PM3 Conformational Analysis of the (3R,5R,6R)-6- Acetylamidopenicillanic Acid. II. Electronic Properties

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SUMMARY

A conformational analysis with the semiempirical PM3 method was performed for (3R,5R,6R)-6-acetylamidopenicillanic acid. 92 distinct conformers were found within 12.14 kcal/mol. Dependence of some electronic properties of these conformers (HOMO and LUMO energies, dipole moment, v_{min} minimum vibration energy, maximum vibration energy $v_{MAX.}$) with respect to some geometric characteristics : pseudochirality of the N14 atom, the *syn-anti* arrangement of the O17 and H28 atoms of the amidic group and the three puckering classes of the thyazolidinic cycle noted with a, b, c.
Keywords: conformational analysis; (3R,5R,6R)-6-acetylamidopenicilanic acid; PM3.

INTRODUCTION

The (3R,5R,6R)-6-acetylamidopenicillanic acid is one of the simplest antibacterial compounds of the penicillin class. Its molecular structure contains two fused rings (a four-membered β-lactamic ring and a five-membered thiazolidinic ring) and three chiral centers is prezented in Figure 1 [1].
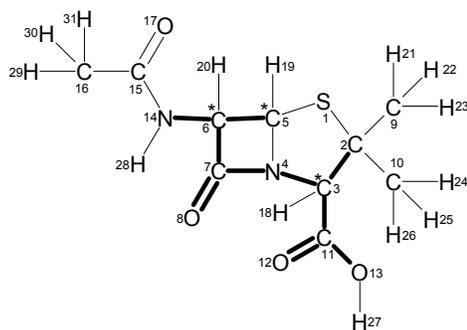
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Fig.1 Atom numbering in *(3R,5R,6R)-6-acetylamidopenicillanic acid* (* denotes the chirality).

In this paper we present an analysis of the dependence of the electronic properties of the (3R,5R,6R)-6-acetylamido-penicillanic acid with respect to the geometrical characteristics of the conformers. The pyramidalization degree of the nitrogen N14 atom resulted from the PM3 method is measured by the "conicity" of the improper angle C6-C15-H28-N14. The electronic properties are analysed with respect to the *anti* or *syn* orientation of atoms O17 and H28 of the exocyclic amidic group and the three puckering classes of the thyazolidinic cycle [1].

MATERIALS AND METHODS

Gas phase equilibrium geometry of conformers was obtained by semiempirical PM3 calculations with an SCF convergence of 10^{-5}, and a RMS gradient of 10^{-2} kcal/Å·mol [2,3]. Conformational search was performed by varying the C2-C3-C11-C12, C5-C6-N14-C15 and C6-N14-C15-C16 dihedrals in the range 0 ±180° with steps of 15°. Energy criterion was set to 20 kcal/mol above the minimum energy conformer. Calculations have been performed with Conformational Search module [4], from HyperChem7.52 package [5].

RESULTS AND DISCUSSION

The semiempirical PM3 method gives 92 conformers [1, 7]. In Table I these conformers are ordered and numbered in ascending order of formation enthalpies. The obtained results for some structural properties (HOMO, LUMO, μ) are presented also in Table I.

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Table I. Numbering of the conformers of the (3R,5R,6R)-6-acetilamidopenicillanic acid arranged in the ascending order of the formation enthalpies computed with PM3 some of their energetic, structural and electronic characteristics

Enegetic order	HOMO (eV)	LUMO (eV)	Chirality N(14)	Pozition 17,28.	μ (Debye)	Vibrations (cm^{-1})		ZPVE (kcal/mol)
						$\nu_{min.}$	$\nu_{MAX.}$	
01(2pm3)	-9.802	-0.482	R	anti	4.123	25.06	3850.03	149.601
02(3pm3)	-9.796	-0.466	R	anti	4.105	27.80	3849.46	149.923
03(4pm3)	-9.776	-0.485	R	syn	3.542	25.85	3849.92	150.133
04(5pm3)	-9.753	-0.453	R	syn	3.255	28.08	3849.60	150.430
05(6pm3)	-9.828	-0.508	R	anti	3.988	28.31	3849.19	149.615
06(7pm3)	-9.773	-0.438	R	anti	3.325	37.03	3847.68	150.012
07(8pm3)	-9.800	-0.510	R	syn	1.613	27.29	3849.55	150.162
08(9pm3)	-9.826	-0.491	R	anti	3.940	31.82	3849.30	149.885
09(10pm3)	-9.780	-0.477	R	syn	1.597	29.14	3848.97	150.399
10(11pm3)	-9.672	-0.396	S	syn	3.414	25.95	3849.70	150.373
11(12pm3)	-9.693	-0.396	R	anti	4.318	20.45	3848.50	149.676
12(13pm3)	-9.680	-0.441	S	syn	3.786	27.32	3849.74	149.983
13(14pm3)	-9.780	-0.462	R	anti	3.236	28.37	3847.48	149.530
14(15pm3)	-9.760	-0.464	R	syn	3.442	27.89	3849.47	150.119
15(16pm3)	-9.731	-0.436	R	syn	3.477	31.53	3847.60	150.493
16(17pm3)	-9.656	-0.397	S	anti	3.936	25.37	3849.51	149.510
17(18pm3)	-9.818	-0.491	R	anti	4.349	36.17	3842.18	150.230
18(19pm3)	-9.754	-0.472	R	syn	3.694	29.09	3847.49	150.084
19(20pm3)	-9.709	-0.473	S	syn	3.811	26.72	3849.88	149.680
20(21pm3)	-9.707	-0.468	S	syn	1.827	29.38	3849.21	150.006
21(22pm3)	-9.696	-0.419	S	syn	1.735	23.61	3849.95	150.344
22(23pm3)	-9.575	-0.314	S	anti	4.338	23.91	3848.11	149.647
23(24pm3)	-9.775	-0.485	R	syn	1.303	31.12	3842.26	150.745
24(25pm3)	-9.787	-0.488	R	syn	1.725	29.20	3849.31	150.092
25(26pm3)	-9.654	-0.384	S	syn	3.652	27.52	3847.56	150.378
26(27pm3)	-9.648	-0.356	S	anti	3.291	33.45	3847.77	149.889
27(28pm3)	-9.736	-0.447	R	syn	3.643	28.48	3847.41	150.129
28(29pm3)	-9.686	-0.426	S	anti	3.896	27.28	3849.07	149.498
29(30pm3)	-9.822	-0.511	R	anti	4.428	24.74	3842.08	149.732
30(31pm3)	-9.733	-0.498	S	syn	1.833	27.89	3849.18	149.707
31(32pm3)	-9.795	-0.519	R	syn	1.406	28.43	3841.81	150.369
32(33pm3)	-9.712	-0.436	S	syn	1.730	27.27	3848.71	150.054
33(35pm3)	-9.601	-0.371	S	syn	4.507	18.11	3848.09	150.125
34(36pm3)	-9.701	-0.437	S	syn	1.497	29.91	3841.94	150.645
35(37pm3)	-9.670	-0.435	S	syn	3.911	31.07	3847.52	149.861
36(38pm3)	-9.652	-0.390	S	anti	3.088	29.91	3847.80	149.409
37(39pm3)	-9.672	-0.403	S	syn	3.668	30.43	3847.25	150.106
38(40pm3)	-9.779	-0.494	R	syn	1.495	27.77	3842.12	150.380
39(41pm3)	-9.693	-0.410	S	anti	4.327	32.54	3842.32	150.110

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Enegetic order	HOMO (eV)	LUMO (eV)	Chirality N(14)	Pozition 17,28.	μ (Debye)	Vibrations (cm^{-1})		ZPVE (kcal/mol)
						$\nu_{min.}$	$\nu_{MAX.}$	
40(42pm3)	-9.630	-0.405	S	syn	4.539	15.08	3847.97	149.805
41(43pm3)	-9.636	-0.367	S	anti	3.705	17.20	3846.72	149.547
42(44pm3)	-9.696	-0.465	S	syn	3.938	30.03	3847.23	149.612
43(45pm3)	-9.717	-0. 455	S	syn	1.495	29.90	3842.19	150.376
44(46pm3)	-9.690	-0. 434	S	anti	4.336	18.48	3842.07	149.578
45(47pm3)	-9.736	-0.509	S	syn	1.674	29.53	3842.03	149.863
46(48pm3)	-9.689	-0.498	S	syn	4.031	31.48	3848.46	150.224
47(49pm3)	-9.811	-0.570	S	anti	4.911	27.28	3849.03	150.180
48(50pm3)	-9.854	-0.600	S	anti	4.148	30.51	3848.83	150.166
49(51pm3)	-9.730	-0.533	S	syn	1.735	33.11	3848.11	150.195
50(52pm3)	-9.582	-0.345	R	syn	3.624	23.89	3849.04	150.177
51(53pm3)	-9.581	-0.412	R	syn	4.708	36.72	3848.25	149.909
52(55pm3)	-9.588	-0.282	S	anti	4.383	38.55	3851.56	149.960
53(56pm3)	-9.625	-0.339	S	anti	4.274	31.16	3851.34	149.664
54(57pm3)	-9.561	-0.254	S	anti	4.049	26.29	3852.07	149.917
55(58pm3)	-9.860	-0.607	S	anti	4.527	38.20	3841.59	150.401
56(59pm3)	-9.602	-0.317	S	anti	4.238	25.22	3851.32	149.582
57(60pm3)	-9.615	-0.380	R	syn	1.458	27.24	3848.64	150.153
58(61pm3)	-9.586	-0.285	S	anti	4.072	28.81	3849.81	149.825
59(63pm3)	-9.625	-0.453	R	syn	2.486	37.24	3847.88	149.880
60(64pm3)	-9.637	-0.352	S	anti	4.084	23.05	3849.86	149.489
61(65pm3)	-9.694	-0.500	S	syn	3.673	26.94	3846.94	150.179
62(66pm3)	-9.708	-0.510	S	syn	1.725	41.91	3844.75	150.309
63(67pm3)	-9.570	-0.327	R	syn	3.062	30.59	3848.06	150.012
64(68pm3)	-9.300	-0.035	R	anti	3.290	28.83	3852.43	149.620
65(69pm3)	-9.329	-0.065	R	anti	4.487	38.34	3851.77	149.645
66(70pm3)	-9.618	-0.335	S	anti	3.865	31.31	3848.37	149.540
67(71pm3)	-9.332	-0.095	R	anti	4.241	31.18	3851.73	149.342
68(72pm3)	-9.737	-0.547	S	syn	1.726	35.76	3842.22	150.417
69(73pm3)	-9.299	-0.064	S	syn	3.325	27.20	3852.02	149.277
70(74pm3)	-9.587	-0.302	S	anti	4.349	34.66	3842.64	150.199
71(75pm3)	-9.326	-0.065	R	anti	4.184	28.72	3850.12	149.503
72(76pm3)	-9.539	-0.201	S	syn	2.244	25.36	3850.32	149.851
73(77pm3)	-9.613	-0.376	R	syn	1.835	33.65	3841.77	150.453
74(78pm3)	-9.344	-0.104	R	anti	4.102	23.49	3850.42	149.175
75(79pm3)	-9.662	-0.385	S	anti	4.308	29.95	3843.65	149.852
76(80pm3)	-9.716	-0.544	S	syn	4.086	29.18	3849.37	150.124
77(81pm3)	-9.741	-0.565	S	syn	3.145	29.85	3848.10	150.089
78(82pm3)	-9.575	-0.236	S	anti	2.888	34.41	3849.19	149.829
79(83pm3)	-9.617	-0.451	R	syn	4.440	29.28	3849.55	150.052
80(84pm3)	-9.326	-0.088	R	anti	4.185	33.78	3842.94	149.864
81(85pm3)	-9.312	-0.080	R	anti	3.812	33.55	3849.50	149.171
82(86pm3)	-9.614	-0.458	R	syn	2.415	35.02	3843.50	150.370
83(87pm3)	-9.650	-0.476	R	syn	3.401	31.30	3848.05	149.948
84(88pm3)	-9.743	-0.566	S	syn	1.976	32.30	3847.70	150.096
85(89pm3)	-9.609	-0.472	R	syn	2.806	40.91	3844.97	149.504
86(90pm3)	-9.293	-0.068	R	anti	4.187	32.34	3848.05	149.456
87(91pm3)	-9.352	-0.126	R	anti	4.130	30.73	3844.38	149.558
88(92pm3)	-9.587	-0.289	R	anti	4.760	30.40	3850.95	150.172

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Enegetic order	HOMO (eV)	LUMO (eV)	Chirality N(14)	Pozition 17,28.	μ (Debye)	Vibrations (cm^{-1})		ZPVE (kcal/mol)
						$\nu_{min.}$	$\nu_{MAX.}$	
89(94pm3)	-9.557	-0.359	R	anti	2.943	19.65	3849.07	149.164
90(95pm3)	-9.570	-0.370	R	anti	2.933	10.75	3849.28	149.746
91(96pm3)	-9.551	-0.340	R	anti	3.308	14.64	3850.39	149.801
92(97pm3)	-9.548	-0.380	R	anti	2.892	31.83	3842.98	149.659

To be sure that the obtained conformers are minima on the potential energy surface (PES) and not saddle points, for each conformer a normal vibration calculation was performed. All vibrations were positive for all conformes. The wavelength number of the maximum vibration, ν_{MAX} and zero point vibration energy, ZPVE are given in Table I, too. A gap of 12.14 kcal/mol resulted between the lowest energy (02pm3) conformer and the highest energy (97pm3) one[1].

After an analysis of the HOMO and LUMO energies (Table I) we cannot find a clusterization of the conformers with respect to the following geometric properties: pseudochirality of the N14 atom, *syn-anti* arrangement of the O17 and H28 atoms of the amidic group or after the puckering class of the thiazolidinic ring (a, b, c) [1]. For comparison of electronic properties their average values were calculated.

The HOMO and LUMO energy average values with respect to the (R, S) pseudochirality of the N14 atom are:

HOMO(R) = -9.724±0.063 eV,   LUMO(R) = -0.446±0.047eV,
HOMO(S) = -9.573±0.152 eV,   LUMO(S) = -0.340±0.169eV,

They are not statistically distinct. However, comparing the average values for the R conformers with the average values of the S conformers it results that the HOMO energies are lower for the (S) conformers, while the LUMO energies are higher for the (S) conformers, and the data dispersion (SD) is narrower. Overall, one can conclude that through the pyramidalization of the N(14) atom the HOMO and LUMO energies are not significantly influenced in the PM3 method.

The HOMO and LUMO energy average values calculated with respect to the *syn-anti* criterion are:

HOMO(*syn*) = -9.641±0.141eV,   LUMO(*syn*) = -0.391 ±0.141eV,
HOMO(*anti*) = -9.645±0.138eV,   LUMO(*anti*) = -0.393 ±0.131eV,

Compared to *anti*, the *syn* conformers have the HOMO energy average values lower and the LUMO energy values higher. Even if they are influenced by the *syn-anti* arrangement, the differences of the HOMO and LUMO energies, respectively, are not significant. In conclusion, the *syn-anti* arrangement of the O17 and H28 atoms has a weak influence on the HOMO and LUMO energy in the PM3 merthod.

The HOMO and LUMO energy average values calculated with respect to the puckering criteria of the thiazolidinic cycle (a, b, c) are:

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HOMO(a) = -9.632±0.156 eV, LUMO(a) = -0.378 ±0.156eV,
HOMO(b) = -9.683 ±0.110 eV, LUMO(b) = -0.425 ±0.092eV.
HOMO(c) = -9.643±0.074eV, LUMO(c) = -0.386 ±0.077 eV,

There is a small difference between the average values of the three puckering classes. Due to the large dispersion for the HOMO in (b) puckering class, we cannot conclude that these average values are statistically distinct. However, we can make some remarks: the (b) puckering class has the lowest HOMO energy average values and the highest LUMO energy values.

To see the measure in which the HOMO and LUMO average values of the (a,b,c) puckering classes are influenced by the pyramidalization at N(14) or by the *syn-anti* arrangement, the average values function of these criteria were calculated.

The HOMO and LUMO average values for the (a,b,c) puckering classes calculated function of the R-S pseudochirality are:

HOMO(R,a) = -9.723±0.060 eV, LUMO(R,a) = - 0. 447±0.046eV,
HOMO(S,a) = -9.555 ±0.171 eV, LUMO(S,a) = - 0.320 ±0.190 eV,

HOMO(R,b) = -9.747±0.055eV, LUMO(R,b) = -0.460±0.035eV,
HOMO(S,b) = -9.609±0.113eV, LUMO(S,b) = -0.384±0.120eV,

HOMO(R,c) = -9.667±0.077eV, LUMO(R,c) = -0.401 ±0.061 eV,
HOMO(S,c) = -9612 ±0.065eV, LUMO(S,c) = -0.366 ±0.101 eV.

The statistical analysis of the data suggests that both for the average values of the HOMO and LUMO energies with respect to the (a), (b) and (c) puckering classes and the R-S N14 pyramidalization, there are no statistically distinct values.

The HOMO and LUMO average values for the (a,b,c) puckering classes calculated with respect to the *syn-anti* criterion are:

HOMO(*syn*,a) = -9.620±0.173eV, LUMO(*syn*,a) = -0.366 ±0.175eV,
HOMO(*anti*,a) = -9.641±0.143 eV, LUMO(*anti*,a) = -0.388 ±0.142eV,
HOMO(*syn*,b) = -9.691±0.087eV, LUMO(*syn*,b) = -0.435 ±0.080eV,
HOMO(*anti*,b) = -9.666 ±0.157 eV, LUMO(*anti*,b) = -0.403 ±0.117eV,

HOMO(*syn*,c) = -9.646±0.090eV, LUMO(*syn*,c) = -0.362 ±0.088eV,
HOMO(*anti*,c) = -9.638 ±0.060 eV, LUMO(*anti*,c) = -0.415 ±0.060 eV.

Even if there is a superimposition of the confidence intervals, we can appreciate that the average values are distinct only for the (c) puckering class. For (a) puckering class, the average values for the HOMO *syn* and *anti* energies are not distinct, while the LUMO energies are distinct and respect the rule of statistical differentiation: the LUMO(*syn*,a) energy is lower than the LUMO(*anti*,a) energy. For the (b) puckering class, the average values of HOMO as well as for LUMO energies are not statistically distinct: the (*anti*,b) average values are lower than the (*syn*,b) average values. For (c) puckering class, the average values of both HOMO and LUMO energies are statistically distinct, and the (*syn*,c)

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average values are lower than the *(anti,*c) average values. In conclusion, only in the (c) puckering class the *syn-anti* orientation influences significantly both the values of the HOMO and the LUMO energies.

These results prove that for all *syn-anti* conformers the HOMO and LUMO energies are influenced more by the spatial arrangement of the exocyclic amidic group, while the N14 atom pseudochirality does not influence significantly these values.

In Figure 2 is given the orbital distribution in HOMO and LUMO levels for three conformers: 02pm3 (with the lowest energy) and 97 pm3 (with the worst concordance with experimental geometry) [1].

For all the conformers the contribution of the sulphur atom, S1 to the HOMO or LUMO level is the most important. For the HOMO level are of importance also the contributions of the σ bonds between C2-C9, C2-C10, C5-C6 and C5-H19 and of lower importance the local contributions of the N4, O8, N14 and O17 atoms. For the LUMO level are of importance the contributions of the C2 and C5 atoms and in lower measure those of the N3, C6, C7 and O8 atoms.
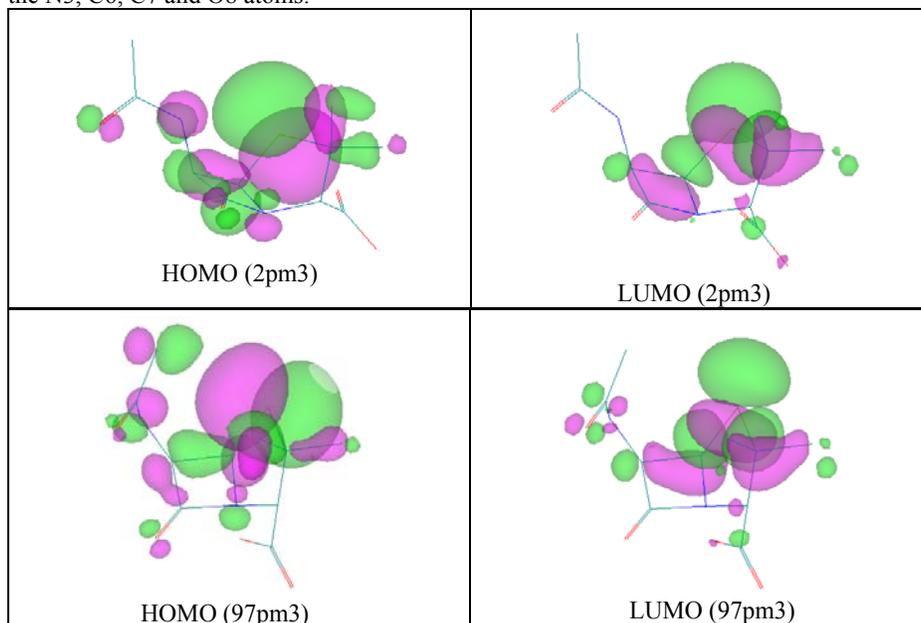

Figure 2. The weight of the Sulphur (S1) atom in HOMO and LUMO of conformers 02pm3 (with the lowest energy) and 97 pm3 (with the worst concordance with experimental geometry) computed with PM3

Analyzing the data in Table I one can observe that there is no influence of the pyramidalization of the N14 atom on the dipole moment, as it results from the average

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values calculated with the R-S criterion: $\mu(R) = 3.199 \pm 1.084$ Debye, $\mu(S) = 3.203 \pm 1.055$. Even if these average values seem different, due to their high standard deviation they are not statistically distinct. .

The influence of the *syn-anti* arrangement on the dipole moment is more obvious. The *syn* structures have lower values of the dipole moment in the interval 1.303 - 4.708 Debye for conformers 24pm3 and 53pm3, respectively. Comparatively, the *anti* structures have higher values in the interval 2.888 - 4.911 Debye for conformers 82pm3 and 49pm3, respectively (Table I). The average values are $\mu(syn) = 2.815 \pm 1.065$ Debye, and $\mu(anti) = 3961 \pm 0.518$ Debye. Statistically these average values are distinct.

The influence of the puckering on the dipole moment is proven by the average values for the three puckering classes (a,b,c):

$$\mu(a) = 3.477 \pm 0.951 \text{ Debye}$$
$$\mu(b) = 2.885 \pm 1.062 \text{ Debye}$$
$$\mu(c) = 4.019 \pm 0.839 \text{ Debye}$$

Even if these average values are different, due to the high dispersion they are not statistically distinct.

The influence of the *syn-anti* arrangement on the average values of the dipole moment calculated with respect to the (a,b,c) puckering classes are:

$$\mu(syn,a) = 2.872 \pm 1.048 \text{Debye}$$
$$\mu(anti,a) = 3.950 \pm 0.507 \text{ Debye}$$

$$\mu(syn,b) = 2.459 \pm 0.942 \text{ Debye}$$
$$\mu(anti,b) = 3.844 \pm 0.600 \text{ Debye}$$

$$\mu(syn,c) = 3.809 \pm 1.070 \text{ Debye}$$
$$\mu(anti,c) = 4.208 \pm 0.434 \text{ Debye}$$

From these data, for each puckering class there is an evident differentiation of the dipole moments function of the *syn-anti* arrangement.

As expected, these average values prove that for all conformers the dipole moment is strongly influenced by the *syn-anti* spatial arrangement of the O17 and H28 atoms of the exocyclic amidic group.

The minimum vibration energy, ν_{min}, is a backbone vibration and all atoms are implicated in it through their out-of-the-plane vibration (Fig. 3). The ν_{min} average value is of 29.00 ± 5.467 cm^{-1}, with a large dispersion, which proves the dependence of this vibration on the conformation. The maximum vibration energy, ν_{MAX}, is an ellongation vibration implicated only in the bond between the O13 atom and the H27 atom and it takes place in the bond plane. Its average value is of 3847.651 ± 2.997 cm^{-1}. Its disperion is small, which proves its non-dependence on the conformation. If the dependence of these vibrations on the

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N14 pyramidalization (R-S pseudochirality), on the *syn-anti* arrangement and on the puckering classes are taken into account, the following average values are obtained:

$\nu_{min.}(R) = 29.282 \pm 5.717$ cm^{-1}　　　　$\nu_{MAX.}(R) = 3847.670 \pm 3.044$cm^{-1}

$\nu_{min.}(S) = 28.731 \pm 5.263$ cm^{-1}　　　　$\nu_{MAX.}(S) = 3847.633 \pm 2.98$ cm^{-1}

$\nu_{min.}(syn) = 29.427 \pm 4.672$cm^{-1}　　　$\nu_{MAX.}(syn) = 3847.320 \pm 2.78$ cm^{-1}

$\nu_{min.}(anti) = 27.879 \pm 6.046$cm^{-1}　　　$\nu_{MAX.}(anti) = 3848.399 \pm 3.210$ cm^{-1}

$\nu_{min.}(a) = 28.758 \pm 5.216$ cm^{-1}　　　$\nu_{MAX.}(a) = 3848.049 \pm 2.981$ cm^{-1}

$\nu_{min.}(b) = 30.339 \pm 3.601$ cm^{-1}　　　$\nu_{MAX.}(b) = 3846.680 \pm 3.257$ cm^{-1}

$\nu_{min.}(c) = 26.669 \pm 9.829$cm^{-1}　　　$\nu_{MAX.}(c) = 3847.938 \pm 1.574$ cm^{-1}

Comparing these average values one observes that the $\nu_{min.}$ backbone vibration depends on the puckering classes, but is not influenced by pseudochirality and the *syn-anti* arrangement. At the same time the $\nu_{MAX.}$ vibration is not influenced neither by the pseudochirality, the *syn-anti* arrangement, nor by the puckering classes. We can generalize that independent of the conformer the vibrations of the functional groups are not influenced by the three factors: pseudochirality, *syn-anti* arrangement and puckering classes, while the vibrations implicating the backbone depend on the puckering classes and do not depend on pseudochirality and *syn-anti* arrangement.
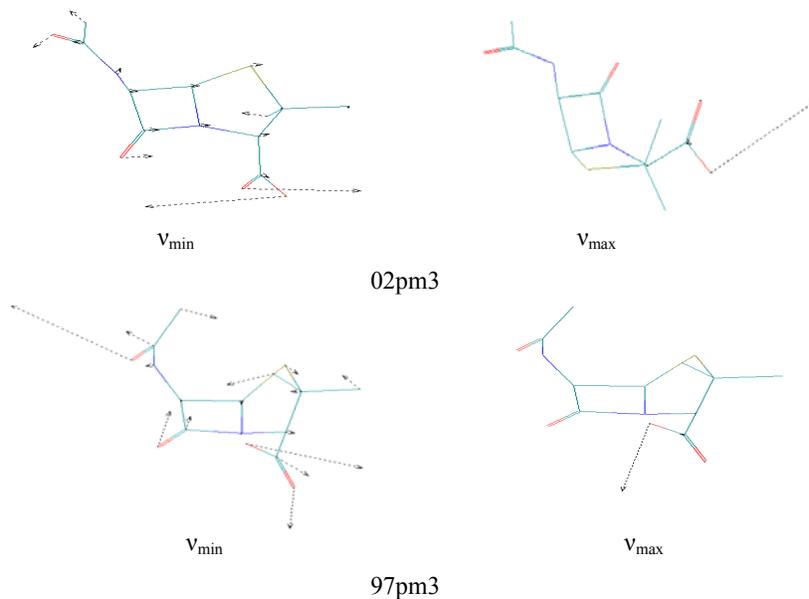

ν_{min}　　　　　　　　ν_{max}

02pm3

ν_{min}　　　　　　　　ν_{max}

97pm3

Figure 3. Movement vectors proportional with force constants for vibration ν_{min} and ν_{MAX} of conformers 02pm3, 97pm3, computed with PM3.

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The average values of the puckering classes calculated for the backbone vibration energies ν_{min}, and ν_{MAX} with respect to the R-S pseudochirality or the *syn-anti* arrangement are:

$\nu_{min.}(a,R) = 27.758\pm5.977\text{cm}^{-1}$ $\nu_{MAX.}(a,R) = 3849.058\pm3.113 \text{ cm}^{-1}$

$\nu_{min.}(a,S) = 29.597\pm4.407\text{cm}^{-1}$ $\nu_{MAX.}(a,S) = 3848.045\pm2.918\text{cm}^{-1}$

$\nu_{min.}(b,R) = 30.734\pm3.065\text{cm}^{-1}$ $\nu_{MAX.}(b,R) = 3846.799\pm3.184 \text{ cm}^{-1}$

$\nu_{min.}(b,S) = 29.879\pm4.236\text{cm}^{-1}$ $\nu_{MAX.}(b,S) = 3846.541 \pm3.478\text{cm}^{-1}$

$\nu_{min.}(c,R) = 33.143\pm8.149\text{cm}^{-1}$ $\nu_{MAX.}(c,R) = 3848.110 \pm2.130 \text{ cm}^{-1}$

$\nu_{min.}(c,S) = 18.575\pm3.776\text{cm}^{-1}$ $\nu_{MAX.}(c,S) = 3847.723\pm0.671\text{cm}^{-1}$

$\nu_{min.}(a,syn) = 29.882\pm3.731\text{cm}^{-1}$ $\nu_{MAX.}(a,syn) = 3847.600 \pm269 \text{ cm}^{-1}$

$\nu_{min.}(a,anti) = 26.16\pm8.87\text{cm}^{-1}$ $\nu_{MAX.}(a,anti) = 3848.64 \pm2.82 \text{ cm}^{-1}$

$\nu_{min.}(b,syn) = 28.744\pm2.404\text{cm}^{-1}$ $\nu_{MAX.}(b,syn) = 3846.889 \pm3.219\text{cm}^{-1}$

$\nu_{min.}(b,anti) = 33.928\pm3.322 \text{ cm}^{-1}$ $\nu_{MAX.}(b,anti) = 3846.186\pm3.511 \text{ cm}^{-1}$

$\nu_{min.}(c,syn) = 29.621\pm12.039\text{cm}^{-1}$ $\nu_{MAX.}(c,syn) = 3847.432\pm1.383\text{cm}^{-1}$

$\nu_{min.}(c,anti) = 22.990 \pm5.648\text{cm}^{-1}$ $\nu_{MAX.}(c,anti) = 3848.570\pm1.761\text{cm}^{-1}$

Comparing these data it results that both pseudochirality and syn – anti arrangement do not influence the ν_{min} and ν_{MAX} vibration energies.

Based on the above results we can conclude that both the backbone vibrations as well as the vibrations of the functional groups do not depend on the *syn*-anti arrangement or the pseudochirality of the N14 atom. But they depend significantly on the puckering class. For all the 92 conformers optimized with the PM3 method, the nature of these two types of vibrations do not change.

The equilibrium energy (ZPVE) is relatively constant around the average value of 149.930 ±0.349 kcal/mol. It is contained in the interval 149.164 kcal/mol and 150.745 kcal/mol. The average calculated values for ZPVE using the *syn-anti* arrangement, R-S pseudochirality and puckering classes criteria lead to the conclusion that this energy does not change. ZPVE is a measure who does not depend significantly on the conformer's nature.

CONCLUSION

From the conformational analysis with the PM3 method it results that for all conformers the pseudochirality of the N14 atom does not influence significantly the HOMO and LUMO energies. On the contratry, the energy of these levels is influenced by the *syn-anti* arrangement of the exocyclic amidic group as well as by the puckering of the thiazolidinic ring

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From the analysis of the orbital contribution to the HOMO and LUMO levels, one can conclude that in these levels the S1 atom has the dominant contribution, while the geometry factors - pseudochirality of the N14 atom, the *syn-anti* arrangement and the puckering of the thiazolidinic cycle do not influence significantly this contribution.

The dipole moment is influenced strongly by the *syn-anti* arrangement. The puckering slightly influences the dipole moment, while the pseudochirality does not influence it at all.

From the vibration analysis one can draw the conclusion that both the backbone vibrations as well as the vibrations of the functional groups do not depend by the *syn-anti* arrangement or by the pseudochirality at the N14 atom, but depend significantly on the puckering. ZPVE does not depend significantly on the geometry of the conformer.

ACKNOWLEDGMENTS

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