Structure-Activity Relationships of Cannabigerol and Cannabigerolic acid Derivatives as Antibacterial Agents Against Gram-Positive Bacteria

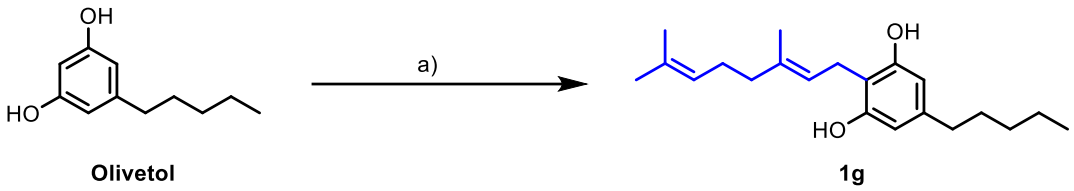
Prashant S. Mandal, Lucy M. Coleman, Vikas Kumar, Daniel E. Walker, Jessica C. Thompson, and Shanteri Singh*

Department of Chemistry & Biochemistry, University of Oklahoma, Norman, Oklahoma 73019, United States.

*Email: shanteri.singh@ou.edu

Table of Content **Page**

Reaction optimization scheme:



Olivetol **1g**

Reaction Condition: a) Olivetol (1.0 equiv.), geraniol (1.0 equiv.), Al_2O_3 (acidic) (2.0, 5.0, and 10.0 equiv.), DCE, 80 °C, 8 h, N_2 atm.

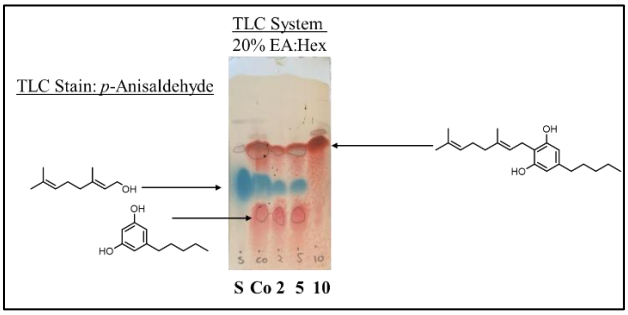


Figure S1: TLC observation of CBG compound

NMR Spectral data

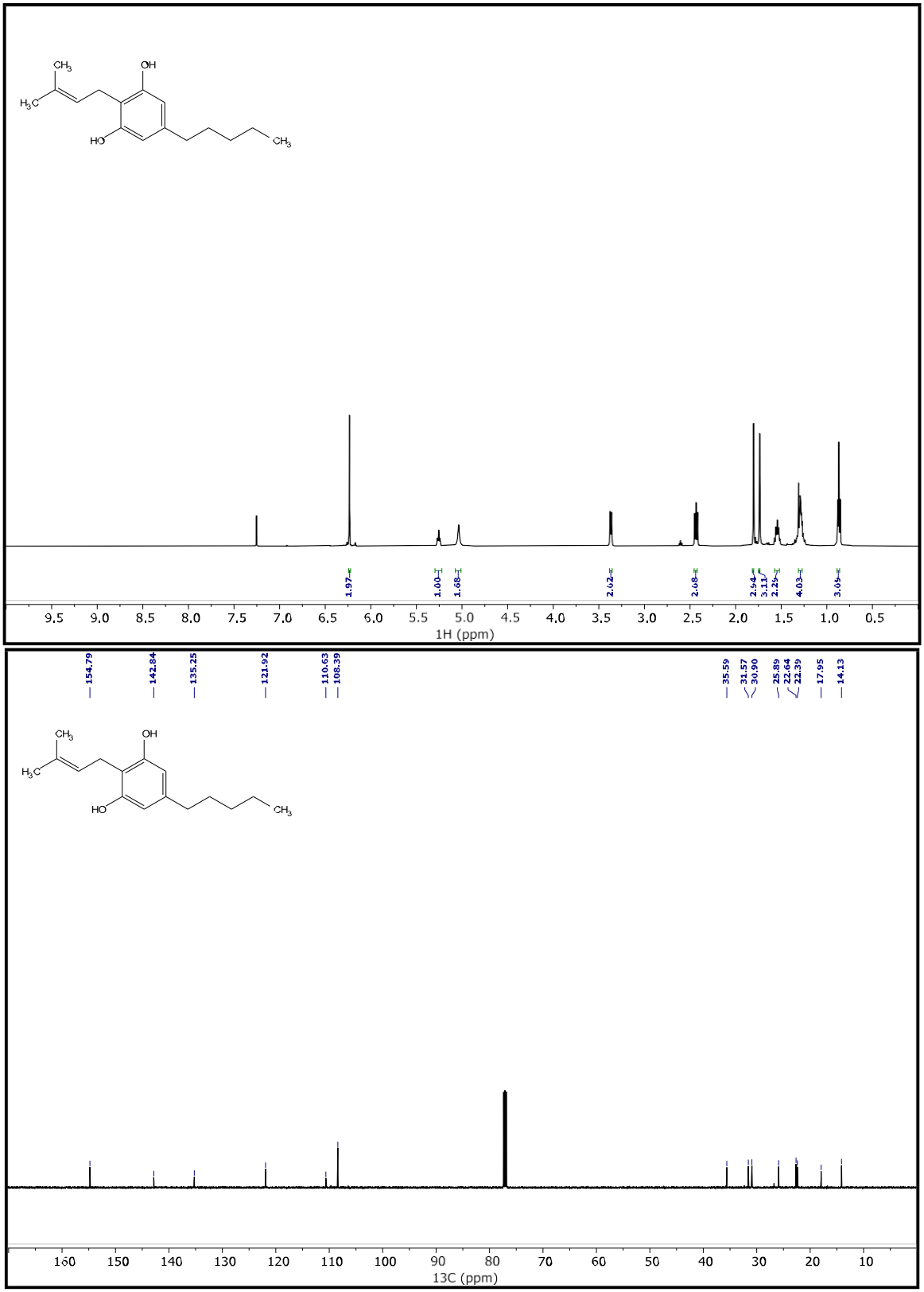


Figure S2: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1a** in $CDCl_3$

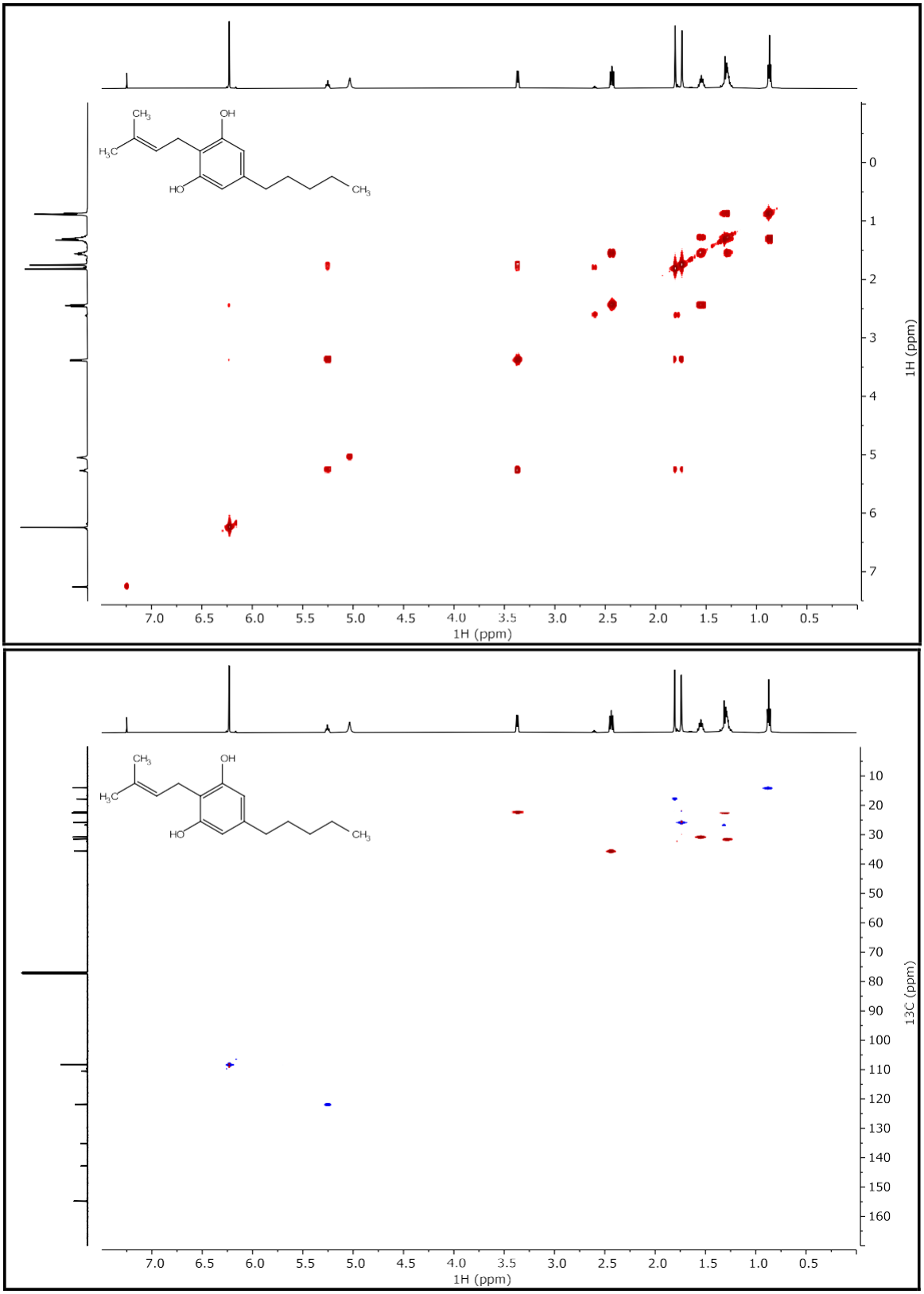


Figure S3: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1a** in $CDCl_3$

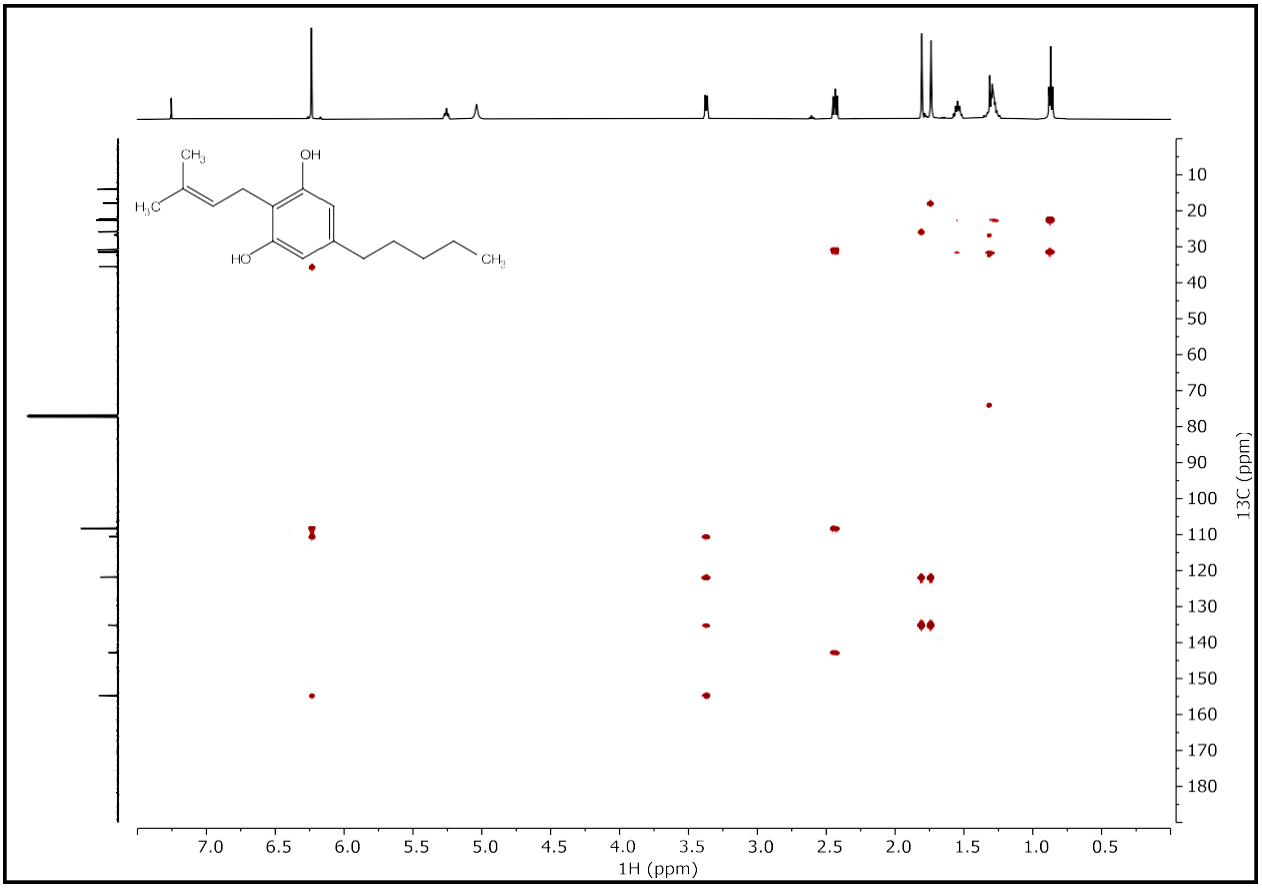


Figure S4: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1a** in $CDCl_3$

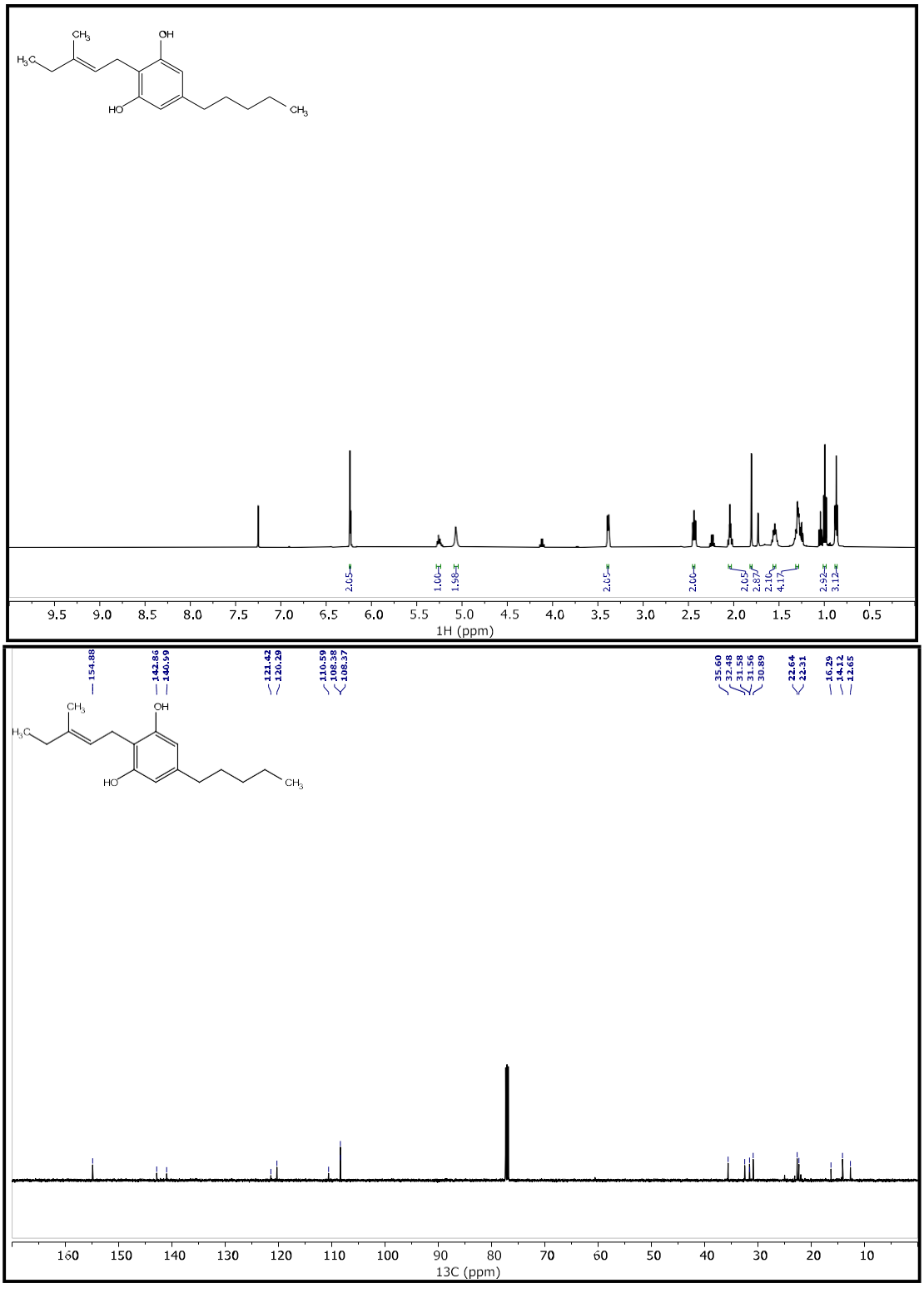


Figure S5: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1b** in $CDCl_3$

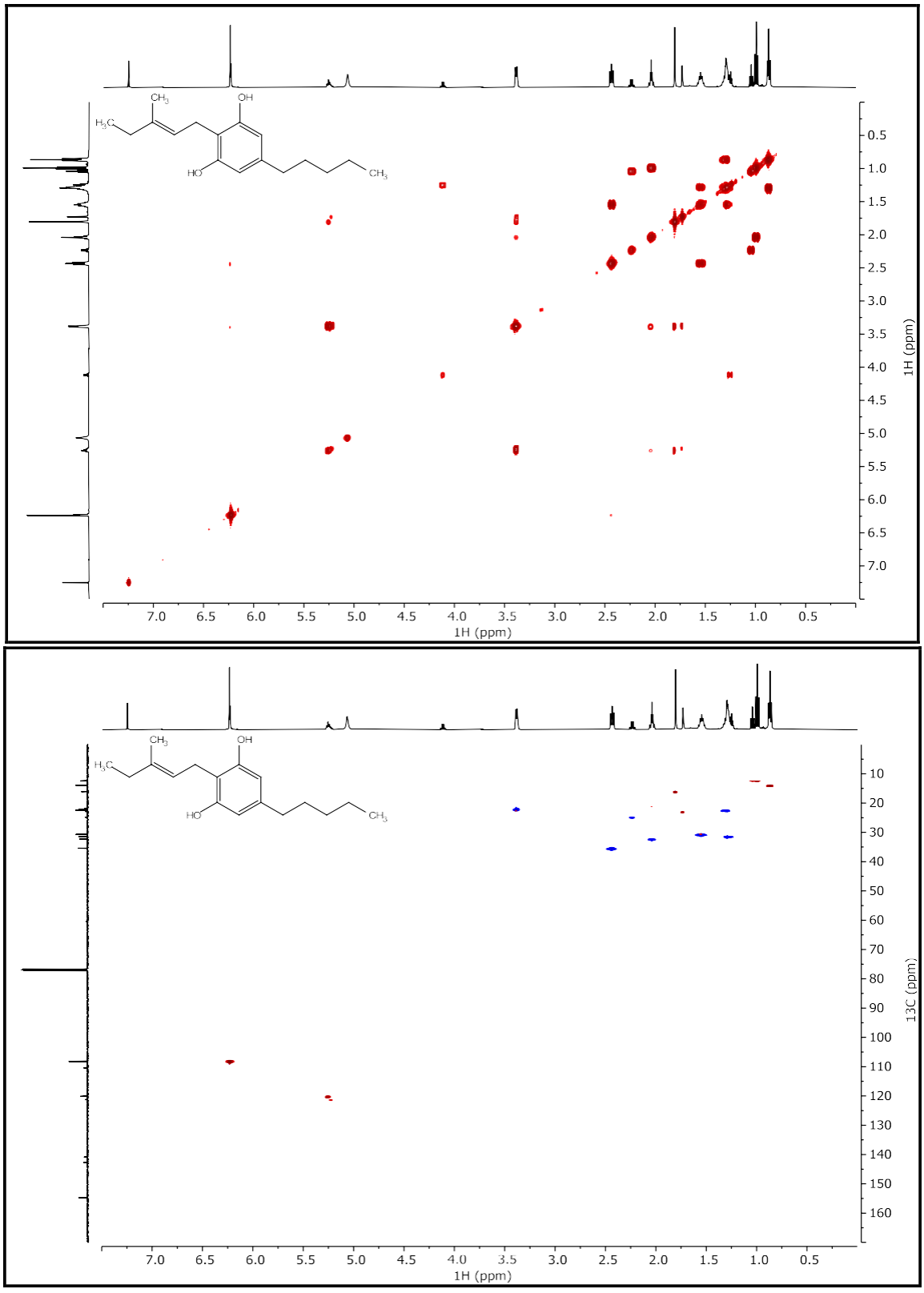


Figure S6: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1b** in $CDCl_3$

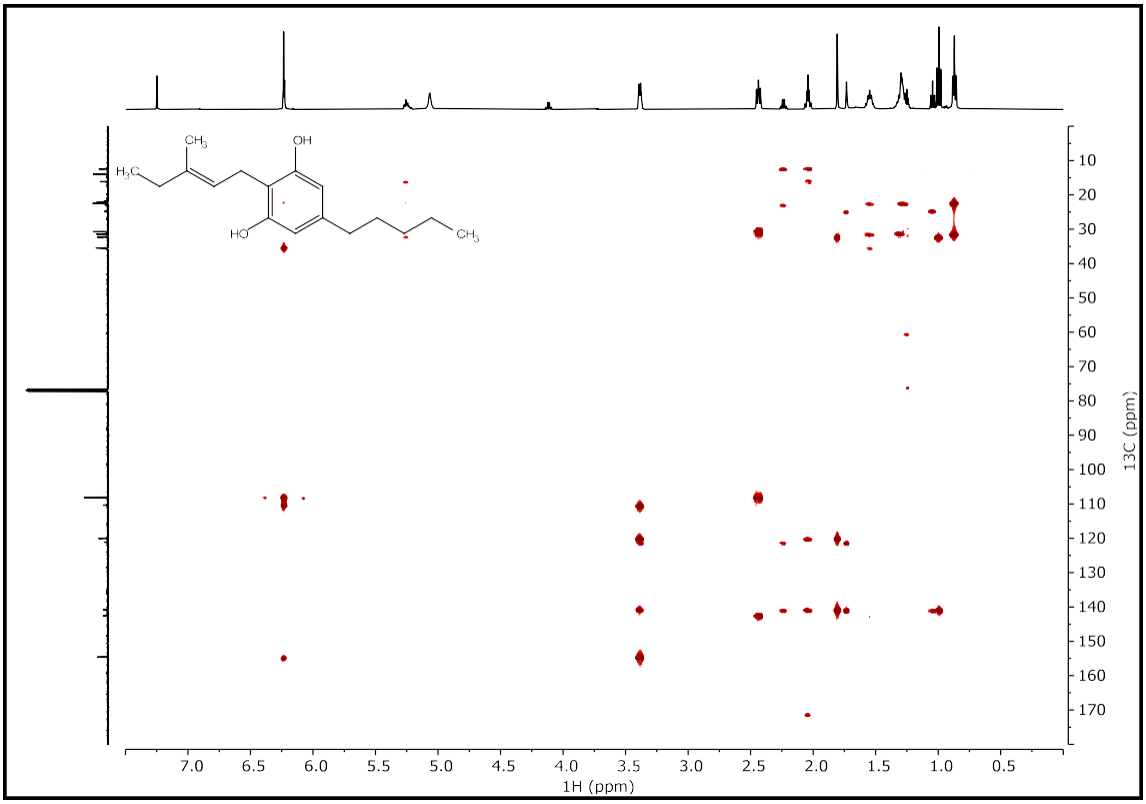


Figure S7: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1b** in $CDCl_3$

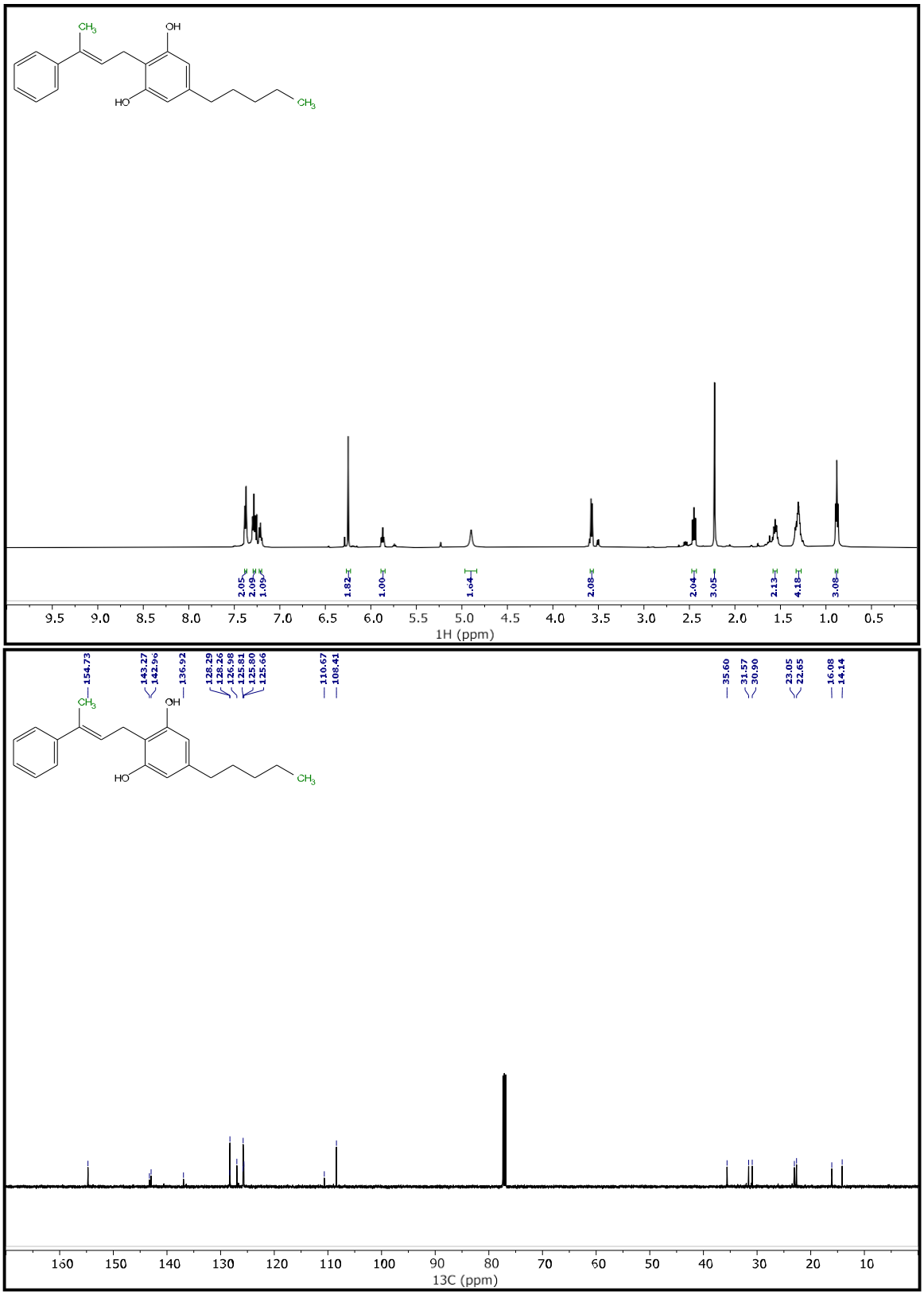


Figure S8: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1c** in $CDCl_3$

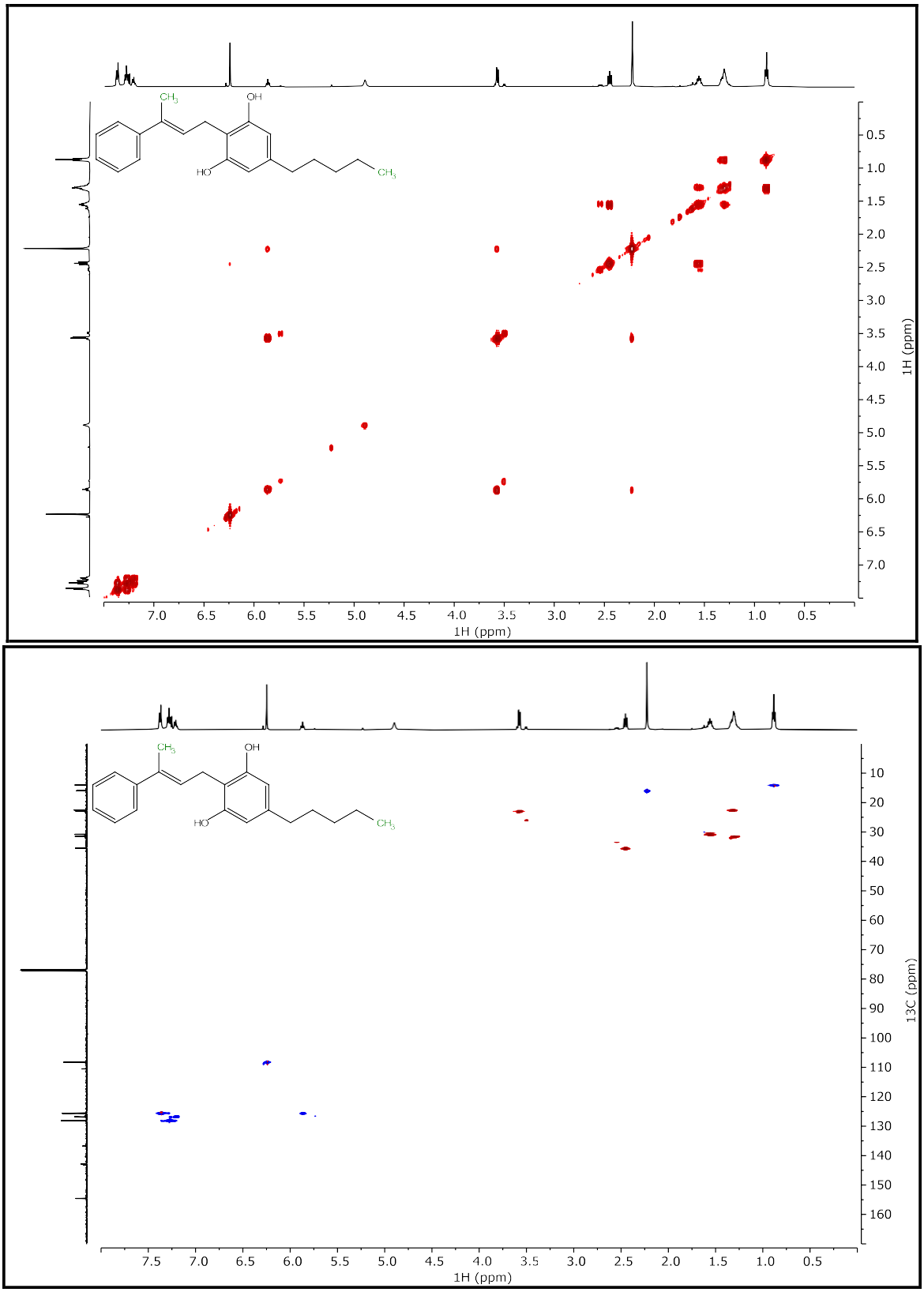


Figure S9: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1c** in $CDCl_3$

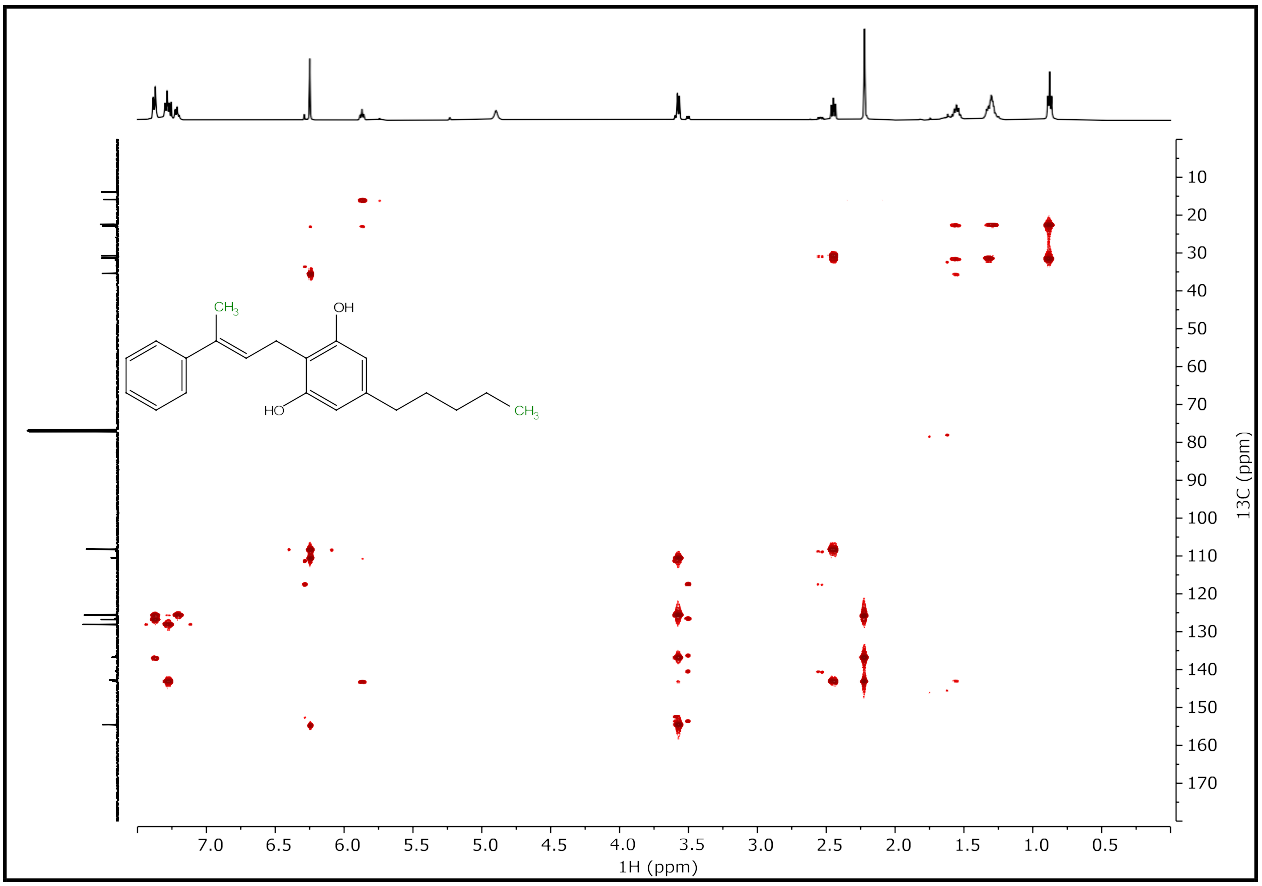


Figure S10: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1c** in $CDCl_3$

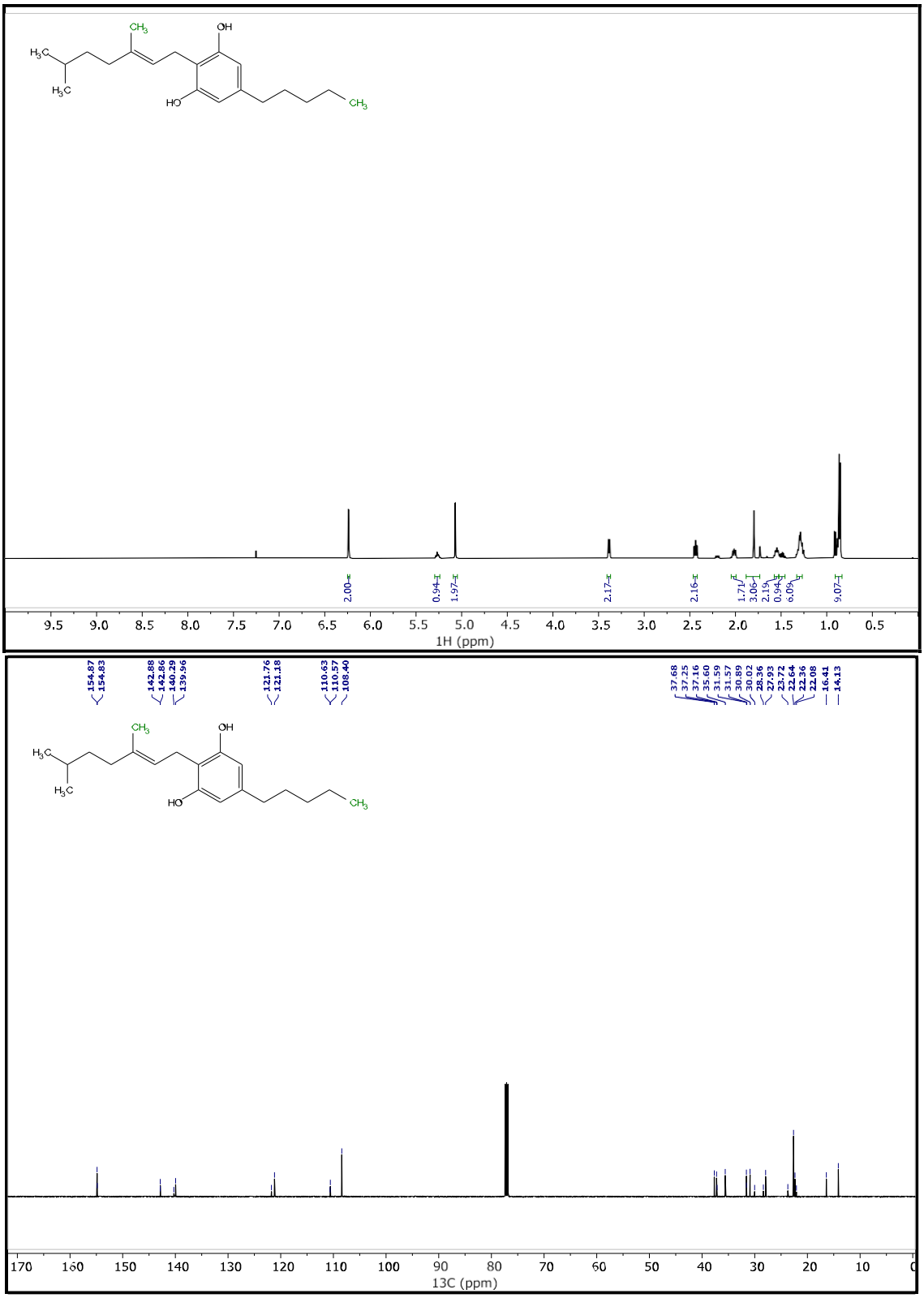


Figure S11: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1d** in $CDCl_3$

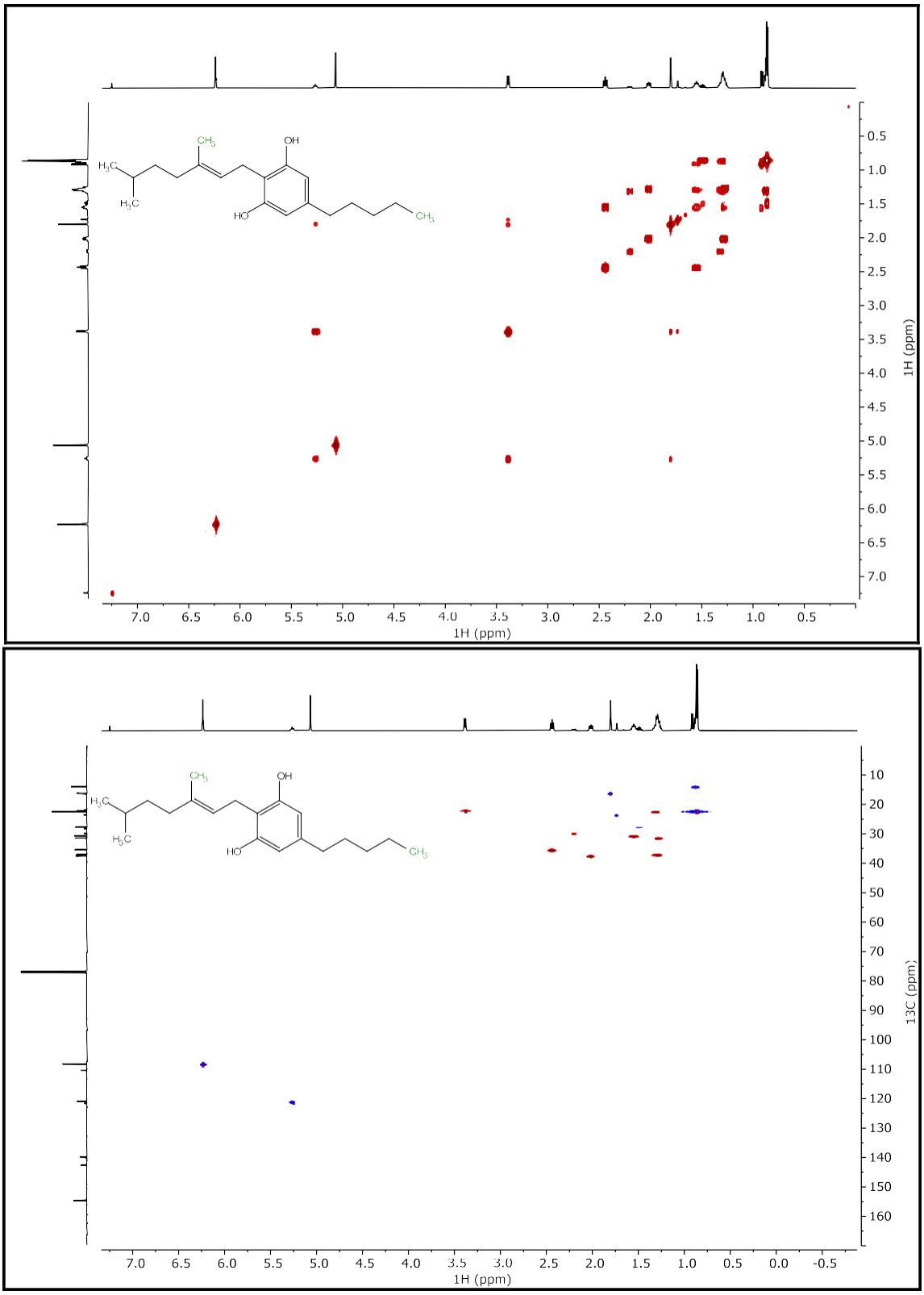


Figure S12: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1d** in $CDCl_3$

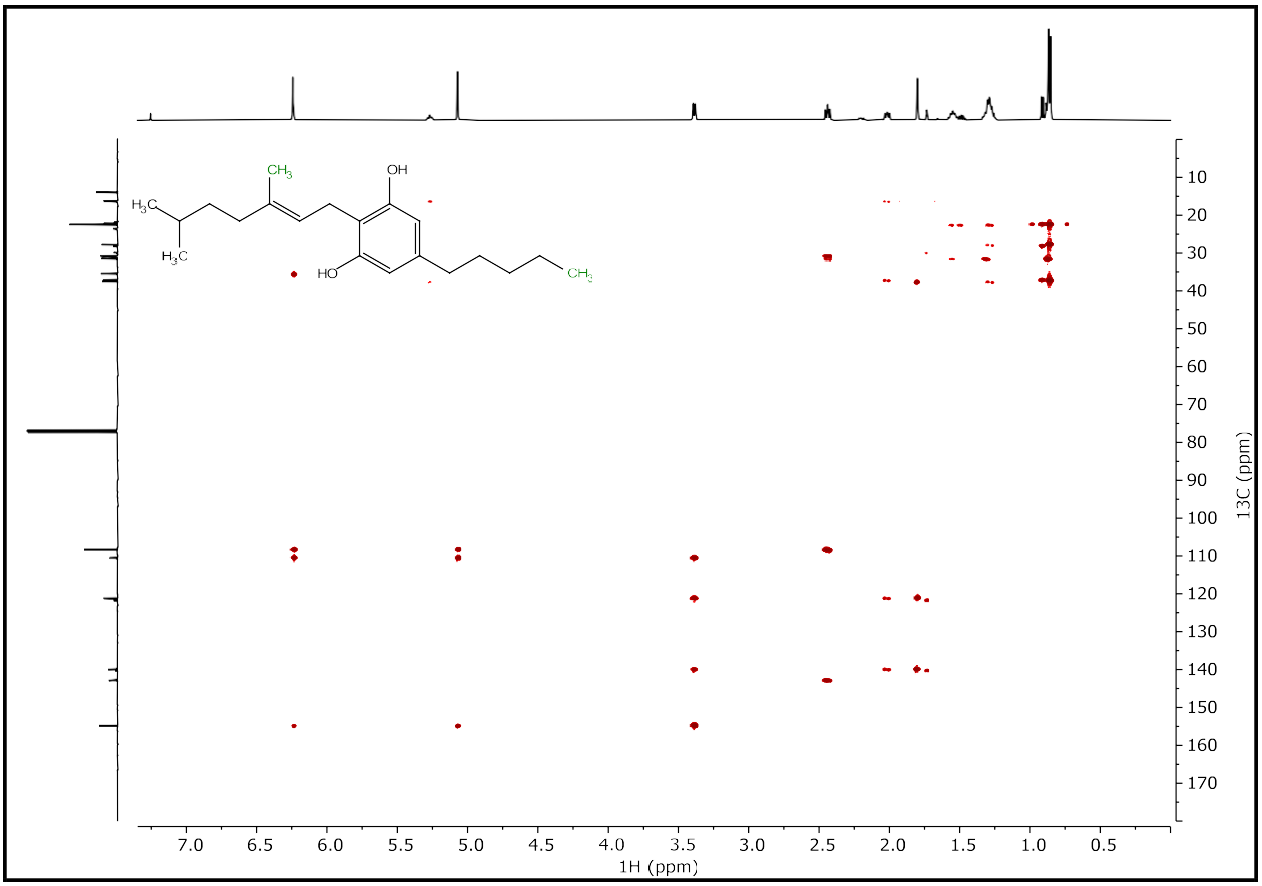


Figure S13: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1d** in $CDCl_3$

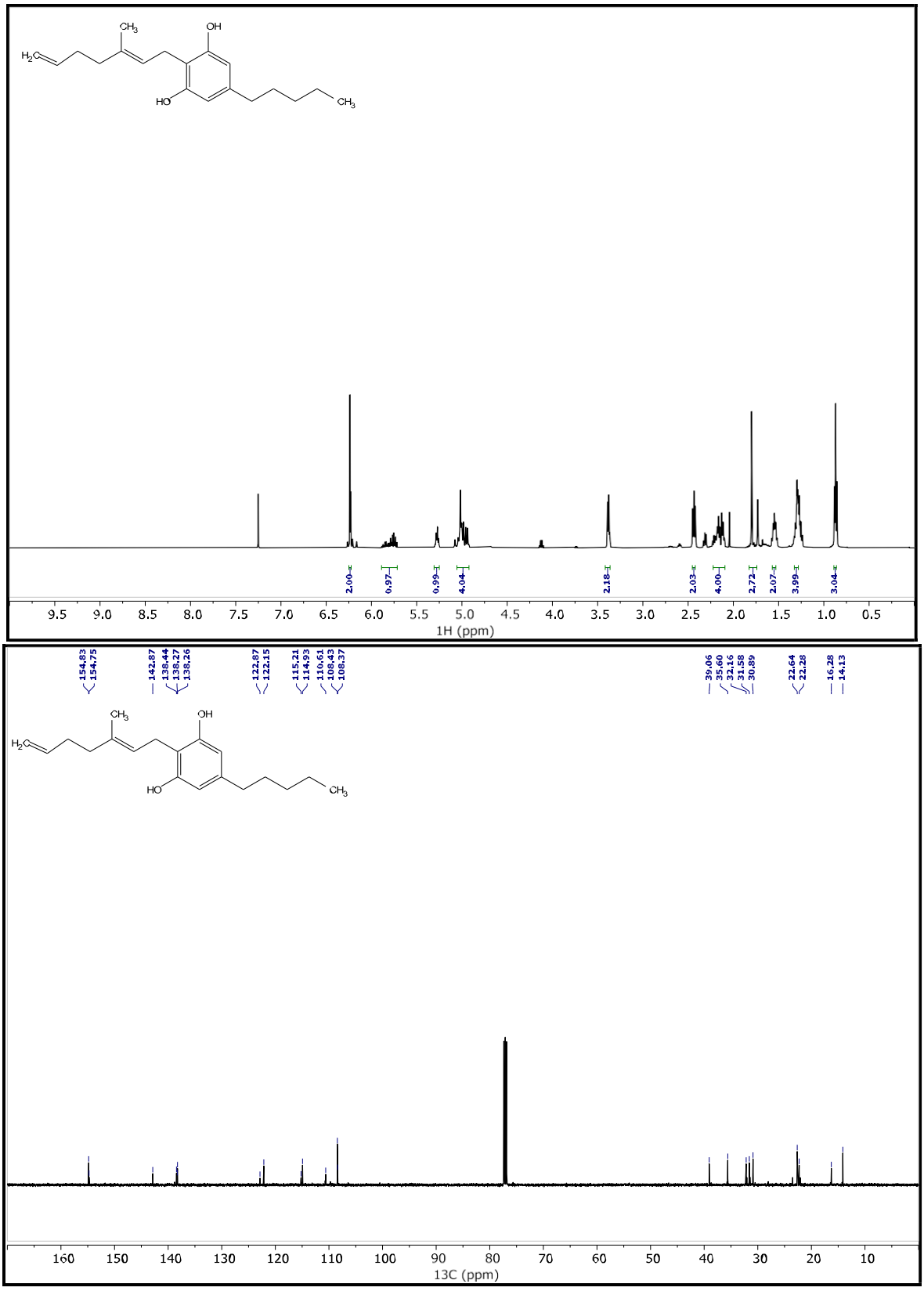


Figure S14: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1e** in $CDCl_3$

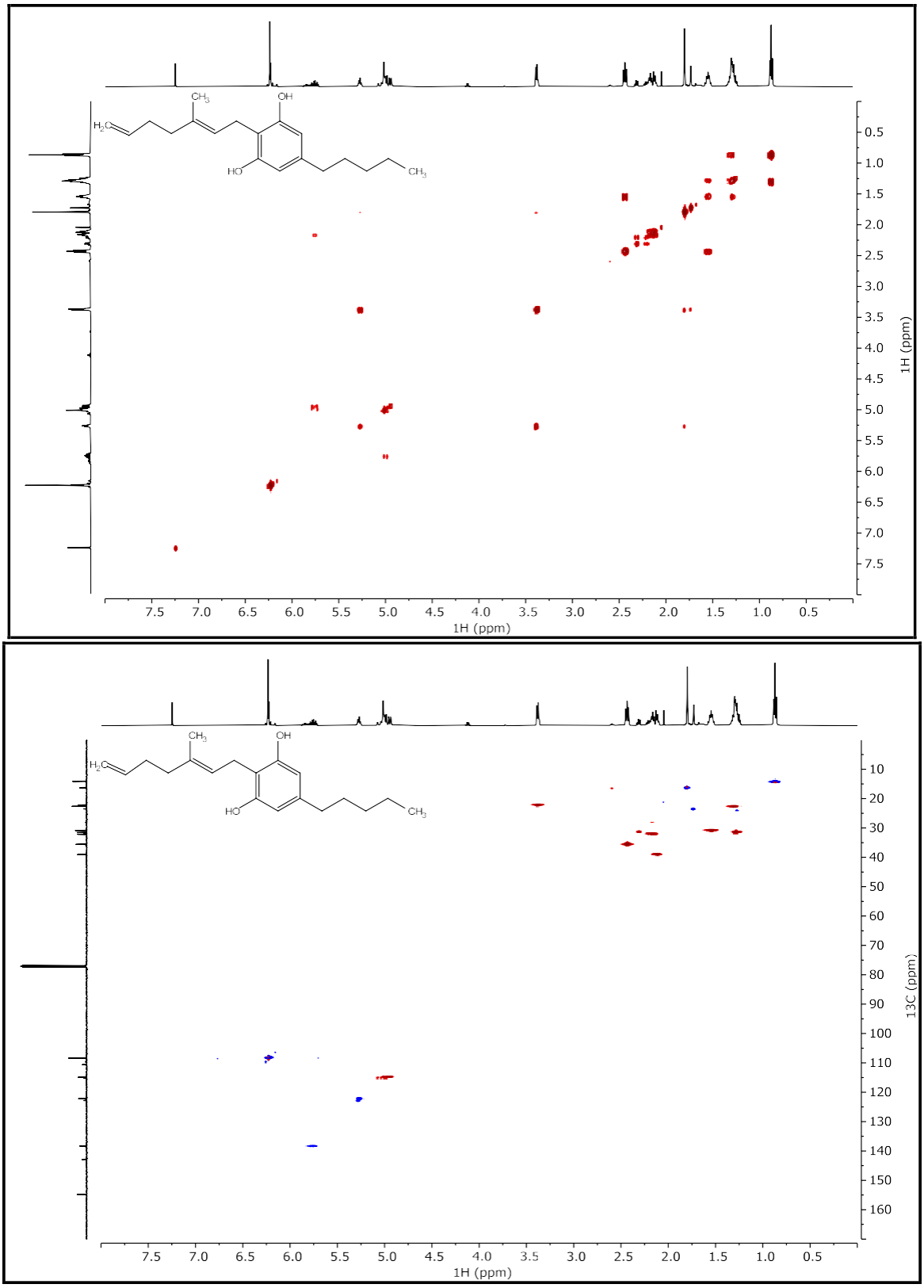


Figure S15: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC NMR spectrum of **1e** in $CDCl_3$

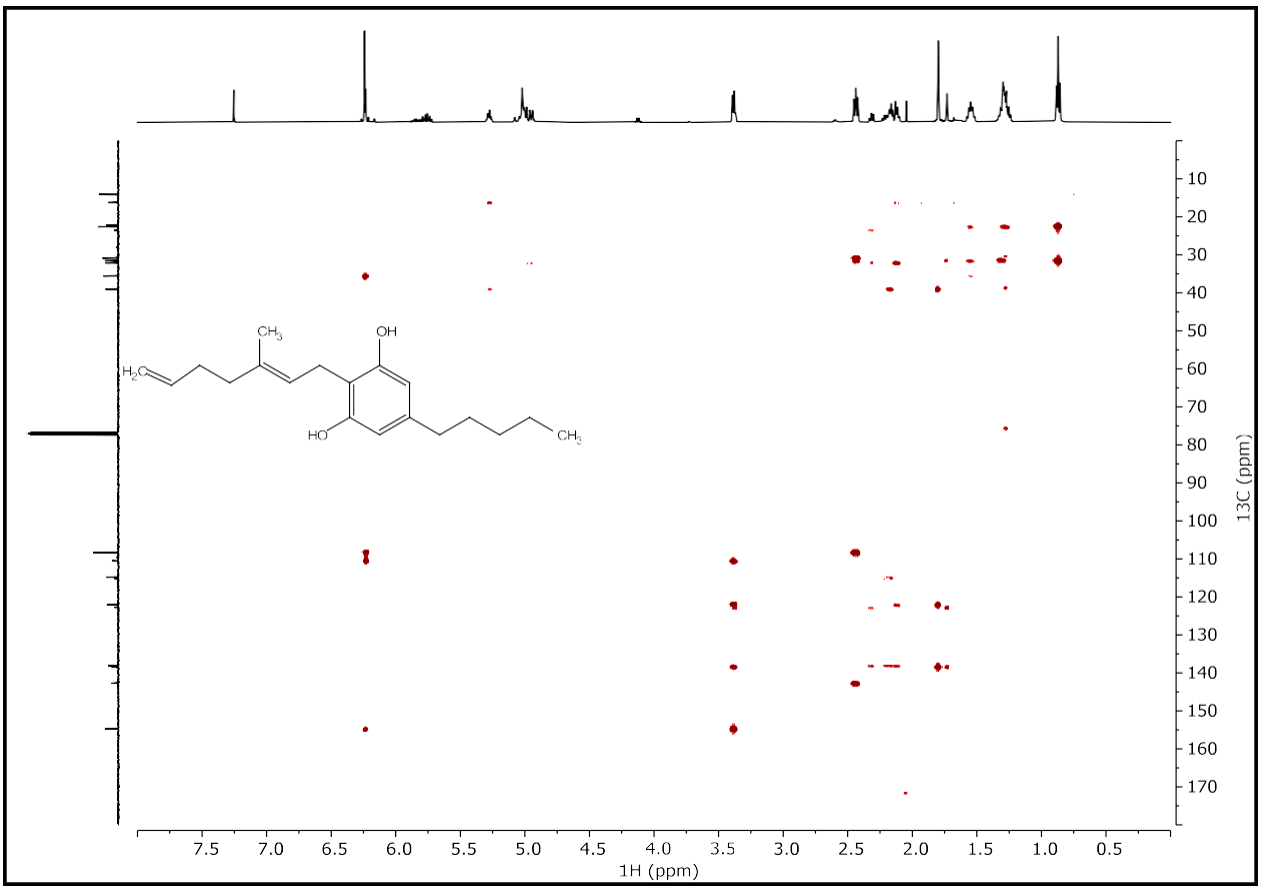


Figure S16: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1e** in $CDCl_3$

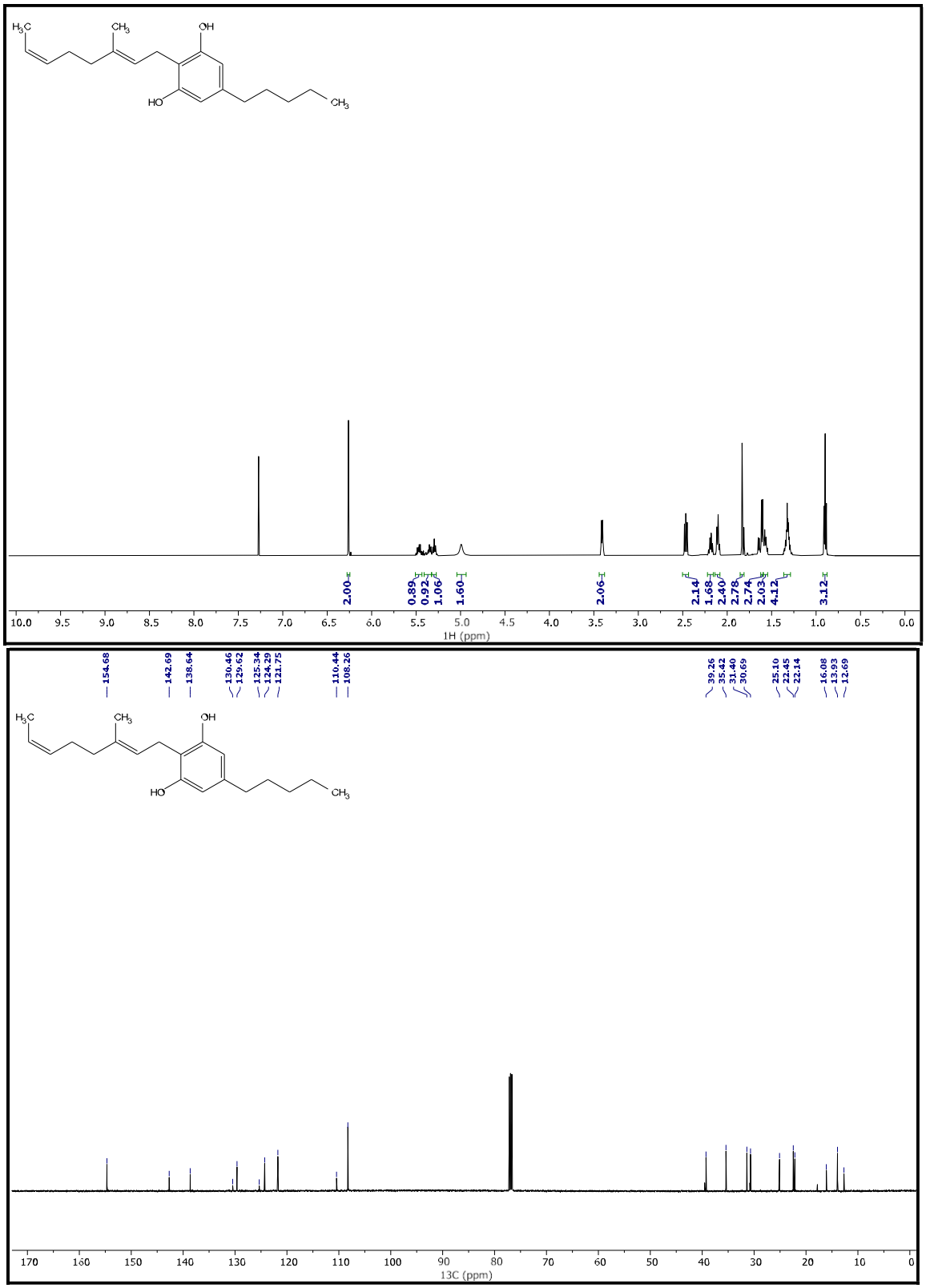


Figure S17: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1f** in $CDCl_3$

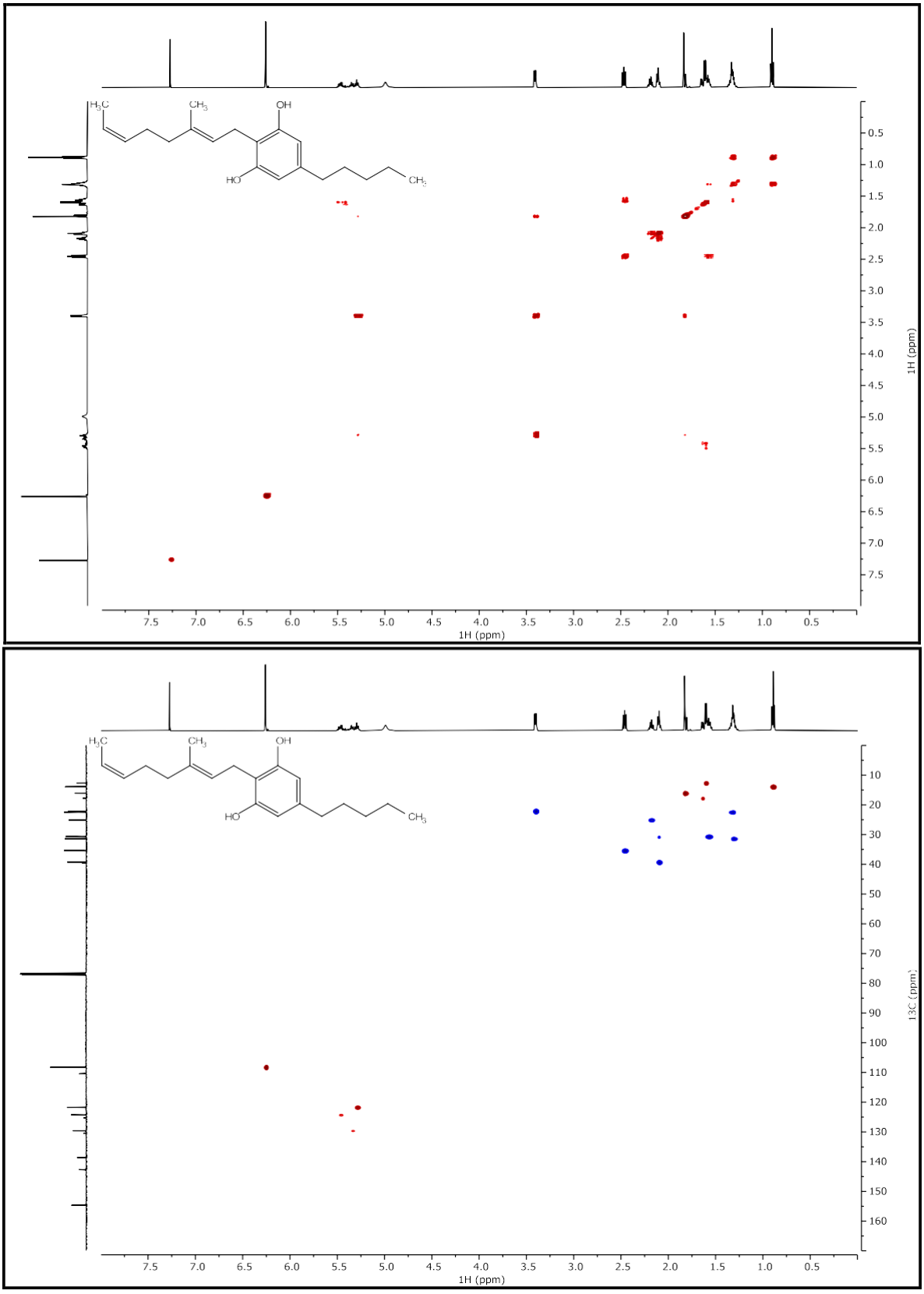


Figure S18: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1f** in $CDCl_3$

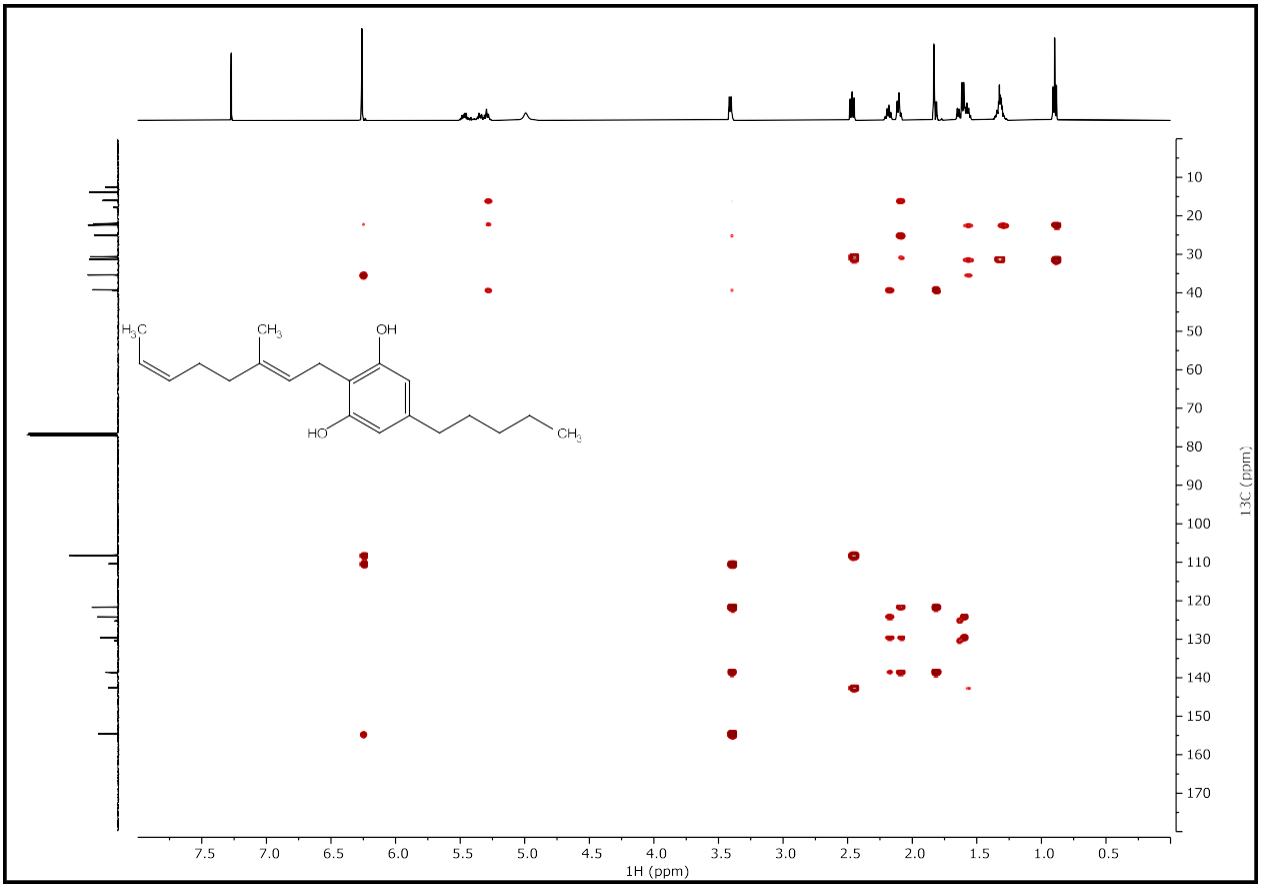


Figure S19: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1f** in $CDCl_3$

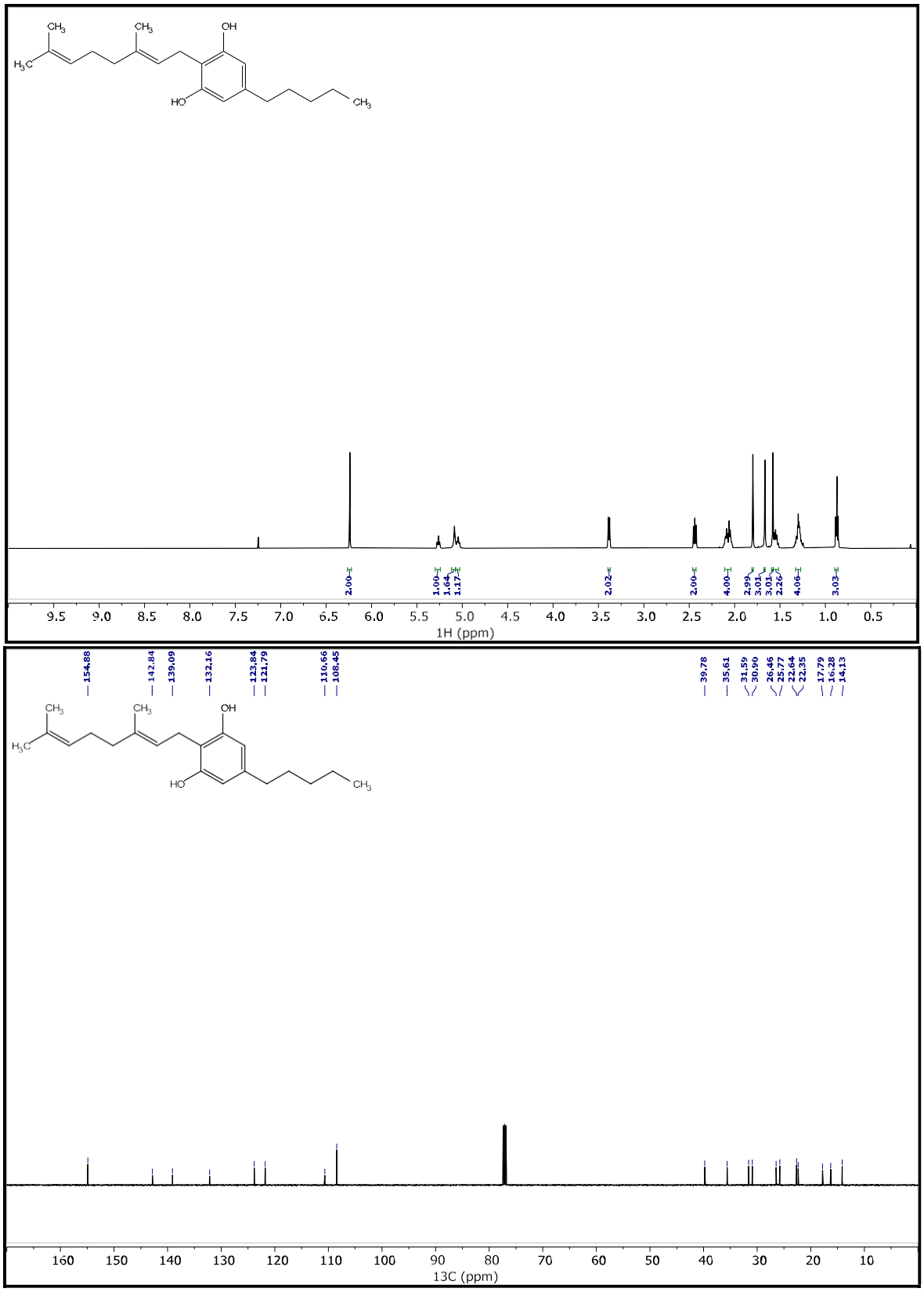


Figure S20: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1g** in $CDCl_3$

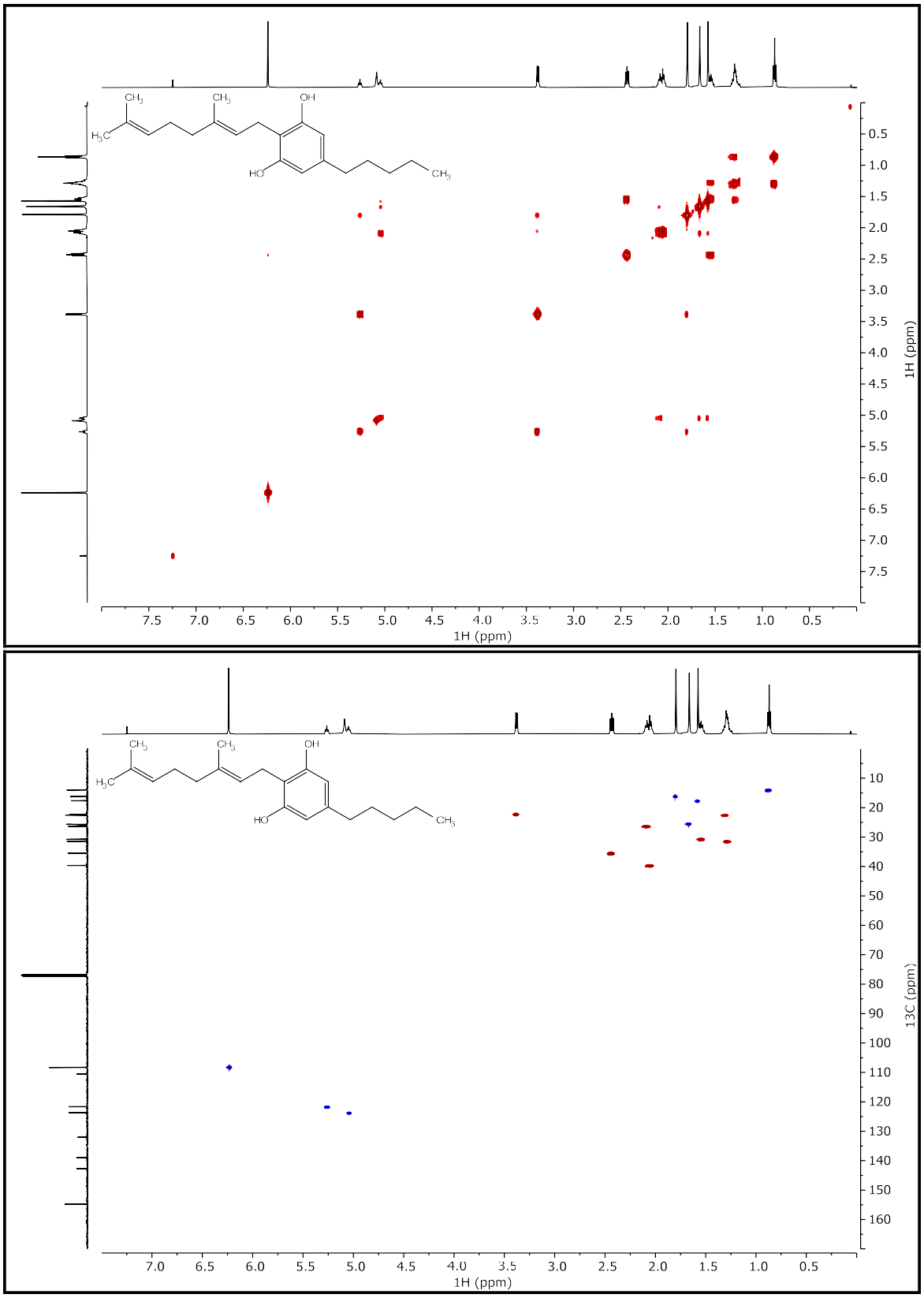


Figure S21: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1g** in $CDCl_3$

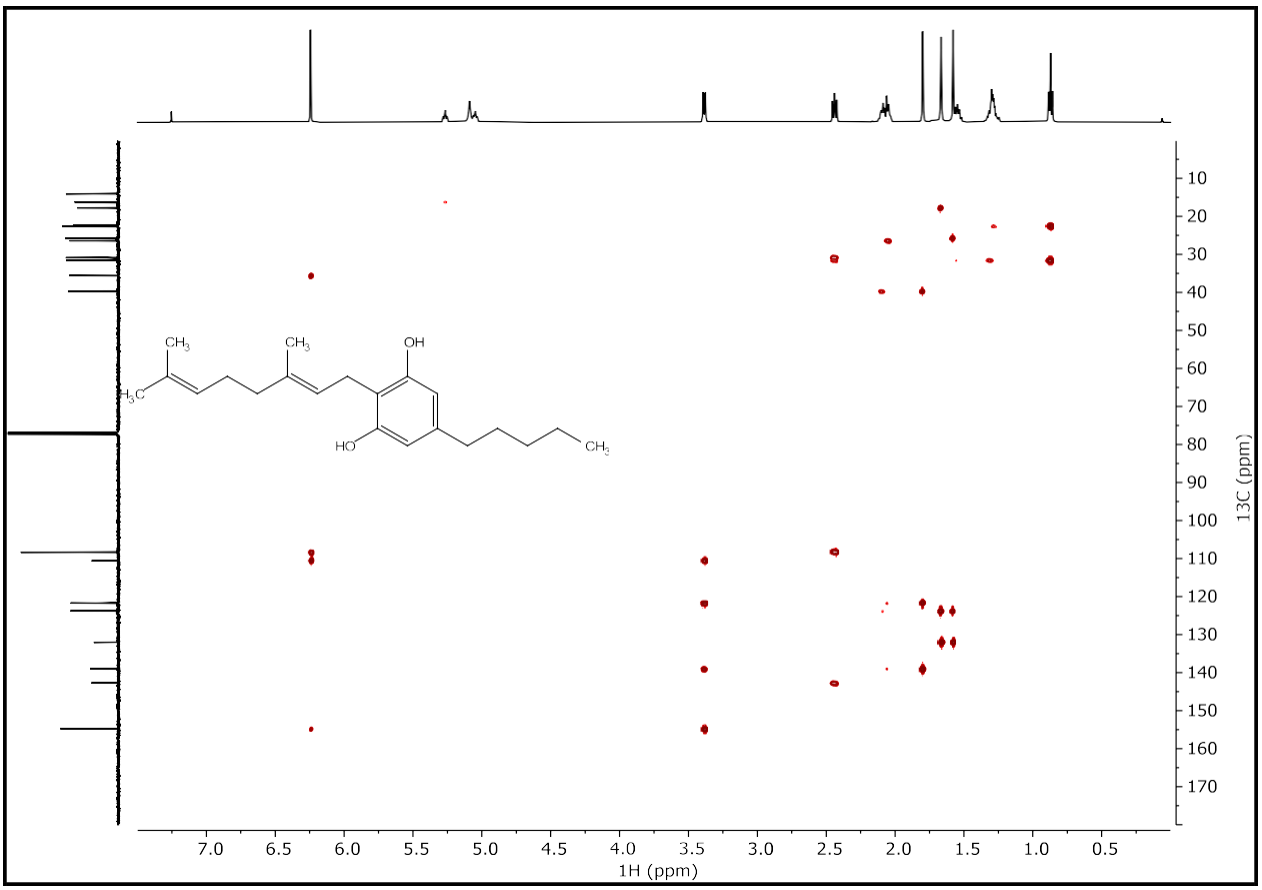


Figure S22: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1g** in $CDCl_3$

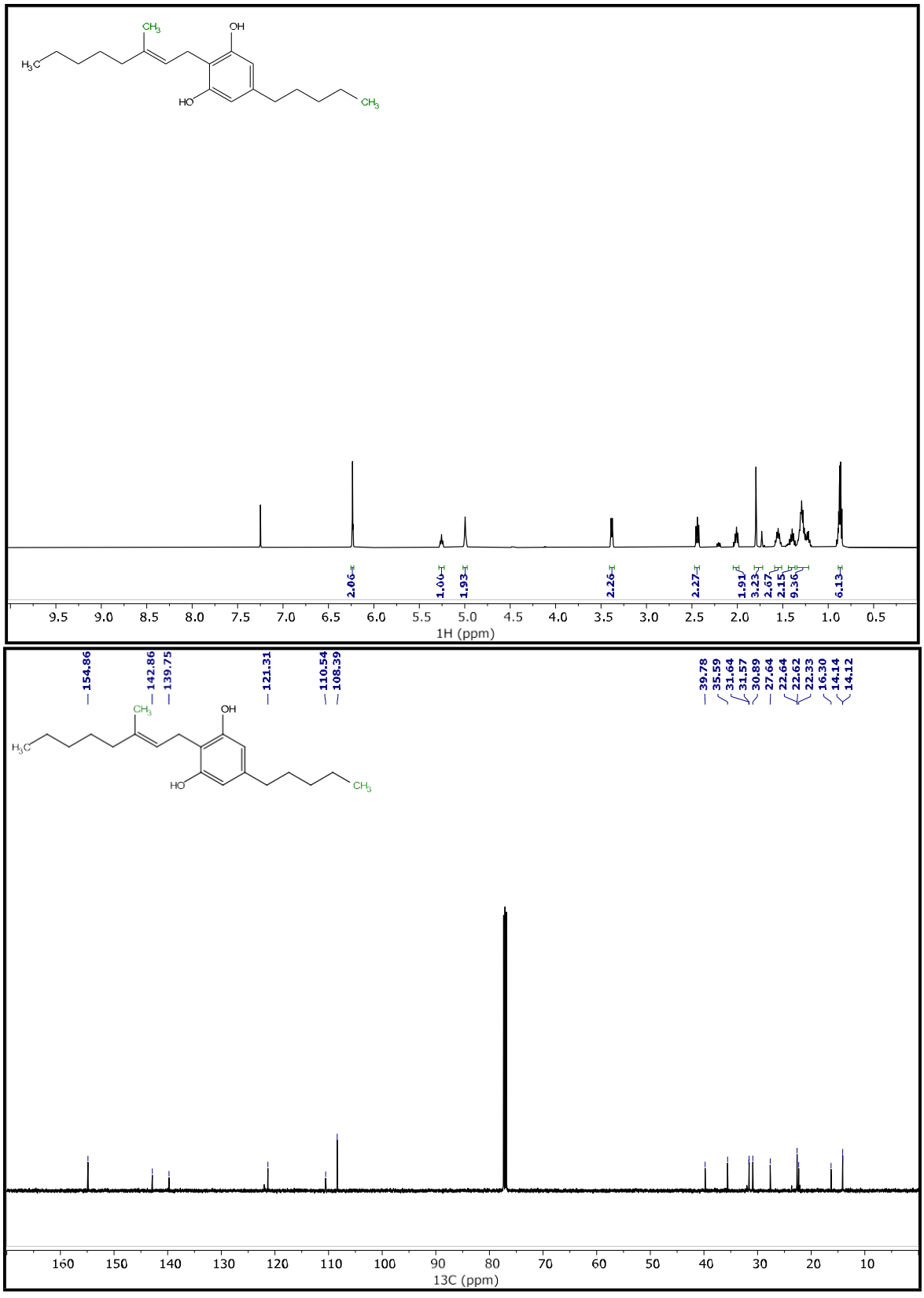


Figure S23: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1h** in $CDCl_3$

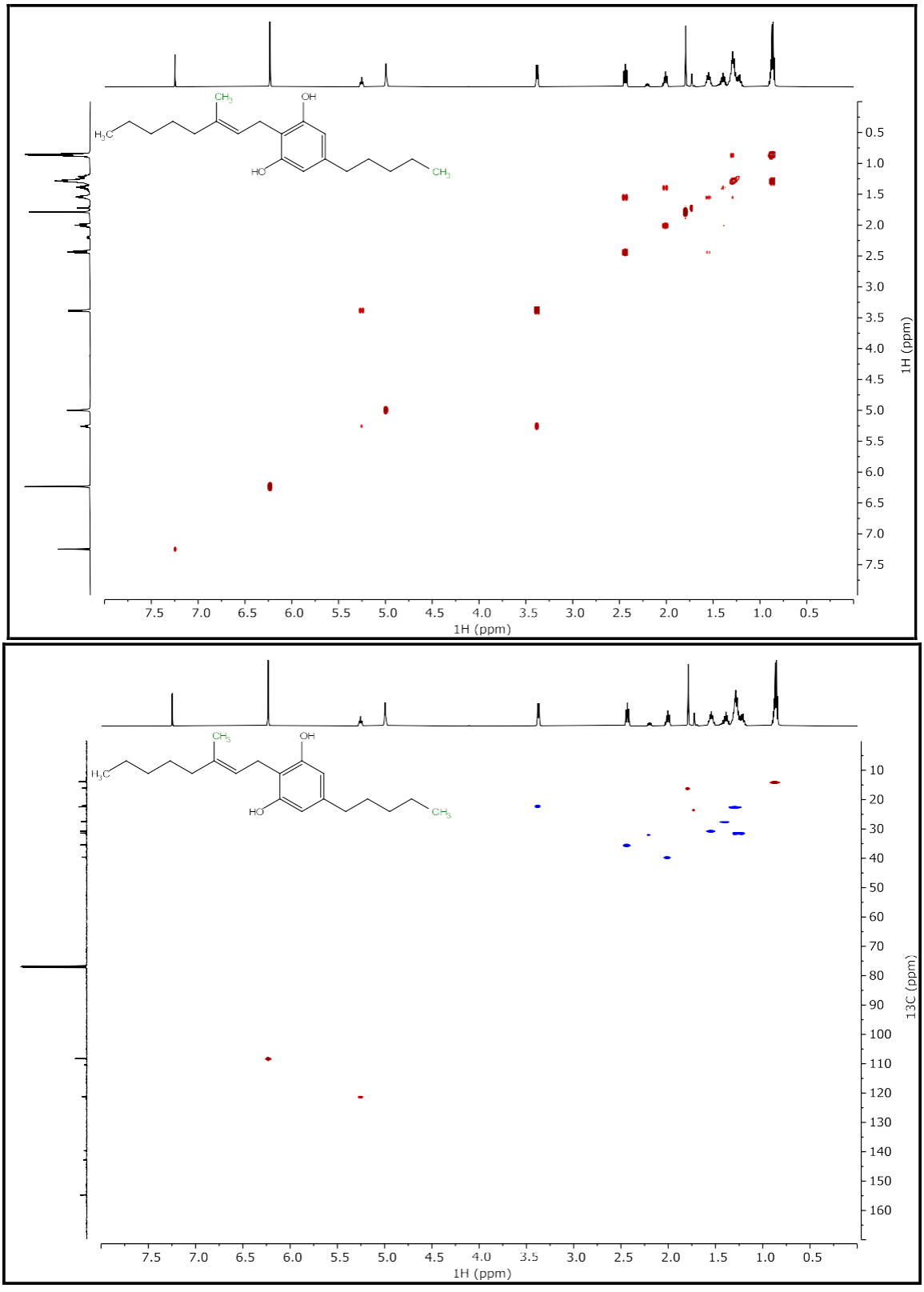


Figure S24: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1h** in $CDCl_3$

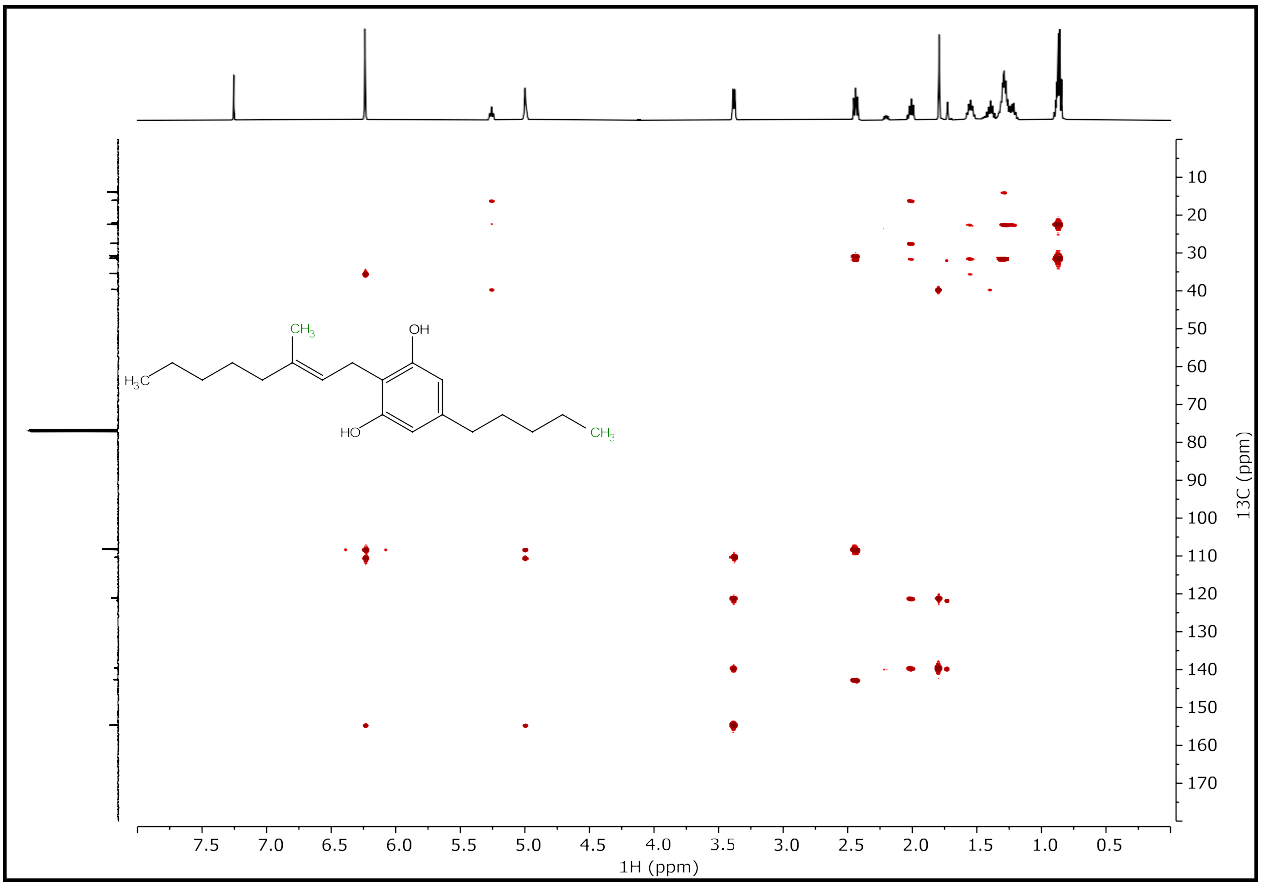


Figure S25: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1h** in $CDCl_3$

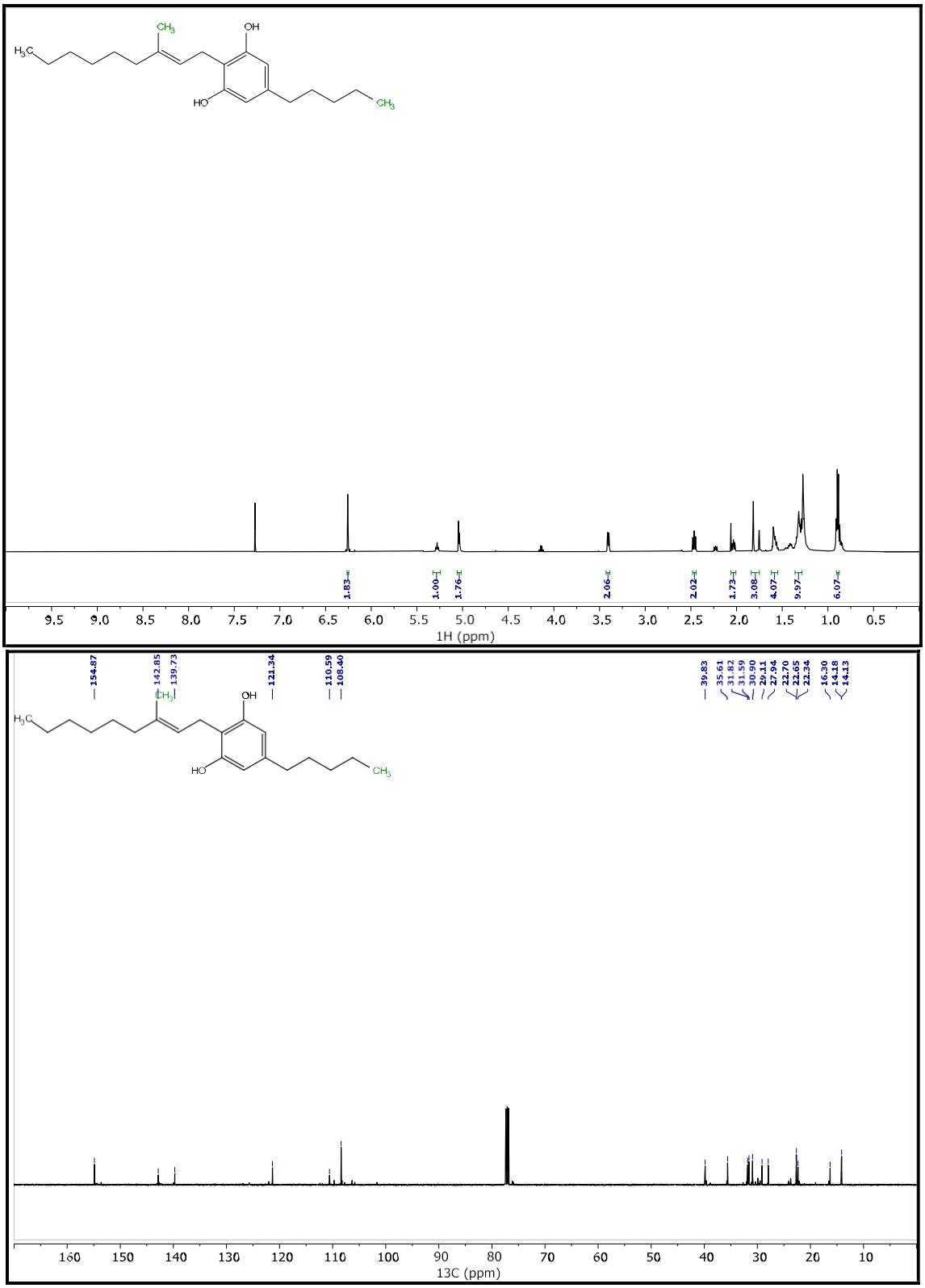


Figure S26: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1i** in $CDCl_3$

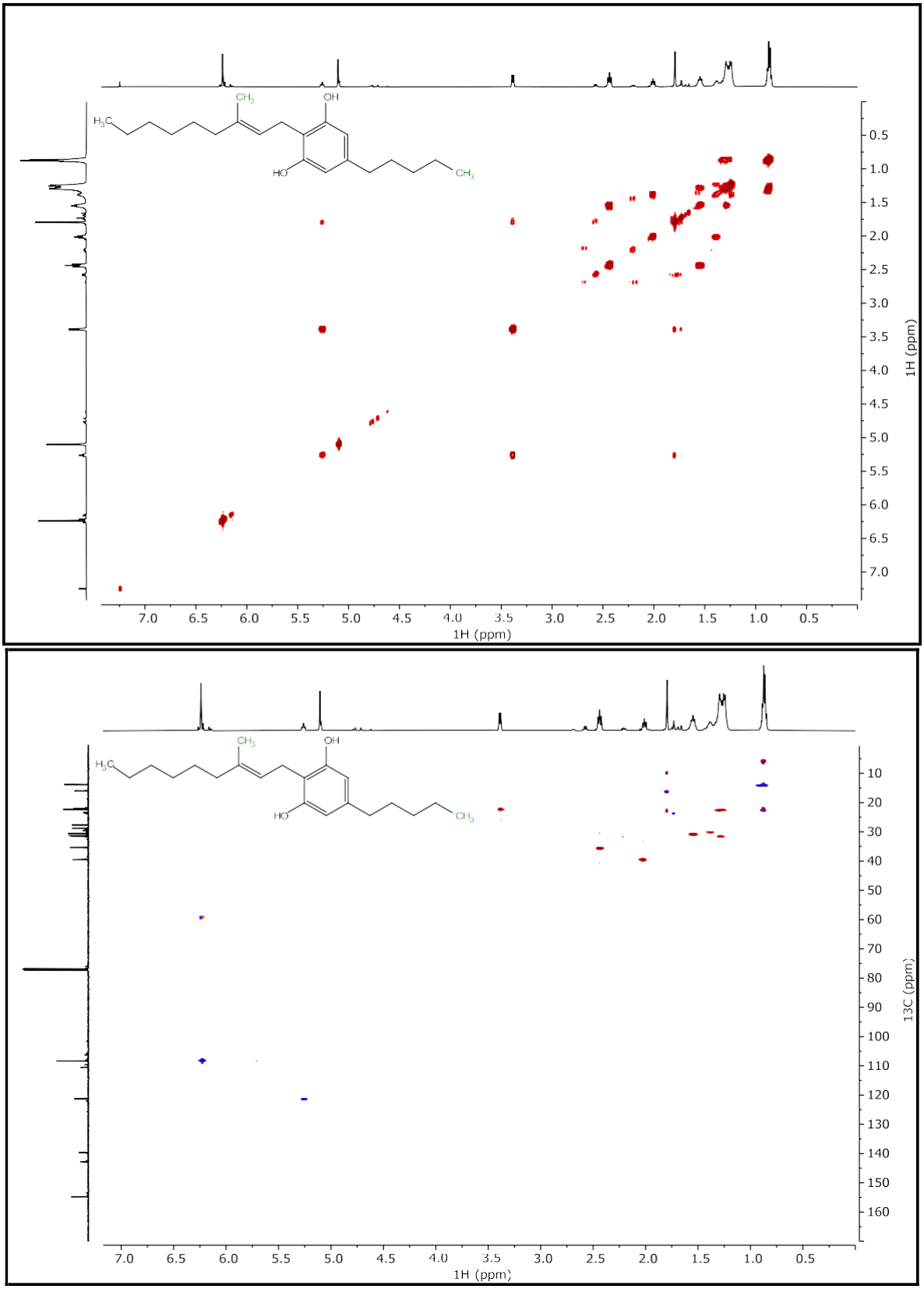


Figure S27: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1i** in $CDCl_3$

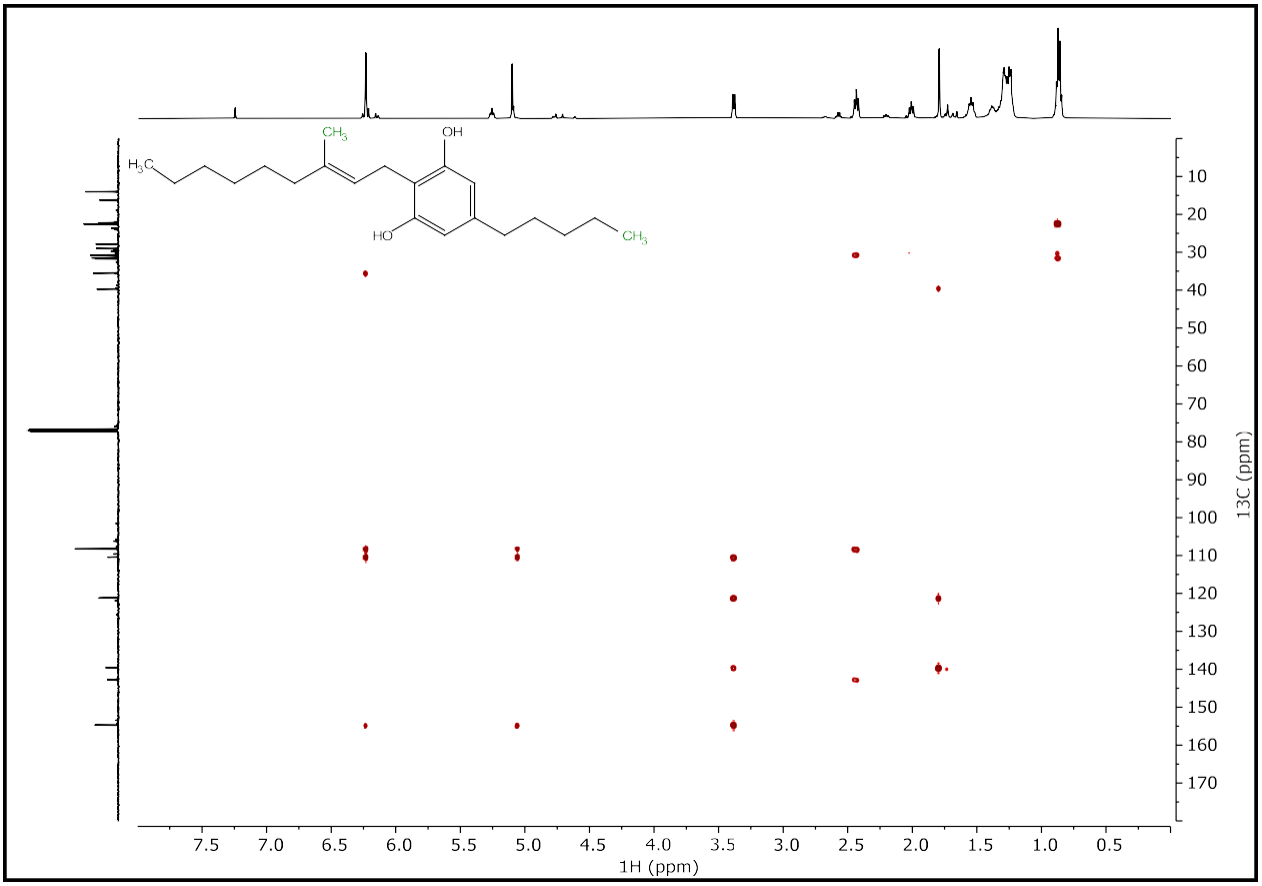


Figure S28: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1i** in $CDCl_3$

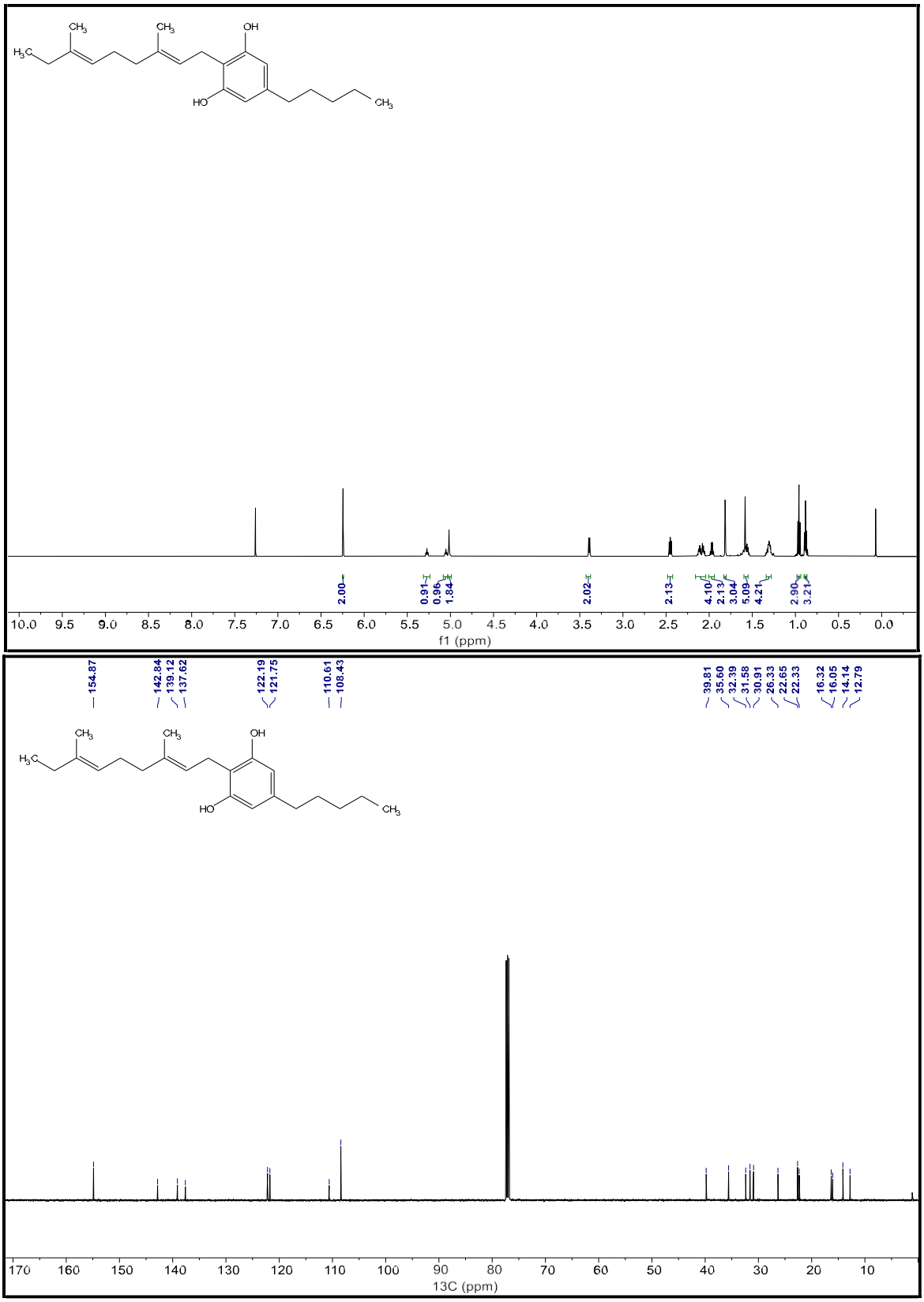


Figure S29: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1j** in $CDCl_3$

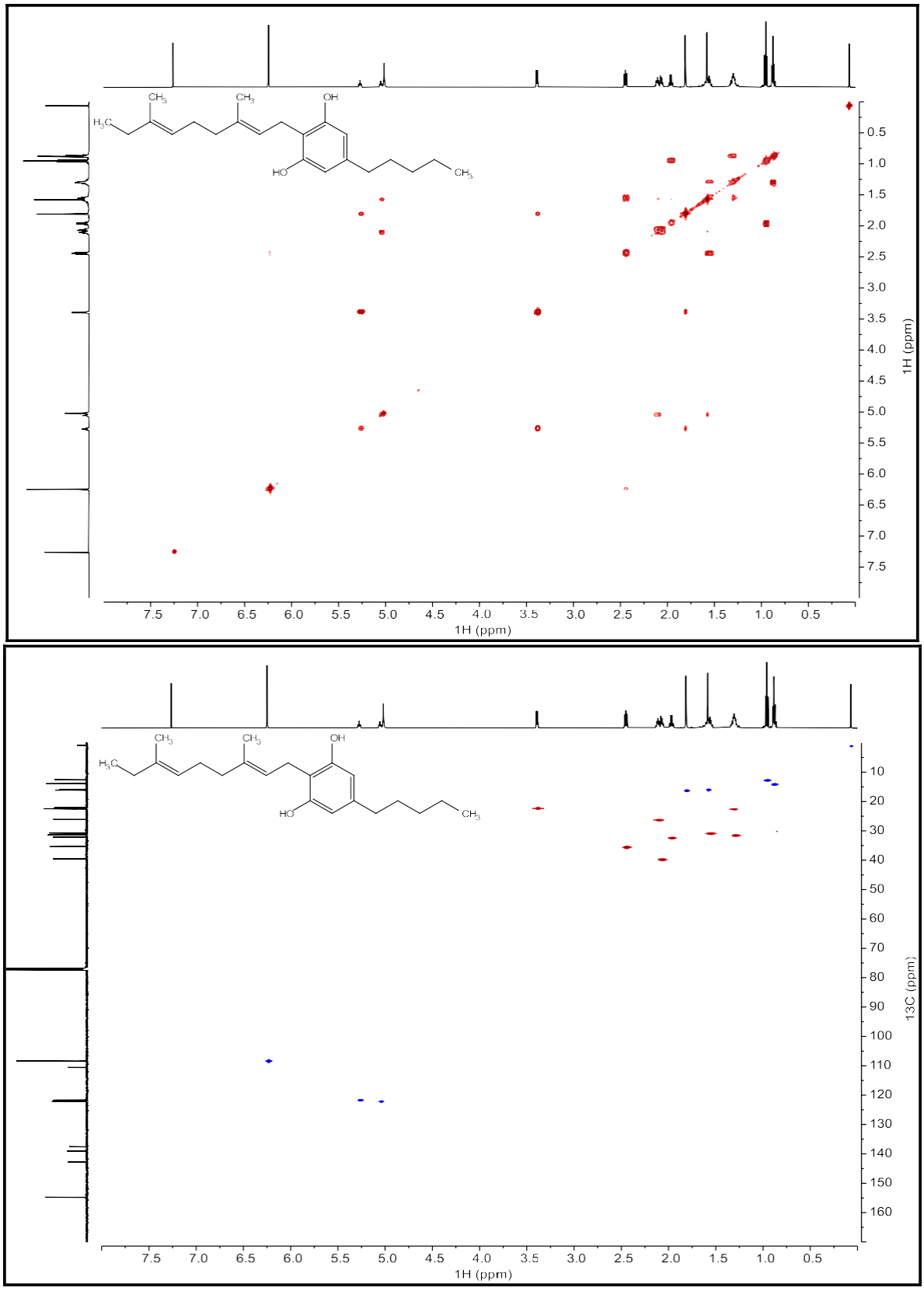


Figure S30: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1j** in $CDCl_3$

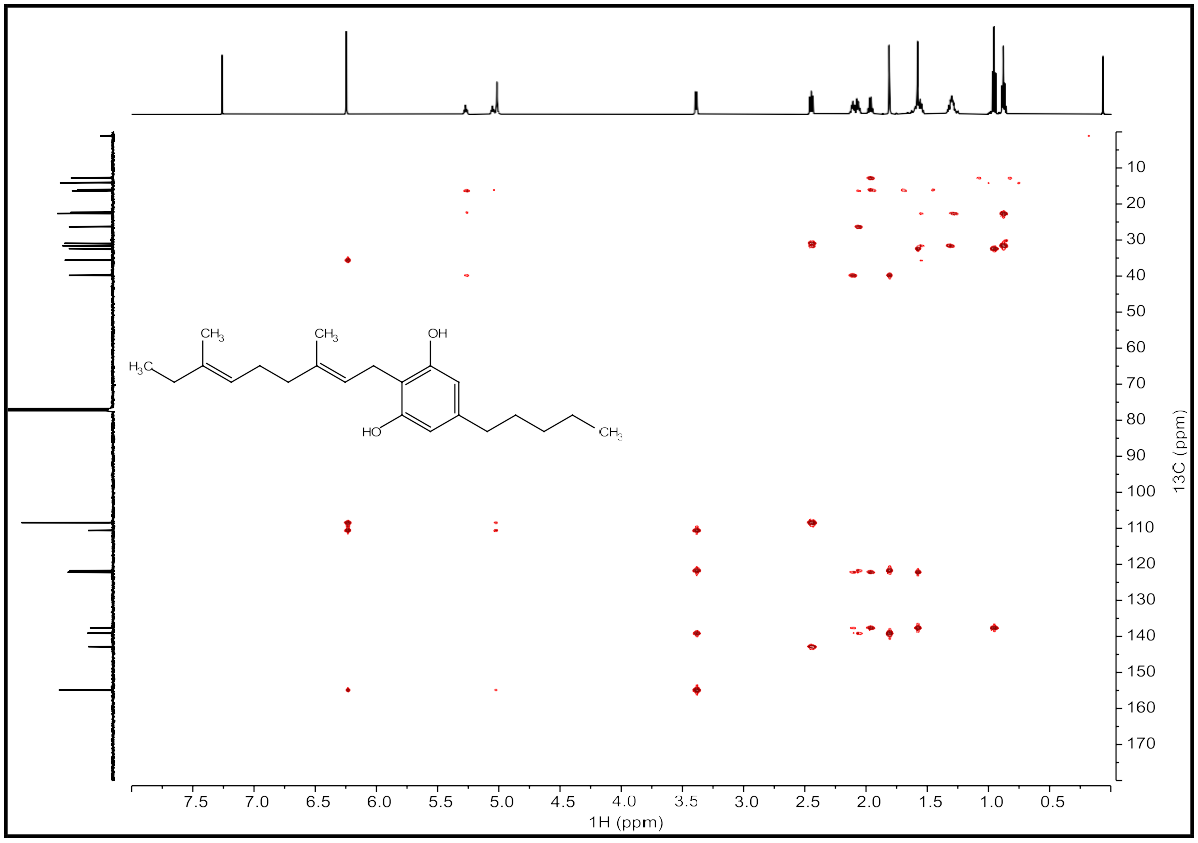


Figure S31: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1j** in $CDCl_3$

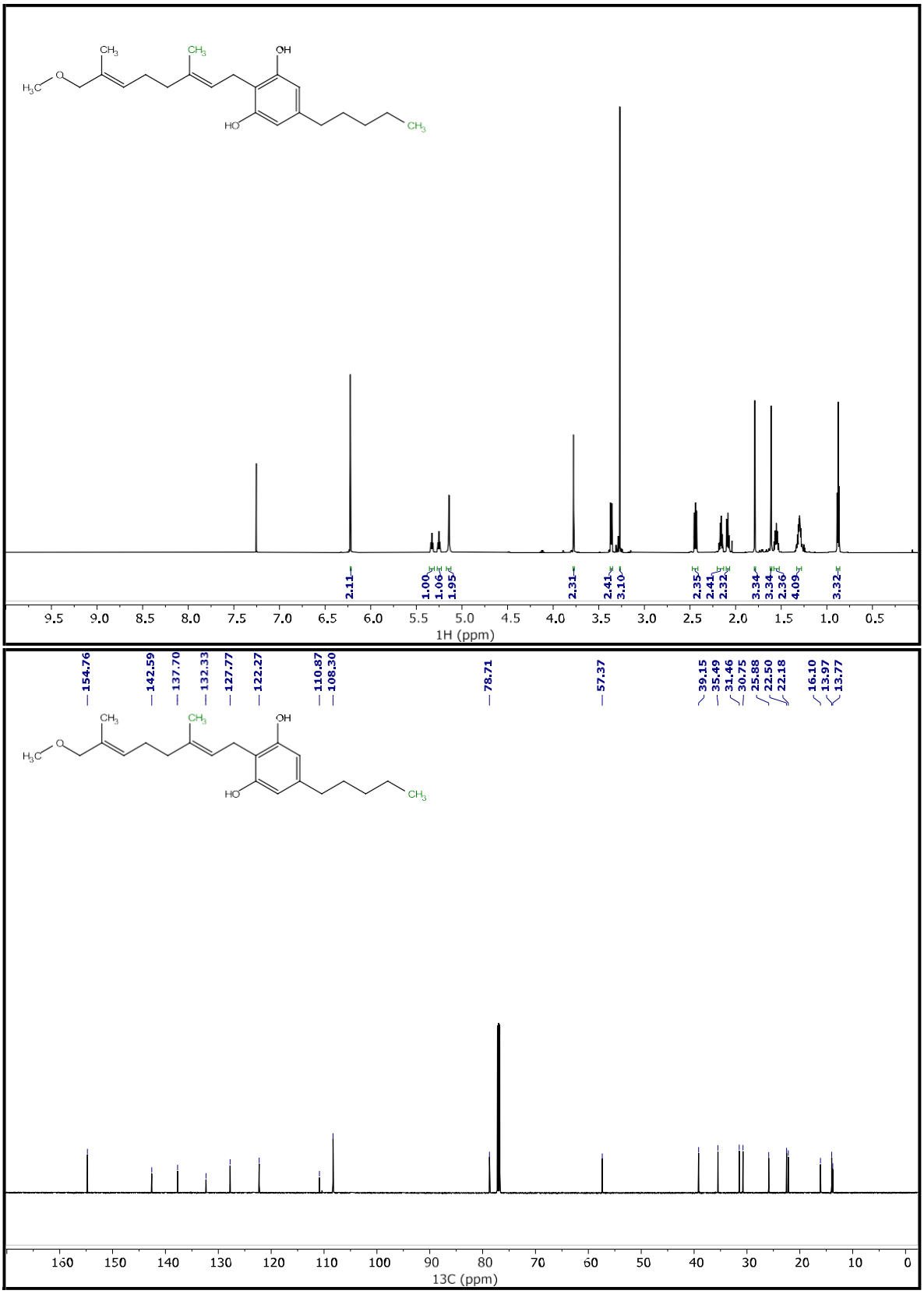


Figure S32: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1k** in $CDCl_3$

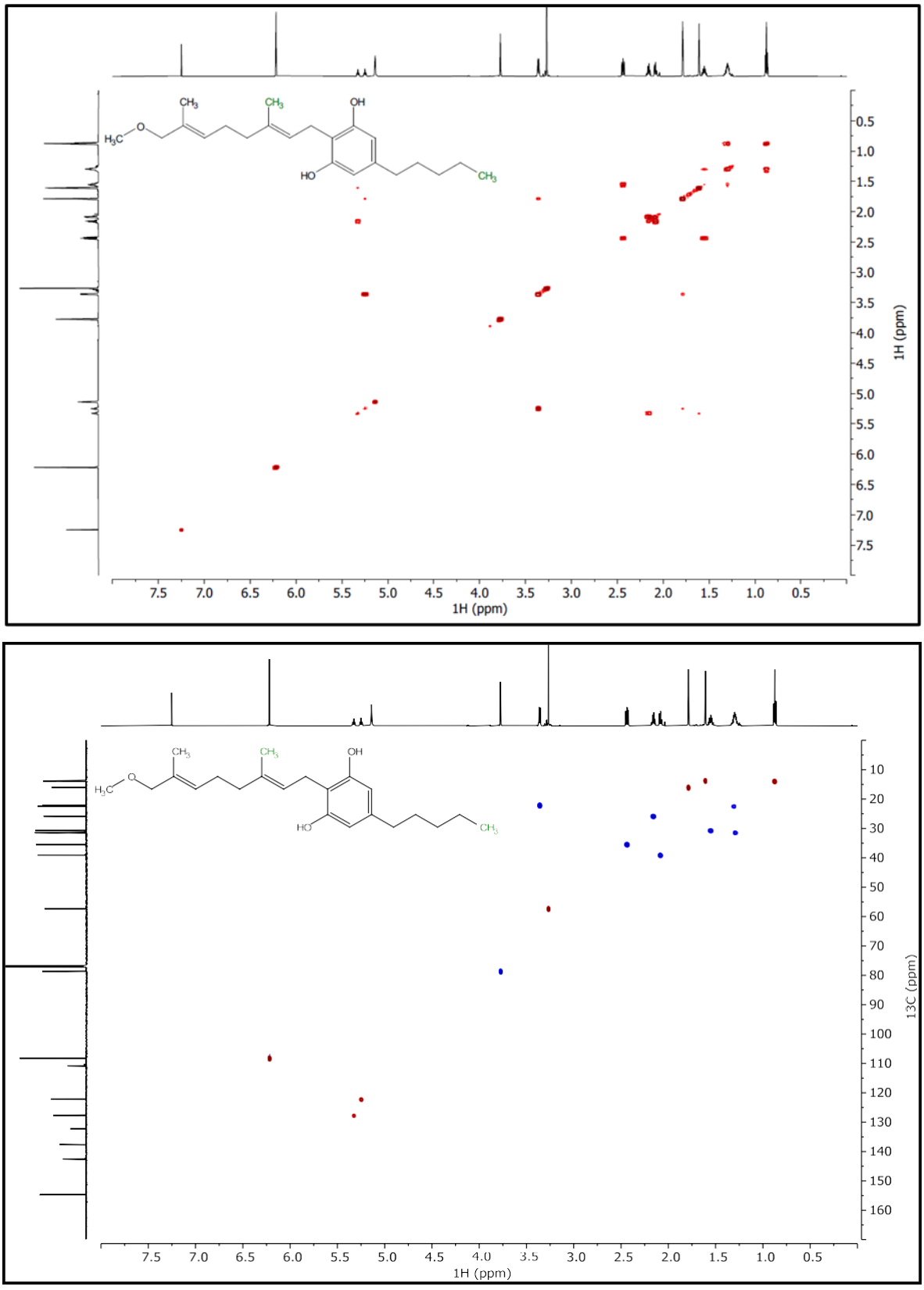


Figure S33: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1k** in $CDCl_3$

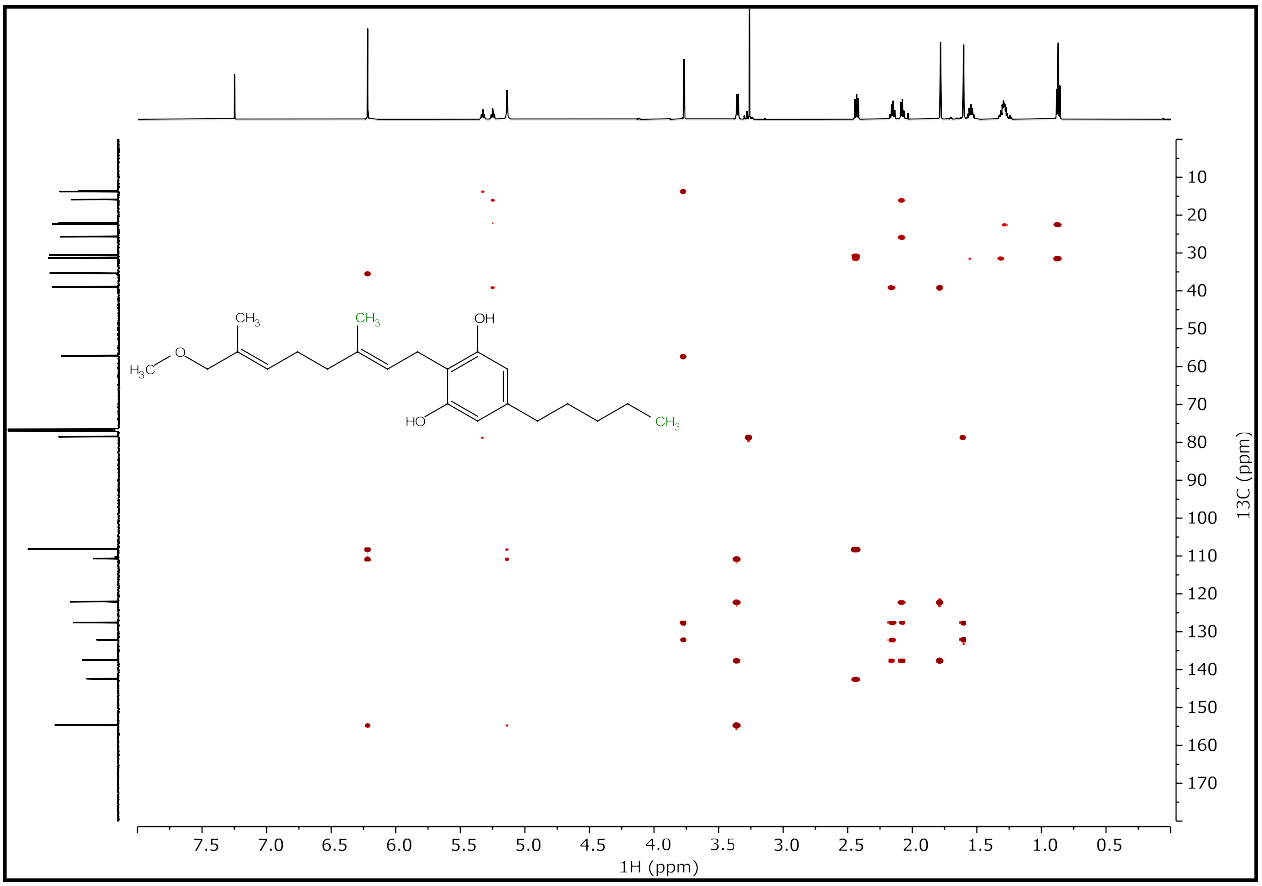


Figure S34: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1k** in $CDCl_3$

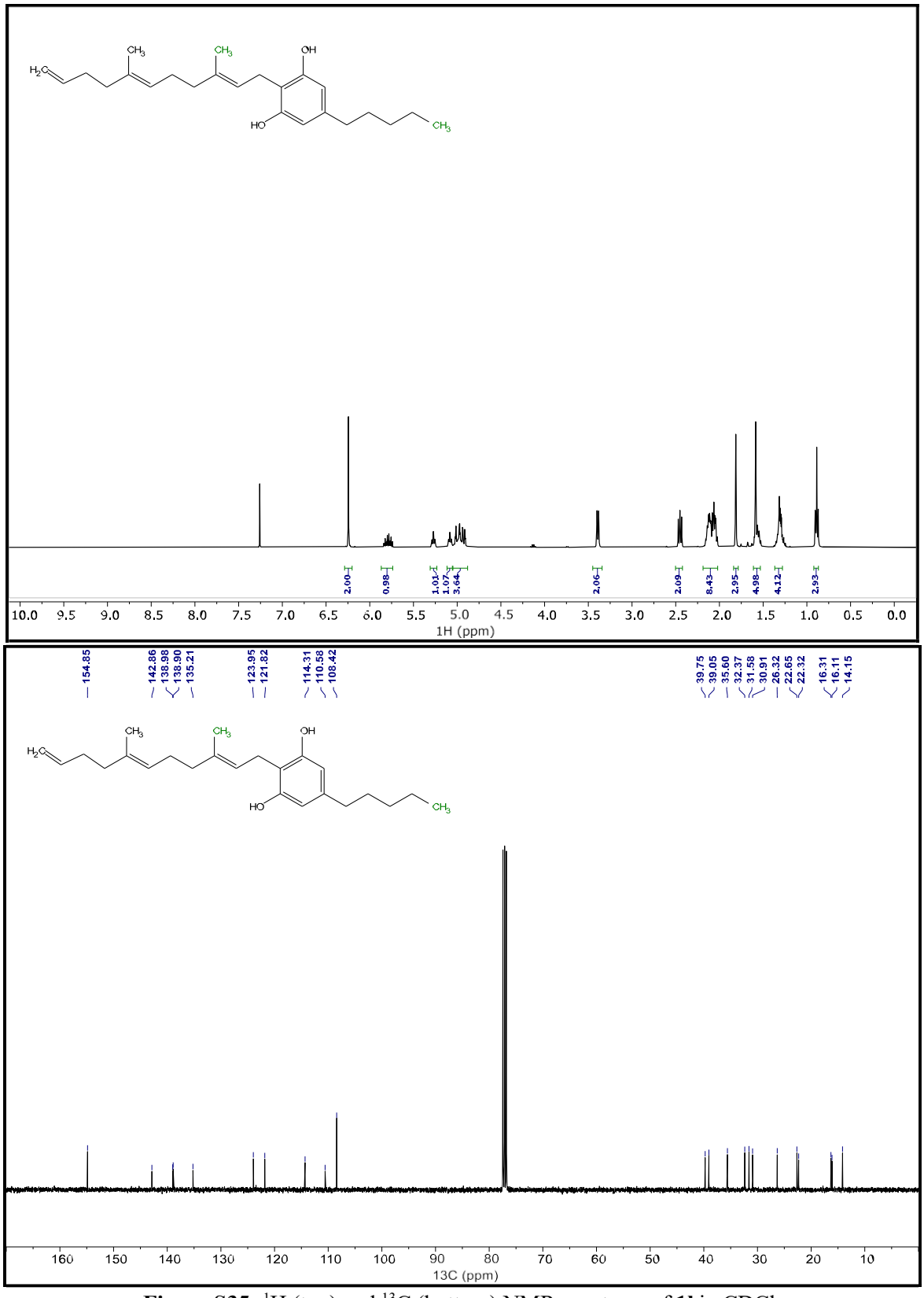


Figure S35: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **11** in $CDCl_3$

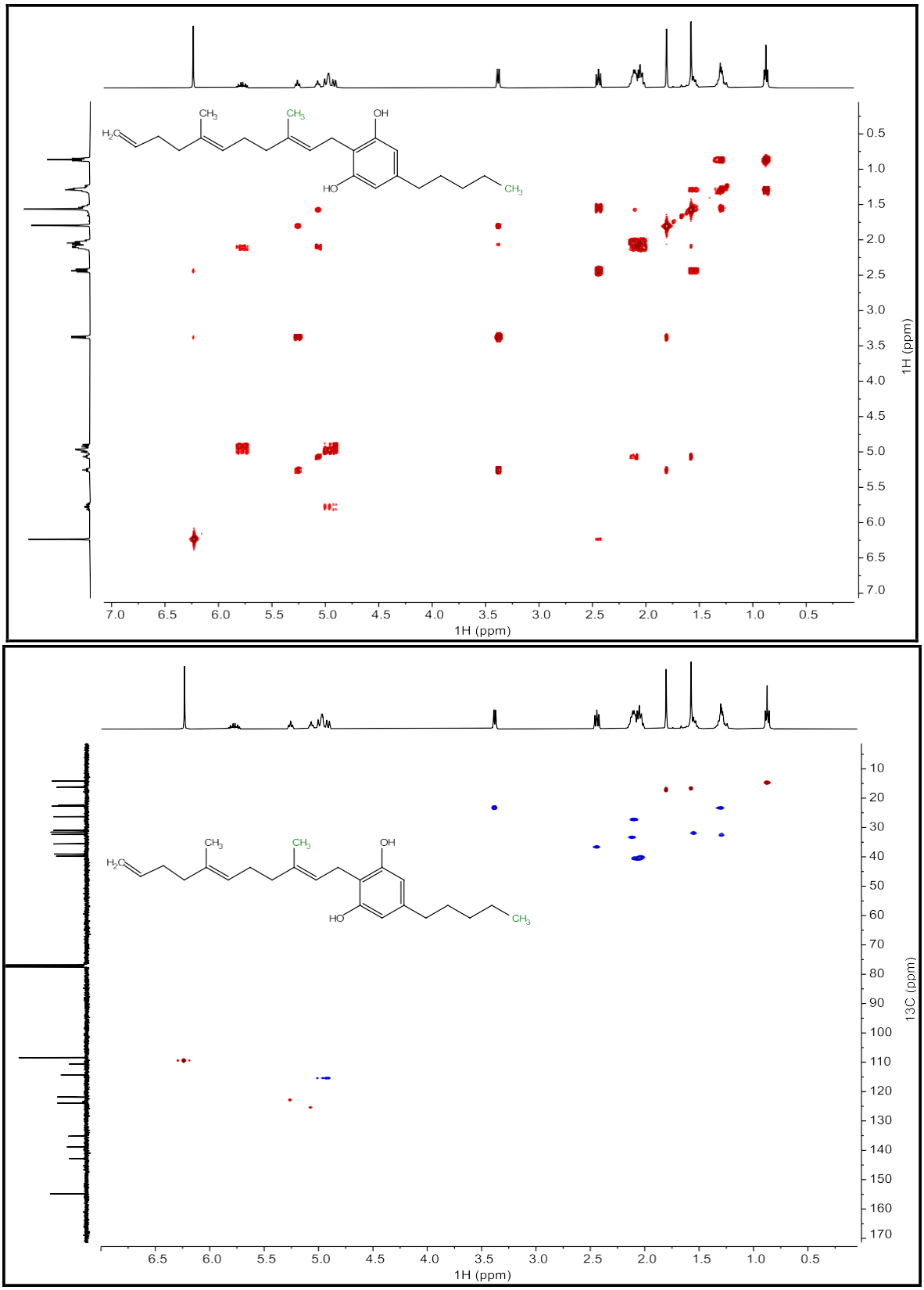


Figure S36: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1l** in $CDCl_3$

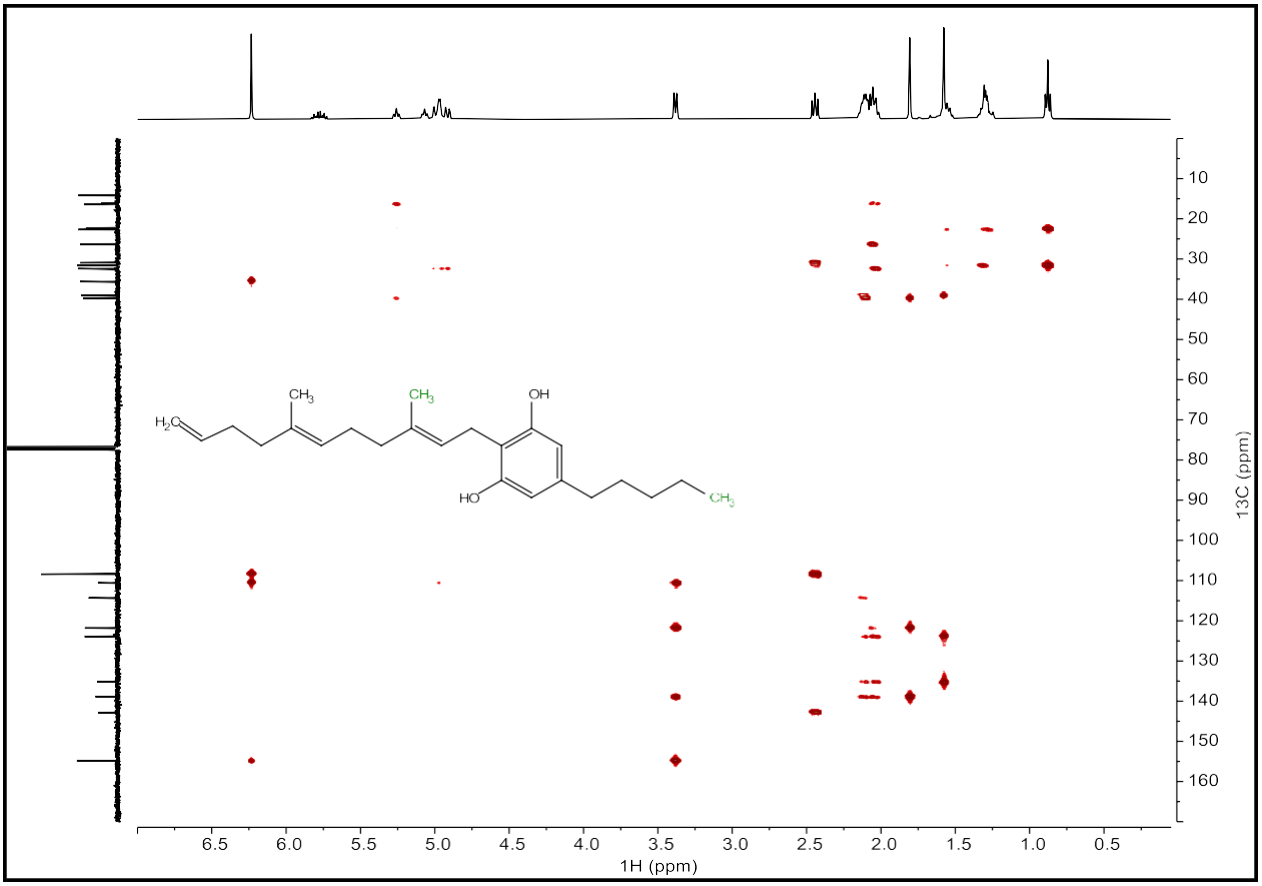


Figure S37: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1l** in $CDCl_3$

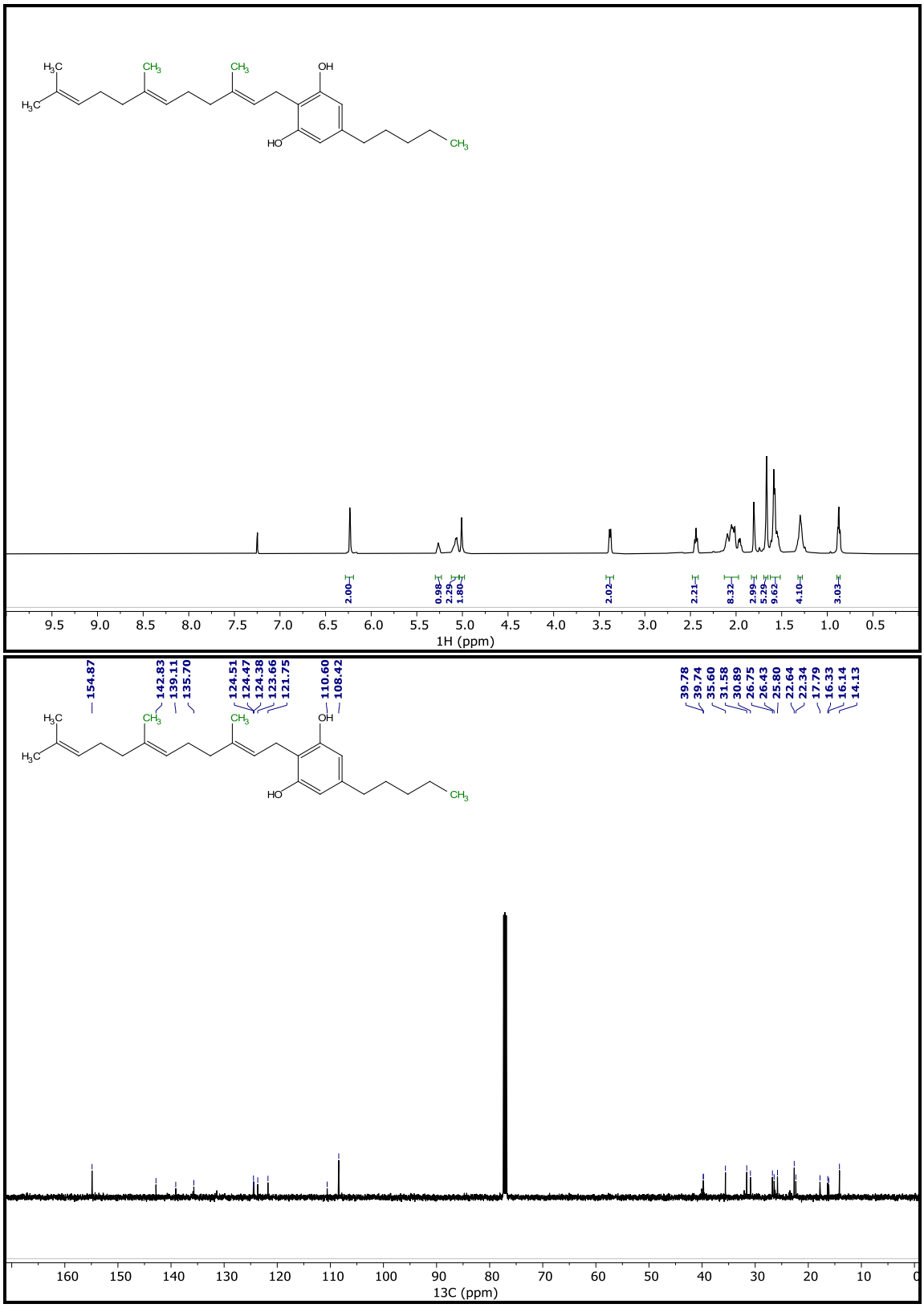


Figure S38: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **1m** in $CDCl_3$

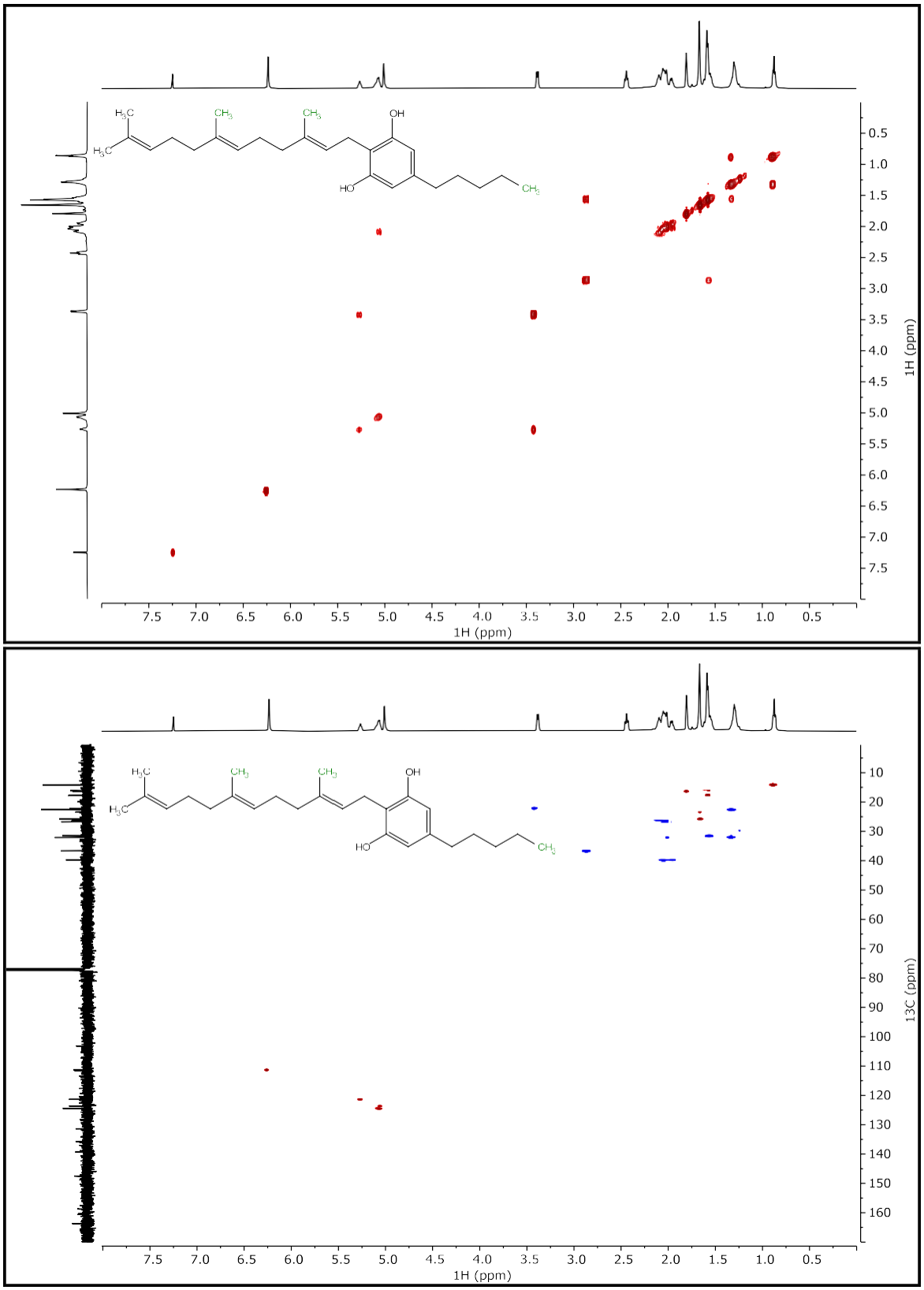


Figure S39: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **1m** in $CDCl_3$

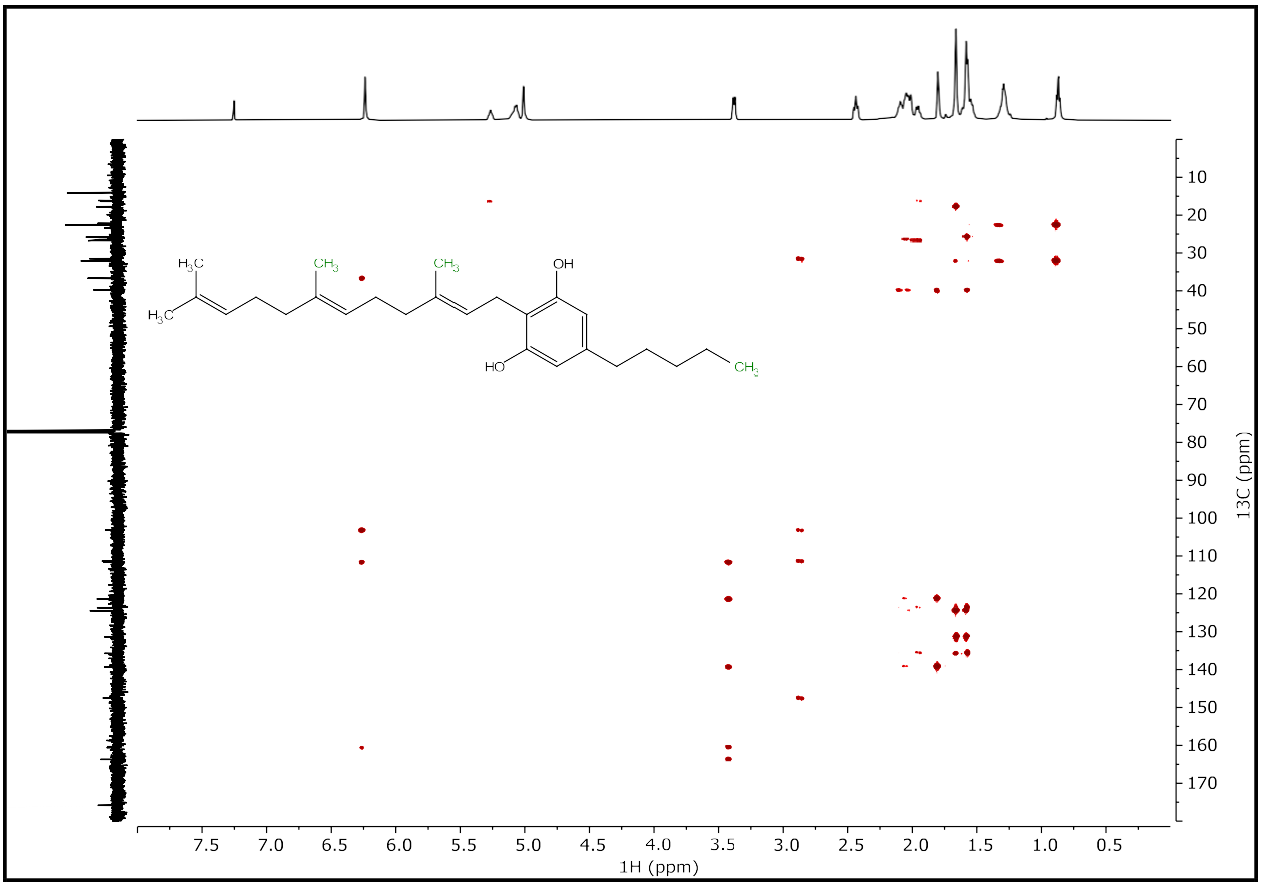


Figure S40: 2D-^{1}H-^{13}C HMBC NMR spectrum of **1m** in $CDCl_3$

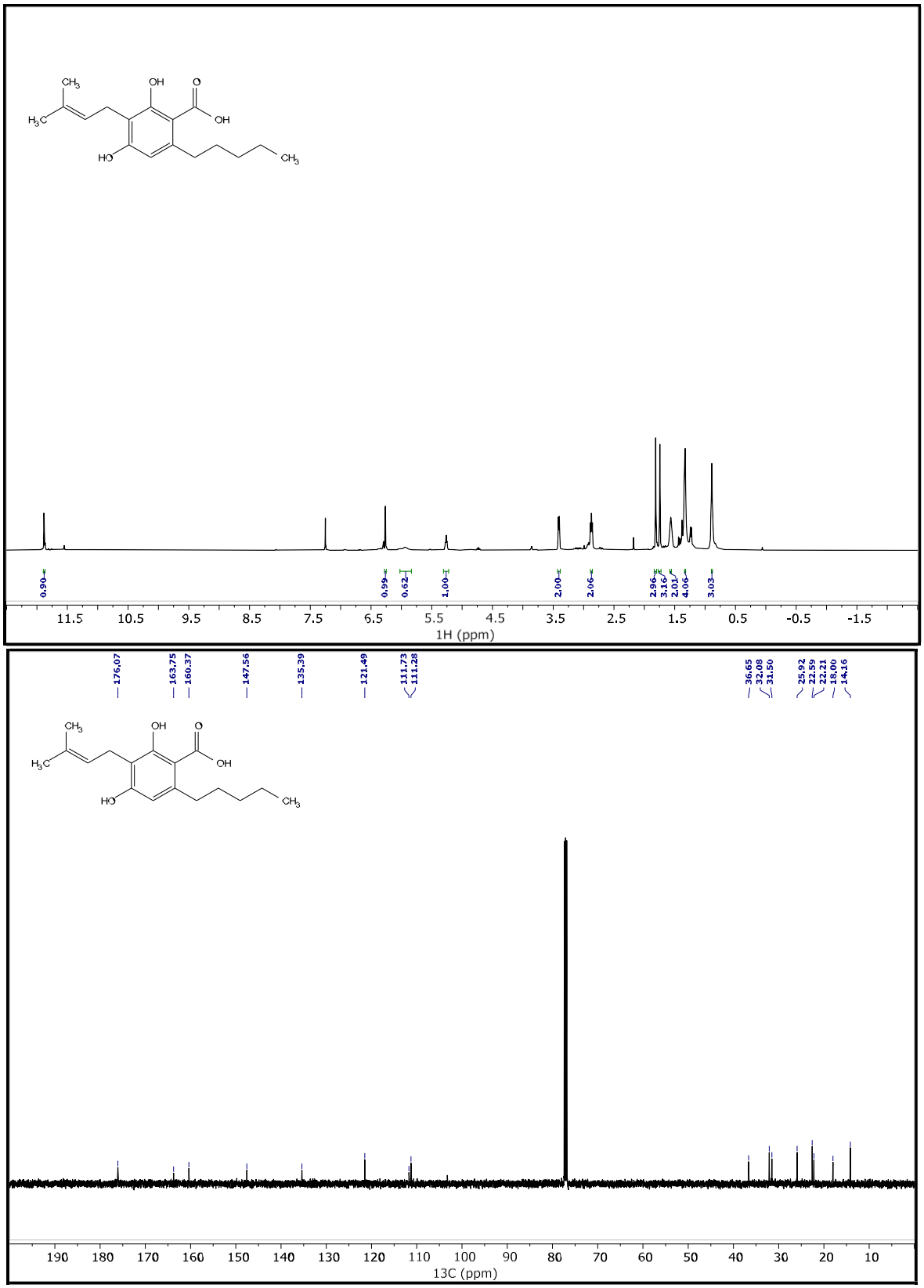


Figure S41: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2a** in $CDCl_3$

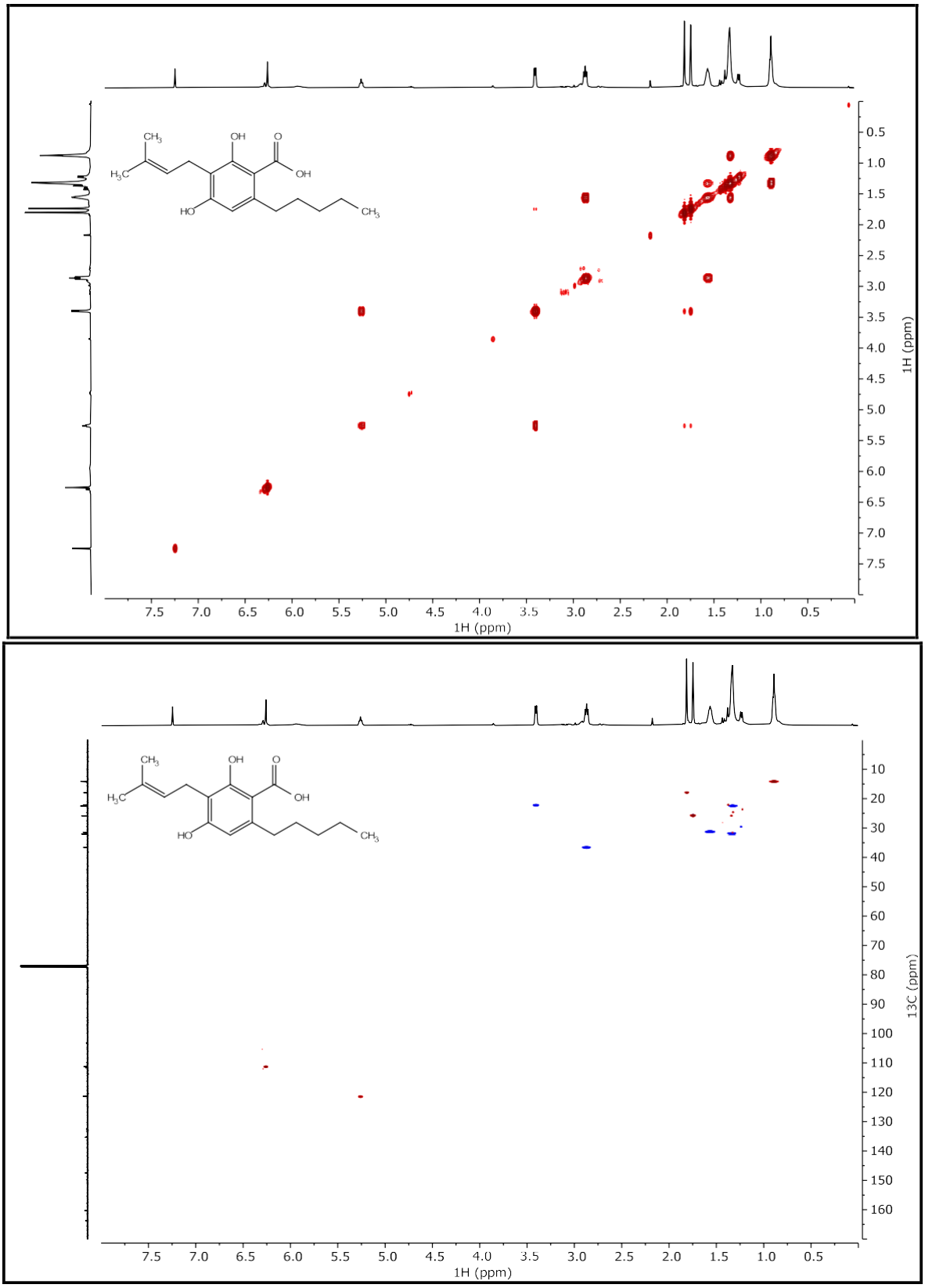


Figure S42: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2a** in $CDCl_3$

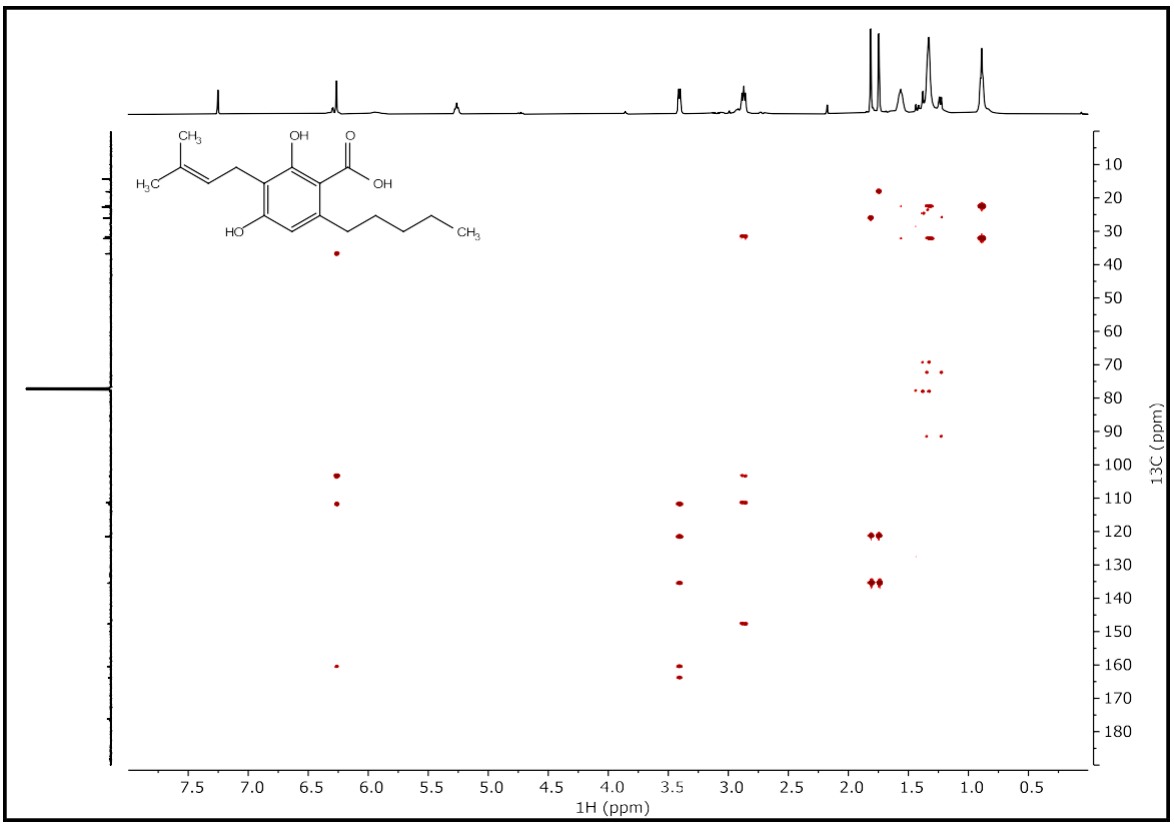


Figure S43: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2a** in $CDCl_3$

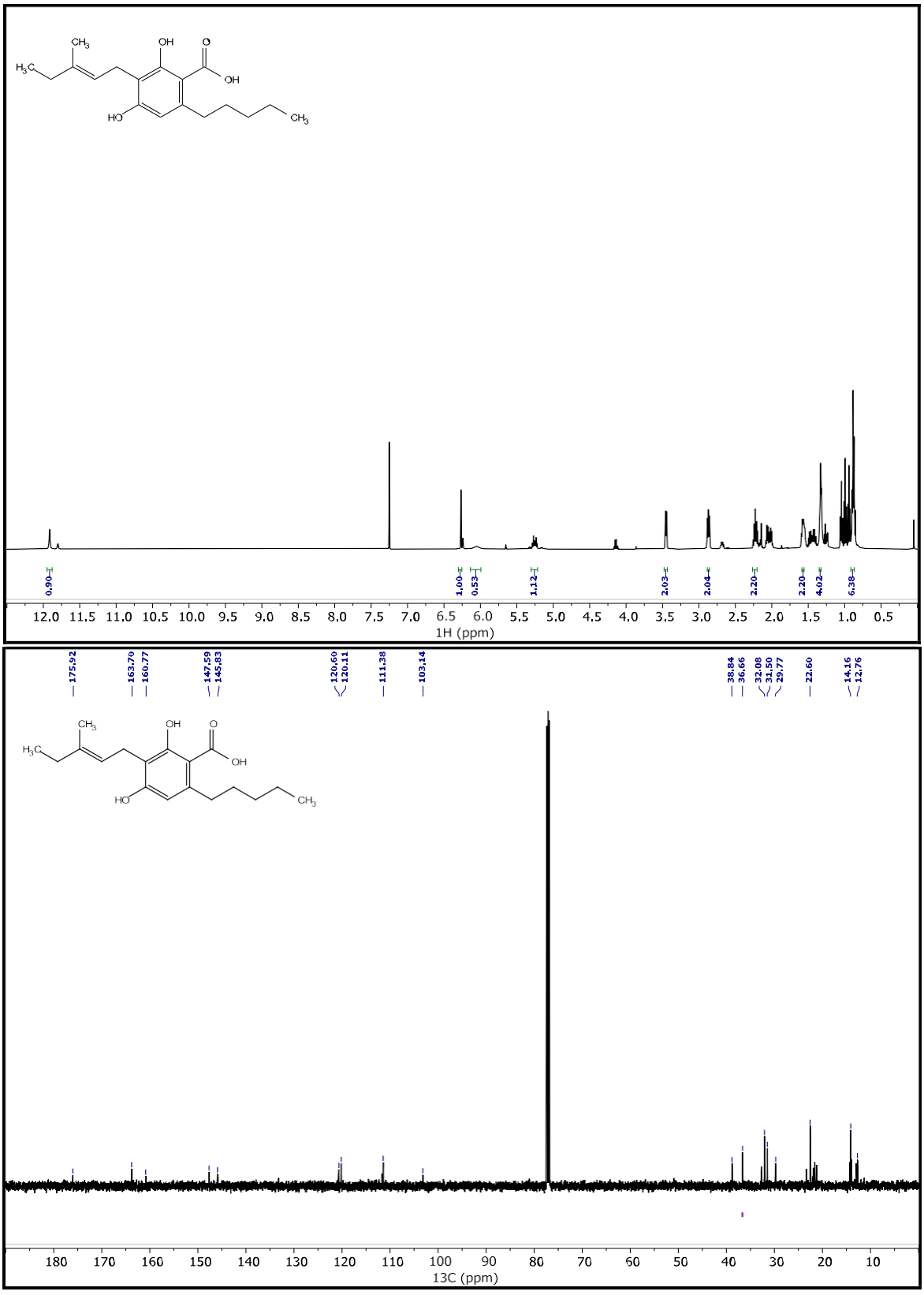


Figure S44: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2b** in $CDCl_3$

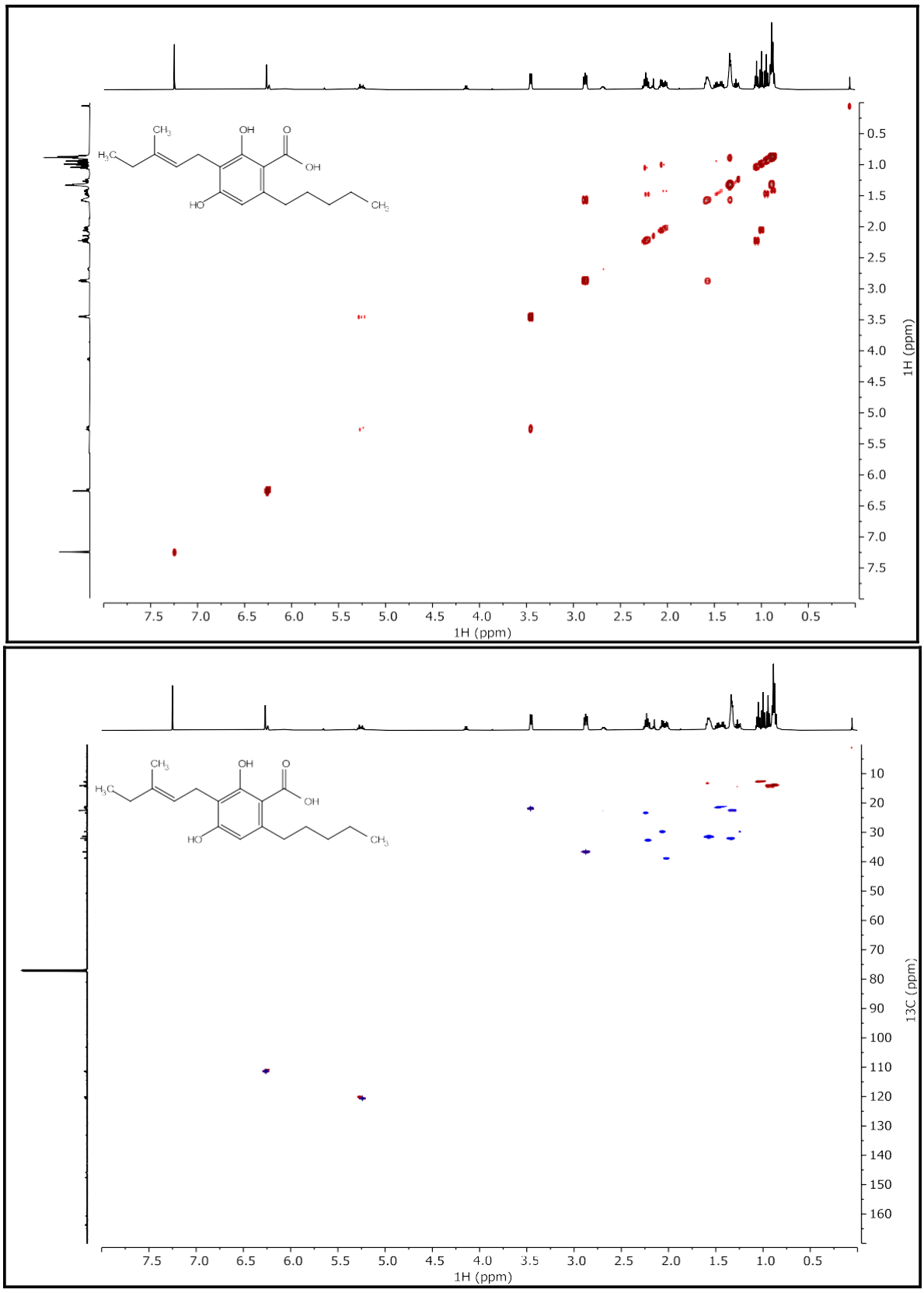


Figure S45: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2b** in $CDCl_3$

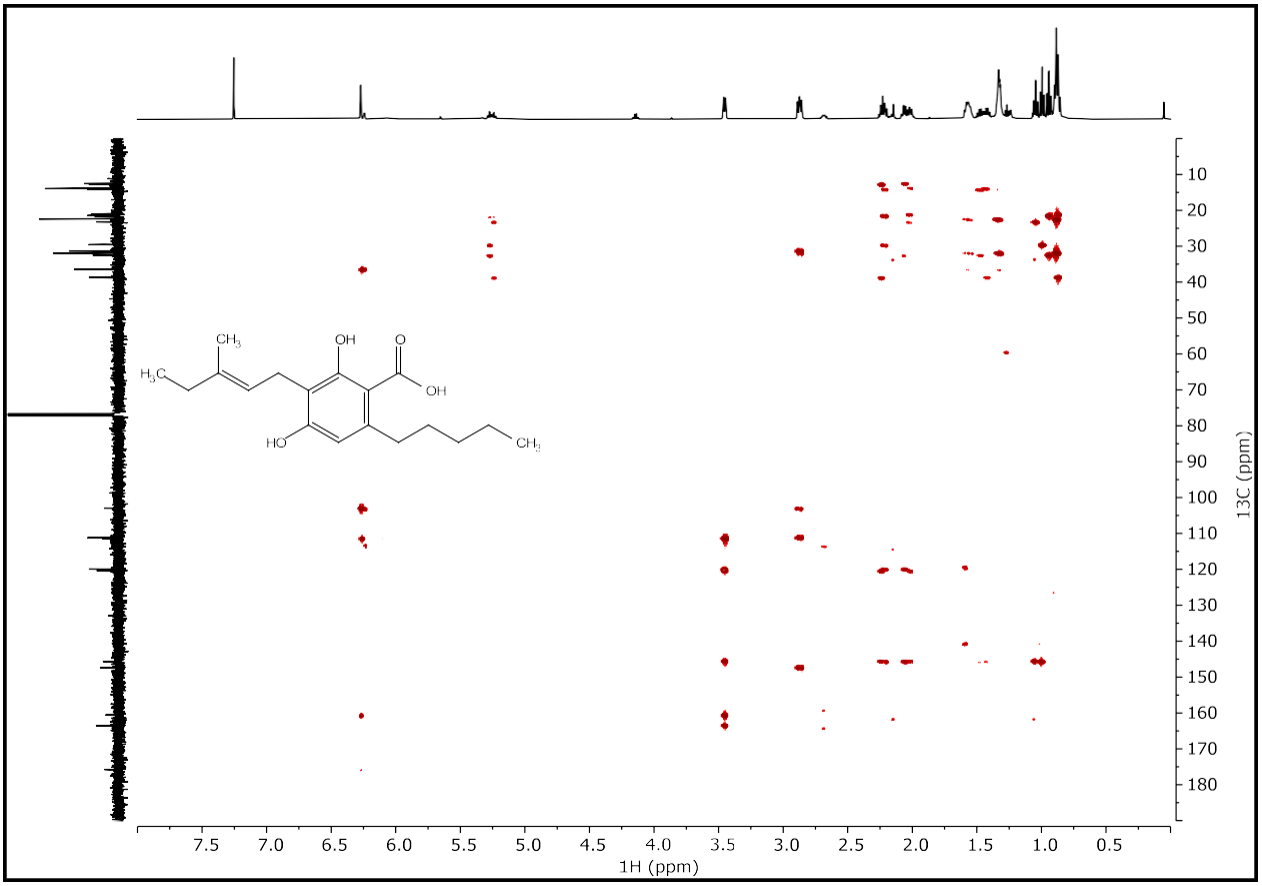


Figure S46: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2b** in $CDCl_3$

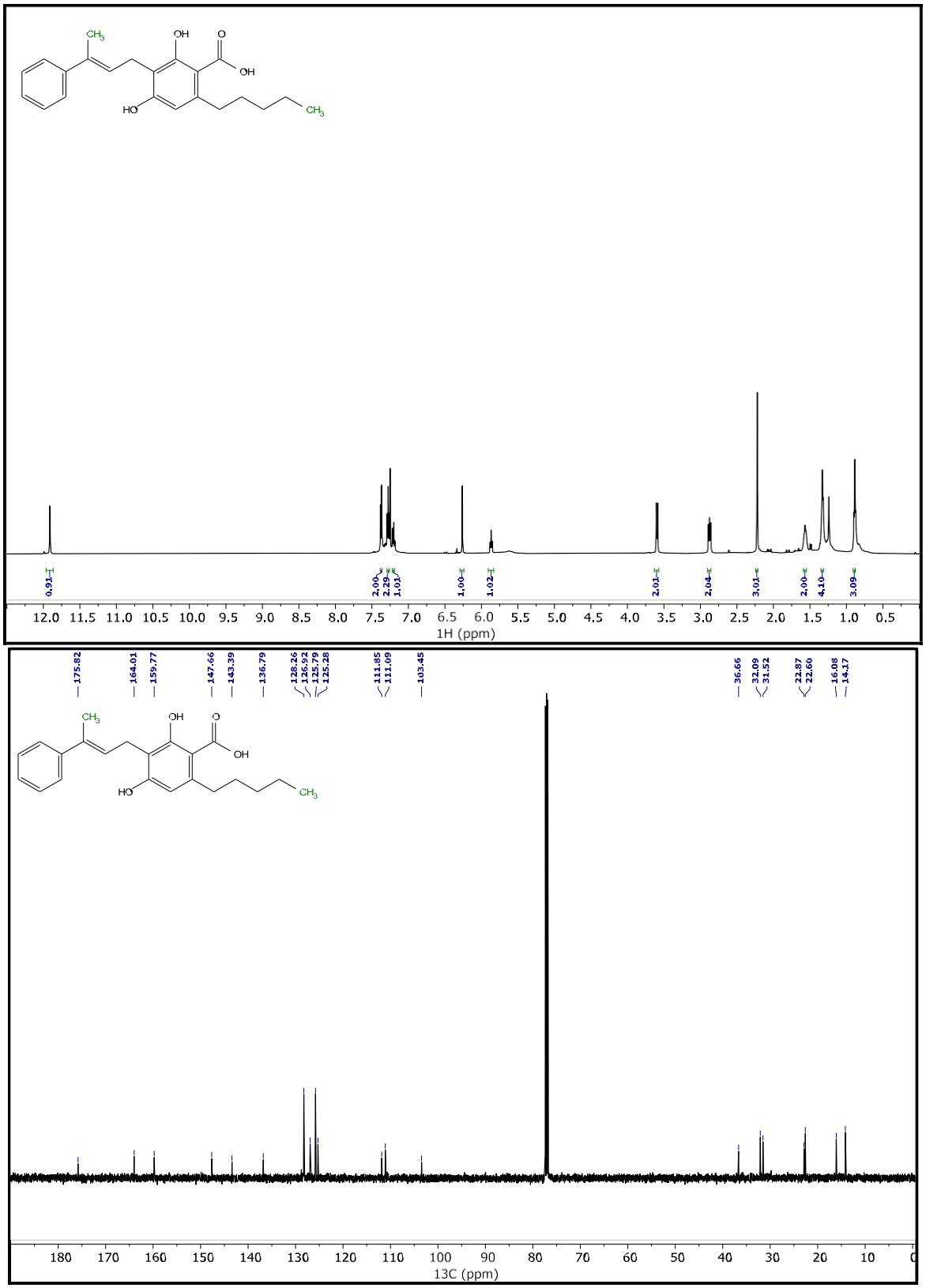


Figure S47: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2c** in $CDCl_3$

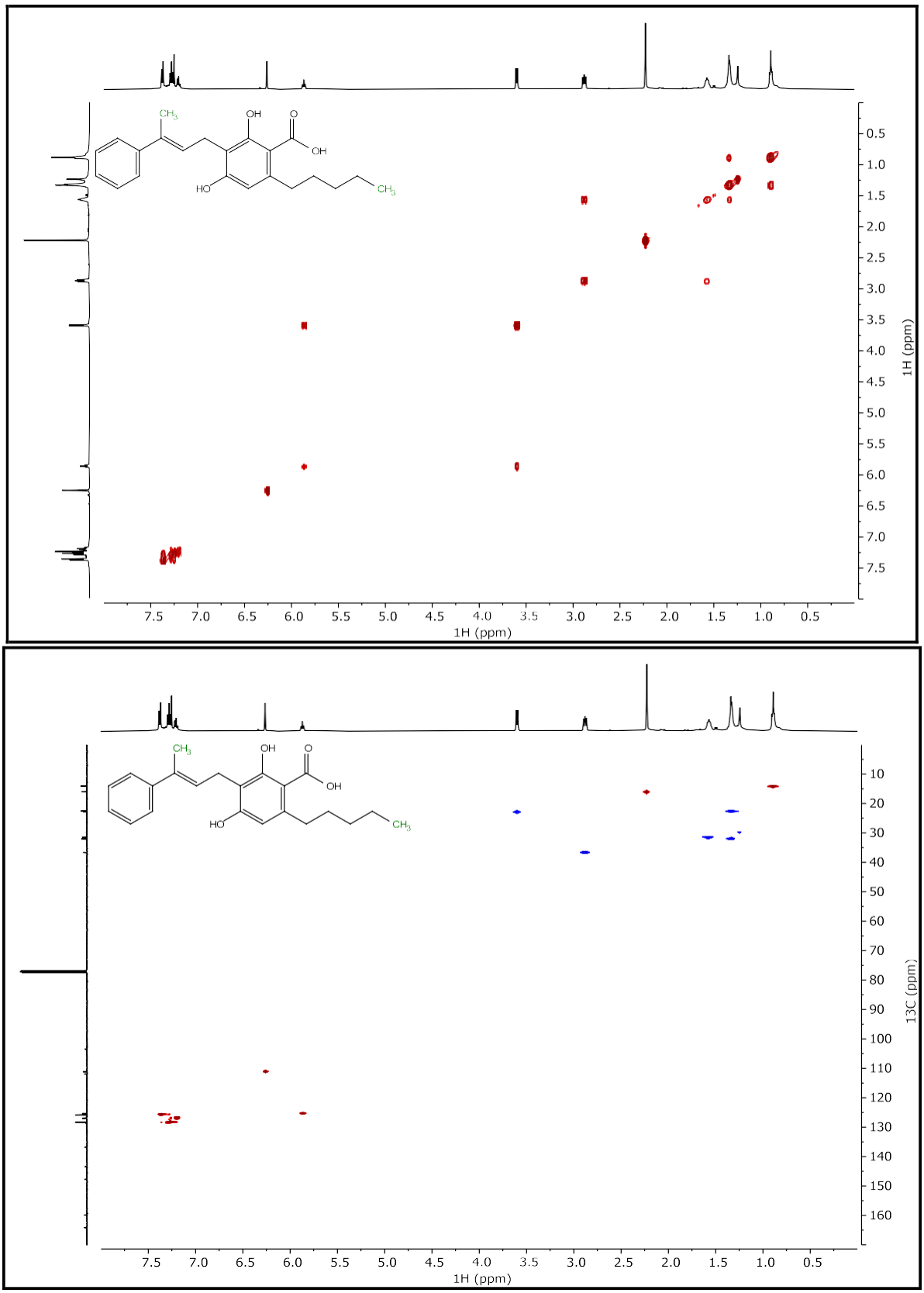


Figure S48: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2c** in $CDCl_3$

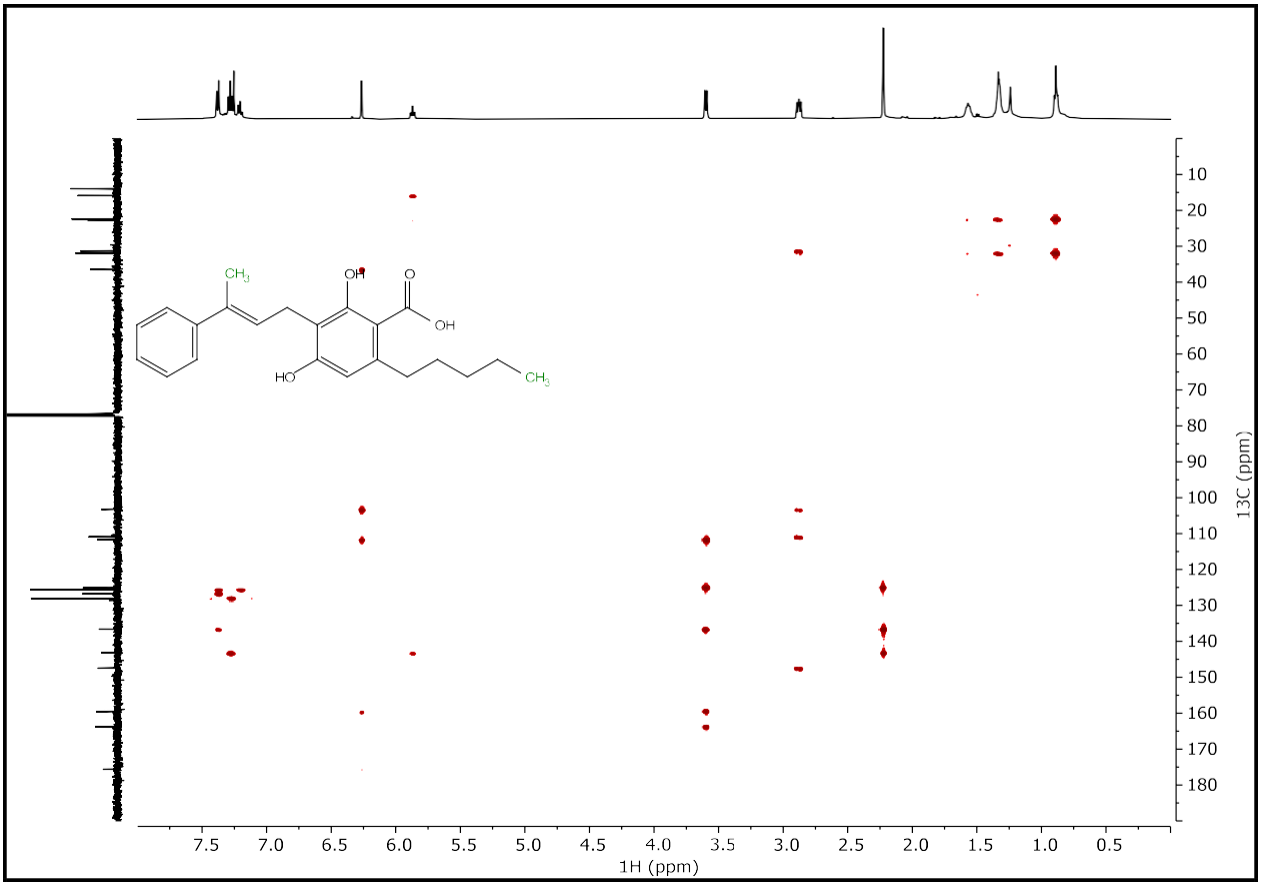


Figure S49: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2c** in $CDCl_3$

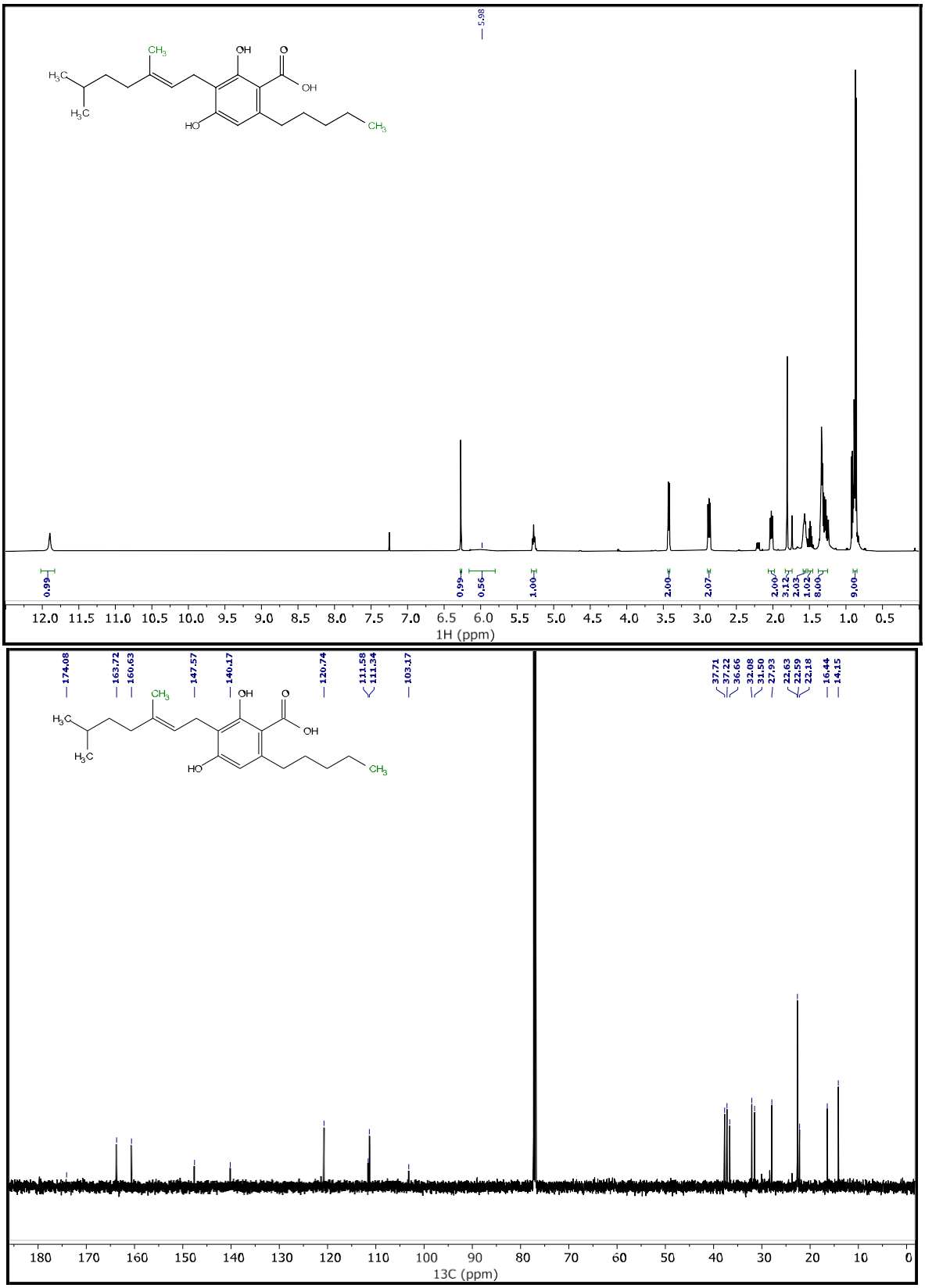


Figure S50: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2d** in $CDCl_3$

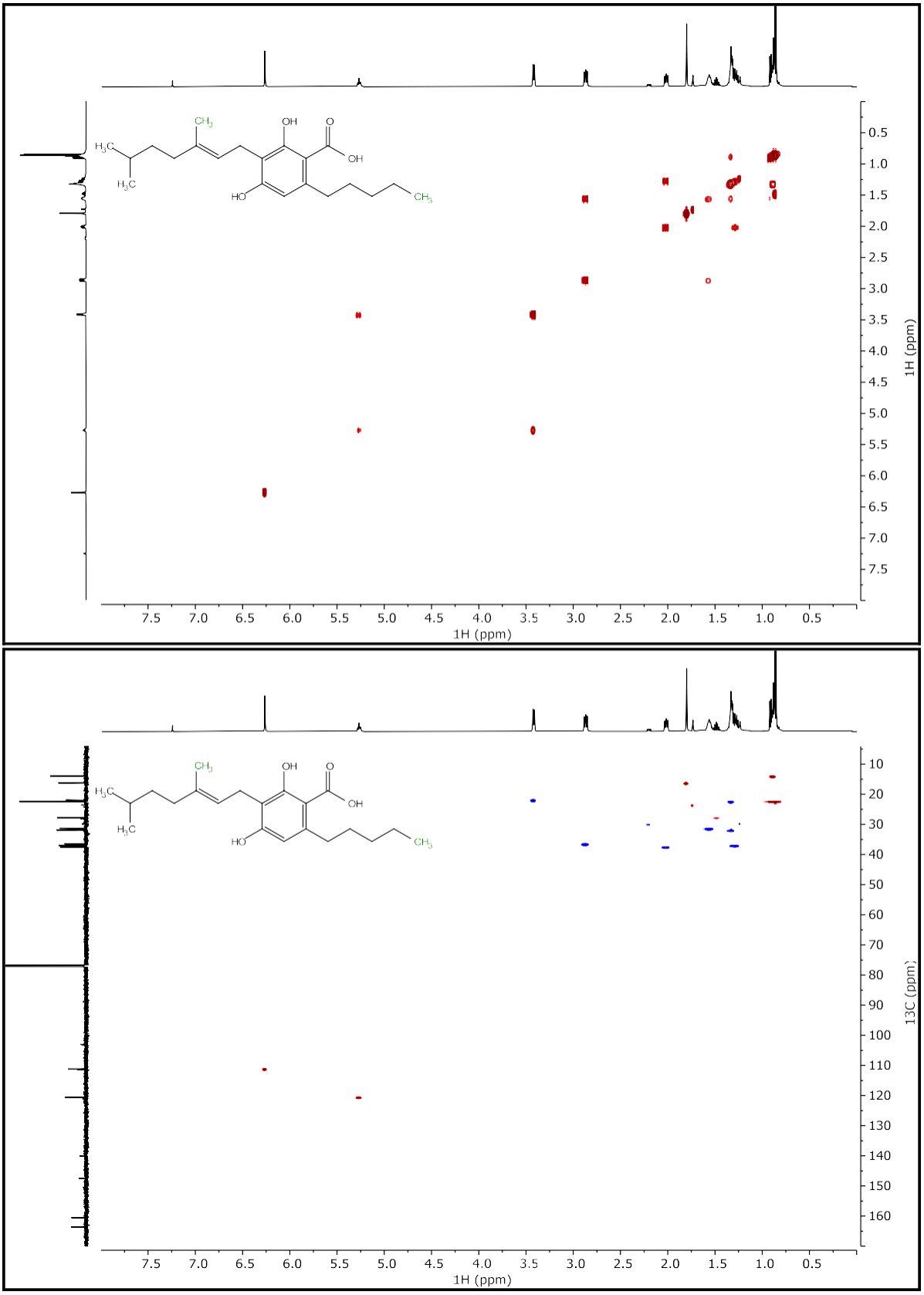


Figure S51: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2d** in $CDCl_3$

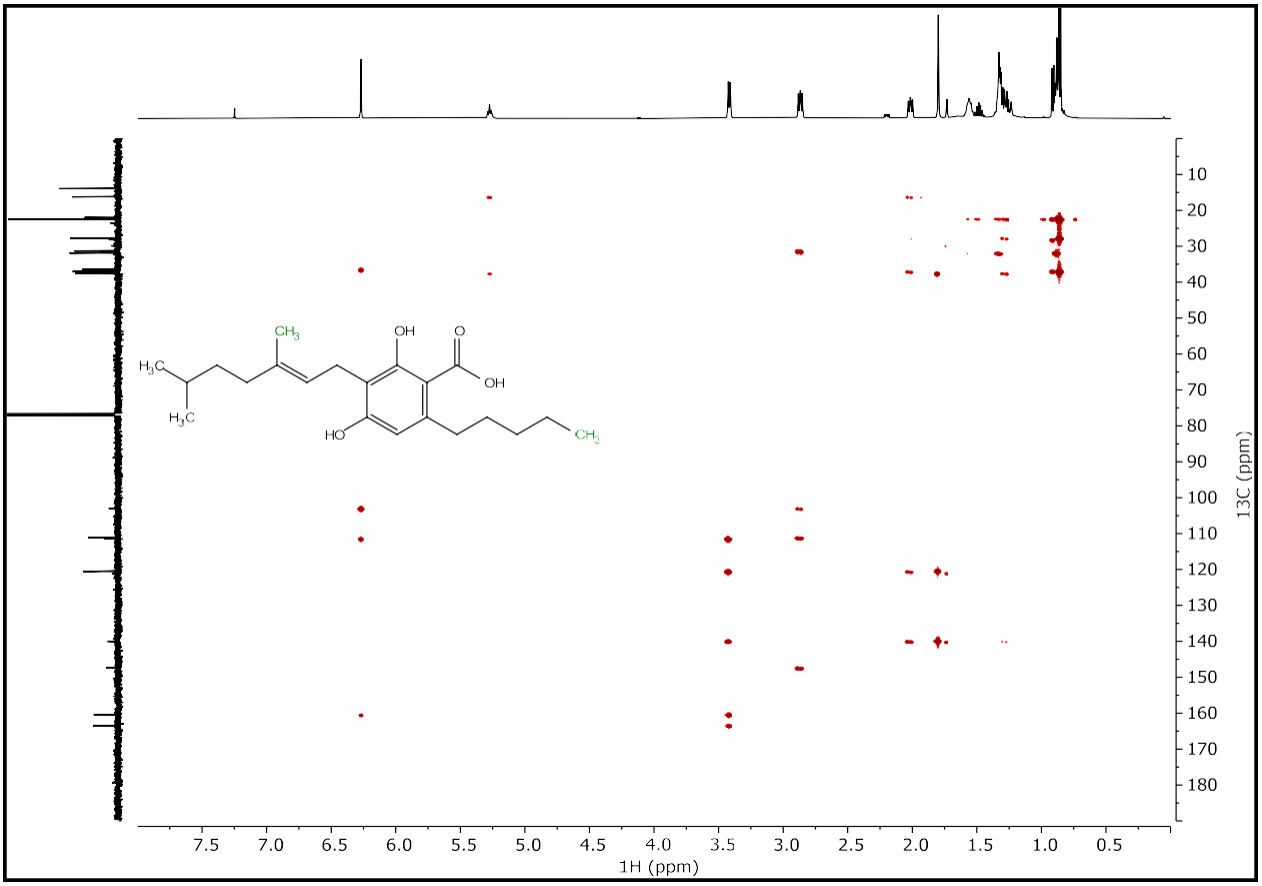


Figure S52: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2d** in $CDCl_3$

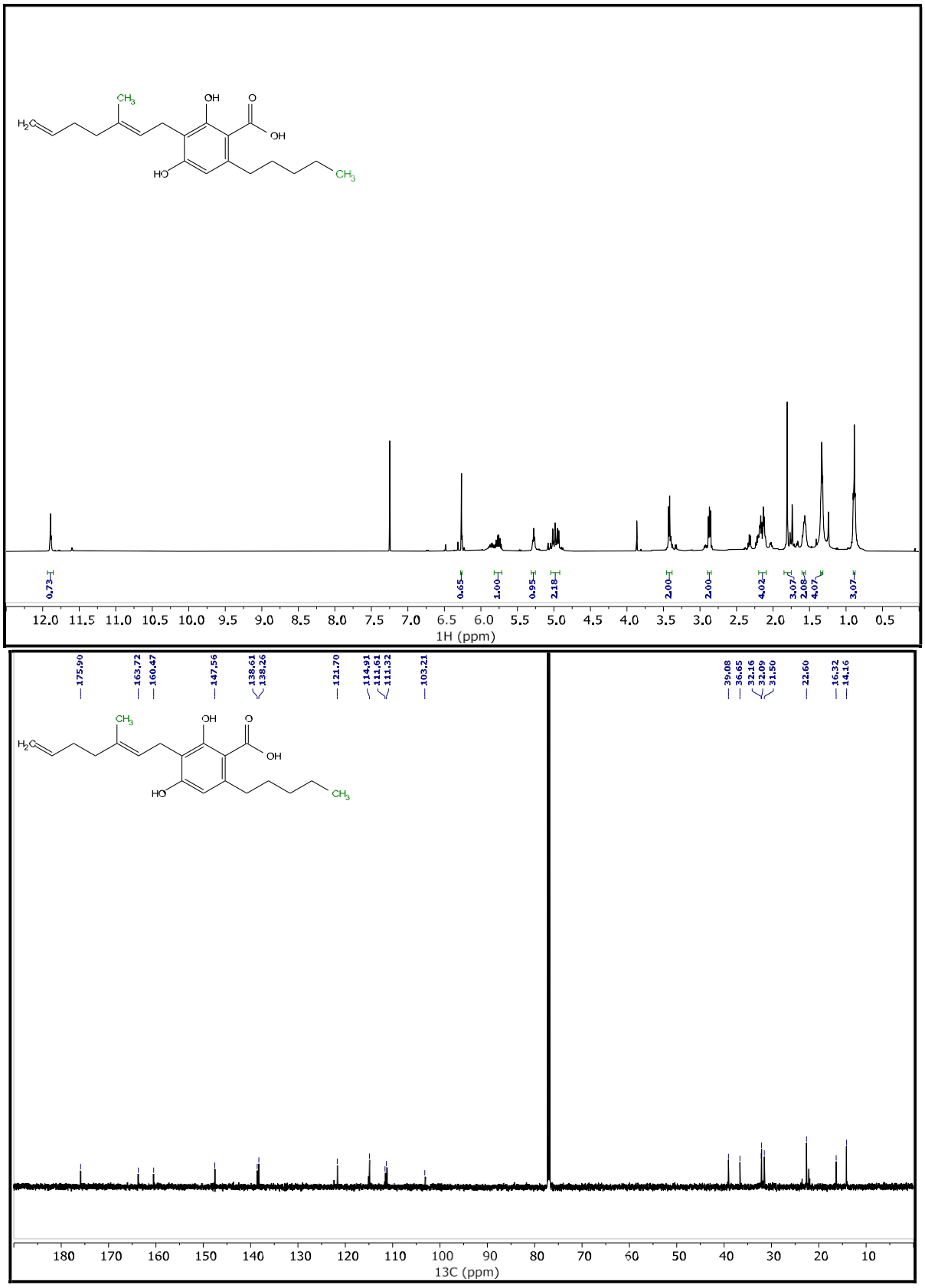


Figure S53: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2e** in $CDCl_3$

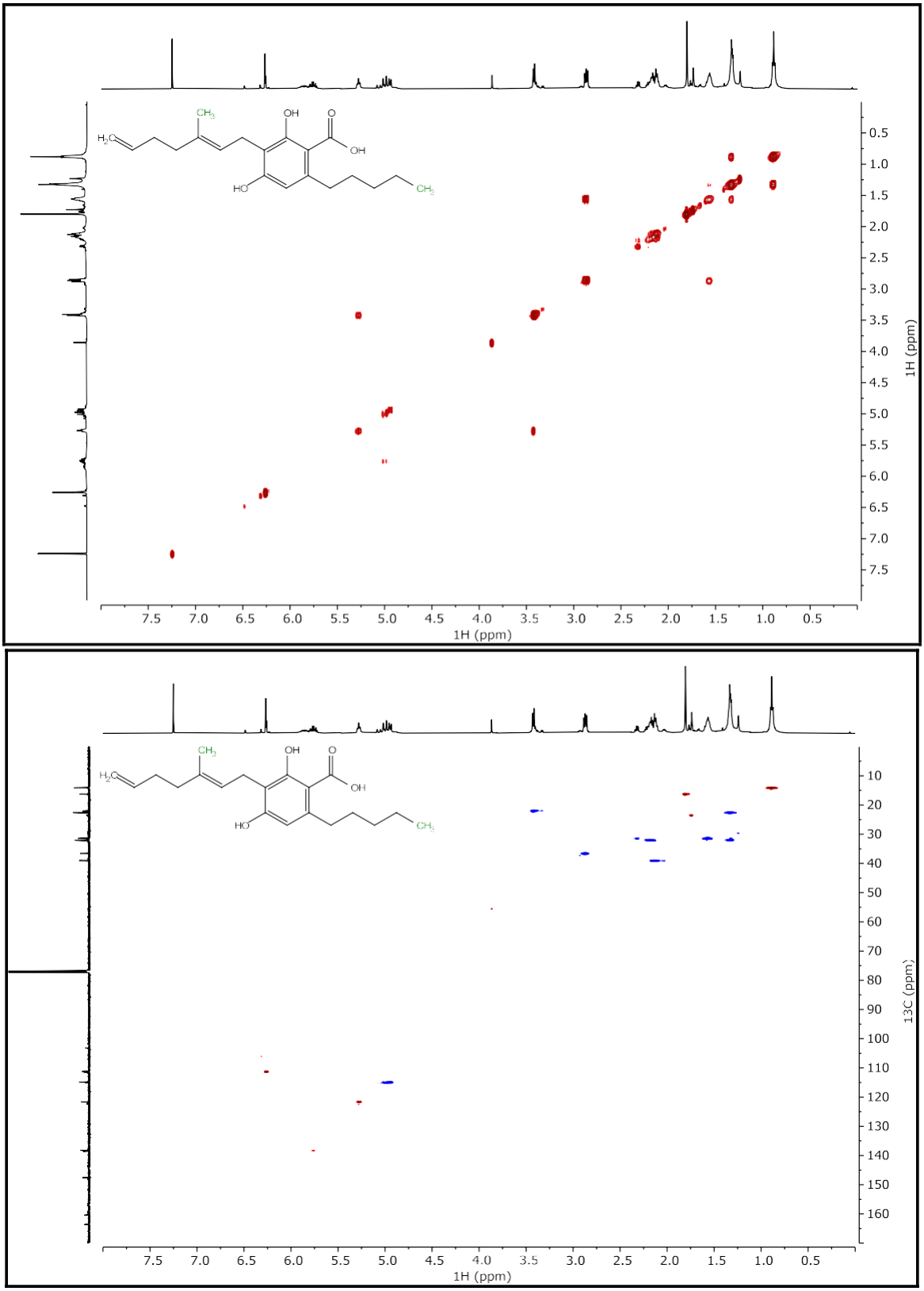


Figure S54: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2e** in $CDCl_3$

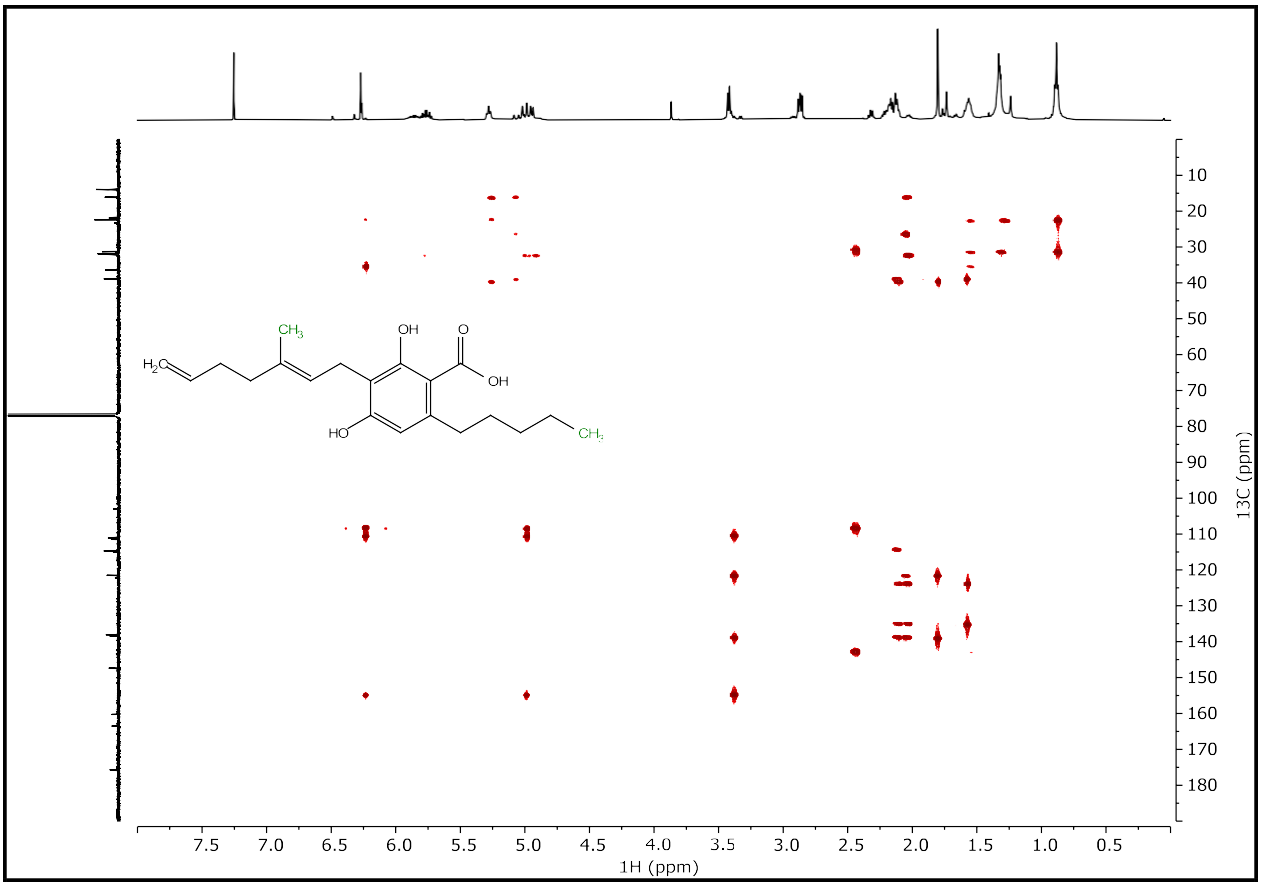


Figure S55: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2e** in CDCl

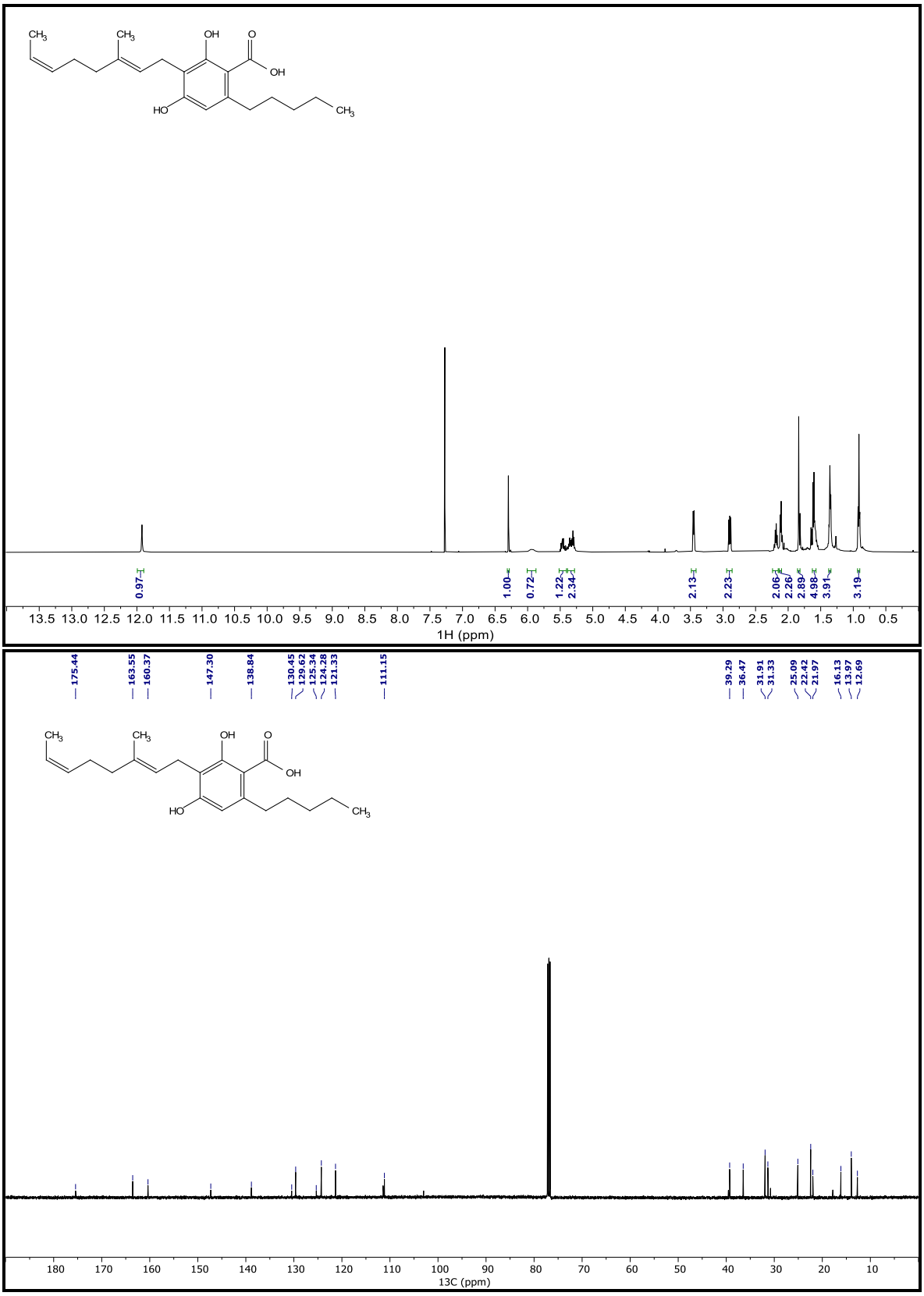


Figure S56: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2f** in $CDCl_3$

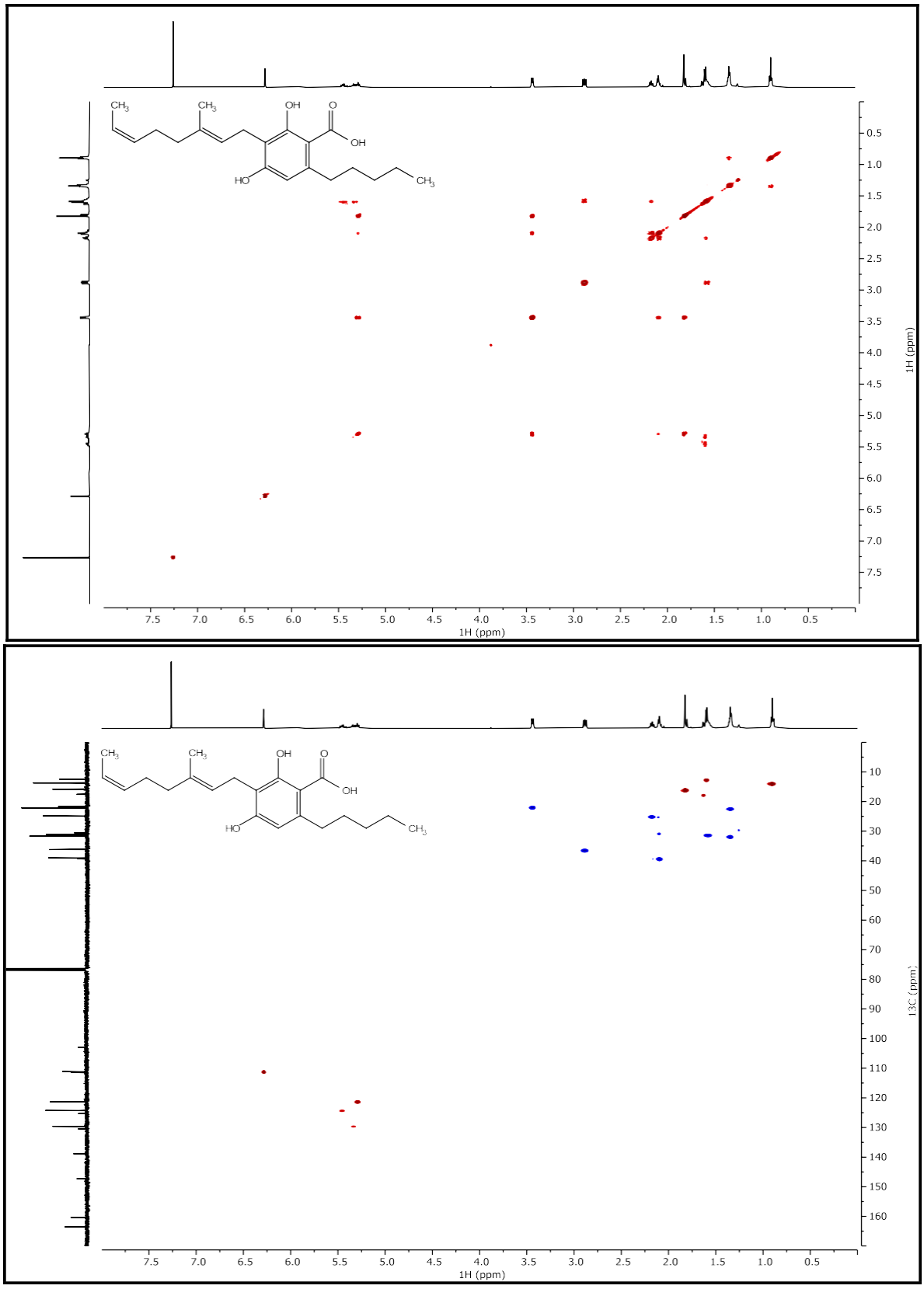


Figure S57: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2f** in $CDCl_3$

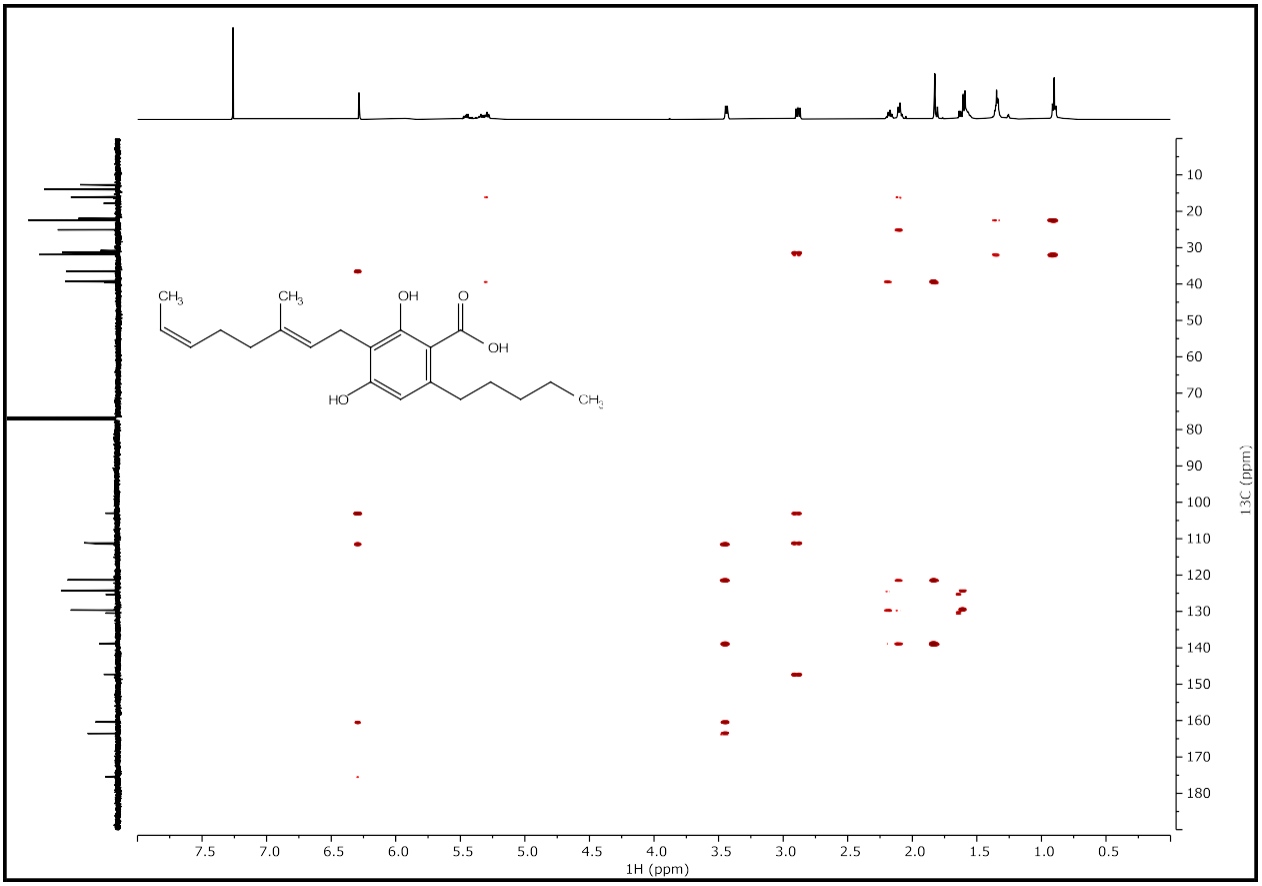


Figure S58: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2f** in $CDCl_3$

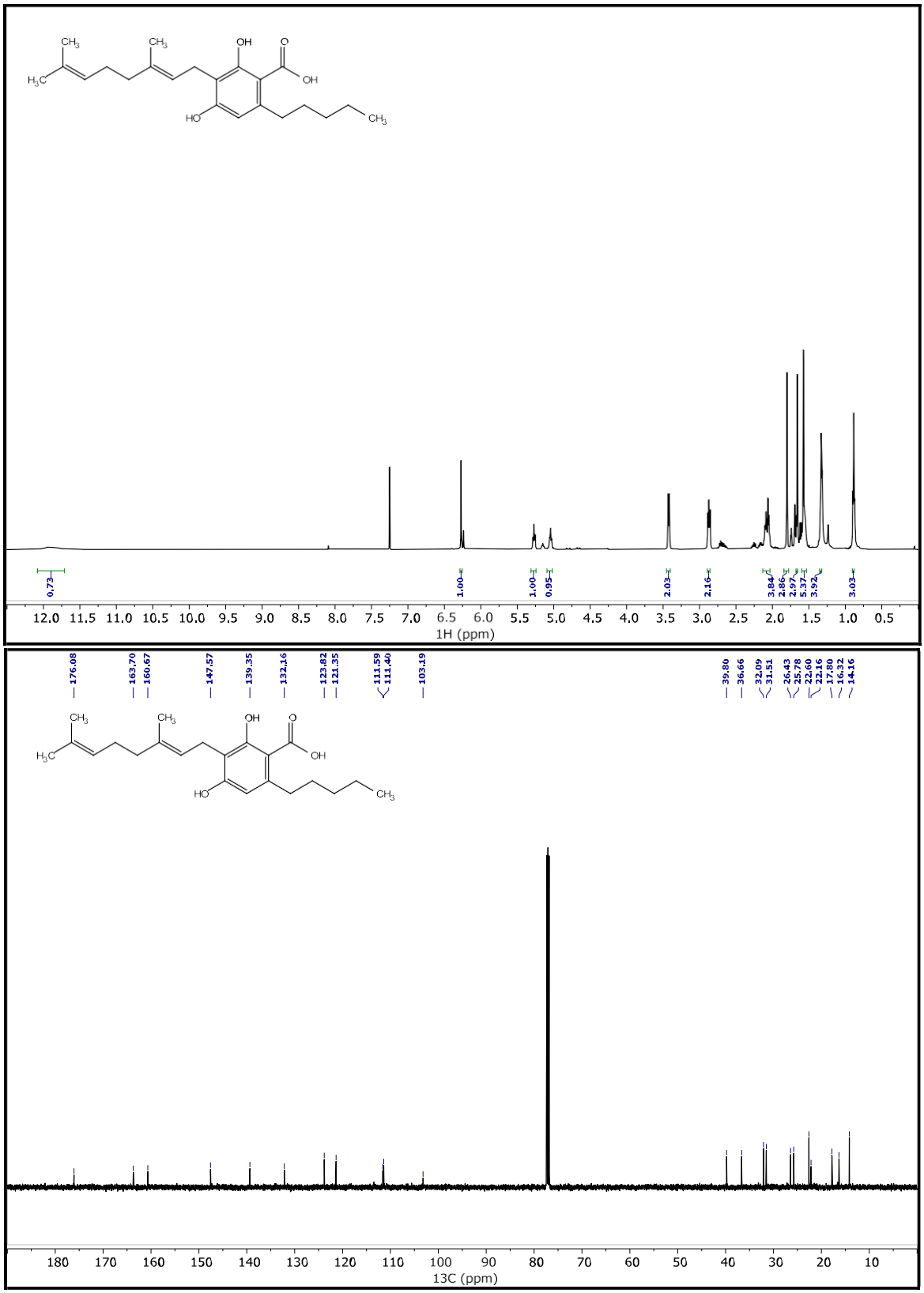


Figure S59: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2g** in $CDCl_3$

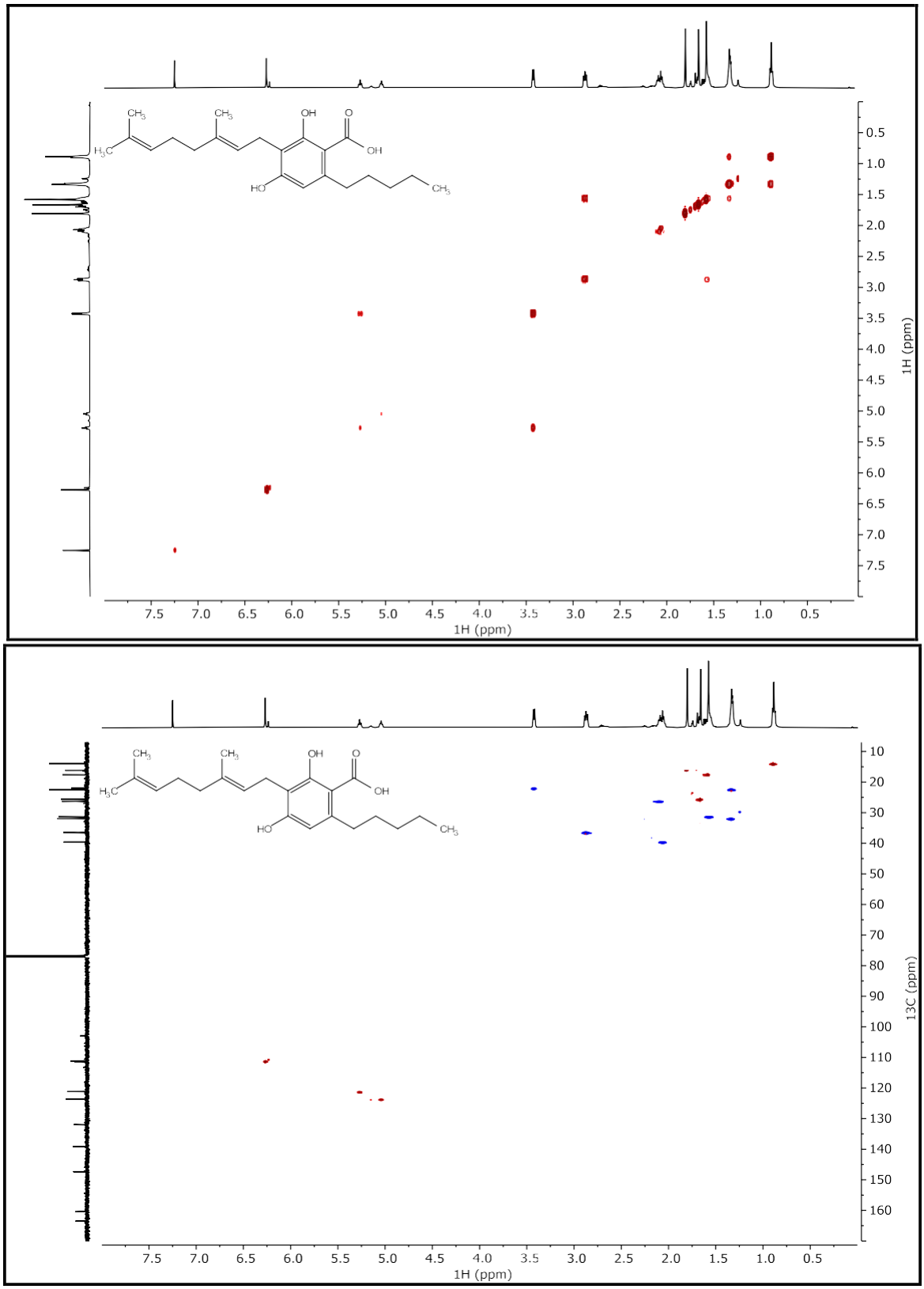


Figure S60: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2g** in $CDCl_3$

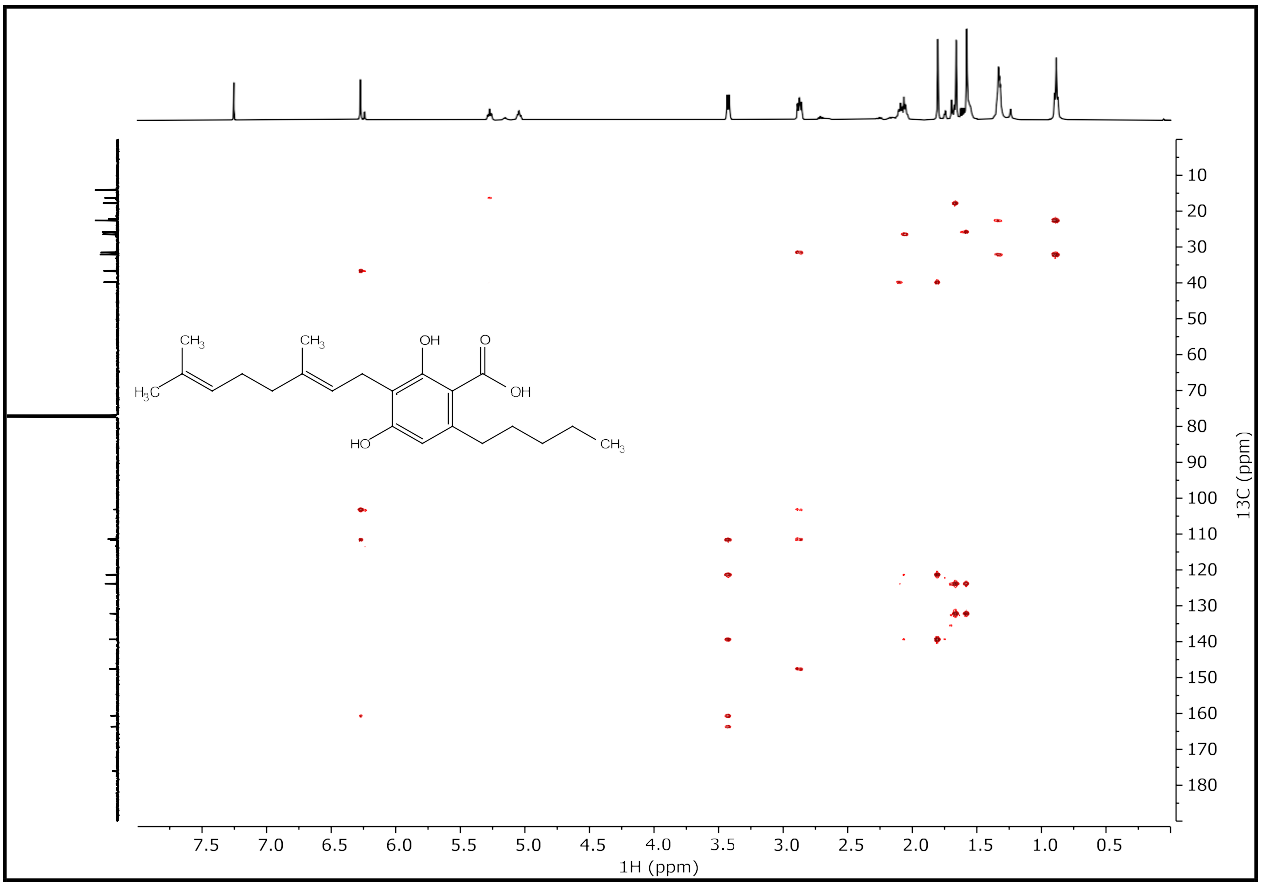


Figure S61: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2g** in $CDCl_3$

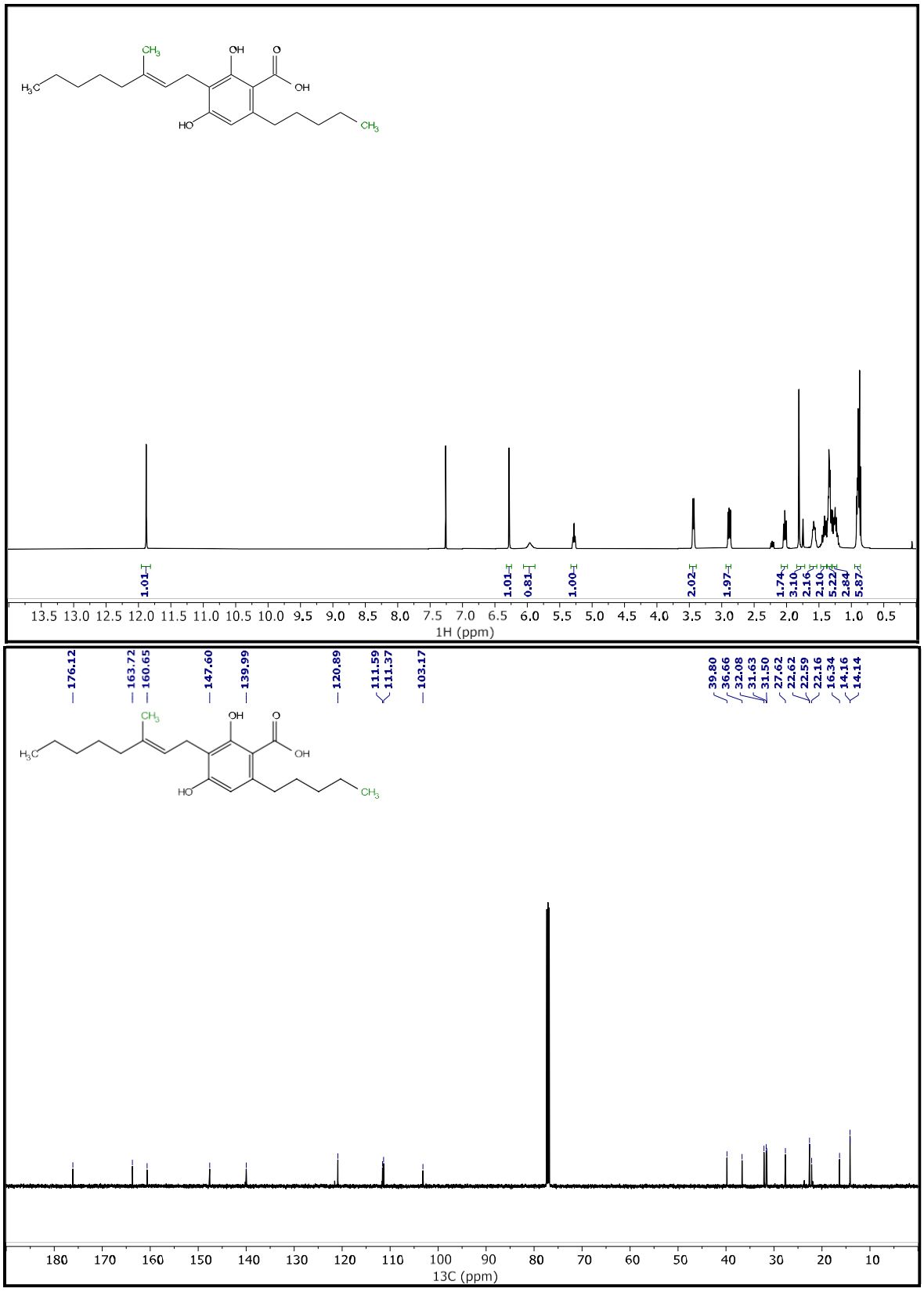


Figure S62: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2h** in $CDCl_3$

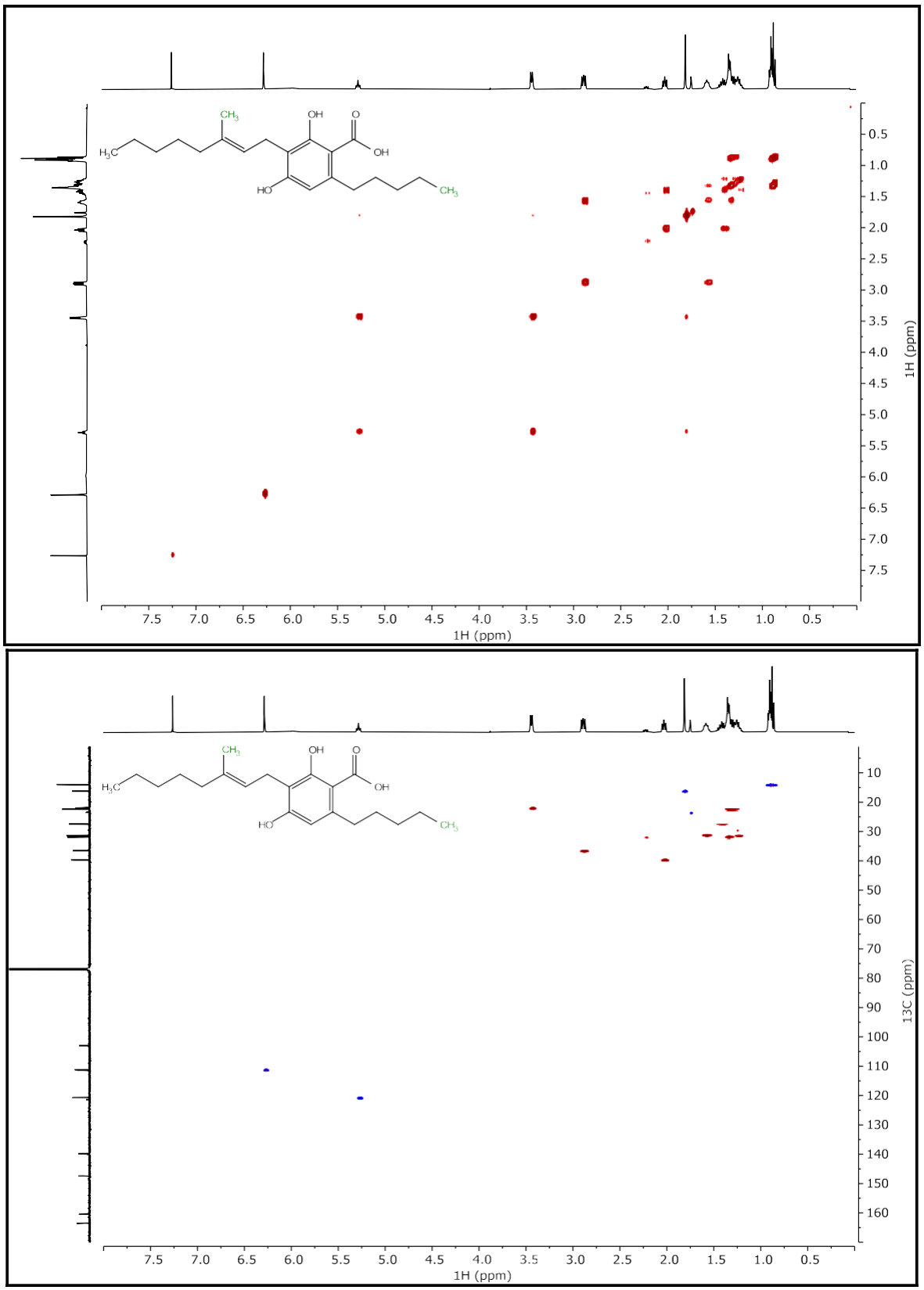


Figure S63: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2h** in $CDCl_3$

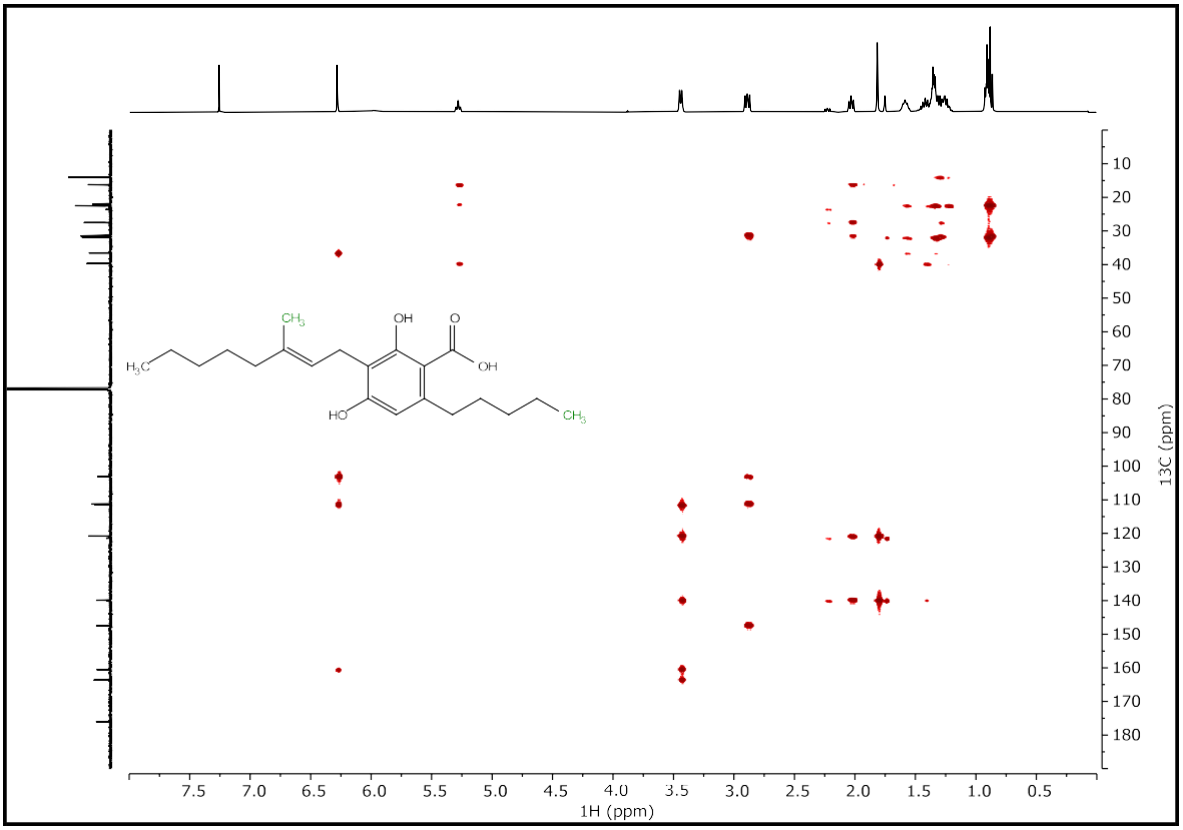


Figure S64: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2h** in $CDCl_3$

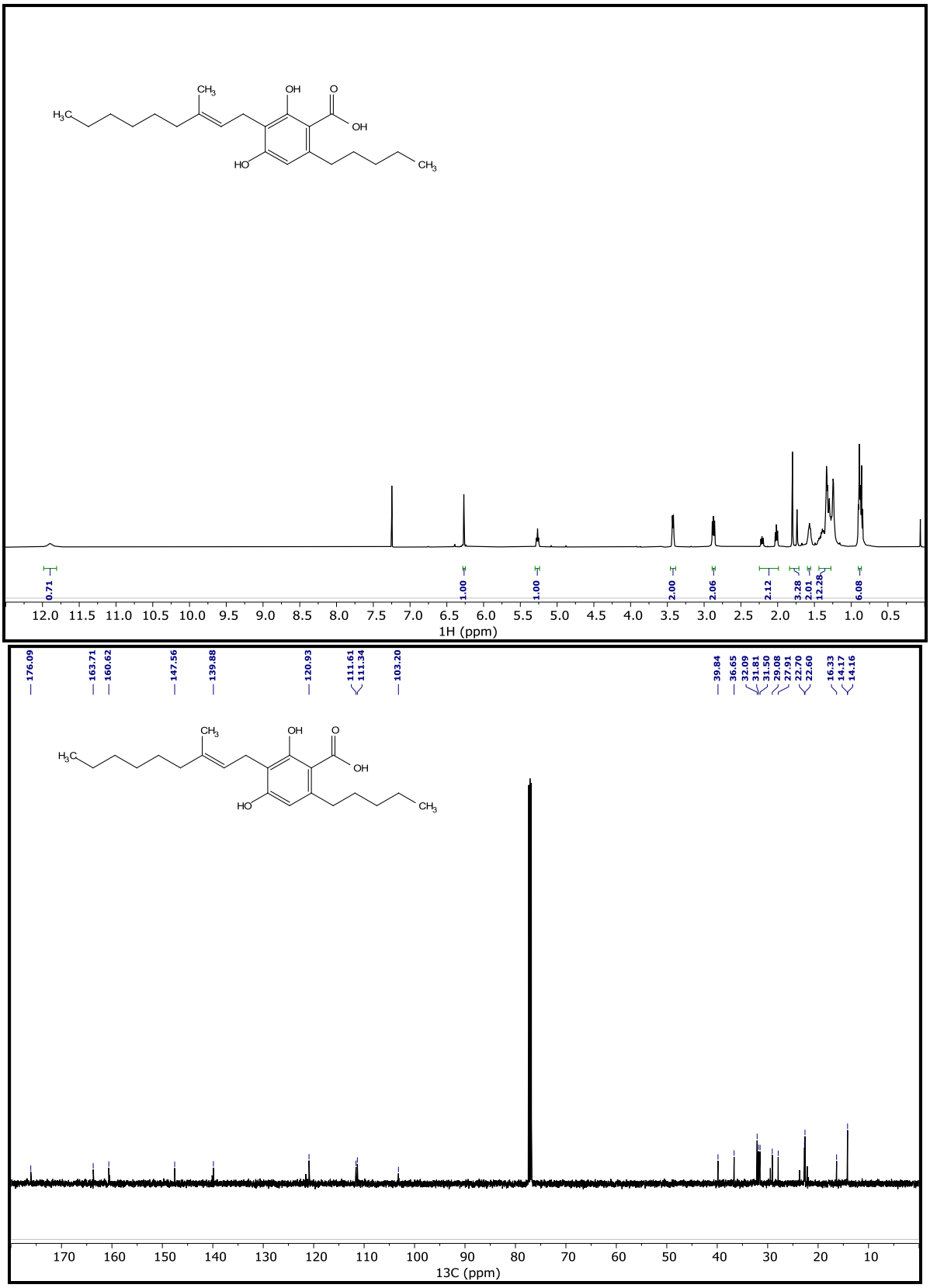


Figure S65: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2i** in $CDCl_3$

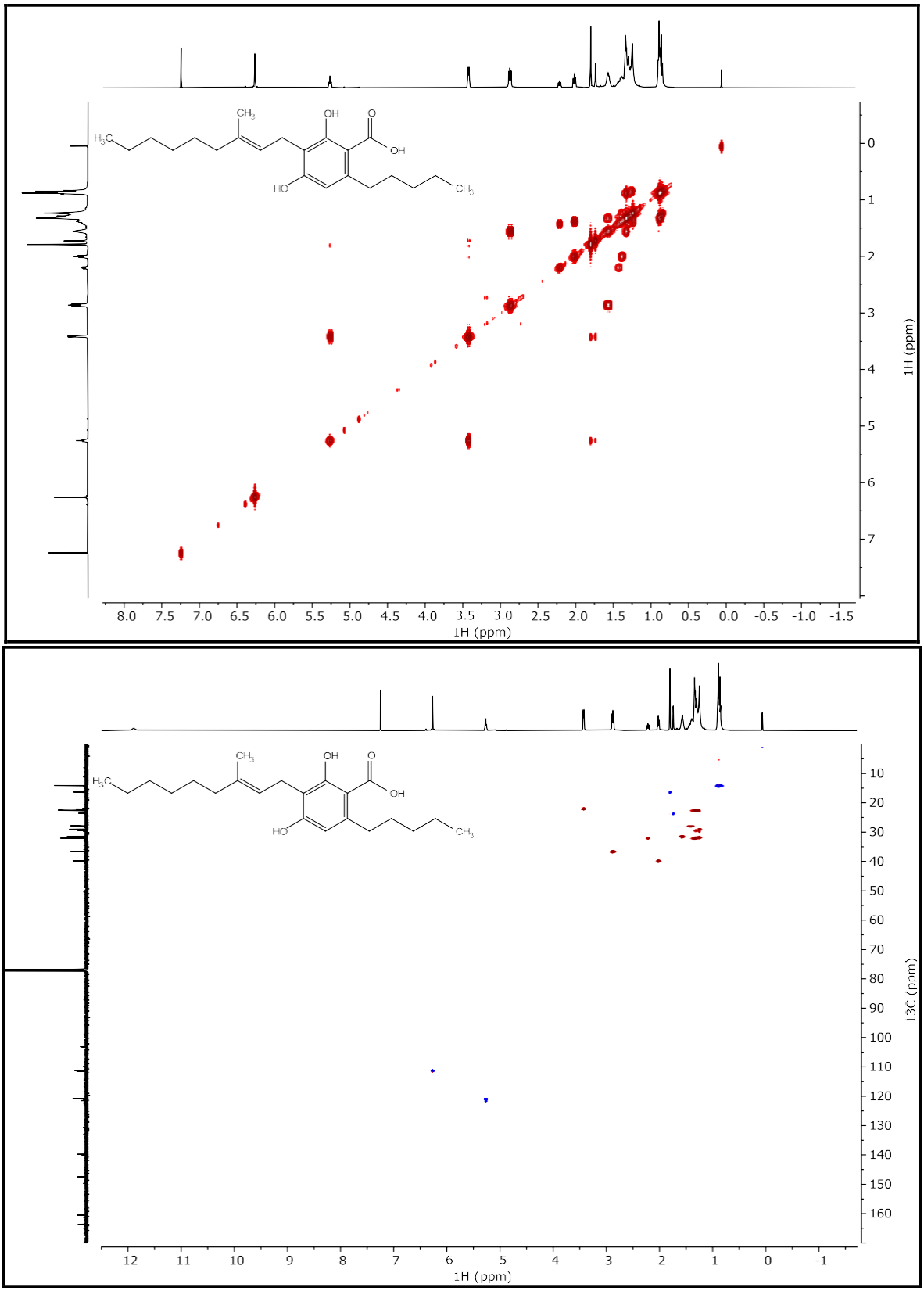


Figure S66: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2i** in $CDCl_3$

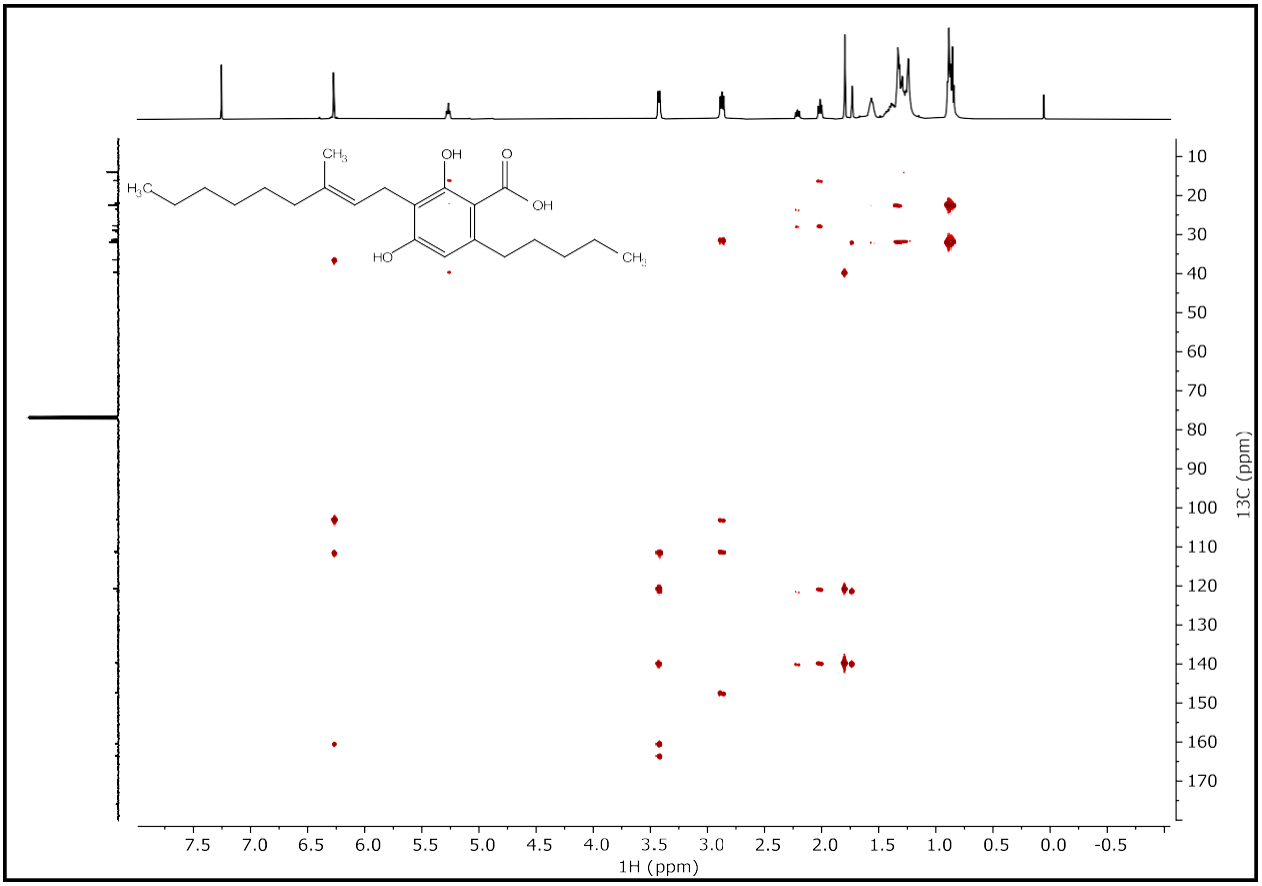


Figure S67: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2i** in $CDCl_3$

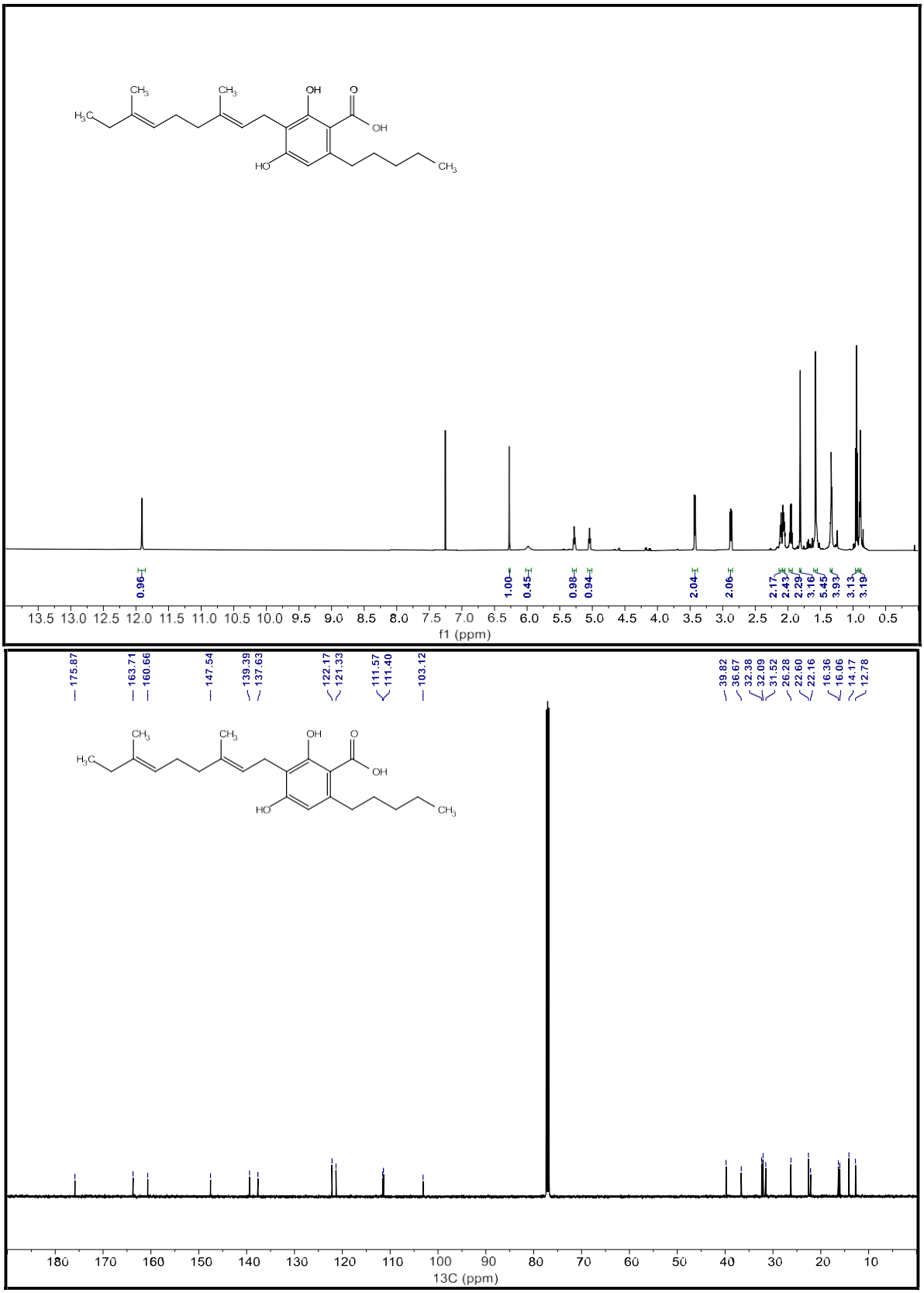


Figure S68: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2j** in $CDCl_3$

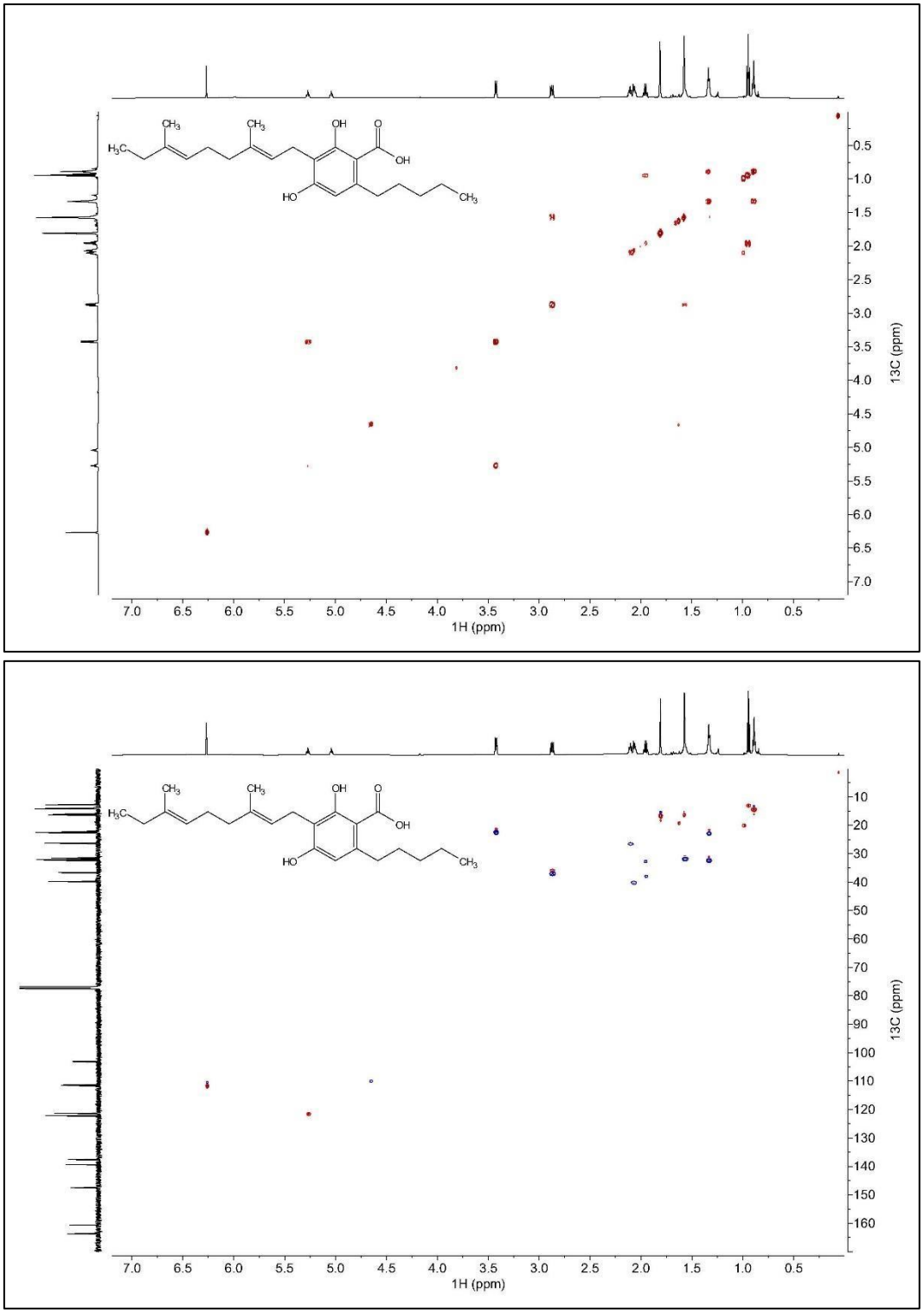


Figure S69: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2j** in $CDCl_3$

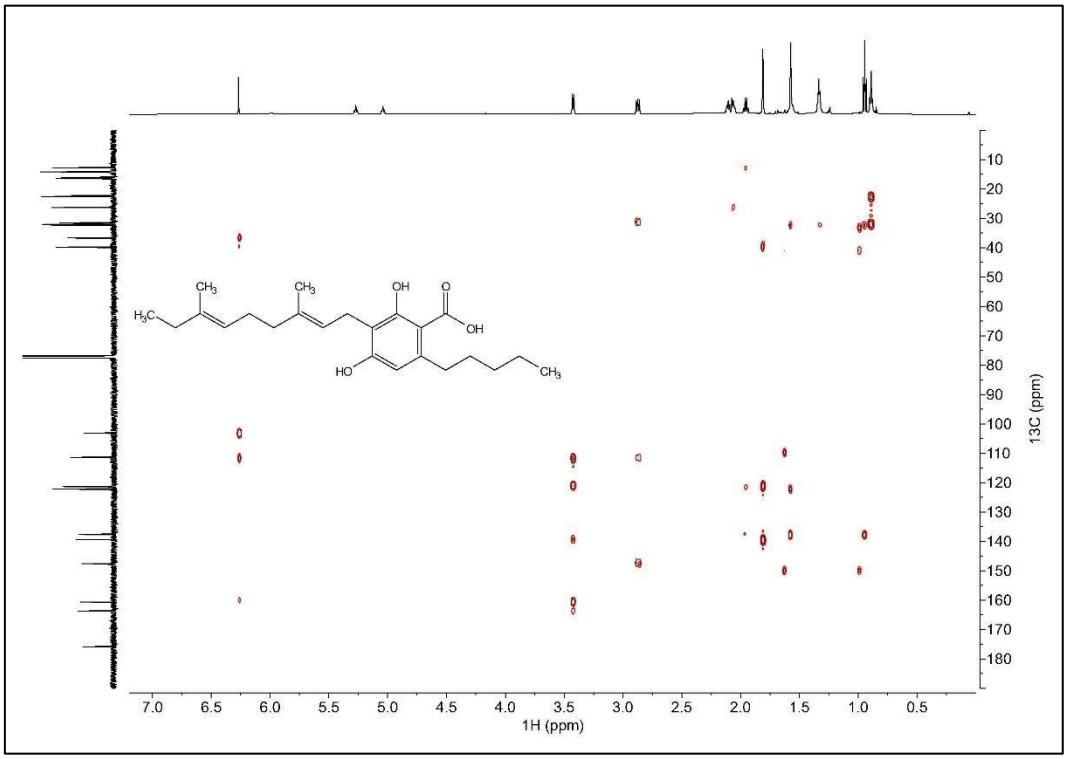


Figure S70: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2j** in $CDCl_3$

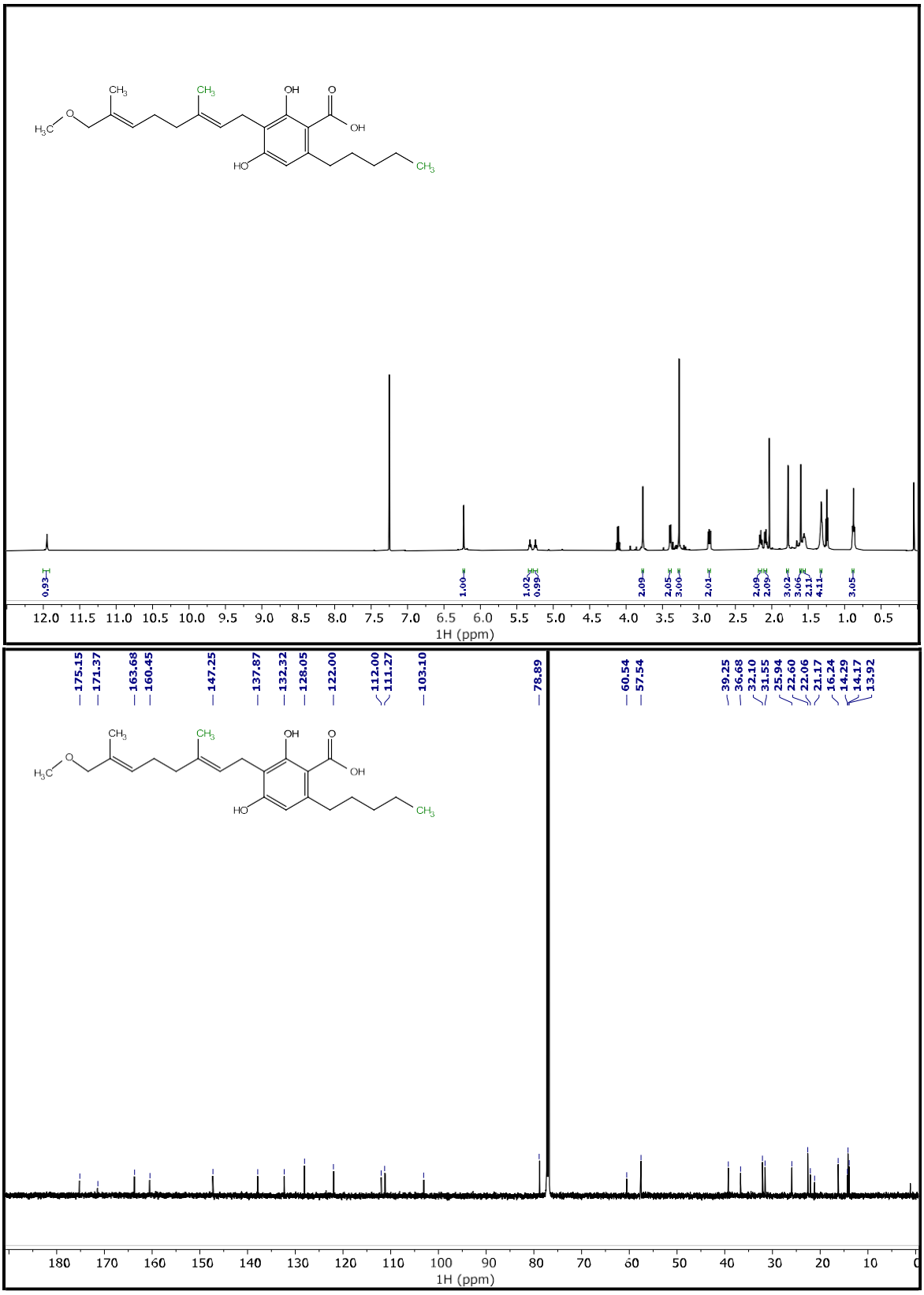


Figure S71: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2k** in $CDCl_3$

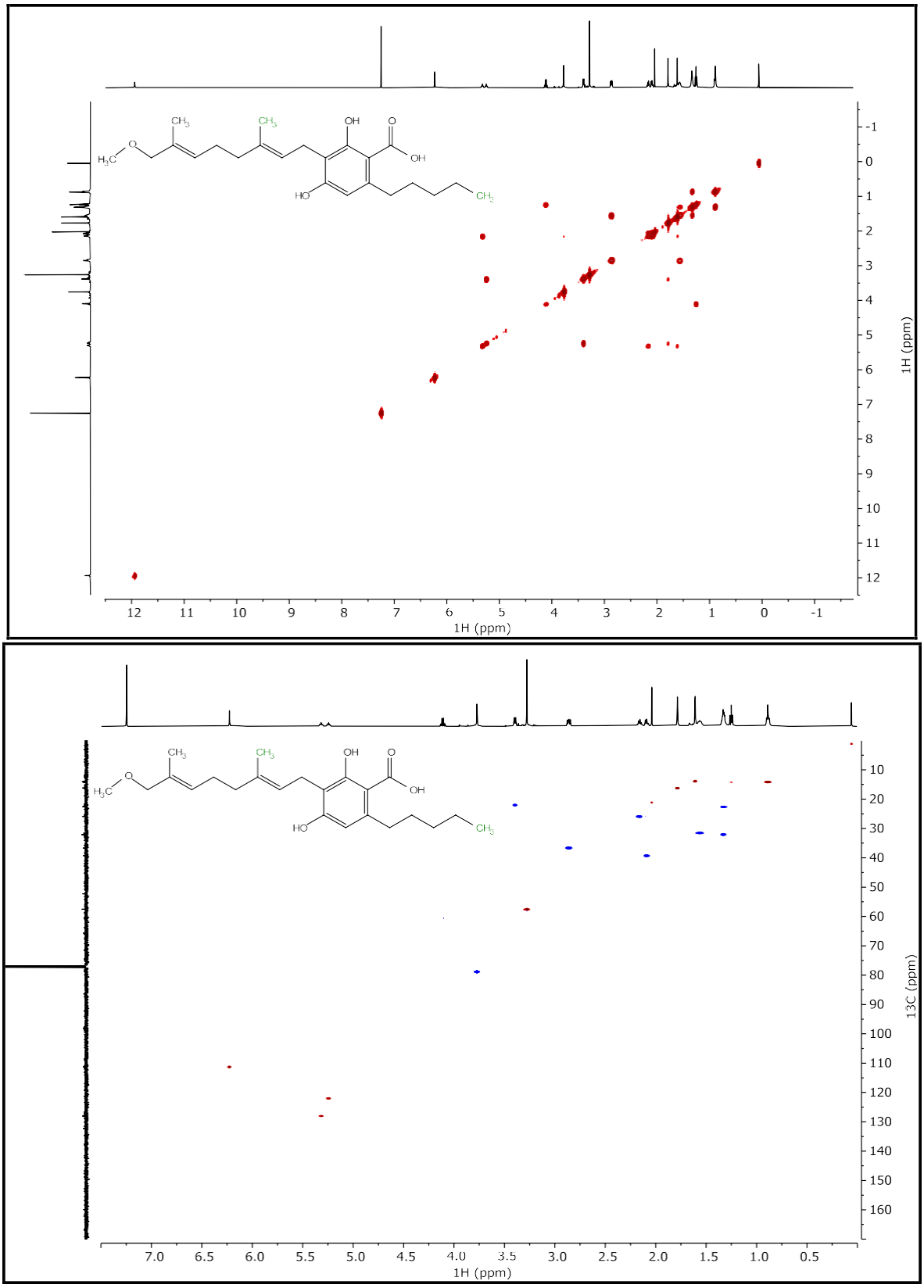


Figure S72: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2k** in $CDCl_3$

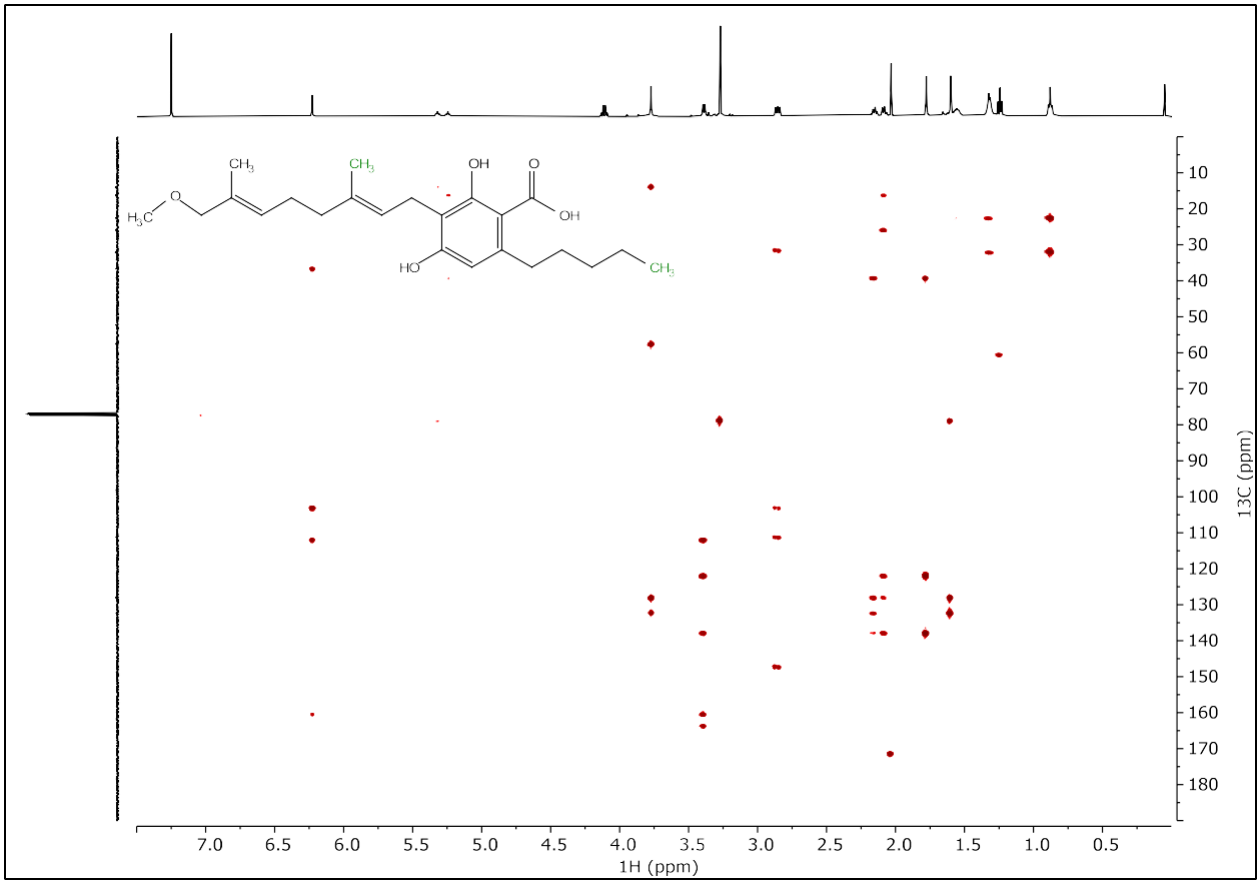


Figure S73: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2k** in $CDCl_3$

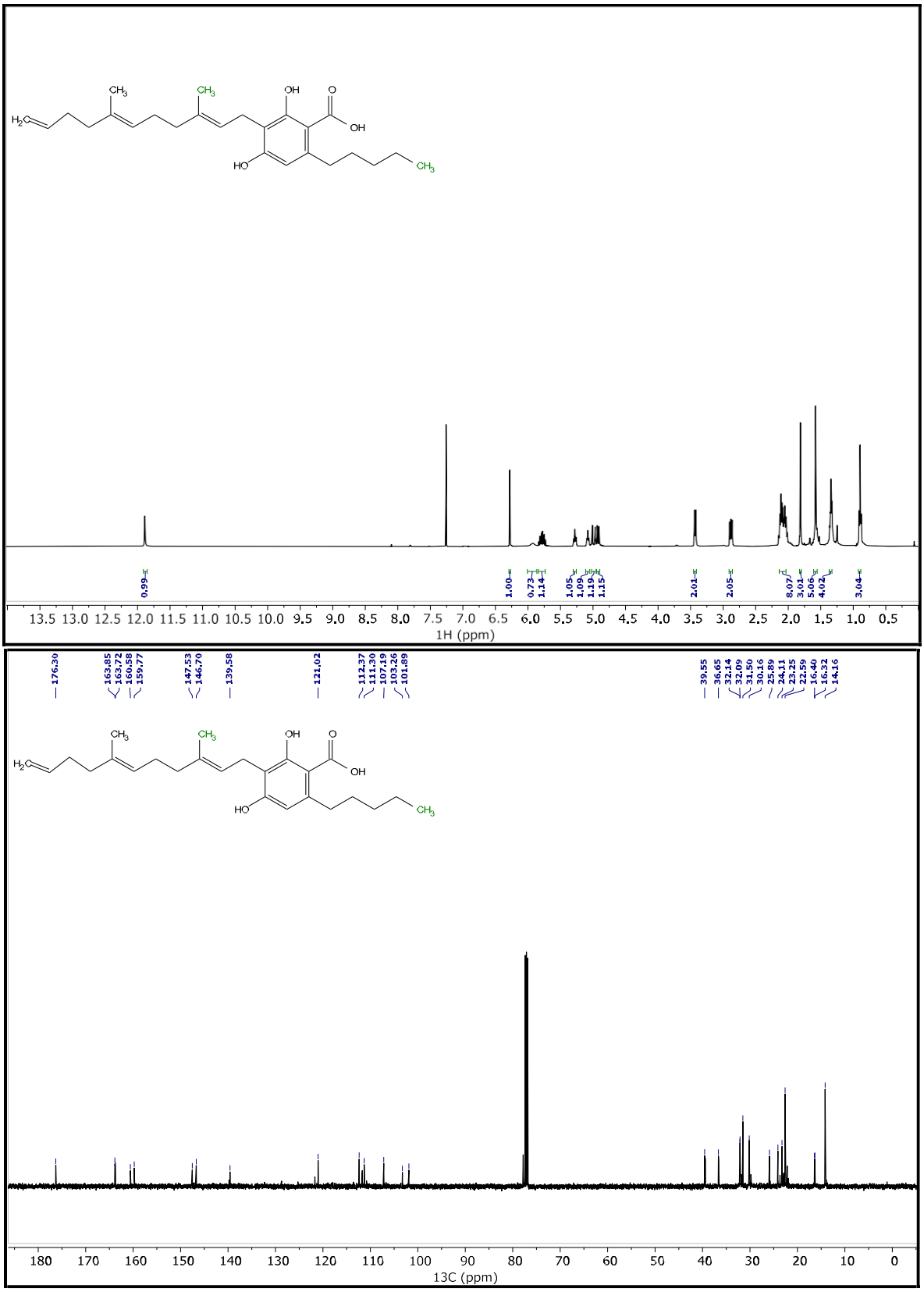


Figure S74: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2l** in $CDCl_3$

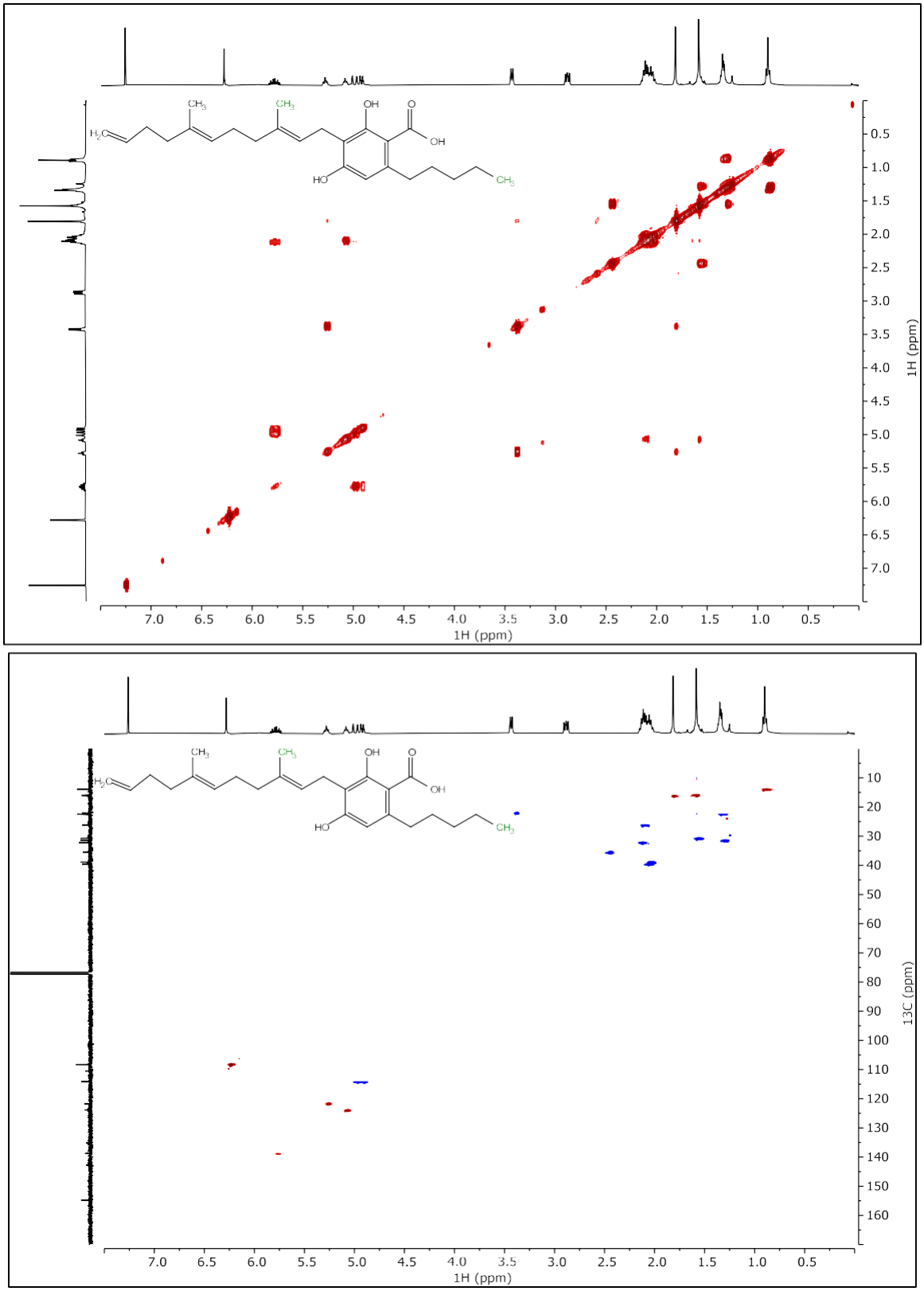


Figure S75: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2l** in $CDCl_3$

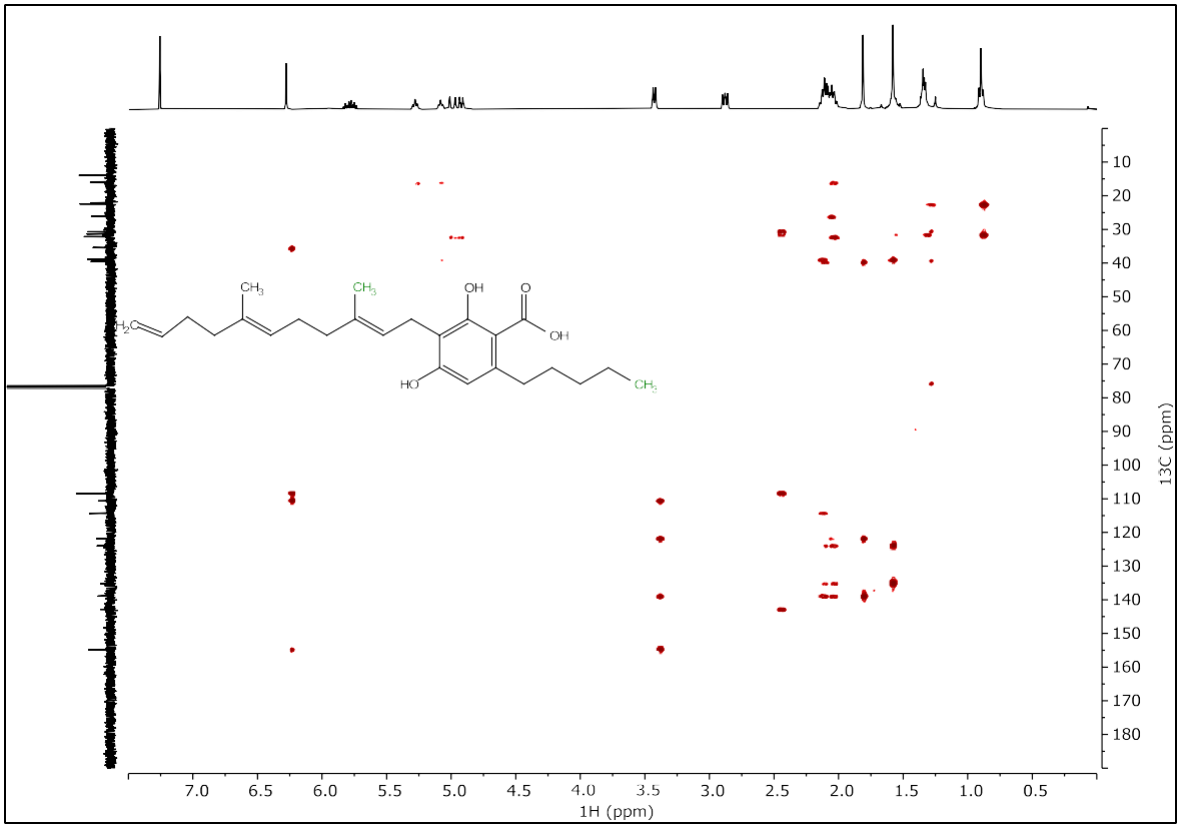


Figure S76: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2l** in $CDCl_3$

Figure S77: ^{1}H (top) and ^{13}C (bottom) NMR spectrum of **2m** in $CDCl_3$

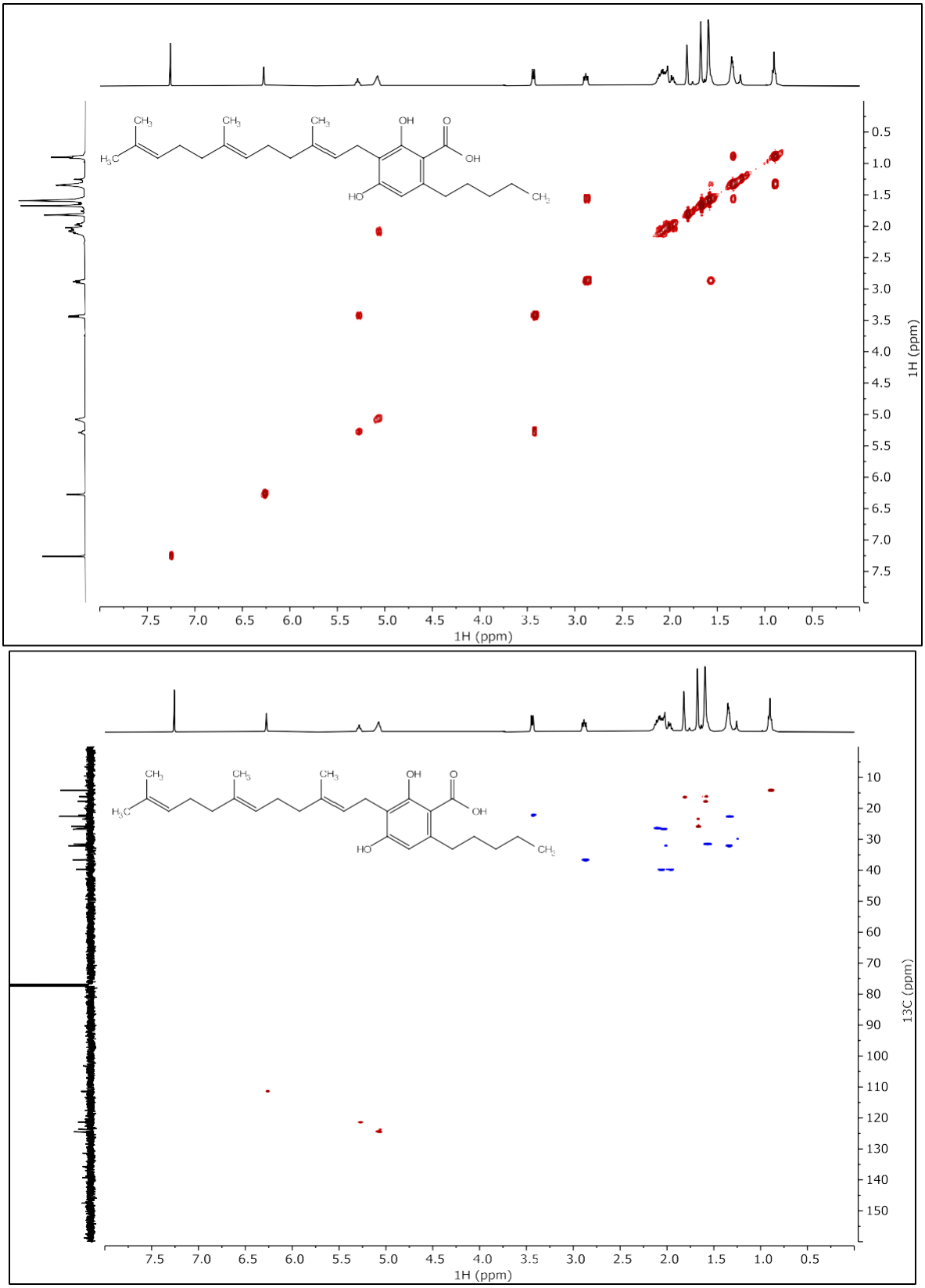


Figure S78: 2D-^{1}H-^{1}H COSY (top) and 2D-^{1}H-^{13}C HSQC (bottom) NMR spectrum of **2m** in $CDCl_3$

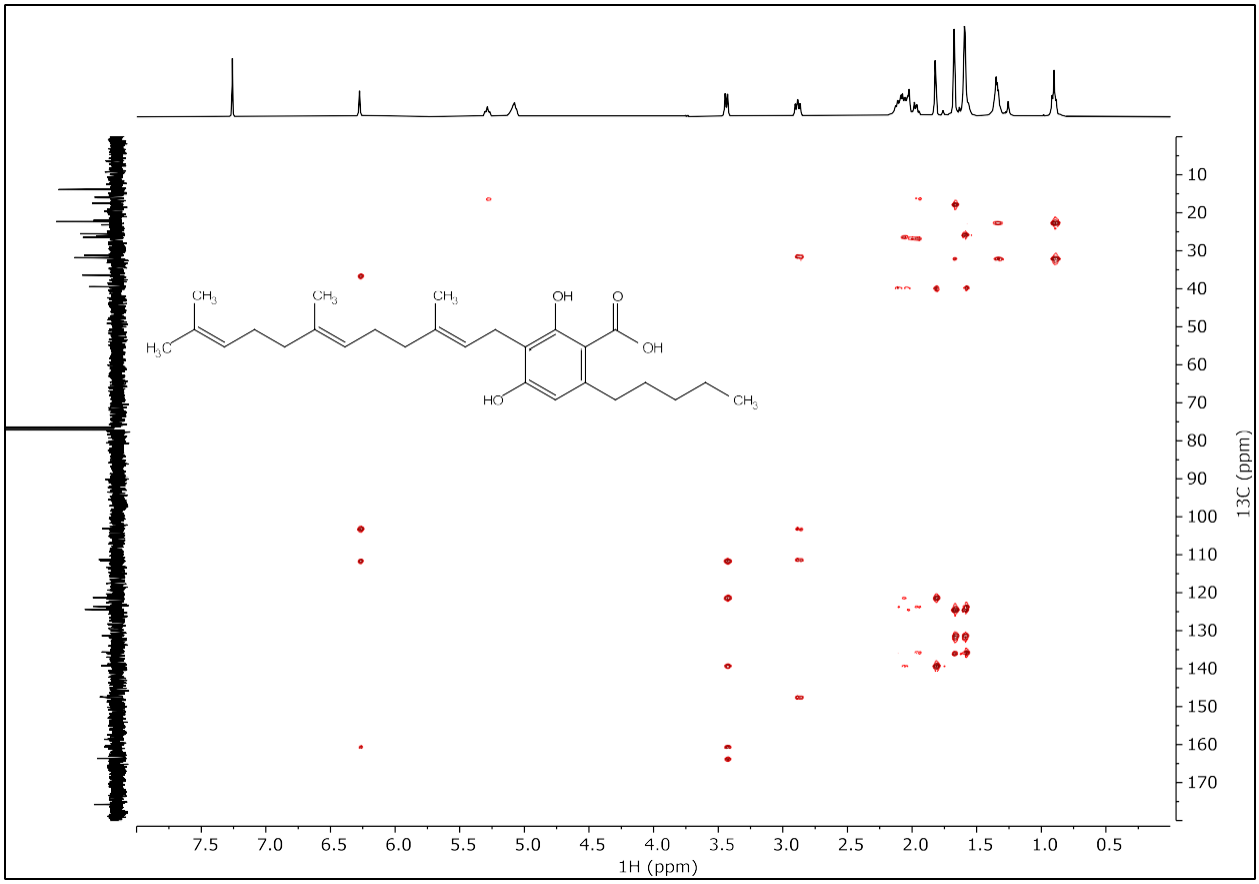
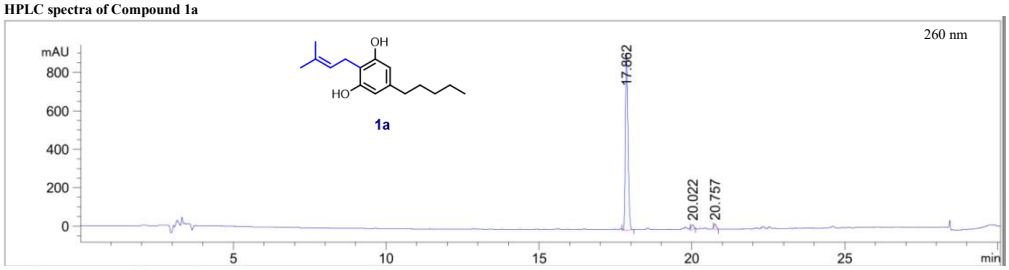


Figure S79: 2D-^{1}H-^{13}C HMBC NMR spectrum of **2m** in $CDCl_3$

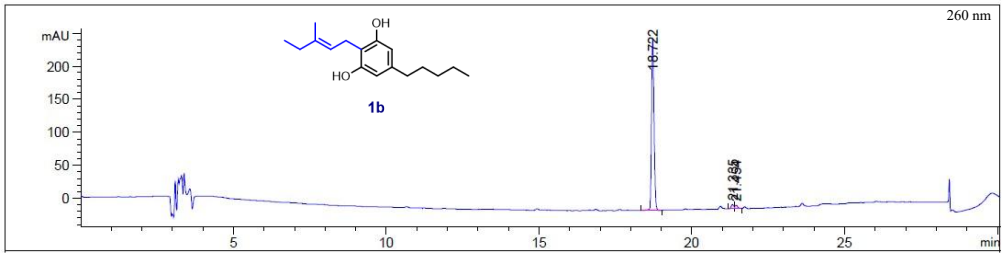
HPLC spectra of Compound 1a



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.862	MM	0.0949	5251.36719	922.71375	95.1769
2	20.022	MM	0.0946	135.09544	23.79102	2.4485
3	20.757	MM	0.0817	131.01985	26.71530	2.3746
Totals :				5517.48248	973.22006	

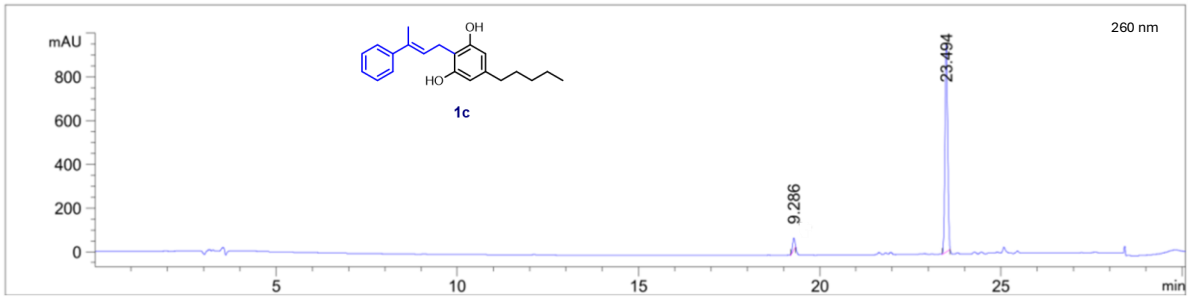
HPLC spectra of Compound 1b



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.722	BB	0.0864	1443.59717	261.60330	95.1685
2	21.335	BV	0.0857	36.51196	6.48396	2.4070
3	21.454	VV	0.0987	36.77714	5.45303	2.4245
Totals :				1516.88627	273.54030	

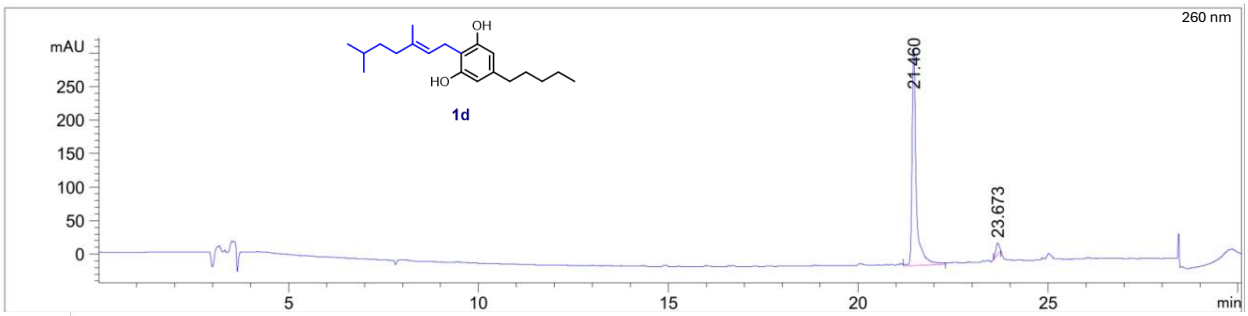
HPLC spectra of Compound 1c



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.286	MM	0.0714	245.14891	57.22861	4.8687
2	23.494	MM	0.0835	4790.04297	955.68701	95.1313
Totals :				5035.19188	1012.91563	

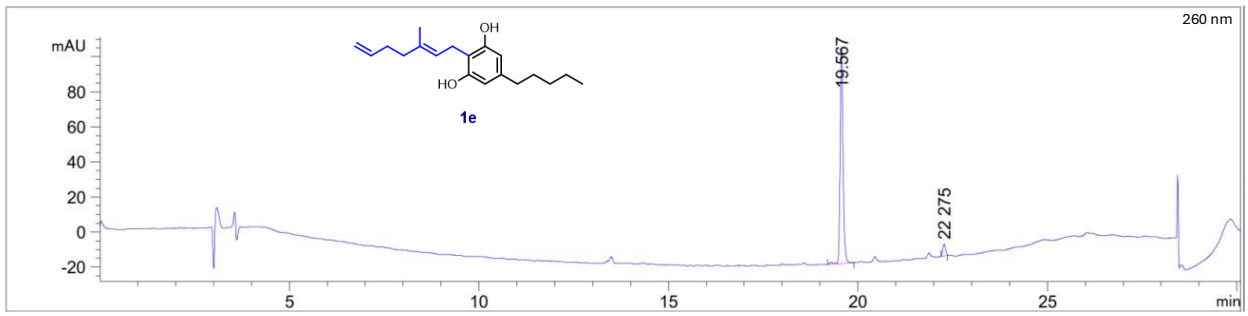
HPLC spectra of Compound 1d



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.460	MM	0.1284	2505.89990	325.35666	95.5001
2	23.673	MM	0.1081	118.07523	18.20720	4.4999
Totals :				2623.97513	343.56386	

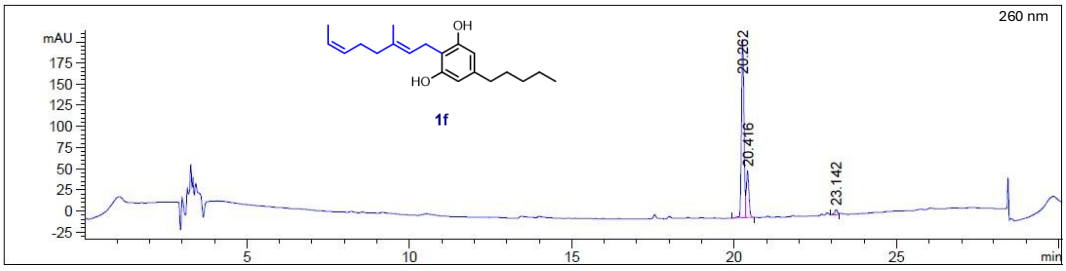
HPLC spectra of Compound 1e



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.567	VB R	0.0846	681.75574	123.14854	95.1449
2	22.275	MM	0.0865	34.78864	6.70246	4.8551
Totals :				716.54438	129.85100	

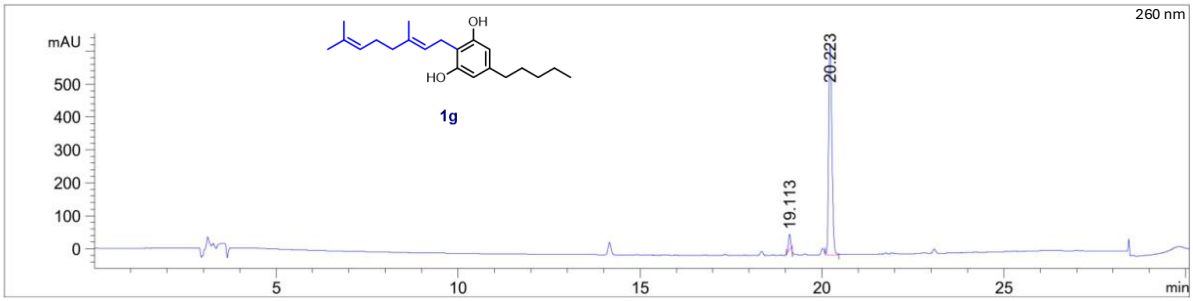
HPLC spectra of Compound 1f



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.262	VV R	0.0832	1153.41199	211.52626	77.0465
2	20.416	VB	0.0815	302.13480	55.53432	20.1822
3	23.142	VV	0.1000	41.48665	6.05014	2.7713
Totals :				1497.03343	273.11072	

E/Z=78:21
Total= 97.22%

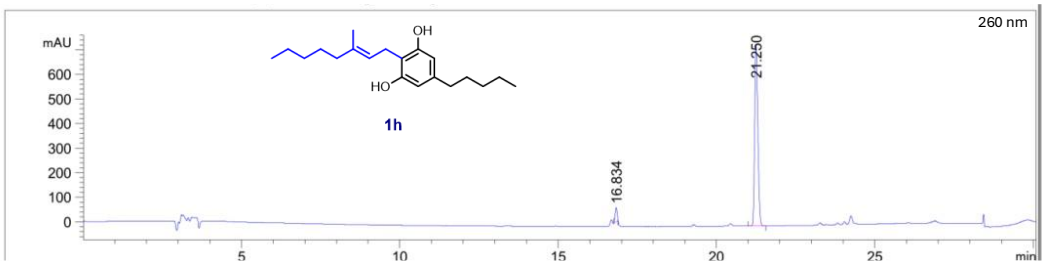
HPLC spectra of Compound 1g



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.113	MM	0.0680	192.43596	47.16096	4.6657
2	20.223	MM	0.1016	3932.02490	645.07843	95.3343
Totals :				4124.46086	692.23939	

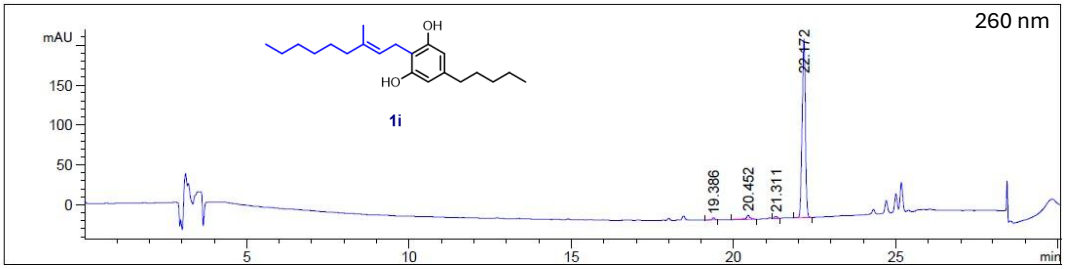
HPLC spectra of Compound 1h



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.834	MM	0.0708	243.57567	57.35545	4.4545
2	21.250	BB	0.1104	5224.48096	739.99799	95.5455
Totals :				5468.05663	797.35344	

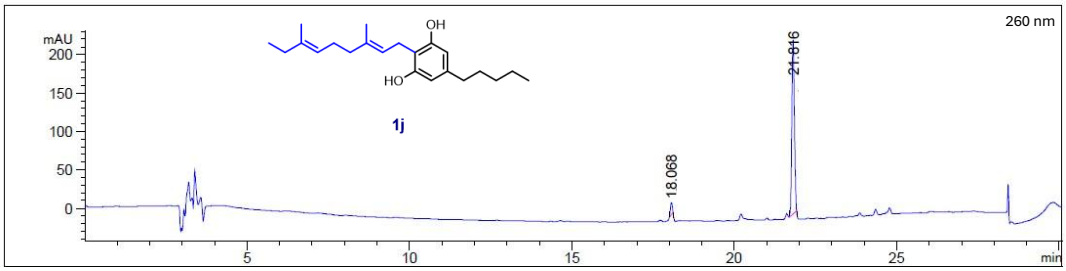
HPLC spectra of Compound 1i



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.386	BB	0.0859	15.53739	2.75059	0.9464
2	20.452	VB R	0.1290	46.17853	5.03717	2.8127
3	21.311	VB	0.1045	16.85205	2.50481	1.0264
4	22.172	BB	0.1055	1563.21826	223.82329	95.2145
Totals :				1641.78623	234.11586	

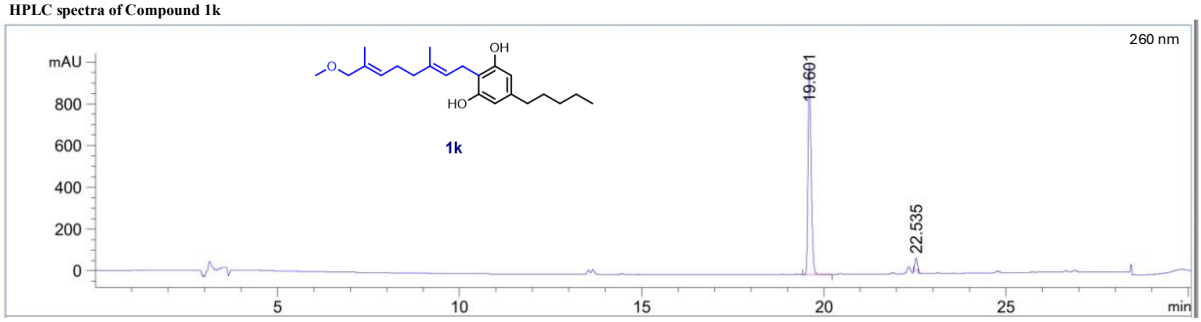
HPLC spectra of Compound 1j



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.068	MM	0.0636	61.64835	16.16594	4.8301
2	21.816	MM	0.0892	1214.69885	227.02464	95.1699
Totals :				1276.34721	243.19059	

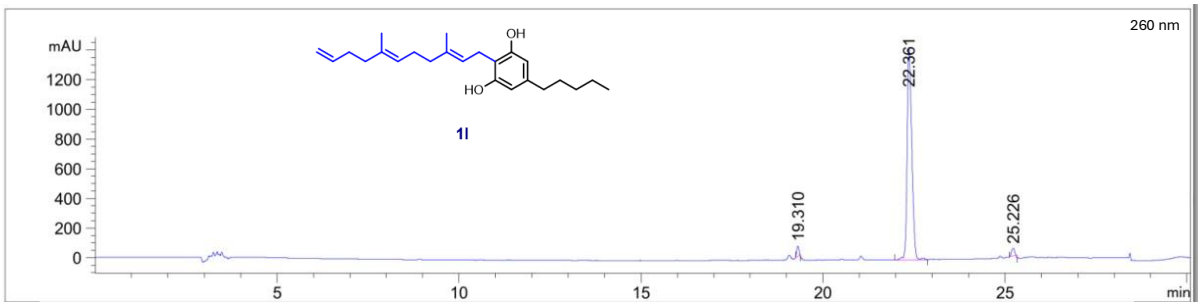
HPLC spectra of Compound 1k



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.601	BV R	0.0933	6185.83057	1010.22913	96.0622
2	22.535	MM	0.0732	253.56789	57.77071	3.9378
Totals :				6439.39845	1067.99984	

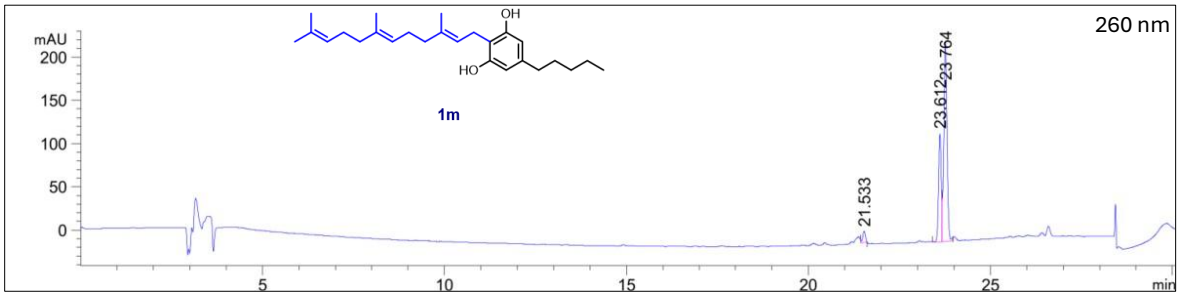
HPLC spectra of Compound 1l



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.310	MM	0.0691	282.14832	68.04646	2.1382
2	22.361	VV R	0.1337	1.26233e4	1430.58826	95.6640
3	25.226	MM	0.0921	290.00366	52.49737	2.1977
Totals :				1.31955e4	1551.13209	

HPLC spectra of Compound 1m



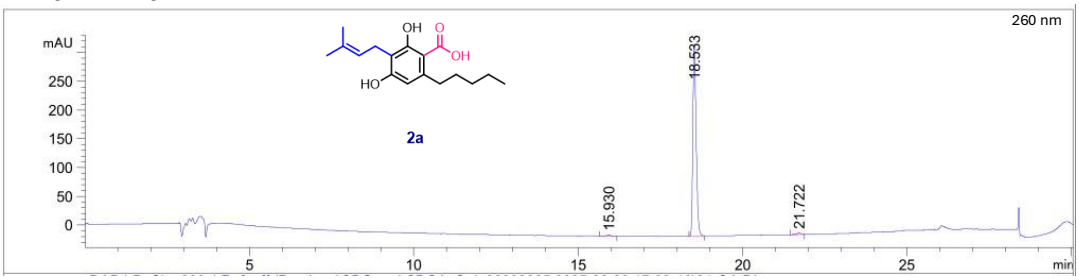

```
Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  21.533 MM    0.0863   66.25224   12.78901   3.1307
   2  23.612 MF    0.0877  659.50250  125.38855  31.1643
   3  23.764 FM    0.1000 1390.45667  231.82675  65.7050

Totals :                  2116.21141  370.00431
```

E/Z=32:67
Total=96.86%

HPLC spectra of Compound 2a

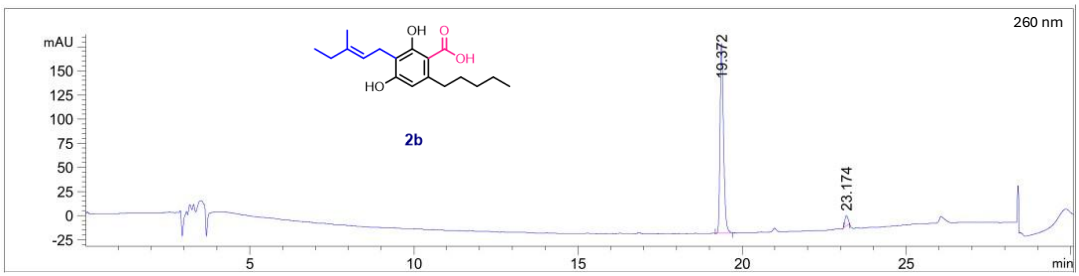



```
Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.930 BB    0.1150   18.56155    2.32852   0.8068
   2  18.533 BB    0.1031 2255.91089  332.75171  98.0591
   3  21.722 BB    0.1269   26.08908    2.95874   1.1340

Totals :                  2300.56153  338.03897
```

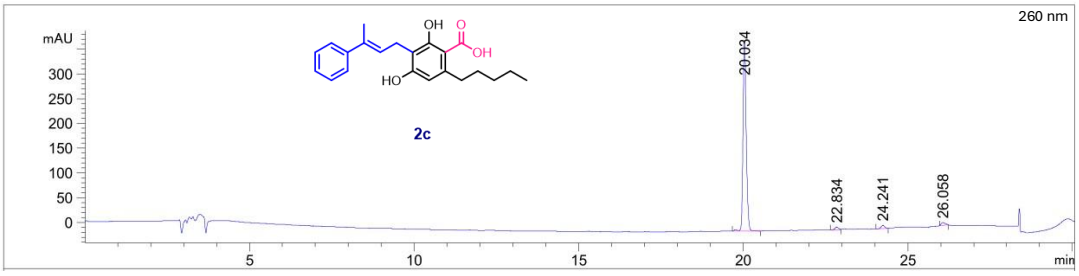
HPLC spectra of Compound 2ab



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.372	MM	0.1255	1481.38086	196.75314	95.5504
2	23.174	MM	0.1057	68.98505	10.87346	4.4496
Totals :				1550.36591	207.62660	

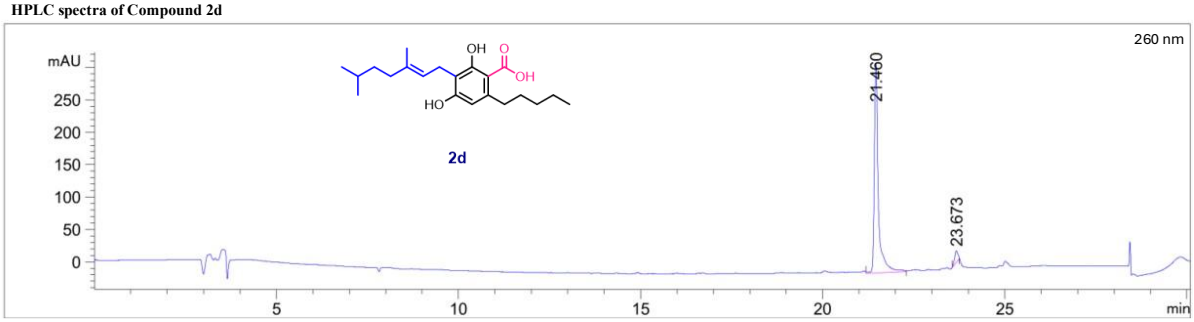
HPLC spectra of Compound 2c



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.034	VB R	0.1033	2647.22803	386.31946	95.4031
2	22.834	BV	0.1092	35.96355	5.04393	1.2961
3	24.241	BB	0.1154	46.99673	6.27367	1.6937
4	26.058	MM	0.1405	44.59488	5.29063	1.6071
Totals :				2774.78318	402.92768	

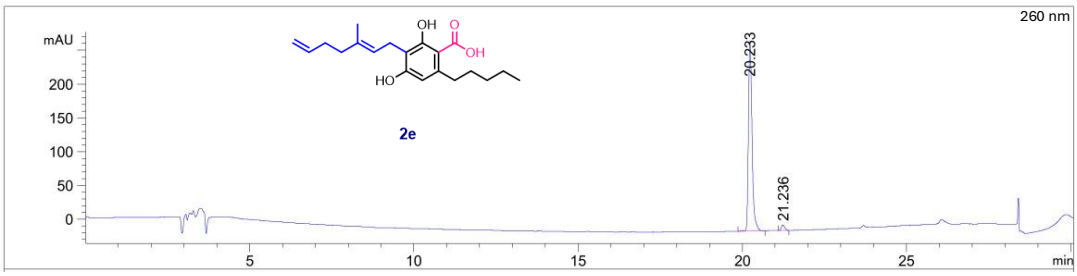
HPLC spectra of Compound 2d



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.460	MM	0.1284	2505.89990	325.35666	95.5001
2	23.673	MM	0.1081	118.07523	18.20720	4.4999
Totals :				2623.97513	343.56386	

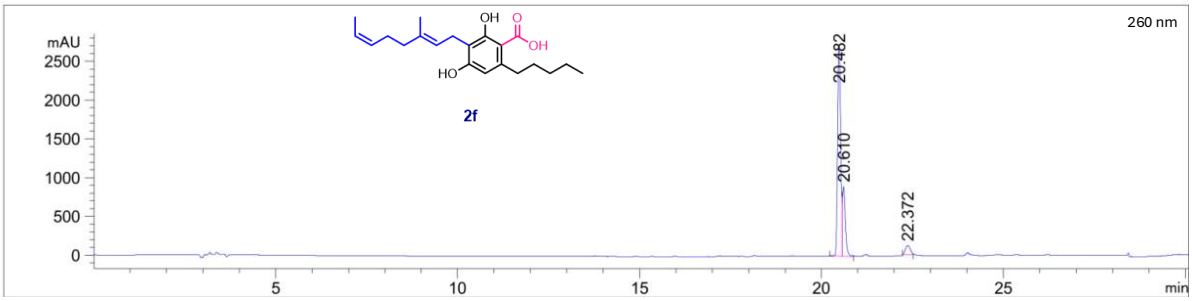
HPLC spectra of Compound 2e



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.233	VB R	0.1170	2146.05786	281.26004	97.3102
2	21.236	BB	0.1139	59.31953	8.05784	2.6898
Totals :				2205.37740	289.31788	

HPLC spectra of Compound 2f

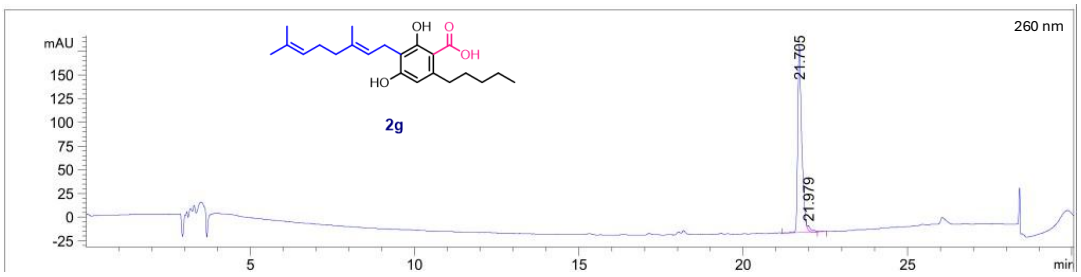


Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.482	MF	0.0982	1.61147e4	2734.88501	72.2374
2	20.610	FM	0.0943	5086.71484	899.22607	22.8022
3	22.372	MM	0.1583	1106.57849	116.50709	4.9604
Totals :				2.23080e4	3750.61817	

E/Z=75:25
Total= 95.03%

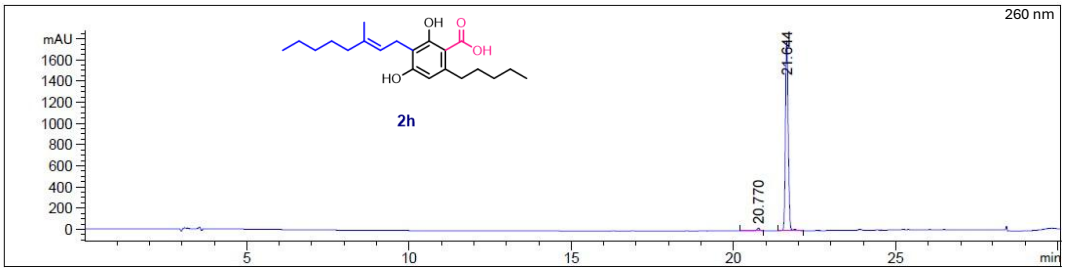
HPLC spectra of Compound 2g



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.705	BV R	0.1259	1704.55273	198.05458	97.5510
2	21.979	VV E	0.1334	42.79163	4.32610	2.4490
Totals :				1747.34436	202.38068	

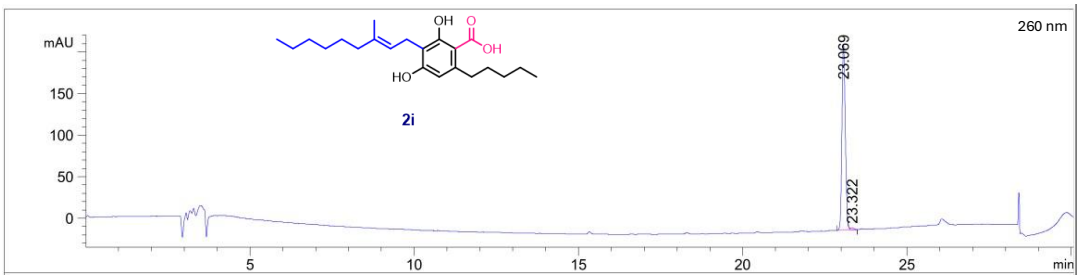
HPLC spectra of Compound 2h



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.770	VB R	0.0896	156.26451	25.20651	1.4615
2	21.644	VV R	0.0915	1.05359e4	1804.64307	98.5385
Totals :				1.06921e4	1829.84958	

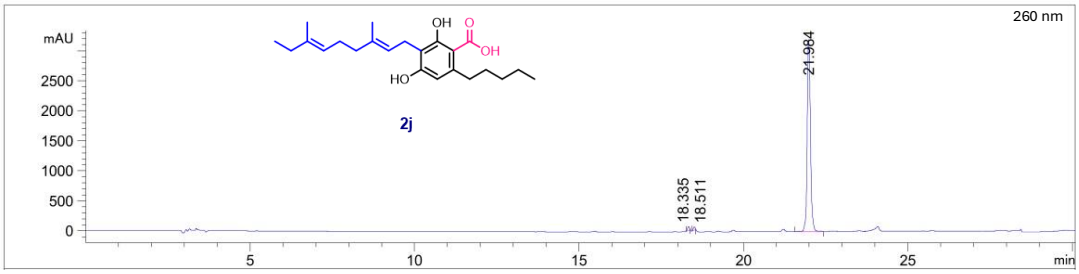
HPLC spectra of Compound 2i



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.069	BV R	0.1080	1573.39612	223.84657	98.8942
2	23.322	VB E	0.1084	17.59359	2.48977	1.1058
Totals :				1590.98970	226.33634	

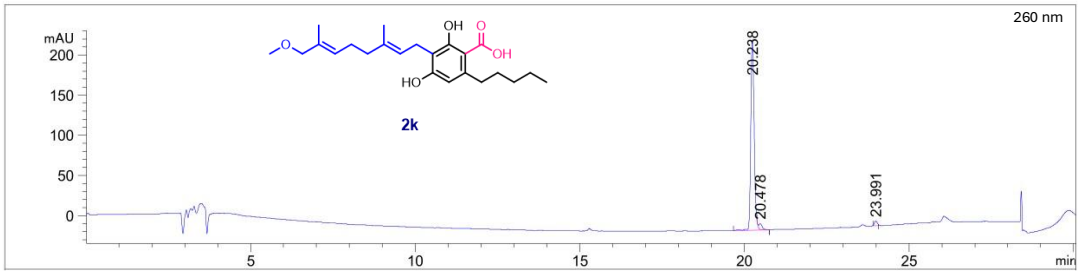
HPLC spectra of Compound 2j



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.335	MM	0.0689	282.62387	68.37981	1.2264
2	18.511	MM	0.0608	193.34044	53.00846	0.8389
3	21.984	VV R	0.1122	2.25698e4	3193.19702	97.9347
Totals :				2.30458e4	3314.58529	

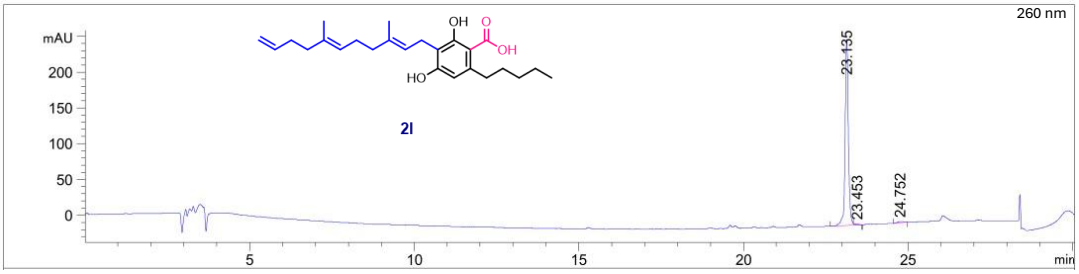
HPLC spectra of Compound 2k



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.238	VV R	0.1090	1683.37708	236.70670	95.2878
2	20.478	VB E	0.1041	50.02013	7.10789	2.8314
3	23.991	MM	0.0995	33.22723	5.56645	1.8808
Totals :				1766.62444	249.38104	

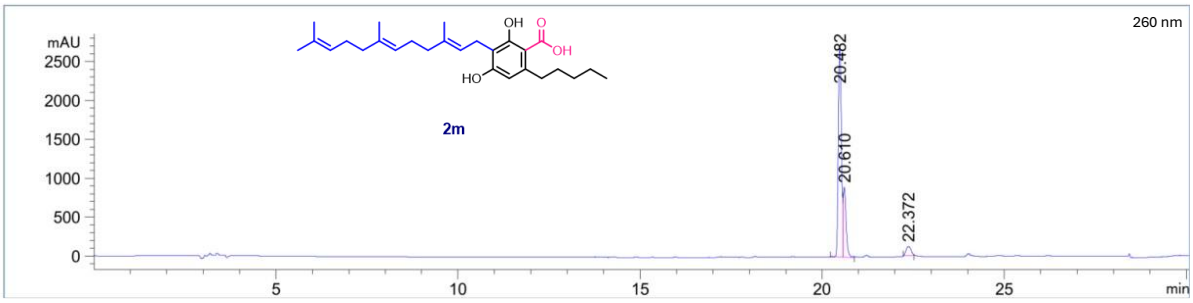
HPLC spectra of Compound 2l



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.135	BV R	0.1052	1806.36145	259.57413	98.3217
2	23.453	VB E	0.1035	9.13491	1.37569	0.4972
3	24.752	BB	0.1513	21.69838	1.98849	1.1811
Totals :				1837.19474	262.93831	

HPLC spectra of Compound 2k



Signal 1: DAD1 A, Sig=260,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.482	MF	0.0982	1.61147e4	2734.88501	72.2374
2	20.610	FM	0.0943	5086.71484	899.22607	22.8022
3	22.372	MM	0.1583	1106.57849	116.50709	4.9604
Totals :				2.23080e4	3750.61817	

E/Z=74:26
Total= 95.04%

Table S1. Table of MICs (μg/mL) for CBG and CBGA analogs performed in biological triplicate (n=3). The > sign indicates that the cells survived at the given maximum concentration.

Compound		*B. subtilis* (ATCC 6051)	*S. epidermidis* (ATCC 12228)	*S. aureus* (ATCC 25923)	*S. aureus*, MRSA (ATCC 700787)	*E. faecalis*, VRE (ATCC 700802)
	Rep1	1.0	0.2	0.5	1.0	1.0
	Rep2	1.0	0.2	0.5	0.5	2.0
Daptomycin	Rep3	1.0	0.5	0.5	0.5	2.0
	Rep1	>21.6	>21.6	>21.6	>21.6	>21.6
	Rep2	>21.6	>21.6	>21.6	>21.6	>21.6
Olivetol	Rep3	>21.6	>21.6	>21.6	>21.6	>21.6
	Rep1	>21.6	>21.6	>21.6	>21.6	>21.6
	Rep2	>21.6	>21.6	>21.6	>21.6	>21.6
Olivetolic acid	Rep3	>21.6	>21.6	>21.6	>21.6	>21.6
	Rep1	1.0	1.0	1.0	2.0	2.0
	Rep2	1.0	2.0	2.0	2.0	2.0
CBG (1g)	Rep3	2.0	2.0	2.0	2.0	4.0
	Rep1	4.6	4.6	4.6	4.6	8.0
	Rep2	2.3	2.3	4.6	4.6	8.0
CBGA (2g)	Rep3	2.3	2.3	4.6	4.6	8.0
	Rep1	3.3	3.3	1.7	1.7	6.6
	Rep2	3.3	6.6	3.3	3.3	6.6
1b	Rep3	6.6	3.3	3.3	3.3	13.2
	Rep1	6.7	6.7	13.4	13.4	>13.4
	Rep2	6.7	6.7	6.7	6.7	13.4
2b	Rep3	6.7	6.7	6.7	6.7	6.7
	Rep1	3.9	2.0	1.0	2.0	3.9
	Rep2	2.0	2.0	2.0	2.0	3.9
1c	Rep3	2.0	3.9	2.0	2.0	7.8
	Rep1	15.7	9.0	4.5	9.0	>15.7
	Rep2	7.9	4.5	4.5	4.5	15.7
2c	Rep3	7.9	4.5	4.5	4.5	7.9
	Rep1	3.8	3.8	3.8	3.8	3.8
	Rep2	3.8	3.8	3.8	3.8	3.8
1d	Rep3	3.9	7.7	7.7	3.9	7.7
	Rep1	>17.6	>17.6	>17.6	>17.6	>17.6
	Rep2	>17.6	>17.6	>17.6	>17.6	>17.6
2d	Rep3	>17.6	>17.6	>17.6	>17.6	>17.6
	Rep1	1.8	1.8	1.8	1.8	1.8
	Rep2	3.6	1.8	1.8	1.8	3.6
1e	Rep3	3.7	3.7	3.7	3.7	3.7
	Rep1	2.8	5.7	4.2	2.1	8.4
2e	Rep2	5.7	2.8	4.2	4.2	8.4

	Rep3	2.8	2.8	4.2	4.2	8.4
	Rep1	3.8	3.8	3.8	3.8	7.7
	Rep2	3.8	3.8	3.8	3.8	7.7
1f	Rep3	3.8	3.8	3.8	3.8	7.7
	Rep1	7.7	7.7	7.7	15.5	15.5
	Rep2	7.7	7.7	7.7	15.5	15.5
2f	Rep3	7.7	7.7	7.7	15.5	15.5
	Rep1	1.9	1.0	1.0	1.0	1.9
	Rep2	1.0	1.0	1.9	1.0	1.9
1h	Rep3	1.9	1.9	1.9	1.0	1.9
	Rep1	3.9	3.9	7.7	7.7	7.7
	Rep2	3.9	7.7	7.7	7.7	7.7
2h	Rep3	3.9	3.9	7.7	7.7	7.7
	Rep1	2.0	2.0	2.0	2.0	4.0
	Rep2	2.0	2.0	2.0	2.0	4.0
1i	Rep3	2.0	2.0	2.0	2.0	4.0
	Rep1	4.6	4.6	8.0	8.0	9.2
	Rep2	2.3	2.3	8.0	8.0	4.6
2i	Rep3	2.3	2.3	8.0	8.0	4.6
	Rep1	1.0	2.1	2.1	2.1	4.2
	Rep2	1.0	2.1	2.1	2.1	4.2
1j	Rep3	1.0	2.1	2.1	2.1	4.2
	Rep1	4.2	4.2	8.4	16.7	8.4
	Rep2	4.2	4.2	8.4	16.7	8.4
2j	Rep3	4.2	4.2	8.4	16.7	16.7
	Rep1	8.8	4.4	4.4	4.4	>17.5
	Rep2	4.4	4.4	4.4	8.8	>17.5
1k	Rep3	4.4	4.4	4.4	8.8	>17.5
	Rep1	19.7	19.7	9.9	9.9	>19.7
	Rep2	9.9	9.9	9.9	9.9	>19.7
2k	Rep3	9.9	9.9	9.9	9.9	>19.7
	Rep1	1.1	1.1	1.1	2.3	1.1
	Rep2	1.1	1.1	2.3	2.3	1.1
1l	Rep3	2.3	2.3	1.1	2.3	2.3
	Rep1	5.1	2.5	5.1	5.1	5.1
	Rep2	2.5	2.5	10.1	5.1	5.1
2l	Rep3	2.5	2.5	5.1	5.1	5.1
	Rep1	>19.4	2.4	9.7	>19.4	9.7
	Rep2	>19.4	1.2	9.7	>19.4	4.9
1m	Rep3	>19.4	2.7	9.7	>19.4	4.9
	Rep1	3.2	3.2	6.4	6.4	6.4
	Rep2	3.2	3.2	6.4	6.4	6.4
2m	Rep3	3.2	3.2	6.4	6.4	12.8

Table S2. Table of MBCs (μg/mL) for CBG and CBGA analogs performed in biological triplicate (n=3). The > sign indicates that the compounds did not cause a 3 log reduction in cell viability.

Compound		*B. subtilis* (ATCC 6051)	*S. epidermidis* (ATCC 12228)	*S. aureus* (ATCC 25923)	*S. aureus*, MRSA (ATCC 700787)	*E. faecalis*, VRE (ATCC 700802)
	Rep1	1.0	1.0	1.0	1.0	1.0
	Rep2	1.0	1.0	1.0	1.0	1.0
Daptomycin	Rep3	1.0	1.0	1.0	1.0	1.0
	Rep1	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep2	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
Olivetol	Rep3	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep1	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep2	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
Olivetolic acid	Rep3	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep1	4.0	> 4.0	4.0	8.0	> 8.0
	Rep2	4.0	> 4.0	4.0	4.0	> 8.0
CBG (1g)	Rep3	4.0	> 4.0	4.0	8.0	> 8.0
	Rep1	9.2	> 9.2	18.4	> 18.4	32.0
	Rep2	9.2	9.2	> 18.4	> 18.4	32.0
CBGA (2g)	Rep3	9.2	9.2	> 18.4	> 18.4	8.0
	Rep1	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep2	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
1a	Rep3	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep1	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep2	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
2a	Rep3	> 86.4	> 86.4	> 86.4	> 86.4	> 86.4
	Rep1	13.2	> 13.2	6.8	> 6.8	13.2
	Rep2	13.2	13.2	6.8	> 6.8	26.4
1b	Rep3	6.6	13.2	> 6.8	> 6.8	13.2
	Rep1	13.4	> 26.8	26.8	> 26.8	> 26.8
	Rep2	13.4	26.8	> 26.8	> 26.8	> 26.8
2b	Rep3	13.4	26.8	> 26.8	> 26.8	> 26.8
	Rep1	> 8.0	> 8.0	8.0	> 8.0	15.6
	Rep2	> 8.0	> 8.0	8.0	> 8.0	15.6
1c	Rep3	> 8.0	8.0	8.0	8.0	7.8
	Rep1	7.9	> 18.0	18.0	> 18.0	> 31.6
	Rep2	15.8	18.0	> 18.0	> 18.0	> 31.6
2c	Rep3	15.8	18.0	> 18.0	> 18.0	31.6

	Rep1	15.2	> 15.2	7.6	15.2	> 15.2
	Rep2	15.2	> 15.2	7.6	15.2	> 15.2
1d	Rep3	7.6	15.2	7.6	15.2	> 15.2
	Rep1	35.2	> 70.4	70.4	> 70.4	70.4
	Rep2	35.2	70.4	> 70.4	> 70.4	> 70.4
2d	Rep3	35.2	70.4	> 70.4	> 70.4	70.4
	Rep1	> 7.2	> 7.2	7.2	7.2	> 7.2
	Rep2	> 7.2	7.2	7.2	7.2	> 7.2
1e	Rep3	> 7.2	7.2	7.2	7.2	> 7.2
	Rep1	11.2	> 11.2	> 16.8	> 16.8	32.0
	Rep2	11.2	> 11.2	16.8	> 16.8	> 32.0
2e	Rep3	11.2	> 11.2	16.8	> 16.8	> 32.0
	Rep1	7.6	3.8	3.8	3.8	7.6
	Rep2	15.2	3.8	3.8	3.8	7.6
1f	Rep3	> 15.2	15.2	3.8	3.8	7.6
	Rep1	7.7	7.7	7.7	15.4	30.8
	Rep2	7.7	15.4	7.7	15.4	30.8
2f	Rep3	7.7	7.7	15.4	15.4	30.8
	Rep1	4.0	> 4.0	2.0	4.0	> 7.6
	Rep2	> 4.0	> 4.0	4.0	4.0	> 7.6
1h	Rep3	> 4.0	> 4.0	2.0	2.0	> 7.6
	Rep1	7.8	15.6	> 30.8	30.8	7.7
	Rep2	7.8	7.8	30.8	> 30.8	30.8
2h	Rep3	15.6	3.9	30.8	> 30.8	30.8
	Rep1	8.0	> 8.0	4.0	8.0	> 16.0
	Rep2	8.0	4.0	8.0	8.0	> 16.0
1i	Rep3	8.0	> 8.0	4.0	8.0	> 16.0
	Rep1	2.3	9.2	16.0	32.0	4.6
	Rep2	2.3	4.6	32.0	> 32.0	18.4
2i	Rep3	9.2	4.6	16.0	> 32.0	4.6
	Rep1	4.0	2.0	8.0	2.0	4.1
	Rep2	4.0	2.0	> 8.0	2.0	4.1
1j	Rep3	4.0	2.0	8.0	2.0	4.1
	Rep1	4.1	4.1	16.6	16.7	8.3
	Rep2	4.1	4.1	8.3	16.7	8.3
2j	Rep3	4.1	4.1	8.3	16.7	8.3
	Rep1	17.6	17.6	4.4	8.8	70.0
	Rep2	17.6	8.8	4.4	17.6	> 70.0
1k	Rep3	17.6	8.8	4.4	> 17.6	17.5
	Rep1	9.9	> 39.6	39.6	> 39.6	19.7
	Rep2	9.9	39.6	> 39.6	> 39.6	78.8
2k	Rep3	39.6	39.6	> 39.6	> 39.6	78.8

	Rep1	4.4	> 4.4	4.6	9.2	> 4.4
	Rep2	4.4	> 4.4	9.2	9.2	> 4.4
1l	Rep3	4.4	> 4.4	9.2	9.2	> 4.4
	Rep1	5.0	5.0	10.2	10.2	5.1
	Rep2	2.5	2.5	10.2	20.4	5.1
2l	Rep3	5.0	2.5	10.2	20.4	5.1
	Rep1	38.8	> 4.8	> 25.6	> 77.6	> 19.6
	Rep2	38.8	> 4.8	> 25.6	> 77.6	> 19.6
1m	Rep3	77.6	> 4.8	> 25.6	> 77.6	> 19.6
	Rep1	3.2	6.4	> 25.6	25.6	12.8
	Rep2	3.2	3.2	> 25.6	> 25.6	6.4
2m	Rep3	3.2	3.2	25.6	> 25.6	6.4

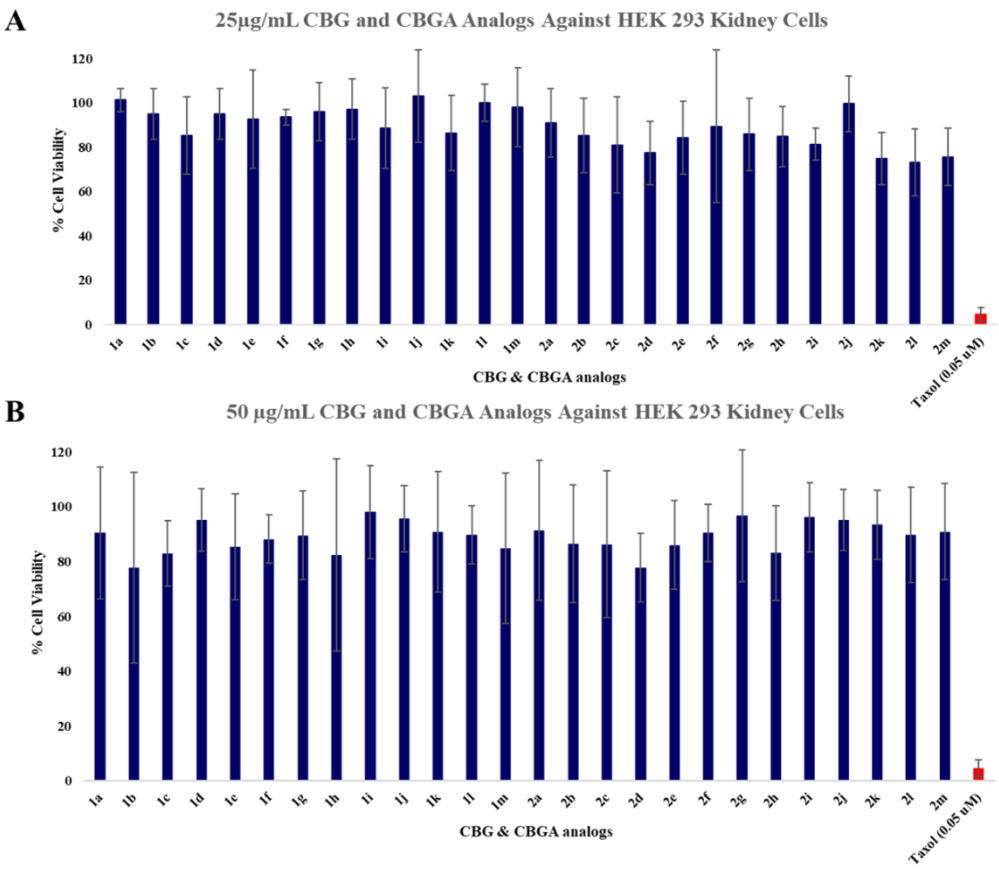


Figure S80. Cytotoxicity of the synthetic compounds CBG and CBGA analogs in HEK293 kidney cells at 25 μg/mL (A) and 50 μg/mL (B). Data are presented as the mean ± from biological triplicate.