Supplementary material

Phytochemical, Antimicrobial, Antioxidant, and *In Vitro* Cytotoxicity Evaluation of *Echinops erinaceus* Kit Tan

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Table S1. NMR spectral data for the mixture of C1[*] and C2[**] in $CDCl_3$.

P.	Type		Compounds C1[*] and C2[**]						Reported [***]	
			HSQC δ_H (*J* in Hz) [*/**]		δ_C [*]	δ_C [**]	HMBC (H→C) [*]	COSY [*]	δ_H	δ_C
	C-1[*]	C-2[**]	C-1[*]	C-2[**]	C-1[*]	C-2[**]	C-1[*]/ C-2[**]	C-1[*]/ C-2[**]	C-1[*]/ C-2[**]	
1	CO	CO			174.3	174.7				180.5
2	CH_2	CH_2	2.22, *q,* (8.0, 15.8)		34.4	34.7	C-1	C-3	2.36	34.0
3	CH_2	CH_2	1.54, *br.s*		25.3	25.3	C-1, C-2, C-4	C-2, C-4	1.64	24.6
4-7	CH_2	CH_2	1.17, 1.22, *m*		29.7- 30.1	29.8-30.1	C-3	C-8	1.30	29-3
8	CH_2	CH_2	1.96, *m*[*], 1.54, *m*[*]	2.70, *m*[**]	25.9	26.0	C-12, C-7	C-7, C-9	2.03	27.1
9	CH	CH	5.30, *m*		128.3	128.4	C-8, C-11	C-8	5.36	130.0
10	CH	CH	5.30, *m*		130.4	130.6	C-8, C-11	C-11	5.36	130.0
11	CH_2	CH_2	1.96, m		27.6	27.6	C-9, C-10, C-12	C-10, C-12	2.03	27.1
12-15	CH_2	CH_2	1.17, 1.22, *m*		29.7-30.1	29.8-31.0			1.30	29.0 - 31.0
16	CH_2	CH_2			31.9	32.3				
17	CH_2	CH_2			23.0	23.1		C-18		22.5
18	CH_3	CH_3	0.80, *s* [*]	0.81, *s* [**]	14.5	14.5	C-17	C-17	0.89	14.1
1`	O-CH_3	O-CH_2	3.59, *s*[*]	4.04, *q, J*= (7.0, 14.0)[**]	51.8	60.5	C-1[*] C-1[**], C-2``[**]	C-2`		51.9 60.4
2`		CH_3		1.17, overlapped		14.6	C-1`[**]	C-1`		

[*] Signals are related to compound **C1**.

[**] Signals are related to compound **C2**.

[***] published data for methyl oleate and ethyl oleate [35,36].

Table S2. NMR spectral data for the compound C4 in $CDCl_3$.

P.	Compound C4								Reported * (600 MHz, acetone-d_6,)	
	HSQC		HMBC (H→C)			COSY	NOESY	HSQC		
	Type	δ_H (*J* in *Hz*) *	δ_C *	$^2J_{CH}$	$^3J_{CH}$	$^4J_{CH}$	^{1}H-^{1}H	^{1}H-^{1}H	δ_H (*J* in *Hz*) *	δ_C *
1	C		36.1							36.5
2	CH_2	1.41, *dd* (14.5, 3.3); 1.90, *d,* (14.5)	47.2	C-1	C-4, C-6, C-10		H-3	H-12, H-10	1.99, *dd* (14.2, 3.7); 1.54, *dd* (14.3, 3.5)	48.0
3	CH	4.24, *br.s*	66.5	C-4	C-1, C-5		H-2, H-4	H-11	4.29, *m*	66.9
4	CH_2	2.4, *d* (13.8); 1.63, *dd* (3.6, 14.0)	45.5		C-2, C-6		H-3	H-12	2.39, *dd* (13.4, 3.7); 1.71, *dd* (13.6, 3.7)	46.5
5	C		87.4							87.1
6	C		183.5							183.5
7	CH	5.60, *s*	112.6	C-8, C-6	C-1, C-5			H-13	5.68, *s*	113.4
8	C		172.6							171.7
9	CH_3	1.18, *s*	30.7		C-6	C-1		H-9	1.26, *s*	30.4
10	CH_3	1.39, *s*	26.4		C-6			H-12	1.47, *s*	27.6
11	CH_3	1.70, *s*	26.9	C-1	C-2, C-6			H-10	1.74, *s*	27.0

* published data [40].

Table S3. NMR spectral data for the Compound C6 in CD_3OD.

P.	Compound C6			
	C6		Reported *	
	δ_H (*J* in *Hz*)	δ_C	δ_H (*J* in *Hz*) *	δ_C *
1		127.1		127.6
2	7.41, *d* (8.5)	130.9	7.41, *d* (8.5)	130.8
3	6.78, *d* (8.5)	116.6	6.78, *d* (8.5)	116.7
4		160.9		160.8
5	6.78, *d* (8.5)	116.6	6.78, *d* (8.5)	116.7
6	7.41, *d* (8.5)	130.9	7.41, *d* (8.5)	130.8
7	7.56, *d* (15.9)	146.3	7.51, *d* (15.9)	145.2
8	6.26, *d* (15.9)	115.8	6.27, *d* (15.9)	116.0
9		177.8		178.0

* published data [56].

Table S4. NMR spectral data for the compound C7 in CD_3OD.

P.	Compound C7						Reported *	
	HSQC		HMBC (H→C)			COSY	(400/100 MHz, DMSO-*d6*)	
	δ_H (*J* in *Hz*)	δ_C	$^2J_{CH}$	$^3J_{CH}$	$^4J_{CH}$	^1H-^1H	δ_H (*J* in *Hz*) *	δ_C *
2	5.25, *dd* (12.8, 2.8)	81.0				H-3	5.37, *dd* (12.5, 3.0)	78.5
3	3.05, *d* (17.2, 12.8)	44.6	C-4	C-10		H-2	3.19, *dd* (17.1, 12.5)	42.1
	2.67, *dd* (17.2, 2.9)		C-2, C-4	C-1`		H-2	2.67, *dd* (17.1, 3.0)	
4		196.5						196.5
5	12.08, *s*	160.9					12.97, *s*	163.0
6	5.87, *d, J*=7.5 Hz	97.6					5.88, *s*	95.9
7		167.0					10.81, *s*	166.7
8	5.87, *d, J*=7.5 Hz	96.7					5.88, *s*	95.1
9		161.8						163.6
10		101.9						101.9
1`		132.3						129.6
2`	6.76, *s*	116.7	C-1`, C-3`	C-2, C-4`			6.75, *s*	114.5
3`		147.4					9.09, *s*	145.8[a]
4`	6.89, *s*	115.2	C-3`/C-5`	C-6`	C-2		6.88, *s*	118.1
5`		147.4					9.04, *s*	145.3[a]
6`	6.76, *s*	119.7	C-1`, C-3`	C-2, C-4`			6.75, *s*	115.5

* Published data [48,55]. [a]: interchangeable values.

Table S5. *In silico* Physicochemical and pharmacokinetics of compounds C1-C7.

Predictive parameters	C1	C2	C3	C4	C5	C6	C7
Pass prediction (Pa/Pi) [a]							
Anti-inflammatory/ Intestinal [a]	0.717/ 0.002[a]	0.672/ 0.019	0.415/ 0.008	0.515/ 0.053	0.325/ 0.139	0.641/ 0.024	0.697/ 0.016
Antimycobacterial/ antibacterial [b]	0.367/ 0.049	0.427/ 0.033	0.312/ 0.056 [b]	0.455/ 0.021 [b]	0.176/ 0.140 [b]	0.457/ 0.026	0.403/ 0.029 [b]
Anti-ulcerative	0.662/ 0.007	0.688/ 0.005				0.581/ 0.013	0.604/ 0.011
Antineoplastic/ Anticarcinogenic [c]	0.343/ 0.044 [c]	0.546/ 0.017	0.366/ 0.118	0.746/ 0.019; 0.305/ 0.032 (Colon cancer); 0.437/ 0.026 [c]	0.591/ 0.047	0.559/ 0.015 [c]	0.662/ 0.007 (Breast cancer)
Antifungal	0.505/ 0.030	0.487/ 0.033	0.380/ 0.054	0.393/ 0.051	0.364/ 0.059	0.451/ 0.039	0.593/ 0.019
TNF expression inhibitor	0.672/ 0.008	0.609/ 0.012	0.323/ 0.089	0.309/ 0.097	0.680/ 0.007	0.737/ 0.005	0.496/ 0.030
CYP2J2 substrate						0.836/ 0.008	0.659/ 0.044
CYP2C12 substrate	0.752/ 0.047	0.812/ 0.033	0.726/ 0.052	0.871/ 0.019			0.898/ 0.012
CYP3A1 substrate	0.700/0.009	0.680/ 0.010	0.535/ 0.036		0.254/ 0.138	0.540/ 0.034	0.580/ 0.024
CYP4A2 substrate	0.696/ 0.002	0.671/ 0.002		0.363/ 0.044			
Oxygen/ free radical scavenger/antioxidant	0.628/ 0.017	0.600/ 0,023		0,297/ 0,023	0,350/ 0,017	0,627/ 0,005	0,828/ 0,003
ADME Prediction [b]							
Physicochemical parameters							
TPSA (^{0}A):	26.30 Å²	26.30 Å²	37.30 Å²	46.53 Å²	113.29 Å²	57.53 Å²	107.22 Å²
Molar Refractivity	94.26	99.06	70.66	52.51	126.50	45.13	73.59
Drug likeness Prediction							
Bioavailability Score	0.55	0.55	0.55	0.55	0.55	0.85	0.55
Synthetic accessibility	3.16	3.34	4.14	3.63	3.63	1.61	3.09

Absorption Prediction							
Log *S* (ESOL)	-5.32	-5.70	-2.65	-1.69	-1.69	-2.02	-3.40
Consensus Log $P_{o/w}$	5.95	6.33	2.72	1.53	1.53	1.26	1.48
Solubility class	Moderately soluble		Soluble	Very soluble	Very soluble	Soluble	Soluble
Distribution Prediction/Pharmacokinetics							
Log *Kp* (skin permeation, cm/s)	-2.82	-2.49	-6.15	-6.79	-6.79	-6.26	-6.46
GI absorption	High	Low	High	High	High	High	High
BBB permeant	No	No	Yes	Yes	Yes	Yes	No
Metabolism Prediction							
P-gp substrate	No	No	No	No	No	No	Yes
CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4 inhibitors	All No, except Yes (CYP1A2)		No	No	No	No	All No, except Yes (CYP3A4)

Where "Pa" is probable activity, "Pi" is probable inactivity, "Å2" polar surface area, "TPSA" Topological polar surface area, and Methyl oleate (**C1**), Ethyl oleate (**C2**), erinaceosin (**C3**), loliolide (**C4**), erinaceol (**C5**), (*E*)-*p*-coumaric acid (**C6**), and 5,7,3`,5`-tetrahydroxy flavanone (**C7**). [a] PASS prediction web tool **[29]**, [b] SwissADME web tool **[30]**.

Table S6. Docking results of isolated compounds against PDB ID:1KZN, 3GNS, 7AFW, 4M6J, and 6C0V enzymes (binding free energies, interaction type derived from the best conformations of each compound into the macromolecule).

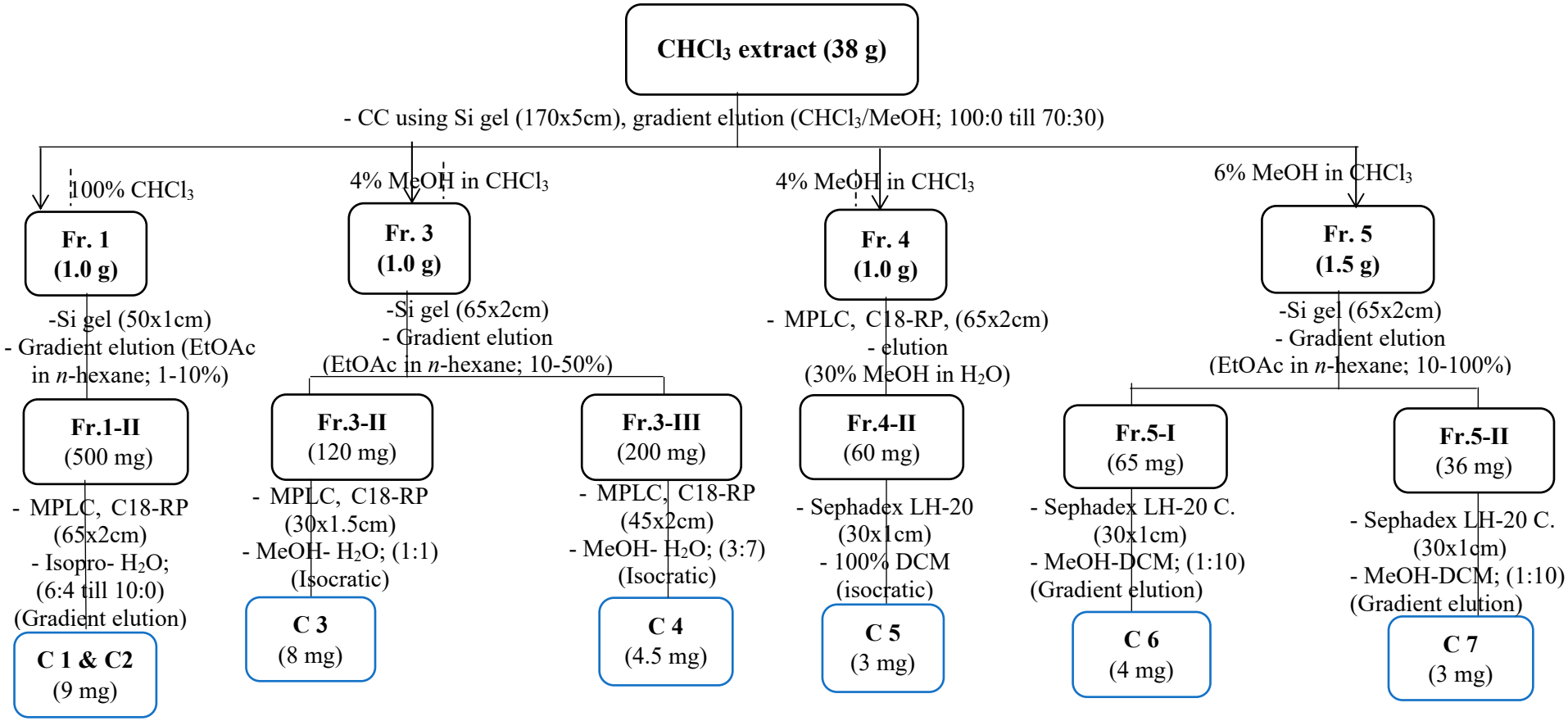
Score/ Interactions	Isolated Compounds							Co-Crystalized Ligand(s)		
	C1	C2	C3	C4	C5	C6	C7	CBN	TRI	
Antimicrobial Molecular Docking										
1. DNA Gyrase Topoisomerase II (*E. coli*), (PDB ID:1KZN)										
BFE[a] (kcal/mol)	-4.5	-4.1	-5.7	-4.9	-5.7	-5.5	-7.7	-7.4		
Amide- π-stucked								**Asn46***		
HB	**Asn46*** **Gly119*** **Val120***		Ala96 **Gly117***	Ala96 **Asn46***	Ala96 **Gly117***, **119*** Ser121	Ala96 **Asn46***	Glu42 **Val120*** Ser121	Arg136 **Asn46*** **Asp73***		
Ha.B								Gly77		
π-alkyl/alkyl	Ala86, 96 Val89	Ala86, 96 **Ile90*** Val89				Ala96 **Ile90***	**Ile90***	Ala47 **Ile90*** Pro79 **Val71***		
π-σ								Thr165		
π-Cation/ π-Anion								Arg76 **Glu50***		
VDW	**Asp49*** **His95*** **Ile90*** Ser121	Ser85 Val84	Asp45 **Asn46*** Glu42 **Gly119*** **His95*** **Ile90*** Ser121 Val93, 118	Gly117, **119*** **His95*** **Ile90*** Ser121 **Val**93, 118, **120***	**Asn46*** **Asp**45, **49*** Glu42 **His95***, 116 **Ile90*** Leu94 Val93, 118, **120***, 122	**Asp49*** **His95*** **Leu94*** **Gly119*** **Val120***	**Asn46*** **Asp**45, **49*** **His95*** **Leu94*** Gly**119*** Val93	Ala86 **Asp49*** Ile78 Met91, 166 Val43, **Val120***, 167		
C:H bond							Gly117			
2. Enoyl-Acyl Carrier Protein Reductase (*S. aureus*) (PDB ID: 3GNS)										
BFE[a] (kcal/mol)	-4.5	-5.1	-6.3	-5.9	-6.0	-5.8	-6.9		-5.8	
Amide- π-stucked						Phe77				
HB	Asn205 **Leu196***	Ala21 Ile20	Arg45 Gln64	Ser19` Thr146`	Ala21` Gly13`	Asn86 Lys134	Gly13` Ser93`		Ser19`	

	Try147*		Glu72 Tyr39		Ile94 Ser93`, 121 Thr145`					
π-alkyl/alky	Ile211 Leu148 Pro192	Ala163 Ile20 Leu148, **196*** Lys164 Met160 **Try147***			Ile20` **Leu196***	Lys134	Ile20` Ala15		Ala15 Ile20` **Leu196***	
VDW	Glu210 Leu207, 208	Ile94 Gly13 Ser19, 93 Thr145, 146	Asn75 Asp66 Gln79 Gly76 Ile65 Leu62 Tyr63	Ala15, 21` Gly13` Ile20, 94` **Leu196*** Thr145` **Tyr147*** Ser93`	Ala15 Arg40 Ile120 Thr146` Tyr91, **147*** Ser19` Val67	Glu78, 131 Gly81, 85 Ile74 Leu135 Pro137	Ala21` Ile14, 94` **Leu196*** Thr145, 146` Tyr91`, **147*** Val24		Ala21` Gly13` Ser93` Thr145, 146` Tyr91`, **147***	
Cytotoxic Molecular Docking										
3. *β*-Catenin (PDB ID: 7AFW)										
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**R9Q**		
BFE[a] (kcal/mol)	-4.3	-4.2	-6.0	-5.3	-5.1	-5.0	-5.9	-6.2		
Amide- π-stucked								Gly245``		
HB		Gly245` Lys242``, 281	Gln203	Thr201	Gln203 **Thr205****	Met202	Asn204 Gln203	**Asn206**** **Thr205****		
π-alkyl/alky	Lys242`` **Pro247****	Lys242`` **Pro247****	Lys242``		Lys242``	Lys242``	Lys242``	**Pro247****		
π-Sulphur							**Met243****	**Met243****		
VDW	Asn204 Gln203 Met202, **243**** **Thr205****	Gln203 **Met243****	**Asn**204, **206**** **Met243**** **Thr205****	Arg200 Asn161, 204 Asp162 Gln165 Leu160 **Thr205**** Val204	**Asn206**** Gly245`` Met202, **243**** **Thr205****	Asn204 Gly203, 245`` Lys281 **Met243**** **Thr205****	**Asn206**** Met202 **Thr205****	Ala211 **Asp207**** Lys242`` **Ser246**** Val208, **248****, 251		
C:H bond	**Asn206****									
4. Crystal structure of human dihydrofolate reductase (DHFR) bound to NADPH (PDB ID:4M6J)										

	C1	C2	C3	C4	C5	C6	C7	NDP	Metho	Cipro
BFE[a] (kcal/mol)	-4.4	-3.8	-5.1	-4.5	-5.3	-4.9	-6.3	-7.1	-7.1	-5.5
Amide- π-stucked							**Ser118*****			**Ser118*****
HB	**Gly20*****	**Gly20*****	**Ser118***** **Gly20**** (DDB)	**Gly20***** (DDB)	Asp145 **Gly20**** Ser118 **Thr146*****	Asp145 Ser118, **119*****	**Arg77***** Ser118 **Glu123***** (AAB)	**Glu123***** **Lys55***** Ser118, **119***** **Thr146*****	Asp145 Glu123 **Gly20*****	Lys122 **Ser118***** Thr146
π-alkyl/alky	Lys122$^{```}$	Lys122$^{```}$					Lys122$^{```}$ Ser118		Lys122$^{```}$	
VDW	Asp145 **Gly17***** **Lys55***** Ser118, **119***** **Thr146*****	Asn19 Asp145 **Gly17***** Ser118, **119***** **Thr146*****	Asn19 Asp145 Lys18 **Ser119***** **Thr146*****	Asn19 Asp21, 145 **Lys55***** **Ser118***** **Thr146*****	Asn19 **Lys55*****, 122 **Ser119*****	Asn19 **Gly20***** Lys18 **Thr146*****	Asn126 **Ser119*****	**Arg77***** Lys122$^{```}$ Phe147 **Val120*****	Arg77*** Asn19, 126 Lys18, **55***** Ser118, **119***** **Thr146*****	**Arg77***** **Lys55***** **Ser119*****
5. Crystal structure of human P-gp (PDB ID: 6C0V)										
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**ATP**	**DOXO**	
BFE[a] (kcal/mol)	-6.9	-6.9	-7.7	-6.5	-8.4	-6.1	-8.0	-7.0	-8.2	
HB	Ala729$^{````}$ **Ser979******					Ile736$^{````}$	Ala729$^{````}$ **Phe336******	Ala729 Leu332 Phe732 Ser979	Leu332 **Phe336******	
π-alkyl/alky	Ile735$^{````}$ Leu332, 339$^{````}$ Phe314, **335******, **728******, 759	Ile735$^{````}$ Leu332$^{````}$, 339, 976 **Phe72******, **728******, 759, **983******, 335, 314	Leu339$^{````}$ **Phe335**$^{````}$		Ile731, 735 Leu339 Phe759$^{````}$ (π- π stucked), **Phe335******	**Phe335******, 759$^{````}$ (π- π stucked)	Leu332$^{````}$		Ile736 Leu332	
π-σ			Phe759	**Phe 335******						
VDW	Ala729$^{````}$ Ile736$^{````}$ Leu976 Phe336, **983******	Ala729$^{````}$ **Ile340****** Phe336, 732 **Ser979******	Ile731$^{````}$, 735 Phe314, 728, **732******	Ile731$^{````}$ Leu332, 339 **Phe336******, **728******,	Ala729$^{````}$ Glu972 **Ile**736, **340******	Ile735$^{````}$ Leu339$^{````}$ Phe314, **732****** Tyr310	Ile731, 735$^{````}$ Leu339 Phe72, 314, **335******,	Ile731, 735, 736 Leu339, 976	Ala729 Glu972 Ile340, 731, 735	

		Tyr310	Tyr307, 310	**732******, 314, 759 Val331	Leu332$^{````}$, **975******, 976 Phe72****, **336******, 728****, 732, **983******,314 Ser733, **979******		728, 732$^{````}$, 759, **983****** **Ser979******	**Phe72******, 314, 335, **336******, **728******, 759, **983******	Leu339, 976 **Phe72******, 314, 335, **728******, 759 **Ser979******	

[a]RMSD < 2; BFE: Binding free energy (kcal/mol); CB=Covalent bond; HB= Hydrogen Bond/ Hydrogen-carbon bond; DDB= unfavorable donor-donor bond; AAB= unfavorable acceptor-acceptor bond; Ha.B= Halogen bond; π= Pi; σ= Sigma; VDW= Van Dar Waals; **CBN**= Clorobiocin (reference ligand ID:1KZN); **TRI**= Triclosan (reference ligand ID: 3GNS); **R9Q**= 3-[(2-R)-4-methyl-5-oxidanylidene-2,3-dihydro-1,4-benzoxazepin-2-yl]benzenecarbonitrile (reference ligand ID: 7AFW); **NADPH**= dihydro-nicotinamide-adenine-dinucleotide phosphate (PDB ID:4M6J); and **DOXO**= Doxorubicin (PubChem ID: 31703), and **ATP**= Adenosine-5'-triphosphate (reference ligand ID:6C0V); *[52], ** [33], ***[34], **** [21], `, ``, ```, ```` shown with co-crystalized ligand. Amino acid residues in bold are reported before as crucial residues.



Flowchart S1. Fractionation and purification of the $CHCl_3$ extract of the *E. erinaceus* aerial flowering parts.

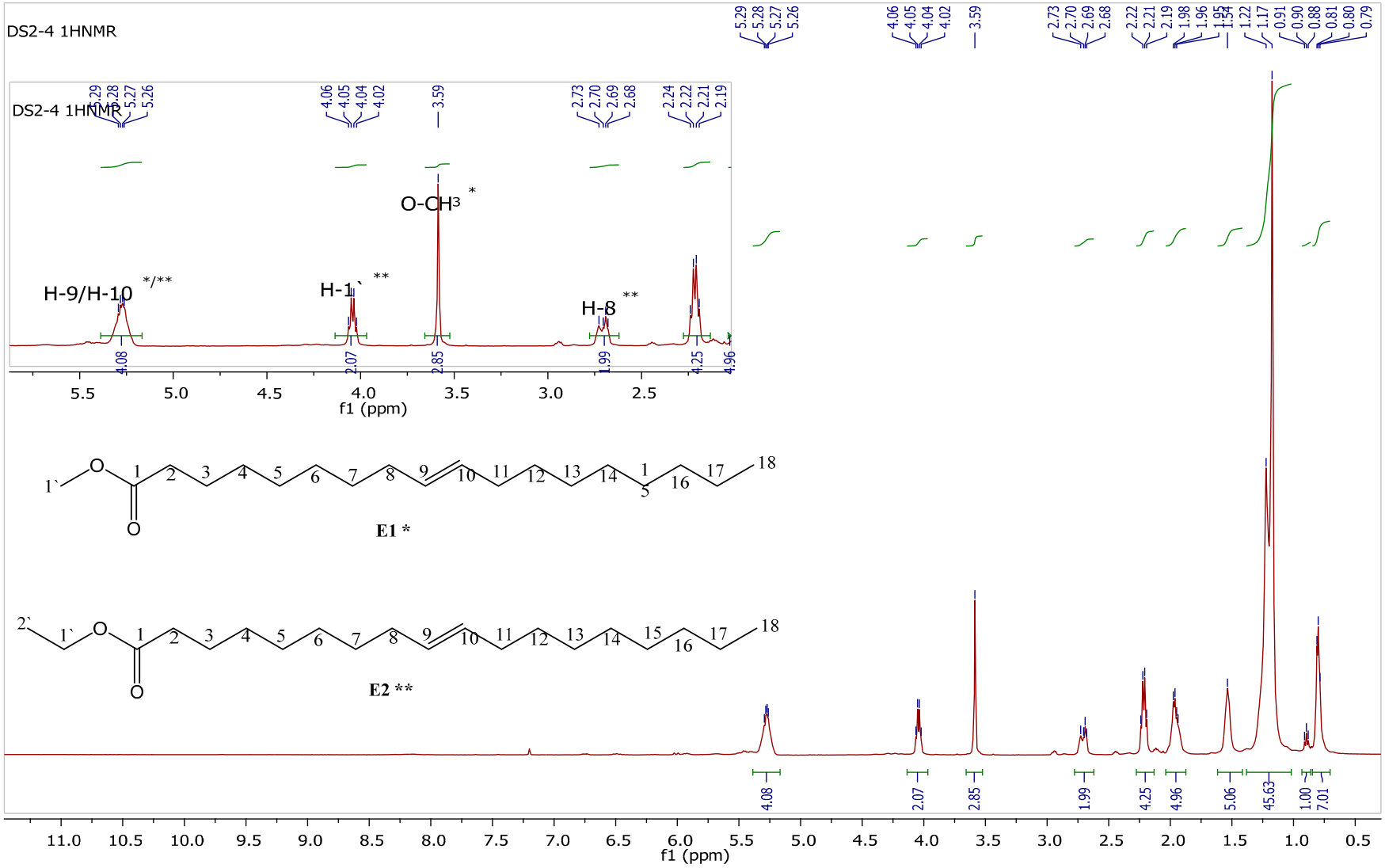


Fig. S1. [1]H-NMR spectrum of mixture of compounds **C1*** and **C2**** in $CDCl_3$.

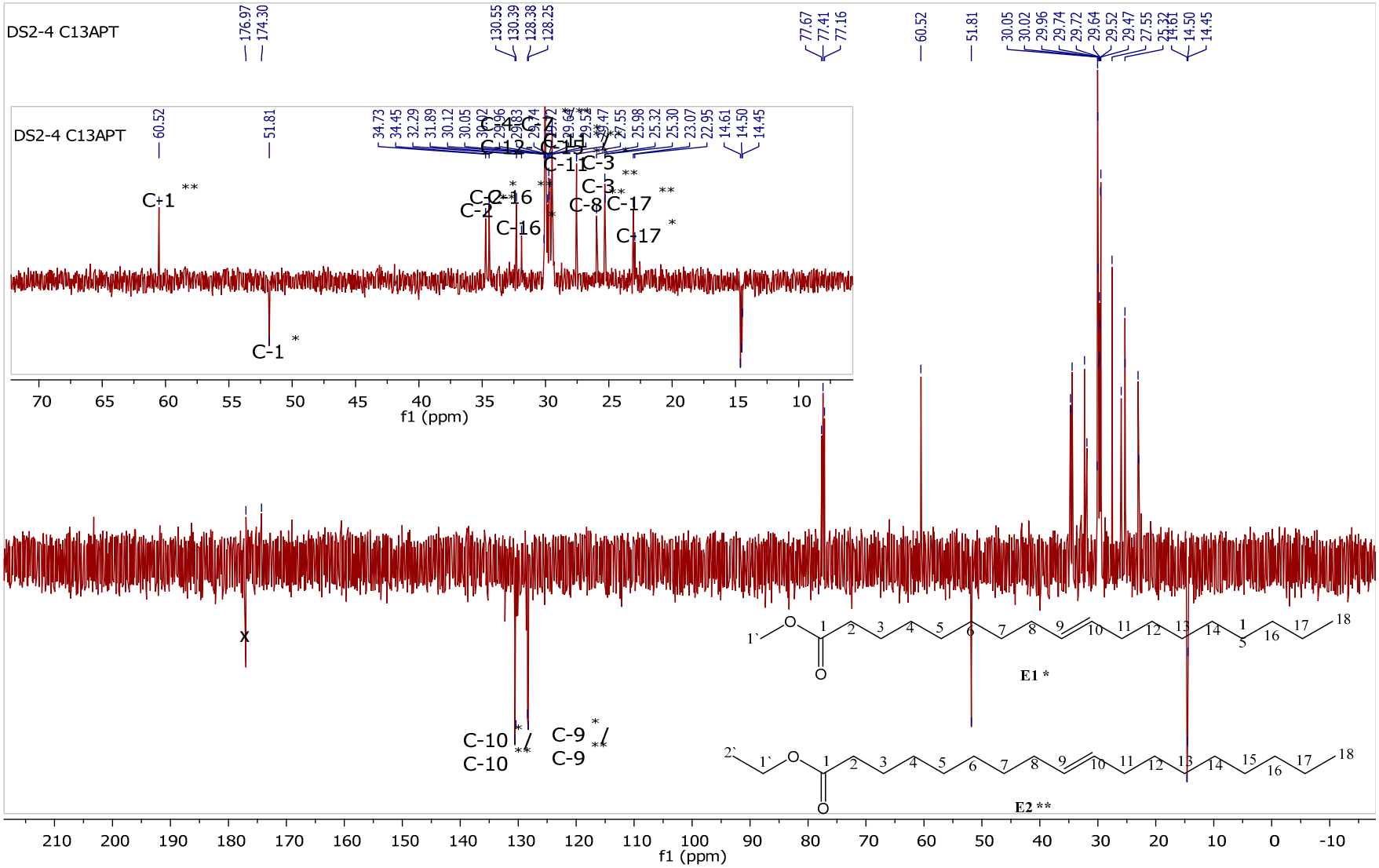


Fig. S2. APT spectrum of mixture of compounds **C1*** and **C2**** in $CDCl_3$.

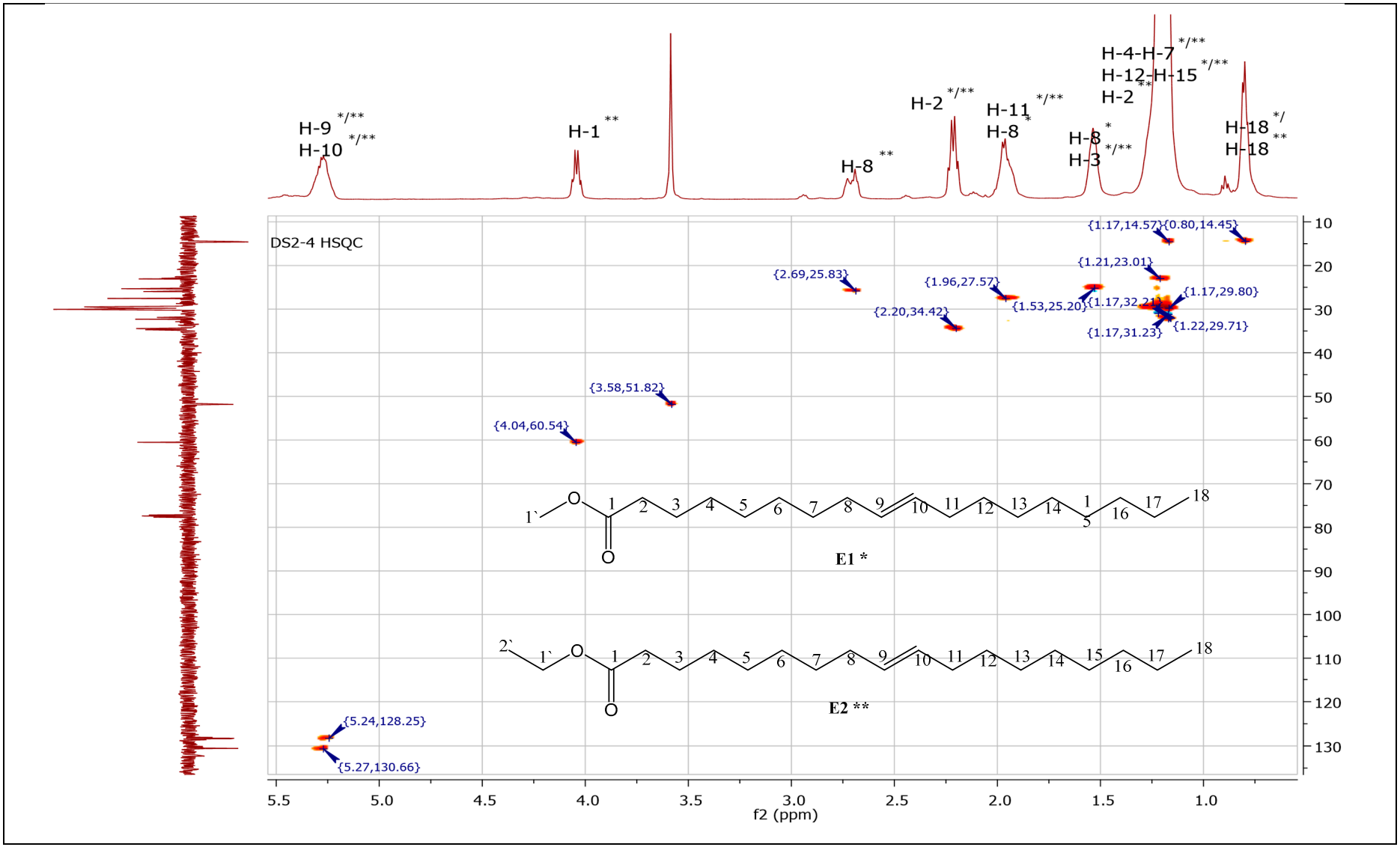


Fig. S3. HSQC spectrum (expansion; 0.5-5.5 ppm) of mixture of compounds **C1*** and **C2**** in $CDCl_3$.

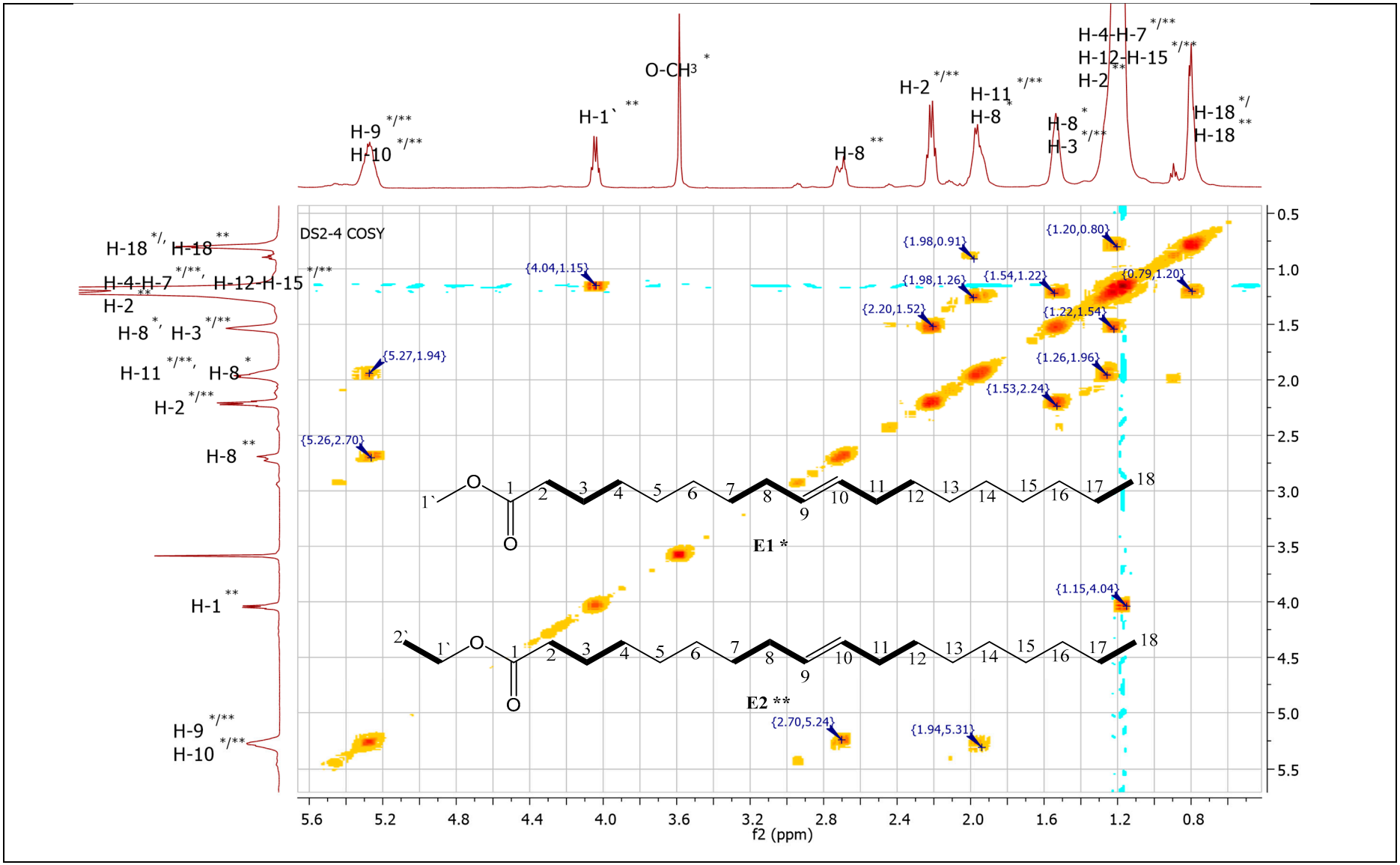
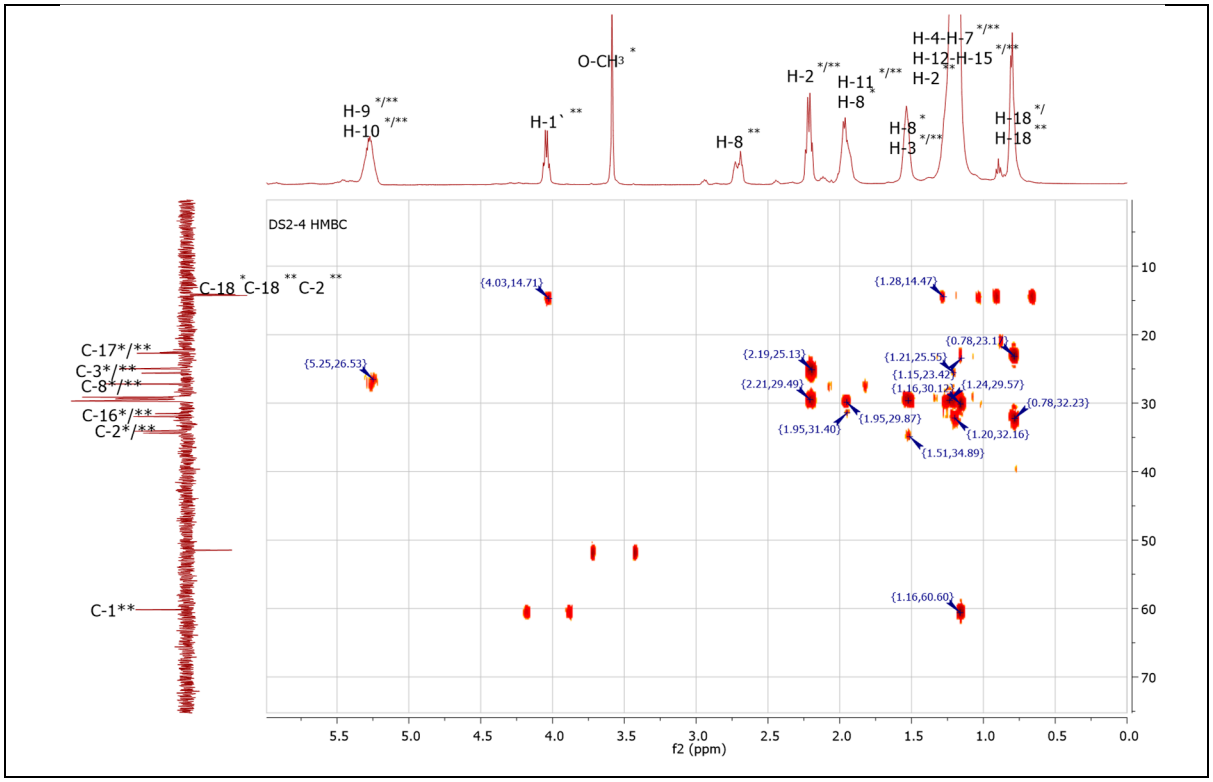
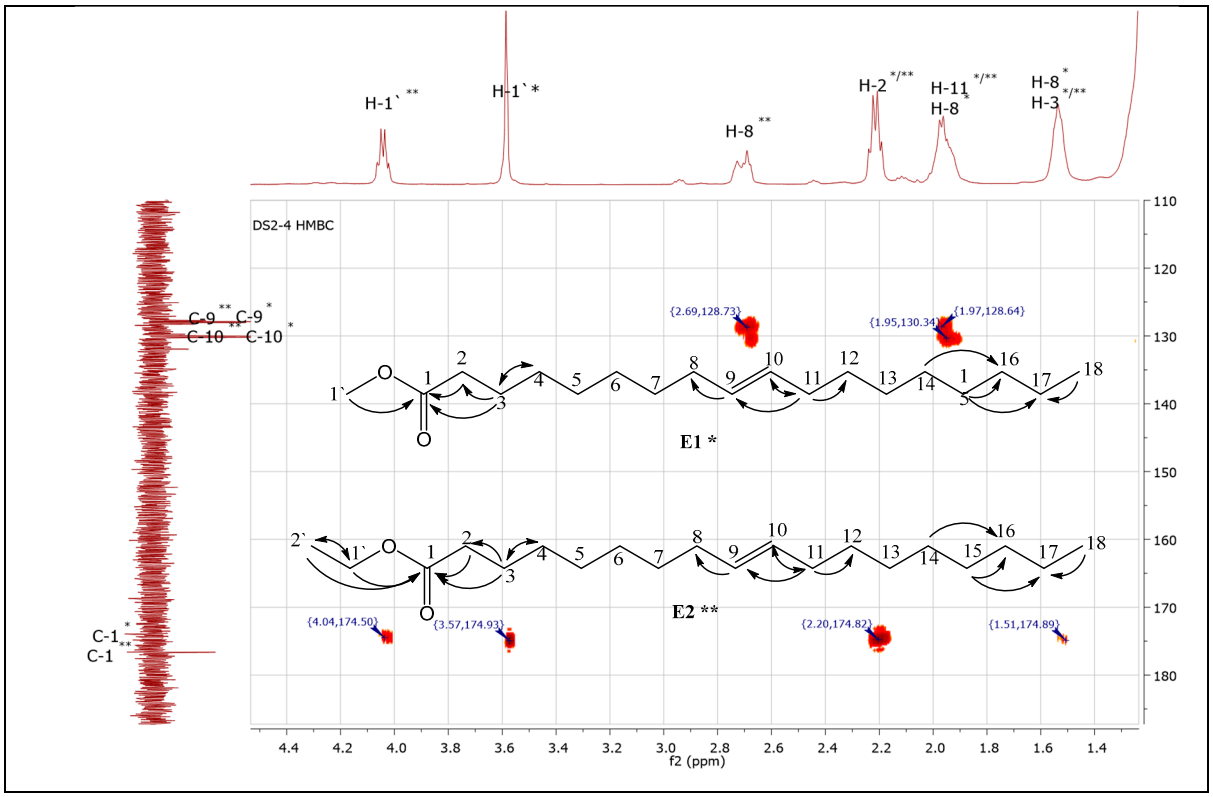


Fig. S4. COSY spectrum (expansion; 0.6-5.6 ppm) of mixture of compounds **C1*** and **C2**** in $CDCl_3$.



Expansion; 0-6.0 ppm



Expansion; 1.3-4.4 ppm

Fig. S5. HMBC spectrum (expansion; 0-6.0 and 1.3-4.4 ppm) of mixture of compounds **C1*** and **C2**** in $CDCl_3$.

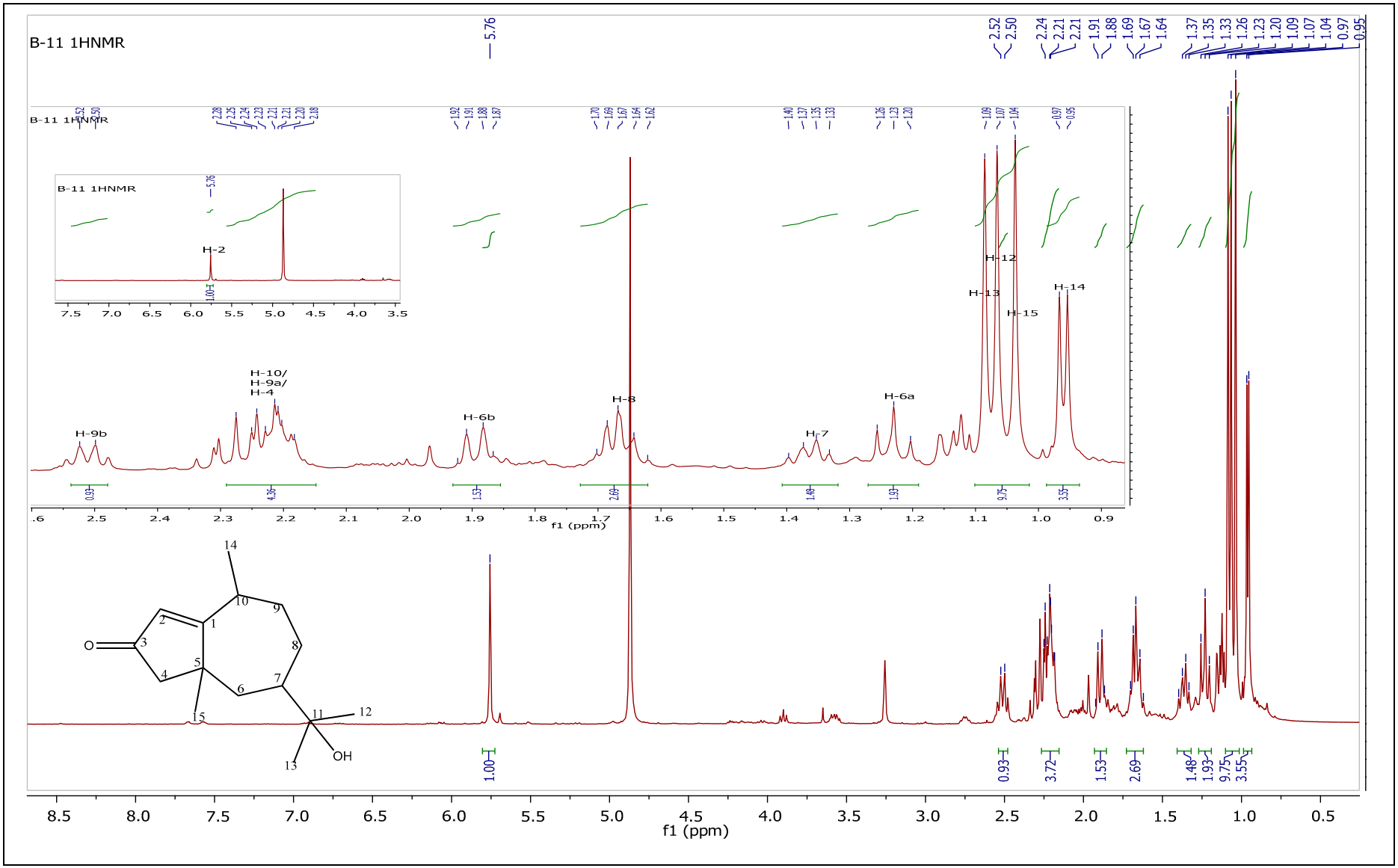


Fig. S6. ^{1}H-NMR spectrum (expansion; 0.5-8.5, 0.9-2.6, 3.5-7.5 ppm) of **C3** in CD_3OD.

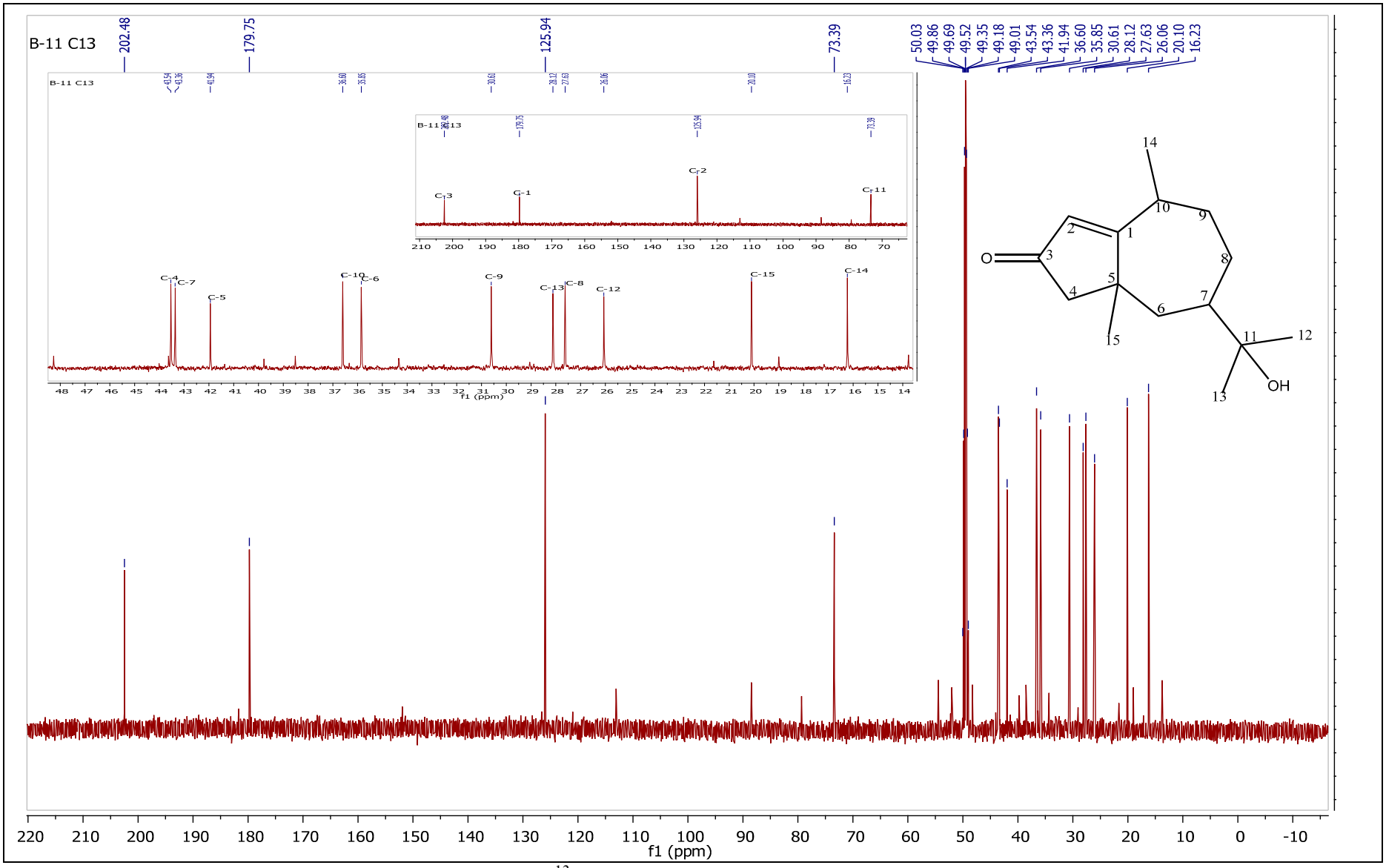


Fig. S7. ^{13}C-NMR spectrum of **C3** in CD_3OD.

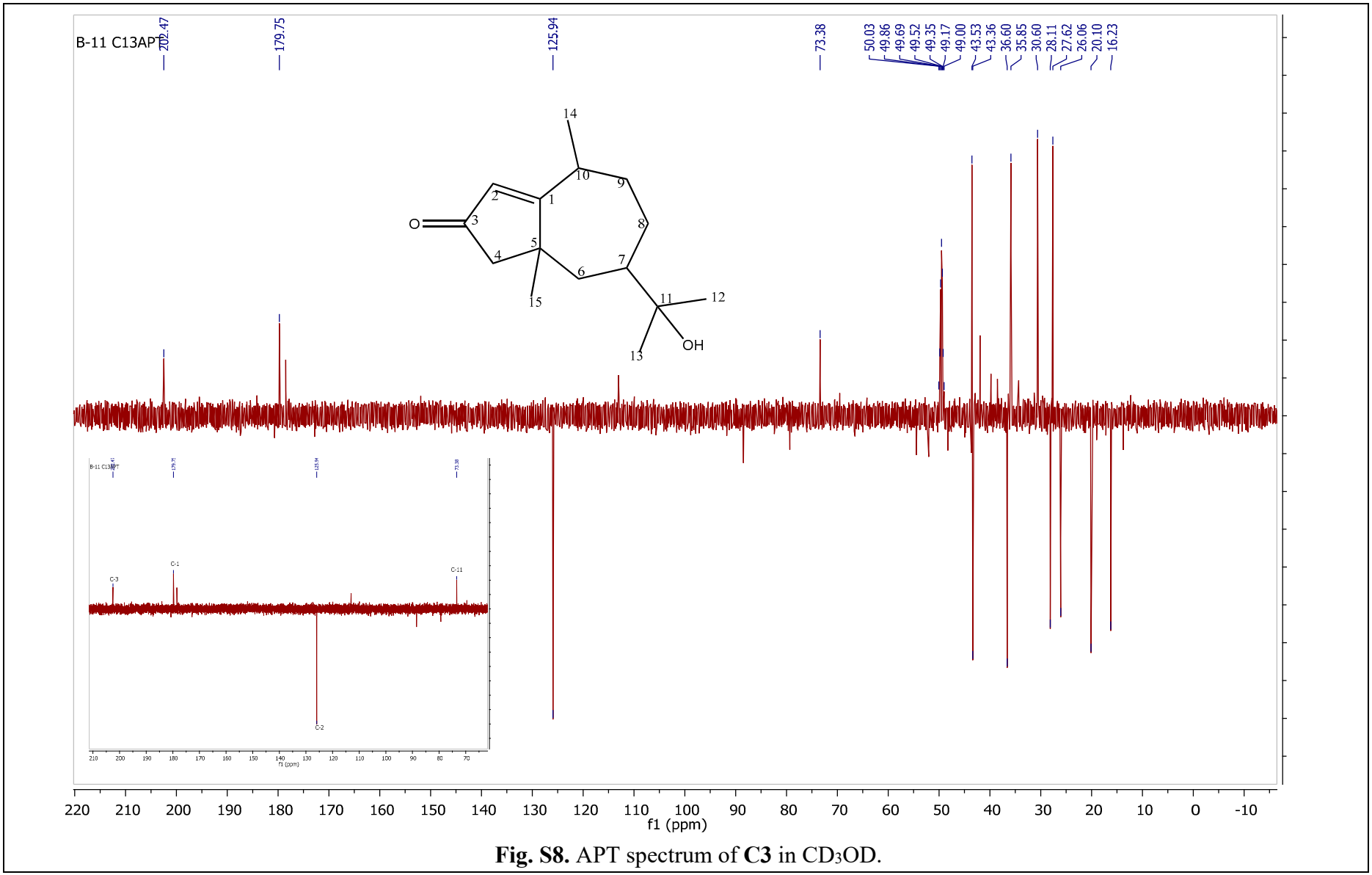


Fig. S8. APT spectrum of **C3** in CD_3OD.

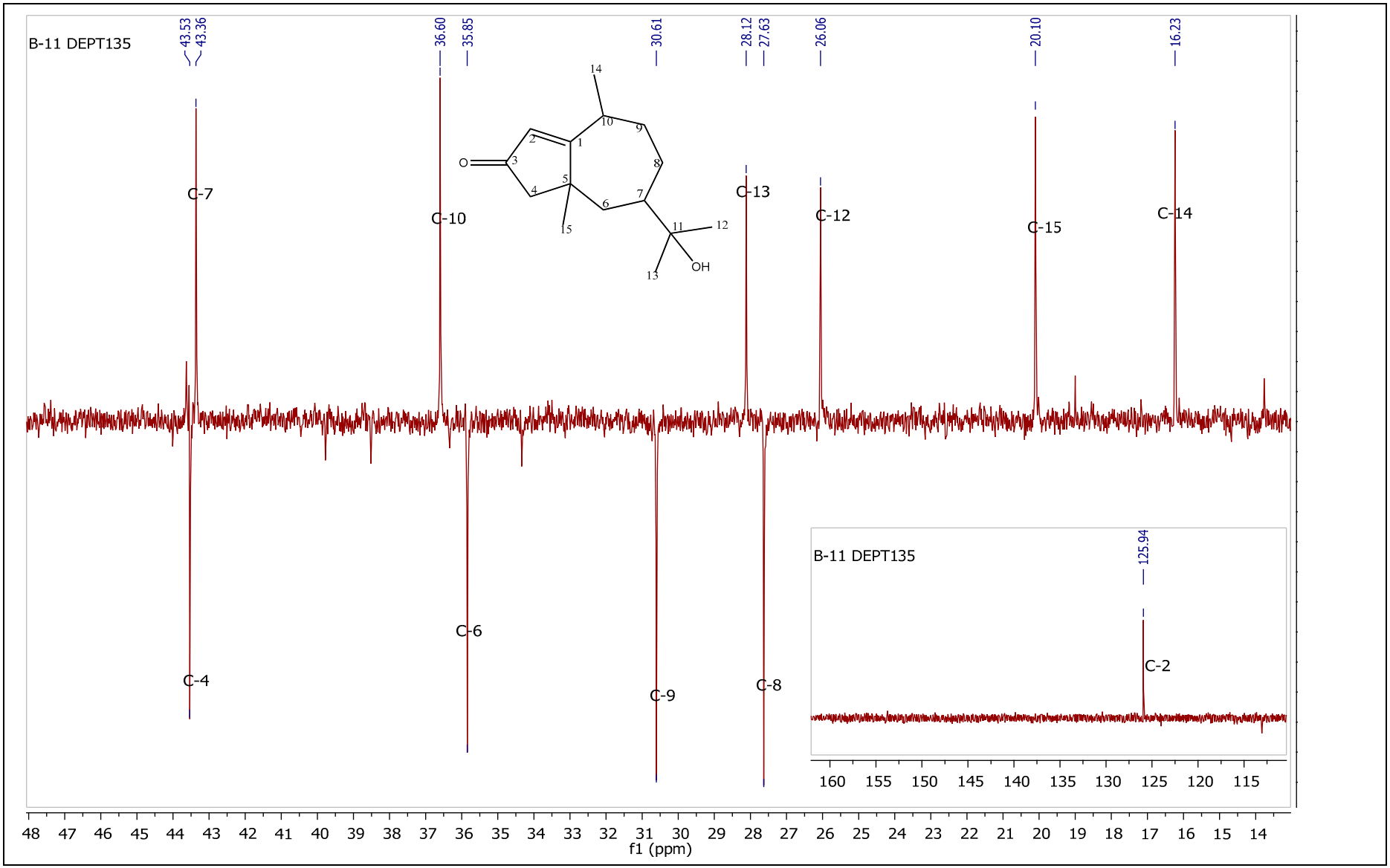
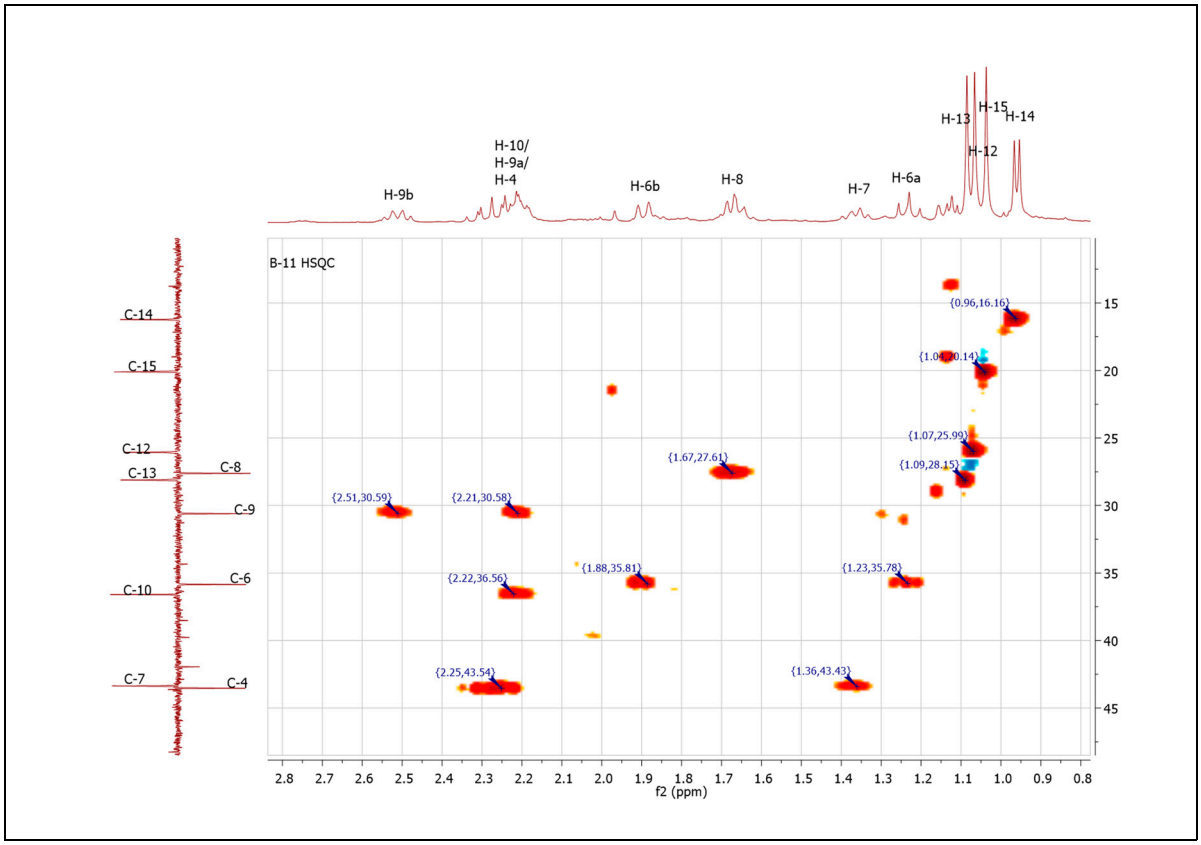
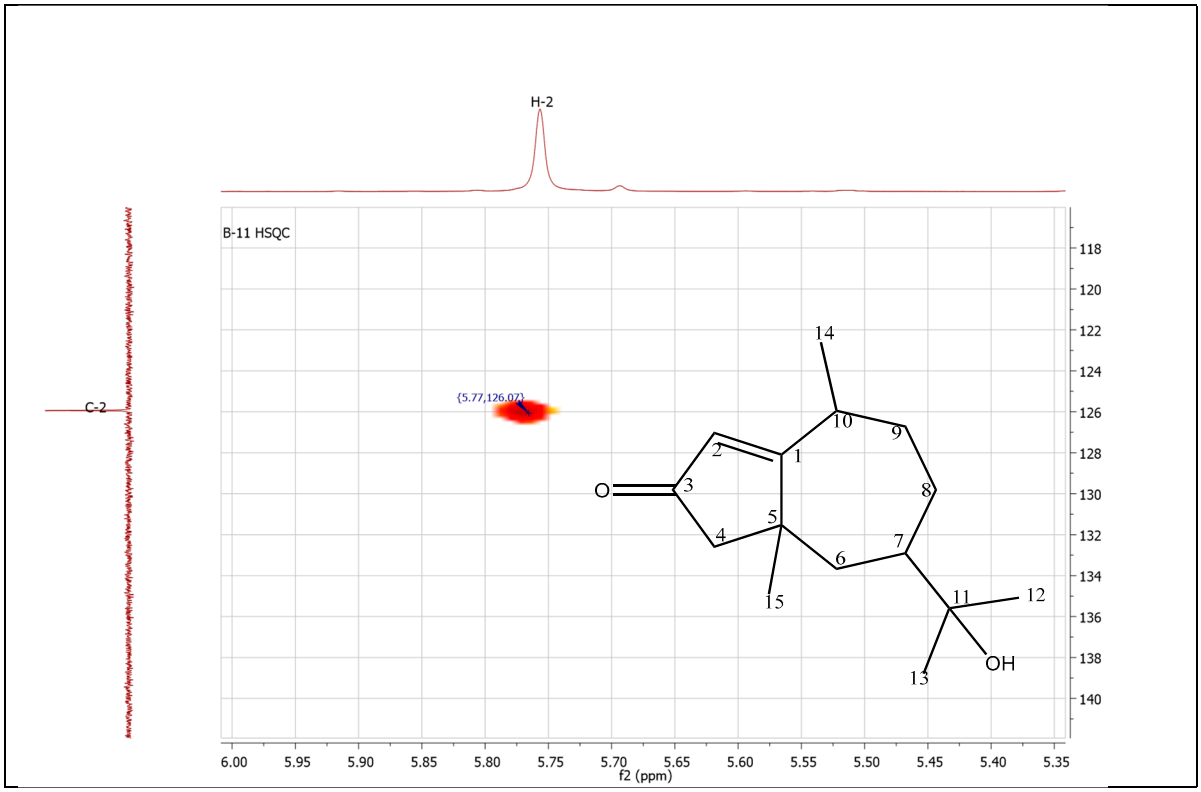


Fig. S9. DEPT spectrum (expansion; 14-48 and 115-160 ppm) of **C3** in CD_3OD.



Expansion; 0.8-2.8 ppm



Expansion; 5.35-6.0 ppm

Fig. S10. HSQC-NMR spectrum (expansion; 0.8-2.8 and 5.35-6.0 ppm) of **C3** in CD_3OD.

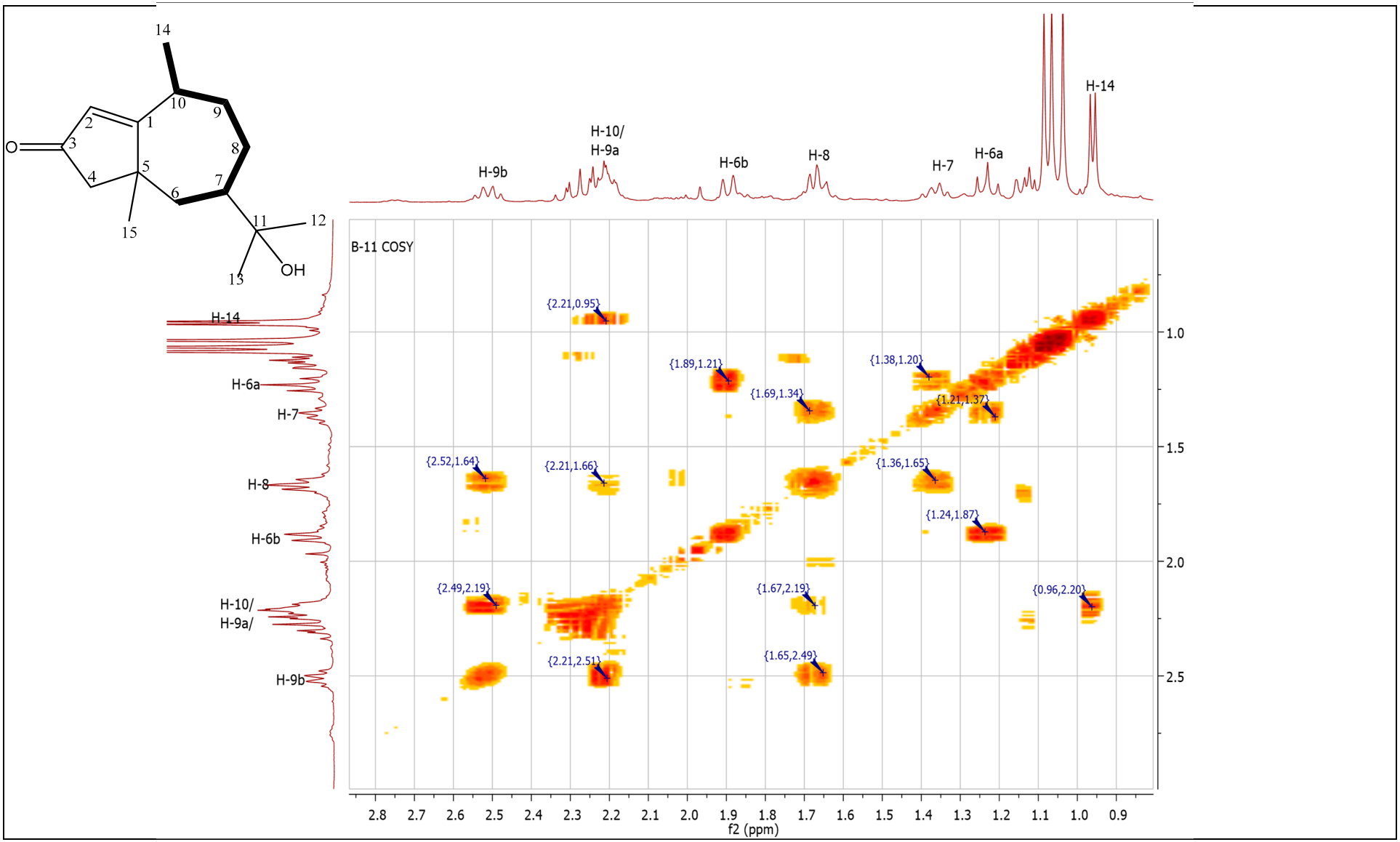


Fig. S11. COSY spectrum (expansion; 0.9-2.8 ppm) of **C3** in CD_3OD.

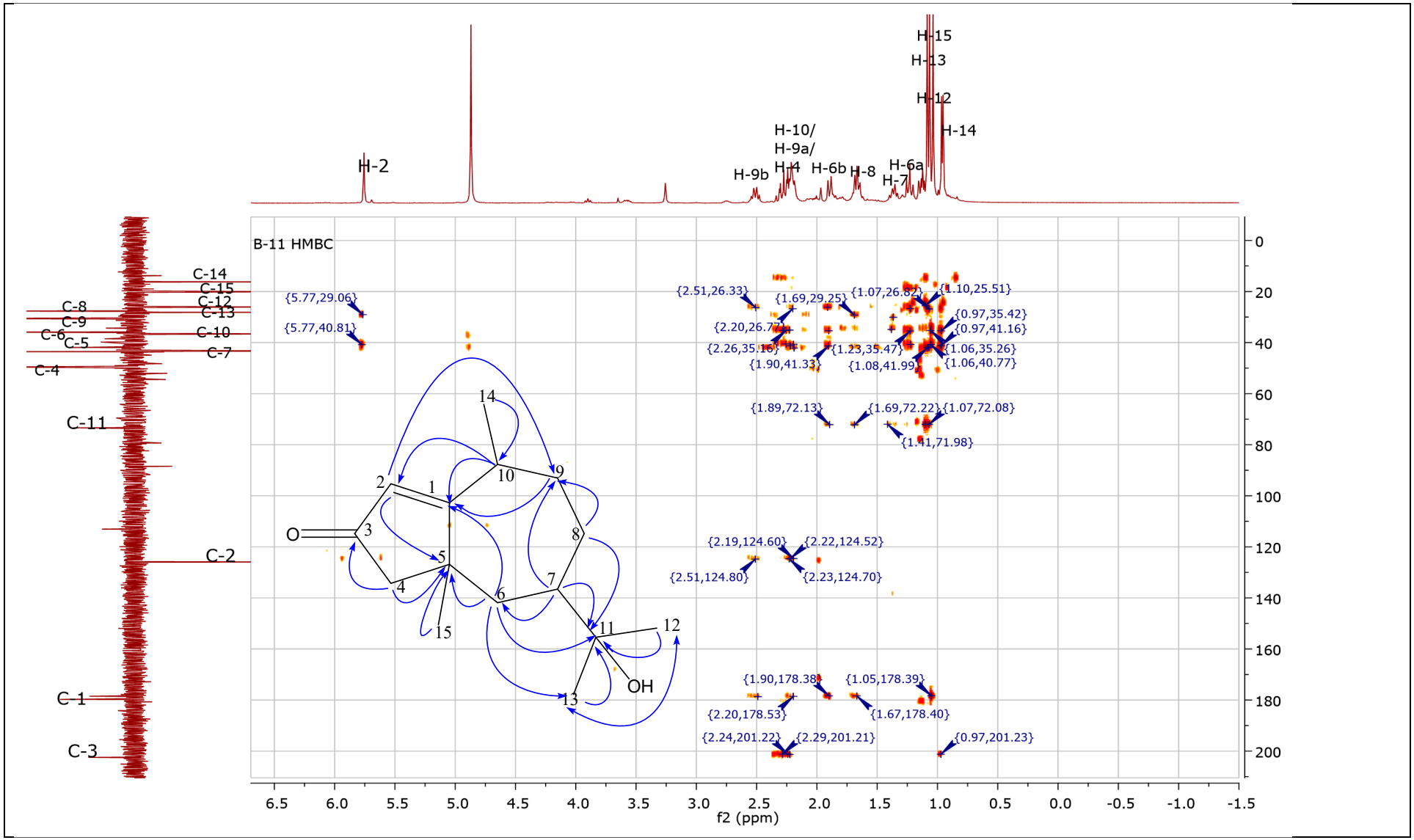
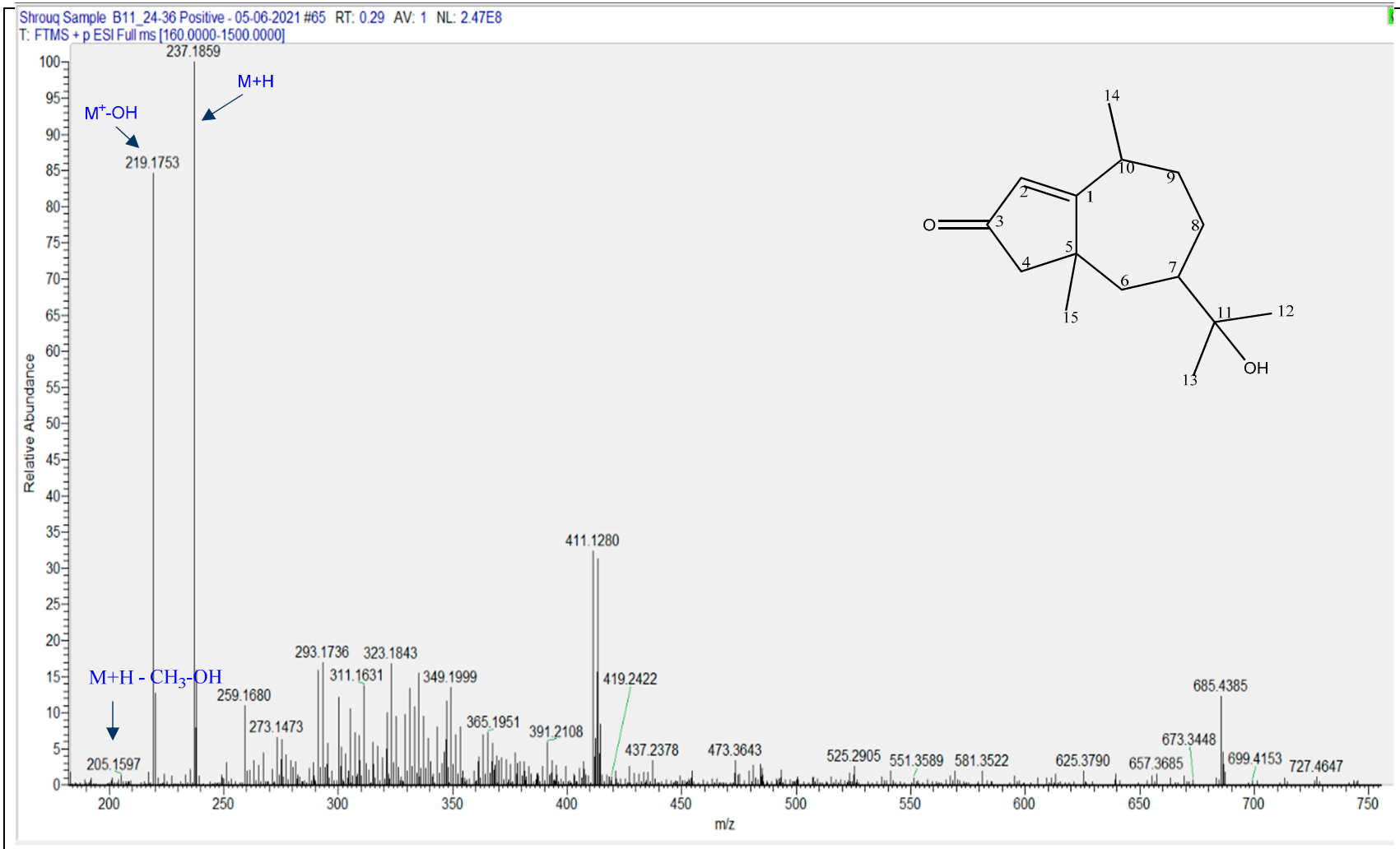


Fig. S12. HMBC spectrum (expansion; -1.5 – 6.5 ppm) of **C3** in CD_3OD.



HR-ESI-MS (+ mode)

Fig. S13. HR-ESI-MS spectrum (positive mode) of **C3**.

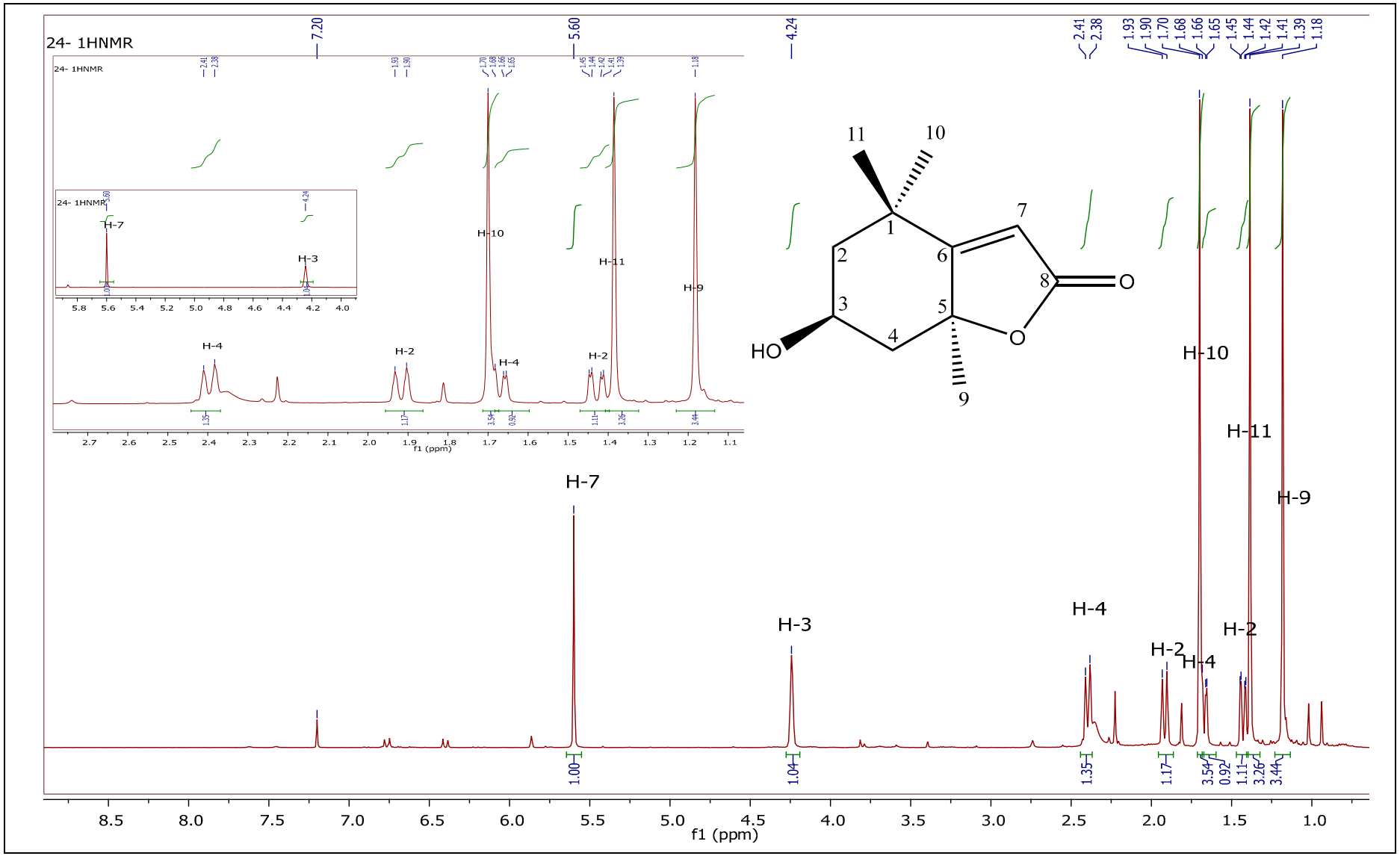


Fig. S14. ^{1}H-NMR spectrum of **C4** in $CDCl_3$.

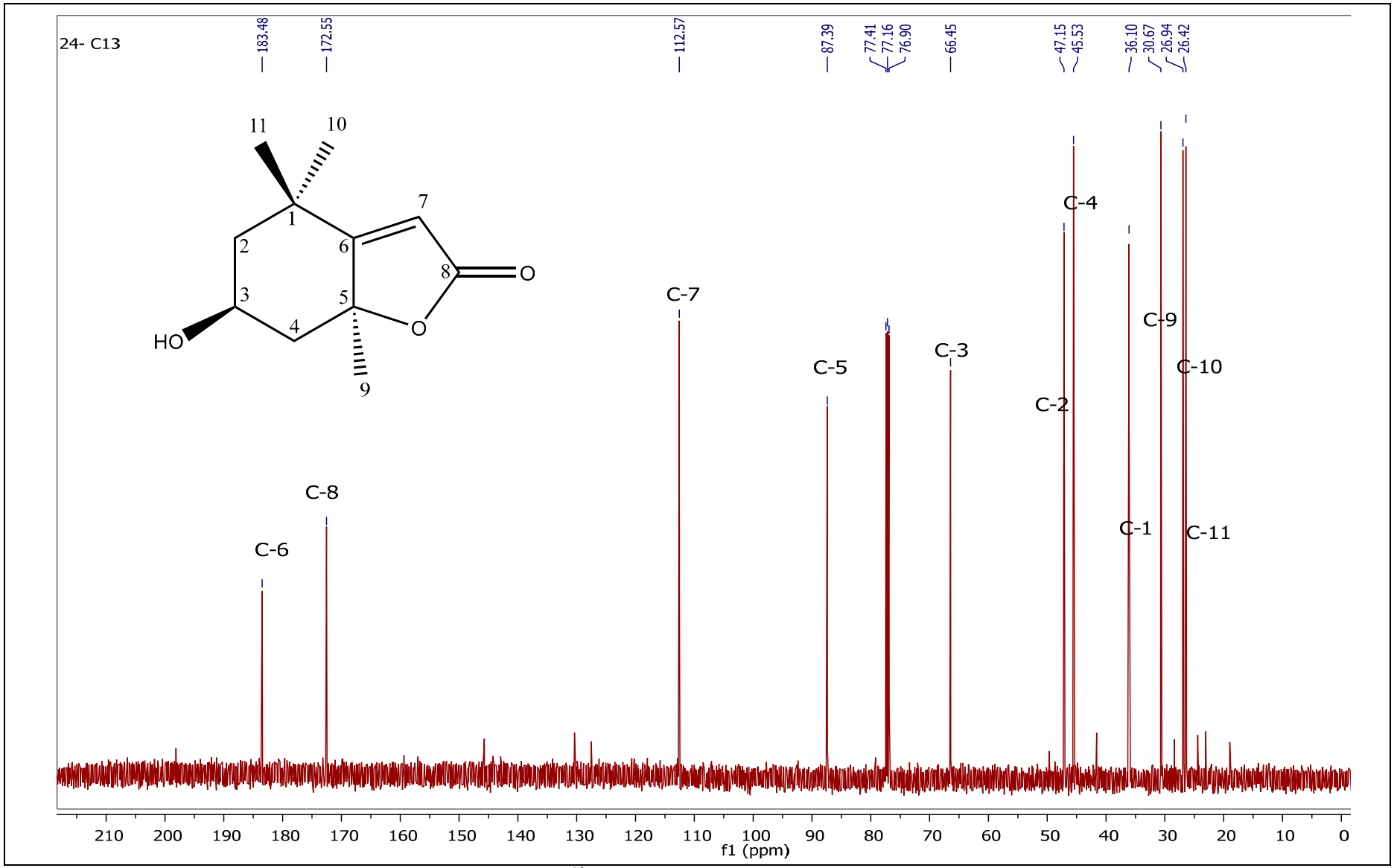


Fig. S15. ^{13}C-NMR spectrum of **C4** in $CDCl_3$.

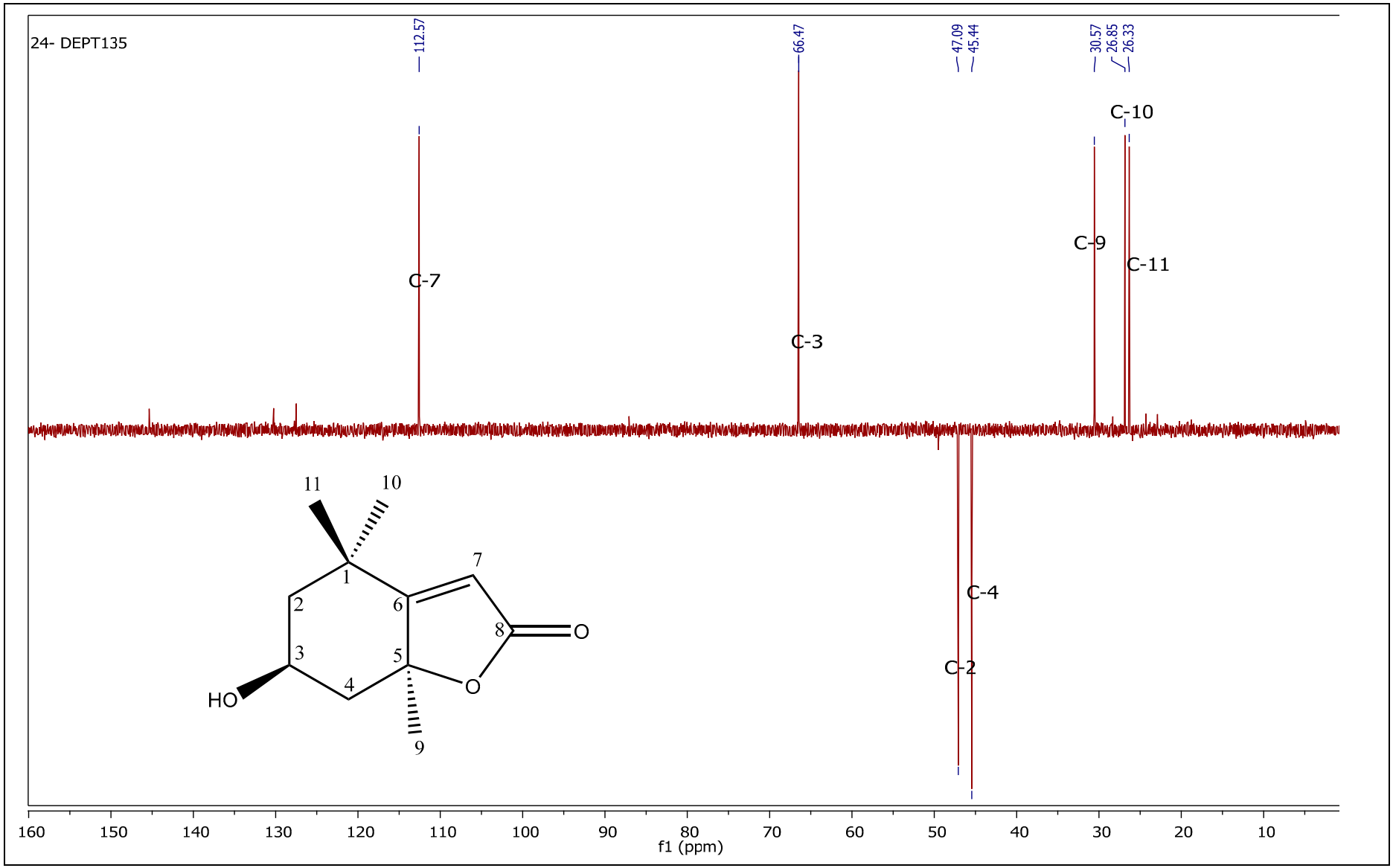
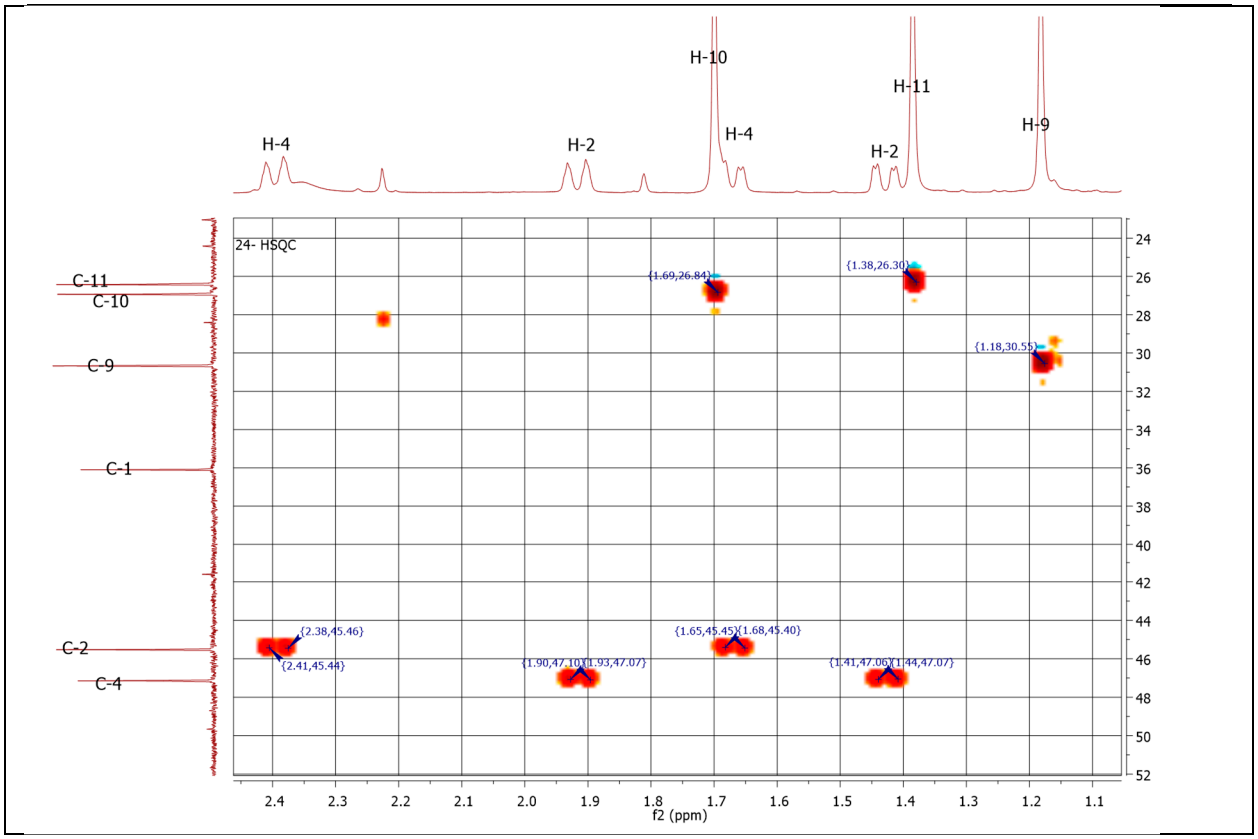
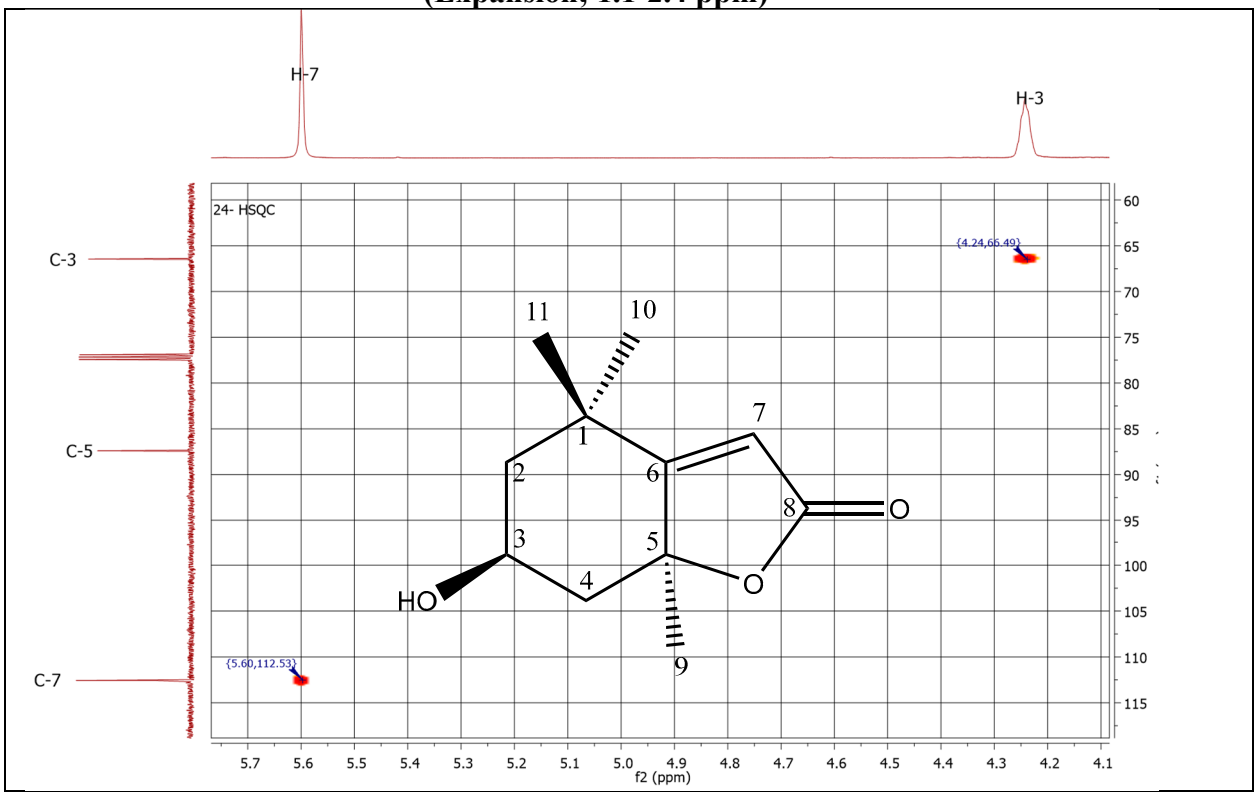


Fig. S16. DEPT spectrum of **C4** in $CDCl_3$.



(Expansion; 1.1-2.4 ppm)



(Expansion; 4.1-5.7 ppm)

Fig. S17. HSQC spectrum (expansion; 1.1-2.4 ppm and 4.1-5.7 ppm) of **C4** in $CDCl_3$.

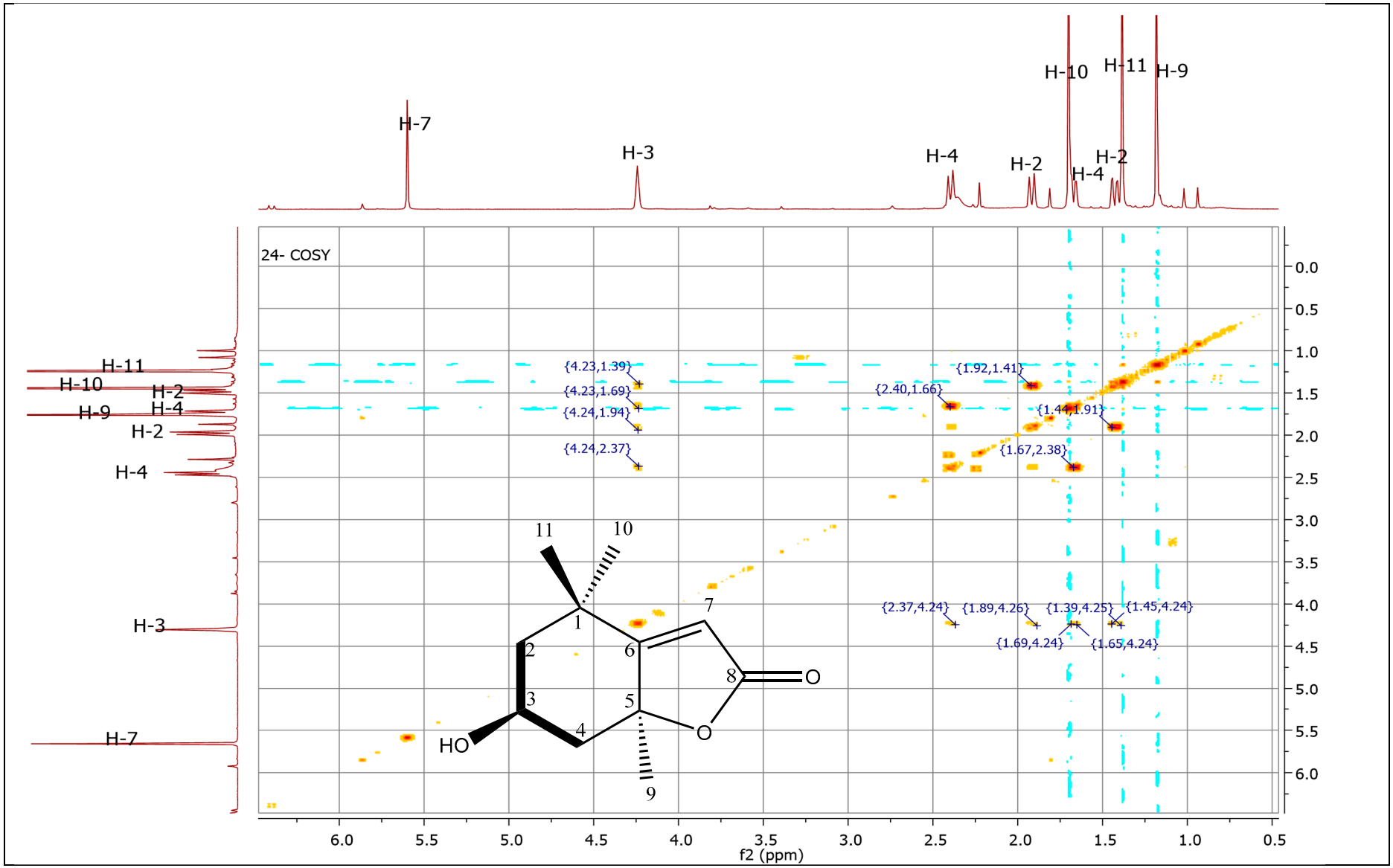
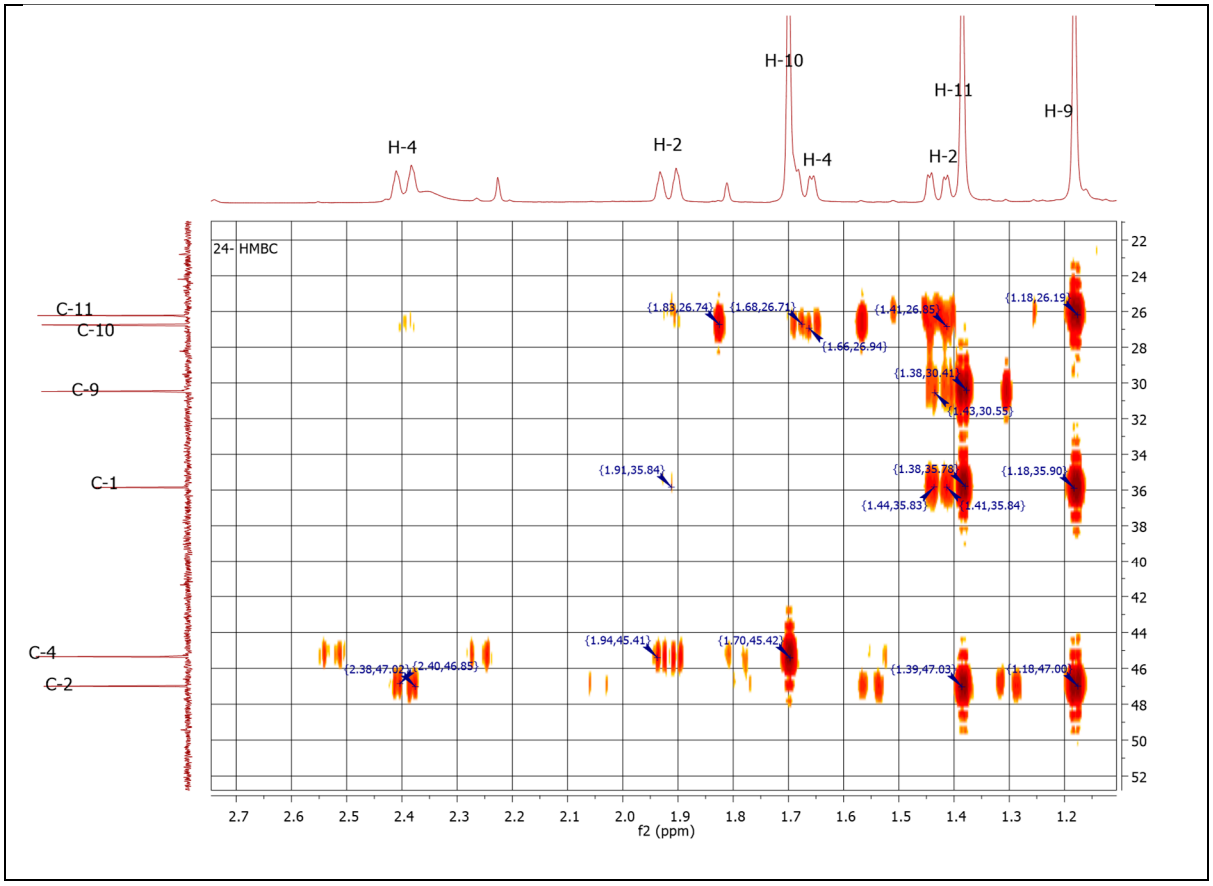
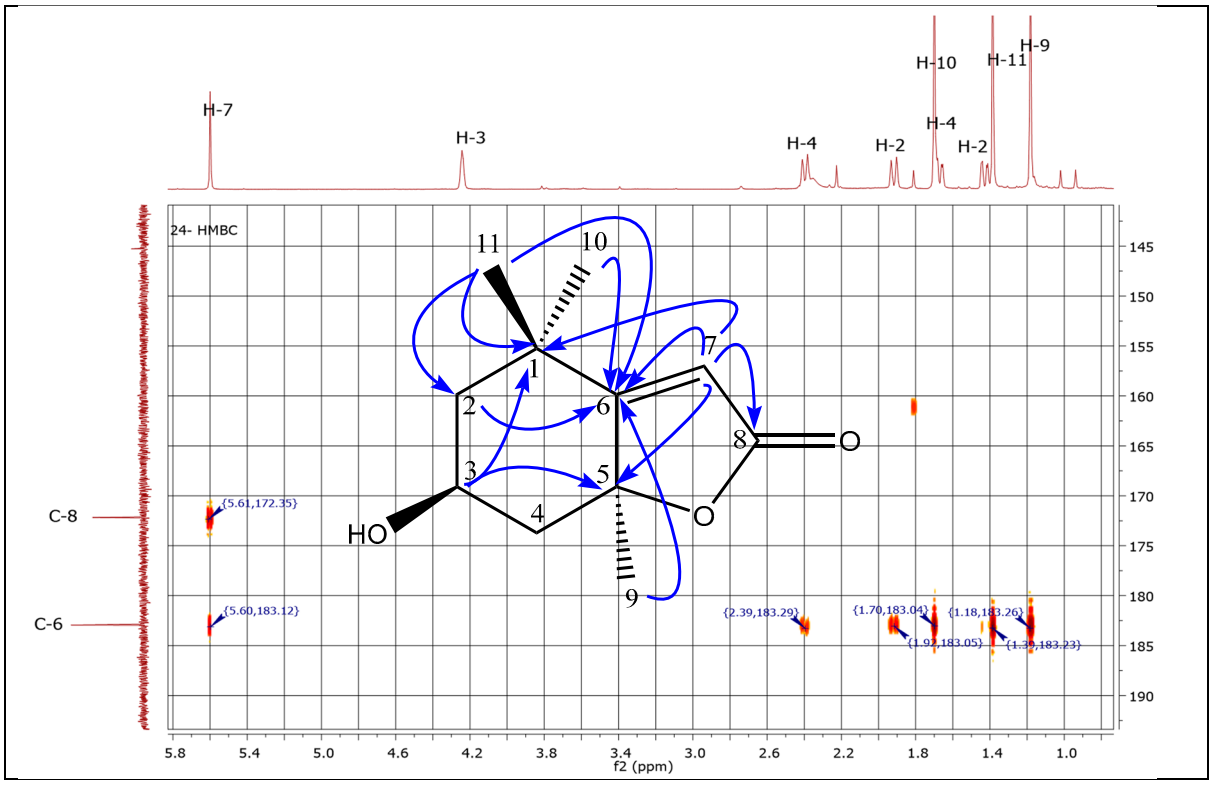


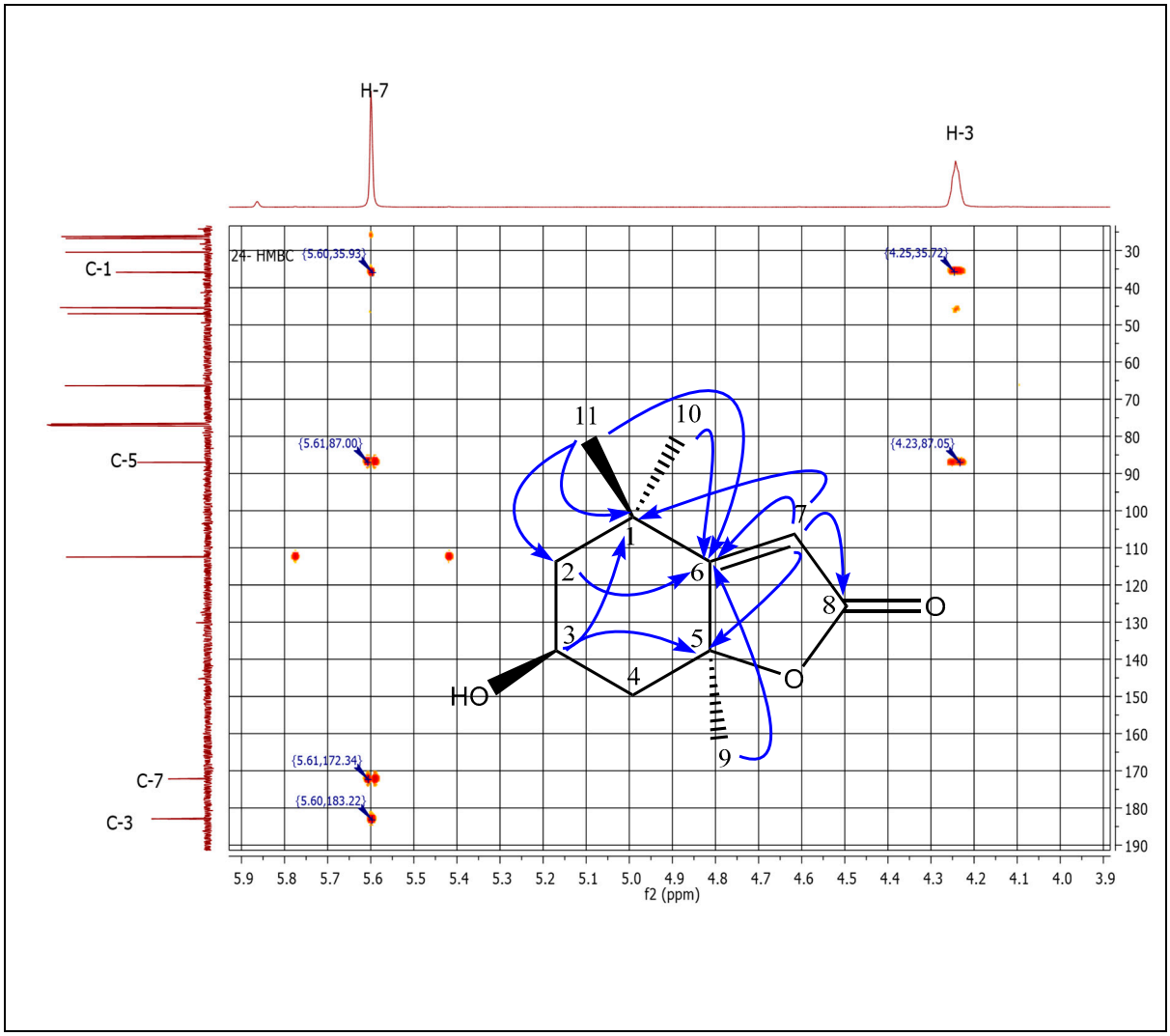
Fig. S18. COSY spectrum (expansion; 0.5-6.5 ppm) of **C4** in $CDCl_3$.



A. Expansion; 1.0-2.7 ppm



B. Expansion; 1.0-5.8 ppm



C. Expansion; 3.9-5.9 ppm

Fig. S19. HMBC spectrum (expansion; A. 1.0-2.7, B. 1.0-5.8, and C. 3.9-5.9 ppm) of **C4** in $CDCl_3$.

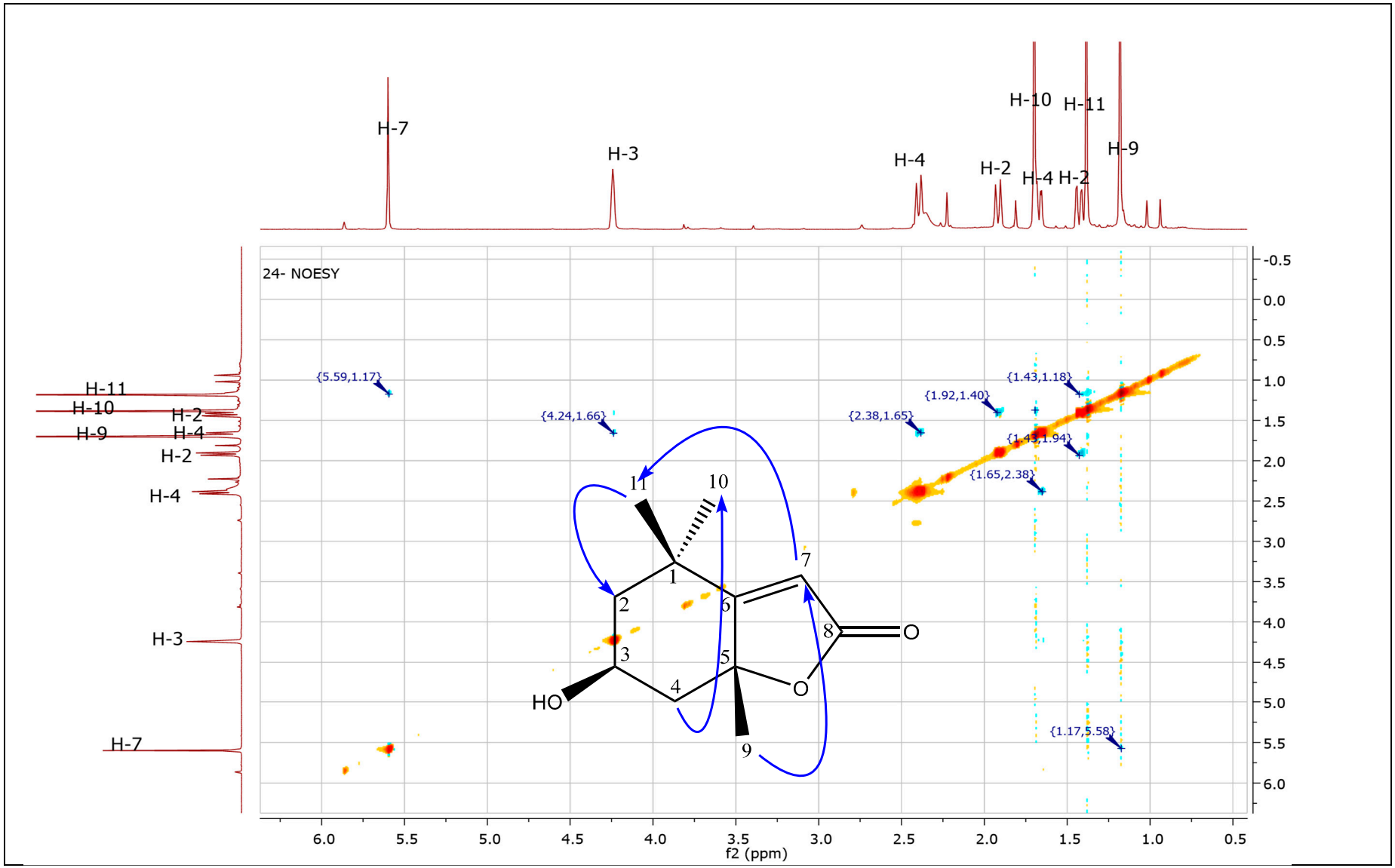


Fig. S20. NOESY spectrum (expansion; 0.5-6.5 ppm) of **C4** in $CDCl_3$.

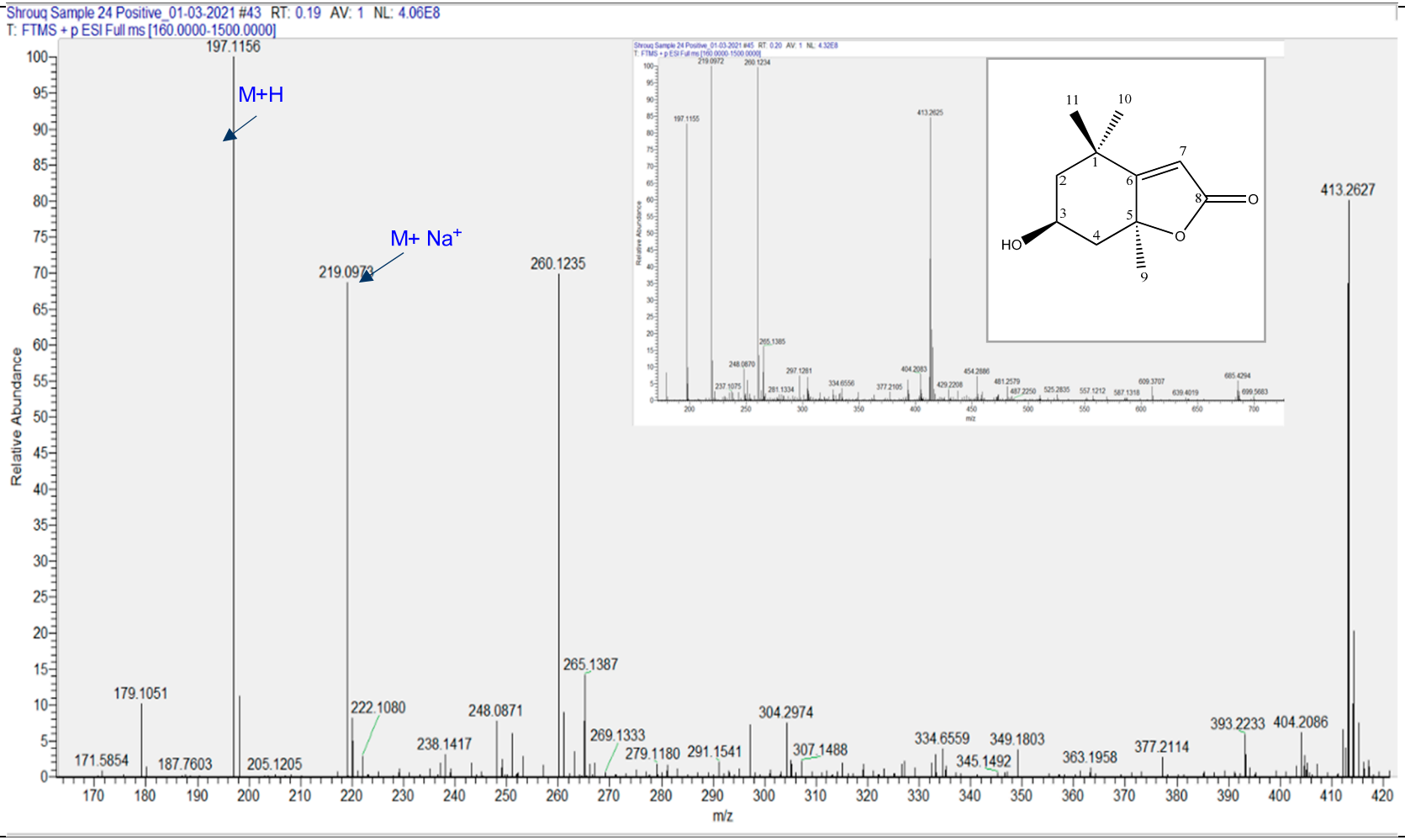


Fig. S21. HR-ESI-MS (+ mode) spectrum (expansion; 170-420 *m/z*) of **C4** in $CDCl_3$.

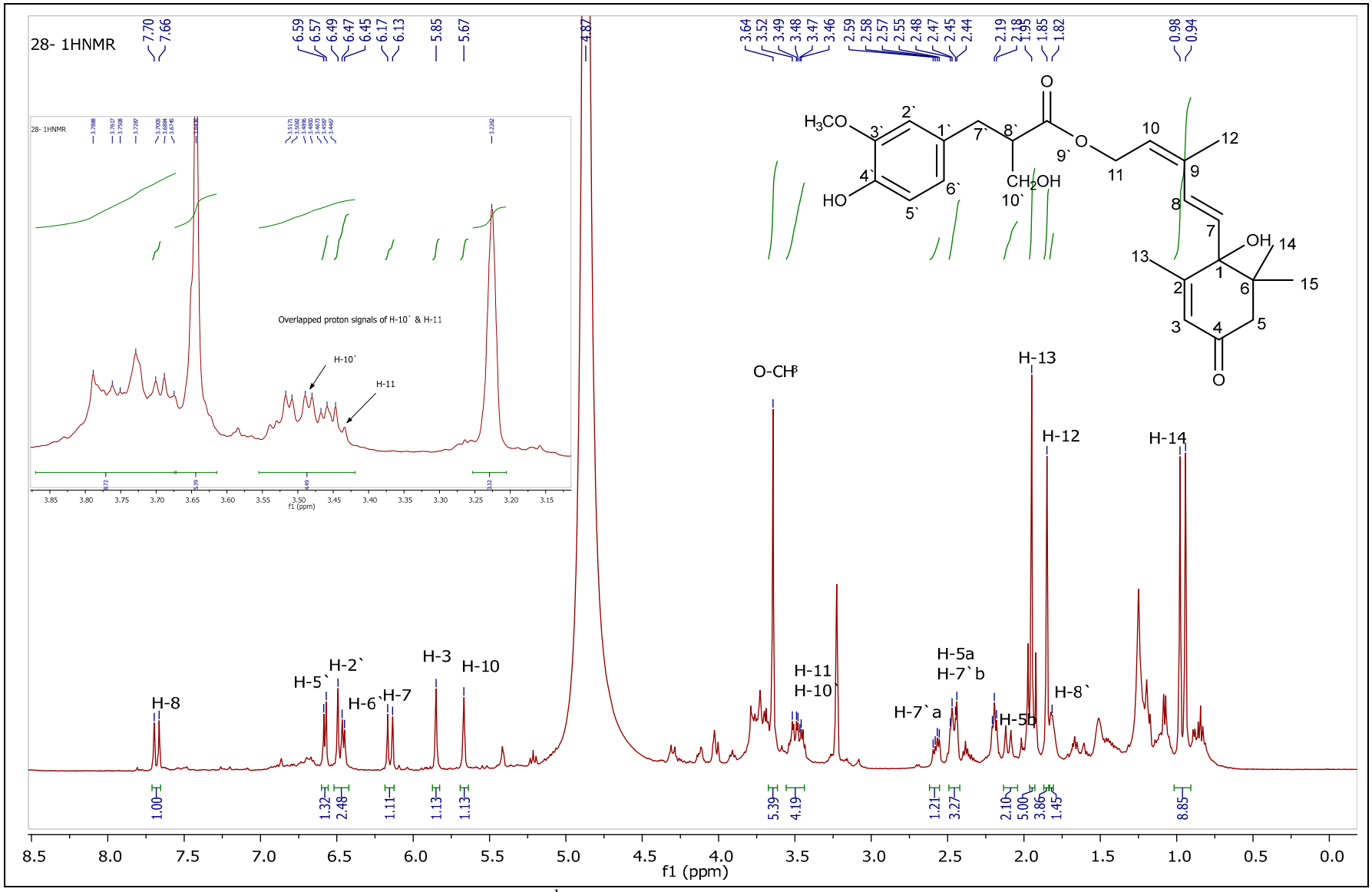


Fig. S22. ^{1}H-NMR spectrum of **C5** in CD_3OD.

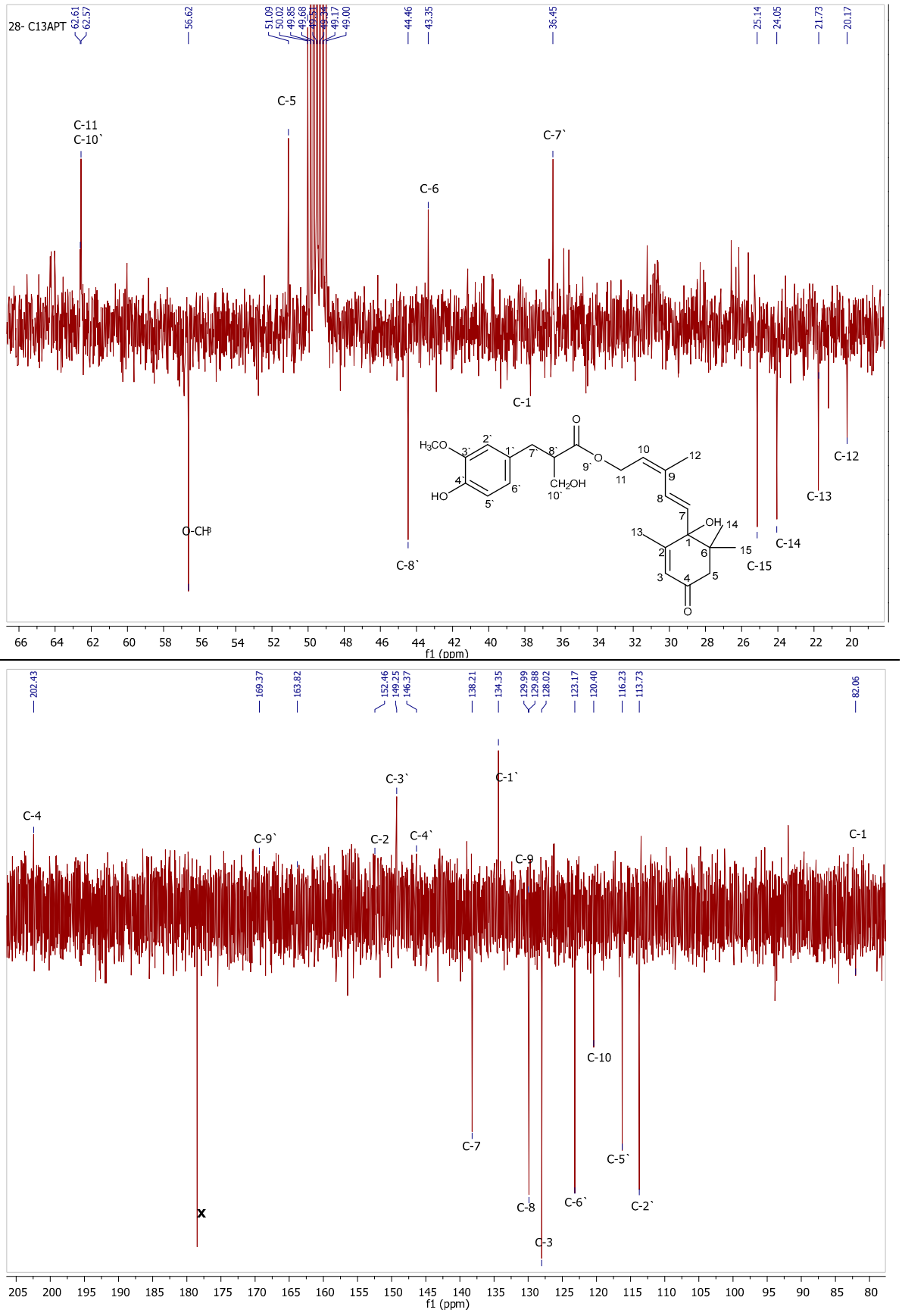


Fig. S23. APT spectrum (expansion; 18-66 and 80-205 ppm) of **C5** in CD_3OD.

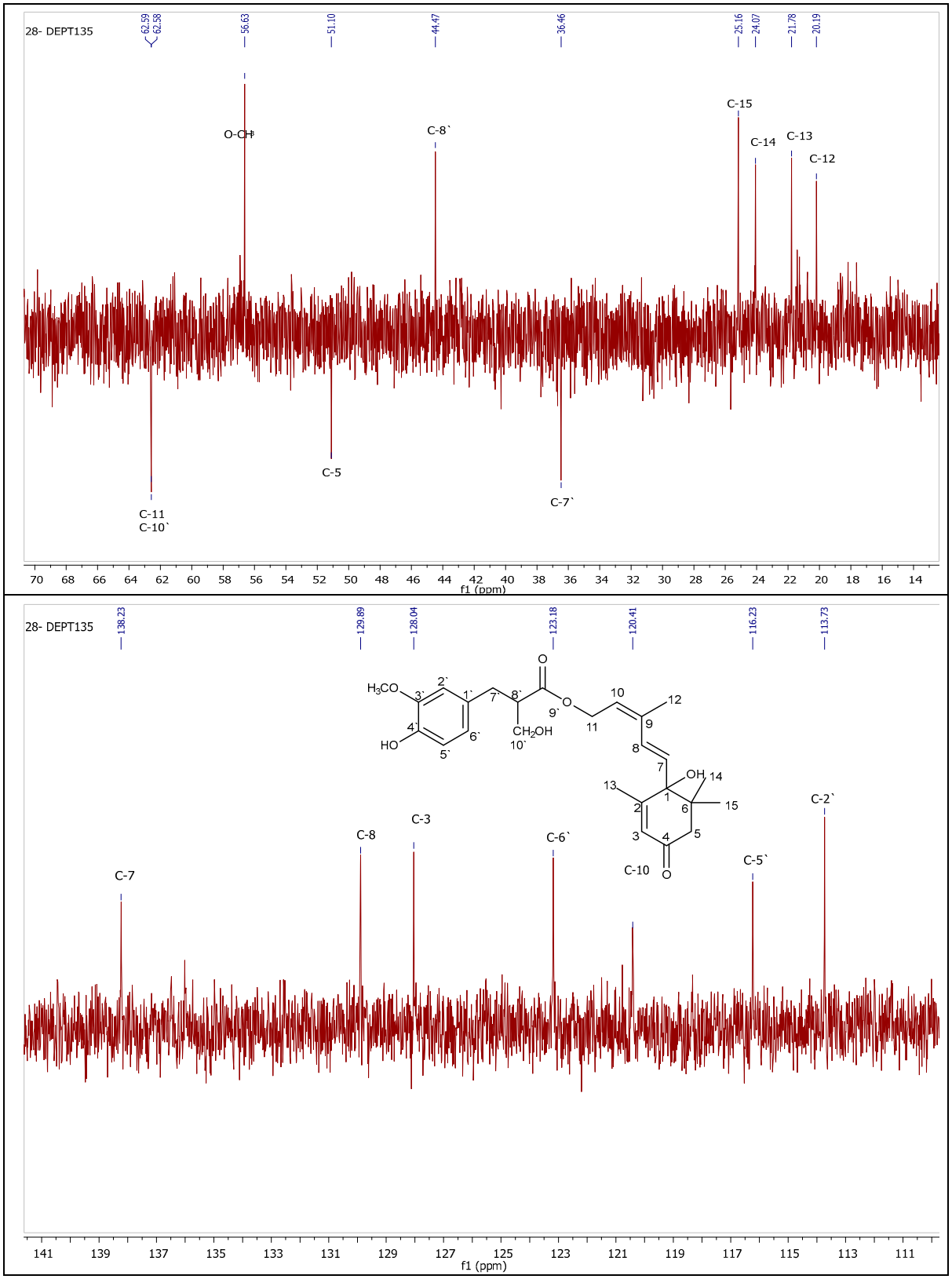
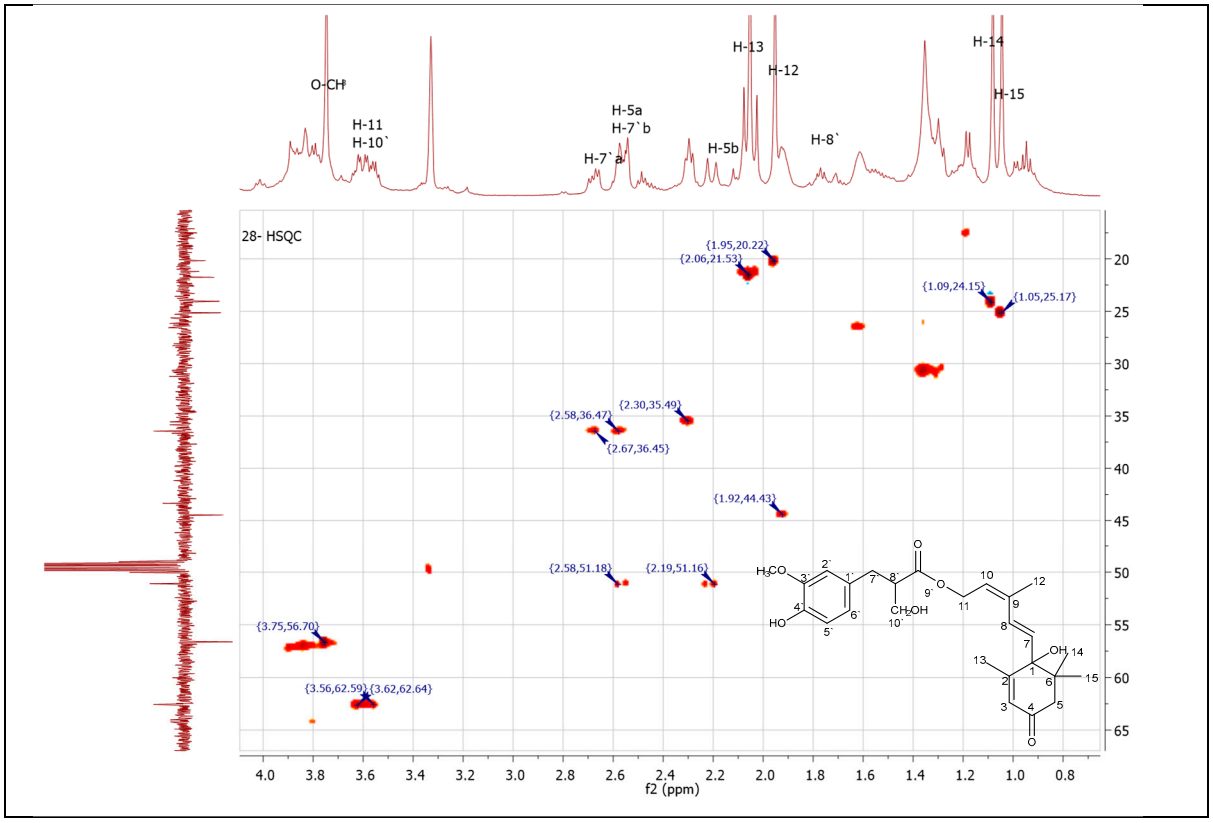
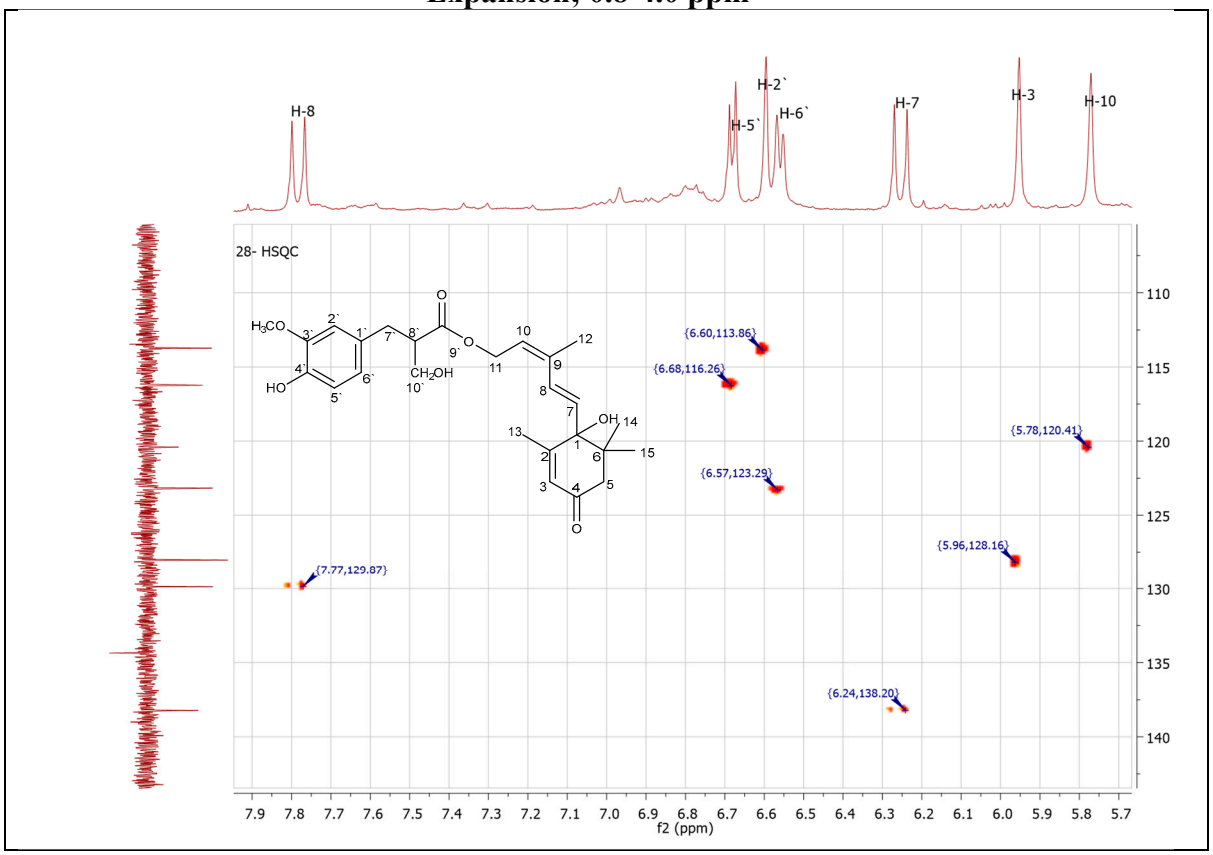


Fig. S24. DEPT spectrum (expansion; 12-70 and 111-141 ppm) of **C5** in CD_3OD.



Expansion; 0.8-4.0 ppm



Expansion; 5.7-7.9 ppm

Fig. S25. HSQC spectrum (expansion; 0.8-4.0 and 5.7-7.9 ppm) of **C5** in CD_3OD.

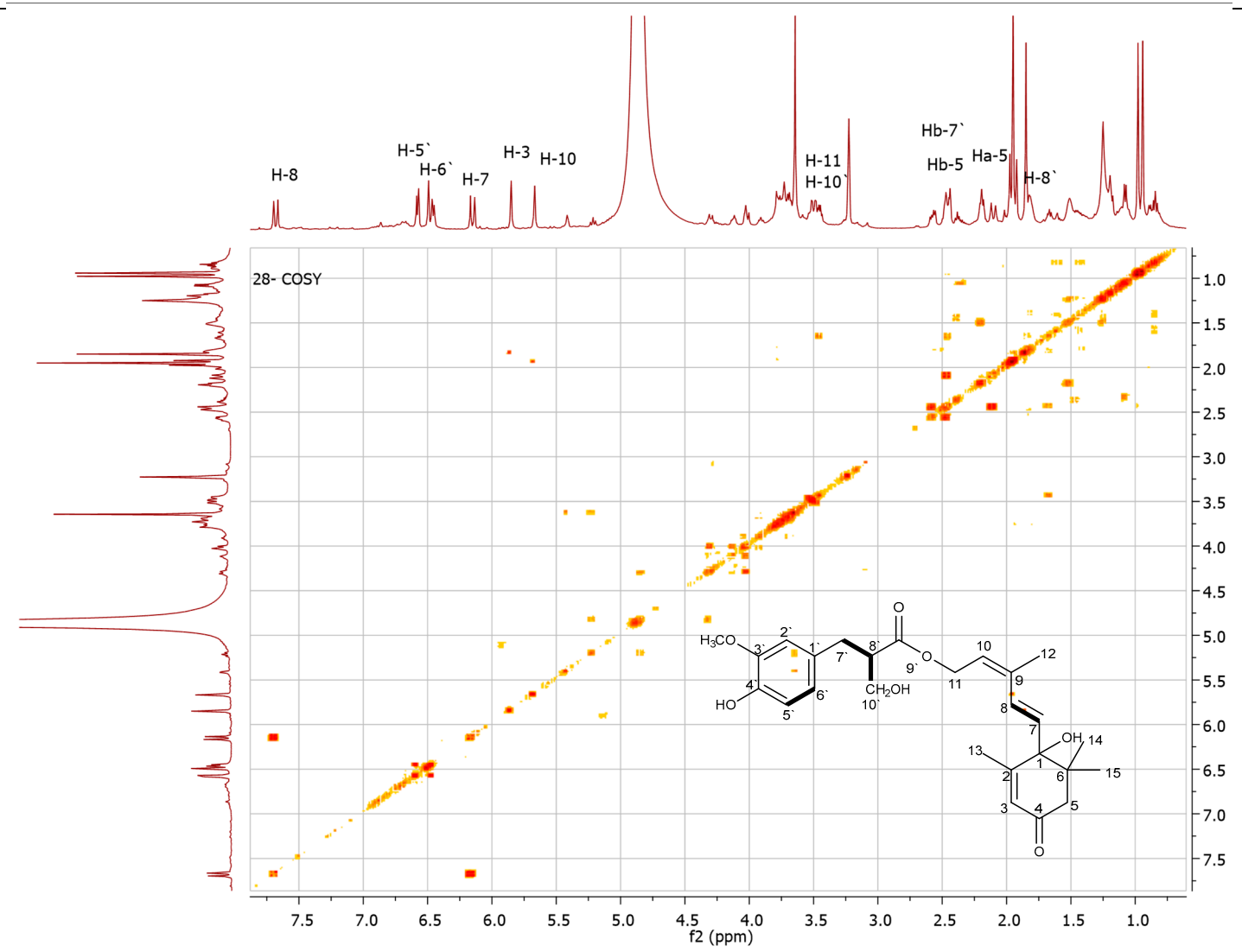


Fig. S26. COSY spectrum of **C5** in CD_3OD.

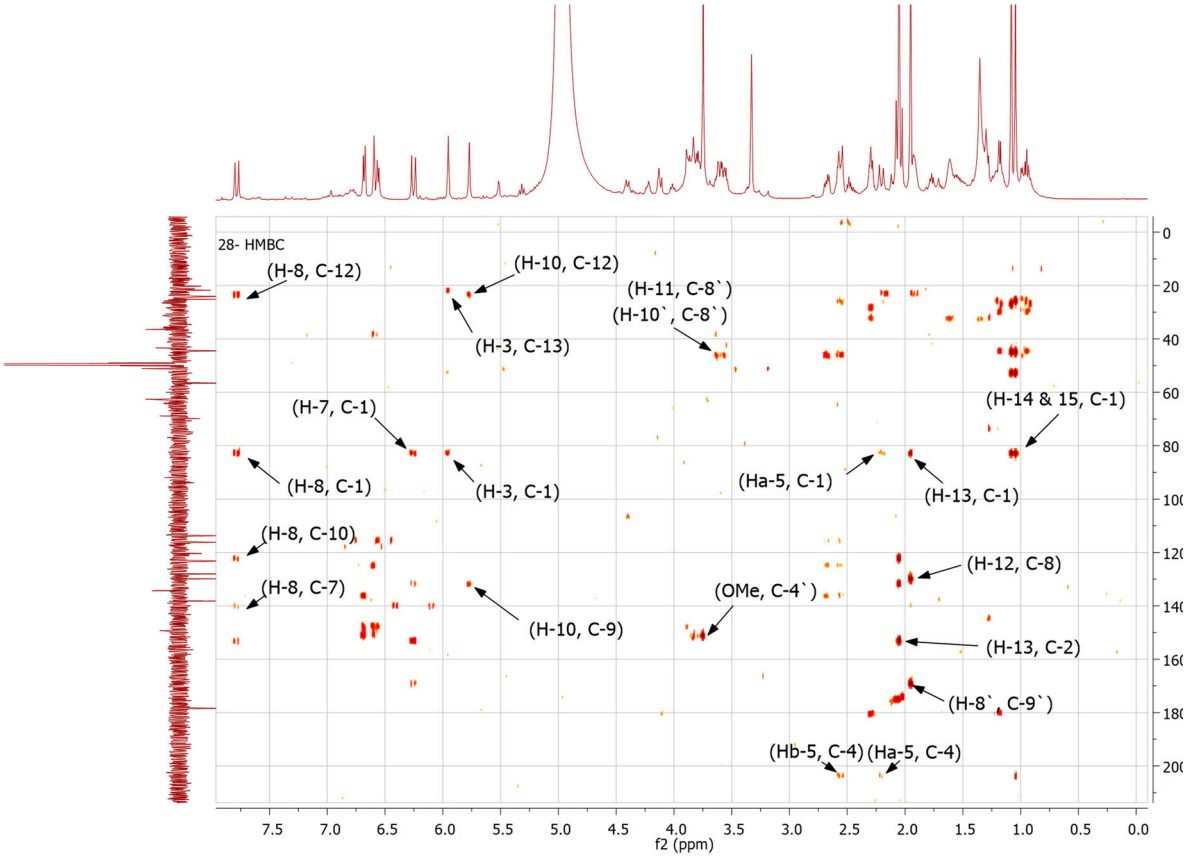


Fig. S27. HMBC spectrum of compound **C5** in CD_3OD.

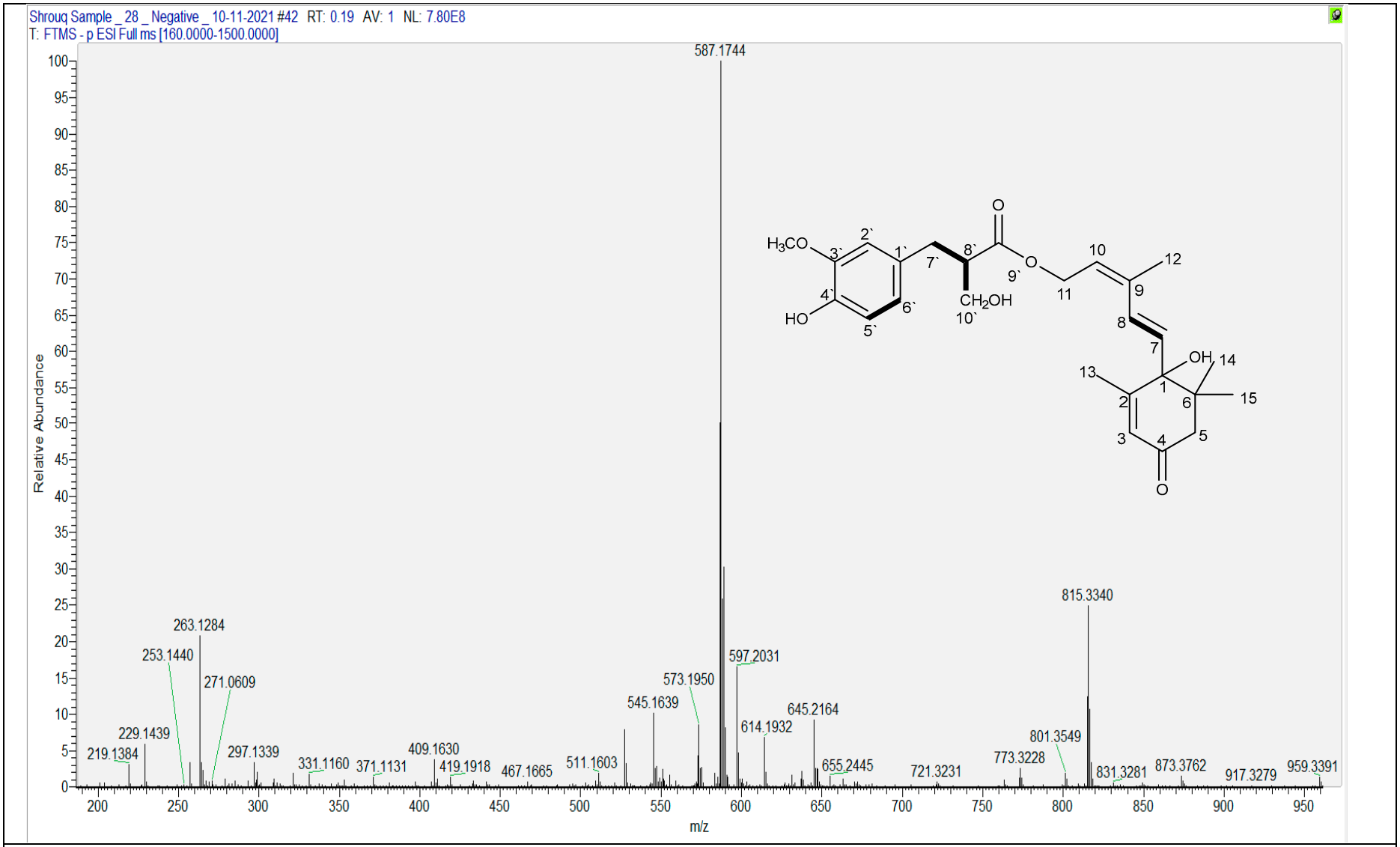


Fig. S28. HR-ESI-MS (- mode) spectrum (expansion; 200-800 *m/z*) of **C5** in CD_3OD.

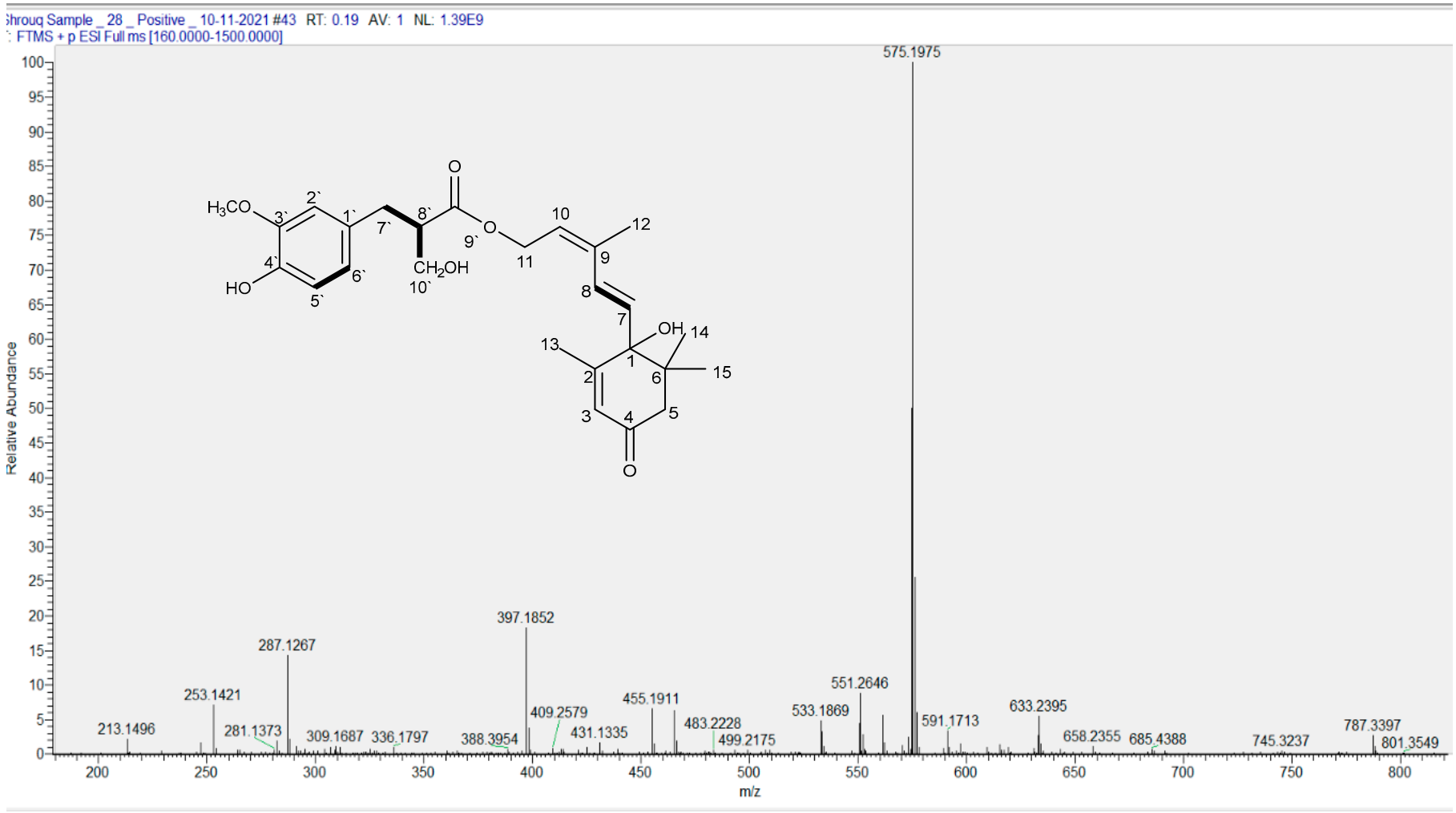


Fig. S29. HR-ESI-MS (+ mode) spectrum (expansion; 200-800 *m/z*) of **C5** in CD_3OD.

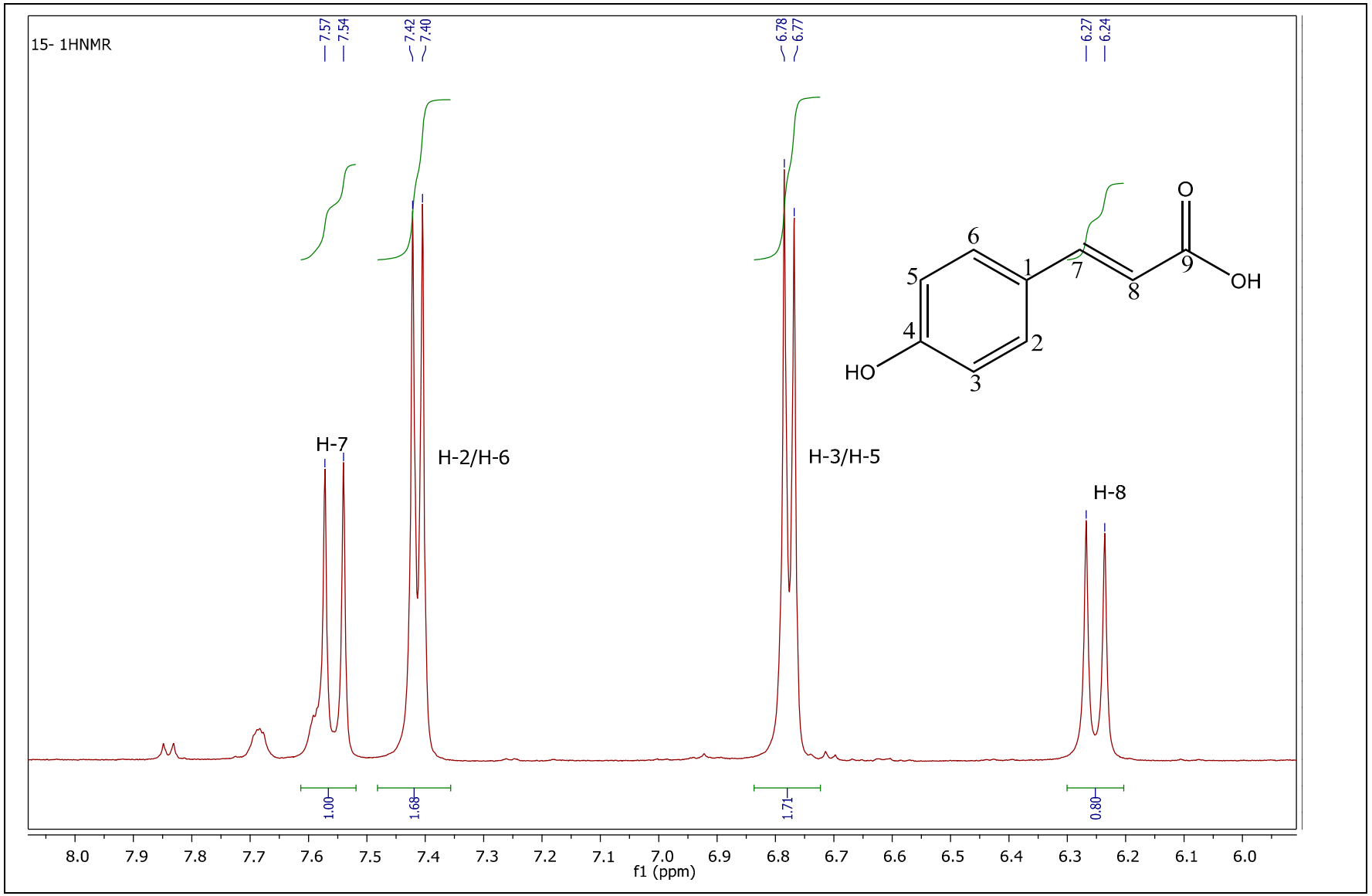


Fig. S30. ^{1}H-NMR spectrum (expansion; 6.0-8.0 ppm) of **C6** in CD_3OD.

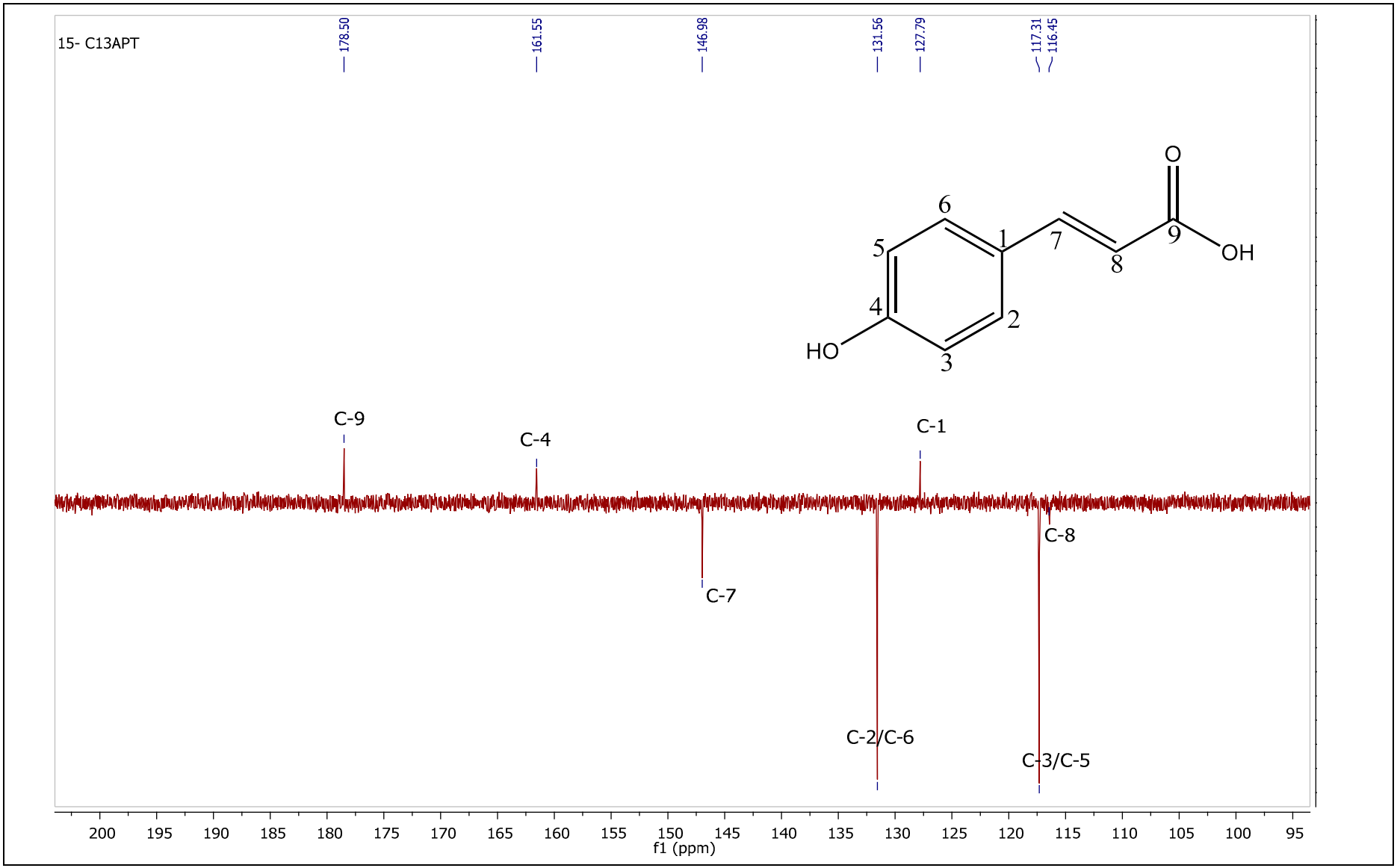


Fig. S31. APT spectrum (expansion; 95-200 ppm) of **C6** in CD_3OD.

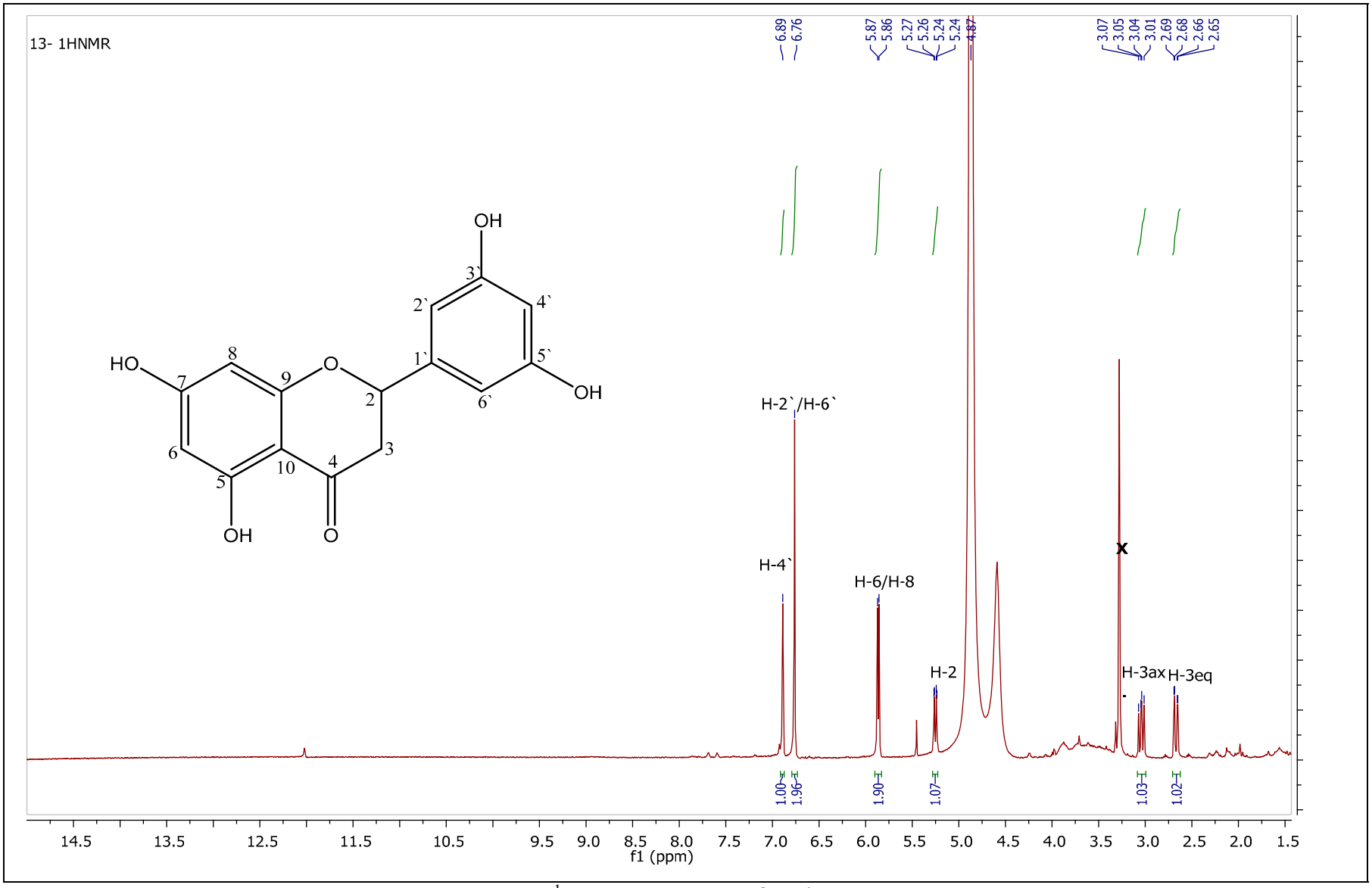


Fig. S32. ^{1}H-NMR spectrum of **C7** in CD_3OD.

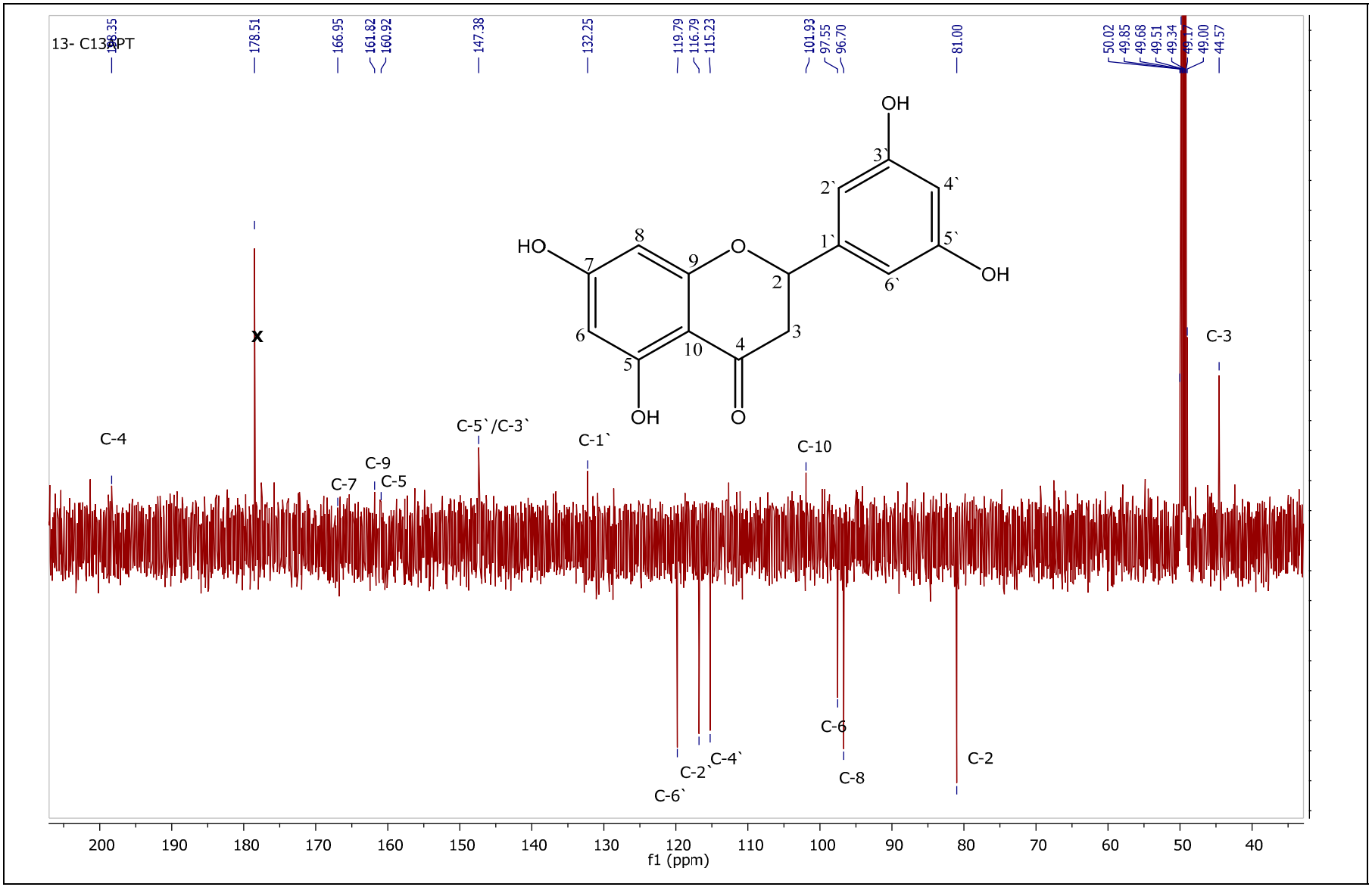


Fig. S33. APT spectrum (expansion; 30-210 ppm) of **C7** in CD_3OD.

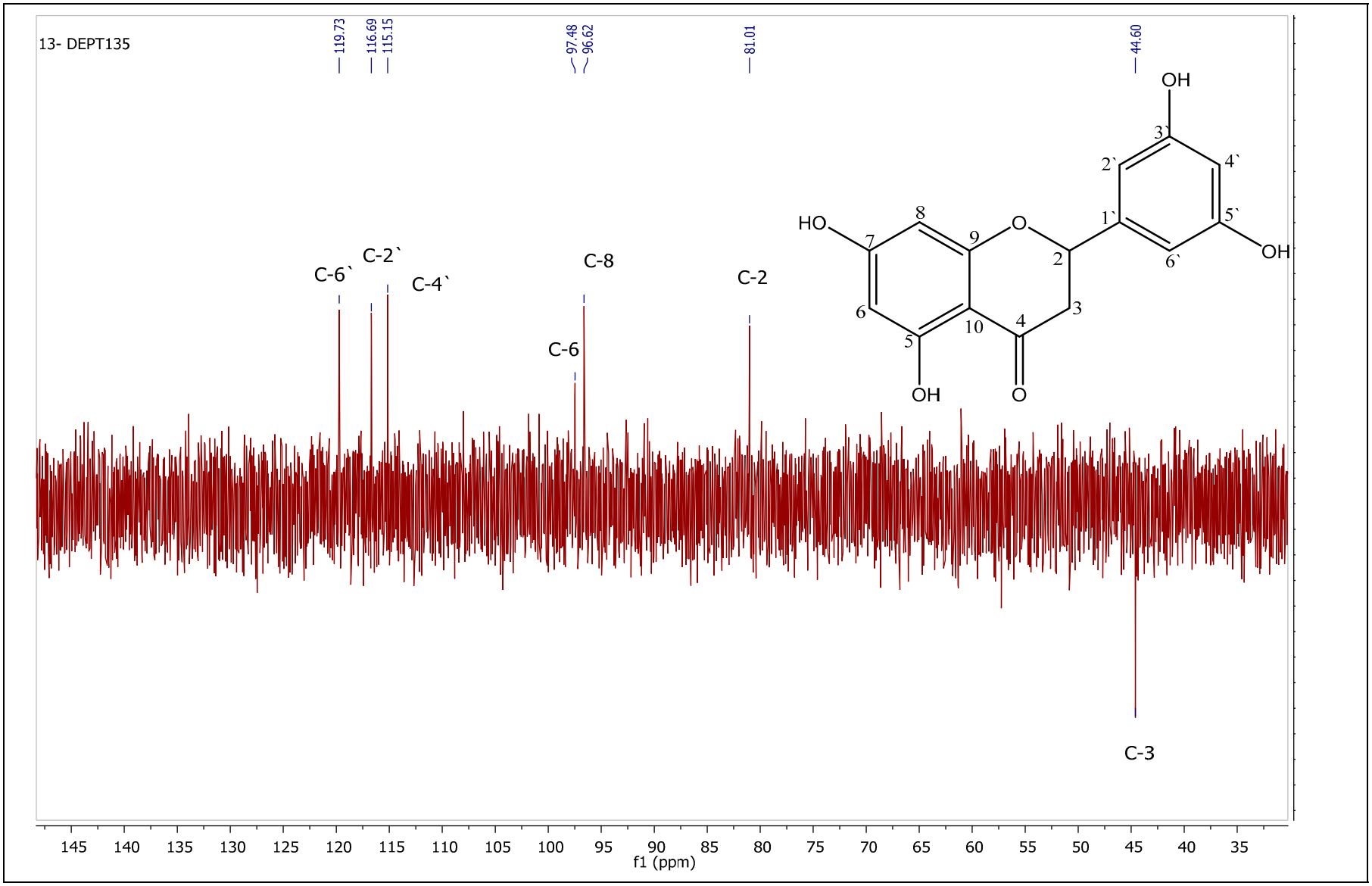


Fig. S34. DEPT spectrum (expansion; 30-145 ppm) of **C7** in CD_3OD.

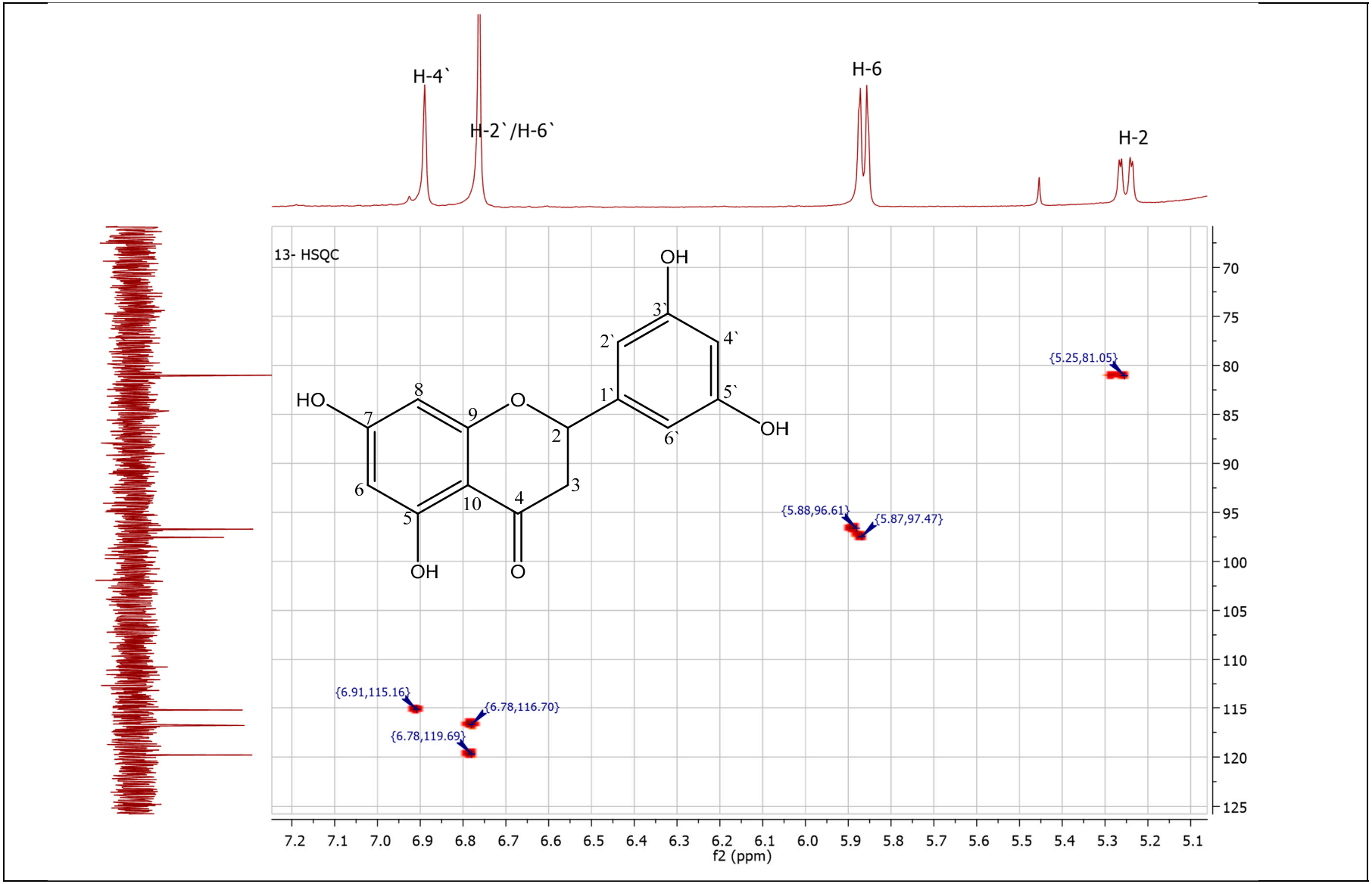


Fig. S35. HSQC spectrum (expansion; 5.1-7.2 ppm) of **C7** in CD_3OD.

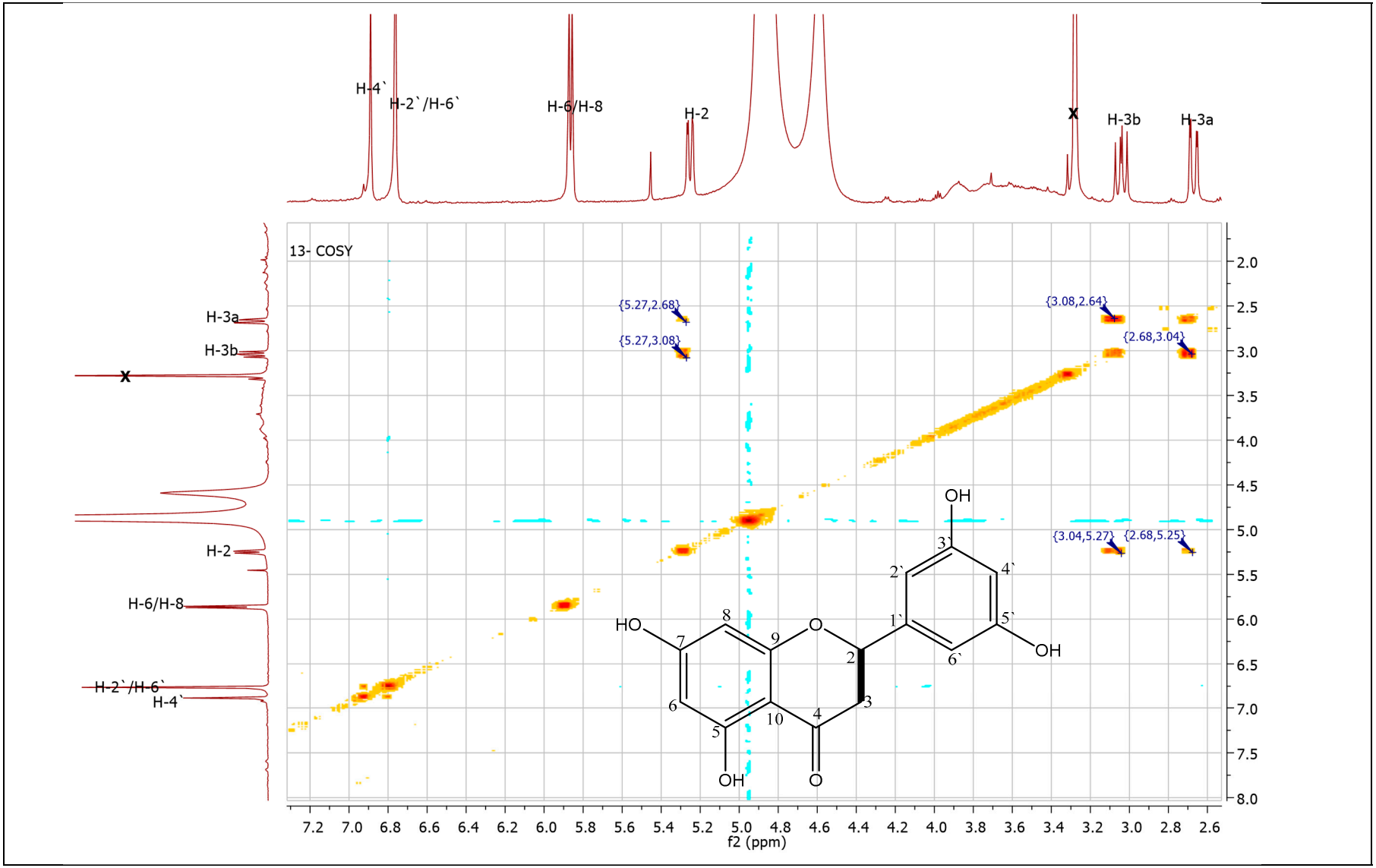


Fig. S36. COSY spectrum (expansion; 2.6-7.2 ppm) of **C7** in CD_3OD.

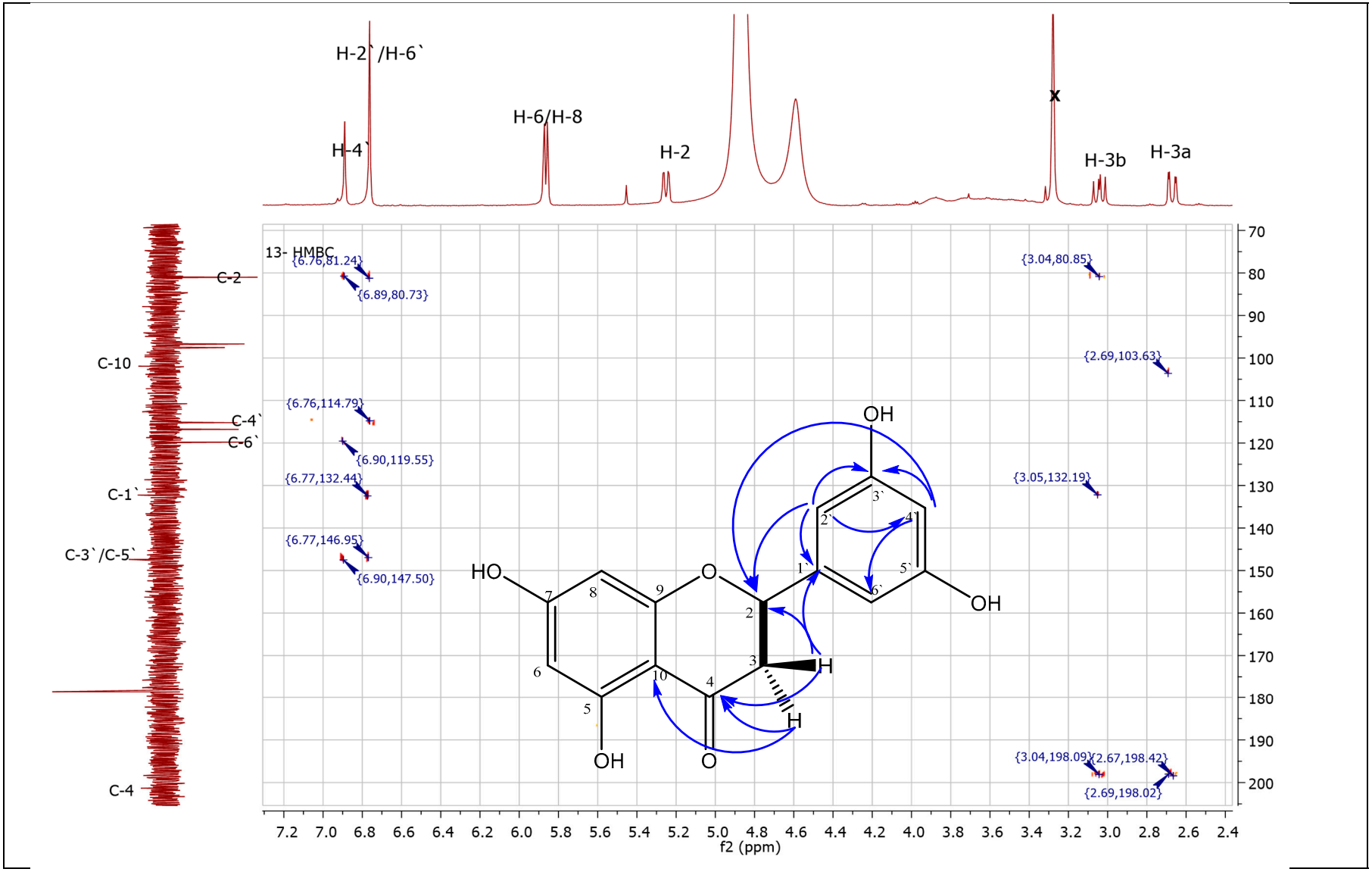
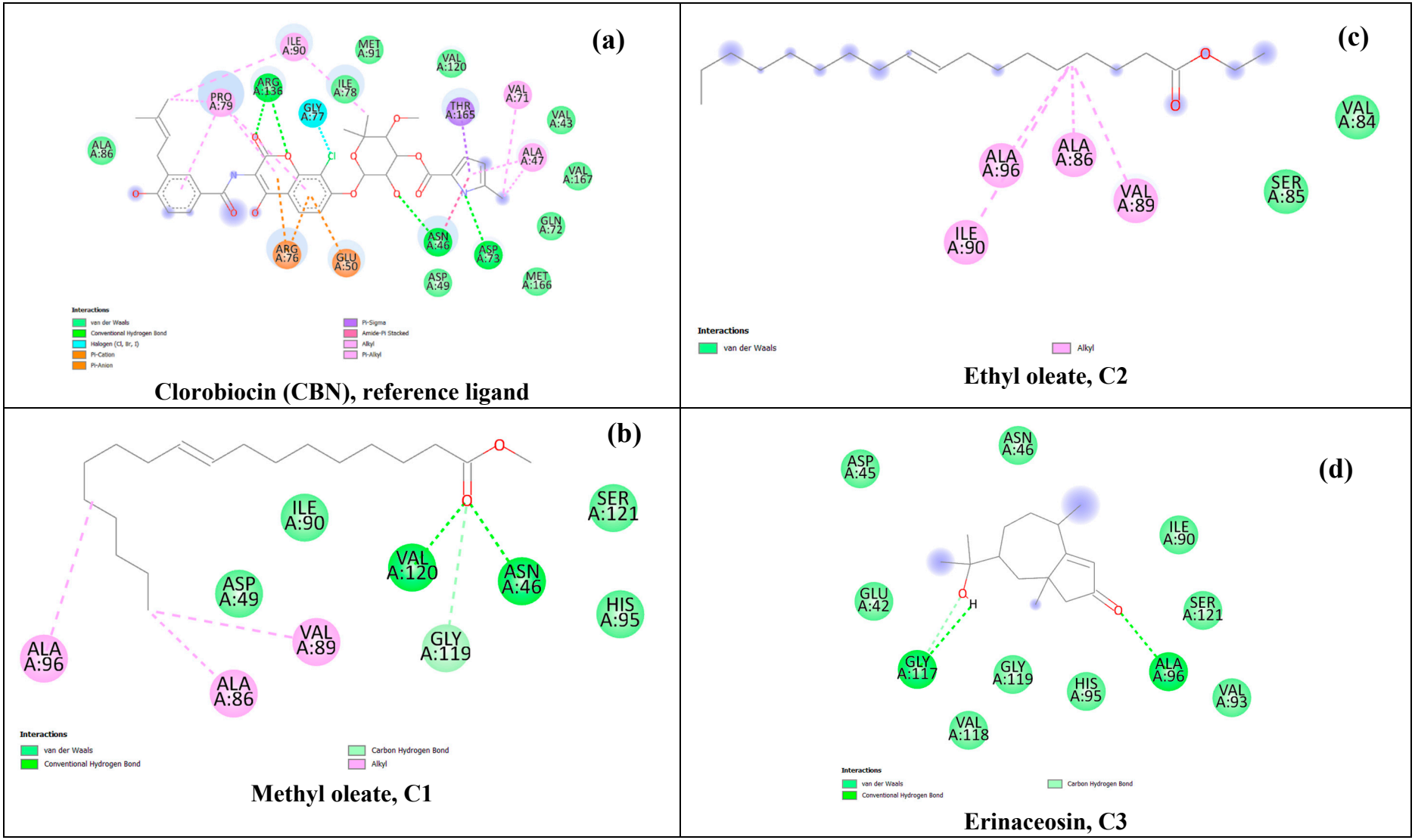
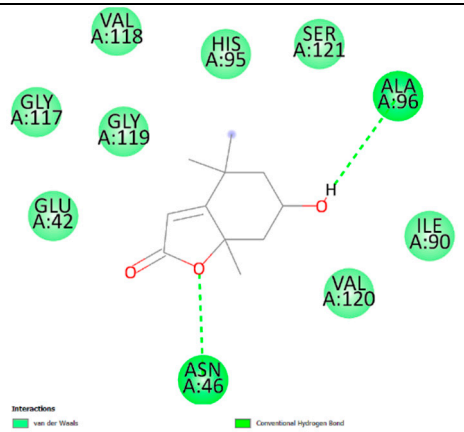
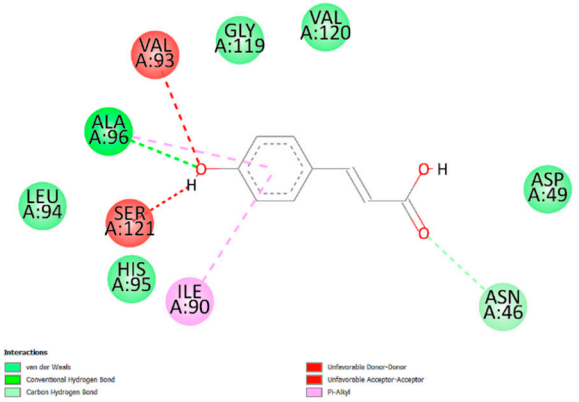


Fig. S37. HMBC spectrum (expansion; 2.4-7.2 ppm) of compound **C7** in CD_3OD.

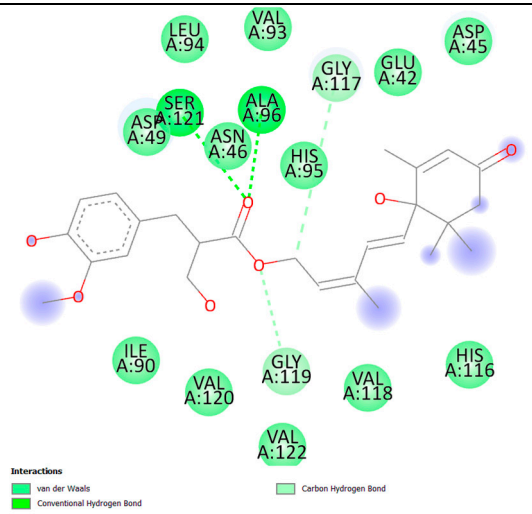

(a)
ILE A:90
MET A:91
VAL A:120
ARG A:138
ILE A:78
PRO A:79
GLY A:77
THR A:165
VAL A:71
VAL A:43
ALA A:86
ALA A:47
VAL A:167
GLN A:72
ASN A:46
ASP A:73
ARG A:76
GLU A:50
ASP A:49
MET A:166
Interactions
van der Waals
Conventional Hydrogen Bond
Halogen (Cl, Br, I)
Pi-Cation
Pi-Anion
Pi-Sigma
Amide-Pi Stacked
Alkyl
Pi-Alkyl
Clorobiocin (CBN), reference ligand
(c)
VAL A:84
ALA A:96
ALA A:86
SER A:85
VAL A:89
ILE A:90
Interactions
van der Waals
Alkyl
Ethyl oleate, C2
(b)
SER A:121
ILE A:90
VAL A:120
ASN A:46
ASP A:49
HIS A:95
VAL A:89
ALA A:96
GLY A:119
ALA A:86
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Alkyl
Methyl oleate, C1
(d)
ASN A:46
ASP A:45
ILE A:90
GLU A:42
SER A:121
GLY A:117
GLY A:119
ALA A:96
HIS A:95
VAL A:93
VAL A:118
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Erinaceosin, C3



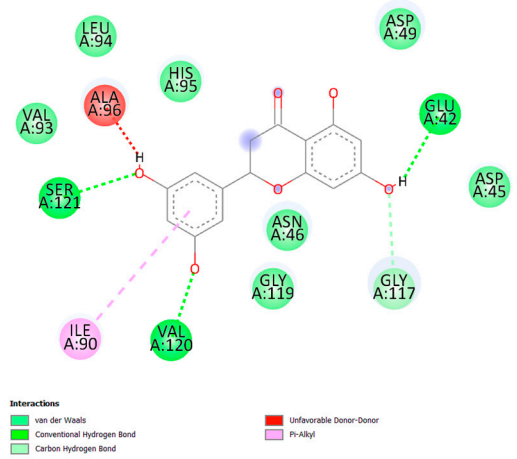
Loliolide, C4



(*E*)-*p*-coumaric acid, C6

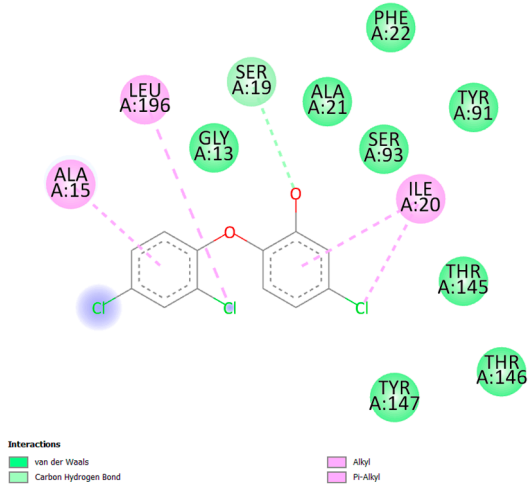


Erinaceol, C5

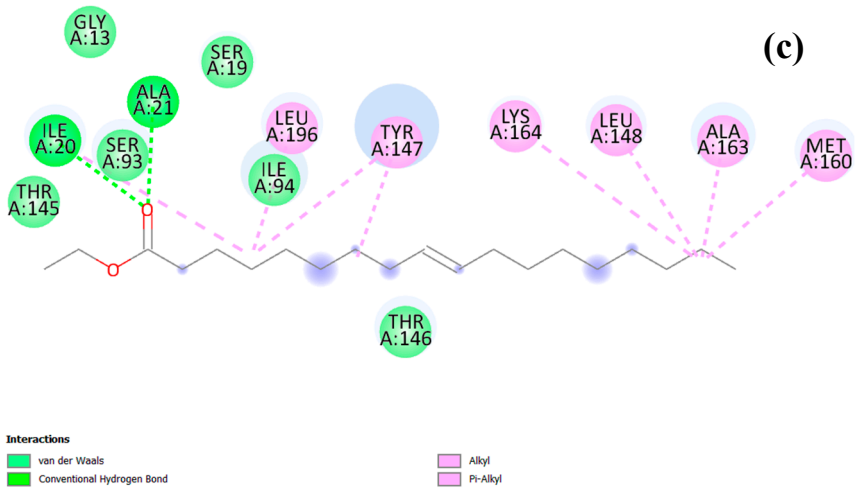


5,7,3`,5`-Tetrahydroxy flavanone, C7

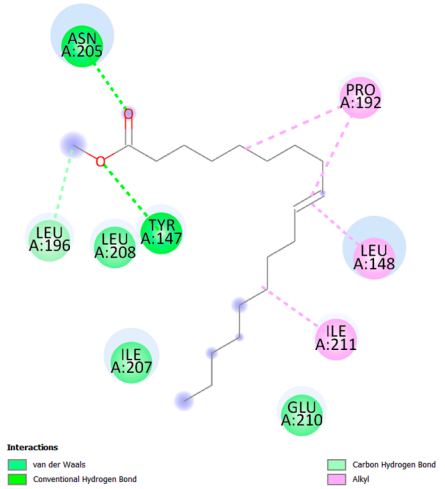
Fig. S38: Two-dimensional (2D) molecular interactions of isolated compounds **(a)** Clorobiocin (CBN), reference inhibitor, **(b-h)** Compounds **C1-C7** with DNA gyrase topoisomerase II (*E. coli*) enzyme (PDB ID:1KZN), (dimensions X:21.0176, Y: 30.3575, Z:27.6357).



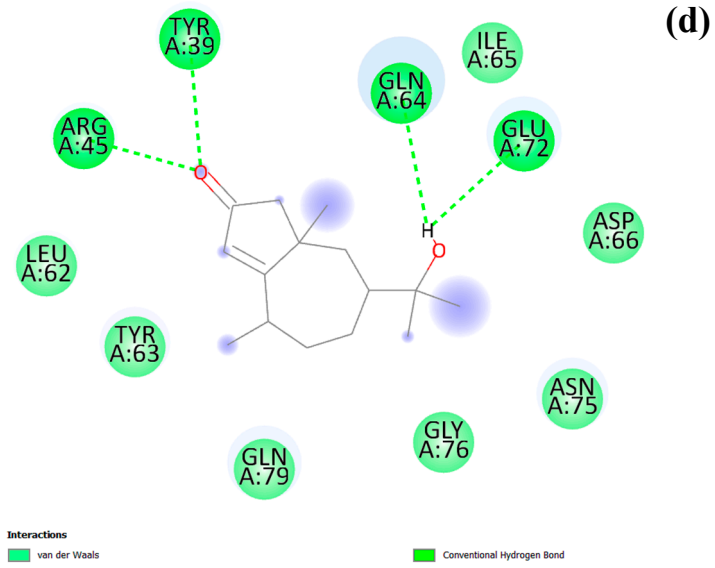
Triclosan, TRI, Reference Ligand



Ethyl oleate, C2



Methyl oleate, C1



Erinaceosin, C3

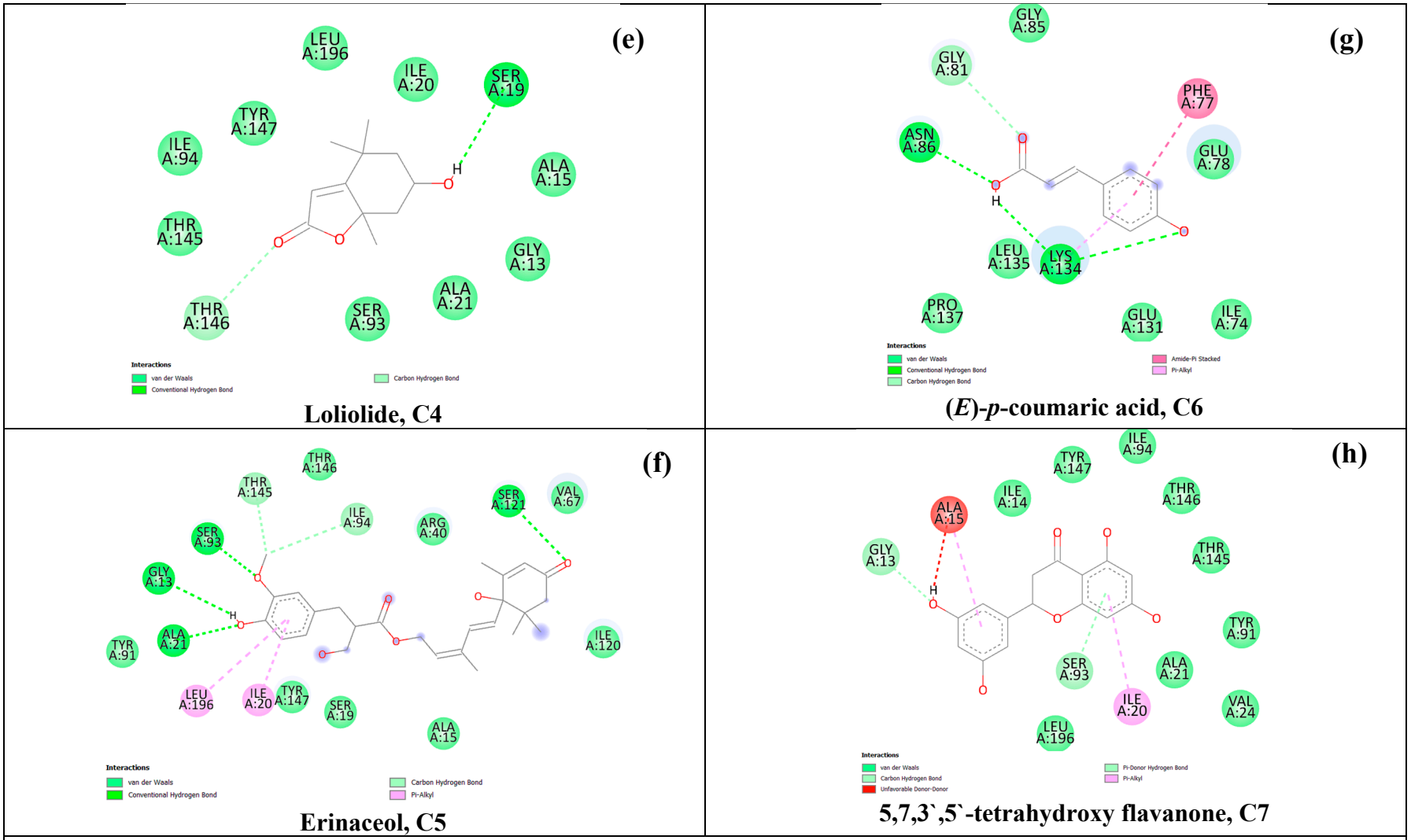
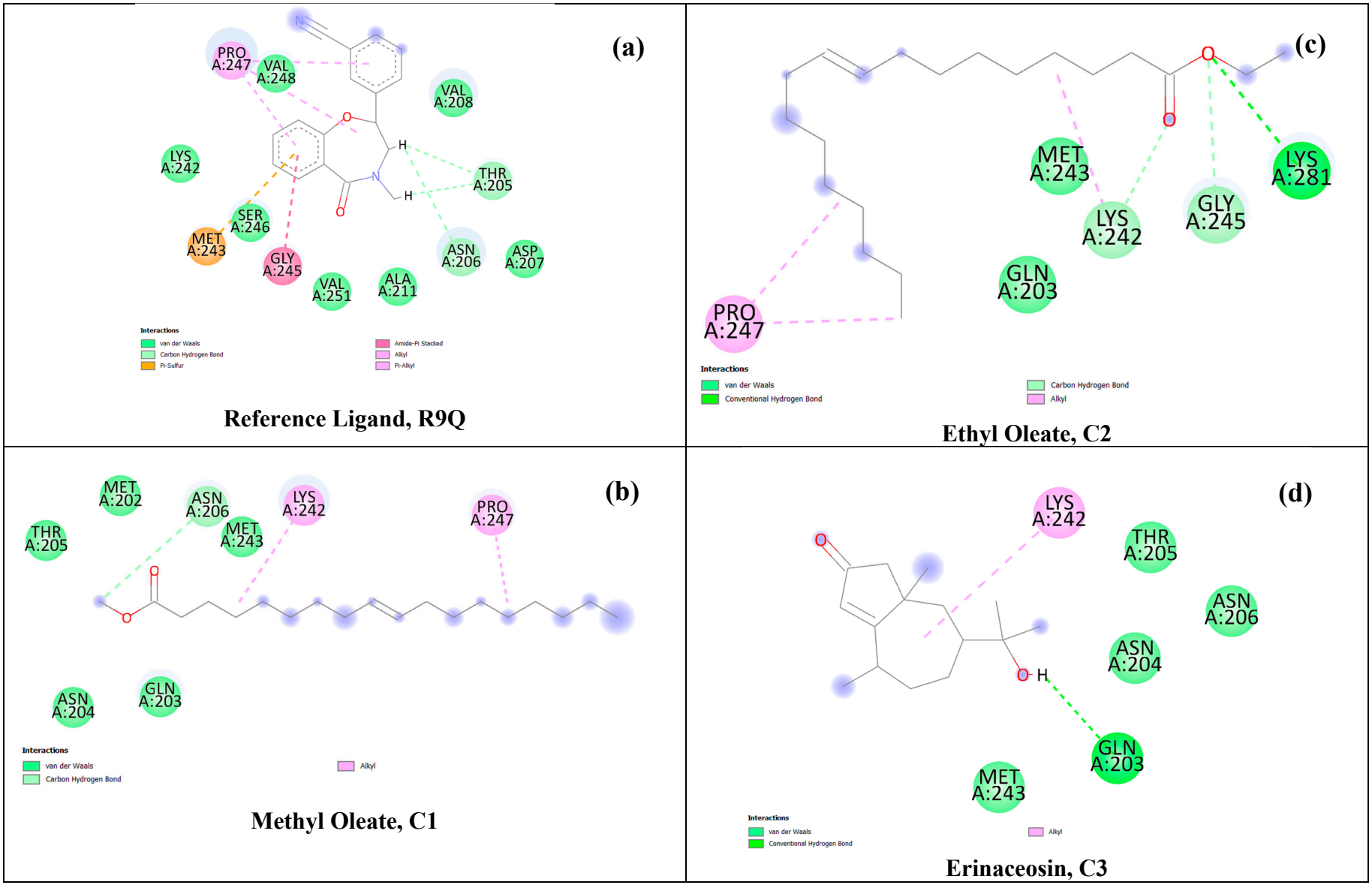


Fig. S39. Two-dimensional (2D) molecular interactions of **(a)** Triclosan, TRI, Reference Ligand, and **(b-h)** compound **C1-C7** with Enoyl-Acyl Carrier Protein Reductase (*S. aureus*), (FabI) (PDB ID:3GNS), (dimensions (Å) X:43.7680, Y: 51.7046, Z:49.0095).


(a)
PRO A:247
VAL A:248
VAL A:208
LYS A:242
THR A:205
SER A:246
MET A:243
GLY A:245
ASN A:206
ASP A:207
VAL A:251
ALA A:211
Interactions
van der Waals
Carbon Hydrogen Bond
Pi-Sulfur
Amide-Pi Stacked
Alkyl
Pi-Alkyl
Reference Ligand, R9Q
(c)
MET A:243
LYS A:242
GLY A:245
LYS A:281
GLN A:203
PRO A:247
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Alkyl
Ethyl Oleate, C2
(b)
MET A:202
ASN A:206
LYS A:242
MET A:243
PRO A:247
THR A:205
ASN A:204
GLN A:203
Interactions
van der Waals
Carbon Hydrogen Bond
Alkyl
Methyl Oleate, C1
(d)
LYS A:242
THR A:205
ASN A:206
ASN A:204
GLN A:203
MET A:243
Interactions
van der Waals
Conventional Hydrogen Bond
Alkyl
Erinaceosin, C3

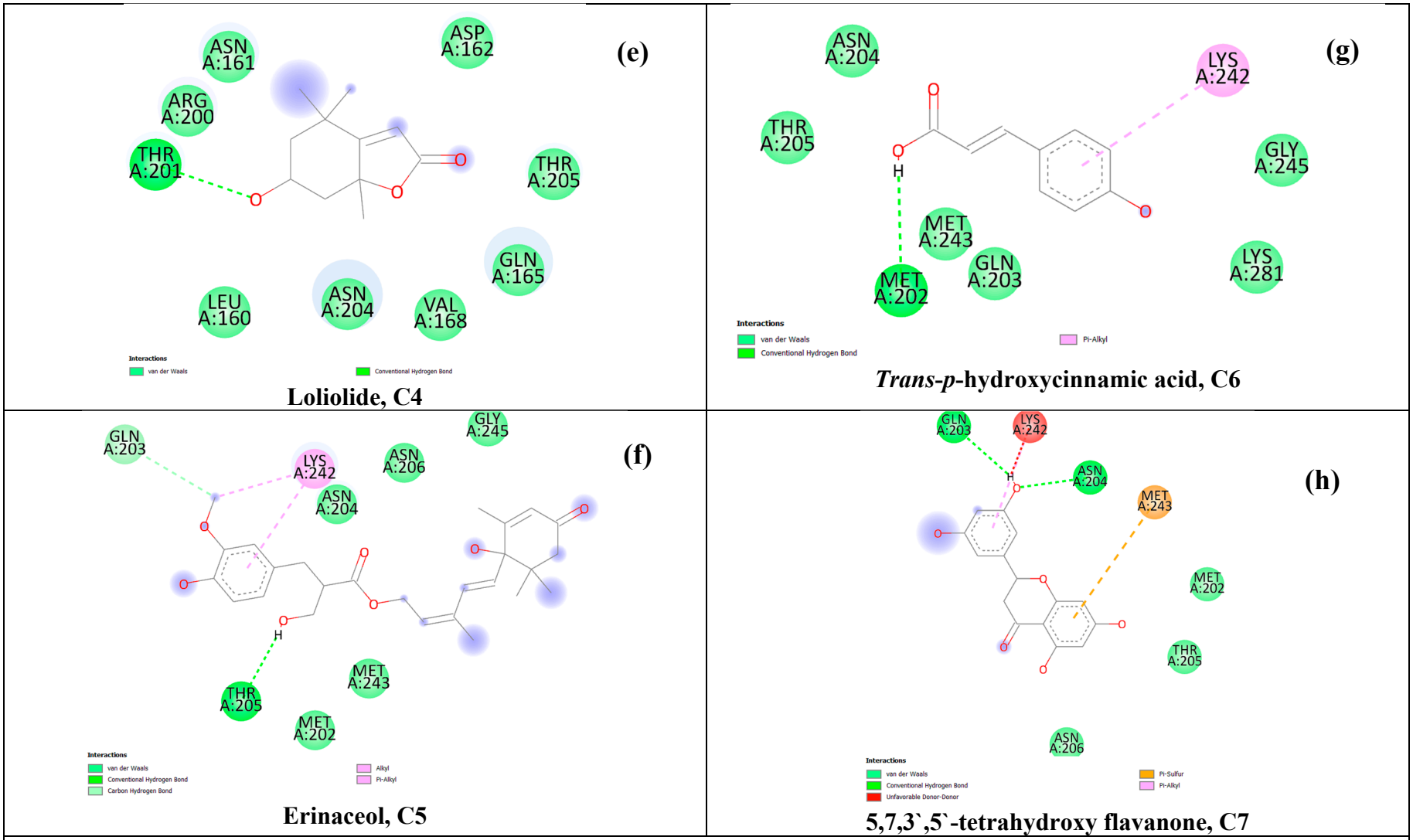
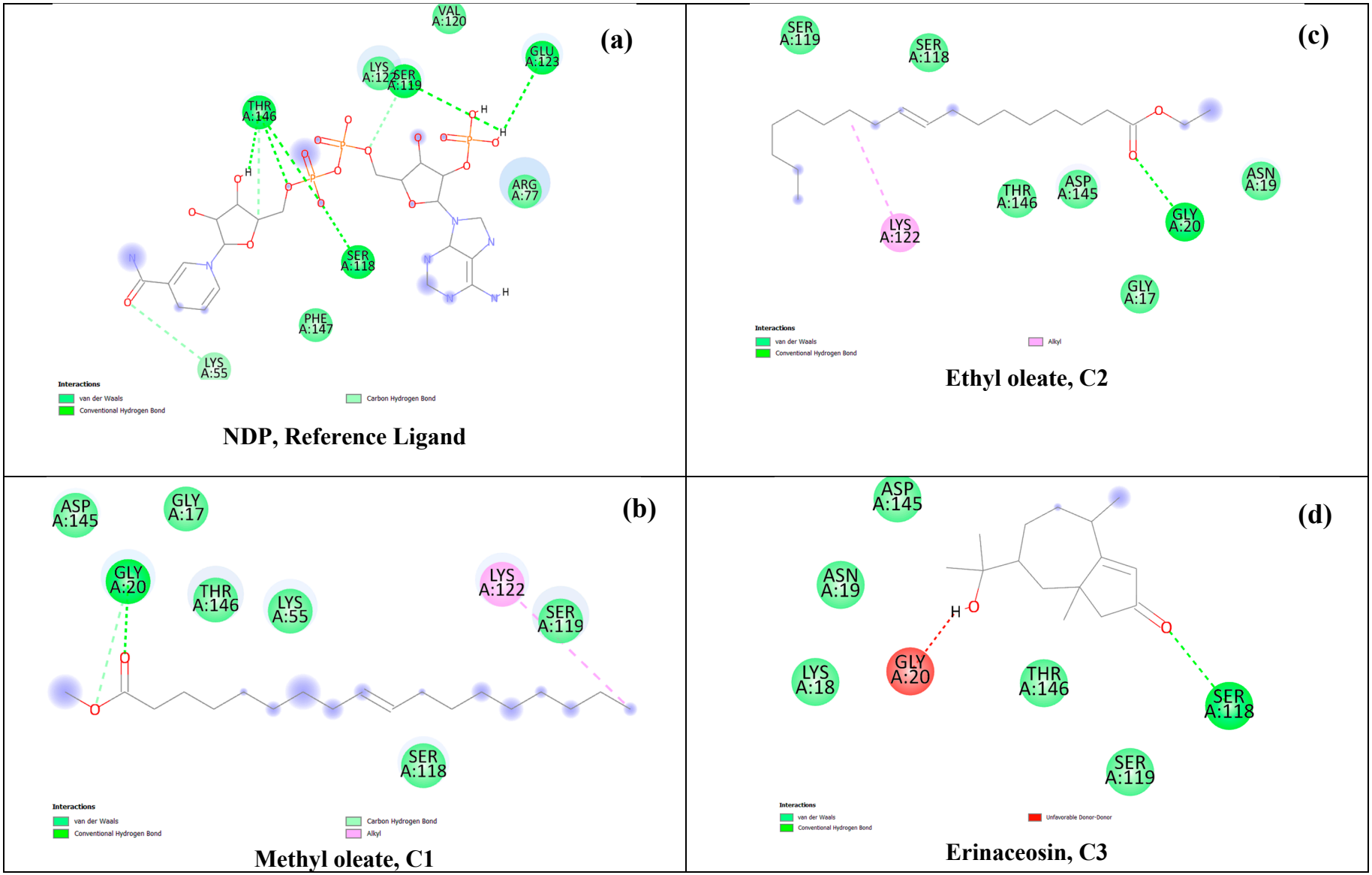
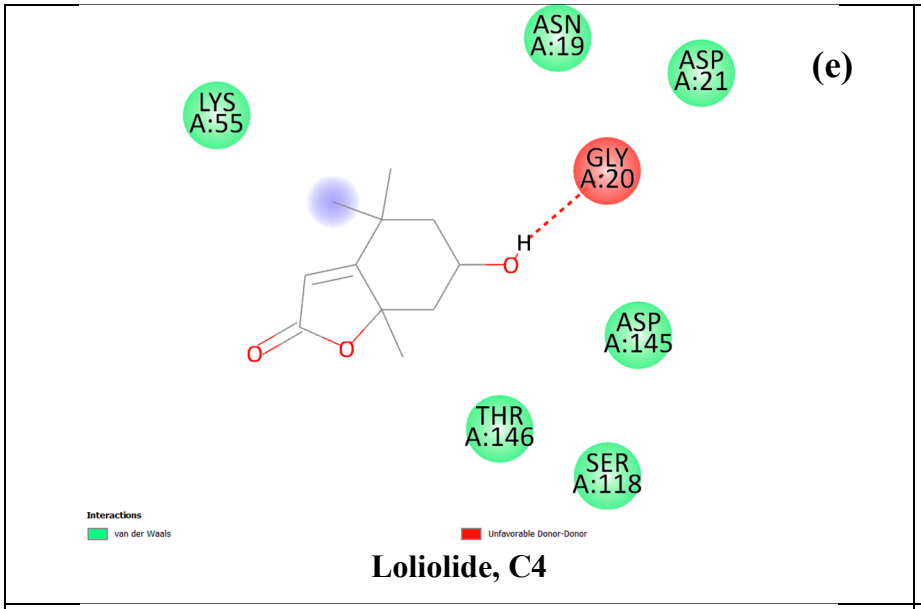
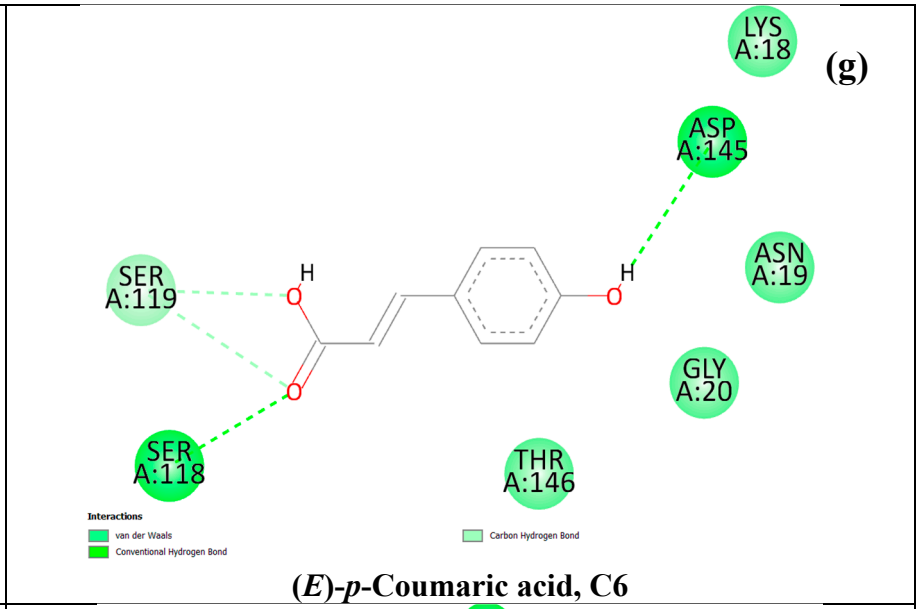


Fig. S40. Two-dimensional (2D) molecular interactions of **(a)** Reference Ligand, R9Q, and **(b-h)** isolated compounds **C1-C-7** with *β*-Catenin (PDB ID:7AFW), (dimensions (Å) X:20.4162, Y: 21.1198, Z:25.0).

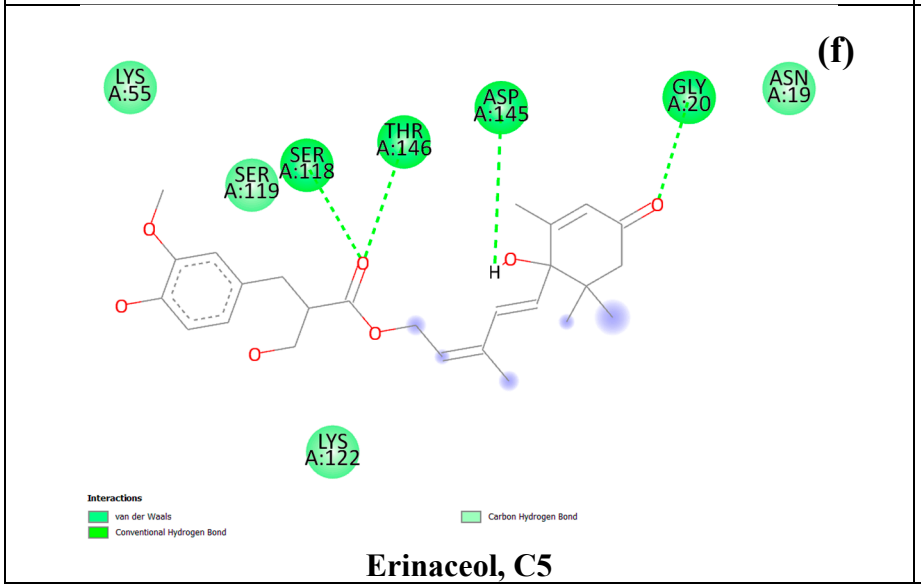

(a)
VAL A:120
GLU A:123
LYS A:122
SER A:119
THR A:146
ARG A:77
SER A:118
PHE A:147
LYS A:55
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
NDP, Reference Ligand
(c)
SER A:119
SER A:118
THR A:146
ASP A:145
ASN A:19
LYS A:122
GLY A:20
GLY A:17
Interactions
van der Waals
Conventional Hydrogen Bond
Alkyl
Ethyl oleate, C2
(b)
ASP A:145
GLY A:17
GLY A:20
THR A:146
LYS A:55
LYS A:122
SER A:119
SER A:118
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Alkyl
Methyl oleate, C1
(d)
ASP A:145
ASN A:19
LYS A:18
GLY A:20
THR A:146
SER A:118
SER A:119
Interactions
van der Waals
Conventional Hydrogen Bond
Unfavorable Donor-Donor
Erinaceosin, C3



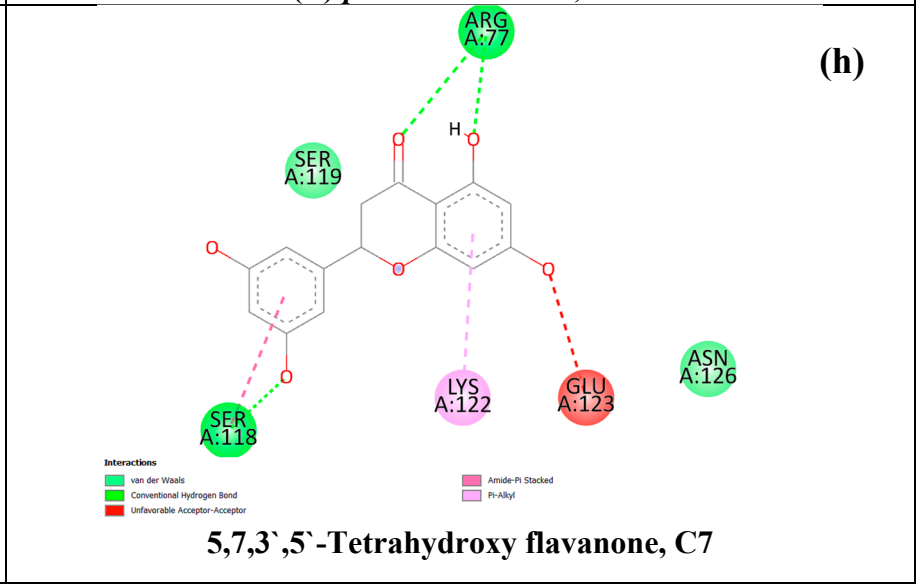
Loliolide, C4



(*E*)-*p*-Coumaric acid, C6



Erinaceol, C5



5,7,3`,5`-Tetrahydroxy flavanone, C7

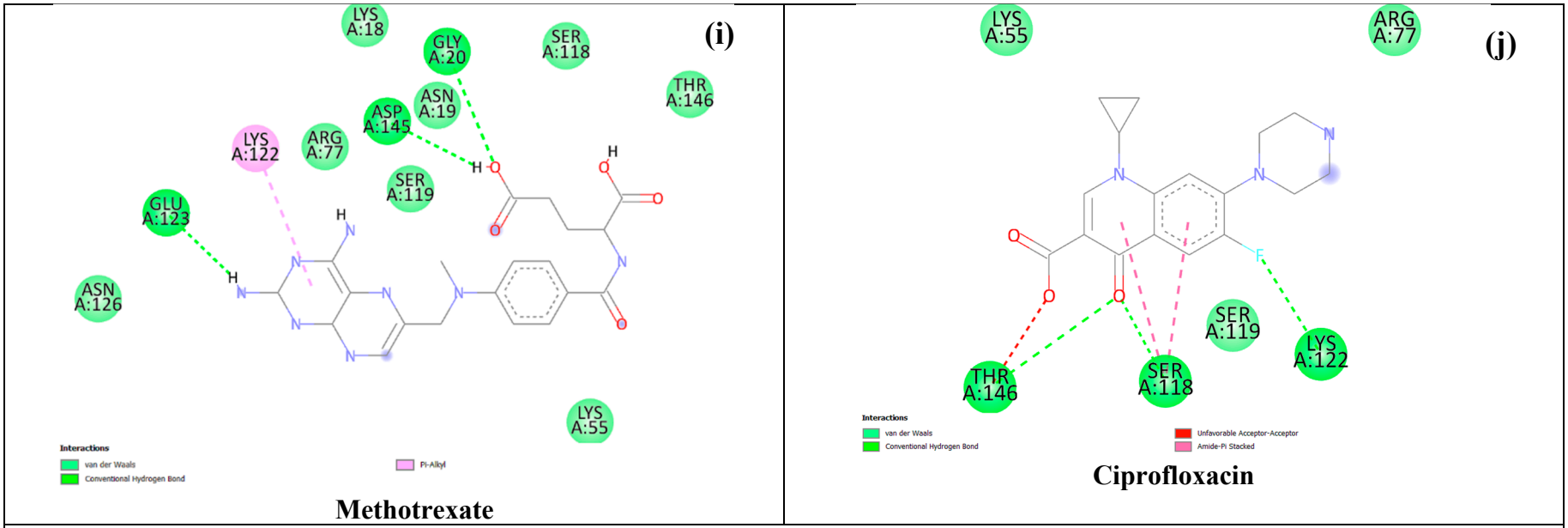
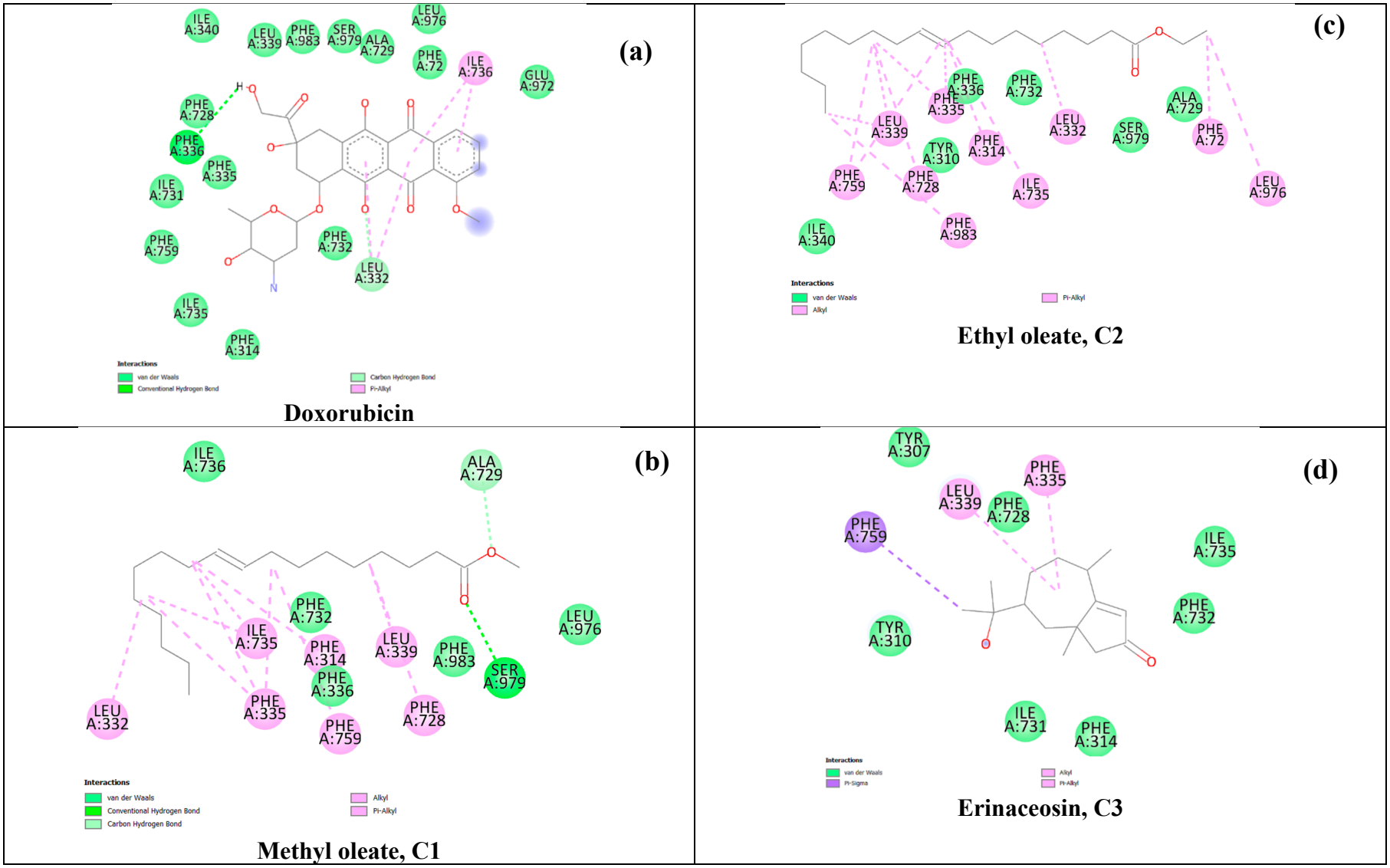


Fig. S41. Two-dimensional (2D) molecular interactions of **(a)** NDP, Reference Ligand, **(b-h)** isolated compounds **C1-C7**, and **(i)** Methotrexate, and **(j)** Ciprofloxacin with Crystal structure of human dihydrofolate reductase (DHFR) bound to NADPH (PDB ID:4M6J), Ciprofloxacin (PubChem ID: 2764), Methotrexate (PubChem ID: 12694), (dimensions (Å) X:20.8191, Y:24.1576, Z:27.1117), (root mean square deviation) RMSD < 2.


(a)
ILE A:340
LEU A:339
PHE A:983
SER A:979
ALA A:729
LEU A:976
PHE A:72
ILE A:736
GLU A:972
PHE A:728
PHE A:336
PHE A:335
ILE A:731
PHE A:759
PHE A:732
LEU A:332
ILE A:735
PHE A:314
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Pi-Alkyl
Doxorubicin
(c)
PHE A:336
PHE A:732
PHE A:335
LEU A:339
LEU A:332
SER A:979
ALA A:729
PHE A:72
TYR A:310
PHE A:314
PHE A:759
PHE A:728
ILE A:735
LEU A:976
PHE A:983
ILE A:340
Interactions
van der Waals
Alkyl
Pi-Alkyl
Ethyl oleate, C2
(b)
ILE A:736
ALA A:729
PHE A:732
LEU A:976
ILE A:735
PHE A:314
LEU A:339
PHE A:983
SER A:979
PHE A:336
LEU A:332
PHE A:335
PHE A:728
PHE A:759
Interactions
van der Waals
Conventional Hydrogen Bond
Carbon Hydrogen Bond
Alkyl
Pi-Alkyl
Methyl oleate, C1
(d)
TYR A:307
PHE A:335
LEU A:339
PHE A:728
PHE A:759
ILE A:735
PHE A:732
TYR A:310
ILE A:731
PHE A:314
Interactions
van der Waals
Pi-Sigma
Alkyl
Pi-Alkyl
Erinaceosin, C3

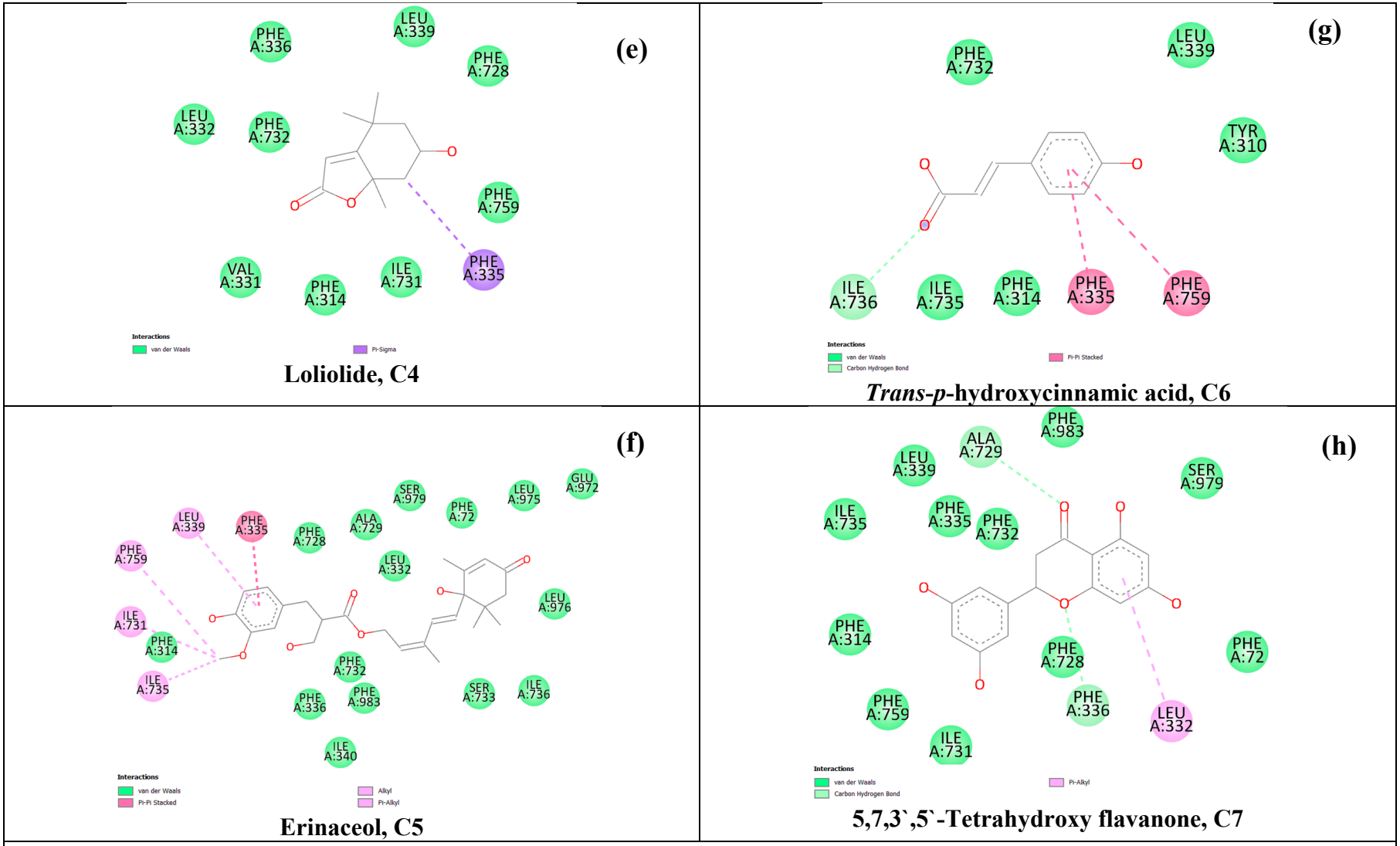
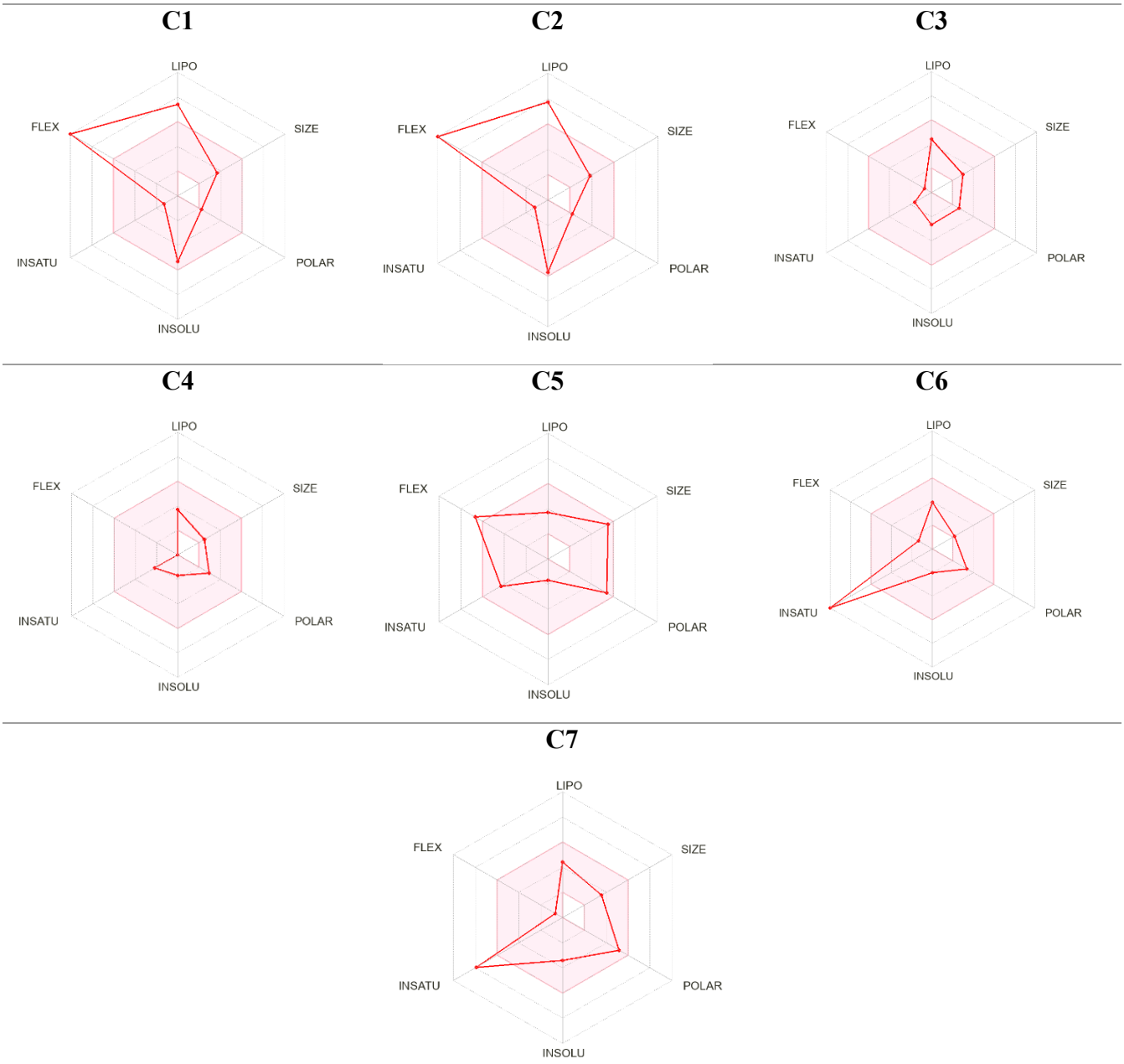


Fig. S42. Two-dimensional (2D) molecular interactions of **(a)** Doxorubicin (PubChem ID: 31703), and isolated compounds; **(b-h)** Compounds **C1**-**C7** with Crystal structure of human P-gp (PDB ID: 6C0V), (dimensions (Å) X:20.8191, Y:24.1576, Z:27.1117), (root mean square deviation) RMSD < 2. Width 995.



(a)

Fig. S43. Bioavailability radar representation of compounds C1-C7 (molecules 1-7).

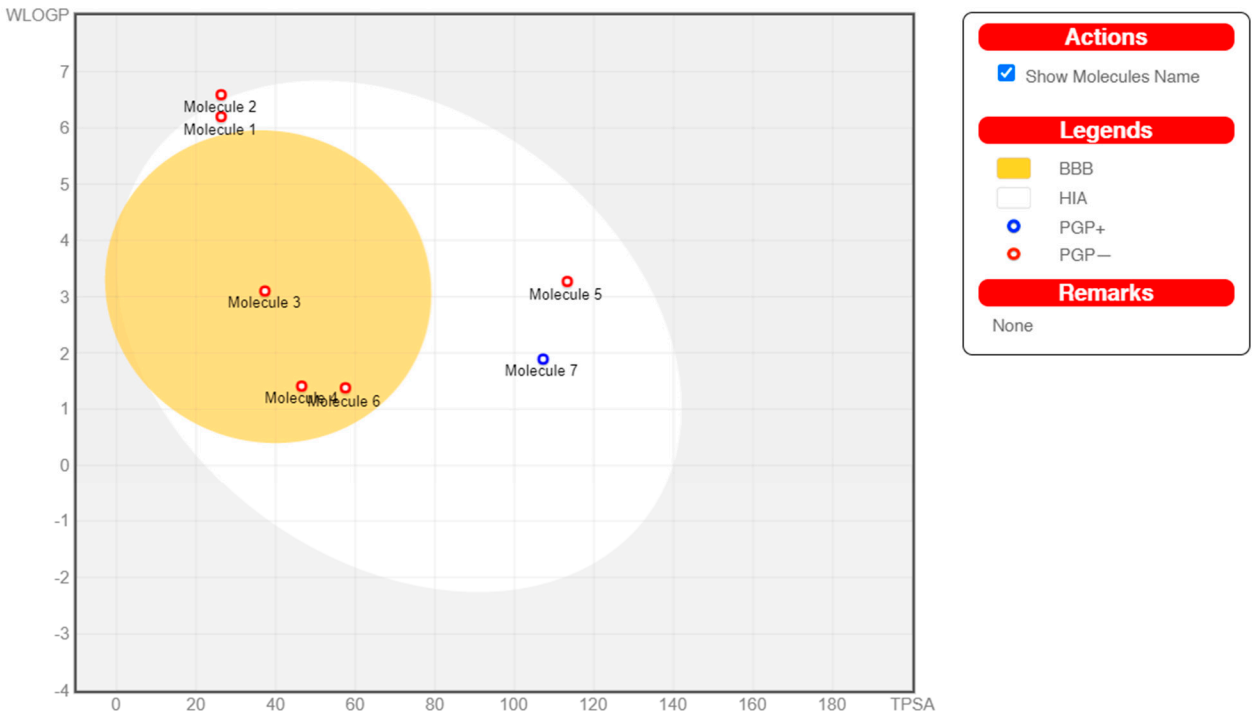


Fig. S44. Predicted BOILED-Egg diagram of compounds **C1-C7** (molecules 1-7, respectively).