Efficient Total Synthesis of (+)-Negamycin, a Potential Chemotherapeutic Agent for Genetic Diseases.

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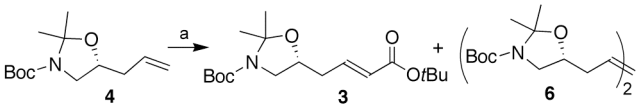
Supporting information

Additional Data

Table A. Optimization for CM reaction



4 **3** **6**

Entry	Catalyst	Conditions	Conversion (%)[c]	**3**/**6** ratio[c]
1	[Ru]-**I**	rt/24 h	50	44/66
2	[Ru]-**I**	reflux/5 h	36	41/59
3	[Ru]-**I**	µW/15 min	47	24/76
4	[Ru]-**II**	rt/24 h	95	97/3
5	[Ru]-**II**	reflux/5 h	96	>99/traces
6b	[Ru]-**II**	reflux/5 h	90	95/5
7	[Ru]-**II**	µW/15 min	100 (83)[d]	100/ 0
8b	[Ru]-**II**	µW/15 min	96	97/3

[a] Reagents and conditions: (i) *tert*-butyl acrylate, [Ru] 5 mol %, CH_2Cl_2. [b] 1 equiv of *tert*-butyl acrylate. [c] Measured by 1H NMR of the crude mixture [d] Isolated yield (SiO_2 column chromatography, eluent : hexane/ethyl acetate = 80/20).

EXPERIMENTAL PART

1. General information

NMR spectra (^{1}H and ^{13}C) were recorded on a JEOL JNM-AL300 (^{1}H:300 MHz; ^{13}C: 75.5 MHz) or a Varian UNITY INOVA 400NB (^{1}H:400 MHz; ^{13}C:100 MHz) spectrometer and the chemical shift values were expressed in parts per million downfield from tetramethysilane (TMS) as an internal standard. All coupling constants (*J* values) were reported in Hertz (Hz). Melting points were taken on a micro hot-stage apparatus (Yanagimoto). Mass spectra (MS) were obtained by electron impact (EI, CI) ionization methods on JEOL GCmate MS-BU20. Elemental analyses were done on a Perkin-Elmer Series CHNS/O Analyzer 2400. Specific Rotations were recorded on a Horiba High-speed Accurate Polarimeter SEPA-300 with a sodium lamp and are reported as follows: $[\alpha]_D^T$ (c g/100 mL, solvent). Microwave experiments were carried out with a CEM Discover oven. Preparative HPLC was carried out using a Waters 600E system equipped with a UV detector. Organic extracts were dried over sodium sulfate (Na_2SO_4), filtered, and concentrated using a rotary evaporator at <40 °C bath temperature. Solids and non volatile oils were vacuum dried at <2 mmHg.

2. Materials

Commercially available chemicals were obtained from Waco Pure Chemical Industries, Ltd. (Osaka, Japan), Nacalai Tesque, Inc. (Kyoto, Japan), Aldrich Chemical Co., Inc. (Milwaukee, WI), Tokyo Kasei Kogyo Co., Ltd. (Tokyo, Japan), Kishida Chemical Co., Ltd. (Osaka, Japan), and used without further purification. Column chromatography was carried on Merck 107734 silica gel 60 (70-230 mesh). Analytical thin layer chromatography (TLC) was performed using Merck 105715 silica gel 60 F_{254} precoated plates (0.25 mm thickness) and compounds were visualized by UV illumination (254 nm) and by heating after spraying ca. 0.7% ethanolic solution of ninhydrin.

3. Total synthesis of (-)-Negamycin

3-1. (*R*)-*tert*-Butyl 5-allyl-2,2-dimethyloxazolidine-3-carboxylate (4)

To a solution of *B*-allyl-diisopinocampheylborane [(+)-Ipc_2B(allyl)] (4 mL of 1M solution in pentane, 4 mmol) dissolved in Et_2O (4 mL) was added at -100°C a solution of N-Boc-2-aminoacetaldehyde (636 mg, 4 mmol) dissolved in Et_2O cooled to -78°C (4 mL). The reaction mixture was stirred for 2 hours at -100°C and MeOH (600 μL), 1N NaOH (4.8 mL) and H_2O_2 (450 μL) were added. Oxidation was completed by refluxing 3h before addition of water for extraction. The aqueous phase was washed twice with EtOAc, the organic layers were combined and dried over Na_2SO_4. After filtration and evaporation of the solvent under reduced pressure, the residue was dissolved in acetone and both 2,2-

Supplementary Material (ESI) for Chemical Communications

dimethoxypropane and boron trifluoride, ethyl ether complex were added at room temperature. The reaction mixture was stirred under reflux at 66 °C for over night. The solution was poured into sat. $NaHCO_3$ aq., and acetone was removed under reduced pressure. The resulting residue was extracted with AcOEt and washed consecutively with sat. $NaHCO_3$ aq., brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, the residue was applied to silica-gel column chromatography ($CHCl_3$:MeOH=15:1) to yield the desired compound **4** with 90% yield as colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.74 (m, 1H), 5.16-5.08 (m, 2H), 4.17-4.05 (m, 1H), 3.55-3.73 (m, 1H), 3.05-3.15 (m, 1H), 2.23-2.50 (m, 2H), 1.46 (br s, 15H); $[\alpha]_D^{24.9}$ -46.8 ° (c 1.00, $CHCl_3$); HRMS (EI+) calculated for $C_{13}H_{23}NO_{35}$ (M^+) 241.3270, found 241.3300.

3-7. (*S*)-*tert*-Butyl 5-[(*E*)-3-(*tert*-butoxycarbonyl)allyl] -2,2-dimethyloxazolidine-3 –carboxylate (3).
In a microwave reactor, to a solution of Grubbs catalyst second generation (10,5 mg, 0.0125 mmol) dissolved in CH_2Cl_2 (250 μL) was added dropwise a mixture of **4** (60 mg, 0.25 mmol) and *tert*-butyl acrylate (108 μL, 1.25 mmol) in CH_2Cl_2 (250 μL). The reaction mixture was irradiated for 15 minutes (Temperature set to 40 °C and automatically controlled by the oven). The residue was then applied to silica-gel column chromatography (hexane:AcOEt=10:1) to yield the desired compound **3** as light-yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (td, *J* = 7.0, 16.0 Hz, 1H), 5.85 (d, *J* = 15.7 Hz, 1H), 4.19-4.14 (m, 1H), 3.73-3.65 (m, 1H), 3.13-3.04 (m, 1H), 2.55-2.42 (m, 2H), 1.57 (br s, 3H), 1.54 (br s, 3H), 1.48 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 152.2, 141.9, 125.8, 93.7, 93.3, 80.4, 79.6, 72.2, 72.0, 50.5, 35.6, 28.4, 28.1, 27.2, 26.2, 25.3, 24.3; $[\alpha]_D^{24.6}$ -26.2 ° (c 1.06, $CHCl_3$); HRMS (EI+) calculated for $C_{18}H_{31}N_1O_5$ (M^+) 341.2202, found 341.2200.

3-8. (*R*)-*tert*-Butyl-5-{(*R*)-3-(*tert*-butoxycarbonyl)-2-[*N*-benzyl-*N*-((2-methoxy-7,7-dimethylbicyclo[2,2,1]heptan-1-yl)methyl)amino]propyl}-2,2-dimethyloxazolidine-3-carboxylate (8).
A 2.6M solution of *n*-butyllithium in hexane (112 μL) was added to a solution of **7** (80.0 mg, 0.298 mmol) in tetrahydrofurane (1.0 mL) and the mixture was stirred at -50 °C. After passing 1 hour, a solution of **3** (50 mg, 0.146 mmol) in tetrahydrofurane (0.7 mL) was added dropwise to the reaction mixture, which was stirred at -40 °C for another 2 hours. After quenching the reaction by adding a saturated solution of sodium sulfate, the mixture was extracted with chloroform. The organic layer was washed with a saturated solution of sodium chloride, dried over anhydrous sodium sulfate, and condensed *in vacuo*. The residue was purified by silica gel column chromatography (n-hexane : ethyl acetate = 10:1) to afford compound **8** (72.1 mg, 80.4%) accompanying with the recovered starting material **3** (8.3 mg, 16.6 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 4H), 7,22-7.18 (m, 1H), 4.31 (br s, 1H), 3.83 (d, *J* = 14 Hz, 1H), 3.67-3.63, 3.57-3.53 (m, total 1H), 3.47 (dd, *J* = 7.2, 2.8 Hz, 1H), 3.32-3.27 (m, 1H), 3.25, 3.21 (s, total 1H), 3.18 (s. 3H), 3.01-2.93 (m, 2H), 2.81-2.70 (m, 2H), 2.18 (d, *J* = 13.6 Hz, 1H), 2.12-2.03 (m, 1H), 1.79-1.73 (m, 2H), 1.65-1.26 (m, 12H), 1.47 (s, 9H), 1.43 (s, 9H), 0.91 (s, 3H), 0.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 152.4, 140.7, 129.2, 128.0, 126.6, 93.2, 92.8, 85.0, 80.2, 79.8, 79.2, 70.7, 70.1, 54.8, 54.0, 52.6, 51.3, 50.9, 47.7, 45.5, 30.8, 28.5, 28.1, 27.4, 27.2, 26.4, 25.3, 24.4, 20.6, 20.4; $[\alpha]_D^{24.6}$ -14.0 ° (c 1.01, $CHCl_3$); HRMS (EI+) calculated for $C_{36}H_{58}N_2O_6$ (M^+) 614.4294, found 614.4286.

3-9. (*R*)-*tert*-Butyl-5-{(*R*)-3-(*tert*-butoxycarbonyl)-2-aminopropyl}-2,2-dimethyl-oxazolidine-3-carboxylate (9).

Under Ar atomosphere, the solution of *tert*-butyl ester **8** (200.00 mg, 0.43 mmol) in anhydrous CH_2Cl_2 (3 mL) was added to NIS (293.00 mg, 1.30 mmol) light shielding at room temperature. The reaction mixture was stirred at room temperature for 2 h. The solution was poured into sat. $NaHCO_3$ aq., and the organic phase was extracted with $CHCl_3$, wash with 10 % $Na_2S_2O_3$aq. and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, the residue was applied to silica-gel column chromatography (hexane:AcOEt=20:1) to yield the desired compound **9** as light-yellow oil (80.4 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.25-4.18 (m, 1H), 3.73-3.65 (m, 1H), 3.40-3.33 (m, 1H), 3.08-3.06 (m, 1H), 2.44 (dd, *J* = 4.0, 15.6 Hz, 1H), 2.24 (dd, *J* = 8.8, 15.6 Hz, 1H), 1.74 (br s, 2H), 1.69 (dd, *J* = 4.6, 7.9 Hz, 1H), 1.64-1.61 (m, 1H), 1.57 (br s, 3H), 1.53 (br s, 3H), 1.47 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 152.2, 93.4, 92.9, 80.7, 80.0, 79.4, 71.2, 70.9, 51.1, 45.8, 44.1, 40.4, 28.4, 28.1, 27.3, 26.3, 25.2, 24.3; $[\alpha]_D^{25.3}$ -11.8 ° (c 1.05, $CHCl_3$); HRMS (EI+) calculated for $C_{18}H_{34}N_2O_5$ (M^+) 358.2467, found 358.2474.

3-10. (*R*)-*tert*-Butyl-5-{(*R*)-3-(*tert*-butoxycarbonyl)-2-*tert*-butoxycarbony-aminopropyl}-2,2-dimethyl oxazolidine-3-carboxylate (11).

To solution of amine **9** (82.40 mg, 0.23 mmol) in THF (2.3 mL) was added to $(Boc)_2O$ (64.2 mg, 0.29 mmol) and Et_3N (48.00 μL, 0.35 mmol) dropwise at 0 °C. The reaction mixture was stirred at room temperature for 5 h. The solvent was removed under reduced pressure. The resulting residue was extracted with AcOEt and washed consecutively with 10% cirtic acid aq., sat. $NaHCO_3$ aq., brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, the residue was applied to silica-gel column chromatography ($CHCl_3$) to yield the desired compound **11** as light-yellow oil (105.2 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (br s, 1H), 4.17-4.10 (m, 1H), 4.08-3.92 (m, 1H), 3.78-3.58 (m, 1H), 3.04 (t, *J* = 9.0 Hz, 1H), 2.50 (d, *J* = 5.7 Hz, 2H), 1.92-1.69 (m, 2H), 1.56 (s, 3H), 1.52 (s, 3H), 1.47 (s, 9H), 1.45 (s, 9H), 1.44 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 155.1, 151.8, 93.3, 93.0,

81.0, 80.0, 79.4, 79.2, 71.6, 71.0, 51.0, 45.7, 40.3, 37.6, 28.4, 28.4, 28.1, 27.3, 26.2, 25.1, 24.2; $[\alpha]_D^{24.2}$ -14.1 ° (c 1.15, $CHCl_3$); HRMS (CI+) calculated for $C_{23}H_{43}N_2O_7$ (M^++H) 459.3070, found 459.3073.

3-11.(*R*)-4-{(*R*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyloxazolidin-5-yl}-3-(*tert*-butoxycarbonylamino)butanoic acid (2).

To solution of *tert*-butyl ester **11** (105.2 mg, 0.23 mmol) in 2M KOH in MeOH (4 mL) was irradiated under microwave cavity with an output at 10 W for 15 min at 100 °C. The solution was poured into 10 % citric acid aq. And the organic phase was extracted with AcOEt, wash brine, and dried over Na_2SO_4. The solvent was removed under pressure. The resulting light-yellow oil (92.1 mg, 99%) was used for next reaction without purification.

3-12. (*R*)-*tert*-Butyl-(*R*)-5-[2-(*tert*-butoxycarbonylamino)-3-{(*tert*-butoxycarbonyl methyl)methylaminocarbamoyl}propyl]-2,2-dimethyloxazolidine-3-carboxylate (13).

Under Ar atomosphere, the solution of acid **2** (73.8 mg, 0.183 mmol) and tert-butyl-2-(N-methylhydrazino)acetate · PTSA **12** (118.2 mg, 0.37 mmol) and HOBt (56.0 mg, 0.37 mmol) in anhydrous CH_2Cl_2 (2.5 mL) was cooled to 0 °C, and Et_3N (51 μL, 0.09 mmol) was added dropwise, then EDC· HCl was added. The reaction mixture was stirred for 2 h at room temperature. The solution was poured into 10 % citric acid aq., and the organic phase was extracted with AcOEt, wash with sat. $NaHCO_3$ aq. brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, the residue was applied to silica-gel column chromatography ($CHCl_3$:MeOH=50:1) to yield the desired compound **13** as light-yellow oil (99.6 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93, 7.33 (br s, total 1H), 5.74-5.22 (m, 1H), 4.16-4.09 (m, 1H), 3.99 (br s, 1H), 3.56 (d, J = 5.6 Hz, 2H), 3.06-3.02 (m, 1H), 2.76, 2.73 (s, total 3H), 2.47-2.36 (m, 2H), 1.98 (br s, 1H), 1.71-1.68 (m, 2H), 1.59 (br s, 3H), 1.55 (br s, 3H), 1.48 (s, 9H), 1.47 (s, 9H), 1.43 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 170.0, 169.0, 155.2, 152.1, 151.7, 93.4, 93.1, 82.3, 82.1, 79.9, 79.3, 79.1, 78.8, 71.8, 59.2, 58.2, 50.9, 46.6, 44.9, 43.8, 38.5, 37.8, 37.0, 28.34, 28.29, 28.0, 27.2, 26.1, 25.0, 24.2; $[\alpha]_D$24.2 -5.5 ° (c 1.07, $CHCl_3$); m.p. 135-136 °C; HRMS (CI+) calculated for $C_{26}H_{48}N_4O_8$ (M^++H) 544.3472, found 544.3470.

3-13. 2-[(3*R*,5*R*)-3,6-Diamino-5-hydroxy-hexanoyl]-1-methylhydrazinoacetic acid. [(+)-Negamycin]

The compound **13** (19.0 mg, 0.04 mmol) was treated with 4M HCl/dioxane (2 mL) at 0 °C. The reaction mixture was stirred at same temperature for 2 h. The solvent was removed under pressure; the remaining crude light-yellow oil was purified by ion exchange chromatography on Amberlite CG50

(NH_4^+ form) or by preparative HPLC. ^{1}H NMR (400 MHz, D_2O) δ 3.97-3.89 (m, 1H), 3.55-3.49 (m, 1H), 3.24 (s, 2H), 2.97 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.80 (dd, *J* = 13.2, 9.2 Hz, 1H), 2.48 (s, 3H), 2.39-2.36 (m, 2H), 1.79-1.56 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 170.8, 64.3, 60.9, 45.5, 44.3, 43.8, 41.8, 39.3; $[\alpha]_D^{25.2}$ +2.4 ° (c 0.36, H_2O), lit. $[\alpha]_D^{29.0}$ +2.5 ° (c 2.00, H_2O); m.p. 135-136 °C; HRMS (FAB+) calculated for $C_9H_{21}N_4O_4$ (M^++H) 249.1563, found 249.1559.

3.14. *tert*-Butyl 2-(*N*-methylhydrazino)acetate.PTSA (12)

At 0 °C, Et_3N (11.1 mL, 79.31 mmol) and *tert*-butyl 2-bromoacetate (1.0 M solution in CH_2Cl_2, 8.4 mL, 56.56 mmol) were added dropwise to a solution of methylhydrazine (3.0 mL, 56.56 mmol) in CH_2Cl_2 (190 mL). The reaction mixture was then stirred at room temperature overnight. Solvent was removed under reduced pressure and residue is dissolved with an AcOEt/MeOH mixture (15:1), filtrated and the resulting solution was evaporated under reduced pressure. The residue was applied to silica-gel column chromatography (AcOEt/MeOH =15:1) to yield the desired compound as colorless oil (7.5 mg). The pure compound was then dissolved in THF (70.0 mL) and *p*-toluenesulfonique acid (8.864g, 46.60 mmol) was added. The reaction mixture was stirred at this temperature for 30 minutes before filtration. The cake was washed with Et_2O. The solution was then evaporated under reduced pressure to yield the desired compound **12** as a white powder (10.4 g, 50% for 2 steps) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 9.0 Hz, 2H), 7.16 (d, *J* = 9.0 Hz, 2H), 3.73 (s, 2H), 2.90 (s, 3H), 2.36 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 141.5, 140.4, 128.9, 126.0, 83.5, 57.7, 43.9, 27.9, 21.3; m.p. 131-133 °C; HRMS (EI+) calculated for $C_7H_{16}N_2O_2$ (M^+) 160.1212, found 160.1214; Anal. Cald for $C_7H_{16}N_2O_2$: C, 50.58; H, 7.28; N. 8.48; found C, 50.48; H, 7.35; N. 8.36.

HCl form

,1 std1h

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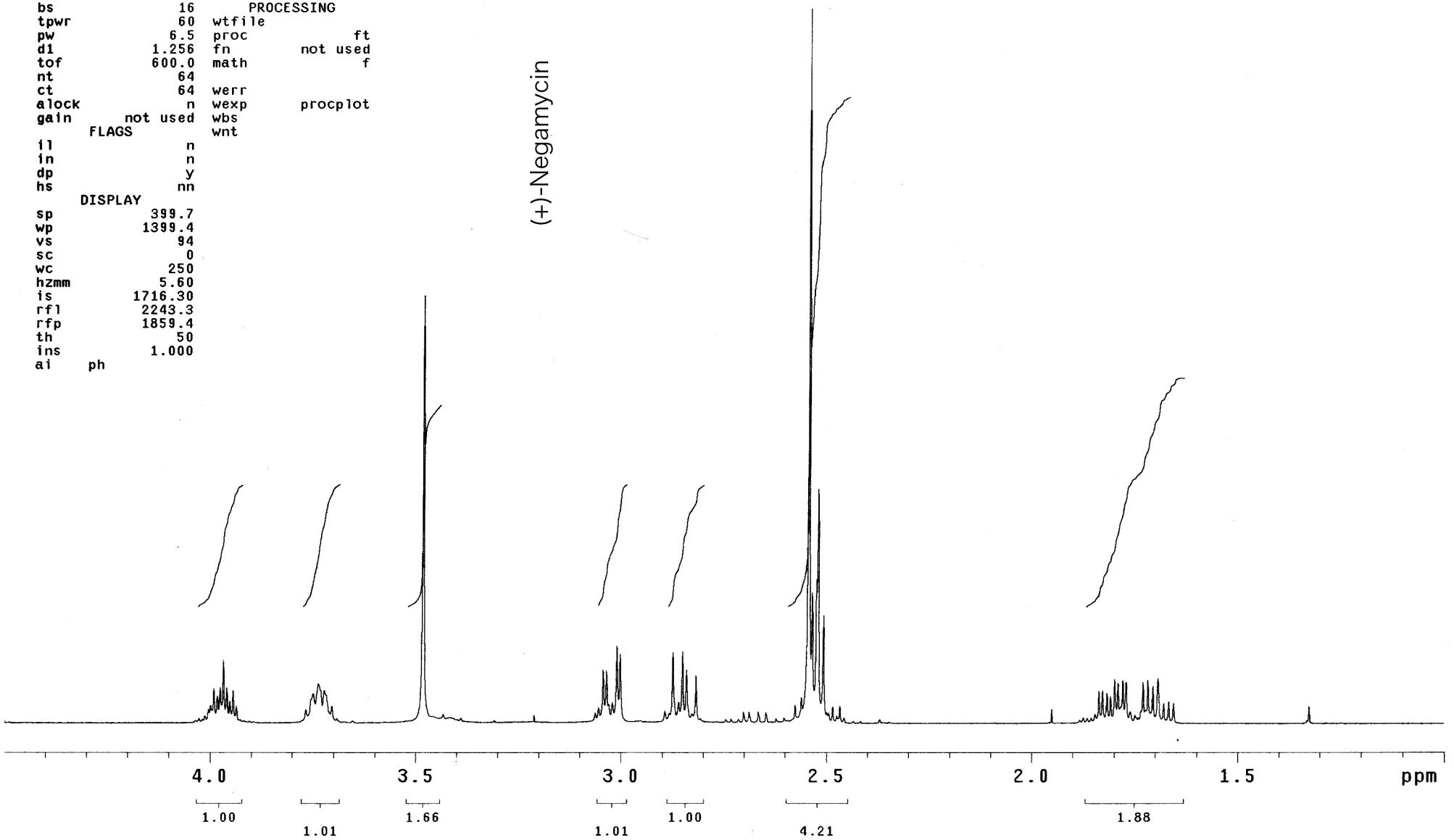
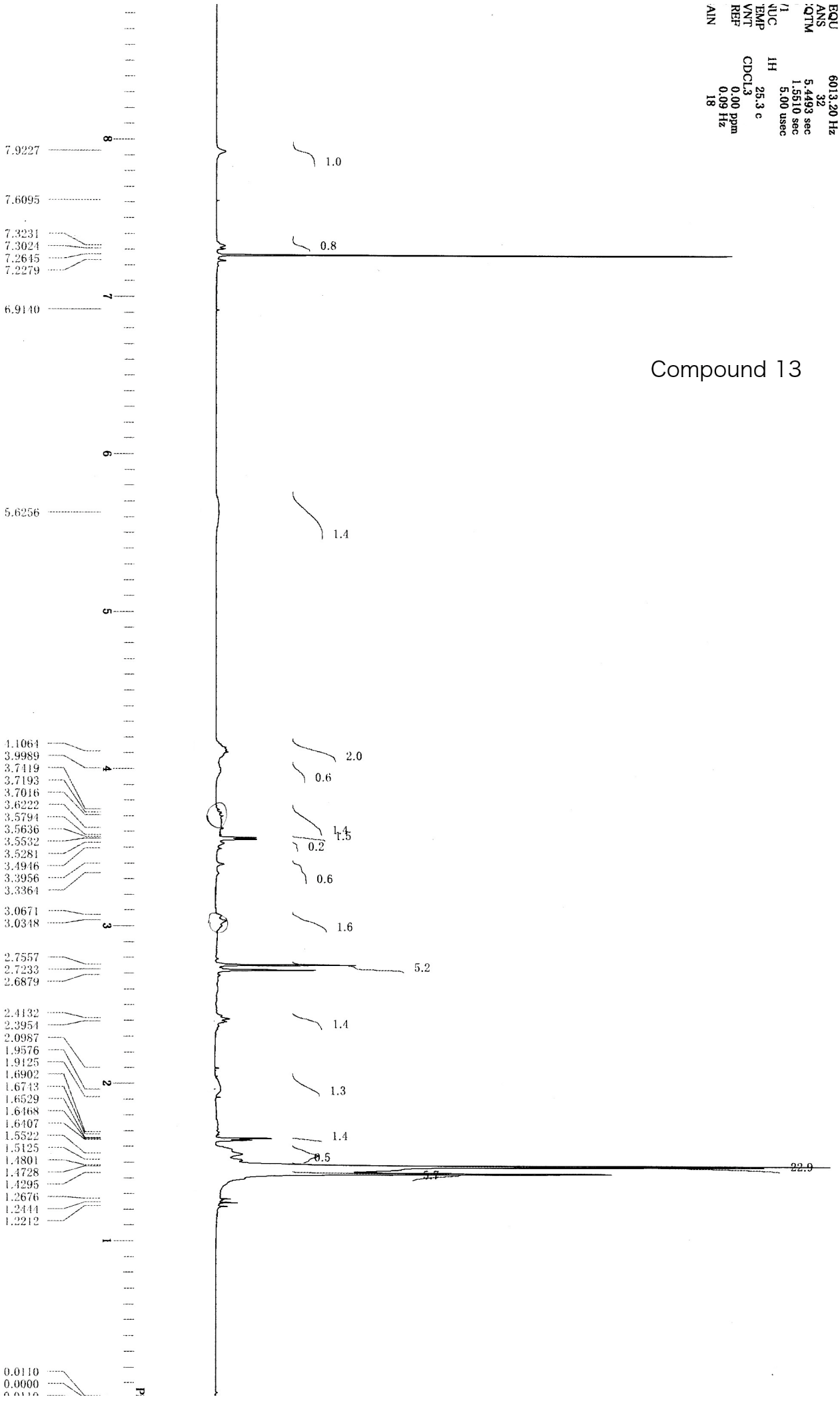
(+)-Negamycin





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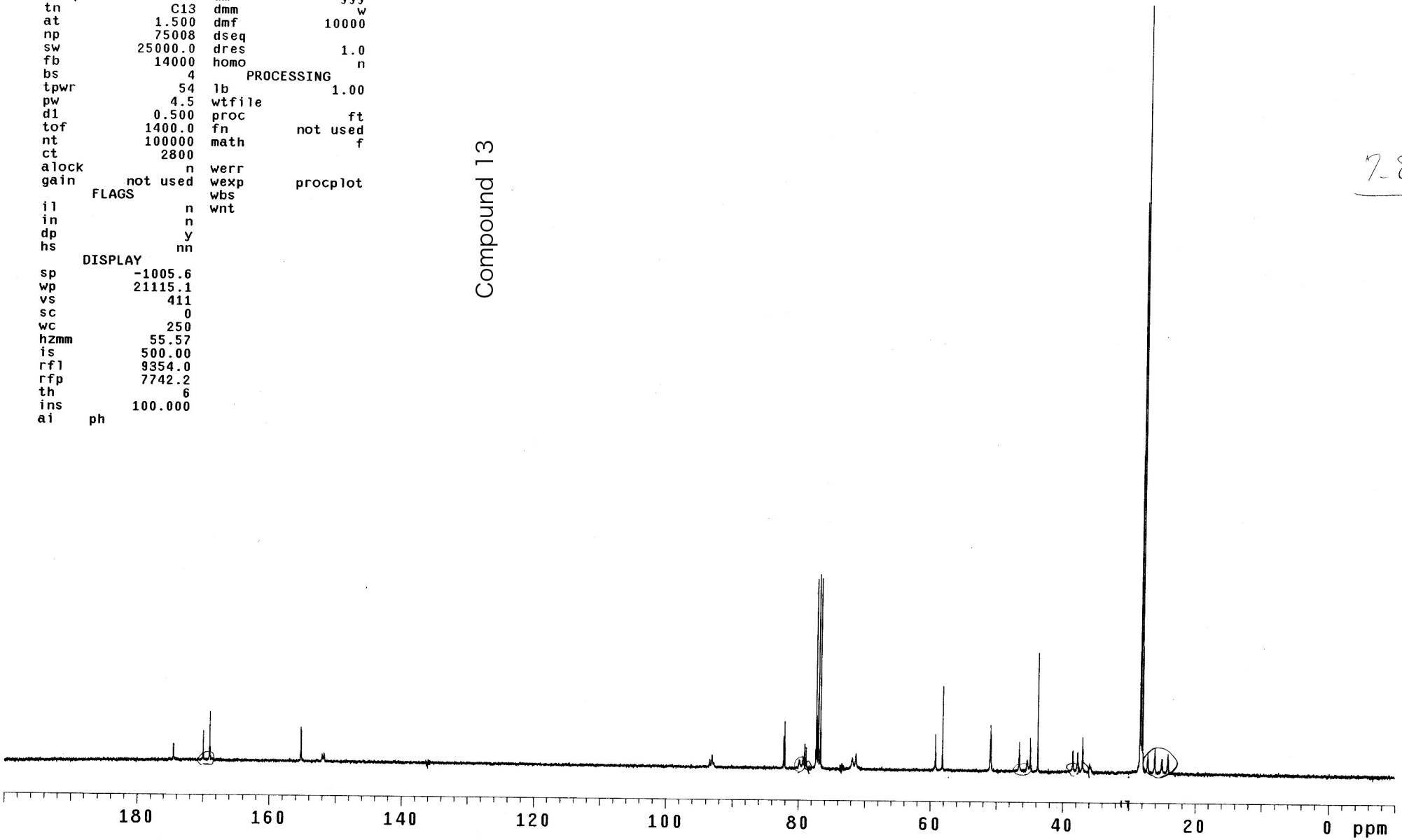
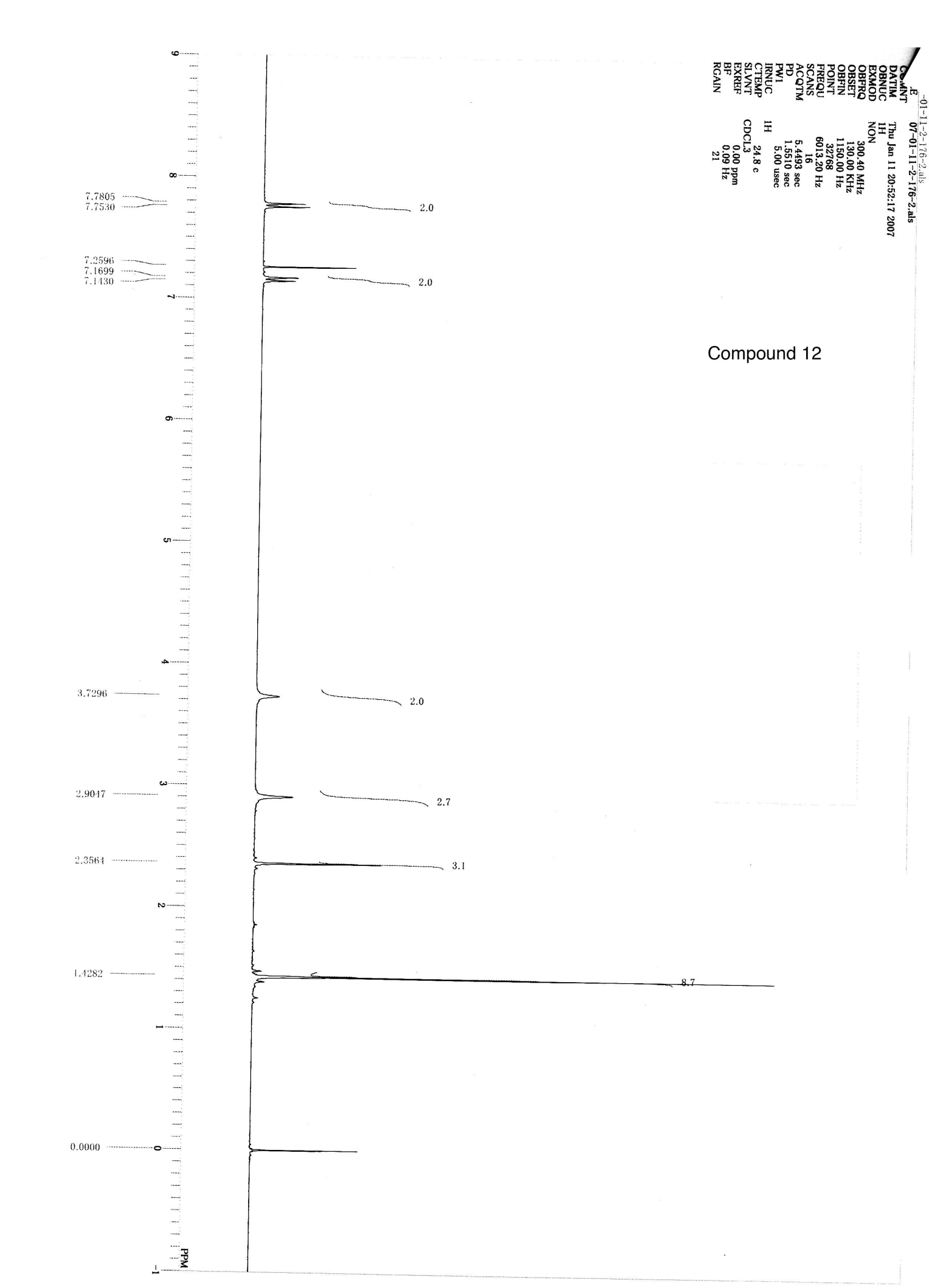
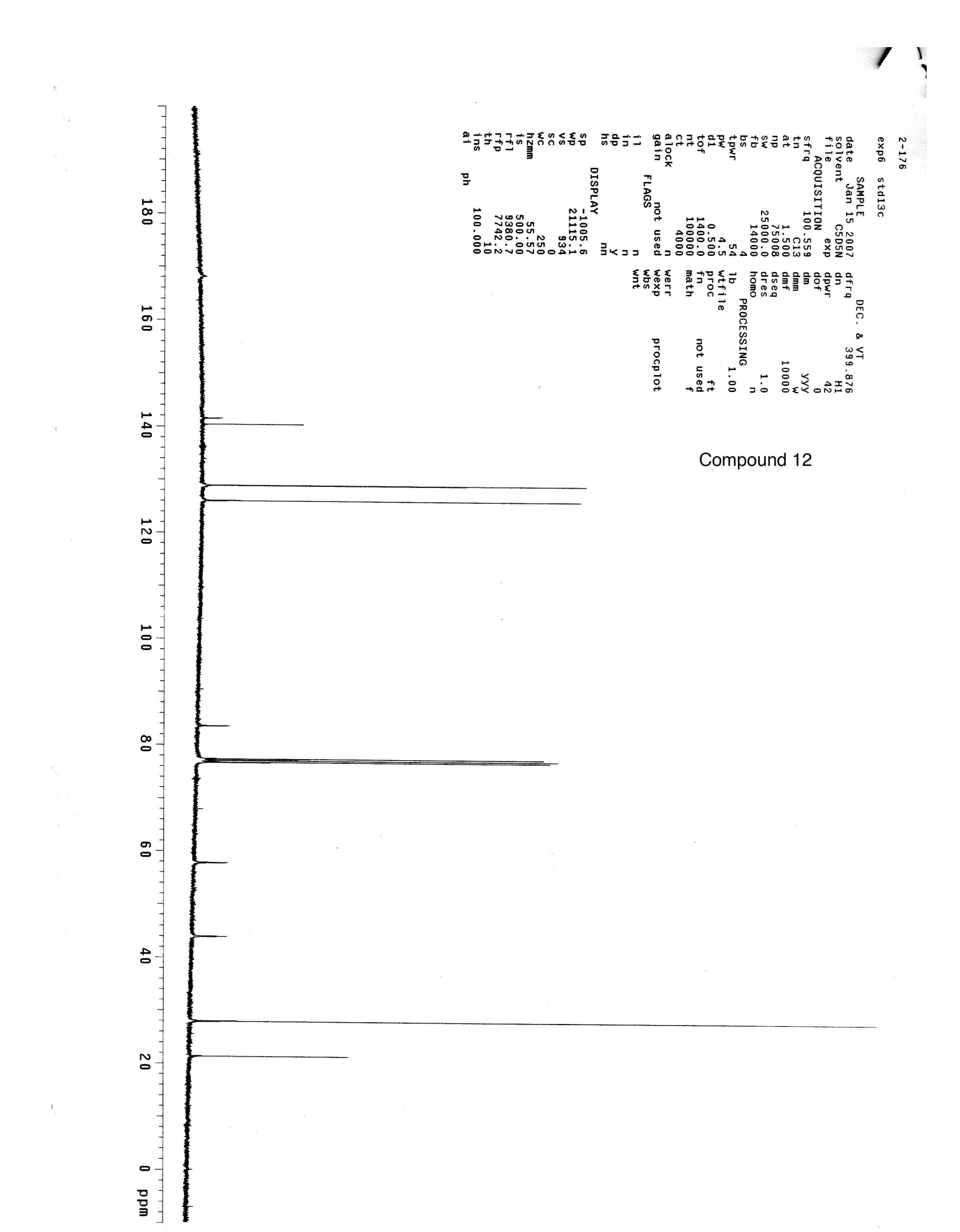
Compound 13

7-8.9





Compound 12



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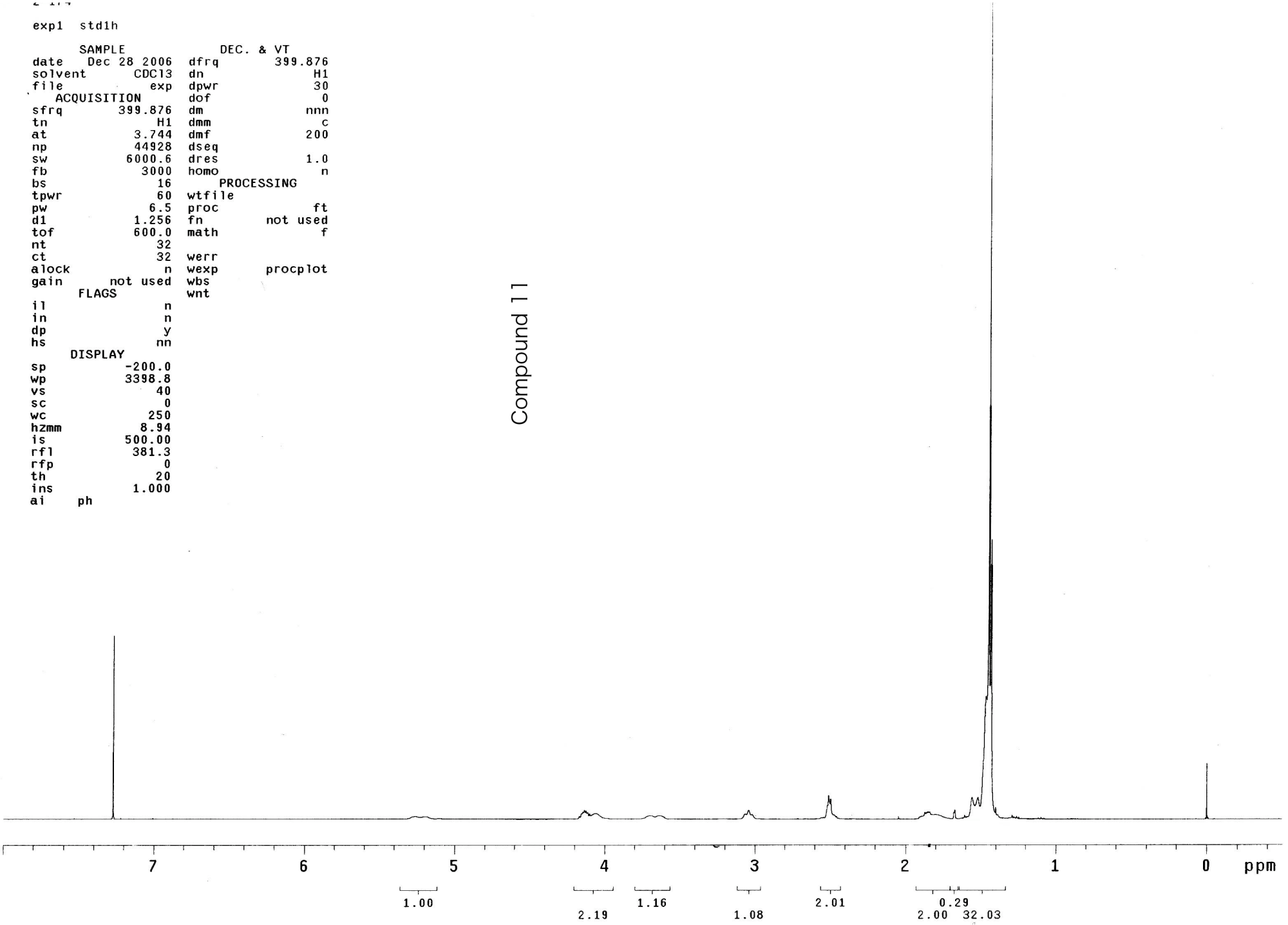
Compound 11



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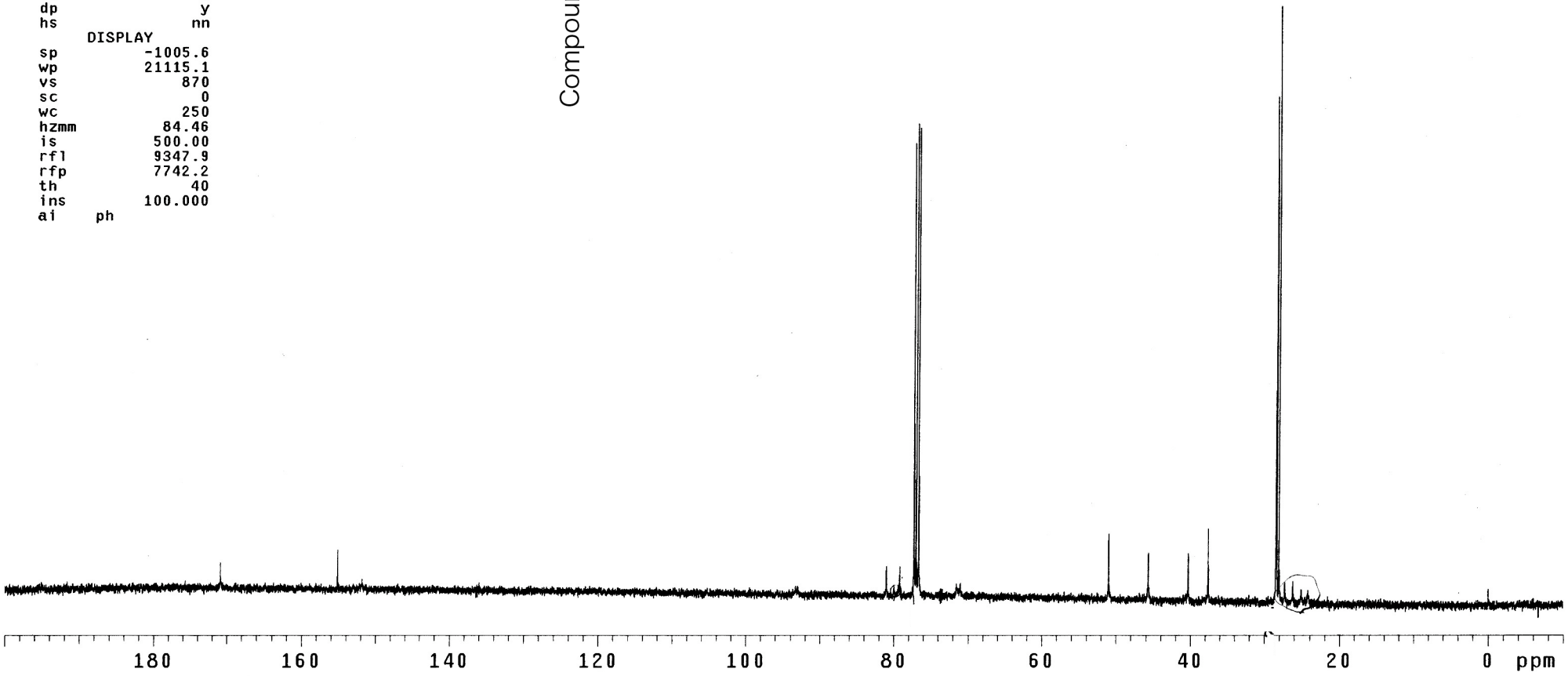
fb	14000	homo	n
bs	4	PROCESSING	
tpwr	54	lb	1.00
pw	4.5	wtfile	
d1	0.500	proc	ft
tof	1400.0	fn	not used
nt	100000	math	f
ct	2400		
alock	n	werr	
gain	not used	wexp	procplot
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1005.6		
wp	21115.1		
vs	870		
sc	0		
wc	250		
hzmm	84.46		
is	500.00		
rfl	9347.9		
rfp	7742.2		
th	40		
ins	100.000		
ai	ph		

Compound 11

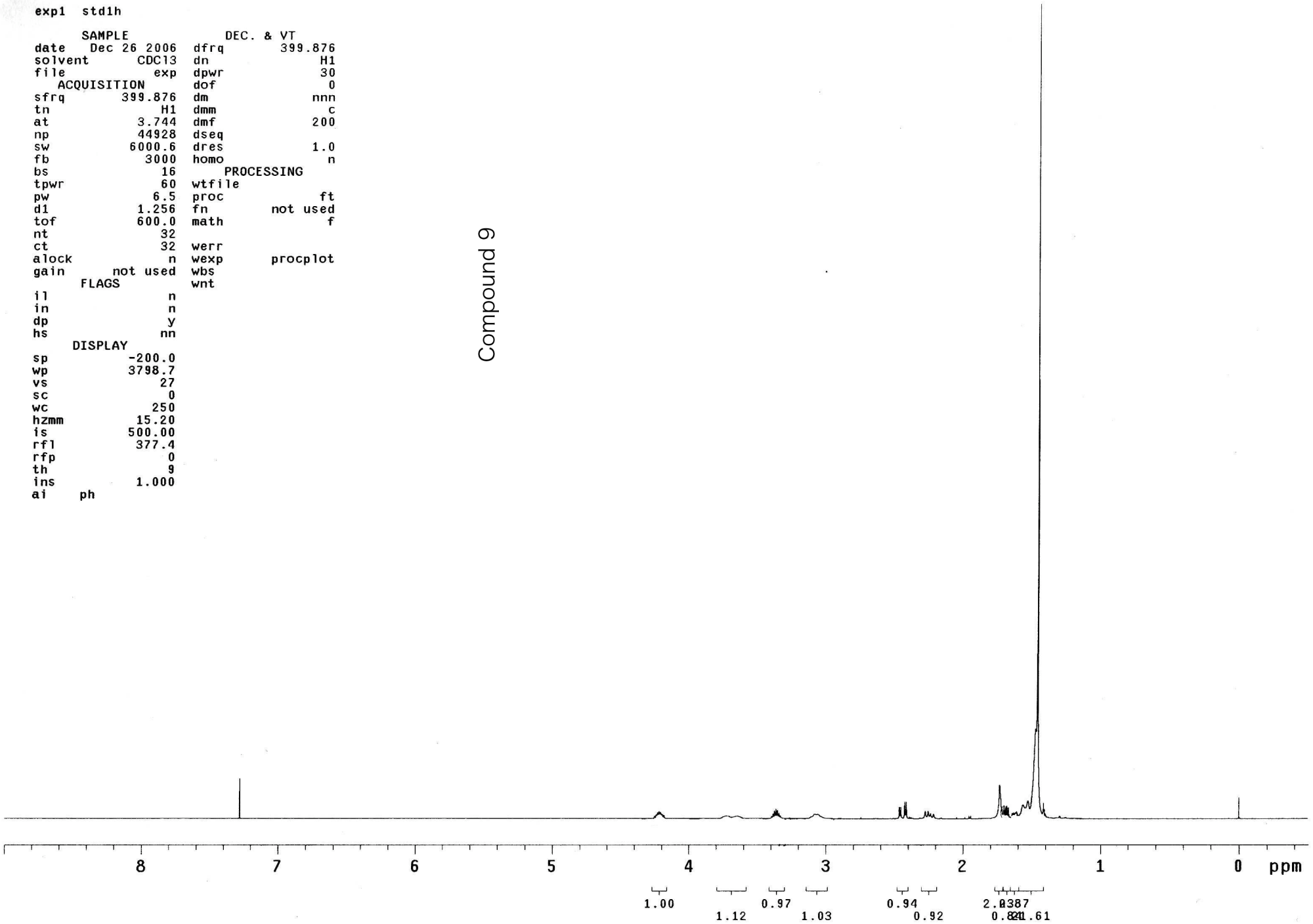


after NIS

exp1 std1h

SAMPLE		DEC. & VT	
date	Dec 26 2006	dfrq	399.876
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	399.876	dm	nnn
tn	H1	dmm	c
at	3.744	dmf	200
np	44928	dseq	
sw	6000.6	dres	1.0
fb	3000	homo	n
bs	16	PROCESSING	
tpwr	60	wtfile	
pw	6.5	proc	ft
d1	1.256	fn	not used
tof	600.0	math	f
nt	32		
ct	32	werr	
alock	n	wexp	procplot
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-200.0		
wp	3798.7		
vs	27		
sc	0		
wc	250		
hzmm	15.20		
is	500.00		
rfl	377.4		
rfp	0		
th	9		
ins	1.000		
ai	ph		

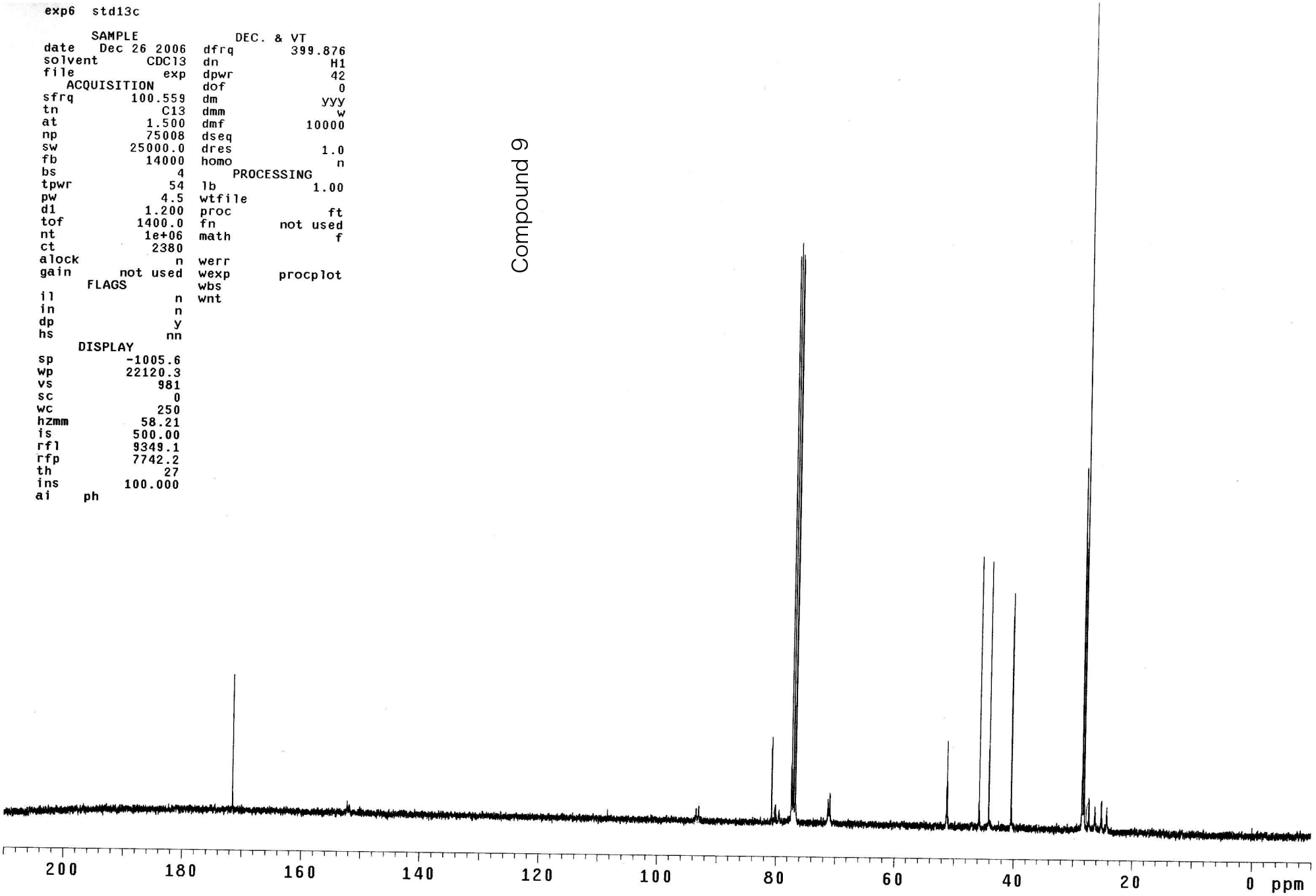
Compound 9



exp6 std13c

SAMPLE		DEC. & VT	
date	Dec 26 2006	dfrq	399.876
solvent	CDCl3	dn	H1
file	exp	dpwr	42
ACQUISITION		dof	0
sfrq	100.559	dm	yyy
tn	C13	dmm	w
at	1.500	dmf	10000
np	75008	dseq	
sw	25000.0	dres	1.0
fb	14000	homo	n
bs	4	**PROCESSING**	
tpwr	54	lb	1.00
pw	4.5	wtfile	
d1	1.200	proc	ft
tof	1400.0	fn	not used
nt	1e+06	math	f
ct	2380		
alock	n	werr	
gain	not used	wexp	procplot
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1005.6		
wp	22120.3		
vs	981		
sc	0		
wc	250		
hzmm	58.21		
is	500.00		
rfl	9349.1		
rfp	7742.2		
th	27		
ins	100.000		
ai	ph		

Compound 9

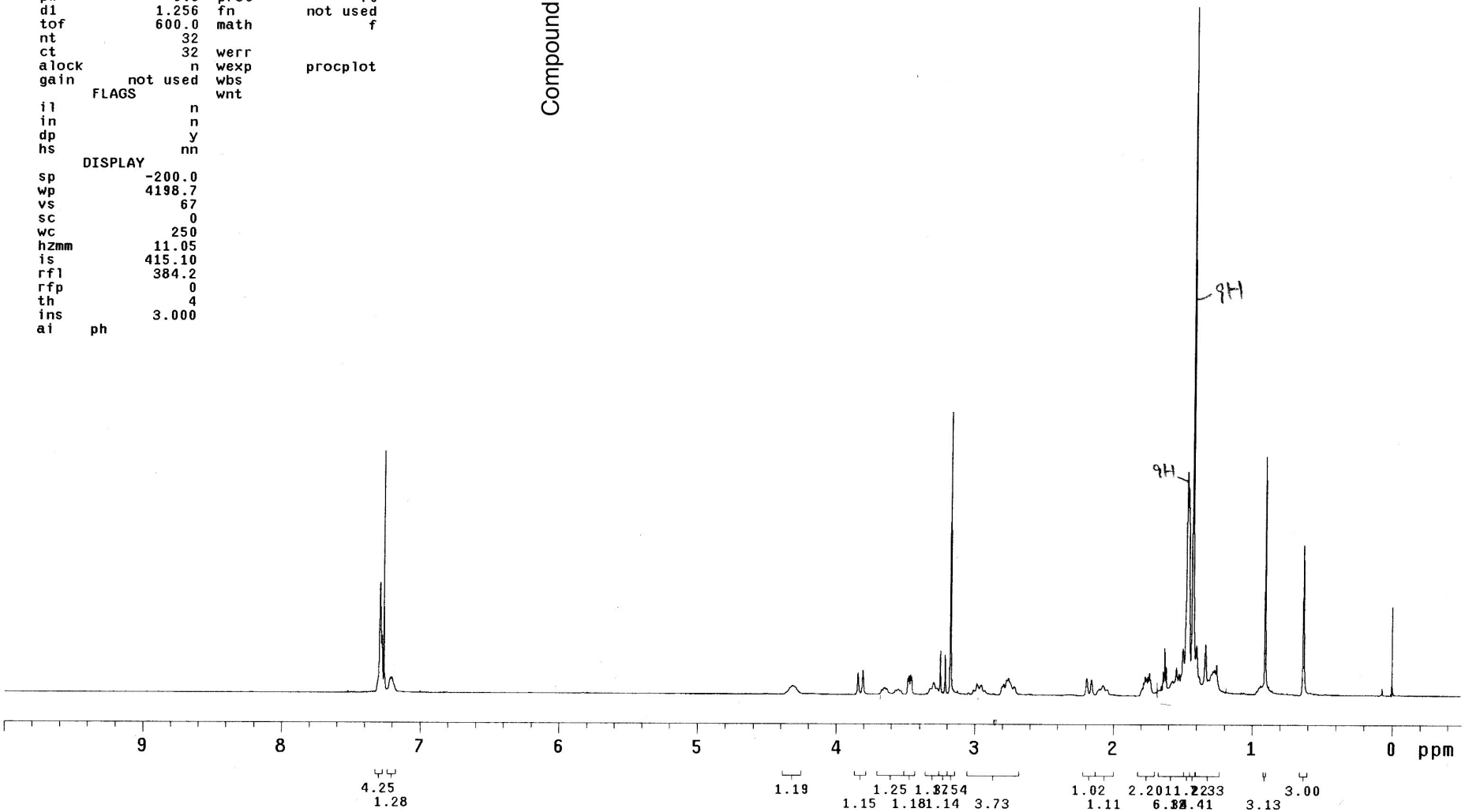


michael

exp1 stdih

SAMPLE		DEC. & VT	
date	Dec 19 2006	dfrq	399.876
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	399.876	dm	nnn
tn	H1	dmm	c
at	3.744	dmf	200
np	44928	dseq	
sw	6000.6	dres	1.0
fb	3000	homo	n
bs	16	PROCESSING	
tpwr	60	wtfile	
pw	6.5	proc	ft
d1	1.256	fn	not used
tof	600.0	math	f
nt	32		
ct	32	werr	
alock	n	wexp	procplot
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-200.0		
wp	4198.7		
vs	67		
sc	0		
wc	250		
hzmm	11.05		
is	415.10		
rfl	384.2		
rfp	0		
th	4		
ins	3.000		
ai	ph		

Compound 8

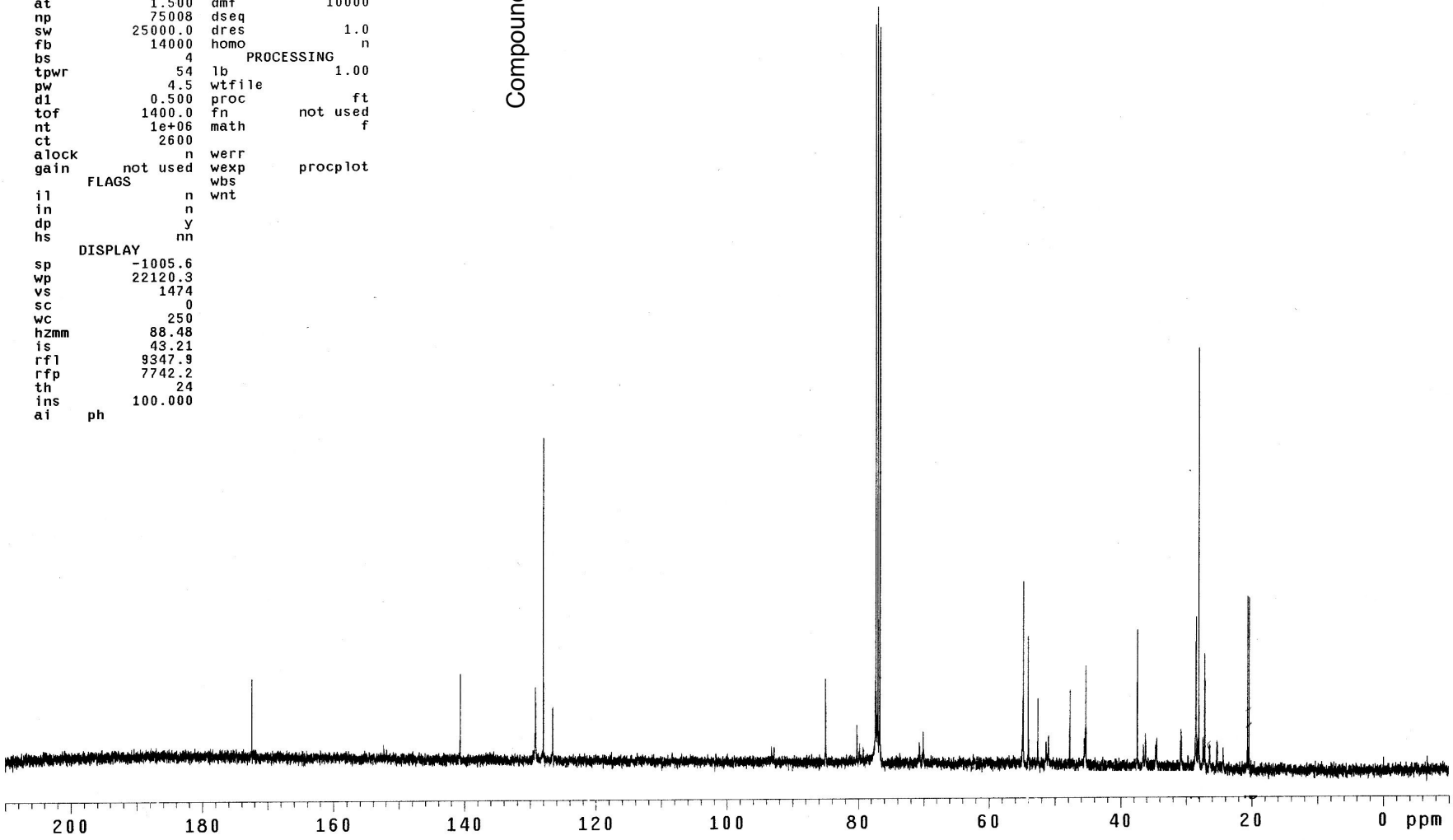


michael

exp6 std13c

SAMPLE		DEC. & VT	
date	Dec 19 2006	dfrq	399.876
solvent	CDCl3	dn	H1
file	exp	dpwr	42
ACQUISITION		dof	0
sfrq	100.559	dm	yyy
tn	C13	dmm	w
at	1.500	dmf	10000
np	75008	dseq	
sw	25000.0	dres	1.0
fb	14000	homo	n
bs	4	PROCESSING	
tpwr	54	lb	1.00
pw	4.5	wtfile	
d1	0.500	proc	ft
tof	1400.0	fn	not used
nt	1e+06	math	f
ct	2600		
alock	n	werr	
gain	not used	wexp	procplot
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1005.6		
wp	22120.3		
vs	1474		
sc	0		
wc	250		
hzmm	88.48		
is	43.21		
rfl	9347.9		
rfp	7742.2		
th	24		
ins	100.000		
ai	ph		

Compound 8

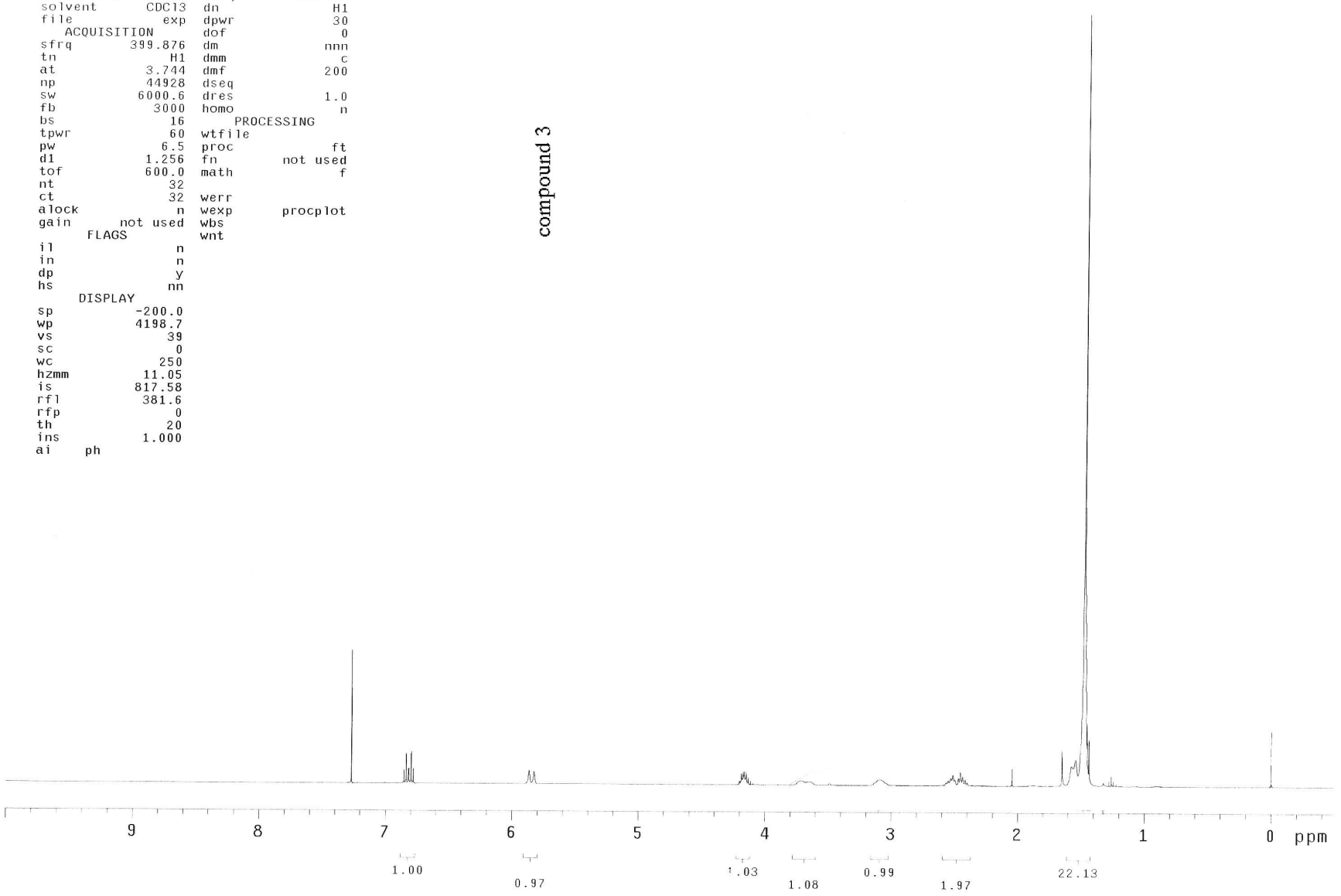


2-160

expl std1h

SAMPLE		DEC. & VT	
date	Dec 5 2006	dfrq	399.876
solvent	CDCl3	dn	H1
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	399.876	dm	nnn
tn	H1	dmm	c
at	3.744	dmf	200
np	44928	dseq	
sw	6000.6	dres	1.0
fb	3000	homo	n
bs	16	PROCESSING	
tpwr	60	wtfile	
pw	6.5	proc	ft
d1	1.256	fn	not used
tof	600.0	math	f
nt	32		
ct	32	werr	
alock	n	wexp	procplot
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-200.0		
wp	4198.7		
vs	39		
sc	0		
wc	250		
hzmm	11.05		
is	817.58		
rfl	381.6		
rfp	0		
th	20		
ins	1.000		
ai	ph		

compound 3

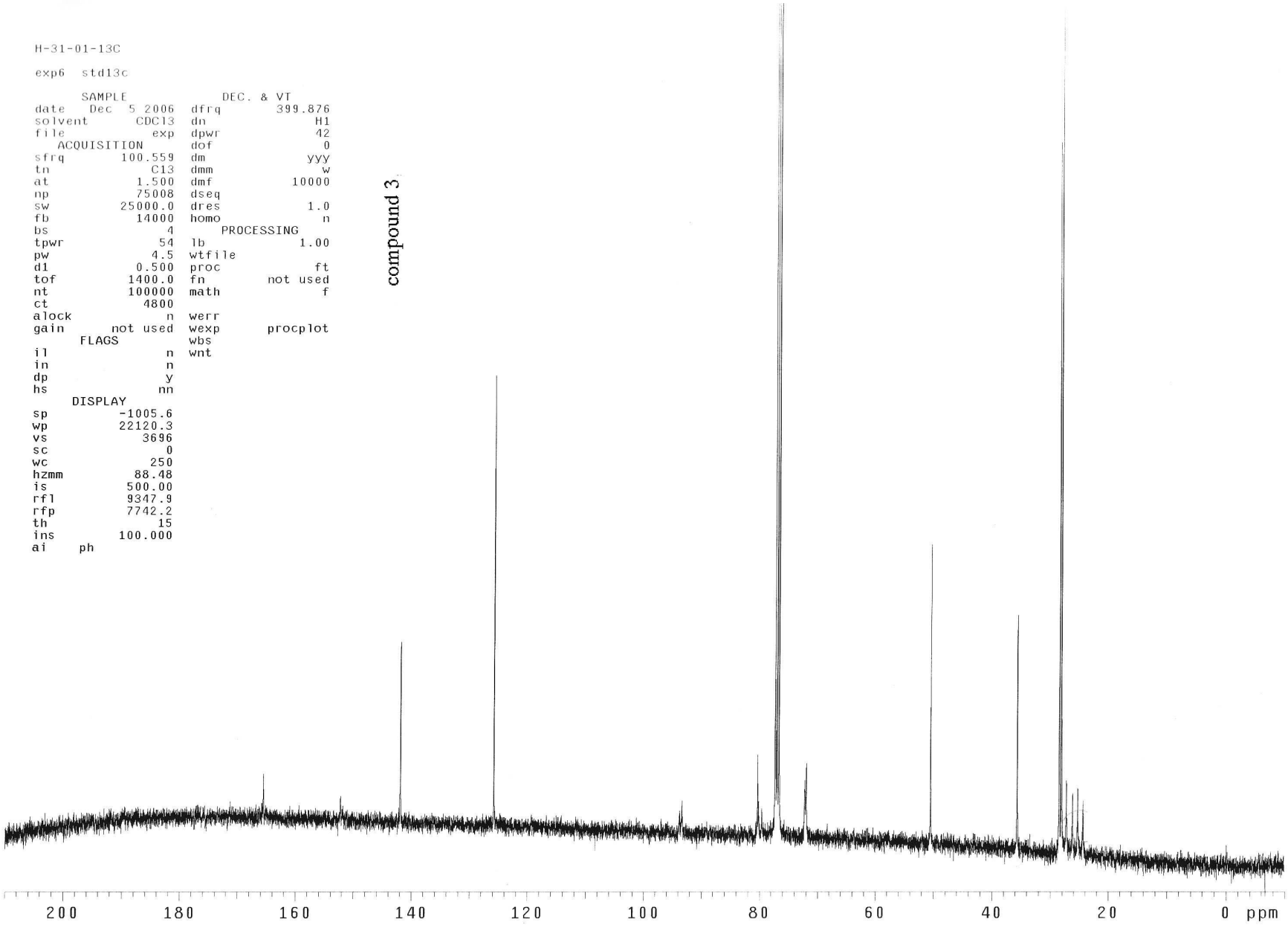


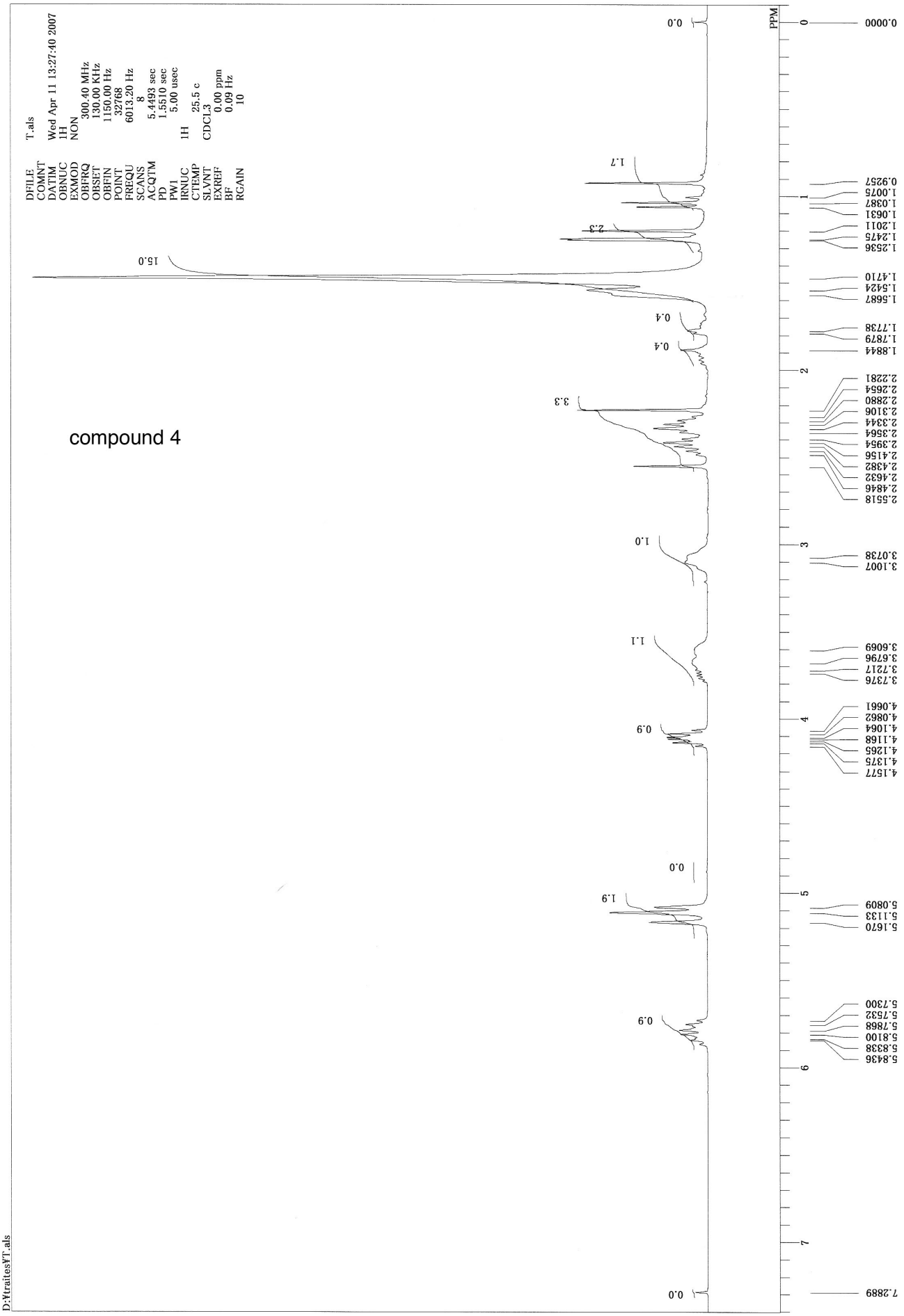
H-31-01-13C

exp6 std13c

SAMPLE		DEC. & VT	
date	Dec 5 2006	dfrq	399.876
solvent	CDCl3	dn	H1
file	exp	dpwr	42
ACQUISITION		dof	0
sfrq	100.559	dm	yyy
tn	C13	dmm	w
at	1.500	dmf	10000
np	75008	dseq	
sw	25000.0	dres	1.0
fb	14000	homo	n
bs	4	PROCESSING	
tpwr	54	lb	1.00
pw	4.5	wtfile	
d1	0.500	proc	ft
tof	1400.0	fn	not used
nt	100000	math	f
ct	4800		
alock	n	werr	
gain	not used	wexp	procplot
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1005.6		
wp	22120.3		
vs	3696		
sc	0		
wc	250		
hzmm	88.48		
is	500.00		
rfl	9347.9		
rfp	7742.2		
th	15		
ins	100.000		
ai	ph		

compound 3





Native (+)-Negamycin