

Supporting Information

Total Synthesis of Scholarisine K and Alstolactine A

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I Experimental Procedures and Spectroscopic Data of Compounds

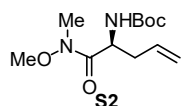
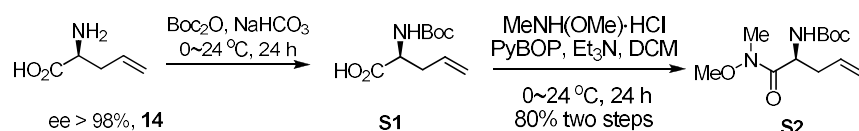
II Comparison of the Spectra of Natural and Synthetic products

III References and Notes

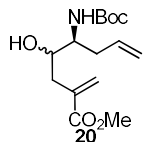
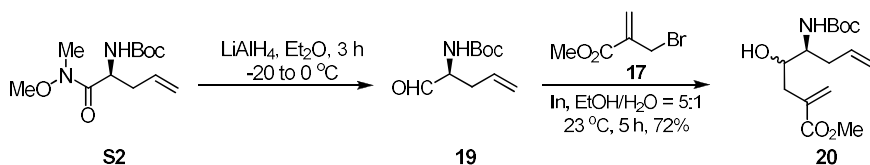
IV ^1H and ^{13}C NMR Spectra of Compounds

General Experimental Procedures: Unless stated otherwise, all reactions were carried out under a nitrogen atmosphere. Dichloromethane, dimethylsulfoxide and dimethylformamide were distilled from calcium hydride. Tetrahydrofuran and was distilled from sodiumbenzophenone in a continuous still under an atmosphere of nitrogen. Flash column chromatography was performed as described by Still (W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923–2925), employing Qingdao Haiyang silica gel 60 (200–300 mesh). TLC analyses were performed on EMD 250 μm Silica Gel HSGF254 plates and visualized by quenching of UV fluorescence ($\lambda_{\text{max}} = 254 \text{ nm}$), or by staining ceric ammonium molybdate, ammonium molybdate, or potassium permanganate. ^1H and ^{13}C NMR spectra were recorded on a Bruker-500, 400 spectrometer. Chemical shifts for ^1H and ^{13}C NMR spectra are reported in ppm (δ) relative to residue protium in the solvent (CDCl_3 : δ 7.26, 77.0 ppm; the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were acquired on a waters GCT premier, and Mass spectra at Agilent 5975C. Infrared (IR) spectra were obtained using a Thermo Electron Corporation Nicolet Nexus 670 FT-IR Spectrometer. The $[\alpha]_{\text{D}}$ was recorded using PolAAr 3005 High Accuracy Polarimeter.

Note: Most of the compounds have at least two isomers and N-Cbz protected compounds mainly have rotational isomers.



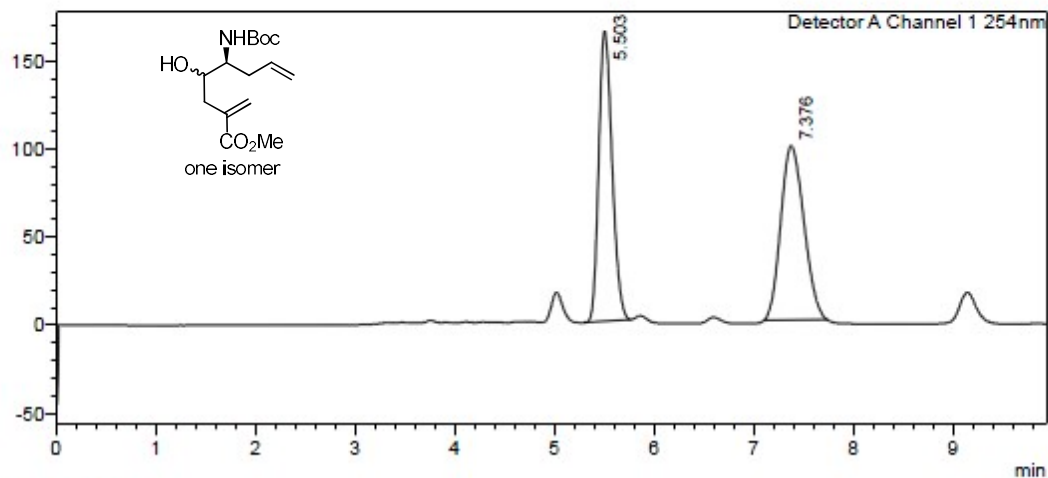
To a stirred solution of *L*-2-Allylglycine (**14**) (12.0 g, 104.2 mmol, 1.0 equiv) in THF (170 mL) and H_2O (170 mL) was added NaHCO_3 (26.4 g, 312.6 mmol, 3.0 equiv) and Boc_2O (30 g, 125.0 mmol, 1.2 equiv) at 0 $^\circ\text{C}$, the resulting mixture was vigorously stirred at 0 $^\circ\text{C}$ for 0.5 h, then the mixture was warmed to 24 $^\circ\text{C}$ and vigorously stirred for another 24 h. THF was removed in vacuo and the resulting aqueous suspension was washed with diethyl ether (100 mL). The aqueous layer was acidified to pH 4 by slowly addition of 1 N HCl at 0 $^\circ\text{C}$, and extracted with ethyl acetate (5 \times 200 mL). The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under vacuum to give **S1** as a colorless oil. To a stirred solution of crude **S1** in 347 mL dichloromethane was added Et_3N (15.9 mL, 114.6 mmol, 1.1 equiv) and PyBOP (54.2 g, 104.2 mmol, 1.0 equiv) at 0 $^\circ\text{C}$. After stirring for 10 min at 0 $^\circ\text{C}$, *N*-methoxymethanamine (11.2 g, 114.6 mmol, 1.1 equiv) was added at the same temperature. After stirring for another 0.5 h, an additional aliquot of Et_3N (1.5 mL, 10.4 mmol, 0.1 equiv) was added. Then the mixture was warmed to 24 $^\circ\text{C}$ and vigorously stirred for another 2 h, an additional aliquot of Et_3N (7.0 mL, 52.1 mmol, 0.5 equiv) was added. After 11 h, H_2O (150 mL) was added, then dichloromethane was removed in vacuo and the resulting mixture was extracted with ethyl acetate (3 \times 200 mL). The combined organic layer was washed with 1 N HCl (100 mL) and saturated aqueous NaHCO_3 (100 mL) and brine (50 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (15:1 to 2:1 petroleum ether-ethyl acetate) to give compound **S2**^[1] (21.4 g, 80%) as a colorless oil. $R_f = 0.23$ (20% ethyl acetate-hexane); $[\alpha]_{\text{D}}^{26} = 5.6$ ($c = 1.0$, CH_2Cl_2).



To a stirred solution of **S2** (6.2 g, 24.0 mmol, 1.0 equiv) in anhydrous diethyl ether (120 mL) was added LiAlH_4 (2.4 M in THF, 13 mL, 31.2 mmol, 1.3 equiv) dropwise at -20°C under N_2 , the resulting mixture was vigorously stirred at -20°C for 10 min, then the mixture was warmed to 0°C and vigorously stirred for another 3 h. The mixture was then cooled to -78°C and treated slowly with aqueous 0.35 M NaHSO_4 (60 mL) which was cooled to 0°C before addition. The reaction mixture was stirred at room temperature for 10 min and added 1 N HCl (50 mL) which was cooled to 0°C before addition, then extracted with pre-cooled diethyl ether at -20°C (3×100 mL). The combined organic layer was washed with 1 N HCl (4×200 mL) and saturated aqueous NaHCO_3 (2×80 mL) and brine (3×80 mL) which were all cooled to 0°C before washed and kept the temperature below 3°C when washed. The solution was dried over anhydrous sodium sulfate at 0°C for 10 min. The dried solution was filtered and concentrated under vacuum at 0°C to afford the desired product **19** as a colorless oil. $[\alpha]_D^{27} = 35.0$ ($c = 1.6$, CH_2Cl_2). (**Note: all the the final treatment was proceeded below 3°C , and the aldehyde was unstable at room temperature, which can be racemization slowly**). The crude product was dissolved in a mixture of EtOH (150 mL), water (30 mL) at 0°C . To a stirred the solution was added **17**^[2] (6.8 g, 38.4 mmol, 1.6 equiv) and indium power (3.0 g, 26.4 mmol, 1.1 equiv). The mixture was warmed to 23°C for 40 min, an additional aliquot of **17** (0.86 g, 4.8 mmol, 0.2 equiv) and indium power (1.1 g, 9.6 mmol, 0.4 equiv) was added. Following 1 h, an additional aliquot of **17** (0.28 g, 2.4 mmol, 0.1 equiv) and indium power (0.55 g, 4.8 mmol, 0.2 equiv) was added again. After 3 h, the mixture was concentrated under vacuum, then extracted with ethyl acetate (3×150 mL). The combined organic layer was washed with 1 N HCl (80 mL) and brine (80 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (15:1 to 3:2 petroleum ether-ethyl acetate) to give compound **20** (5.17 g, 72%, dr = 1.7:1, determined by crude ^1H NMR) as a colorless oil. $R_f = 0.48$ (30% ethyl acetate-hexane); (The two isomers were carefully isolated by preparation thin layer chromatography by 20% petroleum ether-ethyl acetate three times using trace of crude reaction mixture to test ee). Enantiomeric excess: one is 98.9%, the other is 96.7%, determined by HPLC (CHIRALPAK AD-H, hexane/isopropanol = 85/15, flow rate 1.0 mL/min, $T = 30^\circ\text{C}$, 254 nm) 98.9% ee for its $t_R = 5.528$ min (minor), $t_R = 7.383$ min (major); 96.7% ee for its $t_R = 5.781$ min (minor), $t_R = 6.541$ min (major); ^1H NMR (400 MHz, CDCl_3) δ 6.26 (d, $J = 7.8$ Hz, 1H), 5.88 – 5.75 (m, 1H), 5.72 (d, $J = 5.0$ Hz, 1H), 5.19 – 5.01 (m, 2H), 4.82 (s, 0.5H), 4.67 (s, 0.5H), 3.77 (s, 3H), 3.75 – 3.55 (m, 2H), 3.25 (s, 0.36H), 2.97 (s, 0.46 H), 2.64 – 2.16 (m, 4H), 1.43 (s, 9H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 167.8, 167.7, 155.9, 136.8, 136.6, 134.7, 134.6, 128.0, 127.6, 117.0, 116.9, 78.9, 78.7, 72.4, 70.8, 54.4, 53.3, 51.7, 51.6, 37.4, 37.0, 36.2, 34.2, 28.0 ppm; IR ν_{max} 3366, 2977, 1713, 1635, 1514, 1441, 1366, 1248, 1161, 1047, 949, 918 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{15}\text{H}_{25}\text{NO}_5$ $[\text{M}]^+$: 299.1733, found 299.1731.

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mV



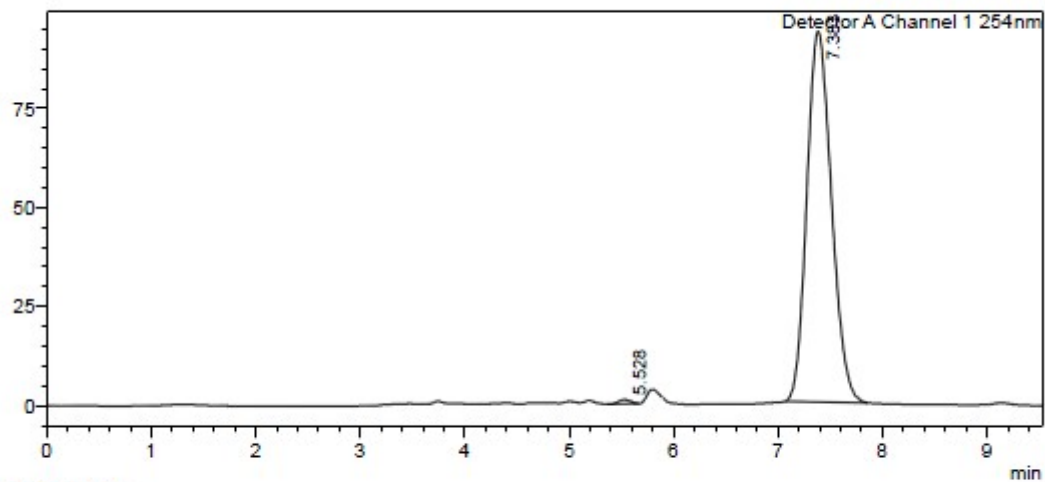
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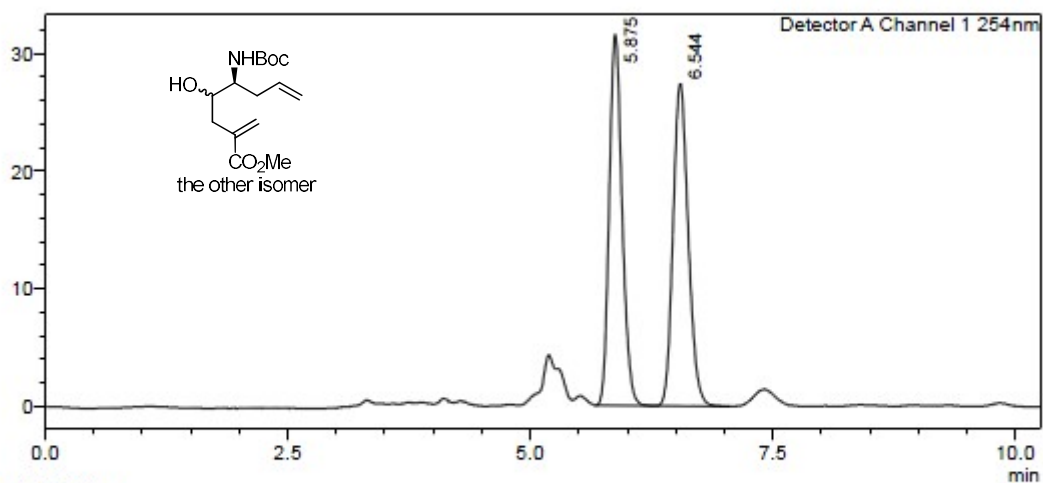
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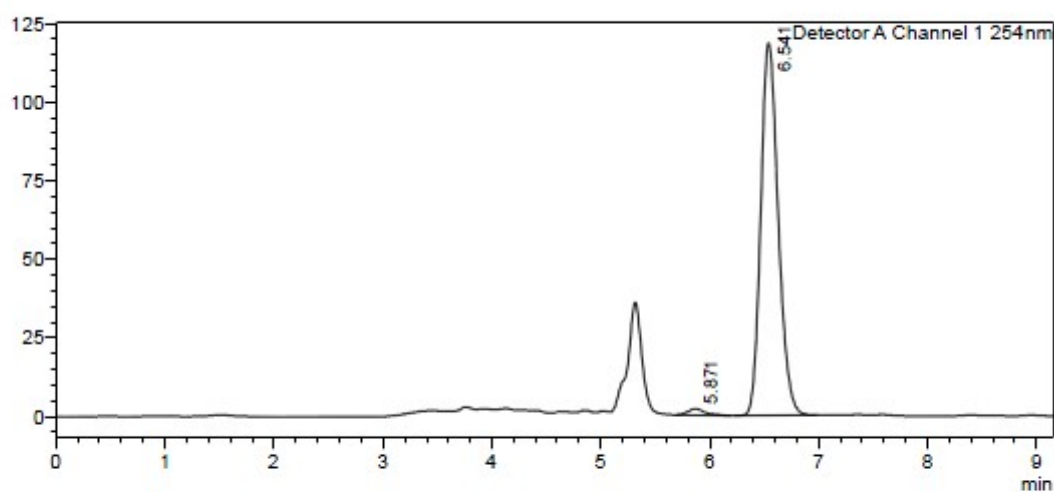
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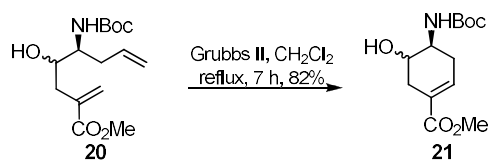
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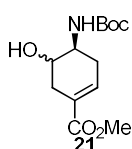


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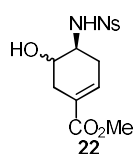
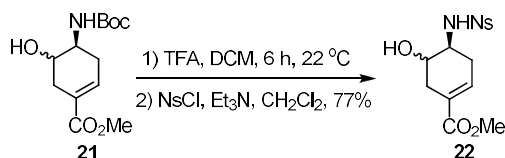
Detector A Channel 1 254nm

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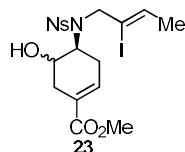
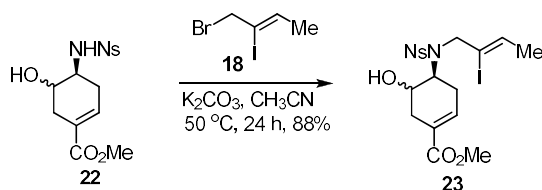




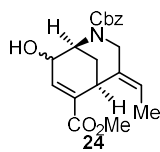
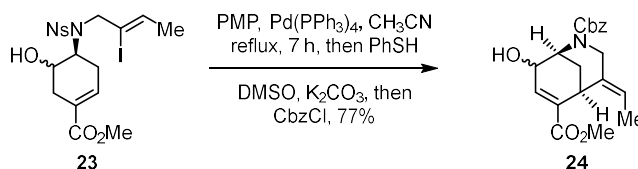
To a solution of **20** (3.0 g, 10.0 mmol, 1.0 equiv) in anhydrous and degassed dichloromethane (380 mL, 0.026 M) in a round-bottom flask was added Grubbs II catalyst (424 mg, 0.5 mmol, 0.05 equiv). The mixture was heated to 55 °C for 7 h. The solution was cooled to room temperature, and removed under vacuum. The residue was purified by a flash column chromatography on silica gel (12:1 to 1:1 petroleum ether-ethyl acetate) to give compound **21** (2.78 g, 82%) as a white solid. R_f = 0.50 (50% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 6.85 (s, 0.44H), 6.79 (s, 0.56H), 5.10 (s, 0.5H), 4.94 (s, 0.50H), 4.05 (s, 0.4H), 3.81 – 3.55 (m, 1.6H), 3.68 (s, 3H), 3.45 (s, 0.60H) 3.29 (s, 0.4H), 2.73 (d, J = 17.9 Hz, 1H), 2.62 – 2.33 (m, 1.4H), 2.26 (dd, J = 18.6, 6.0 Hz, 1H), 2.06 (dd, J = 19.9, 4.7 Hz, 0.6H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 167.2, 166.9, 156.4, 155.9, 136.9, 136.3, 128.0, 126.9, 79.9, 79.6, 68.8, 67.1, 51.7, 51.6, 50.8, 48.7, 31.8, 30.9, 29.5, 28.2 ppm; IR ν_{max} 3493, 3367, 1681, 1521, 1432, 1365, 1310, 1253, 1169, 1083, 1046, 721 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{13}\text{H}_{21}\text{NO}_5$ $[\text{M}]^+$: 271.1420, found 271.1418.



To a solution of **21** (18.4 g, 67.9 mmol, 1.0 equiv) in dichloromethane (200 mL) was added trifluoroacetic acid (200 mL) at 0 °C, then the mixture was warmed to 22 °C and vigorously stirred for 6 h. The solution was removed under vacuum. After azeotropic dehydrating with toluene, the residual solvent was removed with oil pump for 0.5 h. The crude amine was dissolved with dry dichloromethane (350 mL) under nitrogen, Et_3N (95 mL, 679 mmol, 10.0 equiv) was added dropwise at 0 °C, then 2-nitrobenzenesulfonyl chloride (16.5 g, 74.7 mmol, 1.1 equiv) was added at the same temperature. The mixture was warmed to 24 °C and vigorously stirred for 1 h and quenched with water (50 mL). The mixture was extracted with dichloromethane (3×150 mL). The combined organic layer was washed with brine (50 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (10:1 to 2:3 petroleum ether-ethyl acetate) to give compound **22** (18.7 g, 77%) as a white solid. R_f = 0.32 (50% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 8.20 – 8.12 (m, 1H), 7.93 – 7.85 (m, 1H), 7.81 – 7.71 (m, 2H), 6.81 (br, 0.5H), 6.77 (br, 0.50H), 5.74 (t, J = 7.2 Hz, 2H), 4.04 (s, 0.5H), 3.85 – 3.62 (m, 1.5H), 3.73 (s, 3H), 3.35 – 3.45 (m, 0.5H), 2.84 (dd, J = 17.7, 5.3 Hz, 0.5H), 2.78 – 2.68 (m, 0.5H), 2.63 – 2.52 (m, 1H), 2.39 (m, 1H), 2.32 – 2.17 (m, 1.5H), 2.02 (d, J = 5.1, 0.5H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 166.8, 166.5, 147.8, 135.8, 135.6, 134.7, 133.9, 133.8, 133.7, 133.0, 131.0, 130.6, 128.0, 126.9, 125.53, 125.47, 68.4, 66.9, 55.0, 52.7, 51.9, 32.1, 31.9, 28.7 ppm; IR ν_{max} 3529, 3494, 3331, 3092, 2926, 1705, 1536, 1439, 1360, 1302, 1252, 1167, 1078, 780, 730, 655 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_7\text{S}$ $[\text{M}]^+$: 356.0678, found 356.0685.

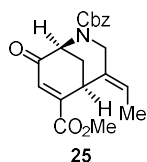
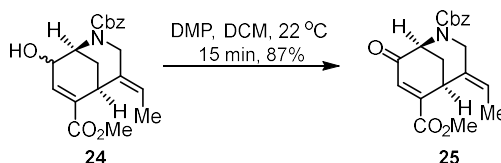


To a solution of **22** (10.7 g, 30.2 mmol, 1.0 equiv) and potassium carbonate (8.3 g, 60.4 mmol, 2.0 equiv) in 150 mL acetonitrile was added **18**^[3] (15.7 g, 60.4 mmol, 2.0 equiv) under nitrogen at room temperature, then the mixture was warmed to 50 °C and vigorously stirred for 24 h and quenched with water (40 mL). The solution was removed under vacuum and the resulting mixture was extracted with ethyl acetate (3×200 mL). The combined organic layer was washed with brine (50 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (10:1 to 1:1 petroleum ether-ethyl acetate) to give compound **23** (14.2 g, 88%) as a white solid. R_f = 0.60 (50% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 8.01 (d, J = 7.6 Hz, 1H), 7.72 – 7.53 (m, 3H), 6.75 (s, 1H), 6.03 (q, J = 6.0 Hz, 1H), 4.47 (d, J = 16.5 Hz, 1H), 4.05 (d, J = 16.5 Hz, 1H), 3.98 – 3.88 (m, 1H), 3.87 – 3.75 (m, 1H), 3.67 (s, 3H), 2.89 (dd, J = 17.2, 5.2 Hz, 1H), 2.74 – 2.63 (m, 1H), 2.61 – 2.39 (m, 2H), 2.25 – 2.05 (m, 1H), 1.65 (d, J = 6.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 166.3, 147.4, 136.7, 134.6, 133.7, 133.6, 131.8, 131.7, 127.6, 124.2, 105.3, 65.9, 60.0, 56.0, 51.7, 33.9, 30.7, 21.8 ppm; IR ν_{max} 3496, 2921, 1706, 1540, 1436, 1357, 1251, 1157, 1075, 1039, 953, 825, 727, 645 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{18}\text{H}_{21}\text{IN}_2\text{O}_7\text{S}$ $[\text{M}]^+$: 536.0114, found 536.0118.



To a solution of **23** (11.0 g, 20.5 mmol, 1.0 equiv) in 380 mL anhydrous and degassed acetonitrile in a round-bottom flask was added 1,2,2,6,6-pentamethylpiperidine (7.4 mL, 41.0 mmol, 2.0 equiv) and tetrakis(triphenylphosphine) palladium (4.7 g, 4.1 mmol, 0.2 equiv) under nitrogen at room temperature. The mixture was warmed to 80 °C and vigorously stirred for 7 h. Acetonitrile (about 190 mL) was removed under vacuum. Potassium carbonate (14.2 g, 102.5 mmol, 5.0 equiv) and thiophenol (8.4 mL, 82 mmol, 4.0 equiv) were added to the resulting mixture under nitrogen at room temperature. The reaction was stirred for 12 h at room temperature and then cooled to 0 °C, benzyl chloroformate (14.4 mL, 102.5 mmol, 5.0 equiv) was added. The mixture was warmed to 24 °C and vigorously stirred for another 7 h and quenched with water (40 mL). The solution was removed under vacuum and the resulting mixture was extracted with ethyl acetate (3×150 mL). The combined organic layer was washed with brine (50 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (15:1 to 3:2 petroleum ether-ethyl acetate) to give compound **24** (5.6 g, 77%) as a colorless oil. R_f = 0.21 (30% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 7.39 – 7.27 (m, 5H), 6.96 (s, 1H), 5.52 – 5.37 (m,

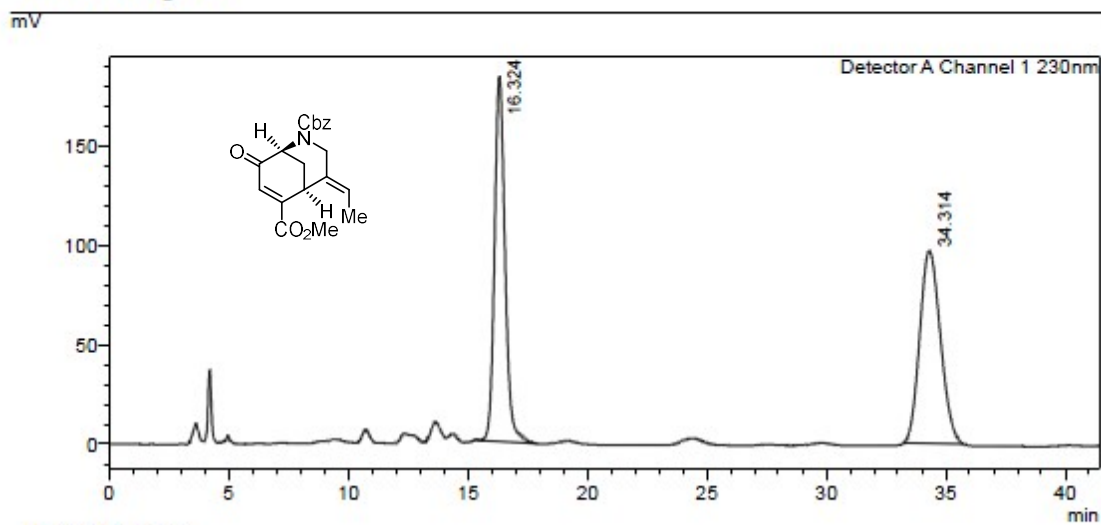
1H), 5.18 – 5.06 (m, 2H), 4.58 (br, 1.66H), 4.46 (br, 0.34H), 4.29 (d, $J = 14.6$ Hz, 0.36H), 4.20 (d, $J = 14.5$ Hz, 0.64H), 3.85 (s, 1H), 3.80 – 3.62 (m, 4H), 1.94 (t, $J = 14.2$ Hz, 1H), 1.85 (dd, $J = 13.1$, 2.8 Hz, 1H), 1.78 – 1.73 (dd, $J = 6.4$, 1.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 166.0, 157.4, 156.3, 140.9, 136.6, 136.5, 132.1, 131.8, 131.5, 131.4, 128.4, 127.8, 127.6, 127.5, 121.4, 121.1, 68.8, 68.1, 67.3, 51.7, 49.5, 49.4, 46.2, 45.9, 31.4, 30.9, 29.3, 12.6 ppm; IR ν_{max} 3420, 2950, 1674, 1426, 1336, 1231, 1097, 911, 730, 697 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{20}\text{H}_{23}\text{NO}_5$ $[\text{M}]^+$: 357.1576, found 357.1575.



To a solution of **24** (5.6 g, 15.7 mmol, 1.0 equiv) in 60 mL dichloromethane was added Dess-Martin periodinane (8.0 g, 18.8 mmol, 1.2 equiv) and 0.12 mL distilled water under nitrogen at 22 °C. The reaction mixture was stirred for 15 min at the same temperature. The solution was removed under vacuum and saturated aqueous NaHCO_3 (50 mL) and saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (50 mL) were added to the resulting mixture.

The mixture was stirred for 0.5 h at room temperature and extracted with ethyl acetate (3×150 mL). The combined organic layer was washed with brine (50 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (15:1 to 2:1 petroleum ether-ethyl acetate) to give compound **25** (4.9 g, 87%) as a yellow solid. $R_f = 0.59$ (30% ethyl acetate-hexane); Enantiomeric excess: 98.4%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 60/40, flow rate 1.0 mL/min, $T = 30$ °C, 230 nm), $t_R = 16.342$ min (minor), $t_R = 34.004$ min (major); $[\alpha]_D^{22} = 106.2$ ($c = 1.0$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.46 – 7.26 (m, 5H), 6.91 (s, 1H), 5.62 (s, 1H), 5.15 (s, 2H), 4.88 (s, 0.4H), 4.76 (s, 0.6H), 4.39 (d, $J = 14.9$ Hz, 0.6H), 4.3 (d, $J = 14.8$ Hz, 0.4H), 4.14 (t, $J = 2.9$ Hz, 1H), 3.82 (s, 3H), 3.67 (m, 1H), 2.24 (d, $J = 12.1$ Hz, 1H), 2.05 (d, $J = 13.1$ Hz, 1H), 1.80 (dd, $J = 6.8$, 2.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 195.9, 195.6, 165.6, 154.8, 148.3, 136.3, 133.3, 128.8, 128.4, 127.9, 127.7, 124.4, 67.5, 54.1, 53.8, 52.70, 52.67, 45.8, 45.5, 33.1, 30.8, 12.8 ppm; IR ν_{max} 2955, 1692, 1141, 1303, 1225, 1100, 1043, 968, 911, 825, 736, 701 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_5$ $[\text{M}]^+$: 355.1420, found 355.1418.

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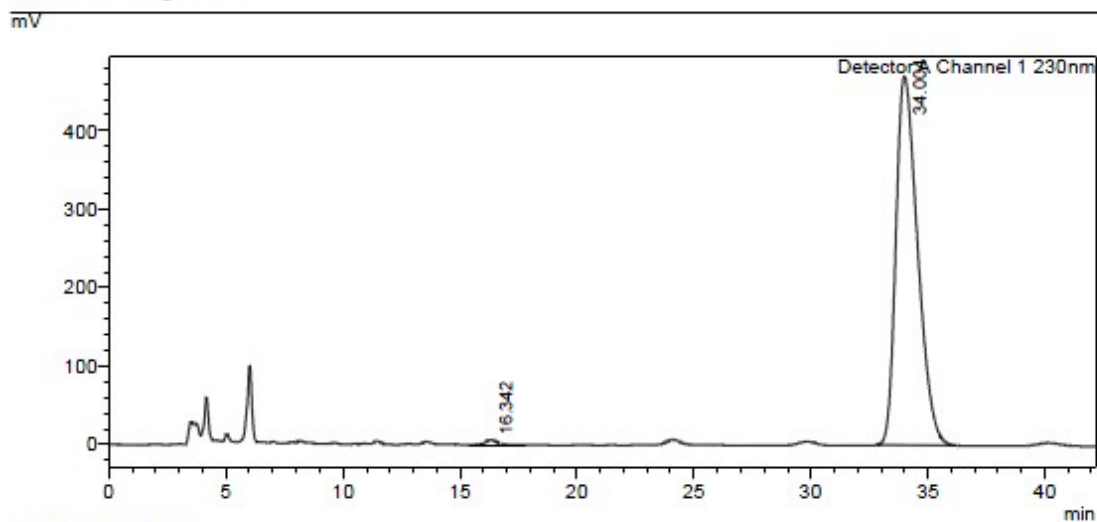


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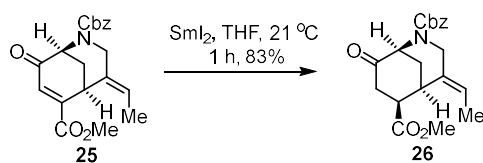
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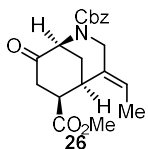


<Peak Table>

Detector A Channel 1 230nm

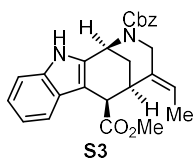
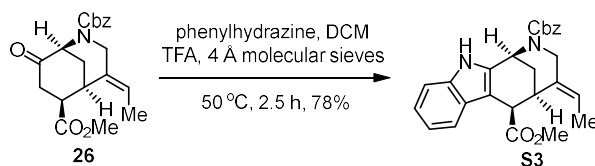
Peak#	Ret. Time	Area	Height	Conc.
1	16.342	234889	6541	0.767
2	34.004	30379766	470281	99.233
Total		30614655	476822	





To compound **25** (200.0 mg, 0.56 mmol, 1.0 equiv) in a dry and round-bottom flask was added samariumdiiiodide (0.1 mol in THF, 16.8 mL, 3.5 equiv) under nitrogen at 21 °C. The reaction mixture was stirred for 1 h at the same temperature. Then the reaction mixture was cooled to -78 °C, 20 mL brine was added dropwise until the blue faded.

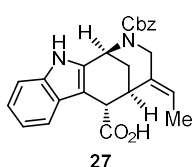
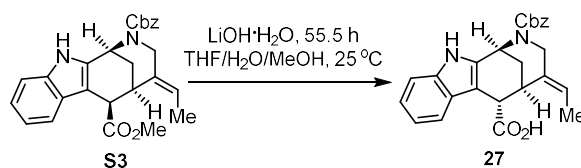
The mixture was warmed to room temperature and the solution was removed under vacuum. The resulting mixture was extracted with ethyl acetate (3×20 mL). The combined organic layer was washed with brine (10 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (15:1 to 3:2 petroleum ether-ethyl acetate) to give compound **26** (165.2 mg, 83%, dr = 5.7:1, determined by crude ¹H NMR) as a colorless oil (The diastereomer cannot be isolated very well). *R_f* = 0.31 (30% ethyl acetate-hexane); ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.27 (m, 5H), 5.56 (s, 1H), 5.20 – 5.02 (m, 2H), 4.62 – 4.62 (m, 1H), 4.30 (d, *J* = 16.2 Hz, 1H), 4.10 (d, *J* = 16.2 Hz, 1H), 3.70 (s, 0.3H), 3.65 (s, 2.7H), 3.43 (d, *J* = 3.5 Hz, 0.9H), 3.33 (s, 0.1 H), 3.13-2.92 (m, 2H), 2.51(d, *J* = 13.1 Hz, 0.9H), 2.43(d, *J* = 14.0 Hz, 0.1H), 2.10 (dt, *J* = 14.0, 7.2, 3.6 Hz, 1H), 2.03 (m, 1H), 1.70 (d, *J* = 6.5 Hz, 0.27H), 1.58 (dd, *J* = 6.9, 1.0 Hz, 2.8H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 205.4, 205.1, 172.9, 171.7, 155.0, 154.8, 136.0, 134.4, 130.1, 128.1, 128.0, 127.7, 127.5, 127.4, 122.9, 122.3, 67.1, 67.0, 58.9, 56.7, 51.9, 51.68, 51.67, 47.7, 46.6, 46.1, 45.5, 45.2, 38.9, 34.7, 32.2, 30.6, 30.2, 27.9, 27.6, 12.7, 12.2 ppm; IR *v*_{max} 2950, 1696, 1407, 1312, 1205, 1170, 1088, 1013, 740, 699 cm⁻¹; HRMS (EI): *m/z* calcd for C₂₀H₂₃NO₅ [M]⁺: 357.1576, found 357.1573.



To a solution of **26** (95.2 mg, 0.27 mmol, 1.0 equiv, dr = 5.7:1) and active 4Å molecular sieves (95 mg) in 5.4 mL anhydrous dichloromethane was added trifluoroacetic acid (0.2 mL, 2.7 mmol, 10.0 equiv) and phenylhydrazine (32 μL, 0.32 mmol, 1.2 equiv) in a tube sealing under nitrogen at 0 °C. The mixture was warmed to 50 °C and vigorously stirred for 2.5 h and cooled to room temperature

and quenched with saturated aqueous NaHCO₃ (2 mL). The resulting mixture was extracted with dichloromethane (3×5 mL). The combined organic layer was washed with brine (2 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (12:1 to 3:2 petroleum ether-ethyl acetate) to give compound **S3** (90.7 mg, 78%, dr = 10:1, determined by crude ¹H NMR) as a white solid (The diastereomer cannot be isolated very well). *R_f* = 0.59 (30% ethyl acetate-hexane); ¹H NMR (400 MHz, CDCl₃) δ 8.59 (s, 1H), 7.66 (s, 0.4H), 7.45 (s, 1.6H), 7.39 – 7.27 (m, 5H), 7.22 – 7.15 (m, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 5.58 – 5.37 (m, 2H), 5.21 – 5.05 (m, 2H), 4.26 (dd, *J* = 17.9, 6.1 Hz, 1H), 4.12 (d, *J* = 14.5 Hz, 1H), 3.81 – 3.72 (m, 1H), 3.68 (s, 3H), 3.54 (dd, *J* = 38.5, 14.3 Hz, 1H), 2.23 – 2.00 (m, 2H), 1.77 (d, *J* = 7.0 Hz, 0.3H), 1.68 (d, *J* = 6.7 Hz, 2.7H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 156.1, 136.4, 135.8, 133.2, 131.7, 128.9, 128.4, 127.9, 127.6, 125.9, 122.5, 122.3, 119.7, 119.1, 111.4, 108.8, 67.2, 51.6, 47.2, 44.6, 44.0, 32.4, 31.4, 12.5 ppm; IR *v*_{max} 3383, 3327,

3296, 2951, 2927, 1675, 1452, 1417, 1309, 1231, 1161, 1097, 1013, 736, 695 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_4$ $[\text{M}]^+$:430.1893, found 430.1897.

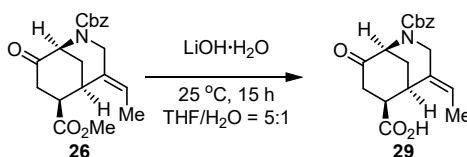


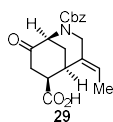
To a solution of **27** (11.1 mg, 0.0264 mmol, 1.0 equiv) in THF (0.3 mL), H_2O (60 μL) and MeOH (0.1 mL) was added lithium hydroxide monohydrate (2.2 mg, 0.106 mmol, 4.0 equiv) at 25 $^\circ\text{C}$ and vigorously stirred for 55.5 h. The mixture was acidified to pH 4 by slowly addition of 1 N HCl at 0 $^\circ\text{C}$, and extracted with dichloromethane (5 \times 5 mL). The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under vacuum to give **27** as a white solid, which was used in the subsequent step without further purification.

The anhydride **28** was prepared with two methods below:

Method A: To a solution of crude **27** (0.0264 mmol) and DMAP (0.6 mg, 0.005 mmol, 0.2 equiv) in 0.6 mL anhydrous dichloromethane was added Et_3N (10 μL , 0.071 mmol, 2.7 equiv) under nitrogen at 0 $^\circ\text{C}$. After stirring for 5 min at 0 $^\circ\text{C}$, bromoacetyl bromide **15** (4.7 μL , 0.053 mmol, 2.0 equiv) was added at the same temperature. After stirring for another 5 min, the mixture was warmed to room temperature and vigorously stirred for 10 h and quenched with water (1 mL). The resulting mixture was extracted with dichloromethane (3 \times 4 mL). The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the crude product was defined by ^1H NMR. No new product was detected and **27** was recovered.

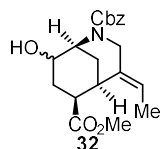
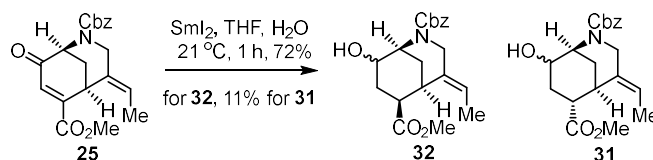
Method B: To a solution of crude **27** (0.0264 mmol) in 0.5 mL anhydrous dichloromethane was added oxalyl chloride (4.6 μL , 0.053 mmol, 2.0 equiv) and DMF (1 μL) under nitrogen at 0 $^\circ\text{C}$. The mixture was warmed to room temperature and vigorously stirred for 1 h. The solvent was removed under vacuum quickly under nitrogen. To the mixture was added bromoacetic acid (15 mg, 0.119 mmol, 4.5 equiv) in 0.6 mL anhydrous dichloromethane under nitrogen at 0 $^\circ\text{C}$. Then Et_3N (15 μL , 0.119 mmol, 4.5 equiv) was added at the same temperature. The mixture was warmed to room temperature and vigorously stirred for 9 h and quenched with water (1 mL). The resulting mixture was extracted with dichloromethane (3 \times 4 mL). The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the crude product was defined by ^1H NMR. No new product was detected and **27** was recovered.



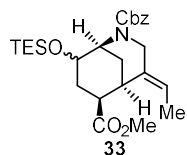
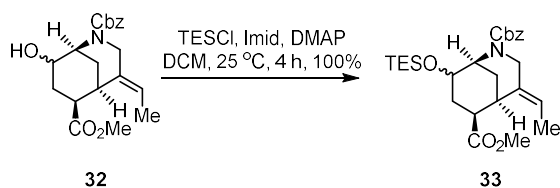


To a solution of **26** (136.5 mg, 0.382 mmol, 1.0 equiv) in THF (3.0 mL) and H₂O (0.6 mL) was added lithium hydroxide, monohydrate (32 mg, 0.764 mmol, 2.0 equiv) at 25 °C and vigorously stirred for 15 h. The mixture was acidified to pH 4 by slowly addition of 1 N HCl at 0 °C, and extracted with dichloromethane (5×10 mL). The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under vacuum to give **29** as a white solid, which was used in the subsequent step without further purification.

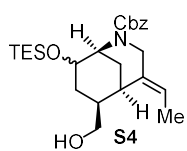
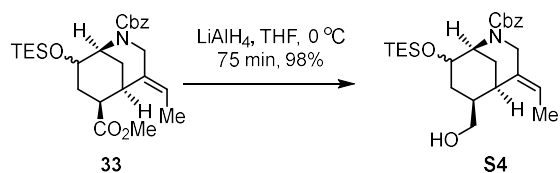
The anhydride **30** was prepared with two methods the same as **28**. No new product was detected and **29** was recovered.



To compound **25** (4.2 g, 11.8 mmol, 1.0 equiv) and degassed distilled water (21.2 mL, 1180 mmol, 100 equiv) in a round-bottom flask was added samariumdiiiodide (0.1 mol in THF, 709 mL, 70.8 mmol, 6.0 equiv) under nitrogen at 21 °C. After stirring for 20 min, an aliquot of samariumdiiiodide (120 mL, 11.8 mmol, 1.0 equiv) was added at the same temperature. Following 20 min, an additional aliquot of samariumdiiiodide (120 mL, 11.8 mmol, 1.0 equiv) was added. The reaction mixture was stirred for another 20 min at the same temperature, and quenched with 50 mL brine. THF was removed in vacuo and the resulting mixture was extracted with ethyl acetate (4×200 mL). The combined organic layer was washed with 80 mL saturated aqueous Na₂S₂O₃ and 50 mL 1 N HCl and 50 mL brine, then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (15:1 to 1:1 petroleum ether-ethyl acetate) to give compound **32** (3.0 g, 72%) as a colorless oil, *R_f* = 0.16 (40% ethyl acetate-hexane), and compound **31** (460 mg, 11%) as a colorless oil, *R_f* = 0.46 (40% ethyl acetate-hexane); **32** for ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.27 (m, 5H), 5.51 – 5.37 (m, 1H), 5.21 – 5.05 (m, 2H), 4.51 (d, *J* = 2.0 Hz, 0.7H), 4.45 – 4.32 (m, 0.5H), 4.19 (q, *J* = 16.2 Hz, 1.5H), 4.06 (d, *J* = 16.3 Hz, 0.3H), 3.97 – 3.88 (m, 0.7H), 3.86 – 3.77 (m, 0.3H), 3.62 (s, 3H), 3.44 (s, 1H), 3.26 (d, *J* = 2.8 Hz, 1H), 2.77 (dt, *J* = 13.1, 4.5 Hz, 1H), 2.11 – 1.99 (m, 1H), 1.96 – 1.68 (m, 3H), 1.53 (d, *J* = 6.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 173.0, 158.2, 156.0, 136.5, 136.4, 131.2, 128.4, 128.0, 127.7, 121.9, 72.7, 71.3, 67.4, 67.2, 51.5, 51.0, 50.7, 50.2, 49.6, 44.6, 31.5, 30.9, 30.5, 30.4, 30.2, 12.4, 12.2 ppm; IR ν_{max} 3419, 2950, 1732, 1677, 1417, 1319, 1235, 1195, 1100, 1008, 968, 739, 698 cm⁻¹; HRMS (EI): *m/z* calcd for C₂₀H₂₅NO₅ [M]⁺:359.1733, found 359.1730; **31** for ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.27 (m, 5H), 5.44 (dq, *J* = 13.8, 6.7 Hz, 1H), 5.19 – 5.04 (m, 2H), 4.27 – 4.12 (m, 2H), 4.12 – 3.99 (m, 2H), 3.62 (s, 3H), 3.28 (d, *J* = 2.3 Hz, 1H), 3.09 (tt, *J* = 13.0, 4.5 Hz, 1H), 2.35 (ddt, *J* = 33.9, 13.3, 2.8 Hz, 1H), 2.13 – 1.98 (m, 1H), 1.90 – 1.77 (m, 1H), 1.62 – 1.49 (m, 4H) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 174.4, 174.2, 155.8, 155.3, 136.6, 136.4, 131.5, 131.4, 128.4, 128.0, 127.81, 127.76, 121.63, 121.55, 67.3, 67.2, 67.0, 66.2, 51.4, 50.5, 50.2, 48.8, 48.6, 40.8, 40.7, 31.2, 31.1, 29.4, 29.0, 26.4, 26.2, 12.41, 12.38 ppm; IR ν_{max} 3445, 2928, 1734, 1695, 1413, 1239, 1093, 1039, 734, 699 cm⁻¹; HRMS (EI): *m/z* calcd for C₂₀H₂₅NO₅ [M]⁺:359.1733, found 359.1737.

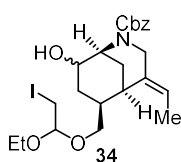
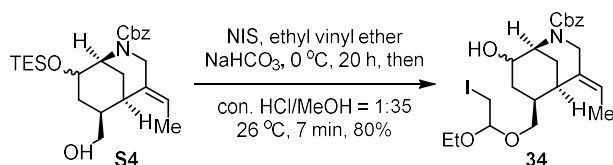


To a solution of **32** (3.8 g, 10.6 mmol, 1.0 equiv) and imidazole (2.2 g, 31.8 mmol, 3.0 equiv) and 4-dimethylaminopyridine (260 mg, 2.1 mmol, 0.2 equiv) in 100 mL anhydrous dichloromethane was added triethylchlorosilane (4.4 mL, 26.5 mmol, 2.5 equiv) under nitrogen at 25 °C. The reaction mixture was stirred for 4 h at the same temperature and quenched with water (40 mL). The resulting mixture was extracted with dichloromethane (3×100 mL). The combined organic layer was washed with brine (50 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (12:1 to 4:1 petroleum ether-ethyl acetate) to give compound **33** (5.0 g, 100%) as a colorless oil. R_f = 0.63 (20% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 7.37 – 7.27 (m, 5H), 5.53 – 5.39 (m, 1H), 5.32 (d, J = 12.4 Hz, 0.5H), 5.12 (q, J = 12.6 Hz, 1H), 4.90 (d, J = 12.4 Hz, 0.5H), 4.51 (dd, J = 6.5, 3.8 Hz, 0.5H), 4.42 – 4.34 (m, 1H), 4.19 (d, J = 12.4 Hz, 0.5H), 4.02 (qt, J = 2.3 Hz, 1H), 3.94 – 3.79 (m, 1H), 3.56 (d, J = 3.9 Hz, 3H), 3.26 (s, 1H), 2.85 – 2.75 (m, 1H), 2.10 – 1.95 (m, 2H), 1.87 – 1.77 (m, 1H), 1.76 – 1.65 (m, 1H), 1.58 – 1.50 (m, 3H), 0.95 (t, J = 8.0 Hz, 4.5H), 0.88 (t, J = 8.0 Hz, 4.5H), 0.61 (ddd, J = 10.2, 7.9, 1.5 Hz, 3H), 0.51 (q, J = 7.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 173.4, 173.2, 156.4, 156.0, 137.2, 137.0, 132.0, 131.8, 128.34, 128.29, 128.0, 127.8, 127.7, 127.6, 121.9, 121.7, 71.1, 71.0, 66.9, 66.7, 51.6, 51.5, 50.8, 50.43, 50.39, 50.37, 45.1, 45.0, 32.64, 32.55, 32.2, 31.8, 31.4, 30.9, 30.7, 30.2, 29.7, 12.30, 12.27, 6.83, 6.78, 4.82, 4.76 ppm; IR ν_{max} 2952, 2876, 1737, 1697, 1417, 1316, 1233, 1100, 1017, 969, 832, 728, 698 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{26}\text{H}_{39}\text{NO}_5\text{Si}$ $[\text{M}]^+$: 473.2598, found 473.2607.

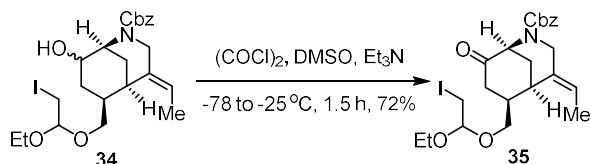


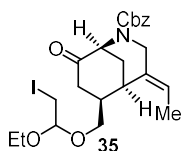
To a solution of **33** (4.2 g, 8.9 mmol, 1.0 equiv) in anhydrous THF (90mL) was added LiAlH_4 (2.4 M in THF, 4.5 mL, 10.7 mmol, 1.2 equiv) dropwise at 0 °C under nitrogen. The reaction mixture was stirred for 75 min at the same temperature and quenched with 10 mL methanol. The resulting mixture was warmed to room temperature and 30 mL saturated aqueous potassium sodium tartrate was added and stirred overnight. THF was removed in vacuo and the resulting mixture was extracted with ethyl acetate (3×100 mL). The combined organic layer was washed with brine (50 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (10:1 to 2:1 petroleum ether-ethyl acetate) to give compound **S4** (3.9 g, 98%) as a colorless oil. R_f = 0.21 (20% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 7.38 – 7.26 (m, 5H), 5.58 – 5.43 (m, 1H), 5.32 (d, J = 12.4 Hz, 0.5H), 5.12 (dd, J = 12.4, 5.6 Hz 1H), 4.89

(d, $J = 12.4$ Hz, 0.5H), 4.50 (dd, $J = 4.0, 2.7$ Hz, 0.5H), 4.42 – 4.33 (m, 1H), 4.28 (d, $J = 16.0$ Hz, 0.5H), 4.05 – 3.81 (m, 2H), 3.53 – 3.40 (m, 2H), 2.98 (q, $J = 3.1$ Hz, 1H), 2.03 – 1.84 (m, 2H), 1.84 – 1.74 (m, 1H), 1.73 – 1.54 (m, 5H), 0.94 (t, $J = 7.9$ Hz, 4H), 0.87 (t, $J = 7.9$ Hz, 5H), 0.61 (ddd, $J = 10.2, 17.9, 1.5$ Hz, 3H), 0.50 (q, $J = 7.8$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 156.5, 156.0, 137.2, 137.0, 133.2, 133.0, 128.34, 128.28, 128.0, 127.74, 127.66, 121.6, 121.5, 71.7, 71.6, 66.9, 66.7, 66.05, 65.99, 51.4, 51.0, 50.9, 50.7, 42.4, 42.2, 34.5, 34.4, 32.2, 31.9, 30.0, 29.8, 12.70, 12.66, 6.85, 6.80, 4.83, 4.77 ppm; IR ν_{max} 2952, 2876, 1737, 1697, 1417, 1233, 1101, 1017, 832, 729 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{25}\text{H}_{39}\text{NO}_4\text{Si}$ $[\text{M}]^+$: 445.2648, found 445.2647.



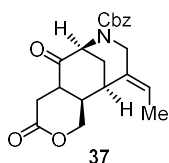
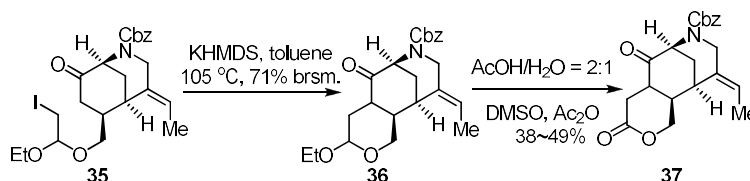
To a solution of **S4** (2.8 g, 6.3 mmol, 1.0 equiv) and NaHCO_3 (1.6 g, 18.9 mmol, 3.0 equiv) in 60 mL anhydrous dichloromethane was added ethyl vinyl ether (3.6 mL, 37.8 mmol, 6.0 equiv) and N-iodosuccinimide (2.8 g, 12.6 mmol, 2.0 equiv) under nitrogen at 0 °C. The reaction mixture was stirred for 20 h at the same temperature in dark. The solvent was removed under vacuum and 72 mL con.HCl/MeOH (1:35) was added at 26 °C. The reaction mixture was stirred for 7 min at the same temperature and then cooled to 0 °C, saturated aqueous NaHCO_3 was added until pH is 7 to 8. The resulting mixture was extracted with ethyl acetate (4×80 mL). The combined organic layer was washed with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (30 mL) and brine (30 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (20:1 to 3:2 petroleum ether-ethyl acetate) to give compound **34** (2.7 g, 80%) as a colorless oil. $R_f = 0.30$ (30% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.27 (m, 5H), 5.58 – 5.45 (m, 1H), 5.23 – 5.05 (m, 2H), 4.62 – 4.48 (m, 2H), 4.37 (d, $J = 17.2$ Hz, 1H), 4.26 (d, $J = 16.2$ Hz, 1H), 4.05 (d, $J = 16.2$ Hz, 1H), 4.00 – 3.80 (m, 1H), 3.67 – 3.49 (m, 2H), 3.34 (d, $J = 6.7$ Hz, 1H), 3.22 – 3.13 (m, 2H), 2.95 (s, 1H), 2.14 – 1.97 (m, 2H), 1.84 – 1.72 (m, 2H), 1.66 – 1.57 (m, 3H), 1.28 – 1.13 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 158.2, 156.0, 136.5, 131.9, 131.8, 128.5, 128.4, 128.04, 127.96, 127.8, 121.9, 121.8, 102.0, 101.9, 73.3, 72.0, 69.9, 69.4, 67.4, 67.2, 62.6, 62.2, 62.1, 51.5, 51.3, 50.7, 50.1, 39.8, 39.6, 33.0, 32.4, 31.5, 31.0, 29.8, 29.7, 15.3, 15.1, 13.2, 13.1, 13.0, 12.9, 5.3, 5.2 ppm; IR ν_{max} 3934, 1736, 1682, 1416, 1321, 1236, 1102, 1046, 740, 698 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{23}\text{H}_{32}\text{NO}_5\text{I}$ $[\text{M}]^+$: 529.1325, found 529.1328.





To a solution of $(\text{COCl})_2$ (0.39 mL, 4.5 mmol, 1.5 equiv) in 28 mL anhydrous dichloromethane was added DMSO (0.64 mL, 9.1 mmol, 3.0 equiv) under nitrogen at -78°C . The reaction mixture was stirred for 15 min at the same temperature and compound **34** (1.6 g, 3.02 mmol, 1.0 equiv) in 2 mL dichloromethane was added.

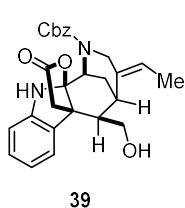
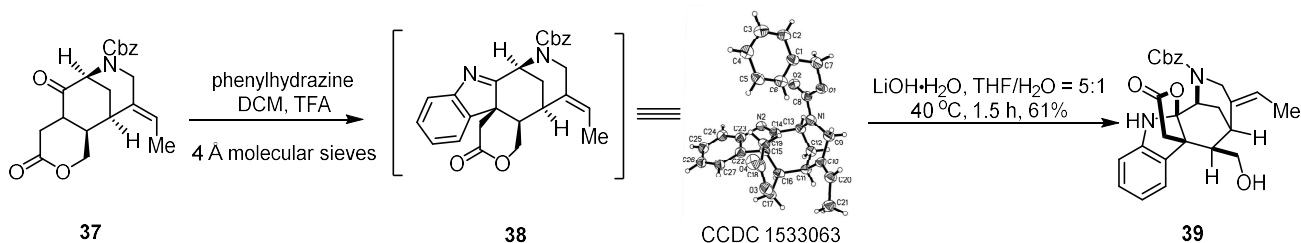
The resulting mixture was stirred for 1.5 h at -78°C , Et_3N (2.1 mL, 15.1 mmol, 5.0 equiv) was added. Then the reaction mixture was slowly warmed to -25°C for 1.5 h and saturated aqueous NaHCO_3 (20 mL) was added and warmed to room temperature for 10 min. The resulting mixture was extracted with dichloromethane (3×50 mL). The combined organic layer was washed with saturated aqueous NaHCO_3 (10 mL) and brine (10 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (15:1 to 2:1 petroleum ether-ethyl acetate) to give compound **35** (1.1 g, 72%) as a colorless oil. $R_f = 0.52$ (30% ethyl acetate-hexane); ^1H NMR (400 MHz, CDCl_3) δ 7.38 – 7.26 (m, 5H), 5.62 (d, $J = 5.2$ Hz, 1H), 5.11 (d, $J = 4.8$ Hz, 2H), 4.53 (dt, $J = 11.6, 5.4$ Hz, 1H), 4.47 (s, 1H), 4.31 (d, $J = 16.3$ Hz, 1H), 4.06 (d, $J = 16.3$ Hz, 1H), 3.66 – 3.47 (m, 2H), 3.46 – 3.32 (m, 1H), 3.24 – 3.06 (m, 3H), 2.54 (d, $J = 13.6$ Hz, 1H), 2.45 – 2.33 (m, 1H), 2.34 – 2.23 (m, 1H), 2.09 (dt, $J = 13.8, 3.2$ Hz, 1H), 1.97 (d, $J = 13.1$ Hz, 1H), 1.72 – 1.62 (m, 3H), 1.20 (td, $J = 7.0, 2.7$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 206.1, 155.2, 136.2, 131.0, 130.8, 128.3, 127.9, 127.6, 123.1, 122.9, 102.0, 101.7, 68.8, 68.7, 67.3, 62.5, 62.1, 57.7, 48.2, 42.5, 41.0, 32.8, 29.81, 29.78, 15.08, 15.06, 13.20, 13.16, 5.0, 4.9 ppm; IR ν_{max} 2975, 1701, 1406, 1372, 1310, 1237, 1105, 1046, 729, 698 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{23}\text{H}_{30}\text{NO}_5\text{I}$ $[\text{M}]^+$: 527.1169, found 527.1179.



To a solution of **35** (1.0 g, 1.9 mmol, 1.0 equiv) in 39 mL anhydrous toluene was added KHMDS (1.0 M in THF, 2.0 mL, 2.0 mmol, 1.05 equiv) under nitrogen at room temperature. The mixture was warmed to 105°C and vigorously stirred for 27 min. The mixture was poured into ice saturated aqueous NH_4Cl (50 mL). The resulting mixture was extracted with ethyl acetate (3×80 mL). The combined organic layer was washed with brine (30 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (20:1 to 2:1 petroleum ether-ethyl acetate) to give compound **36** (430.8 mg, 57%) as a colorless oil and compound **35** (137.1 mg, 14%). $R_f = 0.36$ (30% ethyl acetate-hexane) for **36**.

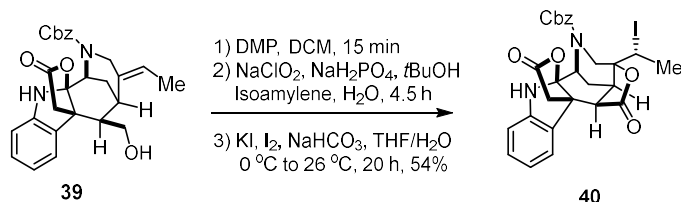
To a solution of **36** (250 mg, 0.63 mmol, 1.0 equiv) in 6 mL AcOH was added 3 mL H_2O at room temperature. The mixture was warmed to 60°C and vigorously stirred for 4.5 h. AcOH was removed in vacuo and the resulting mixture was extracted with dichloromethane (4×10 mL). The combined organic layer was washed with saturated aqueous NaHCO_3 (4 mL) and brine (3 mL), then dried over anhydrous sodium sulfate for 1 h. The solvent was removed under vacuum, and the residue was dissolved in dry DMSO (6 mL). To the solution Ac_2O (0.3 mL, 3.2 mmol, 5.0 equiv) was added under nitrogen at room temperature. The mixture was warmed to 32°C and vigorously stirred for 6 h. The mixture was poured into H_2O (5 mL). The resulting mixture was extracted with ethyl acetate

(3×15 mL). The combined organic layer was washed with H₂O (3×4 mL) and brine (4 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (12:1 to 1:1 petroleum ether-ethyl acetate) to give compound **37** (95.6 mg, 41%) as a white solid. *R*_f = 0.51 (50% ethyl acetate-hexane); [α]_D²² = 60.3 (c = 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.26 (m, 5H), 5.70 (d, *J* = 5.7 Hz, 1H), 5.19 (d, *J* = 12.3 Hz, 1H), 5.07 (t, *J* = 12.1 Hz, 1H), 4.54 – 4.27 (m, 3H), 4.23 – 4.11 (m, 1H), 4.07 (t, *J* = 11.2 Hz, 1H), 3.10 (d, *J* = 2.7 Hz, 1H), 3.00 (td, *J* = 11.9, 5.5 Hz, 1H), 2.82 – 2.58 (m, 2H), 2.55 – 2.27 (m, 2H), 2.20 – 1.96 (m, 3H), 1.63 (d, *J* = 7.0 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 205.5, 205.2, 168.8, 155.4, 154.9, 135.9, 130.6, 128.4, 128.2, 127.9, 124.0, 71.4, 67.7, 67.4, 58.3, 46.1, 45.7, 45.0, 44.8, 41.0, 40.7, 33.0, 32.8, 29.3, 29.2, 28.8, 13.7 ppm; IR ν_{max} 3478, 2926, 1729, 1406, 1313, 1233, 1174, 1114, 1048, 970, 745, 700 cm⁻¹; HRMS (EI): *m/z* calcd for C₂₁H₂₃NO₅ [M]⁺: 369.1576, found 369.1579.

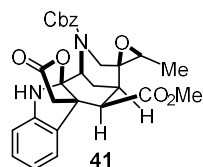
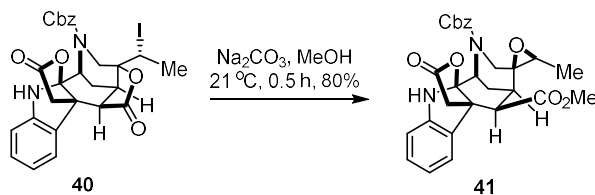


To a solution of **37** (95.0 mg, 0.26 mmol, 1.0 equiv) and active 4Å molecular sieves (95 mg) in 5 mL anhydrous dichloromethane was added trifluoroacetic acid (0.29 mL, 3.9 mmol, 15.0 equiv) and phenylhydrazine (31 μ L, 0.31 mmol, 1.2 equiv) in a tube sealing under nitrogen at 0 °C. The mixture was warmed to 70 °C and vigorously stirred for 10 min and slowly dropped to 63 °C and vigorously stirred for 3 h. Then the mixture was cooled to room temperature and quenched with saturated aqueous NaHCO₃ (2 mL). The resulting mixture was extracted with dichloromethane (4×8 mL), and then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was dissolved in 3.6 mL THF/H₂O (5:1). To the mixture, LiOH·H₂O (27 mg, 0.64 mmol, 2.5 equiv) was added at room temperature. The mixture was warmed to 40 °C and vigorously stirred for 1.5 h. The mixture was poured into H₂O (3 mL). The resulting mixture was extracted with ethyl acetate (3×15 mL). The combined organic layer was washed with brine (4 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (12:1 to 1:1 petroleum ether-ethyl acetate) to give compound **39** (73.5 mg, 61%) as a white solid. *R*_f = 0.49 (50% ethyl acetate-hexane); [α]_D¹⁸ = -43.5 (c = 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.44 – 7.28 (m, 5H), 7.24 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.83 (q, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 5.76 – 5.60 (m, 1H), 5.30 – 5.08 (m, 2.6H), 4.84 (d, *J* = 20.5 Hz, 1H), 4.68 (s, 0.4H), 4.33 (dd, *J* = 33.2, 17.2 Hz, 1H), 4.05 – 3.97 (m, 1H), 3.96 – 3.81 (m, 1H), 3.70 (dt, *J* = 19.6, 9.9 Hz, 1H), 3.18 (s, 1H), 3.02 (dd, *J* = 27.8, 18.1 Hz, 1H), 2.81 (dd, *J* = 18.1, 9.3 Hz, 1H), 2.11 (t, *J* = 15.1 Hz, 1H), 2.03 – 1.91 (m, 2H), 1.76 (d, *J* = 6.9 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ 173.6, 173.4, 156.3, 155.7, 145.2, 144.8, 136.6, 136.4, 135.5, 135.2, 129.7, 129.1, 128.5, 128.0, 127.8, 125.2, 125.0, 124.1, 124.0, 123.9, 120.7, 120.4, 110.3, 105.6,

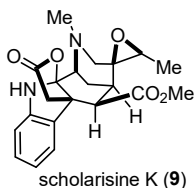
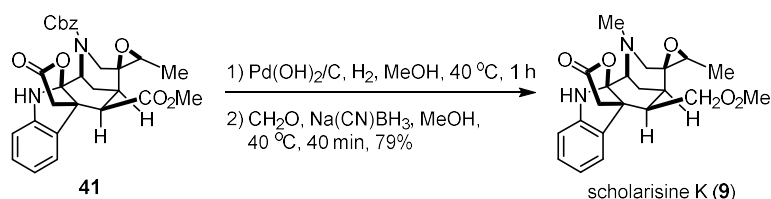
105.0, 67.6, 61.3, 61.1, 50.5, 50.2, 50.0, 49.8, 49.6, 47.5, 47.2, 36.6, 29.5, 29.3, 27.2, 13.3, 13.2 ppm; IR ν_{max} 3397, 3309, 2887, 1757, 1686, 1471, 1413, 1313, 1230, 1106, 1052, 972, 913, 740 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_5$ $[\text{M}]^+$: 460.1998, found 460.2007.



To a solution of **39** (33.9 mg, 0.0736 mmol, 1.0 equiv) in 1.4 mL dichloromethane was added Dess-Martin periodinane (59.0 g, 0.13 mmol, 1.8 equiv) under nitrogen at 25 °C. The reaction mixture was stirred for 15 min at the same temperature. To the solution was added saturated aqueous NaHCO_3 (1 mL) and saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (1 mL). The mixture was stirred for 10 min at room temperature and extracted with ethyl acetate (4×5 mL). The combined organic layer was washed with brine (3 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was dissolved in *t*BuOH (0.6 mL) and 2-methyl-2-butene (0.4 mL). To the solution was added a solution of sodium chlorite (33.0 mg, 0.37 mmol, 5.0 equiv) and monobasic sodium phosphate (69 mg, 0.44 mmol, 6.0 equiv) in H_2O (0.4 mL) at 0 °C. The mixture was warmed to room temperature and vigorously stirred for 4.5 h. The reaction mixture was poured into water (1 mL) and acidified to pH 4 by slowly addition of 1 N HCl at 0 °C, and extracted with dichloromethane (5×6 mL). The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the residue was dissolved in 1.2 mL THF/ H_2O (2:1). To the solution was added NaHCO_3 (15.5 mg, 0.18 mmol, 2.5 equiv) and a solution of KI (49.0 mg, 0.29 mmol, 4.0 equiv) and I_2 (37 mg, 0.15 mmol, 2.0 equiv) in H_2O (0.6 mL) at 0 °C. The reaction mixture was stirred for 0.5 h at the same temperature. The mixture was warmed to room temperature and vigorously stirred for 20 h in dark and quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (1 mL). The resulting mixture was extracted with ethyl acetate (4×5 mL). The combined organic layer was washed with brine (3 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel (10:1 to 1:1 petroleum ether-ethyl acetate) to give compound **40** (23.7 mg, 54%) as a white solid. R_f = 0.58 (4% methanol-dichloromethane); $[\alpha]_{\text{D}}^{18}$ = -57.9 (c = 0.57, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.45 – 7.32 (m, 5H), 7.19 (d, J = 7.4 Hz, 1H), 7.15 (td, J = 7.7, 1.1 Hz, 1H), 6.90 – 6.85 (td, J = 7.5, 0.7 Hz, 1H), 6.68 (d, J = 7.8 Hz, 1H), 5.24 – 5.15 (m, 2H), 5.03 (br, 1H), 4.49 (d, J = 1.9 Hz, 1H), 4.28 (q, J = 6.9 Hz, 1H), 4.23 (d, J = 14.5 Hz, 1H), 3.61 (d, J = 18.0 Hz, 1H), 3.50 (d, J = 14.5 Hz, 1H), 3.34 (d, J = 11.3 Hz, 1H), 2.89 (d, J = 11.2 Hz, 1H), 2.80 (d, J = 18.0 Hz, 1H), 2.01 (d, J = 6.8 Hz, 5H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 173.80, 173.78, 173.2, 173.1, 157.6, 146.04, 146.00, 135.8, 133.4, 129.5, 128.6, 128.30, 128.28, 122.4, 120.7, 109.7, 103.7, 103.6, 85.9, 68.4, 52.0, 49.6, 47.1, 44.1, 40.5, 34.8, 31.9, 22.2, 21.7 ppm; IR ν_{max} 3393, 2933, 1769, 1709, 1611, 1473, 1395, 1317, 1212, 1168, 1102, 1044, 949, 907, 748, 700 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_6\text{I}$ $[\text{M}]^+$: 600.0757, found 600.0754.

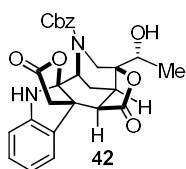
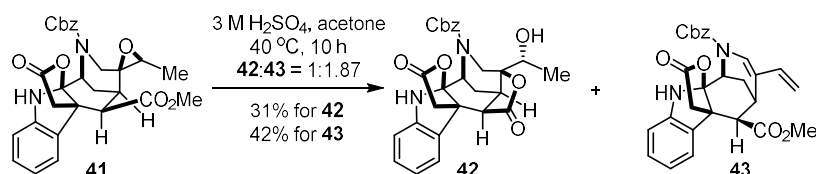


To a solution of **40** (26.0 mg, 0.0433 mmol, 1.0 equiv) in 2.0 mL anhydrous methanol was added Na_2CO_3 (13.8 mg, 0.08 mmol, 3.0 equiv) under nitrogen at 21 °C. The reaction mixture was stirred for 0.5 h at the same temperature and quenched with H_2O (1 mL). The resulting mixture was extracted with dichloromethane (4×5 mL). The combined organic layer was washed with brine (2 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum and was purified by preparation thin layer chromatography (4% methanol – dichloromethane) to give **41** (17.4 mg, 80%) as a white solid. $R_f = 0.57$ (4% methanol-dichloromethane); $[\alpha]_D^{19} = -32.7$ ($c = 1.0$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.56 – 7.28 (m, 6H), 7.13 (t, $J = 7.6$ Hz, 1H), 6.83 (t, $J = 7.5$ Hz, 1H), 6.73 (d, $J = 7.8$ Hz, 1H), 5.17 (s, 2.7H), 4.81 (s, 1H), 4.61 (s, 0.3H), 3.70 (d, $J = 15.3$ Hz, 1H), 3.66 (s, 3H), 3.61 (d, $J = 19.0$ Hz, 1H), 3.55 (d, $J = 19.1$ Hz, 1H), 3.37 (d, $J = 13.5$ Hz, 1H), 2.94 (s, 1H), 2.73 (q, $J = 3.5$ Hz, 1H), 2.60 (d, $J = 3.9$ Hz, 1H), 2.27 (d, $J = 13.9$ Hz, 1H), 2.13 (d, $J = 14.4$ Hz, 1H), 1.34 (d, $J = 5.5$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 174.1, 170.9, 156.8, 145.2, 136.2, 134.7, 129.2, 128.5, 128.2, 128.1, 125.1, 121.0, 110.7, 104.6, 68.0, 60.8, 58.8, 51.8, 51.6, 50.2, 49.5, 48.2, 37.6, 27.2 (two carbon), 11.6 ppm; IR ν_{max} 3325, 2928, 2850, 1701, 1611, 1398, 1335, 1306, 1233, 1177, 1103, 1057, 1020, 909, 873, 850, 814, 750, 699 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{28}\text{H}_{28}\text{N}_2\text{O}_7$ $[\text{M}]^+$: 504.1897, found 504.1904.



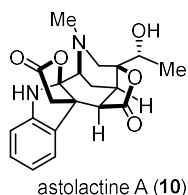
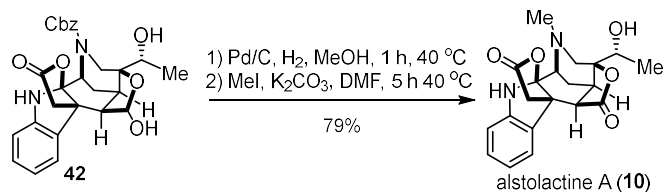
To a solution of **41** (6.0 mg, 0.0119 mmol, 1.0 equiv) in 0.3 mL methanol was added 10 % $\text{Pd(OH)}_2/\text{C}$ (3.3 mg, 0.0024 mmol, 0.2 equiv). The resulting suspension was stirred at 40 °C under H_2 for 1 h, the mixture was filtered and concentrated. The residue was dissolved in 0.3 mL methanol. To the solution was added aqueous CH_2O (50 μL) and Na(CN)BH_3 (7.5 mg, 0.119 mmol, 10.0 equiv) at room temperature. The resultant suspension was stirred at 40 °C for 40 min. To the solution was added saturated aqueous NaHCO_3 (1 mL) at room temperature. The resulting mixture was extracted with dichloromethane (4×4 mL). The combined organic layer was washed with brine (2 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the residue was dissolved in MeOH (1.2 mL) and sodium phosphate buffer (0.3 mL, pH 7.7). To the solution was added silica gel (200 mg) at room temperature. The mixture vigorously stirred for 6 h. The resulting mixture was extracted with dichloromethane (4×5 mL). The combined organic layer was washed with brine (2 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum and was purified by preparation thin layer chromatography (4% methanol – dichloromethane)

to give scholarisine K (**9**) (3.6 mg, 79%) as a white solid. R_f = 0.58 (4% methanol-dichloromethane); $[\alpha]_D^{24}$ = 10.4 (c = 0.13, MeOH), [Lit. $[\alpha]_D^{26}$ = 16.3 (c = 0.13, MeOH)]^[4]; ^1H NMR (500 MHz, CDCl_3) δ 7.34 (d, J = 7.5 Hz, 1H), 7.09 (td, J = 7.7 Hz, 0.9, 1H), 6.80 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 4.63 (s, 1H), 3.75 (d, J = 18.3 Hz, 1H), 3.62 (s, 3H), 3.42 (d, J = 18.3 Hz, 1H), 3.15 (d, J = 13.3 Hz, 1H), 2.99 (dd, J = 4.7, 1.6 Hz, 1H), 2.80 (q, J = 5.5 Hz, 1H), 2.63 (dd, J = 7.5, 3.6 Hz, 1H), 2.49 (d, J = 4.5 Hz, 1H), 2.39 (s, 3H), 2.16 (dt, J = 14.3, 4.3 Hz, 1H), 2.12 (d, J = 13.3 Hz, 1H), 2.04 (dt, J = 14.4, 2.3 Hz, 1H), 1.29 (d, J = 5.6 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 175.3, 171.2, 145.9, 135.4, 128.8, 125.2, 120.8, 110.6, 106.0, 62.2, 58.1, 57.6, 56.4, 51.8, 51.4, 51.2, 45.7, 39.1, 27.2, 25.8, 11.3 ppm; IR ν_{max} 2959, 2921, 2853, 1737, 1466, 1260, 1230, 1172, 1097, 1020, 946, 801, 765, 744 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_5$ $[\text{M}]^+$: 384.1685, found 384.1686.



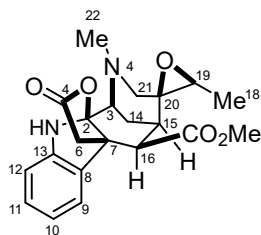
To a solution of **41** (20.0 mg, 0.0396 mmol, 1.0 equiv) in 0.6 mL acetone was added 3 M H_2SO_4 (132 μL , 0.396 mmol, 10.0 equiv) dropwise at 0 $^\circ\text{C}$. The mixture was warmed to 40 $^\circ\text{C}$ and vigorously stirred for 10 h. To the solution was added saturated aqueous NaHCO_3 (1.5 mL) at room temperature. The resulting mixture was extracted with dichloromethane (5 \times 4 mL). The combined organic layer was washed with brine (2 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum and was purified by preparation thin layer chromatography (4% methanol – dichloromethane) to give **42** (6.1 mg, 31%) as a white solid. R_f = 0.25 (4% methanol-dichloromethane); $[\alpha]_D^{19}$ = -44.6 (c = 0.63, CHCl_3); and **43** (8.1 mg, 42%) as a colorless oil, R_f = 0.62 (4% methanol – dichloromethane); $[\alpha]_D^{18}$ = -2.2 (c = 0.88, CHCl_3); **42** for $\delta^1\text{H}$ NMR (500 MHz, CDCl_3) δ 7.40 – 7.30 (m, 5H), 7.24 (d, J = 7.6 Hz, 1H), 7.14 (t, J = 7.3 Hz, 1H), 6.88 (t, J = 7.5 Hz, 1H), 6.68 (d, J = 7.8 Hz, 1H), 5.17 (q, J = 12.2 Hz, 2H), 5.00 (s, 1H), 4.55 (s, 1H), 3.97 (d, J = 15.0 Hz, 1H), 3.72 (d, J = 5.7 Hz, 1H), 3.31 (dd, J = 19.7, 16.5 Hz, 2H), 3.17 (d, J = 10.6 Hz, 1H), 2.99 (d, J = 10.5 Hz, 1H), 2.92 (d, J = 17.8 Hz, 1H), 2.17 – 2.04 (m, 2H), 1.89 (ddd, J = 15.0, 4.3, 2.7 Hz, 1H), 1.29 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 172.6, 157.7, 145.5, 135.9, 134.3, 129.5, 128.6, 128.3, 123.1, 121.3, 110.1, 103.8, 87.5, 70.1, 68.4, 50.7, 48.7, 46.7, 46.5, 40.9, 29.5, 21.0, 17.0 ppm; IR ν_{max} 3470, 3349, 2926, 1760, 1700, 1608, 1474, 1401, 1347, 1214, 1093, 1038, 950, 740, 699 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{27}\text{H}_{26}\text{N}_2\text{O}_7$ $[\text{M}]^+$: 490.1740, found 490.1743. **43** has rotational isomer, ^1H NMR (500 MHz, CDCl_3) δ 7.49 – 7.27 (m, 5H), 7.13 (dd, J = 18.7, 10.2 Hz, 2H), 6.82 (t, J = 7.1 Hz, 1H), 6.74 (d, J = 7.5 Hz, 1H), 6.36 – 6.17 (m, 1H), 5.33 – 5.21 (m, 2H), 5.19 – 5.08 (m, 1H), 5.04 (d, J = 17.4 Hz, 1H), 4.96 (d, J = 11.0 Hz, 1H), 4.84 (d, J = 12.6 Hz, 1H), 3.66 (s, 3H), 3.45 (d, J = 18.7 Hz, 1H), 3.28 (d, J = 18.7 Hz, 1H), 3.21 (d, J = 2.5 Hz, 1H), 2.65 (s, 1H), 2.27 (t, J = 15.8 Hz, 1H), 1.92 (d, J = 13.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 174.2, 174.0, 171.4, 153.0, 152.8, 144.5, 144.2, 135.6, 135.42, 135.36, 135.3, 134.25, 134.17, 129.4, 128.6, 128.4, 128.3, 127.9, 127.2, 124.0, 121.4, 121.2, 117.3, 116.8, 110.9, 110.3, 110.0, 106.0, 105.6, 68.8, 52.8, 51.8, 51.3, 50.5, 49.9, 38.2, 38.0, 27.2, 27.0, 26.7 ppm; IR ν_{max} 3356,

2954, 1711, 1635, 1428, 1392, 1317, 1170, 1104, 1052, 949, 903, 748 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}_6$ $[\text{M}]^+$: 486.1791, found 486.1795.



To a solution of **42** (10.0 mg, 0.02 mmol, 1.0 equiv) in 0.4 mL methanol was added 10 % Pd/C (6.4 mg, 0.006 mmol, 0.3 equiv). The resultant suspension was stirred at 40 °C under H_2 for 1 h, the mixture was filtered and concentrated. The residue was dissolved in 0.3 mL anhydrous DMF. To the mixture was added K_2CO_3 (5.6 mg, 0.04 mmol, 2.0 equiv) and MeI (2.2 μL , 0.036 mmol, 1.8 equiv) under nitrogen. The mixture was warmed to 40 °C and vigorously stirred for 5 h. To the solution was added H_2O (1.5 mL) at room temperature. The resulting mixture was extracted with dichloromethane (5 \times 4 mL). The combined organic layer was washed with brine (2 mL), then dried over anhydrous sodium sulfate. The solvent was removed under vacuum and was purified by preparation thin layer chromatography (4% methanol – dichloromethane) to give alstolactine A (**10**) (5.9 mg, 79%) as a white solid. R_f = 0.44 (4% methanol-dichloromethane); $[\alpha]_{\text{D}}^{24}$ = -77.8 (c = 0.1, MeOH), [Lit. $[\alpha]_{\text{D}}^{25}$ = -98.1 (c = 0.10, MeOH)]^[5]; ^1H NMR (500 MHz, MeOD) δ 7.19 (dd, J = 7.5, 0.6 Hz, 1H), 7.07 (td, J = 7.7, 1.2 Hz, 1H), 6.79 (td, J = 7.5, 0.9 Hz, 1H), 6.61 (d, J = 7.8 Hz, 1H), 3.69 (q, J = 6.5 Hz, 1H), 3.53 (d, J = 17.8 Hz, 1H), 3.17 (d, J = 11.3 Hz, 1H), 2.99 (d, J = 5.5 Hz, 1H), 2.78 (d, J = 17.8 Hz, 1H), 2.81 – 2.78 (m, 1H), 2.77 (d, J = 13.3 Hz, 1H), 2.55 (d, J = 13.3 Hz, 1H), 2.44 (s, 3H), 1.90 (ddd, J = 14.7, 5.5, 2.4 Hz, 1H), 1.84 (ddd, J = 14.7, 4.2, 1.3 Hz, 1H), 1.21 (d, J = 6.5, 3 H) ppm; ^{13}C NMR (125 MHz, MeOD) δ 178.4, 177.2, 148.4, 136.7, 130.2, 124.2, 121.2, 110.4, 109.2, 92.1, 69.2, 59.7, 55.7, 51.4, 49.1, 46.2, 43.8, 31.2, 21.6, 17.3 ppm; IR ν_{max} 2921, 2853, 1742, 1466, 1260, 1081, 1020, 801, 747 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_5$ $[\text{M}]^+$: 370.1529, found 370.1532.

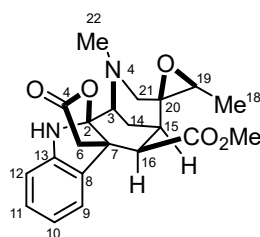
Comparison of ^1H NMR spectroscopic data of natural and synthetic scholarisine K



scholarisine K

position	natural δ ^1H [ppm; mult; J (Hz)] 600 MHz	synthetic δ ^1H [ppm; mult; J (Hz)] 500 MHz	deviation (natural–synthetic) $\Delta\delta$ (ppm)
3	3.00 (br, d, 4.5)	2.99 (dd, 4.7, 1.6)	0.01
5	3.75 (d, 18.4)	3.75 (d, 18.3)	
6	3.43 (d, 18.4)	3.42 (d, 18.3)	0.01
9	7.34 (d, 7.9)	7.34 (d, 7.5)	
10	6.78 (t, 7.9)	6.80 (t, 7.5)	-0.02
11	7.08 (t, 7.9)	7.09 (td, 7.7, 0.9)	-0.01
12	6.68 (d, 7.9)	6.70 (d, 7.8)	-0.02
14	2.16 (dt, 14.3, 4.5)	2.16 (dt, 14.3, 4.3)	
	2.02 (dt, 14.3, 2.2)	2.04 (dt, 14.4, 2.3)	-0.02
15	2.62 (m)	2.63 (dd, 7.5, 3.6)	-0.01
16	2.48 (d, 4.5)	2.49 (d, 4.5)	-0.01
18	1.29 (d, 5.6)	1.29 (d, 5.5)	
19	2.81 (q, 5.6)	2.80 (q, 5.5)	0.01
21	3.14 (d, 13.6)	3.15 (d, 13.3)	-0.01
	2.12 (d, 13.6)	2.12 (d, 13.3)	
22	2.38 (s)	2.39 (s)	-0.01
OMe	3.61 (s)	3.62 (s)	-0.01

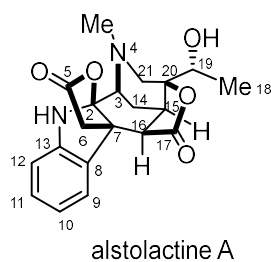
Comparison of ^{13}C NMR spectroscopic data of natural and synthetic scholarisine K



scholarisine K

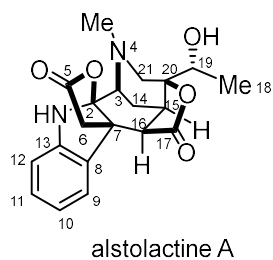
position	natural $\delta^{13}\text{C}$ [ppm] 100 MHz	synthetic $\delta^{13}\text{C}$ [ppm] 125 MHz	deviation (natural–synthetic) $\Delta\delta$ (ppm)
2	106.2	106.0	0.2
3	57.5	57.6	-0.1
5	175.5	175.3	0.2
6	39.1	39.1	
7	51.1	51.2	-0.1
8	135.3	135.4	-0.1
9	125.1	125.2	-0.1
10	120.6	120.8	-0.2
11	128.8	128.8	
12	110.5	110.6	-0.1
13	145.9	145.9	
14	25.8	25.8	
15	27.1	27.2	-0.1
16	51.7	51.8	-0.1
18	11.2	11.3	-0.1
19	58.1	58.1	
20	62.2	62.2	
21	56.3	56.4	-0.1
22	45.6	45.7	-0.1
-CO-	171.3	171.2	0.1
OMe	51.3	51.4	-0.1

Comparison of ^1H NMR spectroscopic data of natural and synthetic alstolactine A



position	natural δ ^1H [ppm; mult; J (Hz)] 600 MHz	synthetic δ ^1H [ppm; mult; J (Hz)] 500 MHz	deviation (natural–synthetic) $\Delta\delta$ (ppm)
3	3.00 (d, 5.4)	2.99 (d, 5.5)	0.01
6	3.55 (d, 18.1)	3.53 (d, 17.8)	0.02
	2.80 (d, 18.1)	2.78 (d, 17.8)	0.02
9	7.21 (d, 7.9)	7.19 (dd, 7.5, 0.6)	0.02
10	6.80 (t, 7.9)	6.79 (td, 7.5, 0.9)	0.01
11	7.08 (t, 7.9)	7.07 (td, 7.7, 1.2)	0.01
12	6.63 (d, 7.9)	6.61 (d, 7.8)	0.02
14	1.89 (dd, 14.7, 5.4)	1.90 (ddd, 14.7, 5.5, 2.4)	-0.01
	1.85 (dd, 14.7, 4.5)	1.84 (ddd, 14.7, 4.2, 1.3)	0.01
15	2.79 (m)	2.79 (m)	
16	3.17 (d, 11.3)	3.17 (d, 11.3)	
18	1.21 (d, 6.4)	1.21 (d, 6.5)	
19	3.71 (q, 6.4)	3.69 (q, 6.5)	0.02
21 β	2.77 (d, 13.6)	2.77 (d, 13.3)	
21 α	2.56 (d, 13.6)	2.55 (d, 13.3)	0.01
NMe	2.44 (s)	2.44 (s)	

Comparison of ^{13}C NMR spectroscopic data of natural and synthetic alstolactine A

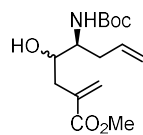


position	natural $\delta^{13}\text{C}$ [ppm] 100 MHz	synthetic $\delta^{13}\text{C}$ [ppm] 125 MHz	deviation (natural–synthetic) $\Delta\delta$ (ppm)
2	109.1	109.2	-0.1
3	59.6	59.7	-0.1
5	177.2	177.2	
6	43.8	43.8	
7	51.3	51.4	-0.1
8	136.6	136.7	-0.1
9	124.2	124.2	
10	121.2	121.2	
11	130.2	130.2	
12	110.5	110.4	0.1
13	148.4	148.4	
14	21.6	21.6	
15	31.2	31.2	
16	49.1	49.1	
17	178.4	178.4	
18	17.3	17.3	
19	69.2	69.2	
20	92.1	92.1	
21	55.6	55.7	-0.1
N-Me	46.2	46.2	

Reference

1. The ^1H NMR and ^{13}C NMR spectroscopic data were the same as reported before, see: a) Goel, O. P.; Kroll, U.; Stier, M.; Kesten, S. *Org. Synth.* **1988**, *67*, 69; b) Han, W.; Hu, L.; Jiang, X.; Decicco, C. P. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 711; c) Rishel, M. J.; Hecht, S. M. *Org. Lett.* **2001**, *3*, 2867.
2. Yu, C. Z.; Liu, B.; Hu, L. Q. *J. Org. Chem.* **2001**, *66*, 5413.
3. Yin, W. Y.; Kabir, M. S.; Wang, Z. J.; Rallapalli, S. K.; Ma, J.; Cook, J. M. *J. Org. Chem.* **2010**, *75*, 3339.
4. Yang, X.-W.; Luo, X.-D.; Lunga, P. K.; Zhao, Y.-L.; Qin, X.-J.; Chen, Y.-Y.; Liu, L.; Li, X.-N.; Liu, Y.-P. *Tetrahedron* **2015**, *71*, 3694.
5. Yang, X.-W.; Qin, X.-J.; Zhao, Y.-L.; Lunga, P. K.; Li, X.-N.; Jiang, S.-Z.; Cheng, G.-G.; Liu, Y.-P.; Luo, X.-D. *Tetrahedron Lett.* **2014**, *55*, 4593.

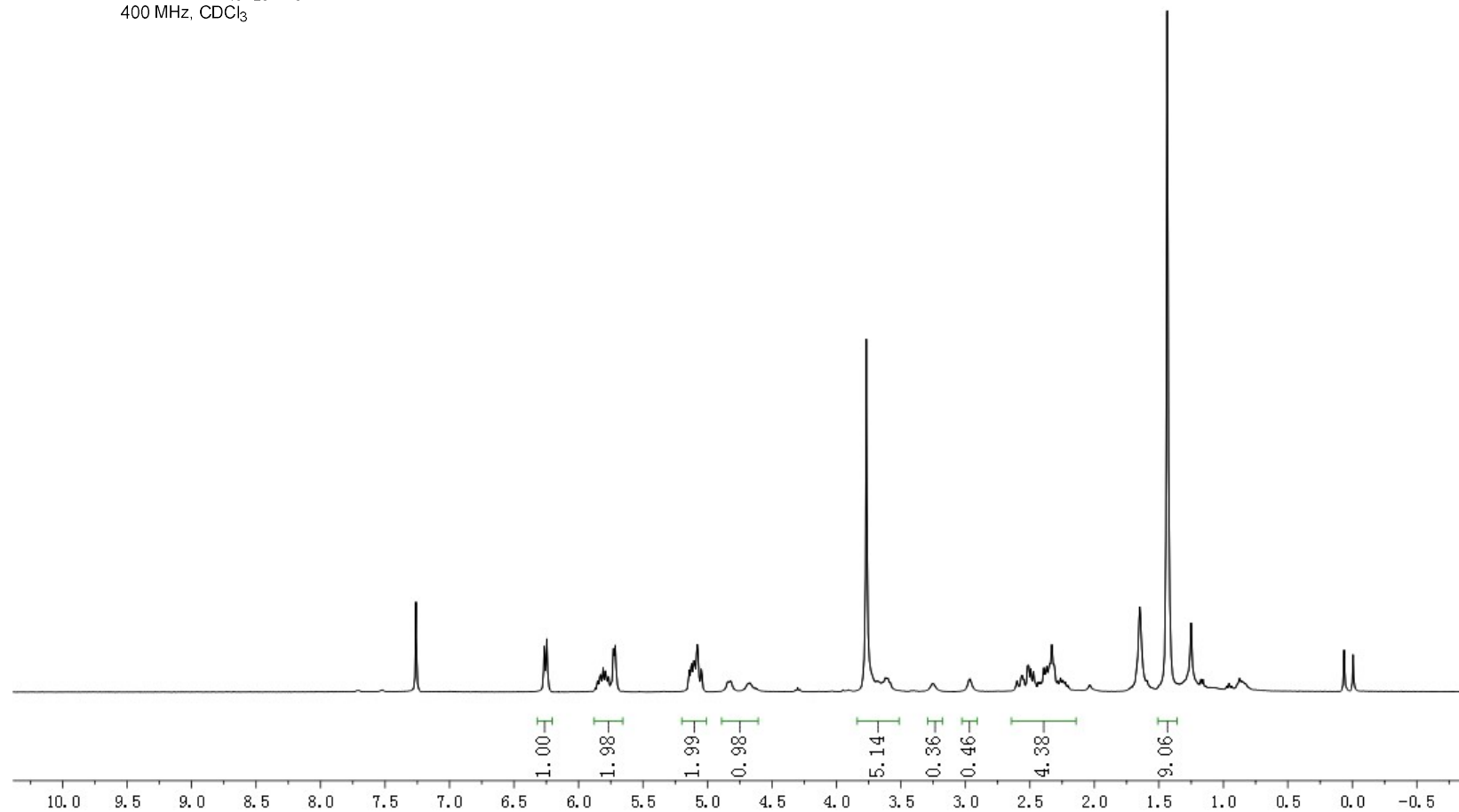
¹H and ¹³C NMR Spectra of Compounds

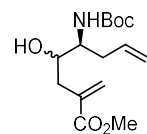


20

Chemical Formula: C₁₅H₂₅NO₅
400 MHz, CDCl₃

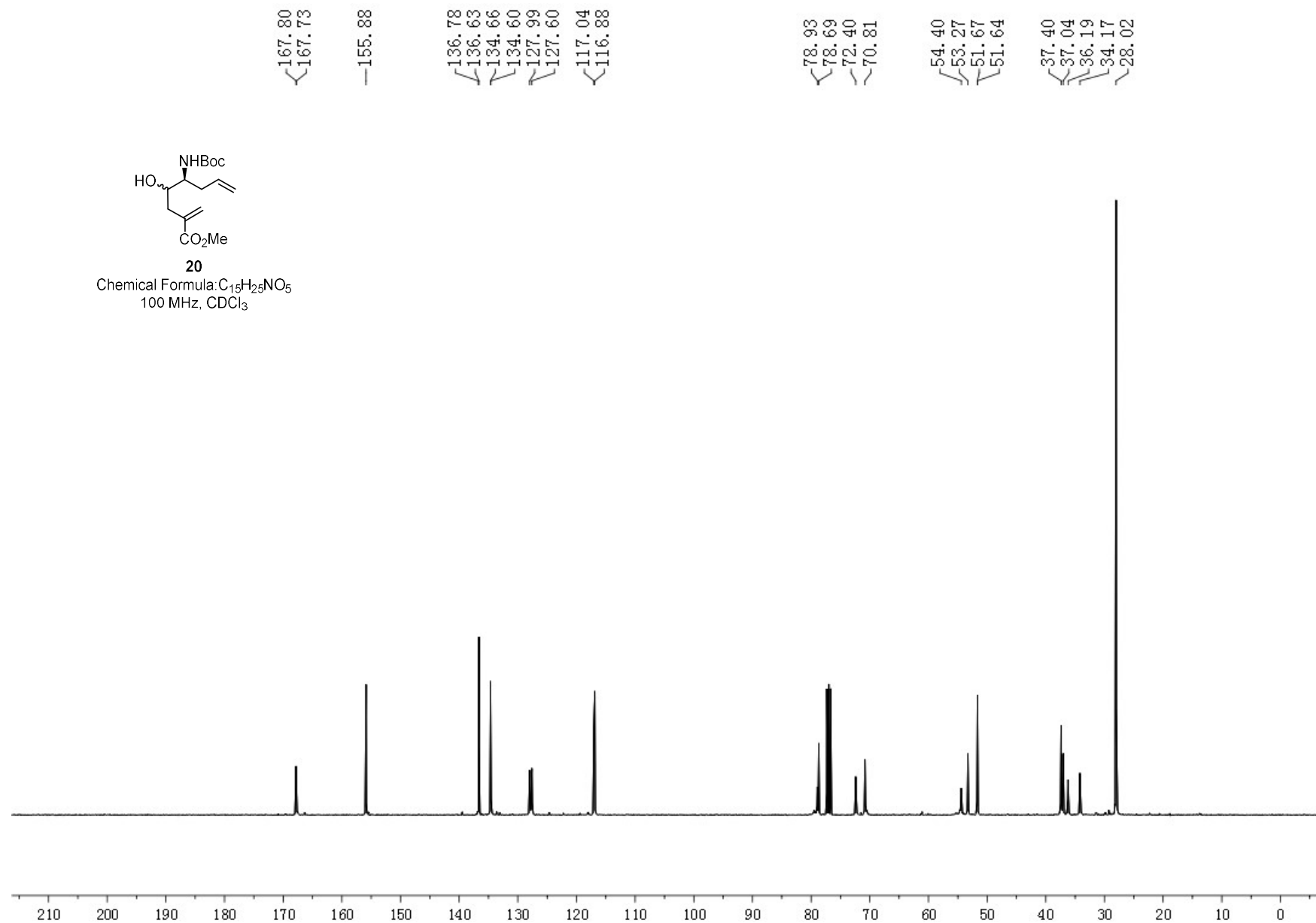
6.27
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5.81
5.73
5.72
5.14
5.12
5.10
5.08
5.05
4.82
4.67
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3.62
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2.51
2.49
2.39
2.37
2.35
2.33
1.45

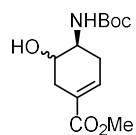




20

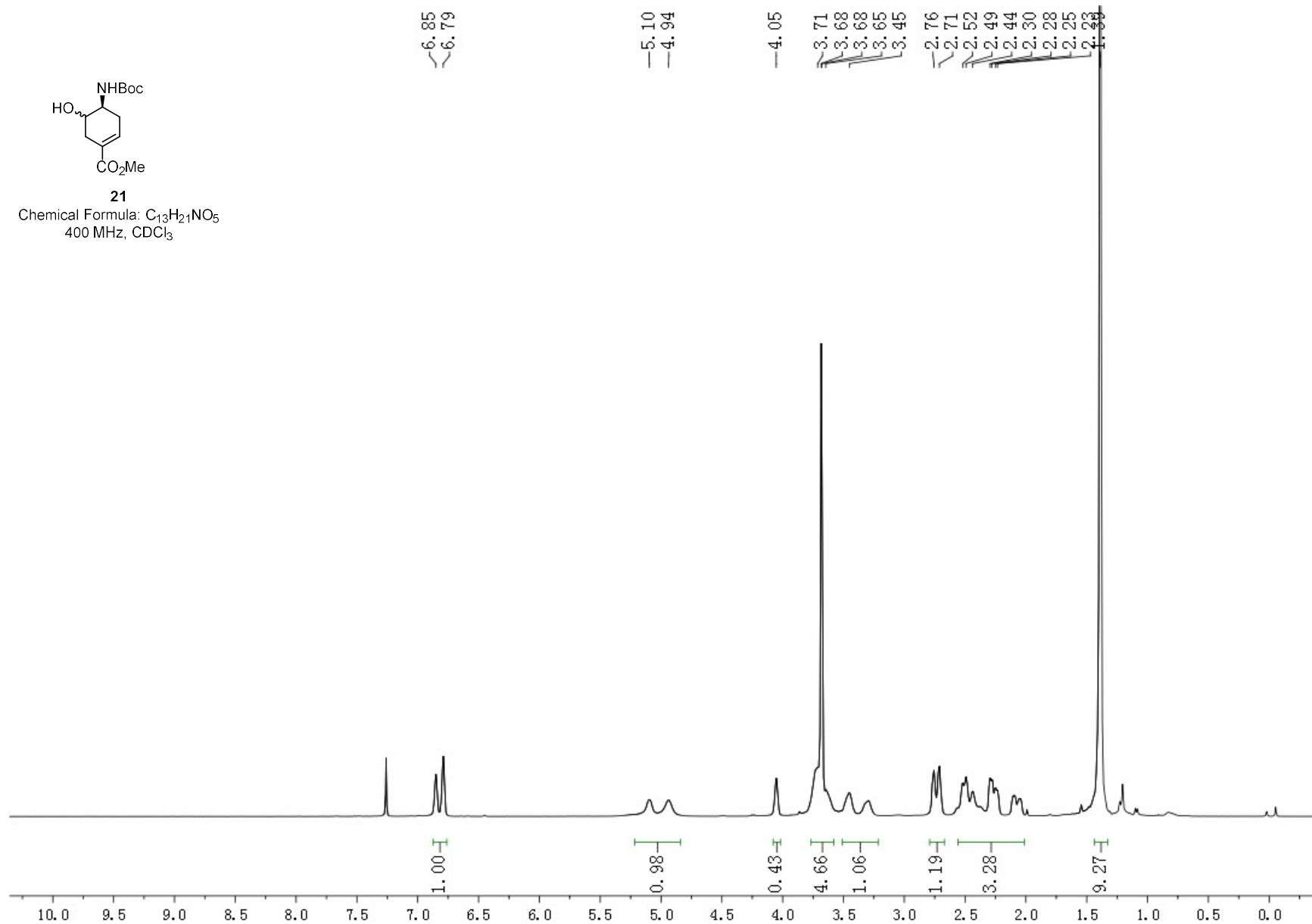
Chemical Formula: $C_{15}H_{25}NO_5$
100 MHz, $CDCl_3$

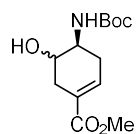




21

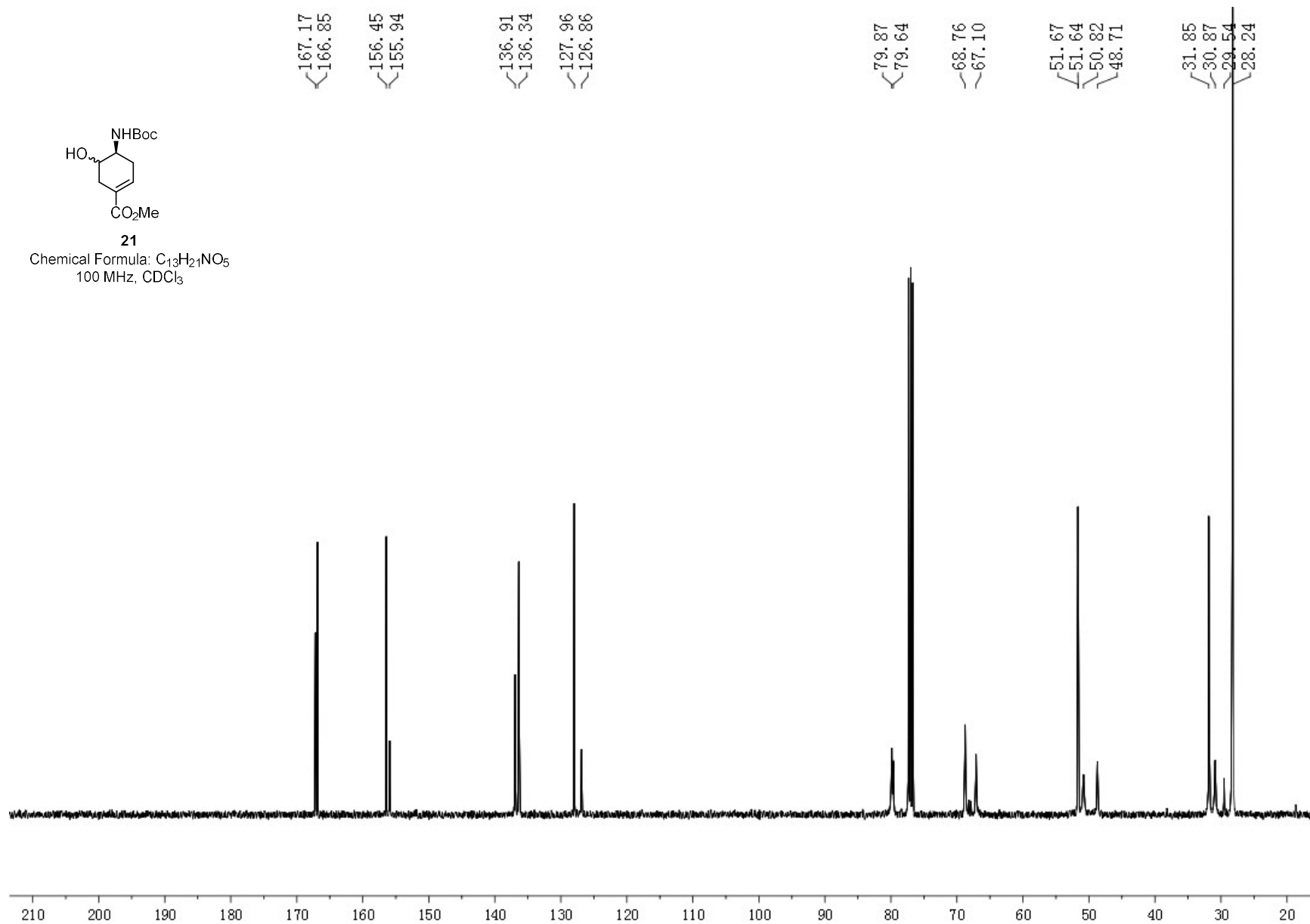
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400 MHz, $CDCl_3$

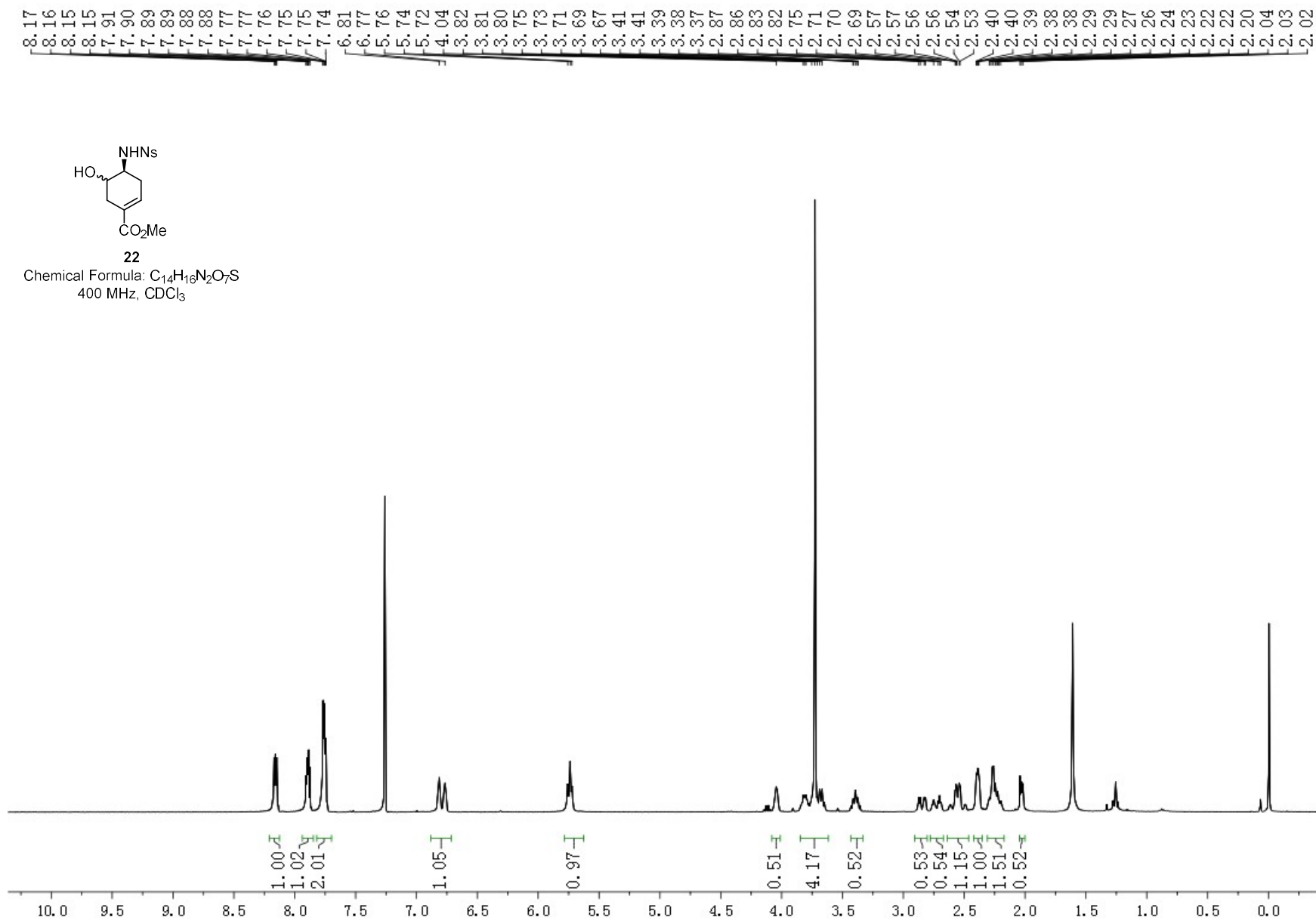


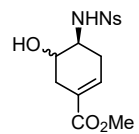


21

Chemical Formula: $C_{13}H_{21}NO_5$
100 MHz, $CDCl_3$

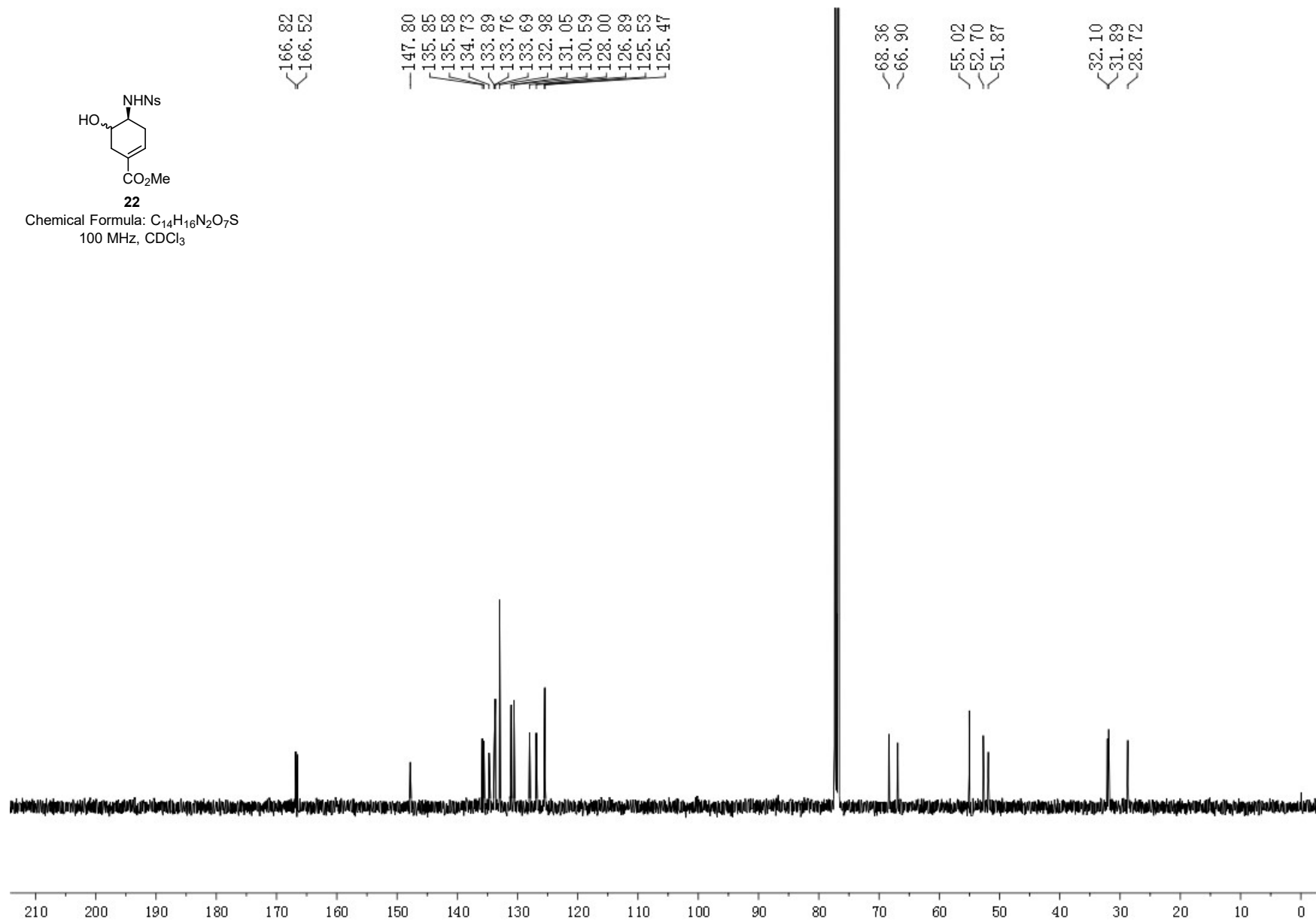


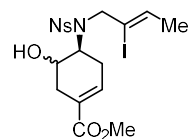




22

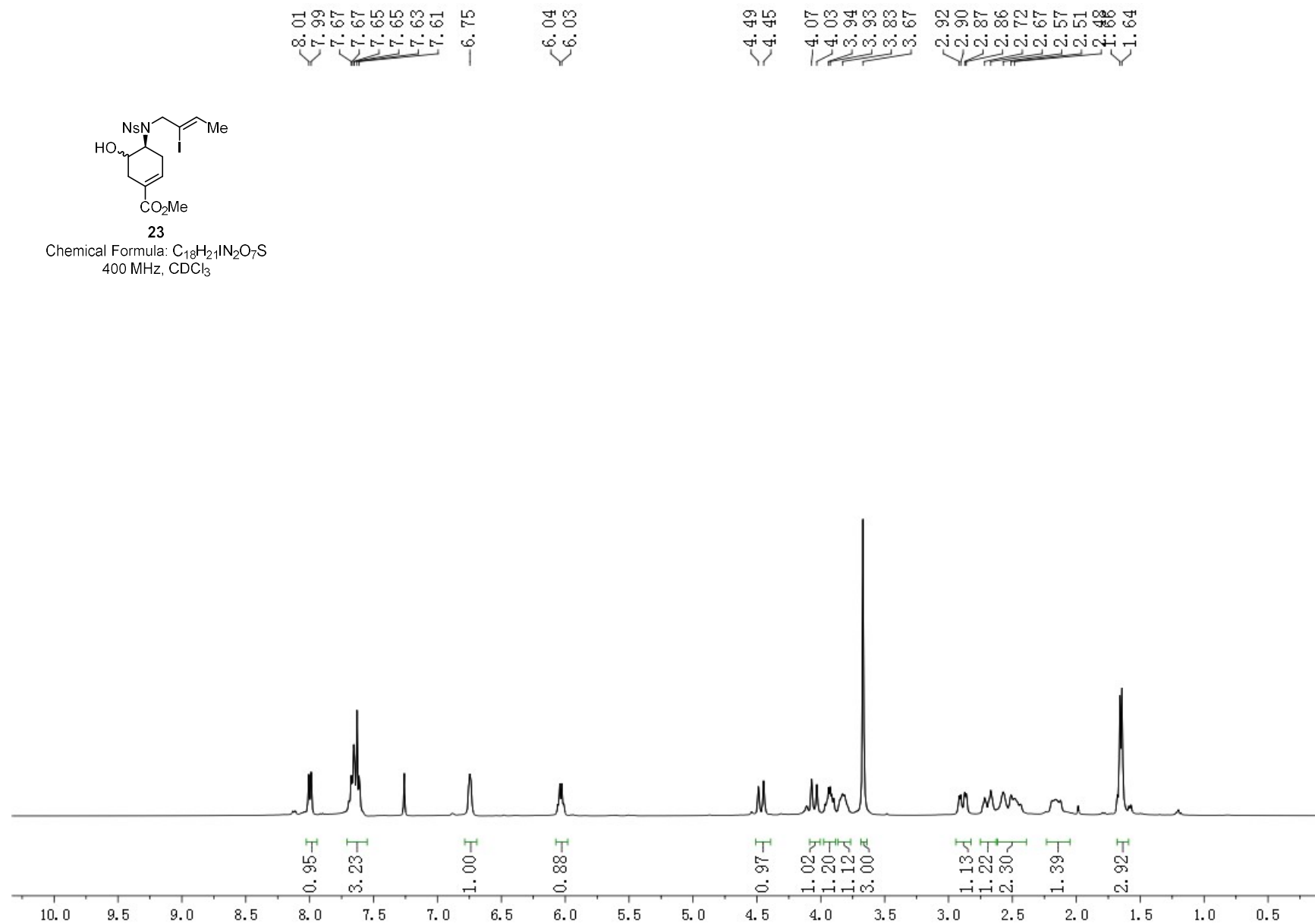
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100 MHz, $CDCl_3$

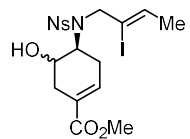




23

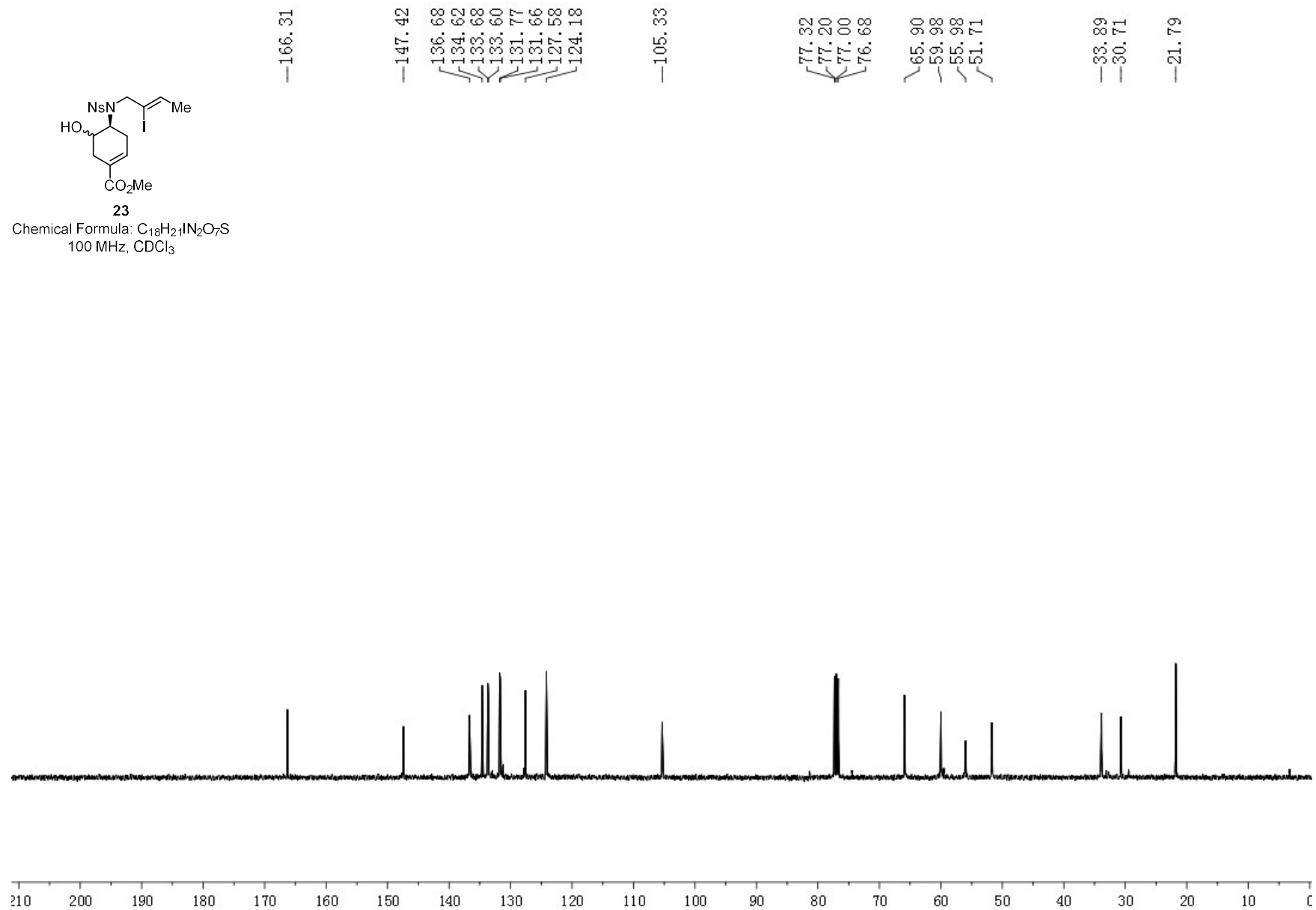
Chemical Formula: $C_{18}H_{21}N_2O_7S$
400 MHz, $CDCl_3$

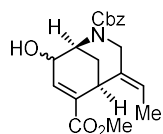




23

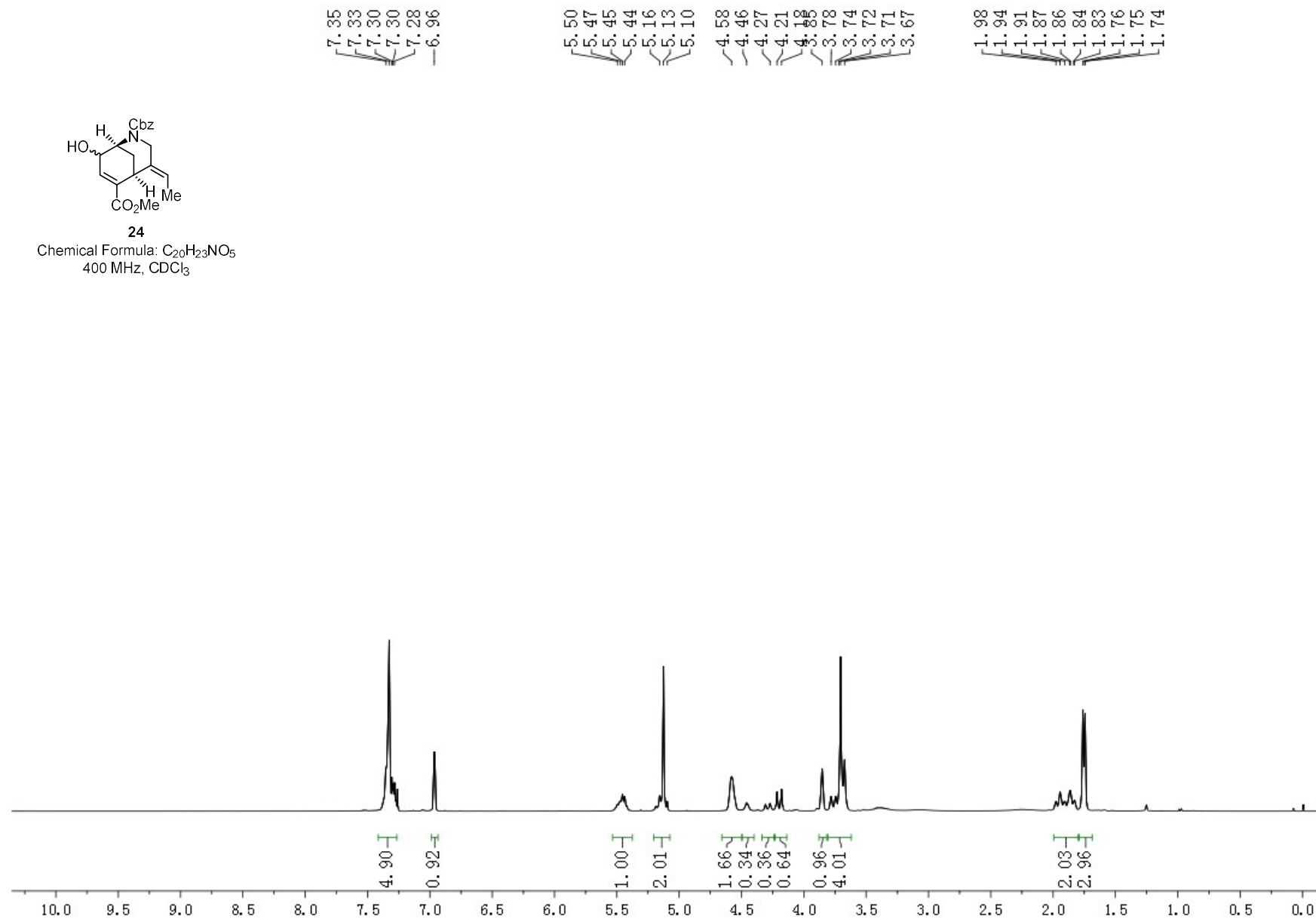
Chemical Formula: $C_{18}H_{21}N_2O_7S$
100 MHz, $CDCl_3$

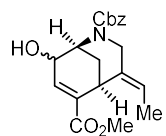




24

Chemical Formula: $C_{20}H_{23}NO_5$
400 MHz, $CDCl_3$

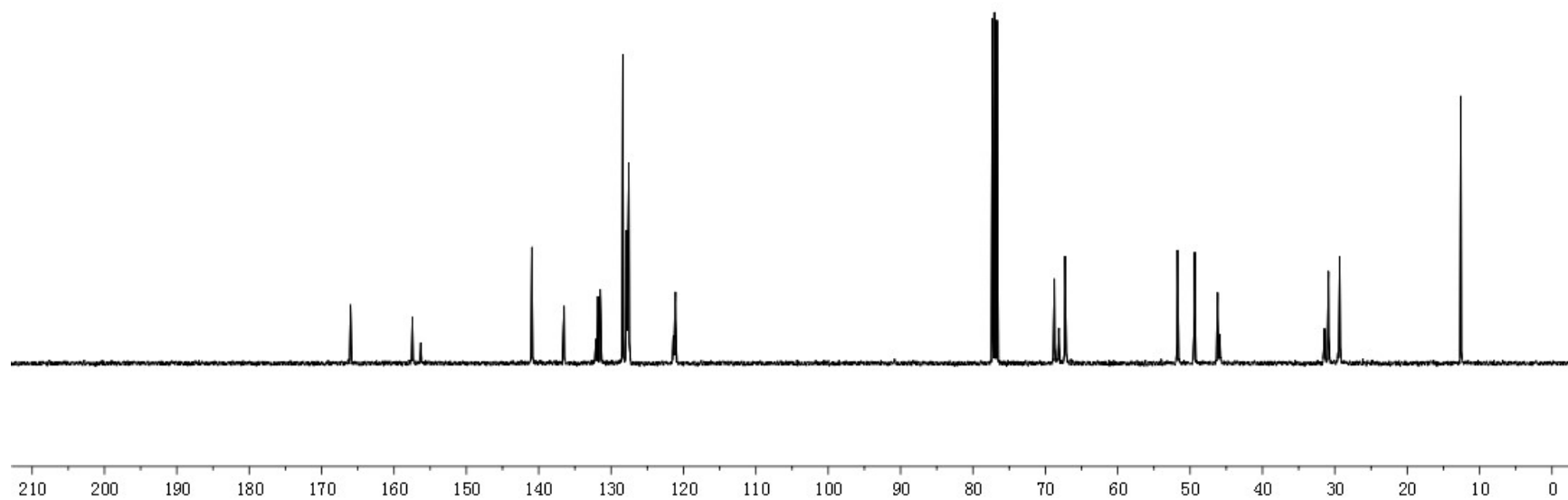


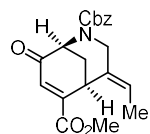


24

Chemical Formula: C₂₀H₂₃NO₅
100 MHz, CDCl₃

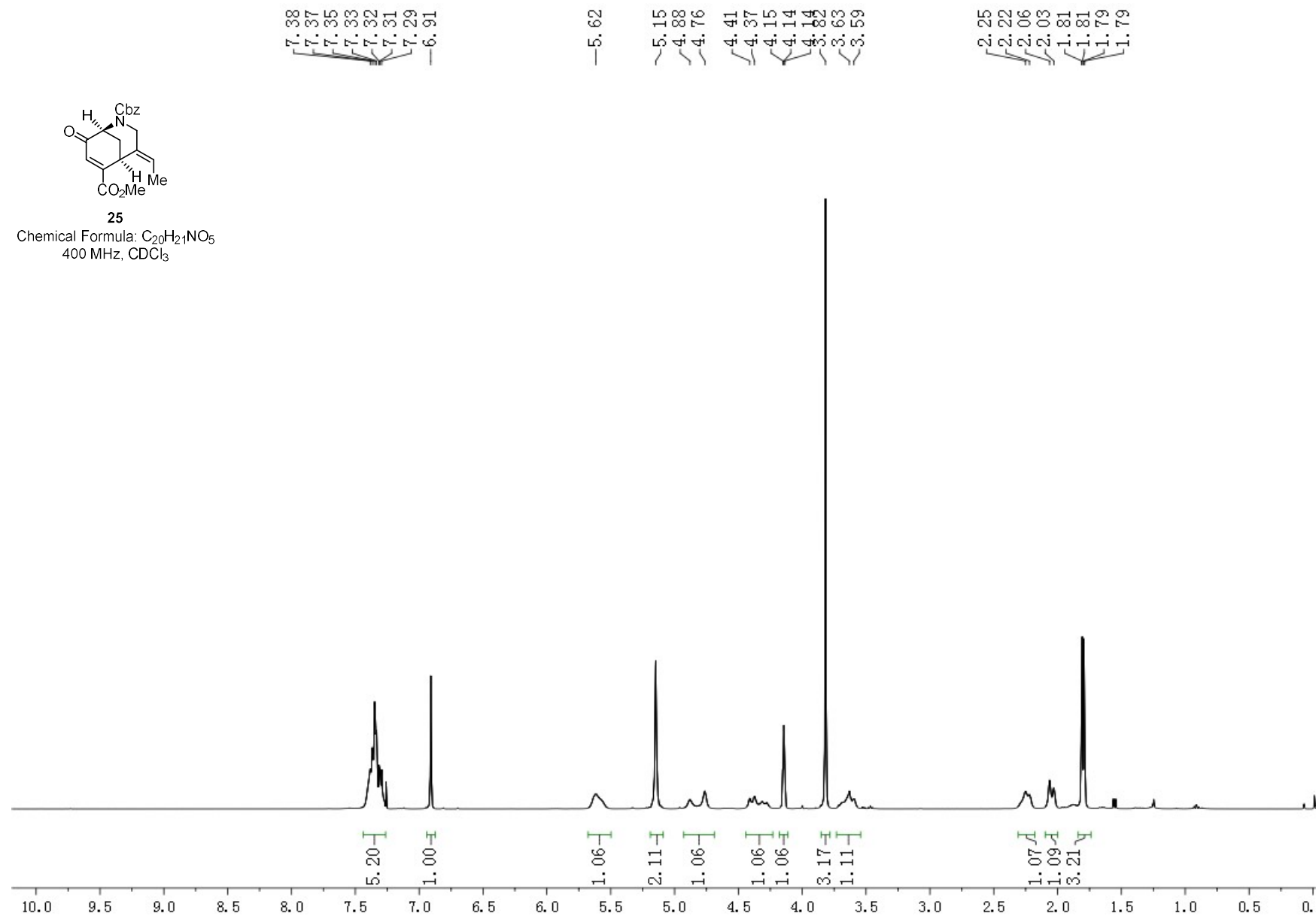
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 121.40
 121.13
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 46.22
 45.89
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 30.89
 29.33
 —12.59



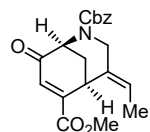


25

Chemical Formula: C₂₀H₂₁NO₅
400 MHz, CDCl₃



195.94
195.59



25

Chemical Formula: C₂₀H₂₁NO₅
100 MHz, CDCl₃

165.59

154.79

148.33

136.26

133.27

128.83

128.38

127.94

127.72

124.35

67.54

54.09

53.78

52.70

52.67

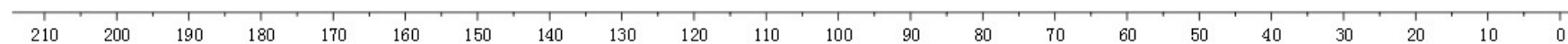
45.79

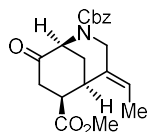
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33.14

30.85

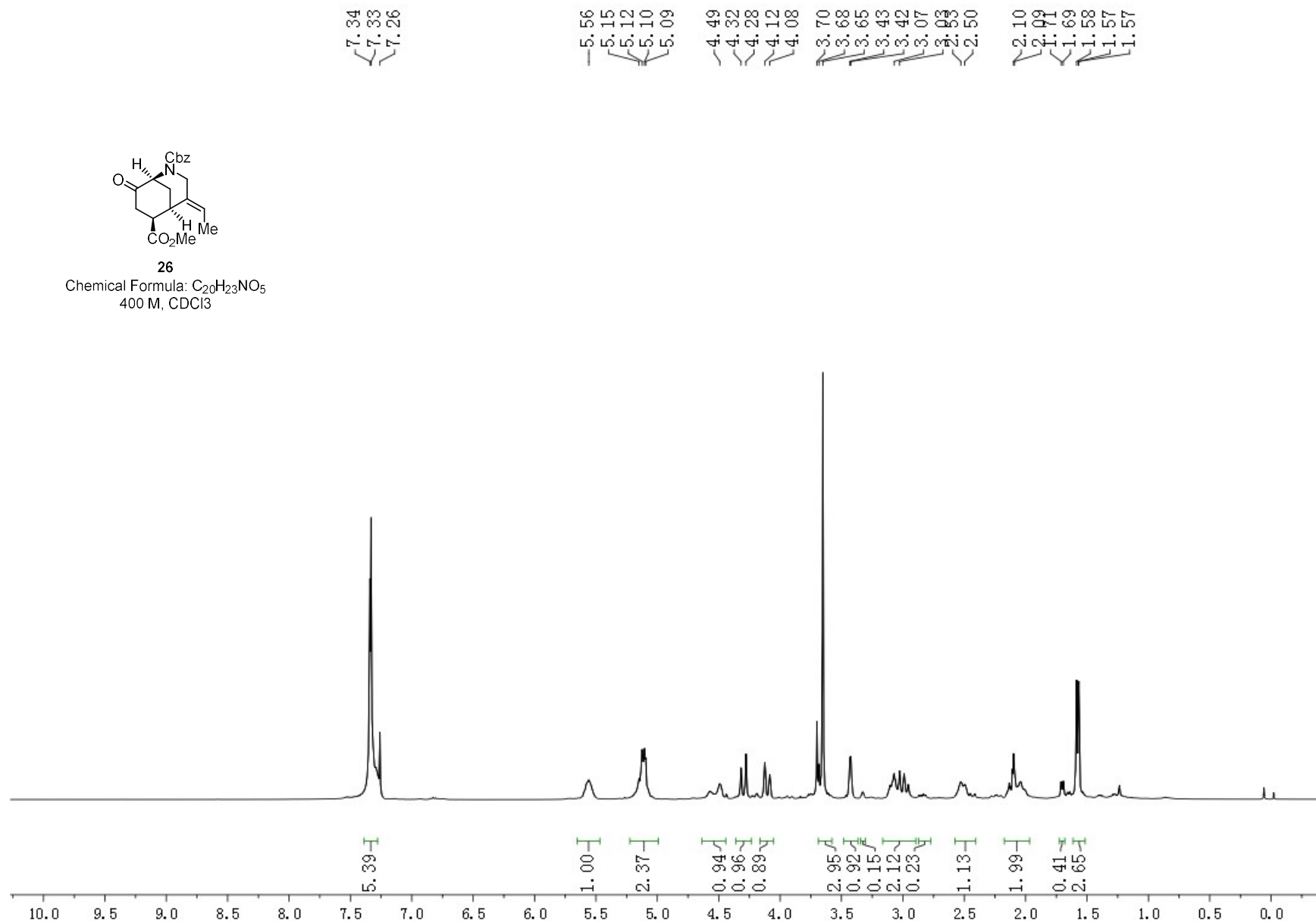
12.79





26

Chemical Formula: $C_{20}H_{23}NO_5$
400 M, $CDCl_3$



205.41
205.06

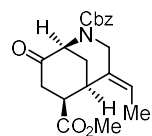
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154.85

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127.66
127.54
127.38
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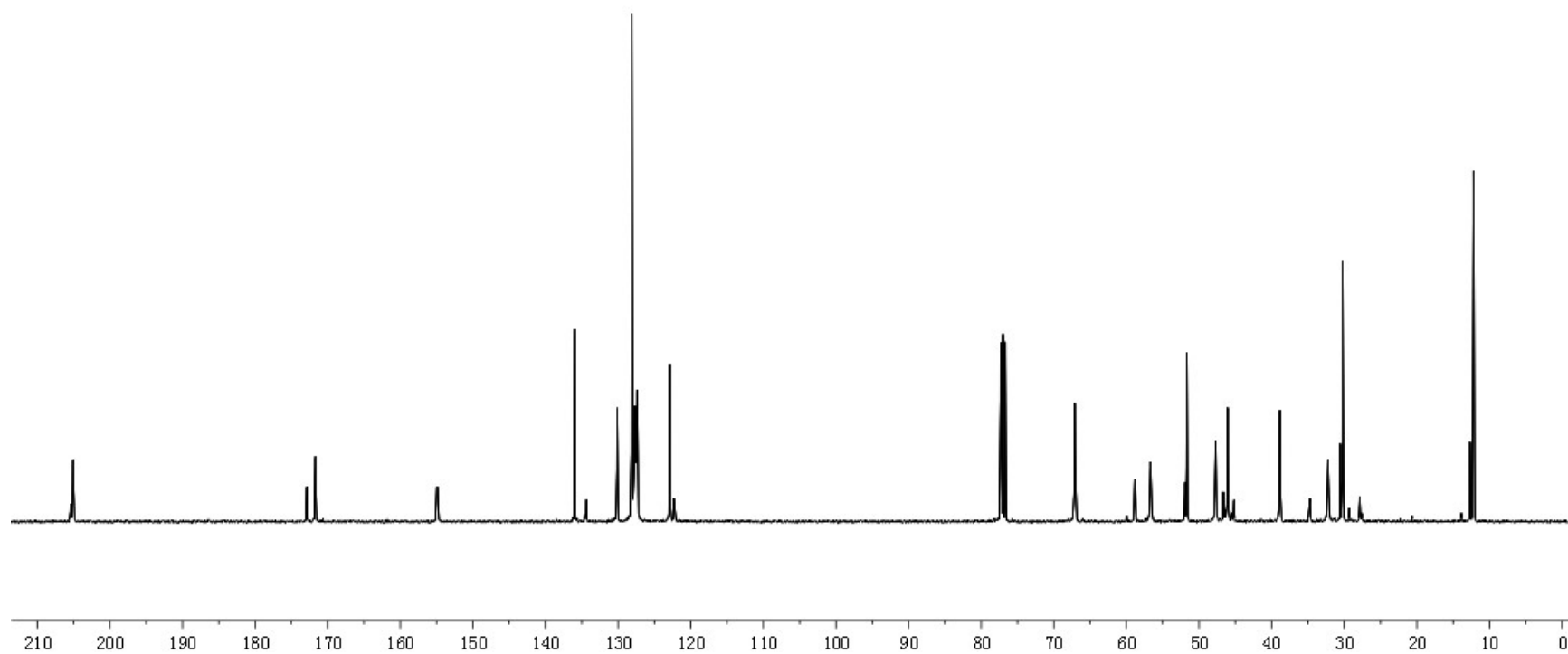
67.11
66.99

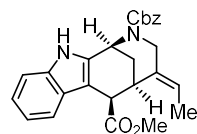
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27.85
12.19



26

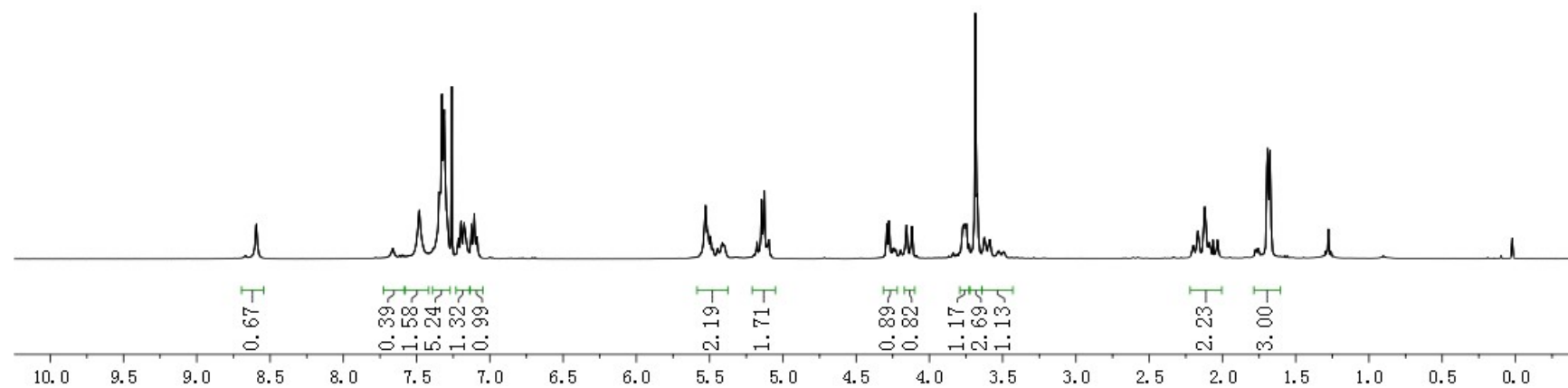
Chemical Formula: C₂₀H₂₃NO₅
100 M, CDCl₃



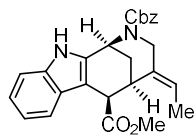


S3

Chemical Formula: $C_{26}H_{26}N_2O_4$
400 MHz, $CDCl_3$

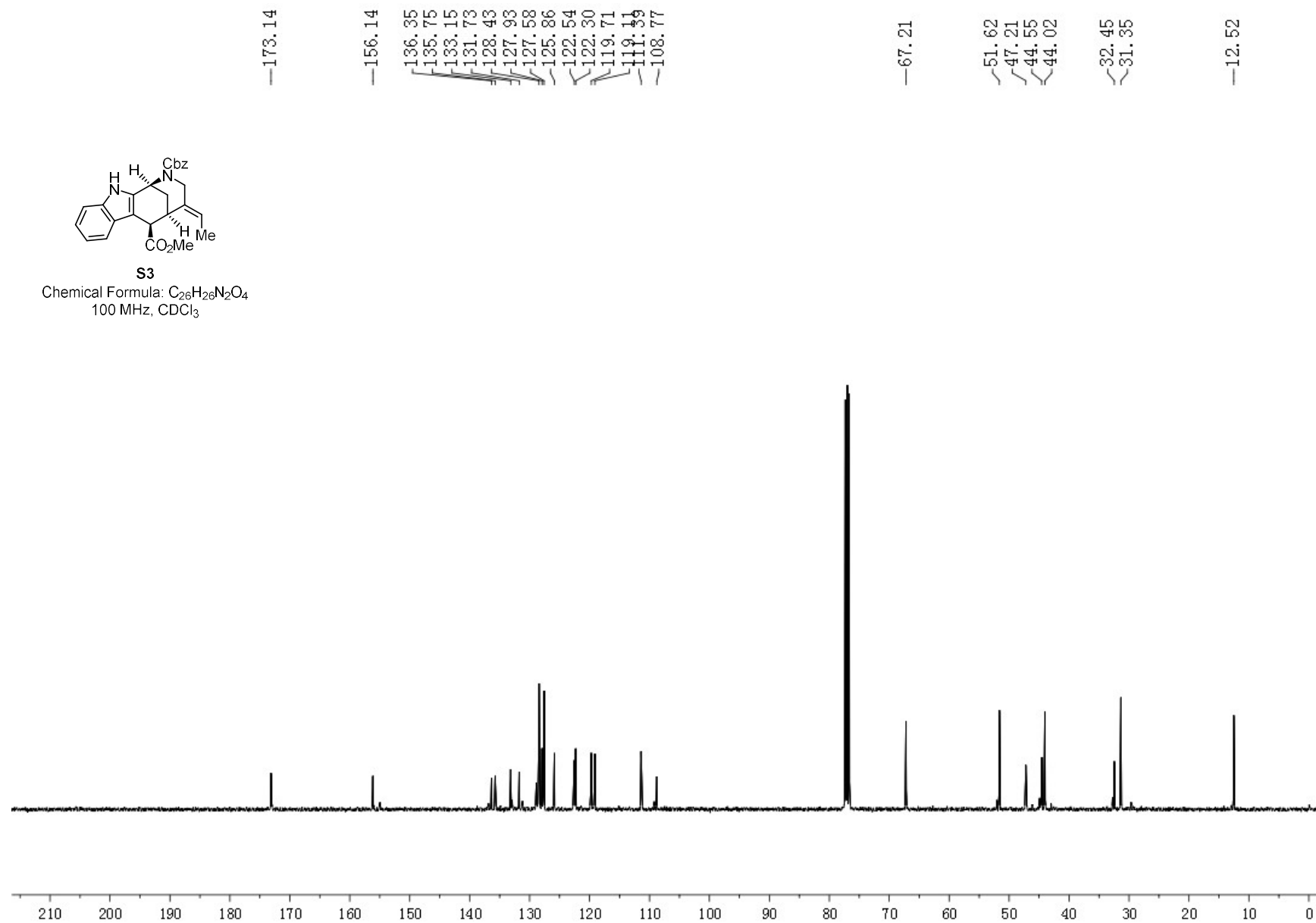


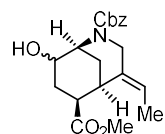
8.59
7.66
7.48
7.35
7.34
7.33
7.31
7.29
7.21
7.20
7.18
7.13
7.11
7.09
5.53
5.51
5.49
5.44
5.41
5.18
5.15
5.13
5.11
5.11
5.10
3.77
3.76
3.75
3.73
3.69
3.67
3.62
3.59
3.53
2.20
2.17
2.12
2.10
2.09
2.06
2.03
1.77
1.76
1.69
1.67



S3

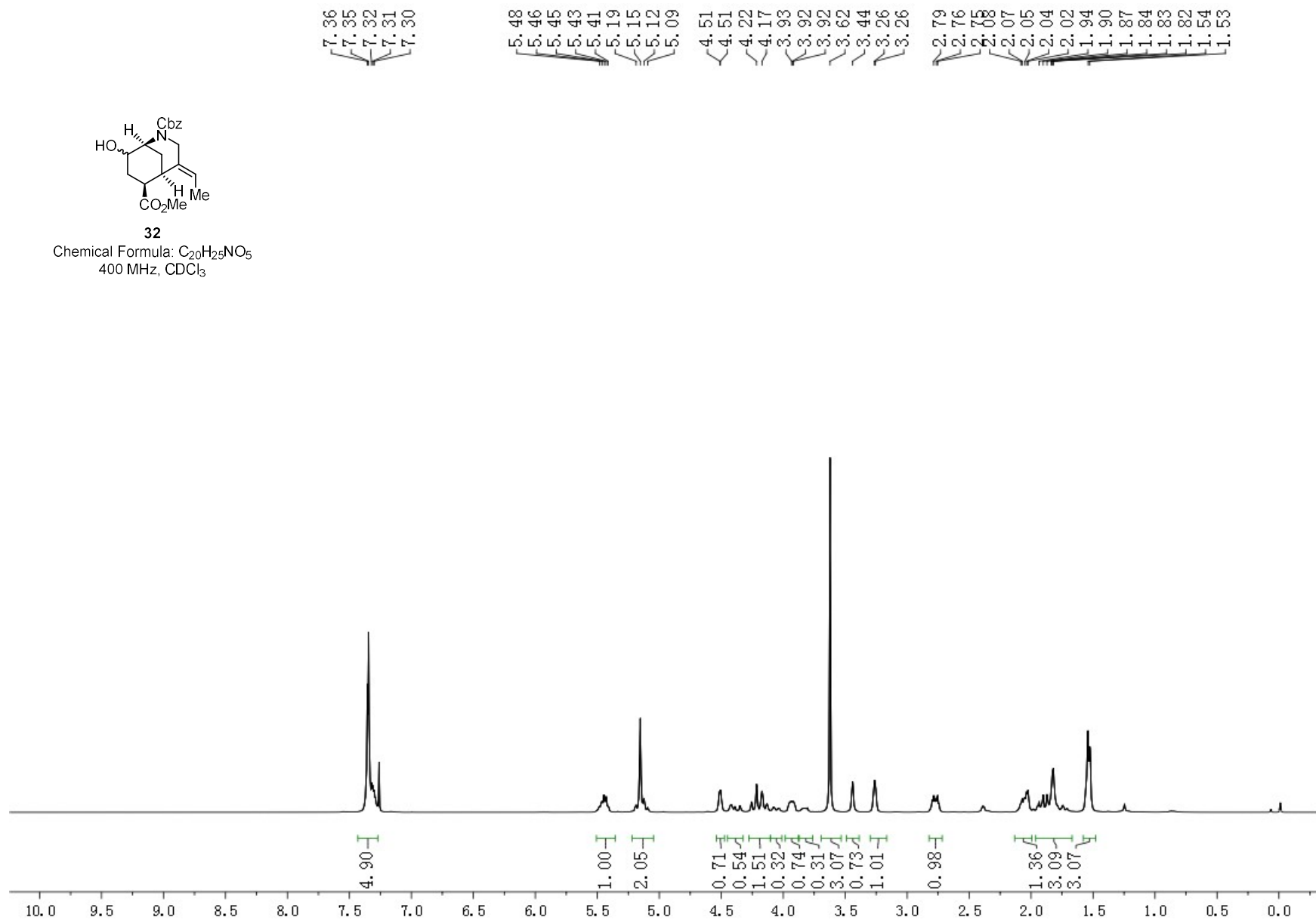
Chemical Formula: $C_{26}H_{26}N_2O_4$
100 MHz, $CDCl_3$

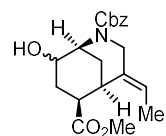




32

Chemical Formula: $C_{20}H_{25}NO_5$
400 MHz, $CDCl_3$





32

Chemical Formula: $C_{20}H_{25}NO_5$
100 MHz, $CDCl_3$

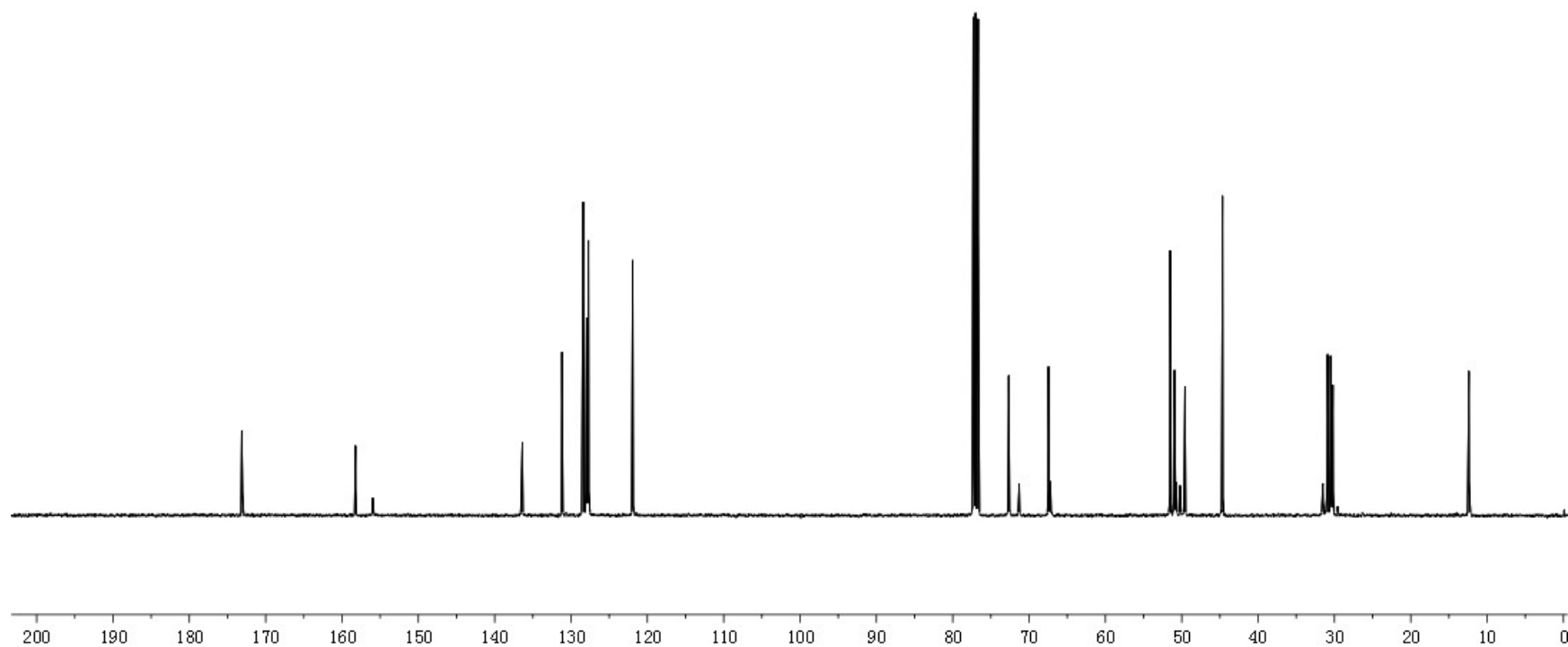
173.12
173.03

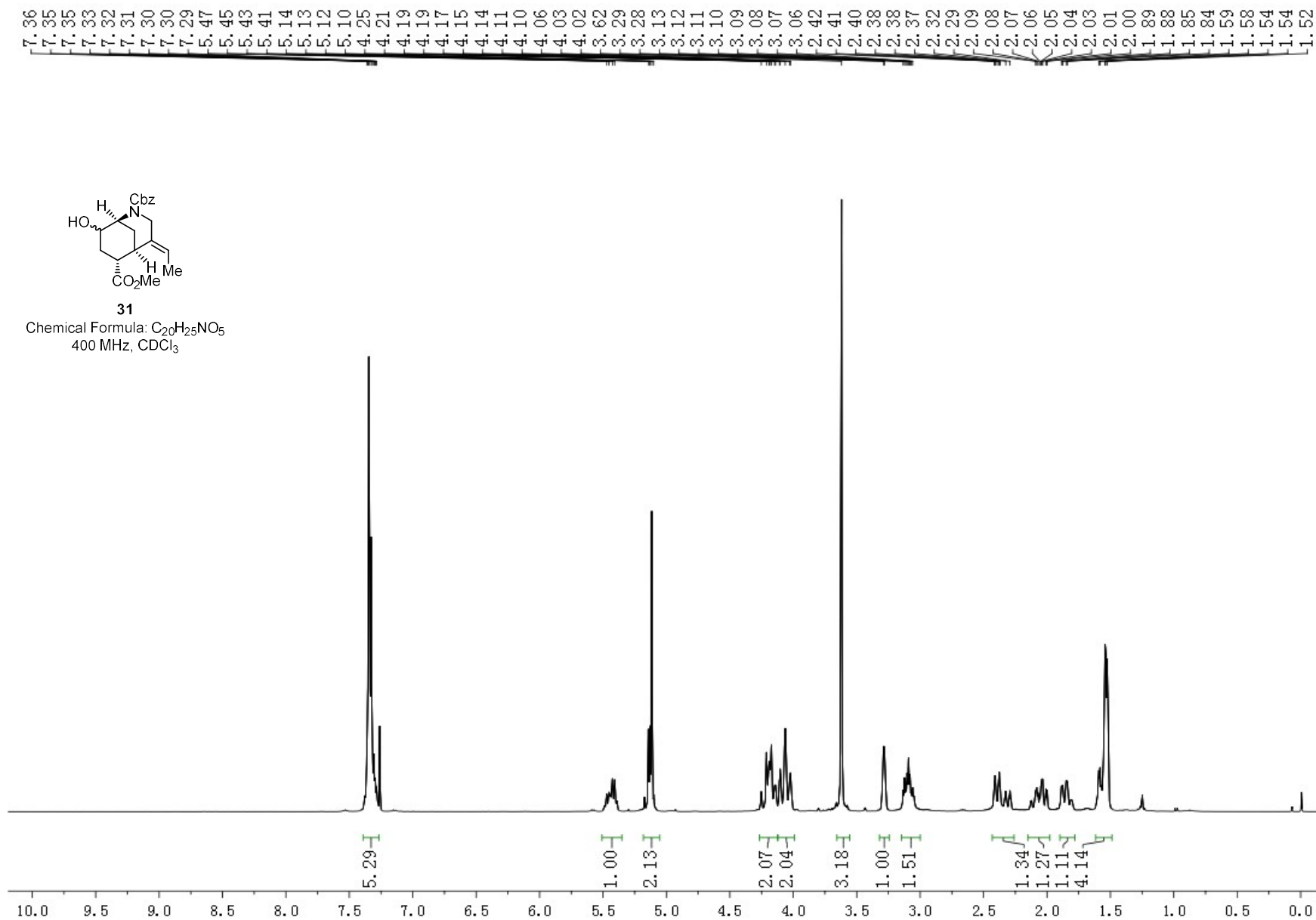
158.24
155.97

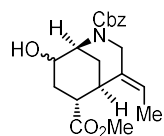
136.51
136.37
131.17
128.42
127.95
127.71
121.92

72.66
71.29
67.45
67.19

51.51
50.95
50.70
50.22
49.58
44.65
31.52
30.89
30.49
30.40
30.21

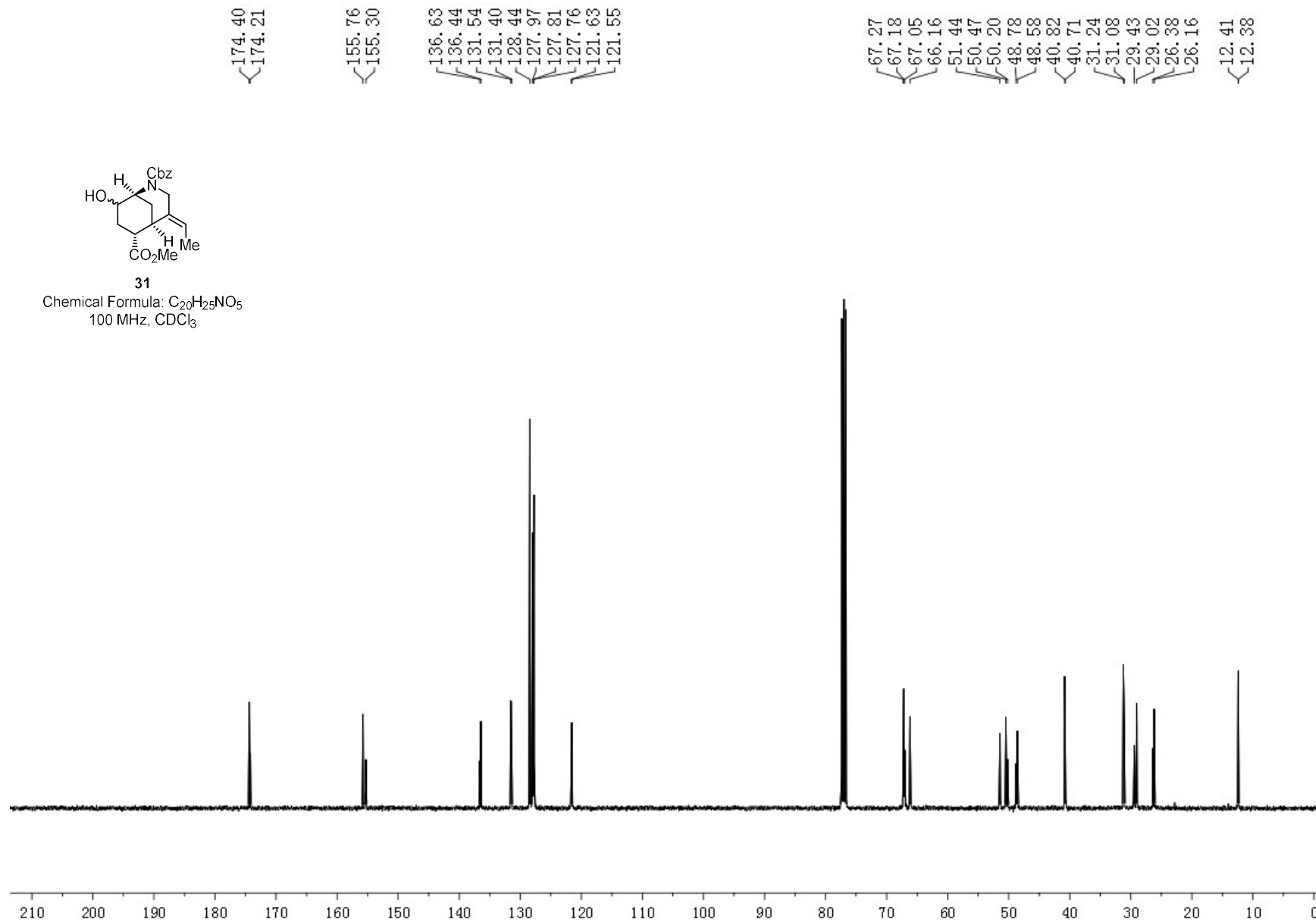


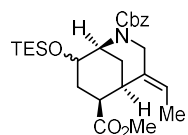




31

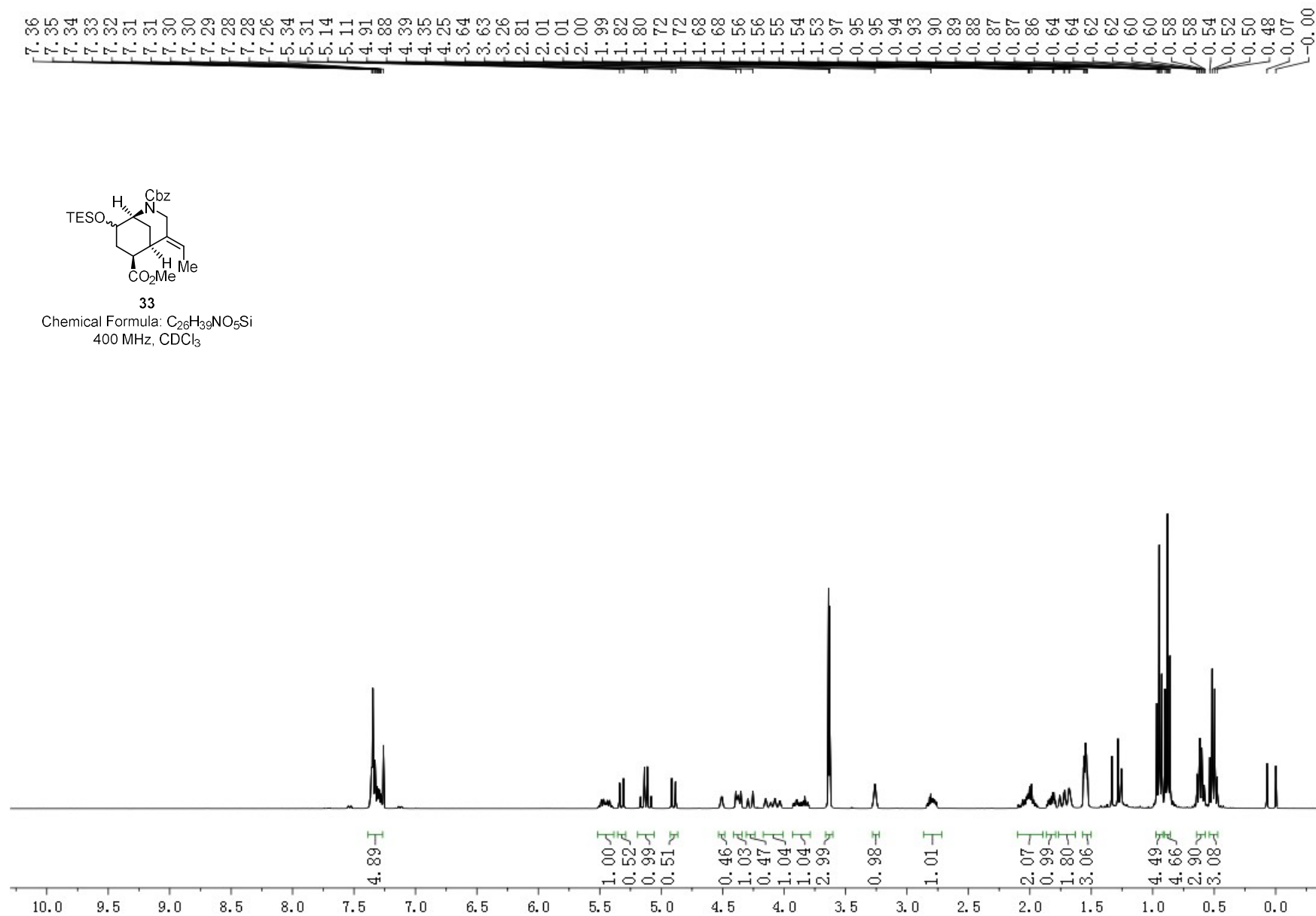
Chemical Formula: $C_{20}H_{25}NO_5$
100 MHz, $CDCl_3$

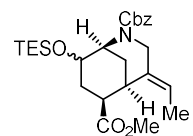




33

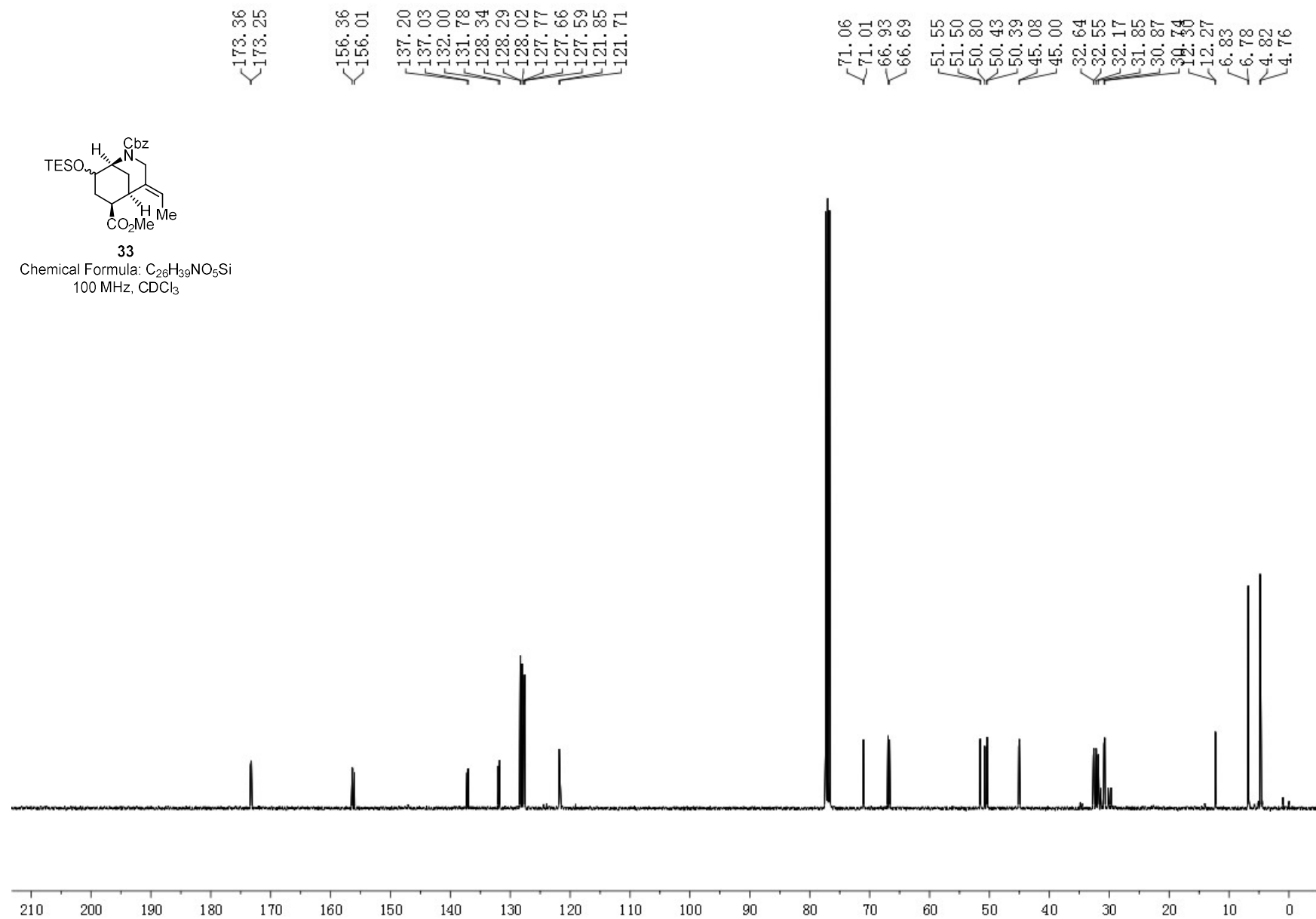
Chemical Formula: C₂₆H₃₉NO₅Si
400 MHz, CDCl₃

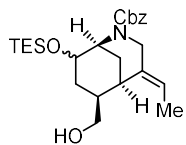
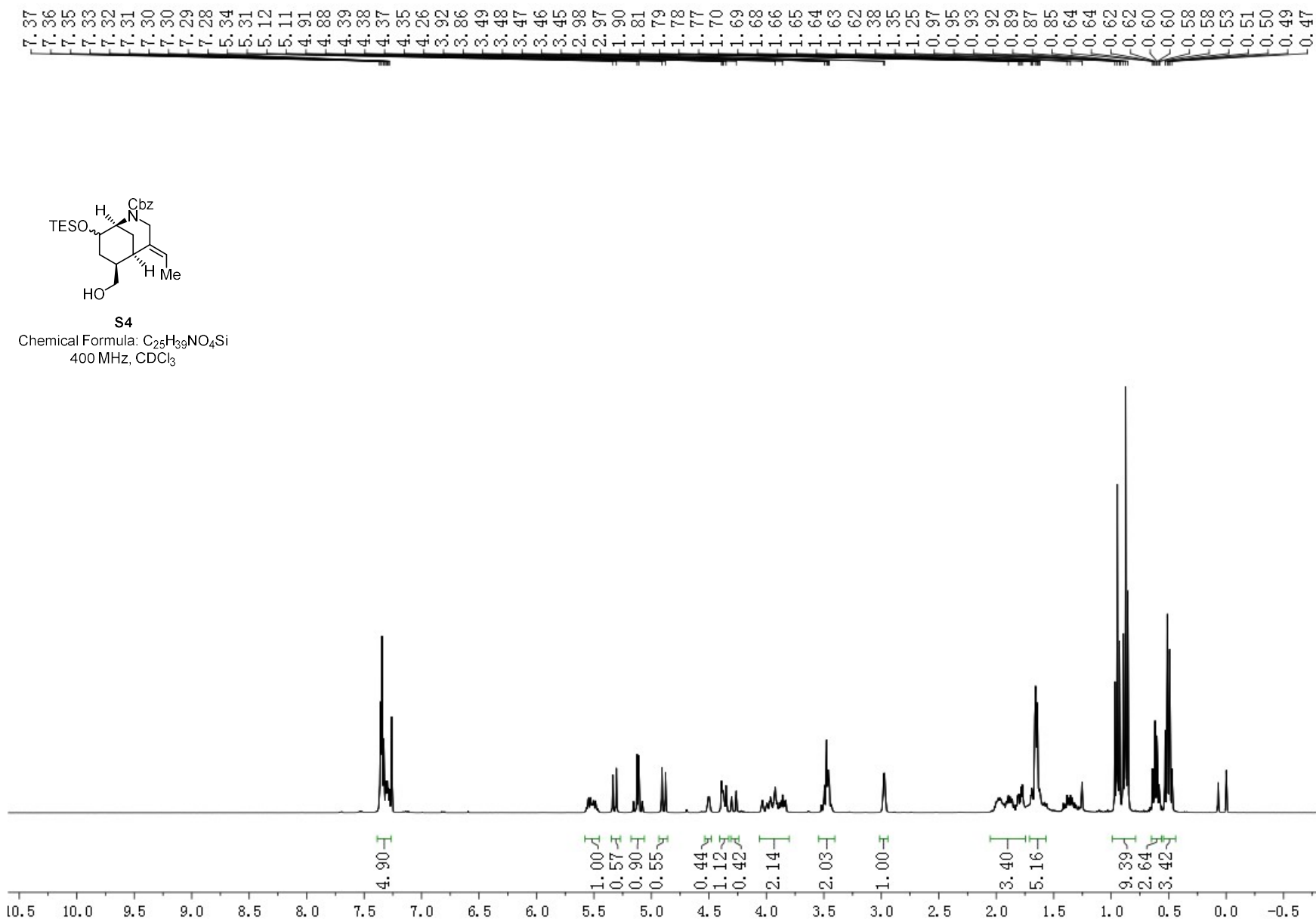




33

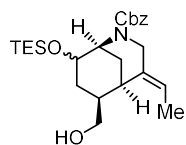
Chemical Formula: $C_{26}H_{39}NO_5Si$
100 MHz, $CDCl_3$



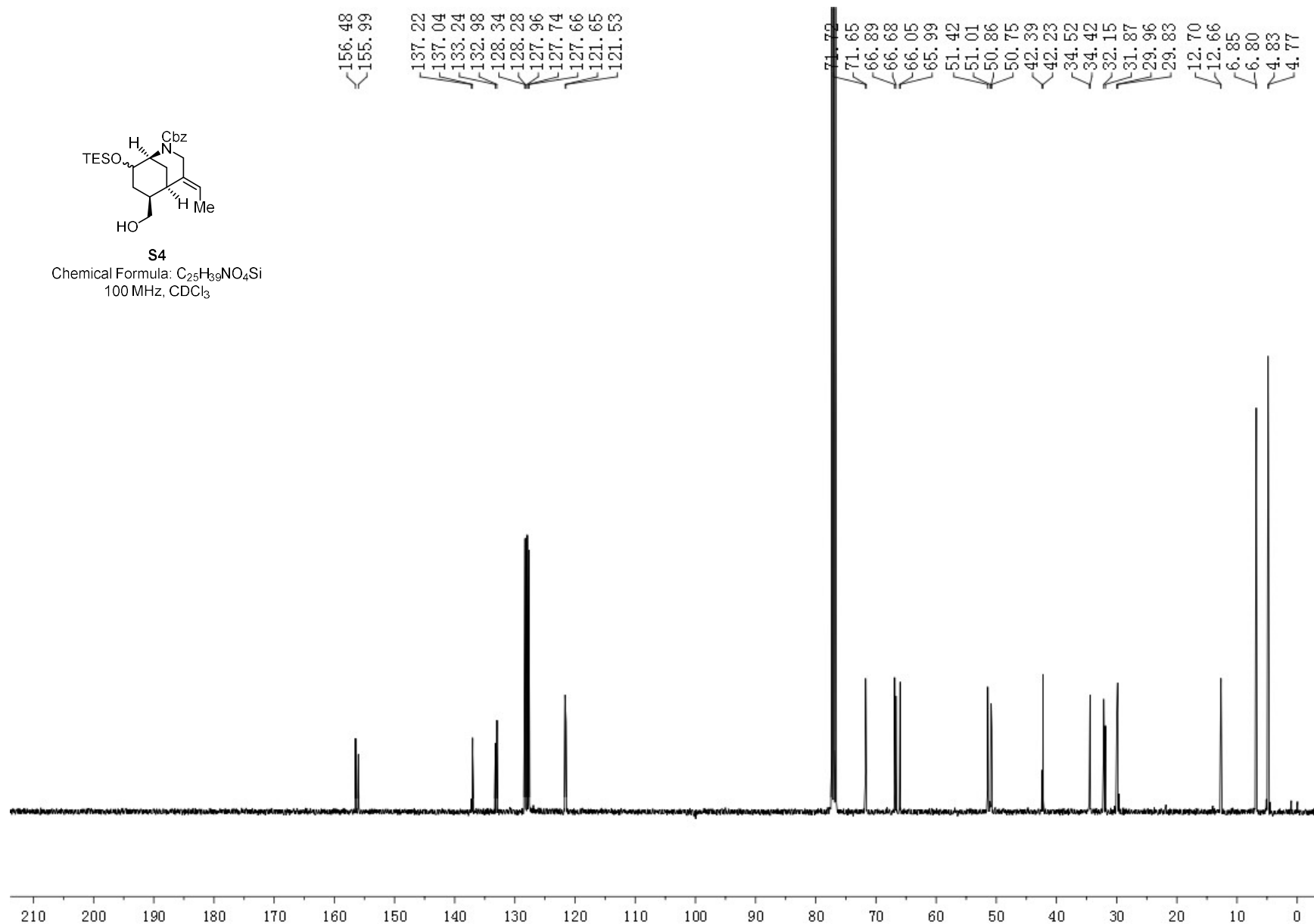


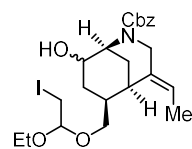
S4

Chemical Formula: C₂₅H₃₉NO₄Si
400 MHz, CDCl₃



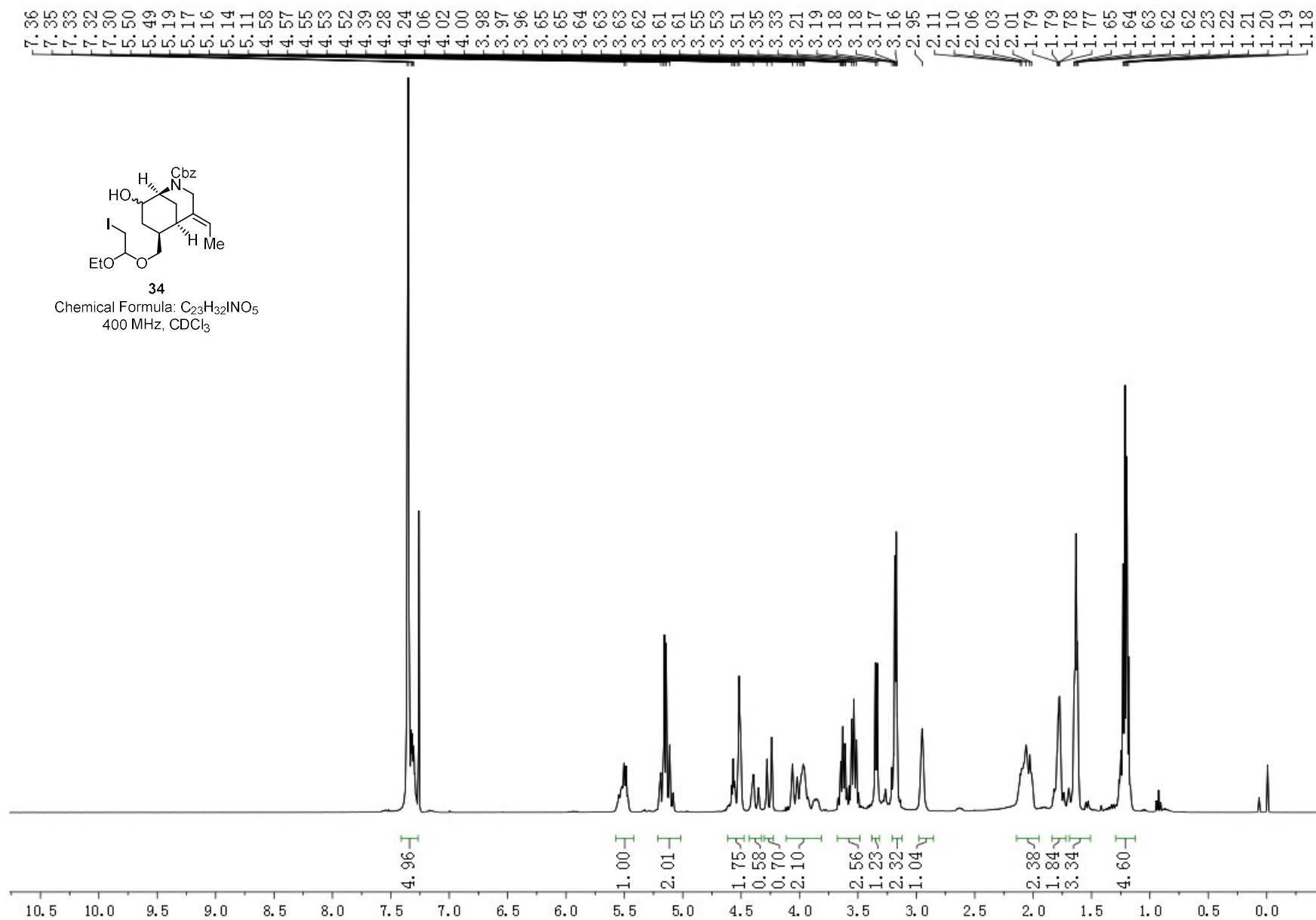
S4
Chemical Formula: $C_{25}H_{39}NO_4Si$
100 MHz, $CDCl_3$



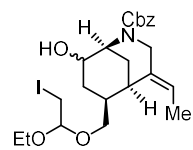


34

Chemical Formula: $C_{23}H_{32}INO_5$
400 MHz, $CDCl_3$

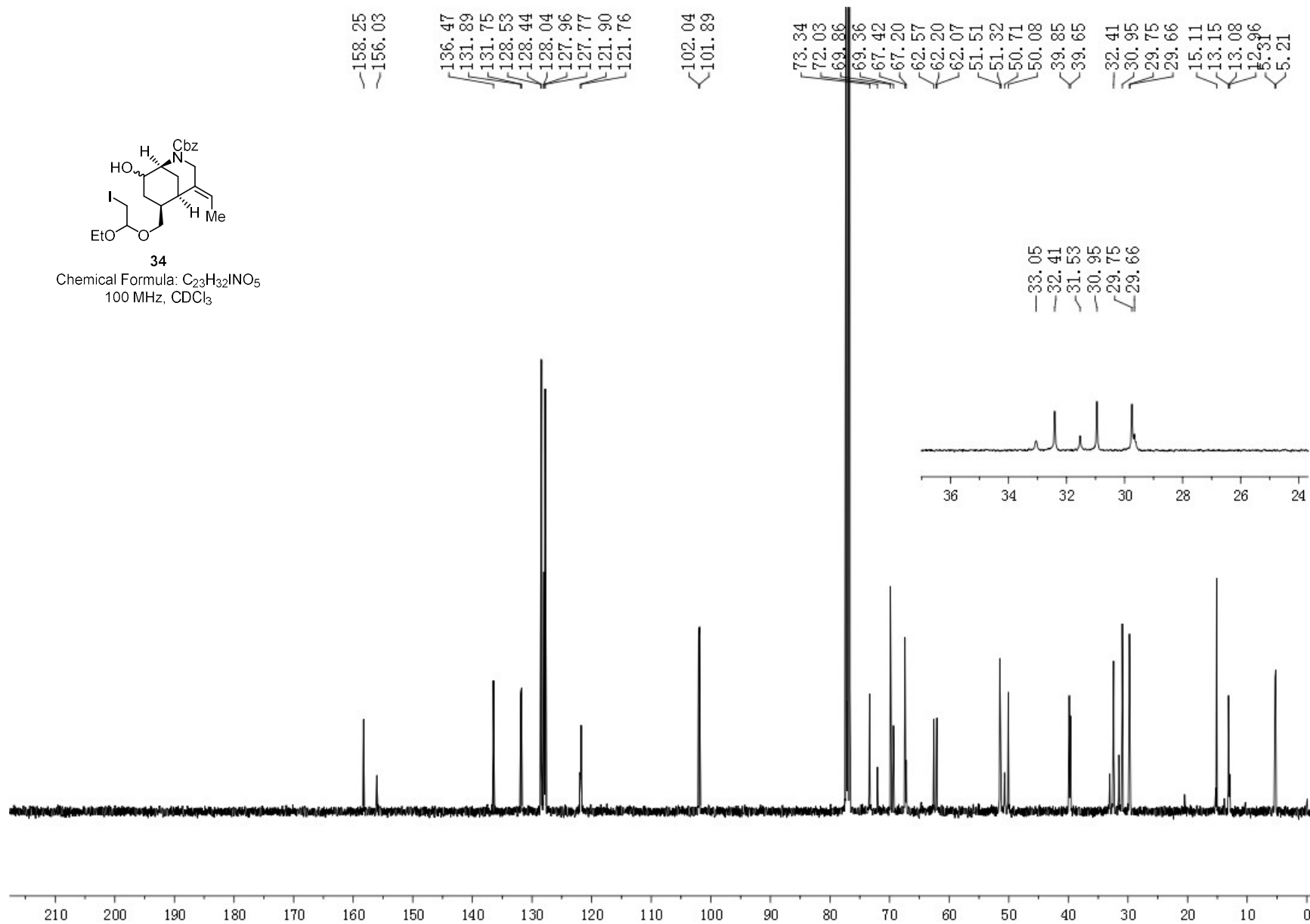


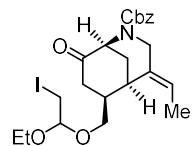
S50



34

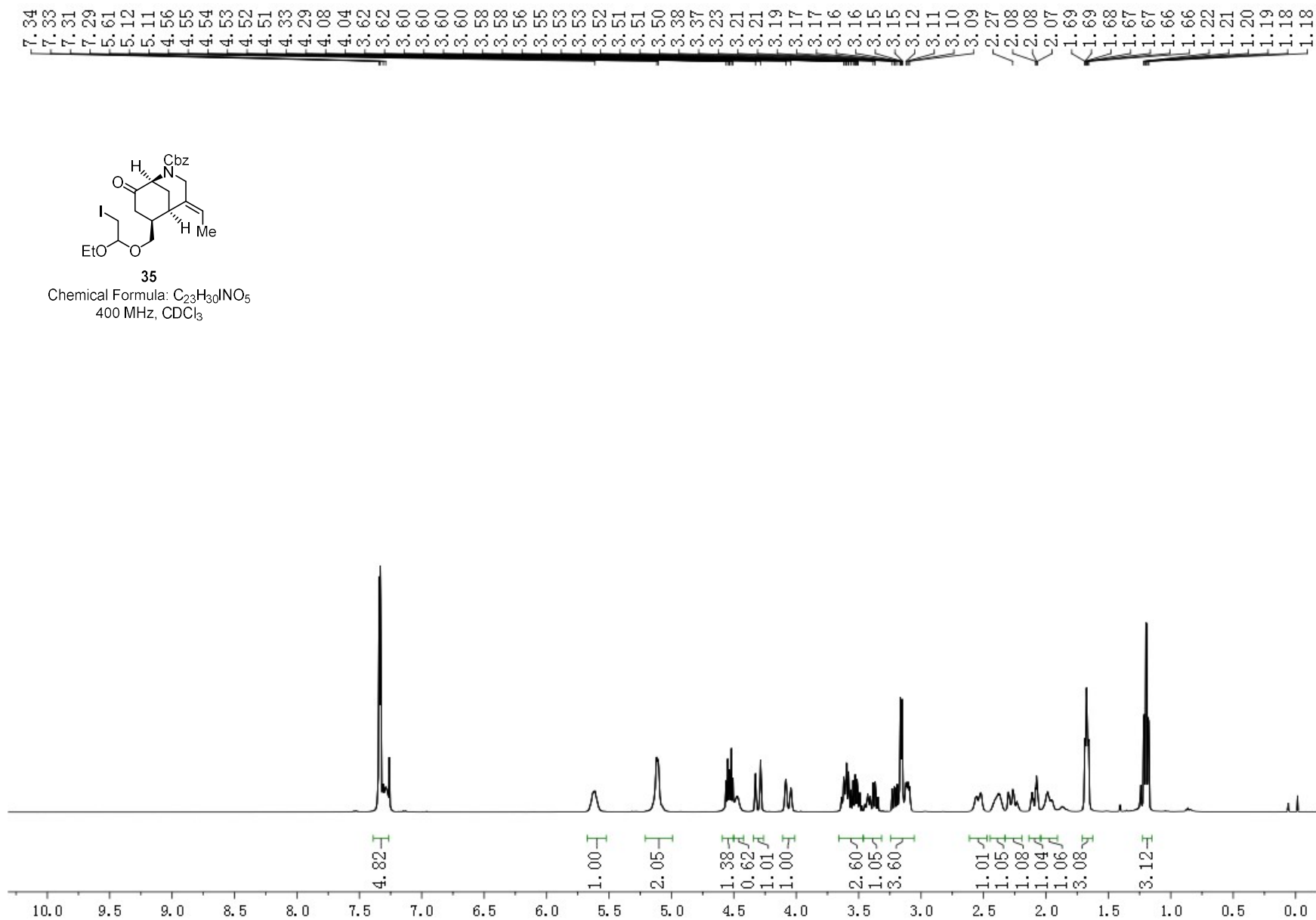
Chemical Formula: C₂₃H₃₂INO₅
100 MHz, CDCl₃

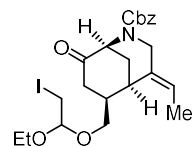




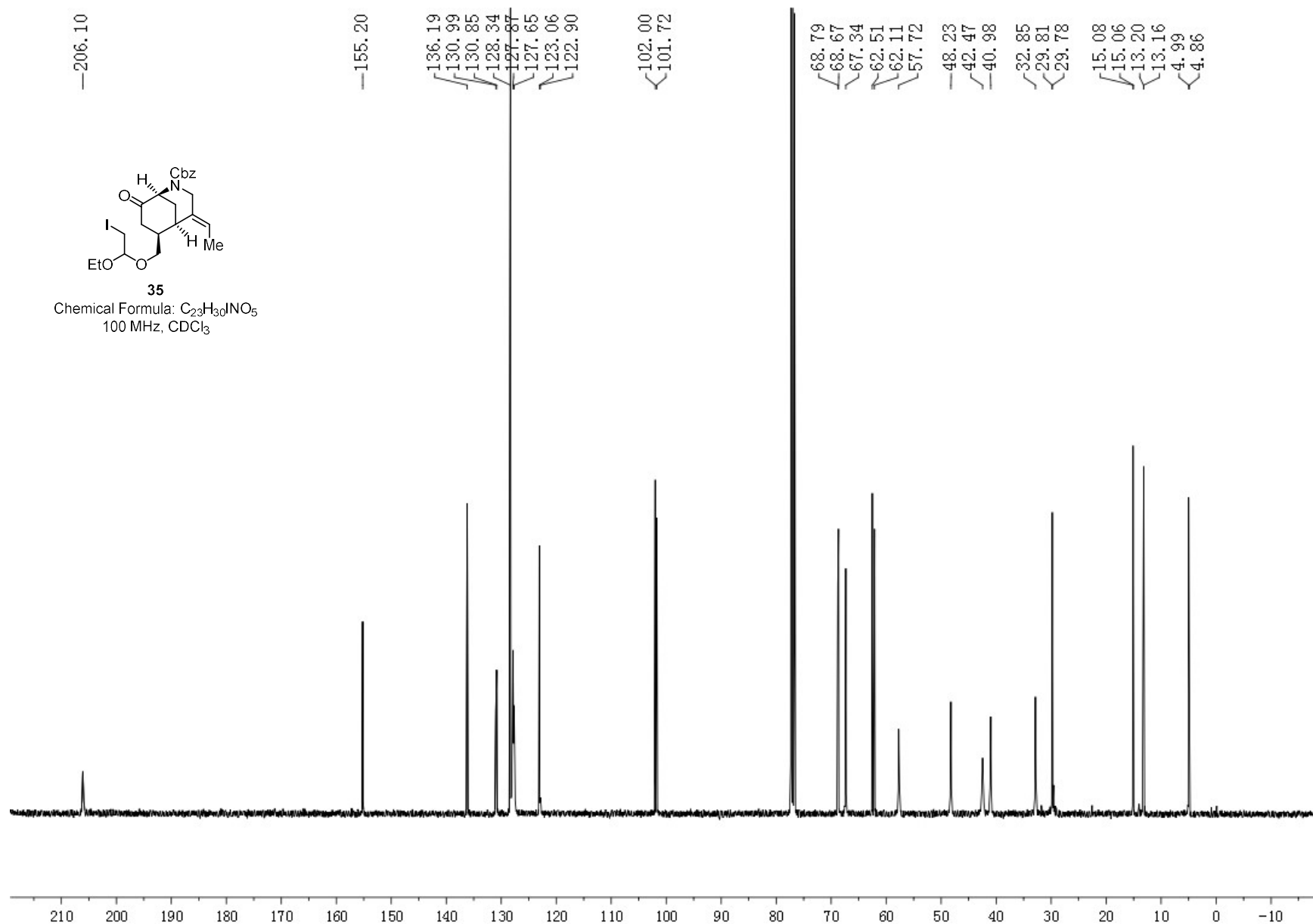
35

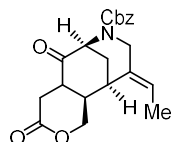
Chemical Formula: $C_{23}H_{30}INO_5$
400 MHz, $CDCl_3$





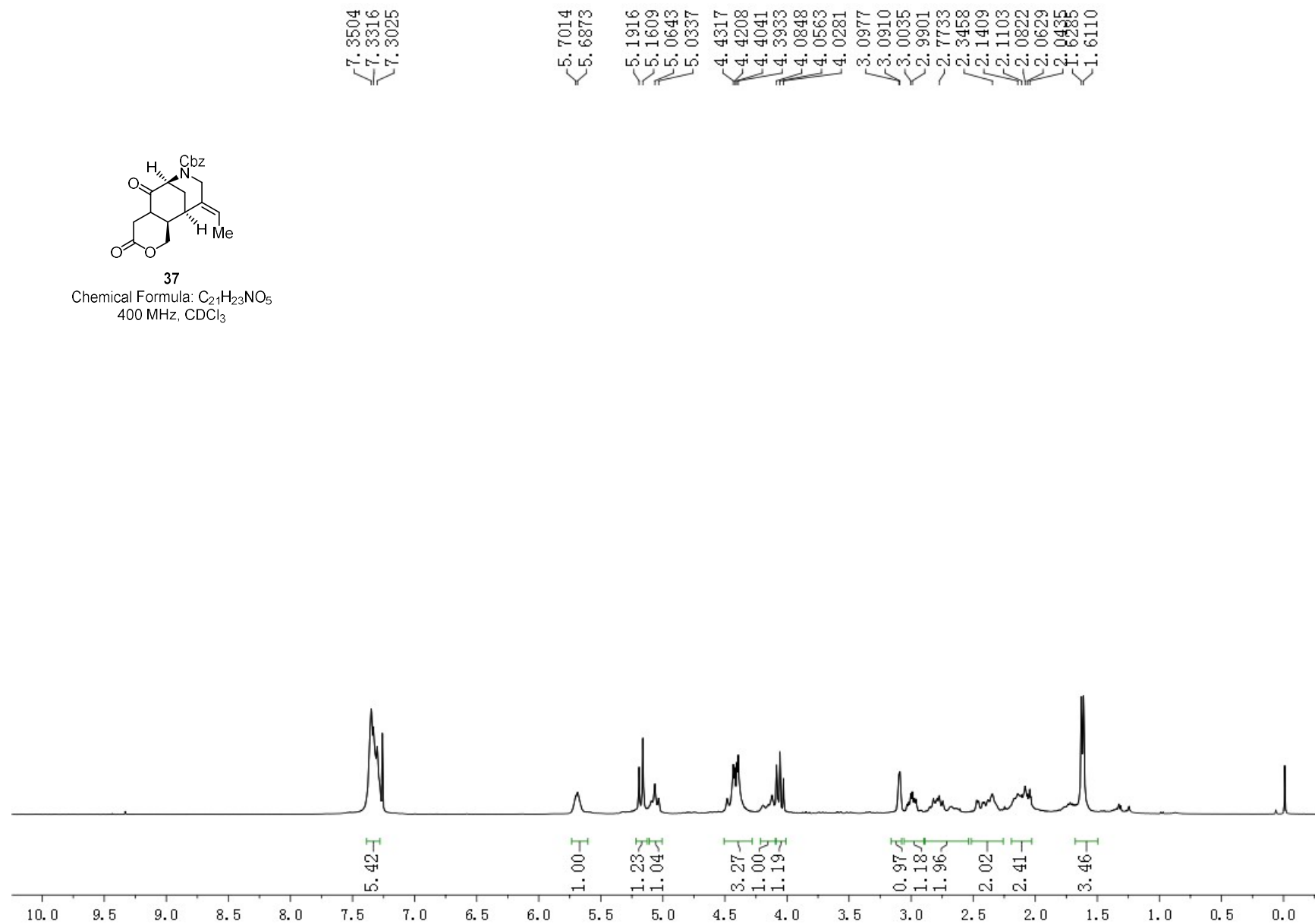
35
Chemical Formula: C₂₃H₃₀INO₅
100 MHz, CDCl₃

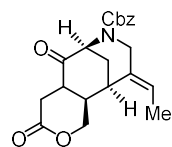




37

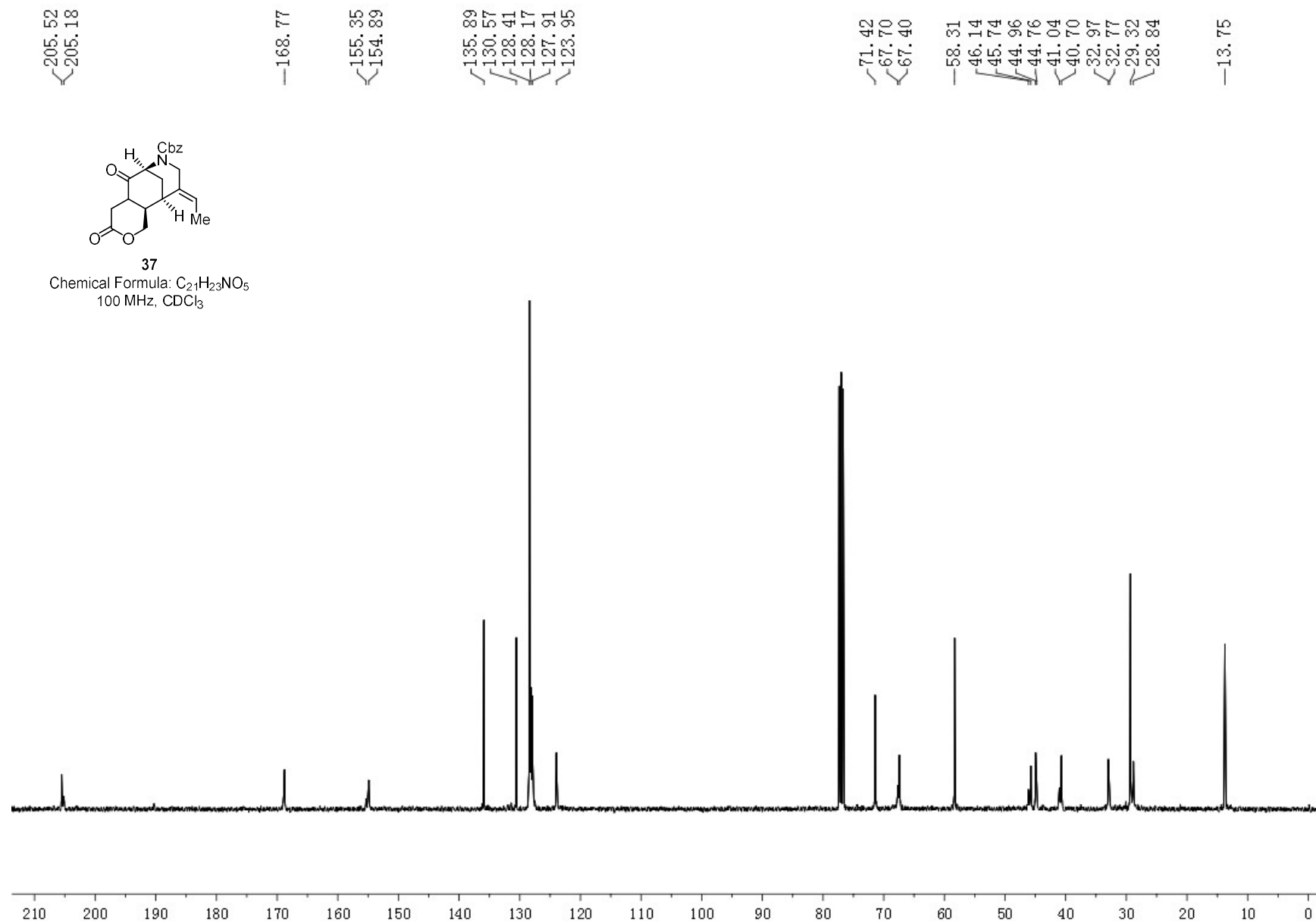
Chemical Formula: $C_{21}H_{23}NO_5$
400 MHz, $CDCl_3$

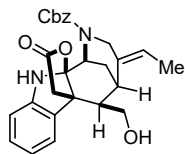




37

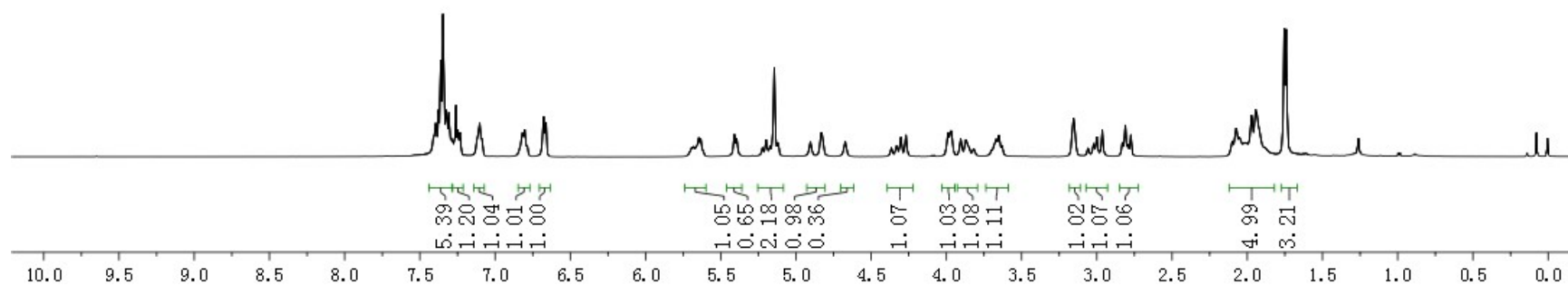
Chemical Formula: $C_{21}H_{23}NO_5$
100 MHz, $CDCl_3$

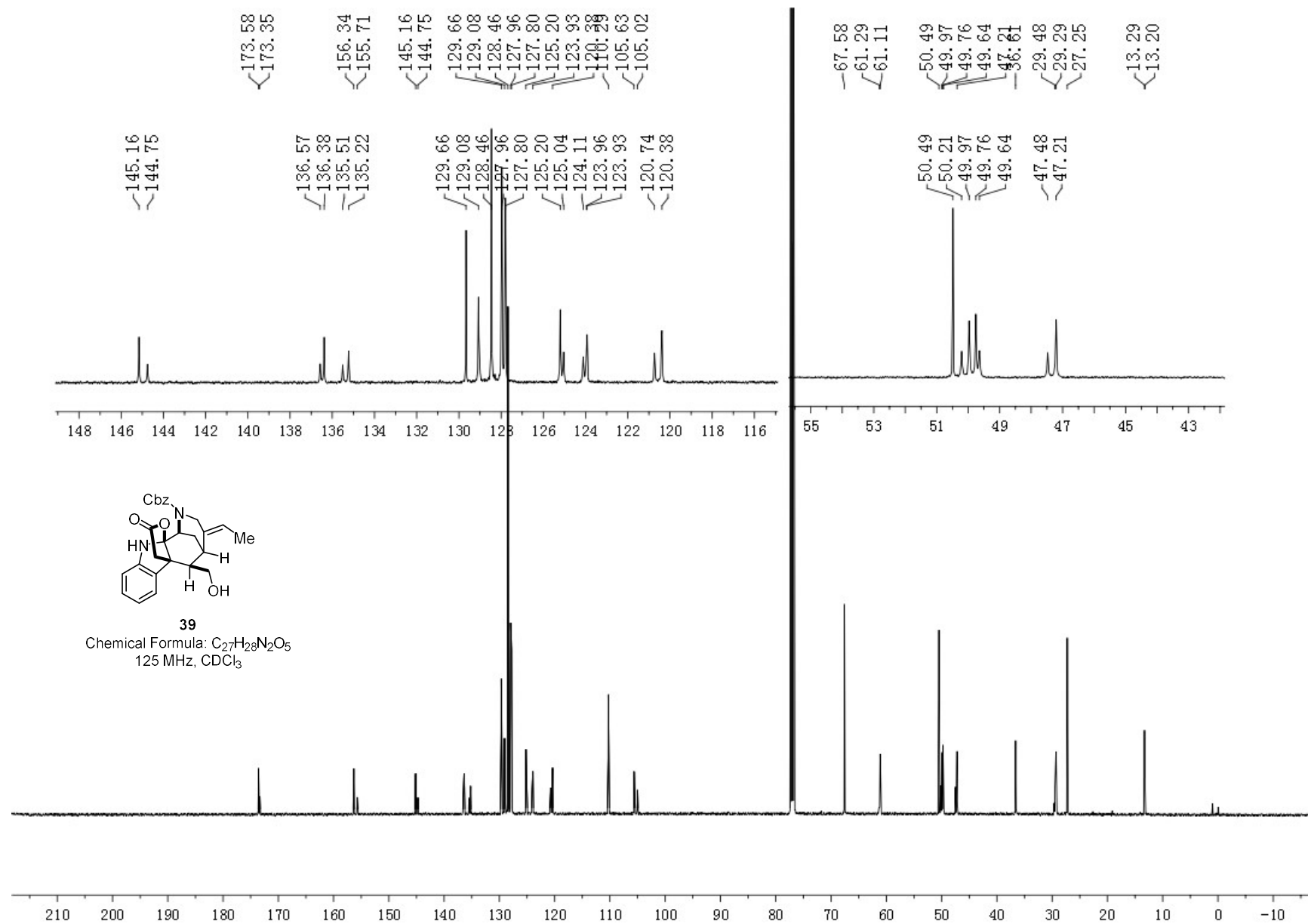


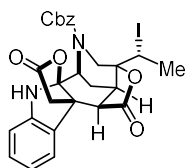


39

Chemical Formula: $C_{27}H_{28}N_2O_5$
500 MHz, $CDCl_3$

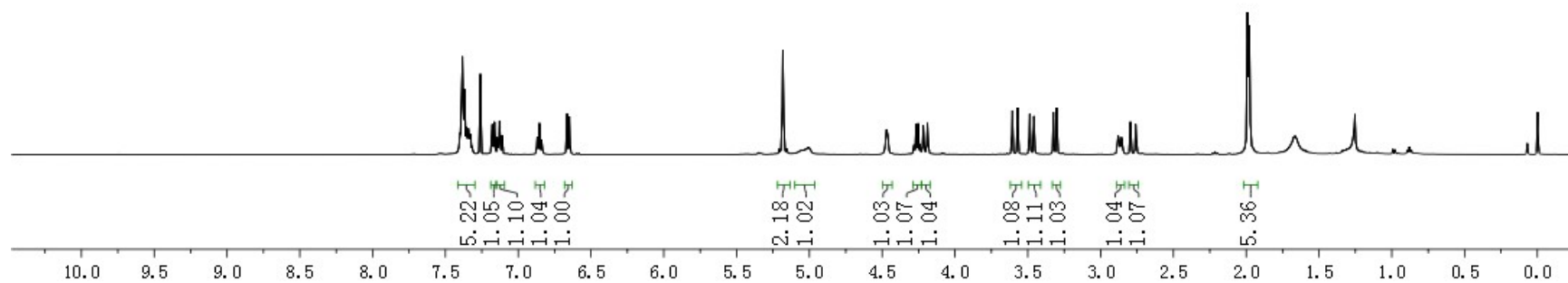


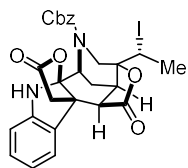




40

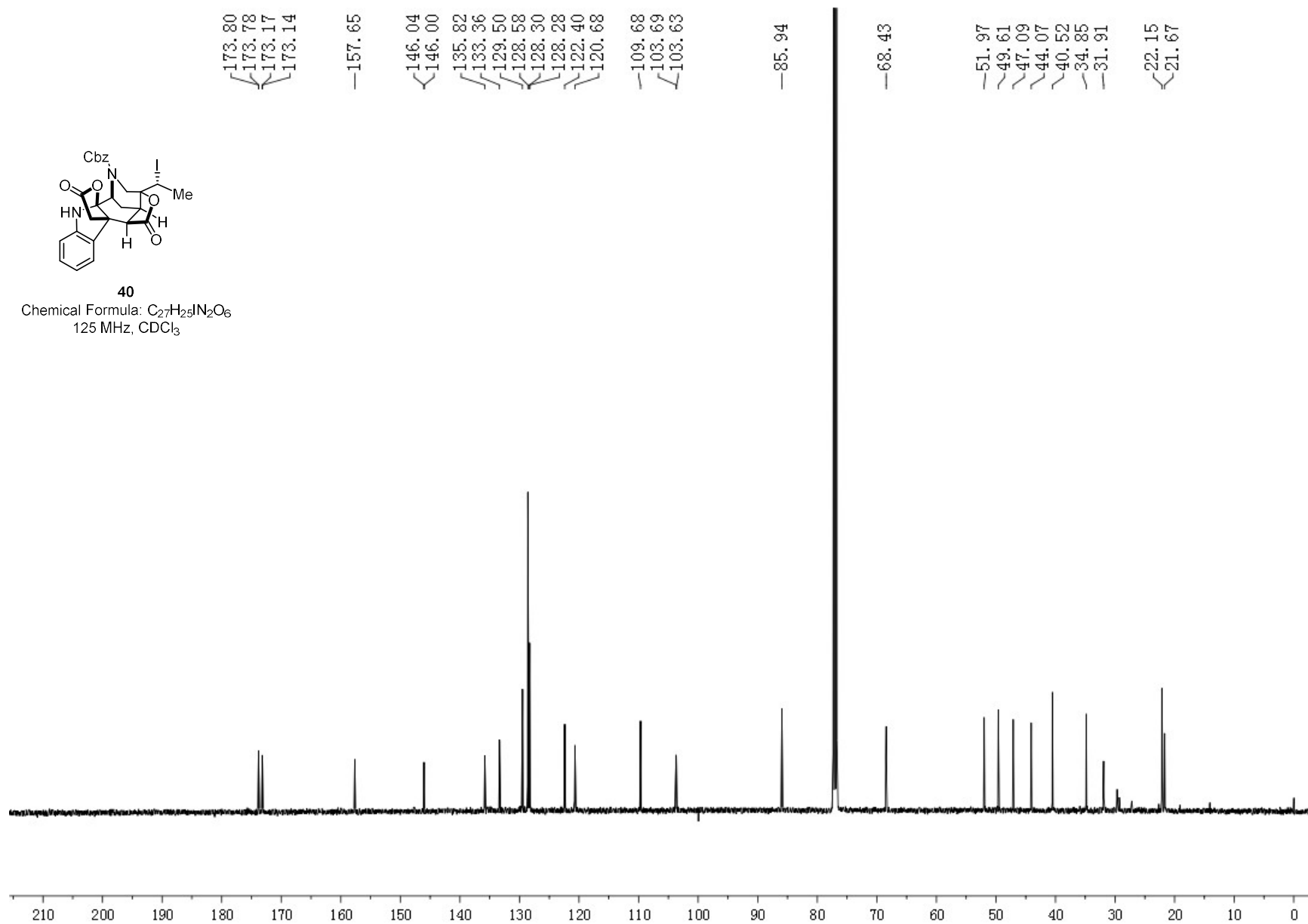
Chemical Formula: $C_{27}H_{25}IN_2O_6$
500 MHz, $CDCl_3$

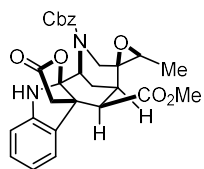




40

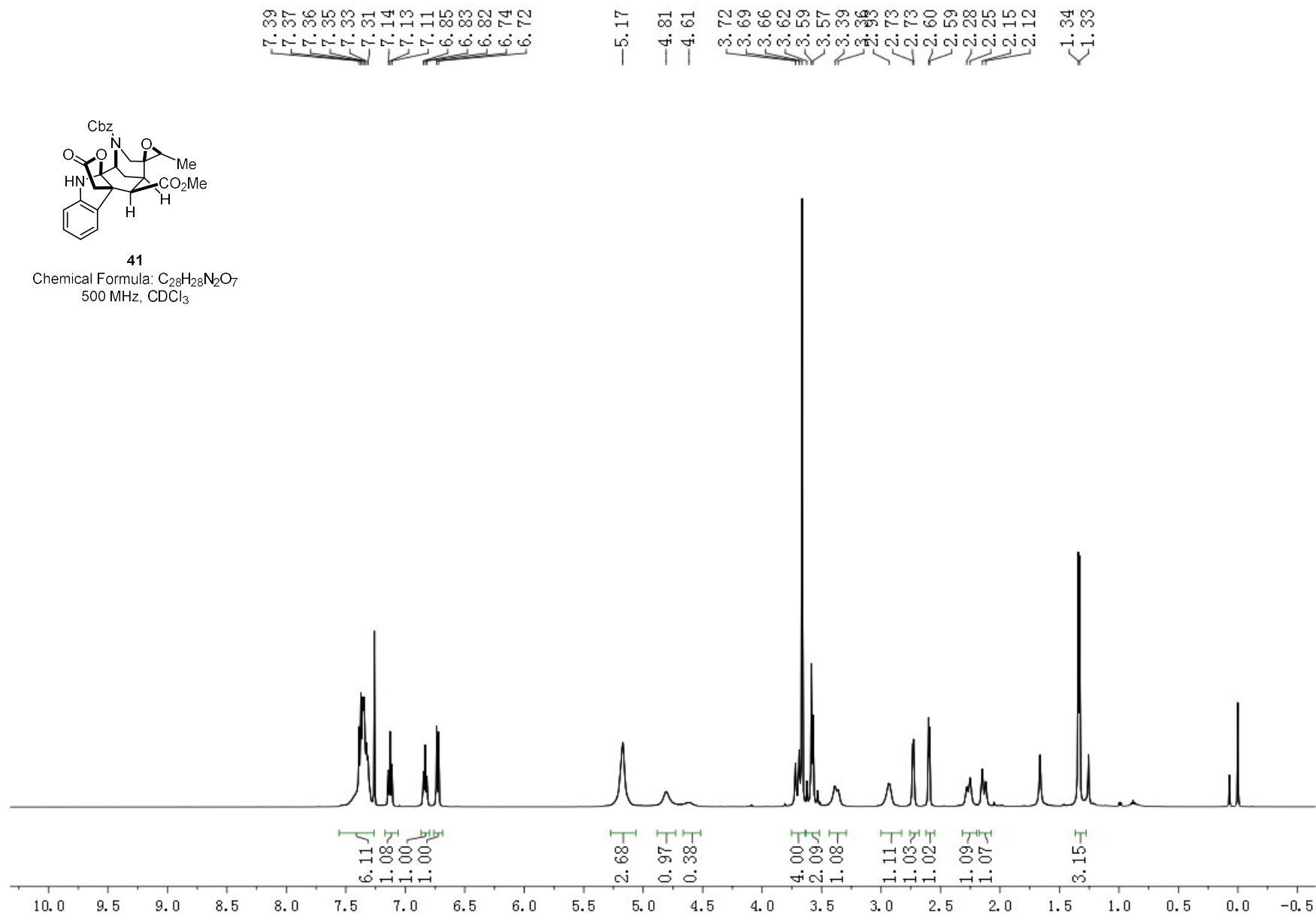
Chemical Formula: $C_{27}H_{25}IN_2O_6$
125 MHz, $CDCl_3$

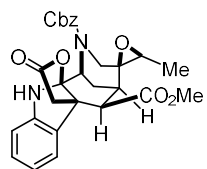




41

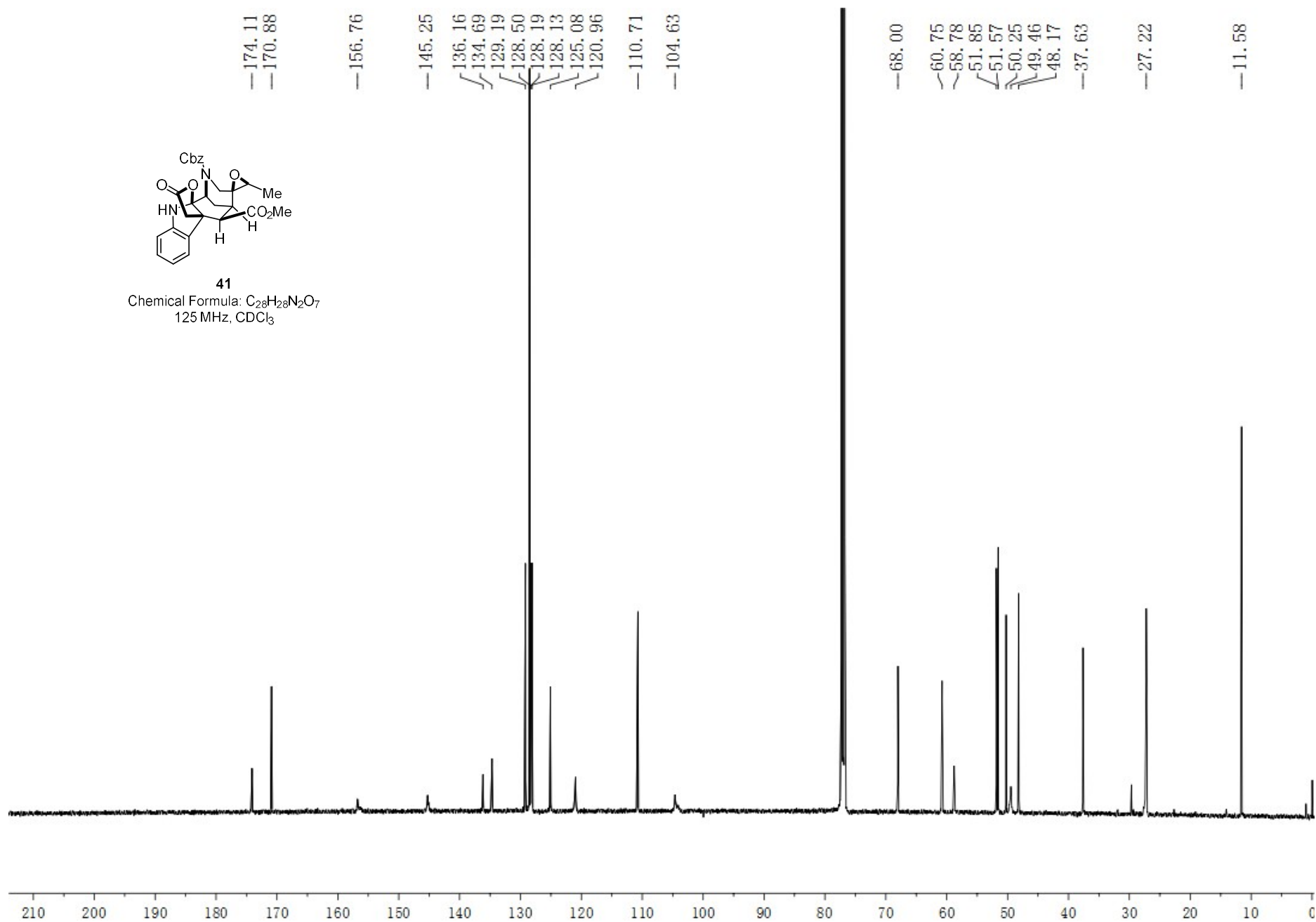
Chemical Formula: $C_{28}H_{28}N_2O_7$
500 MHz, $CDCl_3$

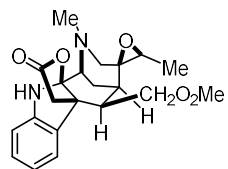




41

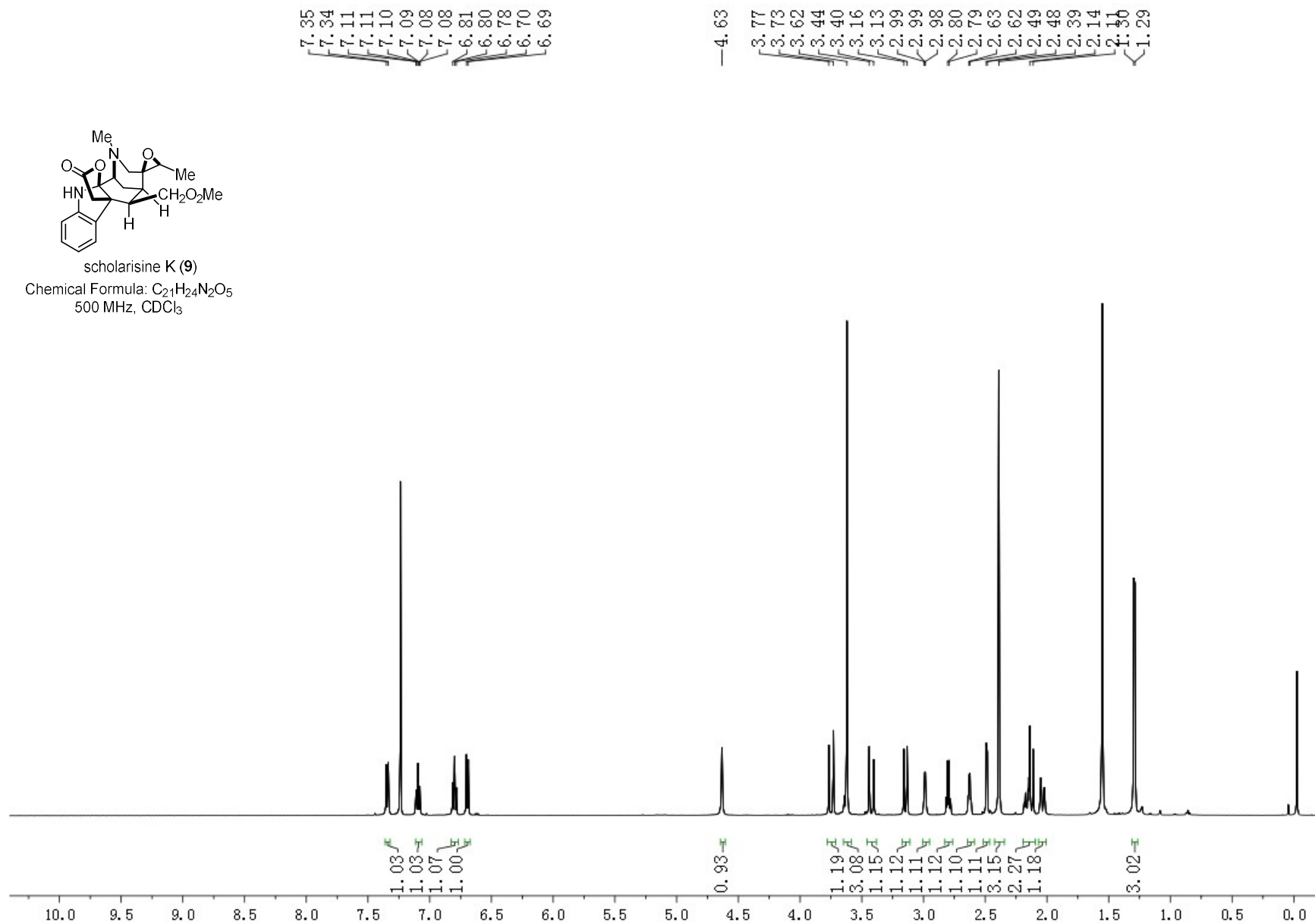
Chemical Formula: C₂₈H₂₈N₂O₇
125 MHz, CDCl₃

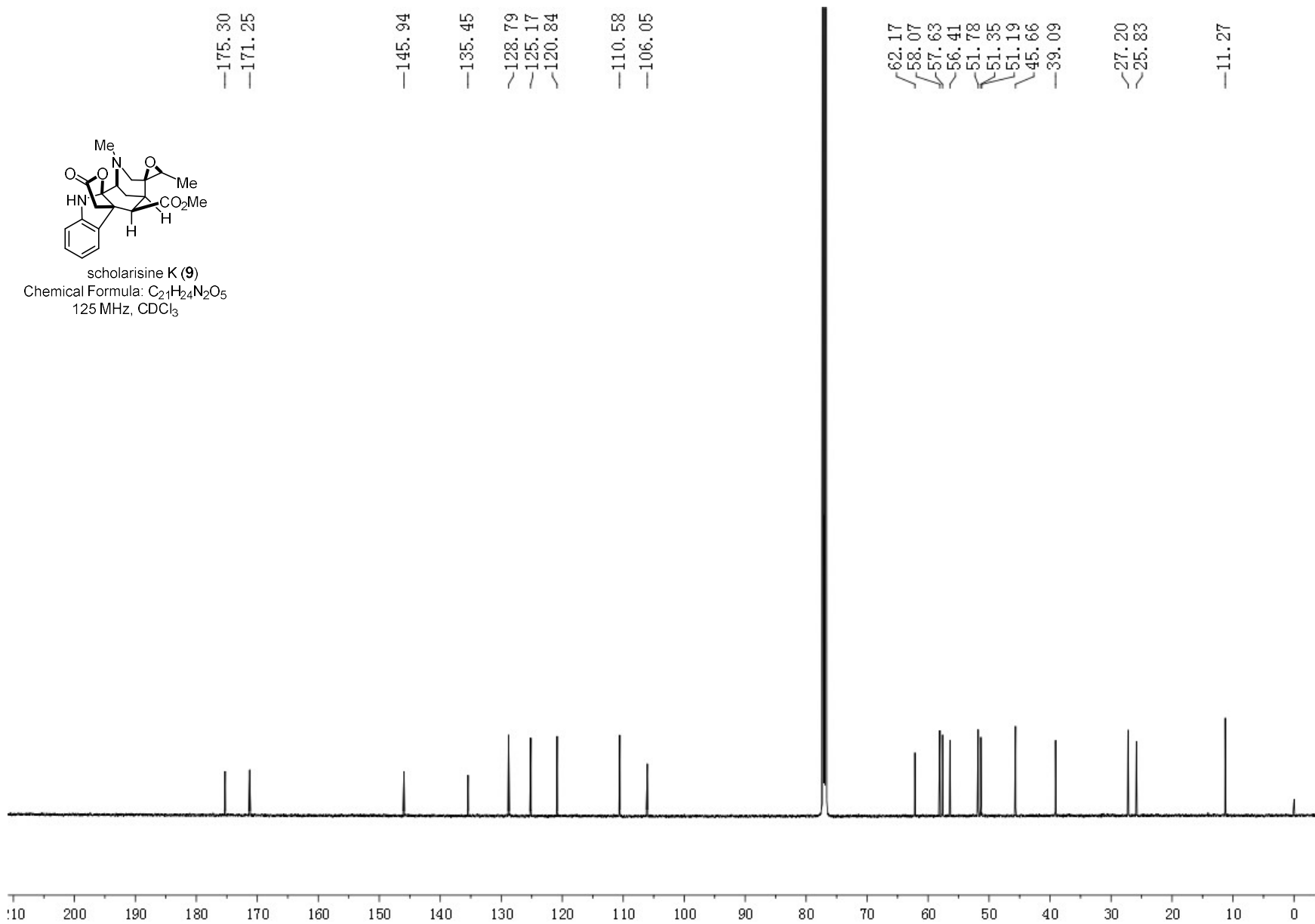




scholarisine K (**9**)

Chemical Formula: $C_{21}H_{24}N_2O_5$
500 MHz, $CDCl_3$



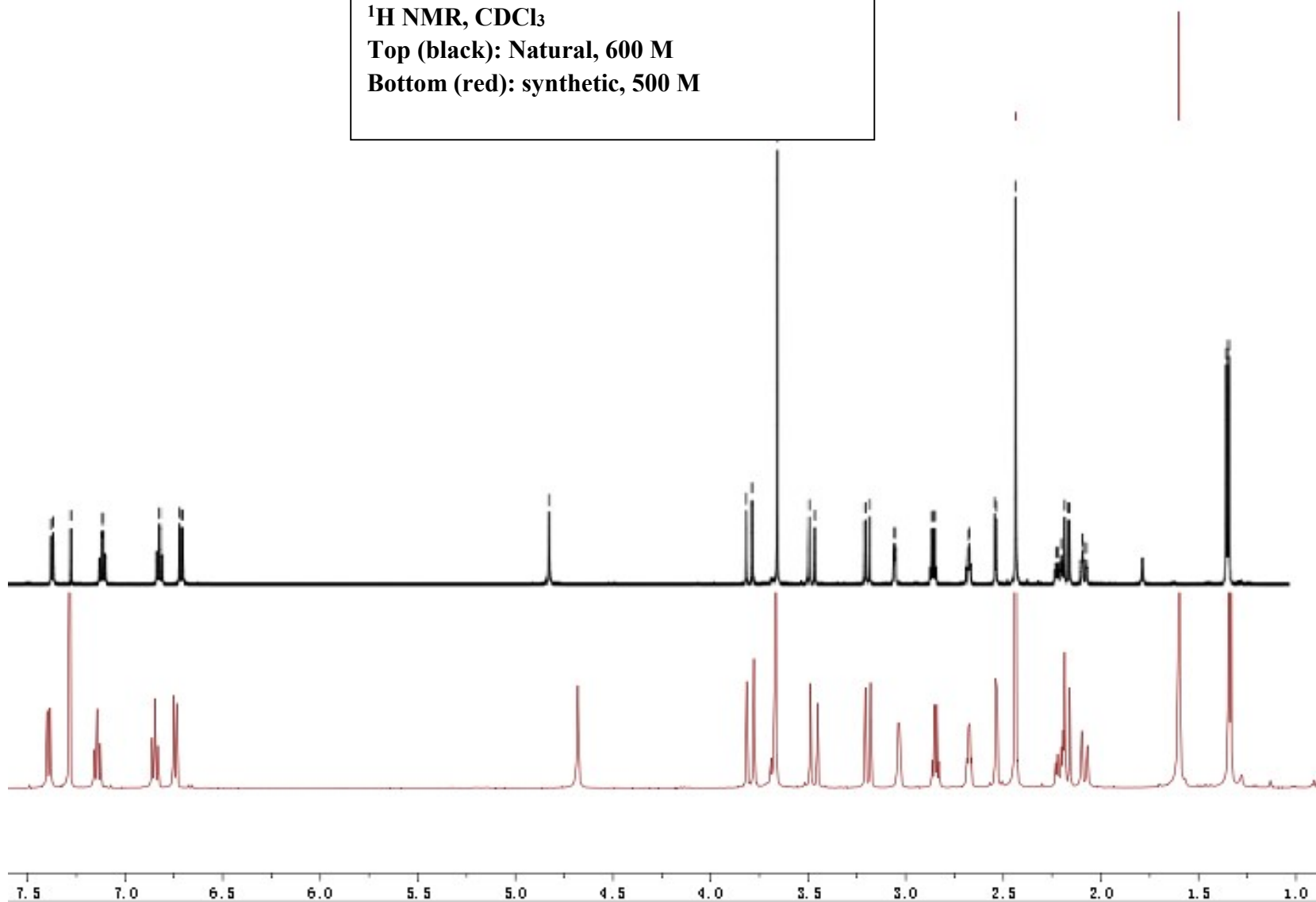


Scholarisine K Comparison Spectra

^1H NMR, CDCl_3

Top (black): Natural, 600 M

Bottom (red): synthetic, 500 M

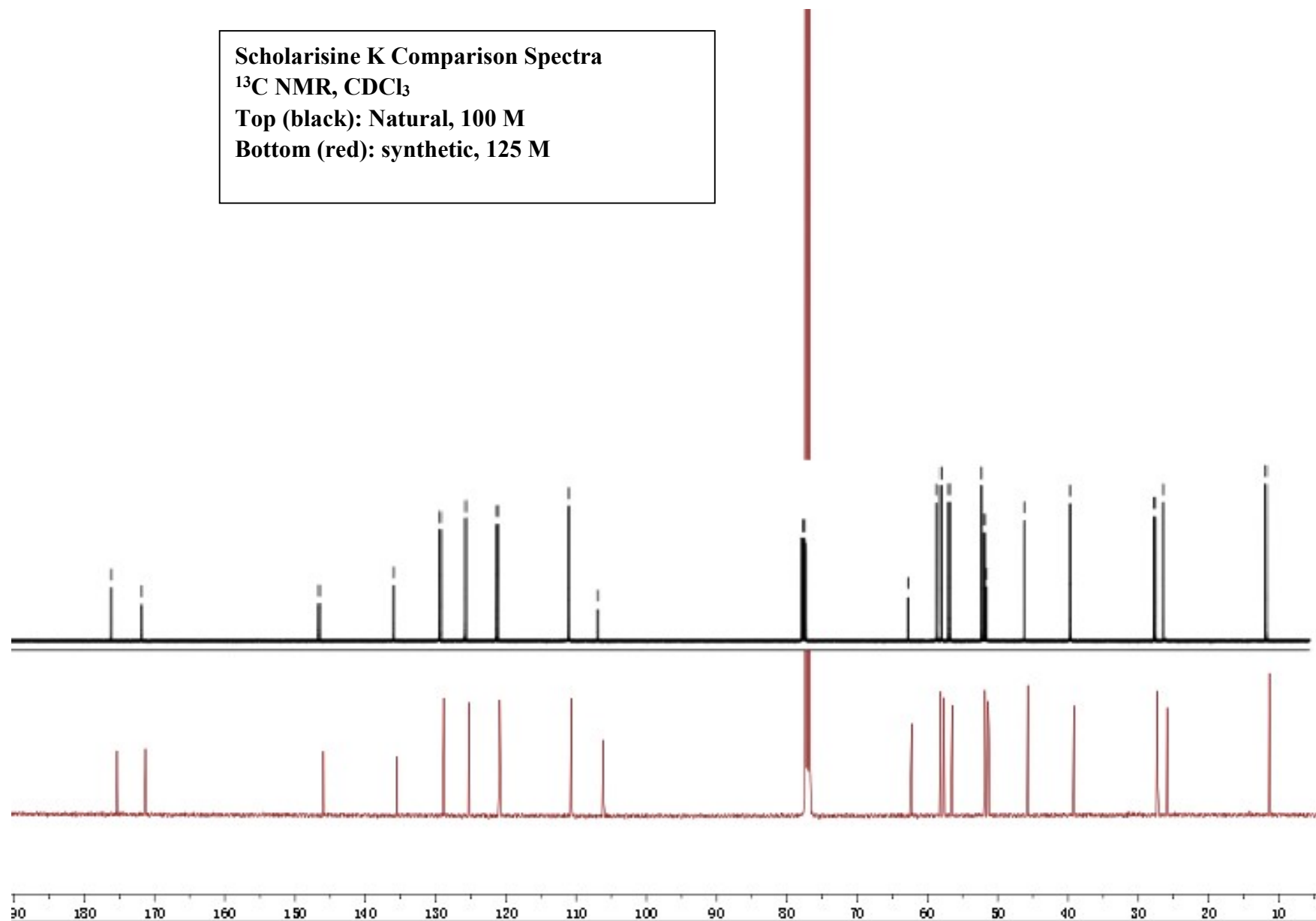


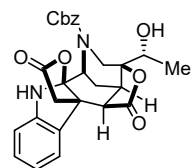
Scholarisine K Comparison Spectra

^{13}C NMR, CDCl_3

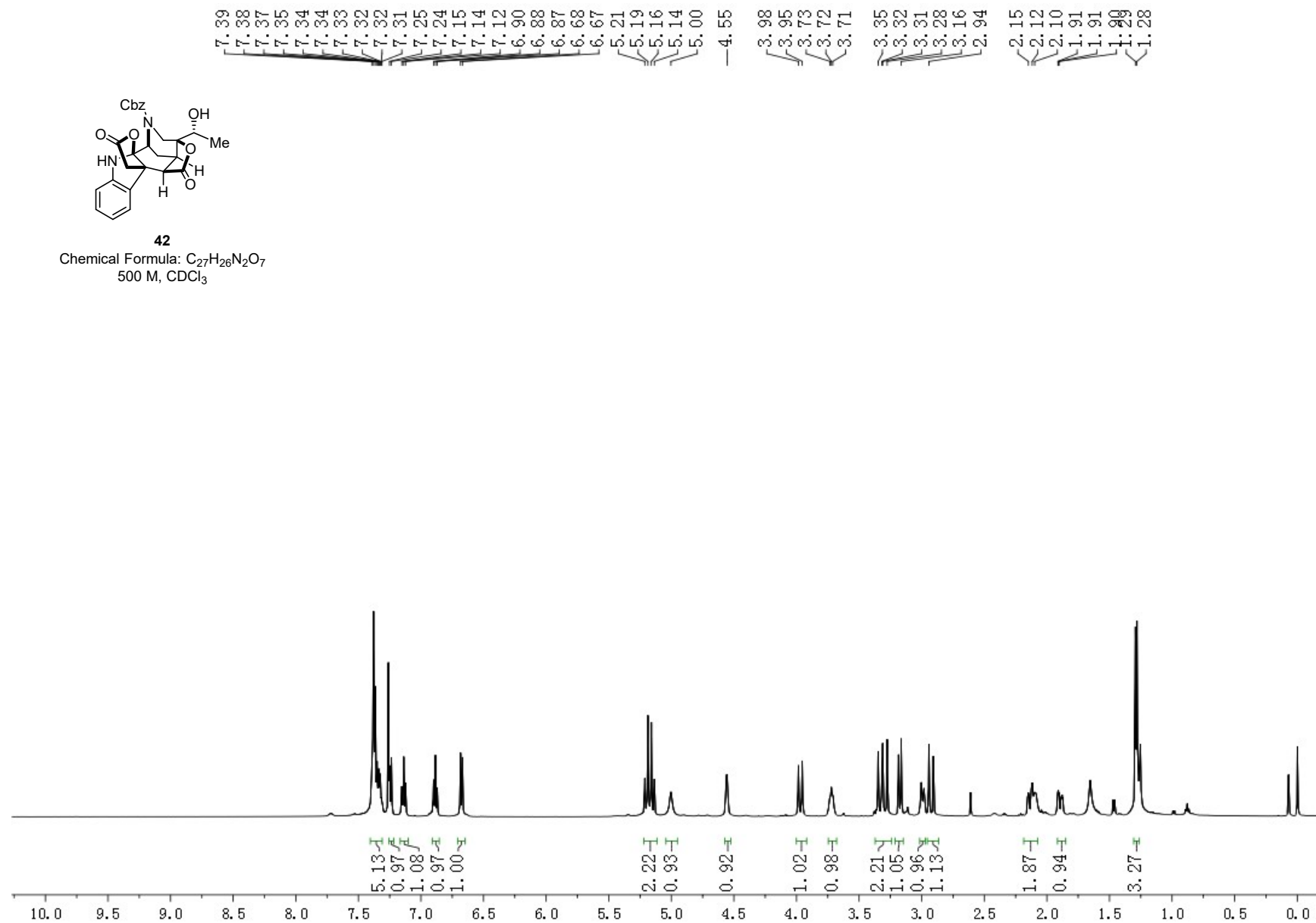
Top (black): Natural, 100 M

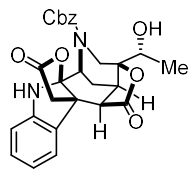
Bottom (red): synthetic, 125 M





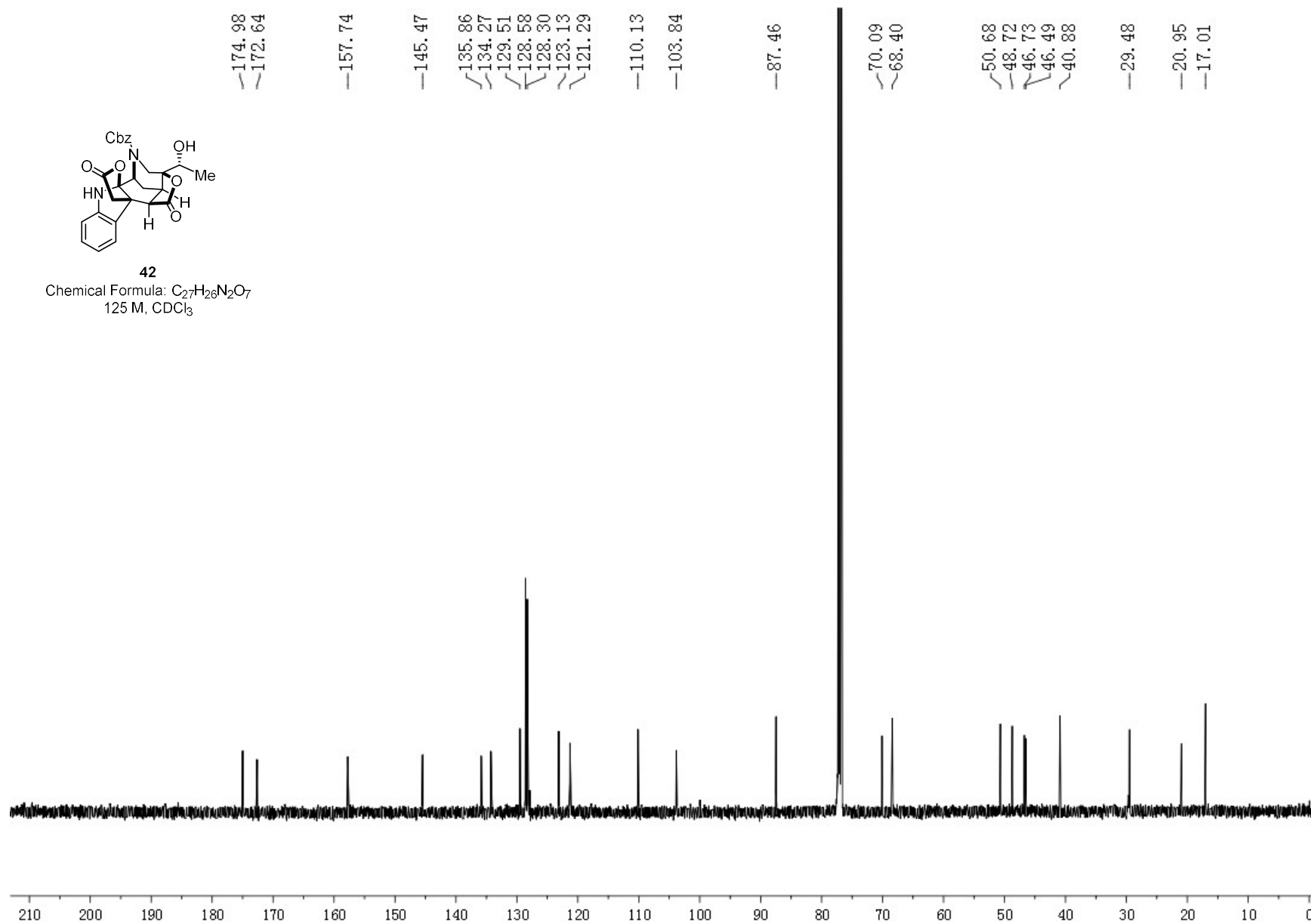
42
Chemical Formula: $C_{27}H_{26}N_2O_7$
500 M, $CDCl_3$

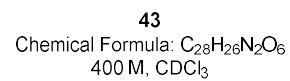


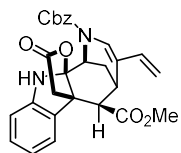


42

Chemical Formula: $C_{27}H_{26}N_2O_7$
125 M, $CDCl_3$

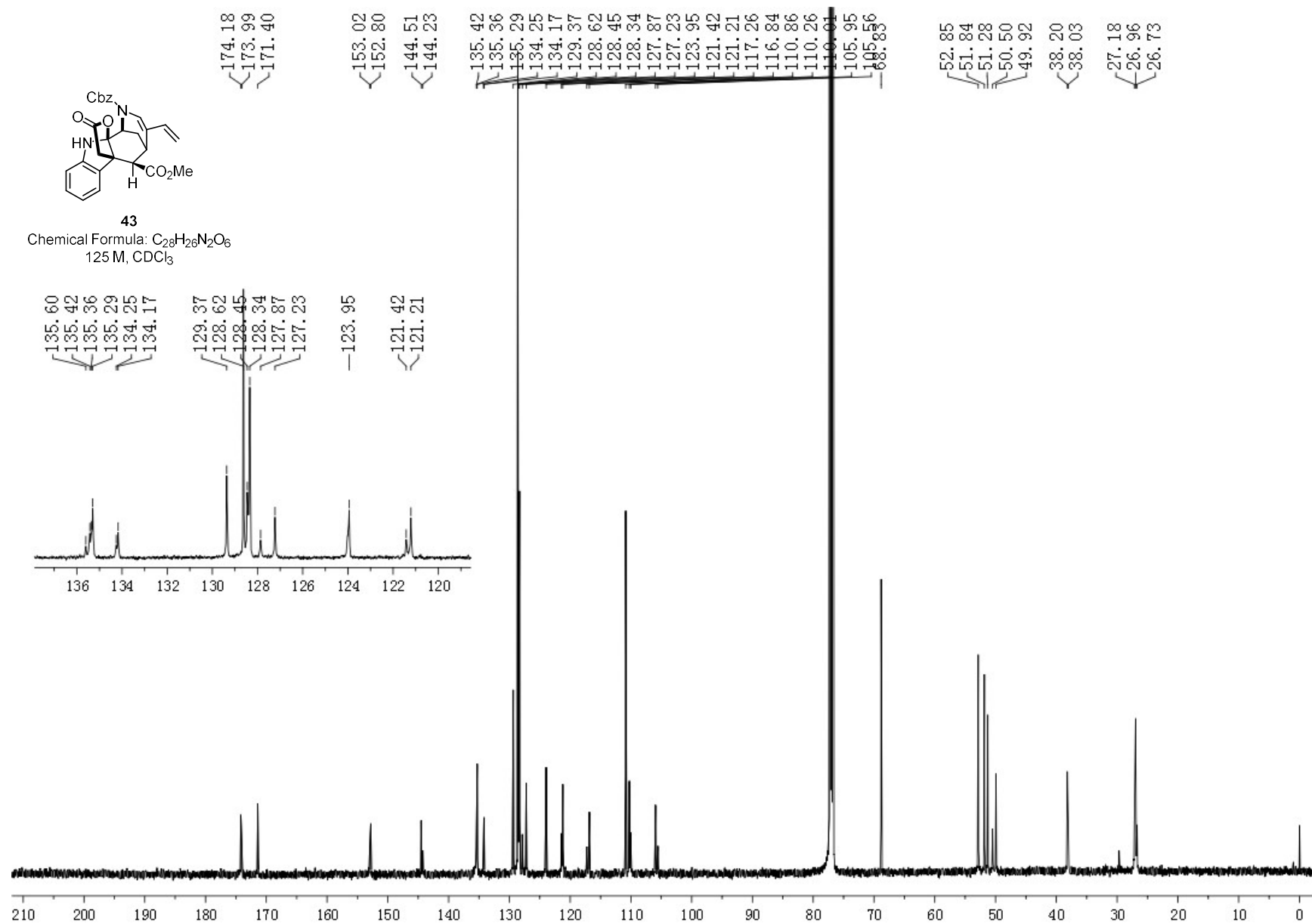


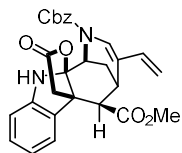




43

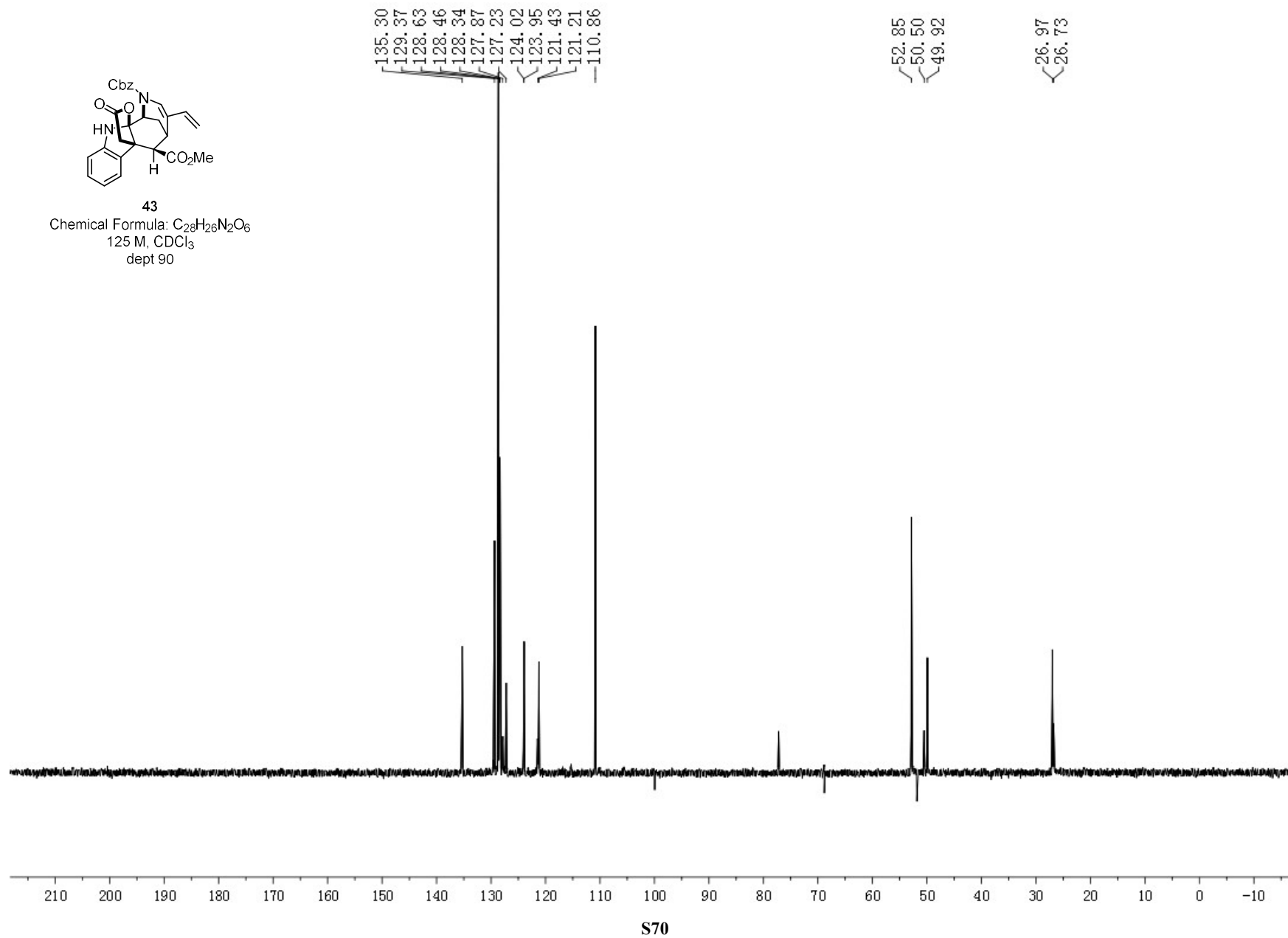
Chemical Formula: $C_{28}H_{26}N_2O_6$
125 M, $CDCl_3$

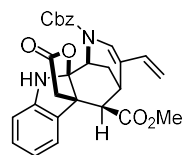




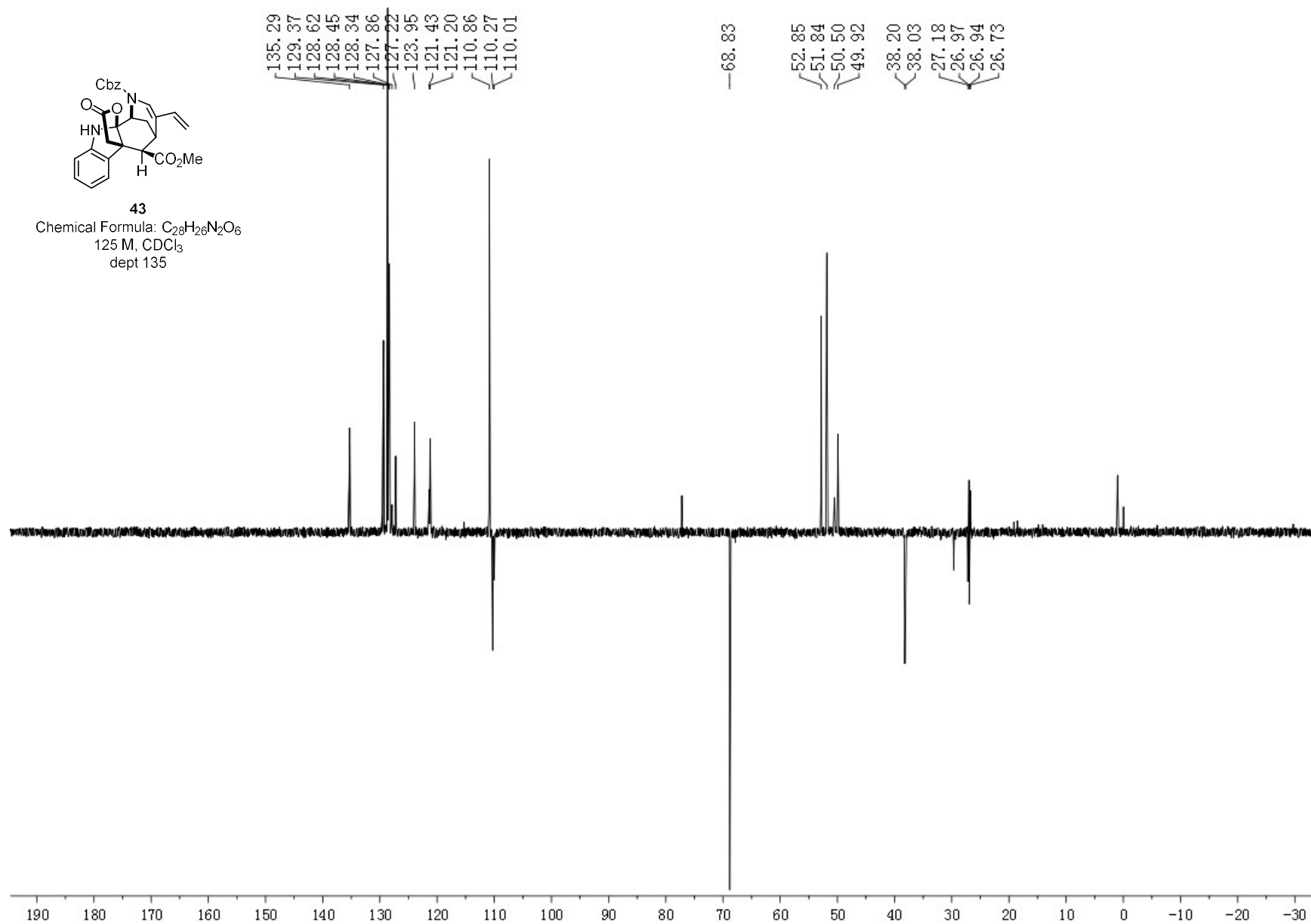
43

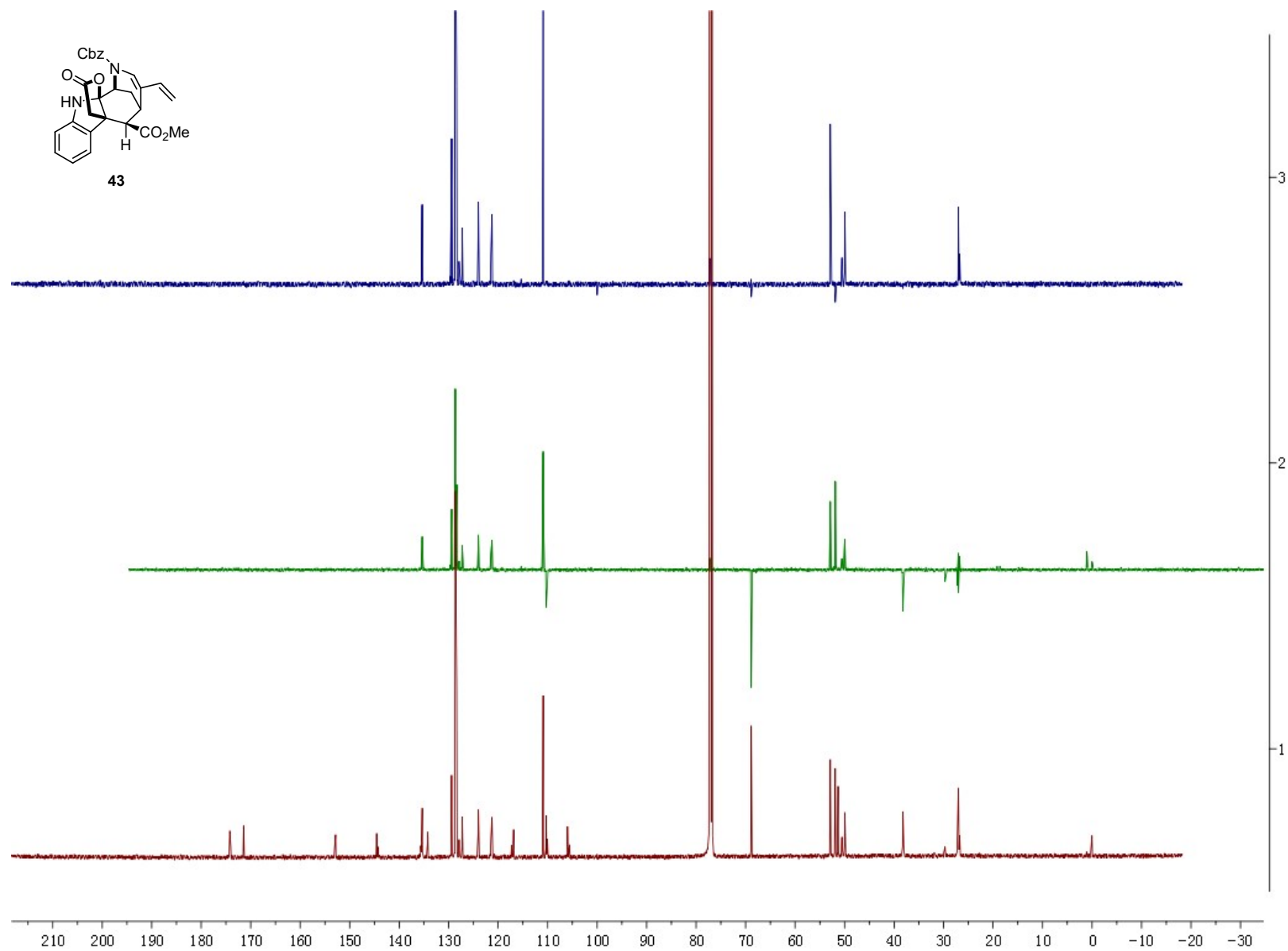
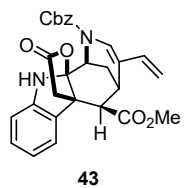
Chemical Formula: $C_{28}H_{26}N_2O_6$
 125 M, $CDCl_3$
 dept 90

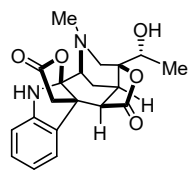




43
 Chemical Formula: $C_{28}H_{26}N_2O_6$
 125 M, $CDCl_3$
 dept 135

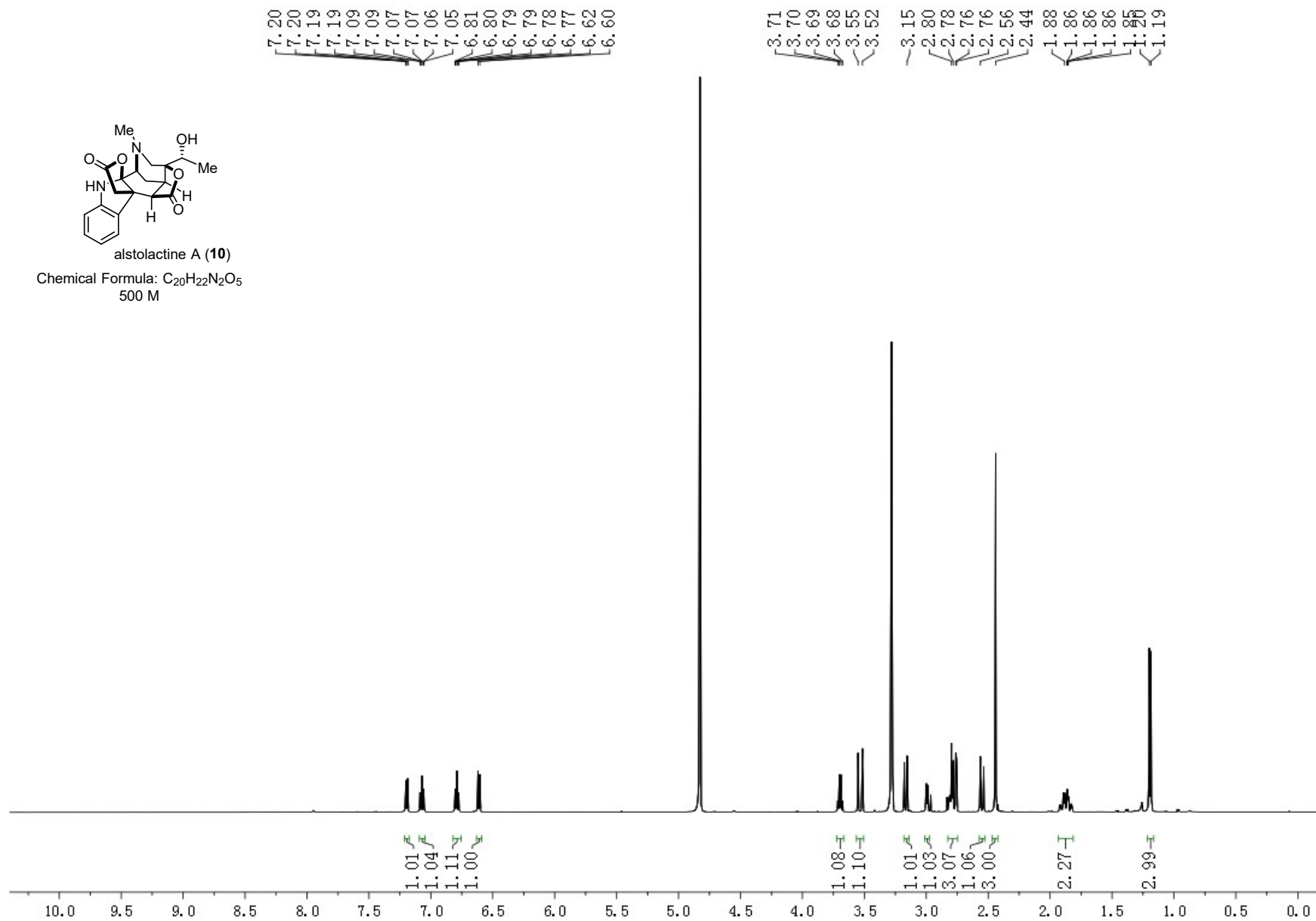


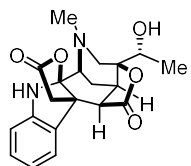




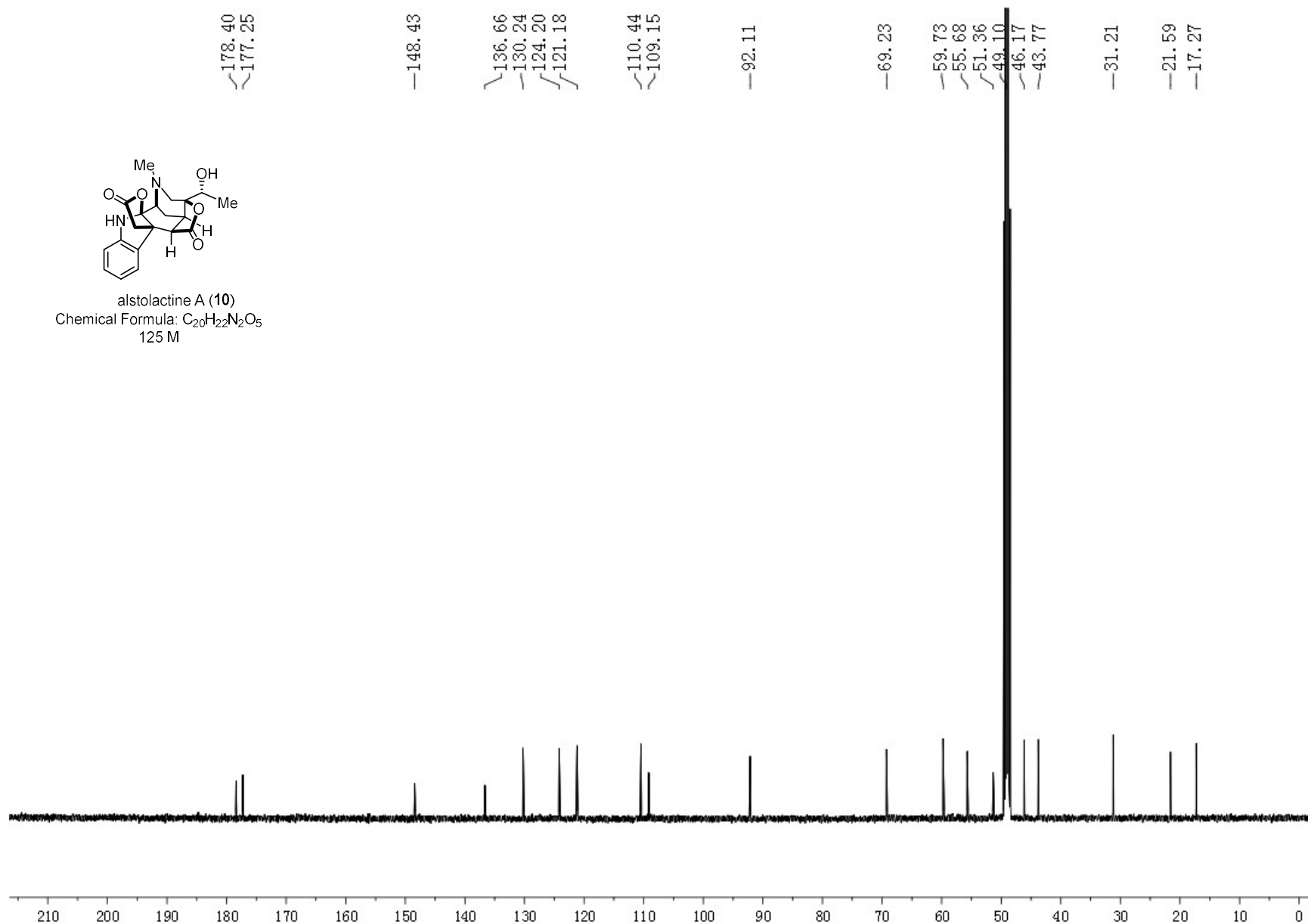
alstolactone A (**10**)

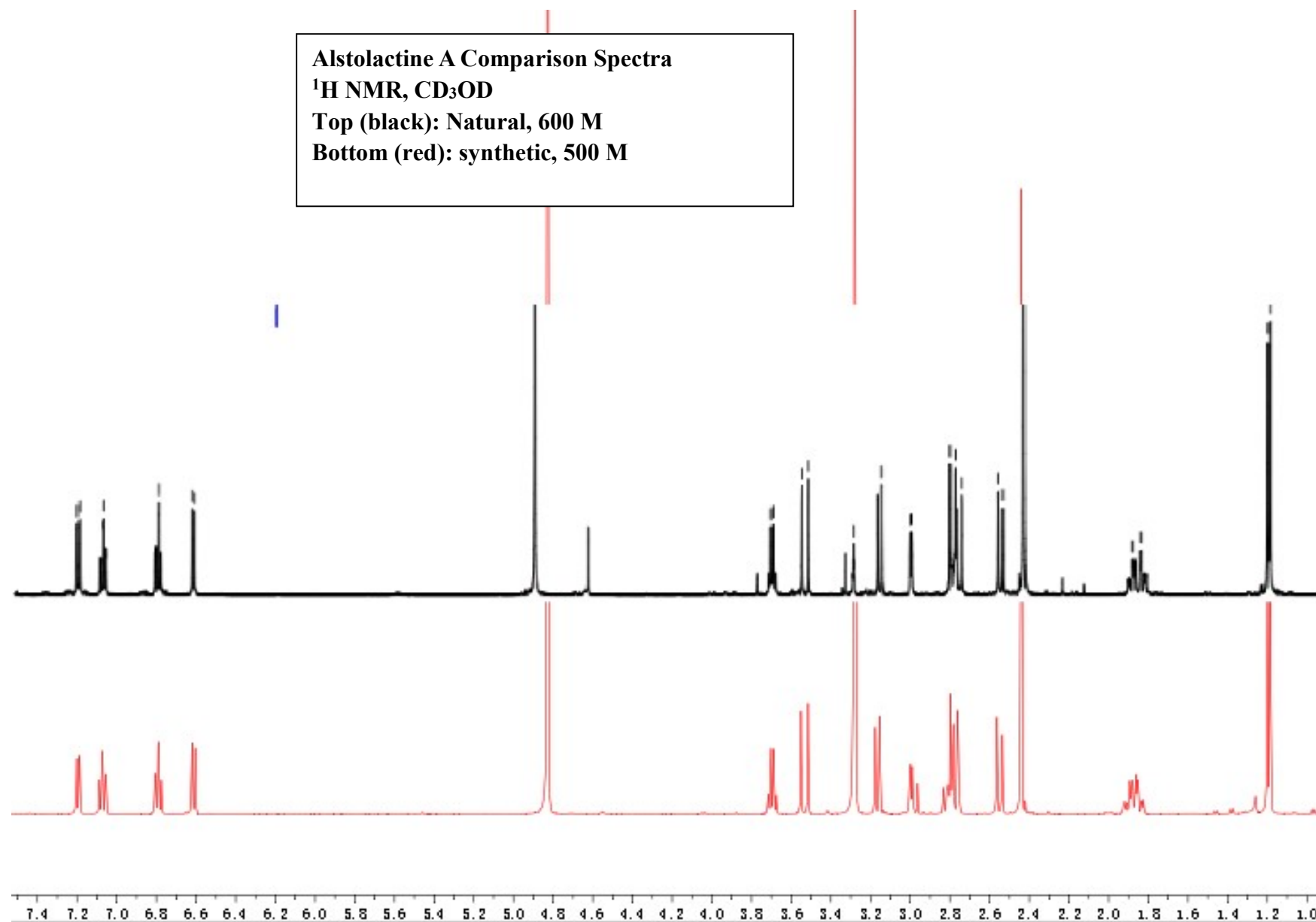
Chemical Formula: $C_{20}H_{22}N_2O_5$
500 M





alstolactine A (**10**)
 Chemical Formula: C₂₀H₂₂N₂O₅
 125 M





Alstolactine A Comparison Spectra

^1H NMR, CD_3OD

Top (black): Natural, 100 M

Bottom (red): synthetic, 125 M

