Supporting Information

Chemo- and Biocatalytic Esterification of Marchantin A and Cytotoxic Activity of Ester Derivatives

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Table S1. Changes in the chemical shifts δ_H of marchantin A ester derivatives after esterification.
Table S2. Changes in the chemical shifts δ_C of marchantin A ester derivatives after esterification.
Table S3. Calculated of physically significant molecular descriptors and pharmaceutically relevant properties.

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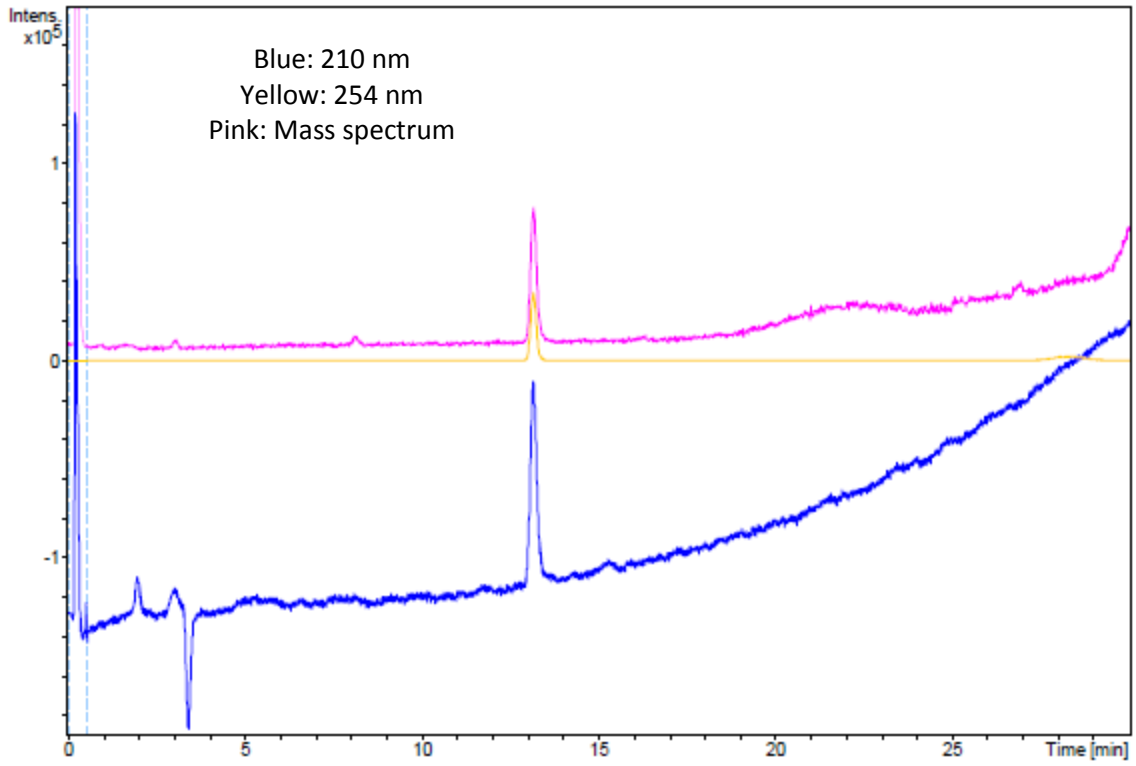
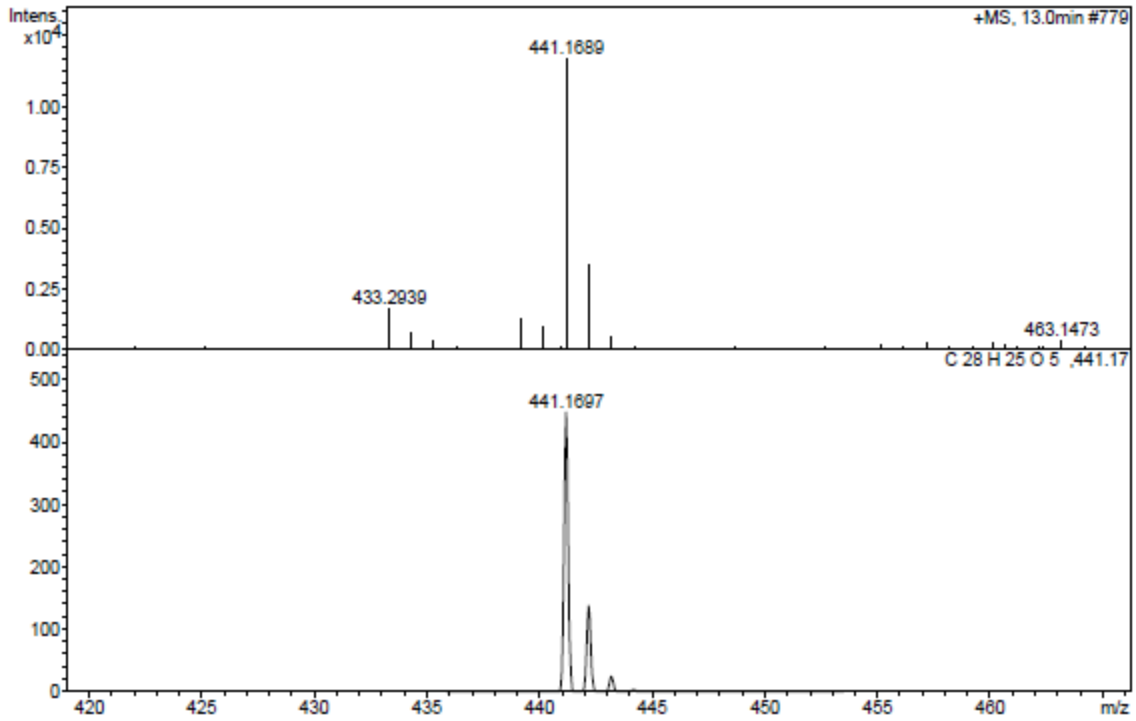
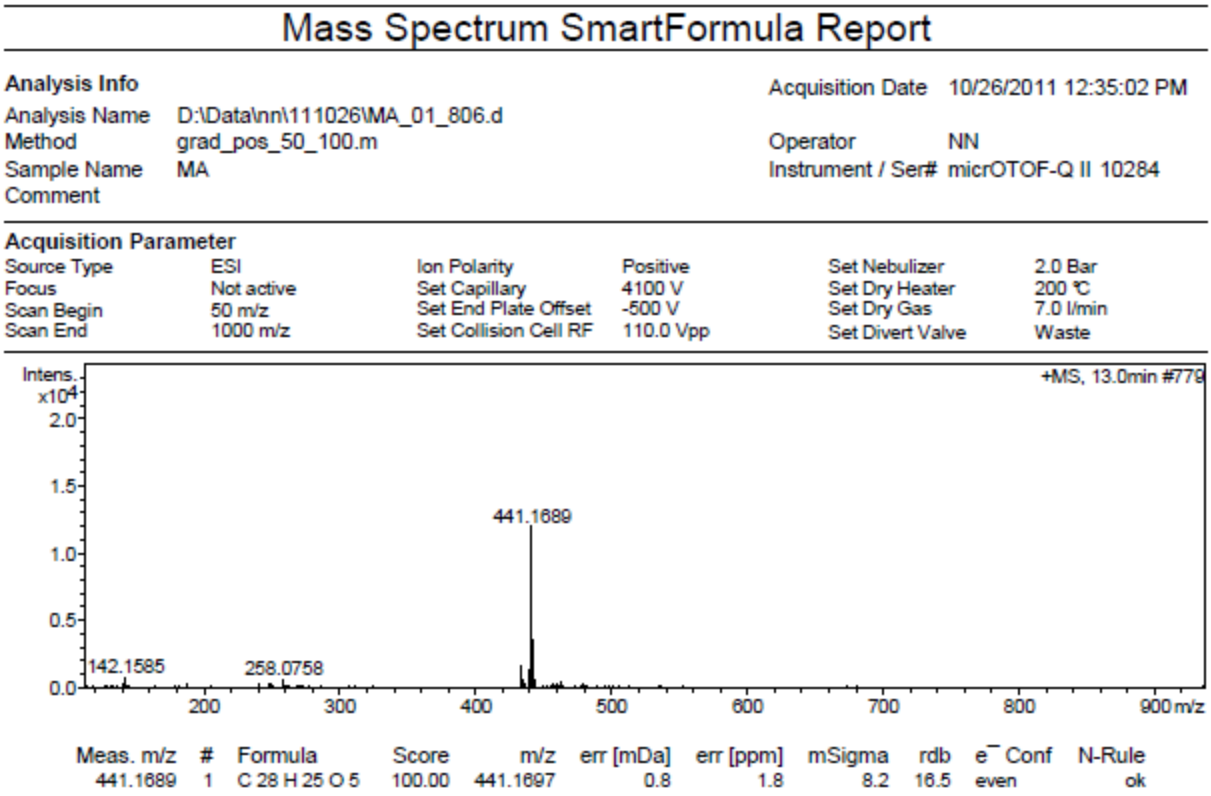






Conditions: Agilent 1100 system consisting of degasser, quaternary pump, auto sampler, column oven, photodiode array detector (PDA) and a 150 × 4.6 mm Phenomenex C18 Luna column with particle size of 5 µm and pore size of 100 Å (Phenomenex, Inc., Torrance, CA). The column was operated at 40 °C. Solvent was delivered at 0.5 ml/min using the following linear gradient elution profile: 50% B to 100% B over 30 min (solvent A: water/acetonitrile 95:5 + 0.1% formic acid; solvent B: acetonitrile/water 95:5 + 0.1% formic acid). The flow from the column was split by a T-piece connected to capillaries of different length and i.d. (10 cm/0.05 µm, 100 cm/0.5 µm), directing < 1% of the column outflow to a micrOTOF-Q mass spectrometer equipped with electrospray ionization (ESI) interface (Bruker Daltonik GmbH, Bremen, Germany). Mass spectra were acquired in positive-ion mode, using drying temperature of 350 °C, nebulizer pressure of 15 psi, and drying gas flow of 15 ml/min. Injection volume was 5 µl.

Figure S1. HPLC-HREIMS spectra of marchantin A

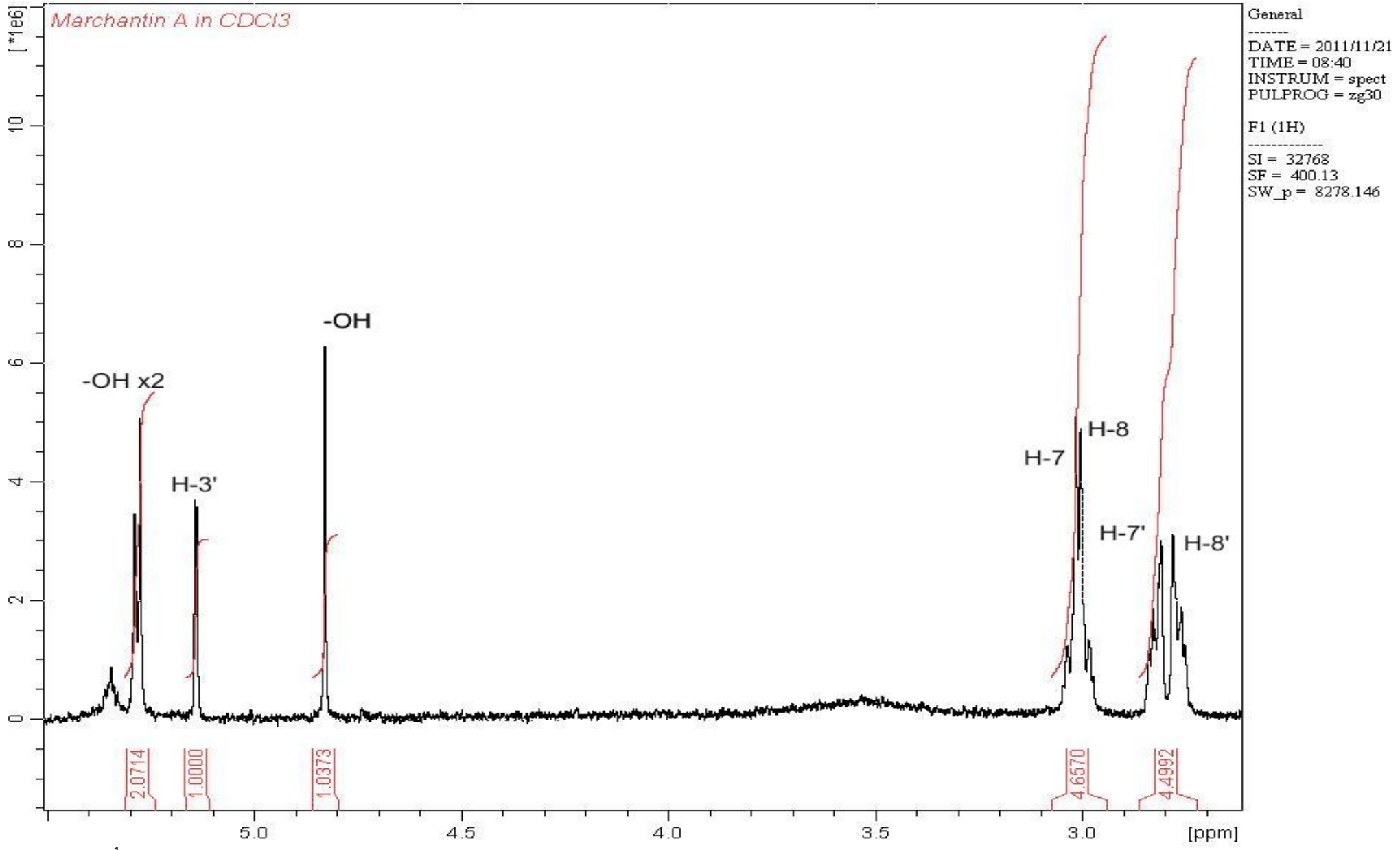


Figure S2. ^{1}H spectrum of marchantin A (2.6-5.5 ppm)

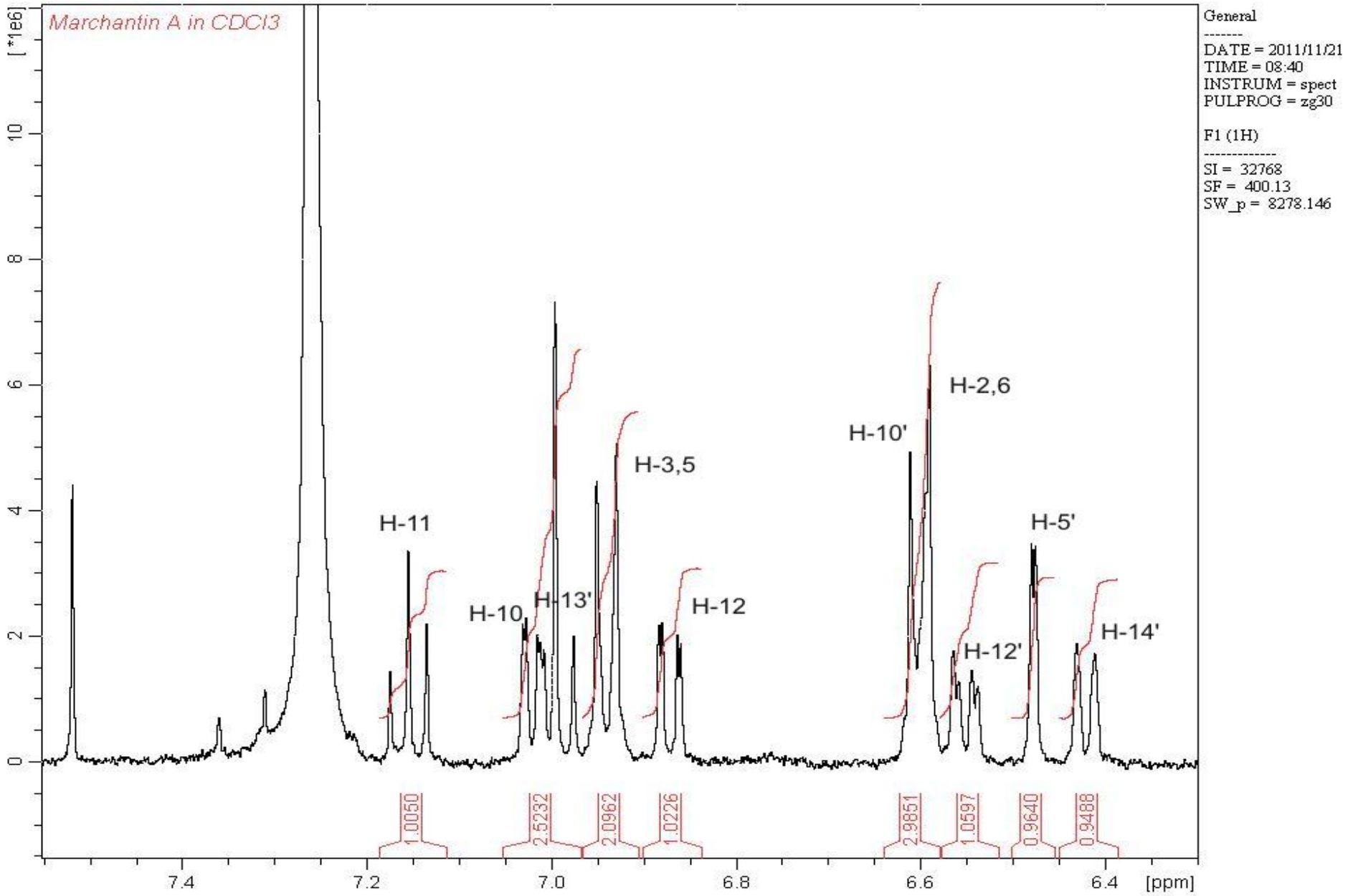


Figure S3. [1]H NMR spectrum of marchantin A (6.30-7.55 ppm)

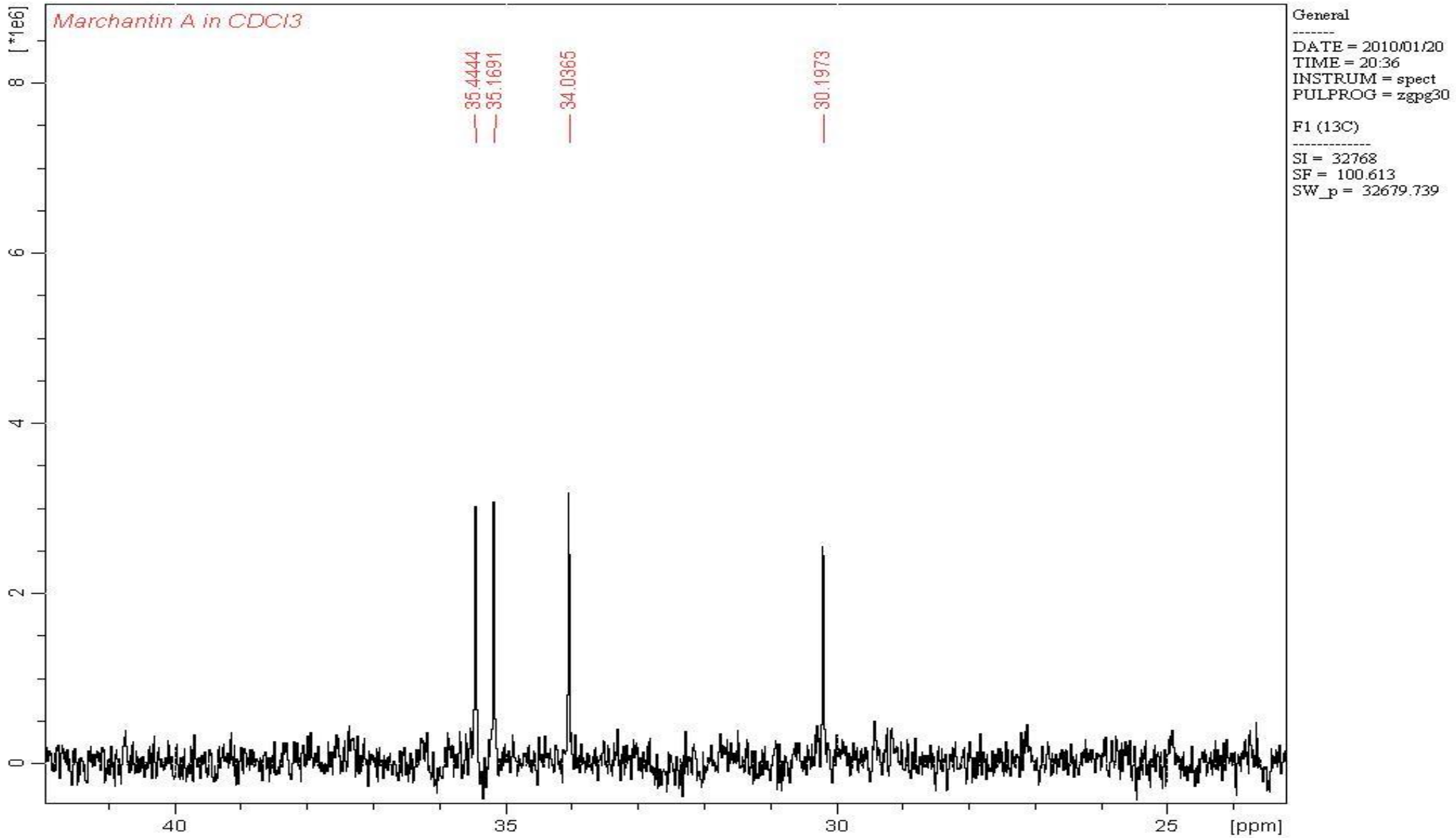


Figure S4. ^{13}C NMR spectrum of marchantin A (23-42 ppm)

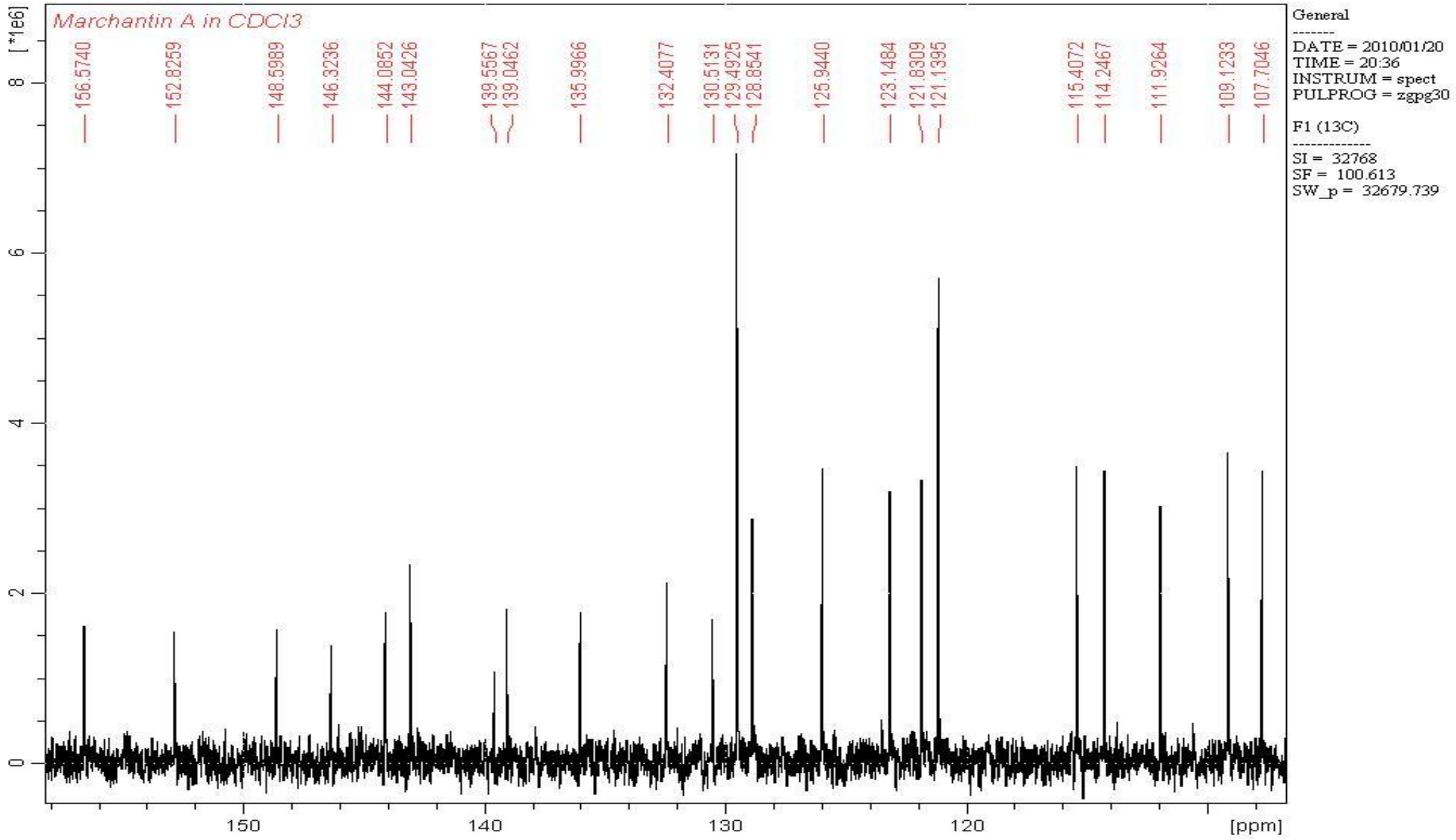


Figure S5. ^{13}C NMR spectrum of marchantin A (107-158 ppm)

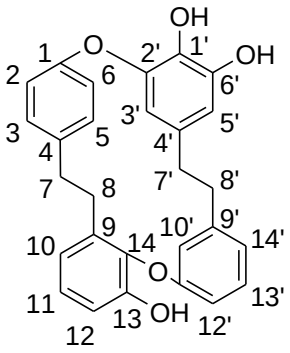
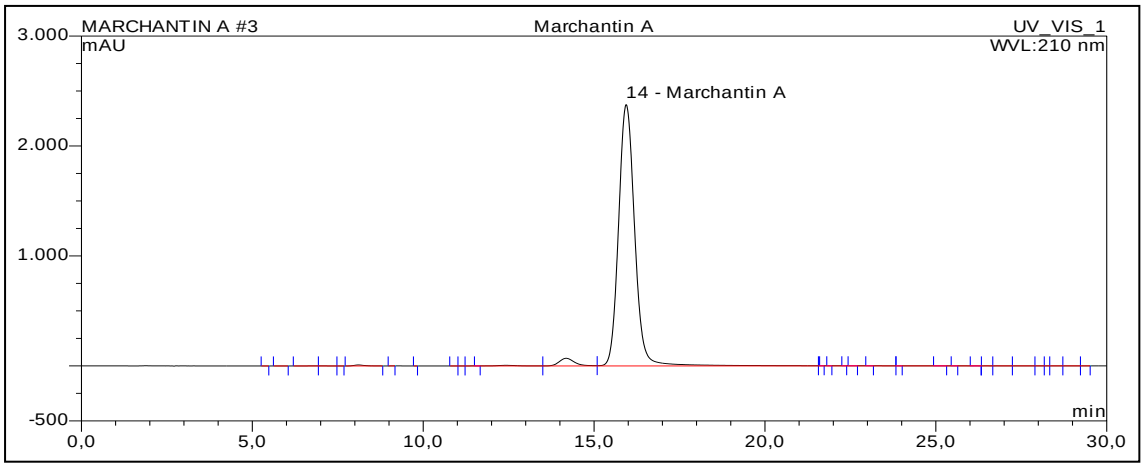


Figure S6. The structure of marchantin A

3	**marchantin A**		
Sample Name:	**marchantin A**	*Injection Volume:*	**10,0**
Vial Number:	**RA1**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**210**
Control Program:	**marchantin 70-30**	*Bandwidth:*	**1**
Quantif. Method:	**MARCHANTIN A -analytical**	*Detection limit:*	**0.001 [signal*min]**
Recording Time:	**7.4.2011 11:09**		
Run Time (min):	**30,00**		



1	5,37	n.a.	0,190	0,022	0,00	n.a.	BMB
2	5,94	n.a.	0,110	0,032	0,00	n.a.	BMB
3	6,81	n.a.	0,569	0,246	0,02	n.a.	BM
4	7,03	n.a.	0,492	0,175	0,01	n.a.	M
5	7,56	n.a.	0,152	0,019	0,00	n.a.	MB
6	8,10	n.a.	8,890	3,025	0,22	n.a.	BMB
7	9,09	n.a.	0,196	0,017	0,00	n.a.	BMB
8	9,78	n.a.	0,083	0,006	0,00	n.a.	BMB
9	10,95	n.a.	0,111	0,017	0,00	n.a.	BM
10	11,20	n.a.	0,245	0,027	0,00	n.a.	M
11	11,64	n.a.	0,046	0,008	0,00	n.a.	Ru
12	12,42	n.a.	5,714	3,927	0,29	n.a.	M
13	14,18	n.a.	69,678	36,061	2,67	n.a.	M
14	15,94	Marchantin A	2376,367	1303,206	96,40	n.a.	M
15	21,68	n.a.	0,067	0,005	0,00	n.a.	Ru
16	21,91	n.a.	0,060	0,005	0,00	n.a.	Ru

17	22,11	n.a.	1,447	2,778	0,21	n.a.	M
18	22,33	n.a.	0,086	0,007	0,00	n.a.	Rd
19	22,60	n.a.	0,098	0,016	0,00	n.a.	Rd
20	23,07	n.a.	0,181	0,023	0,00	n.a.	Rd
21	24,00	n.a.	0,040	0,005	0,00	n.a.	Ru
22	24,15	n.a.	0,965	1,525	0,11	n.a.	M
23	25,01	n.a.	0,090	0,022	0,00	n.a.	Rd
24	25,59	n.a.	0,081	0,007	0,00	n.a.	Rd
25	26,17	n.a.	0,138	0,024	0,00	n.a.	Rd
26	26,48	n.a.	0,466	0,121	0,01	n.a.	M
27	26,78	n.a.	0,399	0,171	0,01	n.a.	M
28	27,33	n.a.	0,317	0,151	0,01	n.a.	M
29	27,98	n.a.	0,204	0,038	0,00	n.a.	M
30	28,26	n.a.	0,169	0,021	0,00	n.a.	M
Total:			2468,111	1351,821	100,00	0,000	

Figure S7. Analytical HPLC chromatogram of marchantin A

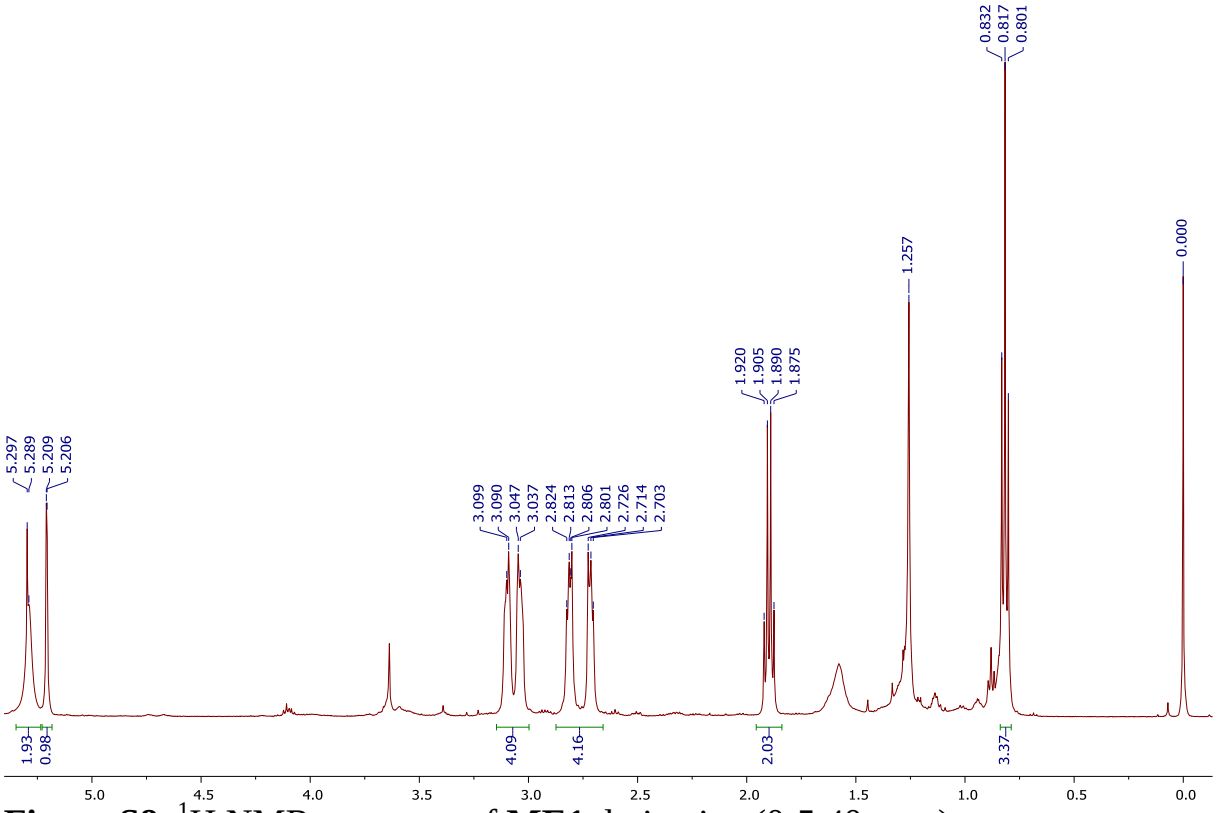


Figure S8. ^{1}H NMR spectrum of **ME1** derivative (0-5.40 ppm)

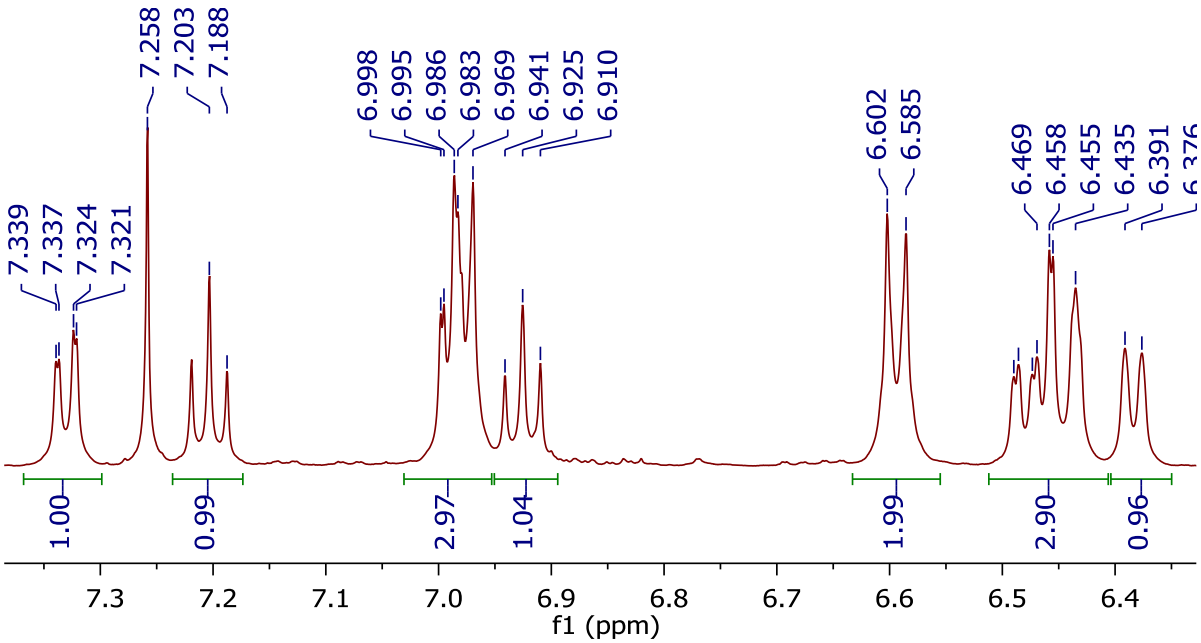


Figure S9. ^{1}H NMR spectrum of **ME1** derivative (6.32-7.40 ppm)

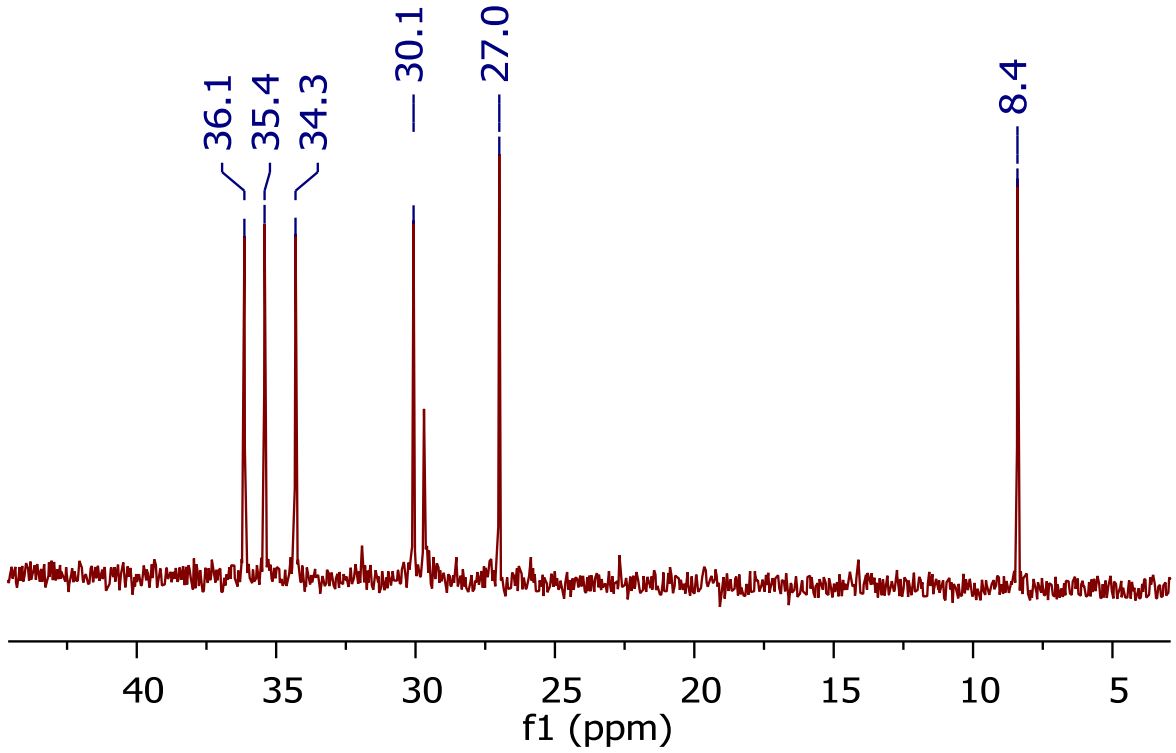


Figure S10. ^{13}C NMR spectrum of **ME1** derivative (3-44 ppm)

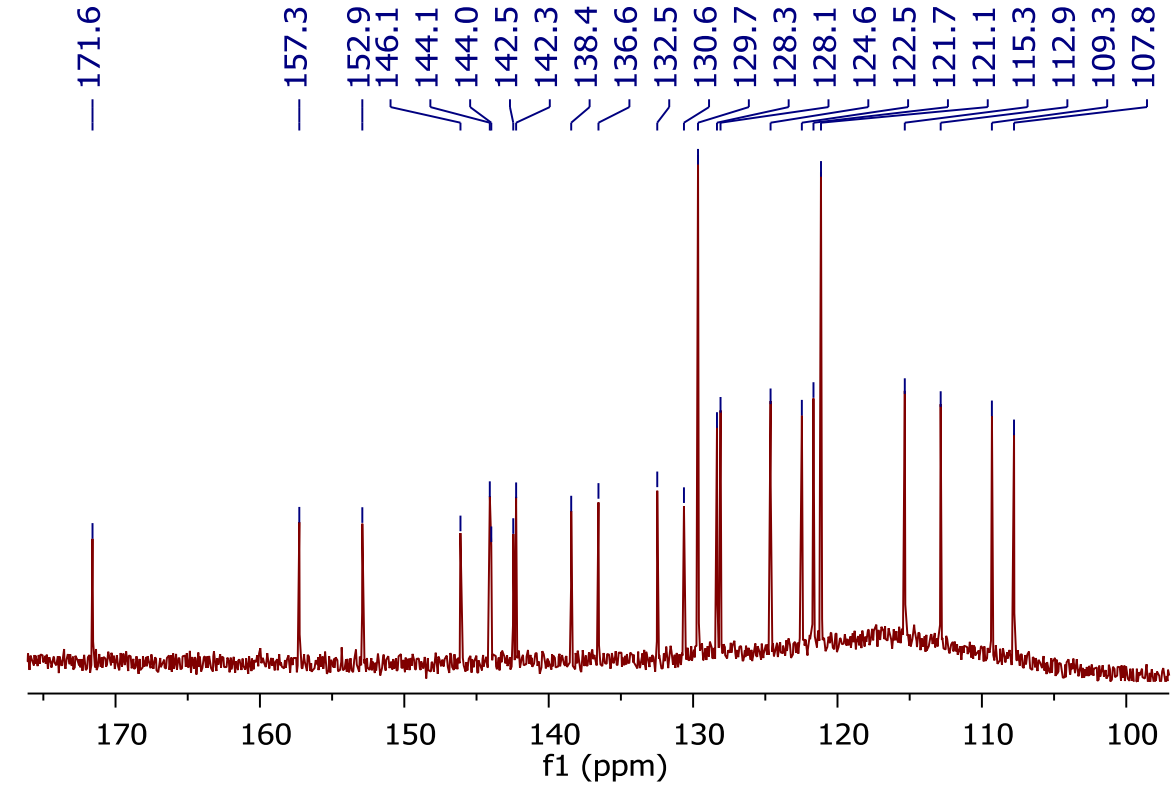


Figure S11. ^{13}C NMR spectrum of **ME1** derivative (98-176 ppm)

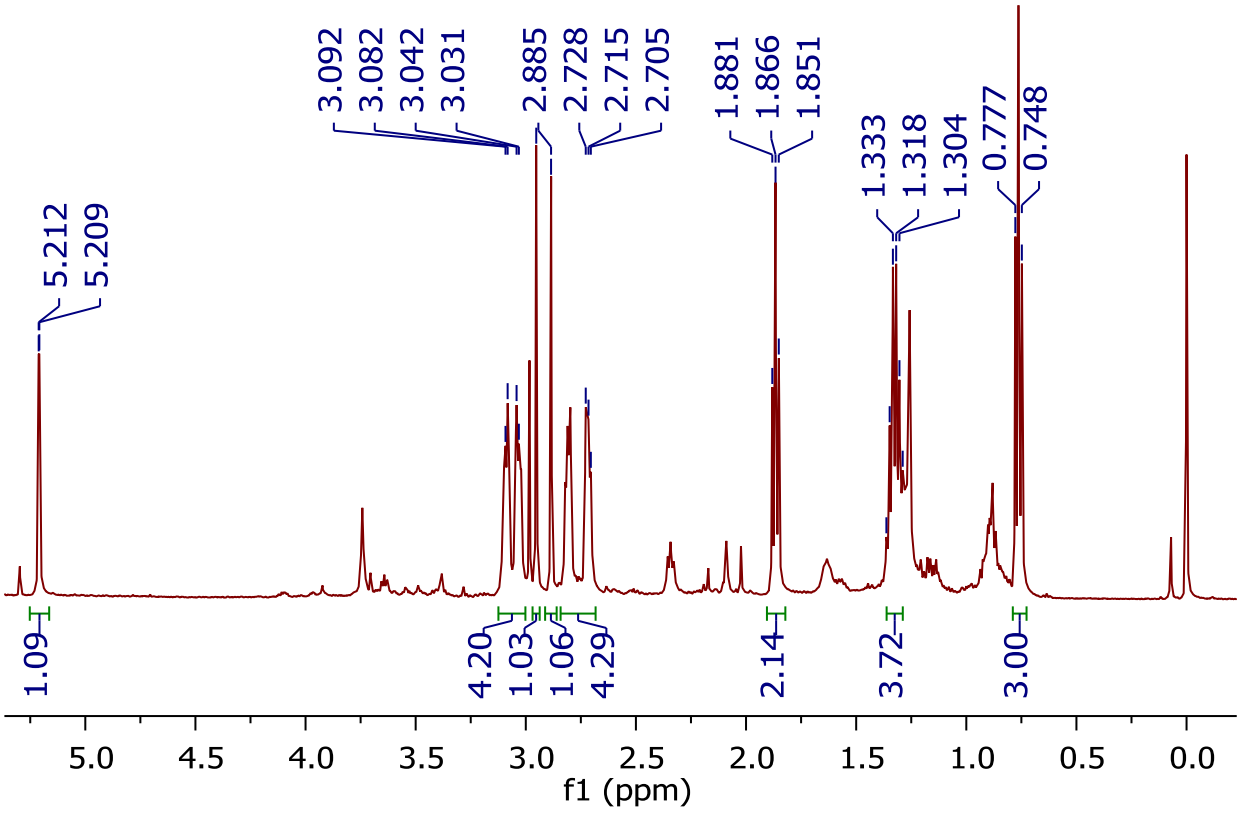


Figure S12. ^{1}H NMR spectrum of **ME2** derivative (0-5.25 ppm)

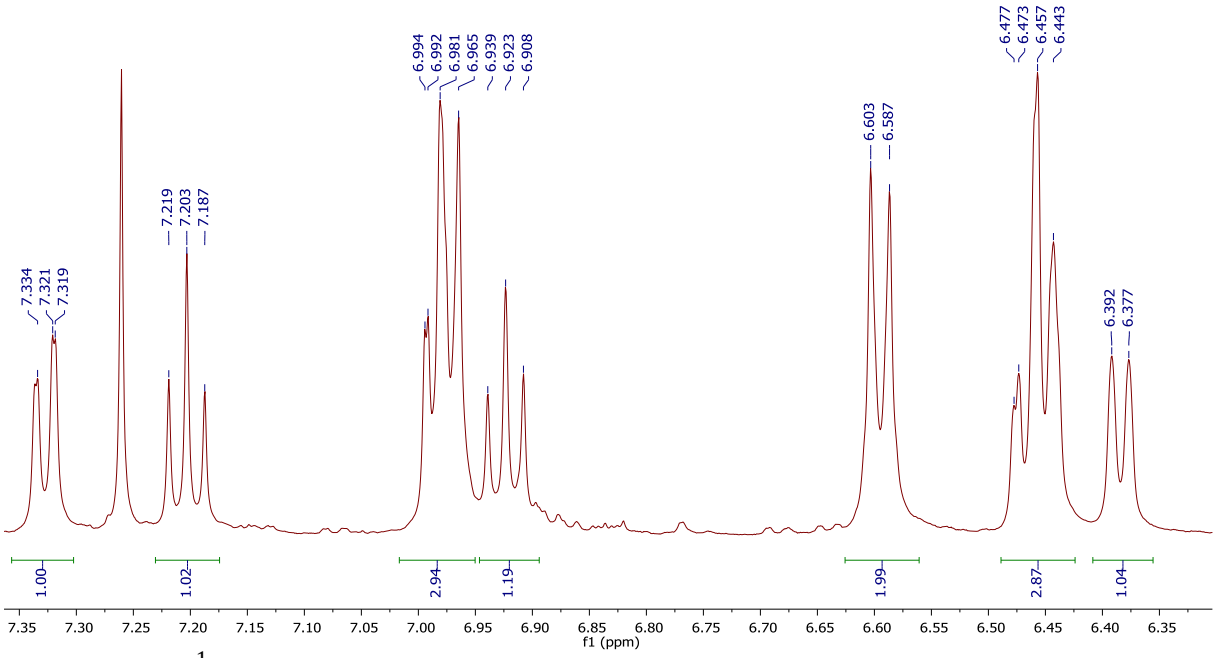


Figure S13. ^{1}H NMR spectrum of **ME2** derivative (6.30-7.37 ppm)

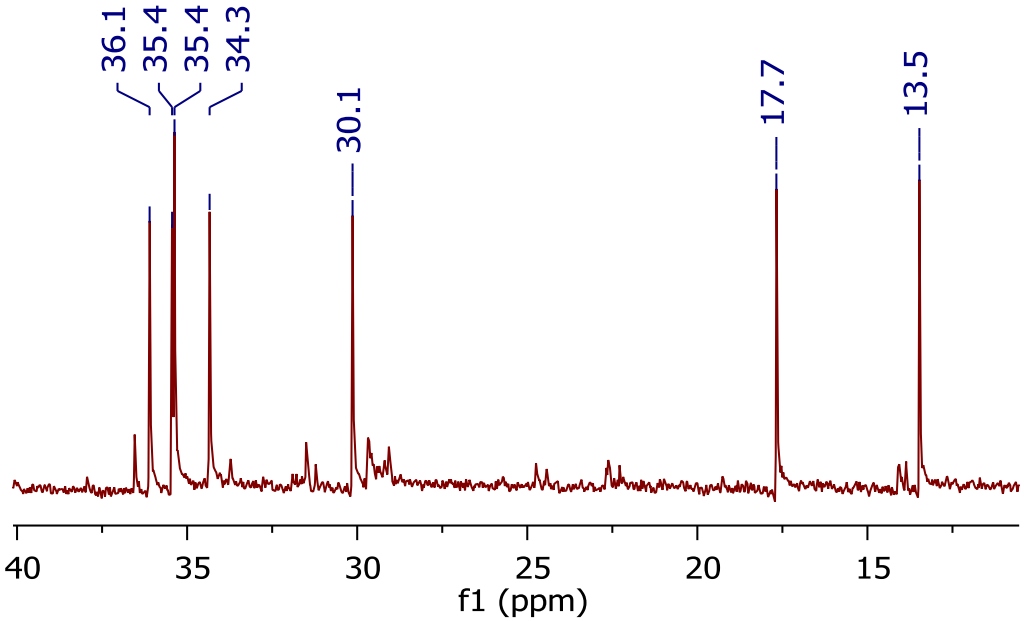


Figure S14. ^{13}C NMR spectrum of **ME2** derivative (12-40 ppm)

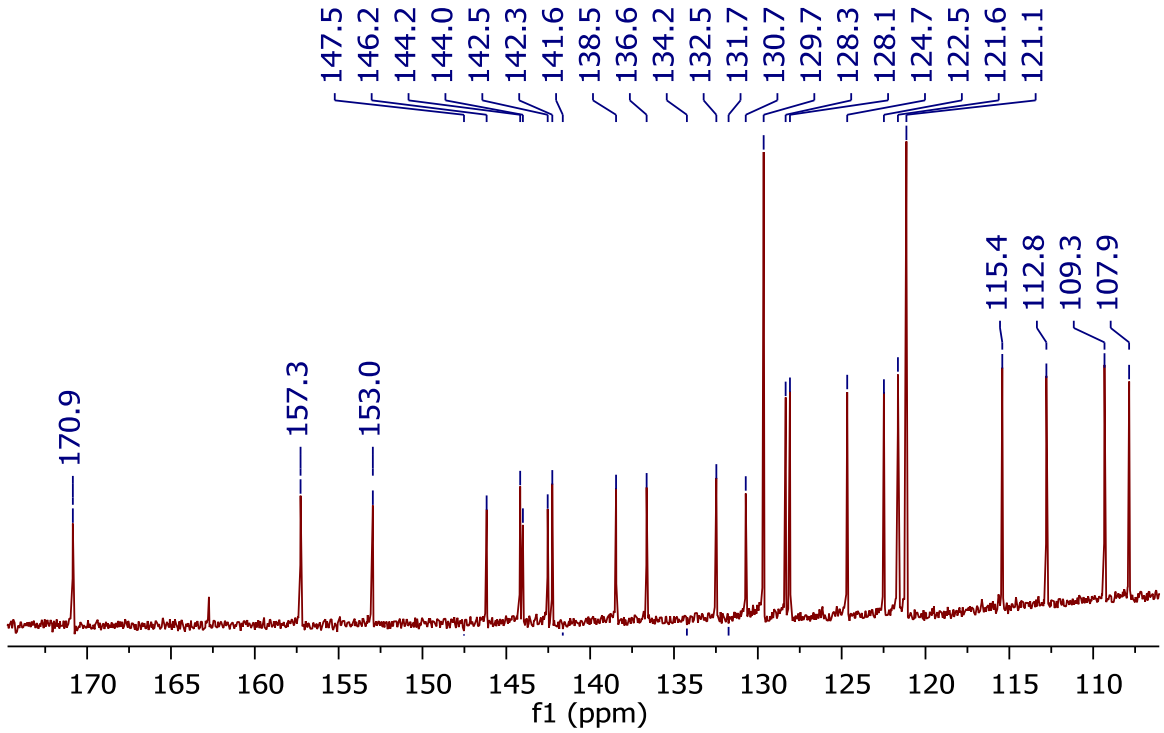


Figure S15. ^{13}C NMR spectrum of **ME2** derivative (107-174 ppm)

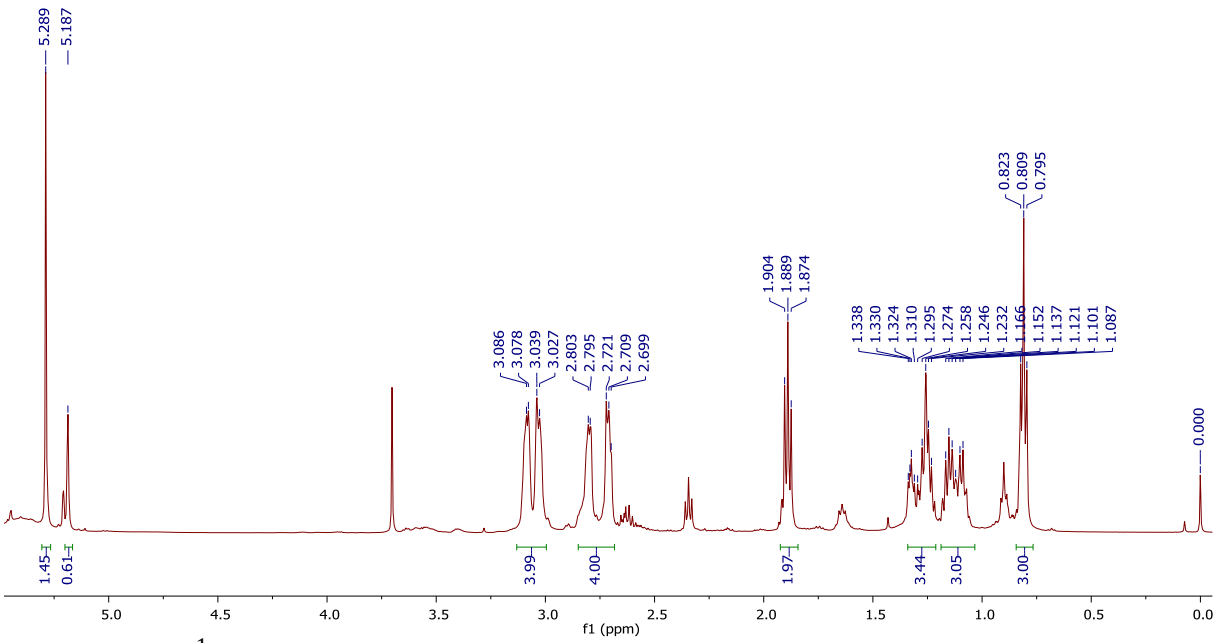


Figure S16. ^{1}H NMR spectrum of **ME3** derivative (0-5.50 ppm)

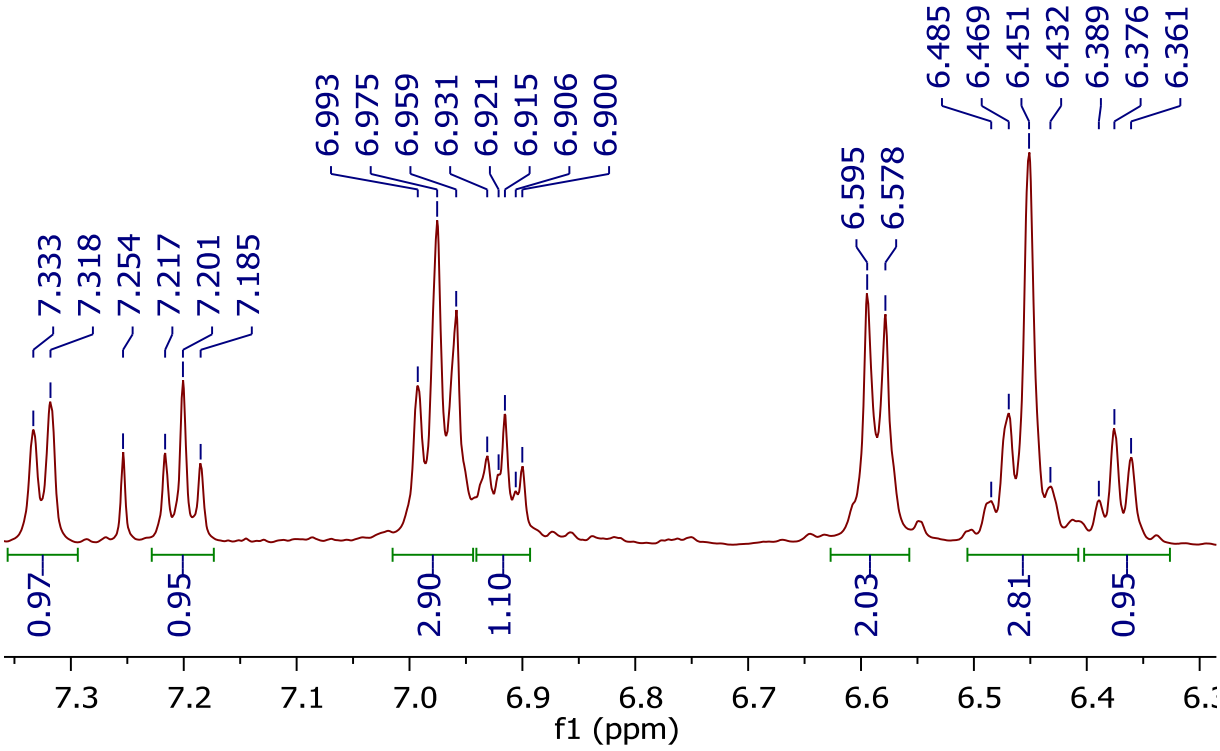


Figure S17. [1]H NMR spectrum of **ME3** derivative (6.30-7.35 ppm)

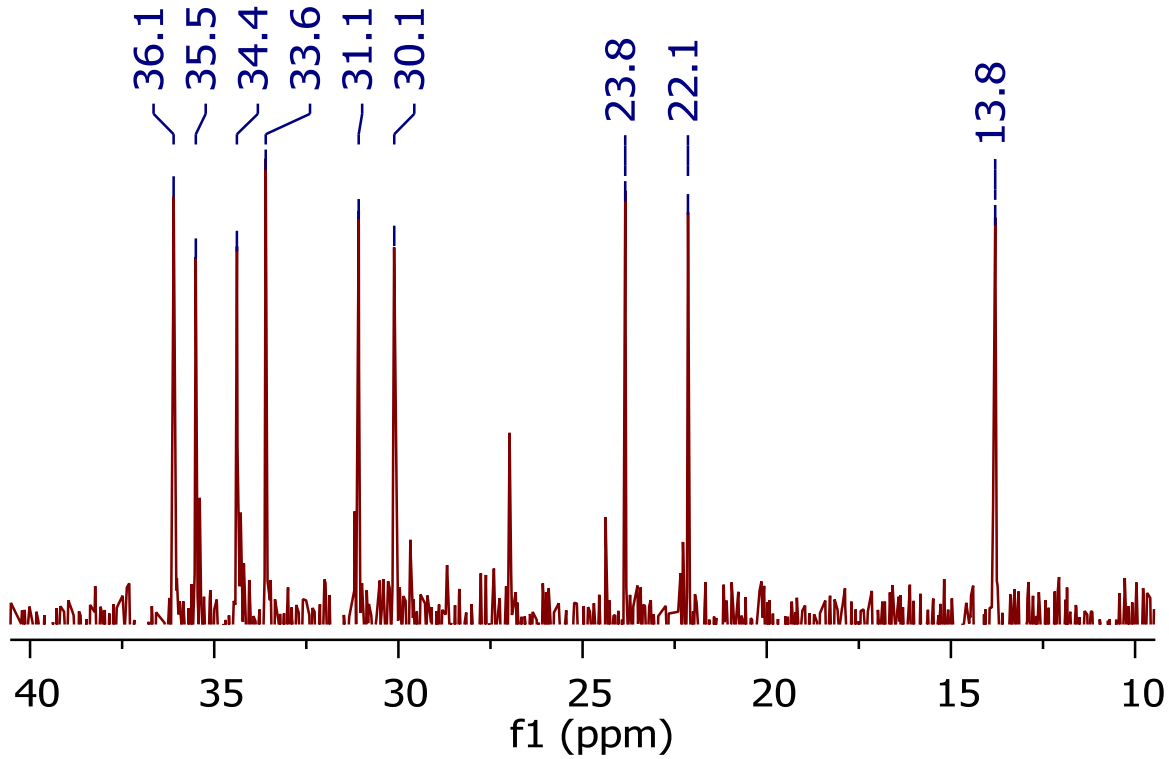


Figure S18. [13]C NMR spectrum of **ME3** derivative (10-40 ppm)

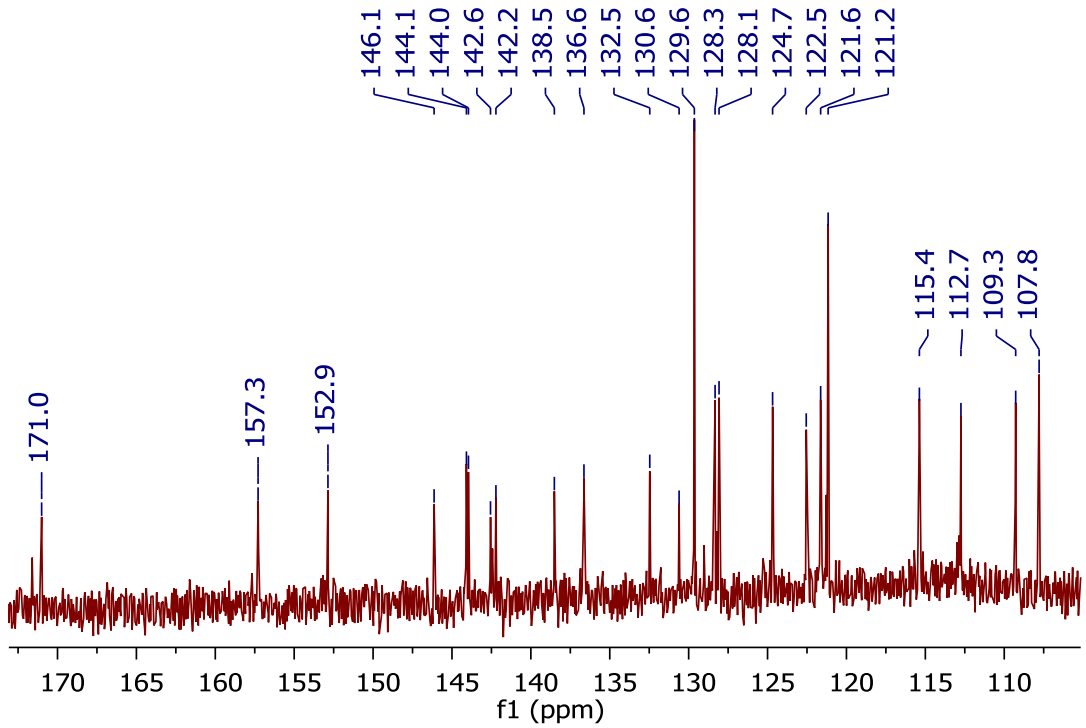


Figure S19. ^{13}C NMR spectrum of **ME3** derivative (105-173 ppm)

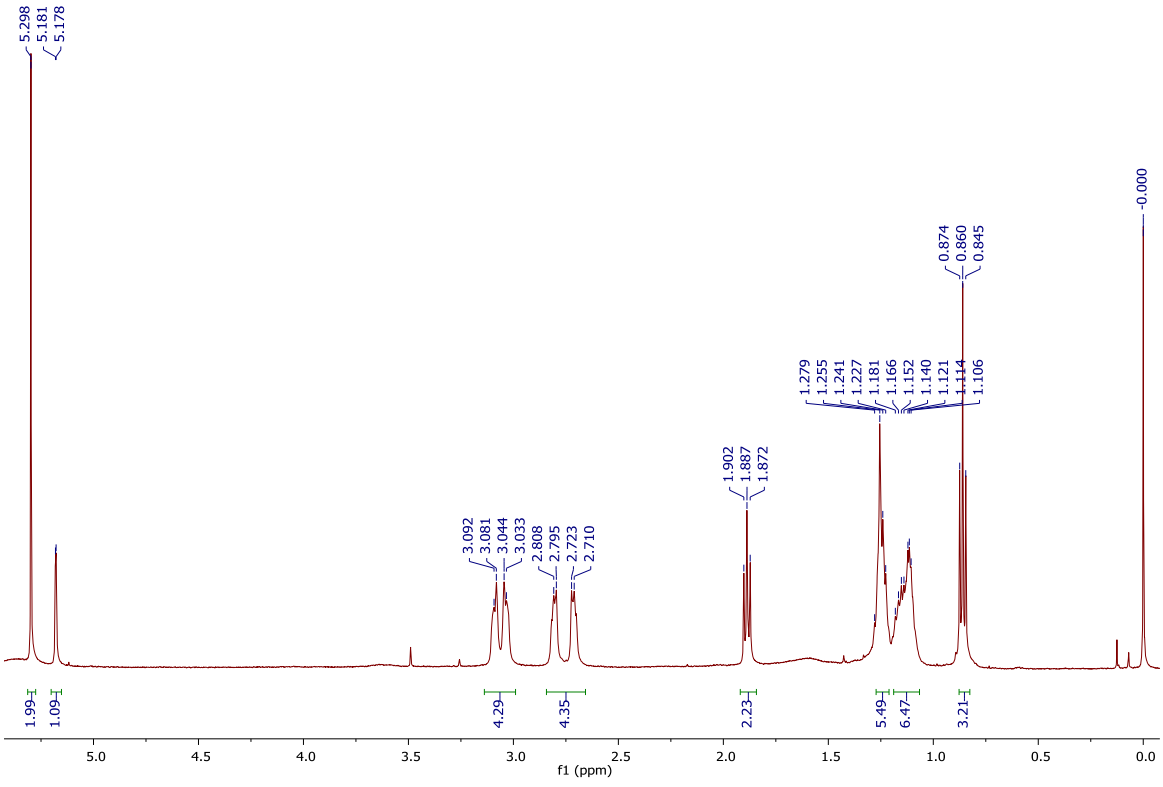


Figure S20. ^{1}H NMR spectrum of **ME4** derivative (0-5.40 ppm)

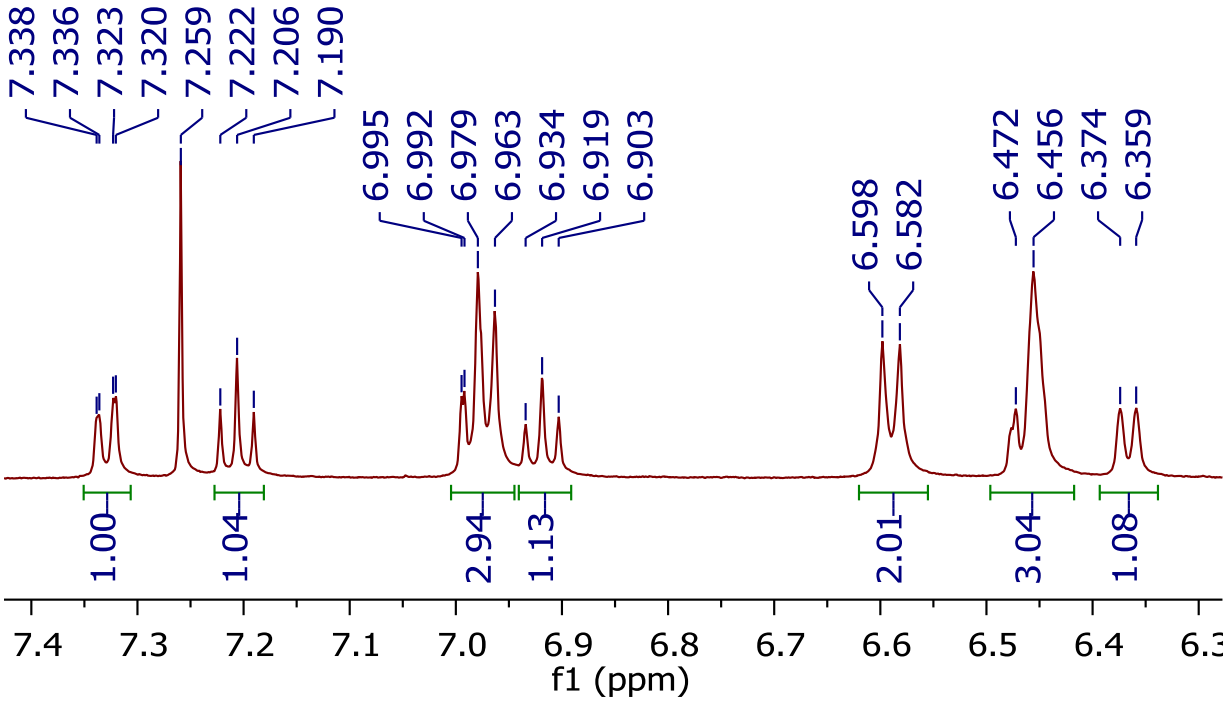


Figure S21. ^{1}H NMR spectrum of **ME4** derivative (6.30-7.45 ppm)

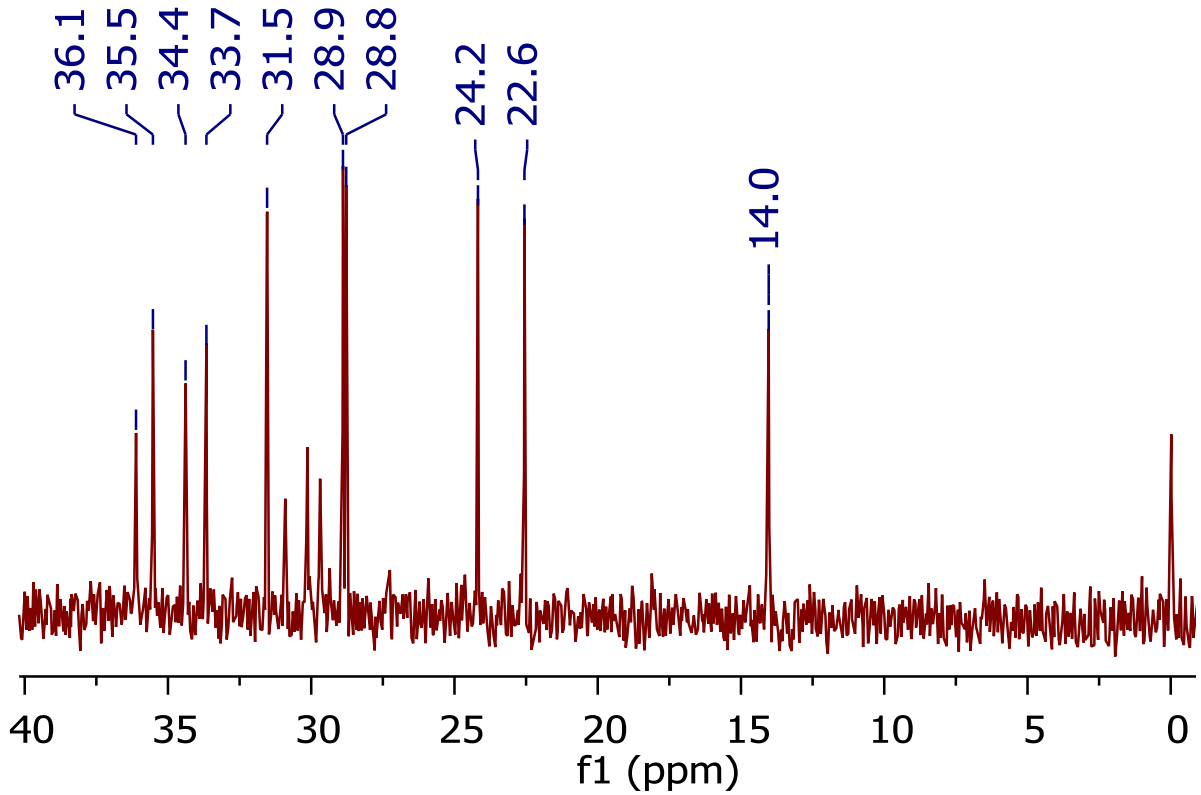


Figure S22. ^{13}C NMR spectrum of **ME4** derivative (0-40 ppm)

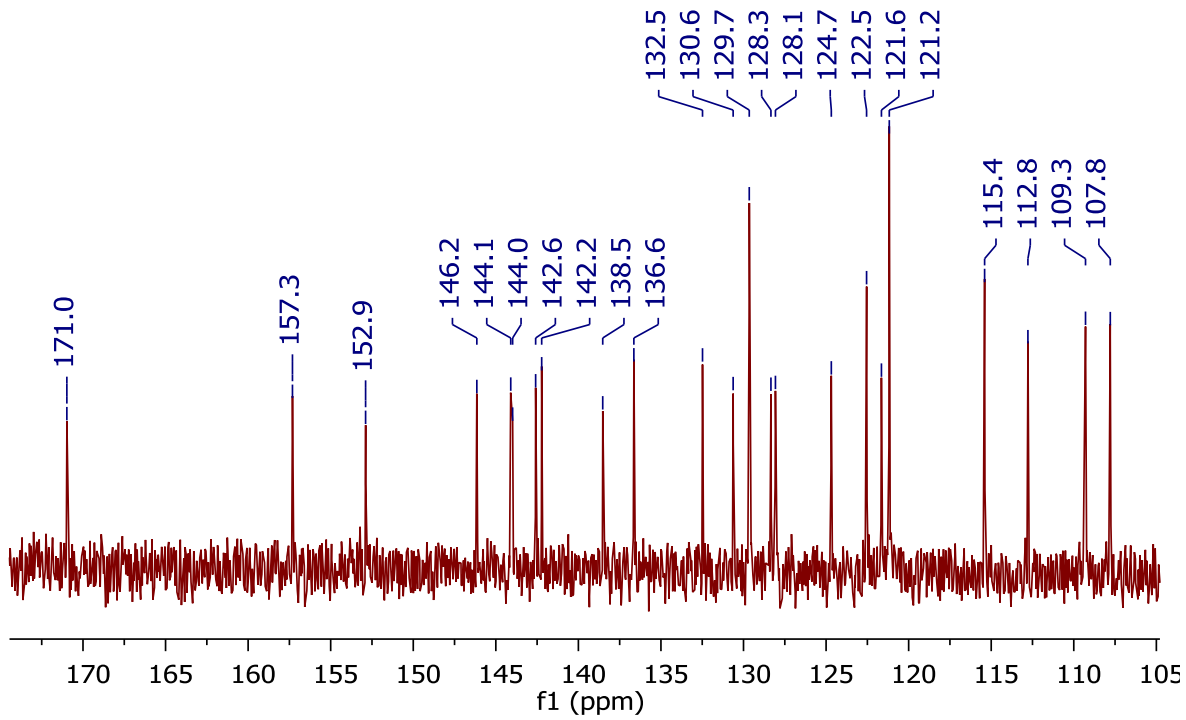


Figure S23. ^{13}C NMR spectrum of **ME4** derivative (105-175 ppm)

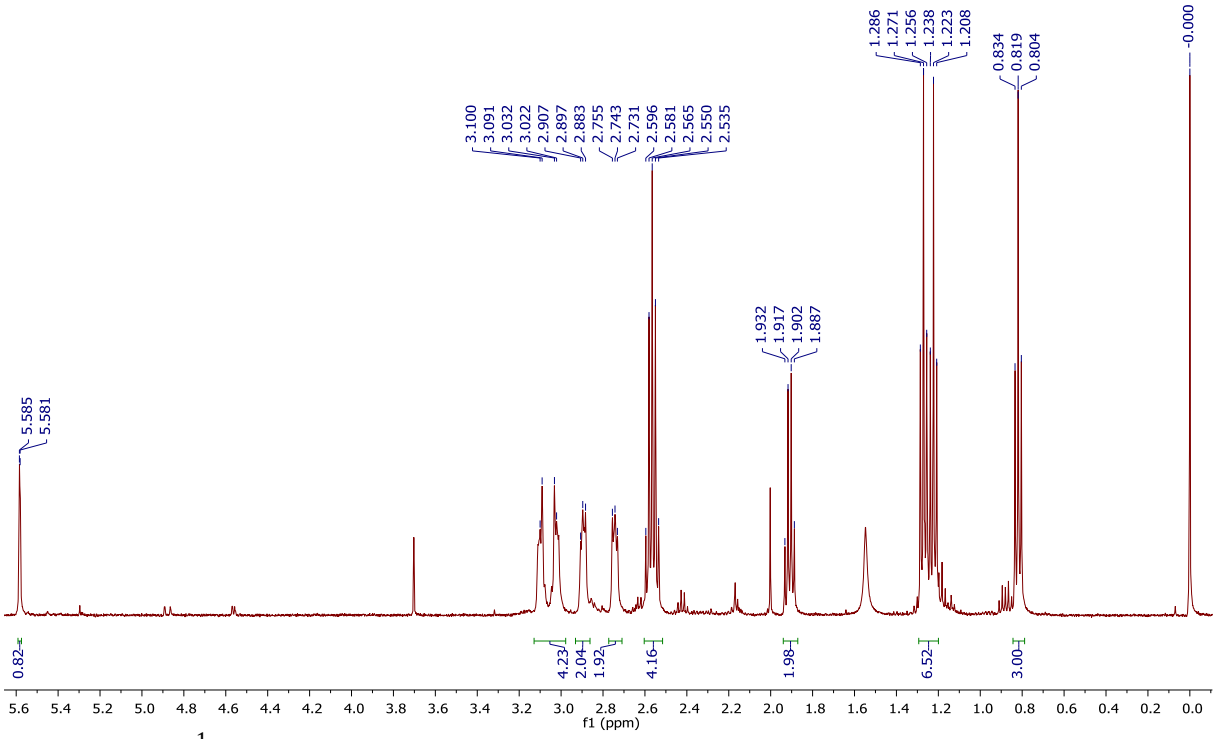


Figure S24. ^{1}H NMR spectrum of **TE1** derivative (0-5.60 ppm)

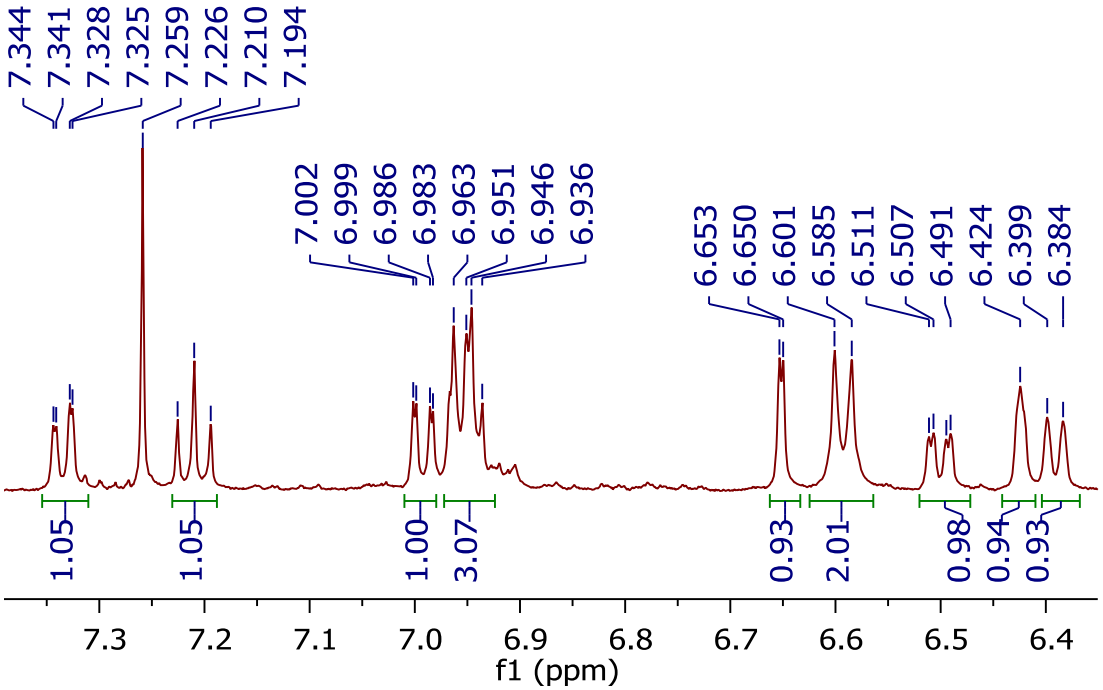


Figure S25. [1]H NMR spectrum of **TE1** derivative (6.35-7.40 ppm)

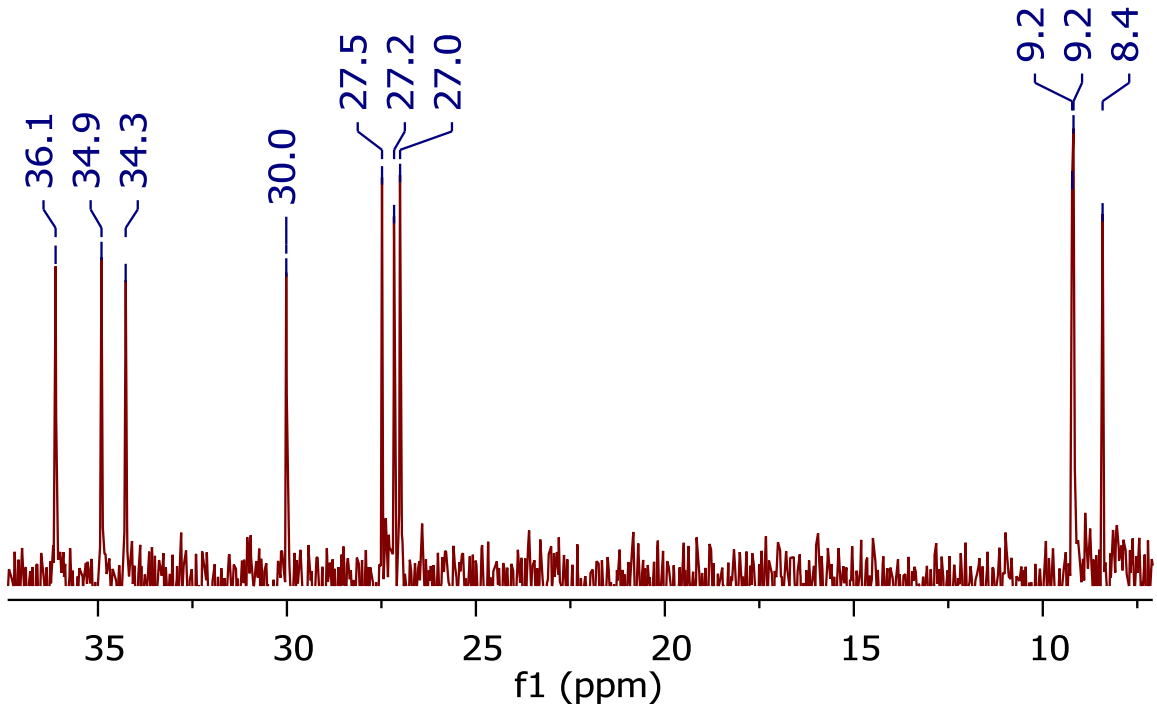


Figure S26. [13]C NMR spectrum of **TE1** derivative (7-37 ppm)

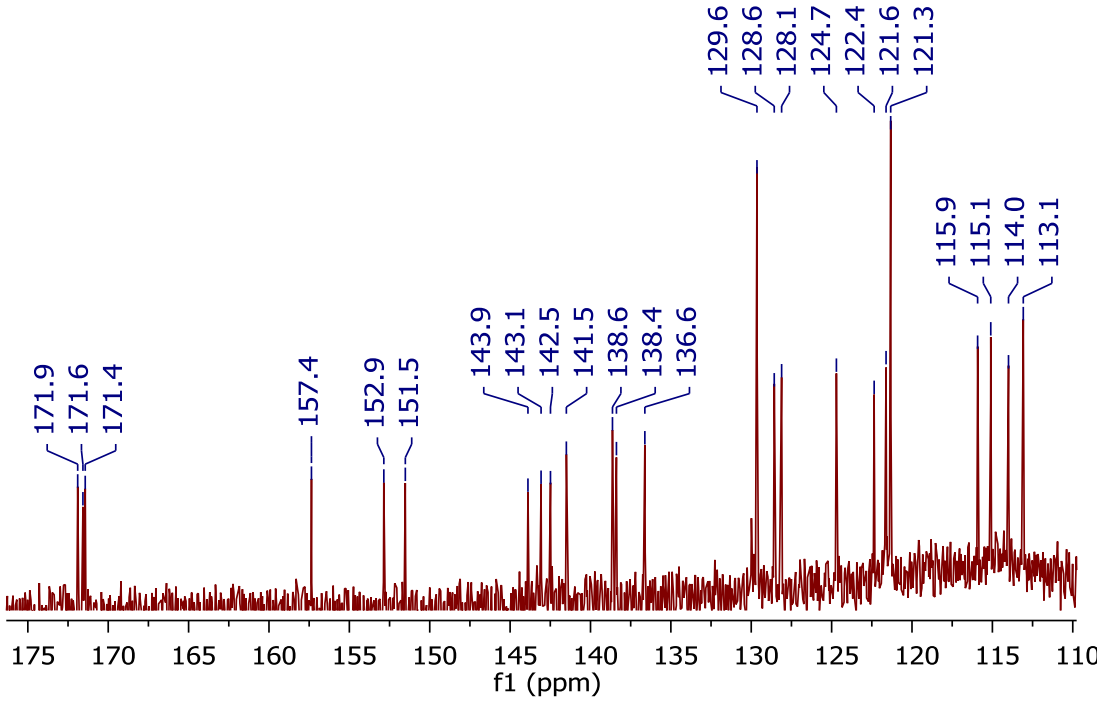


Figure S27. ^{13}C NMR spectrum of **TE1** derivative (110-175 ppm)

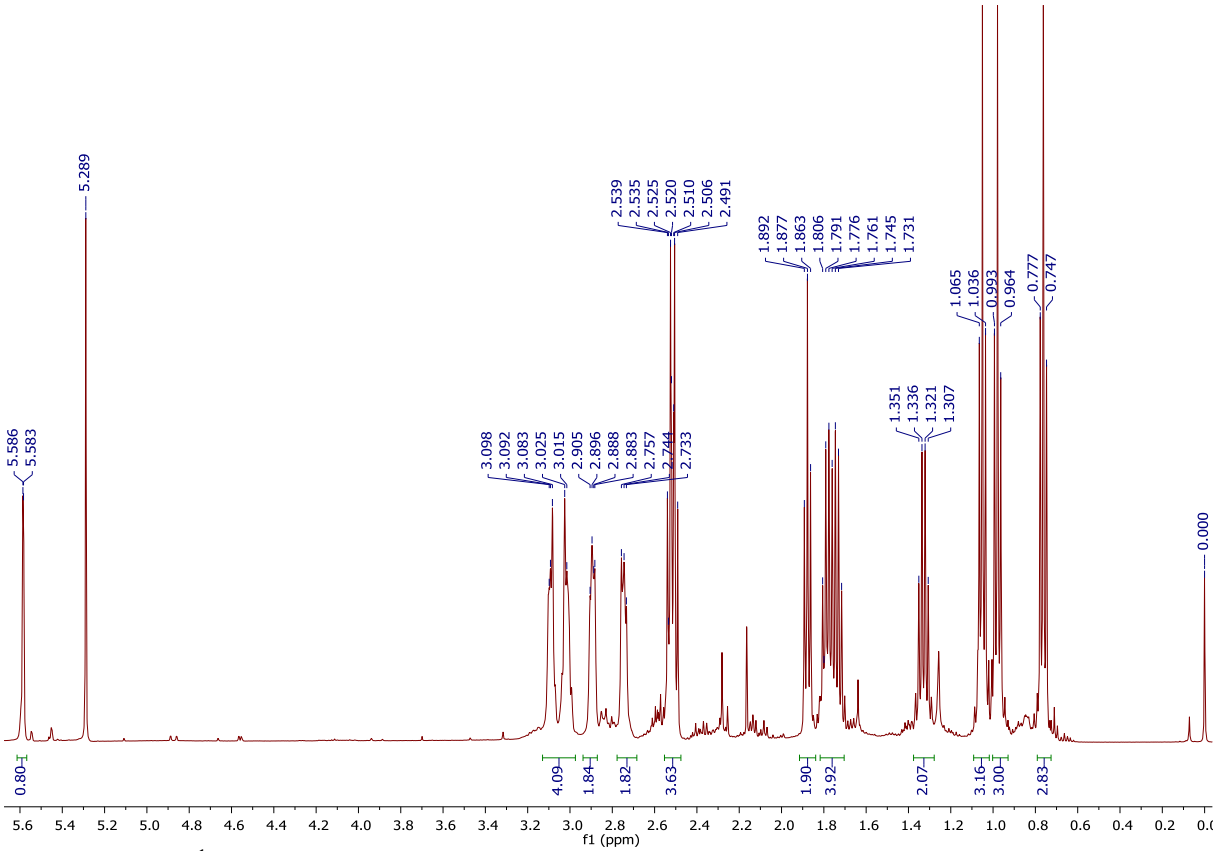


Figure S28. ^{1}H NMR spectrum of **TE2** derivative (0-5.65 ppm)

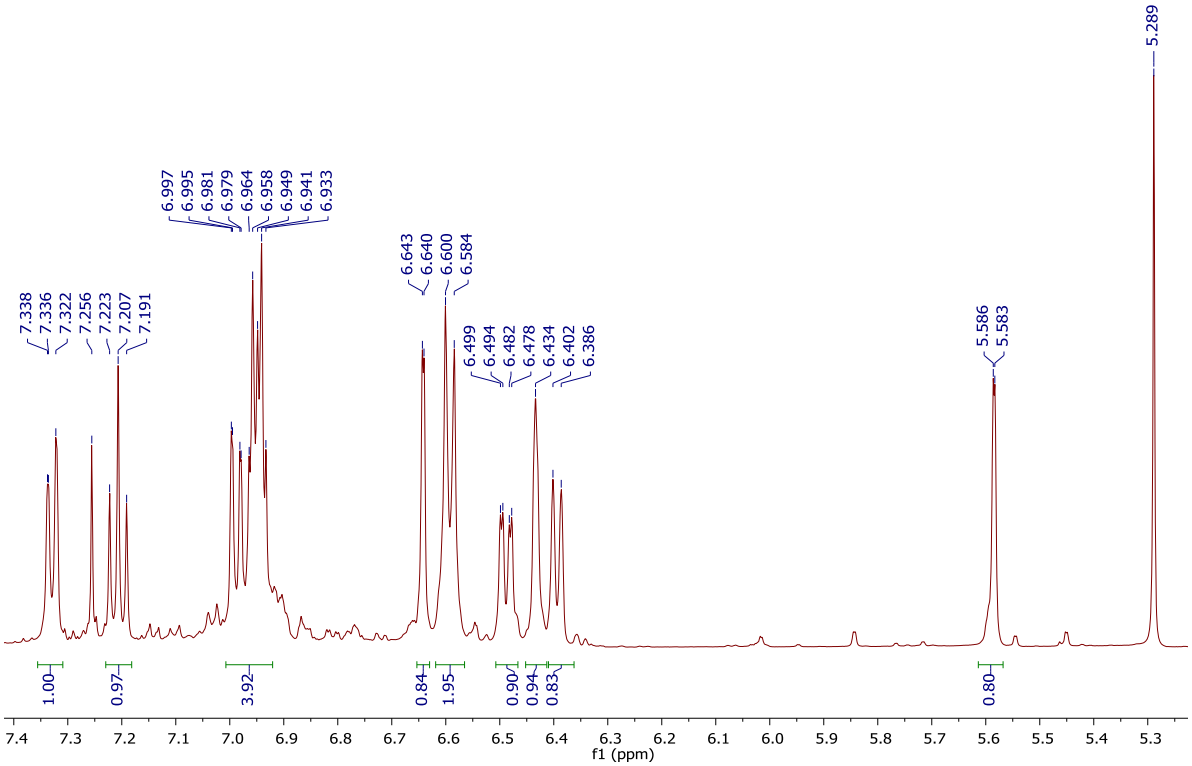


Figure S29. ^{1}H NMR spectrum of **TE2** derivative (5.25-7.40 ppm)

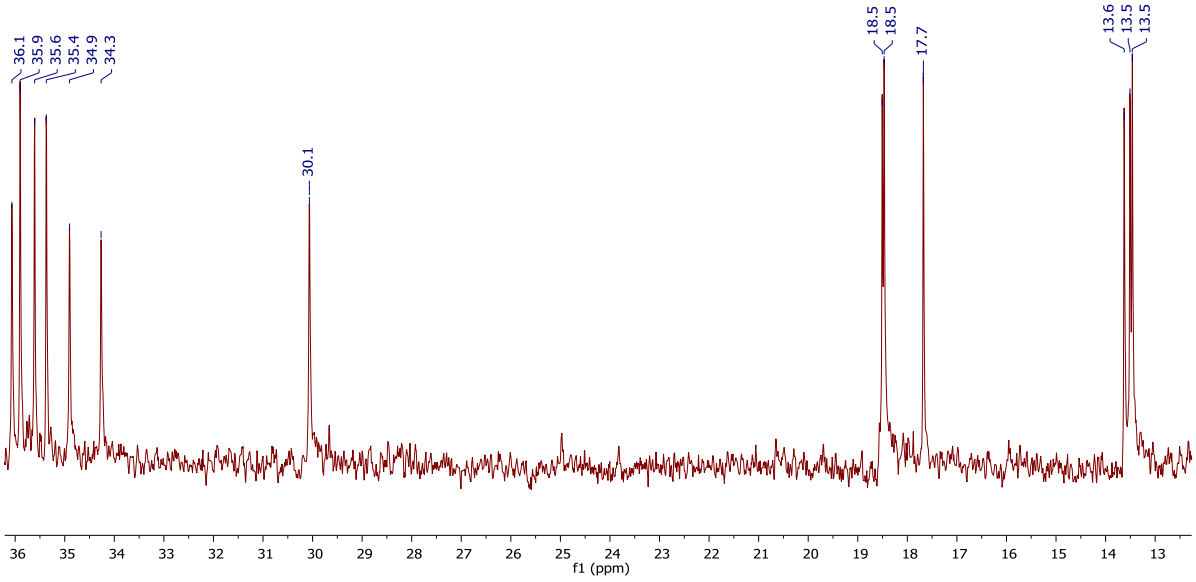


Figure S30. ^{13}C NMR spectrum of **TE2** derivative (12.5-36.5 ppm)

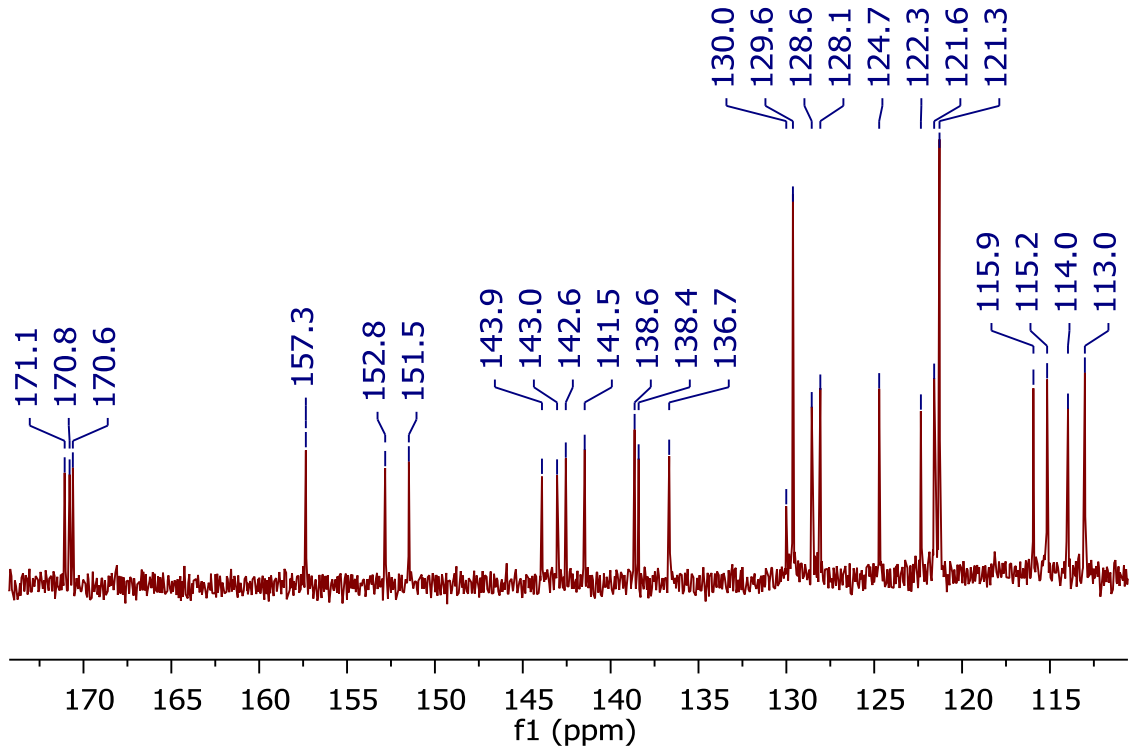


Figure S31. ^{13}C NMR spectrum of **TE2** derivative (111-173 ppm)

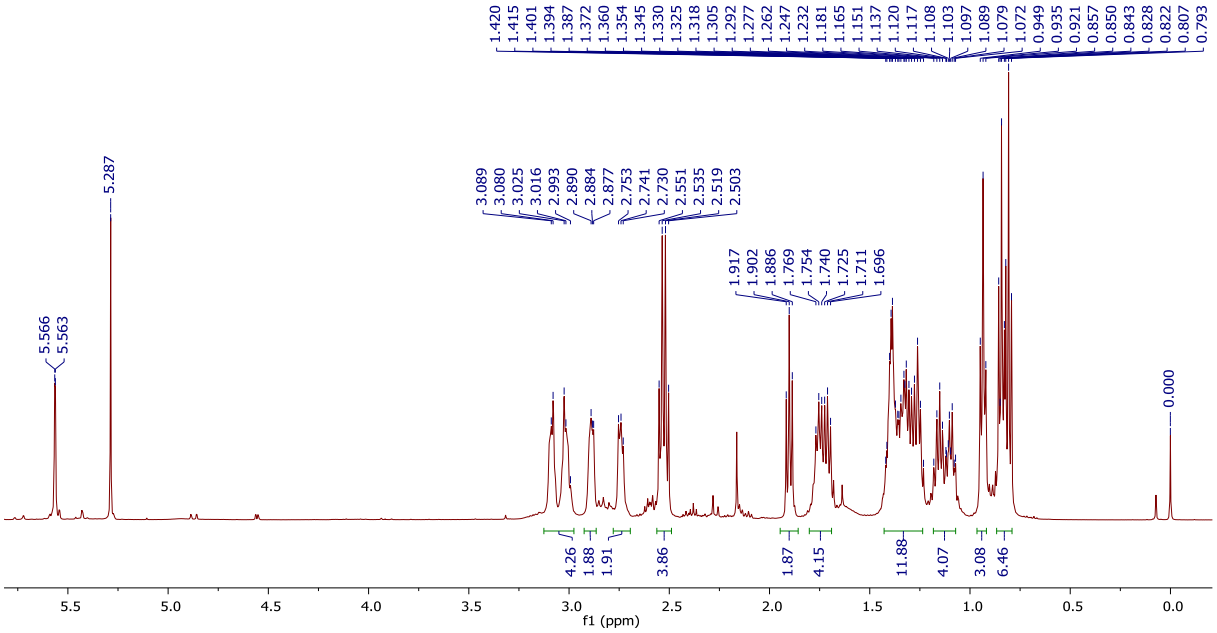


Figure S32. ^{1}H NMR spectrum of **TE3** derivative (0-5.75 ppm)

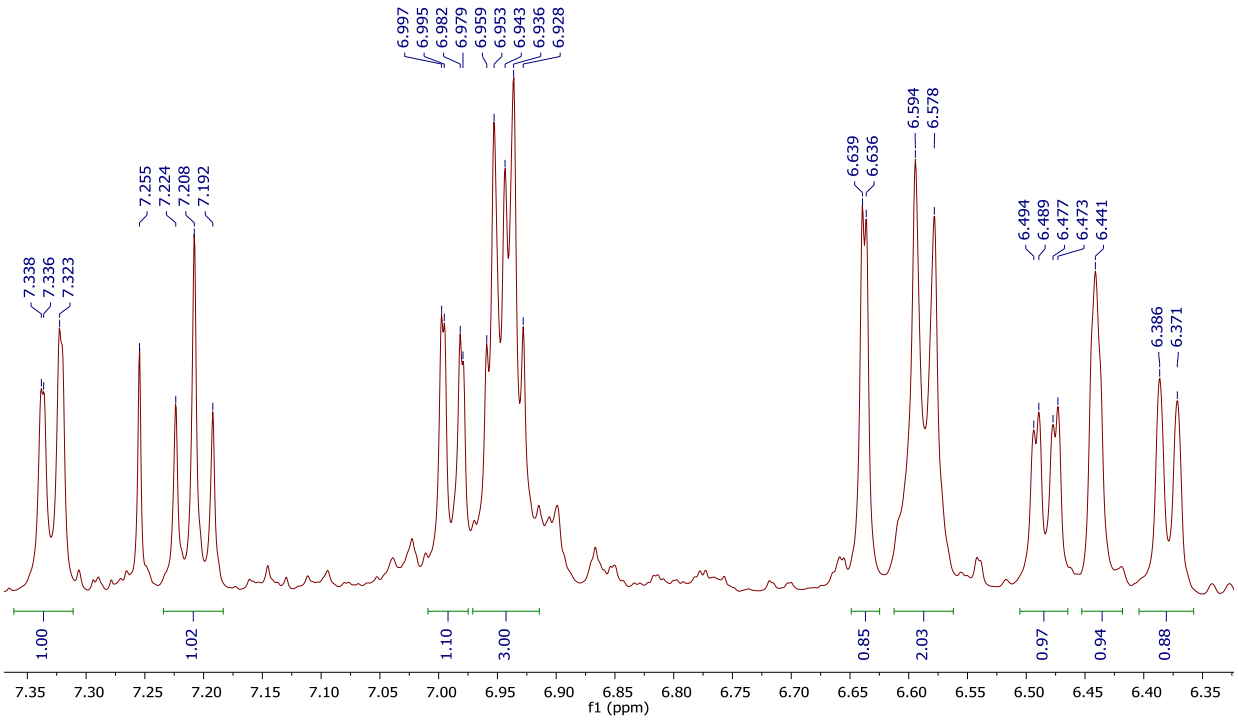


Figure S33. ^{1}H NMR spectrum of **TE3** derivative (6.32-7.37 ppm)

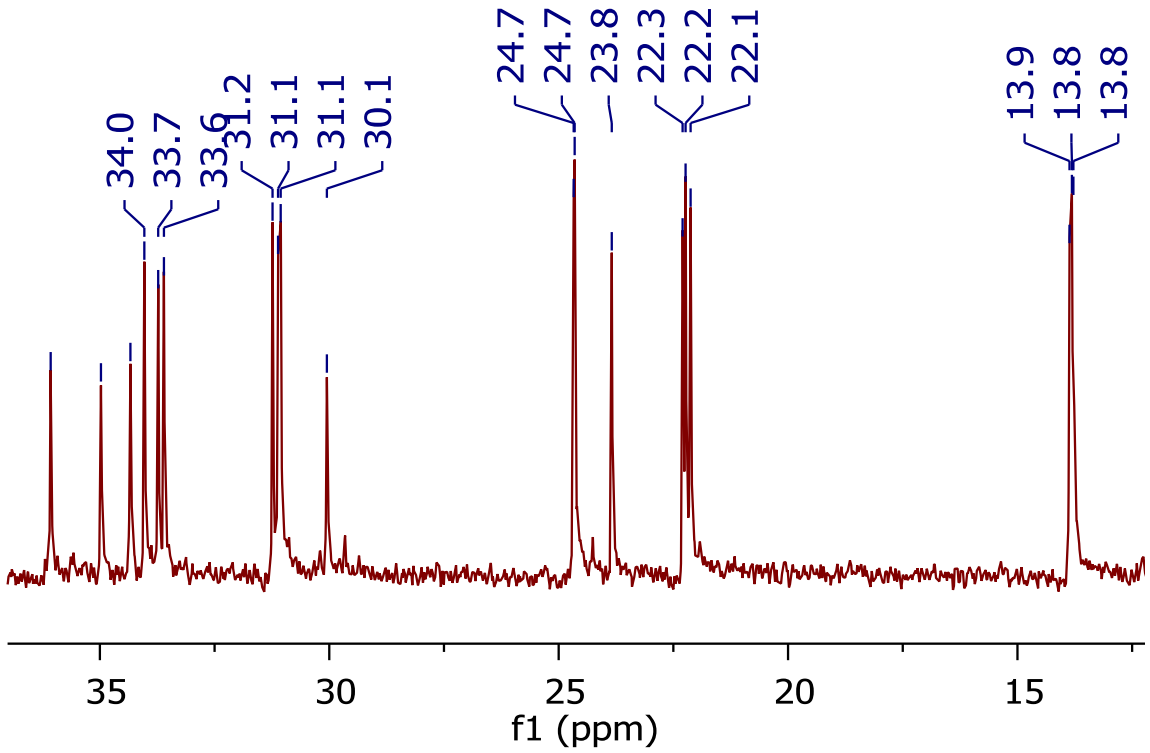


Figure S34. ^{13}C NMR spectrum of **TE2** derivative (12-37 ppm)

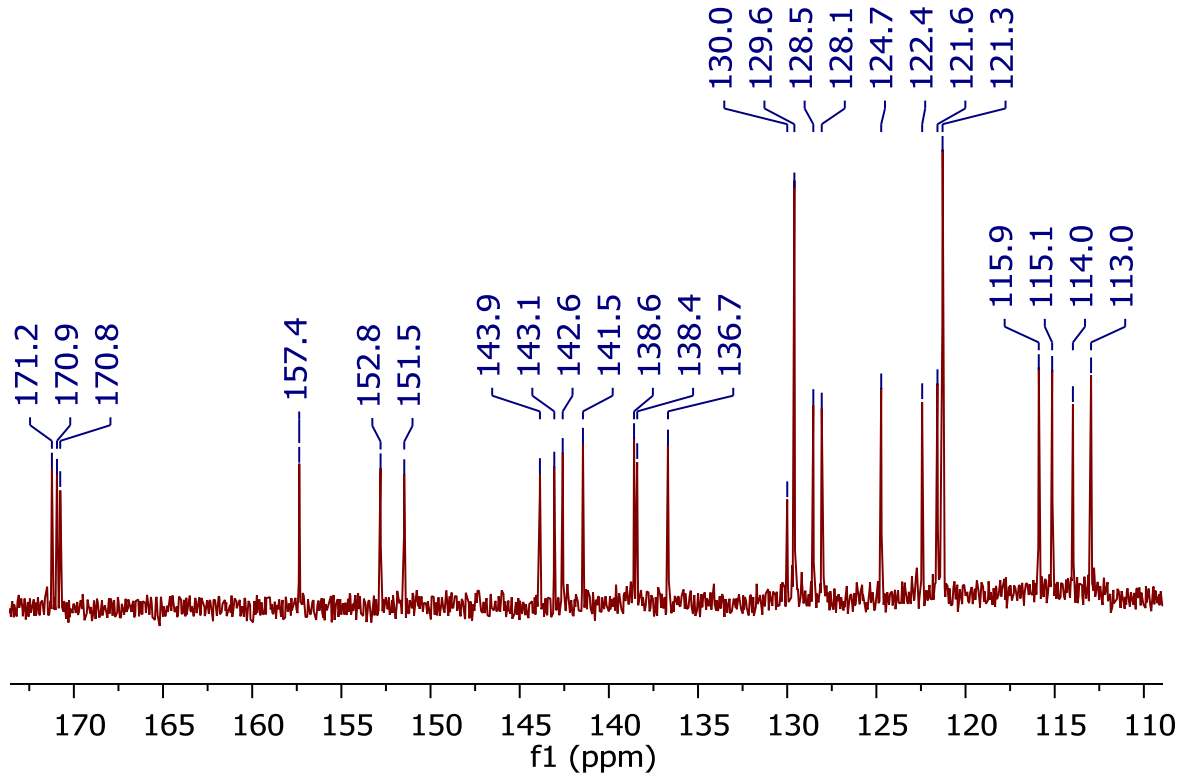


Figure S35. ^{13}C NMR spectrum of **TE2** derivative (110-173 ppm)

Table S1.

Changes in the chemical shifts δ_H of marchantin A ester derivatives after esterification.

Position	MA δ_H/mult	ME1 δ_H/mult	ME2 δ_H/mult	ME3 δ_H/mult	ME4 δ_H/mult	TE1 δ_H/mult	TE2 δ_H/mult	TE3 δ_H/mult
10	**7.02 dd**	**7.33 dd**	**7.32 dd**	**7.32 dd**	**7.33 dd**	**7.33 dd**	**7.33 dd**	**7.33 dd**
11	**7.15 t**	**7.19 t**	**7.20 t**	**7.20 t**	**7.21 t**	**7.21 t**	**7.21 t**	**7.21 t**
12	**6.87 dd**	**6.99 dd**	**6.99 dd**	**6.99 dd**	**6.99 dd**	**6.99 dd**	**6.99 dd**	**6.99 dd**
3'	**5.14 d**	5.21 d	5.21 d	5.19 d	5.19 d	**5.58 d**	**5.58 d**	**5.56 d**
5'	**6.48 d**	6.46 d	6.46 d	6.45 d	6.46 d	**6.65 d**	**6.64 d**	**6.64 d**

*bolded chemical shifts – shifts changed after esterification

Table S2.

Changes in the chemical shifts δ_C of marchantin A ester derivatives after esterification.

Position	MA δ_C	ME1 δ_C	ME2 δ_C	ME3 δ_C	ME4 δ_C	TE1 δ_C	TE2 δ_C	TE3 δ_C
1'	**132.4**	130.6	130.7	130.6	130.6	**129.9**	**130.0**	**130.0**
2'	**146.3**	146.1	146.2	146.1	146.2	**151.5**	**151.5**	**151.5**
3'	**107.7**	107.8	107.9	107.8	107.8	**114.0**	**114.0**	**114.0**
4'	**130.6**	130.6	130.7	130.6	130.6	**138.6**	**138.6**	**138.6**
5'	**109.1**	109.3	109.3	109.3	109.3	**115.9**	**115.9**	**115.9**
6'	**144.1**	144.1	144.2	144.1	144.1	**143.0**	**143.0**	**143.1**
9	**136.0**	136.6	136.6	136.6	136.6	**136.6**	**136.7**	**136.7**
10	**121.8**	**128.1**	**128.1**	**128.1**	**128.1**	**128.1**	**128.1**	**128.1**
11	**126.0**	**124.6**	**124.7**	**124.7**	**124.7**	**124.7**	**124.7**	**124.7**
12	**114.3**	**121.7**	**121.6**	**121.6**	**121.6**	**121.6**	**121.6**	**121.6**
13	**148.7**	**142.5**	**142.5**	**142.6**	**142.6**	**142.4**	**142.6**	**142.6**
14	**139.6**	**144.0**	**144.0**	**144.0**	**144.0**	**143.8**	**143.9**	**143.9**

*bolded chemical shifts – shifts changed after esterification

Table S3. Calculated of physically significant molecular descriptors and pharmaceutically relevant properties.

molecule	#rotor	mol_MW	SASA	FOSA	FISA	volume	IP(eV)
MA	13	440.495	631.316	145.975	137.602	1239.139	8.784
ME1	14	496.559	649.011	207.825	97.371	1365.938	8.885
ME2	15	510.585	680.004	231.146	102.412	1410.856	8.865
ME3	17	538.639	738.305	304.435	136.256	1535.528	8.851
ME4	19	566.693	776.503	354.667	130.893	1624.729	8.937
TE1	16	608.687	858.112	459.822	102.712	1757.838	9.136
TE2	19	650.767	903.729	526.842	86.342	1890.078	9.089
TE3	25	734.928	903.146	533.443	90.259	2064.331	9.354

Table S3 cont.

molecule	Qppolrz	QPlogPC16	QPlogPoct	QPlogPo/w	CIQPlogS	QPPCaco	QPPMDCK	QPlogKp
MA	38.41	13.869	19.013	4.747	-8.054	490.926	229.285	-1.582
ME1	42.805	14.454	20.423	5.384	-8.675	1181.756	592.576	-0.759
ME2	43.986	14.84	20.737	5.623	-8.963	1058.592	526.113	-0.746
ME3	47.224	15.758	21.562	6.108	-9.541	505.572	236.687	-1.35
ME4	49.446	16.421	22.059	6.699	-10.121	568.381	268.624	-1.083
TE1	56.744	17.073	23.487	6.259	-9.495	1051.67	522.395	-0.835
TE2	60.062	18.024	24.496	7.229	-10.389	1503.569	768.775	-0.263
TE3	63.077	18.964	25.901	8.326	-12.176	1380.287	700.875	0.202

List of QikProp properties and descriptors.

#rotor Number of non-trivial (not CX3), non-hindered (not alkene, amide, small ring) rotatable bonds.

mol_MW Molecular weight of the molecule.

SASA Total solvent accessible surface area (SASA) in square angstroms using a probe with a 1.4 Å radius.

FOSA Hydrophobic component of the SASA (saturated carbon and attached hydrogen).

FISA Hydrophilic component of the SASA (SASA on N, O, H on heteroatoms, carbonyl C).

Volume Total solvent-accessible volume in cubic angstroms using a probe with a 1.4 Å radius.

IP(ev) PM3 calculated ionization potential (negative of HOMO energy).

QPpolrz Predicted polarizability in cubic angstroms.

QPlogPC16 Predicted hexadecane/gas partition coefficient.

QPlogPoct Predicted octanol/gas partition coefficient.

QPlogPw Predicted water/gas partition coefficient.

QPlogPo/w Predicted octanol/water partition coefficient.

CIQPlogS Conformation-independent predicted aqueous solubility, log S. S in mol dm^{-3} is the concentration of the solute in a saturated solution that is in equilibrium with the crystalline solid.

QPPCaco Predicted apparent Caco-2 cell permeability in nm/sec. Caco-2 cells are a model for the gut-blood barrier. QikProp predictions are for non-active transport.

QPPMDCK Predicted apparent MDCK cell permeability in nm/sec. MDCK cells are considered to be a good mimic for the blood-brain barrier. QikProp predictions are for non-active transport.

QPlogKp Predicted skin permeability, log