Supporting Information

Investigation of Premyrsinane and Myrsinane Esters in *Euphorbia cupanii* and *Euphobia pithyusa* with *MS2LDA* and Combinatorial Molecular Network Annotation Propagation

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Authors contribution

M.N.-E. and L.-F.N. contributed equally to the manuscript. M.N.-E. and L.-F.N., F.R., J.P., P.D. and M.L. designed the research and wrote the manuscript. D.T. performed the mass spectrometry analysis. M.N.-E. and L.-F.N. analyzed the mass spectrometry data and interpreted the MS2LDA analysis. M.N.-E. performed the isolation and the identification of the compounds. P.R. performed the X-ray diffraction analysis of the crystals. L.-F.N., M.N.-E. and R.R.S. conceived and evaluated the combinatorial network annotation propagation.

Table S1. Botanical characteristic comparison between *Euphorbia pithyusa* and *Euphorbia cupanii*.

species	*Euphorbia pithyusa*	*Euphorbia cupanii*
biological type	chamephyte: initial ramification begins at a certain height from the ground, so that the plant assumes the appearance of a very branched bush	rhizomatous geophyte: simple upright branches, originating from the base, all originating from a bush with several stems
growth areas	sandy and rocky areas of the Mediterranean coast at low altitudes	upright shrub, uncultivated areas such as road borders, and the banks of river at various altitude
repartition	Steno-Mediterranean	Corso-Sardinia-Sicily
height	10 to 130 cm	Until 1 m
leaves	clamped on very branched stems, branches bearing groups of sterile branches leaves of the lower part of the stem are linear or lanceolate, glaucous, somewhat coriaceous, acute and with raised margins, while the upper leaves are larger and less dense	the rhizome of this species emits many branching ascending, glaucous, simple and devoid of leaves underneath leaves are of equal size, linear-lanceolate, increasing and arched in a vegetative period reflected during the flowering
cyathium	May to September umbel with 5 to 7 bifid rays	June to October Umbel with 5 to 10 bifid rays
glands	Yellow, crescent and shaped	Large, semi-lunar, yellow, lateral horns with a rounded apex
capsules	greenish and smooth	globose, ovoid, deeply furrowed and finely striated
seeds	dark and oval with small dimples	ovoid, finely alveolate with whitish areas superimposed on dark areas
number of chromosomes	2n = 28	2n = 36

Figure S2. *Euphorbia pithyusa* and *Euphorbia cupanii* herbaria.

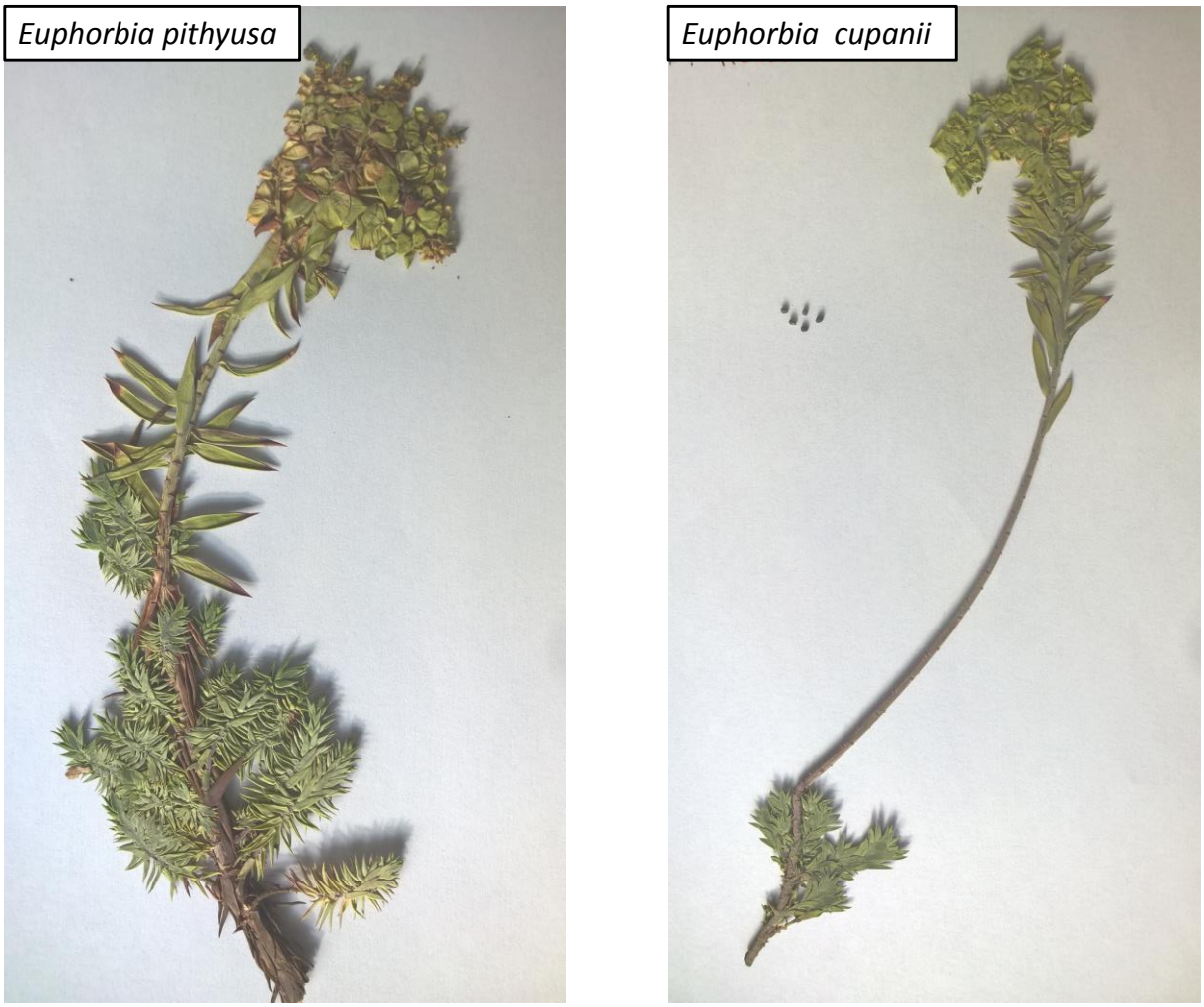


Figure S3. Annotated clusters of the molecular networks from *E. pithyusa* (in blue) and *E. cupanii* (in red) extracts. Cluster annotation as A/ triterpene, B/ diterpene esters and C/ tigliane.

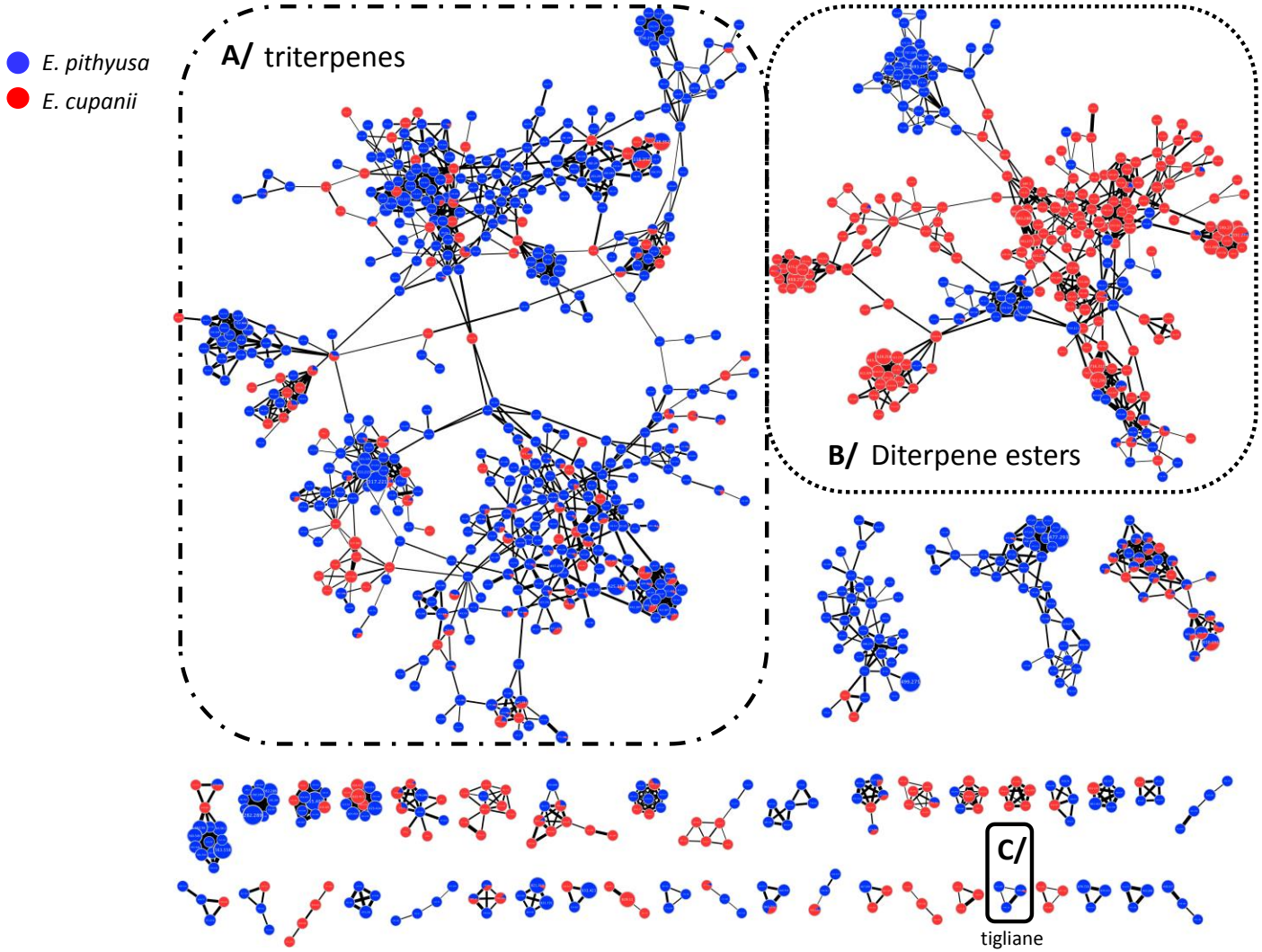


Figure S4. Venn's diagrams for *E. pithyusa* and *E. cupanii* molecular networks. A. Considering all MS/MS spectra. B. Considering only MS/MS spectra from networks and clusters annotated as diterpene esters.

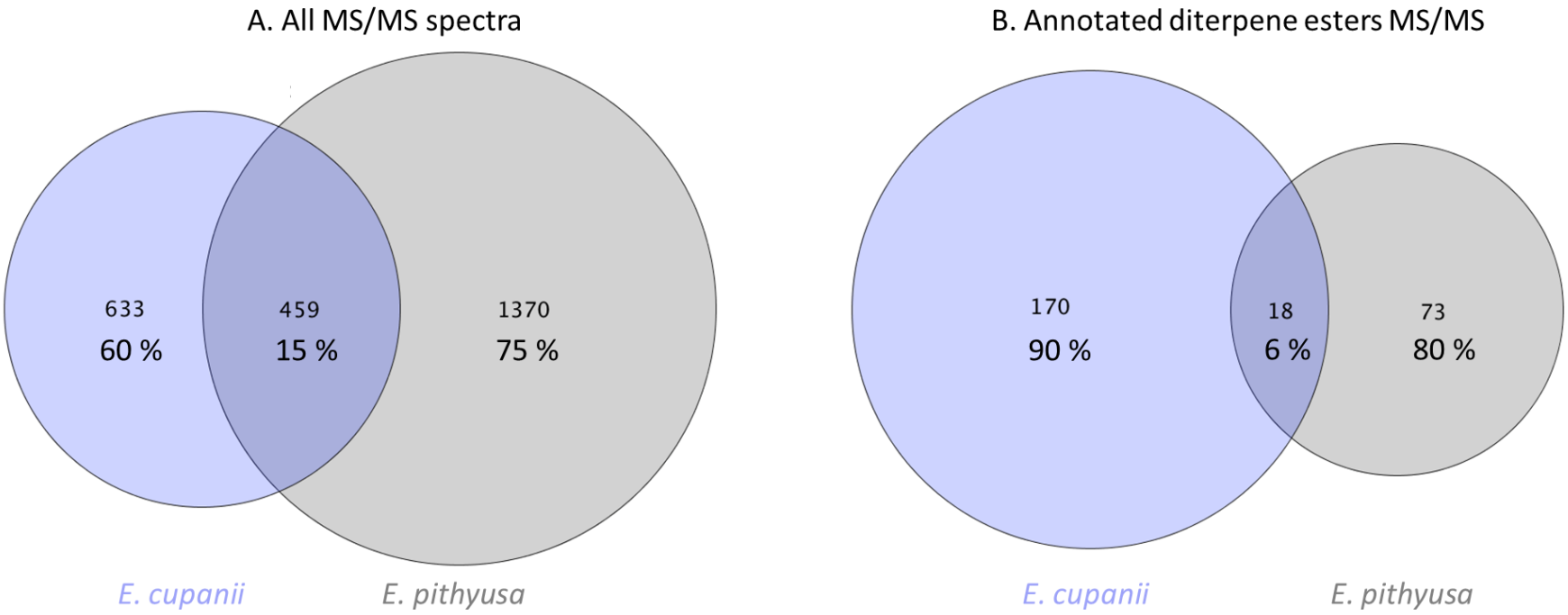


Table S5. The ten first fragment and loss features, and their corresponding probabilities that are explained by the Mass2Motifs 240, 129, 67, 219, 16, 76, 193, and 271.

Mass2Motif 240

Feature	Probability
fragment_267.1750	0.521
fragment_225.1250	0.094
fragment_225.1750	0.087
fragment_267.2250	0.041
fragment_239.1750	0.039
fragment_252.1750	0.035
fragment_239.1250	0.026
fragment_211.1250	0.026
fragment_285.1750	0.024
fragment_193.1250	0.022

129

Feature	Probability
fragment_647.2750	0.082
fragment_465.2250	0.068
fragment_587.2750	0.065
fragment_525.2750	0.043
fragment_317.1750	0.041
fragment_405.2250	0.041
fragment_377.1750	0.041
fragment_267.1750	0.036
loss_120.0250	0.030
loss_180.0750	0.030

67

Feature	Probability
fragment_247.1750	0.180
fragment_277.1750	0.088
fragment_235.1750	0.083
fragment_265.1750	0.039
fragment_259.1750	0.033
fragment_219.1250	0.029
fragment_295.1750	0.027
fragment_232.1250	0.024
fragment_233.1250	0.023
fragment_369.1750	0.021

219

Feature	Probability
fragment_247.1750	0.062
fragment_193.1250	0.050
fragment_235.1750	0.034
fragment_219.1250	0.032
fragment_207.1250	0.028
fragment_131.0750	0.028
fragment_217.1250	0.025
fragment_232.1250	0.024
fragment_179.0750	0.023
fragment_205.1250	0.022

Mass2Motif 16

Feature	Probability
fragment_441.2250	0.062
fragment_279.1750	0.044
fragment_501.2250	0.041
fragment_105.0250	0.040
fragment_249.1750	0.038
fragment_331.2750	0.036
loss_122.0250	0.028
fragment_297.1750	0.022
fragment_561.2750	0.022
fragment_189.1250	0.022

76

Feature	Probability
fragment_279.1750	0.144
fragment_297.1750	0.089
fragment_251.1750	0.054
fragment_209.1250	0.035
fragment_223.1750	0.033
fragment_237.1250	0.033
fragment_361.1750	0.031
fragment_269.2250	0.030
fragment_195.1250	0.026
fragment_261.1750	0.025

193

Feature	Probability
fragment_237.1750	0.672
fragment_223.1750	0.073
fragment_265.1750	0.048
fragment_237.2250	0.021
fragment_211.1750	0.018
fragment_377.1750	0.017
fragment_208.1250	0.017
fragment_194.1250	0.016
fragment_283.1750	0.015
fragment_249.1250	0.009

271

Feature	Probability
fragment_247.1750	0.097
fragment_277.1750	0.063
fragment_235.1750	0.062
fragment_541.2250	0.039
fragment_419.1750	0.027
fragment_265.1750	0.027
fragment_295.1750	0.024
fragment_259.1750	0.021
fragment_233.1250	0.020
fragment_479.2250	0.019

Figure S6. Diterpene esters molecular network from *E. pithyusa* (in grey) and *E. cupanii* extracts, visualized using a fraction layout from *E. cupanii* fractions (F1–F14).

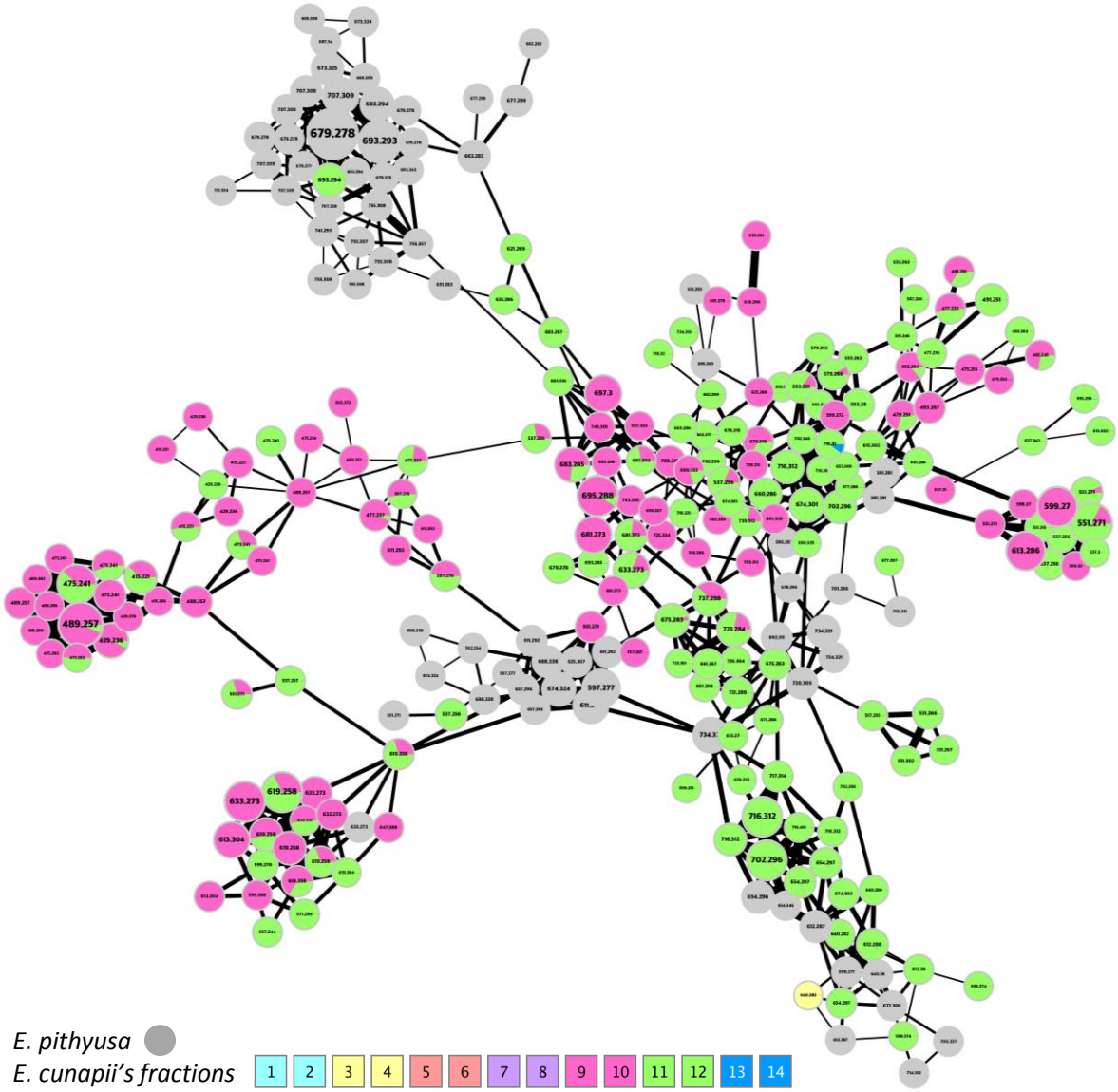


Table S7. ^{1}H NMR Data for Compounds **11a**, **11h**, **13** (500 MHz) and **11b**, **11c**, **12** (300 MHz) in $CDCl_3$ at 300 K, δ_H in ppm, *J* in Hz.

Pos.	**11a**	**11b**	**11c**	**11h**	Pos.	**12**	**13**
1*α*	2.96, dd (16.2, 10.3)	2.96, dd (16.2, 10.3)	2.61, dd (14.9, 10.2)	2.85, dd (16.0, 10.8)	1*α*	2.75, dd (16.0, 10.9)	2.76, d (16.2)
1*β*	2.68, dd (16.2, 9.2)	2.70, dd (16.2, 9.2)	1.53, dd (14.9, 10.2)	2.68, dd (16.0, 9.0)	1*β*	2.57, dd (16.0, 9.4)	2.37, d (16.2)
2	2.23, m	2.23, m	2.15, m	2.18, m	2	2.12, m	-
3	5.25, t (3.5)	5.25, t (3.5)	5.23, t (3.7)	5.28, t (3.6)	3	5.23, t (2.3)	5.66, d (4.4)
4	2.96, dd (10.1, 3.5)	2.96, dd (10.1, 3.5)	2.99, dd (11.3, 3.7)	3.19, dd (11.1, 3.6)	4	3.07, dd (11.1, 3.7)	3.21, dd (11.1, 4.4)
5	4.23, dd (10.1, 2.7)	4.23, dd (10.1, 2.7)	6.08, dd (11.3, 1.3)	6.04, dd (11.1, 1.1)	5	5.87, d (11.1)	5.97, d (11.1)
7	5.63, d (6.6)	5.65, d (6.3)	4.82, d (6.4)	5.11, d (6.4)	7	4.87, d (6.2)	4.91, d (6.9)
8	6.21, ddd (9.7, 6.6, 1.4)	6.21, ddd (9.7, 6.3, 1.4)	6.10, ddd (9.5, 6.5, 1.3)	6.25, ddd (9.8, 6.4, 1.5)	8	6.13, ddd (10.0, 6.6, 1.3)	6.17, ddd (10.0, 6.9, 1.5)
9	5.84, dd (9.7, 5.0)	5.84, dd (9.7, 5.0)	5.83, dd (9.6, 5.7)	5.90, dd (9.8, 5.6)	9	5.94, dd (10.0, 5.6)	5.92, dd (10.0, 5.8)
11	3.28, dd (5.0, 4.1)	3.28, dd (5.0, 4.1)	3.16, dd (5.7, 3.5)	3.27, dd (5.6, 3.5)	11	3.31, dd (5.6, 3.5)	3.17, dd (5.8, 3.5)
12	3.25, d (4.1)	3.25, d (4.1)	3.86, d (3.5)	3.47, d (3.5)	12	3.13, d (3.5)	3.40, d (3.5)
14	5.21, s	5.21, s	5.19, s	5.28, br s	14	5.33, br s	
16	0.89, d (6.8)	0.89, d (6.8)	0.85, d (6.8)	0.80, d (6.8)	16	0.80, d (6.7)	1.60, s
17a	4.20, d (12.0)	4.20, d (12.0)	4.18, d (8.8)	4.11, d (8.6)	17a	4.01, d (8.9)	3.99, d (9.2)
17b	3.48, d (12.0)	3.49, d (12.0)	3.58, d (8.8)	3.60, dd (8.6, 1.5)	17b	3.44, dd (8.9, 1.2)	3.48, d (9.2)
18a	4.92, br s	4.92, br s	4.86, br s	4.87, br s	18	1.46, br s	1.58, s
18b	4.87, br s	4.87, br s	4.74, br s	4.11, br s			
19	1.91, s	1.92, s	1.93, s	1.91, s	19	1.73, s	1.53, s
20	1.29, s	1.29, s	1.30, s	1.31, s	20	1.24, s	1.42, s
3-OR_1	1.69, s	2.08, q (7.6)	1.96, s	2.12, q (7.5)	2-Obz		7.91, d (7.7)
		0.67, t (7.6)		0.93, t (7.5)			7.40, t (7.7)
5-OR_2	3.85, br s	3.94, br s	7.88, d (7.5)	1.94, s			7.52, t (7.7)
			7.39, t (7.5)		3-OAc	2.01, s	1.96, s
			7.51, t (7.5)		5-OAc	1.94, s	1.97, s
7-OR_3	8.01, d (7.6)	8.00, d (7.6)	2.12, s	9.17, br s	7-OAc	1.95, s	2.12, s
	7.38, t (7.6)	7.38, t (7.6)		8.75, br s	10-OAc	2.15, s	2.15, s
	7.53, t (7.6)	7.53, t (7.6)		8.33, br d (7.6)	14-OBz	7.86, d (7.4)	
				7.44, m		7.39, t (7.4)	
14-OR_4	7.94, d (7.6)	7.94, d (7.6)	8.09, d (7.4)	7.94, d (7.4)		7.53, t (7.4)	
	7.41, t (7.6)	7.41, t (7.6)	7.45, t (7.4)	7.42, t (7.4)	15-OAc	1.95, s	1.94, s
	7.55, t (7.6)	7.55, t (7.6)	7.58, t (7.4)	7.56, t (7.4)			
15-OR_5	2.02, s	2.02, s	2.75, br s	2.20, s			

Table S8. ^{1}H NMR Data for Compounds **14a**, **15a**, **15b** (500 MHz) and **14b**, **14c**, **15c** (300 MHz) in $CDCl_3$ at 300 K (δ_H in ppm, J in Hz).

Pos.	**14a**	**14b**	**14c**	**15a**	**15b**	**15c**
1*α*	2.66, dd (15.5, 11.1)	3.35, dd (14.6, 9.9)	3.36, dd (18.0, 12.0)	2.58, dd (14.6, 10.5)	2.46, dd (14.6, 10.1)	2.59, dd (14.5, 10.2)
1*β*	1.75, dd (15.5, 6.8)	1.48, m	1.47, m	1.53, dd (14.6, 10.1)	1.48, dd (14.6, 10.1)	1.52, dd (14.5, 9.8)
2	2.17, m	2.16, m	2.18, m	2.12, m	2.02, m	2.11, m
3	5.32, dd (5.0, 4.1)	5.23, t (4.5)	5.28, t (4.5)	5.16, t (3.8)	4.98, t (3.6)	5.18, br t (3.3)
4	3.11, dd (10.8, 4.1)	2.54, dd (10.4, 4.5)	2.54, dd (12.4, 4.5)	3.07, dd (10.5, 3.8)	2.98, dd (10.4, 3.6)	3.07, dd (10.3, 3.3)
5	5.93, dd (10.8, 1.3)	6.06, d (10.4)	6.06, d (12.4)	5.94, d (10.5)	5.94, d (10.4)	5.92, d (10.3)
7	4.70, dd (11.0, 2.7)	4.77, dd (10.2/2.9)	4.78, dd (10.2, 2.9)	4.67, dd (11.1, 2.6)	4.80, dd (11.1, 2.9)	4.66, dd (10.9, 1.9)
8α	1.87, m	1.88, m	1.88, m	1.84, m	2.00, m	1.84, m
8*β*	1.45, m	1.46, m	1.49, m	1.43, m	1.68, m	1.42, m
9	1.03, m	1.01, m	1.01, m	0.96, m	0.90, m	0.96, dd (17.0, 8.3)
11	0.65, dd (9.6, 7.2)	0.73, m	0.73, m	0.63, dd (9.5, 7.8)	0.68, dd (9.5, 7.5)	0.63, dd (8.3, 7.5)
12	3.06, d (7.2)	2.78, d (6.6)	2.80, d (7.4)	3.48, d (7.8)	3.39, d (7.5)	3.48, d (7.5)
14	-	-	-	5.15, s	4.93, s	5.14, br s
16	0.90, d (7.2)	0.85, d (7.0)	0.85, d (7.0)	0.79, d (6.8)	0.77, d (6.8)	0.78, d (7.0)
17a	4.52, d (9.6)	4.27, d (9.9)	4.25, d (11.7)	4.52, d (9.3)	4.59, d (9.5)	4.51, d (9.3)
17b	3.87, d (9.6)	3.87, d (9.9)	3.86, d (11.7)	3.73, dd (9.3, 0.9)	3.91, dd (9.5, 1.1)	3.73, br d (9.3)
18	1.02, s	1.05, s	1.05, s	1.08, s	1.09, s	1.08, s
19	1.04, s	1.08, s	1.08, s	1.22, s	1.15, s	1.21, s
20	1.38, s	1.51, s	1.51, s	1.27, s	1.26, s	1.27, s
3-OR_1	2.12, s	2.12, s	2.45, q (7.5)	2.13, s	2.08, s	2.49, q (7.4)
			1.21, t (7.5)			1.16, t (7.4)
5-OBz	7.97, d (7.4)	7.90, d (8.0)	7.90, d (8.0)	7.96, d (7.4)	7.57, d (7.3)	7.95, d (7.3)
	7.41, t (7.4)	7.40, t (8.0)	7.40, t (8.0)	7.41, t (7.4)	7.03, t (7.3)	7.41, t (7.3)
	7.53, t (7.4)	7.52, t (8.0)	7.52, t (8.0)	7.51, t (7.4)	7.20, t (7.3)	7.52, t (7.3)
7-OAc	1.26, s	1.35, s	1.36, s	1.29, s	7.52, d (7.3)	1.28, s
or 7-OR_2					7.02, t (7.3)	
					7.20, t (7.3)	
14-OR_3				8.08, d (7.6)	2.15, s	8.07, d (7.5)
				7.47, t (7.6)		7.47, t (7.5)
				7.58, t (7.6)		7.59, t (7.5)
15-OR_2	3.19, br s	2.13, s	2.13, s	2.74, br s	2.78, br s	2.77, br s

Table S9. ^{13}C NMR Data for Compounds **11a**, **11h**, **13, 14a**, **15a**, **15b** (125 MHz), and **11b**, **11c**, **12, 14b**, **14c**, **15c**, (75 MHz), ($CDCl_3$ at 300 K, δ_C in ppm).

Pos.	**11a**	**11b**	**11c**	**11h**	Pos.	**12**	**13**	Pos.	**14a**	**14b**	**14c**	**15a**	**15b**	**15c**
1	43.6	43.6	51.3	44.1		43.2	47.7	1	46.4	42.3	42.3	51.8	51.8	51.8
2	36.2	36.2	36.4	37.0		36.8	88.0	2	33.9	35.4	35.6	36.1	36.5	36.0
3	80.9	80.3	79.1	77.0		77.2	78.8	3	79.3	77.5	77.5	79.3	79.7	79.1
4	55.0	54.7	51.6	52.2		52.1	49.6	4	52.5	53.7	53.9	53.1	53.6	53.1
5	66.4	66.2	70.3	69.7		69.2	68.9	5	68.4	68.4	68.4	68.6	69.0	68.5
6	54.3	54.3	55.2	54.9		54.4	55.7	6	54.7	54.2	54.1	53.5	53.4	53.5
7	65.7	65.6	64.1	65.8		63.3	63.7	7	77.0	77.2	77.2	77.1	77.5	77.2
8	123.2	123.2	123.9	123.7		124.8	125.4	8	25.2	24.3	24.2	25.4	25.9	25.3
9	133.6	133.6	133.5	134.7		131.4	131.0	9	24.8	24.1	24.1	24.6	24.4	24.7
10	147.9	147.7	147.6	147.3		85.9	85.7	10	20.3	19.2	19.2	20.1	20.0	20.3
11	42.1	41.9	41.5	42.0		41.3	44.3	11	16.9	17.6	17.6	17.6	17.5	17.6
12	40.3	40.3	39.5	41.0		37.6	38.9	12	41.3	41.3	41.3	39.3	39.4	39.4
13	89.4	89.4	89.7	90.0		90.4	92.1	13	88.4	88.5	88.5	86.2	86.4	86.3
14	82.2	82.2	82.4	82.2		82.7	200.9	14	202.8	202.9	202.9	82.3	82.4	82.3
15	90.8	90.6	80.8	90.3		90.6	89.3	15	88.3	90.4	90.4	80.7	80.6	80.7
16	14.3	14.3	14.8	14.4		14.2	19.9	16	15.8	15.1	15.1	15.1	15.4	15.1
17	68.6	68.6	69.3	69.6		69.6	70.8	17	74.8	73.4	73.4	73.1	73.4	73.1
18	112.7	112.7	112.0	113.2		23.3	25.4	18	28.3	28.3	28.3	28.4	28.9	28.5
19	20.6	20.6	21.1	21.1		24.6	21.9	19	15.6	16.2	16.2	16.0	16.1	16.0
20	24.6	24.6	24.1	24.7		25.1	21.0	20	29.4	20.4	20.4	23.3	23.8	23.4
3-OR_1	172.2	167.9	170.1	174.5	2-Obz		165.3	3-OR_1	169.9	170.7	173.6	170.1	170.0	173.3
	24.1	27.5	21.3	28.2			130.8		21.3	21.2	28.1	21.4	21.7	28.0
		8.9		9.2			129.8				9.3			9.3
5-OR_2			164.9	169.7			128.6	5-OBz	165.1	164.9	164.9	165.1	164.8	165.1
			130.0	20.9			133.2		130.5	130.3	130.4	130.9	130.0	130.9
			129.6		3-OAc	171.1	170.8		129.8	129.8	129.8	129.8	130.2	129.8
			128.6			21.2	21.2		128.8	128.8	128.8	128.8	128.5	128.7
			133.1		5-OAc	169.4	169.4		133.5	133.5	133.5	133.3	132.9	133.3
7-OR_3	165.6	165.3	170.6	164.6		22.7	21.1	7-OAc	170.9	170.6	170.6	171.0	164.2	170.9
	129.1	129.5	21.4	150.9	7-OAc	170.6	170.6		21.0	21.1	21.1	21.1	129.8	21.1
	128.9	131.9		129.8		21.0	21.4						130.1	
	128.1	128.5		137.9	10-OAc	167.8	169.3						128.5	
	132.6	133.6		123.4		23.0	21.6						133.0	
				153.4	14-OBz	166.4		14-				166.0	170.8	166.0
14-OR_4	165.7	165.7	166.1	166.3		129.6						130.1	21.6	130.1
	129.4	131.9		129.4		130.1						129.8		130.0
	130.3	130.0		130.3		128.4						128.8		128.8
	129.7	128.5		128.9		133.4						133.5		133.5
	132.8	133.3		133.7	15-OAc	170.5	170.5	15-		170.6	170.2			
15-OR_5	167.8	167.8		168.4		21.3	22.7			22.0	20.4			
	22.6	22.6		22.7										

Table S10. Crystal Data of Compounds **11d**, **11f**, **11h**, **12**, and **15b**.

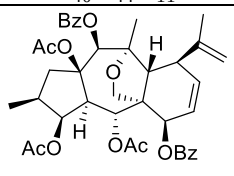
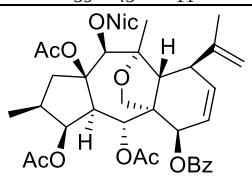
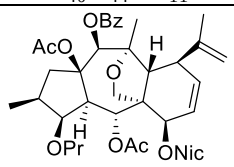
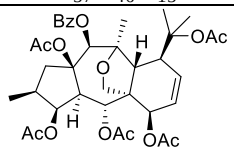
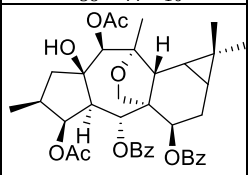
Identification code	**11d**	**11f**	**11h**	**12**	**15b**
Empirical formula	$C_{40}H_{44}O_{11}$	$C_{39}H_{43}NO_{11}$	$C_{40}H_{44}NO_{11}$	$C_{37}H_{46}O_{13}$	$C_{38}H_{44}O_{10}$
Chemdraw Drawing					
Formula weight	700.75	701.74	714.16	698.74	660.73
Temperature (K)	293(2)	293(2)	293(2)	293(2)	293(2)
Wavelength (Å)	1.54187	1.54187	1.54187	1.54187	1.54187
Crystal system, space group	Orthorhombic, $P2_12_12_1$	Orthorhombic, $P2_12_12_1$	Orthorhombic, $P2_12_12_1$	Monoclinic, $P2_1$	Orthorhombic, $P2_12_12_1$
Unit cell dimensions a (Å)	9.5382(3)	9.5854(9)	9.4658(6)	11.9104(12)	10.1182(2)
b (Å)	13.4084(4)	17.8136(17)	13.6587(8)	9.3699(9)	13.8736(2)
c (Å)	28.913(2)	21.264(2)	28.643(2)	17.1206(12)	24.3877(17)
α (°)	90	90	90	90	90
β (°)	90	90	90	105.923(8)	90
γ (°)	90	90	90	90	90
Volume ($Å^3$)	3697.7(3)	3630.9(6)	3703.3(4)	1837.3(3)	3423.4(3)
Z, Calcd Density (Mg/m^3)	4, 1.259	4, 1.284	4, 1.282	2, 1.263	4, 1.282
Abs° coefficient (mm^{-1})	0.754	0.777	0.771	0.796	0.758
F(000)	1488	1488	1516	744	1408
Crystal size (mm)	0.36 x 0.20 x 0.20	0.25 x 0.11 x 0.08	0.06 x 0.03 x 0.02	0.60 x 0.36 x 0.26	0.46 x 0.25 x 0.10
θ range -data collect° (°)	3.548 to 68.237	3.236 to 68.233	3.086 to 63.670	2.684 to 68.247	3.625 to 68.265
Limiting indices	$-11 \le h \le 11$, $-15 \le k \le 16$, $-34 \le l \le 30$	$-9 \le h \le 11$, $-19 \le k \le 20$, $-25 \le l \le 25$	$-9 \le h \le 10$, $-15 \le k \le 15$, $-32 \le l \le 33$	$-14 \le h \le 14$, $-11 \le k \le 11$, $-20 \le l \le 18$	$-8 \le h \le 11$, $-16 \le k \le 16$, $-29 \le l \le 29$
Reflect° collected/unique [R(int)]	44844 / 6764 0.0541	32777 / 6529 0.0654	31812 / 6042 0.0976	35624 / 6592 0.0482	32289 / 6200 0.0458
Completeness to θ_{full} (%)	99.9	98.2 99.5	99.4	99.5	99.6
Absorption correction	Semi-empirical from equivalents				
Max. and min. transmission	0.86 and 0.73	0.94 and 0.78	0.99 and 0.76	0.81 and 0.66	0.93 and 0.73
Refinement method	Full-matrix least-squares on F^2				
Data / restraints / parameters	6759 / 10 / 466	6525 / 0 / 466	6042 / 72 / 74	6583 / 1 / 461	6199 / 0 / 440
Goodness-of-fit on F^2	0.999	0.855	0.900	1.122	0.998
R1 [I>2σ(I)] wR2	0.0550, 0.1291	0.0389, 0.0659	0.0674, 0.1224	0.0360, 0.0883	0.0373, 0.0795
R1 (all data) wR2	0.1448, 0.1937	0.1198, 0.0861	0.2273, 0.1822	0.0479, 0.1069	0.0958, 0.1127
Flack parameter	0.04(7)	0.09(8)	-0.07(16)	-0.04(5)	-0.19(7)
Extinction coefficient	n/a	n/a	n/a	0.0044(4)	n/a
Largest $\Delta_{peak\&hole}$ ($e.Å^3$)	0.181 and -0.232	0.156 and -0.152	0.188 and -0.245	0.182 and -0.181	0.183 and -0.191

Table S11. ^{1}H and ^{13}C NMR Data for Compounds **16a–c** and **17** (600 MHz) in $CDCl_3$ at 300 K

	16a		**16b**		**16c**		**17**	
pos.	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1	7.59, br d (10.4)	161.0	7.59, br s	161.0	7.58, br d (10.4)	161.0	7.65, br s	160.6
2		133.0		133.0		133.0		135.2
3		209.1		209.1		209.1		204.9
4		73.9		73.9		73.9		73.2
5α	2.47, t (19.0)	38.7	2.47, t (19.0)	38.7	2.47, t (18.2)	38.7	6.88, s	138.1
5β	2.51, t (19.0)		2.51, t (19.0)		2.50, t (18.2)			
6		140.5		140.5		140.5		148.5
7	5.68, d (4.9)	129.4	5.68, br d (5.0)	129.4	5.68, br d (5.6)	129.4		201.5
8	3.23, m	39.4	3.23, m	39.4	3.22, m	39.4	3.72, d (5.0)	55.8
9		78.4		78.4		78.4		75.6
10	3.24, d (7.4)	56.4	3.25, d (7.4)	56.4	3.24, d (7.4)	56.4	2.21, m	60.1
11	2.15, m	43.5	2.15, m	43.5	2.15, m	43.5	3.30, br t (2.3)	43.5
12	5.44, d (9.8)	76.9	5.46, d (9.8)	76.9	5.43, d (10.3)	76.9	5.46, d (9.8)	76.3
13		65.4		65.4		65.4		65.7
14	1.04, br s	36.5	1.02, br s	36.5	1.05, br s	36.5	1.80, d (5.3)	30.3
15		26.4		26.4		26.4		25.3
16	1.26, s	16.8	1.26, s	17.2	1.25, s	16.8	1.21, s	17.8
17	1.20, s	23.9	1.20, s	24.1	1.19, s	23.9	1.18, s	24.2
18	0.89, d (6.4)	14.3	0.88, d (6.4)	14.3	0.87, d (6.4)	14.3	0.93, d (6.4)	15.2
19	1.76, d (8.2)	10.2	1.75, d (8.2)	10.2	1.75, d (8.2)	10.2	1.82, d (1.8)	11.0
20a	4.03, d (12.9)	68.2	4.03, d (12.9)	68.2	4.02, d (12.5)	68.2	4.38, d (14.0)	64.5
20b	3.98, d (12.9)		3.98, d (12.9)		3.97, d (12.5)		4.27, d (14.0)	
14-OR								
1'		167.0		167.0		167.0		167.0
2'	5.84, d (15.4)	121.2	5.84, d (15.4)	121.2	5.53, d (11.3)	115.3	5.53, d (11.3)	115.3
3'	7.58, dd (15.4, 11.1)	140.1	7.58, dd (15.4, 11.1)	140.1	6.54, t (11.3)	145.9	6.55, t (11.3)	145.9
4'	6.11, t (11.1)	126.7	6.11, t (11.1)	126.7	7.30, t (11.3, 15.2)	127.0	7.30, t (11.3, 15.2)	127.0
5'	5.86, dd (11.1, 7.4)	121.2	5.86, dd (11.1, 7.4)	121.2	6.06, ddd (15.2, 7.4, 7.1)	146.3	6.07, ddd (15.2, 7.4, 7.1)	146.3
6'	2.26, m	28.5	2.26, m	28.5	2.16, m	33.1	2.16, m	33.1
7'	1.39, m	29.2	1.39, m	29.2	1.40, m	29.1	1.40, m	29.1
8'	1.27, m	31.6	1.27, m	31.6	1.26, m	30.1	1.26, m	28.5
9'	1.26, m	22.9	1.26, m	22.9	1.26, m	28.5	1.26, m	30.1
10’	0.86, t (7.0)	11.8	0.86, t (6.4)	11.8	0.85, t (6.4)	14.2	0.85, t (6.7)	14.2
13-OiBu or MeBu		179.7		178.7		179.7	-	179.7
	2.57, q (7.0)	34.4	2.37, qt (6.9, 7.7)	41.5	2.57, q (7.0)	34.4	2.59, q (7.0)	34.4
	1.18, d (7.0)	18.8	1.12, d (6.9)	16.5	1.18, d (7.0)	18.8	1.18, d (7.0)	18.8
	1.15, d (7.0)	18.7	1.72, qdd (7.6, 7.7, 7.7)	26.4	1.15, d (7.0)	18.7	1.19, d (7.0)	18.7
			1.44, qdd (7.6, 7.7, 7.7)					
			0.92, t (7.6)	11.9				

Table S12. Antiviral Activities of Compounds **16a–c** and **17** against CHIKV in Vero Cells

references	CC_{50} Vero[b]	EC_{50} CHIKV	SI[c]
E. cupanii extract		< 0.6[a]	>12
F12		0.055[a]	129
16a	57.1	< 0.7[b]	77
16b	8.6	< 0.7[b]	12
16c	44	< 0.8[b]	58
17	28.4	4.5 ± 0.6[b]	6
chloroquine	89 ± 28	11 ± 7[b]	8

[a]Data in μg/ml.

[b]Data in μM. Values are the median ± median absolute deviation calculated from at least three independent assays.

[c]SI or window for antiviral selectivity calculated as CC50 Vero/EC50 CHIKV.

Figure S13. ESI-MS/MS spectrum of compound **14c**. The neutral loss and diterpene backbone fragment ions are annotated.

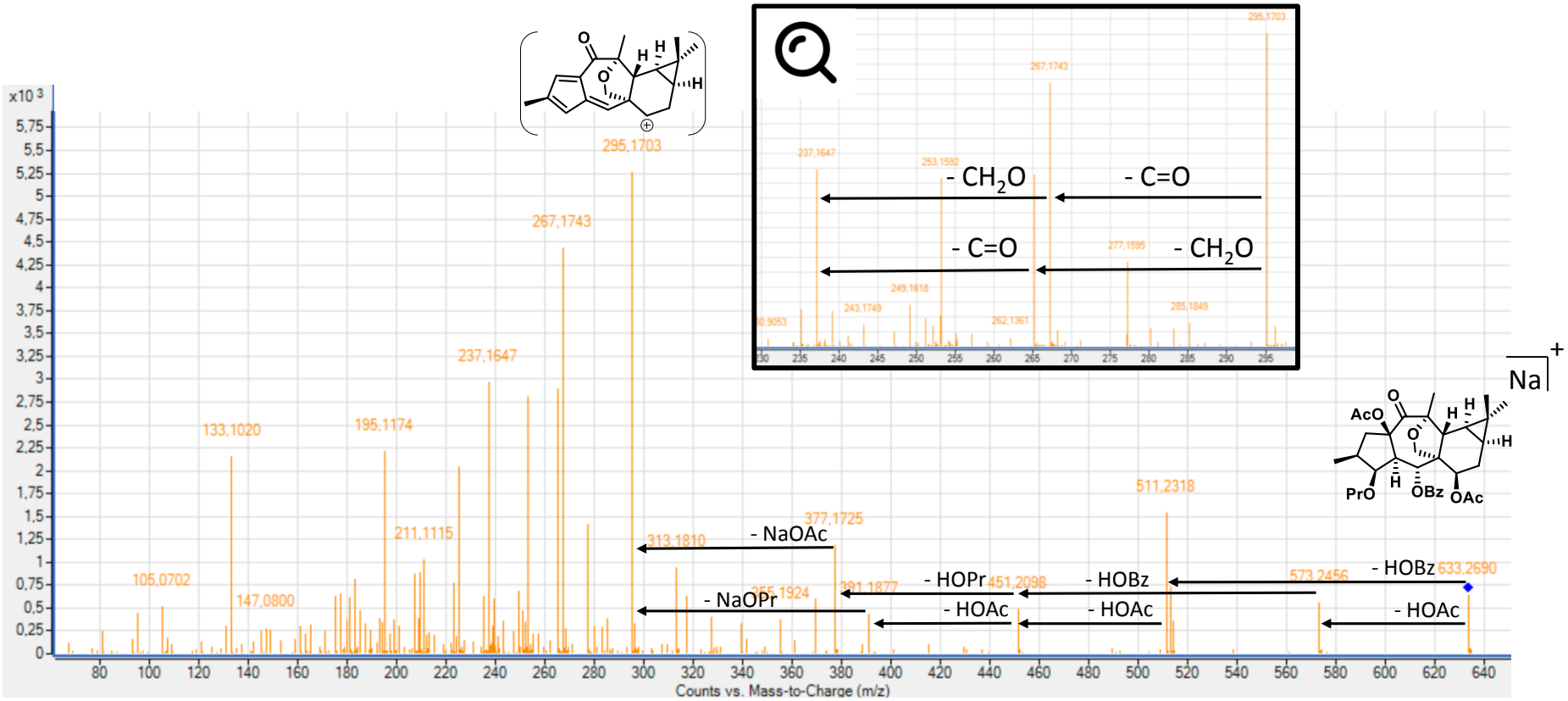


Figure S14. ESI-MS/MS spectrum of compound **15b**. The neutral loss and diterpene backbone fragment ions are annotated.

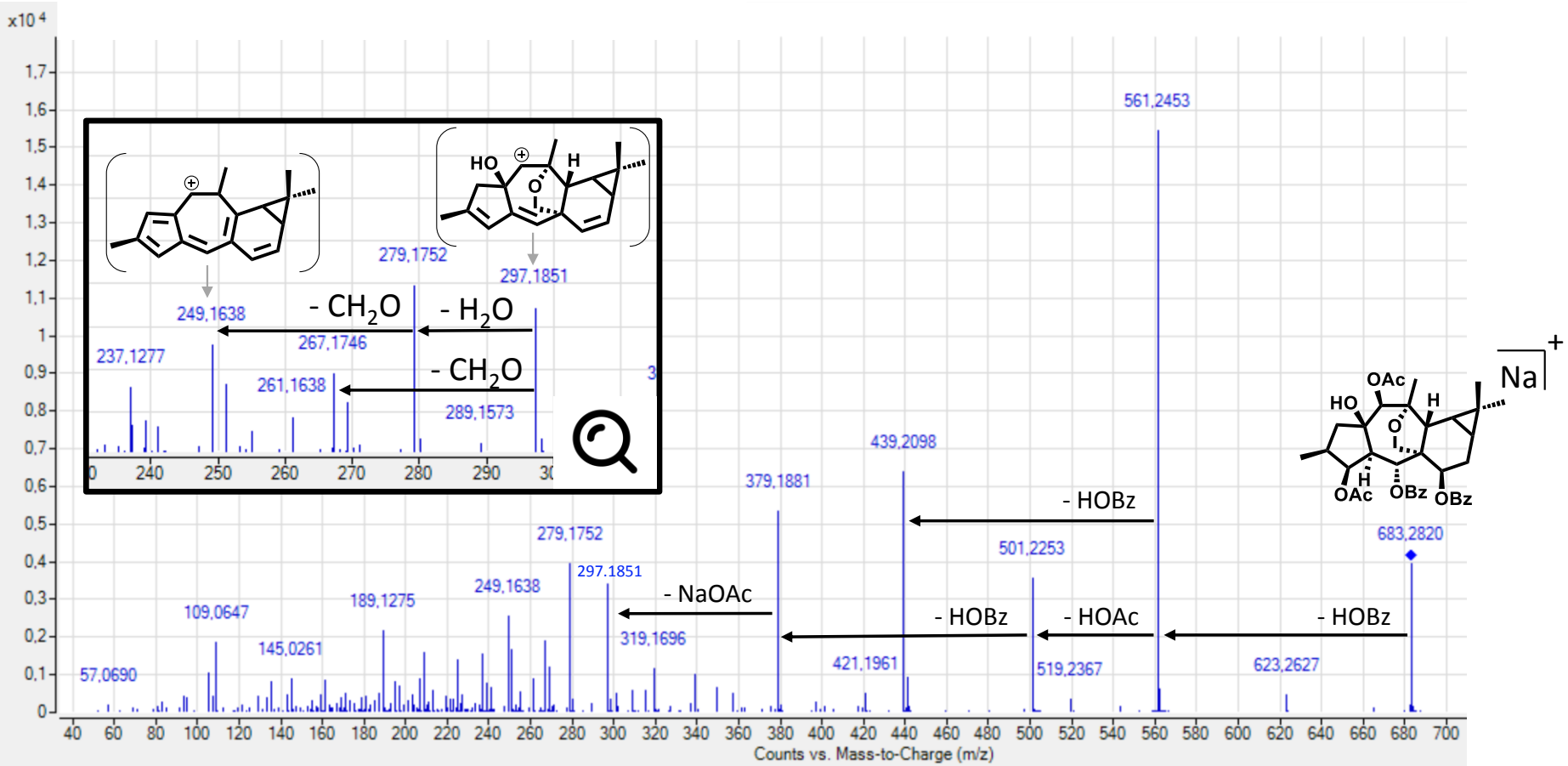


Figure S15. ESI-MS/MS spectrum of compound **13**. The neutral loss and diterpene backbone fragment ions are annotated.

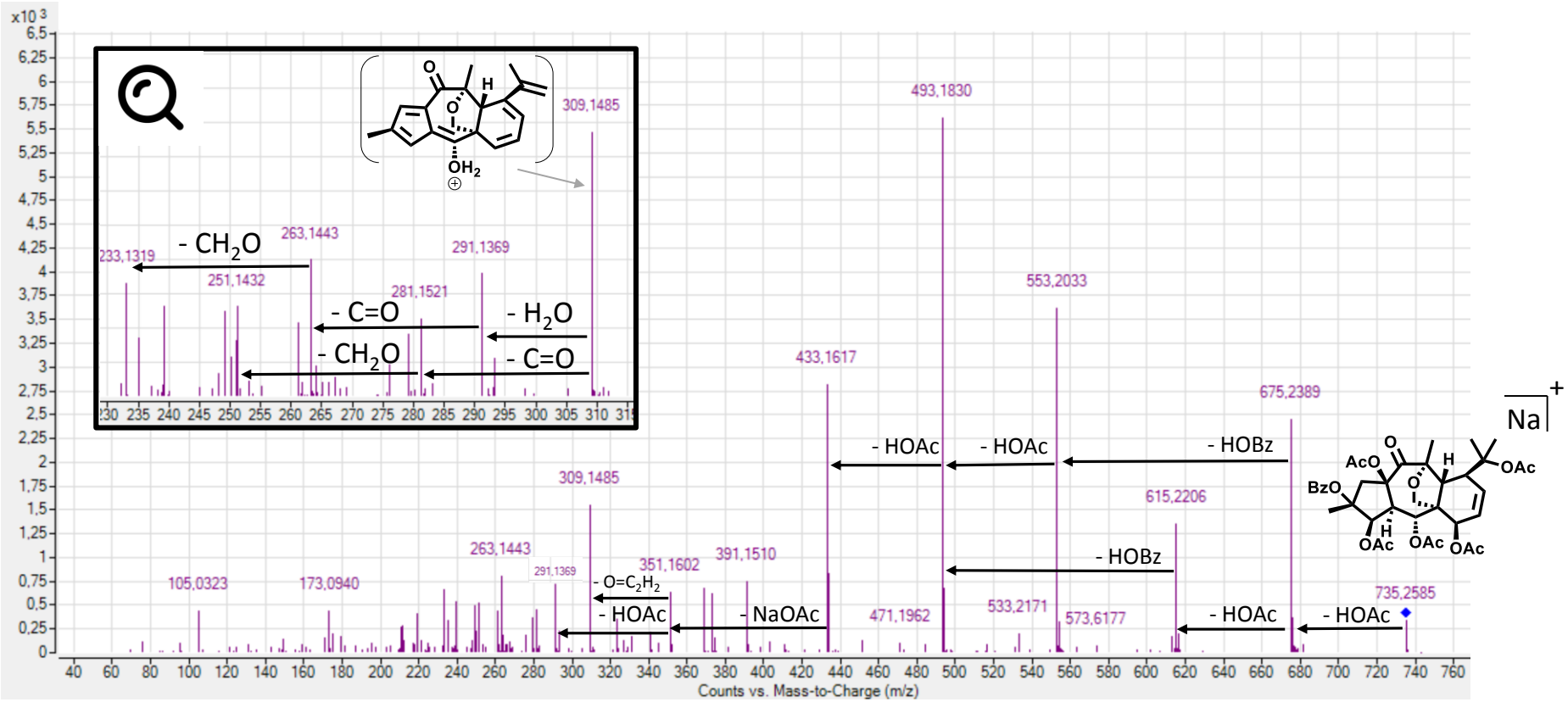


Figure S16. Premyrsinane and myrsinane molecular network annotated with combinatorial network annotation propagation using DNP, UNPD, SUPERNATURAL2 (*Fusion*).

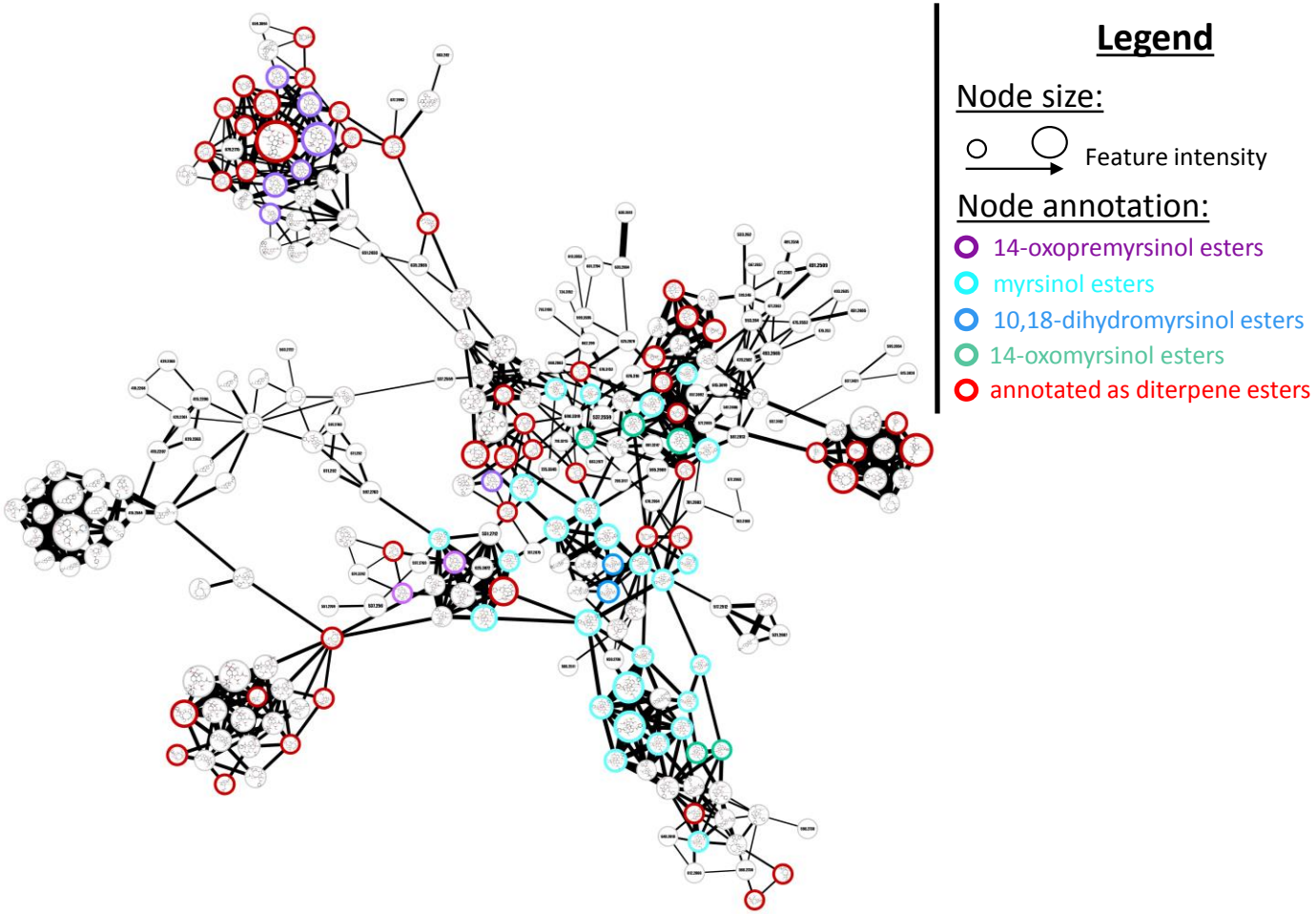
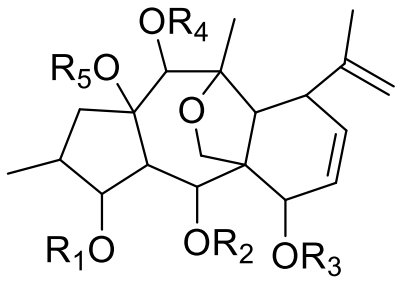
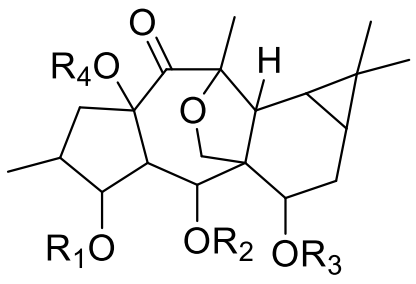


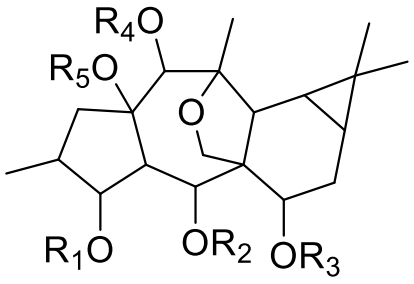
Figure S17. Scaffolds of premyrsinol and myrsinol used for the generation of the Combinatorial Structure Database (CSDB).



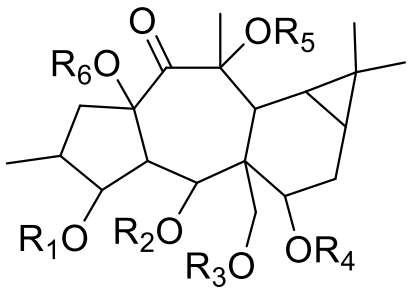
myrsinol
pentahydroxylated



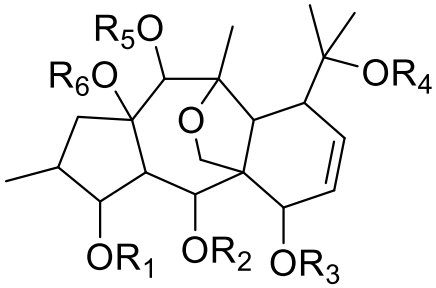
13,17-oxy-14-oxopremyrsinol
tetrahydroxylated



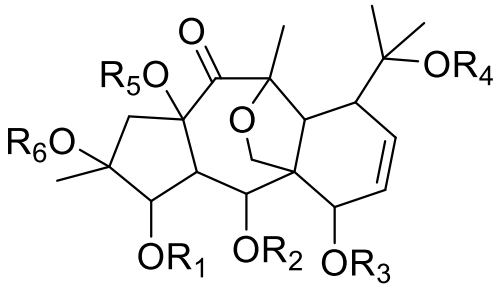
13,17-oxypremyrsinol
pentahydroxylated



14-oxopremyrsinol
hexahydroxylated



10,18-dihydromyrsinol
hexahydroxylated



10,18-dihydro-14-oxomyrsinol
hexahydroxylated

Figure S18. Building blocks of premyrsinol and myrsinol used for the generation of the Combinatorial Structure Database (CSDB).

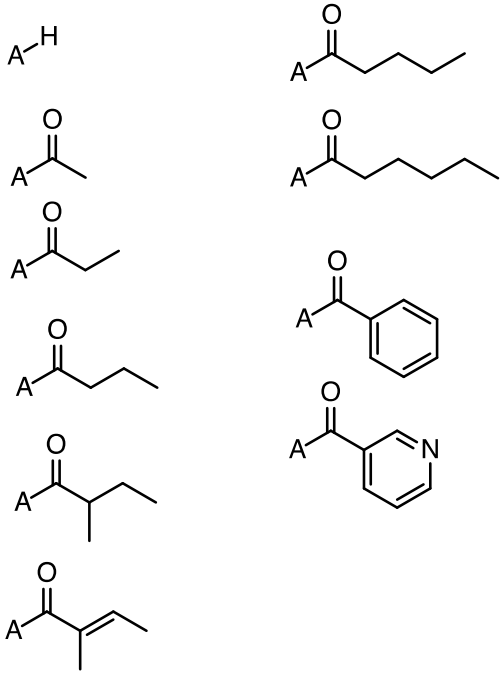


Figure S19. ESI-MS/MS spectrum of the ion at *m/z* 693.294; ProteoSAFeClusterLink:

http://gnps.ucsd.edu//ProteoSAFe/result.jsp?task=8457f016a6604a119141a8e7898a7067&view=cluster_details&protein=520

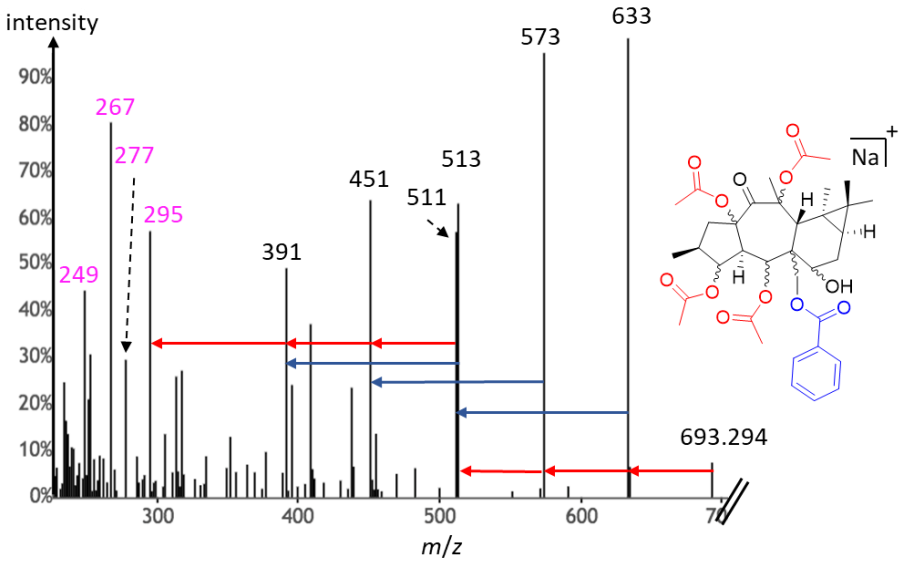


Figure S20. ESI-MS/MS spectrum of the ion at *m/z* 737.298; ProteoSAFeClusterLink:

http://gnps.ucsd.edu//ProteoSAFe/result.jsp?task=8457f016a6604a119141a8e7898a7067&view=cluster_details&protein=802

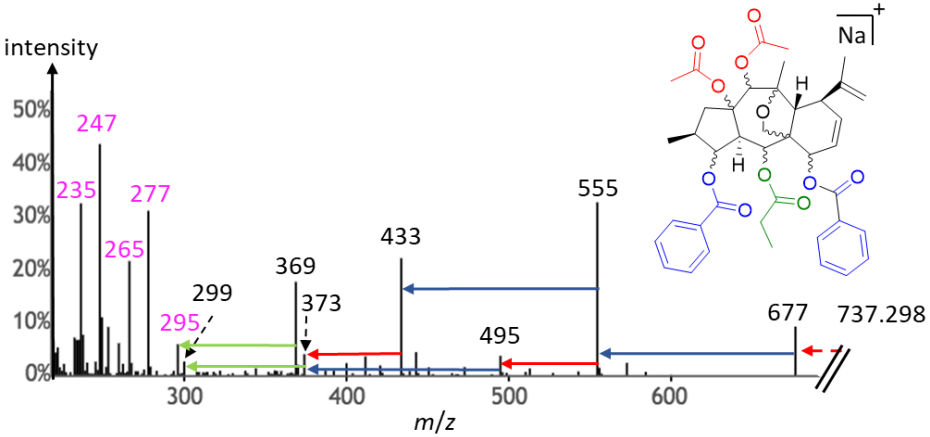
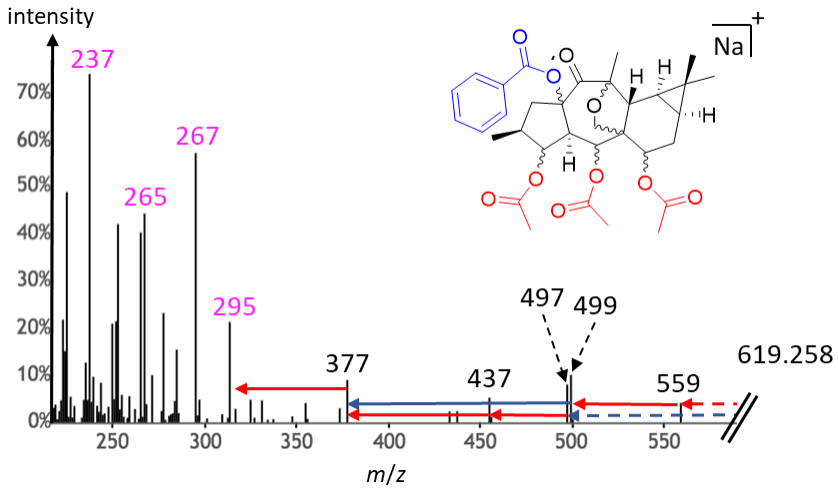


Figure S21. ESI-MS/MS spectrum of the ion at *m/z* 619.258; ProteoSAFeClusterLink:

http://gnps.ucsd.edu//ProteoSAFe/result.jsp?task=8457f016a6604a119141a8e7898a7067&view=cluster_details&protein=762



S22. General Experiment Procedure.

Optical rotations $[\alpha]_D$ were measured on a polarimeter MCP 300 Anton Paar polarimeter at 24 °C. Monochromatic light source is the sodium D-lines. EtOH was used as solvent. IR spectra were obtained on a Perkin Elmer Spectrum BX FT-IR system. UV spectra were recorded on a Varian Cary 100 scan spectrophotometer and they were measured in a 1 cm quartz cell. The 1D- (^{1}H and ^{13}C) and 2D- (COSY, HSQC, HMBC and ROESY) NMR analysis were recorded in $CDCl_3$ at 300 K on a Bruker Avance 600 MHz instrument using a 1.7 mm microprobe for compounds **16a**–**c** and **17**, on a Bruker Avance 500 MHz instrument for compounds, **11a**, **11h**, **15**, **14a**, **15a**, and **15b**, and on a Bruker Avance 300 MHz instrument for compounds **11b**, **11c**, **13, 14b**, **14c**, and **15c**. The data processing software was NMRnotebook® (http://www.nmrtec.com/). Analytical C_{18} columns (Kromasil, 250 × 4.6 mm i.d., 5 μm, Thermo Scientific) was used for HPLC separation on a Waters autopurification system equipped with a binary pump (Waters 2525), a UV–vis diode array detector (190–600 nm, Waters 2996), and a PL-ELS 1000 ELSD Polymer Laboratory detector. This unit was controlled with Masslynx software. Semi-preparative C_{18} column (Kromasil, 250 × 10 mm; i.d. 5 μm) was used for semi-preparative HPLC separation using a Dionex autopurification system equipped with a binary pump (P580), an UV–vis array detector (200–600 nm, Dionex UVD340U), and a PL-ELS 1000 ELSD detector Polymer Laboratory. This unit was controlled with Chromeleon software. The staining reagent used for analytical TLC plates (Silica gel 60 F_{254}, Merck) was the sulfuric molybdate, which was prepared by dissolving ammonium dimolybdate (50 g) in water (450 mL) and slowly adding concentrated sulfuric acid (50 mL) in cold conditions. The plates were observed at 254 nm and 366 nm UV-wavelength. GraceResolv silica cartridges and VersaFlash C_{18} spherical silica were used for flash chromatography using a Combiflash Companion (RF-200, Teledyne Isco) and UV detector. An Acquity Waters UPLC Waters

system coupled with a LCT Premier XE time-of-flight mass spectrometer were used for acquired LC-HRESIMS data. This MS was fitted with an ESI source operating in positive ion mode in the range *m/z* 80-1500. UPLC system was composed of a Waters Acquity PDA dectector, a BEH C_{18} column (2.1 mm × 50 mm, 1.7 μm) at a flow rate of 0.6 mL/min. Elution was conducted with a H_2O−acetonitrile (MeCN) + 0.1% formic acid gradient as follows: 95:5 to 0:100 in 5.5 min. The data were treated with Masslynx® software. All other chemicals and solvents were purchased from SDS (Peypin, France).

S23. Purification and Isolation.

The fraction F10 (830 mg) was mixed with 900 mg of Celite and subjected to flash chromatography on a VersaFlash C_{18} column (Spherical, 23 x 53 mm, 20-45 μm 30 g). The eluted system chose was H_2O–MeCN + 0.1% formic acid (40:60 to 0:100 in 50 minutes), leading to obtain 5 fractions, F10-1 to F10-5. The fraction F10-2 (449 mg) was fractionated by semi-preparative HPLC (Kromasil C_{18}, isocratic H_2O–MeCN + 0.1% formic acid, 30:70 in 40 min) offering three new compounds, compound **14a** (2.3 mg), **14b** (110 mg) and **14c** (117 mg). The fractionation of F10-3 (83.3 mg) by semi-preparative HPLC (Kromasil C_{18}, isocratic H_2O–MeCN + 0.1% formic acid, 20:80 in 40 min) afforded the compound **11c** (4.9 mg). Then, the fraction F10-4 (32.6 mg) was prepared by semi-preparative HPLC (Kromasil C_{18}, isocratic H_2O–MeCN + 0.1% formic acid, 15:85 in 40 min) allowed the isolation of the compound **15c** (7.4 mg). The Fraction F11 (2824 mg) was mixed with 3 g of Celite and subjected to flash chromatography on a pre-packed silica column (GraceResolv, 120 g). The eluted system chose was acetone-heptane (10:90 to 100:0 in 111 minutes), leading to obtaining 10 fractions, F11-1 to F11-10. The fraction F11-2 (1254 mg) was fractionated by semi-preparative HPLC (Kromasil C_{18}, isocratic H_2O–MeCN + 0.1% formic acid, 30:70 in 45 min) leading the isolation of two new compounds, **15a** (32.1 mg) and **11e** (4.7 mg). The fractionation of F11-3 (374.7 mg) by semi-preparative HPLC (Kromasil C_{18}, isocratic H_2O–MeCN + 0.1% formic acid, 30:70 in 40 min) afforded two new compounds, **15b** (3.9 mg) and **11e** (11.8 mg), and one know compound **11d** (12.9), while the fractionation of F11-4 (383.8 mg) in the same conditions allowed the isolation of two new compounds, **11a** (2.9 mg) and **12** (22.7 mg). Then, the fractionation of F11-5 (134.4 mg) by semi-preparative HPLC (Kromasil C_{18}, isocratic H_2O–MeCN + 0.1% formic acid, 20:80 in 40 min) afforded two new compounds, **11h** (3.1 mg) and **13** (2.6 mg), and two know compounds, **11f** (6.4

mg) and **11g** (2.9 mg). The fractionation of F12 (1075 mg) by semi-preparative HPLC (Kromasil C_{18}, isocratic H_2O–MeCN + 0.1% formic acid, 15:85 in 45 min) afforded four new compounds, **16a** (0.8 mg), **16b** (1.2 mg), **16c** (0.5 mg), and **17** (1.7 mg).

S24. X-ray Structure Determination.

Colourless crystals suitable for single-crystal X-ray analysis were obtained after incubation of concentrated Et_2O solutions saturated with hexane vapours at low temperature for the five compounds analysed herein. All the data were collected on a Rigaku diffractometer constituted by a MM007 HF rotating-anode generator, equipped with Osmic CMF confocal optics, and a Rapid II curved Image Plate, operating with Cu-Kα radiation (λ =1.54187 Å). Samples were irradiated at room temperature. The crystal-to-detector distance was 127.40 mm, and in accordance with the IP detector area, allowed us to record 10°-oscillation frames in the range 6-136.5° 2θ. For each sample, ω-scan strategies by the *d*trek* program[1] based upon cell constants and matrix orientation derived from a preliminary scan of few 1°-oscillation images were chosen to optimize the best coverage of Friedel pairs. Data reduction and scaling were carried out with an empirical absorption correction, as well as a treatment for Lorentz and polarization effects using the program *Fs_Process*.[2] Completeness up to 2θ max for all datasets was better than 97%. Compounds **11d**, **11f**, **11h** and **15b** were assigned to the space group P $2_12_12_1$ (n° 19), and finally compound **12**, to the monoclinic space group P 2_1 (n° 4), based upon systematic absences, *E*-statistics, agreement factors for equivalent reflections, and successful solution and refinement of the corresponding structure. The structures were solved by phasing intrinsic methods (SHELXT),[3] and refined by full matrix least squares on F^2 using SHELXL-2014/7.[4] Anisotropic thermal parameters were used for all non-hydrogen atoms and if most of the H atoms were located in residual maps they all were refined as riding and with U_{eq} values set at $1.2U_{eq}$ (parent atom) (1.5 for the methyl groups or hydroxyl oxygen atoms). RIGU rigid-bond restraints were used in SHELXL for the

[1] Pflugrath, J. W. (1999). Acta Cryst. D55, 1718–1725.
[2] Rigaku. (2009) CrystalClear-SM Expert 2.0 r4 Rigaku Corporation, Tokyo, Japan.
[3] Sheldrick, G. M. (2015). *Acta Cryst.* A**71**, 3-8.
[4] Sheldrick, G. M. (2015). *Acta Cryst.* C**71**, 3-8.

bonded atoms in the propenyl substituent at C12 in **11d** and for the atoms in the phenyl and pyridine groups in **11h** to make displacement ellipsoid plots[5] chemically more reasonable.

In absence of strong anomalous scatterers, Bayesian-type analysis[6] of Bijvoet pairs of reflections as implemented within the PLATON[7] program was undertaken for each valuable sample to assign the correct absolute structure. Crystals **11d**, **11f** and **11h** appeared to be weak diffractors despite intense copper radiation and long exposure time (in the range of 60 - 120s per degree of oscillation), therefore the most reliable result that was obtained for **12** was applied to corroborate the other estimates of these family compounds. Hooft[6] parameter [y = -0.02 (4)] and P2 or P3(true) =1 reinforce the significance of the Flack[8] x and Parsons[9] z parameter estimates [x = -0.04 (5) and z = 0.04 (5)] from 3003 Friedel pairs (95% Friedel coverage) and 2310 quotients [(I+)-(I-)]/[(I+)+(I-)]. X-ray crystallography data collection parameters and structure refinement statistics are reported in Table **S10**.

[5] Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453-457.
[6] Hooft, R.W.W., Straver, L. H. & Spek, A. L. (2008). J. Appl. Cryst. 41, 96–103.
[7] Spek, A. L. (2009). *Acta Cryst.* D**65**, 148-155.
[8] Flack, H. D. (1983). *Acta Cryst.* A**39**, 876-881.
[9] Parsons, Flack and Wagner, (2013). *Acta Cryst.* B**69,** 249-259.

S25. Feature Based Molecular Networking with MZmine2.

For MZmine2, the parameters (v2.32) were set as follows: noise level MS1 (1,000); noise level MS2 (75); ADAP chromatogram builder[41] (min. time span 0.03 min; min. highest intensity 2,000; *m*/*z* tolerance of 25 ppm); Chromatogram deconvolution module (Baseline cut-off; min. peak height 2,000; peak duration 0.04-1.5 min; Baseline level 1,000; Wavelets (ADAP); S/N threshold 10; min feature height 10; coefficient/area threshold 110; retention time wavelet range 0.001-0.1 min; *m*/*z* range for MS2 scan pairing of 0.3 Da; retention time range for MS2 scan pairing 0.2 min); Peak grouping (min. intensity for interval selection 0.05; min. intensity overlap 0.55; min. correlation 0.55); Join aligner (*m*/*z* tolerance of 20 ppm; retention time absolute tolerance 0.5 min; isotope *m*/*z* tolerance 5 ppm); Peak finder (intensity tolerance 0.35; *m*/*z* tolerance of 10 ppm; retention time absolute tolerance 0.3); Peak row filter (MS/MS filter; reset row ID); Remove duplicate filter (retention time absolute 0.35; *m*/*z* tolerance of 15 ppm); Peak finder module (intensity tolerance 0.35; retention time tolerance absolute 0.35; *m*/*z* tolerance of 15 ppm). The mgf file exported in MZmine2 with the "GNPS export module" was uploaded on GNPS (http://gnps.ucsd.edu) and the parameters were set with a precursor ion mass tolerance of 0.012 Da and a fragment ion mass tolerance of 0.03 Da. A cosine score of 0.65 and a 6 minimum matched peak were considered to generate the molecular networks. Cytoscape 3.6.1[42] software was used to visualize the molecular networks, where the cosine score and the relative intensity were estimated by the edge and the node size, respectively. The intensity of the ion in each subspecies and fractions is represented in the node's pie chart diagram. The link can be accessed here: https://gnps.ucsd.edu/ProteoSAFe/status.jsp?task=a6ff2e43eb014c7ab53630805f0e32a3

Figure S26. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **11a**

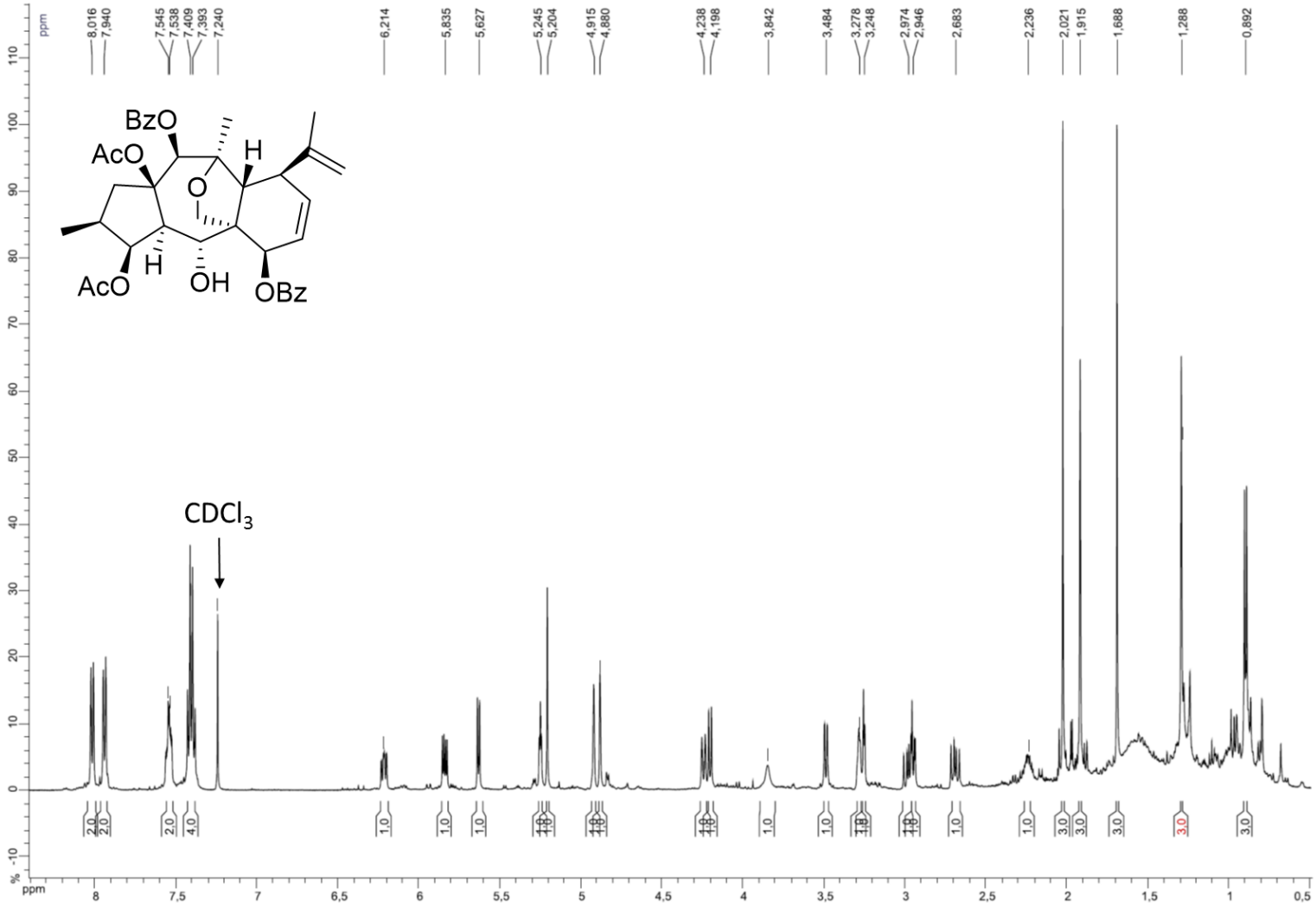


Figure S27. HMBC NMR spectrum ($CDCl_3$, 500 MHz) of **11a**

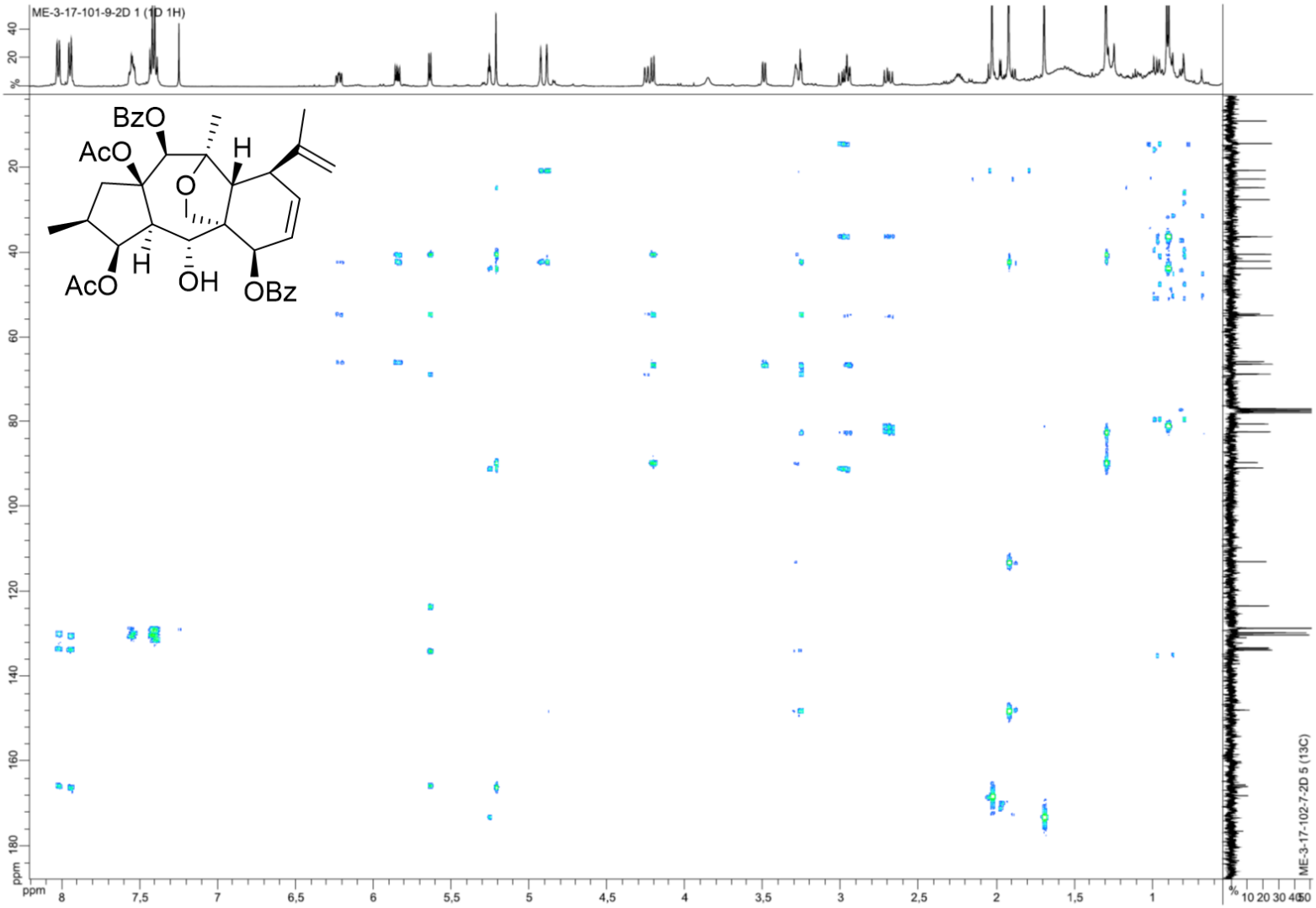
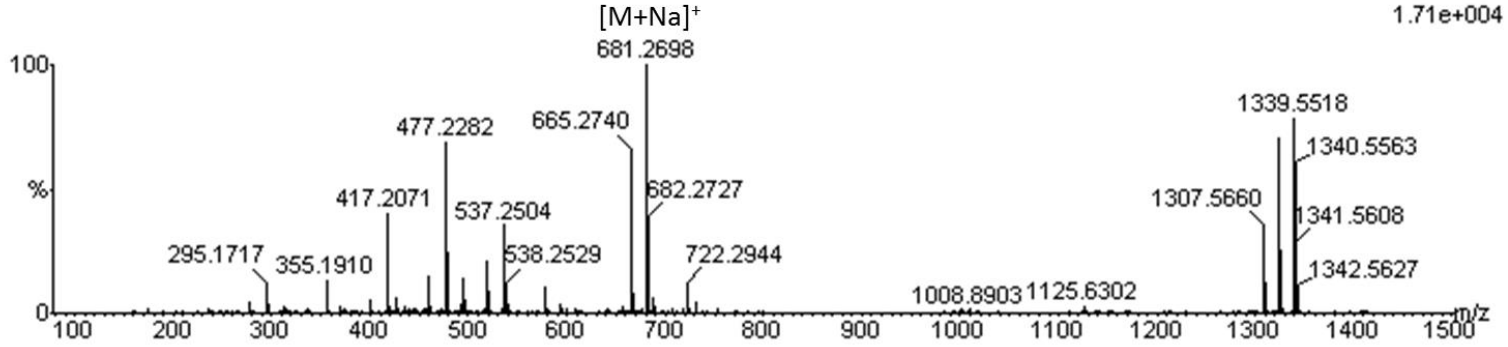


Figure S28. HRESIMS spectrum (TOF) of **11a**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
832 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

08-Jan-2016 16:31:00 LCT Premier XE KE483 ROUSSI_esposito24-2 686 (3.196)
1: TOF MS ES+



Minimum:				-1.5						
Maximum:		5.0	5.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
681.2698	681.2700	-0.2	-0.3	20.5	340.3	0.9	C40	H41	O10	
	681.2676	2.2	3.2	17.5	340.1	0.6	C38	H42	O10	Na [M+Na]+
	681.2665	3.3	4.8	-1.5	342.1	2.7	C22	H49	O23	

Figure S29. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **11b**

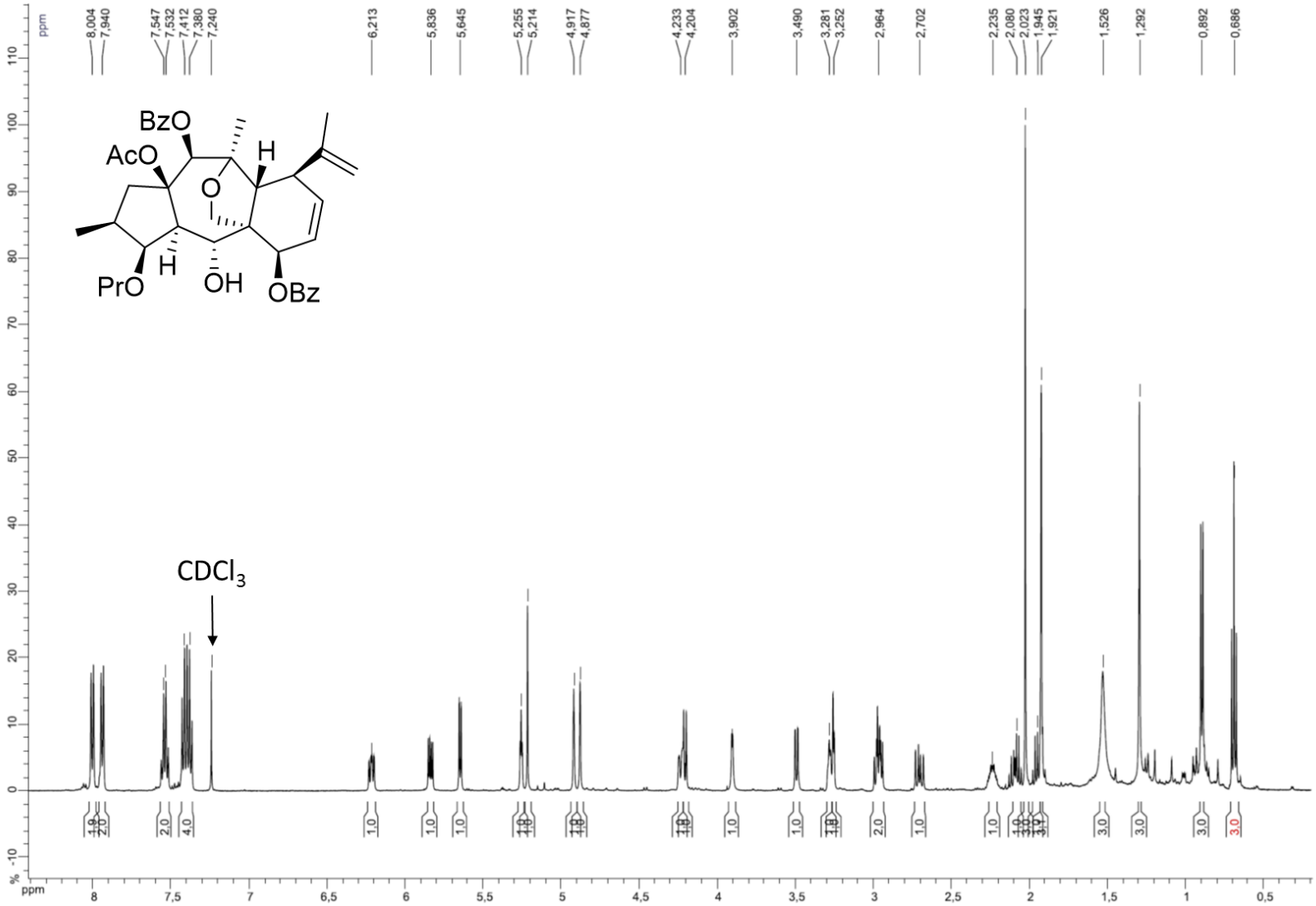


Figure S30. ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) of **11b**

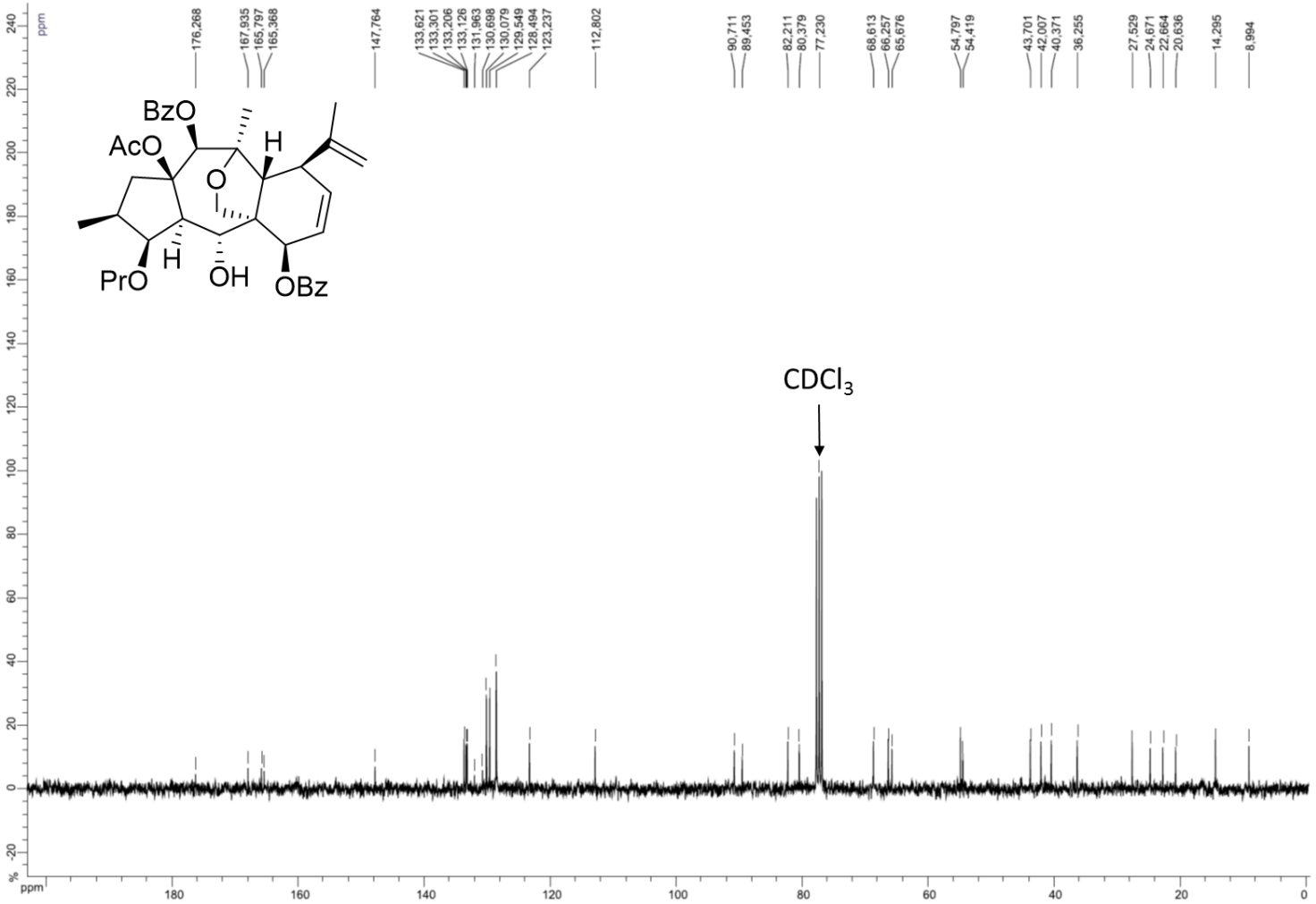


Figure S31. HMBC NMR spectrum ($CDCl_3$, 300 MHz) of **11b**

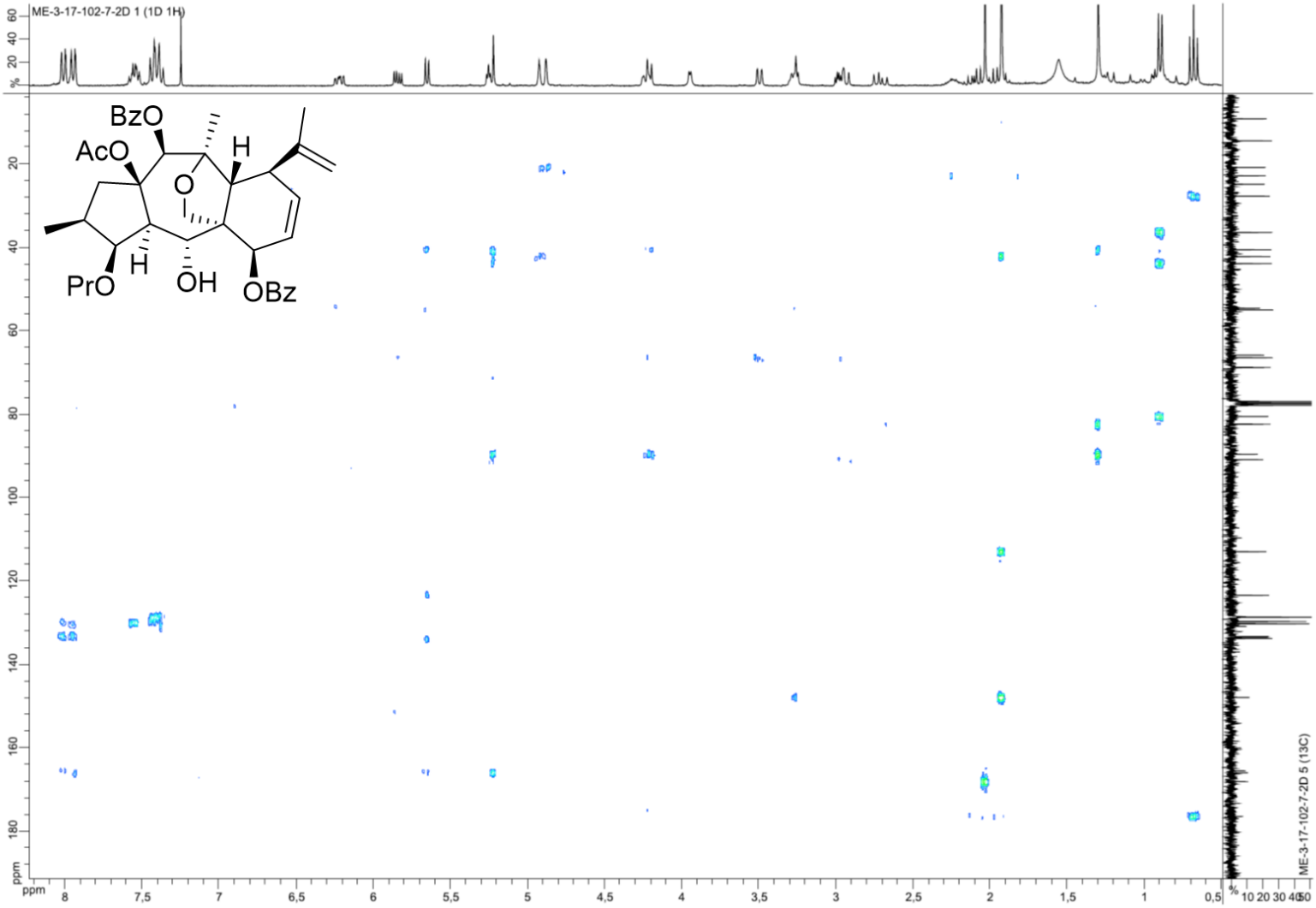


Figure S32. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **11b**

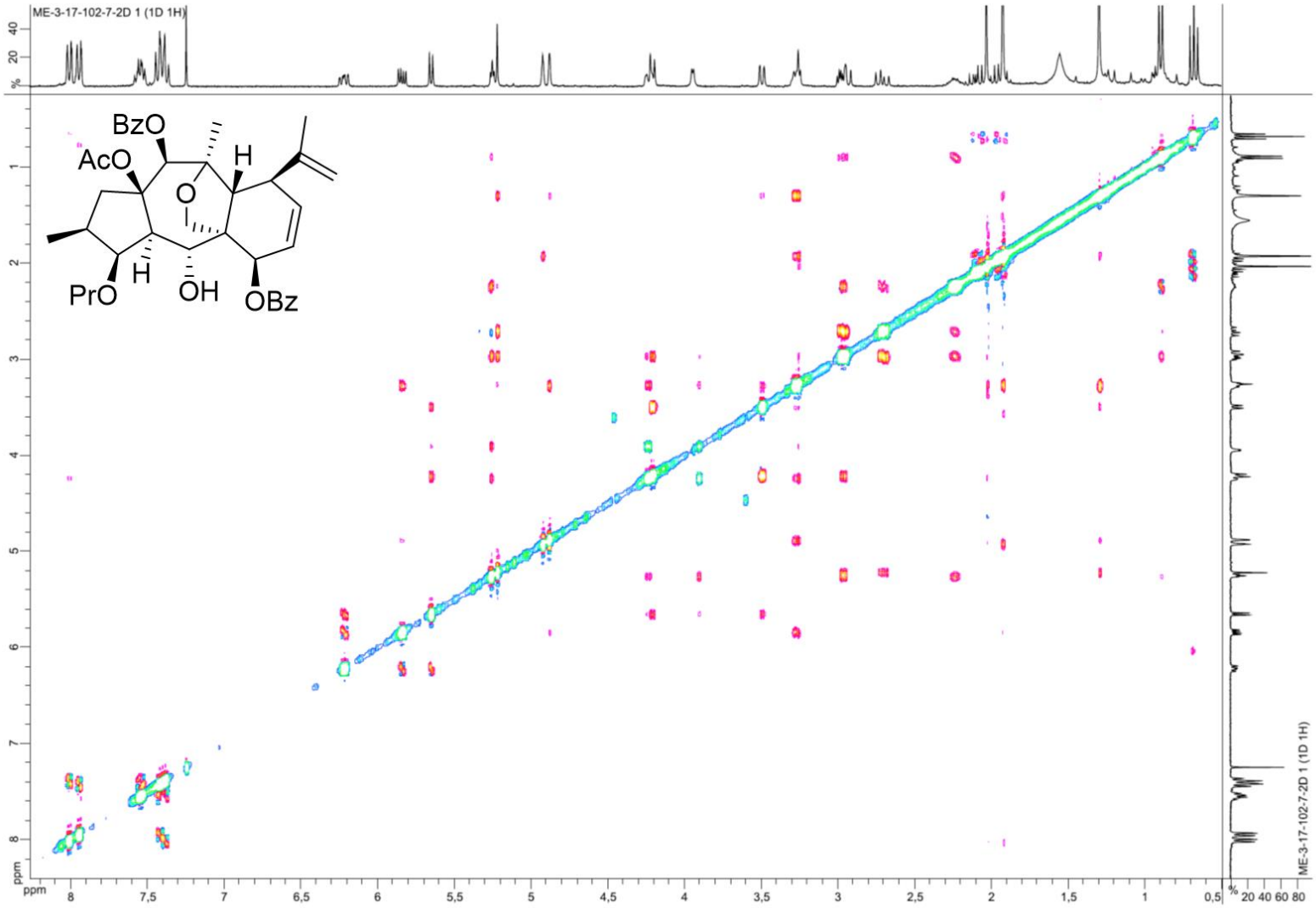


Figure S33. HRESIMS spectrum (TOF) of **11b**

Elemental Composition Report

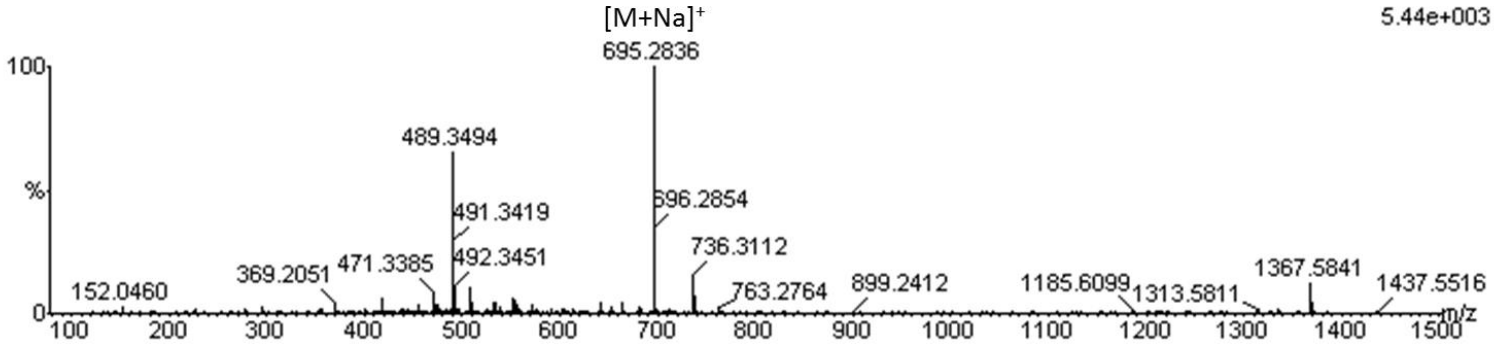
Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
863 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

05-Feb-2016 11:18:15 LCT Premier XE KE483 ROUSSI_esposito29-1 748 (3.454)
1: TOF MS ES+



Minimum:				-1.5						
Maximum:		5.0	5.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
695.2836	695.2832	0.4	0.6	17.5	243.3	3.3	C39	H44	O10	Na [M+Na]+
	695.2821	1.5	2.2	-1.5	240.1	0.0	C23	H51	O23	
	695.2856	-2.0	-2.9	20.5	245.0	4.9	C41	H43	O10	

Figure S34. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **11c**

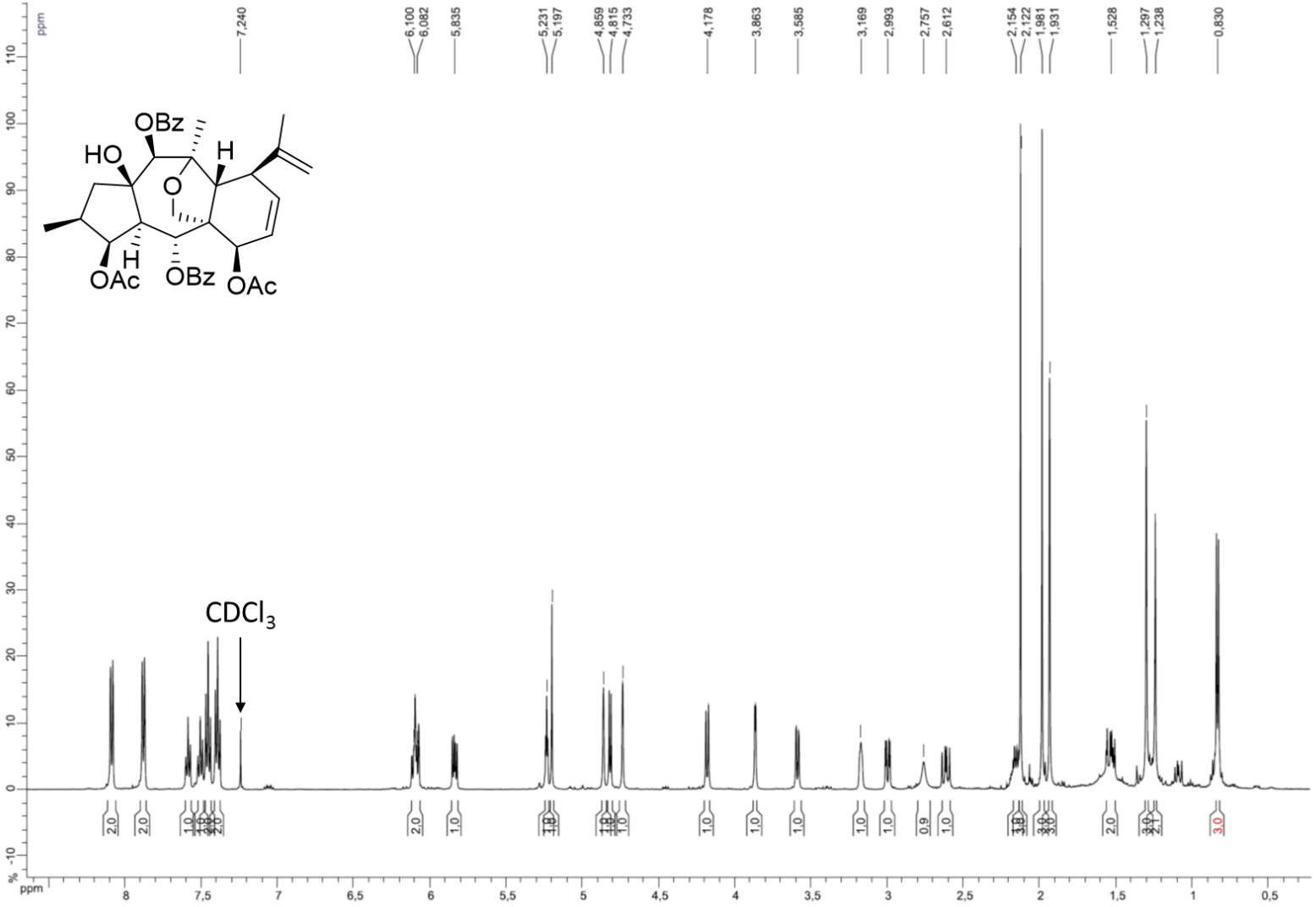


Figure S35. ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) of **11c**

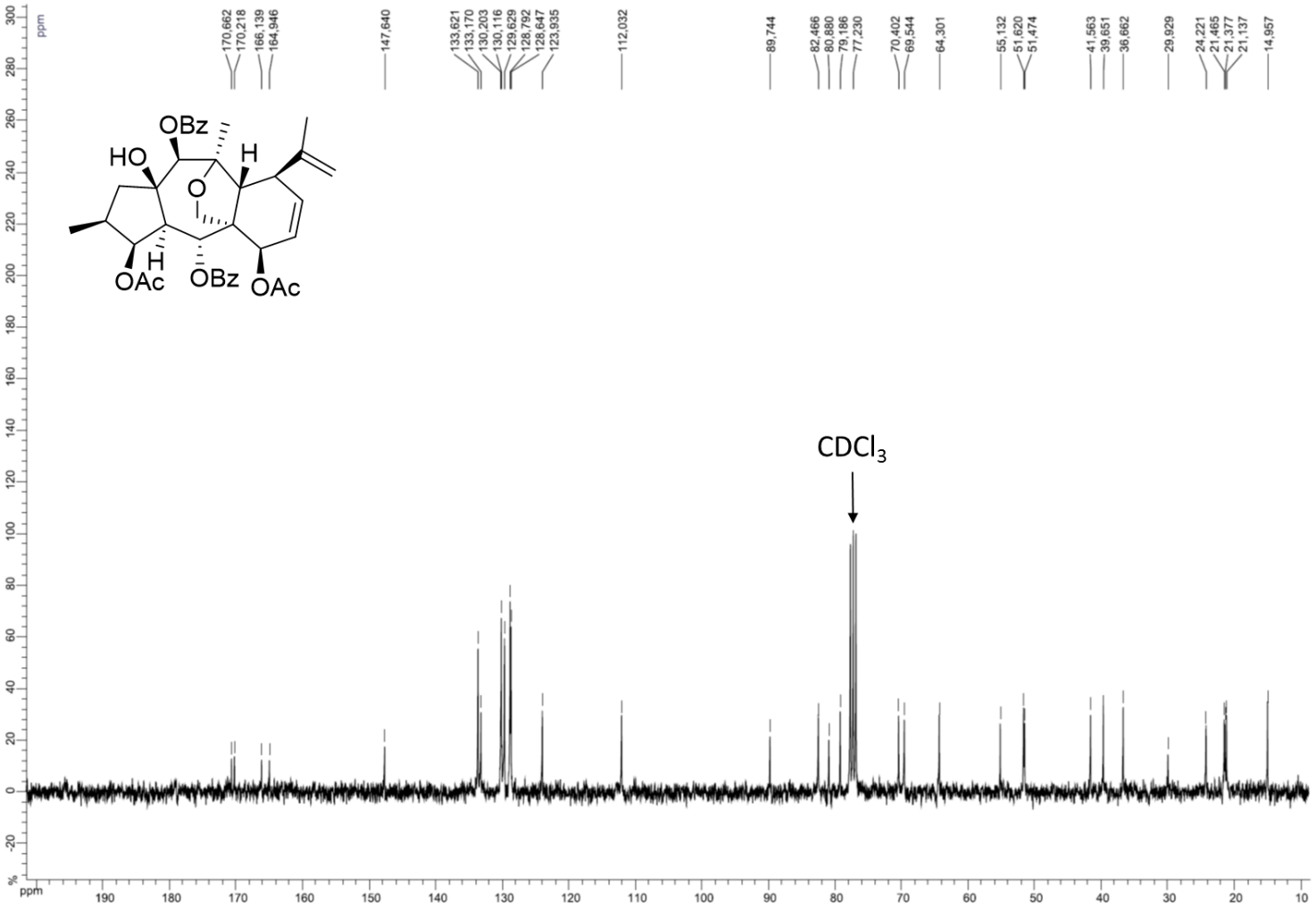


Figure S36. HMBC NMR spectrum ($CDCl_3$, 300 MHz) of **11c**

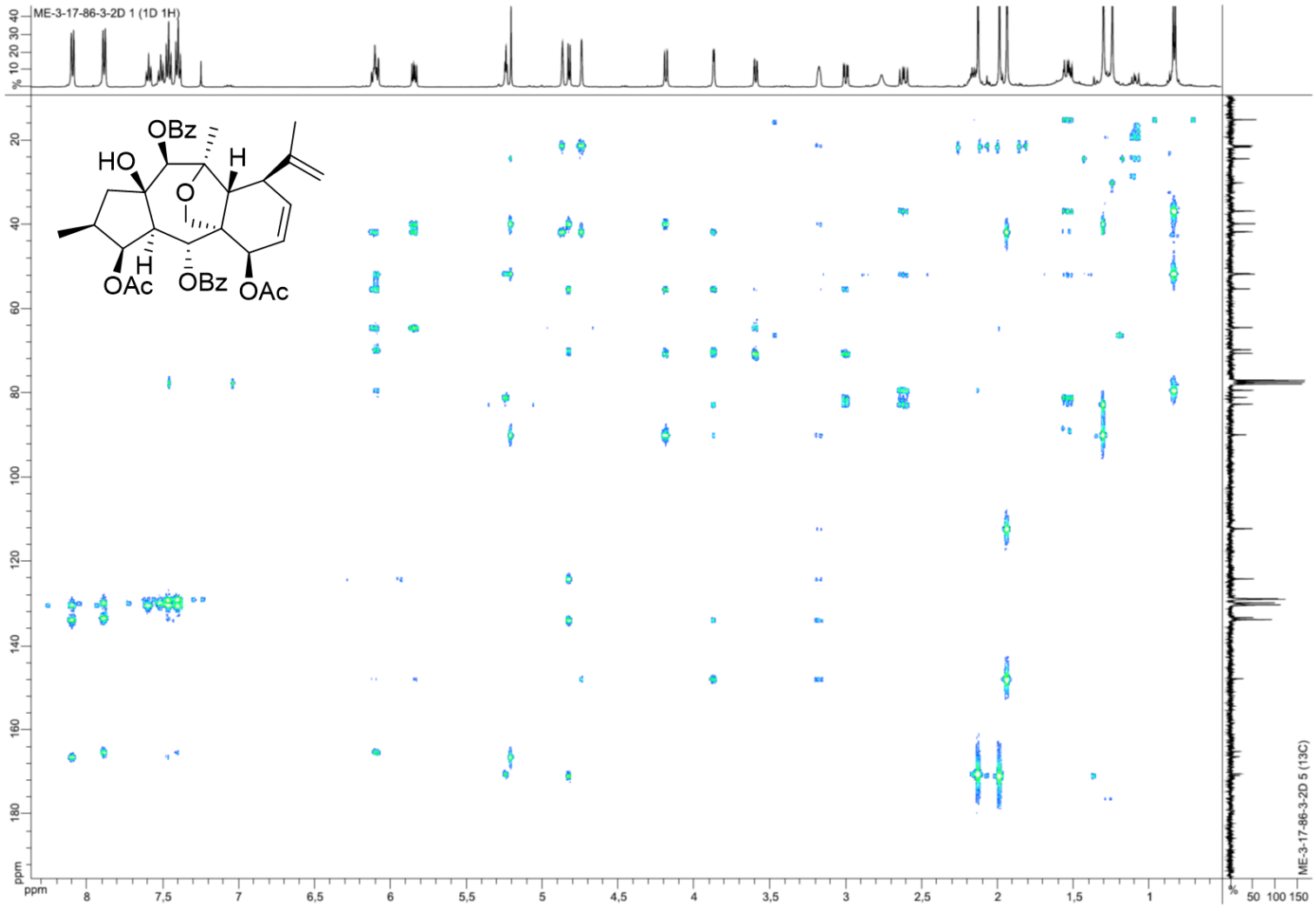


Figure S37. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **11c**

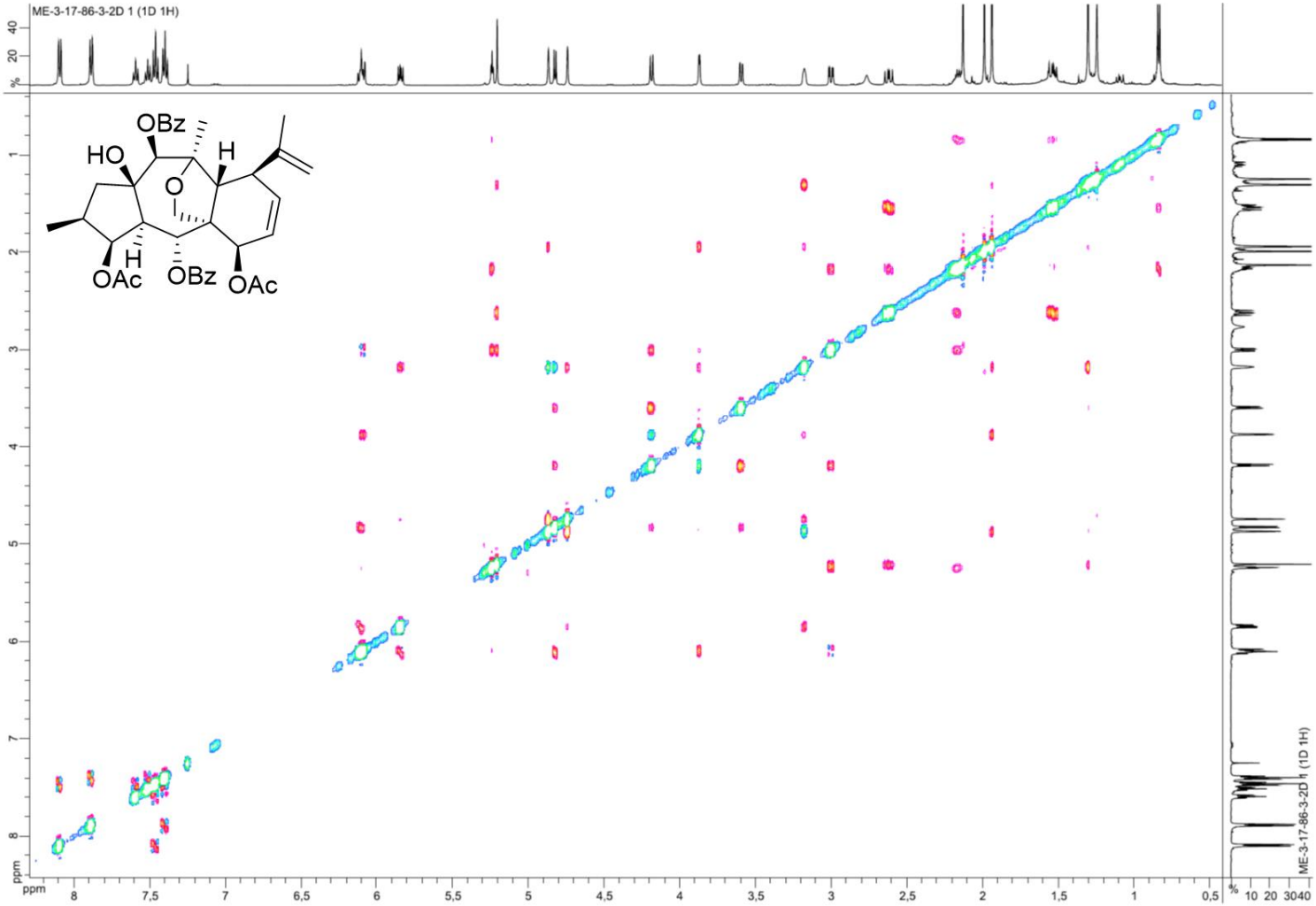


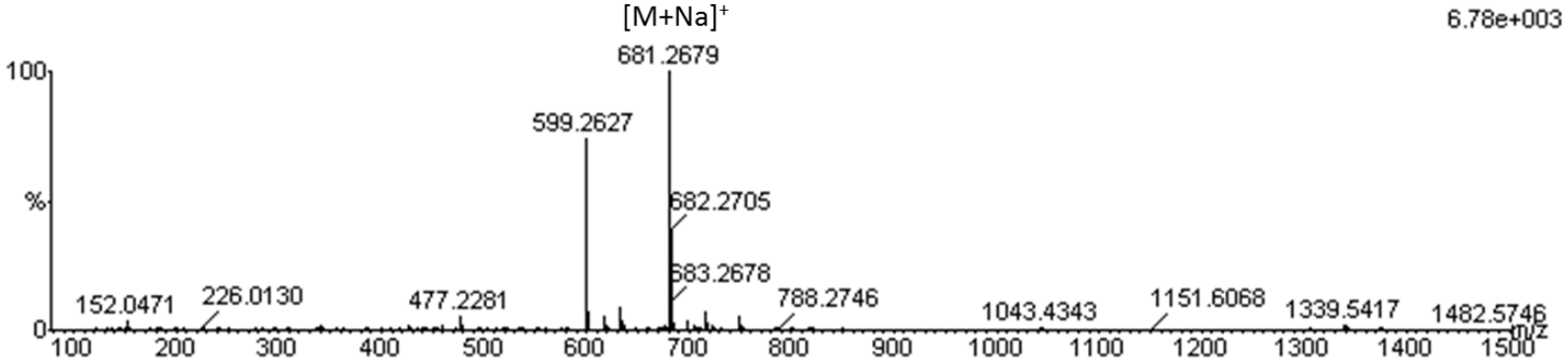
Figure S38. HRESIMS spectrum (TOF) of **11c**

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
832 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

08-Jan-2016 17:50:07 LCT Premier XE KE483 ROUSSI_esposito25-4 709 (3.312)
1: TOF MS ES+



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
681.2679	681.2676	0.3	0.4	17.5	217.1	0.0	C38	H42	O10	Na	[M+Na]+
	681.2665	1.4	2.1	-1.5	226.1	9.1	C22	H49	O23		
	681.2700	-2.1	-3.1	20.5	220.7	3.6	C40	H41	O10		

Figure S39. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **11d**

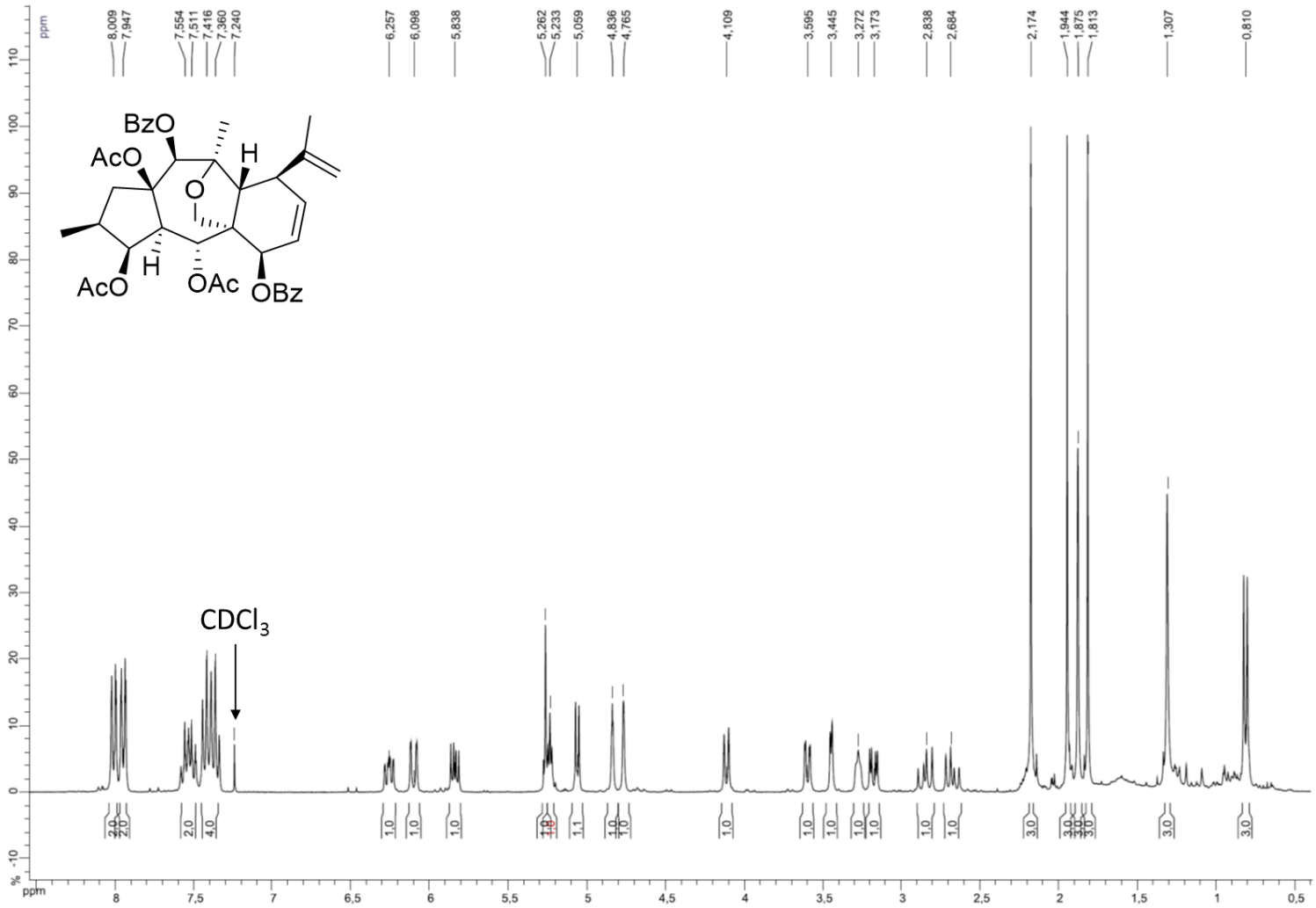


Figure S40. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **11e**

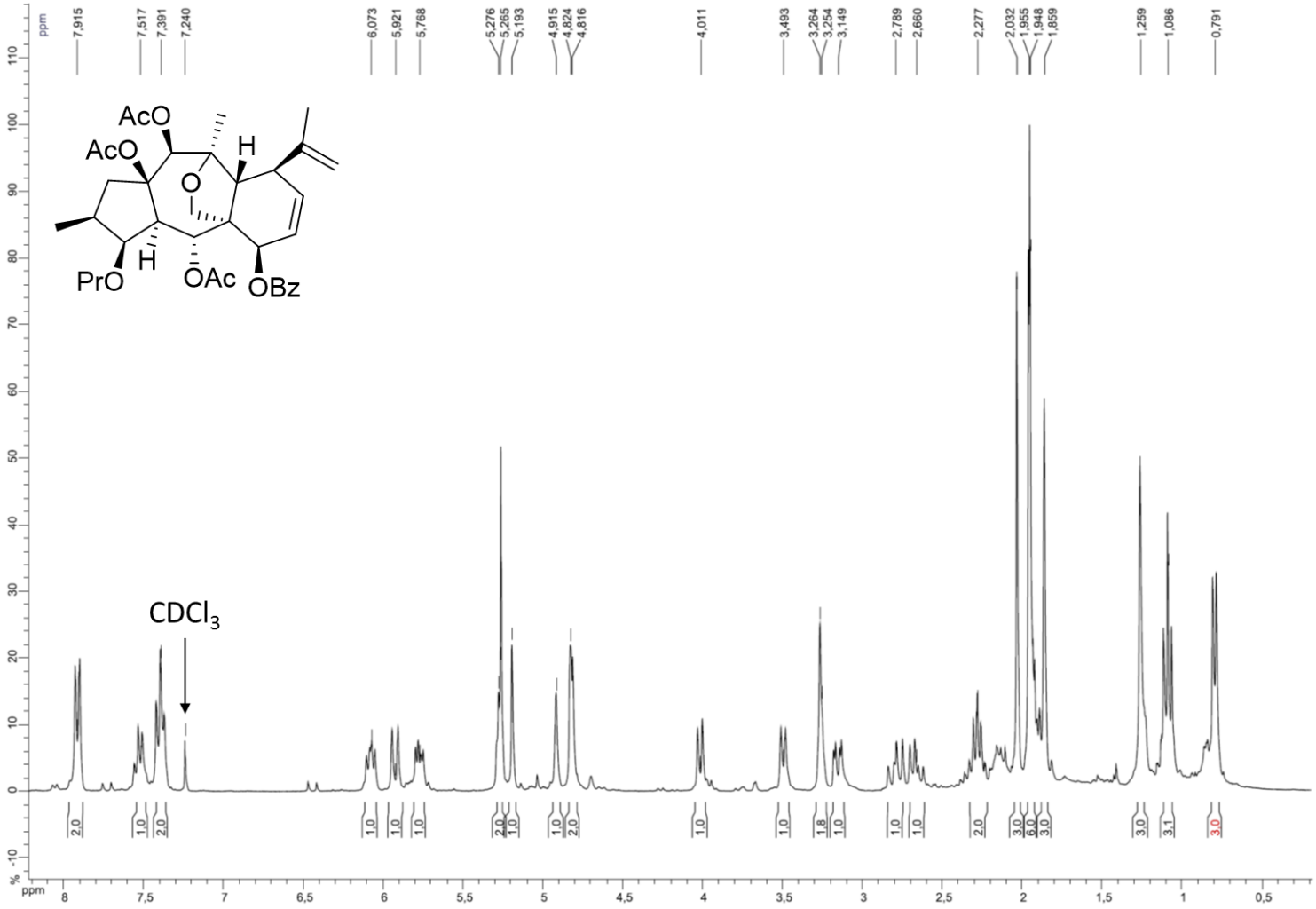


Figure S41. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **11f**

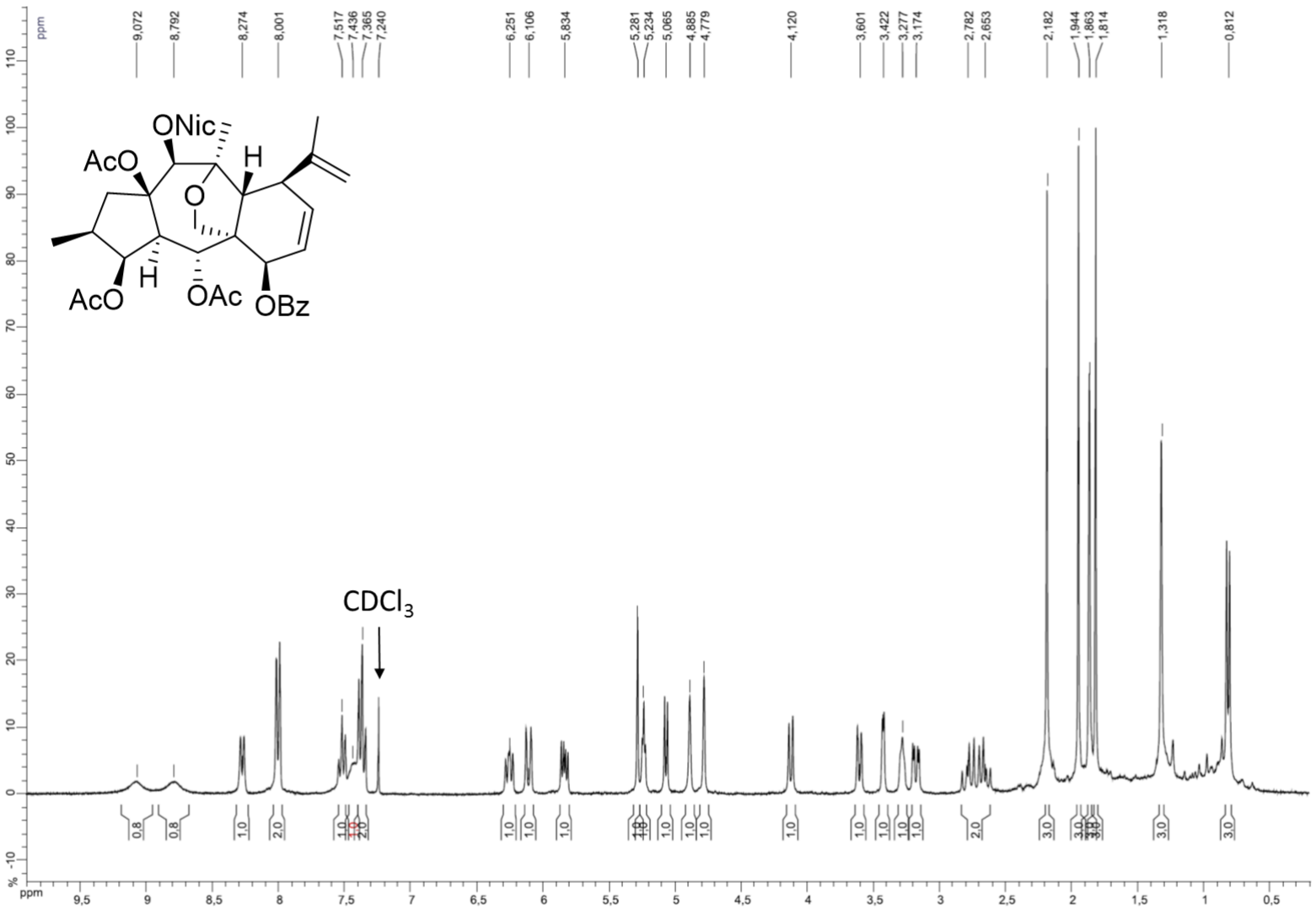


Figure S42. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **11g**

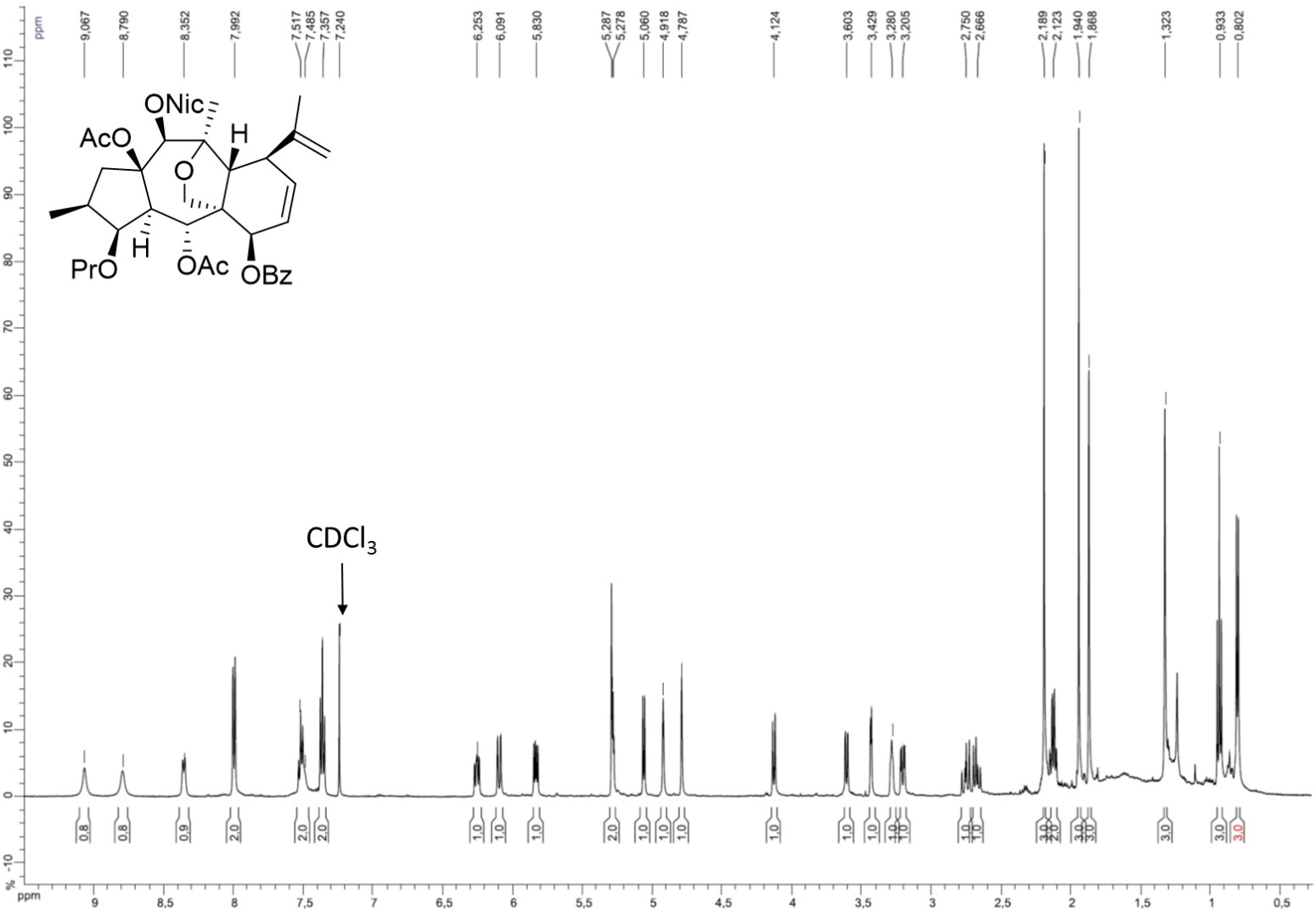


Figure S43. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **11h**

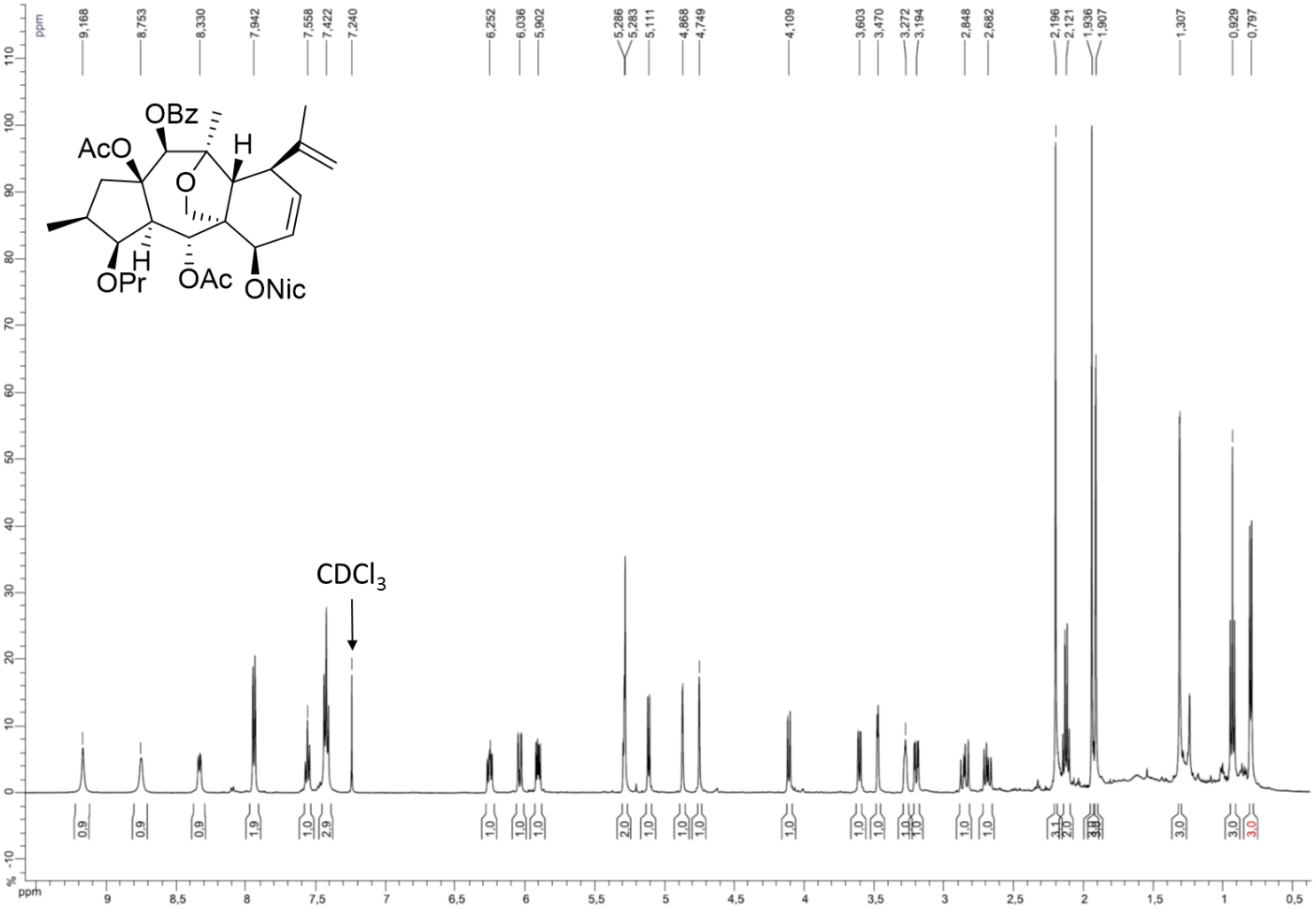


Figure S44. HMBC NMR spectrum ($CDCl_3$, 500 MHz) of **11h**

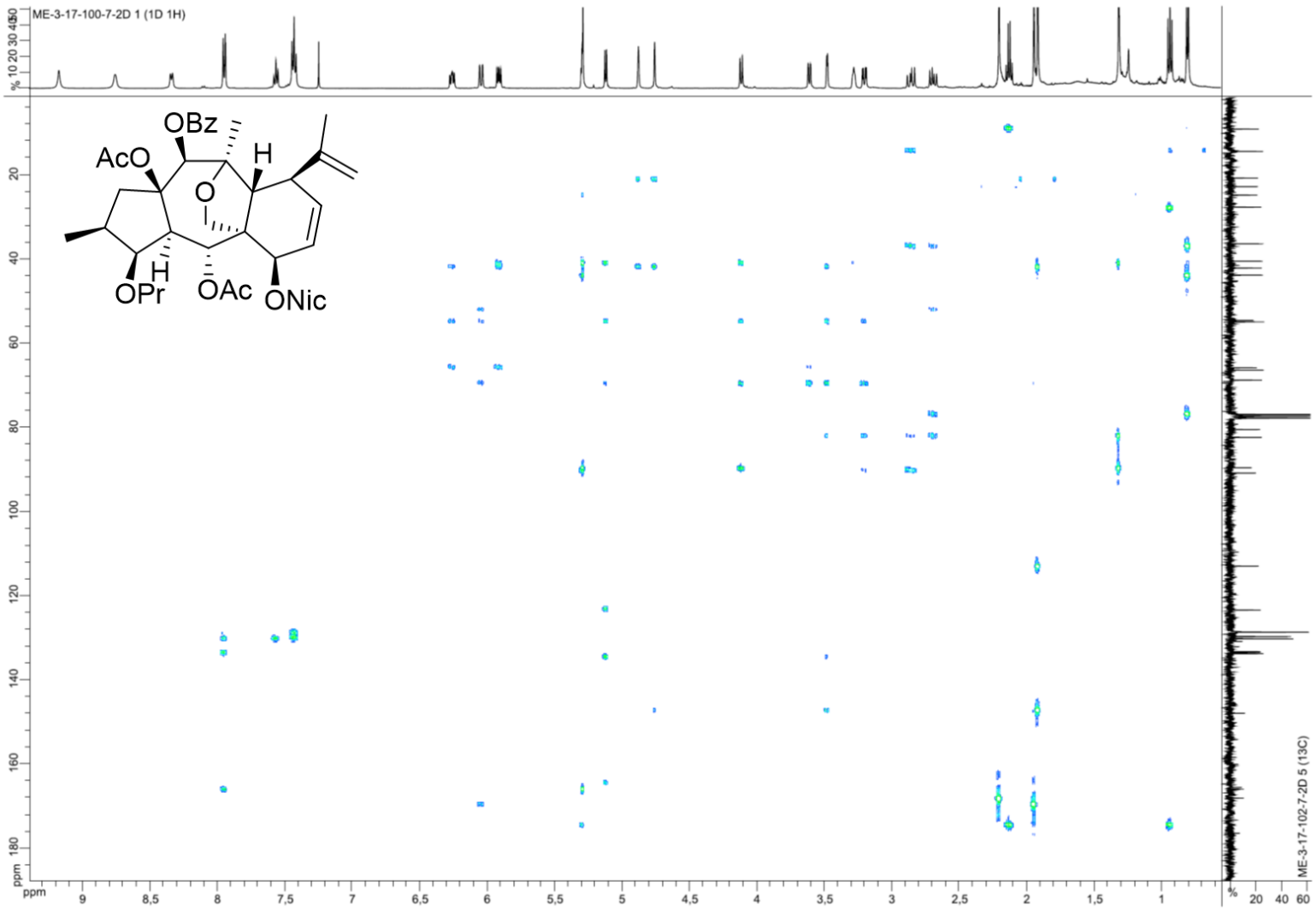


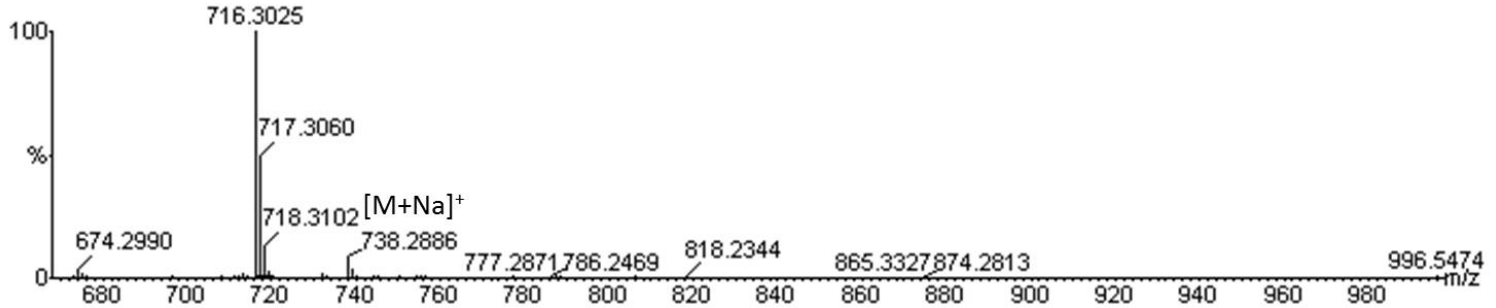
Figure S45. HRESIMS spectrum (TOF) of **11h**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
952 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

08-Jan-2016 16:53:33 LCT Premier XE KE483 ROUSSI_esposito24-4 670 (3.143)
1: TOF MS ES+

7.49e+003



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
738.2886	738.2890	-0.4	-0.5	18.5	102.4	0.8	C40 Na	H45	N	O11	[M+Na]+
	738.2879	0.7	0.9	-0.5	102.3	0.6	C24	H52	N	O24	
	738.2914	-2.8	-3.8	21.5	105.7	4.1	C42	H44	N	O11	
	738.2856	3.0	4.1	30.5	107.0	5.4	C49	H40	N	O6	

Figure S46. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **12**

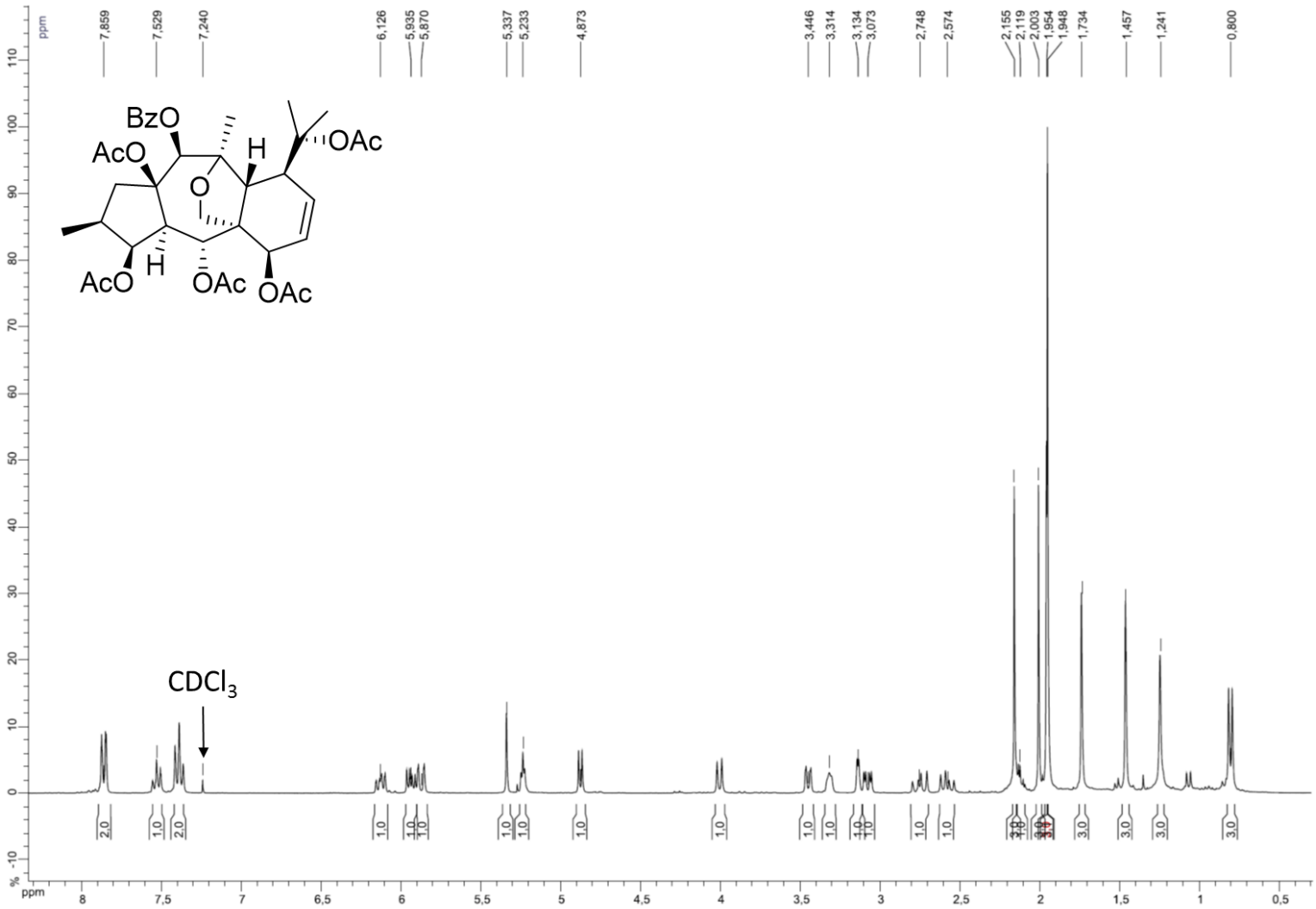


Figure S47. ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) of **12**

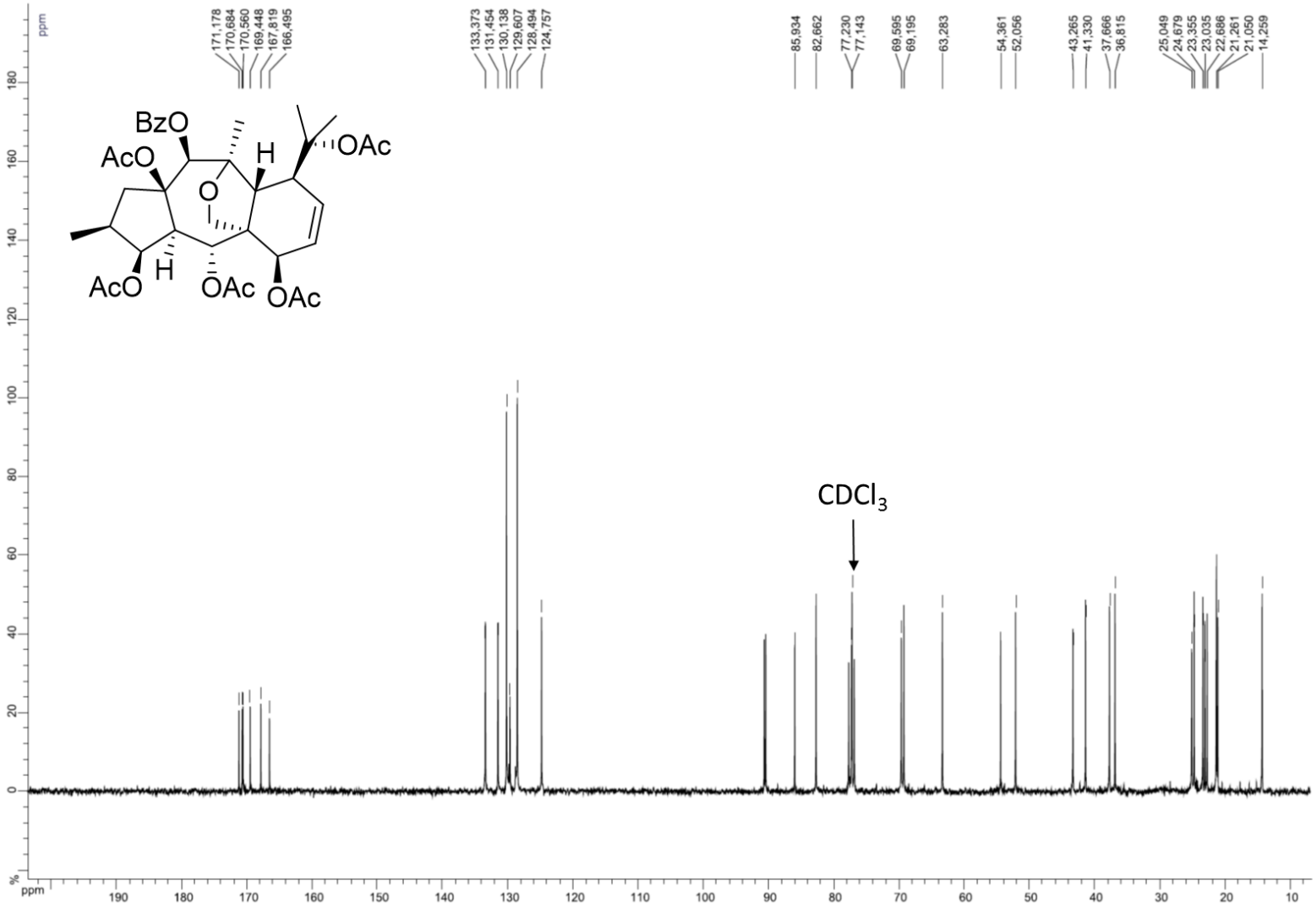


Figure S48. HMBC NMR spectrum ($CDCl_3$, 300 MHz) of **12**

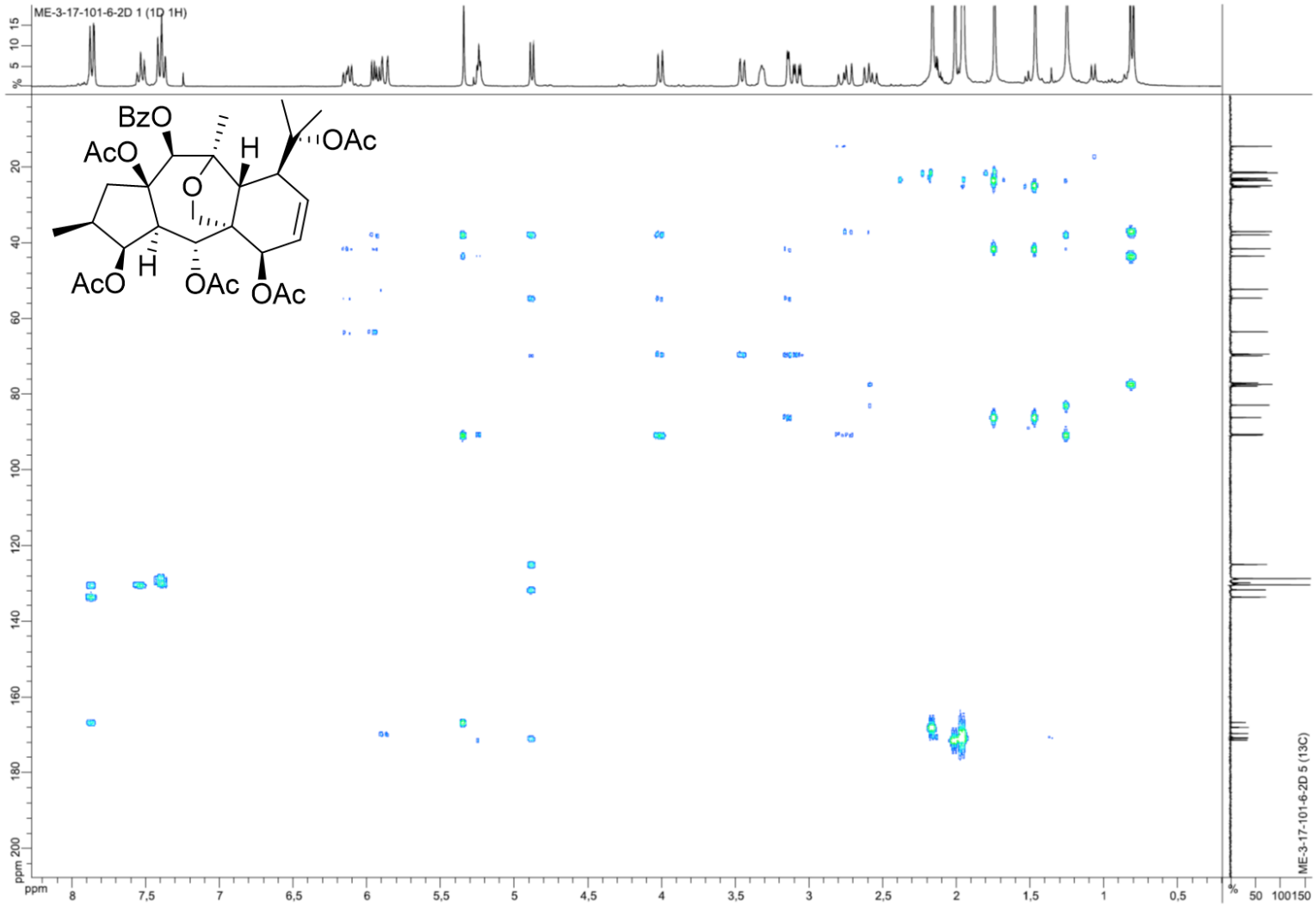


Figure S49. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **12**

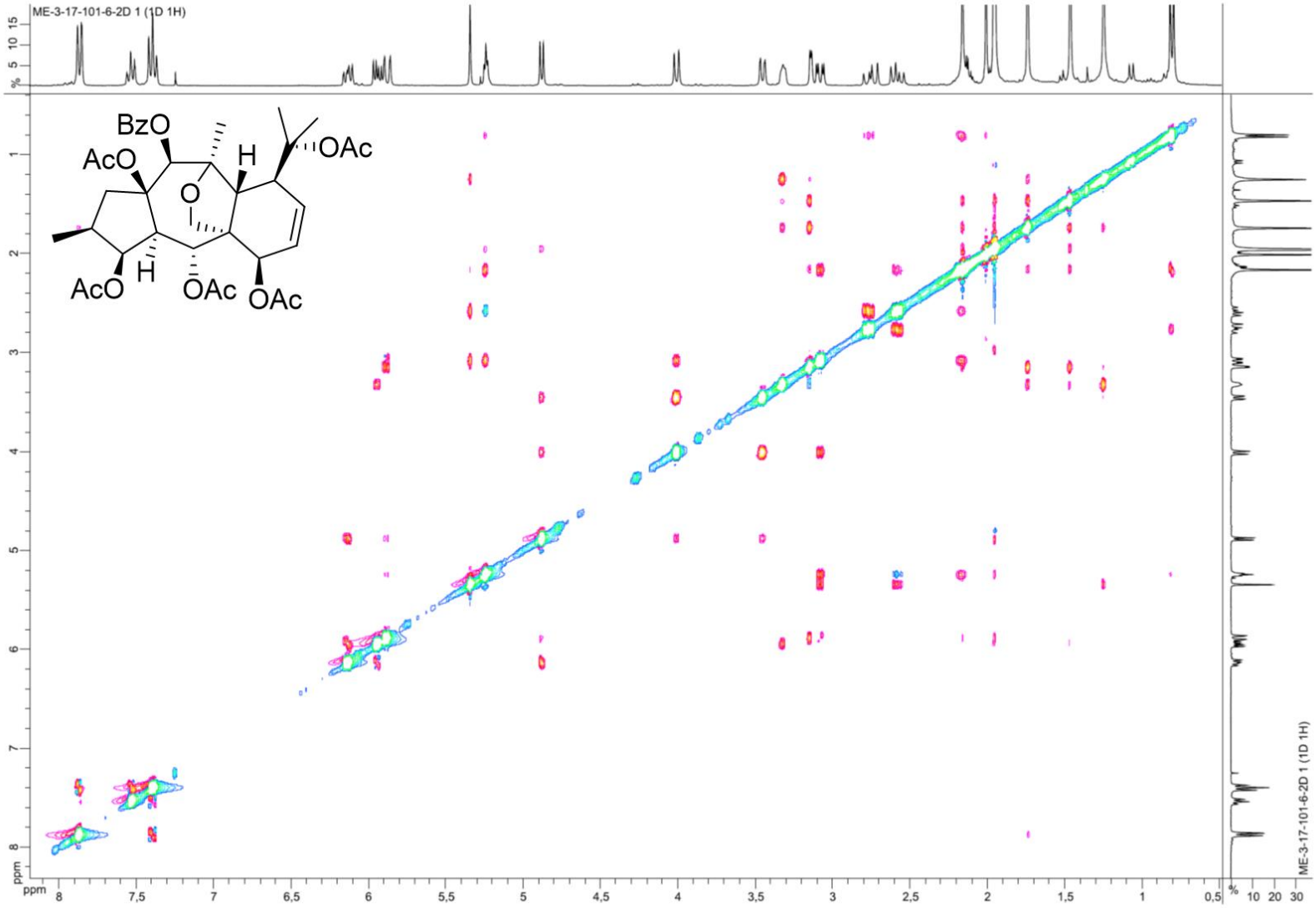
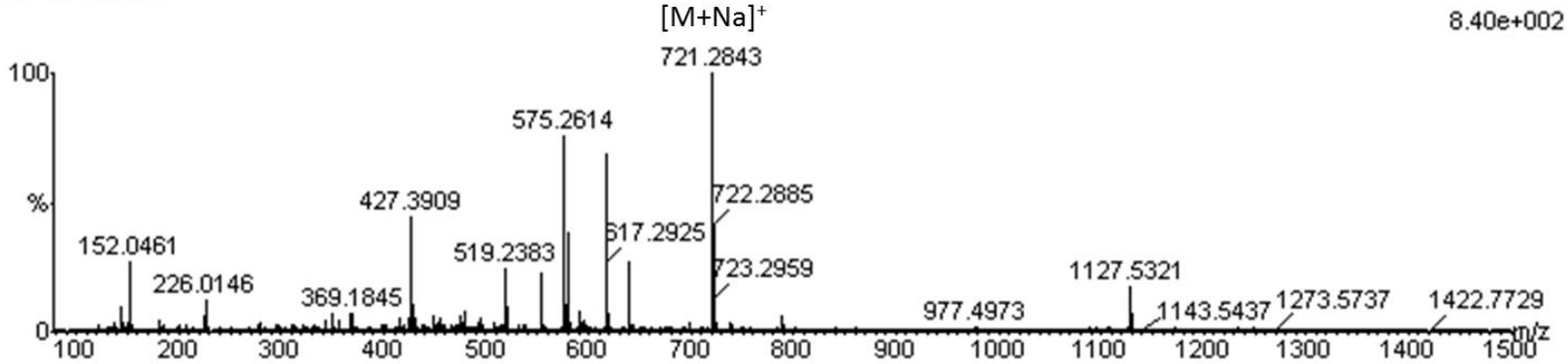


Figure S50. HRESIMS spectrum (TOF) of **12**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
918 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

08-Jan-2016 16:19:44 LCT Premier XE KE483 ROUSSI_esposito24-1 691 (3.214)
1: TOF MS ES+



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
721.2843	721.2836	0.7	1.0	14.5	120.8	0.9	C37	H46	O13	Na	$[M+Na]^+$
	721.2860	-1.7	-2.4	17.5	120.4	0.5	C39	H45	O13		
	721.2871	-2.8	-3.9	36.5	127.9	8.1	C55	H38	Na		

Figure S51. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **13**

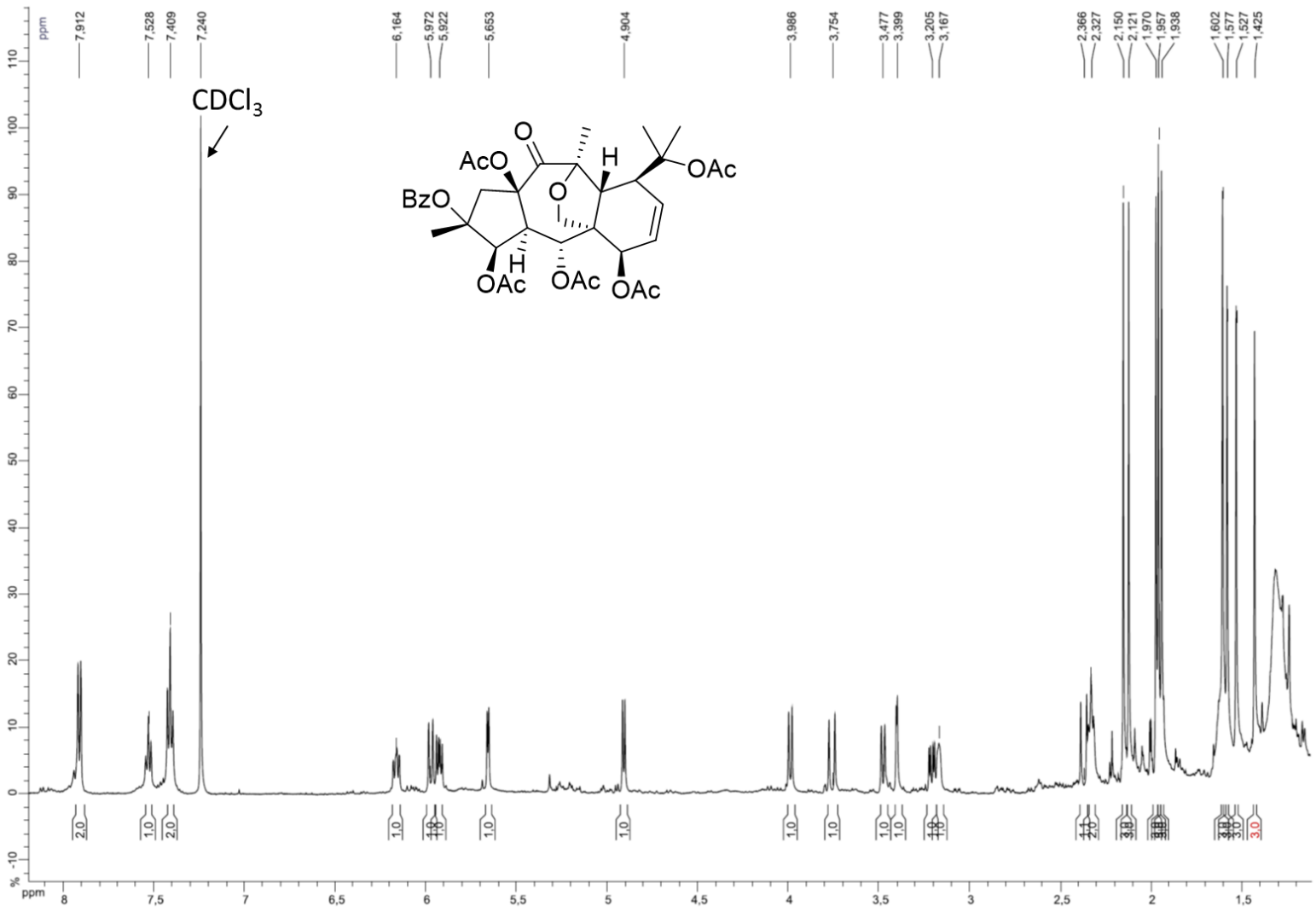


Figure S52. ^{13}C NMR spectrum ($CDCl_3$, 500 MHz) of **13**

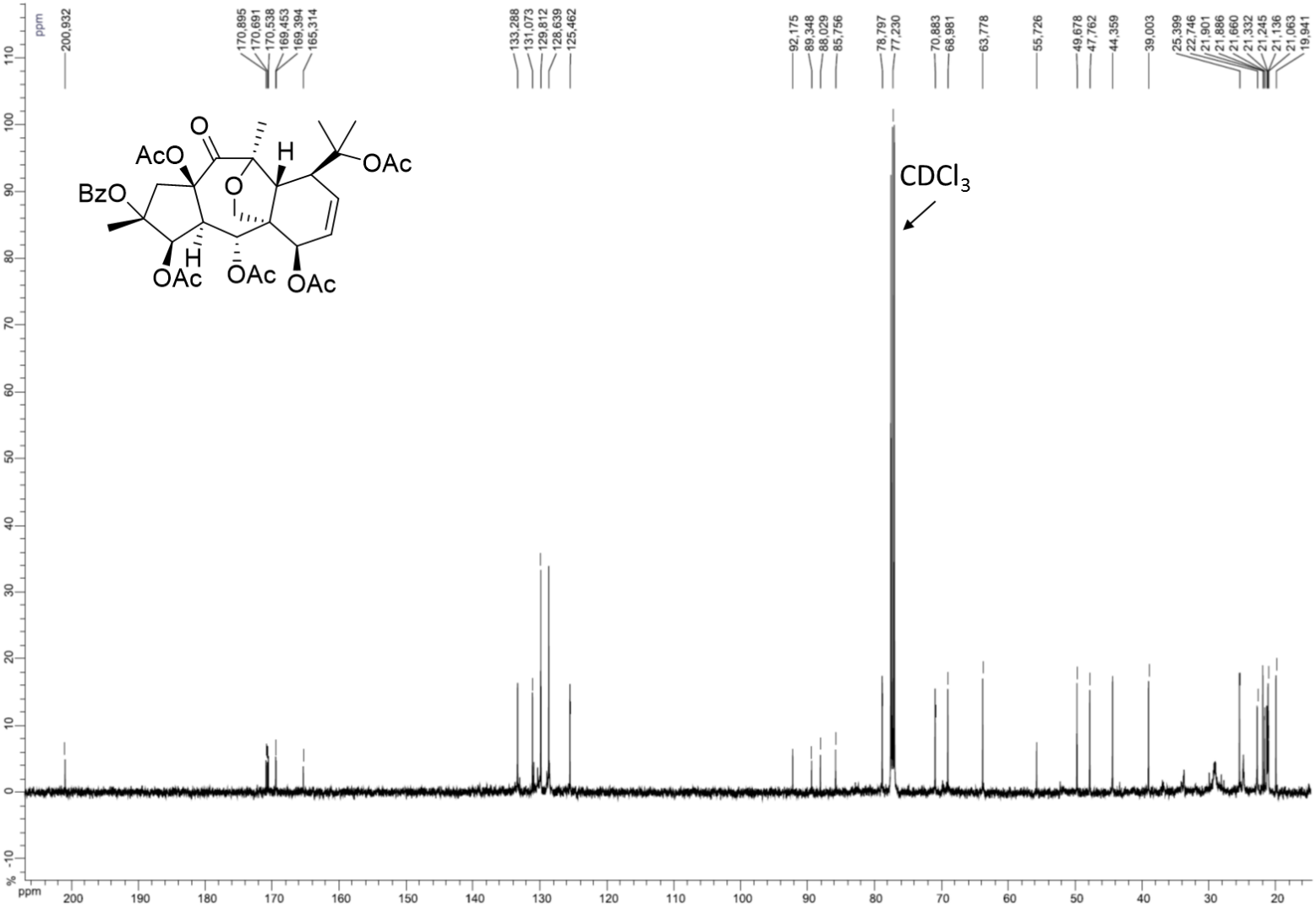


Figure S53. HMBC NMR spectrum ($CDCl_3$, 500 MHz) of **13**

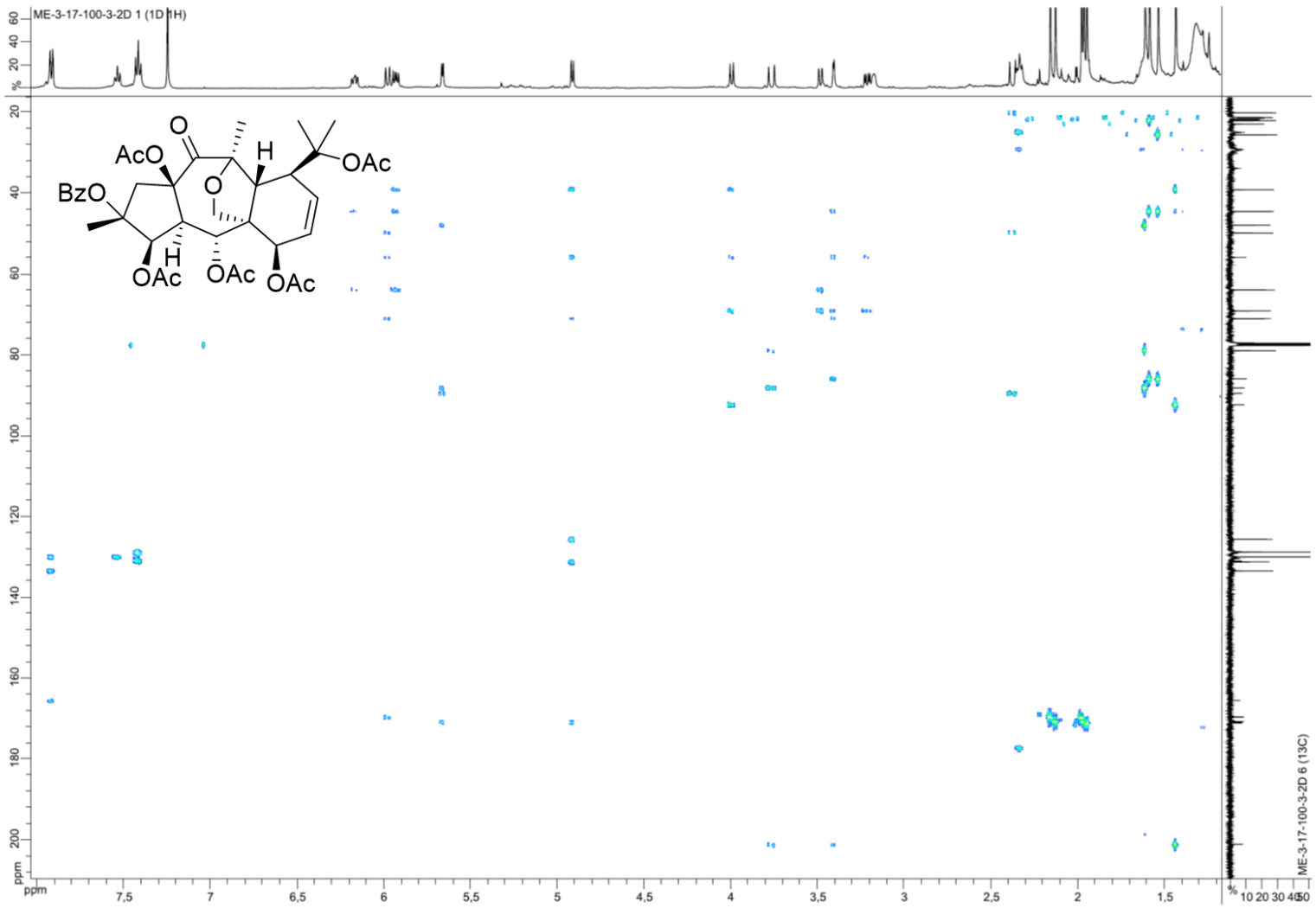


Figure S54. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **13**

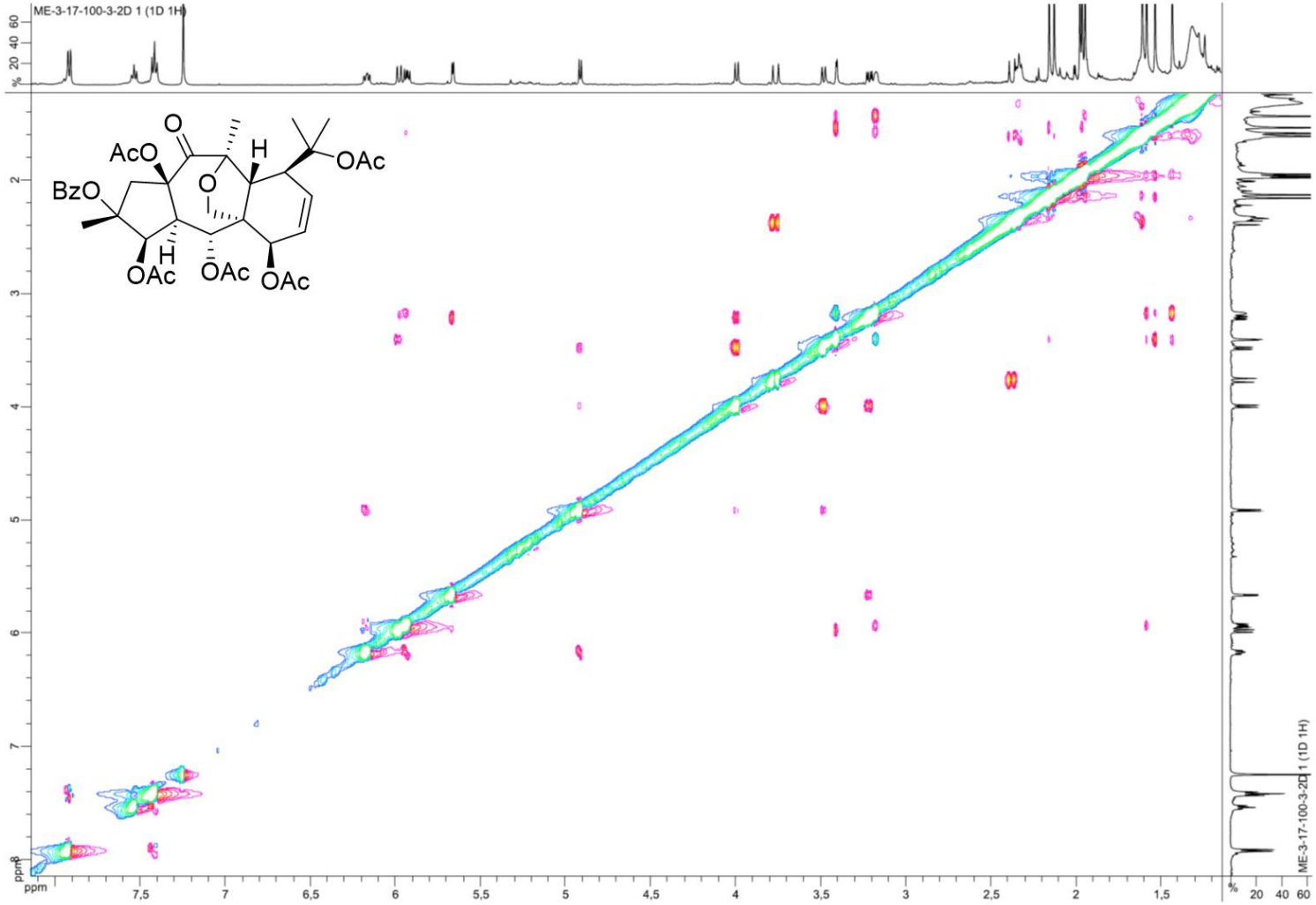
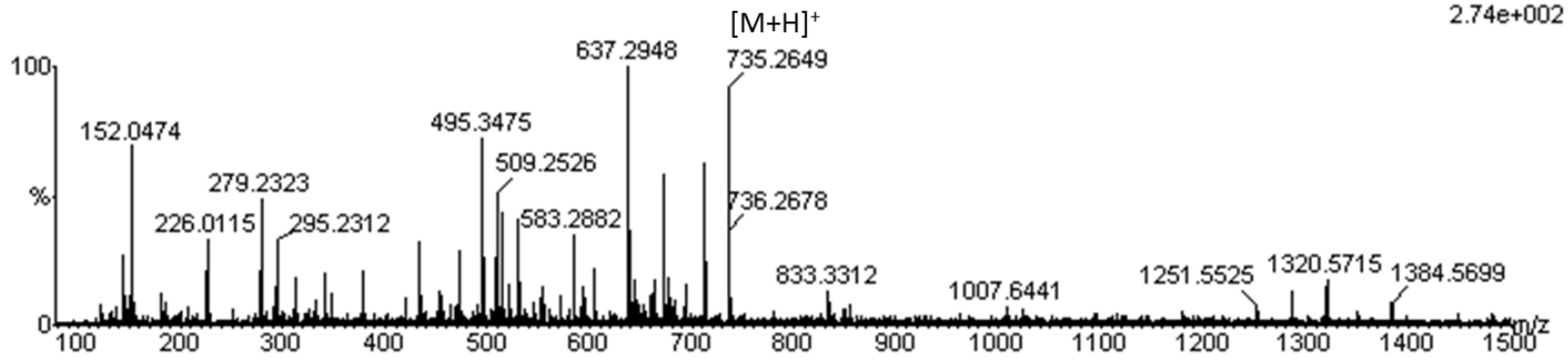


Figure S55. HRESIMS spectrum (TOF) of **13**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
948 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

08-Jan-2016 15:22:33 LCT Premier XE KE483 ROUSSI_esposito23-2 684 (3.159)
1: TOF MS ES+



Minimum:				-1.5			
Maximum:		5.0	5.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
735.2649	735.2653	-0.4	-0.5	18.5	111.8	0.6	C39 H43 O14 $[M+H]^+$
	735.2664	-1.5	-2.0	37.5	115.1	3.9	C55 H36 O Na
	735.2629	2.0	2.7	15.5	112.1	0.9	C37 H44 O14 Na

Figure S56. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **14a**

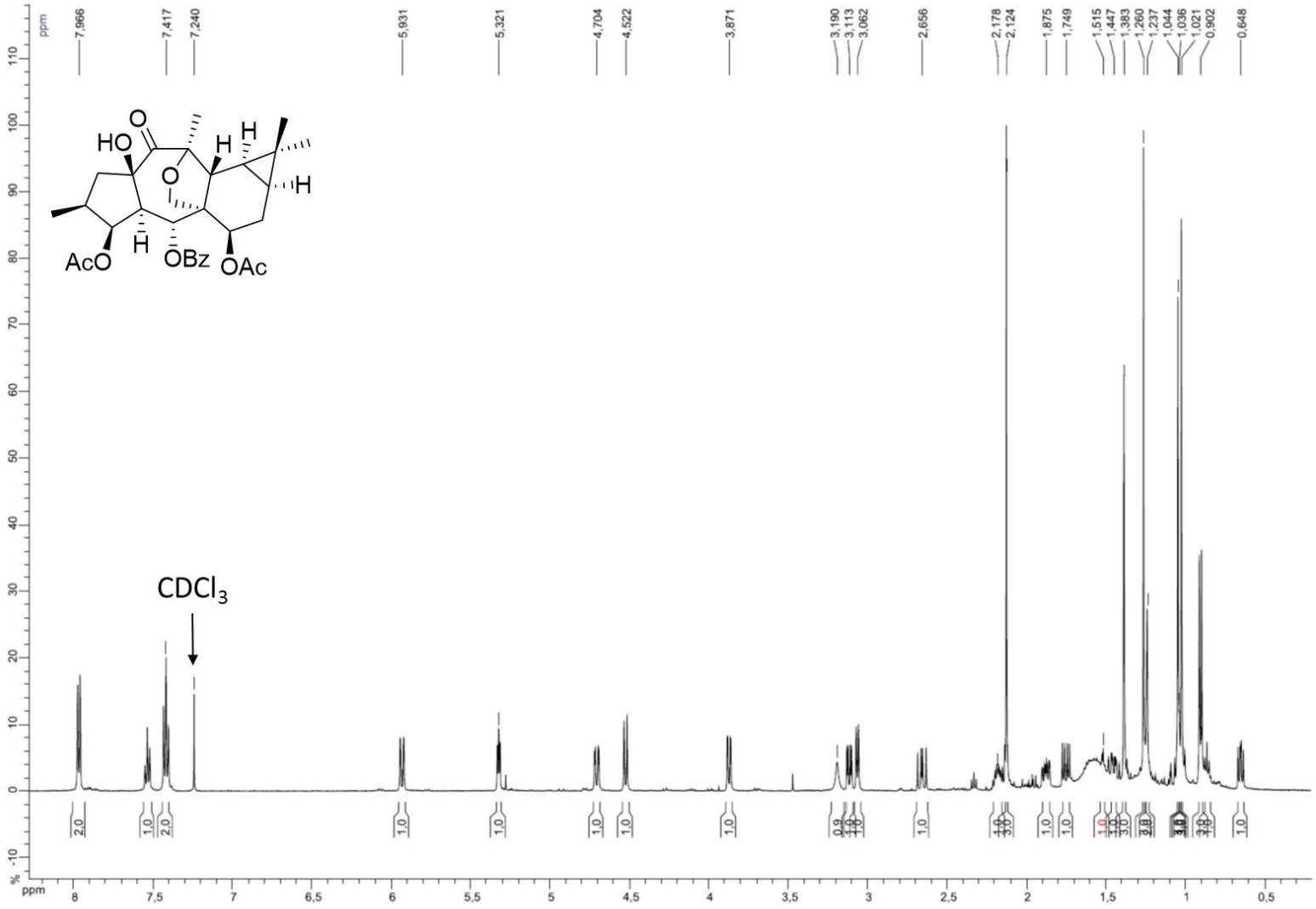


Figure S57. ^{13}C NMR spectrum ($CDCl_3$, 125 MHz) of **14a**

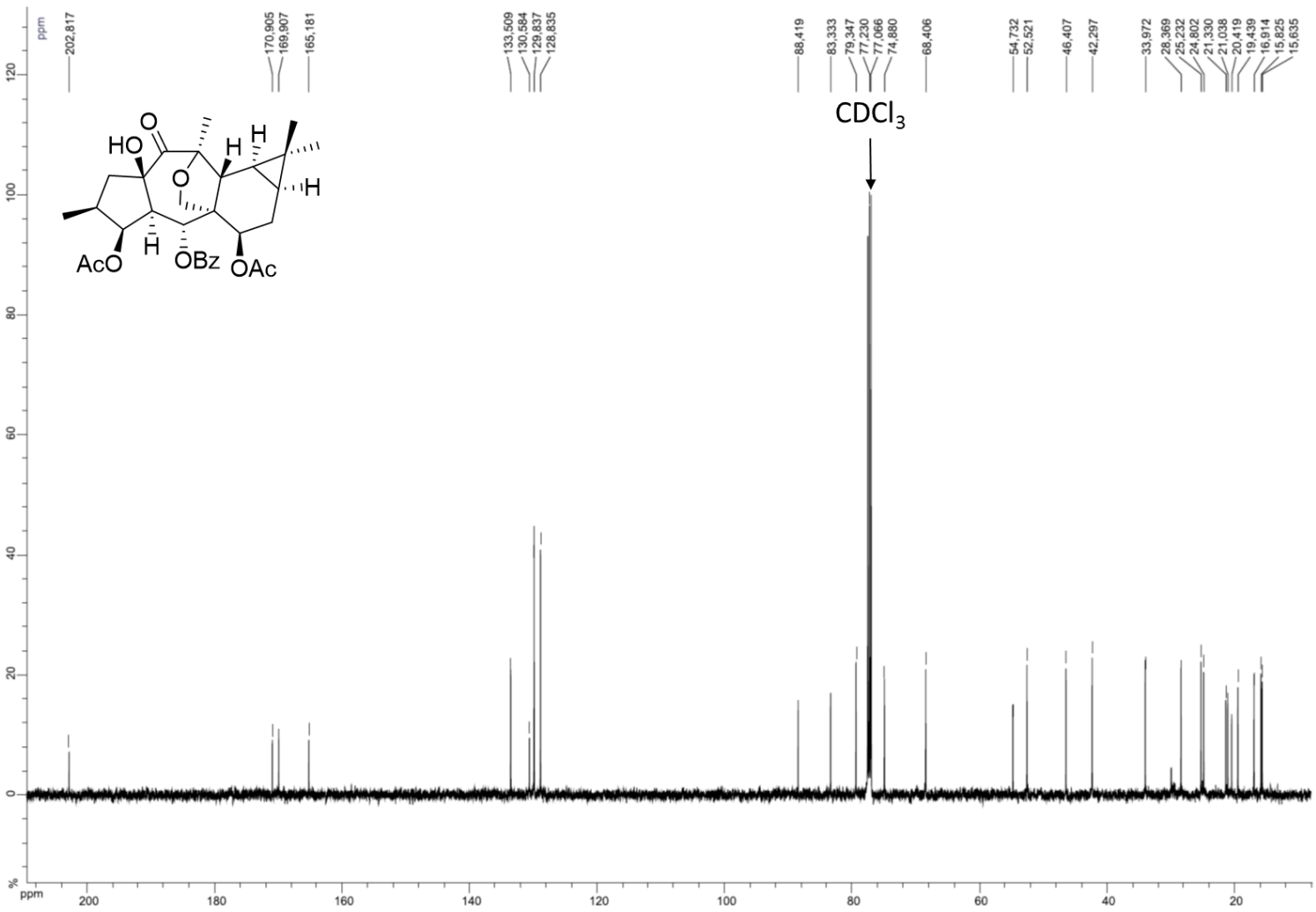


Figure S58. HMBC NMR spectrum ($CDCl_3$, 500 MHz) of **14a**

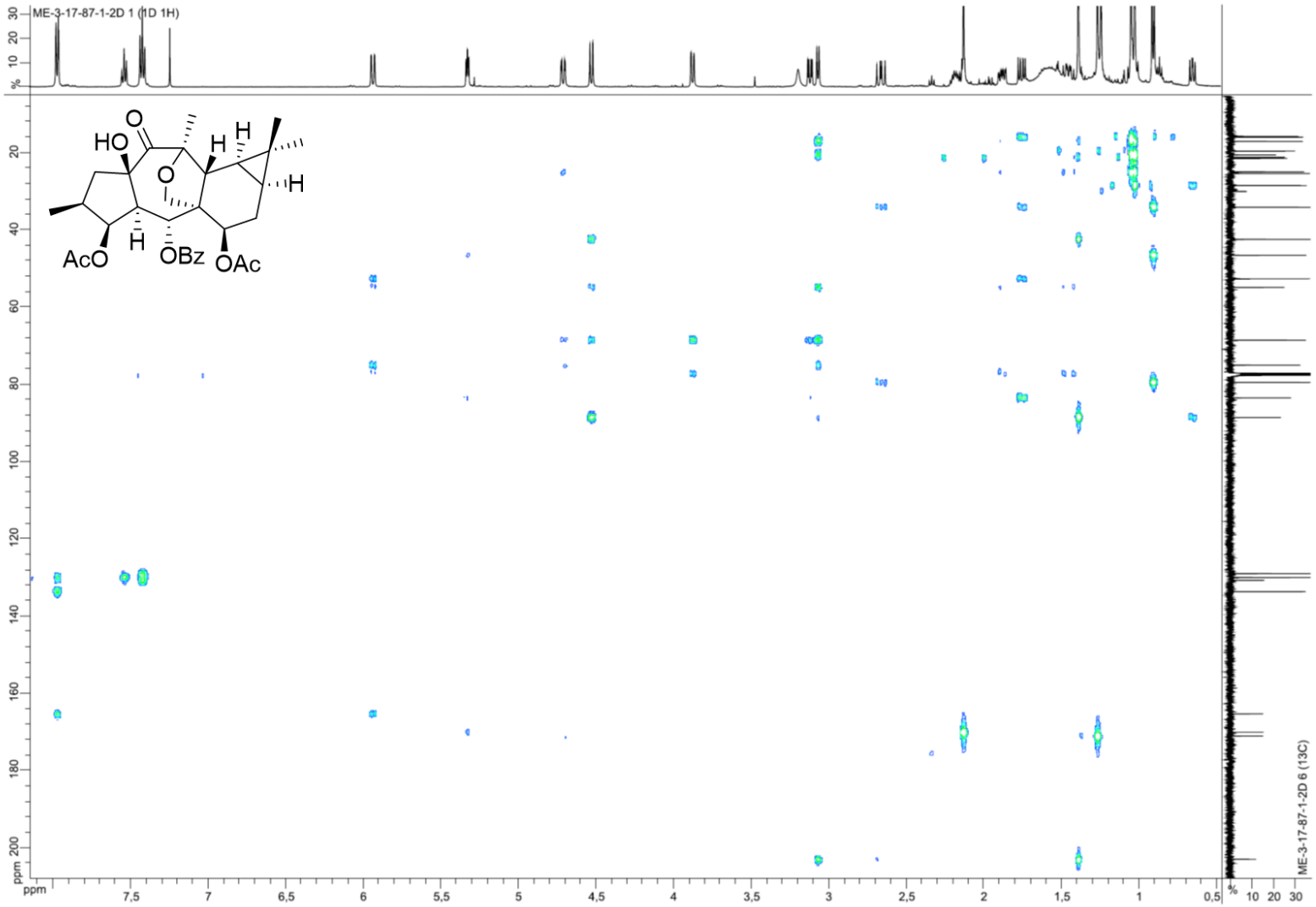


Figure S59. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **14a**

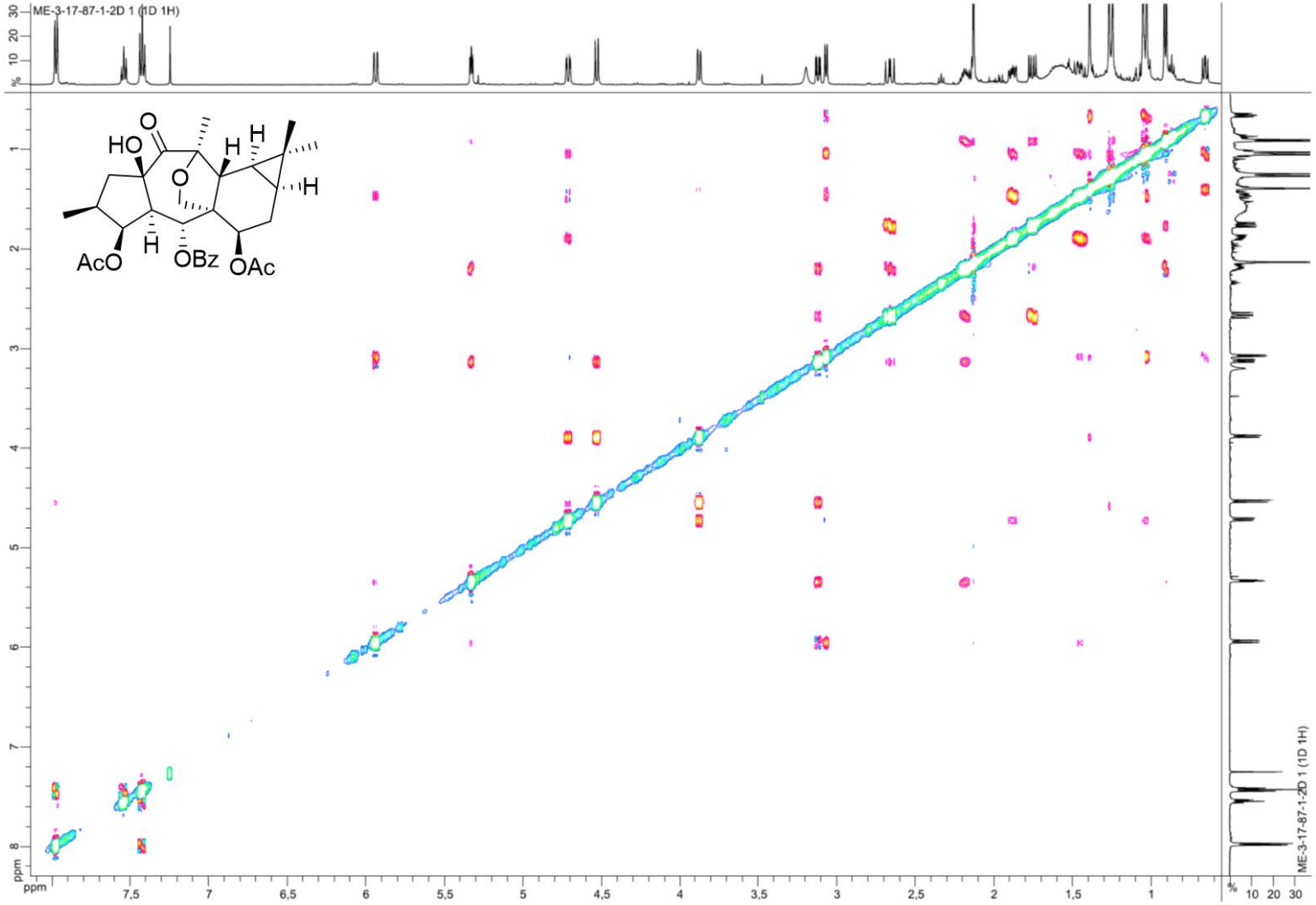


Figure S60. HRESIMS spectrum (TOF) of **14a**

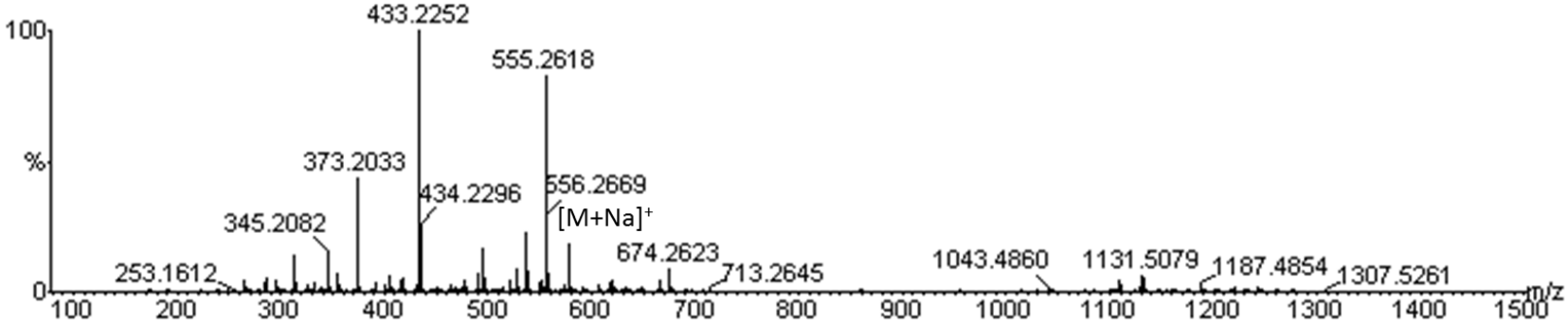
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
307 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-60 H: 0-100 O: 0-50 Na: 0-1

30-May-2015 4::7::7 LCT Premier XE KE483 ROUSSI_esposito18-2 632 (2.786)
1: TOF MS ES+

2.33e+004



Minimum:				-1.5						
Maximum:		5.0	5.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
577.2434	577.2414	2.0	3.5	12.5	267.5	0.4	C31	H38	O9	Na [M+Na]+
	577.2438	-0.4	-0.7	15.5	268.3	1.2	C33	H37	O9	

Figure S61. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **14b**

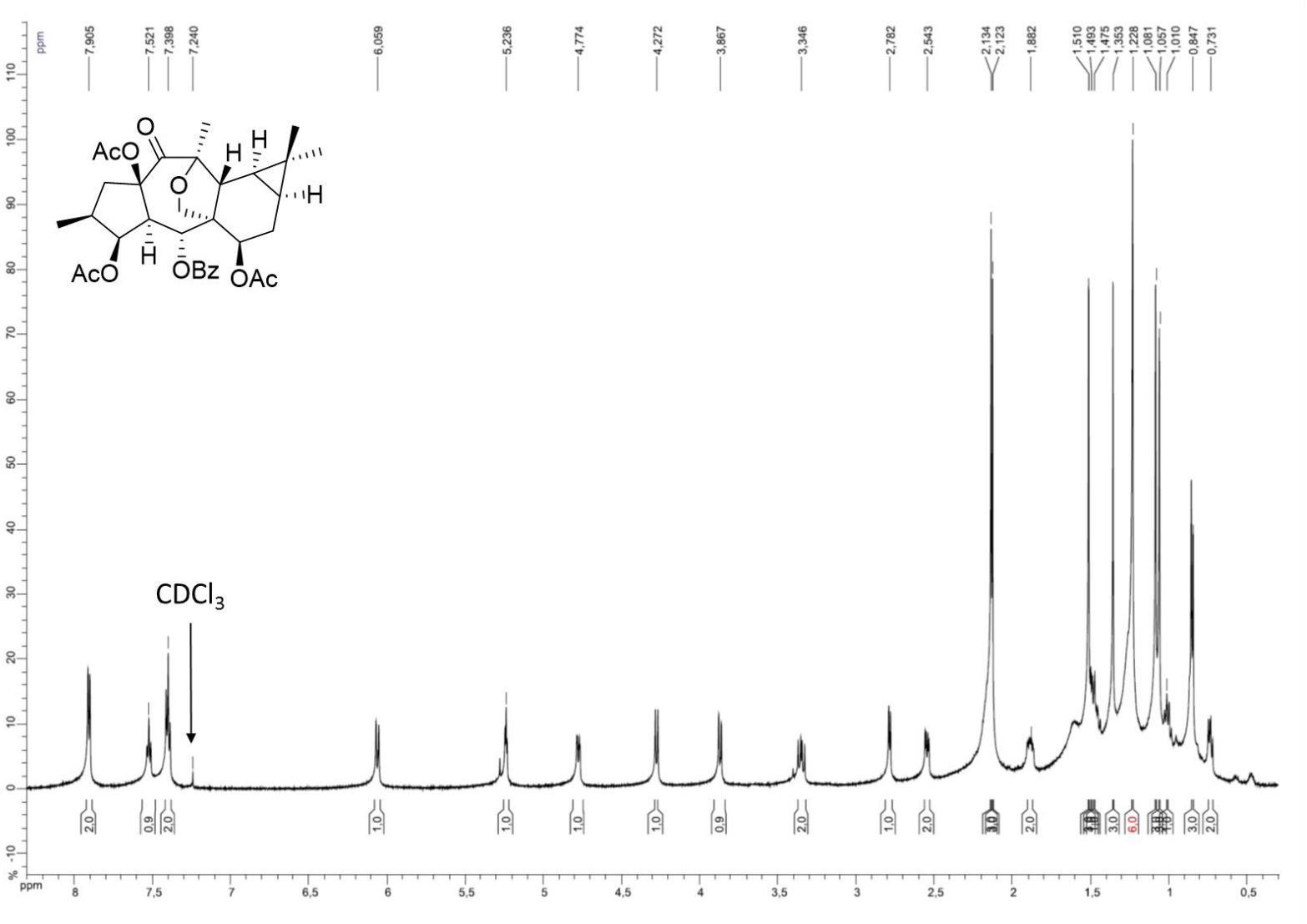


Figure S62. ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) of **14b**

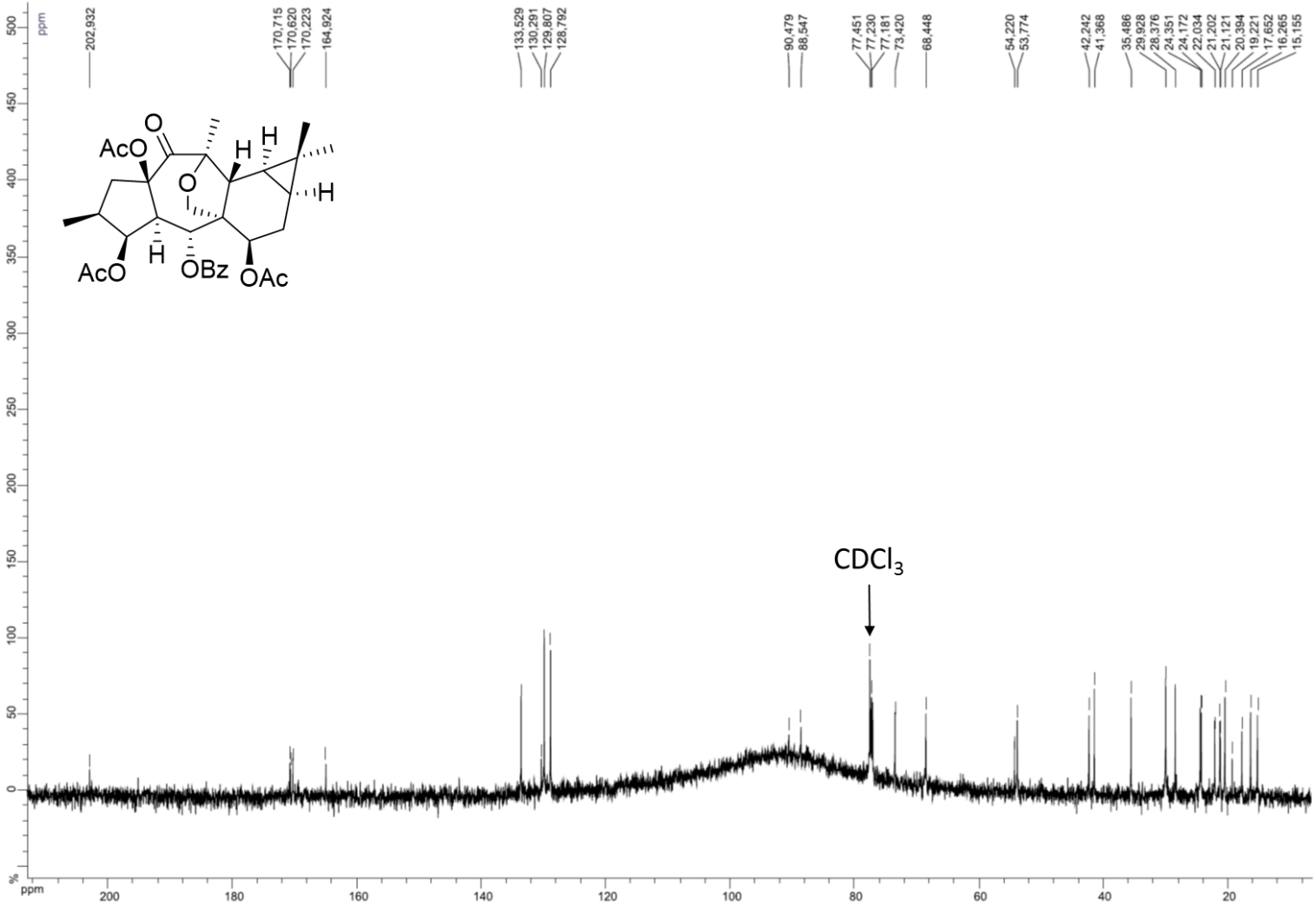


Figure S63. HMBC NMR spectrum ($CDCl_3$, 300 MHz) of **14b**

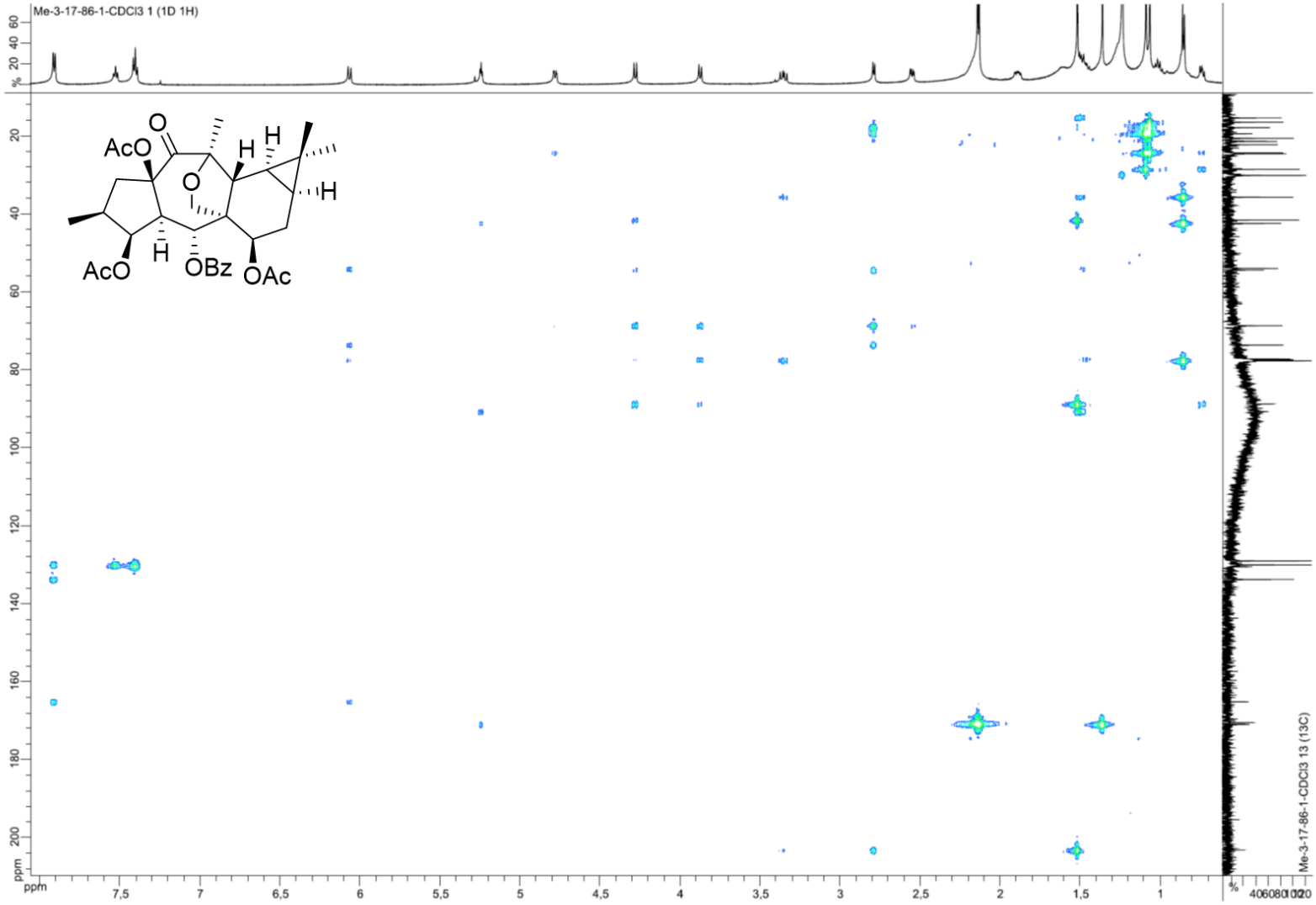


Figure S64. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **14b**

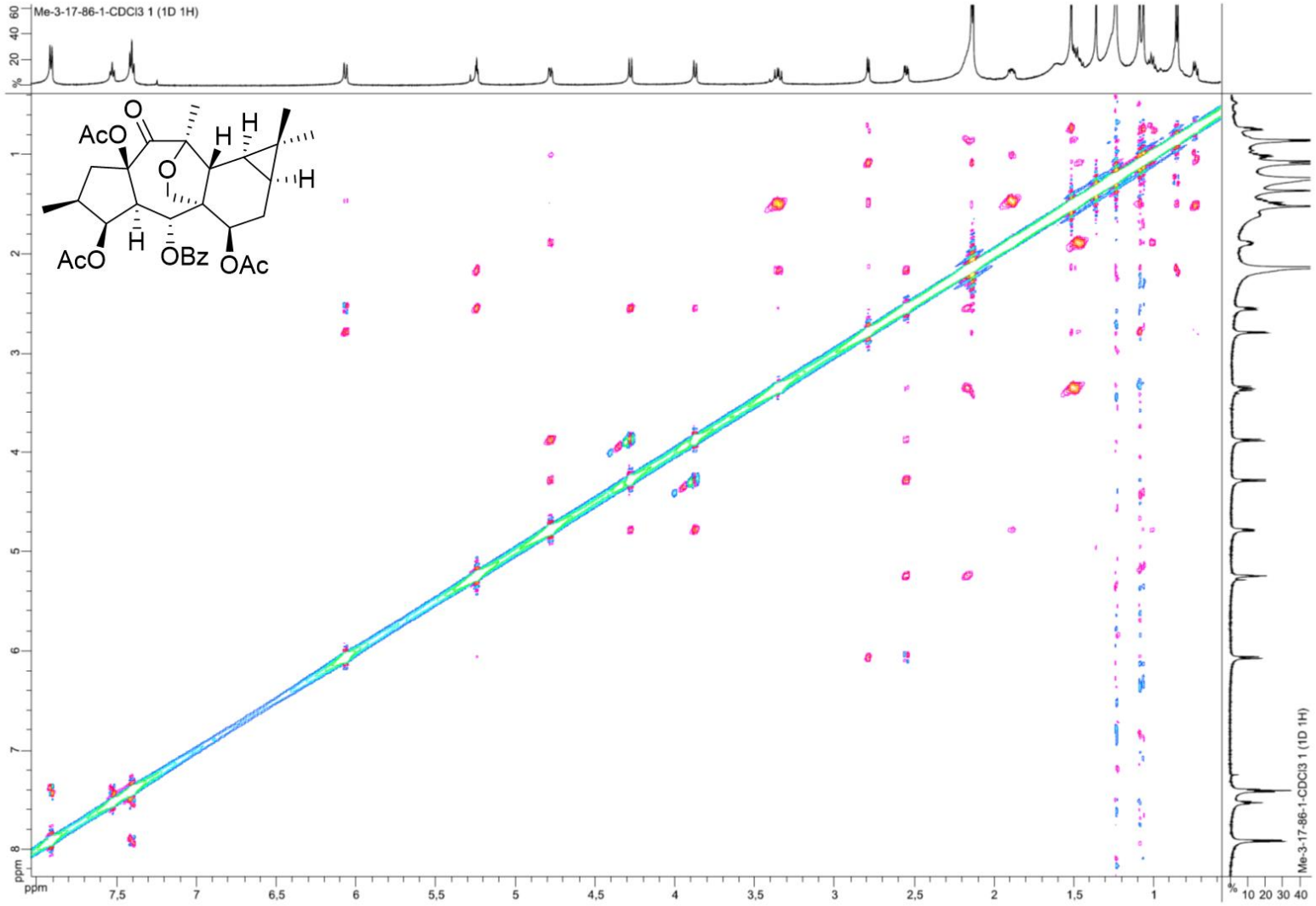
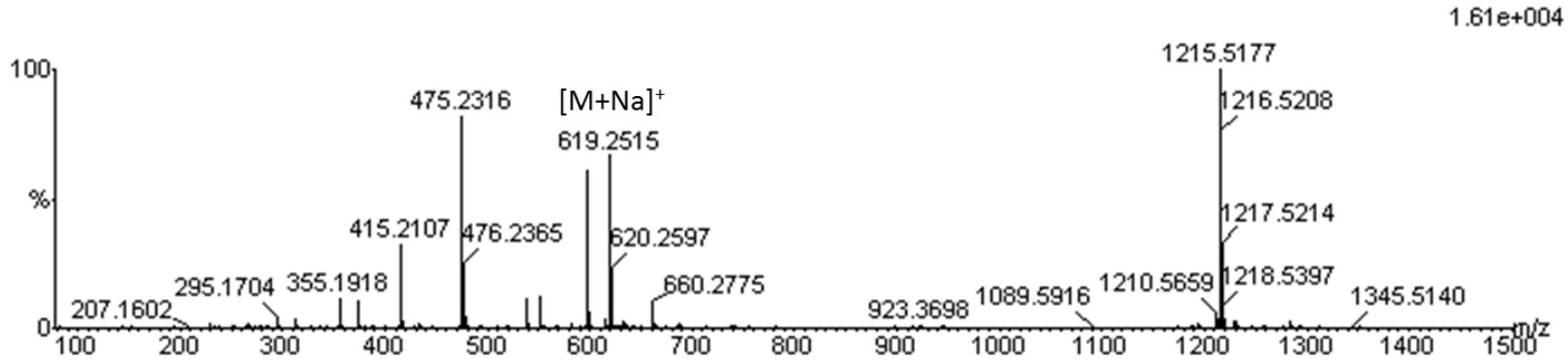


Figure S65. HRESIMS spectrum (TOF) of **14b**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
361 formula(e) evaluated with 4 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-60 H: 0-100 O: 0-50 Na: 0-1

28-May-2015 3::4::8 LCT Premier XE KE483 ROUSSI_esposito17-1 670 (2.946)
1: TOF MS ES+



Minimum:				-1.5							
Maximum:		5.0	10.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
619.2515	619.2519	-0.4	-0.6	13.5	374.3	0.1	C33	H40	O10	Na	[M+Na]+
	619.2543	-2.8	-4.5	16.5	376.9	2.7	C35	H39	O10		
	619.2484	3.1	5.0	25.5	383.2	9.0	C42	H35	O5		
	619.2460	5.5	8.9	22.5	381.6	7.4	C40	H36	O5	Na	

Figure S66. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **14c**

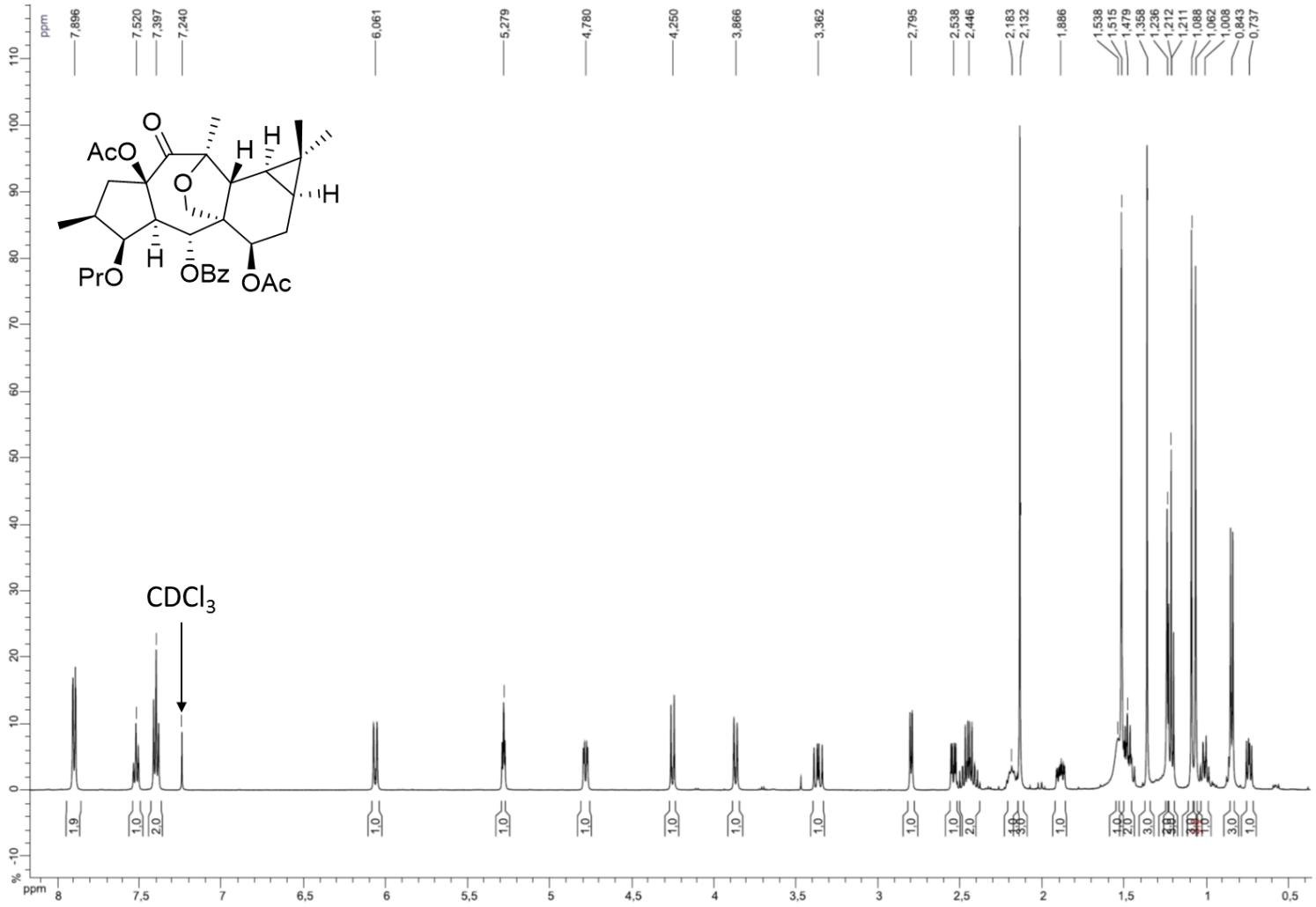


Figure S67. ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) of **14c**

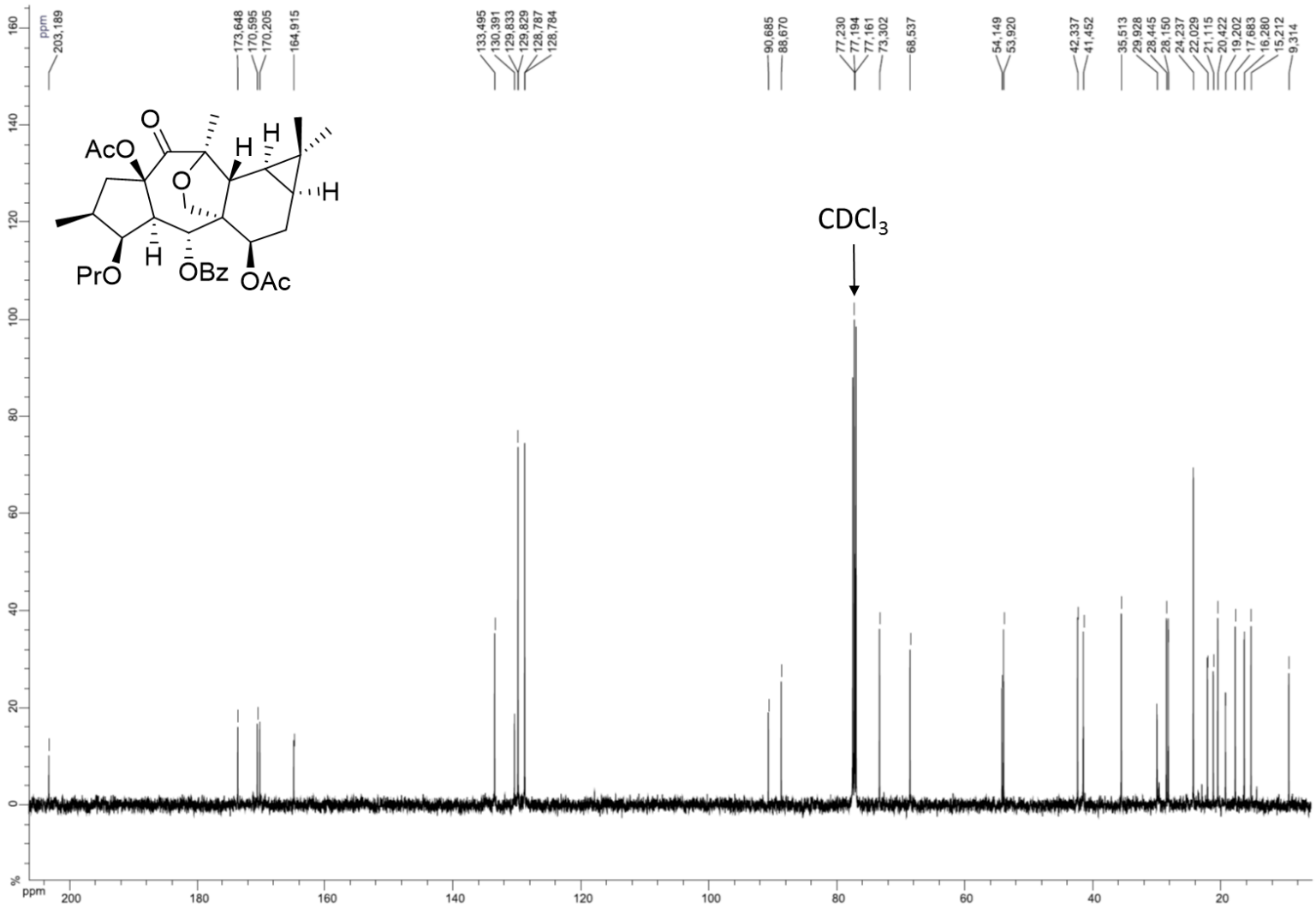


Figure S68. HMBC NMR spectrum ($CDCl_3$, 300 MHz) of **14c**

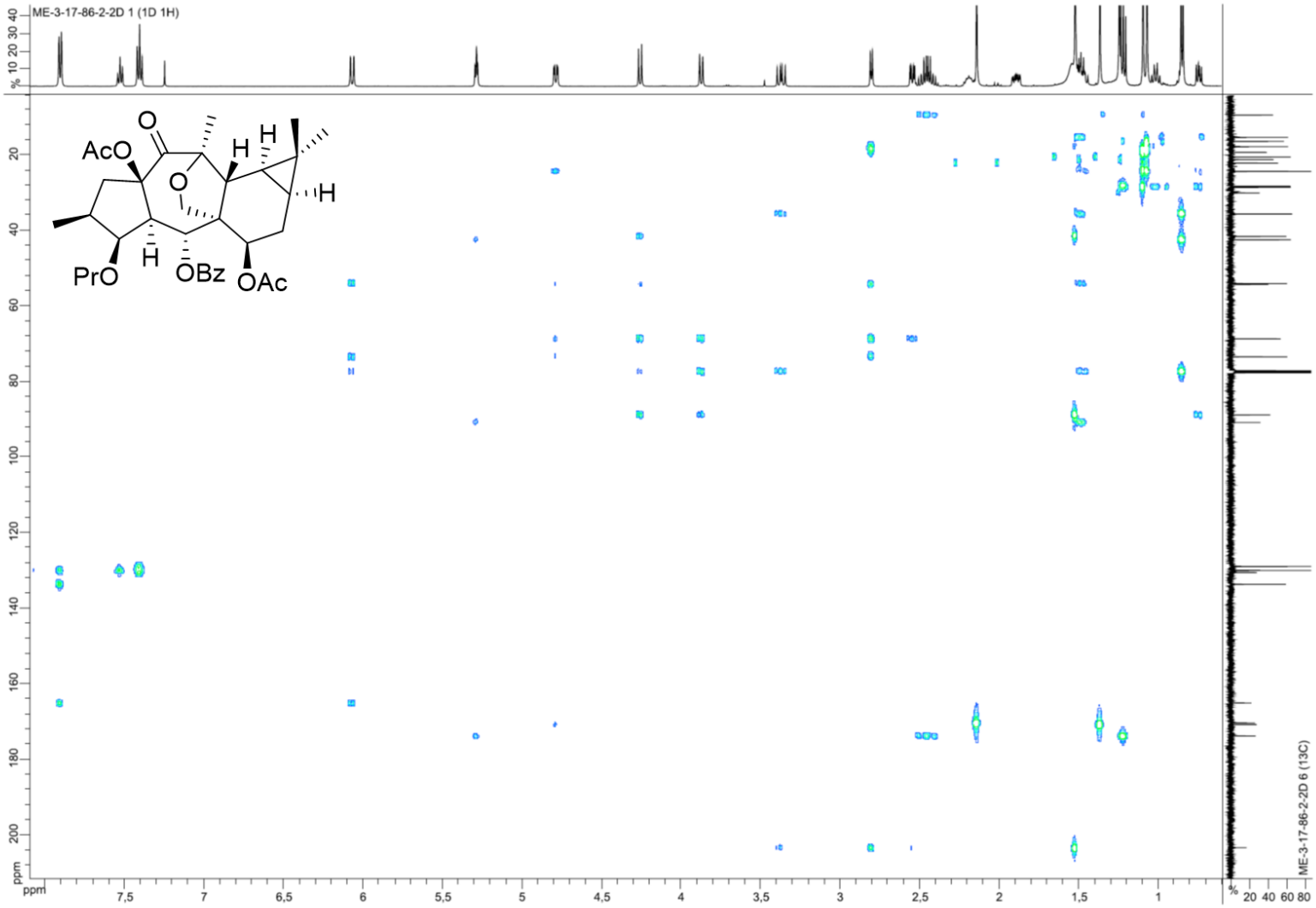


Figure S69. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **14c**

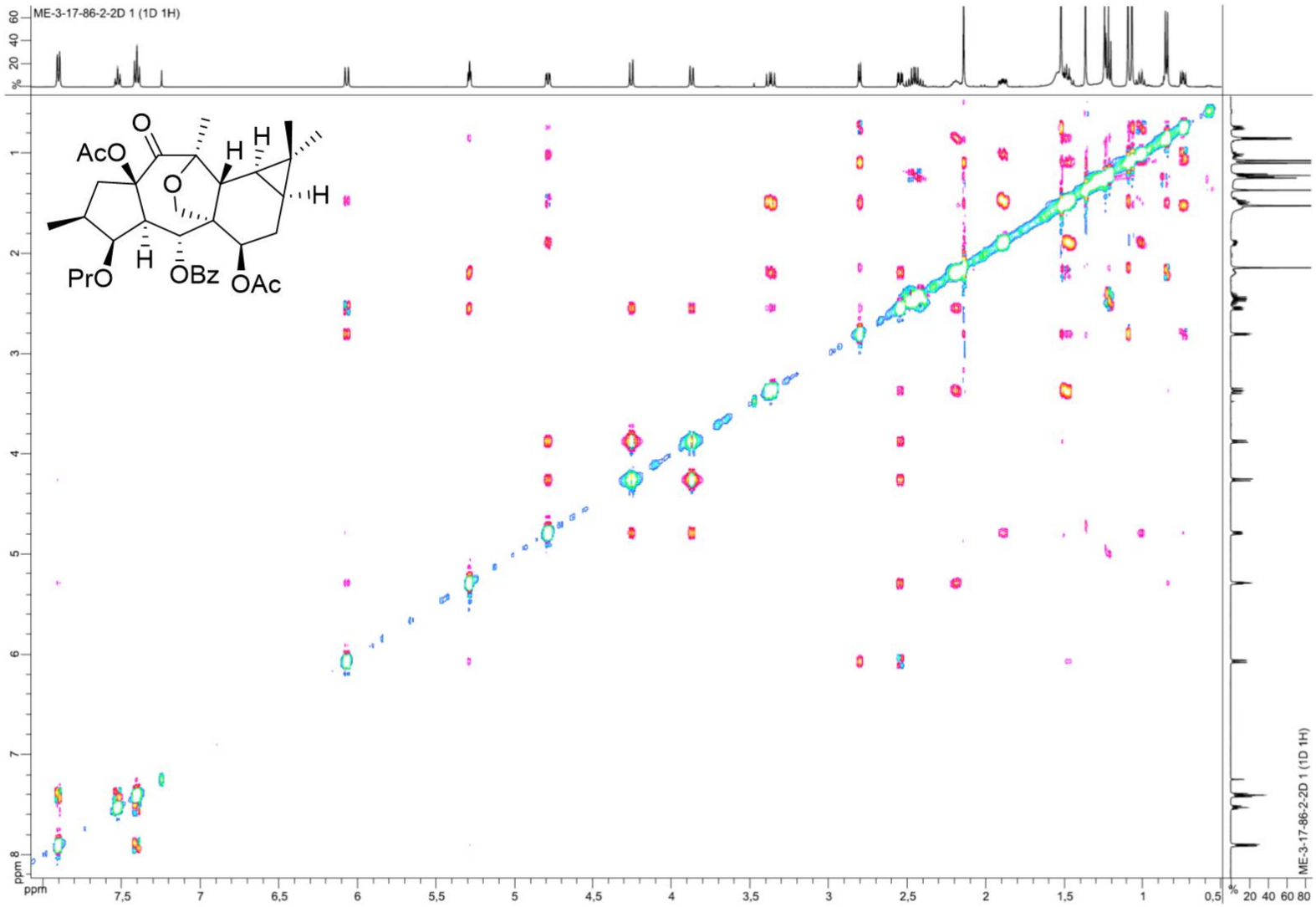


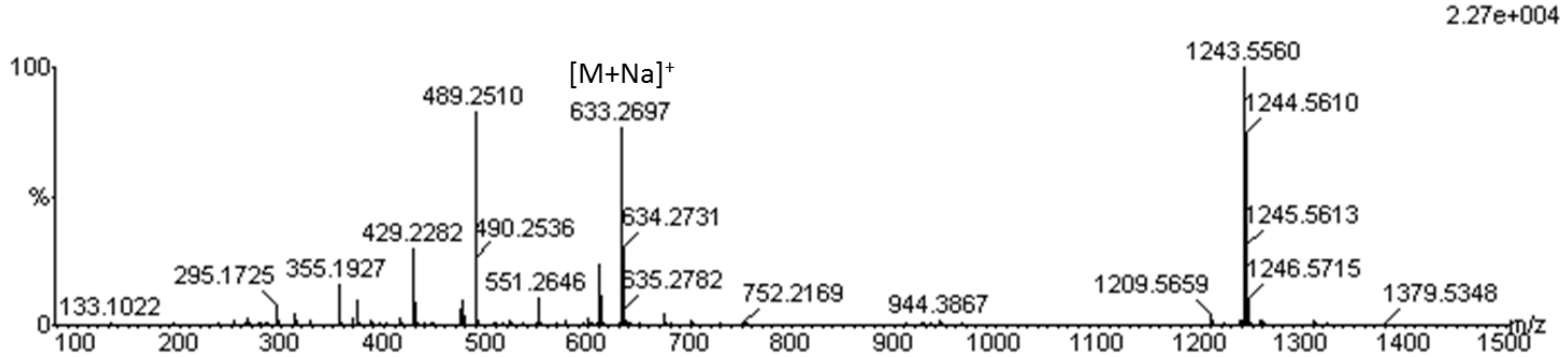
Figure S70. HRESIMS spectrum (TOF) of **14c**

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
363 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-60 H: 0-100 O: 0-50 Na: 0-1

27-May-2015 8::4::6 LCT Premier XE KE483 ROUSSI_esposito16-4 696 (3.057)
1: TOF MS ES+



Minimum:				-1.5						
Maximum:		5.0	10.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
633.2697	633.2700	-0.3	-0.5	16.5	381.0	1.7	C36	H41	O10	
	633.2676	2.1	3.3	13.5	379.6	0.3	C34	H42	O10	Na [M+Na]+
	633.2734	-3.7	-5.8	4.5	383.8	4.5	C27	H46	O15	Na
	633.2641	5.6	8.8	25.5	386.6	7.3	C43	H37	O5	
	633.2758	-6.1	-9.6	7.5	382.6	3.3	C29	H45	O15	

Figure S71. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **15a**

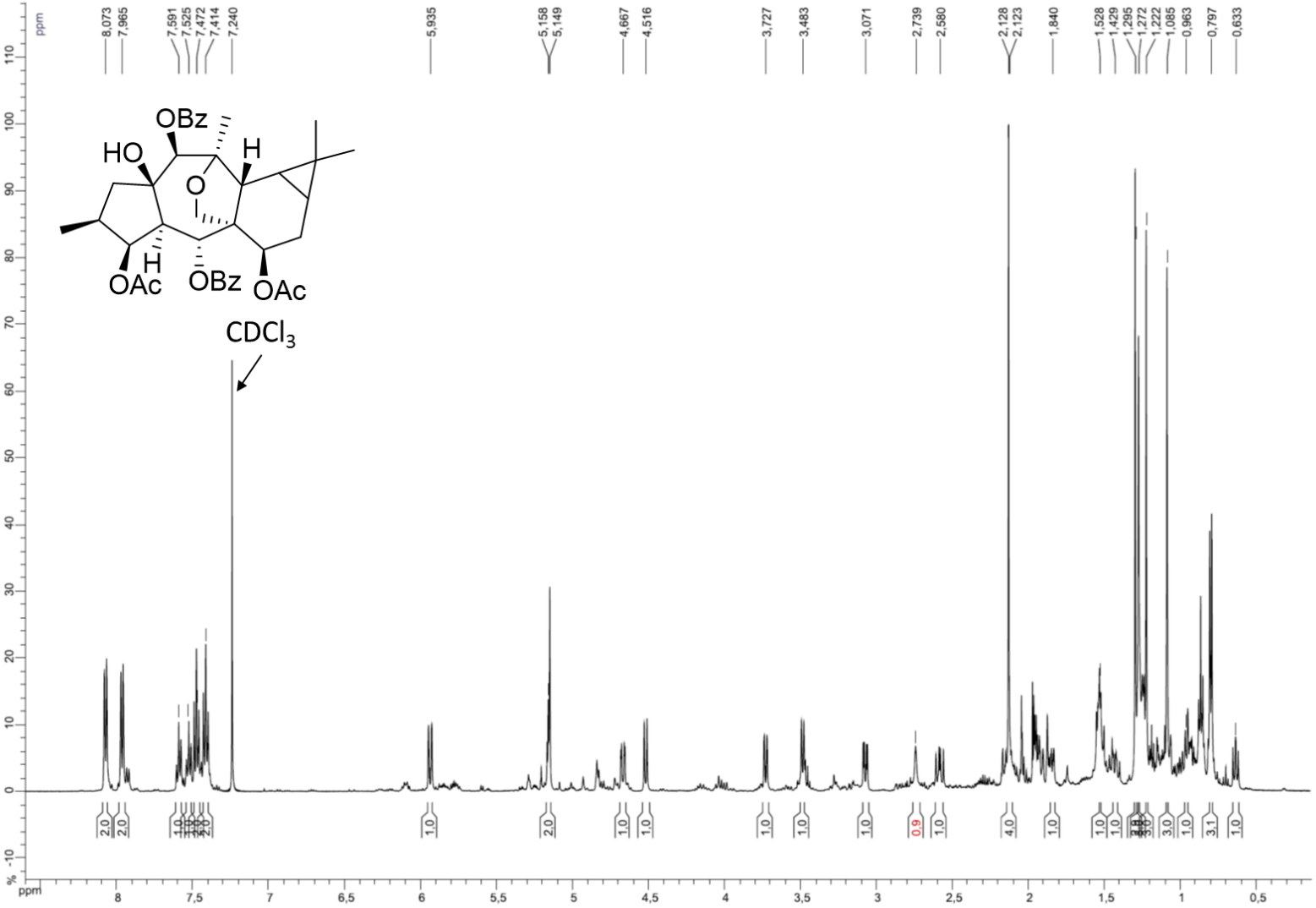


Figure S72. ^{13}C NMR spectrum ($CDCl_3$, 125 MHz) of **15a**

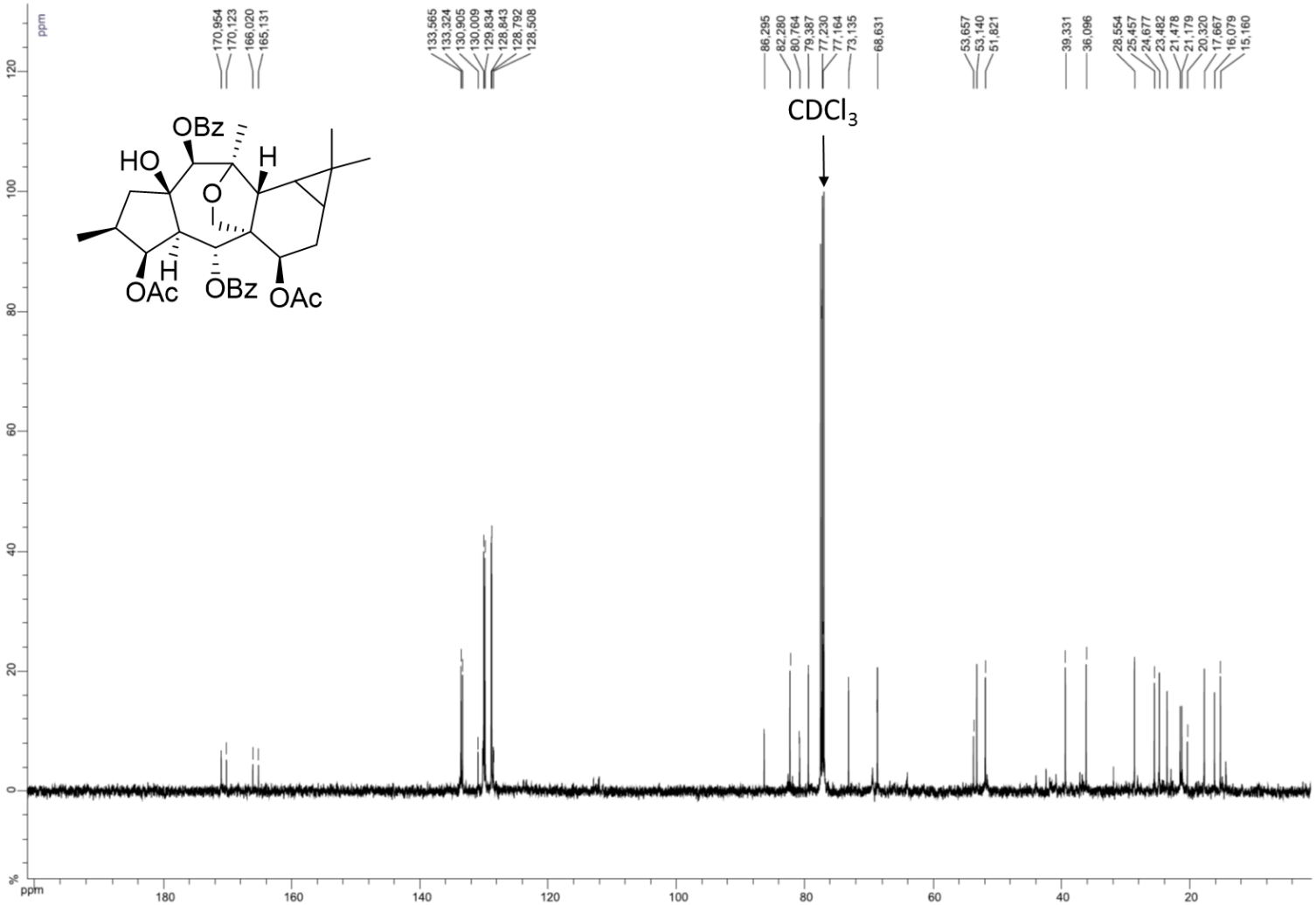


Figure S73. HMBC NMR spectrum ($CDCl_3$, 500 MHz) of **15a**

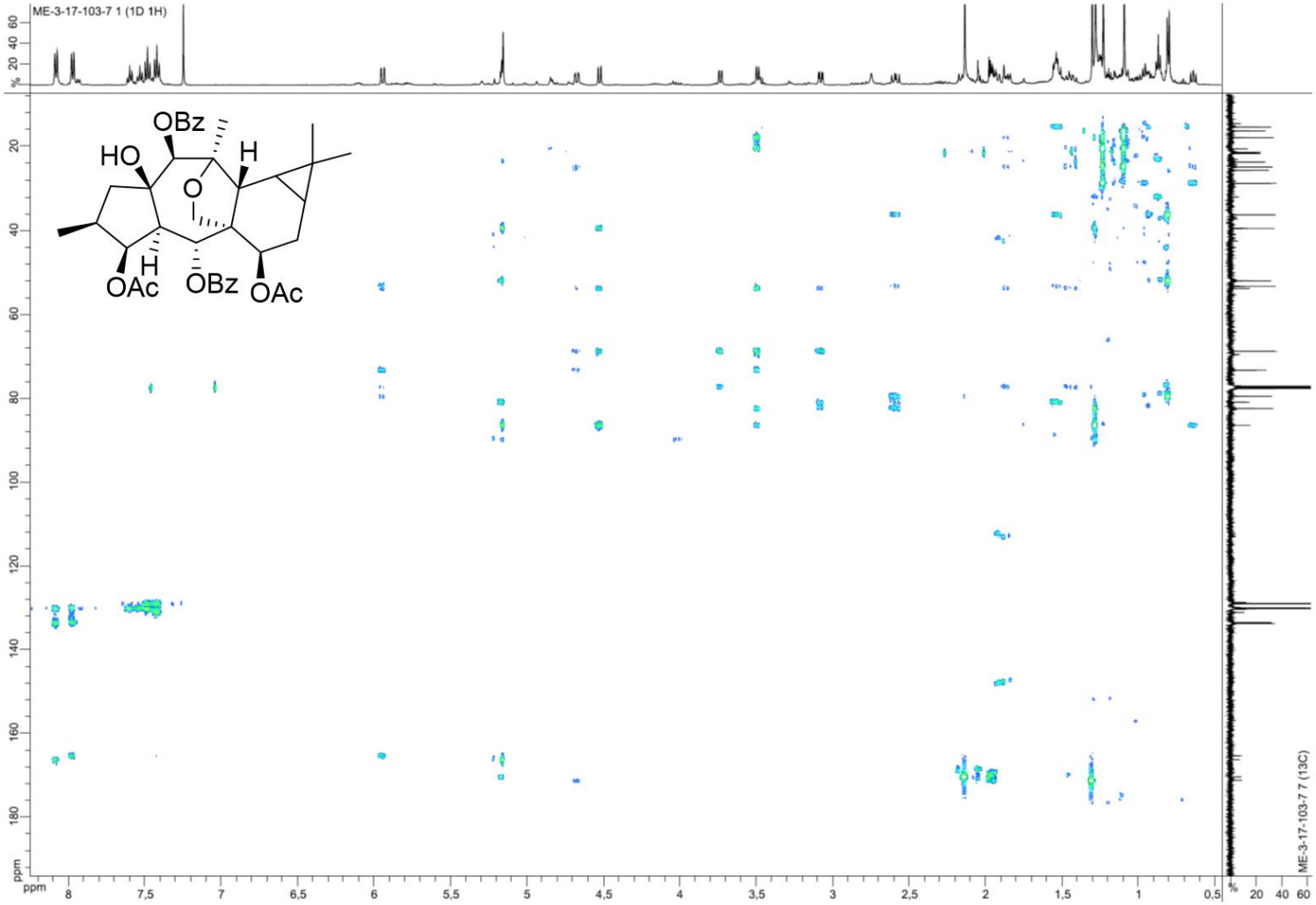


Figure S74. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **15a**

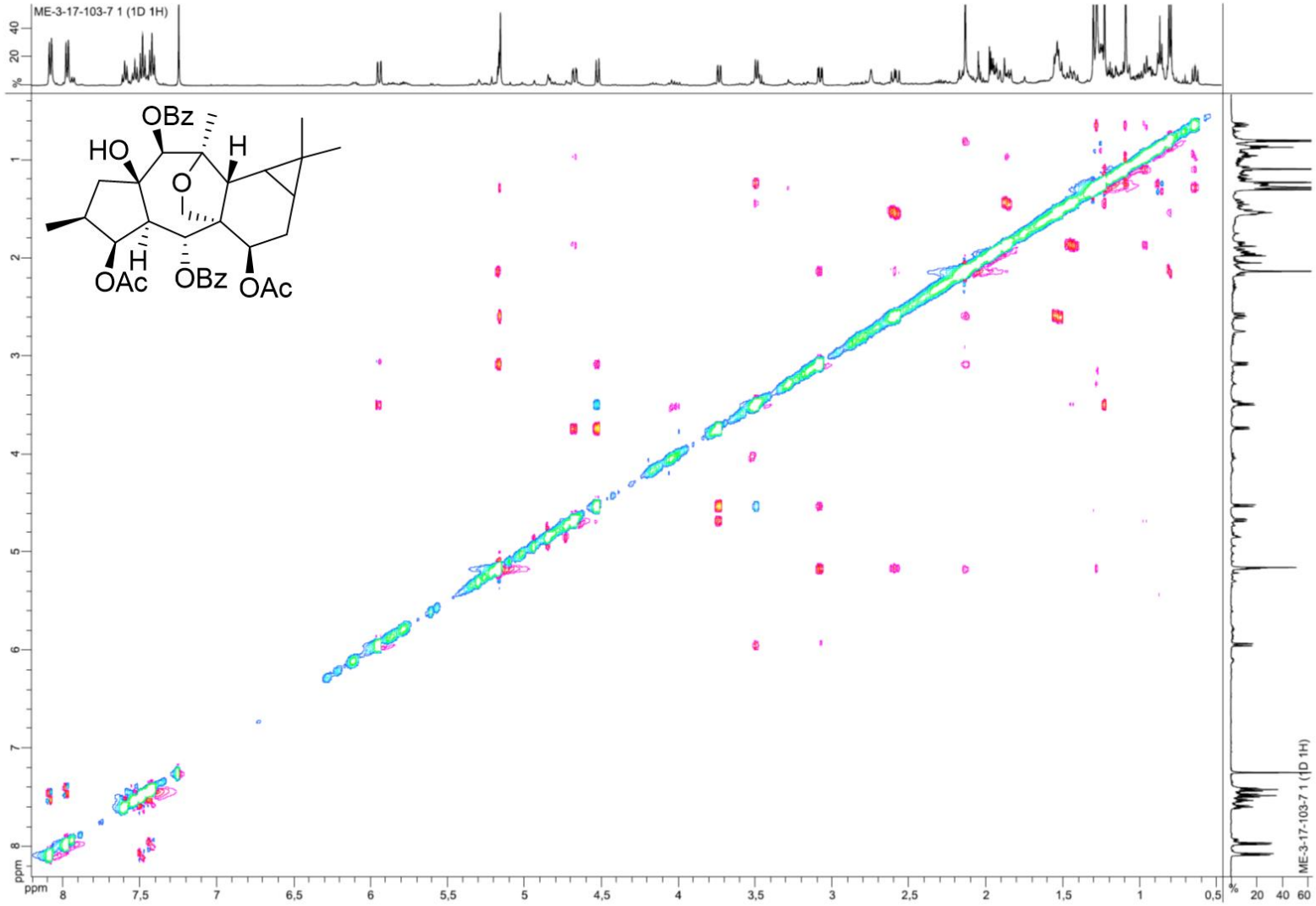


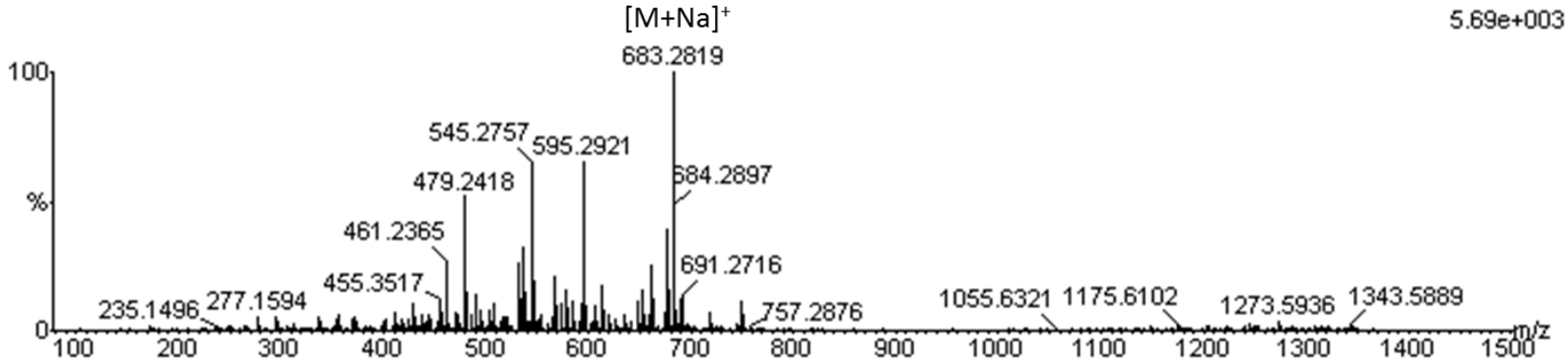
Figure S75. HRESIMS spectrum (TOF) of **15a**

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
836 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

16-Feb-2016 11:10:16 LCT Premier XE KE483 ROUSSI_esposito30-5 684 (3.198)
1: TOF MS ES+



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
683.2819	683.2832	-1.3	-1.9	16.5	290.6	0.4	C38	H44	O10	Na	$[M+Na]^+$
	683.2797	2.2	3.2	28.5	291.4	1.1	C47	H39	O5		

Figure S76. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **15b**

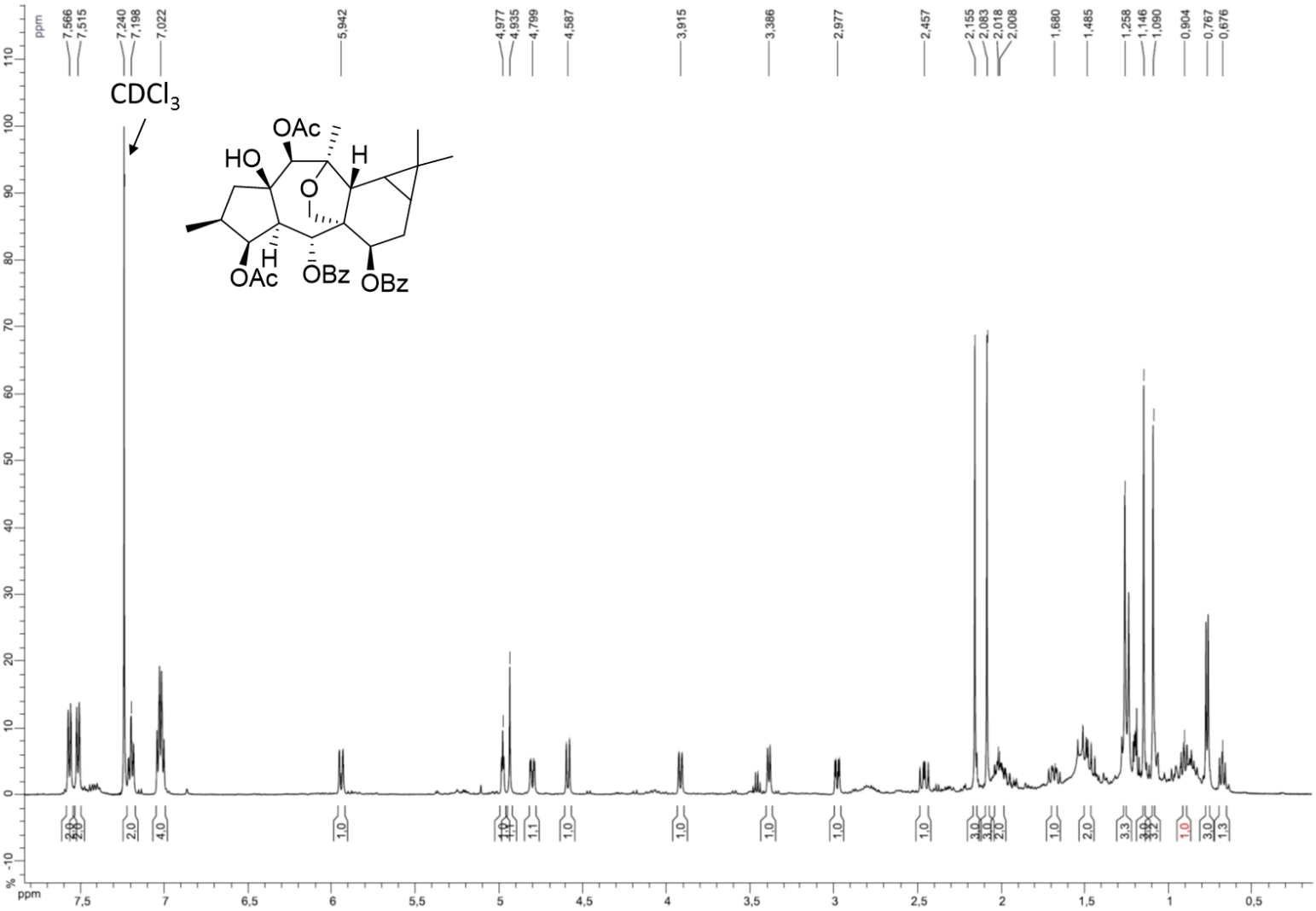


Figure S77. HMBC NMR spectrum ($CDCl_3$, 500 MHz) of **15b**

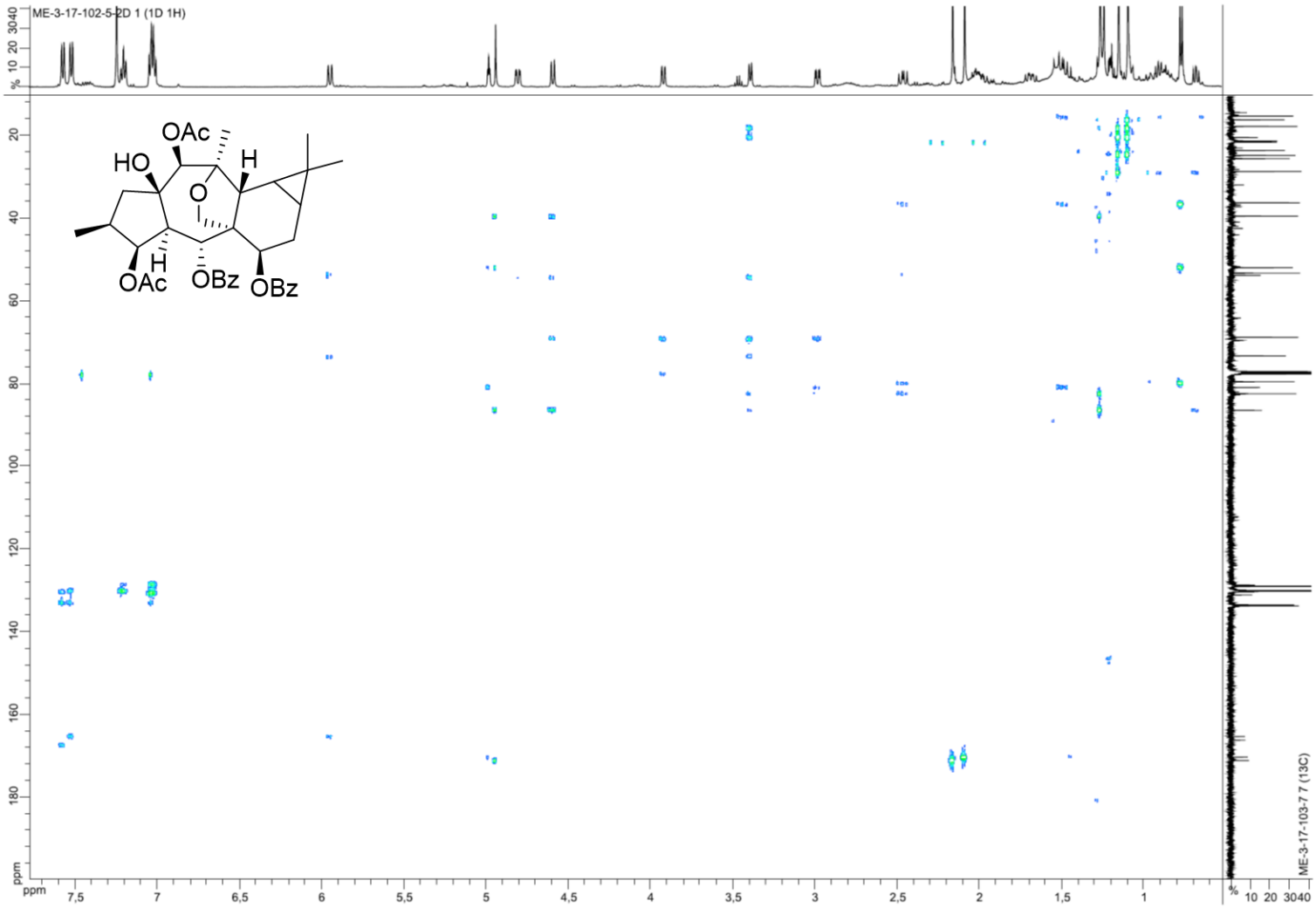


Figure S78. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **15b**

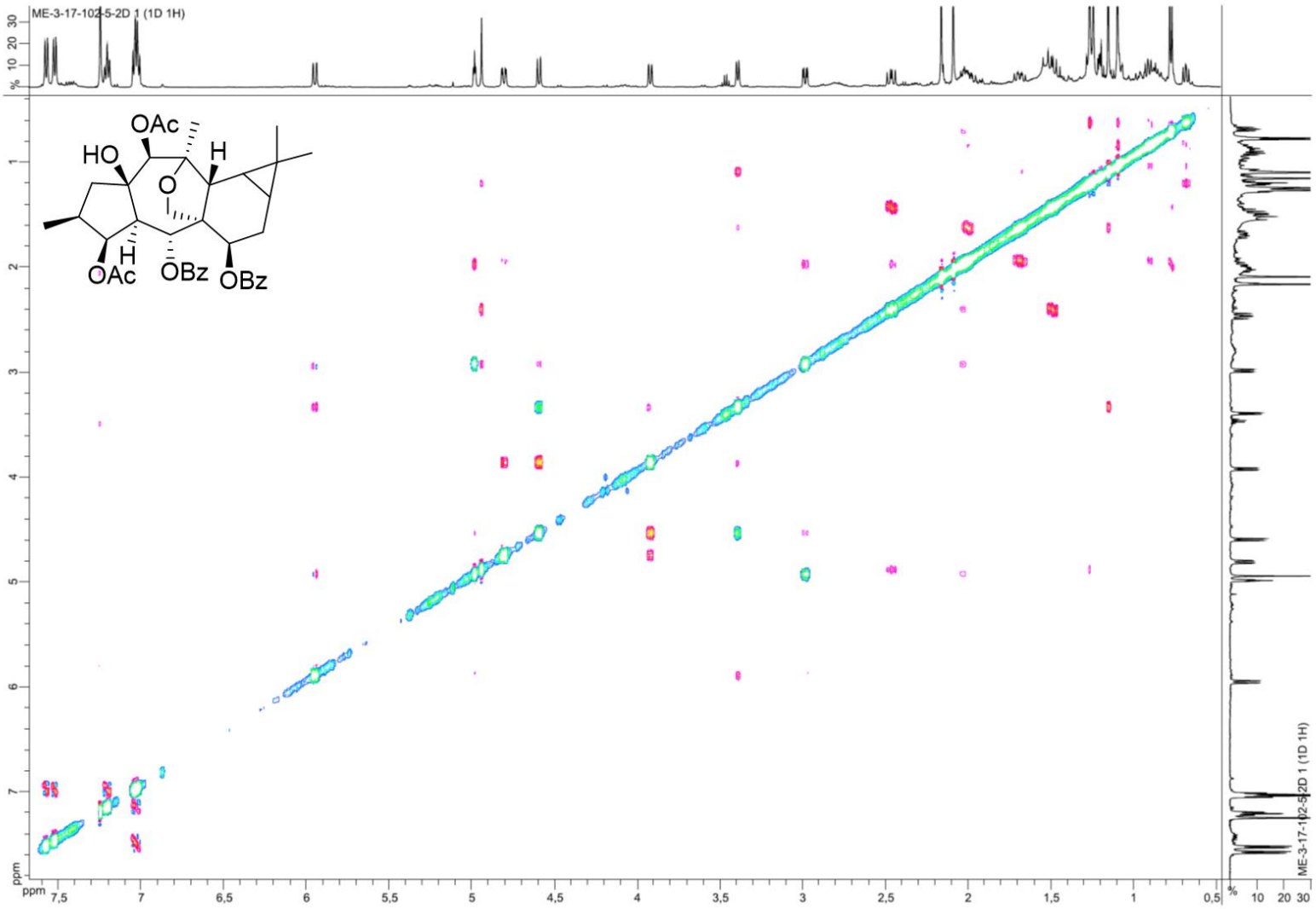
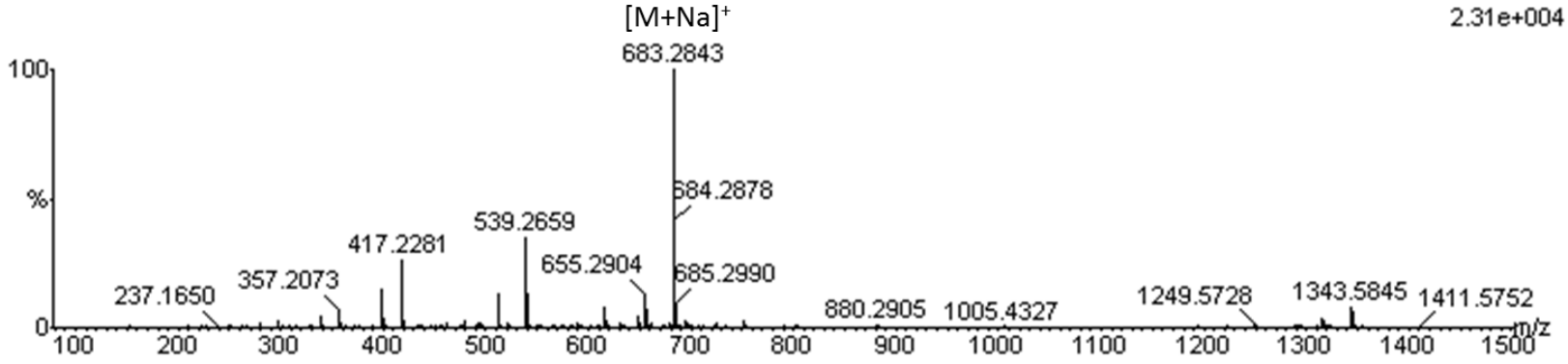


Figure S79. HRESIMS spectrum (TOF) of **15b**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
836 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

08-Jan-2016 15:56:25 LCT Premier XE KE483 ROUSSI_esposito23-5 677 (3.170)
1: TOF MS ES+



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
683.2843	683.2832	1.1	1.6	16.5	338.4	0.2	C38	H44	O10	Na	[M+Na]+
	683.2856	-1.3	-1.9	19.5	340.1	1.9	C40	H43	O10		

Figure S80. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **15c**

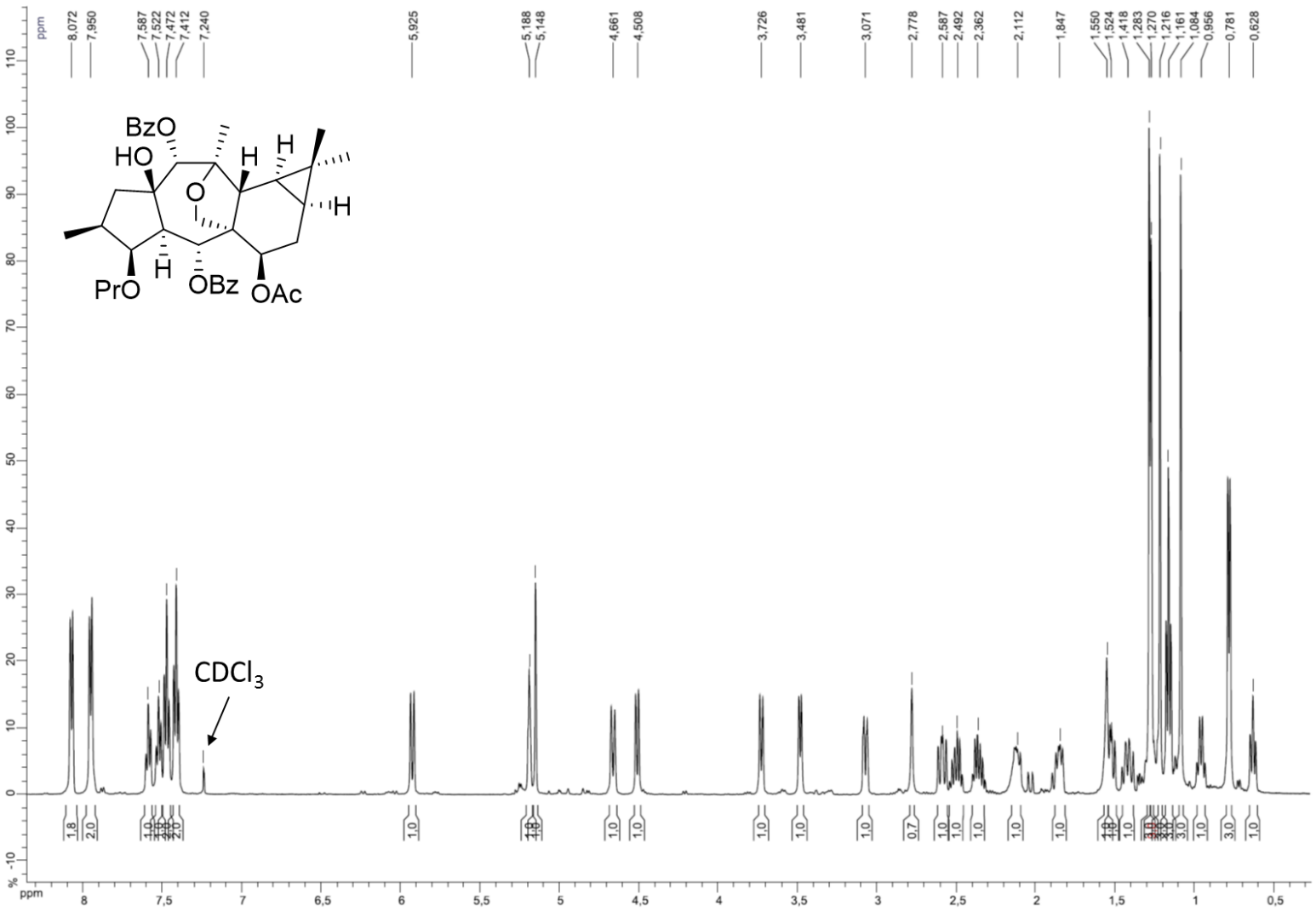


Figure S81. ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) of **15c**

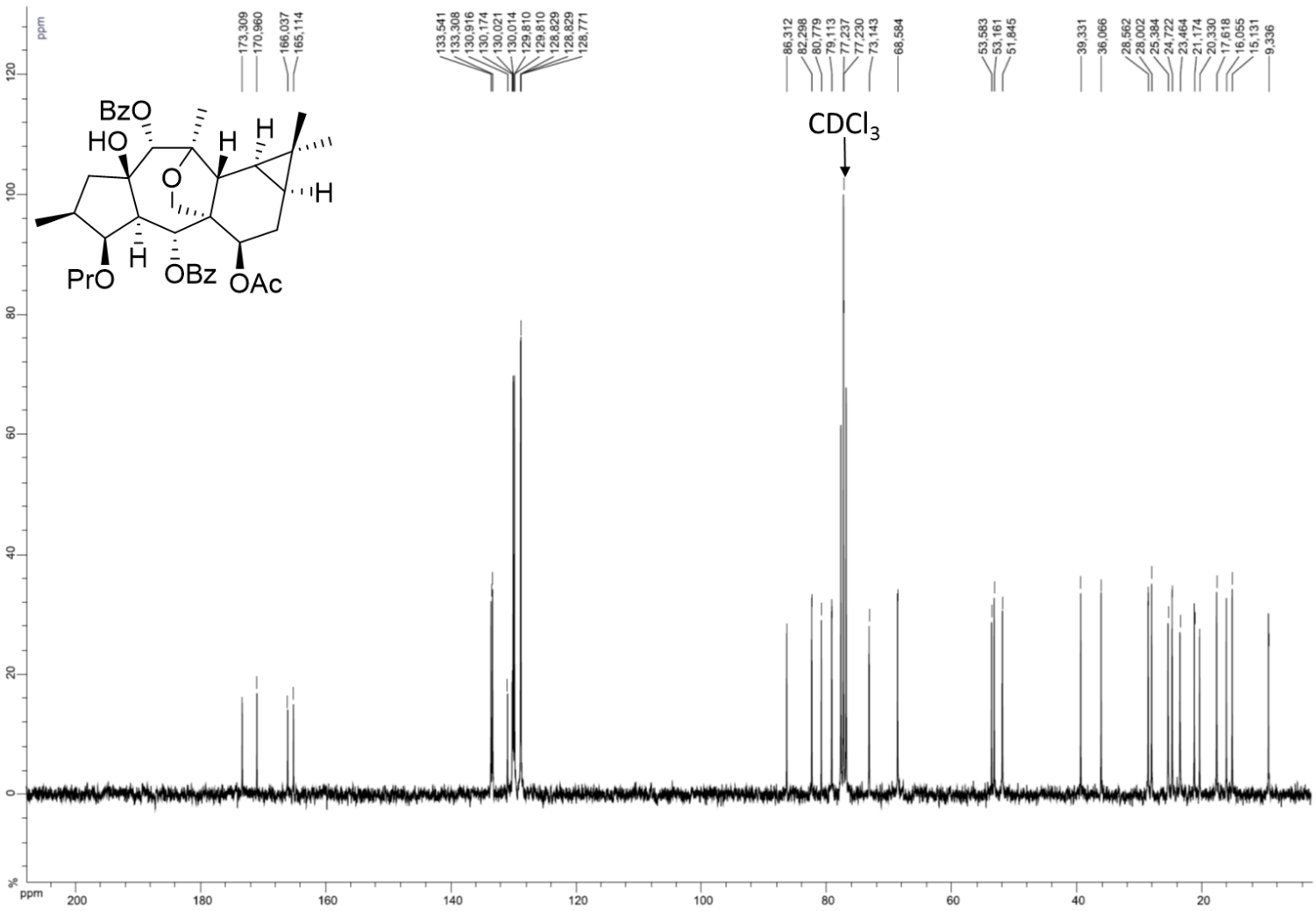


Figure S82. HMBC NMR spectrum ($CDCl_3$, 300 MHz) of **15c**

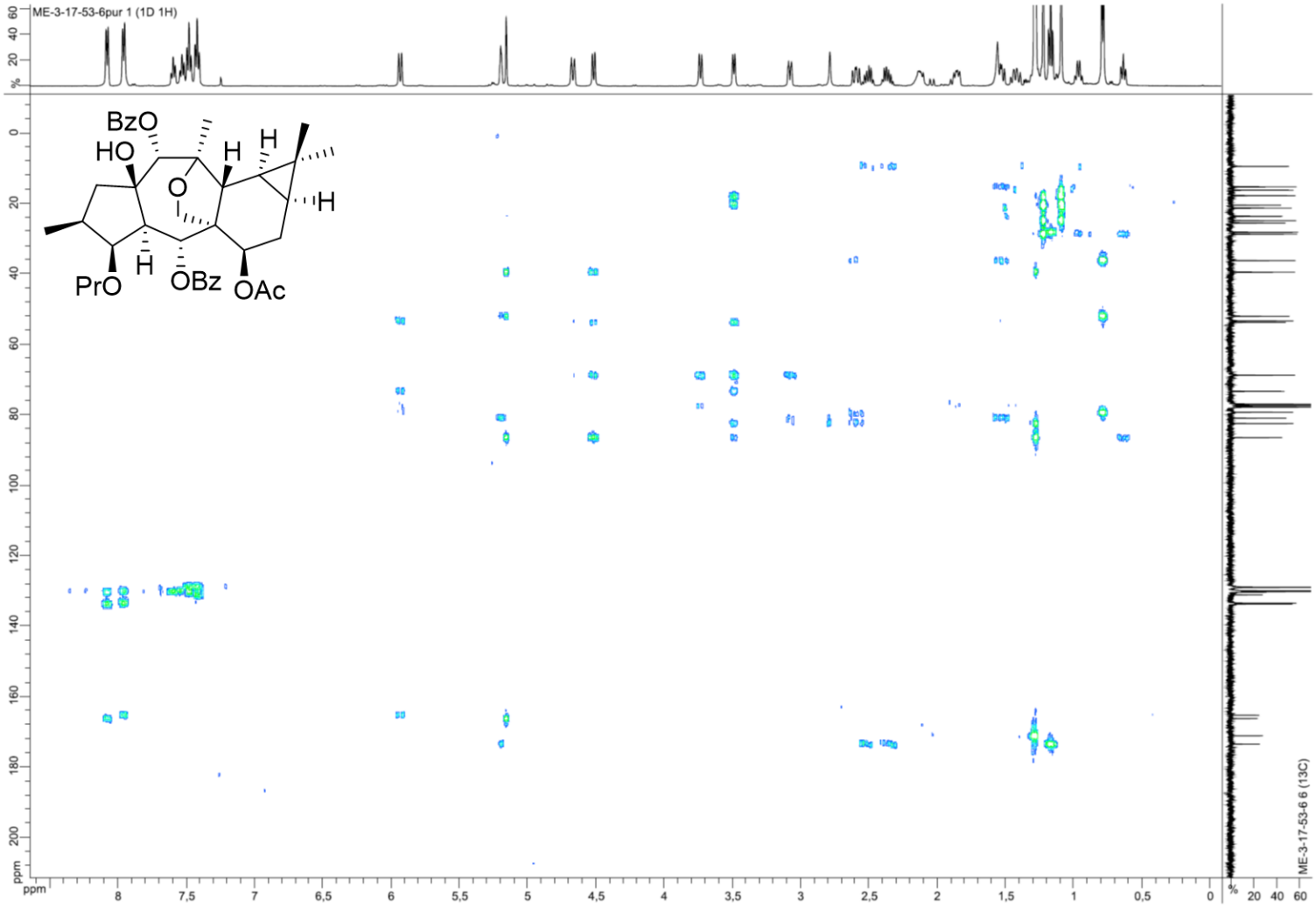


Figure S83. ROESY NMR spectrum ($CDCl_3$, 500 MHz) of **15c**

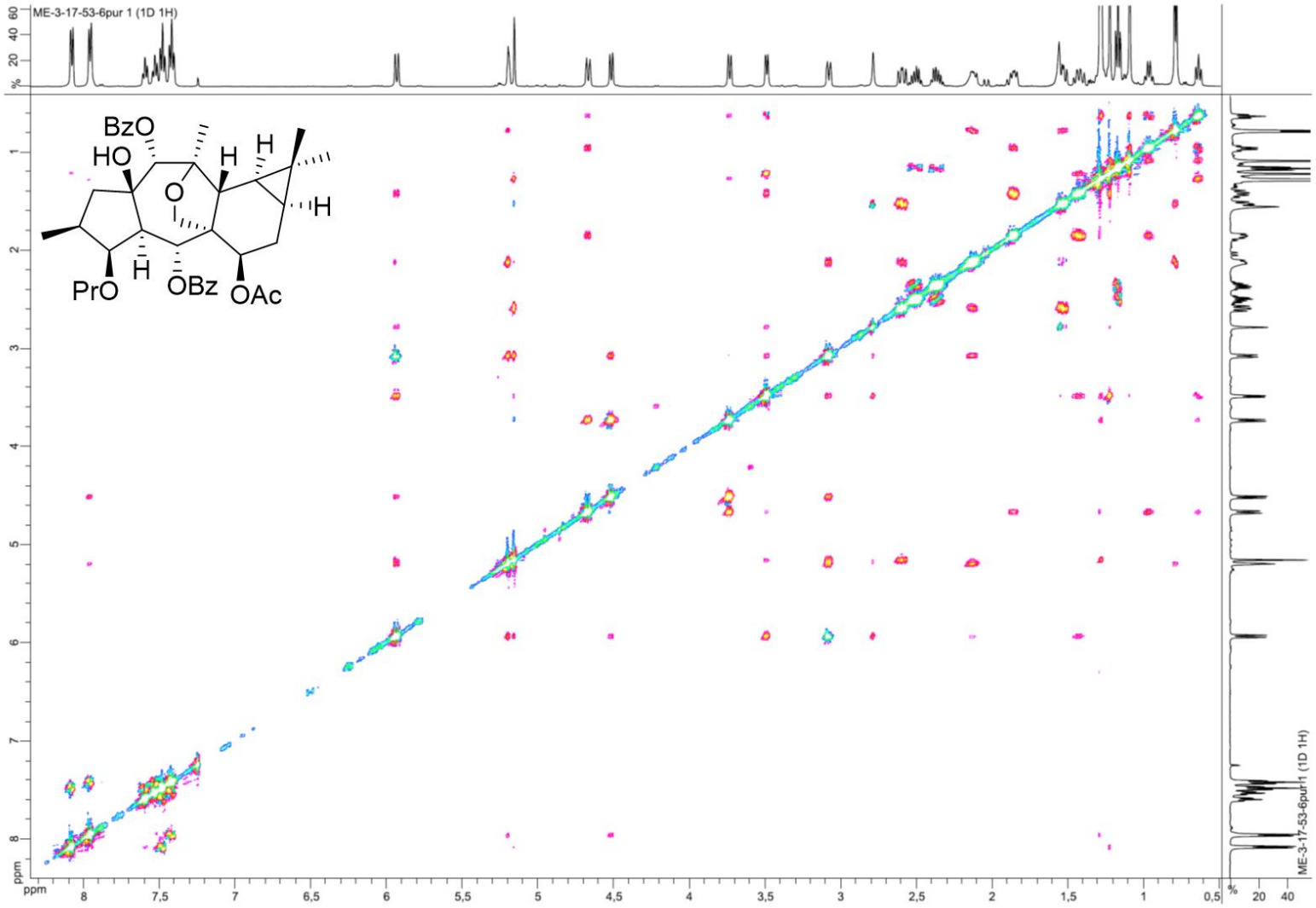


Figure S84. HRESIMS spectrum (TOF) of **15c**

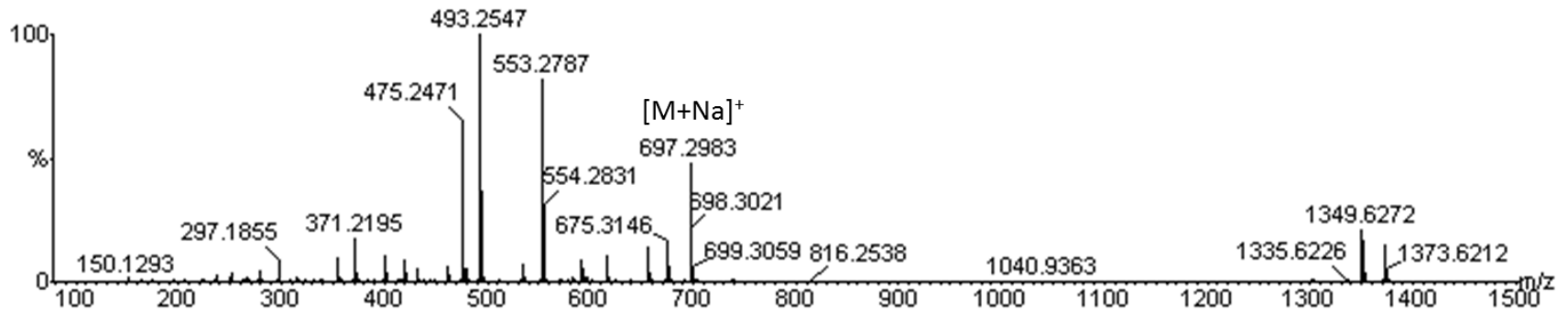
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
436 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-100 H: 0-300 O: 0-50 Na: 0-1

27-Apr-2015 20:11:07 LCT Premier XE KE483 ROUSSI_esposito13-4 761 (3.332)
1: TOF MS ES+

3.89e+004



Minimum:				-1.5							
Maximum:		5.0	5.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula				
697.2983	697.2989	-0.6	-0.9	16.5	339.1	0.8	C39	H46	O10	Na	[M+Na]+
	697.2954	2.9	4.2	28.5	342.4	4.0	C48	H41	O5		
	697.3013	-3.0	-4.3	19.5	339.0	0.7	C41	H45	O10		

Figure S85. ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **16a**

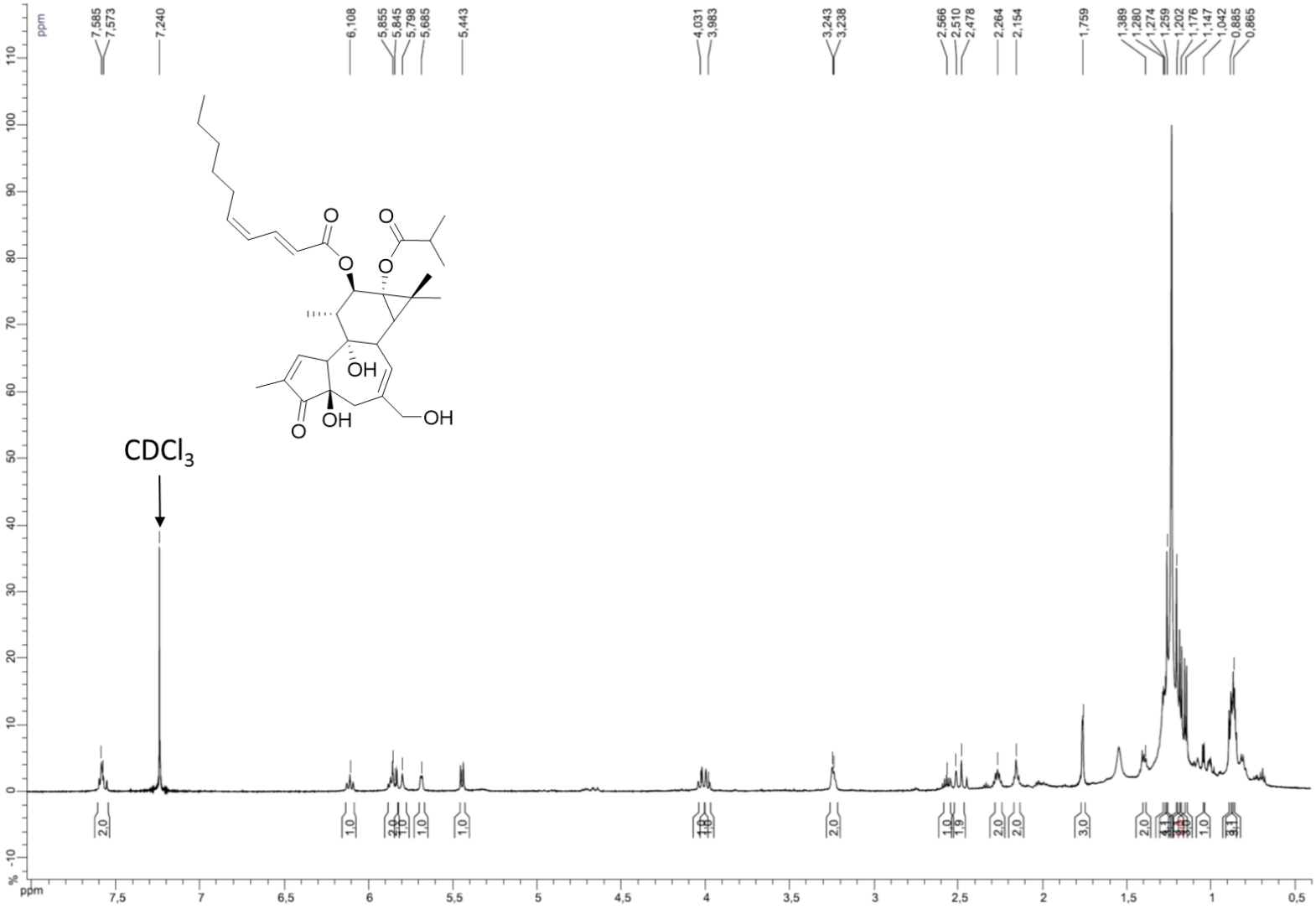


Figure S86. COSY NMR spectrum ($CDCl_3$, 600 MHz) of **16a**

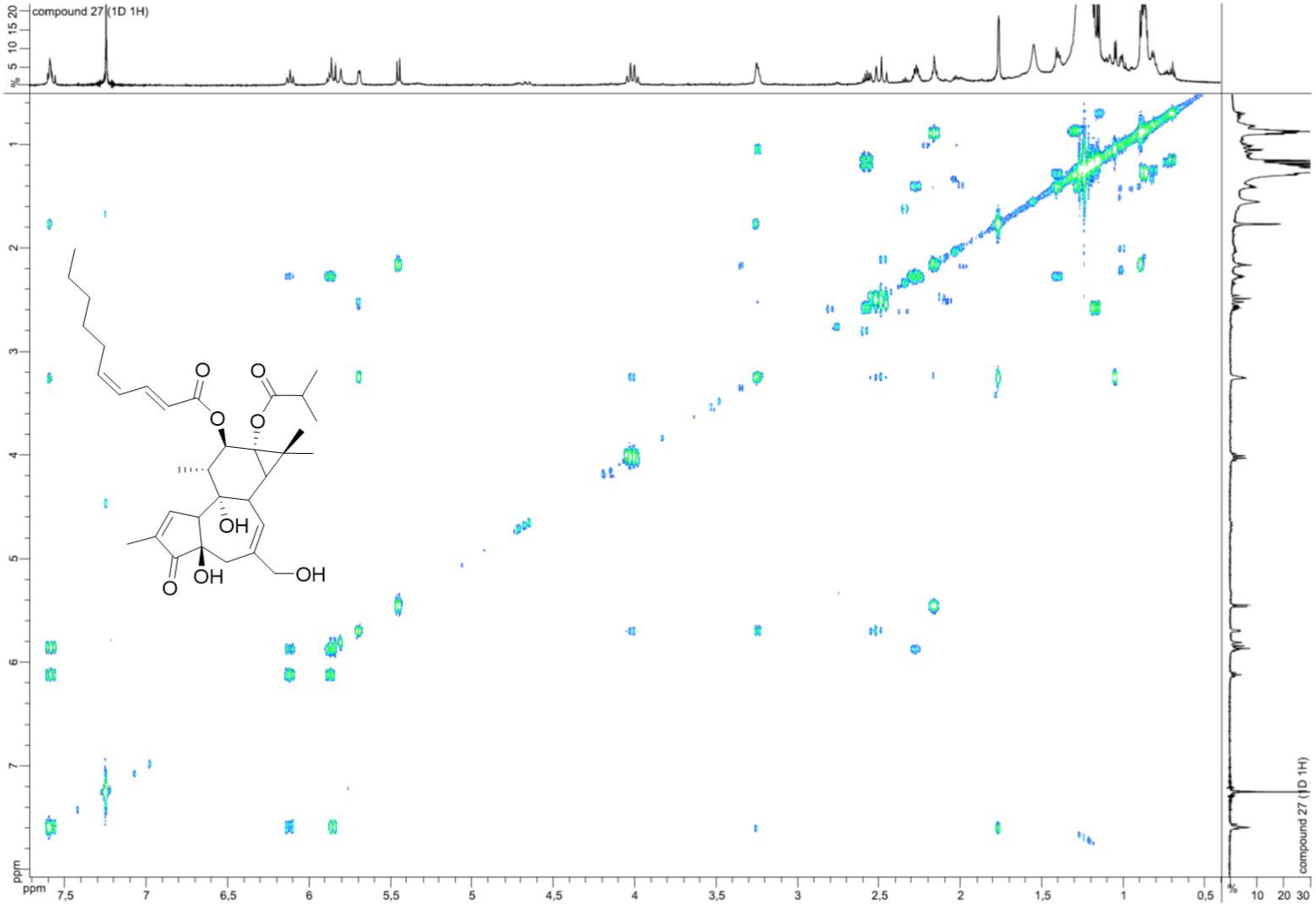


Figure S87. ROESY NMR spectrum ($CDCl_3$, 600 MHz) of **16a**

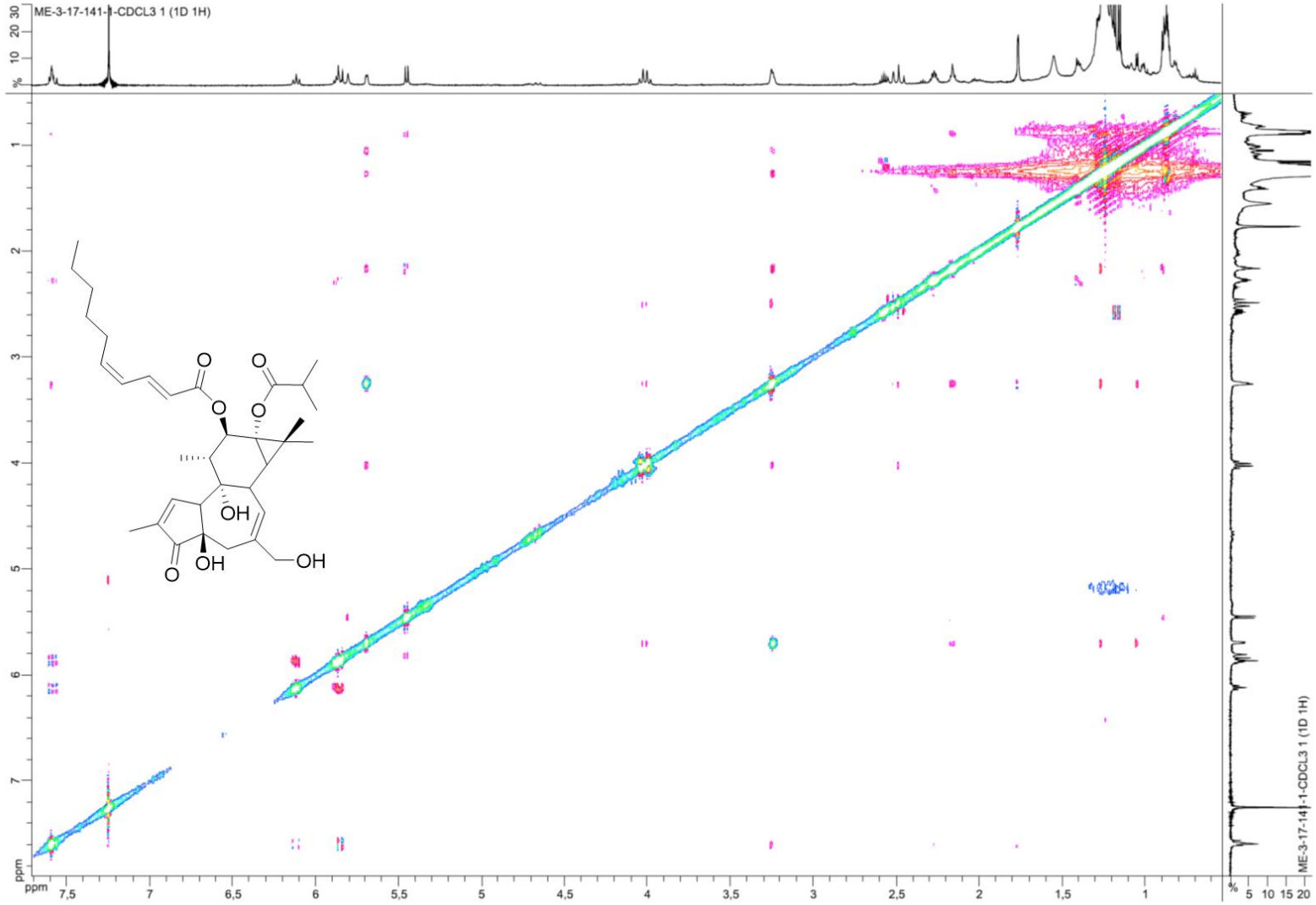


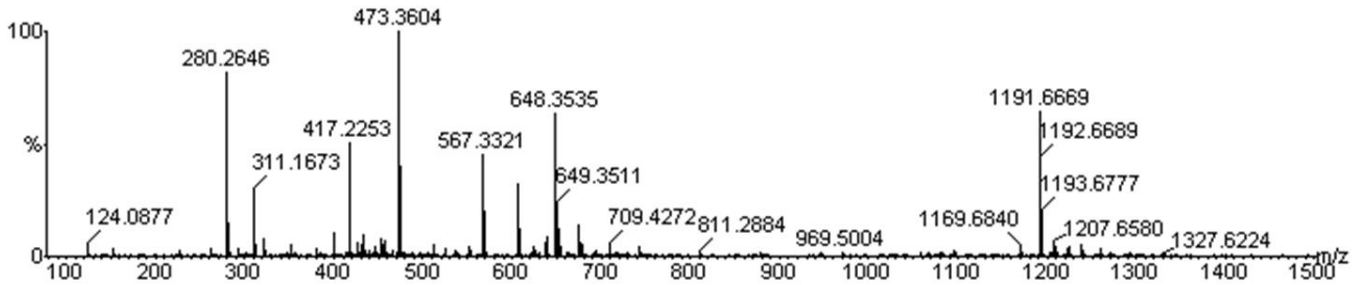
Figure S88. HRESIMS spectrum (TOF) of **16a**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
677 formula(e) evaluated with 5 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

29-Apr-2016 6::9::2 LCT Premier XE KE483 ROUSSI_esposito45-3 711 (3.313)
1: TOF MS ES+

3.82e+003



Minimum:				-1.5			
Maximum:		5.0	10.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
607.3246	607.3247	-0.1	-0.2	10.5	190.3	0.5	C34 H48 O8 Na $[M+Na]^+$
	607.3271	-2.5	-4.1	13.5	191.5	1.7	C36 H47 O8
	607.3212	3.4	5.6	22.5	194.5	4.7	C43 H43 O3
	607.3188	5.8	9.6	19.5	193.5	3.7	C41 H44 O3 Na
	607.3306	-6.0	-9.9	1.5	191.4	1.6	C27 H52 O13 Na

Figure S89. ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **16b**

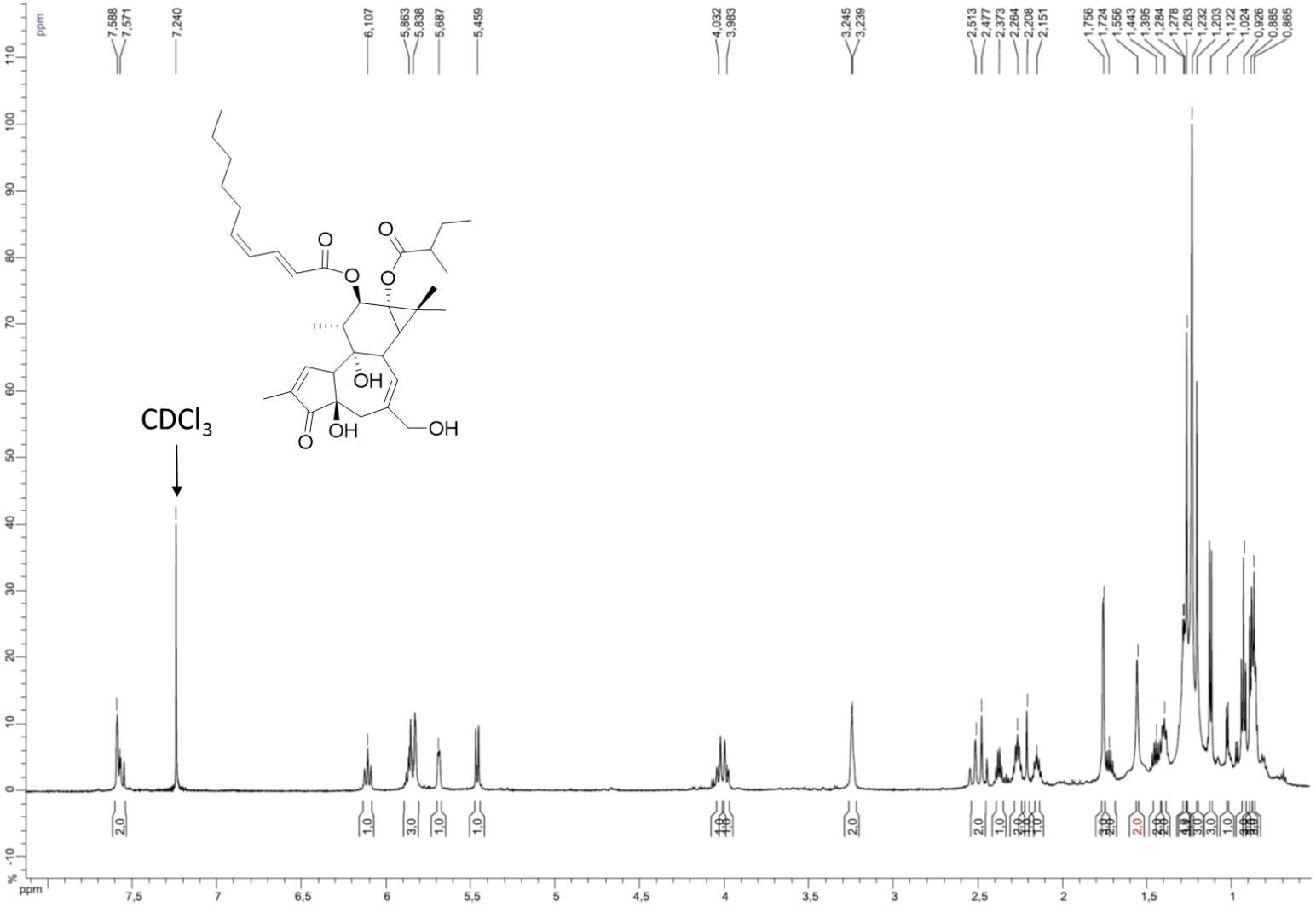


Figure S90. COSY NMR spectrum ($CDCl_3$, 600 MHz) of **16b**

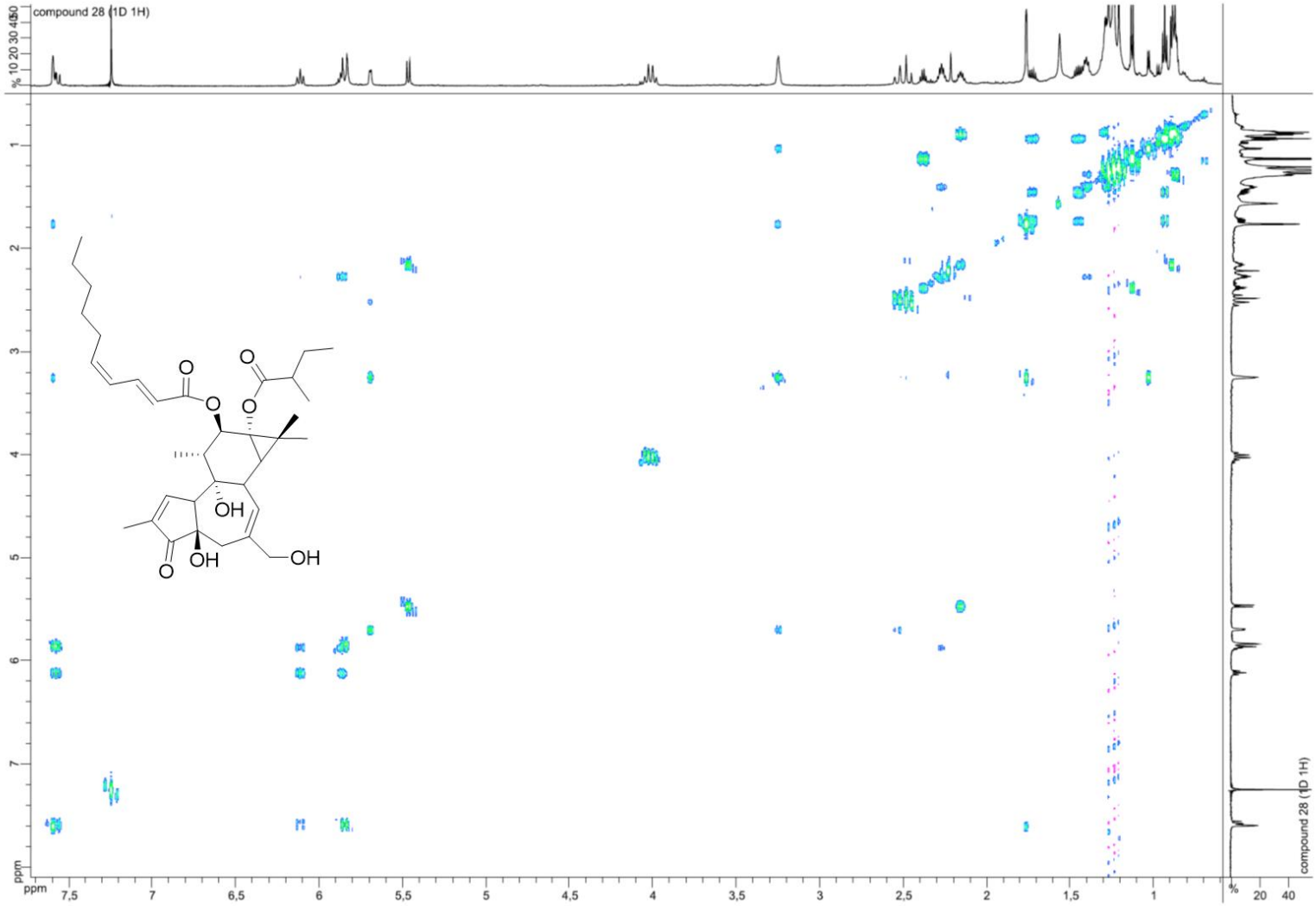


Figure S91. HMBC NMR spectrum ($CDCl_3$, 600 MHz) of **16b**

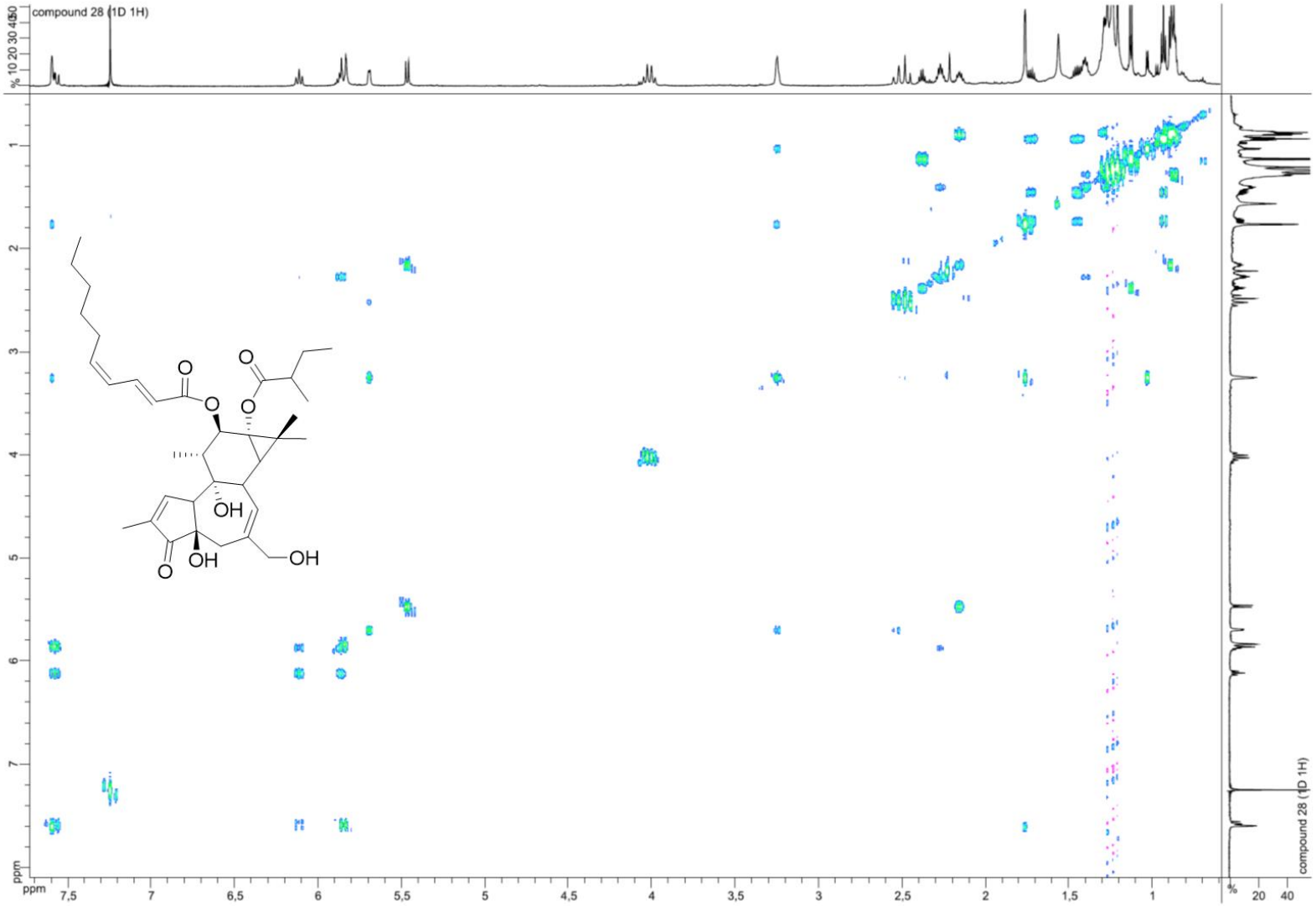


Figure S92. ROESY NMR spectrum ($CDCl_3$, 600 MHz) of **16b**

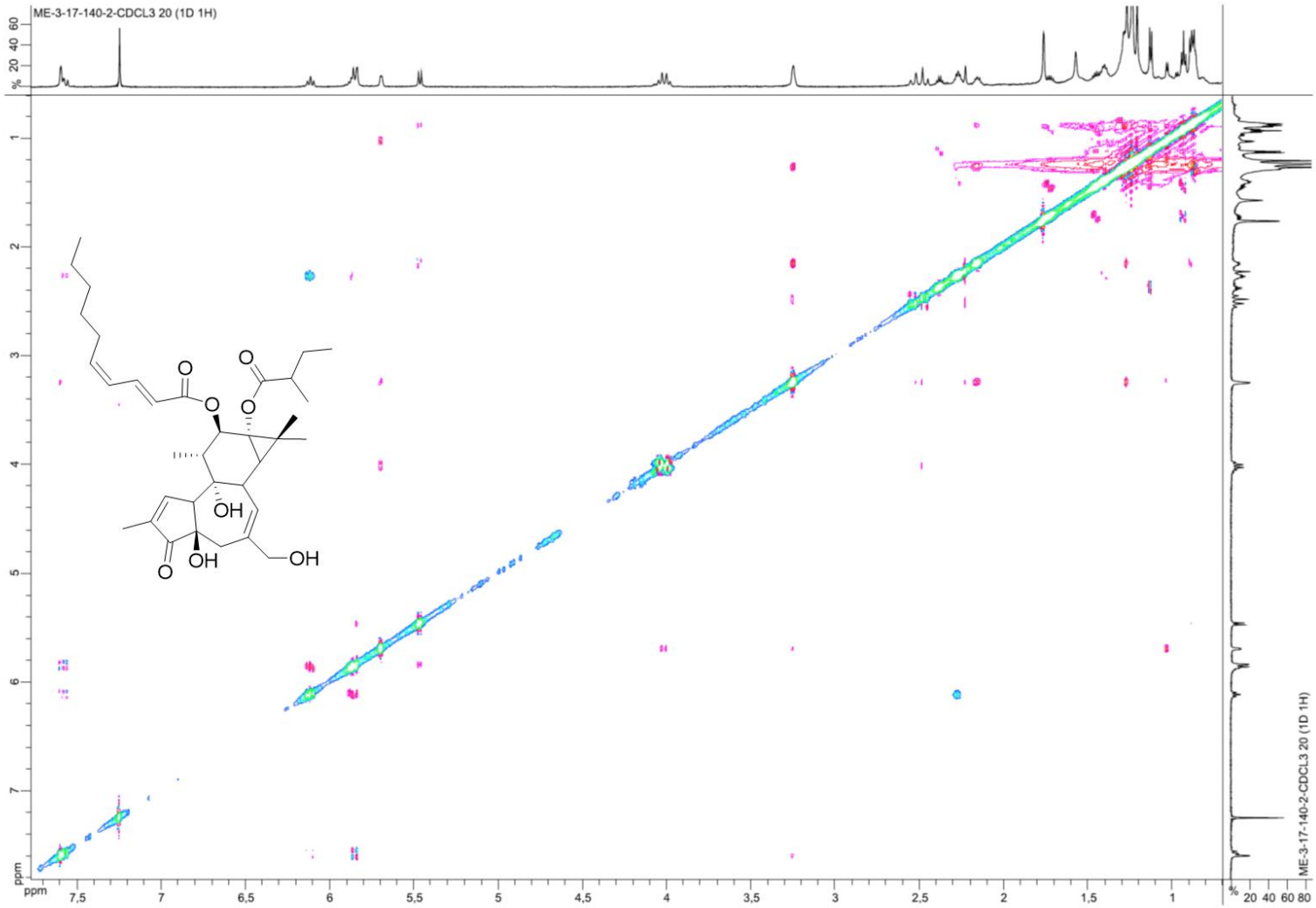
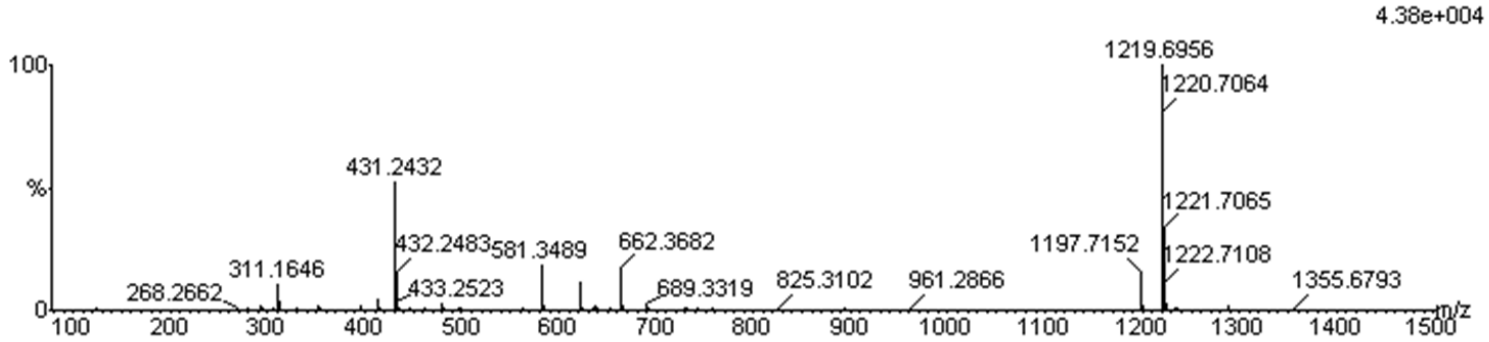


Figure S93. HRESIMS spectrum (TOF) of **16b**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
705 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

29-Apr-2016 6::6::0 LCT Premier XE KE483 ROUSSI_esposito45-1 727 (3.388)
1: TOF MS ES+



Minimum:				-1.5						
Maximum:		5.0	10.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
621.3422	621.3427	-0.5	-0.8	13.5	314.5	2.3	C37	H49	08	
	621.3403	1.9	3.1	10.5	312.3	0.1	C35	H50	08	Na $[M+Na]^+$
	621.3462	-4.0	-6.4	1.5	315.6	3.4	C28	H54	013	Na
	621.3369	5.3	8.5	22.5	319.8	7.6	C44	H45	03	

Figure S94. ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **16c**

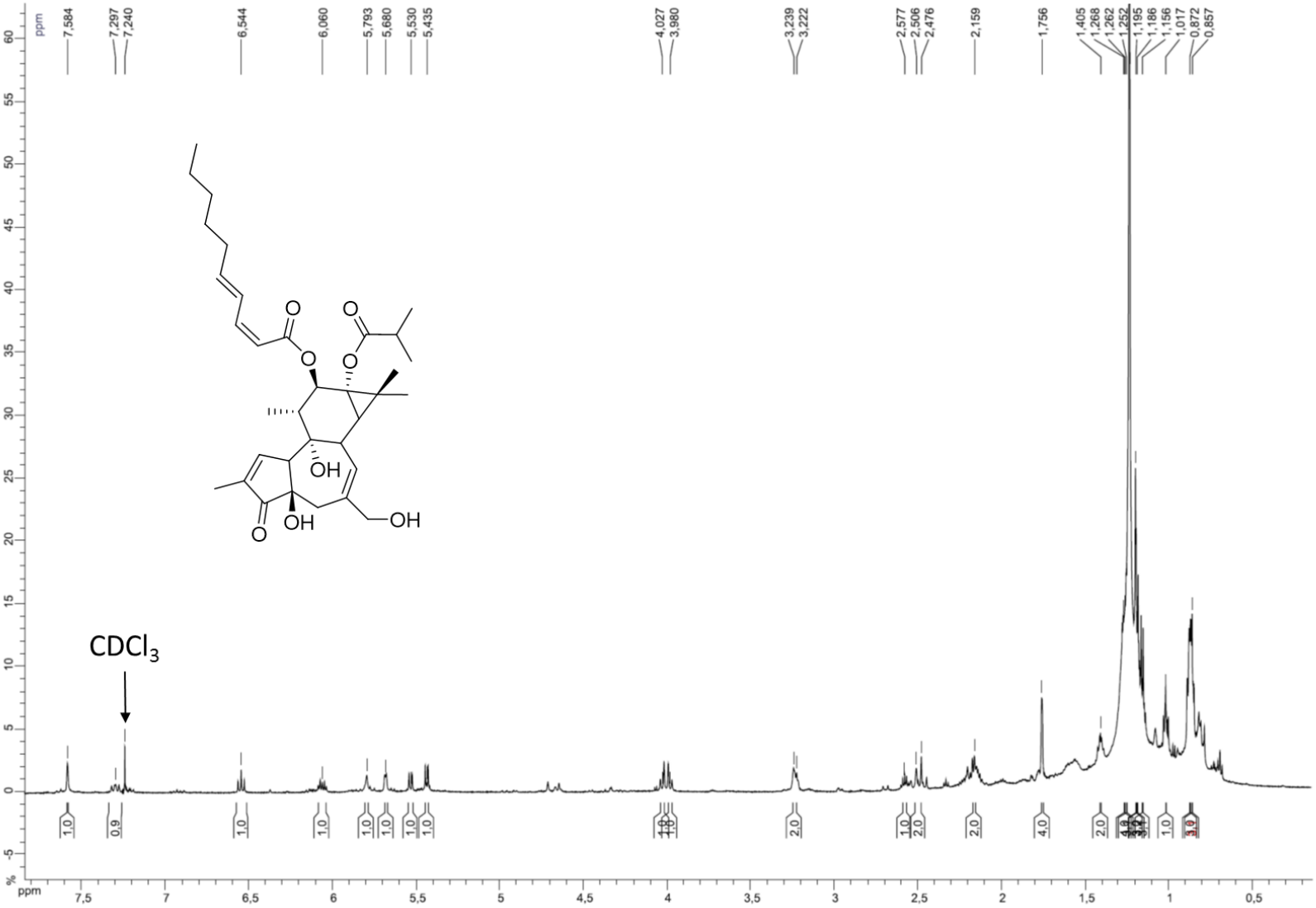


Figure S95. COSY NMR spectrum ($CDCl_3$, 600 MHz) of **16c**

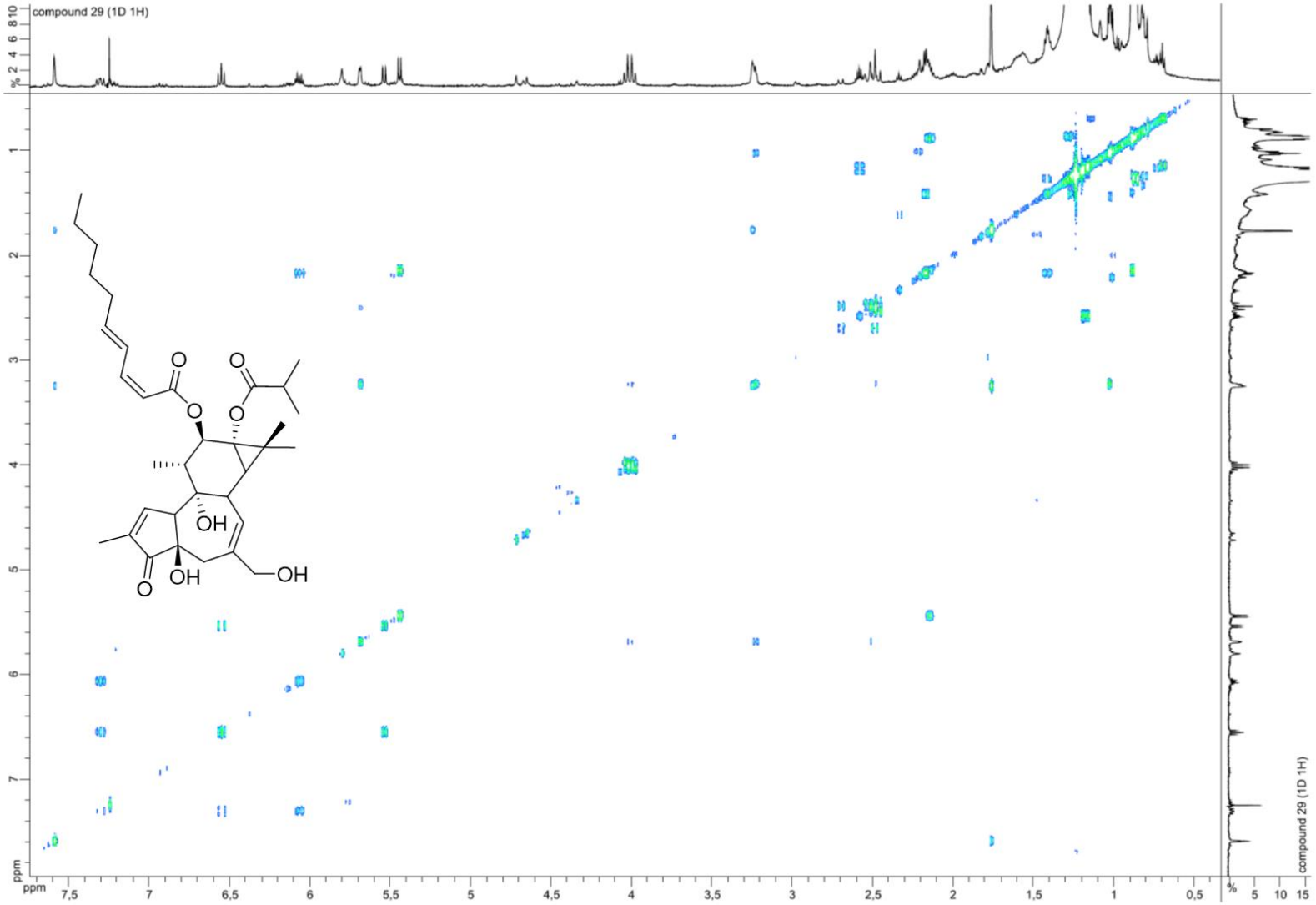


Figure S96. ROESY NMR spectrum ($CDCl_3$, 600 MHz) of **16c**

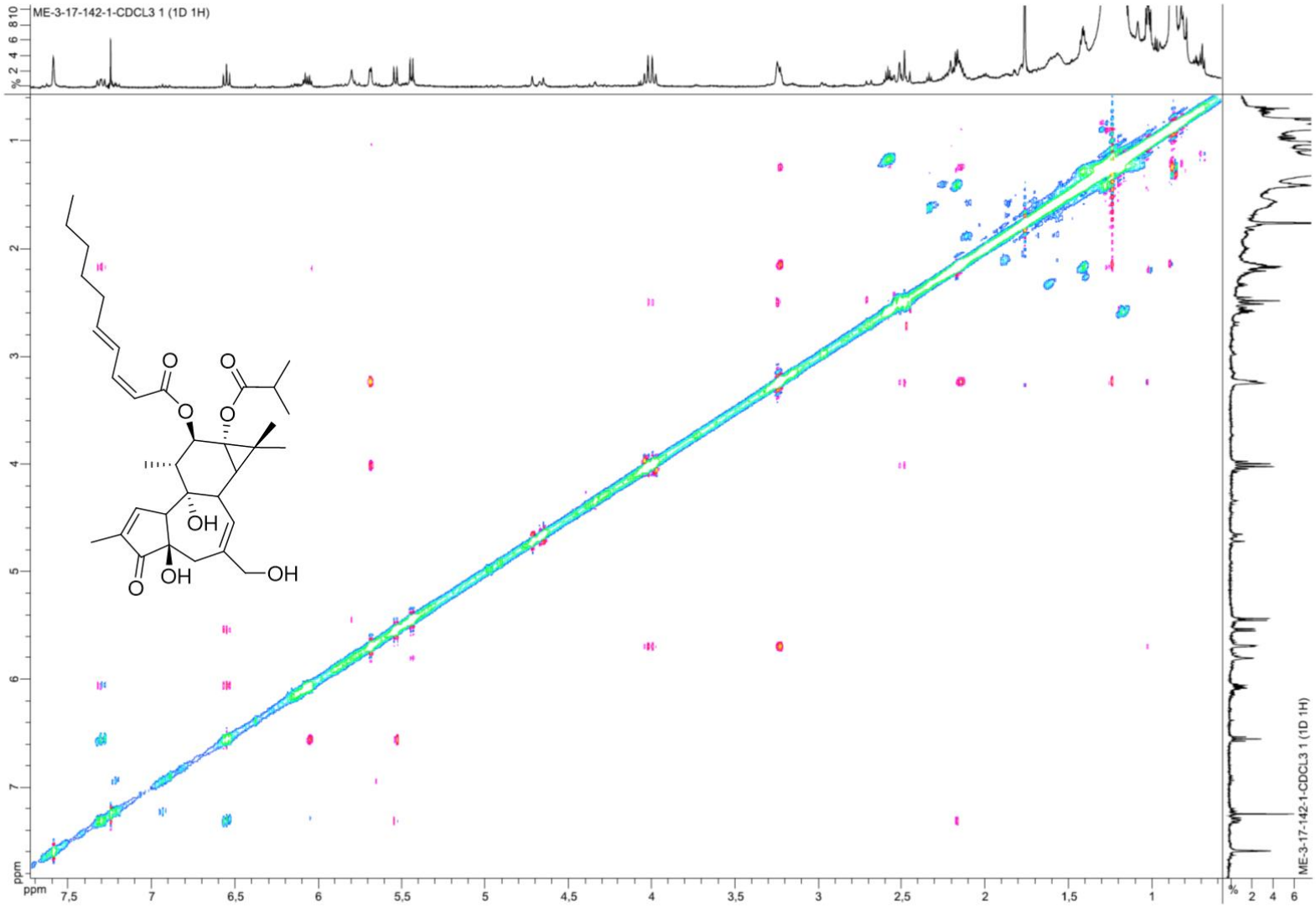


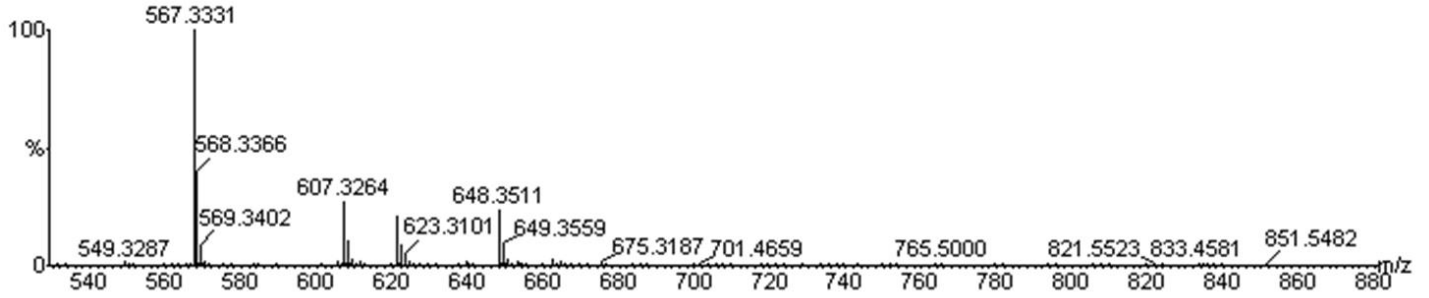
Figure S97. HRESIMS spectrum (TOF) of **16c**

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
677 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

02-May-2016 3::7::3 LCT Premier XE KE483 ROUSSI_esposito46-2 717 (3.322) Cm (716:721)
1: TOF MS ES+

1.06e+005



Minimum:				-1.5						
Maximum:		5.0	10.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
607.3264	607.3271	-0.7	-1.2	13.5	794.6	0.3	C36	H47	08	
	607.3247	1.7	2.8	10.5	799.1	4.8	C34	H48	08	Na $[M+Na]^+$
	607.3306	-4.2	-6.9	1.5	795.8	1.5	C27	H52	013	Na
	607.3212	5.2	8.6	22.5	799.9	5.6	C43	H43	03	

Figure S98. ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **17**

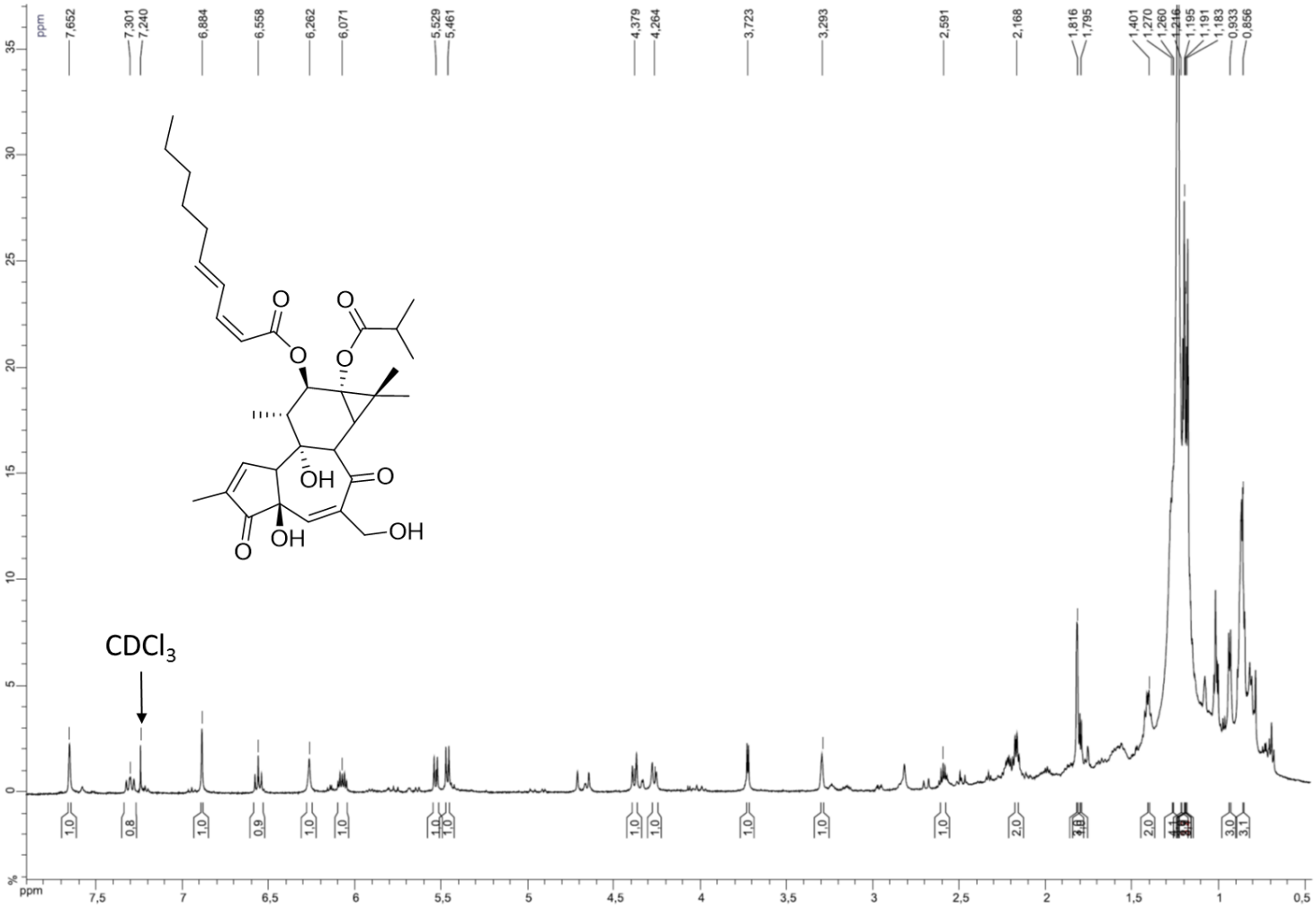


Figure S99. COSY NMR spectrum ($CDCl_3$, 600 MHz) of **17**

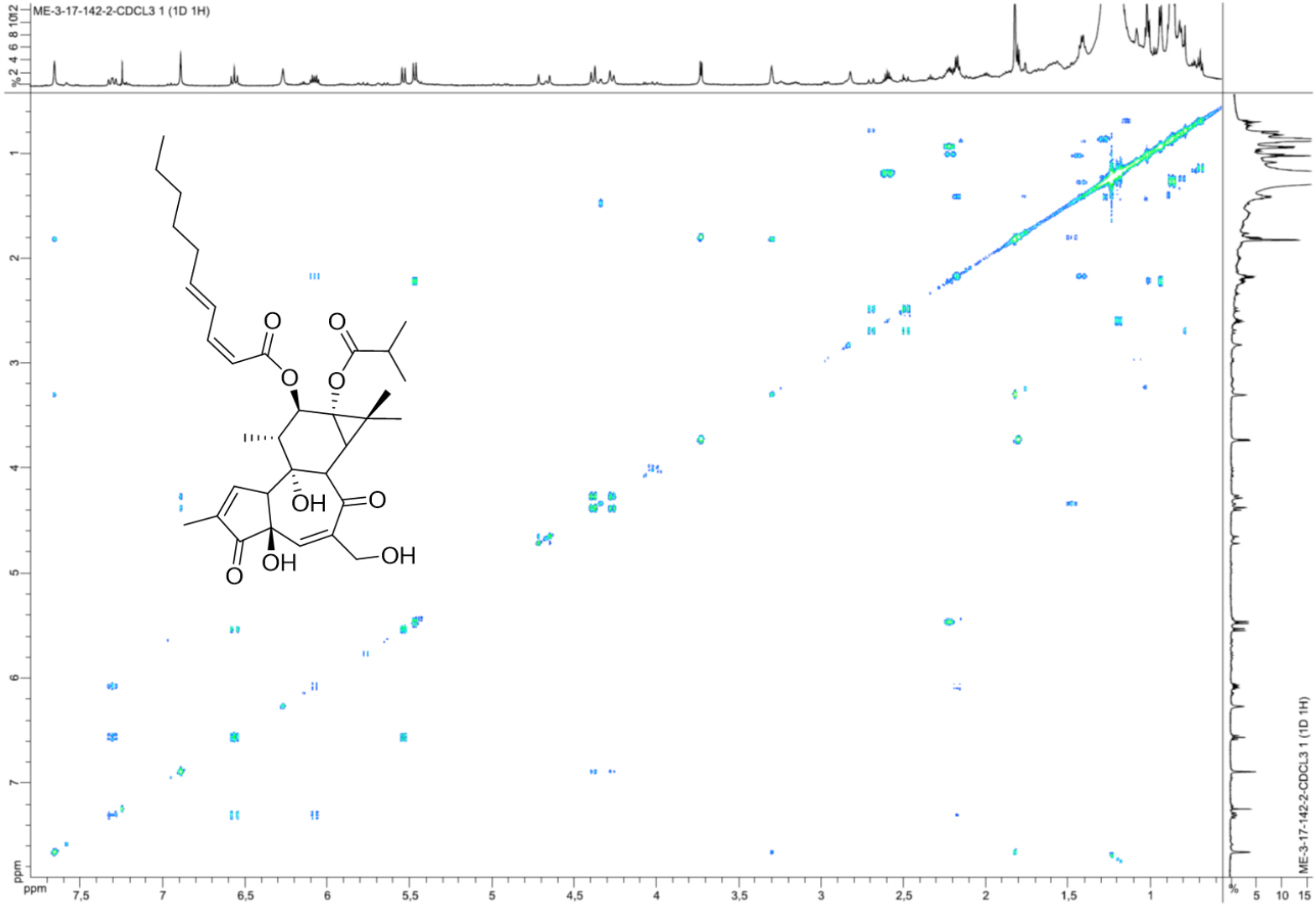


Figure S100. ROESY NMR spectrum ($CDCl_3$, 600 MHz) of **17**

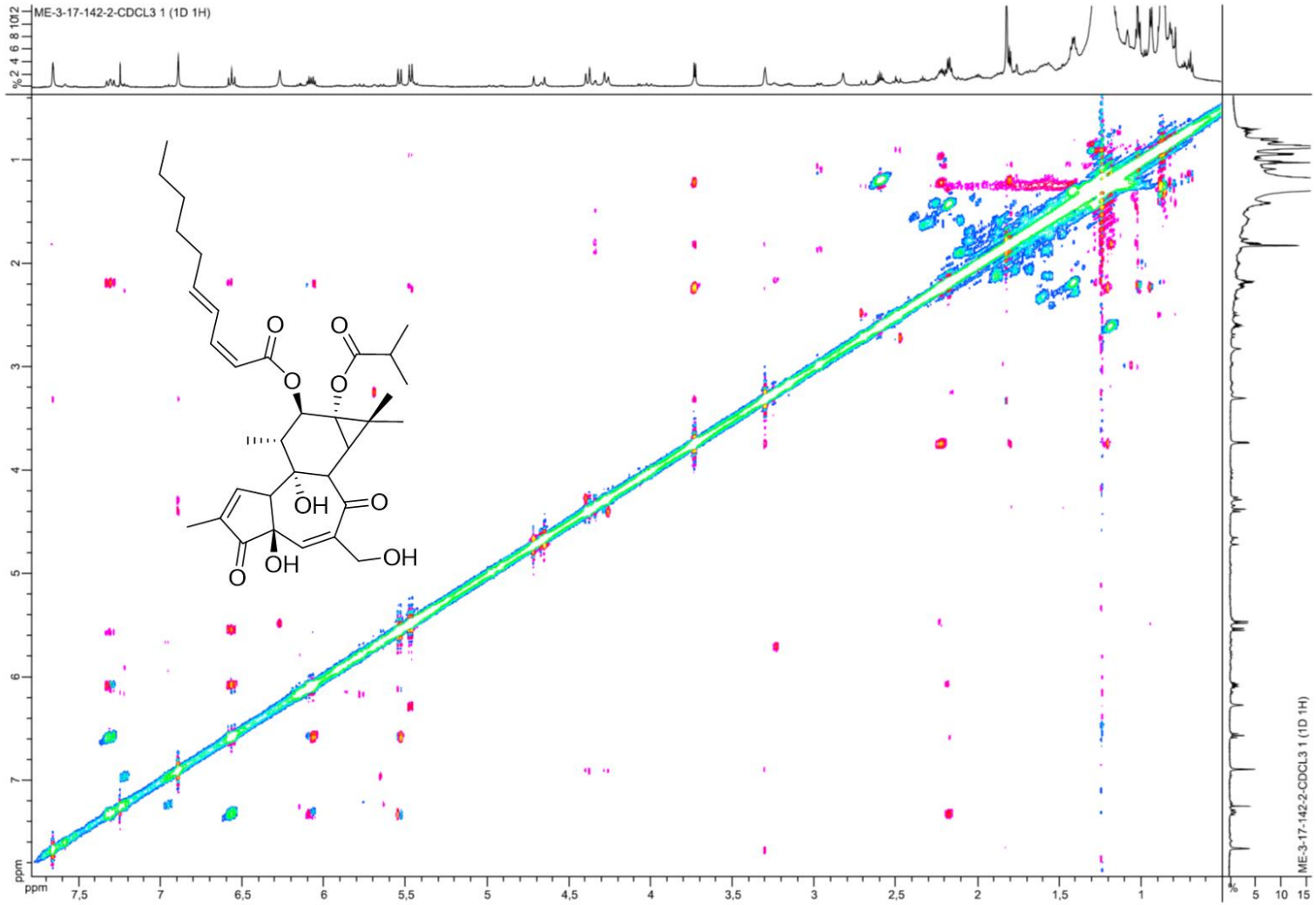


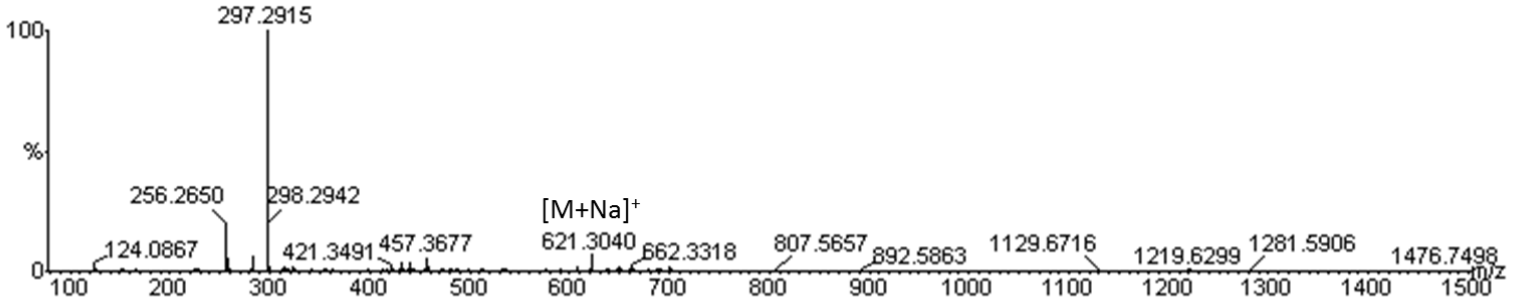
Figure S101. HRESIMS spectrum (TOF) of **17**

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
704 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-60 H: 0-100 N: 0-1 O: 0-50 Na: 0-1

02-May-2016 3::3::4 LCT Premier XE KE483 ROUSSI_esposito46-1 744 (3.460)
1: TOF MS ES+

1.27e+004



Minimum:				-1.5			
Maximum:		5.0	3.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
621.3040	621.3040	0.0	0.0	11.5	163.8	0.0	C34 H46 O9 Na [M+Na]+