Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Total Syntheses of Seven Stemoamide-Type Alkaloids

Tao Shi,[a],‡ Fei Cao,[b],‡ Jinhong Chen,[a] Xiaodong Wang,[a] Gaofeng Yin,[a] Huihong Wang,[b] Zhen Wang[a,b,c]

[a] T.S., J.C., X.W., G.Y., Z.W.*
School of Pharmacy
Lanzhou University
No 199 West Donggang Road
E-mail: zhenw@lzu.edu.cn

[b] F.C., H.W.,* Z.W.*
State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering
Lanzhou University
Lanzhou 730000, Gansu, China
E-mail: hhwang18@lzu.edu.cn

[c] Z.W.*
School of Pharmaceutical Science, Hengyang Medical School
University of South China
Hengyang 421001, Hunan, China

‡ These authors contributed equally to this work.

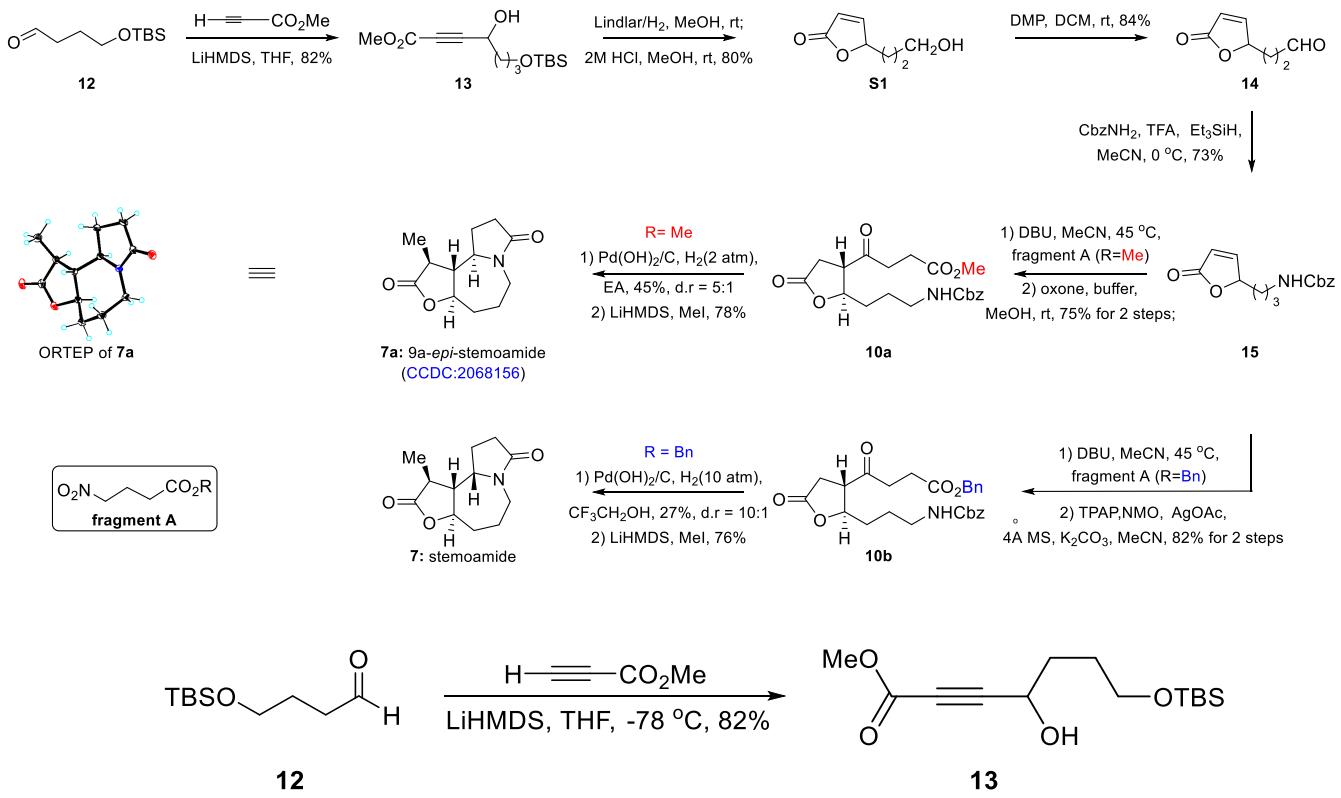
Table of Contents

I. General Information.

All reactions were performed in oven-dried glassware fitted with rubber septa under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Methylene chloride (CH_2Cl_2) was distilled immediately before use from calcium hydride. Diethyl ether and tetrahydrofuran (THF) were distilled immediately before use from sodium-benzophenone ketyl. All other solvents were processed through the reference *Purification of Laboratory Chemicals (Seventh Edition)*. External bath temperatures were used to record all reaction temperatures. Silica gel (300~400 mesh) and petroleum ether, EtOAc, CH_2Cl_2 and MeOH are used for product purification by flash column chromatography. NMR spectra were recorded on Bruker 400 MHz (400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR) spectrometers. Proton chemical shifts are reported relative to a residual solvent peak ($CDCl_3$ at 7.26 ppm) and carbon chemical shifts are reported relative to a residual solvent peak ($CDCl_3$ at 77.0 ppm) in order to compare with natural products conveniently. The following abbreviations were used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were measured on a Brucker Daltonics Apex II 47e Specification (for HRMS). The structures of single crystals were characterized on an Agilent (Supernova) or a Bruker (Smart APEX II) instrument. Non-hydrogen atoms are shown as 30% ellipsoid for the images of crystal structures.

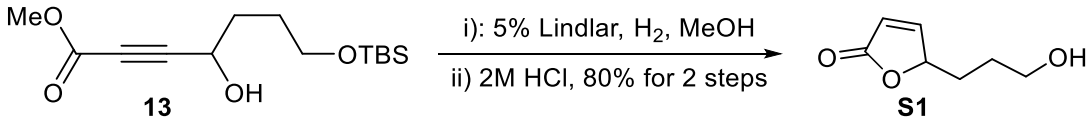
II. Experimental Procedures and Spectroscopic Data of Compounds.

Total Synthesis of Stemoamide (7) and 9a-*epi*-Stemoamide (7a):



methyl 7-((tert-butyldimethylsilyl)oxy)-4-hydroxyhept-2-ynoate (13):

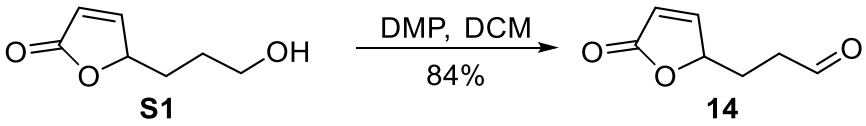
To a stirred mixture of methyl propiolate (1.5 mL, 16.3 mmol, 1.5 eq) in THF (80 mL) was added LiHMDS (1M in THF, 21.8 mL, 21.8 mmol, 2.0 eq) at -78 °C under Ar atmosphere. After stirring at –78 °C for 1 h, a solution of aldehyde **12** (2.2 g, 10.9 mmol, 1.0 eq) in THF (40 mL) was added to a solution of the lithium acetylide *via* syringe at –78 °C.[1] The resulting solution was stirred at –78 °C for 1 h, and quenched with aqueous saturated NH_4Cl solution (40 mL). The mixture was allowed to warm to room temperature, extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine (200 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography with EtOAc/petroleum ether (5:1) to give the product **13** (2.6 g, 82%) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.59 – 4.52 (m, 1H), 3.97 (d, *J* = 6.8 Hz, 1H), 3.77 (s, 3H), 3.74 – 3.70 (m, 1H), 3.67 – 3.61 (m, 1H), 1.96 – 1.80 (m, 3H), 1.77 – 1.66 (m, 1H), 0.90 (s, 9H), 0.08 (d, *J* = 2.9 Hz, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 153.9, 88.4, 76.1, 63.1, 61. 7, 52. 7, 34.8, 28.3, 25.9, 18.3, -5.4, -5.5. **IR (KBr, *ν* / cm^{-1})** 2932, 2954, 2861, 2240, 1720, 1437, 1254, 1098, 837. **HRMS (ESI, m/z):** [M + Na]$^+$ calcd for $[C_{14}H_{26}O_4SiNa]^+$ 309.1493, found 309.1495.



5-(3-hydroxypropyl)furan-2(5H)-one (S1):

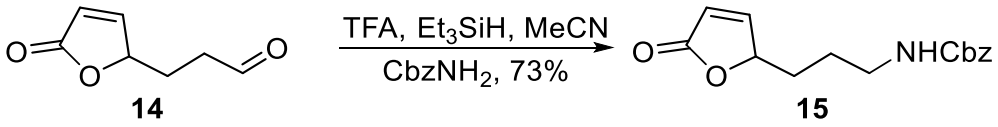
The alkynol **13** (1.0 g, 3.5 mmol, 1.0 eq) and 5% Lindlar (72 mg, 0.35 mmol, 0.1 eq) were dissolved in MeOH (35 mL), and the mixture was continually stirred under hydrogen atmosphere (1 atm) at rt for 12 h. The mixture was filtered, which was used directly in the next step.

To the residue was added dropwise 5 mL of 2M HCl and 35 mL of MeOH, the resulting mixture was stirred at rt for 1 h. The mixture was extracted with DCM (3 × 50 mL) and aqueous saturated NaCl solution (100 mL), dried over Na_2SO_4, and concentrated. The mixture was directly purified by flash column chromatography with EtOAc/petroleum ether (4:1) to give product **S1** (397 mg, 80% for 2 steps) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47 (dd, *J* = 5.7, 1.5 Hz, 1H), 6.11 (dd, *J* = 5.7, 2.0 Hz, 1H), 5.18 – 5.03 (m, 1H), 3.69 (t, *J* = 5.4 Hz, 2H), 1.98 – 1.87 (m, 1H), 1.82 (s, 1H), 1.77 – 1.65 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.2, 156.4, 121.5, 83.2, 61.9, 29.7, 27.9. **IR (KBr, ν / cm^{-1})** 3316, 2932, 1745, 1333, 1169, 1106, 820. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_7H_{10}O_3Na]^+$ 165.0522, found 165.0527.



3-(5-oxo-2,5-dihydrofuran-2-yl)propanal (14):

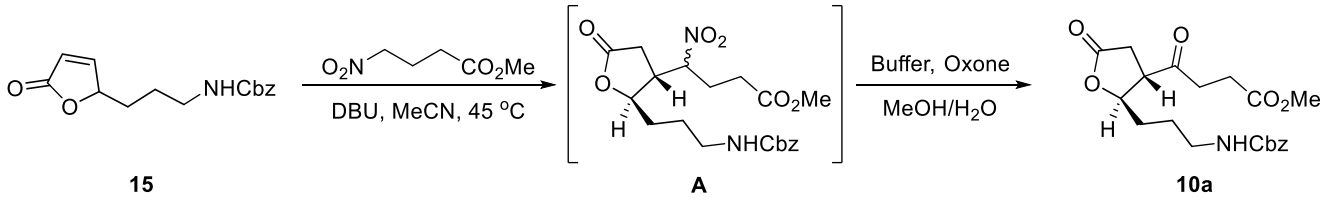
DMP (6.4 g, 15 mmol, 1.5 eq) was slowly added to a stirred solution of **S1** (1.4 g, 10 mmol, 1.0 eq) in CH_2C1_2 (100 mL) at rt for 30 min. The mixture was quenched with saturated aqueous solution of sodium thiosulfate (20 mL), and extracted with DCM (3 × 100 mL) and aqueous saturated NaCl solution (200 mL), dried over Na_2SO_4, and concentrated. Then the mixture was concentrated under reduced pressure and purification by flash column chromatography with EtOAc/petroleum ether (2:3) to give product **14** (1.2 g, 84%) as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.81 – 9.65 (m, 1H), 7.43 (dt, *J* = 5.7, 1.5 Hz, 1H), 6.15 – 5.98 (m, 1H), 5.12 – 5.02 (m, 1H), 2.70 – 2.52 (m, 2H), 2.24 – 2.11 (m, 1H), 1.87 – 1.74 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.3, 172.5, 155.8, 121.7, 81.8, 38.6, 25.0. **IR (KBr, *ν* / cm^{-1})** 3347, 2952, 2363, 1750, 1709, 1532, 1455, 1256, 1164, 1105, 1012, 915, 751. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_7H_8O_3Na]^+$ 163.0366, found 163.0364.



14 **15**

benzyl (3-(5-oxo-2,5-dihydrofuran-2-yl)propyl)carbamate (15):[2]

Trifluoroacetic acid (1.8 mL, 24.2 mmol, 2.0 eq) was added to a stirred solution of **14** (1.7 g, 12.1 mmol, 1.0 eq) and benzyl carbamate (2.7 g, 18.2 mmol, 1.5 eq) in MeCN (60 mL). The resulting solution was cooled to 0 °C and then triethylsilane (4.8 mL, 30.3 mmol, 2.5 eq) was added. After 12 h, saturated $NaHCO_3$ solution (50 mL) was added and the mixture was extracted with diethyl ether (3 x 50 mL). The solvent was removed under reduced pressure and the resulting crude mixture was purified by flash column chromatography with EtOAc/petroleum ether (2:3) to give the desired product **15** (2.4 g, 73%) as a pale oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41 (d, *J* = 5.5 Hz, 1H), 7.37 – 7.29 (m, 5H), 6.09 (dd, *J* = 5.7, 2.0 Hz, 1H), 5.15 – 5.02 (m, 3H), 4.98 – 4.88 (m, 1H), 3.33 – 3.14 (m, 2H), 1.89 – 1.77 (m, 1H), 1.71 – 1.57 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.9, 156.4, 156.0, 136.4, 128.5, 128.1, 128.0, 121.7, 82.7, 66.7, 40.3, 30.2, 25.6. **IR (KBr, ν / cm^{-1})** 3323, 2960, 1708, 1500, 1223, 900, 732. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{15}H_{17}NO_4Na]^+$ 298.1050, found 298.1052.



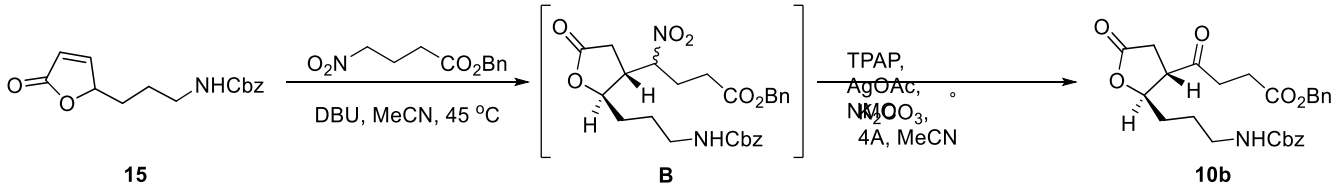
15 **A** **10a**

methyl-2-(3-(((benzyloxy)carbonyl)amino)propyl)-5-oxotetrahydrofuran-3-yl)-4-nitrobutanoate (10a):

1,8-Diazabicyclo[5.4.0]undec-7-ene (2 mL, 13.5 mmol, 0.5 eq) was added to a solution of furanone **15** (7.4 g, 26.9 mmol, 1.0 eq) and methyl 4-nitrobutyrate (5.9 g, 40.35 mmol, 1.5 eq) in MeCN (135 mL), and this mixture was stirred at 45 °C for 12 h. After total consumption of the starting material, the mixture was extracted with DCM (3 × 150 mL) and aqueous saturated NaCl solution (200 mL), dried over Na_2SO_4, and concentrated to give the crude **A** without further purification.

To a solution of the above nitro derivative **A** in 223 mL of MeOH, 223 mL buffer (0.5 M solution of Na_2HPO_4 in 1.0 M solution of NaOH) was added. After 0.5 h, oxone (19.8 g, 32.3 mmol, 1.2 eq) in 33 mL of water was added to the stirred suspension. The resulting mixture was stirred at room temperature for 1 h, then it was acidified with 10% solution of HCl and extracted with CH_2Cl_2 (3 × 250 mL). The combined organic layers were washed with brine, dried and concentrated under reduced pressure. Then the crude mixture was purified by flash column chromatography with EtOAc/petroleum ether (2:3) to give the desired product **10a** (7.8 g, 75% for 2 steps) as a

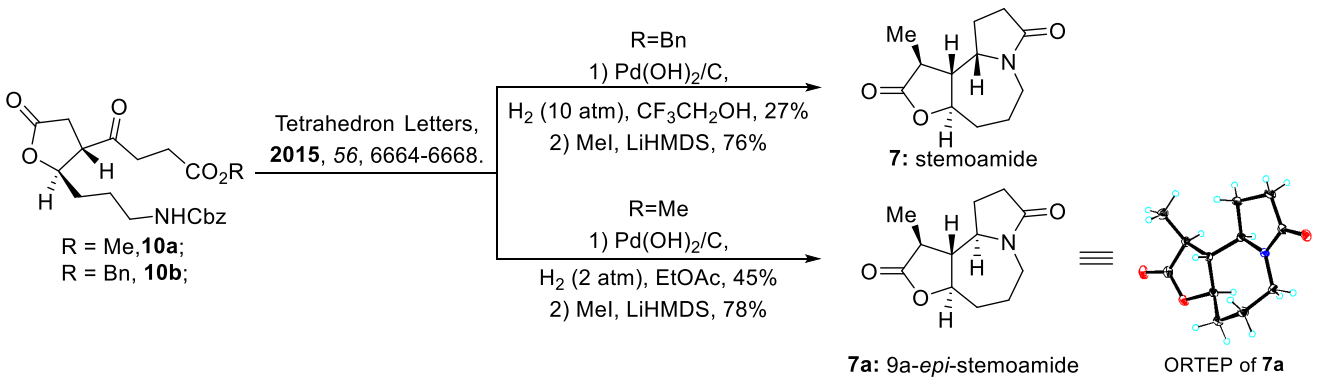
pale oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 – 7.31 (m, 5H), 5.08 (s, 2H), 5.03 – 4.94 (m, 1H), 4.69 – 4.57 (m, 1H), 3.64 (s, 3H), 3.30 – 3.16 (m, 3H), 2.87 (dd, *J* = 17.7, 9.1 Hz, 1H), 2.79 – 2.61 (m, 5H), 1.88 – 1.64 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 205.5, 174.1, 172.9, 156.5, 136.5, 128.5, 128.11, 128.09, 80.4, 66.7, 52.4, 52.1, 40.1, 37.0, 32.5, 31.8, 27.6, 26.1. **IR (KBr, *ν* / cm^{-1})** 3371, 3035, 2954, 1779, 1735, 1530, 1441, 1247, 1027, 844, 738. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{20}H_{25}NO_7Na]^+$ 414.1523, found 414.1525.



benzyl 4-(2-(3-(((benzyloxy)carbonyl)amino)propyl)-5-oxotetrahydrofuran-3-yl)-4-oxobutanoate (10b)[3]

1,8-Diazabicyclo[5.4.0]undec-7-ene (0.1 mL, 0.7 mmol, 0.2 eq) was added to a solution of furanone **15** (1 g, 3.6 mmol, 1.0 eq) and benzyl 4-nitrobutanoate (1.0 g, 4.4 mmol, 1.2 eq) in MeCN (36 mL) and this mixture was stirred at 45 °C for 12 h. After total consumption of the starting material, the mixture was extracted with DCM (3 ×50 mL) and aqueous saturated NaCl solution (50 mL), dried over Na_2SO_4, and concentrated. Then the crude **B** was used without further purification.

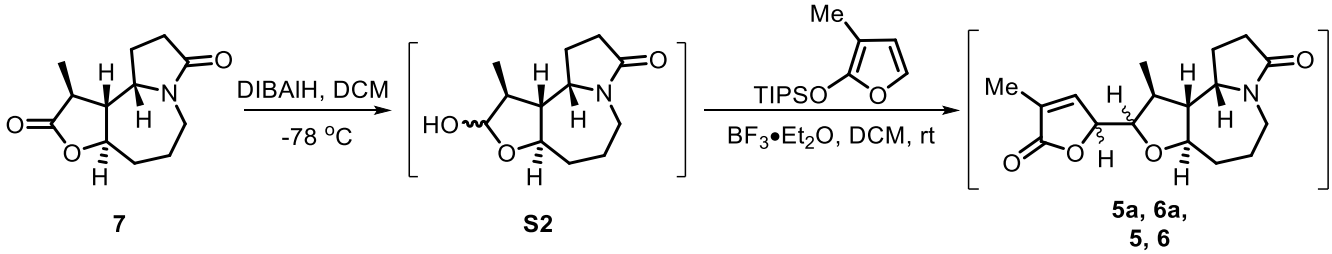
To a solution of **B** in MeCN (132 mL) was added tetrapropylammonium perruthenate (315 mg, 0.9 mmol, 0.25 eq), *N*-methylmorpholine *N*-oxide (505 mg, 4.32 mmol, 1.2 eq), AgOAc (1.2 g, 7.2 mmol, 2 eq), 4 Å molecular sieves (750 mg) and K_2CO_3 (2.48 g, 18 mmol, 5 eq). Then the suspension mixture was stirred for 6 h at the ambient temperature. After evaporation of the solvent, the crude mixture was purified by flash column chromatography with petroleum ether / EtOAc (2:3) to give the desired product **10b** (1.56 g, 93%) as a pale oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 – 7.27 (m, 10H), 5.08 (s, 5H), 4.65 – 4.55 (m, 1H), 3.28 – 3.12 (m, 3H), 2.86 – 2.61 (m, 6H), 1.85 – 1.56 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 205.5, 174.1, 172.2, 156.5, 136.5, 135.4, 128.6, 128.5, 128.4, 128.2, 128.08, 128.05, 80.4, 66.8, 66.6, 52.3, 40.1, 36.93, 32.5, 31.8, 27.8, 26.0. **IR (KBr, *ν* / cm^{-1})** 3371, 3347, 2935, 2365, 1776, 1718, 1530, 1251, 1169, 1027, 699. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{26}H_{29}NO_7Na]^+$ 490.1836, found 490.1840.



Stemoamide (7) and 9a-*epi*-stemoamide (7a): [2]

Stemoamide (7):^{1}H NMR (400 MHz, $CDCl_3$) δ 4.23 – 4.10 (m, 2H), 3.98 (dt, *J* = 10.7, 6.4 Hz, 1H), 2.69 – 2.54 (m, 2H), 2.44 – 2.35 (m, 4H), 2.08 – 2.00 (m, 1H), 1.89 – 1.79 (m, 1H), 1.71 (t, *J* = 11.3 Hz, 1H), 1.59 – 1.44 (m, 2H), 1.29 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 177.4, 174.0, 77.7, 55.9, 52.8, 40.3, 37.4, 34.9, 30.6, 25.7, 22.6, 14.1. **IR (KBr, ν / cm^{-1})** 3449, 2925, 1787, 1653, 1412, 1215, 1194, 997. **HRMS (ESI, m/z):** [M + Na]$^+$ calcd for $[C_{12}H_{17}NO_3Na]^+$ 246.1101, found 246.1104.

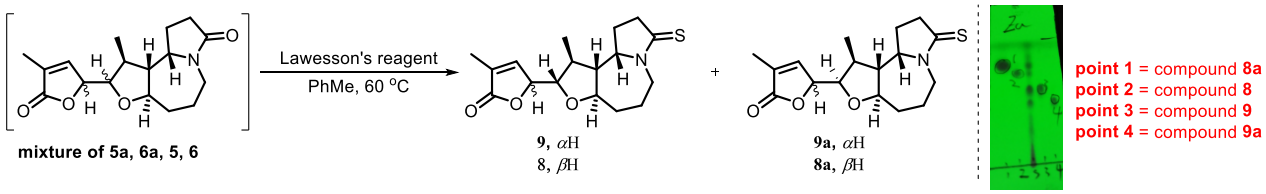
9a-*epi*-stemoamide (7a):^{1}H NMR (400 MHz, $CDCl_3$) 4.31 (ddd, *J* = 10.9, 9.8, 5.2 Hz, 1H), 3.88 (ddd, *J* = 14.7, 6.3, 3.2 Hz, 1H), 3.59 (ddd, *J* = 9.6, 8.6, 6.5 Hz, 1H), 3.14 (ddd, *J* = 14.6, 8.9, 3.3 Hz, 1H), 2.56 – 2.34 (m, 4H), 2.29 – 2.19 (m, 1H), 2.00 – 1.91 (m, 1H), 1.89 – 1.78 (m, 3H), 1.77 – 1.67 (m, 1H), 1.39 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** 177.6, 174.2, 81.1, 62.0, 55.2, 40.2, 39.8, 30.8, 30.3, 24.9, 22.3, 15.4. **IR (KBr, *ν* / cm^{-1})** 3452, 2930, 1783, 1647, 1420, 1218, 1190, 996. **HRMS (ESI, m/z):** [M + Na]$^+$ calcd for $[C_{12}H_{17}NO_3Na]^+$ 246.1101, found 246.1105.



Mixture of 5a, 6a, 5, 6[5]

Diisobutylalminium hydride (1 M in hexane, 1.2 mL, 1.2 mmol, 3.0 eq) was added to a solution of stemoamide (**7**: 90 mg, 0.4 mmol, 1.0 eq) in CH_2Cl_2 (5 mL) at –78 °C. The resulting solution was maintained at –78 °C for 1 h, and then quenched with aqueous saturated (+)-potassium sodium tertrate (10 mL). The mixture was vigorously stirred for 1 h, and extracted with DCM (3 x 20 mL). The combined organic extract was washed with brine (20 mL), dried over Na_2SO_4, and concentrated. The crude compound **S2** was used in the next step without further purification.

BF_3•Et_2O (252 μL, 2.0 mmol, 5.0 eq) was added to a solution of lactol **S2** and 2-siloxyfuran (305 mg, 1.2 mol, 3.0 eq) in CH_2Cl_2 (7 mL) at room temperature. After stirring for 6 h, the reaction mixture was quenched with aqueous saturated $NaHCO_3$ (5 mL) and extracted with DCM (4 x 20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The mixture of **5a, 6a, 5, 6** was used in the next reaction without further purification.



Compounds 8, 9, 8a, 9a

To a stirred solution of the above mixture of **5a, 6a, 5, 6** in PhMe (3 mL), Lawesson's reagent (194 mg, 0.48 mmol, 1.2 eq) was added. After stirring at 60 °C for 1.0 h. The crude residue was purified by column chromatography (PE/ EtOAc = 1:1) to afford compound **9** (12.8 mg, 10%), **8** (15.4 mg, 12%), **9a** (16.7 mg, 13%), **8a** (18.0 mg, 14%) as a white solid.

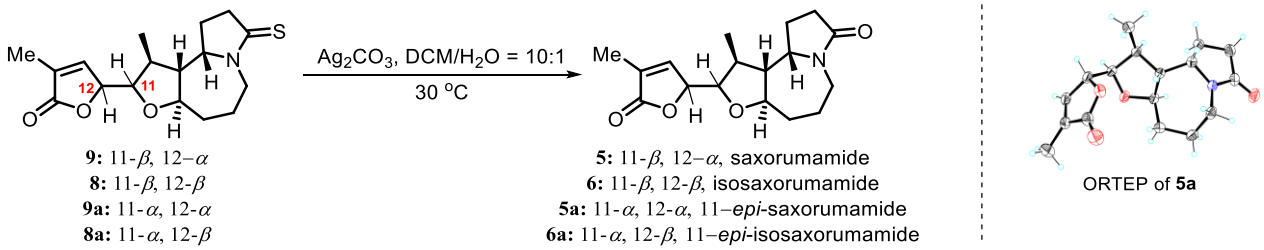
9, a white solid, **^{1}H NMR (400 MHz, $CDCl_3$)** 7.00 (p, *J* = 1.6 Hz, 1H), 4.92 (h, *J* = 2.0 Hz, 1H), 4.77 – 4.70 (m, 1H), 4.23 – 4.16 (m, 1H), 3.87 (dd, *J* = 8.7, 2.2 Hz, 1H), 3.72 (td, *J* = 10.4, 3.1 Hz, 1H), 3.06 (dd, *J* = 17.4, 8.8 Hz, 1H), 2.97 – 2.80 (m, 2H), 2.42 – 2.31 (m, 1H), 2.23 – 2.04 (m, 3H), 1.94 (t, *J* = 1.8 Hz, 3H), 1.89 – 1.74 (m, 2H), 1.72 – 1.60 (m, 1H), 1.48 – 1.36 (m, 1H), 1.16 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.6, 174.0, 145.8, 131.3, 83.4, 80.0, 79.8, 63.8, 54.4, 45.8, 43.3, 38.4, 35.7, 24.2, 23.7, 15.8, 10.9. **IR (KBr, *ν* / cm^{-1})** 2924, 2861, 1752, 1603, 1493, 1301, 1238, 1148, 1079, 790. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{17}H_{23}NO_3SNa]^+$ 344.1291, found 344.1293.

8, a white solid, **^{1}H NMR (400 MHz, $CDCl_3$)** 7.17 (t, *J* = 1.8 Hz, 1H), 4.83 – 4.70 (m, 2H), 4.25 – 4.16 (m, 1H), 3.83 (td, *J* = 10.3, 3.1 Hz, 1H), 3.52 (t, *J* = 7.4 Hz, 1H), 3.07 (dd, *J* = 17.4, 8.8 Hz, 1H), 2.99 – 2.82 (m, 2H), 2.25 – 2.15 (m, 2H), 2.15 – 2.03 (m, 2H), 1.93 (s, 3H), 1.83 – 1.73 (m, 2H), 1.71 – 1.59 (m, 1H), 1.53 – 1.41 (m, 1H), 1.16 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR (76 MHz, $CDCl_3$)** δ 200.6, 173.9, 147.1, 130.8, 85.4, 82.9, 79.4, 63.7, 54.9, 45.8, 43.4, 40.5, 35.7, 24.3, 23.7, 16.4, 10.8. **IR (KBr, *ν* / cm^{-1})** 2938, 2845, 1732, 1615, 1434, 1321, 1224, 1167, 1083, 779. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{17}H_{23}NO_3SNa]^+$ 344.1291, found 344.1294.

9a, a white solid, **^{1}H NMR (400 MHz, $CDCl_3$)** 6.97 (p, *J* = 1.6 Hz, 1H), 4.87 (h, *J* = 1.8 Hz, 1H), 4.69 (dt, *J* = 13.7, 3.1 Hz, 1H), 4.24 – 4.16 (m, 2H), 3.70 – 3.61 (m, 1H), 3.08 – 2.97 (m, 2H), 2.91 – 2.80 (m, 1H), 2.60 – 2.45 (m, 2H), 2.07 – 1.95 (m, 2H), 1.93 (t, *J* = 1.7 Hz, 3H), 1.80 – 1.68 (m, 2H), 1.65 – 1.57 (m, 1H), 1.45 – 1.33

(m, 1H), 1.24 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)**δ 200.2, 174.6, 146.5, 131.0, 80.4, 79.8, 79.7, 64.0, 50.4, 45.8, 43.4, 39.0, 34.8, 23.7, 12.8, 10.8. **IR (KBr, *ν* / cm^{-1})** 2935, 2853, 1746, 1656, 1456, 1334, 1254, 1187, 1054, 770. **HRMS (ESI, m/z):** [M + Na]$^+$ calcd for [$C_{17}H_{23}NO_3SNa$]$^+$ 344.1291, found 344.1298.

8a, a white solid, **^{1}H NMR (400 MHz, CDCl$_3$)** 7.29 – 7.26 (m, 1H), 4.81 – 4.72 (m, 2H), 4.32 – 4.22 (m, 1H), 3.66 (td, *J* = 10.6, 2.9 Hz, 1H), 3.59 (dd, *J* = 9.0, 7.4 Hz, 1H), 3.11 – 2.84 (m, 3H), 2.51 – 2.41 (m, 1H), 2.29 – 2.08 (m, 3H), 1.93 (t, *J* = 1.8 Hz, 3H), 1.85 – 1.68 (m, 3H), 1.52 – 1.39 (m, 1H), 1.24 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 200.7, 174.0, 148.9, 130.6, 83.0, 79.4, 79.0, 64.1, 53.3, 45.7, 43.4, 39.0, 35.7, 24.1, 23.7, 14.2, 10.8. **IR (KBr, *ν* / cm^{-1})** 2943, 2874, 1747, 1654, 1487, 1351, 1246, 1154, 1083, 785. **HRMS (ESI, m/z):** [M + Na]$^+$ calcd for [$C_{17}H_{23}NO_3SNa$]$^+$ 344.1291, found 344.1292.



9: 11-*β*, 12–*α*
8: 11-*β*, 12-*β*
9a: 11-*α*, 12-*α*
8a: 11-*α*, 12-*β*

5: 11-*β*, 12–*α*, saxorumamide
6: 11-*β*, 12-*β*, isosaxorumamide
5a: 11-*α*, 12-*α*, 11–*epi*-saxorumamide
6a: 11-*α*, 12-*β*, 11–*epi*-isosaxorumamide

ORTEP of **5a**

Compounds 5, 6, 5a, 6a

To a stirred solution of **9** (5.5 mg, 0.017 mmol, 1 eq) or **8** (6.0 mg, 0.019 mmol, 1 eq) or **9a** (5.7 mg, 0.018 mmol, 1 eq) or **8a** (6.2 mg, 0.019 mmol, 1 eq) in 0.1M DCM/H_2O (10 : 1), Ag_2CO_3 (1.2 eq) was added at 30 °C. After stirring for 3.0 h, the mixture was filtrated through Celite and the filter cake was washed with DCM : MeOH = 10:1 (10 x 3 mL). The crude residue was purified by column chromatography (EtOAc/MeOH = 15:1-10:1) to respectively afford compound **5** (4.6 mg, 89%), **6** (5.2 mg, 91%), **5a** (4.8 mg, 89%), **6a** (5.4 mg, 92%) as a white solid.

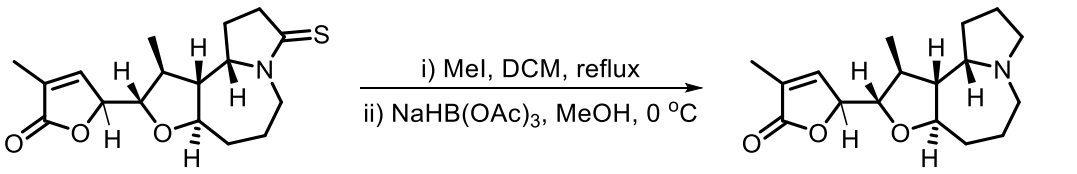
5 (Saxorumamide) a white solid, **^{1}H NMR (400 MHz, CDCl$_3$)** 7.01 (p, *J* = 1.6 Hz, 1H), 4.93 (h, *J* = 2.1 Hz, 1H), 4.10 – 4.03 (m, 1H), 3.92 (dt, *J* = 10.7, 6.3 Hz, 1H), 3.86 (dd, *J* = 8.8, 2.3 Hz, 1H), 3.77 (td, *J* = 10.2, 3.1 Hz, 1H), 2.64 – 2.56 (m, 1H), 2.42 – 2.33 (m, 3H), 2.14 – 2.06 (m, 2H), 2.04 – 1.97 (m, 1H), 1.94 (t, *J* = 1.8 Hz, 3H), 1.81 – 1.70 (m, 2H), 1.44 – 1.31 (m, 2H), 1.14 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (76 MHz, CDCl$_3$)** δ 174.1, 145.9, 131.2, 83.6, 80.1, 56.1, 55.2, 40.4, 37.7, 36.0, 30.8, 25.9, 22.5, 16.0, 10.9. **IR (KBr, *ν* / cm^{-1})** 3285, 2924, 2853, 1754, 1679, 1605, 1422, 1323, 1062, 751. **HRMS (ESI, m/z):** [M + Na]$^+$ calcd for [$C_{17}H_{23}NO_4Na$]$^+$ 328.1519, found 328.1520.

6 (Isosaxorumamide) a white solid, **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.17 (p, *J* = 1.6 Hz, 1H), 4.80 (dp, *J* = 5.7, 1.9 Hz, 1H), 4.12 – 4.05 (m, 1H), 3.96 – 3.85 (m, 2H), 3.55 – 3.50 (m, 1H), 2.66 – 2.58 (m, 1H), 2.37 (dd, *J* =

10.6, 4.5 Hz, 2H), 2.19 – 2.08 (m, 3H), 2.06 – 1.99 (m, 1H), 1.94 (t, *J* = 1.8 Hz, 3H), 1.78 – 1.66 (m, 2H), 1.48 – 1.37 (m, 2H), 1.14 (d, *J* = 5.9 Hz, 3H). **^{13}C NMR (76 MHz, $CDCl_3$)** δ 174.1, 174.0, 147.2, 130.8, 85.6, 83.0, 79.7, 55.9, 55.6, 40.4, 39.7, 36.0, 30.9, 25.9, 22.6, 16.6, 10.8. **IR (KBr, *ν* / cm^{-1})** 3275, 2935, 2847, 1749, 1665, 1645, 1434, 1356, 1074, 731. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{17}H_{23}NO_4Na]^+$ 328.1519, found 328.1527.

5a (11-*epi*-saxorumamide) a white solid, **^{1}H NMR (400 MHz, $CDCl_3$)** 6.97 (p, *J* = 1.7 Hz, 1H), 4.87 (q, *J* = 1.8 Hz, 1H), 4.21 (d, *J* = 7.9 Hz, 1H), 4.07 – 4.00 (m, 1H), 3.96 – 3.88 (m, 1H), 3.73 (td, *J* = 10.1, 2.9 Hz, 1H), 2.72 – 2.64 (m, 1H), 2.58 – 2.42 (m, 2H), 2.39 – 2.32 (m, 2H), 1.96 – 1.92 (m, 4H), 1.75 – 1.64 (m, 3H), 1.42 – 1.30 (m, 2H), 1.24 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.6, 174.0, 146.6, 131.0, 80.5, 80.1, 79.9, 56.2, 51.2, 40.4, 38.4, 35.0, 30.9, 25.8, 22.0, 13.0, 10.8. **IR (KBr, *ν* / cm^{-1})** 3243, 2943, 2872, 1761, 1683, 1643, 1431, 1343, 1053, 743. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{17}H_{23}NO_4Na]^+$ 328.1519, found 328.1524.

6a (11-*epi*-isosaxorumamide) a white solid, **^{1}H NMR (400 MHz, $CDCl_3$)** 7.29 – 7.26 (m, 1H), 4.76 (dt, *J* = 9.2, 2.0 Hz, 1H), 4.13 – 4.06 (m, 1H), 3.97 (dt, *J* = 10.5, 6.4 Hz, 1H), 3.72 (td, *J* = 10.2, 2.8 Hz, 1H), 3.62 – 3.55 (m, 1H), 2.65 (t, *J* = 13.1 Hz, 1H), 2.53 – 2.43 (m, 1H), 2.41 – 2.34 (m, 2H), 2.26 – 2.18 (m, 1H), 2.13 – 2.00 (m, 2H), 1.93 (t, *J* = 1.8 Hz, 3H), 1.80 – 1.72 (m, 1H), 1.68 – 1.63 (m, 1H), 1.52 – 1.34 (m, 2H), 1.23 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.2, 174.0, 149.0, 130.5, 83.2, 79.7, 79.1, 56.3, 54.0, 40.4, 38.3, 36.0, 30.8, 25.9, 22.4, 14.2, 10.8. **IR (KBr, *ν* / cm^{-1})** 3235, 2944, 2848, 1764, 1669, 1632, 1434, 1341, 1072, 773. **HRMS (ESI, m/z):** $[M + Na]^+$ calcd for $[C_{17}H_{23}NO_4Na]^+$ 328.1519, found 328.1528.



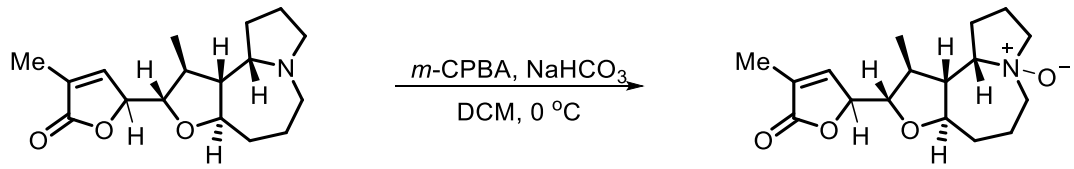
9: 11-*β*, 12–*α*
8: 11-*β*, 12-*β*

2: 11-*β*, 12–*α*, isoneostemocochinir
1: 11-*β*, 12-*β*, neostemocochinine

A mixture of **8** or **9** (10 mg, 0.03 mmol, 1.0 eq), and MeI (19 uL ,0.3 mmol, 10.0 eq) in DCM was heated at reflux until the thiolactam was consumed as monitored by TLC. After cooling to room temperature, the reaction mixture was concentrated. The resulting thioiminium salt was then dissolved in methanol (3 mL) and was immediately treated with sodium triacetoxyborohydride (9.5 mg, 0.045 mmol, 1.5 eq). The resulting mixture was stirred at 0 °C for 0.5 h and then quenched with aqueous saturated $NaHCO_3$ (5 mL) and extracted with DCM : MeOH = 5 : 1 (4 x 20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The crude residue was purified by column chromatography (Al_2O_3/SiO_2 = 10:1, DCM/MeOH = 40:1-20:1) to afford tertiary amine **1** (7.0 mg, 80%) or **2** (6.5 mg, 75%) as a colorless oil.

1, (**Neostemocochinine**) a colorless oil, **^{1}H NMR (600 MHz, $CDCl_3$)**) δ 7.18 (s, 1H), 4.79 (s, 1H), 4.04 (t, *J* = 10.7 Hz, 1H), 3.48 (d, *J* = 7.8 Hz, 1H), 3.05 – 2.85 (m, 3H), 2.73 – 2.52 (m, 2H), 2.14 (d, *J* = 13.3 Hz, 1H), 2.04 (s, 1H), 1.98 – 1.88 (m, 4H), 1.81 (s, 2H), 1.73 – 1.62 (m, 2H), 1.58 – 1.49 (m, 2H), 1.41 – 1.30 (m, 1H), 1.10 (d, *J* = 4.6 Hz, 3H). **^{13}C NMR (76 MHz, $CDCl_3$)** δ 174.1, 147.3, 130.5, 85.3, 83.2, 79.9, 59.7, 55.5, 53.1, 49.2, 42.0, 36.1, 29.7, 27.8, 22.5, 17.0, 10.7. **IR (KBr, ν / cm^{-1})** 2937, 2854, 1758, 1643, 1451, 1353, 1062, 764. **HRMS (ESI, m/z):** $[M + H]^+$calcd for $[C_{17}H_{26}NO_3]^+$ 292.1907, found 292.1898.

2, (**Isoneostemocochinine**) a colorless oil, **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.01 (t, *J* = 1.7 Hz, 1H), 5.10 – 4.82 (m, 1H), 3.93 (td, *J* = 10.4, 3.3 Hz, 1H), 3.79 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.04 – 2.86 (m, 2H), 2.79 – 2.57 (m, 2H), 2.30 – 2.17 (m, 1H), 2.14 – 2.06 (m, 1H), 1.96 – 1.91 (m, 3H), 1.87 – 1.77 (m, 2H), 1.75 – 1.48 (m, 5H), 1.38 – 1.27 (m, 2H), 1.09 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (76 MHz, $CDCl_3$)** δ 174.2, 146.1, 131.1, 83.6, 80.7, 80.3, 59.4, 55.3, 52.9, 49.1, 39.8, 36.2, 27.8, 23.6, 22.7, 16.4, 10.9. **IR (KBr, *ν* / cm^{-1})** 2943, 2864, 1763, 1623, 1441, 1341, 1054, 763. **HRMS (ESI, m/z):** $[M + H]^+$ calcd for $[C_{17}H_{26}NO_3]^+$ 292.1907, found 292.1919.



2: 11-*β*, 12–*α*, isoneostemocochinine
1: 11-*β*, 12-*β*, neostemocochinine

4: 11-*β*, 12–*α*, isoneostemocochinine-N-oxide
3: 11-*β*, 12-*β*, neostemocochinine-N-oxide

m-CPBA (5.2 mg, 0.03 mmol, 1.5 eq) was added to a stirred solution of **2** or **1** (6 mg, 0.02 mmol, 1.0 eq) and $NaHCO_3$ (5.0 mg,0.06 mmol, 3.0 eq) in DCM (2 mL) under argon atmosphere at 0 °C for 0.5 h. The mixture was filtrated through Celite and the filter cake was washed with DCM : MeOH = 10:1 (10 x 3 mL). The crude residue was purified by column chromatography (Al_2O_3/SiO_2 = 10:1, DCM/MeOH = 40:1-20:1) to respectively afford N-oxide **4** (4.4 mg, 72%) or **3** (4.3 mg, 70%) as a a colorless oil.

3, (**Neostemocochinine-N-oxide**) a colorless oil, **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.11 – 7.02 (m, 1H), 5.03 – 4.85 (m, 1H), 4.18 – 4.00 (m, 1H), 3.96 – 3.81 (m, 1H), 3.69 (dd, *J* = 7.7, 5.2 Hz, 1H), 3.65 – 3.53 (m, 2H), 3.53 – 3.45 (m, 1H), 3.42 – 3.30 (m, 1H), 2.50 – 2.39 (m, 2H), 2.39 – 2.29 (m, 1H), 2.24 – 2.13 (m, 2H), 1.94 (t, *J* = 1.8 Hz, 3H), 1.88 – 1.79 (m, 1H), 1.74 – 1.67 (m, 1H), 1.65 – 1.51 (m, 2H), 1.21 – 1.16 (m, 1H), 1.08 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.9, 145.9, 131.3, 84.6, 82.8, 80.6, 80.1, 71.4, 66.0, 48.9, 39.7, 32.1, 24.4, 20.3, 18.7, 16.3, 10.8. **IR (KBr, *ν* / cm^{-1})** 2945, 2853, 1769, 1448, 1217, 1095, 1043, 739. **HRMS (ESI, m/z):** $[M + H]^+$calcd for $[C_{17}H_{26}NO_4]^+$ 308.1856, found 308.1863.

4, (**Isoneostemocochinine-N-oxide**) a colorless oil, **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.00 – 6.96 (m, 1H), 4.89 (q, *J* = 1.9 Hz, 1H), 3.98 – 3.87 (m, 2H), 3.83 (dd, *J* = 8.7, 1.7 Hz, 1H), 3.64 – 3.55 (m, 2H), 3.55 – 3.44 (m, 1H), 3.43 – 3.33 (m, 1H), 2.51 – 2.29 (m, 3H), 2.28 – 2.18 (m, 2H), 2.17 – 2.07 (m, 1H), 1.94 (t, *J* = 1.8 Hz, 3H), 1.90 – 1.77 (m, 1H), 1.64 – 1.53 (m, 1H), 1.51 – 1.42 (m, 1H), 1.22 – 1.18 (m, 1H), 1.15 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.2, 145.9, 131.1, 82.9, 80.8, 80.1, 77.9, 71.3, 66.1, 48.6, 40.1, 32.3, 24.6, 20.4, 18.7, 15.0, 10.9. **IR (KBr, *ν* / cm^{-1})** 2935, 2854, 1773, 1454, 1210, 1091, 1038, 732. **HRMS (ESI, m/z):** [M + H]$^{+}$calcd for $[C_{17}H_{26}NO_4]^{+}$ 308.1856, found 308.1846.

III. Comparison of NMR data of Natural and Synthetic Stemoamide-Type Alkaloids.

Proton	natural sample	our synthetic sample (5)
	^{1}H NMR (300 MHz, $CDCl_3$)	^{1}H NMR (400 MHz, $CDCl_3$)
13-H	6.99 (m, 1H)	7.00 (t, *J* = 1.6 Hz, 1H)
12-H	4.96 (dd, *J* = 3.8, 2.0 Hz, 1H)	4.93 (q, *J* = 2.0 Hz, 1H)
5-H	4.08 (dd, *J* = 14.0, 2.3 Hz, 1H)	4.11 – 4.00 (m, 1H)
9a-H	3.93 (m, 1H)	3.97 – 3.83 (m, 2H)
11-H	3.87 (dd, *J* = 8.8, 2.0 Hz, 1H)	
8-H	3.78 (ddd, J = 13.0, 10.2, 2.7 Hz, 1H)	3.77 (td, *J* = 10.2, 3.1 Hz, 1H)
5-H	2.60 (dd, *J* = 14.0, 12.4 Hz, 1H)	2.64– 2.51 (m, 1H)
2, 10-H	2.38 (m, 1H), 2.37 (m, 2H)	2.43 – 2.31 (m, 3H)
7, 9-H	2.12 (m, 1H), 2.10 (m, 1H)	2.14 – 2.06 (m, 2H)
1-H	2.02 (m, 1H)	2.05 – 1.97 (m, 1H)
16-H	1.94 (dd, *J* = 1.7, 1.7 Hz, 3H)	1.94 (t, *J* = 1.8 Hz, 3H)
1, 6-H	1.77 (m, 1H), 1.74 (m, 1H)	1.82 – 1.68 (m, 2H)
6, 7-H	1.42 (m, 1H), 1.38 (m, 1H)	1.45 – 1.29 (m, 2H)
17-H	1.10 (d, *J* = 6.6 Hz, 3H)	1.14 (d, *J* = 6.5 Hz, 3H)

carbon	natural sample	our synthetic sample (5)
	^{13}C NMR (100 MHz, $CDCl_3$)	^{13}C NMR (76 MHz, $CDCl_3$)
3.15-C	174.1, 174.1	174.1, 174.1
13-C	145.8	145.8
14-C	131.2	131.1
11-C	83.6	83.6
8.12-C	80.1, 80.1	80.1, 80.1
9a-C	56.0	56.0
9-C	55.1	55.1
5-C	40.4	40.4
10-C	37.6	37.6
7-C	36.0	36.0
2-C	30.7	30.7
6-C	25.8	25.8
1-C	22.4	22.4
17-C	15.9	15.9
16-C	10.8	10.8

Proton	natural sample	our synthetic sample (6)
	^{1}H NMR (300 MHz, $CDCl_3$)	^{1}H NMR (400 MHz, $CDCl_3$)
13-H	7.15 (t, *J* = 1.6Hz, 1H)	7.17 (t, *J* = 1.6 Hz, 1H)
12-H	4.78 (ddd, *J* = 6.9, 3.9, 1.8 Hz, 1H)	4.80 (dt, *J* = 6.7, 1.9 Hz, 1H)
5-H	4.08 (m, 1H)	4.13 - 4.04 (m, 1H)
9a-H	3.92 (m, 1H)	3.97 - 3.83 (m, 2H)
8-H	3.88 (m, 1H)	
11-H	3.52 (dd, *J* = 7.9, 6.9 Hz, 1H)	3.55 - 3.49 (m, 1H)
5-H	2.62 (m, 1H)	2.67 - 2.56 (m, 1H)
2-H	2.38 (dd, *J* = 10.5, 4.4 Hz, 2H)	2.45 - 2.33 (m, 2H).
7, 9, 10-H	2.15 (m, 1H), 2.12 (m, 1H), 2.12 (m, 1H)	2.19 - 2.08 (m, 3H)
1-H	2.01 (m, 1H)	2.07 - 1.99 (m, 1H)
16-H	1.93 (dd, *J* = 1.9, 1.7 Hz, 3H)	1.94 (t, *J* = 1.8 Hz, 3H)
1, 6-H	1.75 (m, 1H), 1.70 (m, 1H)	1.78 - 1.64 (m, 2H)
6, 7-H	1.42 (m, 1H), 1.40 (m, 1H)	1.43 (tdd, *J* = 11.9, 8.2, 3.4 Hz, 2H)
17-H	1.13 (d, *J* = 8.0 Hz, 3H)	1.14 (d, *J* = 5.9 Hz, 3H)

carbon	natural sample	our synthetic sample (6)
	^{13}C NMR (100 MHz, $CDCl_3$)	^{13}C NMR (76 MHz, $CDCl_3$)
3.15-C	174.0, 174.0	174.0, 174.0
13-C	147.0	147.1
14-C	130.8	130.7
11-C	85.6	85.5
12-C	82.9	82.9
8-C	79.7	79.7
9a-C	55.9	55.9
9-C	55.6	55.5
5-C	40.4	40.4
10-C	39.7	39.6
7-C	36.0	35.9
2-C	30.8	30.8
6-C	25.9	25.8
1-C	22.6	22.5
17-C	16.5	16.5
16-C	10.7	10.7

Comparison of ^{1}H NMR of **Isoneostemocochinine (2)** and **Neostemocochinine (1)**

δ in ppm rel. to solvent signals (δ(H) $CHCl_3$: 7.26)

Proton	natural sample Isoneostemocochinine	natural sample neostemocochinine	our synthetic sample Isoneostemocochinine (2)	our synthetic sample Neostemocochinine (1)
	^{1}H NMR (400 MHz, $CDCl_3$)		^{1}H NMR (400 MHz, $CDCl_3$)	^{1}H NMR (600 MHz, $CDCl_3$)
1-H	a: 1.78 - 1.85 (m)	a: 1.78 - 1.85 (m)	1.77 – 1.87 (m, 2H)	1.76 – 1.86 (m, 2H)
	b: 1.52 - 1.60 (m)	b: 1.52 - 1.60 (m)	1.48 – 1.75 (m, 5H)	1.49 – 1.58 (m, 2H)
2-H	a: 1.89 - 1.96 (m)	a: 1.89 - 1.96 (m)	1.77 – 1.87 (m, 2H)	1.88-1.98 (m, 4H)
	b: 1.28 - 1.35 (m)	b: 1.33 - 1.41 (m)	1.27 – 1.38 (m, 2H)	1.30– 1.41 (m, 1H)
3-H	2.65 - 2.75 (m)	2.65 - 2.75 (m)	2.57 – 2.79 (m, 2H)	2.52– 2.73 (m, 2H)
5-H	a: 2.95 - 3.05 (m)	a: 2.95 - 3.05 (m)	2.86 – 3.04 (m, 2H)	2.85 – 3.05 (m, 3H)
	b: 2.90 - 3.00 (m)	b: 2.90 - 3.00 (m)		
6-H	a: 1.50 - 1.58 (m)	a: 1.50 - 1.58 (m)	1.48 – 1.75 (m, 5H)	1.49 – 1.58 (m, 2H)
	b: 1.30 - 1.40 (m)	b: 1.30 - 1.40 (m)	1.48 – 1.75 (m, 5H)	1.30– 1.41 (m, 1H)
7-H	a: 2.00 - 2.06 (m)	a: 2.00 - 2.06 (m)	/	2.08 – 2.00 (m, 1H)
	b: 1.24 - 1.30 (m)	b: 1.24 - 1.30 (m)	1.27 – 1.38 (m, 2H)	/
8-H	3.93 (*dt*, *J* = 3.3, 10.4)	4.05 (*dt*, *J* = 3.3, 10.2)	3.93 (td, *J* = 10.4, 3.3 Hz)	4.04 (t, *J* = 10.7 Hz, 1H)
9-H	2.08 - 2.15 (m)	2.10 – 2.17 (m)	2.06 – 2.14 (m, 1H)	2.14 (d, *J* = 13.3Hz, 1H)
9a-H	3.76 - 3.82 (m)	3.76 - 3.82 (m)	/	/
10-H	2.17 - 2.27 (m)	2.17 - 2.27 (m)	2.17 – 2.30 (m, 1H)	2.11-2.15 (m, 1H)
11-H	3.79 (*dd J* = 2.0, 8.8)	3.67 (*dd J* = 6.6, 8.0)	3.79 (dd, *J* = 8.7, 2.7 Hz, 1H)	3.48 (t, J = 7.8 Hz, 1H)
12-H	4.89-4.93 (m)	4.80 (*dt*, *J* = 1.9, 6.6)	4.82 – 5.10 (m, 1H)	4.79 (s, 1H)
13-H	7.00 (*dq*, *J* = 1.6, 3.0)	7.18 (*dq*, *J* = 1.8, 3.2)	7.01 (t, *J* = 1.7 Hz, 1H)	7.18 (s, 1H)
14-H	—	—	—	—
15-H	—	—	—	—
16-H	1.95 (*d*, *J* = 1.6)	1.92 (*d*, *J* = 1.8)	1.91-1.96 (m, 3H)	1.88-1.98 (m, 4H)
17-H	1.11 (*d*, *J* = 6.4)	1.09 (*d*, *J* = 6.4 Hz)	1.09 (d, *J* = 6.5 Hz, 3H).	1.10 (d, *J* = 4.6 Hz, 3H)

Comparison of ^{13}C NMR of **Isoneostemocochinine (2)** and **Neostemocochinine (1)**

δ in ppm rel. to solvent signals (δ(C) $CHCl_3$: 77.0)

Carbon	natural sample Isoneostemocochinine	our synthetic sample Isoneostemocochinine (2)	Deviation (ppm)	natural sample neostemocochinine	our synthetic sample Neostemocochinine (1)	Deviation (ppm)
	^{13}C NMR (101 MHz, $CDCl_3$)	^{13}C NMR (76 MHz, $CDCl_3$)		^{13}C NMR (101 MHz, $CDCl_3$)	^{13}C NMR (76 MHz, $CDCl_3$)	
1-C	23.2	23.6	0.4	23.2	27.8	4.6
2-C	26.3	27.8	1.5	26.3	29.7	3.4
3-C	52.0	55.3	3.3	52.1	55.5	3.4
5-C	49.8	49.1	0.7	49.9	49.2	0.7
6-C	17.5	22.7	5.2	17.7	22.5	4.8
7-C	33.7	36.2	2.5	33.8	36.1	2.3
8-C	82.6	83.6	1.0	82.9	83.2	0.3
9-C	51.4	52.9	1.5	51.8	53.1	1.3
9a-C	60.7	59.4	1.3	60.7	59.7	1.0
10-C	40.2	39.8	0.4	39.8	42.0	2.2
11-C	84.5	80.7	3.8	80.6	85.3	4.7
12-C	78.9	80.3	1.4	78.3	79.9	1.6
13-C	146.0	146.1	0.1	145.9	147.3	1.4
14-C	130.9	131.1	0.2	131.1	130.5	0.6
15-C	174.1	174.2	0.1	173.9	174.1	0.2
16-C	10.6	10.9	0.3	10.7	10.7	0
17-C	14.9	16.4	1.5	16.2	17.0	0.8

Comparison of ^{1}H NMR of **Isoneostemocochinine *N*-oxide (4)** and **Neostemocochinine *N*-oxide (3)**

δ in ppm rel. to solvent signals (δ(H) $CHCl_3$: 7.26)

Proton	natural sample Isoneostemocochinine N-oxide	natural sample Neostemocochinine N-oxide	our synthetic sample Isoneostemocochinine N-oxide (4)	our synthetic sample Neostemocochinine N-oxide (3)
	^{1}H NMR (400 MHz, $CDCl_3$)		^{1}H NMR (400 MHz, $CDCl_3$)	^{1}H NMR (400 MHz, $CDCl_3$)
1-H	1.82 (m)	1.81 (m)	1.79 – 1.90 (m, 1H)	1.79 – 1.88 (m, 1H)
	1.57 (m)	1.57 (m)	1.52 – 1.64 (m, 1H)	1.51 – 1.65 (m, 2H)
2-H	1.91 (m)	1.91 (m)	—	—
	1.37 (m)	1.37 (m)	—	—
3-H	3.48 (m, 2H)	3.48 (m, 2H)	3.44 – 3.55 (m, 1H) 3.43 – 3.34 (m, 1H)	3.45 – 3.53 (m, 1H) 3.42 – 3.32 (m, 1H)
5-H	3.95 (m)	3.95 (m)	3.87 – 3.98 (m, 2H)	—
	3.60 (m)	3.62 (m)	3.55 – 3.64 (m, 2H)	3. 53 – 3.65 (m, 2H)
6-H	1.54 (m)	1.54 (m)	1.42 – 1.51 (m, 1H)	1.51 – 1.65 (m, 2H)
	1.37 (m)	1.37 (m)	—	—
7-H	2.06 (m)	2.06 (m)	2.07 - 2.17 (m, 1 H)	2.13 – 2.24 (m, 2H)
	1.27 (m)	1.27 (m)	1.18 – 1.23 (m, 1H)	1.16 – 1.21 (m, 1H)
8-H	3.94 (m)	4.05 (m)	3.87 – 3.98 (m, 2H)	4.00-4.18 (m, 1H)
9-H	2.11 (m)	2.17 (m)	2.18 – 2.28 (m, 2H)	2.13 – 2.24 (m, 2H)
9a-H	3.89 (m)	3.89 (m)	—	3.81 – 3.96 (m, 1H)
10-H	2.22 (m)	2.20 (m)	2.29 – 2.51 (m, 3H)	2.39 – 2.50 (m, 2H)
11-H	3.72 (m)	3.82 (m)	3.83 (dd, *J* = 8.7, 1.7 Hz, 1H)	3.69 (dd, *J* = 7.7, 5.2 Hz, 1H)
12-H	4.88 (m)	4.93 (m)	4.89 (q, *J* = 1.9 Hz, 1H)	4.85 – 5.03 (m, 1H)
13-H	6.98 (*q*, *J* = 1.7)	7.07 (*q*, *J* = 1.7)	6.96 – 7.00 (m, 1H)	7.02 – 7.11 (m, 1H)
14-H	—	—	—	—
15-H	—	—	—	—
16-H	1.92 (*d*, *J* = 1.7)	1.92 (*d*, *J* = 1.7)	1.94 (t, *J* = 1.8 Hz, 3H)	1.94 (t, *J* = 1.8 Hz, 3H)
17-H	1.15 (*d*, *J* = 6.1)	1.09 (*d*, *J* = 6.1)	1.15 (d, *J* = 6.6 Hz, 3H)	1.08 (d, *J* = 6.6 Hz, 3H)

Comparison of ^{13}C NMR of **Isoneostemocochinine *N*-oxide (4)** and **Neostemocochinine *N*-oxide (3)**

δ in ppm rel. to solvent signals (δ(C) $CHCl_3$: 77.0)

Carbon	natural sample Isoneostemocochinine N-oxide	our synthetic sample Isoneostemocochinine N-oxide (4)		natural sample Neostemocochinine N-oxide	our synthetic sample Neostemocochinine N-oxide (3)
	^{13}C NMR (101 MHz, $CDCl_3$)	^{13}C NMR (101 MHz, $CDCl_3$)		^{13}C NMR (101 MHz, $CDCl_3$)	^{13}C NMR (101 MHz, $CDCl_3$)
1-C	20.5	20.4		20.6	20.3
2-C	24.6	24.6		24.8	24.4
3-C	70.2	71.3		70.4	71.4
5-C	66.0	66.1		66.0	66.0
6-C	18.8	18.7		18.9	18.7
7-C	32.4	32.3		32.1	32.1
8-C	83.0	82.9		82.8	82.8
9-C	48.7	48.6		49.0	48.9
9a-C	80.6	80.8		80.5	80.6
10-C	40.2	40.1		39.6	39.7
11-C	84.6	77.9		84.6	84.6
12-C	80.5	80.1		80.2	80.1
13-C	145.8	145.9		145.8	145.9
14-C	131.1	131.1		131.3	131.3
15-C	174.2	174.2		173.9	173.9
16-C	10.8	10.9		10.7	10.8
17-C	14.9	15.0		16.3	16.3

IV. References

1. Reddy, Chada Raji, Gajula Dharmapuri, and Nagavaram Narsimha Rao. "Synthesis of the macrocyclic core of iriomoteolide 3a." *Org. Lett.* **2009**, *11*, 5730-5733.

2. Gilmar A. Brito, Ariel M. Sarotti, Peter Wipf, Ronaldo A. Pilli. "Cascade cyclization triggered by imine formation. Formal synthesis of the alkaloid (±)-stemoamide and its 9a-epimer." *Tetra. Lett.* **2015**, *56*, 6664-6668.

3. Yuji Tokunaga, Masataka Ihara and Keiichiro Fukumoto. "A mild oxidative transformation of nitro compounds into ketones bytetrapropylammonium perruthenate." *J. Chem. Soc., Perkin Trans 1*, **1997**, *3*, 207-210.

4. Akihiro Takada, Hiroaki Fujiwara, Kenji Sugimoto, Hirofumi Ueda, and Hidetoshi Tokuyama**.** "Total Synthesis of (-)-Isoschizogamine." *Chem. Eur. J.* **2015,** *21*, 16400 – 16403.

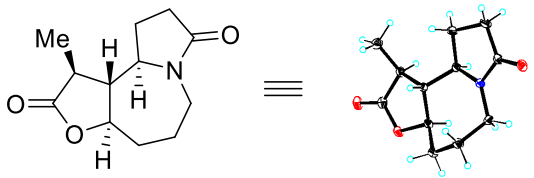
5. M. Yoritate, Y. Takahashi, H. Tajima, C. Ogihara, T. Yokoyama, Y. Soda, T. Oishi, T. Sato, N. Chida, *J. Am. Chem. Soc.* **2017**, *139*, 18386-18391.

V. Cif Check Reports

Crystal Data and Cif Check Report for

compound 7a

(CCDC: 2068156)



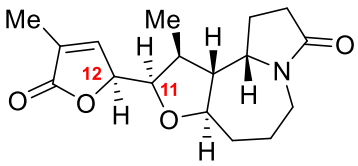
7a: 9a-*epi*-stemoamide ORTEP of **7a**

```
Bond precision:  C-C = 0.0042 A          Wavelength=1.54184

Cell:            a=27.7033(5)     b=7.2169(15)     c=22.9335(18)
                 alpha=90         beta=90          gamma=90
Temperature:     153 K

                 Calculated                Reported
Volume           4585.1(10)                4585.1(10)
Space group      P c a 21                  P c a 21
Hall group       P 2c -2ac                 P 2c -2ac
Moiety formula   2(C12 H17 N O3), H2 O     2(C12 H17 N O3), H2 O
Sum formula      C24 H36 N2 O7             C24 H36 N2 O7
Mr               464.55                    464.55
Dx,g cm-3        1.346                     1.346
Z                8                         8
Mu (mm-1)        0.812                     0.812
F000             2000.0                    2000.0
F000'            2006.44
h,k,lmax         33,8,27                   33,8,27
Nref             8169[ 4198]               8071
Tmin,Tmax        0.907,0.922               0.939,1.000
Tmin'            0.907

Correction method= # Reported T Limits: Tmin=0.939 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.92/0.99      Theta(max)= 66.964

R(reflections)= 0.0375( 7909)     wR2(reflections)= 0.0993( 8071)

S = 1.048                 Npar= 615
```

Crystal Data and Cif Check Report for

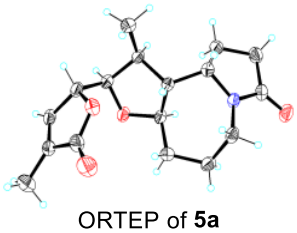
compound 5a

(CCDC: 2068264)



5a: 11-*epi*-saxorumamide

≡



ORTEP of **5a**

Bond precision: C-C = 0.0043 A Wavelength=0.71073

Cell: a=9.519(3) b=8.812(3) c=9.818(3)
alpha=90 beta=106.838(3) gamma=90
Temperature: 296 K

	Calculated	Reported
Volume	788.2(4)	788.3(4)
Space group	P 21	P 21
Hall group	P 2yb	P 2yb
Moiety formula	C17 H23 N O4	?
Sum formula	C17 H23 N O4	C17 H23 N O4
Mr	305.36	305.36
Dx,g cm-3	1.287	1.286
Z	2	2
Mu (mm-1)	0.091	0.091
F000	328.0	328.0
F000'	328.16	
h,k,lmax	12,11,12	12,11,12
Nref	3477[1853]	2958
Tmin,Tmax	0.973,0.982	0.596,0.746
Tmin'	0.973	

Correction method= # Reported T Limits: Tmin=0.596 Tmax=0.746
AbsCorr = MULTI-SCAN

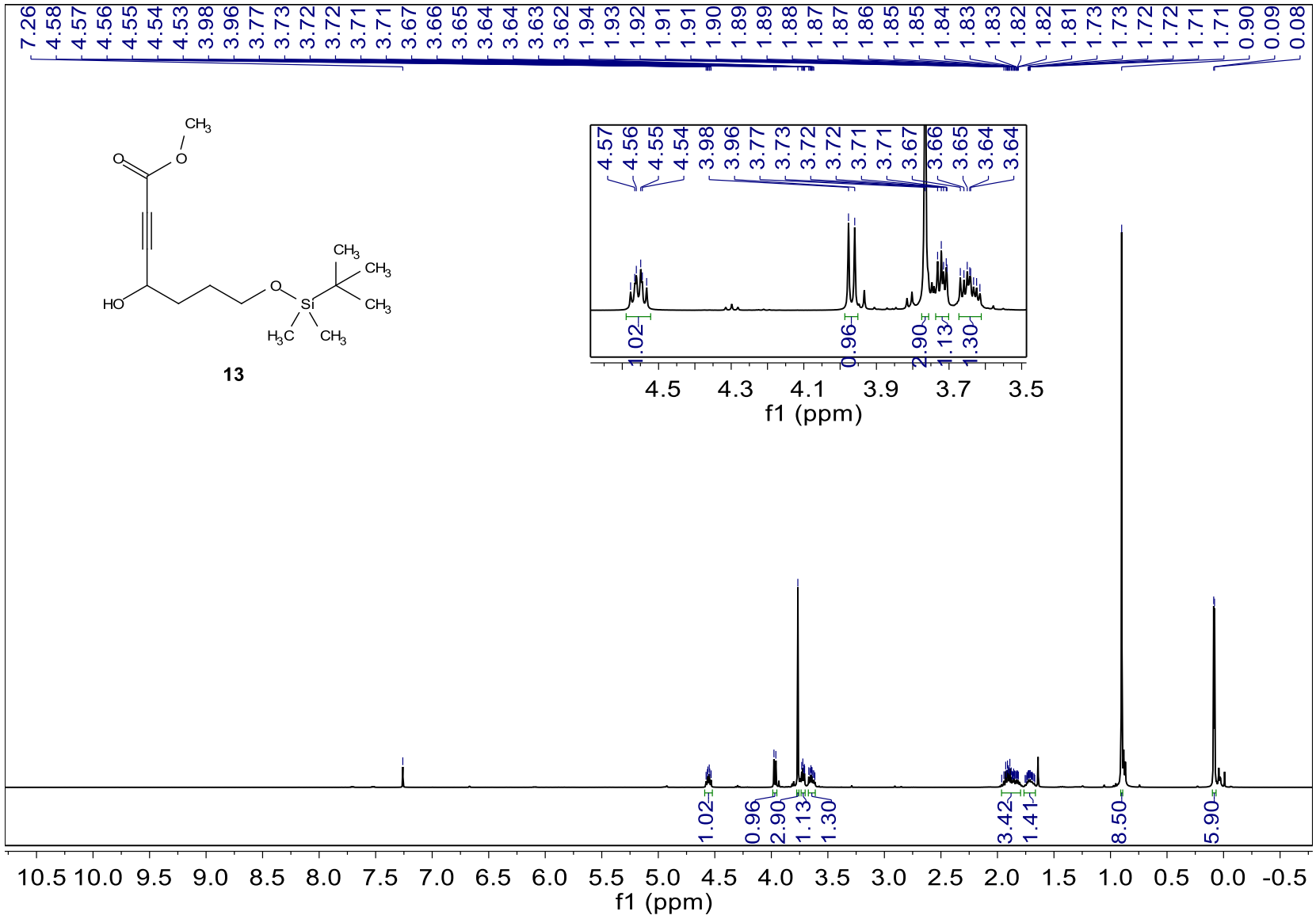
Data completeness= 1.60/0.85 Theta(max)= 27.110

R(reflections)= 0.0382(2323) wR2(reflections)= 0.0861(2958)

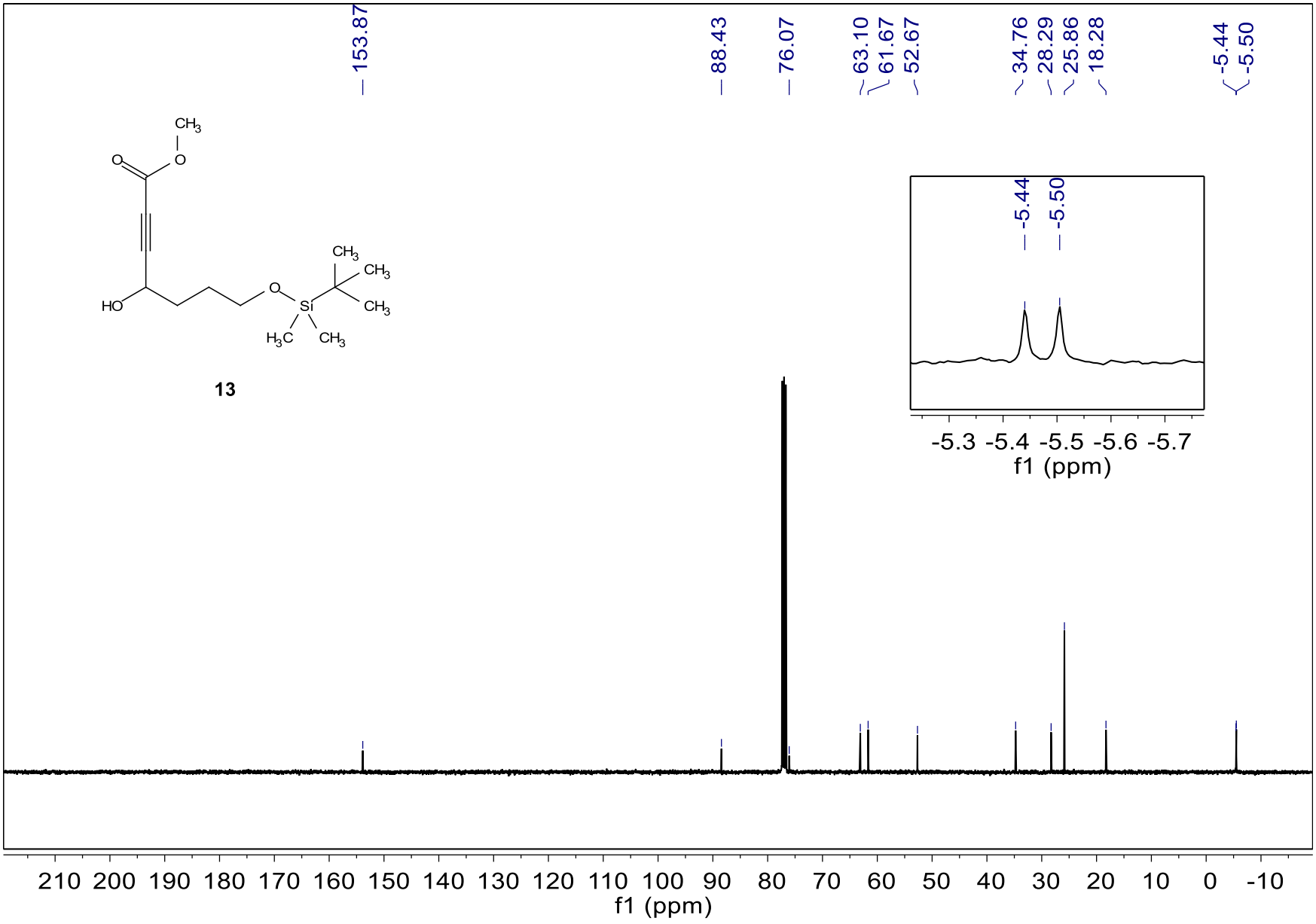
S = 1.003 Npar= 201

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

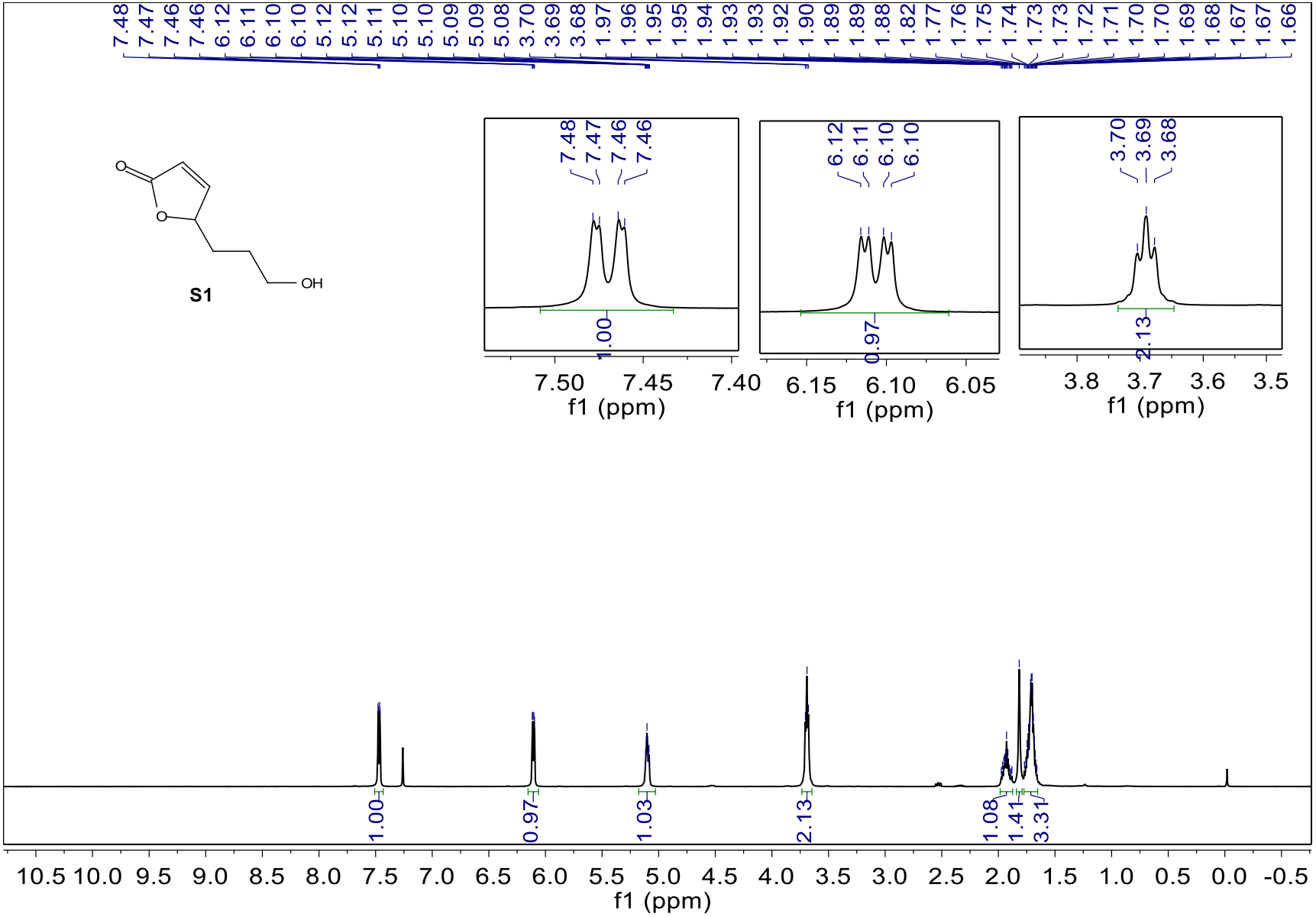
^{1}H NMR Spectrum of 13 (400 MHz, $CDCl_3$)



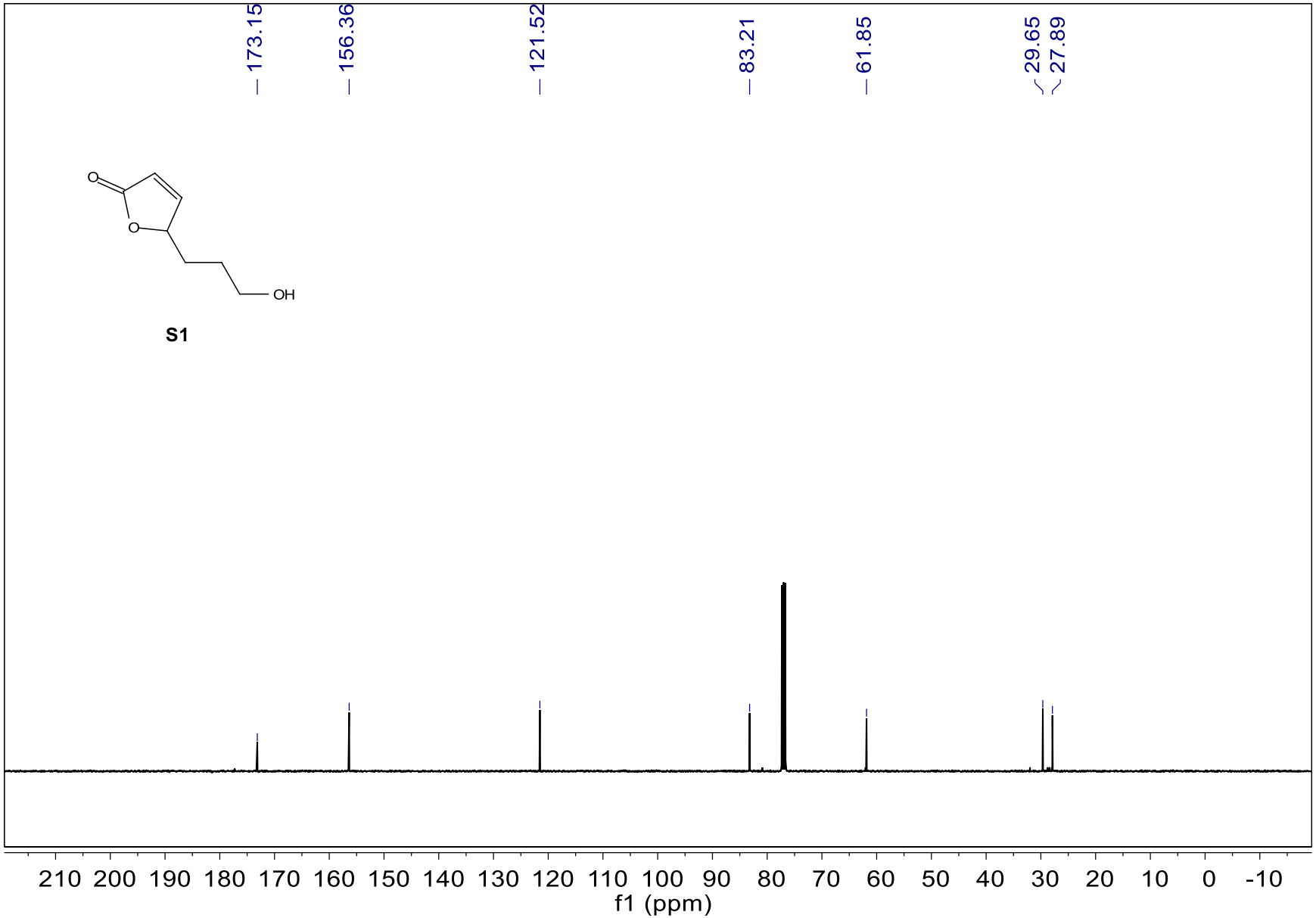
^{13}C NMR Spectrum of 13 (101 MHz, $CDCl_3$)



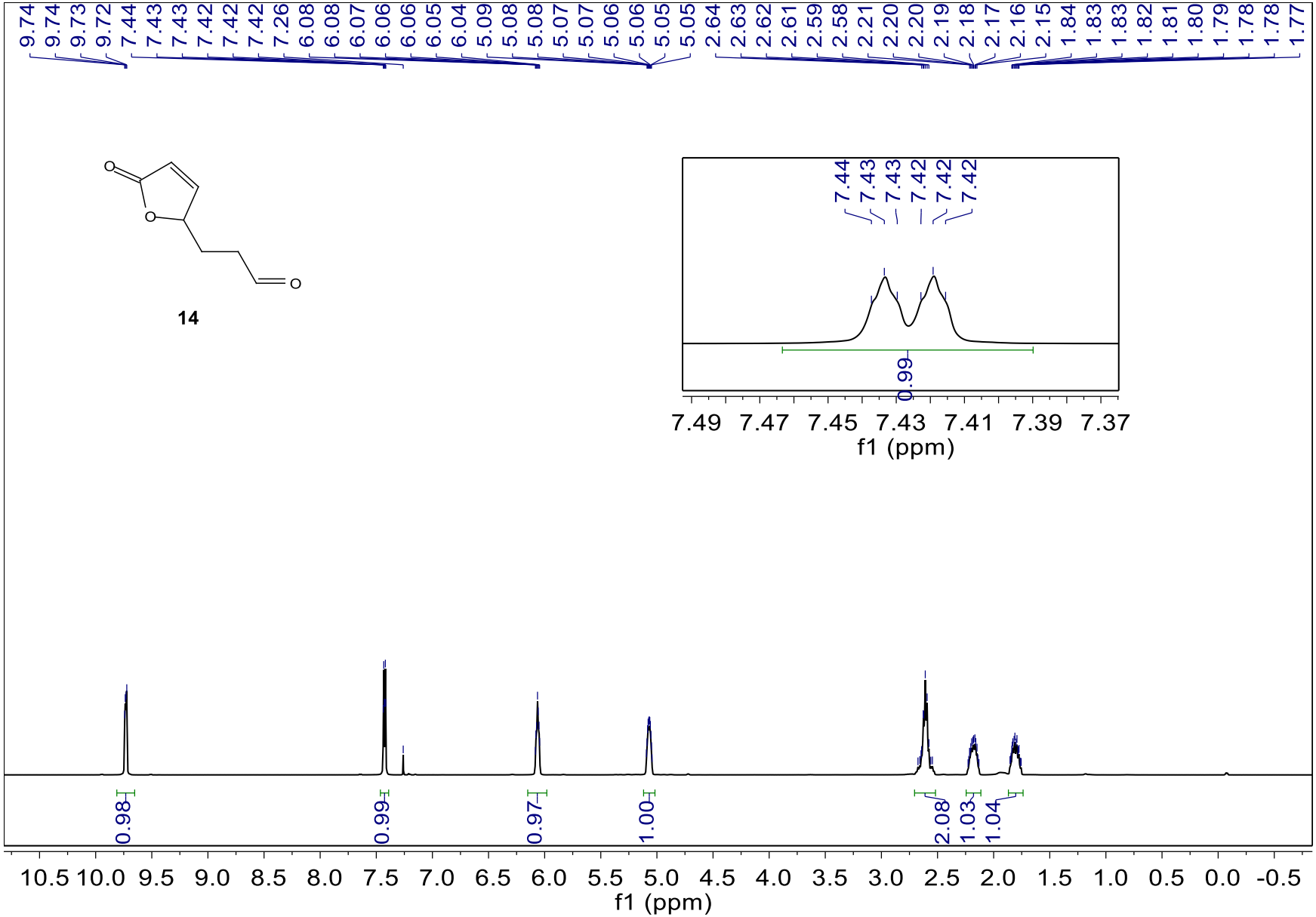
^{1}H NMR Spectrum of S1 (400 MHz, $CDCl_3$)



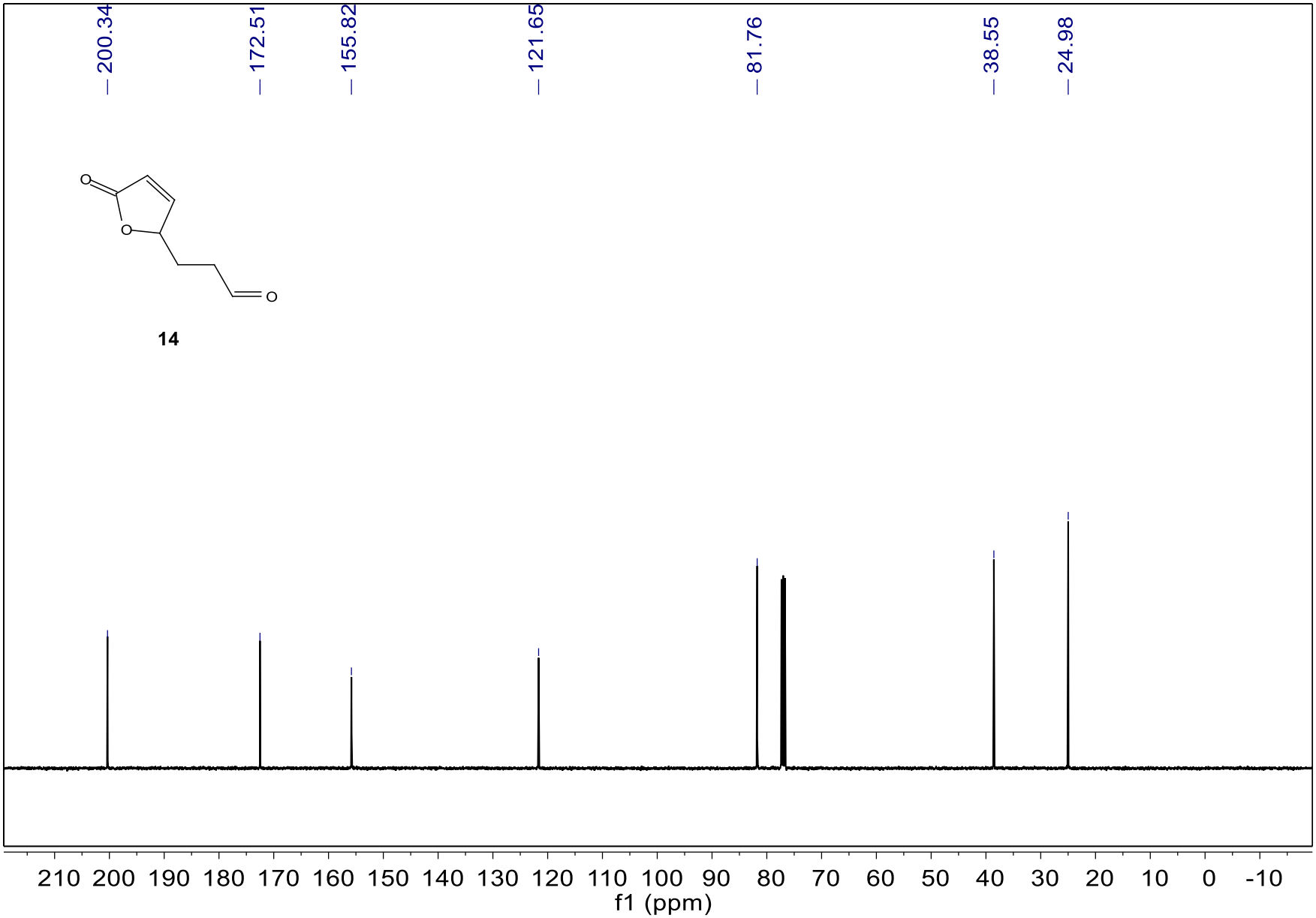
^{13}C NMR Spectrum of S1 (101 MHz, $CDCl_3$)



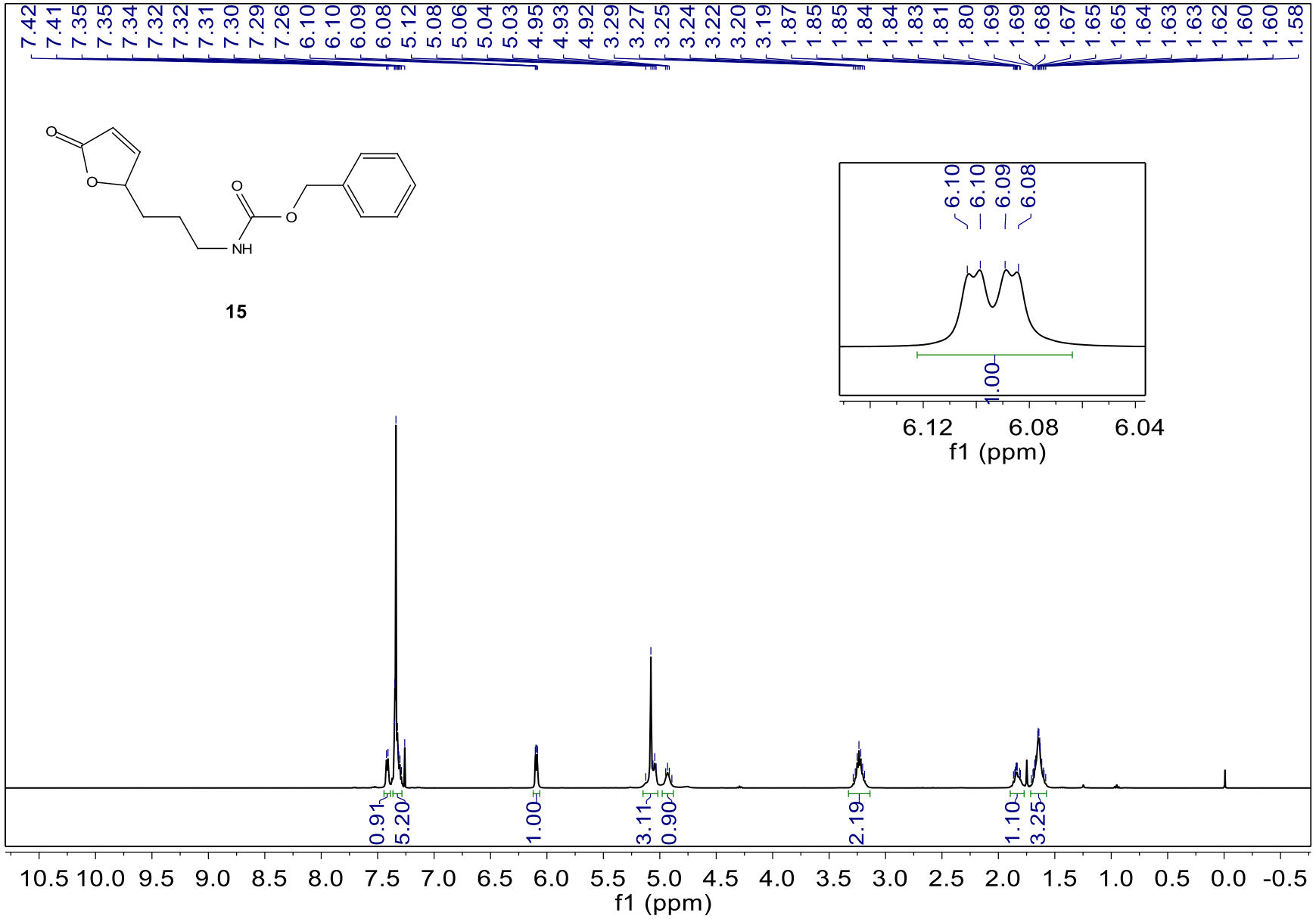
^{1}H NMR Spectrum of 14 (400 MHz, $CDCl_3$)



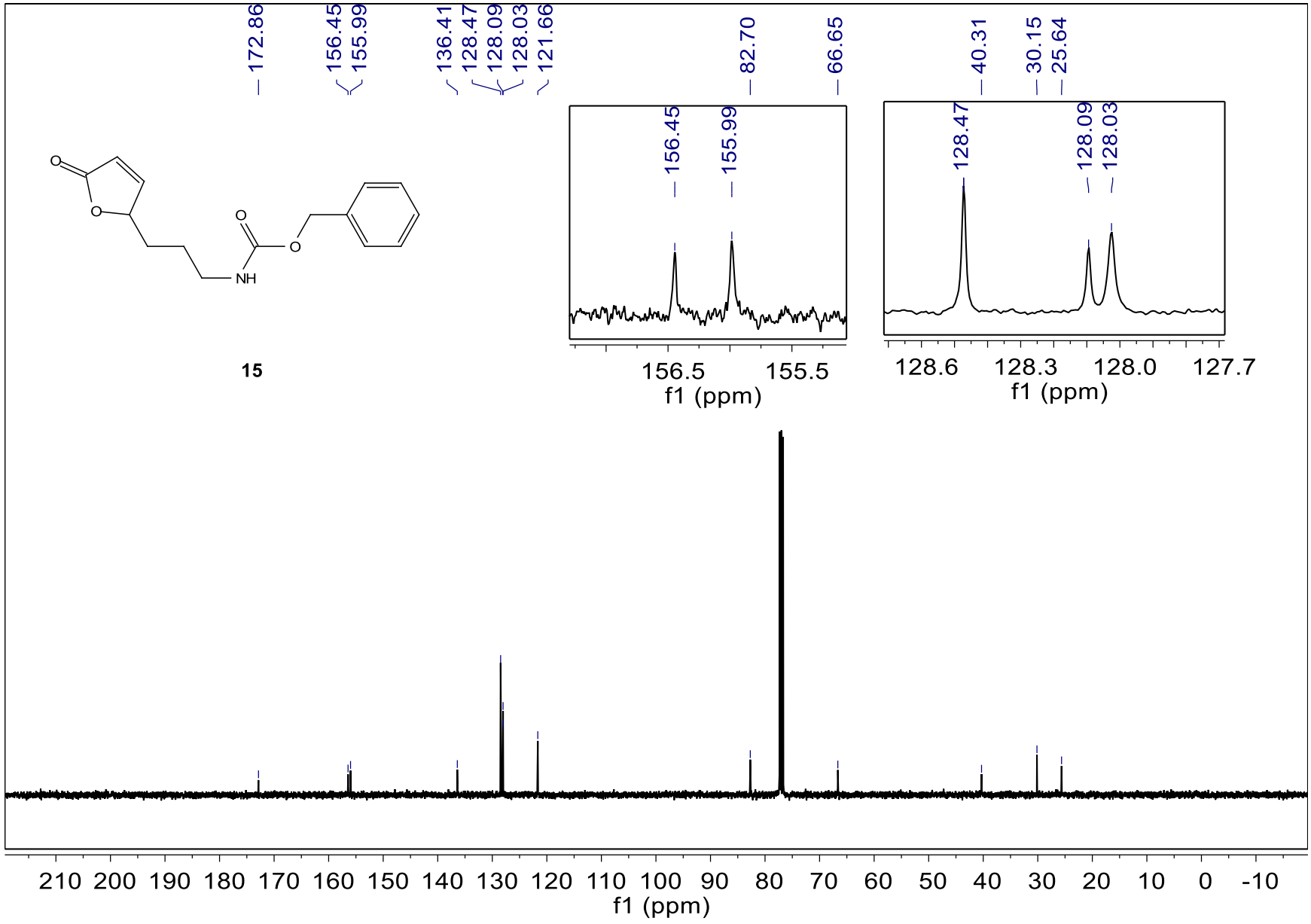
^{13}C NMR Spectrum of 14 (101 MHz, $CDCl_3$)



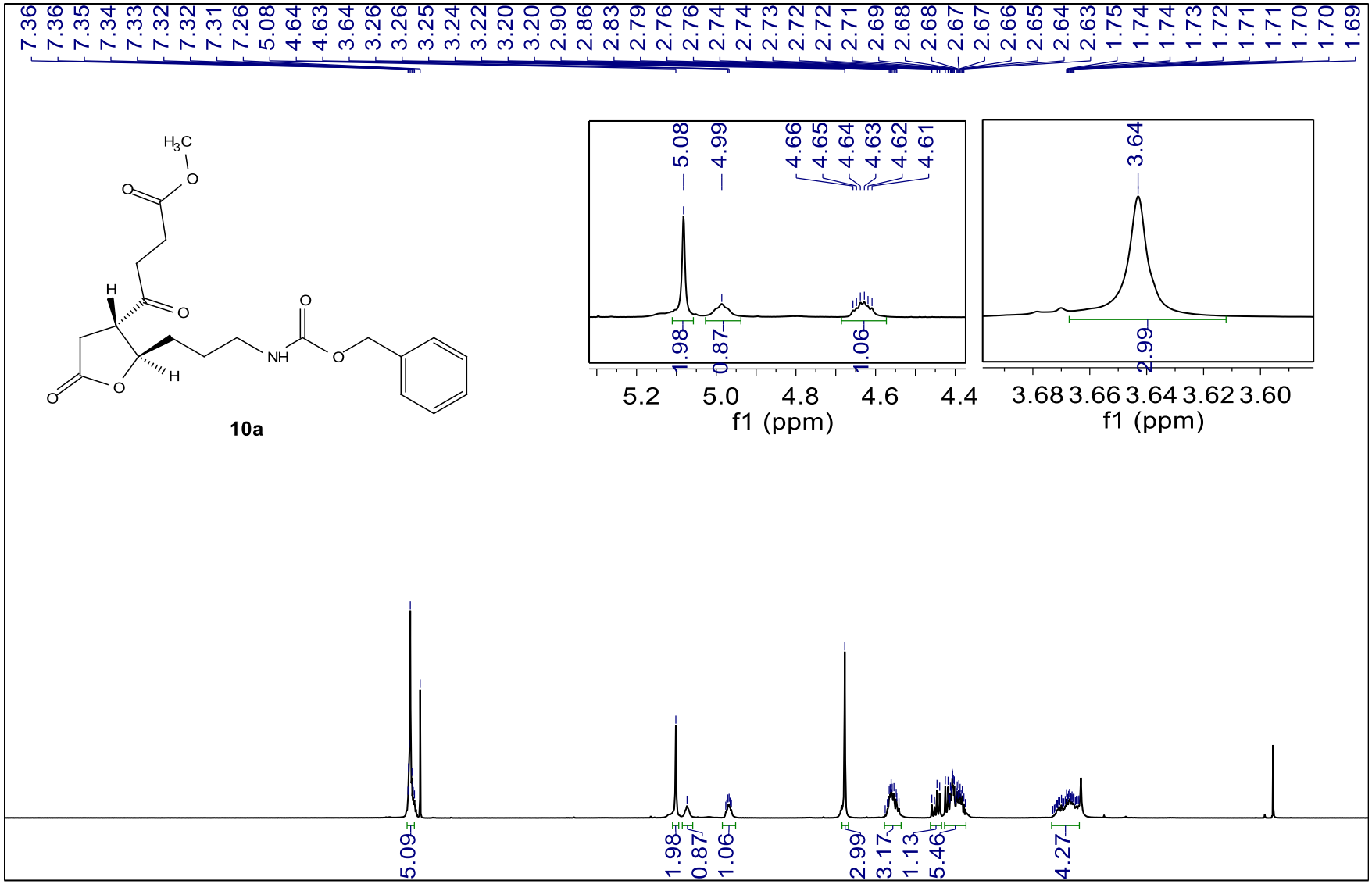
^{1}H NMR Spectrum of 15 (400 MHz, $CDCl_3$)



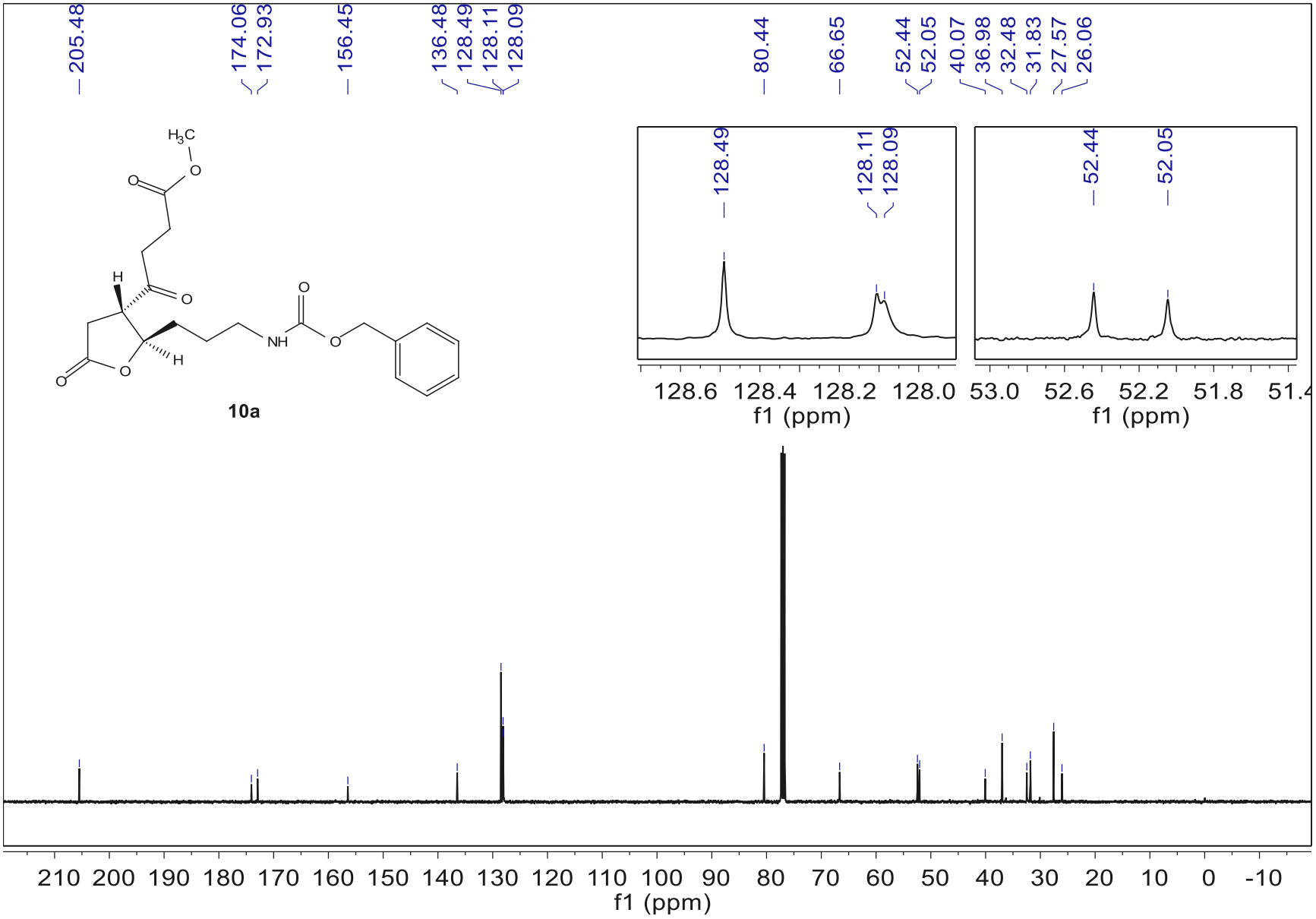
^{13}C NMR Spectrum of 15 (101 MHz, $CDCl_3$)



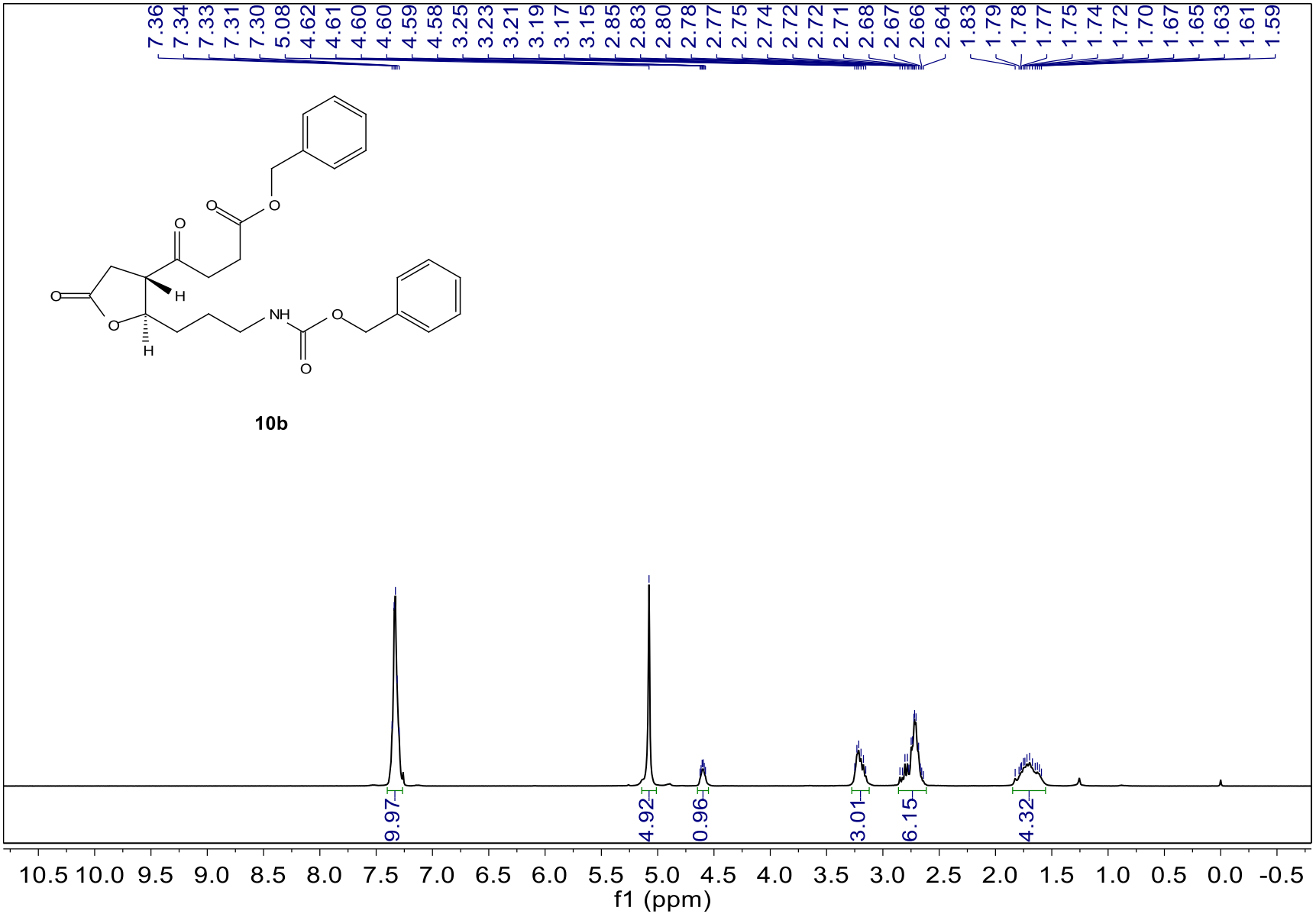
^{1}H NMR Spectrum of 10a (400 MHz, $CDCl_3$)



^{13}C NMR Spectrum of 10a (101 MHz, $CDCl_3$)

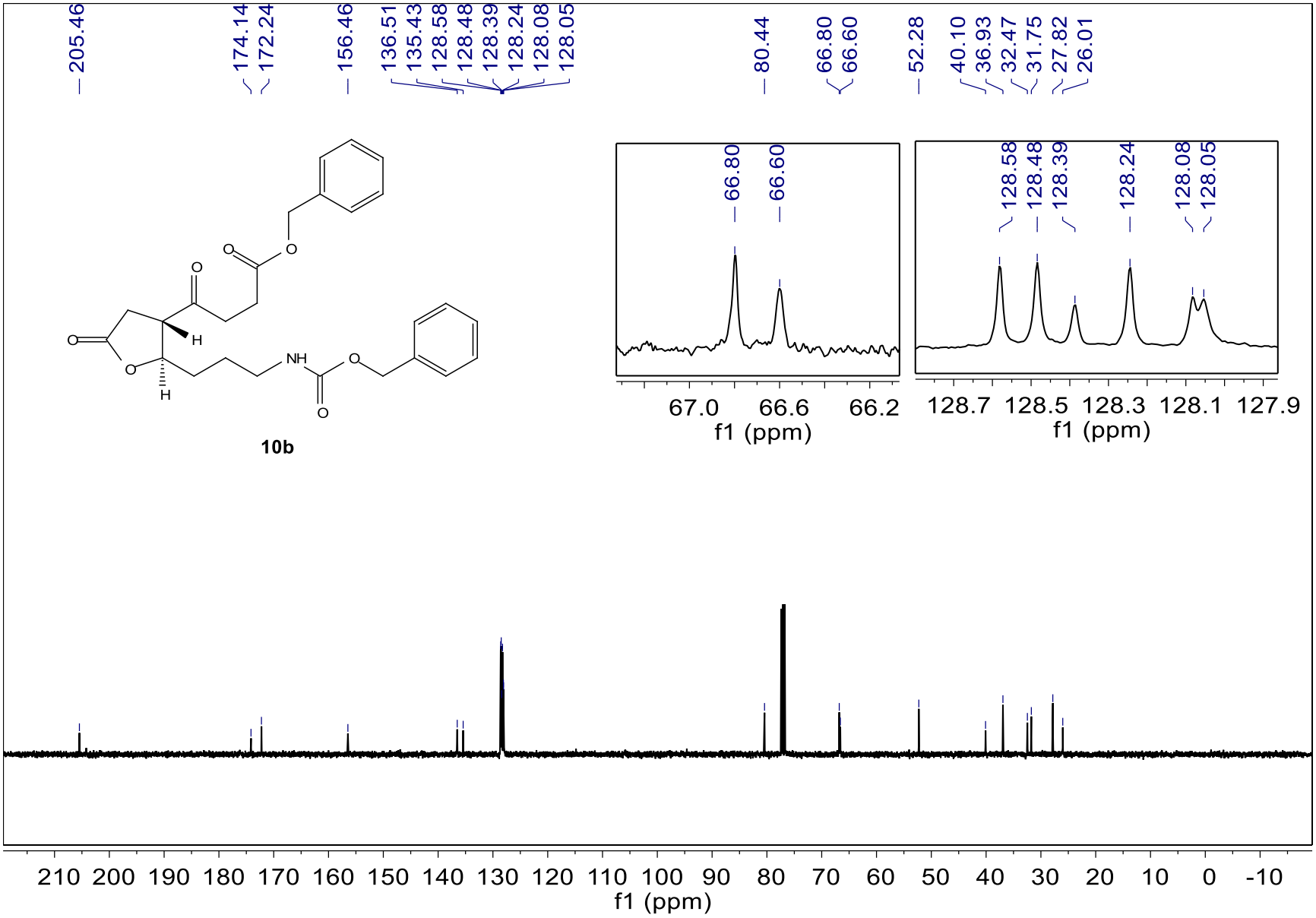


^{1}H NMR Spectrum of 10b (400 MHz, $CDCl_3$)

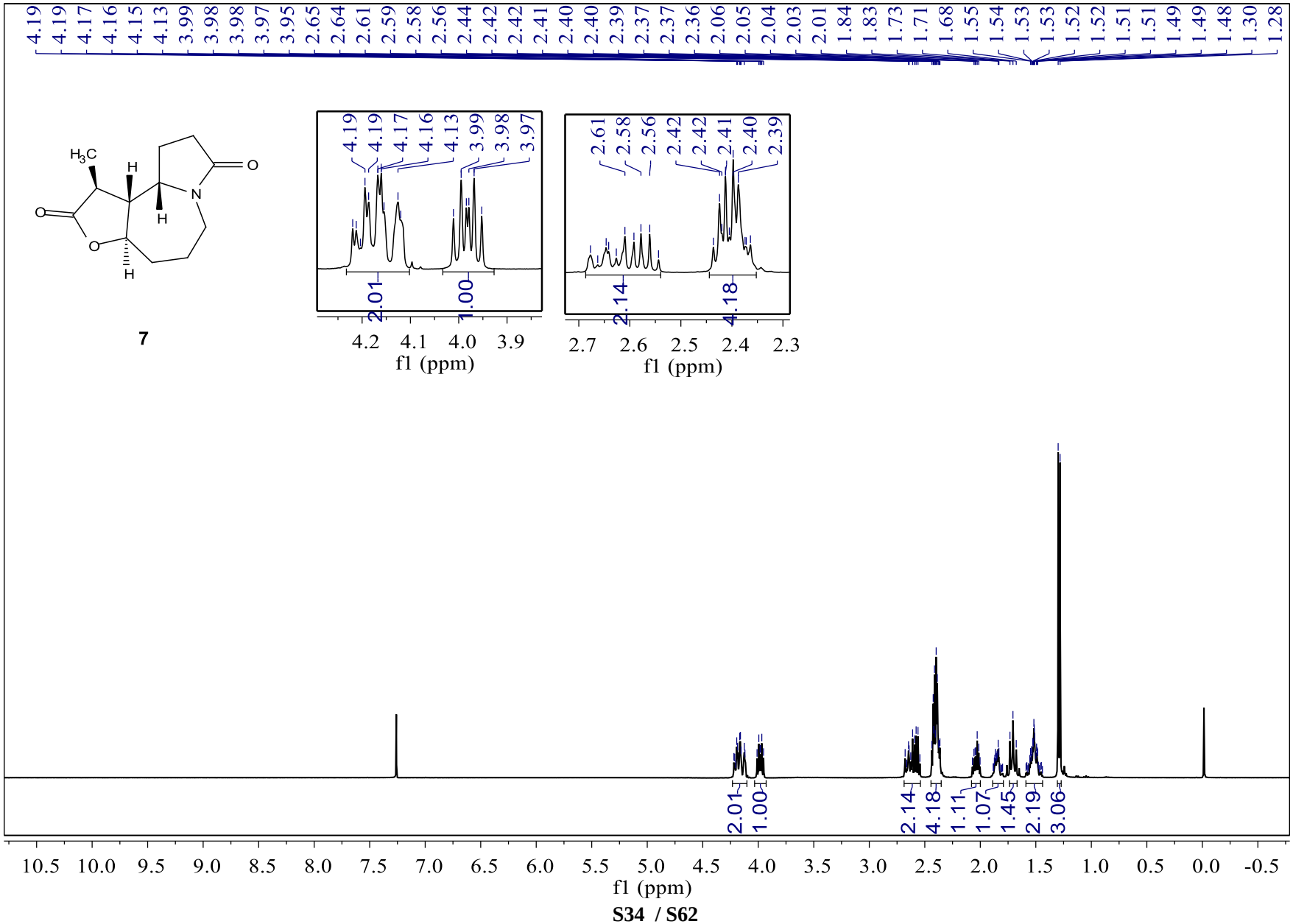


10b

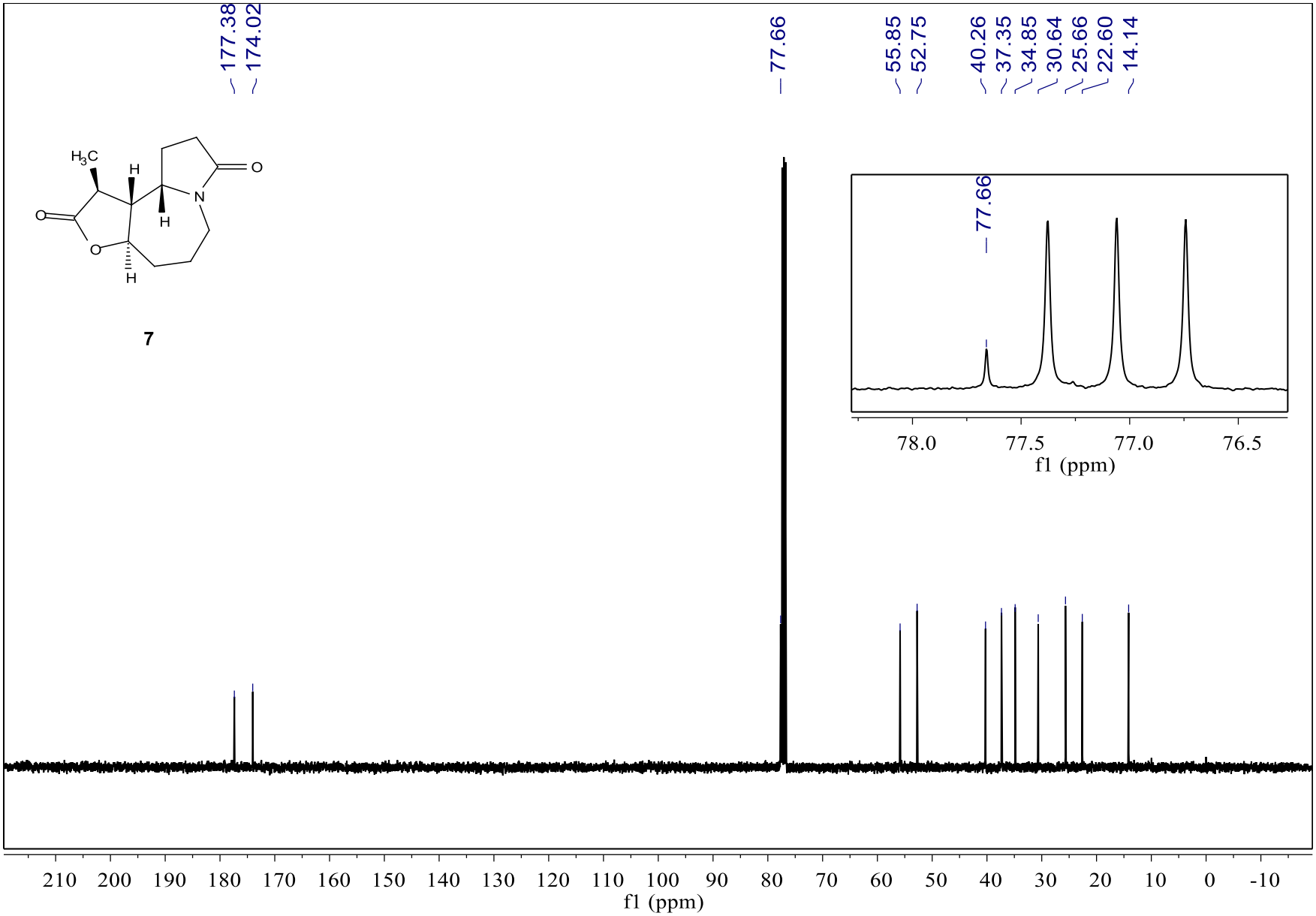
^{13}C NMR Spectrum of 10b (101 MHz, $CDCl_3$)



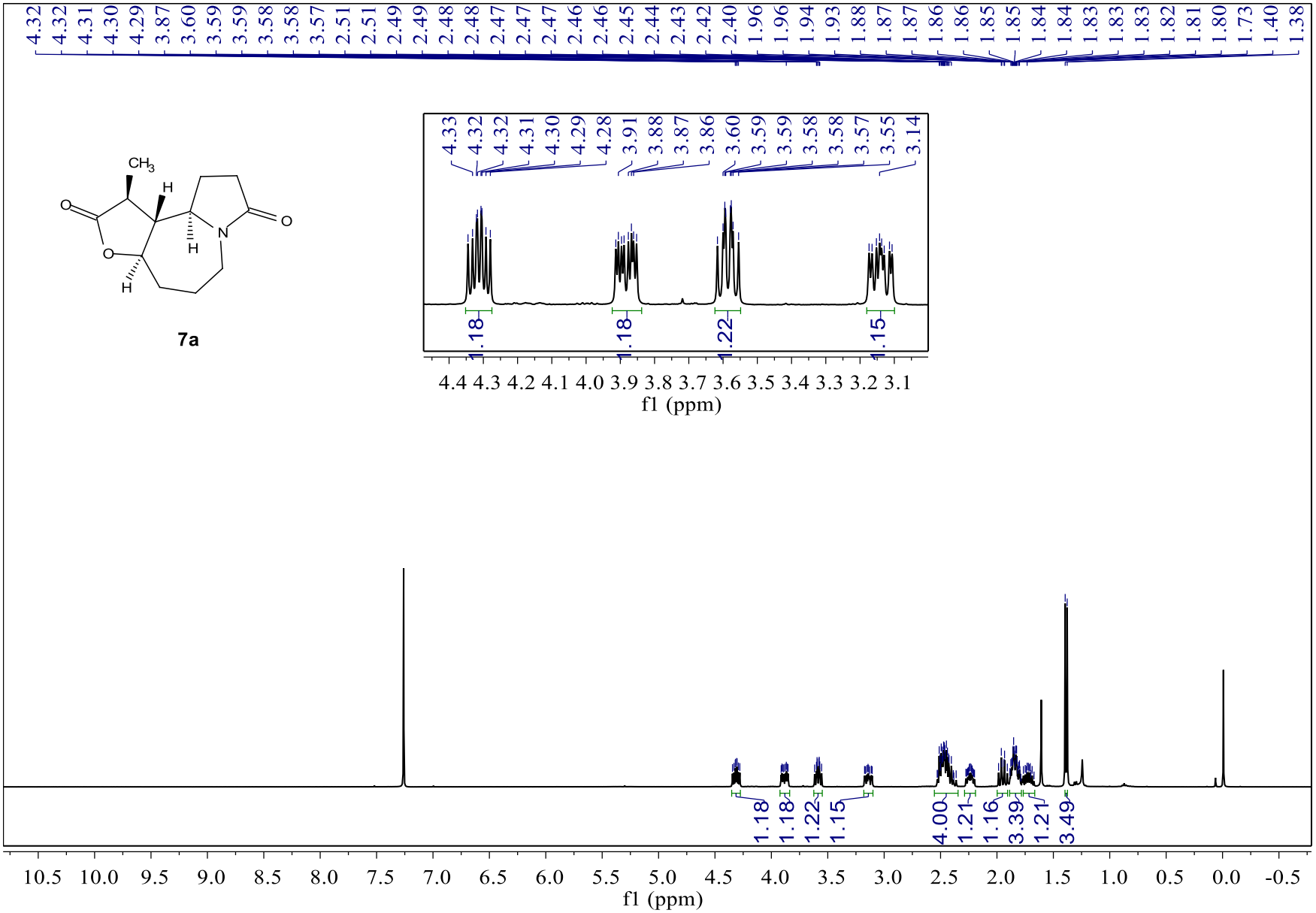
^{1}H NMR Spectrum of 7 (400 MHz, $CDCl_3$)



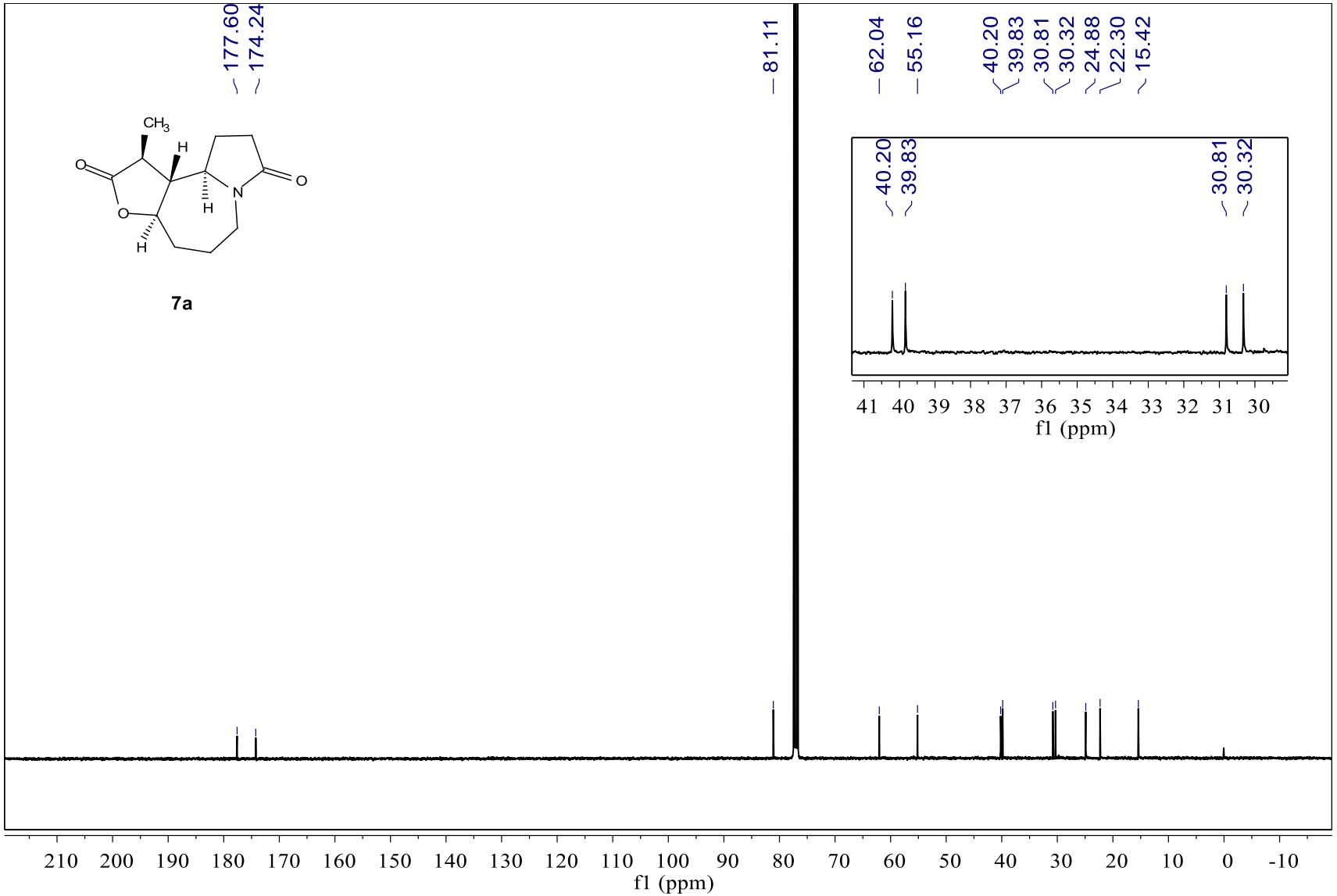
^{13}C NMR Spectrum of 7 (101 MHz, $CDCl_3$)



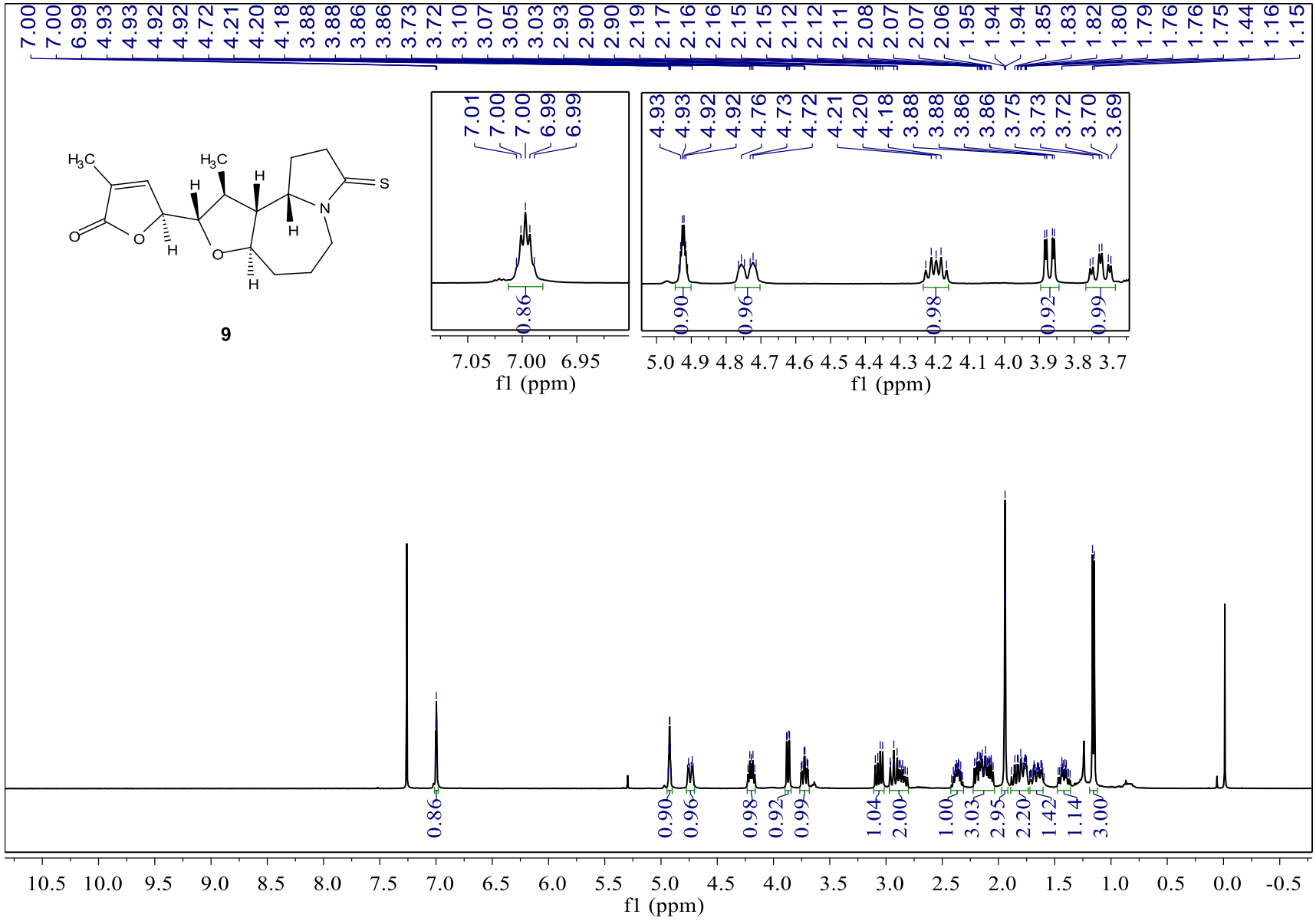
^{1}H NMR Spectrum of 7a (400 MHz, $CDCl_3$)



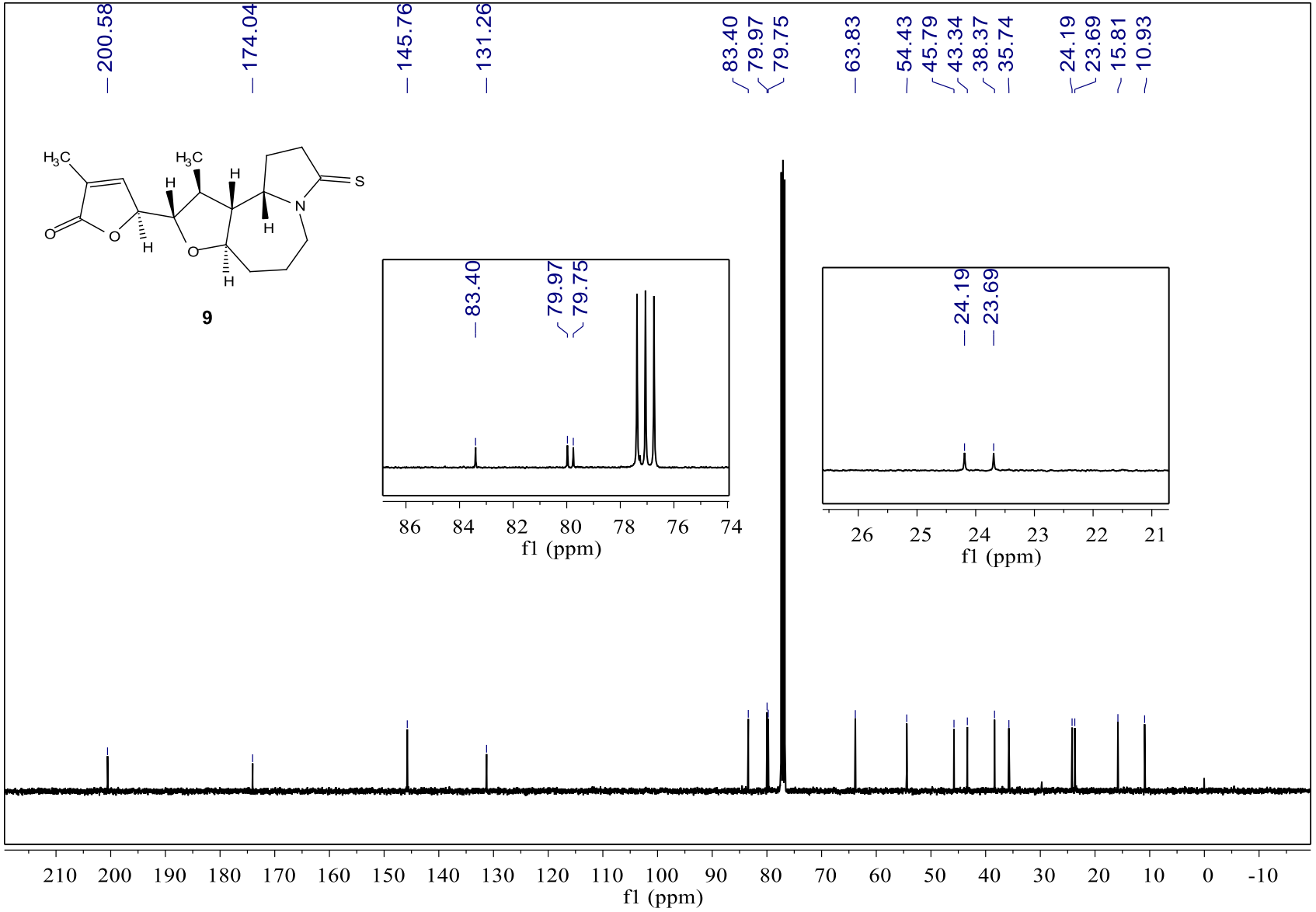
^{13}C NMR Spectrum of 7a (101 MHz, $CDCl_3$)



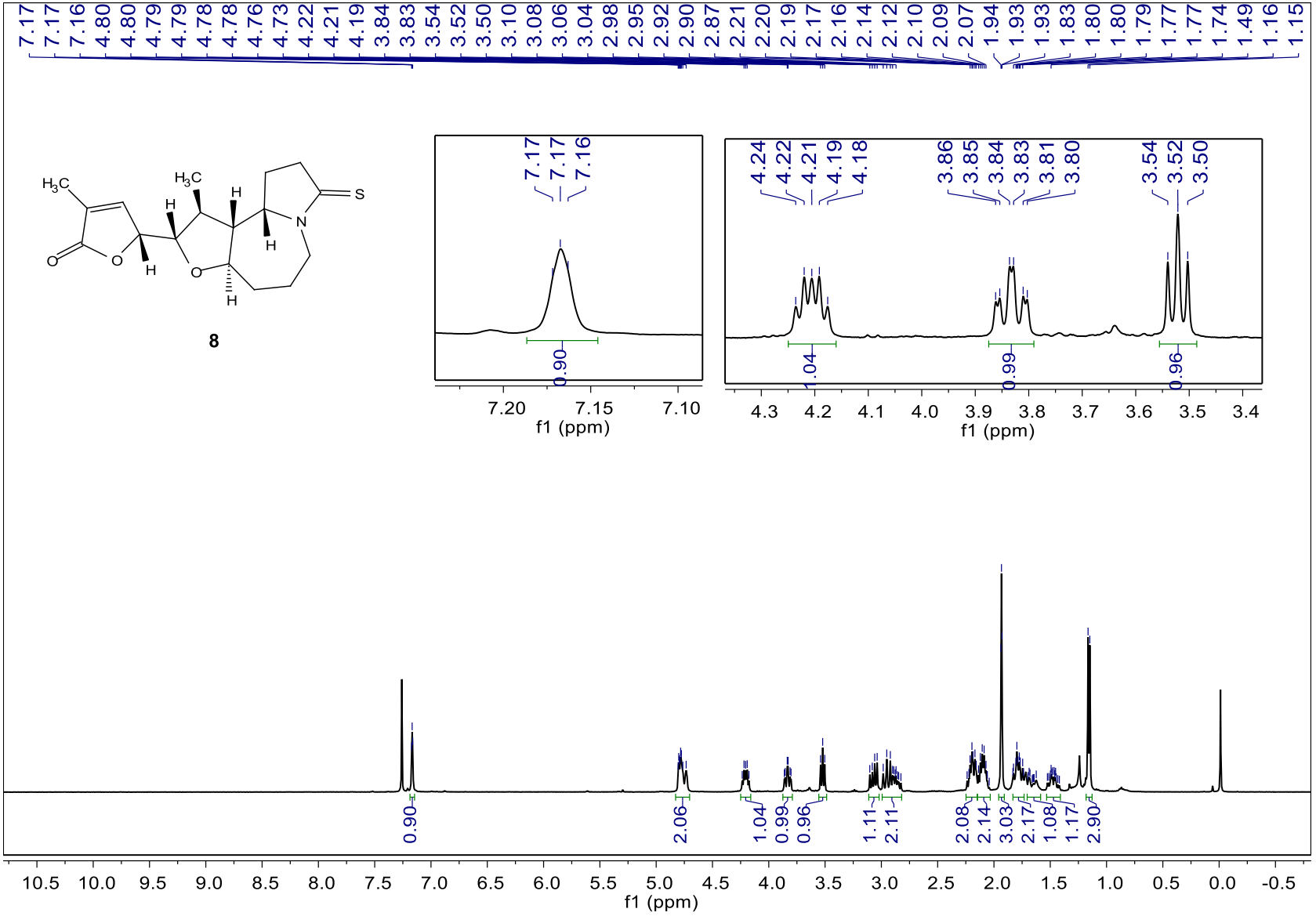
^{1}H NMR Spectrum of 9 (400 MHz, $CDCl_3$)



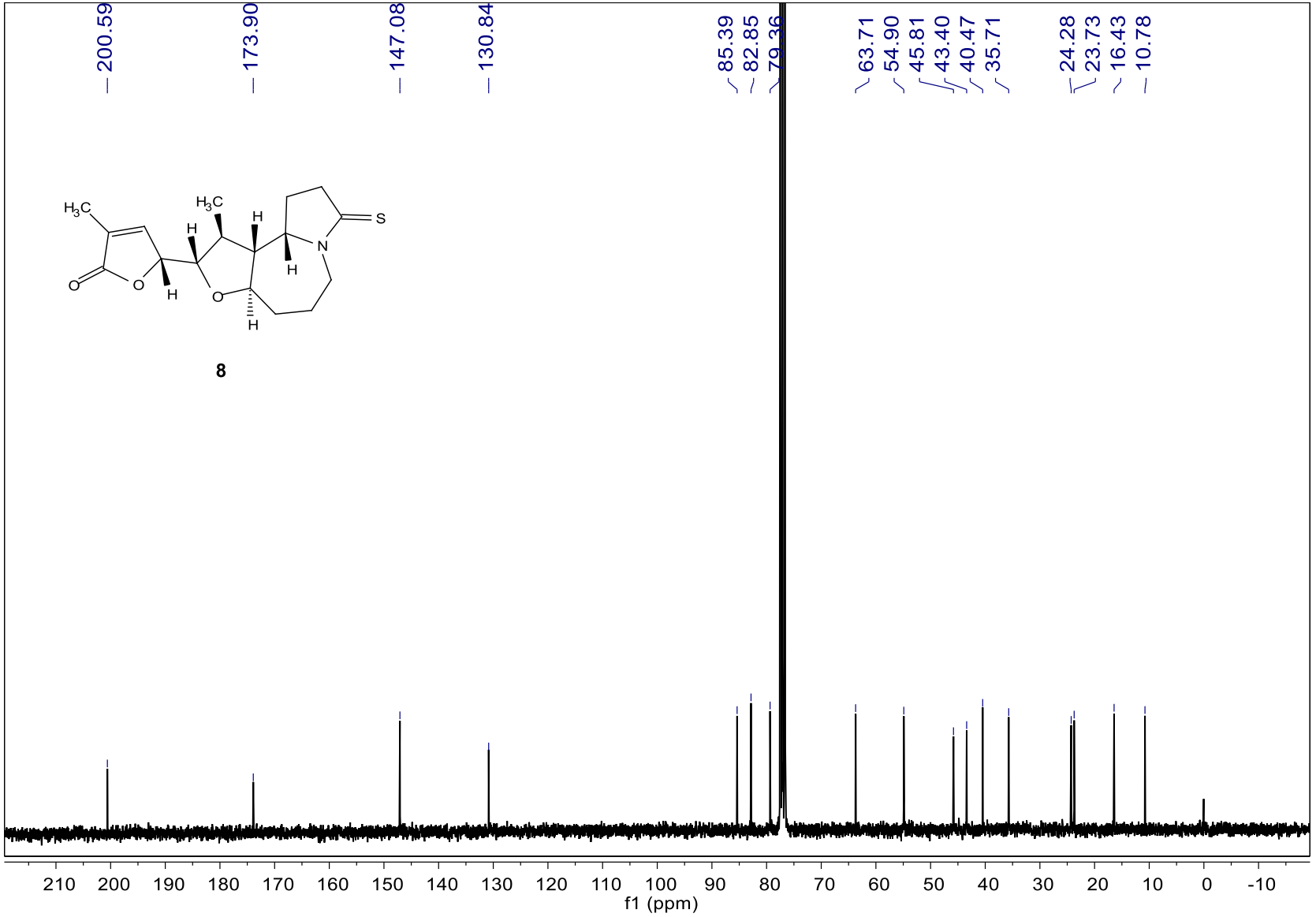
^{13}C NMR Spectrum of 9 (101 MHz, $CDCl_3$)



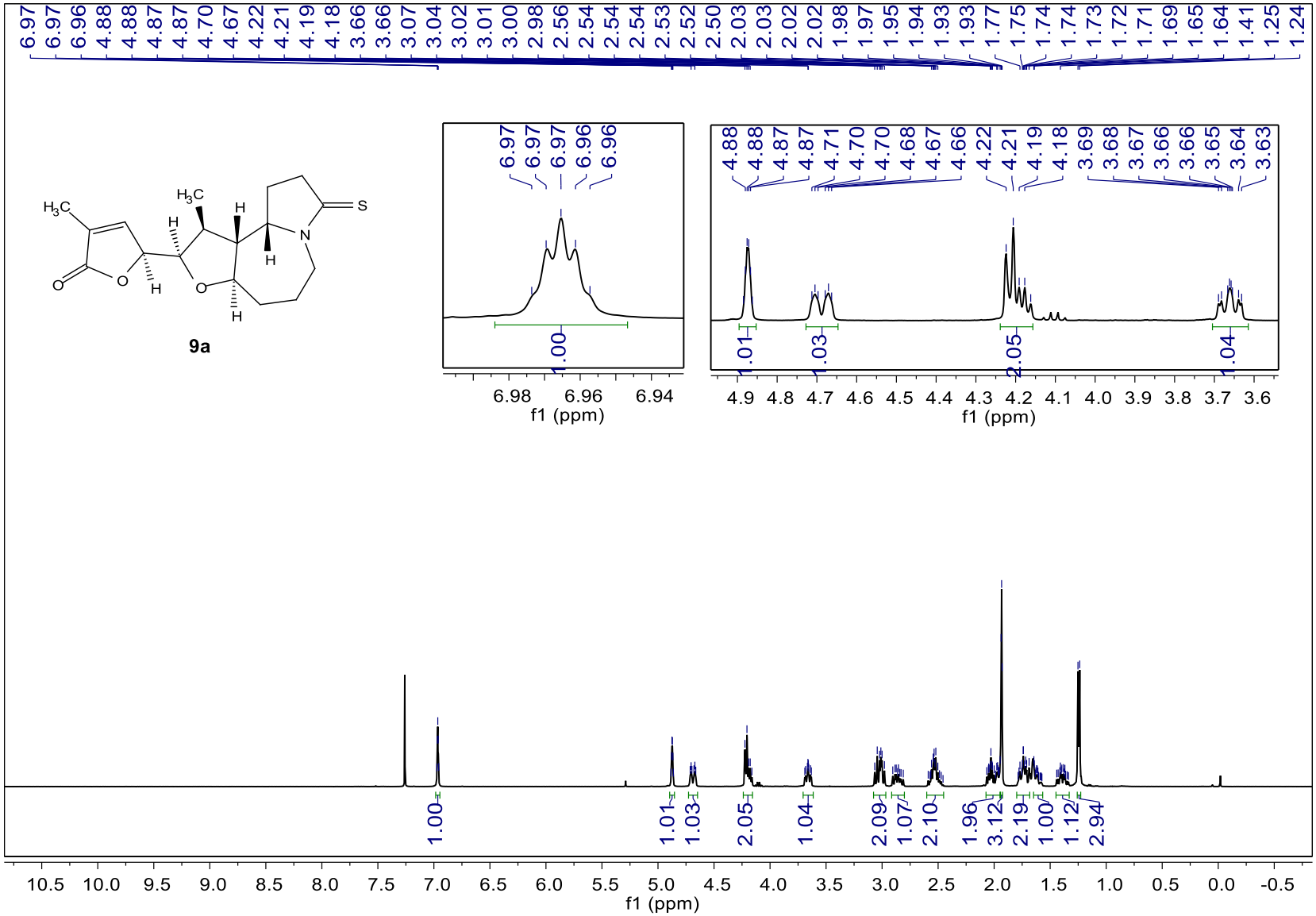
^{1}H NMR Spectrum of 8 (400 MHz, $CDCl_3$)



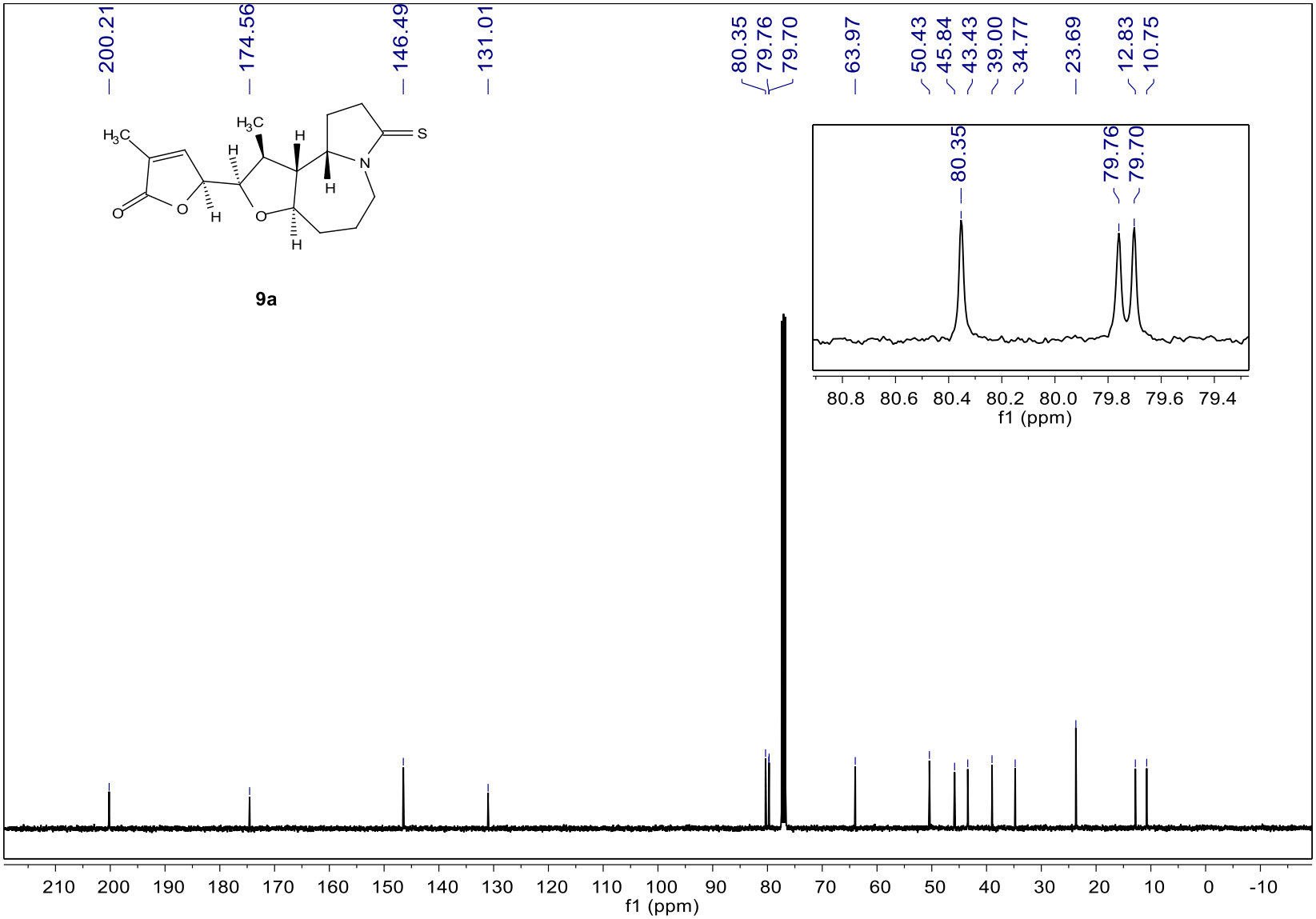
^{13}C NMR Spectrum of 8 (76 MHz, $CDCl_3$)



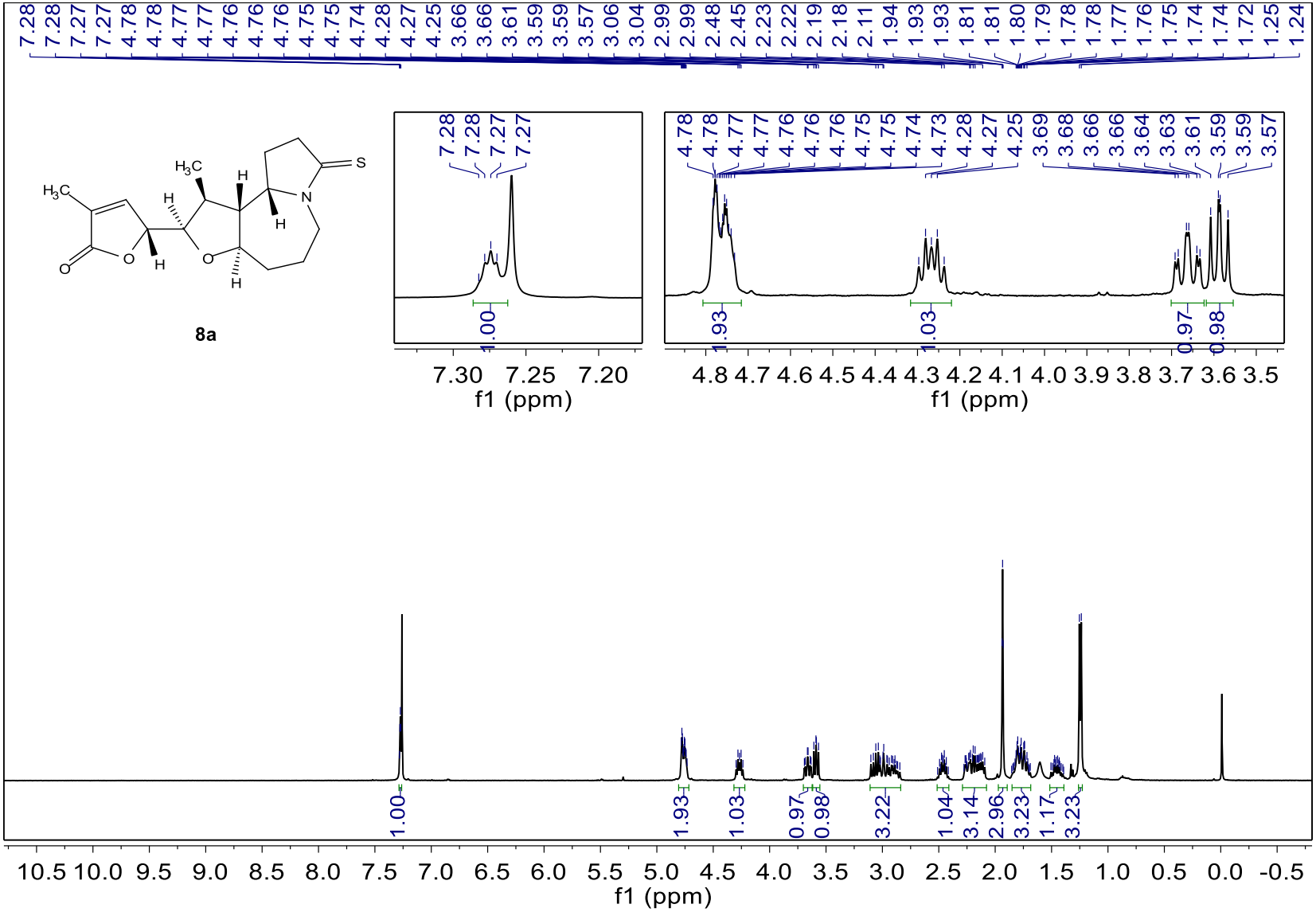
^{1}H NMR Spectrum of 9a (400 MHz, $CDCl_3$)



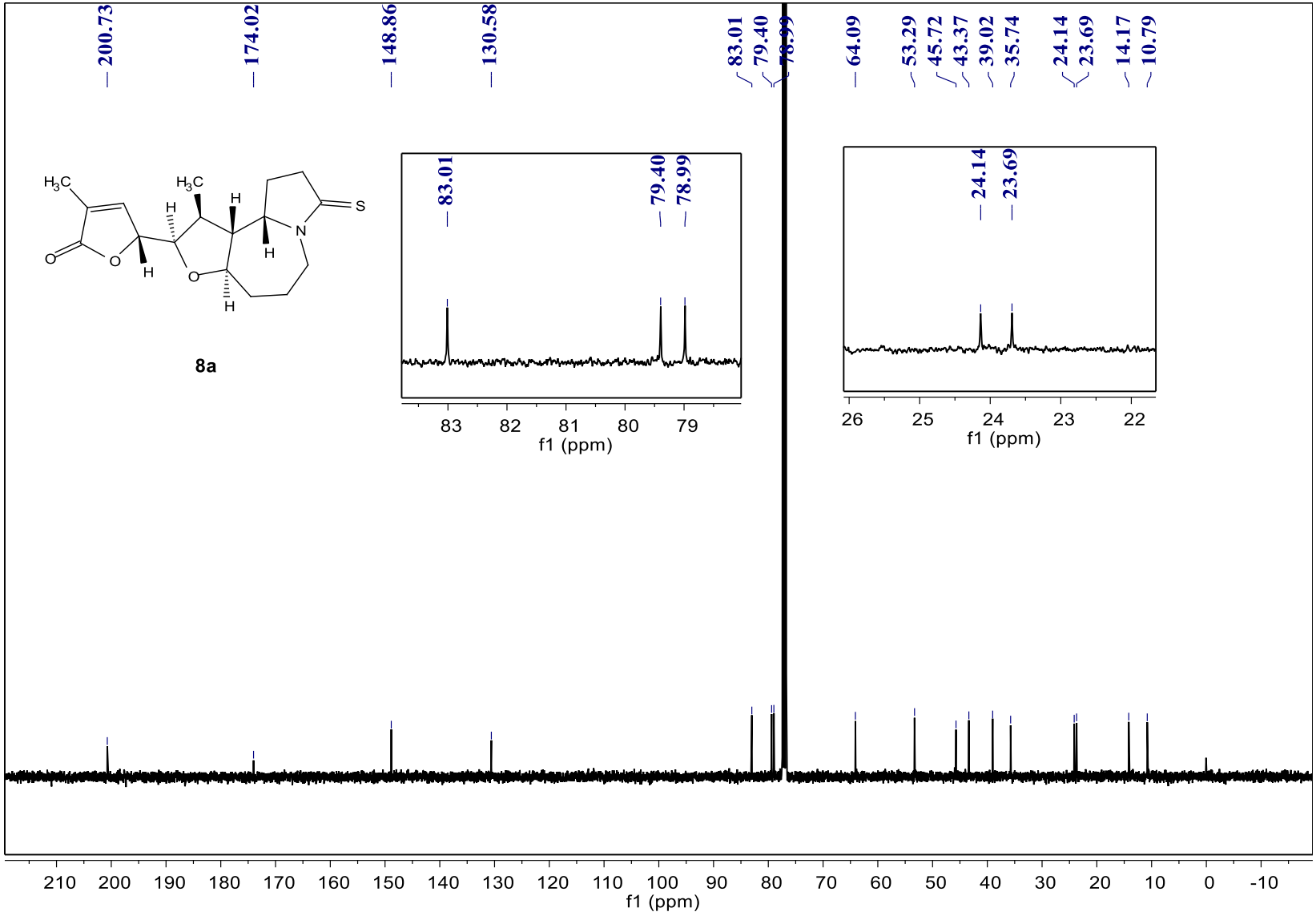
^{13}C NMR Spectrum of 9a (101 MHz, $CDCl_3$)



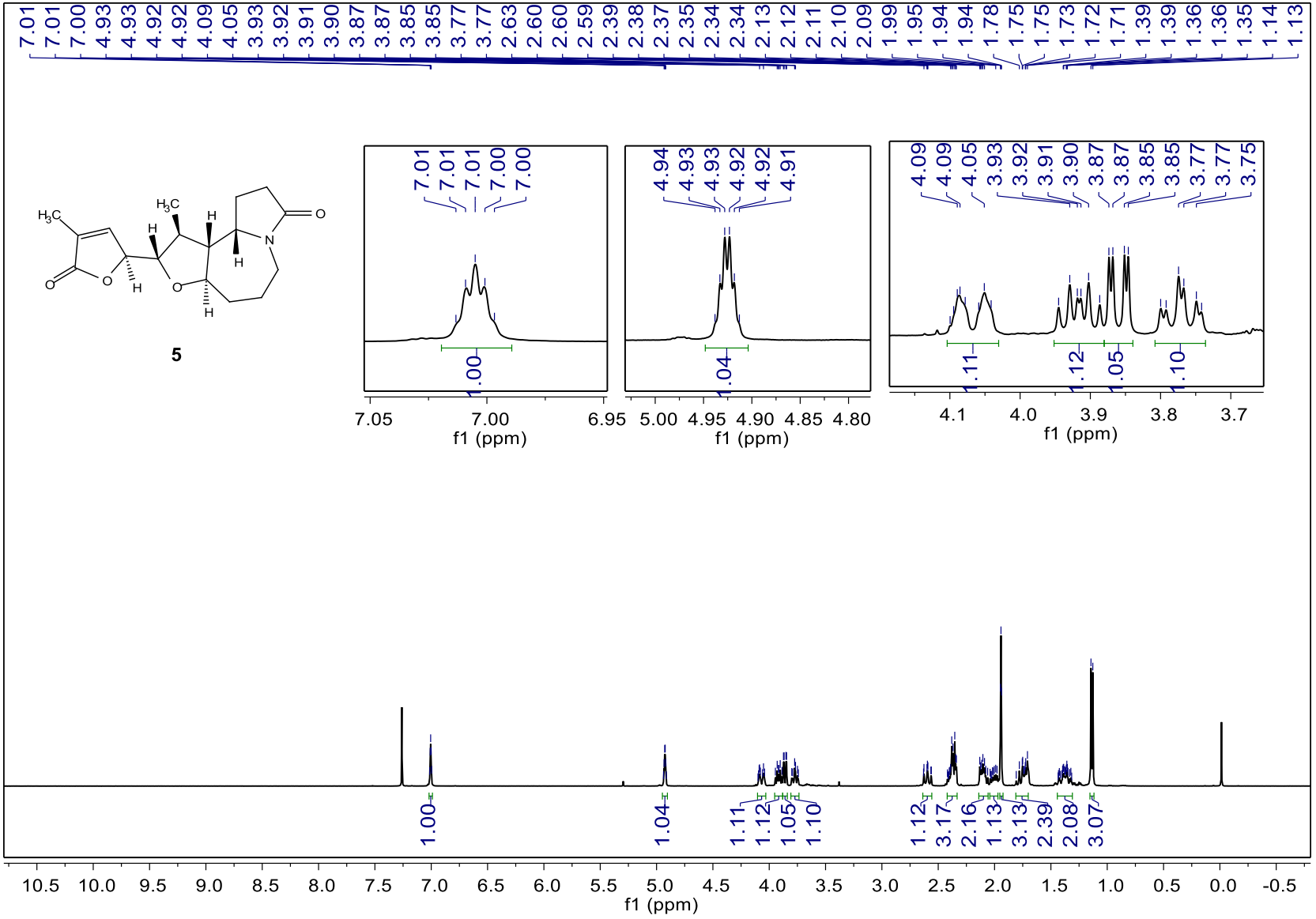
^{1}H NMR Spectrum of 8a (400 MHz, $CDCl_3$)



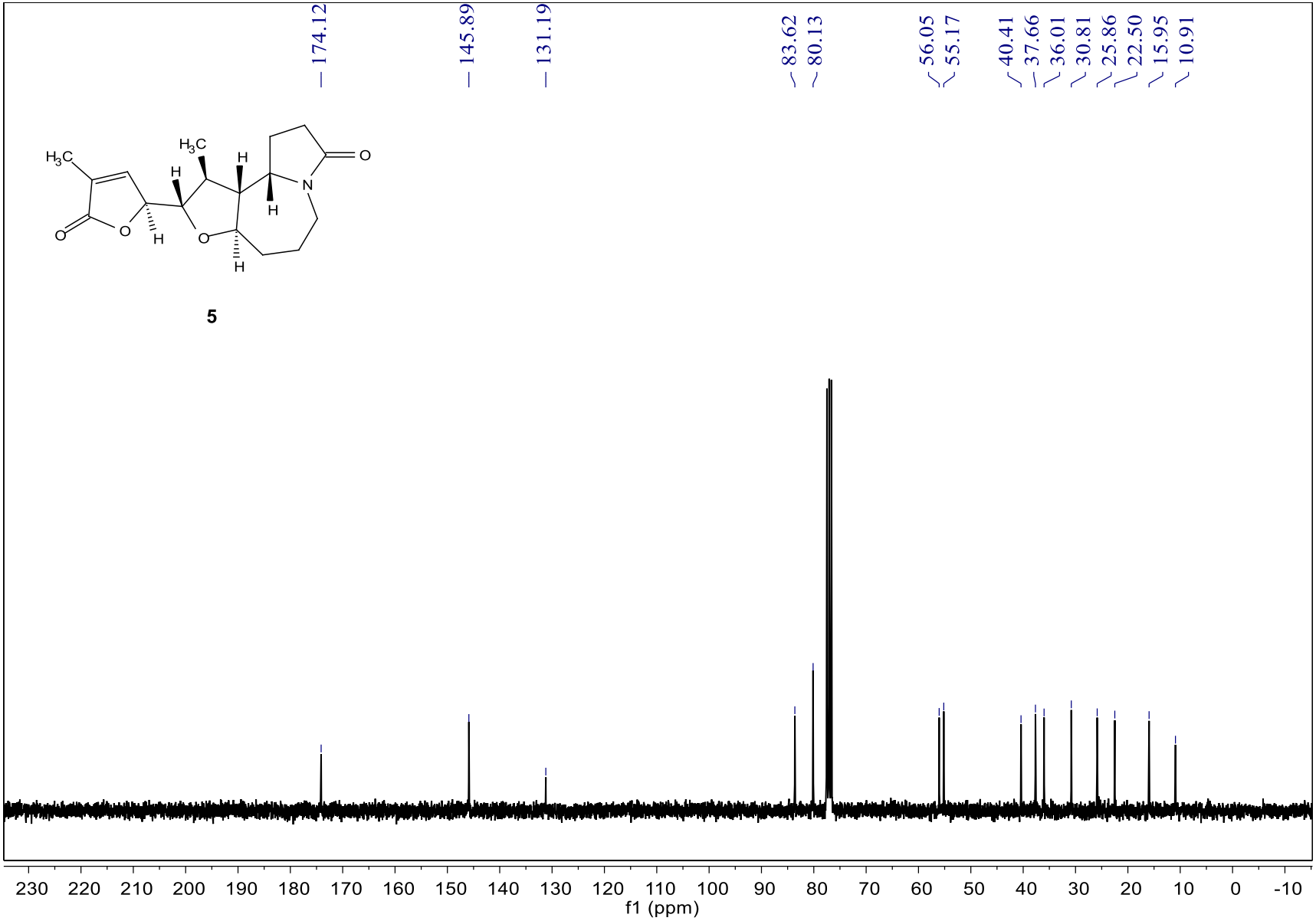
^{13}C NMR Spectrum of 8a (101 MHz, $CDCl_3$)



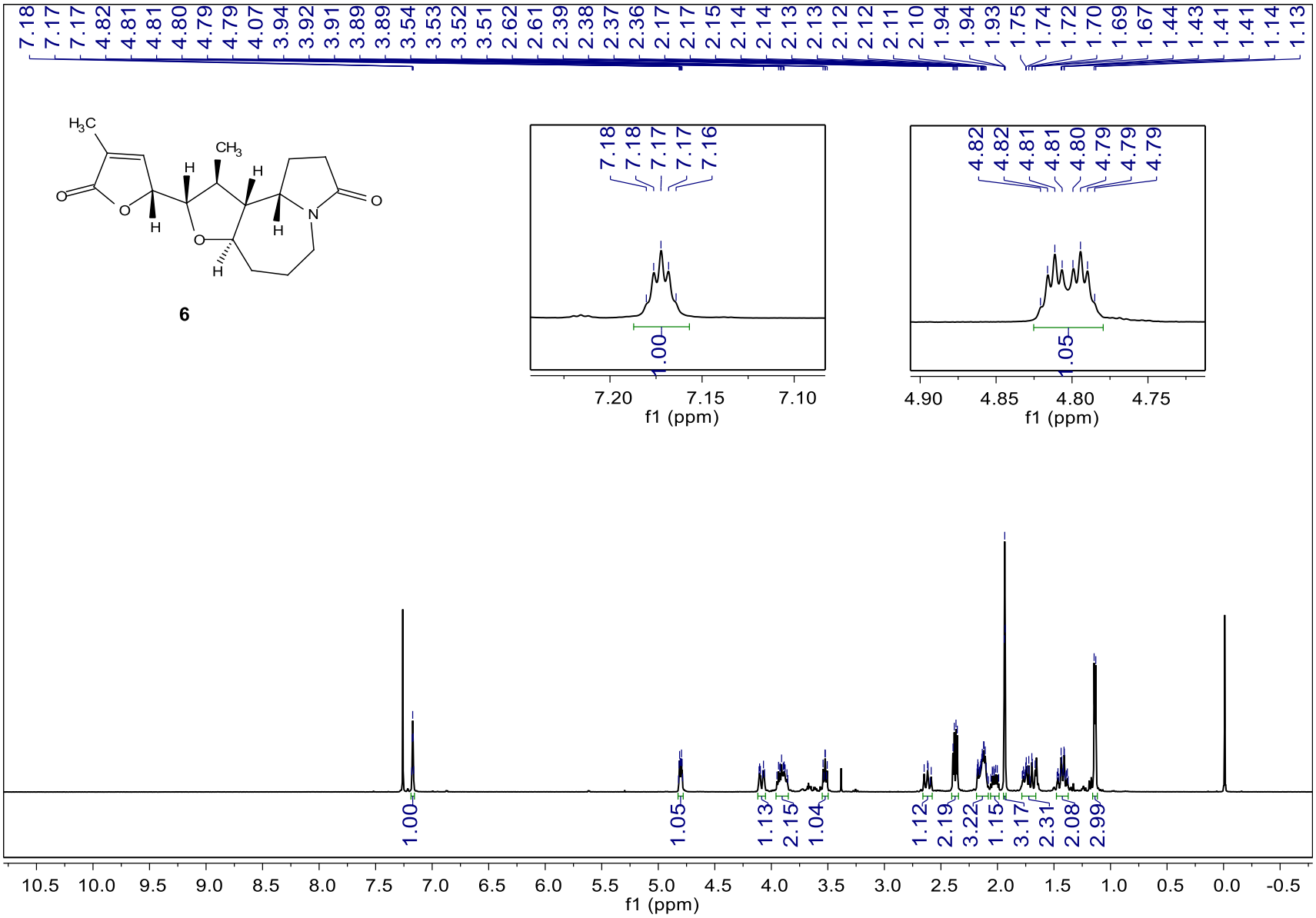
^{1}H NMR Spectrum of 5 (400 MHz, $CDCl_3$)



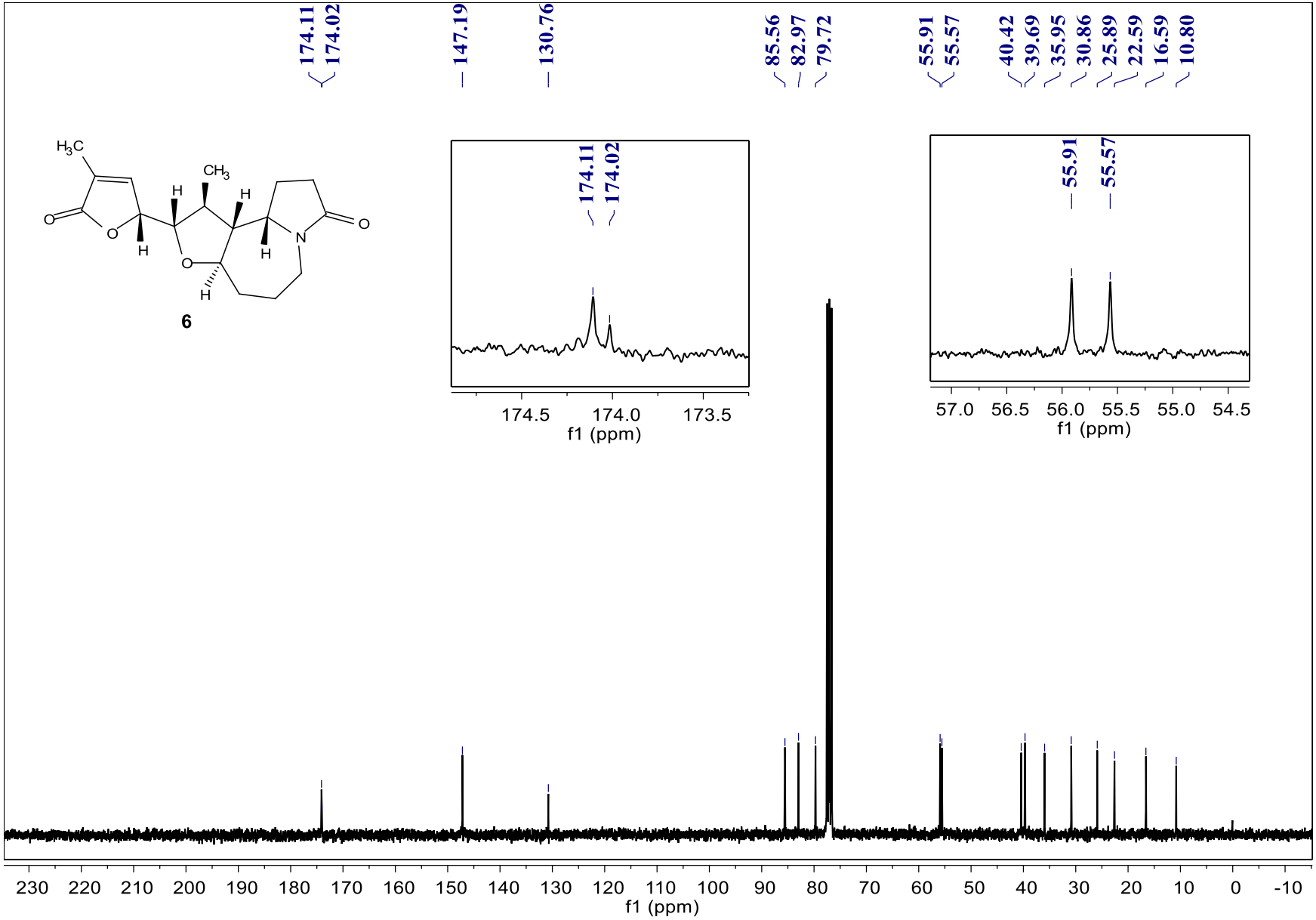
^{13}C NMR Spectrum of 5 (76 MHz, $CDCl_3$)



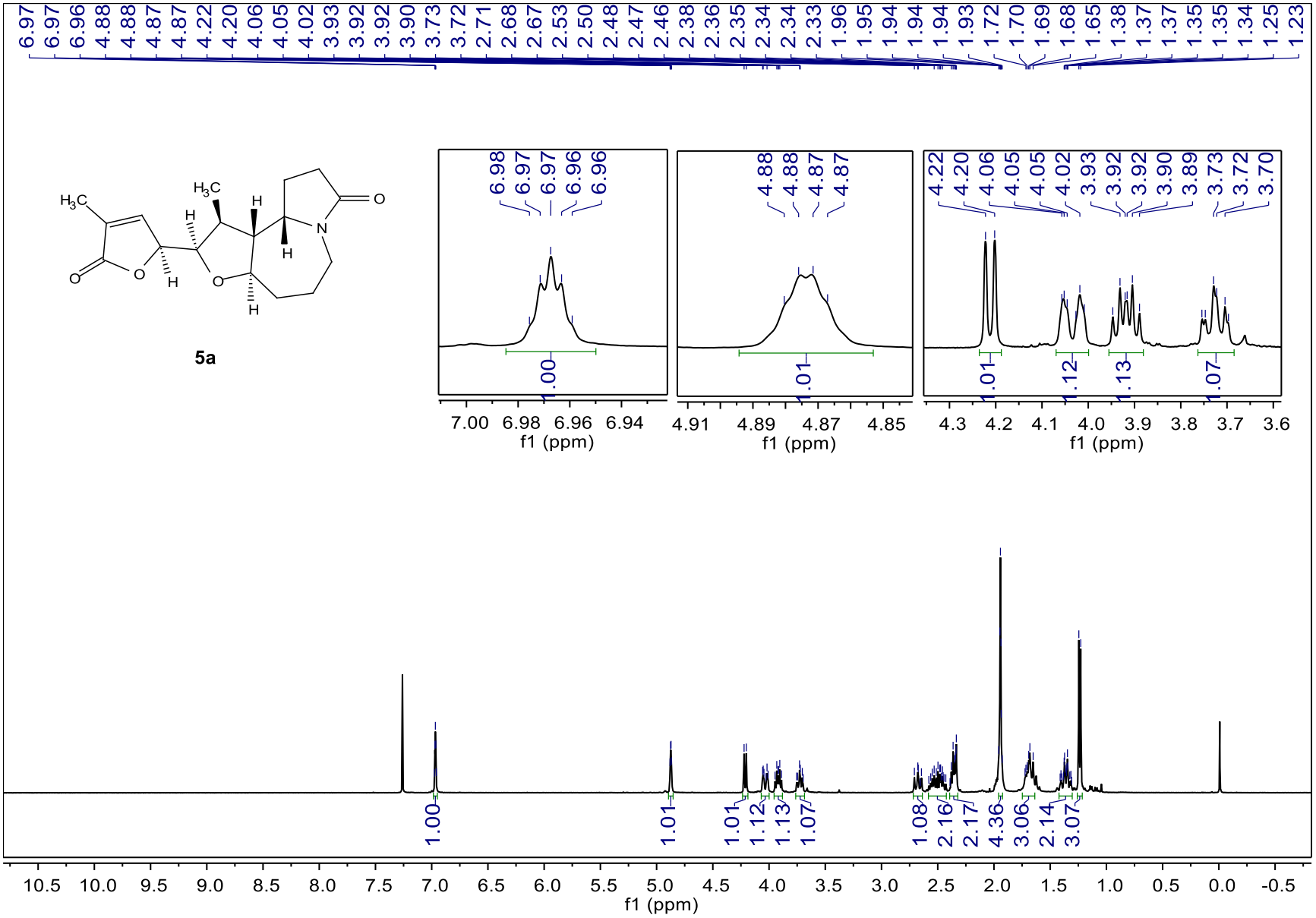
^{1}H NMR Spectrum of 6 (400 MHz, $CDCl_3$)



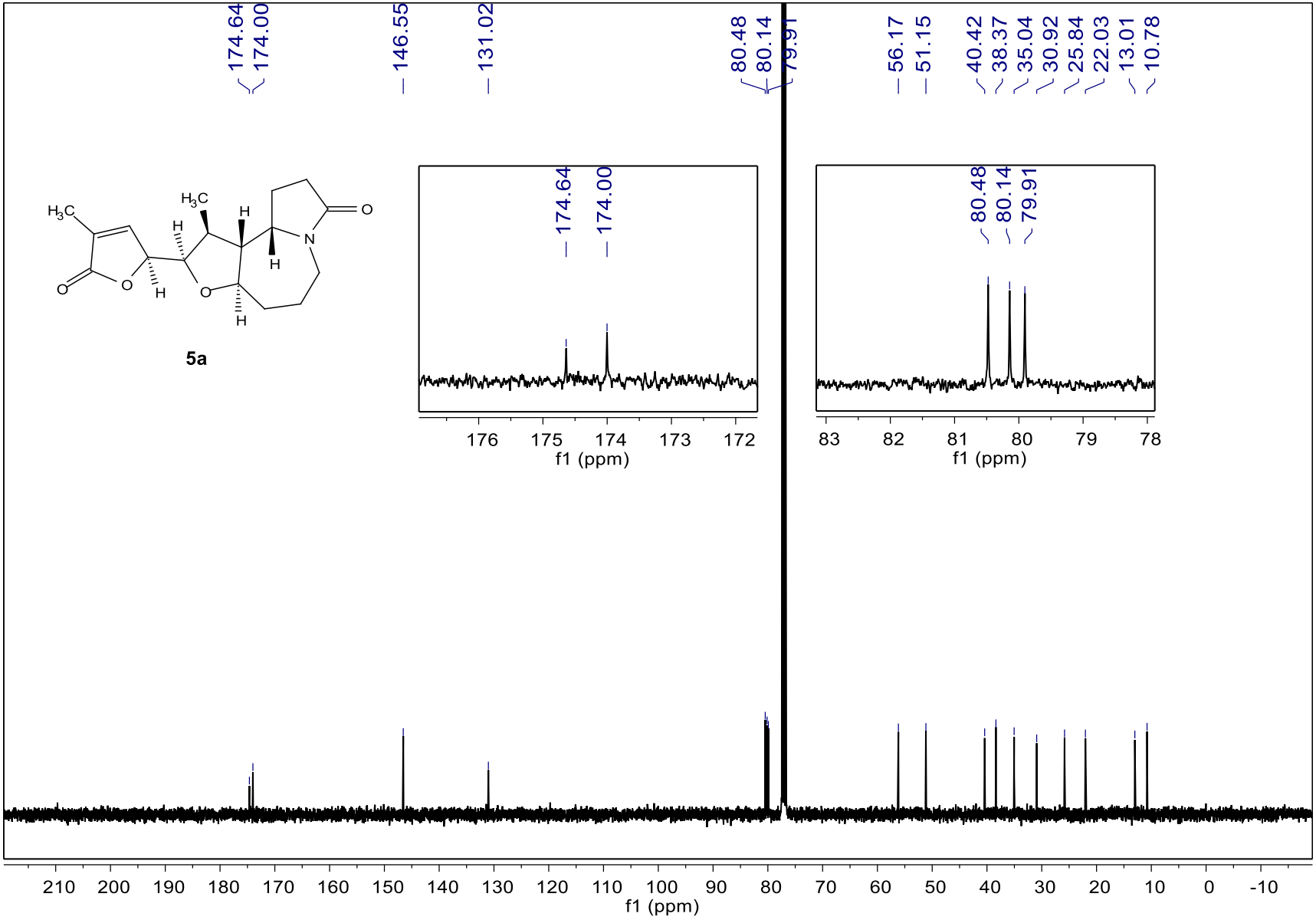
^{13}C NMR Spectrum of 6 (76 MHz, $CDCl_3$)



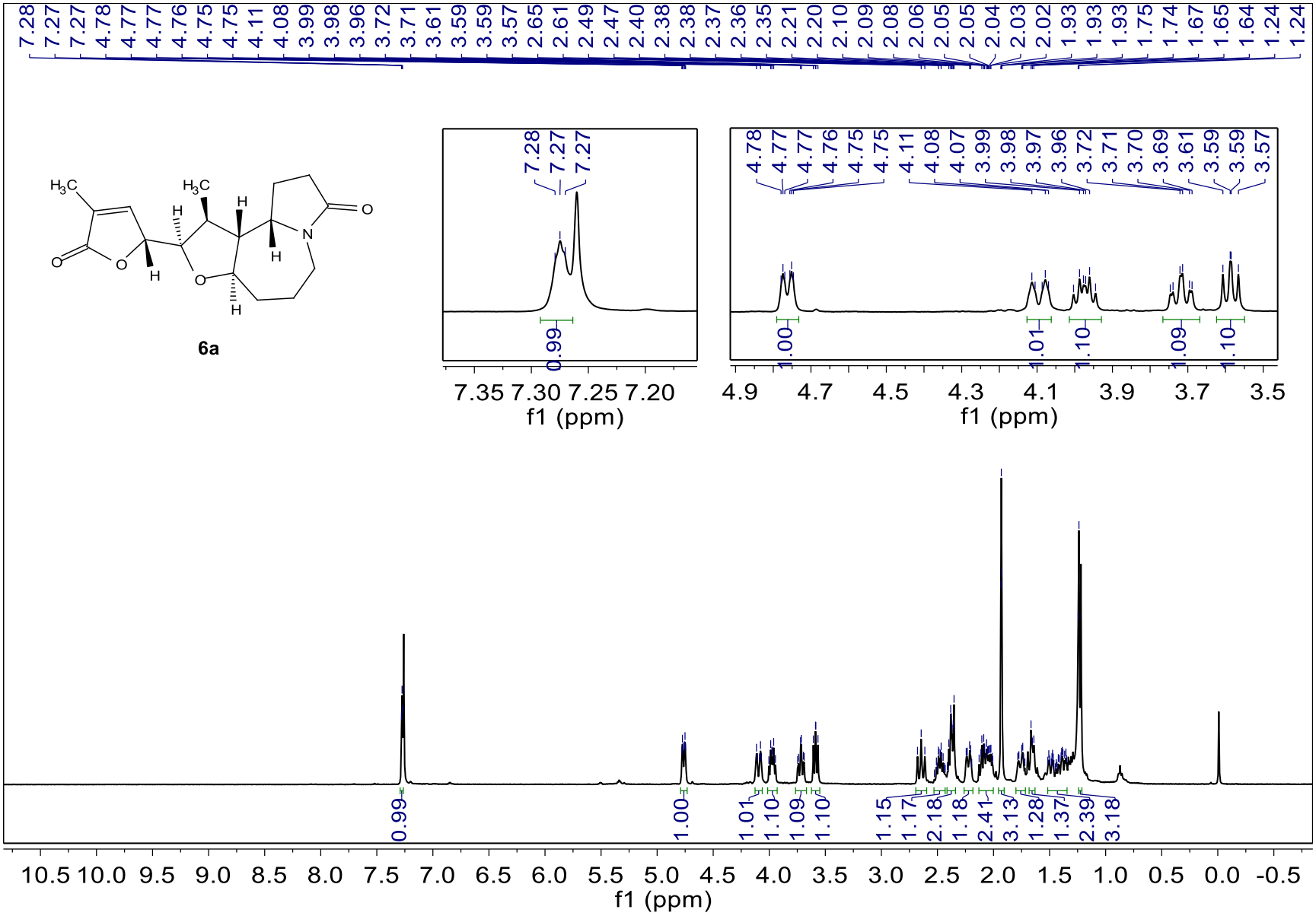
^{1}H NMR Spectrum of 5a (400 MHz, $CDCl_3$)



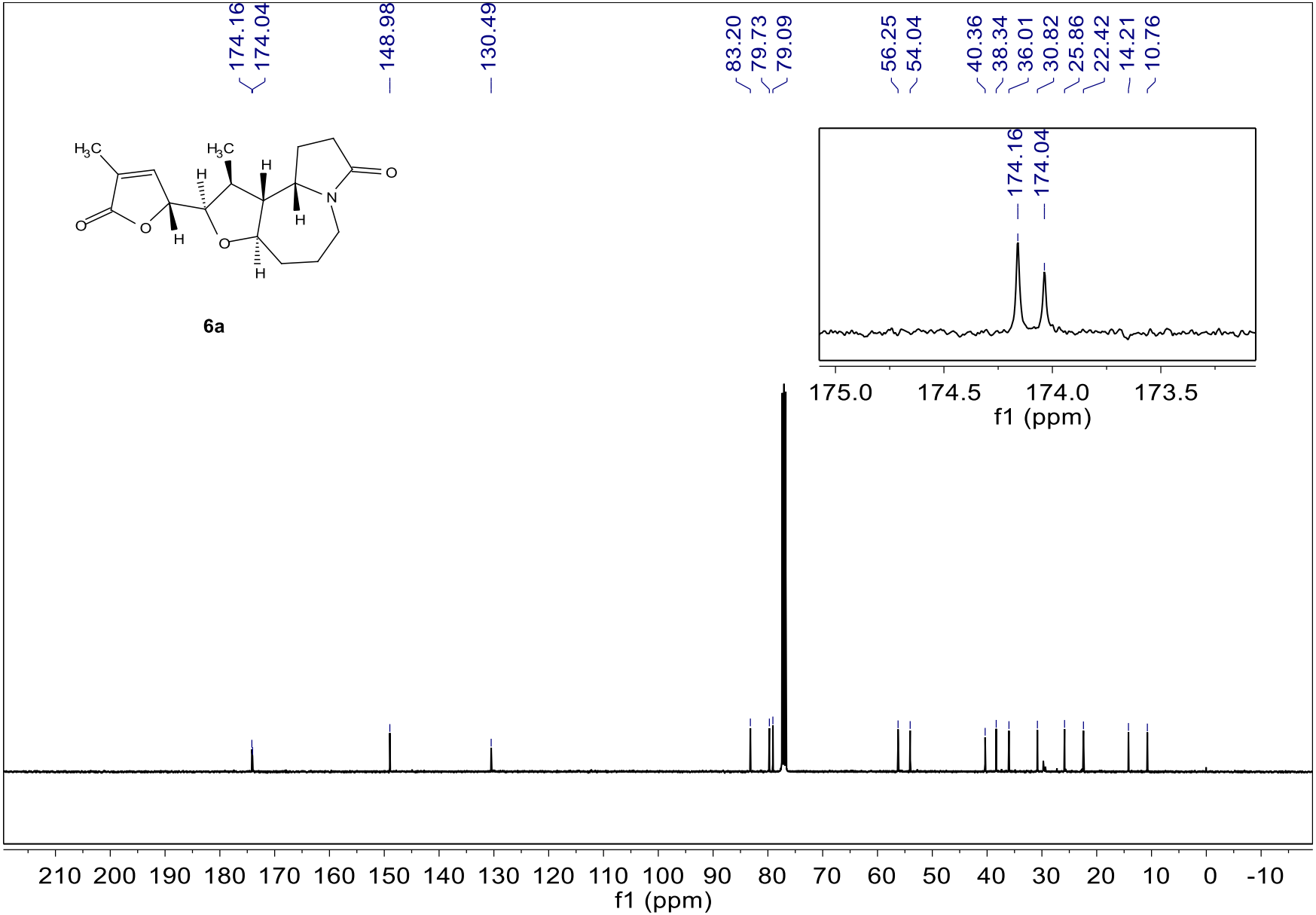
^{13}C NMR Spectrum of 5a (101 MHz, $CDCl_3$)



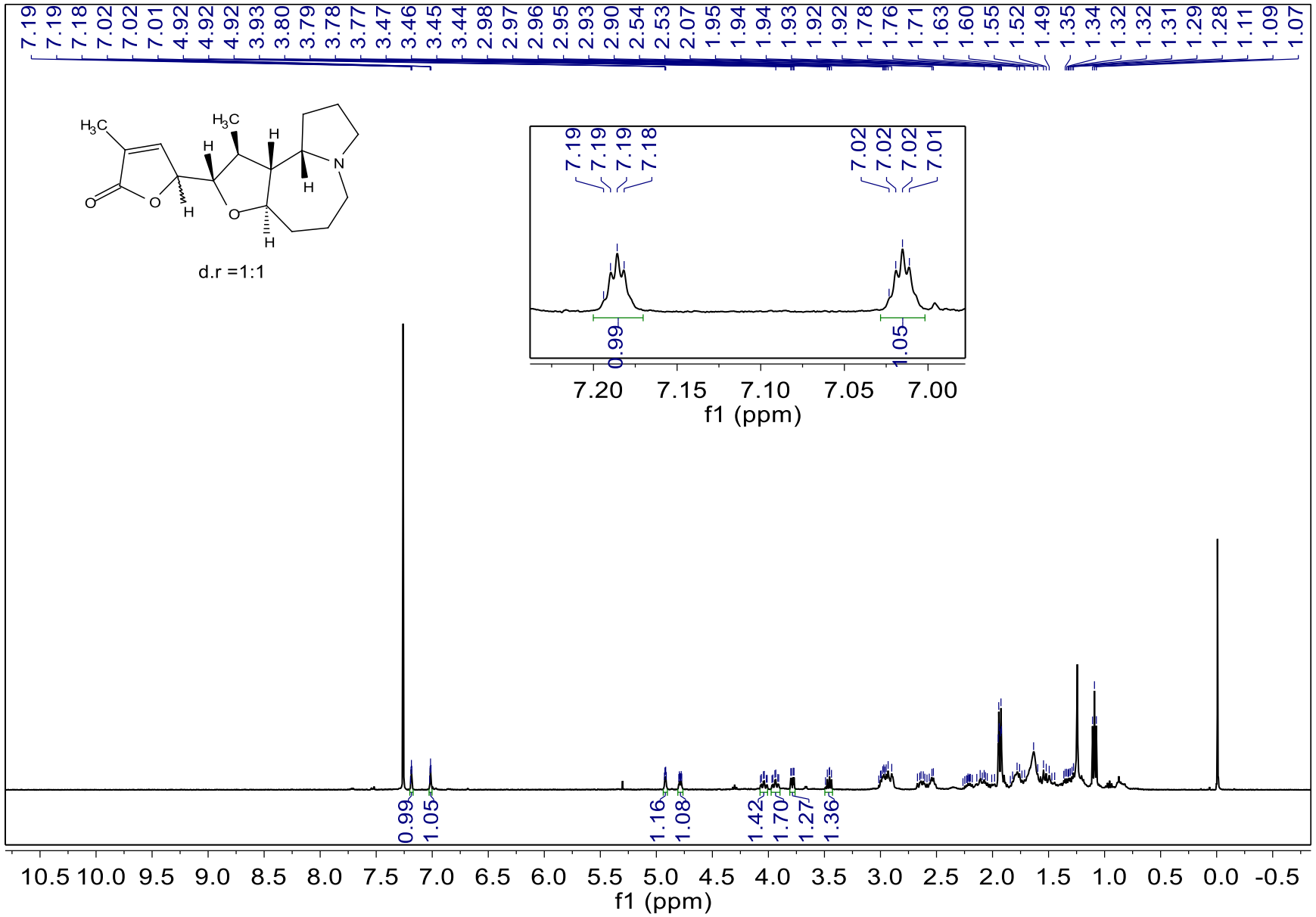
^{1}H NMR Spectrum of 6a (400 MHz, $CDCl_3$)



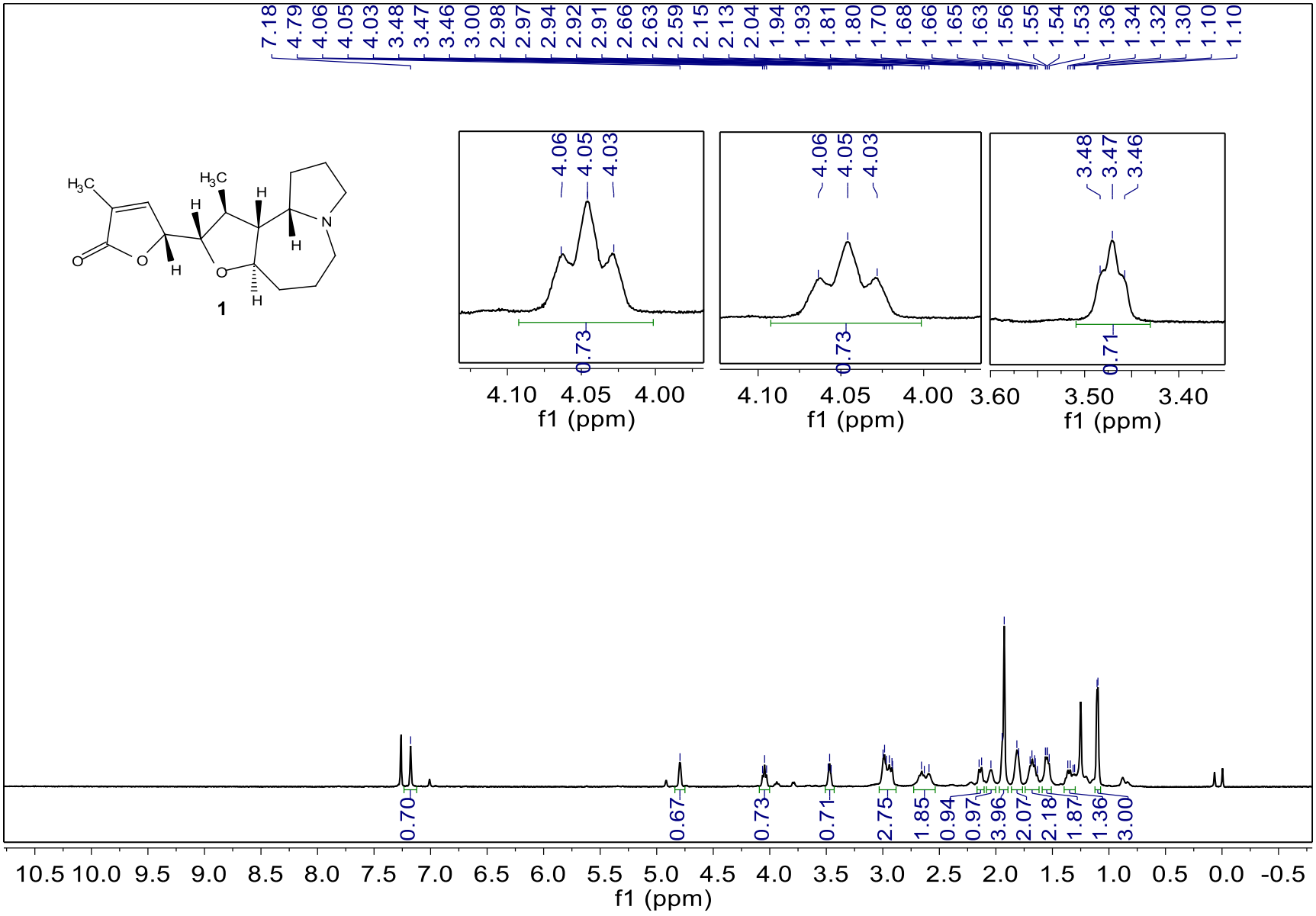
^{13}C NMR Spectrum of 6a (101 MHz, $CDCl_3$)



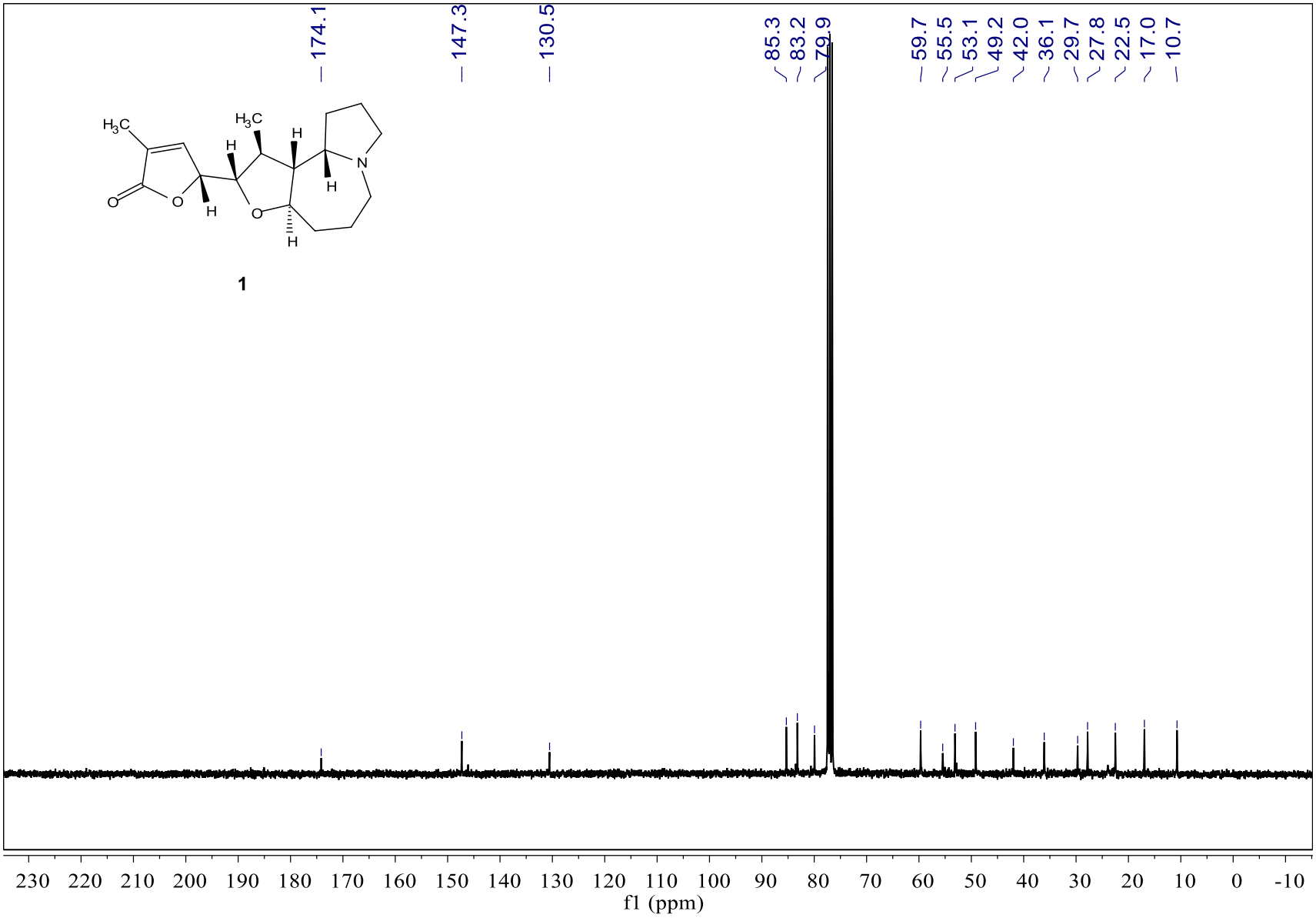
^{1}H NMR Spectrum of 1+2 (400 MHz, $CDCl_3$)



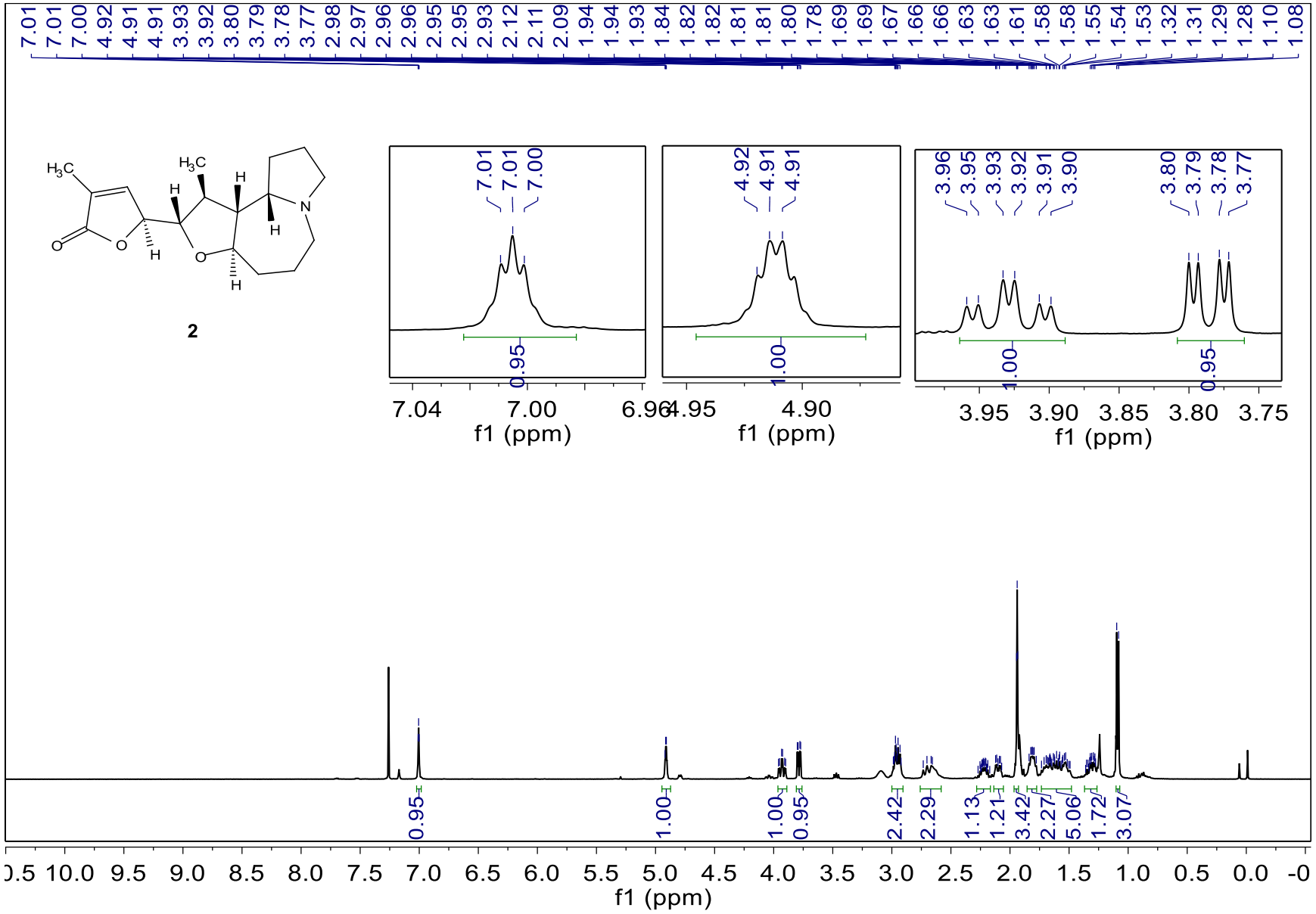
^{1}H NMR Spectrum of 1 (600 MHz, $CDCl_3$)



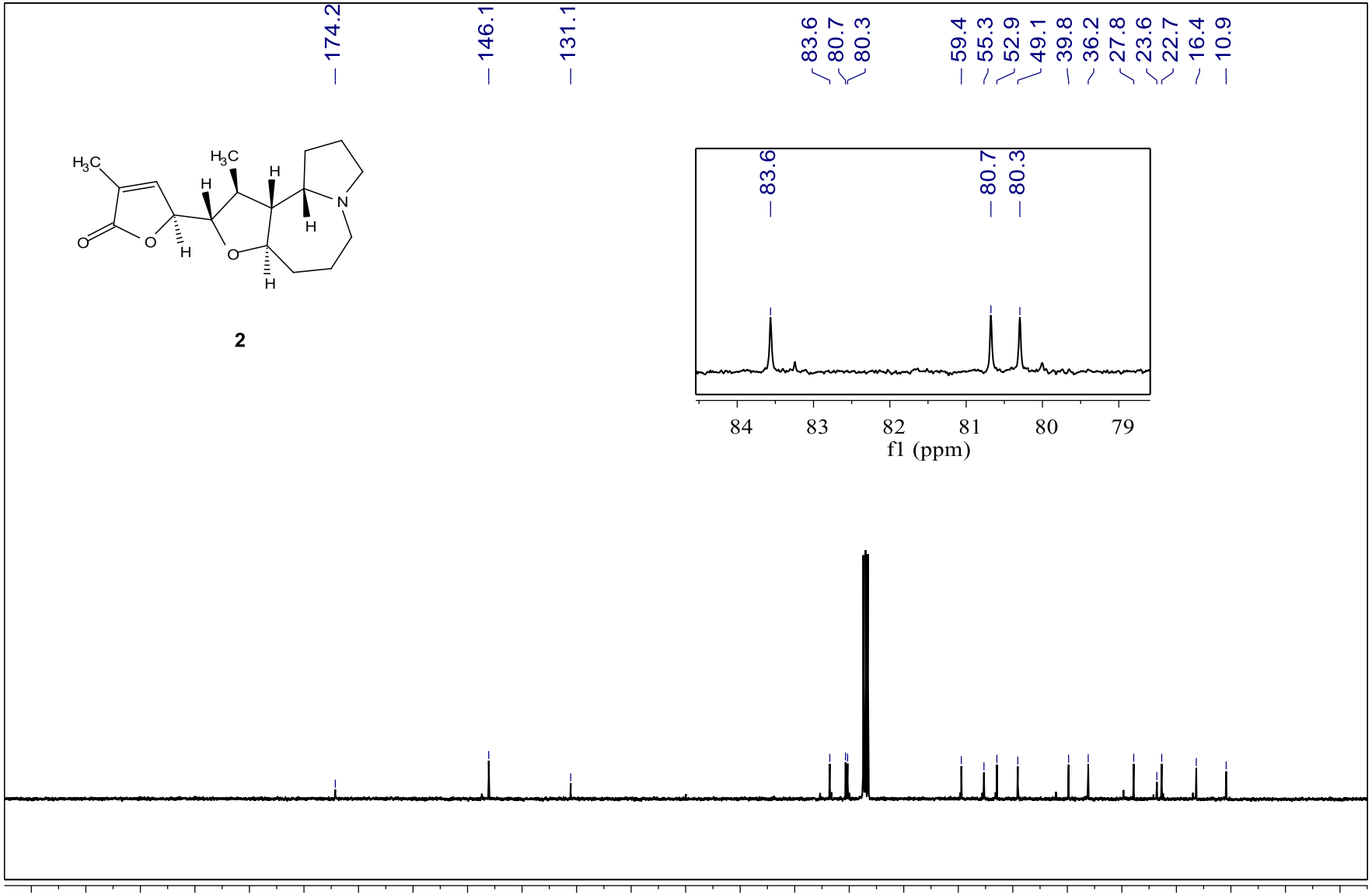
^{13}C NMR Spectrum of 1 (76 MHz, $CDCl_3$)



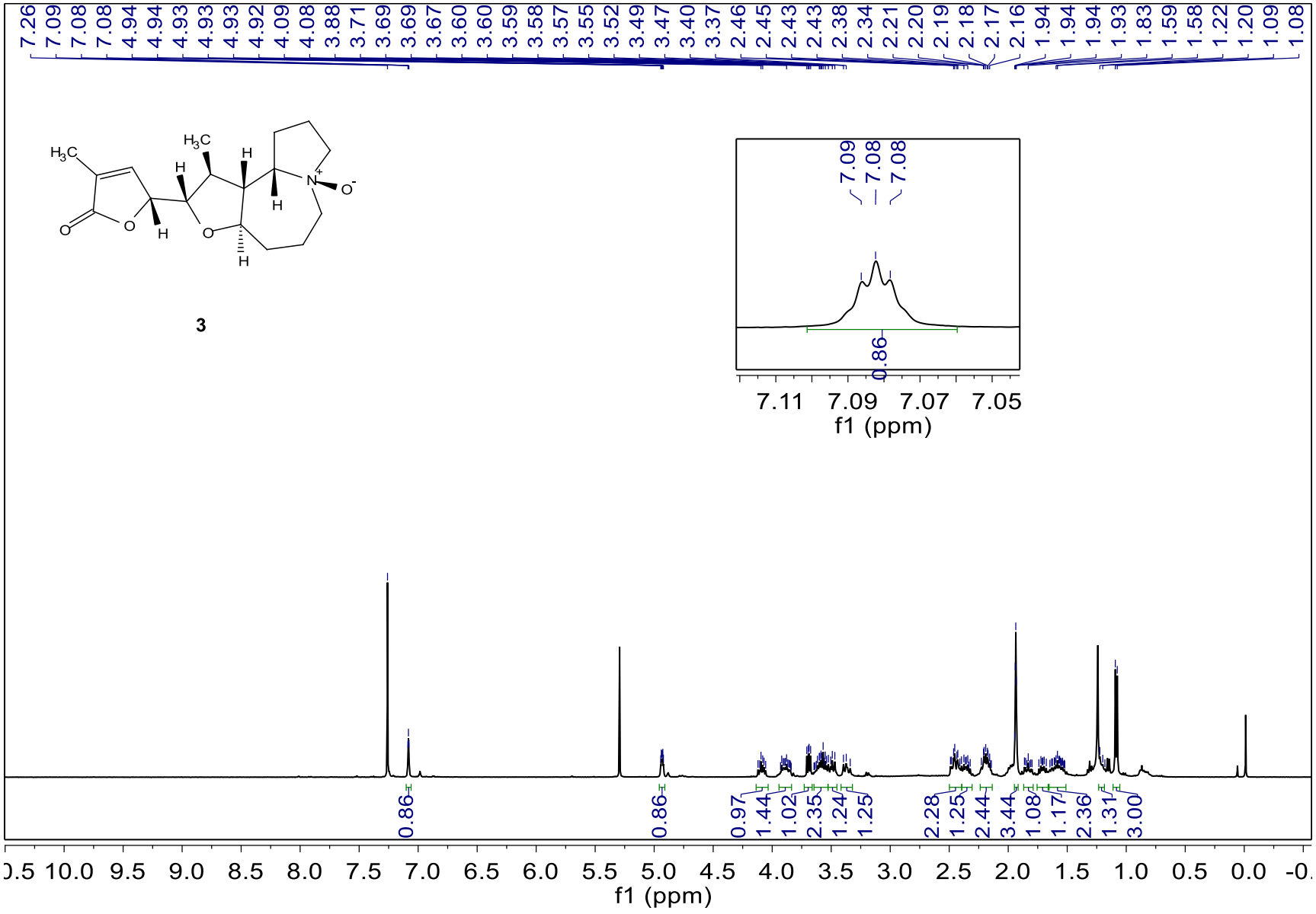
^{1}H NMR Spectrum of 2 (400 MHz, $CDCl_3$)



^{13}C NMR Spectrum of 2 (76 MHz, $CDCl_3$)

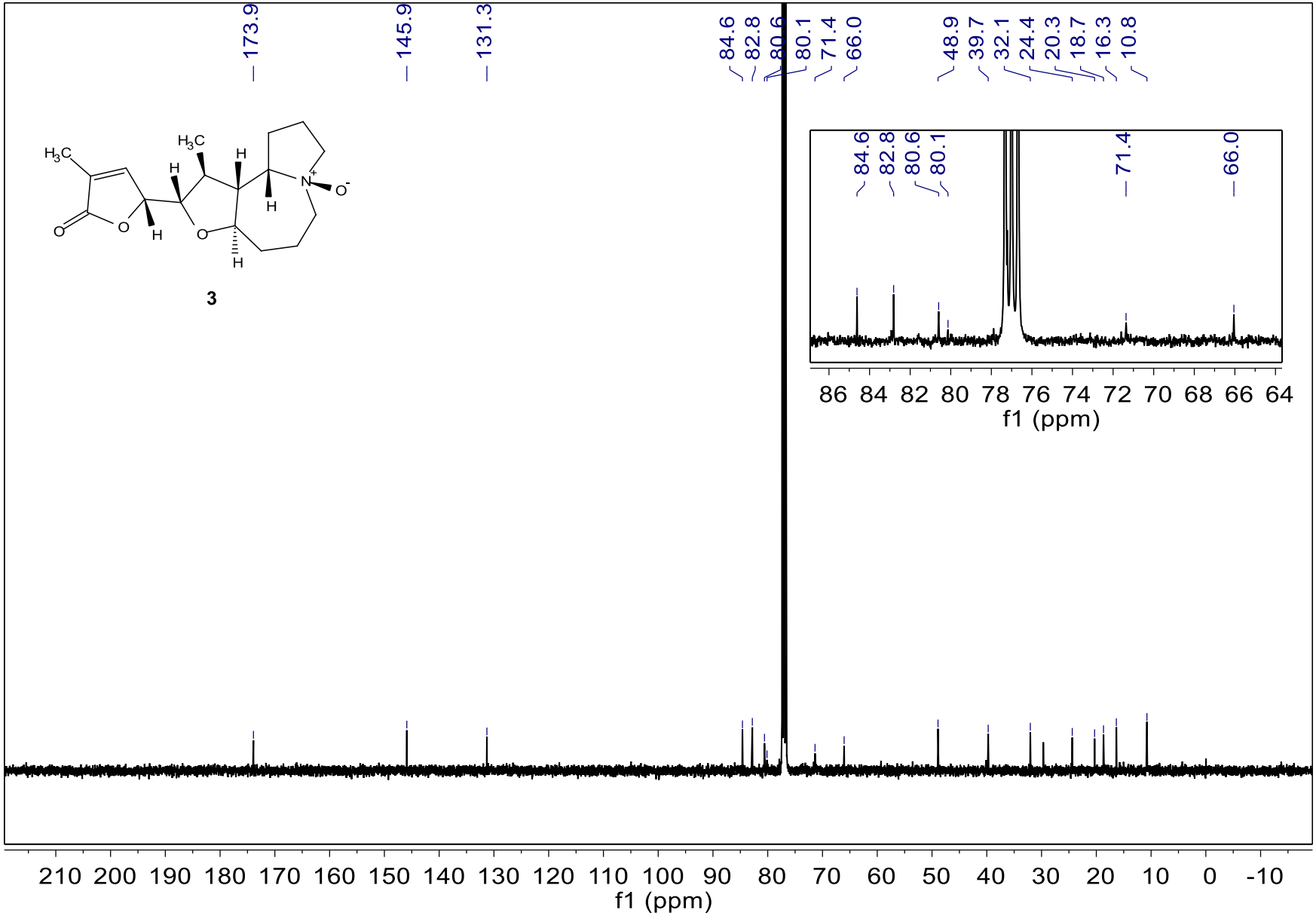


^{1}H NMR Spectrum of 3 (400 MHz, $CDCl_3$)

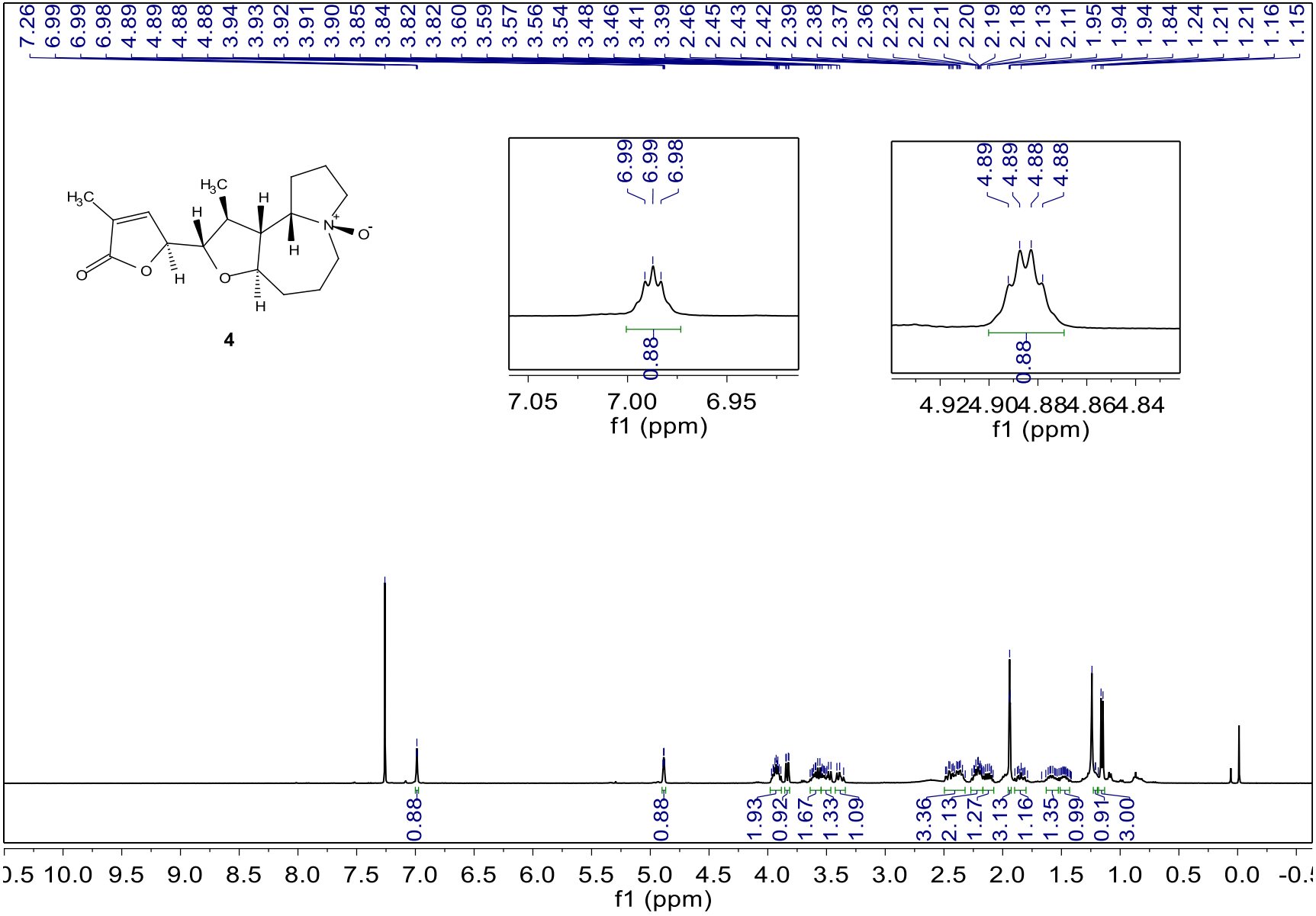


3

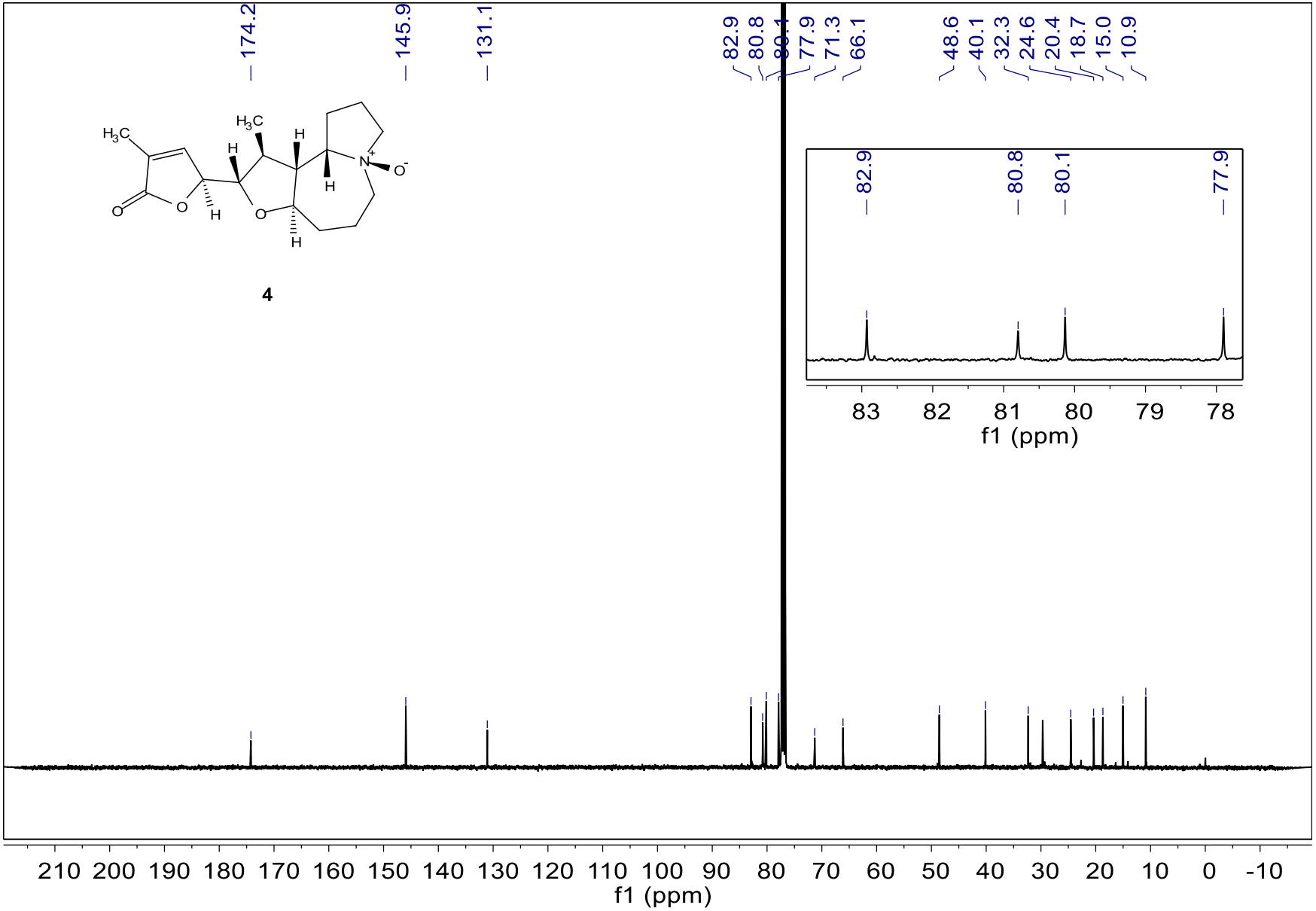
^{13}C NMR Spectrum of 3 (101 MHz, $CDCl_3$)



^{1}H NMR Spectrum of 4 (400 MHz, $CDCl_3$)



^{13}C NMR Spectrum of 4 (101 MHz, $CDCl_3$)



4