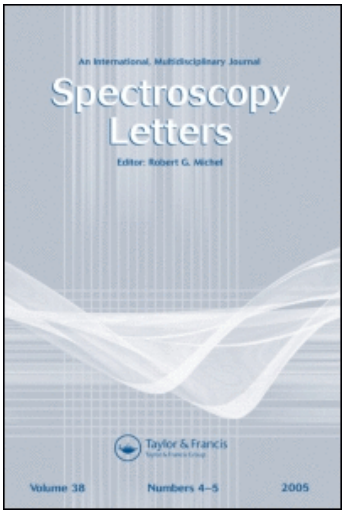


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

The Crystal Structure of Platyphylline and Molecular Conformational Analysis of Integerrimine

S. Öztürk[a]; S. Ide[b]; B. Sener[c]; H. K. Fun[d]
[a] Department of Physics, Faculty of Arts and Sciences, Erciyes University, Kayseri, Turkey [b] Department of Engineering Physics, Hacettepe University, Beytepe, Ankara, Turkey [c] Department of Pharmacognosy, Faculty of Pharmacy, Gazi University, Ankara, Turkey [d] X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, Penang, Malaysia

To cite this Article Öztürk, S. , Ide, S. , Sener, B. and Fun, H. K.(2000) 'The Crystal Structure of Platyphylline and Molecular Conformational Analysis of Integerrimine', Spectroscopy Letters, 33: 4, 495 — 507
To link to this Article: DOI: 10.1080/00387010009350134
URL: http://dx.doi.org/10.1080/00387010009350134

SPECTROSCOPY LETTERS, 33(4), 495–507 (2000)

THE CRYSTAL STRUCTURE OF PLATYPHYLLINE AND MOLECULAR CONFORMATIONAL ANALYSIS OF INTEGERRIMINE

Keywords : Structure, crystal, conformation, Platyphylline, Integerrimine, AM1, PM3, MM3.

S. Öztürk[a], S. İde[b]*, B. Sener[c] and H. K. Fun[d]

[a]Department of Physics, Faculty of Arts and Sciences, Erciyes University, Kayseri-38039 Turkey
[b]Department of Engineering Physics, Hacettepe University, Beytepe, Ankara-06532 Turkey
[c]Department of Pharmacognosy, Faculty of Pharmacy, Gazi University, Ankara-06330 Turkey
[d]X-ray Crystallography Unit, School of Physics,Universiti Sains Malaysia, 11800 USM, Penang Malaysia

ABSTRACT

The title compounds platyphylline ($C_{18}H_{29}NO_5.0.5H_2O$) and integerrimine ($C_{18}H_{25}NO_6$) have been isolated from the serial parts of the Senecio species. The crystal and molecular structures of platyphylline have been determined. The compound crystallises in orthorhombic space group, $P2_12_12_1$. The pyrrolizidine nucleus exhibits exo-buckling conformation. The molecular geometry was stabilized by C-H...O and C-H...N hydrogen bonds. A search for the low energy conformations of integerrimine as a similar alkaloid was also carried out. Force field calculations were undertaken by the MM3 program and some particular conformations were computed with the semi-emprical molecular orbital methods by the AM1 and PM3 programs.

INTRODUCTION

For many years, the *Senecio* species belonging to the family of Asteraceae, are known as a rich source of pyrrolizidine alkaloids. The hepatotoxic nature of the pyrrolizidine alkaloids from the *Senecio* species has enjoyed wide spread interest. Platyphylline as a pyrrolizidine type alkaloid was isolated from *Senecio othonnae* and *Senecio pseudo-orientalis* growing in Turkey. The separation, isolation, and purification of this alkaloid, as well as its spectral data were described in previous

studies [1,2]. The work reported here is part of a project aimed at providing a better understanding of the structural properties of some bioactive natural compounds.

The crystal and molecular structure of platyphylline has been determined in the present work. On the other hand, the certain structure of integerrimine could not be obtained by single crystal X-ray diffraction method due to poor crystalline structure. So, full geometry optimization and molecular mechanic calculations were performed to obtain some useful knowledge about structural properties of integerrimine.

EXPERIMENTAL

Powdered plant materials were percolated with ethanol at room temperature, and the combined ethanolic extracts were evaporated to dryness in vacuo. The separation and isolation of the compound were realized by using standard methods described previously [3].

A summary of the key crystallographic information is given in Table 1. The data was collected on a SMART CCD diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å) with a detector distance of 4 cm and swing angle of -35°. A hemisphere of the reciprocal space was covered by a combination of three sets of exposures; each set had a different ϕ angle (0,88,180°) and each exposure of 30s covered 0.3° in ω. Coverage of the unique set is over 99% complete. Crystal decay was monitored by repeating thirty initial frames at the end of data collection and analysing the duplicate reflections, and was found to be negligible. The collected data were reduced by using the program SAINT[4] and empirical absorption correction was carried out by using the SADABS[5] program.

The data collection was covered over a hemisphere of reciprocal space by a combination of three sets of exposures; each set had a different ω angle (0, 88 and 180°) for the crystal and each exposure of 30 covered 0.3° in ω. The crystal-to-detector distance was 4 cm and the detector swing angle was -30°. Coverage of the unique set is over 99°complete. Crystal decay was monitored by repeating thirty initial frames at the end of data collection and analysing the duplicate reflections, and was found to be negligible. The structure was solved by direct methods and refined by full-matrix least-square techniques. Only water molecule H atoms were located from a difference Fourier map and refined isotropically. The other H-atoms were located geometrically and then refined isotropically with fixed displacement parameters.

The structure of the title compound was solved by direct methods and refined by least-squares on F_{obs}^2 by using the SHELXTL[6] software package. All non–H atoms were anisotropically refined. H-atoms were located geometrically and then refined isotropically with fixed displacement parameters. The final conventional R=0.0499 and ωR=0.1422 for $I>2\sigma(I)$ with weighting scheme, $w=1/[\sigma^2(F_o^2)+(0.1199P)^2+1.1626P]$ where $P=(F_o^2+2F_c^2)/3$.

TABLE 1.

Crystal data and structure refinement for $C_{17}H_{26}NO_6.0.5H_2O$.

Formula	$C_{17}H_{26}NO_6.0.5H_2O$
Formula weight	349.40
Colour	colourless
Crystal system	orthorhombic
Space group	P $2_12_12_1$
a [Å]	9.4250(2)
b [Å]	13.2220(2)
c [Å]	15.3326(3)
V [Å^3]	1910.71(6)
Z	4
$D_{ca.}$ [g·cm^{-3}]	1.215
μ [mm^{-1}]	0.093
F(000)	752
Crystal size [mm]	0.40 x 0.34 x 0.24
θ range [°]	2.65 to 22.50
h , k, l	-10/10, 0/14, 0/16
Reflections collected / unique	8282 / 2493
R_{int}	0.0412
Independent reflections	2493
Absorption correction	None
Extinction coefficient	0.012(3)
No. Parameters	236
GOF	1.104
Final R indices [I > 2 σ (I)]	R = 0.0499, ωR = 0.1422
R indices (all data)	R = 0.0541, ωR = 0.1479
Largest diff. peak and hole [e.Å^{-3}]	0.274 and -0.328

RESULTS AND DISCUSSION

Fig.1. shows the displacement ellipsoid plot of platyphylline with the numbering scheme. The atomic coordinates and the mean temperature factors with estimated standard deviations for non-hydrogen and hydrogen atoms are listed in Tables 2 and 3, respectively, and the bond lengths, bond angles, and torsion angles, are given in Tables 4 and 5. In all essential details the geometry of the molecule in terms of bond lengths and angles show normal values. The pyrrolizidine ring is exo-buckled at an angle of 55.9(2)°. This value slightly larger than the other retronecine alkaloids. Exo-buckling has also been observed in other retronecine alkaloids, and the puckering angles in crystals of senecionine, retrorsine, and jacobine [7,8] have the values of 35.3(4), 36.8(8) and 36.9(4)°. These values are in accord with the conclusion from NMR data that retronecine esters in solution are exo-buckled to about this degree, whereas heliotridine esters in solution exhibit averaging between exo- and endo-buckling [9]. The bond lengths and angles are in good agreement with those reported for other pyrrolizidine alkaloids, Table 4. The C1-C2 (1.527(6)Å) is single bond. The ring-fusion distance, N1-C7, of 1.493(4)Å is similar to the values 1.51(1)Å in retrorsine and 1.486(5)Å in jacobine while the

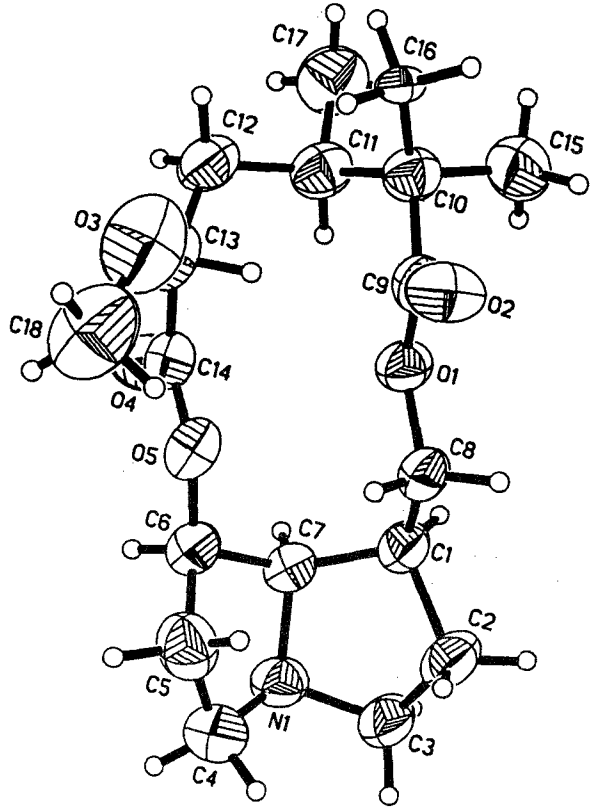


Fig.1. The structure of platyphylline showing 50% probability displacement ellipsoids and atom-numbering scheme.

angles subtended at N1 have a mean value 109.2(4)° with C4-N1-C3 113.3(3)°; the corresponding values in senecionine are 110.6(3) and 115.3(3)° and in retrorsine are 110.7(6) and 114.8(6)° and in jacobine are 110.4(4) and 115.2(4)°. The crystal structure has got intra- and intermolecular H-bonds. The details of the hydrogen bonds are given in Table 6. The molecule is show one-dimensional chain in the [1 0 0] direction and its packing diagram shown in Fig. 2.

In order to optimize the geometry of integerrimine which is shown in Scheme 1., molecular mechanic calculation method (MM3) was used, firstly [10]. Minimum energy value was found as 54.07 kcal/mol. Some similar crystallographic parameters of platyphylline were used in semi-emprical molecular orbital calculations for integerrimine . Minimum energy values obtained from AM1 and

TABLE 2.

Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for $C_{17}H_{26}NO_6.0.5H_2O$. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O1	10941(2)	3938(2)	3389(1)	49(1)
O2	12855(3)	4454(2)	4112(2)	66(1)
O3	14421(3)	4554(2)	2627(2)	63(1)
O4	12067(5)	6743(3)	2961(3)	123(2)
O5	9150(3)	5543(3)	1922(2)	76(1)
O6	9395(3)	5798(2)	3354(1)	53(1)
N1	6251(3)	4325(2)	3977(2)	54(1)
C1	8656(4)	3599(2)	3984(2)	49(1)
C2	7817(4)	3270(3)	4786(3)	66(1)
C3	6283(4)	3370(3)	4491(3)	65(1)
C4	6118(5)	5250(3)	4530(3)	69(1)
C5	7475(5)	5846(3)	4399(3)	69(1)
C6	7941(4)	5504(3)	3504(2)	53(1)
C7	7637(4)	4362(2)	3506(2)	46(1)
C8	10143(4)	3928(3)	4194(2)	49(1)
C9	12307(4)	4204(2)	3447(2)	46(1)
C10	13108(4)	4031(3)	2587(2)	50(1)
C11	12294(4)	4401(3)	1777(2)	56(1)
C12	12161(4)	5553(3)	1716(2)	61(1)
C13	11391(4)	6068(3)	2448(2)	53(1)
C14	9873(4)	5791(3)	2535(2)	53(1)
C15	13351(5)	2884(3)	2574(3)	72(1)
C16	12979(6)	4009(4)	917(3)	81(1)
C17	11444(7)	7388(4)	3677(3)	103(2)
O1W	6322(9)	5070(9)	1328(4)	113(3)

TABLE 3.

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for $C_{17}H_{26}NO_6.0.5H_2O$.

	x	y	z	U(eq)
H1A	8737	3004	3606	58
H2A	8037	2577	4945	79
H2B	8012	3707	5280	79
H3A	6006	2799	4132	78
H3B	5649	3412	4988	78
H4A	6006	5066	5138	83
H4B	5302	5647	4352	83
H5A	7298	6569	4412	82
H5B	8177	5678	4838	82
H6	7337	5829	3066	63
H7A	7494	4135	2904	55
H8A	10135	4598	4453	59
H8B	10572	3463	4606	59
H11	11332	4122	1810	67
H12A	13108	5836	1681	74
H12B	11678	5716	1176	74
H13	11656	5519	2846	64
H15A	13698	2668	3133	108
H15B	14035	2719	2133	108
H15C	12473	2546	2450	108
H16A	12431	4238	428	121
H16B	12998	3283	922	121
H16C	13930	4263	870	121
H17A	11963	8011	3717	154
H17B	11504	7033	4222	154
H17C	10468	7531	3547	154
H1W1	5900(8)	5590(4)	1590(5)	50
H2W1	6520(9)	4430(2)	1450(5)	50

TABLE 4.

Bond lengths(Å), bond angles (°) for $C_{17}H_{26}NO_6.0.5H_2O$.

Bond Lengths			
O1-C9	1.338(4)	C1-C7	1.574(5)
O1-C8	1.446(4)	C2-C3	1.521(6)
O2-C9	1.190(4)	C4-C5	1.516(6)
O4-C13	1.349(5)	C5-C6	1.509(5)
O4-C17	1.510(7)	C6-C7	1.537(5)
O5-C14	1.207(5)	C9-C10	1.537(5)
O6-C14	1.334(4)	C10-O3	1.419(4)
O6-C6	1.443(4)	C10-C15	1.534(5)
N1-C3	1.488(5)	C10-C11	1.538(5)
N1-C4	1.493(5)	C11-C12	1.531(6)
N1-C7	1.493(4)	C11-C16	1.558(5)
C1-C8	1.503(5)	C12-C13	1.499(6)
C1-C2	1.527(5)	C13-C14	1.483(6)
Bond Angles			
C9-O1-C8	116.5(3)	O2-C9-O17	123.3(3)
C13-O4-C17	127.9(5)	O2-C9-C10	124.3(3)
C14-O6-C6	118.0(3)	O1-C9-C10	112.1(3)
C3-N1-C4	113.3(3)	O3-C10-C15	110.6(3)
C3-N1-C7	105.5(3)	O3-C10-C9	108.6(3)
C4-N1-C7	108.7(3)	C15-C10-C9	103.3(3)
C8-C1-C2	113.1(3)	O3-C10-C11	108.4(3)
C8-C1-C7	118.9(3)	C15-C10-C11	112.3(3)
C2-C1-C7	104.0(3)	C9-C10-C11	113.6(3)
C3-C2-C1	103.1(3)	C12-C11-C10	114.0(3)
N1-C3-C2	104.5(3)	C12-C11-C16	108.3(3)
N1-C4-C5	106.3(3)	C10-C11-C16	111.8(3)
C6-C5-C4	102.1(3)	C13-C12-C11	116.5(3)
O6-C6-C5	109.9(3)	O4-C13-C14	124.5(4)
O6-C6-C7	116.2(3)	O4-C13-C12	120.5(4)
C5-C6-C7	103.8(3)	C14-C13-C12	115.0(3)
N1-C7-C6	101.3(3)	O5-C14-O6	123.0(3)
N1-C7-C1	106.7(2)	O5-C14-C13	122.8(3)
C6-C7-C1	121.1(3)	O6-C14-C13	114.2(3)
O1-C8-C1	107.7(3)	H1W1-O1W-H2W1	138(8)

TABLE 5.

Torsion angles (°)

C8-C1-C2-C3	159.0(3)	C8-O1-C9-O2	-2.4(5)
C7-C1-C2-C3	28.6(4)	C8-O1-C9-C10	171.1(3)
C4-N1-C3-C2	-82.4(4)	O2-C9-C10-O3	-20.9(5)
C7-N1-C3-C2	36.4(4)	O1-C9-C10-O3	165.5(3)
C1-C2-C3-N1	-40.6(4)	O2-C9-C10-C15	96.5(4)
C3-N1-C4-C5	115.8(3)	O1-C9-C10-C15	-77.0(3)
C7-N1-C4-C5	-1.1(4)	O2-C9-C10-C11	-141.6(4)
N1-C4-C5-C6	25.9(4)	O1-C9-C10-C11	44.9(4)
C14-O6-C6-C5	-163.4(3)	O3-C10-C11-C12	-51.6(4)
C14-O6-C6-C7	79.1(4)	C15-C10-C11-C12	-174.1(3)
C4-C5-C6-O6	-165.8(3)	C9-C10-C11-C12	69.1(4)
C4-C5-C6-C7	-40.8(4)	O3-C10-C11-C16	71.6(4)
C3-N1-C7-C6	-145.4(3)	C15-C10-C11-C16	-50.9(4)
C4-N1-C7-C6	-23.6(3)	C9-C10-C11-C16	-167.7(4)
C3-N1-C7-C1	-17.8(3)	C10-C11-C12-C13	-60.8(4)
C4-N1-C7-C1	104.0(3)	C16-C11-C12-C13	174.2(3)
O6-C6-C7-N1	160.7(3)	C17-O4-C13-C14	-3.8(6)
C5-C6-C7-N1	39.9(4)	C17-O4-C13-C12	174.9(4)
O6-C6-C7-C1	43.1(4)	C11-C12-C13-O4	117.6(4)
C5-C6-C7-C1	-77.7(4)	C11-C12-C13-C14	-63.6(4)
C8-C1-C7-N1	-134.0(3)	C6-O6-C14-O5	-0.6(5)
C2-C1-C7-N1	-7.1(4)	C6-O6-C14-C13	-177.9(3)
C8-C1-C7-C6	-19.1(5)	O4-C13-C14-O5	149.0(4)
C2-C1-C7-C6	107.8(4)	C12-C13-C14-O5	-29.8(5)
C9-O1-C8-C1	-179.2(3)	O4-C13-C14-O6	-33.7(5)
C2-C1-C8-O1	163.8(3)	C12-C13-C14-O6	147.6(3)
C7-C1-C8-O1	-73.8(4)		

TABLE 6.

Hydrogen-bonding geometry (Å, °).

D - H ... A	D - H	H ... A	D ... A	D - H ... A
C8 H8A .. O5^{I}	0.970	2.421	2.878	108
C11 H11 .. O1^{I}	0.981	2.453	2.842	103
C13 H13 .. O1^{I}	0.980	2.352	3.191	143
C2 H2B .. O1W^{ii}	0.970	2.370	3.330	170
C5 H5B .. O1W^{ii}	0.970	2.515	3.370	145
C16 H16C .. N1^{iii}	0.961	1.908	2.729	142
C16 H16C .. O1W^{iii}	0.960	1.923	2.777	147

Symmetry codes: (*i*) x,y,z ; (*ii*) -x+1/2+1,-y+1,z+1/2 ; (*iii*) x+1,y,z.

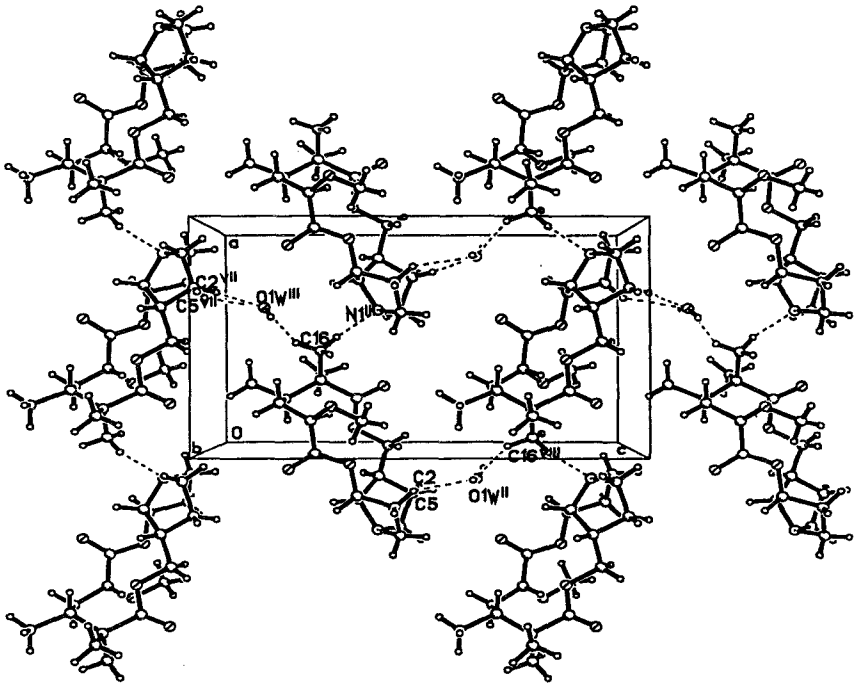
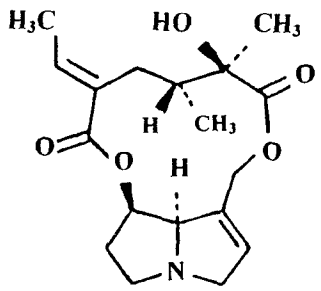


Fig. 2. Packing diagram.



Scheme I.

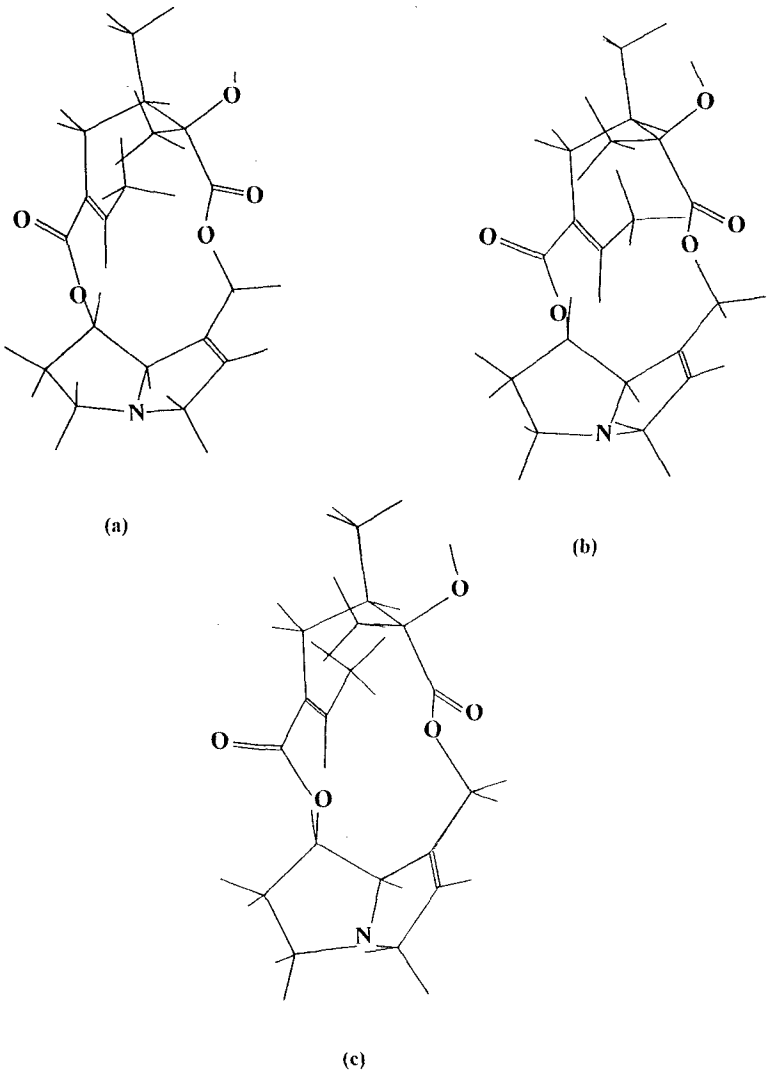


Fig. 3. Three stable conformations of Integerrimine.
The result of a) MM3 b) AM1 c) PM3

TABLE 7.

Computed conformational results

Bond lengths	MM3	PM3	AM1	X-ray results for platyhylline
C1-C2	1.341	1.343	1.347	-
C2-C3	1.519	1.496	1.510	1.521(6)
C3-N1	1.474	1.490	1.476	1.488(5)
N1-C7	1.474	1.514	1.493	1.493(4)
C7-C6	1.536	1.548	1.554	1.537(5)
C6-C5	1.525	1.537	1.529	1.509(5)
C5-C4	1.535	1.528	1.536	1.516(6)
C4-N1	1.474	1.490	1.469	1.493(5)
C1-C8	1.502	1.490	1.477	1.503(5)
C8-O1	1.444	1.427	1.442	1.446(4)
O1-C9	1.361	1.366	1.363	1.338(4)
C9-O2	1.216	1.213	1.231	1.190(4)
C9-C10	1.521	1.552	1.534	1.537(5)
C10-O3	1.446	1.427	1.431	1.419(4)
C10-C11	1.561	1.565	1.545	1.538(5)
C11-C16	1.542	1.527	1.516	1.558(5)
C12-C13	1.551	1.536	1.527	1.531(6)
C11-C12	1.510	1.494	1.489	1.499(6)
C12-C13	1.347	1.342	1.344	-
C13-C17	1.505	1.479	1.473	-
C17-C18	1.502	1.490	1.476	1.483(6)
C13-C14	1.218	1.216	1.234	1.207(5)
C14-O5	1.362	1.369	1.379	1.334(4)
O5-C6	1.445	1.429	1.438	1.443(4)

TABLE 8.

Some of the computed bond angles and torsion angles (°)

C6-C7-C1	113.9	114.2	112.5
C1-C2-C3	111.3	111.6	109.9
C6-C5-C4	100.8	105.9	104.9
C4-N1-C3	114.8	115.9	115.8
C7-C6-C5	102.3	105.2	105.0
C7-C1-C2	109.1	110.8	109.6
C2-C3-N1	105.0	105.0	107.5
C5-C4-N1	103.4	107.9	109.5
C1-C7-N1	106.4	104.6	106.7
C6-C7-N1	103.7	106.0	107.6
O5-C6-C7-C1	-93.1	-101.8	-102.5
C8-C1-C7-C6	68.3	77.6	74.0
C7-C1-C2-C3	0.0	-1.6	-2.1
C1-C2-C3-N1	-1.9	-3.6	-2.2
C2-C3-N1-C4	126.4	129.1	125.0
C3-N1-C7-C1	-3.1	-8.0	-6.5
C6-C7-N1-C4	-8.8	-13.2	-10.3
C6-C5-C4-N1	38.4	16.5	16.9
C7-C6-C5-C4	-43.8	-24.2	-22.2
C13-C14-O5-C6	-143.0	-154.5	-144.2
O2-C9-O1-C8	-2.4	-11.0	0.0

PM3 [10] programs are 42.04 and 42.52 kcal/mol, respectively. Three stable conformations of integerrimine are defined and represented in Fig. 3. Bond lengths and some geometrical parameters showing the results of these studies were given in Table 7 and 8. The C1-C2 double bond in the conformation of integerrimine is more stable than the single bond. This bond was single in the structure of platyphylline. The pyrrolizidine conformations for two compounds were different due to these different bond characters.

ACKNOWLEDGEMENT

This work was supported by Turkish Scientific and Technical Research Council (Project No: TBAG-1621). The authors would like to thank the Malaysian Government and Universiti Sains Malaysia for research grant R&D No. 190-9609-2801. SÖ thanks the Universiti Sains Malaysia for a Visiting Post Doctoral Fellowship.

REFERENCES

[1] B.Şener, S. Küsmenoğlu, F. Ergün and A.E. Karakaya, *J. Fac. Pharm. Gazi*, 3(2), 105 (1986).

[2] B.Şener, S. Küsmenoğlu, F. Ergün and A.E. Karakaya, *J. Fac. Pharm. Gazi*, 5(1), 101 (1986).

[3] B.Şener, S. Küsmenoğlu, F. Ergün and A.E. Karakaya, *Proceeding of The VI. Symposium on Plant Originated Crude Drugs* (Ed. Şener, B.) p. 315-318, Publication of Gazi University, Ankara (1987).

[4] Siemens, *SAINT v4 Software Reference Manual, Siemens Analytical X-Ray Systems, Inc.*, Madison, Wisconsin, USA (1996).

[5] G. M. Sheldrick, *SADABS. Program for Empirical Absorption Correction of Area Dectector Data,* Univ. of Göttingen, Germany (1996).

[6] Siemens, *SHELXTL Version 5 Reference Manual, Siemens Analytical X-Ray Systems*, Inc., Madison, Wisconsin, USA (1996).

[7] M. F. Mackay and C. C. J. Culvenor, *Acta Cryst.* B38, 2754 (1982).

[8] A. Perez-Salazar, F. H. Cano and S. Garcia-Blanco, *Cryst. Struct. Commun.*, 7, 105 (1978).

[9] C. C. J. Culvenor and W. G. Woods, *Aust. J. Chem.* 18, 1625 (1965).

[10] Alchemy 2000 , *A Computational Chemistry Program,* Tripos, Inc. USA (1996)

Date Received: July 10, 1999
Date Accepted: January 20, 2000