Electronic Supplementary Material (ESI) for ChemComm.

Divergent Pathways to Furosesquiterpenes. First Total Syntheses of (+)-Zedoarol and (*Rac*)-Gweicurculactone.

Elissavet E. Anagnostaki, Vera P. Demertzidou and Alexandros L. Zografos*

Contribution from the Department of Chemistry, Laboratory of Organic Chemistry, Aristotle University of Thessaloniki, University Campus, Thessaloniki 54124, Greece

Corresponding Author e-mail: alzograf@chem.auth.gr

Supporting Information

Table of contents

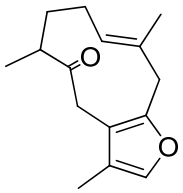
I. General Information

All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions. Dry diethyl ether (Et_2O), and tetrahydrofuran (THF), were obtained by refluxing the solvents with sodium and benzophenone for several hours whereas methylene chloride (CH_2Cl_2) was dried by distillation from CaH_2. The solvents were kept under argon using molecular sieves 4Å in their bottles. Reagents were purchased at the highest commercial quality and used without further purification.

Reactions were monitored by thin-layer chromatography (TLC) carried out on S-2 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and ethanolic *p*-anisaldehyde as developing agent. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Silica gel was neutralized with 1% Et_3N and used in all indicative cases where compounds are sensitive to acidic conditions. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254).

NMR spectra were recorded on Brüker 300 AM and Agilent 500 spectrometer and calibrated using TMS as an internal reference. The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, brd = broad doublet, brt = broad triplet, pst = pseudo triplet. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI-TOF (time of flight) mass spectrometer at a 4000 V emitter voltage. Optical rotations were recorded on a Perkin-Elmer Model 343 polarimeter at 589 nm, and are reported in units of 10^{-1}(deg cm^2 g^{-1}).

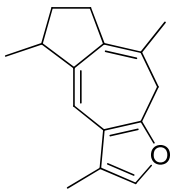
II. Experimental procedures and physical properties of compounds



2

(R,S)-furanogermenone (2)

In a well-dried schlenk tube a solution of compound **1**[1] (235 mg, 1.00 mmol) in dry THF (7ml) was introduced and deoxygenated in high vacuum with the aid of liquid nitrogen. Then oil free KH (40mg, 1.00 mmol) was added at once and the mixture was immediately capped and heated for 10 min at 65 ^{o}C. The mixture was cooled down at room temperature and quenched by the addition of 5 ml of saturated aqueous ammonium chloride. The aqueous layer was extracted with Et_2O (3 X 10 ml) and the combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by neutralized silica gel flash column chromatography (petroleum/ Et_2O = 100:1) gave **2** (193 mg, 82%) as a white solid. Compound **2** lacks of optical activity. R_f = 0.30 (petroleum/ Et_2O = 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.09 (brs, 1H), 5.14 (brt, 1H), 3.44 (d, *J* = 15Hz, 1H), 3.41 – 3.30 (m, 1H), 3.21 (brd, *J* = 15Hz, 2H), 2.60 – 2.46 (m, 1H), 2.31 – 2.06 (m, 2H), 2.02 – 1.88 (m, 1H), 1.88 (s, 3H), 1.82 – 1.76 (m, 1H), 1.69 (brs, 3H), 1.08 (d, *J* = 6Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.3, 148.8, 136.5, 131.8, 131.7, 121.9, 113.7, 47.3, 38.4, 36.4, 36.3, 29.6, 18.3, 17.3, 8.12.

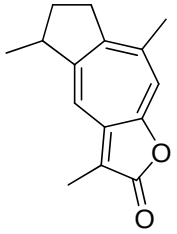


3

Compound 3

In a well-dried schlenk tube, a solution of compound **1**[1] (235 mg, 1.00 mmol) in dry THF (7 ml) was introduced and deoxygenated in high vacuum with the aid of liquid nitrogen. In the resulting solution a 1M solution of KHMDS in toluene (1ml, 1.00 mmol) was introduced and the schlenk was capped and heated to 90 ^{o}C for 10 min. The mixture was cooled down at room temperature and quenched by the addition of 5 ml of saturated aqueous ammonium chloride. The aqueous layer was extracted with Et_2O (3 X 10 ml) and the combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*.

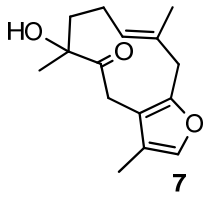
Purification by neutralized silica gel flash column chromatography (petroleum/ Et_2O = 100:1) provided compound **3** as a yellow oil (139 mg, 65%). R_f = 0.73 (petroleum/ Et_2O = 3:1). Compound **3** was obtained as racemic mixture. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 (brs, 1H) 6.36 (brs, 1H), 3.09 [d, (a,b system), *J* = 15.8Hz, 1H], 2.94 [d, (a,b system), *J* = 15.8Hz, 1H], 2.79 – 2.76 (m, 1H), 2.57 – 2.51 (m, 1H), 2.48 – 2.41 (m, 1H), 2.15 – 2.11 (m, 1H), 2.01 (brs, 3H), 1.97 (d, *J* = 1.2Hz, 3H), 1.47 – 1.40 (m, 1H), 1.12 (d, *J* = 7Hz, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.4, 140.5, 139.3, 135.0, 133.3, 119.4, 117.3, 116.0, 44.5, 33.4, 31.2, 23.2, 21.4, 19.6, 7.9; HRMS: calcd for $C_{15}H_{19}O^+$ [M + H^+]: 215.1436, found 215.1439.



Gweicurculactone (4)

Racemic (R,S)-Gweicurculactone (4)

A solution of compound **3** (30 mg, 0.14 mmol) in DCM was stirred at room temperature for 1 day before evaporated to dryness and purified by neutralized silica gel flash column chromatography (petroleum/ Et_2O = 30:1) Racemic compound **4** (11 mg, 35%) was obtained as a reddish solid which was found to be identical to the natural substance[2] except from its optical rotation. ^{1}H NMR (500 MHz, $CDCl_3$): δ =6.86 (s, 1H) 6.70 (s, 1H), 3.10 – 3.00 (m, 1H), 2.84 – 2.74 (m, 1H), 2.71 – 2.61 (m, 1H), 2.21 (s, 3H), 2.14 – 2.05 (m, 1H), 1.95 (s, 3H), 1.51 (m, 1H), 1.28 (d, *J* = 4.8 Hz, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 156.7, 154.9, 146.3, 144.3, 136.6, 118.0, 116.4, 103.7, 44.0, 33.8, 32.1, 24.8, 20.2, 7.8; HRMS: calcd for $C_{15}H_{17}O_2^+$ [M + H^+]: 229.1228, found 229.1223.

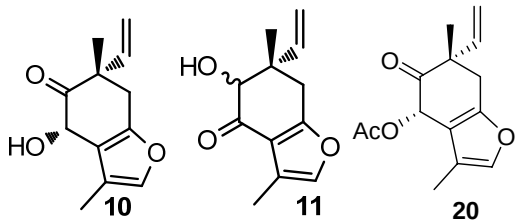


7

(R,S)-5-Hydroxy-furanogermanone (7)

In a well-dried schlenk tube, a solution of compound **1**[1] (50 mg, 0.22 mmol) in dry THF (7 ml) was introduced and it was saturated with dry oxygen gas (passed through anhydrous $CaCl_2$). In the resulting solution, oil free KH (9 mg, 0.22 mmol) was added at once and the mixture was immediately capped and heated for 10 min at 65 ^{o}C. The mixture was cooled down at

room temperature and quenched by the addition of 5 ml of saturated aqueous ammonium chloride. The aqueous layer was extracted with Et_2O (3 X 10 ml) and the combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by neutralized silica gel flash column chromatography (petroleum/ Et_2O = 50:1) gave **7** (24 mg, 45%) as a colourless oil. Compound **7** was obtained as racemic mixture. R_f = 0.13 (petroleum/ Et_2O = 3:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13 (brs, 1H), 5.27 (brt, 1H), 4.23 – 3.96 (m, 1H), 3.92– 3.69 (m, 1H), 3.47– 3.04 (m, 3H), 2.43 – 2.02 (m, 4H), 1.91 (s, 3H), 1.40 (brs, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.5, 148.8, 136.8, 132.5, 130.5, 122.4, 113.6, 78.6, 39.0, 31.1, 28.0, 27.1, 22.5, 17.1, 8.0; HRMS: calcd for $C_{15}H_{21}O_3^+$ [M + H^+]: 249.1490, found 249.1487.

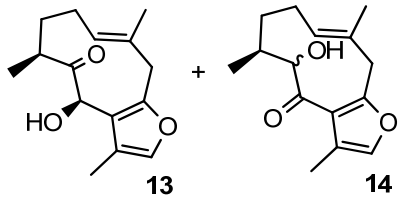


Compound 10 and mixture of compounds 11

To a stirred solution of compound **9**[1] (100 mg, 0.52 mmol) in dry THF (2 ml) was added a solution of 1M LiHMDS in THF (0.48 ml, 0.48mmol) under argon atmosphere at -78 ^oC. After 30 min, R(-)10-camphorosulphonyl oxaziridine (108 mg, 0.48 mmol) dissolved in dry THF (0.5 ml) was added at the same temperature and the resulting solution was stirred for 45 min at the same temperature. Then the reaction mixture was quenched by the addition of 1.5 ml saturated aqueous sodium thiosulphate and the aqueous layer was extracted with Et_2O (3 X 8 ml). The combined organic extracts are dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/ Et_2O = 50:1) provided compound **10** (54 mg, 52%) as a pale yellow oil. The compound was readily transformed to its regioisomeric compounds **11** over 2h at rt or within few minutes when dissolved in $CDCl_3$. R_f = 0.48 (petroleum/ Et_2O = 3:1). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.11 (s, 1H), 5.96 (dd, *J* = 17.4Hz, 10.7Hz, 1H), 5.21 (d, *J* = 10.7Hz, 1H), 5.18 (d, *J* = 17.4Hz, 1H), 3.37 (s, 1H), 3.05 [d, (a,b system), *J* = 1.4Hz, 1H], 2.85 [d, (a,b system), *J* = 1.4Hz, 1H], 2.08 (s, 3H), 1.36 (s, 3H). Its stereochemistry was elucidated by NOESY NMR spectroscopy of its acetyl derivative **21**. Acetyl derivative also fails to give a stable compound and also readily transforms to a mixture of acetylated compounds. <u>For acetyl derivative **20**</u>: Compound **10** (20 mg, 0.10 mmol) was dissolved in DCM (1 ml) and treated with Ac_2O (46 µL, 0.50 mmol) at rt for 6h. The resulting mixture was quenched with water and extracted with Et_2O (3 X 8 ml).

The combined organic extracts are dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/ Et_2O = 50:1) provided **20** (21 mg, 85%) as a pale yellow oil. R_f = 0.62 (petroleum/ Et_2O = 3:1) ^1H NMR (500 MHz, $CDCl_3$): δ = 7.12 (s, 1H), 6.30 (d, *J* = 5 Hz, 1H), 5.92 (dd, *J* = 20 Hz, 10 Hz, 1H), 5.21 (d, *J* = 10Hz, 1H), 5.17 (d, *J* =20Hz, 1H), 3.03 [d, (a,b system), *J* = 20Hz, 1H], 2.85 [d, (a,b system), *J* = 20Hz, 1H], 2.19 (s, 3H), 1.92 (s, 3H), 1.32 (s, 3H); HRMS: calcd for $C_{14}H_{17}O_4^+$ [M + H^+]: 249.1127, found 249.1119.

For compounds **11 (mixture of isomers almost 1:1 ratio)**: ^1H NMR (500 MHz, $CDCl_3$): δ = 7.14 (s, 1H), 7.11 (s, 1H), 6.13 (dd, *J* = 20Hz, *J* =15Hz, 1H), 5.80 (dd, *J* = 20Hz, *J* = 10Hz, 1H), 5.22 (m, 1H), 5.03 (d, *J* = 11Hz , 1H), 4.98 (d, *J* = 18Hz, 1H), 4.17 (brs, 1H), 3.8 (brs, 1H), 3.06 [d, (a,b system), *J* = 17Hz, 1H], 2.78 [d, (a,b system), *J* = 17Hz, 1H], 3.03 [d, (a,b system), *J* = 17Hz, 1H], 2.91 [d, (a,b system), *J* = 17Hz, 1H], 2.2 (s, 3H), 2.18 (s, 3H), 1.43 (s, 1H), 1.03 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.9, 193.9, 165.7, 165.5, 143.8, 140.3, 140.1, 138.0, 119.0, 118.9, 118.3, 117.5, 115.4, 113.5, 80.2, 78.7, 46.8, 46.5, 35.2, 35.0, 25.6, 16.3, 8.7, 8.6.



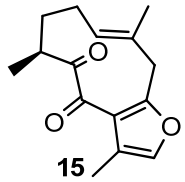
13 **14**

7-hydroxy-furanogermenone (13) and compounds 14

To a stirred solution of furanogermenone **(2)** (48 mg, 0.21 mmol) in dry THF (2 ml) was added a 1.6M solution of *n*BuLi in pentane (0.15 ml, 0.25 mmol) under argon atmosphere at -78 ^oC. After 40 min, the solution was warmed to rt for 15 min before R(-)10-camphorosulphonyl oxaziridine (56 mg, 0.25 mmol) dissolved in dry THF (0.5 ml) introduced to the reaction mixture at -78 ^oC. The reaction was stirred for 45 min at the same temperature. Then, the reaction mixture was quenched by the addition of 1.5 ml saturated aqueous sodium dicarbonate and the aqueous layer was extracted with Et_2O (3 X 7 ml). The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/ Et_2O = 100:1) provided compound **13** (21 mg, 40%) as a colourless oil, along with compound **14** (4 mg, 8%) as a colourless oil and starting material **2** (20 mg, 42%). For compound **13:** R_f = 0.18 (petroleum/ Et_2O = 3:1). $[a]^{25}_D$ = + 4.5 (c 1.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.08 (brs, 1H), 4.96 (brs, 2H), 3.91 (brs, 1H), 3.36 (d, *J* = 16Hz, 1H), 3.09 (d, *J* = 16Hz, 1H), 2.63 – 2.46 (m, 1H), 2.36 – 2.10 (m, 2H), 2.07 (s, 3H), 1.72 – 1.56 (m, 2H), 1.26 (s, 3H), 1.06 (d, *J* =

7Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.5, 154.7, 136.4, 128.8, 122.0, 117.7, 69.9, 39.88, 36.6, 33.1, 29.7, 23.1, 19.9, 17.3, 8.3; HRMS: calcd for $C_{15}H_{21}O_3^+$ [M + H^+]: 249.1490, found 249.1488. For compounds **14**: R_f = 0.27 (petroleum/ Et_2O = 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06 (brs, 1H), 5.50 (t, *J* = 7Hz, 1H), 3.35 (brs, 2H), 2.97 (d, *J* = 15Hz, 1H), 2.38 – 2.23 (m, 2H), 2.10 – 2.02 (m, 1H), 1.97 (s, 3H), 1.84 – 1.78 (m, 1H), 1.72 (s, 3H), 1.57 – 1.48 (m, 2H), 1.05 (d, *J* = 7Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 214.5, 214.0, 149.9, 146.6, 138.7, 136.9, 136.6, 132.2, 129.4, 122.9, 122.0, 116.7, 77.2, 40.6, 39.8, 39.6, 38.6, 32.4, 31.9, 29.7, 27.2, 26.5, 25.8, 23.9, 23.5, 17.8, 13.9, 9.3, 7.9.

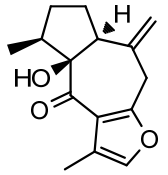
Derivatization of compound **13** using (*S*)-camphanic acid: Compound **13** (4 mg, 0.016 mmol) was dissolved in THF (0.5 ml) before (*S*)-camphanic acid (3.2 mg, 0.016 mmol) and EDC (3 mg, 0.016) introduced in the reaction mixture at rt. The reaction mixture was left for stirring at the same temperature for 12 h before quenched with saturated $NaHCO_3$ (3 ml) and extracted with Et_2O (3 x 5 ml). The combined organic extracts were dried with anhydrous sodium sulfate, filtered and evaporated *in vacuo*. Estimation of the enantiomeric excess of compound **13** was judged by the crude NMR of the reaction mixture.



15

Compound 15

To a stirred suspension of PDC (18 mg, 0.048 mmol) and silica gel (10 mg) in dry CH_2Cl_2 (1 ml) was added dropwise at room temperature a solution of the alcohol **13** (10 mg, 0.04 mmol) in dry CH_2Cl_2 (1 ml). The reaction mixture was vigorously stirred under argon atmosphere for 4h. The resulting dark brown slurry was filtered through a short column of celite, eluted with Et_2O and chromatographed on neutralized silica gel column (petroleum/ Et_2O = 100:1) to give **15** (9 mg, 90%) as a colourless oil. The compound is readily transforms to a mixture of zedoarol (**18**) and several other unidentified compounds. R_f = 0.63 (petroleum/Et_2O = 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10 (brs, 1H), 5.29 – 5.16 (m, 1H), 3.54 [d, (a,b system), *J* = 16.5Hz, 1H], 3.31 [d, (a,b system), *J* = 16.5Hz, 1H], 3.00 – 2.83(m, 1H), 2.32 –1.94 (m, 4H), 2.04 (s, 3H), 1.57 (s, 3H), 1.27 (s, 3H).



Zedoarol (**17**)

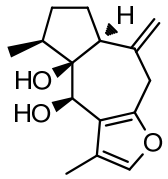
Zedoarol (17)

To a stirred suspension of PDC (55 mg, 0.15 mmol) and silica gel (30 mg) in dry CH_2Cl_2 (1 ml) was added dropwise at room temperature a solution of the alcohols **14** (30 mg, 0.12 mmol) in dry CH_2Cl_2 (1 ml). The reaction mixture was vigorously stirred under argon atmosphere for 24h. The resulting dark brown slurry was filtered through a short column of celite, eluted with Et_2O and chromatographed on neutralized silica gel column (petroleum/ Et_2O = 50:1) to give zedoarol **17** (23 mg, 77%) as a colourless oil.

Alternatively:

A stirred solution of compound **15** (10 mg, 0.04 mmol) in toluene (1 ml) was heated for 4 h at 140^{o}C. Then, the mixture was concentrated *in vacuo.* Purification by neutrlized silica gel flash column chromatography (petroleum/Et_2O = 50: 1) provided zedoarol **17** (8 mg, 80%) as a colourless oil.

R_f = 0.44 (petroleum/Et_2O = 3:1). $[a]^{25}_D$ = + 10.2 (c 1.0, $CHCl_3$) {literature[3] $[a]^{25}_D$ = + 11.6 (c 1.0)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.05 (brs, 1H) 5.30 (brs, 1H), 5.14 (brs, 1H), 3.83 [d, (a,b system), *J* = 18Hz, 1H], 3.65 [d, (a,b system), *J* = 18Hz, 1H], 2.97 (t, *J* = 9.5Hz,1H), 2.58 – 2.48 (m, 1H), 2.13 (brs, 3H), 2.06 (m, 1H), 1.92 (m, 1H), 1.90 (m, 1H), 1.46 (m, 1H), 1.14 (d, *J* = 6.7Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ =196.9, 158.3, 140.6, 138.4, 122.4, 119.7, 115.1, 84.1, 50.9, 40.5, 38.9, 29.9, 27.2, 14.3, 9.5. HRMS: calcd for $C_{15}H_{19}O_3^+$ [M + H^+]: 247.1334, found 247.1329.

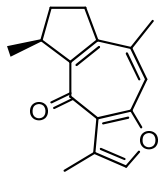


16

Compound 16

A stirred solution of **13** (20 mg, 0.08 mmol) in toluene (1.5 ml) was heated for 4 h at 140^{o}C. Then, the mixture was concentrated *in vacuo.* Purification by neutralized silica gel flash column chromatography (petroleum/Et_2O = 50: 1) provided zedoarol **17** (2 mg, 10%) as a colourless oil, **16** (13 mg, 65%) as a colourless oil. R_f = 0.30 (petroleum/Et_2O = 3:1). $[a]^{25}_D$ = + 3.1 (c 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.03 (brs, 1H), 5.21 (brs, 1H), 5.03 (brs, 1H),

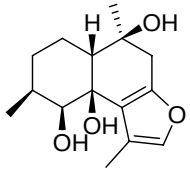
4.52 (d, *J* = 8.6Hz, 1H), 3.76 [d, (a,b system), *J* = 17.7Hz, 1H], 3.52 [d, (a,b system), *J* = 17.7Hz, 1H], 2.67 (t, *J* = 8.7Hz, 1H), 3.42 (d, *J* = 8.8Hz, 1H), 2.26 (q, *J* = 7.3Hz, 1H), 2.07 (brs, 3H), 1.95 – 1.85 (m, 1H), 1.86 – 1.76 (m, 1H), 1.15 (d, *J* = 6.9Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$)= δ 147.3, 143.2, 137.4, 122.6, 119.5, 113.1, 80.4, 74.2, 51.4, 45.9, 37.4, 31.7, 27.9, 15.5, 9.5. HRMS: calcd for $C_{15}H_{21}O_3^+$ [M + H^+]: 249.1490, found 249.1482.



19

Compound 19

A solution of zedoarol (**17**) (30 mg, 0.12 mmol) in MeOH (2.5 ml) was treated with KOH (130 mg, 2.4 mmol) at rt. The reaction was stirred at the same temperature for 30 min before quenched with saturated aqueous NH_4Cl solution and extracted with Et_2O (3 x 7 ml). The combined organic extracts were dried with anhydrous sodium sulfate, filtered and evaporated *in vacuo*. The crude mixture was purified by neutralized silica gel flash column chromatography to provide compound **19** (27 mg, 99%) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 (s, 1H), 7.24 (s, 1H), 3.66 (m, 1H), 3.15 (m, 1H), 2.98 (m, 1H), 2.45 (s, 3H), 2.32 (s, 3H), 1.52 (m, 1H), 1.53 (m, 1H), 1.23 (d, *J* = 5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$)= 179.5, 157.2, 155.3, 147.5, 141.6, 135.4, 125.5, 123.1, 122.6, 42.6, 36.8, 29.5, 24.8, 18.4, 10.6. HRMS: calcd for $C_{15}H_{17}O_2^+$ [M + H^+]: 249.1225, found 249.1228.



Compound 20

A solution of compound **13** (10 mg, 0.04 mmol) in DCM (1 ml) was treated with p-toluenesulfonic acid monohydrate (8 mg, 0.04 mmol) at 0 ^{o}C. The reaction was stirred at the same temperature for 1.5 h before quenched with $NaHCO_3$ and extracted with ether (3 x 10 ml). The combined organic extracts were dried with anhydrous sodium sulfate, filtered and evaporated *in vacuo*. The crude mixture was purified by neutralized silica gel flash column chromatography to provide compound **20** (8 mg, 75%) as a colourless oil. $[a]^{25}_D$ = -4.6 (c 0.2, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.11 (s, 1H), 4.50 (d, *J* = 12 Hz, 1H), 3.17 (s, 1H), 3.08 (d,

J = 15 Hz, 1H), 2.75 (d, *J* = 15 Hz, 1H), 2.58 (d, *J* = 9 Hz, 1H), 2.08 (s, 3H), 1.89-1.80 (m, 4H), 1.62 (m, 1H), 1.33 (s, 1H), 1.15 (d, *J* = 6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$)= 148.4, 137.7, 120.9, 120.8, 91.2, 80.8, 71.4, 46.6, 43.0, 41.6, 35.7, 24.9, 21.8, 12.7, 8.2. HRMS: calcd for $C_{15}H_{23}O_4^+$ [M + H^+]: 267.1596, found 267.1601.

NMR Comparison of synthetic and natural Zedoarol[3]

Position	^{1}H-NMR Shifts ($CDCl_3$)		^{13}C-NMR Shifts ($CDCl_3$)	
	Synthetic (500 MHz)	Natural (400 MHz)	Synthetic (125 MHz)	Natural (100 MHz)
1	2.97 (t, *J* = 9.5 Hz,1H)	2.98 (t, *J* = 9.3 Hz,1H)	50.9	50.8
2	2.06 (m, 1H); 1.90 (m, 1H)	2.05 (m, 1H); 1.90 (m, 1H)	27.2	27.2
3	1.46 (m, 1H); 1.92 (m, 1H)	1.46 (m, 1H); 1.90 (m, 1H)	29.9	29.8
4	2.58 – 2.48 (m, 1H)	2.53 (tq, *J* = 6.8, 9.2 Hz, 1H)	40.5	40.5
5	-	-	84.1	84.1
6	-	-	196.9	197.0
7	-	-	119.7	119.8
8	-	-	158.3	158.3
9	-	-	38.9	39.0
10	-	-	140.6	140.8
11	3.83 (d, *J* = 18 Hz, 1H); 3.65 (d, *J* = 18 Hz, 1H)	3.83 (d, *J* = 18.1 Hz, 1H); 3.66 (d, *J* = 18.1 Hz, 1H)	122.4	122.4
12	7.05 (brs, 1H)	7.05 (brs, 1H)	138.4	138.4
13	2.13 (brs, 3H)	2.12 (d, *J* = 1.4 Hz, 3H)	9.5	9.5
14	1.14 (d, *J* = 6.7Hz, 3H)	1.14 (d, *J* = 6.8 Hz, 3H)	14.3	14.4
15	5.30 (brs, 1H); 5.14 (brs, 1H)	5.32 (brs, 1H); 5.16 (brs, 1H)	115.1	115.2

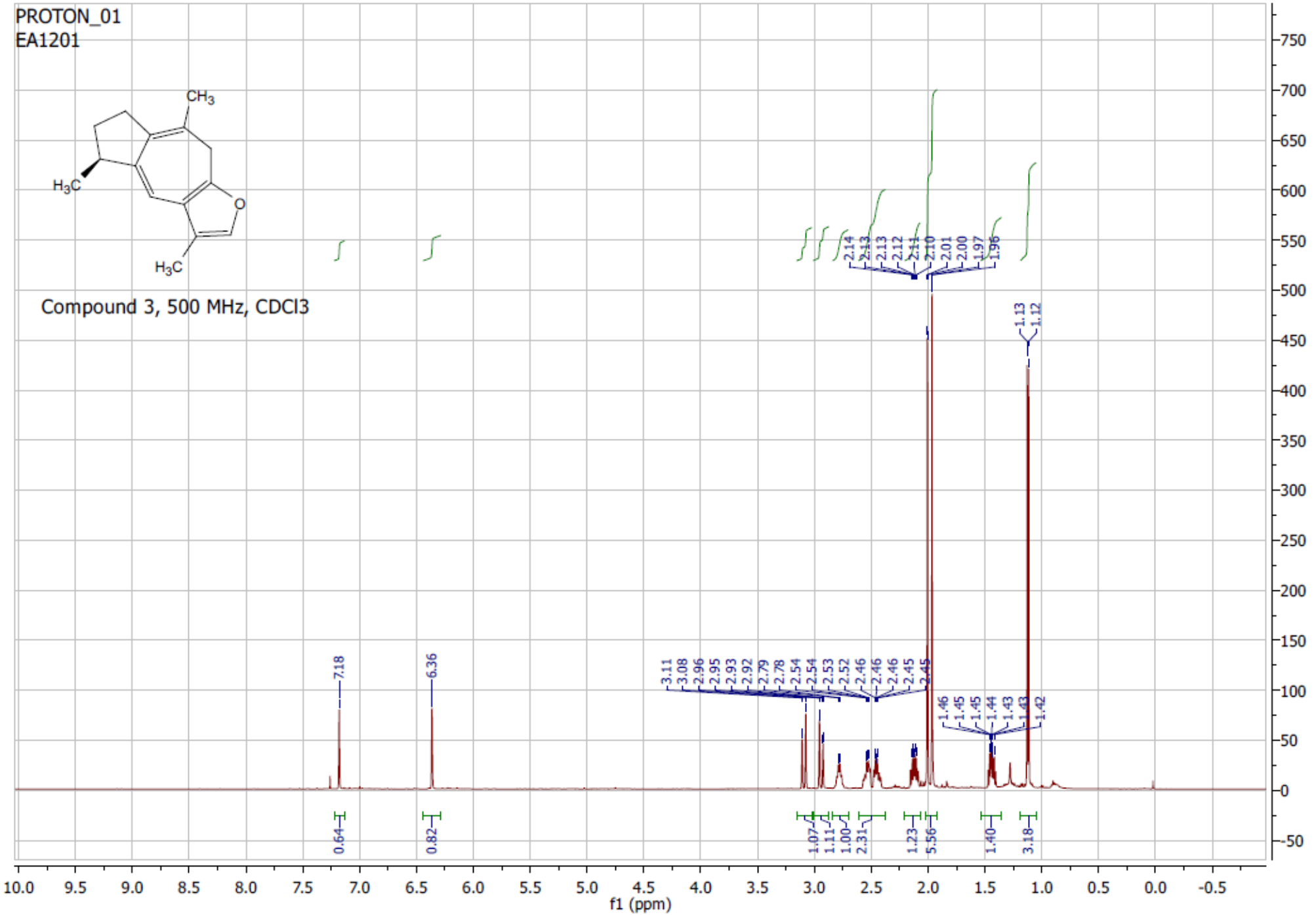
NMR Comparison of synthetic and natural Gweicurculactone[2]

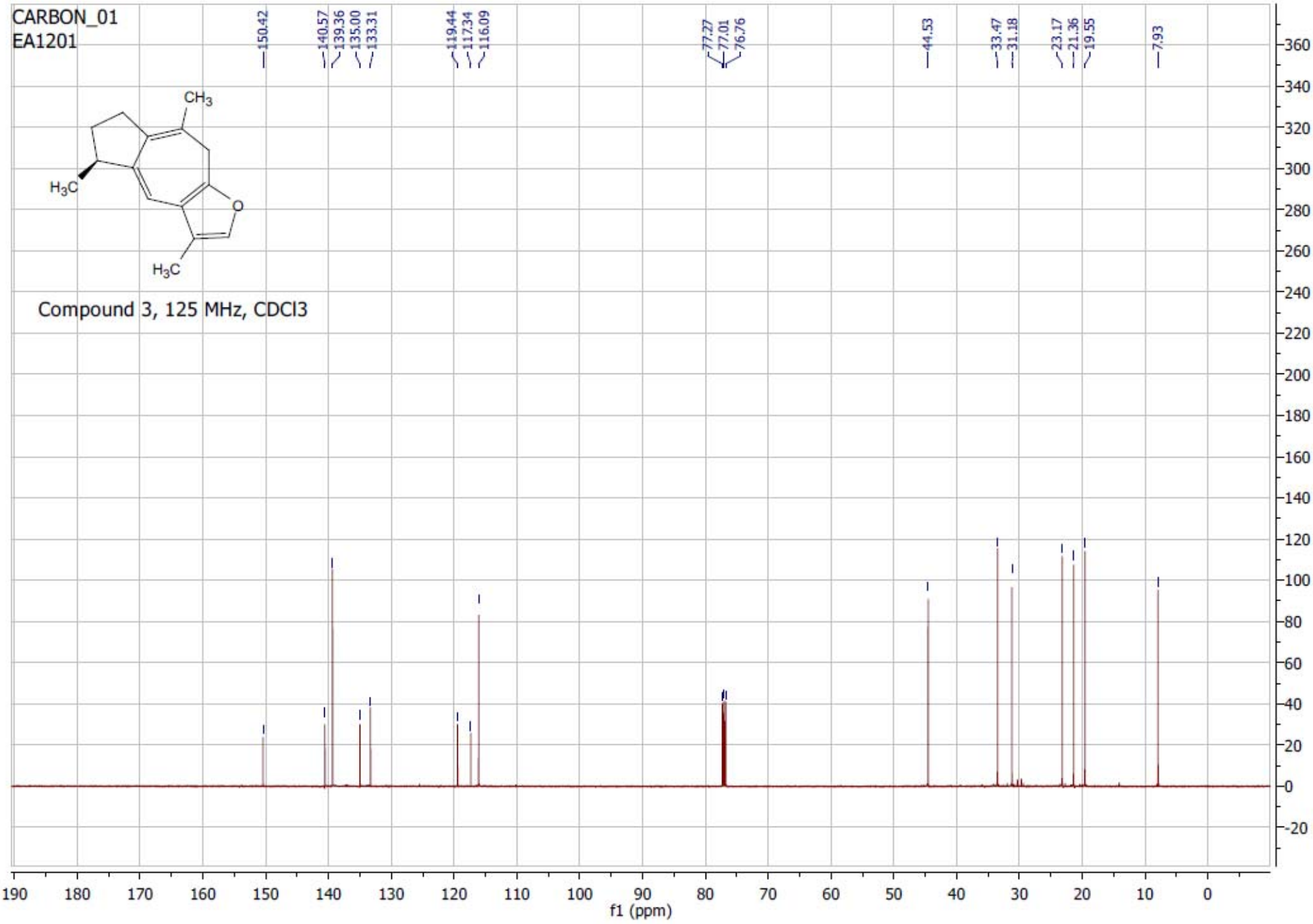
Position	^{1}H-NMR Shifts ($CDCl_3$)		^{13}C-NMR Shifts ($CDCl_3$)	
	Synthetic (500 MHz)	Natural (400 MHz)	Synthetic (125 MHz)	Natural (100 MHz)
1			146.3	146.3
2	2.71 – 2.61 (m, 1H) 2.84 – 2.74 (m, 1H)	2.66 (m, 1H) 2.83 (m, 1H)	32.1	32.0
3	1.51 (m, 1H) 2.14 – 2.05 (m, 1H)	1.51 (m, 1H) 2.10 (m, 1H)	33.8	33.8
4	3.10 – 3.00 (m, 1H)	3.07 (m, 1H)	44.0	43.9
5			156.7	156.7
6	6.86 (s, 1H)	6.86 (s, 1H)	118.0	118.0
7			154.9	154.8
8			144.3	144.4
9	6.70 (s, 1H)	6.70 (s, 1H)	116.4	116.5
10			103.7	103.6
11			136.6	136.6
12			170.7	170.8
13	2.21 (s, 3H)	2.21 (s, 3H)	7.8	7.8
14	1.28 (d, *J* = 4.8 Hz, 3H)	1.27 (d, 4.5 Hz, 3H)	24.8	24.8
15	1.95 (s, 3H)	1.95 (s, 3H)	20.2	20.2

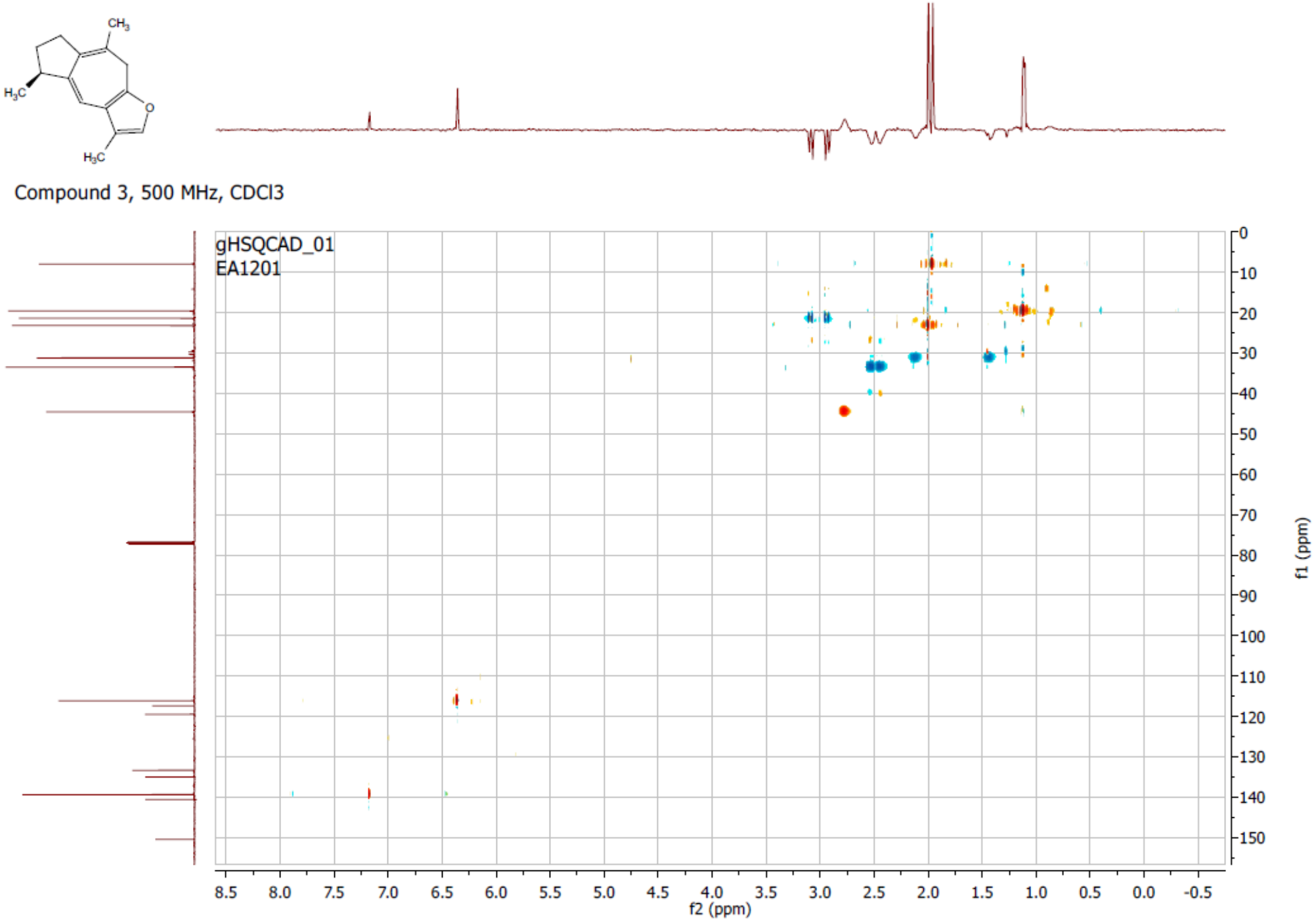
References

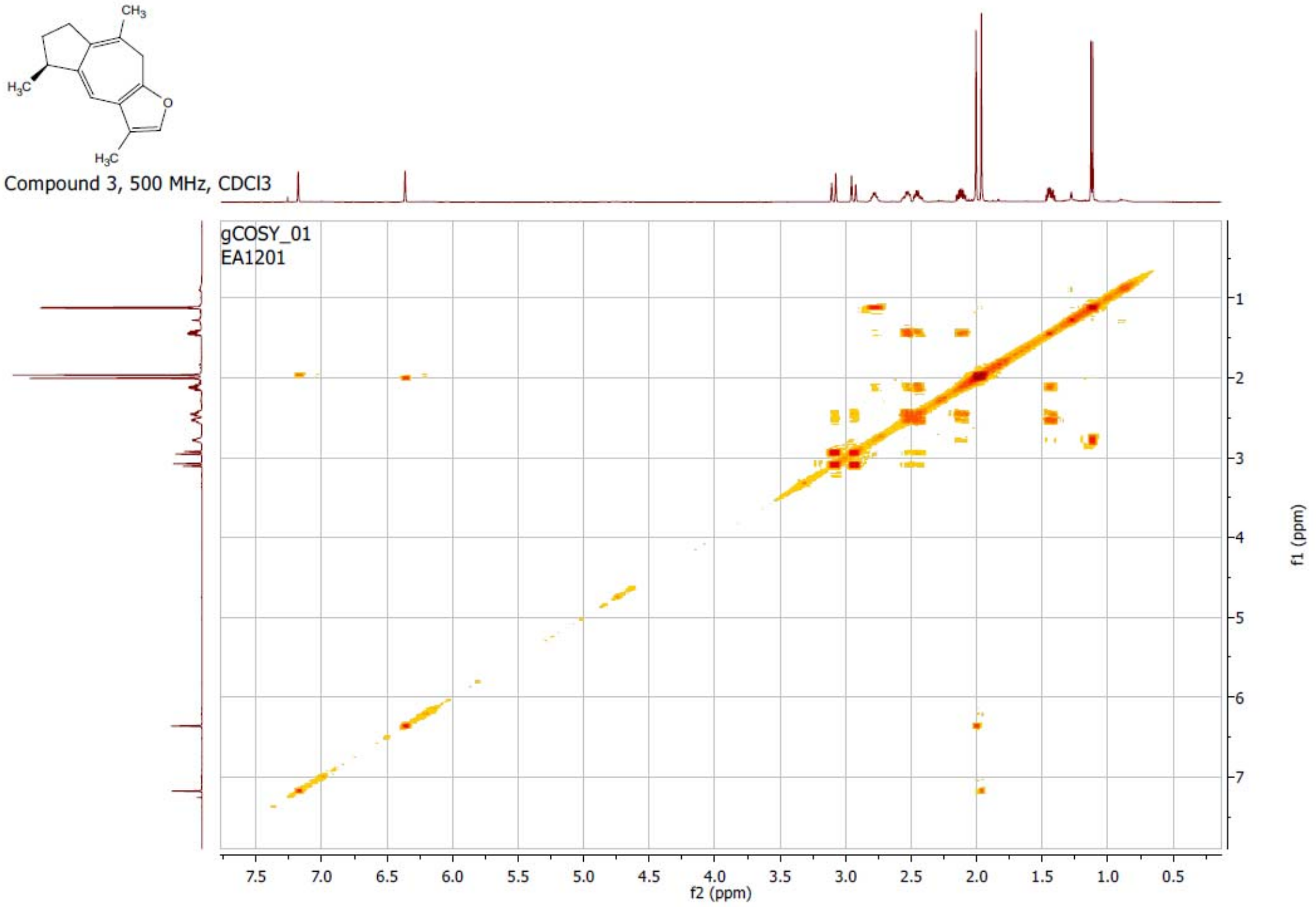
[1] Elissavet E. Anagnostaki and Alexandros L. Zografos, *Org. lett.*, **2013**, *15*, 152-155.
[2] S. D. Asem and W. S. Laitonjam, *Nat. Prod. Res*., 2014, **28**, 477-482.
[3]Y. Shiobara, S. Asakawa, M. Kodama and T. Takemoto, *Phytochemistry*, 1986, **25**, 1351-1353.

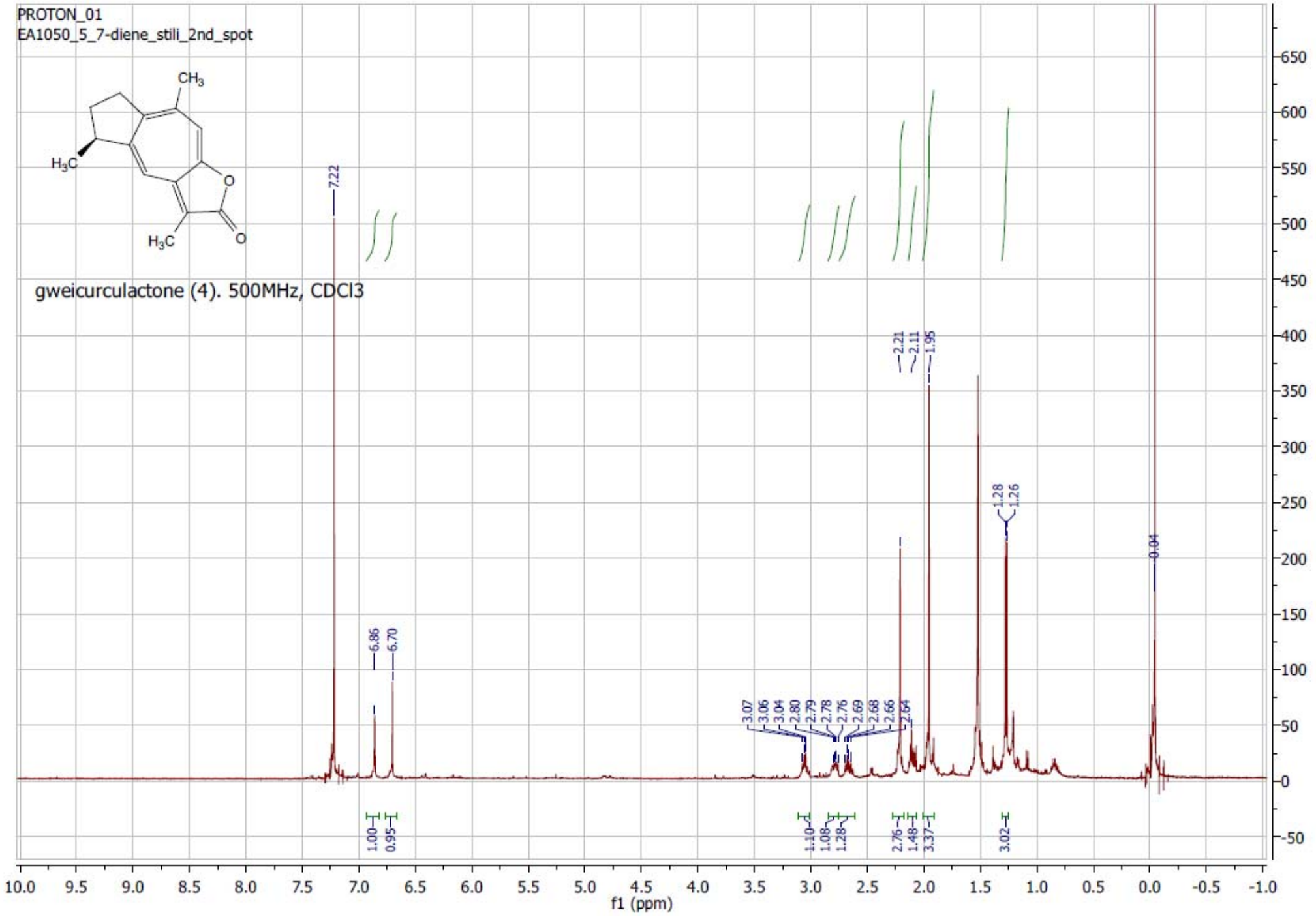
NMR Spectra of compounds

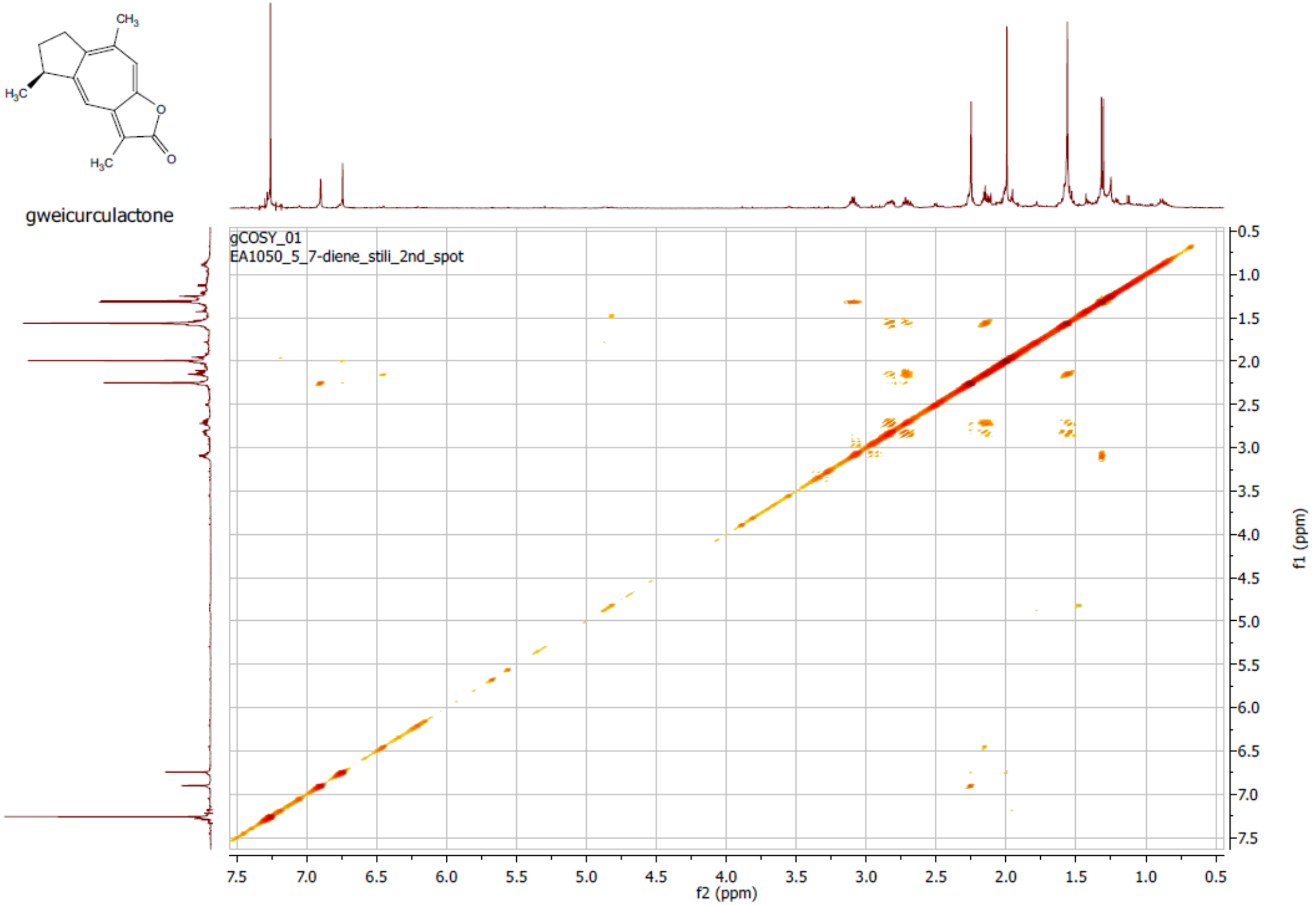

PROTON_01
EA1201
CH3
H3C
O
H3C
Compound 3, 500 MHz, CDCl3
7.18
6.36
0.64
0.82
1.07
1.11
1.00
2.31
1.23
5.56
1.40
3.18
f1 (ppm)

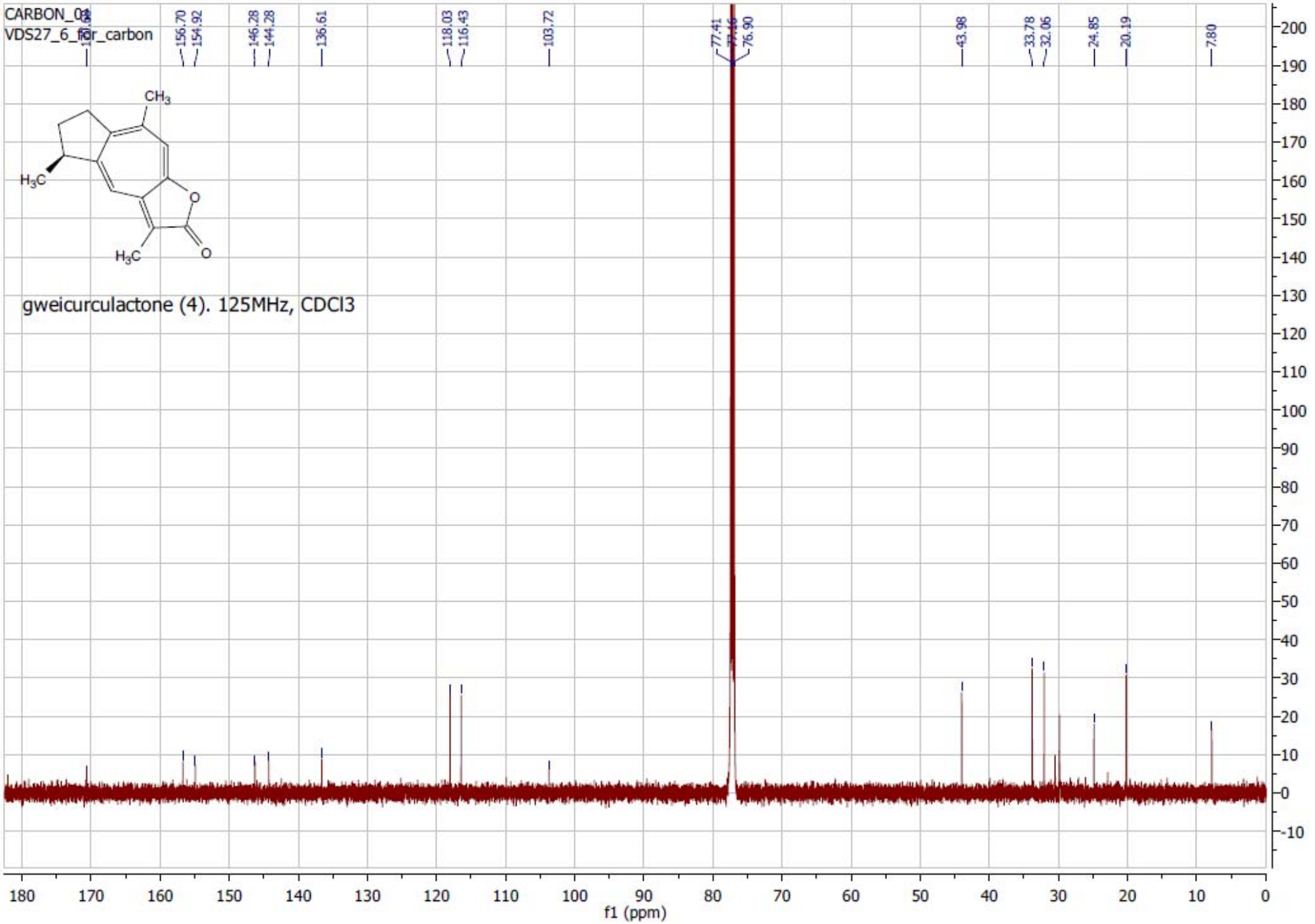

CARBON_01
EA1201
150.42
140.57
139.36
135.00
133.31
119.44
117.34
116.09
77.27
77.01
76.76
44.53
33.47
31.18
23.17
21.36
19.55
7.93
CH3
H3C
O
H3C
Compound 3, 125 MHz, CDCl3
f1 (ppm)

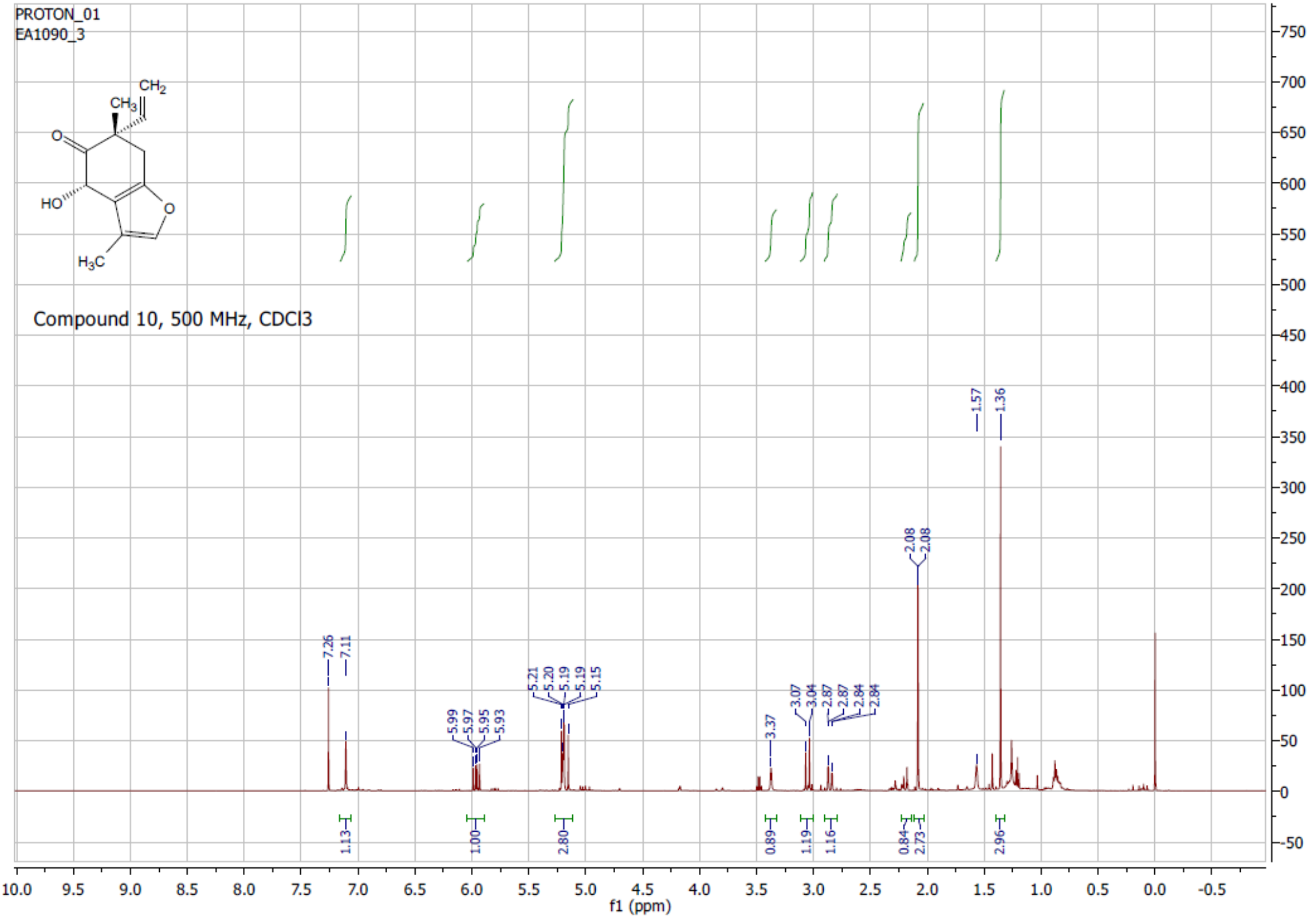

CH3
H3C
O
H3C
Compound 3, 500 MHz, CDCl3
gHSQCAD_01
EA1201
f2 (ppm)
f1 (ppm)

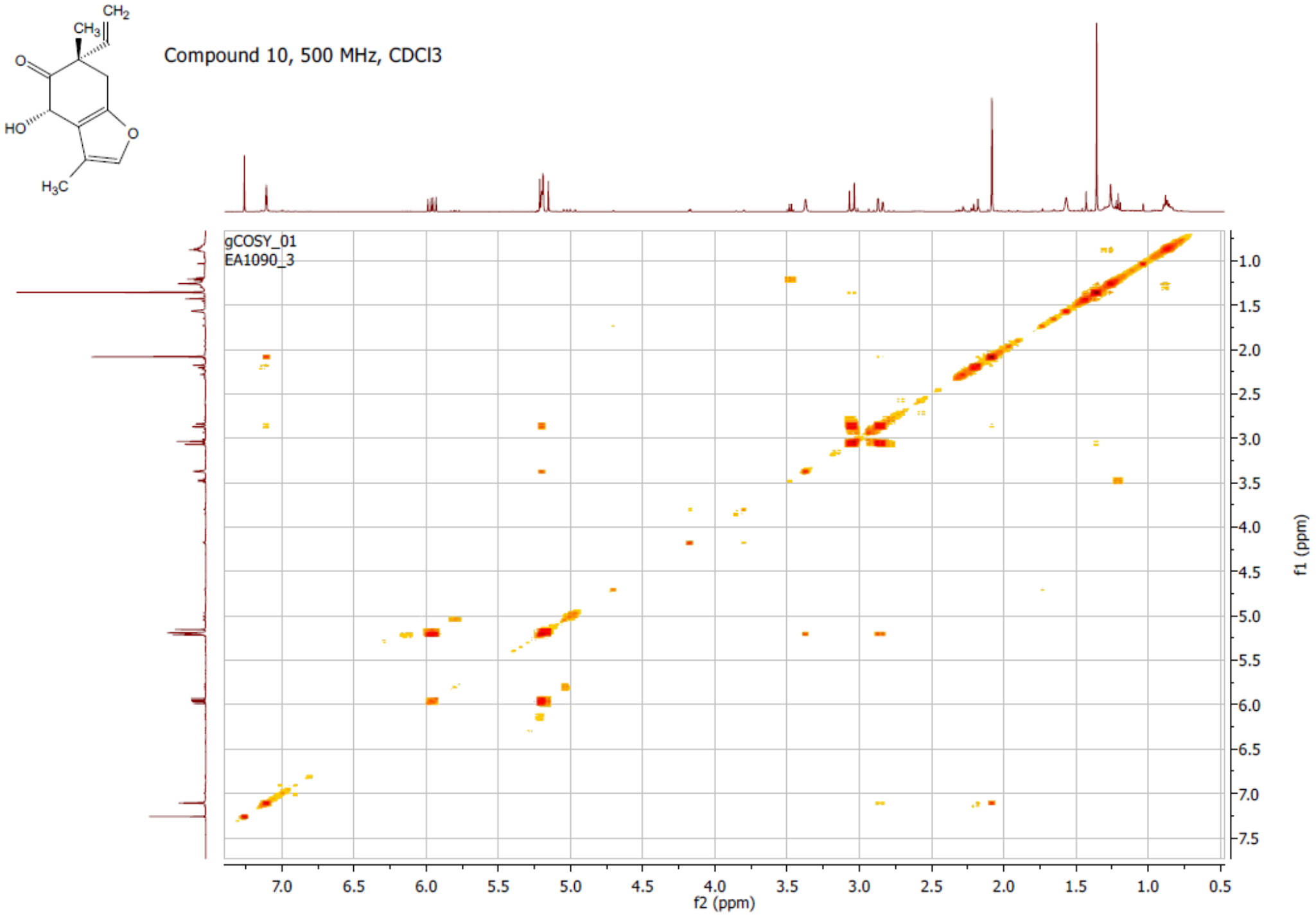

CH3
H3C
O
H3C
Compound 3, 500 MHz, CDCl3
gCOSY_01
EA1201
f2 (ppm)
f1 (ppm)

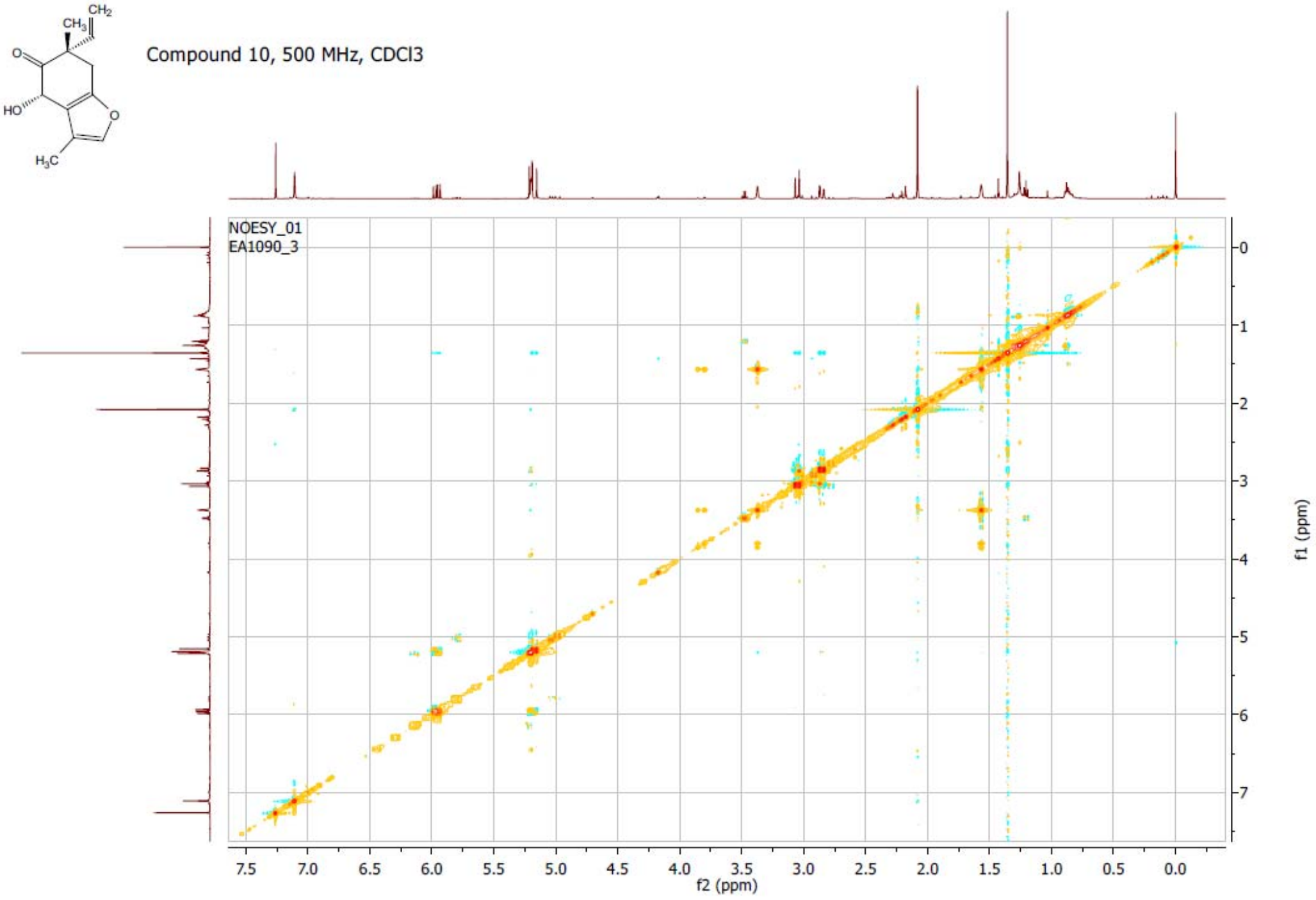

PROTON_01
EA1050_5_7-diene_stili_2nd_spot
CH3
H3C
O
O
H3C
gweicurculactone (4). 500MHz, CDCl3
7.22
6.86
6.70
3.07
3.06
3.04
2.80
2.79
2.78
2.76
2.69
2.68
2.66
2.64
2.21
2.11
1.95
1.28
1.26
0.04
1.00
0.95
1.10
1.08
1.28
2.76
1.48
3.37
3.02
f1 (ppm)

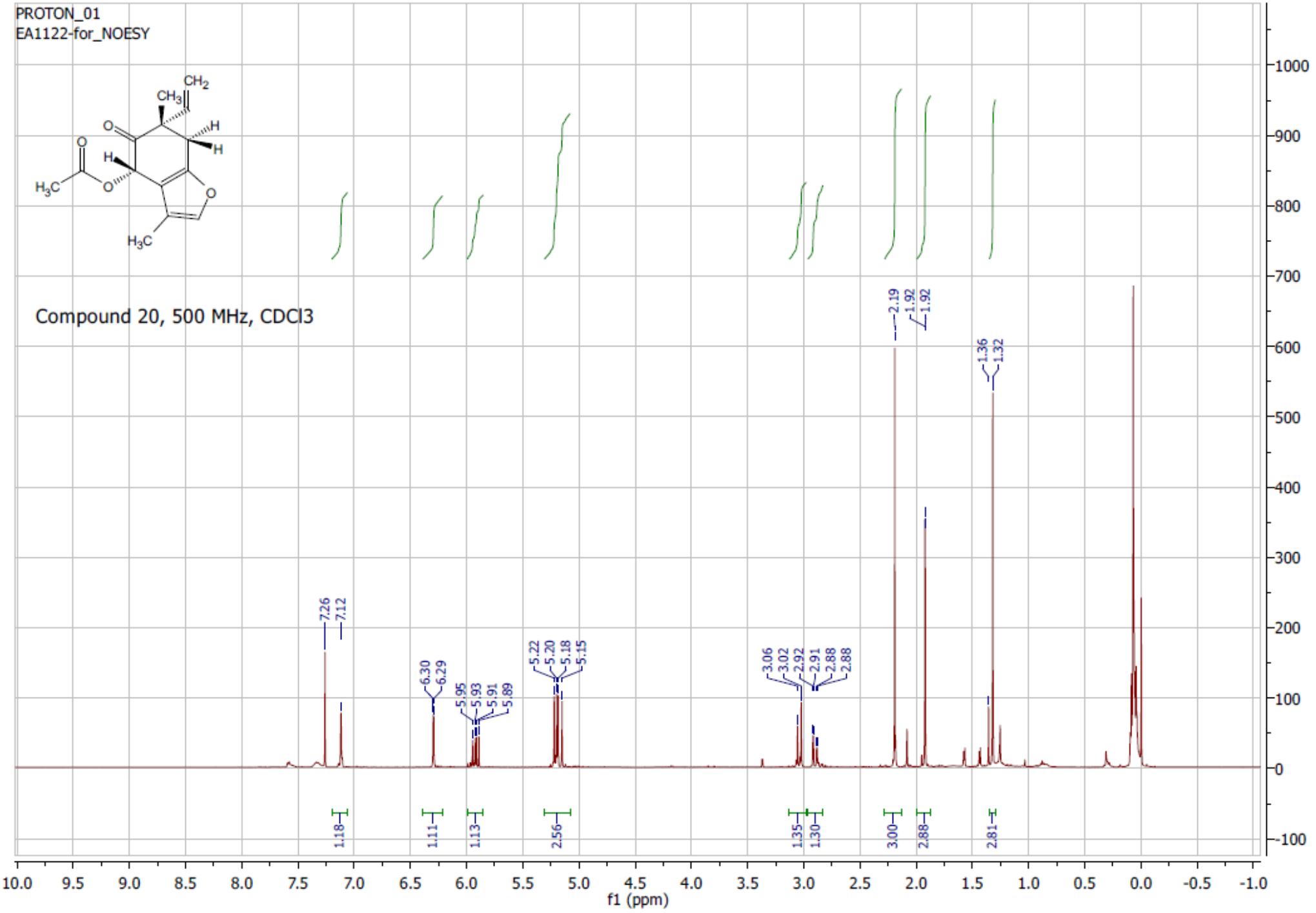

gweicurculactone
gCOSY_01
EA1050_5_7-diene_stili_2nd_spot
f2 (ppm)
f1 (ppm)

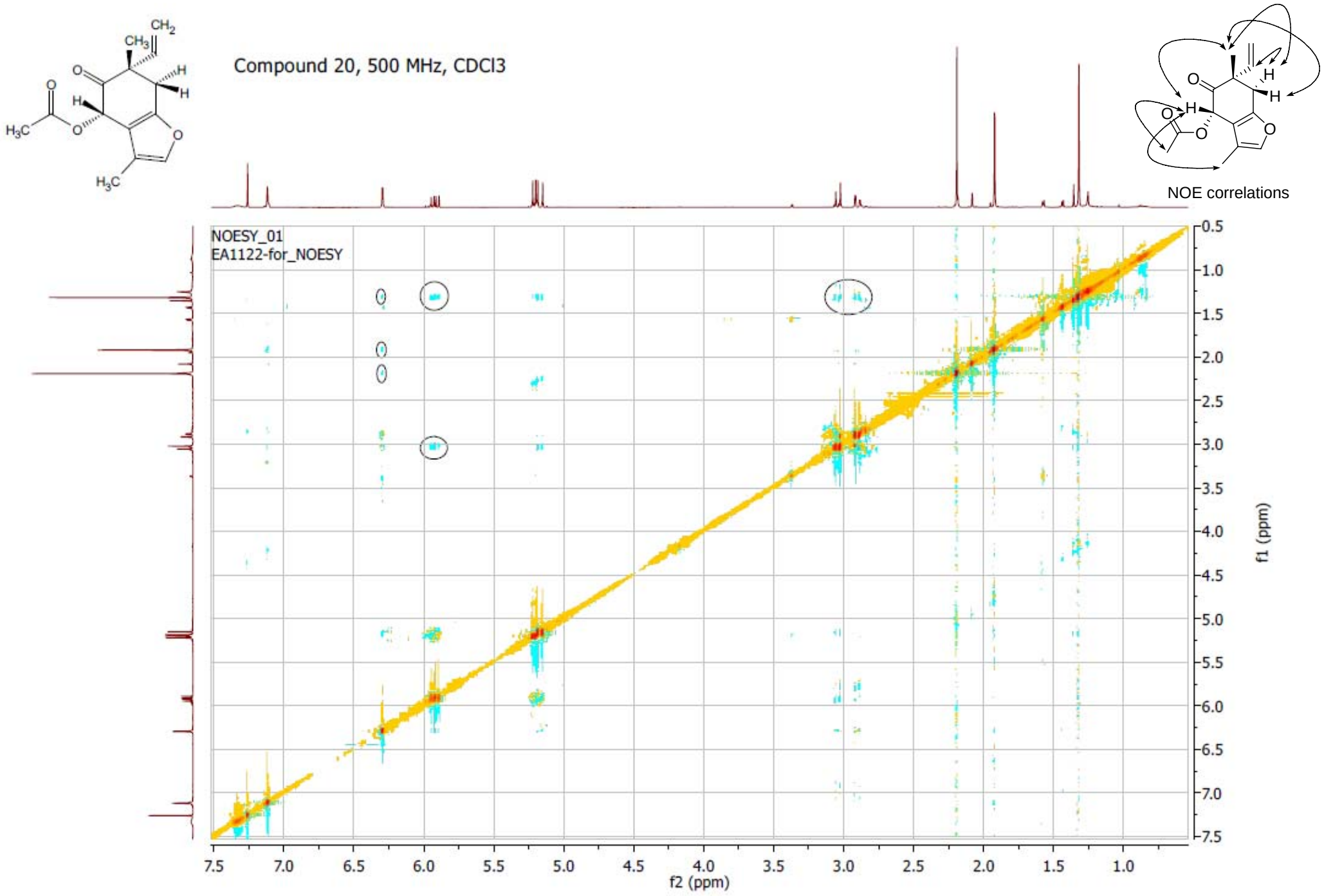

CARBON_01
VDS27_6_for_carbon
156.70
154.92
146.28
144.28
136.61
118.03
116.43
103.72
77.41
77.16
76.90
43.98
33.78
32.06
24.85
20.19
7.80
CH3
H3C
O
O
H3C
gweicurculactone (4). 125MHz, CDCl3
f1 (ppm)

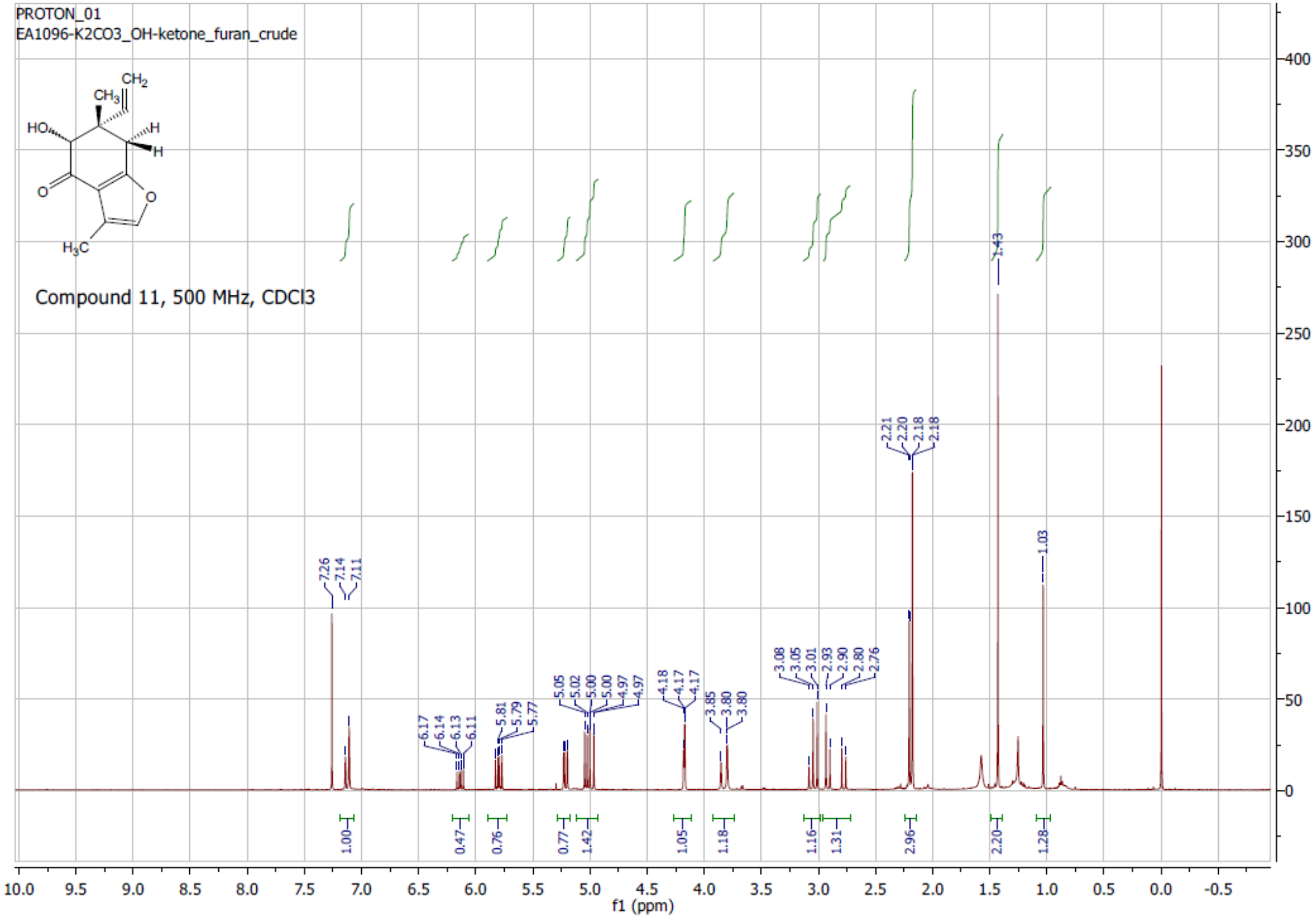

PROTON_01
EA1090_3
Compound 10, 500 MHz, CDCl3
f1 (ppm)

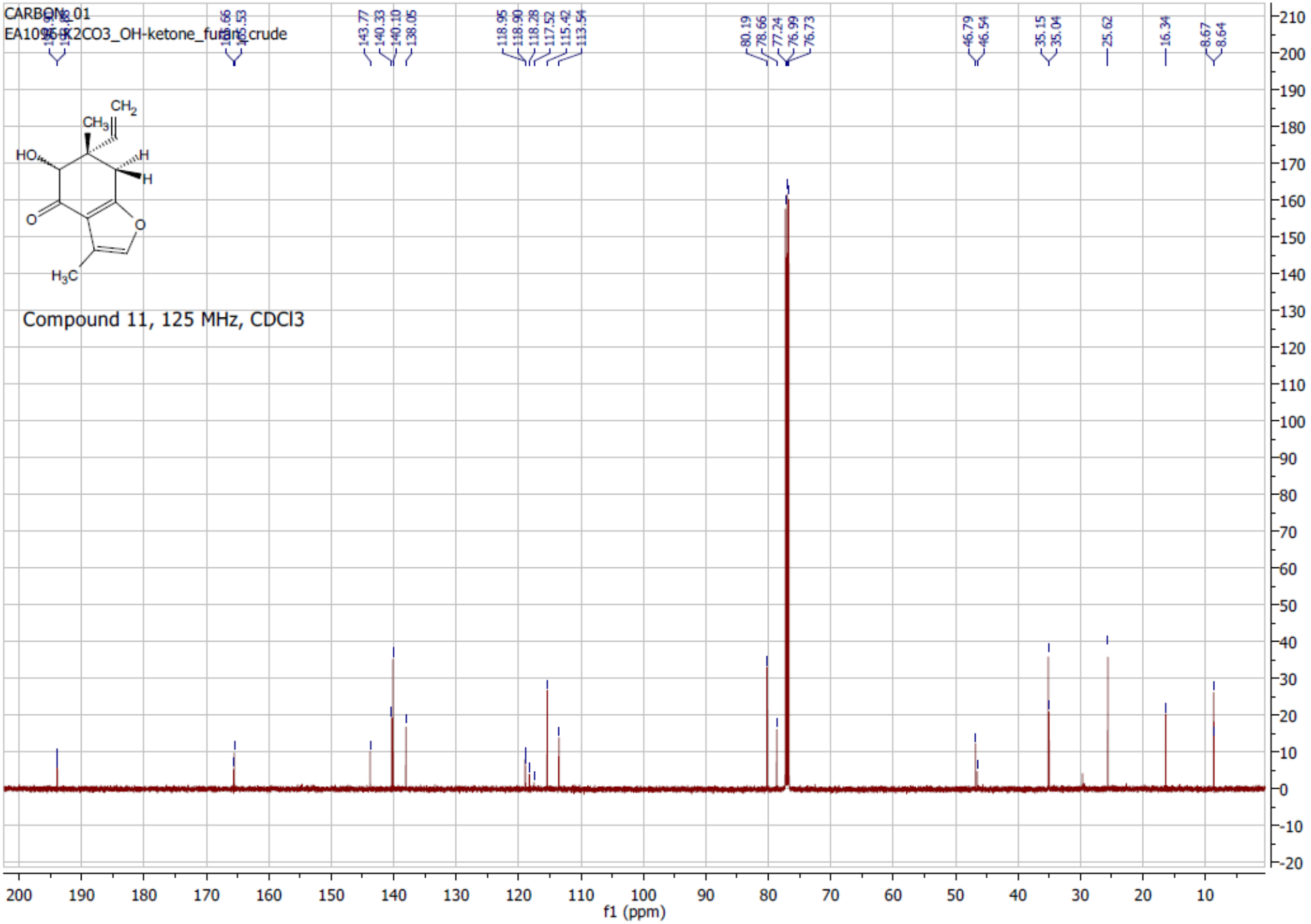

Compound 10, 500 MHz, CDCl3
gCOSY_01
EA1090_3
f2 (ppm)
f1 (ppm)

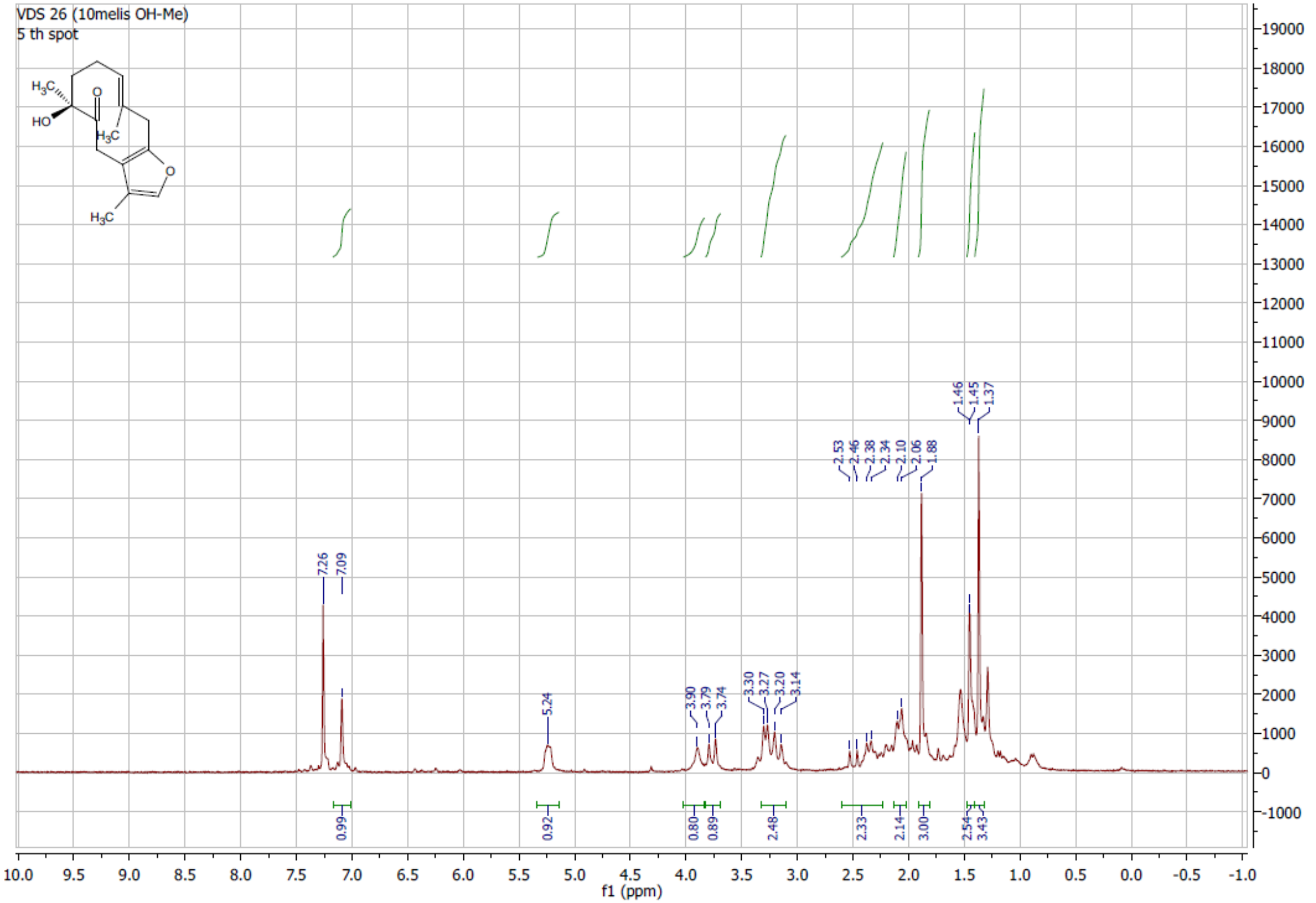

Compound 10, 500 MHz, CDCl3
NOESY_01
EA1090_3
f2 (ppm)
f1 (ppm)

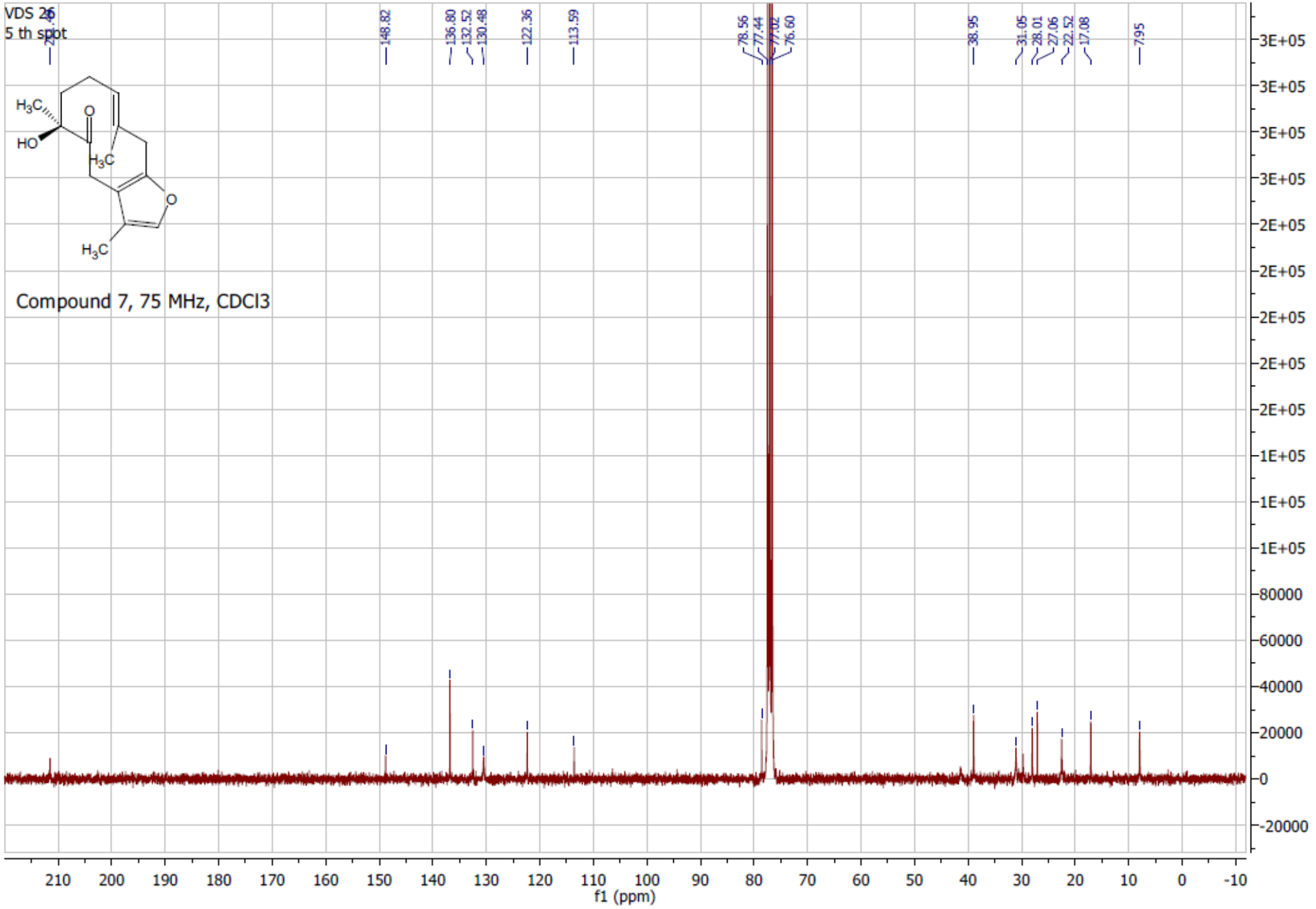

PROTON_01
EA1122-for_NOESY
Compound 20, 500 MHz, CDCl3
7.26
7.12
6.30
6.29
5.95
5.93
5.91
5.89
5.22
5.20
5.18
5.15
3.06
3.02
2.92
2.91
2.88
2.88
2.19
1.92
1.92
1.36
1.32
1.18
1.11
1.13
2.56
1.35
1.30
3.00
2.88
2.81
f1 (ppm)

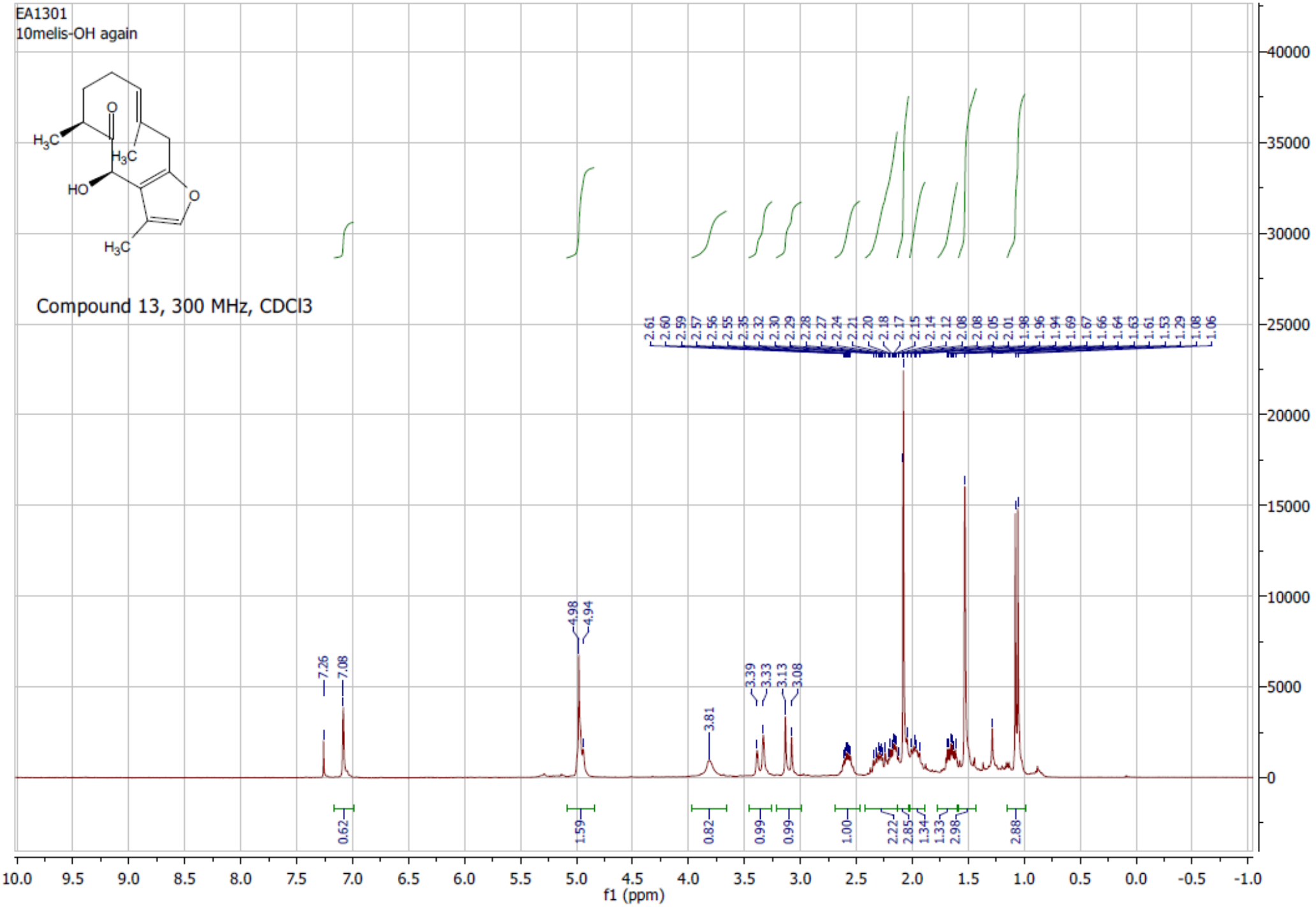

Compound 20, 500 MHz, CDCl3
NOESY_01
EA1122-for_NOESY
NOE correlations
f2 (ppm)
f1 (ppm)

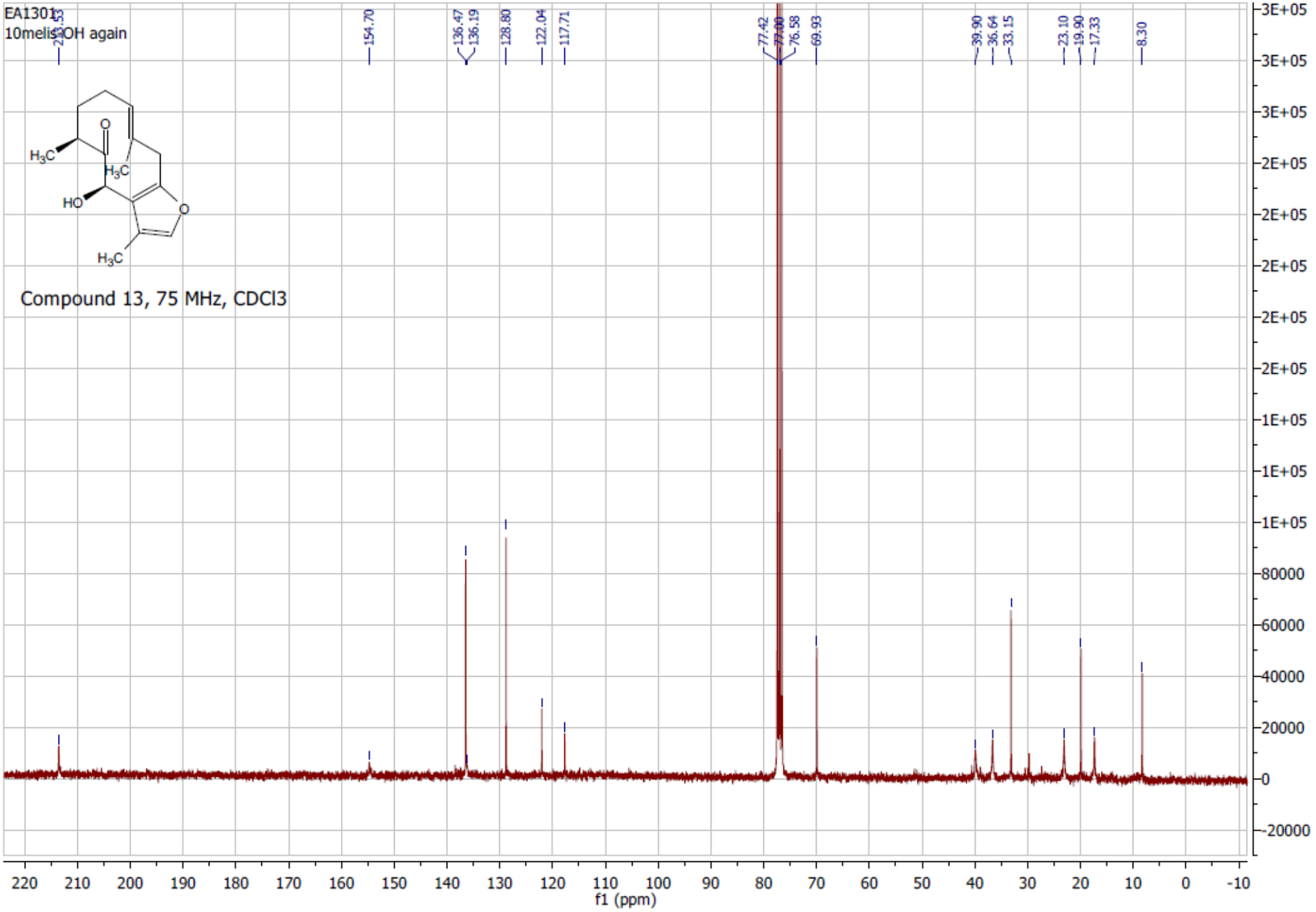

PROTON_01
EA1096-K2CO3_OH-ketone_furan_crude
Compound 11, 500 MHz, CDCl3
f1 (ppm)

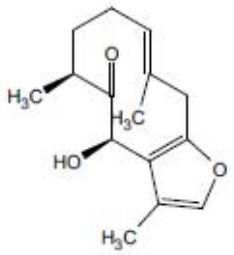

CARBON_01
EA10954K2CO3_OH-ketone_furan_crude
143.77
140.33
140.10
138.05
118.95
118.90
118.28
117.52
115.42
113.54
80.19
78.66
77.24
76.99
76.73
46.79
46.54
35.15
35.04
25.62
16.34
8.67
8.64
Compound 11, 125 MHz, CDCl3
f1 (ppm)


VDS 26 (10melis OH-Me)
5 th spot
H3C
O
HO
H3C
O
H3C
7.26
7.09
5.24
3.90
3.79
3.74
3.30
3.27
3.20
3.14
2.53
2.46
2.38
2.34
2.10
2.06
1.88
1.46
1.45
1.37
0.99
0.92
0.80
0.89
2.48
2.33
2.14
3.00
2.54
3.43
f1 (ppm)

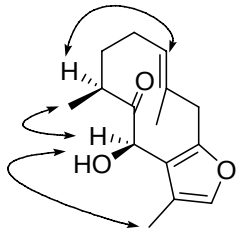

VDS 26
5 th spot
Compound 7, 75 MHz, CDCl3
148.82
136.80
132.52
130.48
122.36
113.59
78.56
77.44
77.02
76.60
38.95
31.05
28.01
27.06
22.52
17.08
7.95
f1 (ppm)


EA1301
10melis-OH again
Compound 13, 300 MHz, CDCl3
f1 (ppm)

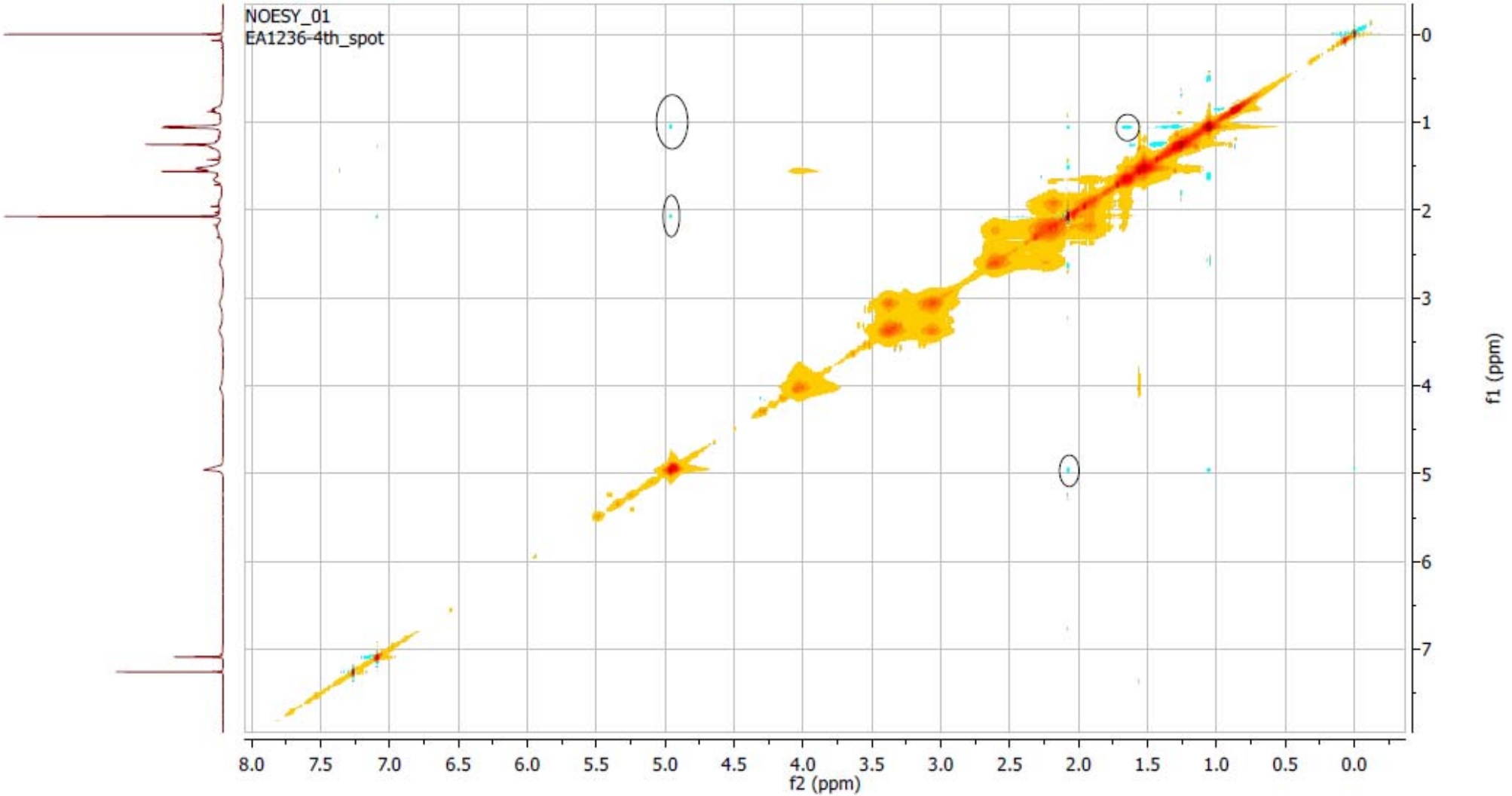

EA1301
10melisOH again
154.70
136.47
136.19
128.80
122.04
117.71
77.42
77.00
76.58
69.93
39.90
36.64
33.15
23.10
19.90
17.33
8.30
O
H3C
H3C
HO
O
H3C
Compound 13, 75 MHz, CDCl3
f1 (ppm)

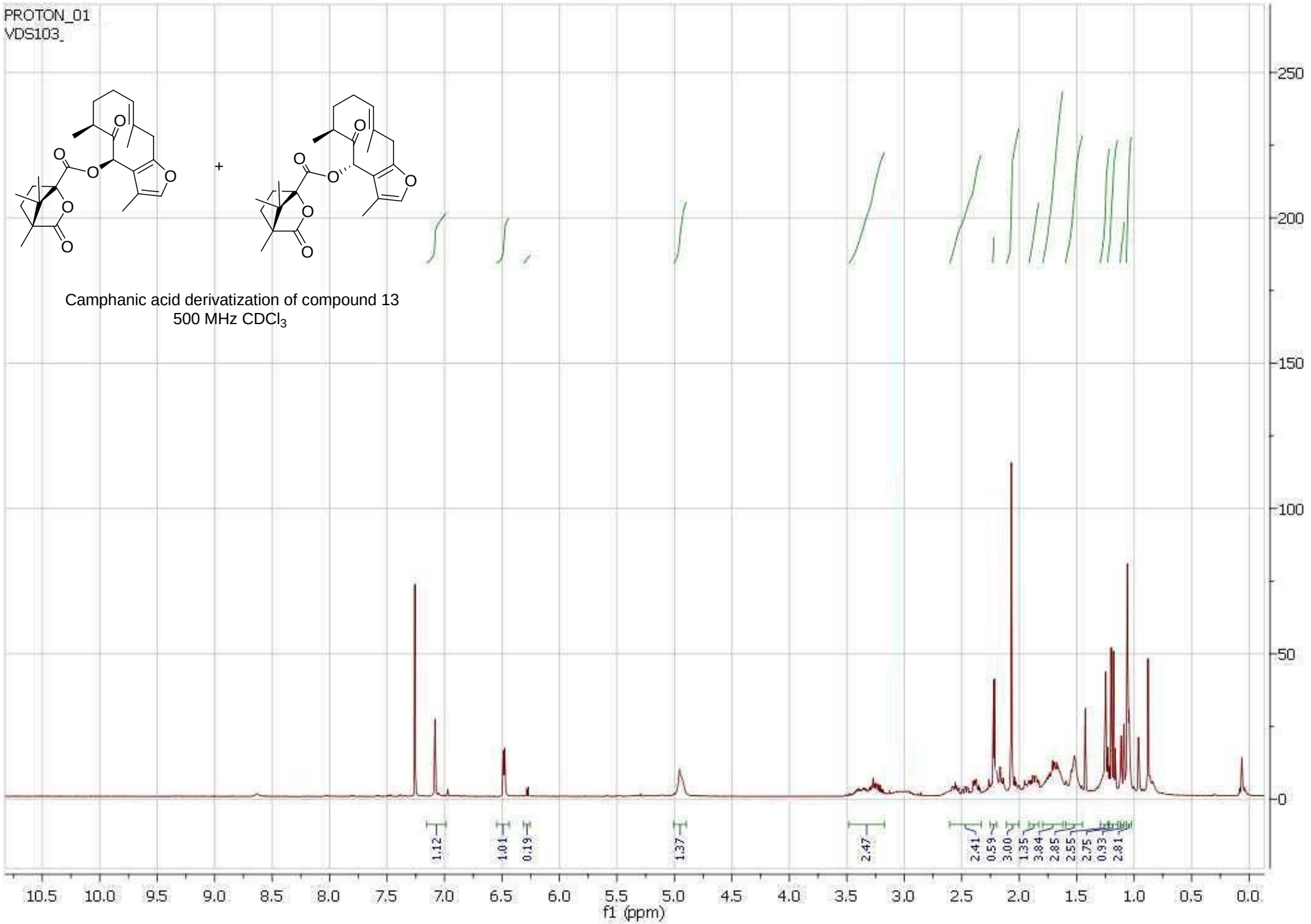


Compound 13, 500 MHz, CDCl3

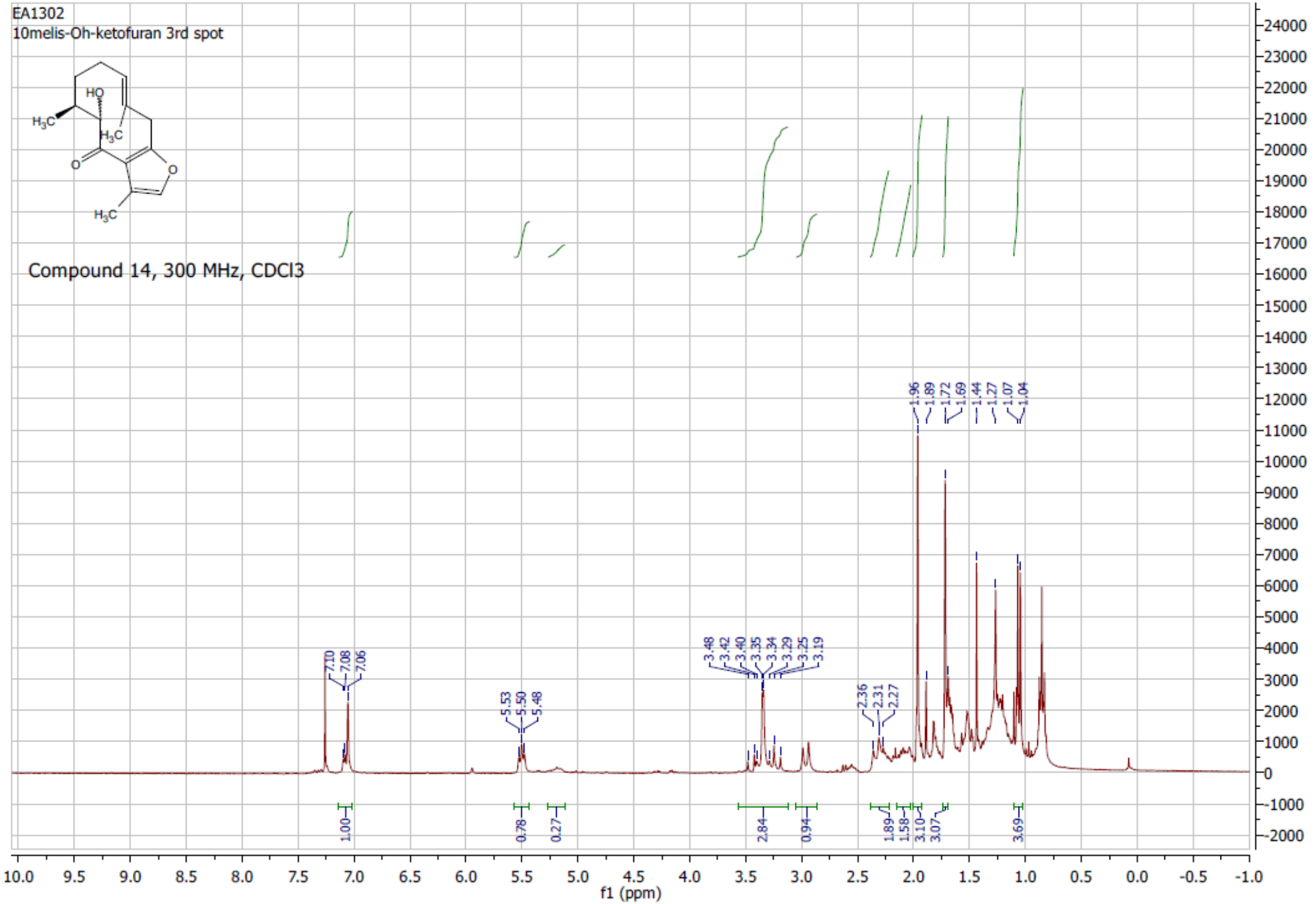


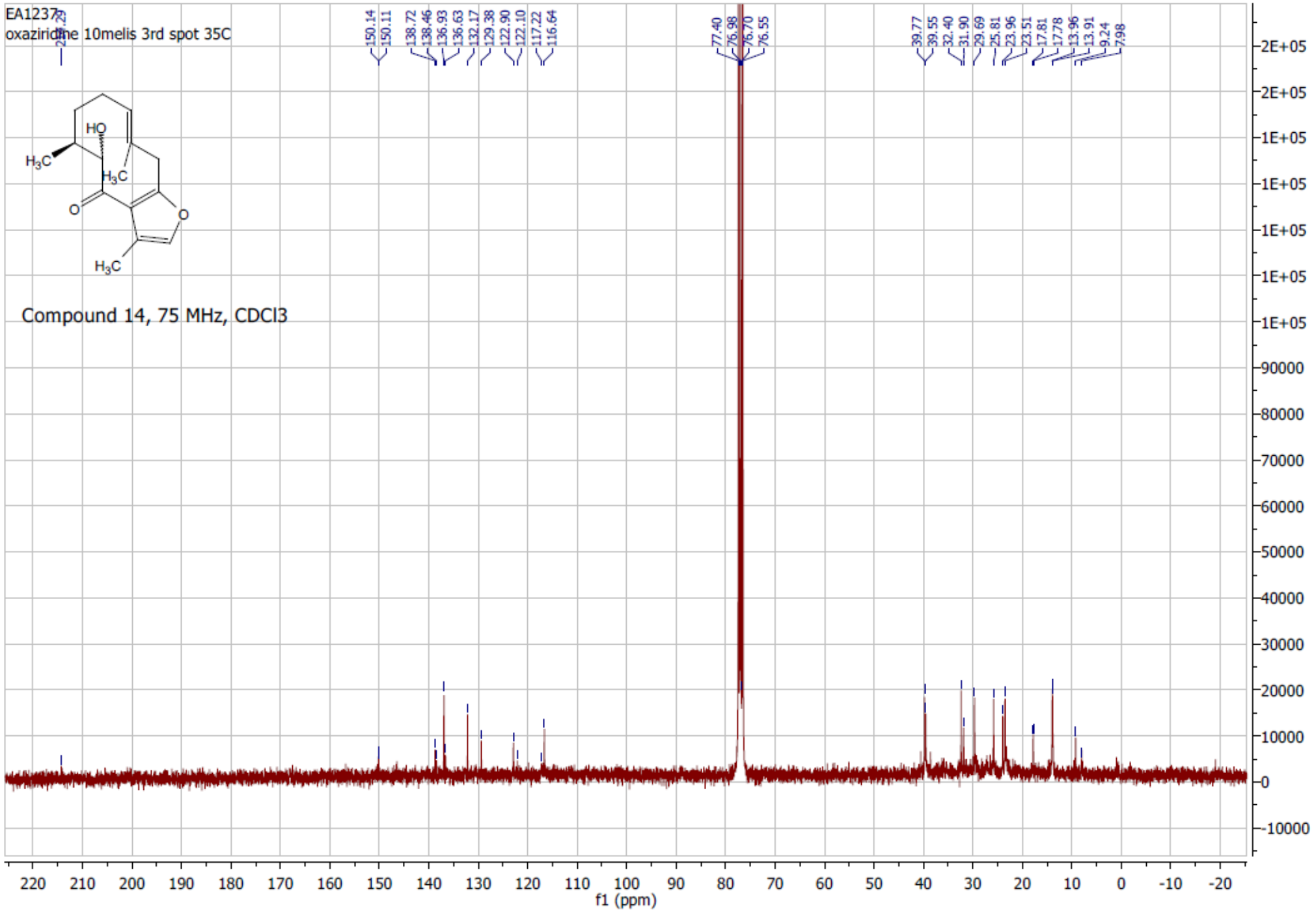
NOE correlations

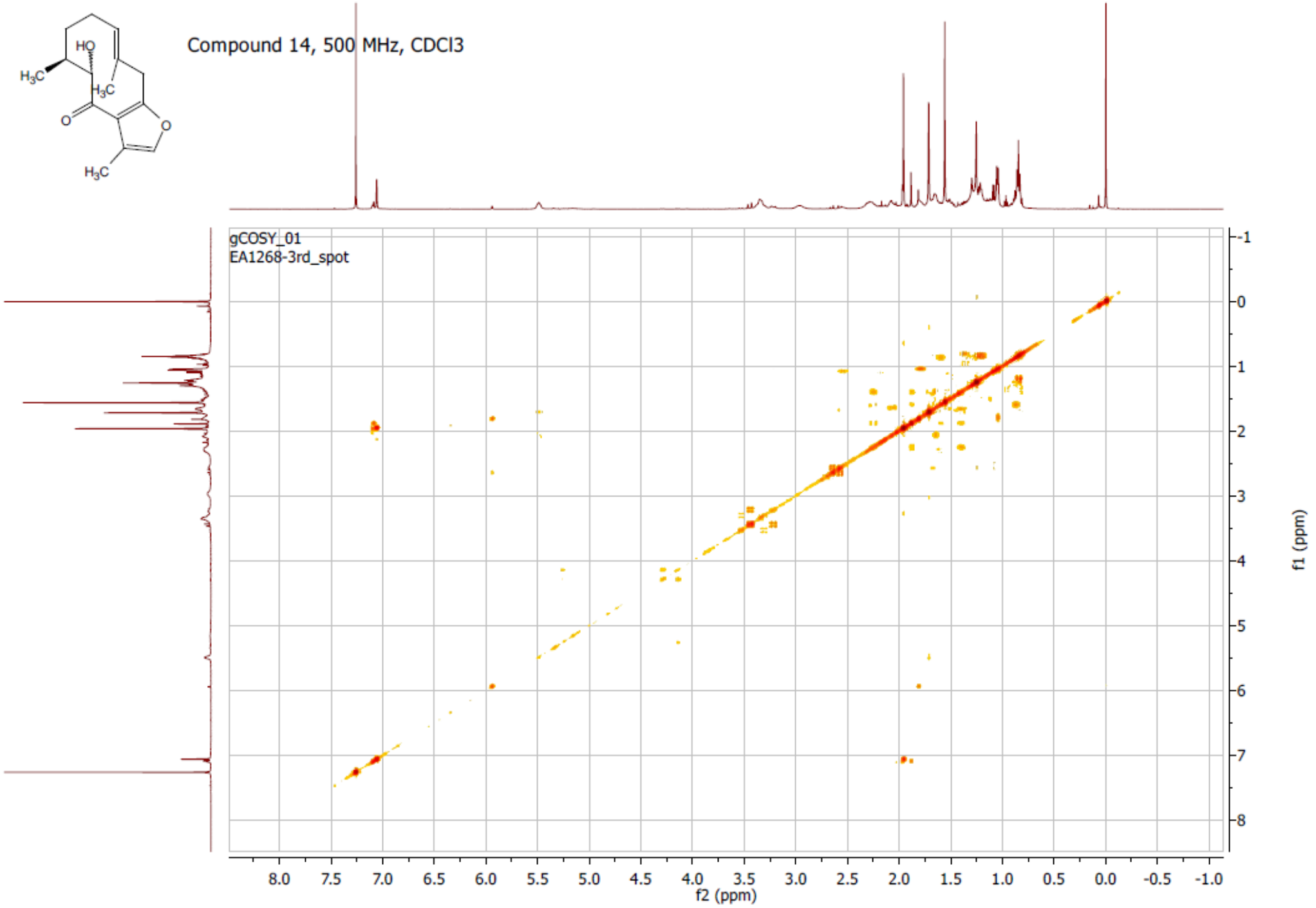


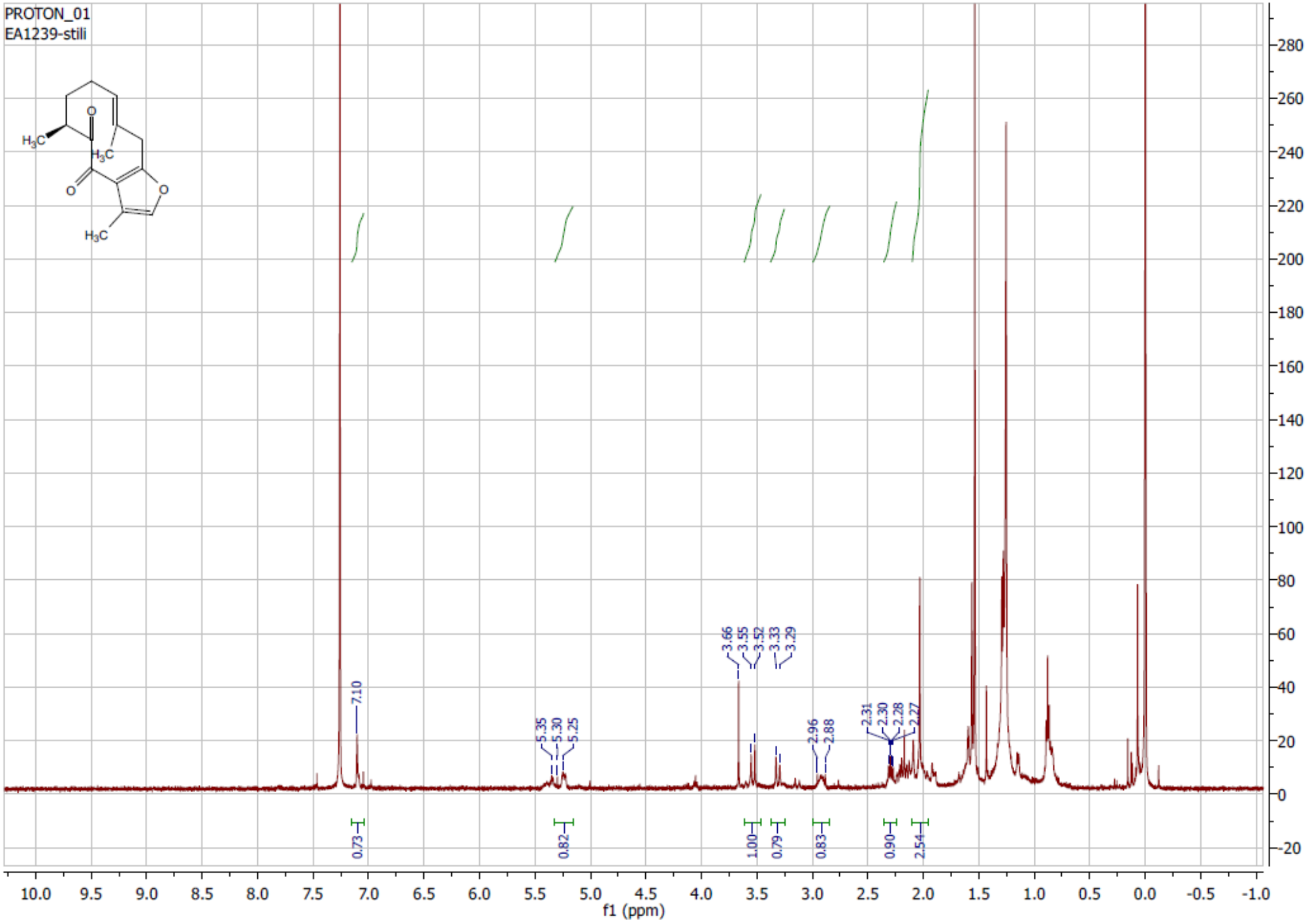


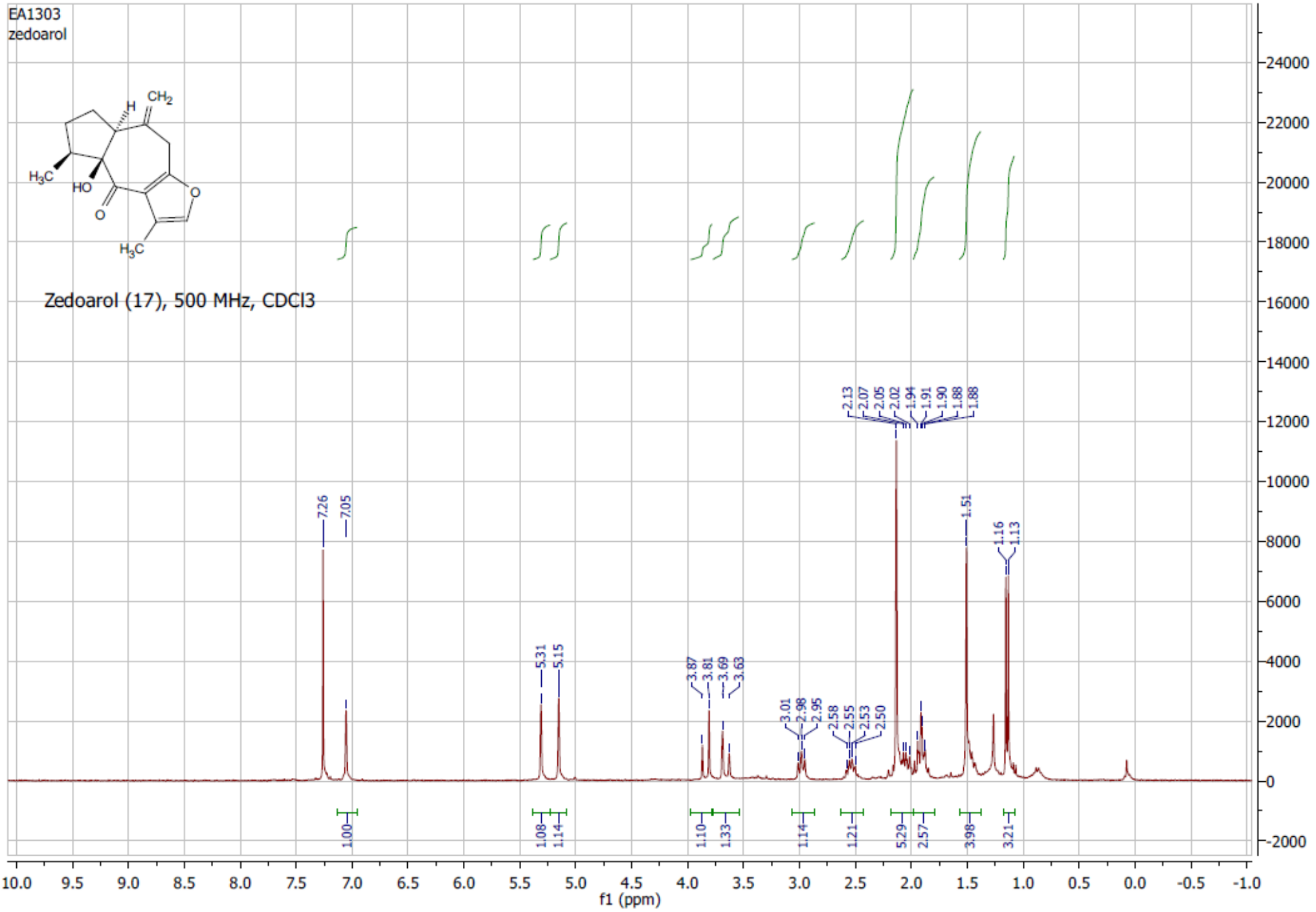
Camphanic acid derivatization of compound 13
500 MHz $CDCl_3$

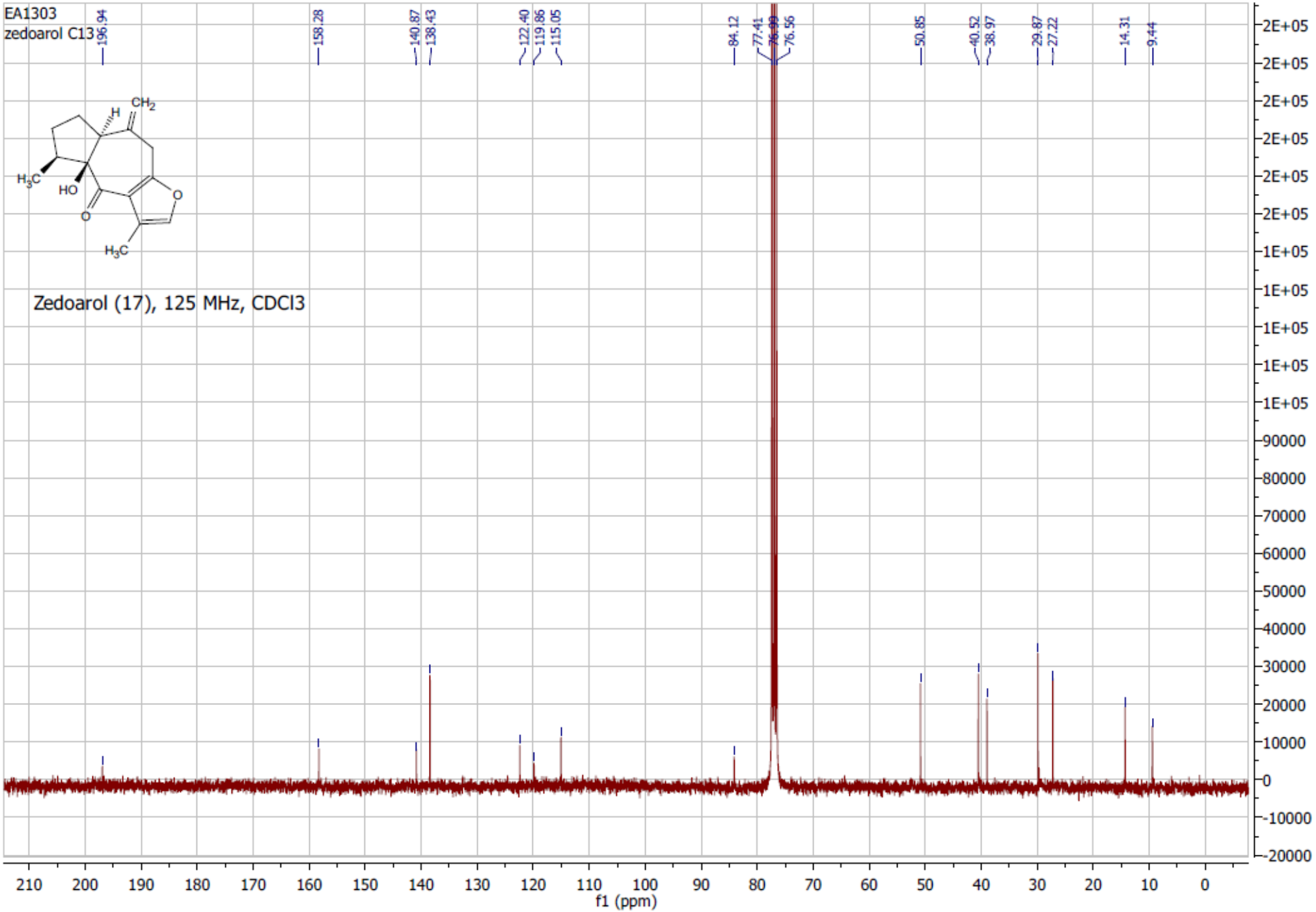

EA1302
10melis-Oh-ketofuran 3rd spot
HO
H3C
H3C
O
O
H3C
Compound 14, 300 MHz, CDCl3
7.10
7.08
7.06
5.53
5.50
5.48
3.48
3.42
3.40
3.35
3.34
3.29
3.25
3.19
2.36
2.31
2.27
1.96
1.89
1.72
1.69
1.44
1.27
1.07
1.04
1.00
0.78
0.27
2.84
0.94
1.89
1.58
3.10
3.07
3.69
f1 (ppm)

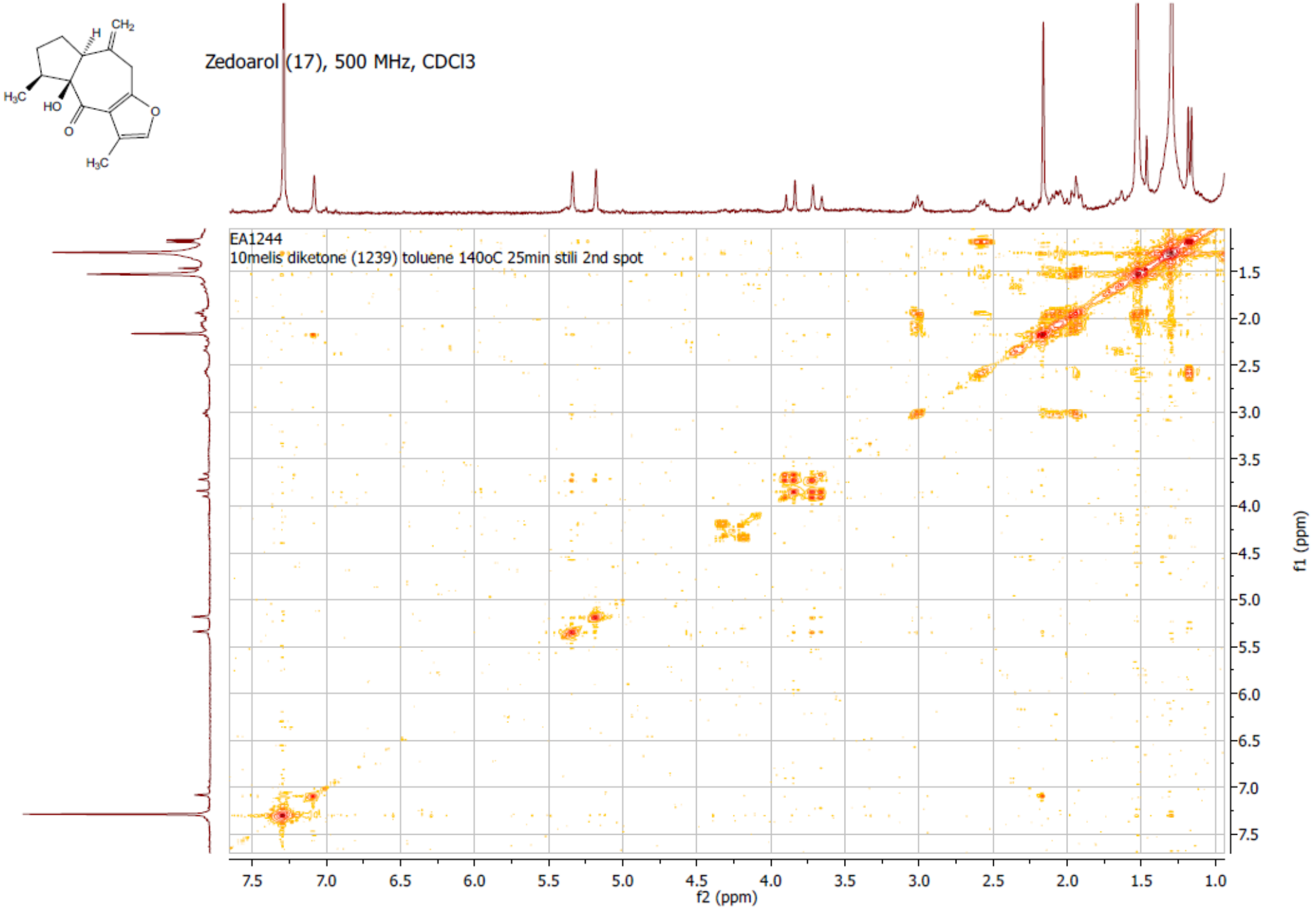

EA1237
oxaziridine 10melis 3rd spot 35C
Compound 14, 75 MHz, CDCl3
f1 (ppm)

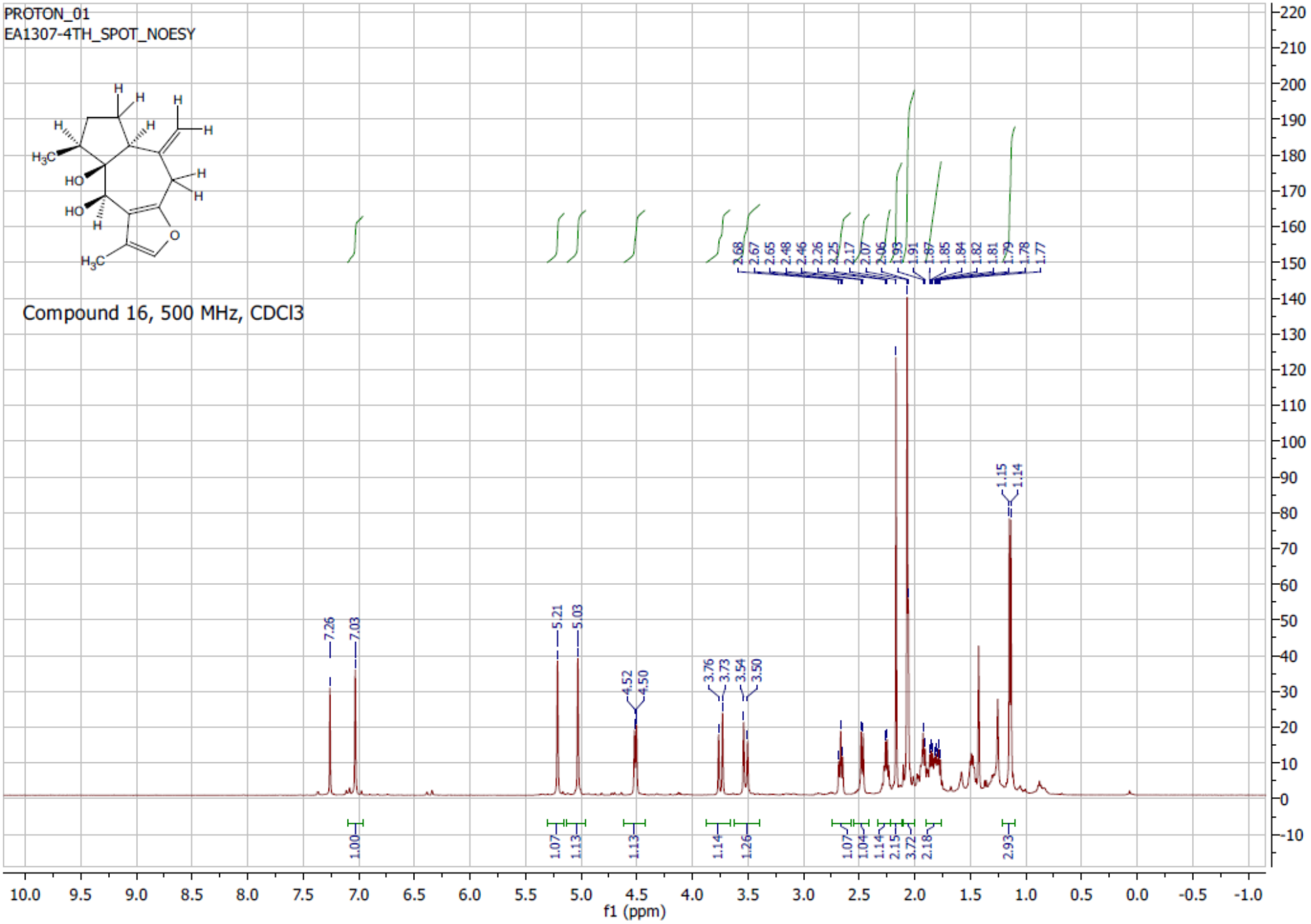

Compound 14, 500 MHz, CDCl3
gCOSY_01
EA1268-3rd_spot
HO
H3C
H3C
O
O
H3C
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f2 (ppm)
-1
0
1
2
3
4
5
6
7
8
f1 (ppm)

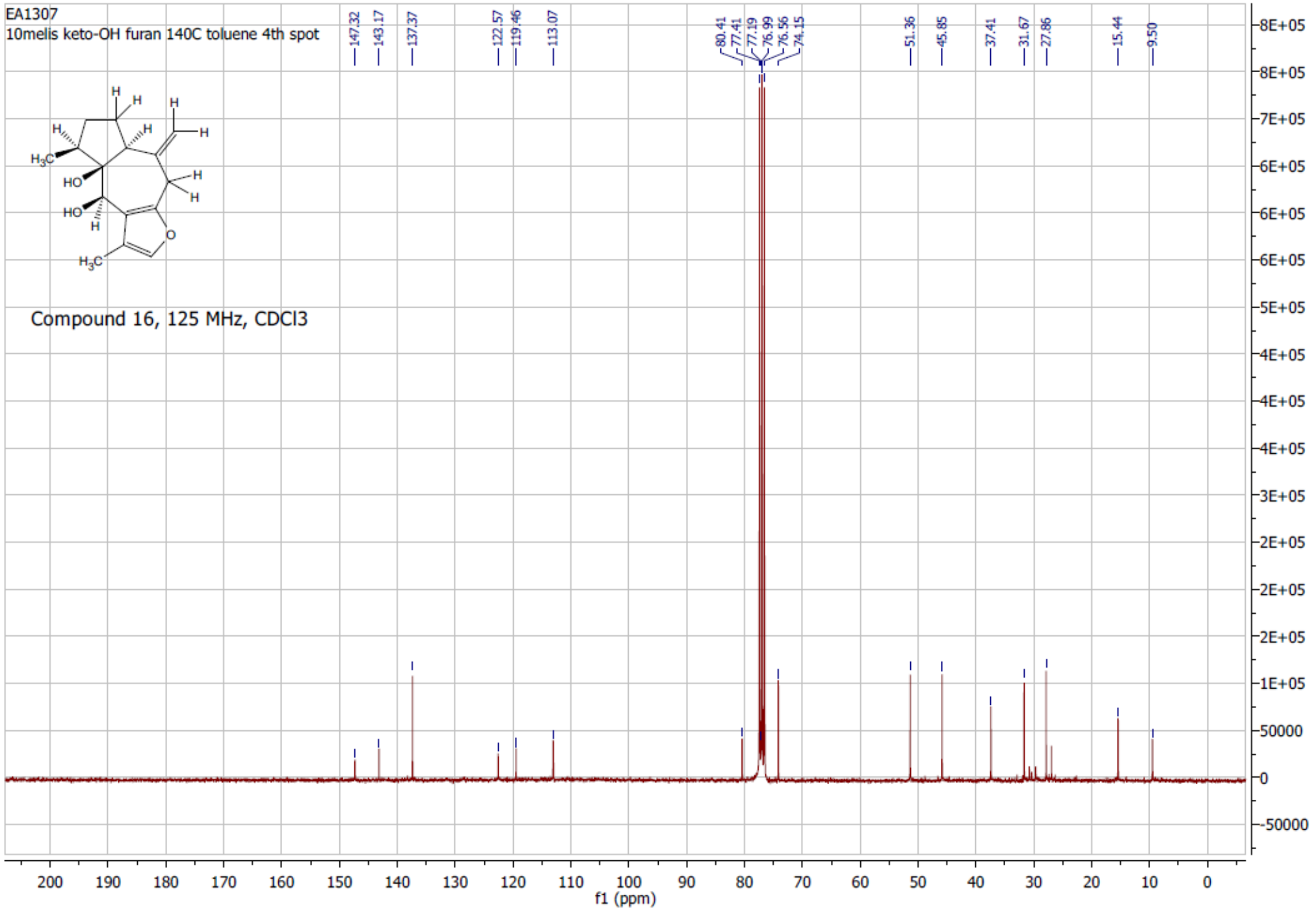

PROTON_01
EA1239-stili
O
H3C
H3C
O
O
H3C
7.10
5.35
5.30
5.25
3.66
3.55
3.52
3.33
3.29
2.96
2.88
2.31
2.30
2.28
2.27
0.73
0.82
1.00
0.79
0.83
0.90
2.54
f1 (ppm)

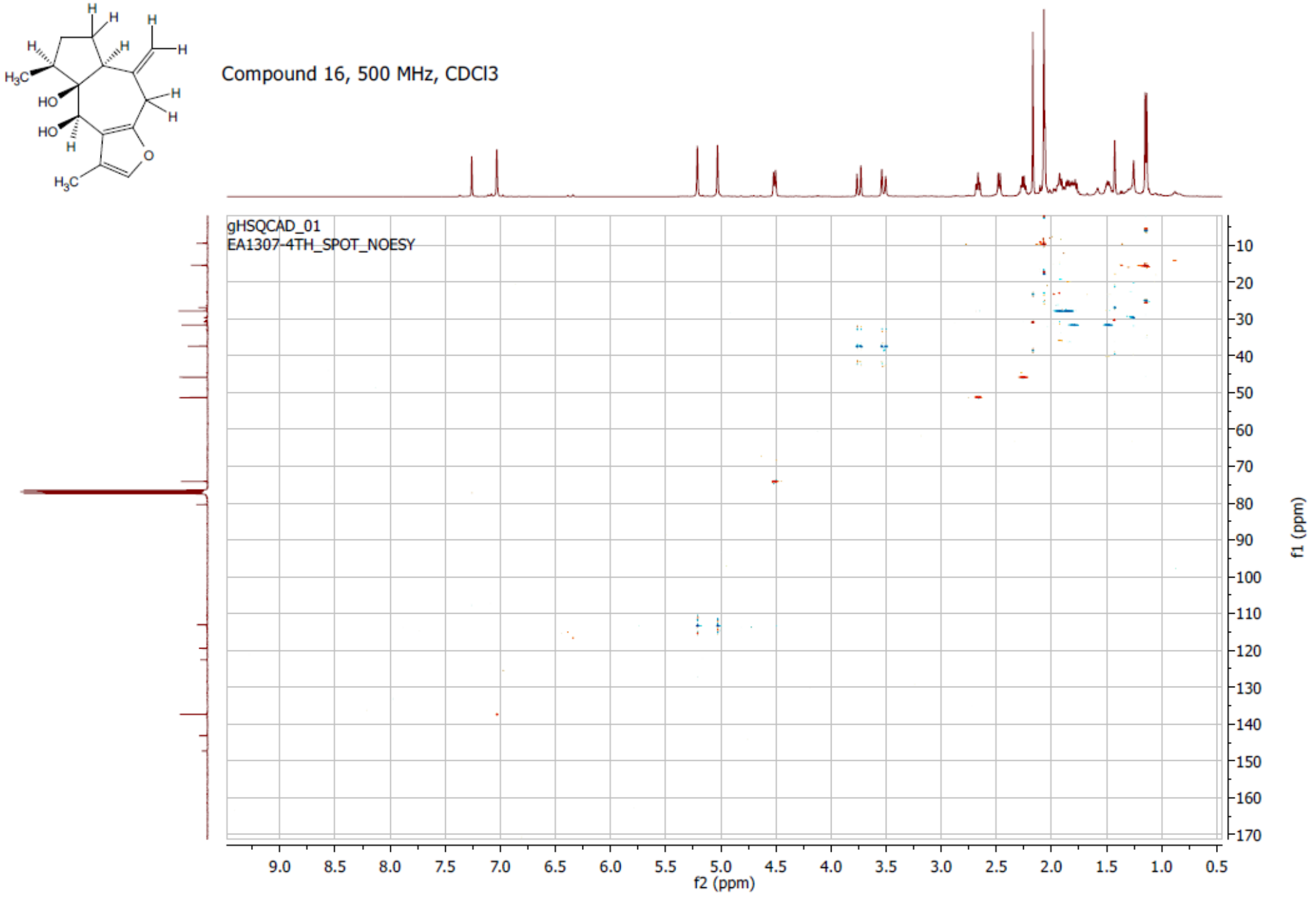

EA1303
zedoarol
Zedoarol (17), 500 MHz, CDCl3
f1 (ppm)

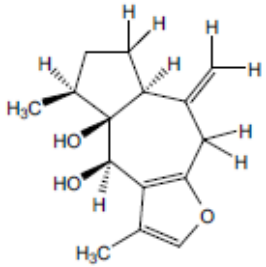

EA1303
zedoarol C13
196.94
158.28
140.87
138.43
122.40
119.86
115.05
84.12
77.41
76.99
76.56
50.85
40.52
38.97
29.87
27.22
14.31
9.44
Zedoarol (17), 125 MHz, CDCl3
f1 (ppm)


Zedoarol (17), 500 MHz, CDCl3
EA1244
10melis diketone (1239) toluene 140oC 25min stili 2nd spot
f2 (ppm)
f1 (ppm)

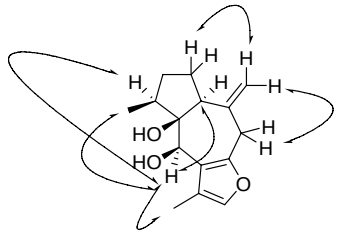

PROTON_01
EA1307-4TH_SPOT_NOESY
Compound 16, 500 MHz, CDCl3
7.26
7.03
5.21
5.03
4.52
4.50
3.76
3.73
3.54
3.50
2.68
2.67
2.65
2.48
2.46
2.26
2.25
2.17
2.07
2.06
1.93
1.91
1.87
1.85
1.84
1.82
1.81
1.79
1.78
1.77
1.15
1.14
1.00
1.07
1.13
1.13
1.14
1.26
1.07
1.04
1.14
2.15
3.72
2.18
2.93
f1 (ppm)


EA1307
10melis keto-OH furan 140C toluene 4th spot
147.32
143.17
137.37
122.57
119.46
113.07
80.41
77.41
77.19
76.99
76.56
74.15
51.36
45.85
37.41
31.67
27.86
15.44
9.50
Compound 16, 125 MHz, CDCl3
f1 (ppm)

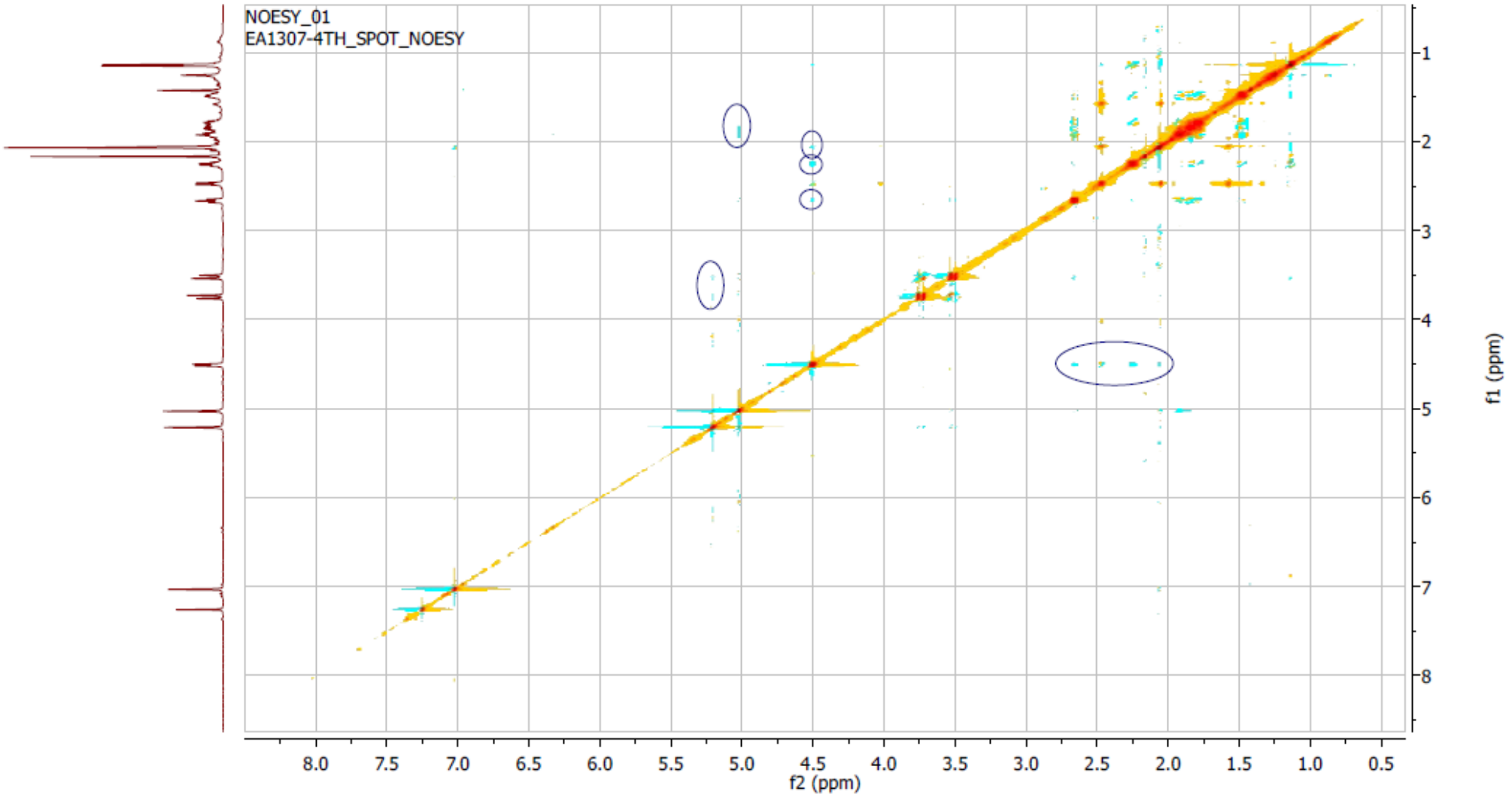

Compound 16, 500 MHz, CDCl3
gHSQCAD_01
EA1307-4TH_SPOT_NOESY
f2 (ppm)
f1 (ppm)

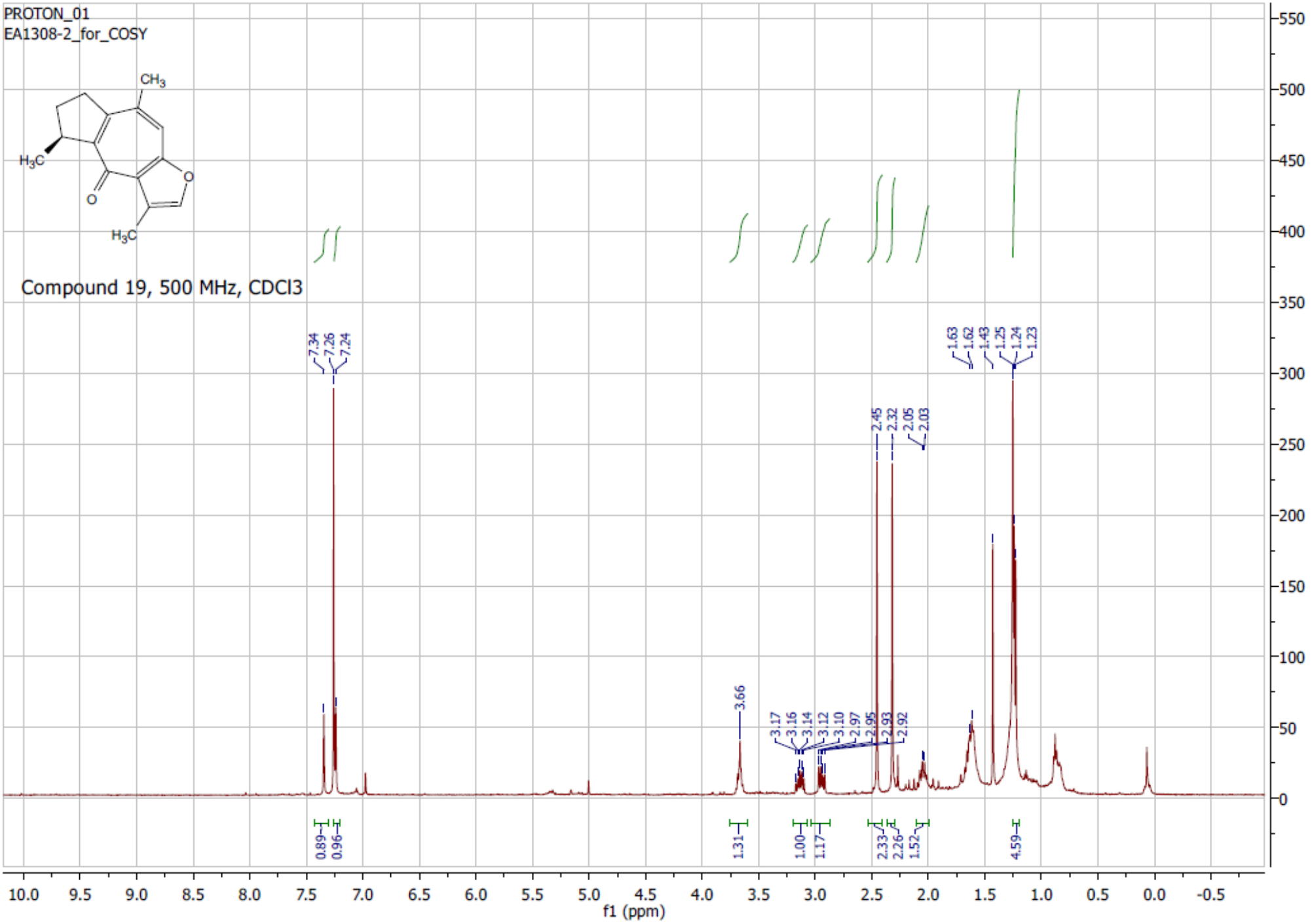


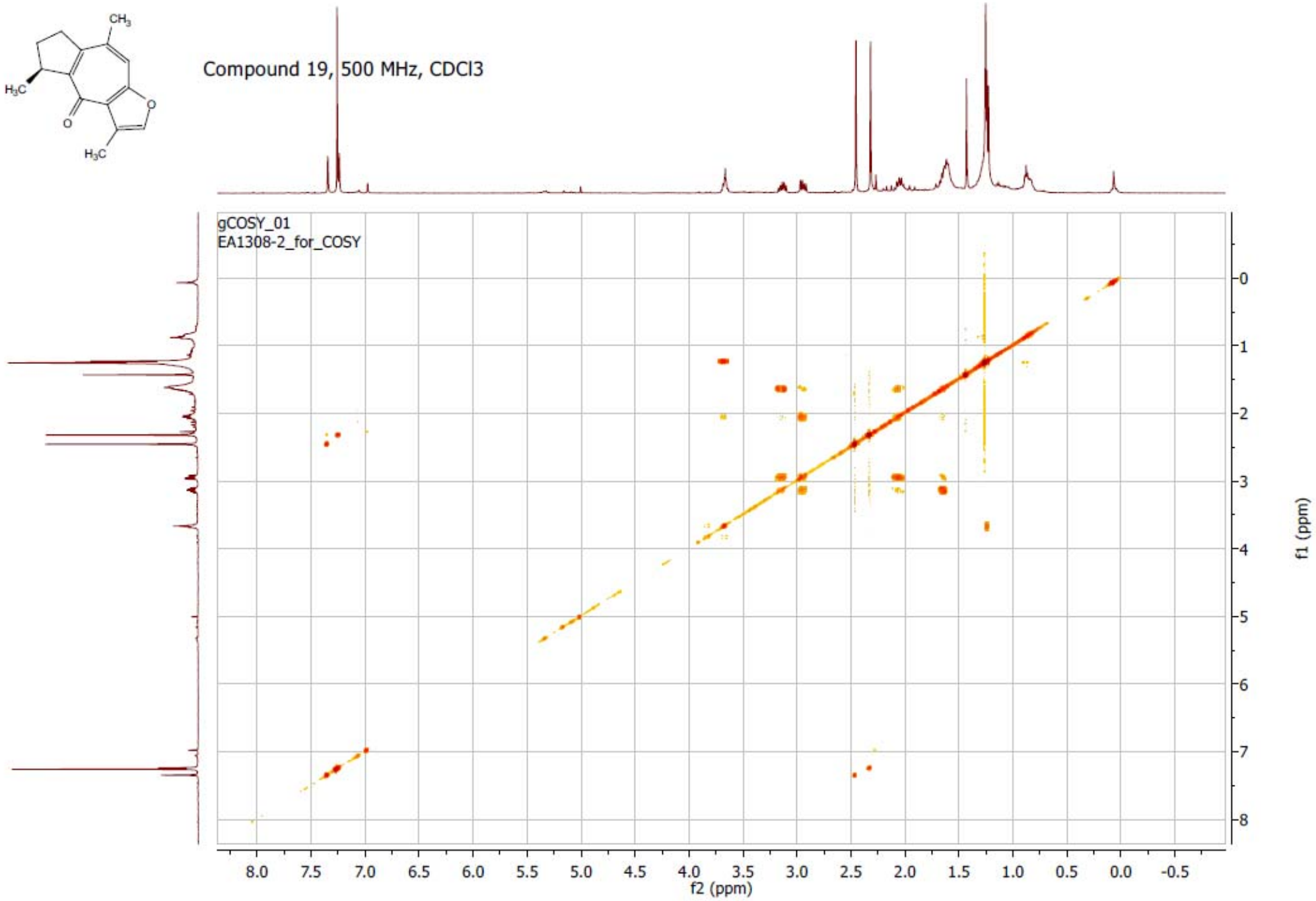
Compound 16, 500 MHz, CDCl3

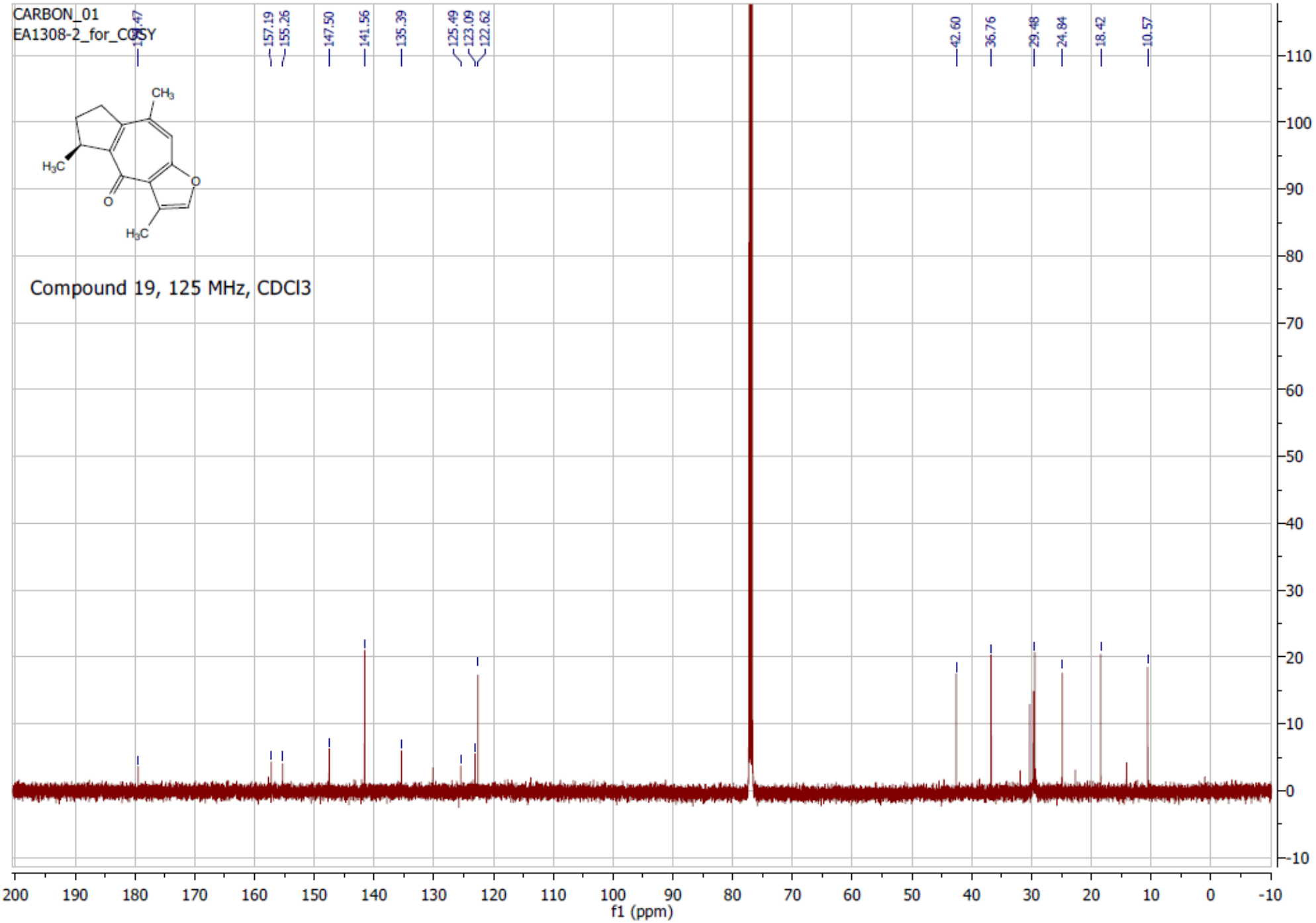


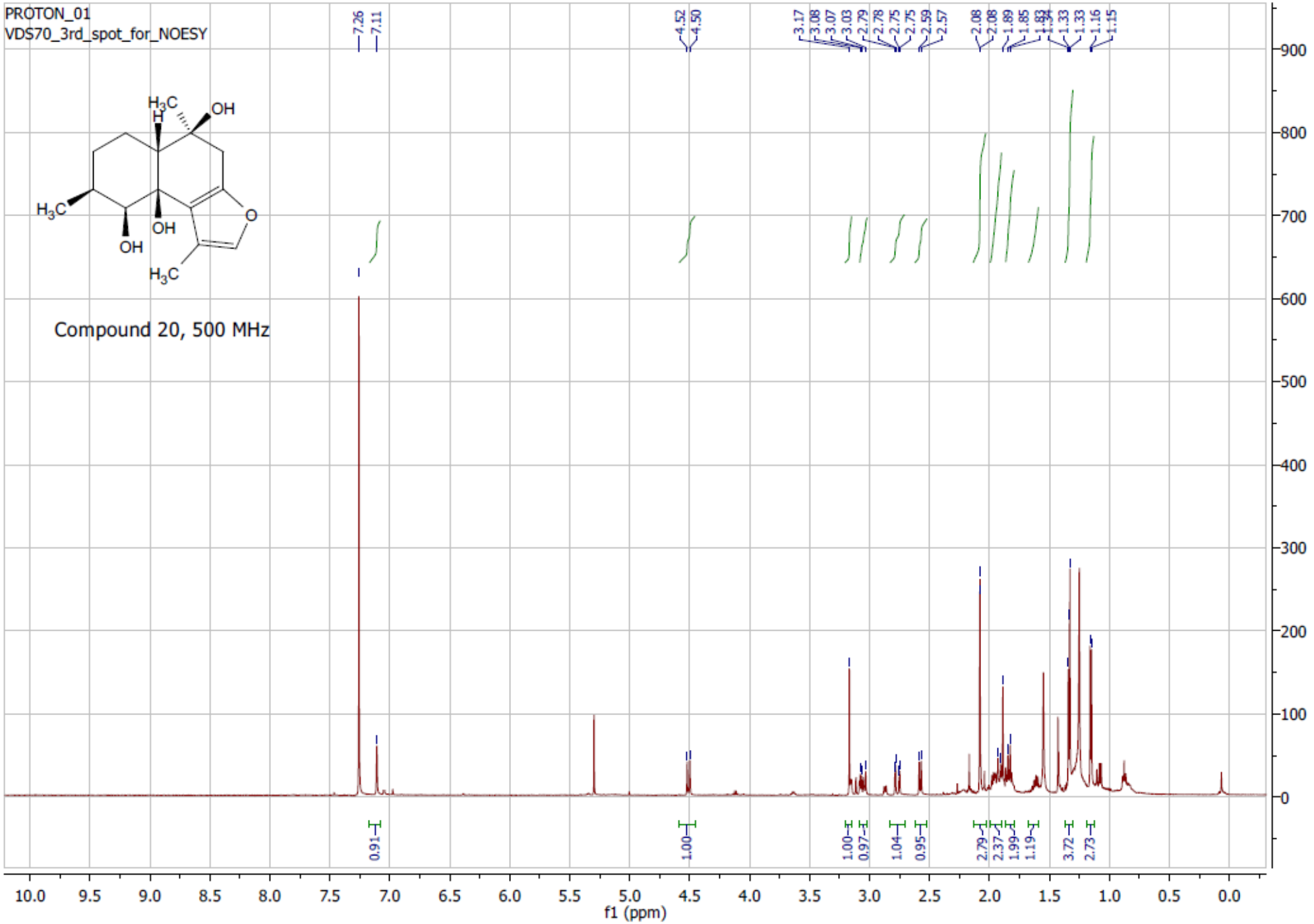
NOE correlations

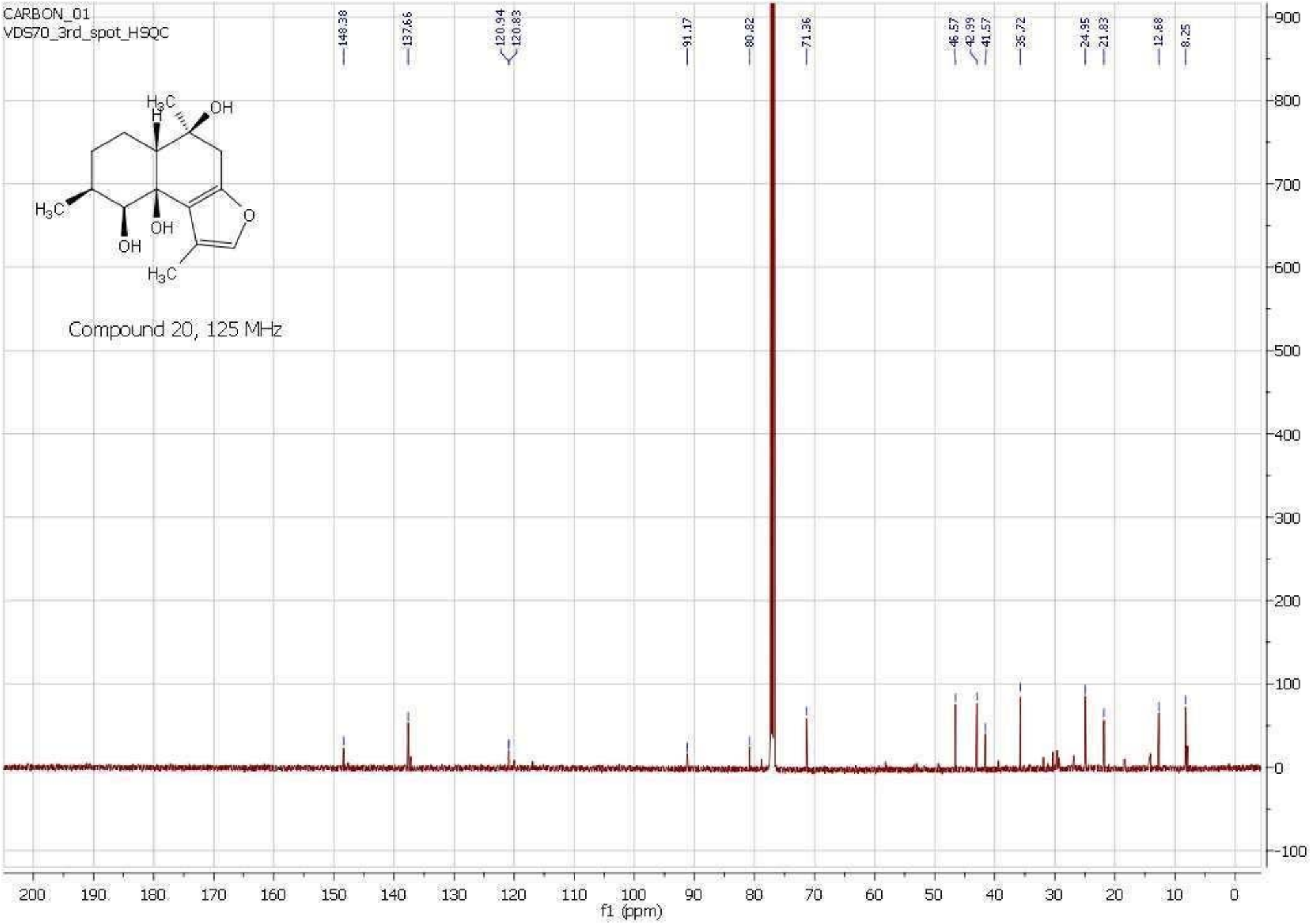


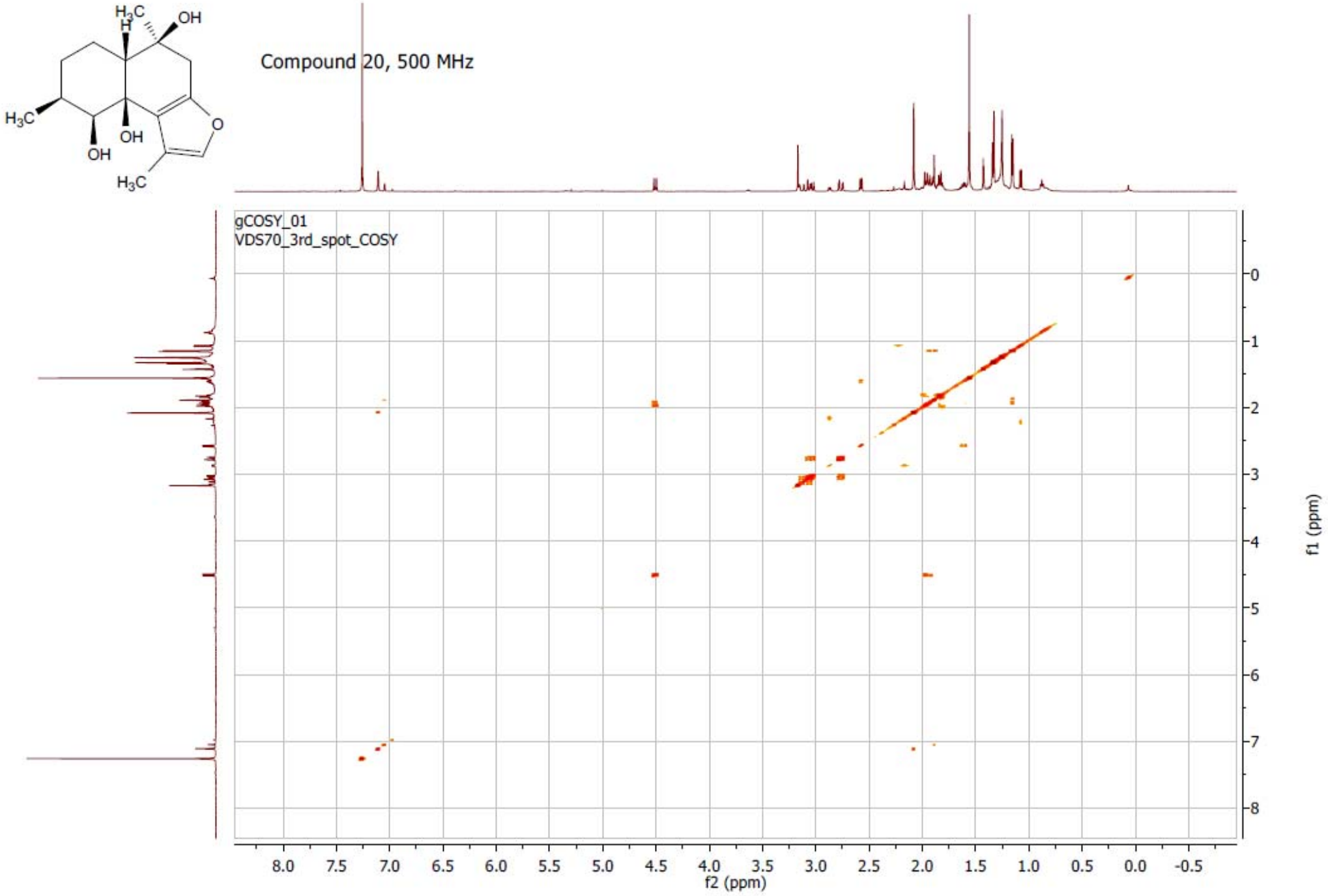

PROTON_01
EA1308-2_for_COSY
Compound 19, 500 MHz, CDCl3
CH3
H3C
O
O
H3C
7.34
7.26
7.24
1.63
1.62
1.43
1.25
1.24
1.23
2.45
2.32
2.05
2.03
3.66
3.17
3.16
3.14
3.12
3.10
2.97
2.95
2.93
2.92
0.89
0.96
1.31
1.00
1.17
2.33
2.26
1.52
4.59
f1 (ppm)

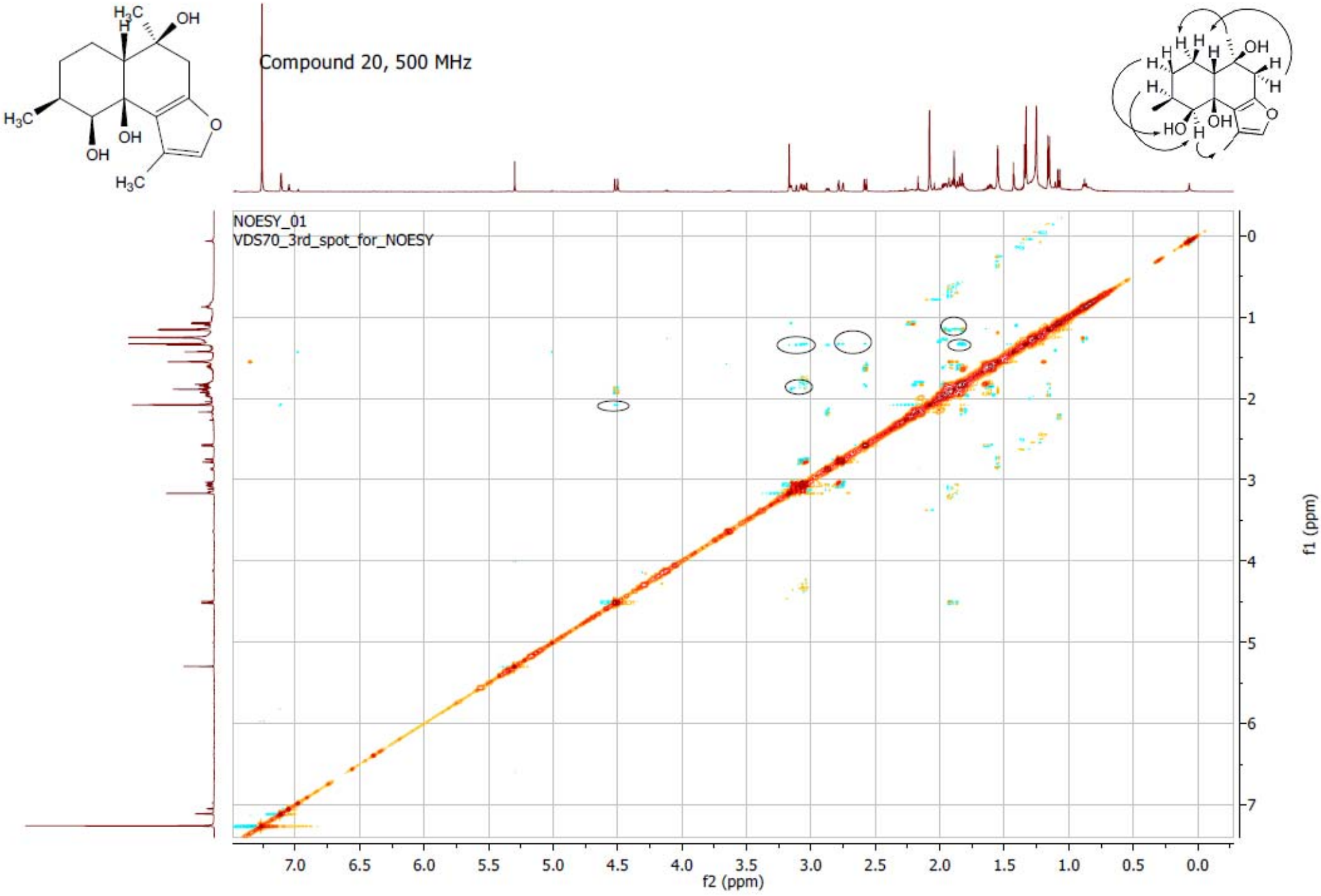

Compound 19, 500 MHz, CDCl3
gCOSY_01
EA1308-2_for_COSY
f2 (ppm)
f1 (ppm)


CARBON_01
EA1308-2_for_COSY
179.47
157.19
155.26
147.50
141.56
135.39
125.49
123.09
122.62
42.60
36.76
29.48
24.84
18.42
10.57
CH3
H3C
O
O
H3C
Compound 19, 125 MHz, CDCl3
f1 (ppm)


PROTON_01
VDS70_3rd_spot_for_NOESY
Compound 20, 500 MHz
f1 (ppm)


CARBON_01
VDS70_3rd_spot_HSQC
148.38
137.66
120.94
120.83
91.17
80.82
71.36
46.57
42.99
41.57
35.72
24.95
21.83
12.68
8.25
Compound 20, 125 MHz
f1 (ppm)


Compound 20, 500 MHz
gCOSY_01
VDS70_3rd_spot_COSY
f2 (ppm)
f1 (ppm)


Compound 20, 500 MHz
NOESY_01
VDS70_3rd_spot_for_NOESY
f2 (ppm)
f1 (ppm)