



Geometry and Vibration Spectrum of Marine β -Carboline Alkaloid

YUANQIANG ZHU^{1,*}, HONG SU¹ and JIANCHUN GUO²

¹School of Chemistry and Chemical Engineering, Southwest Petroleum University, Chengdu 610500, Sichuan Province, P.R. China

²State Key Laboratory of Oil and Gas Reservoir Geology and Exploitation, Southwest Petroleum University, Chengdu 610500, Sichuan, P.R. China

*Corresponding author: E-mail: yqzhu@swpu.edu.cn

Received: 7 July 2014;

Accepted: 10 March 2015;

Published online: 26 May 2015;

AJC-17228

In this study, the geometry and vibration spectrum of 5-bromo-8-methoxy-1-methyl- β -carboline alkaloid was investigated by the density functional theory (DFT) in combination with the scaled quantum mechanism force field method (SQM). The fully optimized geometries at the B3LYP/6-311++G** and B3LYP/aug-cc-pVDZ levels were found to be in good agreement with the X-ray crystal structure. Based on the optimized geometries, a normal coordinate analysis was carried out with the GF matrix method to generate the potential energy distributions. According to potential energy distributions, all vibration modes were assigned reliably to certain vibration frequencies. The strongest absorption peak with a frequency of 1265 cm^{-1} is contributed by the stretching of the N₁₆-C₁₇, N₂₄-C₂₁, C₂₃-C₂₅ bonds and triangle deformation of the C₁₅-C₁₇-C₂₃-N₂₄-C₂₁-C₁₉ six member ring and potential energy distributions of the these modes are 10.85, 14.90, 10.99 and 21.53 %, respectively. This study is helpful to further study the relationship between the structure and the pharmacological activity of β -carboline alkaloid derivatives.

Keywords: β -Carboline alkaloid, Normal coordinate analysis, Vibration spectrum, Density functional theory, Potential energy distributions.

INTRODUCTION

In the past 10 years, new compounds originating from marine actinomycetes have been widely applied in many fields, even more popular than compounds from their terrestrial counterparts. Marine actinomycetes have been more and more considered as an exciting new resource for drug discovery^{1,2}. Actinomycetes are important economical microorganisms and play a leading role in the production of bioactive natural products^{3,4}. The vast majority of bryozoans metabolites isolated to date are alkaloids, such as the β -carboline derivatives^{5,6}. It has been demonstrated that new species of marine actinomycetes are capable of producing novel chemotypes.

β -Carboline derivatives are a kind of indole alkaloids widely distributed in nature and show a wide biological activity⁷⁻⁹. Previous studies¹⁰⁻¹² have found that β -carboline alkaloid derivatives show the activity which affects the central nervous system, especially benzodiazepine receptor demonstrated antispasmodic, anxiolytic and neural pharmacological activity. This very pharmacological activity inspires people to research the β -carboline alkaloid derivatives and pharmacological activity^{12,13}. In recent years, studies have also found that β -carboline alkaloid and its derivatives have anticancer, antitumor and other aspects of biological activity^{14,15}, such as, the Lavendamycin with antimicrobial antitumor and HIV

reverse transcriptase inhibition, harmaline with antitumor activity¹⁶⁻¹⁸. As a marine β -carboline alkaloid derivative recently isolated from bryozoans by Till and Prinsep¹⁹, the 5-bromo-8-methoxy-1-methyl- β -carboline have proven to be an excellent source of novel biologically active compounds. Till and co-workers analyzed its structure with X-ray and NMR diffraction technique and obtained the structure parameters of the skeleton. However, there are no theoretical reports on the microcosmic structure and the vibration spectrum. The geometry and the spectral property of 5-bromo-8-methoxy-1-methyl- β -carboline need further researches.

Herein, we reported the geometry and vibration spectrum of a marine β -carboline alkaloid. The DFT calculations in combination with the scaled quantum mechanical force field were used to analyze vibration spectrum of 5-bromo-8-methoxy-1-methyl- β -carboline. The results will provide support for the relationship of the structure and pharmacological activity of β -carboline alkaloid.

THEORETICAL METHODOLOGIES

The Gaussian 09 program²⁰ were carried out to optimize the geometry of 5-bromo-8-methoxy-1-methyl- β -carboline alkaloid at the B3LYP/6-311++G** and B3LYP/aug-cc-pVDZ levels. The molecular structure was depicted in Fig. 1. Based

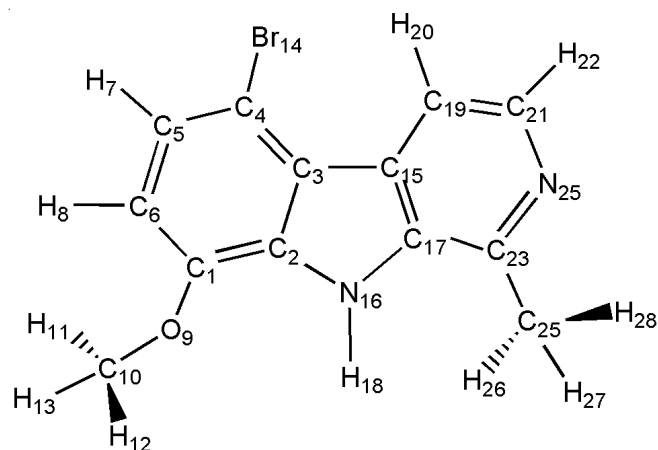


Fig. 1. Molecular structure and atom numbering of 5-bromo-8-methoxy-1-methyl- β -carboline

on the optimized geometry, the vibration frequencies were calculated at the same level to generate the vibration harmonic force constants.

The local internal symmetry coordinates were defined using the method given by Pulay *et al.*²¹. The coordinates were sorted into four types, $s_1 \sim s_{30}$ for bond stretching, $s_{31} \sim s_{57}$ for bond angle deformation, $s_{58} \sim s_{65}$ for out-of-plane bending, $s_{66} \sim s_{78}$ for bond torsion. The local internal symmetry coordinates were not presented in this paper for the space. A normal coordinate analysis was carried out using GF matrix method developed by Wilson to give the scaled vibration frequencies and the potential energy distributions. The theoretical force field F matrix, which was obtained through molecular vibration calculation programs, was transformed from cartesian into the local internal coordinates. In order to make the vibration frequencies in good agreement with the experimental values, we applied SQM procedures given by Pulay *et al.*²² to empirically scale the theoretical force fields:

$$F_{ij}^{\text{Scaled}} = (C_i C_j)^{1/2} F_{ij}^{\text{DFT}} \quad (1)$$

C represents the scaled factor of the i local internal symmetry coordinates; F_{ij}^{DFT} stands for the theoretical force constant in the local internal coordinates and F_{ij}^{Scaled} means the scaled force constant. According to previous studies²³, the scale factors are 0.9679 for the vibration frequency higher than 1000 cm^{-1} and 1.0100 for the vibration frequency lower than 1000 cm^{-1} . The kinetic energy matrix, G , was built up from a set of independent internal coordinates and the optimized molecular geometry. And then the corresponding GF matrix eigen values were calculated. These results lead to the final theoretical frequencies and the potential energy distributions matrix.

RESULTS AND DISCUSSION

Geometry of 5-bromo-8-methoxy-1-methyl- β -carboline:

The two B3LYP/6-311++G** and B3LYP/aug-cc-pVDZ levels give a similar geometry and vibrational frequencies. The calculated vibrational frequencies have no imaginary frequency, which indicates that the optimized geometry is located at the minimum point on the potential energy surface. The following discussions were mainly based on the results calculated by B3LYP method. The calculated geometric parameters were listed in Table-1.

Table-1 showed that the calculated geometric parameters are very close to the experimental X-ray crystal structure¹⁹. The bond distance of the C_1 - C_2 bond is 0.1402 and 0.1400 nm at the B3LYP/6-311++G** and B3LYP/aug-cc-pVDZ levels, respectively. Compared with the experimental results, the difference of the bond length is only 0.0004 nm. The bond angle of the C_6 - C_1 - C_2 three atoms is 117.6 and 117.5 degree at the two levels, respectively. The calculated bond angle of C_6 - C_1 - C_2 is only 0.3 degree larger than that of the experiment value. The dihedral angle of the O_9 - C_1 - C_2 - C_3 four atoms is 0.0 and 0.0 degree at the two levels of theory, respectively. The largest difference between the calculated dihedral angle and the experiment results is only 0.1 degree. From the torsional angles in Table-1, it is concluded that all atoms of the molecular skeleton are in the same plane, which presents the aromatic characteristics.

IR spectrum of 5-bromo-8-methoxy-1-methyl- β -carboline:

Based on the optimized geometry, the vibration frequency was calculated at the same levels. The Gaussian functions were used to describe the infrared spectrum with the vibration frequency and absorption intensity. The infrared spectrum diagrams obtained at the B3LYP/6-311++G** level was depicted in Fig. 2. The 5-bromo-8-methoxy-1-methyl- β -carboline molecule belongs to the point group C_1 and involves 78 free degrees of vibration, all of which are infrared and Raman activity.

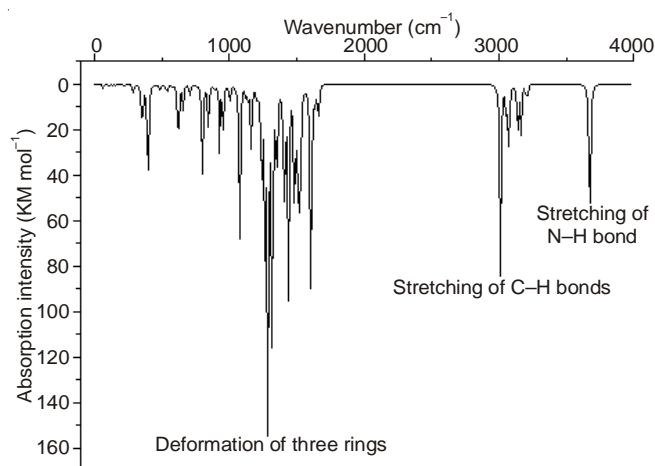


Fig. 2. Calculated IR spectrum of 5-bromo-8-methoxy-1-methyl- β -carboline at B3LYP/6-311++G** level

The interaction between the indole-ring and the pyridine-ring leads to the fundamental frequency distribution below 1633 cm^{-1} . The coupling appears in the vibration modes of characteristic frequency, which makes it difficult to assign the vibration modes to a certain frequency. Therefore, we calculated the harmonic vibration force constants of 5-bromo-8-methoxy- β -carboline and the potential energy distributions of vibration modes. The vibration frequency of 5-bromo-8-methoxy- β -carboline can be clearly assigned according to the potential energy distributions. The results were listed in Table-2. Table-2 showed that there are 78 vibration frequencies from 60 to 3616 cm^{-1} . The strongest absorption peak is the vibration mode 31 with a wave number of 1265 cm^{-1} and an intensity of $159.18 \text{ KM mol}^{-1}$, which is contributed by the stretching of

TABLE-1
CALCULATED AND EXPERIMENTAL GEOMETRIC PARAMETERS OF
5-BROMO-8-METHOXY-1-METHYL- β -CARBOLINE MOLECULE

Name	B3LYP/6-311++G**	B3LYP/aug-cc-pVDZ	Expt. [Ref. 19]	Name	B3LYP/6-311++G**	B3LYP/aug-cc-pVDZ	Expt. [Ref. 19]
Bond length (nm)							
C ₁ -C ₂	0.1402	0.1405	0.1404	C ₁₇ -N ₁₆	0.1384	0.1386	0.1375
C ₂ -C ₃	0.1415	0.1420	0.1415	C ₁₇ -C ₁₅	0.1415	0.1418	0.1414
C ₃ -C ₄	0.1405	0.1409	0.1402	C ₁₅ -C ₃	0.1451	0.1453	0.1443
C ₄ -C ₅	0.1382	0.1386	0.1375	N ₁₆ -H ₁₈	0.1006	0.1008	0.0750
C ₅ -C ₆	0.1410	0.1414	0.1412	C ₁₇ -C ₂₃	0.1402	0.1406	0.1400
C ₆ -C ₁	0.1387	0.1392	0.1385	C ₂₃ -N ₂₄	0.1331	0.1335	0.1339
C ₆ -H ₈	0.1082	0.1087	0.1000	C ₂₁ -N ₂₄	0.1348	0.1351	0.1354
C ₅ -H ₇	0.1082	0.1088	0.0920	C ₂₁ -C ₁₉	0.1387	0.1392	0.1381
C ₁ -O ₉	0.1366	0.1368	0.1361	C ₁₉ -C ₁₅	0.1401	0.1405	0.1405
C ₂ -N ₁₆	0.1377	0.1380	0.1375	C ₂₅ -H ₂₆	0.1096	0.1102	0.1080
C ₄ -Br ₁₄	0.1917	0.1918	0.1900	C ₂₅ -H ₂₇	0.1096	0.1102	0.1030
C ₁₀ -O ₉	0.1424	0.1426	0.1432	C ₂₃ -C ₂₅	0.1505	0.1506	0.1500
C ₁₉ -H ₂₀	0.1081	0.1087	0.0930	C ₂₁ -H ₂₂	0.1085	0.1091	0.0980
Angles (°)							
C ₆ -C ₁ -C ₂	117.61	117.62	117.87	O ₉ -C ₁ -C ₆	126.89	126.72	126.86
C ₁ -C ₂ -C ₃	122.92	122.82	122.28	O ₉ -C ₁ -C ₂	115.50	115.67	115.25
C ₂ -C ₃ -C ₄	117.64	117.75	117.87	O ₉ -C ₁₀ -H ₁₁	111.13	110.99	119.4
C ₃ -C ₄ -C ₅	120.12	120.15	120.57	C ₂₁ -C ₁₉ -C ₁₅	117.34	117.28	117.32
C ₄ -C ₅ -C ₆	121.02	120.93	120.64	O ₉ -C ₁₀ -H ₁₃	111.14	111.01	124.7
C ₅ -C ₆ -C ₁	120.69	120.74	120.75	H ₁₁ -C ₁₀ -H ₁₂	109.47	109.60	117.3
C ₁₅ -C ₃ -C ₂	105.93	105.99	105.74	H ₁₁ -C ₁₀ -H ₁₃	109.66	109.67	120.6
C ₃ -C ₂ -N ₁₆	109.61	109.49	109.96	H ₁₂ -C ₁₀ -H ₁₃	109.46	109.60	118.6
C ₂ -N ₁₆ -C ₁₇	108.85	108.94	108.22	H ₁₈ -N ₁₆ -C ₂	124.17	124.32	123.00
N ₁₆ -C ₁₇ -C ₁₅	108.93	108.93	109.59	H ₁₈ -N ₁₆ -C ₁₇	126.99	126.74	129.00
C ₁₇ -C ₁₅ -C ₃	106.67	106.65	106.46	C ₁₅ -C ₁₉ -H ₂₀	121.98	121.99	122.70
C ₁₉ -C ₁₅ -C ₁₇	117.34	117.40	117.54	C ₁₉ -C ₂₁ -H ₂₂	119.94	119.87	119.00
C ₁₅ -C ₁₇ -C ₂₃	121.57	121.56	121.64	C ₂₁ -C ₁₉ -H ₂₀	120.68	120.73	120.00
C ₁₇ -C ₂₃ -N ₂₄	119.57	119.56	119.37	N ₂₄ -C ₂₁ -H ₂₂	115.40	115.47	116.30
C ₂₃ -N ₂₄ -C ₂₁	119.52	119.55	119.44	C ₁₇ -C ₂₃ -C ₂₅	121.63	121.73	121.40
N ₂₄ -C ₂₁ -C ₁₉	124.66	124.66	124.67	N ₂₄ -C ₂₃ -C ₂₅	118.80	118.72	119.23
C ₅ -C ₄ -Br ₁₄	118.83	118.89	119.86	Br ₁₄ -C ₄ -C ₃	121.05	120.96	119.57
C ₁ -C ₂ -N ₁₆	127.46	127.68	127.71	C ₄ -C ₃ -C ₁₅	136.43	136.27	136.34
N ₁₆ -C ₁₇ -C ₂₃	129.50	129.51	128.74	C ₃ -C ₁₅ -C ₁₉	135.98	135.94	135.98

the N₁₆-C₁₇, N₂₄-C₂₁, C₂₃-C₂₅ bonds and the deformation of the C₁₅-C₁₇-C₂₃-N₂₄-C₂₁-C₁₉ ring. Potential energy distributions of the stretching of the bonds and the deformation of the C₁₅-C₁₇-C₂₃-N₂₄-C₂₁-C₁₉ ring are 10.85, 14.90, 10.99 and 21.53 %, respectively. These three bonds are the characteristic groups of the 5-bromo-8-methoxy-1-methyl- β -carboline, corresponding to the characteristic absorption peak. The weakest one is the vibration mode 45 with a frequency of 910 cm⁻¹ and an intensity of 0.04 KM mol⁻¹. This absorption peak can not be observed in the experimental infrared spectrum, but can be clearly assigned through the potential energy distributions. The vibration mode is contributed by the out-of-plan bend of the C₆-H₈, C₅-H₇ bonds (Table-2). Total potential energy distributions of these vibration patterns is 132.06 %, more than 100 %, which indicates that strong coupling is appearing between these vibration modes.

The vibration mode with the highest frequency of 3616 cm⁻¹ is contributed by the stretching of the N₁₆-H₁₈ bond in indole-ring, which presents a strong absorption intensity of 88.66 KM mol⁻¹ (Table-2). The potential energy distributions of the N₁₆-H₁₈ bond stretching is 99.96 % and the potential energy distributions of other vibration modes are zero, which indicates no other vibration coupling appearing. In Fig. 2, the

sharp absorption peak can be used as the characteristic vibration absorption peak of 5-bromo-8-methoxy- β -carboline. The vibration frequencies with wave number around 3000 cm⁻¹ has relatively weak absorption intensity and the potential energy distributions show that there is no coupling appearing. These vibration frequencies are contributed by the stretching movement of carbon-hydrogen bonds. The carbon-hydrogen bonds' stretching movement can be easily identified based on the potential energy distributions, which is consistent with the experimental data with wave numbers 2925 cm⁻¹. All vibration modes with wave numbers lower than 1700 cm⁻¹ are more than two vibration modes appearing coupling. For instance, the vibration mode 66 is contributed by the in-plan rocking of the C₄-Br₁₄ bond and the perking of the two rings C₁-C₂-C₃-C₄-C₅-C₆, C₃-C₂-N₁₆-C₁₇-C₁₅ and the C₁₅-C₁₇-C₂₃-N₂₄-C₂₁-C₁₉ asymmetry torsion. The wave number of this mode is 293 cm⁻¹ and the absorption intensity is 1.65 KM mol⁻¹. The potential energy distributions of the vibration patterns are 14.27, 32.50 and 30.53 %, respectively. The vibration of the C₄-Br₁₄ bond in the ground state is extremely weak and other vibration mode coupling appears. Therefore, there is no characteristic absorption peak appearing in the IR spectrum for the C₄-Br₁₄ bond.

TABLE-2
ASSIGNMENT OF THE CALCULATED IR SPECTRUM OF
5-BROMO-8-METHOXY-1-METHYL- β -CARBOLINE AT THE B3LYP/6-311++G** LEVEL

No.	B3LYP/6-311++G**			Potential energy distributions (%)	Assignment ^a
	Frequency (cm ⁻¹)	Scaled (cm ⁻¹)	Intensity (KM mol ⁻¹)		
v ₁	3676	3616	88.66	S ₂₅ (99.96)	N ₁₆ -H ₁₈ stretch.
v ₂	3219	3167	4.12	S ₁₉ (98.20)	C ₁₉ -H ₂₀ stretch.
v ₃	3211	3159	3.00	S ₁₆ (58.65), S ₁₇ (41.02)	C ₆ -H ₈ stretch. C ₅ -H ₇ stretch.
v ₄	3197	3145	3.88	S ₁₆ (41.44), S ₁₇ (59.06)	C ₆ -H ₈ stretch. C ₅ -H ₇ stretch.
v ₅	3160	3109	21.46	S ₂₀ (98.47)	C ₂₁ -H ₂₂ stretch.
v ₆	3139	3088	17.60	S ₂₉ (21.97), S ₃₀ (67.28)	C ₁₀ H ₁₃ H ₁₂ H ₁₁ asym. stretch. C ₁₀ H ₁₂ H ₁₁ asym. stretch.
v ₇	3131	3080	6.58	S ₂₃ (90.68)	C ₂₅ H ₂₈ H ₂₇ H ₂₆ asym. stretch.
v ₈	3073	3023	31.51	S ₂₉ (76.12), S ₃₀ (25.77)	C ₁₀ H ₁₃ H ₁₂ H ₁₁ asym. stretch. C ₁₀ H ₁₂ H ₁₁ asym. stretch.
v ₉	3054	3005	19.25	S ₂₄ (100.88)	C ₂₅ H ₂₇ H ₂₆ asym. stretch.
v ₁₀	3011	2963	62.85	S ₂₈ (91.82)	C ₁₀ H ₁₃ H ₁₂ H ₁₁ symm. stretch.
v ₁₁	3010	2961	25.35	S ₂₂ (91.50), S ₂₃ (10.24)	C ₂₅ H ₂₈ H ₂₇ H ₂₆ symm. stretch. C ₂₅ H ₂₈ H ₂₇ H ₂₆ asym. stretch.
v ₁₂	1657	1633	19.37	S ₁ (38.16), S ₄ (13.83), S ₃₃ (10.60)	C ₁ -C ₂ stretch. C ₄ -C ₅ stretch. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. deform.
v ₁₃	1633	1612	8.26	S ₁₁ (26.89), S ₁₄ (16.12), S ₁₅ (11.26), S ₃₇ (10.34)	C ₁₇ -C ₂₃ stretch. C ₂₁ -C ₁₉ stretch. C ₁₉ -C ₁₅ stretch. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. deform.
v ₁₄	1603	1583	104.21	S ₅ (10.64), S ₆ (20.82), S ₃₉ (14.59)	C ₅ -C ₆ stretch. C ₆ -C ₇ stretch. C ₆ -H ₈ i-p rock.
v ₁₅	1597	1577	16.67	S ₉ (14.26), S ₁₂ (12.20), S ₁₅ (25.16), S ₃₈ (10.92)	C ₁₇ -C ₁₅ stretch. C ₂₃ -N ₂₄ stretch. C ₁₉ -C ₁₅ stretch. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. deform.
v ₁₆	1524	1513	76.17	S ₅₄ (23.01), S ₅₅ (67.65)	C ₁₀ H ₁₃ H ₁₂ H ₁₁ asym. deform. C ₁₀ H ₁₃ H ₁₂ H ₁₁ scis.
v ₁₇	1512	1511	24.09	S ₄ (11.31), S ₃₄ (11.12), S ₄₀ (20.47)	C ₄ -C ₅ stretch. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring deform. C ₅ -H ₇ i-p rock.
v ₁₈	1505	1507	30.11	S ₄₃ (14.65), S ₄₇ (25.05)	C ₂₁ -H ₂₂ i-p rock. C ₂₅ H ₂₆ H ₂₇ H ₂₈ scis.
v ₁₉	1491	1498	9.76	S ₅₄ (71.75), S ₅₅ (24.95)	C ₁₀ H ₁₃ H ₁₂ H ₁₁ asym. deform. C ₁₀ H ₁₃ H ₁₂ H ₁₁ scis.
v ₂₀	1486	1494	9.66	S ₄₆ (69.90), S ₄₇ (23.85)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ asym. deform. C ₂₅ H ₂₆ H ₂₇ H ₂₈ scis.
v ₂₁	1482	1484	45.18	S ₄₇ (18.20), S ₅₃ (54.76)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ scis. C ₁₀ H ₁₃ H ₁₂ H ₁₁ symm deform.
v ₂₂	1476	1480	6.30	S ₄₃ (14.94), S ₄₇ (16.78), S ₅₃ (39.44)	H ₂₂ i-p rock. C ₂₅ H ₂₆ H ₂₇ H ₂₈ scis. C ₁₀ H ₁₃ H ₁₂ H ₁₁ symm. deform.
v ₂₃	1441	1432	94.60	S ₈ (21.51), S ₉ (11.31), S ₄₂ (25.38)	N ₁₆ -C ₁₇ stretch. C ₁₇ -C ₁₅ stretch. C ₁₉ -H ₂₀ i-p rock.
v ₂₄	1417	1410	18.67	S ₄₅ (87.36)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ symm. deform.
v ₂₅	1410	1403	36.00	S ₂ (25.38), S ₃₉ (12.07), S ₅₀ (16.47)	C ₂ -C ₃ stretch. C ₆ -H ₈ i-p rock. N ₁₆ -H ₁₈ i-p rock.
v ₂₆	1403	1395	14.13	S ₃ (21.68), S ₄ (17.87), S ₇ (22.91), S ₅₀ (10.14)	C ₃ -C ₄ stretch. C ₄ -C ₅ stretch. C ₂ -N ₁₆ stretch. N ₁₆ -H ₁₈ i-p rock.
v ₂₇	1356	1341	53.71	S ₁ (14.61), S ₂ (20.21), S ₄ (12.39), S ₆ (22.81), S ₇ (11.25), S ₄₀ (10.15)	C ₁ -C ₂ stretch. C ₂ -C ₃ stretch. C ₄ -C ₅ stretch. C ₆ -C ₇ stretch. C ₂ -N ₁₆ stretch. C ₅ -H ₇ i-p rock.
v ₂₈	1331	1320	45.18	S ₁₀ (19.47), S ₁₂ (22.13), S ₁₅ (12.78), S ₄₃ (18.80)	C ₁₅ -C ₃ stretch. C ₂₃ -N ₂₄ stretch. C ₁₉ -C ₁₅ stretch. C ₂₁ -H ₂₂ i-p rock.
v ₂₉	1311	1295	109.20	S ₉ (23.71), S ₁₂ (25.10), S ₁₄ (14.32)	C ₁₇ -C ₁₅ stretch. C ₂₃ -N ₂₄ stretch. C ₂₁ -C ₁₉ stretch.
v ₃₀	1286	1276	41.23	S ₂₆ (12.00), S ₃₉ (22.81)	C ₁ -O ₉ stretch. C ₆ -H ₈ i-p rock.
v ₃₁	1280	1265	159.18	S ₈ (10.85), S ₁₃ (14.90), S ₂₁ (10.99), S ₃₆ (21.53)	N ₁₆ -C ₁₇ stretch. N ₂₄ -C ₂₁ stretch. C ₂₃ -C ₂₅ stretch. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ triangle deform.
v ₃₂	1260	1247	64.94	S ₁₃ (23.61), S ₂₆ (14.12)	N ₂₄ -C ₂₁ stretch. C ₁ -O ₉ stretch.
v ₃₃	1236	1229	53.92	S ₈ (13.83), S ₄₀ (12.59)	N ₁₆ -C ₁₇ stretch. C ₅ -H ₇ i-p rock.
v ₃₄	1205	1206	7.79	S ₅₆ (13.81), S ₅₇ (42.92)	C ₁₀ H ₁₃ H ₁₂ H ₁₁ asym. deform. C ₁₀ H ₁₃ H ₁₂ H ₁₁ scis.
v ₃₅	1168	1174	0.78	S ₅₆ (70.82), S ₅₇ (24.59)	C ₁₀ H ₁₃ H ₁₂ H ₁₁ asym. deform. C ₁₀ H ₁₃ H ₁₂ H ₁₁ scis.
v ₃₆	1161	1149	27.89	S ₂₇ (11.51), S ₃₆ (2.71), S ₅₀ (14.80)	O ₉ -C ₁₀ stretch. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ triangle deform. N ₁₆ -H ₁₈ i-p rock.
v ₃₇	1137	1128	8.15	S ₅ (36.14), S ₃₉ (19.26)	C ₅ -C ₆ stretch. C ₆ -H ₈ i-p rock.
v ₃₈	1121	1116	3.52	S ₁₃ (12.56), S ₁₄ (12.43), S ₄₂ (22.45), S ₄₈ (14.23)	N ₂₄ -C ₂₁ stretch. C ₂₁ -C ₁₉ stretch. C ₁₉ -H ₂₀ i-p rock. C ₂₅ H ₂₆ H ₂₇ H ₂₈ asym. deform.
v ₃₉	1079	1063	72.50	S ₂₇ (40.67)	O ₉ -C ₁₀ stretch.
v ₄₀	1053	1059	1.40	S ₄₉ (77.84), S ₆₃ (10.84)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ scis. C ₂₅ H ₂₆ H ₂₇ H ₂₈ o-o-p rock.
v ₄₁	1007	997	9.11	S ₂₇ (20.21), S ₄₈ (27.76)	O ₉ -C ₁₀ stretch. C ₂₅ H ₂₆ H ₂₇ H ₂₈ asym. deform.
v ₄₂	971	976	0.07	S ₆₁ (51.25), S ₆₂ (79.59)	C ₁₉ -H ₂₀ o-o-p rock. C ₂₁ -H ₂₂ o-o-p rock.
v ₄₃	958	949	23.11	S ₁₂ (11.99), S ₂₇ (13.49), S ₄₈ (23.74)	C ₂₃ -N ₂₄ stretch. O ₉ -C ₁₀ stretch. C ₂₅ H ₂₆ H ₂₇ H ₂₈ asym. deform.
v ₄₄	928	914	35.26	S ₇ (12.71), S ₁₈ (21.01), S ₃₁ (32.47)	C ₂ -N ₁₆ stretch. C ₄ -Br ₁₄ stretch. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ triangle deform.
v ₄₅	905	910	0.04	S ₅₈ (53.87), S ₅₉ (78.19)	C ₆ -H ₈ o-o-p rock. C ₅ -H ₇ o-o-p rock.

V ₄₆	886	875	1.91	S ₃₆ (41.74), S ₃₈ (14.80)	C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ triangle deform. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym deform.
V ₄₇	842	846	22.27	S ₆₁ (69.64), S ₆₂ (43.90)	C ₁₉ -H ₂₀ o-o-p rock. C ₂₁ -H ₂₂ o-o-p rock.
V ₄₈	809	803	1.36	S ₅₈ (65.31), S ₅₉ (32.30), S ₆₅ (24.06), S ₆₆ (21.74), S ₆₇ (10.24)	C ₆ -H ₈ o-o-p rock. C ₅ -H ₇ o-o-p rock. O ₉ C ₁₀ H ₁₃ H ₁₂ H ₁₁ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ perk. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors.
V ₄₉	799	797	39.70	S ₂₁ (10.47), S ₂₆ (10.99)	C ₂₃ -C ₂₅ stretch. C ₁ -O ₉ stretch.
V ₅₀	790	793	1.64	S ₆₃ (11.76), S ₆₆ (15.71), S ₆₉ (36.05), S ₇₂ (78.09)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ perk. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ perk.
V ₅₁	757	761	1.02	S ₅₉ (13.90), S ₆₅ (16.31), S ₆₆ (82.31), S ₇₀ (33.89), S ₇₂ (31.01)	C ₅ -H ₇ o-o-p rock. O ₉ C ₁₀ H ₁₃ H ₁₂ H ₁₁ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ perk. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ perk.
V ₅₂	708	697	5.66	S ₃₃ (18.70), S ₃₅ (13.22), S ₃₇ (17.61)	C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. deform. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring deform. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. deform.
V ₅₃	660	656	10.86	S ₆ (10.89), S ₃₄ (17.55), S ₅₁ (22.97), S ₅₂ (16.66)	C ₆ -C ₇ stretch. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring deform. O ₉ C ₁₀ H ₁₃ H ₁₂ H ₁₁ i-p rock. C ₁ -O ₉ -C ₁₀ bend.
V ₅₄	627	630	5.76	S ₆₃ (13.87), S ₆₅ (25.38), S ₆₇ (19.28), S ₆₉ (22.99), S ₇₁ (14.43), S ₇₂ (22.73), S ₇₃ (11.46), S ₇₄ (14.46)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ o-o-p rock. O ₉ C ₁₀ H ₁₃ H ₁₂ H ₁₁ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ perk. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors.
V ₅₅	625	615	31.88	S ₁₈ (15.95), S ₃₂ (20.67), S ₃₄ (11.89), S ₃₅ (12.76), S ₃₇ (18.97)	C ₄ -Br ₁₄ stretch. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. deform. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring deform. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring deform. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. deform.
V ₅₆	589	584	0.07	S ₆₅ (37.58), S ₆₇ (11.32), S ₆₈ (13.48), S ₇₀ (29.46), S ₇₃ (19.85), S ₇₅ (11.77)	O ₉ C ₁₀ H ₁₃ H ₁₂ H ₁₁ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk.
V ₅₇	581	582	0.93	S ₃₃ (35.14), S ₃₇ (18.91)	C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym deform. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym deform.
V ₅₈	566	569	0.06	S ₆₀ (49.00), S ₆₆ (39.48), S ₆₇ (43.75), S ₆₈ (16.23), S ₇₁ (10.32)	Br ₁₄ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ perk. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk.
V ₅₉	536	533	5.25	S ₂₁ (13.03), S ₃₈ (44.81)	C ₂₃ -C ₂₅ stretch. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. deform.
V ₆₀	550	522	0.36	S ₆₃ (44.63), S ₆₈ (12.08), S ₇₃ (21.30), S ₇₄ (39.37), S ₇₅ (17.64)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk.
V ₆₁	485	479	4.01	S ₃₂ (17.31), S ₄₄ (15.24)	C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. deform. C ₂₅ H ₂₆ H ₂₇ H ₂₈ i-p rock.
V ₆₂	396	398	60.33	S ₆₄ (71.19), S ₆₈ (22.74)	N ₁₆ -H ₁₈ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors.
V ₆₃	370	369	0.27	S ₄₁ (25.22), S ₄₄ (18.27), S ₅₂ (17.38)	C ₄ -Br ₁₄ i-p rock. C ₂₅ H ₂₆ H ₂₇ H ₂₈ i-p rock. C ₁ -O ₉ -C ₁₀ bend.
V ₆₄	355	356	26.89	S ₆₀ (22.99), S ₆₄ (45.20), S ₆₅ (15.85), S ₆₈ (13.19), S ₇₀ (21.78), S ₇₁ (10.61)	C ₄ -Br ₁₄ o-o-p rock. C ₆ -H ₁₈ o-o-p rock. O ₉ C ₁₀ H ₁₃ H ₁₂ H ₁₁ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk.
V ₆₅	340	337	0.49	S ₁ (11.48), S ₅₂ (32.43)	C ₁ -C ₂ stretch. C ₁ -O ₉ -C ₁₀ bend.
V ₆₆	292	293	1.65	S ₆₀ (14.27), S ₇₁ (32.50), S ₇₄ (30.53)	C ₄ -Br ₁₄ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors.
V ₆₇	289	291	1.75	S ₆₃ (16.33), S ₆₄ (63.61), S ₆₈ (12.69), S ₆₉ (23.78), S ₇₀ (19.19), S ₇₃ (11.73), S ₇₅ (39.84)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ o-o-p rock. N ₁₆ -H ₁₈ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk.
V ₆₈	282	279	0.37	S ₁₈ (24.27), S ₃₂ (19.83), S ₄₄ (20.18)	C ₄ -Br ₁₄ stretch. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. deform. C ₂₅ H ₂₆ H ₂₇ H ₂₈ i-p rock.
V ₆₉	228	229	0.05	S ₇₈ (83.64)	O ₉ -C ₁₀ tors.
V ₇₀	223	221	1.22	S ₁₈ (18.20), S ₄₄ (20.74)	C ₄ -Br ₁₄ stretch. C ₂₅ H ₂₆ H ₂₇ H ₂₈ i-p rock.
V ₇₁	202	203	0.31	S ₆₃ (12.89), S ₇₃ (15.02), S ₇₄ (20.33), S ₇₈ (10.16)	C ₂₅ H ₂₆ H ₂₇ H ₂₈ o-o-p rock. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. O ₉ -C ₁₀ tors.
V ₇₂	151	151	0.82	S ₄₁ (34.23), S ₅₁ (29.13)	C ₄ -Br ₁₄ i-p rock. O ₉ C ₁₀ H ₁₃ H ₁₂ H ₁₁ i-p rock.
V ₇₃	129	130	1.01	S ₆₇ (27.35), S ₇₀ (10.42), S ₇₇ (47.64)	C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁ -O ₉ tors.
V ₇₄	109	109	0.20	S ₃₃ (14.95), S ₄₁ (22.40)	C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. deform. C ₄ -Br ₁₄ i-p rock.
V ₇₅	104	105	0.95	S ₇₆ (103.99)	C ₂₃ -C ₂₅ tors.
V ₇₆	94	95	0.23	S ₆₄ (13.95), S ₆₇ (23.70), S ₆₉ (17.95), S ₇₀ (10.41), S ₇₁ (13.51), S ₇₃ (12.18), S ₇₅ (19.13)	N ₁₆ -H ₁₈ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk.
V ₇₇	65	65	0.50	S ₆₀ (18.31), S ₆₇ (10.79), S ₆₈ (11.64), S ₇₃ (23.18), S ₇₇ (11.11)	C ₄ -Br ₁₄ o-o-p rock. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₁₅ -C ₁₇ -C ₂₃ -N ₂₄ -C ₂₁ -C ₁₉ asym. tors. C ₁ -O ₉ tors.
V ₇₈	60	60	1.68	S ₆₈ (12.21), S ₇₀ (12.28), S ₇₁ (11.33), S ₇₇ (76.19), S ₇₈ (22.62)	C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ asym. tors. C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ ring tors. C ₁ -C ₂ -C ₃ -C ₄ -C ₅ -C ₆ , C ₃ -C ₂ -N ₁₆ -C ₁₇ -C ₁₅ perk. C ₁ -O ₉ tors. O ₉ -C ₁₀ tors.

Notes: We neglect the vibrational modes, potential energy distributions of which are lower than 10 %. ^a abbreviations used: stretch., stretching; bend., bending; deform., deformation; twis., twisting; scis., scissoring; rock., rocking; wagg., wagging; tors., torsion; i-p, in-plane; o-o-p, out-of-plane; asym., asymmetry; sym., symmetry. ^bFrequencies and intensities were calculated from the unscaled B3LYP/6-311++G** force field.

Raman spectrum of 5-bromo-8-methoxy-1-methyl- β -carboline: We have also predicted the Raman spectrum of the 5-bromo-8-methoxy-1-methyl- β -carboline molecule at the B3LYP/6-311++G** level. All vibration modes indicate Raman active. The calculated Raman spectrum was shown in Fig. 3. The strongest absorption peak is the symmetric stretching of three hydrogen atoms of the methoxy group with vibration frequency of 2947 cm^{-1} and absorption intensity of 497.15 KM mol^{-1} .

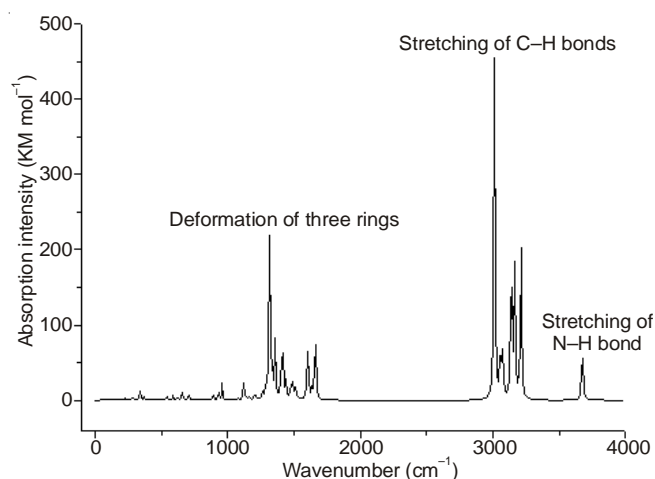


Fig. 3. Calculated Raman spectrum of 5-bromo-8-methoxy-1-methyl- β -carboline at B3LYP/6-311++G** level

The highest absorption peak is assigned to the stretching of the N-H bond. The absorption peak with vibration frequency around 3000 cm^{-1} is assigned to the stretching of C-H bond. The absorption peaks with vibration frequencies lower than 2000 cm^{-1} are complex and an absorption peak may correspond to several different vibration modes, appearing coupling.

Conclusion

The B3LYP method with the 6-311++G** and aug-cc-pVDZ basis sets was applied to study the geometry and vibration spectrum of 5-bromo-8-methoxy-1-methyl- β -carboline alkaloid. Wilson GF matrix method was used to analyze the normal internal coordinate. The fully optimized geometry is in consistent with the experimental results. The vibration modes were assigned reasonably according to the potential energy distributions. The total 78 vibration modes from 60 to 3616 cm^{-1} indicate Infrared and Raman active. The highest one is contributed exclusively by the stretching of the $\text{N}_{16}\text{-H}_{18}$ bond with potential energy distributions of 99.96 %. These results are helpful for further study of the relationship between molecular structure and pharmacological activity of the alkaloids.

ACKNOWLEDGEMENTS

This project has been supported by the Open Fund (No. PLN1124) of State Key Laboratory of Oil and Gas Reservoir Geology and Exploitation, Southwest Petroleum University.

REFERENCES

- W. Fenical and P.R. Jensen, *Nat. Chem. Biol.*, **2**, 666 (2006).
- T. Arai, M. Wasai and N. Yokoyama, *J. Org. Chem.*, **76**, 2909 (2011).
- J. Berdy, *J. Antibiot.*, **58**, 1 (2005).
- H. Huang, Y. Yao, Z. He, T. Yang, J. Ma, X. Tian, Y. Li, C. Huang, X. Chen, W. Li, S. Zhang, C. Zhang and J. Ju, *J. Nat. Prod.*, **74**, 2122 (2011).
- M.M. Parvez, N. Haraguchi and S. Itsuno, *Macromolecules*, **47**, 1922 (2014).
- V. Swathi, P.R. Pratap, N. Monila and S. Harshini, *Int. J. Pharm. Chem. Sci.*, **1**, 1098 (2012).
- R.H. Cao, W. Peng, Z. Wang and A. Xu, *Curr. Med. Chem.*, **14**, 479 (2007).
- Y. Lee, R.S. Klausen and E.N. Jacobsen, *Org. Lett.*, **13**, 5564 (2011).
- L. Salassa, *Eur. J. Inorg. Chem.*, **2011**, 4931 (2011).
- M. Cain, O. Campos, F. Guzman and J.M. Cook, *J. Am. Chem. Soc.*, **105**, 907 (1983).
- J. Asgarpanah and F. Ramezanloo, *Afr. J. Pharm. Pharmacol.*, **6**, 1573 (2012).
- Y. Li, R. Sattler, E.J. Yang, A. Nunes, Y. Ayukawa, S. Akhtar, G. Ji, P.-W. Zhang and J.D. Rothstein, *Neuropharmacology*, **60**, 1168 (2011).
- E.D. Cox, H. Diaz-Arauzo, Q. Huang, M.S. Reddy, C.R. Ma, B. Harris, R. McKernan, P. Skolnick and J.M. Cook, *J. Med. Chem.*, **41**, 2537 (1998).
- A.E. Laine, C. Lood and A.M.P. Koskinen, *Molecules*, **19**, 1544 (2014).
- H.J. Guan, H.S. Chen, W.L. Peng, Y. Ma, R.H. Cao, X.D. Liu and A.L. Xu, *Eur. J. Med. Chem.*, **41**, 1167 (2006).
- W.J. Zhang, Z. Liu, S.M. Li, T.T. Yang, Q. Zhang, L. Ma, X.P. Tian, H.B. Zhang, C.G. Huang, S. Zhang, J.H. Ju, Y.M. Shen and C.S. Zhang, *Org. Lett.*, **14**, 3364 (2012).
- M.R. Prinsep, B. Yao, B.K. Nicholson and D.P. Gordon, *Phytochem. Rev.*, **3**, 325 (2004).
- M. Schumacher, M. Kelkel, M. Dicato and M. Diederich, *Biotechnol. Adv.*, **531**, 29 (2011).
- M. Till and M.R. Prinsep, *J. Nat. Prod.*, **72**, 796 (2009).
- M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, Ö. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski and D.J. Fox, Gaussian 09, Revision D.01, Gaussian, Inc., Pittsburgh, PA (2013).
- P. Pulay, G. Fogarasi, G. Pang and J.E. Boggs, *J. Am. Chem. Soc.*, **101**, 2550 (1979).
- P. Pulay, G. Fogarasi, G. Pongor, J.E. Boggs and A. Vargha, *J. Am. Chem. Soc.*, **105**, 7037 (1983).
- M.P. Andersson and P. Uvdal, *J. Phys. Chem. A*, **109**, 2937 (2005).