New Cladiellin-type Diterpenoids from the South China Sea Soft Coral *Cladiella krempfi*: Structures and Molecular Docking analysis in EGFRs

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Table S1. EGFR inhibitory data of compounds **1**–**6** and the positive control staurosporine.

Compound ID	Concentration (nM)	Mean	SD
1	20000	-9.9	4.5
2	20000	-12.5	4.2
3	20000	-3.8	5.3
4	20000	-3.4	5.8
5	20000	-7.5	3.1
6	20000	-4.9	3.7
Staurosporine	**IC_{50}** = 82.3 **nM**		

Table S2. In silico docking parameters between compounds **2-6** and the ligand of 7XO site of 5X2A

EGFR crystal structure	Compound ID	Number of hydrogen bonds	Binding Energy (kcal mol^{-1})	Van der Waals Energy (kcal mol^{-1})	-CDOCKER ENERGY (kcal mol^{-1})	-CDOCKER INTERACTION ENERGY (kcal mol^{-1})
5X2A	**2**	3	3.57	-19.62	-21.53	56.27
	3	1	1.83	-13.54	-28.67	47.16
	4	3	0.13	-14.00	-24.37	55.77
	5	1	8.52	-15.53	-25.47	54.58
	6	2	3.72	-14.21	-30.33	49.82

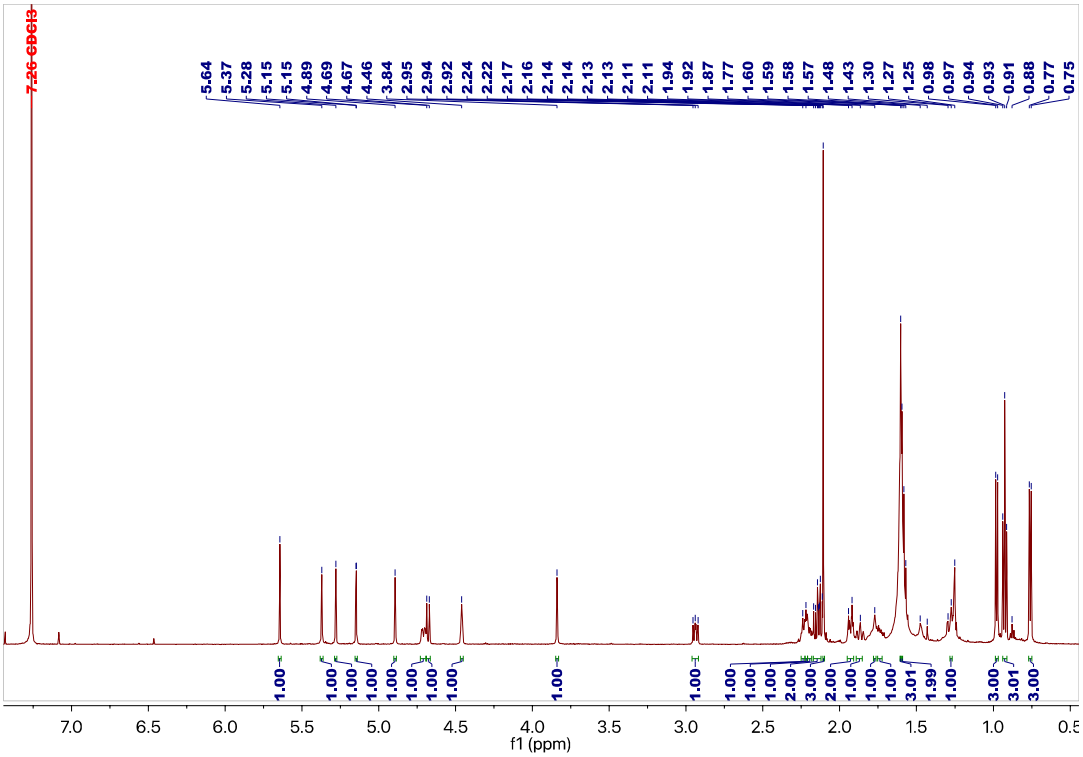


Figure S1. ^{1}H NMR spectrum of compound **1** in $CDCl_3$

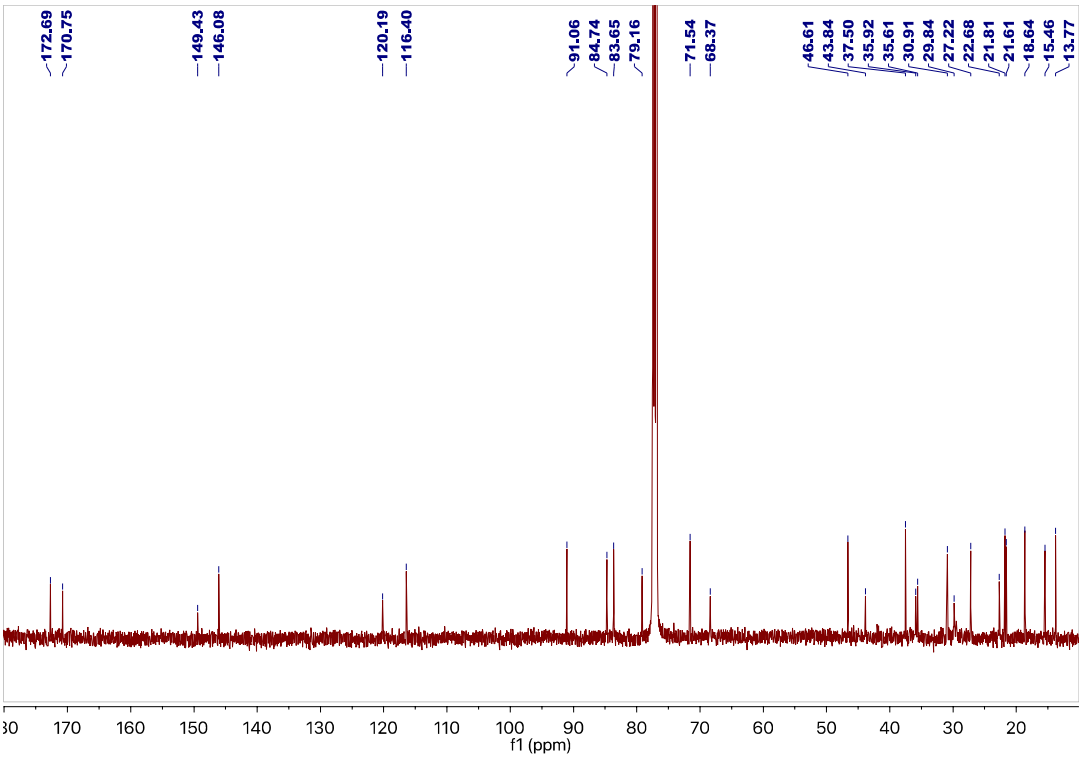


Figure S2. ^{13}C NMR spectrum of compound **1** in $CDCl_3$

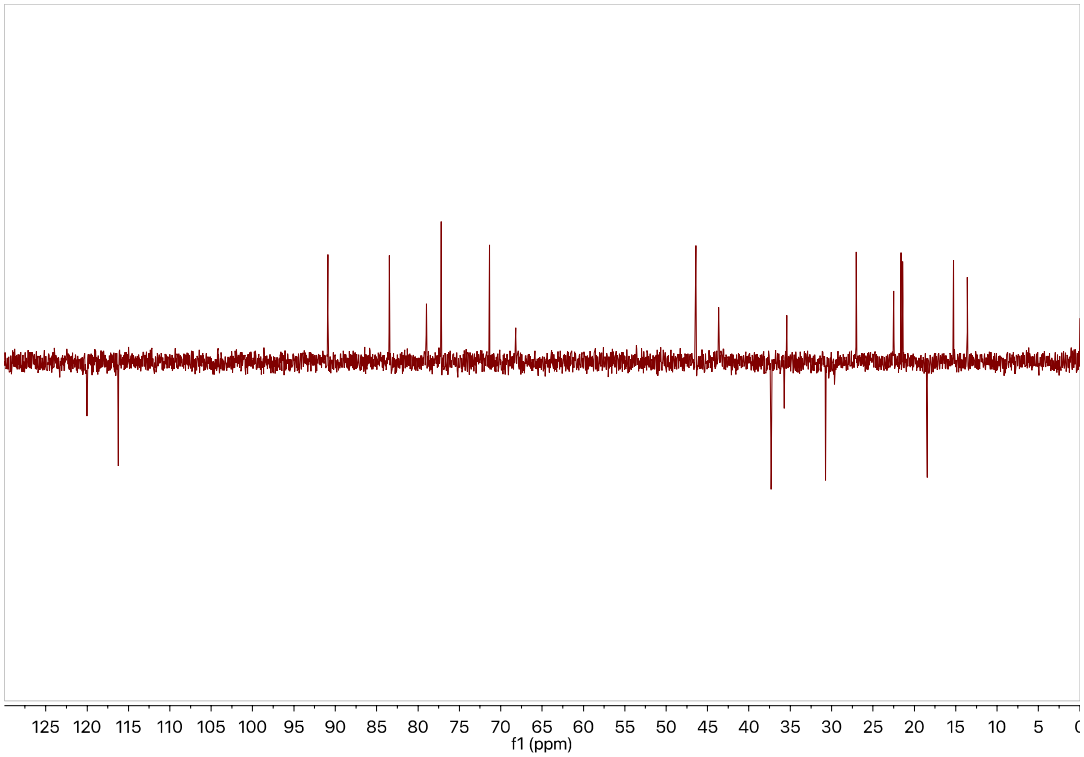


Figure S3. DEPT135 spectrum of compound **1** in $CDCl_3$

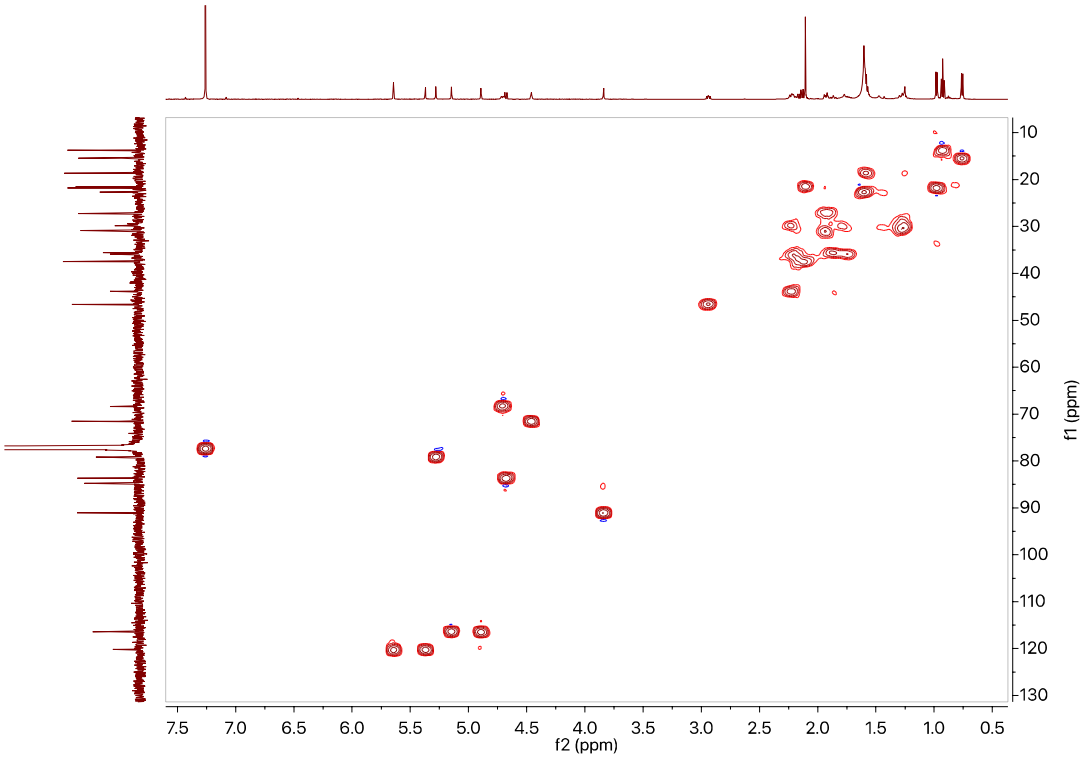


Figure S4. HSQC spectrum of compound **1** in $CDCl_3$

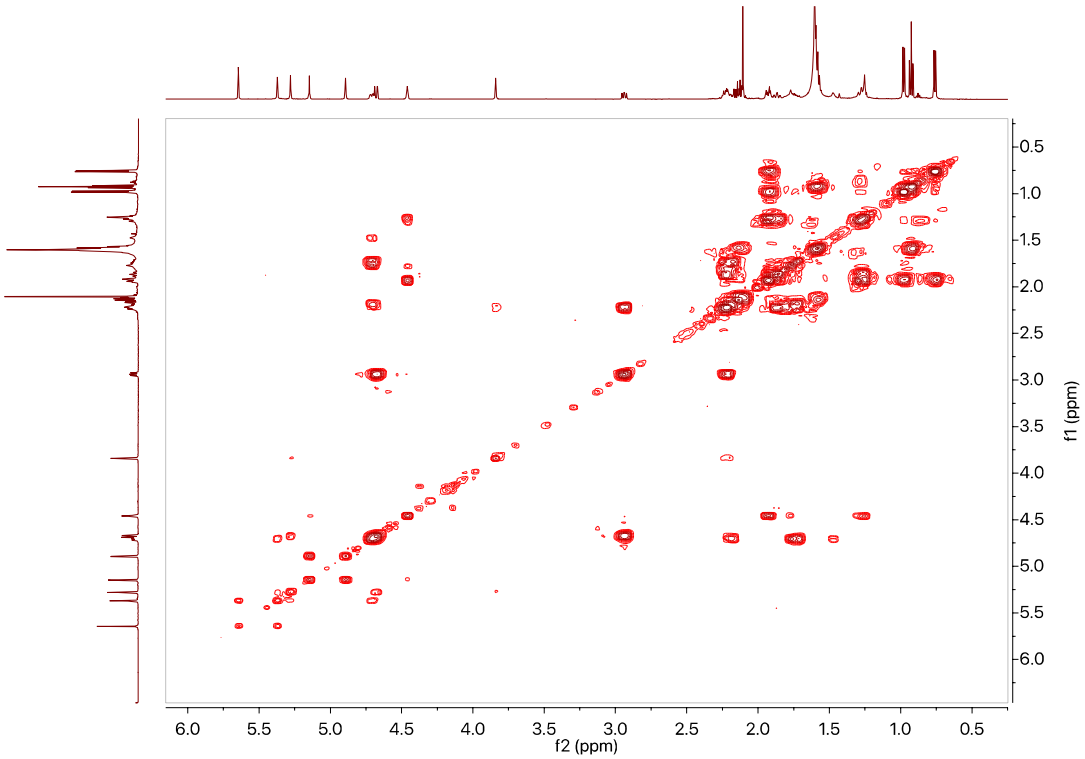


Figure S5. ^{1}H-^{1}H COSY spectrum of compound **1** in $CDCl_3$

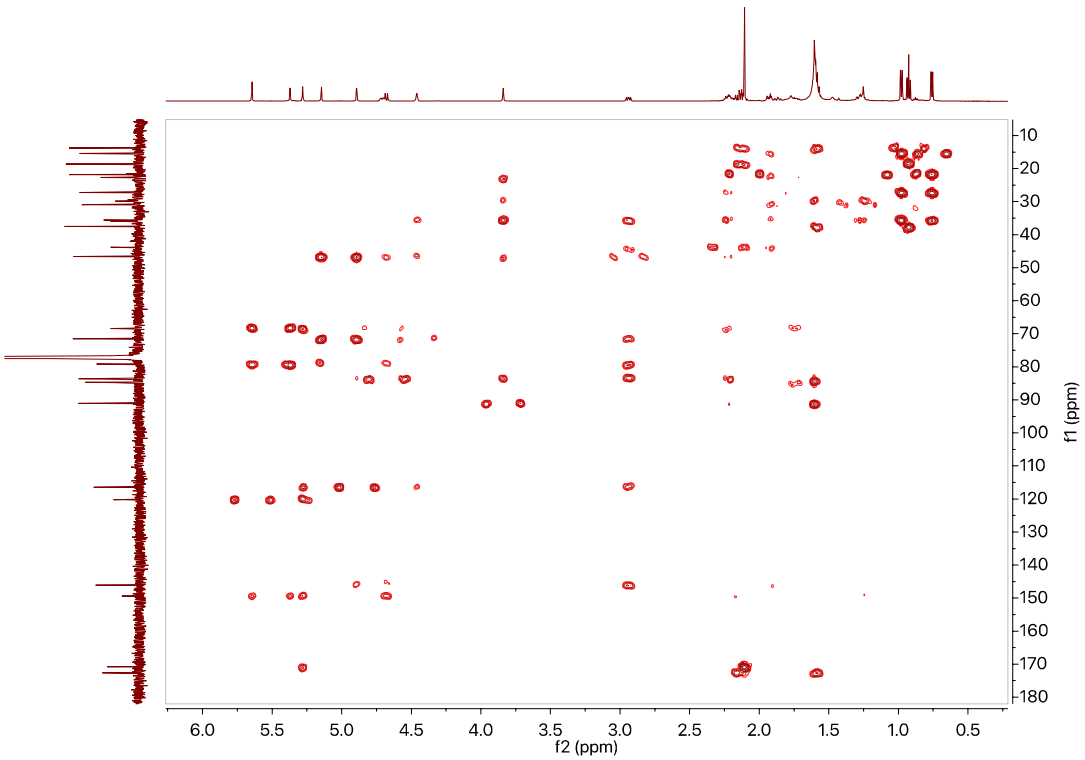


Figure S6. HMBC spectrum of compound **1** in $CDCl_3$

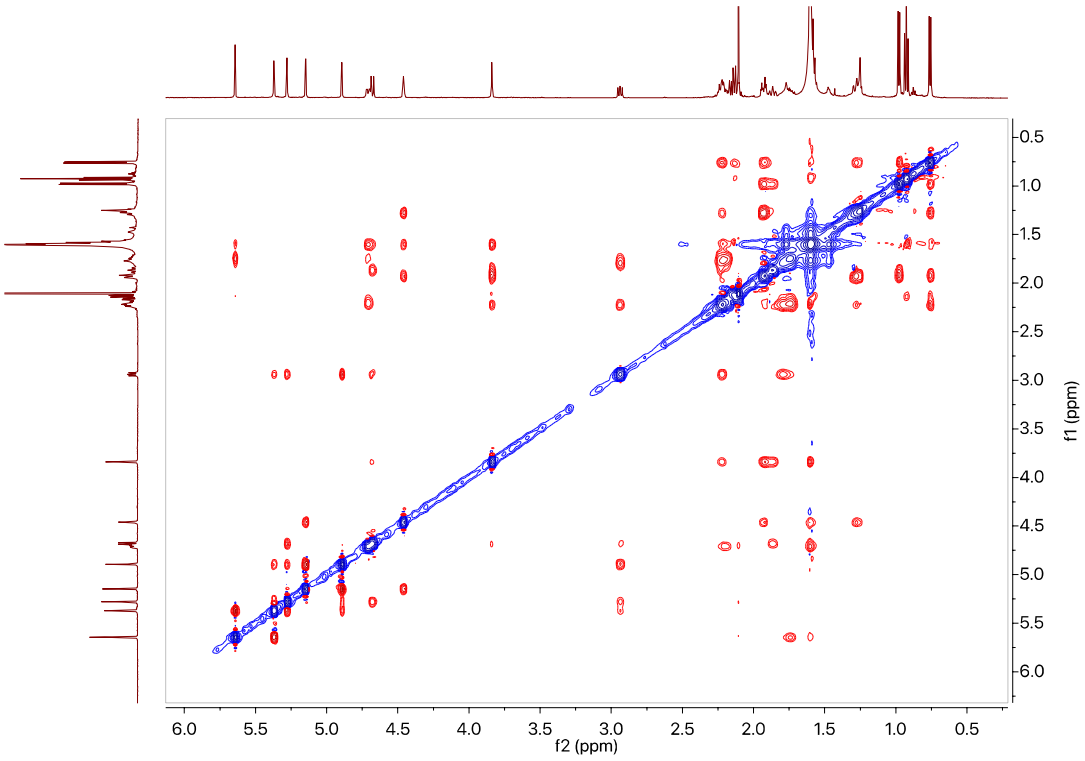


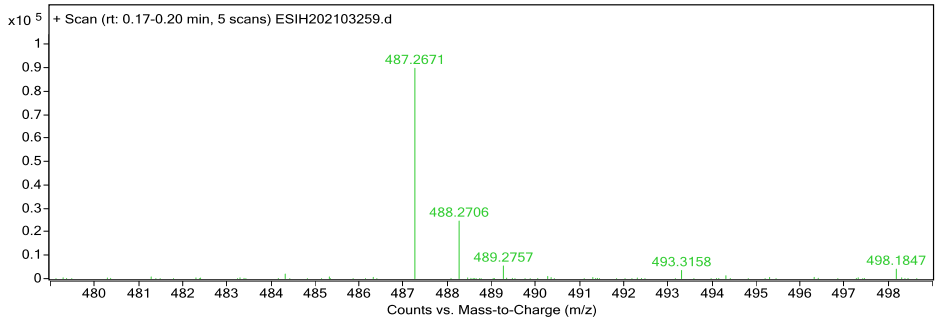
Figure S7. NOESY spectrum of compound **1** in $CDCl_3$

Qualitative Analysis Report

Data Filename	ESIH202103259.d	**Sample Name**	A8-A8-E3B
Sample ID		**Position**	P1-E3
Instrument Name	Agilent G6520 Q-TOF	**Acq Method**	20160322_MS_ESIH_POS_1min.m
Acquired Time	7/1/2021 19:56:48	**IRM Calibration Status**	Success
DA Method	small molecular data analysis method.m	**Comment**	ESIH by zhuzhenyun

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
487.2671	487.2666	-0.47	-0.97	C26 H40 Na O7	(M+Na)+

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Figure S8. HR-ESI-MS spectrum of compound **1**

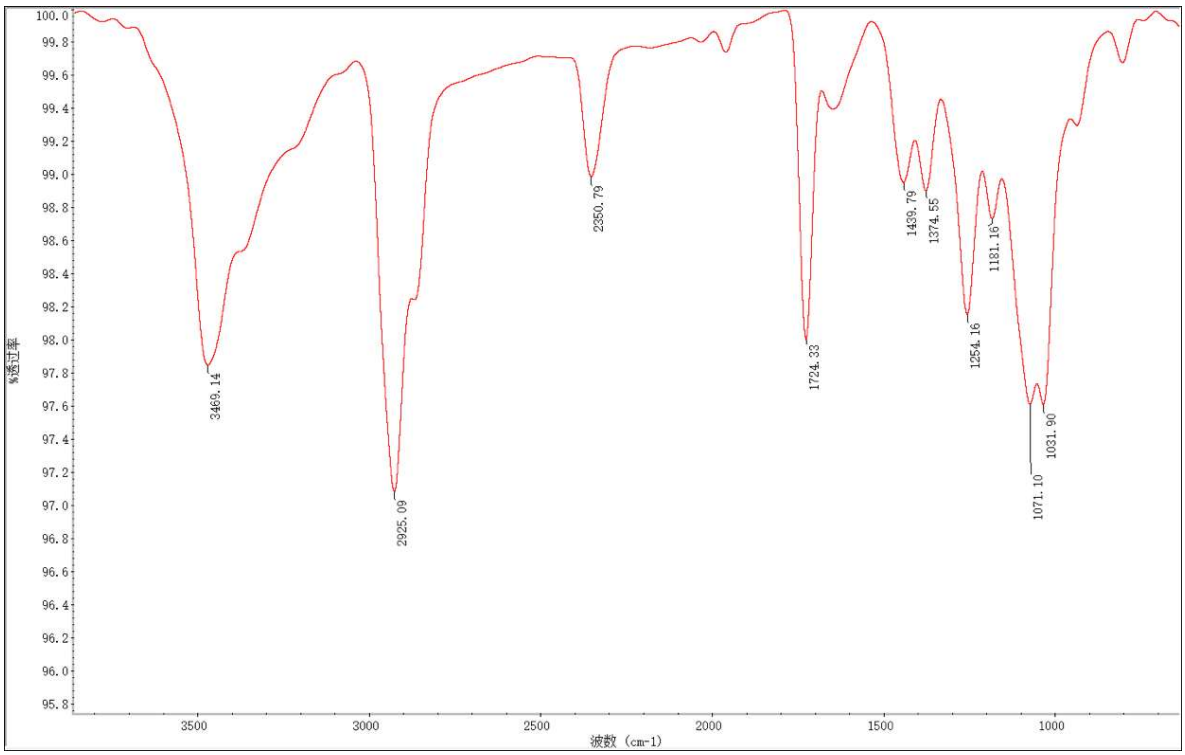


Figure S9. IR spectrum of compound **1**

day, 06/28/2021

sample was measured on an Autopol VI, serial number 901
ufactured by Rudolph Research Analytical,Hackettstown,N

): E3B-2
Temperature : OFF
p Corr : OFF

	Average	Std.Dev.
	24.881	2.9282

lo	Sample ID	Time	Result
	E3B-2	05:56:35 PM	23.571
	E3B-2	05:56:59 PM	28.571
	E3B-2	05:57:10 PM	23.571
	E3B-2	05:57:20 PM	22.143
	E3B-2	05:57:27 PM	22.143
	E3B-2	05:57:41 PM	29.286

ature

Figure S10. ORD spectrum of compound **1**

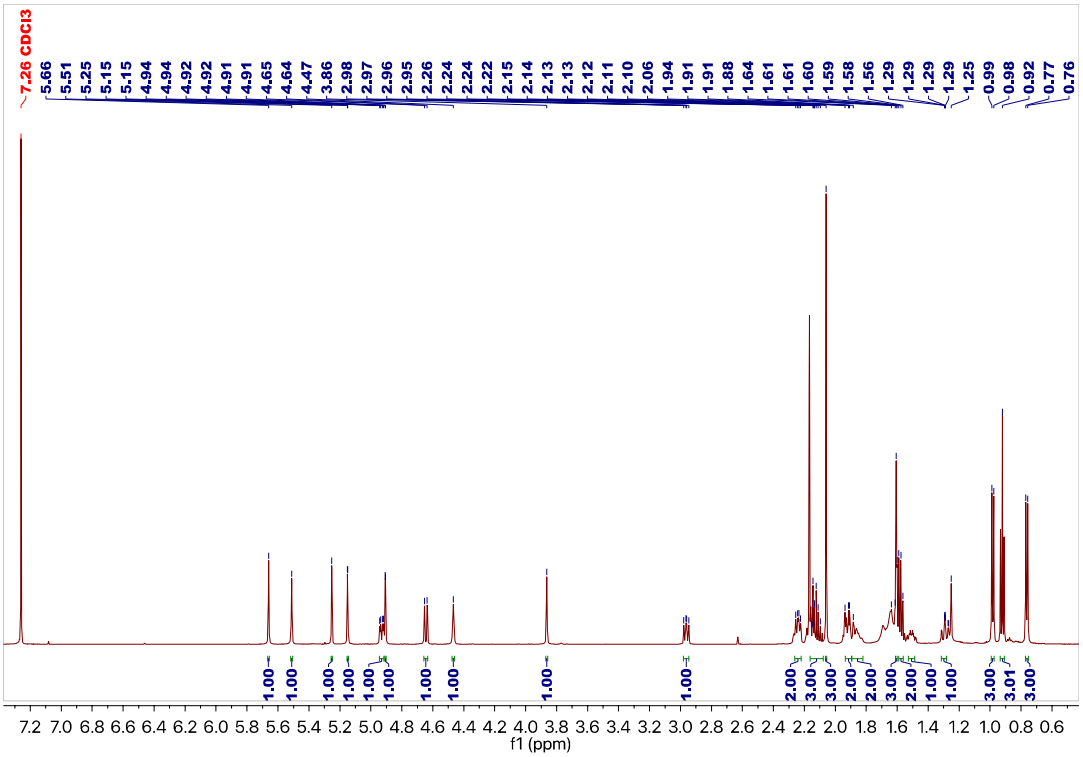


Figure S11. ^{1}H NMR spectrum of compound **2** in $CDCl_3$

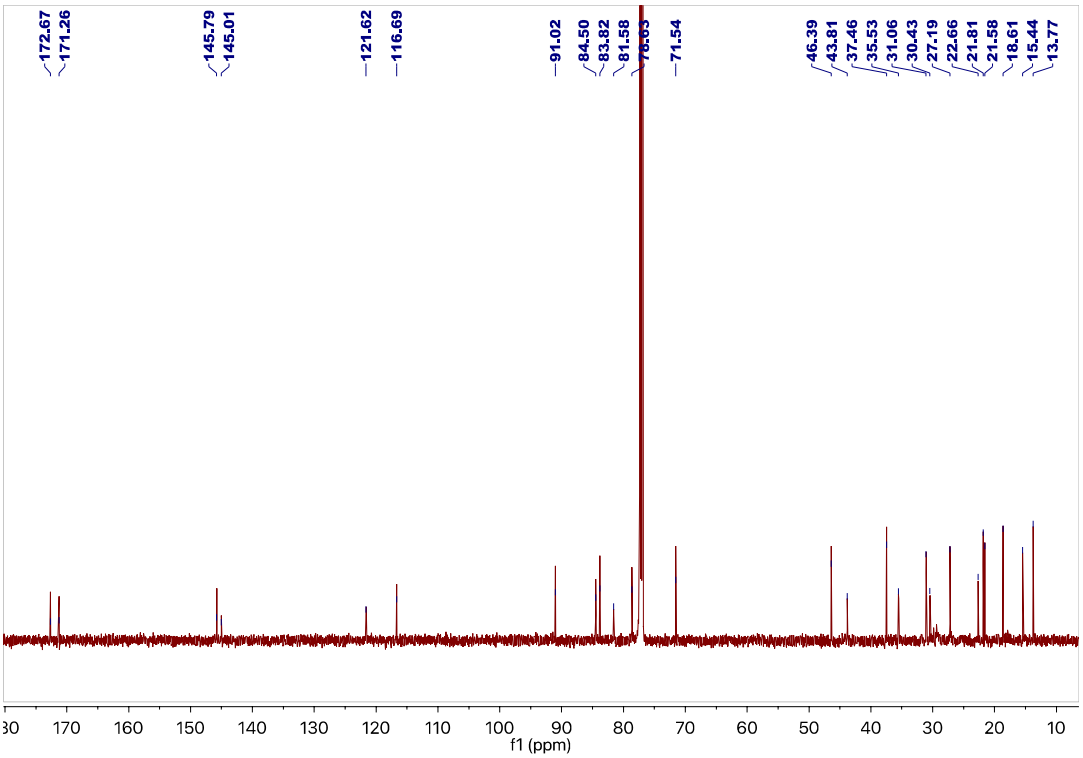


Figure S12. ^{13}C NMR spectrum of compound **2** in $CDCl_3$

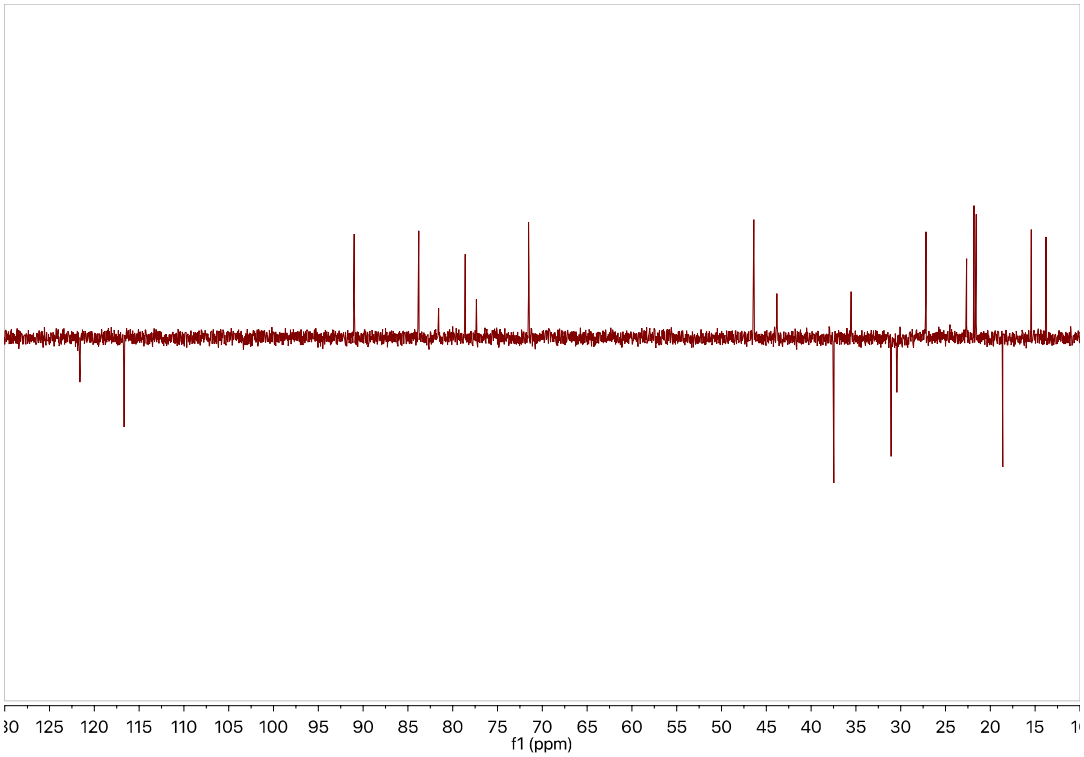


Figure S13. DEPT135 spectrum of compound **2** in $CDCl_3$

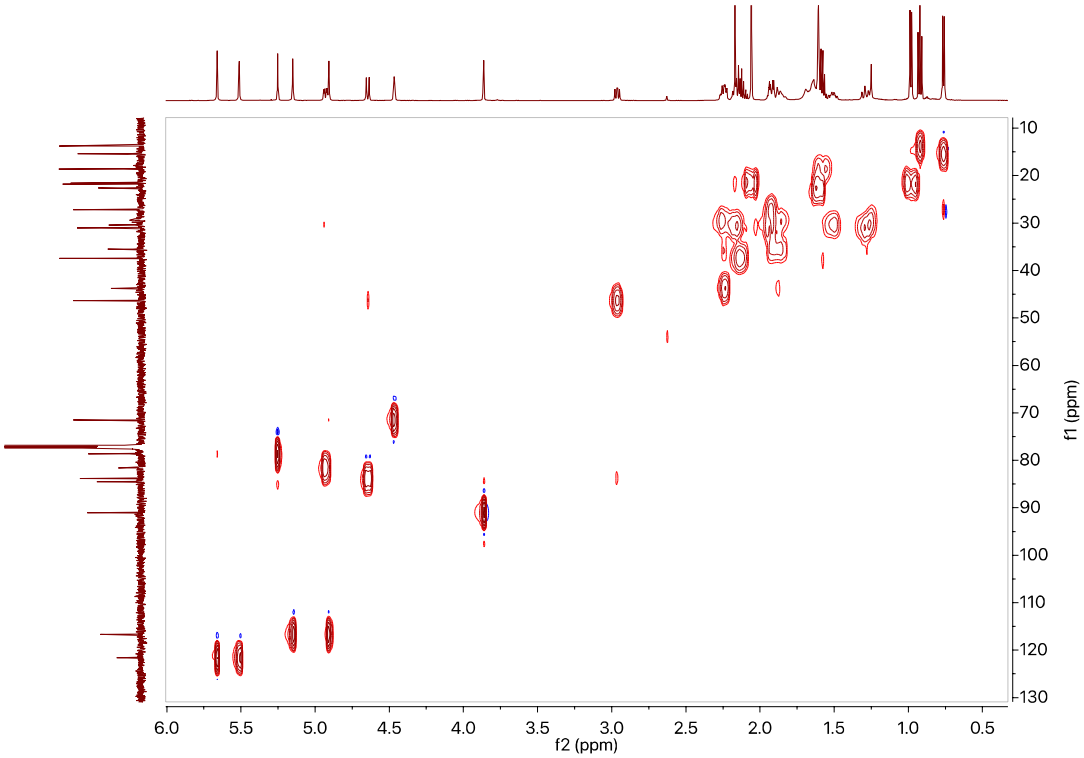


Figure S14. HSQC spectrum of compound **2** in $CDCl_3$

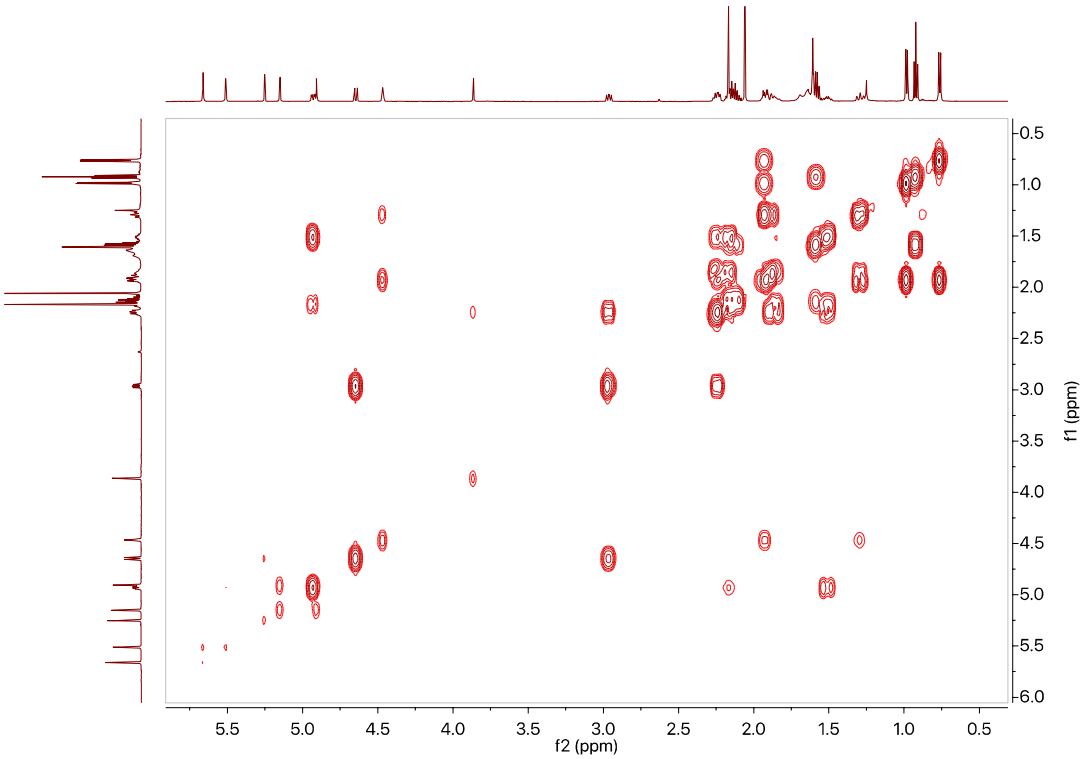


Figure S15. ^{1}H-^{1}H COSY spectrum of compound **2** in $CDCl_3$

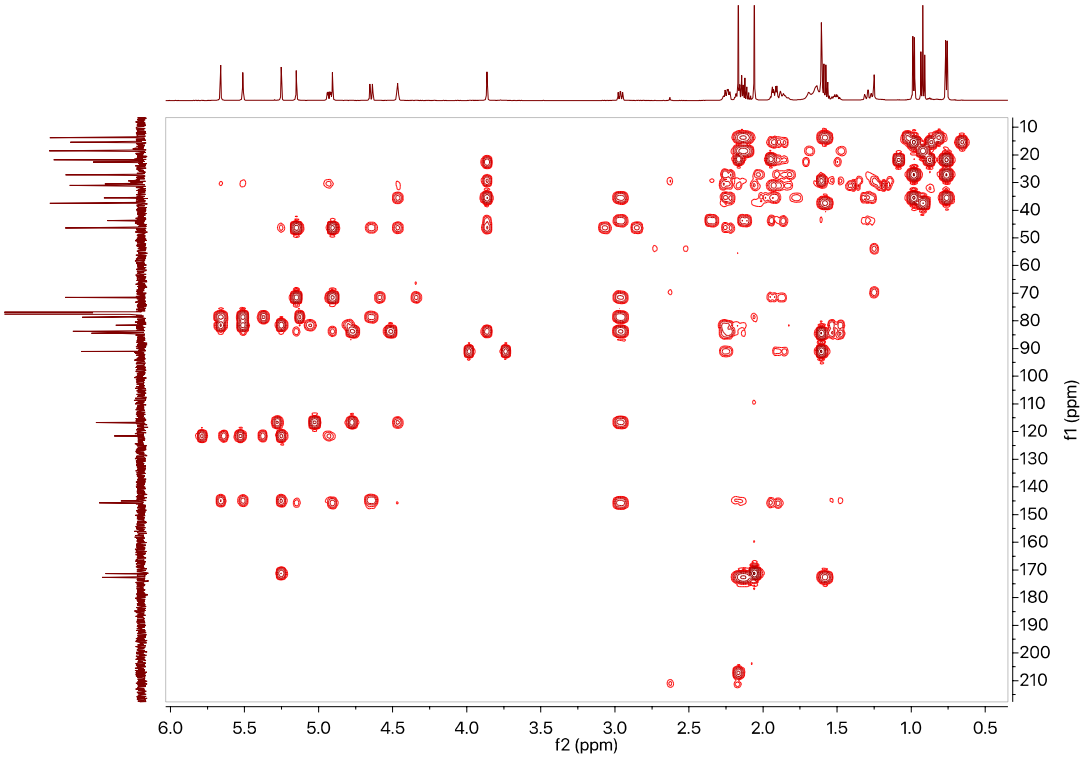


Figure S16. HMBC spectrum of compound **2** in $CDCl_3$

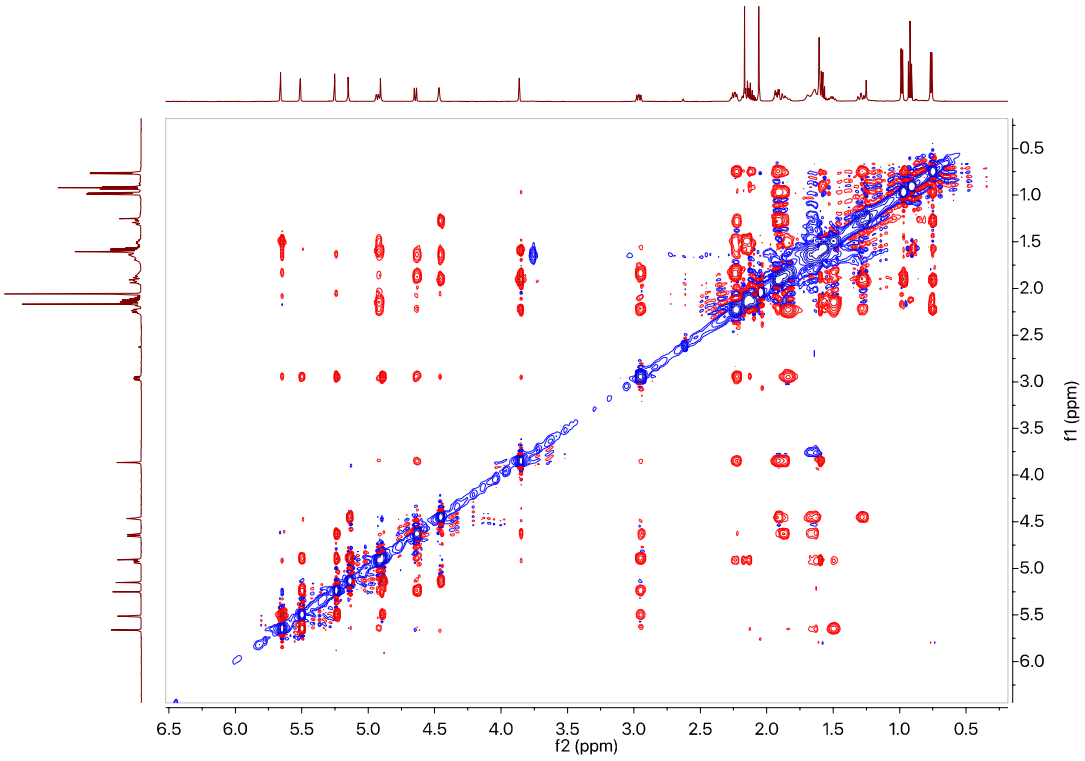


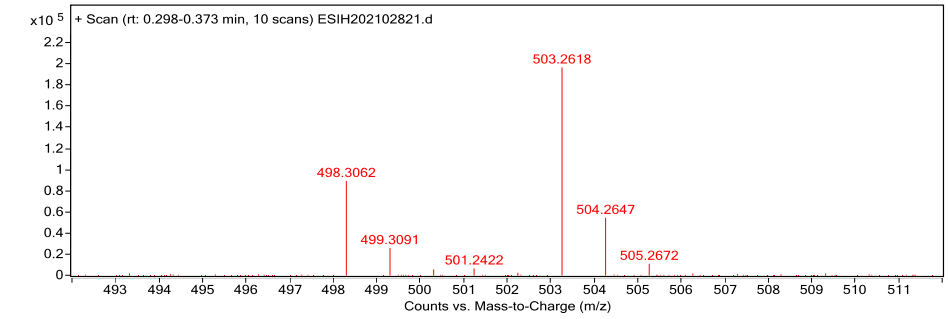
Figure S17. NOESY spectrum of compound **2** in $CDCl_3$

Qualitative Analysis Report

Data Filename	ESIH202102821.d	**Sample Name**	A8-A8-E4A
Sample ID		**Position**	P2-D2
Instrument Name	Agilent G6520 Q-TOF	**Acq Method**	20160322_MS_ESIH_POS_1min.m
Acquired Time	5/24/2021 17:23:13	**IRM Calibration Status**	Success
DA Method	small molecular data analysis method.m	**Comment**	ESIH by zhuzhenyun

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
503.2618	503.2615	-0.31	-0.62	C26 H40 Na O8	(M+Na)+
498.3062	498.3061	-0.03	-0.05	C26 H44 N O8	(M+NH4)+

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Figure S18. HR-ESI-MS spectrum of compound **2**

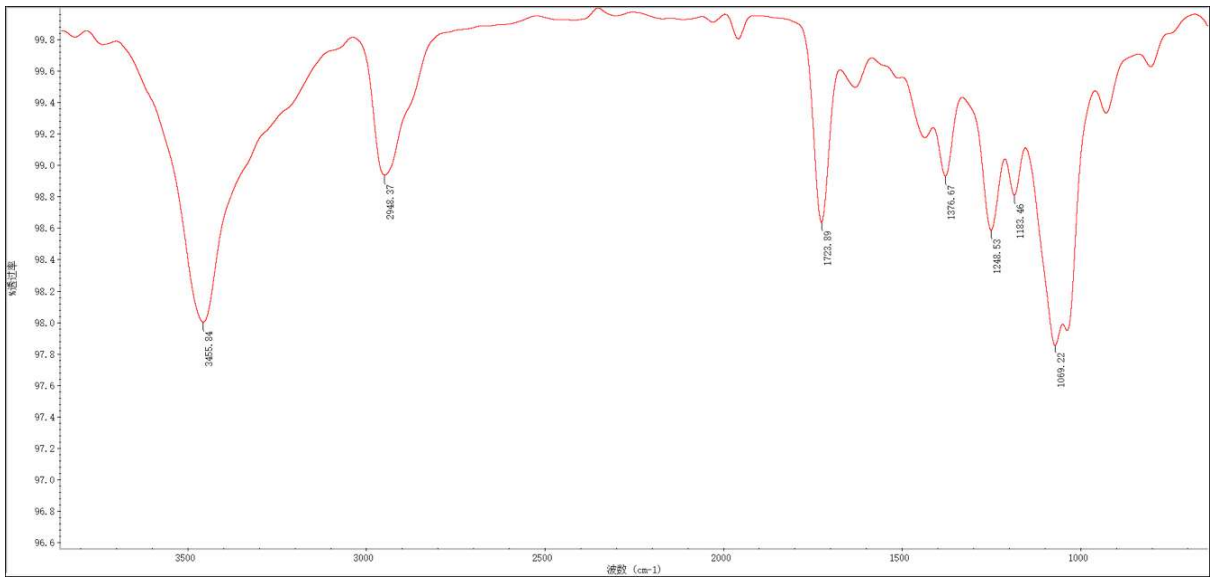


Figure S19. IR spectrum of compound **2**

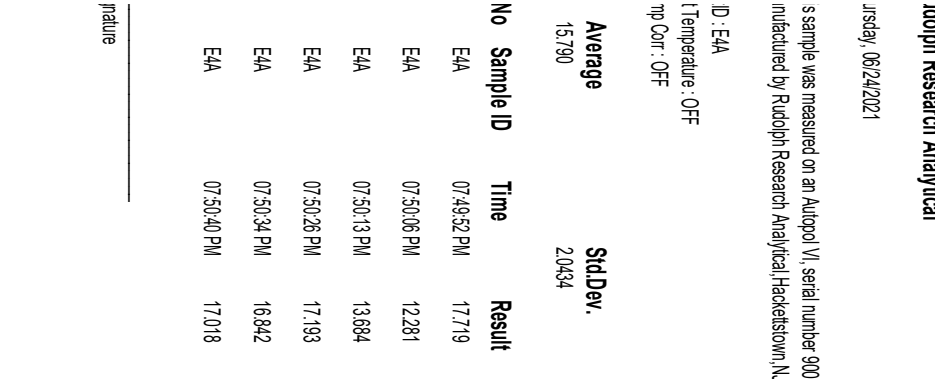


Figure S20. ORD spectrum of compound **2**

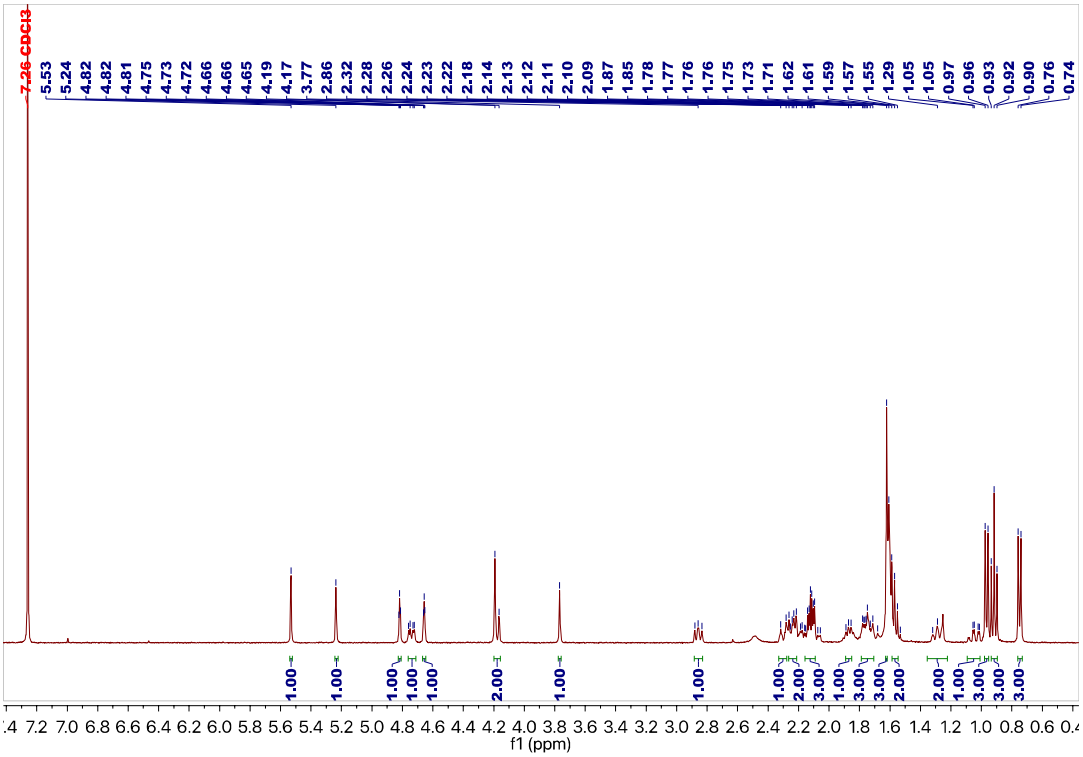


Figure S21. ^{1}H NMR spectrum of compound **3** in $CDCl_3$

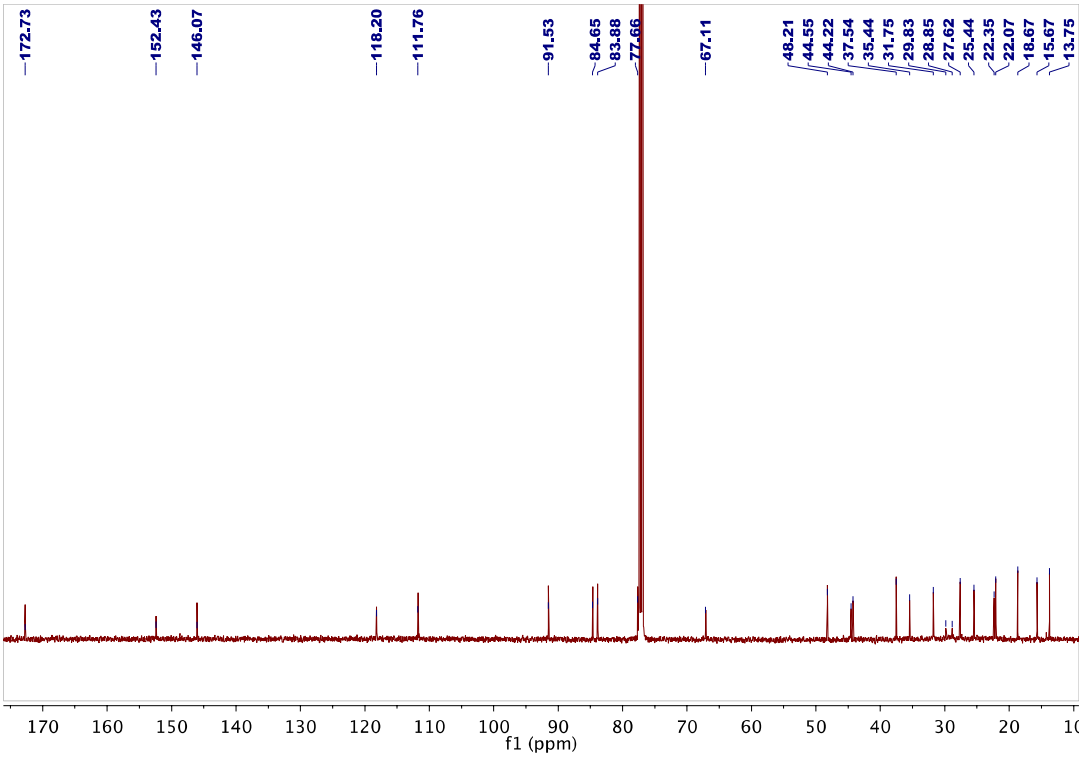


Figure S22. ^{13}C NMR spectrum of compound **3** in $CDCl_3$

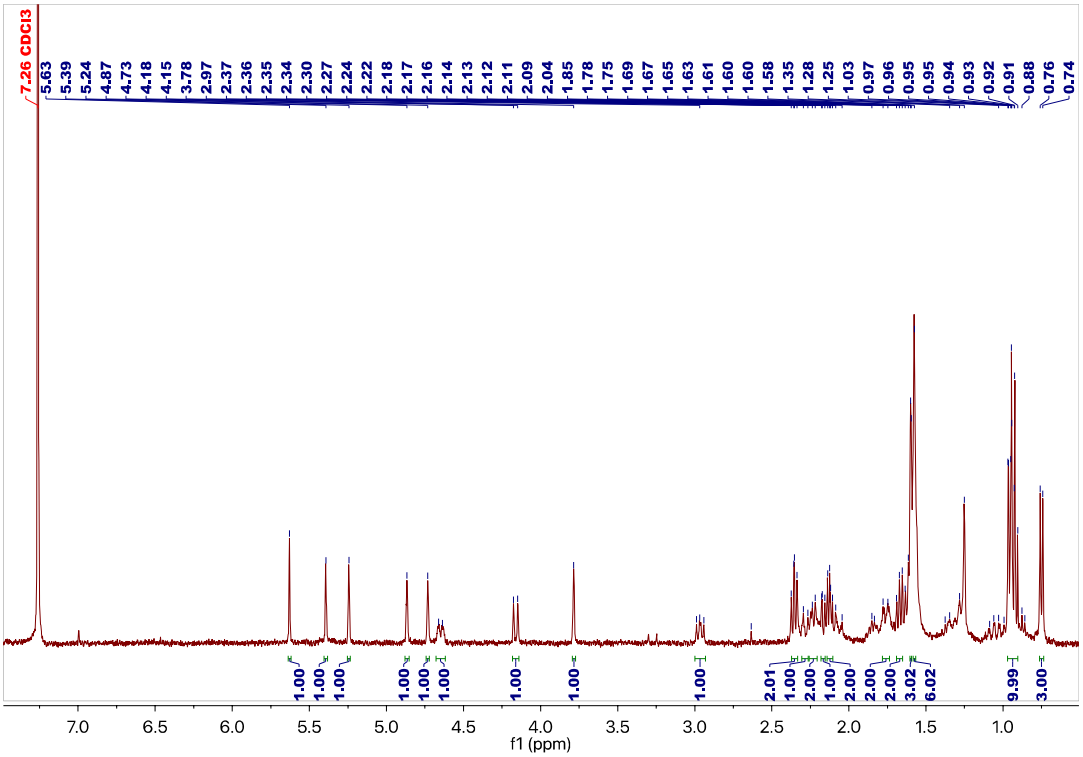


Figure S23. ^{1}H NMR spectrum of compound **4** in $CDCl_3$

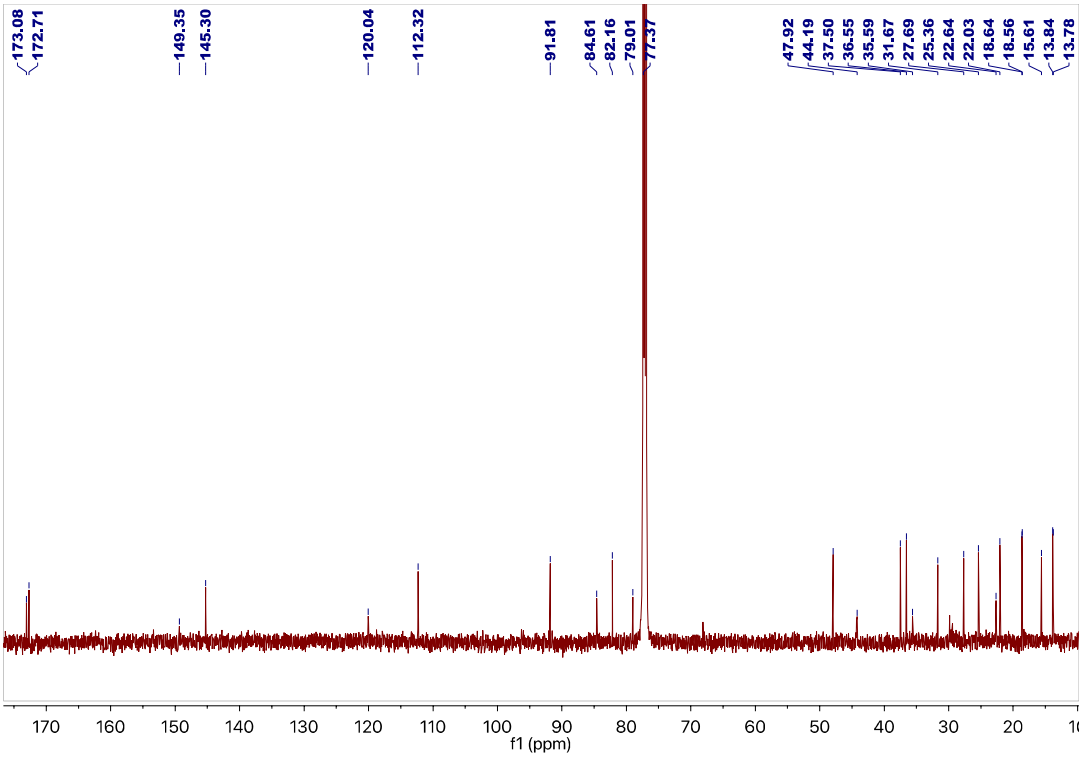


Figure S24. ^{13}C NMR spectrum of compound **4** in $CDCl_3$

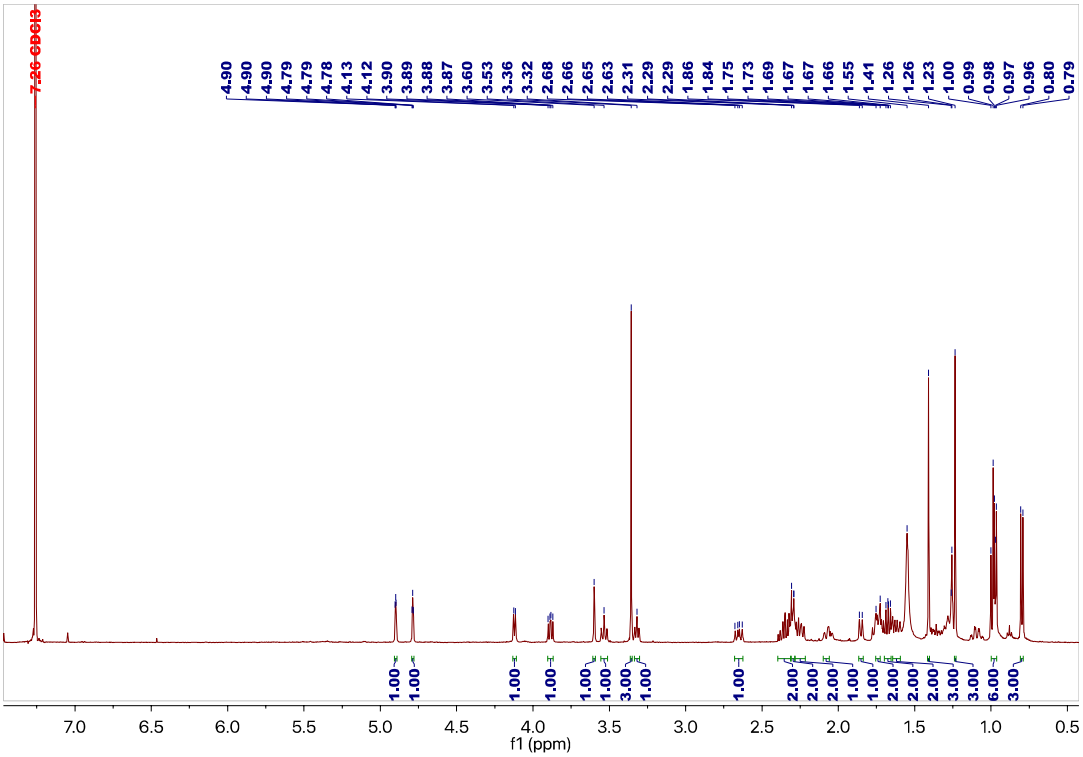


Figure S25. ^{1}H NMR spectrum of compound **5** in $CDCl_3$

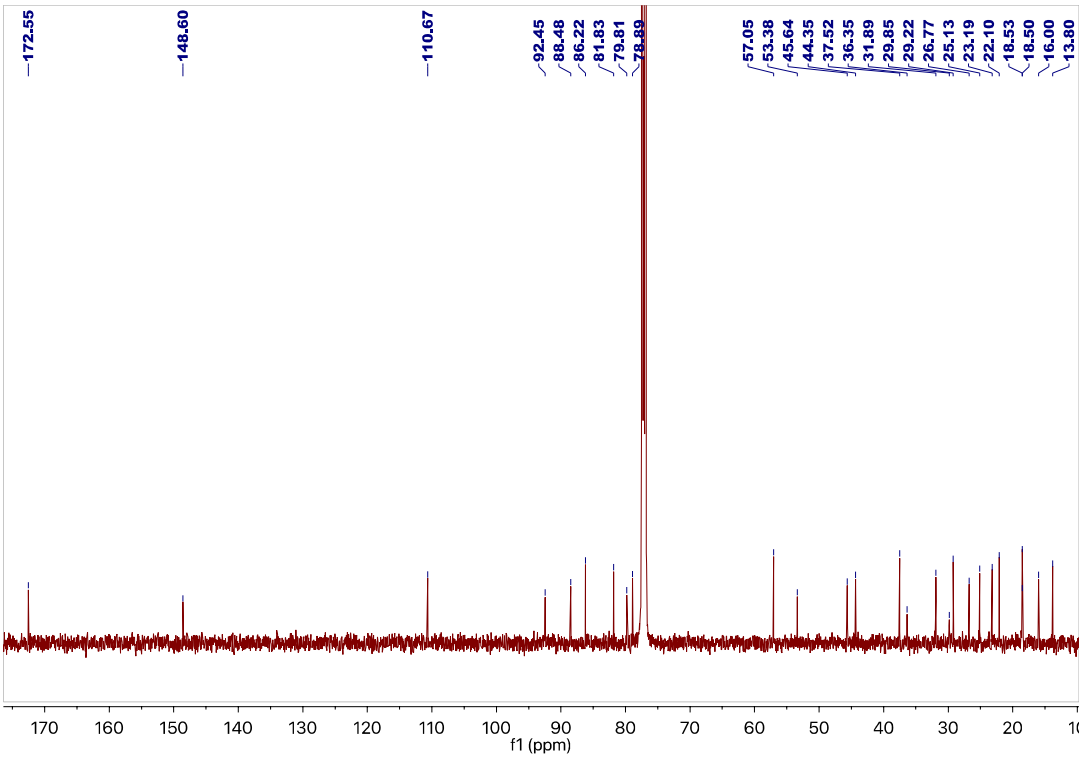


Figure S26. ^{13}C NMR spectrum of compound **5** in $CDCl_3$

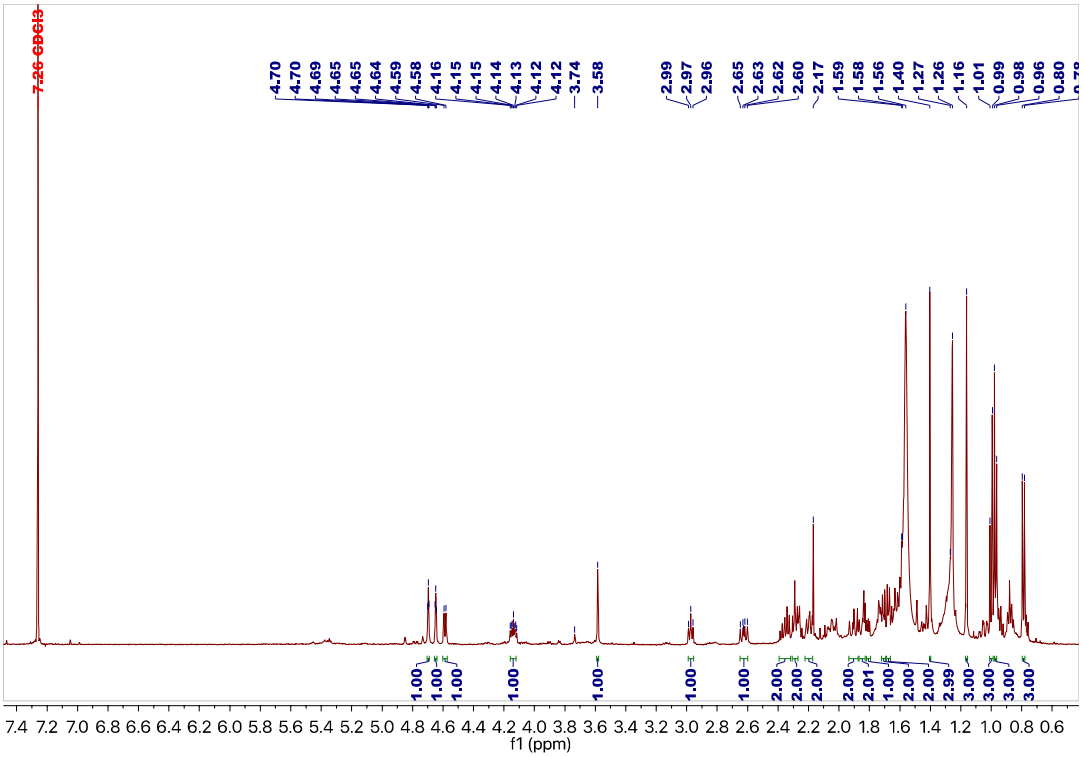


Figure S27. ^{1}H NMR spectrum of compound **6** in $CDCl_3$

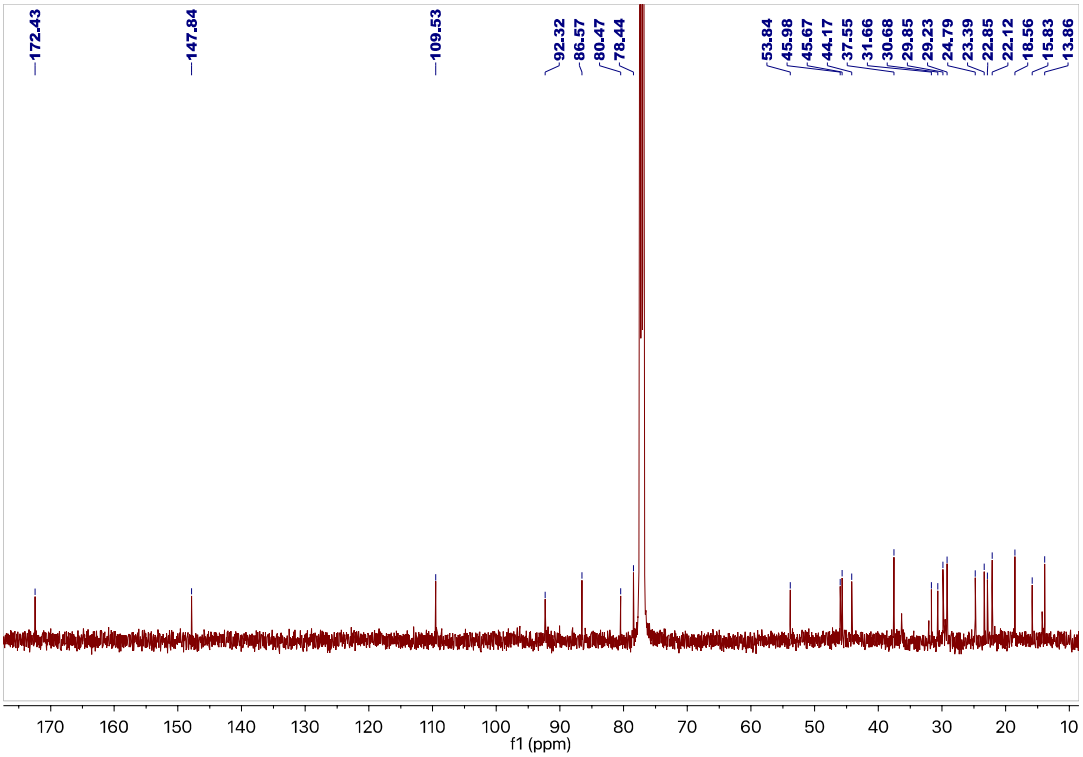


Figure S28. ^{13}C NMR spectrum of compound **6** in $CDCl_3$

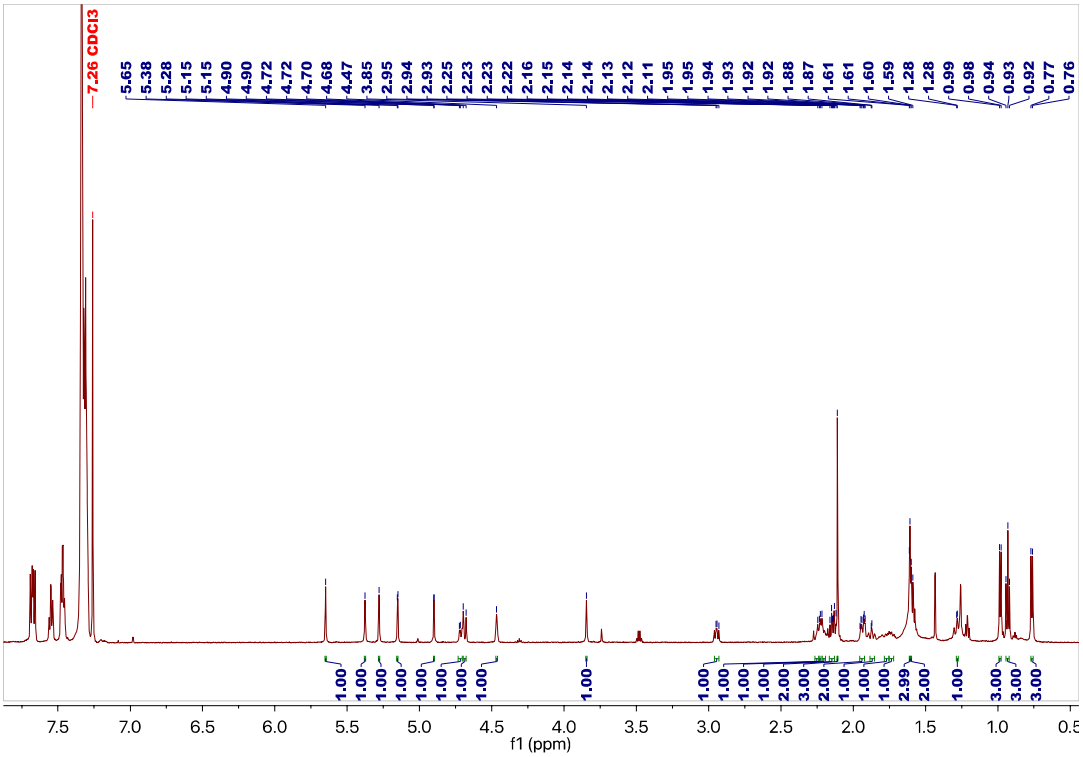


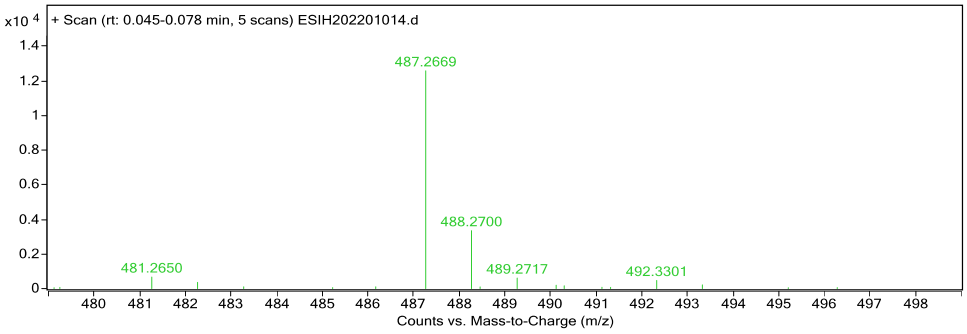
Figure S29. ^{1}H NMR spectrum of mixture in $CDCl_3$

Qualitative Analysis Report

Data Filename	ESIH202201014.d	**Sample Name**	A8-A8-E4A0302
Sample ID		**Position**	P1-B2
Instrument Name	Agilent G6520 Q-TOF	**Acq Method**	20160322_MS_ESIH_POS_1min.m
Acquired Time	3/2/2022 13:53:10	**IRM Calibration Status**	Success
DA Method	small molecular data analysis method.m	**Comment**	ESIH by fangsu

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI



Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
487.2669	487.2666	-0.27	-0.55	C26 H40 Na O7	(M+Na)+

--- End Of Report ---

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Figure S30. HR-ESI-MS spectrum of mixture

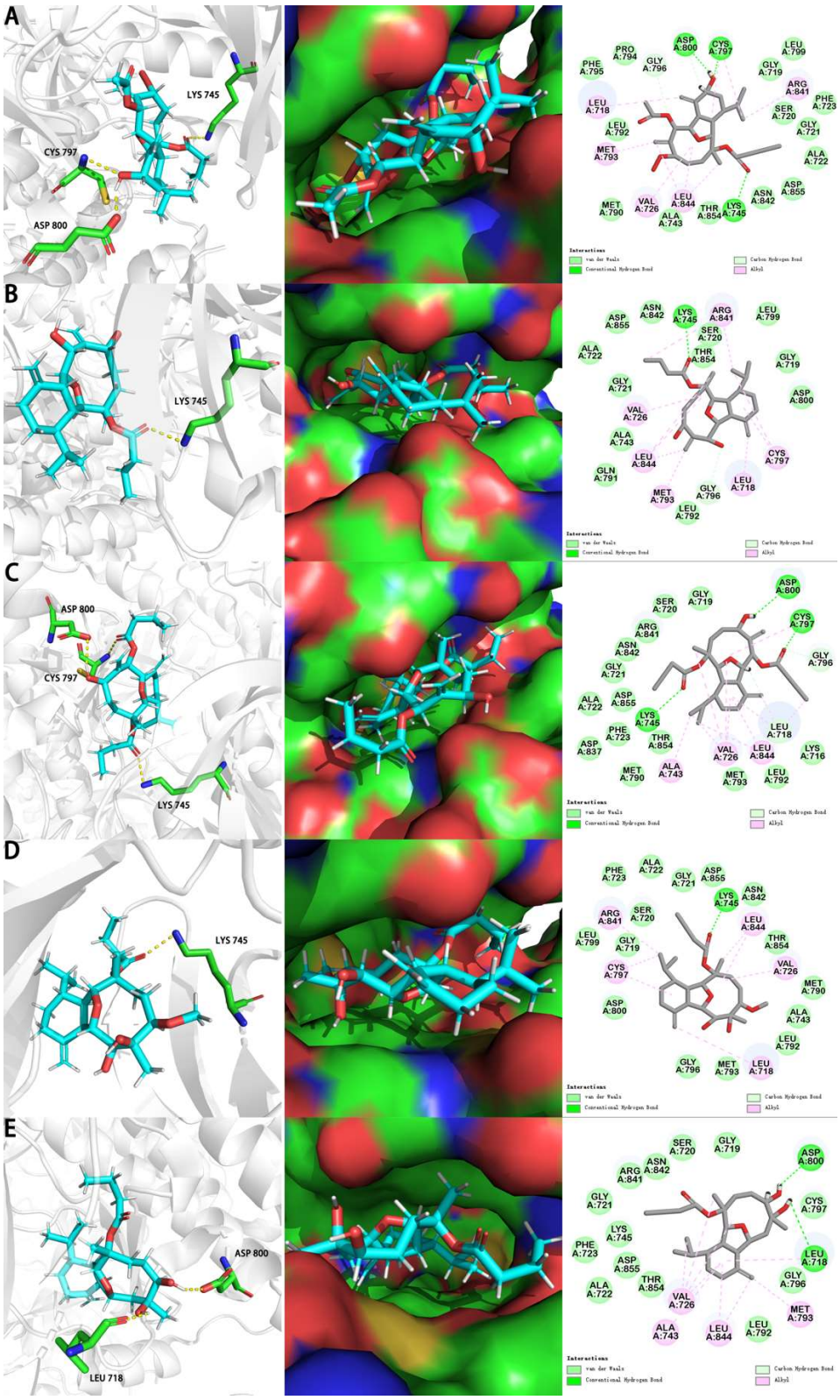

Figure S31. In silico binding mode of compounds **2**–**6** at EGFR kinase crystal structure 5X2A.