Suberitamides A-C, Aryl Alkaloids from a *Pseudosuberites* sp. Marine Sponge that Inhibit Cbl-b Ubiquitin Ligase Activity

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Table S1. ^{13}C NMR (150 MHz) and ^{1}H NMR Data (600 MHz) of Compound 1 in DMSO-d_6.

Position	δ_C (type)	δ_H (J in Hz)	HMBC
2	109.1, C		
2-OCH_3	51.6, CH_3	3.40, s	2
3	53.3, CH	4.09, d (13.8)	2, 4, 16, 26, 27, 31
4	54.6, CH	3.91, d (13.8)	3, 5, 6, 32, 33, 37
5	102.3, C		
5-OH		7.40, s	4, 5, 6
6	169.4, C		
7-NH		10.52, d (10.2)	6
8	120.2, CH	7.29, dd (14.6, 10.2)	6, 9, 10
9	114.8, CH	6.43, d (14.6)	8, 10, 11, 15
10	126.9, C		
11, 15	126.8, CH	7.24, d (8.4)	9, 11, 13, 15
12, 14	115.6, CH	6.72, d (8.4)	10, 12, 13, 14
13	156.4, C		
13-OH		9.47, s	12, 13, 14
16	166.0, C		
17-NH		10.50, d (10.2)	
18	120.1, CH	7.04, dd (14.6, 10.2)	16, 19, 20
19	114.3, CH	6.29, d (14.6)	18, 20, 21, 25
20	126.9, C		
21, 25	126.7, CH	7.18, d (8.4)	19, 21, 23, 25
22, 24	115.6, CH	6.70, d (8.4)	20, 22, 23, 24
23	156.3, C		
23-OH		9.44, s	22, 23, 24
26	124.8, C		
27	115.8, CH	6.52, d (1.8)	2[a], 3, 29, 31
28	144.4, C		
28-OH		8.71, s	27, 28, 29
29	144.5, C		
29-OH		8.74, s	28, 29, 30
30	115.0, CH	6.50, d (8.4)	26, 28
31	119.2, CH	6.36, d (8.4, 1.8)	2[a], 3, 27, 29
32	125.0, C		
33	116.6, CH	6.55, d (1.8)	4, 5[a], 35, 37
34	144.7, C		
34-OH		8.68, s	33, 34, 35
35	144.6, C		
35-OH		8.69, s	34, 35, 36
36	115.2, CH	6.51, d (8.4)	32, 34
37	120.1, CH	6.38, dd (8.4, 1.8)	4, 5[a], 33, 35

[a] J_{CH}= 2 Hz optimized HMBC experiment

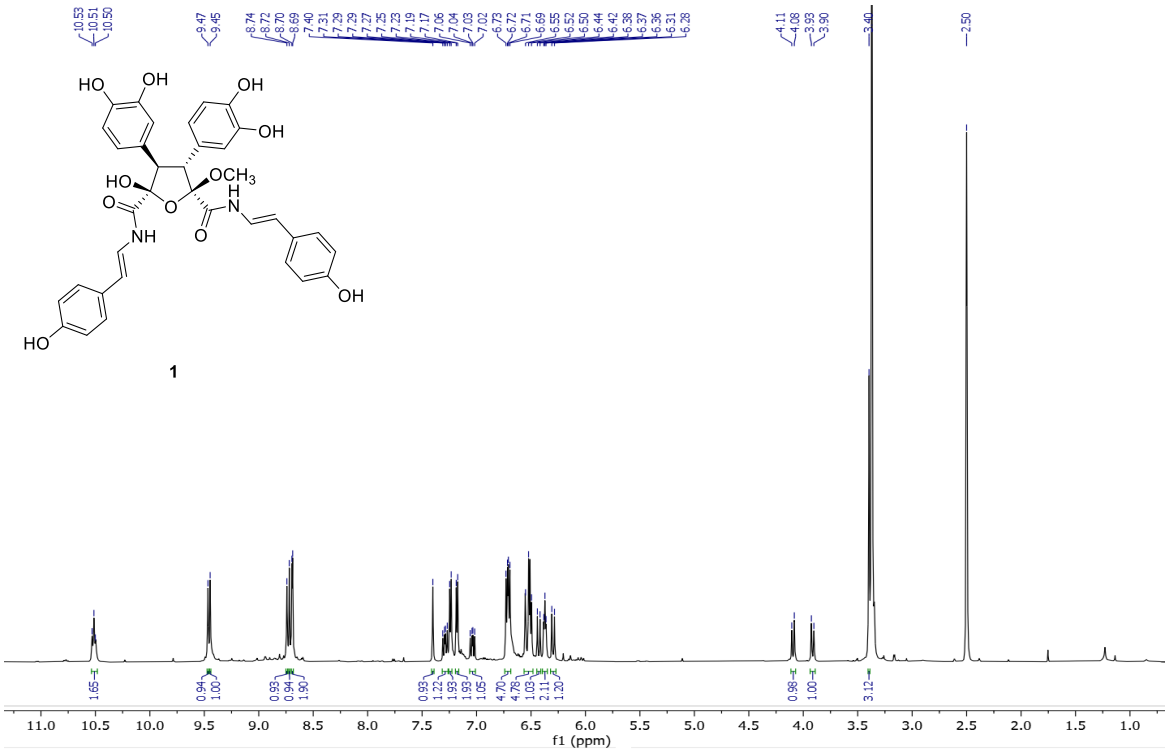


Figure S1. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of **1**

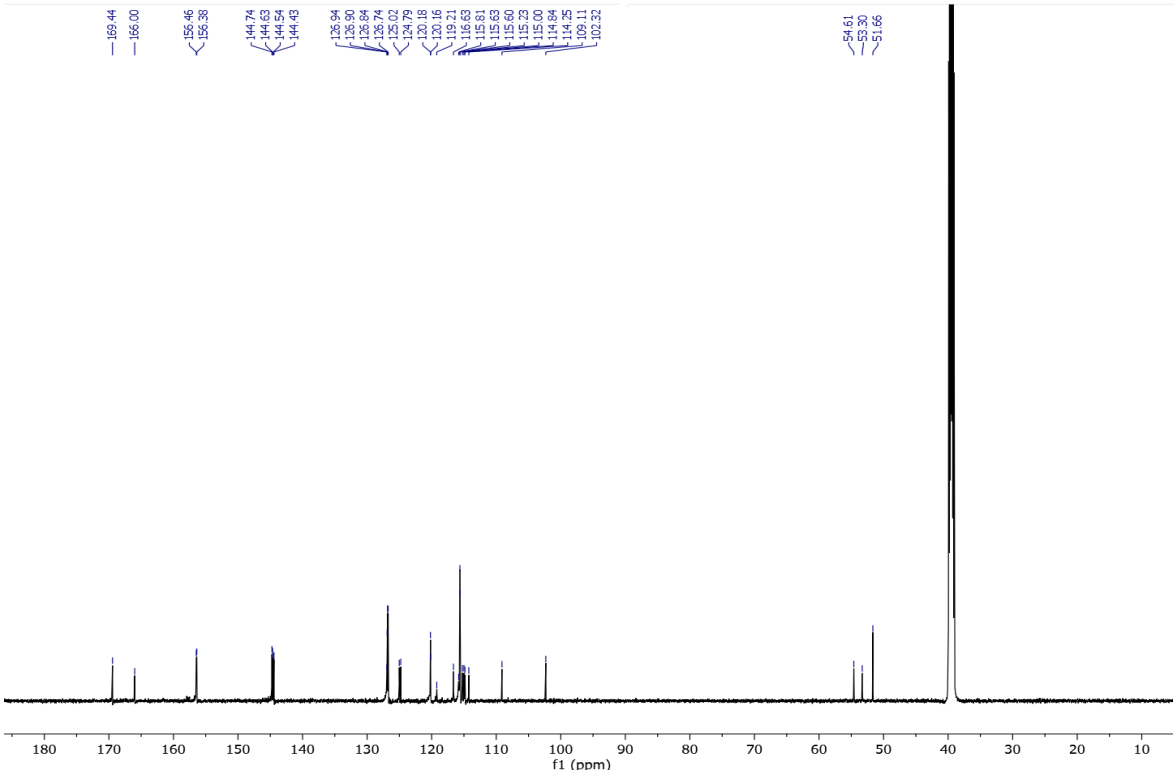


Figure S2. ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of **1**

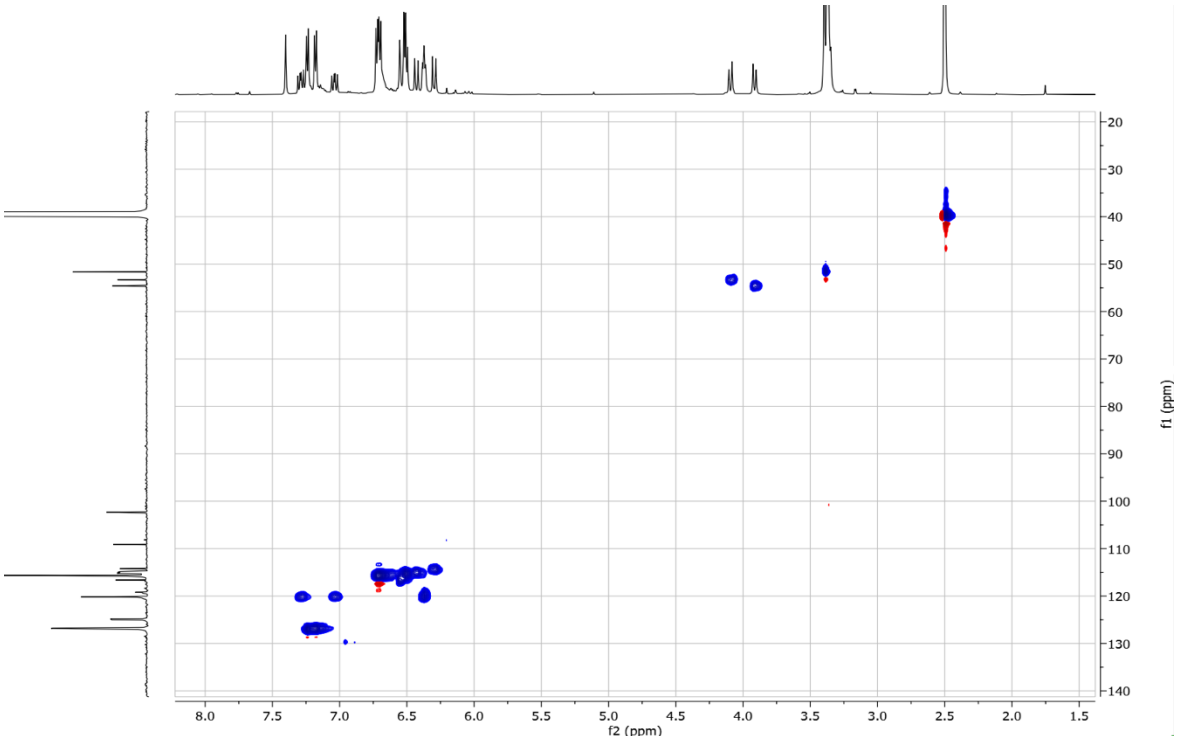


Figure S3. Edited HSQC NMR (DMSO-d_6) spectrum of **1**

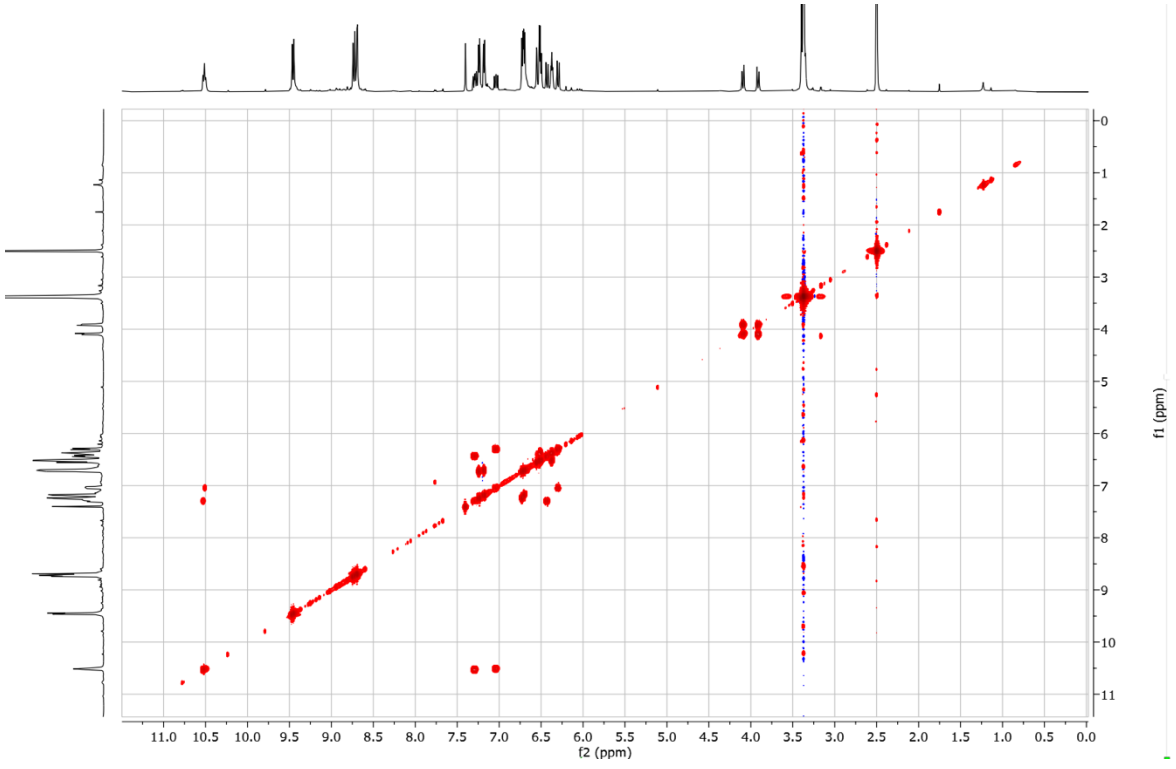


Figure S4. COSY NMR (600 MHz, DMSO-d_6) spectrum of **1**

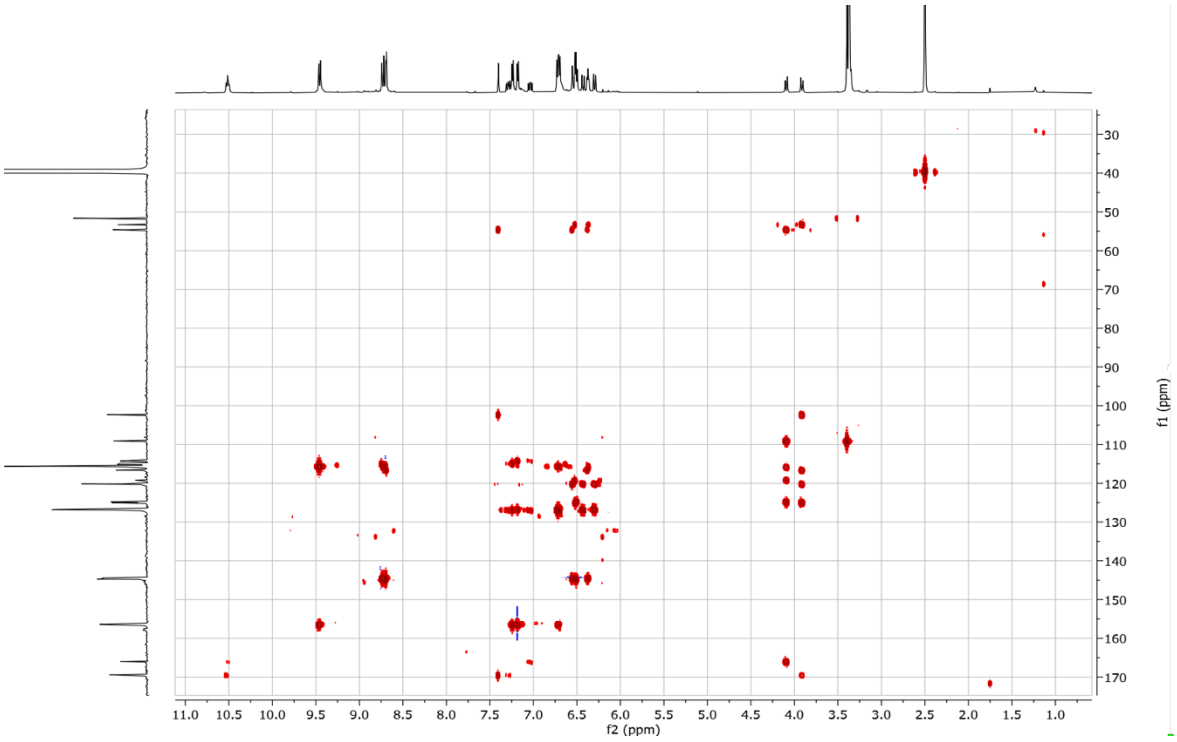


Figure S5. HMBC NMR (DMSO-d_6) spectrum of **1**

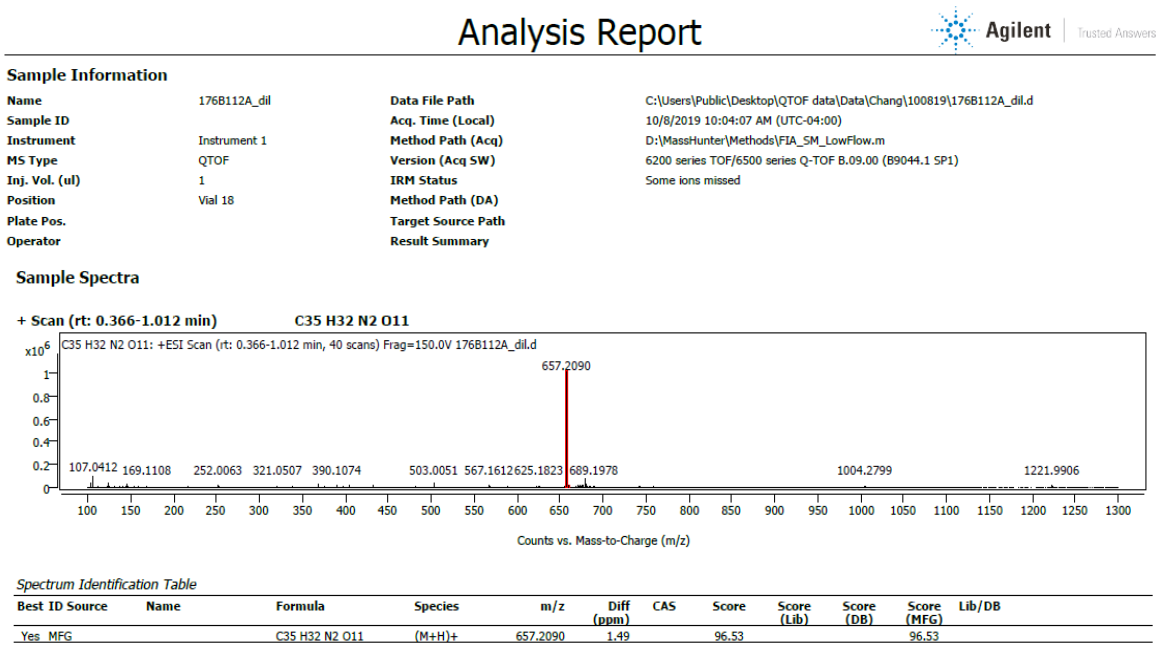
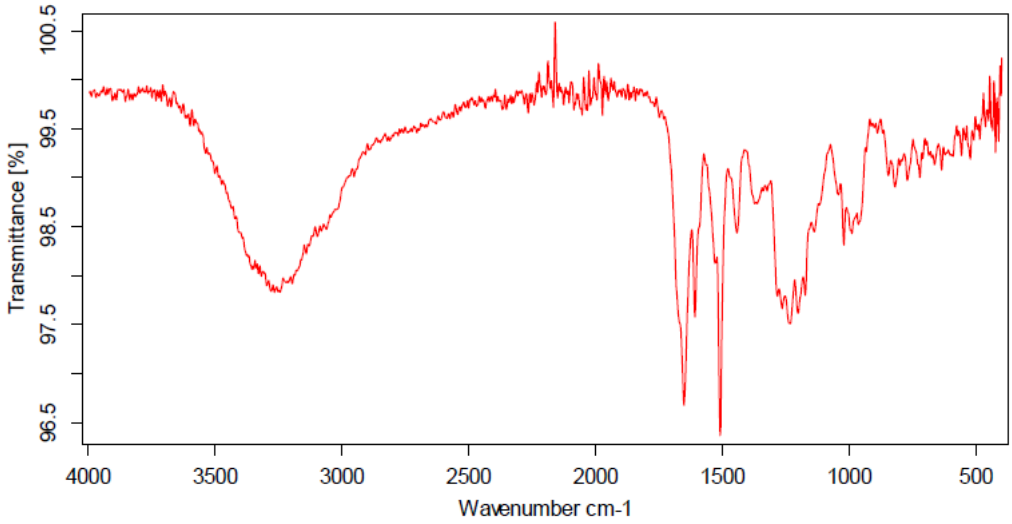


Figure S6. ESI-HR MS data of **1**

IR Spectrum Report

Instrument type	Alpha II
Accessory	ATR platinum Diamond 1 Refl #24C8F5322D
Spectrum file name	176B112A.0
Spectrum file path	T:\Data\MEAS\Chang
Measurement date and time	15/10/2019 22:20:54 (GMT-7)
Sample name	176B112A
Sample form	Instrument type and / or accessory

Spectrum



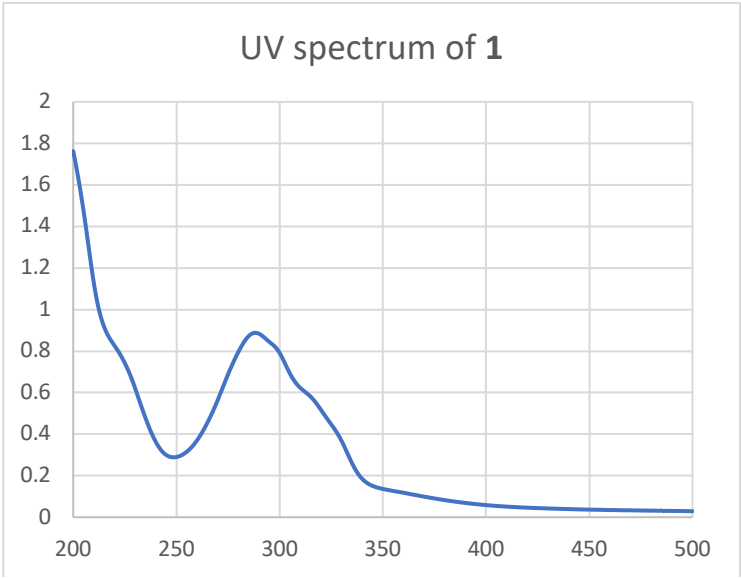


Figure S7. IR & UV spectra of **1**

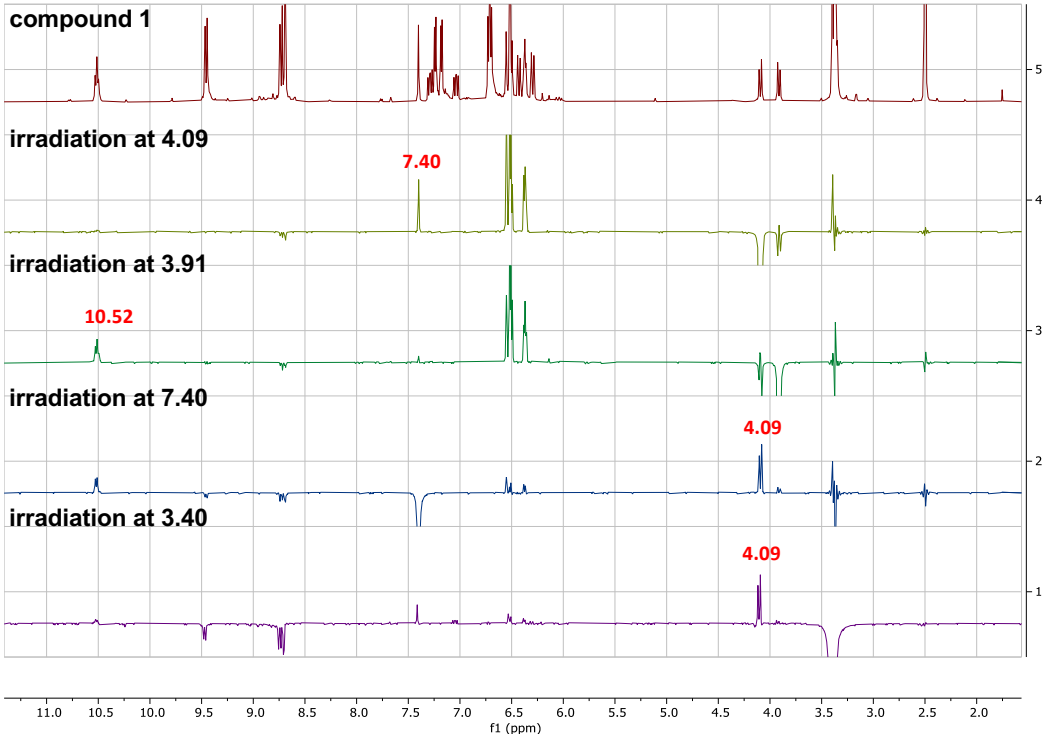


Figure S8. 1D-Selective ROESY NMR (600 MHz, DMSO-d_6) spectra of **1**

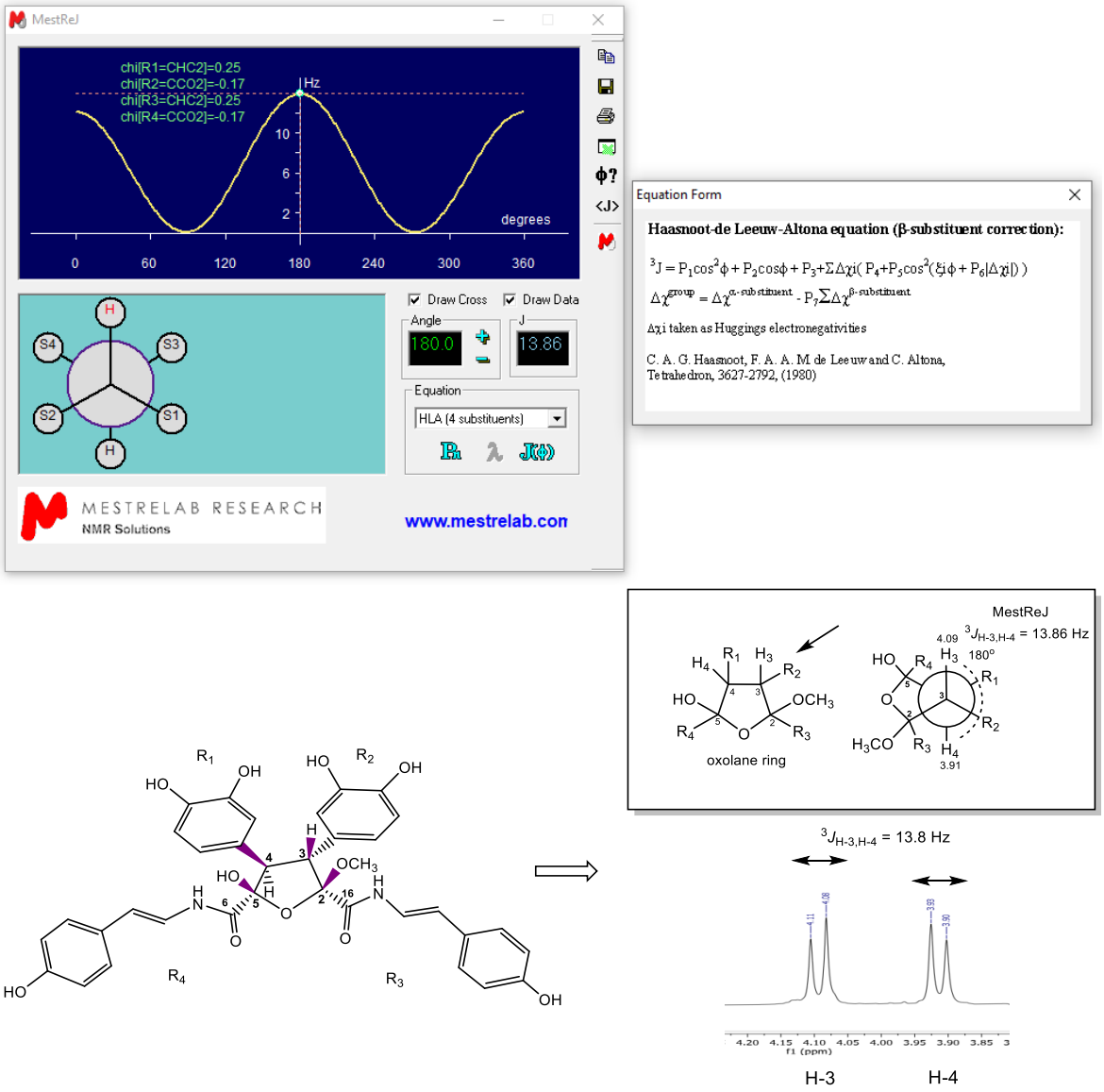


Figure S9. Calculated dihedral angle along the C-3/C-4 bond using MestReJ v1.1 for **1** in DMSO-d_6

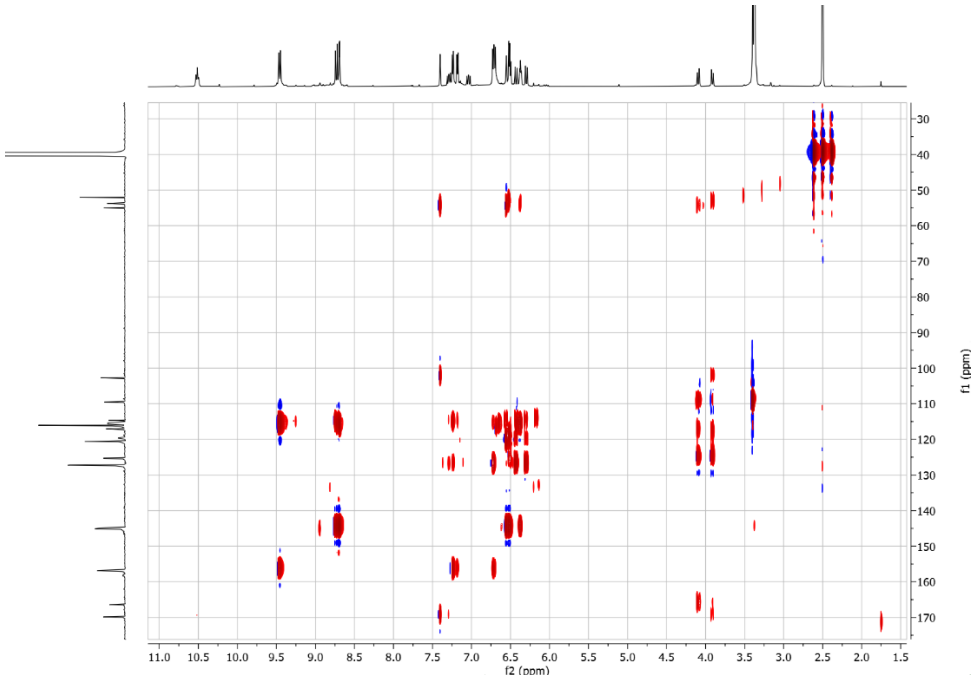


Figure S10. IP PIP-HSQMBC NMR (*cnst* 25 = 0, DMSO-d_6) spectrum of **1**

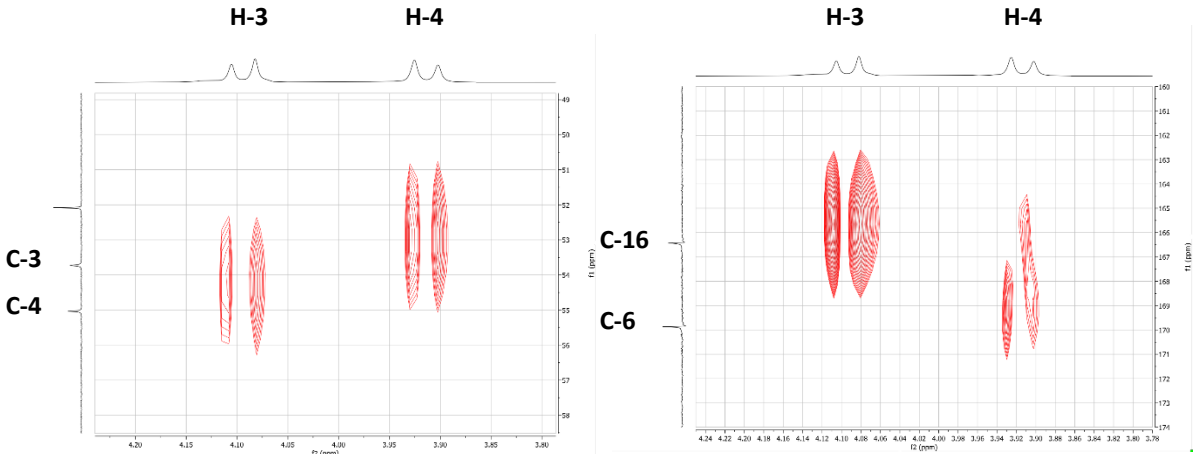


Figure S11. Expanded IP PIP-HSQMBC NMR (*cnst* 25 = 0, DMSO-d_6) spectrum of **1**

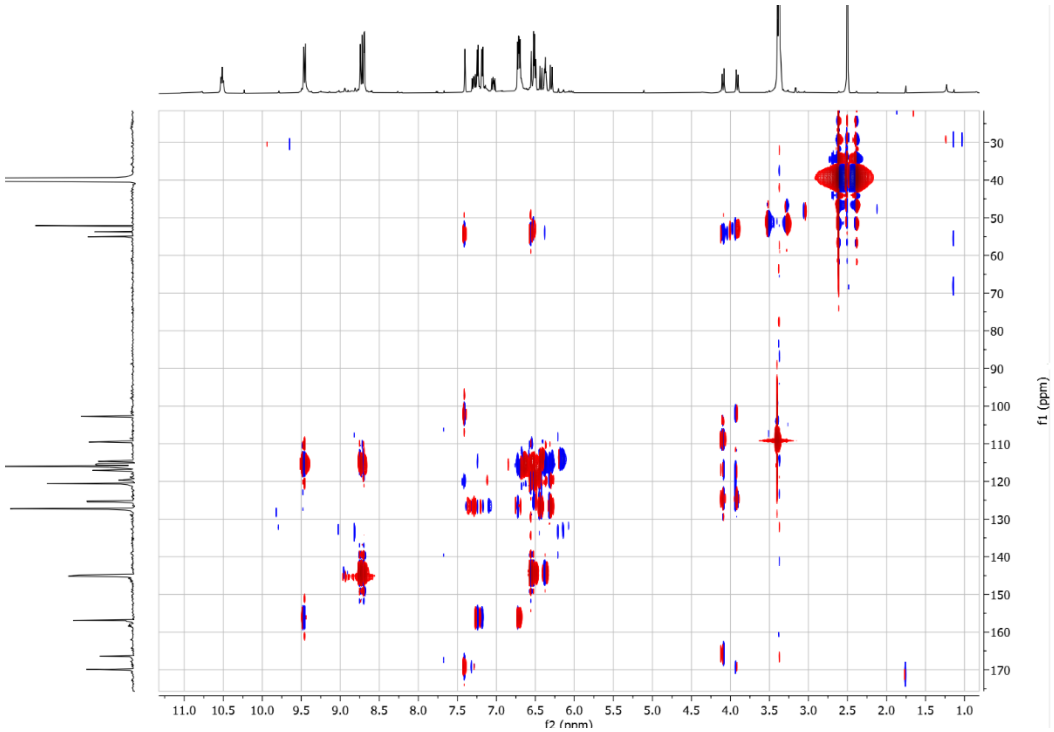


Figure S12. AP PIP-HSQMBC NMR (*cnst* 25 = 1, DMSO-d_6) spectrum of **1**

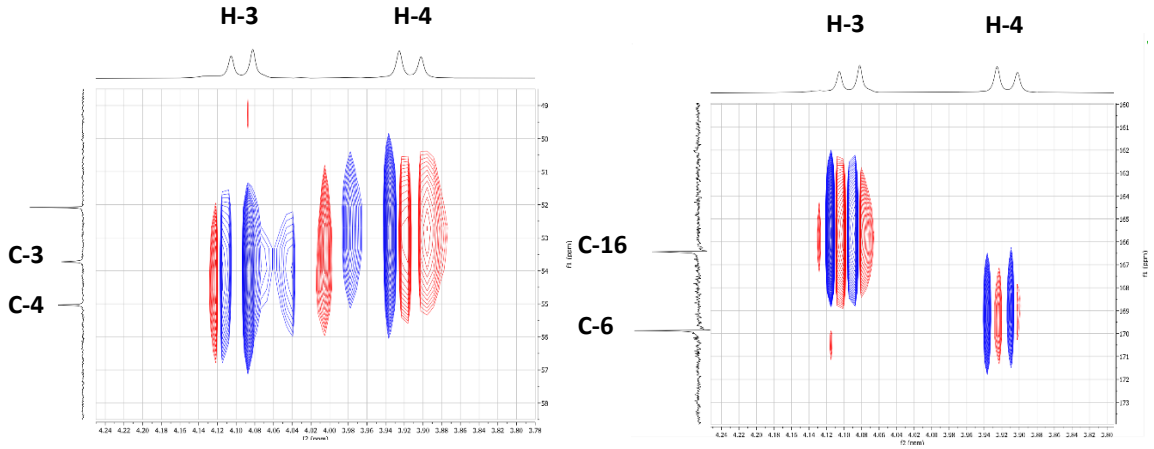


Figure S13. Expanded AP PIP-HSQMBC NMR (*cnst* 25 = 1, DMSO-d_6) spectrum of **1**

S14. IPAP: addition/subtraction procedure using “adsu” in TopSpin 4.0.7

referred from Magn. Reson. Chem. **2020**, *58*, 363–375.

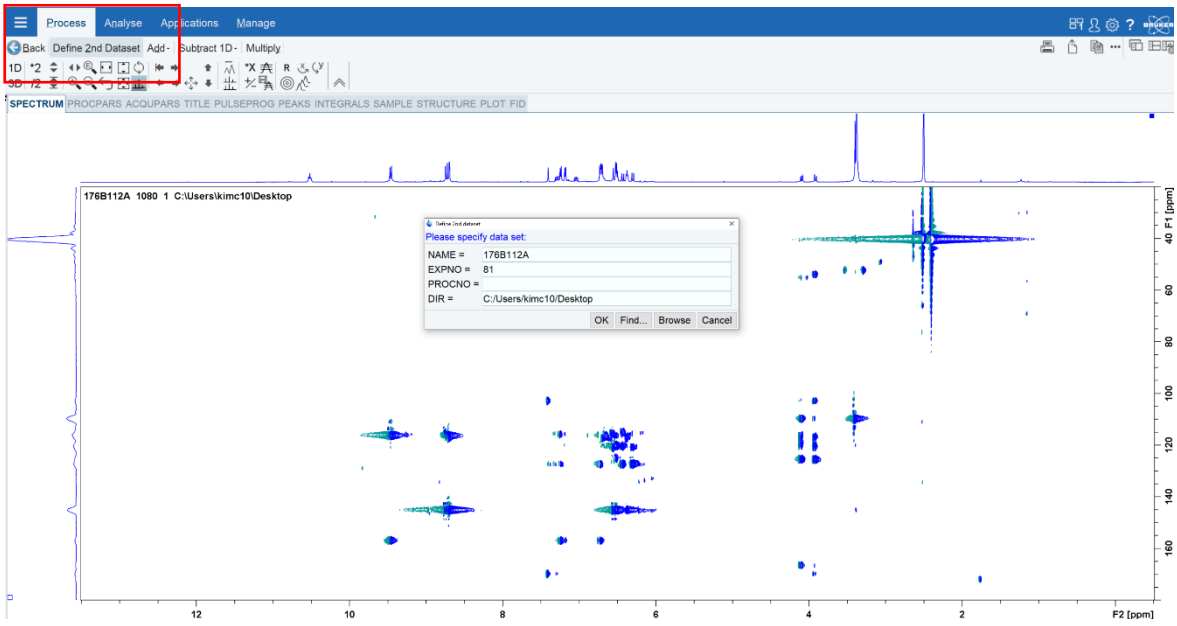
Once IP dataset and AP dataset have been acquired, follow the steps below:

First thing we have to do is to create two new subspectra: copy IP experiment (let’s say expno 80) into two new data set by typing “wrpa 1080” and then “wrpa 1081”.

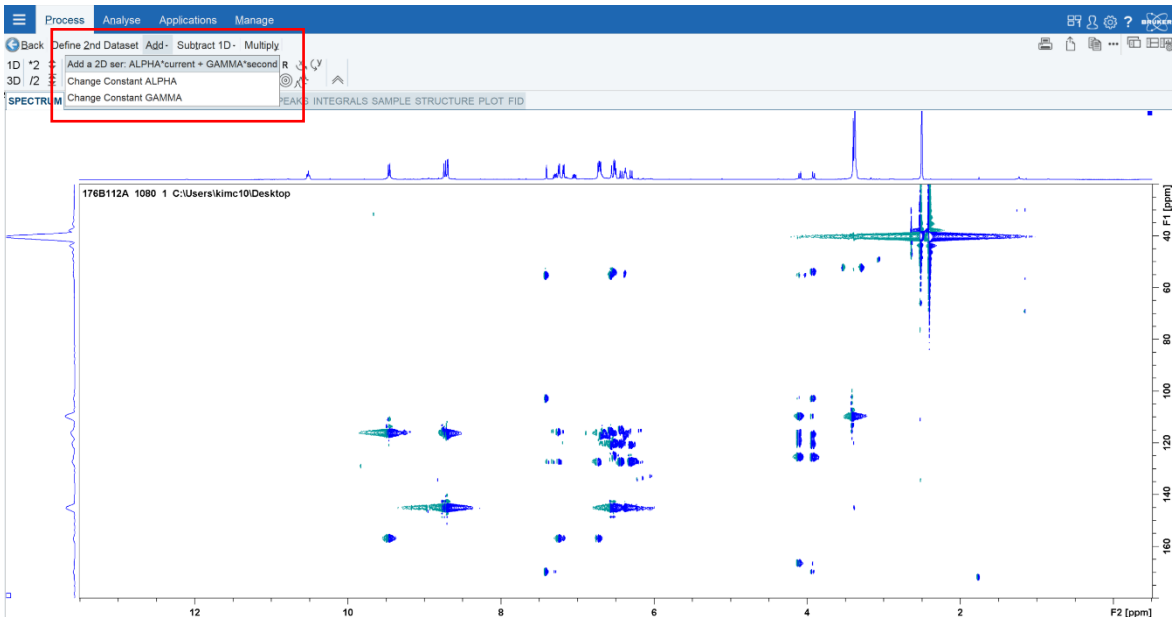
> *In 1080 we will add the AP dataset (expno81), so that 1080 will eventually be IP+AP.*
> *In 1081 we will subtract the AP dataset (expno81), so that 1081 will eventually be IP-AP.*

1. Open 1080 dataset and then type “adsu” in the command line.

2. Click on “Define 2nd dataset” in the top panel
   In the pop-up window, we type “81” (which is the AP data we want to add) in the expno box, and we type “1” in the procno box.
   Click OK.



3. We then click on “Add” in the top panel. Make sure you click on the arrow section of the icon (indicated by the black arrow)



The equation is ALPHA*current (dataset) + GAMMA*second (dataset).

Since we are now adding the second dataset to get the IP+AP subspectra, we set ALPHA and GAMMA both to be 1 by clicking “change constant ALPHA” and “change constant GAMMA”, respectively.

4. When ALPHA and GAMMA have been set, we then click on “Add a 2D ser” option. Again, make sure you click on the arrow section of the icon (indicated by the black arrow)

   TopSpin will ask if we are sure we want to add, we click OK.

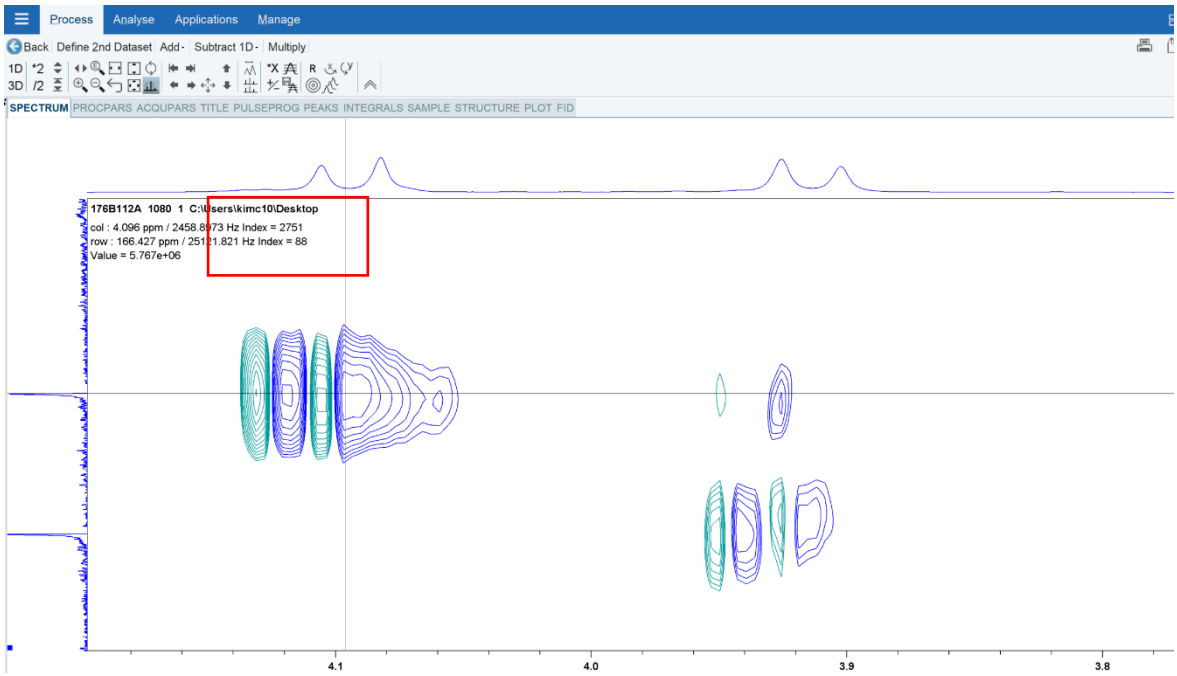
5. We then process the data typing “xfb”.

6. We now open 1081 dataset and repeat steps 2-5 with the only exception that GAMMA must be set to -1 in this case as we want to do the subtraction step here to get the IP-AP subspectra.

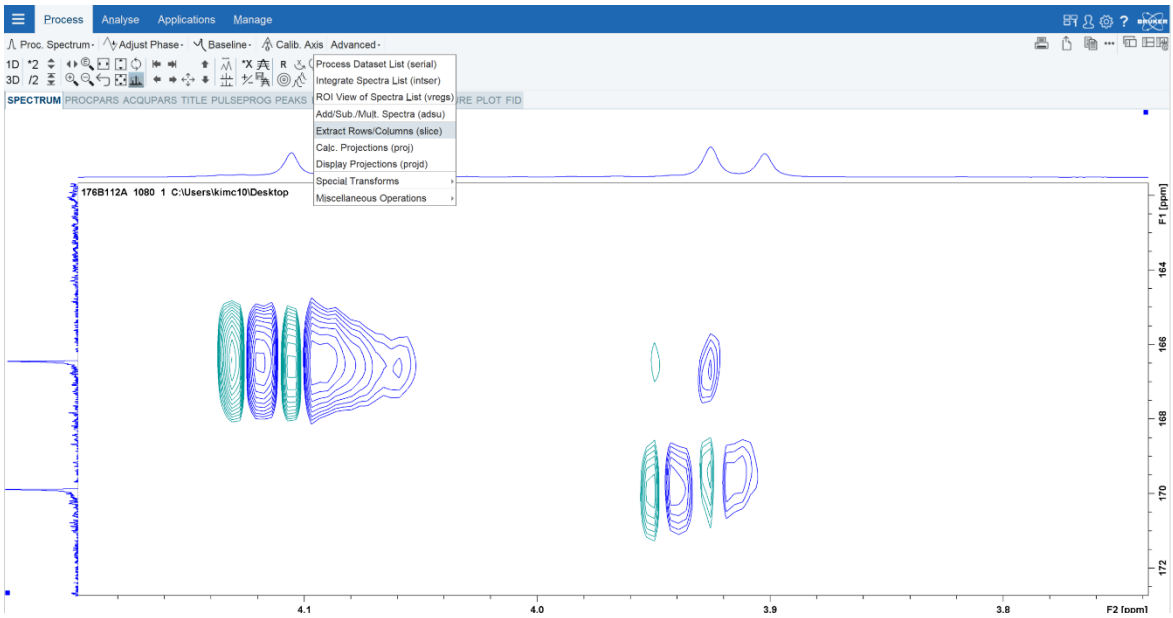
We now have both subspectra (IP+AP, and IP-AP) ready to be analyzed.

After **extracting 1D slices** at the carbon frequencies of interest from the IP+AP dataset (1080) and IP-AP dataset (1081), we can overlap them to measure with high accuracy the long-range proton-carbon coupling constant just by looking at their relative displacement.

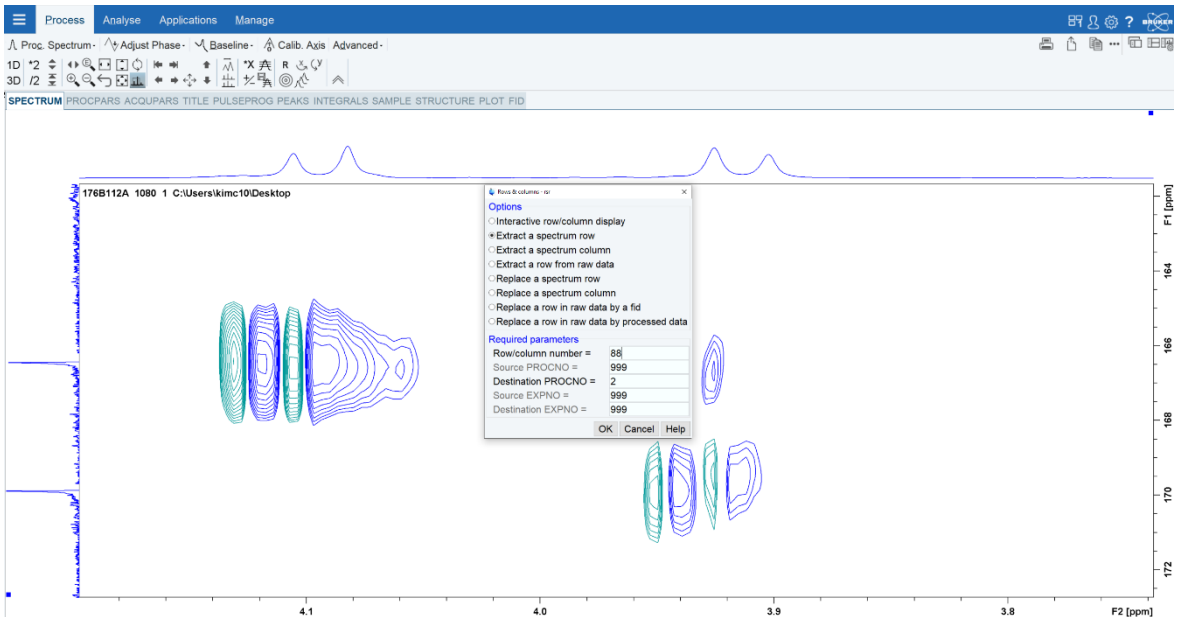
Extracting 1D slices at the carbon frequencies



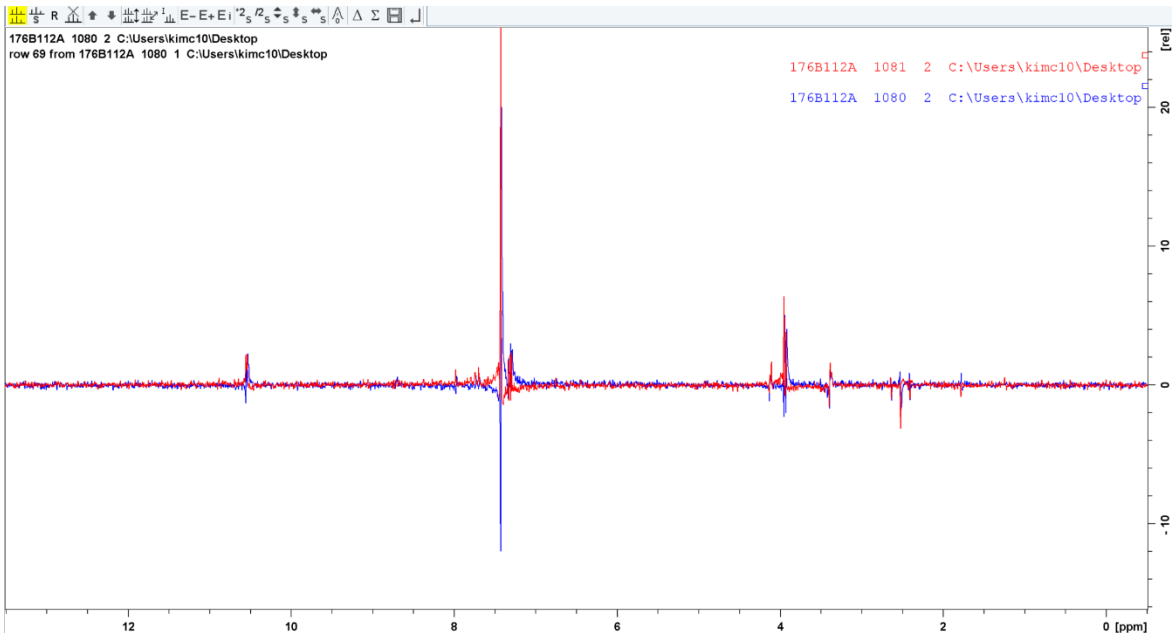
We need to write down for the index value of interesting signals. Then, we click on “Advanced” in the top panel and Extract Rows/Columns (slice).

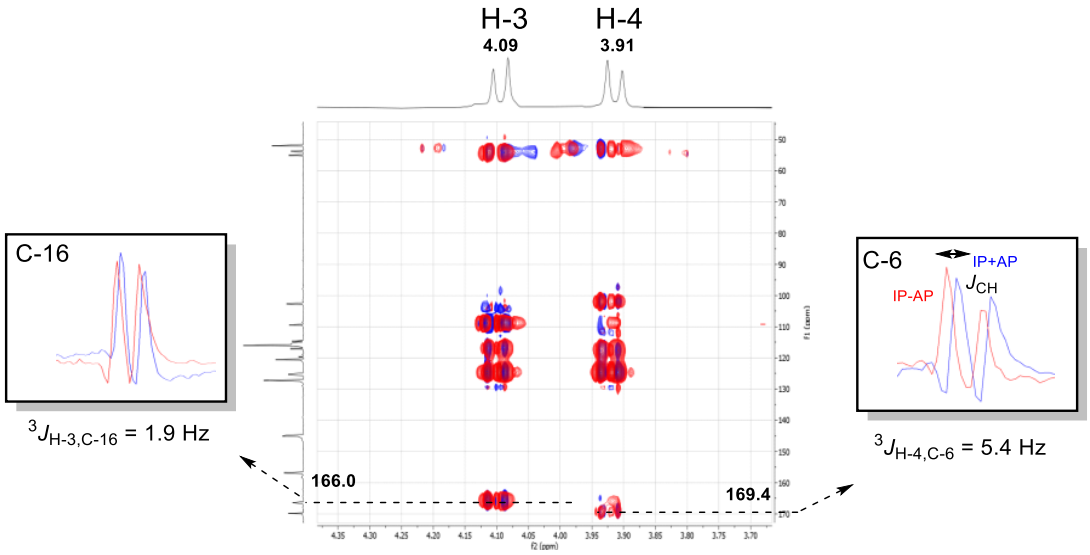


Lastly, we put the index value into the Row/column and designated 2 as a PROCNO number.



Peak overlapping





2D PIP-HSQMBC-IPAP

-extracting 1D slices at the carbon frequencies

-relative sign information cannot be extracted from the PIP-HSQMBC experiment.

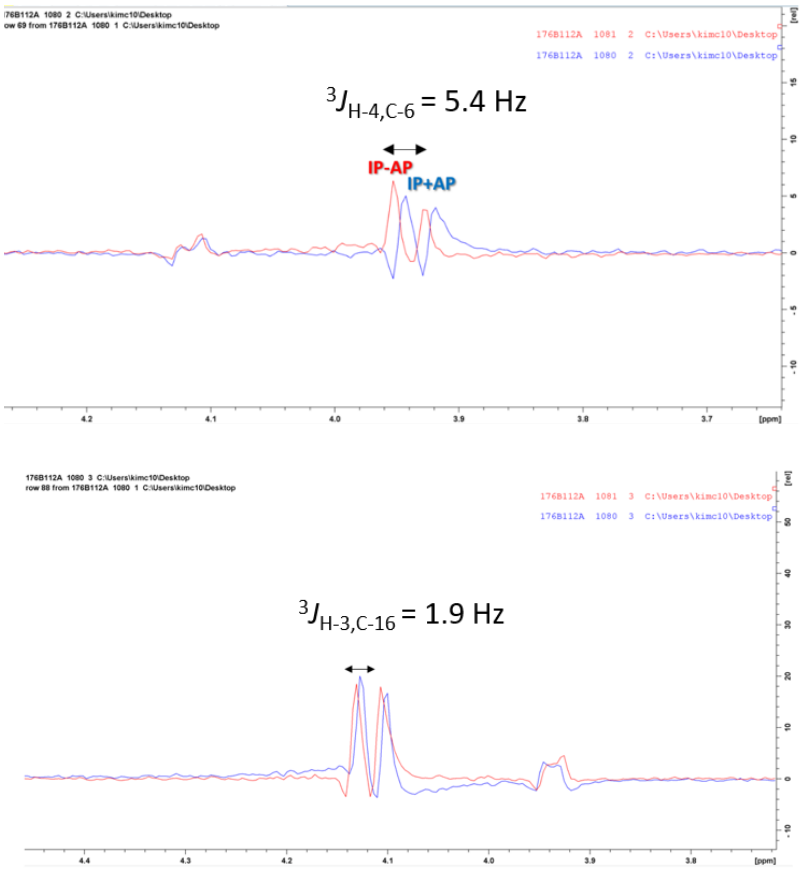
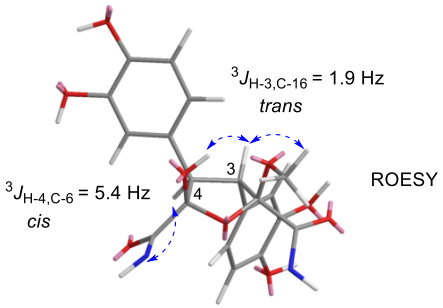
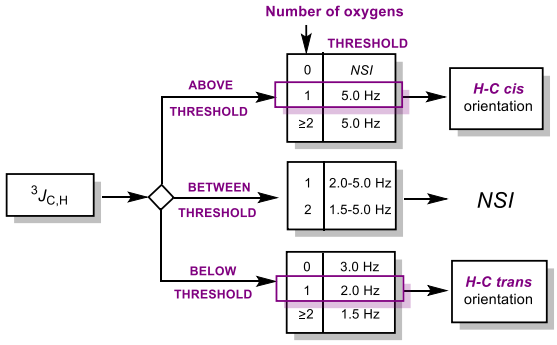


Figure S15. Extracted 1D carbon slices (DMSO-d_6) from spectra of **1**



J measured	value (Hz)	relative orientation
1) $^3J_{H\text{-}3,C\text{-}16}$	1.9	C-H *trans*
2) $^3J_{H\text{-}4,C\text{-}6}$	5.4	C-H *cis*



(NSI: no stereochemical information can be extracted).

Chem. Eur. J. **2011**, *17*, 6338 - 6347

Figure S16. Flow chart to use $^3J_{C,H}$ values for configurational analysis of five-membered rings.

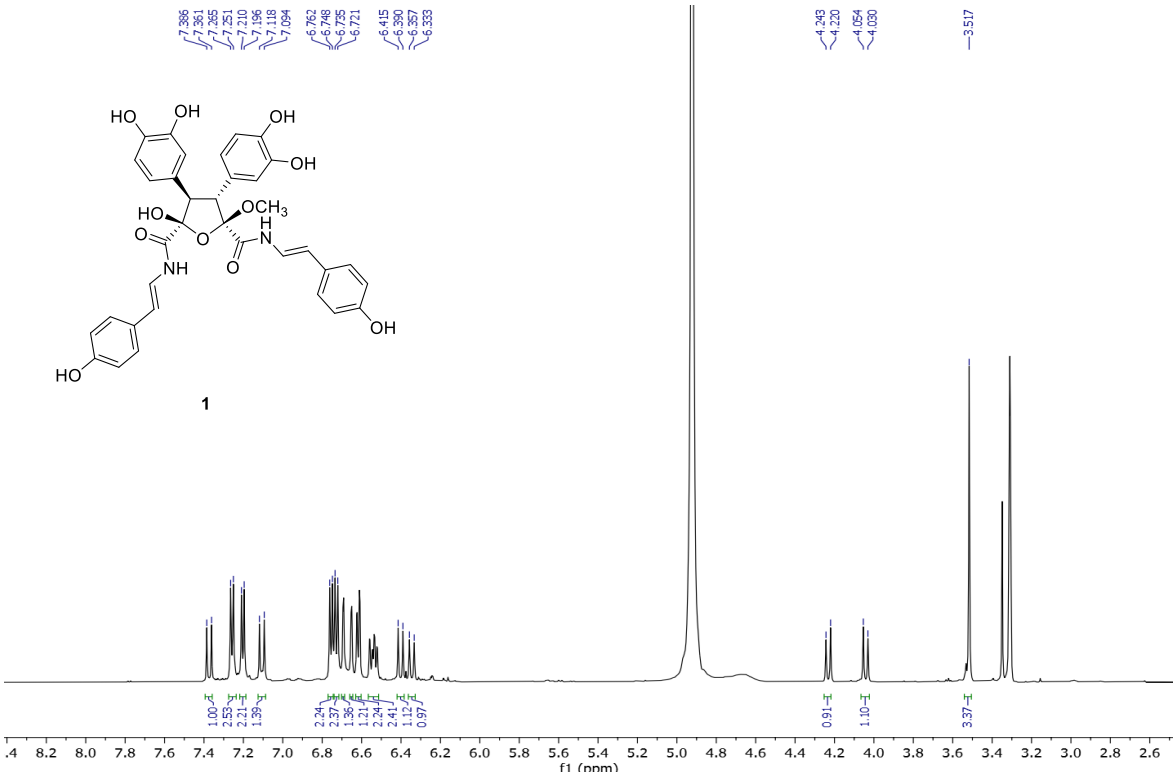


Figure S17. ^{1}H NMR (600 MHz, MeOH-d_4) spectrum of **1**

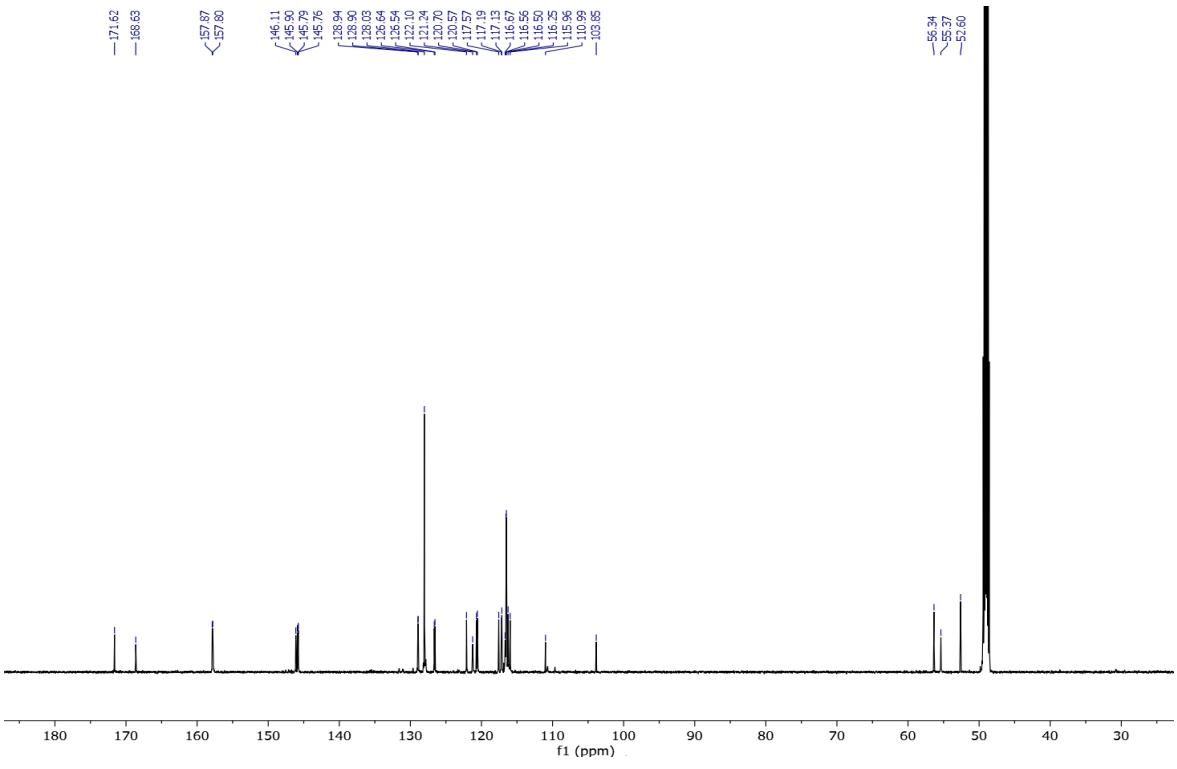


Figure S18. ^{13}C NMR (150 MHz, MeOH-d_4) spectrum of **1**

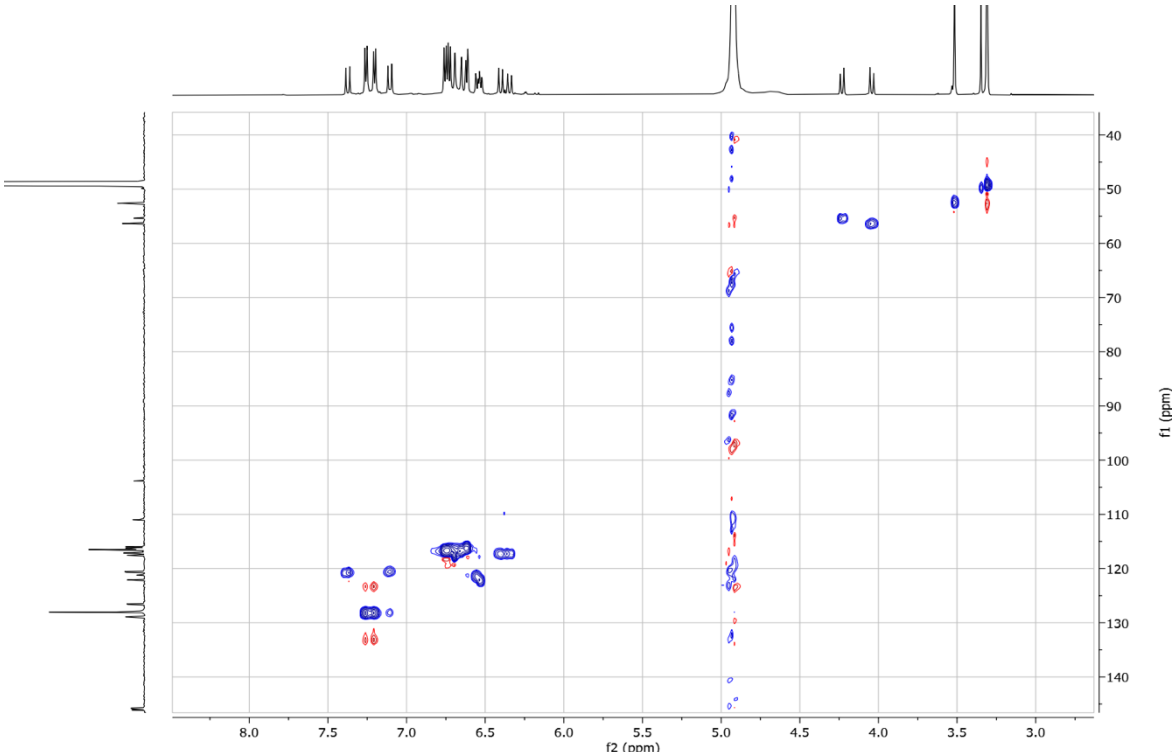


Figure S19. Edited HSQC NMR (MeOH-d_4) spectrum of **1**

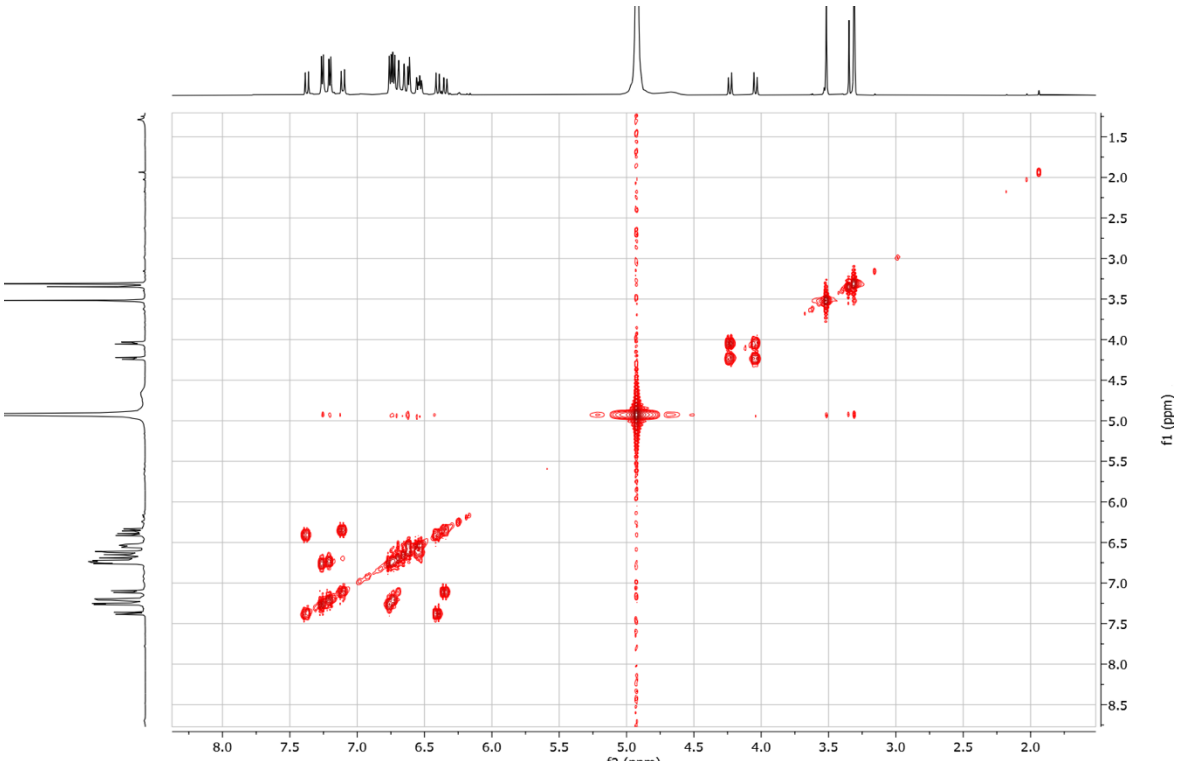


Figure S20. COSY NMR (600 MHz, MeOH-d_4) spectrum of **1**

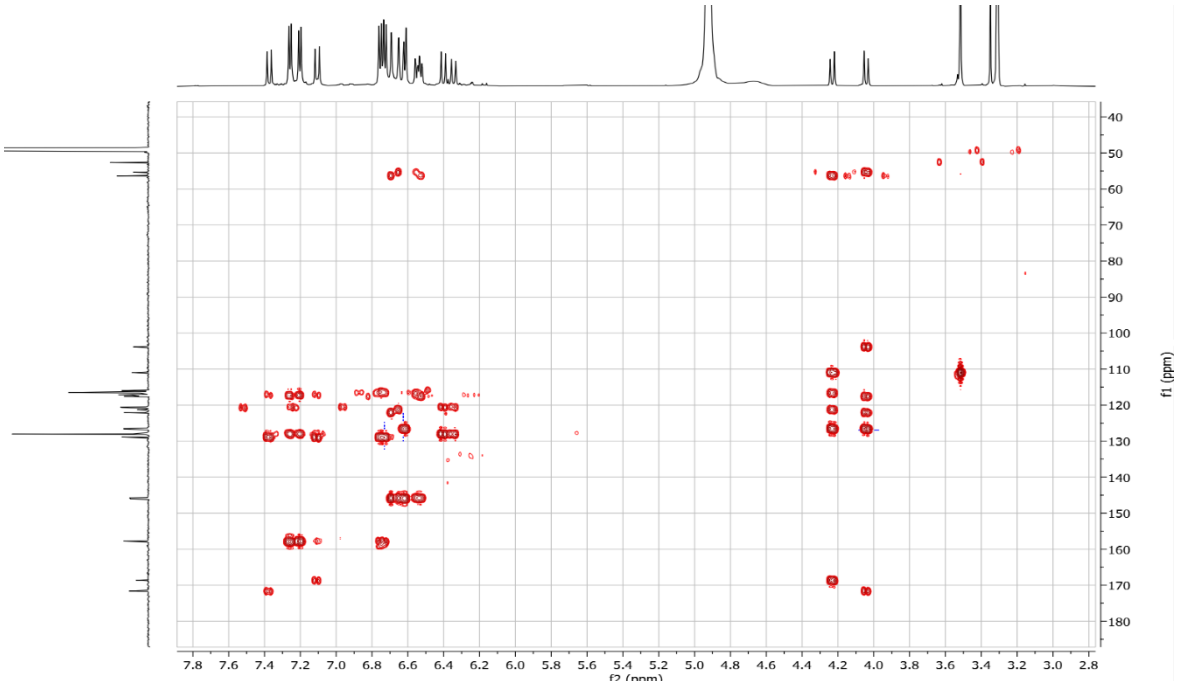


Figure S21. HMBC NMR (MeOH-d_4) spectrum of **1**

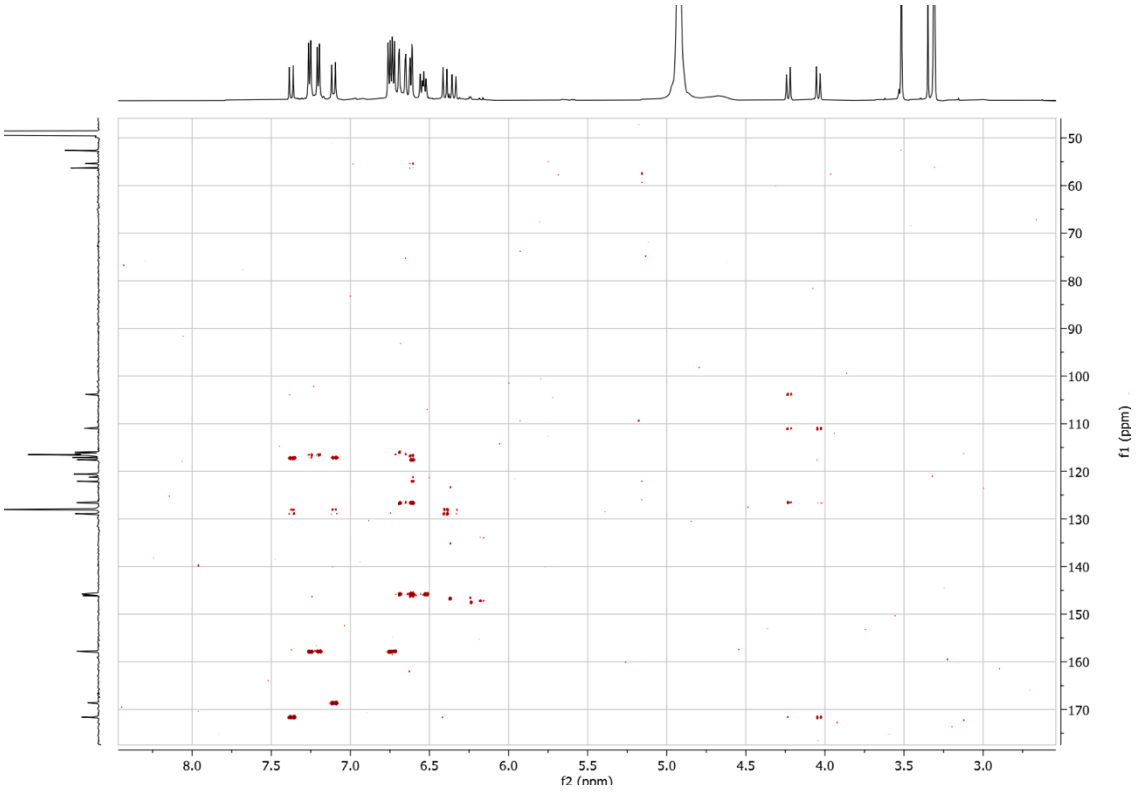


Figure S22. LR-HSQMBC NMR (MeOH-d_4) spectrum of **1**

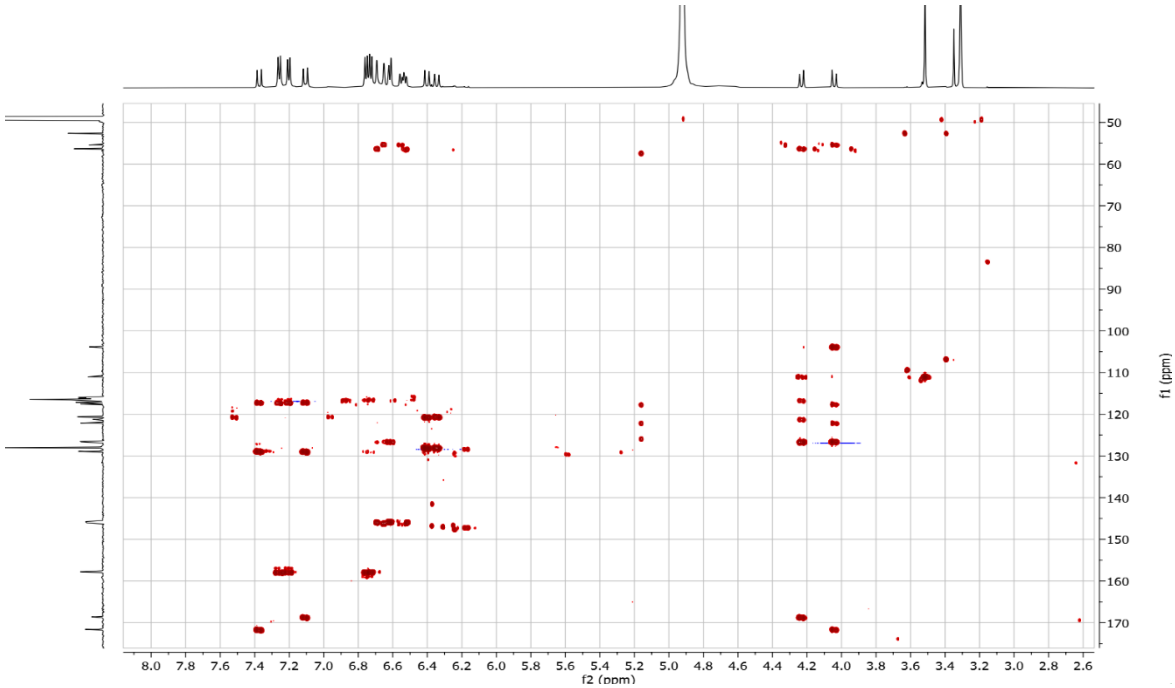


Figure S23. HMBC NMR (J_{CH} = 3.5 Hz, MeOH-d_4) spectrum of **1**

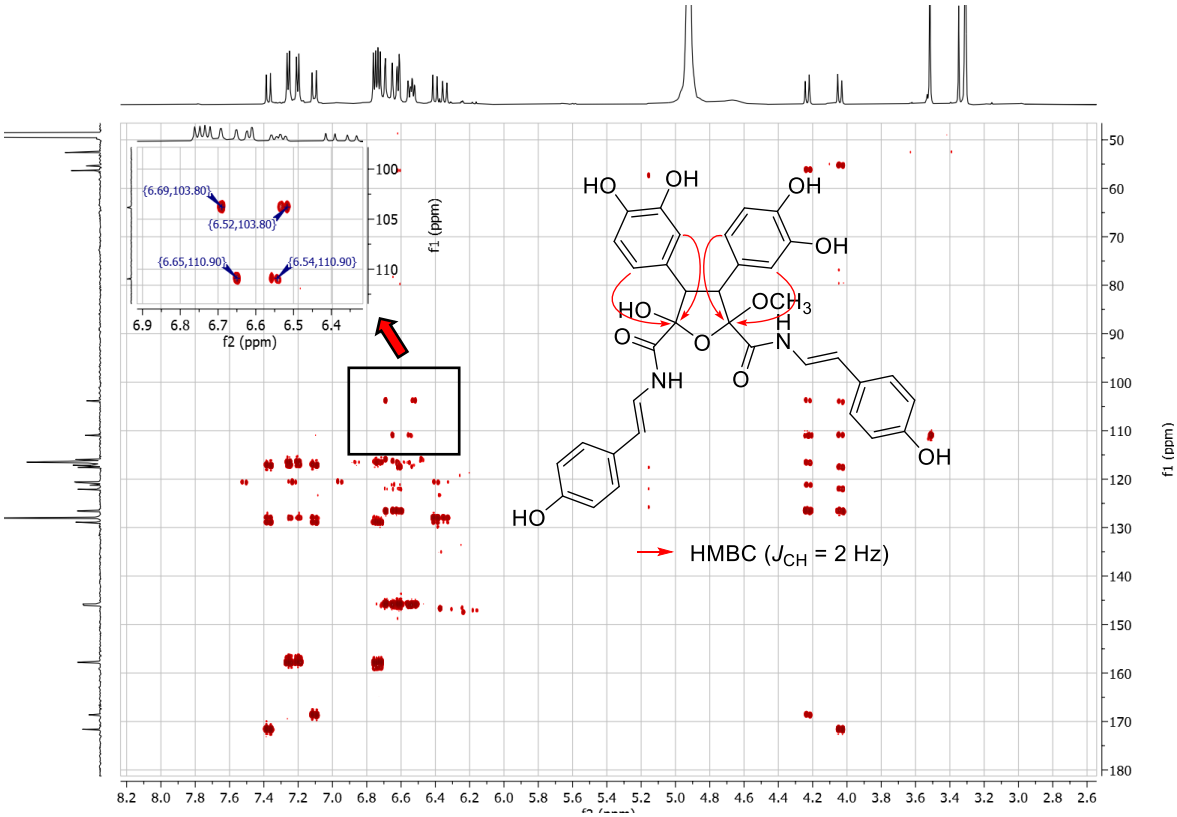


Figure S24. HMBC NMR (J_{CH} = 2.0 Hz, MeOH-d_4) spectrum of **1**

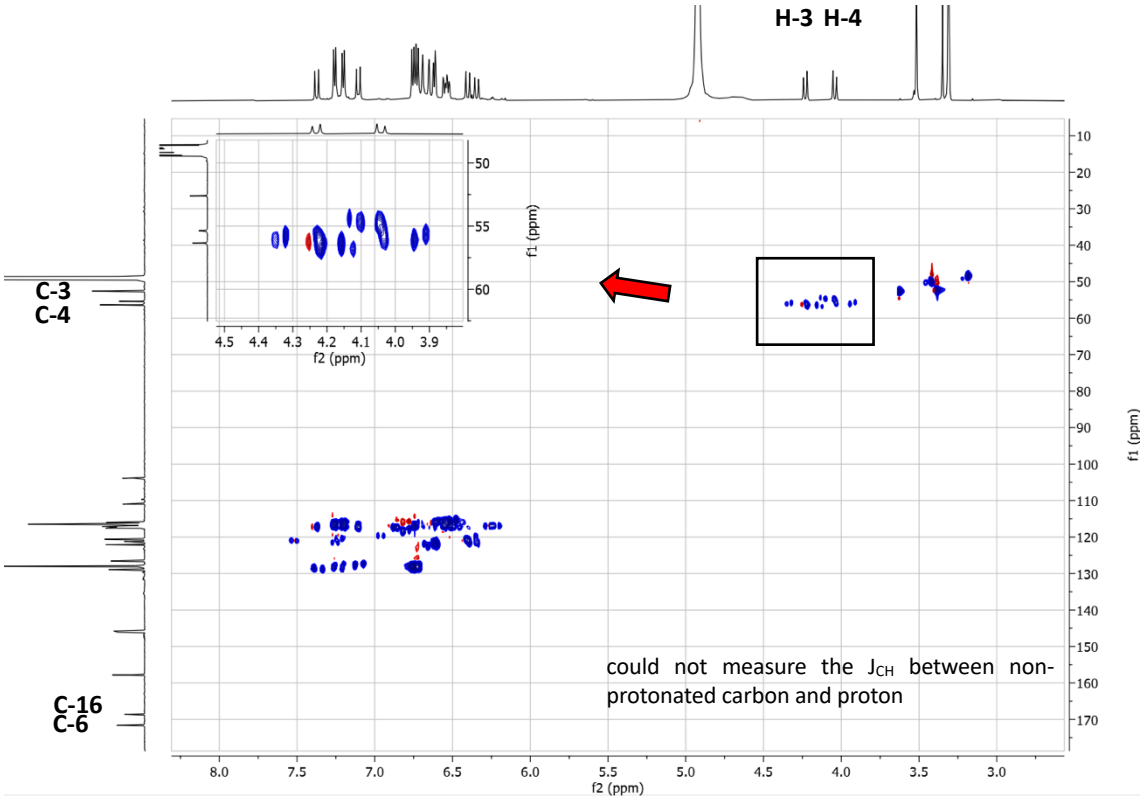
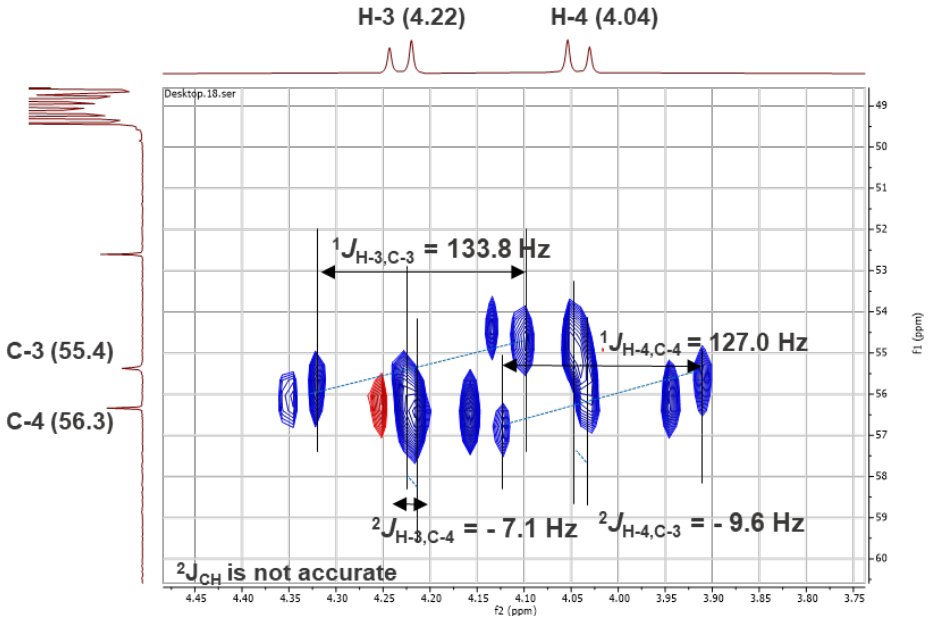


Figure S25. HSQC-HECADE NMR (MeOH-d_4) spectrum of **1**



all positive couplings will be tilted as "/", while negative couplings will form a backward slash "\"

Figure S26. Expanded HSQC-HECADE NMR (MeOH-d_4) spectrum of **1**

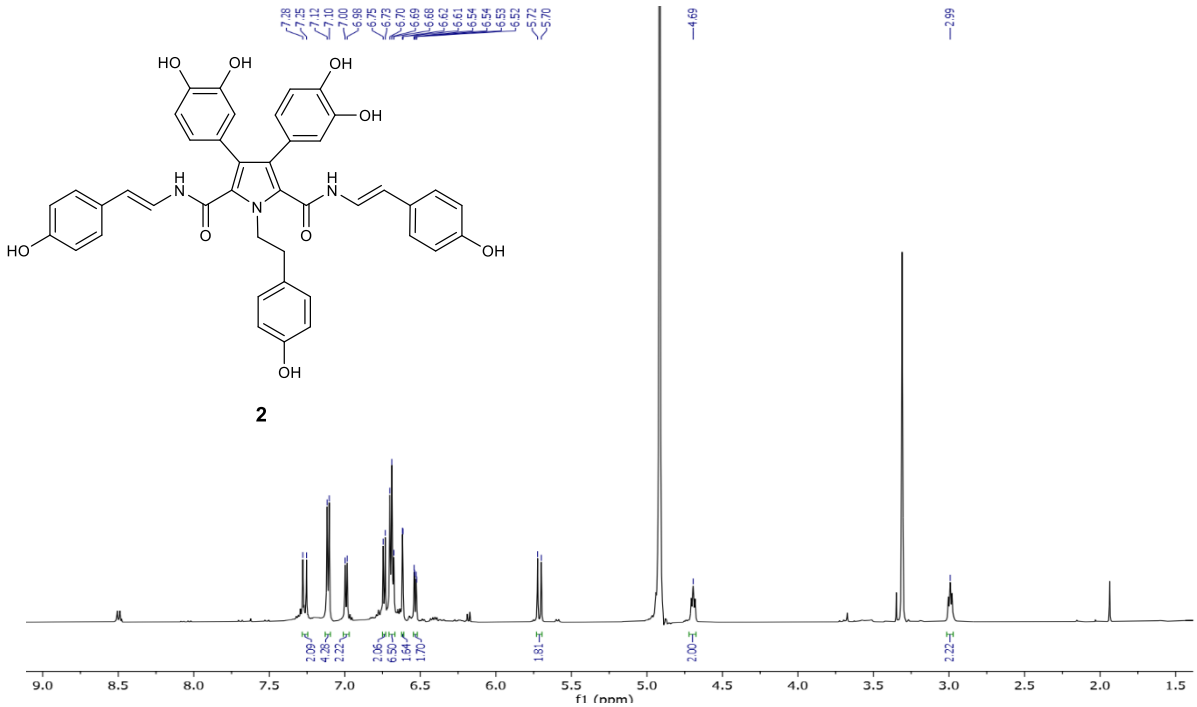


Figure S27. ^{1}H NMR (600 MHz, MeOH-d_4) spectrum of **2**

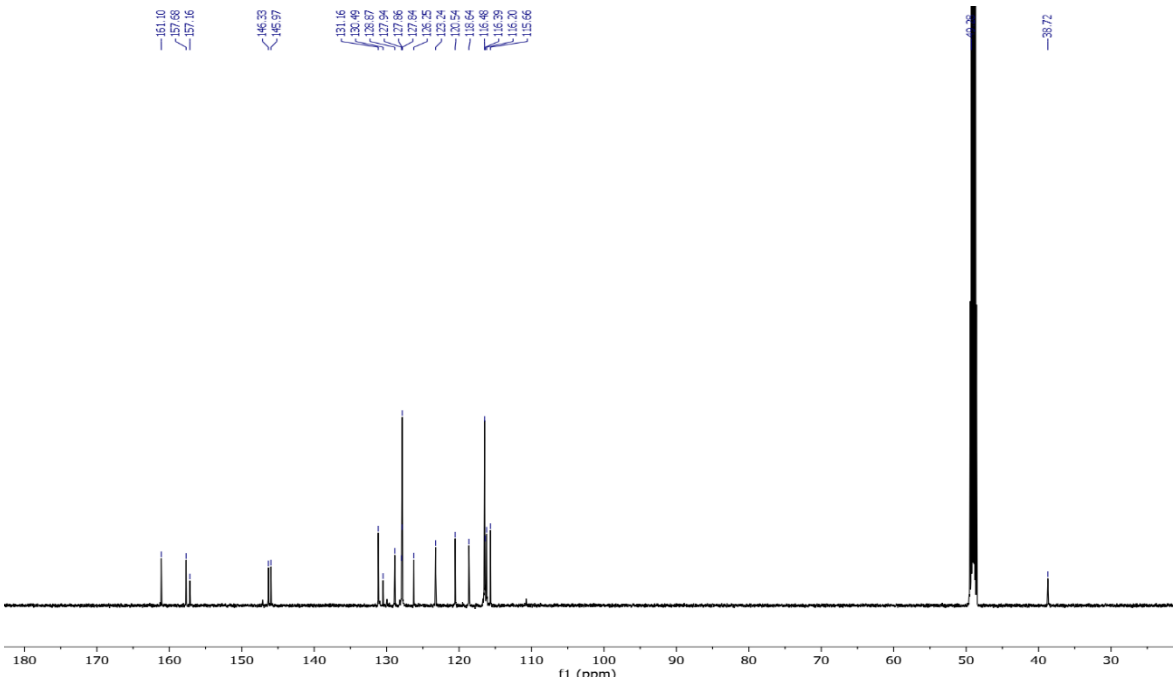


Figure S28. ^{13}C NMR (150 MHz, MeOH-d_4) spectrum of **2**

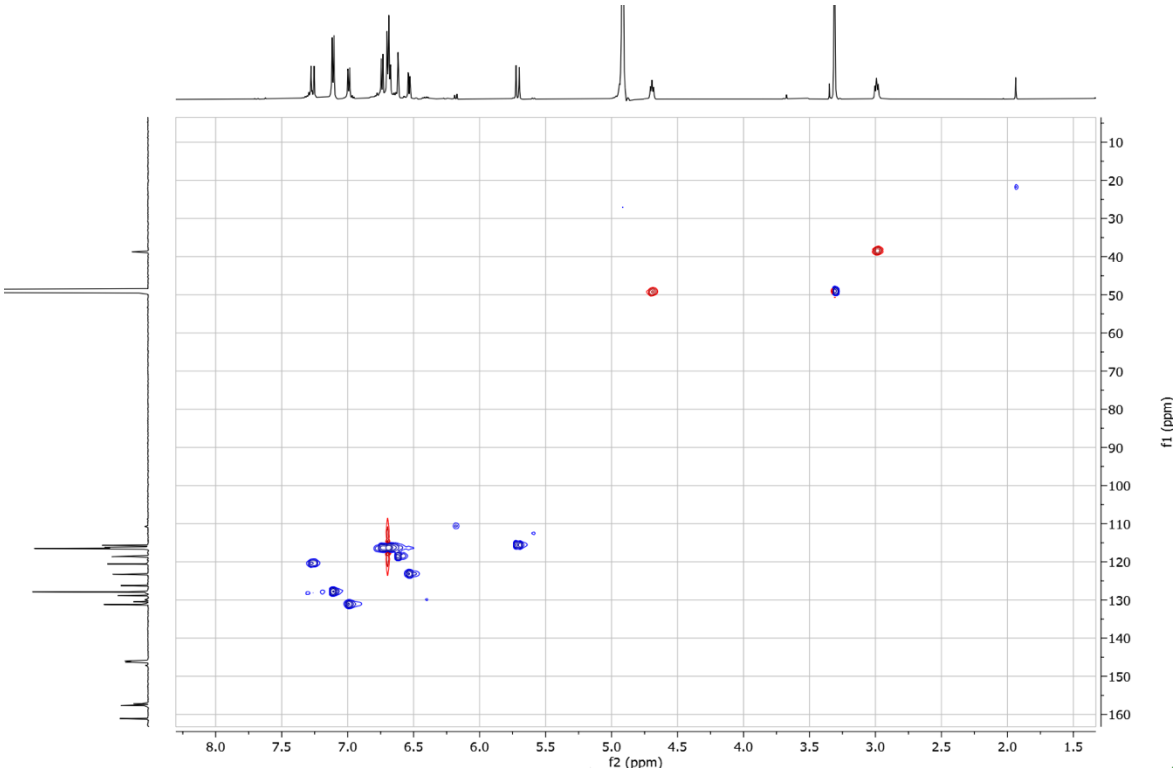


Figure S29. Edited HSQC NMR (MeOH-d_4) spectrum of **2**

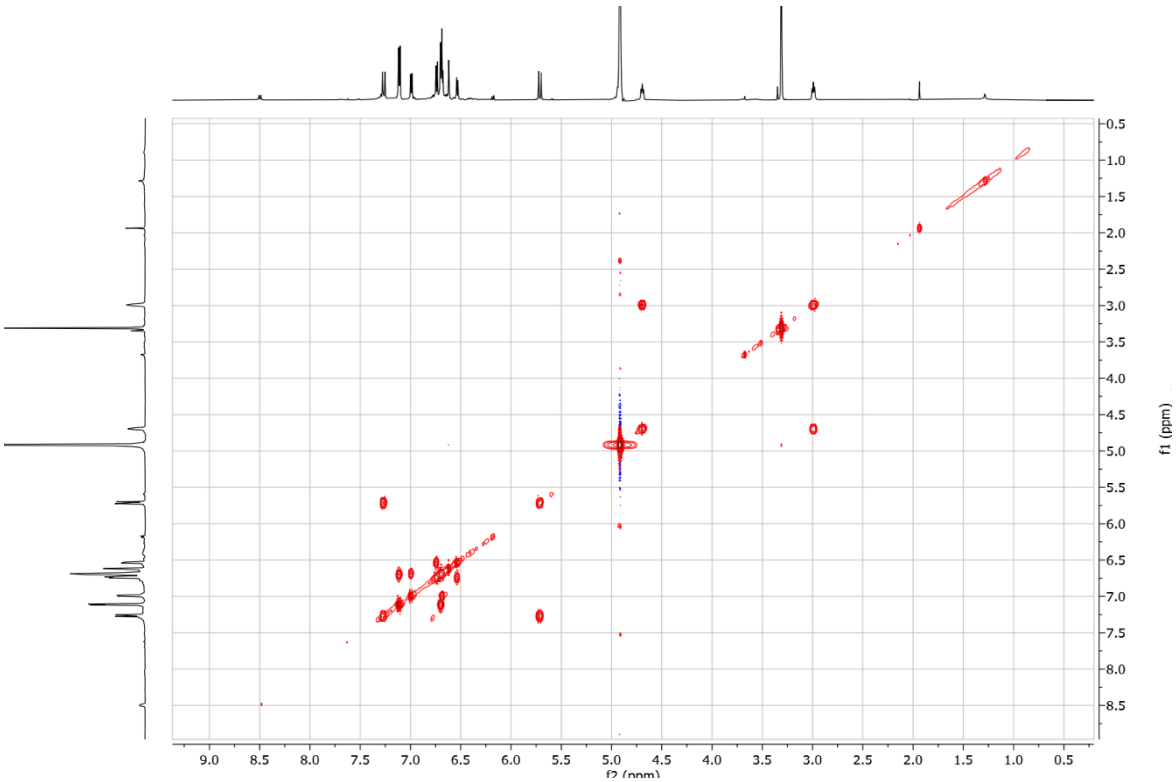


Figure S30. COSY NMR (600 MHz, MeOH-d_4) spectrum of **2**

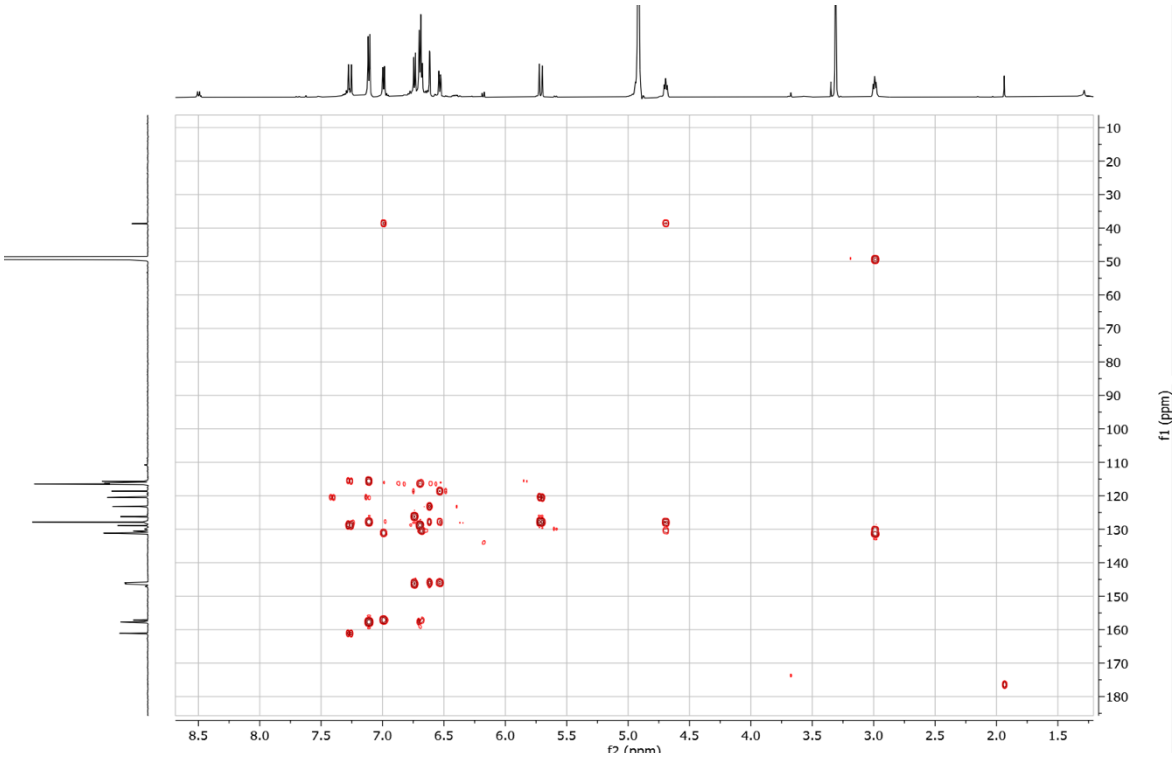


Figure S31. HMBC NMR (MeOH-d_4) spectrum of **2**

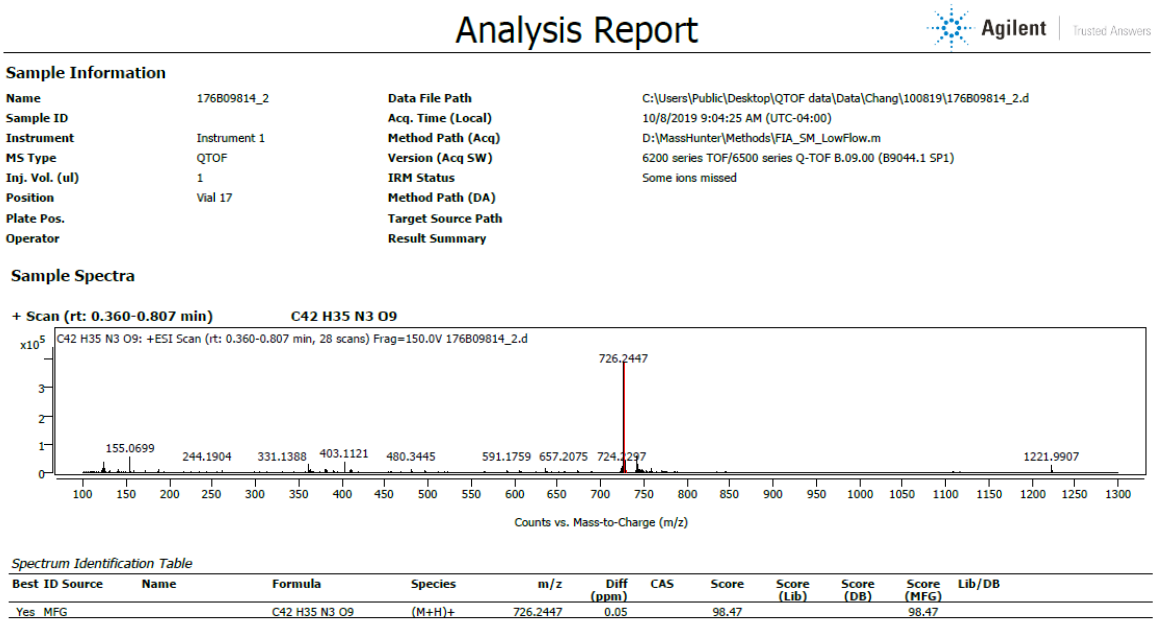
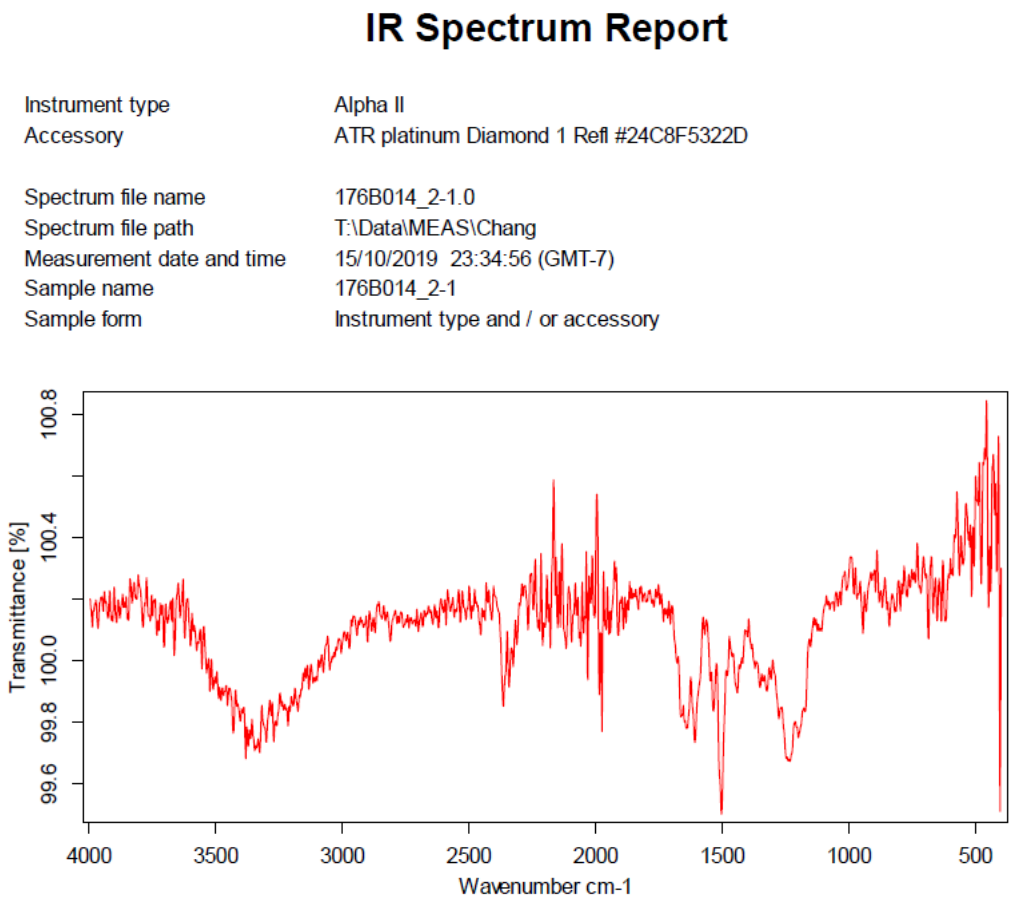


Figure S32. ESI- HRMS data of **2**



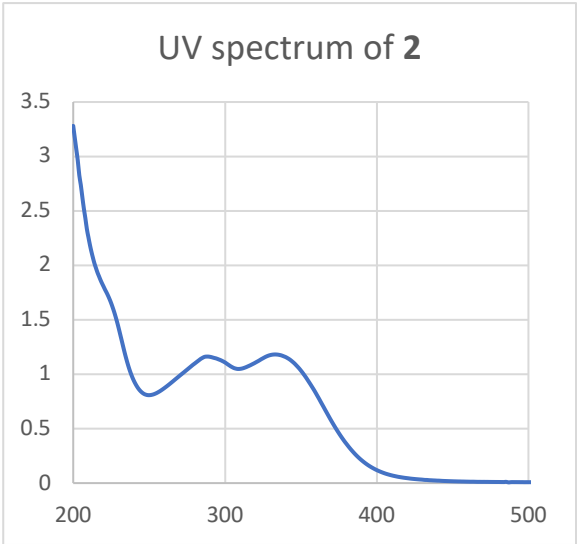


Figure S33. IR & UV spectra of **2**

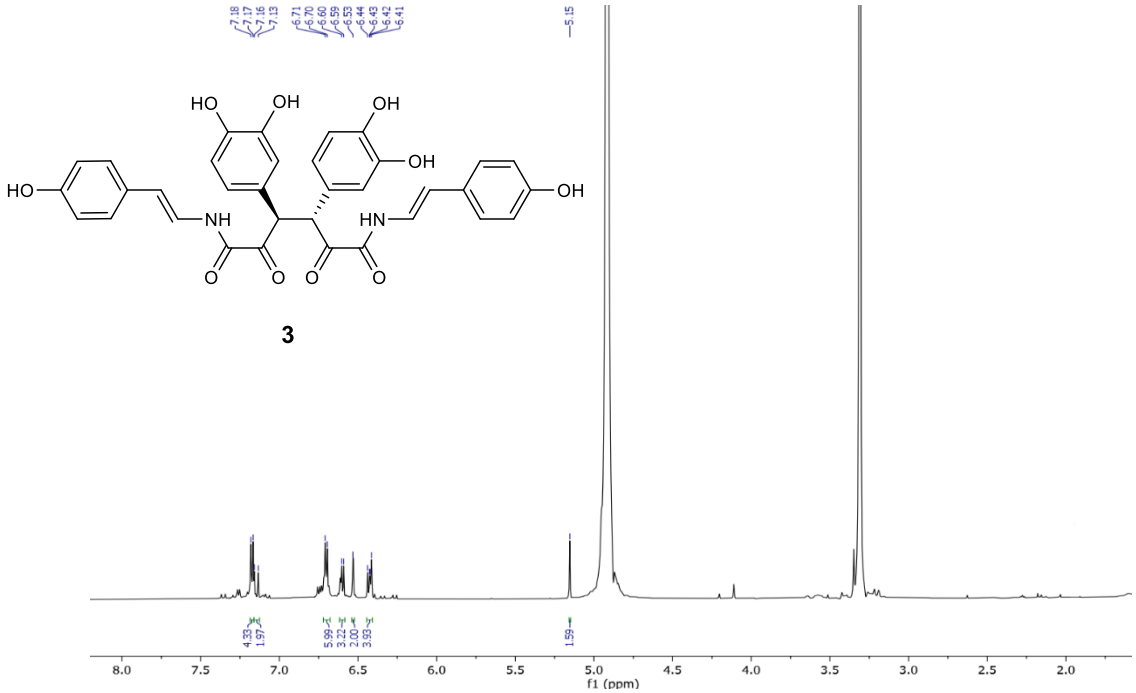


Figure S34. ^{1}H NMR (600 MHz, MeOH-d_4) spectrum of **3**

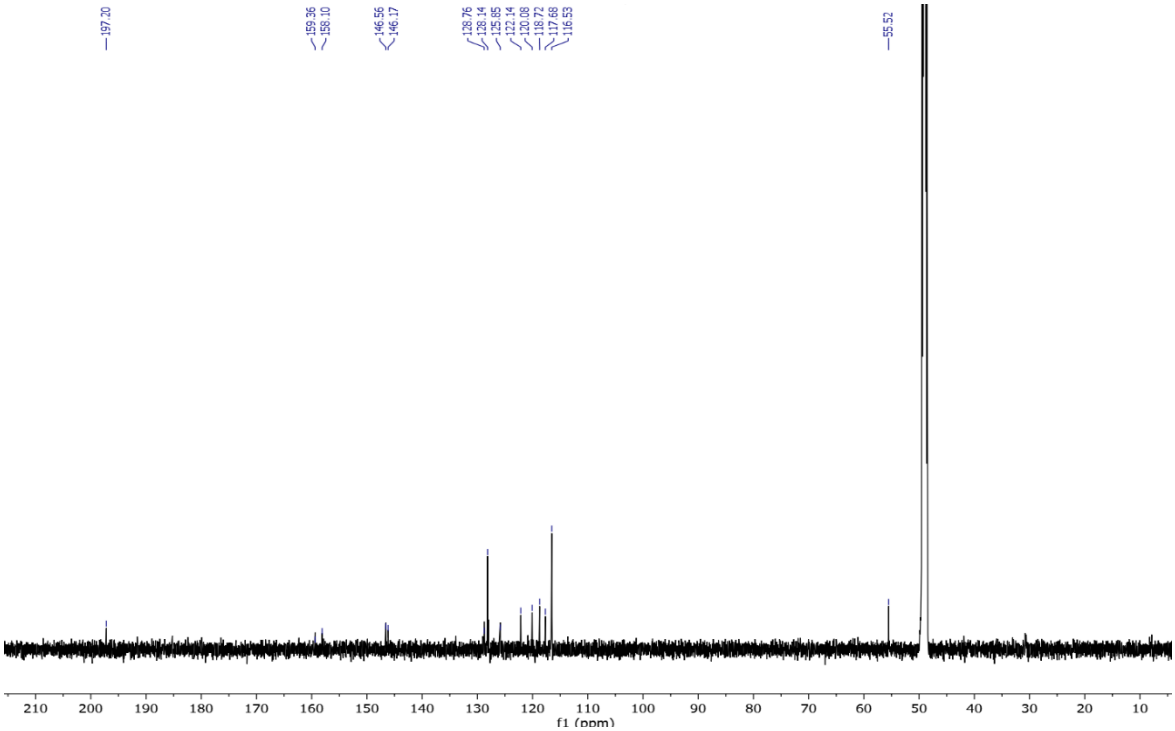


Figure S35. ^{13}C NMR (150 MHz, MeOH-d_4) spectrum of **3**

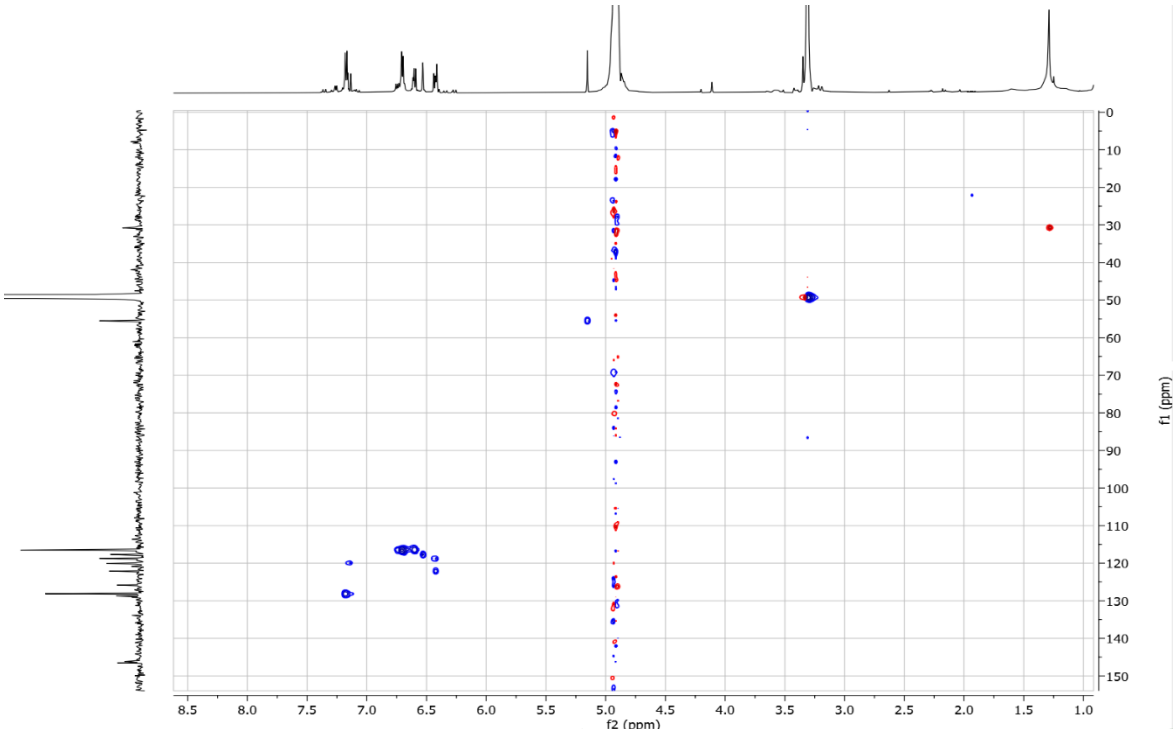


Figure S36. Edited HSQC NMR (MeOH-d_4) spectrum of **3**

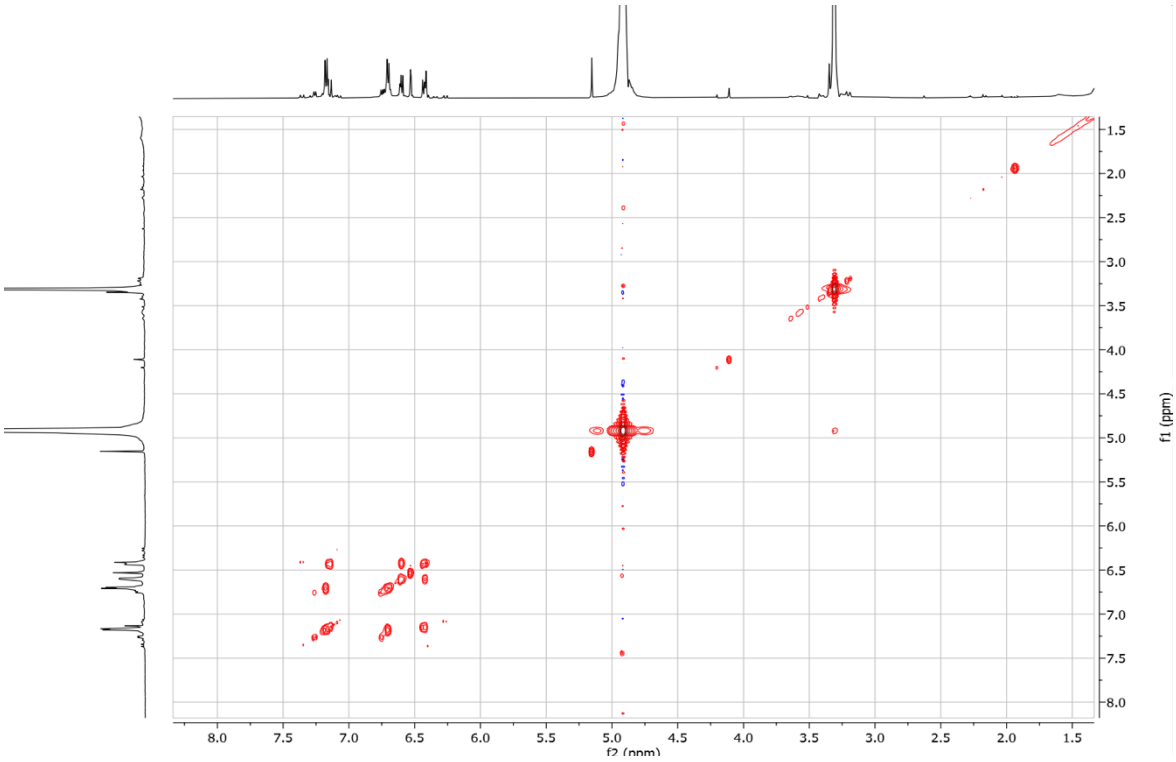


Figure S37. COSY NMR (600 MHz, MeOH-d_4) spectrum of **3**

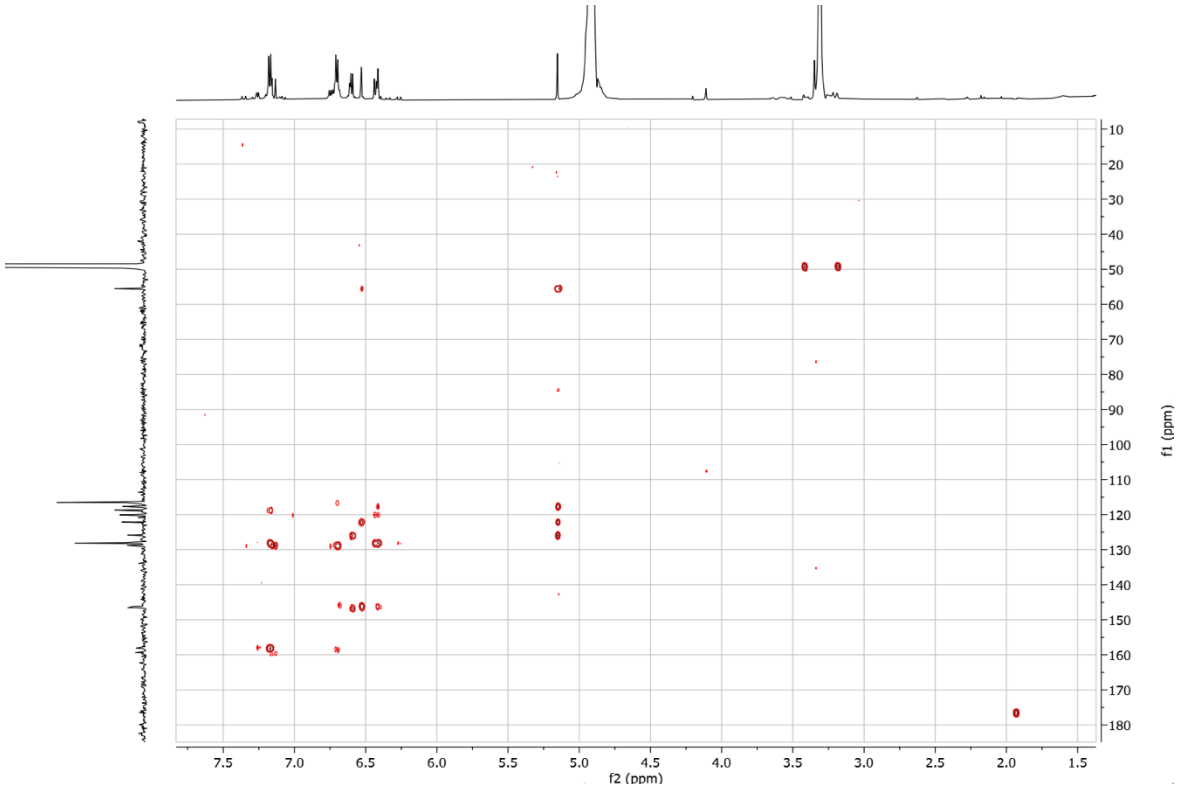


Figure S38. HMBC NMR (MeOH-d_4) spectrum of **3**

Analysis Report

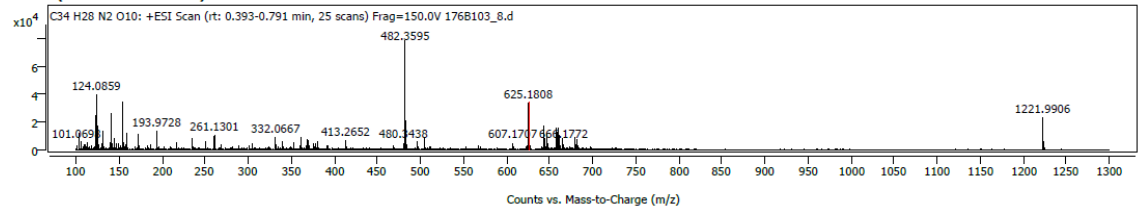
Agilent Trusted Answers

Sample Information

Name	176B103_8	**Data File Path**	C:\Users\Public\Desktop\QTOF data\Data\Chang\100819\176B103_8.d
Sample ID		**Acq. Time (Local)**	10/8/2019 9:15:21 AM (UTC-04:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\FIA_SM_LowFlow.m
MS Type	QTOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF B.09.00 (B9044.1 SP1)
Inj. Vol. (ul)	1	**IRM Status**	Some ions missed
Position	Vial 19	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Spectra

+ Scan (rt: 0.393-0.791 min) **C34 H28 N2 O10**



Spectrum Identification Table

Best	ID Source	Name	Formula	Species	m/z	Diff (ppm)	CAS	Score	Score (Lib)	Score (DB)	Score (MFG)	Lib/DB
Yes	MFG		C34 H28 N2 O10	(M+H)+	625.1808	-1.39		98.15			98.15	

Figure S39. ESI- HRMS data of **3**

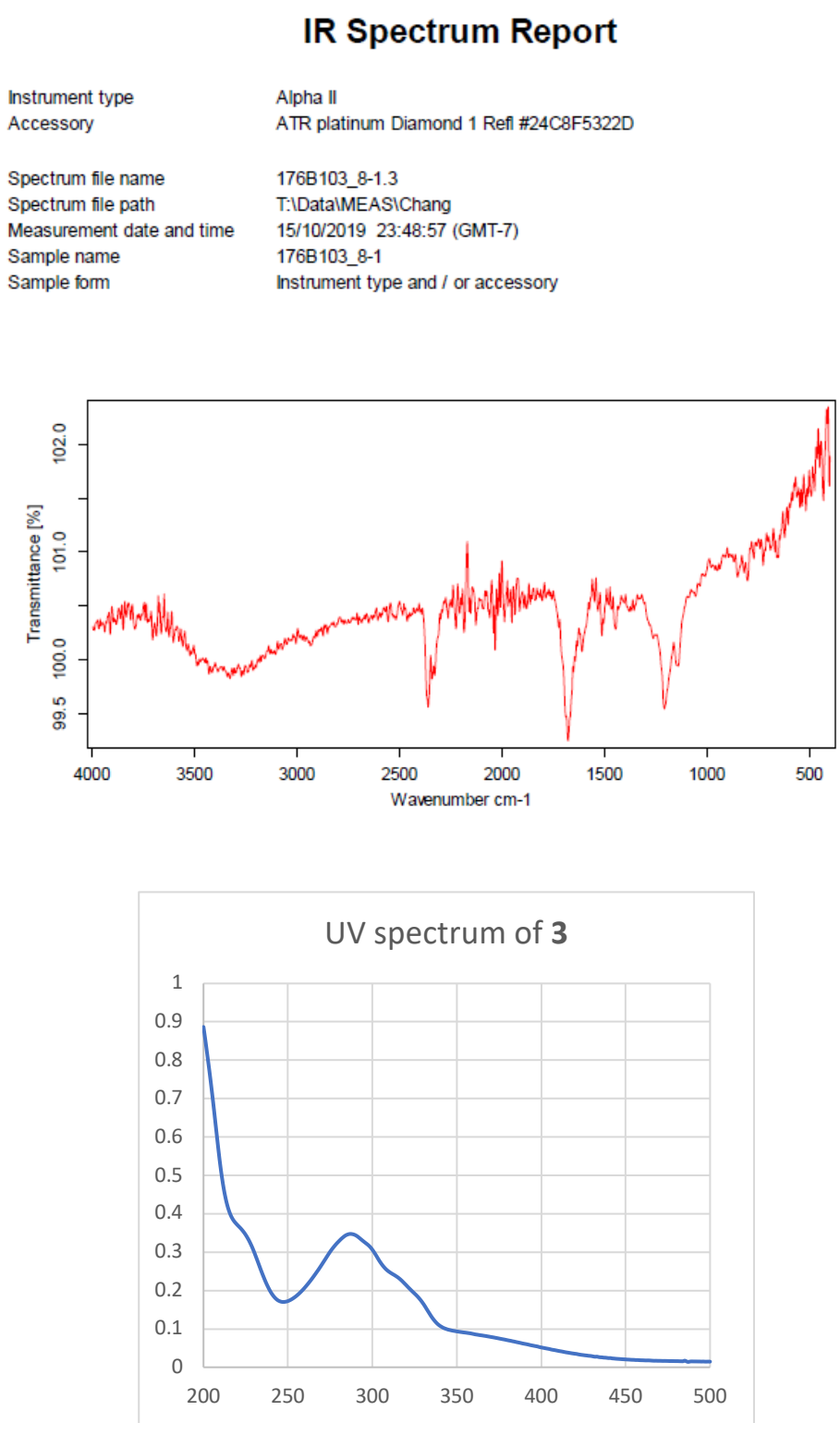
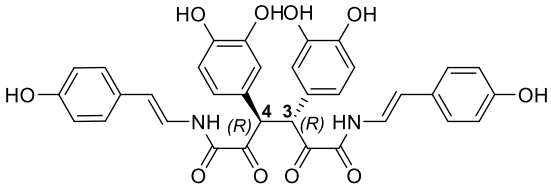
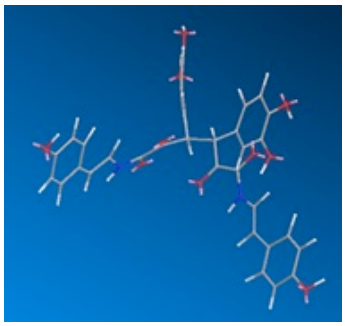


Figure S40. IR & UV spectra of **3**

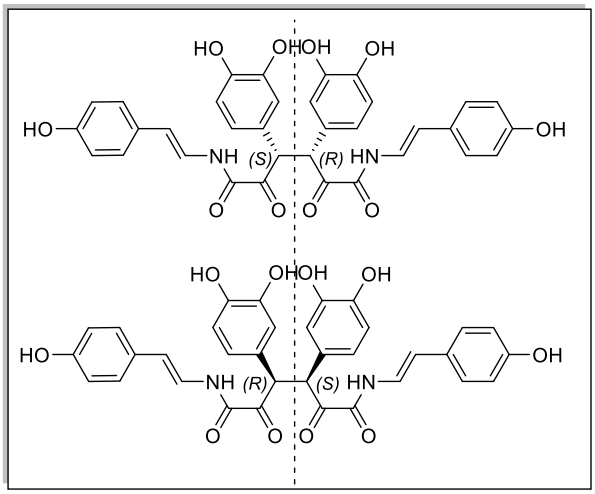


3

$[\alpha]_D$ = +86.7



Energy minimization model using Chem 3D



A meso compound (3*R*,4*S* or 3*S*,4*R*) of **3** would be achiral

Figure S41. Relative configuration of compound **3**

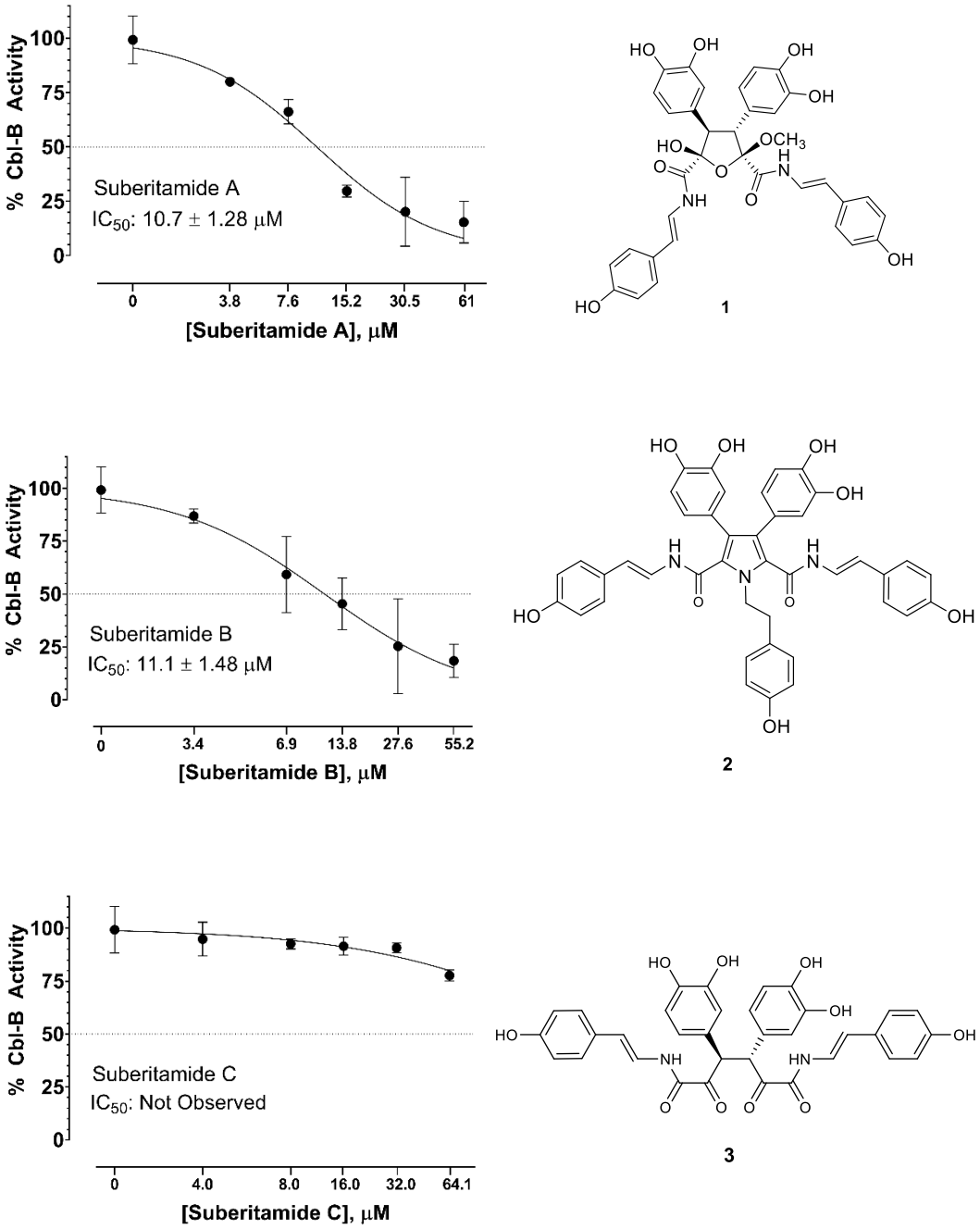


Figure S42. Dose-response curves of Cbl-b inhibitory activity for **1-3**