Supplementary Material (ESI) for Chemical Communications


# Asymmetric total synthesis of *ent*-heliespirones A & C

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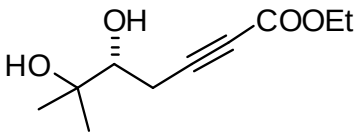
# Experimental Section

**General**. All the reactions were carried out under an atmosphere of argon or nitrogen in dried glassware unless otherwise indicated. Materials were obtained from commercial suppliers and used without further purification except when otherwise noted. Solvents were dried and distilled according to the standard protocols. Flash column chromatography was performed on silica gel using the indicated solvent.

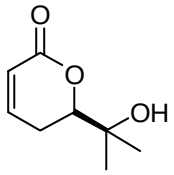
## （5R）-5，6-Dihydroxy-6-methylhept-2-ynethiote (2)




A 250-mL round-bottomed flask, equipped with a magnetic stirrer, was charged with $K_2CO_3$ (4.19 g, 30 mmol), $K_3Fe(CN)_6$ (9.98 g, 30 mmol), $(DHQD)_2$-PHAL (410.0 mg, 0.5 mmol), $K_2OsO_4 \cdot H_2O$ (37.2 mg, 0.1 mmol), water (50 ml) and tert-butyl alcohol (50 mL). The resulting mixture was stirred at room temperature till it produced two clear phases. Methanesulfonamide (971.0 mg, 1.0 mmol) was added in one-portion and the reaction mixture was stirred for additional 1.5 h. The reaction mixture was cooled to 0℃. Olefin **1** (1.5 ml, 8.0 mmol) was added at once, and the heterogeneous slurry was stirred vigorously at 0 ℃ overnight. Solid sodium sulfite (5.63 g) was added at 0℃ and the mixture was allowed to warm to room temperature and stirred for 90 min. EtOAc (100 ml) and water (50 ml) were added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc (60 ml*3). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. This crude product was purified by flash chromatography on silica gel with EtOAc-Pet (33：67 v/v) as eluent to give diol **2** (1.57 g, 98%, over 96% ee) as a colorless oil. $[\alpha]^{13.0}_D$ +40.0 (c 0.10 in $CH_2Cl_2$); IR (neat): 3409, 2237, 1706, 1465, 1370, 1258, 1070, 1033 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3 + D_2O$) δ 4.21 (q, $J$ = 7.1 Hz, 2H), 3.64

(dd, *J* = 8.9 Hz, 3.3 Hz, 1H), 2.60 (A of AB, dd, *J* = 17.2 Hz, 3.6Hz, 1H), 2.50 (B of AB, dd, *J* = 17.2 Hz, 8.8 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.24 (s, 3H), 1.17 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.0, 87.8, 75.7, 74.3, 72.4, 62.1, 26.0, 24.3, 22.6, 14.0. HRMS (ES) m/z calcd for $C_{10}H_{16}O_4Na$ $[M+Na]^+$ 223.0946, found 223.0944. Enantiomeric excess was determined by HPLC analysis [CHIRALCEL OD-H column, 10% isopropanol-hexane, 1.0 mL/min, λ = 210 nm, retention times 7.17 min (S) and 8.14 min (R)].

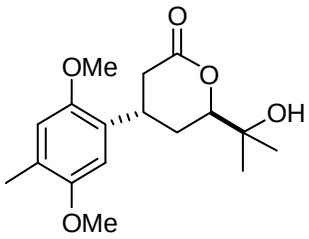
## (R)-6-(2-hydroxypropan-2-yl)-5,6-dihydro-2H-pyran-2-one (4)




To a solution of ester **2** (373.3 mg, 1.86 mmol) in ethanol (19 ml), Lindlar's catalyst (39.7 mg, 1.0 mol%) and quinoline (0.93 mL, 7.44 mmol) were added. The resulting mixture was stirred at room temperature for 30 min then exposed to an atom. pressure of hydrogen at the same temperature. The reaction mixture was stirred for 2.5 h. After this time, the mixture was filtered through Celite, washed with EtOAc and the volatiles were removed under reduced pressure. Then the residue was redissolved in EtOAc (50 ml) and the solution was washed with 1 N HCl (15 ml*2). The aqueous layer was saturated with NaCl and extracted with EtOAc (15 ml*3). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. The crude product was redissolved in toluene (13 ml). TsOH (0.5 eq.) was added at 25℃. The resulting mixture was stirred overnight. The reaction was quenched with sat. aq $NaHCO_3$ (10 ml), diluted with EtOAc (20 ml) and water (10 ml). The organic layer was separated and the aqueous layer was saturated with NaCl and extracted with DCM (20 ml*5). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. This crude product was purified by flash chromatography on silica gel with EtOAc-Pet (50：50 v/v) as eluent to give lactone **4** (247.0 mg, 85%) as a colorless oil. $[\alpha]^{13.0}_D$ +125.2 (c 0.10 in $CH_2Cl_2$); IR (neat): 3448, 2979, 2904, 1715, 1469,

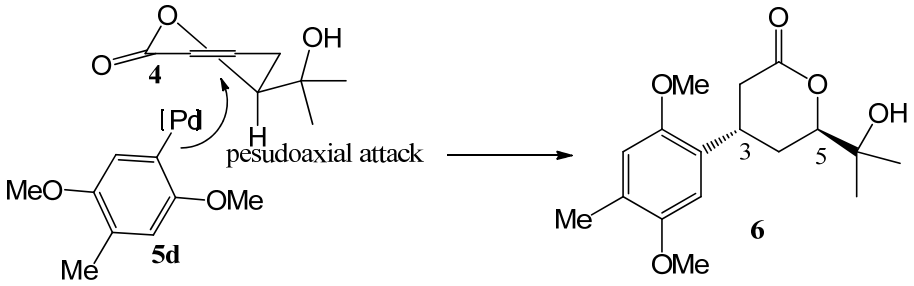
1385, 1261, 1040 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.91 (ddd, *J* = 8.7 Hz, 6.4 Hz, 1.9 Hz, 1H), 6.00 – 5.97 (m, 1H), 4.21 (dd, *J* = 12.7 Hz, 3.9 Hz, 1H), 2.53 – 2.31 (m, 3H), 1.28 (s, 3H), 1.22 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 164.2, 145.9, 120.6, 83.8, 70.8, 25.4, 24.8, 24.2. HRMS (ES) *m/z* calcd for $C_8H_{12}O_3NH_4$ $[M+NH_4]^+$ 174.1130, found 174.1128.

## (4S,6R)-4-(2,5-dimethoxy-4-methylphenyl)-6-(2-hydroxypropan-2-yl)tetrahydro-2H-pyran-2-one (6)

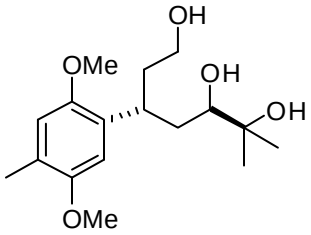



To a 25-mL one-neck flask, $Pd_2(dba)_3$ (68.7 mg, 0.075 mmol), $PPh_3$ (40.2 mg, 0.150 mmol), 2,5-Dimethoxy-4-methylphenylboronic acid **5d** (1.03 g, 5.0 mmol), cesium carbonate (977.5 mg, 3.0 mmol), chloroform (6.3 μl, 0.075 mmol), lactone **4** (387.3 mg, 2.42 mmol) and toluene (5 mL) were added. The resulting solution was stirred at room temperature for 80 min. The reaction mixture was immersed into a 60℃ oil-bath for 90 min. The reaction mixture was cooled down to room temperature, diluted with brine (30 ml) and EtOAc (30 ml). The organic layer was separated and the aqueous layer was extracted with EtOAc (30 ml*2). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. This crude product was purified by flash chromatography on silica gel with EtOAc-Pet (33：67 v/v) as eluent to give lactone **6** (657.0 mg, 88%) as a colorless oil. $[\alpha]^{14.5}_D$ +14.3 (c 0.57 in $CHCl_3$); IR (neat): 3446, 2973, 2935, 1735, 1508, 1465, 1399, 1212, 1043 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.72 (s, 1H), 6.55 (s, 1H), 4.23 (dd, *J* = 11.1 Hz, 4.2 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.52 – 3.38 (m, 1H), 2.92 (A of AB, dd, *J* = 16.2 Hz, 8.6 Hz, 1H), 2.64 (B of AB, dd, *J* = 16.2 Hz, 6.1 Hz, 1H), 2.20 (s, 3H), 2.16 – 1.95 (m, 2H), 1.25 (s, 3H), 1.20 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 173.0, 151.5, 150.5, 128.5, 126.0, 114.1, 110.8, 83.6, 71.3, 56.0, 55.6, 34.3, 31. 6, 28.5, 25.9, 24.3, 16.1. HRMS (ES) *m/z* calcd for $C_{17}H_{25}O_5$ $[M+H]^+$ 309.1702, found 309.1704.

The stereochemistry of the compound **6** was confirmed by the NOE experiments which have not shown any enhancement between the 3-H and 5-H. The transition state of the palladium-catalyzed Michael addition can also explain the stereochemistry of the resulting adduct.



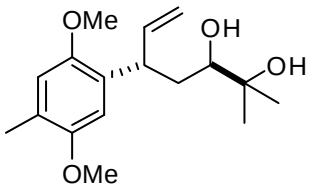

## (3R,5R)-3-(2,5-dimethoxy-4-methylphenyl)-6-methylheptane-1,5,6-triol (7)




To a solution of lactone **6** (313.1 mg, 1.01 mmol) in ether (10.0 ml), a solution of $LiBH_4$ in THF (0.51 ml, 4.0M in THF, 2.02 mmol) was added dropwise at 0℃ and the resulting mixture was stirred for 10 min at the same temperature. The reaction mixture was warmed slowly to room temperature and stirred for 40 min. The reaction was quenched with 1.0 N NaOH ( 5.0 ml) at 0℃, warmed slowly to room temperature and stirred for additional 2 h. The mixture was diluted with EtOAc (30 ml) and water (15 ml). The aqueous layer was saturated with NaCl. The organic layer was separated and the aqueous layer was extracted with DCM (15 ml*6). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. This crude product was purified by flash chromatography on silica gel with DCM-Methanol (9：91 v/v) as eluent to give triol **7** (315.5 mg, quant.) as a colorless oil. $[\alpha]^{13.0}_{D}$ +29.2 (c 0.10 in $CH_2Cl_2$); IR (neat): 3395, 2936, 1505, 1465, 1399, 1209, 1044 $cm^{-1}$; $^1H$ NMR (300 MHz,

$CDCl_3$) δ 6.71 (s, 1H), 6.64 (s, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.56 – 3.51 (m, 2H), 3.46 – 3.30 (m, 2H), 2.19 (s, 3H), 2.12 – 2.01 (m, 1H), 1.88 – 1.80 (m, 1H), 1.70 – 1.58 (m, 2H), 1.19 (s, 3H), 1.13 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 152.4, 150.7, 131.2, 125.3, 114.8, 110.4, 76.5, 73.0, 60.7, 56.7, 56.2, 38.0, 37.3, 31.3, 26.1, 23.5, 16.3. HRMS (ES) *m/z* calcd for $C_{17}H_{28}O_5Na$ $[M+Na]^+$ 335.1834, found 335.1837.

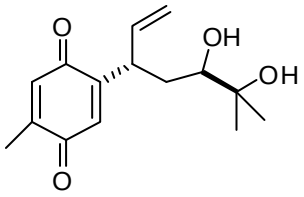
## (3R,5S)-5-(2,5-dimethoxy-4-methylphenyl)-2-methylhept-6-ene-2,3-diol (8)




To a solution of triol **7** (93.7 mg, 0.3 mmol) and o-Nitrophenylselenocyanate (175.8 mg, 0.75 mmol) in THF (3.0 ml), tributylphosphine (0.19 ml, 0.75 mmol) was added dropwise at 0℃ and stirred for 1h. The reaction was quenched with water (1.0 ml). The reaction mixture was diluted with $Et_2O$ (15 ml) and water (15 ml). The organic layer was separated and the aqueous layer was extracted with $Et_2O$ (15 ml*3). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. The crude product was re-dissolved in THF (3.0 ml), and $H_2O_2$ (1.5 ml, 30%wt) was added dropwise at 0℃ and the resultant was stirred for 1 d. The reaction was quenched with sat. aq $Na_2S_2O_3$ (2.0 ml), diluted with $Et_2O$ (20 ml) and brine ( 15 ml). The organic layer was separated and the aqueous layer was extracted with $Et_2O$ (15 ml*3). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. This crude product was purified by flash chromatography on silica gel with EtOAc-Pet (20：80 v/v, 200 ml, 25:75 v/v, 320 ml, 33:67 v/v 120 ml) as eluent to give compound **8** (67.1 mg, 76%) as a faint yellow oil. $[\alpha]^{14.5}_D$ +36.3 (c 0.25 in $CHCl_3$); IR (neat): 3423, 2932, 1506, 1464, 1396, 1209, 1044 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.71 (s, 1 H), 6.67 (s, 1 H), 6.02 (ddd, *J* = 17.2 Hz, 10.0 Hz, 8.0 Hz, 1H), 5.15 (d, *J* = 17.2 Hz, 1H), 5.11 (d, *J* = 10.8 Hz, 1H), 3.94 – 3.88 (m,

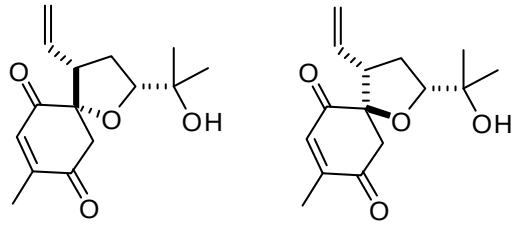
1H), 3.80 (s, 3H), 3.79(s, 3 H), 3.52 (d, *J* = 10.3 Hz, 1H), 2.33 (brs, 2H), 2.20 (s, 3H), 1.93 (A of AB, ddd, *J* = 12.0 Hz, 10.4 Hz, 1.2 Hz, 1H), 1.60 (B of AB, ddd, *J* = 14.4 Hz, 10.8 Hz, 4.4 Hz, 1H), 1.21 (s, 3H), 1.14 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.9, 150.2, 140.3, 131.1, 125.1, 115.4, 114.8, 110.7, 76.3, 73.0, 56.5, 56.1, 40.3, 36.9, 26.1, 23.4, 16.2. HRMS (ES) *m/z* calcd for $C_{17}H_{26}O_4Na$ $[M+Na]^+$ 317.1729, found 317.1722.

## 2-((3S,5R)-5,6-dihydroxy-6-methylhept-1-en-3-yl)-5-methylcyclohexa-2, 5-diene-1,4-dione (9)




To a solution of compound **8** (10.0 mg, 0.034 mmol) in MeCN (0.5 ml), CAN aq. (47.0 mg in 0.1 ml water) was added dropwise at 0℃ and the resultant was stirred for 30 min at 0℃. The reaction mixture was diluted with EtOAc (10 ml) and brine (5 ml). The organic layer was separated and the aqueous layer was extracted with EtOAc (10 ml*3). The combined organic extracts was washed with sat. aq $NaHCO_3$ (10 ml*2). The resulting aqueous layer was extracted with EtOAc (10 ml*2). The combined organic extracts were dried over anhydrous sodium sulfate and concentrated to give the crude product. This crude product was purified by flash chromatography on silica gel with EtOAc-Pet (33：67 v/v) as eluent to give compound **9** (8.8 mg, 98%) as a yellow oil. $[\alpha]^{14.5}_D$ +20.5 (c 0.108 in $CHCl_3$); TLC (EtOAc : Pet, 1 : 1 v/v): $R_f$ = 0.41; IR (neat): 3415, 2968, 2924, 1653, 1376, 1259, 1165, 1071, 1015, 917 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.59 (s, 1H), 6.53 (s, 1H), 5.77 (ddd, *J* = 17.8 Hz, 9.4 Hz, 1H), 5.23 – 5.18 (m, 2H), 3.75 – 3.69 (m, 1H), 3.45 (d, *J* = 10.7 Hz, 1H), 2.03 (s, 3H), 1.75 – 1.69 (m, 2H), 1.57 – 1.50 (m, 1H), 1.20 (s, 3H), 1.14 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 188.4, 187.3, 151.5, 145.5, 137.4, 133.9, 132.0, 118.3, 76.0, 73.0, 39.5, 35.8, 26.5, 23.6, 15.5. HRMS (ESI) *m/z* calcd for $C_{15}H_{21}O_4$ $[M+H]^+$ 265.1440, found 265.1440.

## (+)-heliespirone A and (-)-heliespirone C




(+)-heliespirone A (-)-heliespirone C

To a solution of compound **9** (67.1 mg, 0.254 mmol) in THF (1.0 ml), LiCl (215.3 mg, 5.08 mmol) was added at room temperature. The resulting mixture was immersed into an oil-bath (70℃) and stirred till there were no further increasing of the reaction products. The reaction mixture was cooled down to room temperature, diluted with EtOAc, filtered through Celite and concentrated to give the crude products. This crude products were purified by flash chromatography on silica gel with EtOAc-Pet (20：80 v/v, 200 ml, 25:75 v/v, 160 ml, 33:67 v/v, 90 ml) as eluent to give (+)-heliespirone A (15.2 mg, 23%, brsm 31%) as a colorless oil and (-)-heliespirone C (17.5 mg, 26%, brsm 36%) as a faint yellow oil. Recycled compound **9** (18.1 mg, 27%).

### (+)-heliespirone A

$[\alpha]^{14.5}_{D}$ +17.6 (c 0.09 in $CHCl_3$), {lit.[1] $[\alpha]^{25}_{D}$ -29.0 (c = 0.1 in $CHCl_3$)}. TLC (EtOAc : Pet, 1 : 1 v/v): $R_f$ = 0.70; IR (neat): 3454, 2974, 2930, 1679, 1621, 1241, 1062 $cm^{-1}$; $^1$H-NMR (600 MHz, $CDCl_3$) δ 6.62 (q, *J* = 1.4 Hz, 1H), 5.30 (ddd, *J* = 17.0 Hz, 9.7 Hz, 9.7 Hz, 1H), 5.07 (d, *J* = 16.9 Hz, 1H), 4.97 (d, *J* = 10.0 Hz, 1H), 4.04 (dd, *J* = 10.6 Hz, 5.2 Hz, 1H), 3.25 (A of AB, d, *J* = 15.5 Hz, 1H), 2.97 (B of AB, d, *J* = 15.5 Hz, 1H), 2.92 (ddd, *J* = 12.6 Hz, 9.5 Hz, 6.5 Hz, 1H), 2.15 (ddd, *J* = 12.6 Hz, 10.9 Hz, 1H), 1.96 (d, *J* = 1.4 Hz, 3H), 1.98-1.94 (m, 1H), 1.33 (s, 3H), 1.10 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 201.4, 195.6, 153.6, 137., 135.4, 118.6, 87.6, 86.7, 70.3, 57.1, 51.8, 31.9, 28.4, 25.3, 16.0. HRMS (ES) *m/z* calcd for $C_{15}H_{20}O_4Na$ $[M+Na]^+$ 287.1259, found 287.1261.

### (-)-heliespirone C

$[\alpha]^{14.5}_{D}$ -31.8 (c 0.11 in $CHCl_3$), {lit.[2] $[\alpha]^{25}_{D}$ +14.4 (c = 0.1 in $CHCl_3$)}. TLC (EtOAc : Pet, 1 : 1 v/v): $R_f$ = 0.58; IR (neat): 3469, 2975, 1688, 1622, 1420, 1378, 1250, 1115,

1071 $cm^{-1}$; $^{1}$H-NMR (600 MHz, $CDCl_3$) δ 6.68 (q, *J* = 1.4 Hz, 1H), 5.59 (ddd, *J* = 16.8 Hz, 10.3 Hz, 8.6 Hz, 1H), 5.12 (dd, *J* = 9.3 Hz, 0.8 Hz, 1H), 5.11 (dd, *J* = 17.0 Hz, 0.8 Hz, 1H), 3.96 (dd, *J* = 10.7 Hz, 5.1 Hz, 1H), 3.30-3.26 (m, 1H), 2.95 (A of AB, d, *J* = 16.1 Hz, 1H), 2.84 (B of AB, d, *J* = 16.2 Hz, 1H), 2.07-2.03 (m, 1H), 1.99 (d, *J* = 1.4 Hz, 3H), 1.96-1.89 (m, 1H), 1.24 (s, 3H), 1.13 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 196.9, 196.3, 151.9, 137.1, 134.6, 119.9, 86.9, 86.7, 70.3, 48.9, 47.0, 32.4, 27.6, 24.6, 16.2. HRMS (ES) *m/z* calcd for $C_{15}H_{20}O_4Na$ $[M+Na]^+$ 287.1259, found 287.1257.

**Table 1.** Comparison of $^{1}$H NMR data between synthetic (+)-heliespirone A and natural (-)-heliespirone A reported data[1].

| Synthetic (+)-heliespirone A $^{1}$H NMR ($CDCl_3$, 600 MHz) (δ, multiplicity, coupling constant (Hz)) | Natural (-)-heliespirone A $^{1}$H NMR ($CDCl_3$, 400 MHz, reported in ref. 1) (δ, multiplicity, coupling constant (Hz)) |
|---|---|
| 6.62, q , 1.4 | 6.61, s |
| 5.30, ddd, 17.0, 9.7, 9.7 | 5.29, ddd, 9.8 |
| 5.07, d, 16.9 | 5.06, ddd, 16.8, 1.3, 0.7 |
| 4.97, d, 10.0 | 4.96, dd, 10.0 |
| 4.04, dd, 10.6, 5.2 | 4.03, dd |
| 3.25, A of AB, d, 15.5 | 3.23, d, 15.5 |
| 2.97, B of AB, d, 15.5 | 2.95, d, 15.5 |
| 2.92, ddd, 12.6, 9.5, 6.5 | 2.91, ddd, 12.7, 6.4 |
| 2.15, ddd, 12.6, 10.9 | 2.14, ddd, 10.6 |
| 1.96, d, 1.4 | 1.96, d, 1.5 |
| 1.98-1.94, m | 1.96, ddd, 12.7, 5.2 |
| 1.33, s | 1.32, s |
| 1.10, s | 1.09, s |

**Table 2.** Comparison of $^{13}$C NMR data between synthetic (+)-heliespirone A and natural (-)-heliespirone A reported data[1].

| Synthetic (+)-heliespirone A ($CDCl_3$, 100 MHz) | Natural (-)-heliespirone A ($CDCl_3$, 100 MHz, reported in ref. 1) |
|---|---|
| 201.4 | 201.5 |
| 195.6 | 179.5* |
| 153.6 | 153.4 |
| 137.1 | 137.0 |
| 135.4 | 135.3 |
| 118.6 | 118.4 |
| 87.6 | 87.6 |
| 86.7 | 86.7 |
| 70.3 | 70.1 |
| 57.1 | 57.1 |
| 51.8 | 51,8 |
| 31.9 | 31.9 |
| 28.4 | 28.3 |
| 25.3 | 25.3 |
| 16.0 | 15.9 |

*This chemical shift was mis-read in Macias' original paper and should be read as about 196 ppm; please compare this data with the spectra in the original paper (ref. 1).

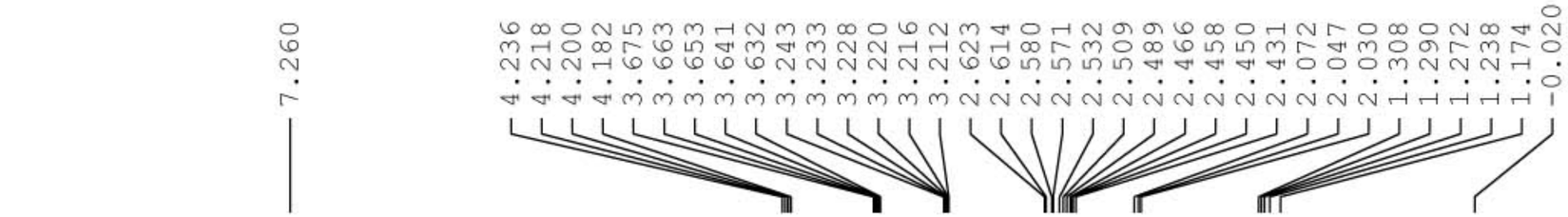
**Table 3.** Comparison of $^{1}$H NMR data between synthetic (-)-heliespirone C and natural (+)-heliespirone C reported data[2].

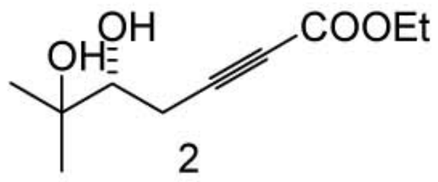
| Synthetic (-)-heliespirone C $^{1}$H NMR ($CDCl_3$, 600 MHz) (δ, multiplicity, coupling constant (Hz)) | Natural (+)-heliespirone C $^{1}$H NMR ($CDCl_3$, 400 MHz, reported in ref. 2) (δ, multiplicity, coupling constant (Hz)) |
|---|---|
| 6.68, q, 1.4 | 6.63, q, 1.5 |
| 5.59, ddd, 16.8, 10.3, 8.6 | 5.61, ddd, 16.4, 10.5, 8.5 |
| 5.12, dd, 9.3, 0.8 | 5.12, dd, 8.5, 1.1 |
| 5.11, dd, 17.0, 0.8 | 5.09, dd, 16.4, 1.1 |
| 3.96, dd, 10.7, 5.1 | 3.95, dd, 10.7, 5.1 |
| 3.30-3.26, m | 3.26, brddd, 12.2, 12.2, 10.7 |
| 2.95, A of AB, d, 16.1 | 2.95, d, 16.2 |
| 2.84, B of AB, d, 16.2 | 2.83, d,16.2 |
| 2.07-2.03, m | 2.04, ddd, 12.2, 7.1, 5.1 |
| 1.99, d, 1.4 | 1.98, d, 1.5 |
| 1.96-1.89, m | 1.92, ddd, 12.2, 12.2, 10.7 |
| 1.24, s | 1.23, s |
| 1.13, s | 1.12, s |

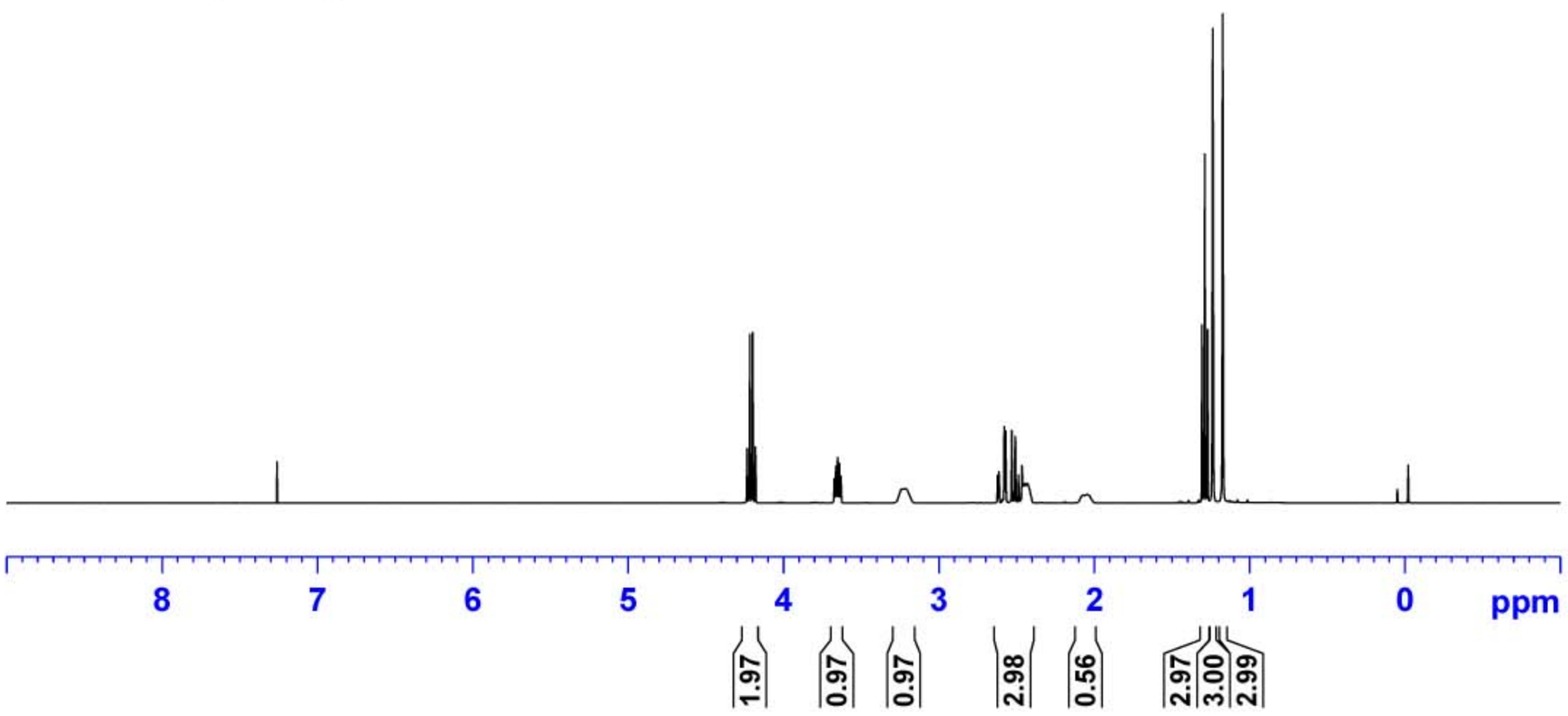
**Table 4.** Comparison of $^{13}$C NMR data between synthetic (-)-heliespirone C and natural (+)-heliespirone C reported data[2].

| Synthetic (-)-heliespirone C ($CDCl_3$, 100 MHz) | Natural (+)-heliespirone C ($CDCl_3$, 100 MHz, reported in ref. 2) |
|---|---|
| 196.9 | 196.5 |
| 196.3 | 196.3 |
| 151.9 | 151.7 |
| 137.1 | 136.9 |
| 134.6 | 134.6 |
| 119.9 | 119.6 |
| 86.9 | 86.9 |
| 86.7 | 86.7 |
| 70.3 | 70.3 |
| 48.9 | 48.5 |
| 47.0 | 47.0 |
| 32.4 | 32.4 |
| 27.6 | 27.5 |
| 24.6 | 24.5 |
| 16.2 | 16.1 |

References: 1 F. A. Macias, R. M. Varela, A. Torres and J. M.G. Molinillo, *Tetrahedron Lett.,* 1998, **39**, 427-430.
2 F. A. Marcias, J. L. G. Galindo, R. M. Varela, A. Torres, J. M. G. Molinillo, F. R. Fronczek, *Org. Lett.,* 2006, **8**, 4513-4516.




```
Current Data Parameters
NAME                      124
EXPNO                       4
PROCNO                      1

F2 - Acquisition Parameters
Date_              20091112
Time                   2.25
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                        8
DS                        0
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                      101
DW                   60.800 usec
DE                    6.50 usec
TE                   295.8 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                   12.00 usec
PL1                  -2.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF            400.1300094 MHz
WDW                      GM
SSB                       0
LB                   -0.20 Hz
GB                      0.1
PC                     1.00
```

hc-2-119-bp H1 CDCl3 2009-11-12

Pulse Sequence: s2pul

D2O.

400 MHz

7.283

4.746

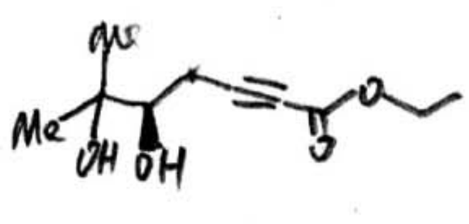
4.256
4.238
4.220
4.202

3.680
3.672
3.658
3.649

2.636
2.627
2.593
2.584
2.570
2.547
2.525
2.504
2.482
2.180

1.327
1.310
1.292
1.253
1.190

-0.000



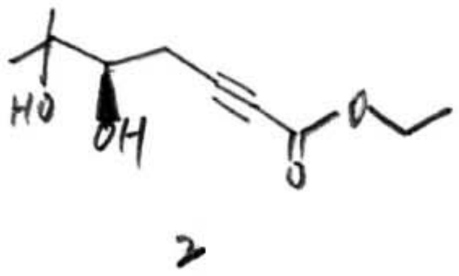

2

10 9 8 7 6 5 4 3 2 1 ppm

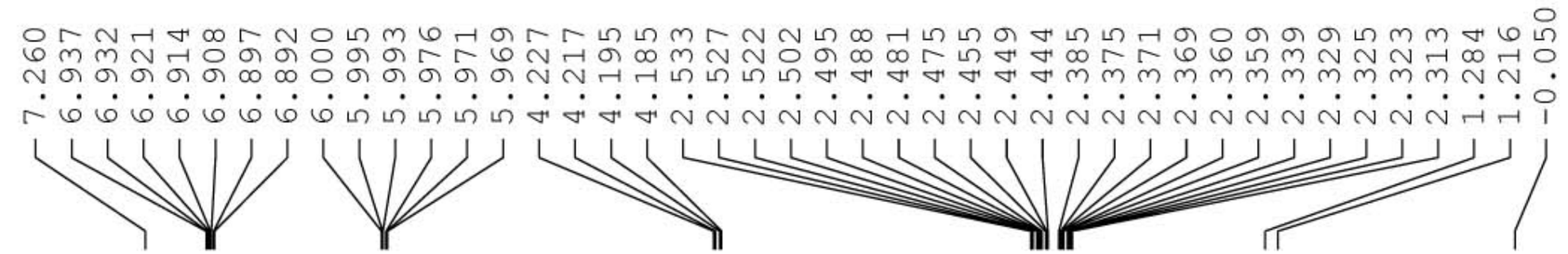
0.29 2.00 0.89 0.12 3.05

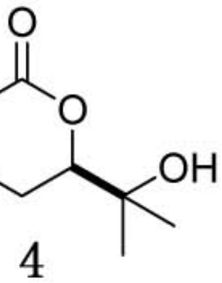
HC-2-124-C-CDCL3-C13-2010-1-15 100 MHz

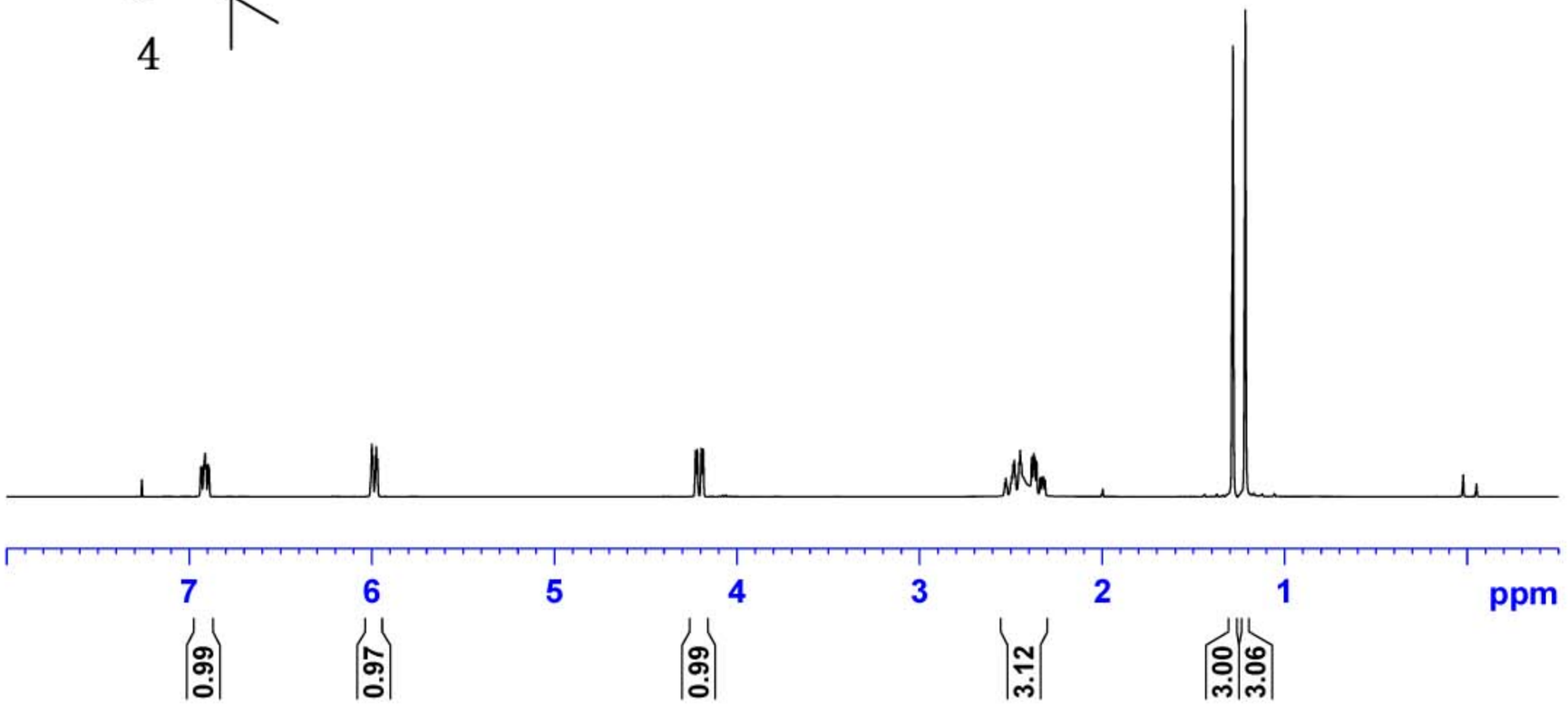
Pulse Sequence: s2pul



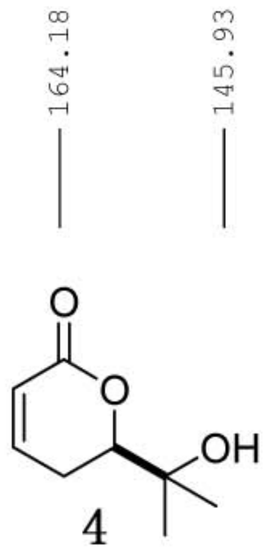

2



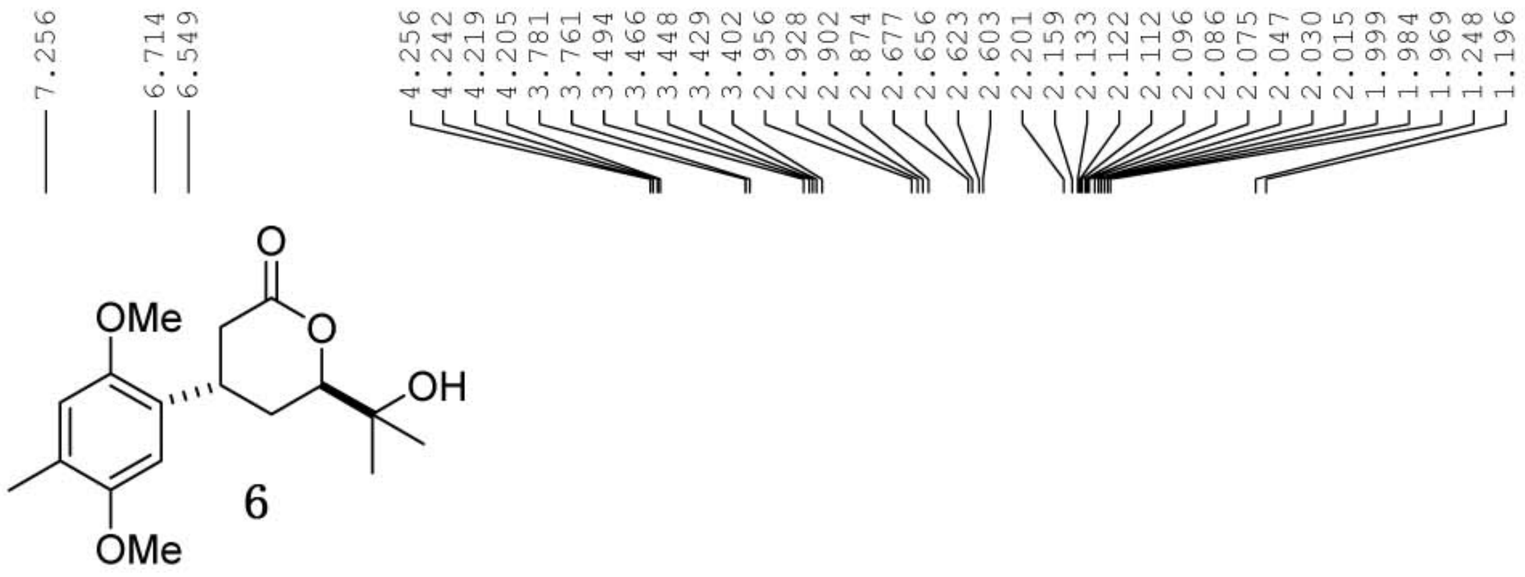

```
Current Data Parameters
NAME                  138
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20091230
Time                1.16
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                      8
DS                      0
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                   80.6
DW                 60.800 usec
DE                  6.50 usec
TE                 294.7 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 12.00 usec
PL1                -2.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF           400.1300094 MHz
WDW                    GM
SSB                     0
LB                 -0.20 Hz
GB                    0.1
PC                   1.00
```




4




```
Current Data Parameters
NAME                  138
EXPNO                  18
PROCNO                  1

F2 - Acquisition Parameters
Date_           20091230
Time_               2.48
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     0
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631988 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                296.3 K
D1             2.00000000 sec
d11            0.03000000 sec
DELTA          1.89999998 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                 15.50 usec
PL1                -1.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2              60.00 usec
PL12               11.35 dB
PL13               13.05 dB
PL2                -2.00 dB
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF           100.6127734 MHz
WDW                   EM
SSB                    0
LB                  0.60 Hz
GB                     0
PC                  1.40
```



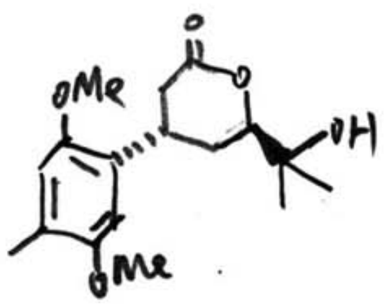

```
Current Data Parameters
NAME            cd-1b-14
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20100107
Time                2.38
INSTRUM            av300
PROBHD   5 mm QNP 1H/13
PULPROG             zg30
TD                 32768
SOLVENT              D2O
NS                    11
DS                     0
SWH             5995.204 Hz
FIDRES          0.182959 Hz
AQ              2.7329011 sec
RG                   128
DW                83.400 usec
DE                 6.00 usec
TE                292.6 K
D1             1.00000000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                10.50 usec
PL1                0.10 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF          300.1300135 MHz
WDW                   GM
SSB                    0
LB                -0.20 Hz
GB                   0.1
PC                  1.00
```

hc-2--170-5-C-CDCL3-C13-2010-1-7

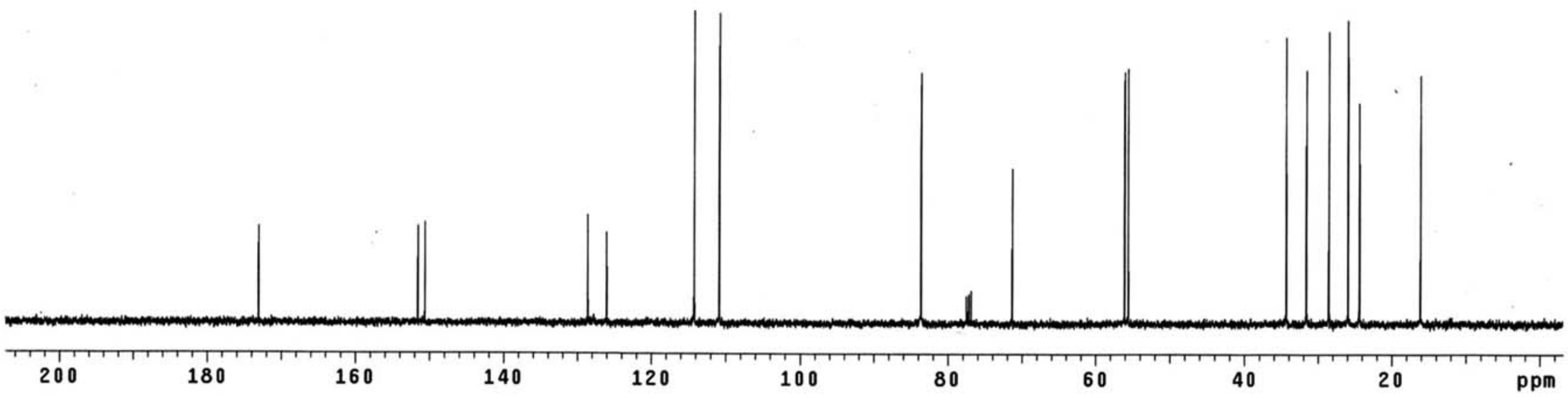
Pulse Sequence: s2pul

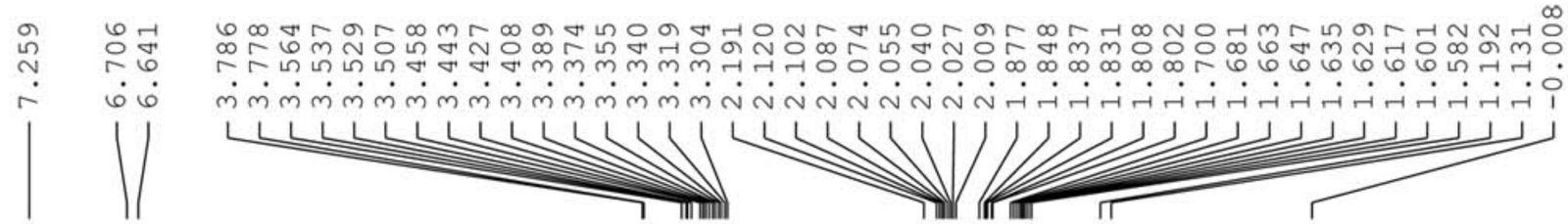
100 MHz

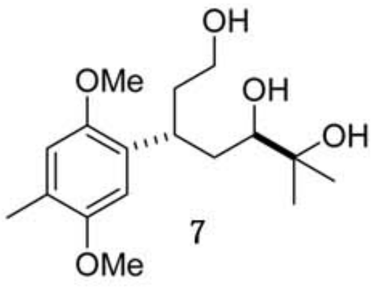
173.090
151.542
150.596
128.591
126.015
114.198
110.873
83.622
77.517
77.197
76.882
71.340
56.084
55.606
34.335
31.602
28.521
25.910
24.352
16.113



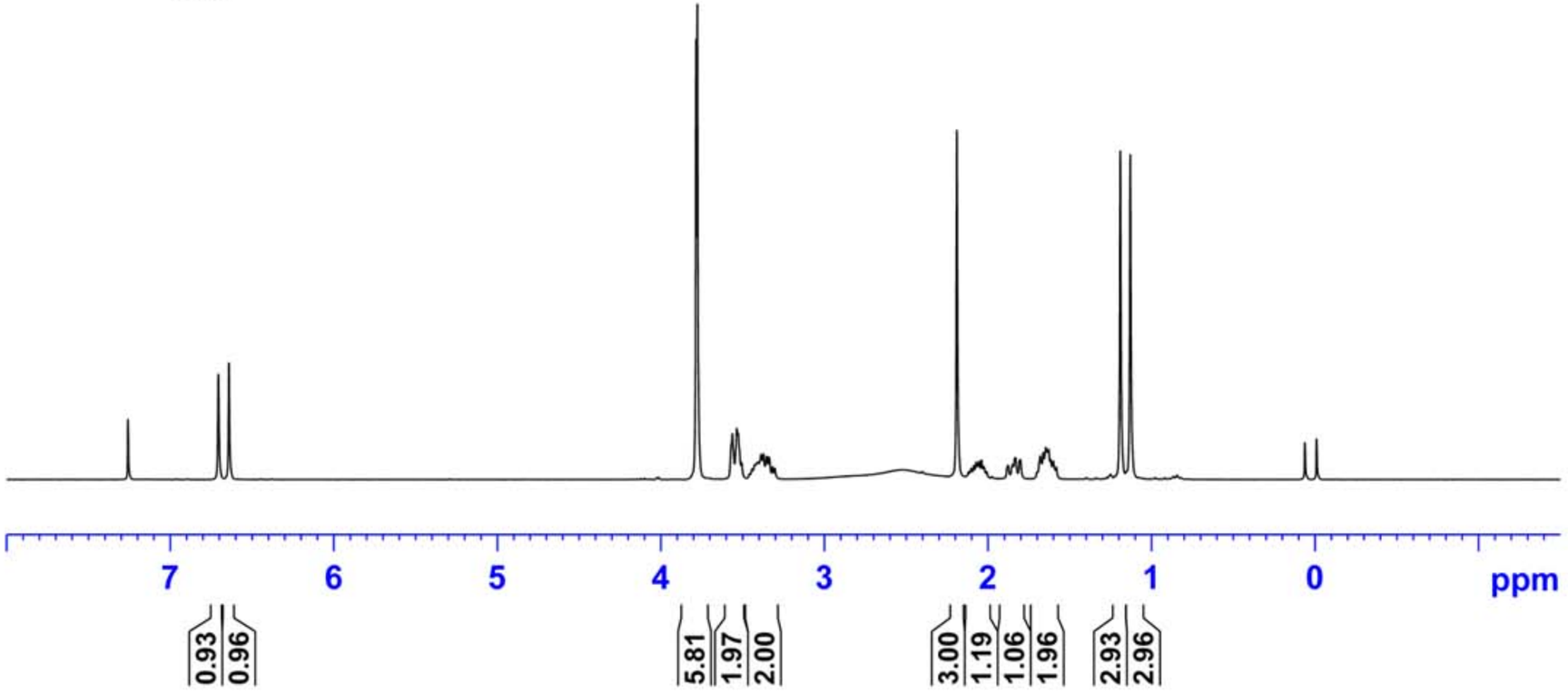

6






7



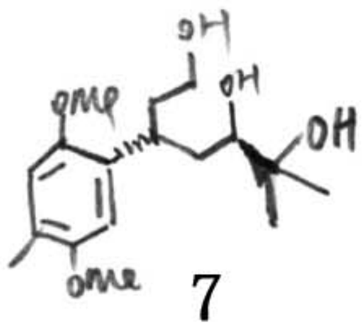

```
Current Data Parameters
NAME                  cd-lb-15
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20100107
Time                      2.41
INSTRUM                  av300
PROBHD    5 mm QNP 1H/13
PULPROG                   zg30
TD                       32768
SOLVENT                    D2O
NS                           8
DS                           0
SWH                   5995.204 Hz
FIDRES                0.182959 Hz
AQ                    2.7329011 sec
RG                         128
DW                      83.400 usec
DE                       6.00 usec
TE                      292.6 K
D1                 1.00000000 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                        1H
P1                      10.50 usec
PL1                      0.10 dB
SFO1               300.1318534 MHz

F2 - Processing parameters
SI                       32768
SF                 300.1300129 MHz
WDW                         GM
SSB                          0
LB                      -0.20 Hz
GB                         0.1
PC                        1.00
```

hc-2-173-4-C-CDCL3-C13-2010-1-6

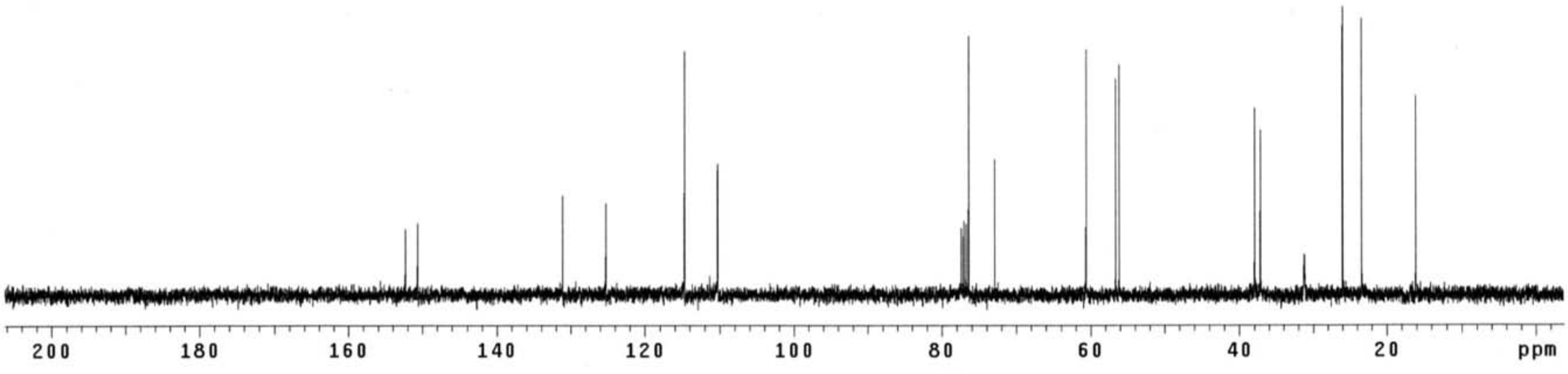
Pulse Sequence: s2pul

100 MHz

152.276
150.651
131.107
125.218
114.675
110.266
77.383
77.067
76.748
76.416
72.906
60.600
56.596
56.096
37.936
37.163
31.203
25.993
23.394
16.144



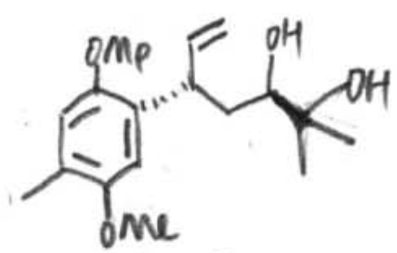

7



Hel-0110-1-H H1 CDCl3 2010-1-7

Pulse Sequence: s2pul

400 MHz




8

7.263
6.709
6.672
6.070
6.050
6.045
6.027
6.025
6.007
6.002
5.982
5.179
5.136
5.131
5.104
3.940
3.930
3.915
3.909
3.895
3.884
3.799
3.789
3.532
3.506
2.328
2.201
1.967
1.963
1.941
1.937
1.932
1.928
1.906
1.903
1.636
1.625
1.609
1.600
1.591
1.575
1.564
1.213
1.148
0.080
0.006

10 9 8 7 6 5 4 3 2 1 ppm

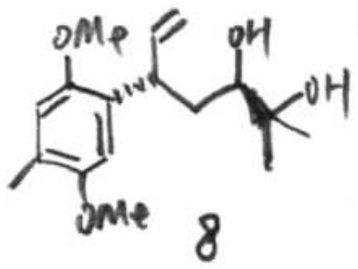
1.93 0.94 2.03 6.04 1.03 1.00 1.84 2.89 1.26 1.00 3.06 2.95

hel-0110-1-C-CDCL3-C13-2010-1-8

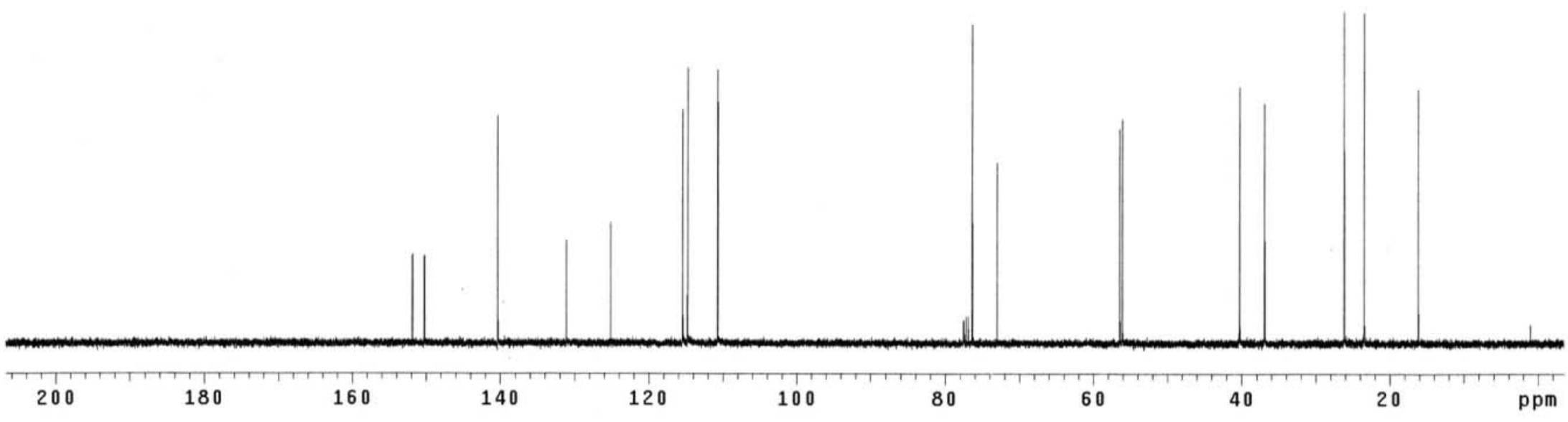
Pulse Sequence: s2pul

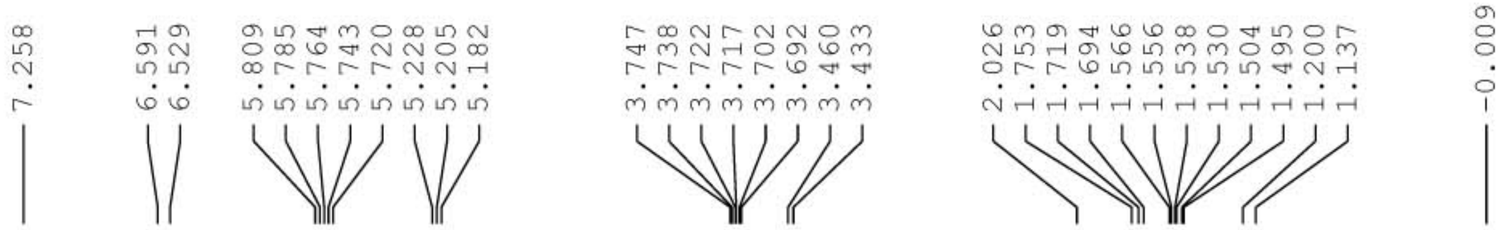
100 MHz

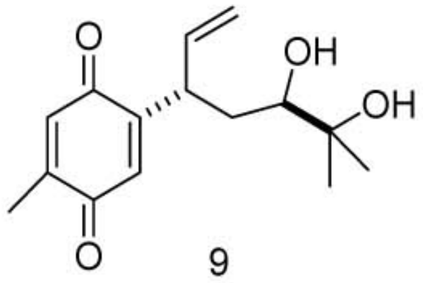
151.872
150.230
140.342
131.080
125.108
115.452
114.769
110.720
77.480
77.165
76.843
76.346
73.018
56.457
56.119
40.282
36.900
26.129
23.444
16.150



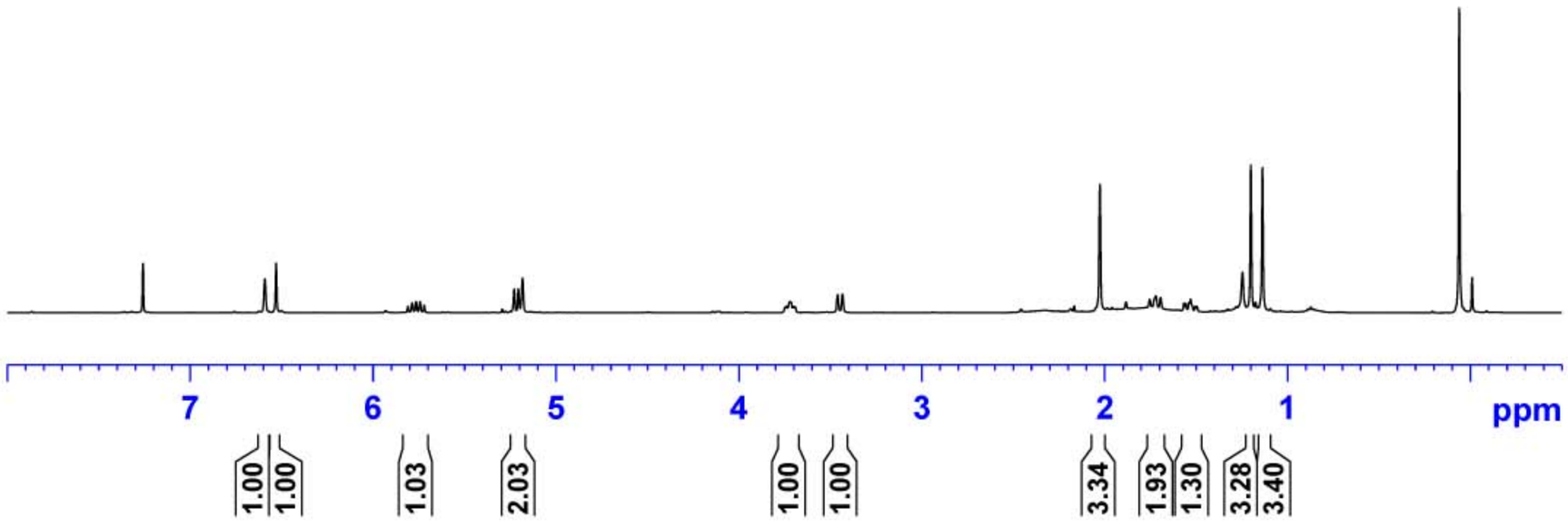

8





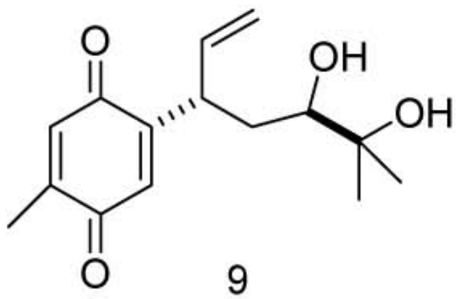




9

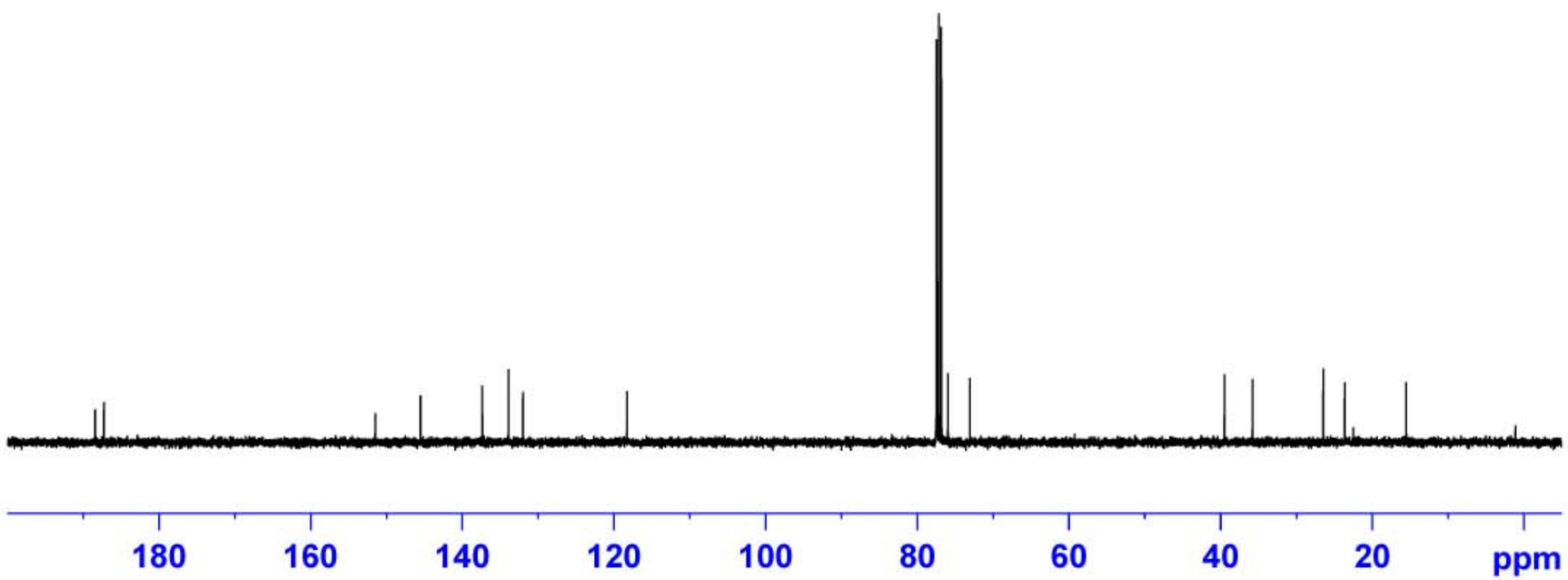



```
Current Data Parameters
NAME          hel-0111-1
EXPNO                 14
PROCNO                 1

F2 - Acquisition Parameters
Date_           20091013
Time               4.12
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    0
SWH            8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG                  287
DW               60.800 usec
DE                6.50 usec
TE               295.8 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                  1H
P1                12.00 usec
PL1               -2.00 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                32768
SF          400.1300104 MHz
WDW                  GM
SSB                   0
LB               -0.20 Hz
GB                  0.1
PC                 1.00
```

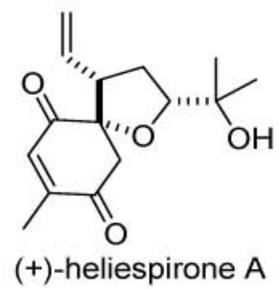
188.43
187.27
151.48
145.53
137.36
133.90
132.00
118.27
77.47
77.15
76.83
75.96
73.04
39.50
35.78
26.48
23.64
15.54




9

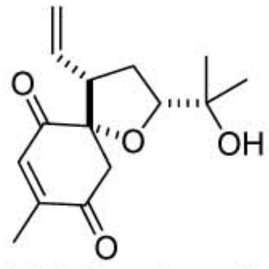



```
Current Data Parameters
NAME          hel-0111-1
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20100120
Time               5.13
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  128
DS                    0
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ            1.3631988 sec
RG                 1290
DW               20.800 usec
DE                6.50 usec
TE               294.7 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                15.50 usec
PL1               -1.00 dB
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             60.00 usec
PL12              11.35 dB
PL13              13.05 dB
PL2               -2.00 dB
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF          100.6127583 MHz
WDW                    EM
SSB                    0
LB                0.60 Hz
GB                     0
PC                1.40
```




(+)-heliespirone A




(+)-heliespirone A

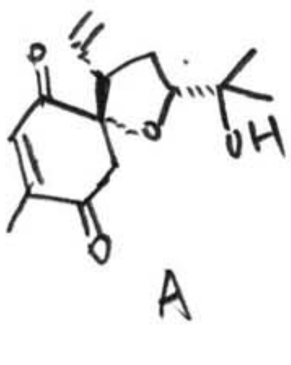
add $D_2O$

hc-2-191-top-c-CDCL3-C13-2010-1-20

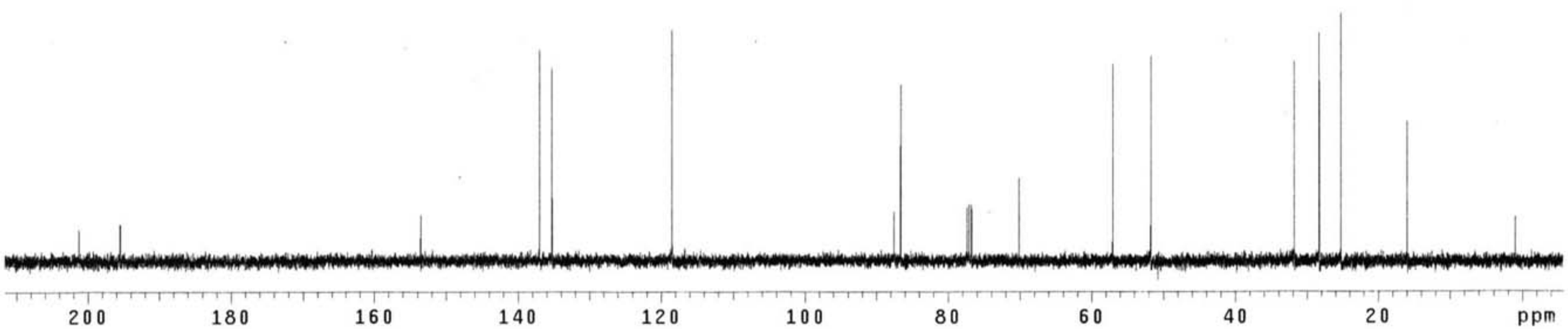
Pulse Sequence: s2pul

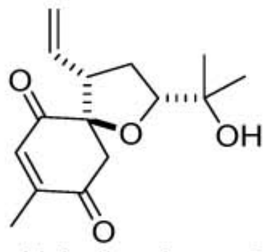
100 MHz

201.263
195.470
153.521
136.964
135.254
118.454
87.493
86.591
77.359
77.040
76.722
70.129
57.014
51.710
31.770
28.290
25.219
15.922
0.980



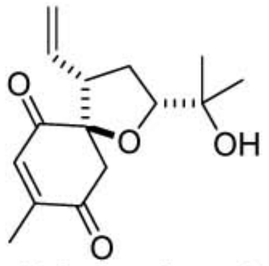

A





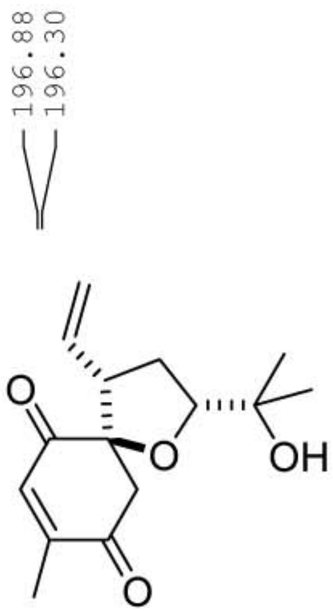

(-)-heliespirone C



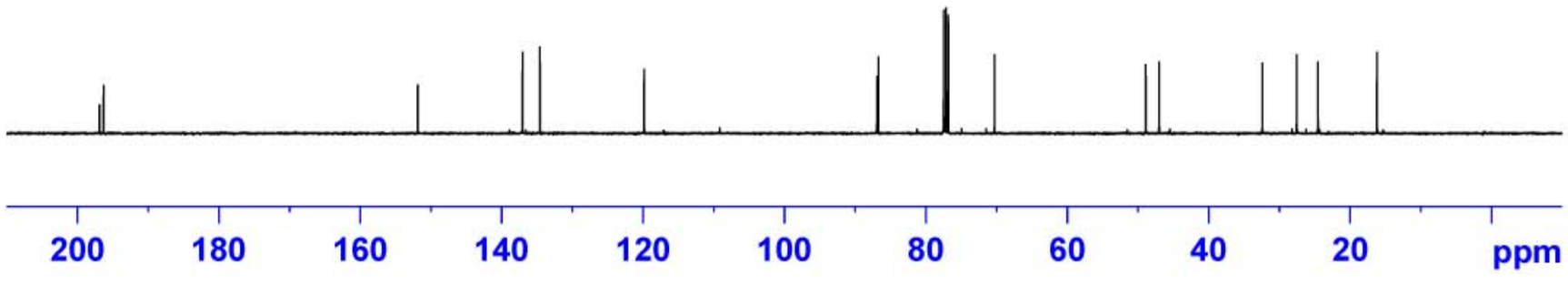




(-)-heliespirone C

add $D_2O$



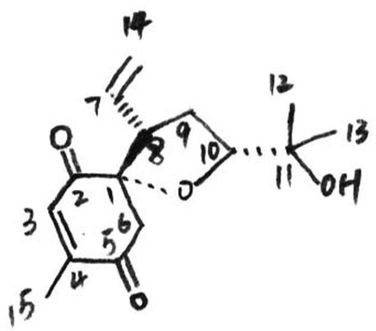

(-)-heliespirone C

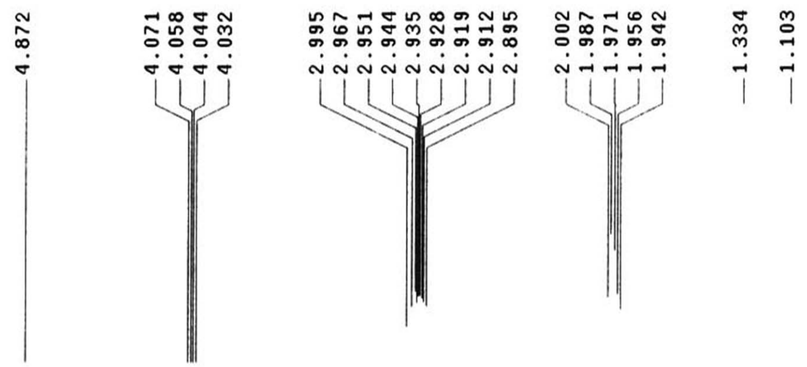

```
Current Data Parameters
NAME                      C
EXPNO                    18
PROCNO                    1

F2 - Acquisition Parameters
Date_              20100120
Time                   5.26
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      128
DS                        0
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                1.3631988 sec
RG                     1620
DW                   20.800 usec
DE                    6.50 usec
TE                   294.6 K
D1              2.00000000 sec
d11             0.03000000 sec
DELTA           1.89999998 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    15.50 usec
PL1                   -1.00 dB
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                 60.00 usec
PL12                  11.35 dB
PL13                  13.05 dB
PL2                   -2.00 dB
SFO2           400.1316005 MHz

F2 - Processing parameters
SI                      32768
SF             100.6127607 MHz
WDW                        EM
SSB                         0
LB                     0.60 Hz
GB                          0
PC                      1.40
```

A NOEDS4.05 CDCl3 2010-5-17

Pulse Sequence: cyclenoe




(+) A



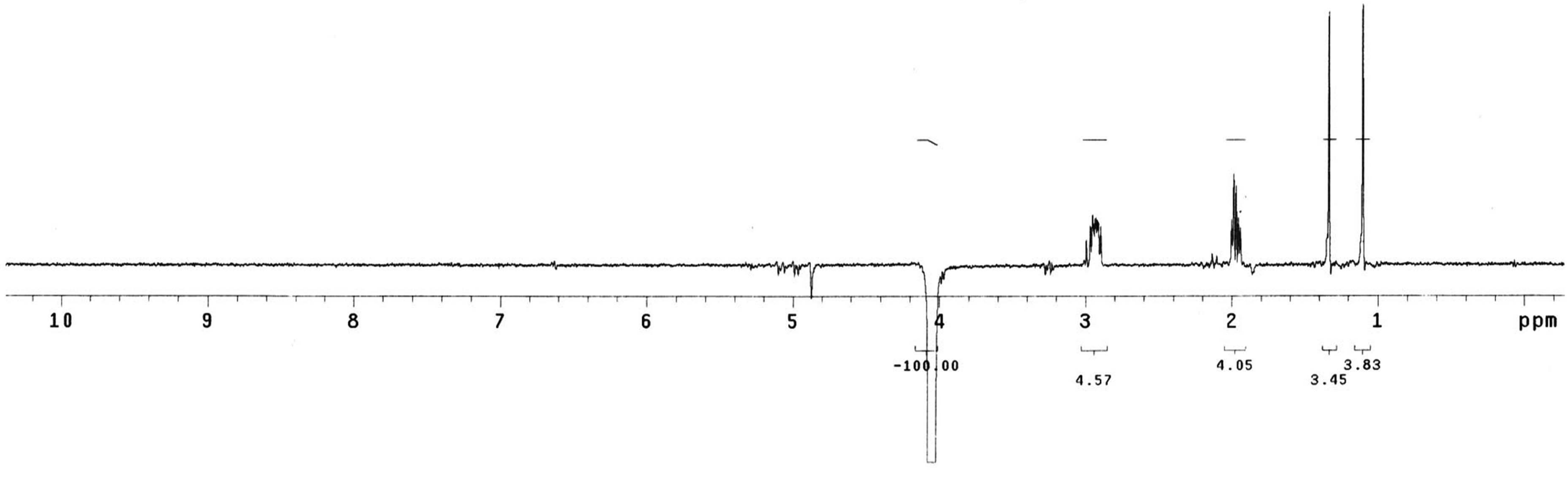

Irradition of H-10;

provoked: H-6β + H-8, 4.57%

H-9β, 4.05%

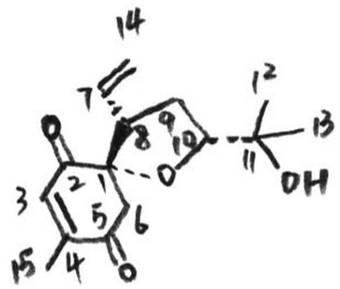
H-13, 3.45%

H-12, 3.83%

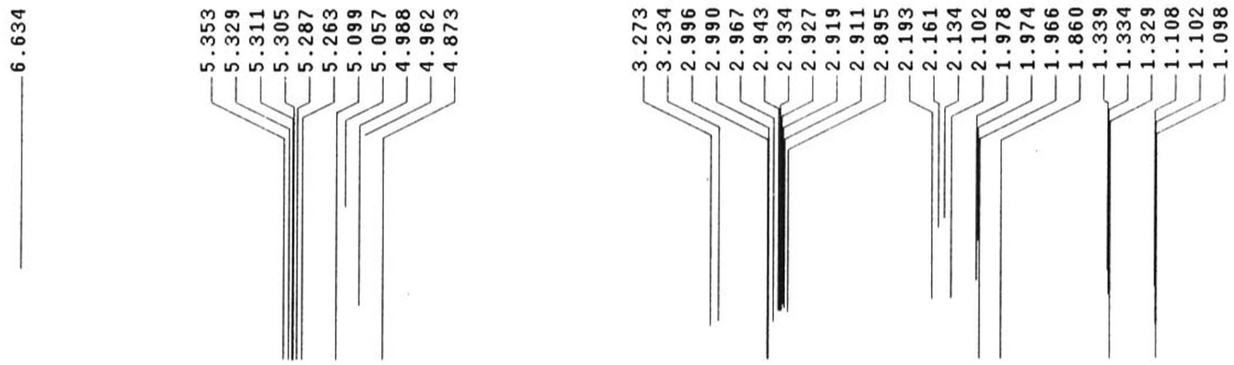


A NOEDS5.31 CDCl3 2010-5-17

Pulse Sequence: cyclenoe




(+) A



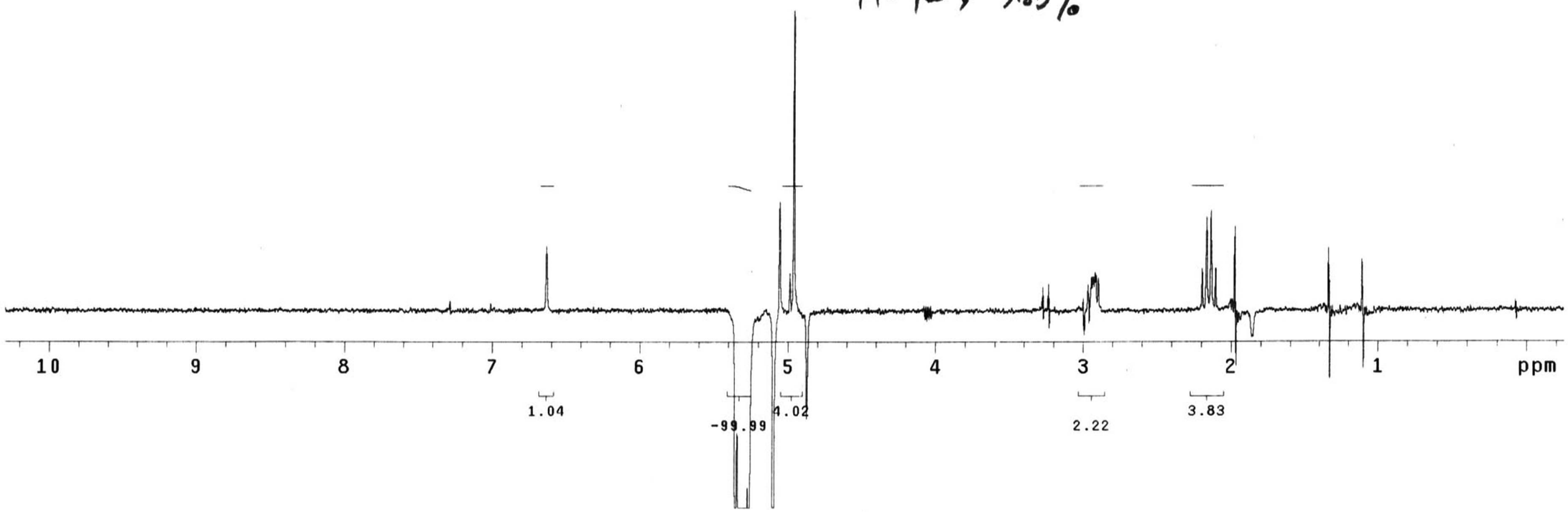

Irradition of H-7;

provoked: H-3, 1.04%

H-14 cis, 4.02%

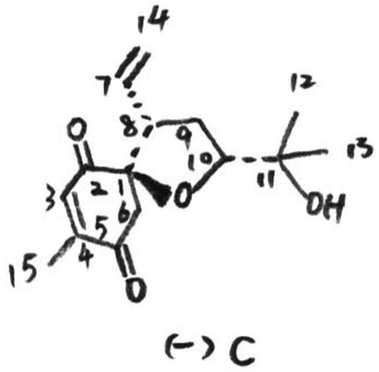
H-8, 2.22%

H-9d, 3.83%



C NOEDS3.92 CDCl3 2010-5-17

Pulse Sequence: cyclenoe




(-) C

6.652
6.649
5.097
3.944
3.931
3.917
3.904
3.265
3.245
3.236
3.226
3.217
3.197
2.907
2.836
2.831
2.050
2.037
2.020
2.006
1.976
1.956
1.953
1.951
1.947
1.945
1.913
1.884
1.205
1.193
1.095
1.083

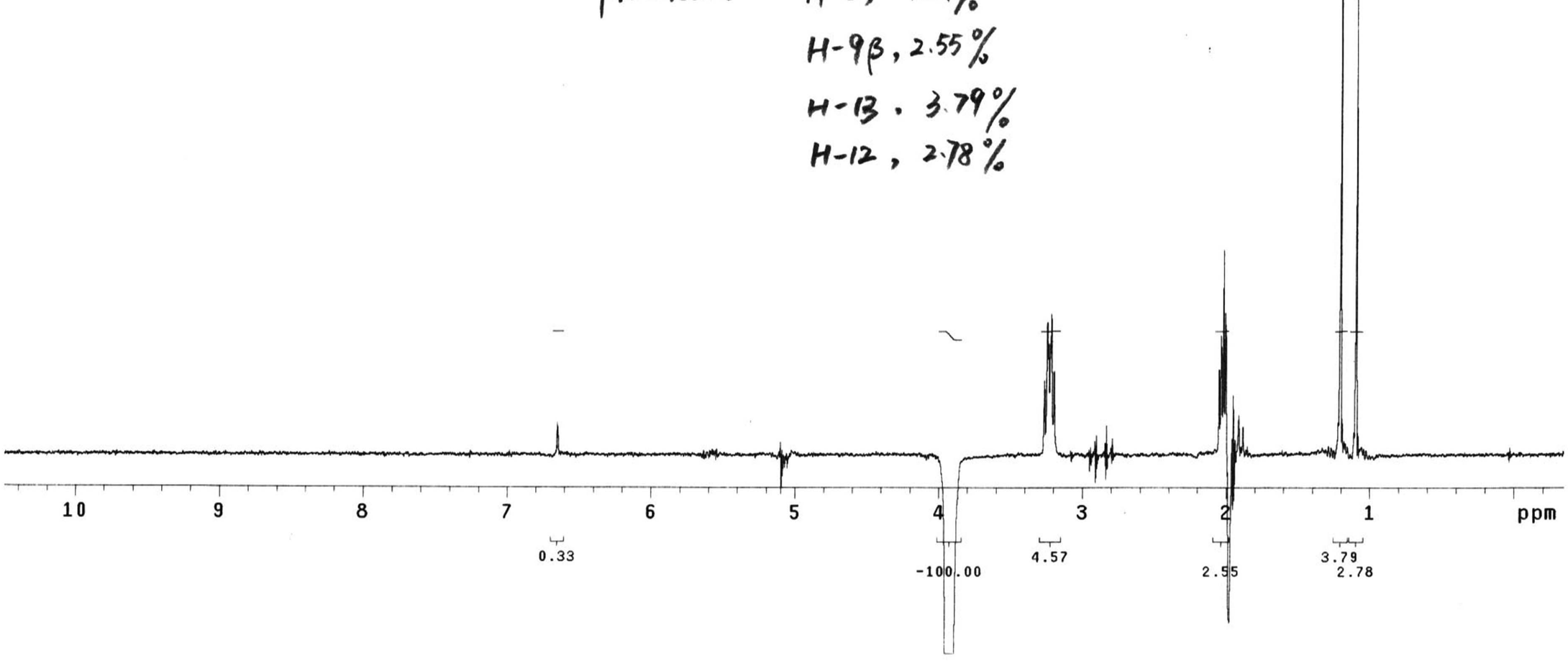
Irradition of H-10;

prowoked: H-8, 4.57%

H-9β, 2.55%

H-13, 3.79%

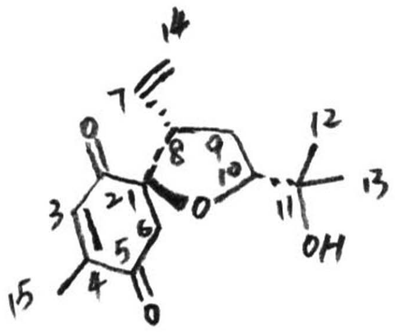
H-12, 2.78%



C NOEDS5.59 CDCl3 2010-5-17

Pulse Sequence: cyclenoe

6.654
6.646
5.636
5.615
5.610
5.595
5.588
5.574
5.569
5.547
5.096
5.068
5.050
3.946
3.942
3.934
3.929
3.919
3.915
3.906
3.903
3.263
3.244
3.235
3.225
3.215
3.196
2.945
2.904
2.836
2.831
2.795
2.791
2.022
2.017
1.990
1.977
1.956
1.948
1.938
1.910
1.881
1.852
1.207
1.203
1.097
1.093
0.032
0.028




(-).C

Irradition of H-7;

provoked: H-14 cis. 3.07%

H-8, 2.37%

H-6α, 2.74%

H-9α, 2.05%