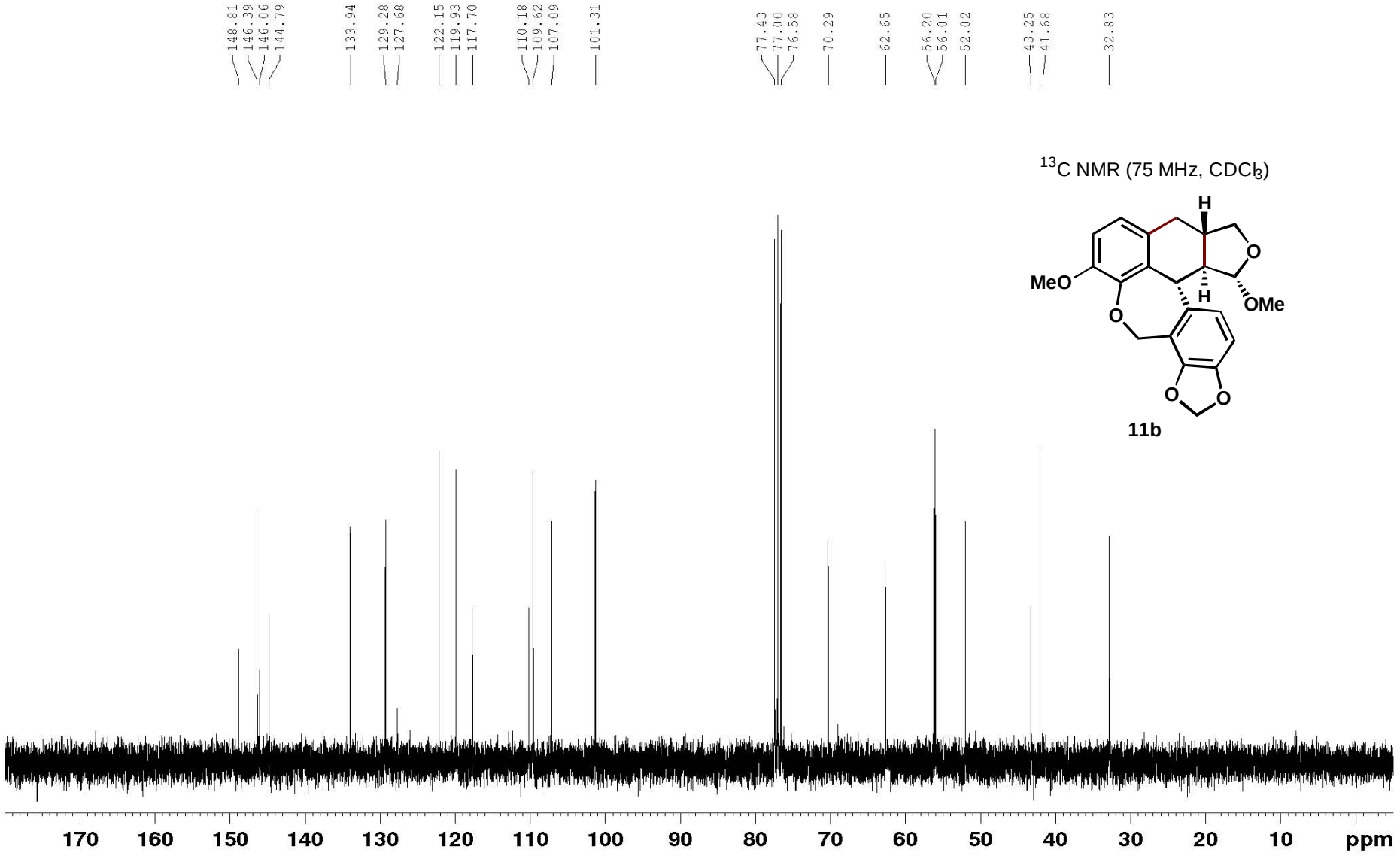

7.302
7.294
7.272
7.265
6.877
6.870
6.850
6.843
6.756
6.727
6.662
6.649
6.623
5.969
5.965
5.948
5.931
5.929
5.883
5.880
5.872
5.868
5.483
5.476
5.446
5.438
5.424
5.419
5.413
5.398
5.383
5.367
5.362
5.356
5.234
5.229
5.199
5.194
4.988
4.976
4.939
4.885
4.717
4.327
4.311
4.061
4.054
3.976
3.962
3.957
3.939
3.934
3.914
3.869
3.419
3.329
3.315
0.000
1H NMR (300 MHz, CDCl3)
Br
O
MeO
Br
OMe
O
O
O
2
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
1.14
1.00
1.01
0.96
1.71
1.26
1.14
0.90
0.63
0.82
0.42
0.14
0.33
0.87
0.44
0.18
0.64
0.36
0.97
1.13
3.12
0.19
2.04
0.59
0.08

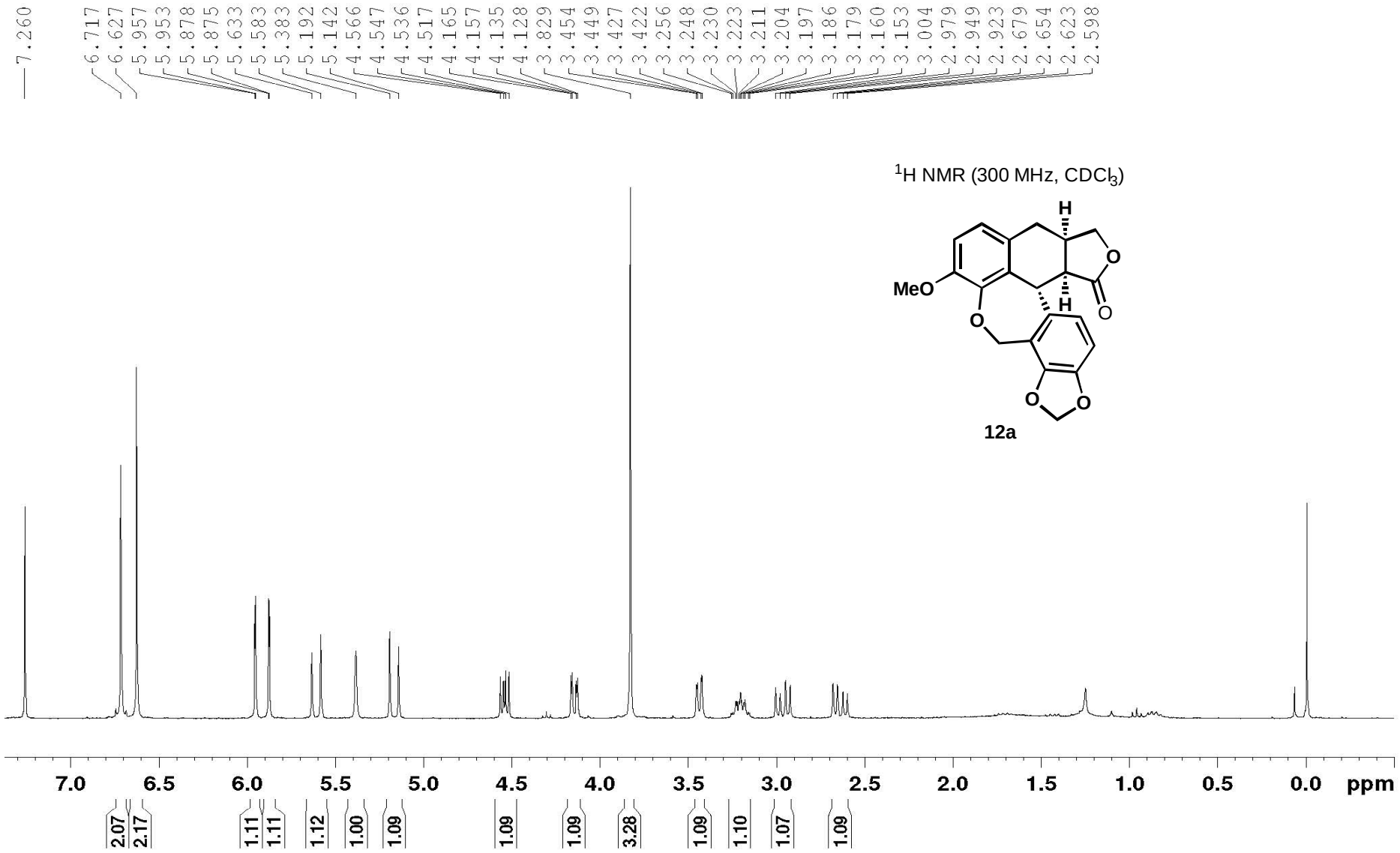

151.86
151.78
146.69
146.60
145.54
143.96
143.92
138.20
137.48
134.02
133.90
129.21
128.89
128.23
125.66
124.88
118.03
117.61
116.79
114.89
112.42
112.27
106.64
106.20
102.11
101.93
101.63
101.53
77.42
77.00
76.58
69.81
69.03
68.87
67.61
58.11
56.05
55.99
55.69
55.57
55.31
52.89
52.57
^{13}C NMR (75 MHz, CDCl$_3$)
Br
O
MeO
Br
OMe
O
O
O
2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

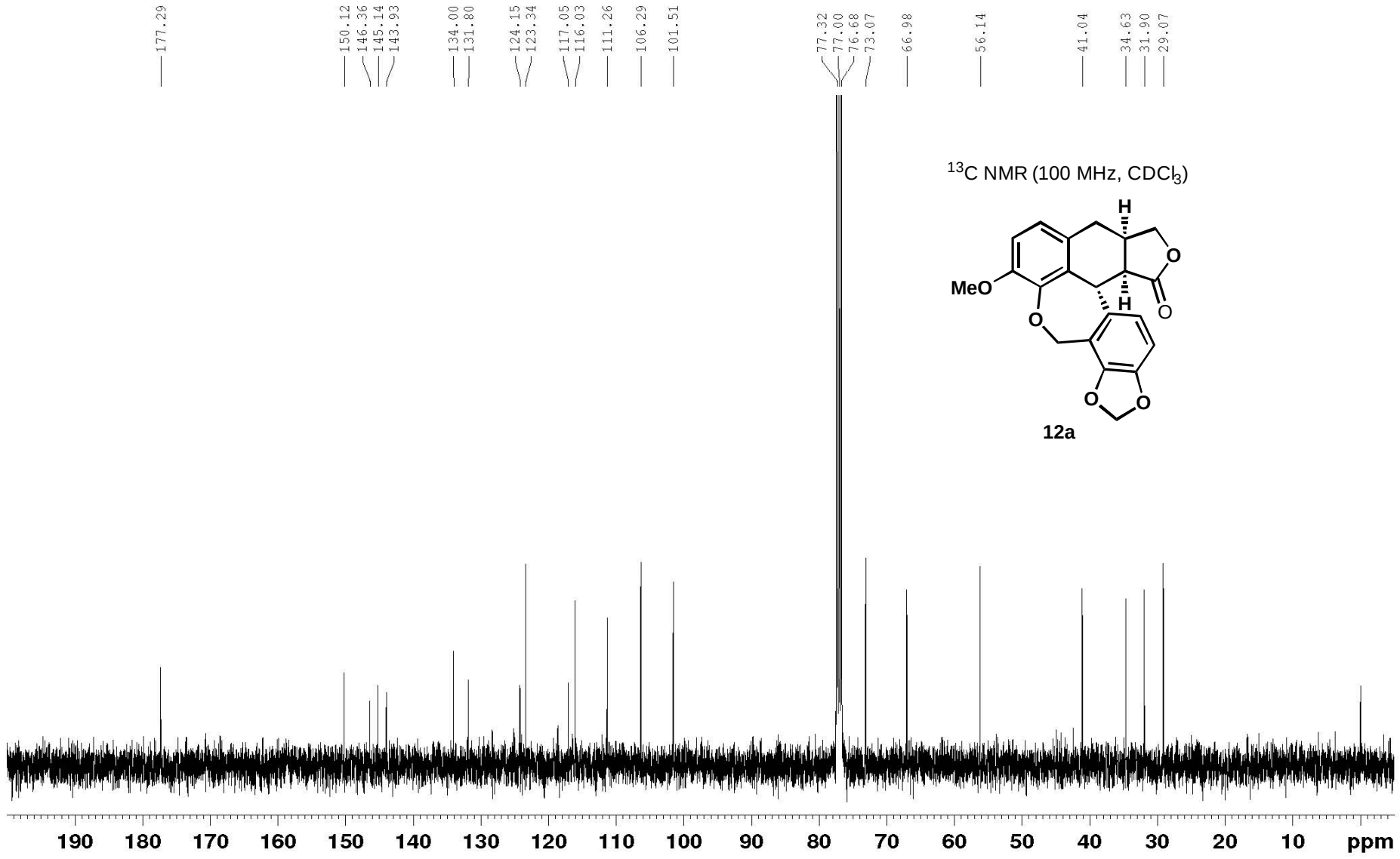

7.260
6.935
6.914
6.731
6.711
6.702
6.681
6.636
6.616
5.973
5.970
5.947
5.944
5.461
5.429
4.945
4.912
4.623
4.612
4.472
4.445
4.198
4.177
4.155
3.827
3.779
3.763
3.758
3.741
3.398
2.840
2.806
2.775
2.674
2.663
2.651
2.636
2.628
2.617
2.610
2.389
2.373
2.368
2.360
2.341
2.331
2.311
2.299
2.283
^{1}H NMR (400 MHz, CDCl$_3$)
MeO
OMe
O
H
H
O
O
O
11a
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
0.97
1.12
0.98
0.99
0.91
1.04
1.16
1.10
0.98
0.94
1.00
2.82
1.14
2.78
0.99
1.94
1.07


149.26
149.13
145.87
145.19
133.95
133.76
128.37
122.90
119.86
118.87
108.20
107.57
104.38
101.23
77.32
77.00
76.68
71.03
67.32
56.06
54.04
53.11
41.15
39.40
34.05
^{13}C NMR (100 MHz, CDCl$_3$)
H
O
MeO
H
OMe
O
O
O
11a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.259
7.210
7.182
6.721
6.702
6.693
6.674
6.669
6.657
6.640
5.967
5.963
5.949
5.944
5.662
5.617
5.330
5.285
5.022
4.984
4.779
4.762
4.099
4.078
4.072
4.052
3.800
3.785
3.773
3.764
3.737
3.378
2.842
2.809
2.793
2.769
2.720
2.591
2.575
2.553
2.536
2.514
2.497
2.267
2.248
2.231
2.212
2.193
2.174
2.156
2.137
2.118
0.000
1H NMR (300 MHz, CDCl3)
MeO
OMe
H
H
O
O
O
O
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
1.03
1.17
1.99
1.05
1.05
1.00
0.97
1.07
0.97
1.07
4.20
3.01
2.08
1.03
0.99

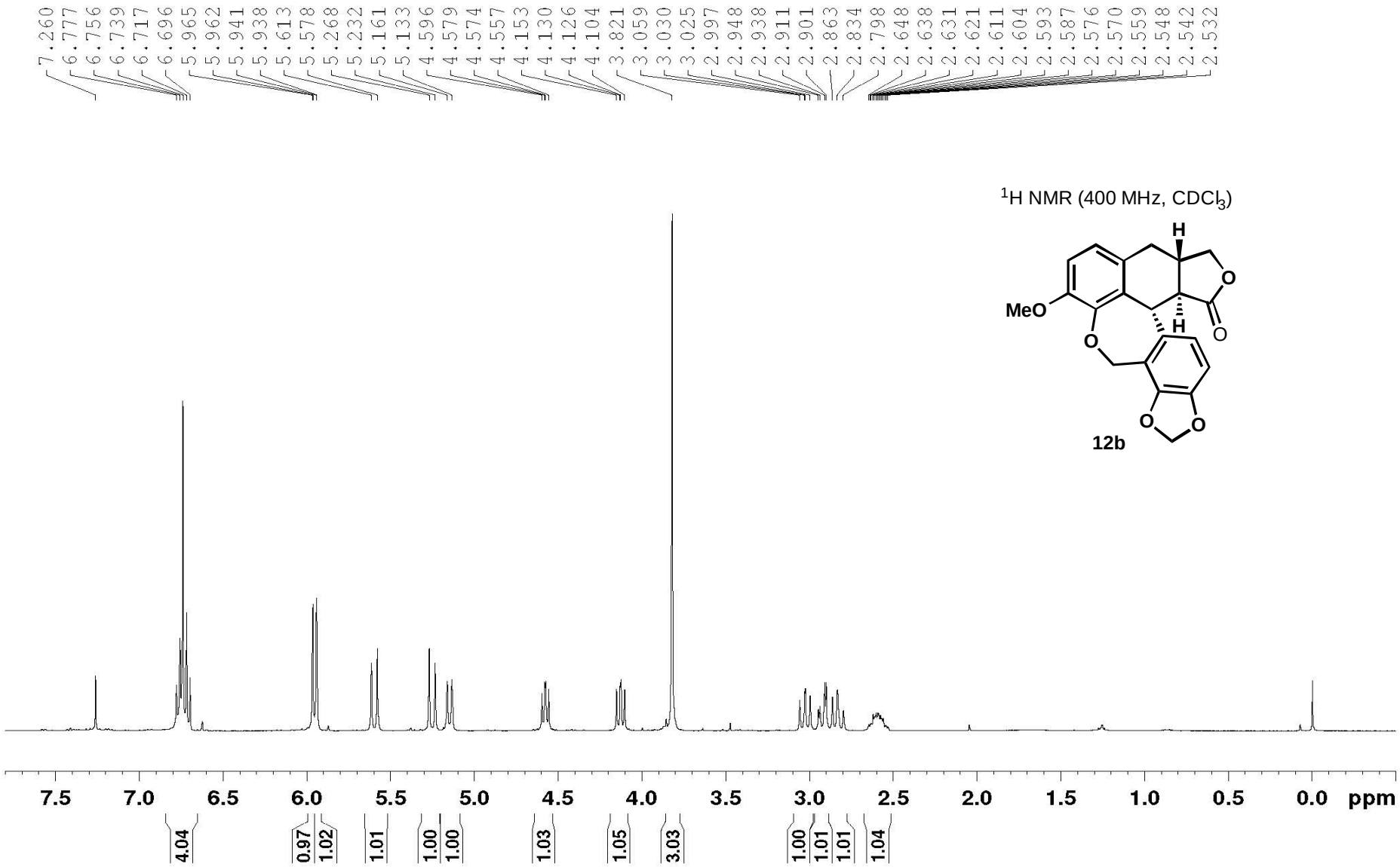

148.81
146.39
146.06
144.79
133.94
129.28
127.68
122.15
119.93
117.70
110.18
109.62
107.09
101.31
77.43
77.00
76.58
70.29
62.65
56.20
56.01
52.02
43.25
41.68
32.83
^{13}C NMR (75 MHz, CDCl$_3$)
MeO
OMe
H
H
O
O
O
O
11b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

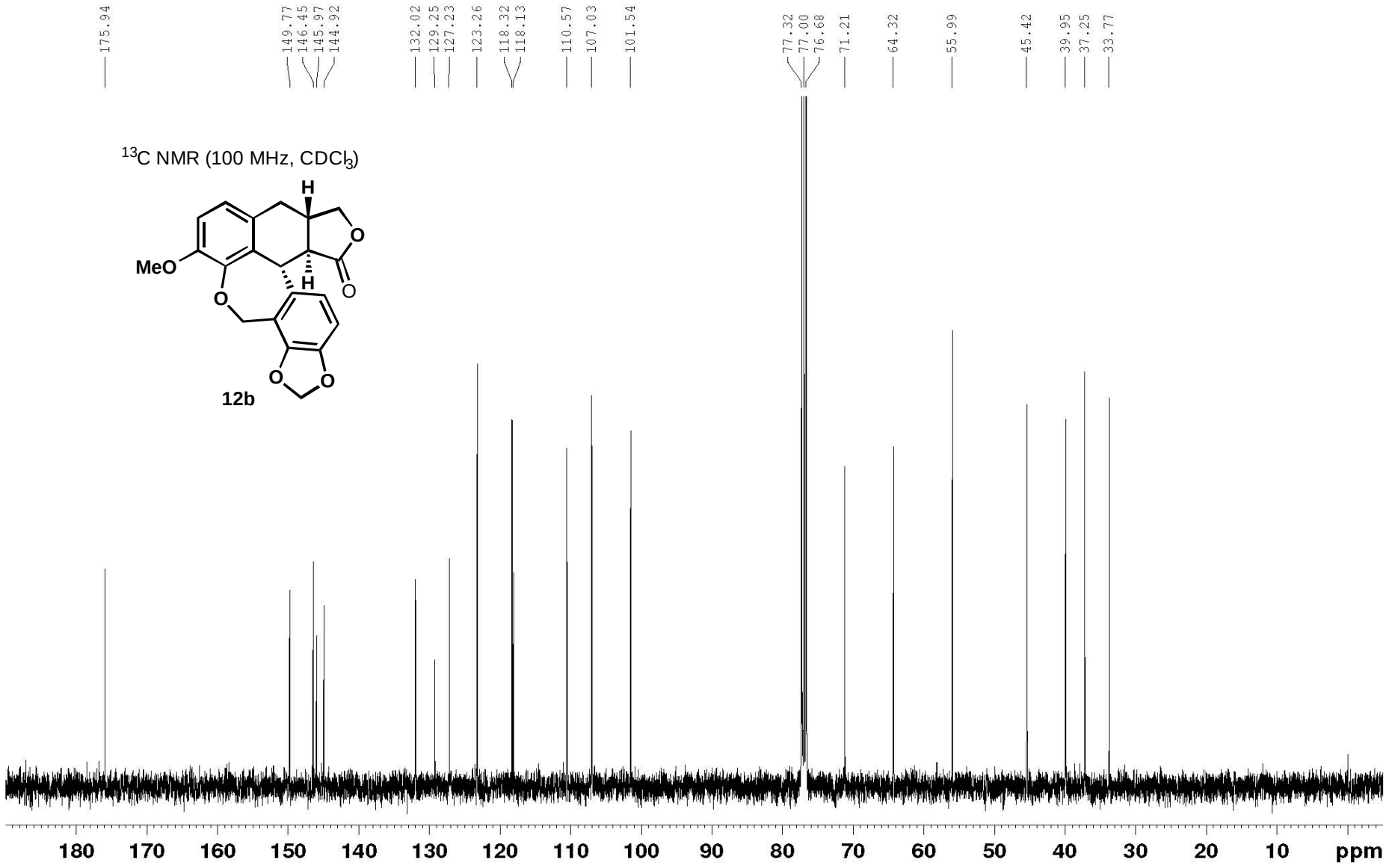

7.260
6.717
6.627
5.957
5.953
5.878
5.875
5.633
5.583
5.383
5.192
5.142
4.566
4.547
4.536
4.517
4.165
4.157
4.135
4.128
3.829
3.454
3.449
3.427
3.422
3.256
3.248
3.230
3.223
3.211
3.204
3.197
3.186
3.179
3.160
3.153
3.004
2.979
2.949
2.923
2.679
2.654
2.623
2.598
^{1}H NMR (300 MHz, CDCl$_3$)
MeO
H
H
O
O
O
O
O
12a
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
2.07
2.17
1.11
1.11
1.12
1.00
1.09
1.09
1.09
3.28
1.09
1.10
1.07
1.09

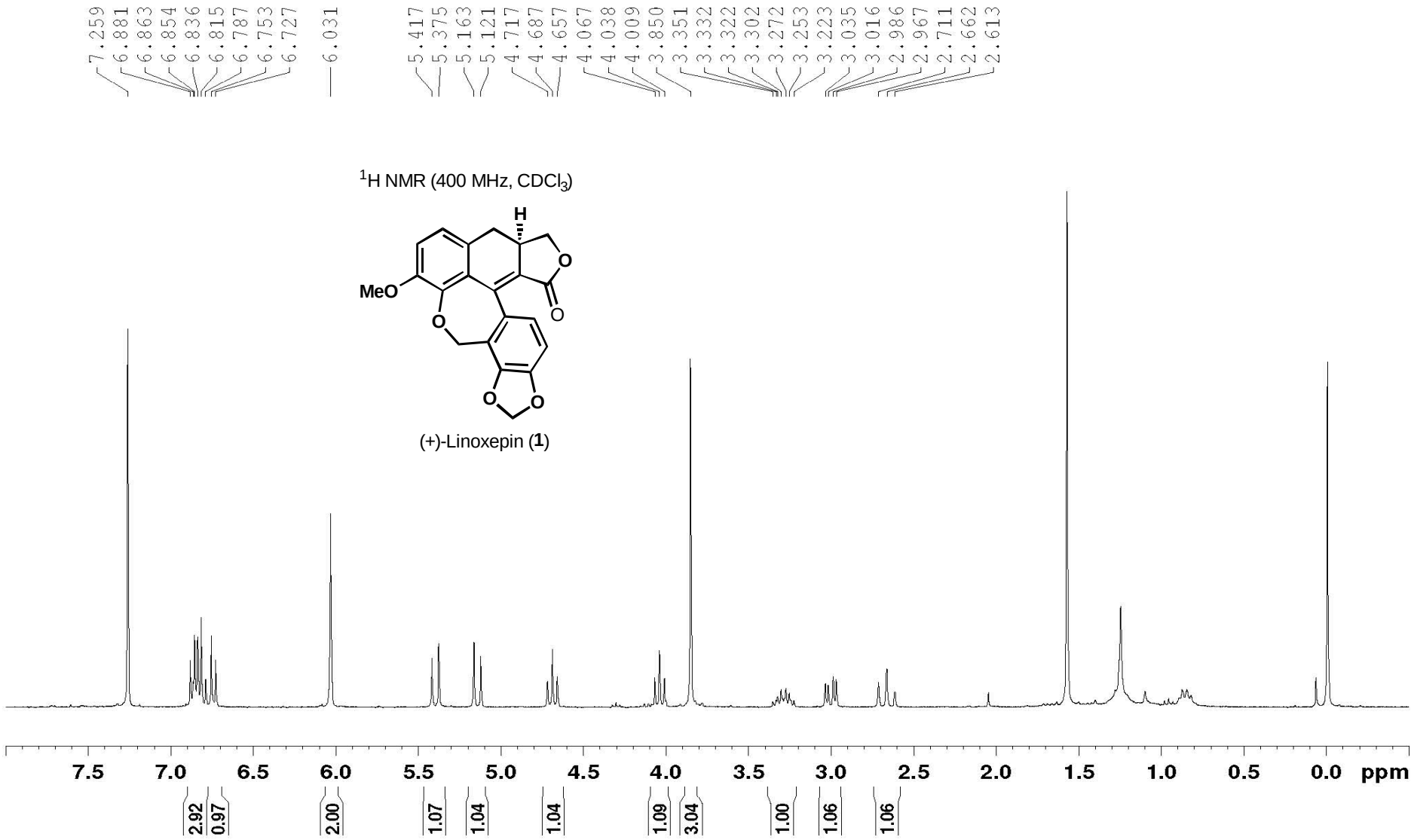


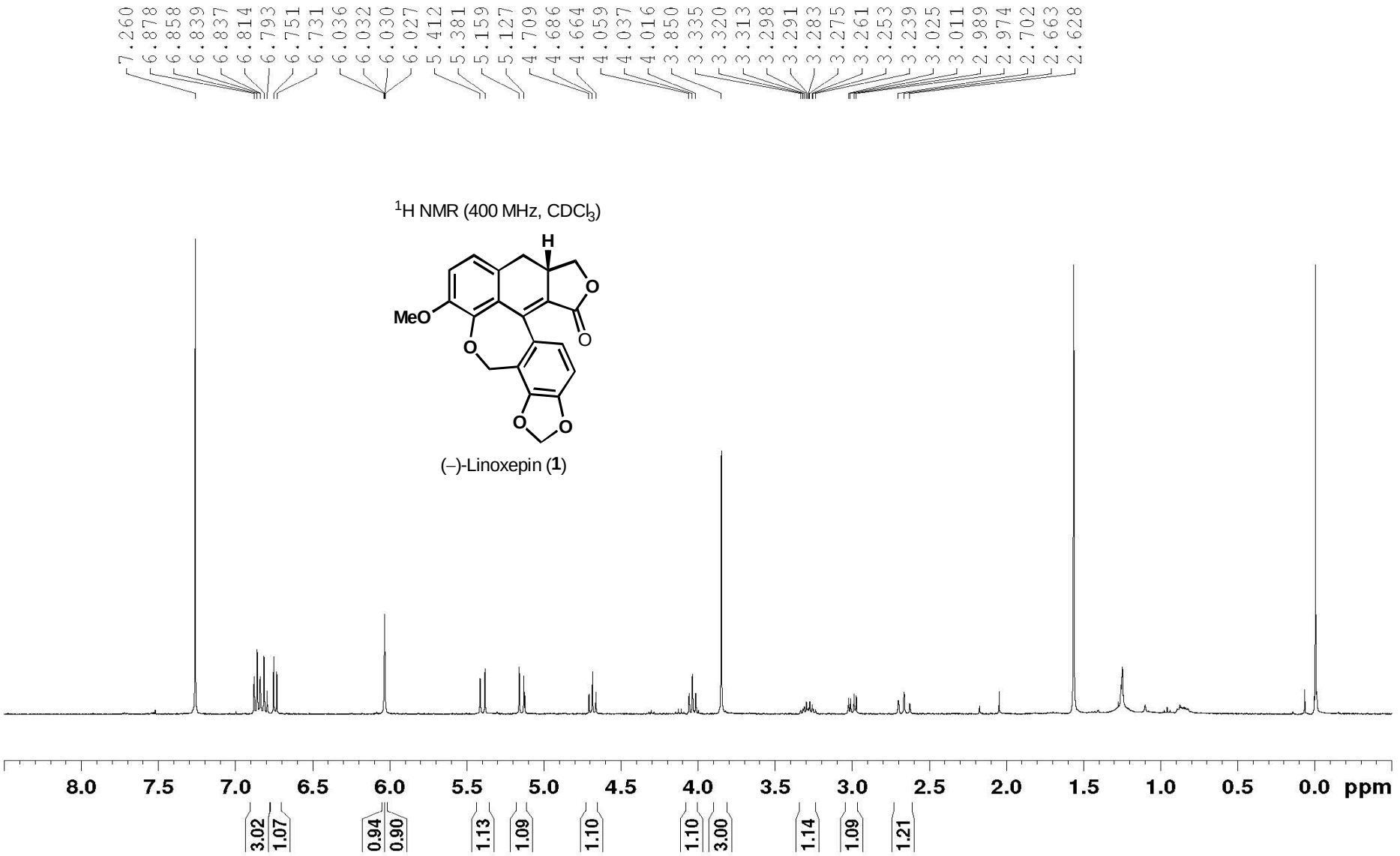
^{13}C NMR (100 MHz, $CDCl_3$)

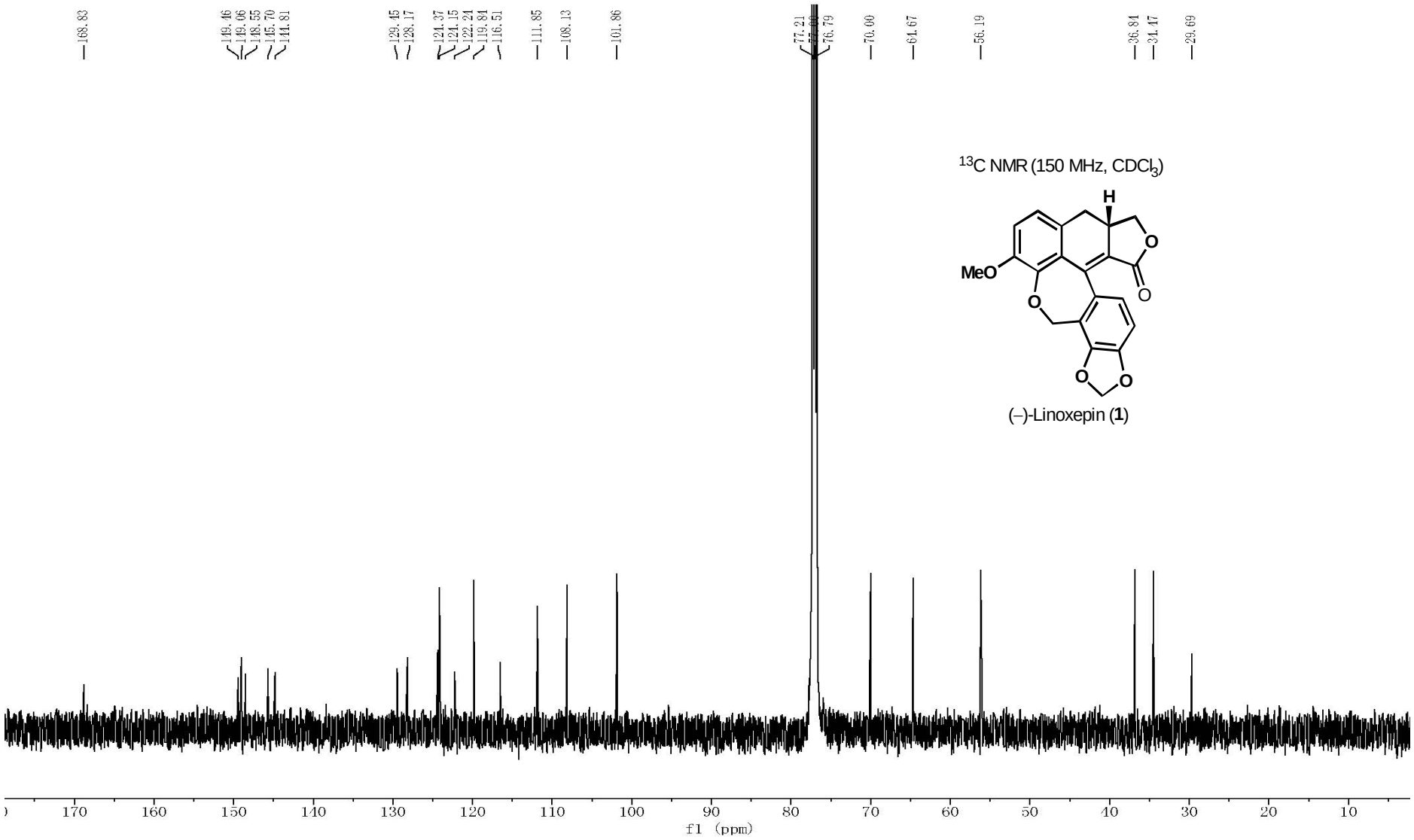
12a


7.260
6.777
6.756
6.739
6.717
6.696
5.965
5.962
5.941
5.938
5.613
5.578
5.268
5.232
5.161
5.133
4.596
4.579
4.574
4.557
4.153
4.130
4.126
4.104
3.821
3.059
3.030
3.025
2.997
2.948
2.938
2.911
2.901
2.863
2.834
2.798
2.648
2.638
2.631
2.621
2.611
2.604
2.593
2.587
2.576
2.570
2.559
2.548
2.542
2.532
^{1}H NMR (400 MHz, $CDCl_3$)
MeO
H
H
O
O
O
O
O
O
12b
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
4.04
0.97
1.02
1.01
1.00
1.00
1.03
1.05
3.03
1.00
1.01
1.01
1.04


175.94
149.77
146.45
145.97
144.92
132.02
129.25
127.23
123.26
118.32
118.13
110.57
107.03
101.54
77.32
77.00
76.68
71.21
64.32
55.99
45.42
39.95
37.25
33.77
13C NMR (100 MHz, CDCl3)
MeO
H
H
O
O
O
O
O
12b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

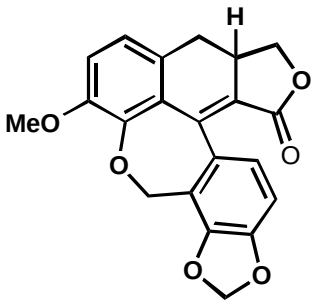

7.259
6.881
6.863
6.854
6.836
6.815
6.787
6.753
6.727
6.031
5.417
5.375
5.163
5.121
4.717
4.687
4.657
4.067
4.038
4.009
3.850
3.351
3.332
3.322
3.302
3.272
3.253
3.223
3.035
3.016
2.986
2.967
2.711
2.662
2.613
^{1}H NMR (400 MHz, CDCl$_3$)
MeO
H
O
O
O
O
O
(+)-Linoxepin (**1**)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.92
0.97
2.00
1.07
1.04
1.04
1.09
3.04
1.00
1.06
1.06


7.260
6.878
6.858
6.839
6.837
6.814
6.793
6.751
6.731
6.036
6.032
6.030
6.027
5.412
5.381
5.159
5.127
4.709
4.686
4.664
4.059
4.037
4.016
3.850
3.335
3.320
3.313
3.298
3.291
3.283
3.275
3.261
3.253
3.239
3.025
3.011
2.989
2.974
2.702
2.663
2.628
^{1}H NMR (400 MHz, $CDCl_3$)
H
MeO
O
O
O
O
O
(–)-Linoxepin (**1**)
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
3.02
1.07
0.94
0.90
1.13
1.09
1.10
1.10
3.00
1.14
1.09
1.21

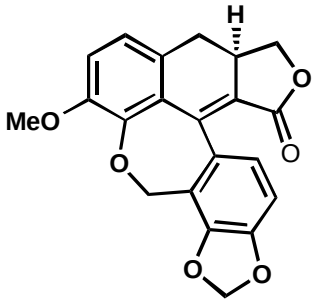


^{13}C NMR (150 MHz, $CDCl_3$)

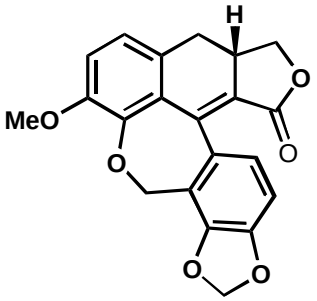
(–)-Linoxepin (**1**)



***rac*-Linoxepin**



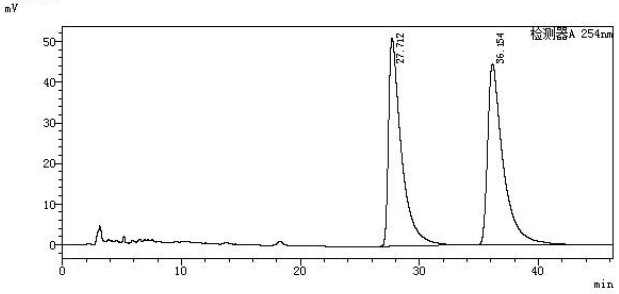
(+)-Linoxepin



(–)-Linoxepin

样品名	: Linoxepin-消旋-IA- (85: 15)		
样品ID	: Linoxepin-消旋-IA- (85: 15)		
数据文件名	: Linoxepin-消旋-IA- (85: 15) 1.lcd		
方法文件名	: tlh85.15 - 70min.lcm		
批处理文件名	:		
样品瓶号	: 1-1	样品类型	: 未知
进样体积	: 20 uL		
分析日期	: 2023/03/17 08:54:48	分析者	: System Administrator
处理日期	: 2023/03/17 09:41:09	处理者	: System Administrator

<色谱图>



<峰表>

检测器A 254nm

峰号	保留时间	面积	高度	浓度	浓度单位	标记	化合物名
1	27.712	3848102	51104	48.823			
2	36.154	4033561	44624	51.177			
总计		7881663	95728				

样品名	: Linoxepin-顺IA- (85: 15)		
样品ID	: Linoxepin-顺-IA- (85: 15)		
数据文件名	: Linoxepin-顺-IA- (85: 15) 1.lcd		
方法文件名	: tlh85.15 - 70min.lcm		
批处理文件名	:		
样品瓶号	: 1-3	样品类型	: 未知
进样体积	: 20 uL		
分析日期	: 2023/03/17 09:50:40	分析者	: System Administrator
处理日期	: 2023/03/17 10:37:42	处理者	: System Administrator

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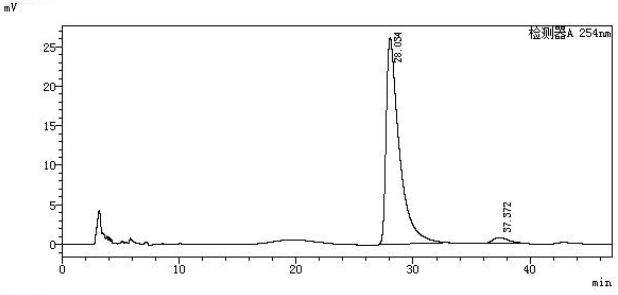

<峰表>

检测器A 254nm

峰号	保留时间	面积	高度	浓度	浓度单位	标记	化合物名
1	28.034	2035735	26140	96.722			
2	37.372	68993	729	3.278		M	
总计		2104728	26869				

样品名	: Linoxepin-反IA- (85: 15)		
样品ID	: Linoxepin-反-IA- (85: 15)		
数据文件名	: Linoxepin-反-IA- (85: 15) 1.lcd		
方法文件名	: tlh85.15 - 70min.lcm		
批处理文件名	:		
样品瓶号	: 1-2	样品类型	: 未知
进样体积	: 10 uL		
分析日期	: 2023/03/17 10:41:33	分析者	: System Administrator
处理日期	: 2023/03/17 11:26:42	处理者	: System Administrator

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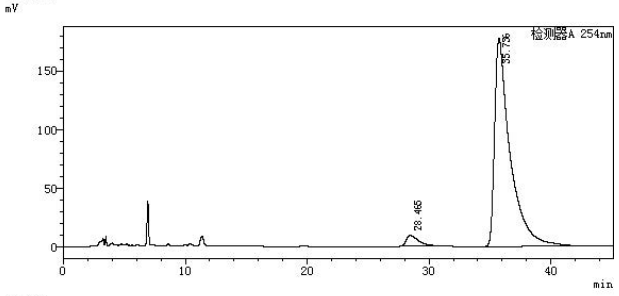

<峰表>

检测器A 254nm

峰号	保留时间	面积	高度	浓度	浓度单位	标记	化合物名
1	28.465	561605	8476	3.442		M	
2	35.736	15754997	177602	96.558			
总计		16316601	186078				