Supporting Information

***Rec. Nat. Prod*. 17:2 (2023) 377-381**

Plagranline A, a Novel *β*-carboline and the First Alkaloid isolated from *Platycodon grandiflorus*

Ju-Tao Wang [1,2,3], Lan Ding [1], Ren-Nai Yang [1], Liang-Ping Zha[1,3]

Yang Yu [1,2,3], and Shuang-Ying Gui [1,4,5,6]

[1] School of Pharmacy, Anhui University of Chinese Medicine, Hefei, 230012, PR China

[2] Institute of Medicinal Chemistry, Anhui Academy of Chinese Medicine, Hefei 230012, PR China

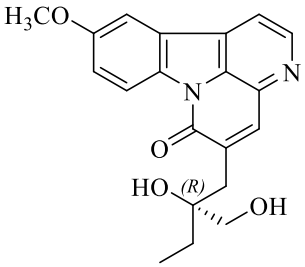
[3] Anhui Province Key Laboratory of Research & Development of Chinese Medicine, Hefei, 230012, PR China

[4] Institute of Pharmaceutics, Anhui Academy of Chinese Medicine, Hefei 230012, PR China

[5] Anhui Province Key Laboratory of Pharmaceutical Preparation Technology and Application, Hefei, Anhui, 230012, PR China

[6] Engineering Technology Research Center of Modernized Pharmaceutics，Anhui Education Department (AUCM), Hefei, Anhui, 230012, PR China

Table of Contents — **Page**



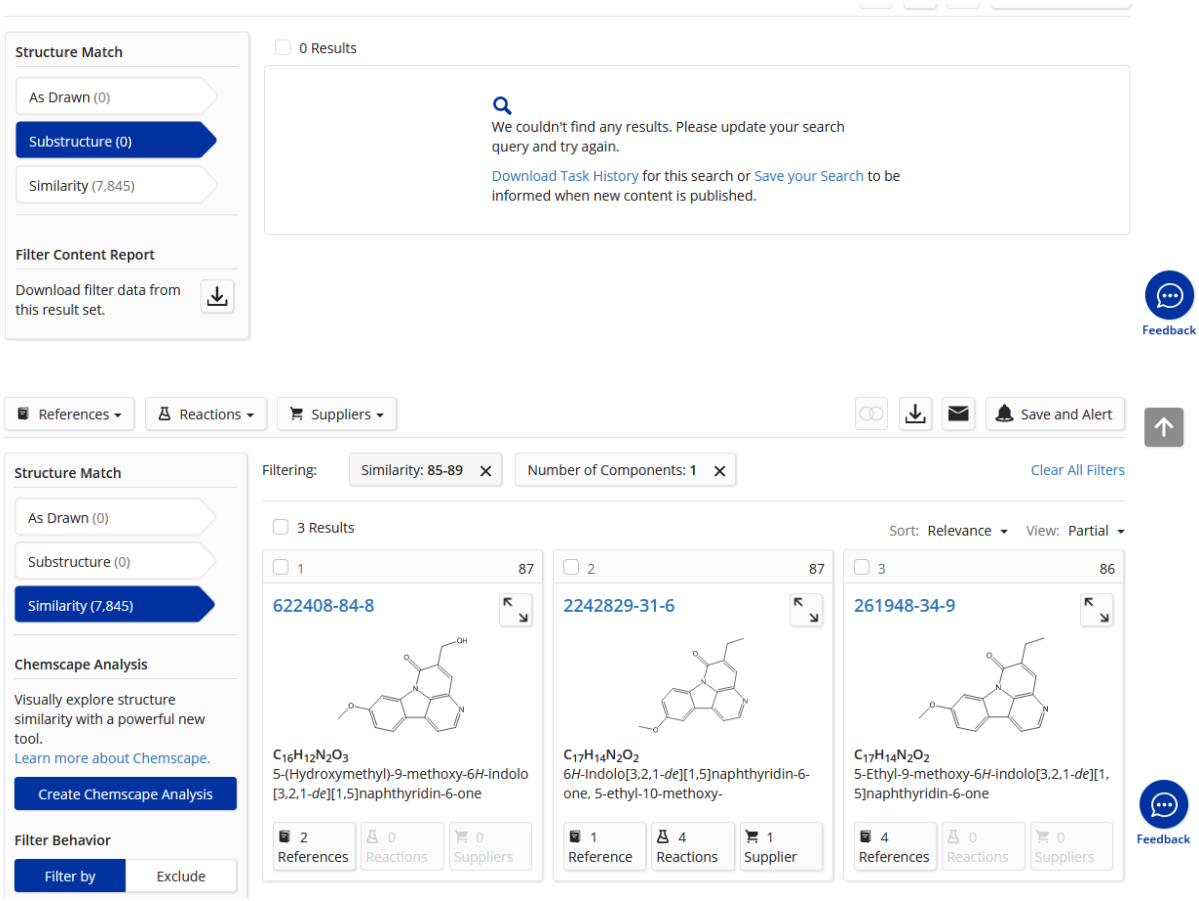
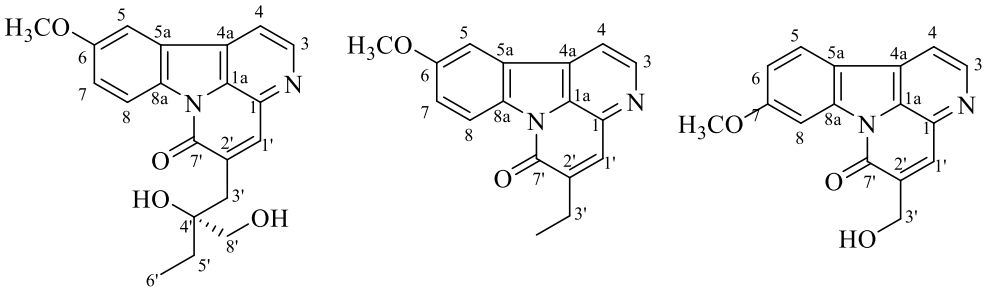


Figure S1: New compound (**1**) search report of SciFinder



1 **3** **4**

Figure S2: Most similar compounds **3** and **4** for the new compound **1**

Table S1. ^{1}H and ^{13}C NMR spectroscopic data for **1**, **3** and **4** (δ in ppm and J in Hz)

NO.	**1**[a]		**3**[b]		**4**[c]	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		137.4, C		136.8, C		130.7, C
1a		132.4, C		131.4, C		135.3, C
3	8.83 (d, 4.9)	146.9, CH	8.76 (d, 5.0)	145.7. CH	8.78 (d, 5.0)	146.0, CH
4	8.20 (d, 4.9)	117.1, CH	7.84 (d, 5.0)	115.3, CH	8.17 (d, 5.0)	115.7, CH
4a		130.5, C		129.6, C		129.2, C
5	7.94 (d, 2.5)	107.9, CH	7.52 (d, 2.5)	106.6, CH	8.29 (d, 8.7)	124.6, CH
5a		127.3, C		126.0, C		117.5, C
6		159.1, C		157.8, C		113.2, C
7	7.36 (dd, 8.8, 2.5)	118.6, CH	7.23 (dd, 10.0, 2.5)	118.0, CH	7.20 (dd, 8.7, 2.3)	113.2, CH
8	8.54 (d, 8.8)	118.5, CH	8.55 (5.0)	117.6, CH	8.09 (d, 2.3)	101.1, CH
8a		134.5, C		133.8, C		140.3, C
6-OCH_3	3.97 (s)	56.2, CH_3	3.95 (s)	55.9, CH_3		55.8, CH_3
1′	8.06 (s)	139.8, CH	7.81 (s)	133.9, CH	8.02 (s)	133.1, CH
2′		138.7, C		143.8, C		141.3, C
3′	2.97 (d, 13.7) 3.13 (d, 13.7)	38.4, CH_2	2.83 (q, 7.5)	24.2, CH_2	4.60 (d, 5.4)	58.7, CH_2
4′		75.5, C	1.36 (t, 7.5)	12.7, CH_3		
4′-OH	3.91 (s)					
5′	1.64 (q, 7.5) 1.69 (q, 7.5)	30.7, CH_2				
6′	1.00 (t, 7.5)	7.8, CH_3				
7′		162.3, C		159.7, C		158.4, C
8′	3.37 (dd, 11.3, 5.6) 3.41 (dd, 11.3, 6.9)	66.6, CH_2				

a): the ^{1}H and ^{13}C NMR data of compound **1** were recorded at 800 MHz and 200 MHz, with acetone-*d6*as solvent, respectively. b): the ^{1}H and ^{13}C NMR data of the compound **3** reported in the literature [1] were recorded with a Bruker DRX-500, with DMSO-d_6 as solvent . c): the ^{1}H and ^{13}C NMR data of the compound **4** reported in the literature [2] were recorded with a Bruker DRX-400, with DMSO-d_6 as solvent .

Formula Predictor Report - G-2.lcd

Page 1 of 1

Data File: E:\DATA\2022\0530\1\G-2.lcd

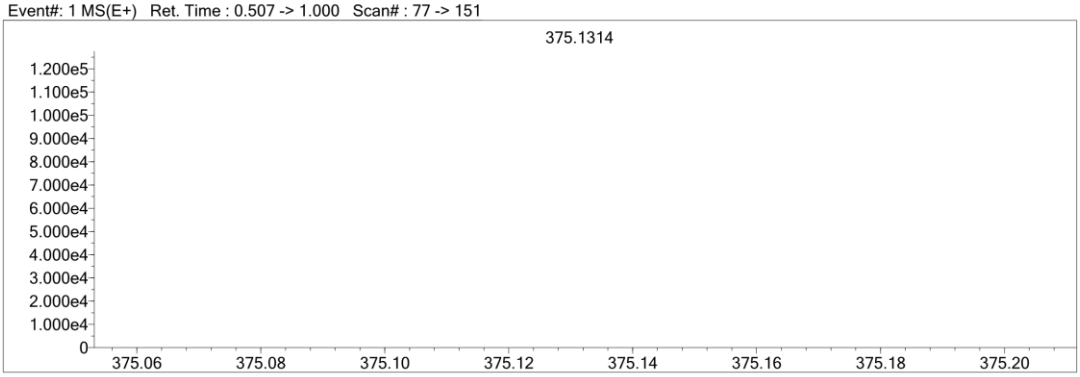
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	5	100	F	1	0	0	Cl	1	0	0	Ag	1	0	0	H
2H	1	0	0	Na	1	0	0	Co	2	0	0	I	3	0	0	Na
B	3	0	0	Mg	2	0	0	Cu	2	0	0	Ir	3	0	0	
C	4	5	50	Si	4	0	0	Se	2	0	0					
N	3	0	5	P	3	0	0	Br	1	0	0					
O	2	0	30	S	2	0	0	Pd	2	0	0					

Error Margin (ppm): 5
HC Ratio: unlimited
Max Isotopes: all
MSn Iso RI (%): 75.00

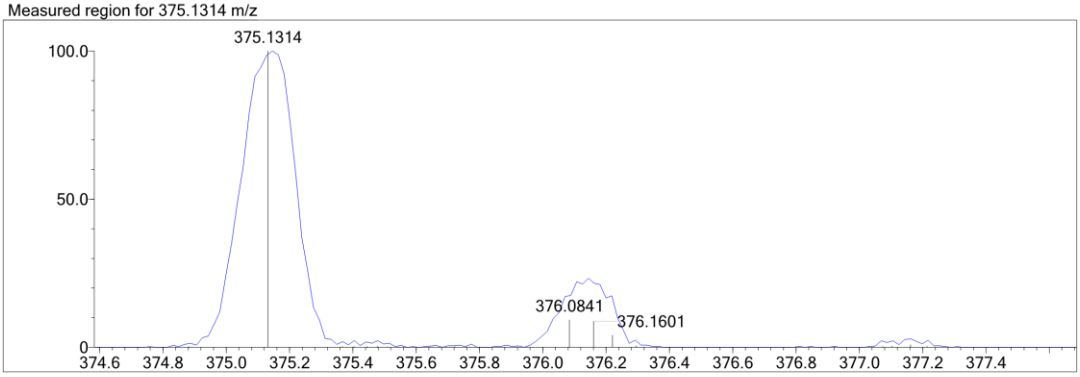
DBE Range: not fixed
Apply N Rule: no
Isotope RI (%): 1.00
MSn Logic Mode: OR

Electron Ions: both
Use MSn Info: yes
Isotope Res: 10000
Max Results: 30

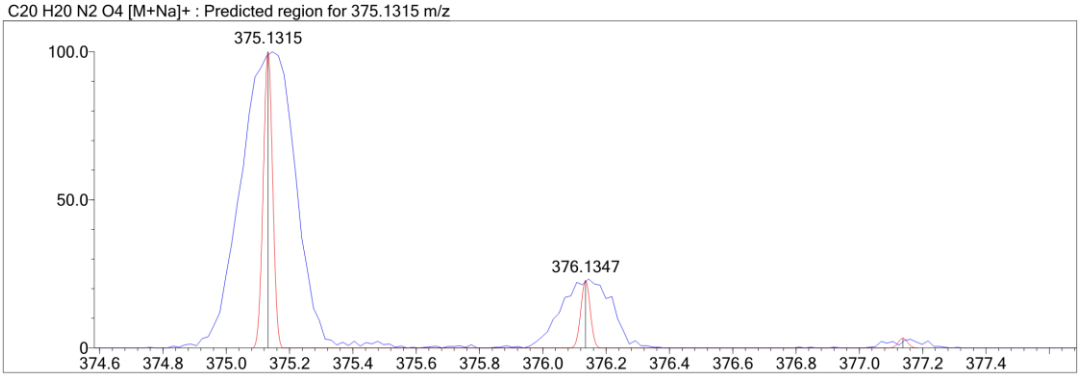
Event#: 1 MS(E+) Ret. Time : 0.507 -> 1.000 Scan# : 77 -> 151



Measured region for 375.1314 m/z



C20 H20 N2 O4 [M+Na]+ : Predicted region for 375.1315 m/z



Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	DBE
C20 H20 N2 O4	[M+Na]+	375.1314	375.1315	-0.1	-0.27	12.0

Figure S3: HR-ESI-MS spectrum of **1** ((Plagranline A)

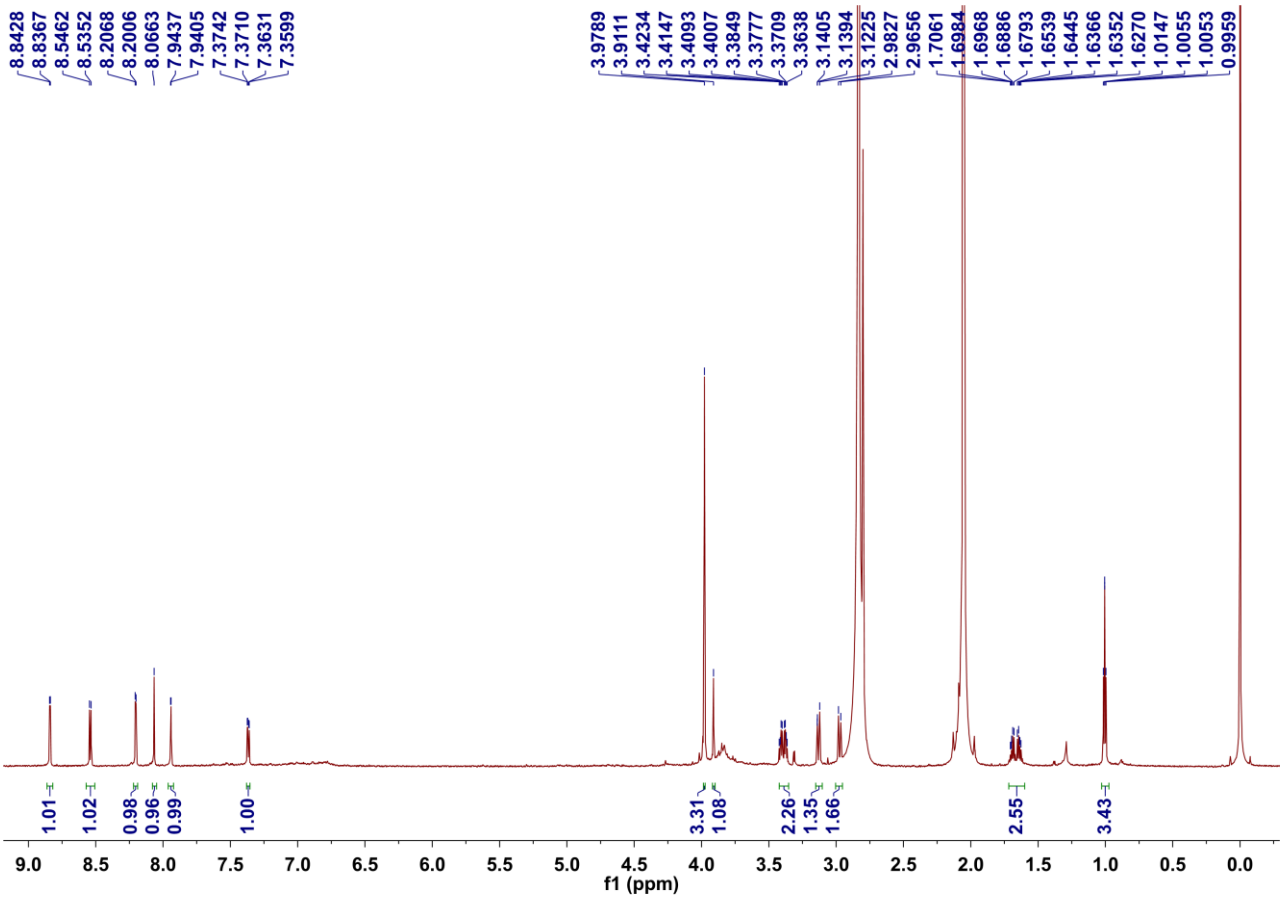


Figure S4: ^{1}H-NMR (800 MHz, acetone-*d6*) spectrum of **1** (Plagranline A)

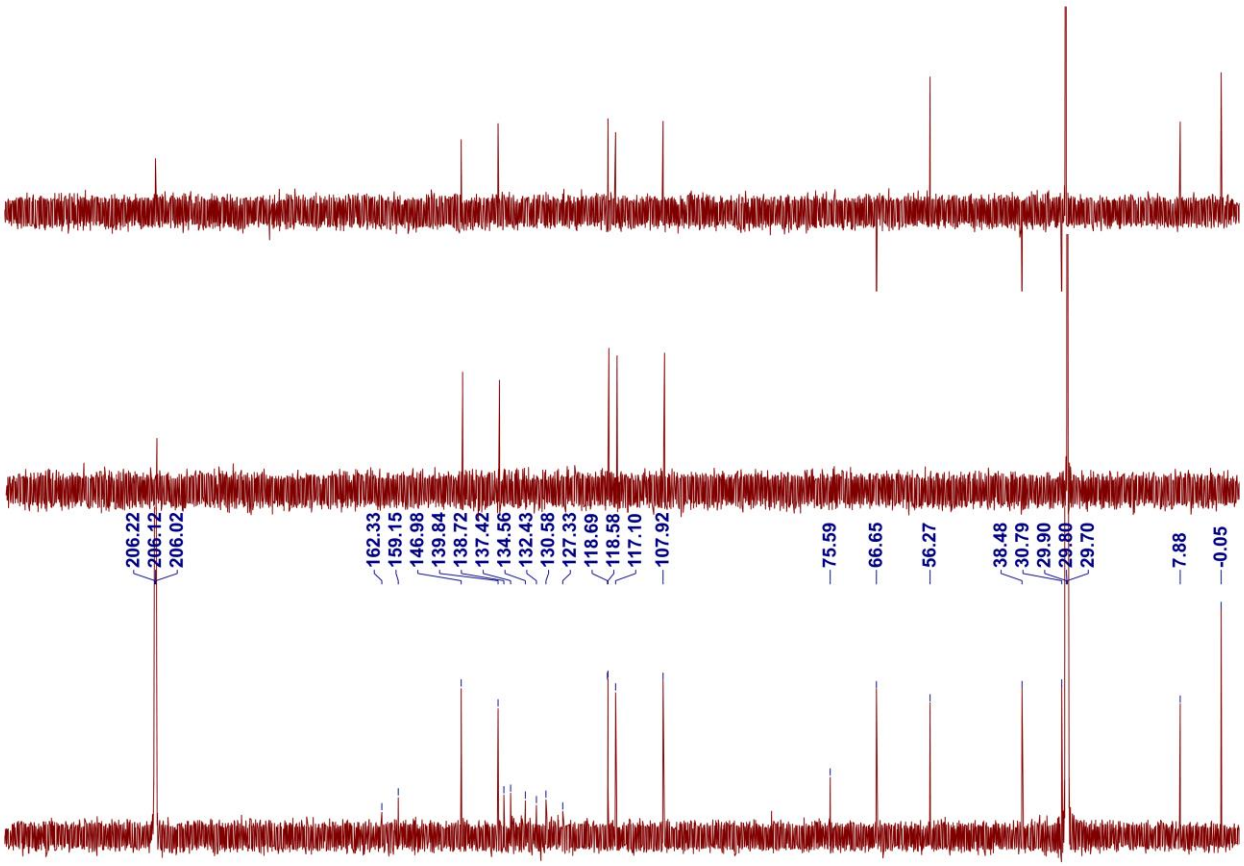


Figure S5: ^{13}C-NMR and DEPT (200 MHz, acetone-*d6*) spectrum of **1** (Plagranline A)

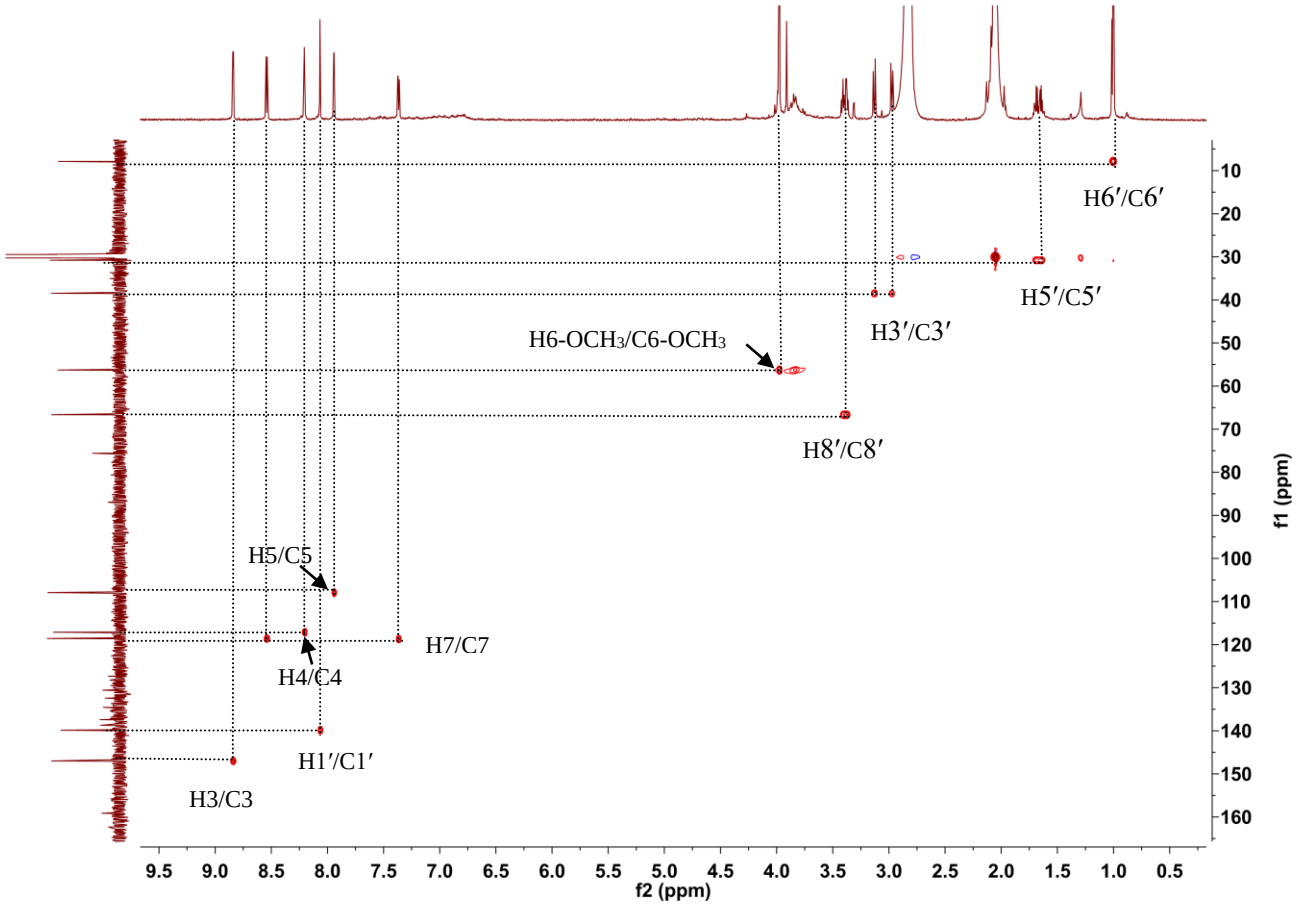


Figure S6: HSQC spectrum of **1** (Plagranline A)

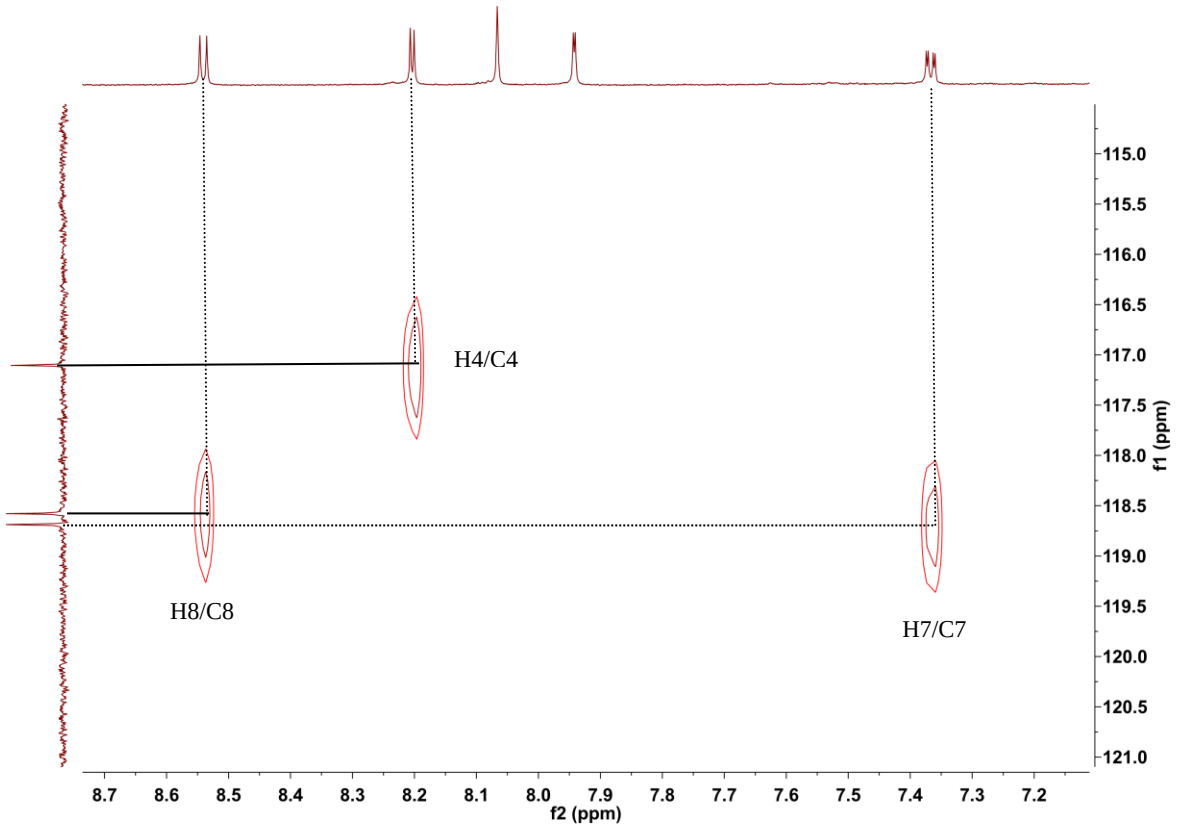


Figure S7: HSQC spectrum of **1** (Plagranline A) (From δ_C115 ppm to δ_C 120 ppm)

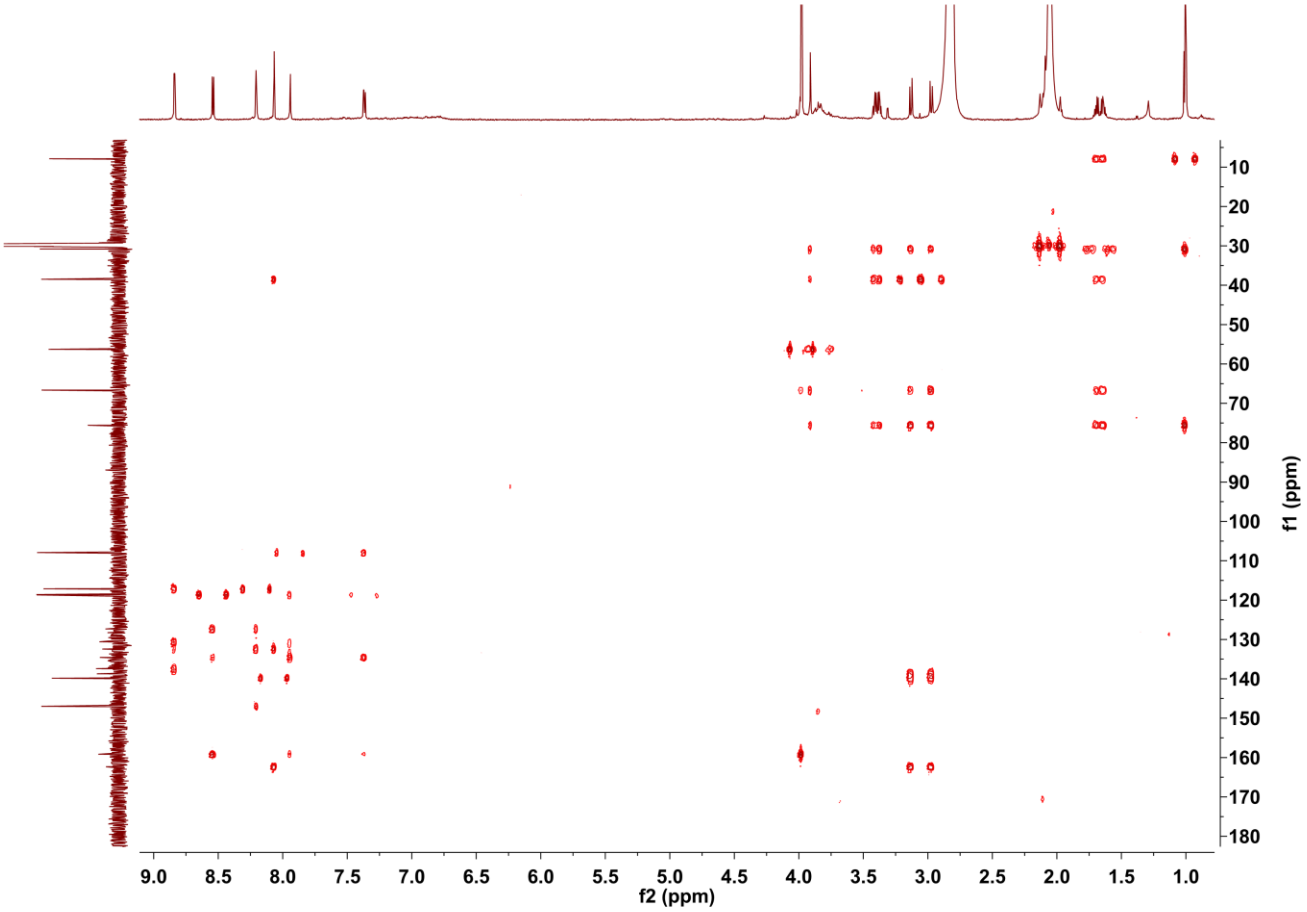


Figure S8: HMBC spectrum of **1** (Plagranline A)

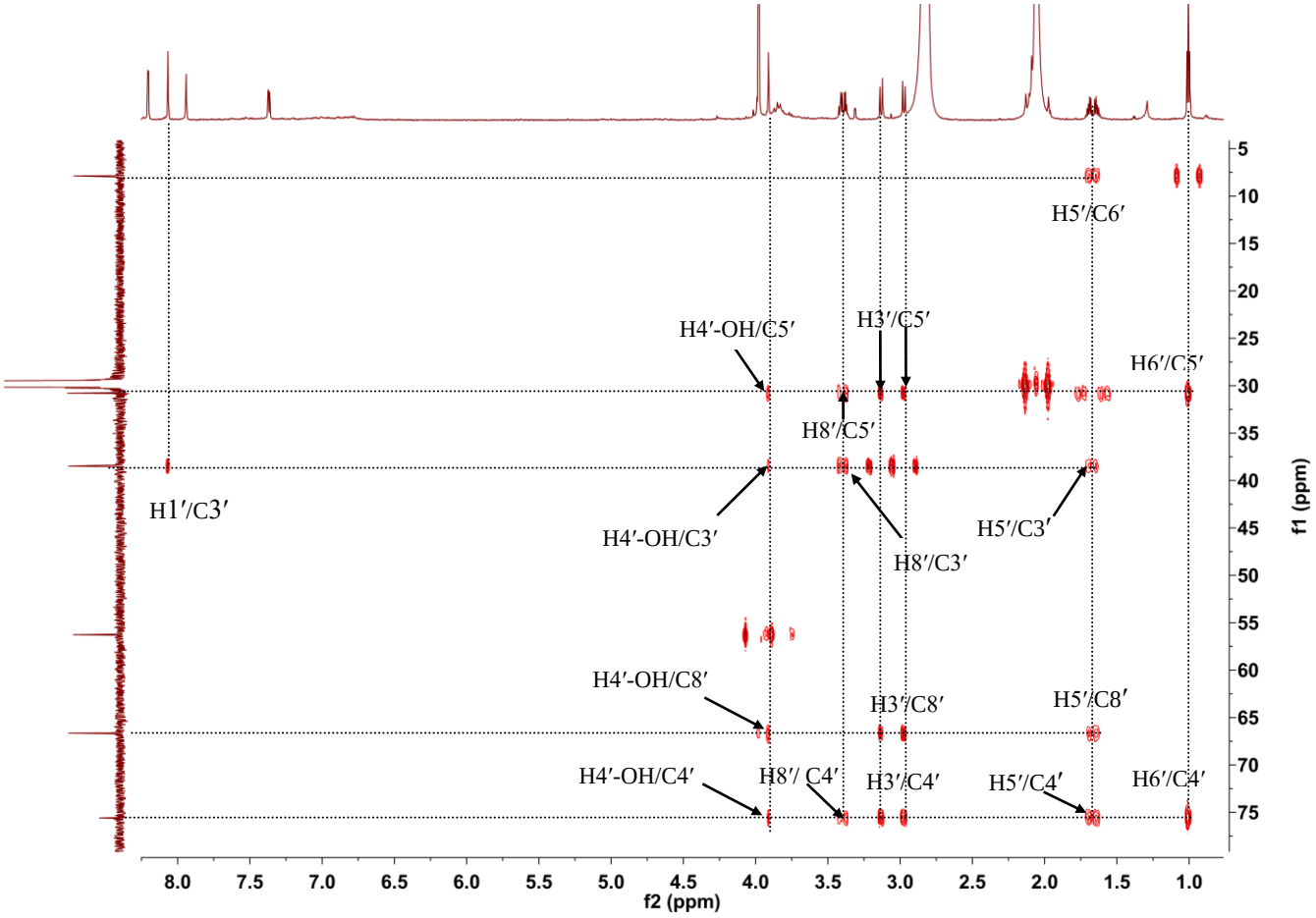


Figure S9: HMBC spectrum of **1** (Plagranline A) (From δ_C 5 pm to δ_C 75 ppm)

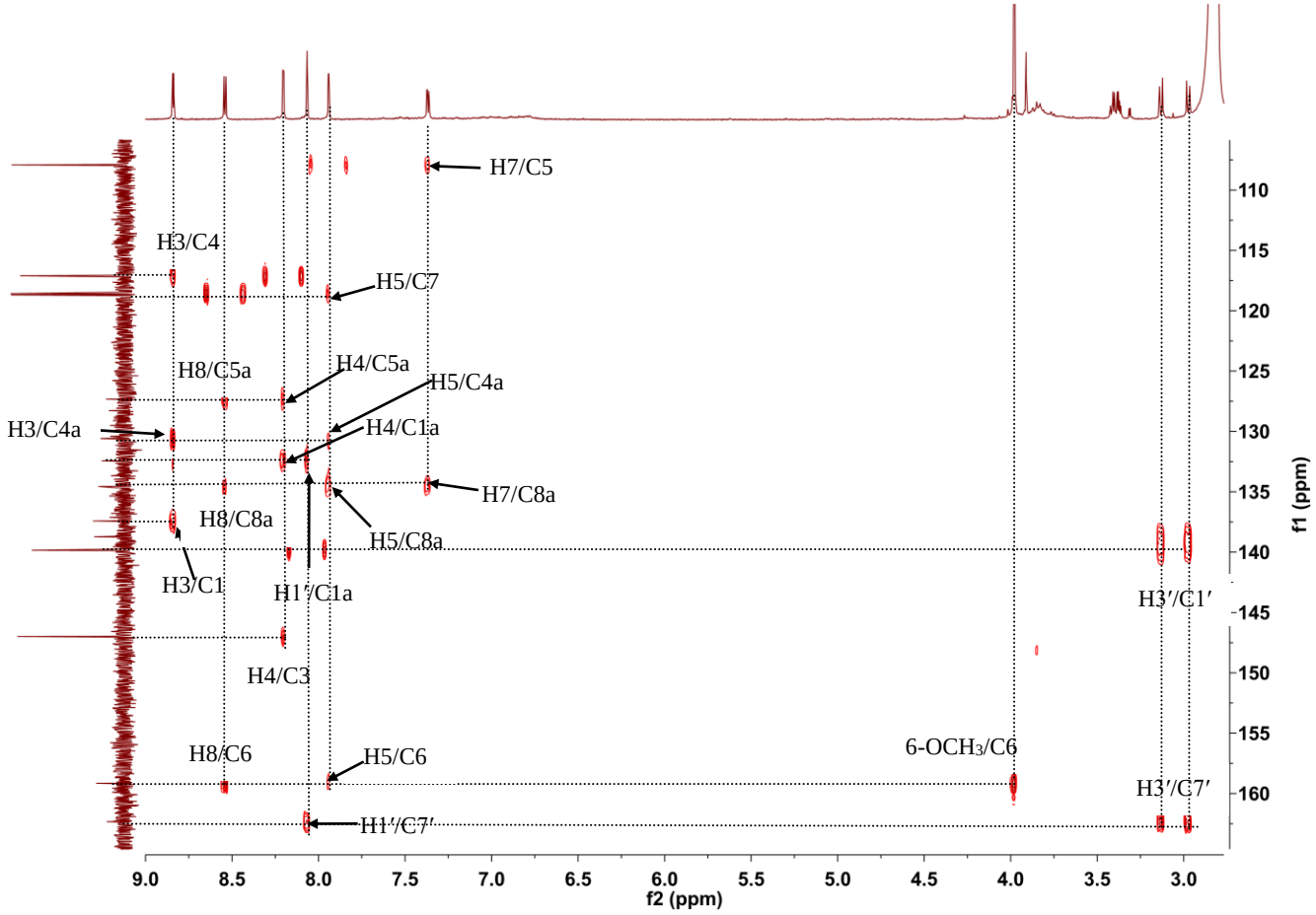


Figure S10: HMBC spectrum of **1** (Plagranline A) (From δ_C 110 ppm to δ_C 160 ppm)

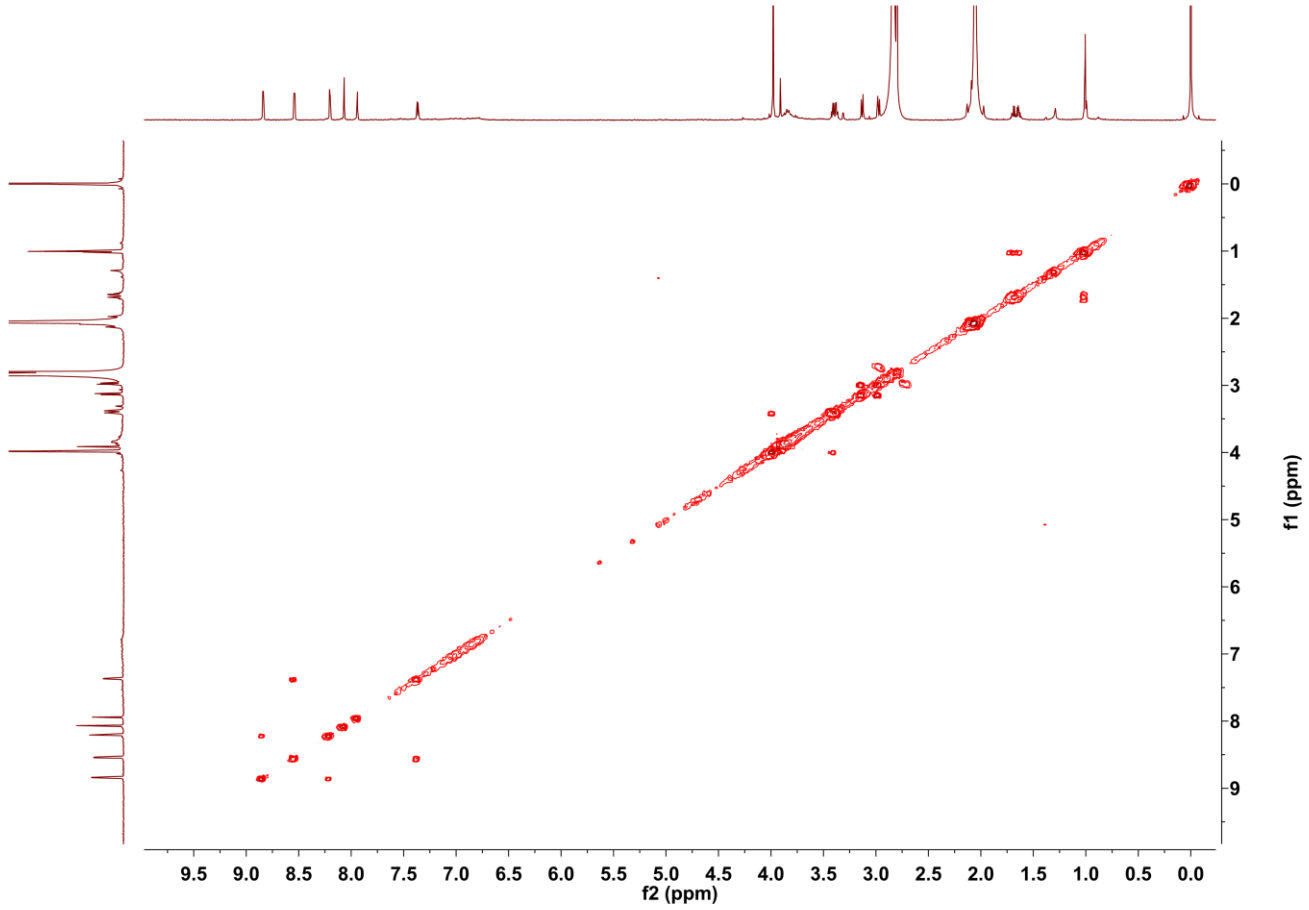


Figure S11: ^{1}H-^{1}H COSY spectrum of **1** (Plagranline A)

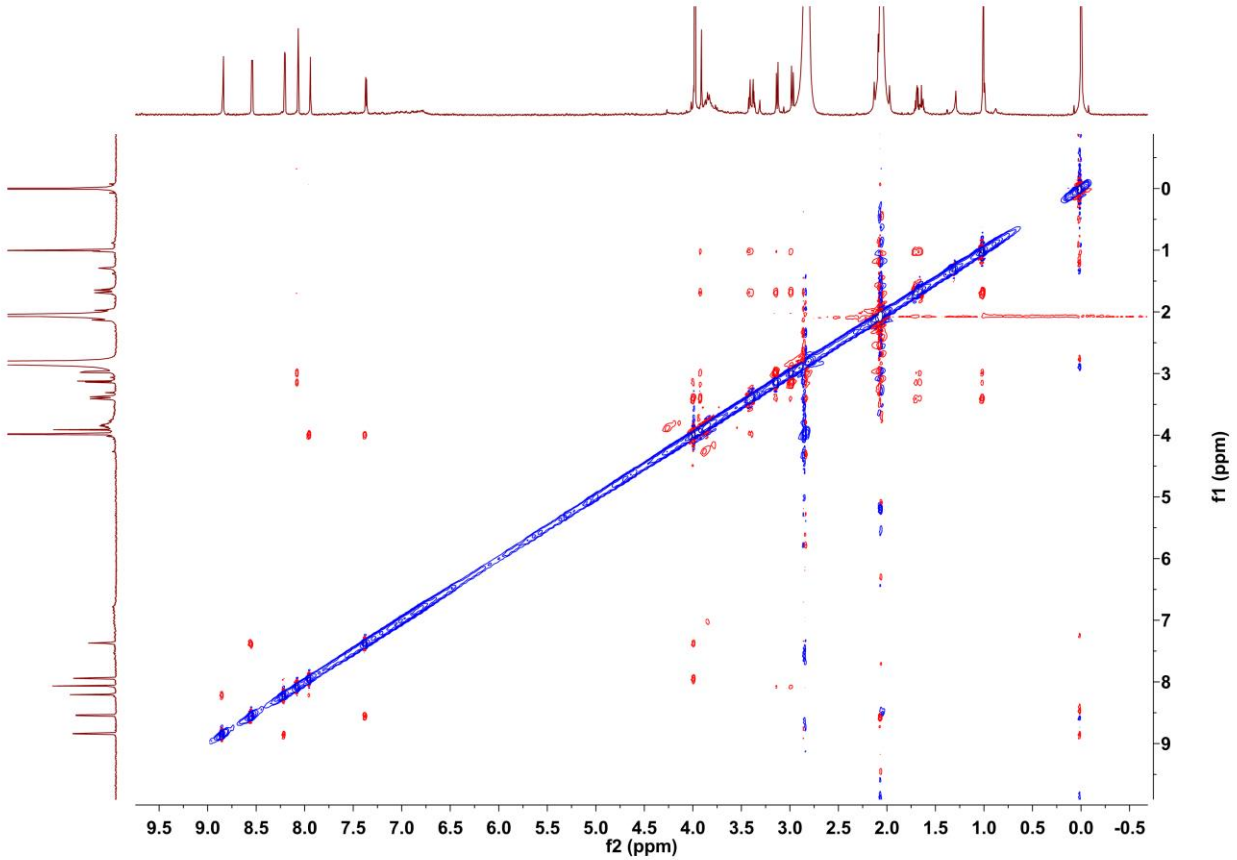


Figure S12: NOESY spectrum of **1** (Plagranline A)

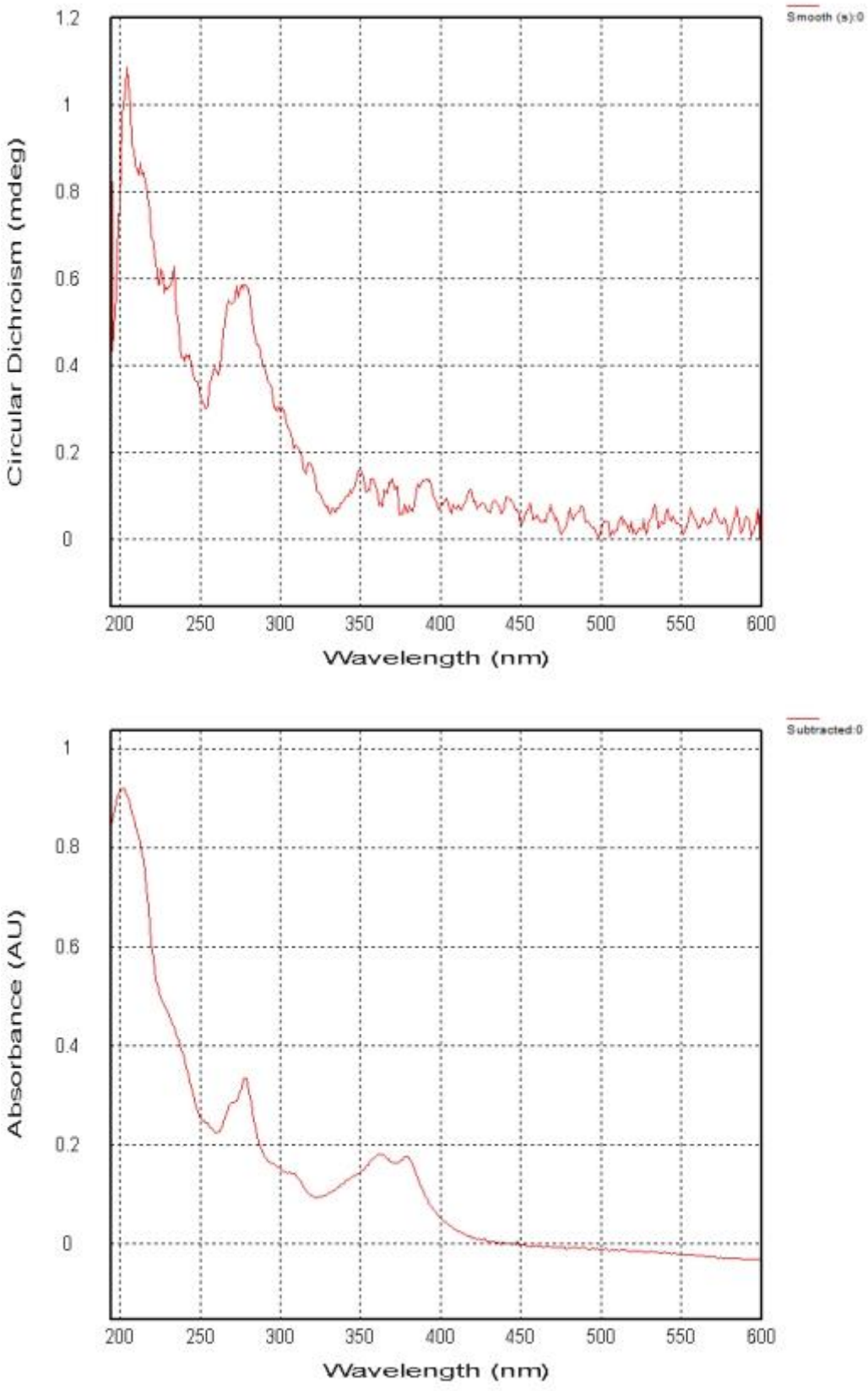


Figure S13: CD and UV spectrum of compound **1** in MeOH

Rudolph Research Analytical

This sample was measured on an Autopol VI, Serial #91058
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Measurement Date : Saturday, 28-MAY-2022

Set Temperature : OFF

Time Delay : Disabled

Delay between Measurement : Disabled

n	Average	Std.Dev.	% RSD	Maximum	Minimum
5	-21.30	1.11	-5.21	-19.67	-22.33

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG.nm	Lg.mm	Conc.g/100ml	Temp.
1	G-2	11:04:09 AM	-20.67	SR	-0.0124	589	100.00	0.060	24.3
2	G-2	11:04:17 AM	-21.83	SR	-0.0131	589	100.00	0.060	24.3
3	G-2	11:04:26 AM	-22.33	SR	-0.0134	589	100.00	0.060	24.3
4	G-2	11:04:34 AM	-22.00	SR	-0.0132	589	100.00	0.060	24.3
5	G-2	11:04:42 AM	-19.67	SR	-0.0118	589	100.00	0.060	24.3

Page 1 of 1

Figure S14: ORD spectrum of compound **1** in MeOH

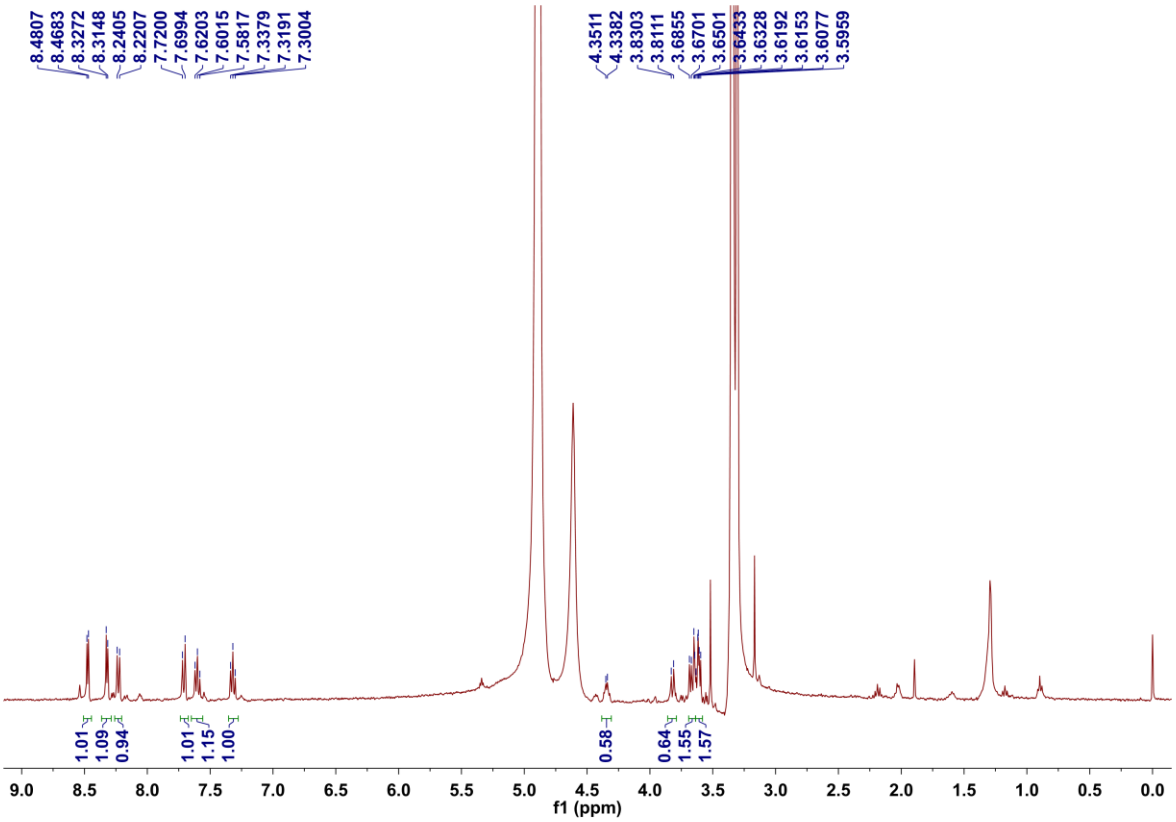


Figure S15: ^{1}H-NMR spectrum of compound **2** in CD_3OD

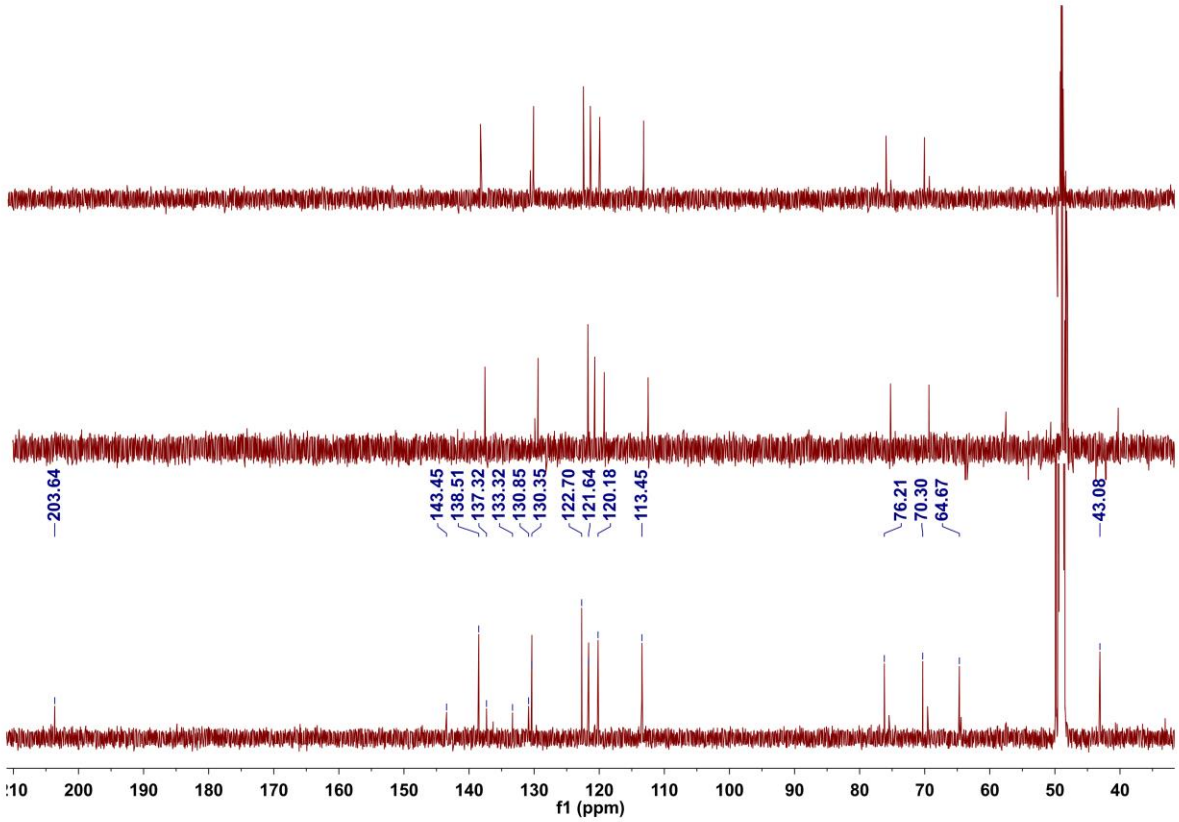


Figure S16: ^{13}C NMR and DEPT spectrum of compound **2** in MeOH

S1: ECD Computational details of compound 1

The initial conformational analysis of compounds **1** was performed using Monte Carlo searching algorithm via the MMFF94 molecular mechanics force field [3], with the aid of SPARTAN'16 program package, leading to a panel of relatively favored conformations in an energy range of 3 kcal/mol above the global minimum. The force field minimum energy conformers were subsequently optimized by applying the density functional theory (DFT) with the B3LYP/def2-SVP level in a vacuum, implemented in the Gaussian 09 software package. Harmonic vibrational frequencies were also analyzed to confirm no imaginary frequencies of the optimized conformers. These predominant conformers were subjected to theoretical calculation of ECD by utilizing Time-dependent density functional theory (TDDFT) calculations at the M06-2X-D3/def2-TZVP level in MeOH solvent using the Polarizable Continuum Model (PCM) and ORD by TDDFT at the APFD/6-311++g(2d,2p) (589 nm). The energies, oscillator strengths, and rotational strengths of each conformer were calculated with Gaussian 09 software package. Theoretical calculations of ECD spectra and ORD value for each conformer were then approximated by the Gaussian distribution. The final ECD and ORD data of individual conformer was summed up based on Boltzmann-weighed population contribution by the SpecDisv 1.64 [4].

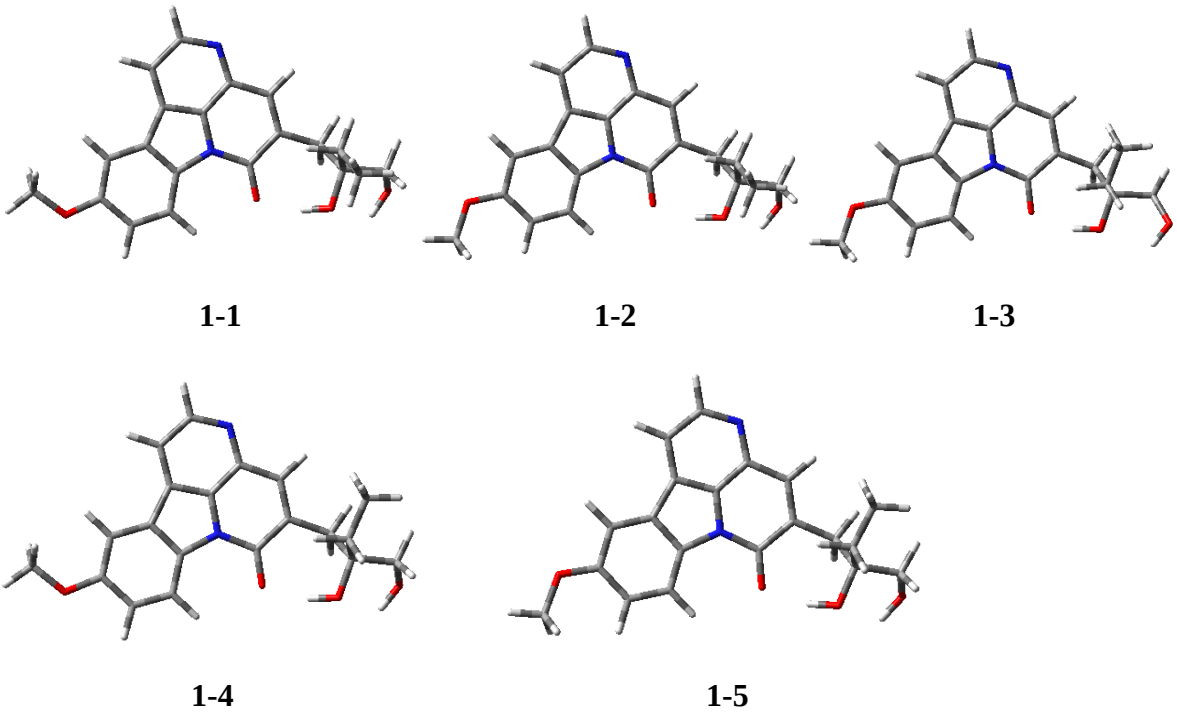


Figure S17 : Optimized geometries of 5 dominant conformers of **1**

at the B3LYP/def2-SVP level in the gas phase

Table S2 : Important thermodynamic parameters (A. U.) of the optimized conformers of **1** in the gas phase

Conformers	**Electronic energy(A. U.)**	**Thermal correction to Gibbs Free Energy (A. U.)**	**Gibbs free energy (kcal/mol)**
1-1	-1183.73021	0.321644	-742599.9993
1-2	-1183.729722	0.32191	-742599.6781
1-3	-1183.729572	0.321518	-742599.5262
1-4	-1183.727601	0.320196	-742599.271
1-5	-1183.727004	0.320245	-742598.8651

Table S3 : Conformational analysis of the optimized conformers of **1** in the gas phase (T=298.15 K)

Conformers	ΔG (kcal/mol)	Population
1-1	0.0000	40.48%
1-2	0.3213	23.53%
1-3	0.4731	18.21%
1-4	0.7284	11.83%
1-5	1.1342	5.96%

Table S4 : Cartesian coordinates of low-energy conformers of **1** optimized at B3LYP/def2-SVP level in gas phase

Atom	Conformers 1-1			Conformers 1-2			Conformers 1-3		
	X	Y	Z	X	Y	Z	X	Y	Z
C	-4.38335	-1.56063	0.067375	-4.50097	-1.17947	0.112157	-4.44465	-1.454	0.153493
C	-3.31366	-2.4612	-0.14225	-3.50056	-2.14784	-0.10921	-3.4109	-2.41118	0.033612
C	-2.00094	-2.02155	-0.28314	-2.1566	-1.7834	-0.26199	-2.07853	-2.03816	-0.11537
C	-1.76782	-0.64624	-0.21072	-1.83429	-0.43337	-0.18973	-1.78831	-0.67214	-0.14392
C	-2.82609	0.275501	-0.00022	-2.83209	0.559498	0.033885	-2.80996	0.305747	-0.02567
C	-4.14383	-0.18095	0.140077	-4.16449	0.183855	0.18433	-4.14798	-0.08387	0.12425
N	-0.5518	0.078512	-0.32135	-0.57551	0.213578	-0.31023	-0.54093	-0.00848	-0.28611
C	-0.85602	1.411547	-0.17855	-0.79207	1.563541	-0.16121	-0.79124	1.342641	-0.25333
C	-2.23139	1.611931	0.022465	-2.14877	1.854653	0.053274	-2.16008	1.614467	-0.09628
C	0.080552	2.439484	-0.22109	0.20974	2.528221	-0.21016	0.187994	2.324533	-0.36171
N	-0.32274	3.714742	-0.06646	-0.10798	3.826876	-0.04886	-0.16314	3.623603	-0.319
C	-1.62543	3.936131	0.125643	-1.391	4.133104	0.15574	-1.45825	3.912839	-0.17072
C	-2.62822	2.941179	0.181227	-2.45673	3.205599	0.218736	-2.50284	2.967357	-0.05391
C	0.755127	-0.36373	-0.50744	0.697269	-0.31193	-0.50901	0.748317	-0.51789	-0.41908
C	1.783883	0.708136	-0.59391	1.792693	0.690212	-0.60089	1.824344	0.500817	-0.56323
C	1.446387	2.028282	-0.44807	1.54347	2.0294	-0.44946	1.538281	1.840873	-0.5301
O	1.004158	-1.56646	-0.58991	0.86651	-1.52874	-0.59702	0.943056	-1.73317	-0.41527
C	3.201026	0.291203	-0.91354	3.177907	0.18198	-0.92911	3.231106	0.008504	-0.82302
C	4.003789	-0.53956	0.136665	3.931526	-0.69449	0.119887	3.968938	-0.80718	0.284299
C	3.888545	0.083948	1.544123	3.870322	-0.05684	1.524211	3.837854	-0.18777	1.689686
O	3.587607	-1.90097	0.149409	3.423173	-2.02437	0.144847	3.50489	-2.15256	0.326634
C	5.469097	-0.61609	-0.34768	5.384518	-0.87313	-0.37513	5.450107	-0.96097	-0.13256
C	4.570447	-0.7029	2.665169	4.501239	-0.88469	2.645615	4.447759	1.201105	1.895063
O	5.554329	-1.30437	-1.5709	5.413449	-1.5768	-1.59218	5.560523	-1.73864	-1.29632
O	-5.60784	-2.12955	0.186619	-5.8165	-1.4684	0.268325	-5.69376	-1.96124	0.293385
C	-6.73551	-1.30947	0.395837	-6.2484	-2.81042	0.214247	-6.78854	-1.08208	0.421333
H	-3.55216	-3.5254	-0.19066	-3.76035	-3.20475	-0.16472	-3.69351	-3.46525	0.0624
H	-1.17737	-2.71528	-0.44368	-1.38161	-2.52902	-0.43192	-1.2829	-2.77565	-0.20695
H	-4.95221	0.531508	0.301455	-4.95806	0.912732	0.357165	-4.92755	0.671915	0.214253
H	-1.9188	4.984953	0.248292	-1.61372	5.198577	0.283264	-1.70913	4.97925	-0.13982
H	-3.66929	3.227781	0.344361	-3.47569	3.557688	0.392366	-3.53343	3.308786	0.064043
H	2.209093	2.807998	-0.51647	2.355364	2.757408	-0.52174	2.332431	2.582198	-0.64856
H	3.215057	-0.29395	-1.84701	3.148082	-0.40661	-1.86005	3.243021	-0.62513	-1.72477
H	3.771493	1.209816	-1.11664	3.804804	1.061464	-1.139	3.842569	0.890355	-1.06372
H	4.275206	1.119067	1.508395	4.330442	0.947532	1.480304	2.765882	-0.16453	1.952217
H	2.815072	0.17466	1.783254	2.807664	0.111946	1.768939	4.29652	-0.90594	2.389308
H	2.640713	-1.9496	-0.093	2.475254	-2.01065	-0.09877	2.556232	-2.17119	0.087406

H	5.886146	0.393982	-0.49218	5.866987	0.105357	-0.53279	5.91364	0.017603	-0.3333
H	6.069833	-1.11775	0.43509	5.957122	-1.4065	0.407851	5.992497	-1.42017	0.720685
H	4.319069	-0.27502	3.648554	4.286354	-0.43546	3.628138	4.284569	1.544152	2.929032
H	4.237361	-1.75131	2.648373	4.094827	-1.90698	2.635742	5.535436	1.206732	1.721058
H	5.668025	-0.69747	2.577267	5.595959	-0.9573	2.551862	4.000556	1.957202	1.230469
H	5.009437	-2.09741	-1.43126	4.815194	-2.32829	-1.44144	4.959058	-2.48584	-1.13364
H	-7.60273	-1.97993	0.459598	-7.33554	-2.79397	0.367992	-7.68421	-1.70961	0.519558
H	-6.65734	-0.73576	1.33713	-6.03334	-3.27277	-0.76593	-6.6999	-0.4432	1.318695
H	-6.89038	-0.60314	-0.43984	-5.78469	-3.42405	1.007455	-6.90151	-0.43459	-0.46705

Atom	Conformers **1-4**			Conformers **1-5**		
	X	Y	Z	X	Y	Z
C	-4.51255	-1.1492	0.180205	-4.55298	-1.05157	0.159785
C	-3.53236	-2.13511	-0.05366	-3.59453	-2.0761	0.021212
C	-2.1872	-1.7931	-0.24334	-2.23353	-1.78286	-0.1345
C	-1.84257	-0.44746	-0.19499	-1.85112	-0.44672	-0.14931
C	-2.82011	0.562973	0.040014	-2.80614	0.602251	-0.01058
C	-4.15401	0.20955	0.227032	-4.15606	0.297175	0.14348
N	-0.5771	0.178824	-0.35136	-0.56262	0.13436	-0.29117
C	-0.77037	1.532956	-0.21365	-0.72042	1.499294	-0.23777
C	-2.11746	1.847695	0.027505	-2.06553	1.864278	-0.06816
C	0.243928	2.481315	-0.29765	0.3243	2.412762	-0.33692
N	-0.04967	3.78691	-0.14749	0.063721	3.732436	-0.27326
C	-1.32289	4.115602	0.081613	-1.20698	4.108698	-0.1134
C	-2.40074	3.205264	0.181612	-2.31434	3.235846	-0.00392
C	0.682431	-0.37112	-0.57607	0.687121	-0.46017	-0.43702
C	1.793174	0.613575	-0.69148	1.830422	0.483489	-0.56841
C	1.564704	1.957888	-0.55439	1.637264	1.839677	-0.51639
O	0.821243	-1.59089	-0.6652	0.796729	-1.68667	-0.4526
C	3.171785	0.087698	-1.03079	3.200454	-0.10168	-0.83208
C	3.863122	-0.91518	-0.06116	3.875069	-0.97877	0.268691
C	3.654564	-0.58517	1.434248	3.776473	-0.36926	1.680988
O	3.420147	-2.24497	-0.3031	3.319651	-2.2898	0.292306
C	5.362239	-0.97875	-0.42439	5.344589	-1.22913	-0.14156
C	4.163646	0.770173	1.929323	4.478756	0.971654	1.909737
O	5.995702	-2.03795	0.243256	5.409282	-2.0001	-1.31317
O	-5.82788	-1.41624	0.372381	-5.88211	-1.27034	0.31468
C	-6.27987	-2.75261	0.352658	-6.37308	-2.59245	0.35328
H	-3.80917	-3.18852	-0.09007	-3.90117	-3.12179	0.033622
H	-1.42829	-2.55272	-0.42307	-1.49135	-2.57234	-0.24065
H	-4.932	0.952538	0.410284	-4.91789	1.070794	0.253162
H	-1.5267	5.185963	0.199243	-1.38316	5.189328	-0.06564
H	-3.40997	3.575444	0.373523	-3.31882	3.644044	0.125668
H	2.385337	2.673553	-0.64854	2.480651	2.526002	-0.62551
H	3.126944	-0.42302	-2.00837	3.170992	-0.72457	-1.74088
H	3.82918	0.961459	-1.16229	3.873075	0.737945	-1.06002
H	2.577669	-0.6863	1.655088	2.706273	-0.27636	1.935562

H	4.156403	-1.39007	1.993087	4.179184	-1.12617	2.374217
H	2.447617	-2.23104	-0.3993	2.373123	-2.23972	0.04868
H	5.439663	-1.08493	-1.52708	5.875672	-0.28282	-0.32935
H	5.877274	-0.04572	-0.14541	5.848876	-1.73343	0.709644
H	3.94208	0.894599	3.001306	4.328866	1.312685	2.946393
H	5.25494	0.864045	1.814074	5.566026	0.903738	1.746446
H	3.695702	1.61752	1.403459	4.092548	1.765215	1.250568
H	5.393675	-2.79284	0.13768	4.756776	-2.70585	-1.16251
H	-7.36211	-2.71784	0.535177	-7.4599	-2.51693	0.490743
H	-6.09805	-3.23441	-0.62489	-6.16915	-3.13512	-0.58732
H	-5.80343	-3.35951	1.143491	-5.94537	-3.16544	1.195574

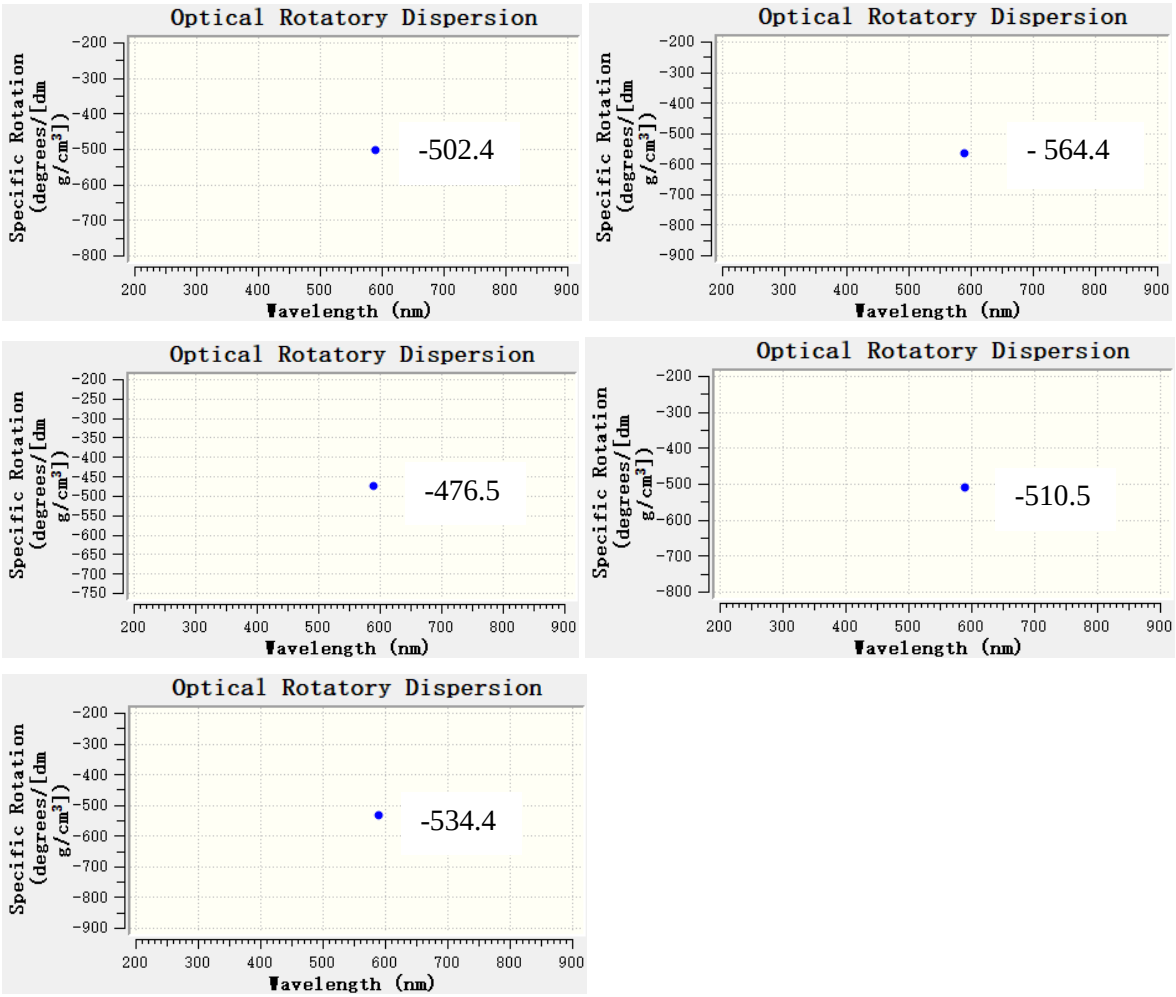


Figure S18 : Calculated specific rotation of compound **1-1-1-5** (**1**: Boltzmann-weighed population: -(502.4 × 40.48% + 564.4 ×23.53% +476.5 ×18.21 % + 510.5 ×11.83%+ 534.4 ×5.96%)= -515.1).

References

[1] J. K. Dai, W. J. Dan, Y. Y. Zhang, M. F. He and J. R. Wang (2018). Design and synthesis of C-10 modified and ring-truncated canthin-6-one analogues as effective membrane-active antibacterial agents, *Bioorg. Med. Chem. Lett*. **28**, 3123-3128.

[2] P. C. Kuo, L. S. Shi, A. G. Damu, C. R. Su, C. H. Huang, C. H. Ke, J. B. Wu, A. J. Lin, K. F. Bastow, K. H. Lee and T. S. Wu (2003). Cytotoxic and antimalarial β-carboline alkaloids from the roots of *Eurycoma longifolia*, *J. Nat. Prod*. **66**, 1324-1327.

[3] T. A. Halgren (1999). MMFF VII. Characterization of MMFF94, MMFF94s, and other widely available force fields for conformational energies and for intermolecular-interaction energies and geometries, *J. Comput. Chem*. **20**, 730-748.

[4] T. Bruhn, A. Schaumloffel, Y. Hemberger and G. Bringmann (2013). SpecDis: Quantifying the comparison of calculated and experimental electronic circular dichroism spectra, *Chirality* **25**, 243-249.