Supporting Information

***Rec. Nat. Prod*. 17:3 (2023) 529-535**

Eupalinolide N, a Previously Undescribed Sesquiterpene Lactone with Anti-inflammatory Activity from *Eupatorium lindleyanum*

Jie Yan[1, 2, 3], Wenxiu Guo[2], Xueyan Huo[2], Yunjie Hu[2], Lanyu Zhou[2], Xiaofang Xie[1, 2], Jin Pei[1, 2], Yun Deng[1, 2], Bin Xiao[3], Ding Liu[3], Dale Guo[1, 2] and Cheng Peng [2]

[1] State Key Laboratory of Southwestern Chinese Medicine Resources, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China

[2] College of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China

[3] Chengdu Push Bio-technology Co., Ltd, Chengdu 610000, China

Table of Contents	Page

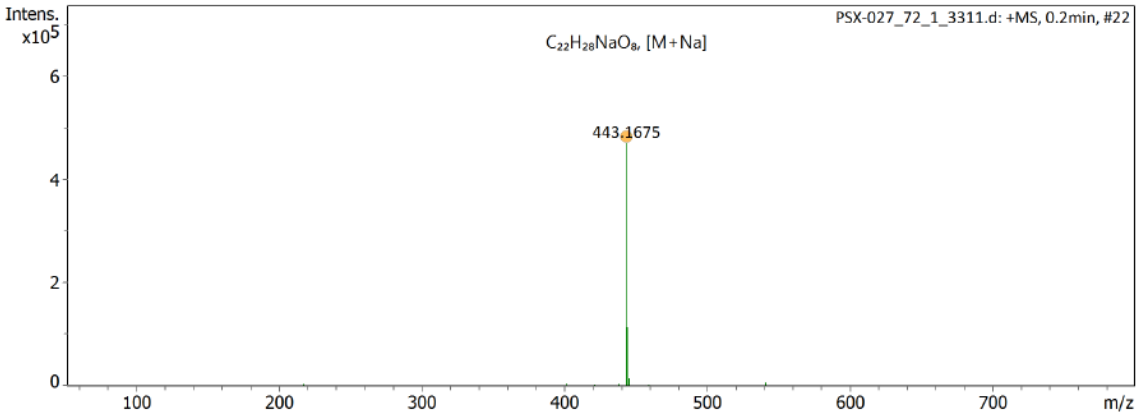


Figure S1: HR-ESI-MS spectrum of compound **1**

Figure S2: The IR spectrum of compound **1**

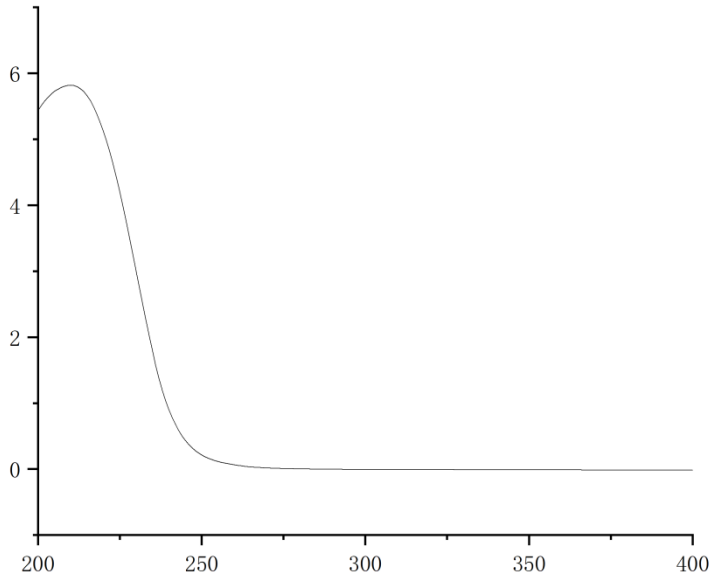


Figure S3: The UV spectrum of compound **1**

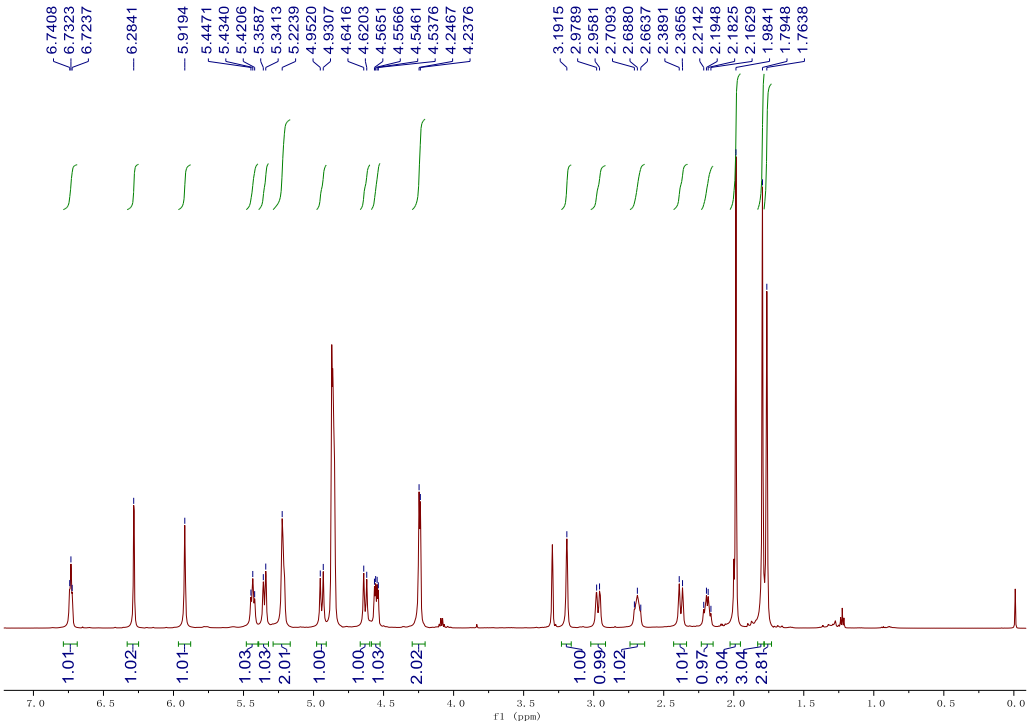


Figure S4: ^{1}H-NMR (700 MHz, CD_3OD) spectrum of compound **1**

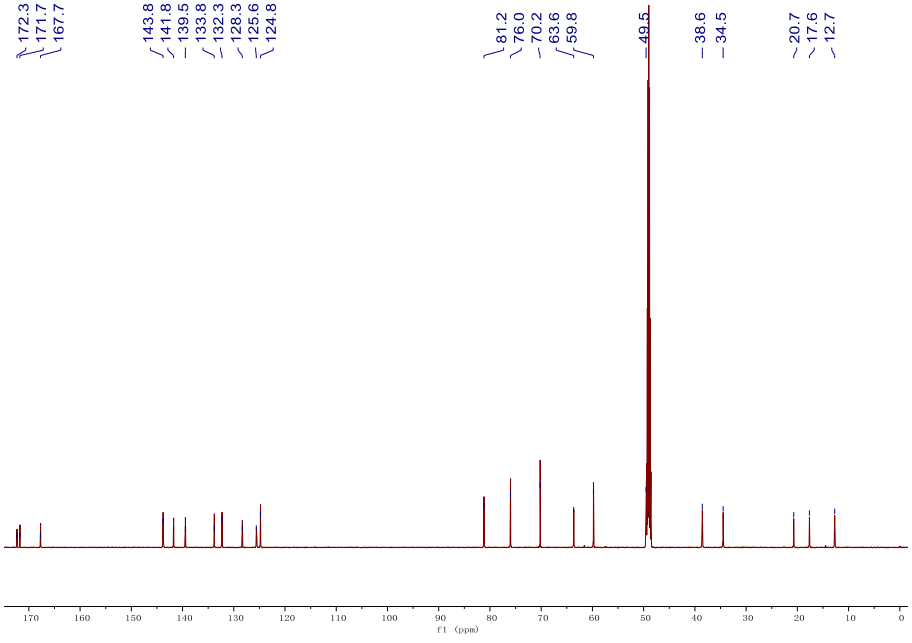


Figure S5: ^{13}C-NMR (175 MHz, CD_3OD) spectrum of compound **1**

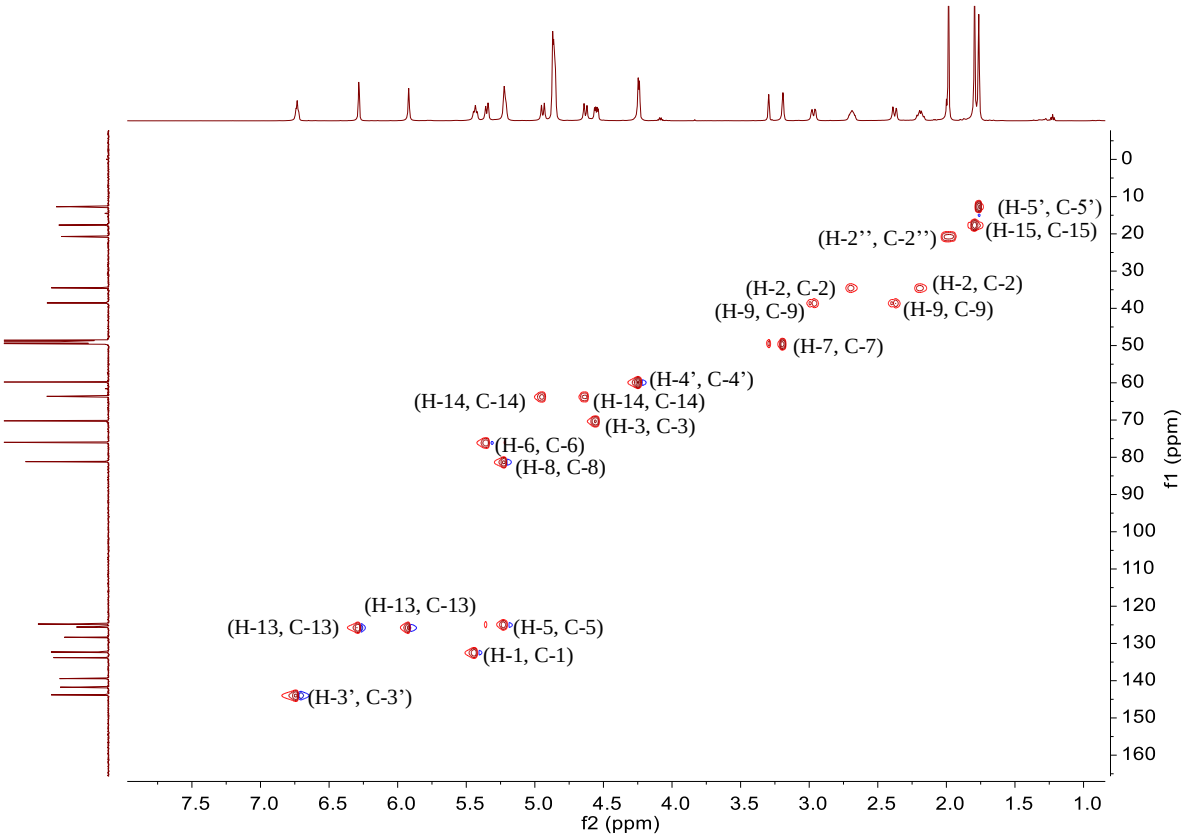


Figure S6: HSQC spectrum of compound **1**

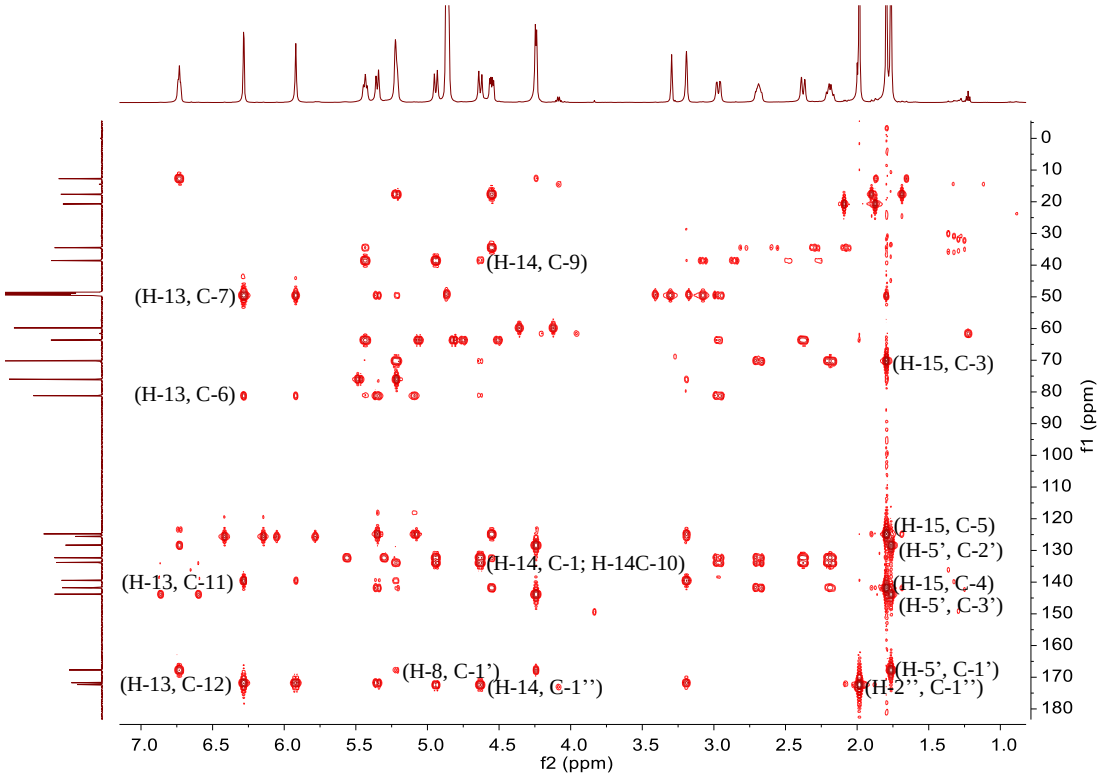


Figure S7: HMBC spectrum of compound **1**

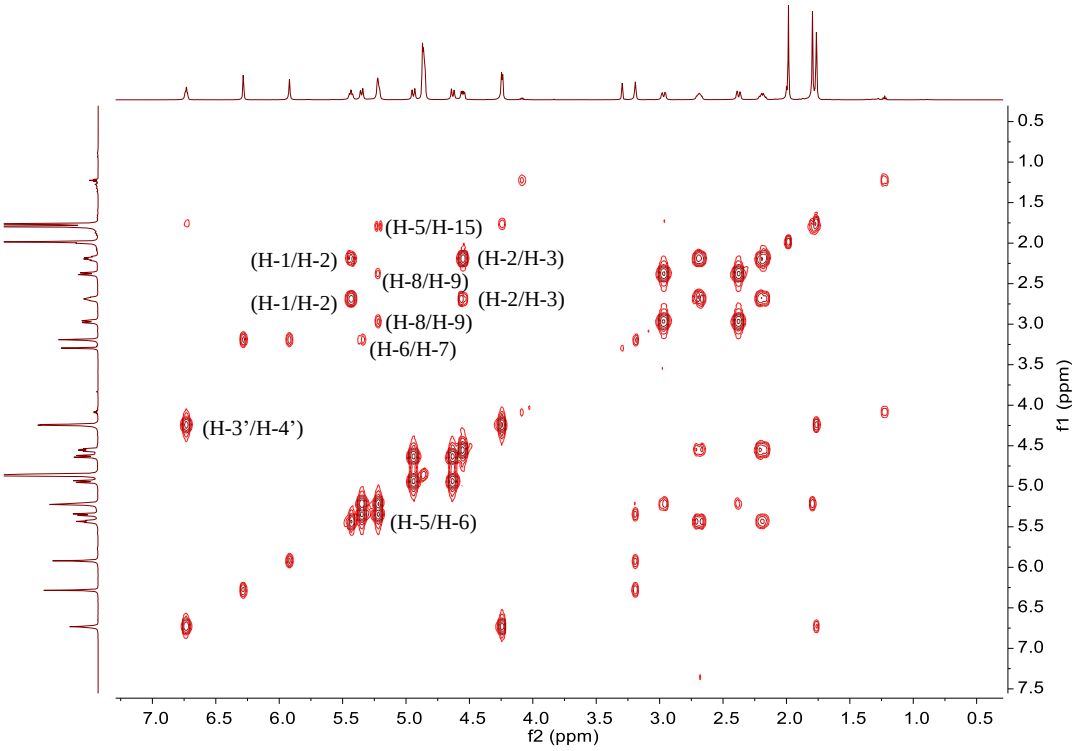


Figure S8: $^{1}H-^{1}H$ COSY spectrum of compound **1**

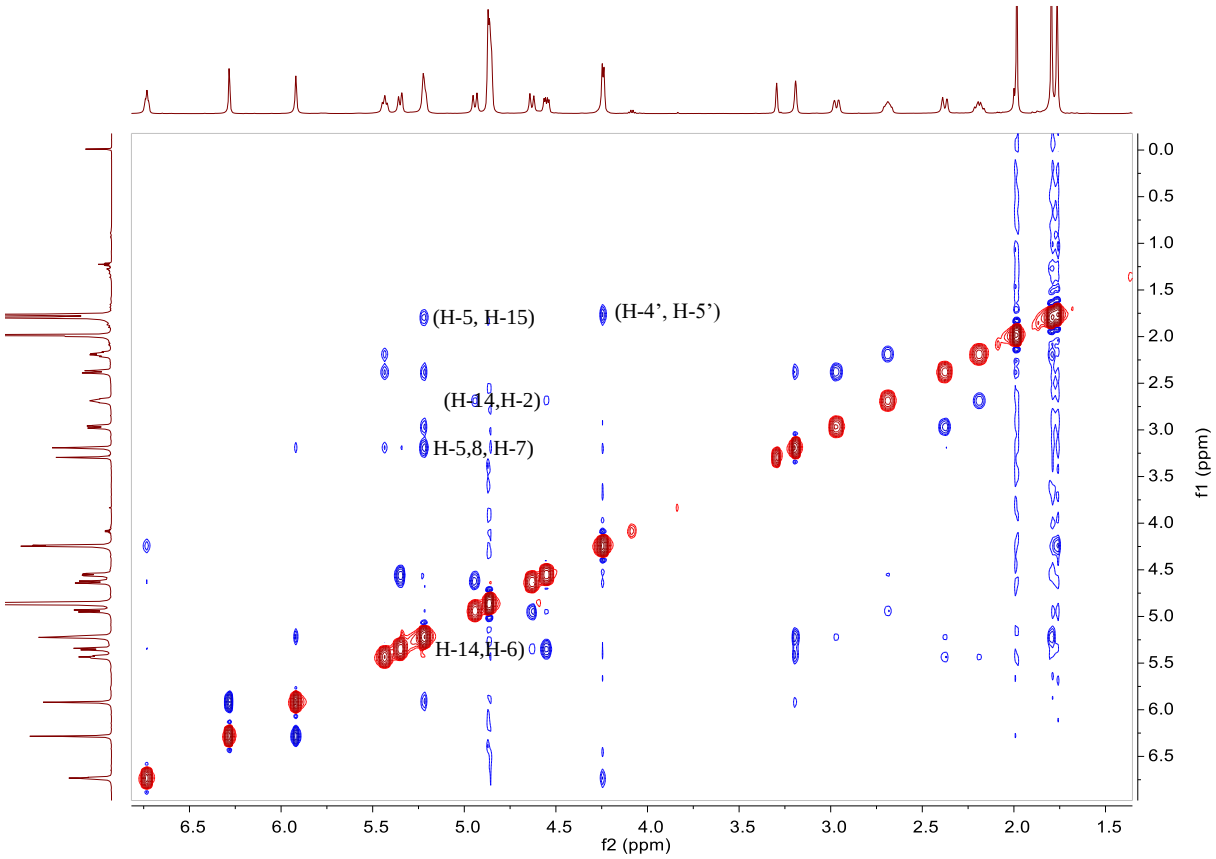


Figure S9: NOESY spectrum of compound **1**

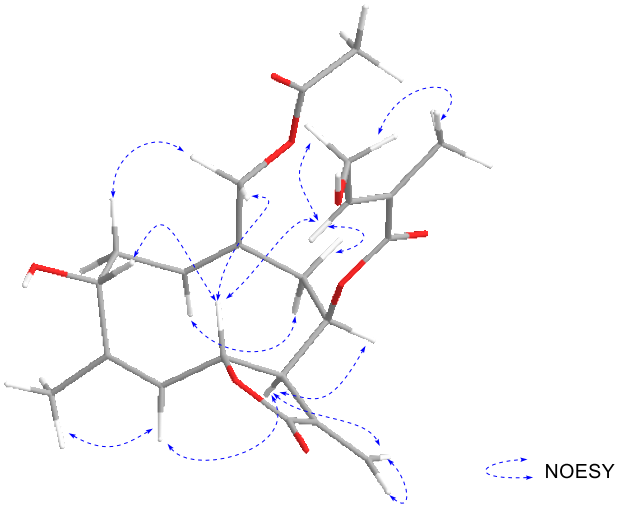


Figure S10: Key NOESY correlations of **1**

S1: Computational Details

The theoretical calculations of compound **1** was performed using Gaussian 16.[1] Conformational analysis was initially carried out using Conflex 8 to generate conformations by Boltzman Jump, then minimize them by Smart Minimizer using the MMFF molecular mechanics force field. All geometries with relative energy from 0-5.0 kcal/mol were used in optimizations at the B3LYP/6-31G (d, p) in the gas and further at WB97XD/DGDZVP in the methanol. Room-temperature equilibrium populations were calculated according to the Boltzmann distribution law. The theoretical calculation of ECD was performed using TD-DFT at the CAM-B3LYP/DGDZVP level in the methanol. The ECD spectra were obtained by weighing the Boltzmann distribution rate of each geometric conformation. SpecDis 1.71 was used to sum up single CD spectra after a Boltzmann statistical weighting, and for the Gauss curve generation (σ = 0.16-0.3 eV) and for the comparison with experimental data.[2]

References

[1] M.J.Frisch, G.W.Trucks, H.B. Schlegel, G :E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, G.A. Petersson, H. Nakatsuji, *et.al*. Gaussian 16, Revision B.01, Gaussian, Inc., Wallingford CT, 2016.

[2] Bruhn T., Schaumlöffel A., Hemberger Y., Pescitelli G., SpecDis version 1.71, Berlin, Germany, 2017.

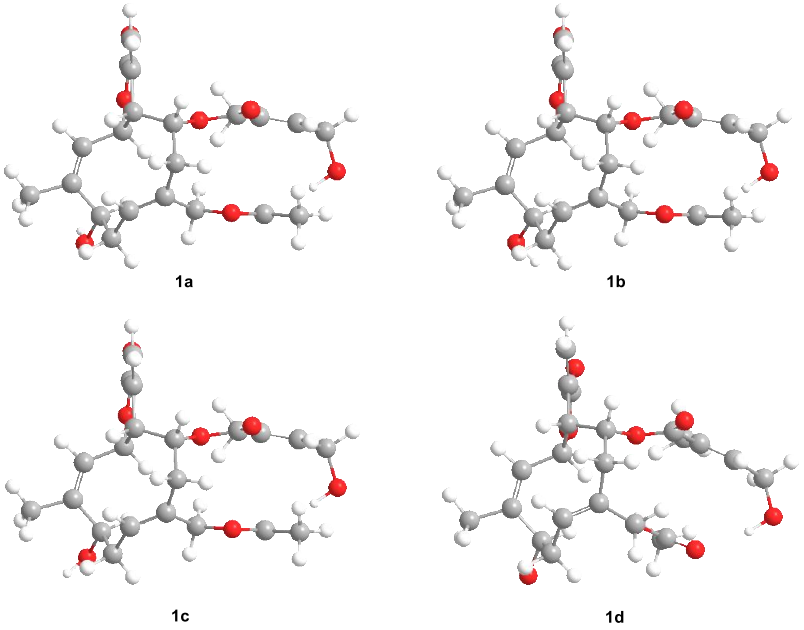


Figure S11 : Most stable conformers of 1*Z*,4*Z*,2'*Z*,3*R*,6*R*,7*R*,8*R*-**1** calculated with DFT at the CAM-B3LYP/DGDZVP level.

Table S1 : Optimized Z-Matrixes of 1*Z*,4*Z*,2'*Z*,3*R*,6*R*,7*R*,8*R*-**1** with simplified structures in the methanol at WB97XD/DGDZVP level.

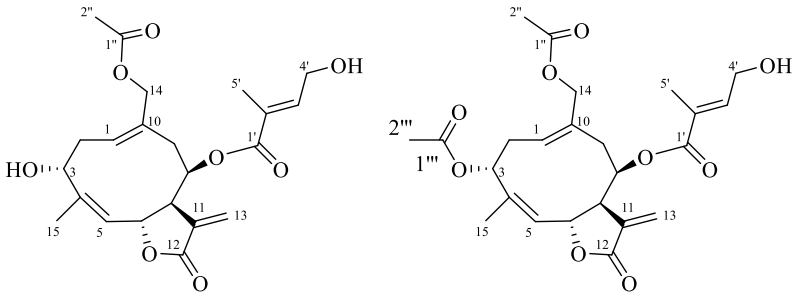
	1a			**1b**			**1c**		
C	-2.04998	0.766186	-0.3572	-2.05271	0.761505	-0.35564	-2.04791	0.769582	-0.35287
C	-1.83634	-2.00804	1.347267	-1.82881	-2.00315	1.35462	-1.83959	-1.9997	1.345663
C	-1.68869	1.407037	1.01669	-1.69286	1.407512	1.01599	-1.68344	1.411708	1.019352
C	-0.30901	1.021043	1.574778	-0.31036	1.029652	1.572476	-0.30392	1.022697	1.575569
C	-0.22813	-0.35917	2.242597	-0.22247	-0.34889	2.242417	-0.2258	-0.35802	2.242424
C	-0.59241	-1.51361	1.339078	-0.5857	-1.50631	1.342278	-0.59343	-1.5109	1.338186
O	-1.96557	1.841875	-1.33776	-1.97652	1.836159	-1.33853	-1.95616	1.842253	-1.33597
C	-1.75744	2.880243	0.710513	-1.76993	2.87971	0.707159	-1.74808	2.884474	0.710353
C	-1.83571	3.04895	-0.76296	-1.85223	3.044938	-0.76651	-1.82296	3.050166	-0.76368
C	-1.75471	3.915102	1.547906	-1.77072	3.916116	1.542623	-1.7443	3.92095	1.545718
O	-1.79358	4.071615	-1.41403	-1.81702	4.066677	-1.41954	-1.77566	4.071213	-1.41686
O	0.595225	1.119761	0.457565	0.591983	1.129641	0.4538	0.599153	1.119174	0.457276
C	1.904506	1.319107	0.687478	1.901212	1.331137	0.682434	1.909263	1.31482	0.686071
O	2.371607	1.488432	1.7978	2.368564	1.504537	1.792025	2.37763	1.482382	1.796142
C	2.670436	1.249883	-0.59518	2.666866	1.258429	-0.60014	2.674071	1.243879	-0.59713
C	3.988839	1.029459	-0.48577	3.984888	1.036004	-0.49015	3.992162	1.021177	-0.48843
C	4.942567	0.72758	-1.60731	4.939067	0.731922	-1.61065	4.944774	0.717114	-1.61032
C	1.87945	1.328788	-1.87436	1.875941	1.336425	-1.87946	1.882461	1.323808	-1.87585
O	5.33699	-0.64245	-1.5647	5.338389	-0.63644	-1.5618	5.337426	-0.6534	-1.56663
C	0.455776	-1.97257	0.357752	0.462524	-1.96646	0.361748	0.453885	-1.97407	0.357859
O	1.702769	-2.08329	1.073012	1.708762	-2.08063	1.077937	1.700521	-2.08555	1.073185
C	-2.43113	-2.95306	0.341416	-2.42676	-2.95196	0.355327	-2.43686	-2.94363	0.340828
C	-2.81983	-2.18633	-0.93567	-2.81526	-2.19232	-0.93573	-2.83503	-2.17764	-0.94059

C	-3.80582	-1.06354	-0.64104	-3.80181	-1.07553	-0.64945	-3.81374	-1.04782	-0.64591
C	-5.25508	-1.47039	-0.56839	-5.2508	-1.48392	-0.58985	-5.26717	-1.44137	-0.5913
C	2.832537	-2.11767	0.36053	2.838667	-2.11548	0.36561	2.830388	-2.12241	0.360659
C	4.037496	-2.17677	1.253653	4.043759	-2.17611	1.258377	4.035142	-2.18165	1.254018
O	2.85458	-2.09368	-0.85992	2.860621	-2.09113	-0.85486	2.852307	-2.10026	-0.85973
C	-3.43935	0.201724	-0.39541	-3.43823	0.188108	-0.39328	-3.44054	0.213466	-0.3927
O	-3.3586	-3.14539	-1.83786	-3.41523	-3.0689	-1.88179	-3.32979	-3.06566	-1.93493
H	-1.30038	0.048011	-0.67302	-1.29911	0.047861	-0.67202	-1.30249	0.046105	-0.66658
H	-2.53477	-1.58491	2.066303	-2.527	-1.5771	2.072132	-2.53748	-1.57281	2.062845
H	-2.43492	1.133155	1.765143	-2.43641	1.131288	1.766239	-2.42937	1.141292	1.769333
H	-0.01905	1.76642	2.319087	-0.0226	1.77785	2.314797	-0.01122	1.767107	2.319765
H	0.780918	-0.47418	2.643602	0.788176	-0.45997	2.640478	0.783224	-0.47607	2.642455
H	-0.90958	-0.33227	3.096594	-0.90114	-0.32294	3.098656	-0.90651	-0.33027	3.096964
H	-1.7975	4.929295	1.163132	-1.81965	4.929371	1.156113	-1.78372	4.934487	1.158856
H	-1.71264	3.780663	2.62418	-1.72551	3.783854	2.61905	-1.70469	3.788508	2.622332
H	4.410328	0.96406	0.514853	4.406032	0.971355	0.510705	4.414142	0.955484	0.511974
H	4.520935	0.976477	-2.58467	4.516193	0.974713	-2.589	4.522882	0.965642	-2.58764
H	5.857153	1.309749	-1.48092	5.851651	1.317947	-1.48736	5.860213	1.29817	-1.48499
H	2.524353	1.371821	-2.75049	2.52093	1.379669	-2.75552	2.526955	1.366287	-2.7523
H	1.240258	2.214416	-1.87904	1.236209	2.221645	-1.88452	1.244195	2.210091	-1.88011
H	1.224422	0.45997	-1.9788	1.221349	0.467237	-1.98383	1.226458	0.455743	-1.98023
H	4.528037	-1.18421	-1.54475	4.531273	-1.18086	-1.54032	4.527757	-1.19407	-1.54681
H	0.222111	-2.94284	-0.08252	0.227533	-2.93586	-0.07994	0.218671	-2.94478	-0.08062
H	0.58783	-1.25396	-0.45536	0.597101	-1.2472	-0.4503	0.586854	-1.25728	-0.45682
H	-1.73827	-3.7479	0.052596	-1.73129	-3.75215	0.082698	-1.74525	-3.73815	0.048428
H	-3.32059	-3.43608	0.753671	-3.31849	-3.4294	0.768571	-3.32112	-3.42855	0.766076
H	-1.90345	-1.77066	-1.36992	-1.89956	-1.77515	-1.37029	-1.92537	-1.76842	-1.38368
H	-5.88205	-0.63831	-0.24491	-5.88207	-0.64935	-0.2812	-5.89375	-0.60432	-0.28154
H	-5.61555	-1.82041	-1.53867	-5.59107	-1.84213	-1.56381	-5.61358	-1.78495	-1.5698
H	-5.39005	-2.29846	0.134223	-5.39455	-2.30579	0.118423	-5.4279	-2.261	0.117729
H	4.946313	-2.11541	0.659942	4.952371	-2.11312	0.66452	4.944075	-2.12188	0.660325
H	4.023483	-3.11142	1.817693	4.030253	-3.11219	1.820079	4.020121	-3.11562	1.819166
H	4.002189	-1.35445	1.970251	4.00846	-1.35565	1.977035	4.000525	-1.35844	1.969637
H	-4.21529	0.928585	-0.1555	-4.21848	0.909653	-0.15183	-4.21272	0.945398	-0.15619
H	-3.48953	-2.71589	-2.69377	-2.76264	-3.74106	-2.11871	-4.02067	-3.61884	-1.54609
	1d								
C	-1.79541	0.739147	-0.44897						
C	-1.77458	-1.48596	1.863732						
C	-1.59779	1.738843	0.73171						
C	-0.3065	1.540045	1.544992						
C	-0.34598	0.397717	2.57252						
C	-0.54283	-0.97306	1.971517						
O	-1.58465	1.512652	-1.66985						
C	-1.59542	3.071354	0.02901						
C	-1.49829	2.830636	-1.43366						
C	-1.666	4.295722	0.54689						
O	-1.36092	3.639301	-2.32816						

O	0.721127	1.34395	0.556426						
C	2.009988	1.477724	0.90363						
O	2.37569	1.836291	2.007282						
C	2.893078	1.066861	-0.23019						
C	4.064154	0.513272	0.115404						
C	5.078939	-0.12761	-0.78737						
C	2.347067	1.243034	-1.62274						
O	5.400082	-1.43728	-0.33386						
C	0.681481	-1.69274	1.455453						
O	0.671829	-1.68586	0.006334						
C	-2.17596	-2.68737	1.06067						
C	-2.493	-2.27116	-0.39006						
C	-3.51477	-1.14388	-0.45861						
C	-4.96095	-1.56309	-0.41645						
C	1.751222	-2.17174	-0.6093						
C	1.587886	-2.21327	-2.1008						
O	2.739911	-2.56152	-0.00796						
C	-3.17669	0.152817	-0.4922						
O	-2.94995	-3.44665	-1.05278						
H	-1.01637	-0.01612	-0.46341						
H	-2.59569	-0.90727	2.282365						
H	-2.43884	1.672344	1.424747						
H	-0.09405	2.466081	2.085579						
H	0.575897	0.442665	3.157219						
H	-1.16665	0.628506	3.256849						
H	-1.64032	5.165656	-0.10202						
H	-1.75167	4.461173	1.616332						
H	4.303642	0.45242	1.175029						
H	4.746539	-0.14821	-1.82975						
H	6.009916	0.443646	-0.75056						
H	3.028656	0.862519	-2.3826						
H	2.174114	2.303277	-1.82869						
H	1.384132	0.740089	-1.73033						
H	4.570614	-1.94488	-0.29366						
H	1.600493	-1.21503	1.79978						
H	0.702538	-2.73457	1.783416						
H	-1.38417	-3.44018	1.018623						
H	-3.06175	-3.15955	1.494951						
H	-1.55649	-1.94645	-0.84928						
H	-5.62262	-0.69694	-0.3686						
H	-5.22584	-2.15645	-1.2949						
H	-5.15241	-2.19402	0.457349						
H	2.535716	-1.97327	-2.58063						
H	0.803946	-1.53902	-2.44078						
H	1.3162	-3.23437	-2.37961						
H	-3.97377	0.896266	-0.50825						
H	-2.99461	-3.25923	-1.99971						

Table S2 : Energy analysis for 1*Z*,4*Z*,2'*Z*,3*R*,6*R*,7*R*,8*R*-**1**

Conf.	Steric Energy (kJ/mol)	Relative Energy (kJ/mol)	Distribution (%)[a]
1a	-1456.4846427	0	42.76
1b	-1456.4842800	0.0003627	29.11
1c	-1456.4839543	0.0006884	20.61
1d	-1456.4830024	0.0016403	7.51



eupalinolide N (**1**) eupalinolide I

Figure S12: The structures of eupalinolide N (**1**) and eupalinolide **I**

Table S3 : The ^{1}H and ^{13}C NMR data of **1** and eupalinolide I

	1		eupalinolide I	
Position	δ_H	δ_C	δ_H	δ_C
1	5.44, t (8.0)	132.3	5.42-5.44, m	129.9
2	2.69, t (13.7)	34.5	2.83-2.90, m	30.2
	2.18, q (11.7)		2.19-2.27, m	
3	4.56, dd (11.4, 5.1)	70.2	5.52, dd (11.5, 5)	71.3
4	-	141.8	-	135.4
5	5.19-5.23, m	124.8	5.25-5.29, m	125.0
6	5.35, d (10.5)	76.0	5.36, d (11)	74.0
7	3.19, s	49.4	3.07, s	48.0
8	5.19-5.23, m	81.2	5.25, s	78.9
9	2.97, d (12.5)	38.6	3.00, d (13)	38.1
	2.37, d (14.1)		2.35, d (14)	
10	-	133.8	-	133.6
11	-	139.5	-	136.9
12	-	171.8	-	169.3
13	6.27	125.6	6.34 d (2)	124.9
	5.92		5.85	
14	4.92, d (12.8)	63.7	4.96, d (13)	62.2
	4.62, d (12.8)		4.67, d (13)	
15	1.79, s	17.7	1.80, s	17.7
1′	-	167.5	-	166.3
2′	-	128.3	-	126.9
3′	6.73, t (5.1)	143.8	6.77, t (5.5)	142.5
4′	4.24, d (5.5)	59.8	4.29, d (6)	59.0
5′	1.76, s	12.6	1.78, s	12.3
1″	-	172.3		170.6
2″	1.99, s	20.7	2.10	20.7
1‴				169.9
2‴			2.02	20.5