

# Supporting Information

## **Atkamine: A new pyrroloiminoquinone scaffold from the cold water Aleutian Islands *Latrunculia* sponge**

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## 1. NMR spectra data for atkamine

Table S1. 1D and 2D NMR data of atkamine

Atom No.	$\delta$ C (in DMSO)	$\delta$ H (mult, J, Hz) (in DMSO)	COSY (in DMSO)	HMBC (in DMSO)	NOESY (in DMSO)
NH-1		13.20,brs			
2	127.1	7.31,s		C-3,C-7,C-10,C-11,C-12	
3	119.8				
4	18.5	2.89,m,2H	2H-5	C-2,C-3,C-5,C-12	H-2,2H-5
5	43.3	3.84,t,J=7.1 Hz,2H	2H-4	C-3,C-4,C-7	2H-4
NH-6		10.57,s			
7	153.6				
8	98.3				
9	147.3				
10	166.4				
11	124.2				
12	122.2				
NH-13		10.32,brs			
14	90.2	5.23,s		C-9,C-15,C-16,C-23,C-24	H-15,H-17
15	69.0	3.90,s		C-14,C-16,C-17,C-20,C-21,C-24,C-25	H-14,H-17,H-25a,H-25b
16	131.0				
17	129.2	7.23,s		C-14,C-15,C-16,C-18,C-19,C-21	H-14,H-15
18	105.3				
19-OH	154.8	9.86-11.34,brs			
20	108.2	6.72,s		C-16,C-18,C-19,C-21	

21	143.2				
S-22					
23	78.3				
24	81.1	5.42,s		C-7, C-8, C-9,C-10,C-14,C-15,C-23	H-25a,H-25b
25a	35.1	1.76,m,2H	H-25b,2H-26	C-23,C-25b,C-26	2H-24,2H-25b,2H-26,H-27
25b	35.1	1.87,m,2H	H-25a,2H-26	C-23,C-25a,C-26	2H-24,2H-25a,2H-26,2H-27
26	25.9	1.48,m,2H	H-25a,H-25b	C-(28 to 34, & 41)	2H-25,2H-27,H-(28 to 34, & 41)
27	29.5	1.2,m,2H	2H-26,H-(28 to 34, & 41)	C-26,C-(28 to 34, & 41)	2H-25,2H-26,H-(28 to 34, & 41)
28-34	28.5-29.5	1.1-1.3,m,14H	2H-27,2H-35,2H-42,2H-40	C-(28 to 34, & 41)	2H-26,2H-27,2H-39,2H-40,
35	29.5	1.2,m,2H	2H-36,H-(28 to 34, & 41)	C-36,C-(28 to 34, & 41)	2H-36,H-(28 to 34, & 41)
36	26.9	1.94,m,2H	2H-35,H-37	C-35,C-37,C-(28 to 34, & 41)	2H-35,H-37,H-(28 to 34, & 41)
37	130.04	5.28,dt,J=9.3,10.8 Hz	2H-36,H-38	C-35,C-36,C-38	2H-36,H-38
38	130.06	5.30,dt,J=9.3,10.8 Hz	2H-39,H-37	C-37,C-39,C-40	H-37,2H-39
39	27.0	1.95,m,2H	2H-40,H-38	C-38	H-38,2H-40,2H-41
40	29.7	1.2,m,2H	2H-39,H-(28 to 34, & 41)	C-38,C-39,C-(28 to 34, & 41)	2H-39,2H-41,H-(28 to 34, & 41)
41	28.5-29.5	1.1-1.3,m,2H	2H-27,2H-35,2H-42,2H-40	C-(28 to 34, & 41)	2H-26,2H-27,2H-39,2H-40,
42	31.6	1.2,m,2H	2H-41,2H-43	C-44,C-(28 to 34, & 41)	3H-44,H-(28 to 34, & 41)
43	22.5	1.2,m,2H	2H-42,3H-44	C-42,C-44,C-(28 to 34, & 41)	3H-44,H-(28 to 34, & 41)
44	14.3	0.81,t,3H	2H-43	C-42,C-43	2H-43,2H-42

Figure S1.  $^1\text{H}$  NMR spectrum of atkamine in  $\text{MeOD-}d_4$

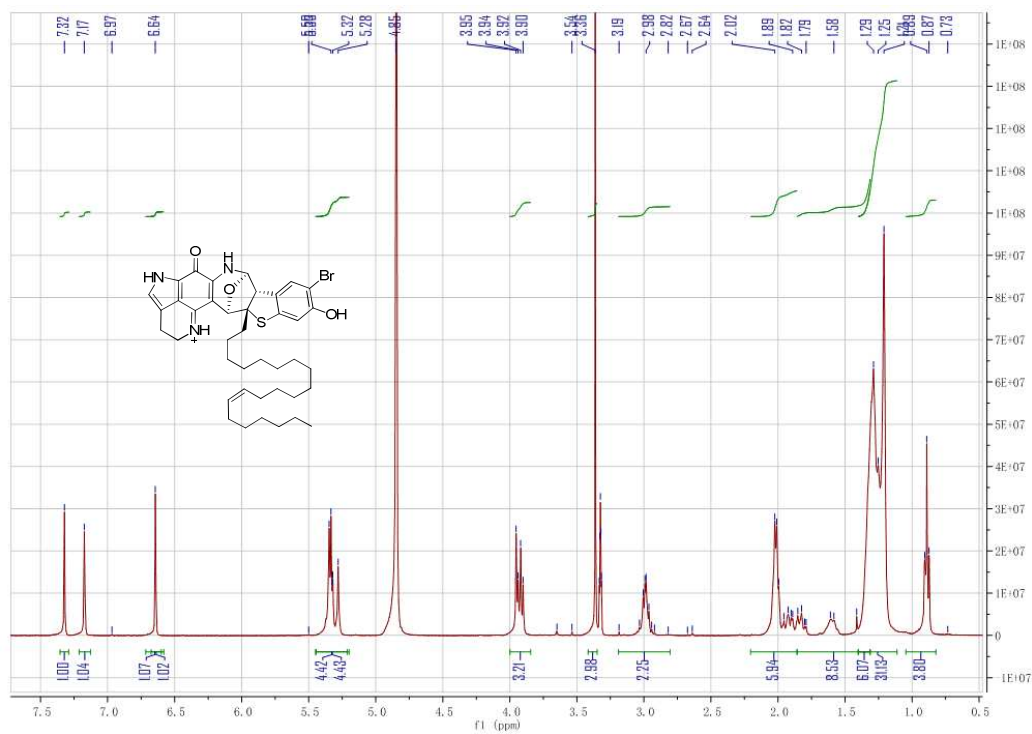
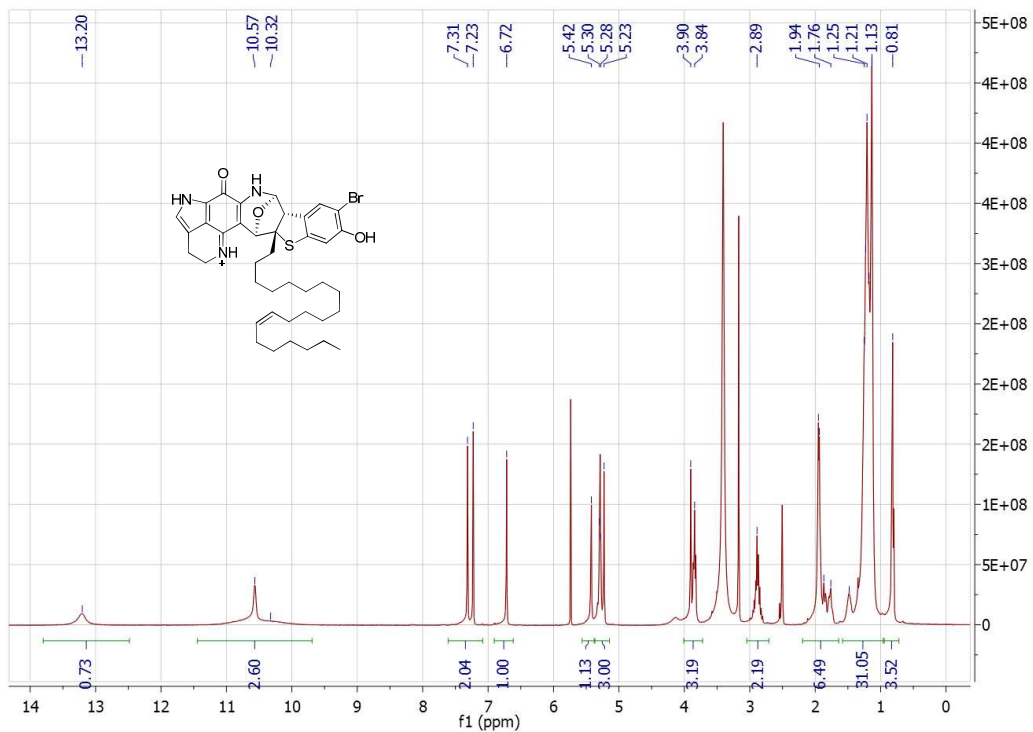
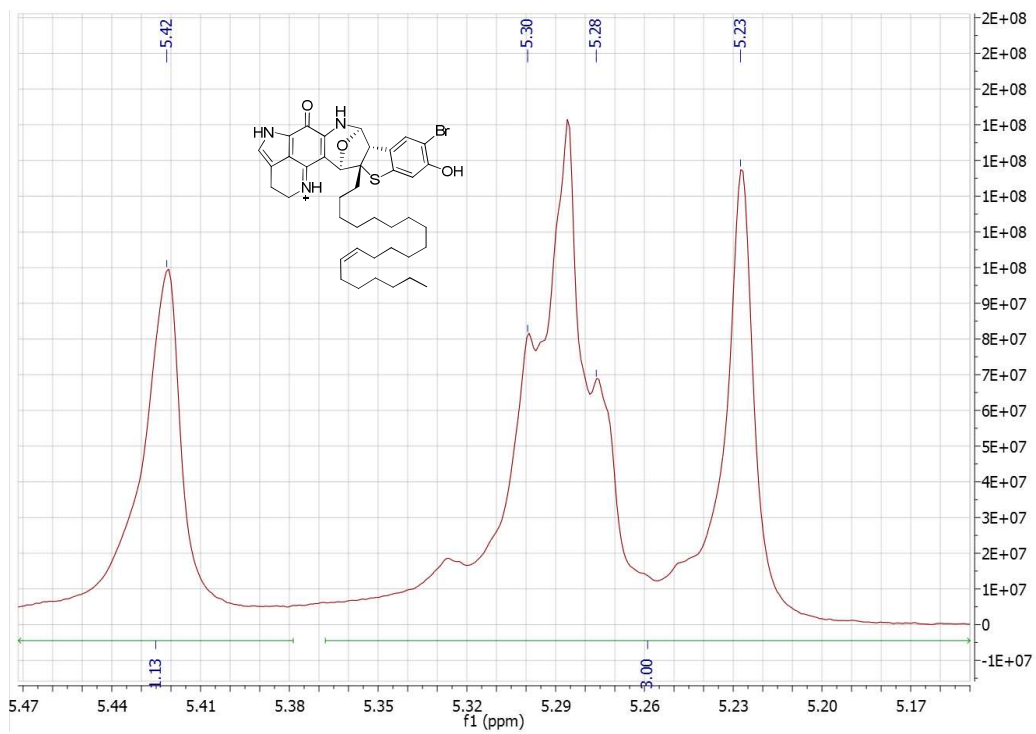
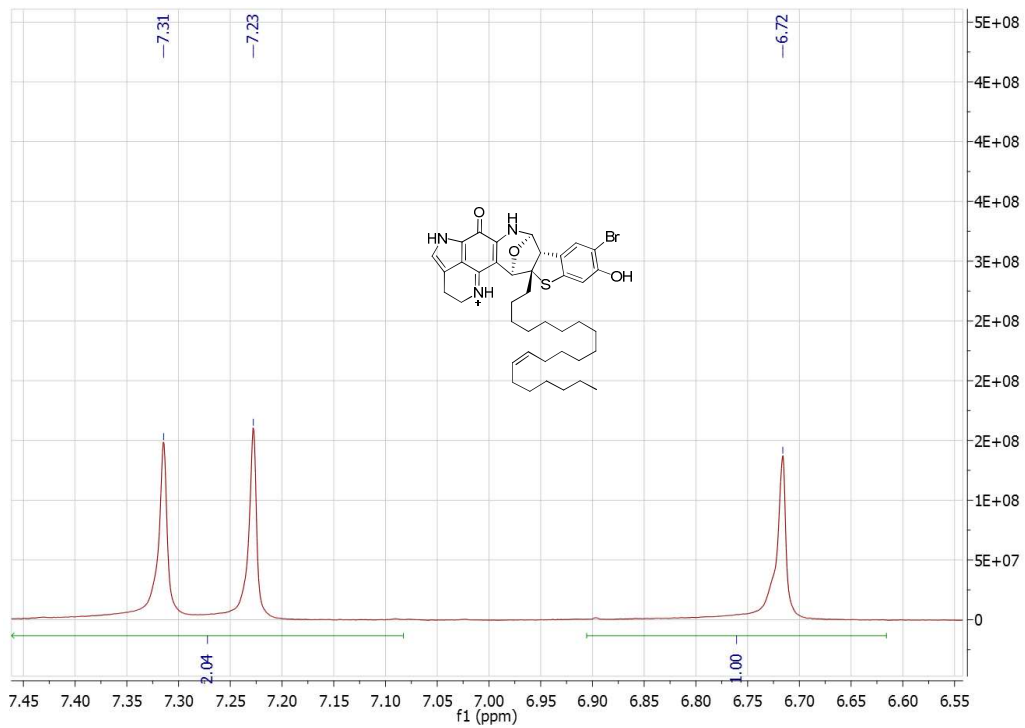


Figure S2.  $^1\text{H}$  NMR spectrum of atkamine in  $\text{DMSO-}d_6$





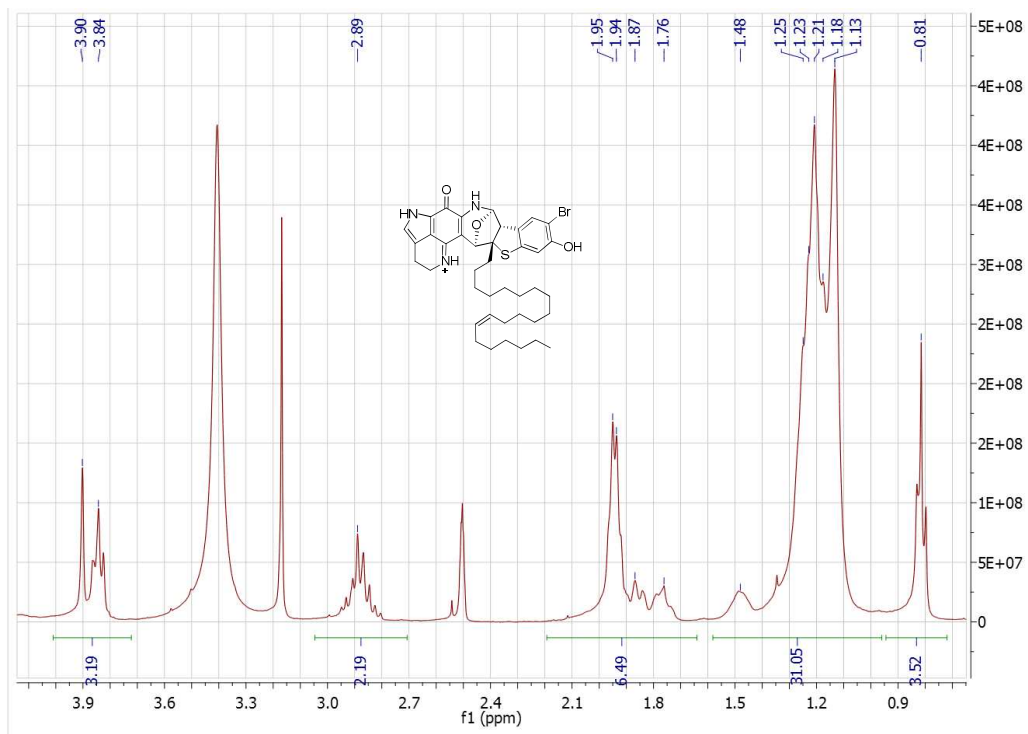


Figure S3.  $^{13}\text{C}$  NMR spectrum of atkamine in  $\text{MeOD-}d_4$

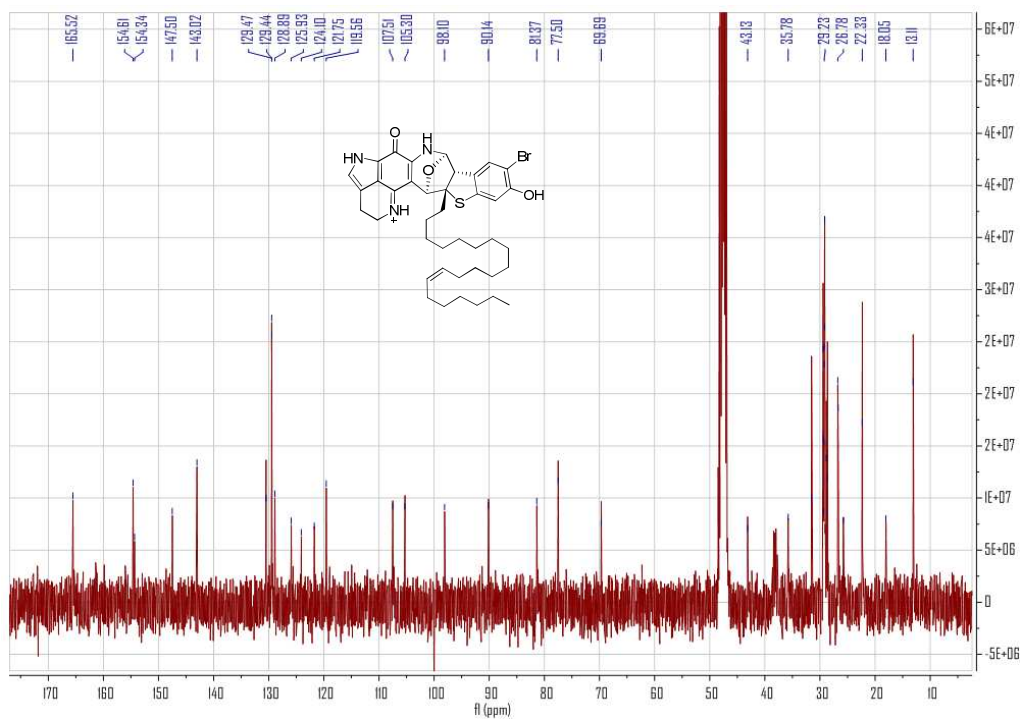
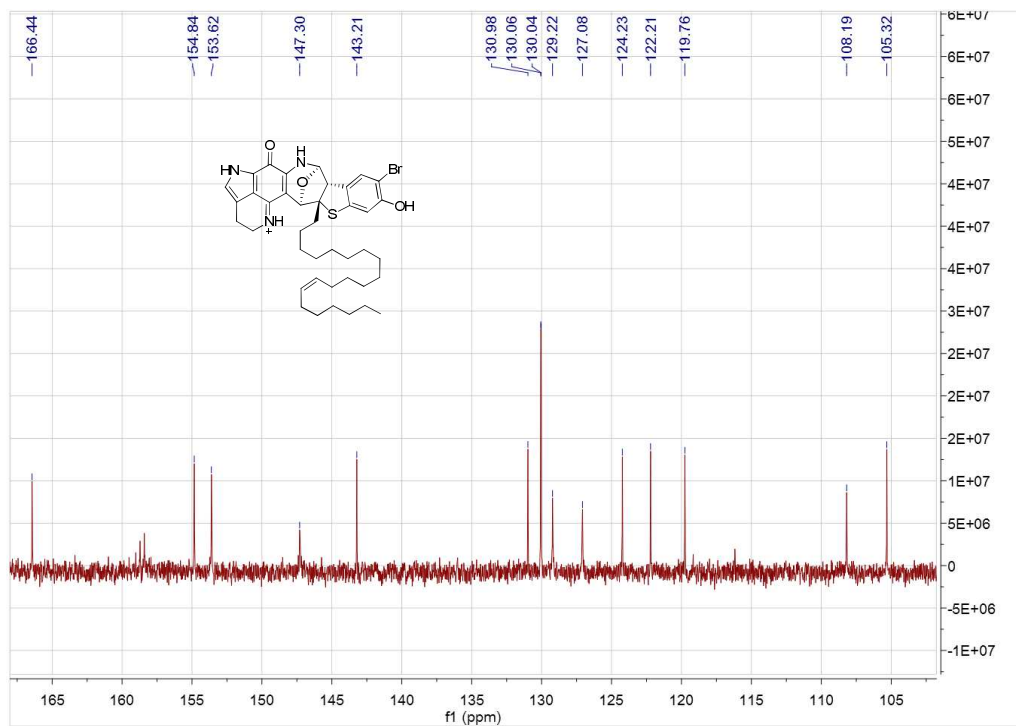
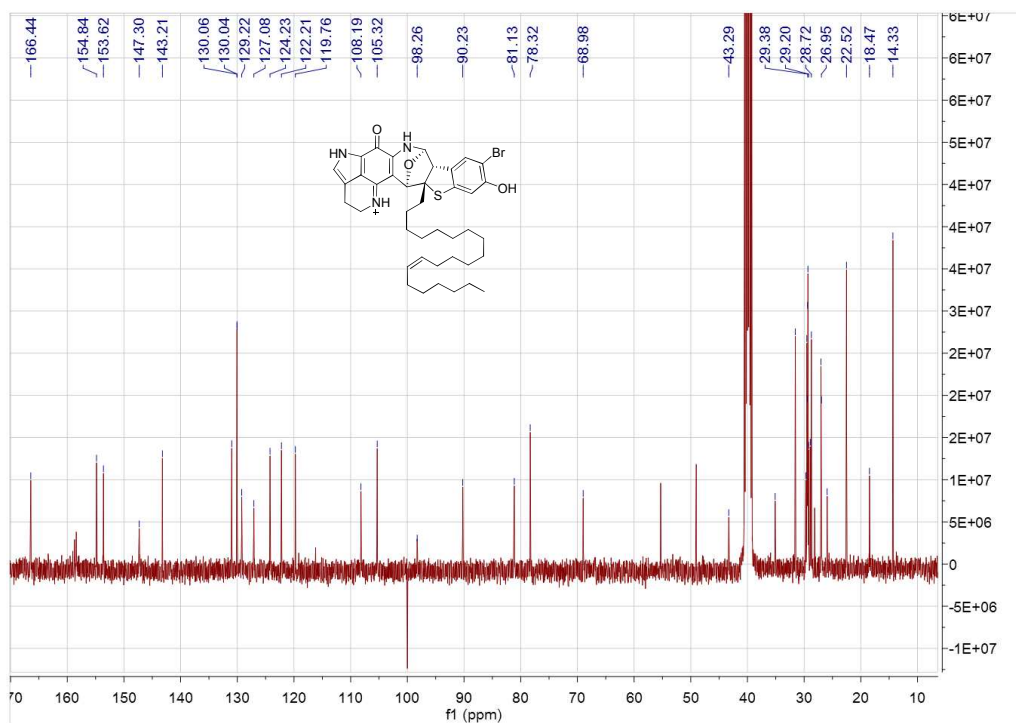


Figure S4.  $^{13}\text{C}$  NMR spectrum of atkamine in  $\text{DMSO-}d_6$



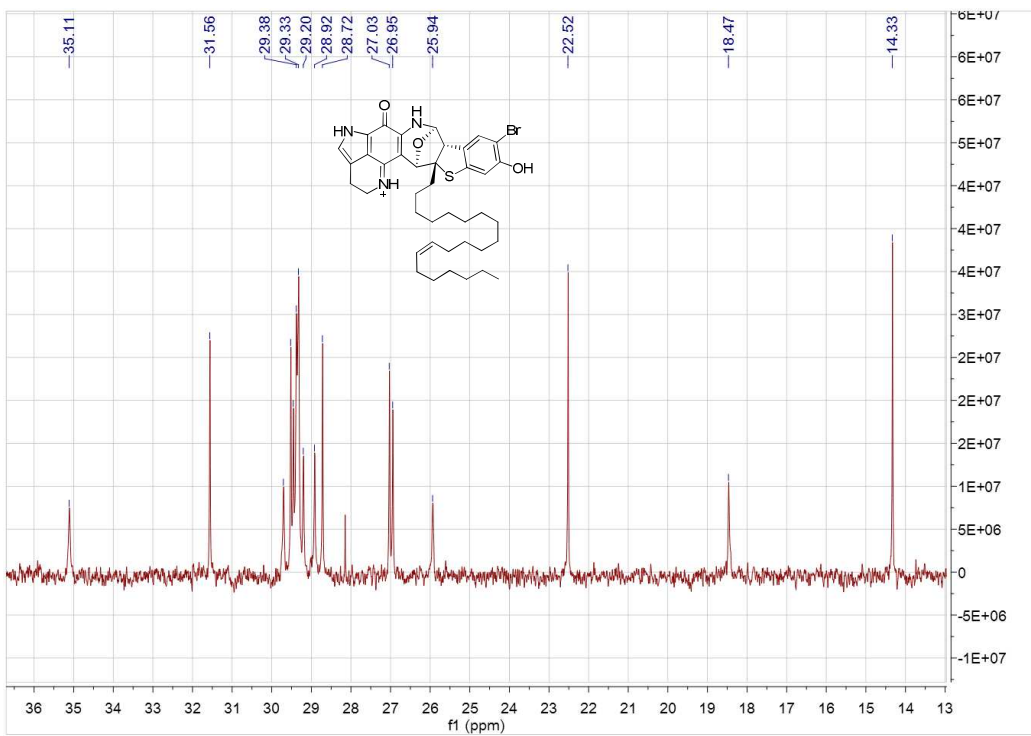
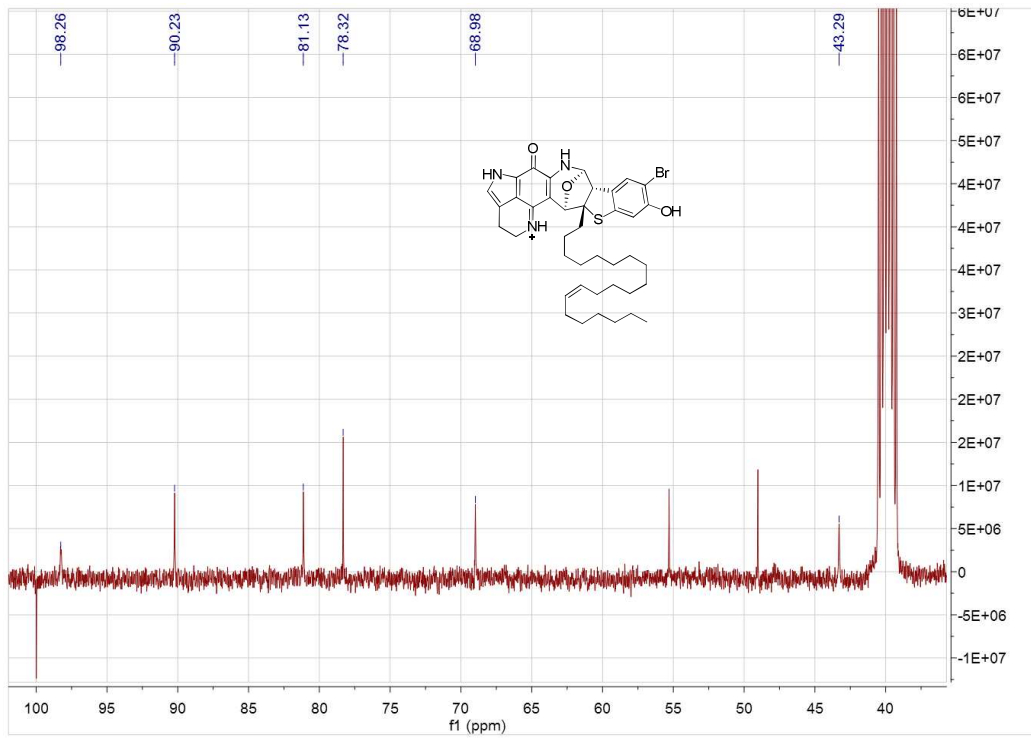




Figure S5. DEPT 135 NMR spectrum of atkamine in DMSO-*d*<sub>6</sub>

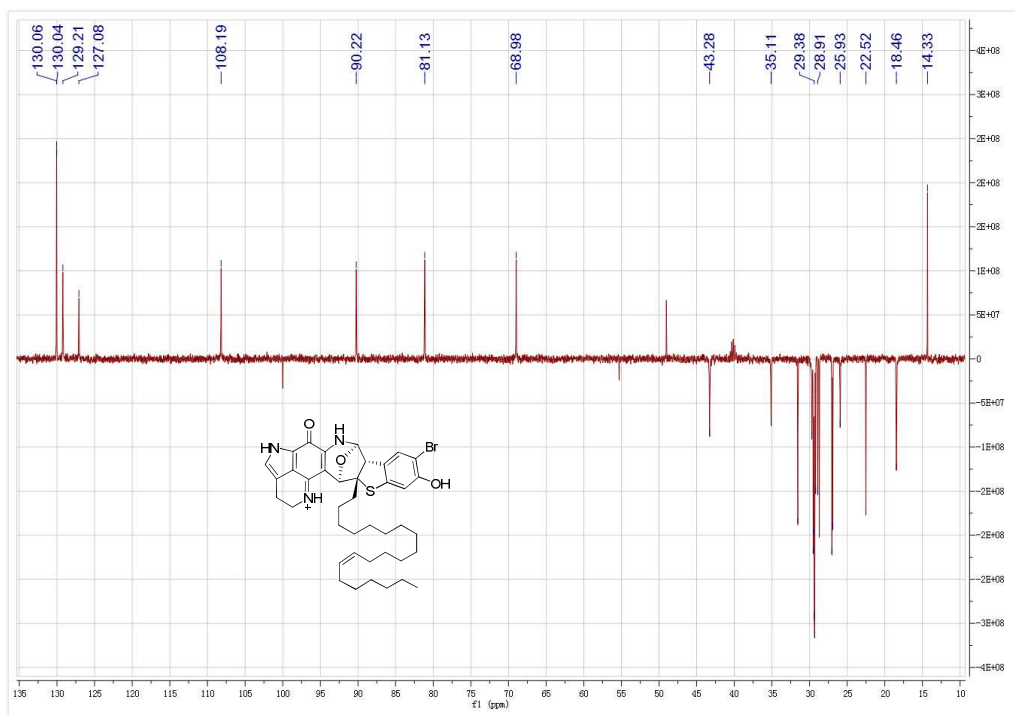


Figure S6. 2D <sup>1</sup>H-<sup>13</sup>C HSQC NMR spectrum of atkamine in DMSO-*d*<sub>6</sub>

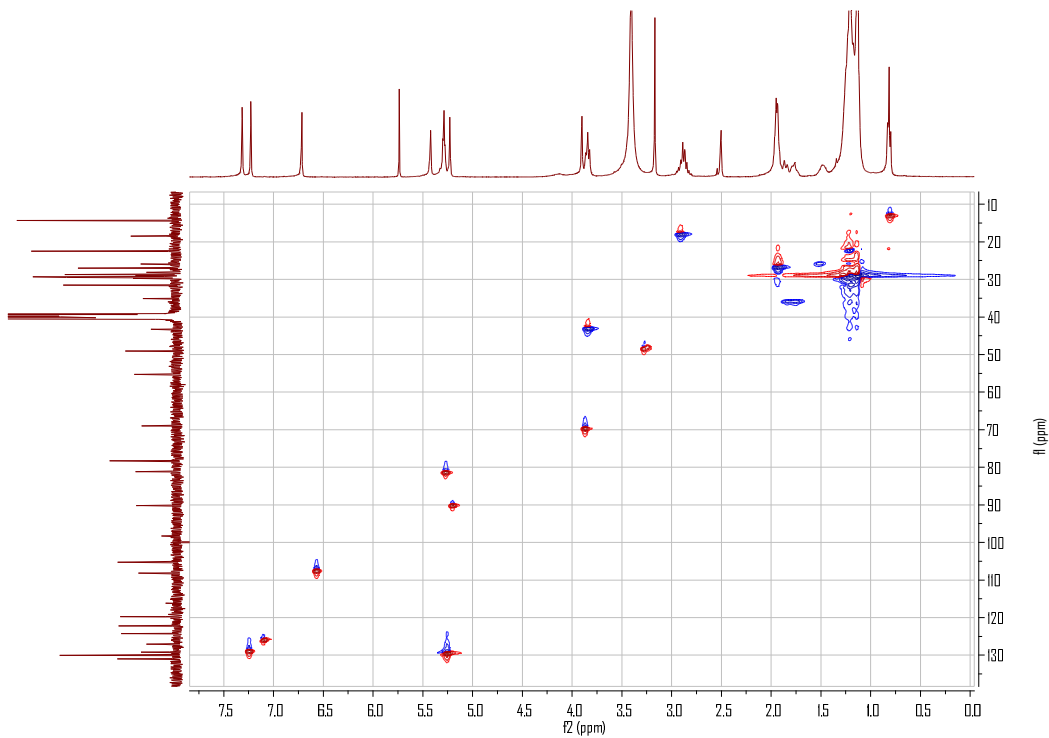


Figure S7. 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC NMR spectrum of atkamine in  $\text{DMSO-}d_6$

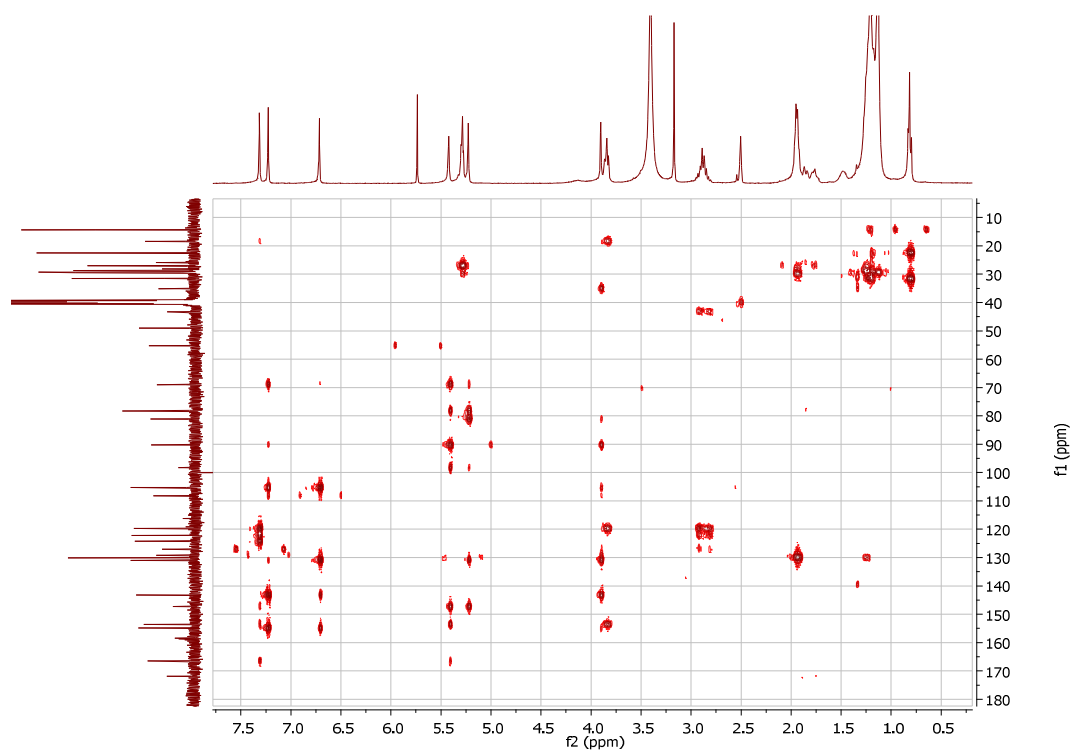
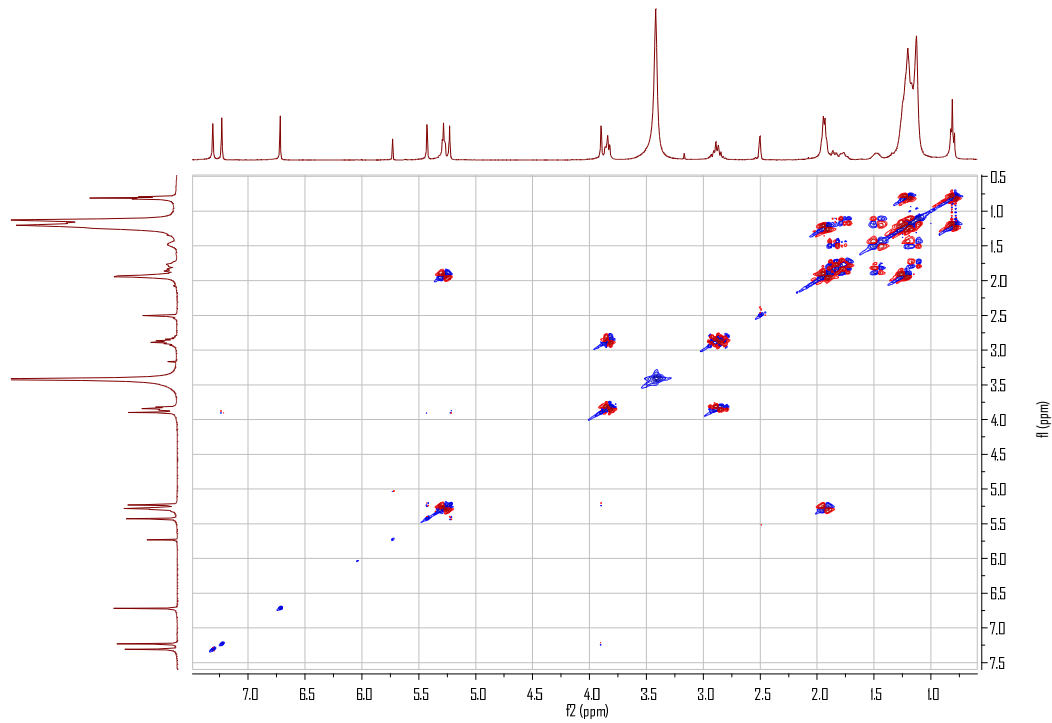


Figure S8. 2D  $^1\text{H}$ - $^1\text{H}$  DQF COSY NMR spectrum of atkamine in  $\text{DMSO-}d_6$





## 2. Isolation procedure

Frozen sample of a *Latrunculia* sp. (4 kg) recovered during the NOAA deep ocean surveys was cut into 2-3 cm<sup>3</sup> pieces and extracted with ethanol (95%) with the help of an ultrasonicator at room temperature. The solvent was removed under vacuum and yielded a brownish crude extraction (225 g) which was then loaded on a flash silica gel column eluting under vacuum with a gradient elution system of hexane-ethyl acetate (50:50, 0:100) followed by ethyl acetate-methanol (75:25, 50:50, 0:100) then methanol-water (50:50). The fractions of ethyl acetate-methanol (75:25, 50:50) were combined and separated by using Sephadex LH-20 with an elution system of dichloromethane-methanol (50:50). The fractions with molecular weight range from 300-700 Daltons (monitored by using LC-MS) were further isolated by using C18 MPLC eluted with methanol-water (0.03% trifluoroacetic acid). The fractions eluted with 10-60% methanol were subjected to preparative HPLC (Phenomenex C<sub>8</sub> column, 21.2 × 250 mm with flow rate at 10 ml/min) using the elution system of MeCN- H<sub>2</sub>O (0.05% trifluoroacetic acid) (9:1) to yield atkamine (5 mg) named after Atka Island. Green-purple solid as TFA salt. HRESIMS 734.3006 [M+H]<sup>+</sup> and 736.3008 [M+H+2]<sup>+</sup> (calcd. for C<sub>40</sub>H<sub>53</sub>BrN<sub>3</sub>O<sub>3</sub>S, Δ 2.79ppm). UV λ<sub>max</sub>=360nm.

## 3. Olefin metathesis of atkamine

**Atkamine** (2 mg, 0.003 mmol) was dissolved in anhydrous dichloromethane (0.5 ml). Grubbs' catalyst generation II (2 mg) was then added in the solution, and the mixture was flushed with ethylene gas for fifteen minutes by using an ethylene balloon. The mixture was stirred at room temperature under ethylene atmosphere for overnight (approximately 12 hours). The reaction mixture was then diluted with dichloromethane and filtered. The crude mixture was analyzed by LC-MS. A peak cluster at m/z 650[M+H]<sup>+</sup> and 652 [M+2]<sup>+</sup> was detected by LC-MS which supported the olefinic double bond was placed between C-37 and C-38.

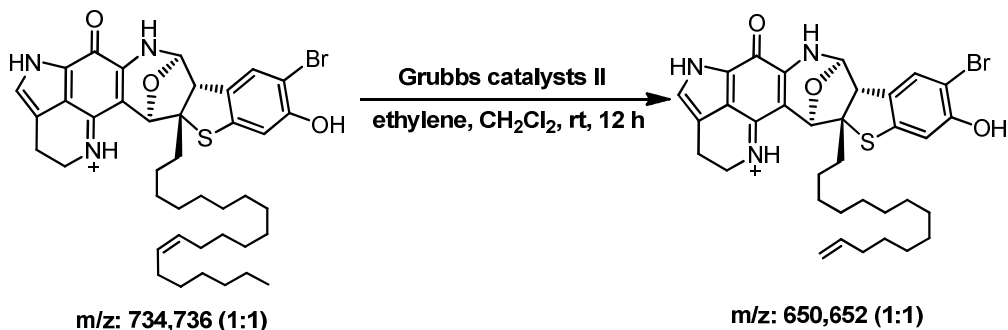
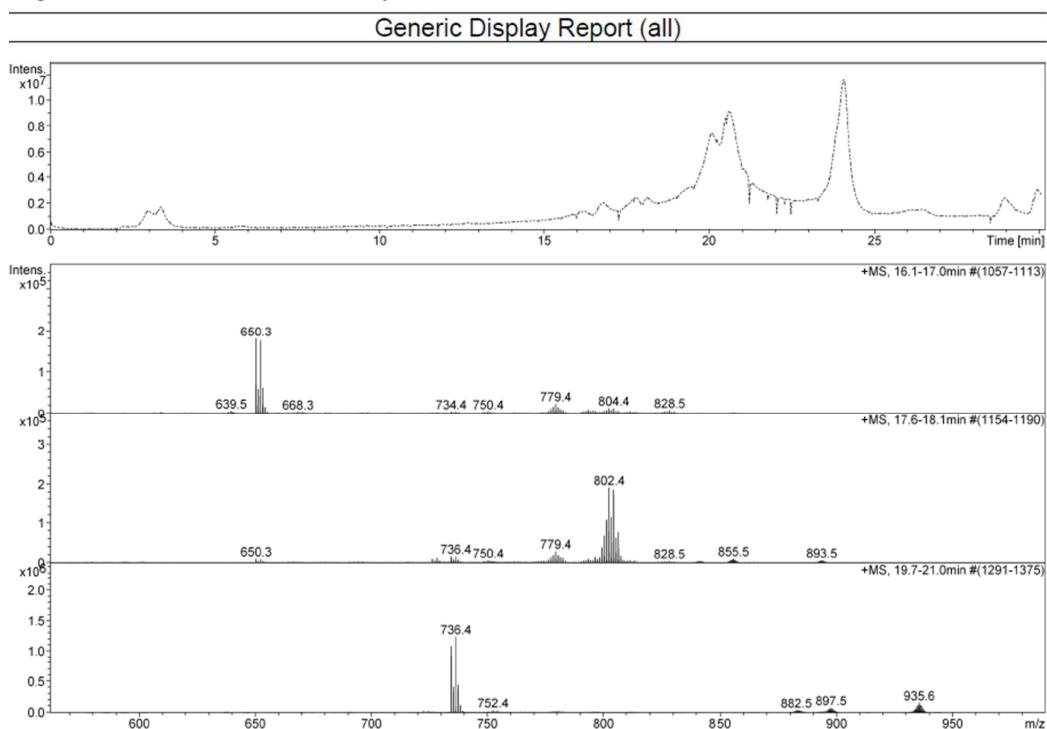


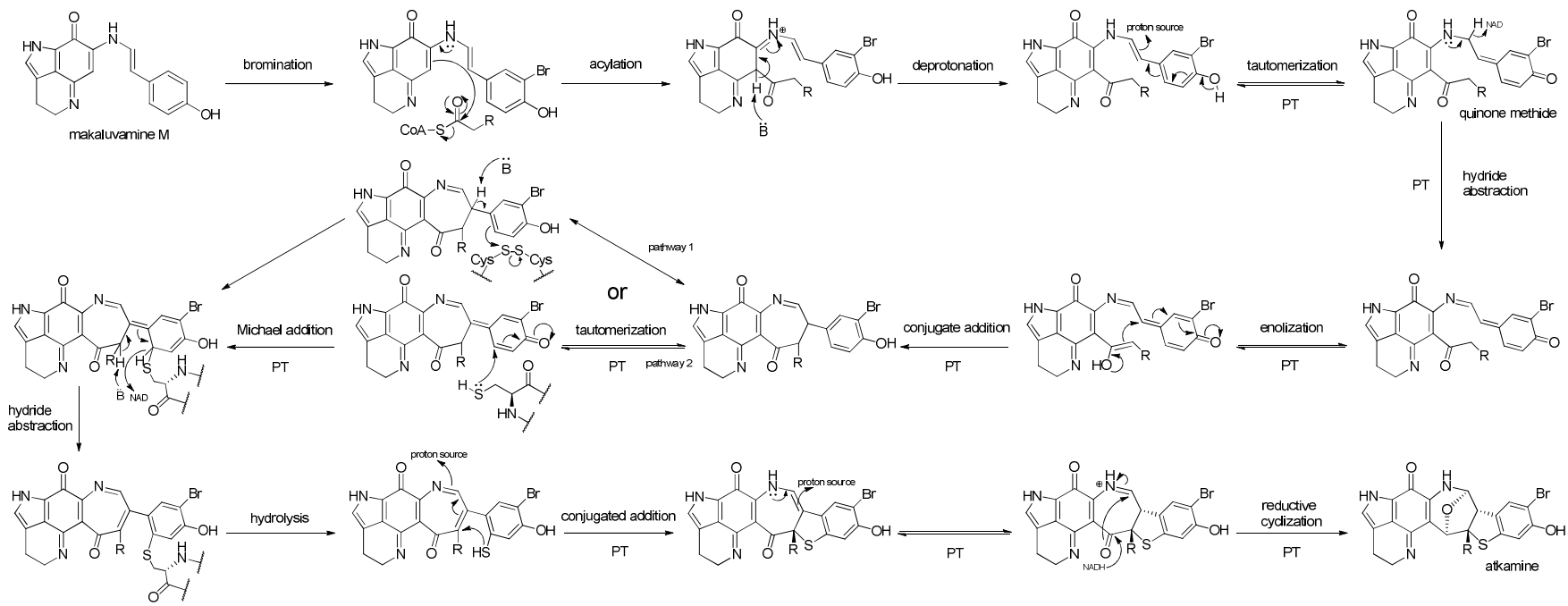
Figure S10. LC-ESI-TOF analysis of the reaction mixture.



#### 4. Proposed biotransformation of atkamine from makaluvamine F.

A proposed biogenesis of atkamine maybe initiated by bromination<sup>1</sup>. The following acylation is done by the nucleophilic attack of the enamine motif to the carbonyl on the VLCFAs (very long-chain fatty acids) precursor<sup>2</sup> from the unsaturated fatty acids biosynthesis pathway<sup>3,4</sup>. A deprotonation of the  $\alpha$ -position happens to regenerate the conjugation and the enamine motif. Then, the quinone methide intermediate<sup>5</sup> is generated through tautomerization. NAD hydride abstraction could follow to generate the imine moiety conjugated to the pyrroloiminoquinone core. Then the acyl group is enolized to perform a conjugate addition on the quinone methide<sup>6</sup> to construct the seven membered ring. The following sulfur incorporation could be via two possible pathways. The first one included a disulfide linkage serving as a sulfur electrophile, and the second pathway could be a Michael addition to the quinone methide moiety<sup>7</sup> via a cysteine thiol group as a nucleophile. Both pathways lead to a dearomatized intermediate and subsequently recover the aromaticity and the conjugation by the assistance of NAD. A hydrolysis releases the free thiol which could undergo a conjugated addition to form the core ring system. The iminium moiety is then reformed from a reductive cyclization to form atkamine.

Figure S11. Proposed biogenesis of atkamine.



R=fatty acid side chain

## 5. Configuration assignment of atkamine

### General computation procedure.

All calculations were performed by using Gaussian 09 software package. The visualization process was performed by using the Gaussian View software and the Molekel software. The aliphatic chain part was pre-optimized to the lowest energy conformation. Conformational analysis was then conducted, and two low energy conformations were generated. Each conformation was minimized by using the MMFF method and then used for the geometry optimization and the frequency calculation by the hybrid DFT calculation with the B3LYP or BH&HLYP methods with the 6-31G(d,p) or TZVP basis set and the PCM solvation model with the dielectric constant representing methanol to generate the optimized structure and a set of thermodynamic data. This structure was then used for the excited-state TDDFT calculations to generate the excitation energies and rotational strengths as well as the electronic structures. The resulted excitation energies and rotational strengths of different conformers were Boltzmann averaged and fitted to a Gaussian function to generate the computed ECD spectrum.

Figure S12. Optimized structure of the lowest energy conformation of atkamine by using the DFT calculation with the B3LYP method and the 6-31G(d,p) basis set with the PCM solvation model.

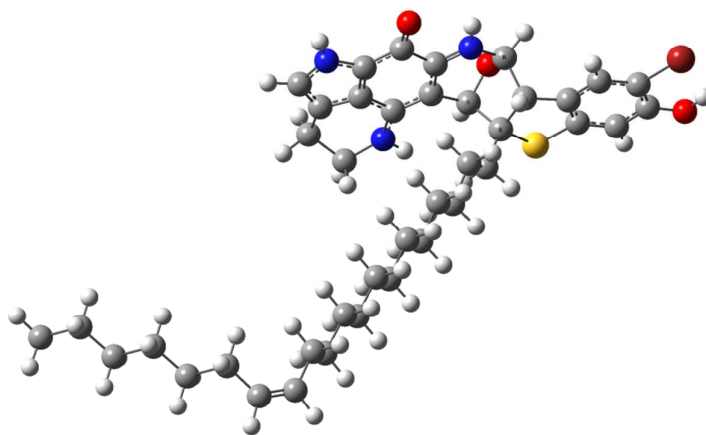


Figure S13. ESP (electrostatic potential) surface of the lowest energy conformation of atkamine by using the DFT calculation with the B3LYP method and the 6-31G(d,p) basis set with the PCM solvation model.

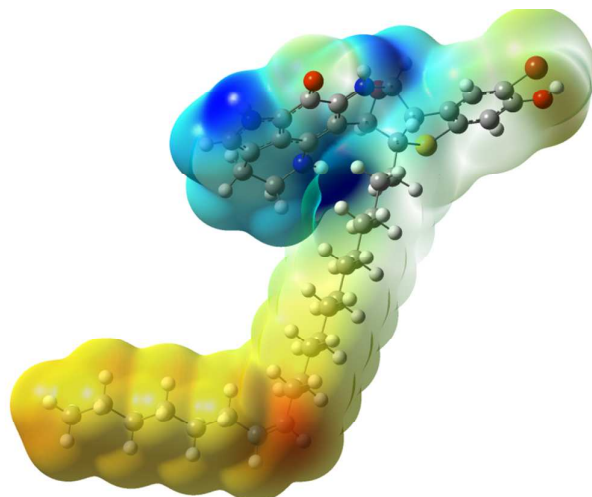


Figure S14. Calculated HOMO and LUMO of the lowest energy conformation of atkamine by using using the TDDFT calculation with the B3LYP method and the 6-31G(d,p) basis set with the PCM solvation model.

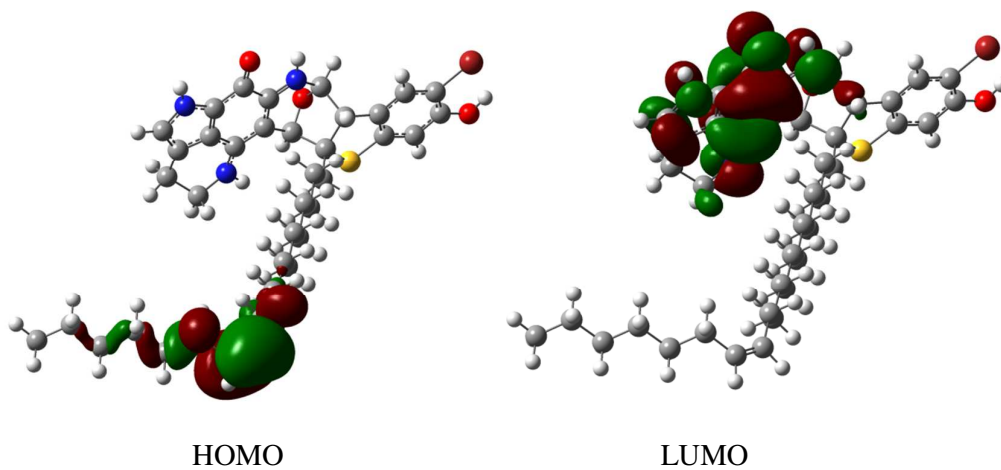




Figure S15.  $^{13}\text{C}$  NMR prediction of atkamine

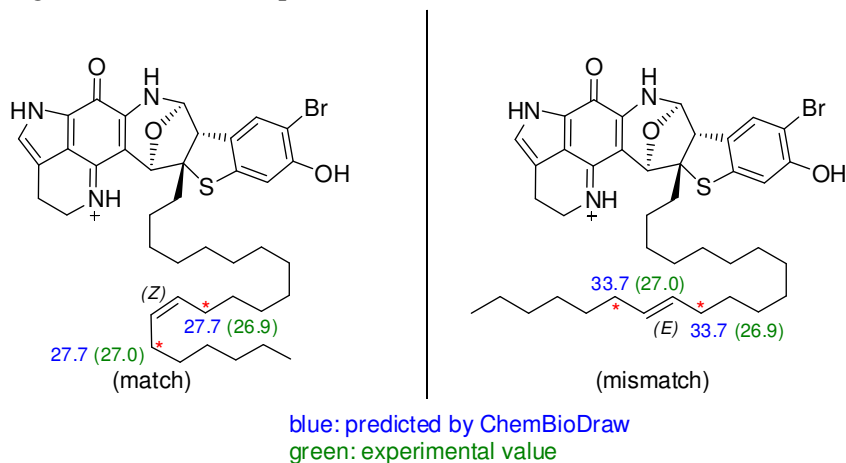


Figure S16. Experimental UV spectra of atkamine (in MeOH).

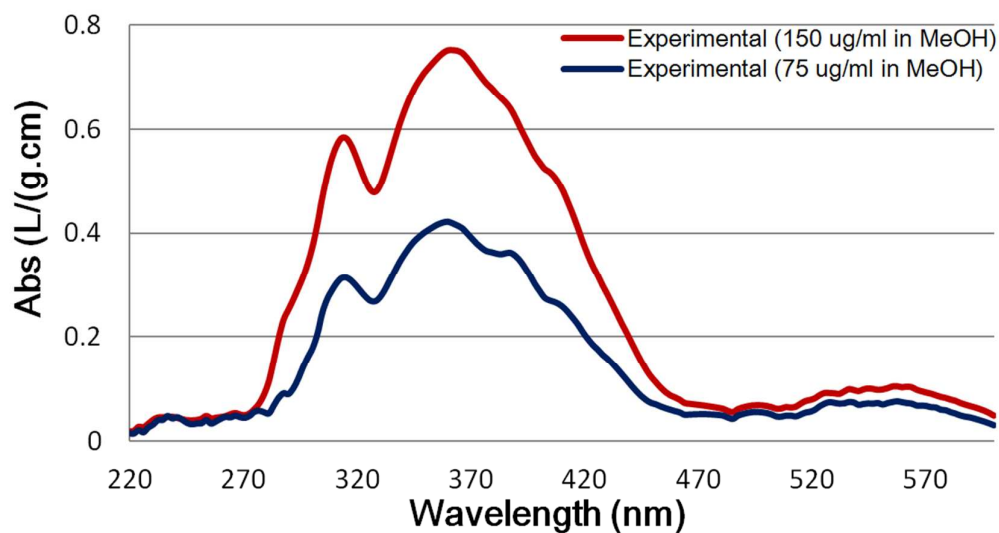


Figure S17. Experimental ECD spectrum (in MeOH).

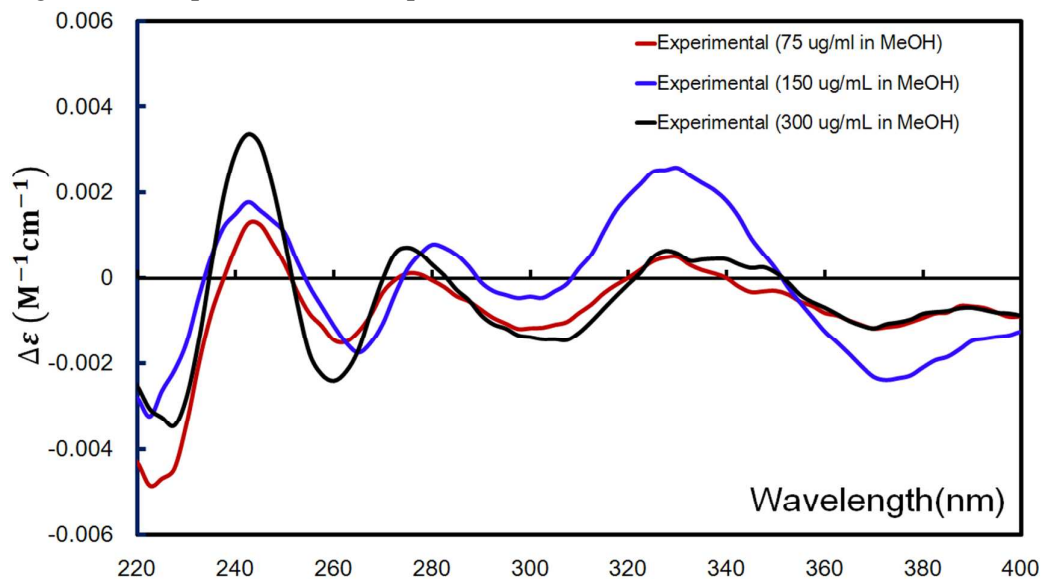
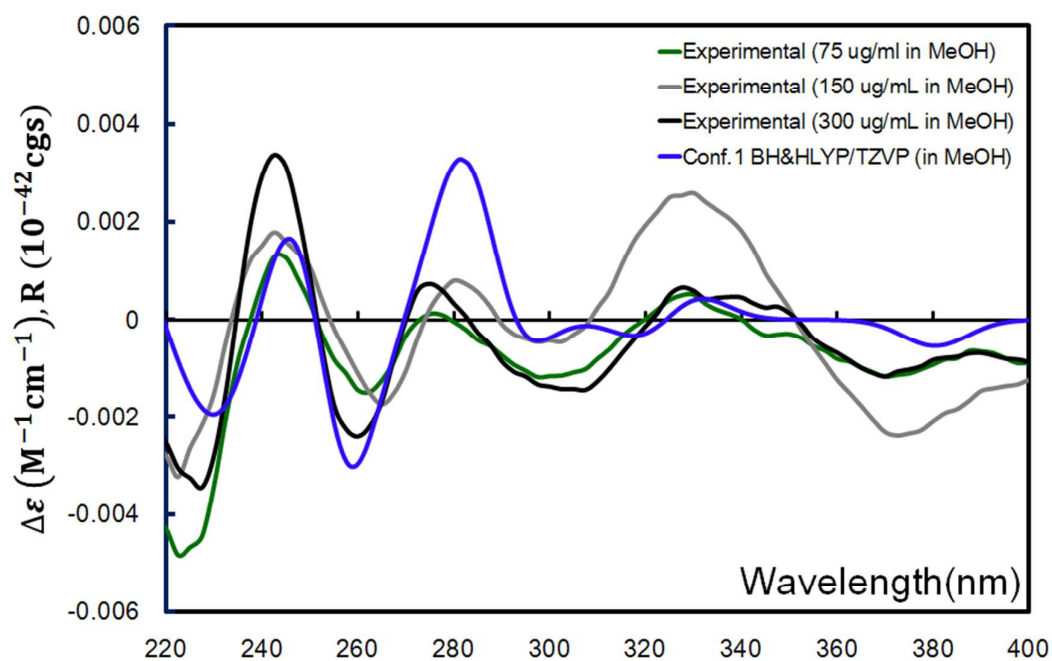
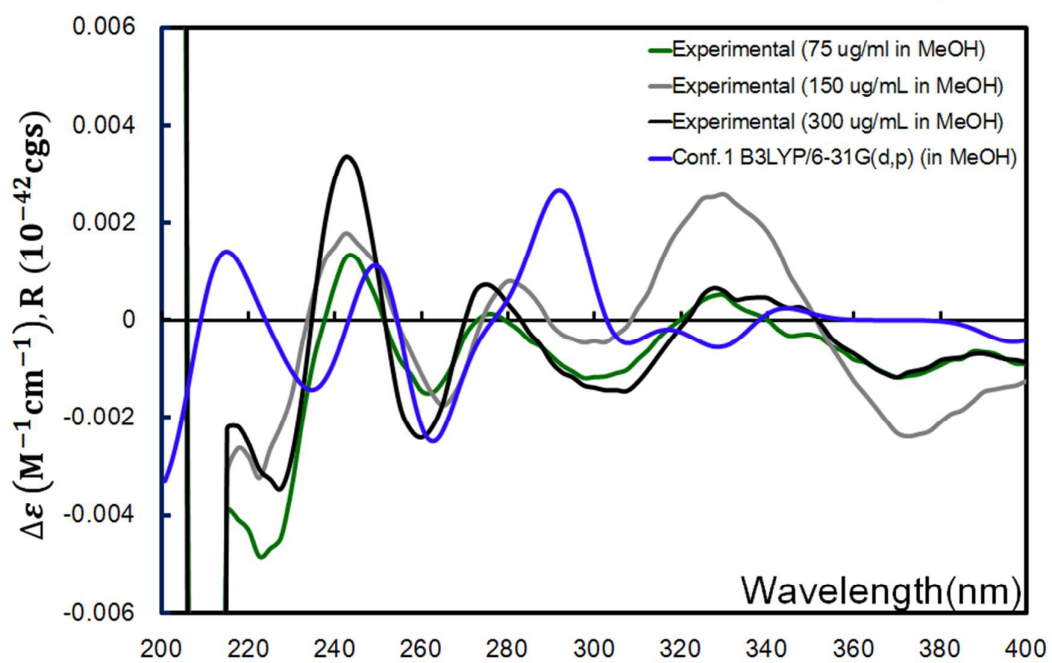
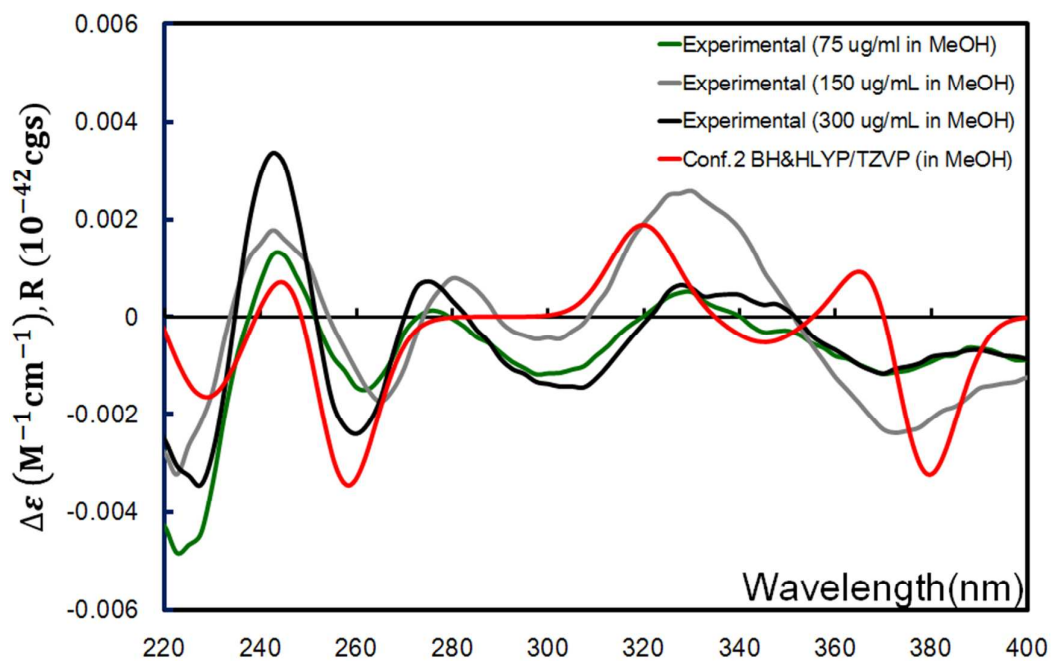


Table S2. Experimental Cotton effects and  $\lambda_{\max} (\pm)$  (in MeOH).

75 ug/mL		150 ug/mL		300 ug/mL	
$\lambda_{\max}(\pm)$	molar ellipticity	$\lambda_{\max}(\pm)$	molar ellipticity	$\lambda_{\max}(\pm)$	molar ellipticity
222.5 (-)	-0.004839112	222.5 (-)	-0.003229054	227.5 (-)	-0.003444437
242.5 (+)	0.001284360	242.5 (+)	0.001785502	242.5 (+)	0.003368910
262.5 (-)	-0.001487745	265.0 (-)	-0.001745095	260.0 (-)	-0.002402288
275.0 (+)	0.000116295	280.0 (+)	0.000796648	275.0 (+)	0.000729253
297.5 (-)	-0.001184914	297.5 (-)	-0.000461056	307.5 (-)	-0.001450019
330.0 (+)	0.000510744	330.0 (+)	0.002586853	327.5 (+)	0.000652272
370.0 (-)	-0.001175774	372.5 (-)	-0.002383184	370.0 (-)	-0.001171420

Figure S18. Calculated ECD curves of different low energy conformations of at-kamine by using the B3LYP/6-31G(d,p) and the BH&HLYP/TZVP methods with the PCM solvation model.





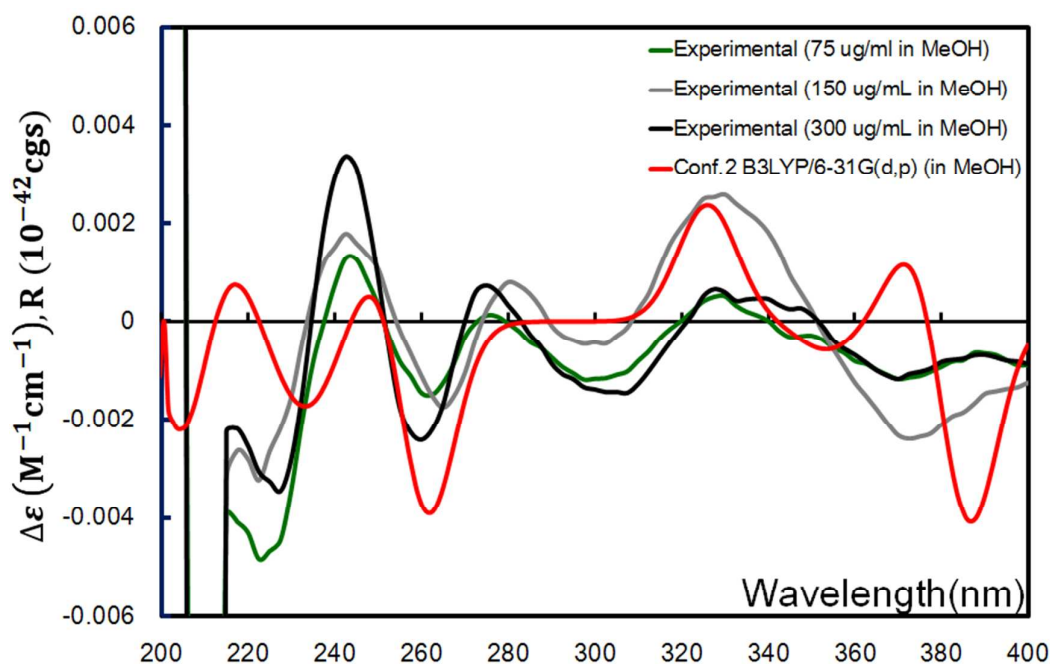


Table S3. Cartesian coordinates of the optimized structures of atkamine using the B3LYP/6-31G (d, p) method with the PCM solvation model representing methanol.

Conf.1	X	Y	Z	Conf.2	X	Y	Z
C	6.421083	-1.009428	0.000119	C	6.440178	-0.981396	-0.012514
C	6.944015	-1.903768	0.931003	C	6.981268	-1.875987	0.907704
C	8.008281	-2.726184	0.569781	C	8.064712	-2.671332	0.539949
C	8.568848	-2.678075	-0.717756	C	8.628992	-2.595525	-0.743528
C	8.036101	-1.783924	-1.655383	C	8.080072	-1.700801	-1.671077
C	6.973511	-0.963196	-1.288310	C	6.997354	-0.908116	-1.298620
C	4.829714	0.607452	-1.103203	C	4.823023	0.622811	-1.090455
S	6.183790	0.201355	-2.358864	S	6.184609	0.253080	-2.354134
C	5.748626	1.211740	1.072760	C	5.711504	1.205854	1.113314
C	4.961654	2.135922	-0.803817	C	4.923338	2.145657	-0.756535
N	4.641717	1.753062	1.880049	N	4.612897	1.688516	1.932030
C	3.744635	2.546752	1.307567	C	3.679745	2.510975	1.363745
C	3.794761	2.778951	-0.073586	C	3.729819	2.739450	-0.034470
C	2.706731	3.134565	2.277127	C	2.707572	3.108446	2.291459
C	1.758679	3.977626	1.607721	C	1.735198	3.918589	1.613089
C	1.834231	4.212432	0.241366	C	1.770869	4.117259	0.234379
C	2.814852	3.623227	-0.639259	C	2.760842	3.568078	-0.621831
O	2.778988	2.870036	3.473291	O	2.770087	2.893608	3.534760
N	2.683385	3.947153	-1.924446	N	2.628987	3.898728	-1.952253
C	1.472940	4.611224	-2.471209	C	0.507756	5.217984	-1.619967
C	0.873664	5.681091	-1.536742	C	0.677694	4.931830	-0.153573
C	0.884336	5.173877	-0.123779	C	-0.006666	5.225631	1.009655
C	0.211766	5.502144	1.055051	N	0.639396	4.611836	2.071914

N	0.747209	4.773705	2.080563	O	9.680367	-3.352485	-1.144285
O	9.600650	-3.461260	-1.112515	Br	8.817610	-3.912289	1.793457
Br	8.739253	-3.966239	1.834327	O	6.051530	2.191805	0.144648
O	6.086274	2.178809	0.103377	C	3.479081	0.135145	-1.687861
C	3.484286	0.106358	-1.685606	C	5.296020	-0.036577	0.255725
C	5.296576	-0.038049	0.257104	C	2.320229	-0.172950	-0.722750
C	2.300229	-0.121329	-0.728745	C	1.022074	-0.485634	-1.480991
C	1.025691	-0.509855	-1.492632	C	-0.135561	-0.882551	-0.556941
C	-0.150210	-0.845138	-0.567218	C	-1.444902	-1.170864	-1.301769
C	-1.440841	-1.196985	-1.317447	C	-2.593821	-1.589772	-0.376315
C	-2.602862	-1.567804	-0.387842	C	-3.911223	-1.861428	-1.113055
C	-3.907412	-1.887836	-1.128038	C	-5.051809	-2.297779	-0.185299
C	-5.056752	-2.286630	-0.194246	C	-6.376004	-2.554255	-0.915362
C	-6.373862	-2.574919	-0.925218	C	-7.509510	-3.004098	0.014635
C	-7.512130	-2.997334	0.011751	C	-8.838167	-3.247054	-0.710969
C	-8.838657	-3.257132	-0.711832	C	-9.968691	-3.706647	0.229887
C	-9.970332	-3.698740	0.236031	C	-11.251208	-4.003246	-0.501131
C	-11.254560	-4.001220	-0.489564	H	4.473898	-0.553101	0.754454
H	4.466132	-0.528810	0.768636	H	6.578438	1.017346	1.746841
H	6.601680	1.036745	1.726592	H	5.191444	2.735986	-1.636225
H	5.243716	2.707815	-1.689487	H	6.567753	-1.960218	1.907291
H	6.531583	-1.966254	1.932509	H	8.512408	-1.654640	-2.664547
H	8.464784	-1.760292	-2.651028	H	-1.742744	-0.278059	-1.869983
H	-1.736324	-0.346805	-1.948691	H	-1.272798	-1.961071	-2.046574
H	-1.245491	-2.032346	-2.004801	H	-4.752144	-3.208737	0.352418
H	-4.761186	-3.173719	0.384080	H	-5.206808	-1.528713	0.585003
H	-5.220358	-1.486284	0.541708	H	0.153652	-1.769673	0.024328
H	0.131433	-1.684816	0.083730	H	-0.305300	-0.081429	0.176422
H	-0.341481	0.006625	0.100906	H	-6.681356	-1.639876	-1.443847
H	-6.678907	-1.680852	-1.487579	H	-6.220735	-3.316312	-1.692462
H	-6.209460	-3.362886	-1.674070	H	0.086576	6.209598	-1.813689
H	1.461403	6.605222	-1.597745	H	-0.173581	4.486929	-2.075475
H	-0.132484	5.917859	-1.892512	H	-0.895993	5.814803	1.179526
H	-0.597943	6.193569	1.233732	H	2.580589	-1.038979	-0.100935
H	2.545032	-0.925578	-0.024031	H	2.145058	0.663180	-0.039798
H	2.095186	0.768623	-0.127412	H	4.692487	1.748272	2.939860
H	1.756188	5.053532	-3.426316	H	0.353180	4.664346	3.037776
H	0.730876	3.828337	-2.667488	H	9.950870	-3.931052	-0.411351
H	4.591056	1.627415	2.886953	H	3.148636	0.885345	-2.418392
H	0.443131	4.816892	3.044243	H	3.679652	-0.772576	-2.265651
H	9.863957	-4.036793	-0.374396	H	0.730238	0.391986	-2.074745
H	3.181788	0.800382	-2.480734	H	1.204951	-1.294908	-2.202256
H	3.685160	-0.843206	-2.190982	H	-7.207943	-3.924350	0.535150
H	0.740605	0.312686	-2.163435	H	-7.657750	-2.247186	0.798082

H	1.237053	-1.372673	-2.139530	H	-9.150559	-2.327950	-1.224654
H	-7.214204	-3.903553	0.558322	H	-9.635645	-4.617808	0.749757
H	-7.662276	-2.219262	0.773883	H	3.405908	3.687088	-2.563935
H	-9.150725	-2.349093	-1.245054	H	-2.756169	-0.806033	0.377506
H	-9.640015	-4.603168	0.769326	H	-2.298490	-2.489865	0.181724
H	3.327113	3.564084	-2.604862	H	-3.747802	-2.636316	-1.875740
H	-2.781018	-0.742894	0.316923	H	-4.213706	-0.956870	-1.659931
H	-2.312381	-2.432666	0.225587	H	-10.124021	-2.950793	1.007259
H	-3.727402	-2.698787	-1.848227	H	-8.692554	-4.001526	-1.496742
H	-4.209198	-1.014522	-1.723899	C	-12.454432	-3.439885	-0.329083
H	-10.122894	-2.931069	1.002326	C	-12.849887	-2.358422	0.641264
H	-8.690576	-4.027489	-1.481588	H	-12.003207	-2.062057	1.269818
C	-12.458628	-3.440602	-0.314385	H	-13.615547	-2.755658	1.325078
C	-12.853183	-2.357929	0.655017	C	-13.427740	-1.113635	-0.059182
H	-12.004554	-2.057150	1.278852	H	-14.265808	-1.417778	-0.701801
H	-13.614001	-2.756311	1.343544	H	-12.666319	-0.693300	-0.729908
C	-13.438954	-1.116745	-0.045168	C	-13.903453	-0.033979	0.920114
H	-14.279303	-1.425124	-0.682748	H	-13.063551	0.271297	1.560437
H	-12.682504	-0.695164	-0.720744	H	-14.657966	-0.464386	1.594153
C	-13.913243	-0.036777	0.934502	C	-14.488832	1.203439	0.229150
H	-13.071199	0.272088	1.570313	H	-15.330027	0.898497	-0.409850
H	-14.663185	-0.468306	1.612891	H	-13.735403	1.633334	-0.446487
C	-14.505646	1.197774	0.244412	C	-14.964377	2.284807	1.207455
H	-15.348948	0.889322	-0.390087	C	-15.550664	3.516137	0.510172
H	-13.756751	1.628914	-0.435476	H	-14.123002	2.590543	1.844212
C	-14.979806	2.279156	1.223389	H	-15.715640	1.854513	1.883720
C	-15.572740	3.507871	0.527122	H	-15.880093	4.268356	1.234545
H	-14.136419	2.588152	1.855929	H	-14.811149	3.988211	-0.146889
H	-15.726742	1.847649	1.903647	H	-16.415530	3.246901	-0.107028
H	-15.901129	4.260074	1.251981	H	-11.165434	-4.773604	-1.269550
H	-14.837513	3.981199	-0.133843	H	-13.266371	-3.790229	-0.968891
H	-16.439554	3.235330	-0.085865	C	1.888385	5.127853	-2.309434
H	-11.169783	-4.774245	-1.255409	H	2.480542	6.013167	-2.034877
H	-13.272269	-3.795199	-0.949651	H	1.767261	5.131123	-3.394710

Table S4. Cartesian coordinates of the optimized structures of atkamine using the BH&HLYP/TZVP method with the PCM solvation model representing methanol.

Conf.1	X	Y	Z	Conf.2	X	Y	Z
C	6.371182	-0.996347	-0.010414	C	6.408860	-0.942511	-0.024376
C	6.886674	-1.885076	0.906825	C	6.958207	-1.826061	0.878140
C	7.939607	-2.702898	0.549455	C	8.040767	-2.599849	0.508690
C	8.490612	-2.649335	-0.723891	C	8.589958	-2.506628	-0.762247
C	7.966018	-1.760690	-1.648726	C	8.033188	-1.623067	-1.672895
C	6.916277	-0.948444	-1.283601	C	6.953416	-0.855513	-1.296597

C	4.796607	0.614519	-1.094466	C	4.783631	0.637475	-1.073535
S	6.131684	0.217996	-2.341426	S	6.124746	0.297961	-2.333789
C	5.709055	1.202973	1.061862	C	5.660236	1.205244	1.110831
C	4.928709	2.126577	-0.790991	C	4.870813	2.144552	-0.732407
N	4.615773	1.740785	1.865538	N	4.567349	1.671862	1.925442
C	3.724779	2.521939	1.302475	C	3.625518	2.471348	1.370646
C	3.772389	2.760401	-0.059424	C	3.681061	2.717930	-0.010986
C	2.687499	3.106786	2.264535	C	2.630293	3.024128	2.275564
C	1.728723	3.925759	1.596700	C	1.651384	3.811142	1.603260
C	1.804851	4.154923	0.248713	C	1.703786	4.027501	0.246429
C	2.784478	3.575022	-0.626549	C	2.709027	3.515958	-0.596242
O	2.764887	2.862667	3.440331	O	2.666245	2.796158	3.500606
N	2.648432	3.884592	-1.893381	N	2.583835	3.853573	-1.910486
C	1.442815	4.534936	-2.438804	C	0.441506	5.102604	-1.599963
C	0.849420	5.602217	-1.521976	C	0.598858	4.805810	-0.145121
C	0.860391	5.103538	-0.117163	C	-0.101930	5.057648	0.997319
C	0.196405	5.428803	1.047474	N	0.540316	4.454172	2.052953
N	0.729686	4.713194	2.065660	O	9.640965	-3.238371	-1.173862
O	9.512468	-3.424413	-1.124137	Br	8.795991	-3.825283	1.755709
Br	8.650581	-3.934797	1.814142	O	5.980334	2.190475	0.160936
O	6.038230	2.161079	0.103579	C	3.455957	0.137797	-1.659061
C	3.461455	0.121287	-1.668958	C	5.262171	-0.020278	0.253848
C	5.258149	-0.028824	0.250484	C	2.310981	-0.169018	-0.698956
C	2.297768	-0.123689	-0.713770	C	1.029039	-0.497011	-1.450466
C	1.027175	-0.485650	-1.469372	C	-0.118103	-0.882848	-0.531169
C	-0.131920	-0.831908	-0.549365	C	-1.410938	-1.186079	-1.270904
C	-1.415519	-1.165421	-1.292112	C	-2.552205	-1.587115	-0.350514
C	-2.563728	-1.539838	-0.369156	C	-3.852927	-1.871360	-1.083925
C	-3.858049	-1.849938	-1.103386	C	-4.988539	-2.284026	-0.161639
C	-4.996488	-2.245593	-0.177142	C	-6.295746	-2.551029	-0.890047
C	-6.300061	-2.532717	-0.904370	C	-7.426308	-2.973363	0.034041
C	-7.429989	-2.946431	0.024387	C	-8.737851	-3.224271	-0.691456
C	-8.740315	-3.211638	-0.698164	C	-9.865250	-3.654034	0.243029
C	-9.864292	-3.640171	0.240926	C	-11.134000	-3.956677	-0.487588
C	-11.133274	-3.952076	-0.485359	H	4.457619	-0.547183	0.744649
H	4.437395	-0.515407	0.756668	H	6.517985	1.023108	1.739089
H	6.553514	1.025355	1.707372	H	5.127064	2.737814	-1.598746
H	5.201112	2.696926	-1.666755	H	6.551461	-1.919173	1.868782
H	6.476872	-1.947920	1.898523	H	8.456740	-1.564494	-2.658627
H	8.389939	-1.733605	-2.635529	H	-1.706139	-0.312234	-1.849345
H	-1.708166	-0.313294	-1.903252	H	-1.234258	-1.982803	-1.991613
H	-1.228181	-1.985784	-1.982789	H	-4.696204	-3.176422	0.389330
H	-4.703560	-3.124732	0.394405	H	-5.146564	-1.505374	0.582802
H	-5.160074	-1.451378	0.549469	H	0.171058	-1.752017	0.057103

H	0.149528	-1.676191	0.077352	H	-0.293272	-0.077973	0.180557
H	-0.315909	0.001477	0.126469	H	-6.592204	-1.655638	-1.433813
H	-6.600492	-1.648450	-1.463928	H	-6.137741	-3.324268	-1.640048
H	-6.135600	-3.317604	-1.640720	H	0.002372	6.076522	-1.781937
H	1.433510	6.515450	-1.586354	H	-0.207253	4.364906	-2.065206
H	-0.147933	5.832856	-1.873659	H	-1.003750	5.611006	1.158678
H	-0.606720	6.113540	1.222748	H	2.574811	-1.019639	-0.076722
H	2.543739	-0.939120	-0.040062	H	2.127233	0.662831	-0.030516
H	2.101478	0.742602	-0.094674	H	4.647554	1.686222	2.922318
H	1.720029	4.964212	-3.389447	H	0.238930	4.488189	3.004233
H	0.710159	3.755801	-2.621929	H	9.940524	-3.819847	-0.475596
H	4.583776	1.606156	2.860008	H	3.121361	0.867320	-2.392824
H	0.425915	4.759234	3.018665	H	3.664131	-0.766726	-2.219021
H	9.793678	-4.005181	-0.417552	H	0.736000	0.362110	-2.050841
H	3.151907	0.817488	-2.444681	H	1.217790	-1.309229	-2.150376
H	3.659315	-0.811520	-2.183594	H	-7.134659	-3.875436	0.569274
H	0.742902	0.345012	-2.112464	H	-7.576694	-2.205414	0.790976
H	1.227864	-1.328254	-2.128168	H	-9.037970	-2.322488	-1.220599
H	-7.135429	-3.840222	0.571761	H	-9.547036	-4.549083	0.776374
H	-7.583623	-2.169042	0.770984	H	3.353381	3.657160	-2.517385
H	-9.046125	-2.316367	-1.235060	H	-2.718579	-0.796469	0.379317
H	-9.541387	-4.530725	0.778999	H	-2.260806	-2.468867	0.217828
H	3.295640	3.522424	-2.566213	H	-3.686089	-2.655593	-1.820547
H	-2.737815	-0.727350	0.334448	H	-4.149199	-0.985951	-1.644035
H	-2.274961	-2.402802	0.228511	H	-10.021588	-2.888742	0.994846
H	-3.682327	-2.651870	-1.818488	H	-8.590222	-3.990005	-1.450572
H	-4.155708	-0.980859	-1.687790	C	-12.325429	-3.402335	-0.326119
H	-10.022423	-2.871117	0.988533	C	-12.724132	-2.324428	0.630145
H	-8.588568	-3.983160	-1.450566	H	-11.885801	-2.018394	1.245686
C	-12.328795	-3.408580	-0.317520	H	-13.476629	-2.721805	1.310416
C	-12.732960	-2.336823	0.643347	C	-13.309241	-1.103681	-0.074305
H	-11.895113	-2.025959	1.257141	H	-14.141332	-1.417298	-0.701651
H	-13.479873	-2.742504	1.324835	H	-12.560979	-0.686305	-0.744545
C	-13.330490	-1.118677	-0.055130	C	-13.782480	-0.028967	0.890399
H	-14.161498	-1.437245	-0.681383	H	-12.948543	0.284711	1.516002
H	-12.587714	-0.692354	-0.725848	H	-14.525196	-0.453989	1.563489
C	-13.810548	-0.051690	0.914811	C	-14.372903	1.187139	0.195884
H	-12.977942	0.266443	1.539961	H	-15.208540	0.874094	-0.428003
H	-14.548270	-0.485548	1.587715	H	-13.631398	1.611148	-0.479349
C	-14.412506	1.162198	0.226367	C	-14.844912	2.264650	1.158871
H	-15.246464	0.844599	-0.397434	C	-15.435925	3.474757	0.455819
H	-13.675818	1.595398	-0.448302	H	-14.009514	2.578779	1.780745
C	-14.892175	2.231548	1.194688	H	-15.584590	1.840755	1.834542
C	-15.494385	3.439630	0.497687	H	-15.764022	4.225759	1.166807



H	-14.058551	2.550045	1.816738	H	-14.706788	3.938106	-0.202248
H	-15.627232	1.798482	1.869558	H	-16.293249	3.194238	-0.148884
H	-15.827737	4.184789	1.212355	H	-11.044799	-4.725199	-1.242292
H	-14.770143	3.911873	-0.159451	H	-13.125585	-3.757171	-0.960155
H	-16.350204	3.154486	-0.106955	C	1.821232	5.055997	-2.261796
H	-11.040628	-4.718391	-1.241888	H	2.381497	5.942651	-1.970185
H	-13.128542	-3.768991	-0.948898	H	1.716778	5.068783	-3.337770

Table S5. Calculated thermodynamic data and ZPVE-corrected energies (in eV) of the low energy conformations of atkamine.

B3LYP/6-31G(d,p)/PCM(MeOH)					
Species	$E_{\text{total}}$	$E_{\text{zpe}}$	$U_{273\text{K}}$	$H_{273\text{K}}$	$G_{273\text{K}}$
Conf.1	-4915.961716	-4915.091033	-4915.042438	-4915.041494	-4915.183487
Conf.2	-4915.962515	-4915.091720	-4915.043189	-4915.042245	-4915.184661
BH&HLYP/TZVP/PCM(MeOH)					
Species	$E_{\text{total}}$	$E_{\text{zpe}}$	$U_{273\text{K}}$	$H_{273\text{K}}$	$G_{273\text{K}}$
Conf.1	-4917.745392	-4916.846715	-4916.799330	-4916.798386	-4916.938354
Conf.2	-4917.745820	-4916.847580	-4916.800061	-4916.799116	-4916.939653

Table S6. Calculated Boltzmann population of the low energy conformations of atkamine.

B3LYP/6-31G(d,p)/PCM(MeOH)					
Species	$E_{\text{total}}$	$E_{\text{zpe}}$	$U_{273\text{K}}$	$H_{273\text{K}}$	$G_{273\text{K}}$
Conf.1	69.87%	67.32%	68.79%	68.79%	77.47%
Conf.2	30.13%	32.68%	31.21%	31.21%	22.53%
BH&HLYP/TZVP/PCM(MeOH)					
Species	$E_{\text{total}}$	$E_{\text{zpe}}$	$U_{273\text{K}}$	$H_{273\text{K}}$	$G_{273\text{K}}$
Conf.1	61.07%	71.30%	68.33%	68.31%	79.68%
Conf.2	38.93%	28.70%	31.67%	31.69%	20.32%

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