Supporting Information

Selective Molecular Sequestration with Concurrent Natural Product Functionalization and Derivatization: From Crude Natural Product Extracts to a Single Natural Product Derivative in One Step

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General Information

Commercially available ACS grade solvents were used without further purification. Peppercorns were purchased from Pepper-Passion Inc. (Issaquah, WA, www.pepper-passion.com), Allspice, cloves and ground cloves were obtained from Martin's supermarket, South Bend, IN, USA. The Rink resin (100-200 mesh, 1% DVB, 0.75 mmol/g) and Wang resin (100-200 mesh, 1% DVB, 1.0 mmol/g) were from Advanced ChemTech (Louisville, KY, www.peptide.com), the hydroxymethyl resin (100-200 mesh, 1% DVB, 0.98 mmol/g) from NovaBiochem (San Diego, CA, www.emdbiosciences.com/html/NBC/home.html). Synthesis was carried out on Domino Blocks in disposable polypropylene reaction vessels. A Labquake Tube Rotator was used for gentle but efficient tumbling of resin slurry.

All NMR spectra were recorded using 600 MHz or 800 MHz spectrometers. ^{1}H and ^{13}C chemical shifts, δ_H and δ_C, are reported relative to the corresponding residual solvent signal (CD_3OD δ_H=3.31 ppm, δ_C=49.00 ppm; CD3CN δ_H=1.94 ppm, δ_C=1.39 ppm).

All reactions were carried out at ambient temperature (~21 ^{o}C) unless stated otherwise. The volume of wash solvent was 10 mL per 1 g of resin. For washing, resin slurry was shaken with the fresh solvent for at least 1 min before changing the solvent. After adding a reagent solution, the resin slurry was manually vigorously shaken to break any potential resin clumps. Resin-bound intermediates were dried by a stream of nitrogen for prolonged storage and/or quantitative analysis.

For the LC/MS analyses, a sample of resin (~5 mg) was treated with TFA in dichloromethane (DCM), the cleavage cocktail was evaporated by a stream of nitrogen, and cleaved compounds extracted into 0.5 mL of MeOH. Alternatively, a sample of resin-bound product on a silicon-based linker was cleaved by 0.1 M TBAF in THF for 30 min, the solution was diluted with MeOH and analyzed.

Types of peppercorn and amounts of materials extracted.

Table 1. Total extracts and content of piperine and piperettine in peppercorns.

Entry	Peppercorn	Total extract	piperine	piperettine
1	Lampong Black	292 mg	116 mg	19.7 mg
2	Malabar Black	241 mg	77 mg	14.5 mg
3	Madagascar Black	248 mg	89 mg	16.6 mg
4	Sarawak Black	204 mg	61 mg	12.6 mg
5	Tellicherry Black	248 mg	71 mg	14.8 mg
6	Talamanca Del Caribe Black	252 mg	80 mg	8.7 mg
7	Vietnamese Black	223 mg	63 mg	11.0 mg
8	Pohnpei peppercorns	278 mg	82 mg	15.1 mg
9	Muntok White	213 mg	68 mg	12.3 mg
10	Talamanca Del Caribe White	249 mg	87 mg	9.3 mg
11	Sarawak Extra Fancy White	227 mg	60 mg	12.3 mg
12	Freeze Dried Green peppercorns	315 mg	68 mg	15.8 mg

Table 2. The effect of spice, its quantity and freshness on yield.

Entry	Spice	Quantity	Age	Yield
1	Lampong Black	50 mg	freshly ground	2 %
2	Lampong Black	100 mg	freshly ground	7 %
3	Lampong Black	200 mg	freshly ground	19 %
4	Lampong Black	400 mg	freshly ground	37 %
5	Lampong Black	800 mg	freshly ground	46 %
6	Lampong Black	800 mg	freshly ground	45 %
7	Lampong Black	800 mg	1 day old[a]	21 %
8	Lampong Black	800 mg	2 days old[a]	20 %
9	Lampong Black	800 mg	2 days old[a]	18 %
10	Lampong Black	800 mg	2 days old[b]	36 %
11	Lampong Black	800 mg	4 days old[a]	6 %

12	Allspice	800 mg	freshly ground	20 %
13	cloves	800 mg	freshly ground	69 %
14	ground cloves	800 mg	freshly opened	65 %

Note: Yield was estimated from UV response on LC traces and calculated with respect to the initial resin loading; [a]exposed to open air; [b]in a sealed container

The LC/MS analyses were carried out using a 3 x 50 mm C18 reverse phase column. Mobile phases: 10 mM ammonium acetate in HPLC grade water (A) and HPLC grade acetonitrile (B). A gradient was formed from 5% to 80% of B in 10 min at 0.7 mL/min. The MS electrospray source operated at capillary voltage 3.5 kV and a desolvation temperature 300 ^{o}C.

Purification was carried out on a C18 column (19 x 100 mm, 5 um particles). A solvent gradient was formed from 10 mM aqueous ammonium acetate and acetonitrile with a flow rate of 15 mL/min.

General Procedure for Agar Diffusion Antibiotic Susceptibility Assay

Antibacterial activity of the compounds was determined by an agar diffusion assay.[1] All test organisms used in this study were from sources provided in **Table 3**. Overnight cultures of test organisms were grown in LB broth for 18-24 hours and standard suspensions of ~1.5 x 10^6 cfu/mL were prepared in sterile saline solution (0.9% NaCl) according to a $BaSO_4$ 0.5 McFarland Standard (bioMérieux, Inc).[2,3] This standardized suspension (0.1 mL) was added to 34 mL of sterile, melted, and tempered (47-50 ºC) Mueller-Hinton No. 2 agar (HiMedia Laboratories). After gentle mixing, the inoculated melted agar was poured into a sterile petri dish (145 mm x 20 mm, Greiner Bio-One) and allowed to solidify. Wells of 9 mm diameter were cut from the petri dish agar and filled with 50 µL of the test sample solution. The petri dish was incubated at 37 ºC for 18-24 hours and the inhibition zone diameters were measured (mm) with an electronic caliper after 24-48 hours. The results are summarized in **Table 4**.

Table 3. Test organisms used in this research.

Strain	Marker	Origin/Reference
Gram-positive bacteria		
Bacillus subtilis ATCC 6633	Wild Type	American Type Culture Collection
Staphylococcus aureus SG511	Wild Type	Hans Knöll Institute, Jena, Germany
Mycobacterium vaccae IMET 10670	Wild Type	Hans Knöll Institute, Jena, Germany
Mycobacterium smegmatis mc^2155	Wild Type	Snapper et al. **1990**[4]
Micrococcus luteus ATCC 10240	Wild Type	American Type Culture Collection
Gram-negative bacteria		
Pseudomonas aeruginosa KW799/WT	Wild Type	Zimmermann **1980**[5]
Pseudomonas aeruginosa KW799/61	Antibiotic Susceptible Penetration Mutant	Zimmermann **1980**[5]
Escherichia coli X580	β-Lactam Hypersensitive	Eli Lilly & Co.

Table 4. Antibacterial activity of compounds in the agar diffusion assay

	Growth inhibition zones in mm (9 mm well diameter)							
	Gram-positive bacteria					Gram-negative bacteria		
	B. subtilis	*S. Aureus*	*M.smegmatis*	*M. vaccae*	*M. luteus*	*P. aeruginosa*		*E. coli*
compd[a]	6633 ATTC	SG511	MC155	10670 IMET	10240 ATTC	KW799/WT	K799/61	X580
4	14	15	15P[c]	15	20	12	13	14
12	18p[b]	19P	15ps	19	17	11	13	0
13	12/14p	13/16P	17s	19	21	16	18p	15
16	14P	18P	28s	17	26s	11	12	13P
17	0	12	15ps	19	38s	15	0	17
Cipro	26/30	-	18/27P	25	0	22	33	31

[a] 50 µL of a 2.0 mM solution in DMSO : MeOH (1 : 9) of each compound was filled in 9 mm wells in agar media (Standard I Nutrient Agar, Serva or Mueller Hinton II Agar, Becton, Dickinson and Company). Inhibition zones read after incubation at 37 °C for 24 h. Cipro (ciprofloxacin) was dissolved in H_2O to give a 5 mg/mL solution. [b] p, partially clear inhibition zone/colonies in the inhibition zone. [c] P, unclear inhibition zone/many colonies in the inhibition zone. [d] s, indicates single colonies in the inhibition zone.

Table 5. ^{1}H and ^{13}C NMR data for compounds **4**, **12**, **13** in CD_3OD at 298 K**.**

4				**12**				**13**			
Substructural unit	δ_C [ppm]	δ_H [ppm]	Proton multiplicity[a] $J(H_i,H_j)$ [Hz]	Substructural unit	δ_C [ppm]	δ_H [ppm]	Proton multiplicity[a] $J(H_i,H_j)$ [Hz]	Substructural unit	δ_C [ppm]	δ_H [ppm]	Proton multiplicity[a] $J(H_i,H_j)$ [Hz]
C-1	170.7			CH_2-1	61.6	3.68	t, 5.8	CH_2-1	61.5	3.68	t, 5.8
C-2	120.1			CH_2-2	43.3	3.47	t, 5.8	CH_2-2	43.1	3.47	t, 5.8
CH-3	148.4	8.57	dd, 0.7, 2.4	C-3	169.0			C-3	168.5		
C-4	165.3			C-4	120.9			C-4	120.6		
CH-5	108.1	7.10	dd, 2.4, 9.0	CH-5	148.5	8.60	dd, 2.5, 0.7	CH-5	147.9	8.55	d, 2.2
CH-6	138.3	8.01	dd, 0.7, 9.0	C-6	165.3			C-6	165.3		
CH-7	68.5	4.50	dd, 4.7, 12.6	CH-7	108.4	7.04	dd	CH-7	107.8	7.10	d, 9.0
CH_2-8	24.0	2.41	mt, ΣJ=43.4	CH-8	137.5	7.96	dd, 8.9	CH-8	137.6	7.99	d, 9.0
		1.58	mt	CH-9	62.5	5.14	dd, 3.8, 11.9	CH-9	68.6	4.49	dd, 4.7, 12.6
CH_2-9	40.2	1.48	mt, ΣJ=20.4	CH_2-10	30.5	2.30	mt, ΣJ=34.0	CH_2-10	23.6	1.57	mt
		1.35	ddd 4.2, 13.1, 13.2			1.60	mt			2.40	mt, ΣJ=35.5
C-10	33.9			CH_2-11	34.2	2.39	qd, 13.6, 4.8	CH_2-11	39.9	1.34	mt
CH_2-11	51.6	1.94	dd, 3.0, 13.3			1.90	mt			1.47	mt
		1.26	d, 13.2	C-12	153.6			C-12	33.6		
C-12	77.9			CH-13	47.5	2.34	mt, ΣJ=20.6	CH_2-13	51.4	1.26	d, 13.4
CH_2-13	37.6	2.28	ddd, 4.1, 7.5, 13.9	CH-14	55.9	1.83	mt			1.94	dd, 2.9, 13.4
		1.37	mt	CH_2-15	34.1	1.77	dtd, 14.0, 4.2, 1.0	C-14	77.6		
CH_2-14	24.2	1.59	mt			1.47	mt	CH_2-15	37.3	1.38	ddd, 4.5, 9.2, 14.4
		1.50	ddd, 3.9, 9.1, 9.3	CH_2-16	38.2	2.35	dt, 13.6, 4.8			2.29	ddd, 3.9, 7.7, 14.4
CH-15	48.2	1.71	ddd, 5.5, 8.7, 12.2			1.88	mt	CH_2-16	23.9	1.51	mt

CH-16	41.61	2.12	ddd, 8.0, 11.1, 11.4	C-17	147.26					1.59	mt, ΣJ=27.0
CH_2-17	37.4	1.54	dd, 7.9, 9.6	CH_2-18	37.8	1.82	mt	CH-17	47.9	1.71	mt, ΣJ=26.2
		1.40	mt			1.61	mt	CH-18	41.3	2.12	ddd, 8.0, 10.8, 11.2
C-18	35.5			C-19	33.8			CH_2-19	37.2	1.40	t, 8.1
CH_3-19	30.9	1.01	s	CH_3-20	22.0	1.00	S			1.54	dd, 8.1, 9.6
CH_3-20	21.0	1.03	s	CH_3-21	30.0	1.02	s	C-20	36.2		
CH_3-21	27.0	0.87	s	CH_2-22	109.9	4.98	mt	CH_3-21	30.6	1.01	s
						4.87	t, 1.3	CH_3-22	20.7	1.03	s
				CH_2-23	115.5	5.10	d, 2.0	CH_3-23	26.8	0.86	s
						5.09	d, 2.0				

a) Due to overlap of several proton signals the values of coupling constants or ΣJ could not be always determined.

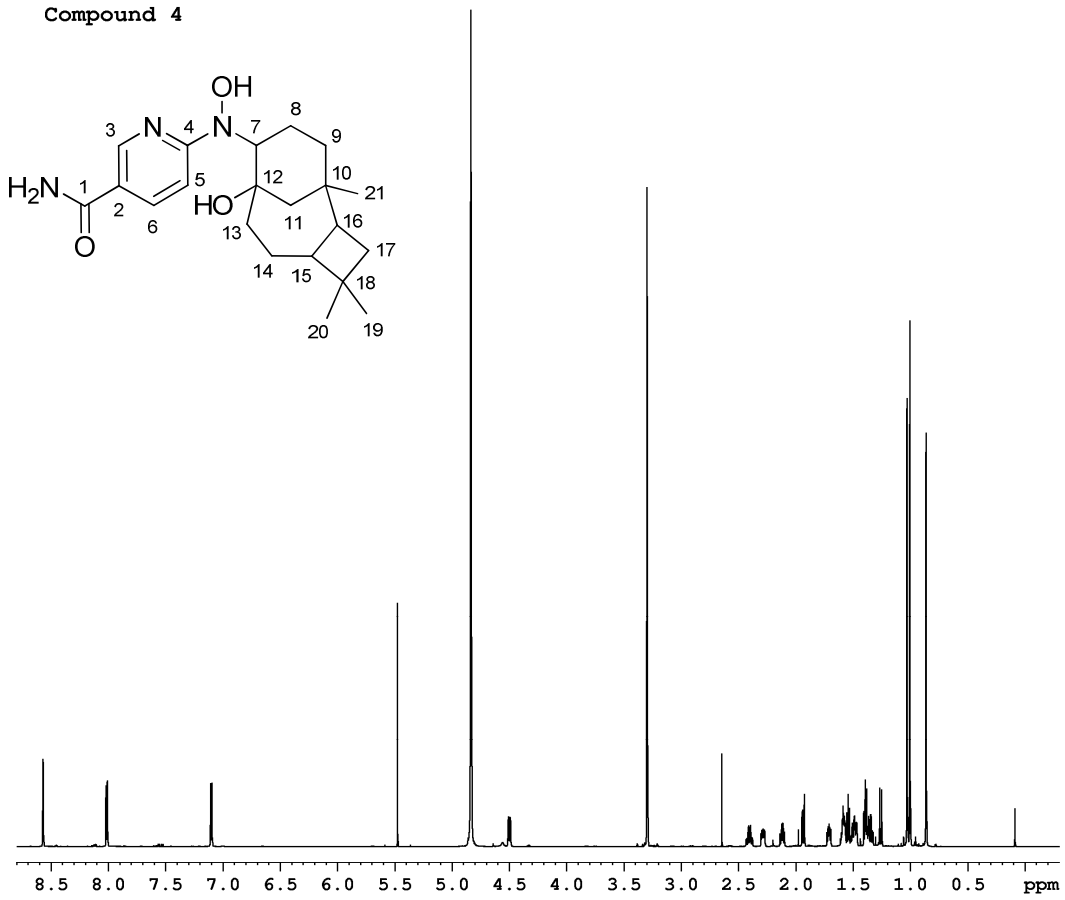
Table 6. ^{1}H and ^{13}C NMR data for compounds **16** and **17** in CD_3OD at 298 K.

16[a]				**17**			
Substructural unit	δ_C [ppm]	δ_H [ppm]	Proton multiplicity[b] $J(H_i,H_j)$ [Hz]	Substructural unit	δ_C [ppm]	δ_H [ppm]	Proton multiplicity[b] $J(H_i,H_j)$ [Hz]
CH_2-1	61.5	3.610	t, 5.5	CH_2-1	61.3	3.70	t, 5.9
CH_2-2	43.1	3.425	t, 5.5	CH_2-2	43.2	3.49	t, 5.9
C-3	167.9			C-3	169.9		
C-4	134.9			C-4	134.9		
CH-5,9	127.9	7.780	d, 8.3	CH-5,9	128.2	7.82	d, 8.4
CH-6,8	128.2	7.422	d, 8.3	CH-6,8	128.3	7.50	d, 8.4
C-7	140.8			C-7	141.7		
NH		7.233	t, 5.3	CH_2-10	67.5	5.23	d, 13.1
CH_2-10	67.1	5.583	d, 13.1			5.20	d, 13.1
		5.092	d, 13.1	C-11	159.0		
C-11	157.3			CH-12	67.5	4.02	dd, 13.1
CH-12	61.8	4.715	bs	CH_2-13	24.4	2.32	qd, 13.5, 4.4
CH_2-13	24.1	2.340	mt			1.57	mt
		1.679	mt	CH_2-14	39.7	1.47	mt
CH_2-14	38.5	1.473	mt			1.32	mt
		1.423	mt	C-15	33.7		
C-15	34.1			CH_2-16	51.0	1.86	dd, 2.9, 13.4
CH_2-16	44.6	2.351	mt			1.16	d, 13.4
		1.952	mt	C-17	77.0		
C-17	97.4			CH_2-18	36.7	2.23	ddd, 3.8, 8.1, 14.3
CH_2-18	33.9	2.357	mt			1.34	mt
		1.824	mt	CH_2-19	23.6	1.56	mt
CH_2-19	23.6	1.688	mt			1.44	mt
		1.444	mt	CH-20	47.7	1.69	ddd, 5.7, 8.5, 12.1
CH-20	46.8	1.74	ddd, 5.2, 9.1,12.0	CH-21	41.1	2.07	ddd, 8.0, 10.8, 11.8
CH-21	40.7	2.019	ddd, 8.1, 10.9, 11.1	CH_2-22	37.1	1.52	dd, 8.0, 9.6

CH_2-22	36.64	1.518	dd, 8.1, 9.5			1.37	dd, 9.6, 10.6
		1.387	t, 10.0	C-23	35.3		
C-23	34.8			CH_3-24	30.6	0.99	s
CH_3-24	30.3	0.993	s	CH_3-25	20.7	1.00	s
CH_3-25	20.6	0.996	s	CH_3-26	26.7	0.84	s
CH_3-26	26.5	0.867	s				

a) In CD_3CN

b) Due to overlap of several proton signals the values of coupling constants or ΣJ could not be always determined.



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SOLVENT	MeOD
NS	64
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FIDRES	0.125483 Hz
AQ	3.9846387 sec
RG	45.2
DW	60.800 usec
DE	30.00 usec
TE	301.9 K
D1	1.00000000 sec
TD0	1
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NUC1	1H
P1	6.00 usec
PL1	1.00 dB
SFO1	800.1837640 MHz
SI	131072
SF	800.1800262 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

^{1}H spectrum of **4** in CD_3OD at 25^o C.

Acquisition Time (sec)	1.7826	***Comment***	**Compound 4**			***Date***	Feb 10 2009
Date Stamp	Feb 10 2009						
Frequency (MHz)	150.85	***Nucleus***	13C	***Number of Transients***	7200	***Original Points Count***	65536
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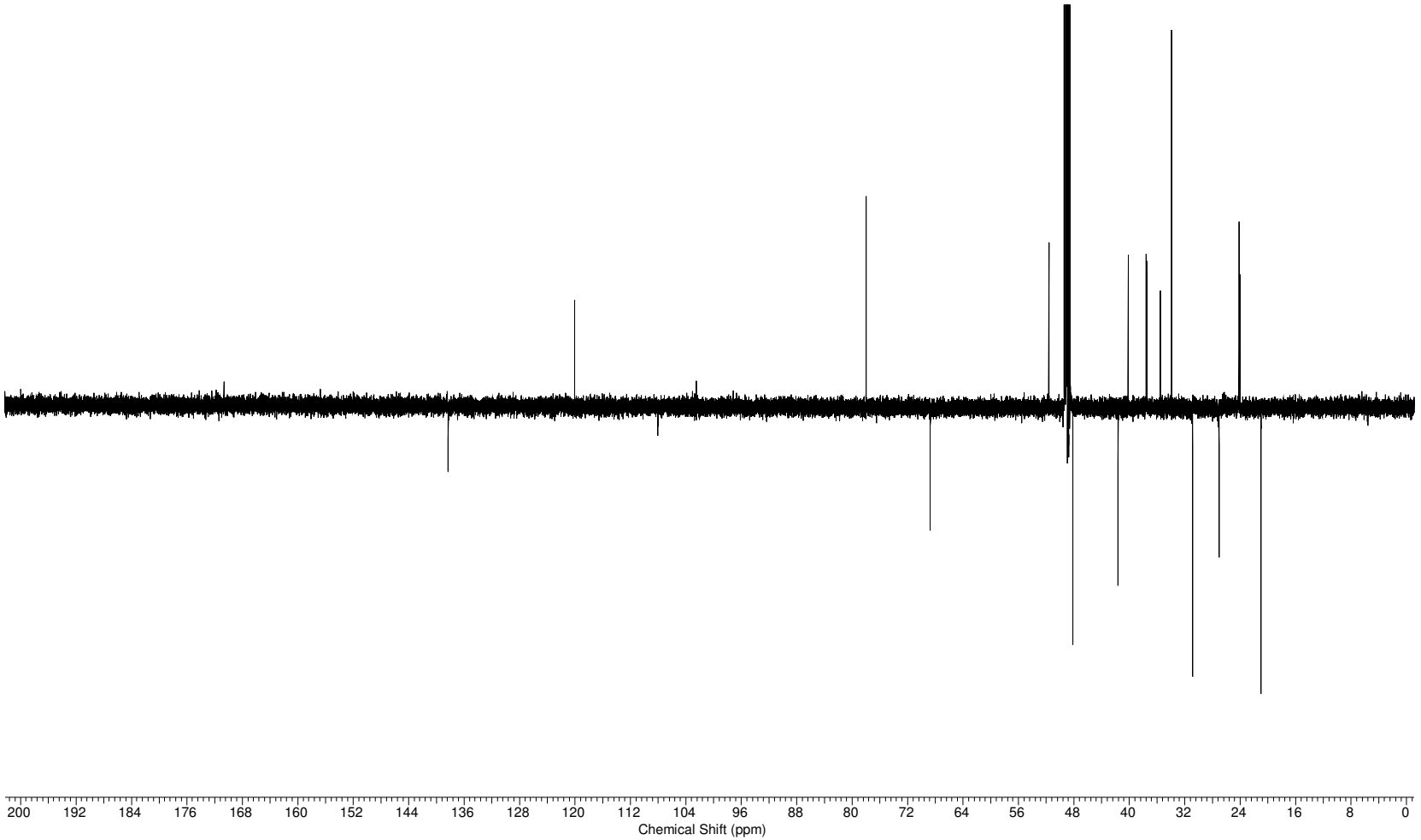
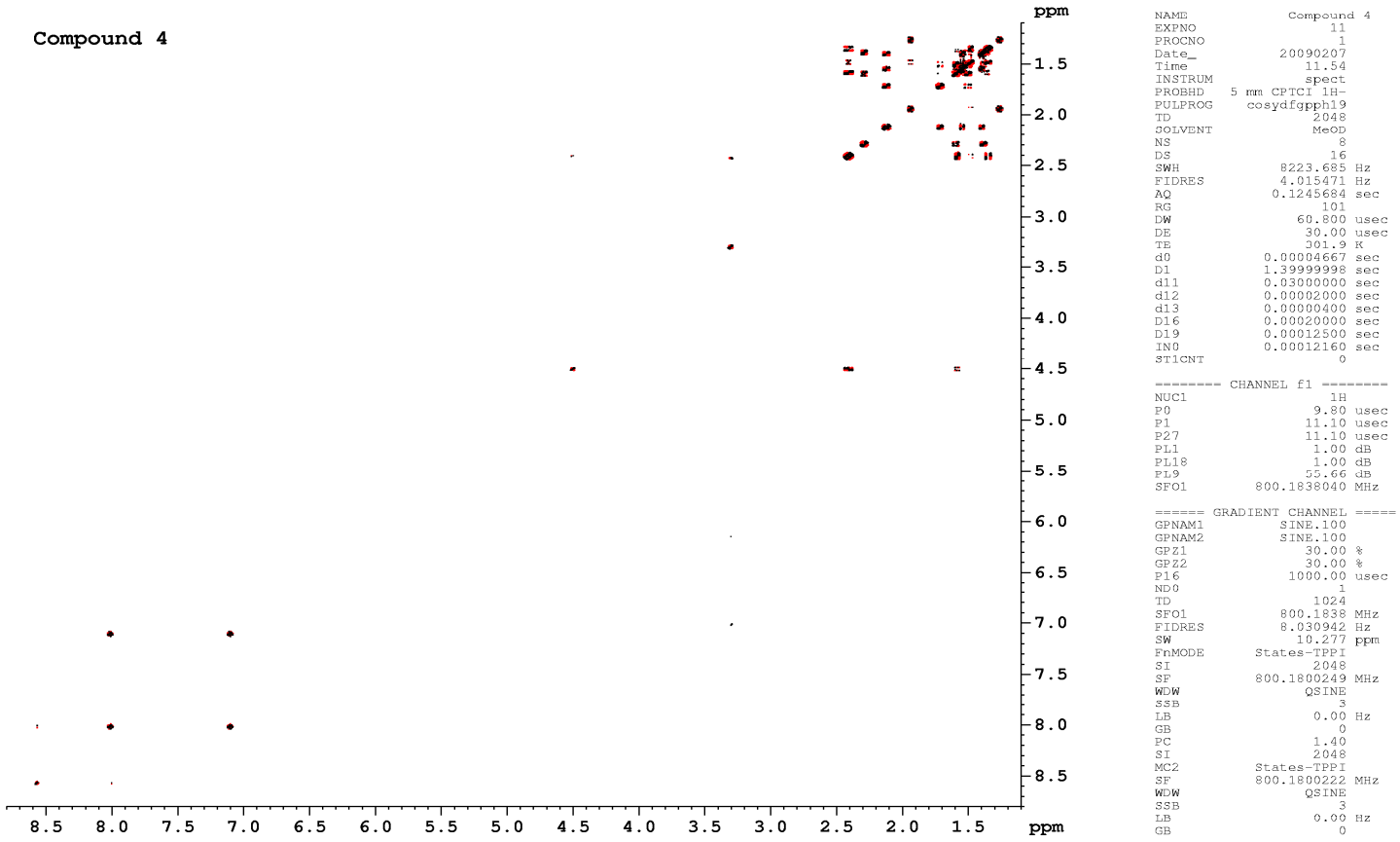


^{13}C APT spectrum of **4** in CD_3OD at 25^{o} C.

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TD                        2048
SOLVENT                   MeOD
NS                           8
DS                          16
SWH                   8223.685 Hz
FIDRES                4.015471 Hz
AQ                   0.1245684 sec
RG                         101
DW                      60.800 usec
DE                      30.00 usec
TE                      301.9 K
d0                   0.00004667 sec
D1                   1.39999998 sec
d11                  0.03000000 sec
d12                  0.00002000 sec
d13                  0.00000400 sec
D16                  0.00020000 sec
D19                  0.00012500 sec
IN0                  0.00012160 sec
ST1CNT                       0

======== CHANNEL f1 ========
NUC1                        1H
P0                        9.80 usec
P1                       11.10 usec
P27                      11.10 usec
PL1                       1.00 dB
PL18                      1.00 dB
PL9                      55.66 dB
SFO1                800.1838040 MHz

====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPNAM2                SINE.100
GPZ1                     30.00 %
GPZ2                     30.00 %
P16                    1000.00 usec
ND0                          1
TD                        1024
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FIDRES               8.030942 Hz
SW                     10.277 ppm
FnMODE            States-TPPI
SI                        2048
SF                 800.1800249 MHz
WDW                      QSINE
SSB                          3
LB                        0.00 Hz
GB                           0
PC                        1.40
SI                        2048
MC2               States-TPPI
SF                 800.1800222 MHz
WDW                      QSINE
SSB                          3
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GB                           0
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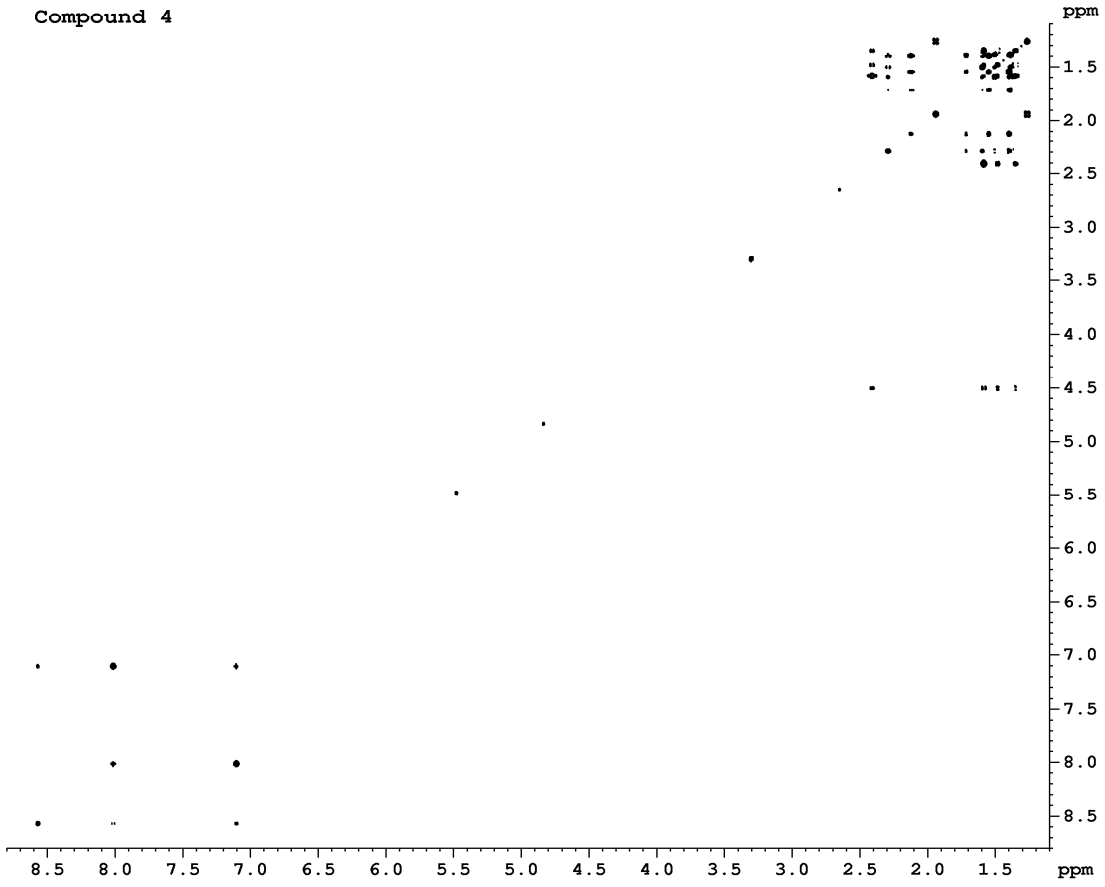
2D DQF-COSY spectrum of **4** in CD_3OD at 25° C. The black and red contours represent positive and negative peaks, respectively.



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TD	2048
SOLVENT	MeOD
NS	8
DS	16
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FIDRES	4.015471 Hz
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RG	114
DW	60.800 usec
DE	30.00 usec
TE	301.9 K
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d13	0.00000400 sec
D16	0.00020000 sec
D19	0.00012500 sec
D20	0.00001000 sec
D21	0.00001000 sec
D9	0.06100000 sec
DELTA	0.00120300 sec
FACTOR1	11
IN0	0.00012160 sec
l1	22
ST1CNT	0
======== CHANNEL f1 ========	
NUC1	1H
P0	9.80 usec
P1	11.10 usec
p2	22.20 usec
P27	11.10 usec
P6	24.00 usec
PL1	1.00 dB
PL10	7.70 dB
PL18	1.00 dB
PL9	55.66 dB
SFO1	800.1838040 MHz
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GPNAM2	SINE.100
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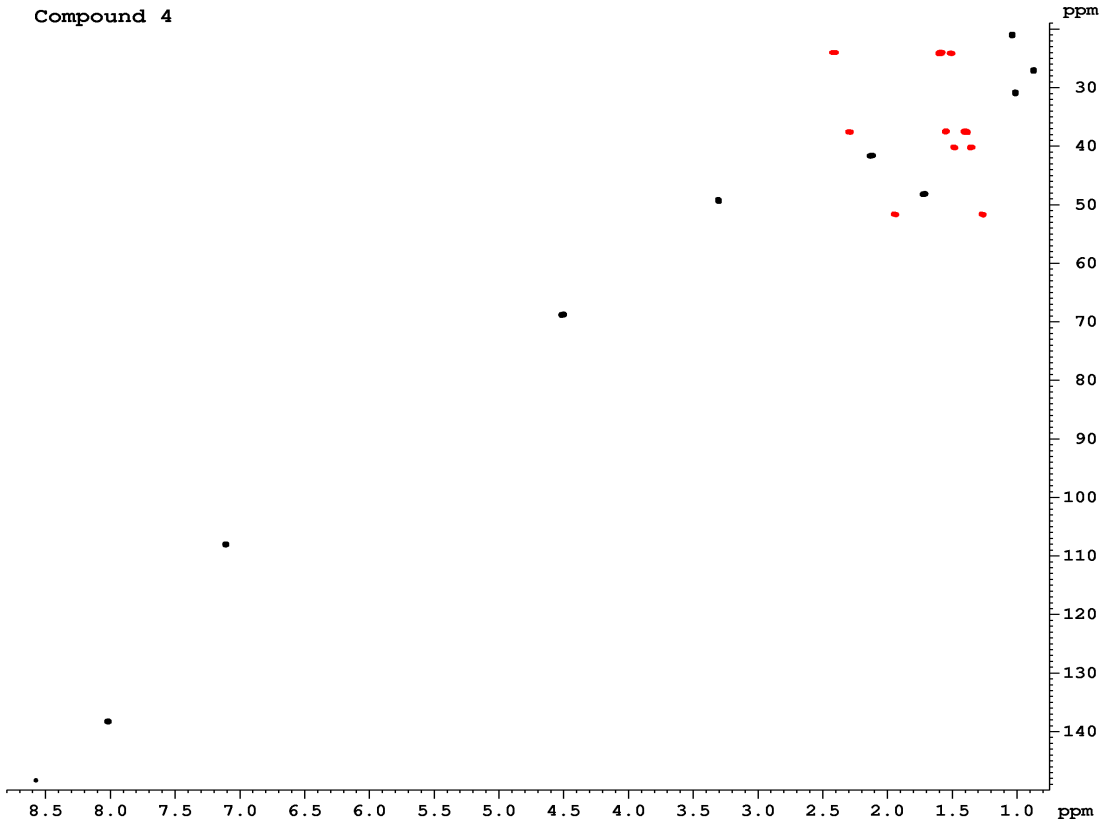
GPZ2	20.00 %
GPZ3	50.00 %
P16	1000.00 usec
ND0	1
TD	1024
SFO1	800.1838 MHz
FIDRES	8.030942 Hz
SW	10.277 ppm
FnMODE	Echo-Antiecho
SI	2048
SF	800.1800249 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.40
SI	2048
MC2	echo-antiecho
SF	800.1800250 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0

2D TOCSY spectrum of **4** in CD_3OD at 25^o C.

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SOLVENT                   MeOD
NS                            16
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RG                          4600
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DE                         6.00 usec
TE                        301.9 K
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CNST2                 145.0000000
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D21                    0.00345000 sec
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IN0                    0.00001460 sec
ST1CNT                        0

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NUC1                         1H
P1                         11.10 usec
p2                         22.20 usec
P28                      1000.00 usec
PL1                         1.00 dB
SFO1                800.1838040 MHz

======== CHANNEL f2 ========
CPDPRG2                 p5m4sp180
NUC2                          13C
P14                        500.00 usec
P24                       2000.00 usec
P3                          15.00 usec
PCPD2                     1500.00 usec
PL0                        120.00 dB
PL12                        10.00 dB
PL2                         -2.25 dB
SFO2                201.2225235 MHz
SP3                         1.08 dB
SP7                         1.08 dB
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SPNAM7       Crp60comp.4
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SPOAL3                      0.500
SPOAL7                      0.500
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SPOFFS3                     0.00 Hz
SPOFFS7                     0.00 Hz

====== GRADIENT CHANNEL =====
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GPNAM2                 SINE.100
GPNAM3                 SINE.100
GPNAM4                 SINE.100
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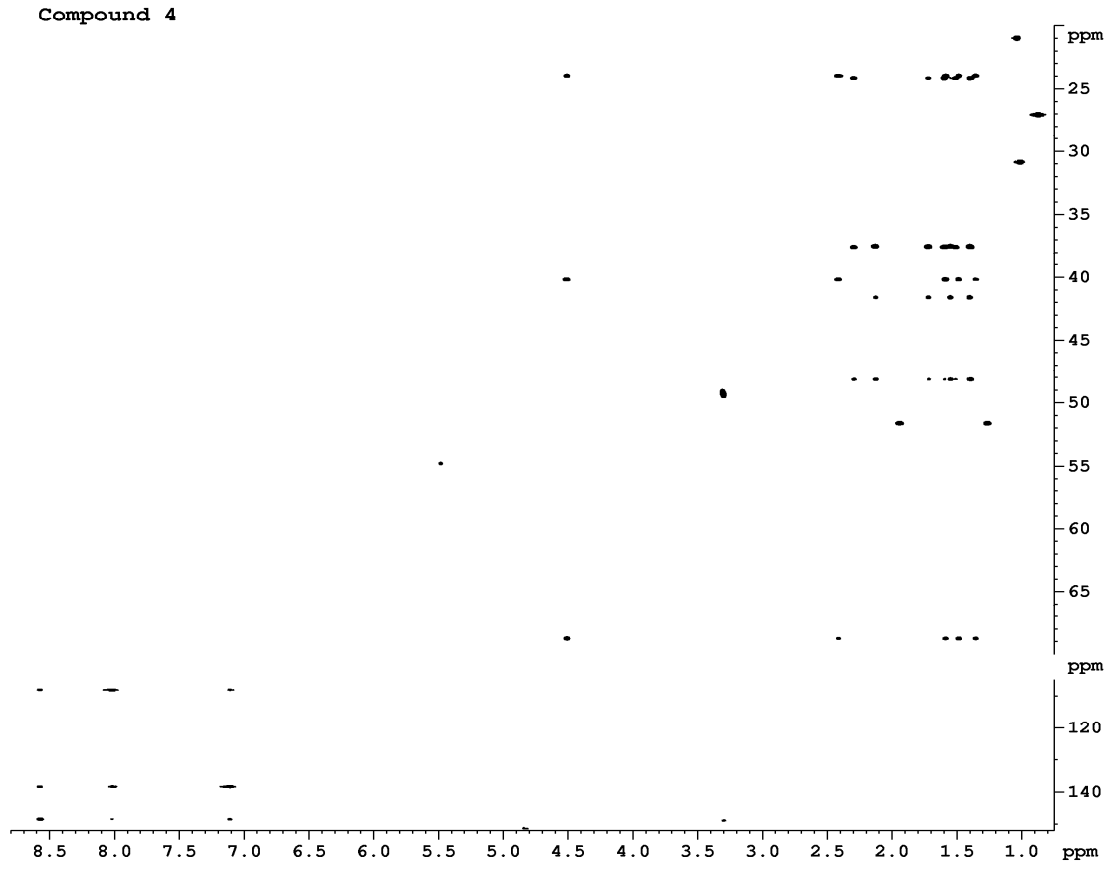
GPZ2                       20.10 %
GPZ3                       11.00 %
GPZ4                       -5.00 %
P16                      1000.00 usec
P19                       500.00 usec
ND0                           2
TD                          512
SFO1                201.2225 MHz
FIDRES                66.887640 Hz
SW                       170.193 ppm
FnMODE           Echo-Antiecho
SI                         2048
SF                  800.1800215 MHz
WDW                       QSINE
SSB                           2
LB                         0.00 Hz
GB                            0
PC                         1.00
SI                         2048
MC2                echo-antiecho
SF                  201.2051388 MHz
WDW                       QSINE
SSB                           2
LB                         0.00 Hz
GB                            0
```

2D ^{13}C-HSQC spectrum of **4** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The black cross-peaks correspond to CH_3 and CH groups, the red cross-peaks correspond to CH_2 groups.



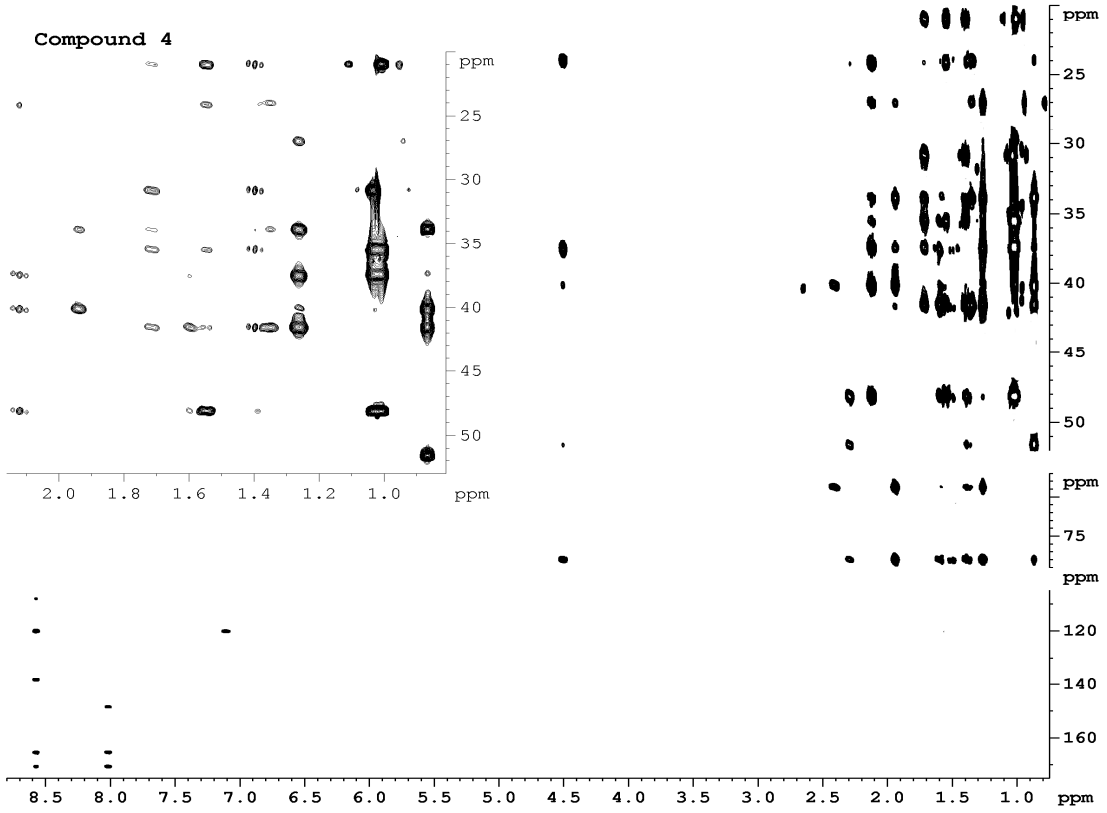

```
NAME                  Compound 4
EXPNO                         14
PROCNO                         1
Date_               20090207
Time                      22.47
INSTRUM                    spect
PROBHD     5 mm CPTCI 1H-
PULPROG    hsqcdietgpsisp.2
TD                         1024
SOLVENT                    MeOD
NS                           16
DS                           32
SWH                  8223.685 Hz
FIDRES               8.030942 Hz
AQ                   0.0623092 sec
RG                        4600
DW                       60.800 usec
DE                       30.00 usec
TE                       301.9 K
CNST17                -0.5000000
CNST2               145.0000000
d0                   0.00000300 sec
D1                   1.50000000 sec
d11                  0.03000000 sec
D16                  0.00020000 sec
D24                  0.00086200 sec
d4                   0.00172414 sec
D9                   0.06100000 sec
DELTA                0.00122420 sec
DELTA1               0.00120800 sec
DELTA2               0.00147014 sec
DELTA3               0.00135800 sec
FACTOR1                      11
IN0                  0.00001655 sec
l1                           22
ST1CNT                        0

======== CHANNEL f1 ========
NUC1                         1H
P1                        11.10 usec
p2                        22.20 usec
P28                     1000.00 usec
P6                        24.00 usec
PL1                        1.00 dB
PL10                       7.70 dB
SFO1                800.1837640 MHz

======== CHANNEL f2 ========
CPDPRG2                 p5m4sp180
NUC2                         13C
P14                      500.00 usec
P24                     2000.00 usec
P3                        15.00 usec
PCPD2                   1500.00 usec
PL0                      120.00 dB
PL12                      10.00 dB
PL2                       -2.25 dB
SFO2                201.2265114 MHz
SP3                        1.08 dB
SP7                        1.08 dB
SPNAM15    Crp,80,1.5,10.nd
SPNAM3     Crp60,0.5,20.1
SPNAM7       Crp60comp.4
SPOAL15                  0.500
SPOAL3                   0.500
SPOAL7                   0.500
SPOFFS15                 0.00 Hz
SPOFFS3                  0.00 Hz
SPOFFS7                  0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPNAM2                SINE.100
GPZ1                     80.00 %
GPZ2                     20.10 %
P16                    1000.00 usec
ND0                          2
TD                        1024
SFO1                201.2205 MHz
FIDRES              29.503399 Hz
SW                    150.141 ppm
FnMODE          Echo-Antiecho
SI                        2048
SF                  800.1800211 MHz
WDW                      QSINE
SSB                          2
LB                        0.00 Hz
GB                           0
PC                        1.00
SI                        2048
MC2             echo-antiecho
SF                  201.2051388 MHz
WDW                      QSINE
SSB                          2
LB                        0.00 Hz
GB                           0
```

2D ^{13}C-HSQC-TOCSY spectrum of **4** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively.



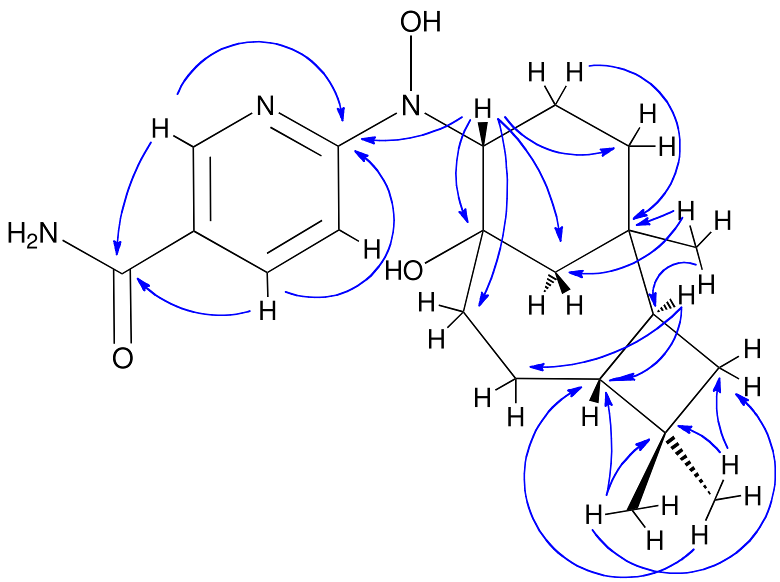

```
NAME                Compound 4
EXPNO                       15
PROCNO                       1
Date_                 20090208
Time                      6.27
INSTRUM                  spect
PROBHD     5 mm CPTCI 1H-
PULPROG     hmbcgpl2ndqf
TD                        2048
SOLVENT                   MeOD
NS                          40
DS                         256
SWH                  8223.685 Hz
FIDRES               4.015471 Hz
AQ                  0.1245684 sec
RG                       5160
DW                     60.800 usec
DE                     30.00 usec
TE                     301.9 K
CNST13              8.0000000
CNST6             125.0000000
CNST7             175.0000000
d0                  0.00000300 sec
D1                  1.39999998 sec
D16                 0.00020000 sec
d6                  0.06250000 sec
DELTA1              0.00280000 sec
DELTA2              0.00165714 sec
DELTA3              0.06129600 sec
IN0                 0.00001380 sec

======== CHANNEL f1 ========
NUC1                        1H
P1                      11.10 usec
p2                      22.20 usec
PL1                      1.00 dB
SFO1               800.1838040 MHz

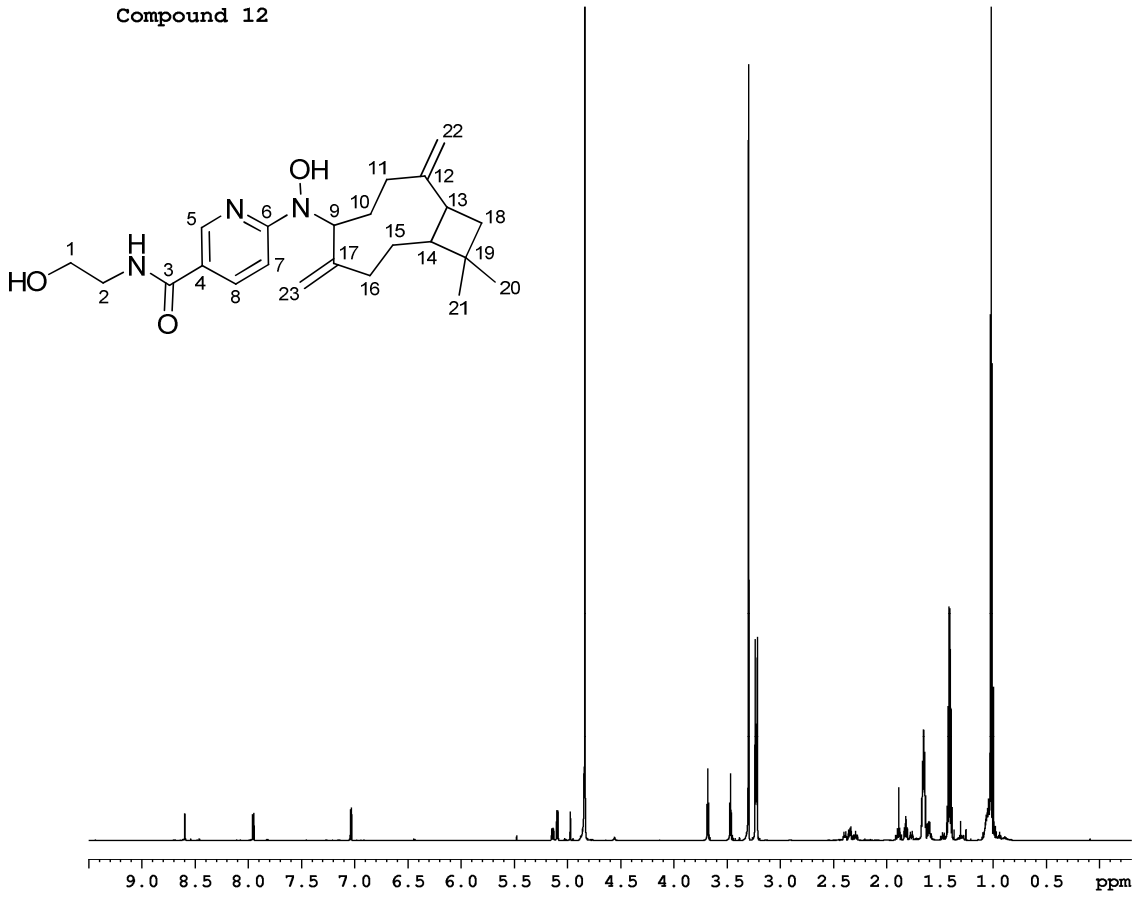
======== CHANNEL f2 ========
NUC2                        13C
P3                      15.00 usec
PL2                     -2.25 dB
SFO2               201.2235295 MHz

------ GRADIENT CHANNEL -----
GPNAM1                SINE.100
GPNAM2                SINE.100
GPNAM3                SINE.100
GPNAM4                SINE.100
GPNAM5                SINE.100
GPNAM6                SINE.100
GPZ1                    50.00 %
GPZ2                    30.00 %
GPZ3                    40.10 %
GPZ4                    15.00 %
GPZ5                   -10.00 %
GPZ6                    -5.00 %
P16                  1000.00 usec
ND0                         2
TD                        512
SFO1               201.2235 MHz
FIDRES              70.765396 Hz
SW                    180.058 ppm
FnMODE                     QF
SI                       2048
SF                 800.1800241 MHz
WDW                    QSINE
SSB                         0
LB                       0.00 Hz
GB                          0
PC                       1.40
SI                       2048
MC2                        QF
SF                 201.2051395 MHz
WDW                    QSINE
SSB                         0
LB                       0.00 Hz
GB                          0
```

2D ^{13}C-HMBC spectrum of **4** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The insert in the upper left corner represents an expansion of the high field region plotted with reduced cross-peaks intensities for a better clarity.

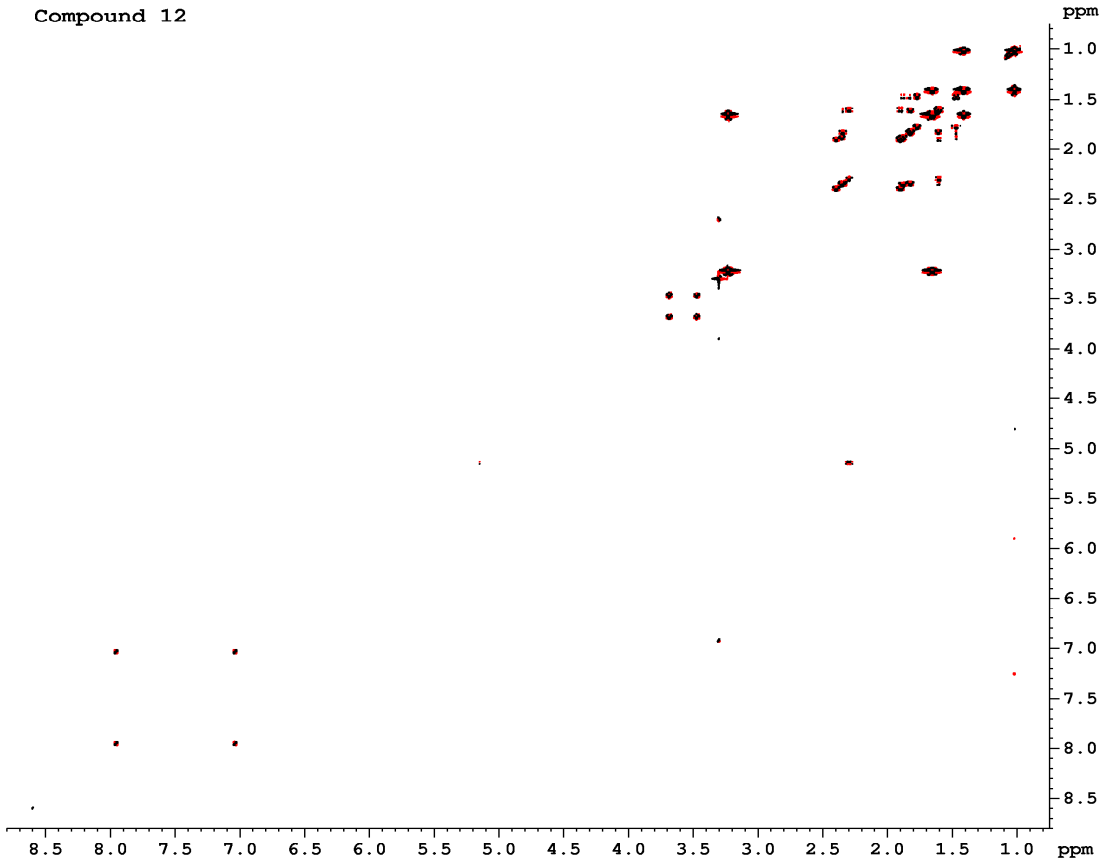


Correlation diagram for compound **4**. The HMBC correlations (in blue), together with proton-proton correlations in DQF-COSY and TOCSY spectra and one bond proton-carbon correlations in the HSQC spectrum unambiguously establish the proposed structure of compound **4**.



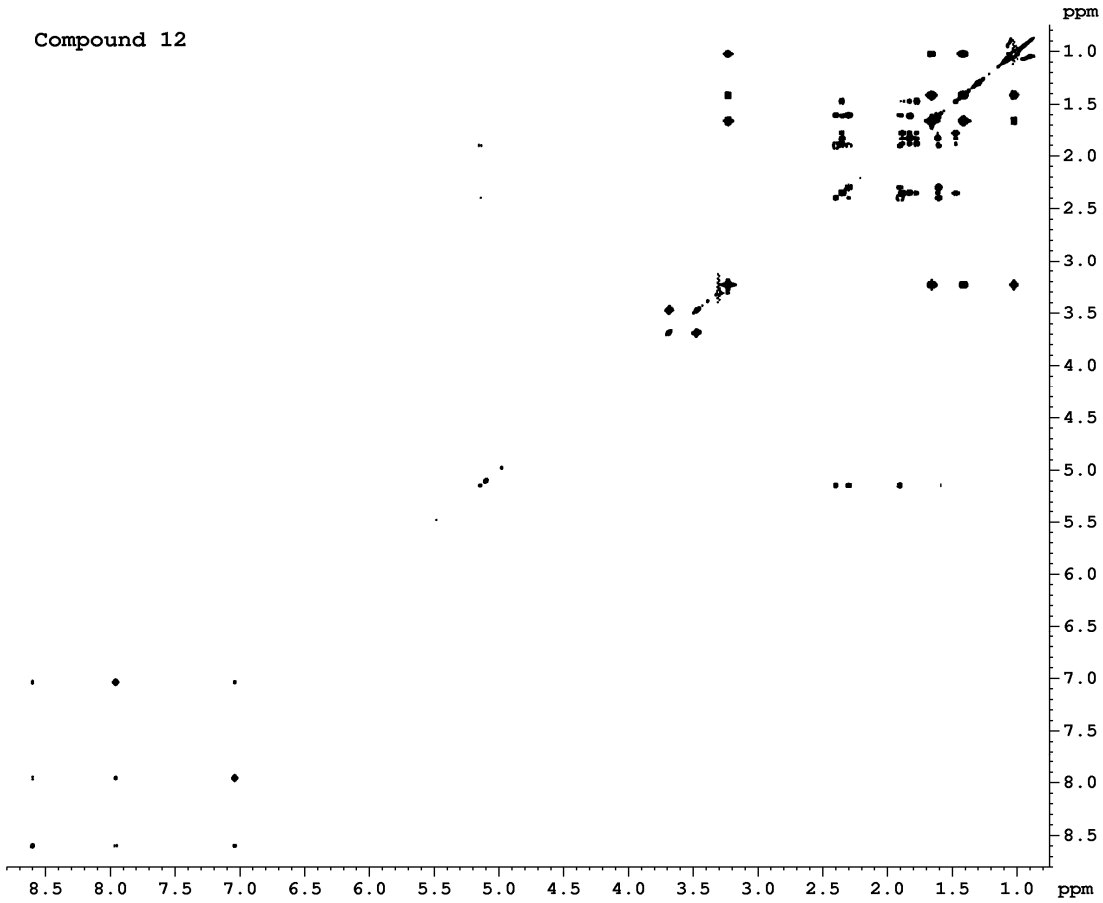
NAME	Compound 12
EXPNO	1
PROCNO	1
Date_	20091117
Time	11.47
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	zg
TD	65536
SOLVENT	MeOD
NS	256
DS	4
SWH	8223.685 Hz
FIDRES	0.125483 Hz
AQ	3.9846387 sec
RG	32
DW	60.800 usec
DE	30.00 usec
TE	301.9 K
D1	0.10000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	10.30 usec
PL1	0.20 dB
SFO1	800.1837640 MHz
SI	131072
SF	800.1800263 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

^{1}H spectrum of **12** in CD_3OD at 25^{o} C.



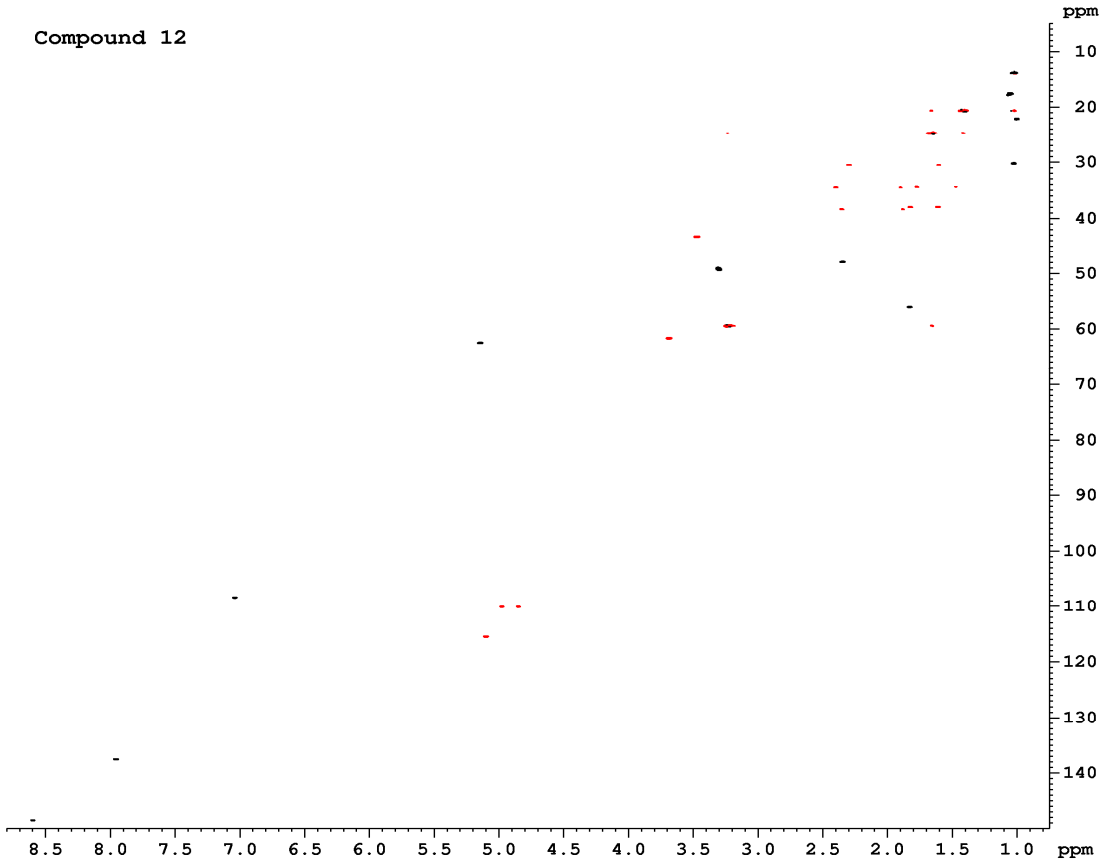
NAME	Compound 12	
EXPNO	2	
PROCNO	1	
Date_	20091117	
Time	13.35	
INSTRUM	spect	
PROBHD	5 mm CPTCI 1H-	
PULPROG	cosydfgpph19	
TD	2048	
SOLVENT	MeOD	
NS	24	
DS	16	
SWH	8223.685	Hz
FIDRES	4.015471	Hz
AQ	0.1245684	sec
RG	114	
DW	60.800	usec
DE	30.00	usec
TE	301.9	K
d0	0.00004769	sec
D1	1.39999998	sec
d11	0.03000000	sec
d12	0.00002000	sec
d13	0.00000400	sec
D16	0.00020000	sec
D19	0.00012500	sec
IN0	0.00012160	sec
ST1CNT	0	
======== CHANNEL f1 ========		
NUC1	1H	
P0	9.20	usec
P1	10.30	usec
P27	10.30	usec
PL1	0.20	dB
PL18	0.20	dB
PL9	55.66	dB
SFO1	800.1838776	MHz
====== GRADIENT CHANNEL =====		
GPNAM1	SINE.100	
GPNAM2	SINE.100	
GPZ1	30.00	%
GPZ2	30.00	%
P16	1000.00	usec
ND0	1	
TD	1024	
SFO1	800.1839	MHz
FIDRES	8.030942	Hz
SW	10.277	ppm
FnMODE	States-TPPI	
SI	2048	
SF	800.1800263	MHz
WDW	QSINE	
SSB	3	
LB	0.00	Hz
GB	0	
PC	1.40	
SI	2048	
MC2	States-TPPI	
SF	800.1800264	MHz
WDW	QSINE	
SSB	3	
LB	0.00	Hz
GB	0	

2D DQF-COSY spectrum of **12** in CD_3OD at 25^{o} C. The black and red contours represent positive and negative peaks, respectively.

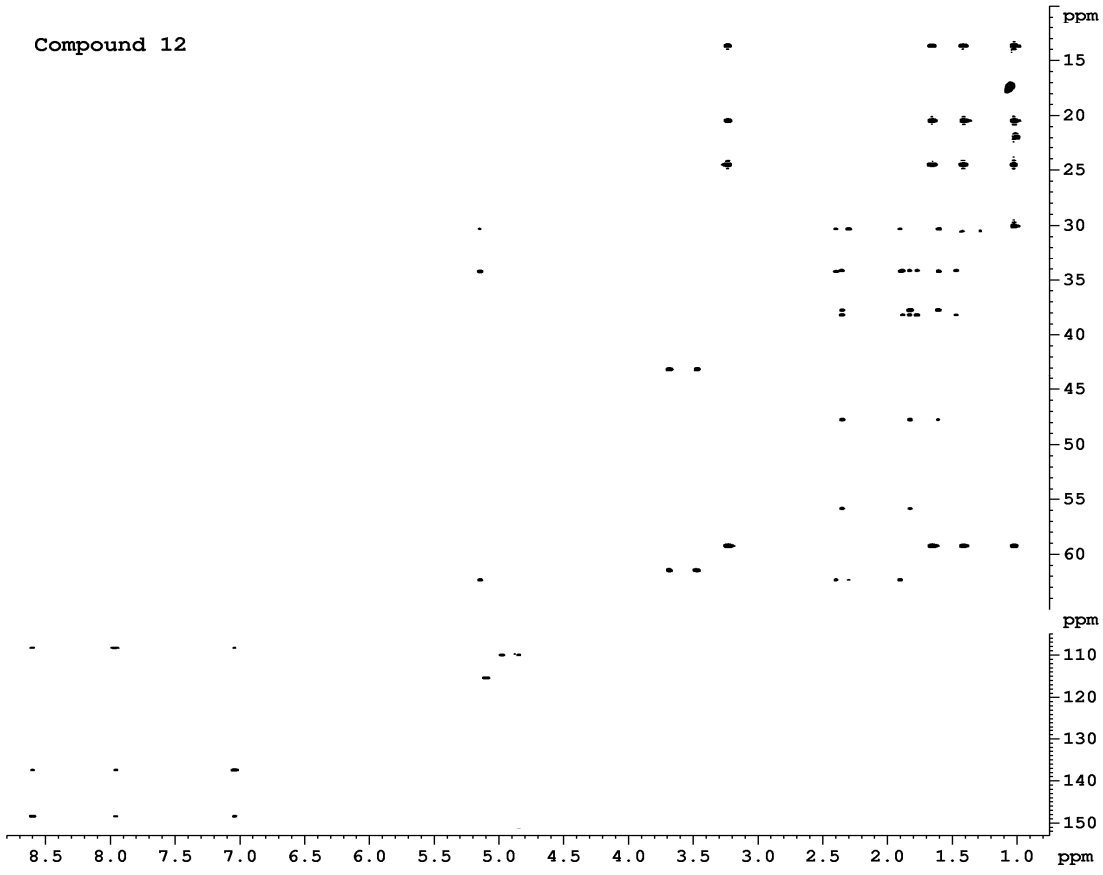


NAME	Compound 12
EXPNO	3
PROCNO	1
Date_	20091118
Time	0.28
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	dipsi2etgpsi19
TD	2048
SOLVENT	MeOD
NS	24
DS	16
SWH	8223.685 Hz
FIDRES	4.015471 Hz
AQ	0.1245684 sec
RG	101
DW	60.800 usec
DE	30.00 usec
TE	301.9 K
d0	0.00000300 sec
D1	1.39999998 sec
d11	0.03000000 sec
d12	0.00002000 sec
d13	0.00000400 sec
D16	0.00020000 sec
D19	0.00012500 sec
D20	0.00001000 sec
D21	0.00001000 sec
D9	0.06000000 sec
DELTA	0.00120300 sec
FACTOR1	11
IN0	0.00012160 sec
l1	22
ST1CNT	0
======== CHANNEL f1 ========	
NUC1	1H
P0	10.30 usec
P1	10.30 usec
p2	20.60 usec
P27	10.30 usec
P6	24.00 usec
PL1	0.20 dB
PL10	7.55 dB
PL18	0.20 dB
PL9	55.66 dB
SFO1	800.1838676 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPNAM2	SINE.100
GPNAM3	SINE.100
GPZ1	30.00 %
GPZ2	20.00 %
GPZ3	50.00 %
P16	1000.00 usec
ND0	1
TD	1024
SFO1	800.1839 MHz
FIDRES	8.030942 Hz
SW	10.277 ppm
FnMODE	Echo-Antiecho
SI	2048
SF	800.1800244 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.40
SI	2048
MC2	echo-antiecho
SF	800.1800244 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0

2D TOCSY spectrum of **12** in CD_3OD at 25° C.



2D ^{13}C-HSQC spectrum of **12** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The black cross-peaks correspond to CH_3 and CH groups, the red cross-peaks correspond to CH_2 groups.



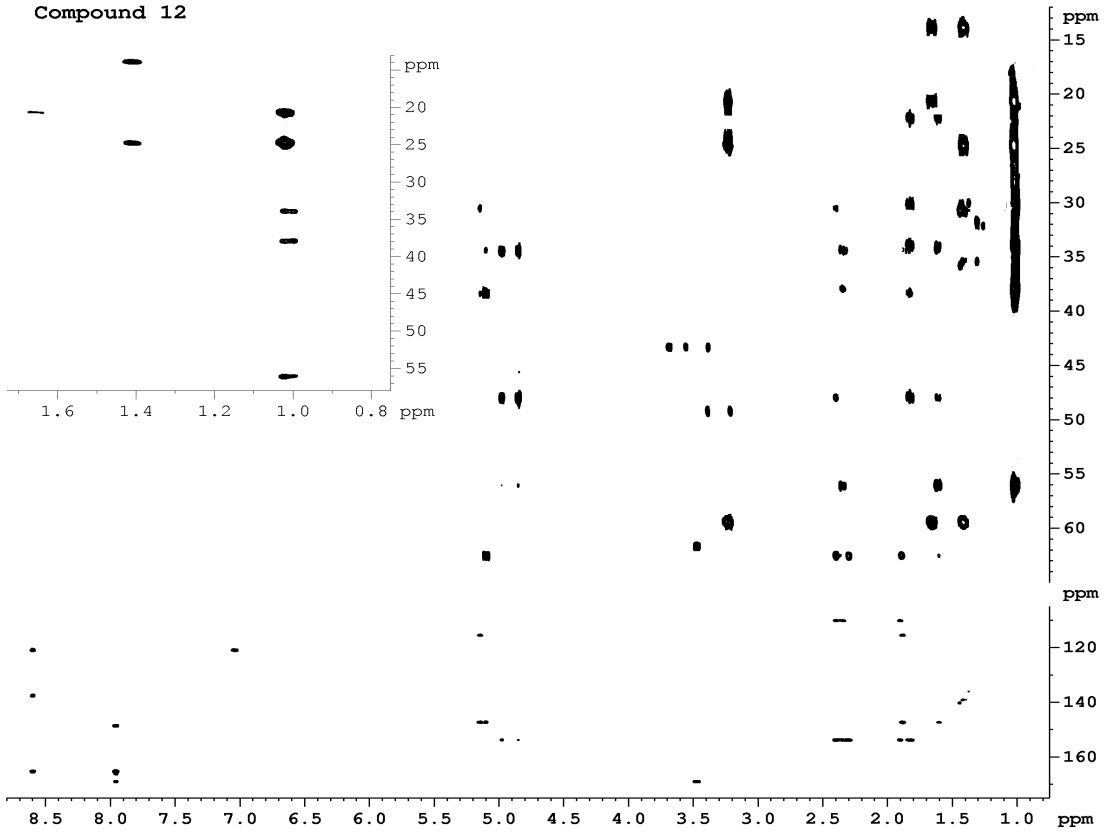

```
NAME                Compound 12
EXPNO                         5
PROCNO                        1
Date_                  20091119
Time                       1.28
INSTRUM                   spect
PROBHD     5 mm CPTCI 1H-
PULPROG    hsqcdietgpsisp.2
TD                         1024
SOLVENT                   MeOD
NS                           32
DS                           32
SWH                   8223.685 Hz
FIDRES                8.030942 Hz
AQ                    0.0623092 sec
RG                        2580
DW                      60.800 usec
DE                      30.00 usec
TE                      301.9 K
CNST17                -0.5000000
CNST2               145.0000000
d0                    0.00000300 sec
D1                    1.50000000 sec
d11                   0.03000000 sec
D16                   0.00020000 sec
D24                   0.00086200 sec
d4                    0.00172414 sec
D9                    0.06000000 sec
DELTA                 0.00122260 sec
DELTA1                0.00120800 sec
DELTA2                0.00147014 sec
DELTA3                0.00135800 sec
FACTOR1                       11
IN0                   0.00001655 sec
l1                            22
ST1CNT                         0

======== CHANNEL f1 ========
NUC1                          1H
P1                       10.30 usec
p2                       20.60 usec
P28                    1000.00 usec
P6                       24.00 usec
PL1                       0.20 dB
PL10                      7.55 dB
SFO1                800.1838676 MHz

======== CHANNEL f2 ========
CPDPRG2               p5m4sp180
NUC2                        13C
P14                     500.00 usec
P24                    2000.00 usec
P3                       14.00 usec
PCPD2                  1500.00 usec
PL0                     120.00 dB
PL12                     10.00 dB
PL2                      -2.00 dB
SFO2                201.2205114 MHz
SP3                       1.08 dB
SP7                       1.08 dB
SPNAM15    Crp,80,1.5,10.nd
SPNAM3     Crp80,0.5,20.1
SPNAM7       Crp80comp.4
SPOAL15                0.500
SPOAL3                 0.500
SPOAL7                 0.500
SPOFFS15               0.00 Hz
SPOFFS3                0.00 Hz
SPOFFS7                0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPZ1                   80.00 %
GPZ2                   20.10 %
P16                  1000.00 usec
ND0                           2
TD                         1024
SFO1                201.2205 MHz
FIDRES              29.503399 Hz
SW                    150.141 ppm
FnMODE       Echo-Antiecho
SI                         2048
SF                  800.1800219 MHz
WDW                      QSINE
SSB                           2
LB                       0.00 Hz
GB                            0
PC                         1.00
SI                         2048
MC2          echo-antiecho
SF                  201.2051870 MHz
WDW                      QSINE
SSB                           2
LB                       0.00 Hz
GB                            0
```

2D ^{13}C-HSQC-TOCSY spectrum of **12** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively.



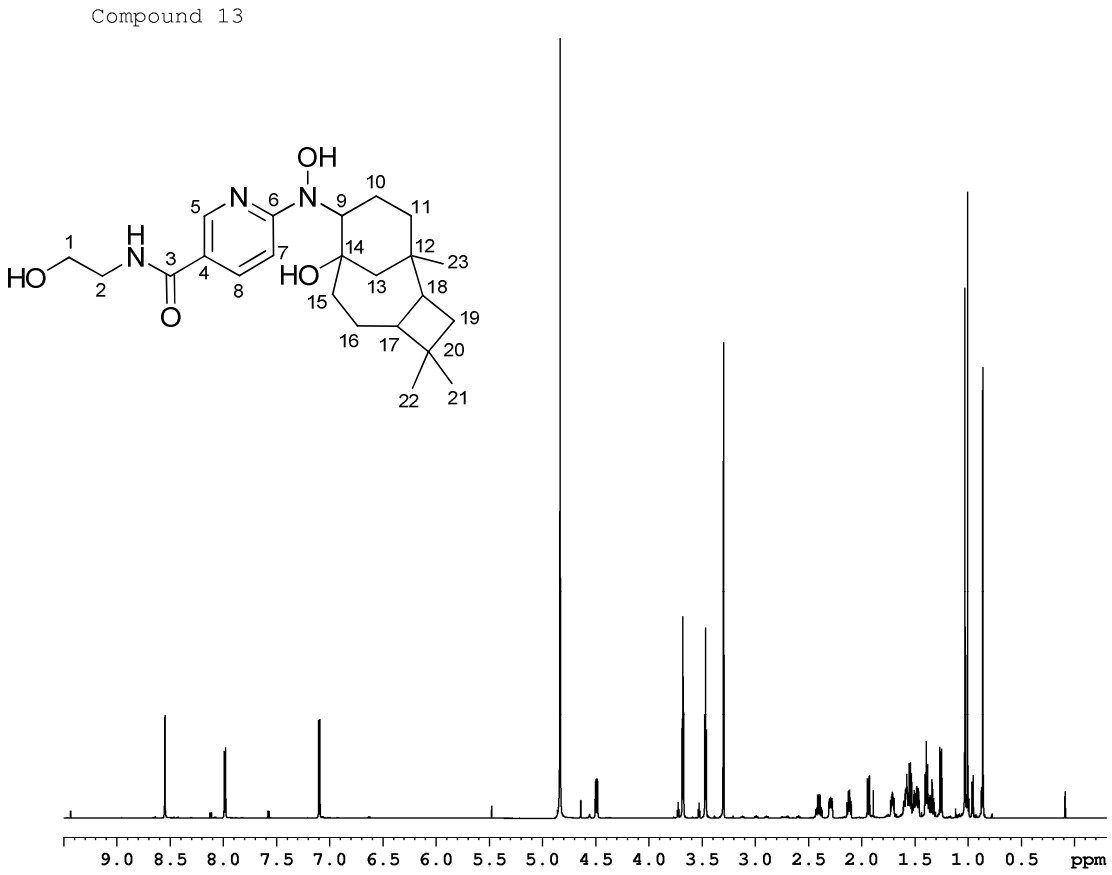

```
NAME                 Compound 12
EXPNO                          6
PROCNO                         1
Date_                   20091119
Time                       16.34
INSTRUM                     spect
PROBHD     5 mm CPTCI 1H-
PULPROG      hmbcgpl2ndqf
TD                          2048
SOLVENT                     MeOD
NS                            80
DS                            64
SWH                     8223.685 Hz
FIDRES                  4.015471 Hz
AQ                     0.1245684 sec
RG                          2890
DW                        60.800 usec
DE                        30.00 usec
TE                        301.9 K
CNST13                 8.0000000
CNST6                125.0000000
CNST7                175.0000000
d0                     0.00000300 sec
D1                     1.39999998 sec
D16                    0.00020000 sec
d6                     0.06250000 sec
DELTA1                 0.00280000 sec
DELTA2                 0.00165714 sec
DELTA3                 0.06129600 sec
IN0                    0.00001310 sec

======== CHANNEL f1 ========
NUC1                         1H
P1                        10.30 usec
p2                        20.60 usec
PL1                        0.20 dB
SFO1                800.1838676 MHz

======== CHANNEL f2 ========
NUC2                        13C
P3                        14.80 usec
PL2                       -2.00 dB
SFO2                201.2245355 MHz

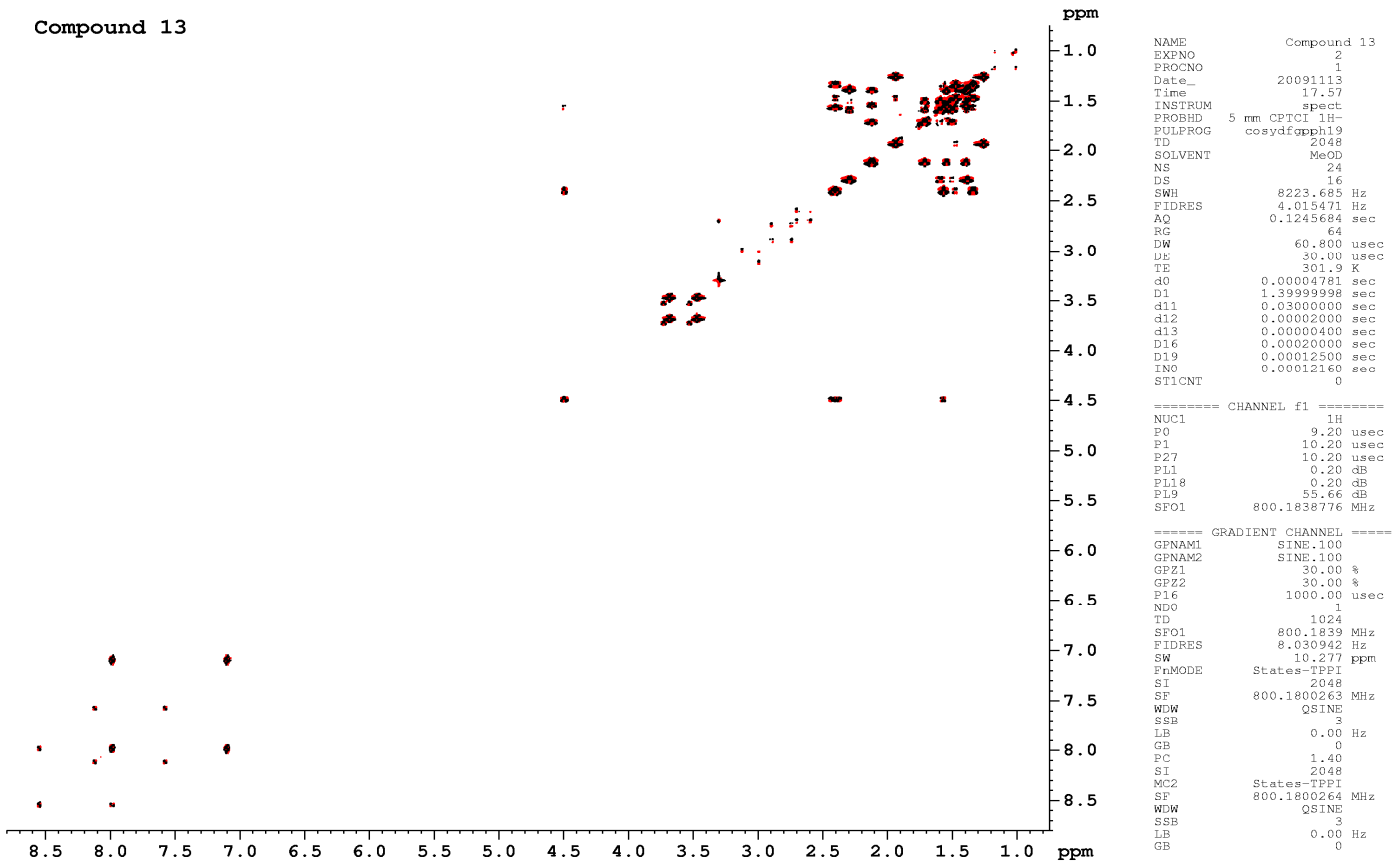
====== GRADIENT CHANNEL =====
GPNAM1                 SINE.100
GPNAM2                 SINE.100
GPNAM3                 SINE.100
GPNAM4                 SINE.100
GPNAM5                 SINE.100
GPNAM6                 SINE.100
GPZ1                      50.00 %
GPZ2                      30.00 %
GPZ3                      40.10 %
GPZ4                      15.00 %
GPZ5                     -10.00 %
GPZ6                      -5.00 %
P16                     1000.00 usec
ND0                           2
TD                          512
SFO1                201.2245 MHz
FIDRES               74.546753 Hz
SW                     189.678 ppm
FnMODE                       QF
SI                          2048
SF                  800.1800248 MHz
WDW                       QSINE
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.40
SI                          2048
MC2                          QF
SF                  201.2051470 MHz
WDW                       QSINE
SSB                           0
LB                         0.00 Hz
GB                            0
```

2D ^{13}C-HMBC spectrum of **12** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The insert in the upper left corner represents an expansion of the high field region plotted with reduced cross-peaks intensities for a better clarity.



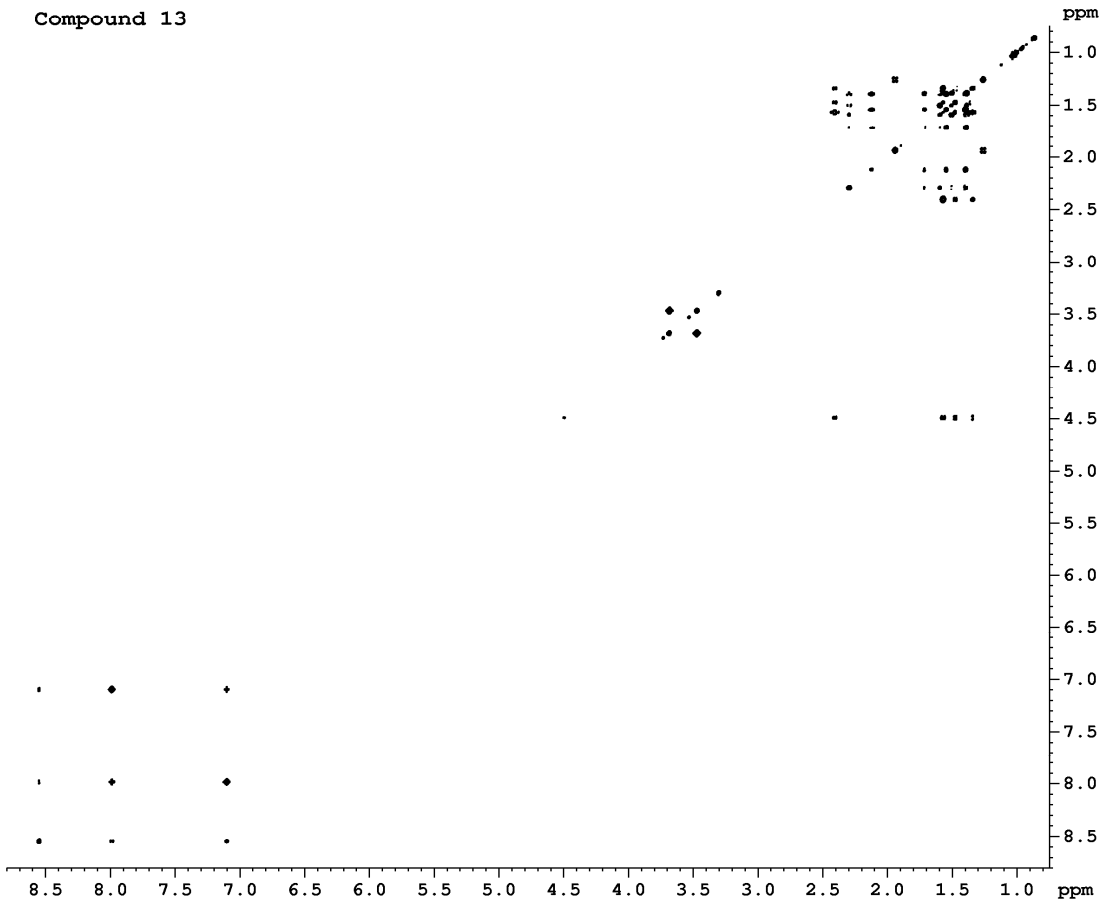
NAME	Compound 13
EXPNO	1
PROCNO	1
Date_	20091113
Time	17.27
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	zg
TD	65536
SOLVENT	MeOD
NS	64
DS	0
SWH	8223.685 Hz
FIDRES	0.125483 Hz
AQ	3.9846387 sec
RG	32
DW	60.800 usec
DE	30.00 usec
TE	301.9 K
D1	0.10000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	6.00 usec
PL1	0.20 dB
SFO1	800.1837640 MHz
SI	131072
SF	800.1800262 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

^{1}H spectrum of **13** in CD_3OD at 25^{o} C.



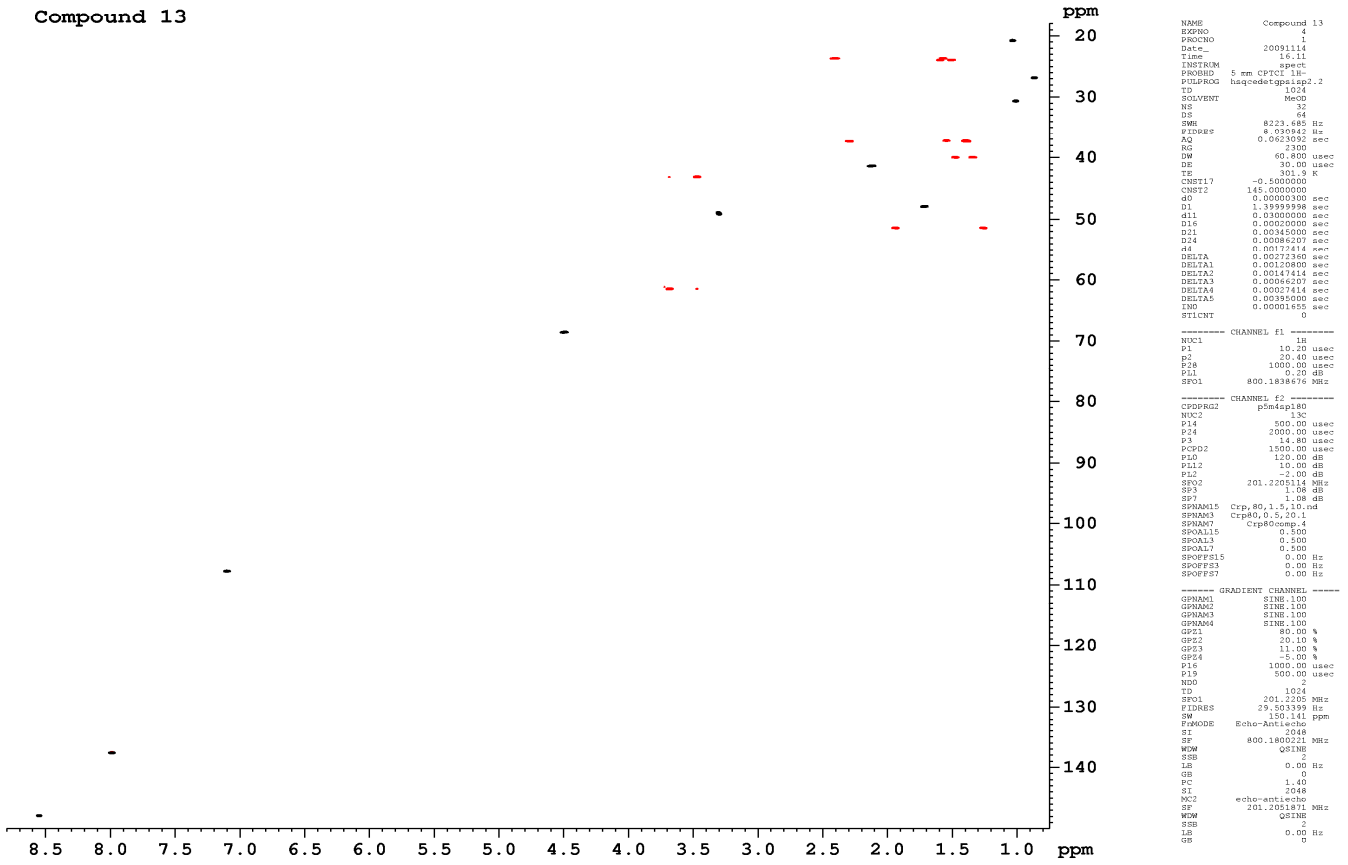
NAME	Compound 13	
EXPNO	2	
PROCNO	1	
Date_	20091113	
Time	17.57	
INSTRUM	spect	
PROBHD	5 mm CPTCI 1H-	
PULPROG	cosydfqppph19	
TD	2048	
SOLVENT	MeOD	
NS	24	
DS	16	
SWH	8223.685	Hz
FIDRES	4.015471	Hz
AQ	0.1245684	sec
RG	64	
DW	60.800	usec
DE	30.00	usec
TE	301.9	K
d0	0.00004781	sec
D1	1.39999998	sec
d11	0.03000000	sec
d12	0.00002000	sec
d13	0.00000400	sec
D16	0.00020000	sec
D19	0.00012500	sec
INO	0.00012160	sec
ST1CNT	0	
======== CHANNEL f1 ========		
NUC1	1H	
P0	9.20	usec
P1	10.20	usec
P27	10.20	usec
PL1	0.20	dB
PL18	0.20	dB
PL9	55.66	dB
SFO1	800.1838776	MHz
====== GRADIENT CHANNEL =====		
GPNAM1	SINE.100	
GPNAM2	SINE.100	
GPZ1	30.00	%
GPZ2	30.00	%
P16	1000.00	usec
ND0	1	
TD	1024	
SFO1	800.1839	MHz
FIDRES	8.030942	Hz
SW	10.277	ppm
FnMODE	States-TPPI	
SI	2048	
SF	800.1800263	MHz
WDW	QSINE	
SSB	3	
LB	0.00	Hz
GB	0	
PC	1.40	
SI	2048	
MC2	States-TPPI	
SF	800.1800264	MHz
WDW	QSINE	
SSB	3	
LB	0.00	Hz
GB	0	

2D DQF-COSY spectrum of **13** in CD_3OD at 25° C. The black and red contours represent positive and negative peaks, respectively.

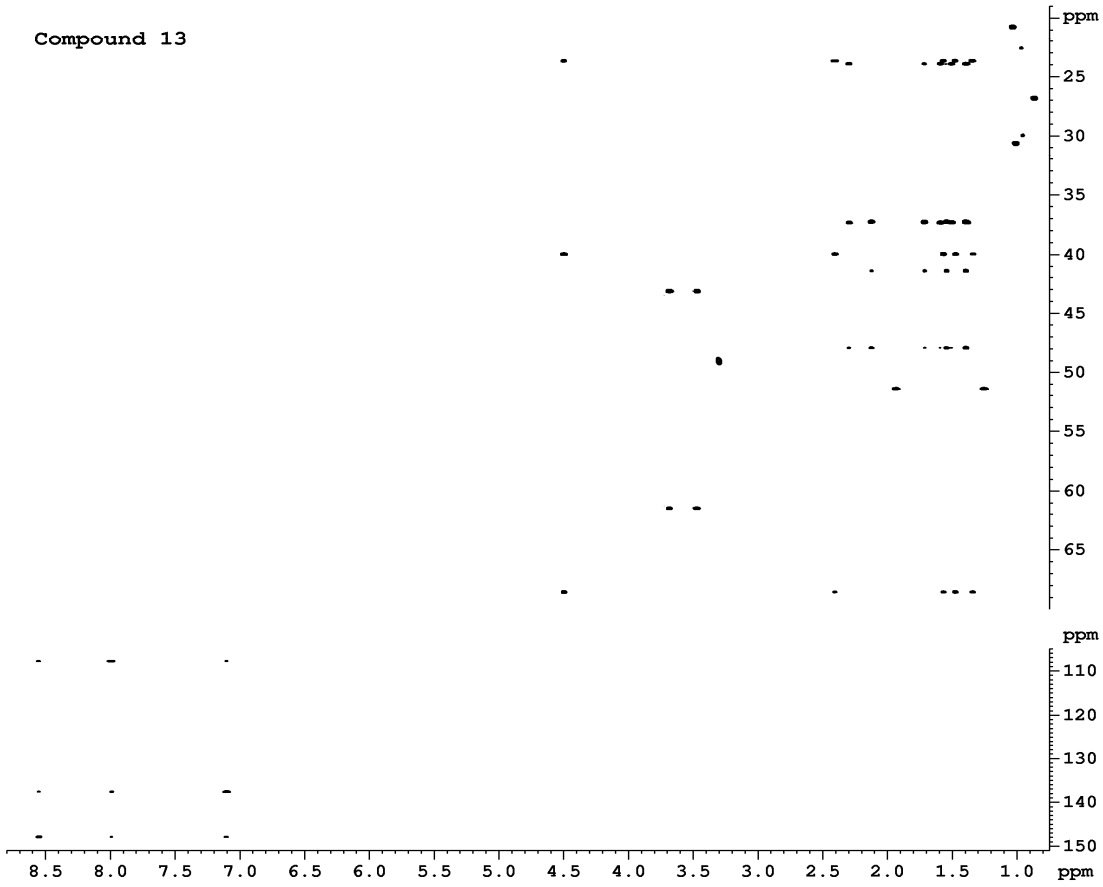


NAME	Compound 13
EXPNO	3
PROCNO	1
Date_	20091114
Time	4.50
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	dipsi2etgpsi19
TD	2048
SOLVENT	MeOD
NS	24
DS	16
SWH	8223.685 Hz
FIDRES	4.015471 Hz
AQ	0.1245684 sec
RG	101
DW	60.800 usec
DE	30.00 usec
TE	301.9 K
d0	0.00000300 sec
D1	1.39999998 sec
d11	0.03000000 sec
d12	0.00002000 sec
d13	0.00000400 sec
D16	0.00020000 sec
D19	0.00012500 sec
D20	0.00001000 sec
D21	0.00001000 sec
D9	0.06000000 sec
DELTA	0.00120300 sec
FACTOR1	11
IN0	0.00012160 sec
l1	22
ST1CNT	0
======== CHANNEL f1 ========	
NUC1	1H
P0	10.20 usec
P1	10.20 usec
p2	20.40 usec
P27	10.20 usec
P6	24.00 usec
PL1	0.20 dB
PL10	7.63 dB
PL18	0.20 dB
PL9	55.66 dB
SFO1	800.1838676 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPNAM2	SINE.100
GPNAM3	SINE.100
GPZ1	30.00 %
GPZ2	20.00 %
GPZ3	50.00 %
P16	1000.00 usec
ND0	1
TD	1024
SFO1	800.1839 MHz
FIDRES	8.030942 Hz
SW	10.277 ppm
FnMODE	Echo-Antiecho
SI	2048
SF	800.1800244 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.40
SI	2048
MC2	echo-antiecho
SF	800.1800244 MHz
WDW	QSINE
ssb	2
LB	0.00 Hz
GB	0

2D TOCSY spectrum of **13** in CD_3OD at 25° C.



2D ^{13}C-HSQC spectrum of **13** in CD_3OD at 25° C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The black cross-peaks correspond to CH_3 and CH groups, the red cross-peaks correspond to CH_2 groups.



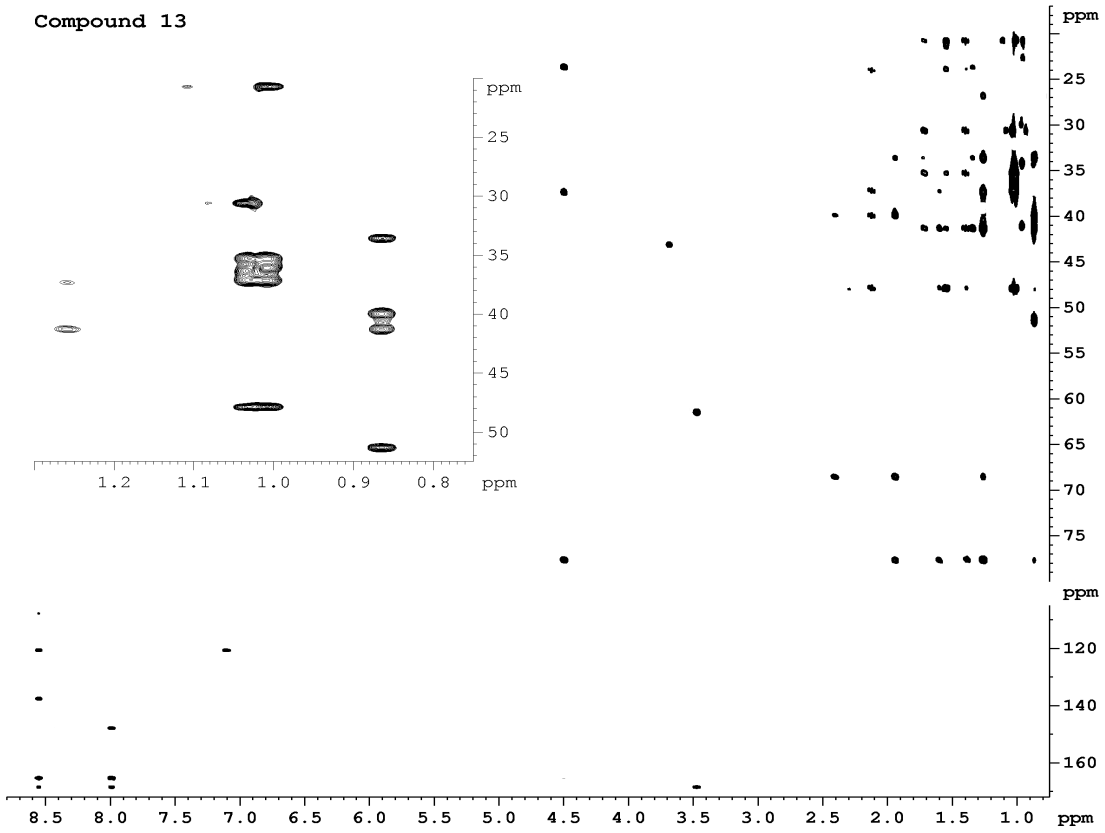

```
NAME                 Compound 13
EXPNO                         5
PROCNO                        1
Date_                  20091115
Time                       5.50
INSTRUM                   spect
PROBHD     5 mm CPTCI 1H-
PULPROG    hsqcdietgpsisp.2
TD                         1024
SOLVENT                    MeOD
NS                           32
DS                           32
SWH                    8223.685 Hz
FIDRES                 8.030942 Hz
AQ                     0.0623092 sec
RG                          2300
DW                       60.800 usec
DE                       30.00 usec
TE                       301.9 K
CNST17                -0.5000000
CNST2                145.0000000
d0                    0.00000300 sec
D1                    1.50000000 sec
d11                   0.03000000 sec
D16                   0.00020000 sec
D24                   0.00086200 sec
d4                    0.00172414 sec
D9                    0.06000000 sec
DELTA                 0.00122240 sec
DELTA1                0.00120800 sec
DELTA2                0.00147014 sec
DELTA3                0.00135800 sec
FACTOR1                      11
IN0                   0.00001655 sec
l1                           22
ST1CNT                        0

======== CHANNEL f1 ========
NUC1                         1H
P1                        10.20 usec
p2                        20.40 usec
P28                     1000.00 usec
P6                        24.00 usec
PL1                        0.20 dB
PL10                       7.63 dB
SFO1                800.1838676 MHz

======== CHANNEL f2 ========
CPDPRG2              p5m4sp180
NUC2                       13C
P14                     500.00 usec
P24                    2000.00 usec
P3                       14.80 usec
PCPD2                  1500.00 usec
PL0                     120.00 dB
PL12                     10.00 dB
PL2                      -2.00 dB
SFO2               201.2205114 MHz
SP3                       1.08 dB
SP7                       1.08 dB
SPNAM15   Crp,80,1.5,10.nd
SPNAM3    Crp80,0.5,20.1
SPNAM7      Crp80comp.4
SPOAL15               0.500
SPOAL3                0.500
SPOAL7                0.500
SPOFFS15              0.00 Hz
SPOFFS3               0.00 Hz
SPOFFS7               0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1             SINE.100
GPNAM2             SINE.100
GPZ1                  80.00 %
GPZ2                  20.10 %
P16                 1000.00 usec
ND0                          2
TD                        1024
SFO1               201.2205 MHz
FIDRES            29.503399 Hz
SW                   150.141 ppm
FnMODE     Echo-Antiecho
SI                        2048
SF                 800.1800219 MHz
WDW                     QSINE
SSB                          2
LB                        0.00 Hz
GB                           0
PC                        1.00
SI                        2048
MC2          echo-antiecho
SF                 201.2051870 MHz
WDW                     QSINE
SSB                          2
LB                        0.00 Hz
GB                           0
```

2D ^{13}C-HSQC-TOCSY spectrum of **13** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively.




```
NAME            Compound 13
EXPNO                     6
PROCNO                    1
Date_              20091115
Time                  20.57
INSTRUM                spect
PROBHD    5 mm CPTCI 1H-
PULPROG     hmbcgpl2ndqf
TD                     2048
SOLVENT                MeOD
NS                       80
DS                       64
SWH                8223.685 Hz
FIDRES             4.015471 Hz
AQ                0.1245684 sec
RG                     2300
DW                   60.800 usec
DE                   30.00 usec
TE                   301.9 K
CNST13           8.0000000
CNST6          125.0000000
CNST7          175.0000000
d0              0.00000300 sec
D1              1.39999998 sec
D16             0.00020000 sec
d6              0.06250000 sec
DELTA1          0.00280000 sec
DELTA2          0.00165714 sec
DELTA3          0.06129600 sec
IN0             0.00001310 sec

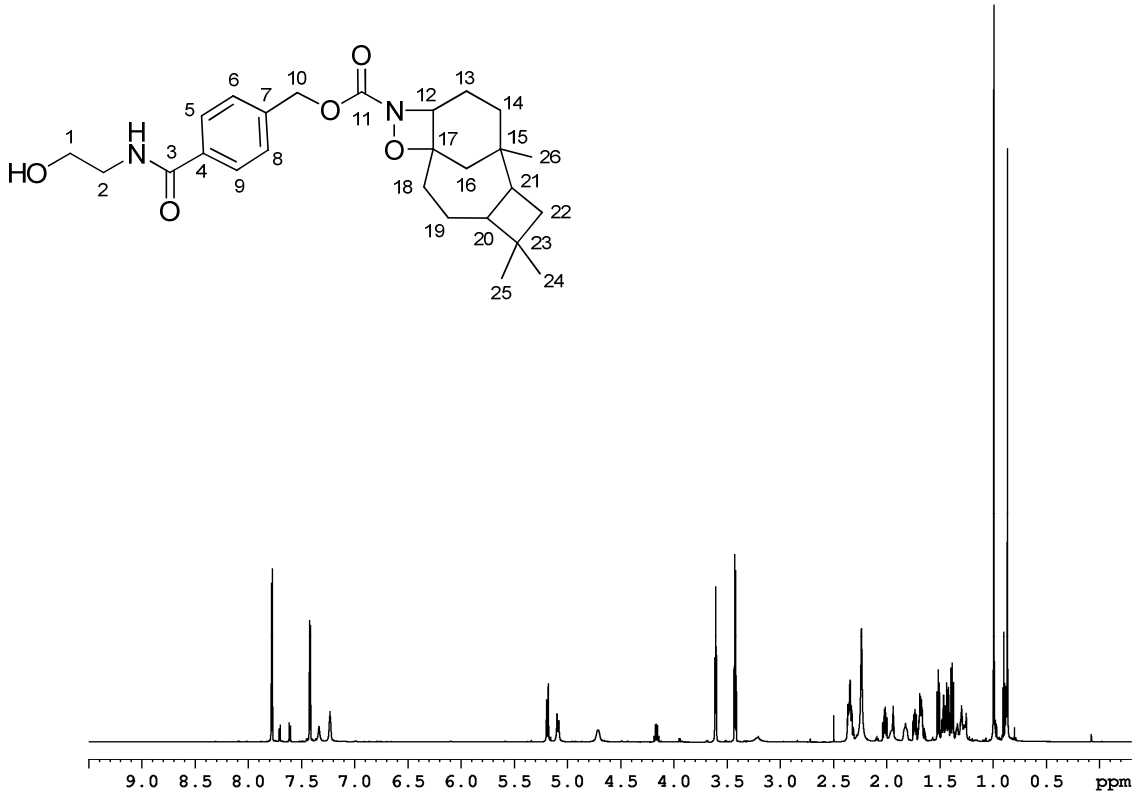
======== CHANNEL f1 ========
NUC1                    1H
P1                   10.20 usec
p2                   20.40 usec
PL1                   0.20 dB
SFO1          800.1838676 MHz

======== CHANNEL f2 ========
NUC2                   13C
P3                   14.80 usec
PL2                  -2.00 dB
SFO2          201.2245355 MHz

====== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPNAM3              SINE.100
GPNAM4              SINE.100
GPNAM5              SINE.100
GPNAM6              SINE.100
GPZ1                 50.00 %
GPZ2                 30.00 %
GPZ3                 40.10 %
GPZ4                 15.00 %
GPZ5                -10.00 %
GPZ6                 -5.00 %
P16                1000.00 usec
ND0                       2
TD                      512
SFO1            201.2245 MHz
FIDRES          74.546753 Hz
SW                189.678 ppm
FnMODE                   QF
SI                     2048
SF            800.1800239 MHz
WDW                   QSINE
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
SI                     2048
MC2                      QF
SF            201.2051930 MHz
WDW                   QSINE
SSB                       0
LB                     0.00 Hz
GB                        0
```

2D ^{13}C-HMBC spectrum of **13** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The insert in the upper left corner represents an expansion of the high field region plotted with reduced cross-peaks intensities for a better clarity.

Compound 16

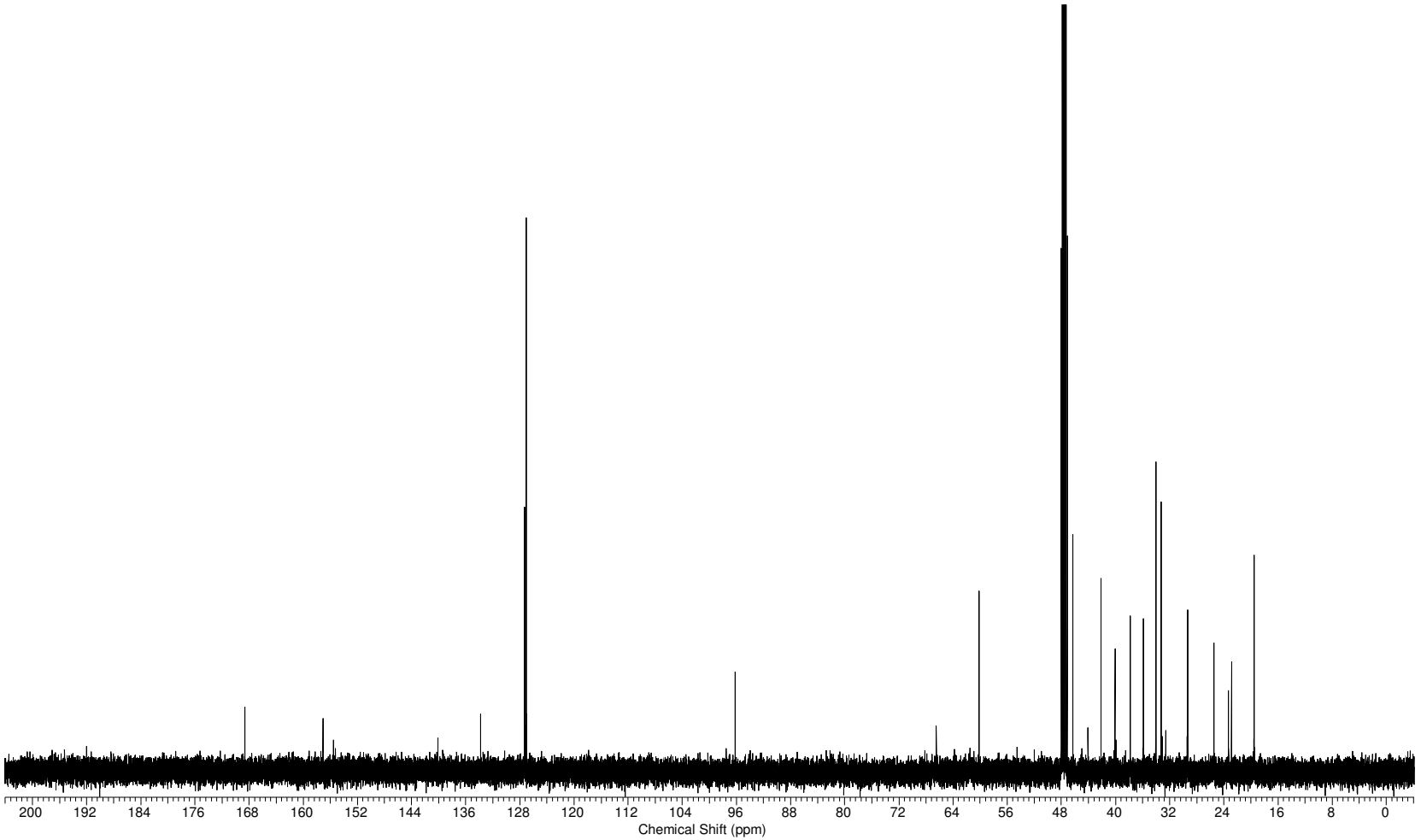



```
NAME            Compound 16
EXPNO                     1
PROCNO                    1
Date_              20091123
Time                   9.15
INSTRUM               spect
PROBHD   5 mm CPTCI 1H-
PULPROG                  zg
TD                    65536
SOLVENT               CD3CN
NS                      128
DS                        4
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9846387 sec
RG                       32
DW                   60.800 usec
DE                   30.00 usec
TE                   280.0 K
D1                0.10000000 sec
TD0                       1

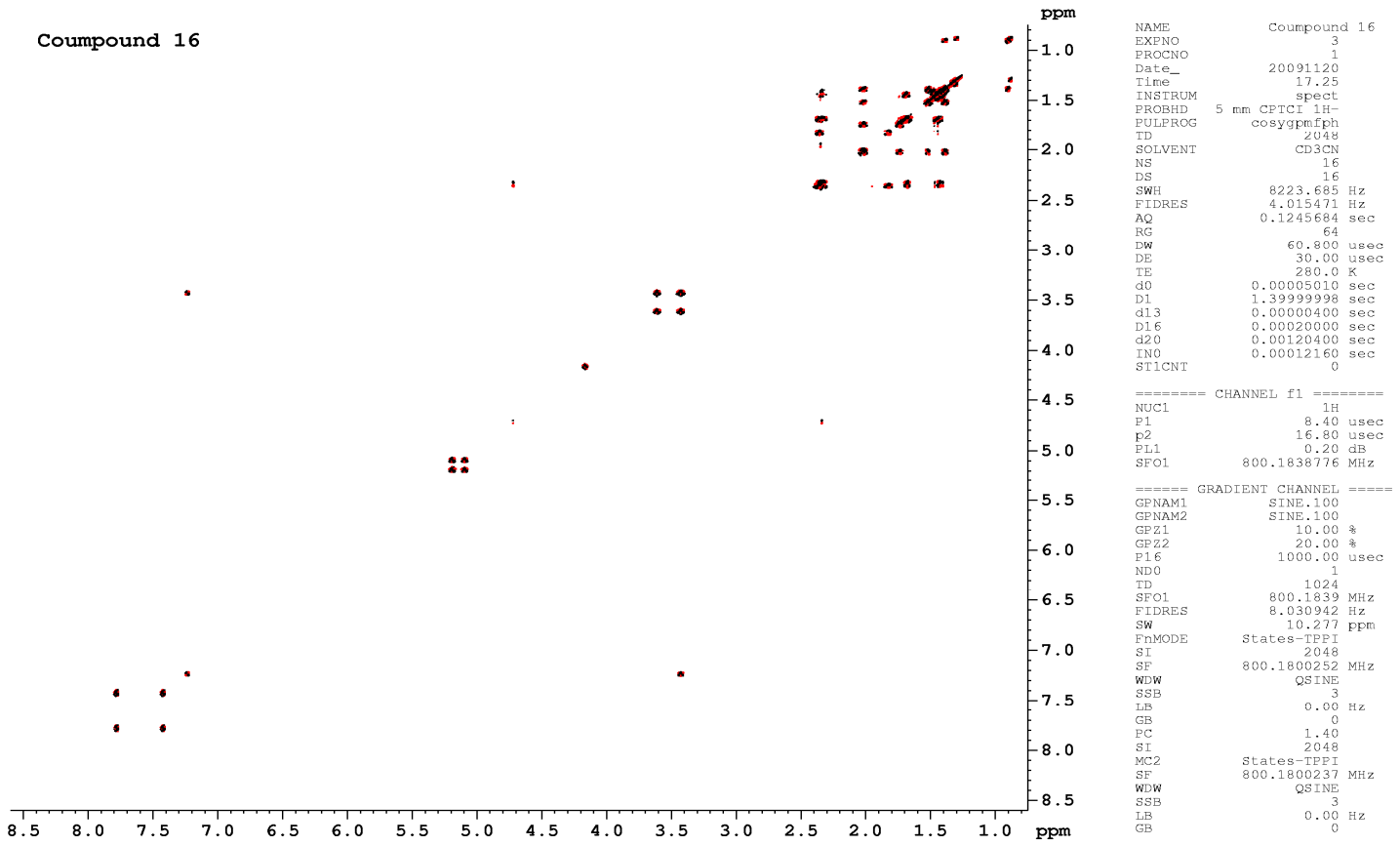
======== CHANNEL f1 ========
NUC1                     1H
P1                    8.40 usec
PL1                   0.20 dB
SFO1           800.1837640 MHz
SI                   131072
SF             800.1800262 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.00
```

^{1}H spectrum of **16** in CD_3CN at 25^{o} C.

Acquisition Time (sec)	1.7826	***Comment***	**Compound 16**	***Date***	May 27 2009	***Date Stamp***	May 27 2009
						Frequency (MHz)	150.85
Nucleus	13C	***Number of Transients***	256	***Original Points Count***	65536	***Points Count***	65536
Pulse Sequence	s2pul	***Receiver Gain***	60.00	***Solvent***	METHANOL-d4		
Spectrum Offset (Hz)	15838.1133	***Sweep Width (Hz)***	36764.71	***Temperature (degree C)***	22.000		



$^{13}C\{^{1}H\}$ spectrum of **16** in CD_3OD at 25° C.

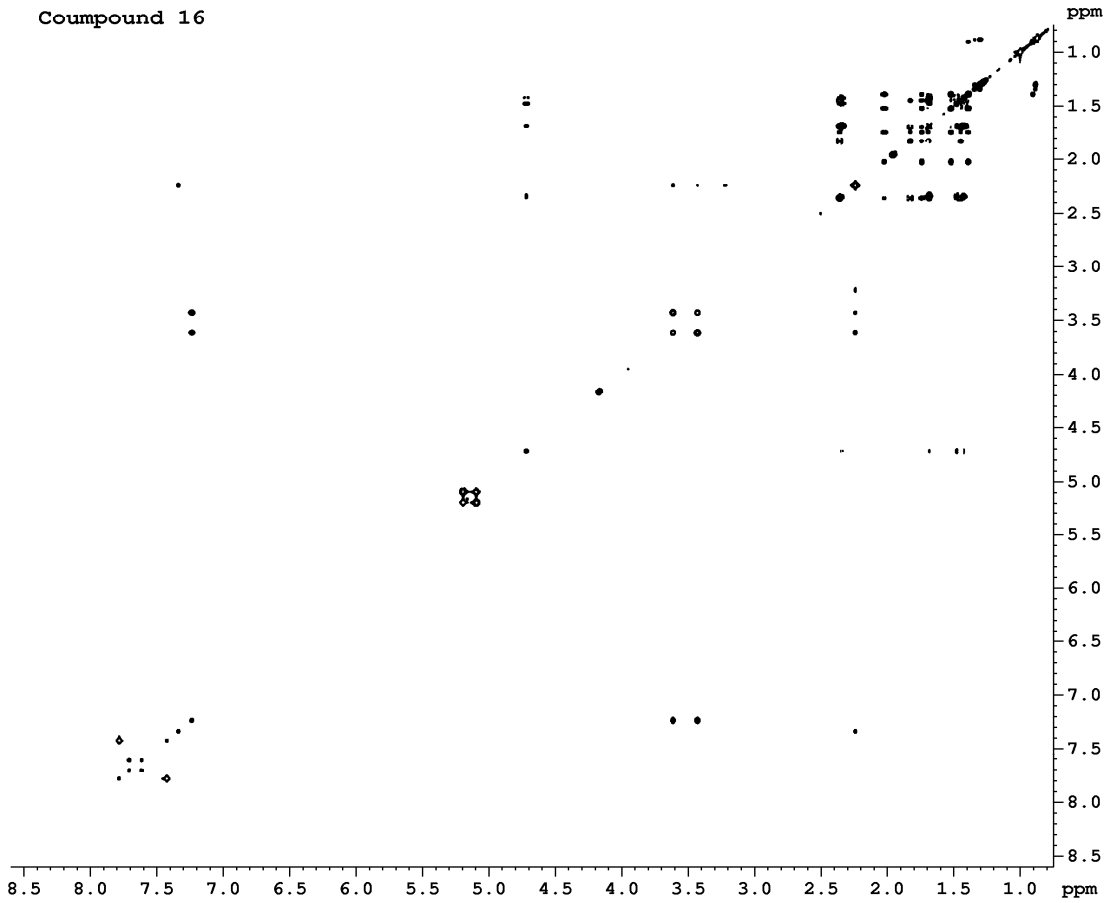



```
NAME              Coumpound 16
EXPNO                        3
PROCNO                       1
Date_              20091120
Time                    17.25
INSTRUM                  spect
PROBHD     5 mm CPTCI 1H-
PULPROG          cosygpmfph
TD                        2048
SOLVENT                 CD3CN
NS                          16
DS                          16
SWH                  8223.685 Hz
FIDRES               4.015471 Hz
AQ                   0.1245684 sec
RG                         64
DW                      60.800 usec
DE                      30.00 usec
TE                      280.0 K
d0                   0.00005010 sec
D1                   1.39999998 sec
d13                  0.00000400 sec
D16                  0.00020000 sec
d20                  0.00120400 sec
IN0                  0.00012160 sec
ST1CNT                       0

======== CHANNEL f1 ========
NUC1                        1H
P1                       8.40 usec
p2                      16.80 usec
PL1                      0.20 dB
SFO1              800.1838776 MHz

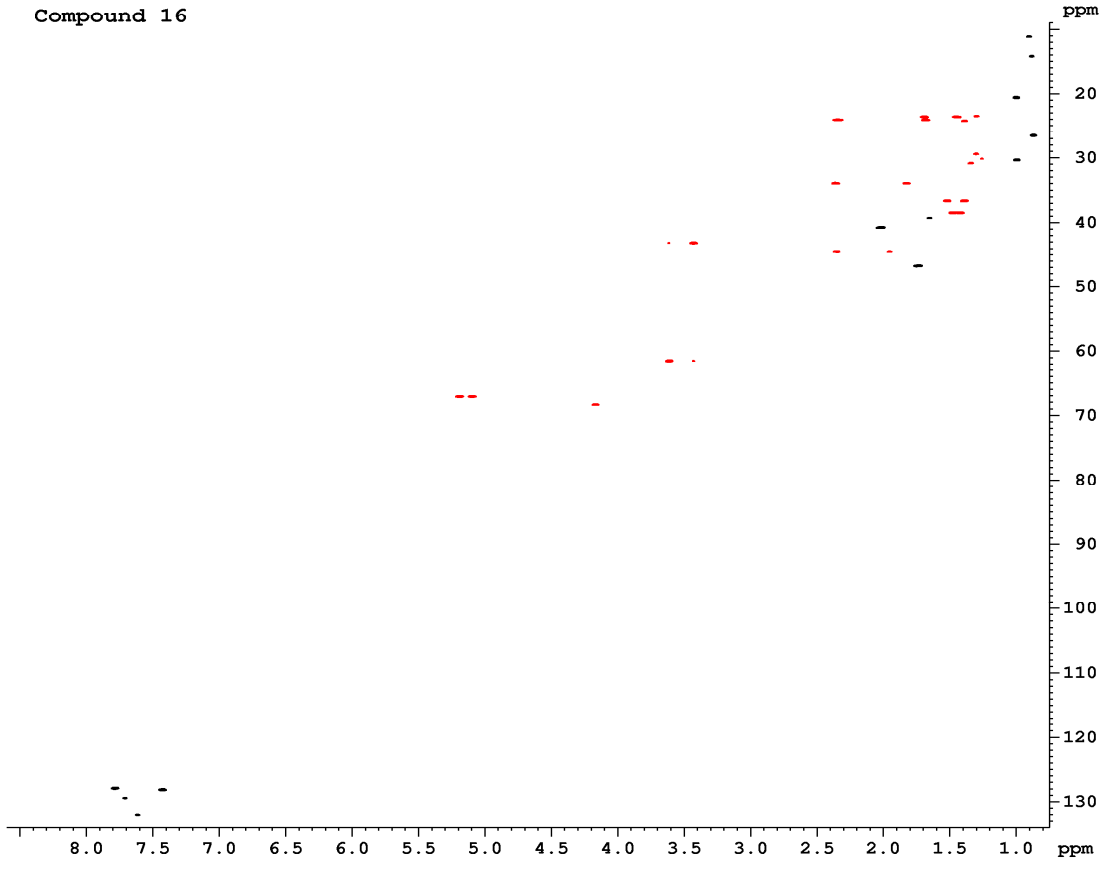
====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPNAM2                SINE.100
GPZ1                    10.00 %
GPZ2                    20.00 %
P16                   1000.00 usec
ND0                          1
TD                        1024
SFO1                 800.1839 MHz
FIDRES               8.030942 Hz
SW                     10.277 ppm
FnMODE             States-TPPI
SI                        2048
SF                   800.1800252 MHz
WDW                      QSINE
SSB                          3
LB                       0.00 Hz
GB                           0
PC                       1.40
SI                        2048
MC2                States-TPPI
SF                   800.1800237 MHz
WDW                      QSINE
SSB                          3
LB                       0.00 Hz
GB                           0
```

2D DQF-COSY spectrum of **16** in CD_3CN at 25° C. The black and red contours represent positive and negative peaks, respectively.

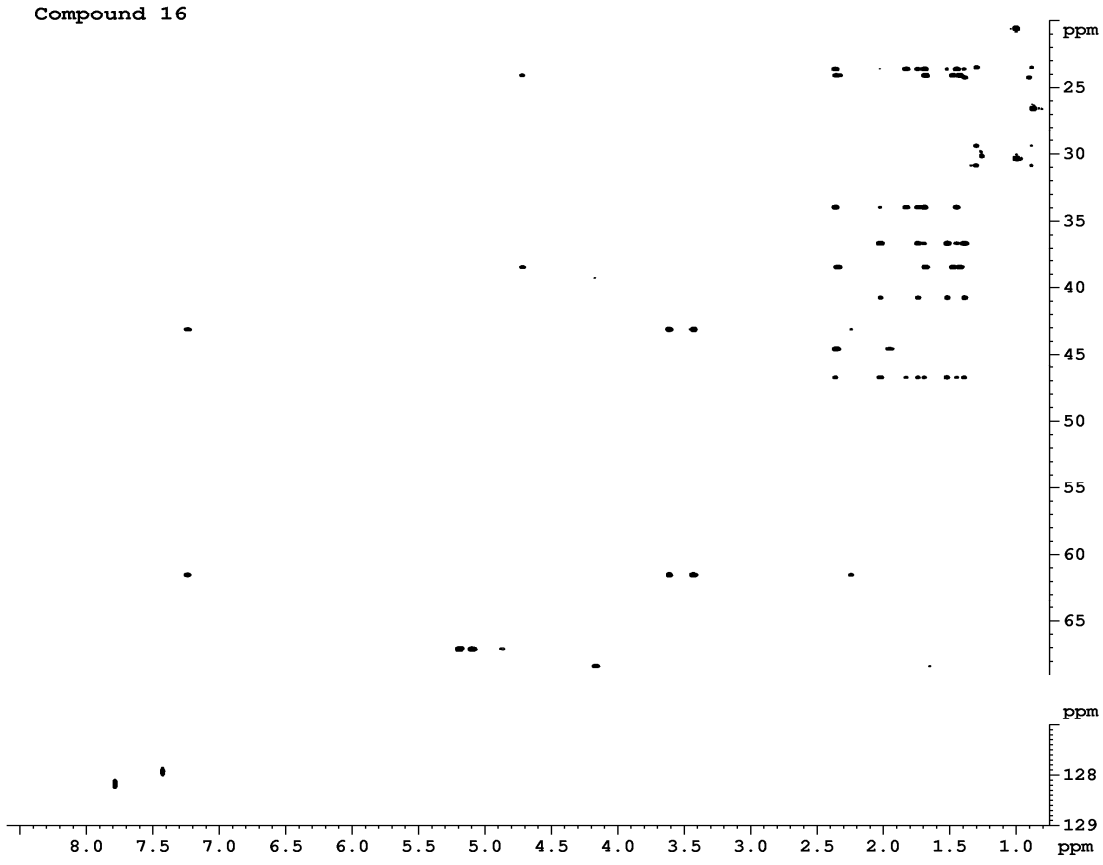


NAME	Compound 16	
EXPNO	4	
PROCNO	1	
Date_	20091121	
Time	0.32	
INSTRUM	spect	
PROBHD	5 mm CPTCI 1H-	
PULPROG	dipsi2etgpsi	
TD	2048	
SOLVENT	CD3CN	
NS	16	
DS	16	
SWH	8223.685	Hz
FIDRES	4.015471	Hz
AQ	0.1245684	sec
RG	64	
DW	60.800	usec
DE	30.00	usec
TE	280.0	K
d0	0.00000300	sec
D1	1.39999998	sec
d11	0.03000000	sec
D16	0.00020000	sec
D20	0.00001000	sec
D21	0.00001000	sec
D9	0.06000000	sec
DELTA	0.00120300	sec
DELTA1	0.00120800	sec
FACTOR1	11	
IN0	0.00012160	sec
l1	22	
ST1CNT	0	
======== CHANNEL f1 ========		
NUC1	1H	
P1	8.40	usec
p2	16.80	usec
P6	24.00	usec
PL1	0.20	dB
PL10	9.32	dB
SFO1	800.1838676	MHz
====== GRADIENT CHANNEL =====		
GPNAM1	SINE.100	
GPNAM2	SINE.100	
GPZ1	30.00	%
GPZ2	30.00	%
P16	1000.00	usec
ND0	1	
TD	1024	
SFO1	800.1839	MHz
FIDRES	8.030942	Hz
SW	10.277	ppm
FnMODE	Echo-Antiecho	
SI	2048	
SF	800.1800240	MHz
WDW	QSINE	
SSB	2	
LB	0.00	Hz
GB	0	
PC	1.40	
SI	2048	
MC2	echo-antiecho	
SF	800.1800239	MHz
WDW	QSINE	
SSB	2	
LB	0.00	Hz
GB	0	

2D TOCSY spectrum of **16** in CD_3CN at 25° C.



2D ^{13}C-HSQC spectrum of **16** in CD_3CN at 25° C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The black cross-peaks correspond to CH_3 and CH groups, the red cross-peaks correspond to CH_2 groups.



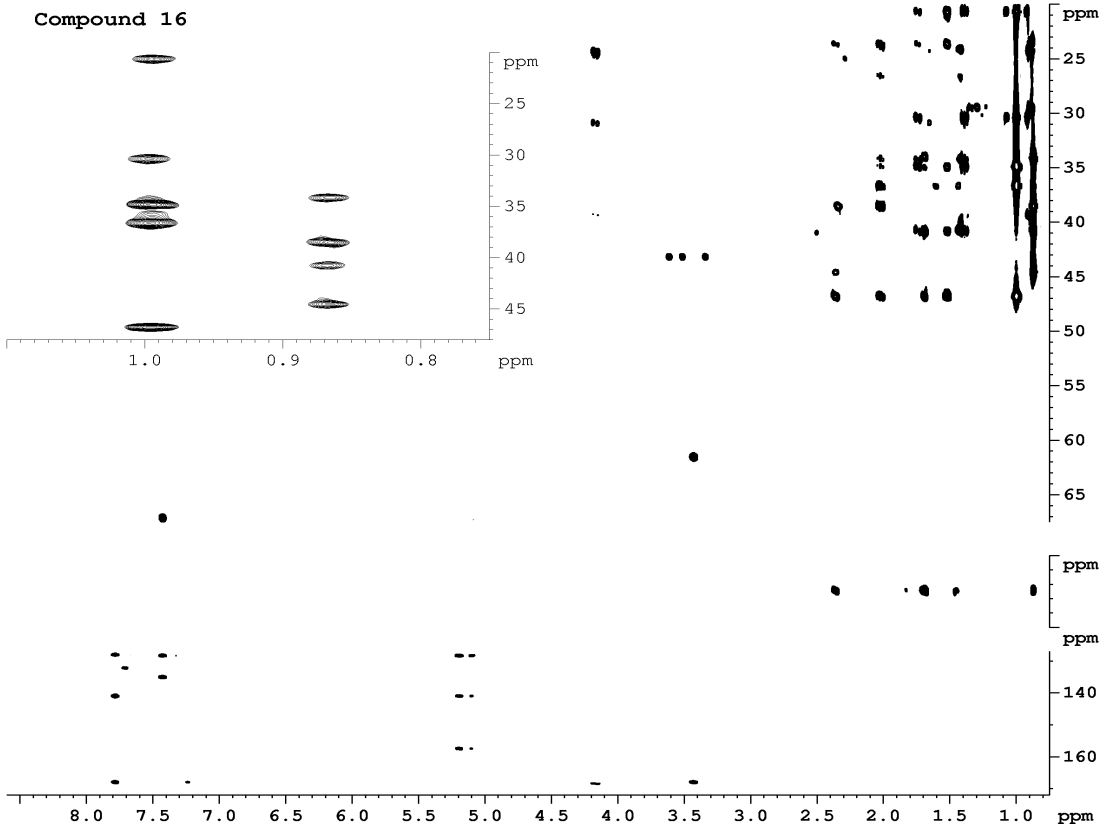

```
NAME              Compound 16
EXPNO                       6
PROCNO                      1
Date_             20091121
Time                  21.49
INSTRUM                spect
PROBHD     5 mm CPTCI 1H-
PULPROG    hsqcdietgpsisp.2
TD                       1024
SOLVENT                 CD3CN
NS                         32
DS                         64
SWH                8223.685 Hz
FIDRES             8.030942 Hz
AQ                 0.0623092 sec
RG                      2300
DW                    60.800 usec
DE                    30.00 usec
TE                    280.0 K
CNST17            -0.5000000
CNST2            145.0000000
d0                 0.00000300 sec
D1                 1.50000000 sec
d11                0.03000000 sec
D16                0.00020000 sec
D24                0.00086200 sec
d4                 0.00172414 sec
D9                 0.06000000 sec
DELTA              0.00121880 sec
DELTA1             0.00120800 sec
DELTA2             0.00147014 sec
DELTA3             0.00135800 sec
FACTOR1                    11
IN0                0.00001655 sec
l1                         22
ST1CNT                      0

======== CHANNEL f1 ========
NUC1                       1H
P1                       8.40 usec
p2                      16.80 usec
P28                   1000.00 usec
P6                      24.00 usec
PL1                      0.20 dB
PL10                     9.32 dB
SFO1            800.1838676 MHz

======== CHANNEL f2 ========
CPDPRG2          p5m4sp180
NUC2                      13C
P14                    500.00 usec
P24                   2000.00 usec
P3                      14.80 usec
PCPD2                 1500.00 usec
PL0                    120.00 dB
PL12                    10.00 dB
PL2                     -2.00 dB
SFO2            201.2205114 MHz
SP3                      1.08 dB
SP7                      1.08 dB
SPNAM15   Crp,80,1.5,10.nd
SPNAM3    Crp80,0.5,20.1
SPNAM7         Crp80comp.4
SPOAL15                0.500
SPOAL3                 0.500
SPOAL7                 0.500
SPOFFS15               0.00 Hz
SPOFFS3                0.00 Hz
SPOFFS7                0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GP21                   80.00 %
GP22                   20.10 %
P16                   1000.00 usec
ND0                        2
TD                      1024
SFO1              201.2205 MHz
FIDRES            29.503399 Hz
SW                  150.141 ppm
FnMODE       Echo-Antiecho
SI                      2048
SF              800.1800209 MHz
WDW                   QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
PC                      1.00
SI                      2048
MC2          echo-antiecho
SF              201.2052705 MHz
WDW                   QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
```

2D ^{13}C-HSQC-TOCSY spectrum of **16** in CD_3CN at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively.



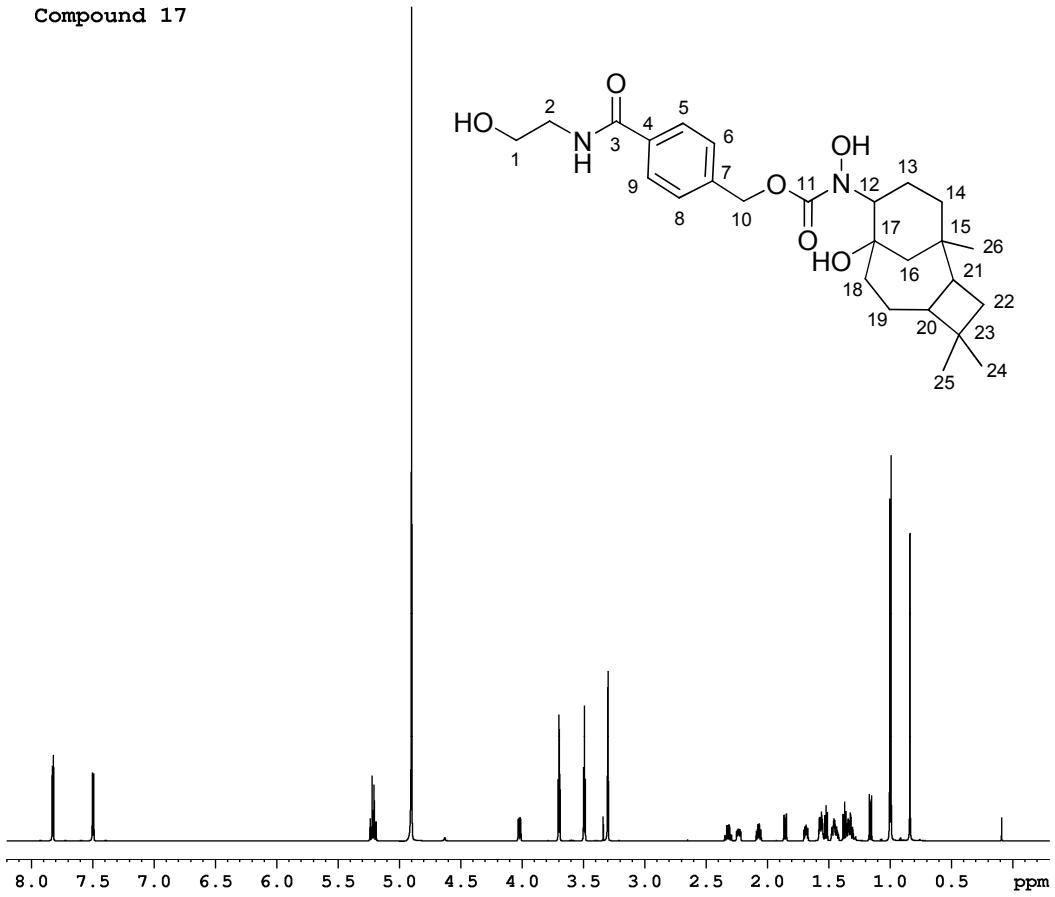

```
NAME                Coumpound 16
EXPNO                          7
PROCNO                         1
Date_                   20091122
Time                       12.57
INSTRUM                    spect
PROBHD     5 mm CPTCI 1H-
PULPROG      hmbcgpl2ndqf
TD                          2048
SOLVENT                   CD3CN
NS                             80
DS                            128
SWH                    8223.685 Hz
FIDRES                 4.015471 Hz
AQ                    0.1245684 sec
RG                          2300
DW                        60.800 usec
DE                        30.00 usec
TE                        280.0 K
CNST13                 8.0000000
CNST6                125.0000000
CNST7                175.0000000
d0                    0.00000300 sec
D1                    1.39999998 sec
D16                   0.00020000 sec
d6                    0.06250000 sec
DELTA1                0.00280000 sec
DELTA2                0.00165714 sec
DELTA3                0.06129600 sec
IN0                   0.00001310 sec

--------- CHANNEL f1 ---------
NUC1                         1H
P1                         8.40 usec
p2                        16.80 usec
PL1                        0.20 dB
SFO1                800.1838676 MHz

--------- CHANNEL f2 ---------
NUC2                        13C
P3                        14.80 usec
PL2                       -2.00 dB
SFO2                201.2245355 MHz

------- GRADIENT CHANNEL ------
GPNAM1                  SINE.100
GPNAM2                  SINE.100
GPNAM3                  SINE.100
GPNAM4                  SINE.100
GPNAM5                  SINE.100
GPNAM6                  SINE.100
GPZ1                       50.00 %
GPZ2                       30.00 %
GPZ3                       40.10 %
GPZ4                       15.00 %
GPZ5                      -10.00 %
GPZ6                       -5.00 %
P16                     1000.00 usec
ND0                            2
TD                           512
SFO1                201.2245 MHz
FIDRES               74.546753 Hz
SW                     189.678 ppm
FnMODE                      QF
SI                        2048
SF                  800.1800233 MHz
WDW                     QSINE
SSB                            0
LB                      0.00 Hz
GB                             0
PC                          1.40
SI                          2048
WDW                         QF
SF                  201.2052644 MHz
WDW                     QSINE
SSB                            0
LB                      0.00 Hz
GB                             0
```

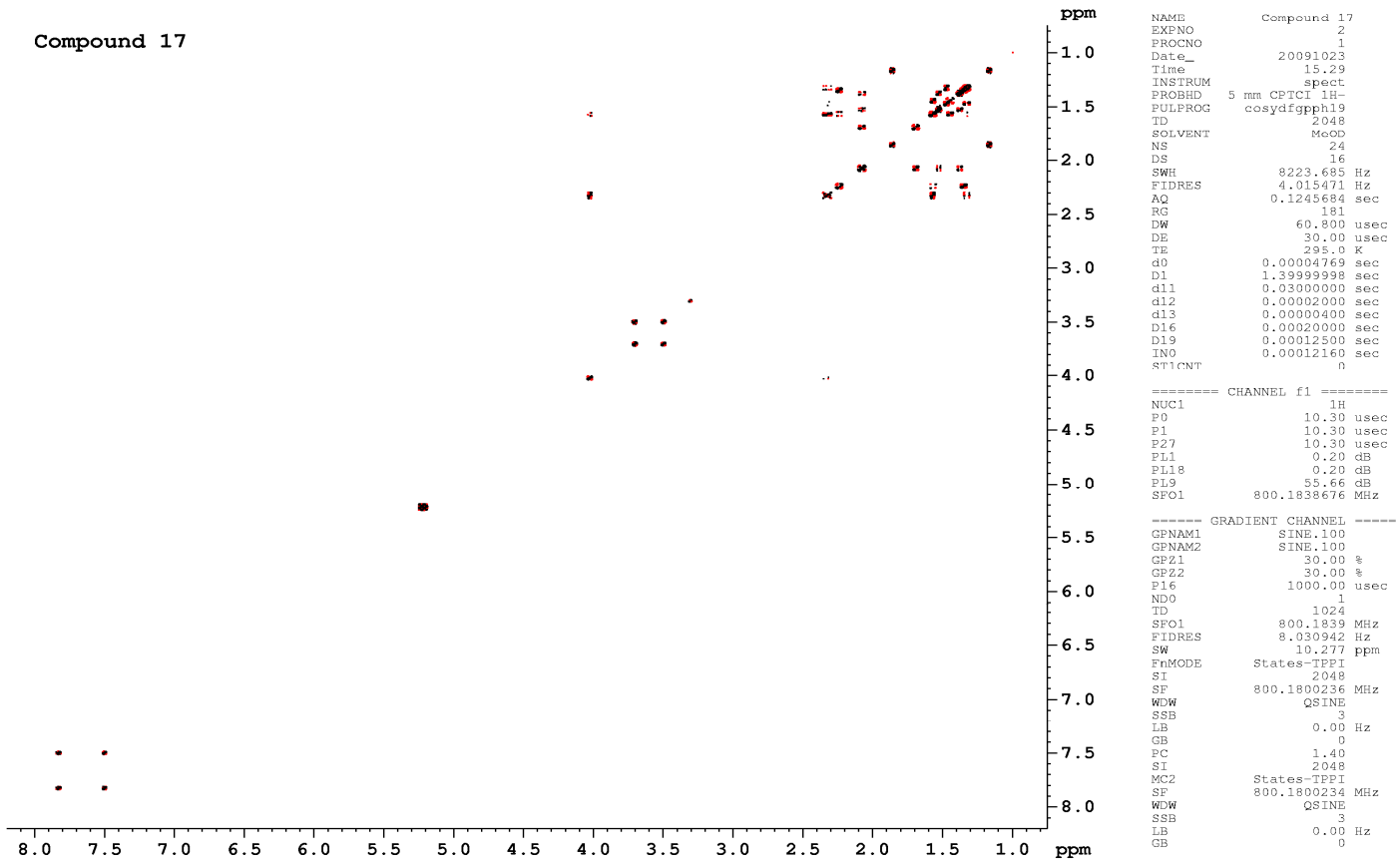
2D ^{13}C-HMBC spectrum of **16** in CD_3CN at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The insert in the upper left corner represents an expansion of the high field region plotted with reduced cross-peaks intensities for a better clarity.




```
NAME          Coumpound 17
EXPNO                    1
PROCNO                   1
Date_             20091023
Time                 15.28
INSTRUM              spect
PROBHD   5 mm CPTCI 1H-
PULPROG                 zg
TD                   65536
SOLVENT               MeOD
NS                     128
DS                       4
SWH               8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                    71.8
DW                  60.800 usec
DE                  30.00 usec
TE                  295.0 K
D1              0.10000000 sec
TD0                      1

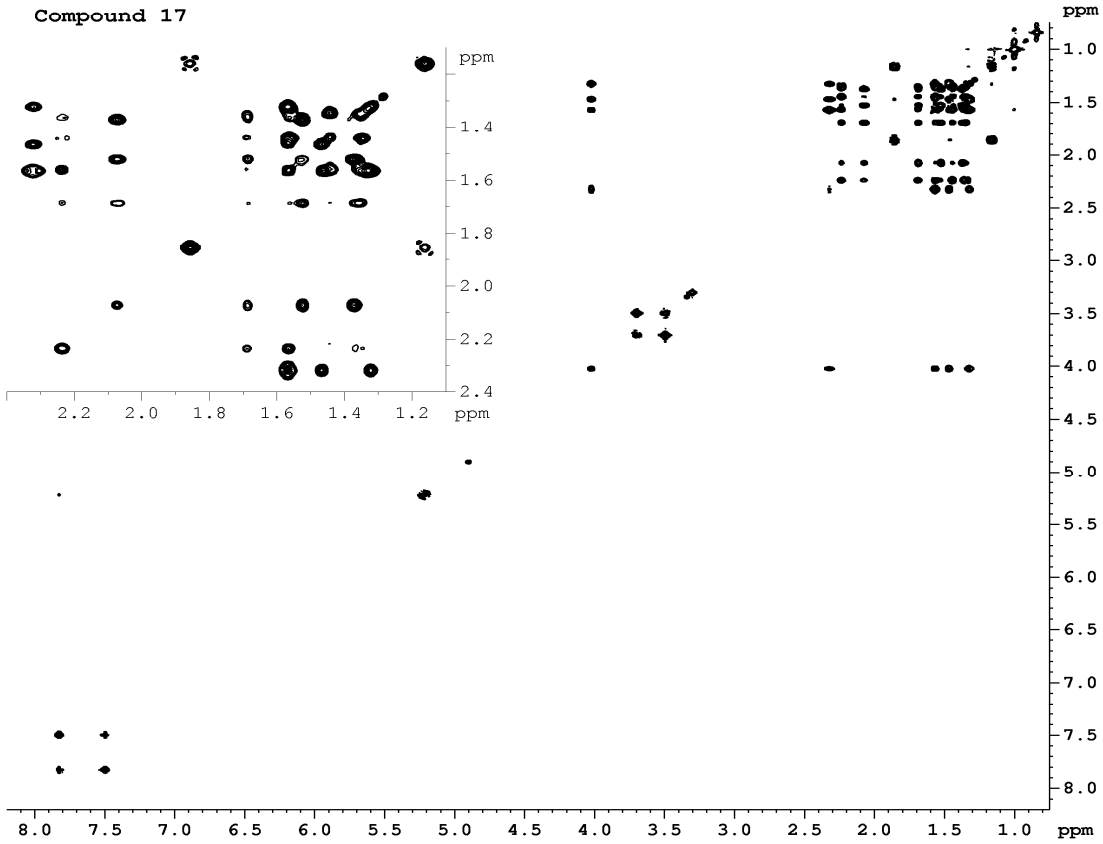
======== CHANNEL f1 ========
NUC1                    1H
P1                   10.30 usec
PL1                   0.20 dB
SFO1          800.1837640 MHz
SI                  131072
SF            800.1800265 MHz
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00
```

^{1}H spectrum of **17** in CD_3OD at 25^o C.



NAME	Compound 17
EXPNO	2
PROCNO	1
Date_	20091023
Time	15.29
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	cosydfgpph19
TD	2048
SOLVENT	MeOD
NS	24
DS	16
SWH	8223.685 Hz
FIDRES	4.015471 Hz
AQ	0.1245684 sec
RG	181
DW	60.800 usec
DE	30.00 usec
TE	295.0 K
d0	0.00004769 sec
D1	1.39999998 sec
d11	0.03000000 sec
d12	0.00002000 sec
d13	0.00000400 sec
D16	0.00020000 sec
D19	0.00012500 sec
IN0	0.00012160 sec
ST1CNT	0
======== CHANNEL f1 ========	
NUC1	1H
P0	10.30 usec
P1	10.30 usec
P27	10.30 usec
PL1	0.20 dB
PL18	0.20 dB
PL9	55.66 dB
SFO1	800.1838676 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPNAM2	SINE.100
GPZ1	30.00 %
GPZ2	30.00 %
P16	1000.00 usec
ND0	1
TD	1024
SFO1	800.1839 MHz
FIDRES	8.030942 Hz
SW	10.277 ppm
FnMODE	States-TPPI
SI	2048
SF	800.1800236 MHz
WDW	QSINE
SSB	3
LB	0.00 Hz
GB	0
PC	1.40
SI	2048
MC2	States-TPPI
SF	800.1800234 MHz
WDW	QSINE
SSB	3
LB	0.00 Hz
GB	0

2D DQF-COSY spectrum of **17** in CD_3OD at 25° C. The black and red contours represent positive and negative peaks, respectively.

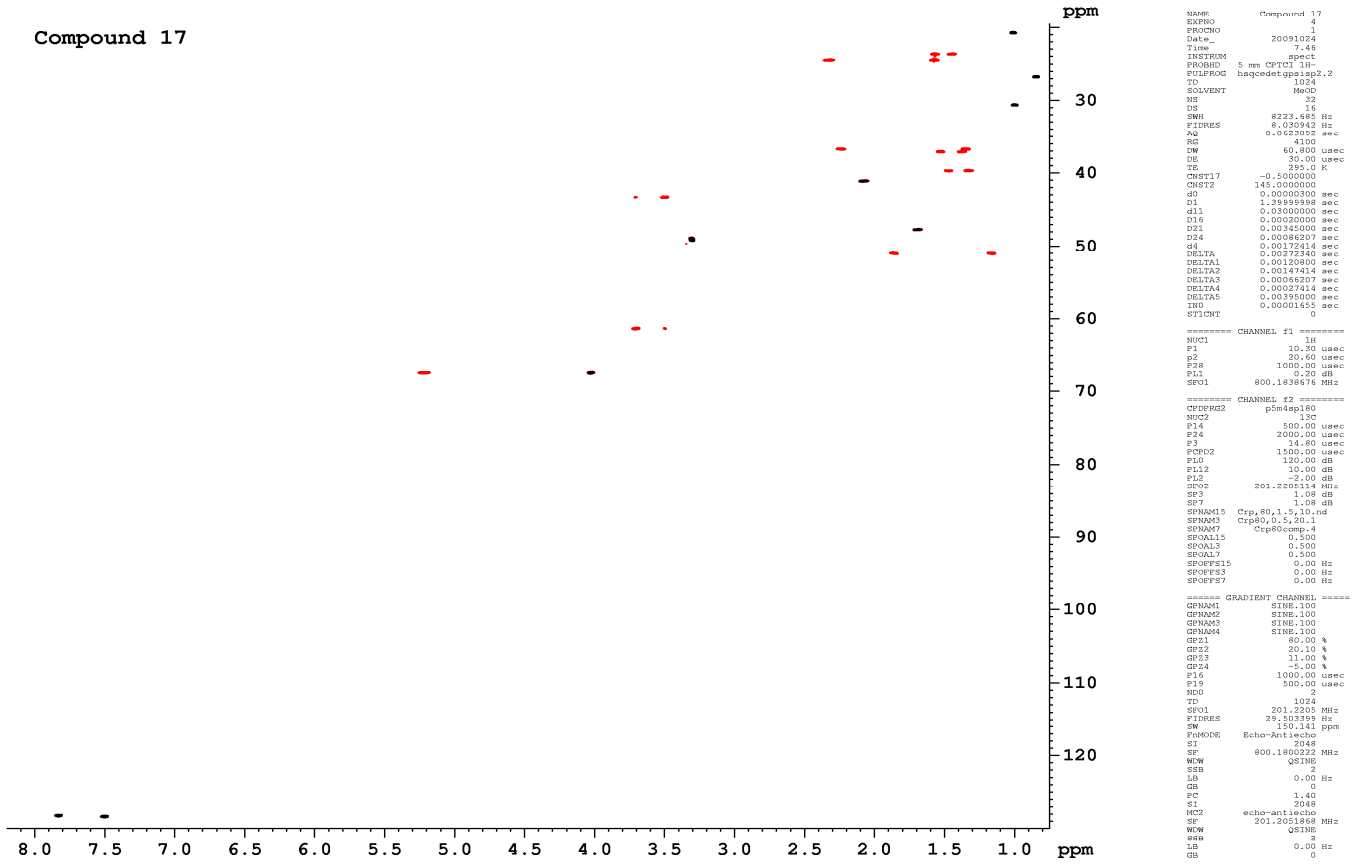



```
NAME            Compound 17
EXPNO                     3
PROCNO                    1
Date_              20091024
Time                   2.22
INSTRUM               spect
PROBHD   5 mm CPTCI 1H-
PULPROG  dipsi2etgpsi19
TD                     1024
SOLVENT                MeOD
NS                       24
DS                       16
SWH                8223.685 Hz
FIDRES             8.030942 Hz
AQ                 0.0623092 sec
RG                       406
DW                  60.800 usec
DE                  30.00 usec
TE                  295.0 K
d0                 0.00000300 sec
D1                 1.39999998 sec
d11                0.03000000 sec
d12                0.00002000 sec
d13                0.00000400 sec
D16                0.00020000 sec
D19                0.00012500 sec
D20                0.00001000 sec
D21                0.00001000 sec
D9                 0.06000000 sec
DELTA              0.00120300 sec
FACTOR1                  11
IN0                0.00012160 sec
l1                       22
ST1CNT                    0

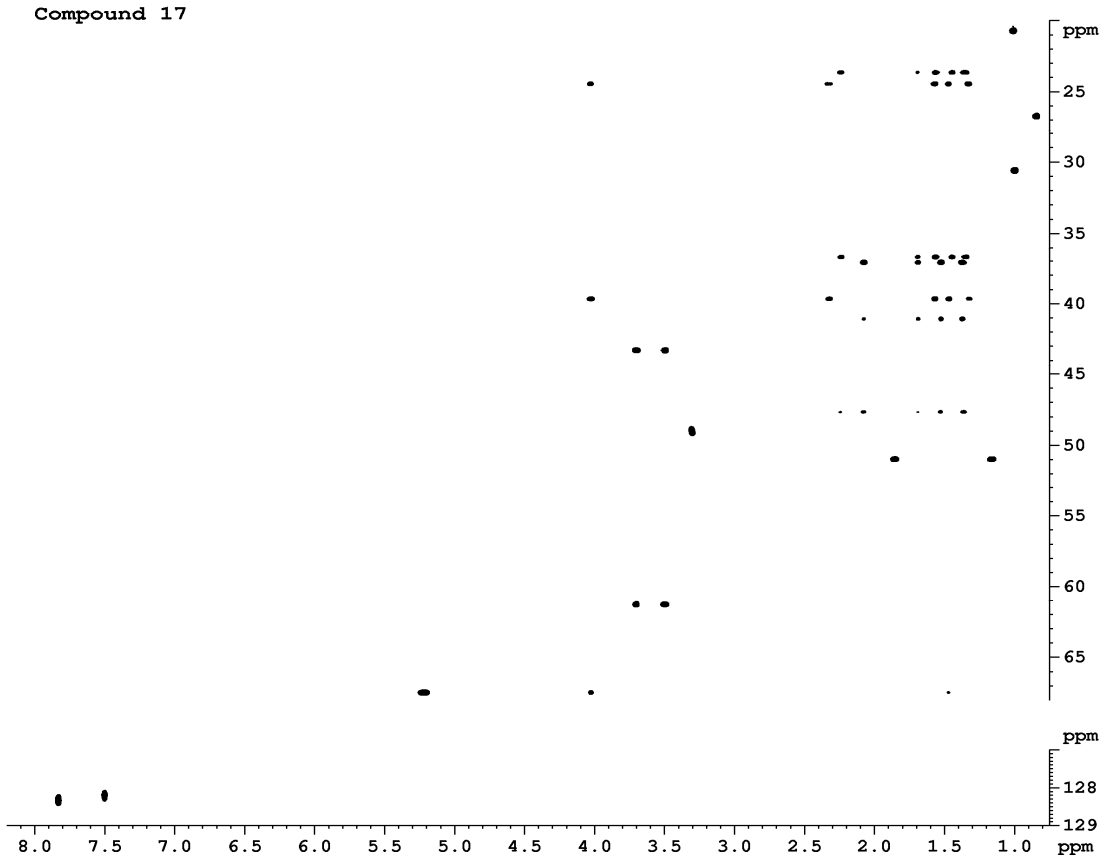
======== CHANNEL f1 ========
NUC1                      1H
P0                   10.30 usec
P1                   10.30 usec
p2                   20.60 usec
P27                  10.20 usec
P6                   24.00 usec
PL1                   0.20 dB
PL10                  7.55 dB
PL18                  0.20 dB
PL9                  55.66 dB
SFO1           800.1838676 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPNAM3           SINE.100
GPZ1                30.00 %
GPZ2                20.00 %
GPZ3                50.00 %
P16               1000.00 usec
ND0                       1
TD                      512
SFO1            800.1839 MHz
FIDRES         16.061884 Hz
SW                 10.277 ppm
FnMODE     Echo-Antiecho
SI                     2048
SF           800.1800239 MHz
WDW                 QSINE
SSB                       2
LB                   0.00 Hz
GB                        0
PC                    1.40
SI                     2048
MC2        echo-antiecho
SF           800.1800240 MHz
WDW                 QSINE
SSB                       2
LB                   0.00 Hz
GB                        0
```

2D TOCSY spectrum of **17** in CD_3OD at 25° C. The insert in the upper left corner represents an expansion of the high field region plotted with reduced cross-peaks intensities for a better clarity.



2D ^{13}C-HSQC spectrum of **17** in CD_3OD at 25° C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The black cross-peaks correspond to CH_3 and CH groups, the red cross-peaks correspond to CH_2 groups.



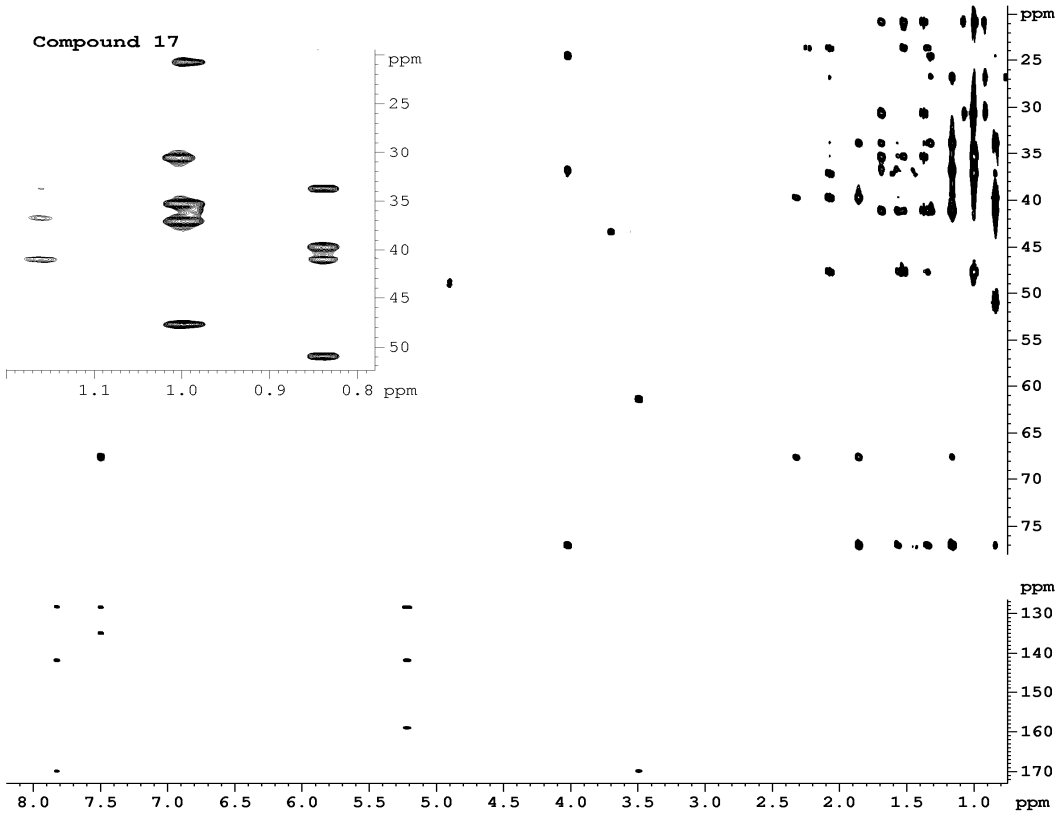

```
NAME            Compound 17
EXPNO                     5
PROCNO                    1
Date_              20091024
Time                 21.25
INSTRUM               spect
PROBHD   5 mm CPTCI 1H-
PULPROG   hsqcdietgpsisp.2
TD                     1024
SOLVENT                MeOD
NS                       40
DS                       16
SWH                8223.685 Hz
FIDRES             8.030948 Hz
AQ                0.0623092 sec
RG                     4100
DW                   60.800 usec
DE                   30.00 usec
TE                   295.0 K
CNST17          -0.5000000
CNST2          145.0000000
d0              0.00000300 sec
D1              1.50000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
D24             0.00086200 sec
d4              0.00172414 sec
D9              0.06000000 sec
DELTA           0.00122260 sec
DELTA1          0.00120800 sec
DELTA2          0.00147014 sec
DELTA3          0.00135800 sec
FACTOR1                  11
IN0             0.00001655 sec
l1                       22
ST1CNT                    0

======== CHANNEL f1 ========
NUC1                     1H
P1                    10.30 usec
P2                    20.60 usec
P28                 1000.00 usec
P6                    24.00 usec
PL1                    0.20 dB
PL10                   7.55 dB
SFO1          800.1836676 MHz

======== CHANNEL f2 ========
CPDPRG2          p5m4sp180
NUC2                    13C
P14                  500.00 usec
P24                 2000.00 usec
P3                    14.80 usec
PCPD2               1500.00 usec
PL0                  120.00 dB
PL12                  10.00 dB
PL2                   -2.00 dB
SFO2          201.2205114 MHz
SP3                    1.08 dB
SP7                    1.08 dB
SPNAM15   Crp,80,1.5,10.nd
SPNAM3    Crp80,0.5,20.1
SPNAM7       Crp80comp.4
SPOAL15              0.500
SPOAL3               0.500
SPOAL7               0.500
SPOFFS15              0.00 Hz
SPOFFS3               0.00 Hz
SPOFFS7               0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPZ1                 80.00 %
GPZ2                 20.10 %
P16                1000.00 usec
ND0                      2
TD                    1024
SFO1            201.2205 MHz
FTMRES          79.503399 Hz
SW                150.141 ppm
FnMODE     Echo-Antiecho
SI                    2048
SF            800.1800222 MHz
WDW                  QSINE
SSB                      2
LB                    0.00 Hz
GB                       0
PC                    1.00
SI                    2048
MC2        echo-antiecho
SF            201.2051871 MHz
WDW                  QSINE
SSB                      2
LB                    0.00 Hz
GB                       0
```

2D ^{13}C-HSQC-TOCSY spectrum of **17** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively.



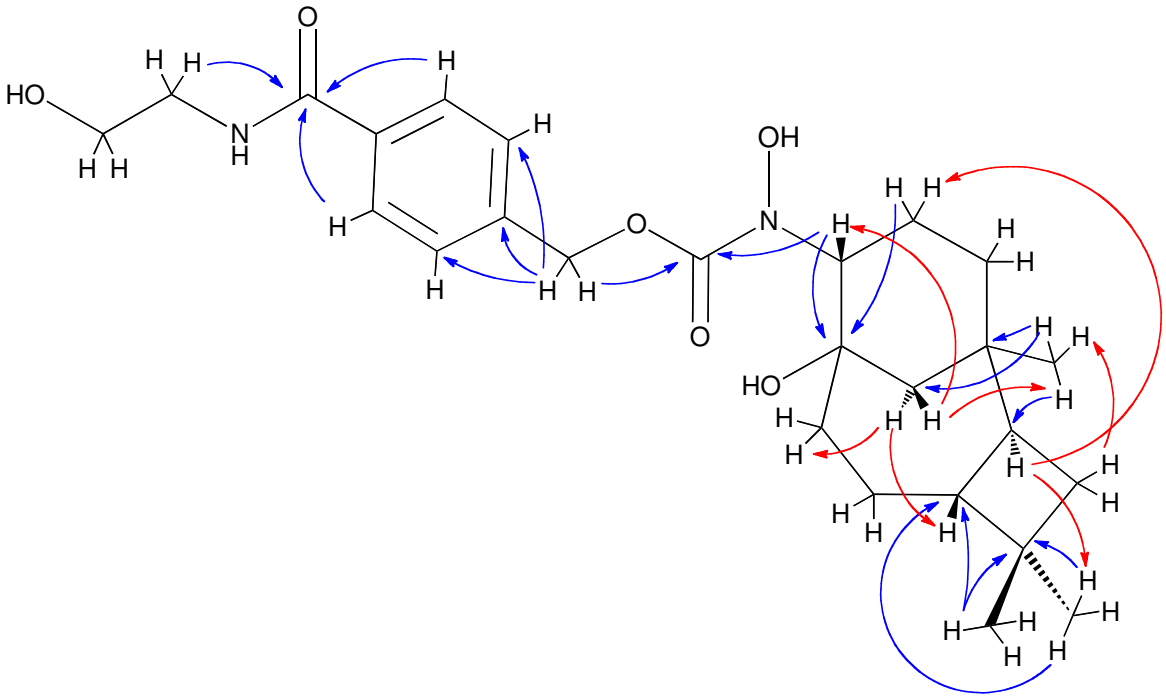

```
NAME            Compound 17
EXPNO                     6
PROCNO                    1
Date_              20091025
Time                  16.16
INSTRUM               spect
PROBHD   5 mm CPTCI 1H-
PULPROG     hmbcgpl2ndqf
TD                     2048
SOLVENT                MeOD
NS                       80
DS                       16
SWH                8223.685 Hz
FIDRES             4.015471 Hz
AQ                0.1245684 sec
RG                     4600
DW                   60.800 usec
DE                   30.00 usec
TE                   295.0 K
CNST13          8.0000000
CNST6         125.0000000
CNST7         175.0000000
d0             0.00000300 sec
D1             1.39999998 sec
D16            0.00020000 sec
d6             0.06250000 sec
DELTA1         0.00280000 sec
DELTA2         0.00165714 sec
DELTA3         0.06129600 sec
IN0            0.00001310 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   10.30 usec
p2                   20.60 usec
PL1                   0.20 dB
SFO1          800.1838676 MHz

======== CHANNEL f2 ========
NUC2                  13C
P3                   14.80 usec
PL2                  -2.00 dB
SFO2          201.2245355 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPNAM3           SINE.100
GPNAM4           SINE.100
GPNAM5           SINE.100
GPNAM6           SINE.100
GPZ1                 50.00 %
GPZ2                 30.00 %
GPZ3                 40.10 %
GPZ4                 15.00 %
GPZ5                -10.00 %
GPZ6                 -5.00 %
P16                1000.00 usec
ND0                       2
TD                      512
SFO1            201.2245 MHz
FIDRES          74.546753 Hz
SW                189.678 ppm
FnMODE                  QF
ST                    2048
SF            800.1800240 MHz
WDW                 QSINE
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.40
SI                    2048
MC2                     QF
SF            201.2051846 MHz
WDW                 QSINE
SSB                       0
LB                    0.00 Hz
GB                        0
```

2D ^{13}C-HMBC spectrum of **17** in CD_3OD at 25^{o} C. The horizontal and vertical axes display ^{1}H and ^{13}C chemical shifts, respectively. The insert in the upper left corner represents an expansion of the high field region plotted with reduced cross-peaks intensities for a better clarity.



Correlation diagram for compound **17.** The HMBC (in blue) and NOE (in red) correlations, together with proton-proton correlations in the DQF-COSY and TOCSY spectra and one bond proton-carbon correlations in the HSQC spectrum unambiguously establish the proposed structure of compound **17** and conformation of its β-caryophyllene unit (segment).

References and Notes

1. For a detailed account of this antibiotic susceptibility assay see: Afonin, S.; Glaser, R. W.; Berditchevskaja, M.; Wadhwani, P.; Gührs, K.-H.; Möllmann, U.; Perner, A.; Ulrich, A. S. "4-Fluoro-phenylglycine as a Label for ^{19}F-NMR Structure Analysis of Membrane Associated Peptides." *ChemBioChem* **2003**, *4*, 1151-1163.

2. Murray, P. R.; Baron, E. J.; Pfaller, M. A.; Tenover, F. C.; Yolken, R. H. *Manual of Clinical Microbiology*, 7th ed.; American Society for Microbiology: Washington, DC, **1999**.

3. The test organisms *Mycobacterium vaccae* IMET 10670 and *Mycobacterium smegmatis* mc^2155 required longer incubation times for overnight LB cultures (24-48 hours) and were used in the agar diffusion assay directly from the LB culture broth without dilution and standardization. The test organism *Bacillus subtilis* ATCC 6633 was used in the agar diffusion assay directly from the LB culture broth without dilution and standardization.

4. Snapper, S. B.; Melton, R. E.; Mustafa, S.; Kieser, T.; Jacobs, W. R. "Isolation and Characterization of Efficient Plasmid Transformation Mutants of *Mycobacterium smegmatis*." *Mol. Microbiol.* **1990**, *4*, 1911-1919.

5. Zimmermann, W. "Penetration of β-Lactam Antibiotics into their Target Enzymes in *Pseudomonas aeruginosa*: Comparison of a Highly Sensitive Mutant with its Parent Strain." *Antimicrob. Agents Chemother.* **1980**, *18*, 94-100.