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FTIR Spectra and Vibrational Spectroscopy of Lantadene A

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Abstract

The molecular geometry and vibrational frequencies of Lantadene A in the ground state have been calculated by Semi-empirical AM1 and PM3 parametrizations. Semi-empirical methods can produce reasonable results on relatively large molecules (near 100s of atoms) in a reasonable amount of time. The experimental frequencies of Lantadene A and the frequencies calculated by AM1 and PM3 methods are nearly the same. Quantum chemical calculations have been carried out to understand the dynamical behaviour of the bioactive molecule Lantadene A.

Keywords- Lantadene A, FTIR Spectra, Vibrational analysis

Introduction

Natural products have been the subject of investigation for many reasons. They have got wide applications, such as antibiotics, pharmacologically active agents or otherwise of interest in human or animal medicine. They hold great potential as probes of the cellular processes in which they interfere. Structural and conformational studies lead to hypothesis concerning target ligand interactions while synthesis is a means to test these hypotheses by eventual total synthesis of derivatives [1, 2]. Lantadene A, [22fl(Z)]-2-methylisocrotonoyloxy-3-oxoolean-12-en-28-oic acid, is the major triterpenoid constituent of *L. Camara*, red variety. Mixed toxin preparation from lantana leaves has been found to exist in two molecular forms, of which only one was found to be hepatotoxic to guinea pigs [3]. *Lantana* plant has been reported to possess a number of medicinal properties [4, 5]. Some metabolites isolated from their leaves possess antitumor activity [6], antithrombin activity [7], anti-inflammatory, antinociceptive and antipyretic activity [8]. During our program at CDRI, *lantana camara* (stem) has shown anti filarial activity [9].

The main objective of the present study is to investigate in detail the vibrational spectra of the important biological molecule Lantadene A that has been isolated from lantana camara leaves having anti filarial activity [10] along with other lantadenes and phinylpropanol glycosides. By AM1 [11] and PM3 [12] methods, which can possibly help in understanding its dynamical behavior. So far, to the best of our knowledge, no detailed quantum chemical calculations have been performed on Lantadene A in the literature.

Results and Discussion

Molecular geometry and Thermodynamic properties

The calculations of the geometry optimization locates the lowest energy conformer in close proximity to the specified starting structure [13,14,15]. The *A/B* and *B/C* rings are in *trans* conformation while the *D/E* rings are *cis* fused. The packing of the molecule is stabilized by O--H.--O hydrogen bonds. Bond lengths and angles (Table 1) agree with the values observed in similar structures such as maytenfolic acid, maytenfoliol (Nozaki, Suzuki, Lee & McPhail, 1982), cantoniensistriol triacetate (Mak, Chang & Chang, 1982) and in [3fl(E)]-acetoxyolean-12-en-28fl-oic acid *etc.* (Roques, Declercq & Germain, 1978). Three of the five six-membered rings (B, D and E) are in the chair conformation, while rings A and C are in sofa and half-chair conformations, respectively (Duax, Weeks & Rohrer, 1976) (Fig. 1). The presence of a double bond in ring C accounts for its twist conformation [16, 17, 18].

The bond lengths of the (C-C) stretch calculated by AM1 and PM3 methods are in the range from 1.473--1.572 and 1.479--1.586, which match well with the X-ray data (1.400--1.601). The bond angles of the (C-C-C) bend calculated by AM1 and PM3 methods are in the ranges from 106.67--120.24 and 105.78--124.77 and match well with the X-ray data (106.30--121.30) of the title compound.

The optimized structure parameters of Lantadene A, calculated by AM1 and PM3 methods are listed in Table-1. On the basis of vibrational analysis by AM1 and PM3 methods, the standard thermodynamic functions: internal thermal energy (E), constant volume heat capacity C_v and entropy S have been calculated and are given in the Table 2, respectively. They provide helpful information for the further study on the title compound**.** Here we have discussed the spectra in the range of 3500-400 cm^{-1}.

Assignments of vibrational spectra

Assignments of the IR frequencies are achieved by comparing the band positions and intensities observed in the IR spectra with wave numbers and intensities from molecular modeling calculations. The molecule Lantadene A (Fig-1) has 92 atoms with 270 normal modes of vibration. The calculated vibrational frequencies and the experimental values (Fig-2) are listed in Table-3. Here we are discussing only FTIR active modes in Table 3. The experimental frequencies of Lantadene A and frequencies calculated by AM1 and PM3 methods are nearly the same.

Table-1: Calculated bond lengths (angstroms) and bond angle (degrees) for Lantadene A, which were optimized at the semi-empirical AM1 and PM3 methods

	X-ray	AM1	PM3
Bond Lengths			
(C-C)	1.400--1.601	1.473--1.572	1.479--1.586
(C=C)	1.334--1.338	1.344--1.346	1.338--1.342
(C-O)	1.327--1.459	1.373--1.442	1.367--1.438
(C=O)	1.199--1.221	1.233--1.235	1.214--1.217
(C-H)	--	1.103--1.133	1.097--1.128
(O-H)	--	0.971	0.952
Bond Angles			
(C-C-C)	106.30--121.30	106.67--120.24	105.78--124.77
(C=C-C)	117.40--130.80	118.62--125.12	117.82--125.05
(C-C-H)	--	104.06--115.99	104.62--115.84
(C-O-C)	117.90	117.94	119.52
(C-O-H)	--	109.40	109.12
(C-C=O)	119.30--119.90	122.18--112.76	121.51--122.47
(C=C-H)	--	118.88--120.14	119.11--120.14
(O=C-O)	122.60--123.10	115.96--118.02	114.06--120.58
(H-C-H)	--	106.54--109.02	104.47--108.26

Table-2: Calculated Thermodynamic Properties of Lantadene A by Semi-empirical AM1 and PM3 methods

	E (Thermal) (KCal/Mol)		CV (Cal/Mol-Kelvin)		S (Cal/Mol-Kelvin)	
	AM1	PM3	AM1	PM3	AM1	PM3
Total	546.317	534.457	154.731	158.880	233.882	227.265
Translational	0.889	0.889	2.981	2.981	44.812	44.812
Rotational	0.889	0.889	2.981	2.981	37.921	37.927
Vibrational	544.540	532.680	148.769	152.918	151.148	144.525

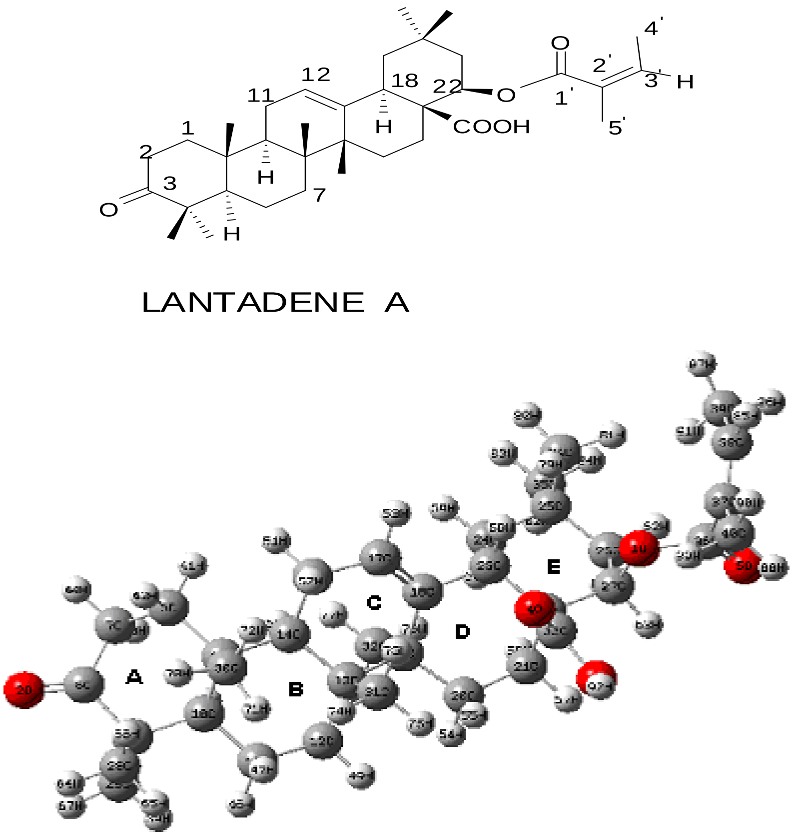

Fig. 1. Molecular structure of Lantadene A

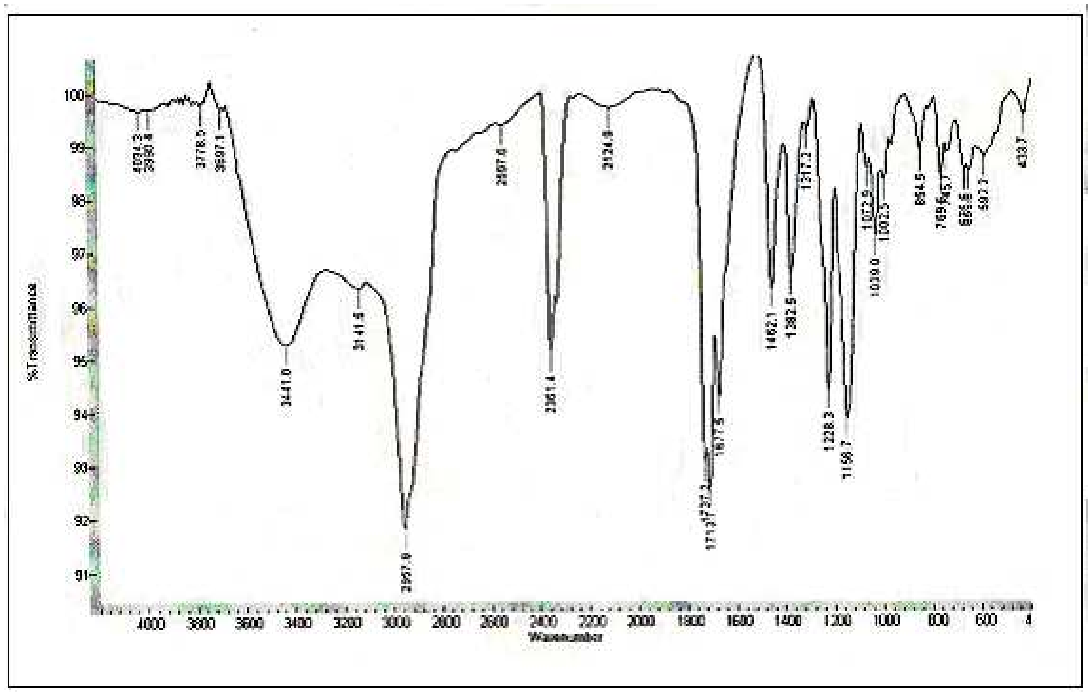

Fig. 2.FTIR Spectra of Lantadene A

Spectral region over 2800 cm^{-1}

The bands located in the high frequency region of the spectra of Lantadene A are easy to identify and belong to O-H and C–H stretching modes. The characteristic ν_{OH} stretching vibration is expected to appear at 3759 cm^{-1} (PM3), which is in good agreement with the experimental data. The characteristic ν_{CH} stretching vibrations of heteroaromatic structure are expected to appear in 2700-3100 cm^{-1} frequency ranges. The ν_{CH} stretching vibrations of the title compound were observed at 2957 and 3098 cm^{-1} (PM3) and the corresponding bands are given at 2957 and 3141 cm^{-1} in the experimental spectrum.

Spectral region 1750–1000 cm^{-1}

In middle region, the stretching vibration of the C=C band observed at 1794 (AM1) and 1838 cm^{-1} (PM3) and corresponding band is given at 1713 cm^{-1} in FTIR spectrum. The H-C–H scissor predicted at 1440 cm^{-1} (PM3) is in reasonable agreement with the 1462 cm^{-1} observed in FTIR. (C–C–H) angle-bending mode observed at 1319 and 1382 cm^{-1} (PM3) and 1326 and 1367 cm^{-1} (AM1) and corresponding band is given at 1317 and 1382 cm^{-1} in FTIR spectrum.

Table-3: Comparison of the observed and calculated Vibrational spectra of Lantadene A by Semi-empirical AM1 and PM3 methods

AM1 (I-R intensities)	PM3 (I-R intensities)	I-R (EXP.)	VIBRATIONAL ASSIGNMENTS
411(2.9424)	437(0.2434)	433	τ (Rings)
597(11.294)	580(1.7131)	592	τ (Rings)
684(5.5954)	666(5.8906)	659	τ (Rings)
701(16.324)	680(4.8402)	676	τ (Rings)
773(0.7507)	732(1.1632)	745	{β (C-C-C)+ β (C-C-H)} adj all rings
778(7.5875)	746(4.7487)	769	β (C-C=O) adj ring A+ β (C-C-H)} adj rings A & B
898(4.2834)	865(5.0003)	854	{β (C-C-C)+ β (C-C-H)} adj ring A & B
1026(10.495)	1000(7.8179)	1002	β (C-C-H) adj ring E
1085(4.0875)	1044(14.016)	1039	β (C-C-H) adj all rings
1105(5.2865)	1072(9.6915)	1072	β (C-C-H) adj all rings
1206(2.7215)	1159(5.2095)	1156	{β (C-C-C)+ β (C-C-H)} adj all rings
1289(8.8331)	1229(15.512)	1228	{β (C-C-C) + β (C-C-H)} adj ring E
1326(5.1613)	1319(5.4640)	1317	β (C-C-H) adj all rings
1367(48.765)	1382(41.609)	1382	β (C-C-H) adj all rings
1415(1.0557)	1440(4.2082)	1462	S (H70-C30-H71)
1794(66.006)	1838(4.6974)	1713	ν(C17=C18)
1795(7.7184)	1850(30.601)	1737	ν(C37=C38)
2919(0.0525)	2957(11.398)	2957	ν(C17-H53)
3011(0.4939)	3098(3.0308)	3141	ν(C-H) adj ring E
3270(117.80)	3759(31.838)	3778	ν(O3-H92)

Abbreviations: ν: Stretching; β: in plane bending; τ: torsion S; scissoring.

Spectral region 1000–400 cm^{-1}

The ring torsion, wag along with the out of plane ring bend, all of them appear in the frequency range 400-900 cm^{-1}.The experimental modes 676, 659 and 433 cm^{-1} matches well with the modes 680, 666 and 437 cm^{-1} (ring tors) [PM3].

Materials and Methods

The experimental and computational methods are given in this section to analyze Lantadene A.

Experimental methods

Isolation of Lantadene A from Lantana camara

Plant *Lantana camara* (leaves collective from Goeshwer, Uttranchal, India, 3.5 kg) was extracted with95% ethanol (3X12 L). Ethanolic extract after concentration under vaccuo gave greenish-black residue (274g). The ethanolic extract after adding to it water (1L), was extracted with hexane (3x800ml), chloroform (3x800ml), and butanol (3x600ml). Successively. The organic solvents were to give hexane fraction (98g), chloroform (65g) and butanol (60g) fractions respectively.

Chloroform fraction (20g) of ethanolic extract of *L. camara* leaves was subjected to flash column chromatography on a column of silica gel (800gm, 200-400 mesh) in Hexane. Column was eluted with Hexane, followed by increasing the % of acetone in hexane (10, 20, 25, 30, 35, 40 and 70% Acetone / Hexane). Chromatographic fractions were mixed according to TLC pattern to make two gross fractions A (5g), and B (2g), which were subjected repeated chromatography separately for further separation.

Isolation of Lantadene- A

Fraction A (5gm), was rechromatograped over column of flash silica gel (70 gm) packed in hexane. Elution was started with hexane, followed by Ethyl acetate –hexane system. Polarity of eluting solvent system was increased from 5, 10, 12, 15 and 20% of Ethyl acetate in hexane. Finally, column was eluted with ethyl acetate. Fractions eluted with 12 % of Ethyl acetate/hexane on concentration gave white solid which was recrystallized from acetone to give white crystalline Lantadene A

Yield: 500 mg**; mp:** .280-82°C**, ESMS:** m/z 553(M^++1)

^{1}H NMR (300M.Hz, $CDCl_3$) 0.84(s, 3H, CH_3), 0.90(s, 3H, CH_3), 1.01(s, 3H, CH_3), 1.07(s, 6H, 2XCH_3), 1.10(s, 3H, CH_3), 1.18, (s, 3H, CH_3), 1.789 (bs, 3H,C=CH_3), 1.98 (d, 6Hz, 3, CH= CH_3), 3.0(m, 1H,H-*18*), 5.1 (bs, 1H,H-*22*), 5.40(bs, 1H, *H-12*), 6.0(bs, 1H, *H-3*$'$).

Computational Methods

All the calculations were performed by using the AM1 and PM3 methods using the GAUSSIAN 03 suite of program [19]. Semi-empirical methods such as AM1 and PM3, simplify the schrodinger equation considerably by simplifying certain integrals in the calculations, but then compensate for this by parameterization of some of them so that the calculations reproduce experimental information on for example, the entropy, once the various approximations are made, the molecular properties to which the parameters are fitted, and the molecules used in the fitting, define a model Hamiltonian, of which the most commonly used are AM1 and PM3

Hamiltonians. A major advantage of the semi-empirical method is the speed of computation compared to full Ab-initio calculations. The vibrational frequencies for this molecule were calculated with these methods and then scaled [20] by 0.9532 and 0.9761 respectively. The aim of this study is to calculate vibrational spectra and thermodynamic properties of Lantadene A. By combining the results of the GAUSSVIEW'S program [21] with symmetry considerations, vibrational frequency assignments were made with a high degree of accuracy**.**

Conclusion

The frequency assignments for Lantadene A have been done for the first time from FT-IR spectra. The equilibrium geometries and harmonic frequencies of Lantadene A were determined and analyzed both at AM1 and PM3 level of theories. The difference between the observed and scaled frequencies is very small. The calculated vibrational frequencies and the experimental values (FTIR) indicate that both the methods AM1 and PM3 can explain the vibrational spectra of the title compound well. It can also be concluded that with a comparable results and lower computational time, semi empirical method could be used to study the spectra of Lantadene A. On the other hand for accurate and precise structural and vibrational data, DFT method could be used with a good agreement with experimental results, as it takes electron electron correlation into account.

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