A non-Natural Elemane as the "Stepping Stone" for the Synthesis of Germacrane and Guaiane Sesquiterpenes

Elissavet E. Anagnostaki, 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

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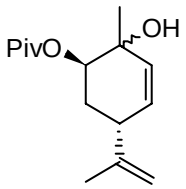
I. General Information

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. 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

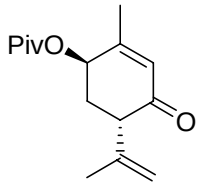


11

(1S,5S)-2-hydroxy-2-methyl-5-(prop-1-en-2-yl)cyclohex-3-enyl pivalate (11)

A stirred solution of 5-isopropenyl-2-methyl-cyclohex-2-enol **10** (540 mg, 3.54 mmol) with Methylene Blue (11 mg, 0.03 mmol) in CH_3CN (5 ml) was irradiated by a visible lamp (400W) under oxygen atmosphere at room temperature for 45 h. The mixture was concentrated to dryness and the residue was dissolved in dry CH_2Cl_2 (5 ml) and treated with $(CH_3)_2S$ (0.38 ml, 5.31 mmol) at room temperature overnight. The mixture was concentrated to dryness and the residue was fractionated by silica gel column chromatography with petroleum : AcOEt (15 : 1) to give (1R,5S)-2-methylene-5-(prop-1-en-2-yl)cyclohexane-1,3-diol and (1R,5S)-2-methylene-5-(prop-1-en-2-yl)cyclohexane-1,3-diol as a mixture in ratio 1:2 (396 mg, 66%) as a pale yellow oil and 167 mg (31%) of **10** (starting material). Then, to the stirred solution of (1R,5R)-2-methyl-5-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol (396 mg, 2.35 mmol) in dry CH_2Cl_2 (18 ml) was added Et_3N (2.6 ml, 18.83 mmol) and DMAP (2.9 mg) successively at room temperature under argon atmosphere. After 15 min, PivCl (1.1 ml, 9.4 mmol) was added at the same temperature and the solution was stirred for 8 h. The reaction mixture was quenched by the addition of 14 ml saturated aqueous ammonium chloride and the aqueous layer was extracted with CH_2Cl_2 (3 X 15 ml). The combined organic extracts are dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/AcOEt = 15:1) to give **11** (517 mg, 87%) as a pale yellow oil. R_f = 0.40 (petroleum/AcOEt = 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ

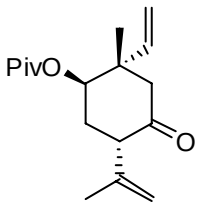
= 5.67 (s, 2H), 4.93 (dd, *J* = 7.2Hz, 3.7Hz, 1H), 4.83 (s, 1H), 4.78 (s, 1H), 2.84 (pst, *J* = 6.4Hz, 1H), 2.08 (brs, 1H), 1.95 – 1.87 (m, 2H), 1.76 (s, 3H), 1.26 (s, 3H), 1.21 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3, 146.6, 132.5, 130.6, 111.6, 75.1, 69.8, 40.4, 38.9, 28.9, 27.1, 24.0, 21.1; HRMS: calcd for $C_{15}H_{25}O_3^+$ [M + H$^+$]: 253.3629, found 253.3631.



12

(1S,5S)-2-hydroxy-2-methyl-5-(prop-1-en-2-yl)cyclohex-3-enyl pivalate (12)

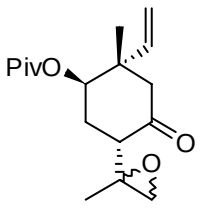
To a stirred suspension of PCC (635 mg, 2.95 mmol) and silica gel (660 mg) in dry CH_2Cl_2 (15 mL) was added dropwise at room temperature a solution of the alcohol **11** (488 mg, 1.96 mmol) in dry CH_2Cl_2 (1 mL). The reaction mixture was vigorously stirred under argon atmosphere for 16 h. The resulting dark brown slurry was filtered through a short column of silica, eluted with CH_2Cl_2 and chromatographed on a silica gel column (petroleum/EtOAc = 15:1) to give **12** (280 mg, 58%) as a colourless oil. R_f = 0.47 (petroleum/AcOEt = 3:1). $[\alpha]^{35}_D$ = +58 (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.96 (s, 1H), 5.50 (pst, *J* = 5.1Hz, 1H), 4.97 (s, 1H), 4.77 (s, 1H), 3.21 (dd, *J* = 8.4Hz, 4.8Hz, 1H), 2.41 (ddd, *J* = 13.3Hz, 8.5Hz, 4.2Hz, 1H), 2.15 – 2.04 (m, 1H), 1.93 (s, 3H), 1.76 (s, 3H), 1.24 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.9, 177.6, 156.2, 141.8, 128.7, 113.6, 68.5, 50.4, 38.9, 32.6, 26.9, 20.9, 20.5; HRMS: calcd for $C_{15}H_{23}O_3^+$ [M + H$^+$]: 251.1642, found 251.1643.



13

(1S,2S,5R)-2-methyl-4-oxo-5-(prop-1-en-2-yl)-2-vinylcyclohexyl pivalate (13)

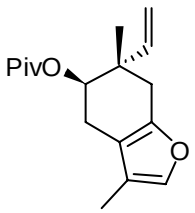
In a well-dried schlenk tube which contained CuI (404 mg, 2.12 mmol) and was degassed three times, vinyl magnesium bromide (4.2 ml, 4.24 mmol) was added under argon atmosphere at -78 ^{o}C. Afterwards, the temperature was raised at 0 ^{o}C for 10 min until the slurry turned jet black and lowered again at -78 ^{o}C. At the same temperature **12** (442 mg, 1.77 mmol) dissolved in dry Et_2O (8.9 ml) was added slowly. After 20 min of stirring at the same temperature, the mixture was quenched by the addition of 6 ml saturated aqueous ammonium chloride and the aqueous layer was extracted with Et_2O (3 X 6 ml). The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/AcOEt = 15:1) gave **13** (384 mg, 78%) as a colourless solid. R_f = 0.63 (petroleum/AcOEt = 3:1). $[\alpha]^{35}_D$ = –107 (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.66 (dd, *J* = 17.4Hz, 11.1Hz, 1H), 5.07 (d, *J* = 1.2Hz, 1H), 5.01 (d, *J* = 8.0Hz, 1H), 5.01 - 4.95 (m, 1H), 4.86 (s, 1H), 4.67 (s, 1H), 3.06 (dd, *J* = 12.0Hz, 6.1Hz, 1H), 2.46 [dd, (a,b system), *J* = 22.6Hz, 14.4Hz, 2H], 2.15 (tt, *J* = 11.8Hz, 2.4Hz, 1H) 1.97 – 1.88 (m, 1H), 1.69 (s, 3H), 1.16 (s, 9H), 1.01 (s, 3H); ^{13}C NMR (75 MHz, CDCl3): δ = 207.9, 177.2, 142.3, 141.9, 115.3, 113.6, 73.2, 52.5, 46.9, 45.2, 39.0, 31.5, 27.1, 24.1, 20.2; HRMS: calcd for $C_{17}H_{27}O_3^+$ [M + H$^+$]: 279.1955, found 279.1950.



(1S,2S,5R)-2-methyl-5-((S)-2-methyloxiran-2-yl)-4-oxo-2-vinylcyclohexyl pivalate

To a stirred solution of **13** (1.42 g, 5.09 mmol) in dry CH_2Cl_2 (70 ml) was added at 0 ^{o}C a portion of solid $NaHCO_3$, *m*CPBA (1.32g, 5.60 mmol)

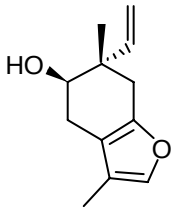
dissolved in dry CH_2Cl_2 (10 ml). The mixture was stirred overnight at room temperature, quenched by the addition of 45 ml saturated aqueous sodium thiosulfate and the aqueous layer was extracted with CH_2Cl_2 (3 X 40 ml). The combined organic extracts were washed with saturated aqueous sodium dicarbonate, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to give (1R,2R,5S)-2-methyl-5-(2-methyloxiran-2-yl)-4-oxo-2-vinylcyclohexyl pivalate (1.40 g, 94%) as a white solid. R_f = 0.64 (petroleum/AcOEt = 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.72 – 5.62 (m, 1H), 5.12 – 4.94 (m, 3H), 2.67 (d, *J* = 4.5Hz, 1H), 2.53 – 2.41 (m, 3H), 2.12 (dd, *J* = 12.9Hz, 11.1Hz, 2H), 1.22 (s, 3H), 1.17 (s, 9H), 1.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.7, 207.2, 177.1, 142.2, 142.1, 115.5, 115.5, 72.8, 72.7, 55.2, 55.1, 54.9, 51.8, 50.9, 50.0, 47.1, 46.7, 45.1, 45.1, 39.0, 28.9, 28.7, 24.7, 24.6, 20.1, 17.2.



14

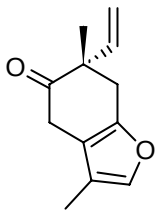
(5S,6S)-3,6-dimethyl-6-vinyl-4,5,6,7-tetrahydrobenzofuran-5-yl pivalate (14)

To a stirred solution of (1R,2R,5S)-2-methyl-5-(2-methyloxiran-2-yl)-4-oxo-2-vinylcyclohexyl pivalate (153 mg, 0.52 mmol) in MeOH (1.9 ml) at room temperature was added 1.15 ml of aq. KOH (40%). After 4 h, the mixture was quenched by the addition of 2 ml saturated aqueous ammonium chloride and the aqueous layer was extracted with Et_2O (3 X 2 ml). The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/AcOEt = 5:1) gave **14** (125 mg, 87%) as a colourless oil. R_f = 0.68 (petroleum/AcOEt = 3:1). $[\alpha]^{35}_D$ = –36 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04 (s, 1H), 5.79 (dd, *J* = 17.5Hz, 10.8Hz, 1H), 5.08 (d, *J* = 17.2Hz, 1H), 5.03 (d, *J* = 9.9Hz, 1H), 4.94 (pst, 5.4Hz, 1H), 2.71 – 2.51 (m, 3H), 2.33 (dd, *J* = 16.1Hz, 5.8Hz, 1H), 1.87 (s, 3H), 1.16 (s, 9H), 1.15 (s, 3H); ^{13}C NMR (75 MHz, CDCl3): δ = 177.6, 148.3, 143.3, 137.6, 119.3, 113.8, 113.6, 74.0, 40.8, 38.8, 33.3, 27.0, 24.0, 20.0, 7.8; HRMS: calcd for $C_{17}H_{25}O_3^+$ [M + H^+]: 277.1798, found 277.1800.



(5S,6S)-3,6-dimethyl-6-vinyl-4,5,6,7-tetrahydrobenzofuran-5-ol

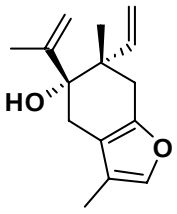
In a sealed tube which contained a stirred solution of **14** (250 mg, 0.90 mmol) in MeOH (40 ml) was added K_2CO_3 (376 mg, 2.70 mmol). The mixture was heated at 110 ^{o}C for 24 h and then was quenched by the addition of 25 ml saturated aqueous ammonium chloride and the aqueous layer was extracted with CH_2Cl_2 (3 X 20 ml). The combined organic extracts are dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/AcOEt = 5:1) to give (5R,6R)-3,6-dimethyl-6-vinyl-4,5,6,7-tetrahydrobenzofuran-5-ol (174 mg, 99%) as a colourless oil. R_f = 0.35 (petroleum/AcOEt = 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.05 (s, 1H), 5.83 (dd, *J* = 17.7Hz, 10.6Hz, 1H), 5.18 (d, *J* = 3.4Hz, 1H), 5.13 (d, *J* = 1.7Hz, 1H), 3.72 (pst, *J* = 6.4Hz, 1H), 2.69 (dd, *J* = 15.8Hz, 5.0Hz, 1H), 2.55 [dd (a,b system), *J* = 33.0Hz, 16.5Hz, 2H], 2.31 (dd, *J* = 15.9Hz, 7.0Hz, 1H), 1.91 (s, 3H), 1.11(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.3, 144.5, 137.7, 119.5, 114.4, 72.4, 42.2, 33.3, 26.2, 17.9, 7.9.



15

(S)-3,6-dimethyl-6-vinyl-6,7-dihydrobenzofuran-5(4H)-one (15)

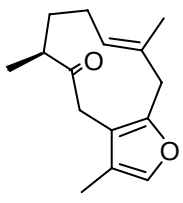
To a stirred solution of (5R,6R)-3,6-dimethyl-6-vinyl-4,5,6,7-tetrahydrobenzofuran-5-ol (123 mg, 0.64 mmol) in dry CH_2Cl_2 (10 ml) was added a portion of solid $NaHCO_3$, Dess-Martin periodinane (325 mg, 0.77 mmol) dissolved in dry CH_2Cl_2 (2 ml) at 0 ^oC under argon atmosphere. The mixture was stirred for 15 min at the same temperature and was quenched by the addition of 7 ml saturated aqueous sodium bicarbonate and the aqueous layer was extracted with CH_2Cl_2 (3 X 7 ml). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/AcOEt = 15:1) gave **15** (87 mg, 71%) as a pale yellow oil and 37 mg (29%) of (5R,6R)-3,6-dimethyl-6-vinyl-4,5,6,7-tetrahydrobenzofuran-5-ol (starting material). R_f = 0.50 (petroleum/AcOEt = 3:1). $[\alpha]^{35}_D$ = –46 (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10 (s, 1H), 5.99 (dd, *J* = 17.4Hz, 10.7Hz, 1H), 5.15 (d, *J* = 10.7Hz, 1H), 5.13 (d, *J* = 17.4Hz, 1H), 3.24 [dd, (a,b system), *J* = 60Hz, 19.7Hz, 2H], 2.91 [dd, (a,b system), *J* = 60Hz, 16.3Hz, 2H], 1.90 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.8, 147.1, 140.9, 138.5, 119.3, 115.4, 114.8, 50.5, 35.8, 34.0, 22.4, 7.8; HRMS: calcd for $C_{12}H_{15}O_2^+$ [M + H^+]: 191.1066, found 191.1068.



5

(5S,6R)-3,6-dimethyl-5-(prop-1-en-2-yl)-6-vinyl-4,5,6,7-tetrahydrobenzofuran-5-ol (5)

To a stirred solution of 2-bromopropene (0.31 ml, 3.47 mmol) in dry Et_2O (4.5 ml) was added at -78 ^oC *t*-BuLi (1.44 ml, 2.31 mmol) under argon atmosphere. The mixture was stirred for 10 min at the same temperature and a solution of **15** (110 mg, 0.58 mmol) in dry Et_2O (0.7 ml) was added dropwise. After 15 min, the mixture was quenched by the addition of the addition of 3 ml saturated aqueous ammonium chloride, the aqueous layer was extracted with CH_2Cl_2 (3 X 5 ml), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/Et_2O = 90:1) gave **5** (94 mg, 70%) as a colourless oil. R_f = 0.36 (petroleum/Et_2O = 3:1). $[\alpha]^{25}_D$ = +49 (c 0.3, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.09 (s, 1H), 6.08 (dd, *J* = 15Hz, 10Hz, 1H), 5.14 (d, *J* = 10Hz, 1H), 5.12 (d, *J* = 15Hz, 1H), 5.06 – 5.0 (m, 1H), 4.95 (s, 1H), 2.90 (dd, *J* = 15Hz, 10Hz, 2H), 2.37 (dd, 20Hz, 15Hz, 2H), 1.91 (s, 3H), 1.86 (s, 3H), 1.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.7, 148.2, 143.5, 137.7, 119.6, 113.5, 113.2, 113.1, 77.9, 45.0, 33.3, 32.6, 22.3, 20.8, 8.0; HRMS: calcd for $C_{15}H_{21}O_2^+$ [M + H^+]: 233.1536, found 233.1536.

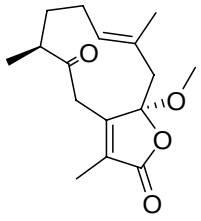


4

3,6,10-trimethyl-6,7,8,11-tetrahydro-4H-cyclodeca[b]furan-5-one (4)

A stirred solution of **5** (134 mg, 0.58 mmol) in toluene (10 ml) was heated for 7 h at 120 ^oC. Then, the mixture was concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/Et_2O = 100:1) gave **4** (56 mg, 42%) as a white solid and 40 mg (30%) of **5** (starting material). R_f = 0.30 (petroleum/Et_2O = 3:1). $[\alpha]^{25}_D$ = +117 (c 0.1 $CHCl_3$). ^{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),

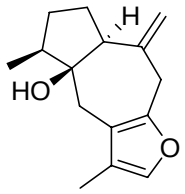
2.31 – 2.06 (m, 2H), 2.02 – 1.88 (m, 1H), 1.88 (s, 3H), 1.82 – 1.76 (m, 1H), 1.69 (brs, 3H), 1.08 (d, *J* = 6Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.3, 148.8, 136.5, 131.8, 131.7, 121.9, 113.7, 47.3, 38.4, 36.4, 36.3, 29.6, 18.3, 17.3, 8.12; HRMS: calcd for $C_{15}H_{21}O_2^+$ [M + H$^+$]: 233.1536, found 233.1531.



17

(6S,11aR,E)-11a-methoxy-3,6,10-trimethyl-7,8,11,11a-tetrahydrocyclodeca[b]furan-2,5(4H, 6H)-dione or Methyl-Curdionolide (17)

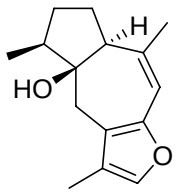
A stirred solution of **4** (40 mg, 0.17 mmol) with Methylene Blue (0.6 mg, 0.002 mmol) in MeOH (1 ml) was irradiated by a visible lamp (400W) under oxygen atmosphere at room temperature for 15 min. Then, the mixture was treated with $(CH_3)_2S$ (13 µl, 0.34 mmol) at room temperature for 6 h. The mixture was concentrated to dryness and the residue was fractionated by silica gel column chromatography with petroleum/Et_2O = 90:1 to give **17** (8 mg, 19%) as pale yellow oil. R_f = 0.13 (petroleum/Et_2O = 3:1). $[\alpha]^{25}_D$ = +66 (c 0.2 CH_3OH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.90 – 4.87 (m, 1H), 3.86 (d, J = 15.5Hz, 1H), 3.24 (d, *J* = 15.5Hz, 1H), 3.11 (s, 3H), 2.94 (d, *J* = 14Hz, 1H), 2.48 – 2.39 (m, 1H), 2.26 (d, J = 14Hz, 1H), 2.25 – 2.21 (m, 1H), 2.15 – 1.97 (m, 2H), 1.97 (s, 3H), 1.87 (s, 3H), 1.71 – 1.65 (m, 1H), 1.06 (d, J = 7Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 210.2, 176.2, 156.6, 133.9, 132.3, 130.4, 119.6, 50.5, 49.2, 47.9, 39.9, 36.1, 27.4, 18.5, 16.6, 9.6; HRMS: calcd for $C_{16}H_{23}O_4^+$ [M + H$^+$]: 279.1591, found 279.1583.



20

(S,E)-3,6,10-trimethyl-6,7,8,11-tetrahydrocyclodeca[b]furan-5(4H)-one (20)

A stirred solution of **4** (40 mg, 0.17 mmol) in toluene (2 ml) was heated for 12 h at 140^{o}C. Then, the mixture was concentrated *in vacuo.* Purification by silica gel flash column chromatography (petroleum/Et_2O = 100: 1) gave **20** (23 mg, 58%) as a colourless oil and **22** (5 mg, 8%) as a colourless oil. For **20**: R_f = 0.37 (petroleum/Et_2O = 3:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.01 (s, 1H), 5.16 (s, 1H), 5.00 (s, 1H), 3.52 (d, *J* = 15Hz, 1H), 3.35 (d, *J* = 15Hz, 1H), 2.82 (d, *J* = 15Hz, 1H), 2.64 (t, *J* = 10Hz, 1H), 2.31 (d, *J* = 15Hz, 1H), 1.96 – 1.91 (m, 3H), 1.90 (s, 3H), 1.88 – 1.85 (m, 2H), 1.78 – 1.71 (m, 1H), 1.08 (d, *J* = 10Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.6, 142.1, 136.2, 122.2, 114.6, 113.8, 78.0, 56.7, 45.0, 39.0, 32.9, 29.5, 26.0, 13.4, 8.2; HRMS: calcd for $C_{15}H_{21}O_2^+$ [M + H$^+$]: 233.1536, found 233.1537.

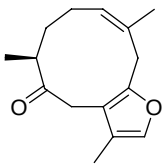


22

(4aS,5S,7aS)-3,5,8-trimethyl-4,4a,5,6,7,7a-hexahydroazuleno[6,5-b]furan-4a-ol (22)

The experimental procedure is described above.

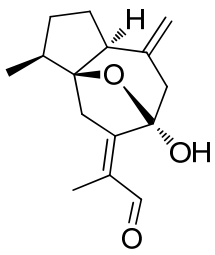
R_f = 0.35 (petroleum/Et_2O = 3:1). For **22**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.07 (s, 1H), 6.28 (s, 1H), 2.82 (d, *J* = 15Hz, 1H), 2.82 – 2.76 (m, 1H), 2.49 (d, *J* = 15Hz, 1H), 2.02 – 1.83 (m, 5H), 1.91 (s, 3H), 1.89 (s, 3H), 1.10 (d, *J* = 5Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.4, 137.4, 132.7, 122.4, 120.7, 115.9, 79.2, 54.0, 46.1, 34.7, 33.9, 26.2, 24.6, 13.6, 8.3; HRMS: calcd for $C_{15}H_{21}O_2^+$ [M + H$^+$]: 233.1536, found 233.1534.



21

(S,Z)-3,6,10-trimethyl-6,7,8,11-tetrahydrocyclodeca[b]furan-5(4H)-one (21)

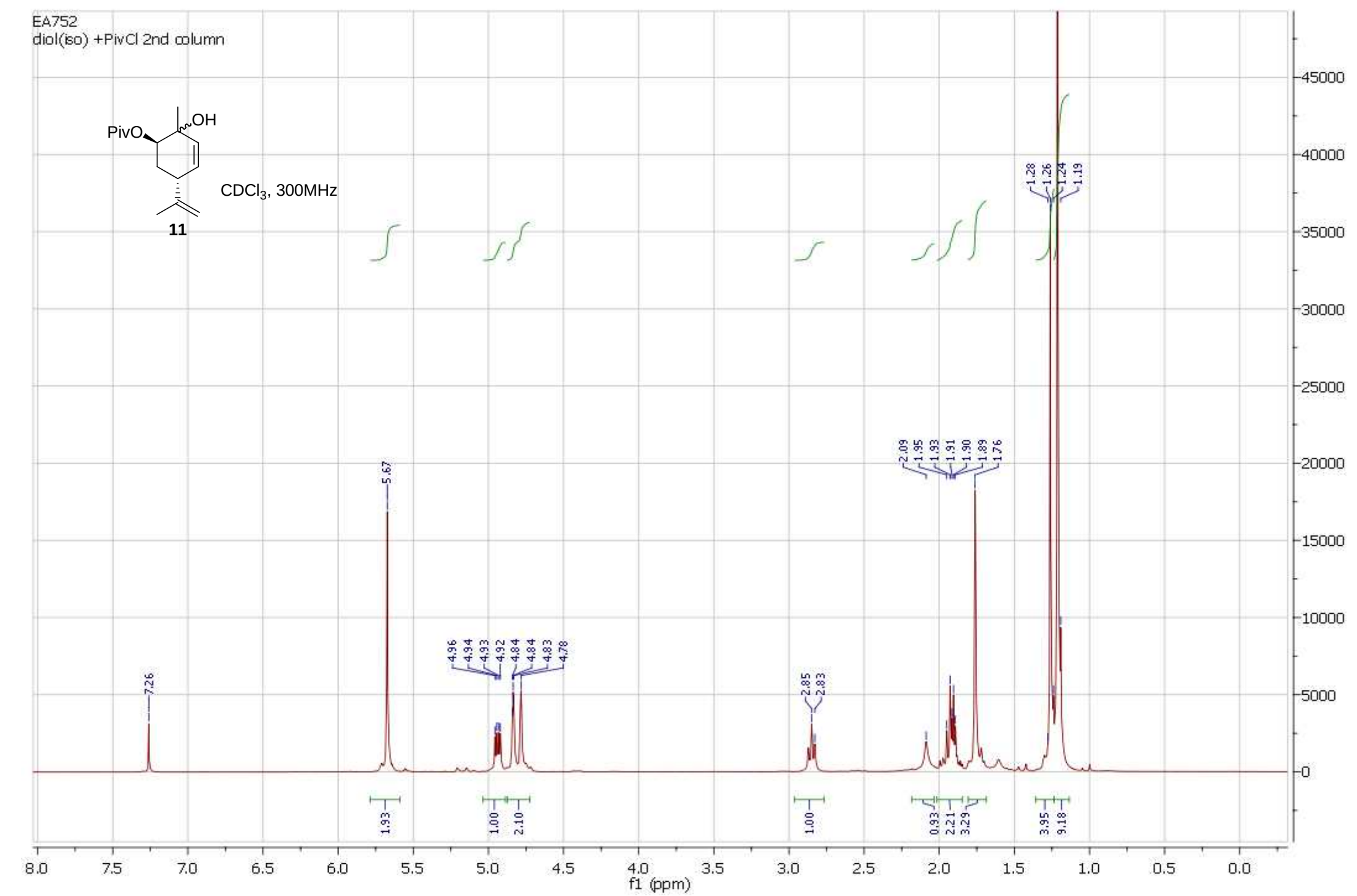
To stirred solution of **20** (22 mg, 0.09 mmol) in CH_2Cl_2 (1.5 ml) at 0 ^oC was added CF_3COOH (7 μL, 0.09 mmol). After 10 min the temperature was raised to room temperature for 1.5 h. Then the mixture was quenched by the addition of 1 ml saturated aqueous sodium hydrogen carbonate, the aqueous layer was extracted with CH_2Cl_2 (3 X 2 ml), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum/Et_2O = 100:1) gave **21** (21 mg, 98%) as a colourless oil. R_f = 0.35 (petroleum/ Et_2O = 3:1). $[\alpha]^{25}_D$ = +136 (c 0.2 $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.12 (s, 1H), 5.16 (t, *J* = 10Hz, 1H), 3.44 (d, *J* = 15Hz, 1H), 3.40 (d, *J* = 15Hz, 1H), 3.30 (d, *J* = 15Hz, 1H), 3.07 (d, *J* = 15Hz, 1H), 2.80 – 2.76 (m, 1H), 2.15 (q, *J* = 10Hz, 1H), 2.02 – 1.90 (m, 2H), 1.89 (s, 3H), 1.85 (s, 3H), 1.85 – 1.83 (m, 1H), 0.94 (d, *J* = 5Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.7, 150.7, 137.1, 134.9, 126.8, 122.4, 115.9, 39.6, 38.5, 33.6, 29.5, 26.1, 24.5, 18.6, 8.1; HRMS: calcd for $C_{15}H_{21}O_2^+$ $[M + H^+]$: 233.1536, found 233.1534.

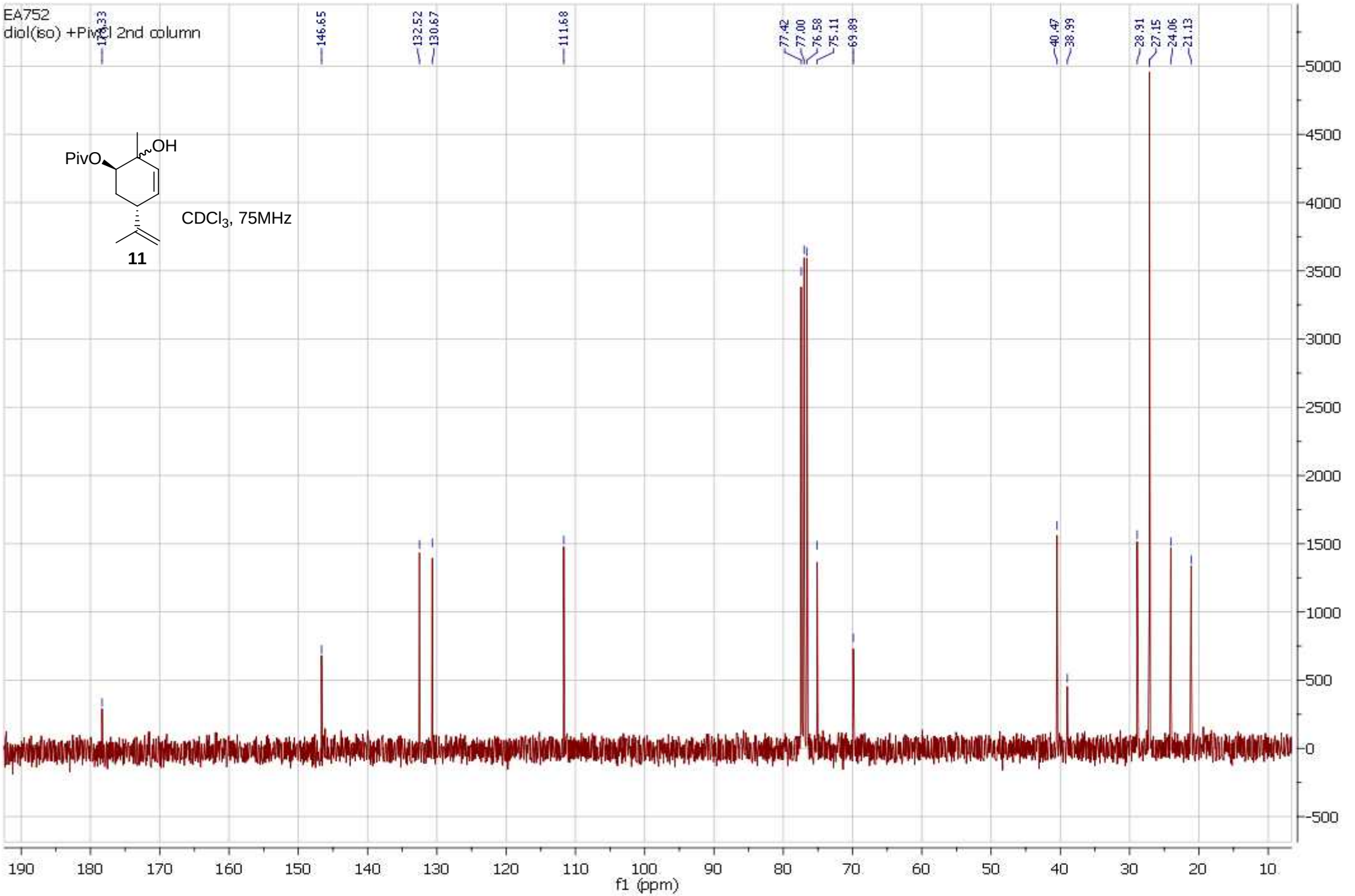


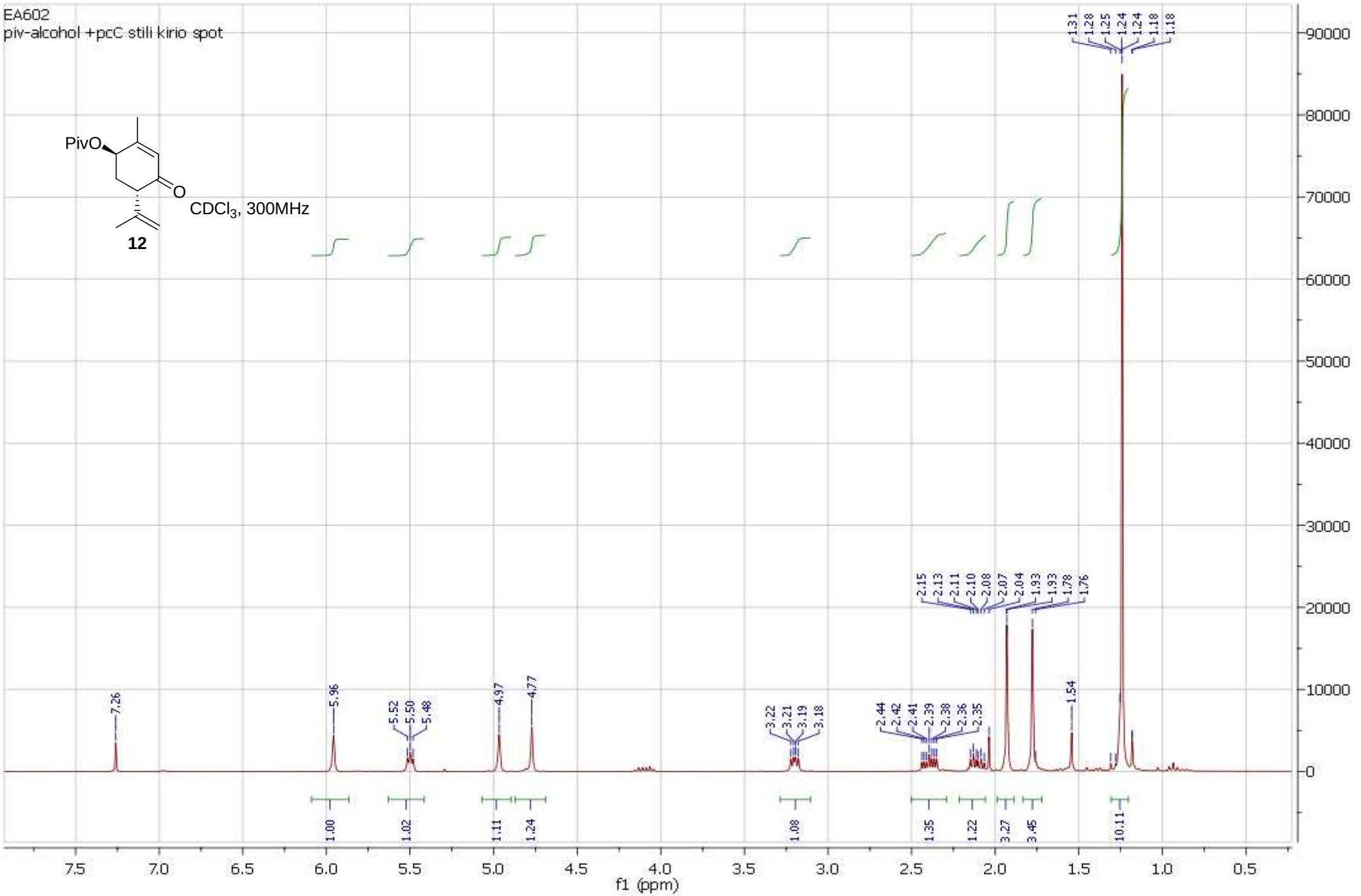
25

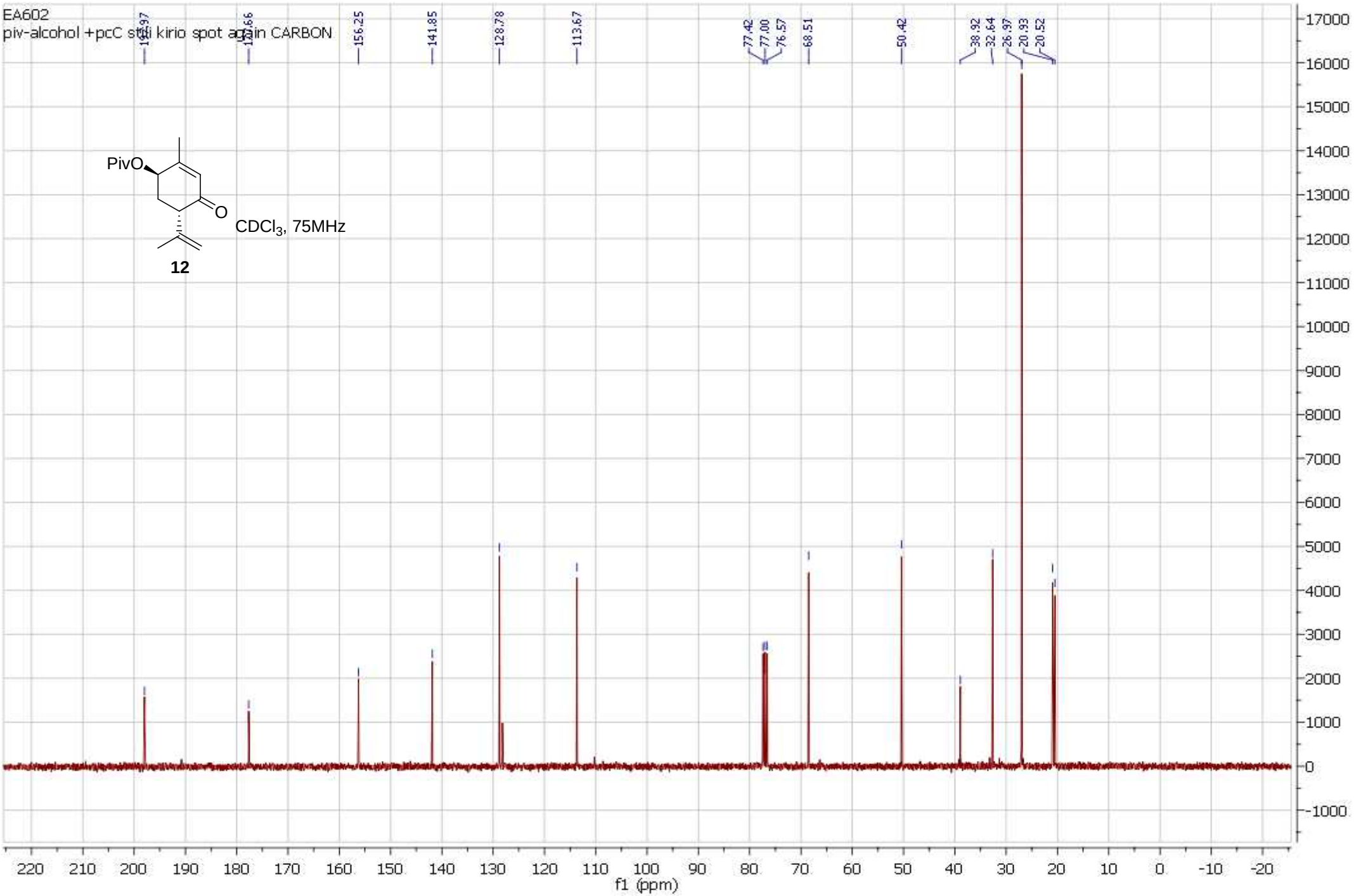
2-(8-hydroxy-2-methyl-6-methylene-11-oxa-tricyclo[6.2.1.01,5] undec-9-ylidene)-propionaldehyde (25)

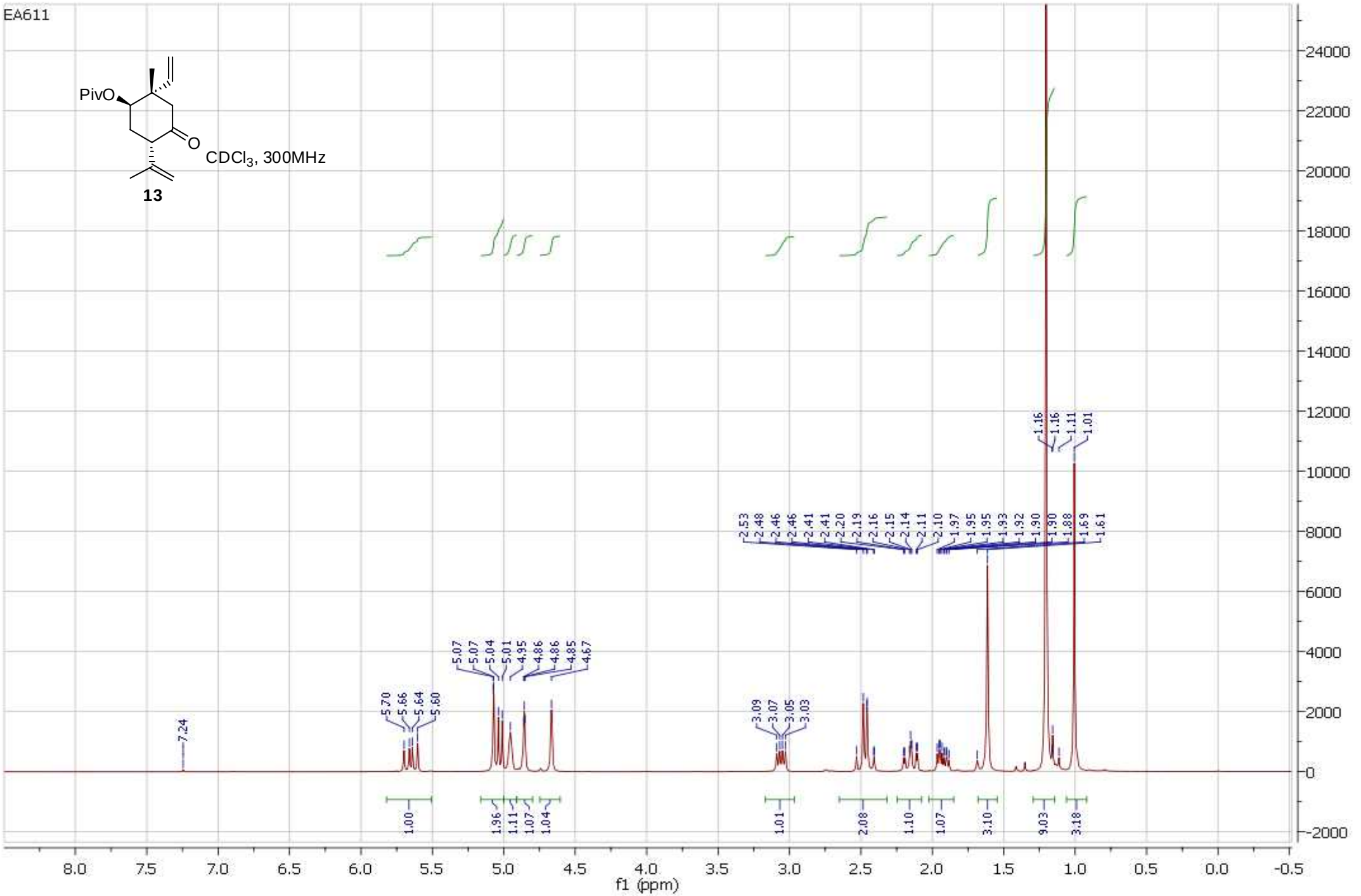
A solution of **20** (5 mg, 0.02 mmol) in $CDCl_3$ (purchased from Aldrich Ltd) was left for 2 d at 5 ^oC in order to form **25** (5 mg, 99%) as a colourless oil. $[\alpha]^{25}_D$ = +64 (c 0.8 $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 10.35 (s, 1H), 4.86 (s, 1H), 4.79 (s, 1H), 3.51 (s, 1H), 2.91 (d, *J* = 15Hz, 1H), 2.78 (d, *J* = 20Hz, 1H), 2.60 (d, *J* = 15Hz, 1H), 2.29 (t, *J* = 10Hz, 2H), 2.04 – 2.01 (m, 2H), 1.82 – 1.75 (m, 1H), 1.72 (s, 3H), 1.58 – 1.55 (m, 1H), 1.25 (s, 3H), 1.04 (d, *J* = 5Hz, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.4, 160.7, 142.5, 131.5, 114.1, 104.2, 88.0, 52.2, 44.8, 38.6, 37.8, 30.6, 29.6, 27.8, 12.3; HRMS: calcd for $C_{15}H_{21}O_3^+$ $[M + H^+]$: 249.1485, found 249.1486.

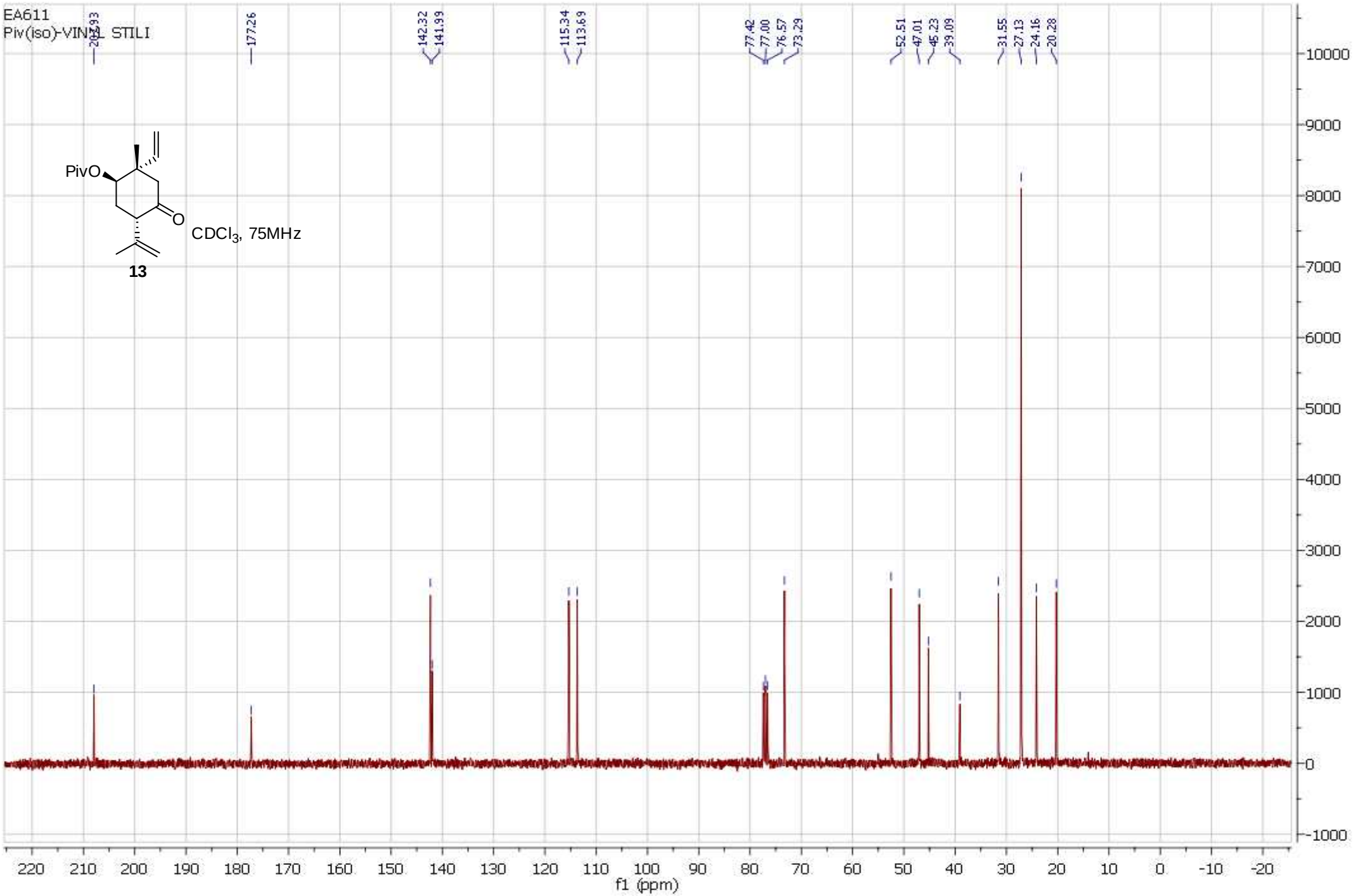

EA752
diol(iso) +PivCl 2nd column
PivO
OH
CDCl3, 300MHz
11
7.26
5.67
4.96
4.94
4.93
4.92
4.84
4.84
4.83
4.78
2.85
2.83
2.09
1.95
1.93
1.91
1.90
1.89
1.76
1.28
1.26
1.24
1.19
1.93
1.00
2.10
1.00
0.93
2.21
3.29
3.95
9.18
f1 (ppm)

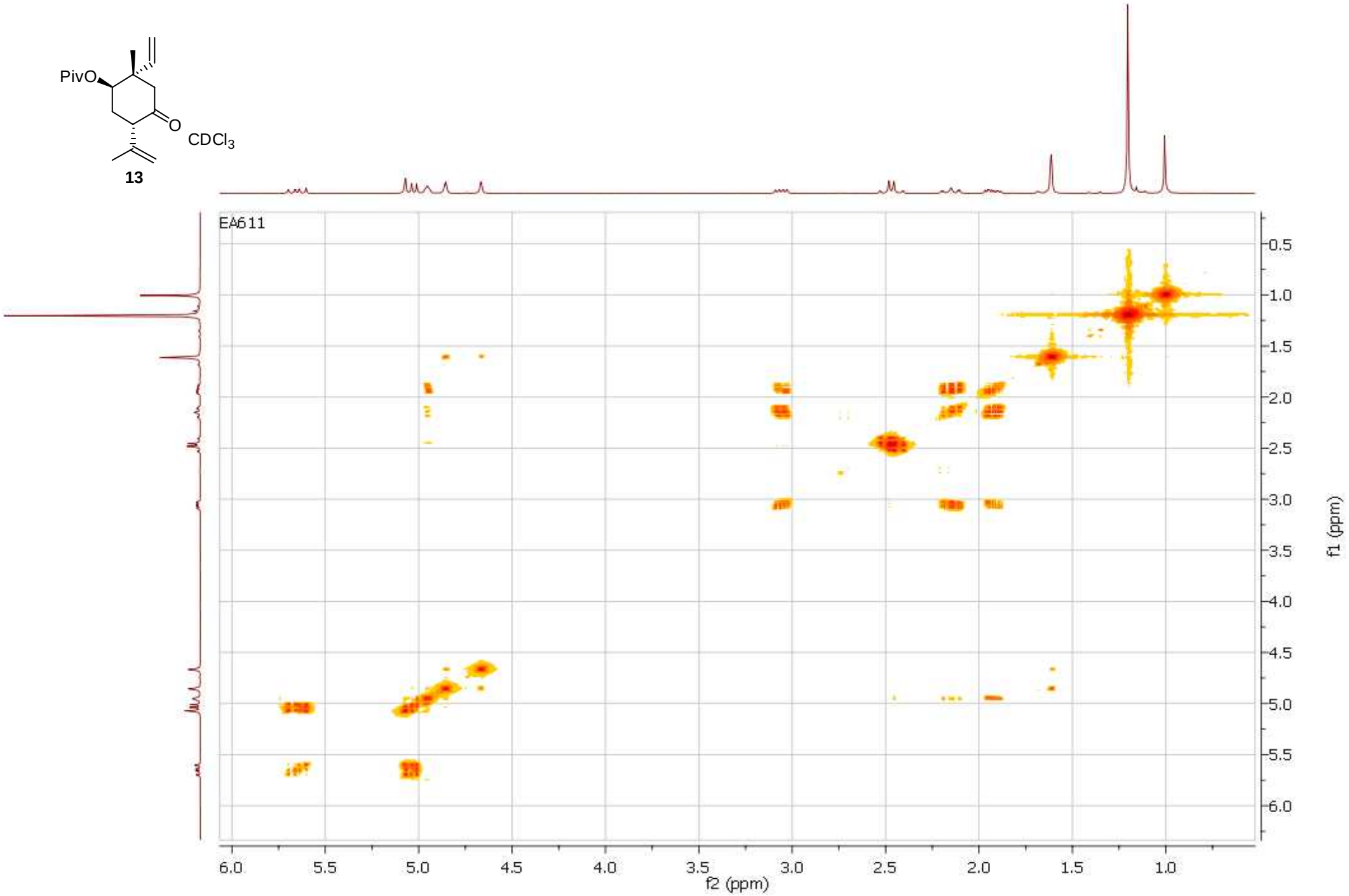

EA752
diol(iso) +Piv 2nd column
178.33
146.65
132.52
130.67
111.68
77.42
77.00
76.58
75.11
69.89
40.47
38.99
28.91
27.15
24.06
21.13
PivO
OH
CDCl3, 75MHz
11
f1 (ppm)

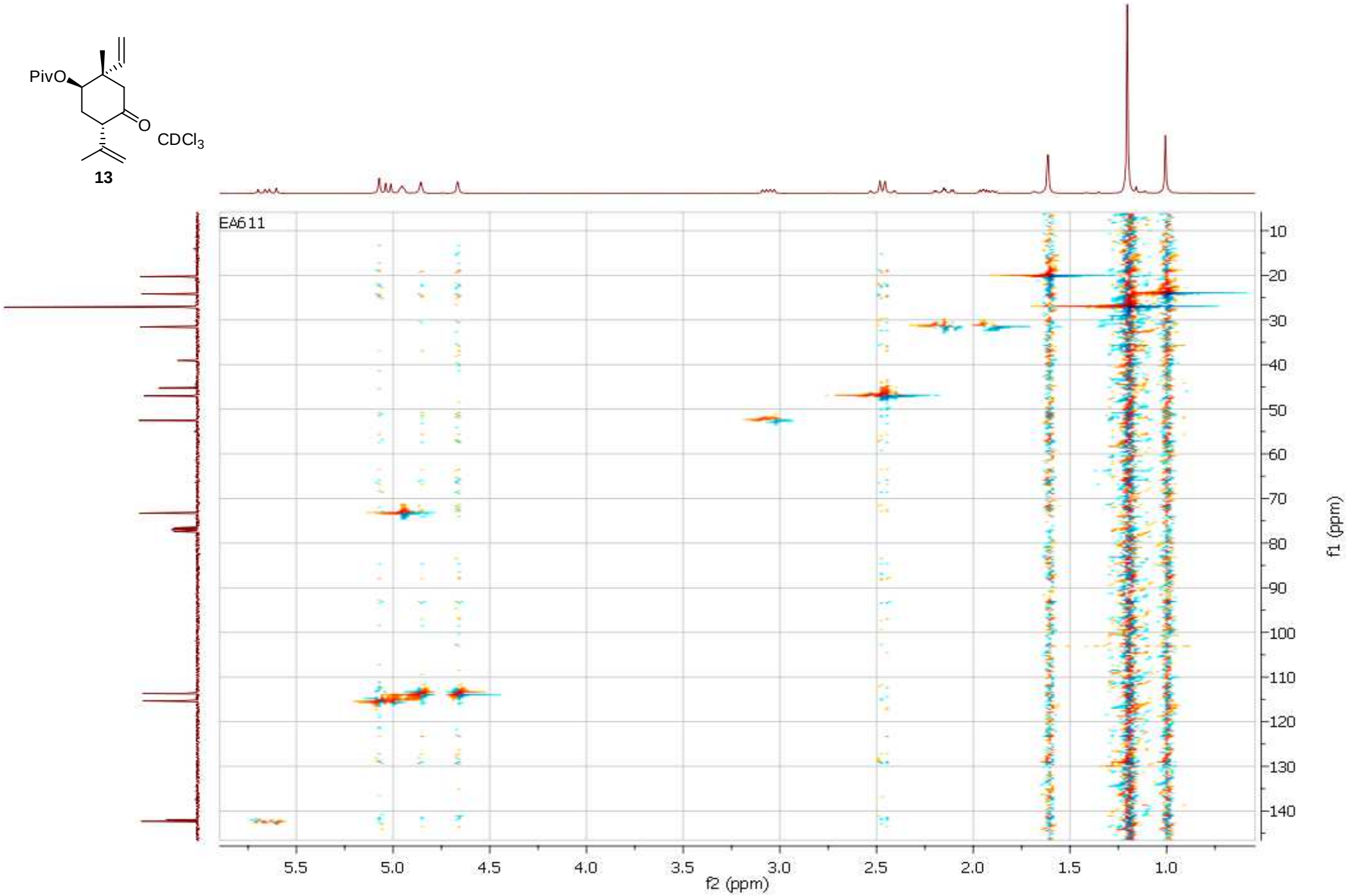

EA602
piv-alcohol +pcC stili kirio spot
PivO
O
CDCl3, 300MHz
12
7.26
5.96
5.52
5.50
5.48
4.97
4.77
3.22
3.21
3.19
3.18
2.44
2.42
2.41
2.39
2.38
2.36
2.35
2.15
2.13
2.11
2.10
2.08
2.07
2.04
1.93
1.93
1.78
1.76
1.54
1.31
1.28
1.25
1.24
1.24
1.18
1.18
1.00
1.02
1.11
1.24
1.08
1.35
1.22
3.27
3.45
10.11
f1 (ppm)

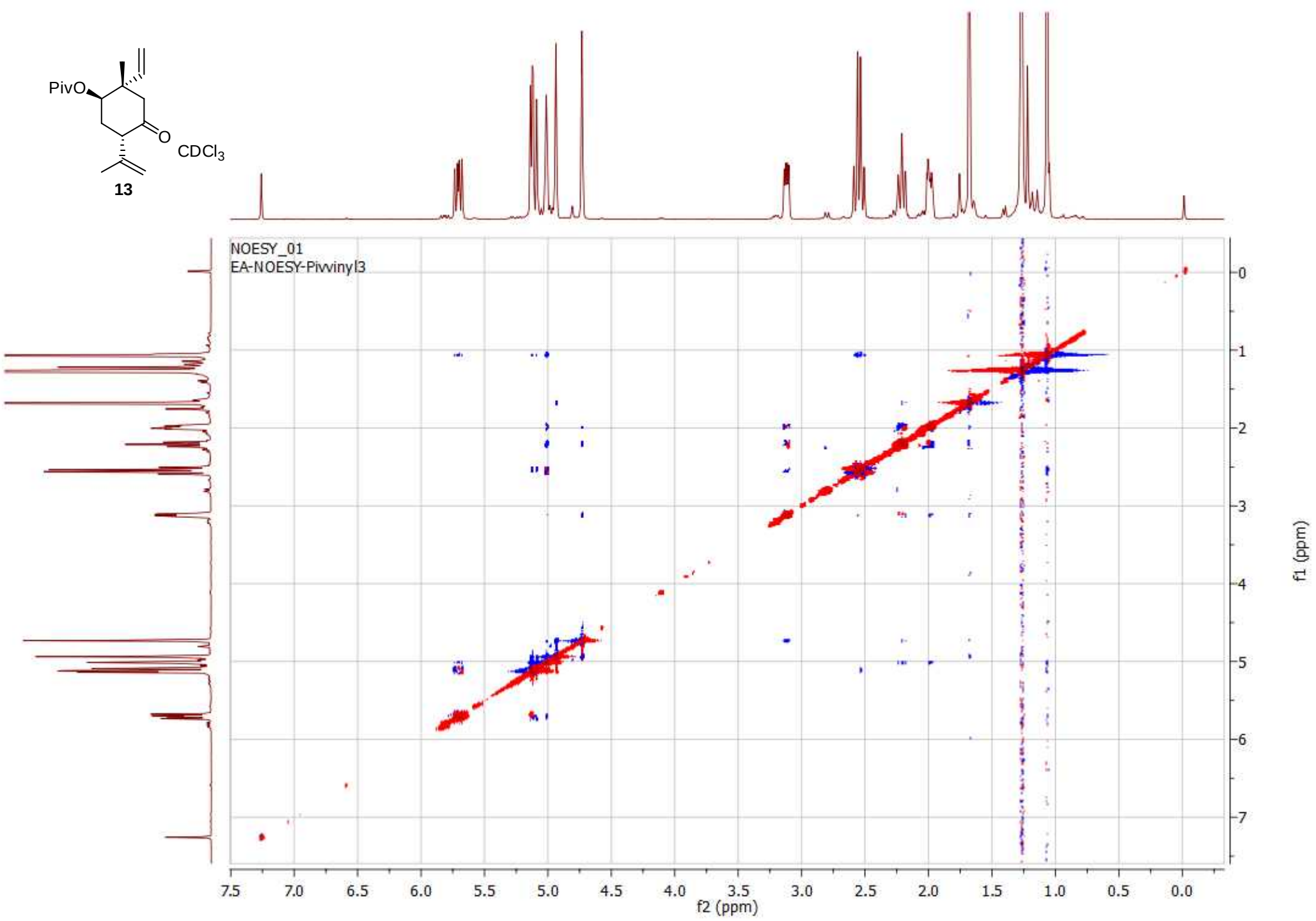

EA602
piv-alcohol +pcC stil kirio spot again CARBON
142.97
133.66
156.25
141.85
128.78
113.67
77.42
77.00
76.57
68.51
50.42
38.92
32.64
26.97
20.93
20.52
PivO
O
CDCl3, 75MHz
12
f1 (ppm)

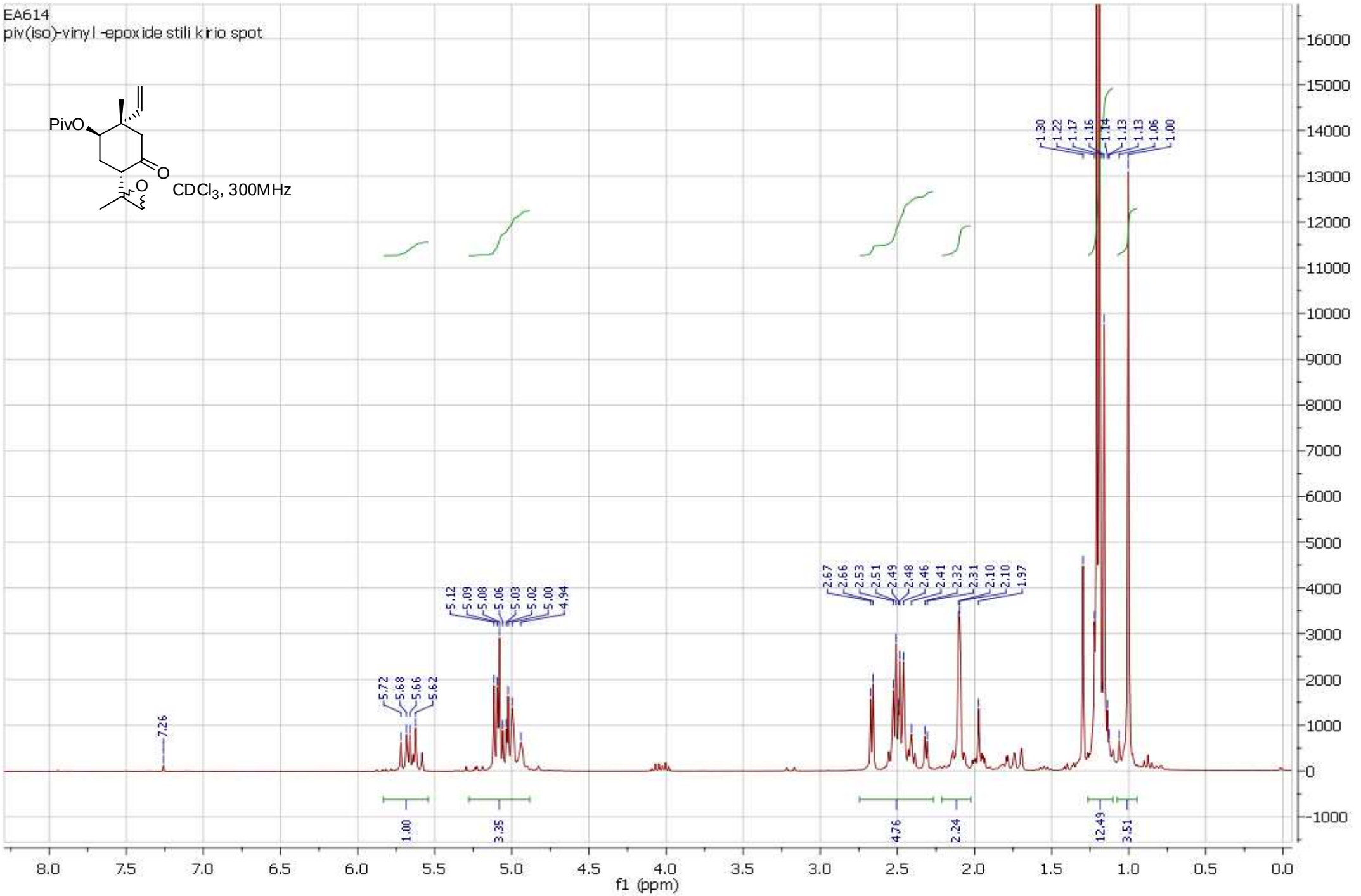

EA611
PivO
O
CDCl3, 300MHz
13
f1 (ppm)

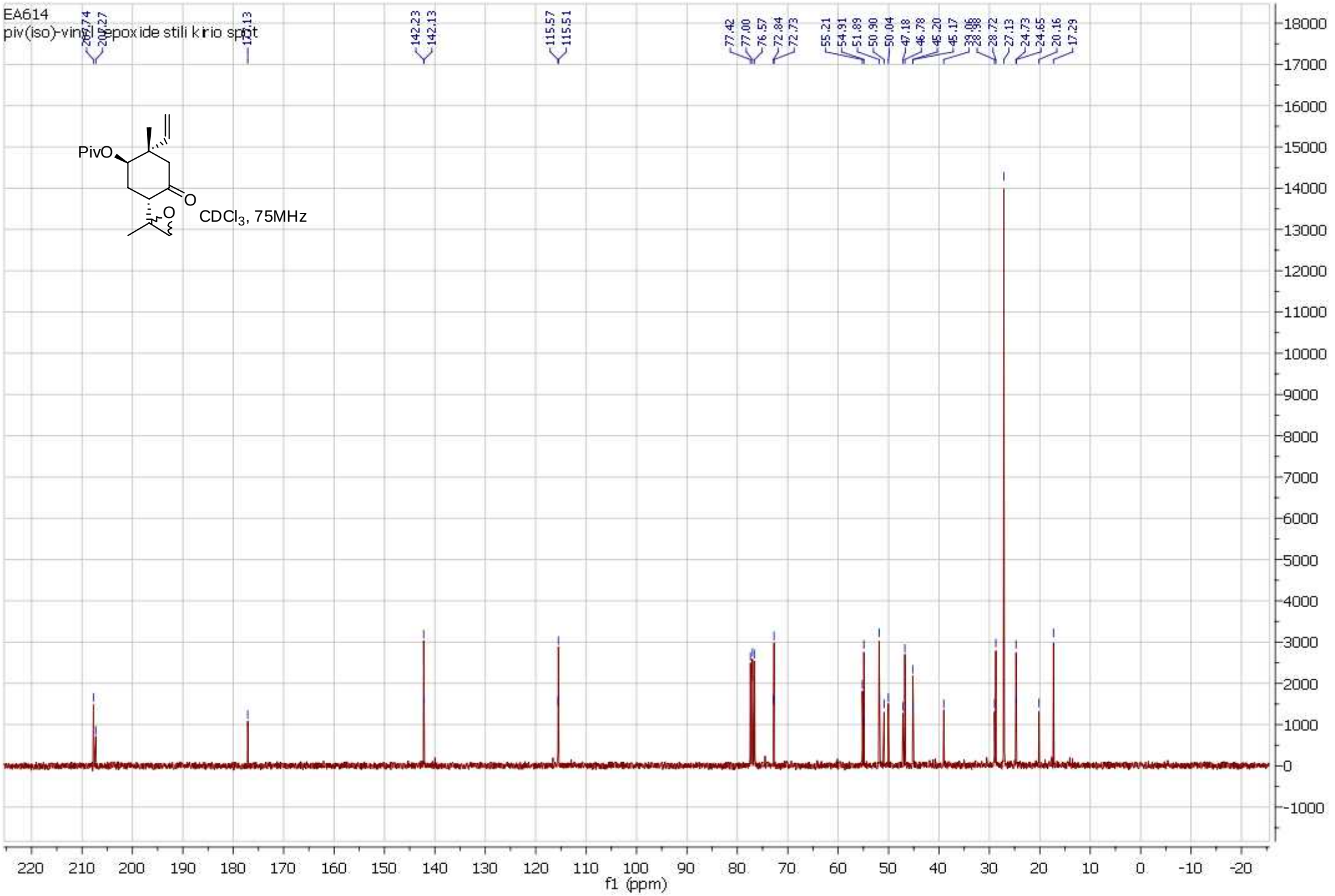

EA611
Piv(iso)-VINYL STILI
208.93
177.26
142.32
141.99
115.34
113.69
77.42
77.00
76.57
73.29
52.51
47.01
45.23
39.09
31.55
27.13
24.16
20.28
PivO
O
CDCl3, 75MHz
13
f1 (ppm)

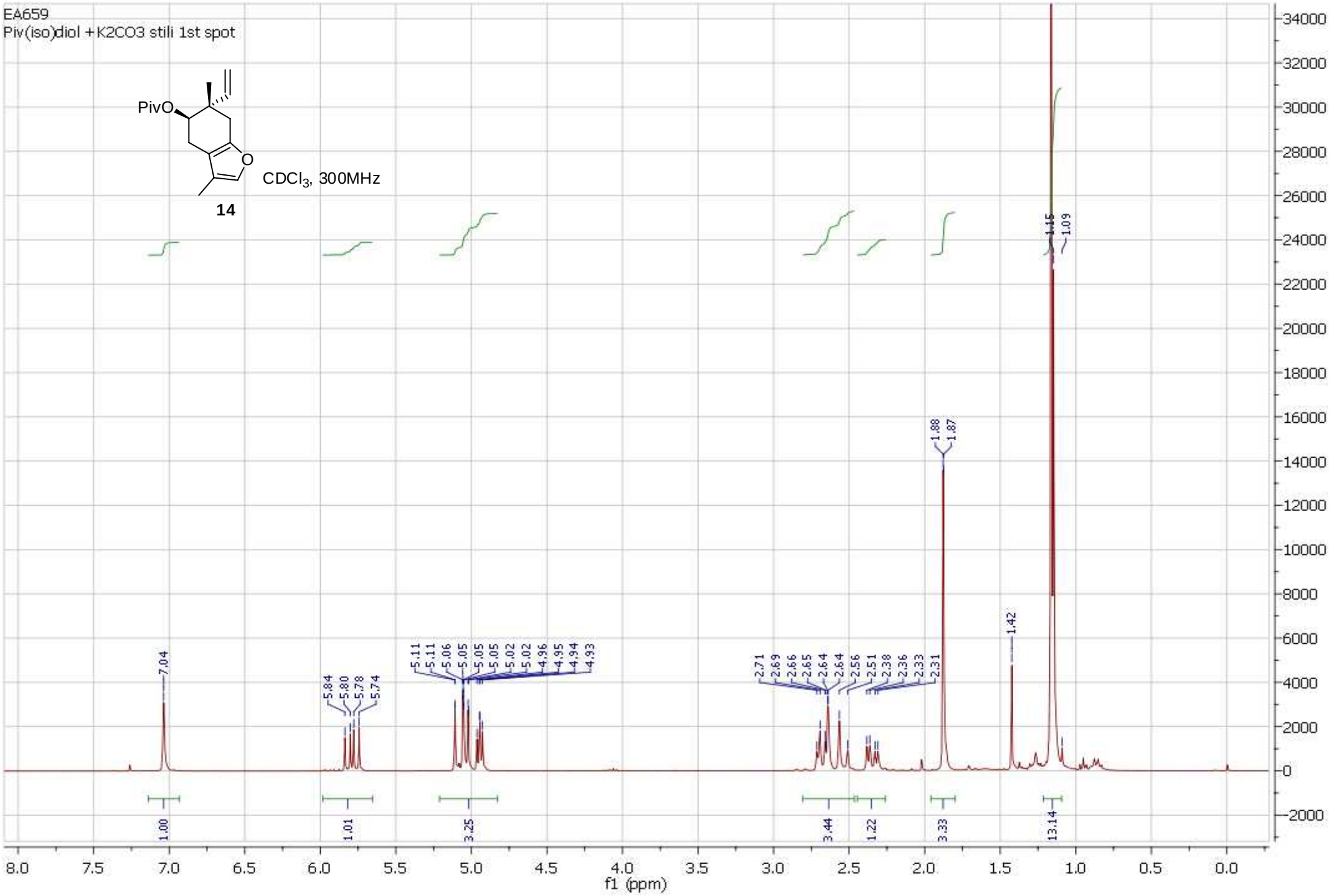

PivO
O
$CDCl_3$
13
EA611
f2 (ppm)
f1 (ppm)

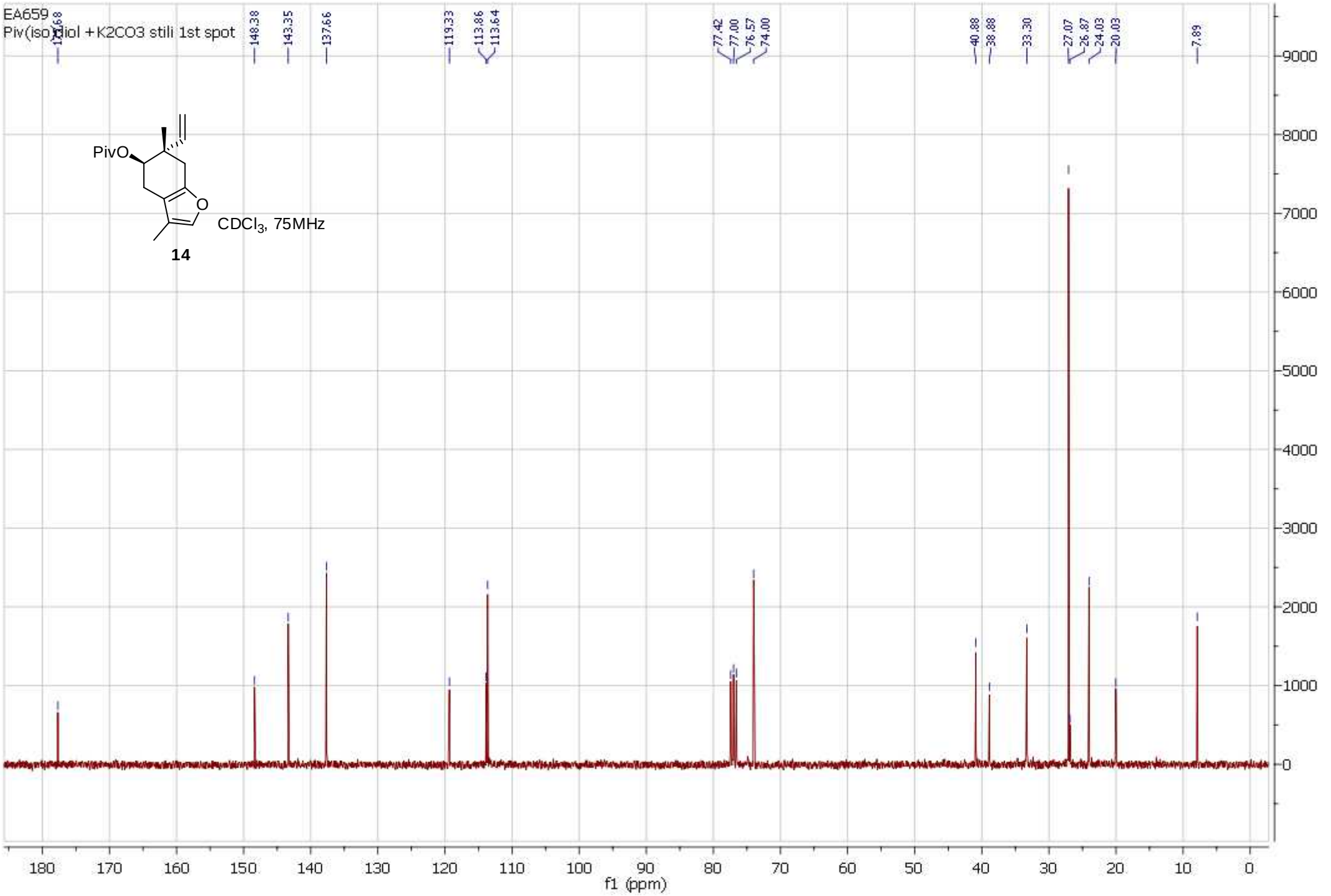

PivO
O
CDCl3
13
EA611
f2 (ppm)
f1 (ppm)

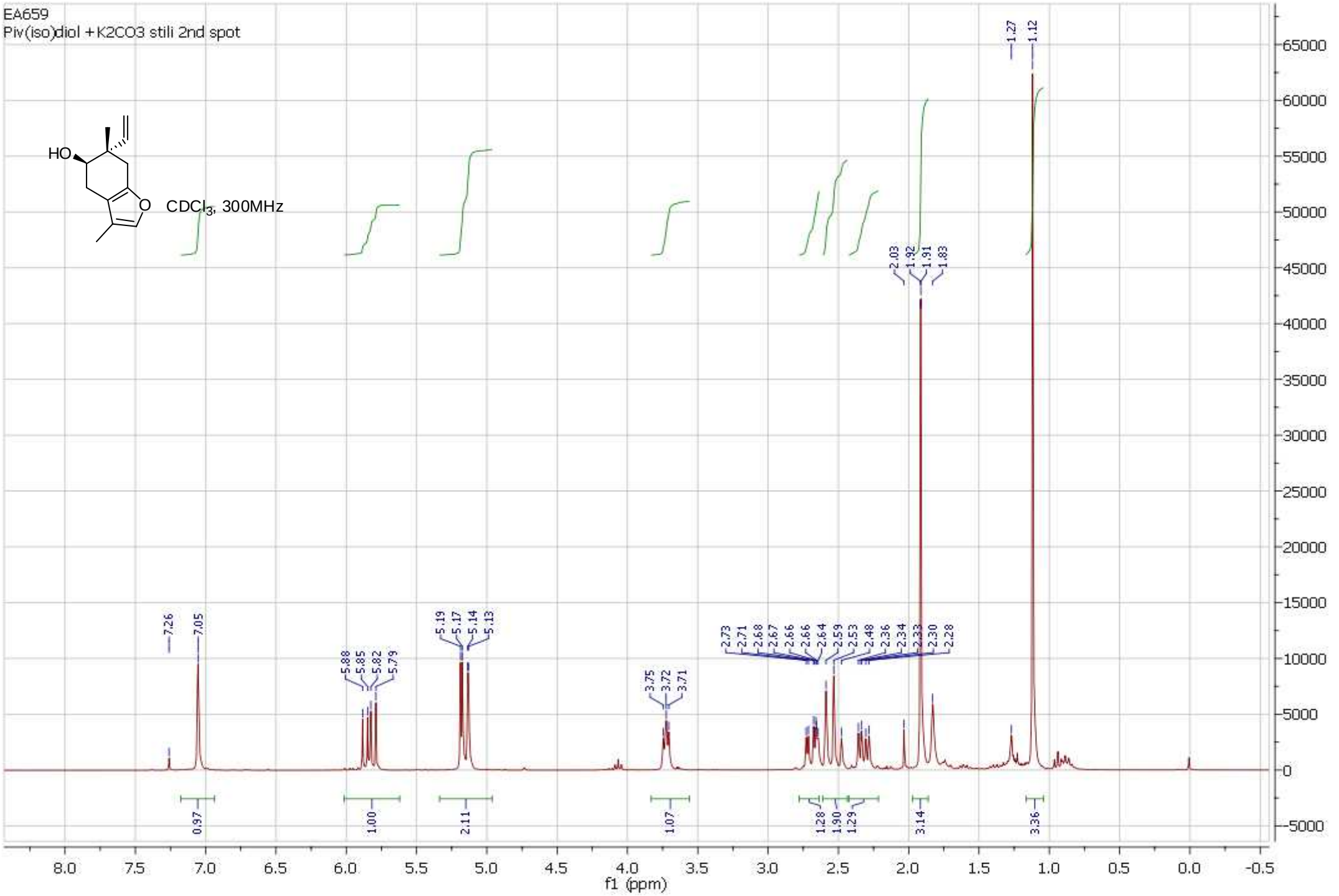

PivO
O
CDCl3
13
NOESY_01
EA-NOESY-Pivvinyl3
f2 (ppm)
f1 (ppm)

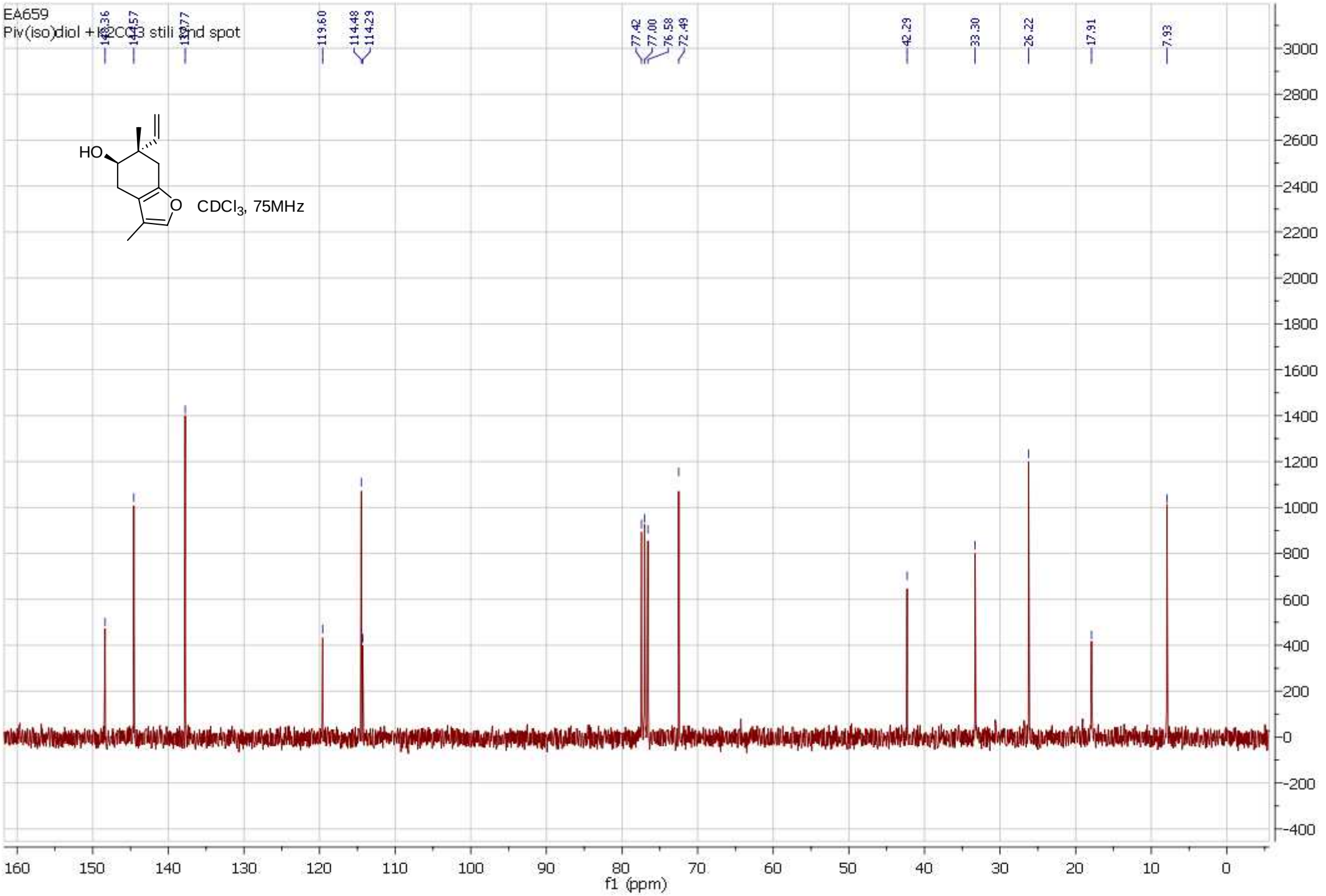

EA614
piv(iso)-vinyl -epoxide stili kirio spot
PivO
O
O
CDCl3, 300MHz
1.30
1.22
1.17
1.16
1.14
1.13
1.13
1.06
1.00
2.67
2.66
2.53
2.51
2.49
2.48
2.46
2.41
2.32
2.31
2.10
2.10
1.97
5.12
5.09
5.08
5.06
5.03
5.02
5.00
4.94
5.72
5.68
5.66
5.62
7.26
1.00
3.35
4.76
2.24
12.49
3.51
f1 (ppm)

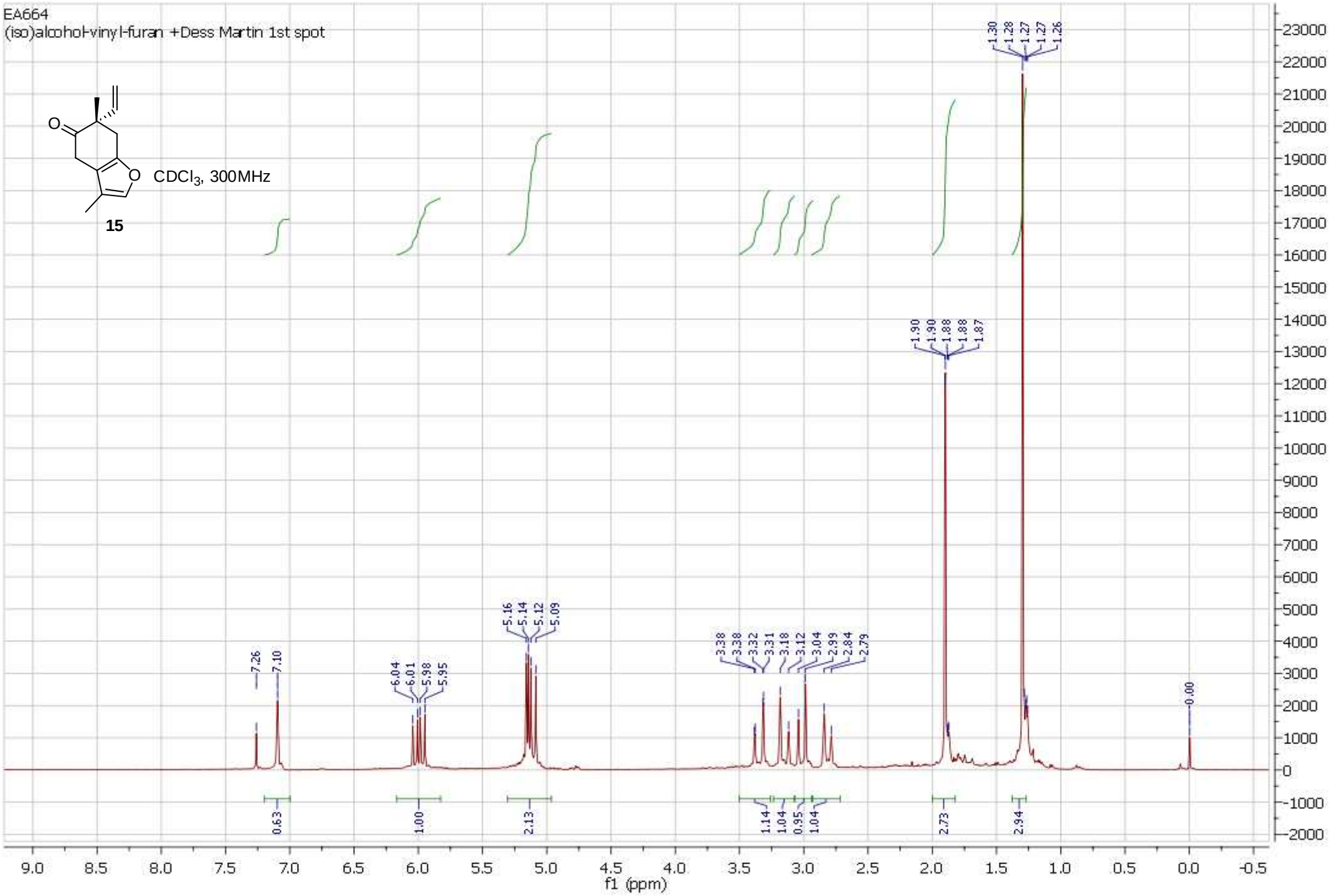

EA614
piv(iso)-vinyl epoxide stili kirio spot
207.74
205.27
142.23
142.13
115.57
115.51
77.42
77.00
76.57
72.84
72.73
55.21
54.91
51.89
50.90
50.04
47.18
46.78
45.20
45.17
33.06
28.98
28.72
27.13
24.73
24.65
20.16
17.29
PivO
O
O
CDCl3, 75MHz
f1 (ppm)

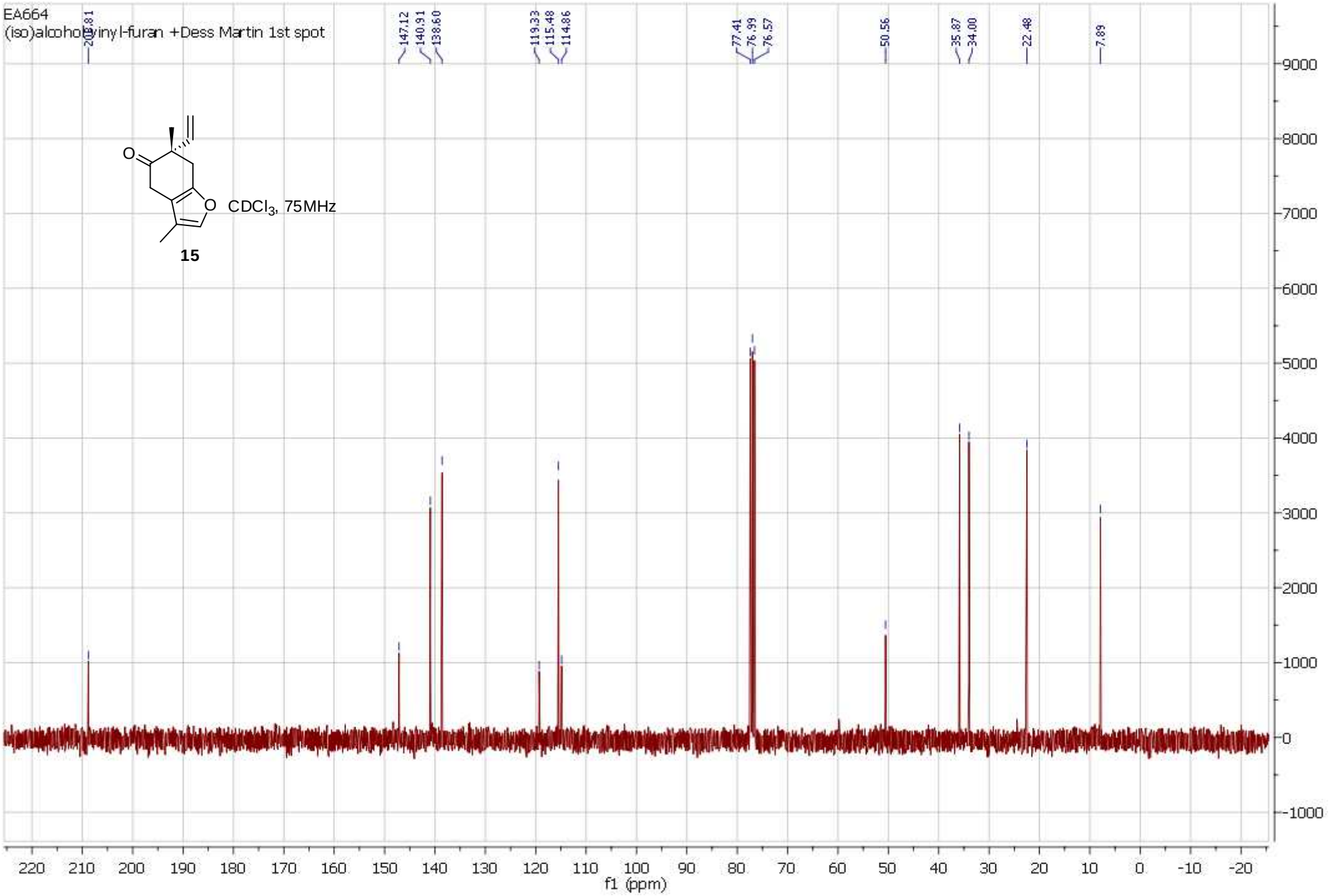

EA659
Piv(iso)diol +K2CO3 stili 1st spot
PivO
O
CDCl3, 300MHz
14
7.04
5.84
5.80
5.78
5.74
5.11
5.11
5.06
5.05
5.05
5.05
5.02
5.02
4.96
4.95
4.94
4.93
2.71
2.69
2.66
2.65
2.64
2.64
2.56
2.51
2.38
2.36
2.33
2.31
1.88
1.87
1.42
1.15
1.09
1.00
1.01
3.25
3.44
1.22
3.33
13.14
f1 (ppm)

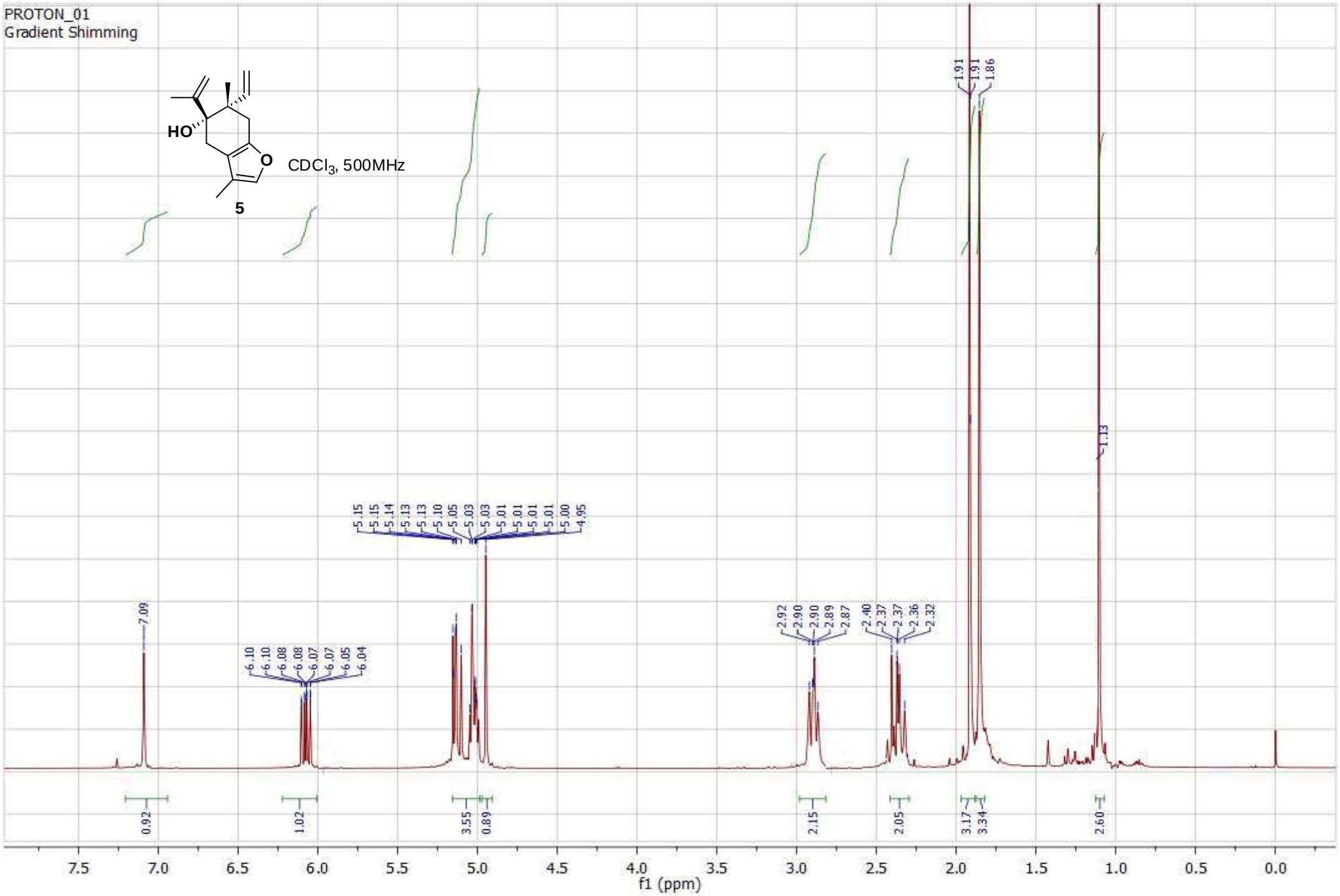

EA659
Piv(iso)diol +K2CO3 stili 1st spot
148.38
143.35
137.66
119.33
113.86
113.64
77.42
77.00
76.57
74.00
40.88
38.88
33.30
27.07
26.87
24.03
20.03
7.89
PivO
O
CDCl3, 75MHz
14
f1 (ppm)

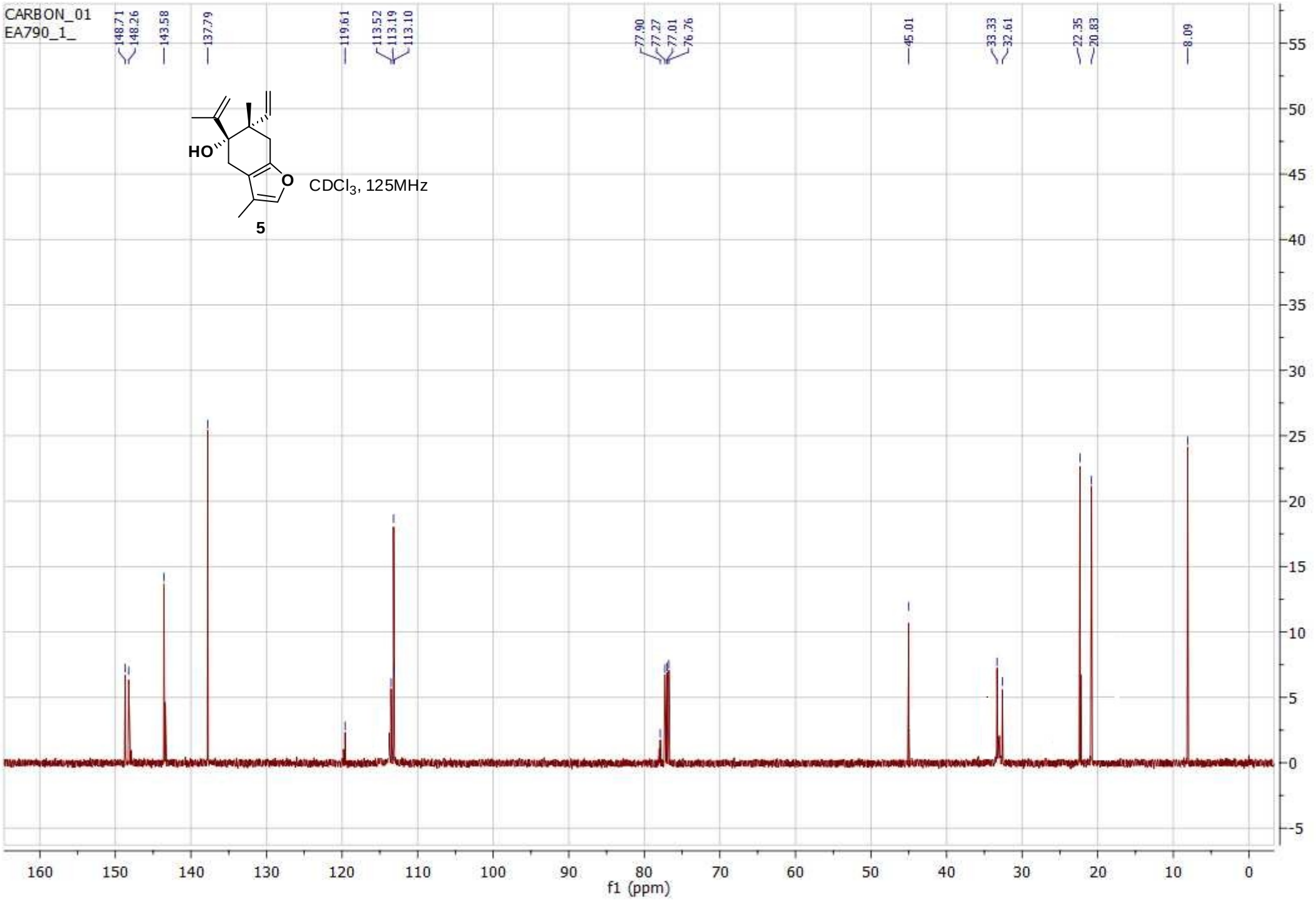

EA659
Piv(iso)diol + K2CO3 stili 2nd spot
HO
O
CDCl3, 300MHz
7.26
7.05
5.88
5.85
5.82
5.79
5.19
5.17
5.14
5.13
3.75
3.72
3.71
2.73
2.71
2.68
2.67
2.66
2.66
2.64
2.59
2.53
2.48
2.36
2.34
2.33
2.30
2.28
2.03
1.92
1.91
1.83
1.27
1.12
0.97
1.00
2.11
1.07
1.28
1.90
1.29
3.14
3.36
f1 (ppm)

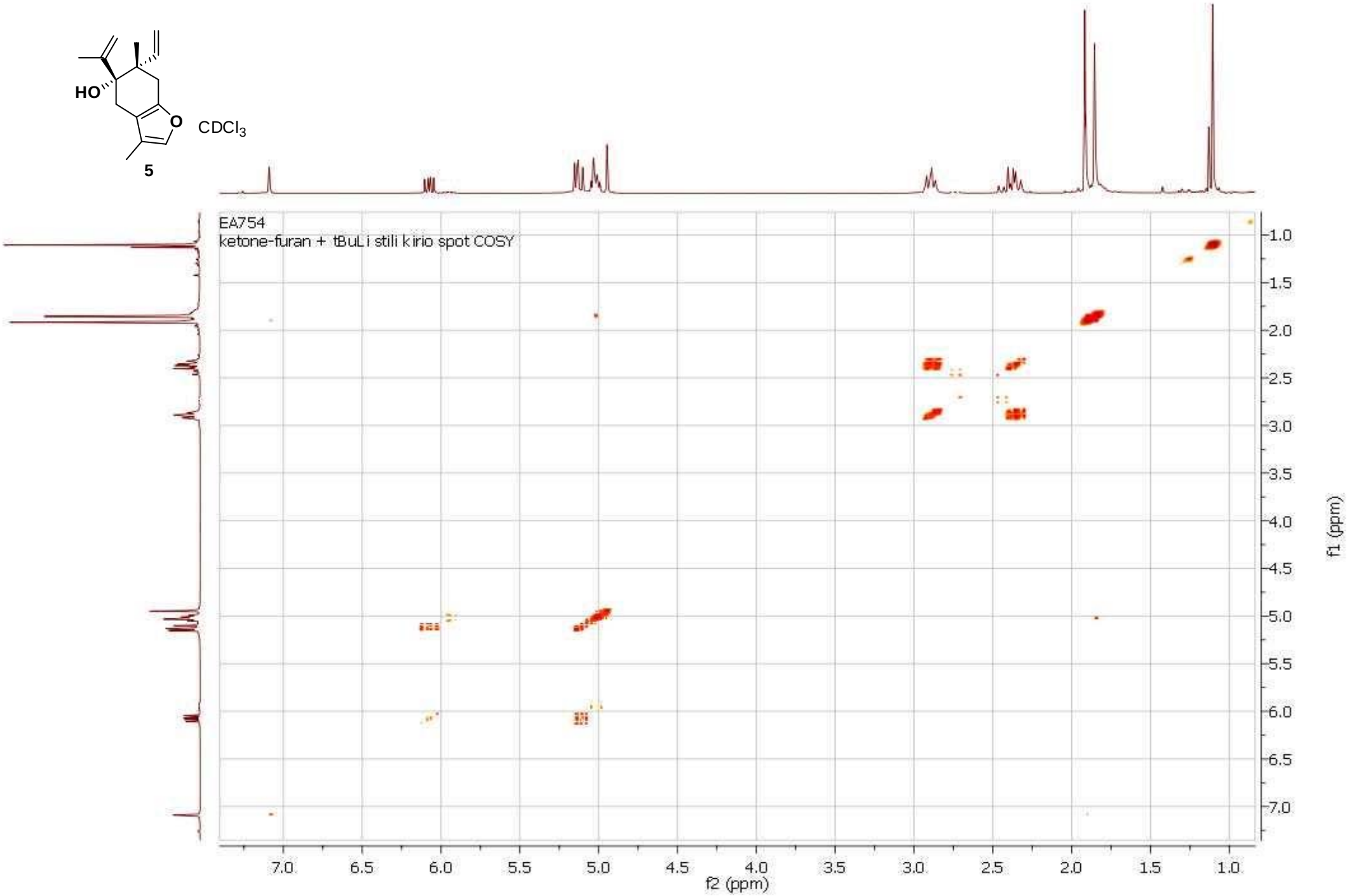

EA659
Piv(iso)diol + K2CO3 stili 2nd spot
148.36
144.57
137.77
119.60
114.48
114.29
77.42
77.00
76.58
72.49
42.29
33.30
26.22
17.91
7.93
HO
O
CDCl3, 75MHz
f1 (ppm)

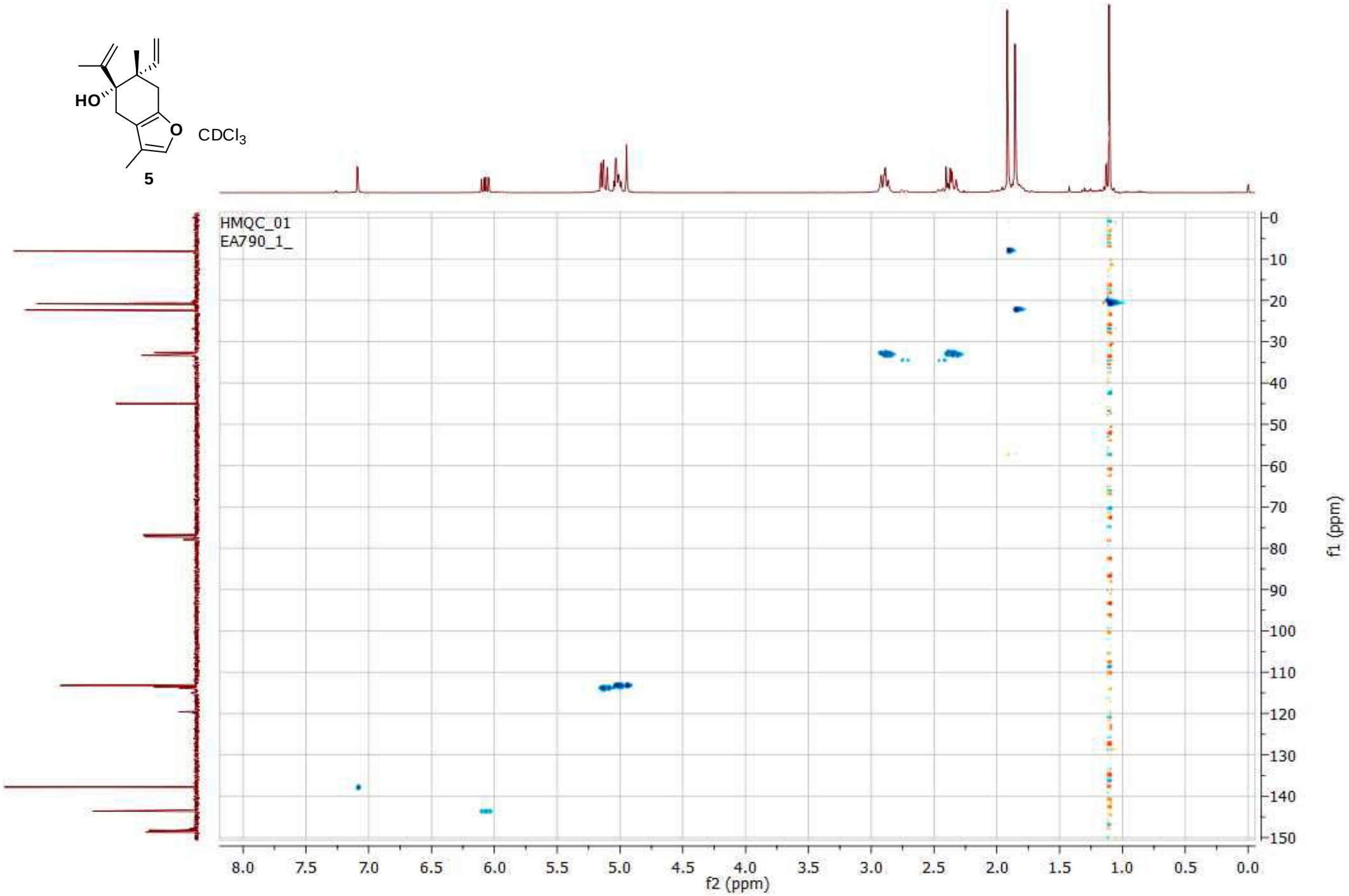

EA664
(iso)alcohol-vinyl-furan +Dess Martin 1st spot
O
O
15
CDCl3, 300MHz
7.26
7.10
6.04
6.01
5.98
5.95
5.16
5.14
5.12
5.09
3.38
3.38
3.32
3.31
3.18
3.12
3.04
2.99
2.84
2.79
1.90
1.90
1.88
1.88
1.87
1.30
1.28
1.27
1.27
1.26
0.00
0.63
1.00
2.13
1.14
1.04
0.95
1.04
2.73
2.94
f1 (ppm)

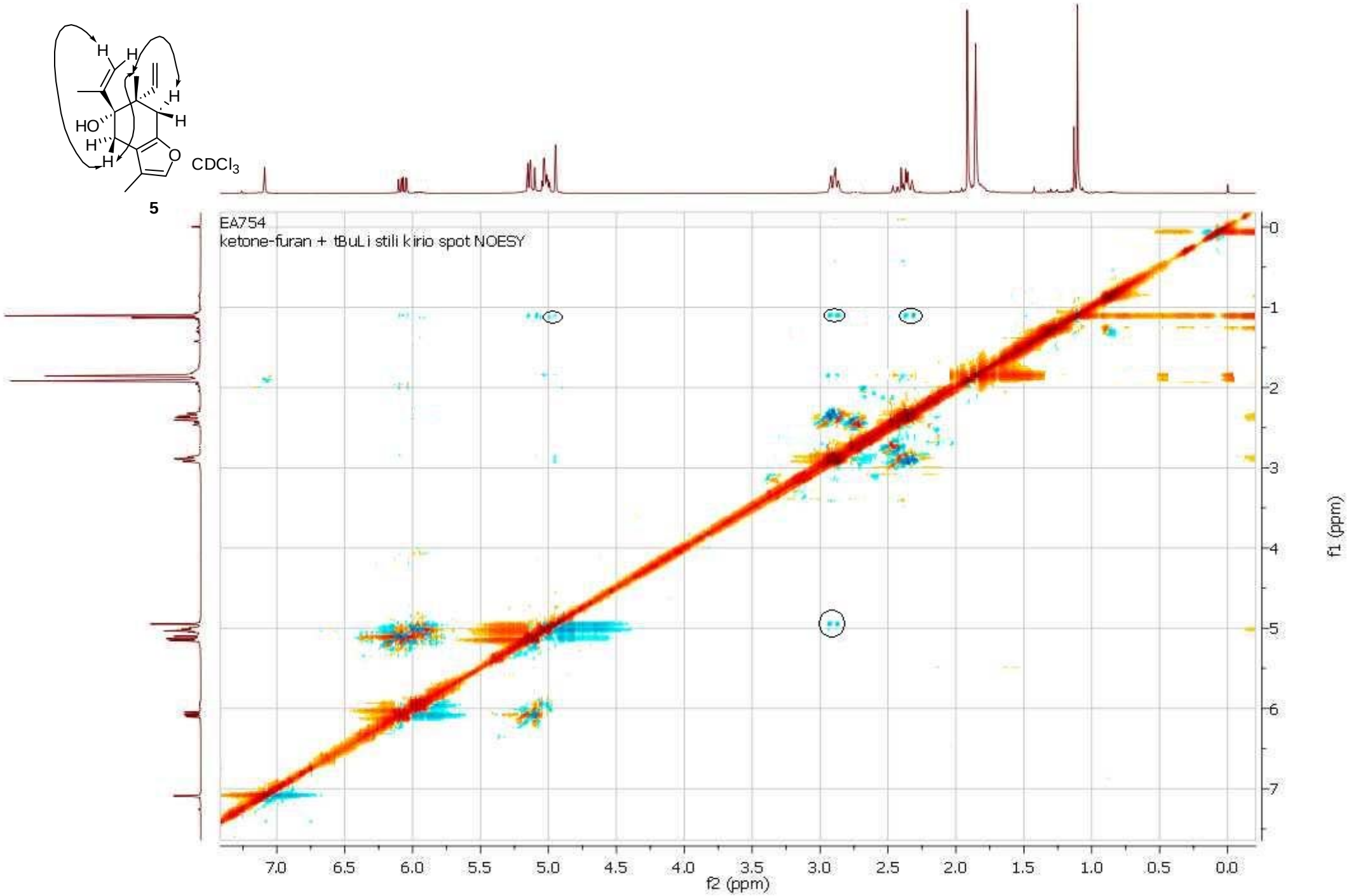

EA664
(iso)alcohol-vinyl-furan +Dess Martin 1st spot
209.81
147.12
140.91
138.60
119.33
115.48
114.86
77.41
76.99
76.57
50.56
35.87
34.00
22.48
7.89
O
O
CDCl3, 75MHz
15
f1 (ppm)

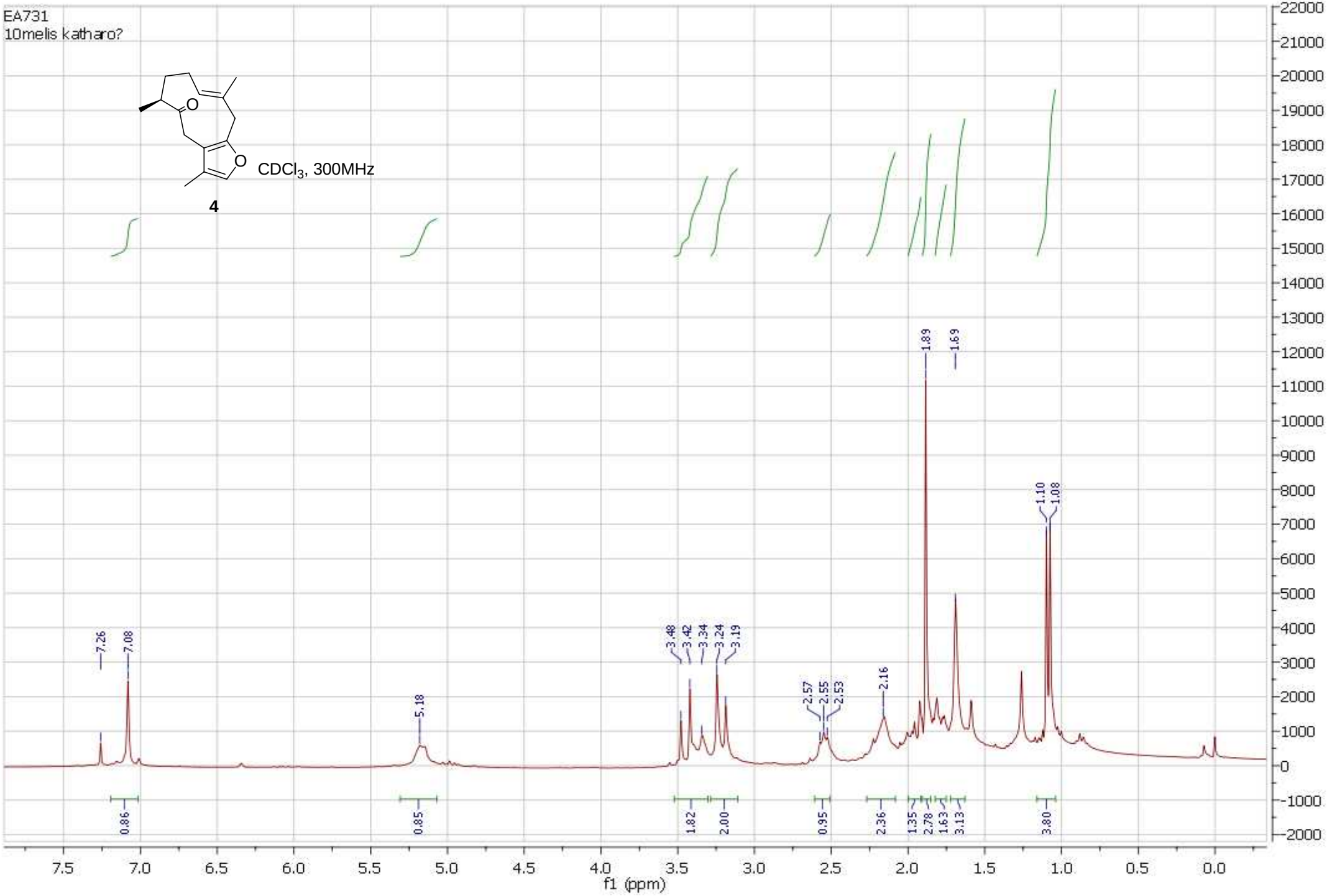

PROTON_01
Gradient Shimming
HO
O
CDCl3, 500MHz
5
7.09
6.10
6.10
6.08
6.08
6.07
6.07
6.05
6.04
5.15
5.15
5.14
5.13
5.13
5.10
5.05
5.03
5.03
5.01
5.01
5.01
5.01
5.00
4.95
2.92
2.90
2.90
2.89
2.87
2.40
2.37
2.37
2.36
2.32
1.91
1.91
1.86
1.13
0.92
1.02
3.55
0.89
2.15
2.05
3.17
3.34
2.60
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

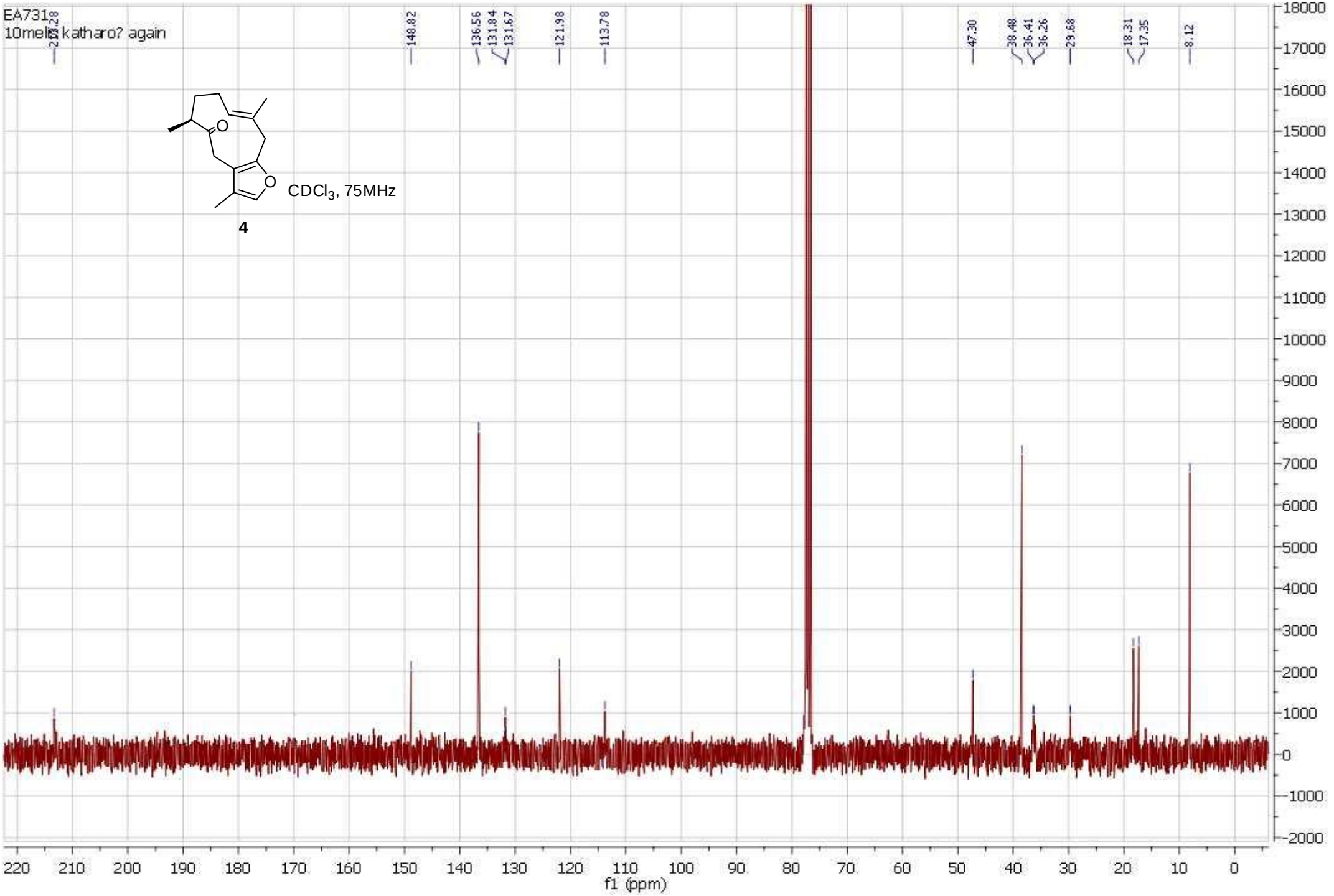

CARBON_01
EA790_1_
148.71
148.26
143.58
137.79
119.61
113.52
113.19
113.10
77.90
77.27
77.01
76.76
45.01
33.33
32.61
22.35
20.83
8.09
HO
O
CDCl3, 125MHz
5
f1 (ppm)

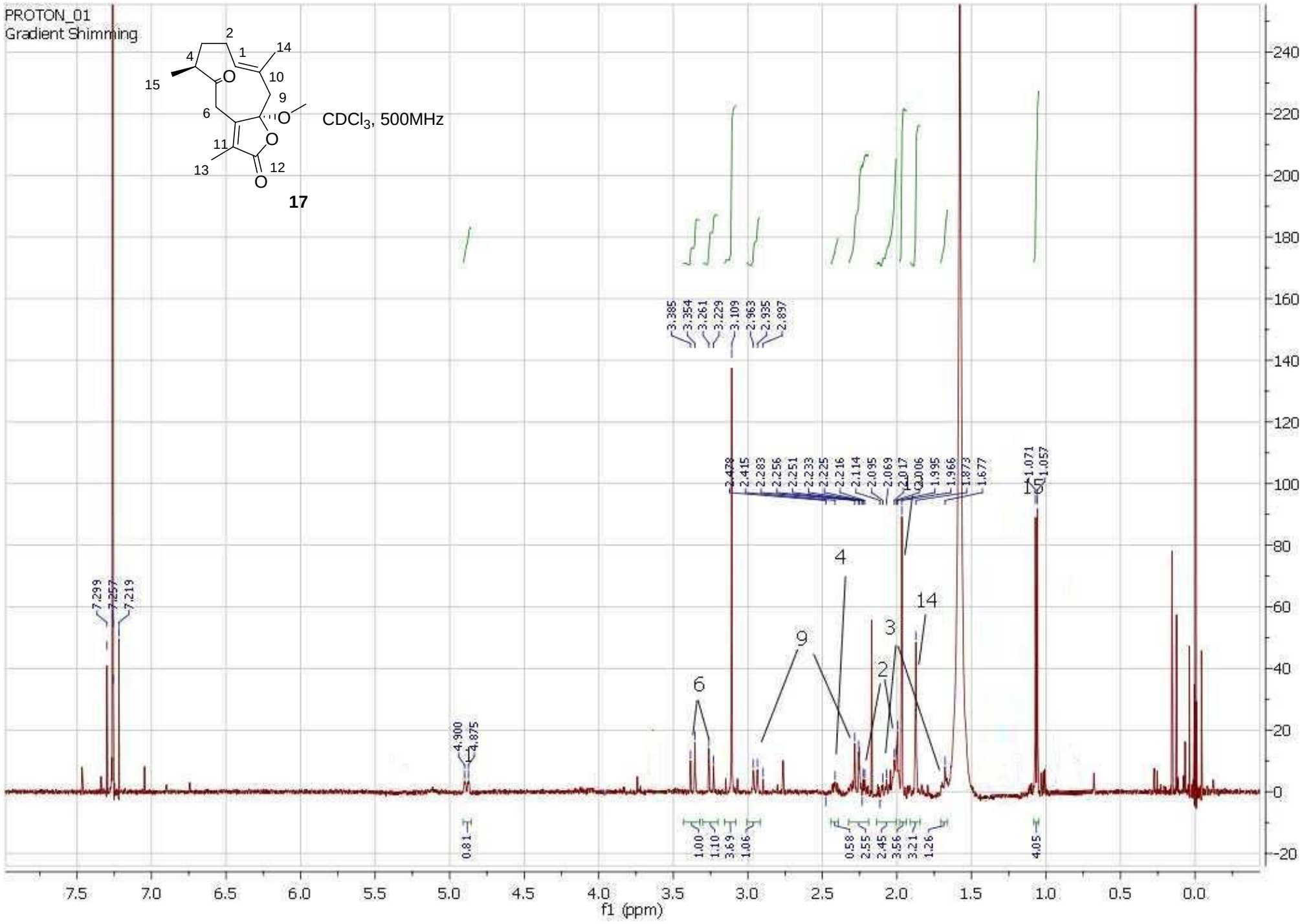

HO
O
CDCl3
5
EA754
ketone-furan + tBuLi stili kirio spot COSY
f2 (ppm)
f1 (ppm)

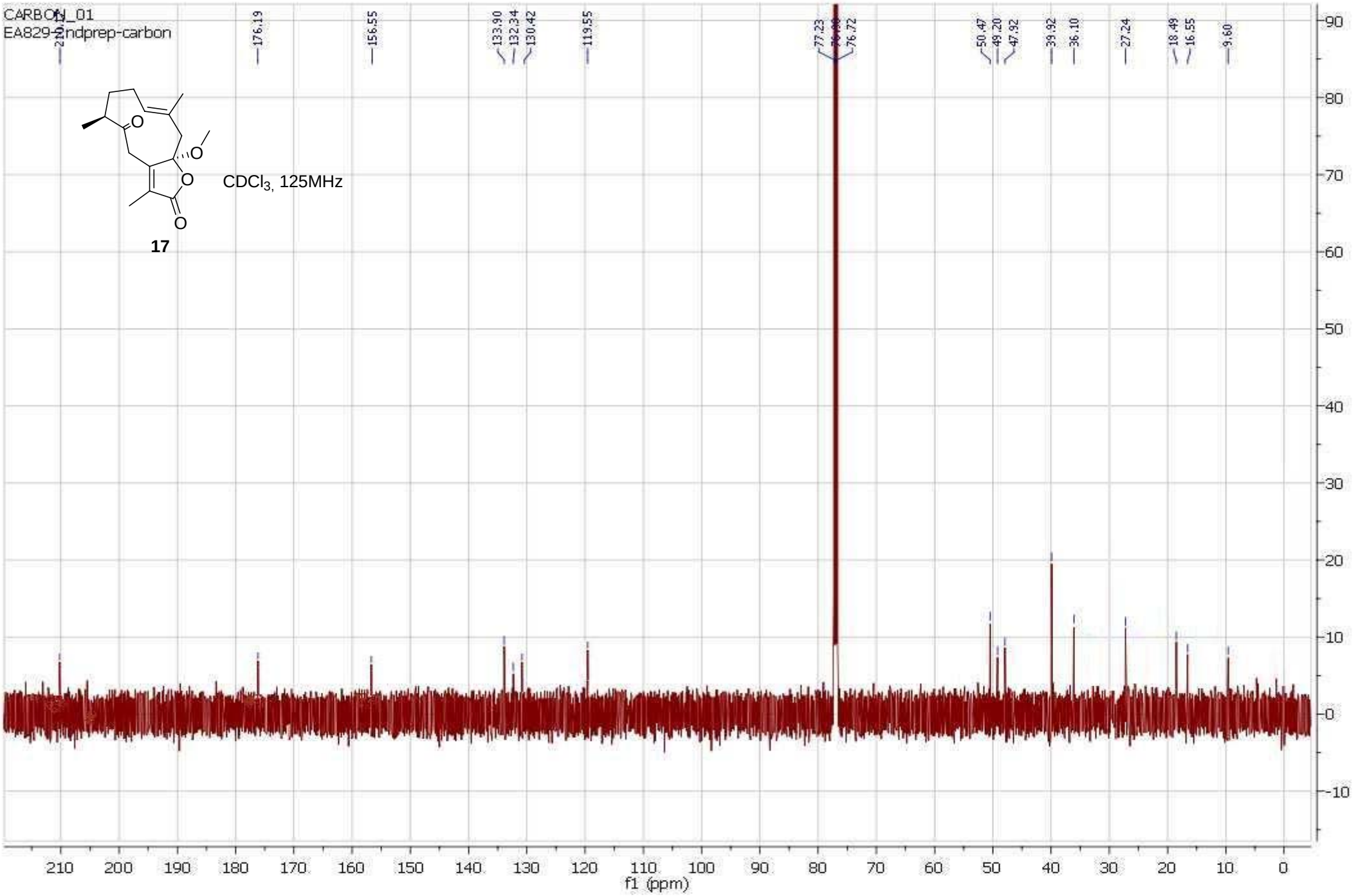

HO
O
CDCl3
5
HMQC_01
EA790_1_
f2 (ppm)
f1 (ppm)

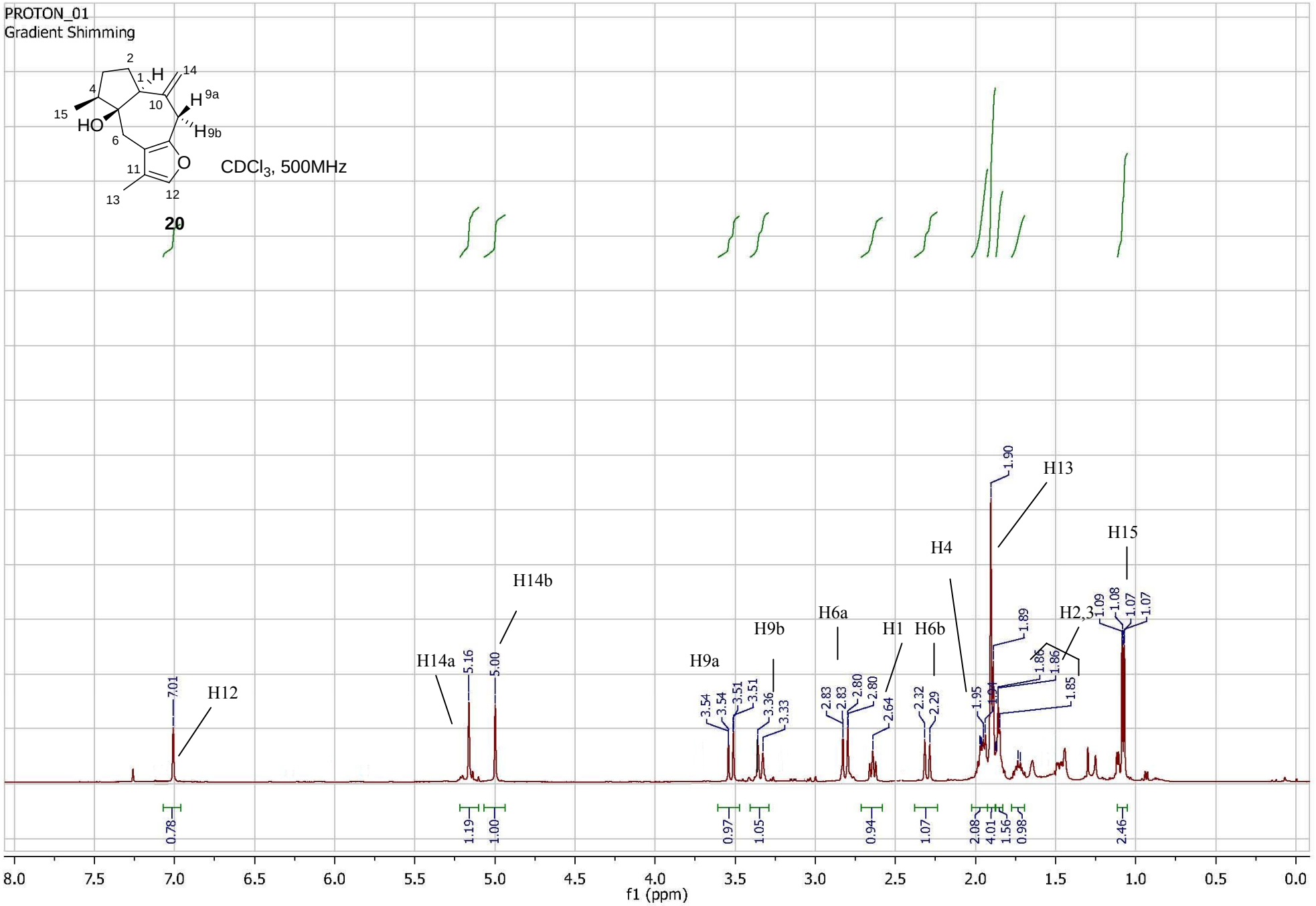

H
H
H
HO
H
H
O
CDCl3
5
EA754
ketone-furan + tBuLi stili kirio spot NOESY
f2 (ppm)
f1 (ppm)

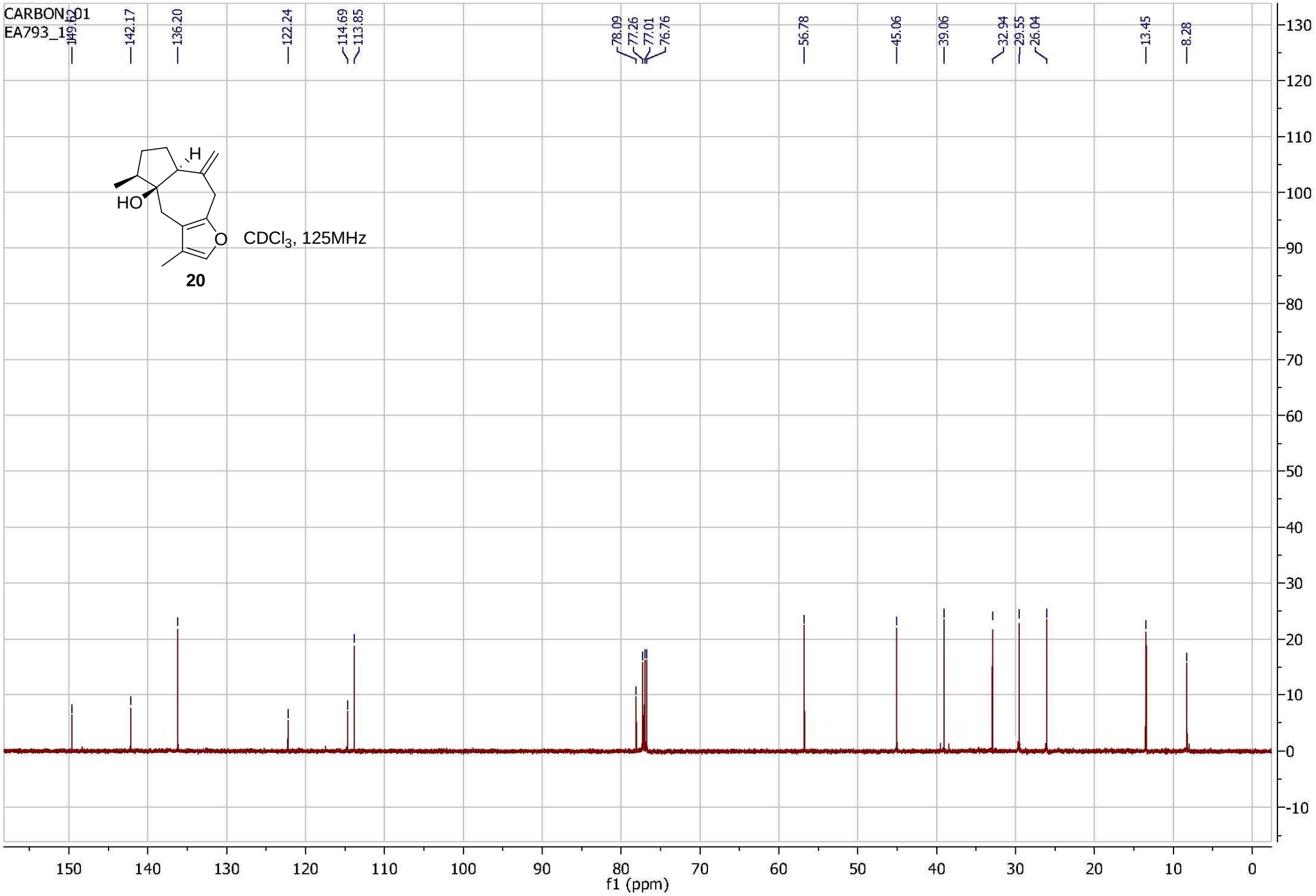

EA731
10melis katharo?
O
O
CDCl3, 300MHz
4
7.26
7.08
5.18
3.48
3.42
3.34
3.24
3.19
2.57
2.55
2.53
2.16
1.89
1.69
1.10
1.08
0.86
0.85
1.82
2.00
0.95
2.36
1.35
2.78
1.63
3.13
3.80
f1 (ppm)

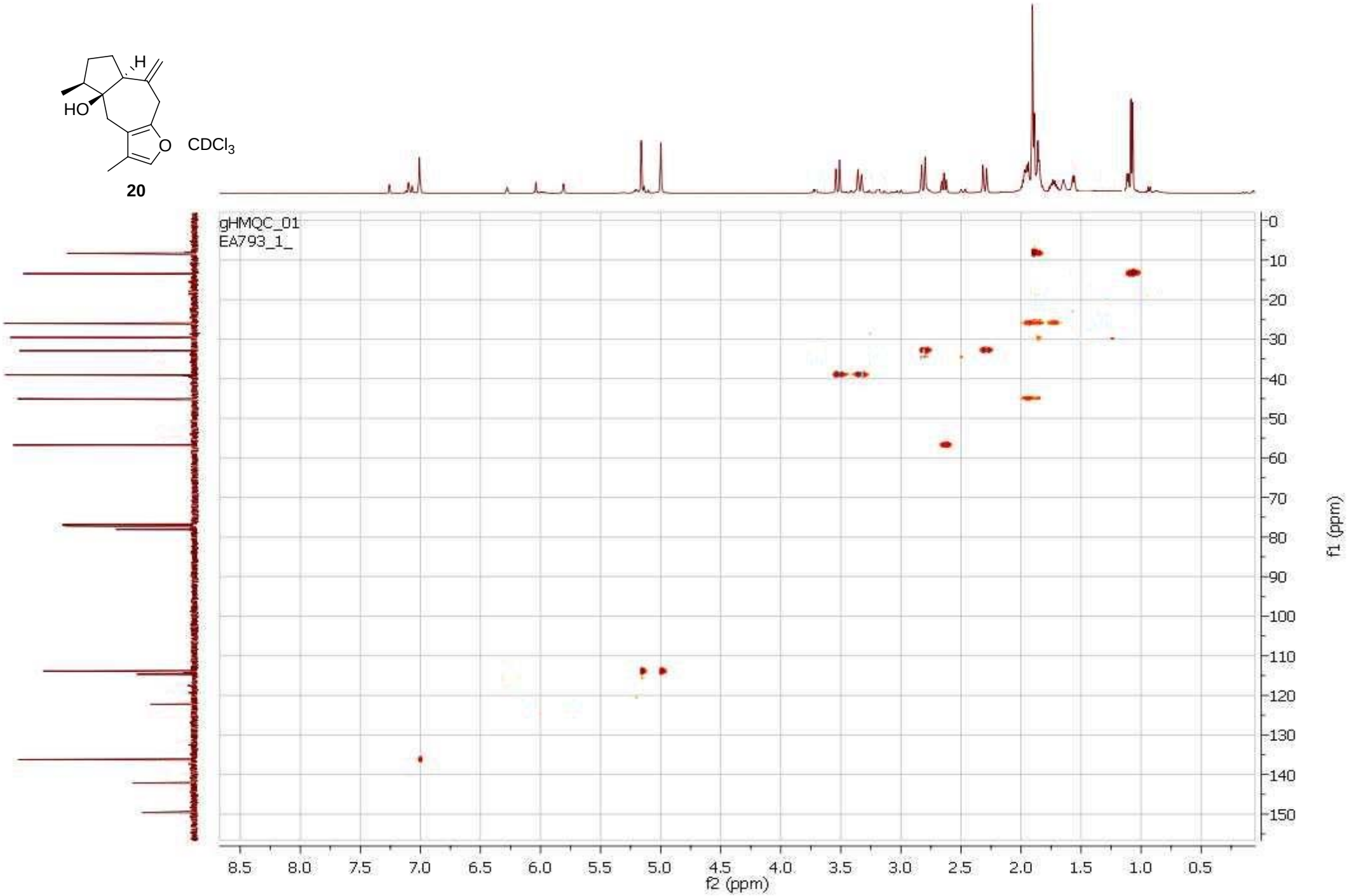

EA731
10melis katharo? again
213.28
148.82
136.56
131.84
131.67
121.98
113.78
47.30
38.48
36.41
36.26
29.68
18.31
17.35
8.12
O
O
CDCl3, 75MHz
4
f1 (ppm)

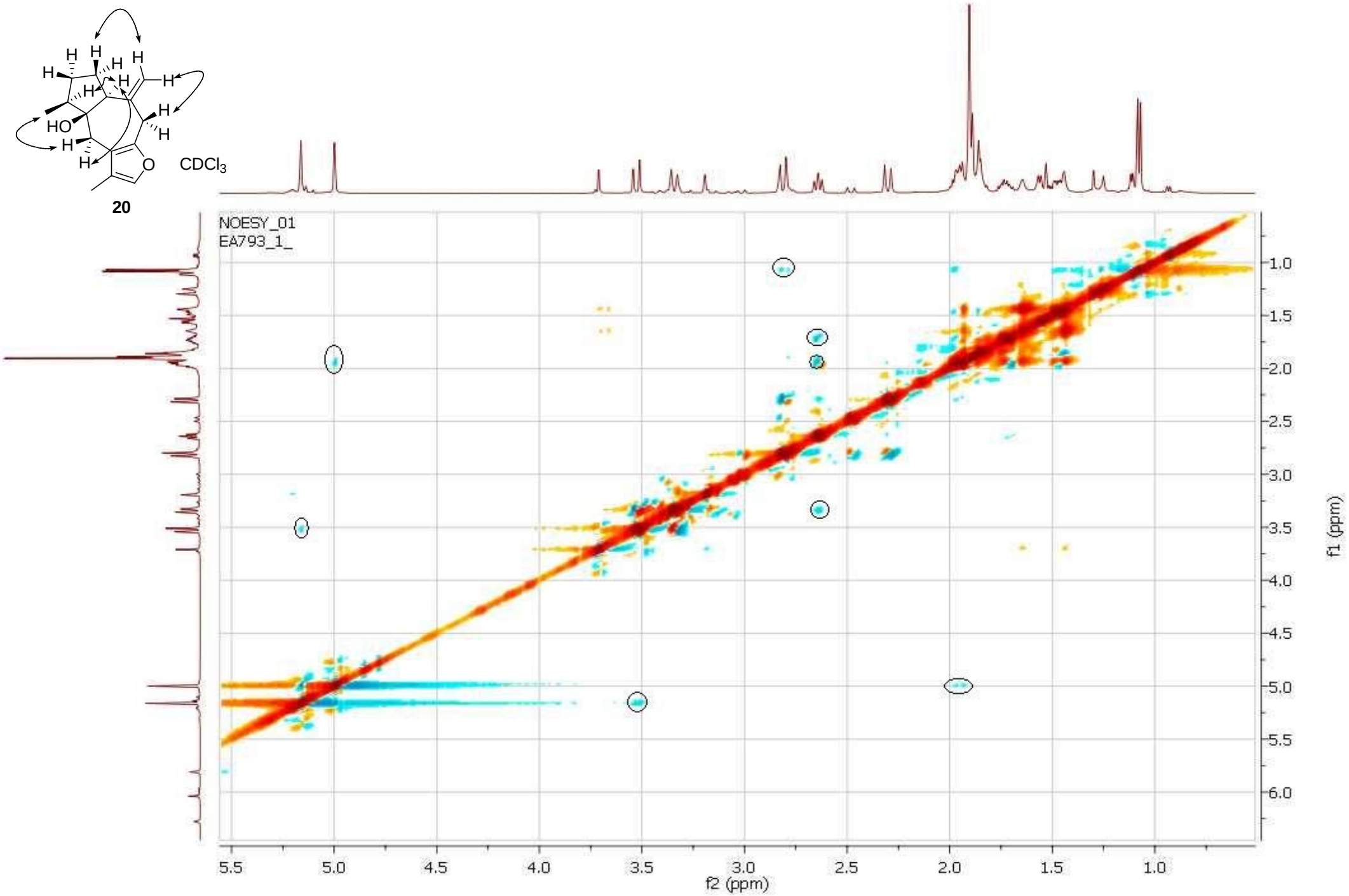

PROTON_01
Gradient Shimming
CDCl3, 500MHz
17
f1 (ppm)


CARBON_01
EA829-2-ndprep-carbon
176.19
156.55
133.90
132.34
130.42
119.55
77.23
76.72
50.47
49.20
47.92
39.92
36.10
27.24
18.49
16.55
9.60
O
O
O
O
CDCl3, 125MHz
17
f1 (ppm)

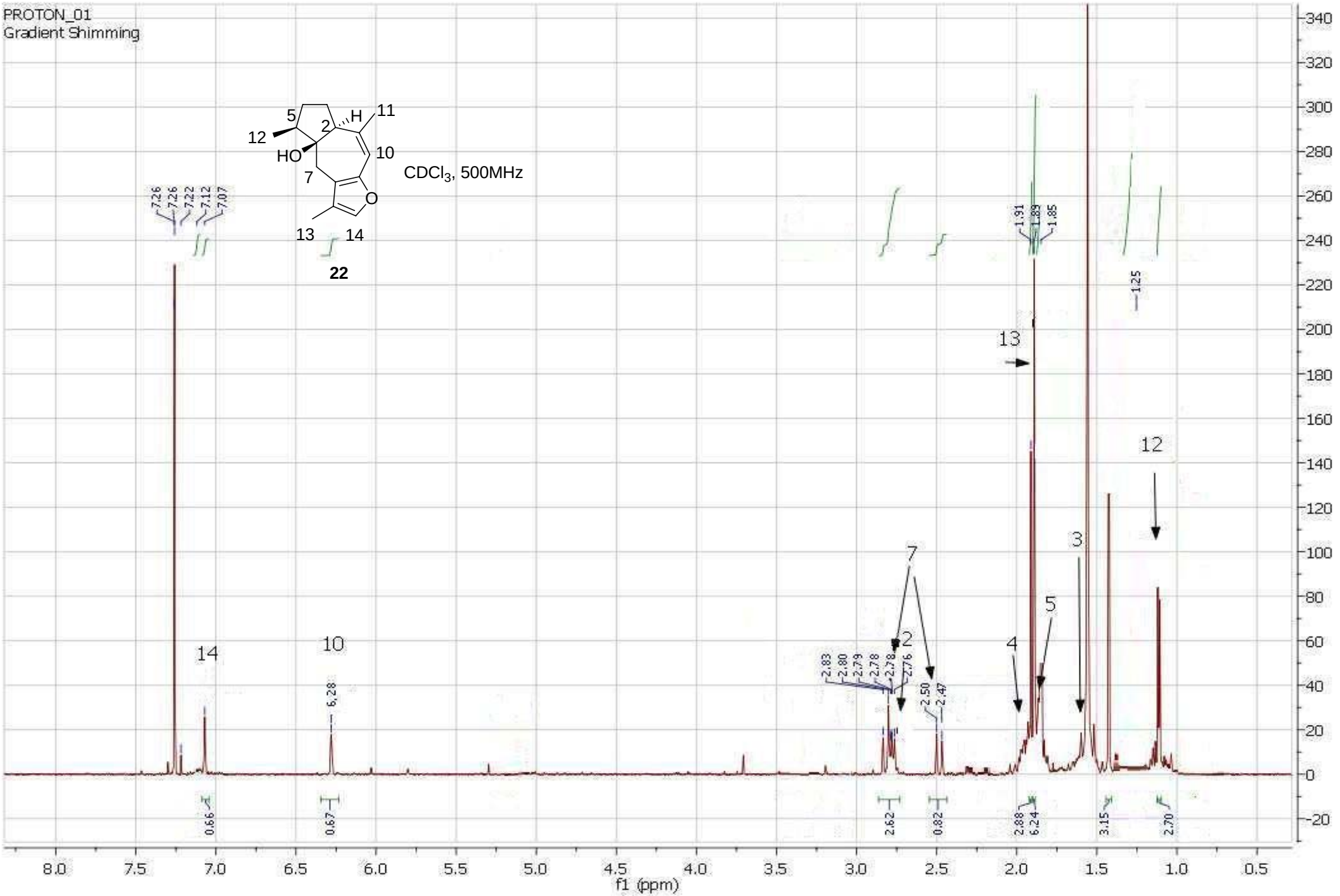

PROTON_01
Gradient Shimming
CDCl3, 500MHz
20
H12
H14a
H14b
H9a
H9b
H6a
H1
H6b
H4
H13
H15
H2,3
7.01
5.16
5.00
3.54
3.54
3.51
3.51
3.36
3.33
2.83
2.83
2.80
2.80
2.64
2.32
2.29
1.95
1.90
1.89
1.88
1.86
1.85
1.09
1.08
1.07
1.07
0.78
1.19
1.00
0.97
1.05
0.94
1.07
2.08
4.01
1.56
0.98
2.46
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

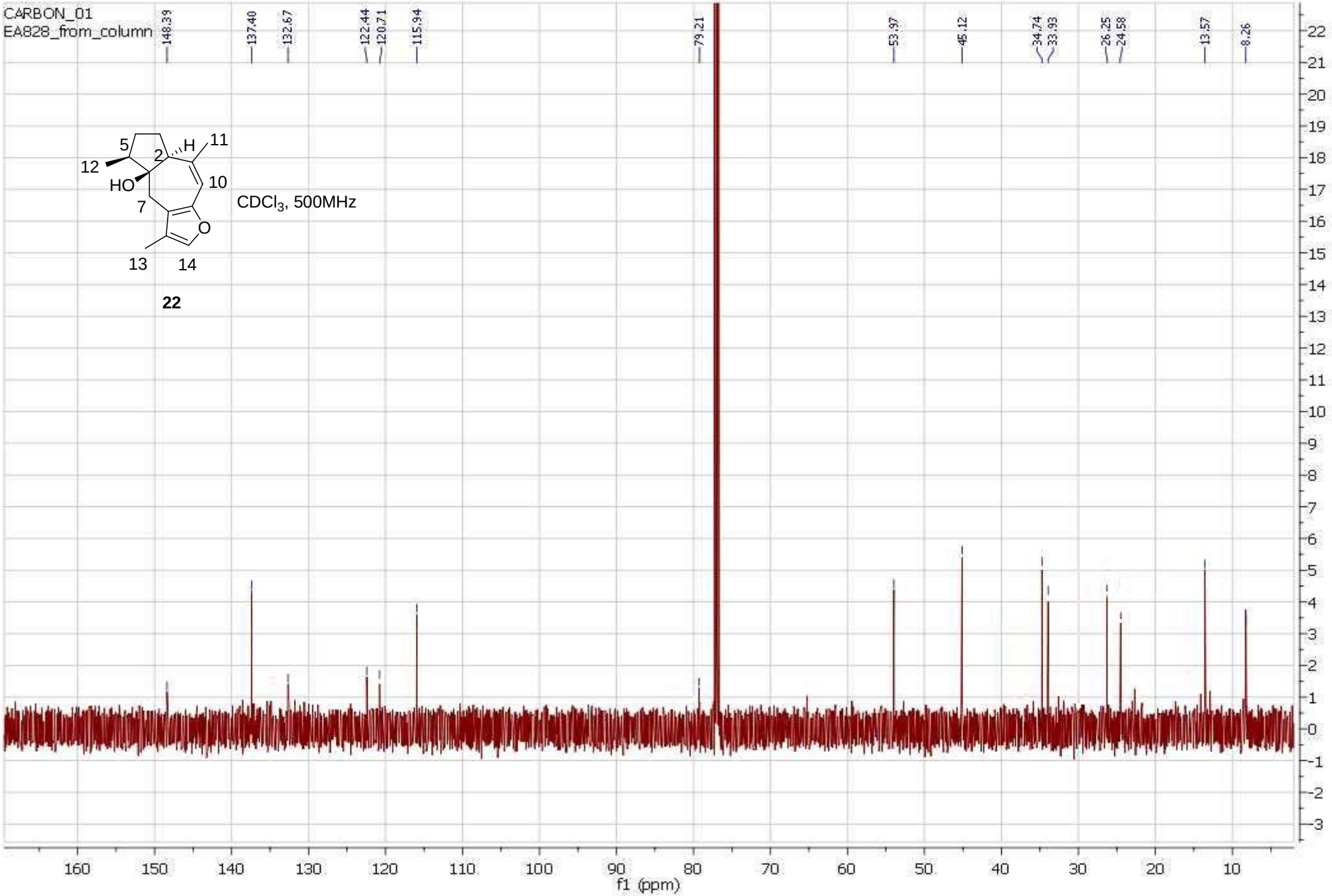

CARBON_01
EA793_1
149.62
142.17
136.20
122.24
114.69
113.85
78.09
77.26
77.01
76.76
56.78
45.06
39.06
32.94
29.55
26.04
13.45
8.28
HO
H
O
CDCl3, 125MHz
20
f1 (ppm)

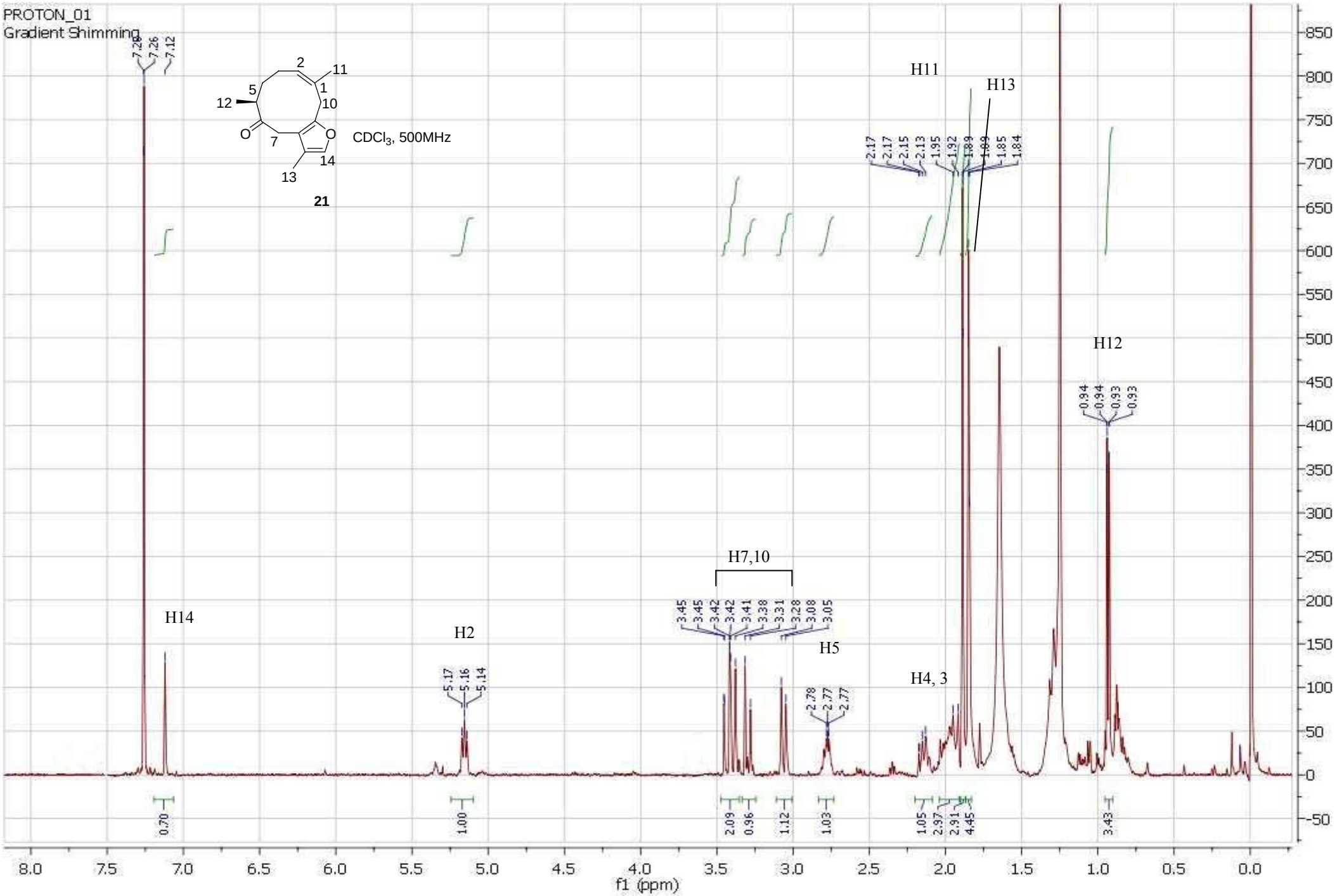

HO
H
O
CDCl3
20
gHMQC_01
EA793_1_
f2 (ppm)
f1 (ppm)

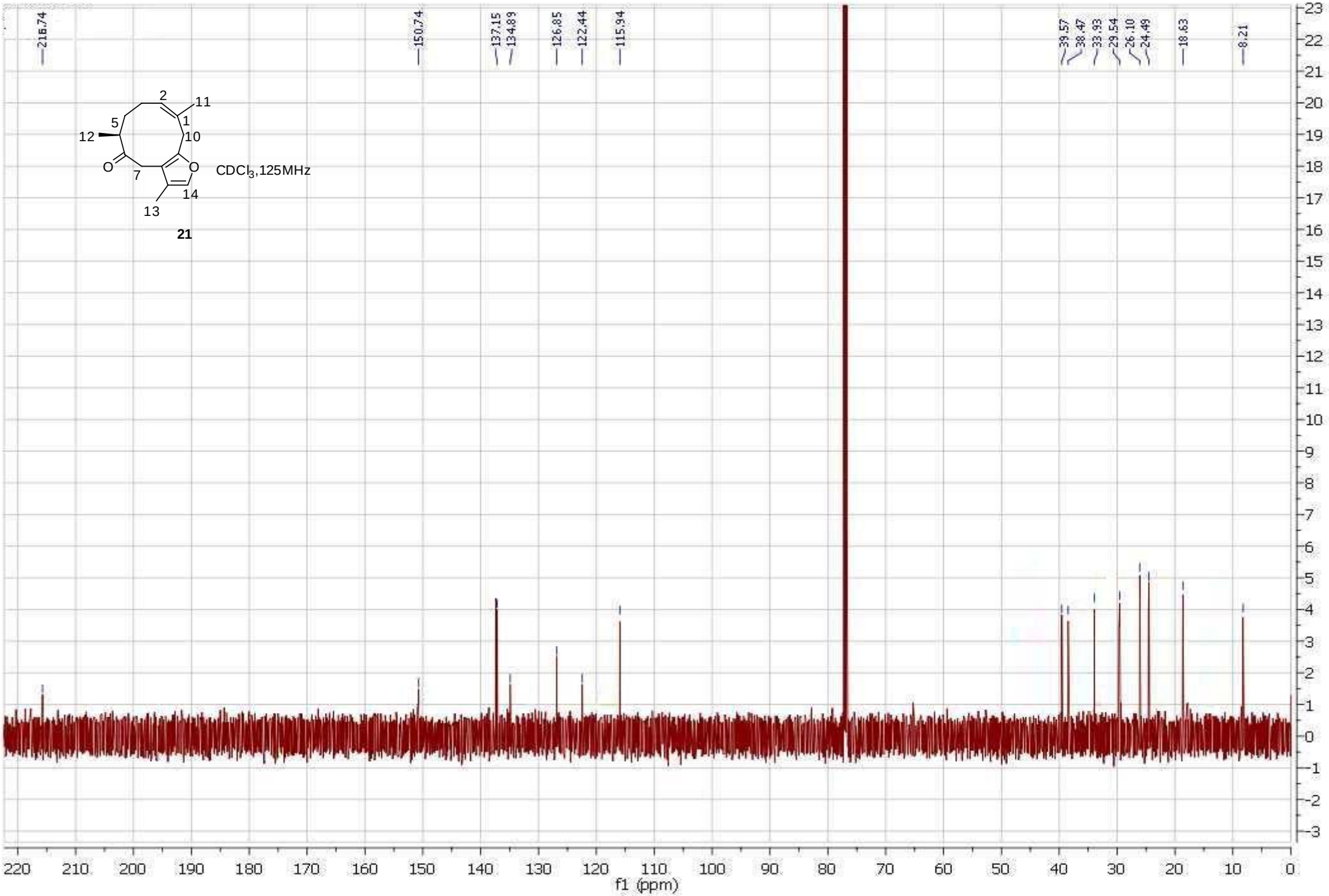


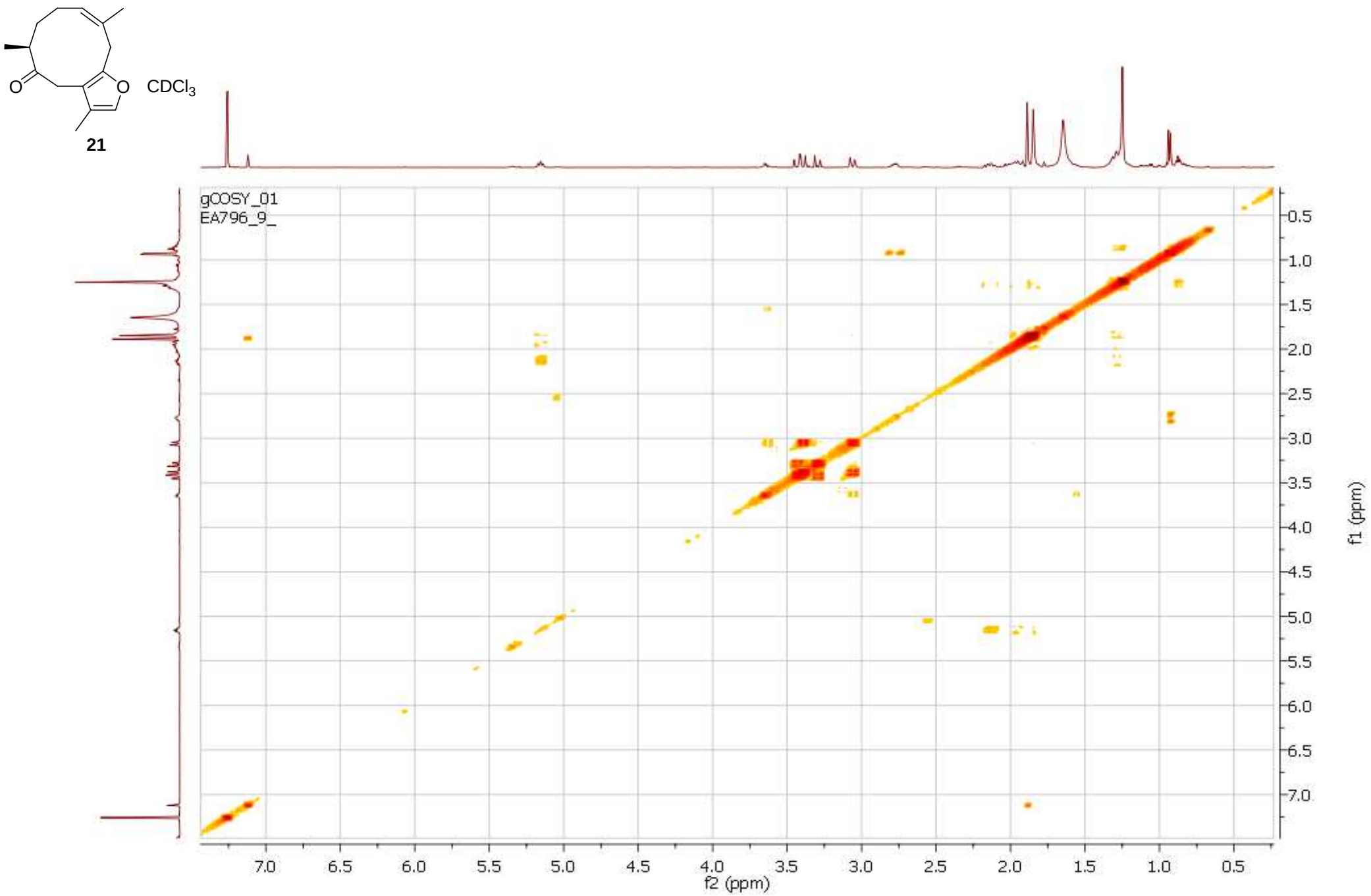
20

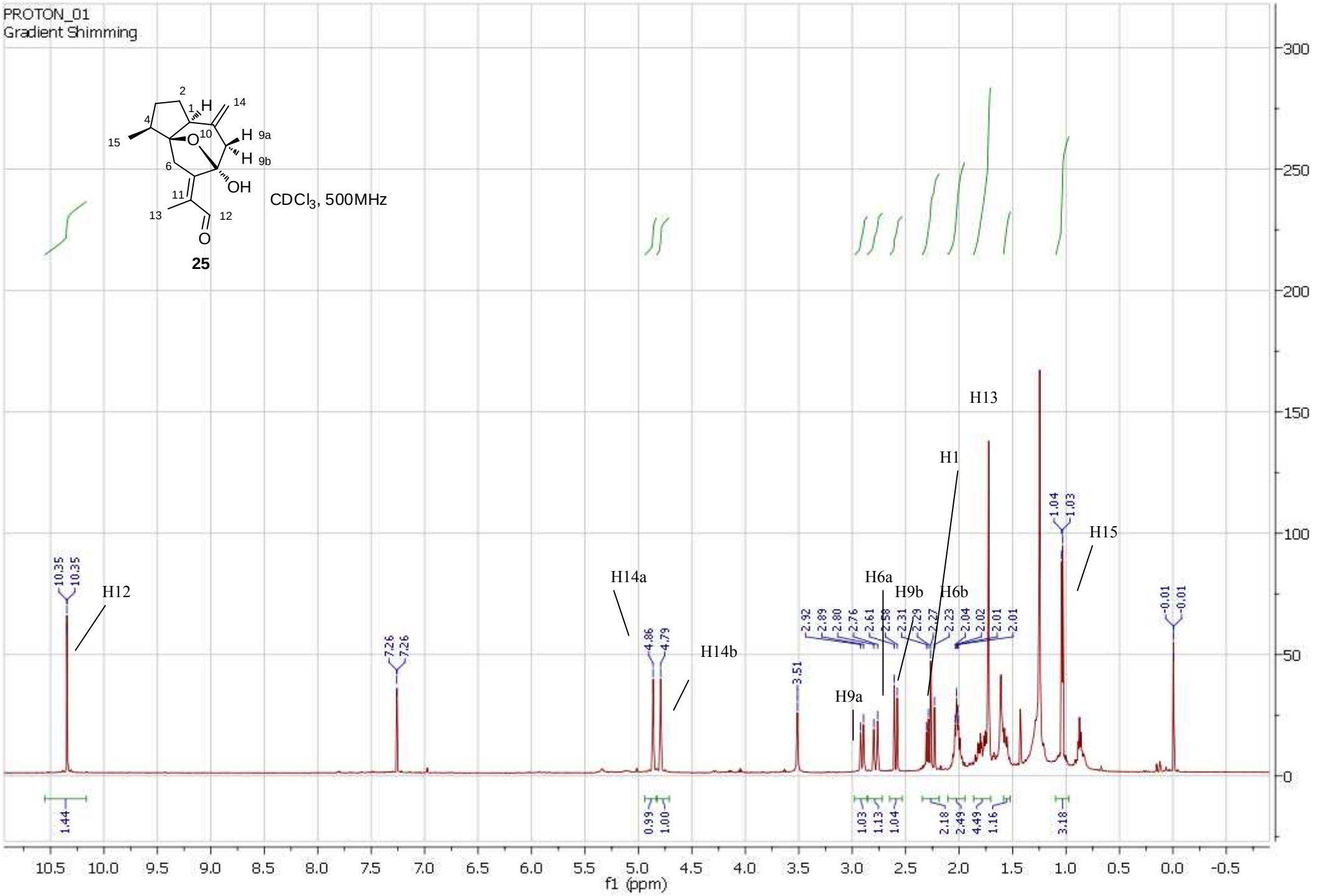

PROTON_01
Gradient Shimming
5
2
H
11
12
HO
10
7
O
13
14
22
CDCl3, 500MHz
7.26
7.26
7.22
7.12
7.07
1.91
1.89
1.85
1.25
13
12
3
7
5
4
2
14
10
6.28
2.83
2.80
2.79
2.78
2.78
2.76
2.50
2.47
0.66
0.67
2.62
0.82
2.88
6.24
3.15
2.70
f1 (ppm)

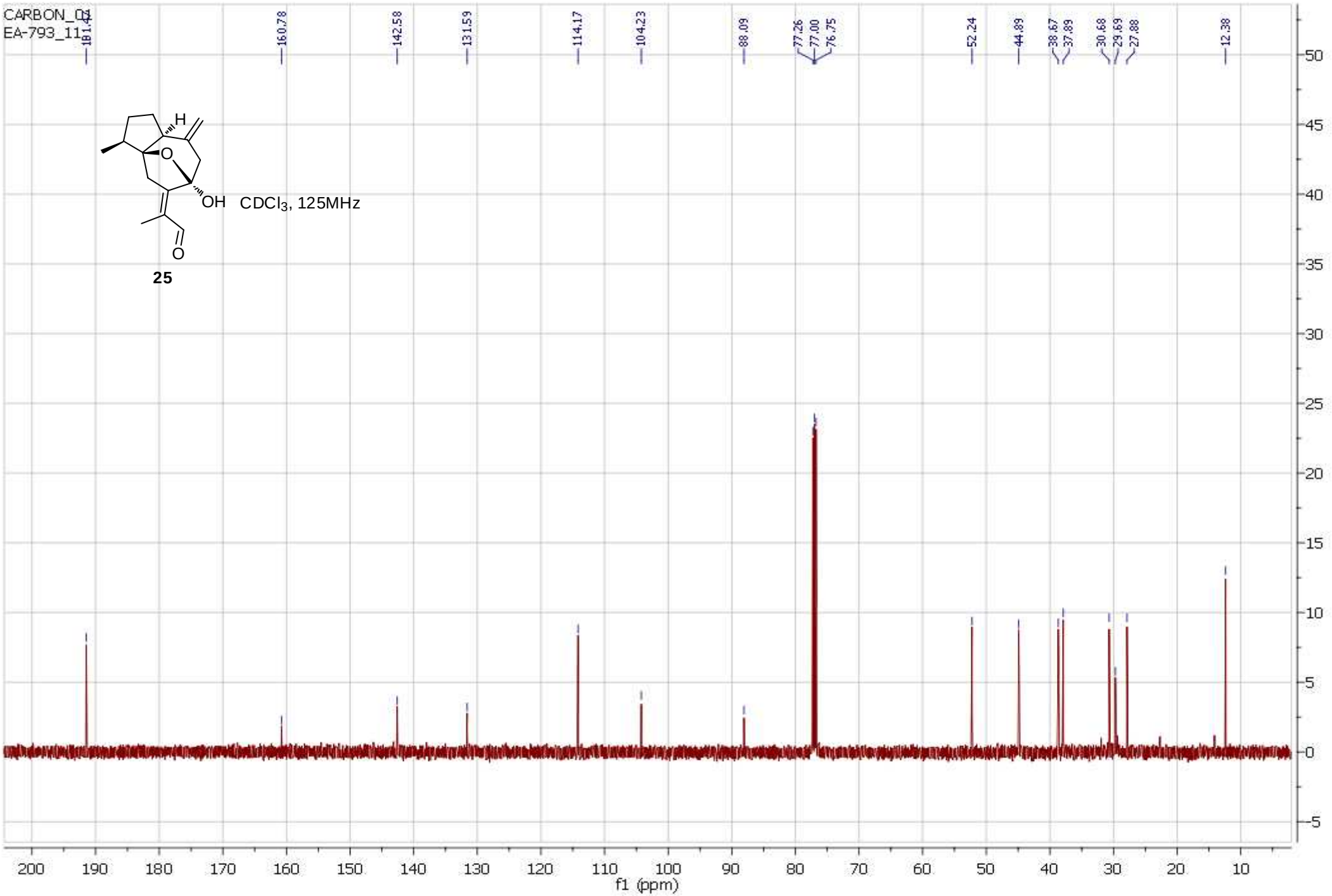

CARBON_01
EA828_from_column
148.39
137.40
132.67
122.44
120.71
115.94
79.21
53.97
45.12
34.74
33.93
26.25
24.58
13.57
8.26
5
2
H
11
12
HO
10
7
O
13
14
CDCl3, 500MHz
22
f1 (ppm)

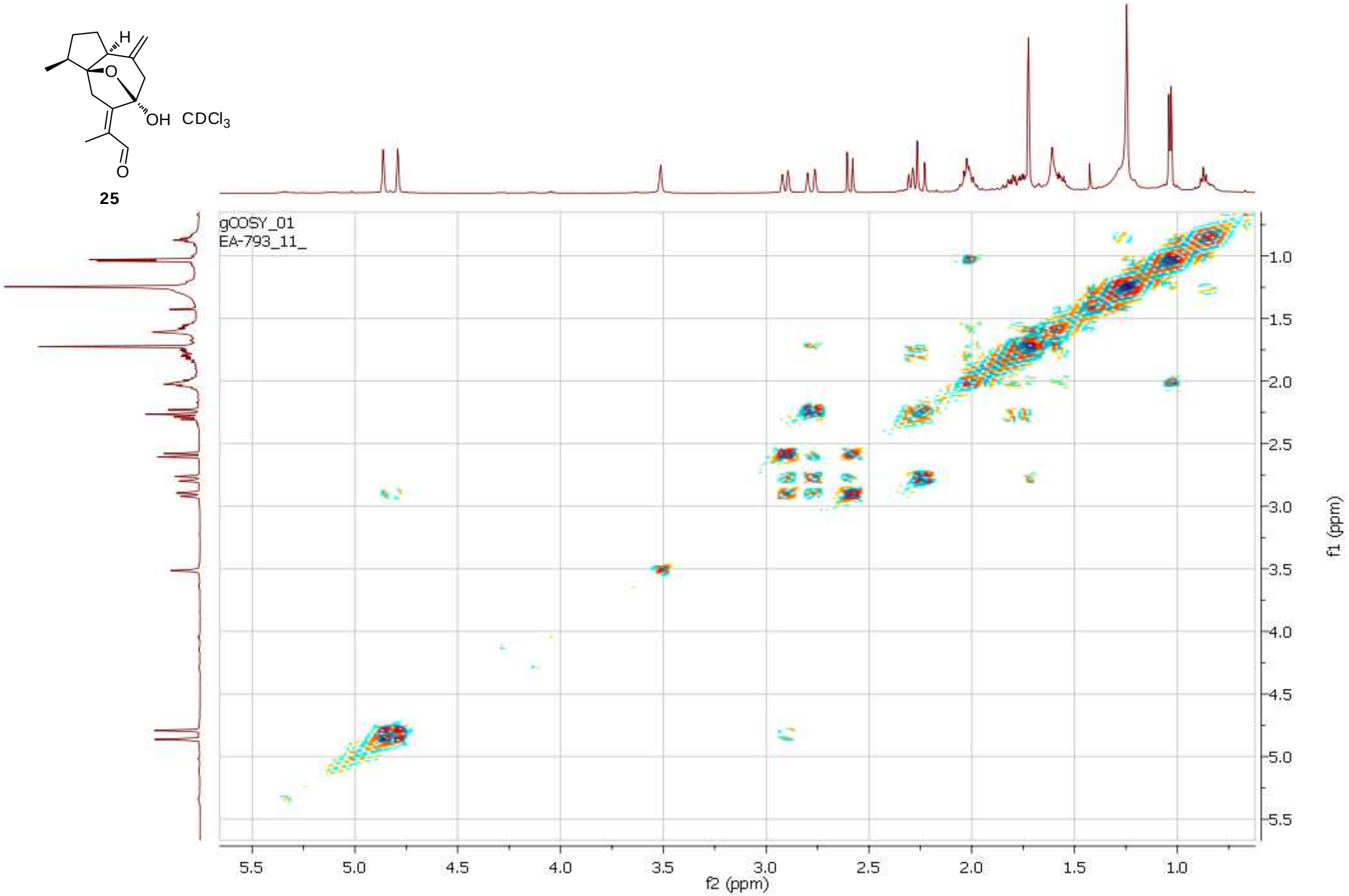

PROTON_01
Gradient Shimming
CDCl3, 500MHz
21
H11
H13
H12
H7,10
H14
H2
H5
H4, 3
f1 (ppm)

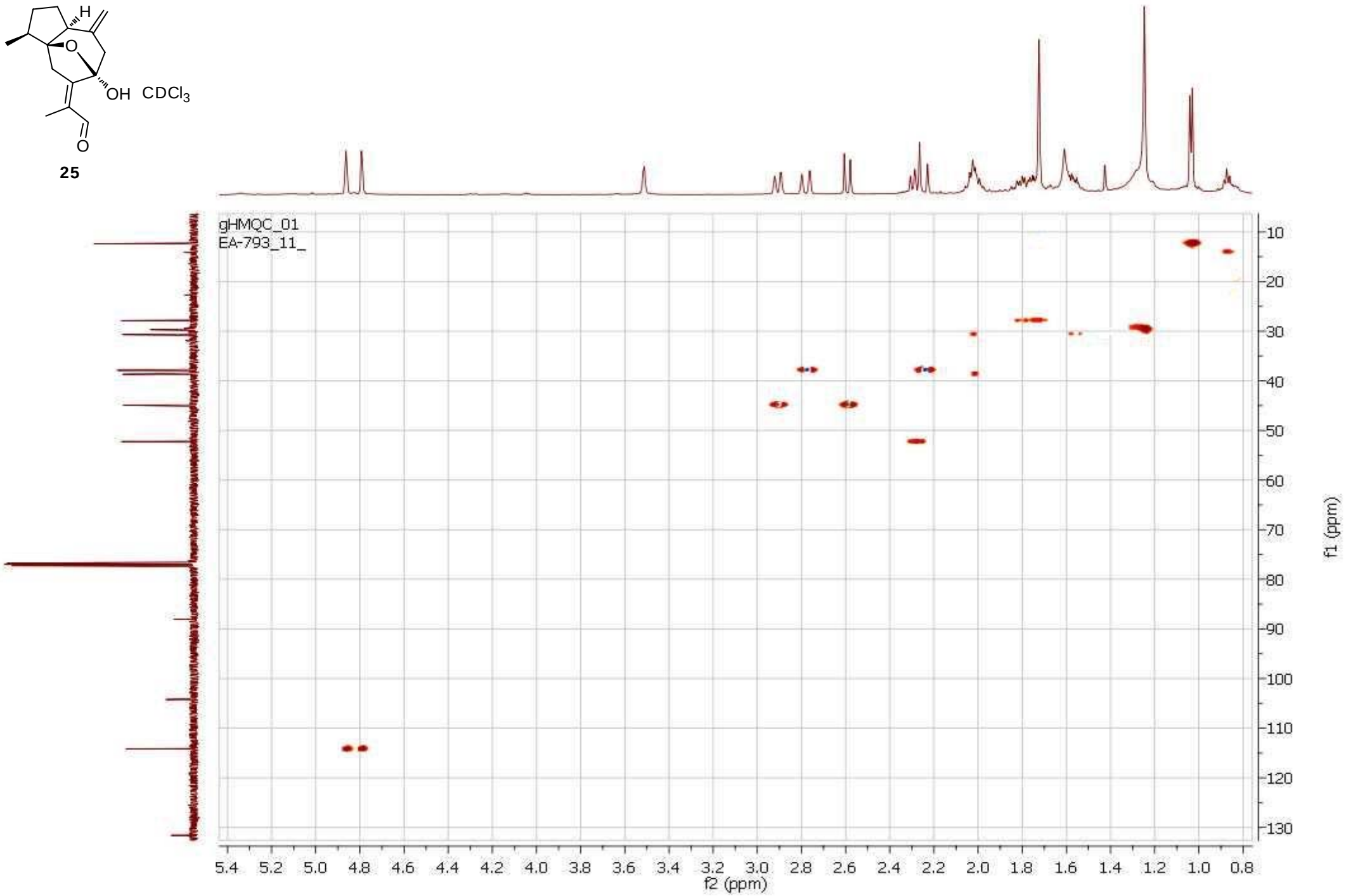

216.74
150.74
137.15
134.89
126.85
122.44
115.94
39.57
38.47
33.93
29.54
26.10
24.49
18.63
8.21
2
11
1
5
12
10
O
7
O
14
13
CDCl3,125MHz
21
f1 (ppm)

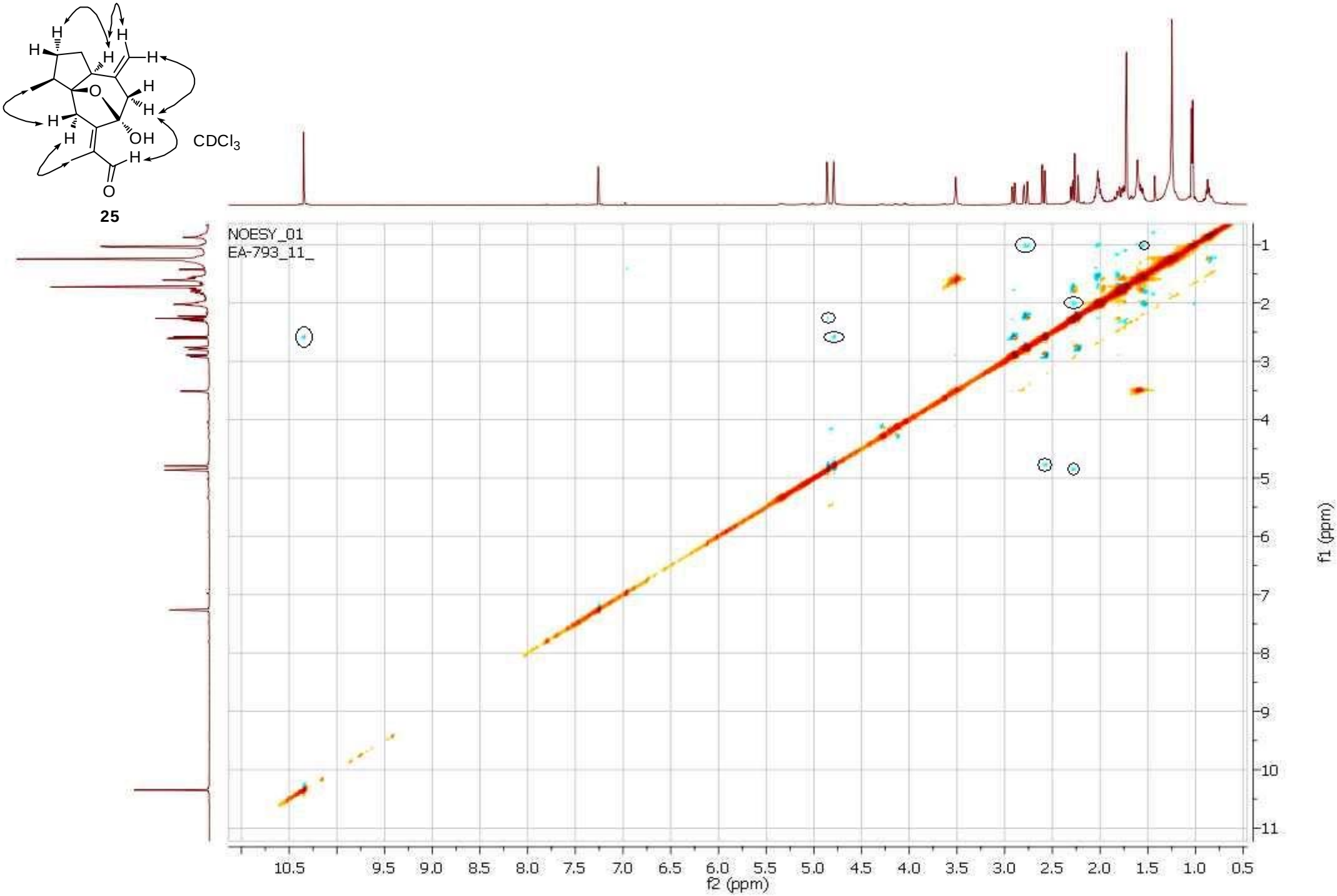

O
O
CDCl3
21
gCOSY_01
EA796_9_
f2 (ppm)
f1 (ppm)

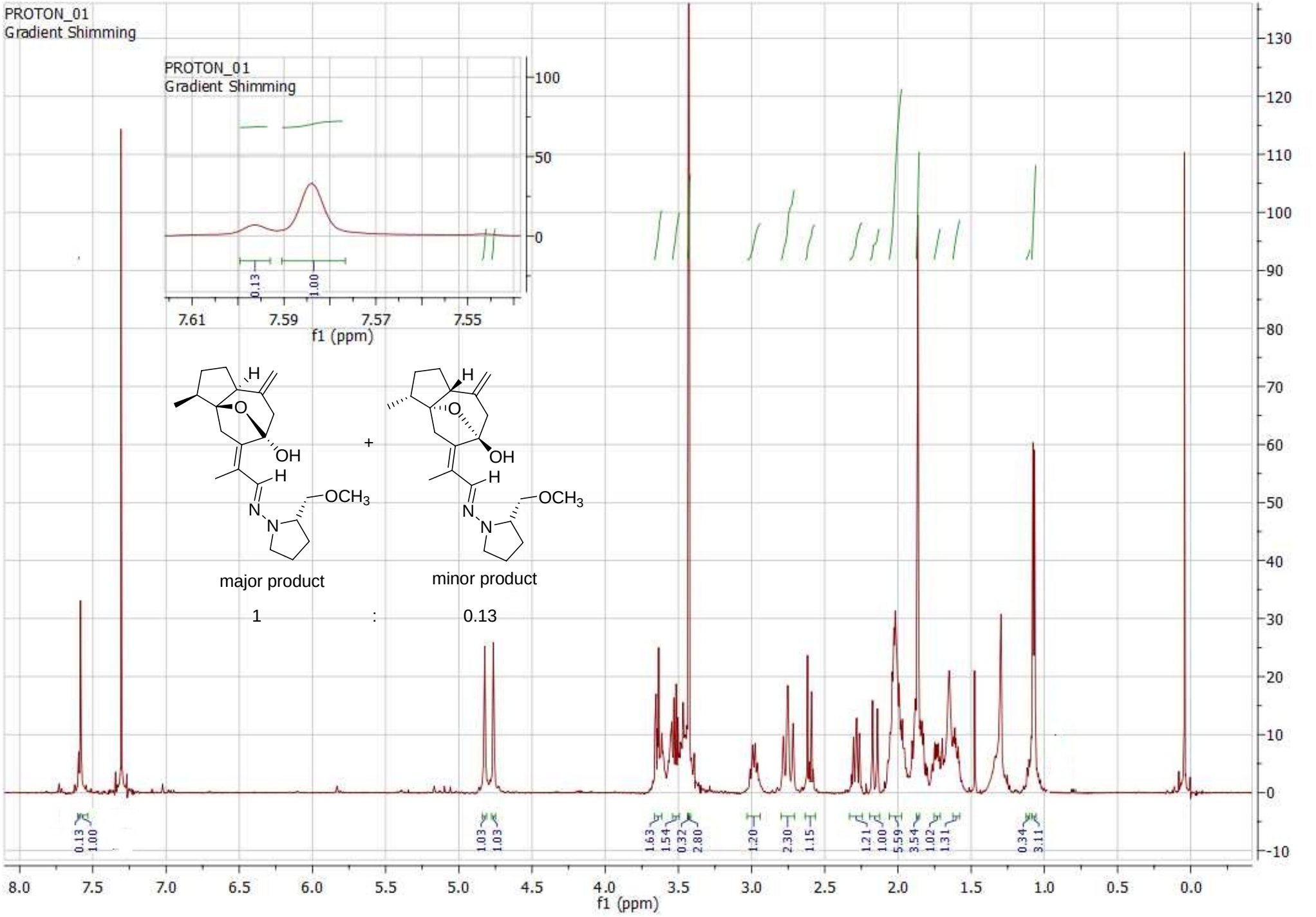

PROTON_01
Gradient Shimming
CDCl3, 500MHz
25
H12
H14a
H14b
H9a
H6a
H9b
H6b
H1
H13
H15
f1 (ppm)


CARBON_01
EA-793_11
181.44
160.78
142.58
131.59
114.17
104.23
88.09
77.26
77.00
76.75
52.24
44.89
38.67
37.89
30.68
29.63
27.88
12.38
H
O
OH
O
CDCl3, 125MHz
25
f1 (ppm)


H
O
OH
O
CDCl3
25
gCOSY_01
EA-793_11_
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
f1 (ppm)


H
O
OH
CDCl3
O
25
gHMQC_01
EA-793_11_
f2 (ppm)
f1 (ppm)


H
H
H
H
H
O
H
H
H
H
OH
H
O
CDCl3
25
NOESY_01
EA-793_11_
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
1
2
3
4
5
6
7
8
9
10
11
f1 (ppm)


PROTON_01
Gradient Shimming
PROTON_01
Gradient Shimming
7.61
7.59
7.57
7.55
f1 (ppm)
major product
minor product
1 : 0.13
f1 (ppm)