

Histone Deacetylase Inhibitors from *Burkholderia thailandensis*

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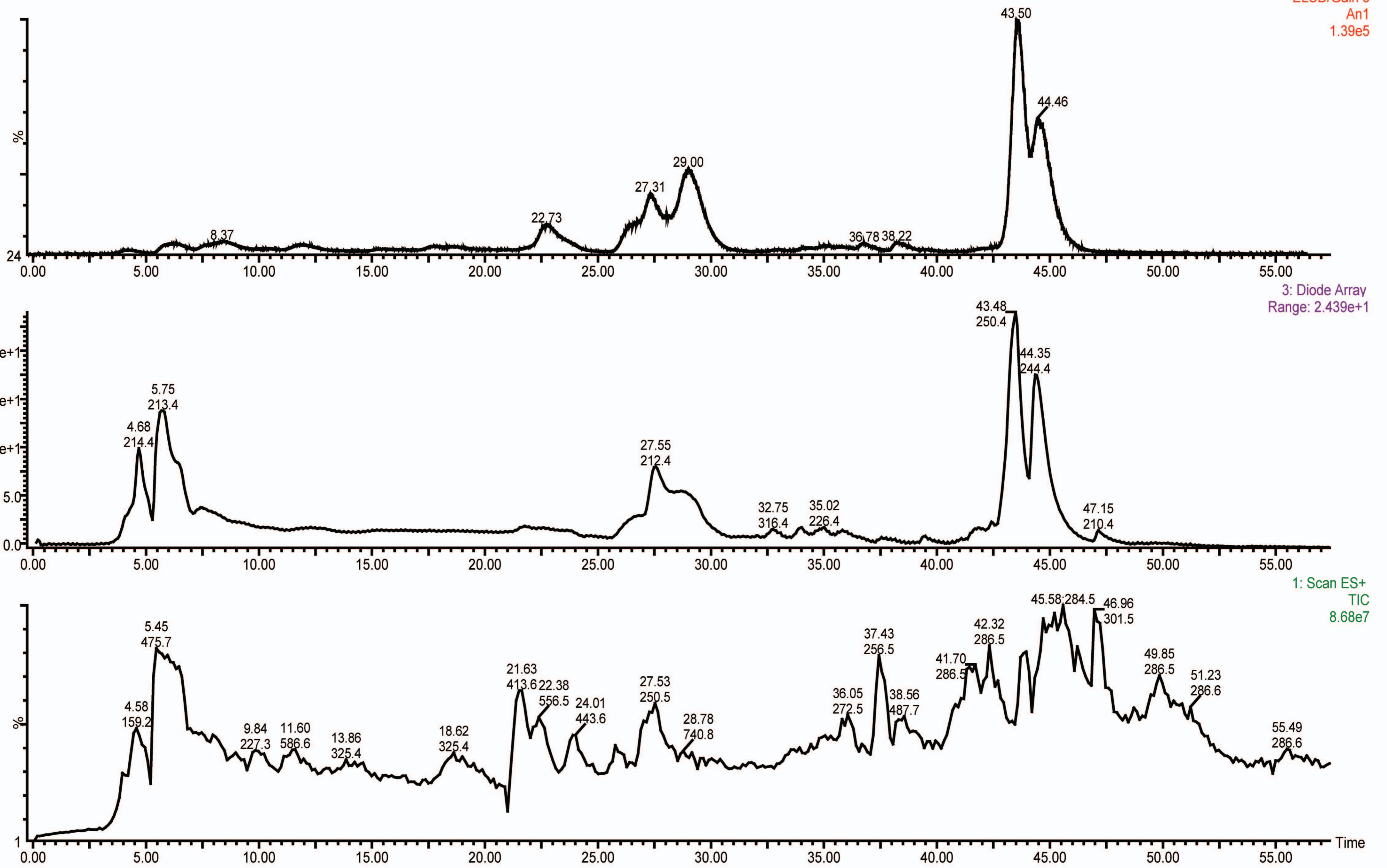
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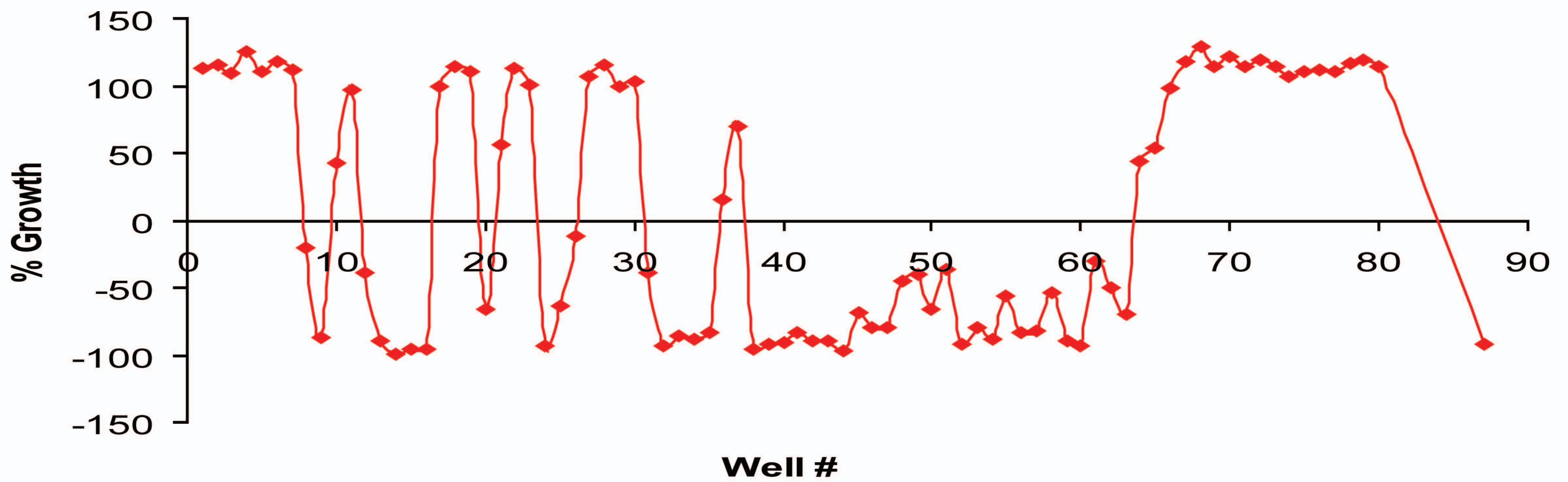
- S3.** HPLC dereplication of crude extract
- S4.** Fractionation diagram
- S5.** Exact mass determination of Spiruchostatin C (**2**)
- S6.** Exact mass determination of dimer of **2**
- S7.** ¹H NMR spectrum of **2** in CDCl₃/CD₃OD (9:1)
- S8.** COSY NMR spectrum of **2** in CDCl₃/CD₃OD (9:1)
- S9.** HSQC NMR spectrum of **2** in CDCl₃/CD₃OD (9:1)
- S10.** HMBC NMR spectrum of **2** in CDCl₃/CD₃OD (9:1)
- S11.** TOCSY NMR spectrum of **2** in CDCl₃/CD₃OD (9:1)
- S12.** Circular dichroism spectrum of **2** in methanol
- S13.** Circular dichroism spectrum of dimer of **2** in methanol
- S14.** Circular dichroism spectrum of FK228 (**1**) in methanol
- S15.** Assignments diagram of **2**
- S16.** Comparative HILIC HPLC of the hydrolysates of **1** and **2**
- S17.** NCI 60 data for FK228 (**1**)
- S18.** NCI 60 data for **2**
- S19.** NCI 60 for selected cell lines – **1** (upper) and **2** (lower)
- S20.** *In vivo* Hollow Fiber Results for Spiruchostatin C (**2**) and FK228 (**1**).

S3 HPLC Dereplication

Burkholderia
C18 Dynamax 60A, 8uM, 60A, 250X21 mm, T=ambient
ACN-H2O, 0-5=(30:70), 25=(50:50), 45-60=(100:0), 15mL/min

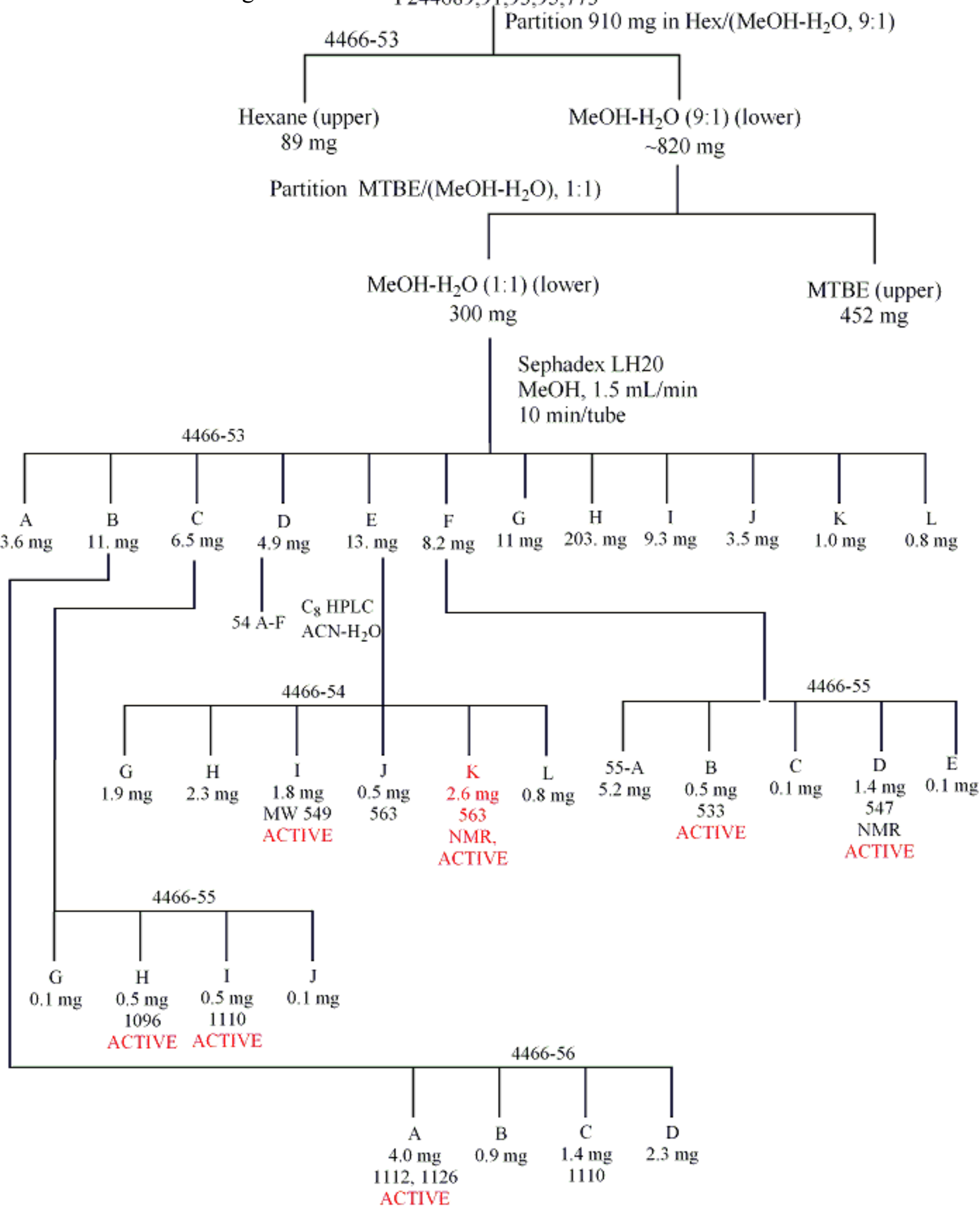


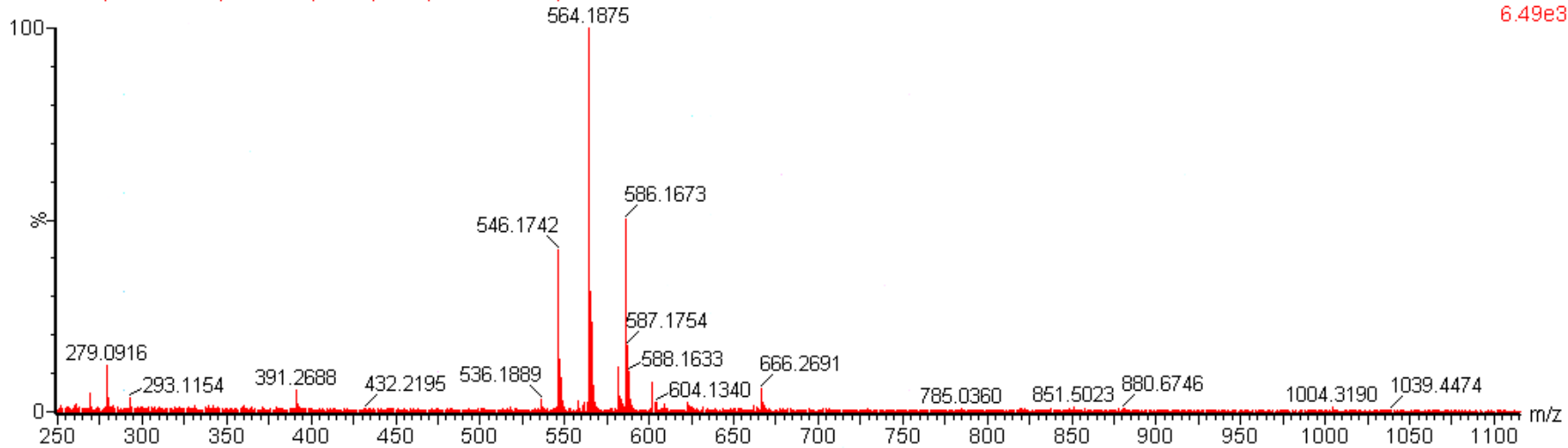
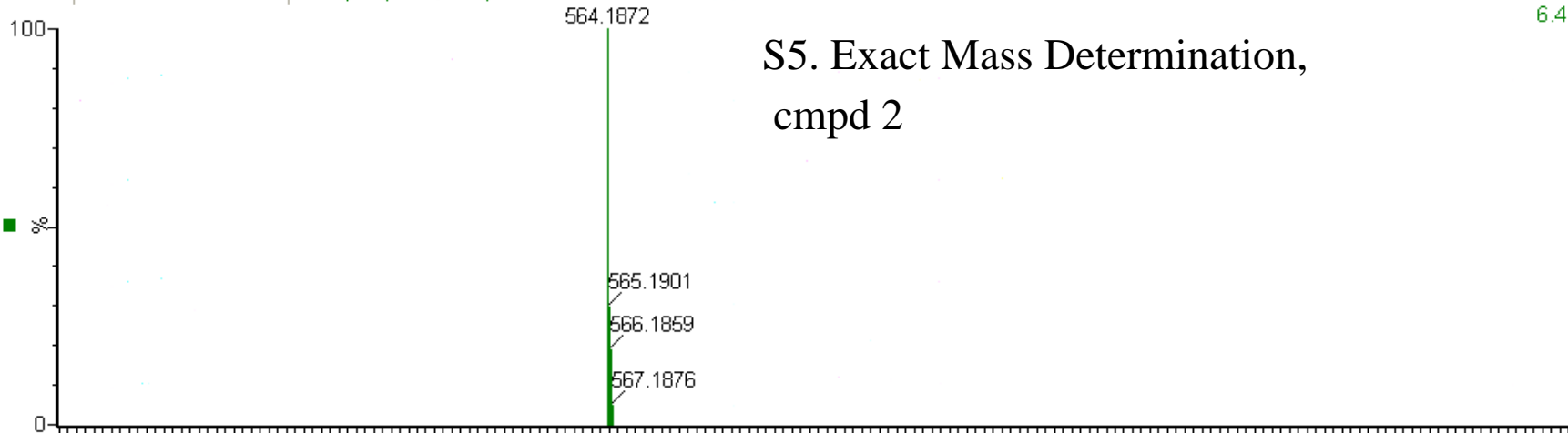
COLO 205



S4. Fractionation Diagram

0G0S6418
Burkholderia thailandensis
Combine 5 EtOAc. extracts
F244689,91,93,95,773

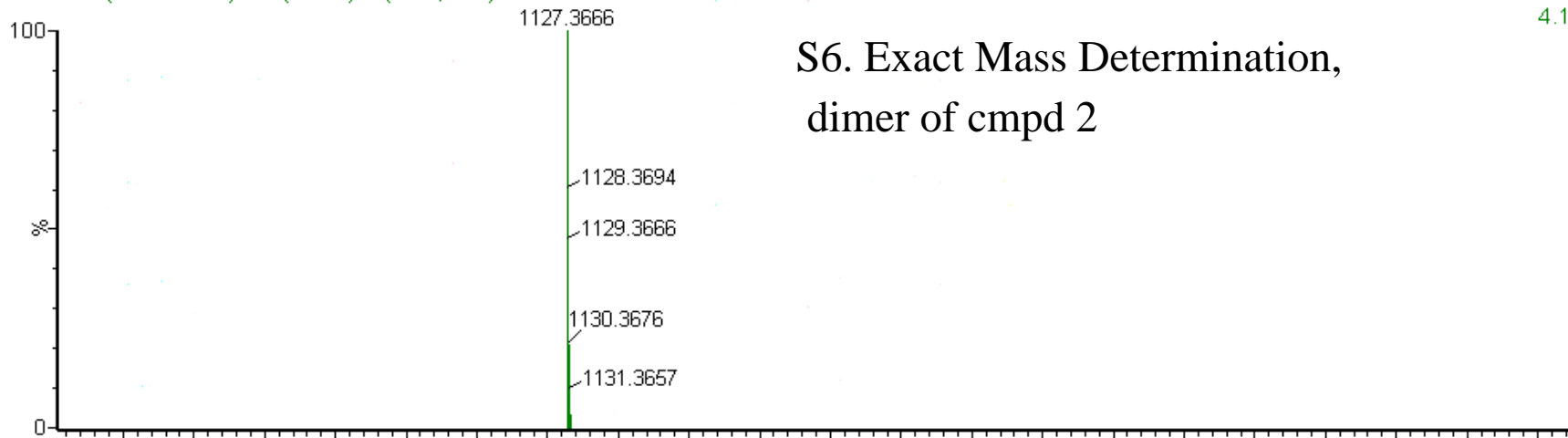


S5. Exact Mass Determination,
cmpd 2

ACN-H₂O w/0.1% FA, 0-1=(1:9), 5=(3:7), 7-8=(9:1), 8.2-9=(1:9), 0.75 mL/min

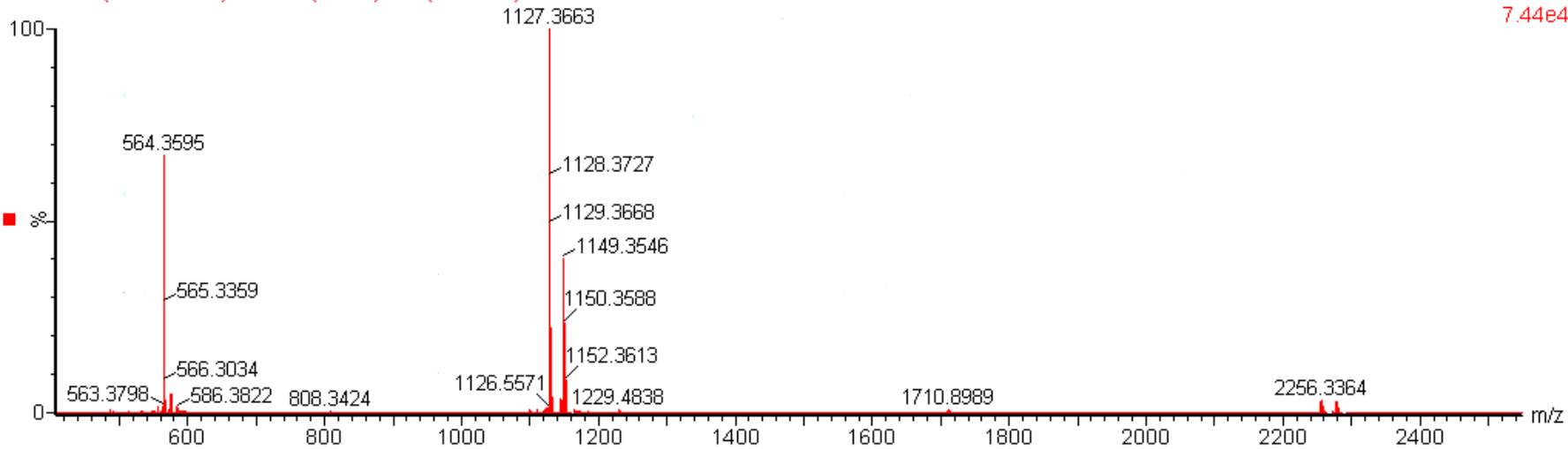
4473-4-D (11 17 2010) T1 (0.018) Is (1.00,1.00) C₄₆H₇₄N₆O₁₄S₆

1: TOF MS ES+
4.14e12



4473-4-D (11 17 2010) T1 477 (5.395) Cm (476:478)

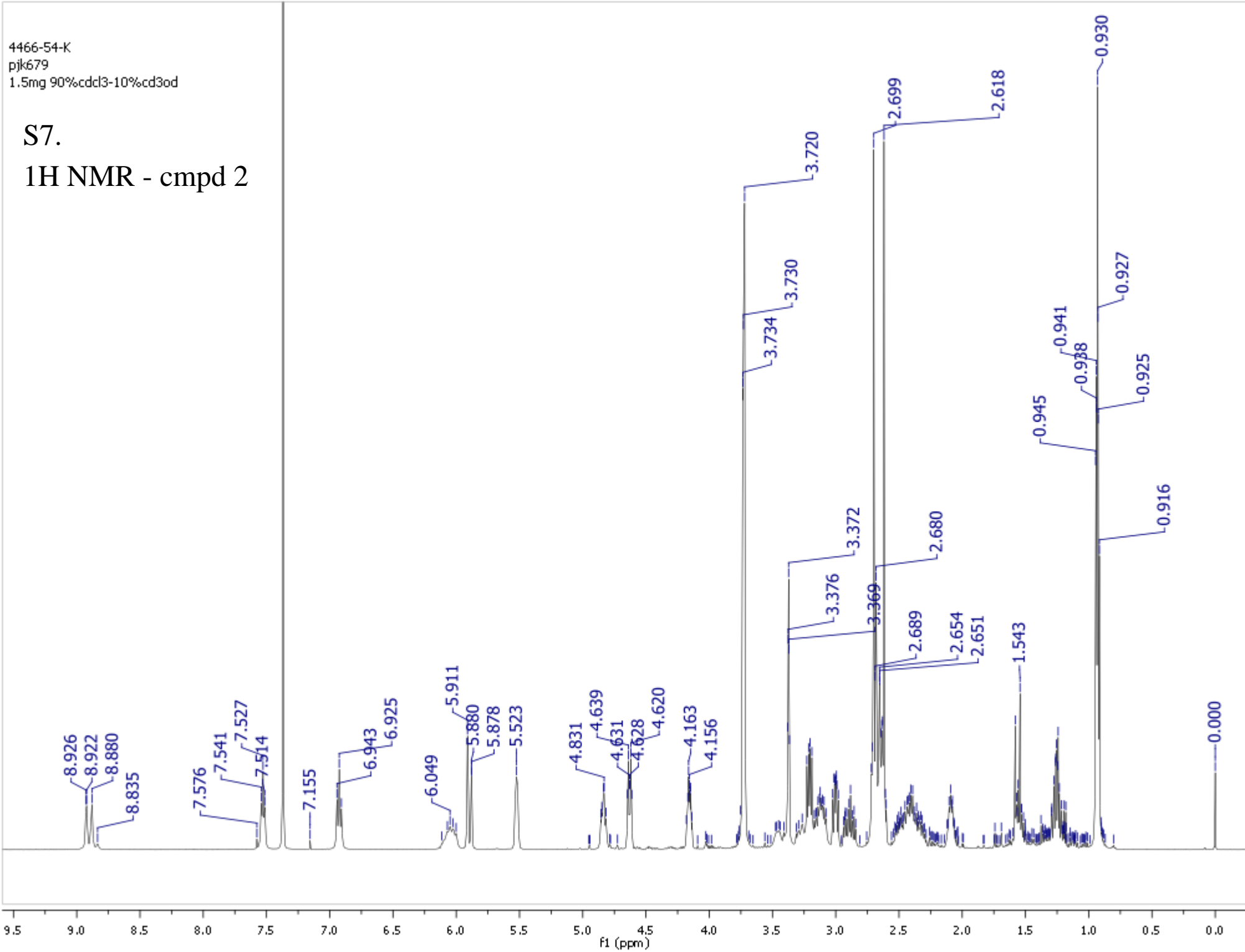
1: TOF MS ES+
7.44e4



4466-54-K
pjk679
1.5mg 90%cdcl3-10%cd3od

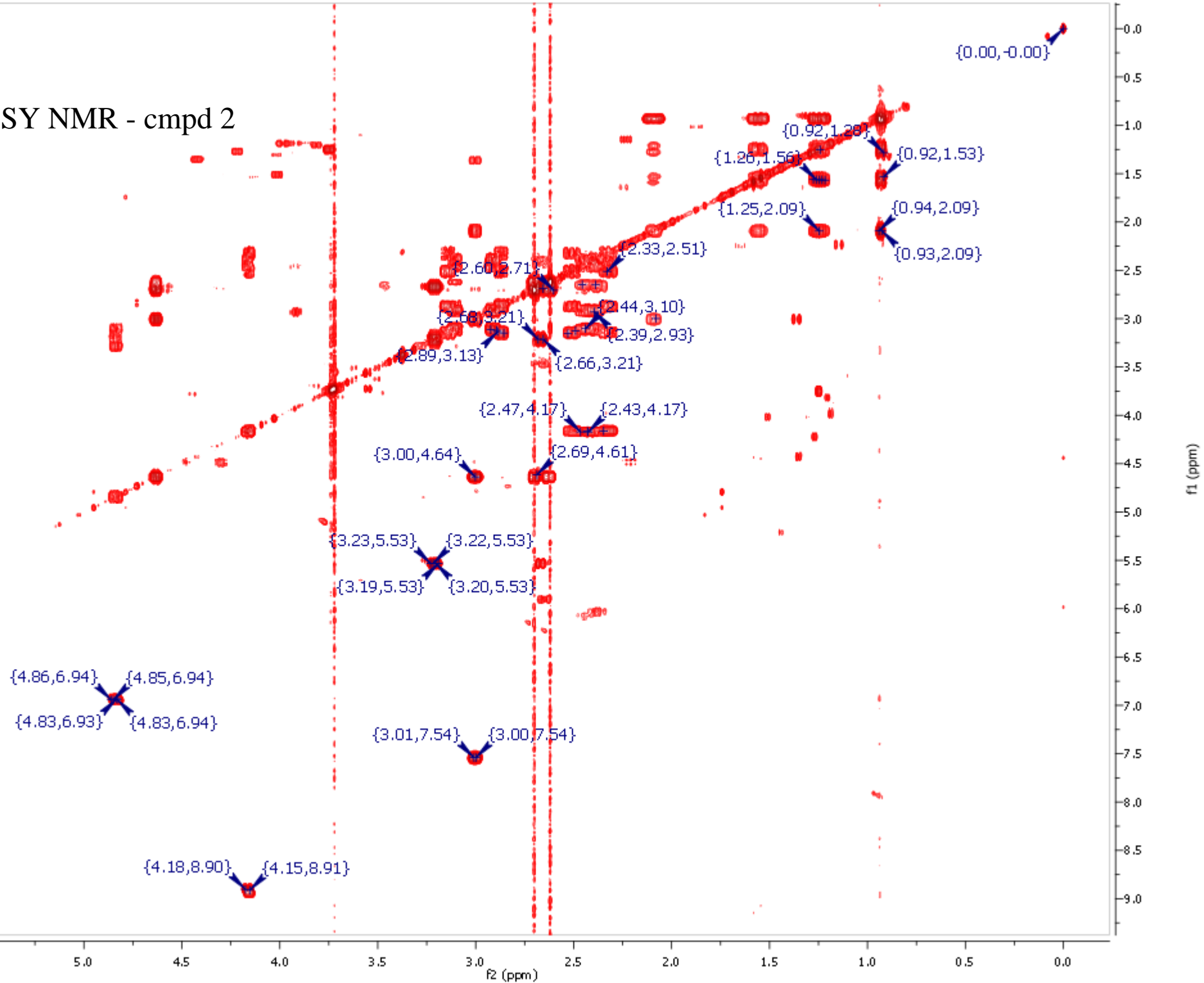
S7.

¹H NMR - compd 2



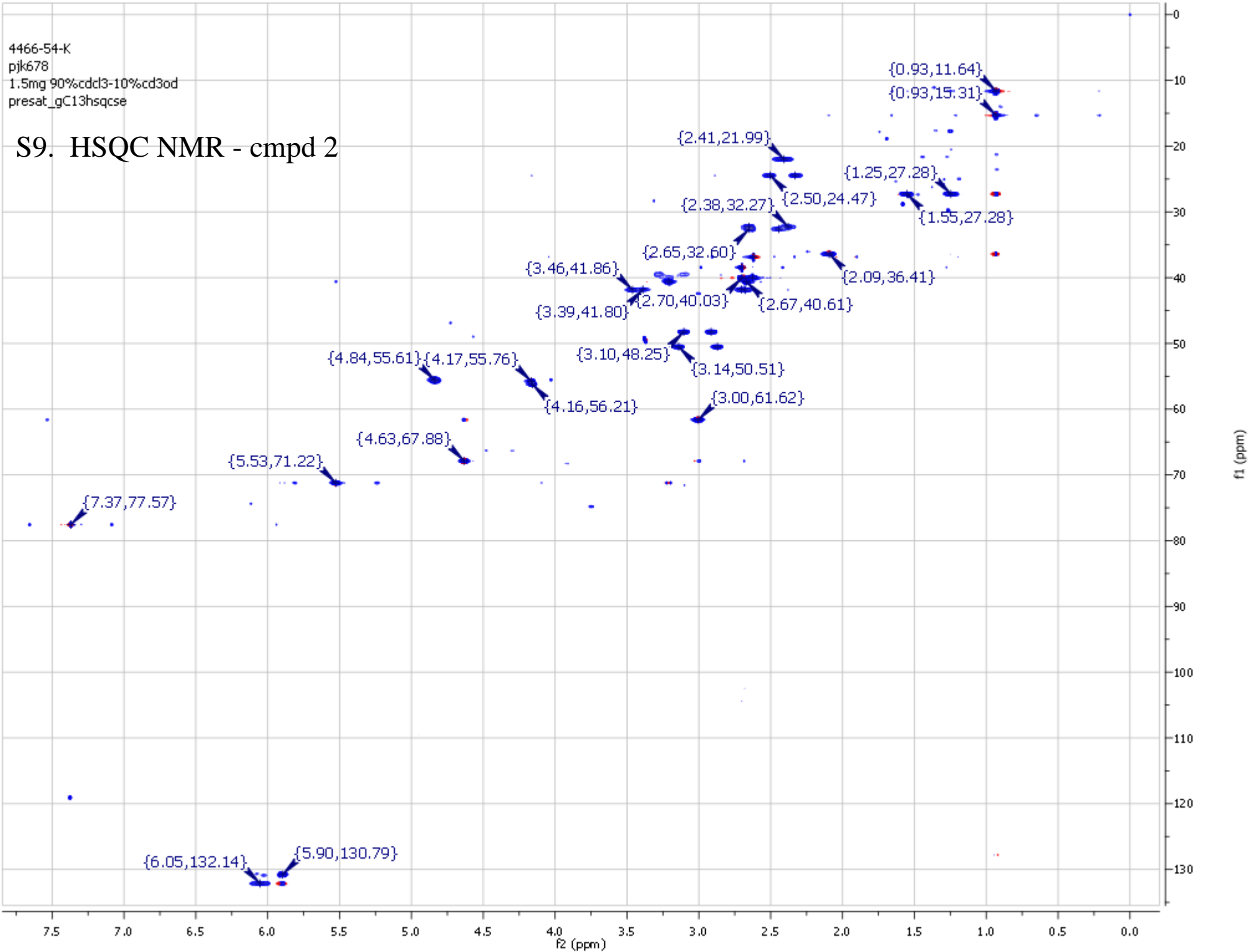
S8.

COSY NMR - compd 2

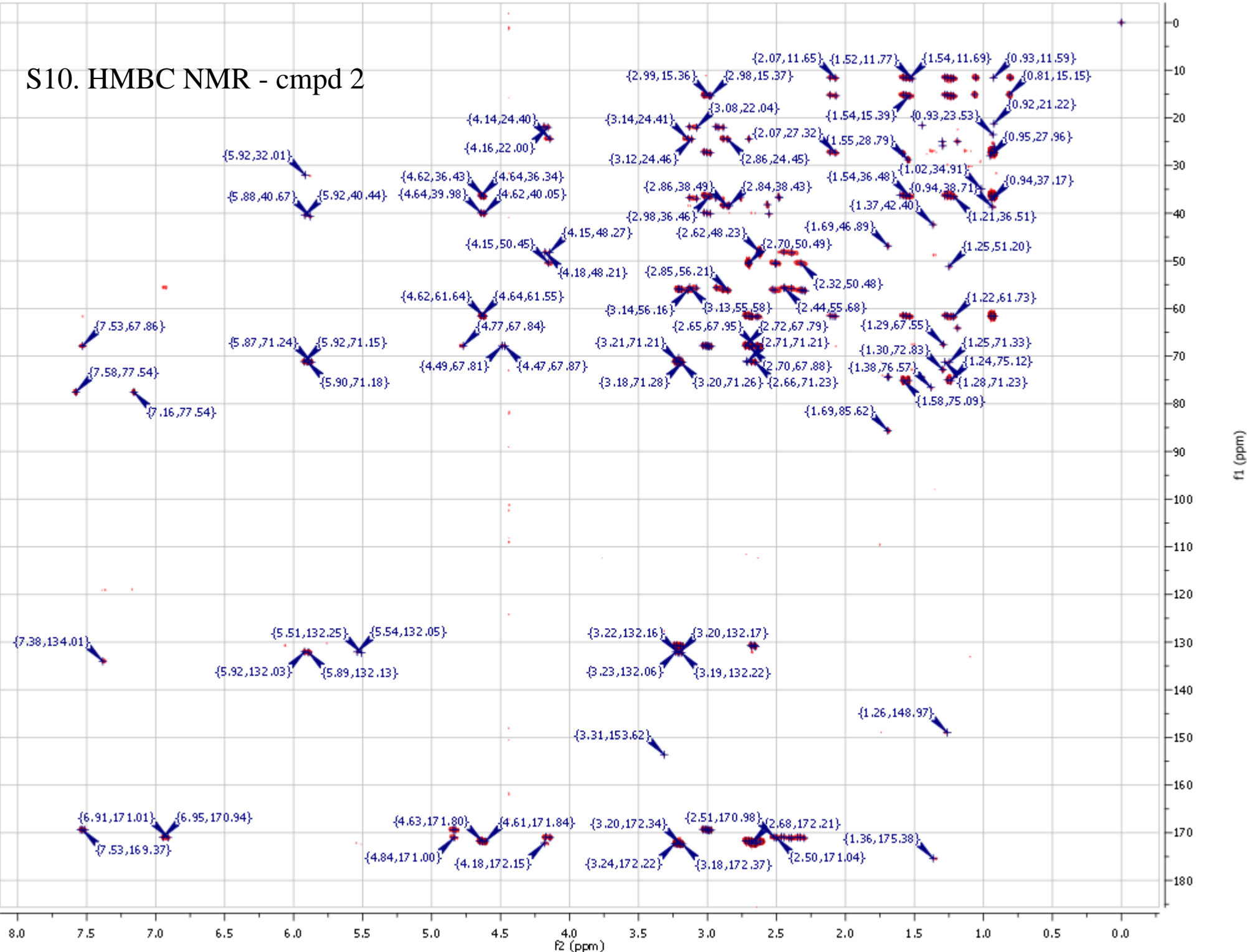


4466-54-K
pjk678
1.5mg 90%cdcl3-10%cd3od
presat_gC13hsqcse

S9. HSQC NMR - compd 2

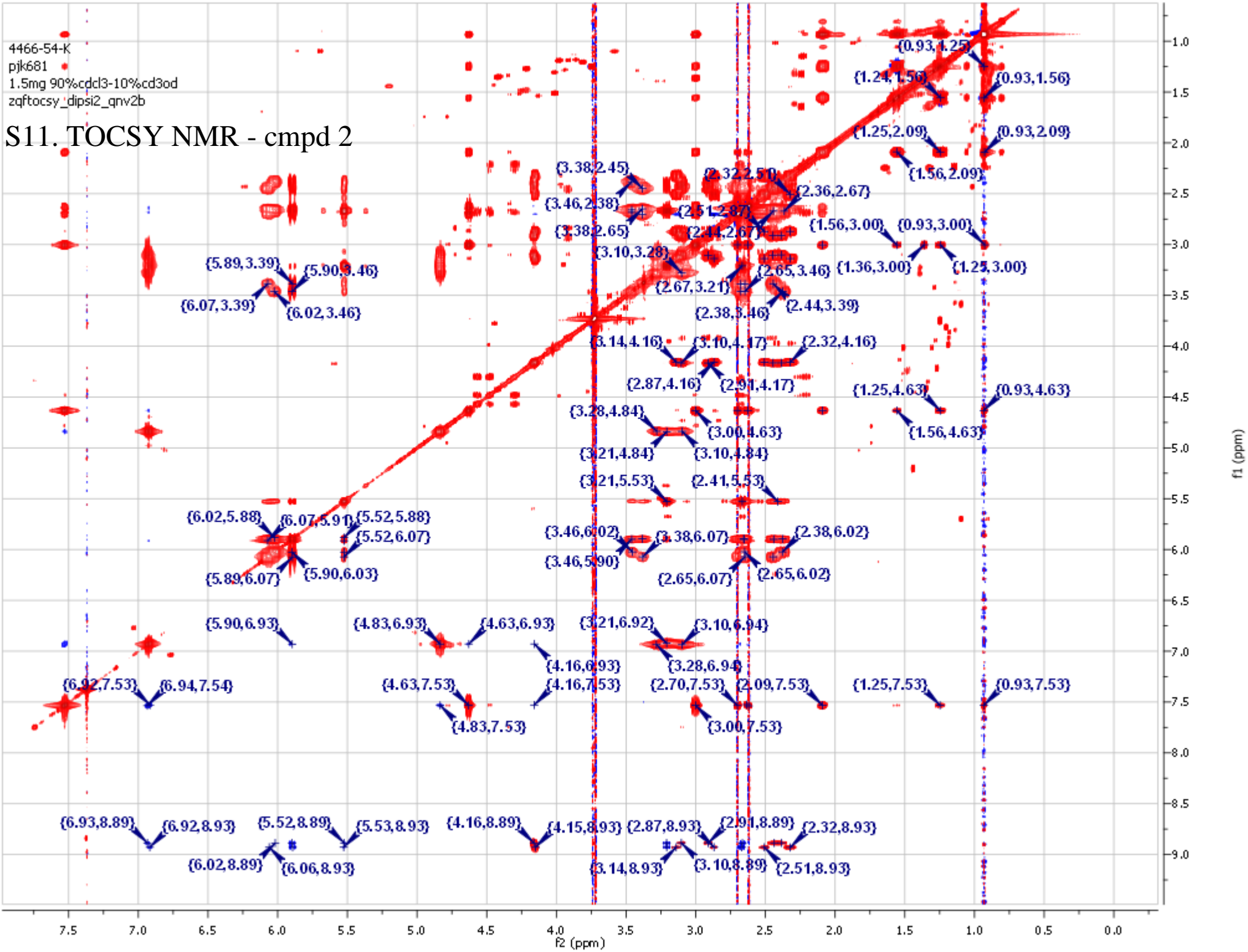


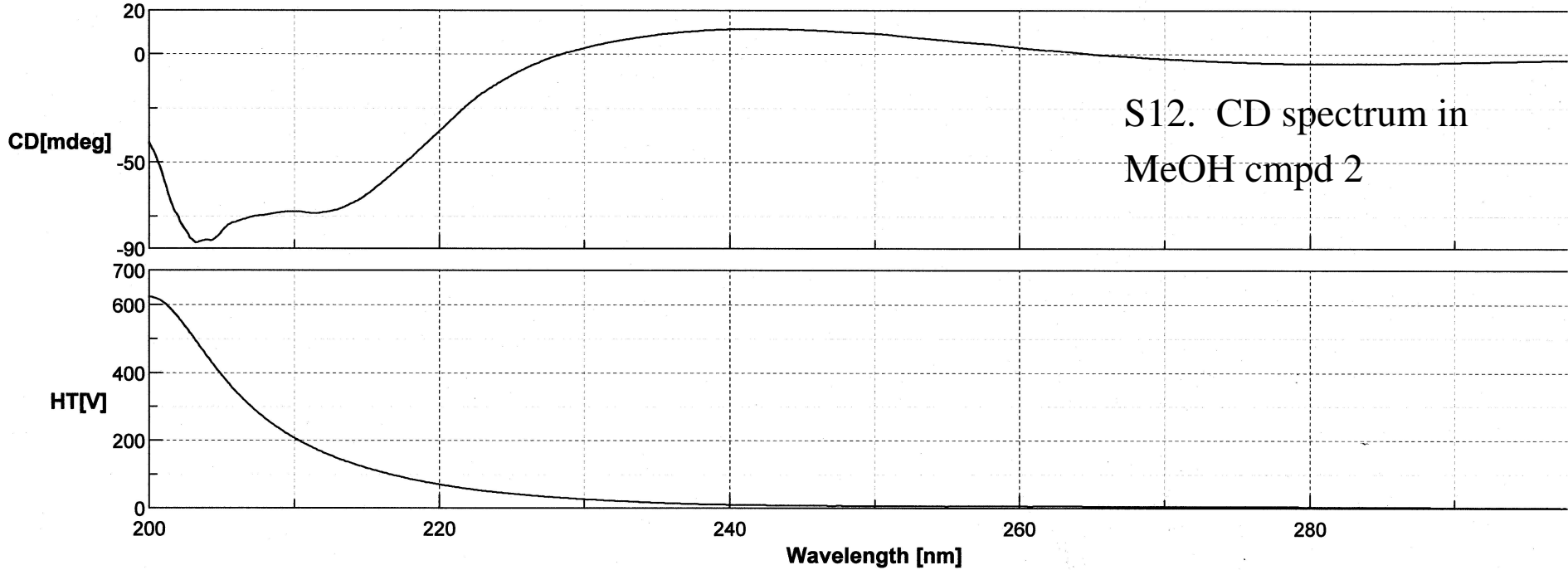
S10. HMBC NMR - compd 2

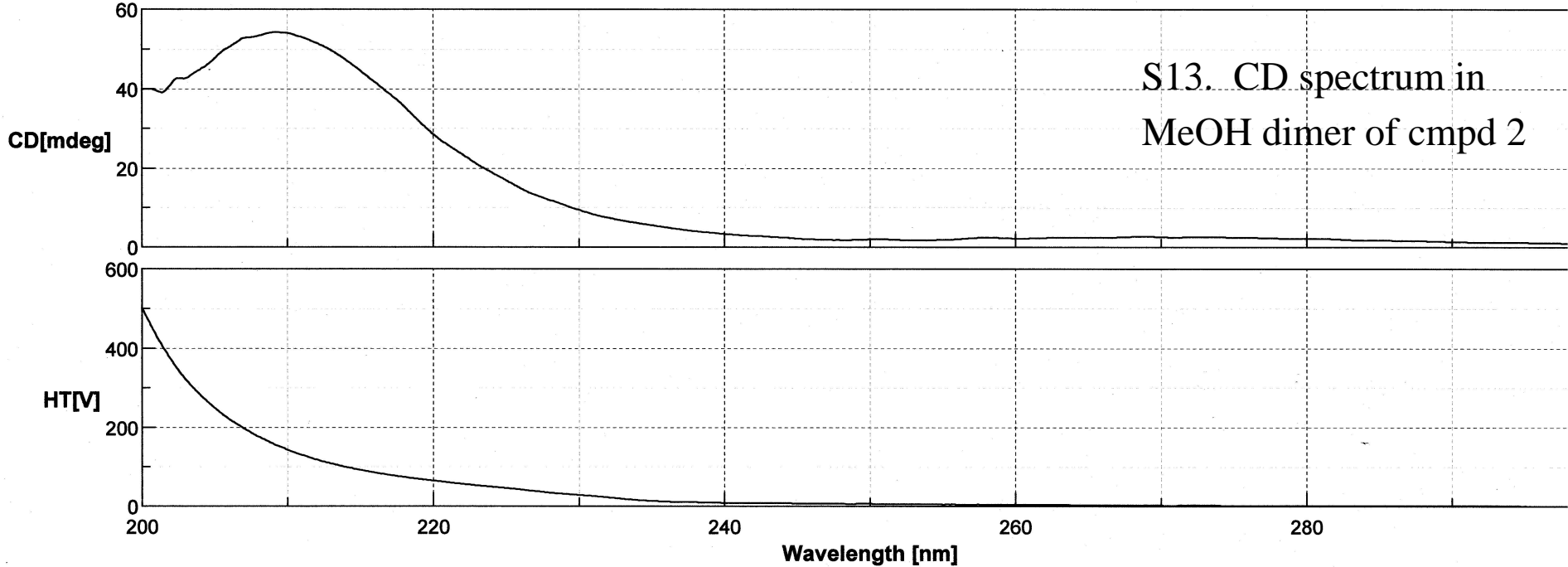


4466-54-K
pjk681
1.5mg 90%cdcl3-10%cd3od
zqftocsy_dipsi2_qnv2b

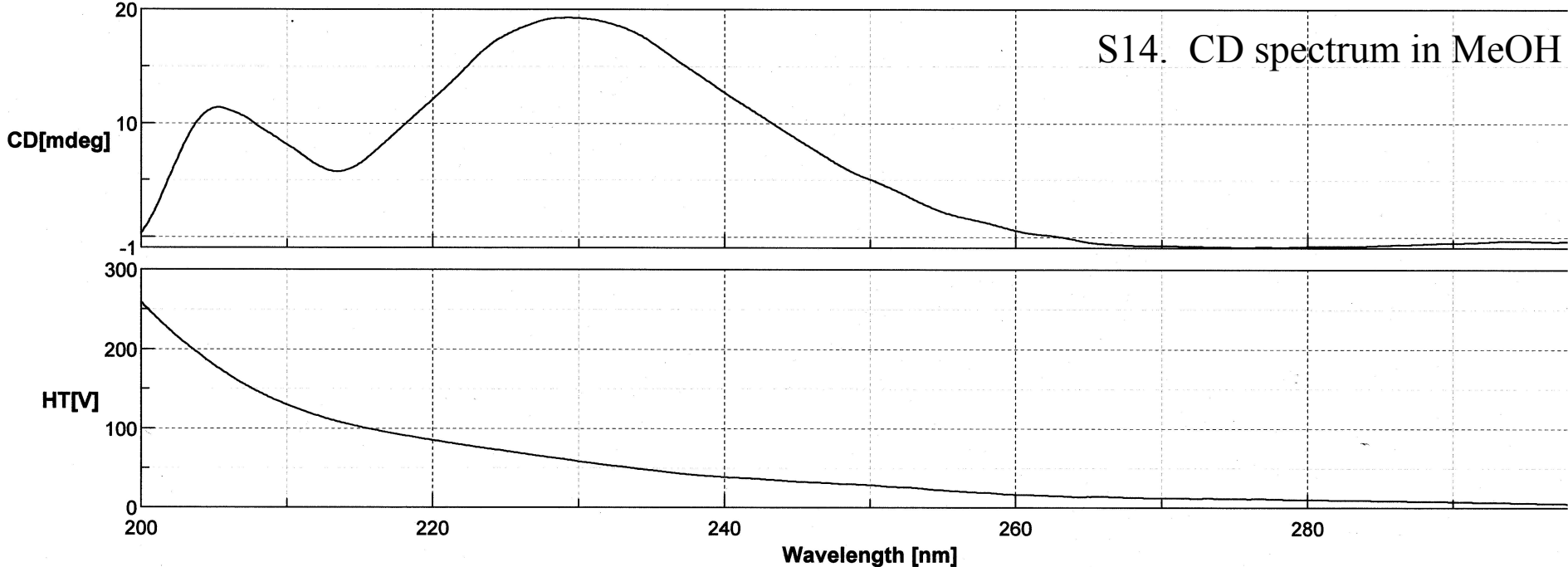
S11. TOCSY NMR - cmpd 2



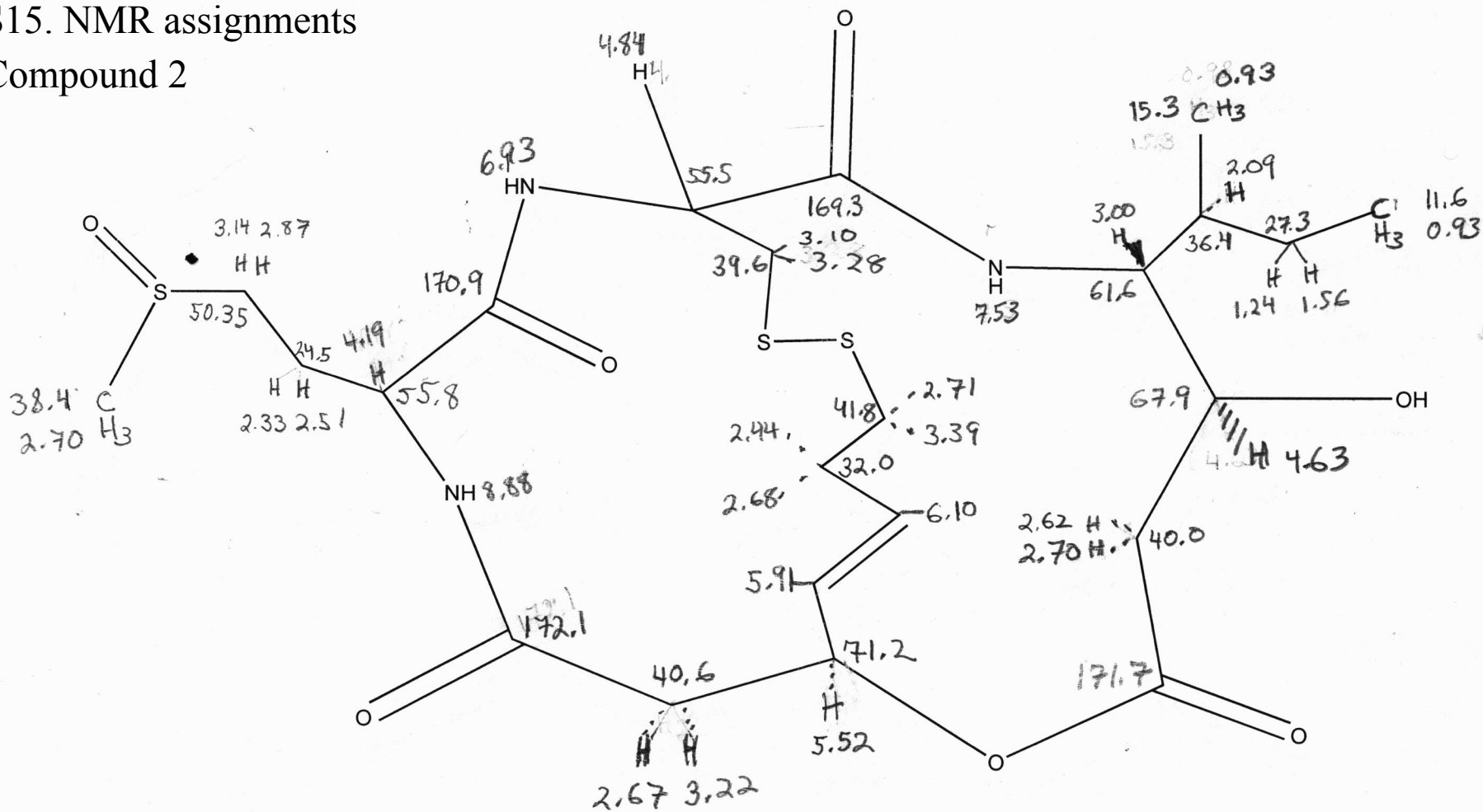




S14. CD spectrum in MeOH

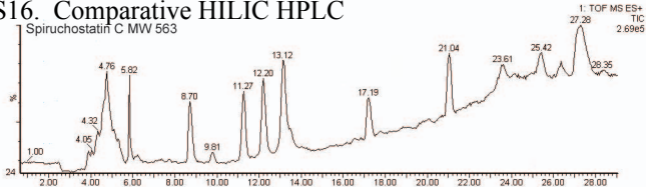


S15. NMR assignments
Compound 2

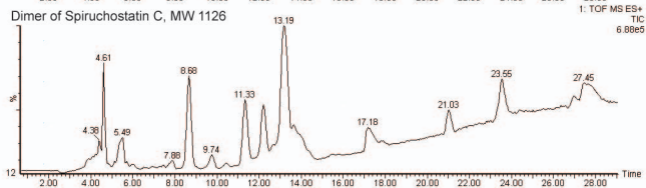


S16. Comparative HILIC HPLC

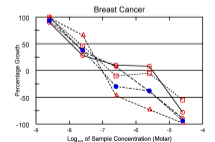
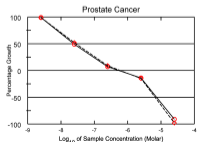
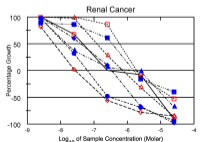
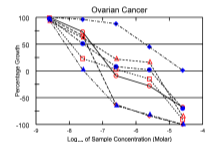
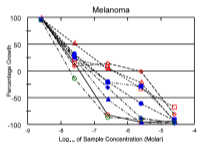
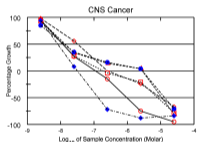
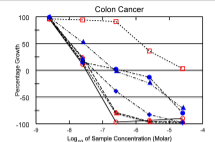
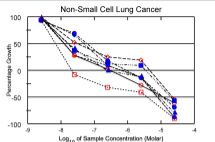
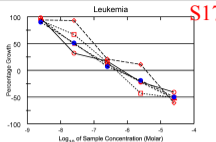
Spiruchostatin C MW 563



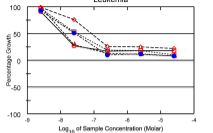
Dimer of Spiruchostatin C, MW 1126



S17.

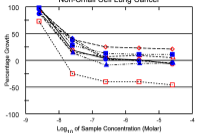


Leukemia



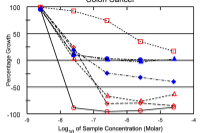
CCRF-CEM
MOLT-4
HL-60(TB)
SR
K-562

Non-Small Cell Lung Cancer



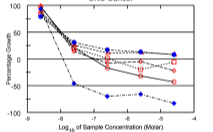
A549/ATCC
HOP-82
NCI-H322M
EKVX
NCI-H226
NCI-H460
HOP-62
NCI-H23
NCI-H223

Colon Cancer



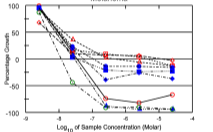
COLO 205
HCT-15
SW-620
HCC-2998
HT29
HCT-116
KM12

CNS Cancer



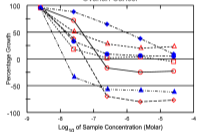
SF-298
SNB-19
SF-295
SNB-75
SF-539
U251

Melanoma



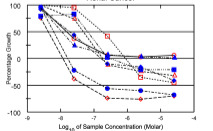
LOX IMVI
MALME-3M
M14
MDA-MB-435
SK-MEL-2
SK-MEL-28
SK-MEL-5
UACC-257
UACC-62
SK-MEL-3

Ovarian Cancer



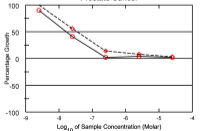
IGROV1
OVCAR-3
OVCAR-4
OVCAR-5
OVCAR-8
NCIADR-RES
SK-OV-3

Renal Cancer



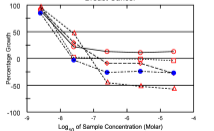
786-O
CAKI-1
TK-10
A498
RXF 383
RXF 383
UO-31
ACHN
SN12C

Prostate Cancer



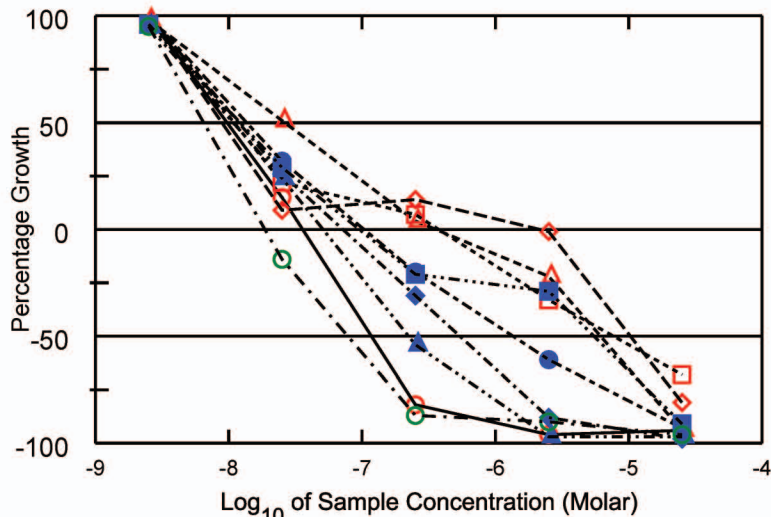
PC-3
DU-145

Breast Cancer



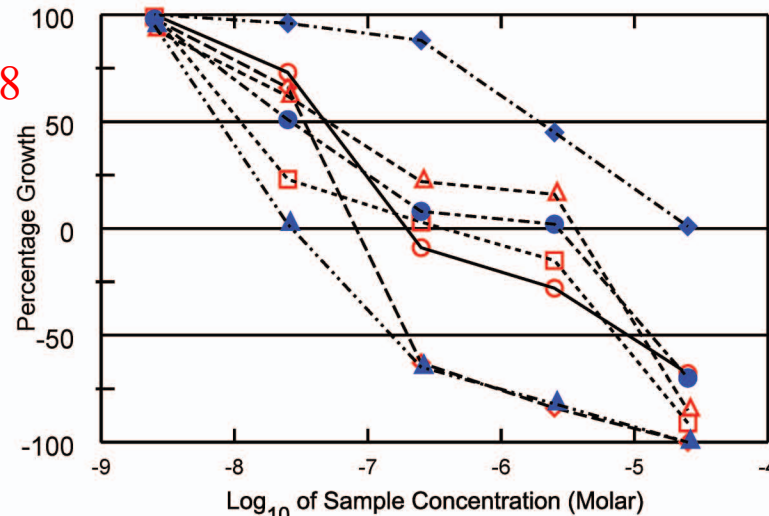
MCF7
T-47D
MDA-MB-231
MDA-MB-468
BT-649

Melanoma

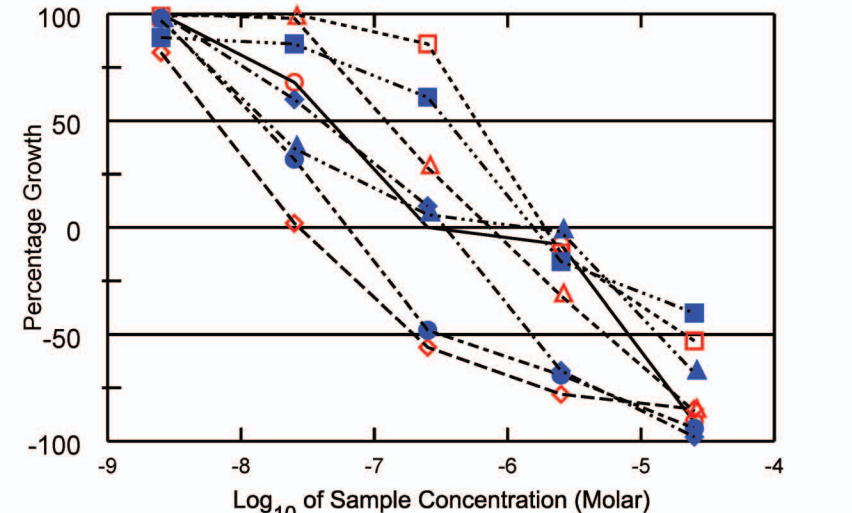


S19.
FK 228

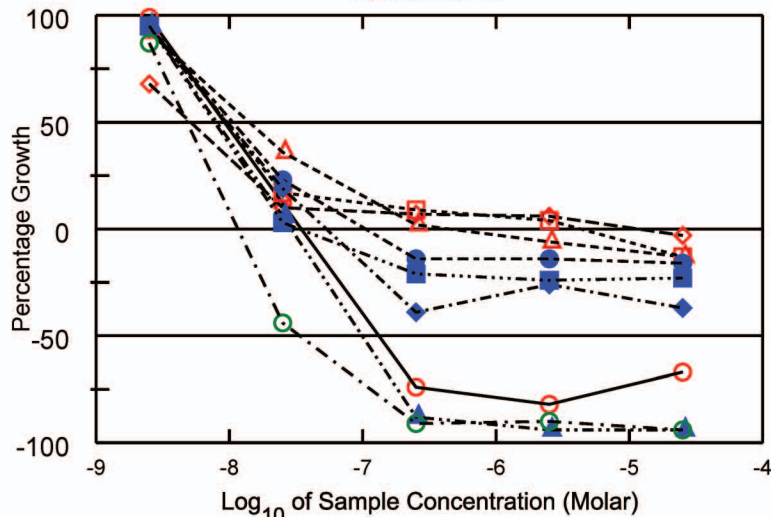
Ovarian Cancer



Renal Cancer

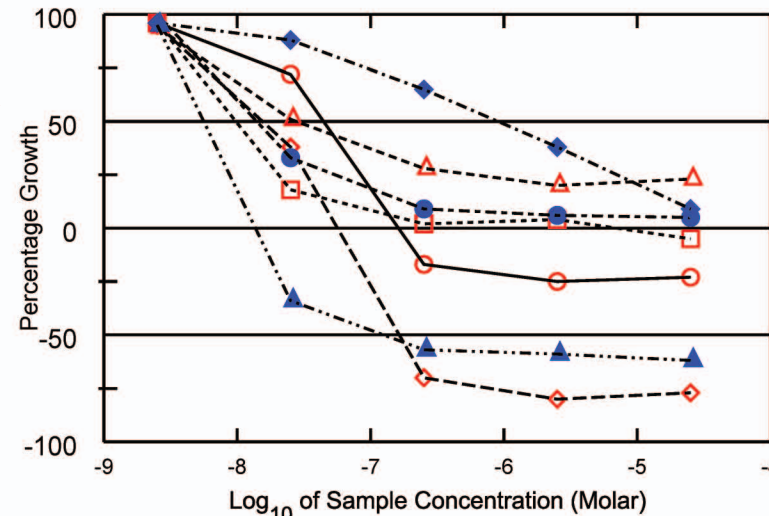


Melanoma

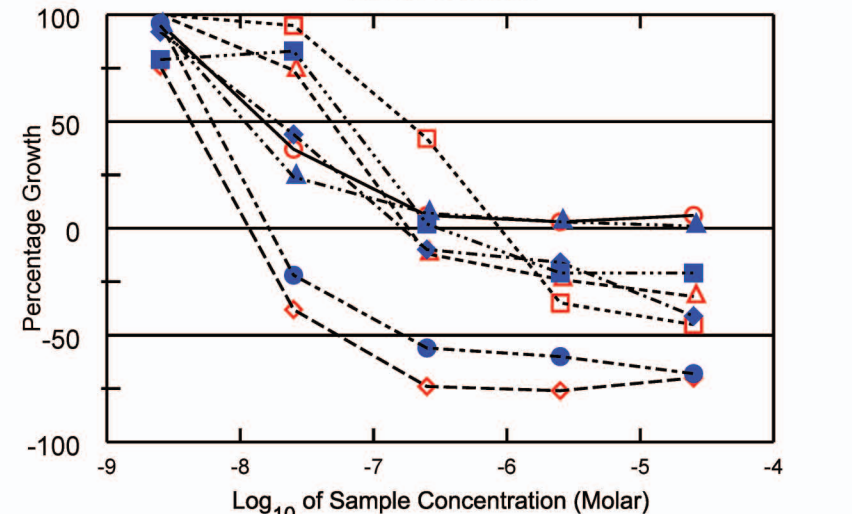


compd 2

Ovarian Cancer



Renal Cancer



S20. *In vivo* Hollow Fiber Results for Spiruchostatin C (2) and FK228 (1).

a. Tumor cells implanted intraperitoneally.

		Tumor Cell Growth (%T/C)			
		Spir. C	FK228	Spir. C	FK228
Tumor Cell Panel	Cell Line	2.4 ^a	2.4	1.6	1.6
Breast	MDA-MB-231	41	26	43	23
CNS	SF-295	>100	48	>100	57
CNS	U251	91	26	76	37
Colon	COLO 205	77	46	73	46
Colon	SW-620	84	55	89	63
Melanoma	LOX IMVI	45	10	22	9
Melanoma	MDA-MB-435	78	51	82	59
Melanoma	UACC-62	50	26	65	29
Non-Small Cell Lung	NCI-H23	92	71	80	64
Non-Small Cell Lung	NCI-H522	45	20	46	50
Ovarian	OVCAR-3	66	47	86	49
Ovarian	OVCAR-5	95	42	90	35

^a amount of drug administered in units of mg/kg/dose

b. Tumor cells implanted subcutaneously

		Tumor Cell Growth (%T/C)			
		Spir. C	FK228	Spir. C	FK228
Tumor Cell Panel	Cell Line	2.4 ^a	2.4	1.6	1.6
Breast	MDA-MB-231	>100	>100	95	76
CNS	SF-295	>100	>100	100	>100
CNS	U251	>100	>100	>100	>100
Colon	COLO 205	87	>100	81	84
Colon	SW-620	80	88	77	77
Melanoma	LOX IMVI	89	84	76	86
Melanoma	MDA-MB-435	>100	>100	86	>100
Melanoma	UACC-62	79	83	79	85
Non-Small Cell Lung	NCI-H23	86	92	65	73
Non-Small Cell Lung	NCI-H522	92	94	95	92
Ovarian	OVCAR-3	56	90	71	76
Ovarian	OVCAR-5	>100	100	>100	>100

^a amount of drug administered in units of mg/kg/dose