

Supplementary Information

Synthesis and antiproliferative activity of derivatives of the phyllanthusmin class of aryl-naphthalene lignan lactones

John L. Woodard, Andrew C. Huntsman, Pratiq A. Patel, Hee-Byung Chai, Ragu Kanagasabai, Soumendrakrishna Karmahapatra, Alexandria N. Young, Yulin Ren, Denisse Herrera, Jack C. Yalowich, A. Douglas Kinghorn, Joanna E. Burdette, James R. Fuchs*

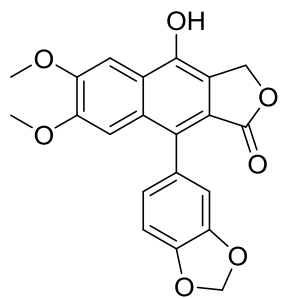
Additional Biological Data:	S1
¹H and ¹³C NMR Spectra:	S2
Additional NMR Spectra of 5 and 16:	S43
HPLC Traces for Tested Compounds:	S51

MDA-MB-435 and MDA-MB-231 cell proliferation assays

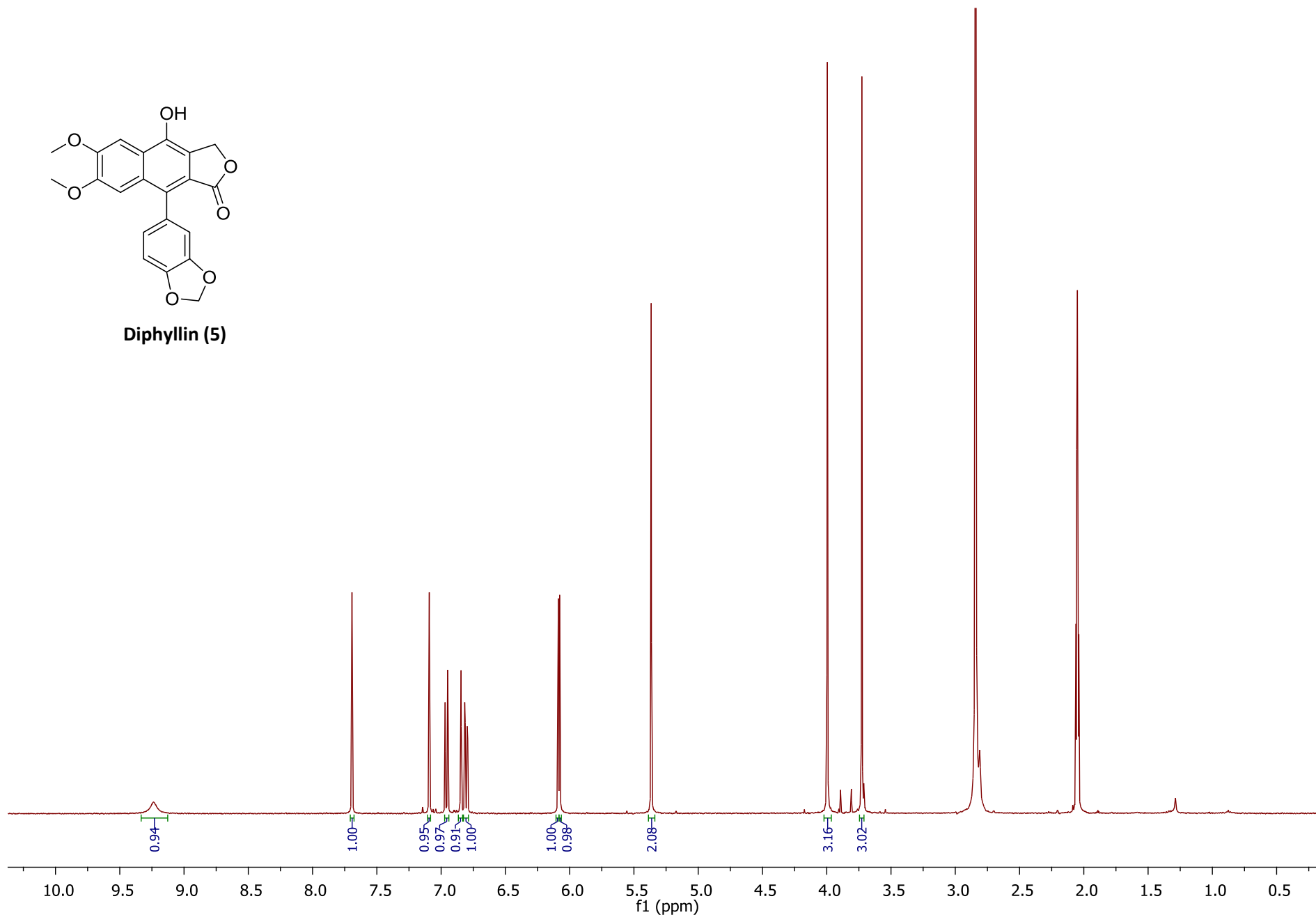
The cytotoxicity of the tested compounds was screened against MDA-MB-435 and MDA-MB-231 cell lines using the previously reported protocol:¹

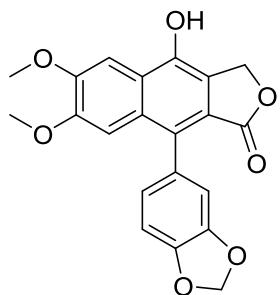
<i>Cmpd</i>	<i>Carbohydrate</i>	<i>Substitution</i>	<i>MDA-MB-435</i>	<i>MDA-MB-231</i>
6a	L-arabinose	-OAc	0.14	1.0
6b	L-arabinose	-OH	NT	NT
6c	L-arabinose	-OMe	0.14	0.65
7a	D-xylose	-OAc	0.23	5.1
7b	D-xylose	-OH	NT	NT
7c	D-xylose	-OMe	NT	NT
8a	D-glucose	-OAc	0.040	2.3
8b	D-glucose	-OH	NT	NT
9a	D-galactose	-OAc	0.41	1.2
9b	D-galactose	-OH	NT	NT
10	D-arabinose	-OAc	0.50	2.2
11	lactose	-OAc	>10	>10
12	D-xylose	-OMe	NT	NT
13	L-arabinose	-OAc	NT	NT
17	L-arabinose	-OAc	NT	NT
18	L-arabinose	-OAc	NT	NT

1.) Guo B, Onakpa MM, Huang X-J, Santarsiero BD, Chen W-L, Zhao M, Zhang X-Q, Swanson SM, Burdette JE, Che C-T. Di-nor- and 17-nor-pimaranes from *Icacina trichantha*. *J Nat Prod.* 2016;79:1815–1821.

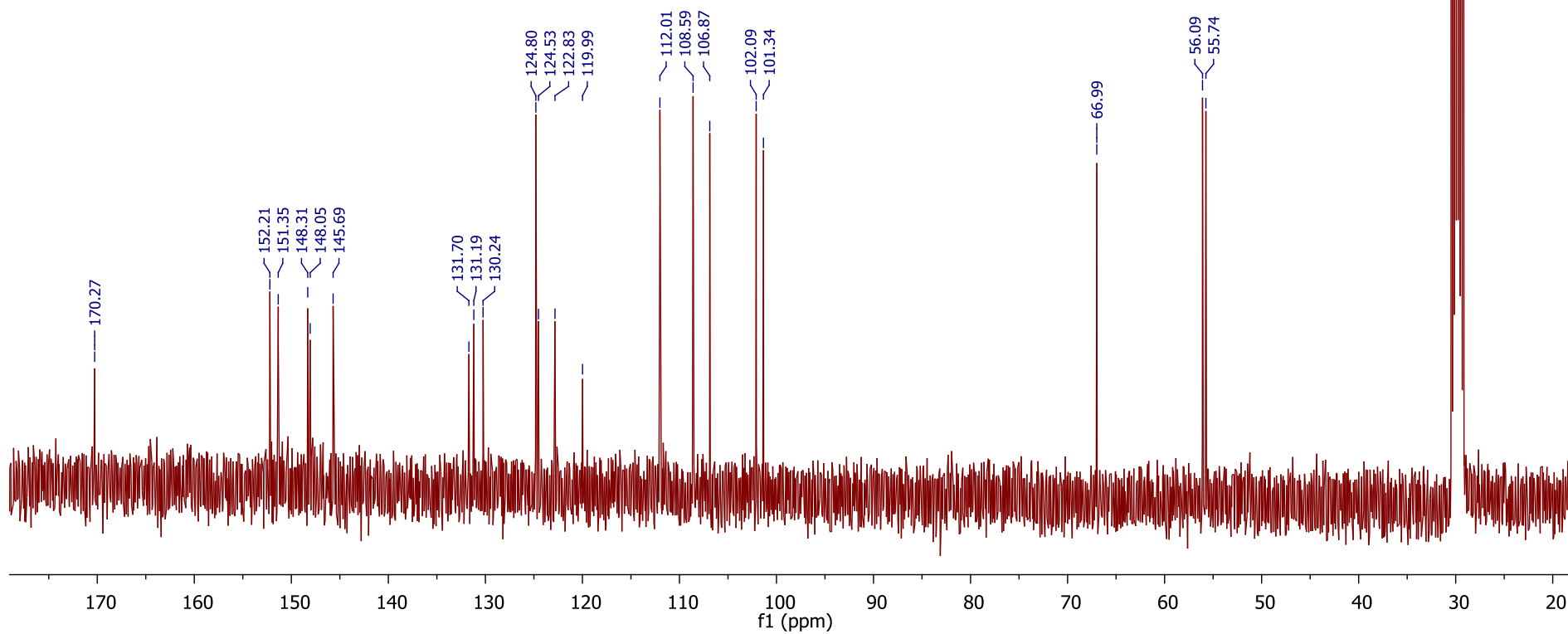


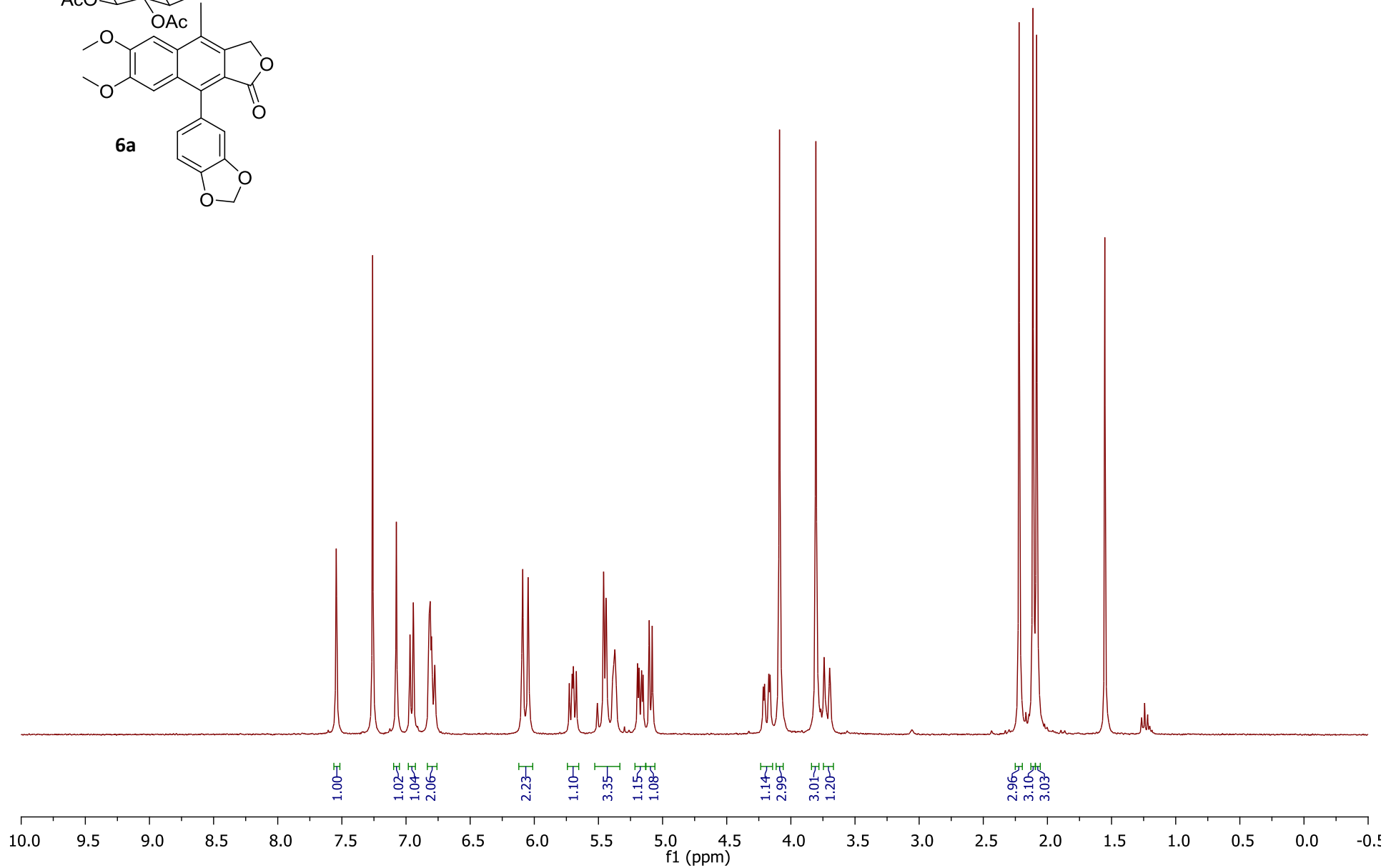
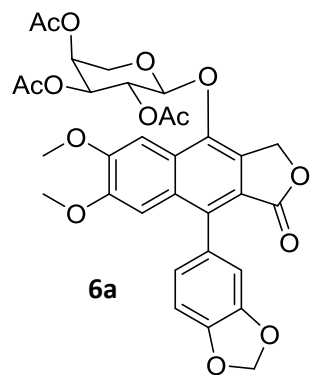
Diphyllin (5)

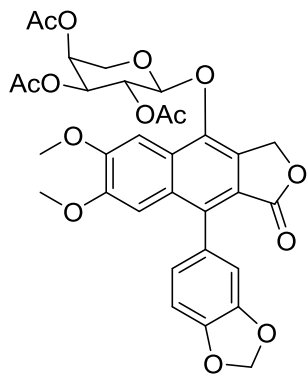




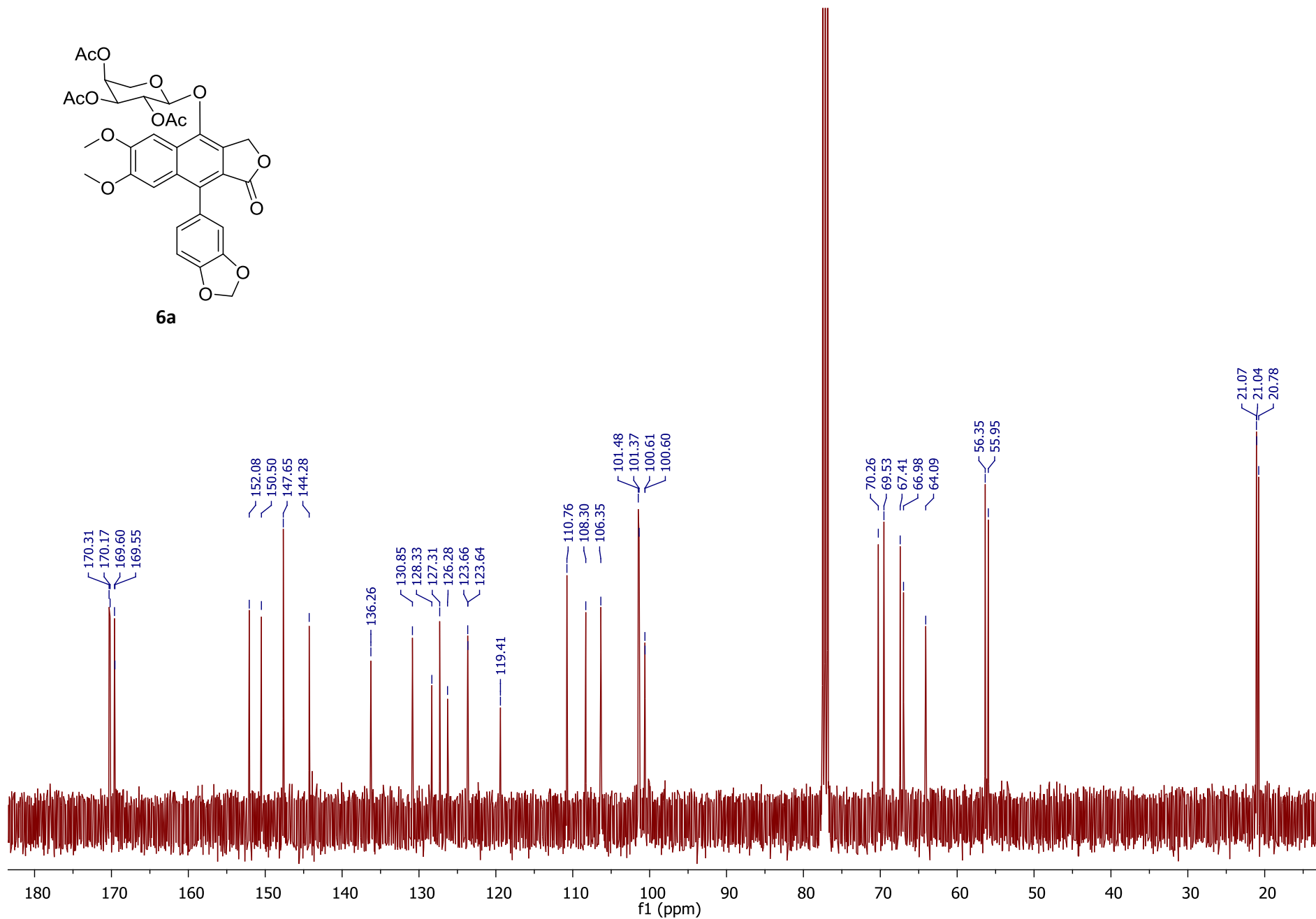
Diphyllin (5)

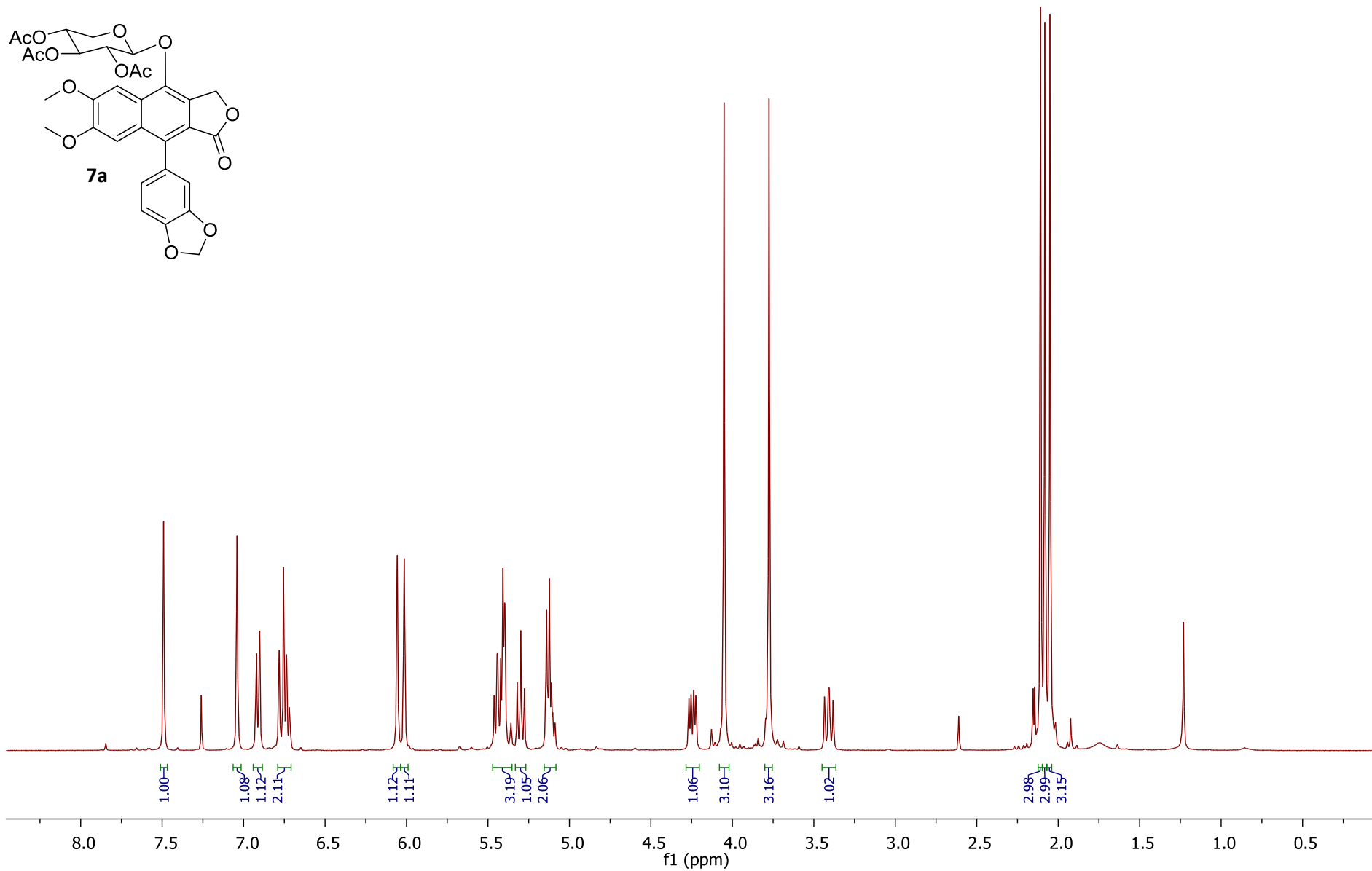
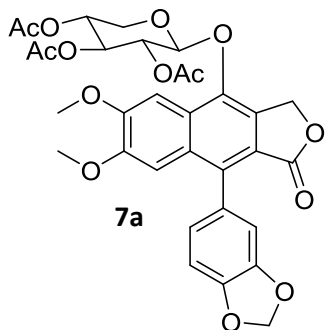


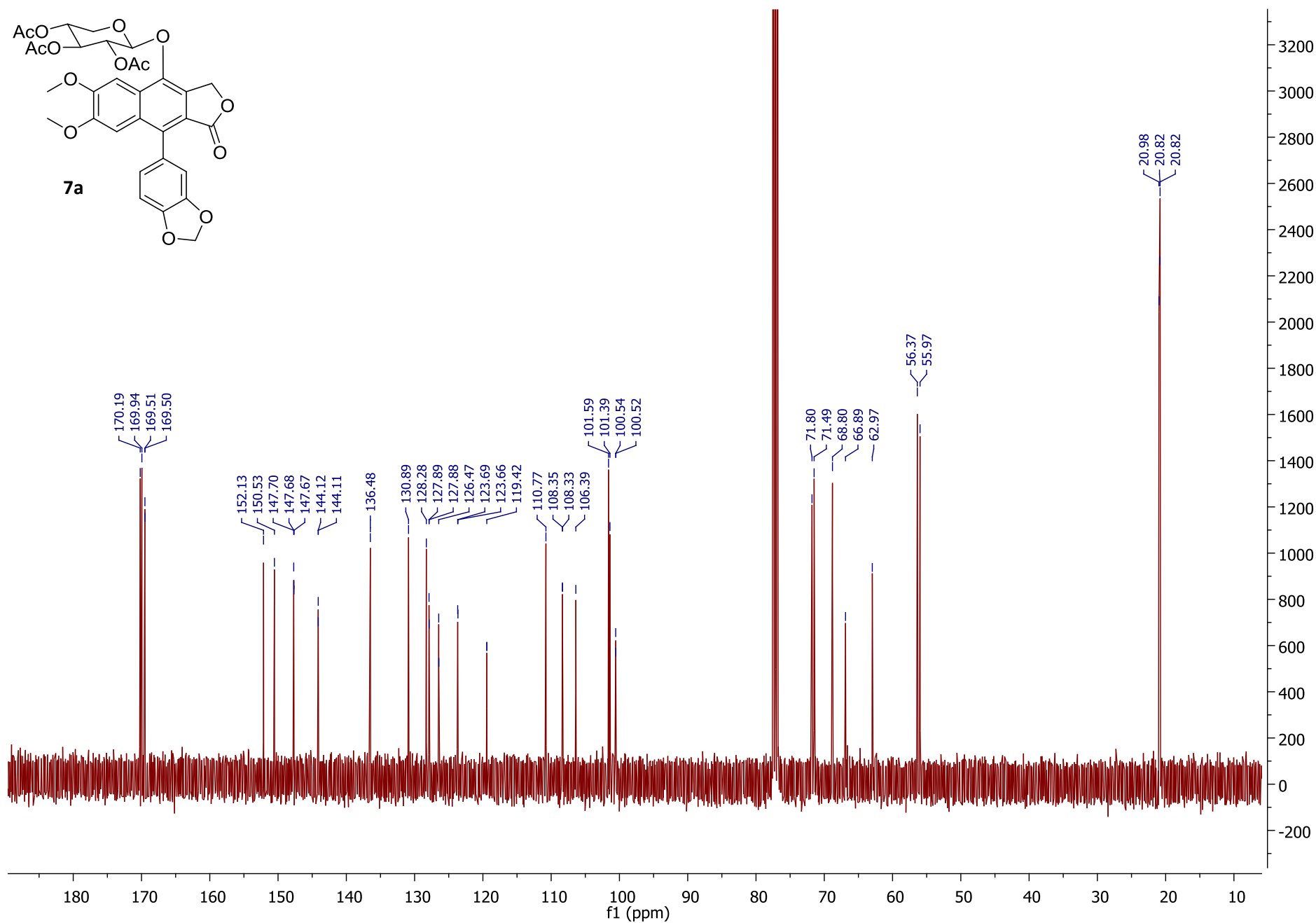
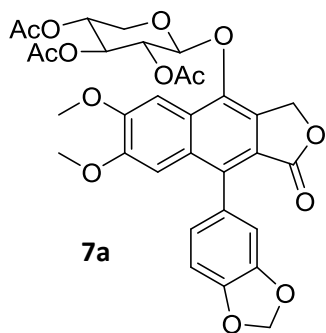


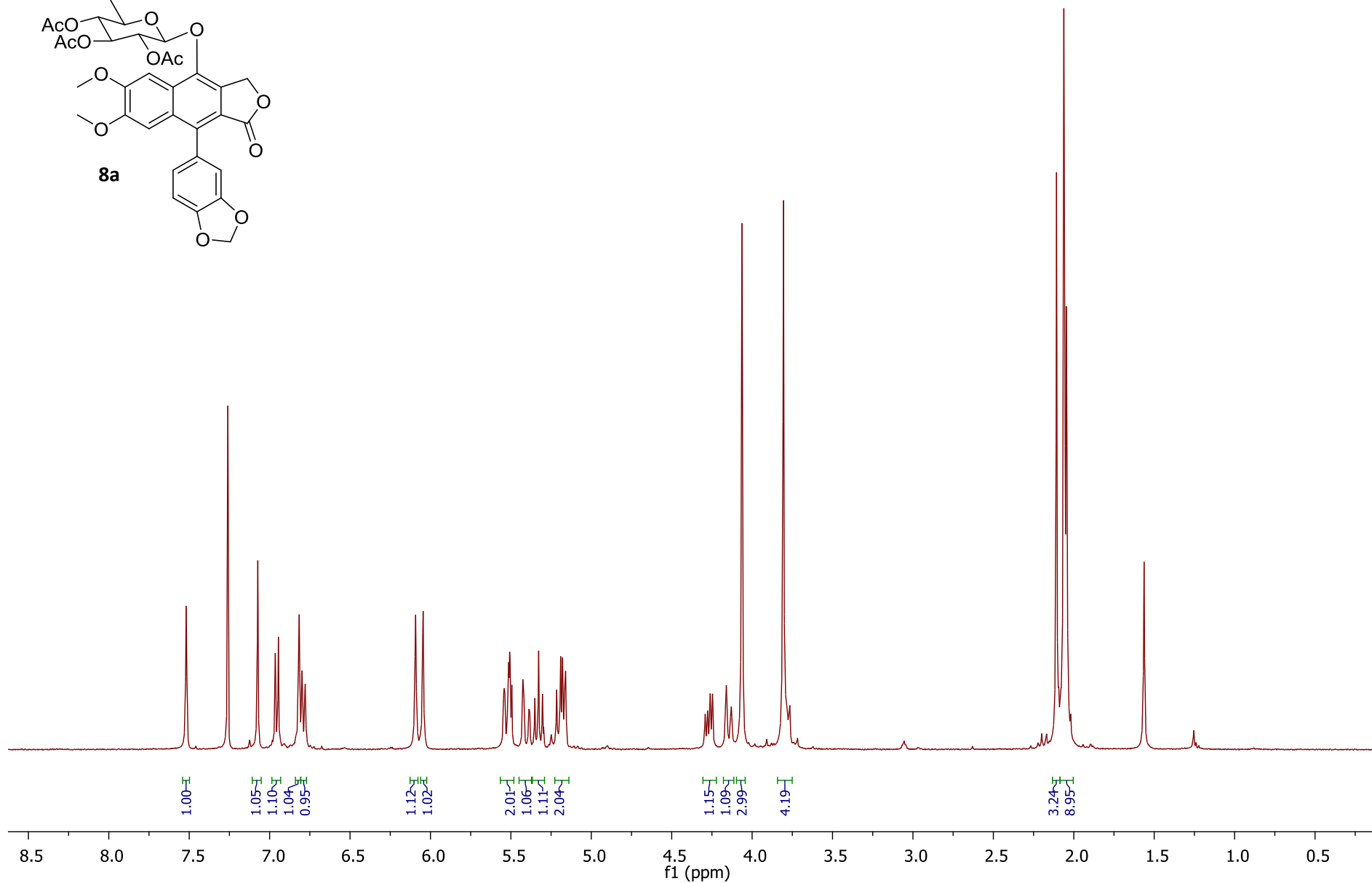
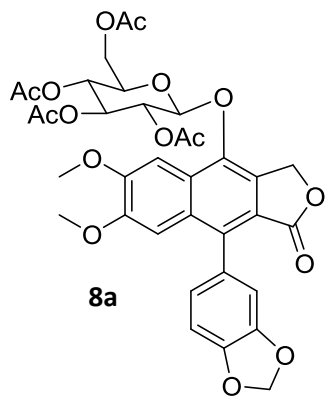


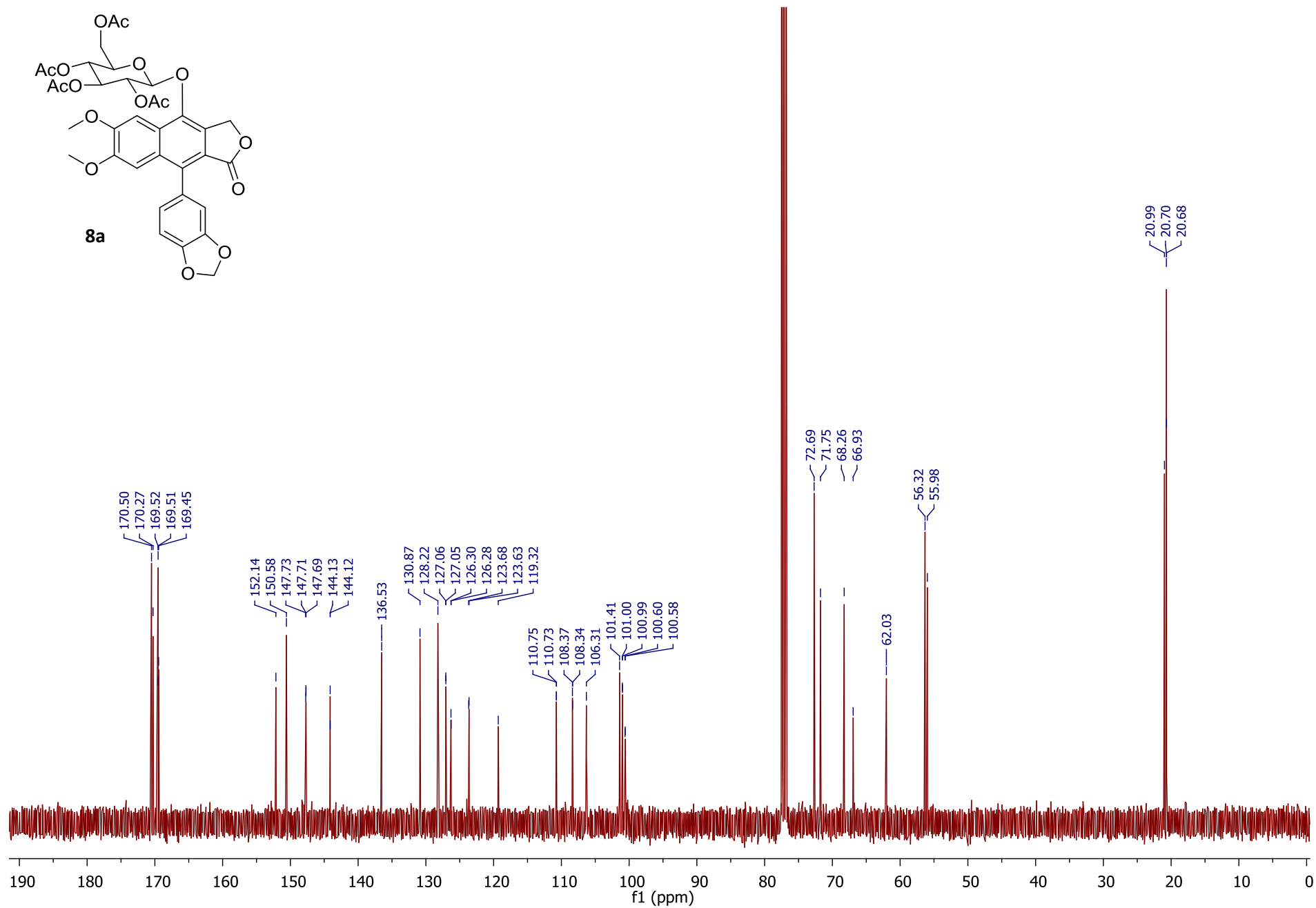
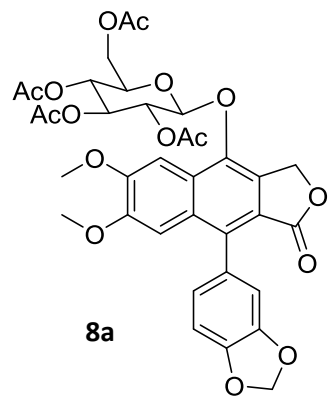
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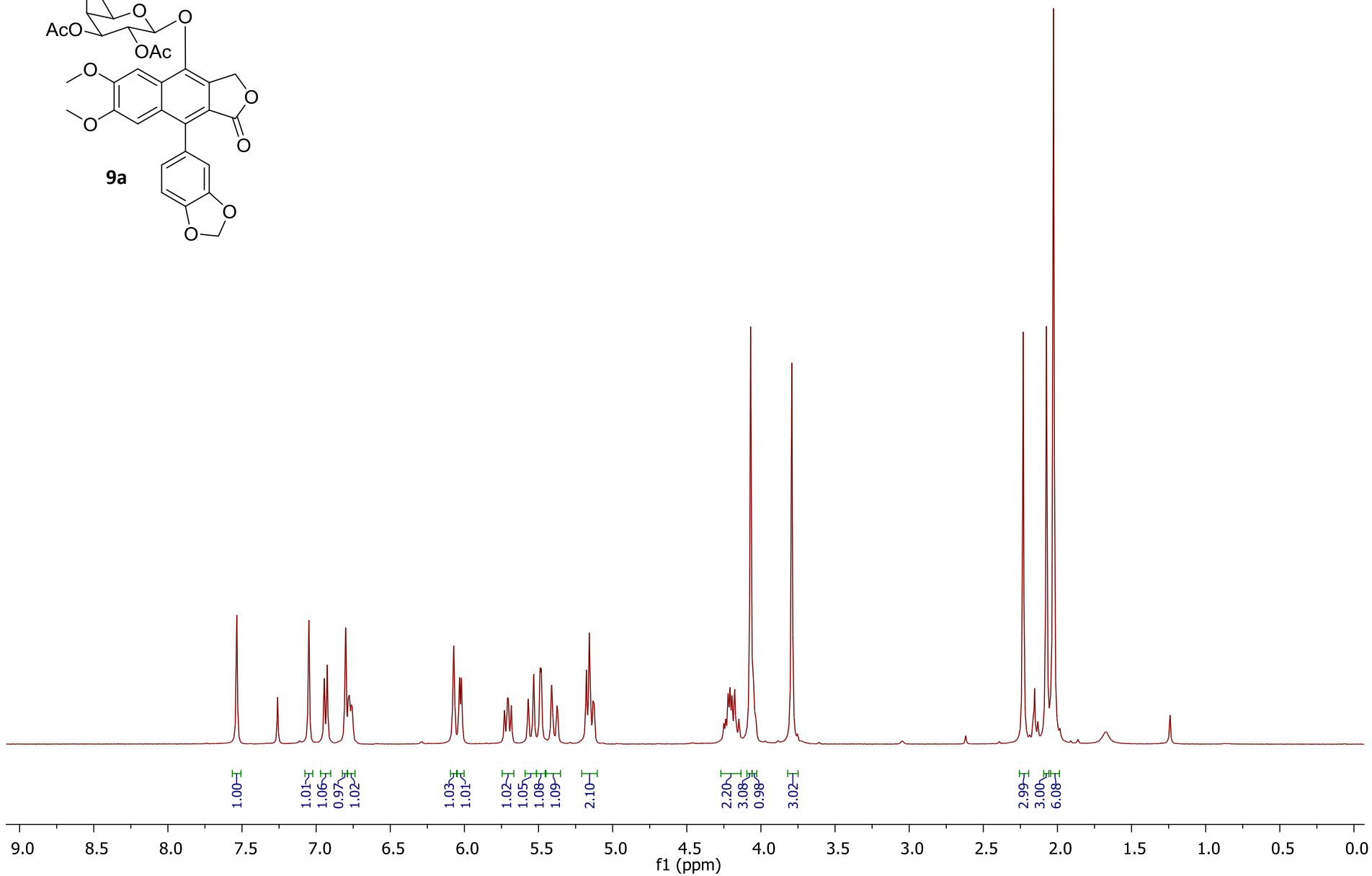
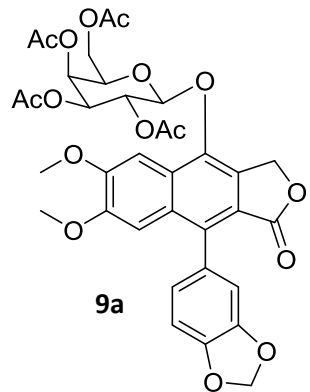


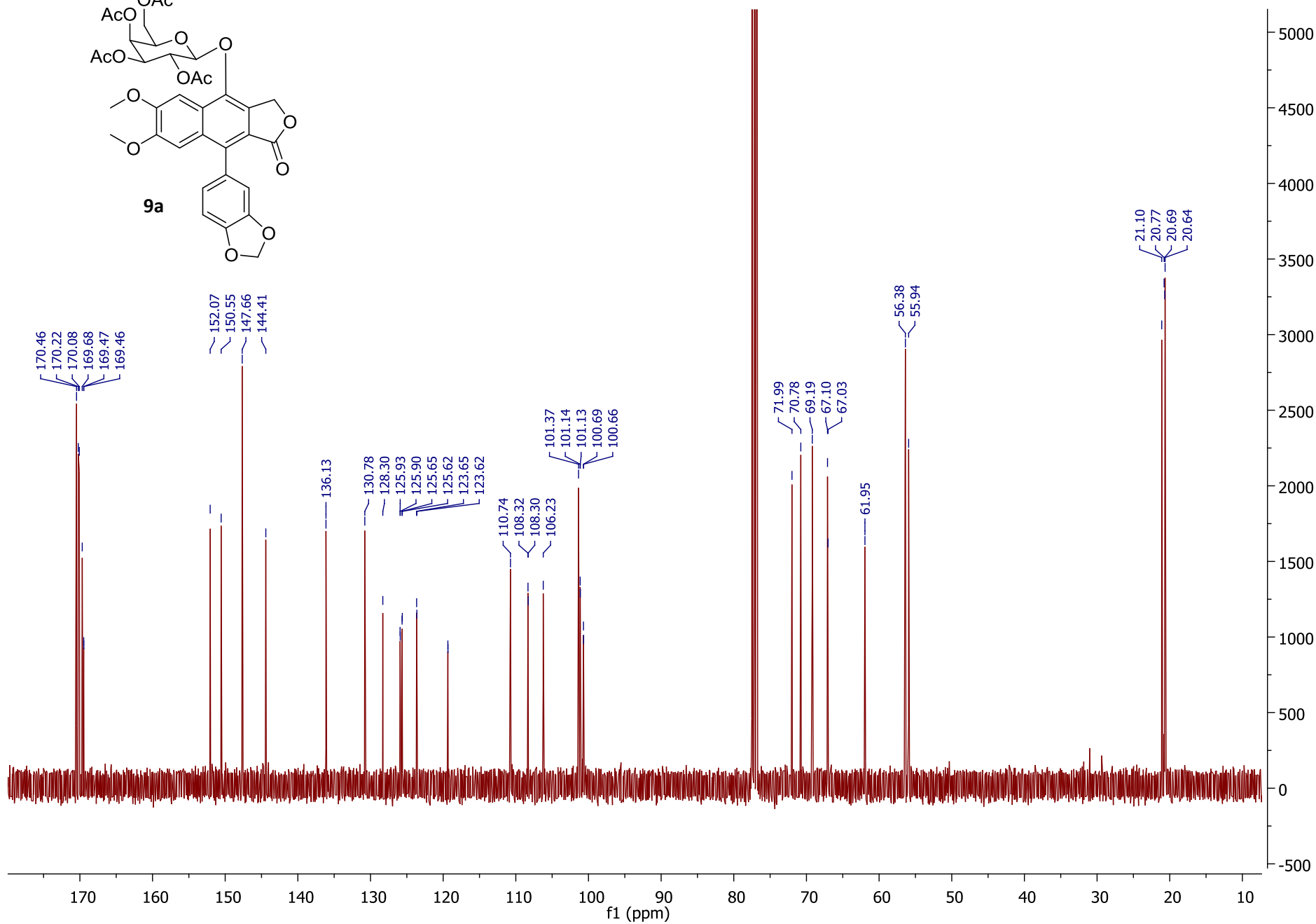
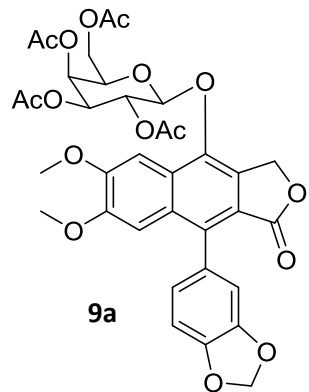


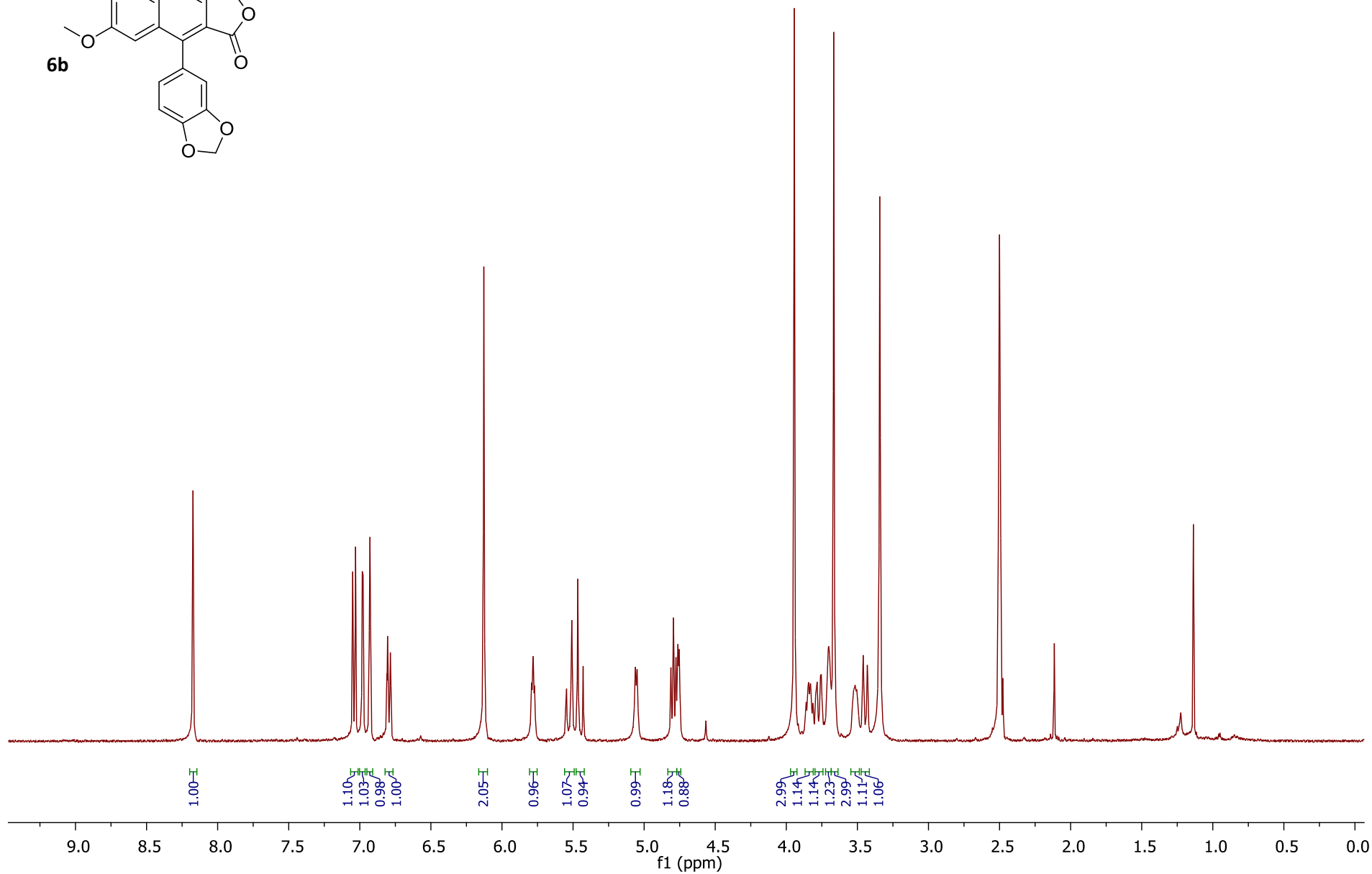
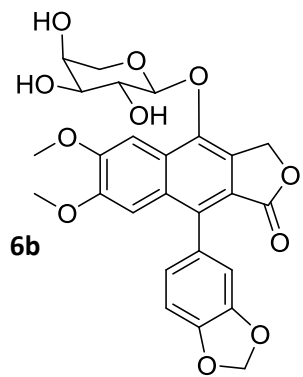


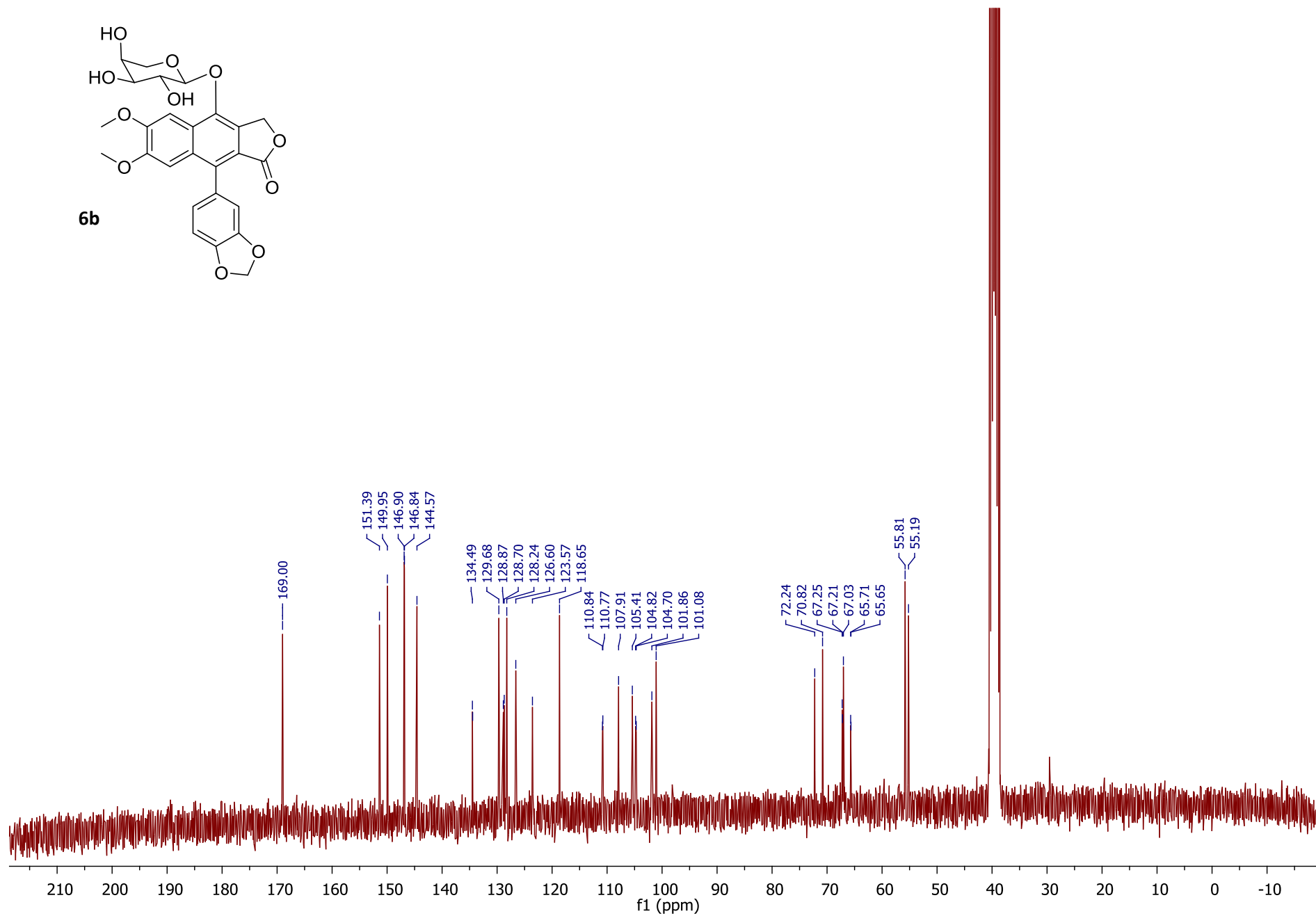
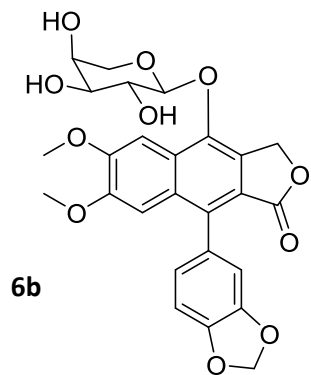


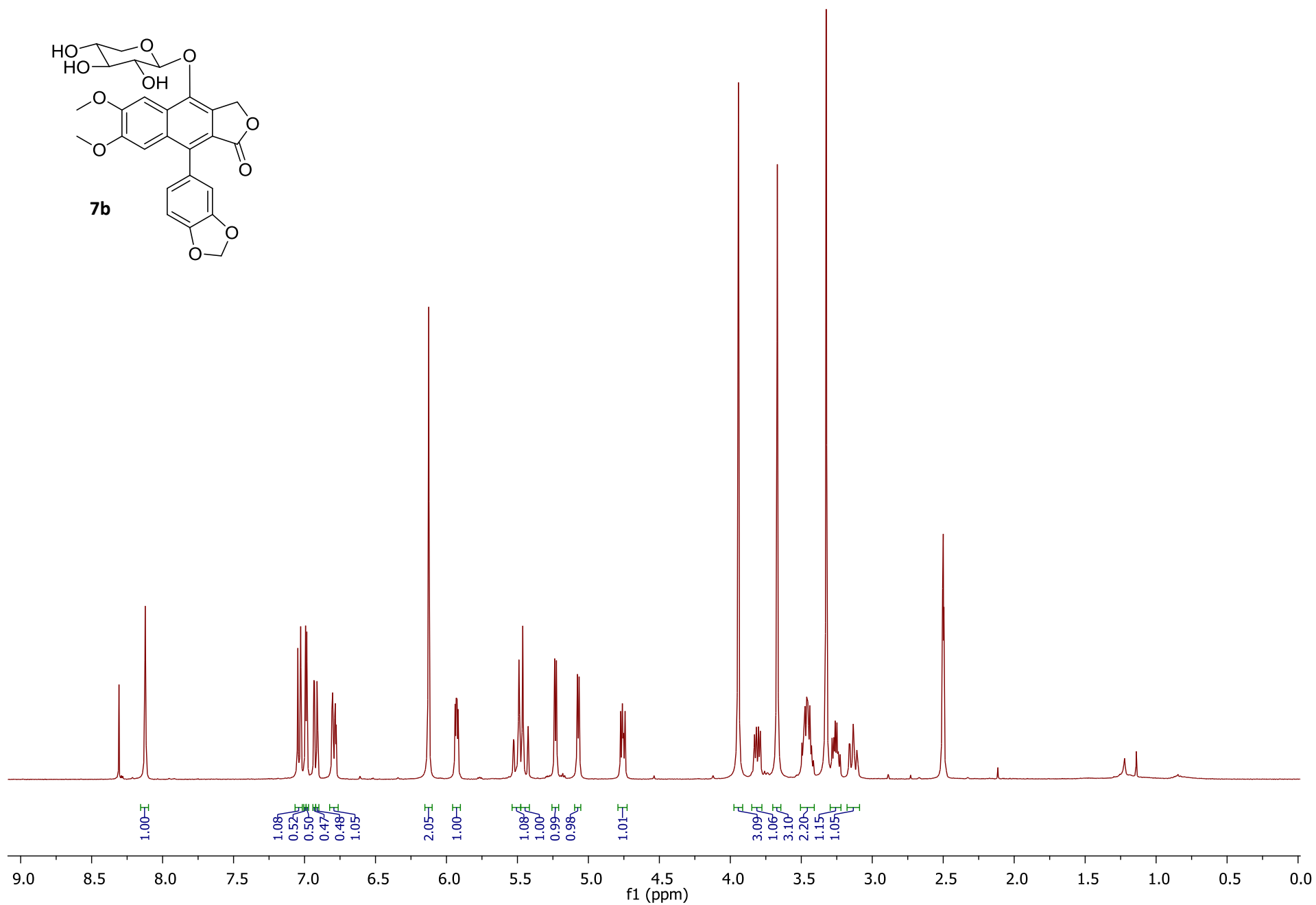
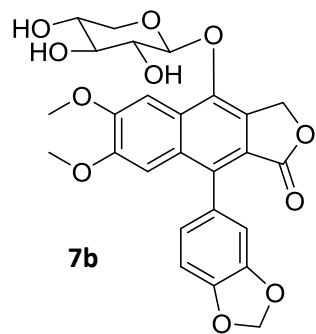


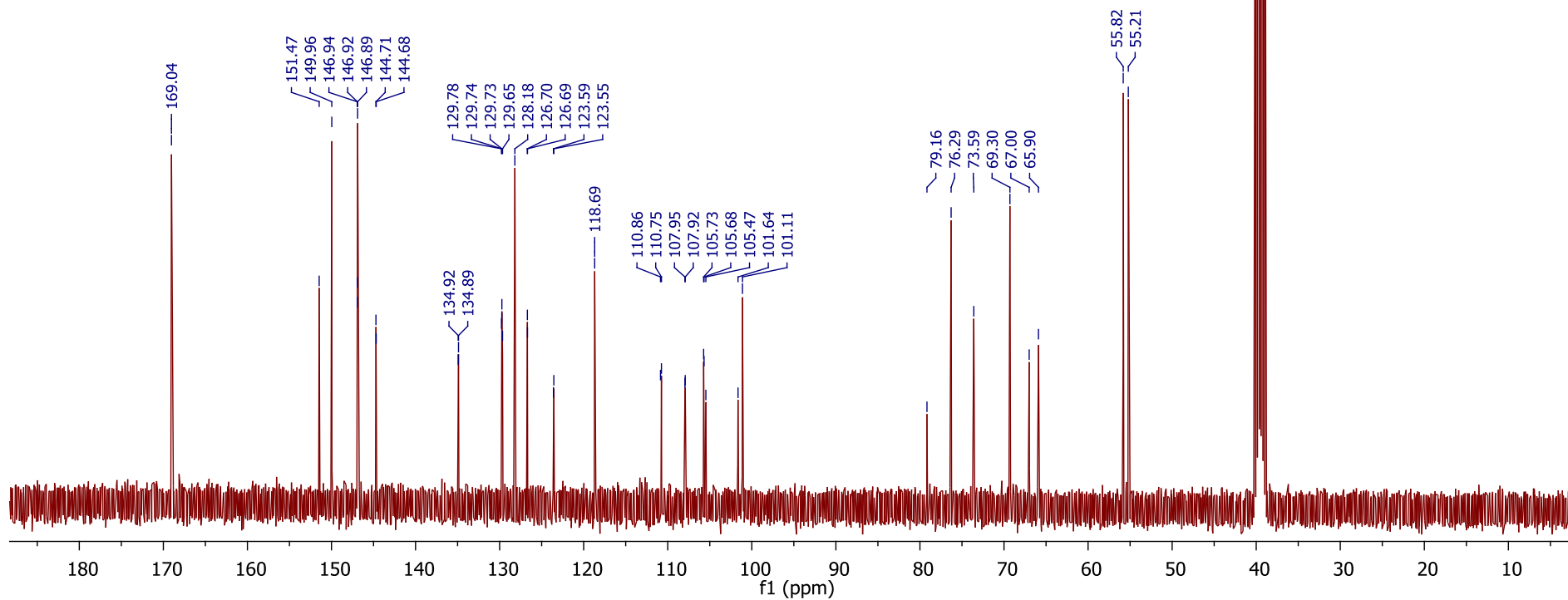
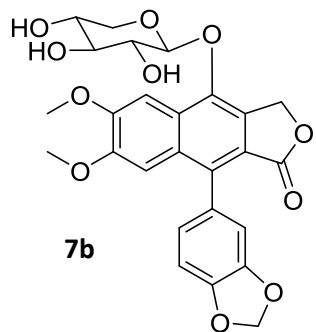


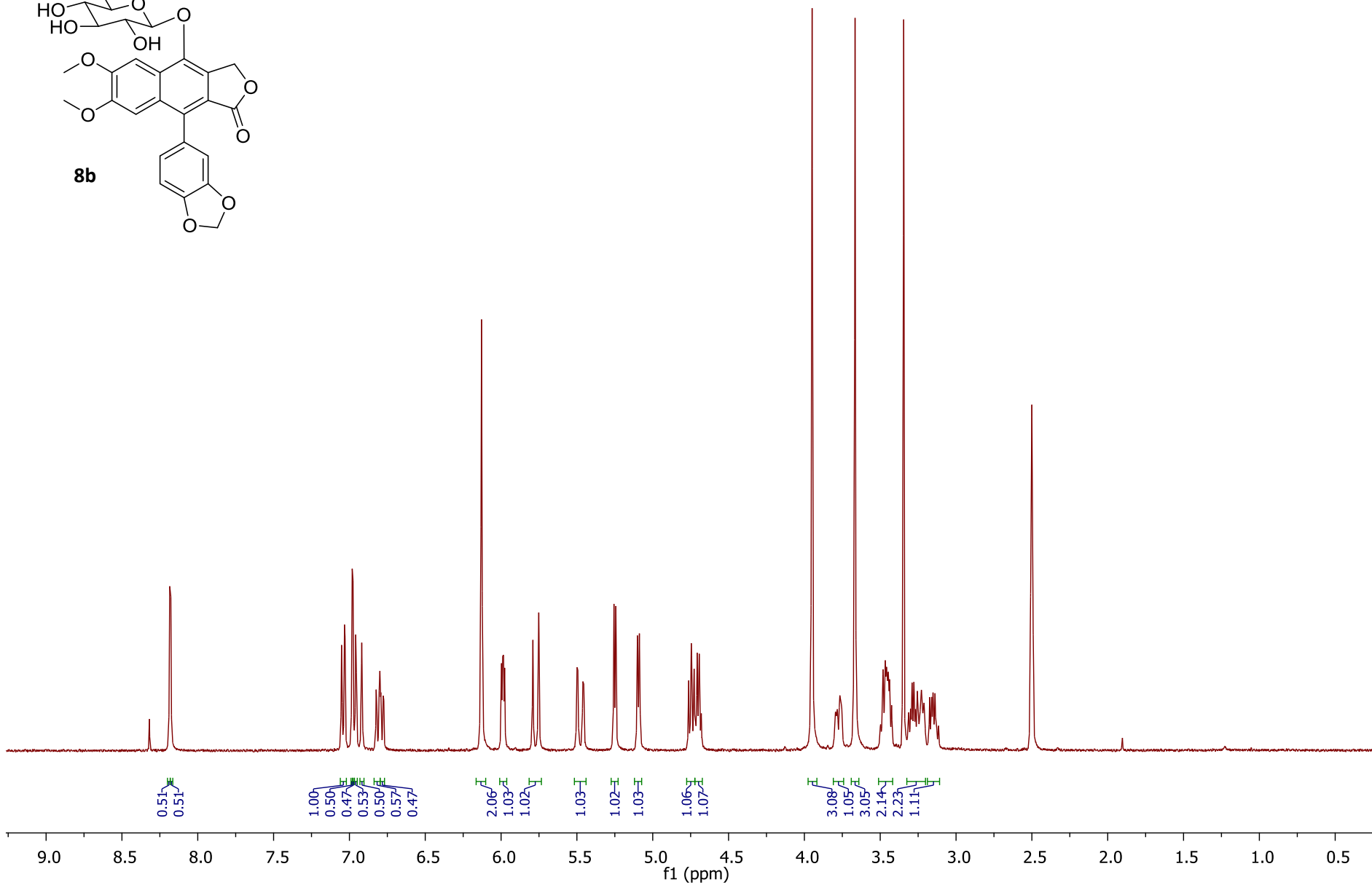
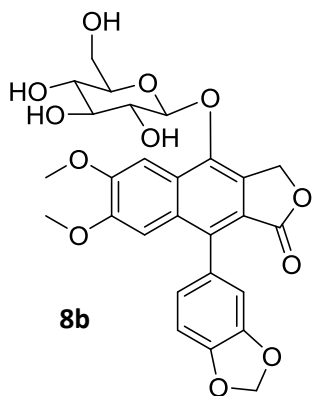


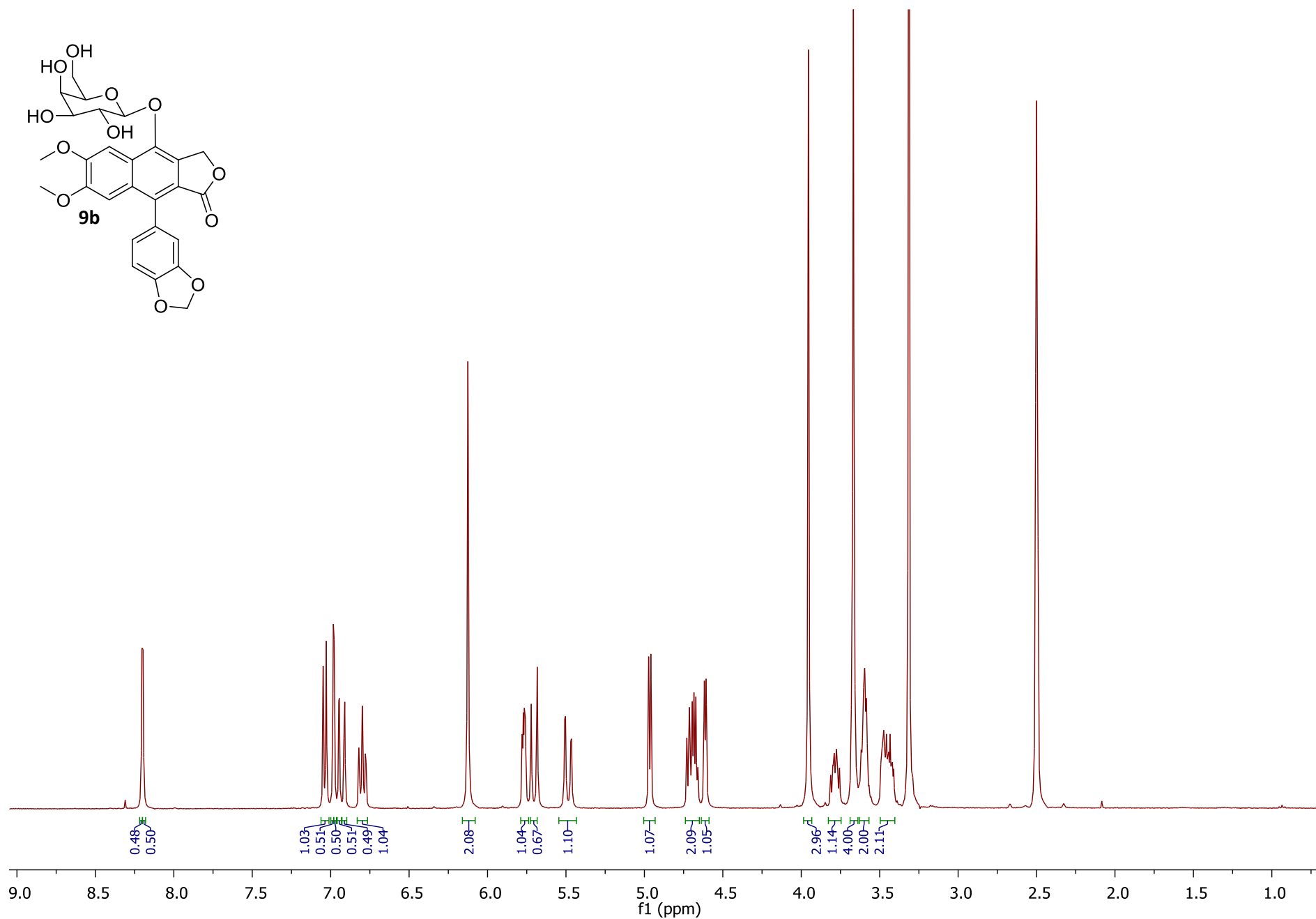
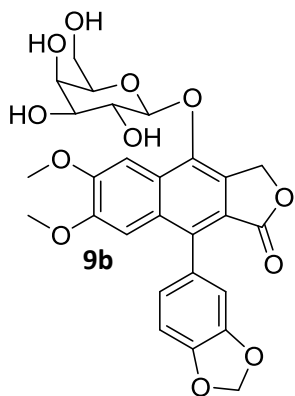


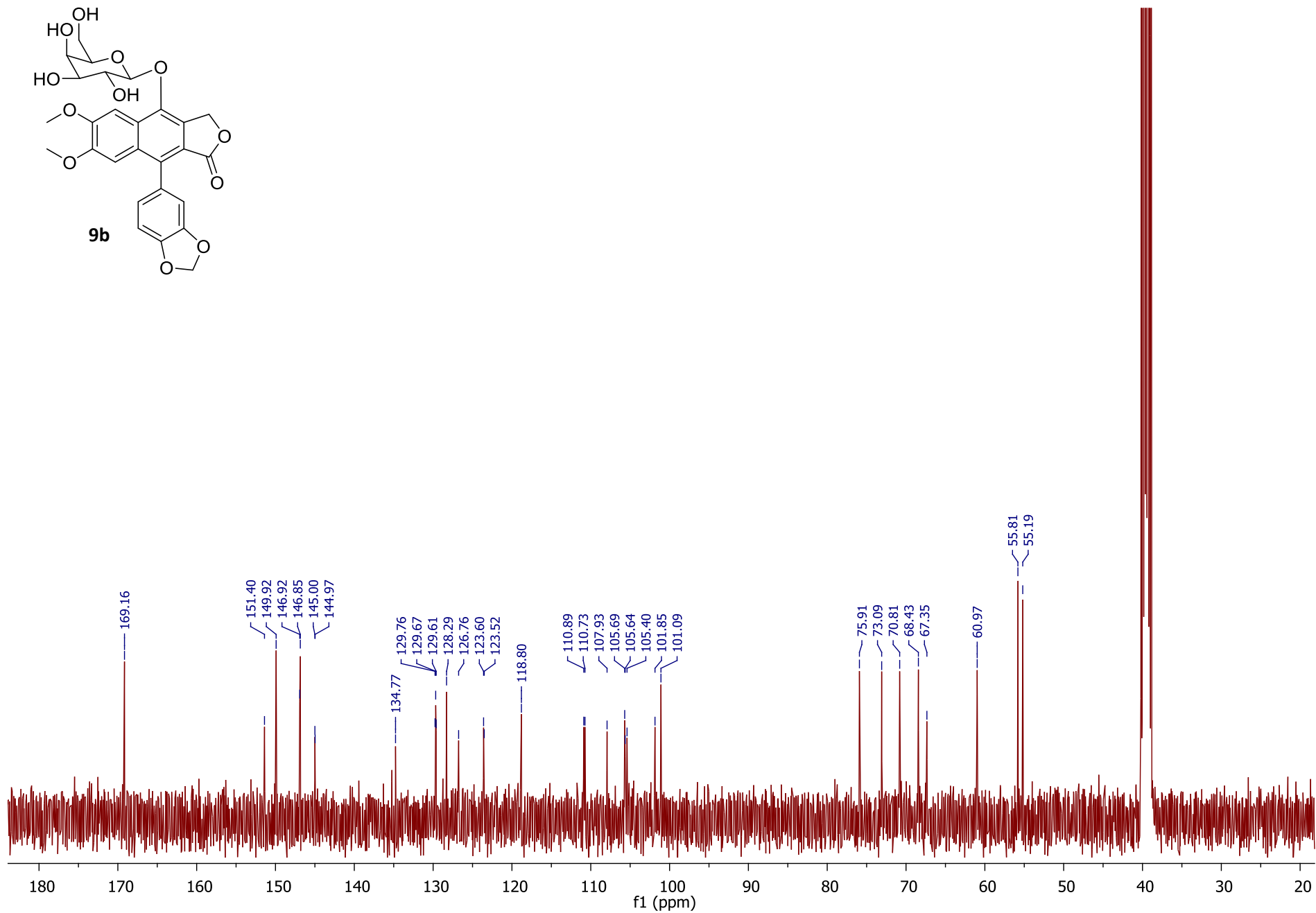
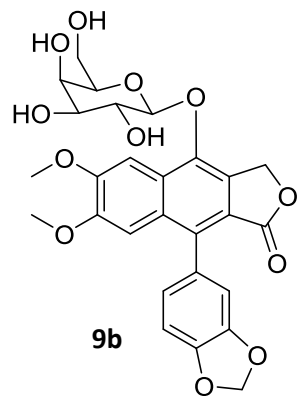


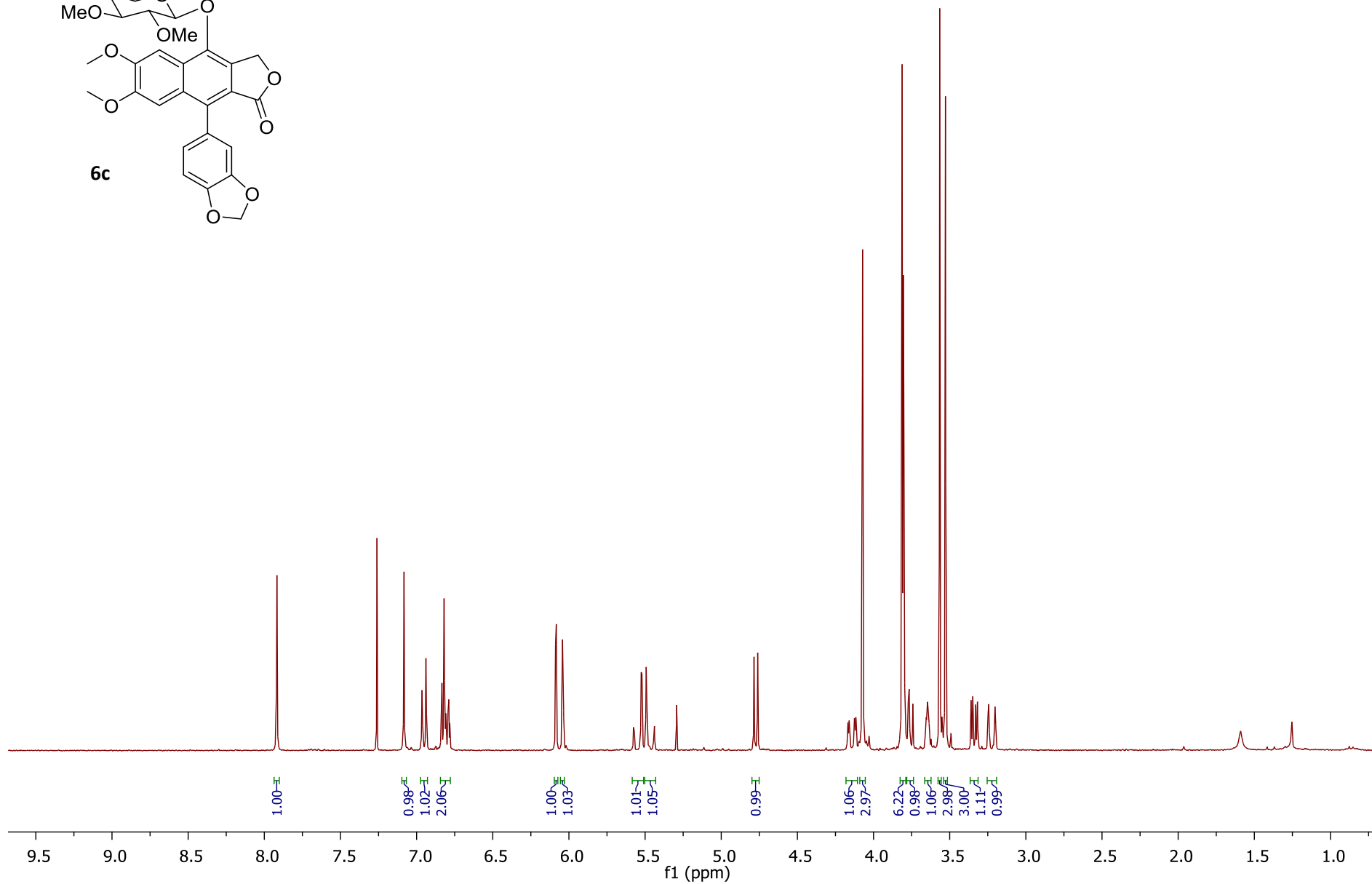
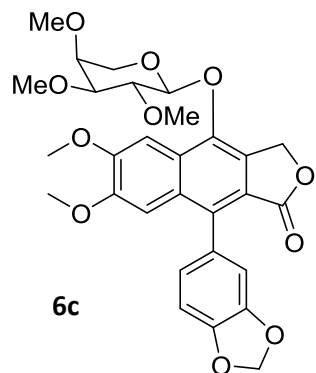


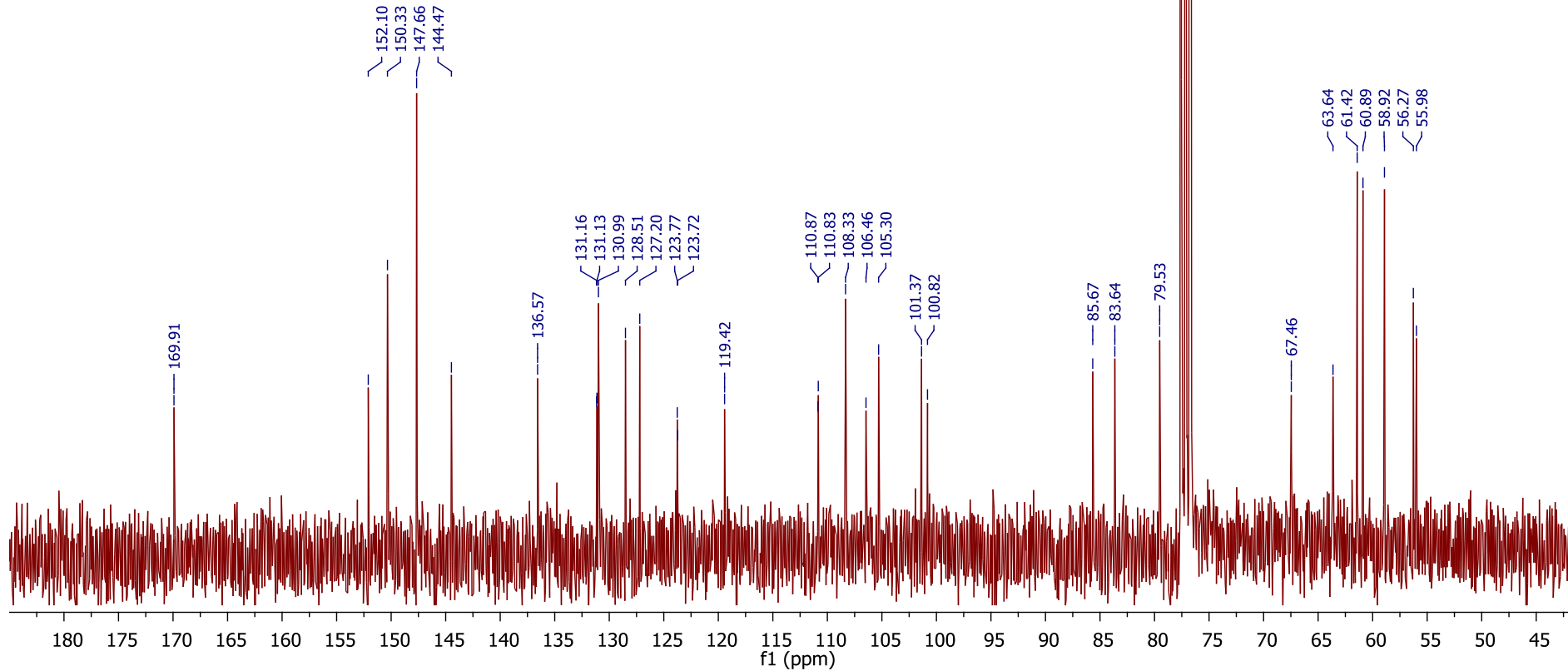
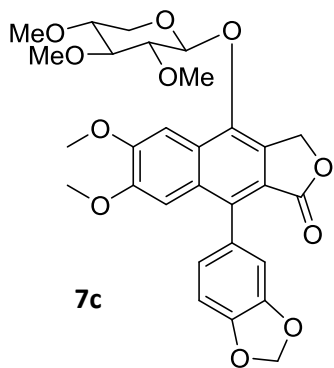


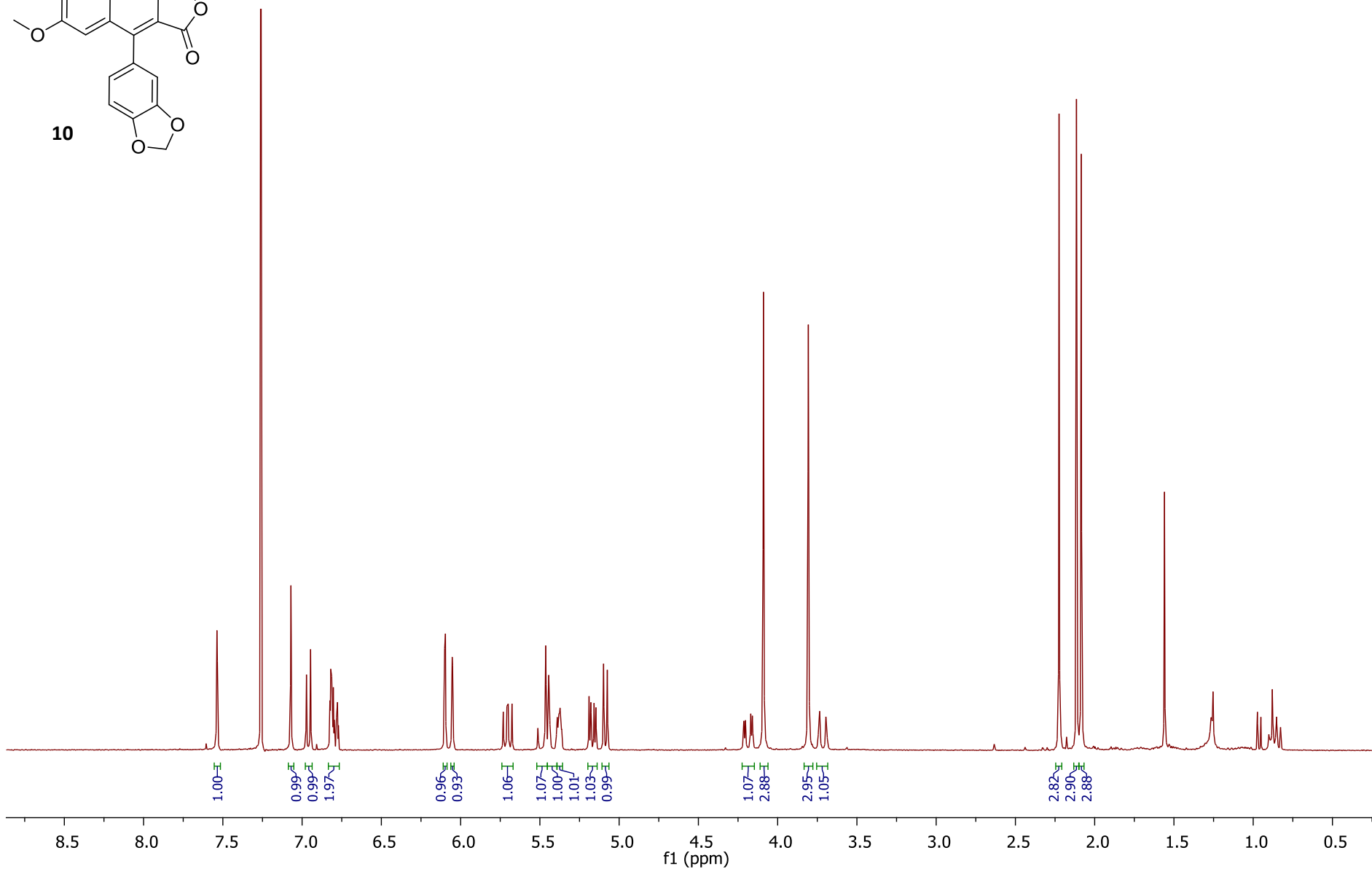
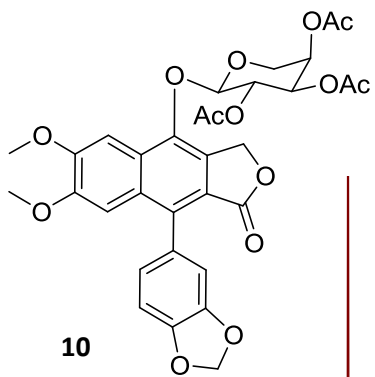


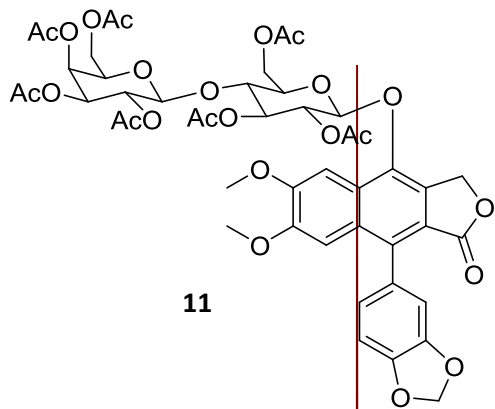




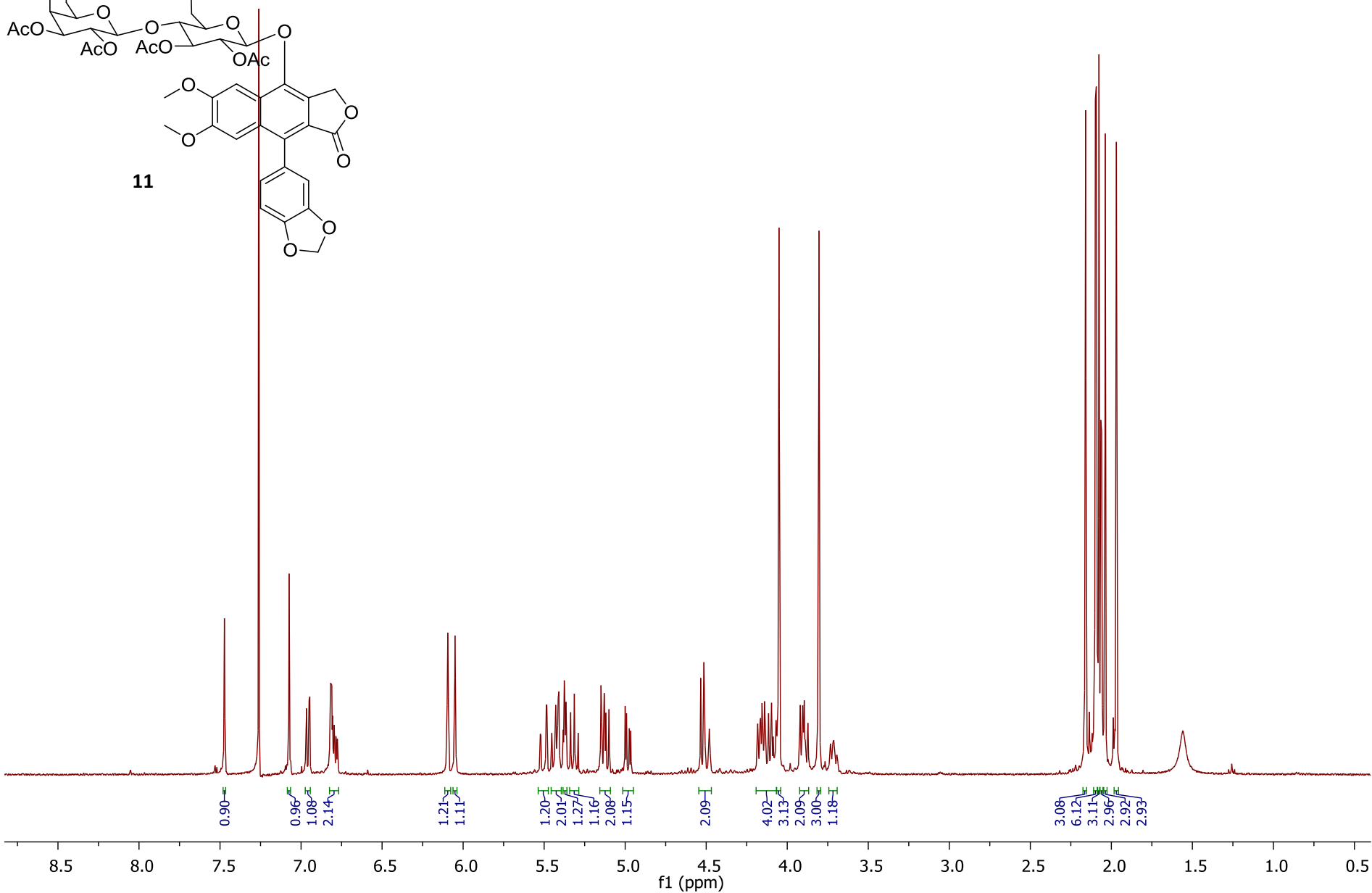




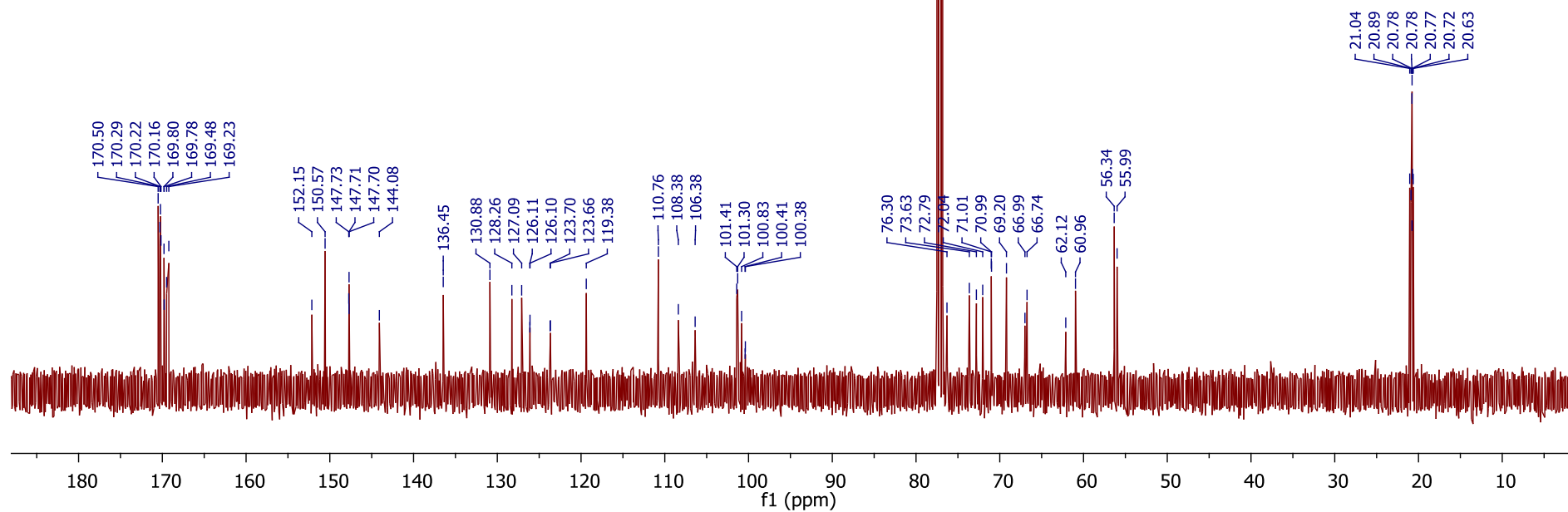
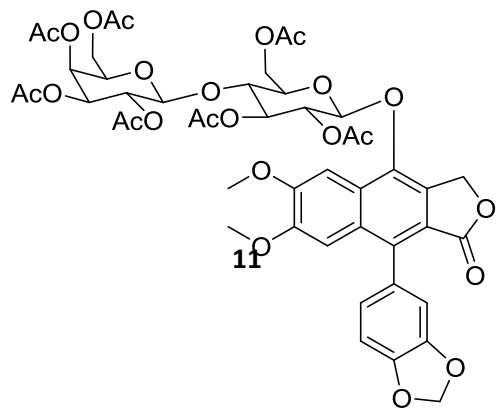


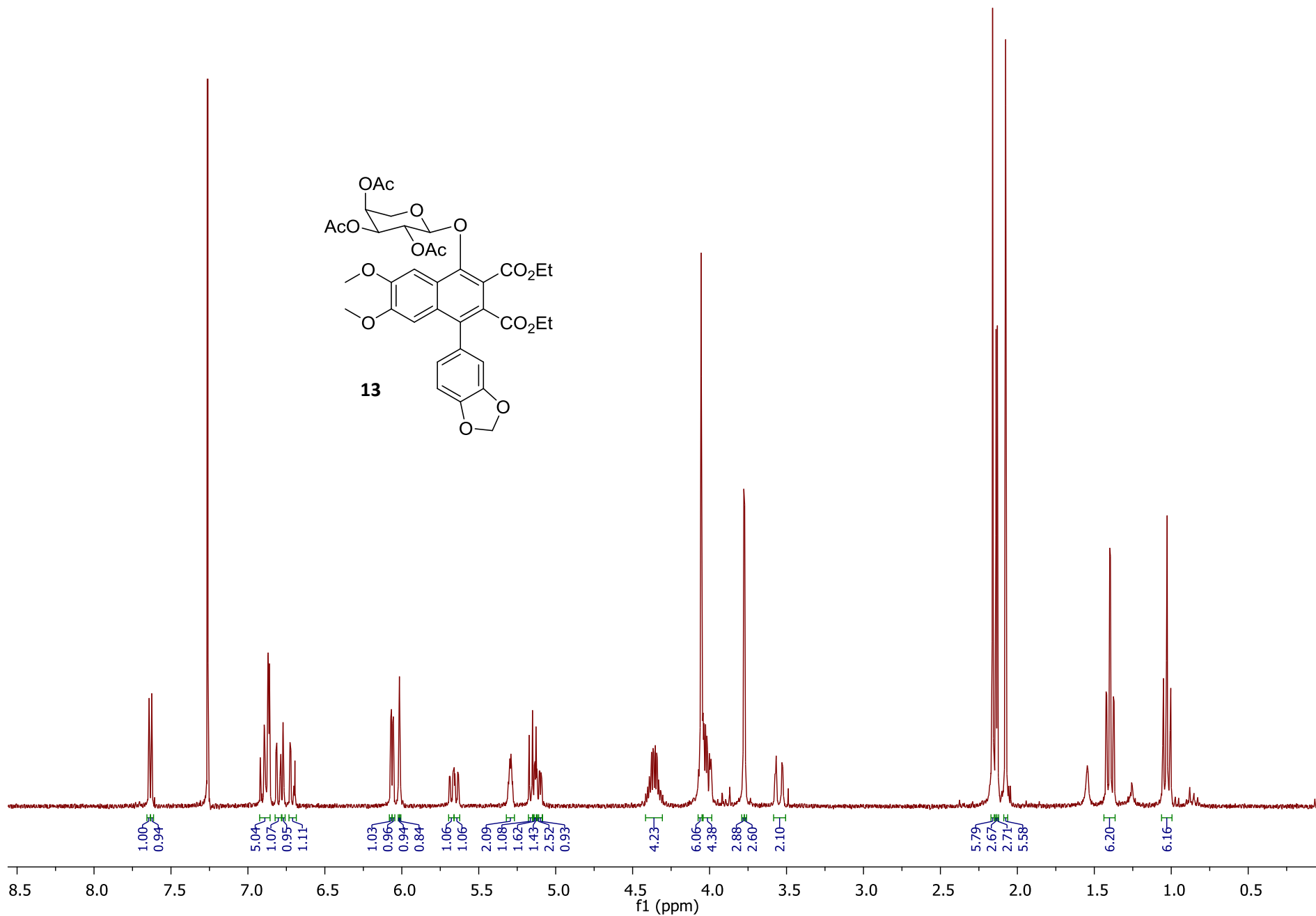
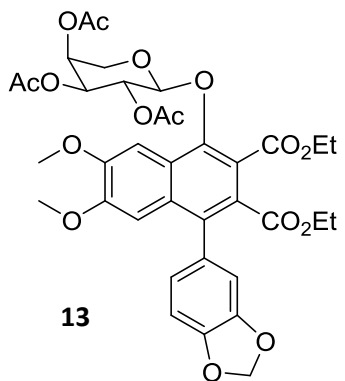


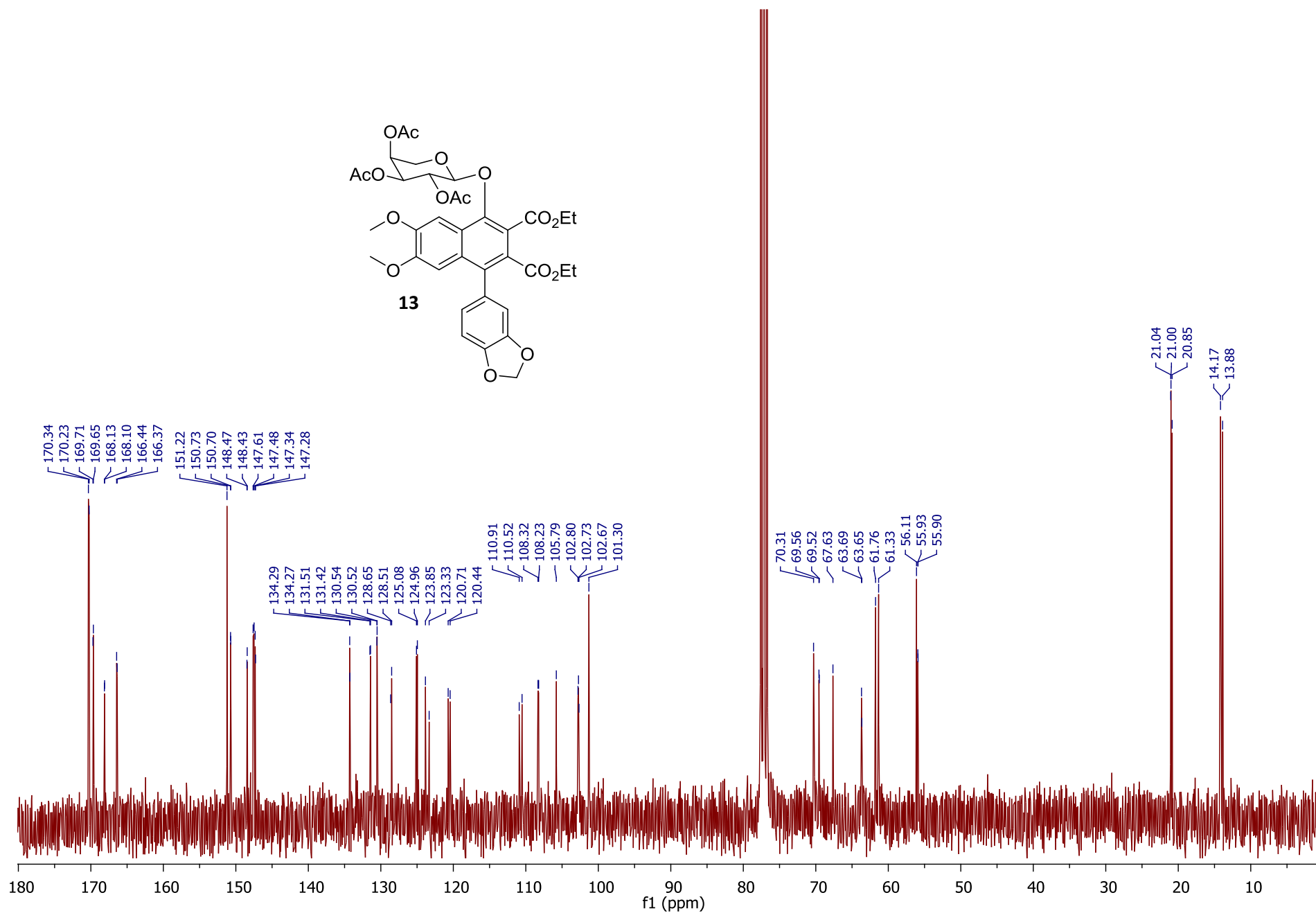
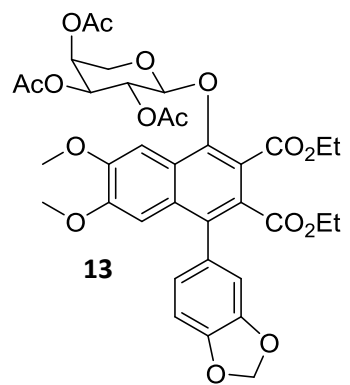
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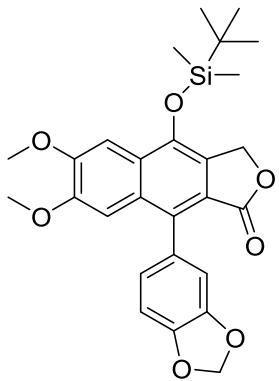


S25

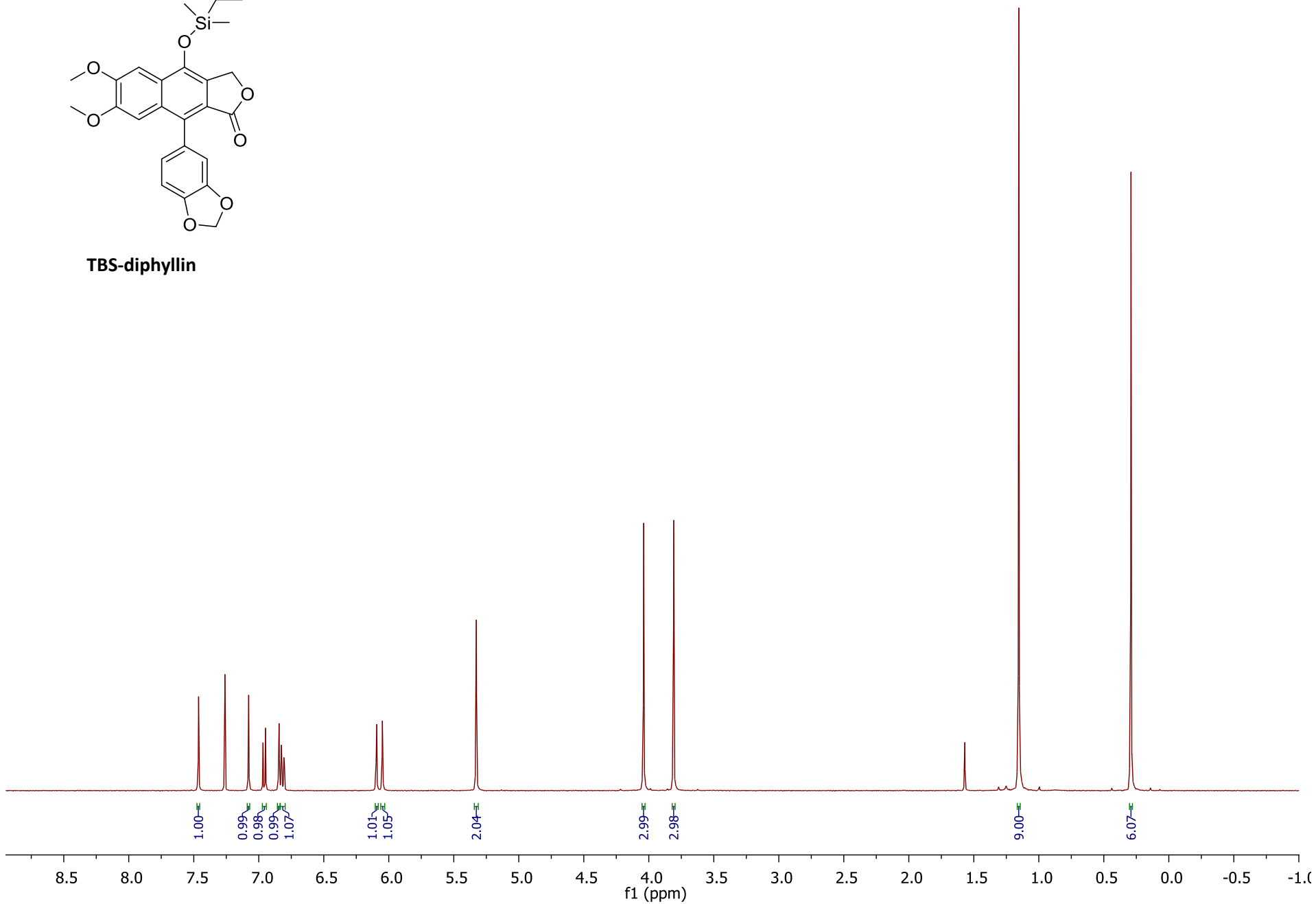


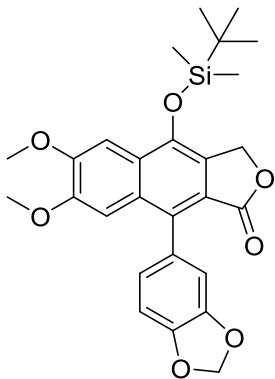




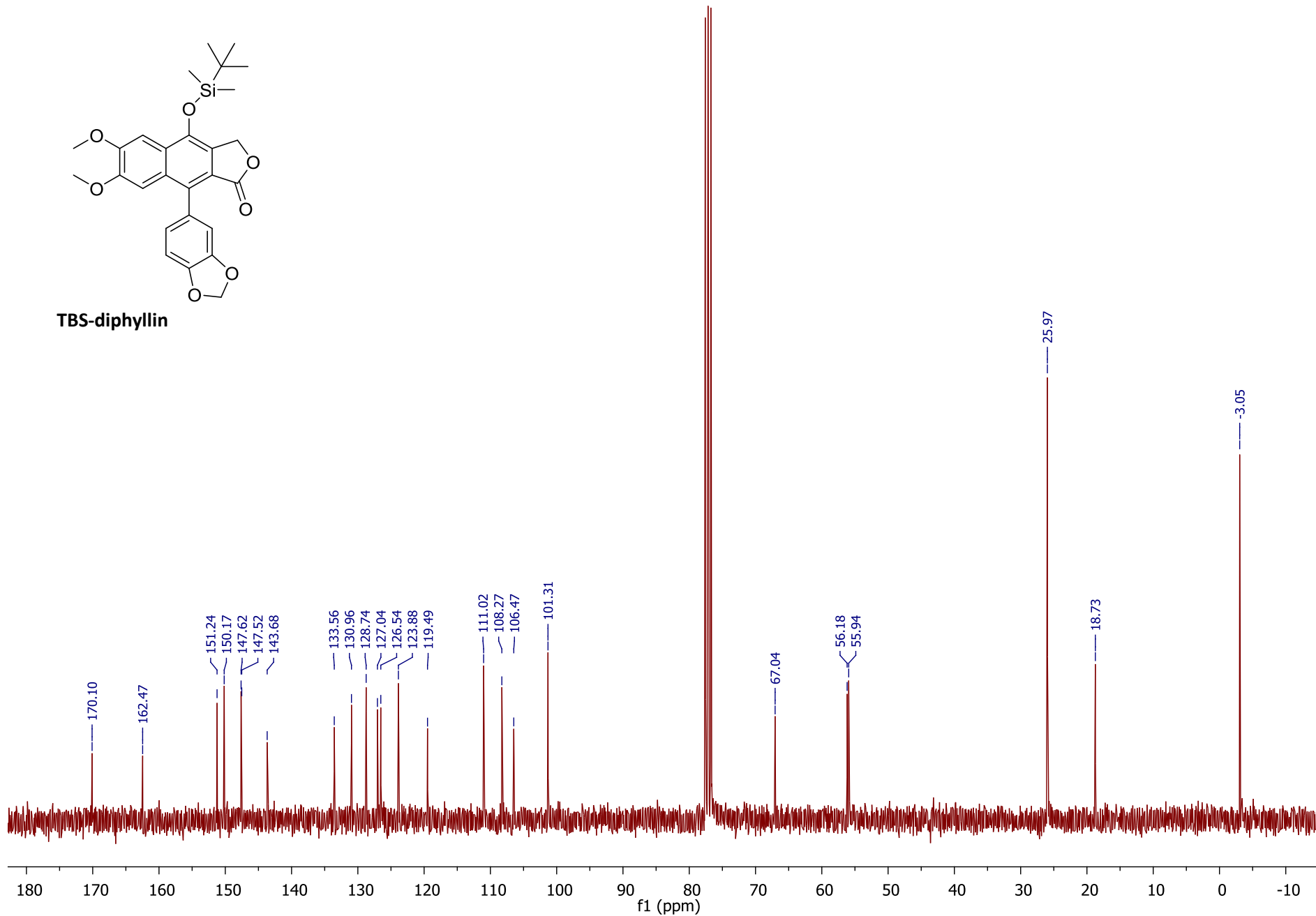


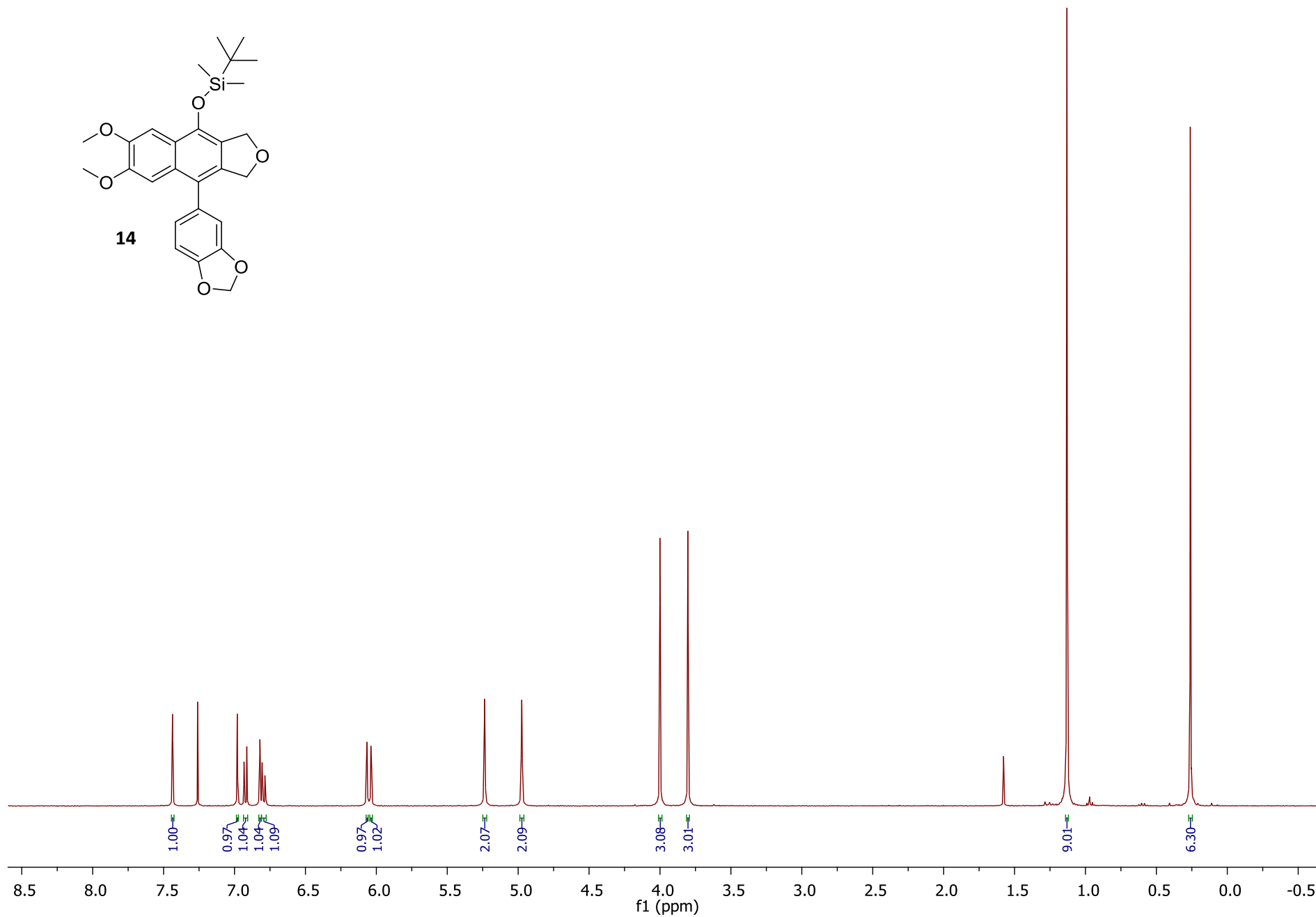
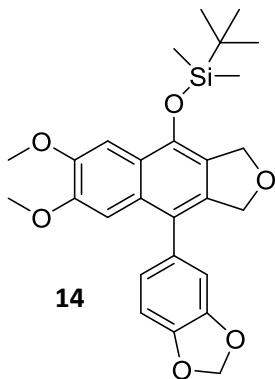
TBS-diphyllin



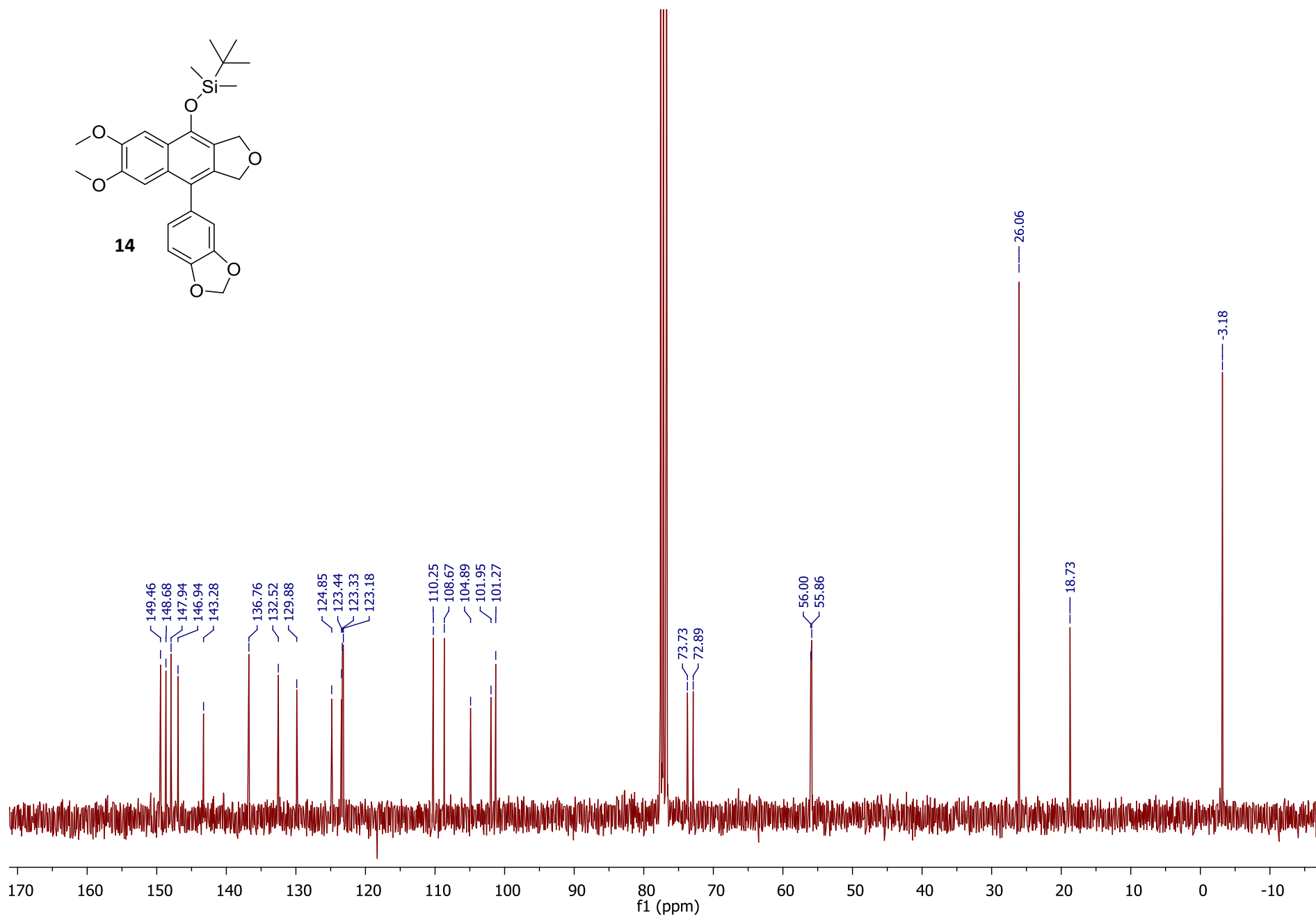
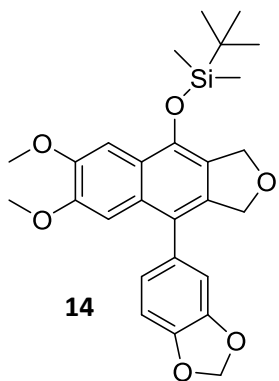


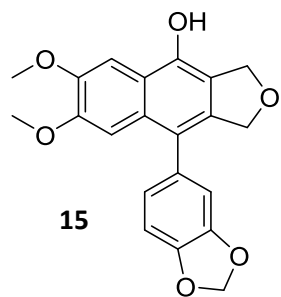
TBS-diphyllin



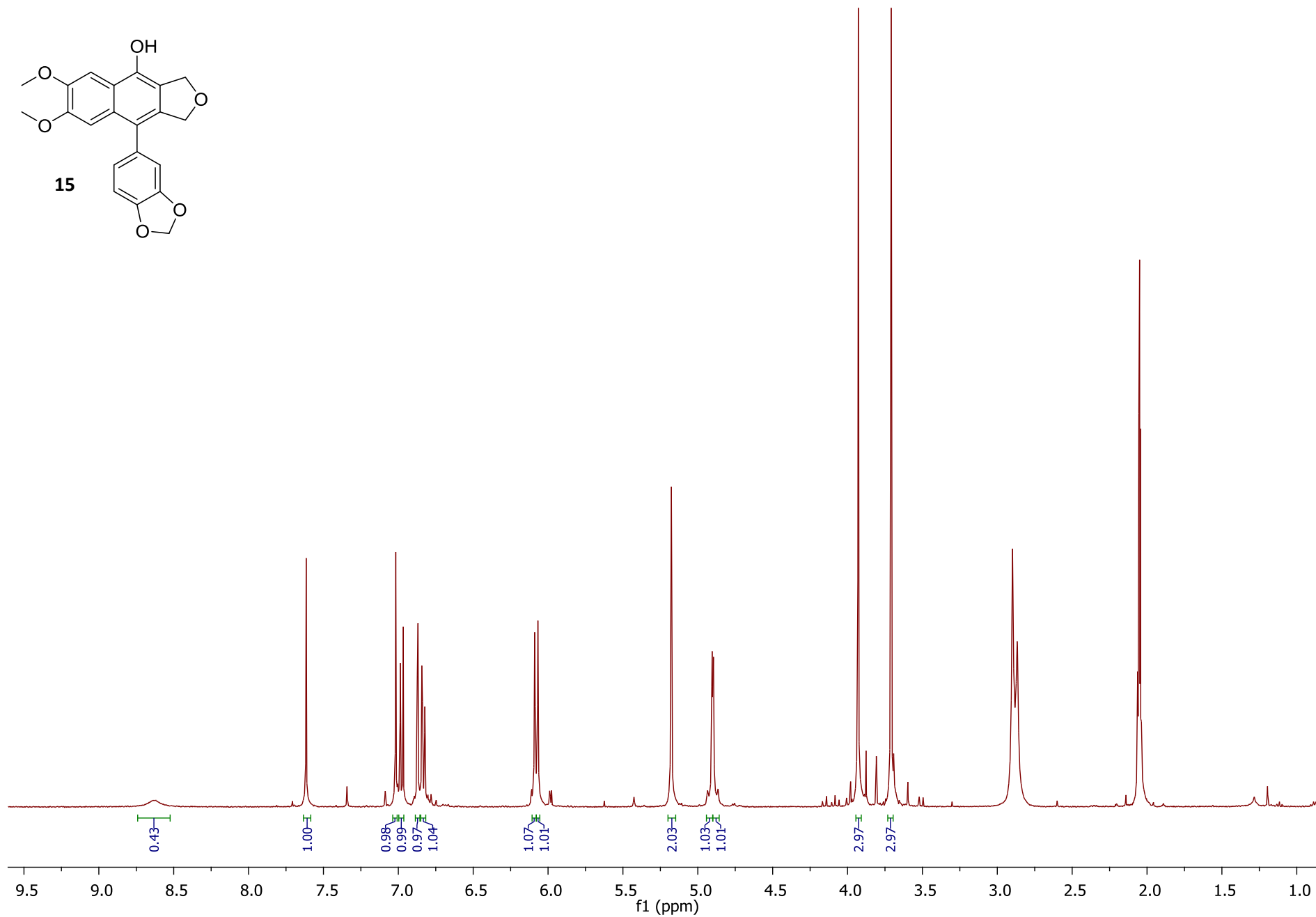


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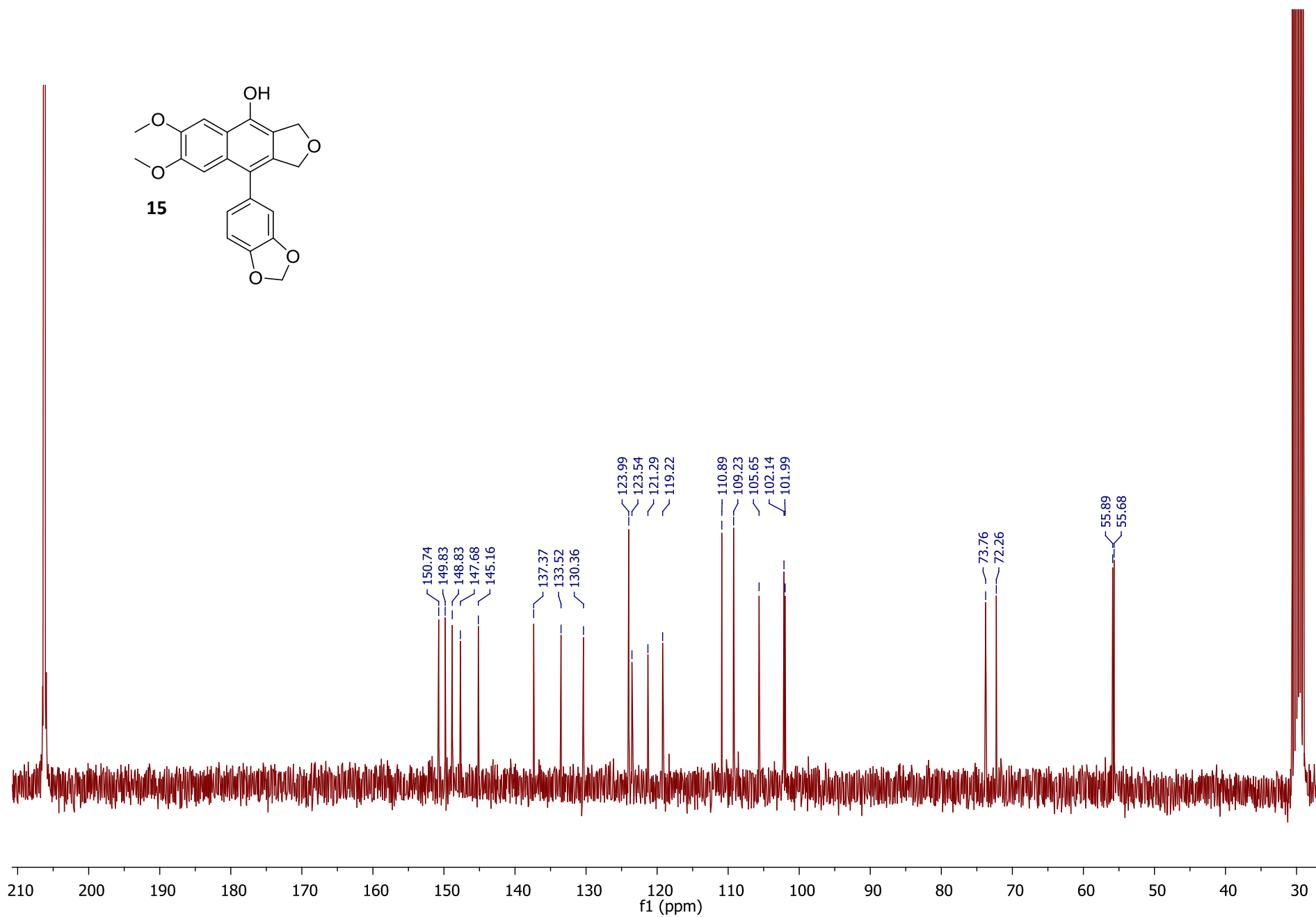
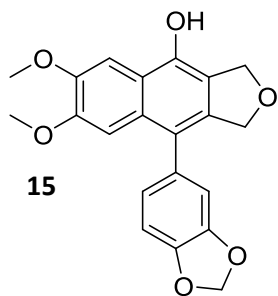


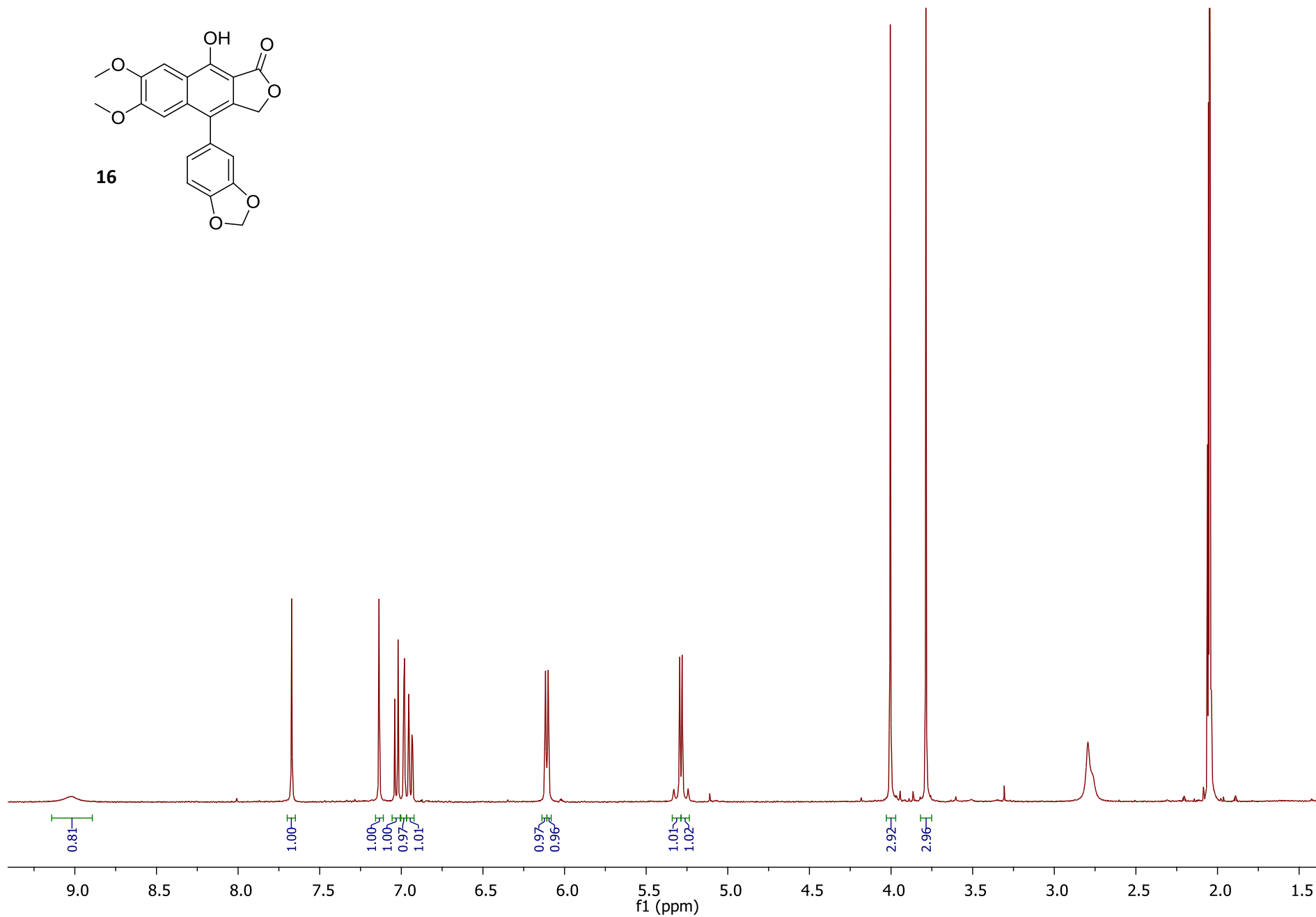
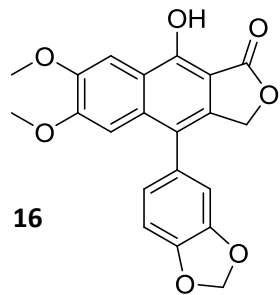


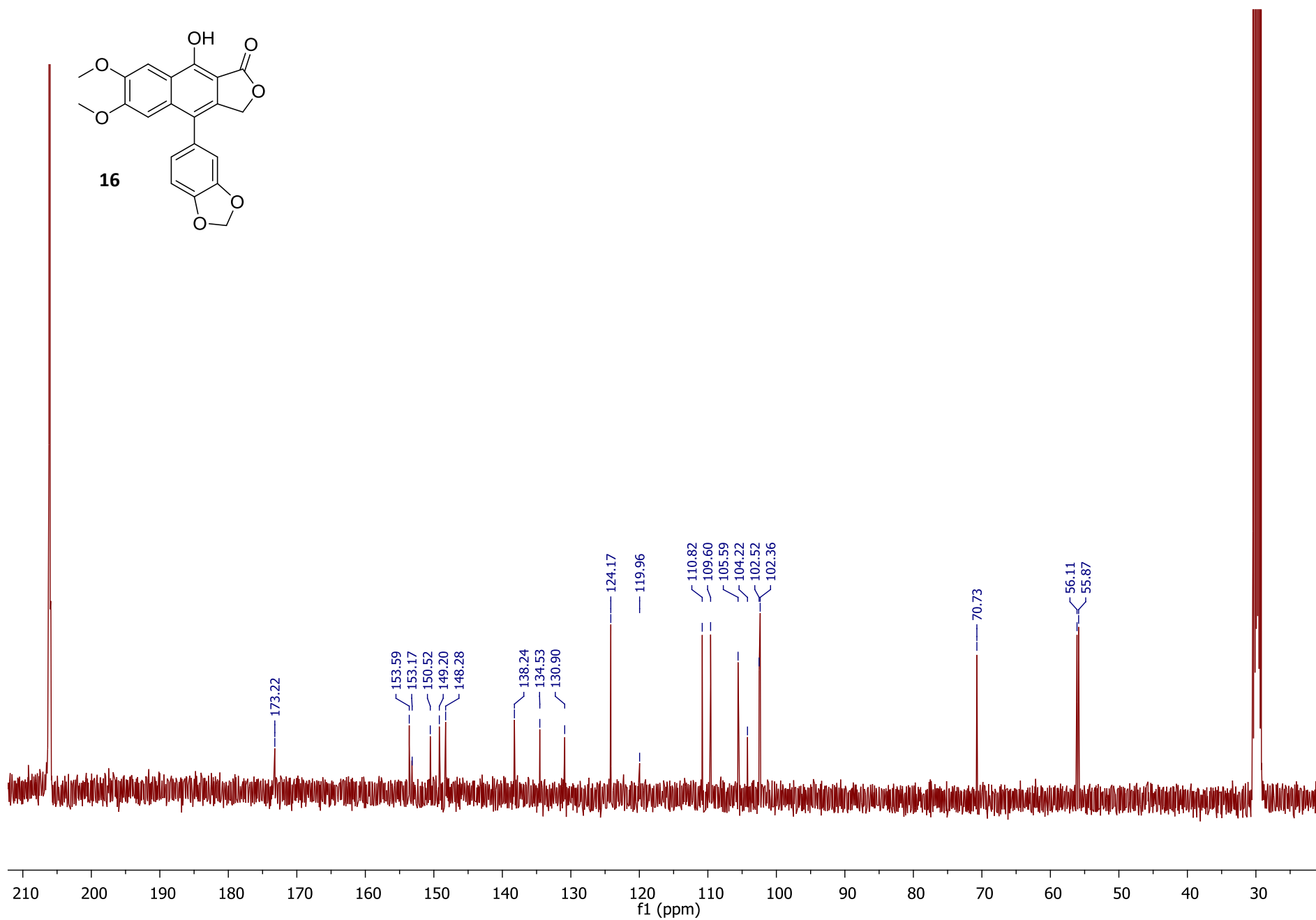
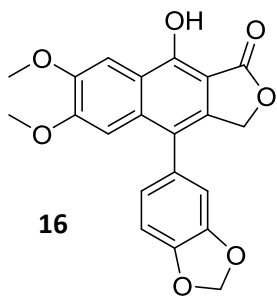
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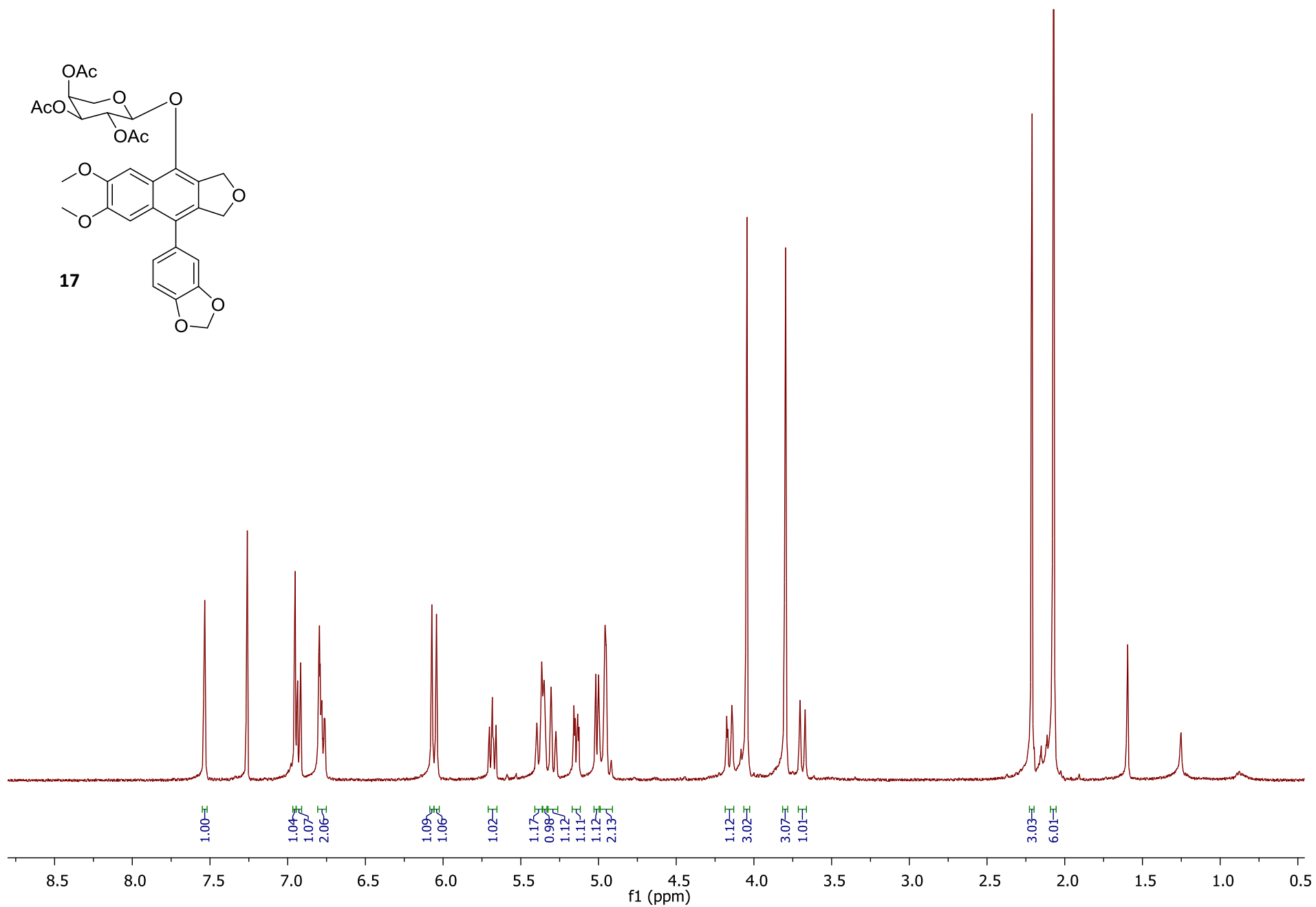
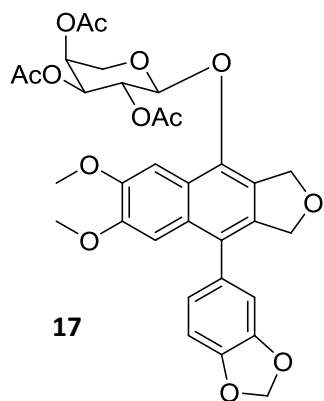


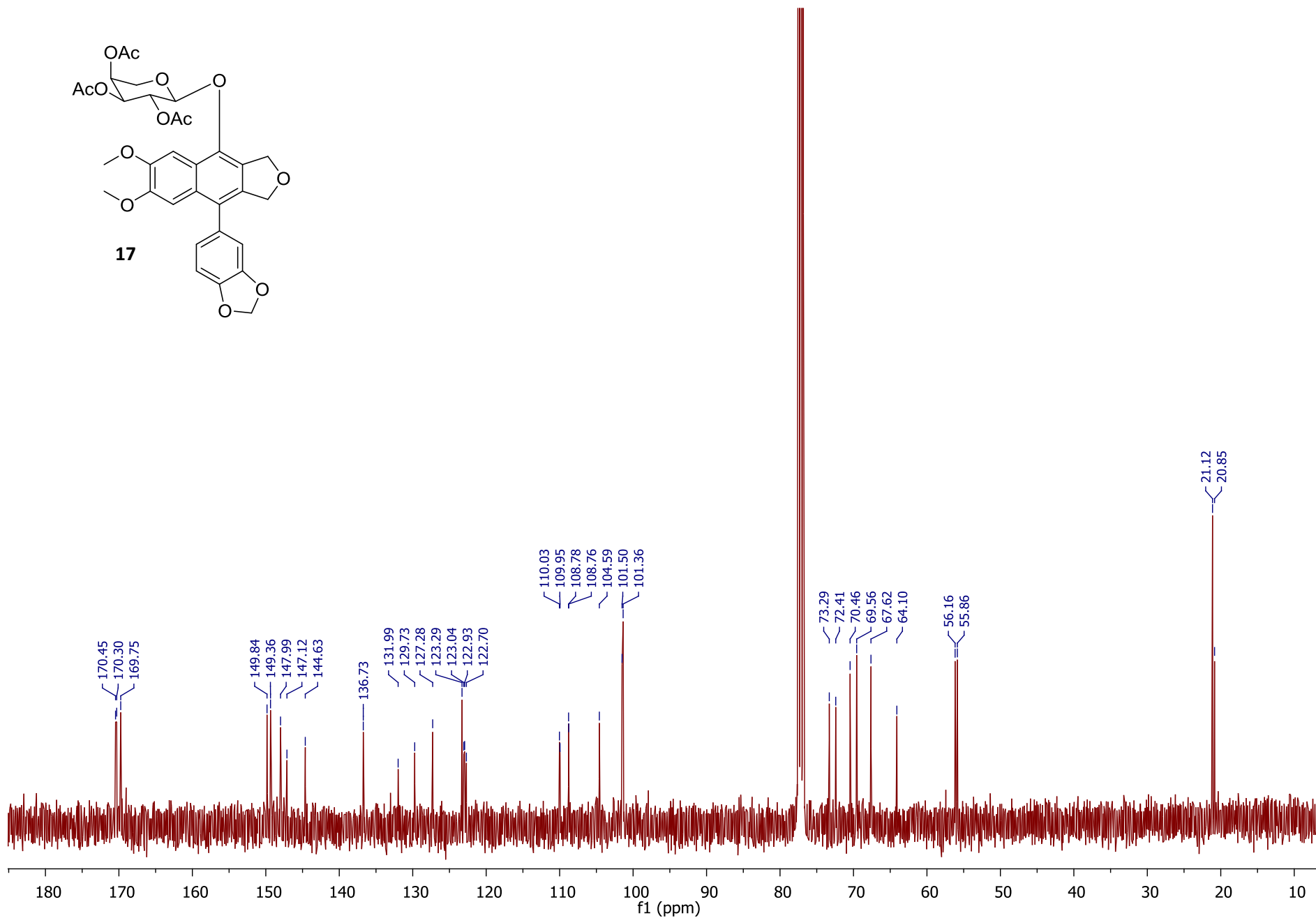
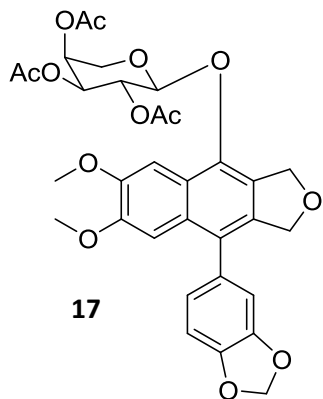
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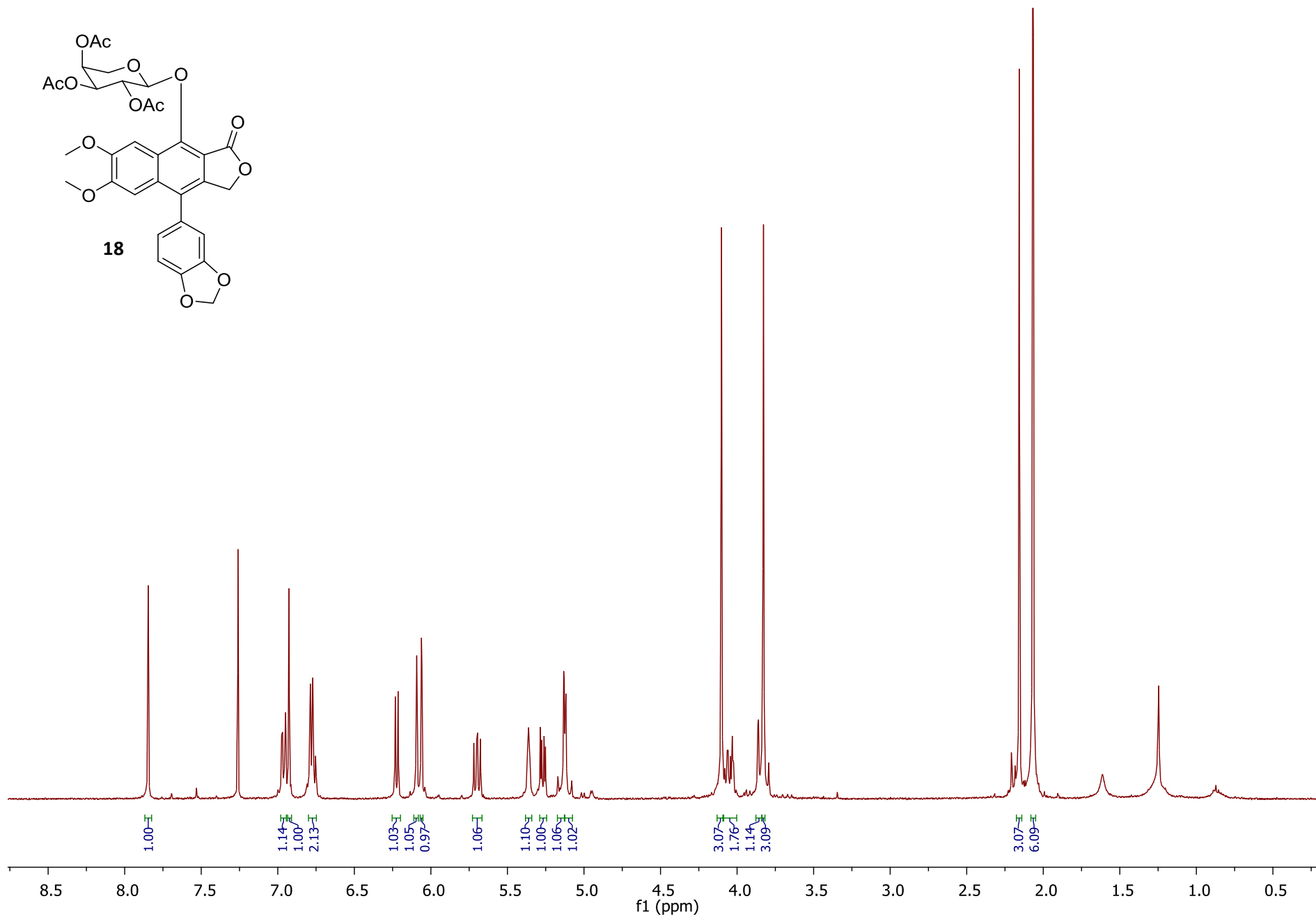
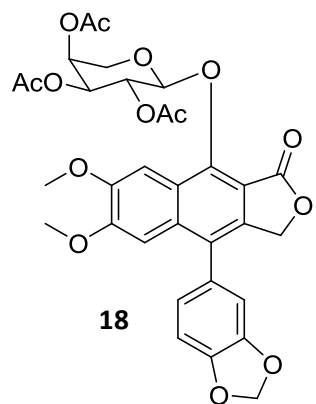






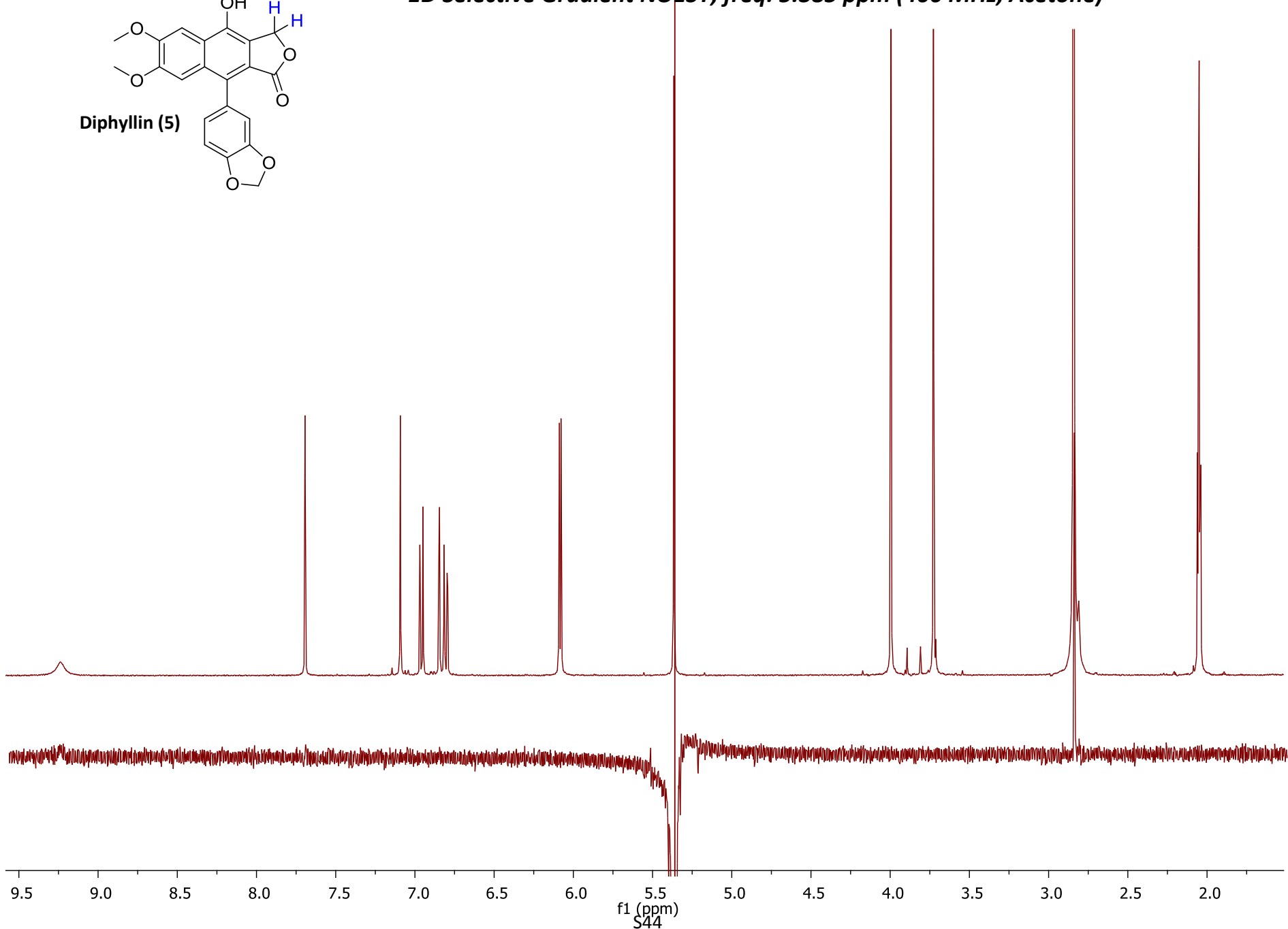
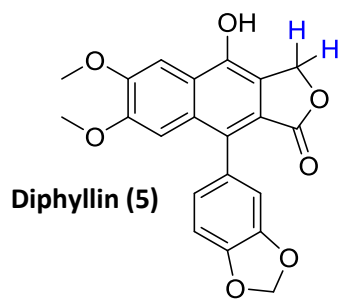


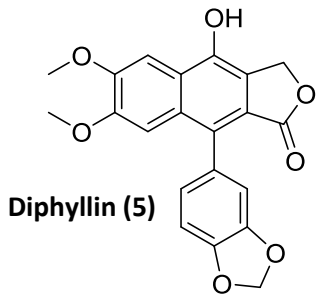




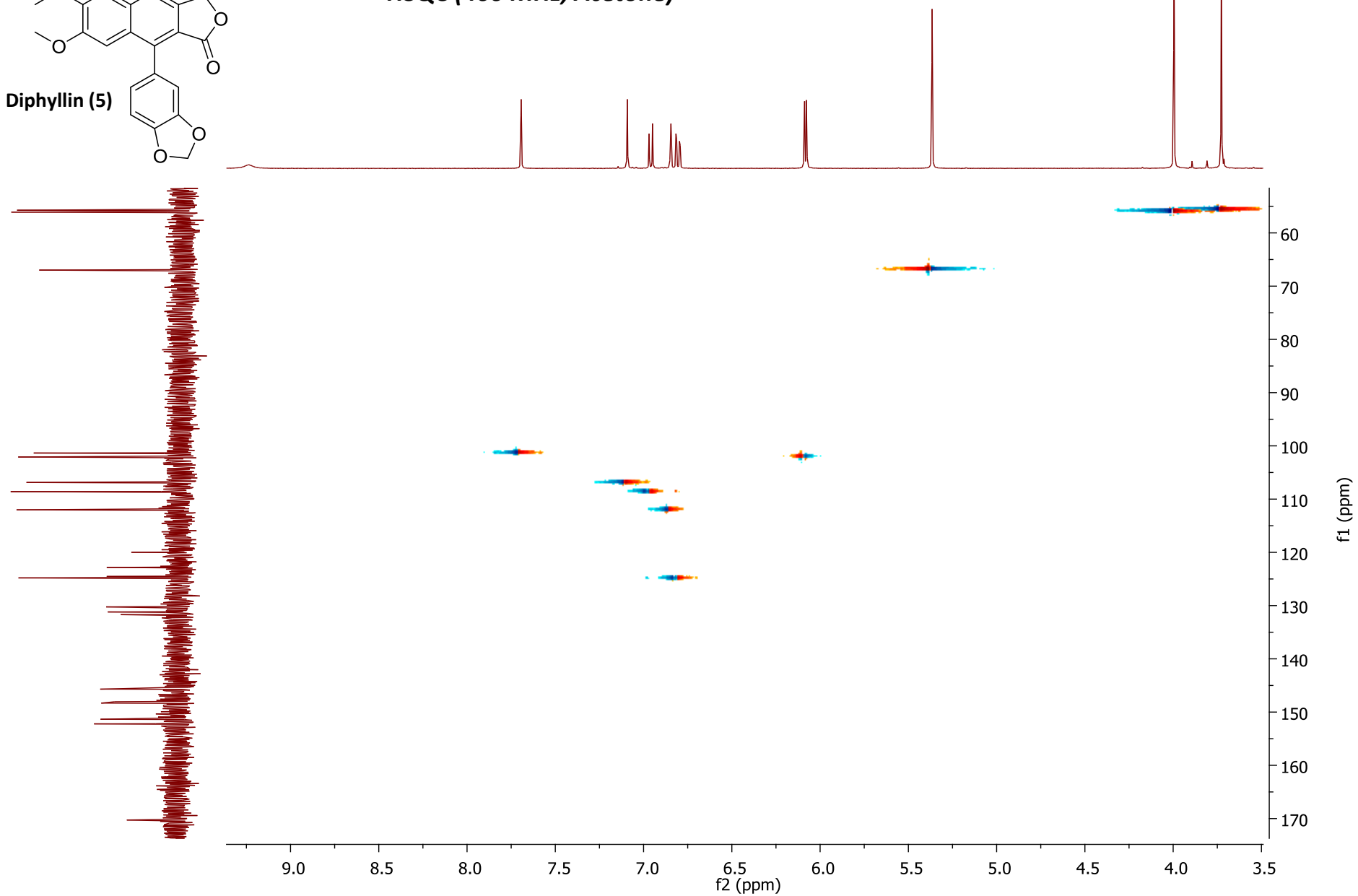
Additional NMR Spectra of 5 and 16

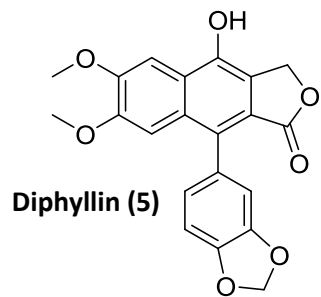
1D Selective Gradient NOESY, freq: 5.385 ppm (400 MHz, Acetone)



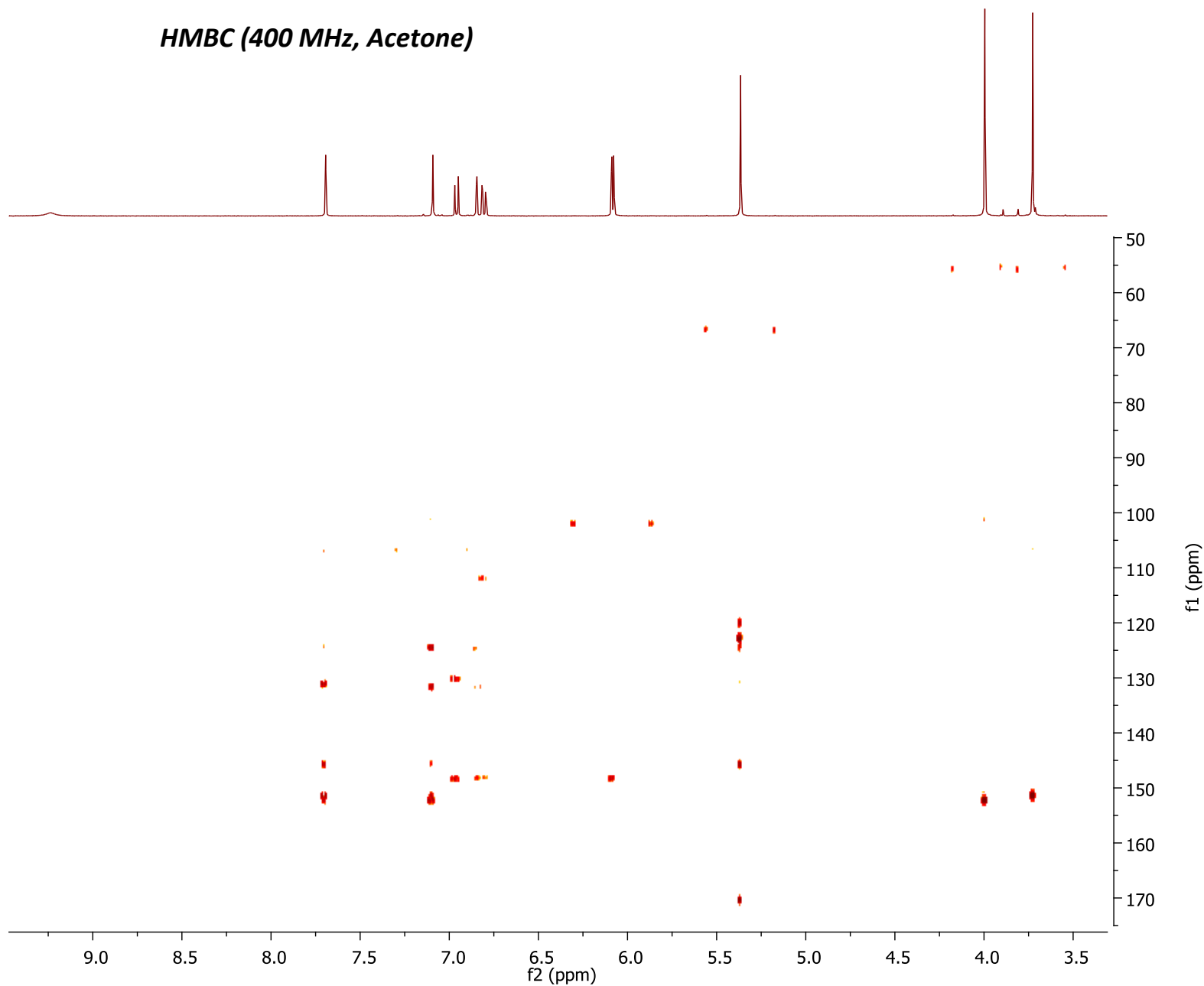


HSQC (400 MHz, Acetone)

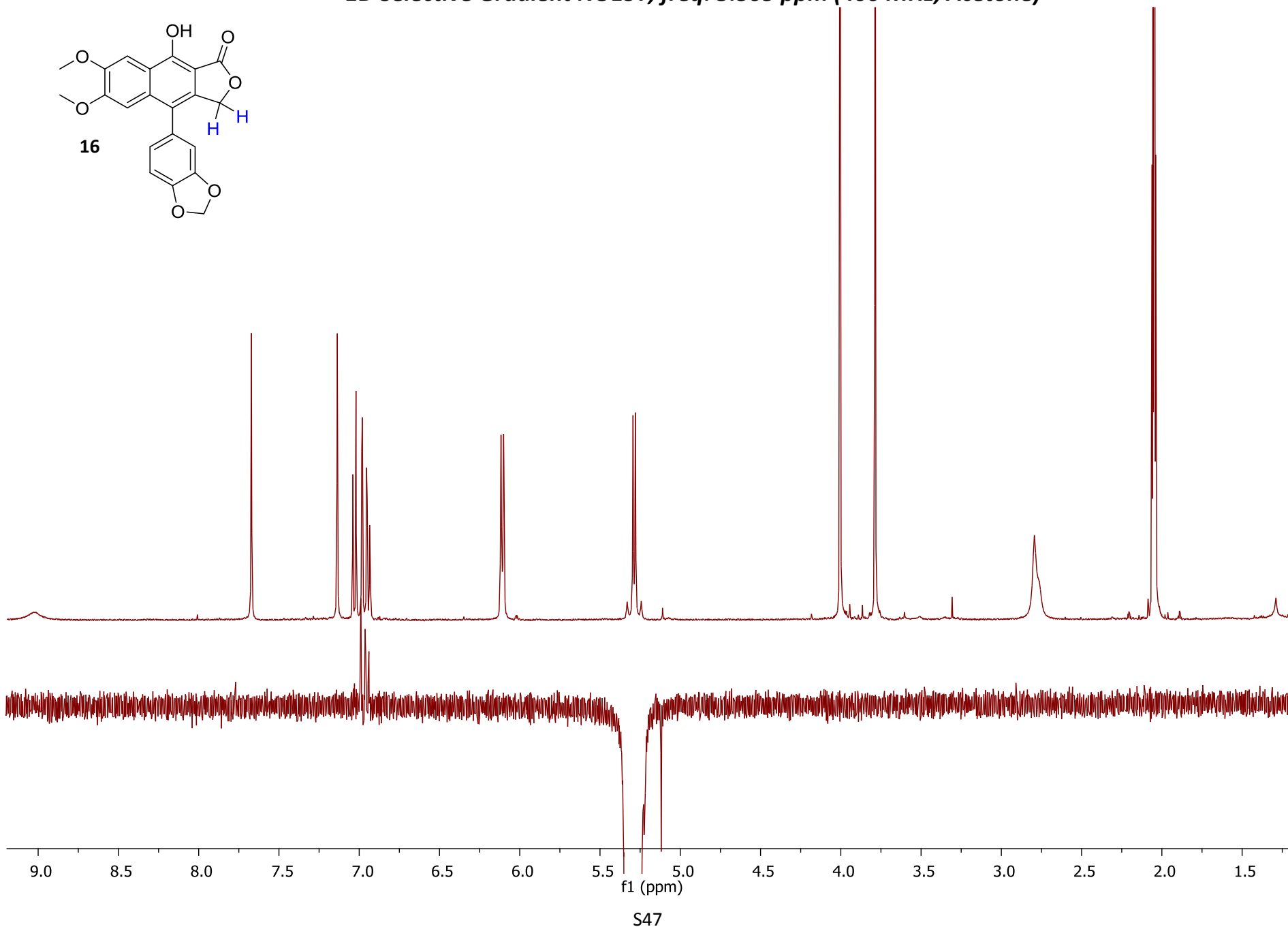
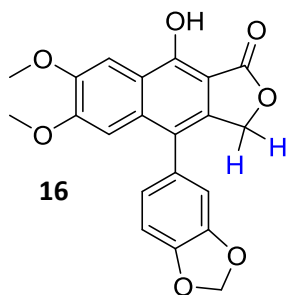


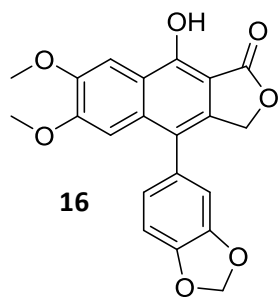


HMBC (400 MHz, Acetone)

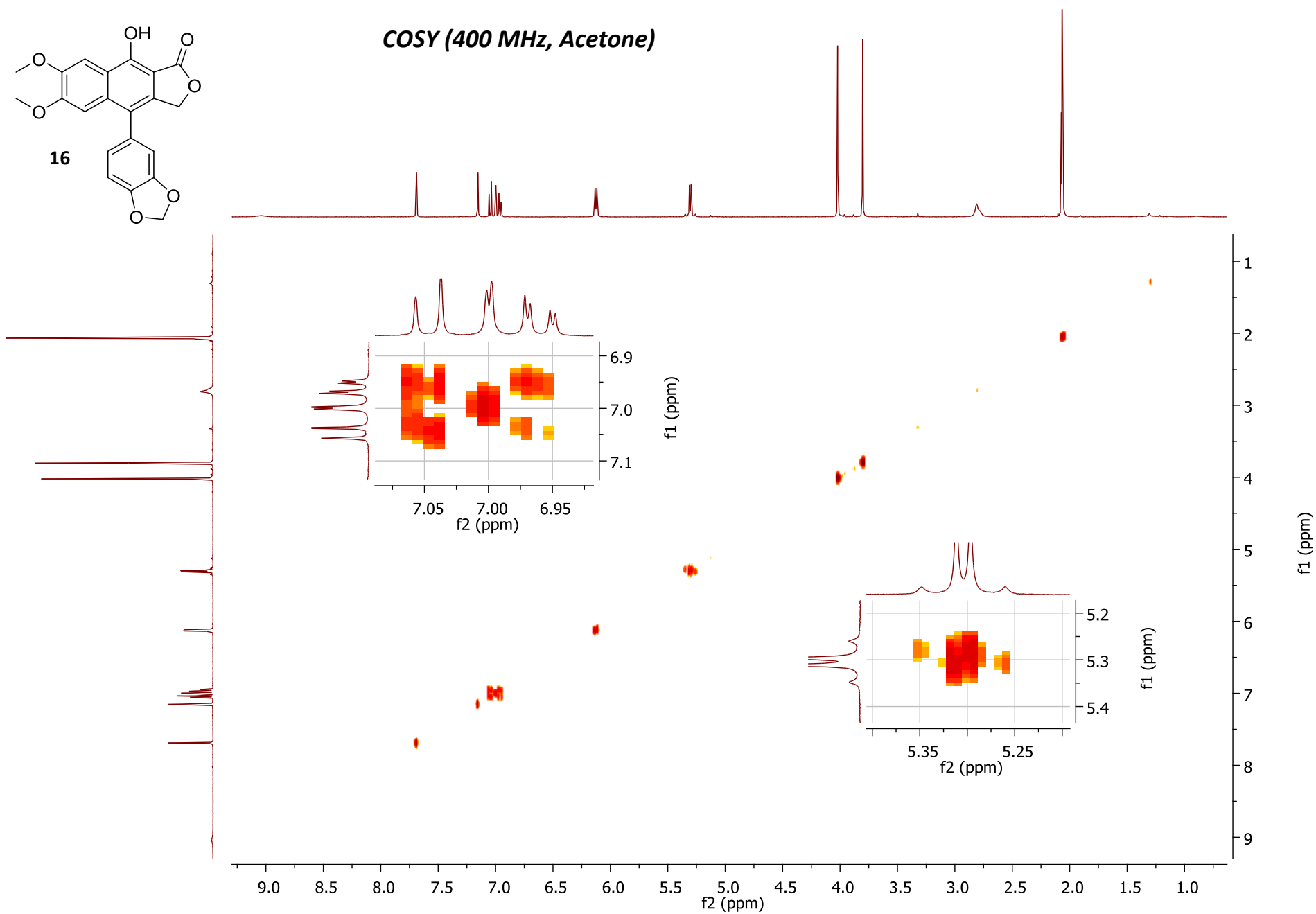


1D Selective Gradient NOESY, freq: 5.303 ppm (400 MHz, Acetone)

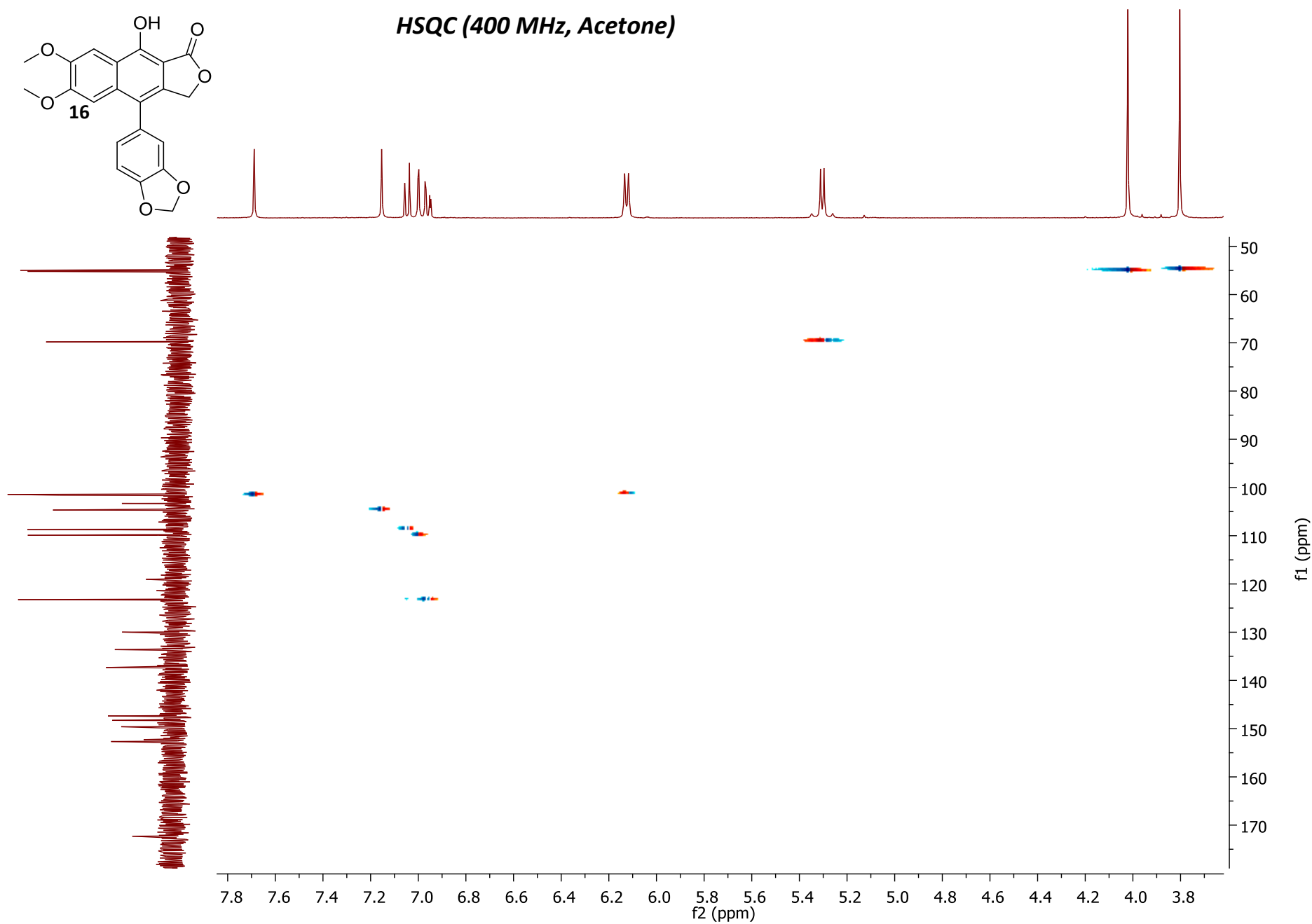
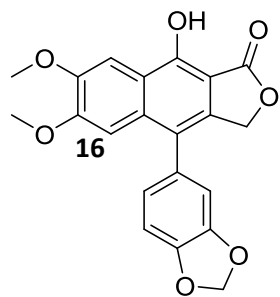


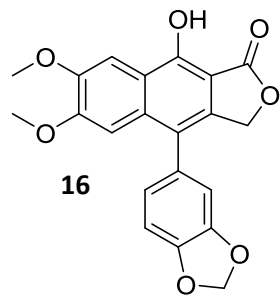


COSY (400 MHz, Acetone)

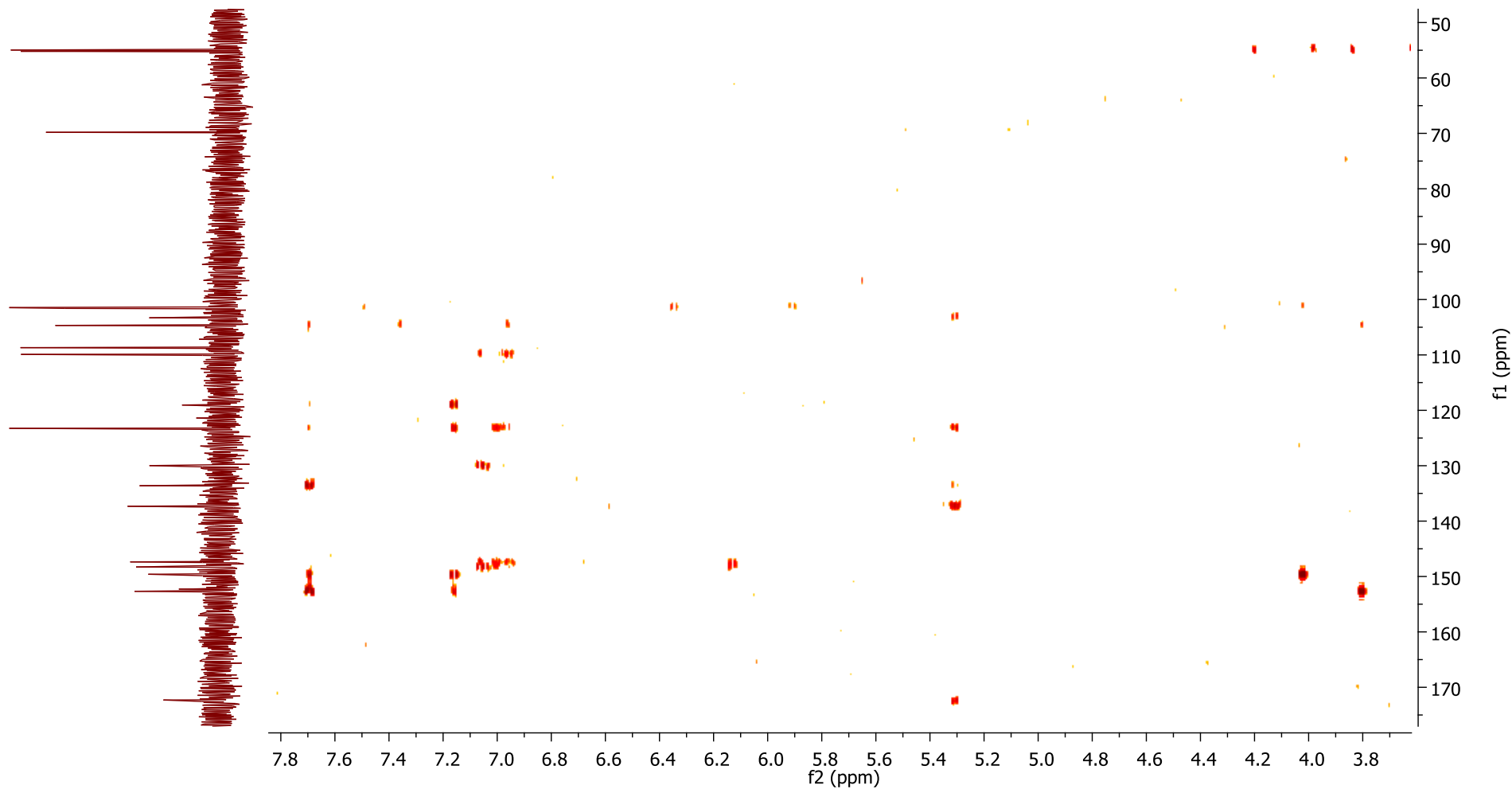
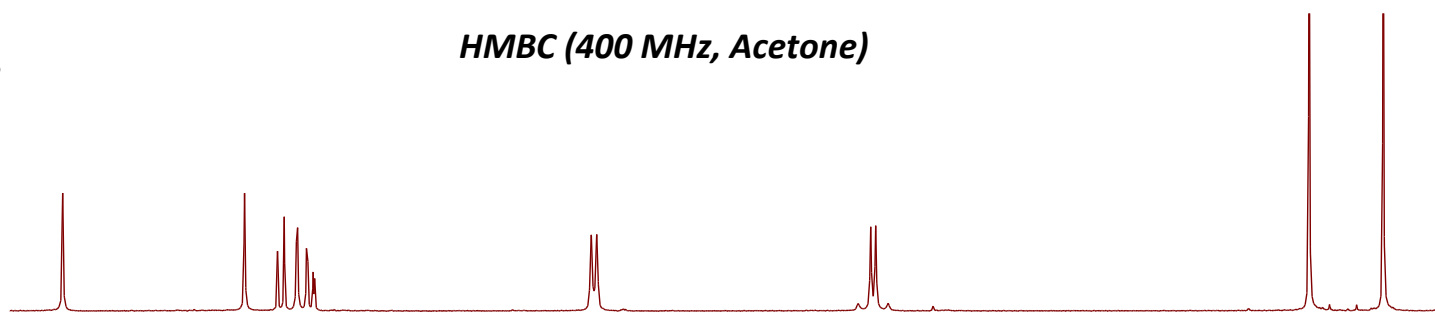


HSQC (400 MHz, Acetone)

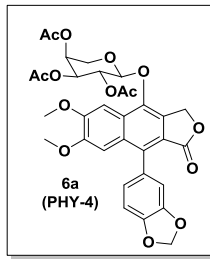




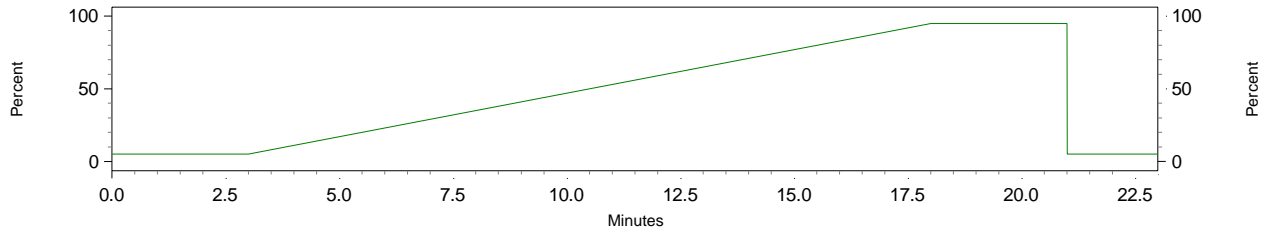
HMBC (400 MHz, Acetone)



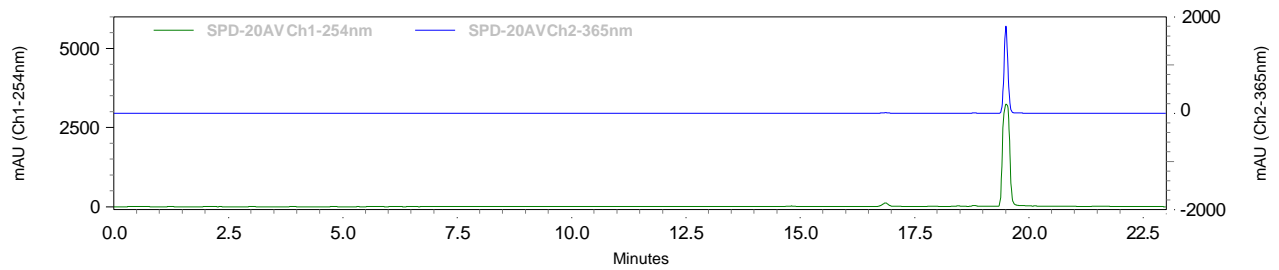
HPLC Traces for Tested Compounds



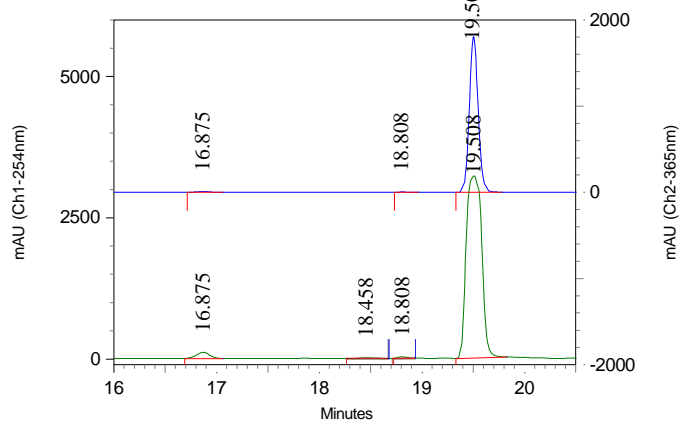
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



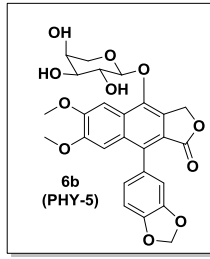
HPLC Trace (254 nm & 365 nm)



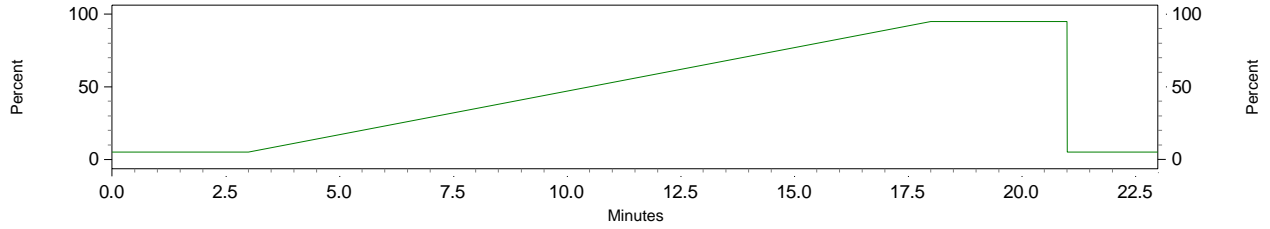
Zoomed View of Relevant Peaks



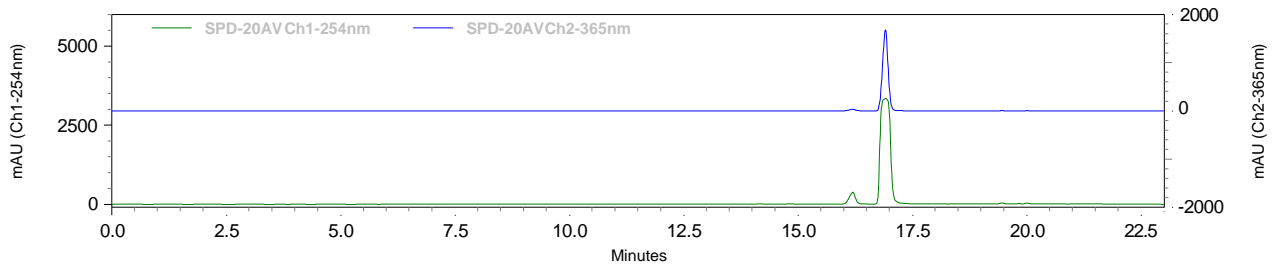
Ch1-254nm		Ch2-365nm	
Retention Time	Area %	Retention Time	Area %
14.825	0.42	16.875	0.68
16.875	2.77	18.808	0.19
18.458	0.35	19.508	99.14
18.808	0.44	Total:	100.00
19.508	96.02		
Total:	100.00		



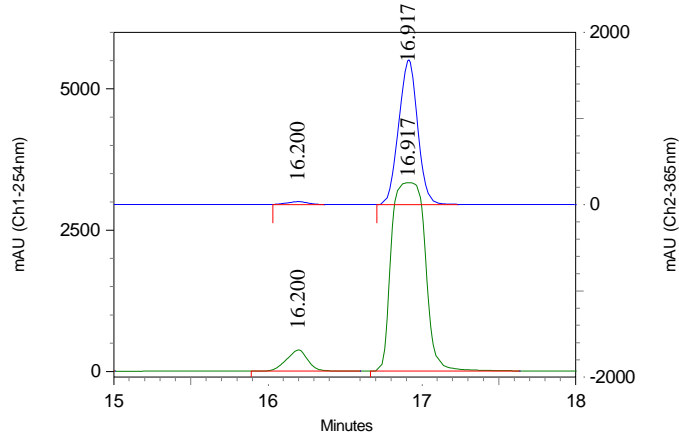
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



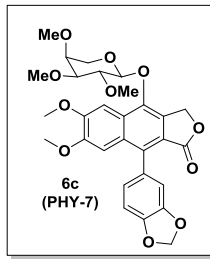
HPLC Trace (254 nm & 365 nm)



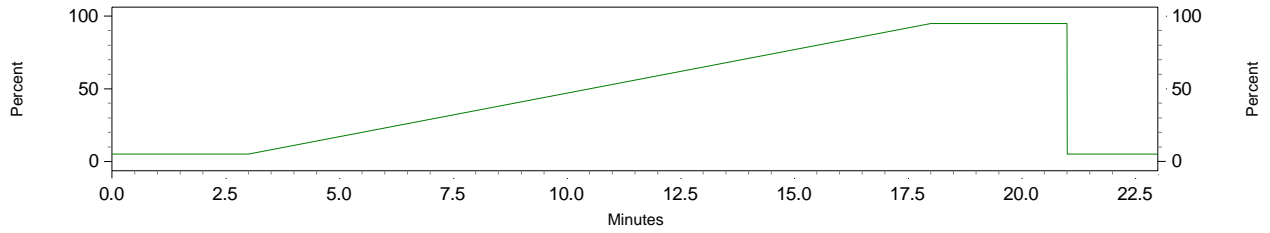
Zoomed View of Relevant Peaks



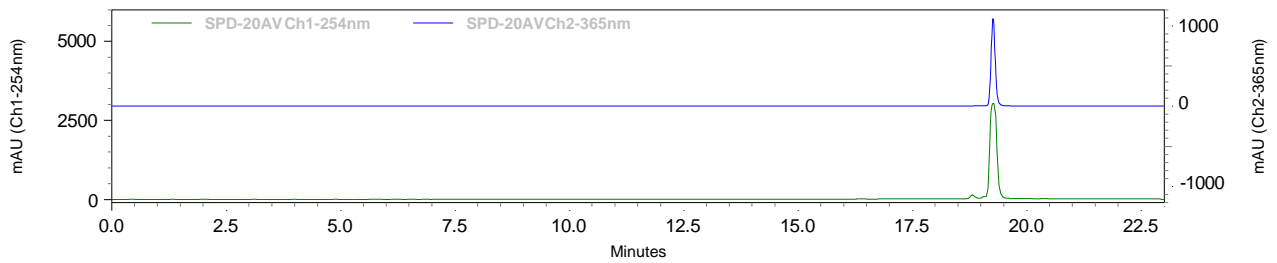
Ch1-254nm		Ch2-365nm	
Retention Time	Area %	Retention Time	Area %
14.183	0.16	16.200	1.93
14.833	0.18	16.917	97.97
16.200	6.64	19.458	0.11
16.917	92.35	Total:	100.00
19.458	0.38		
20.008	0.28		
Total:	100.00		



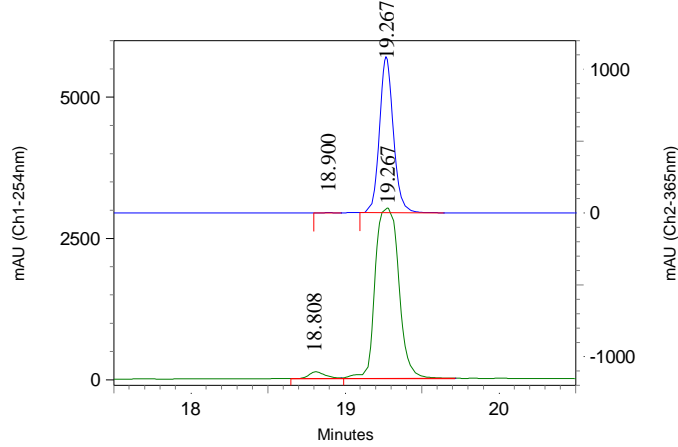
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



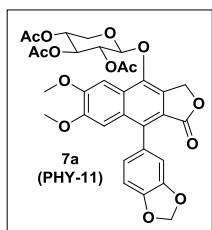
HPLC Trace (254 nm & 365 nm)



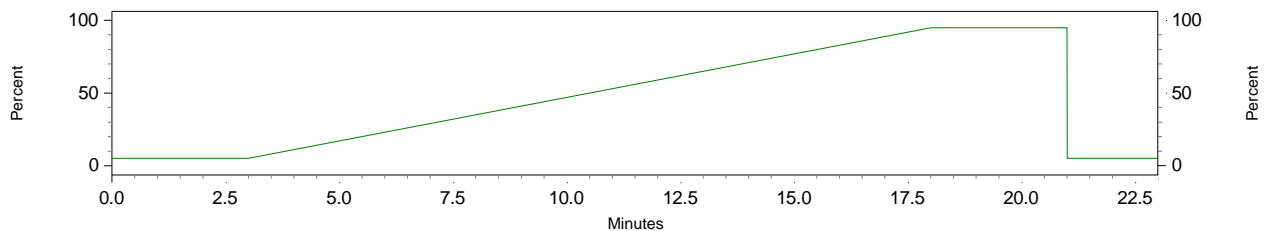
Zoomed View of Relevant Peaks



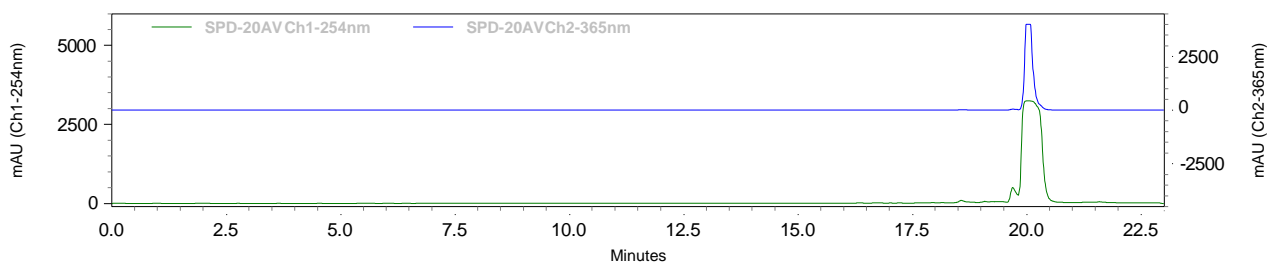
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
18.808	2.65	18.900	0.09
19.267	97.35	19.267	99.91
Total:	100.00	Total:	100.00



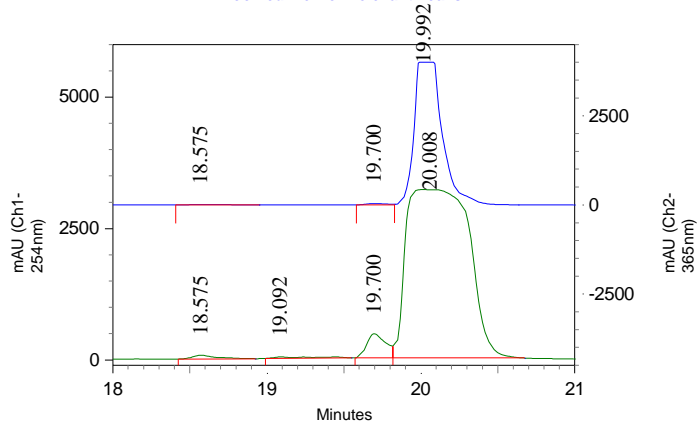
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



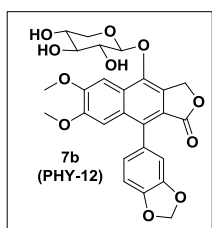
HPLC Trace (254 nm & 365 nm)



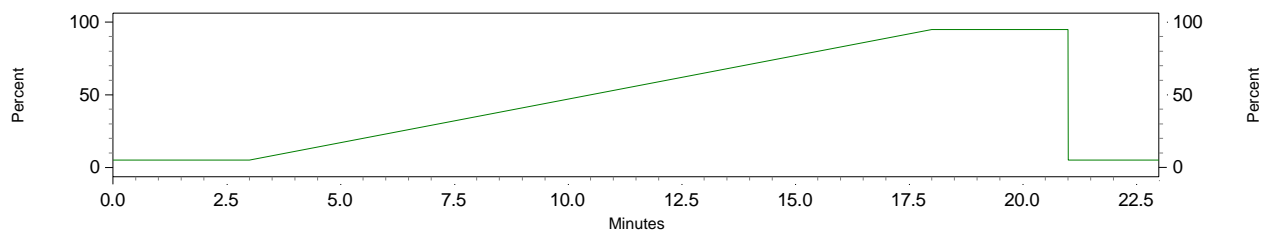
Zoomed View of Relevant Peaks



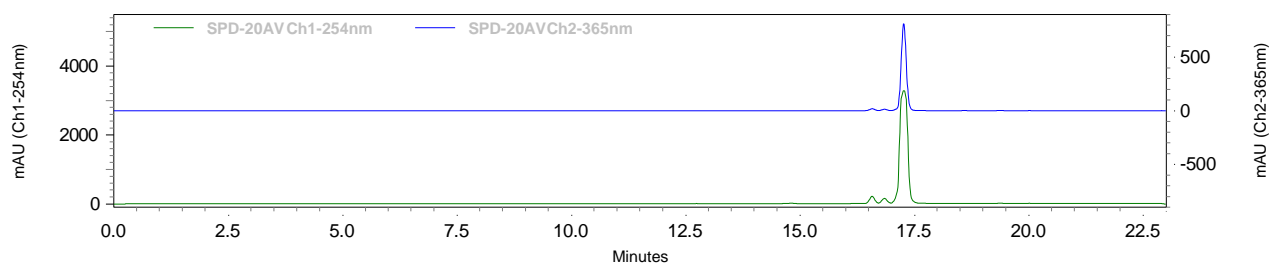
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
18.575	0.76	18.575	0.21
19.092	0.55	19.700	0.58
19.700	4.03	19.992	99.21
20.008	94.12	Total:	100.00
21.592	0.54		
Total:	100.00		



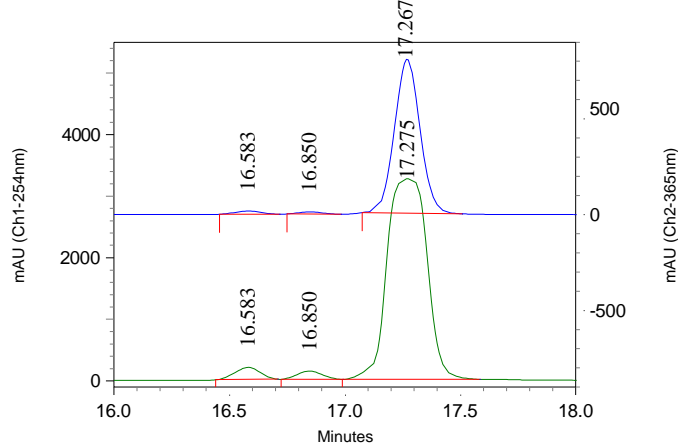
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



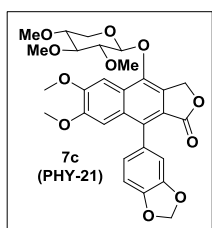
HPLC Trace (254 nm & 365 nm)



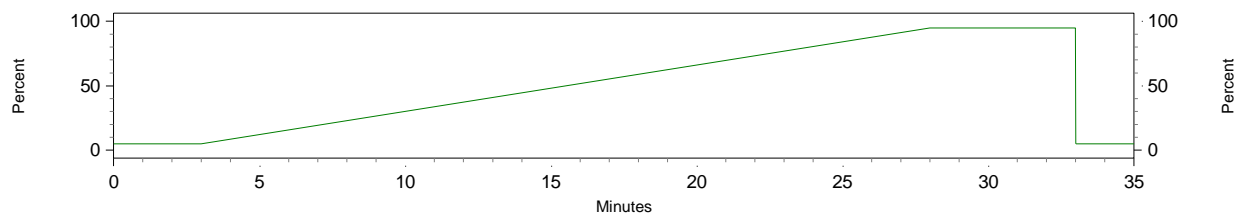
Zoomed View of Relevant Peaks



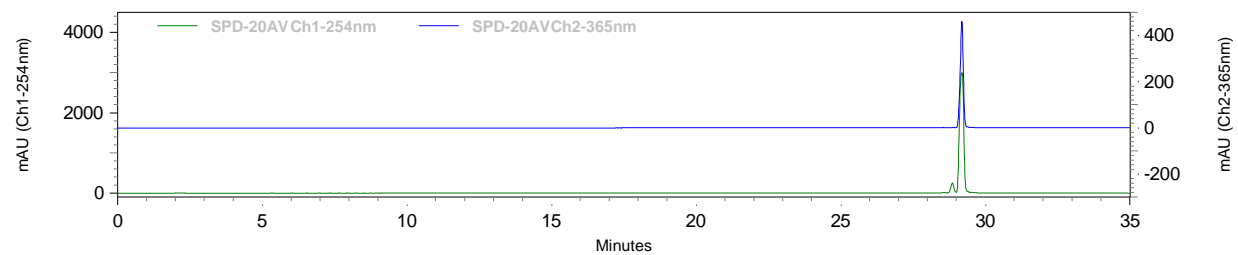
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
16.583	3.60	16.583	1.95
16.850	2.40	16.850	1.23
17.275	93.99	17.267	96.82
Total:	100.00	Total:	100.00



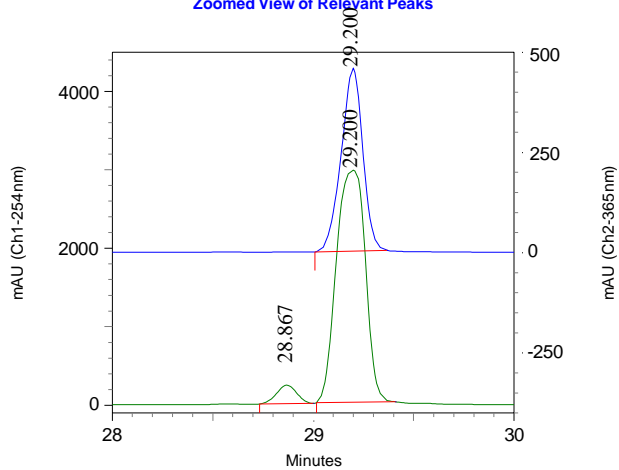
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



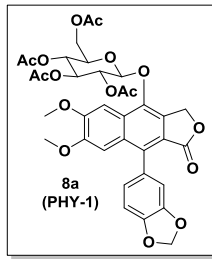
HPLC Trace (254 nm & 365 nm)



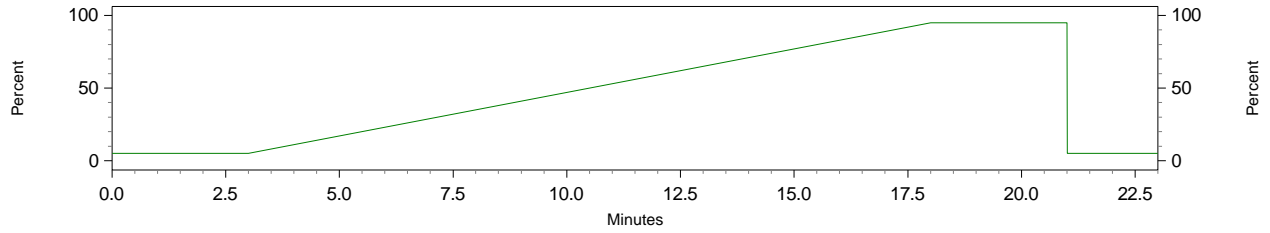
Zoomed View of Relevant Peaks



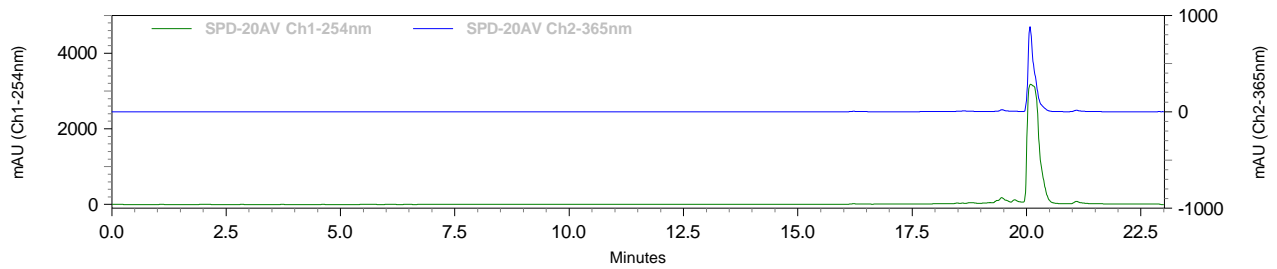
Ch1-254nm		Ch2-365nm	
Retention Time	Area %	Retention Time	Area %
28.867	5.32	29.200	100.00
29.200	94.68	Total:	100.00
Total:	100.00		



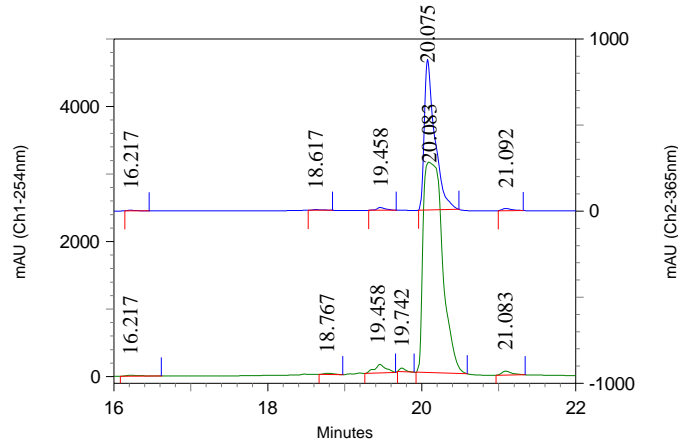
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



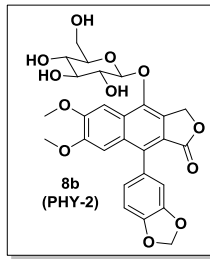
HPLC Trace (254 nm & 365 nm)



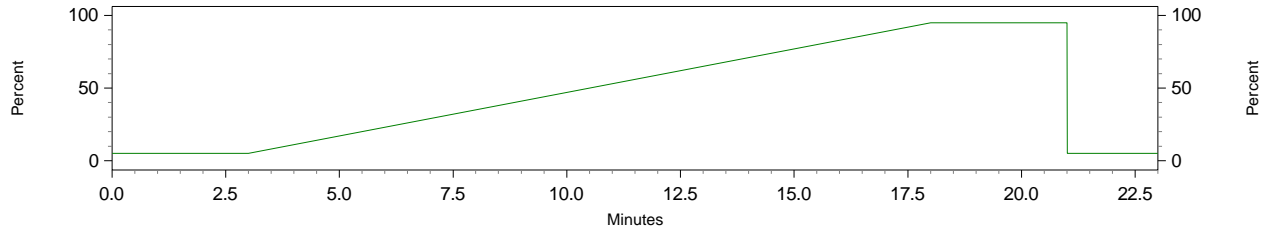
Zoomed View of Relevant Peaks



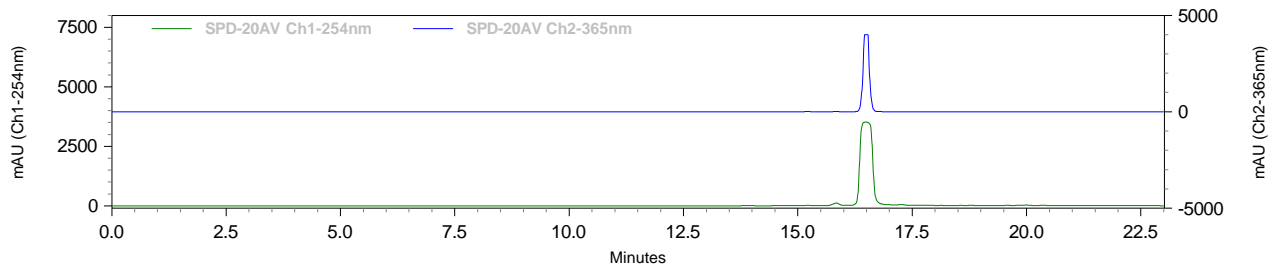
Ch1-254nm		Ch2-365nm	
Retention Time	Area %	Retention Time	Area %
16.217	0.28	16.217	0.28
18.767	0.32	18.617	0.51
19.458	2.31	19.458	1.55
19.742	0.49	20.075	96.38
20.083	95.66	21.092	1.28
21.083	0.93	Total:	100.00
Total:	100.00		



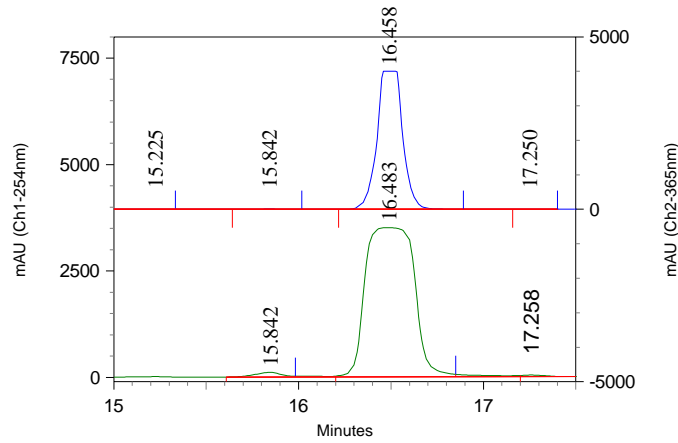
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



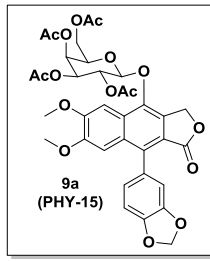
HPLC Trace (254 nm & 365 nm)



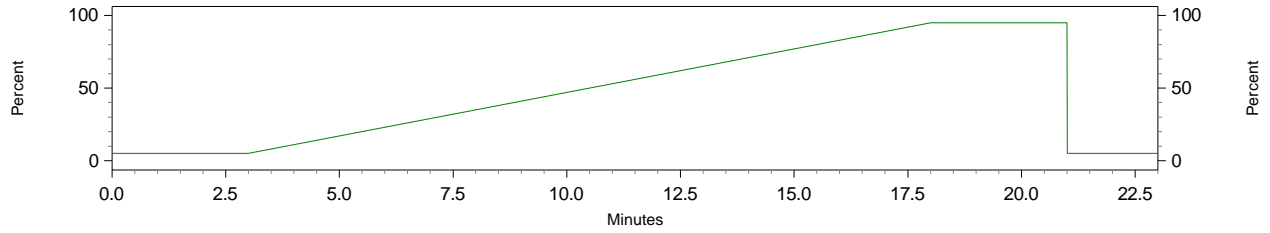
Zoomed View of Relevant Peaks



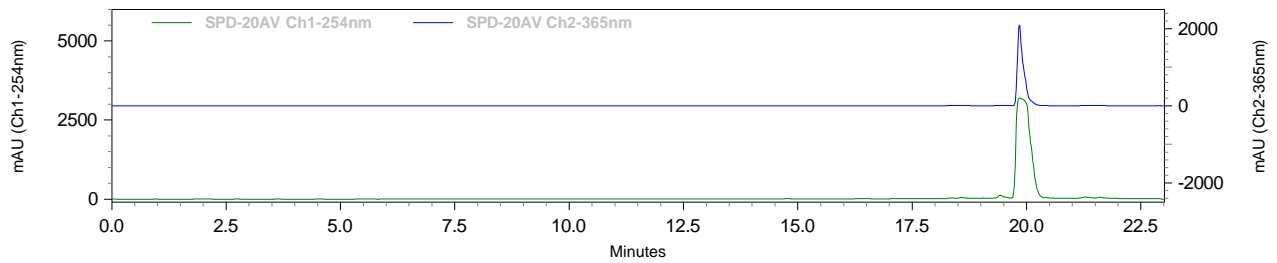
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
15.842	1.64	15.225	0.23
16.483	97.92	15.842	0.22
17.258	0.43	16.458	99.48
Total:	100.00	17.250	0.07
		Total:	100.00



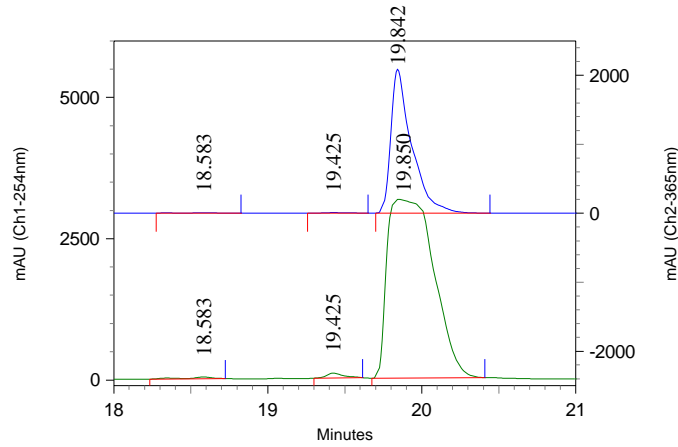
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



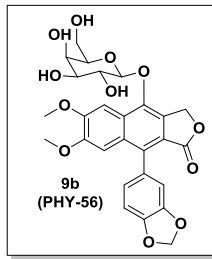
HPLC Trace (254 nm & 365 nm)



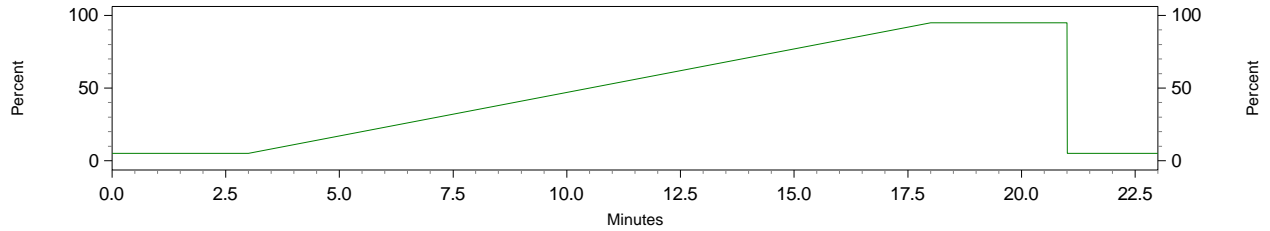
Zoomed View of Relevant Peaks



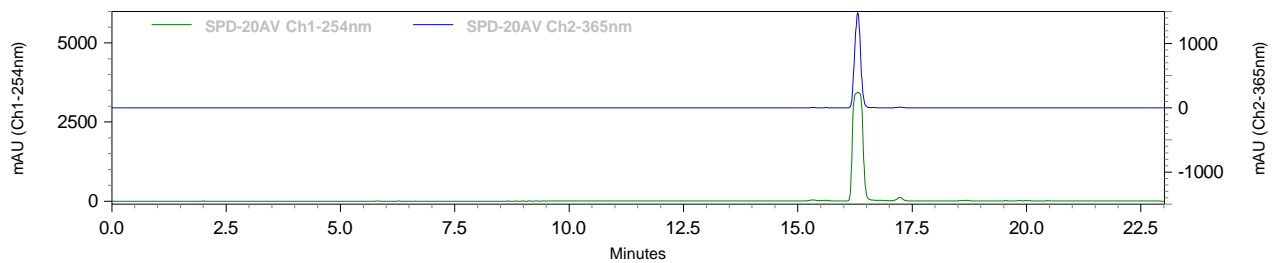
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
18.583	0.53	18.583	0.28
19.425	0.94	19.425	0.32
19.850	97.30	19.842	99.06
21.300	1.23	21.300	0.34
Total:	100.00	Total:	100.00



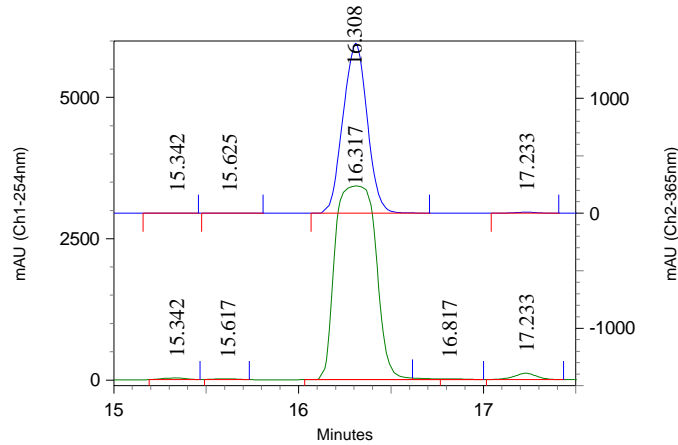
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



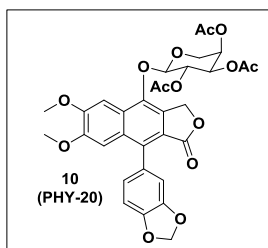
HPLC Trace (254 nm & 365 nm)



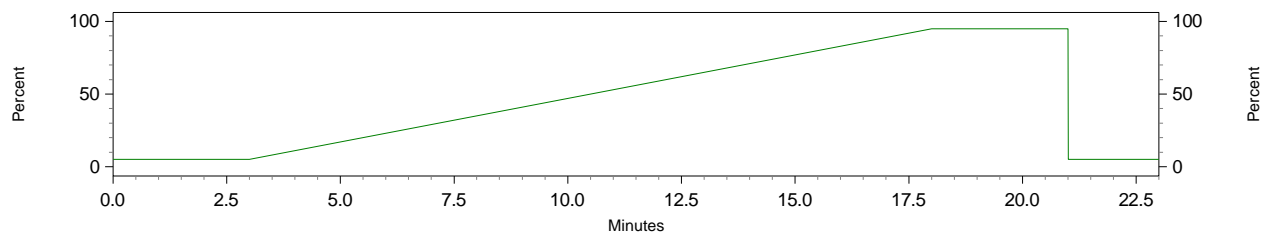
Zoomed View of Relevant Peaks



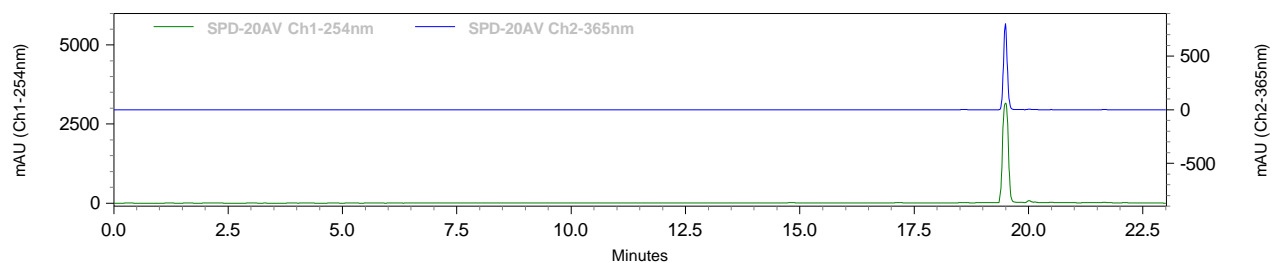
Ch1-254nm		Ch2-365nm	
Retention Time	Area %	Retention Time	Area %
15.342	0.47	15.342	0.13
15.617	0.21	15.625	0.09
16.317	97.23	16.308	99.27
16.817	0.19	17.233	0.51
17.233	1.77	Total:	100.00
18.675	0.14		
Total:	100.00		



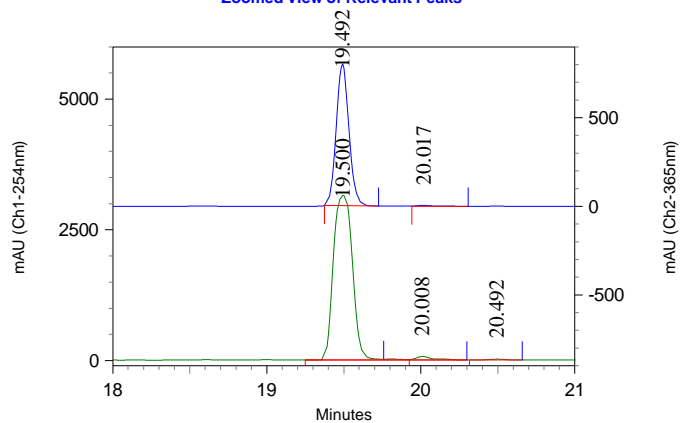
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



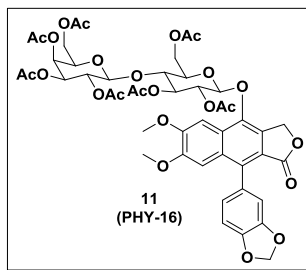
HPLC Trace (254 nm & 365 nm)



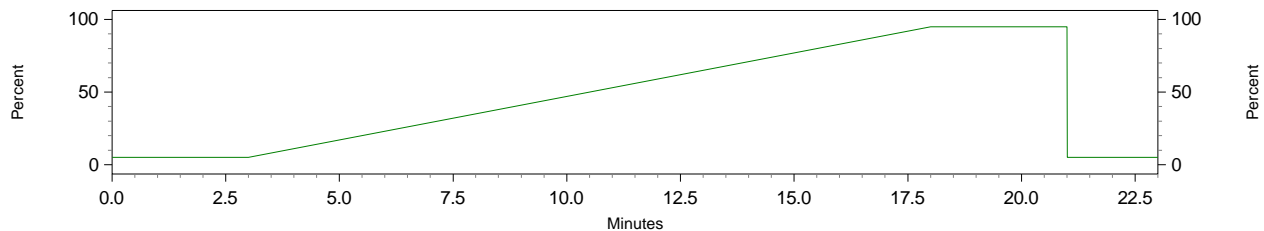
Zoomed View of Relevant Peaks



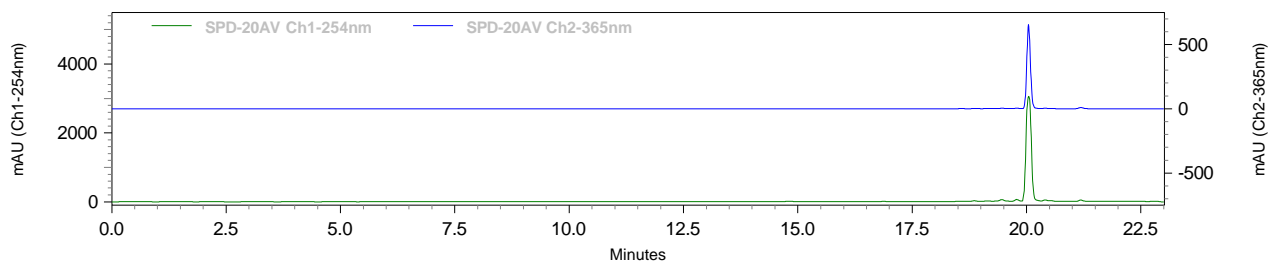
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
14.825	0.41	19.492	99.19
19.500	96.98	20.017	0.81
20.008	1.89	Total:	100.00
20.492	0.41		
21.658	0.32		
Total:	100.00		



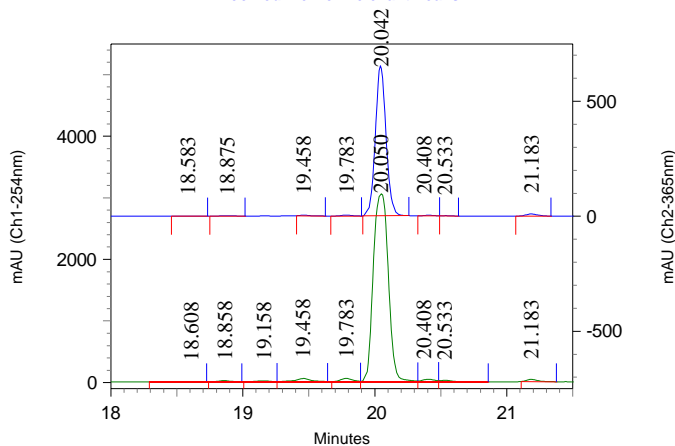
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



HPLC Trace (254 nm & 365 nm)



Zoomed View of Relevant Peaks

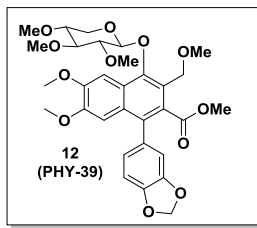


Ch1-254nm

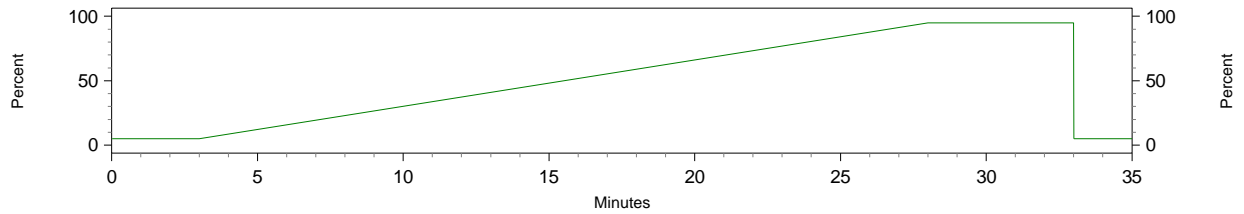
Retention Time	Area %
14.825	0.39
16.875	0.10
18.608	0.22
18.858	0.63
19.158	0.64
19.458	2.03
19.783	1.50
20.050	91.87
20.408	1.11
20.533	0.71
21.183	0.79
Total:	100.00

Ch2-365nm

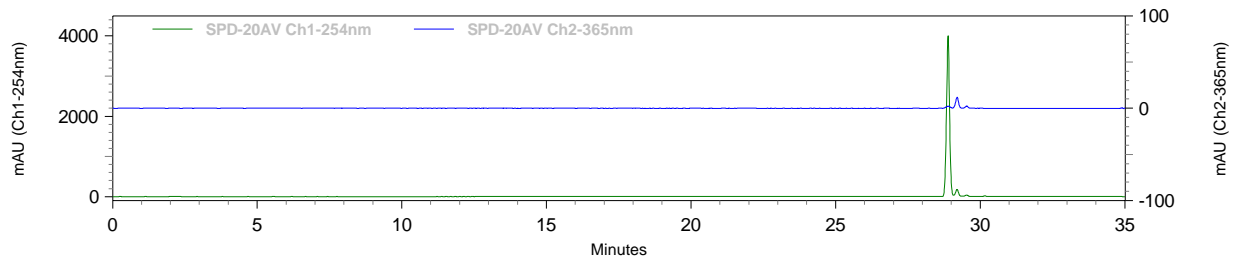
Retention Time	Area %
18.583	0.12
18.875	0.29
19.458	0.33
19.783	0.56
20.042	96.76
20.408	0.31
20.533	0.10
21.183	1.52
Total:	100.00



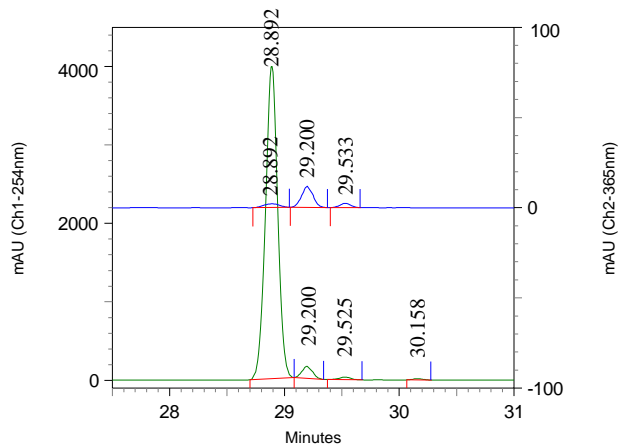
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



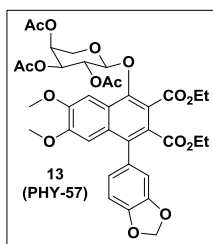
HPLC Trace (254 nm & 365 nm)



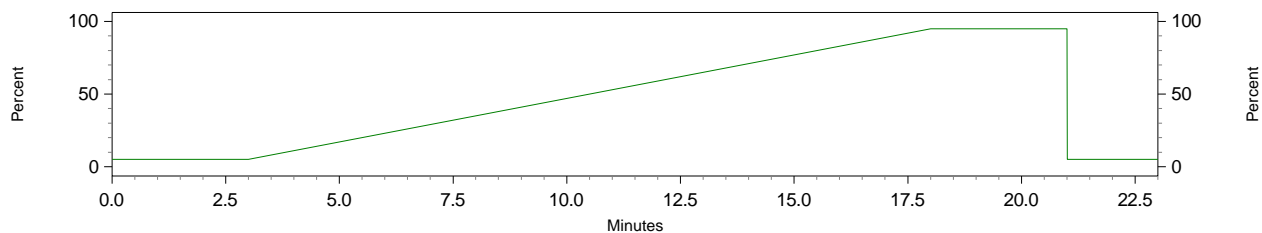
Zoomed View of Relevant Peaks



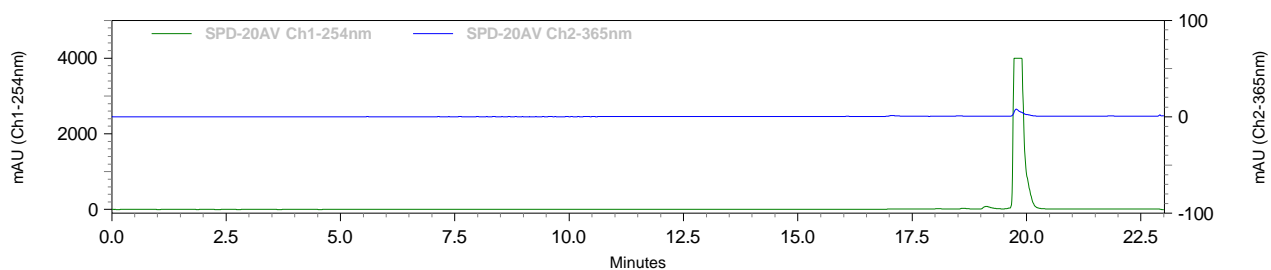
Ch1-254nm		Ch2-365nm	
Retention Time	Area %	Retention Time	Area %
28.892	95.66	28.892	16.96
29.200	3.29	29.200	70.13
29.525	0.74	29.533	12.91
30.158	0.31	Total:	100.00
Total:	100.00		



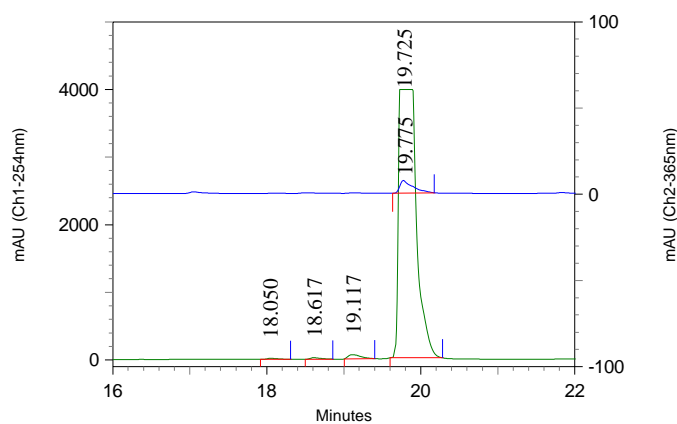
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



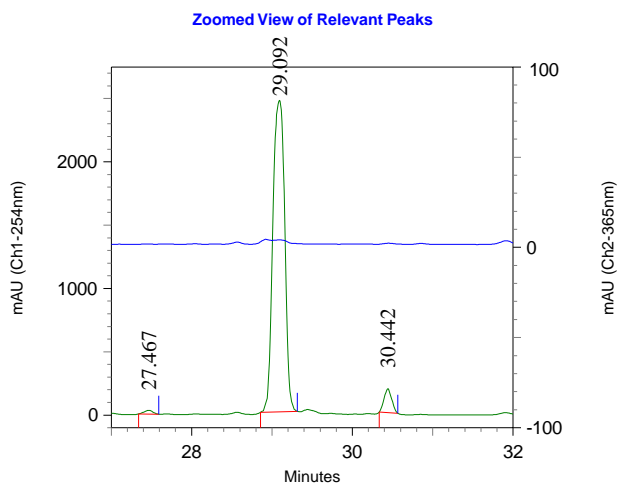
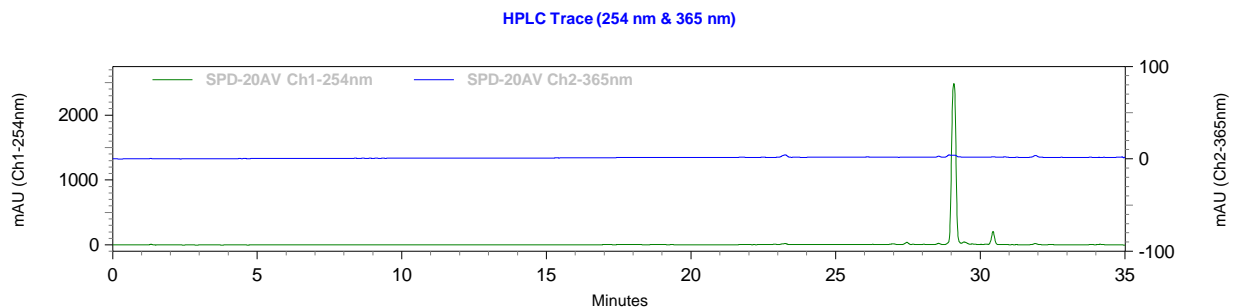
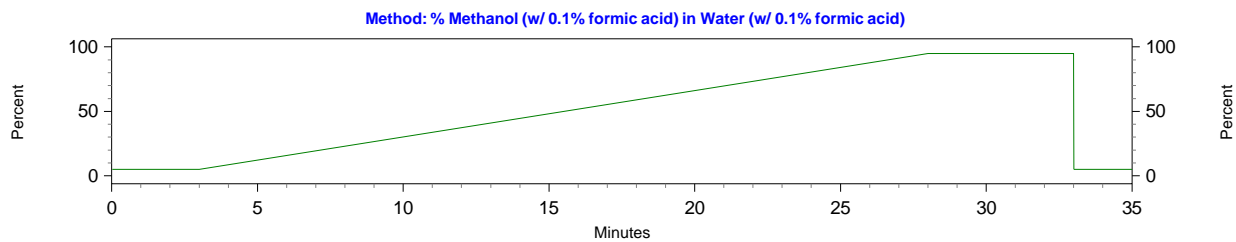
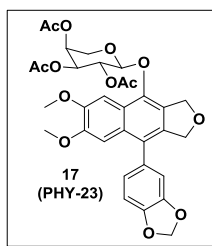
HPLC Trace (254 nm & 365 nm)



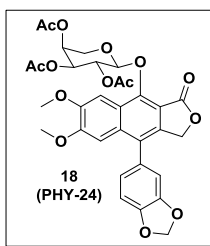
HPLC Trace (254 nm & 365 nm)



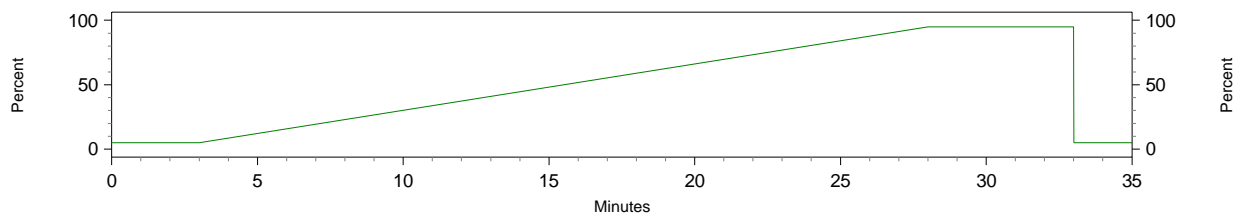
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
18.050	0.21	19.775	100.00
18.617	0.29	Total:	100.00
19.117	1.04		
19.725	98.46		
Total:	100.00		



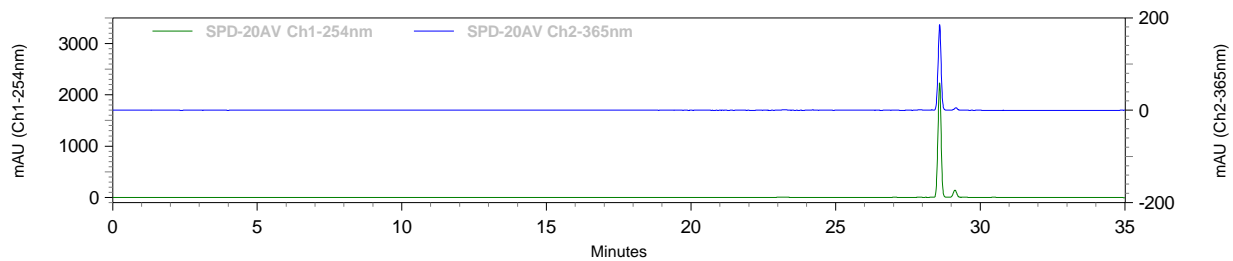
<u>Ch1-254nm</u>		<u>Ch2-365nm</u>	
Retention Time	Area %	Retention Time	Area %
27.467	0.82	----	----
29.092	94.46	----	----
30.442	4.72	----	----
Total:	100.00		



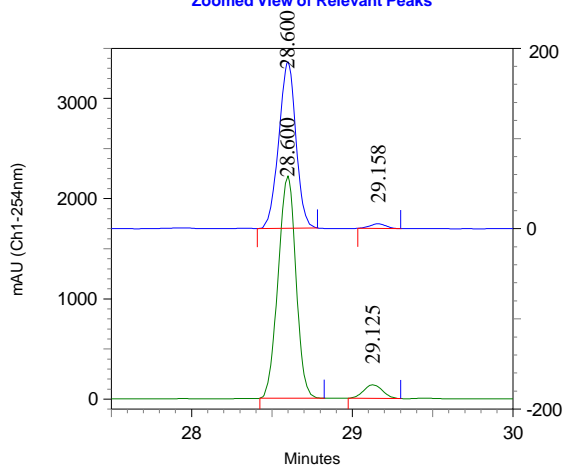
Method: % Methanol (w/ 0.1% formic acid) in Water (w/ 0.1% formic acid)



HPLC Trace (254 nm & 365 nm)



Zoomed View of Relevant Peaks



Ch1-254nm		Ch2-365nm	
Retention Time	Area %	Retention Time	Area %
28.600	93.86	28.600	97.41
29.125	6.14	29.158	2.59
Total:	100.00	Total:	100.00