Supporting Information

for

A case study of empirical and computational chemical shift analyses: Reassignment of the relative configuration of phomopsichalasin to that of diaporthichalasin

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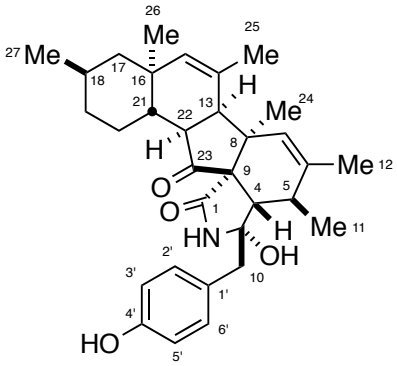
I. Contents of Supporting Information

II. General Experimental Protocols

^{1}H and ^{13}C NMR spectra were recorded on Bruker 850 (850 MHz), Bruker 500 (500 MHz), or Varian Inova 500 (500 MHz) instrument. ^{1}H NMR chemical shifts in $CDCl_3$ are referenced to TMS (0.00 ppm), in d_4-methanol to 3.31 ppm (CHD_2OD), and in d_6-DMSO to 2.50 ppm (CHD_2SOCD_3). ^{13}C NMR chemical shifts in $CDCl_3$ are referenced to TMS (0.00 ppm), in d_4-methanol to 49.0 ppm, and in d_6-DMSO to 39.52 ppm. The following format is used to report resonances: chemical shift in ppm (multiplicity, coupling constant(s) in Hz, integral value, and assignment). Coupling constant analysis was guided by methods we have described elsewhere.[1]

High-resolution mass spectra were recorded on a Bruker BioTOF II (ESI-TOF) instrument using PEG (MW 600) as an internal calibrant. A solution of **7** in methanol and then of the PEG-600 were plug-loaded into a 100 μL syringe and injected into the ESI-TOF ionization chamber. Seven swaths of data (ca. 500 scans each) were analyzed, and the median value was recorded.

III. NMR Spectroscopic Data for Diaporthichalasin (7)



Diaporthichalasin (**7**)

atom numbering

^{1}H NMR (850 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.5 Hz, 2H, *H2'/6'*), 6.84 (d, *J* = 8.5 Hz, 2H, *H3'/5'*), 6.07 (br s, 1H, O*H*), 5.49 (br s, 1H, O*H*), 5.39 (dq, *J* = 1.9, 1.3 Hz, 1H, *H15*), 5.32 (dq, *J* = 1.6, 1.6, 1H, *H7*), 3.12 (d, *J* = 13.5 Hz, 1H, *H10*), 2.98 (d, *J* = 13.4 Hz, 1H, *H10*), 2.98 (d, *J* = 8.0 Hz, 1H, *H13*), 2.91 (d, *J* = 2.1 Hz, 1H, *H4*), 2.44 (dd, *J* = 8.3, 12.9 Hz, 1H, *H22*), 2.35 (s, 1H, N*H*), 2.35 (ddqq, *J* = 2.1, 2.1, 0.9, 7.5 Hz, 1H, *H5*), 1.88 (dd, *J* = 0.9, 1.4 Hz, 3H, *H25*), 1.75 (dd, *J* = 0.9, 1.3 Hz, 3H, *H12*), 1.72 (from HMQC, 1H, *H19eq*), 1.64 (dddd, *J* = 3, 3, 3, 13.5 Hz, 1H, *H20eq*), 1.63 (from COSY, 1H, *H18*), 1.46 (s, 3H, *H24*), 1.45 (ddd, *J* = 1.9, 3.8, 13 Hz, 1H, *H17eq*), 1.40 (ddd, *J* = 2.8, 12.7, 12.7 Hz, 1H, *H21*), 1.21 (dddd, *J* = 3.5, 13, 13, 13 Hz, 1H, *H20ax*), 1.01 (d, *J* = 7.4 Hz, 3H, *H11*), 0.82 (s, 3H, *H26*), 0.82 (d, *J* = 6.5 Hz, 3H, *H27*), 0.72 (dd, *J* = 12.4, 12.4 Hz, 1H, *H17ax*), and 0.60 (dddd, *J* = 4.1, 13.1, 13.1, 13.1 Hz, 1H, *H19ax*).

^{13}C NMR (125 MHz, $CDCl_3$) δ 218.5, 175.1, 155.5, 139.0, 135.3, 131.2, 127.7, 127.1, 126.4, 116.2, 86.8, 64.8, 53.5, 50.4, 49.2, 48.1, 45.8, 43.8, 41.1, 36.0, 35.7, 29.4, 27.1, 25.6, 25.1, 23.4, 22.7, 22.4, 21.0 and 19.7.

^{1}H NMR (850 MHz, d_4-methanol) δ 7.15 (d, *J* = 8.5 Hz, 2H, *H2′/6′*), 6.75 (d, *J* = 8.5 Hz, 2H, *H3′/5′*), 5.37 (dq, *J* = 1.9, 1.9 Hz, 1H, *H15*), 5.21 (dq, *J* = 1.4, 1.4, 1H, *H7*), 3.0 (br s, *2*H, *H10*), 2.86 (d, *J* = 8.0 Hz, 1H, *H13*), 2.73 (d, *J* = 1.7 Hz, 1H, *H4*), 2.25 (dd, *J* = 8.1, 13.0 Hz, 1H, *H22*), 2.09 (br q, *J* = 7.3 Hz, 1H, *H5*), 1.89 (dd, *J* = 0.9, 1.3 Hz, 3H, *H25*), 1.69 (dddd, Σ(*J*s) = 25.7 Hz including *J*s of 1.8 & 12.7 Hz, *H19eq*), 1.65 (s, 3H, *H12*), 1.62 (ddddq, *J* = 4.1, 4.1, 12.3, 12.3, 6.5 Hz, 1H, *H18*), 1.53 (s, 3H, *H24*), 1.52 (dddd, *J* = 3.3, 3.3, 3.3, 13.6 Hz, 1H, *H20eq*), 1.45 (ddd, *J* = 1.8, 3.8, 12.7 Hz, 1H, *H17eq*), 1.45 (ddd, *J* = 2.9, 12.7, 12.7 Hz, 1H, *H21*), 1.1 (dddd, *J* = 4.3, 13.2, 13.2, 13.2 Hz, 1H, *H20ax*), 0.81 (s, 3H, *H26*), 0.81 (d, *J* = 6.5 Hz, 3H, *H27*), 0.81 (d, *J* = 7.3 Hz, *3H*, *H11*), 0.68 (dd, *J* = 12.4, 12.4 Hz, 1H, *H17ax*), and 0.57 (dddd, *J* = 4.3, 13.2, 13.2, 13.2 Hz, 1H, *H19ax*).

^{13}C NMR (125 MHz, d_4-methanol) δ 221.2, 178.2, 157.5, 139.7, 136.6, 132.7, 129.5, 128.0, 127.5, 116.1, 89.6, 66.1, 52.4, 51.9, 50.8, 49.5, 46.3, 45.2, 42.2, 37.0, 36.9, 30.7, 28.4, 26.3, 25.5, 24.5, 23.1, 22.7, 21.0 and 19.9.

^{1}H NMR (850 MHz, d_6-DMSO) δ 9.25 (br s, 1H, O*H*), 8.59 (br s, 1H, N*H*), 7.09 (d, *J* = 8.4 Hz, 2H, *H2′/6′*), 6.67 (d, *J* = 8.5 Hz, 2H, *H3′/5′*), 5.64 (br s, 1H, O*H*), 5.32 (s, 1H, *H15*), 5.08 (dq, *J* = 1.4, 1.5 Hz, 1H, *H7*), 2.87 (d, *J* = 14.1 Hz, 1H, *H10*), 2.85 (d, *J* = 14.1 Hz, 1H, *H10*), 2.73 (d, *J* = 8.1 Hz, 1H, *H13*), 2.48 (d, *J* = 1.4 Hz, 1H, *H4*), 2.04 (dd, *J* = 8.1, 12.9 Hz, 1H, *H22*), 2.03 (br q, *J* = 7.3 Hz, 1H, *H5*), 1.83 (dd, *J* = 0.8, 1.3 Hz, 3H, *H25*), 1.62 (dddd, Σ(*J*s) = 24.7 Hz including *J*s of 1.2 & 12.2 Hz, *H19eq*), 1.58 (dd, *J* = 0.8, 1.4 Hz, 3H, *H12*), 1.55 (ddddq, *J* = 3.9, 3.9, 12.8, 12.8, 6.4 Hz, 1H, *H18*), 1.47 (s, 3H, *H24*), 1.41 (ddd, *J* = 1.7, 3.6, 12.6 Hz, 1H, *H17eq*), 1.37 (dddd, *J* = 3.4, 3.4, 3.4, 13.3 Hz, 1H, *H20eq*), 1.32 (ddd, *J* = 2.9, 12.8, 12.8 Hz, 1H, *H21*), 0.99 (dddd, *J* = 3.5, 13.4, 13.4, 13.4 Hz, 1H, *H20ax*), 0.75 (d, *J* = 6.4 Hz, 3H, *H27*), 0.74 (s, 3H, *H26*), 0.71 (d, *J* = 7.4 Hz, 3H, *H11*), 0.58 (dd, *J* = 12.3, 12.3 Hz, 1H, *H17ax*), and 0.47 (dddd, *J* = 4.2, 12.9, 12.9, 12.9 Hz, 1H, *H19ax*).

^{13}C NMR (125 MHz, d_6-DMSO) δ 218.8, 174.7, 155.9, 137.9, 134.7, 131.5, 128.8, 126.6, 126.1, 114.7, 87.9, 63.6, 50.0, 49.2, 48.6, 47.7, 44.1, 43.6, 40.3, 35.5, 35.3, 28.7, 26.6, 25.4, 24.9, 22.9, 22.6, 22.3, 20.0 and 19.9.

HRMS (ESI-TOF): Calcd for $(C_{32}H_{41}NO_4Na)^+$ 526.2928. Found 526.2948.

Table S1. NMR spectral data for diaporthichalasin (**7**) in $CDCl_3$.

#	δ_H (mult, *J*, Hz)	COSY H→ #	Carbon	HMBC (H → C)
1	-	-	175.1	
2	not assigned	-	-	
3	-	-	86.8	
4	2.91 (d, 2.1)	5	53.5	3,5,6,7,8,9,11,23
5	2.35 (ddqq, 2.1, 2.1, 0.9, 7.5)	4,7,11	29.4	3,4,6,11
6	-	-	135.3	
7	5.32 (dq, 1.6, 1.6)	5, 12	127.1	5,8,9,12
8	-	-	43.8	
9	-	-	64.8	
10	3.12 (d, 13.5) 2.98 (d, 13.4)	10 10	45.8	$1^{\prime}$,$2^{\prime}$/$6^{\prime}$, 3
11	1.01 (d, 7.4)	5	21.0	4,5,6
12	1.75 (dd, 0.9, 1.3)	5, 7	22.4	5,6,7
13	2.98 (d, 8.0)	15, 22, 25	50.4	8,15,21,22,24
14	-	-	127.7	
15	5.39 (dq, 1.9, 1.3)	13, 25	139.0	13,16,21,25
16	-	-	36.0	
17_{ax}	0.72 (dd, 12.4, 12.4)	17_{eq},18	48.1	16,27
17_{eq}	1.45 (ddd, 1.9, 3.8, 13)	18,		
18	1.63 (from COSY)	27	27.1	
19_{ax}	0.60 (dddd, 4.1, 13.1, 13.1, 13.1)	18,19_{eq}, 27	35.7	
19_{eq}	1.72 (from HMQC)	20_{ax}		
20_{ax}	1.21 (dddd, 3.5, 13, 13, 13)	19_{eq} ,20_{eq},21	23.4	
20_{eq}	1.64 (dddd, 3,3,3,13.5)	20_{ax}		
21	1.40 (ddd, 2.8, 12.7, 12.7)	22	41.1	
22	2.44 (dd, 8.3, 12.9)	13,21	49.2	8,21,16,23
23	-	-	218.5	
24	1.46 (s)	-	25.6	7,8,9,13
25	1.88 (dd, 0.9, 1.4)	13, 15	25.1	13,14,15
26	0.82 (s)	-	19.7	16,17,21
27	0.82 (d, 6.5)	18	22.7	17,18
1´	-	-	126.4	
2´,6´	7.15 (d, 8.5)	3´, 5´	131.2	$4^{\prime}$,$1^{\prime}$, $3^{\prime}$/$5^{\prime}$
3´,5´	6.84 (d, 8.5)	2´, 6´	116.2	$4^{\prime}$,$2^{\prime}$/$6^{\prime}$, 10
4´	-	-	155.5	
OH	5.49 (br s)	-	-	3,4,9
OH	6.07 (br s)	-	-	

Table S2. NMR spectral data for diaporthichalasin (**7**) in d_4-methanol (UMN).

#	δ_H (mult, *J*, Hz) of "1"[2]	δ_H (mult, *J*, Hz) of 7	COSY of 7 H → #	Carbon of "1"[2]	Carbon of 7	HMBC of 7 (CD_3OD, H → C)
1	-	-	-	178.2	178.2	
2	-	-	-	-	-	
3	-	-	-	89.7	89.6	
4	2.73 (d, 1.7)	2.73 (d, 1.7)	5	52.4	52.4	3,5,6,8,9,11,23
5	2.09 (br q, 7.3)	2.09 (br q, 7.3)	4,7,11	30.7	30.7	3,4,6,7,9,11
6	-	-	-	136.6	136.6	
7	5.20 (br s)	5.21 (dq, 1.4, 1.4)	11,12,5	127.5	127.5	5,8,9,12,13
8	-	-	-	45.2	45.2	
9	-	-	-	66.1	66.1	
10	2.99 (br s)	3.0 (br s)	2'/6'	46.3	46.3	1',2'/6',3,4
11	0.81 (d, 7.4)	0.81 (d,7.3)		21	21.0	overlaps w/ 26 & 27
12	1.64 (br s)	1.65 (s)	7	22.7	22.7	*overlaps w/ 19 but can *ca.* 5,6,7,24
13	2.85 (br d, 8.0)	2.86 (d, 8)	15,22,25	52.0	51.9	7,8,14,15,21,22,24
14	-	-	-	129.5	129.5	
15	5.36 (br s)	5.37 (dq, 1.9, 1.9)	13,20_{eq},25	139.7	139.7	13,16,17,21,25
16	-	-	-	37.0	37.0	
17_{ax}	0.67 (dd, 12.2)	0.68 (dd, 12.4, 12.4)	17_{eq},18			
17_{eq}	1.45 (m)	1.45(ddd, 1.8, 3.8, 12.7)	17_{ax},20,22	49.4	49.5	16,18,21,26,27
18	1.62 obsc	1.62 (ddddq, 4.1, 4.1, 12.3, 12.3, 6.5)	17_{ax},27	28.4	28.4	overlaps w/ 12
19_{ax}	0.56 (dq, 3.7, 12.7)	0.57 (dddd, 4.3, 13.2, 13.2,13.2)				
19_{eq}	1.64 obsc	1.69 (dddd, Σ(*J*s) = 25.7 Hz including *J*s of 1.8 & 12.7)	18, 20_{ax},20_{eq}	36.9	36.9	16,21
20_{ax}	1.1 (dddd, 12.7, 2.2, 2.4)	1.1 (dddd, 4.3, 13.2, 13.2, 13.2)	18, 19_{ax},21	24.5	24.5	
20_{eq}	1.5 (obsc)	1.51 (dddd, 3.3, 3.3, 3.3, 13.6)	15, 19_{ax}			
21	1.42 (m)	1.42 (ddd, 2.9, 12.7, 12.7)	17_{ax},20_{ax},22	42.2	42.2	overlaps w/ 17
22	2.24 (dd, 8.0, 12.7)	2.25 (dd, 8.1, 13.0)	13,17_{eq}	50.8	50.8	8,9,16,21,23
23	-	-	-	221.3	221.2	
24	1.52 (br s)	1.53 (s)		26.3	26.3	7,8,9,12,13
25	1.88 (br s)	1.89 (dd, 0.9, 1.3)	15	25.5	25.5	13,14,15,26
26	0.80 (s)	0.81 (s)		19.9	19.9	overlaps w/ 11,27
27	0.78 (d, 2.2)	0.81 (d, 6.5)		23.1	23.1	overlaps w/ 11,26
1´	-	-	-	128.0	128.0	
2´,6´	7.14 (d, 8.5)	7.15 (d, 8.5)	3'/5',10	132.8	132.7	1',2'/6',4',3'/5',10
3´,5´	6.74 (d, 8.5)	6.75 (d, 8.5)	2'/6'	116.1	116.1	1',3'/5',4'
4´	-	-	-	157.6	157.5	
OH	-	-	-	-	-	
OH	-	-	-	-	-	

Table S3. NMR spectral data for diaporthichalasin (**7**) in d_6-DMSO.

#	δ_H (mult, *J*, Hz) (2007[3])	δ_H (mult, *J*, Hz) (UMN)	Carbon (2007[3])	Carbon (UMN)
1	-		174.83	174.6
2	8.58 (s)	8.59 (s)	-	-
3	-	-	87.99	87.9
4	2.47 (s)	2.48 (d, 1.4)	49.27	49.2
5	2.03 (m)	2.03 (br q, 7.3)	28.82	28.7
6	-	-	134.77	134.7
7	5.08 (s)	5.08 (dq, 1.4, 1.5)	126.13	126.0
8	-	-	43.64	43.6
9	-	-	63.62	63.6
10	2.86 (s)	2.87 (d, 14.1) 2.85 (d, 14.1)	44.07	44.1
11	0.71 (d, 7.2)	0.71 (d, 7.4)	20.44	20.0
12	1.58 (s)	1.58 (dd, 0.8, 1.4)	22.44	22.3
13	2.72 (d, 8.0)	2.73 (d, 8.1)	50.14	50.0
14	-	-	128.13	128.8
15	5.36 (s)	5.32 (s)	137.95	137.8
16	-	-	35.56	35.5
17_{ax}	0.58 (dd, 12.4, 12.0)	0.58 (dd, 12.3, 12.3)	47.8	47.7
17_{eq}	1.41 (br d, 12.8)	1.41 (ddd, 1.7, 3.6, 12.6)		
18	1.54 (m)	1.55 (ddddq, 3.9, 3.9, 12.8, 12.8, 6.4)	26.72	26.6
19_{ax}	0.46 (br q, 12.4)	0.47 (dddd, 4.2, 12.9, 12.9, 12.9)	35.37	35.3
19_{eq}	1.62 (br d, 9.2)	1.62 (dddd, Σ(*J*s) = 24.7 Hz including *J*s of 1.2 & 12.2)		
20_{ax}	0.98 (br q, 12.4)	0.99 (dddd, 3.5, 13.4, 13.4, 13.4)	22.99	22.9
20_{eq}	1.37 (m)	1.37 (dddd, 3.4, 3.4, 3.4, 13.3)		
21	1.32 (dd, 12.8, 13.2)	1.32 (ddd, 2.9, 12.8, 12.8)	40.34	40.3
22	2.03 (dd, 12, 8.4)	2.04 (dd, 8.1, 12.9)	48.75	48.6
23	-	-	218.95	218.8
24	1.47 (s)	1.47 (s)	25.49	25.4
25	1.82 (s)	1.83 (dd, 0.8, 1.3)	24.98	24.9
26	0.74 (s)	0.74 (s)	19.52	19.9
27	0.75 (d, 7.6)	0.75 (d, 6.4)	22.66	22.6
1´	-	-	126.69	126.6
2´,6´	7.09 (d, 8.4)	7.09 (d, 8.4)	131.6	131.5
3´,5´	6.67 (d, 8.4)	6.67 (d, 8.5)	114.83	114.7
4´	-	-	155.93	155.9
OH	5.63 (s)	5.64 (br s)	-	-
OH	9.26(br s)	9.25 (br s)	-	-

Table S4. Summary of reported and recollected proton (left half) and carbon (right half) NMR chemical shift data for phomopsichalasin (once known as **1**)[2] and diaporthichalasin (**7**)[3] in three different solvents.

Nucleus	**δ ^{1}H**					**δ ^{13}C**				
Sample	**Diap.** $CDCl_3$-*UMN*	**Phom.** MeOH-*1995*	**Diap.** MeOH-*UMN*	**Diap.** DMSO-*2007*	**Diap.** DMSO-*UMN*	**Diap.** $CDCl_3$-*UMN*	**Phom.** MeOH-*1995*	**Diap.** MeOH-*UMN*	**Diap.** DMSO-*2007*	**Diap.** DMSO-*UMN*
Atom #										
1	-	-	-	-	-	175.1	178.2	178.2	174.83	174.65
2	n/a[a]	-	n/a[a]	8.58	8.59	-	-	-	-	-
3	-	-	-	-	-	86.8	89.7	89.6	87.99	87.86
4	2.91	2.73	2.73	2.47	2.48	53.5	52.4	52.4	49.27	49.21
5	2.35	2.09	2.09	2.03	2.03	29.4	30.7	30.7	28.82	28.74
6	-	-	-	-	-	135.3	136.6	136.6	134.77	134.68
7	5.32	5.20	5.21	5.08	5.08	127.1	127.5	127.5	126.13	126.05
8	-	-	-	-	-	43.8	45.2	45.2	43.64	43.57
9	-	-	-	-	-	64.8	66.1	66.1	63.62	63.57
10a **10b**	3.12 2.98	2.99	3.00	2.86	2.87 2.85	45.8	46.3	46.3	44.07	44.06
11	1.01	0.81	0.81	0.71	0.71	21.0	21.0	21.0	20.44	19.95
12	1.75	1.64	1.65	1.58	1.58	22.4	22.7	22.7	22.44	22.33
13	2.98	2.85	2.86	2.72	2.73	50.4	52.0	51.9	50.14	50.02
14	-	-	-	-	-	127.7	129.5	129.5	128.13	128.79
15	5.39	5.36	5.37	5.36	5.32	139.0	139.7	139.7	137.95	137.85
16	-	-	-	-	-	36.0	37.0	37.0	35.56	35.48
17_{ax} **17_{eq}**	0.72 1.45	0.67 1.45	0.68 1.45	0.58 1.41	0.58 1.41	48.1	49.4	49.5	47.8	47.73
18	1.63	1.62	1.62	1.54	1.55	27.1	28.4	28.4	26.72	26.63
19_{ax} **19_{eq}**	0.60 1.72	0.56 1.64	0.57 1.69	0.46 1.62	0.47 1.62	35.7	36.9	36.9	35.37	35.29
20_{ax} **20_{eq}**	1.21 1.64	1.10 1.50	1.10 1.52	0.98 1.37	0.99 1.37	23.4	24.5	24.5	22.99	22.91
21	1.40	1.42	1.45	1.32	1.32	41.1	42.2	42.2	40.34	40.26
22	2.44	2.24	2.25	2.03	2.04	49.2	50.8	50.8	48.75	48.63
23	-	-	-	-	-	218.5	221.3	221.2	218.95	218.75
24	1.46	1.52	1.53	1.47	1.47	25.6	26.3	26.3	25.49	25.39
25	1.88	1.88	1.89	1.82	1.83	25.1	25.5	25.5	24.98	24.87
26	0.82	0.80	0.81	0.74	0.74	19.7	19.9	19.9	19.52	19.94
27	0.82	0.78	0.81	0.75	0.75	22.7	23.1	23.1	22.66	22.56
1′	-	-	-	-	-	126.4	128.0	128.0	126.69	126.59
2′/6′	7.15	7.14	7.15	7.09	7.09	131.2	132.8	132.7	131.6	131.48
3′/5′	6.84	6.74	6.75	6.67	6.67	116.2	116.1	116.1	114.83	114.72
4′	-	-	-	-	-	155.5	157.6	157.5	155.93	155.86
OH	5.49			5.63	5.64	-	-	-	-	-
OH	6.07			9.26	9.25	-	-	-	-	-

[a] n/a = not assigned.

V. Figures S1 and S2.

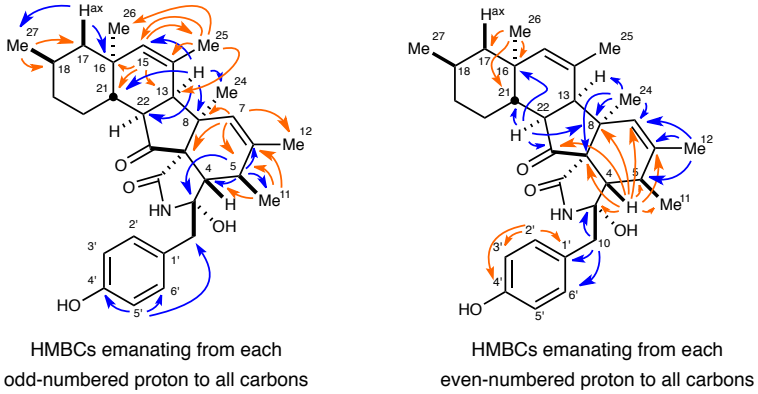


Figure S1. HMBC interactions observed for diaporthichalasin (**7**) in $CDCl_3$. Orange and blue arrows are used merely to help distinguish one set of correlations from another; they carry no additional specific meaning.

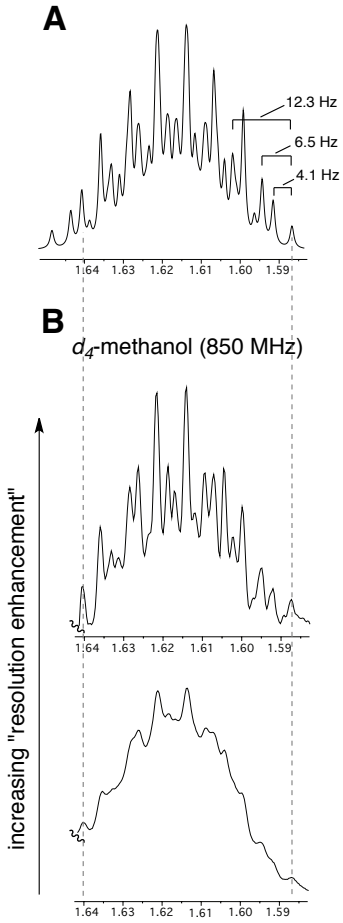


Figure S2. Panel **B**: Multiplet for the axial H18 proton in **7** (850 MHz, d_4-MeOH). Resolution enhancement allows determination[1] of the *J* values for this ddddq of 4.1, 4.1, 12.3, 12.3, and 6.5 Hz. Panel **A**: Simulated first-order multiplet using these deduced coupling constants.

VI. Computational Protocols and Results

A. Molecular Mechanics and DFT Calculations

Molecular mechanics calculations were carried out using MacroModel[4] as implemented in the Maestro[5] graphical user interface. Each of **10a** and **10b** was subjected to a Monte Carlo Multiple Minimum (MCMM)[6] conformational search where all minima within a 5.02 kcal•mol^{-1} (21.0 kJ•mol^{-1}) energetic window were retained. Each of these conformations was optimized with PRCG (500 steps) employing the MMFFs force field and the GB/SA continuum solvation treatment for chloroform.

DFT calculations were carried out using the Gaussian 09 electronic structure modeling platform.[7]

The conformational minima obtained as described were fully optimized at the density functional level of theory employing the hybrid meta-GGA functional M06-2X[8] and the 6-31+G(d,p) basis set. Frequency calculations conducted at the same level of theory provided the free energy values that were used to determine Boltzmann-weighted chemical shifts (where applicable). Solvation effects for methanol and chloroform were included by specifying the integral equation formalism polarized continuum model (IEFPCM).[9] The solute cavities were constructed using united-atom radii.[10]

Single-point GIAO NMR calculations were carried out with the hybrid GGA functional WP04[11] in combination with Jensen's pcS-2 basis set.[12] Solvation effects for methanol and chloroform were included by specifying the integral equation formalism polarized continuum model (IEFPCM). The solute cavities were constructed using Bondi radii.[13]

In order to calculate the chemical shifts for a particular structure, the isotropic chemical shifts for all unique proton nuclei (σ^x) within that structure were referenced to the isotropic chemical shifts of the proton nuclei of tetramethylsilane (σ^{TMS}) according to the following equation:

$$\delta^{x}_{\mathbf{DFT}} = \left| \sigma^{TMS} - \sigma^{x} \right|$$

The values computed for σ^{TMS} (31.7699 and 31.7768 from calculations carried out with methanol and chloroform PCM solvation, respectively) were determined at the same level of theory. Isotropic chemical shifts for proton nuclei that were symmetry-related (i.e., methyl groups) were arithmetically averaged prior to being referenced.

In situations where more than one conformation merits consideration, the referenced chemical shifts are reported as a Boltzmann-weighted average ($\delta^{x}_{\mathbf{DFT}}$) across all conformers:

$$\delta^{x}_{\mathbf{DFT}} = \frac{\sum_{i} \delta^{x}_{i} \, e^{\left(-\Delta E_i / RT\right)}}{\sum_{i} e^{\left(-\Delta E_i / RT\right)}}$$

In the above equation, δ^{x}_{i} is the referenced chemical shift of nucleus x in conformer i, ΔE_i is the difference in free energy (sum of electronic and thermal free energies) between the ith conformer and the most stable (global minimum) conformer, R is the universal gas constant, and T = 298 K.

Finally, the mean absolute error (MAE) was determined according to:

$$\mathbf{MAE} = \sum_{i}^{N} \left| \delta^{x}_{\mathrm{DFT}} - \delta^{x}_{\mathrm{EXP}} \right| / N$$

where $\delta^{x}_{\mathbf{DFT}}$ and $\delta^{x}_{\mathbf{EXP}}$ are the computed and experimental chemical shifts, respectively, for nucleus x, where N is the total number of nuclei being compared.

B. Sample Gaussian input files for the DFT calculations.

i. Representative Gaussian 09 *.com file for geometry optimization and frequency calculation.

M06-2X density functional and the **6-31+G(d,p) basis set** with methanol solvation (for chloroform solvation, 'solvent=methanol' was replaced with 'solvent=chloroform'):

```
%NProcShared=4
%Mem=7900mb
%nproc=4
%chk=Diaporth_trunc_OPT_M062X-6-31+G-dp_MeOH.chk

# M062X/6-31+G(d,p) opt freq=noraman integral(ultrafinegrid)
scrf=(iefpcm,read,solvent=methanol)

GEOMETRY OPTIMIZATION/FREQUENCY CALCULATION WITH METHANOL SOLVATION FOR MODEL
COMPOUND 10B, STARTING FROM THE FOLLOWING INPUT GEOMETRY, WHICH RESULTS FROM THE
INIITAL MCMM SEARCH.

0 1
 C  -5.993542   0.952039  -5.171179
 C  -5.764000   0.202437  -3.856289
 C  -5.707315   1.129910  -2.636173
 C  -6.917411   2.080734  -2.593839
 H  -5.102494   1.530195  -5.438189
 H  -6.123336   0.203607  -5.959751
 H  -6.573317  -0.527735  -3.723604
 H  -4.833980  -0.374362  -3.928494
 H  -4.788995   1.726202  -2.699113
 H  -7.826794   1.497371  -2.390329
 H  -6.803873   2.770150  -1.746141
 C  -7.232181   1.857710  -5.079577
 C  -7.584445   2.582938  -6.388224
 C  -8.900582   3.391860  -6.252487
 C  -9.169665   3.967023  -4.878024
 C  -8.357250   3.729847  -3.831271
 C  -7.101793   2.878379  -3.908259
 H  -8.072702   1.183580  -4.847628
 H  -6.772352   3.237450  -6.723608
 C  -5.927533   3.870155  -4.084999
 H  -6.069033   4.523688  -4.953332
 H  -5.833502   4.523613  -3.208519
 H  -4.964249   3.370131  -4.214540
 C  -5.624745   0.312198  -1.346506
 H  -5.540939   0.969921  -0.474945
 H  -6.513137  -0.314525  -1.213690
 H  -4.746979  -0.342548  -1.357730
 C -10.372935   4.860129  -4.745094
 H -11.293313   4.296405  -4.925530
 H -10.447775   5.303924  -3.746627
 H -10.317943   5.680749  -5.467685
```

```
 H  -8.568330   4.200425  -2.871567
 C  -9.401943   1.665656  -7.870504
 H  -9.804770   0.654489  -7.958921
 H  -9.537371   2.220619  -8.803222
 C  -9.997778   2.411941  -6.690465
 H -10.924170   2.922519  -6.973924
 H -10.242624   1.707364  -5.885185
 H  -8.861169   4.220234  -6.974561
 C  -7.938874   1.643103  -7.525021
 O  -7.122179   0.959985  -8.131984

radii=UA0
```

ii. Representative Gaussian 09 *.com file for GIAO DFT NMR calculation.

WP04 density functional and the **pcS-2 basis set** with methanol solvation (for chloroform solvation, 'solvent=methanol' was replaced with 'solvent=chloroform'):

```
%NProcShared=4
%Mem=7900mb
%nproc=4
%chk=Diaporth_trunc_OPT_M062X-6-31+G-dp_MeOH.chk

# BLYP/GEN IOp(3/76=1000001189,3/77=0961409999,3/78=0000109999) NMR=GIAO guess=read
geom=checkpoint scrf=(iefpcm,read,solvent=methanol)

NMR CALCULATION WITH METHANOL SOLVATION

0 1

H     0
S   4   1.00
      0.754226E+02           0.406941E-02
      0.113499E+02           0.322324E-01
      0.259926E+01           0.150651E+00
      0.735130E+00           0.500000E+00
S   1   1.00
      0.231669E+00           1.0000000
S   1   1.00
      0.741474E-01           1.0000000
P   2   1.00
      0.960000E+01           0.181540E-01
      0.160000E+01           0.500000E+00
P   1   1.00
      0.450000E+00           1.0000000
D   1   1.00
      0.125000E+01           1.0000000
****
C     0
S   7   1.00
      0.785710E+04           0.642223E-03
      0.117865E+04           0.493018E-02
      0.268325E+03           0.255246E-01
      0.759483E+02           0.969662E-01
      0.245586E+02           0.278279E+00
      0.862118E+01           0.500000E+00
      0.312784E+01           0.369563E+00
S   7   1.00
      0.117865E+04           0.220880E-04
      0.268325E+03          -0.202720E-03
      0.759483E+02          -0.889512E-03
      0.245586E+02          -0.199457E-01
      0.862118E+01          -0.690043E-01
      0.312784E+01          -0.230090E+00
```

```
      0.822020E+00           0.500000E+00
S   1   1.00
      0.330170E+00           1.0000000
S   1   1.00
      0.114628E+00           1.0000000
P   4   1.00
      0.219536E+03           0.971271E-03
      0.337748E+02           0.202494E-01
      0.767659E+01           0.138773E+00
      0.223567E+01           0.500000E+00
P   1   1.00
      0.764466E+00           1.0000000
P   1   1.00
      0.262325E+00           1.0000000
P   1   1.00
      0.846377E-01           1.0000000
D   1   1.00
      0.140000E+01           1.0000000
D   1   1.00
      0.450000E+00           1.0000000
F   1   1.00
      0.950000E+00           1.0000000
****
O     0
S   7   1.00
      0.147824E+05           0.607282E-03
      0.221733E+04           0.467273E-02
      0.504741E+03           0.241672E-01
      0.142873E+03           0.929122E-01
      0.463005E+02           0.270386E+00
      0.163373E+02           0.500000E+00
      0.598281E+01           0.392630E+00
S   7   1.00
      0.221733E+04           0.904080E-05
      0.504741E+03          -0.170992E-03
      0.142873E+03          -0.136132E-02
      0.463005E+02          -0.192022E-01
      0.163373E+02          -0.817923E-01
      0.598281E+01          -0.233115E+00
      0.167180E+01           0.500000E+00
S   1   1.00
      0.646621E+00           1.0000000
S   1   1.00
      0.216687E+00           1.0000000
P   4   1.00
      0.392755E+03           0.983308E-03
      0.604239E+02           0.199046E-01
      0.139351E+02           0.137896E+00
      0.415313E+01           0.500000E+00
P   1   1.00
      0.141579E+01           1.0000000
P   1   1.00
```

```
      0.475491E+00           1.0000000
P   1   1.00
      0.145292E+00           1.0000000
D   1   1.00
      0.220000E+01           1.0000000
D   1   1.00
      0.650000E+00           1.0000000
F   1   1.00
      0.110000E+01           1.0000000
****

radii=bondi
```

C. Total electronic energies [E(RM062X)], free energies (sum of electronic and thermal free energies), and Cartesian coordinates for **10a** (2 conformers) and **10b** (1 conformer).

i. **METHANOL** PCM solvation.

10a—Conformer 1:

```
SCF Done: E(RM062X) = -699.117102949
Sum of electronic and thermal Free Energies = -698.787921
---------------------------------------------------------------------
      1        6          -0.000021337   -0.000018190    0.000014195
      2        6           0.000019355   -0.000013904    0.000000074
      3        6          -0.000002603   -0.000000907    0.000002901
      4        6           0.000002954    0.000000505    0.000002233
      5        1           0.000004717    0.000004725   -0.000000251
      6        6           0.000006964    0.000012953   -0.000020327
      7        6          -0.000006789    0.000007191    0.000005979
      8        6          -0.000001040   -0.000003849   -0.000001085
      9        6           0.000002739   -0.000004061    0.000002085
     10        6           0.000003080    0.000000327   -0.000003808
     11        6           0.000001226   -0.000007037    0.000004767
     12        1           0.000001107   -0.000001407    0.000004122
     13        1           0.000001525    0.000000534   -0.000000461
     14        1           0.000002785    0.000000780   -0.000002647
     15        1          -0.000002667    0.000002647   -0.000000071
     16        1          -0.000001149    0.000005288    0.000002395
     17        1           0.000003600    0.000003175    0.000001394
     18        1          -0.000001312   -0.000000967    0.000000526
     19        1           0.000000691    0.000000704    0.000001112
     20        6          -0.000004866    0.000009762   -0.000002097
     21        1           0.000001263   -0.000003944   -0.000004775
     22        1           0.000002002   -0.000002568   -0.000002004
     23        1           0.000002183   -0.000005102   -0.000002643
     24        6          -0.000010732    0.000000622   -0.000005097
     25        1           0.000000916    0.000003484   -0.000000536
     26        1           0.000002481   -0.000000633    0.000003010
     27        1           0.000000641    0.000000249   -0.000003021
     28        6           0.000001300   -0.000004168   -0.000002889
     29        1           0.000000627   -0.000001635    0.000002007
     30        1          -0.000000274   -0.000000586    0.000002520
     31        1           0.000003047   -0.000001384    0.000002468
     32        1          -0.000001477   -0.000001637    0.000000470
     33        6           0.000011661    0.000020604    0.000016075
     34        1           0.000000332   -0.000004618   -0.000003437
     35        1          -0.000003923   -0.000001003   -0.000000276
     36        6          -0.000004842    0.000002947   -0.000023996
     37        1          -0.000003985    0.000000324    0.000004479
     38        1           0.000000373   -0.000000715    0.000005920
     39        1          -0.000002016    0.000002011    0.000002406
     40        6          -0.000009779    0.000001476    0.000004784
     41        8           0.000001222   -0.000001993   -0.000006501
 ---------------------------------------------------------------------
```

10a—Conformer 2:

SCF Done: E(RM062X) = -699.114503903
Sum of electronic and thermal Free Energies = -698.785631

1	6	0.000014719	0.000077072	0.000039437
2	6	0.000019052	-0.000028973	-0.000040288
3	6	-0.000026403	0.000028492	-0.000007970
4	6	0.000004695	0.000007894	0.000005325
5	1	-0.000001970	-0.000012210	-0.000004848
6	6	-0.000034758	-0.000008505	-0.000021320
7	6	0.000038181	0.000010117	0.000034483
8	6	-0.000013195	-0.000027280	-0.000014968
9	6	-0.000001451	0.000002291	-0.000004931
10	6	-0.000003682	0.000005919	0.000011192
11	6	0.000018533	-0.000014925	0.000019790
12	1	0.000004749	0.000011764	0.000011788
13	1	-0.000003508	0.000003376	-0.000005966
14	1	0.000005459	-0.000009295	0.000010355
15	1	-0.000006973	-0.000003879	-0.000014283
16	1	0.000000976	0.000001312	-0.000001192
17	1	-0.000005367	-0.000011398	-0.000004227
18	1	-0.000011383	-0.000003113	0.000012764
19	1	-0.000002492	-0.000000173	-0.000006990
20	6	0.000018793	-0.000002442	-0.000016096
21	1	-0.000007933	-0.000001571	0.000002457
22	1	-0.000001127	0.000002950	0.000001610
23	1	-0.000005019	0.000002523	0.000006775
24	6	-0.000001631	-0.000006264	-0.000009447
25	1	0.000001407	-0.000003792	0.000003181
26	1	0.000001091	-0.000003026	0.000000805
27	1	0.000002329	-0.000000630	0.000002071
28	6	0.000008524	0.000001874	0.000012590
29	1	-0.000003885	0.000000479	-0.000003527
30	1	0.000005161	0.000000074	-0.000007723
31	1	-0.000005918	0.000000945	0.000001138
32	1	-0.000001410	-0.000004451	0.000003062
33	6	-0.000022627	0.000015726	0.000077010
34	1	-0.000004795	0.000006303	-0.000015887
35	1	-0.000001085	-0.000003995	-0.000012312
36	6	0.000007238	-0.000007887	-0.000037698
37	1	0.000005942	0.000000181	0.000002355
38	1	-0.000000335	-0.000005833	-0.000001548
39	1	-0.000002350	0.000002367	0.000008170
40	6	0.000024423	-0.000041205	-0.000066569
41	8	-0.000011978	0.000019188	0.000031437

10b—Conformer 1:

SCF Done: E(RM062X) = -699.123397669
Sum of electronic and thermal Free Energies = -698.794624

1	6	-0.000006082	0.000002184	0.000007319
2	6	0.000000382	-0.000002155	-0.000006069
3	6	0.000003940	0.000003151	0.000007850
4	6	-0.000000112	0.000002441	0.000002383
5	1	0.000000626	-0.000002182	-0.000000036
6	1	0.000000489	-0.000003023	0.000000104
7	1	0.000001138	0.000000926	0.000004771
8	1	-0.000001060	-0.000000535	0.000001804
9	1	-0.000000437	-0.000002545	-0.000001154
10	1	0.000002458	0.000003657	0.000002645
11	1	0.000000984	0.000003194	-0.000000361
12	6	-0.000002223	-0.000006726	-0.000012247
13	6	-0.000004085	-0.000007507	0.000011320
14	6	0.000004896	-0.000009283	-0.000011175
15	6	-0.000008875	0.000004500	-0.000008525
16	6	0.000008052	0.000007637	0.000008132
17	6	0.000005979	0.000007860	-0.000001206
18	1	0.000003587	0.000000640	0.000000121
19	1	-0.000003100	-0.000004970	-0.000005071
20	6	-0.000003863	-0.000001447	0.000000773
21	1	0.000001865	0.000001384	-0.000001924
22	1	0.000001930	0.000001899	-0.000003697
23	1	-0.000001595	0.000000940	-0.000004629
24	6	0.000000635	0.000004444	-0.000001161
25	1	0.000001555	0.000004698	0.000001084
26	1	0.000001586	0.000003741	0.000004020
27	1	0.000001054	0.000003128	0.000002236
28	6	0.000000263	-0.000002464	-0.000001435
29	1	0.000000516	0.000000265	-0.000000366
30	1	-0.000000588	0.000002690	-0.000001940
31	1	0.000003291	0.000000685	-0.000000325
32	1	-0.000000932	0.000002770	-0.000004893
33	6	-0.000001551	0.000008469	0.000013034
34	1	-0.000002913	-0.000003724	0.000003275
35	1	-0.000000687	-0.000005760	-0.000000268
36	6	0.000008790	-0.000012351	-0.000005817
37	1	-0.000003017	0.000000756	0.000002218
38	1	-0.000001777	0.000000832	0.000002594
39	1	-0.000003321	-0.000000272	0.000000846
40	6	-0.000013129	0.000001560	-0.000002141
41	8	0.000005330	-0.000009506	-0.000002087

ii. **CHLOROFORM** PCM solvation

10a—Conformer 1:

```
SCF Done: E(RM062X) = -699.115128310
Sum of electronic and thermal Free Energies = -698.785781
-----------------------------------------------------------------
      1        6           0.000010699    0.000045331    0.000034646
      2        6           0.000017683   -0.000019180   -0.000016100
      3        6           0.000007664   -0.000002376    0.000008205
      4        6          -0.000008683   -0.000005486    0.000010874
      5        1          -0.000000948   -0.000010244   -0.000008590
      6        6          -0.000008765   -0.000024865   -0.000009243
      7        6           0.000004639   -0.000001201   -0.000001473
      8        6           0.000001244   -0.000003754   -0.000002632
      9        6           0.000000463    0.000005175    0.000001674
     10        6          -0.000002500   -0.000003371    0.000003007
     11        6           0.000007589    0.000005200   -0.000002460
     12        1           0.000000613   -0.000001020    0.000004935
     13        1          -0.000000592    0.000002621    0.000000732
     14        1          -0.000002384    0.000003050    0.000001134
     15        1          -0.000000816    0.000003563    0.000000352
     16        1          -0.000000574    0.000002423    0.000000645
     17        1          -0.000000129    0.000000459    0.000002613
     18        1           0.000000566    0.000002104   -0.000000198
     19        1           0.000000663    0.000002628   -0.000000834
     20        6          -0.000004466   -0.000005182   -0.000005035
     21        1          -0.000000767    0.000001710   -0.000001764
     22        1          -0.000000332    0.000004839   -0.000001265
     23        1           0.000001509    0.000000608   -0.000000898
     24        6           0.000003911    0.000003026   -0.000001550
     25        1          -0.000000393    0.000000428   -0.000000561
     26        1           0.000001069    0.000002522   -0.000002236
     27        1          -0.000000227    0.000000552   -0.000000256
     28        6           0.000002664    0.000007195   -0.000003801
     29        1           0.000000832   -0.000001713    0.000000209
     30        1          -0.000002778   -0.000004327    0.000003687
     31        1           0.000002752   -0.000003627    0.000001054
     32        1          -0.000004059   -0.000000664   -0.000003921
     33        6          -0.000033925    0.000003364    0.000016638
     34        1           0.000005639   -0.000002359   -0.000003442
     35        1           0.000008365   -0.000000251   -0.000002092
     36        6          -0.000005862   -0.000002176   -0.000012802
     37        1           0.000001196   -0.000001311    0.000004654
     38        1           0.000001892   -0.000001199    0.000002221
     39        1          -0.000000213    0.000004861    0.000003438
     40        6          -0.000002924    0.000001791   -0.000014033
     41        8          -0.000000314   -0.000009145   -0.000005529
 -----------------------------------------------------------------
```

10a—Conformer 2:

SCF Done: E(RM062X) = -699.112486839
Sum of electronic and thermal Free Energies = -698.783479

1	6	0.000009311	0.000058716	0.000051544
2	6	0.000011735	-0.000030883	-0.000020583
3	6	-0.000003221	0.000004068	0.000001070
4	6	-0.000000671	-0.000002017	0.000009395
5	1	-0.000006450	-0.000012816	-0.000007440
6	6	-0.000007392	-0.000014284	-0.000007506
7	6	0.000020076	0.000002995	0.000005776
8	6	-0.000003368	-0.000009200	-0.000007589
9	6	-0.000002342	-0.000002422	-0.000003297
10	6	-0.000006461	-0.000013079	0.000007156
11	6	0.000008931	0.000019385	-0.000002094
12	1	0.000000161	0.000007045	0.000002188
13	1	0.000002776	0.000004323	0.000001723
14	1	0.000004093	-0.000004050	0.000003409
15	1	-0.000000124	0.000000906	-0.000002974
16	1	0.000001523	-0.000001360	-0.000001472
17	1	-0.000003889	-0.000002425	-0.000002975
18	1	-0.000002669	-0.000000629	0.000004656
19	1	-0.000001339	-0.000000635	-0.000000935
20	6	0.000002129	-0.000008778	0.000000750
21	1	-0.000002896	-0.000001735	0.000002522
22	1	0.000000097	0.000003028	0.000000196
23	1	-0.000000523	0.000002560	0.000002595
24	6	0.000000431	-0.000002892	-0.000003212
25	1	0.000000130	-0.000000341	-0.000000502
26	1	0.000000166	-0.000001841	0.000001019
27	1	0.000000644	-0.000001122	-0.000000873
28	6	0.000000870	0.000007567	-0.000007298
29	1	0.000000933	0.000003070	-0.000001011
30	1	-0.000002507	-0.000001290	0.000001595
31	1	0.000000083	-0.000000179	0.000000222
32	1	-0.000002920	0.000006336	-0.000002390
33	6	-0.000039940	0.000013184	0.000028620
34	1	0.000005634	-0.000000651	-0.000002234
35	1	0.000011949	0.000001036	-0.000006363
36	6	0.000001063	-0.000003755	-0.000017920
37	1	0.000003159	0.000002778	-0.000002619
38	1	0.000002285	-0.000001191	0.000000717
39	1	0.000001515	0.000000913	0.000004093
40	6	-0.000004234	-0.000015333	-0.000019852
41	8	0.000001251	-0.000005002	-0.000008106

10b—Conformer 1:

SCF Done: E(RM062X) = -699.121415688
Sum of electronic and thermal Free Energies = -698.792447

1	6	-0.000001824	-0.000009873	0.000013411
2	6	0.000000618	0.000001871	-0.000016391
3	6	0.000008460	0.000009547	0.000001087
4	6	-0.000002751	-0.000000423	0.000004315
5	1	-0.000002873	-0.000005037	-0.000001577
6	1	-0.000001455	-0.000008011	-0.000004395
7	1	-0.000003063	-0.000000094	0.000002947
8	1	-0.000004243	-0.000002561	0.000001864
9	1	0.000001979	0.000005820	-0.000003531
10	1	-0.000000612	0.000003428	0.000002072
11	1	-0.000001093	0.000002576	-0.000002262
12	6	-0.000011801	0.000012717	-0.000030053
13	6	-0.000000953	-0.000039917	0.000064899
14	6	-0.000018248	-0.000027621	-0.000025103
15	6	-0.000017962	-0.000009215	-0.000007317
16	6	0.000012348	0.000007009	0.000019517
17	6	0.000000929	0.000018068	0.000000655
18	1	0.000001811	-0.000001227	0.000000848
19	1	0.000003177	0.000001526	-0.000012700
20	6	0.000020559	0.000010676	-0.000001011
21	1	-0.000000938	-0.000002983	-0.000001480
22	1	0.000003053	0.000001095	-0.000004486
23	1	-0.000003008	-0.000006744	-0.000000764
24	6	0.000001726	0.000004599	0.000001837
25	1	0.000001049	0.000003571	-0.000001374
26	1	-0.000000135	0.000003679	0.000003434
27	1	-0.000000667	0.000003016	-0.000000738
28	6	0.000003242	0.000004819	0.000010374
29	1	0.000006587	0.000001318	-0.000004363
30	1	0.000000417	0.000002564	-0.000003646
31	1	0.000003918	0.000005063	-0.000003105
32	1	-0.000000875	0.000004703	-0.000004917
33	6	-0.000019759	0.000040864	-0.000013430
34	1	-0.000004006	-0.000009739	0.000010056
35	1	-0.000010082	-0.000017093	0.000001646
36	6	0.000033187	-0.000000768	0.000003926
37	1	0.000000994	-0.000002003	-0.000006042
38	1	-0.000001051	-0.000004410	0.000001968
39	1	0.000004251	0.000003110	-0.000000606
40	6	0.000010751	-0.000008575	-0.000007742
41	8	-0.000011655	0.000004653	0.000012175

D. Table of computed isotropic chemical shifts.

Table S5. Isotropic chemical shifts (σ_{DFT}) for the conformers of structures **10a** and **10b** that were computed at the two different levels of theory employed in this study.

LEVEL OF THEORY	WP04 / pcS-2 // M06-2X / 6-31+G(d,p)						B3LYP / 6-31G(d,p) // MMFFs		
	σ_{DFT}[a] [IEFPCM = methanol]			σ_{DFT}[b] [IEFPCM = chloroform]			σ_{DFT}[c] [gas phase]		
ATOM #	*10a-1*	*10a-2*	*10b-1*	*10a-1*	*10a-2*	*10b-1*	*10a-1*	*10a-2*	*10b-1*
13	29.09	29.17	29.07	29.18	29.26	29.16	29.36	29.41	29.34
15	26.27	26.35	26.35	26.30	26.39	26.38	26.07	26.18	26.15
17_{eq}	30.32	30.74	30.37	30.36	30.77	30.40	30.42	30.75	30.34
17_{ax}	30.36	30.22	30.85	30.37	30.22	30.87	30.11	30.01	30.75
18	29.97	30.15	30.12	29.99	30.19	30.15	29.86	29.98	29.99
19_{eq}	30.39	30.46	30.19	30.37	30.50	30.18	30.21	30.35	30.01
19_{ax}	30.42	30.38	30.96	30.46	30.37	31.00	30.29	30.20	30.91
20_{eq}	30.33	30.22	30.22	30.23	30.17	30.12	29.87	29.65	29.72
20_{ax}	30.32	30.33	30.45	30.35	30.30	30.47	30.27	30.15	30.39
21	30.25	29.87	30.28	30.34	29.97	30.38	30.25	29.86	30.30
22	29.43	29.43	29.43	29.48	29.48	29.48	29.59	29.58	29.61
25	30.04	30.02	30.02	30.06	30.04	30.04	30.14	30.14	30.12
26	30.78	30.85	30.87	30.78	30.86	30.88	30.65	30.79	30.76
27	30.70	30.97	30.96	30.71	30.97	30.96	30.66	30.94	30.96

[a] Values for σ_{DFT} were referenced to the isotropic chemical shift for the protons of tetramethylsilane to obtain the Boltzmann-weighted values of δ_{DFT} (methanol) listed in Table 1 (manuscript). [b] Values for σ_{DFT} were referenced to the isotropic chemical shift for the protons of tetramethylsilane (σ_{REF} = 31.78) to obtain the Boltzmann-weighted values of δ_{DFT} (chloroform) provided in Table S6. [c] Values for σ_{DFT} were referenced to the isotropic chemical shift for the protons of tetramethylsilane (σ_{REF} = 31.83) and then empirically scaled to obtain the values of δ_{DFT} that were used in the DP4 analysis.

E. Description of data input into the Goodman DP4 applet.[14]

---------- **COMPUTED DATA** [B3LYP / 6-31G(d,p) // MMFF]

Empirically scaled proton chemical shifts:

H-15, H-17eq, H-17ax, H-18, H-19eq, H-19ax, H-20ax, H-20eq, H-21, H-22, H-13, Me-25, Me-26, and Me-27.

5.99, 0.98, 1.41, 1.66, 1.26, 1.21, 1.24, 1.71, 1.31, 2.00, 2.25, 1.36, 0.76, and 0.72. (**10a**; isomer #1)

5.68, 1.30, 0.88, 1.67, 1.64, 0.70, 1.25, 1.95, 1.34, 2.07, 2.34, 1.53, 0.86, and 0.66. (**10b**; isomer #2)

---------- **EXPERIMENTAL DATA**

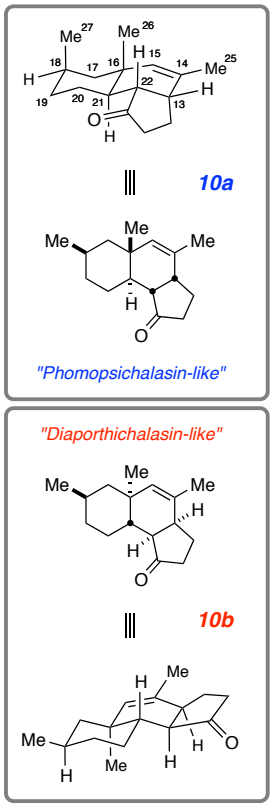
7 ($CDCl_3$): 5.39 (H-15), 1.45 (H-17eq or H-17ax), 0.72 (H-17eq or H-17ax), 1.63 (H-18), 1.72 (H-19eq or H-19ax), 0.60 (H-19eq or H-19ax), 1.21 (H-20ax or H-20eq), 1.64 (H-20ax or H-20eq), 1.40 (H-21), 2.44 (H-22), 2.98 (H-13), 1.88 (Me-25), 0.82 (Me-26), and 0.82 (Me-27).

'1' (CD_3OD): 5.36 (H-15), 1.45 (H-17eq or H-17ax), 0.67 (H-17eq or H-17ax), 1.62 (H-18), 1.64 (H-19eq or H-19ax), 0.56 (H-19eq or H-19ax), 1.10 (H-20ax or H-20eq), 1.50 (H-20ax or H-20eq), 1.42 (H-21), 2.24 (H-22), 2.85 (H-13), 1.88 (Me-25), 0.80 (Me-26 or Me-27), and 0.78 (Me-26 or Me-27).

F. Table S6 of chloroform data (analogous to Table 1 in the manuscript).

Table S6. Comparison of the computed (with chloroform solvation) proton NMR chemical shifts (δ_{DFT}) for structures **10a** and **10b** with the experimentally observed shifts (δ_{EXP}) for the analogous subset of nuclei in the spectrum of diaporthichalasin (**7**) in $CDCl_3$.

ATOM #	δ_{DFT}[a] (chloroform)		δ_{EXP}	$\lvert\Delta\delta\rvert$ for δ_{DFT}[a] vs. δ_{EXP}	
	10a	***10b***	**7**	***10a*** vs. **7**	***10b*** vs. **7**
13	2.59	2.62	2.98	0.39	0.36
15	5.47	5.40	5.39	0.08	0.01
17_{eq}	1.39	1.38	1.45	0.06	0.07
17_{ax}	1.42	0.91	0.72	0.70	0.19
18	1.77	1.63	1.63	0.14	0.00
19_{eq}	1.39	1.60	1.72	0.33	0.12
19_{ax}	1.33	0.78	0.60	0.73	0.18
20_{eq}	1.56	1.66	1.64	0.08	0.02
20_{ax}	1.43	1.31	1.21	0.22	0.10
21	1.46	1.40	1.40	0.06	0.00
22	2.30	2.30	2.44	0.14	0.14
25	1.72	1.74	1.88	0.16	0.14
26	0.99	0.90	0.82	0.17	0.08
27	1.05	0.82	0.82	0.23	0.00
			MAE_{full}[b] =	***0.25***	***0.10***
			MAE_{lite}[c] =	***0.34***	***0.09***
			DP4 probability[d]	***<0.5%***	***>99.5%***



[a] Values for δ_{DFT} were determined by referencing the computed isotropic chemical shifts (σ_{DFT}) for all nuclei to the isotropic chemical shift for the protons of tetramethylsilane (σ_{REF}), both of which were computed at the IEFPCM-WP04/pcS-2//M06-2X/6-31+G(d,p) level of theory. [b] Mean absolute error ($|\Delta\delta_{AVE}|$). Calculation includes all proton nuclei that are listed in the table. [c] Including only the subset of proton nuclei 17-19, 26 and 27. [d] Scaled δ_{DFT} values derived from chemical shifts computed at the B3LYP/6-31G(d,p)//MMFF level of theory (i.e., the level used by Smith and Goodman[15]) were employed.

VII. References and Notes for the Supporting Information

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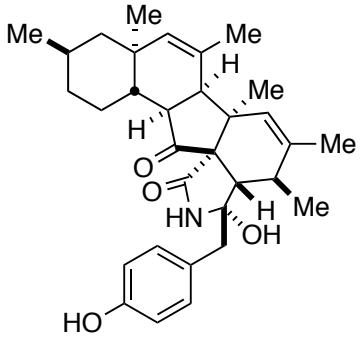
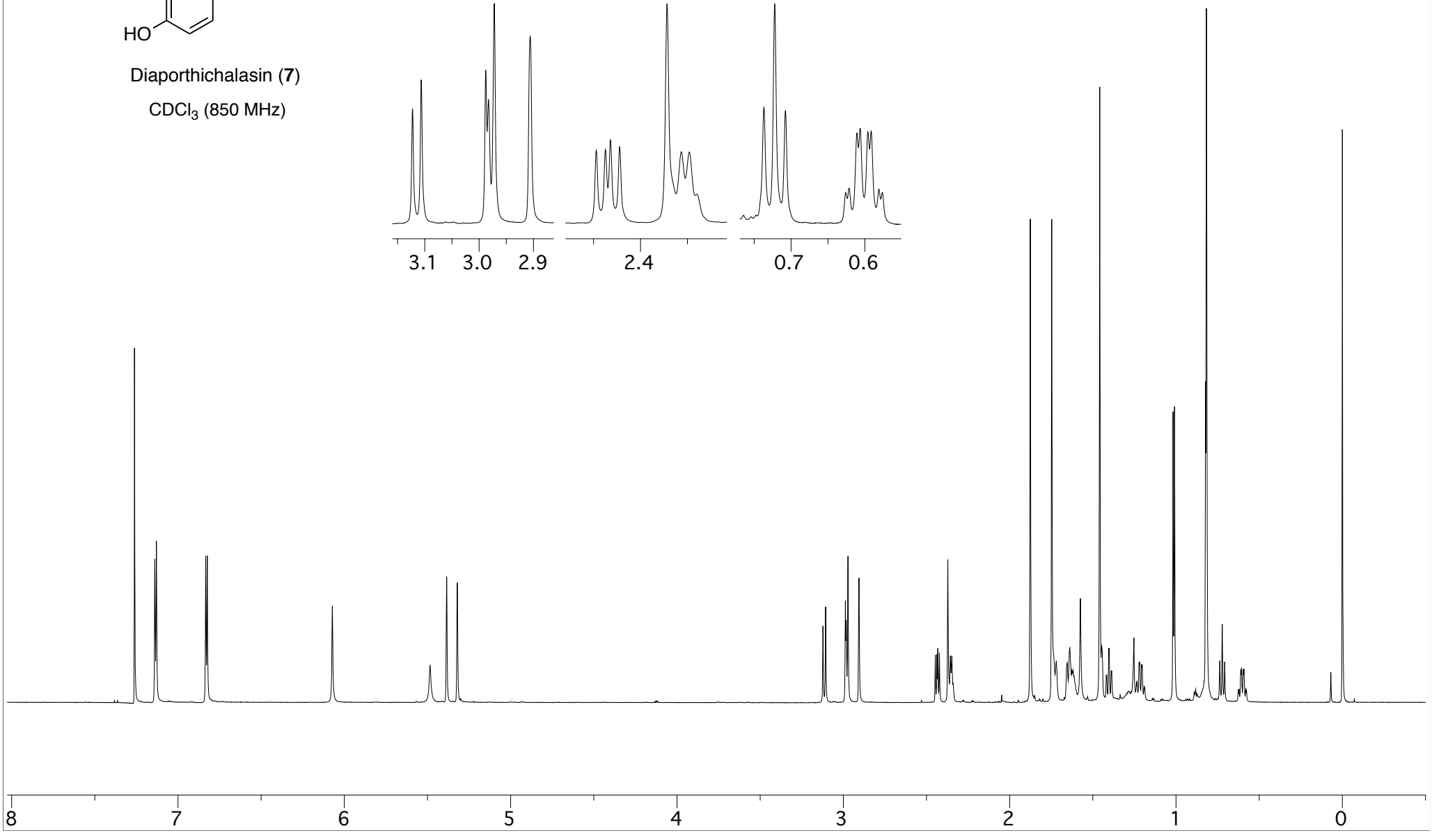
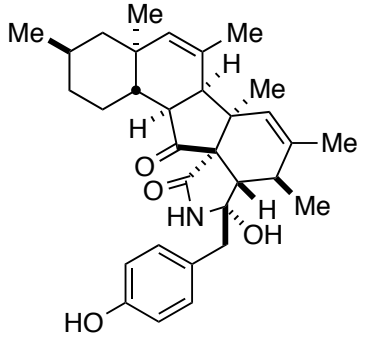
VIII. Copies of ^{1}H and ^{13}C NMR spectra in $CDCl_3$, d_4-MeOH, and d_6-DMSO



Diaporthichalasin (**7**)

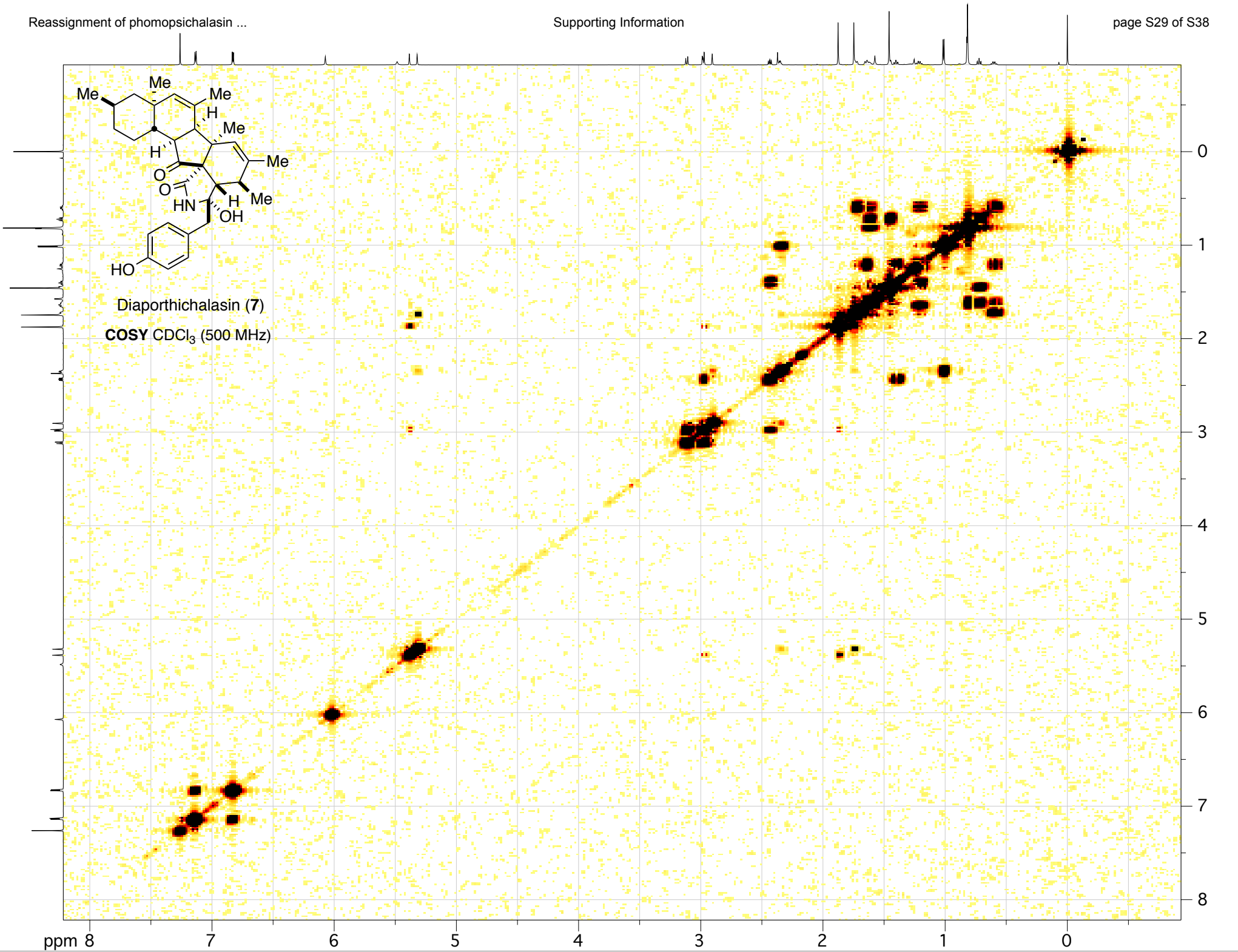
$CDCl_3$ (850 MHz)





Diaporthichalasin (**7**)

$CDCl_3$ (500 MHz)


Me
Me
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Me
H
Me
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O
HN
H
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OH
HO
Diaporthichalasin (7)
COSY CDCl3 (500 MHz)
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6
5
4
3
2
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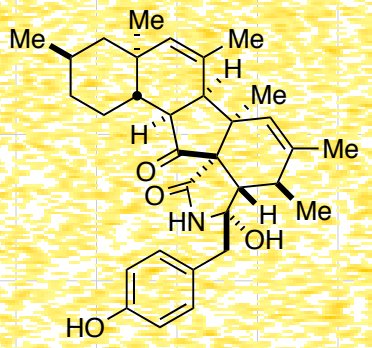
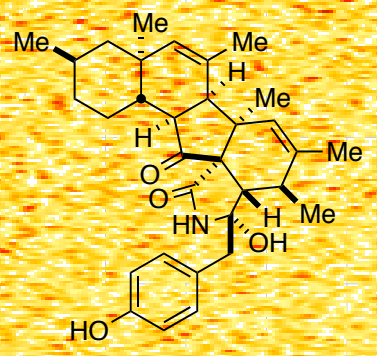
0
0
1
2
3
4
5
6
7
8



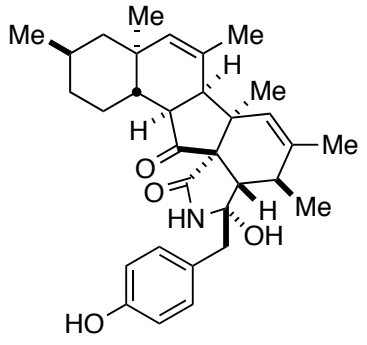
Diaporthichalasin (**7**)

HMQC $CDCl_3$ (500 MHz)



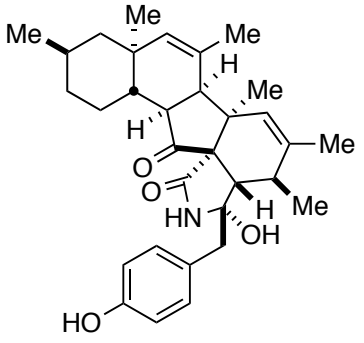
Diaporthichalasin (**7**)

HMBC $CDCl_3$ (500 MHz)



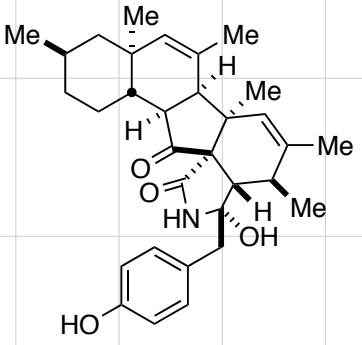
Diaporthichalasin (**7**)

d_4-methanol (850 MHz)



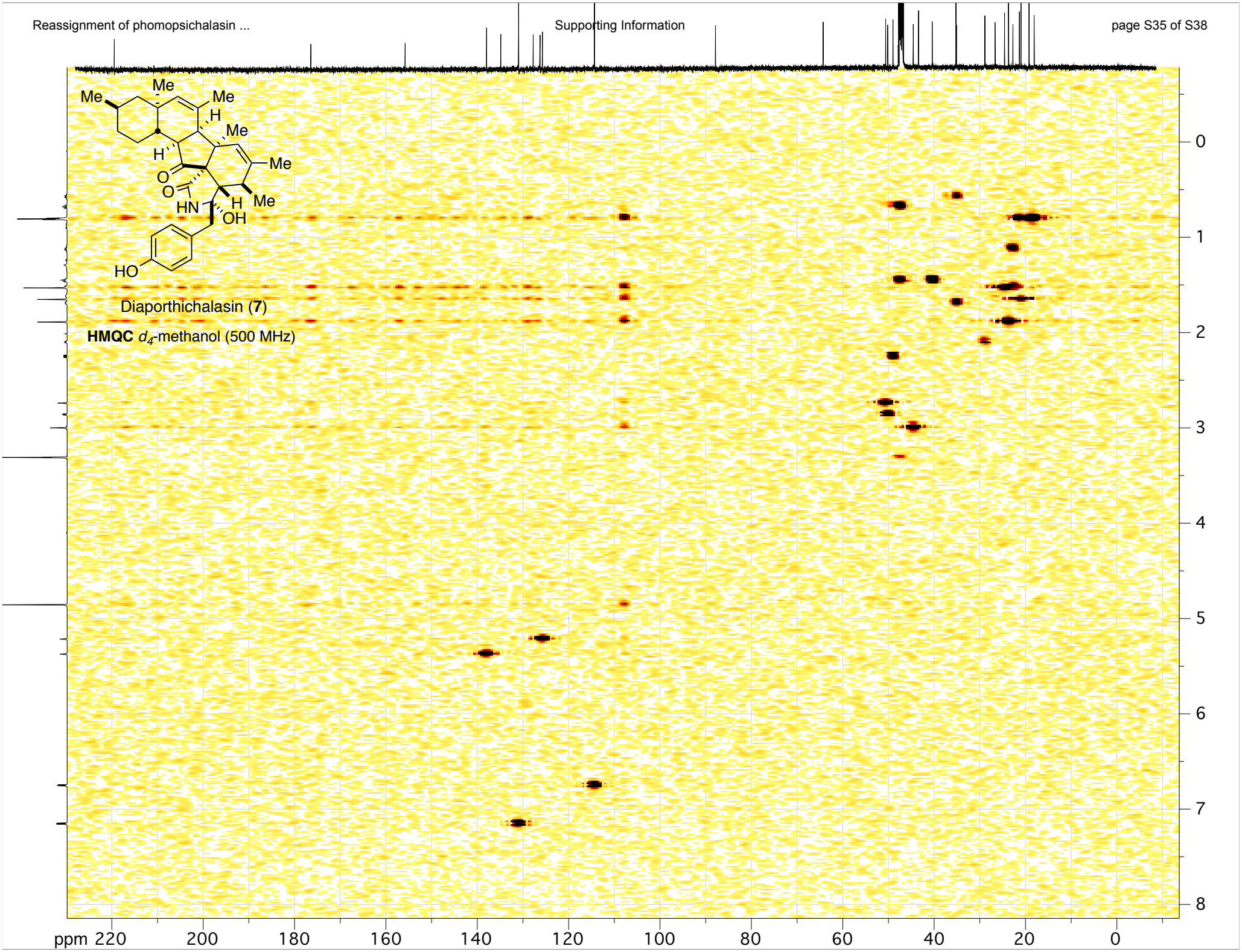
Diaporthichalasin (**7**)

d$_4$-methanol (500 MHz)



Diaporthichalasin (**7**)

COSY d_4-methanol (500 MHz)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H
Me
H
Me
O
O
HN
H
Me
OH
HO
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ppm 220
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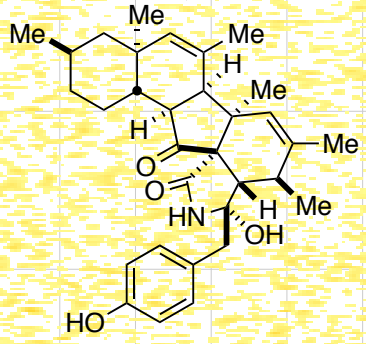
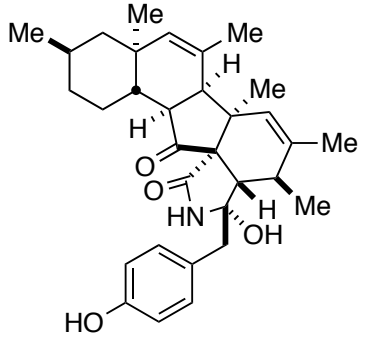
120
100
80
60
40
20
0
0
1
2
3
4
5
6
7
8



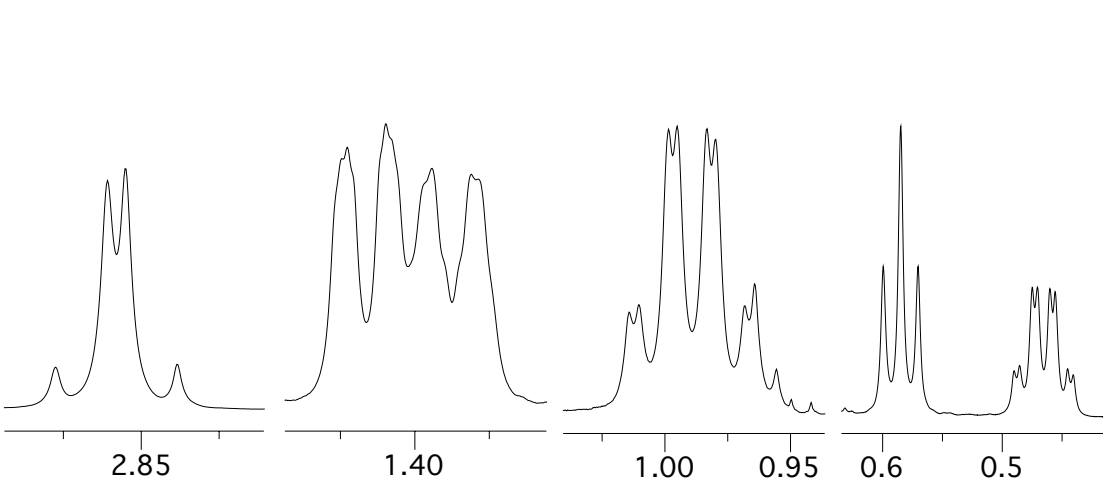
Diaporthichalasin (**7**)

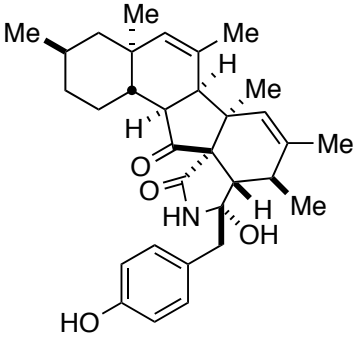
HMBC d_4-methanol (500 MHz)



Diaporthichalasin (**7**)

d_6-DMSO (850 MHz)





Diaporthichalasin (**7**)

d$_6$-DMSO (500 MHz)