Supporting Information

Liposomal Circular Dichroism. Assignment of Remote Stereocenters in Plakinic Acids K and L from a *Plakortis-Xestospongia* Sponge Association

Doralyn S. Dalisay[§], Tim Quach[§] and Tadeusz F. Molinski[§,†,]*

[§]Department of Chemistry and Biochemistry, and [†]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, 9500 Gilman Drive, La Jolla, California 92093.

tmolinski@ucsd.edu

Content *Page*

General Procedures: All non-aqueous reactions were carried out in oven-dried glassware under a nitrogen atmosphere, unless otherwise noted. All solvents were reagent grade. Solvents for dry reactions (DCM, DMF, THF, toluene, acetonitrile, Et_2O) were passed through twin alumina columns (J. C. Meyer, Glass Contour). DMSO was distilled from calcium hydride under reduced pressure and stored over 4 Å molecular sieves. Dry MeOH was prepared and stored over 4Å molecular sieves. Triethylamine and pyridine were distilled from calcium hydride. All other commercially available reagents were used as received. Reactions were monitored by thin layer chromatography (TLC) using 0.25-mm E. Merck per-coated silica gel plates.

CD spectra were recorded on a Jasco J810 spectropolarimeter in 0.2 cm quartz cells at 23 ˚C unless otherwise stated. UV-Vis spectra were recorded in a dual beam Jasco V630 spectrometer in 1 cm quartz cells. Intensities of CD spectra in DSPC liposomes were normalized to absorbance (MeOH).

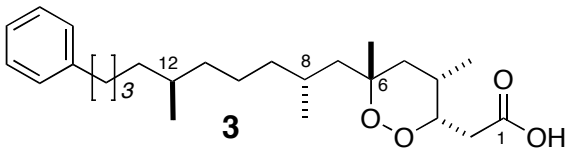
Routine ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using either a Varian Mercury-400 (400 MHz and 75 MHz), Varian Unity-500 (500 MHz), JEOL ECA 500 (500 MHz and 125 MHz), or Bruker DMX-600 (600 MHz) equipped with a 1.7 mm $\{^{13}C\}^{1}H$ TXI probe. NMR spectra were referenced to solvent signals (^{1}H, residual $CHCl_3$ at δ 7.26 ppm; ^{13}C, δ 77.16 ppm). HRMS measurements were carried out at the University of California, Riverside (ESI-MS), or University of California, San Diego (EI-MS) mass spectrometry facilities. Optical rotations were measured on a Jasco P-1010 or P-2000 model digital polarimeter in cells of 10 mm pathlength (*c ,* g/100 mL). IR spectra were recorded on a Jasco 4100 FTIR using ATR (ZnSe plate). LCMS was carried out on a ThermoFisher Accela LC coupled to an MSQ single quadrupole mass spectrometer in positive ion mode, unless otherwise stated. Semi-preparative HPLC was carried out on a Varian SD200 system equipped with a dual-pump and UV-1 UV detector under specified conditions.

Purification and Characterization of Plakinic acids K (3) and L (4).

The sponge *Plakortis halichondroides–Xestospongia deweerdtae* Lehnert & van Soest, 1999 was collected from reef habitat in the Bahamas (lat. 24° 25.163', long. 75° 58.435', accession number, 07-26-171) at a depth of –27 m during the June 2007 cruise of the *RV Seward Johnson*, and frozen immediately until used. The sponge was identified by Sven Zea (Universidad Nacional de Colombia).

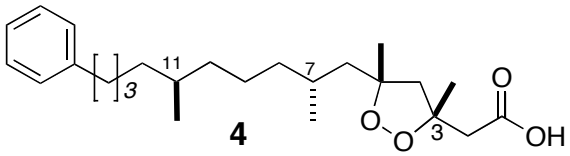
Extraction and Isolation. A frozen sample of the sponge *P. halichondroides-X. deweerdtae* (07-26-171; 200 g) was extracted with MeOH:CH_2Cl_2 with stirring overnight at rt. (100 mL x 2), the combined extracts were filtered and concentrated under reduced pressure. The methanol extract was fractionated using sequential solvent-solvent partitioning with adjustment of the H_2O content at each step: 0% v/v H_2O, hexane (100 mL, Fraction A), 40% v/v H_2O, $CHCl_3$ (100 mL x 2, Fraction B). The MeOH was removed under reduced pressure and the aqueous residue extracted with *n*-BuOH (100 mL x 2, Fraction D). Fraction B (1.41 g) was subjected to silica flash chromatography (2 x 12.5 cm, 0 to 100% MeOH, stepwise 20% increment in $CHCl_3$) to yield fractions #1-8. Fraction #2 (320 mg) was further purified by silica gel flash chromatography (Analogix, RS-4 cartridge, 4g, 50 μm 60Å) using mixtures of hexane and ethyl acetate of increasing polarity (0-100%). Fractions were pooled according to their TLC profiles. The early-eluting Fraction 1 (153 mg) was purified by reversed phase HPLC (C_{18} Luna Phenomenex, 250 x 10 mm) under gradient conditions (70:30 $CH_3CN:H_2O$ to 100% CH_3CN, 3 mL/min, UV detection λ = 254 nm) to give pure plakinic acid K (**3**, 31 mg, 0.0155 % wet weight), plakinic acid L (**4**, 28 mg, 0.014%) and plakinic acid M (, 41 mg, 0.0205 % wet weight).

Plakinic acid K (**3**) colorless oil. $[\alpha]_D^{24}$ –113 (*c* 3.39, $CHCl_3$), UV (MeOH) λ_{max} 260 nm (ε 285), 268 (203), FTIR (ATR, neat) ν 2921, 2850, 1710, 1371, 1294, 738, 697 cm^{-1}. ^1H and ^{13}C NMR data (see Table S1). HREIMS *m/z* 418.3081 $[M]^+$, calcd. 418.3083 for $C_{26}H_{42}O_4$.



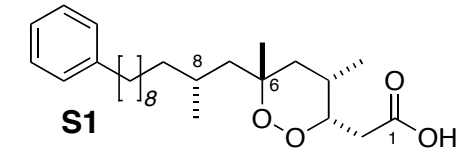
3

Plakinic acid L (**4**). colorless oil; $[\alpha]_D^{24}$ –26.2 (*c* 1.90, $CHCl_3$); UV (MeOH) λ_{max} 268 nm (ε 155), 261 (225); FTIR (ATR, neat) n 2926, 2850, 1710, 1456, 1381, 1305, 1213, 743, 697 cm^{-1}; ^1H and ^{13}C NMR (see Table S2). HREIMS *m/z* 404.2918 $[M]^+$, calcd. 404.2927 for $C_{25}H_{40}O_4$.



4

Plakinic acid M (**S1**). colorless oil; $[\alpha]_D^{24}$ –137 (*c* 1.31, $CHCl_3$); UV (MeOH) l_{max} 269 nm (ε 162), 261 (234); FTIR (ATR, neat) ν 2920, 2850, 1715, 1456, 1371, 1290, 1026, 743, 697 cm^{-1}; ^1H and ^{13}C NMR (see Table S3). HREIMS *m/z* = 418.3081 $[M^+]$ calcd. 418.3083 for $C_{26}H_{42}O_4$.



S1

Table S1. ^{1}H (600 MHz) and ^{13}C NMR (100 MHz) for plakinic acid K (**3**) ($CDCl_3$)

No.	^{1}H, δ, mult. (*J* in Hz)	^{13}C, δ, mult.	HMBC, $^{1}H \rightarrow {}^{13}C$
1		177.6, C	
2	2.49, dd (16.0, 4.0)	31.7, CH_2	1, 3, 4
	2.99, dd (16.0, 9.0)		1, 3, 4
3	4.43, ddd (9.0, 5.0, 4.0)	79.4, CH	1, 2, 4, 5
4	2.45, m	27.9, CH	1, 2, 3, 5, 21
5	1.41, m	37.2, CH_2	3, 4, 6, 7, 21, 22
	1.30, m		
6		81.4, C	
7	1.43, m	48.4, CH_2	5, 6, 8, 9, 22
	1.26, m		5, 6, 8, 9, 22
8	1.62, m	28.4, CH	
9	1.07, m	39.0, CH_2	7, 8, 10, 11
	1.28, m		7, 8, 10, 11
10	1.16, m	24.5, CH_2	7, 8, 9, 11
	1.30, m		
11	1.04, m	37.3, CH_2	9, 12, 24
	1.24, m		9, 12
12	1.35, m	32.8, CH	14, 24
13	1.11, m	36.9, CH_2	11, 12, 14, 24
14	1.32, m	26.9, CH_2	12, 13, 24
15	1.60, m	31.9, CH_2	14, 16, 17
16	2.60, t (7.6)	36.1, CH_2	14, 15, 17, 18
17			
18	7.18, m	128.3, CH	16, 19, 20
19	7.27, t (8.0)	128.5, CH	17, 18
20	7.16, m	125.6, CH	17, 19
21	0.87, d (6.9)	17.3, CH_3	3, 4, 5
22	1.38, s	21.7, CH_3	5, 6, 7
23	0.92, d (6.6)	22.1, CH_3	7, 8, 9
24	0.83, d (6.6)	19.8, CH_3	12, 13

Table S2. ^{1}H (600 MHz) and ^{13}C NMR (100 MHz) for plakinic acid L (**4**) ($CDCl_3$)

No.	^{1}H, δ, mult. (*J* in Hz)	^{13}C, δ, mult.[a]	HMBC, $^{1}H \rightarrow {}^{13}C$
1		176.2, C	
2	2.72, d (15.2)	44.7, CH_2	1, 3, 4
	2.82, d (15.2)		1, 3, 4
3		83.8, CH	1, 2, 4, 5
4	2.19, d (12.8)	56.8, CH	2, 3, 5, 20, 21
	2.59, d (12.8)		2, 3, 5, 20, 21
5		87.4, CH_2	
6	1.38, dd (7.6, 14.0)	45.6, C	4, 5, 7, 8, 21, 22
	1.67, dd (4.9, 14.0)		4, 5, 7, 8, 21, 22
7	1.58, m	29.7, CH_2	4, 6
8	1.12, m	38.5, CH	6, 7, 11, 12
	1.31, m		
9	1.18, m	24.7, CH_2	7, 8, 10, 11
10	1.12, m	37.1, CH_2	7, 9, 11, 12, 13, 22, 23
	1.31, m		
11	1.38, m	32.9, CH_2	8, 7, 10
12	1.05, m	37.4, CH	8, 9, 10, 11, 23
	1.25, m		
13	1.32, m	27.0, CH_2	9, 11, 23
14	1.60, m	32.0, CH_2	15
15	2.60, t (7.6)	36.2, CH_2	14, 16, 17
16		143.0, CH_2	
17	7.17, m	128.5, CH	
18	7.27, t (8.0)	128.3, CH	
19	7.16, m	128.5, CH	
20	1.48, s	23.8, CH	2, 3, 4
21	1.35, s	25.1, CH_3	4, 5, 6
22	0.89, d (6.6)	21.1, CH_3	6, 7, 8
23	0.83, d (6.6)	19.9, CH_3	11,

[a] Determined from DEPT and HSQC.

Table S3. ^{1}H (600 MHz) and ^{13}C NMR (100 MHz) for plakinic acid M (**S1**) ($CDCl_3$)

No.	^{1}H (mult. (*J* in Hz)	^{13}C (mult.)[b]
1		177.6 (C)
2	2.49 (dd, 16.0, 9.2) 2.99 (dd, 16.0, 4.0)	31.9 (CH_2)
3	4.43 (ddd, 4.6, 5.0, 8.9)	79.6 (CH)
4	2.45 (m)	28.1 (CH)
5	1.40 (m)	37.6 (CH_2)
6		81.7 (C)
7	1.44 (m)	48.7 (CH_2)
8	1.60 (m)	28.6 (CH)
9	1.29 (m)	38.9 (CH_2)
10	1.50 (m)	27.3 (CH_2)
11	1.29 (br s[a])	29.8 (CH_2)[a]
12	1.29 (br s[a])	29.9 (CH_2)[a]
13	1.29 (br s[a])	30.0 (CH_2)[a]
14	1.29 (br s[a])	30.0 (CH_2)[a]
15	1.29 (br s[a])	30.1 (CH_2)[a]
16		
17		
18	1.60 (m)	30.3 (CH_2)
19	2.60 (t, 8.0)	36.3 (CH_2)
20	7.26 (d, 6.4)	128.5 (CH)
21	7.27 (t, 8.0)	128.7 (CH)
22	7.18 (d, 7.2)	125.8 (CH)
23	0.87 (d, 6.8)	17.5 (CH_3)
24	1.38 (s)	22.3 (CH_3)
25	0.91 (d, 6.8)	22.0 (CH_3)

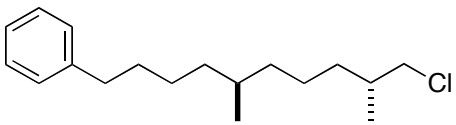
[a] Interchangable, unresolved methylene envelope. [b,] determined from DEPT and HSQC.

$FeCl_2$-Promoted Fragmentation of Plakinic acid K (3) and Plakinic acid L (4).

Commercial AR grade $FeCl_2 \cdot 4H_2O$ (washed with 6 M HCl, dried, to remove Fe(III) impurities) was prepared as a stock solution in degassed distilled H_2O. A solution of plakinic acid K (**3**) (15.0 mg, 35.8 μmol) in CH_3CN/H_2O (8:2, 1.0 mL, deaerated, N_2 purge, 40 min) was treated with $FeCl_2$ solution (1.0 M, 102 μL, 102.5 μmol) and stirred under an atmosphere of N_2 for 30 min, then quenched by adding 4 drops of 1.0 M citric acid and was added with 4 volumes of hexane, vortexed for 1 min and centrifuged to separate the organic layer. The aqueous layer was washed twice with hexane. The combined hexane layer was concentrated under reduced pressure and the residue was purified on a short SiO_2 column (pipette) using the following solvent system: 1:10, 2:10 and 3:10 EtOAc:hexanes to obtain colorless oil of **5** (1.0 mg, 6.6%)**.**

Plakinic acid L (**4**) was treated with $FeCl_2$, as described above, to obtain **5** which was converted through the same sequence of reactions, described below. The intermediates were the same (^{1}H NMR) and the product **7** (~200 μg) was identical (^{1}H NMR, LRESIMS *m/z* 468.30 $[M+Na]^+$, HPLC rt, L-CD) to that derived from **3**.

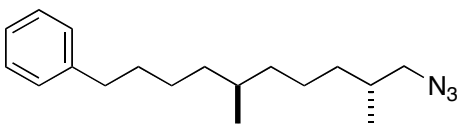
(10-Chloro-5,9-dimethyldecyl)benzene, 5



5

5 from **3**. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (t, *J* = 8 Hz, 2H), 7.17 (d, *J* = 6.6 Hz, 3H), 3.48 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.40 (dd, *J* = 10.8, 6.0 Hz, 1H), 2.60 (t, *J* = 8 Hz, 2H), 1.80 (m, 1H), 1.60 (m, 2H), 1.40 (m, 2H), 1.30-1.28 (m, 7H), 1.15 (m, 3H), 0.99 (d *J* = 6.4 Hz, 3H), 0.84 (d *J* = 6.8 Hz, 3H).

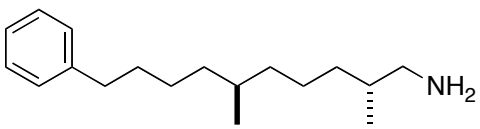
(10-Azido-5,9-dimethyldecyl)benzene, 6 derived from 3



6

Dried NaN_3 (1.16 mg, 17.0 μmol) was added to **5** (1.0, 3.0 μmol) in 50 μL of DMF. The reaction mixture was stirred vigorously at 100 °C for 4 h. The reaction was stopped and added with 200 μL of H_2O and extracted with hexanes (3 x 500 μL) to yield **6** (0.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (t, *J* = 8 Hz, 3H), 7.18 (d, *J* = 7.1 Hz, 2H), 3.20 (dd, *J* = 11.8, 5.9 Hz, 1H), 3.09 (dd, *J* = 12.1, 6.8 Hz, 1H), 2.60 (t, *J* = 7.2 Hz, 2H), 1.80 (m, 1H), 1.60 (m, 2H), 1.35-1.25 (m, 7H), 1.15 (m, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.84 (d, *J* = 6.2 Hz, 3H).

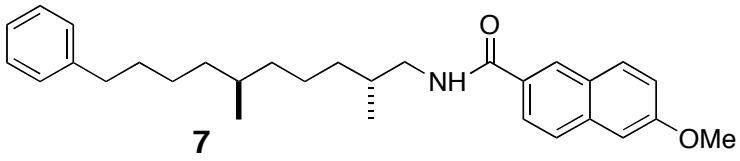
2,6-dimethyl-10-phenyldecan-1-amine, S2 derived from 3



S2

Azide **6** **(**0.6 mg, 2.0 μmol) was dissolved in 1 mL of EtOH:hexanes (3:1) and added with 0.8 mg of Pd/C (10% wt) and purged with H_2 for 1 h. The Pd/C was removed by syringe filter and the solvent was dried by rotaevaporation to yield **S2** (1.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (t, *J* = 8 Hz, 3H), 7.18 (d, *J* = 7.1 Hz, 2H), 2.60 (t, *J* = 8.1 Hz, 2H), 2.45 (dd, 14.2, 5.1 Hz, 1H), 1.60 (m, 2H), 1.41 (m, 1H), 1.30-1.27 (m, 13H), 1.09 (m, 1H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 8.0 Hz, 3H) LRESIMS *m/z* 262.17 $[M+H]^+$.

***N*-(2,6-dimethyl-10-phenyldecyl)-6-methoxy-2-naphthamide, 7 derived from 3**



7

6-Methoxy-2-naphthoyl chloride (2.20 mg, 9 μmol) was added to a solution of (**S2** (1.0 mg, 4 μmol) in 50 μL of CH_2Cl_2. A catalytic amount (~ 0.1 mg) of DMAP and Et_3N (1.43 mg, 1.4 μmol) were added to the solution and stirred vigorously for 2 h at r.t. then quenched by adding DMAPA (0.40 mg, 4 μmol). The reaction mixture was purified by silica column (pencil) using 3:10 EtOAc:hexanes and further purified by RPHPLC (Phenylhexyl analytical column, 250 x 4.6 mm; 90:10 MeOH:H_2O; 1 ml/min; detector 254 nm) to afford **7** (~400 μg). ^{1}H NMR (400 MHz, $CDCl_3$): d 8.20 (s, 1H), 7.81 (m, 3H), 7.29-7.15 (m, 7H), 6.23 (m, 1H), 3.94 (s, 3H), 3.45 (m, 1H), 3.31 (m, 1H), 2.60 (t, *J* = 8.0 Hz, 2H), 1.77 (m, 1H), 1.60 (m, 2H), 1.40-1.25 (m, 14H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H). LRESIMS *m/z* 468.30 $[M+Na]^+$.

Preparation of DSPC Liposomes and Liposomal CD (L-CD) Measurements

Liposomal naphthamides were prepared as previously described.[1] Briefly, a solution of 1,2-distearoyl-*sn*-glycero-3-phosphocholine (DSPC, 2 mg/mL in $CHCl_3$) was added to a solution of naphthamide in $CHCl_3$, concentrated in a round bottom flask. To the dried liposome, 2 mL of HPLC grade H_2O was added. The resulting suspension was sonicated for 2 min, heated (60 °C) and cooled (r.t.) (repeated twice). Uniform liposomes were prepared from this mixture by repeated extrusion (x25) through a 100 nm polycarbonate membrane secured between two 0.5 mL gas tight syringes (Liposofast, Avestin, Toronto, Canada). CD measurements were carried out on the resulting clear preparations under the following parameters: *T* = 23 °C; sensitivity, 100 mdeg; scanning speed, 50 nm/min; wavelength, from 180 to 400 nm; *N* = 15 accumulations. The CD spectra were subtracted from the baseline spectra recorded for DSPC liposomes without added naphthamides. Sample concentrations for L-CD were determined from absorbance at λ 238 nm in MeOH and ε values.

(1). (a) MacMillan, J. B.; Molinski, T. F. *J. Am. Chem. Soc.* **2004,** 12, 9944-5. b) Macmillan, J. B.; Linington, R. G.; Andersen, R. J.; Molinski, T. F. *Angew Chem Int Ed Engl.* **2004,** *43,* 5946-51

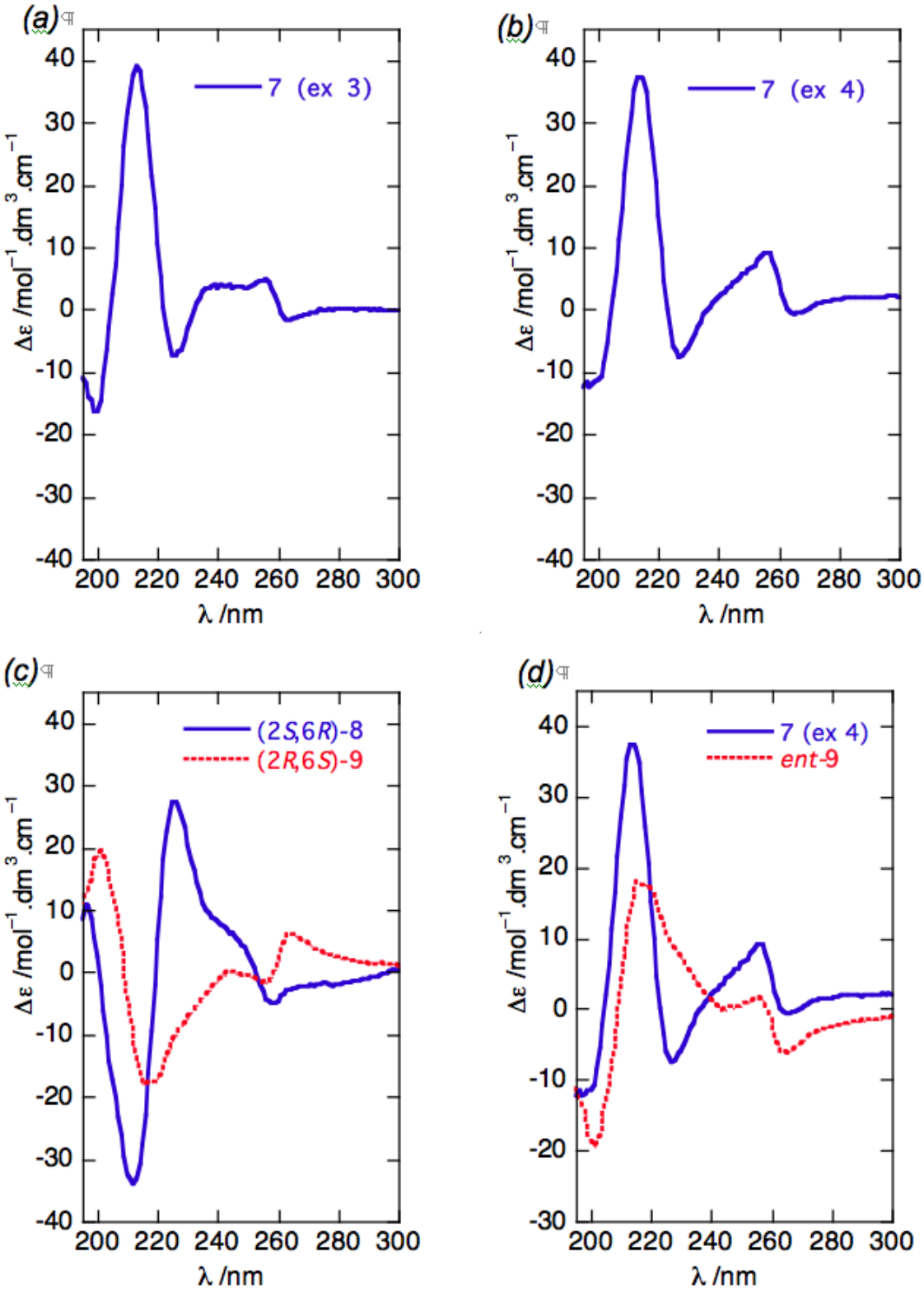


Figure S1. Liposomal circular dichroism (L-CD) spectra (T= 23 ^{0}C; liposomes, H_2O, diastearoyl-*sn*-3-glycero-phosphocholine, 2 mg/mL; mole ratio of phospholipid:naphthamide = 20:1). (a) **7,** prepared from **3**. (b) **7**, prepared from **4** (c = 4.4 x 10^{-4} M). (c) (2*S*,6*R*)-**8** (c = 2.25 x 10^{-4} M) and (2*R*,6*R*)-**9** (c = 2.47 x 10^{-4} M). (d) **7,** prepared from **4** and calculated L-CD spectrum of (2*S*,6*S*)-**9** (inversion of L-CD of **9**).

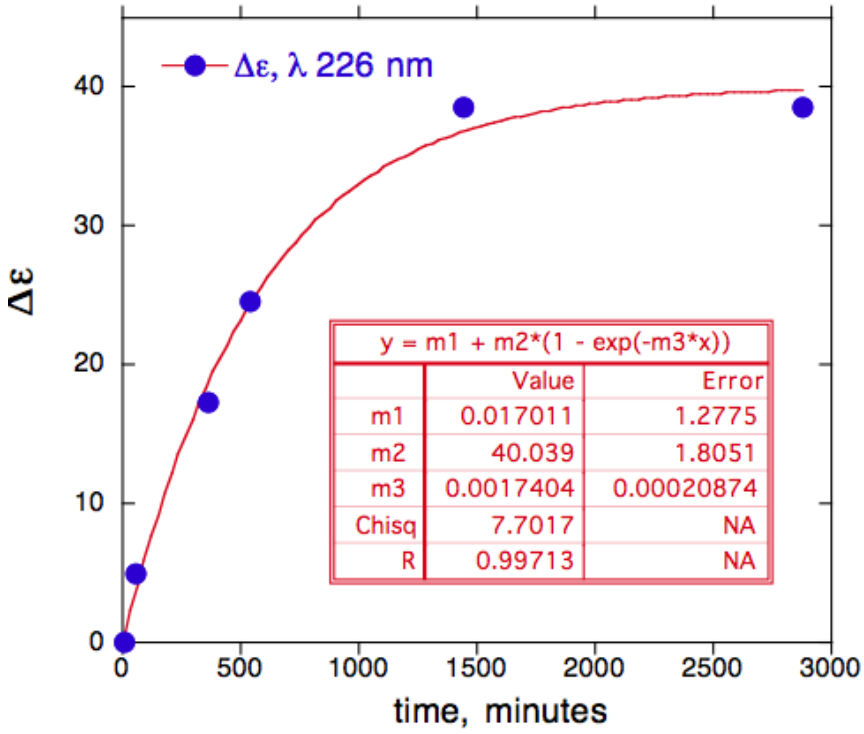


Figure S2. Time-dependent 'growth curve (T = 23 ˚C) of the Cotton effect (λ 226 nm) in the L-CD spectrum of **7** [see Figure 2(c)]. Insert shows exponential fit ($t_{1/2}$ = 385 min).

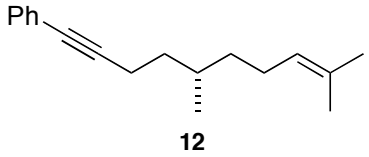
Table S4. Tabulated Cotton effects in L-CD spectra of (2*R*,6*S*)-**7**, (2*S*,6*R*)-**8**, (2*R*,6*R*)-**9** and (2*S*,6*S*)-**9** from Figure S1.

#	(2*R*,6*S*)-**7**		(2*S*,6*R*)-**8**		(2*R*,6*R*)-**9**		(2*S*,6*S*)-**9**[a]	
	λ nm	Δε	λ nm	Δε	λ nm	Δε	λ nm	Δε
1	197	–12.3	196	11.0	201	–19.5	201	+19.5
2	213	+37.2	212	–34.0	217	+17.5	217	–17.5
3	227	–7.6	226	+27.3	256	+1.7	256	–1.7
4	255	+4.7	258	–4.9	265	–6.2	255	+6.2

[a] calculated by inversion of L-CD of (2*R*,6*R*)-**9**

Synthesis of Standards 8 and 9:

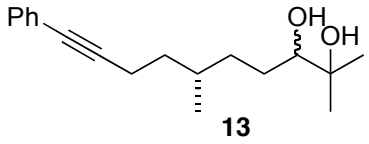
(*S*)-(5,9-Dimethyldec-8-en-1-ynyl)benzene (12)



12

n-BuLi (2.5 M in hexanes, 9.00 mL, 22.5 mmol) was added to a solution of phenylacetylene (2.64 mL, 24.0 mmol) in THF (60 mL) at 0 °C and the mixture warmed to r.t. then heated at reflux for three hours. The reaction was cooled to r.t., the (*S*)-tosylate **11**[2] (2.33 g, 7.50 mmol), prepared from (–)-**10** (obtained by $NaBH_4$ reduction of (–)-(*S*)-citronellal, Takasago, 98% ee) according to standard procedures, was added dropwise and the resulting mixture heated at reflux for a further 19 hours. The reaction was cooled to r.t., diluted with Et_2O and carefully quenched with water. The aqueous phase was extracted with Et_2O and the combined organic extracts washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (hexanes) gave the alkyne **12** (1.65 g, 92%) as a colorless liquid; FTIR (ATR): ν 2961, 2913, 2852, 2233, 1599, 1490, 1452, 1442, 1377, 1358, 1323, 1112, 1069, 1025, 911, 829, 754, 690 cm^{-1}; $[\alpha]_D^{20}$ –3.21 (*c* 3.00, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.43-7.41 (m, 2H), 7.30-7.28 (m, 3H), 5.15 (dt, *J* = 7.2, 1.6 Hz, 1H), 2.52-2.37 (m, 2H), 2.12-1.96 (m, 2H), 1.72 (s, 3H), 1.68 (m, 1H), 1.65 (s, 3H), 1.51-1.37 (m, 2H), 1.27-1.18 (m, 2H), 0.96 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.5 (CH), 131.1 (C), 128.1 (CH), 127.4 (CH), 124.8 (CH), 124.1 (C), 90.4 (C), 80.5 (C), 36.7 (CH_3), 35.7 (CH_3), 31.7 (CH_2), 25.7 (CH_2), 25.4 (CH), 19.1 (CH_2), 17.6 (CH_2), 17.1 (CH_3); HRESIMS *m/z* 241.1952 $[M+H]^+$, calcd. 241.1951 for $C_{18}H_{25}$.

(*R*)-2,6-Dimethyl-10-phenyldec-9-yne-2,3-diol (13)

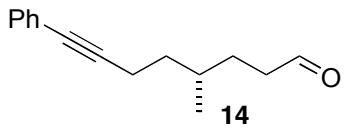


13

OsO_4 (0.2 M in *t*-BuOH, 818 μL, 0.164 mmol) and a solution of alkene **12** (786 mg, 3.27 mmol) in acetone (3.7 mL) were added to a suspension of $K_3Fe(CN)_6$ (3.23 g, 9.81 mmol) and K_2CO_3 (1.36 g, 9.81 mmol) in *t*-BuOH/ water (1:1 v/v, 25 mL) and the mixture stirred at r.t. for 15 hours. A second batch of OsO_4 (0.2 M in *t*-BuOH, 409 μL, 0.0820 mmol) was added and the mixture stirred at r.t. for a further 22 hours. The reaction was quenched with sat. aq. Na_2SO_3 and the aqueous phase extracted with EtOAc. The combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (5:95 → 30:70 EtOAc:hexanes) gave the diol **13** (719 mg, 80%, 1:1 mixture of diastereomers) as a colorless oil; FTIR (ATR): ν 3385, 2950, 2924, 2869, 2854, 1598, 1490, 1461, 1442, 1378, 1323, 1278, 1158, 1098, 1068, 963, 948, 914, 754, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39-7.37 (m, 2H), 7.29-7.24 (m, 3H), 3.32 (m, 1H), 2.72 (br s, 1H), 2.54 (br s), 2.50-2.34 (m, 2H), 1.72-1.59 (m, 2H), 1.55-1.17 (m, 5H), 1.19 (s, 3H), 1.14 (s, 3H), 0.94 (d, *J* = 6.4 Hz, 1.5H), 0.93 (d, *J* = 6.4 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.4 (CH), 128.1 (CH), 127.4 (CH), 123.91/123.89 (C), 90.32/90.29 (C), 80.49/80.47 (C), 78.9/78.6 (CH), 73.18/73.15 (C), 35.8/35.5 (CH_2), 33.8/33.5 (CH_2), 32.1/31.9 (CH), 29.0/28.9 (CH_2), 26.43/26.42 (CH_3), 23.0 (CH_3), 19.3/19.0 (CH_3), 17.08/17.05 (CH_2); HRESIMS *m/z* 292.2282 $[M+NH_4]^+$, calcd. 292.2271 for $C_{18}H_{30}NO_2$.

(2) (a) Mori, K.; Masuda, S.; Suguro, T. *Tetrahedron* **1981**, *37*, 1329-1340. (b) Mori, K.; Harashima, S. *Liebigs Ann. Chem.* **1993**, 391-401.

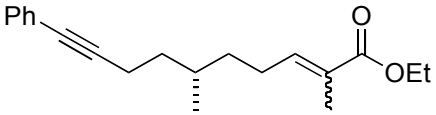
(*R*)-4-Methyl-8-phenyloct-7-ynal (14)



14

$NaIO_4$ (377 mg, 1.76 mmol) was added to a solution of the diol **13** (372 mg, 1.35 mmol) in THF/water (1:1 v/v, 24 mL) and the mixture stirred at r.t. for 13 hours. The reaction was diluted with water and the aqueous phase extracted with Et_2O. The combined organic extracts were washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (10:90 EtOAc:hexanes) gave the aldehyde **14** (247 mg, 85%) as a colorless oil; FTIR (ATR): ν 2956, 2927, 2871, 1708, 1599, 1490, 1453, 1442, 1380, 1280, 1175, 1070, 1023, 913, 756, 692 cm^{-1}; $[\alpha]_D^{20}$ –3.86° (*c* 2.36, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 9.79 (t, *J* = 6.0 Hz, 1H), 7.40-7.37 (m, 2H), 7.29-7.26 (m, 3H), 2.54-2.32 (m, 3H), 1.77-1.61 (m, 4H), 1.54-1.43 (m, 2H), 0.95 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7 (CH), 131.5 (CH), 128.2 (CH), 127.5 (CH), 123.9 (C), 89.9 (C), 80.7 (C), 41.6 (CH_2), 35.4 (CH_2), 31.6 (CH), 28.5 (CH_2), 19.0 (CH_3), 17.1 (CH_2); HREIMS *m/z* 214.1352 $[M]^+$, calcd. 214.1358 for $C_{15}H_{18}O$.

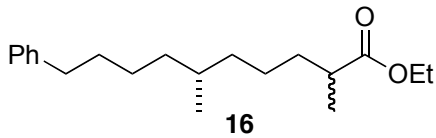
***E*/*Z*-(*S*)-Ethyl 2,6-dimethyl-10-phenyldec-2-en-9-ynoate (15)**



E/*Z*-**15**

n-BuLi (2.25 M in hexanes, 232 μL, 0.522 mmol) was added to a solution of triethyl 2-phosphonopropionate (126 μL, 0.588 mmol) in THF (3.3 mL) at –78 °C and the mixture stirred at –78 °C for 30 minutes. The reaction was then warmed to 0 °C for 10 minutes and re-cooled to –78 °C. The aldehyde **13** (70.0 mg, 0.327 mmol) in THF (1.2 mL) was added and the mixture stirred at –78 °C for 1.5 hours. The reaction was quenched with sat. aq. NH_4Cl, warmed to r.t. and the aqueous phase extracted with Et_2O. The combined organic extracts were washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (5:95 EtOAc:hexanes) gave the alkene **15** (73.3 mg, 75%, 1:1 *E*:*Z*) as a colorless oil; FTIR (ATR): ν 2955, 2926, 2871, 2854, 1709, 1649, 1599, 1490, 1456, 1442, 1376, 1368, 1271, 1248, 1211, 1177, 1146, 1095, 1071, 1028, 912, 756, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.37 (m, 2H), 7.30-7.24 (m, 3H), 6.77 (dt, *J* = 7.6, 1.6 Hz, 0.5H), 5.92 (dt, *J* = 7.6, 1.6 Hz, 0.5H), 4.20 (q, *J* = 7.6 Hz, 1H), 4.17 (q, *J* = 7.6 Hz, 1H), 2.57-2.35 (m, 3H), 2.21 (m, 1H), 1.89 (d, *J* = 1.6 Hz, 1.5H), 1.85 (d, *J* = 1.6 Hz, 1.5H), 1.71-1.62 (m, 2H), 1.57-1.42 (m, 2H), 1.30 (m, 1H), 1.30 (t, *J* = 7.6 Hz, 1.5H), 1.28 (t, *J* = 7.6 Hz, 1.5Hz), 0.95 (d, *J* = 6.4 Hz, 1.5H), 0.94 (d, *J* = 6.4 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.13/168.05 (C), 142.9/142.1 (CH), 131.4 (CH), 128.09/128.08 (CH), 127.6/127.0 (C), 127.42/127.37 (CH), 124.0/123.9 (C), 90.2/90.1 (C), 80.6/80.5 (C), 60.3/60.0 (CH_2), 36.1/35.3 (CH_2), 35.55/35.51 (CH_2), 31.7 (CH), 27.0/26.2 (CH_2), 20.6 (CH_3), 19.0/18.9 (CH_3), 17.0 (CH_2), 14.2/12.3 (CH_3); HRESIMS *m/z* 299.2006 $[M+H]^+$, calcd. 299.2001 for $C_{20}H_{26}O_2$.

(2ξ,6*R*)-Ethyl 2,6-dimethyl-10-phenyldecanoate (16)

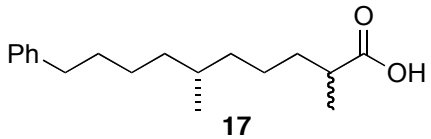


16

A mixture of the enyne **15** (185 mg, 0.620 mmol) and Pd/C (10% wt, 33.0 mg, 0.0310 mmol) in MeOH (4 mL) was stirred under 1 atm of H_2 for five hours. The reaction mixture was evacuated, then filtered through a short pad of Celite and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (4:96 EtOAc:hexanes) gave the saturated ester **16** (179 mg, 95%. 1:1 mixture of C2 epimers) as a colorless oil; FTIR (ATR): ν 3026, 2929, 2857, 1734, 1496, 1463, 1455, 1377, 1257, 1178, 1160, 1096, 1030,

746, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.26 (m, 2H), 7.20-7.16 (m, 3H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.43 (m, 1H), 1.70-1.56 (m, 4H), 1.46-1.24 (m, 10H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.15 (d, *J* = 7.2 Hz, 3H), 1.16-1.10 (m, 2H), 0.85 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9 (C), 142.8 (C), 128.3 (CH), 128.2 (CH), 125.5 (CH), 60.0 (CH_2), 39.54/39.51 (CH), 36.80 (CH_2), 36.78 (CH_2), 36.0 (CH_2), 34.10/34.06 (CH_2), 32.5 (CH), 31.8 (CH_2), 26.7 (CH_2), 24.63/24.60 (CH_2), 19.6 (CH_3), 17.1/17.0 (CH_3), 14.2 (CH_3); HRESIMS *m/z* 305.2478 $[M+H]^+$, calcd. 305.2475 for $C_{20}H_{33}O_2$.

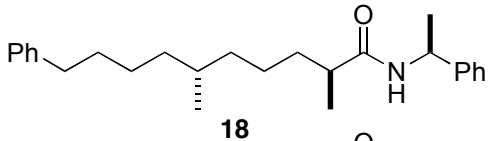
(*R*)-2,6-Dimethyl-10-phenyldecanoic acid (17)



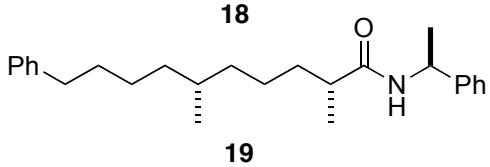
17

LiOH (1.25 M in water, 3.36 mL, 4.20 mmol) was added to a solution of ester **16** (160 mg, 0.526 mmol) in THF/water (7:3 v/v, 5 mL) and the mixture stirred at r.t. for 20 hours then at 100 °C for a further 20 hours. The organic solvent was removed under reduced pressure and the aqueous residue acidified to pH 2 with 2.4M HCl then extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product, which was purified by flash chromatography (0.1:15:94.9 AcOH:EtOAc:hexanes) to give the acid **17** (135 mg, 93%, 1:1 mixture of diastereomers) as a colorless oil; FTIR (ATR): ν 3026, 2926, 2855, 1703, 1604, 1496, 1463, 1455, 1416, 1378, 1290, 1238, 1030, 941, 910, 744, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (m, 2H), 7.22-7.19 (m, 3H), 2.64 (t, *J* = 8.0 Hz, 2H), 2.49 (m, 1H), 1.78-1.59 (m, 4H), 1.50-1.29 (m, 10H), 1.22 (d, *J* = 7.2 Hz, 3H), 1.18-1.13 (m, 2H), 0.80 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.6 (C), 142.8 (C), 128.4 (CH), 128.2 (CH), 125.5 (CH), 39.41/39.38 (CH), 36.81 (CH_2), 36.78 (CH_2), 36.0 (CH_2), 33.8/33.7 (CH_2), 32.5 (CH), 31.8 (CH_2), 27.0 (CH_2), 24.57/24.55 (CH_2), 19.6 (CH_3), 16.8/16.7 (CH_3); HRESIMS *m/z* 275.2011 $[M-H]^-$, calcd. 275.2011 for $C_{18}H_{27}O_2$.

(2*S*,6*R*)-2,6-Dimethyl-10-phenyl-*N*-((*S*)-1-phenylethyl)decanamide (18) and (2*R*,6*R*)-2,6-Dimethyl-10-phenyl-*N*-((*S*)-1-phenylethyl)decanamide (19)



18

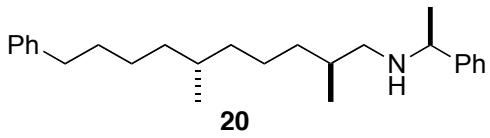


19

(*S*)-(–)-1-Phenylethylamine (74.8 μL, 0.588 mmol), HATU (224 mg, 0.588 mmol) and *i*-Pr_2NEt (137 μL, 0.784 mmol) were added to a solution of acid **17** (135 mg, 0.490 mmol) in DMF (10 mL) and the mixture stirred at r.t. for 19 hours. Evaporation of the solvent under reduced pressure gave the crude product, which was purified by flash chromatography (24:76 → 40:60 Et_2O:hexanes, dry-load) to give amides **18** (87.6 mg, 47%) and **19** (87.1 mg, 47%) as white solids; Data for **18**: FTIR (ATR): ν 3280, 3084, 3061, 3027, 2962, 2927, 2854, 1637, 1539, 1495, 1452, 1375, 1242, 1127, 1110, 1073, 1030, 1019, 943, 908, 745, 696 cm^{-1}; $[\alpha]_D^{21}$ –50.6 (*c* 3.33, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 7.36-7.25 (m, 7H), 7.19-7.15 (m, 3H), 5.62 (br d, *J* = 7.8 Hz, 1H), 5.15 (dq, *J* = 7.2, 7.2 Hz, 1H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.14 (m, 1H), 1.68-1.55 (m, 3H), 1.49 (d, *J* = 6.9 Hz, 3H), 1.40-1.21 (m, 8H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.15-1.05 (m, 2H), 0.83 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.5 (C), 143.3 (C), 142.8 (C), 128.5 (CH), 128.3 (CH), 128.1 (CH), 127.2 (CH), 126.1 (CH), 125.5 (CH), 48.3 (CH), 41.5 (CH), 36.9 (CH_2), 36.8 (CH_2), 35.9 (CH_2), 34.6 (CH_2), 32.5 (CH), 31.7 (CH_2), 26.7 (CH_2), 24.8 (CH_2), 21.6 (CH_3), 19.6 (CH_3), 17.9 (CH_3); HRESIMS *m/z* 380.2947 $[M+H]^+$, calcd. 380.2953 for $C_{26}H_{38}NO$. Data for **19**: FTIR (ATR): ν 3280, 3084, 3062, 3027, 2962, 2926, 2854, 1638, 1540, 1495, 1452, 1376, 1241, 1129, 1073, 1030, 1019, 941, 908, 745, 697 cm^{-1}; $[\alpha]_D^{21}$ –35.0 (*c* 3.33, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 7.34-7.22 (m, 7H), 7.19-7.16

(m, 3H), 5.63 (br d, J = 7.7 Hz, 1H), 5.15 (dq, J = 6.9, 6.9 Hz, 1H), 2.59 (t, J = 7.7 Hz, 2H), 2.14 (m, 1H), 1.62-1.53 (m, 3H), 1.49 (d, J = 6.9 Hz, 3H), 1.37-1.20 (m, 8H), 1.14 (d, J = 6.9 Hz, 3H), 1.12-1.01 (m, 2H), 0.78 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6 (C), 143.4 (C), 142.8 (C), 128.5 (CH), 128.3 (CH), 128.2 (CH), 127.2 (CH), 126.1 (CH), 125.5 (CH), 48.3 (CH), 41.6 (CH), 36.9 (CH_2), 36.8 (CH_2), 35.9 (CH_2), 34.7 (CH_2), 32.6 (CH), 31.8 (CH_2), 26.7 (CH_2), 24.9 (CH_2), 21.6 (CH_3), 19.5 (CH_3), 17.8 (CH_3); HRESIMS *m/z* 380.2949 $[M+H]^+$, calcd. 380.2953 for $C_{26}H_{38}NO$.

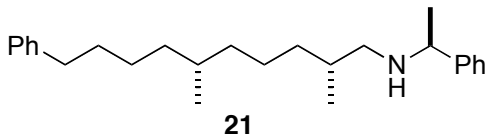
(2*S*,6*R*)-2,6-Dimethyl-10-phenyl-*N*-((*S*)-1-phenylethyl)decan-1-amine (20)



20

BH_3•THF (1.0 M in THF, 474 μL, 0.474 mmol) was added dropwise to the amide **18** (36.0 mg, 0.0948 mmol) in THF (575 μL) at 0 °C and the mixture heated at reflux for 3.5 hours. The reaction was cooled to 0 °C, quenched with 20% aq. NaOH (1 mL) and heated at 50 °C for 45 minutes. The mixture was re-cooled to r.t., extracted with CH_2Cl_2 and the combined organic extracts dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (1:99 → 8:92 MeOH:CH_2Cl_2) gave the amine **20** (31.2 mg, 90%) as a colorless oil; FTIR (ATR): ν 3084, 3061, 3025, 2924, 2854, 1604, 1552, 1494, 1452, 1376, 1369, 1352, 1304, 1248, 1208, 1126, 1073, 1029, 991, 909, 760, 745, 698 cm^{-1}; $[\alpha]_D^{21}$ –29.4 (*c* 3.11, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.24 (m, 7H), 7.19-7.17 (m, 3H), 3.74 (q, J = 6.4 Hz, 1H), 2.61 (t, J = 7.6 Hz, 2H), 2.45 (dd, J = 11.6, 5.2 Hz, 2H), 2.17 (dd, J = 11.6, 7.6 Hz, 2H), 1.83 (br s, 1H), 1.65-1.54 (m, 2H), 1.36 (d, J = 6.8 Hz, 3H), 1.42-1.02 (m, 12H), 0.88 (d, J = 6.4 Hz, 3H), 0.82 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.9 (C), 142.9 (C), 128.34 (CH), 128.33 (CH), 128.2 (CH), 126.7 (CH), 126.6 (CH), 125.5 (CH), 58.4 (CH), 54.2 (CH_2), 37.3 (CH_2), 36.8 (CH_2), 36.0 (CH_2), 35.4 (CH_2), 33.3 (CH), 32.7 (CH), 31.8 (CH_2), 26.7 (CH_2), 24.5 (CH_3), 24.4 (CH_2), 19.7 (CH_3), 18.2 (CH_3); HRESIMS *m/z* 366.3153 $[M+H]^+$, calcd. 366.3161 for $C_{26}H_{40}N$.

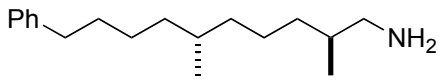
(2*R*,6*R*)-2,6-Dimethyl-10-phenyl-*N*-((*S*)-1-phenylethyl)decan-1-amine (21)



21

BH_3•THF (1.0 M in THF, 327 μL, 0.327 mmol) was added dropwise to the amide **19** (24.8 mg, 0.0654 mmol) in THF (350 μL) at 0 °C and the mixture heated at reflux for four hours. The reaction was cooled to 0 °C, quenched with 20% aq. NaOH (1 mL) and heated at 50 °C for 45 minutes. The mixture was re-cooled to r.t., extracted with CH_2Cl_2 and the combined organic extracts dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (1:99 → 5:95 MeOH:CH_2Cl_2) gave the amine **21** (17.1 mg, 72%) as a colorless oil; FTIR (ATR): ν 3084, 3061, 3025, 2924, 2854, 1604, 1552, 1494, 1452, 1376, 1351, 1303, 1246, 1211, 1126, 1074, 1029, 909, 760, 744, 697 cm^{-1}; $[\alpha]_D^{20}$ –23.6 (*c* 3.19, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35-7.22 (m, 7H), 7.19-7.16 (m, 3H), 3.74 (q, J = 6.6 Hz, 1H), 2.61 (t, J = 7.7 Hz, 2H), 2.31 (d, J = 6.6 Hz, 2H), 1.71 (br s, 1H), 1.64-1.53 (m, 2H), 1.36 (d, J = 6.6 Hz, 3H), 1.40-1.19 (m, 10H), 1.15-0.99 (m, 2H), 0.87 (d, J = 6.9 Hz, 3H), 0.83 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.9 (C), 142.9 (C), 128.4 (CH), 128.3 (CH), 128.2 (CH), 126.8 (CH), 126.6 (CH), 125.5 (CH), 58.4 (CH), 54.3 (CH_2), 37.2 (CH_2), 36.9 (CH_2), 36.0 (CH_2), 35.0 (CH_2), 33.3 (CH), 32.6 (CH), 31.9 (CH_2), 26.8 (CH_2), 24.4 (CH_3), 24.2 (CH_2), 19.6 (CH_3), 18.1 (CH_3); HRESIMS *m/z* 366.3157 $[M+H]^+$, calcd. 366.3161 for $C_{26}H_{40}N$.

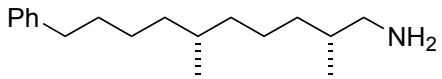
(2*S*,6*R*)-2,6-Dimethyl-10-phenyldecan-1-amine (22)



22

A mixture of secondary amine **20** (27.3 mg, 74.7 μmol) and Pd/C (10% wt, 15.9 mg, 14.9 μmol) in CF_3CH_2OH (3.8 mL) was stirred under 1 atm of H_2 for 17 hours. The reaction mixture was evacuated, then filtered through a short pad of Celite and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (4:6 MeOH:CH_2Cl_2) gave the primary amine **22** (18.0 mg, 92%) as a yellow oil; FTIR (ATR): ν 2925, 2855, 1571, 1496, 1463, 1455, 1377, 1308, 745, 698 cm^{-1}; $[\alpha]_D^{21}$ +5.33 (*c* 3.08, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_3OD): δ 7.26-7.22 (m, 2H), 7.16-7.11 (m, 3H), 2.88 (dd, *J* = 12.4, 6.0 Hz, 1H), 2.71 (dd, *J* = 12.4, 8.0 Hz, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.78 (m, 1H), 1.62-1.12 (m, 13H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD): δ 143.9 (C), 129.4 (CH), 129.2 (CH), 126.6 (CH), 48.0 (CH), 38.4 (CH_2), 37.9 (CH_2), 36.9 (CH_2), 36.3 (CH), 35.7 (CH_2), 33.9 (CH), 33.0 (CH_2), 27.7 (CH_2), 25.4 (CH_2), 20.1 (CH_3), 17.8 (CH_3); HRESIMS *m/z* 262.2528 $[M+H]^+$, calcd. 262.2535 for $C_{18}H_{32}N$.

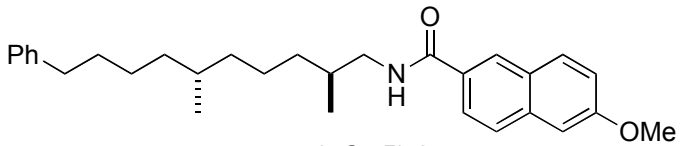
(2*R*,6*R*)-2,6-Dimethyl-10-phenyldecan-1-amine (23)



23

A mixture of secondary amine **21** (10.5 mg, 28.7 μmol) and Pd/C (10% wt, 6.1 mg, 5.7 μmol) in CF_3CH_2OH (1.5 mL) was stirred under 1 atm of H_2 for 20 hours. The reaction mixture was evacuated, then filtered through a short pad of Celite and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (4:6 MeOH:CH_2Cl_2) gave the primary amine **23** (5.4 mg, 72%) as a yellow oil; FTIR (ATR): ν 2925, 2854, 1573, 1496, 1463, 1455, 1377, 1327, 1309, 1277, 748, 698 cm^{-1}; $[\alpha]_D^{21}$ –4.60 (*c* 2.96, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_3OD): δ 7.25-7.22 (m, 2H), 7.16-7.12 (m, 3H), 2.87 (dd, *J* = 12.8, 5.9 Hz, 1H), 2.70 (dd, *J* = 12.8, 8.0 Hz, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.77 (m, 1H), 1.62-1.56 (m, 2H), 1.43-1.26 (m, 9H), 1.21-1.11 (m, 2H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD): δ 144.0 (C), 129.4 (CH), 129.2 (CH), 126.6 (CH), 48.7 (CH), 38.4 (CH_2), 38.1 (CH_2), 36.9 (CH_2), 36.5 (CH), 35.7 (CH_2), 33.9 (CH), 33.1 (CH_2), 27.7 (CH_2), 25.4 (CH_2), 20.1 (CH_3), 17.7 (CH_3); HRESIMS *m/z* 262.2535 $[M+H]^+$, calcd. 262.2535 for $C_{18}H_{32}N$.

***N*-((2*S*,6*R*)-2,6-Dimethyl-10-phenyldecyl)-6-methoxy-2-naphthamide (8)**

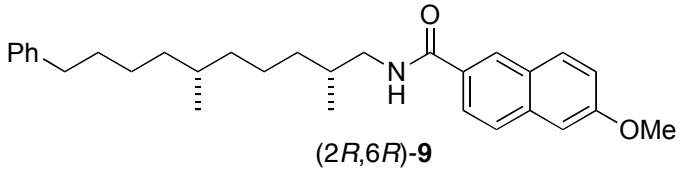


(2*S*,6*R*)-**8**

6-Methoxy-2-naphthoyl chloride (8.6 mg, 39 μmol), Et_3N (9.1 μL, 65 μmol) and DMAP (1 crystal) were added to the amine **22** (3.4 mg, 13 μmol) in CH_2Cl_2 (350 μL) and the mixture stirred at r.t. for 16 hours. 3-(Dimethylamino)propylamine (4.9 μL, 39 μmol) was added and the resulting mixture stirred vigorously at r.t. for 30 minutes. The solvent was evaporated under reduced pressure to give the crude product, which was purified by flash chromatography (15:85 EtOAc/hexanes) to give the naphthamide (2*S*,6*R*)-**8** (3.7 mg, 64%) as a white solid; FTIR (ATR): ν 3317, 2923, 2851, 1629, 1604, 1541, 1503, 1481, 1462, 1455, 1390, 1299, 1261, 1214, 1165, 1093, 1031, 904, 855, 807, 746, 698 cm^{-1}; $[\alpha]_D^{21}$ +1.82 (*c* 3.14, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.83-7.76 (m, 3H), 7.29-7.25 (m, 5H), 7.21-7.16 (m, 2H), 6.23 (m, 1H), 3.94 (s, 3H), 3.46 (m, 1H), 3.31 (m, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.78 (m, 1H), 1.43-1.08 (m, 15H), 1.00 (d, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.7 (C), 158.9 (C), 142.9 (C), 136.1 (C), 130.4 (CH), 129.9 (C), 128.4 (CH), 128.2

(CH), 128.0 (C), 127.1 (CH), 127.0 (CH), 125.5 (CH), 124.1 (CH), 119.7 (CH), 105.6 (CH), 55.3 (CH_3), 46.1 (CH_2), 37.3 (CH_2), 36.8 (CH_2), 36.0 (CH_2), 34.9 (CH_2), 33.5 (CH), 32.7 (CH), 31.8 (CH_2), 26.7 (CH_2), 24.4 (CH_2), 19.7 (CH_3), 17.8 (CH_3); HRESIMS *m/z* 446.3046 $[M+H]^+$, calcd. 446.3059 for $C_{30}H_{40}NO_2$.

***N*-((2*R*,6*R*)-2,6-Dimethyl-10-phenyldecyl)-6-methoxy-2-naphthamide (9)**



(2*R*,6*R*)-**9**

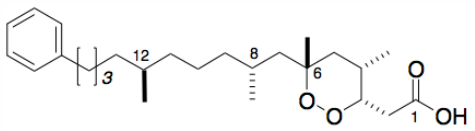
6-Methoxy-2-naphthoyl chloride (22.3 mg, 101 μmol), Et_3N (21.1 μL, 151 μmol) and DMAP (1 crystal) were added to the amine **23** (6.6 mg, 25 μmol) in CH_2Cl_2 (0.7 mL) and the mixture stirred at r.t. for 16 hours. 3-(Dimethylamino)propylamine (12.7 μL, 101 μmol) was added and the resulting mixture stirred vigorously at r.t. for 30 minutes. The solvent was evaporated under reduced pressure to give the crude product, which was purified by flash chromatography (1:9 EtOAc/hexanes) to give the naphthamide (2*R*,6*R*)-**9** (6.2 mg, 55%) as a white solid; FTIR (ATR): ν 3326, 2923, 2850, 1631, 1604, 1542, 1503, 1481, 1462, 1455, 1391, 1298, 1261, 1215, 1166, 1092, 1031, 855, 805, 746, 698 cm^{-1}; $[\alpha]_D^{21}$ –3.41 (*c* 3.02, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.83-7.76 (m, 3H), 7.29-7.25 (m, 5H), 7.21-7.16 (m, 2H), 6.23 (m, 1H), 3.94 (s, 3H), 3.45 (m, 1H), 3.32 (m, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.79 (m, 1H), 1.43-1.10 (m, 15H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.6 (C), 159.0 (C), 142.9 (C), 136.2 (C), 130.4 (CH), 129.9 (C), 128.4 (CH), 128.2 (CH), 128.0 (C), 127.1 (CH), 127.0 (CH), 125.5 (CH), 124.1 (CH), 119.7 (CH), 105.6 (CH), 55.4 (CH_3), 46.1 (CH_2), 37.2 (CH_2), 36.9 (CH_2), 36.0 (CH_2), 34.8 (CH_2), 33.5 (CH), 32.7 (CH), 31.8 (CH_2), 26.8 (CH_2), 24.4 (CH_2), 19.6 (CH_3), 17.8 (CH_3); HRESIMS *m/z* 446.3051 $[M+H]^+$, calcd. 446.3059 for $C_{30}H_{40}NO_2$.

07.26.171.B.2.1.2.16

Figure S3: 1H NMR (400 MHz, CDCl3)

exp2 std1h

SAMPLE		DEC. & VT	
date	Oct 2 2007	dfrq	400.056
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	400.056	dm	nnn
tn	H1	dmm	c
at	1.993	dmf	200
np	23936	PROCESSING	
sw	6006.0	wtfile	
fb	not used	proc	ft
bs	16	fn	not used
tpwr	57		
pw	7.0	werr	
d1	1.000	wexp	
tof	0	wbs	
nt	160	wnt	
ct	64		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-1031.8		
wp	6005.6		
vs	150		
sc	0		
wc	250		
hzmm	3.34		
is	500.00		
rfl	1032.2		
rfp	0		
th	20		
ins	100.000		
nm cdc ph			



Plakinic acid K (**3**)

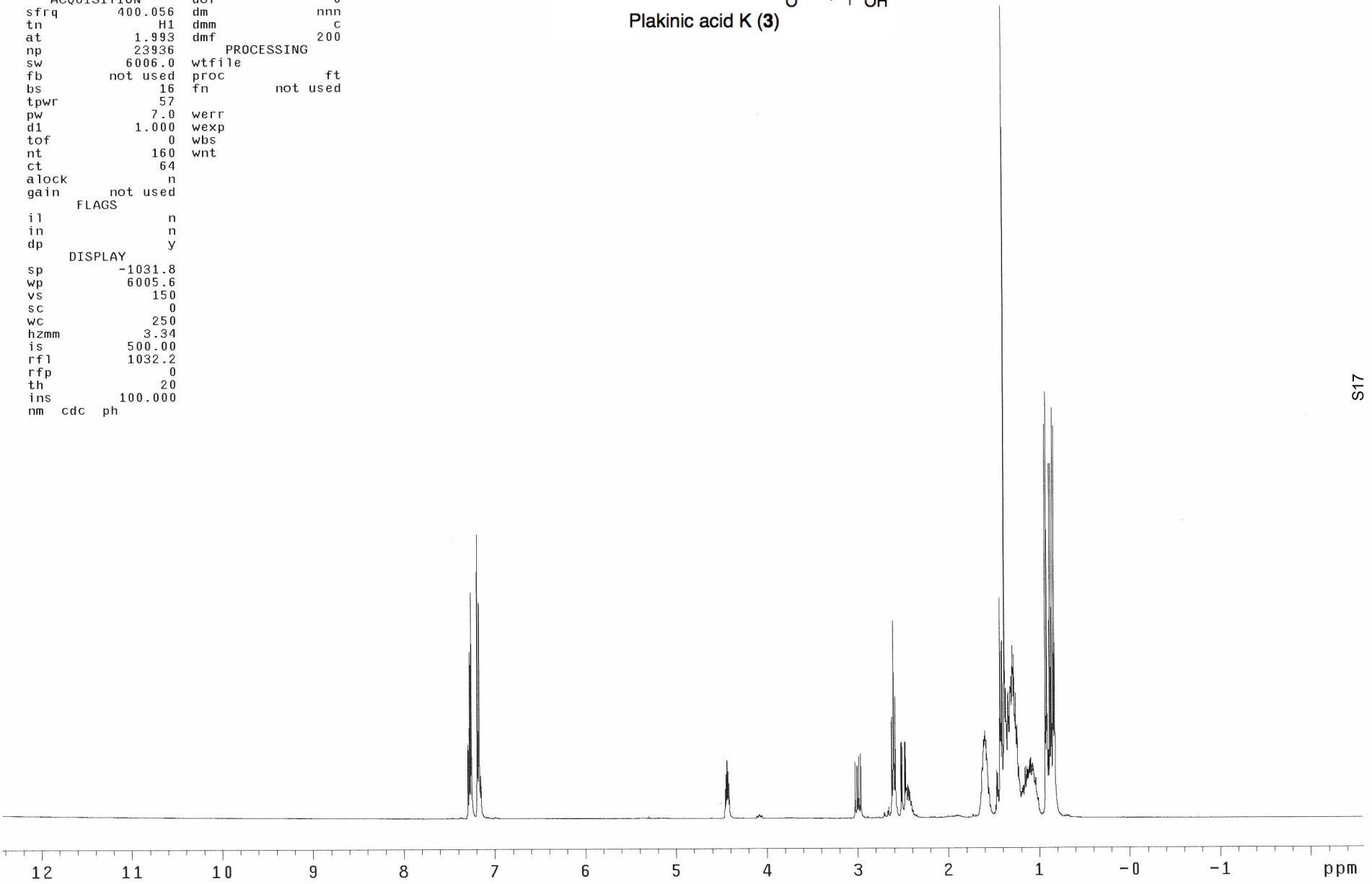
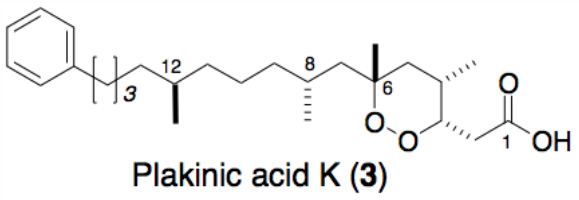


Figure S4: 13C NMR (100 MHz, CDCl3)



Plakinic acid K (**3**)

```
07.26.171.B.2.1.B.16.13C

exp2  std13c

      SAMPLE                DEC. & VT
date    Oct  5 2007   dfrq        399.911
solvent       CDCl3   dn               H1
file            exp   dpwr             38
   ACQUISITION        dof               0
sfrq        100.567   dm              yyy
tn              C13   dmm               w
at            1.500   dmf            9700
np            75000       PROCESSING
sw          25000.0   lb             3.00
fb            13800   wtfile
bs               16   proc             ft
ss                4   fn         not used
tpwr             58
pw              6.5   werr
d1            2.000   wexp
tof               0   wbs
nt            10000   wnt
ct              272
alock             n
gain      not used
      FLAGS
il                n
in                n
dp                y
     DISPLAY
sp         -2987.8
wp         24999.6
vs             112
sc               0
wc             250
hzmm          1.63
is          500.00
rfl        10747.1
rfp         7759.0
th              20
ins         100.000
nm    ph
```

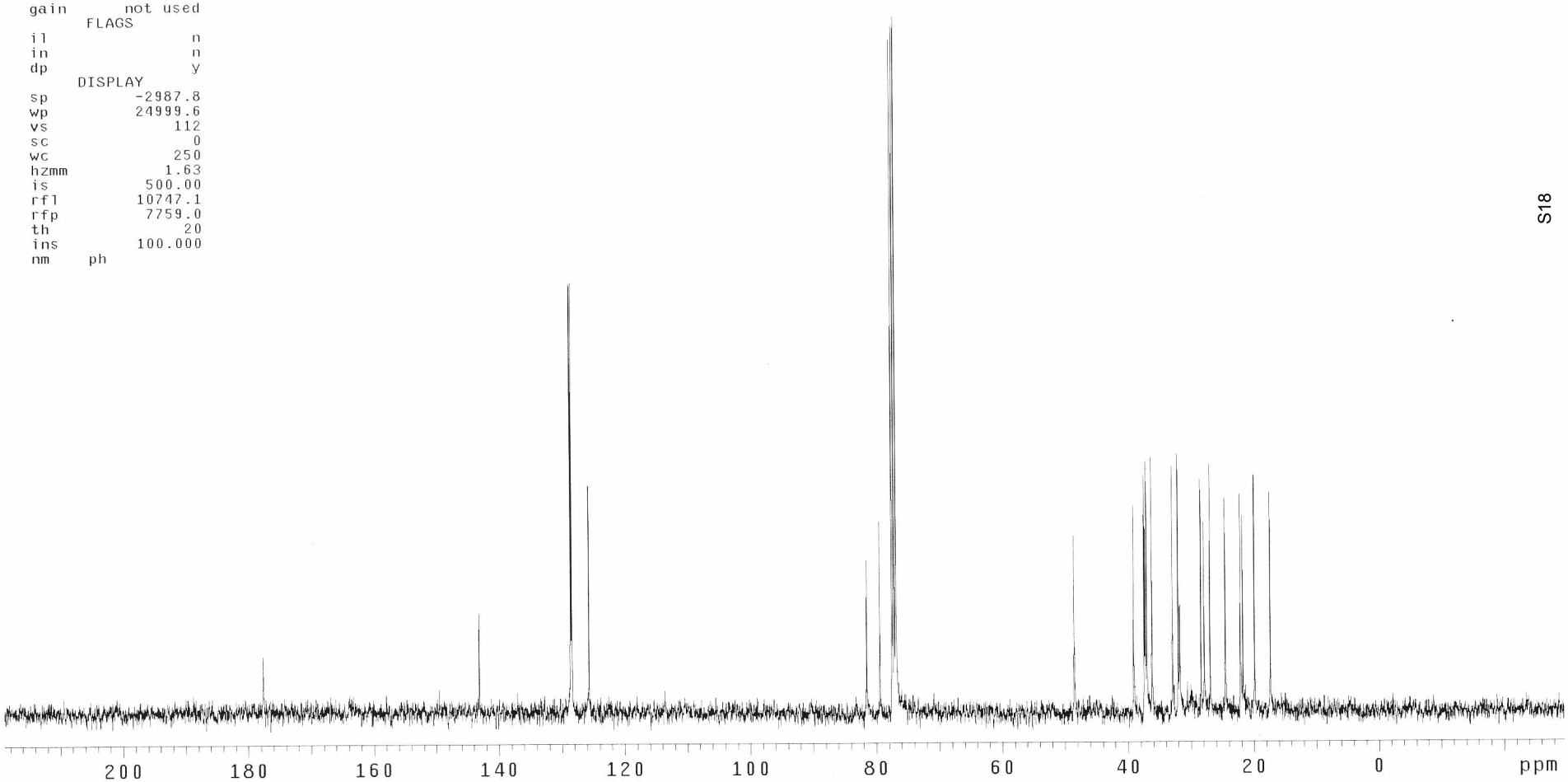
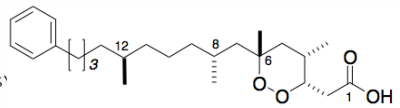


Figure S5: COSY (CDCl3, 400MHz)

07.26.171.B.2.1.B.16.gCOSY

Pulse Sequence: gCOSY
Solvent: CDCl3
Ambient temperature
File: 07.26.171.B.2.1.B.16.gCOSY
Mercury-400BB "hg402"

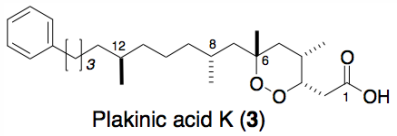
Relax. delay 1.000 sec
Acq. time 0.168 sec
Width 3052.5 Hz
2D Width 3052.5 Hz
4 repetitions
128 increments
OBSERVE H1, 399.9089997 MHz
DATA PROCESSING
Sq. sine bell 0.084 sec
F1 DATA PROCESSING
Sq. sine bell 0.042 sec
FT size 1024 x 1024
Total time 11 min, 28 sec



Plakinic acid K (**3**)

COSY (CDCl3, 400MHz)

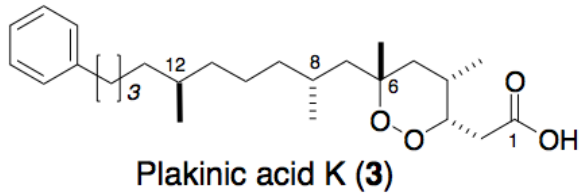
Figure S6: HSQC (CDCl3, 600 MHz)



Plakinic acid K (**3**)

BRUKER

```
Current Data Parameters
NAME       0726171B21216
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20080502
Time              18.10
INSTRUM           spect
PROBHD   1.7 mm PATXI 1
PULPROG         hsqcetgp
TD                1024
SOLVENT           CDCl3
NS                  32
DS                  32
SWH            5040.323 Hz
FIDRES         4.922190 Hz
AQ             0.1016308 sec
RG                2050
DW               99.200 usec
DE                6.50 usec
TE               295.9 K
CNST2        145.0000000
d0            0.00000300 sec
D1            1.50000000 sec
d11           0.03000000 sec
d13           0.00000400 sec
D16           0.00020000 sec
d4            0.00172414 sec
DELTA         0.00121600 sec
DELTA1        0.00071614 sec
IN0           0.00001655 sec
ST1CNT             128
ZGOPTNS

======== CHANNEL f1 ========
NUC1                1H
P1                5.00 usec
p2               10.00 usec
P28            1000.00 usec
PL1               3.00 dB
SFO1         599.8224317 MHz

======== CHANNEL f2 ========
CPDPRG2           garp
NUC2               13C
P3                6.50 usec
p4               13.00 usec
PCPD2            70.00 usec
PL12             21.64 dB
PL2               1.00 dB
SFO2         150.8391874 MHz

====== GRADIENT CHANNEL =====
GPNAM1         SINE.100
GPNAM2         SINE.100
GPZ1              80.00 %
GPZ2              20.10 %
P16             1000.00 usec

F1 - Acquisition parameters
ND0                  2
TD                 256
SFO1         150.8392 MHz
FIDRES       118.013596 Hz
SW             200.289 ppm
FnMODE    Echo-Antiecho

F2 - Processing parameters
SI                1024
SF         599.8200196 MHz
WDW               QSINE
SSB                  2
LB                0.00 Hz
GB                   0
PC                1.40

F1 - Processing parameters
SI                1024
MC2       echo-antiecho
SF         150.8248590 MHz
WDW               QSINE
SSB                  2
LB                0.00 Hz
GB                   0
```



Plakinic acid K (**3**)

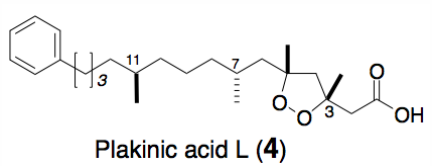
Figure S7: HMBC (600 MHz, CDCl3)

Figure S8: 1H NMR (400 MHz, CDCl3)

07.26.171.B.2.1.2.14

exp2 std1h

SAMPLE		DEC. & VT	
date	Oct 5 2007	dfrq	400.056
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	400.056	dm	nnn
tn	H1	dmm	c
at	1.993	dmf	200
np	23936	PROCESSING	
sw	6006.0	lb	0.15
fb	not used	wtfile	
bs	16	proc	ft
ss	4	fn	not used
tpwr	57		
pw	7.0	werr	
d1	1.000	wexp	
tof	0	wbs	
nt	320	wnt	
ct	96		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-1031.8		
wp	6005.6		
vs	77		
sc	0		
wc	250		
hzmm	2.38		
is	500.00		
rfl	1032.2		
rfp	0		
th	20		
ins	100.000		
nm cdc ph			



Plakinic acid L (**4**)

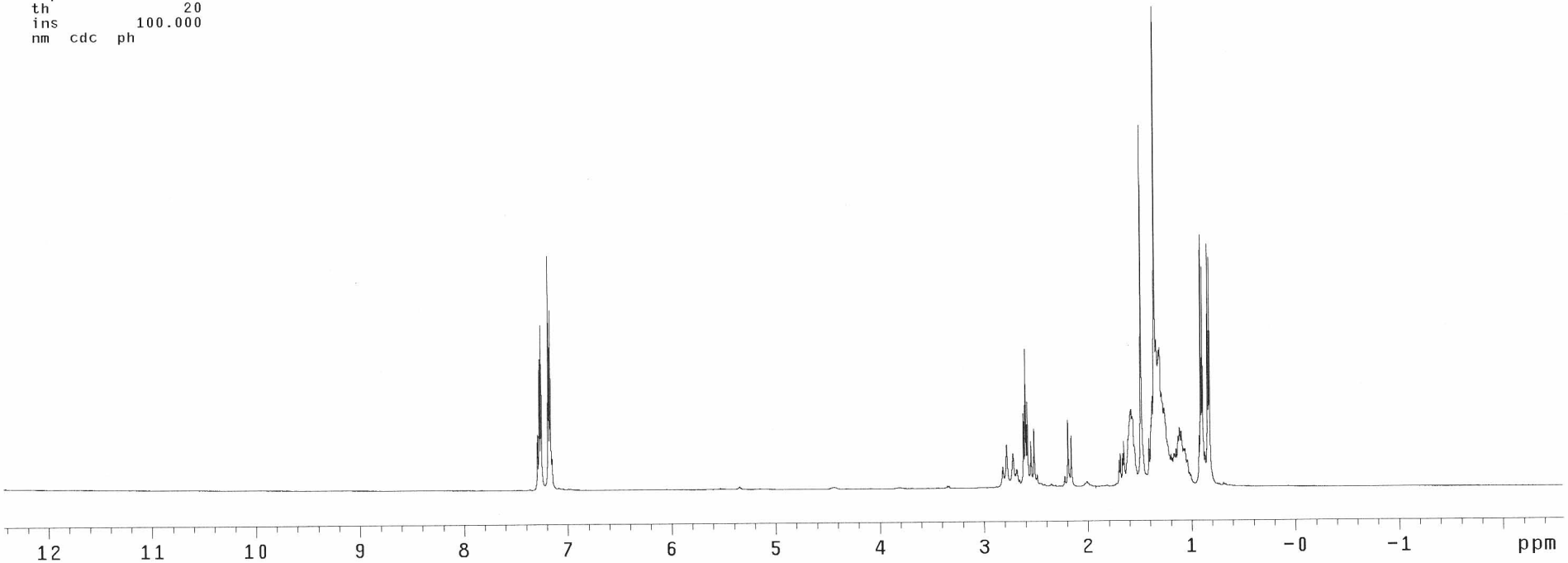
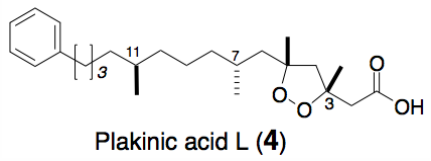


Figure S9: 13C NMR (100 MHz, CDCl3)



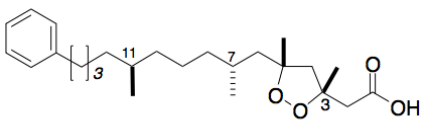
Plakinic acid L (**4**)

```
07.26.171.B.2.1.2.14.13C

exp1  std13c

      SAMPLE              DEC. & VT
date    Oct  7 2007  dfrq        399.911
solvent      CDCl3   dn               H1
file /export/home/~  dpwr             38
molinski/ddalisay/~  dof               0
07.26.171.B.2.1.2.~  dm              yyy
        14.13C.fid   dmm               w
   ACQUISITION       dmf            9700
sfrq        100.567       PROCESSING
tn              C13  lb            5.00
at            2.000  wtfile
np           100000  proc             ft
sw          25000.0  fn         not used
fb            13800
bs               16  werr
ss                4  wexp
tpwr             58  wbs
pw              6.5  wnt
d1            3.000
tof               0
nt            10000
ct            10000
alock             n
gain      not used
      FLAGS
il                n
in                n
dp                y
     DISPLAY
sp         -2977.6
wp         24999.6
vs             749
sc               0
wc             250
hzmm         16.95
is          500.00
rfl         2977.9
rfp              0
th              20
ins         100.000
nm  no  ph
```

07.26.171.B.2.1.2.14.gCOSY

exp1 gCOSY

SAMPLE		FLAGS	
date	Oct 7 2007	hs	nn
solvent	CDCl3	sspul	n
sample	undefined	hsglvl	994
ACQUISITION		SPECIAL	
sw	3448.3	temp	not used
at	0.148	gain	20
np	1024	spin	0
fb	not used	F2 PROCESSING	
ss	16	sb	-0.074
d1	1.000	sbs	not used
nt	6	fn	1024
2D ACQUISITION		F1 PROCESSING	
sw1	3448.3	sb1	-0.037
ni	128	sbs1	not used
TRANSMITTER		proc1	lp
tn	H1	fn1	1024
sfrq	399.911	DISPLAY	
tof	-444.0	sp	-135.7
tpwr	55	wp	3441.5
pw	13.900	sp1	-131.6
GRADIENTS		wp1	3441.5
gzlvl1	994	rfl	142.4
gt1	0.001000	rfp	0
gstab	0.000500	rfl1	138.3
DECOUPLER		rfp1	0
dn	H1	PLOT	
dm	nnn	wc	155.0
		sc	10.0
		wc2	155.0
		sc2	0
		vs	65
		th	7
		ai cdc av	



Plakinic acid L (**4**)

Figure S10: COSY (400 MHz, CDCl3)

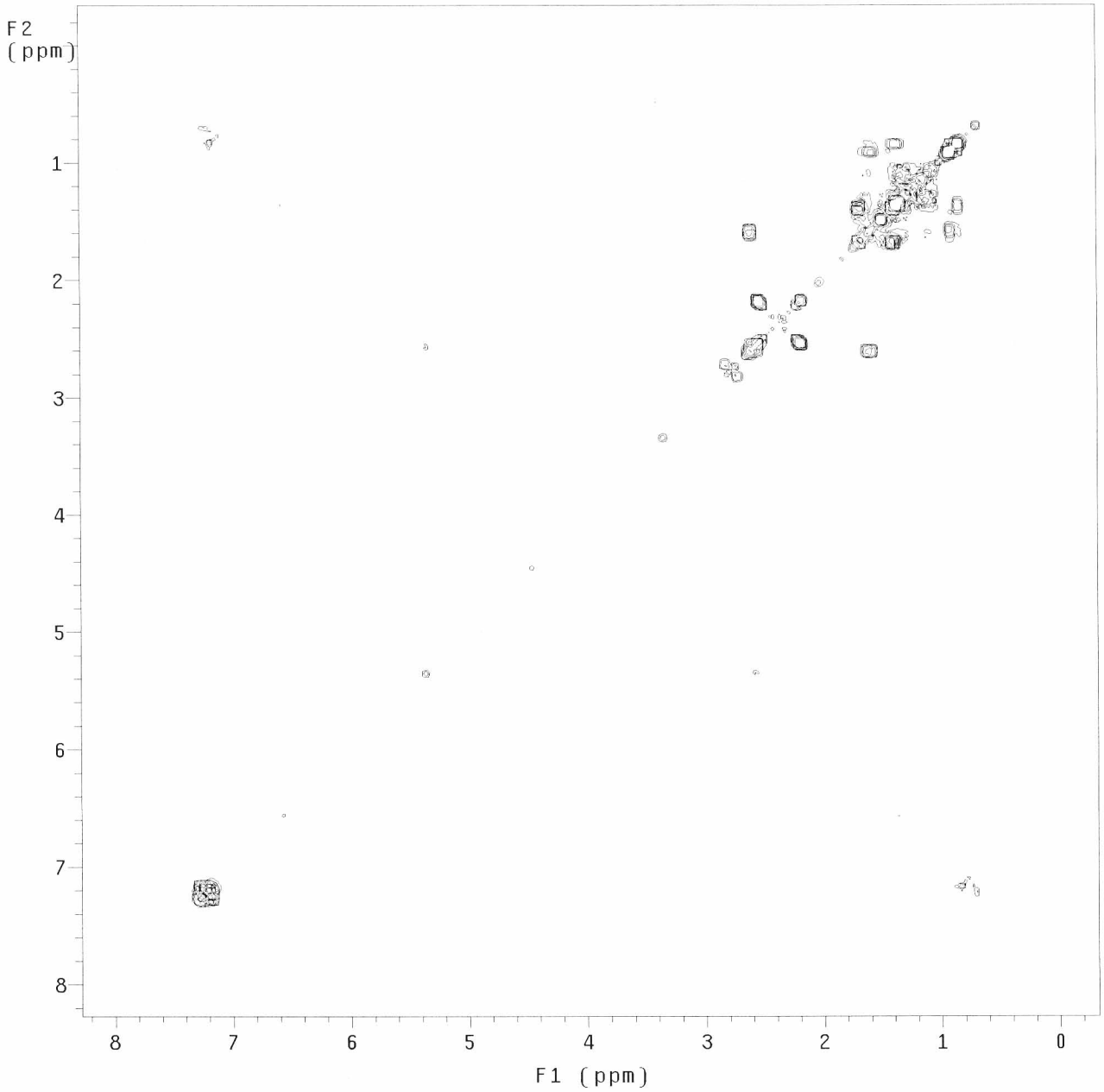
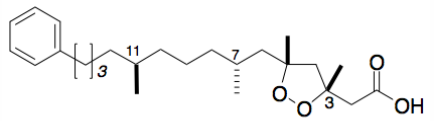
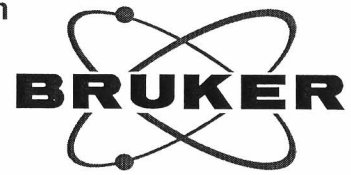


Figure S11: HSQC (CDCl3, 600 MHz)

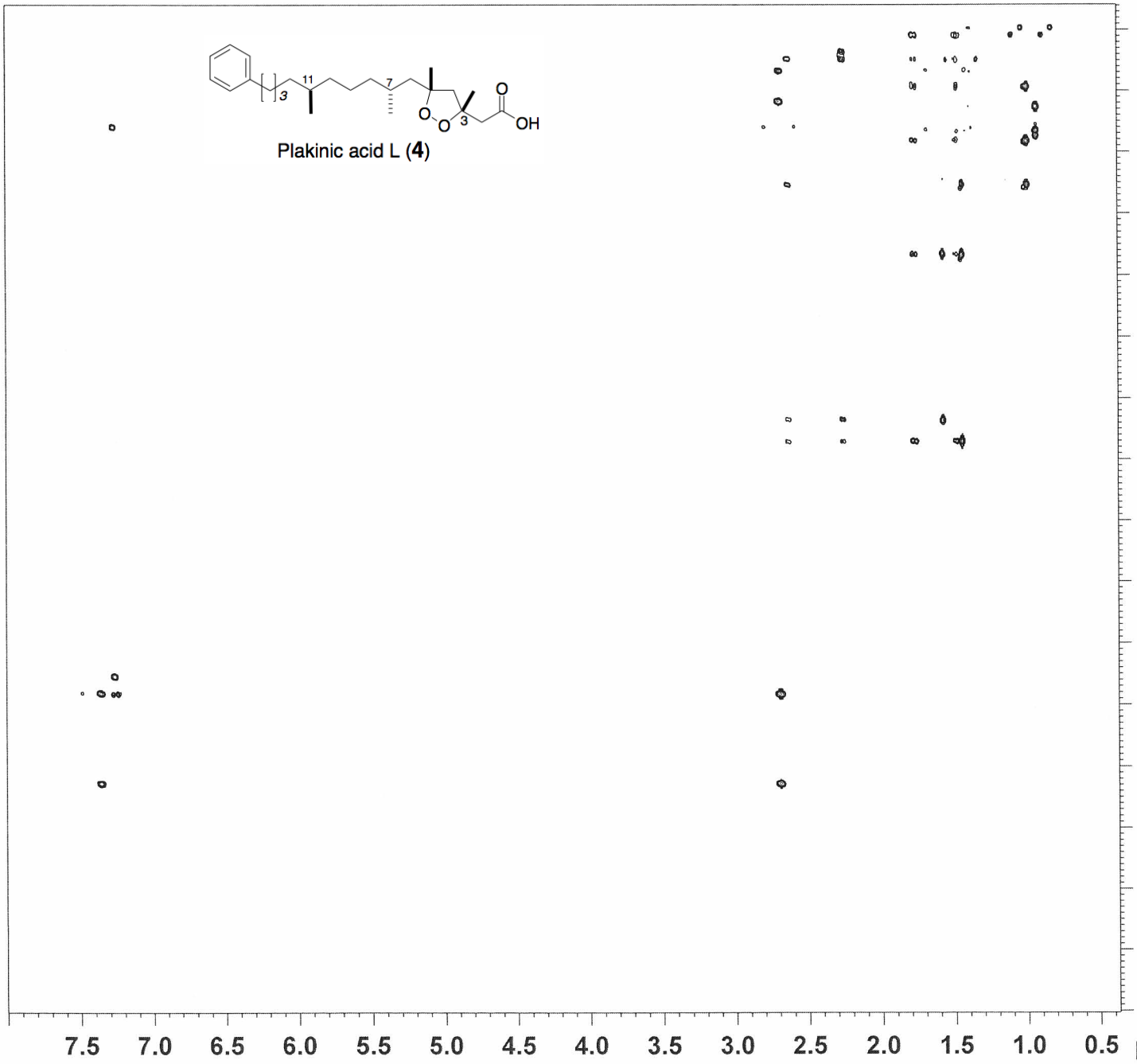


Plakinic acid L (**4**)




```
Current Data Parameters
NAME        0726171B21214
EXPNO                   3
PROCNO                  1

F2 - Acquisition Parameters
Date_            20080508
Time                18.52
INSTRUM             spect
PROBHD   1.7 mm PATXI 1
PULPROG         hsqcetgp
TD                  1024
SOLVENT             CDCl3
NS                    32
DS                    32
SWH             5040.323 Hz
FIDRES          4.922190 Hz
AQ            0.1016308 sec
RG                  2050
DW                99.200 usec
DE                 6.50 usec
TE                296.0 K
CNST2         145.0000000
d0             0.00000300 sec
D1             1.50000000 sec
d11            0.03000000 sec
d13            0.00000400 sec
D16            0.00020000 sec
d4             0.00172414 sec
DELTA          0.00121600 sec
DELTA1         0.00071614 sec
IN0            0.00001655 sec
ST1CNT                128
ZGOPTNS

======== CHANNEL f1 ========
NUC1                  1H
P1                 5.00 usec
p2                10.00 usec
P28             1000.00 usec
PL1                3.00 dB
SFO1         599.8224317 MHz

======== CHANNEL f2 ========
CPDPRG2             garp
NUC2                13C
P3                 6.50 usec
p4                13.00 usec
PCPD2             70.00 usec
PL12              21.64 dB
PL2                1.00 dB
SFO2         150.8391874 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPZ1               80.00 %
GPZ2               20.10 %
P16              1000.00 usec

F1 - Acquisition parameters
ND0                   2
TD                  256
SFO1          150.8392 MHz
FIDRES        118.013596 Hz
SW              200.289 ppm
FnMODE    Echo-Antiecho

F2 - Processing parameters
SI                  1024
SF          599.8200000 MHz
WDW                 QSINE
SSB                   2
LB                 0.00 Hz
GB                    0
PC                 1.40

F1 - Processing parameters
SI                  1024
MC2        echo-antiecho
SF          150.8248590 MHz
WDW                 QSINE
SSB                   2
LB                 0.00 Hz
GB                    0
```

Figure S12: HMBC (CDCl3, 600 MHz)



BRUKER

```
Current Data Parameters
NAME          0726171B21214
EXPNO                     4
PROCNO                    1

F2 - Acquisition Parameters
Date_              20080508
Time                  22.35
INSTRUM               spect
PROBHD   1.7 mm PATXI 1
PULPROG     hmbcgplpndqf
TD                    4096
SOLVENT               CDCl3
NS                      32
DS                      64
SWH              5040.323 Hz
FIDRES           1.230548 Hz
AQ               0.4063732 sec
RG                    2050
DW                 99.200 usec
DE                  6.50 usec
TE                 295.8 K
CNST13           8.0000000
CNST2          145.0000000
d0              0.00000300 sec
D1              1.50000000 sec
D16             0.00020000 sec
d2              0.00344828 sec
d6              0.06250000 sec
IN0             0.00001655 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                   5.00 usec
p2                  10.00 usec
PL1                  3.00 dB
SFO1          599.8223837 MHz

======== CHANNEL f2 ========
NUC2                   13C
P3                   6.50 usec
PL2                  1.00 dB
SFO2          150.8391874 MHz

====== GRADIENT CHANNEL =====
GPNAM1            SINE.100
GPNAM2            SINE.100
GPNAM3            SINE.100
GPZ1                50.00 %
GPZ2                30.00 %
GPZ3                40.10 %
P16               1000.00 usec

F1 - Acquisition parameters
ND0                     2
TD                    256
SFO1          150.8392 MHz
FIDRES        118.013596 Hz
SW              200.289 ppm
FnMODE                 QF

F2 - Processing parameters
SI                    1024
SF          599.8199645 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.40

F1 - Processing parameters
SI                    1024
MC2                    QF
SF          150.8248590 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0
```

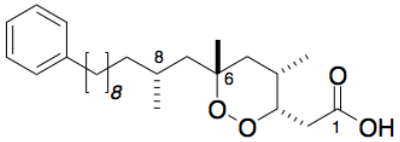
07.26.171.B.2.1.2.17

exp1 std1h

SAMPLE		DEC. & VT	
date	Oct 2 2007	dfrq	400.056
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	400.056	dm	nnn
tn	H1	dmm	c
at	1.993	dmf	200
np	23936	PROCESSING	
sw	6006.0	wtfile	
fb	not used	proc	ft
bs	16	fn	not used
tpwr	57		
pw	7.0	werr	
d1	1.000	wexp	
tof	0	wbs	
nt	160	wnt	
ct	80		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-1031.8		
wp	6005.6		
vs	90		
sc	0		
wc	250		
hzmm	2.30		
is	500.00		
rfl	1032.2		
rfp	0		
th	20		
ins	100.000		

nm cdc ph

Figure S13: 1H NMR (CDCl3, 400 MHz)



Plakinic acid M (**S1**)

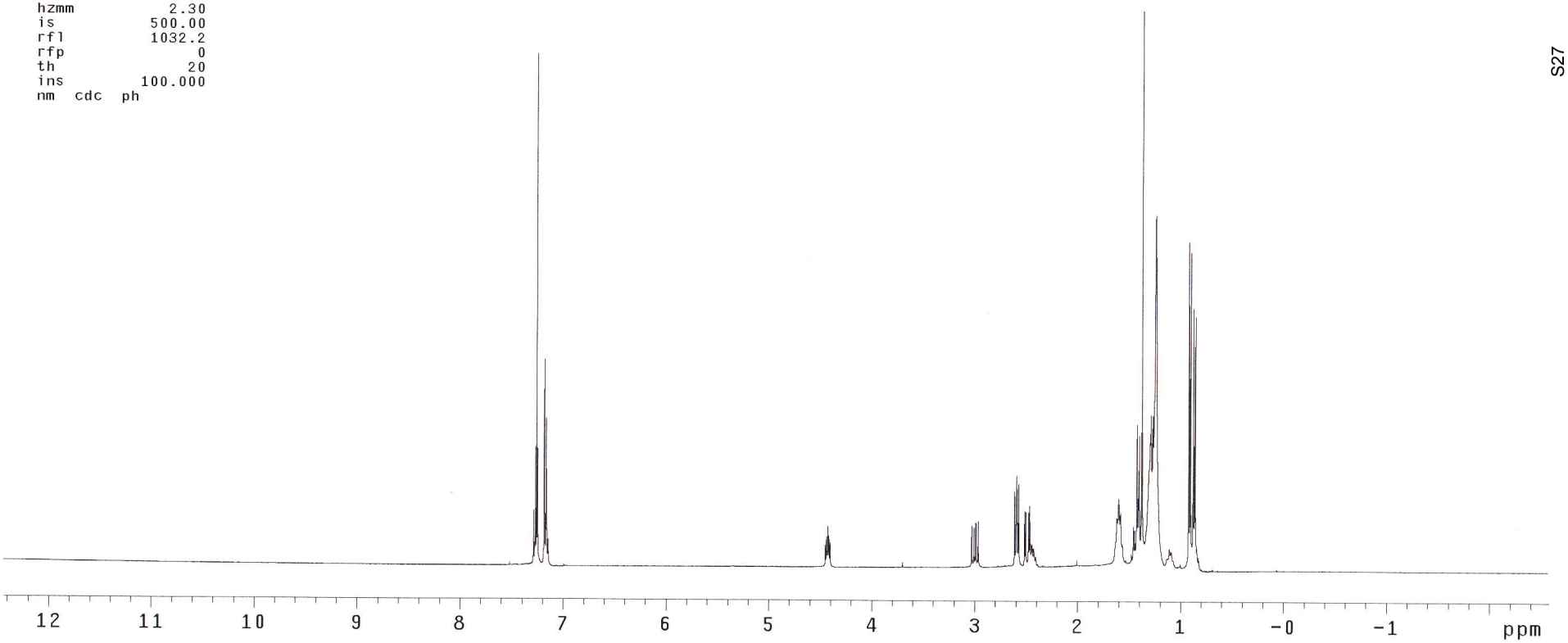
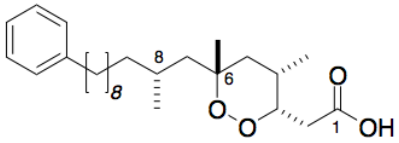


Figure S14: 13C NMR (CDCl3, 100 MHz)

07.26.171.B.2.1.2.17.13C

exp1 std13c

SAMPLE		DEC. & VT	
date	Oct 7 2007	dfrq	399.911
solvent	CDCl3	dn	H1
file	/export/home/~	dpwr	38
	molinski/ddalisay/~	dof	0
	07.26.171.B.2.1.2.~	dm	yyy
	17.13C.fid	dmm	w
ACQUISITION		dmf	9700
sfrq	100.567	PROCESSING	
tn	C13	lb	5.00
at	1.500	wtfile	
np	75000	proc	ft
sw	25000.0	fn	not used
fb	13800		
bs	16	werr	
ss	4	wexp	
tpwr	58	wbs	
pw	6.5	wnt	
d1	2.000		
tof	0		
nt	10000		
ct	1408		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-2986.2		
wp	24999.6		
vs	874		
sc	0		
wc	250		
hzmm	4.98		
is	500.00		
rfl	10745.6		
rfp	7759.0		
th	20		
ins	100.000		
nm no ph			

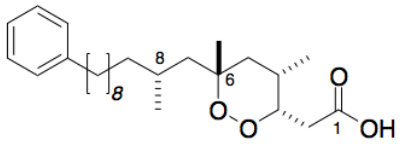


Plakinic acid M (**S1**)

07.26.171.B.2.1.2.17.gCOSY

exp1 gCOSY

SAMPLE		FLAGS	
date	Oct 7 2007	hs	nn
solvent	CDCl3	sspul	n
sample	undefined	hsglvl	994
ACQUISITION		SPECIAL	
sw	4132.2	temp	not used
at	0.248	gain	20
np	2048	spin	0
fb	not used	F2 PROCESSING	
ss	16	sb	-0.124
d1	1.000	sbs	not used
nt	8	fn	2048
2D ACQUISITION		F1 PROCESSING	
sw1	4132.2	sb1	-0.031
ni	128	sbs1	not used
TRANSMITTER		proc1	lp
tn	H1	fn1	2048
sfrq	399.911	DISPLAY	
tof	-329.9	sp	-366.3
tpwr	55	wp	4128.2
pw	13.900	sp1	-364.6
GRADIENTS		wp1	4128.2
gzlvl1	994	rfl	370.4
gt1	0.001000	rfp	0
gstab	0.000500	rfl1	368.7
DECOUPLER		rfp1	0
dn	H1	PLOT	
dm	nnn	wc	155.0
		sc	10.0
		wc2	155.0
		sc2	0
		vs	113
		th	7
		ai cdc av	



Plakinic acid M (**S1**)

Figure S15: COSY (CDCl3, 400 MHz)

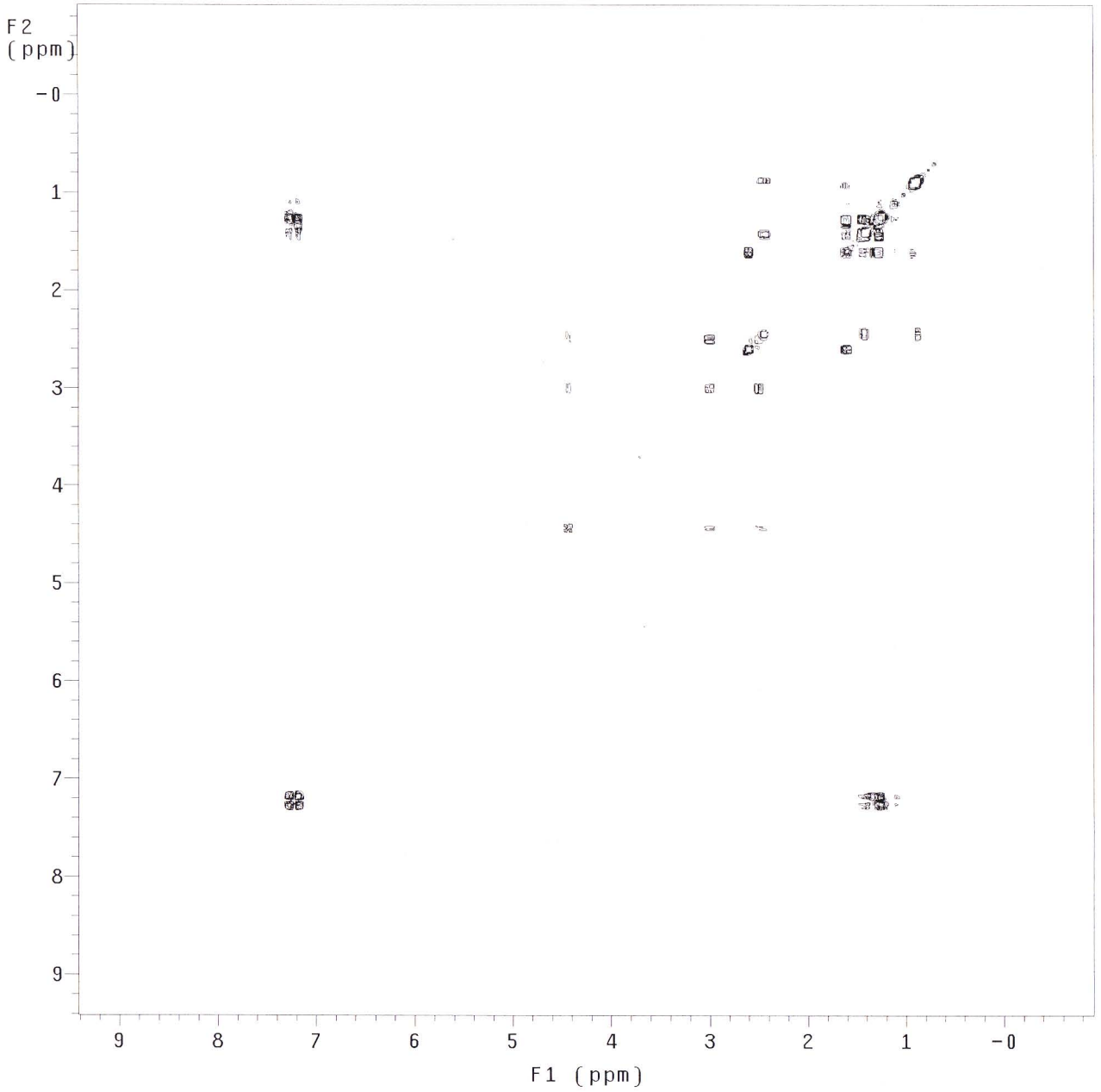


Figure S16: ^{1}H NMR spectrum of enyne **12** (400 MHz, $CDCl_3$).

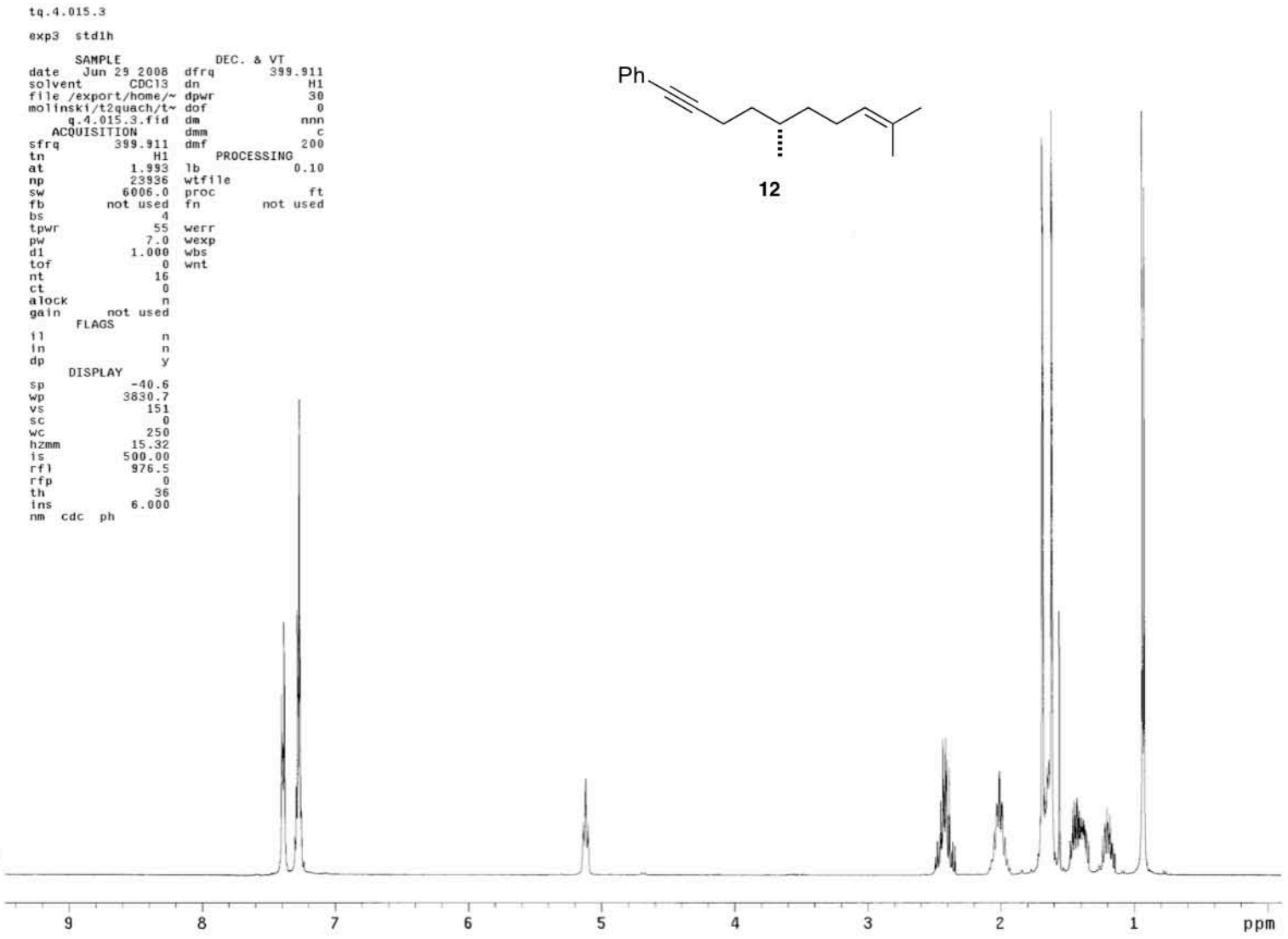


Figure S17: ^{13}C NMR spectrum of enyne **12** (100 MHz, $CDCl_3$).

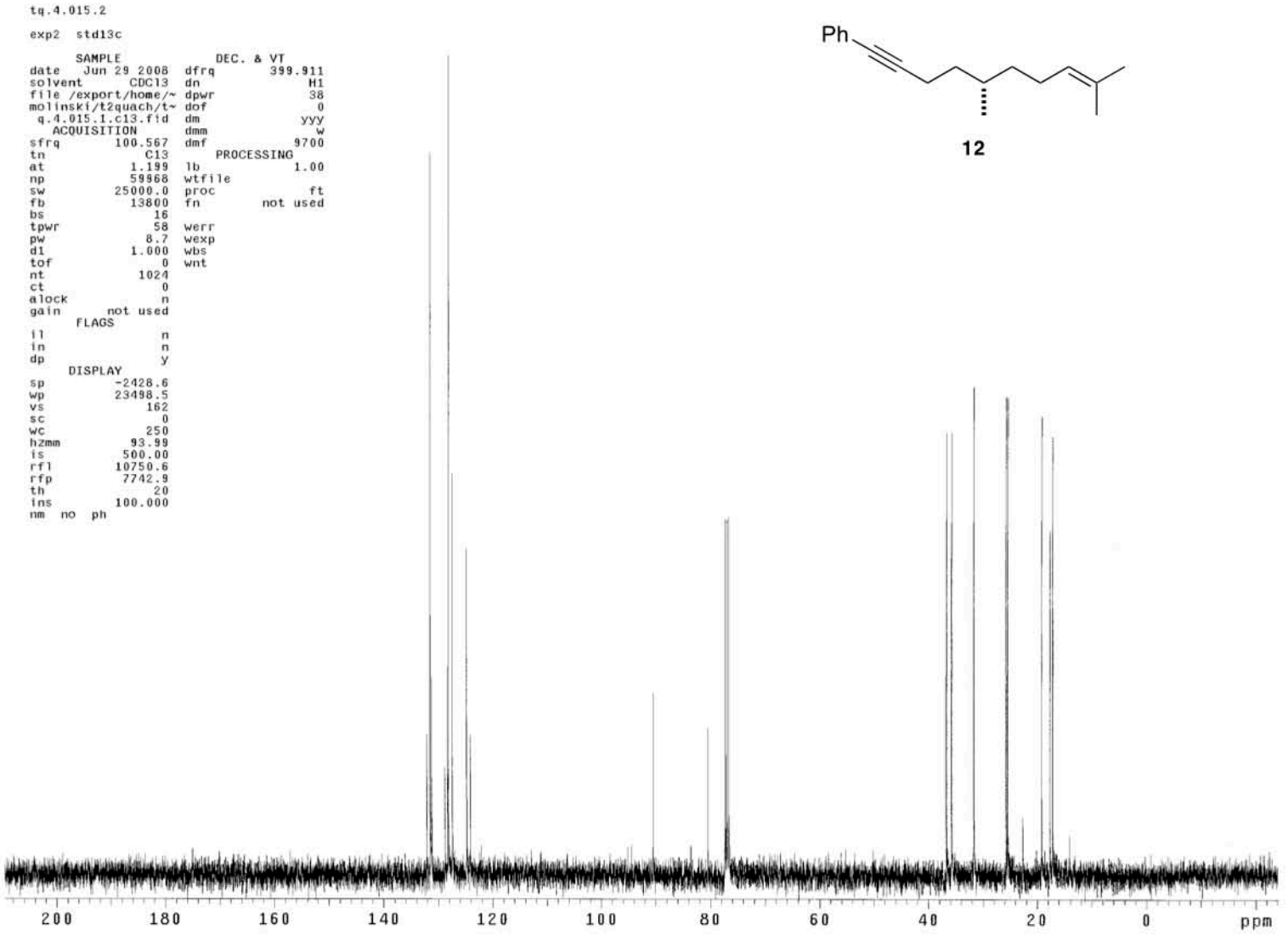


Figure S18: ^{1}H NMR spectrum of diol **13** (400 MHz, $CDCl_3$).

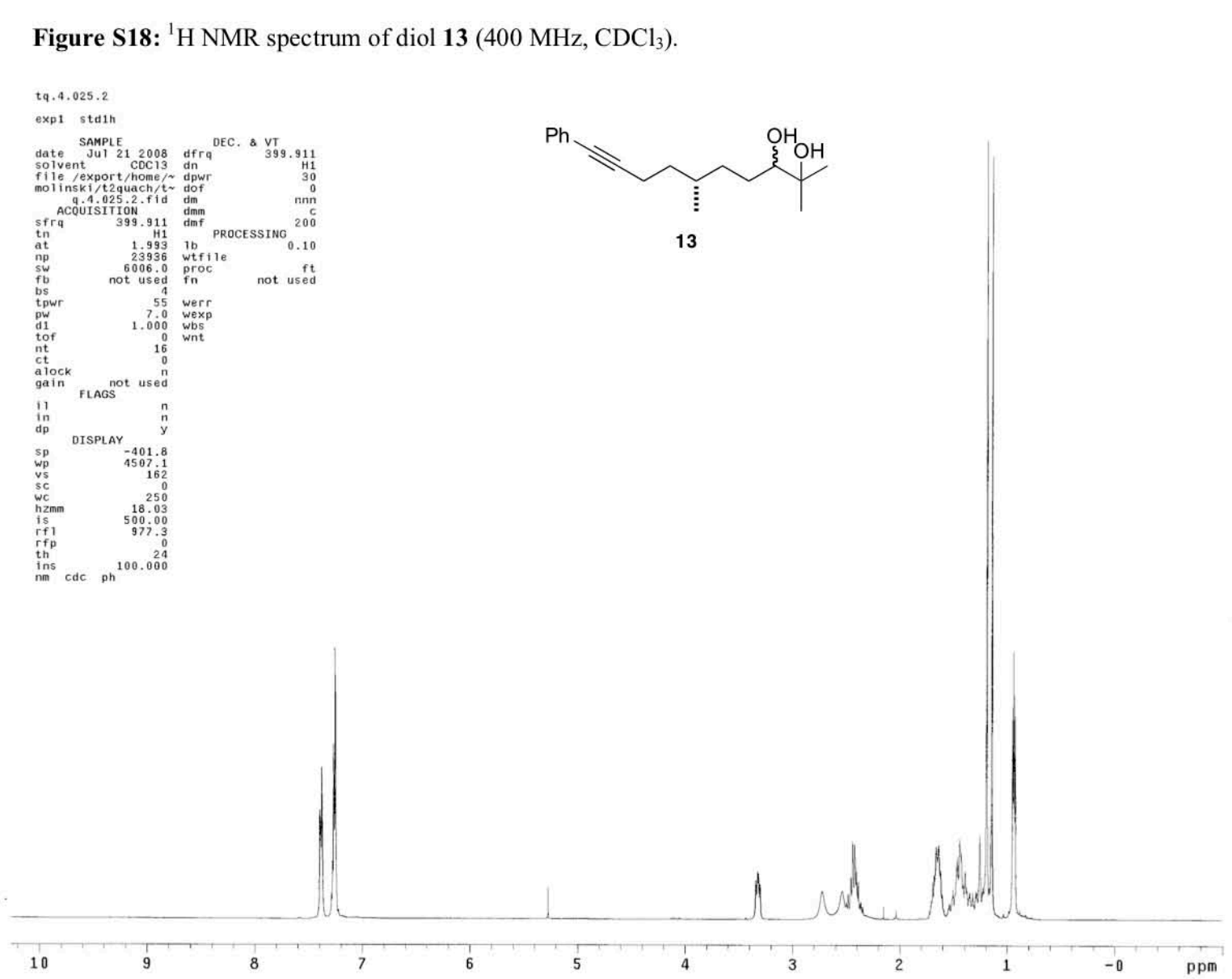


Figure S19: ^{13}C NMR spectrum of diol **13** (100 MHz, $CDCl_3$).

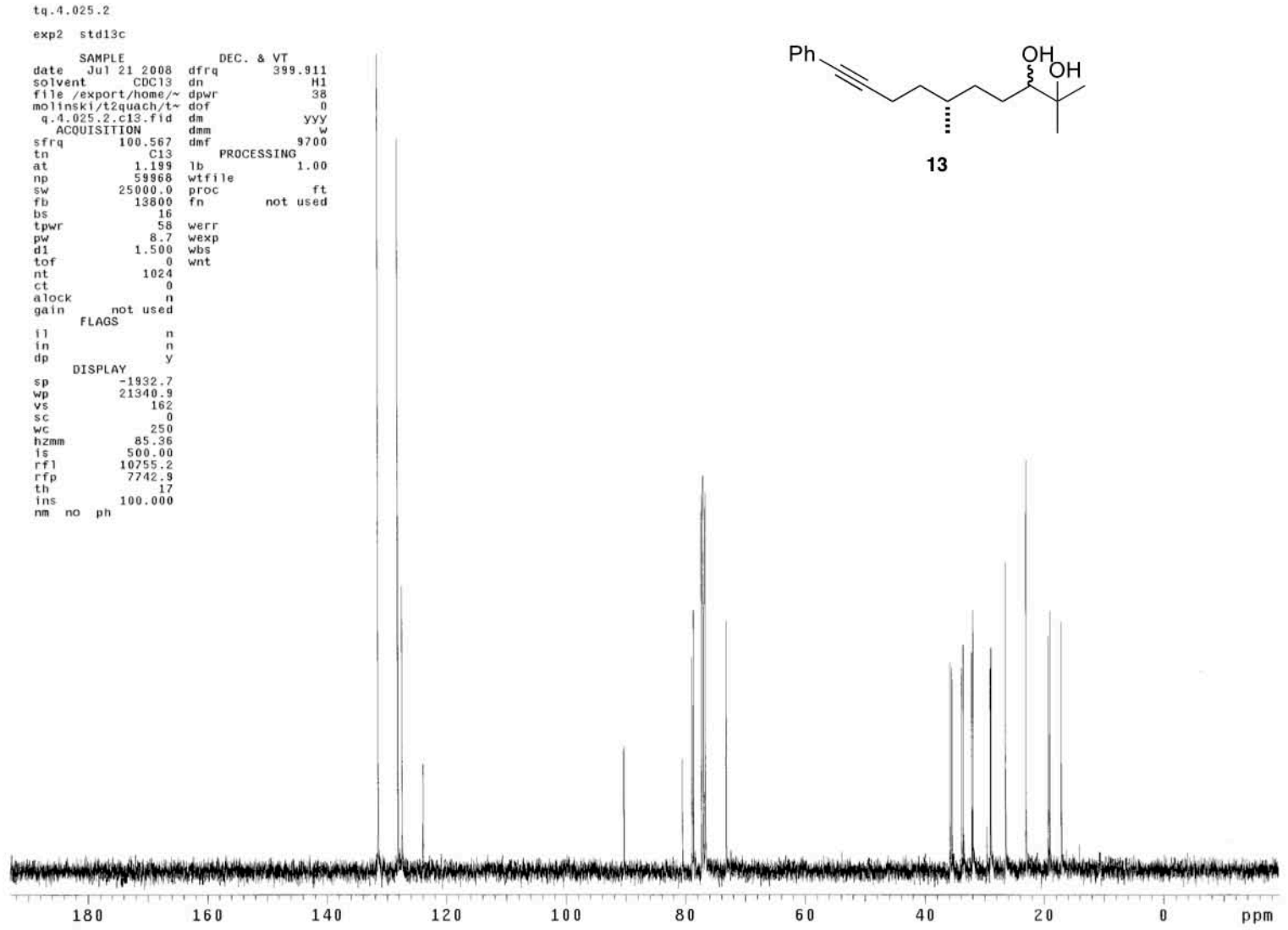


Figure S20: ^{1}H NMR spectrum of aldehyde **14** (400 MHz, $CDCl_3$).

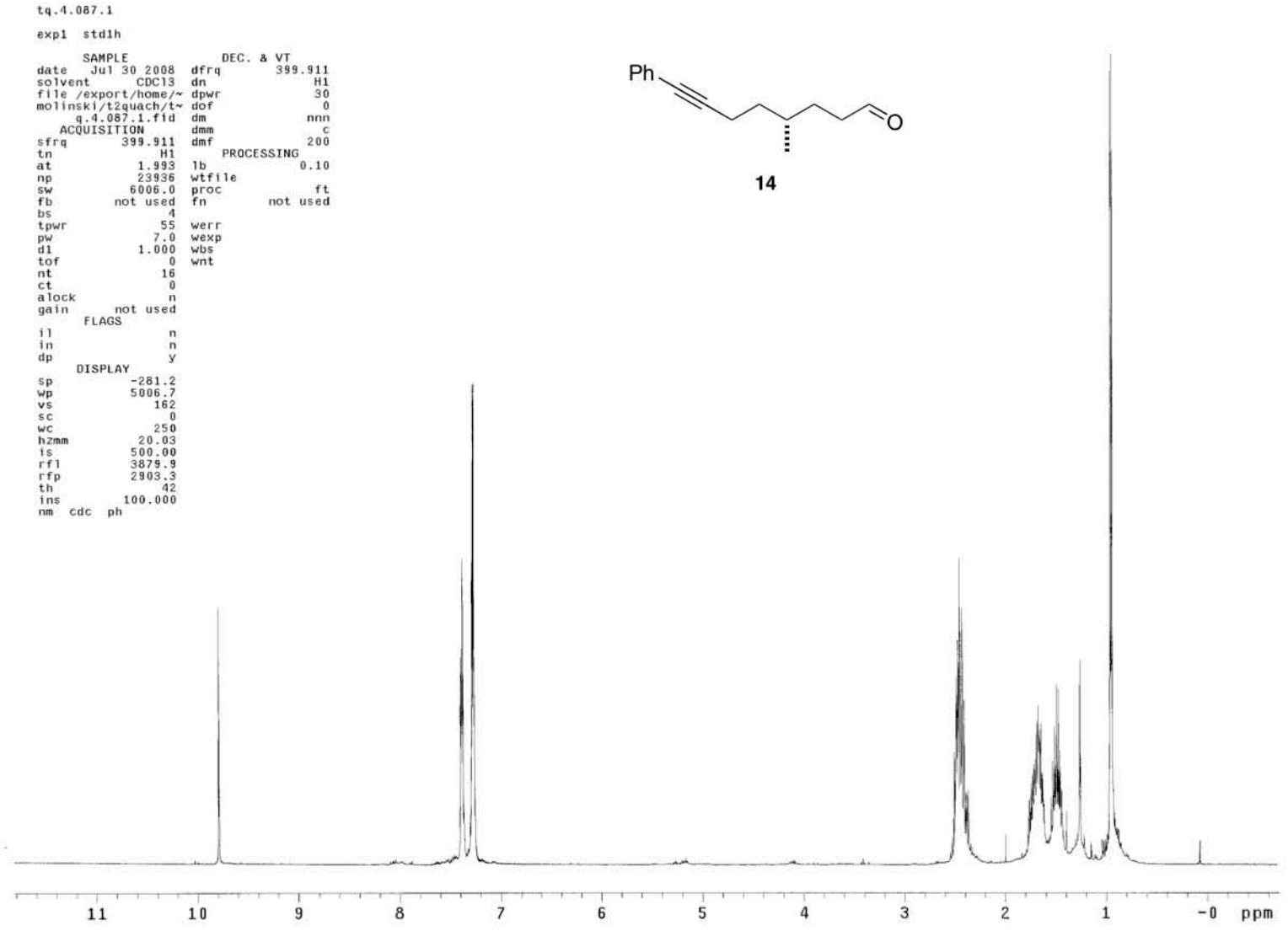


Figure S21: ^{13}C NMR spectrum of aldehyde **14** (100 MHz, $CDCl_3$).

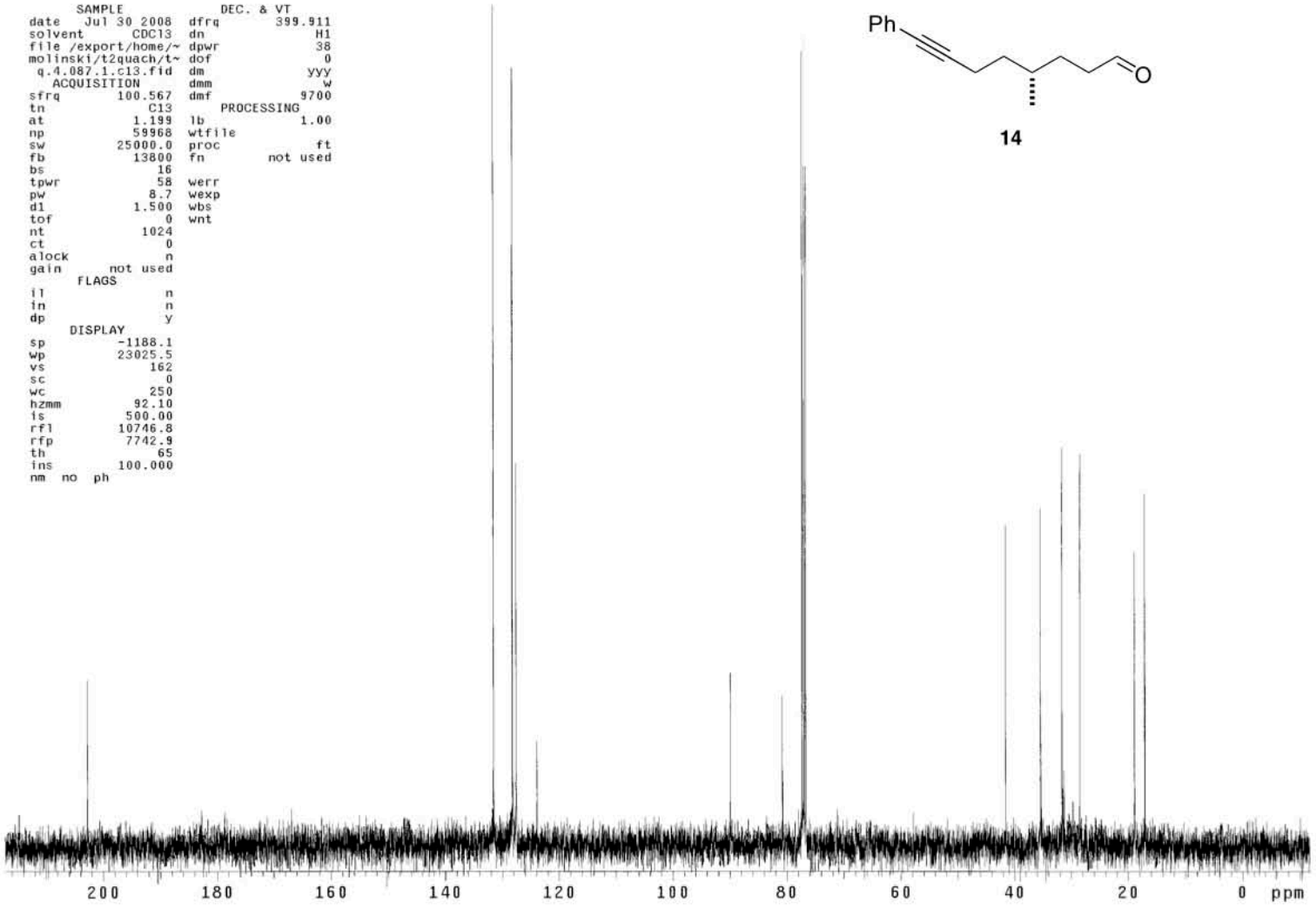


Figure S22: ^{1}H NMR spectrum of unsaturated ester **15** (400 MHz, $CDCl_3$).

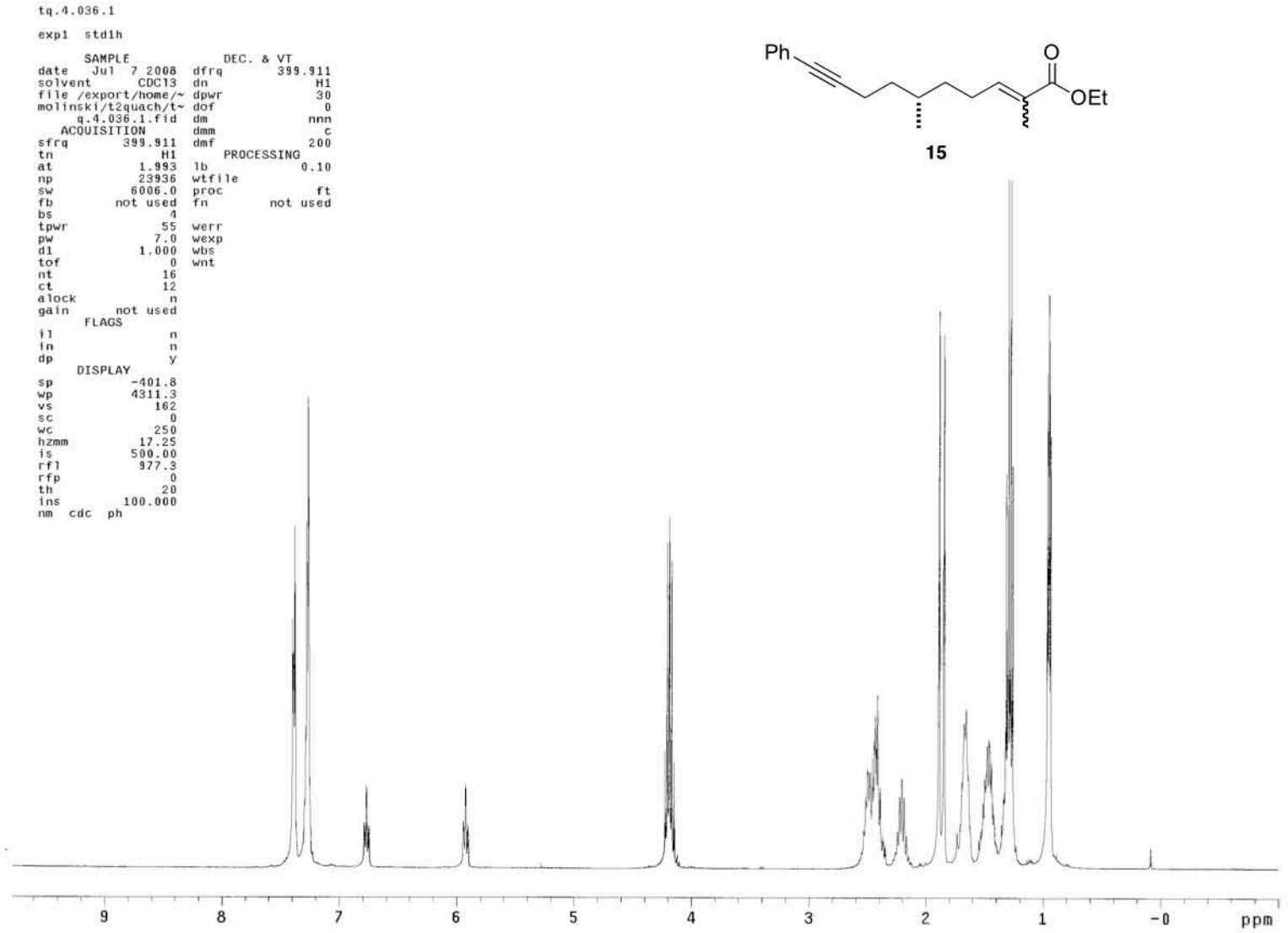


Figure S23: ^{13}C NMR spectrum of unsaturated ester **15** (100 MHz, $CDCl_3$).

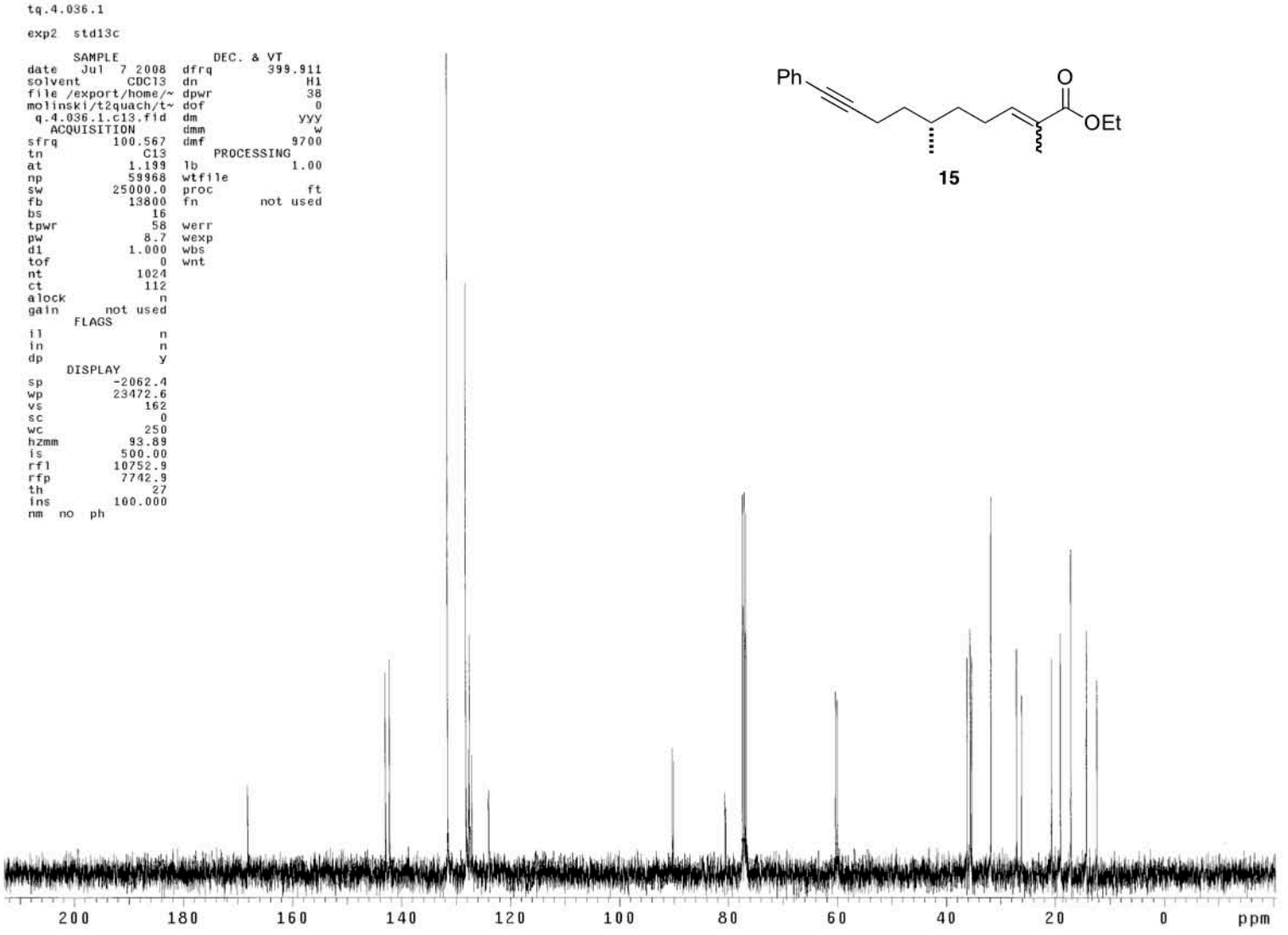


Figure S24: ^{1}H NMR spectrum of saturated ester **16** (400 MHz, $CDCl_3$).

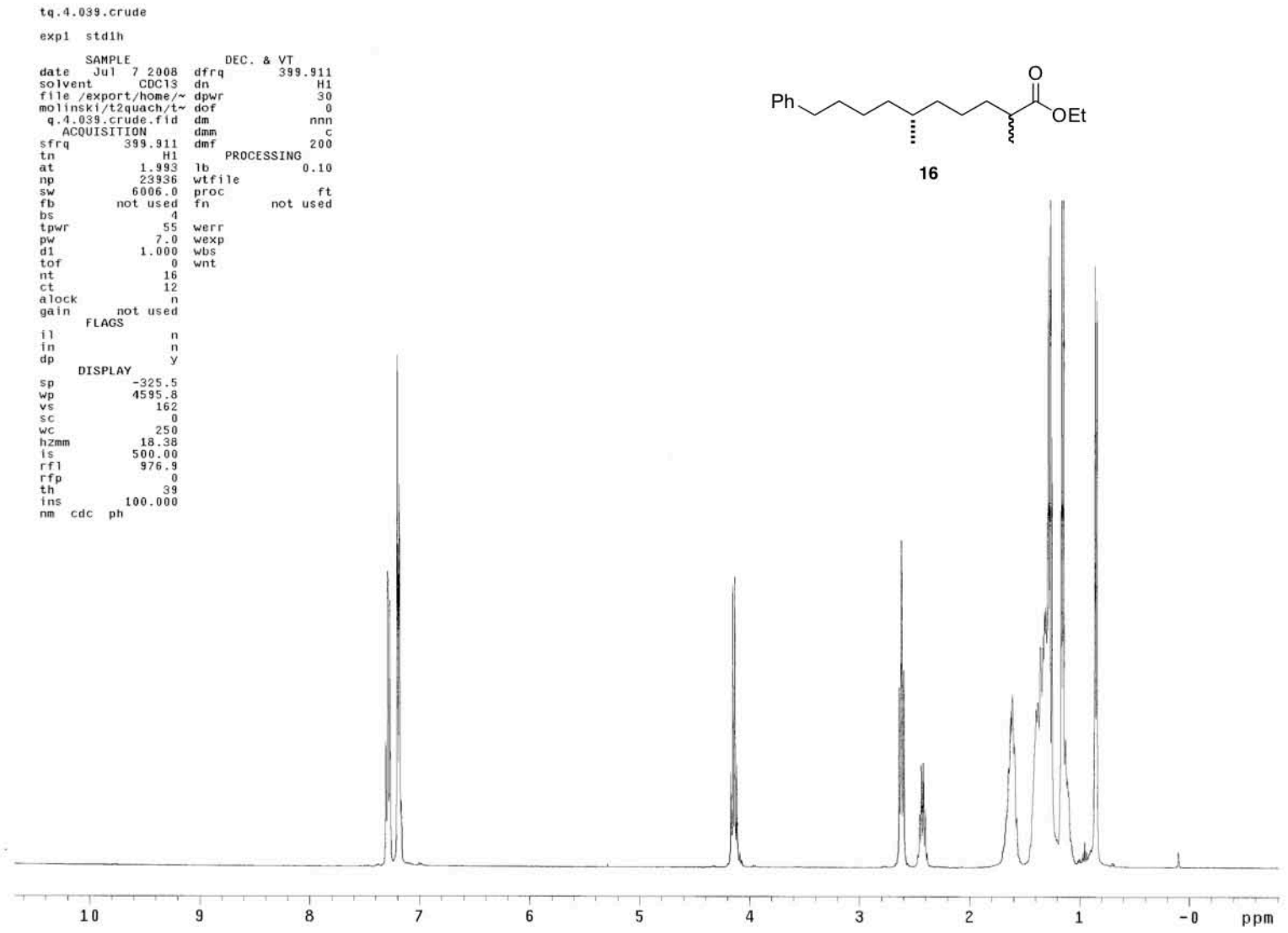


Figure S25: ^{13}C NMR spectrum of saturated ester **16** (100 MHz, $CDCl_3$).

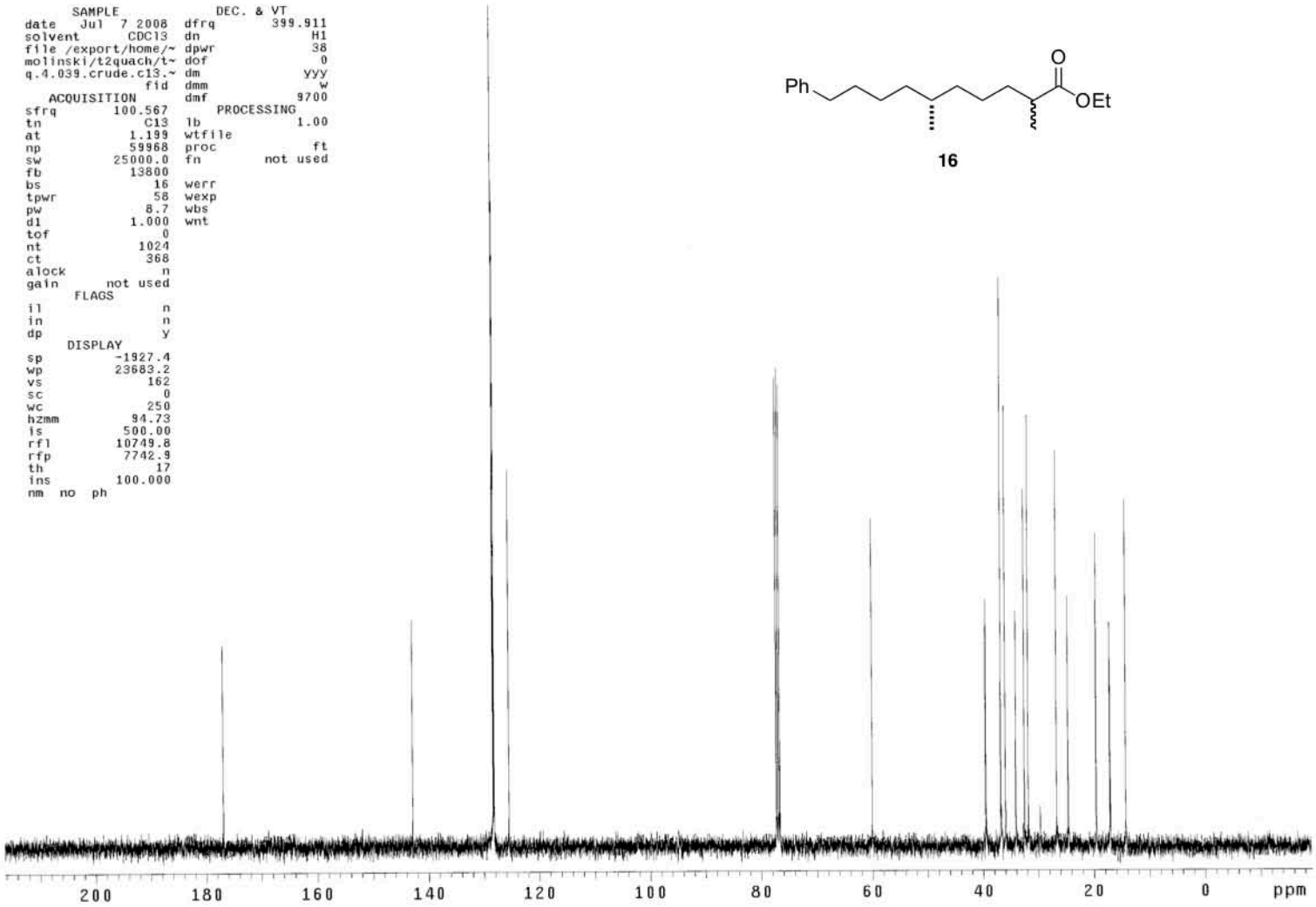


Figure S26: ^{1}H NMR spectrum of acid **17** (400 MHz, $CDCl_3$).

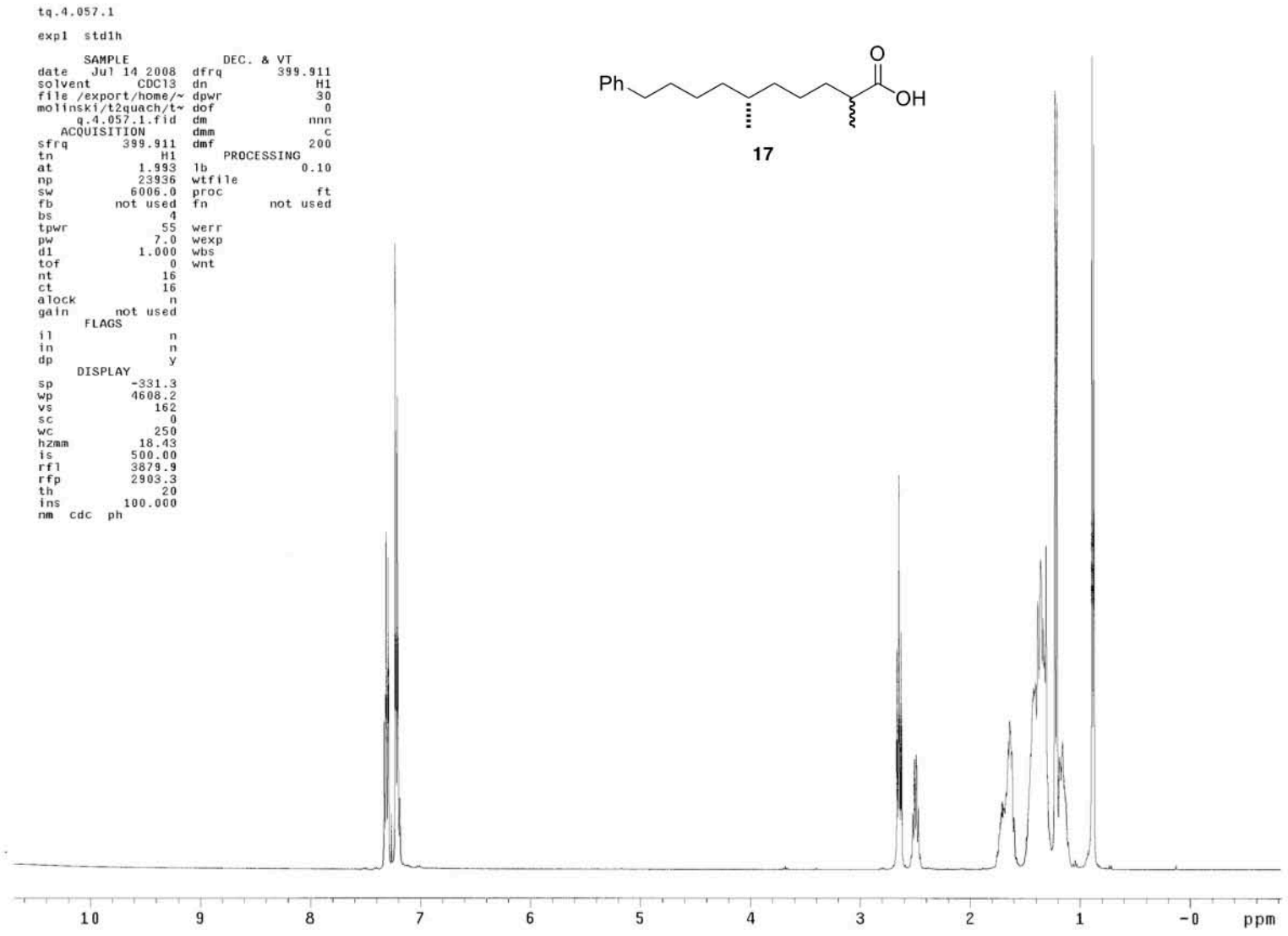


Figure S27: ^{13}C NMR spectrum of acid **17** (100 MHz, $CDCl_3$).

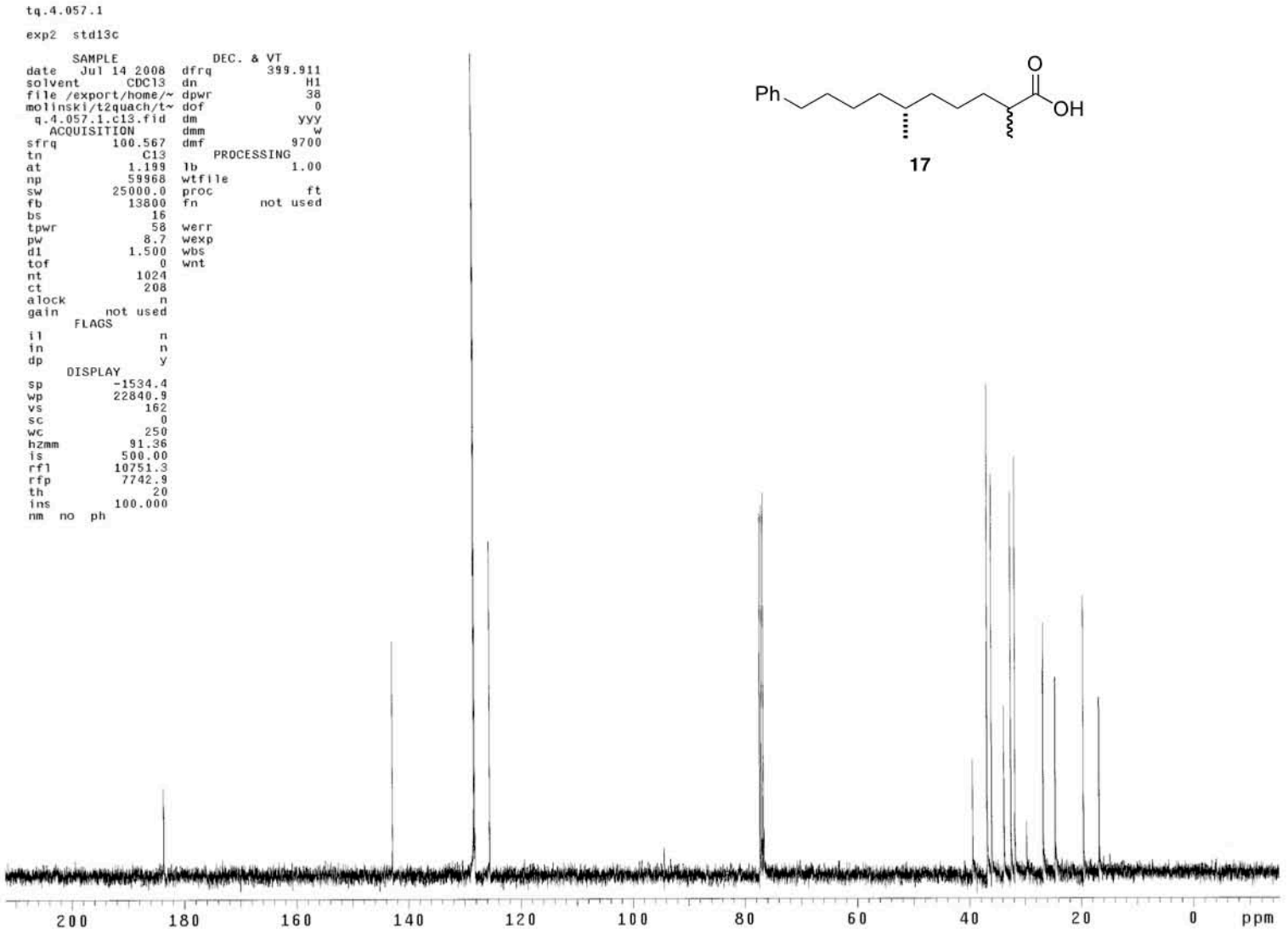


Figure S28: ^{1}H NMR spectrum of amide (2*S*,6*R*)-**18** (400 MHz, $CDCl_3$).

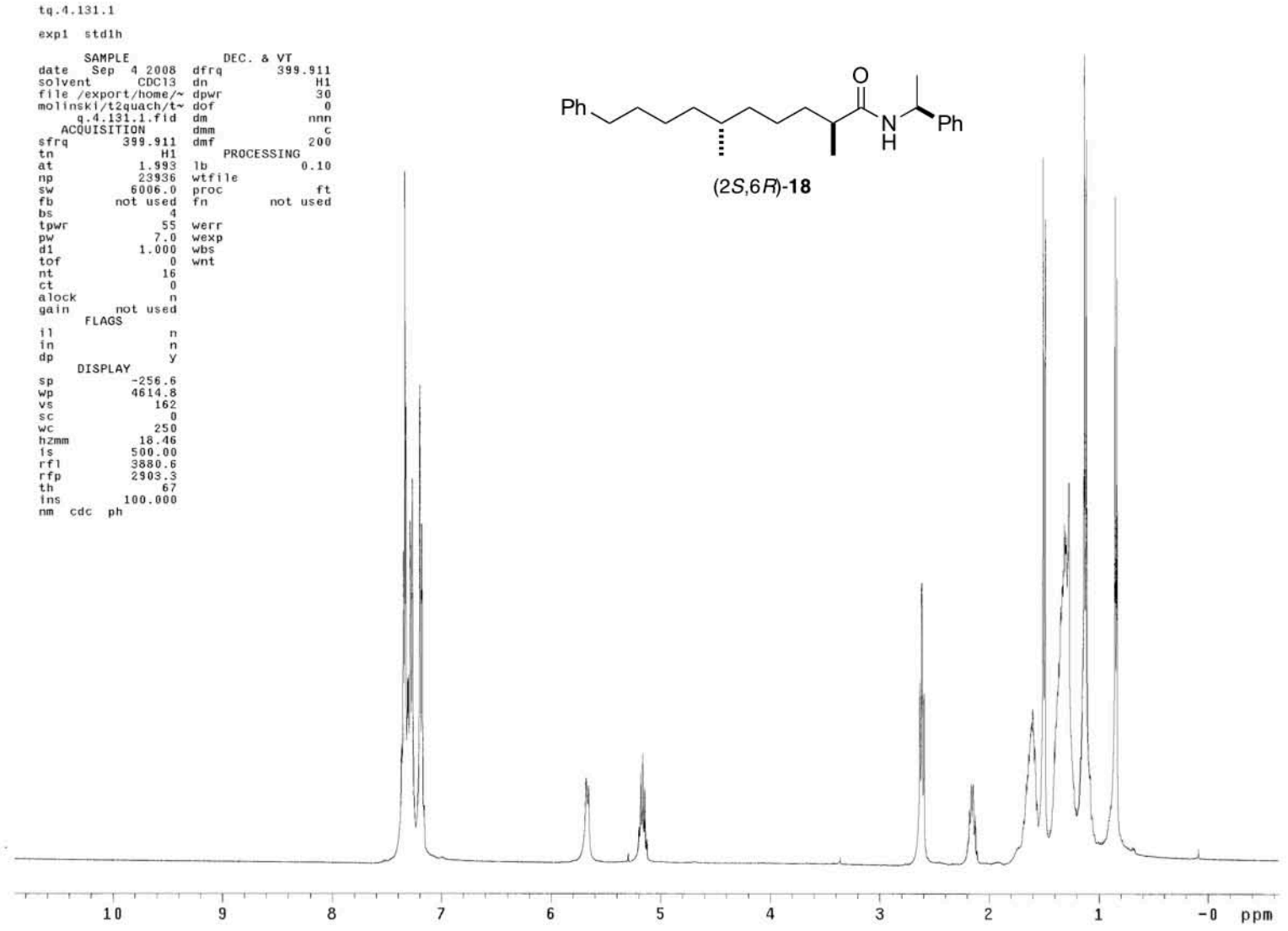


Figure S29: ^{13}C NMR spectrum of amide (2*S*,6*R*)-**18** (100 MHz, $CDCl_3$).

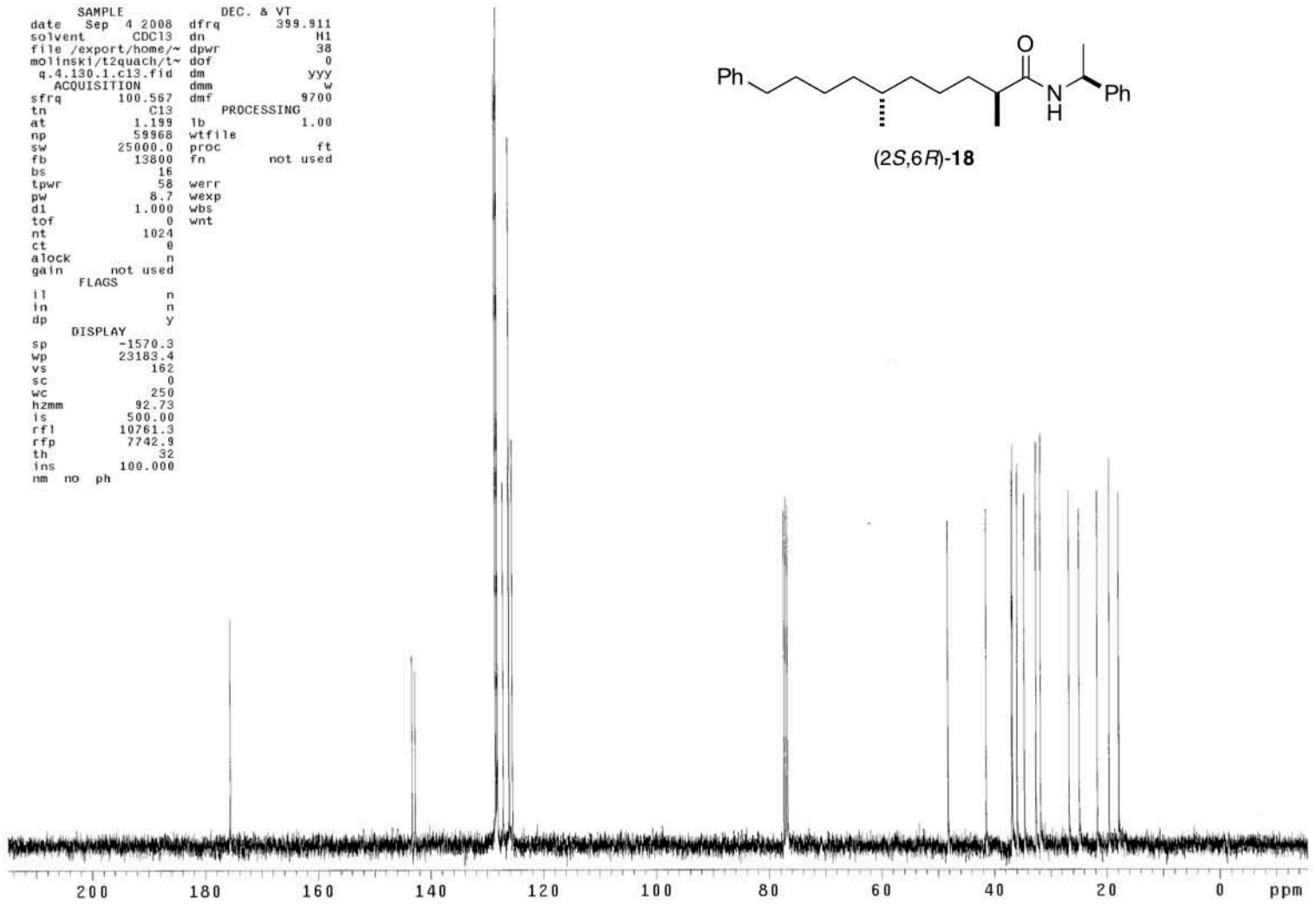


Figure S30: ^{1}H NMR spectrum of amide (2*R*,6*R*)-**19** (400 MHz, $CDCl_3$).

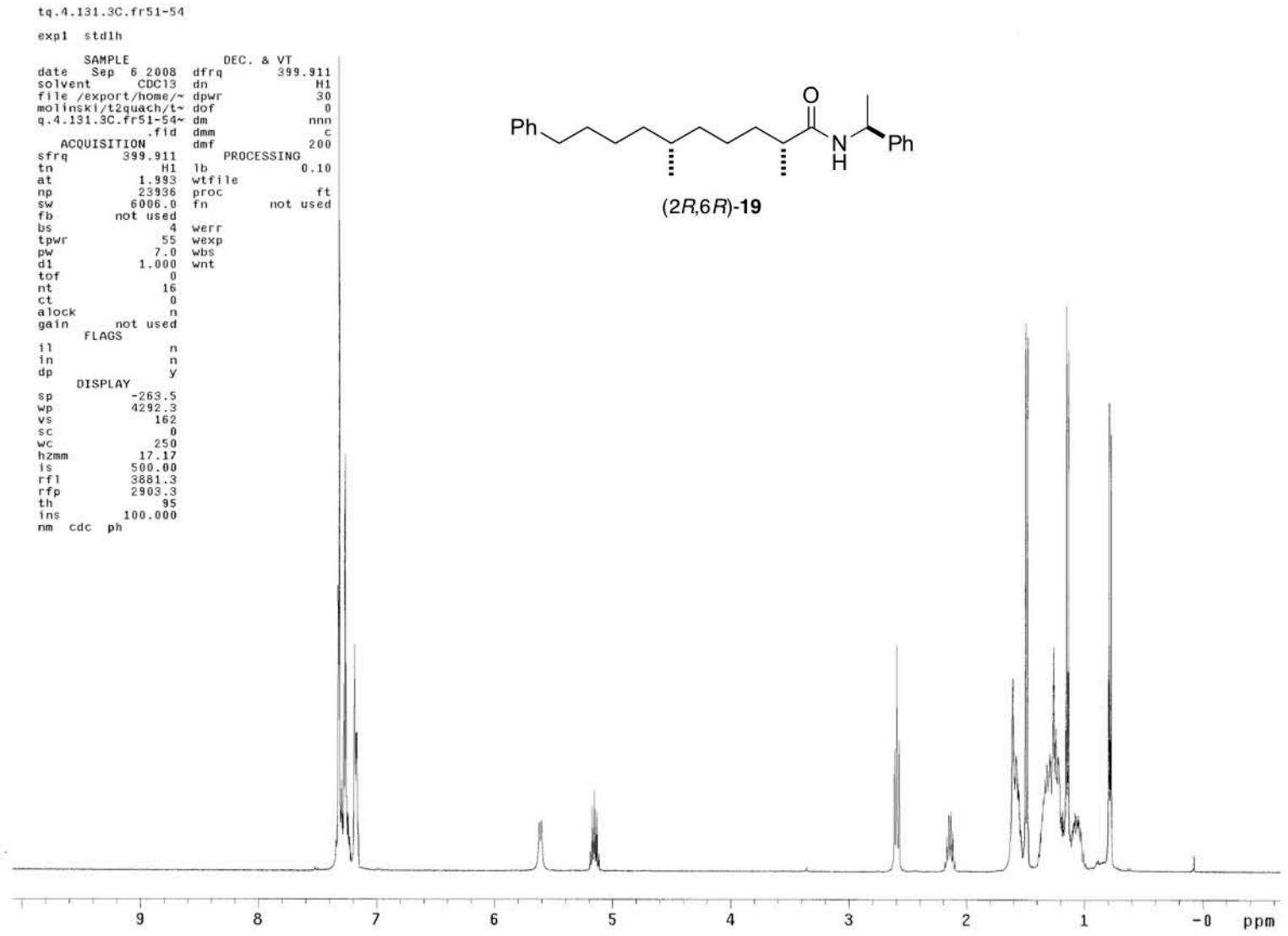


Figure S31: ^{13}C NMR spectrum of amide (2*R*,6*R*)-**19** (100 MHz, $CDCl_3$).

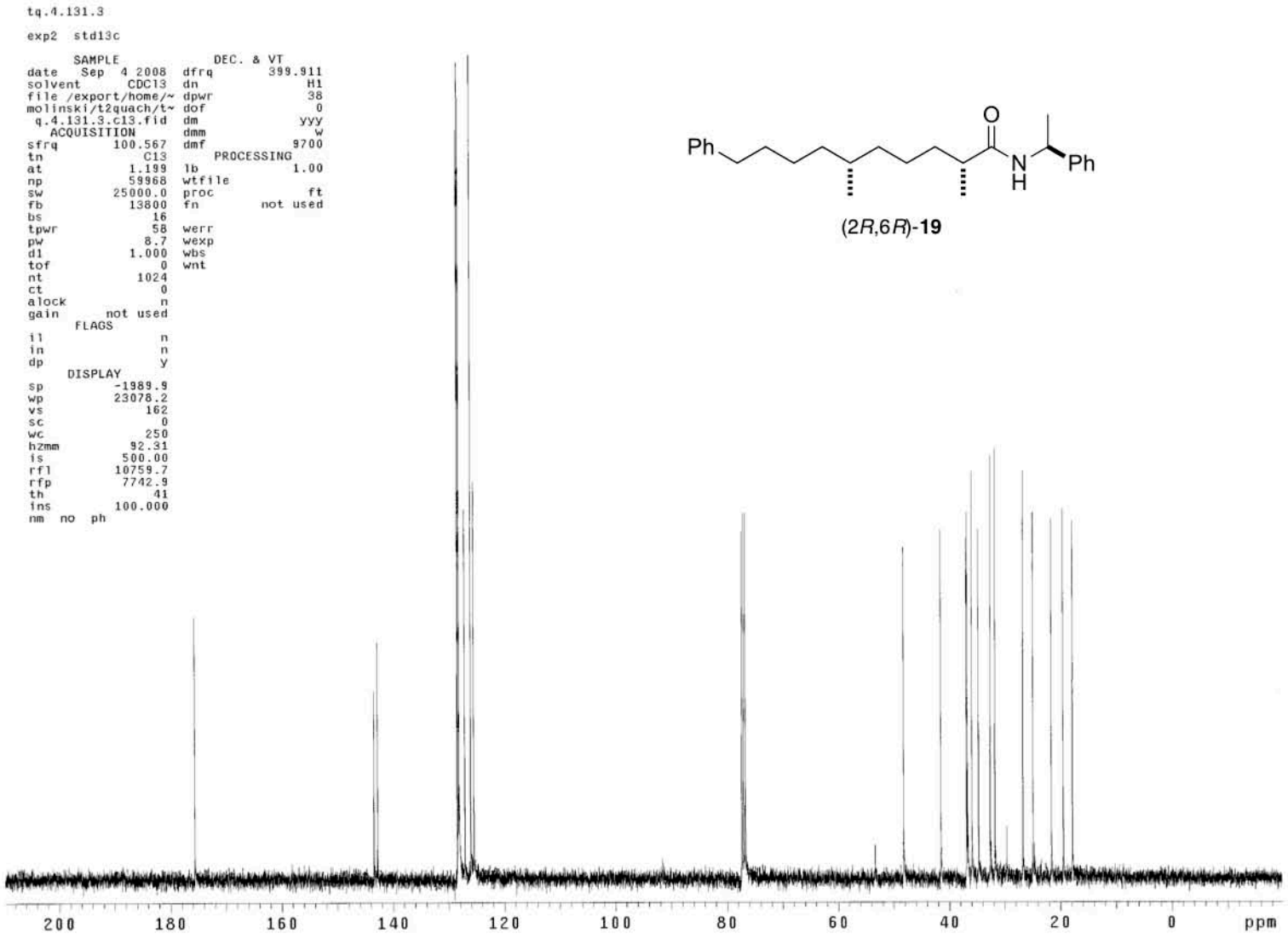


Figure S32: ^{1}H NMR spectrum of secondary amine (2*S*,6*R*)-**20** (400 MHz, $CDCl_3$).

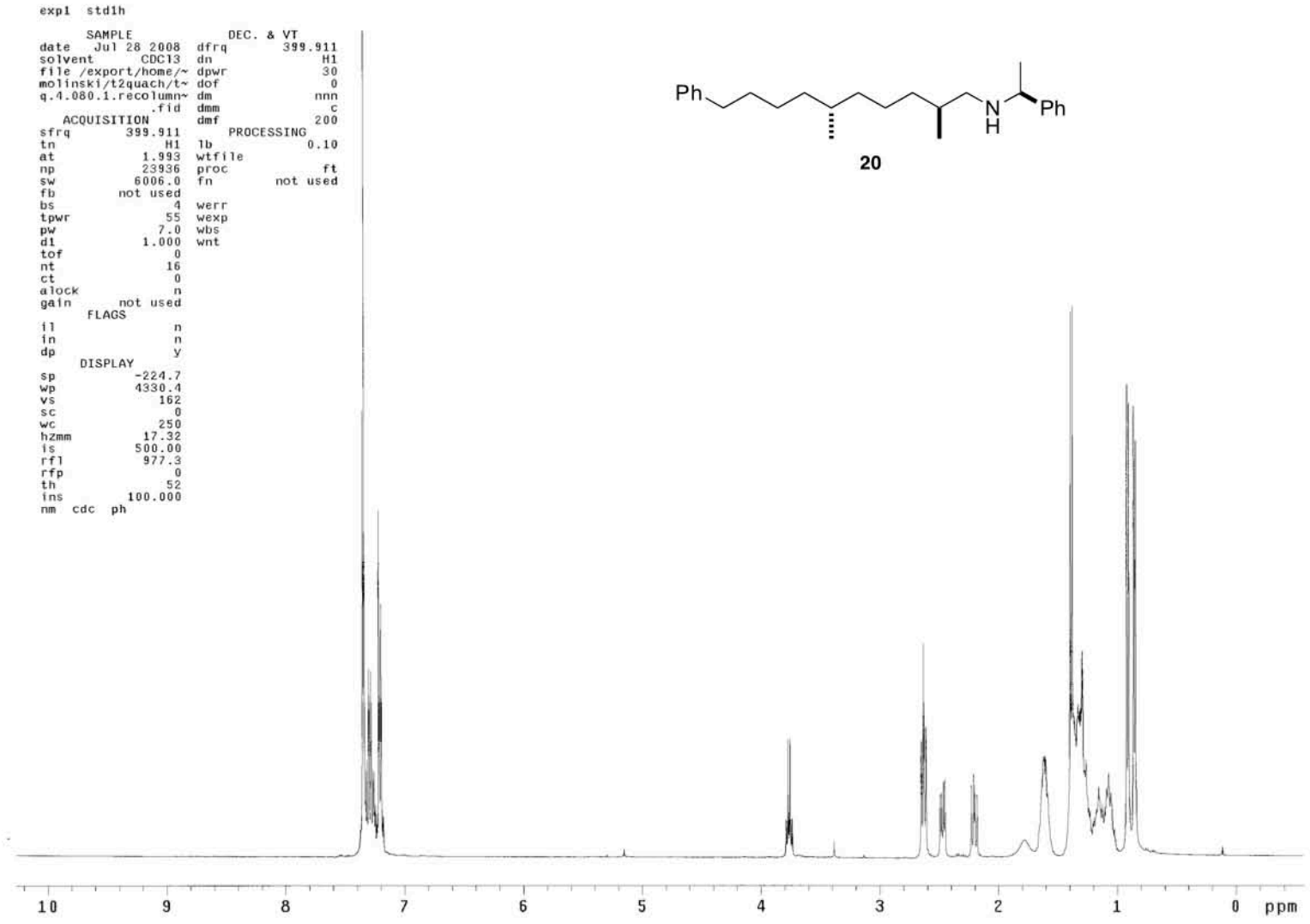


Figure S33: ^{13}C NMR spectrum of secondary amine (2*S*,6*R*)-**20** (100 MHz, $CDCl_3$).

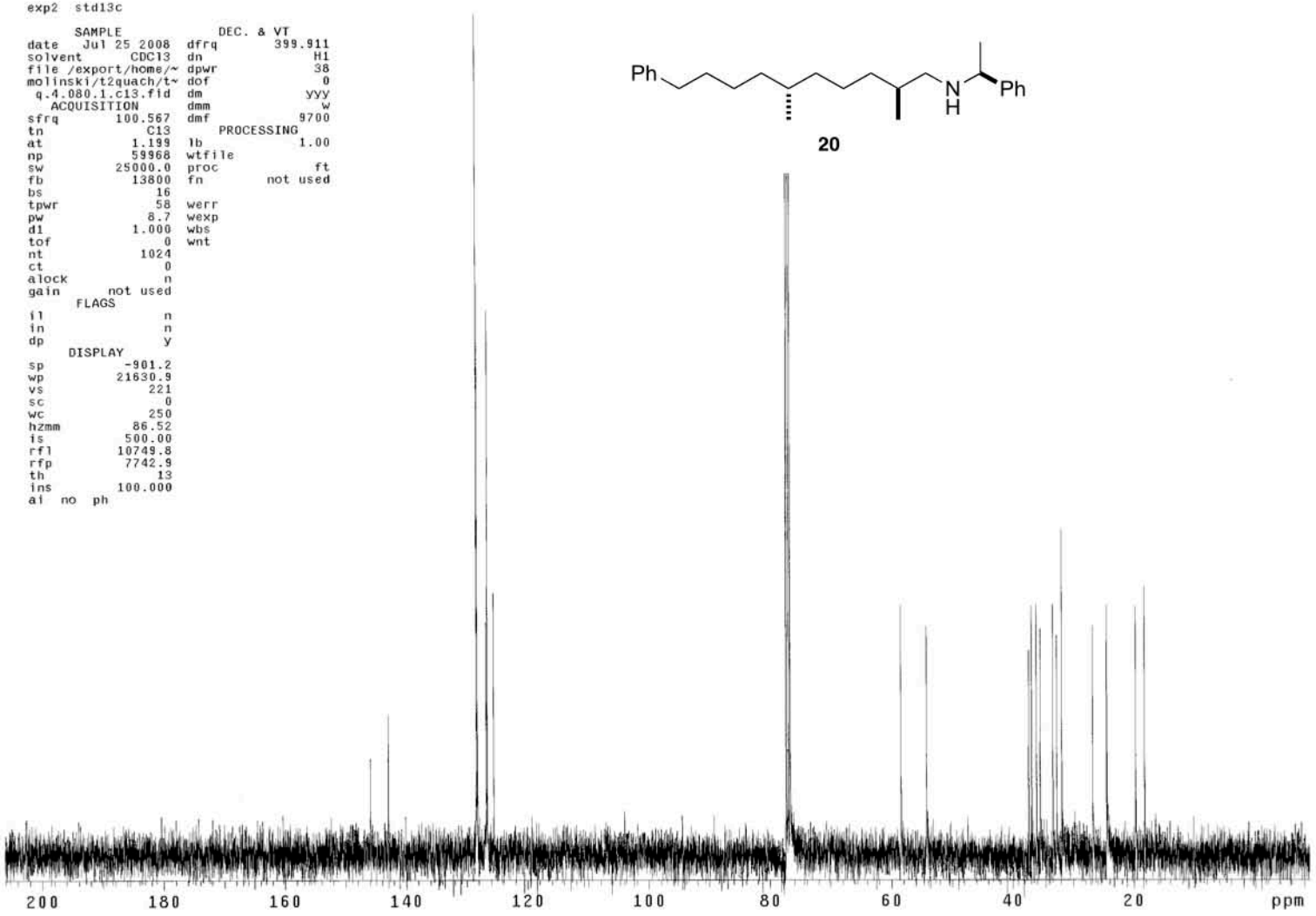


Figure S34: ^{1}H NMR spectrum of secondary amine (2*R*,6*R*)-**21** (500 MHz, $CDCl_3$).

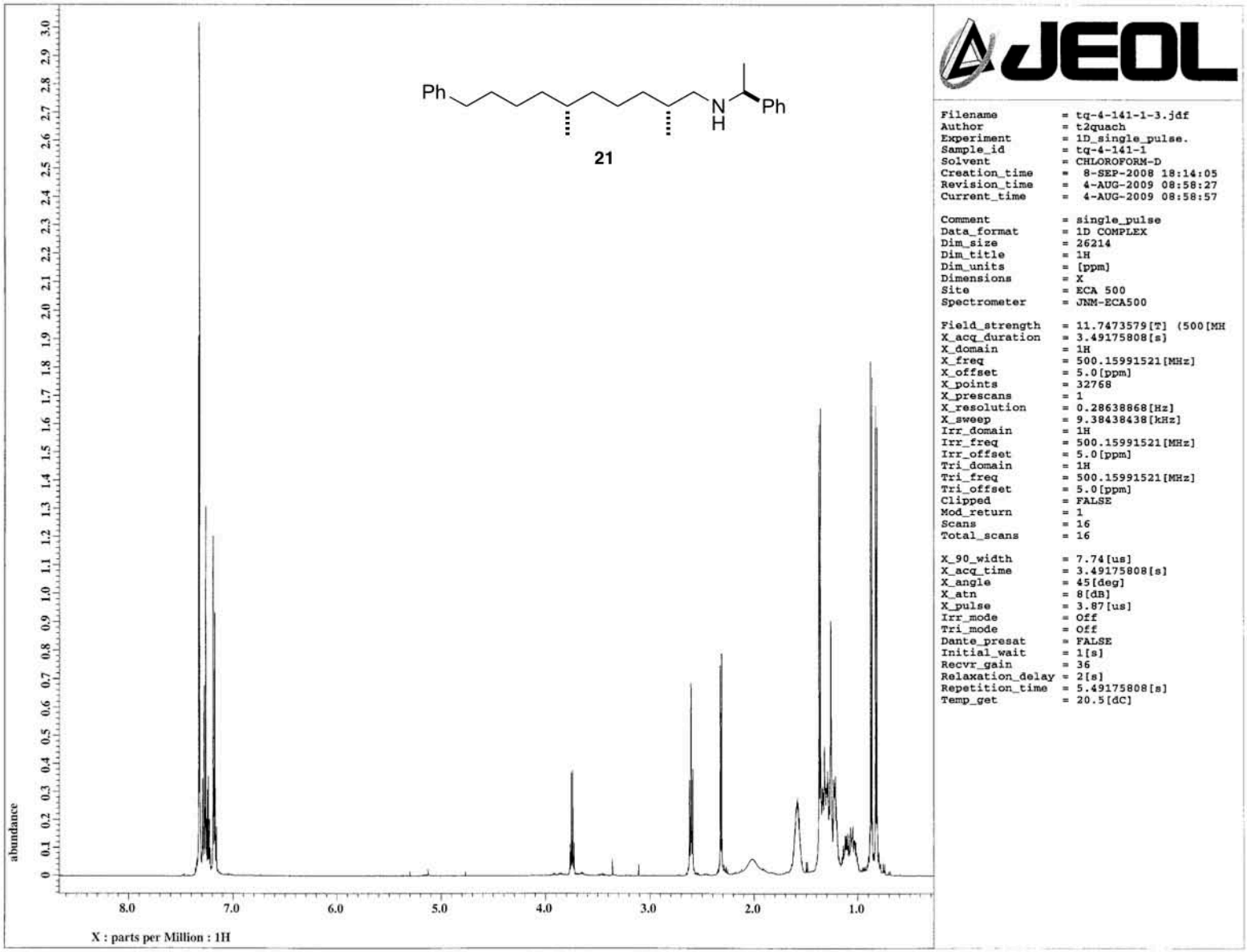


Figure S35: ^{13}C NMR spectrum of secondary amine (2*R*,6*R*)-**21** (125 MHz, $CDCl_3$).

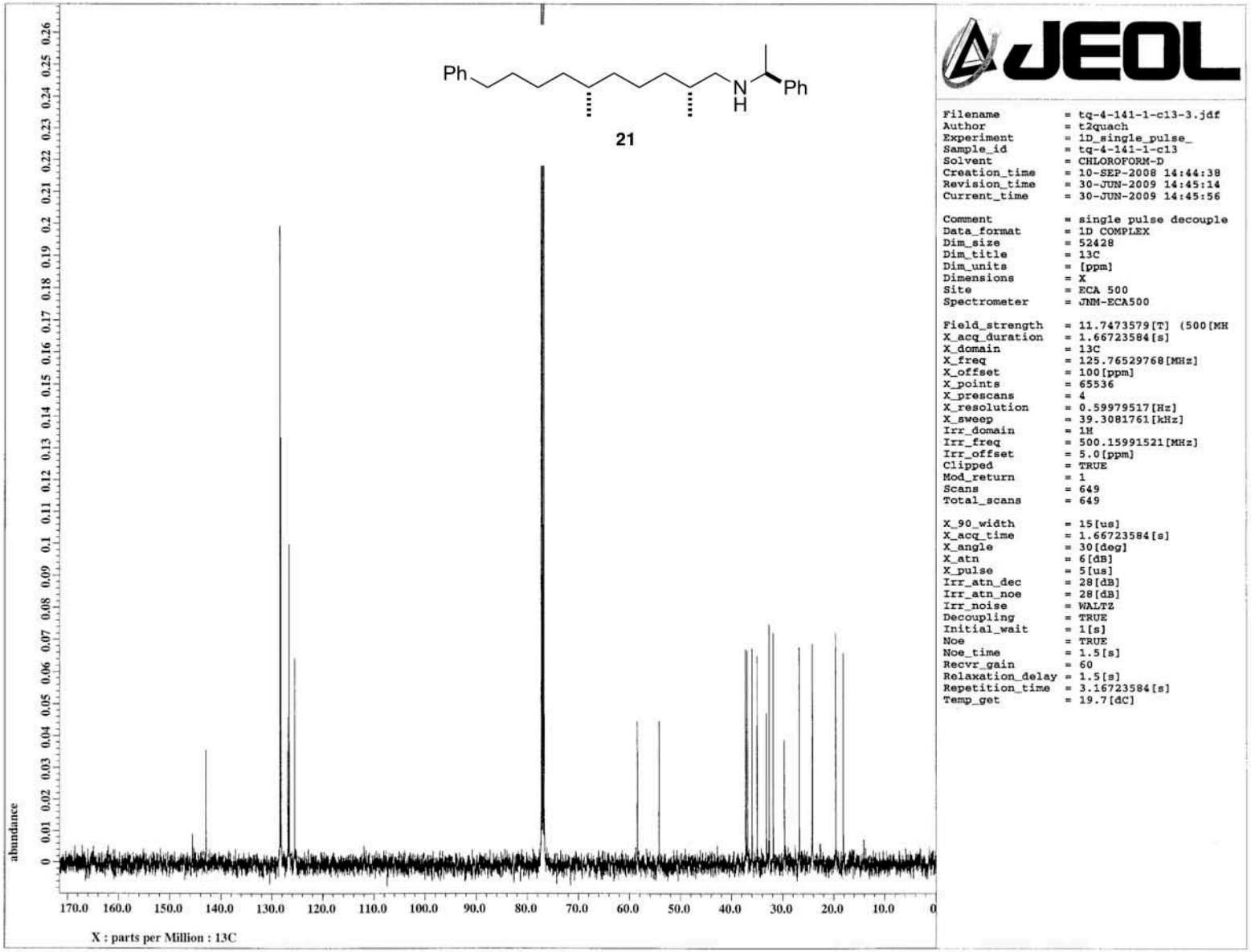


Figure S36: ^{1}H NMR spectrum of primary amine (2*S*,6*R*)-**22** (400 MHz, $CDCl_3$).

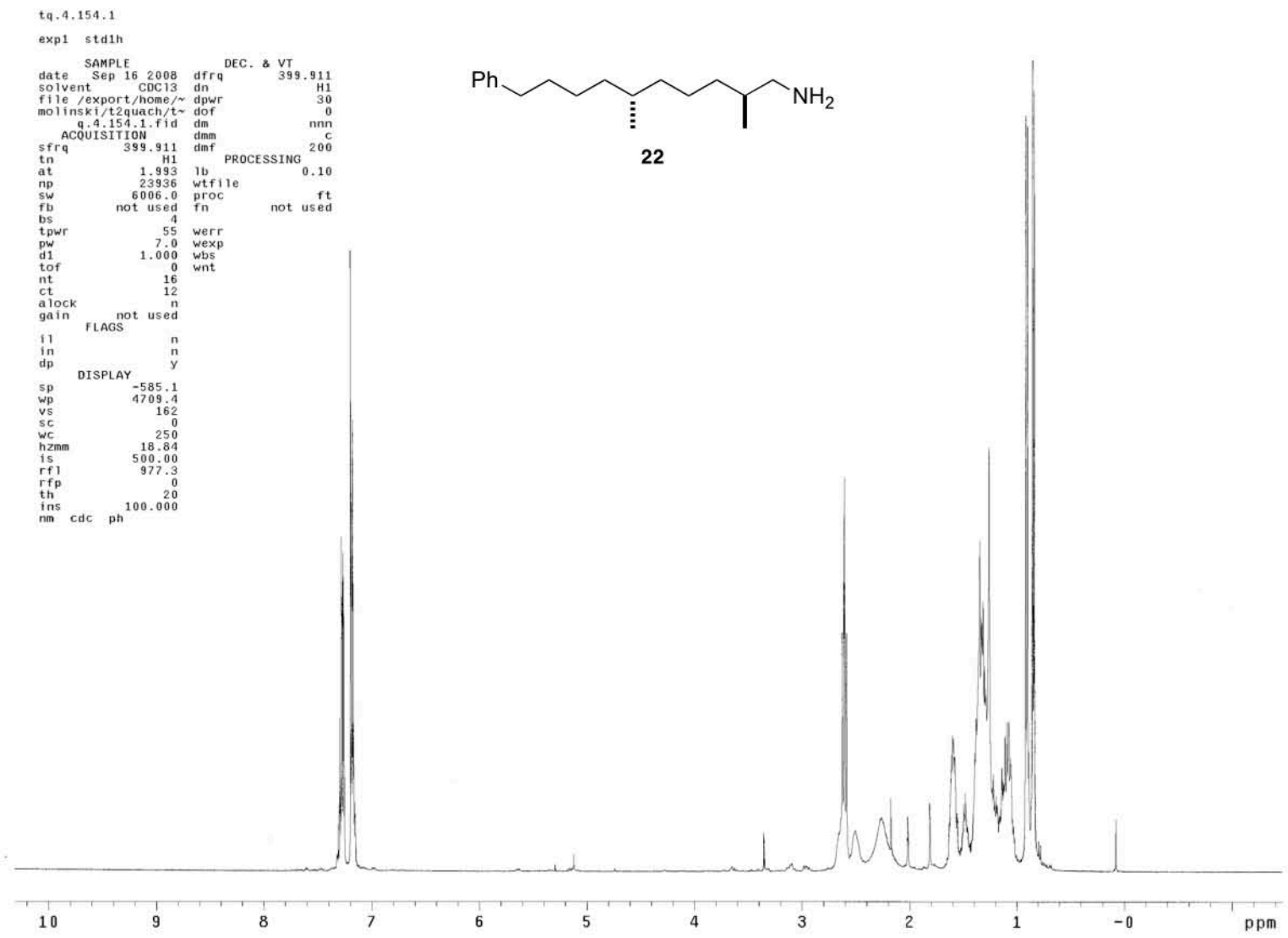
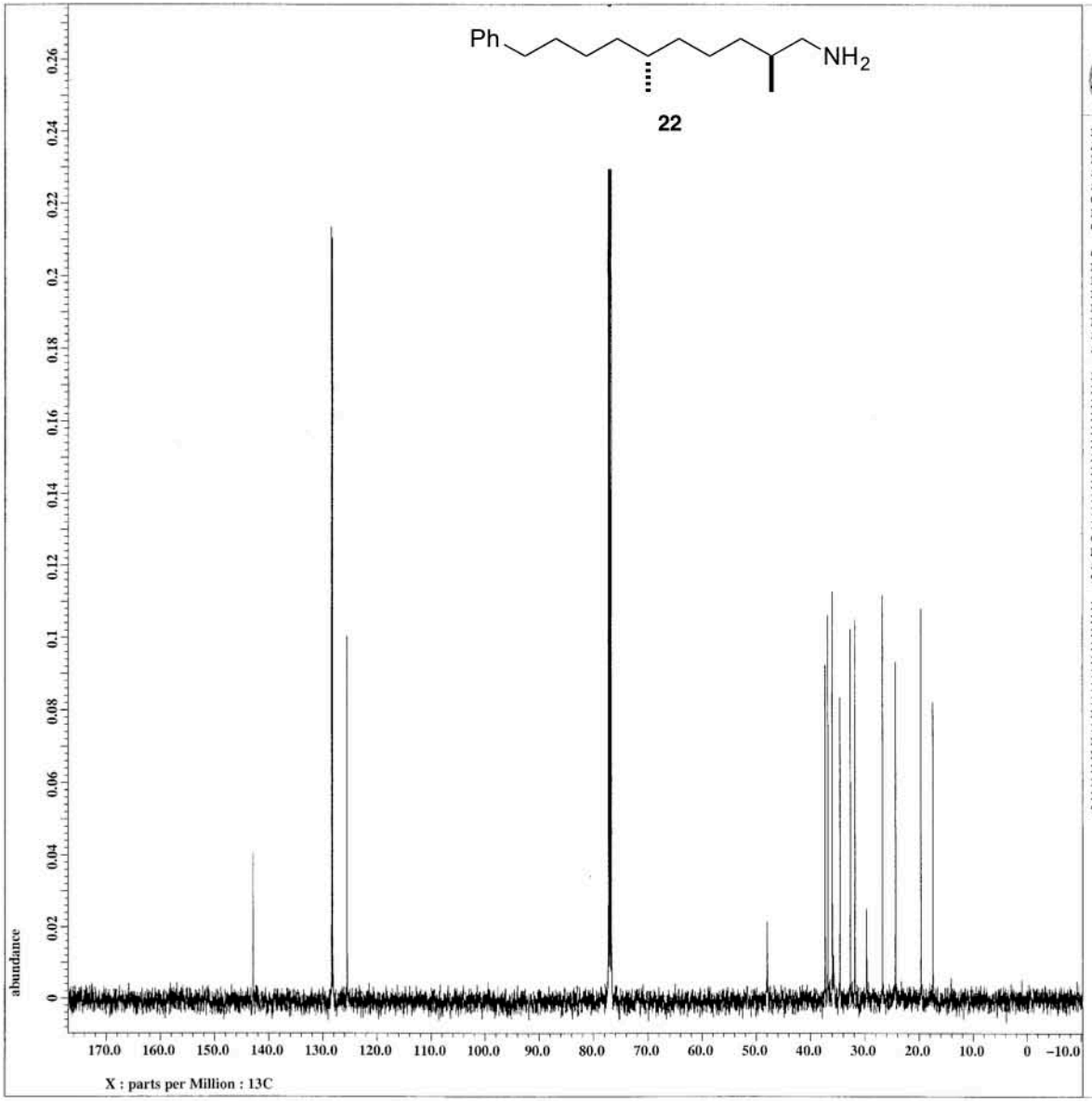


Figure S37: ^{13}C NMR spectrum of primary amine (2*S*,6*R*)-**22** (125 MHz, $CDCl_3$).



JEOL

```
Filename          = tq-4-154-1-c13-5.jdf
Author            = t2quach
Experiment        = 1D_single_pulse_
Sample_id         = tq-4-154-1-c13
Solvent           = CHLOROFORM-D
Creation_time     = 16-SEP-2008 18:03:21
Revision_time     = 30-JUN-2009 14:49:15
Current_time      = 30-JUN-2009 14:49:49

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.66723584[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.59979517[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = TRUE
Mod_return        = 1
Scans             = 733
Total_scans       = 733

X_90_width        = 15[us]
X_acq_time        = 1.66723584[s]
X_angle           = 30[deg]
X_atn             = 6[dB]
X_pulse           = 5[us]
Irr_atn_dec       = 28[dB]
Irr_atn_noe       = 28[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 1.5[s]
Recvr_gain        = 60
Relaxation_delay  = 1.5[s]
Repetition_time   = 3.16723584[s]
Temp_get          = 20.8[dC]
```

Figure S38: ^{1}H NMR spectrum of primary amine (2*R*,6*R*)-**23** (400 MHz, $CDCl_3$).

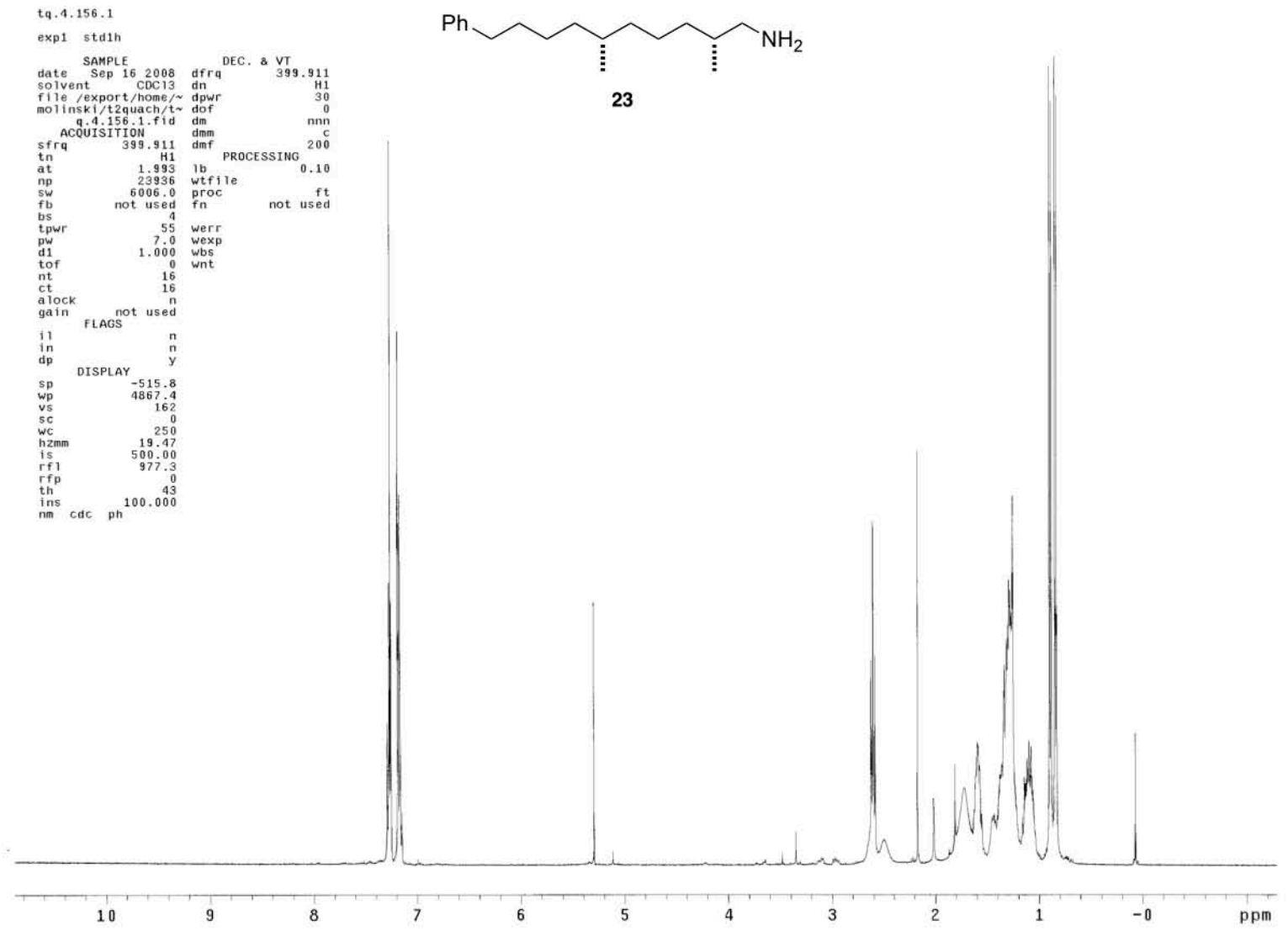


Figure S39: ^{13}C NMR spectrum of primary amine (2*R*,6*R*)-**23** (125 MHz, CD_3OD).

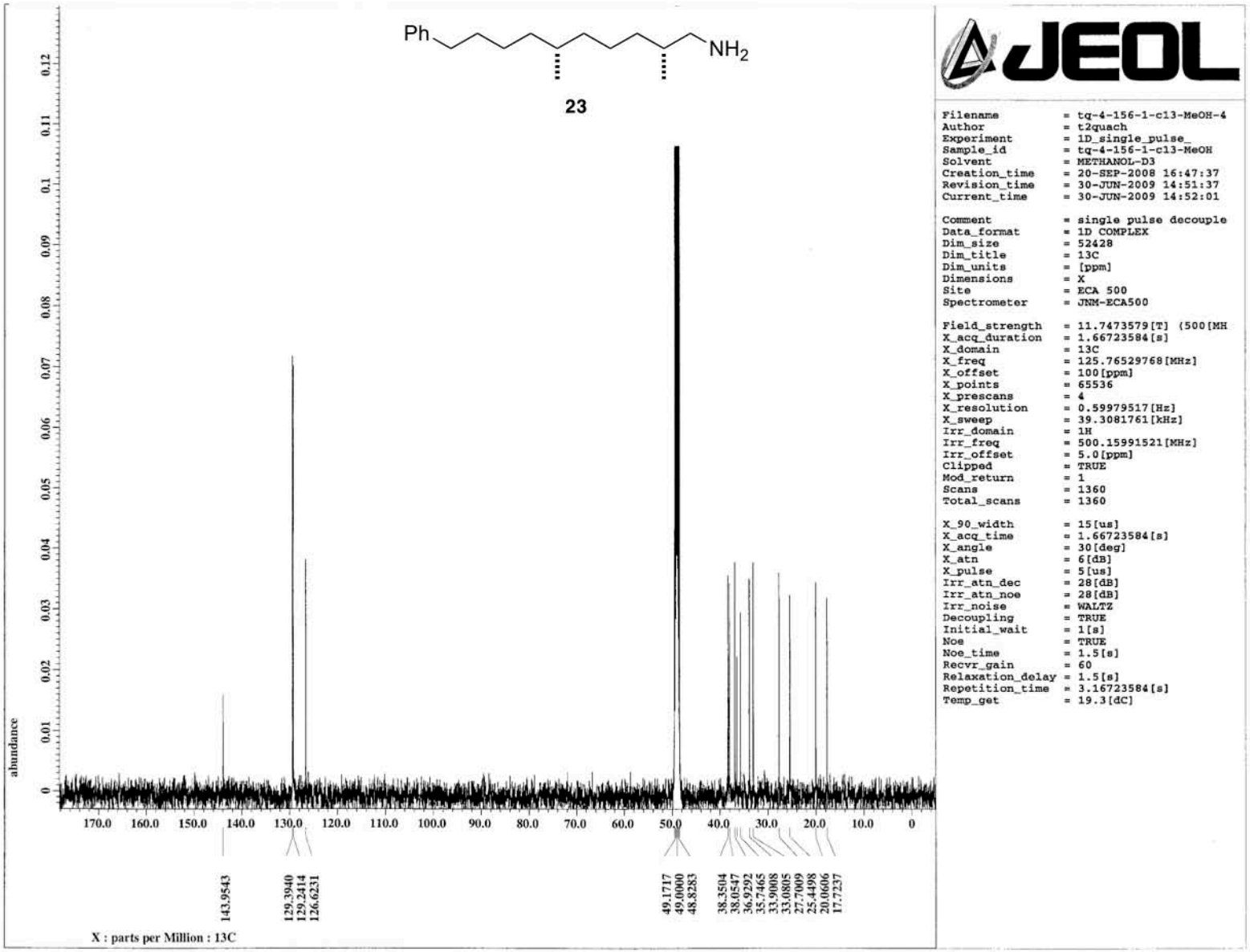
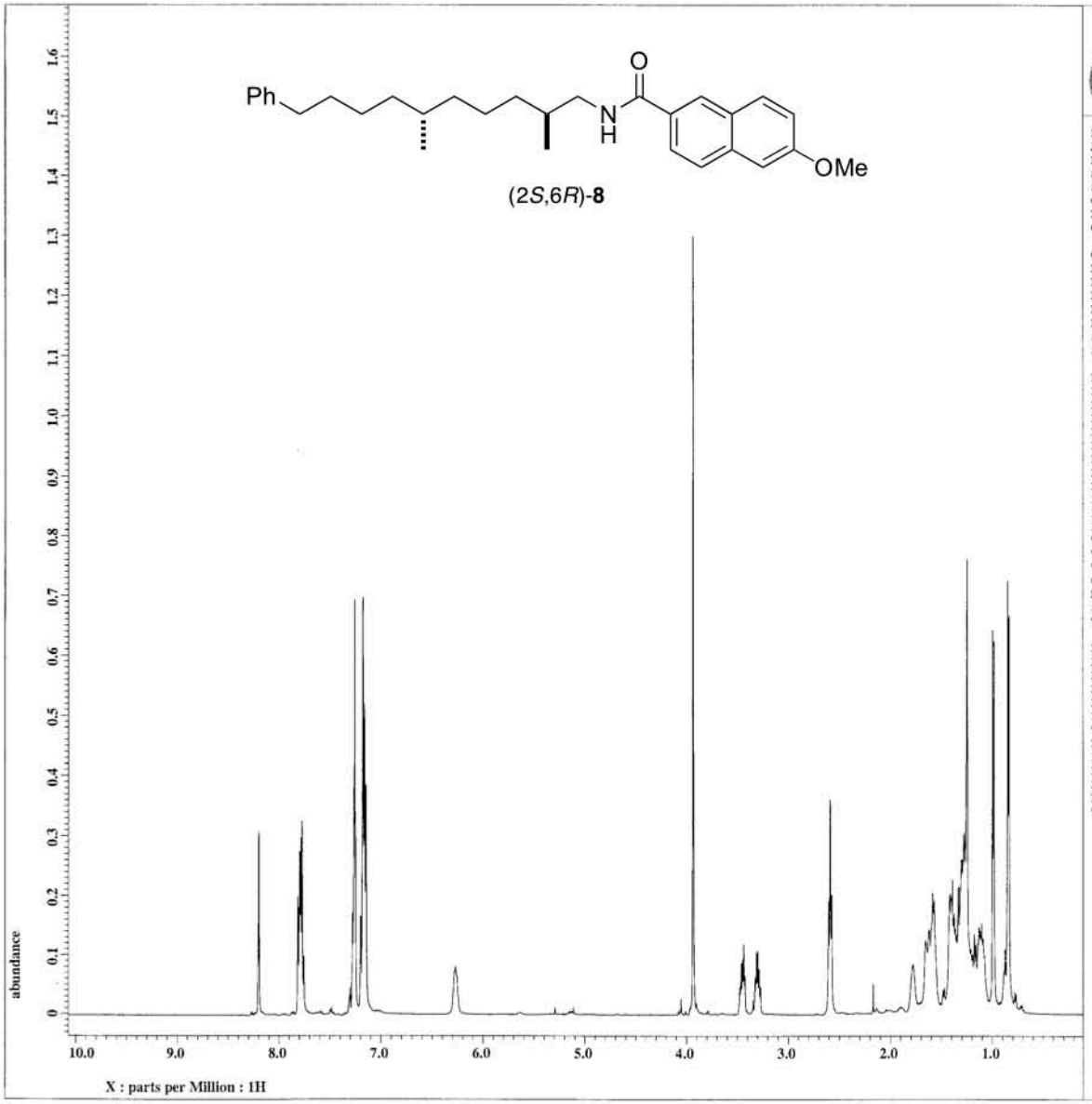
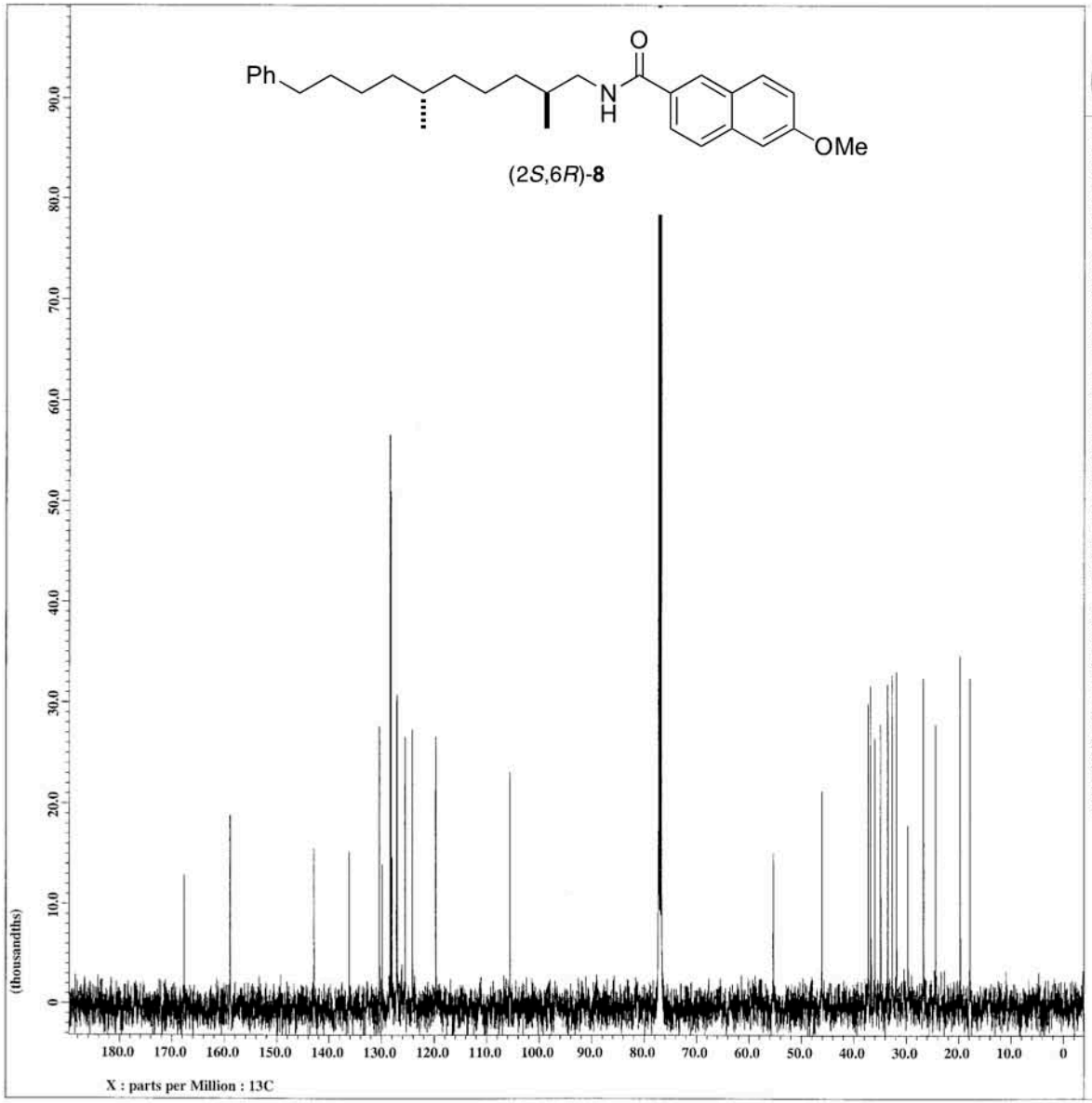


Figure S40: ^{1}H NMR spectrum of naphthamide (2*S*,6*R*)-**8** (500 MHz, $CDCl_3$).




```
Filename          = tq-4-162-1-4.jdf
Author            = t2quach
Experiment        = 1D_single_pulse.
Sample_id         = tq-4-162-1
Solvent           = CHLOROFORM-D
Creation_time     = 21-SEP-2008 15:11:16
Revision_time     = 14-JUL-2009 09:38:38
Current_time      = 14-JUL-2009 09:39:16

Comment           = single_pulse
Data_format       = 1D COMPLEX
Dim_size          = 26214
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 3.49175808[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 32768
X_prescans        = 1
X_resolution      = 0.28638868[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 7.74[us]
X_acq_time        = 3.49175808[s]
X_angle           = 45[deg]
X_atn             = 8[dB]
X_pulse           = 3.87[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 38
Relaxation_delay  = 2[s]
Repetition_time   = 5.49175808[s]
Temp_get          = 18.3[dC]
```

Figure S41: ^{13}C NMR spectrum of naphthamide (2*S*,6*R*)-**8** (125 MHz, $CDCl_3$).



JEOL

```
Filename          = tq-4-162-1-c13-3.jdf
Author            = t2quach
Experiment        = 1D_single_pulse_
Sample_id         = tq-4-162-1-c13
Solvent           = CHLOROFORM-D
Creation_time     = 21-SEP-2008 16:40:05
Revision_time     = 30-JUN-2009 14:53:19
Current_time      = 30-JUN-2009 14:53:40

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.66723584[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.59979517[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = TRUE
Mod_return        = 1
Scans             = 1635
Total_scans       = 1635

X_90_width        = 15[us]
X_acq_time        = 1.66723584[s]
X_angle           = 30[deg]
X_atn             = 6[dB]
X_pulse           = 5[us]
Irr_atn_dec       = 28[dB]
Irr_atn_noe       = 28[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 1.5[s]
Recvr_gain        = 60
Relaxation_delay  = 1.5[s]
Repetition_time   = 3.16723584[s]
Temp_get          = 18.7[dC]
```

Figure S42: ^{1}H NMR spectrum of naphthamide (2*R*,6*R*)-**9** (400 MHz, $CDCl_3$).

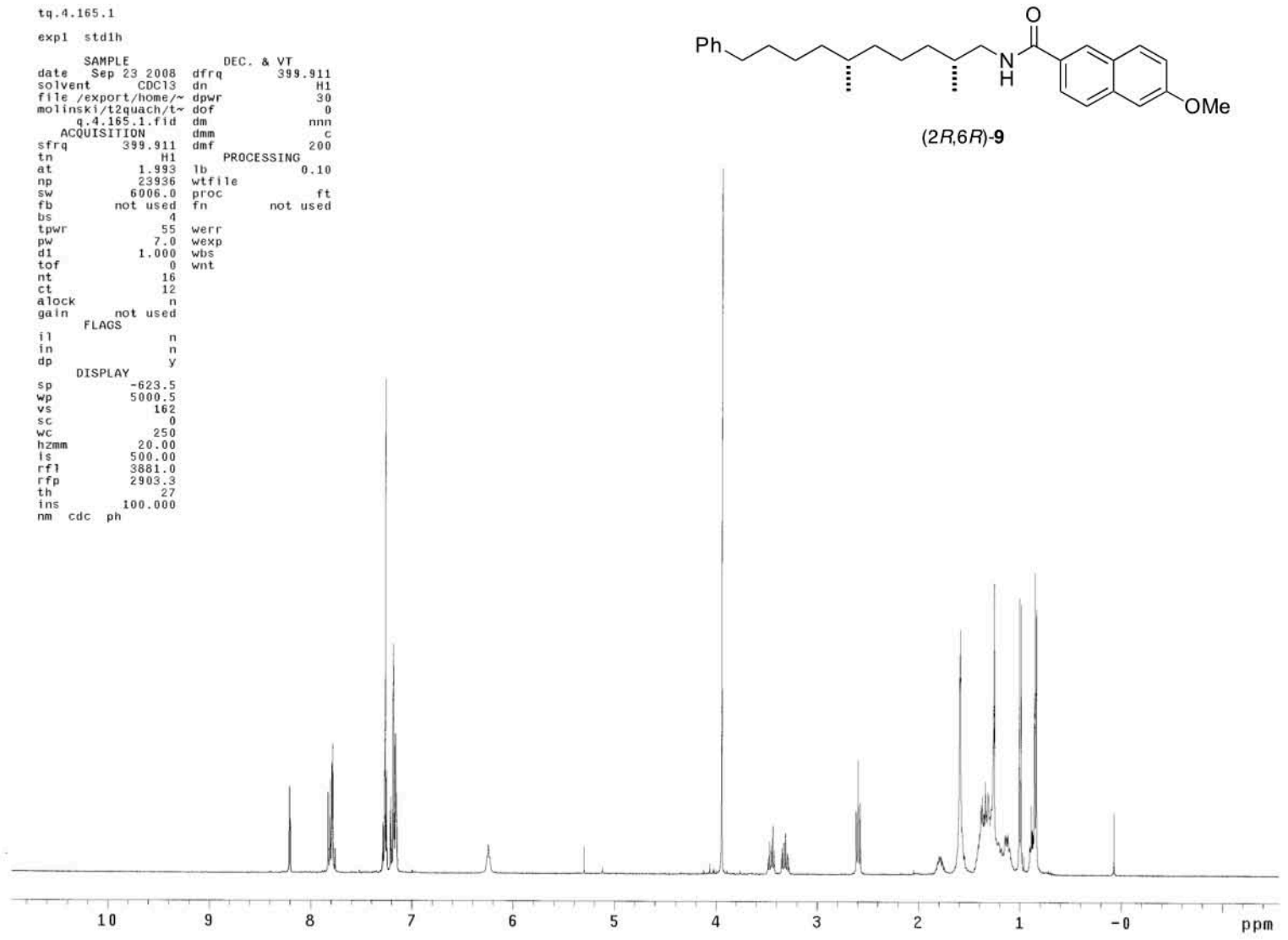
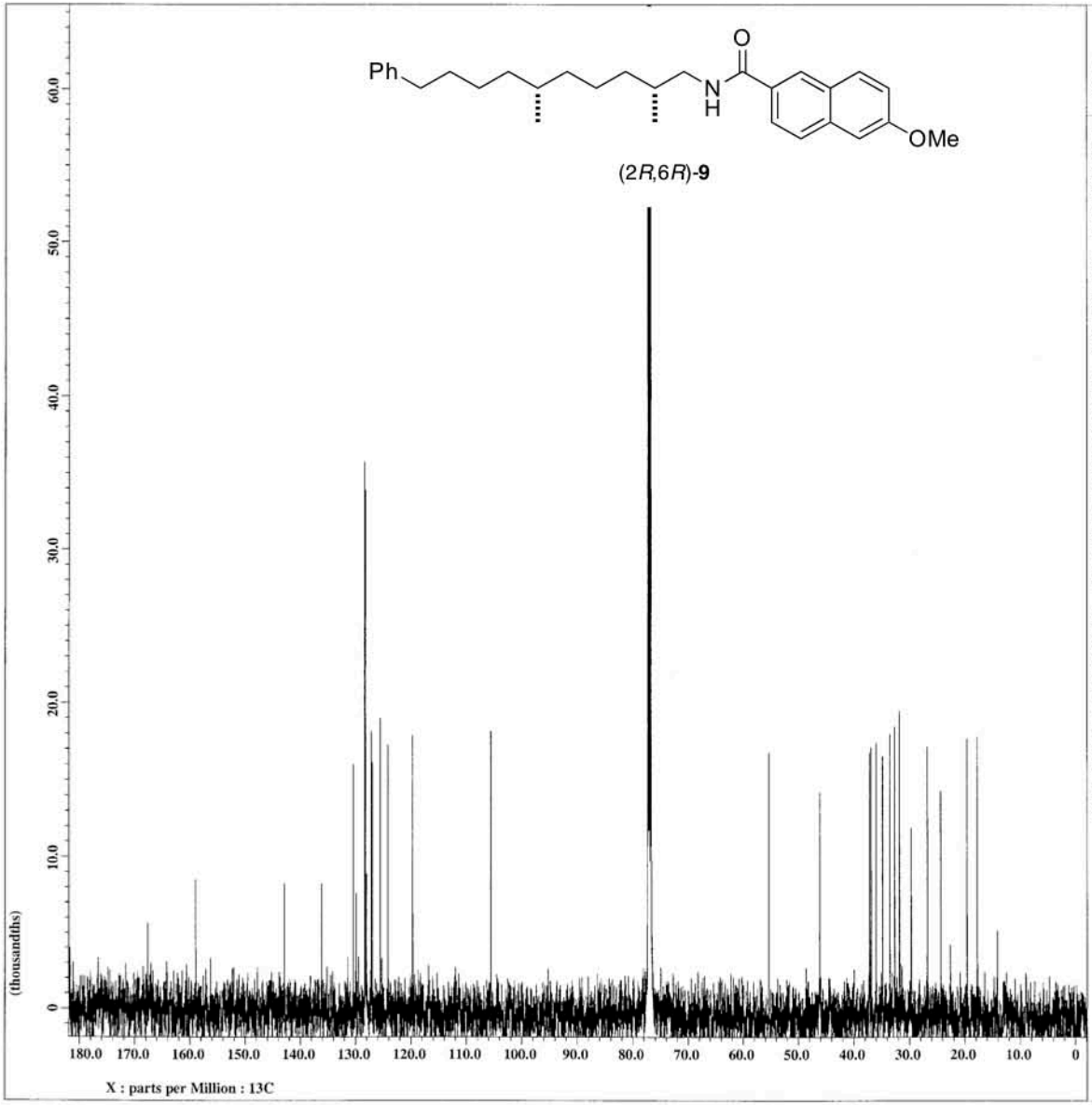


Figure S43: ^{13}C NMR spectrum of naphthamide (2*R*,6*R*)-**9** (125 MHz, $CDCl_3$).



JEOL

```
Filename          = tq-4-165-1-c13-3.jdf
Author            = t2quach
Experiment        = 1D_single_pulse_
Sample_id         = tq-4-156-1-c13
Solvent           = CHLOROFORM-D
Creation_time     = 24-SEP-2008 17:18:25
Revision_time     = 30-JUN-2009 14:54:33
Current_time      = 30-JUN-2009 14:54:51

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.66723584[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.59979517[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = TRUE
Mod_return        = 1
Scans             = 1809
Total_scans       = 1809

X_90_width        = 15[us]
X_acq_time        = 1.66723584[s]
X_angle           = 30[deg]
X_atn             = 6[dB]
X_pulse           = 5[us]
Irr_atn_dec       = 28[dB]
Irr_atn_noe       = 28[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 1.5[s]
Recvr_gain        = 60
Relaxation_delay  = 1.5[s]
Repetition_time   = 3.16723584[s]
Temp_get          = 21.6[dC]
```