ChemistrySelect

Supporting Information

Targeting Neuroblastoma by Limonoids from the Underutilized Fruits of *Xylocarpus granatum*

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Supporting Information

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Experimental Section

General Experimental Procedures

IR spectra were recorded on a Nicolet-740 FT-IR spectrophotometer. The NMR spectra were recorded with Bruker Avance (400 and 500 MHz) for ^{1}H and ^{13}C NMR spectra (100 and125 MHz) in $CDCl_3$ with TMS as an internal standard. Coupling constants are given in Hz. ESI-MS experiment was performed on Waters Xevo G2-XS QTOF mass spectrometer. The specific rotations were measured on JASCO P-2000 polarimeter.

Plant Material

The fruits of *Xylocarpus granatum* were collected from the Nizampatnam (latitude: 15°53′ N, longitude: 80°38′ E) seacoast of Andhra Pradesh, India in March 2017 and were identified by Prof. B. Kondala Rao, Marine Living Resources, Andhra University, Visakhapatnam. A voucher specimen (#IIC-MG-121) has been deposited in the herbarium of Centre for Natural Products and Traditional Knowledge, CSIR-IICT, Hyderabad, India.

Extraction and Isolation

The air-dried fruits of *Xylocarpus granatum* (10 kg) were powdered and extracted with chloroform in a Soxhlet apparatus. The chloroform extract (450 g) was subjected to Si gel (230-400 mesh) vacuum liquid chromatography (VLC), eluted with gradient mixture of *n*-hexane: acetone (0:100) to yield 24 fractions. The first four fractions were pooled and chromatographed over a column of Si gel using gradient mixture of (*n*-Hexane:EtOAc 0:100) as eluent to yield 60 sub fractions. Sub fractions 9 to 26 on repeated Si gel column chromatography (CC) using dichloromethane-EtOAc (100:0 to 70:30) as eluent to yield photogedunin epimers(1 + 2, 7.6 mg), 3 (2.3 g), 4 (6 mg), 5 (12 mg) and 6 (14 mg). Subfractions 29 to 46 on repeated CC, eluted with gradient mixture of dichloromethane-EtOAc to afford compounds 7 (7 mg), 8 (5 mg), 9 (8 mg), 10 (22 mg), 11 (6 mg) and 12 (2 mg).

Acetylation

Photogedunin epimers (1+2, 2 mg) were dissolved in C_5H_5N (0.1 mL) and Ac_2O (0.1 mL) was added and the solution was left overnight at ambient temperature. After usual work-up, the product was purified by recrystallization from *n*-hexane to afford (1+2, 3.5 mg).

*Photogedunin epimers (1+2)***.** White solid, $[\alpha]^{20}_{D}$ +15 ($CHCl_3$; *c* 0.02); IR(KBr) υ_{max}: 3421, 1755, 1707, 1660, 1590 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 10.6 Hz, 1H), 7.11 (t, *J* = 8.4 Hz, 2H), 6.20 (dd, *J* = 50.0, 32.7 Hz, 2H), 5.89 (dd, *J* = 13.5, 10.2 Hz, 2H), 5.63 – 5.48 (m, 2H), 4.55 (d, *J* = 14.5 Hz, 2H), 3.53 (d, *J* = 7.6 Hz, 2H), 2.10 (s, 6H), 1.23 (s, 12H), 1.15 (d, *J* = 7.4 Hz, 7H), 1.07 (d, *J* = 3.3 Hz, 12H) and ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 203.1, 170.0, 169.1, 166.3, 156.5, 151.0, 150.1, 132.1, 125.2, 97.5, 96.9, 75.5, 75.2, 72.5, 69.0, 56.0, 45.3, 43.4, 42.0, 39.5, 38.7, 38.6, 26.5, 24.7, 22.6, 20.6, 20.5, 19.2, 17.7, 16.6, 16.5, 14.2.

Epimeric Photogedunin acetates (1a+2b). White solid, mp: 289-292 °C, IR(KBr) υ_{max}: 1750, 1710, 1660, 1590 cm-1; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (t, *J* = 7.7 Hz), 7.38 – 7.30 (m), 7.11 (d, *J* = 10.2 Hz), 6.91 (t, *J* = 1.6 Hz), 5.87 (d, *J* = 10.2 Hz), 5.57 (s), 5.30 (s), 4.54 (s), 3.52 (s), 2.45 (dd, *J* = 12.8, 5.9 Hz), 2.18 (s), 2.10 (s), 1.23 (d, *J* = 3.7 Hz), 1.17 (s), 1.07 (d, *J* = 1.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 204.4, 169.8, 168.5, 166.8, 157.2, 148.6, 148.1, 134.3, 125.6, 92.8, 92.0, 76.1, 76.0, 73.2, 69.4, 56.4, 45.8, 43.9, 42.5, 39.9, 39.3, 39.2, 26.8, 25.2, 23.0, 21.0, 20.44, 19.55, 18.1, 17.0, 17.2, 14.6.

Gedunin (3). Colorless crystals, ($CHCl_3$−MeOH); $[\alpha]^{20}_{D}$ -44 ($CHCl_3$); IR(KBr) υ_{max}: 1668,1709 cm^{-1}; mp: 194-198 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J* = 1.2 Hz, 2H), 7.11 (d, *J* = 10.2 Hz, 1H), 6.34 (s, 1H), 5.87 (d, *J* = 10.2 Hz, 1H), 5.62 (s, 1H), 4.57 – 4.54 (m, 1H), 3.53 (s, 1H), 2.49 (dd, *J* = 12.8, 6.1 Hz, 1H), 2.17 (dd, *J* = 13.3, 2.4 Hz, 1H), 2.11 (s, 3H), 1.64 – 1.55 (m, 1H), 1.25 (s, 3H), 1.23 (s, 3H), 1.16 (s, 3H), 1.07 (d, *J* = 3.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.9, 169.8, 167.4, 156.9, 143.0, 141.2, 126.0, 120.4, 109.8, 78.2, 73.2, 69.7, 56.8, 46.0, 44.0, 42.6, 40.0, 39.5, 38.7, 27.1, 25.9, 23.2, 21.2, 21.0, 19.7, 18.3, 17.7, 14.9; ESIMS *m/z* 505.2101 $[M+Na]^+$ for $C_{28}H_{34}O_7$.

Deacetyl gedunin (4). Colorless crystals, ($CHCl_3$−MeOH) ; $[\alpha]^{28}_{D}$ +60.7 (*c* 0.1, $CHCl_3$) mp: 246–247 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 7.40 (dd, *J* = 7.7, 6.0 Hz, 2H), 7.10 (d, *J* = 10.2 Hz, 1H), 6.36 (d, *J* = 1.0 Hz, 1H), 5.93 (d, *J* = 10.2 Hz, 1H), 5.47 (s, 1H), 3.88 (s, 1H), 2.92 (t, *J* = 14.4 Hz, 1H), 2.42 (dd, *J* = 13.9, 3.2 Hz, 1H), 2.29 – 2.09 (m, 2H), 2.00 (dd, *J* = 12.9, 9.6 Hz, 1H), 1.92 – 1.69 (m, 2H), 1.36 (s, 3H), 1.22 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 1.14 (s, 3H) and ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.1, 203.3, 166.8, 155.9, 143.1, 141.0, 126.4, 120.2, 109.8, 78.0, 77.2, 65.6, 54.6, 53.6, 53.4, 47.6, 45.2, 39.6, 37.7, 36.7, 32.2, 29.7, 27.0, 20.9, 20.6, 19.8, 17.4, 17.2; ESIMS *m/z* 463.2101 $[M+Na]^+$ for $C_{26}H_{32}O_6$.

7-deacetyl 7-oxogedunin (5). Yellow amorphous powder; $[\alpha]^{20}_{D}$ -30 (*c* 0.1, MeOH,); ^1H NMR (400 MHz, $CDCl_3$): δ 7.42 (dt, *J* = 1.5, 0.8 Hz, 1H), 7.40 (t, *J* = 1.7 Hz, 1H), 7.10 (d, *J* = 10.2 Hz, 1H), 6.36 (dd, *J* = 1.8, 0.8 Hz, 1H), 5.93 (d, *J* = 10.2 Hz, 1H), 5.47 (s, 1H), 3.88 (s, 1H), 3.72 (d, *J* = 3.8 Hz, 1H), 2.98 – 2.86 (m, 1H), 2.42 (d, *J* = 13.9 Hz, 1H), 2.20 (t, *J* = 12.4 Hz, 3H), 2.10 (d, *J* = 7.5 Hz, 1H), 1.36 (s, 3H), 1.22 (s, 3H), 1.16 (s, 3H), 1.14 (d, *J* = 2.5 Hz, 6H) and ^{13}C NMR (125 MHz, $CDCl_3$): δ 208.1, 203.2, 166.8, 155.9, 143.1, 141.0, 126.4, 120.2, 109.8, 78.0, 65.6, 54.6, 53.6, 53.4, 47.6, 45.2, 39.6, 37.7, 36.7, 32.2, 27.0, 20.9, 20.6, 19.8, 17.4, 17.2. ESIMS *m/z* 461.43 $[M+Na]^+$ for $C_{26}H_{30}O_6$.

Xyloccensin T (6). White amorphous powder; $[\alpha]^{20}_{D}$ +81.0 (c 0.05, MeOH); IR (KBr) υ_{max}: 3410, 2927, 1735, 1605, 1422, 1384, 1239 and 1037 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 6.1 Hz, 2H), 6.54 (s, 1H), 6.31 (s, 1H), 5.88 (s, 1H), 5.23 (s, 1H), 5.19 (d, *J* = 12.0 Hz, 1H), 4.82 (dd, *J* = 13.5, 4.1 Hz, 1H), 4.63 (d, *J* = 3.8 Hz, 1H), 3.82 (s, 3H), 3.52 (s, 1H), 3.14 (dd, *J* = 11.9, 3.8 Hz, 1H), 1.69 (s, 3H), 1.60 (s, 3H), 1.58 (s, 3H), 1.53 (s, 3H), 1.49 (s, 3H), 0.91 (s, 3H) and ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 170.8, 163.6, 154.1, 143.3, 141.9, 123.2, 121.3, 119.9, 110.4, 87.4, 82.2, 82.0, 79.0, 78.8, 74.8, 71.2, 69.2, 53.2, 48.8, 46.1, 45.9, 44.9, 44.1, 43.1, 32.5, 29.9, 22.0, 20.1, 17.2, 16.8, 15.7, 14.6; ESIMS *m/z* 723.1212 $[M+Na]^+$ for $C_{35}H_{41}O_{15}$.

6-deoxy destigloylswietenine acetate (7). Colourless powder, $[\alpha]^{20}_{D}$ -150(*c* 0.34, Me_2CO); mp: 260-265 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.42 (t, *J* = 1.6 Hz, 1H), 6.47 (d, *J* = 1.2 Hz, 1H), 5.71 (s, 1H), 5.36 (dd, *J* = 5.2, 1.8 Hz, 1H), 4.75 (d, *J* = 9.4 Hz, 1H), 3.72 (s, 3H), 3.50 (dd, *J* = 8.8, 7.5 Hz, 1H), 3.36 (dd, *J* = 7.6, 4.2 Hz, 1H), 2.96 – 2.79 (m, 2H), 2.40 – 2.35 (m, 2H), 2.24 (s, 2H), 2.09 (s, 3H), 1.15 (s, 3H), 1.09 (s, 3H), 0.82 (s, 3H), 0.79 (s, 3H) and ^{13}C NMR (100 MHz, $CDCl_3$): δ 217.0, 174.1, 170.9, 169.6, 142.9, 141.9, 138.4, 122.9, 120.7, 109.7, 77.5, 56.4, 52.2, 49.9, 48.4, 45.1, 41.5, 38.1, 36.7, 34.3, 32.9, 30.0, 29.7, 22.5, 22.0, 20.4, 20.3, 15.8; ESIMS *m/z* 535.2380 $[M+Na]^+$ for $C_{29}H_{36}O_{8.}$

Odoratone (8). Colorless needles, ($CHCl_3$−MeOH); $[\alpha]^{20}D$ -70.3 (c 0.5; CH_2Cl_2); IR (KBr) υ_{max} 3520, 3360, 2870, 1718, 1678,1430, 1360, 1220, 1160, 780 $cm^{-}1$; m.p: 201-203 $^{\circ}C$; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.31 (dd, *J* = 6.4, 3.3 Hz, 1H), 3.98 (q, *J* = 6.1 Hz, 1H), 3.82 (dd, *J* = 6.4, 1.3 Hz, 1H), 3.66 (t, *J* = 6.1 Hz, 1H), 2.76 (td, *J* = 14.5, 5.5 Hz, 1H), 2.43 (d, *J* = 6.3 Hz, 1H), 2.36 – 2.20 (m, 3H), 2.09 (dd, *J* = 8.2, 4.7 Hz, 2H), 2.05 – 1.96 (m, 2H), 1.86 (dd, *J* = 19.5, 8.6 Hz, 2H), 1.72 (dd, *J* = 9.5, 8.0 Hz, 1H), 1.22 (s, 6H), 1.12 (s, 3H), 1.05 (s, 6H), 1.01 (s, 3H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.83 (s, 3H) and ^{13}C NMR (100 MHz, $CDCl_3$): δ 217.3, 145.9, 146.0, 117.8, 83.7, 80.9, 72.9, 52.4, 51.2, 49.3, 48.5, 47.9, 43.5, 38.5, 37.5, 35.0, 35.0, 34.1, 33.5, 27.8, 27.7, 24.5, 24.4, 21.8, 21.6, 21.3, 18.3, 12.8, 12.4; ESIMS *m/z* 495.3212 $[M+Na]^+$ for $C_{30}H_{48}O_{4.}$

Moluccensin V (9). Colorless crystals, ($CHCl_3$−MeOH); $[\alpha]^{25}D$ -51(*c* 0.34, Me_2CO); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.41 (m, 2H), 6.35 (s, 1H), 5.42 (s, 1H), 5.38 – 5.31 (m, 1H), 4.97 (d, *J* = 9.2 Hz, 1H), 4.38 (d, *J* = 11.9 Hz, 1H), 3.93 (d, *J* = 11.8 Hz, 1H), 3.65 – 3.55 (m, 1H), 3.11 (dd, *J* = 11.7, 7.5 Hz, 1H), 2.87 (ddd, *J* = 19.4, 18.4, 3.5 Hz, 2H), 2.64 (qd, *J* = 18.3, 9.6 Hz, 2H), 2.11 (s, 3H), 1.16 (s, 3H), 1.03 (s, 6H) and ^{13}C NMR (125 MHz, $CDCl_3$): δ 214.6, 170.2, 169.7, 169.1, 143.5, 140.4, 139.0, 122.1, 120.7, 109.2, 77.5, 75.5, 74.4, 55.8, 48.8, 47.7, 45.0, 38.7, 36.6, 35.69, 33.9, 31.6, 29.9, 21.8, 21.3, 20.3, 16.8, 15.9. ESIMS *m/z* 519.1962 $[M+Na]^+$ for $C_{28}H_{32}O_8$.

6-Desoxyswietenine (10). Colorless solid, mp: 106-109 ^{o}C; IR (KBr) υ_{max}: 1735-1710, 1500, 880 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.42 (t, *J* = 1.7 Hz, 1H), 6.93 (dq, *J* = 7.0, 1.3 Hz, 1H), 6.50 – 6.45 (m, 1H), 5.63 (s, 1H), 5.34 (dt, *J* = 7.0, 1.8 Hz, 1H), 4.84 (d, *J* = 9.3 Hz, 1H), 3.73 (s, 3H), 3.56 – 3.44 (m, 2H), 2.82 (d, *J* = 6.2 Hz, 2H), 2.37 (s, 2H), 1.83 (s, 3H), 1.74 (d, *J* = 7.1 Hz, 3H), 1.15 (s, 3H), 1.08 (s, 3H), 0.84 (s, 3H), 0.81 (s, 3H) and ^{13}C NMR (100 MHz, CDCl3) *δ*: 217.3, 174.1,

168.9, 167.1, 143.0, 141.9, 139.6, 138.5, 127.5, 123.1, 120.8, 109.7, 77.1, 76.6, 56.8, 52.2, 49.8, 48.8, 45.2, 41.3, 38.6, 37.0, 34.5, 32.9, 30.0, 22.7, 21.7, 20.7, 20.2, 15.8, 14.1, 11.8. ESIMS *m/z* 575.10 $[M+Na]^+$ for $C_{32}H_{40}O_{8.}$

Granatumin L (11). Colorless crystals ($CHCl_3$−MeOH), $[\alpha]^{25}D$ -56 (*c* 0.19, acetone);m.p: 248-250 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.42 (t, *J* = 1.7 Hz, 1H), 6.96 (qd, *J* = 6.9, 1.3 Hz, 1H), 6.46 (d, *J* = 1.1 Hz, 1H), 5.46 (s, 1H), 5.33 – 5.26 (m, 1H), 4.87 (d, *J* = 10.0 Hz, 1H), 3.95 (d, *J* = 9.6 Hz, 1H), 3.71 (s, 3H), 3.52 (dd, *J* = 9.6, 1.7 Hz, 1H), 2.96 (s, 2H), 2.82 (d, *J* = 4.0 Hz, 2H), 1.81 (s, 3H), 1.65 (d, *J* = 7.1 Hz, 4H), 1.08 (s, 6H), 0.66 (s, 3H) and ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 169.3, 143.0, 141.6, 139.3, 138.5, 127.6, 120.8, 120.0, 109.7, 96.9, 76.3, 75.1, 67.9, 52.1, 48.1, 45.5, 45.0, 41.6, 37.0, 36.4, 34.9, 34.5, 31.9, 29.7, 21.6, 19.6, 15.0, 14.7, 14.4, 11.7. ESIMS *m/z* 591.2380 $[M+Na]^+$ for $C_{32}H_{40}O_9$.

Azadiraindin G (12). White amorphous powder; $[\alpha]^{24}D$ +65.4(c 0.09,$CHCl_3$); IR (KBr) υ_{max}: 3441, 2936, 1748, 1731, 1665, 1646, 1246 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.23 (t, *J* = 1.3 Hz, 1H), 7.10 (d, *J* = 10.2 Hz, 1H), 5.87 (d, *J* = 10.2 Hz, 1H), 5.79 (t, *J* = 1.4 Hz, 1H), 5.57 (t, *J* = 1.3 Hz, 1H), 4.57 – 4.50 (m, 1H), 3.63 (s, 3H), 3.51 (s, 1H), 2.44 (dd, *J* = 12.8, 6.0 Hz, 1H), 2.17 (d, *J* = 13.3 Hz, 1H), 1.92 (s, 1H), 1.91 – 1.74 (m, 2H), 1.56 – 1.32 (m, 2H), 1.23 (d, *J* = 2.5 Hz, 6H), 1.16 (s, 3H), 1.07 (d, *J* = 3.6 Hz, 6H) and ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.0, 169.8, 166.8, 156.8, 148.4, 134.3, 126.0, 102.6, 75.9, 73.2, 69.5, 57.9, 56.7, 46.0, 44.0, 42.6, 40.0, 39.4, 27.1, 25.4, 23.2, 21.2, 21.1, 19.7, 18.3, 17.2, 14.8; ESI-MS: *m/z* 551.2263 [M+Na] for $C_{29}H_{36}O_{9.}$

Biological activity

Cell Culture

The mammalian cancer cell lines MIAPaCa-2 (pancreatic), HeLa (cervical), IMR-32 (neuroblastoma), and MCF-7 (breast carcinoma) of human origin were procured from the American Type Culture Collection (ATCC, Manassas, VA, USA). The cells were grown in Dulbecco's modified Eagle's medium (DMEM; Gibco BRL) with 10% FBS (Invitrogen) supplementation and 1% Penstrep (Invitrogen). After attaining 70–80% confluency, regular passaging was carried out. Initially, trypsinization using 1 × trypsin and 0.05% EDTA was performed, followed by resuspension of the cells in DMEM complete medium. The cells were cultured and maintained at 37 °C in 95% air atmosphere and 5% $CO_{2.}$

Cell viability by SRB Assay

The antiproliferative effect of compounds (**1**+**2**, **3**-**12**) was determined by SRB assay against MIAPaCa-2 (pancreatic), HeLa (cervical), IMR-32 (Neuroblastoma) and MCF-7 (breast cancer) cancer cell lines. All the compounds were dissolved in DMSO (Sigma Chemical Co., St. Louis, Missouri, USA). In brief, 96 well plates were seeded with selected cell lines, and test samples were added. After incubation for 24 h and 48 h, anchorage-dependant cells were fixed with 5% trichloroacetic acid (TCA) and stained with SRB for 30 min. The protein-bound dye was dissolved in 10 mM Tris base solution, and absorbance was measured at 510 nm using a multimode microplate reader (Multimode Varioskan Flash, Thermo Fisher Scientific, MA, USA). Experimental data were derived from three independent experiments.

Hoechst 33342 staining

Before the treatment, IMR-32 cells were seeded into the 12-well plates at 1×10^5 cells / well for 24h. After treating cells with the compound for 24 h, cells were stained with Hoechst 33342 (1 µg / mL) (Invitrogen, Karlsruhe, Germany), then incubated for 30 min at 37 °C in the dark. Cells were washed with PBS, and a fluorescence microscope was used to observe the fluorescent Hoechst-stained nuclei (Olympus, Tokyo, Japan).

Cell cycle analysis using flow cytometry

IMR-32 cells were seeded at approximately 1 $X10^6$ to culture plates, cultured for 24, and 48 h at two different concentrations (25 and 50 µM) of C-23 photogedunin epimers and standard. After the treatment, the cells were washed with PBS, harvested and centrifuged at 3000 rpm, 4 °C for 5-10 min and the supernatant was removed. 70% ethanol was added slowly to fix cells at 4 °C and kept overnight. Later, ethanol was removed by centrifugation and cells were washed twice with PBS. Then, Propidium iodide solution (1X propidium iodide (PI), 5µl/mL of RNase A, and 50µL/mL of Triton X-100) was added and cells were incubated at 37 °C for 1h for cell cycle analysis by using a flow cytometer (Amnis Flow sight Flow Cytometer, USA).

Dihydroethidium staining

Dihydroethidium is a permeable cell dye that responds to the formation of ethidium with O_2^-, which in turn intercalates with the DNA, producing fluorescence with an emission wavelength of 610 nm and excitation wavelength of 520 nm. IMR-32 cells were seeded in a 6-well plate. When cells were 70% confluent, they were treated with the photogedunin epimers. The cells were then incubated for 48h at 37°C. After 48h, cells were stained with dihydroethidium, and images were obtained using a fluorescence microscope (Olympus, Tokyo, Japan).

Western blotting analysis

Following compound treatment, cells were washed in ice-cold PBS and lysed in Laemmli sample buffer. The samples were then separated by SDS-PAGE and transferred to a PVDF membrane (Merck Millipore, Massachusetts, USA). The membrane was blocked with 5% skimmed milk in TBST for 1 h at room temperature (TBS with Tween 20 (0.05% (v/v) TBST), followed by incubation with the primary antibody overnight at 4 °C. (PARP (#9542), CST, Massachusetts, USA). The blots were incubated overnight with the primary antibodies (diluted 1:1000 as per manufacturer's instructions) at 4 °C followed by TBST wash. After washing, the membrane was incubated with HRP-conjugated secondary antibodies (Santa Cruz Biotechnology, Texas, USA) for 1 h at room temperature. The blots were then detected by G-BOX, (Syngene, USA). The protein expression was normalized relative to β-actin expression.

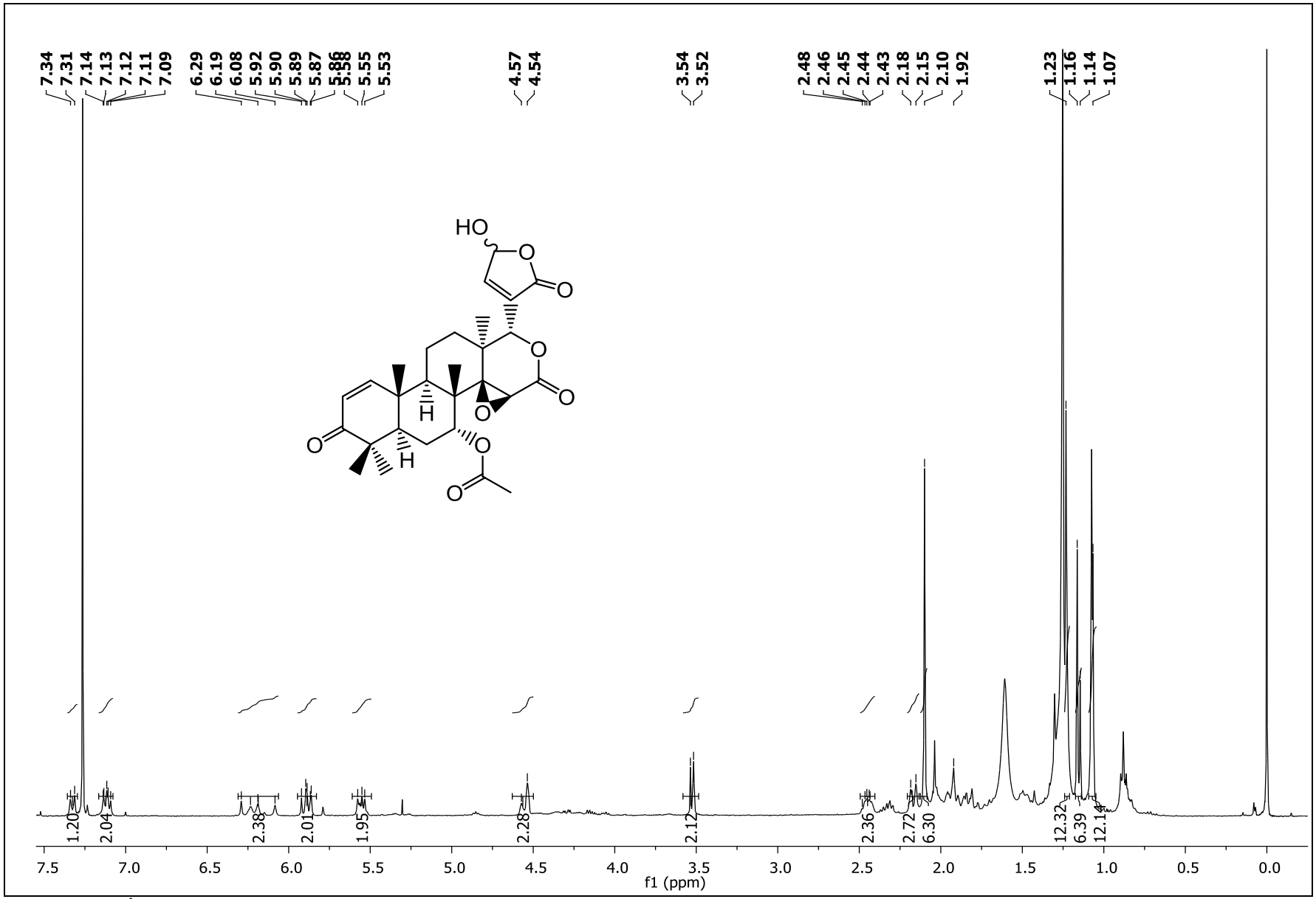


Figure S2: ^{1}H NMR Spectrum of photogedunin epimers (1+2) ($CDCl_3$, 400 MHz)

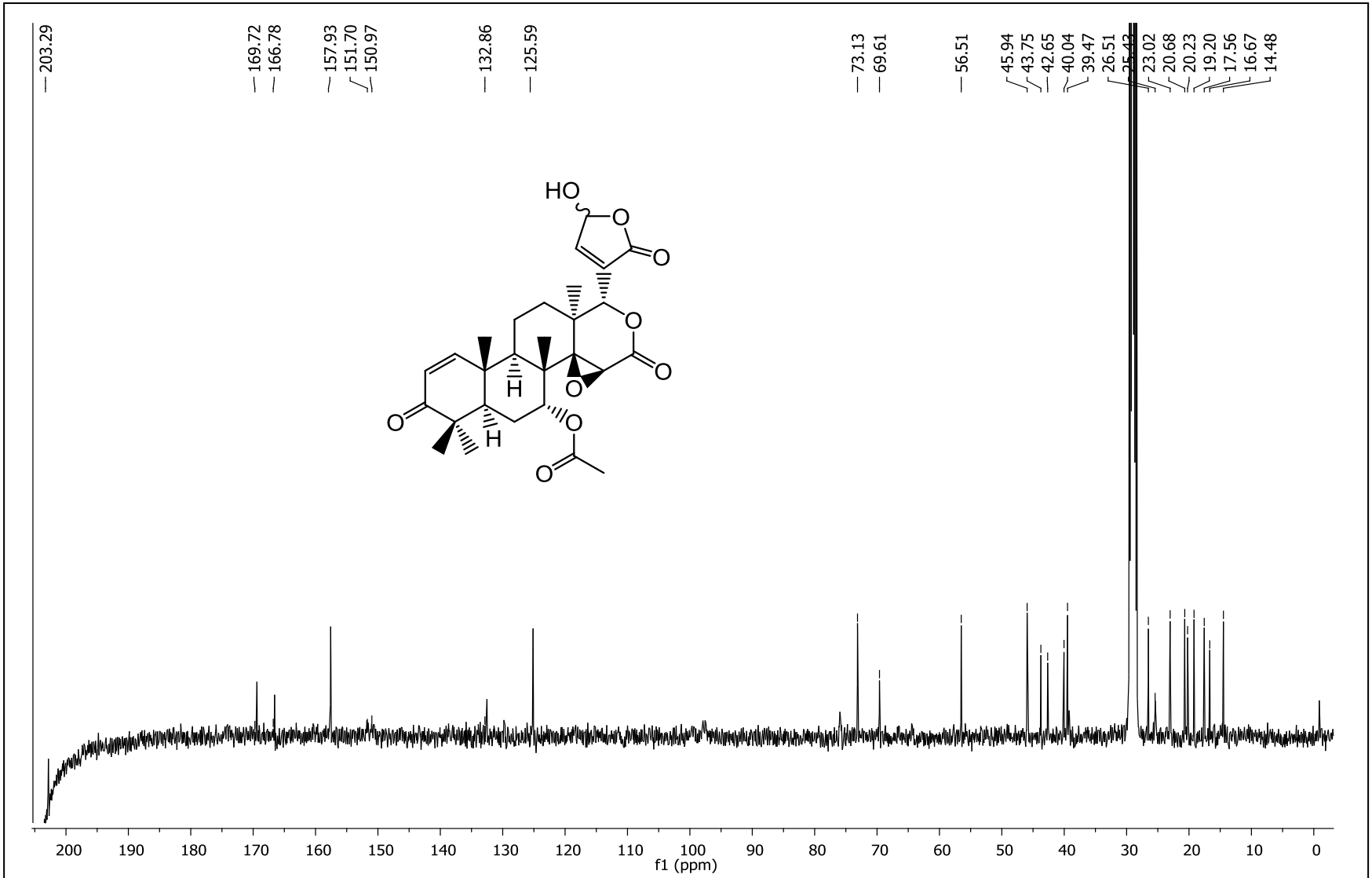


Figure S3: ^{13}C NMR Spectrum of photogedunin epimers (1+2) (Acetone-D_6, 100 MHz)

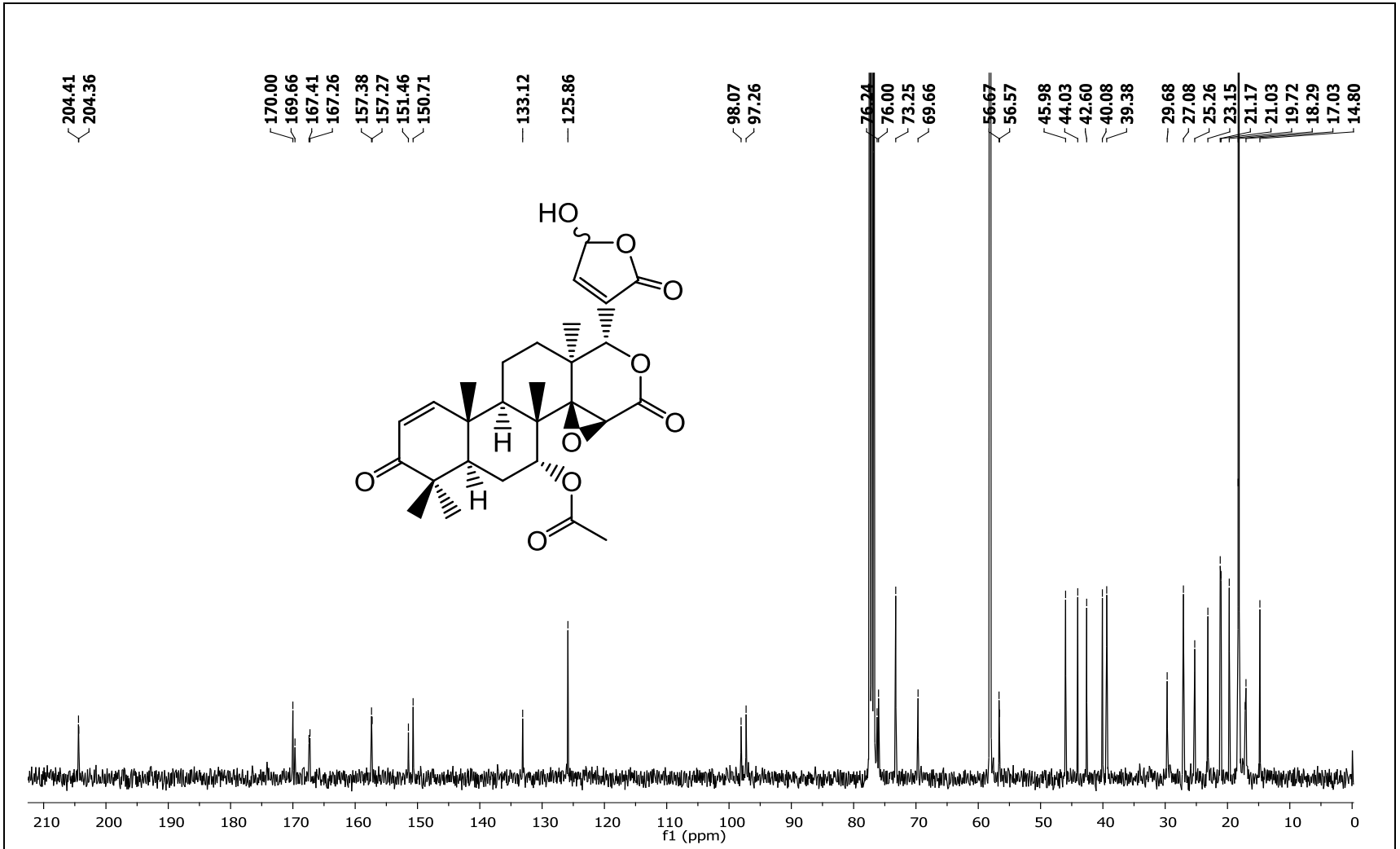


Figure S4: ^{13}C NMR Spectrum of photogedunin epimers (1+2) ($CDCl_3$+CD_3OD, 100 MHz)

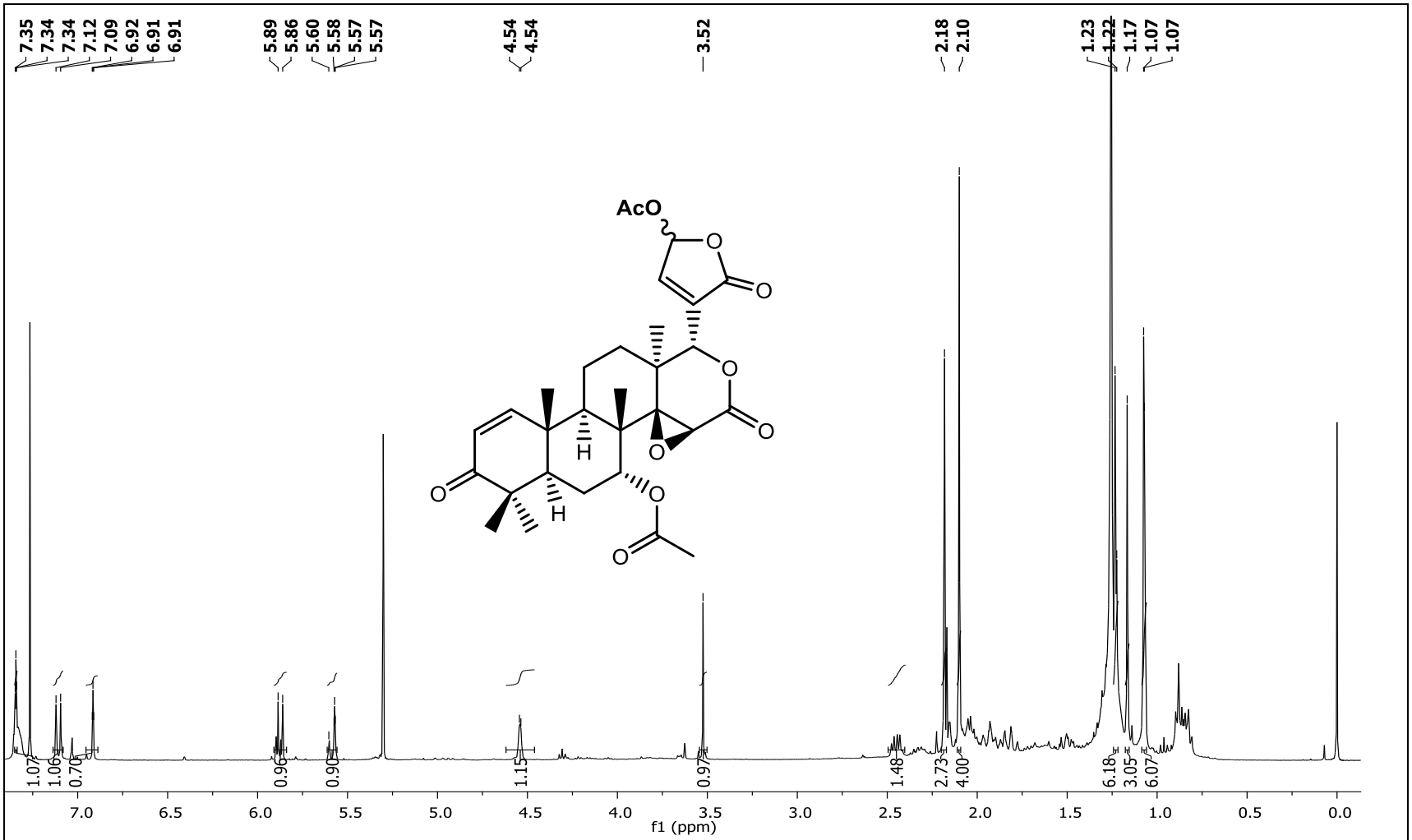


Figure S5: ^{1}H NMR Spectrum of an acetyl photogedunin epimers (1a+2b) ($CDCl_3$, 400 MHz)

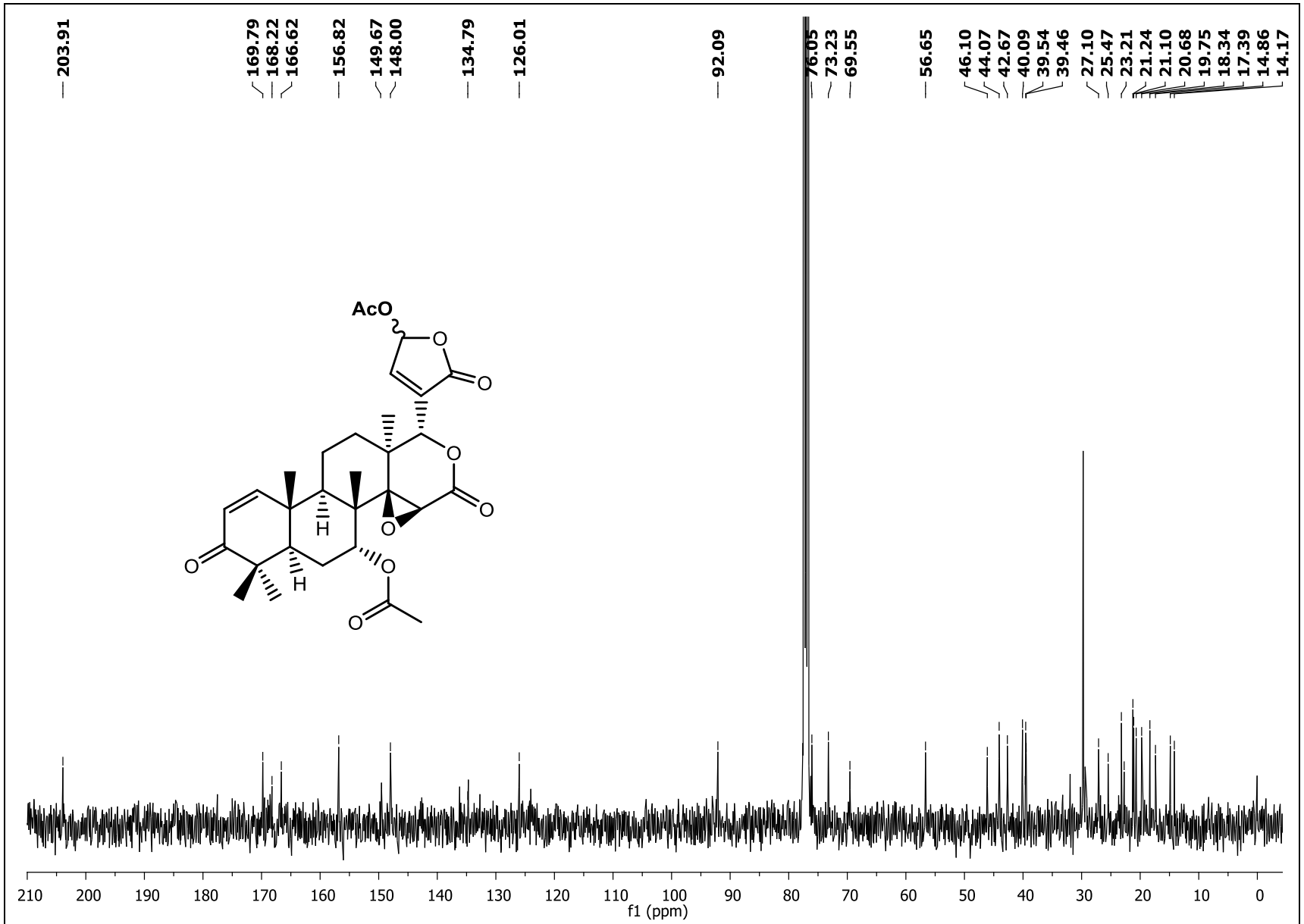


Figure S6: ^{13}C NMR Spectrum of an acetyl photogedunin epimers (1a+2b) ($CDCl_3$, 100 MHz)

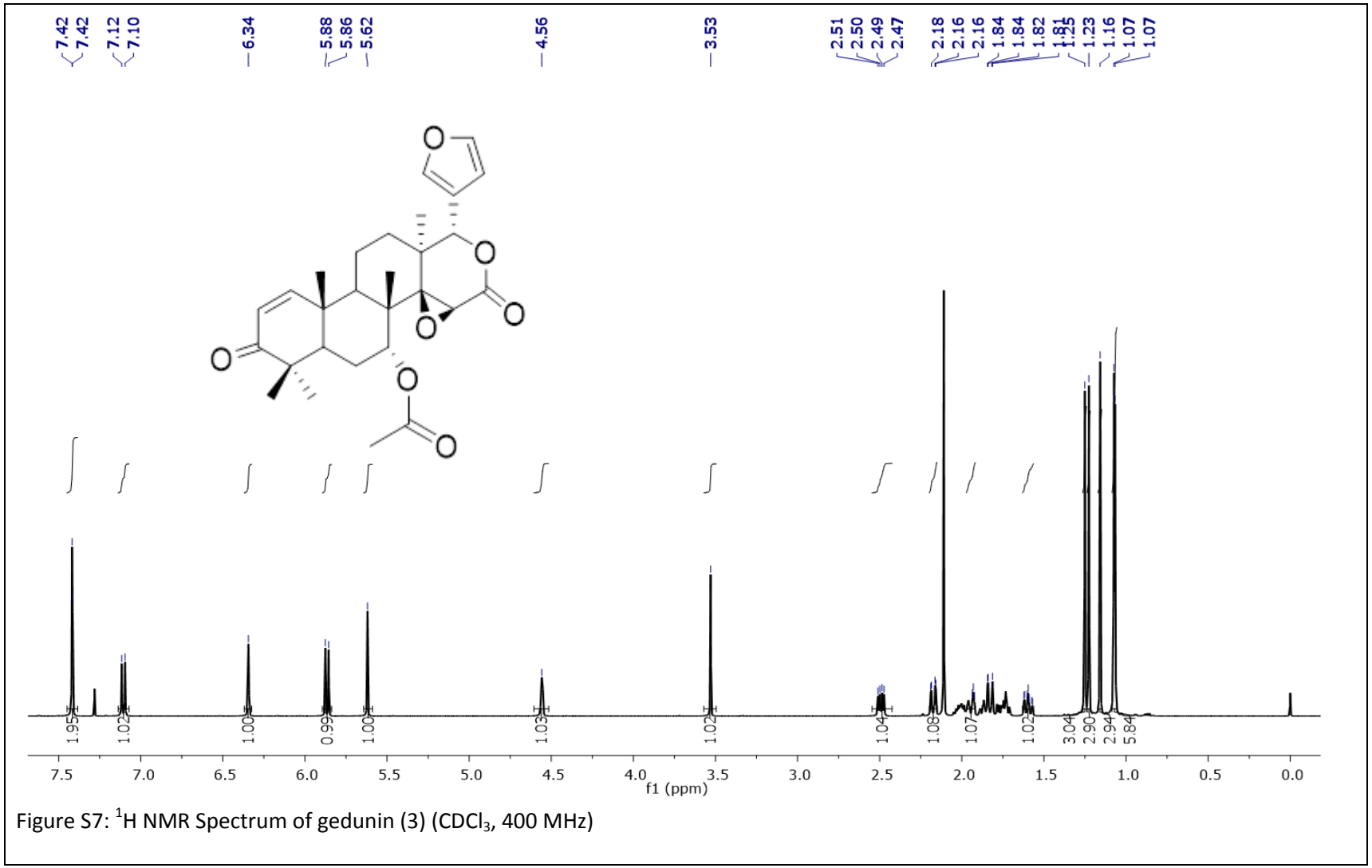


Figure S7: ^{1}H NMR Spectrum of gedunin (3) ($CDCl_3$, 400 MHz)

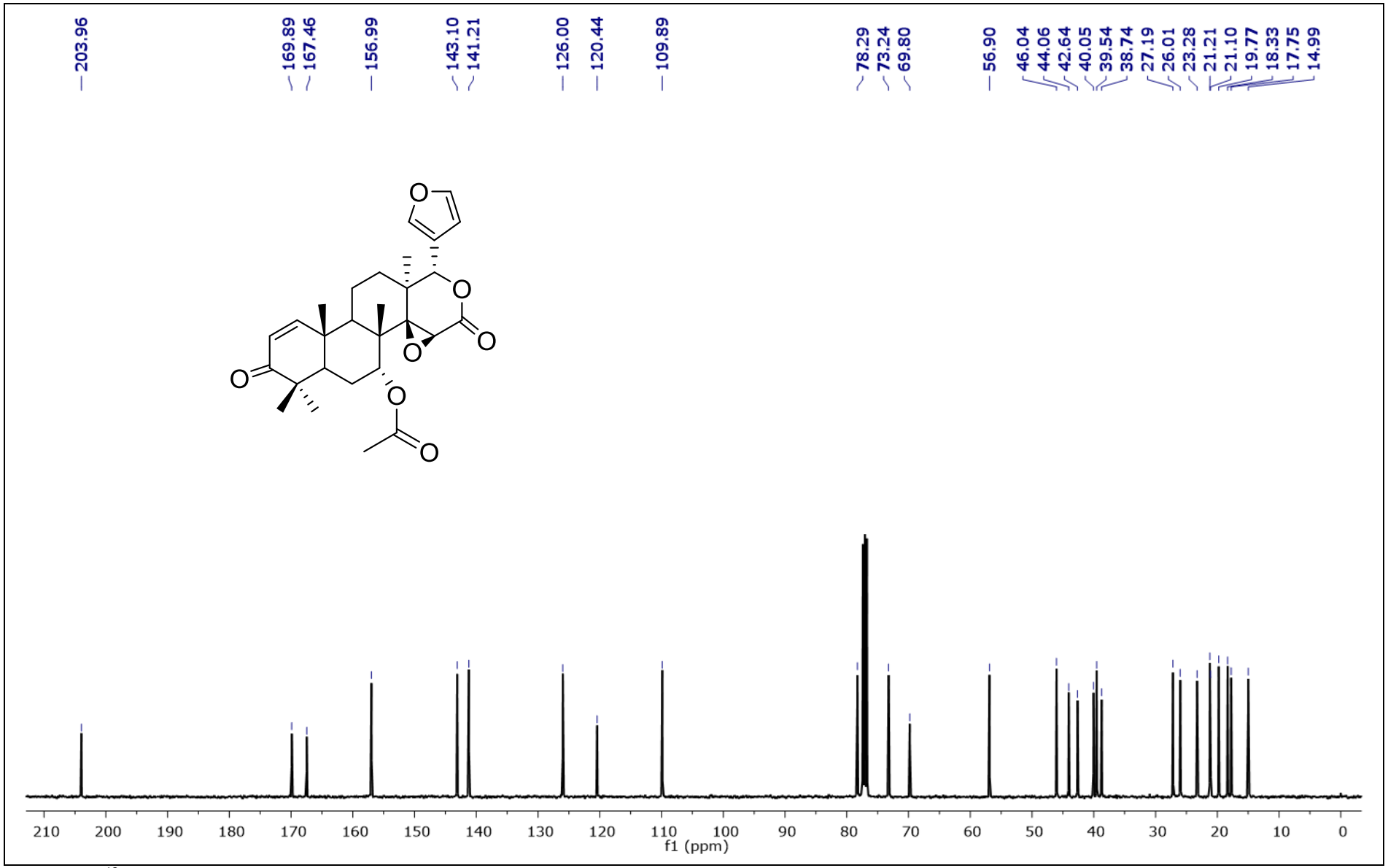


Figure S8: ^{13}C NMR Spectrum of gedunin (3) ($CDCl_3$, 100 MHz)

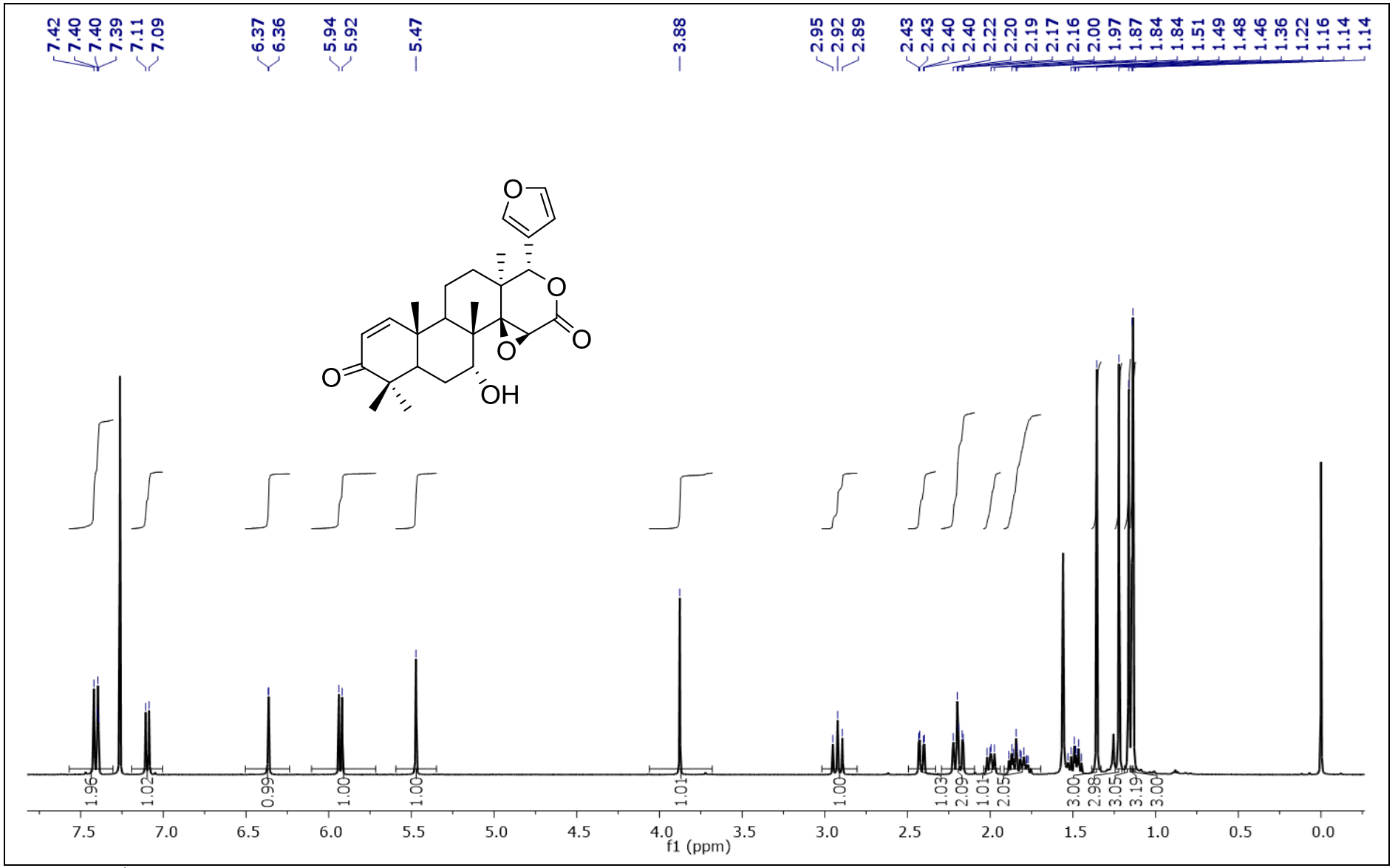


Figure S9: ^{1}H NMR Spectrum of deacetylgedunin (4) ($CDCl_3$, 500 MHz)

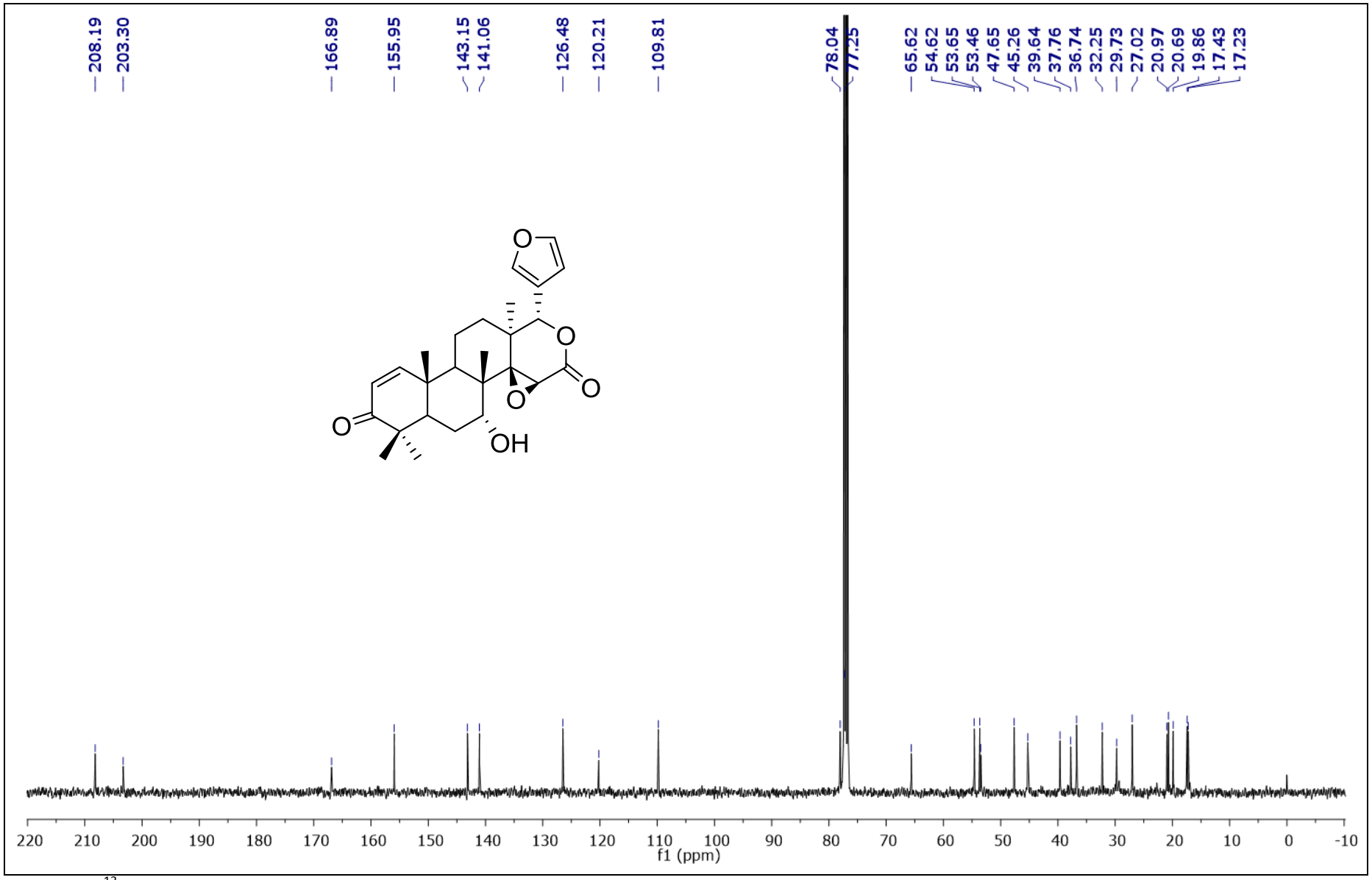


Figure S10: ^{13}C NMR Spectrum of deacetylgedunin (4) ($CDCl_3$, 100 MHz)

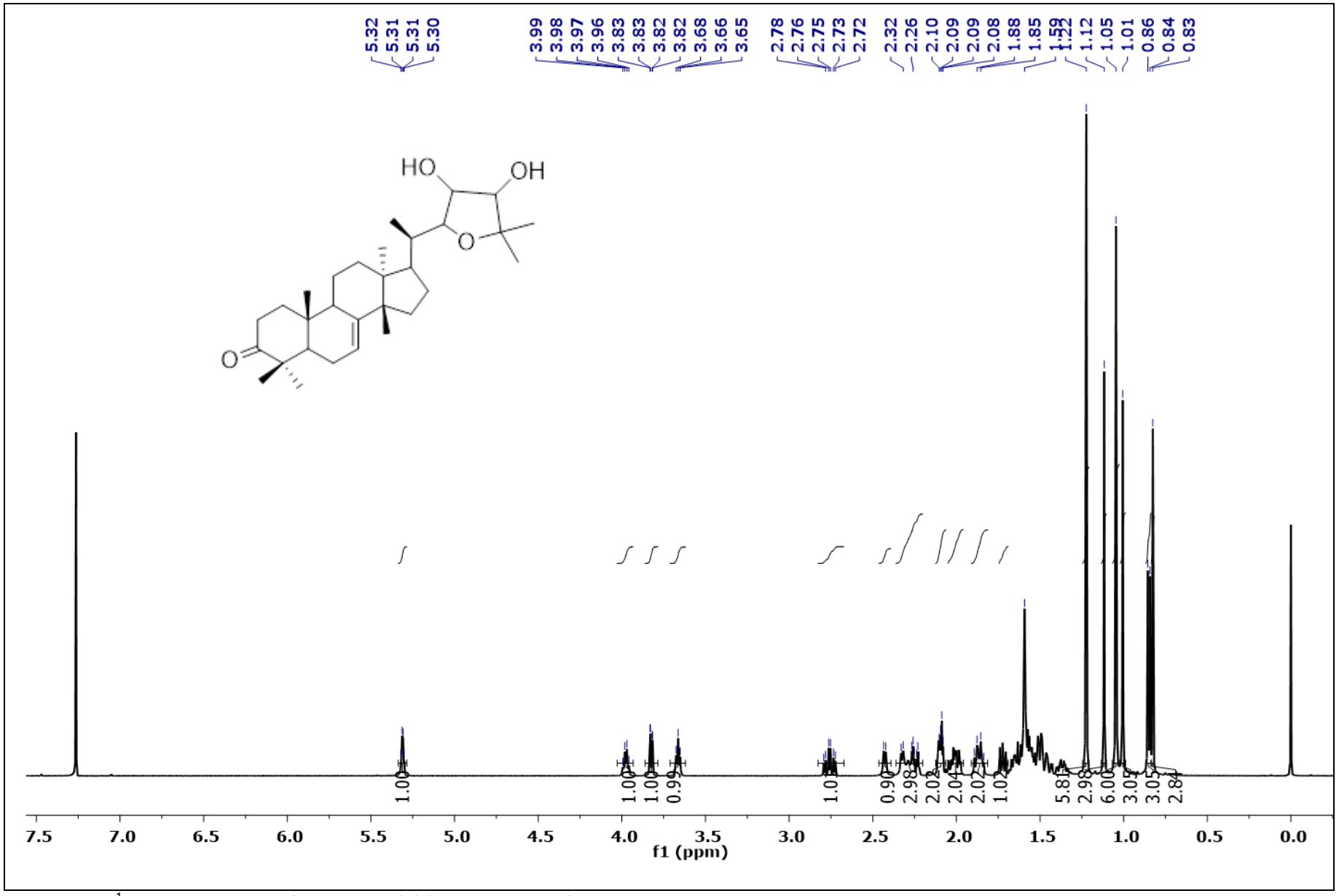


Figure S11: ^{1}H NMR Spectrum of odoratone (5) ($CDCl_3$, 500 MHz)

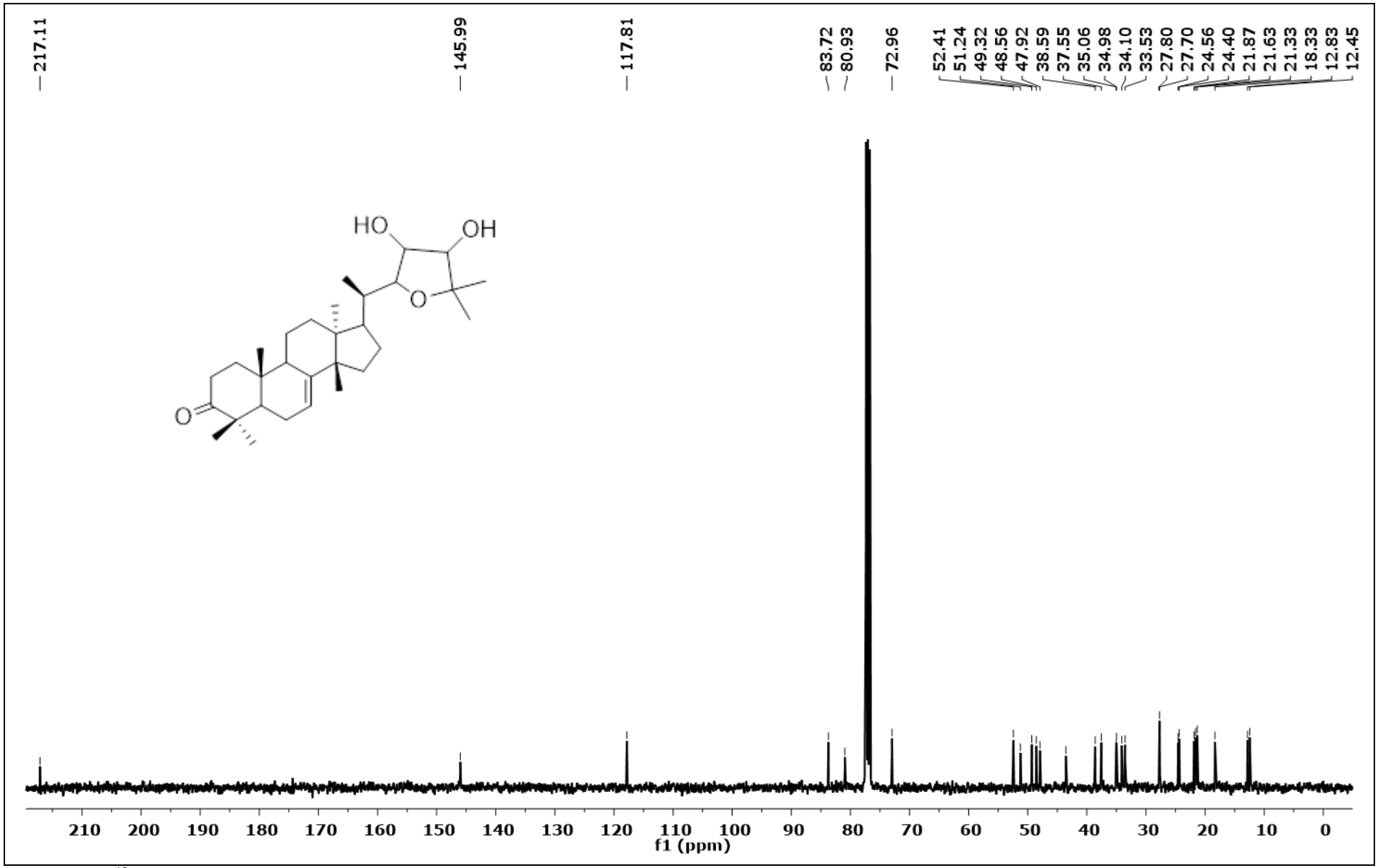


Figure S12: ^{13}C NMR Spectrum of odoratone (5) ($CDCl_3$, 100 MHz)

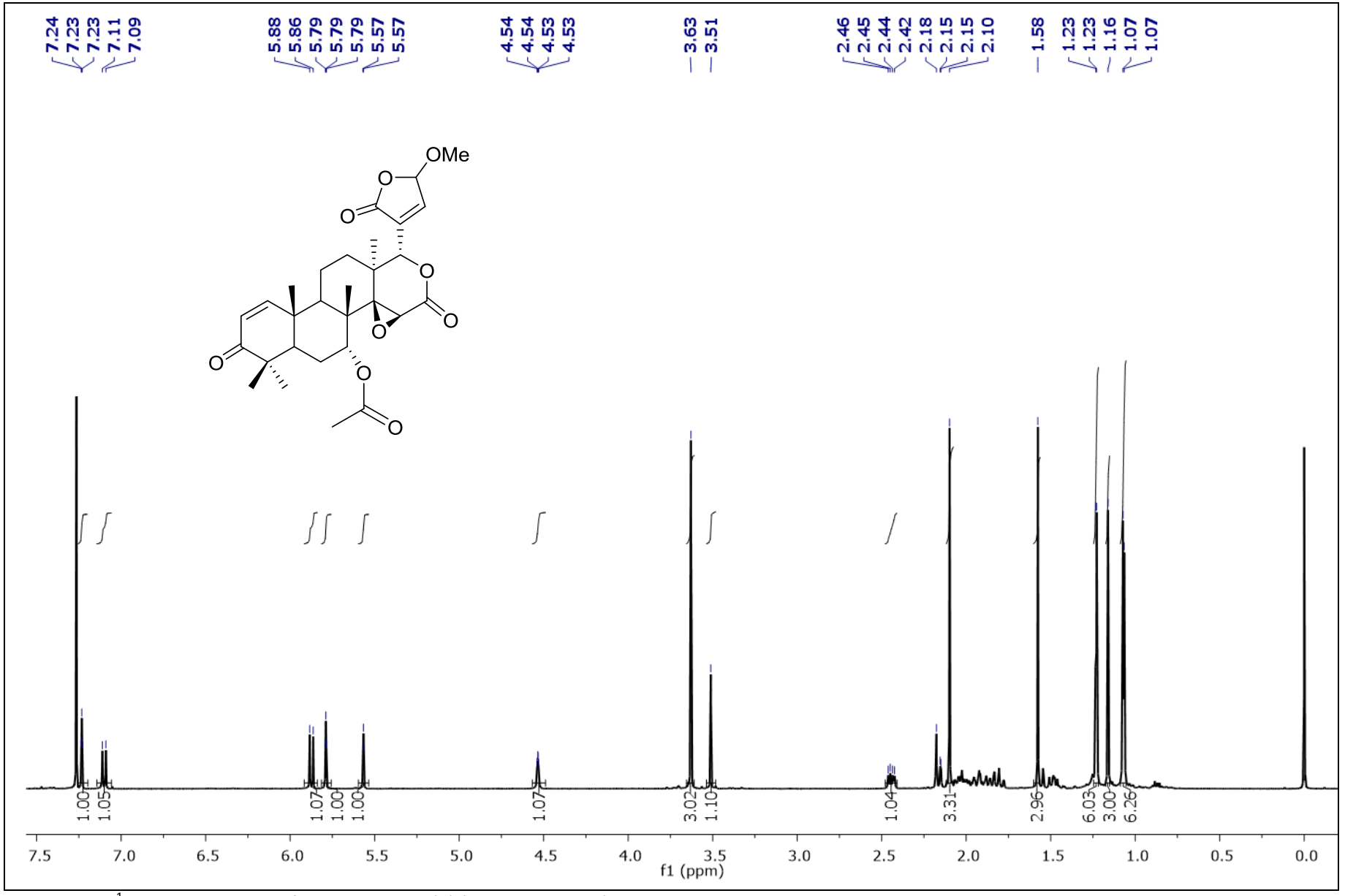


Figure S13: ^{1}H NMR Spectrum of azadiraindin G (6) ($CDCl_3$, 500 MHz)

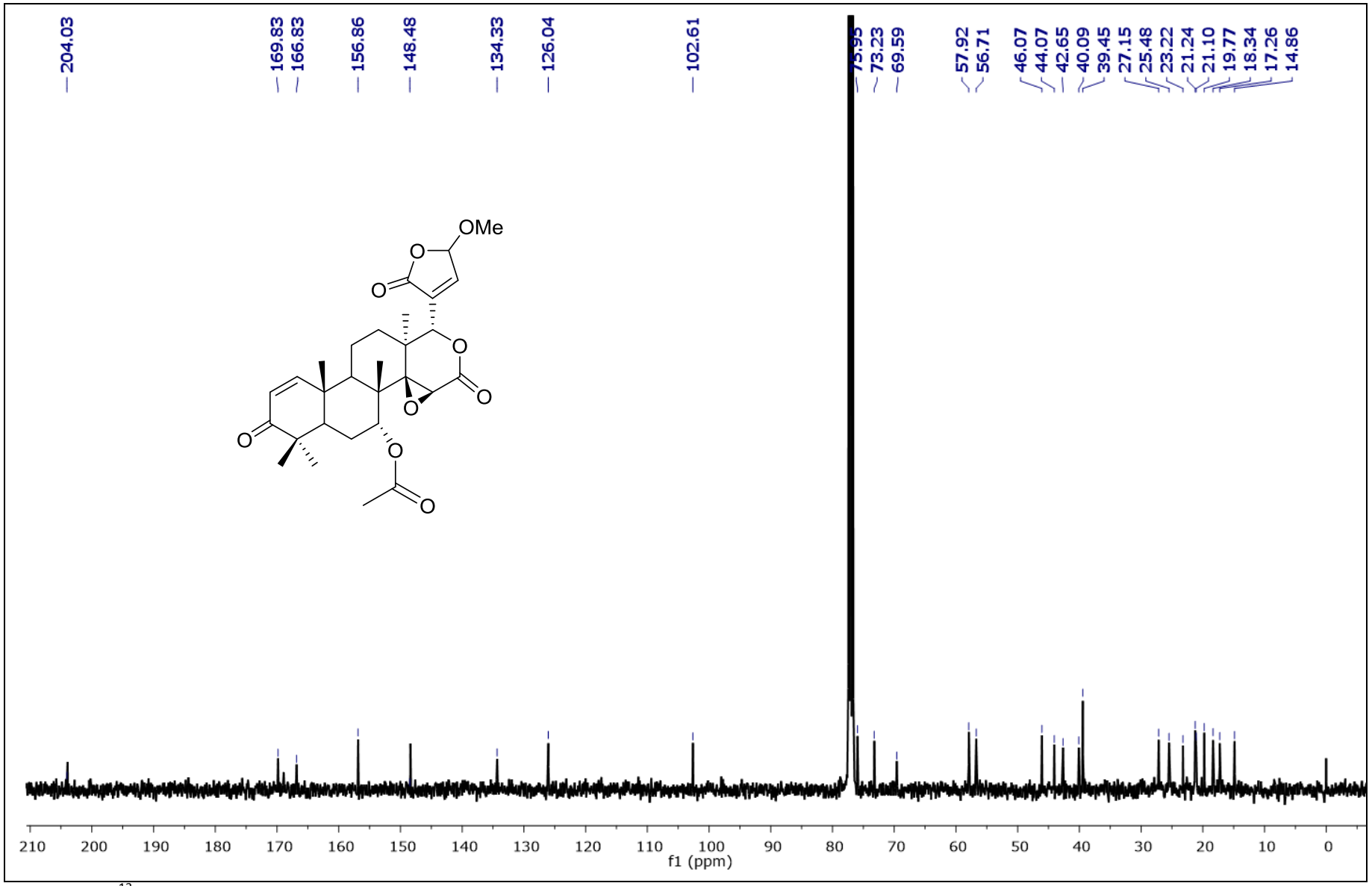


Figure S14: ^{13}C NMR Spectrum of azadiraindin G (6) ($CDCl_3$, 100 MHz)

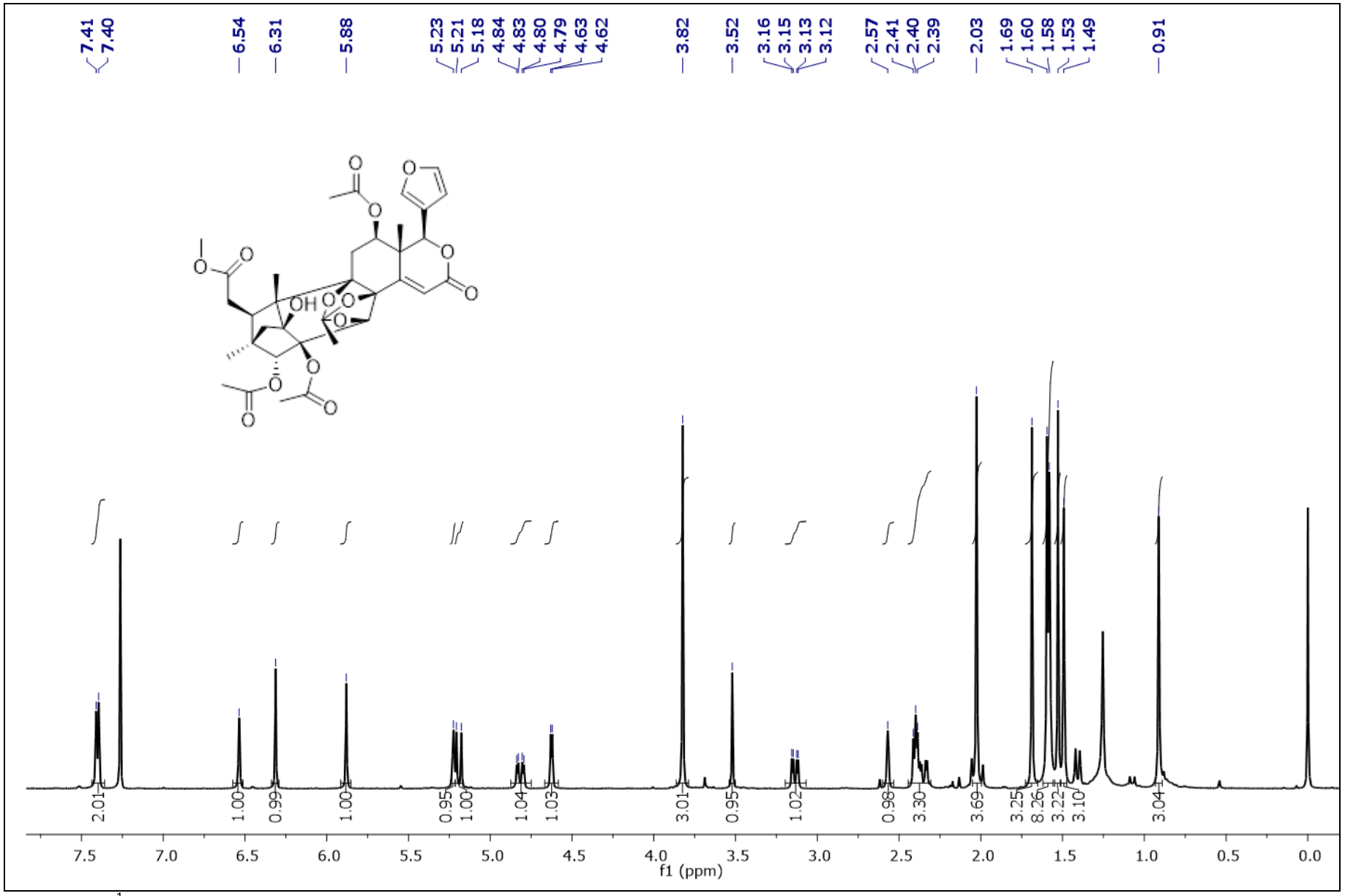


Figure S15: ^{1}H NMR Spectrum of xyloccensin T (7) ($CDCl_3$, 500 MHz)

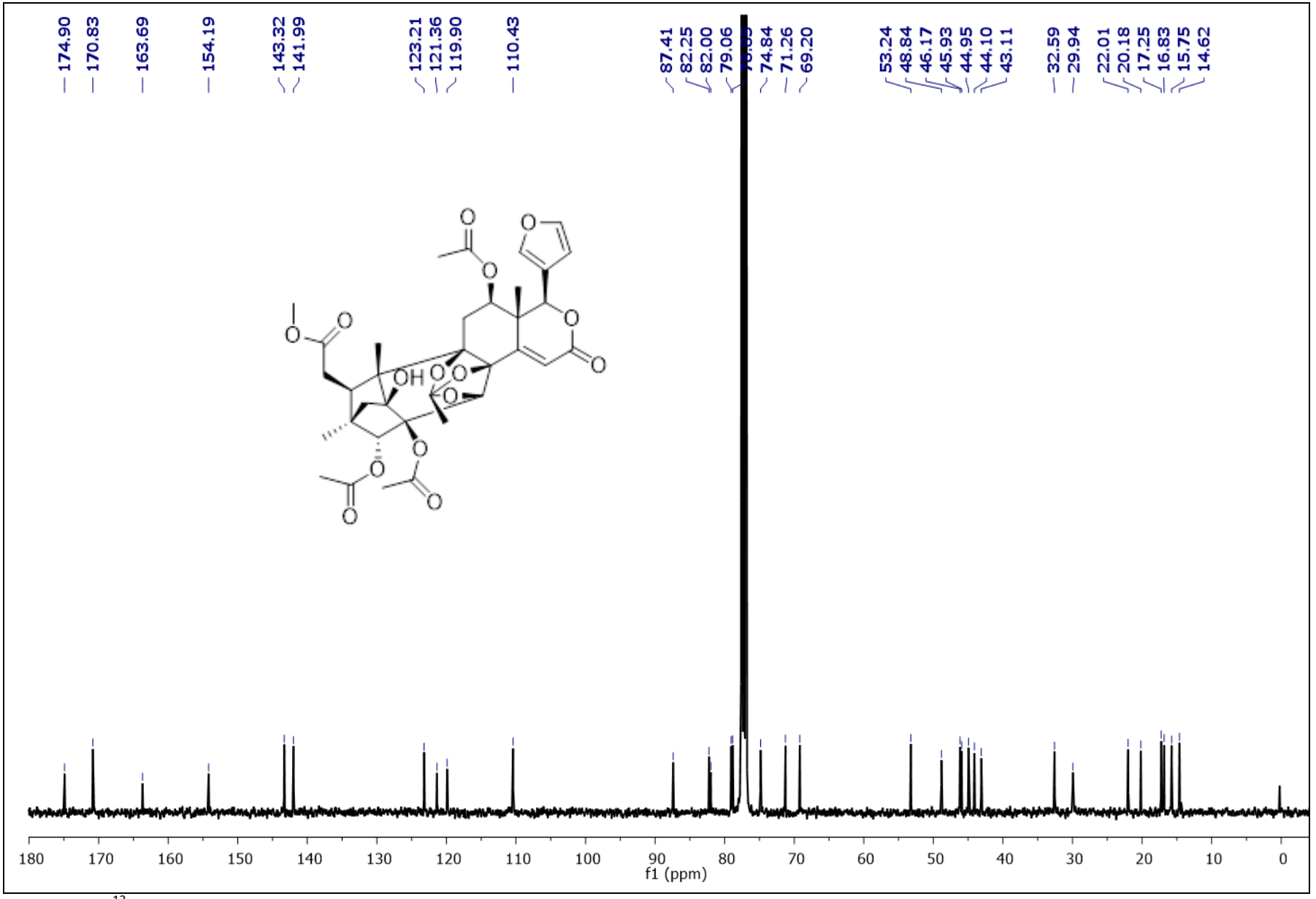


Figure S16: ^{13}C NMR Spectrum of xyloccensin T (7) ($CDCl_3$, 100 MHz)

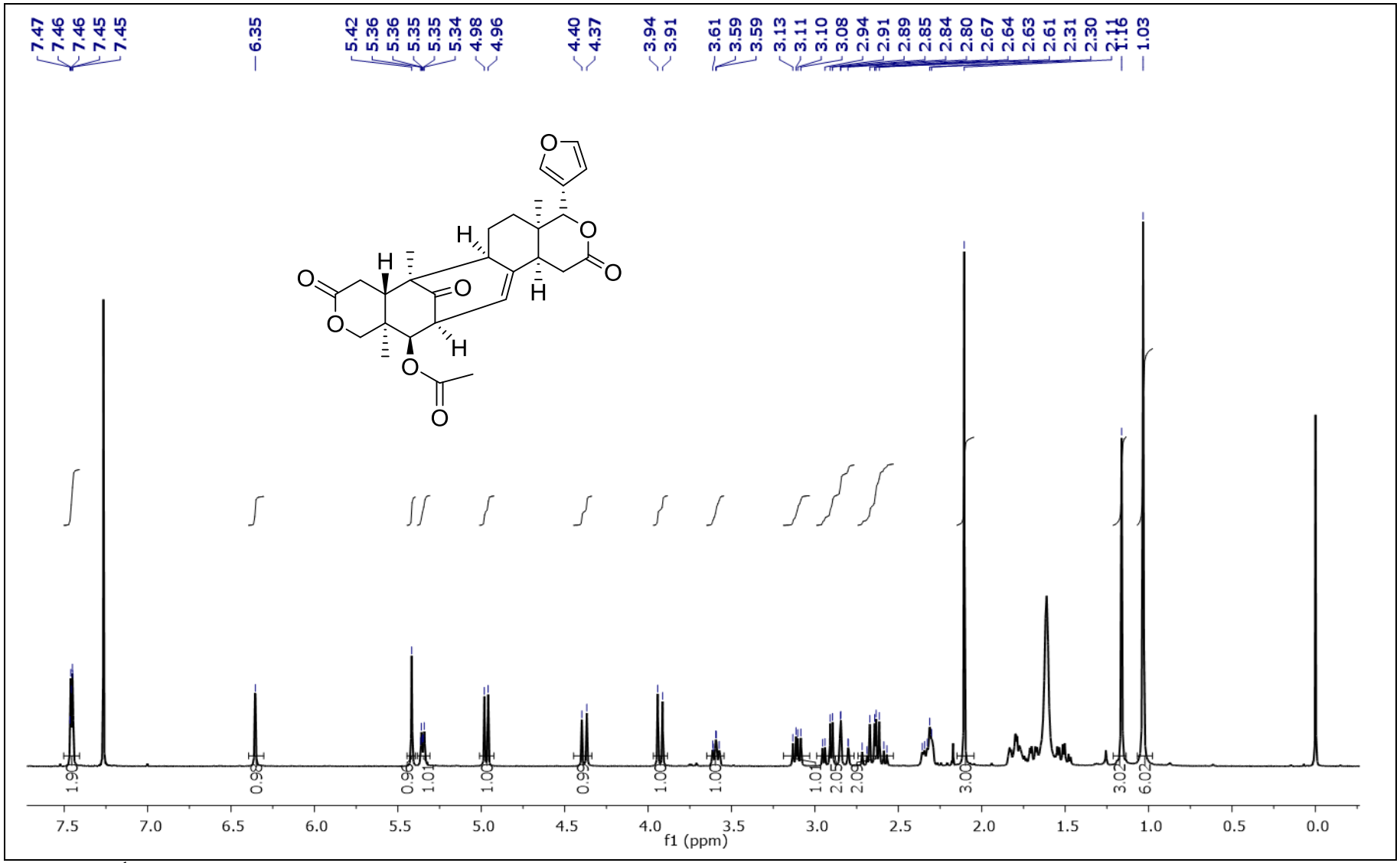


Figure S17: ^{1}H NMR Spectrum of moluccensin V (8) ($CDCl_3$, 400 MHz)

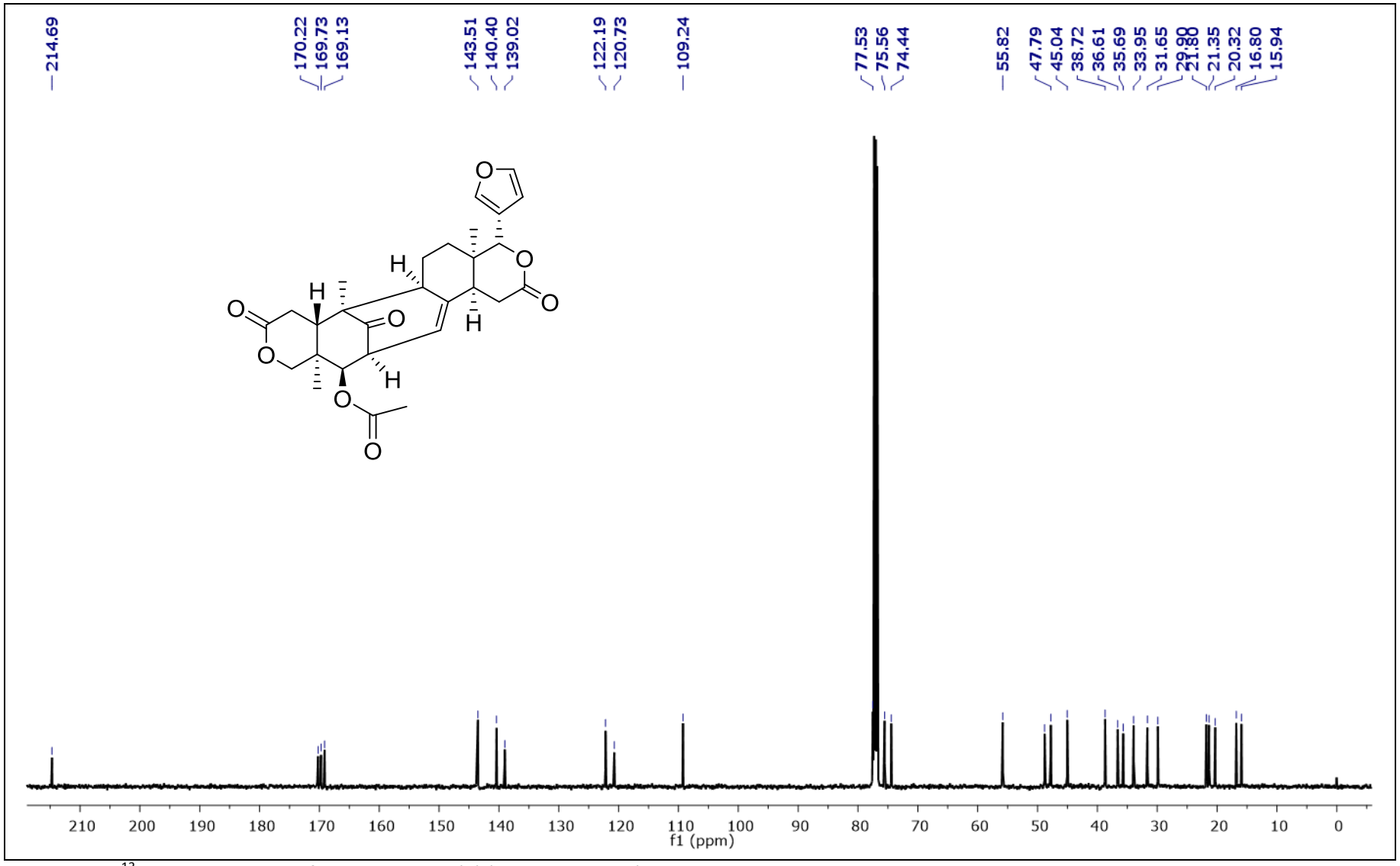


Figure S18: ^{13}C NMR Spectrum of moluccensin V (8) ($CDCl_3$, 125 MHz)

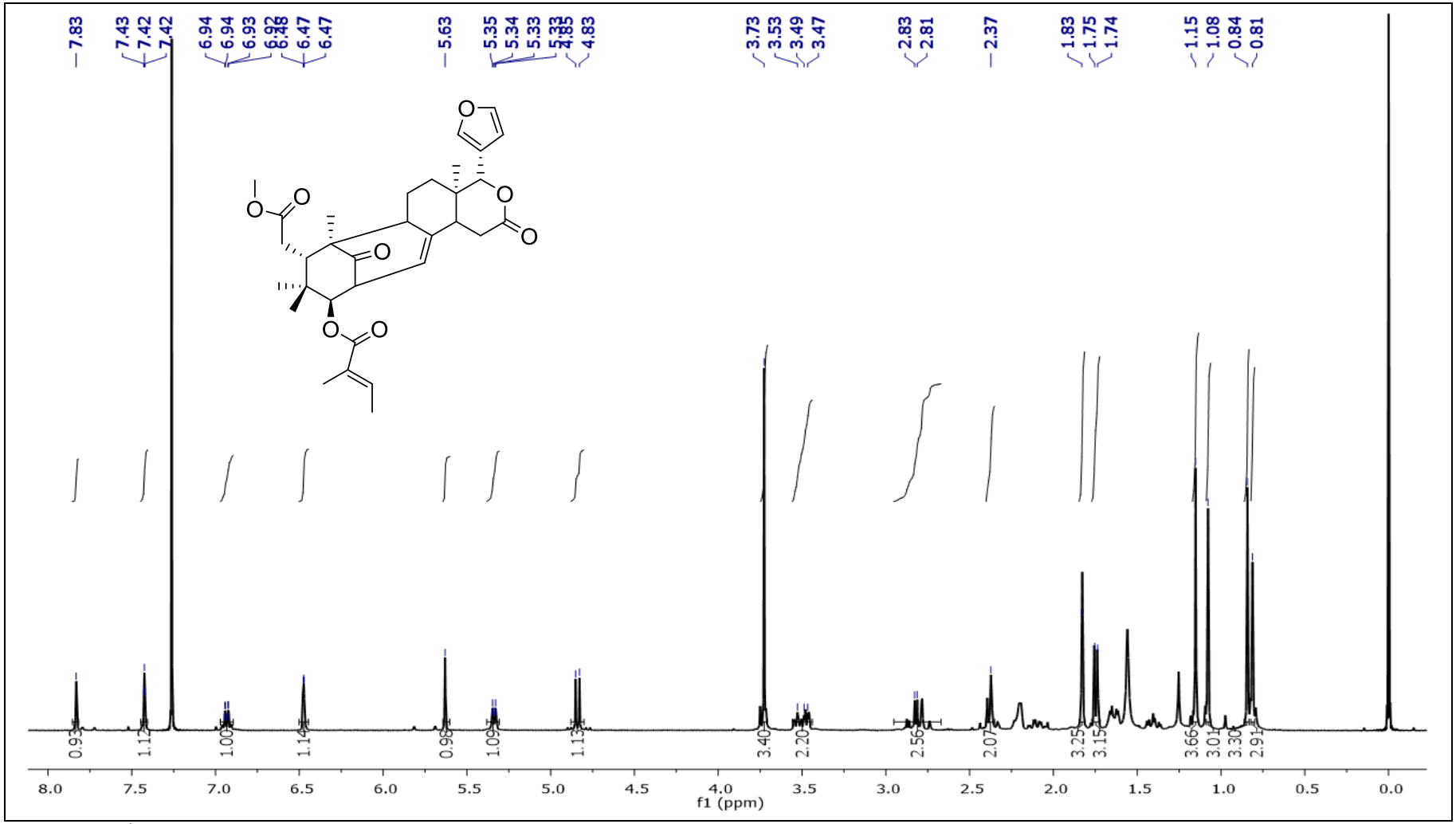


Figure S19: ^{1}H NMR Spectrum of 6-Desoxyswietenine (9) ($CDCl_3$, 500 MHz)

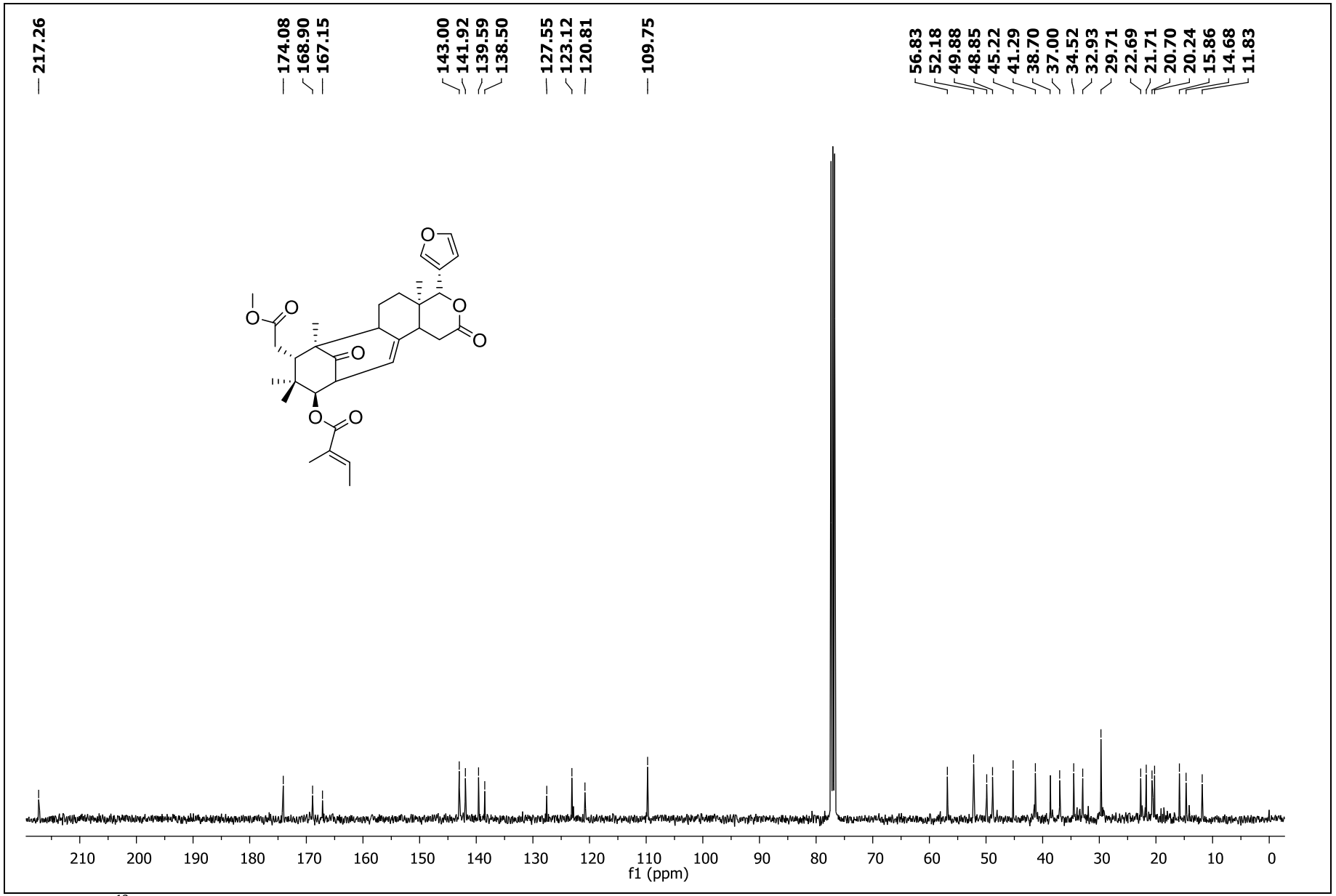


Figure S20: ^{13}C NMR Spectrum of 6-Desoxyswietenine (9) ($CDCl_3$, 125 MHz)

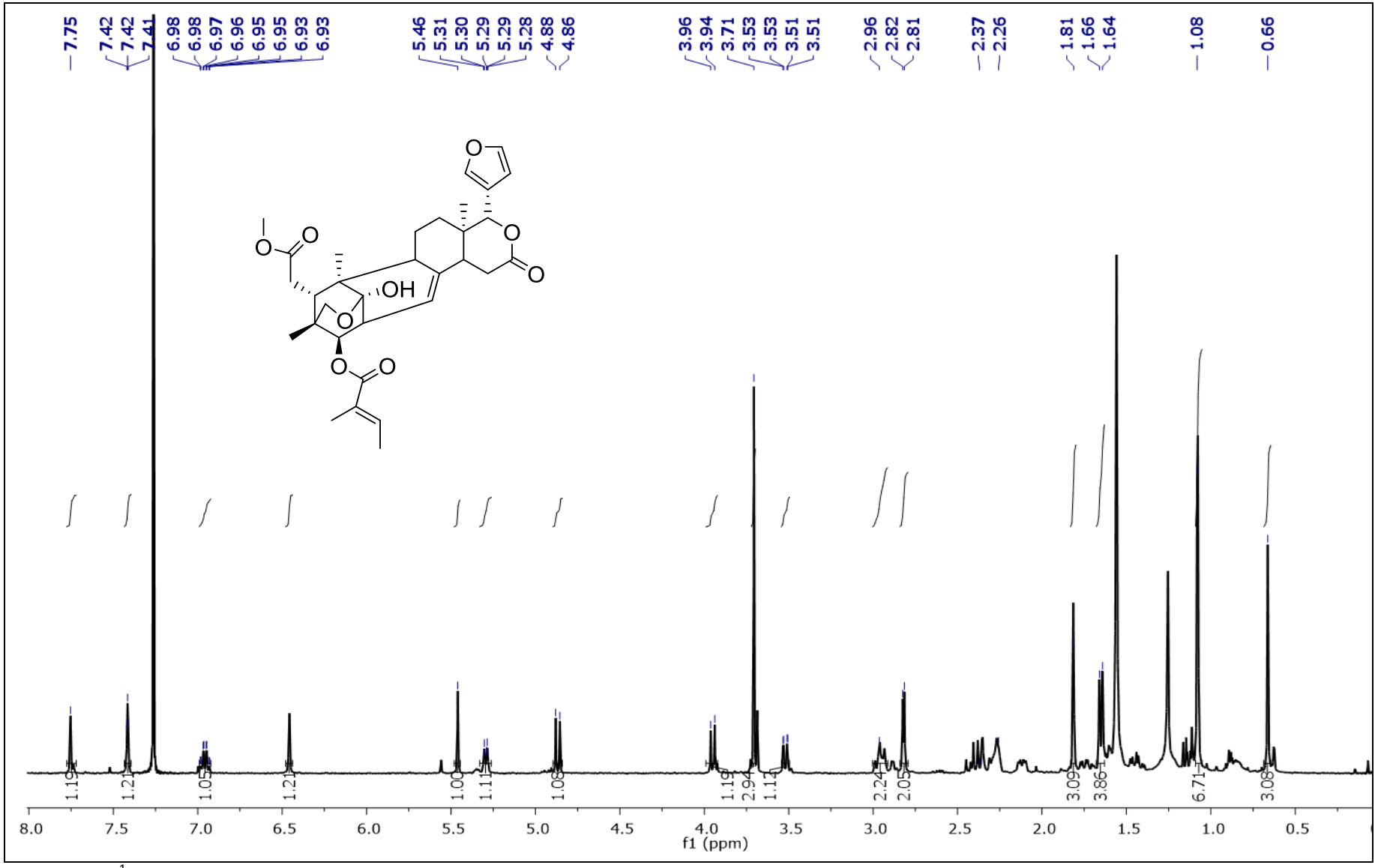


Figure S21: ^{1}H NMR Spectrum of granatumin L (10) ($CDCl_3$, 500 MHz)

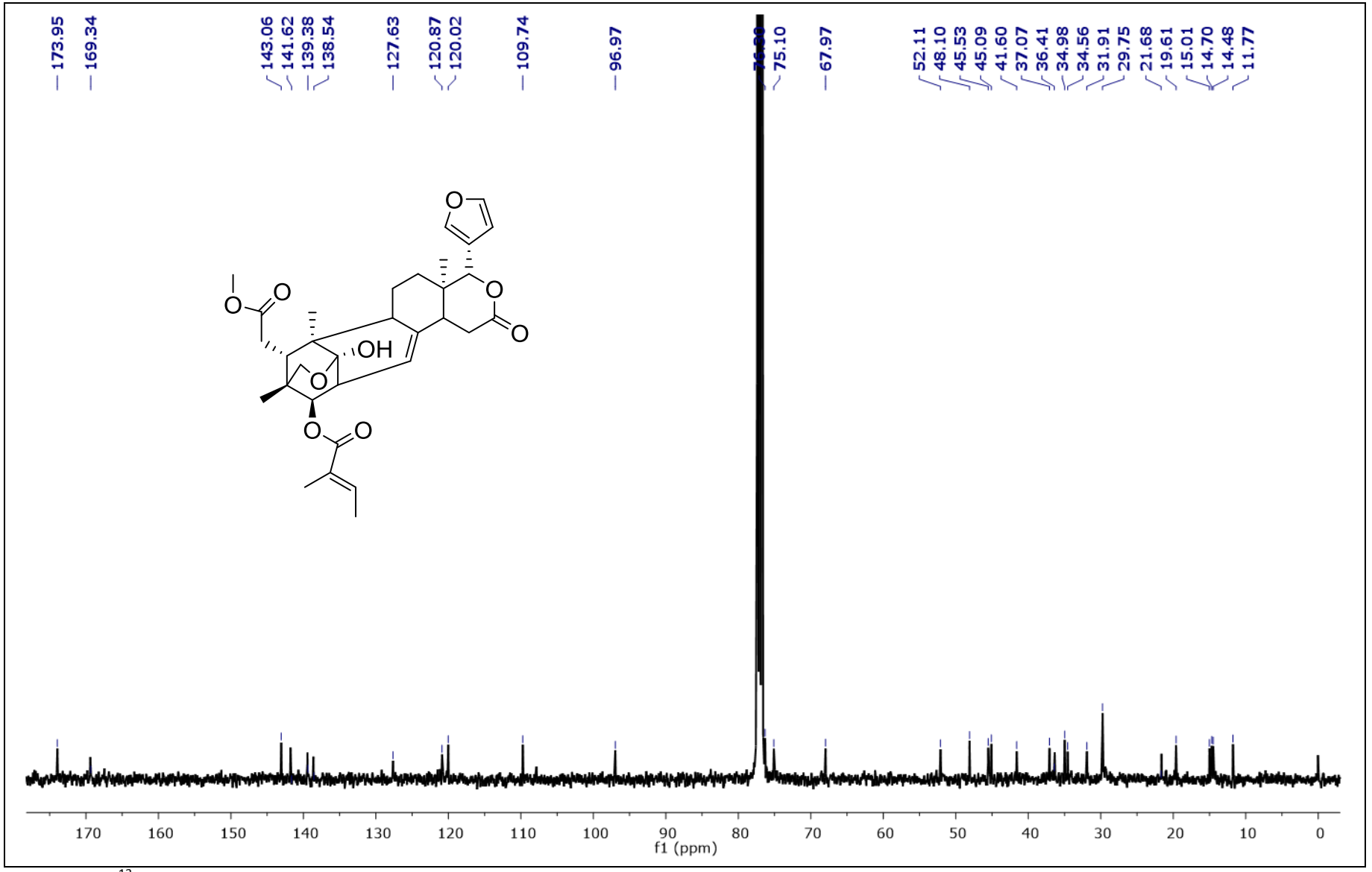


Figure S22: ^{13}C NMR Spectrum of granatumin L (10) ($CDCl_3$, 100 MHz)

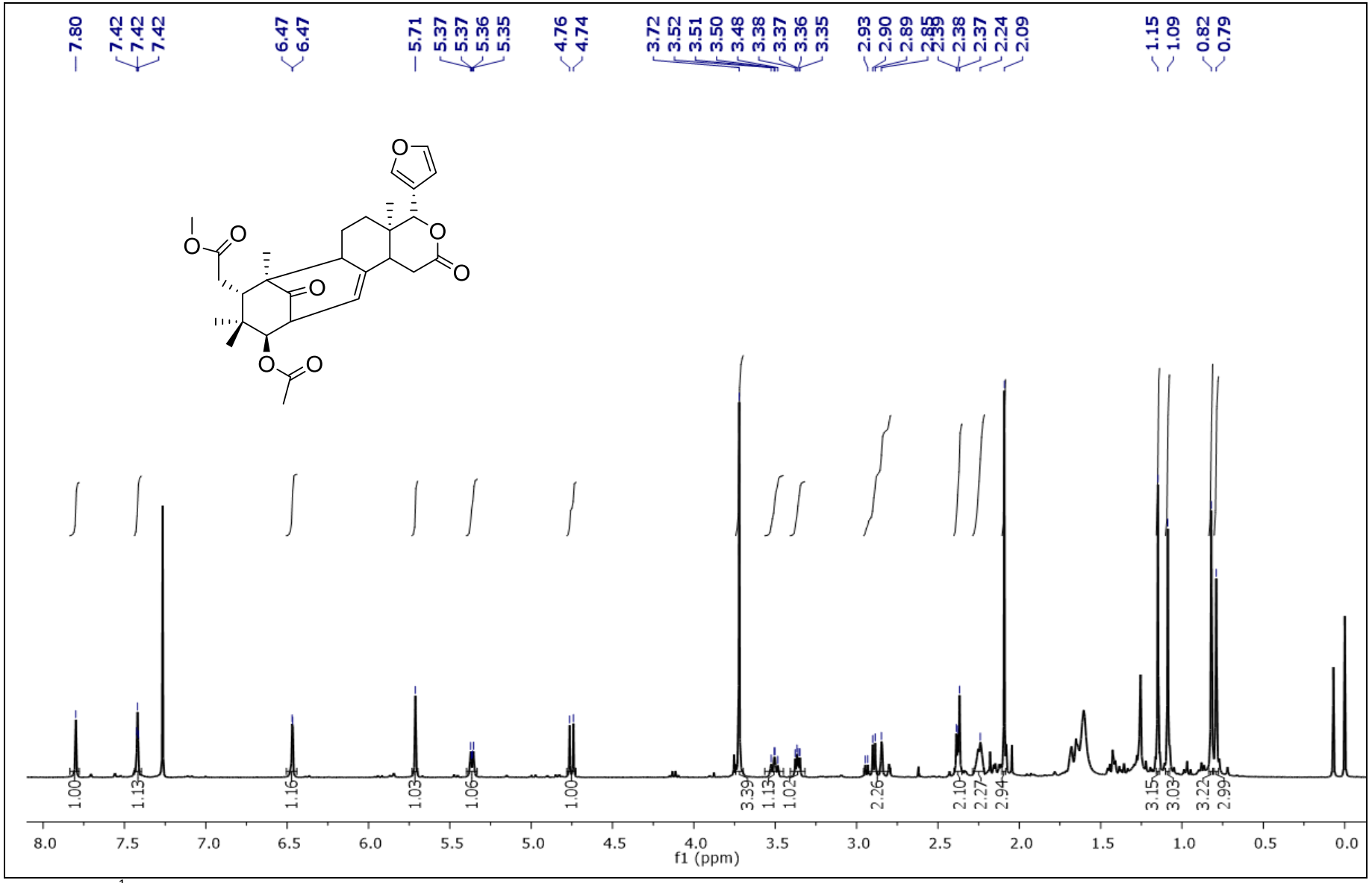


Figure S23: ^{1}H NMR Spectrum of 6-deoxy destigloylswietenine acetate (11) ($CDCl_3$, 400 MHz)

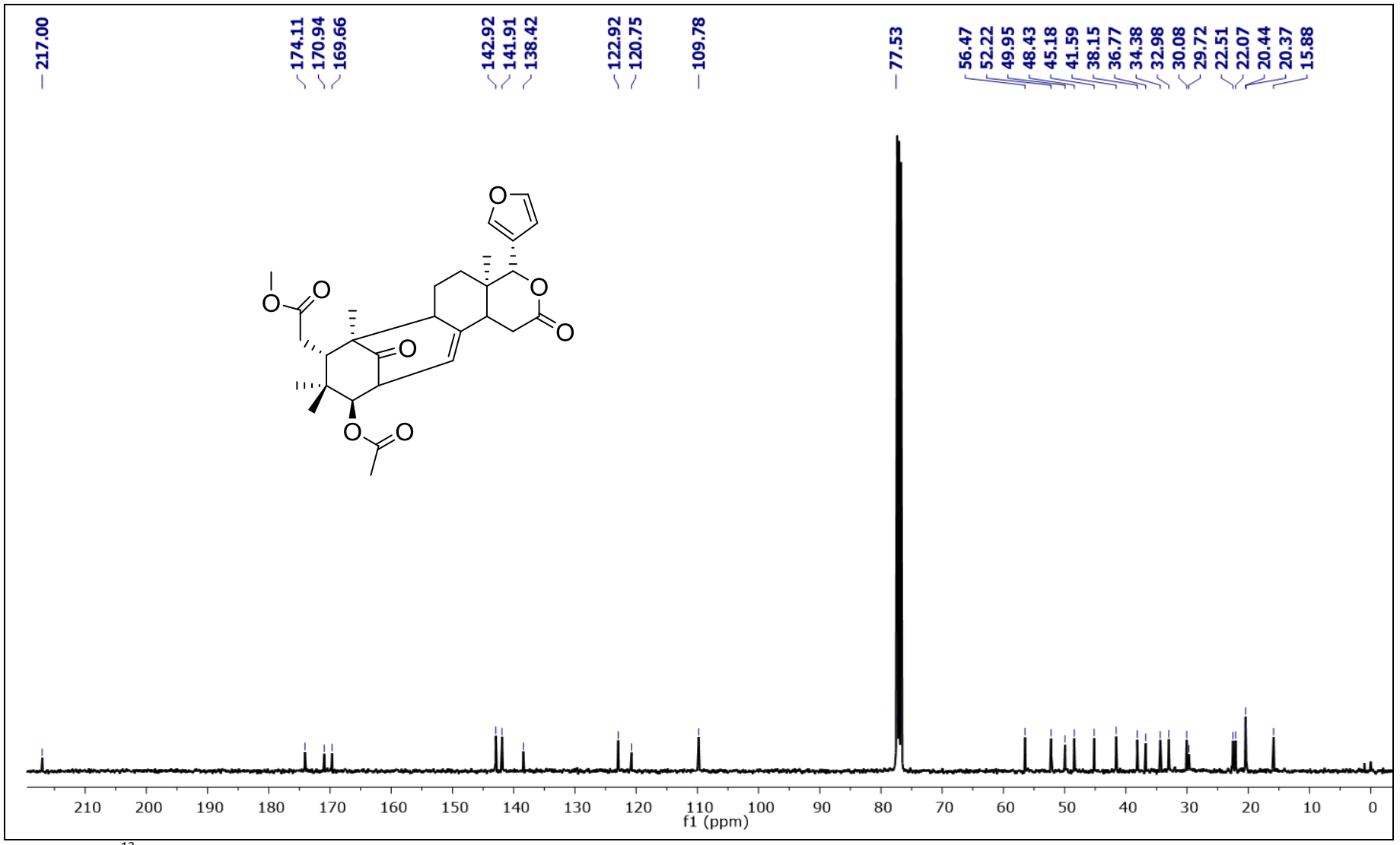


Figure S24: ^{13}C NMR Spectrum of 6-deoxy destigloylswietenine acetate (11) ($CDCl_3$, 100 MHz)

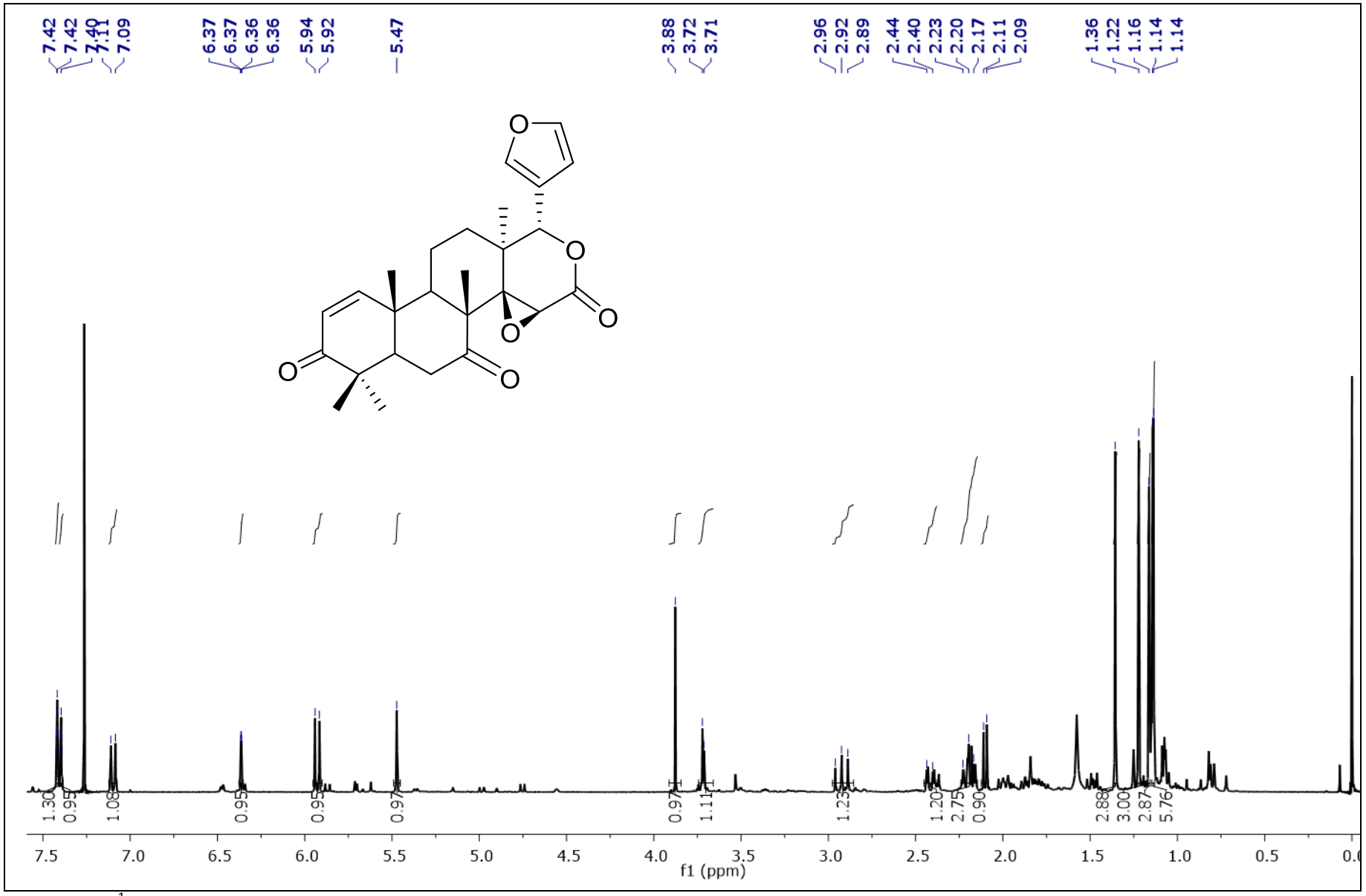


Figure S25: ^{1}H NMR Spectrum of 7-deacetyl 7-oxygedunin (12) ($CDCl_3$, 400 MHz)

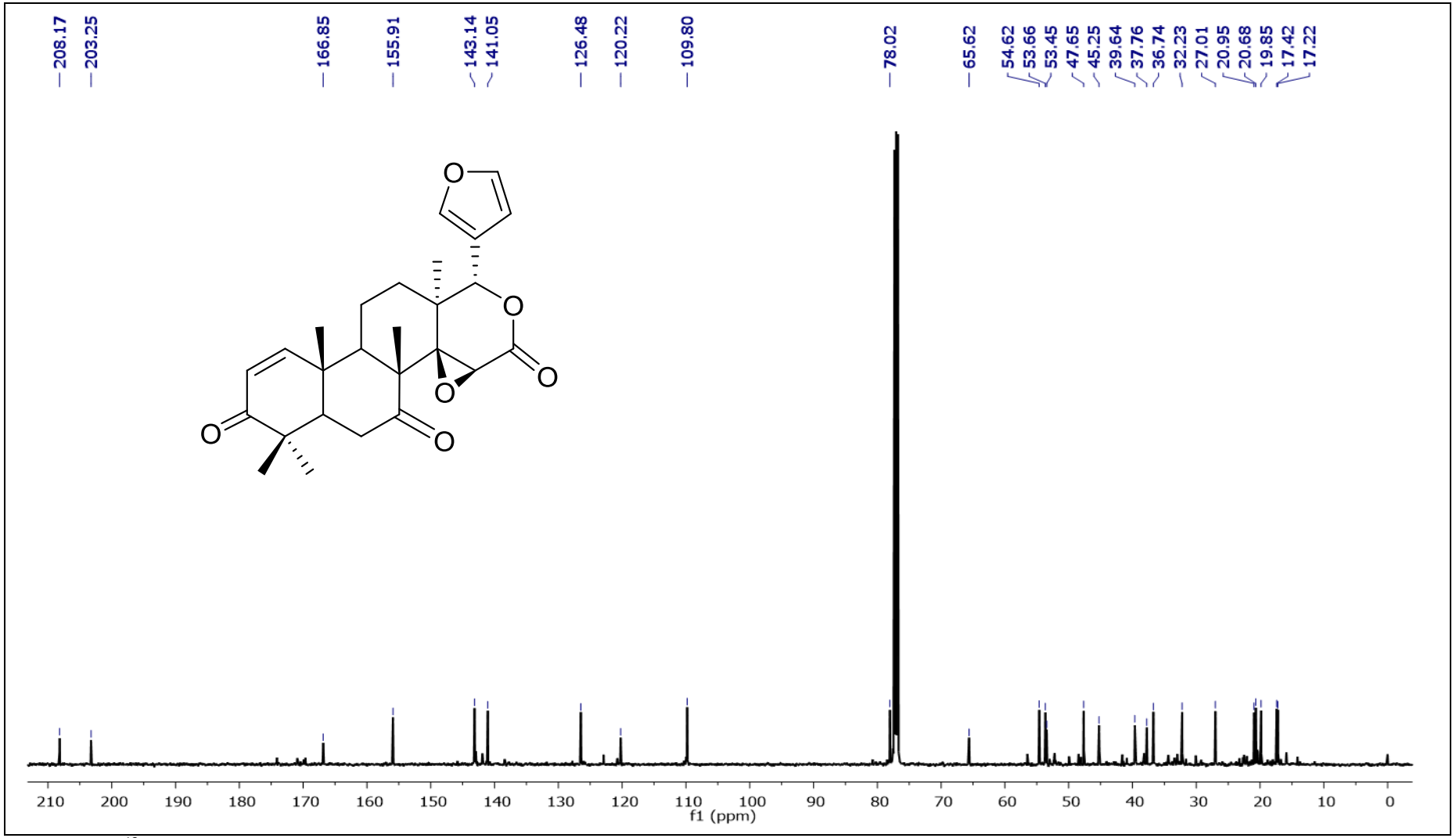


Figure S26: ^{13}C NMR Spectrum of 7-deacetyl 7-oxygedunin (12) ($CDCl_3$, 125 MHz)