

Supporting Information

Synthetic and Biological Studies of Juglorubin and Related Naphthoquinones

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Results of DFT Calculations for Compounds **24a** and **24b**.

Table S1. Total Energy, Number of Imaginary Frequencies, and Atom Coordinates for 24a

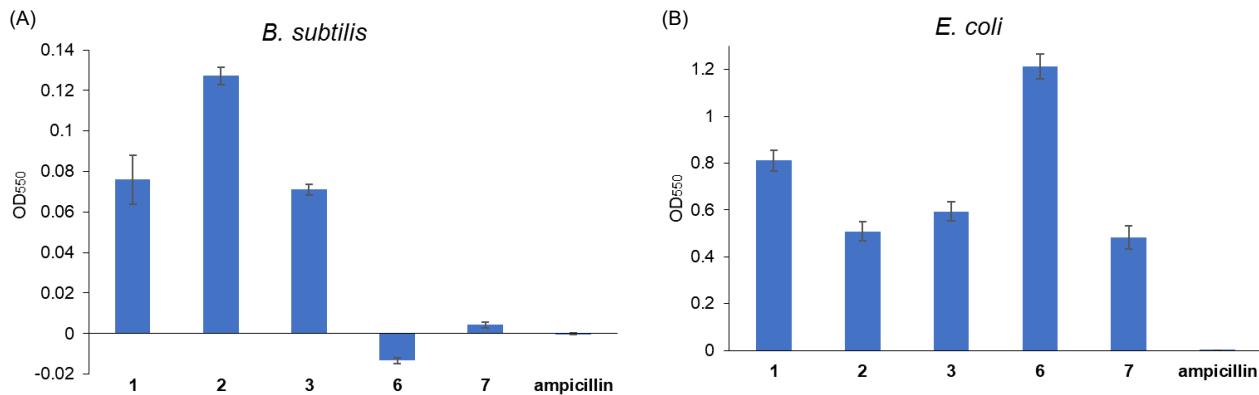
Optimized by DFT/B3LYP/6-31G+(d,p) Level with SMD (CH_2Cl_2). page S19

Table S2. Total Energy, Number of Imaginary Frequencies, and Atom Coordinates for 24b

Optimized by DFT/B3LYP/6-31G+(d,p) Level with SMD (CH_2Cl_2). page S24

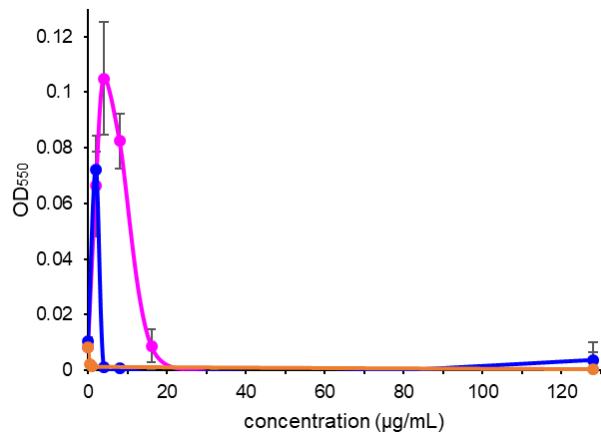
Reference page S29

Figure S1. Antibacterial activity of synthetic compounds at 128 $\mu\text{g}/\text{mL}$.^{a, S1}



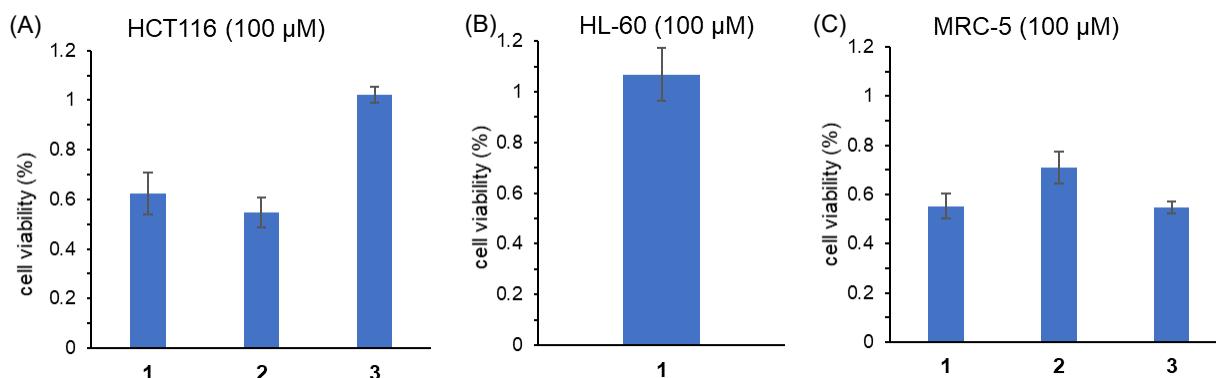
^aBacterial growth was observed in triplicate wells, visually and by measuring the optical density at 550 nm (OD₅₅₀). Bacteria (5×10^5 CFU/mL) were incubated with 128 $\mu\text{g}/\text{mL}$ compounds for 18 h. Ampicillin was used as a positive control.

Figure S2. Dose-response curves of **6** and **7** for the antibacterial activity against *B. subtilis*.^a



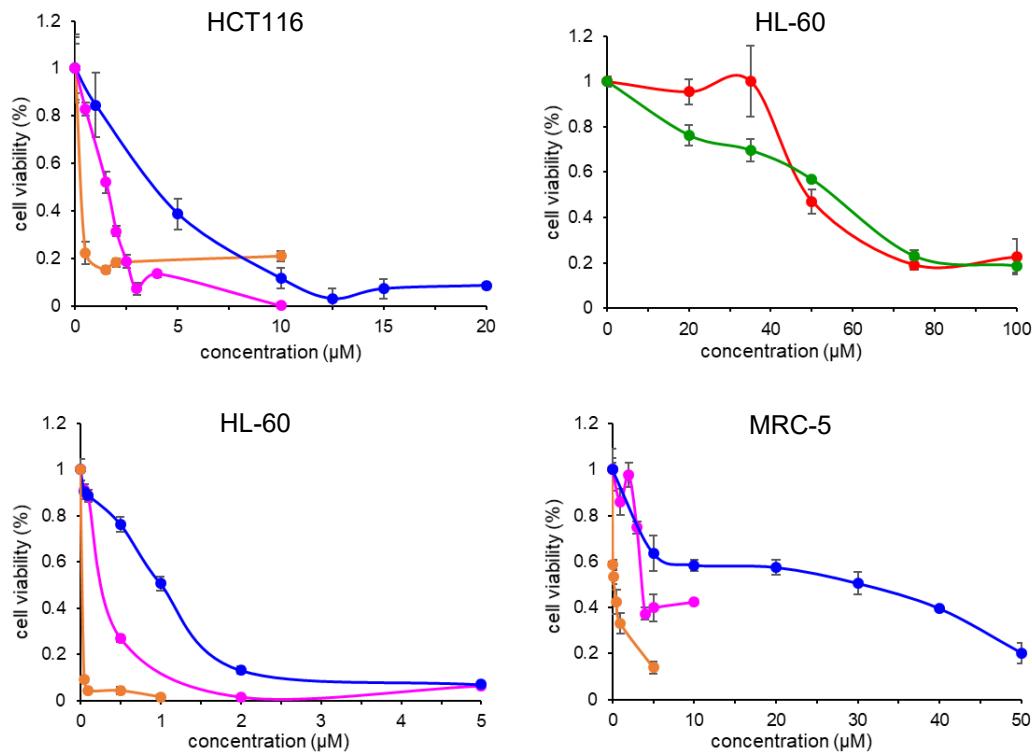
^aBacterial growth was determined by microdilution method. Bacteria (5×10^5 CFU/mL) were incubated with various concentrations of compounds for 18 h. *B. subtilis* were treated with compounds **6** (pink: —) and **7** (blue: —). Ampicillin (orange: ▲) was used as a positive control.

Figure S3. Cytotoxic activity of compounds **1–3** at 100 μM .^a



^aCell viability was determined by WST-8 assay. HCT116 and MRC-5 cells were cultured in a 96-well plate with each well containing 4000 cells in a total volume of 200 μL and HL-60 cells were cultured in a 96-well plate with each well containing 4000 cells in a total volume of 100 μL . The plates were incubated with 100 μM of compounds for 48 h. At the end of incubation, 10 μL of the WST-8 solution was added, and the resultant mixture was incubated for 2 h at 37 °C. Indicated cells were treated with 100 μM of compounds **1–3**.

Figure S4. Dose-response curves of **2**, **3**, **6**, and **7** for the cytotoxic activity.^a



^aCell viability was determined by WST-8 assay. The adherent HCT116 and MRC-5 cells were cultured in a 96-well plate with each well containing 4000 cells in a total volume of 200 μL and the suspension HL-60 cells were cultured in a 96-well plate with each well containing 4000 cells in a total volume of 100 μL . The plates were incubated with various concentrations of compounds for 48 h. At the end of incubation, 10 μL of the WST-8 solution was added, and the resulting mixture was incubated for 2 h at 37 °C. Indicated cells were treated with compounds **2** (red: —), **3** (green: —), **6** (pink: —), **7** (blue: —), and SN-38 (orange: —).

Figure S5. ^1H NMR spectrum (400 MHz, CDCl_3 , TMS) of compound **12a**.

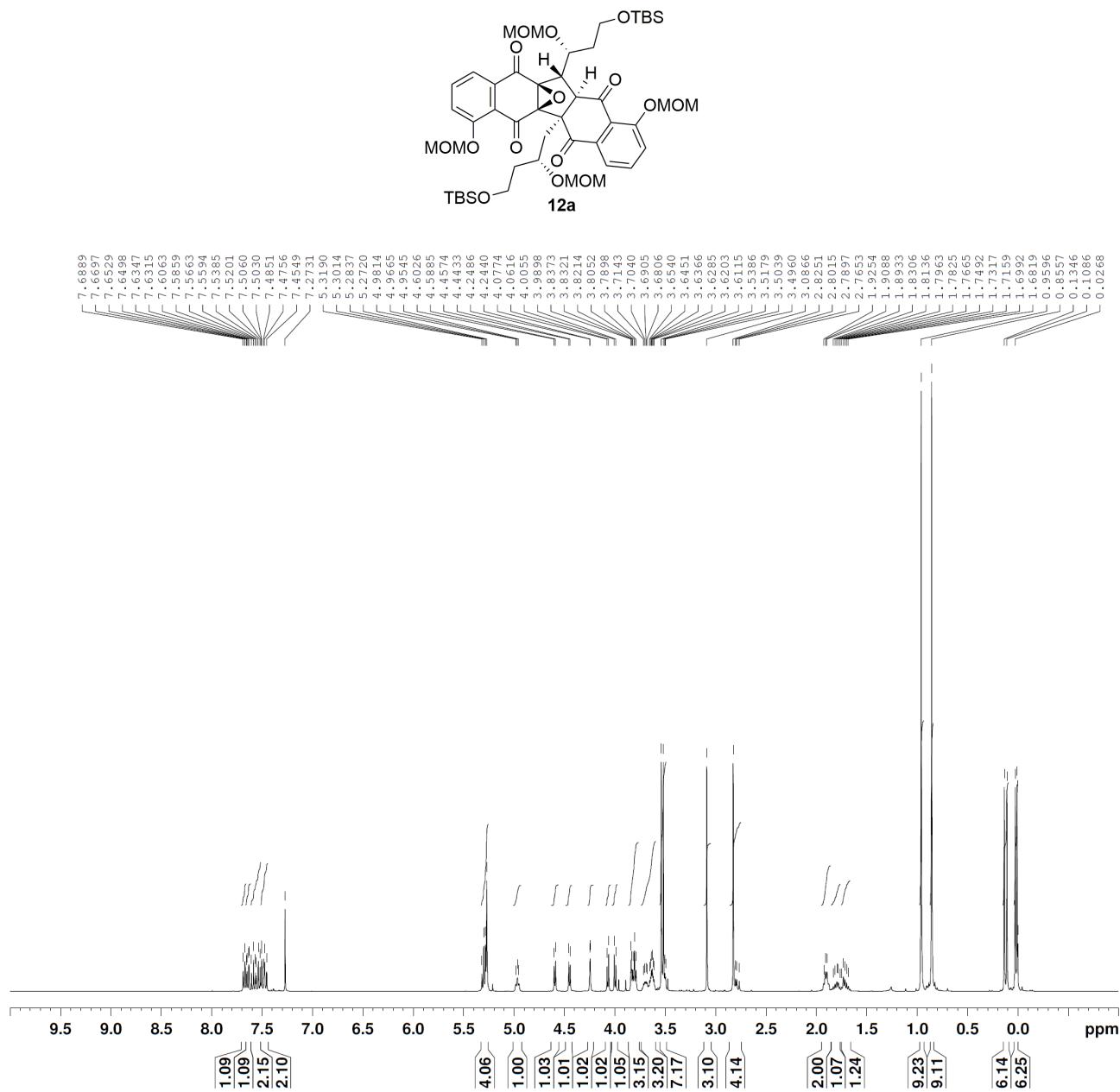


Figure S6. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **12b**.

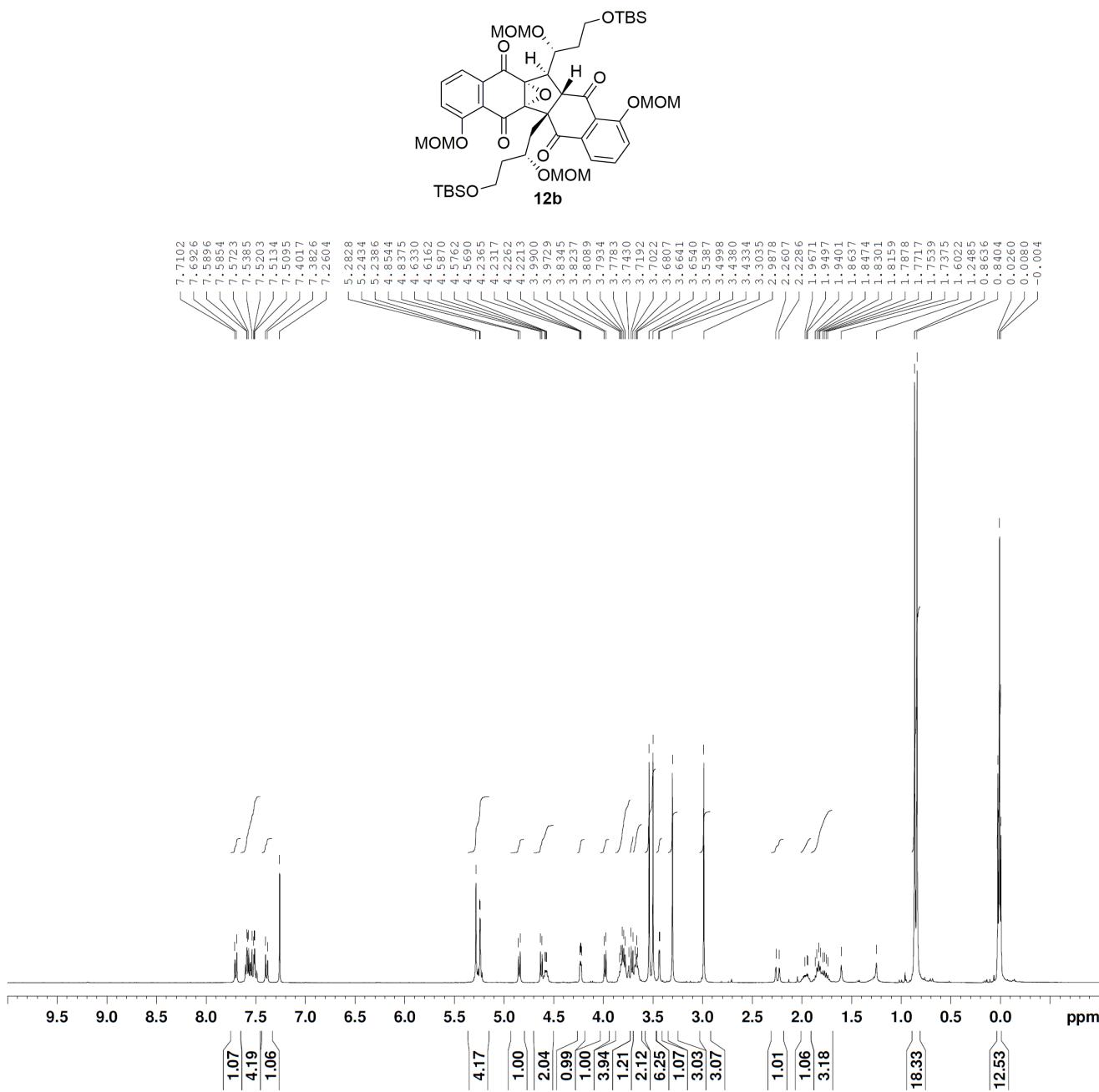


Figure S7. $^{13}\text{C}\{\text{H}\}$ NMR spectrum (100 MHz, CDCl_3) of compound **12b**.

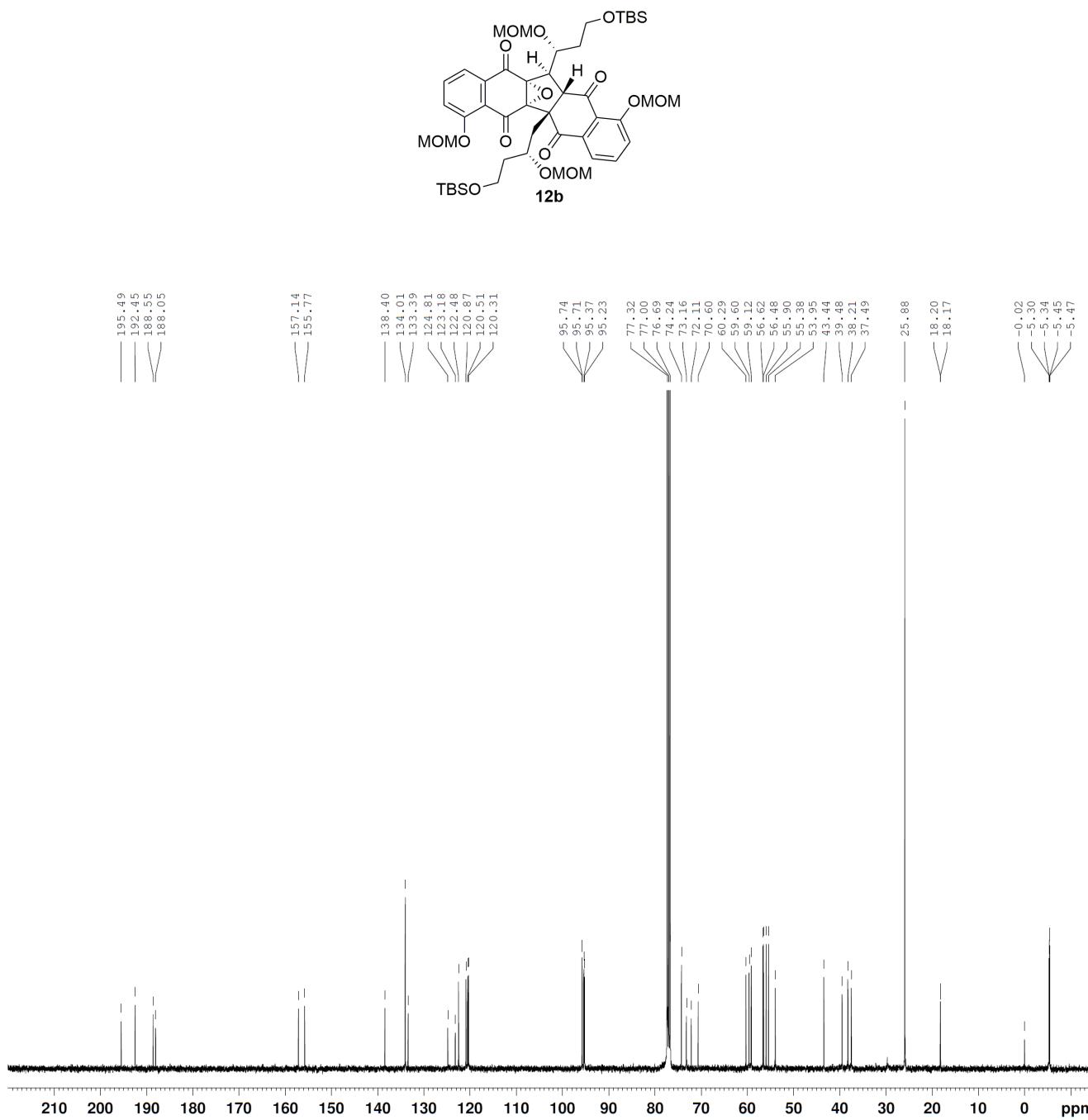


Figure S8. ^1H NMR spectrum (400 MHz, acetone- d_6) of compound **13b**.

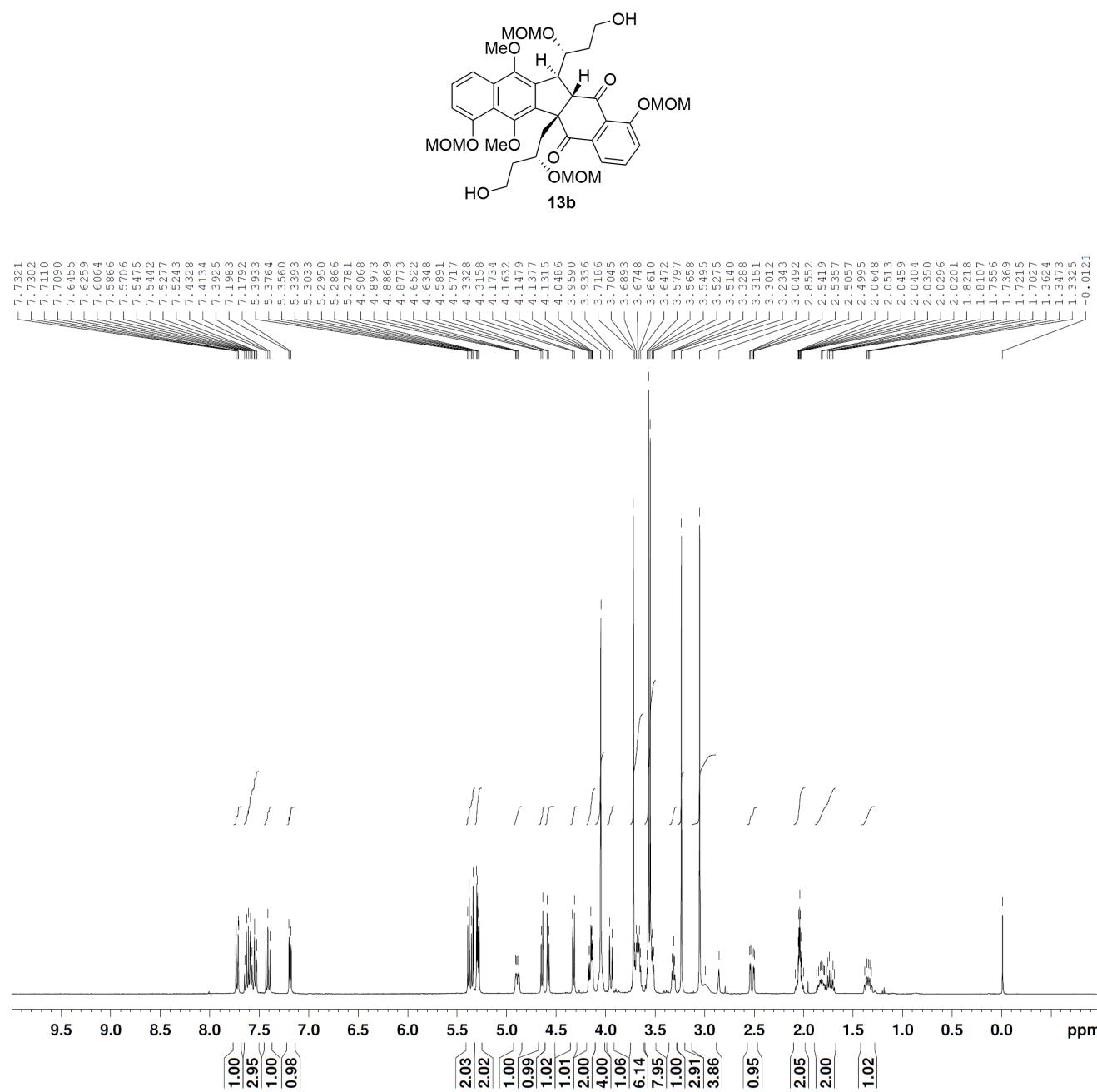


Figure S9. $^{13}\text{C}\{\text{H}\}$ NMR spectrum (100 MHz, acetone- d_6) of compound **13b**.

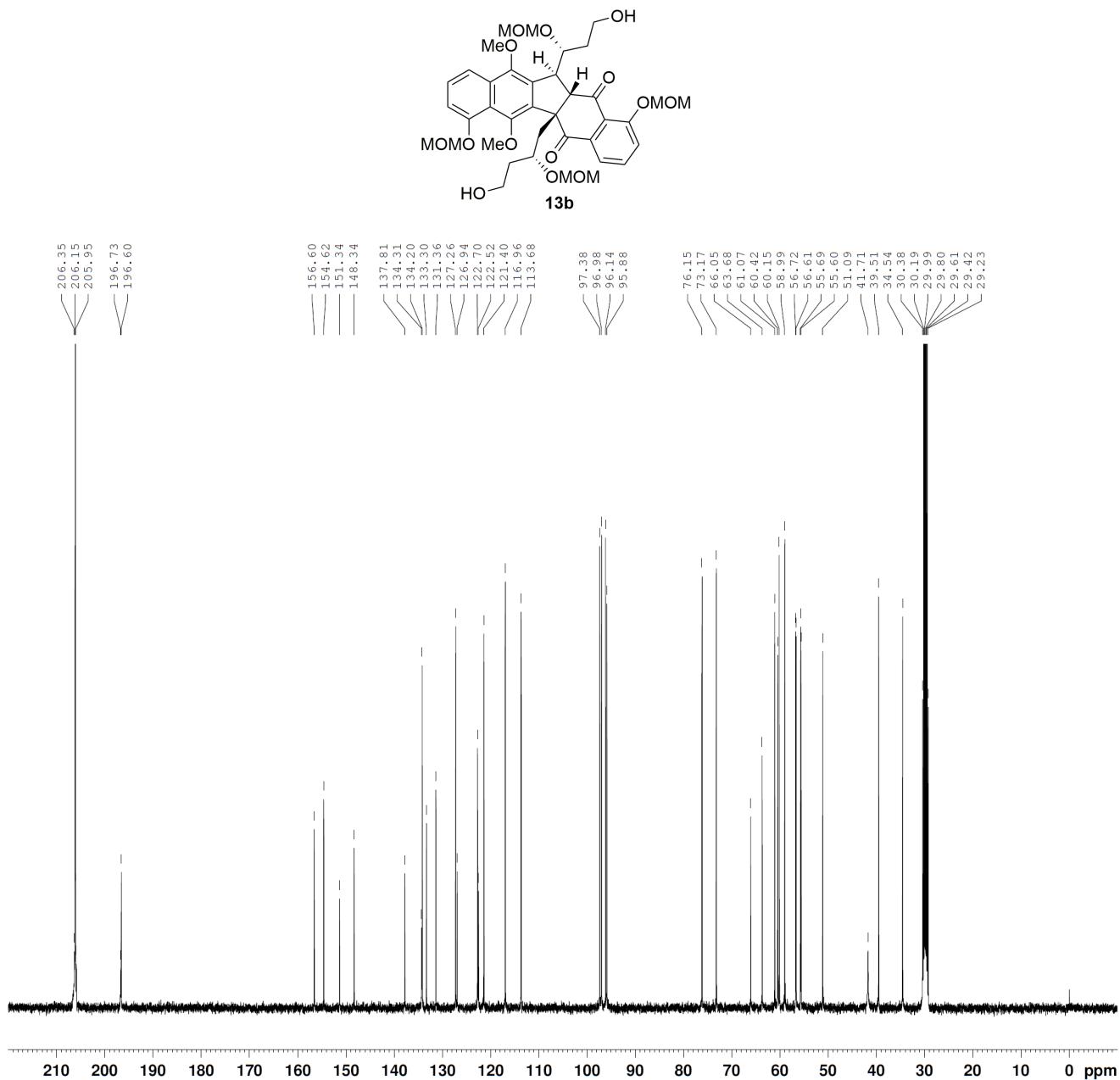


Figure S10. NOESY spectrum (5.0–1.0 ppm) of compound **13b**.

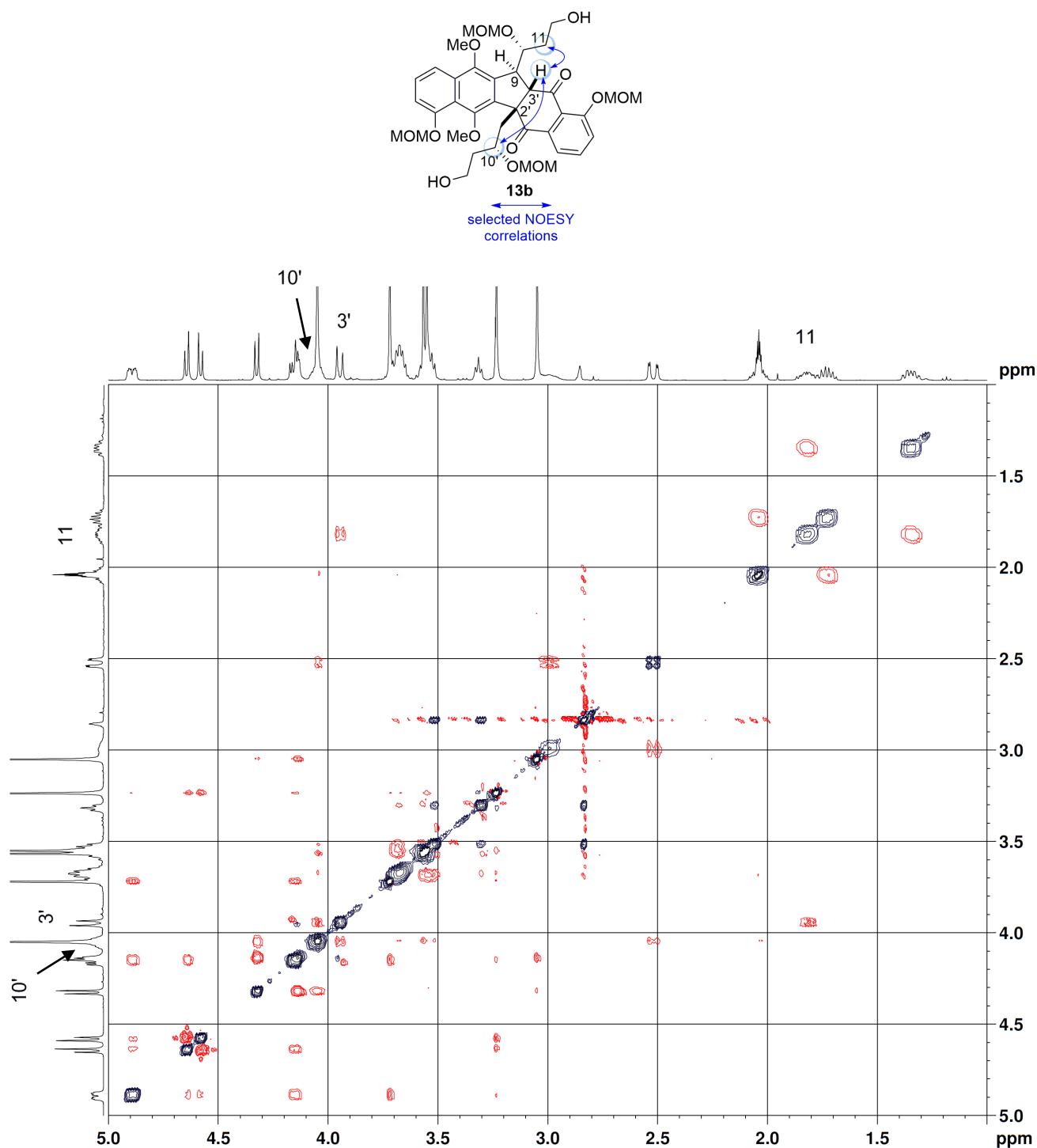


Figure S11. ^1H NMR spectrum (400 MHz, CDCl_3 , TMS) of compound **21b**.

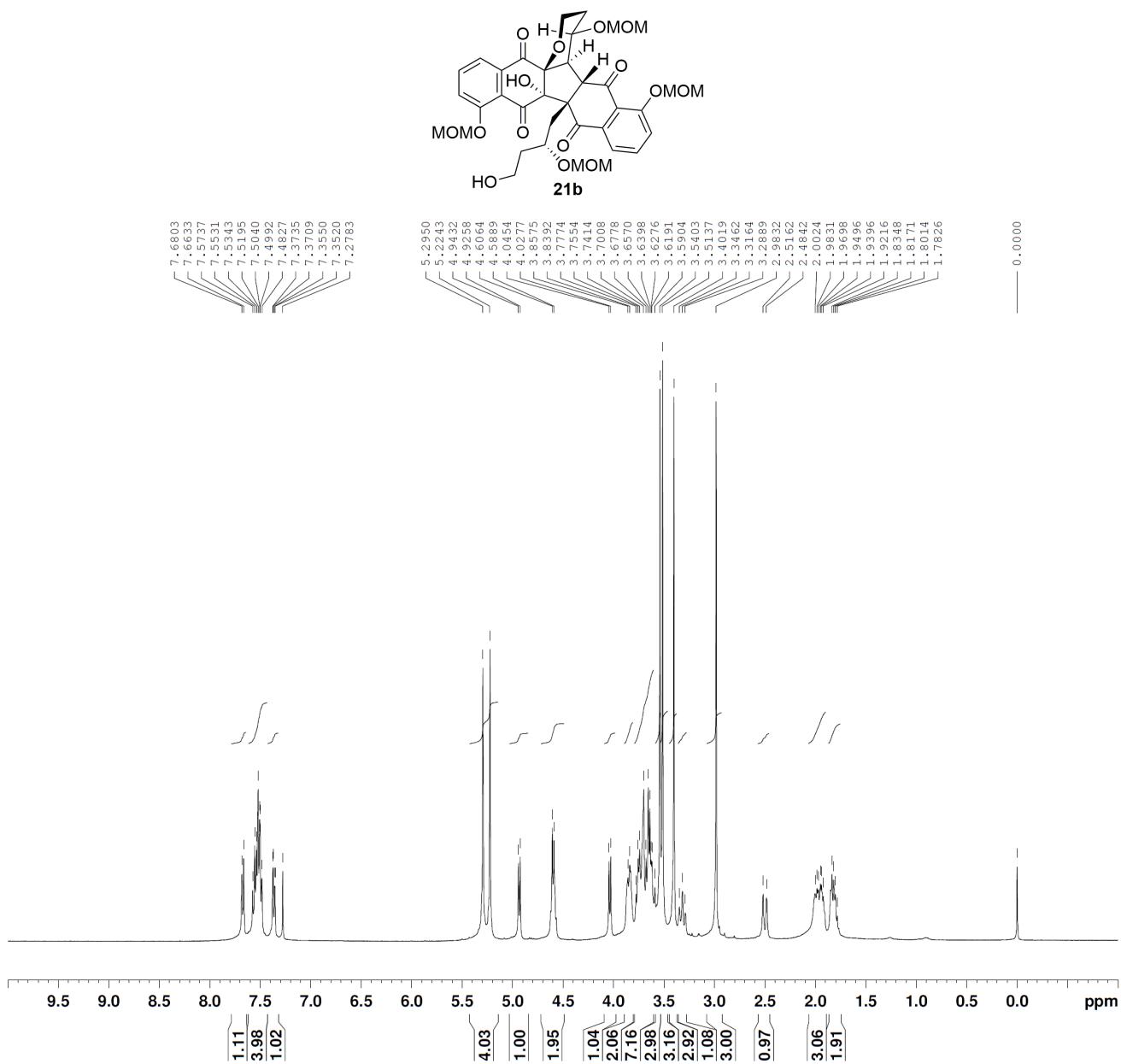


Figure S12. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (100 MHz, CDCl_3) of compound **21b**.

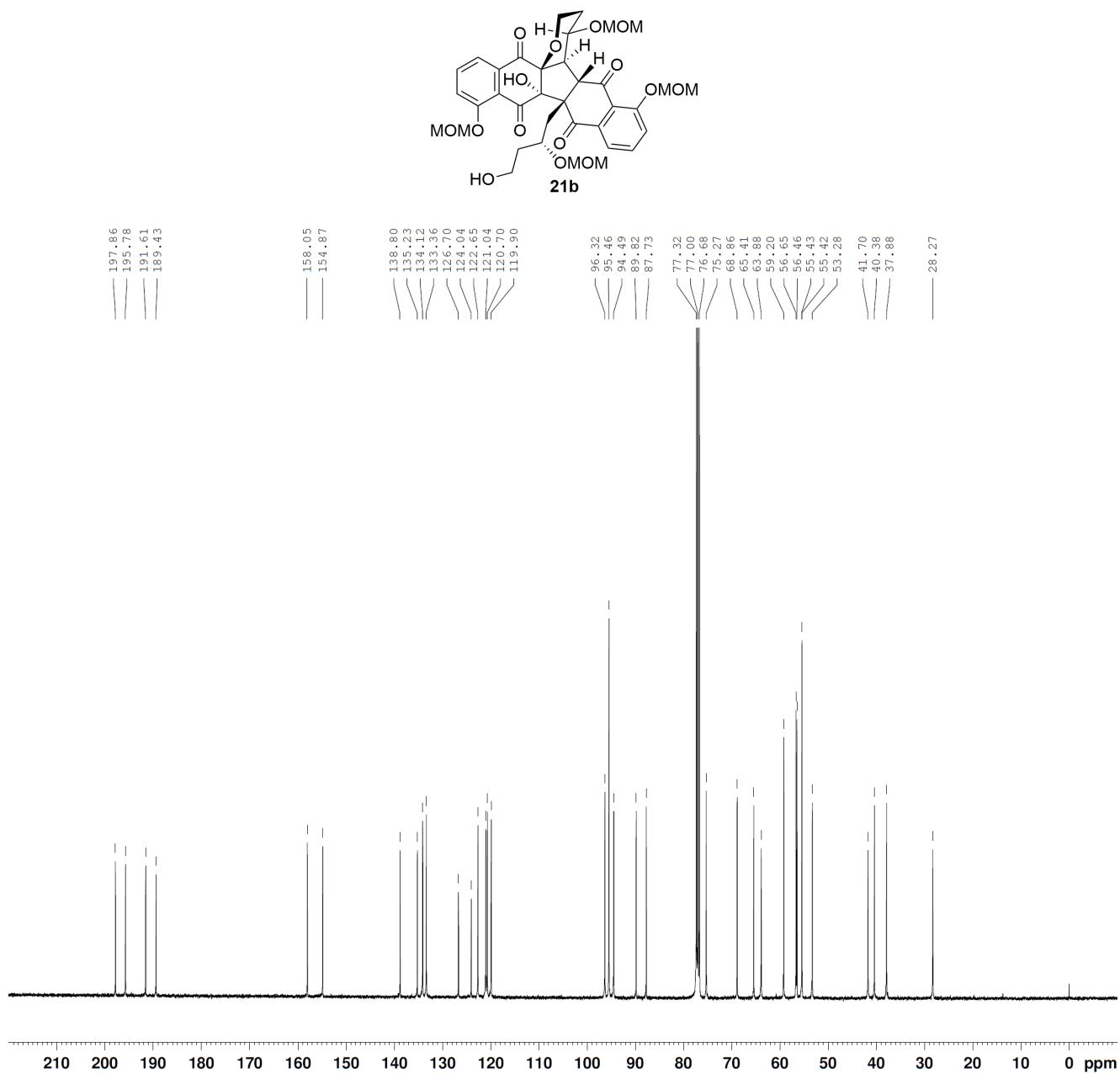


Figure S13. ^1H NMR spectrum (400 MHz, CDCl_3 , TMS) of compound **22b**.

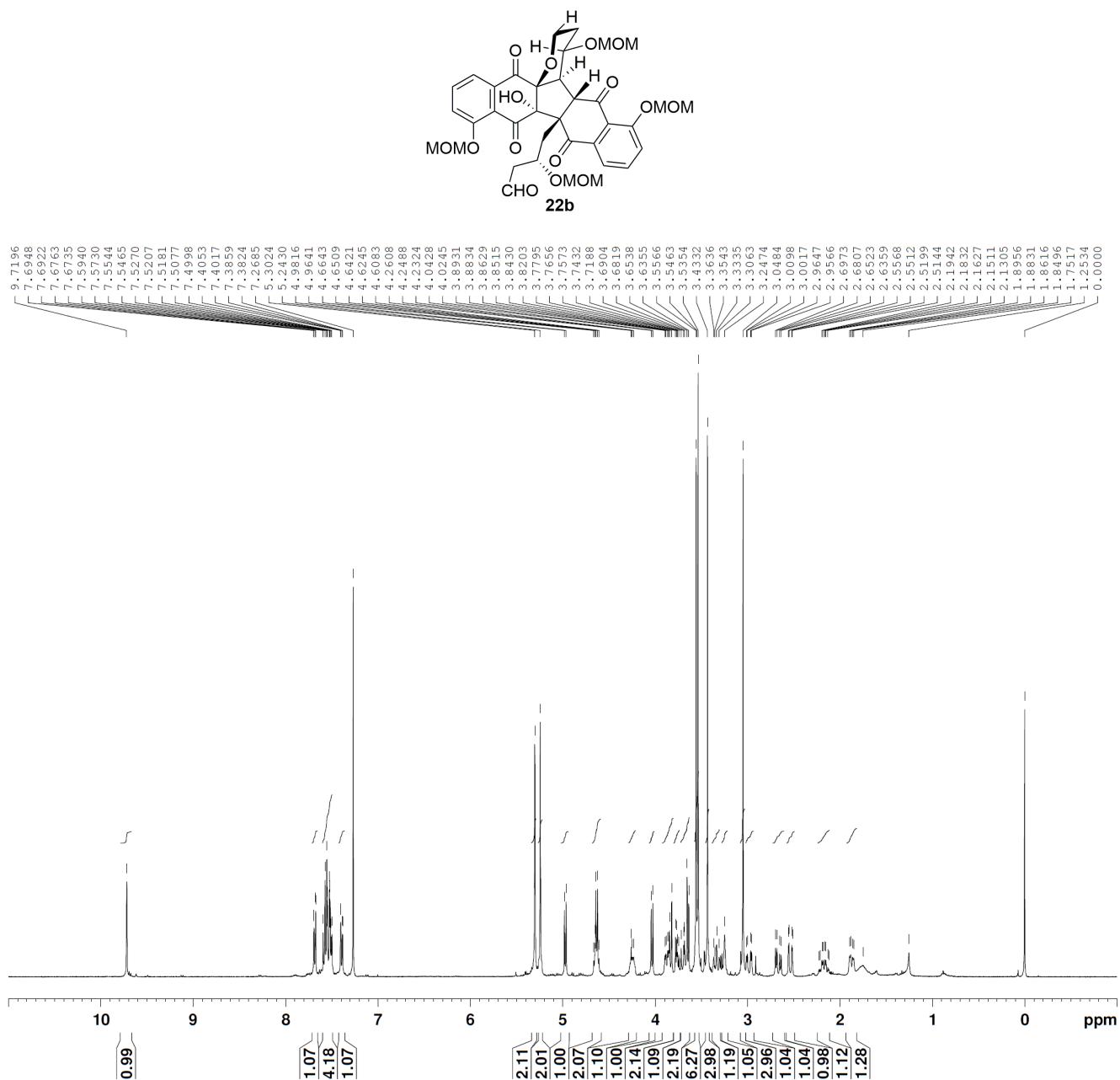


Figure S14. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (100 MHz) of compound **22b**.

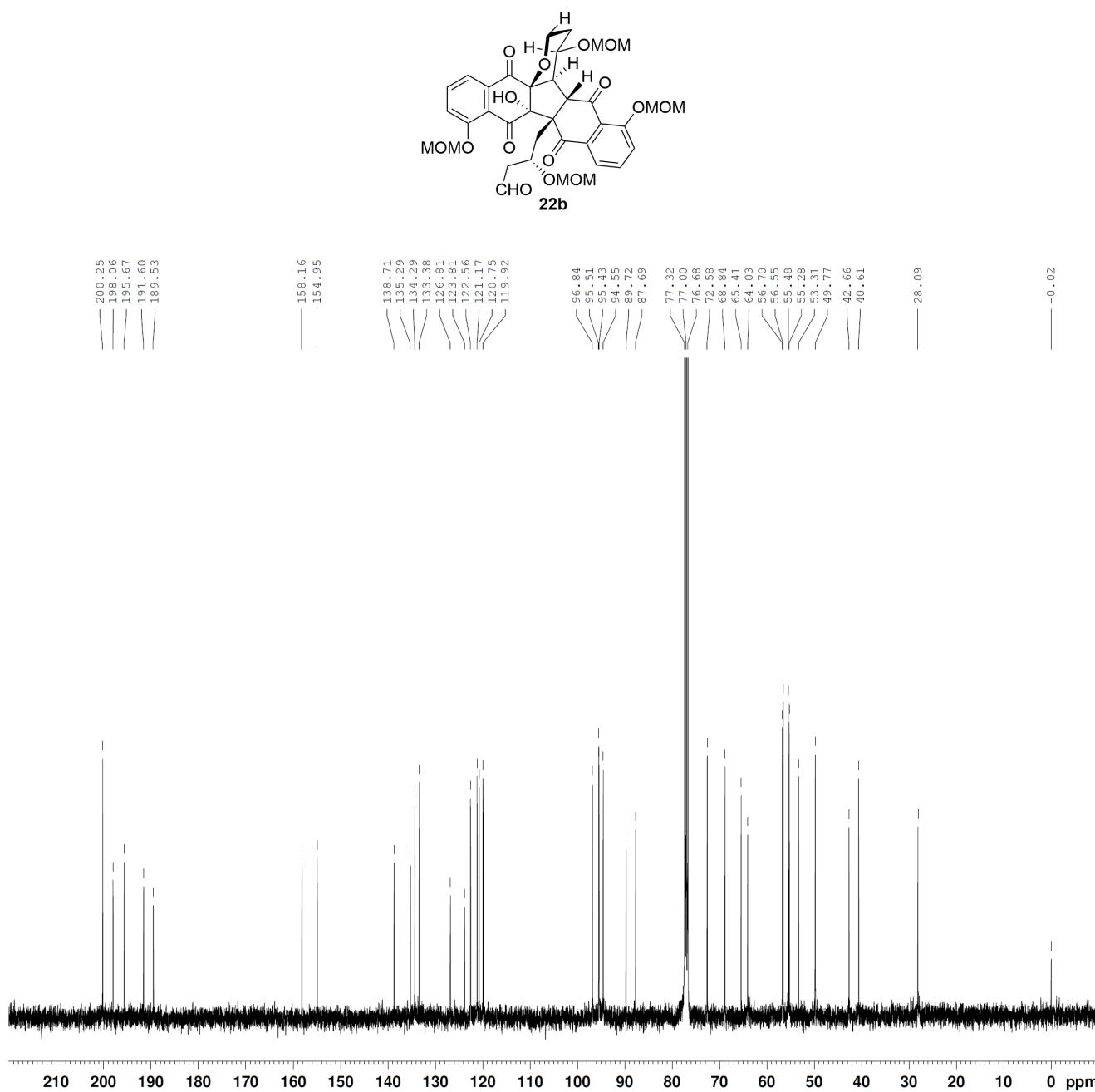


Figure S15. HMBC spectrum (91.0–86.0, 4.0–2.5 ppm) of compound **22b**.

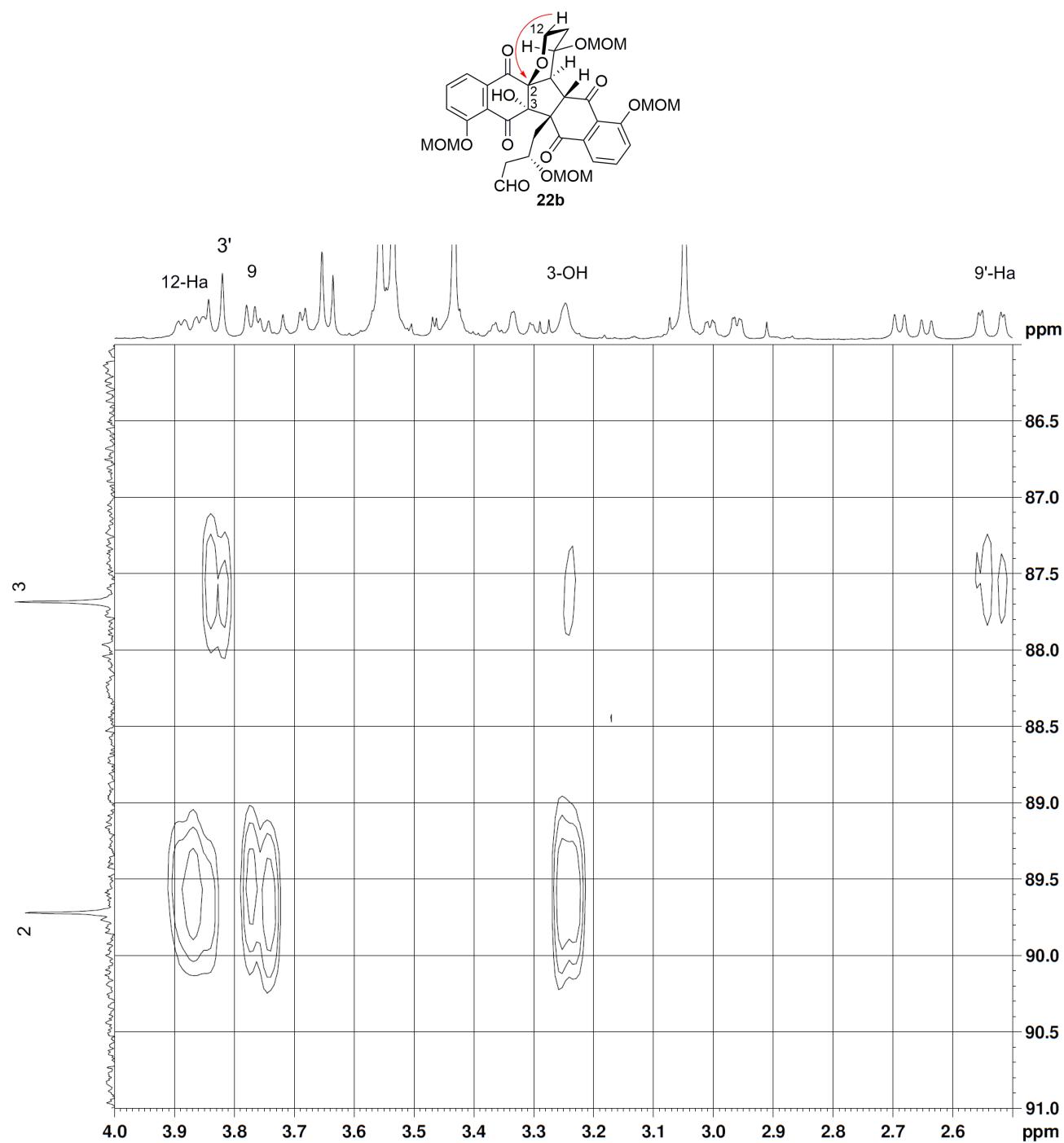


Figure S16. ^1H NMR spectrum (400 MHz, acetone- d_6) of compound **14b**.

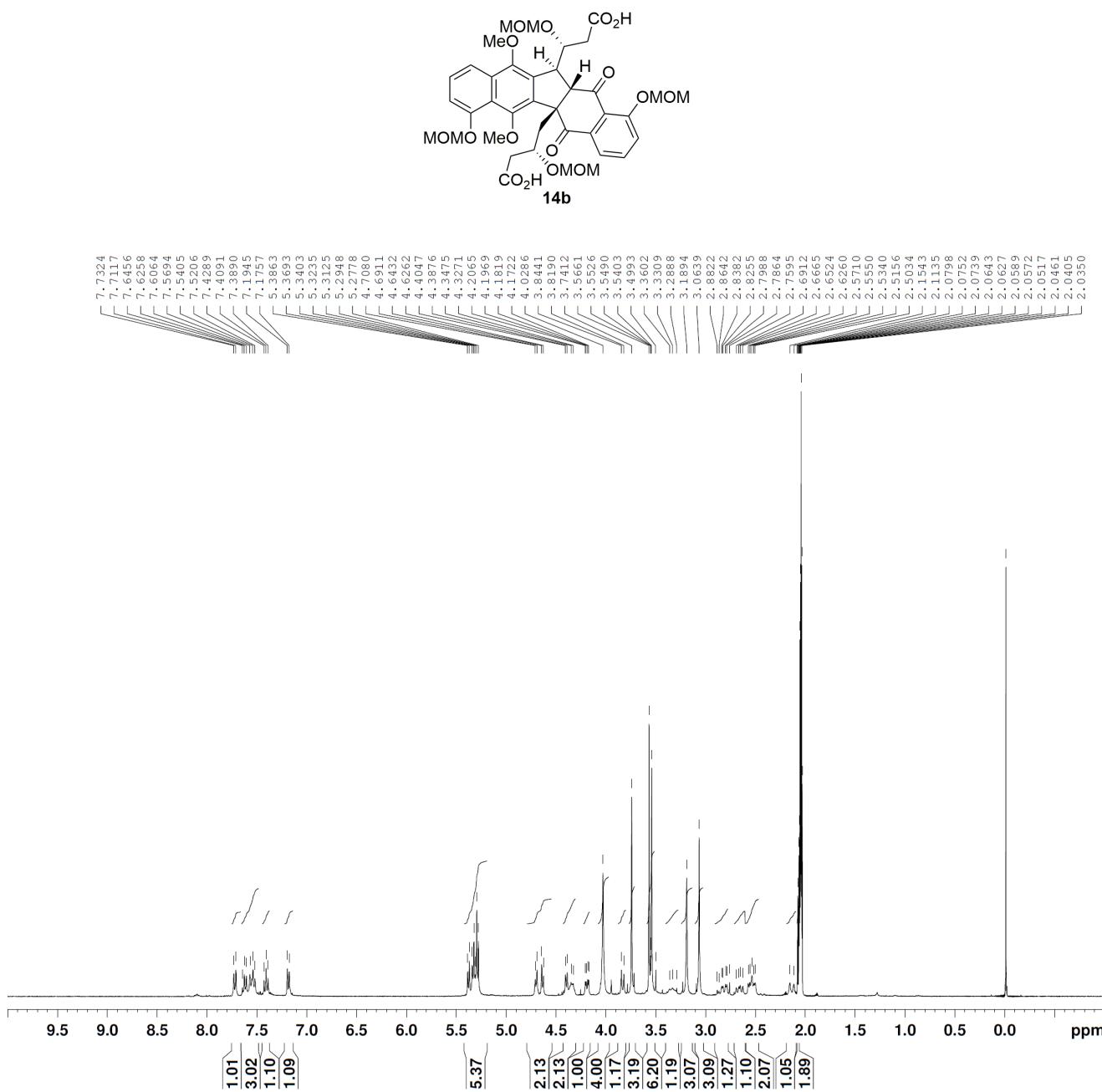


Figure S17. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (100 MHz, acetone- d_6) of compound **14b**.

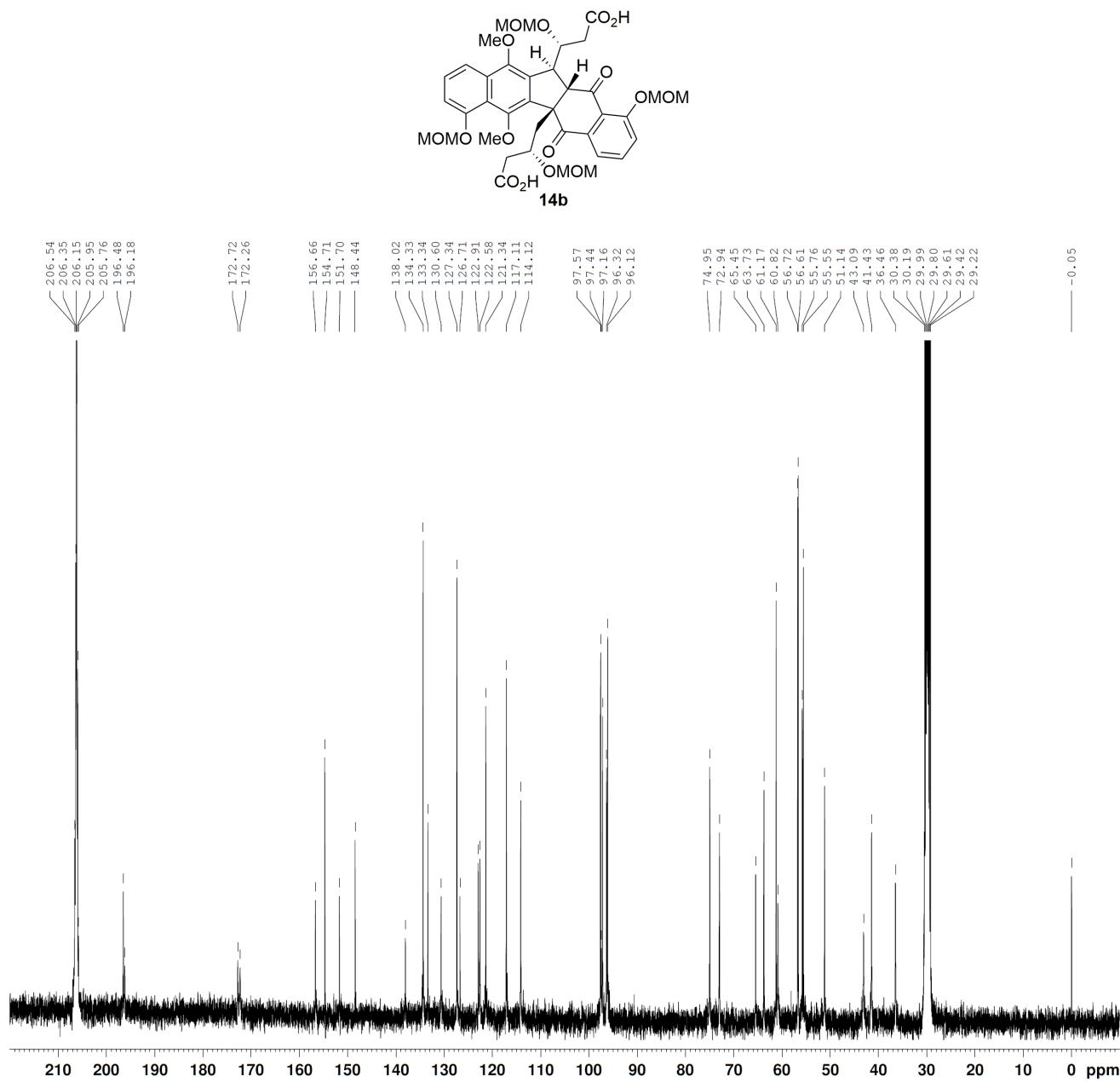
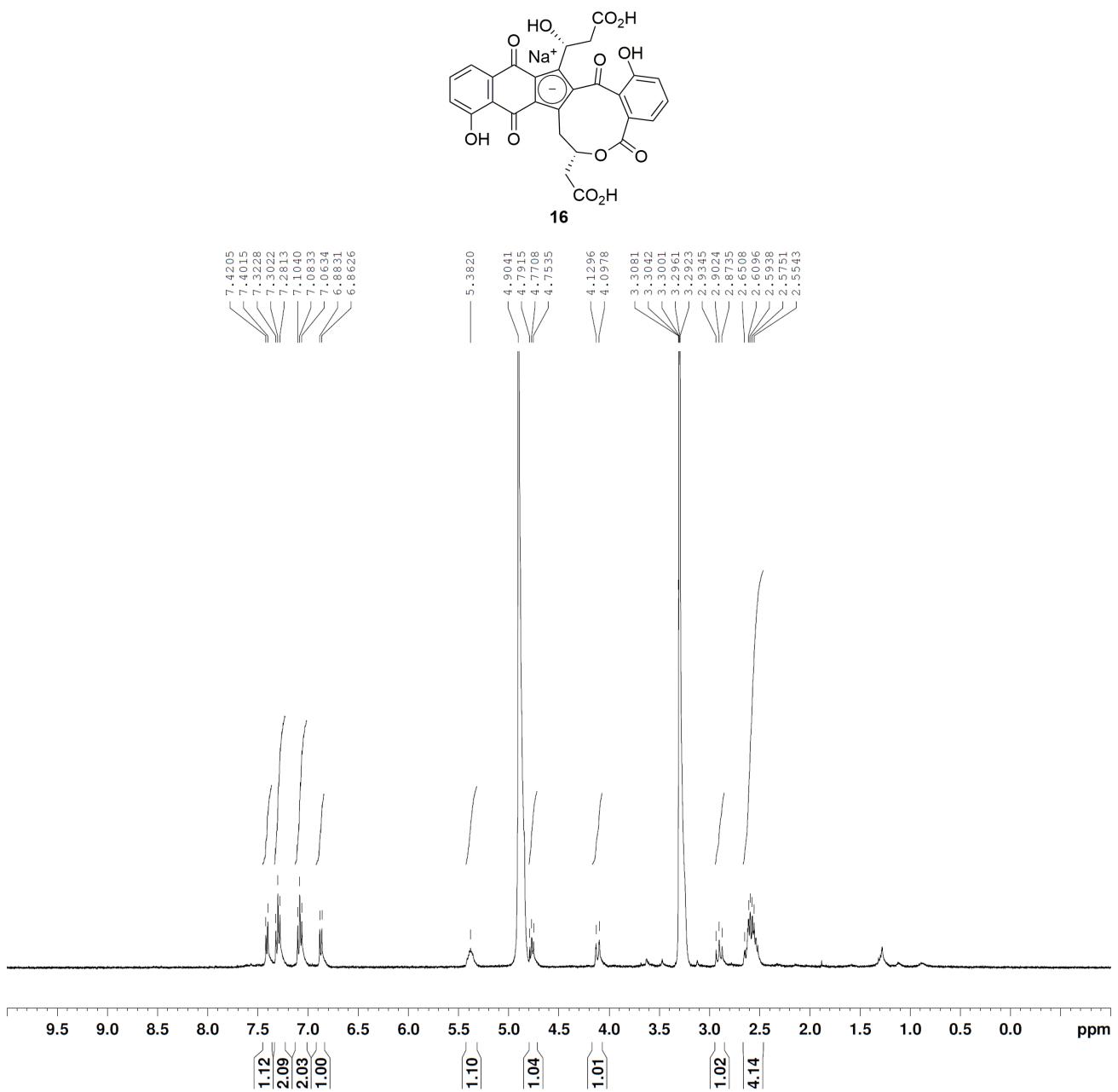
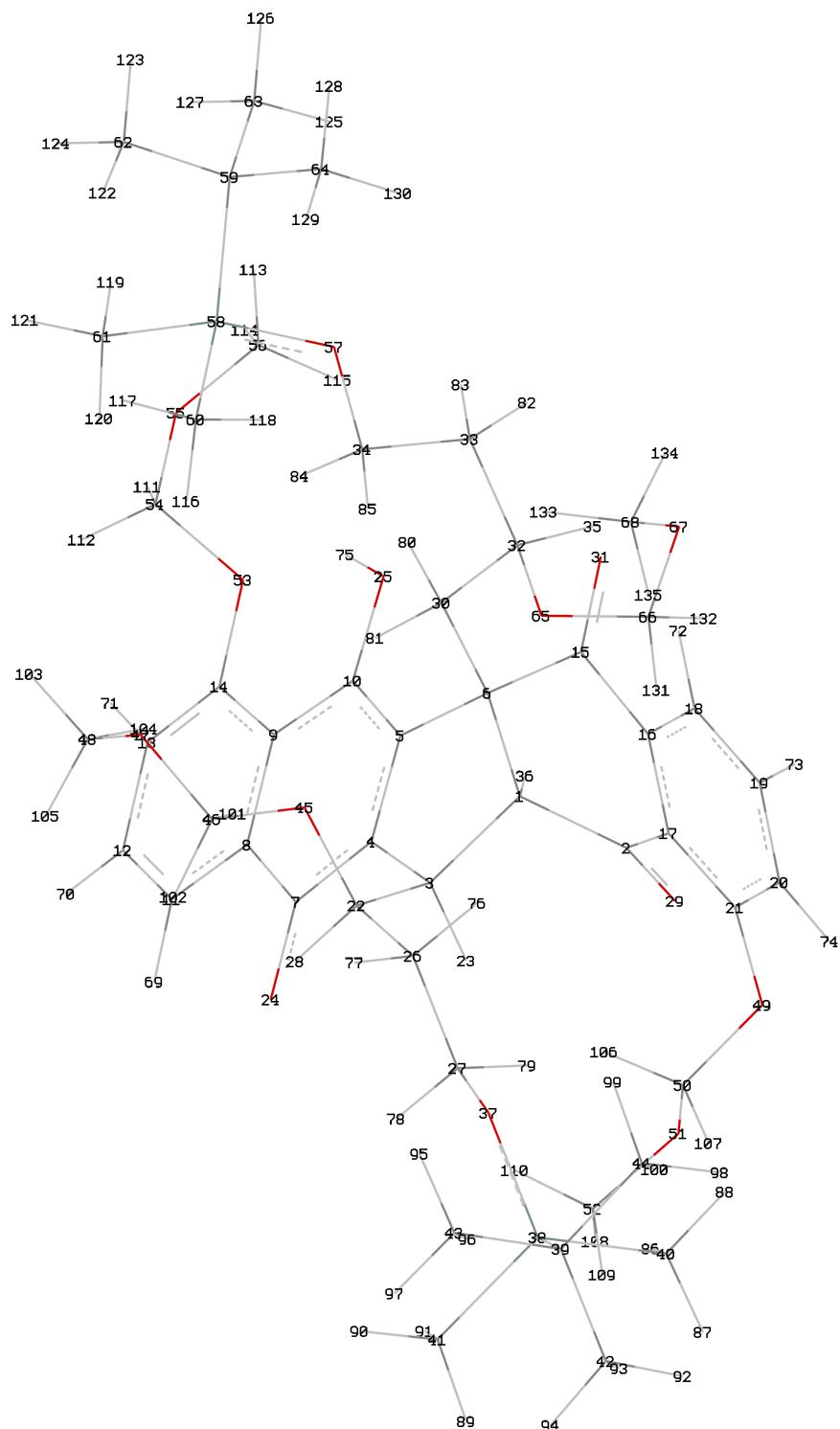


Figure S18. ^1H NMR spectrum (400 MHz, CD_3OD) of compound **16**.



Results of DFT Calculations for Compounds 24a and 24b.

Table S1. Total Energy, Number of Imaginary Frequencies, and Atom Coordinates for Compound 24a Optimized by DFT/B3LYP/6-31G+(d,p) Level with SMD (CH_2Cl_2).^{S1}



24a

Total energy [E(RB3LPY)] = - 3504.41511964 au. Number of imaginary frequencies = 0.

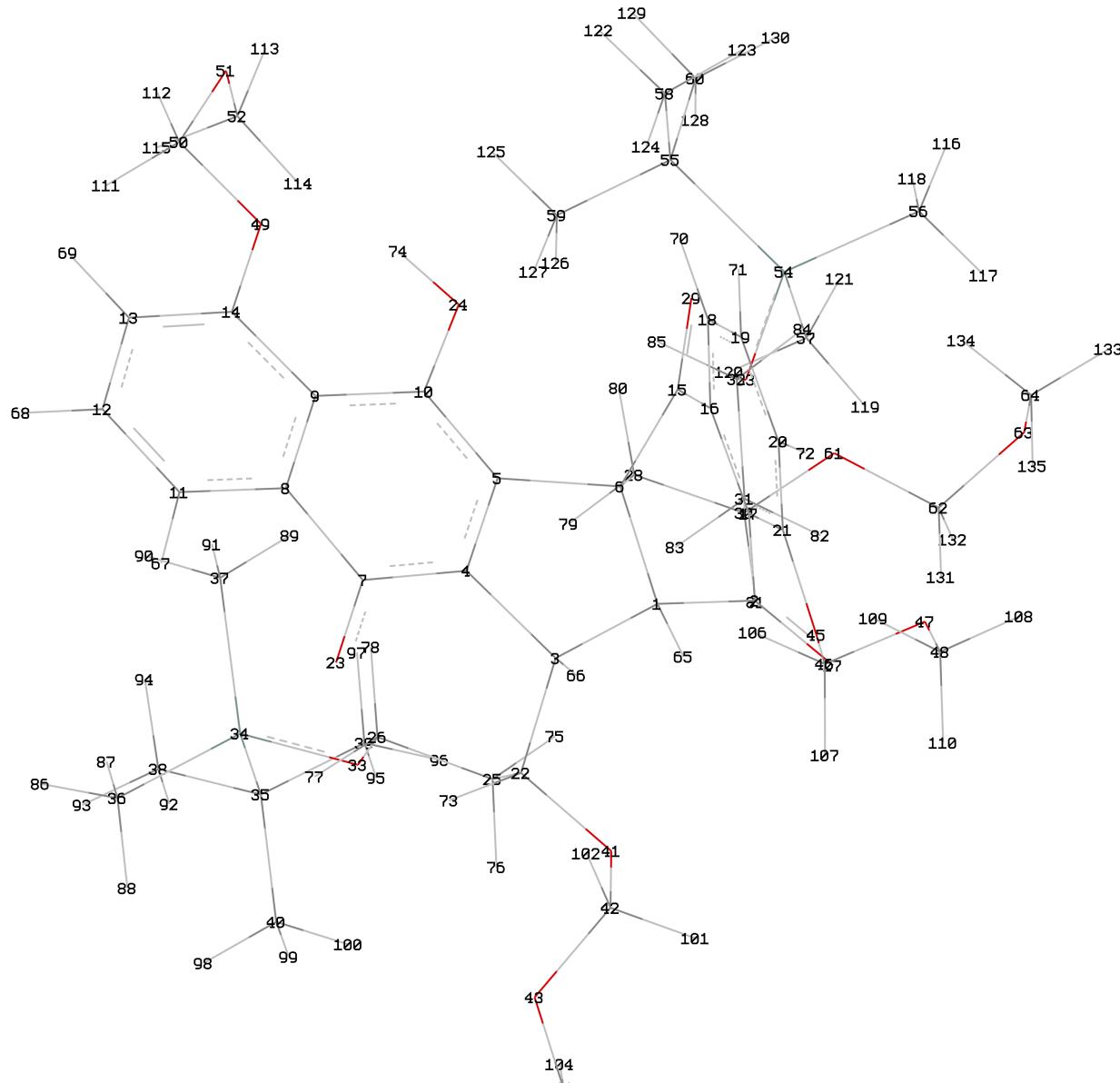
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	0.940383	0.292638	0.925794
2	6	0	2.023847	0.624737	1.940599
3	6	0	1.516579	0.636636	-0.50046
4	6	0	0.732775	1.851925	-0.9186
5	6	0	-0.36797	2.093609	-0.07329
6	6	0	-0.42784	1.064594	1.07747
7	6	0	1.058493	2.665178	-2.02844
8	6	0	0.137376	3.783751	-2.26134
9	6	0	-1.02242	4.000006	-1.42446
10	6	0	-1.25486	3.136845	-0.30762
11	6	0	0.394521	4.664696	-3.33803
12	6	0	-0.43054	5.738371	-3.61448
13	6	0	-1.573	5.962788	-2.81331
14	6	0	-1.86289	5.110158	-1.76703
15	6	0	-0.49252	1.840232	2.398708
16	6	0	0.749705	2.553157	2.835344
17	6	0	2.012345	1.977825	2.577391
18	6	0	0.633849	3.741989	3.564841
19	6	0	1.781408	4.392493	4.011671
20	6	0	3.042277	3.850819	3.746754
21	6	0	3.163427	2.652296	3.042858
22	6	0	1.473821	-0.52044	-1.52722
23	1	0	2.581912	0.893483	-0.42747
24	8	0	2.079735	2.458241	-2.78736
25	8	0	-2.32734	3.322218	0.546727
26	6	0	2.353949	-1.7339	-1.1786
27	6	0	3.855005	-1.45169	-1.16791
28	1	0	1.823612	-0.08591	-2.4746
29	8	0	2.890013	-0.20465	2.208117
30	6	0	-1.66168	0.13541	0.908301
31	8	0	-1.50828	1.921972	3.079011
32	6	0	-1.94745	-0.91407	1.997071
33	6	0	-3.38349	-1.46202	1.908528
34	6	0	-3.74521	-2.11048	0.574564

35	1	0	-1.82942	-0.46539	2.988377
36	1	0	0.758471	-0.77684	1.019272
37	8	0	4.551735	-2.70106	-1.09189
38	14	0	6.228853	-2.8696	-1.1113
39	6	0	6.524413	-4.76069	-1.00743
40	6	0	6.988021	-1.95587	0.357811
41	6	0	6.926724	-2.13293	-2.70635
42	6	0	8.041599	-5.05281	-1.02563
43	6	0	5.862994	-5.46895	-2.20974
44	6	0	5.920715	-5.31988	0.299333
45	8	0	0.10574	-0.93263	-1.69826
46	6	0	-0.16613	-1.6852	-2.86928
47	8	0	-1.4822	-1.46755	-3.29142
48	6	0	-1.71299	-0.1706	-3.85021
49	8	0	4.433452	2.141812	2.87406
50	6	0	4.992976	2.210369	1.583055
51	8	0	5.495527	3.516166	1.381488
52	6	0	5.9658	3.7112	0.048018
53	8	0	-2.99761	5.370565	-0.97997
54	6	0	-4.27725	5.20522	-1.65343
55	8	0	-5.2603	5.872749	-0.94818
56	6	0	-5.64694	5.257446	0.288277
57	8	0	-5.0466	-2.70274	0.689651
58	14	0	-5.86679	-3.4233	-0.59556
59	6	0	-7.45993	-4.14771	0.186887
60	6	0	-4.78761	-4.76589	-1.37333
61	6	0	-6.26019	-2.12589	-1.91225
62	6	0	-8.34088	-4.77771	-0.91527
63	6	0	-8.26036	-3.03095	0.891743
64	6	0	-7.097	-5.23475	1.22184
65	8	0	-0.98677	-1.99758	1.884323
66	6	0	-0.46388	-2.49383	3.090932
67	8	0	-1.34396	-3.32537	3.820538
68	6	0	-1.5856	-4.59253	3.207911
69	1	0	1.276231	4.465272	-3.939
70	1	0	-0.20962	6.412921	-4.43726

71	1	0	-2.22895	6.80616	-3.00926
72	1	0	-0.3525	4.146471	3.765109
73	1	0	1.701424	5.325412	4.561928
74	1	0	3.946827	4.347089	4.082531
75	1	0	-2.78199	4.134631	0.252326
76	1	0	2.051093	-2.15718	-0.21351
77	1	0	2.180989	-2.50859	-1.9351
78	1	0	4.141349	-0.91678	-2.08527
79	1	0	4.128032	-0.82437	-0.31051
80	1	0	-2.54216	0.779813	0.839713
81	1	0	-1.54668	-0.37283	-0.05234
82	1	0	-3.52011	-2.20252	2.703713
83	1	0	-4.08019	-0.63757	2.107987
84	1	0	-3.74602	-1.36564	-0.23126
85	1	0	-3.00657	-2.8804	0.316981
86	1	0	6.826866	-0.87474	0.266579
87	1	0	8.071749	-2.11874	0.408521
88	1	0	6.552557	-2.27771	1.310802
89	1	0	8.013196	-2.27382	-2.76415
90	1	0	6.480061	-2.58703	-3.59858
91	1	0	6.737289	-1.05325	-2.75203
92	1	0	8.561228	-4.59325	-0.17622
93	1	0	8.218551	-6.13678	-0.96716
94	1	0	8.520293	-4.69526	-1.94534
95	1	0	4.780485	-5.30133	-2.2354
96	1	0	6.02913	-6.5548	-2.14905
97	1	0	6.277959	-5.12932	-3.1664
98	1	0	6.378651	-4.87094	1.188904
99	1	0	4.840263	-5.14628	0.355437
100	1	0	6.086004	-6.40592	0.359614
101	1	0	-0.10166	-2.76044	-2.66404
102	1	0	0.549645	-1.40738	-3.66184
103	1	0	-2.74048	-0.16866	-4.22169
104	1	0	-1.59583	0.617106	-3.09979
105	1	0	-1.02528	0.02126	-4.68582
106	1	0	4.24841	1.973424	0.810929

107	1	0	5.805311	1.473026	1.566396
108	1	0	6.325376	4.740625	-0.01204
109	1	0	6.793866	3.027588	-0.18895
110	1	0	5.160088	3.56631	-0.68479
111	1	0	-4.48631	4.126874	-1.72633
112	1	0	-4.22184	5.656608	-2.64581
113	1	0	-6.5579	5.762823	0.615358
114	1	0	-5.85396	4.189244	0.143127
115	1	0	-4.87368	5.382459	1.054583
116	1	0	-3.89646	-4.3261	-1.83794
117	1	0	-5.33184	-5.30318	-2.15992
118	1	0	-4.45032	-5.50206	-0.63436
119	1	0	-6.87514	-1.3102	-1.51438
120	1	0	-5.33654	-1.68552	-2.30758
121	1	0	-6.79591	-2.57118	-2.75966
122	1	0	-7.82587	-5.58954	-1.44329
123	1	0	-9.25262	-5.2051	-0.47266
124	1	0	-8.65794	-4.03996	-1.66215
125	1	0	-7.68335	-2.56384	1.697487
126	1	0	-9.17785	-3.44427	1.336606
127	1	0	-8.5644	-2.24018	0.195279
128	1	0	-8.00984	-5.64131	1.682113
129	1	0	-6.56141	-6.07525	0.764297
130	1	0	-6.47044	-4.83662	2.027971
131	1	0	0.438866	-3.05407	2.812186
132	1	0	-0.21192	-1.67557	3.776458
133	1	0	-2.11016	-4.48783	2.25111
134	1	0	-2.21051	-5.16438	3.898191
135	1	0	-0.64243	-5.133	3.042252

Table S2. Total Energy, Number of Imaginary Frequencies, and Atom Coordinates for 24b Optimized by DFT/B3LYP/6-31G+(d,p) Level with SMD (CH_2Cl_2).^{S2}



24b

Total energy [E(RB3LPY)] = -3504.41390268 au. Number of imaginary frequencies = 0.

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.966354	-0.529269	-0.844325
2	6	0	-3.038071	-1.598099	-0.939171
3	6	0	-2.649035	0.846434	-0.516595
4	6	0	-2.012571	1.287934	0.773366
5	6	0	-0.958451	0.441355	1.169484
6	6	0	-0.861025	-0.801266	0.251674
7	6	0	-2.41875	2.4256	1.509013
8	6	0	-1.604275	2.714968	2.692538
9	6	0	-0.481214	1.887448	3.064765
10	6	0	-0.173115	0.724637	2.284738
11	6	0	-1.93366	3.852054	3.472597
12	6	0	-1.205696	4.19255	4.591564
13	6	0	-0.09701	3.401658	4.981395
14	6	0	0.254774	2.291127	4.236263
15	6	0	-1.228348	-1.983011	1.176811
16	6	0	-2.686897	-2.250616	1.41493
17	6	0	-3.603017	-2.058685	0.36443
18	6	0	-3.108552	-2.755446	2.650696
19	6	0	-4.458738	-3.030865	2.847335
20	6	0	-5.389469	-2.833706	1.821654
21	6	0	-4.96901	-2.350925	0.577255
22	6	0	-2.558899	1.886911	-1.667385
23	8	0	-3.417824	3.168246	1.176001
24	8	0	0.867057	-0.127938	2.601362
25	6	0	-1.163255	2.25406	-2.192784
26	6	0	-0.372875	3.237235	-1.330644
27	8	0	-3.418018	-2.049903	-2.014257
28	6	0	0.558255	-0.984589	-0.346088
29	8	0	-0.388705	-2.645345	1.768889
30	6	0	0.714787	-1.916117	-1.556607
31	6	0	2.173712	-1.970177	-2.05767
32	6	0	3.181387	-2.568022	-1.077608

33	8	0	0.798031	3.633215	-2.060629
34	14	0	1.949032	4.715953	-1.472526
35	6	0	3.228574	4.883968	-2.890815
36	6	0	1.124919	6.368243	-1.068261
37	6	0	2.732829	4.030211	0.10386
38	6	0	4.363419	5.839098	-2.457742
39	6	0	3.835477	3.504173	-3.226002
40	6	0	2.548904	5.45379	-4.155009
41	8	0	-3.293056	1.377941	-2.812761
42	6	0	-4.663232	1.687562	-2.844166
43	8	0	-4.939403	3.006287	-3.275274
44	6	0	-4.6283	3.241745	-4.64847
45	8	0	-5.823643	-2.108333	-0.463818
46	6	0	-7.20955	-2.056472	-0.225239
47	8	0	-7.716288	-3.371301	-0.14087
48	6	0	-9.130365	-3.386379	0.052324
49	8	0	1.332876	1.492777	4.581127
50	6	0	2.213548	1.894108	5.649568
51	8	0	3.271906	1.005711	5.699389
52	6	0	4.245209	1.174924	4.658217
53	8	0	4.45984	-2.632551	-1.72216
54	14	0	5.744909	-3.639976	-1.30033
55	6	0	6.564341	-3.078413	0.349025
56	6	0	5.145399	-5.427946	-1.18234
57	6	0	6.937613	-3.457905	-2.747717
58	6	0	5.671138	-3.430493	1.559237
59	6	0	6.797917	-1.552326	0.323718
60	6	0	7.925767	-3.791329	0.515936
61	8	0	0.221797	-3.226708	-1.21341
62	6	0	-0.166848	-4.014751	-2.333253
63	8	0	-0.24406	-5.35927	-1.967189
64	6	0	-1.327936	-5.675545	-1.08803
65	1	0	-1.506757	-0.483034	-1.830487
66	1	0	-3.728231	0.702602	-0.359768
67	1	0	-2.78505	4.442427	3.149482
68	1	0	-1.469324	5.064324	5.18458

69	1	0	0.464083	3.675364	5.866977
70	1	0	-2.381257	-2.916997	3.438752
71	1	0	-4.80273	-3.410696	3.805142
72	1	0	-6.431407	-3.077786	1.987065
73	1	0	-3.052053	2.795576	-1.305452
74	1	0	1.292446	0.206108	3.410241
75	1	0	-0.558251	1.356476	-2.367083
76	1	0	-1.312193	2.726538	-3.170218
77	1	0	-0.991213	4.118428	-1.110732
78	1	0	-0.08067	2.785077	-0.3778
79	1	0	0.919237	0.000426	-0.662537
80	1	0	1.205978	-1.316846	0.465409
81	1	0	0.109664	-1.530854	-2.389525
82	1	0	2.216872	-2.55388	-2.984677
83	1	0	2.482993	-0.950457	-2.319582
84	1	0	2.853542	-3.568469	-0.770142
85	1	0	3.263117	-1.950009	-0.175716
86	1	0	1.865442	7.111411	-0.747396
87	1	0	0.405631	6.251927	-0.248228
88	1	0	0.585251	6.779812	-1.92919
89	1	0	3.205659	3.055374	-0.062697
90	1	0	3.495928	4.713365	0.49707
91	1	0	1.975816	3.902564	0.887331
92	1	0	5.098521	5.945553	-3.269025
93	1	0	3.991617	6.843972	-2.223322
94	1	0	4.90278	5.467338	-1.578198
95	1	0	4.571026	3.599893	-4.038577
96	1	0	3.070546	2.792273	-3.555335
97	1	0	4.355391	3.063488	-2.366938
98	1	0	2.131164	6.452984	-3.982449
99	1	0	3.279995	5.542574	-4.972417
100	1	0	1.737058	4.807489	-4.507181
101	1	0	-5.116301	0.961602	-3.532908
102	1	0	-5.122082	1.609407	-1.852608
103	1	0	-4.959056	4.257555	-4.878663
104	1	0	-3.551707	3.162241	-4.839322

105	1	0	-5.161107	2.532715	-5.2991
106	1	0	-7.427965	-1.493144	0.695276
107	1	0	-7.634504	-1.533693	-1.09122
108	1	0	-9.431327	-4.434884	0.097525
109	1	0	-9.411349	-2.888239	0.991186
110	1	0	-9.651365	-2.896332	-0.78242
111	1	0	2.549641	2.923267	5.458455
112	1	0	1.682422	1.823131	6.603734
113	1	0	5.069329	0.498788	4.893194
114	1	0	3.833301	0.915459	3.677199
115	1	0	4.613451	2.208891	4.639286
116	1	0	5.976652	-6.105036	-0.949213
117	1	0	4.717842	-5.747333	-2.141088
118	1	0	4.378635	-5.568422	-0.412468
119	1	0	6.420556	-3.691302	-3.68657
120	1	0	7.330331	-2.43762	-2.829134
121	1	0	7.789462	-4.142133	-2.657612
122	1	0	6.148994	-3.096255	2.492278
123	1	0	5.505971	-4.510607	1.647664
124	1	0	4.689303	-2.946502	1.506667
125	1	0	7.294479	-1.227614	1.250301
126	1	0	7.438069	-1.246958	-0.512988
127	1	0	5.857085	-0.996386	0.242266
128	1	0	8.6292	-3.529173	-0.283034
129	1	0	8.390972	-3.499527	1.469213
130	1	0	7.823143	-4.883603	0.527494
131	1	0	-1.140057	-3.656423	-2.709368
132	1	0	0.582177	-3.962414	-3.131072
133	1	0	-1.37153	-6.765655	-1.026413
134	1	0	-1.164588	-5.26388	-0.086483
135	1	0	-2.278656	-5.297179	-1.487487

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