



DIHEDRAL ANGLES CALCULATED WITH 3-SPHERE APPROACH AS INTEGER IN CONFORMATIONAL ANALYSIS ON D-, L- RIBITOL SERIES

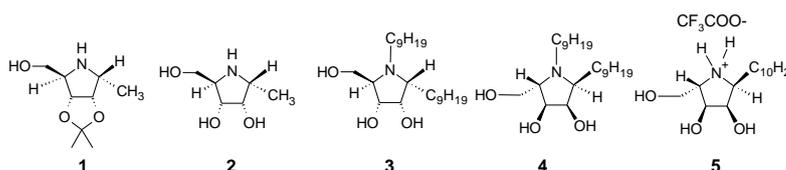
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Torsional angles calculated with 3-sphere approach from the NMR data (chemical shift δc [ppm], vicinal coupling constant $^3J_{HH}$ [Hz]) can be used instead of endocyclic torsional angles on Altona-Sundaralingam pseudorotational phase angle (P) and the AS puckering amplitude. The *trans-aa*, *trans-ee* torsional angles are calculated in relationship of ± 120 [deg] from the Karplus dihedral angles[35], and the 3-sphere torsional angles results from corresponding dihedral angles subtracted from 180[deg] for *trans-aa* and 120 for *trans-ee* stereochemistry. The conformational parameters of iminocyclitols **1-5** with α -D, β -L ribitol stereochemistry are calculated with JavaScript program.



$$P = \tan^{-1}[\theta_{1,2} - \theta_{3,4}/2\theta_{2,3}(\sin\pi/5 + \sin2\pi/5)][\text{deg}], \theta_m = (\theta_{2,3}/\cos P)[\text{deg}],$$

$$\alpha\text{-D: } P = 180 - P^{\text{calc}}, \theta_m = \theta_{2,3}/\cos P^{\text{calc}}, \text{ for } \theta_{2,3} \text{ negative,}$$

$$\beta\text{-L: } P = P^{\text{calc}}, \theta_m = \theta_{2,3}/\cos(180 + P^{\text{calc}}), \text{ for } \theta_{2,3} \text{ negative.}$$

THEORY

The conformational analysis of iminosugar ring have at origins earlier studies on the cyclopentane ring. Analyzing gaseous entropy of cyclopentane, Aston *et al.* demonstrated the contribution of the torsional forces associated with the single C-C bonds as responsible for ring puckered conformation.^{1,2} Lower energy of the puckered conformation relative to a planar ring was demonstrated by Pitzer analyzing the strain energy semi-quantitatively.³ “The rotation of the maximum angle pucker around the ring”, the free pseudorotation of the cyclopentane ring was state by Kilpatrick, Pitzer and Spitzer,⁴ and confirmed by McCullough⁵ with heat capacity measurements.

The puckering in five membered ring was expressed by Kilpatrick, Pitzer and Spitzer as the atomic displacement (Z_j) of j^{th} carbon atom perpendicular to the reference plane of the unpuckered ring, where q and ξ are both orthogonal to each other, and to translation and rotation of the whole molecule.^{4,6}

$$Z_j = (2/5)^{1/2} q \cos[(2\pi/5)j + \xi], \quad j = 1, \dots, 5,$$

$$\xi = l\pi/10 \text{ for } C_s, \xi = (2l+1)\pi/20 \text{ for } C_2,$$

where: l is any integer, q the amplitude [\AA^0] and ξ the phase angle of the pucker [deg].

Cremer and Pople⁷⁻⁹ introduce a unique mean plane for a monocyclic puckered ring, applicable on all the rings size. The amplitude and the phase coordinates are in direct relationship with the

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nuclear positions of the atoms in the ring. The puckering amplitude does not depend on which atom is chosen as number one. The positions of the five atoms on a puckered ring can be presented in Cartesian coordinates (X_j , Y_j , Z_j) or vectors positions R_j ($j = 1, 2, N$). For $N = 5$, the model has only two parameters to describe the conformational space (amplitude - q_m [A°], phase angle ϕ_m [deg]), and the displacement expression become equal with the Kilpatrick equation.⁷ Two distinct ring puckering are v_a and v_b , the first described the envelope (C_s) and the second the twist or half-chair conformation (C_2). If the barrier of interconversion between two is low, the molecule will pass through intermediate conformations with no symmetry (C_1), corresponding to linear combinations.⁷

$$v_a(e_a'') : z_i^{(a)} = z_0 \cos[4\pi(i-1)/5],$$

$$v_b(e_a'') : z_i^{(b)} = z_0 \sin[4\pi(i-1)/5].$$

The generalized ring-puckering coordinates was represented as a set with amplitude q_m ($q_m > 0$) and phase angle ϕ_m ($0 < \phi_m < 2\pi$). The five membered ring has an infinite number of puckered ring conformations along the pseudorotational itinerary ($\phi = 0 - 360^\circ$): 10 envelopes (E) with $\phi = (0 + K360/10)$ and 10 twist (T) with $\phi = (18 + K360/10)$.⁸

$$A = q_m \cos \phi_m = (2/N)^{1/2} \sum_{j=1}^N z_j \cos[2\pi m(j-1)/N],$$

$$B = q_m \sin \phi_m = -(2/N)^{1/2} \sum_{j=1}^N z_j \sin[2\pi m(j-1)/N],$$

$$q_{N/2} = N^{-1/2} \sum_{j=1}^N \cos[(j-1)\pi] = N^{-1/2} \sum_{j=1}^N (-1)^{j-1} z_j,$$

$$q_m^2 = A^2 + B^2; \quad \phi_m = \arctan(B/A).$$

In case of six membered ring $N = 6$ are required three parameters to describe the conformational space: a radius Q and two-phase angles Φ , θ ; and all accessible conformers are represented on Stoddart's diagrams, or most recently Davie's diagrams.¹⁰

$$q_x = Q \sin \theta \sin \Phi, \quad q_y = Q \sin \theta \cos \Phi,$$

where: q_x , q_y – spherical representation of the pyranose ring in two dimensions projection, conformational space used for plotting and visualization of the free energy surface in a continuous space.

Chan *et al.* model's convert Cramer-Pople puckering coordinates to ring torsional angles; the endocyclic torsional angles upon pseudorotation can be analyzed, and estimate the puckering preference with kernel density estimation (KDE).¹¹

A second representation proposed by Cremer used in plane ring deformation coordinates.¹² The

origin of the Cartesian framework must coincide with geometrical center of the atoms involved in the ring structure, and the Z axis must be perpendicular to a mean-plane chosen to pass through the origin on which the vector r' and r'' lie.¹³

$$\hat{Z} = r' \times r'' / |r' \times r''|, \quad Z_j = r_j \cdot \hat{Z},$$

$$r' = \sum_{j=1}^N z_j \sin[2\pi(j-1)/N], \quad r'' = \sum_{j=1}^N z_j \cos[2\pi(j-1)/N],$$

where: Z_j – coordinate of each atom involved in the ring structure.

Altona-Sundaralingam pseudorotational parameters are the maximum angle of torsion (θ_m [deg]) and the phase angle of pseudorotation (P [deg]), with five torsional angles as integer. The amplitude of the phase angle is the maximum distance of a ring atom from the plane of the ring, and also a measure of the magnitude of the deviation from planarity. The phase of the pseudorotation P indicates which part of the ring is out of the planarity. With only three endocyclic torsional angles the conformational parameters of the five membered ring can be calculated from the experimental data empirically.¹⁴ The maximum torsional angle (θ_m) for five membered ring D of the steroids is relatively constant (47°), with a slightly tendency to increase with increasing phase angle.^{15,16} Altona, Geise and Romers used two ellipses with their main axes at 45° to represent the relation between two torsional angles adjacent to each other ($\theta_0 - \theta_1$) in cyclopentane.¹⁵ The maximum torsional angle for the furanose ring has values between $35-45^\circ$, depending on the functional groups at the anomeric position.¹⁴

$$\theta_j = \theta_m \cos(P + j\delta) = \theta_m \cos(P + 4\pi j/5), \\ j = 0-4, \quad \delta = 144^\circ,$$

$$P = \tan^{-1}[(\theta_2 + \theta_4) - (\theta_1 + \theta_3)/2\theta_0(\sin\pi/5 + \sin 2\pi/5)][\text{deg}], \quad \theta_m = (\theta_0/\cos P)[\text{deg}].$$

The pseudo-rotational wheel of the furanose ring is represented by a circle, the twist conformation alternates the envelope conformations. The symmetrical twist (T) conformations are placed at even multiples of 18° of the phase angle P , and symmetrical envelope (E) conformations at odd multiples of P . The upper or northern half of the circle ($P = 0 + /-90^\circ$) comprises all conformations that show a positive value of θ_0 (C_2-C_3), whereas the southern half ($P = 180 + /-90^\circ$) contains all conformations with a negative value of θ_0 .^[14]

Levitt and Warshel for both θ_j and Z_j , the out of plane displacement of the ring atom C_j' ($j = 0$ for $O1'$), reported simple analytical functions: amplitude (θ_{\max} or q) and phase angle P .¹⁷

$$\theta_j = \theta_{\max} \cos(P + j \times 144^\circ - 288^\circ),$$

$$z_j = (2/5)^{1/2} q \cos(w + j \times 144^\circ - 90^\circ).$$

DeTar and Luthra¹⁸ calculate the conformation of proline from the vertical displacement of a given atom in average plane, represented also by a torsion or a bond angle:

$$\lambda_i = a^\circ \cos[t + 4\pi(i - 2)/5], i = 1-5.$$

where: a° is the puckering amplitude, the maximum value assumed by λ , $t = 0, 36, 72$ [deg] (C_2 symmetry "half chair"), $18, 54$ [deg] (C_s symmetry "envelope").

$$\lambda_1 = -0.809\lambda_2 - d_1; \lambda_3 = -0.809\lambda_2 + d_1;$$

$$\lambda_4 = 0.309\lambda_2 + d_2; \lambda_5 = 0.309\lambda_2 - d_2;$$

$$t = \tan^{-1}[-d_1/\lambda_2/\sin(4\pi/5)], a^\circ = \lambda_2/\cos t$$

The conformational parameters can be visualized¹⁹ on Altona - Sundaralingam conformational map.^{14,20} Eccentricity of the Lissajous oval,²¹ the transformation from the sphere to ellipse with parametric equation: $X = A \sin(at + \delta)$, $Y = B \sin(bt)$.

The model reported by Czinki - Császár²² used the differences between two torsional angles on the same sides, relative to Altona formalism where the differences are in opposite, and $\lambda_0 = \lambda_{XC1}$ for the calculation of the puckering amplitude.

$$A \sin P = (\lambda_1 - \lambda_2 + \lambda_3 - \lambda_4) / -2(\sin 4\pi/5 + \sin 2\pi/5),$$

$$A \cos P = \lambda_0.$$

Huang *et al.*²³ reported a mathematic model for the puckered conformation of the RNA sugar conformation, highly related to those developed by Soto and Altona, requiring only two endocyclic torsional angles ($\theta_{1,2}$ and $\theta_{3,4}$), where Z_x and Z_y represent the linear combinations of these angles. From the relationship between the cartesian and polar coordinates results the phase P and the amplitude A .

$$Z_x = (\theta_4 + \theta_1) / 2 \cos(4\pi/5); Z_y = (\theta_4 - \theta_1) / 2 \sin(4\pi/5),$$

$$P = \arctan(Z_y/Z_x), A = (Z_x^2 + Z_y^2)^{1/2}.$$

The correlation between the value of the phase angle of the pseudorotation and the conformation on the Altona's map is realized with Euler theory:²⁴

$$*x + yi = r(\cos\theta + i\sin\theta); r = (x^2 + y^2)^{1/2};$$

$$\text{if } x > 0: \theta = \arctan y/x,$$

$$\theta = \arctan[(y/x) + \pi] \text{ if } x < 0; \text{ if } y < 0, x > 0:$$

$$\theta = \arctan[(y/x) + 2\pi].$$

Rao *et al.* proposed a method based on the endocyclic torsion angles, where the amplitude and

phase of the second order Fourier wave of period $4\pi/5$ corresponds to the AS parameters (θ_m, P). To the calculated value of P if $\chi_2 < 2$ 180[deg] is added. With this method the small dependence of θ_m on the choice of the origin atom was overcome.²⁵

$$\tan P = B/A, \theta_m^2 = A^2 + B^2,$$

$$P = \tan^{-1} B/A + \pi/2, q^2 = A^2 + B^2,$$

$$A = X \cos P = (2/5) \sum \theta_j \cos 4\pi j/5,$$

$$B = X \sin P = -(2/5) \sum \theta_j \sin 4\pi j/5,$$

where $X = \theta_m$ - the angle of deviation from planarity[deg],

or q - the puckering amplitude [A^0], $j = 0-4$.

Rao's coordinate from the Cremer and Pople point of view us the puckering amplitude $q[A^\circ]$ and phase of the pseudorotation $P[\text{deg}]$. The factor $\pi/2$ correlates the CP and AS maps, establishing zero phase angle at 3_2T conformation.²⁶

Dunitz established a mathematical derivation of the Altona, Geise, Romers¹⁵ empirical relationships, where θ_{jk} is the torsion angle and θ_{\max} the maximum torsion angle.²⁷

$$\theta_{jk} = 2.828q \cos\{4\pi/5(j/2 + k/2) + P + \pi/2\},$$

$$\theta_{\max} = 2.828q, \theta_{\max}[\text{deg}] = 162q,$$

$$\theta_{\max}[\text{deg}] = 150q; 0.1 < q < 0.3, [0, 3\pi] [0, \pi/3].$$

The out of plane deformation decreases the bond angle (δ_j) at atom j , the sum of the bond angles deformation ($\sum \delta_j$) and torsional angles ($\sum \theta_{jk}^2$) are independent on the pucker but dependent on amplitude.

$$\theta_j = (3\pi/5) - \delta_j,$$

$$\sum z_j z_{j+1} = -[(2.23 + 1)/4]q^2,$$

$$\sum z_j z_{j+2} = [(2.23 - 1)/4]q^2.$$

Allen *et al.*²⁸ points out the differences between CP and AS approaches; the former has an envelope (E) conformer at $\phi = 0^\circ$,^{29,30} and the latter a twist (T) conformer at $P = 0^\circ$.¹⁴ The transformation of the cyclic to rectangular coordinates reduces the differences. The cartesian coordinate (eq. 1, 2) of the CP coordinates: CP1 corresponding to the vertical axis (E conformations at $\phi_2 = 0, 36, 72^\circ$), and CP2 to the horizontal axis (T conformations, or any T axis with $n \times 36^\circ$, $n = 1, 2, 3$). If AS1 and CP1 coincides exactly, AS2 and CP2 will be oriented at 180° to one another; E axes are $n \times 36^\circ$ and T axes are $180 + n \times 36^\circ$ out of plane.²⁸

Yang *et al.* claim the existence of three possible conformations along the pseudo-rotational map, as a function of the pseudo-rotational angle ϕ with values of 0° and 180° for C_s (envelope), $\pm 90^\circ$ for C_2 symmetry (twisted 0, and $\pm(50 - 60^\circ)$ or $\pm(120 - 130^\circ)$ for C_1 symmetry.³¹

$$CP1 = q_2 \cos \phi_2, CP2 = q_2 \sin \phi_2.$$

$$AS1 = \theta_m \sin P, AS2 = \theta_m \cos P.$$

Allen used topological symmetry with 2D representation for a chemical fragment, process which successively places a given fragment into each of the possible asymmetric units of the relevant conformation space. The GSTST program fulfil permutation and inversion operations to the atomic coordinates set for each local fragment.²⁸

The deviation from a linear relationship between $P(AS)$ and $P(CP)$ is a periodic function of P . For small puckering amplitude the correlations between RWS, AS and CP are given by the follow equation:³²

$$P_{CP} = P_{AS} - 4 \sin(2P_{AS}),$$

$$P_{AS} = \phi_m + 90^\circ.$$

$$\theta_{m(RWS)} = 1.03 \theta_{m(AS)},$$

$$\theta_{m(RWS)}[\text{deg}] = 102.5 q_{(CP)}[A^\circ],$$

$$\theta_{m(AS)}[\text{deg}] = 99.5 q_{(CP)}[A^\circ].$$

The maximum deviation of the endocyclic torsion (θ_m) from 0° gives accurate results only for small deviation from planarity, for larger puckering amplitudes a constant factor of 94.9 should be used in place of the 102.5.²⁷

METHOD

3-manifold locally reassembles Euclidean 3-dimensional space, and can be considered the shape of the universe, as well as a sphere looks like

a plane to a small distance relative to observer, and earth was flat before the modern word demonstrate it is round. One dimensional manifold includes lines and circles, but not figure eight. Two dimensionally manifold is also called surfaces, and have plane, sphere, and torus. Poincare conjecture is a theory about 3-sphere, a hypersphere that bound the unit ball in four dimensionally space, were a point increase to circle, and then is transforms to a torus. Einstein field equation of general relativity is other example, a vectorially approach for the translation from 2 to 4-dimensional space. 4-Manifold can be explained better by physics, since in general relativity space - time is modeled as a pseudo-Riemannian 4-manifold. Platonic solids or Catalan solids, with pentagon faces, are homeomorphic to the sphere. Poincare dodecahedron space is binary icosahedral group of order 120.³³

Our aim is to analyze the conformation of the iminocyclitols **1-5**³⁴ using the dihedral angles θ_{HnHN+1} of the H-C-C-H fragment calculated from chemical shift $\delta[\text{ppm}]$ and vicinal coupling constant ${}^3J_{HnHn+1}[\text{Hz}]$ with 3-sphere approach. The empiric methods for the calculation of the conformation from the torsional angles know to date are Altona-Sundaralingam and Huang, the first one required three torsional angles and the second one only two. PSEUDOROT program provides the identities of the two conformers, using correlations between the exocyclic HCCH dihedral angles (θ_{exo}), predicted from vicinal constant couplings ${}^3J_{HH}$, with endocyclic torsional angles: $\theta_{\text{exo}} = A + B\theta_{\text{endo}}$. The trigonal projection symmetry of the tetrahedral bound angles equals with $A=1$, $B=0$ in case of *cis* stereochemistry, and $A=1$, $B=120$ in case of *trans* stereochemistry, with deviations from the ideal values in case of the furanose ring. The exocyclic HCCH dihedral angles in PSEUDOROT program are calculated with Karplus generalized equation.³⁵

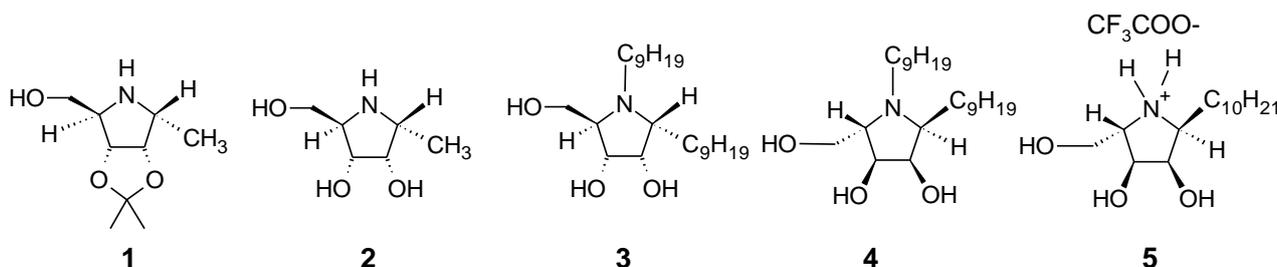


Fig. 1 – Iminocyclitols with α -D-ribitol (**1-3**) and β -L-ribitol (**4, 5**) stereochemistry.

Dihedral angle $\theta_{H_n H_{n+1}}$ [deg] with *cis*, *trans*-stereochemistry, in close relationships with the vicinal angle Φ [deg], are calculated with hypersphere trigonometric equation and conic section as manifold from chemical shift and vicinal coupling constant ${}^3J_{HH}$ [Hz].^{36,37} Dihedral angles with *cis* stereochemistry can be considered torsional angles, and dihedral angles with *trans* stereochemistry must be transformed under 120 rule. The main advantages of the dihedral angles calculated with 3-sphere approach are the sign and the stereochemistry,^{38,39} angles which replaced better the endocyclic torsional angles on Altona's model.

RESULTS AND DISCUSSION

In Table 1 are calculated the phase angle of the pseudorotation P [deg] and the angle of deviation from planarity θ_m [deg] for iminocyclitols **1-5** with Altona-Sundaralingam model¹⁴ (Fig. 2) and Java script program (Fig. 3), using torsional angles calculated with 3-sphere approach^{36,37} from the differences between two consecutive atoms of carbon instead of Karplus torsional angles.

$$P = \tan^{-1}[\theta_{1,2} - \theta_{3,4}/2\theta_{2,3}(\sin\pi/5 + \sin2\pi/5)] [\text{deg}],$$

$$\theta_m = (\theta_{2,3}/\cos P) [\text{deg}],$$

$$\alpha\text{-D: } P = 180 - P^{\text{calc}}, \theta_m = \theta_{2,3}/\cos P^{\text{calc}},$$

for $\theta_{2,3}$ negative,

$$\beta\text{-L: } P = P^{\text{calc}}, \theta_m = \theta_{2,3}/\cos(180 + P^{\text{calc}}),$$

for $\theta_{2,3}$ negative,

where: P [deg] – the phase angle of the pseudorotation, θ_m [deg] – angle of deviation from planarity, $\theta_{n,n+1}$ [deg] – torsional angles.

The phase angle of the pseudorotation⁴⁰ in D ribose series result from the inverse trigonometric

function if $\theta_{H_2H_3}$ is positive, or 180 [deg] is added to the calculated values if $\theta_{H_2H_3}$ is negative ($\alpha\text{-D}$). In the L-ribose series if $\theta_{H_2H_3}$ is positive 180 [deg] is added to calculated value of P , and for $\theta_{H_2H_3}$ negative 180 [deg] is subtracted ($\beta\text{-L}$). The *trans-aa*, *trans-ee* Karplus torsional angles are calculated in relationship of ± 120 [deg] from the dihedral angles,³⁵ and the 3-sphere torsional angles results from corresponding dihedral angles subtracted from 180 [deg] for *trans-aa* and 120 for *trans-ee* stereochemistry. The torsional angles of *trans-aa* stereochemistry are in accord with the corresponding *cis* angles results from vicinal coupling constant. In case of *trans-ee* stereochemistry, from the trigonometric equation^{38,39} both must have equal torsional angles: *trans-ee*^{4,1}, *-ee*^{3,2} = *cis*^{6,1}, relative to 120 [deg] rule where *trans-ee*^{4,1} = *cis*^{6,1} and *trans-ee*^{3,2} = *cis*^{5,2}.

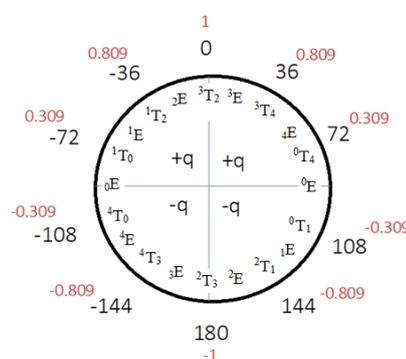


Fig. 2 – Phase angle of pseudorotation P [deg] and the amplitude $q_m[\pi]$ in $\alpha\text{-D}$, $\beta\text{-L}$ ribitol series.

The equations for $\alpha\text{-D}$, $\beta\text{-L}$ ⁴¹ are established analyzing the sign of the torsional angles, the value of P^{calc} on the Altona's map (Fig. 2), and molecular models.

Table 1

Phase angle of the pseudorotation and the angle of deviation from planarity

Entry	$H_n H_{n+1}$	${}^3J_{HH}^{\text{exp(a)}}$ [Hz] ^a	θ^{pred} [deg]	R_{mC} [π] ^b	$\theta_{H_n H_{n+1}}$ [deg]	${}^3J_{HH}^{\text{calc}}$ [Hz]	P^{calc}, P [deg]	θ_m [deg]	E, T
$\alpha\text{-D}$									
1.	1-H₁H₂	4.1	22.76	0.7759	ea ^{6,1} : 20.88	4.15	-30.43 ^b -149.56	-33.29 ^b	⁴ T ₃ – ³ E
2.	1-H₂H₃	5.4	-26.639	0.0224	ae ^{6,1} : -28.71	5.44			
3.	1-H₃H₄	0 (d, H ₃)	90	0.5154	ee ^{3,2} : -88.97 ^b	0.506			
4.	2-H₁H₂	3.1	51.55	0.3949	ae ^{5,2} : 50.209	3.15 ^c	34.01 ^b	35.79 ^b	³ T ₄ ^b
5.	2-H₂H₃	3.9	29.15	0.0056	ea ^{6,1} : 29.67	3.88	-36.88 ^c	-51.24 ^c	³ E- ⁴ T ₃ ^c
6.	2-H₃H₄	8.8	167.43	0.1375	aa ^{6,1} : -168.6 ^b	8.87 ^c	-143.12 -24.12 ^c -155.87	32.510	¹ T ₂ - ² E ^c
7.	3-H₁H₂	4.8	-2.159	0.2464	ea ^{6,1} : -2.918	4.81 ^c	-27.49 ^b -152.50	-21.64 ^b	⁴ T ₃ – ³ E
8.	3-H₂H₃	5.2	-18.15	0.0420	ae ^{6,1} : -19.197	5.22			
9.	3-H₃H₄	0 (t, H ₃)	90	0.1316	ee ^{3,2} : -86.34 ^b	0.95			

Table 1 (continued)

β -L									
10.	4-H ₁ H ₂	4.8	-2.16	0.0756	ea ^{6,1} : -2.168	4.8	30.77	22.26	³ T ₄
11.	4-H ₂ H ₃	5.2	-18.159	0.0448	ae ^{6,1} : -19.14	5.22			
12.	4-H ₃ H ₄	0 (t, H ₃)	90	0.05042	ee ^{3,2} : 87.10	0.85			
13.	5-H ₁ H ₂	2.8	58.63	0.22969	ae ^{5,2} : 56.55	2.89	20.019	40.805	³ E
14.	5-H ₂ H ₃	3.6	38.159	0.03641	ea ^{5,2} : 38.34	3.59			
15.	5-H ₃ H ₄	8.8	167.43	0.28291	aa ^{6,1} : 166.434	8.74	-20.56° -159.44	40.70	³ T ₂ , ³ 2E ^b 2E ^c

a. δ_c , δ_H [ppm], ¹H 400MHz, ¹³C 75MHz: 1-CDCl₃, 2-D₂O, 3-CDCl₃, 4-CDCl₃, δ_H 5-CDCl₃, δ_c 5-CD₃OD[34]; b. sign of θ_{H3H4} in D-ribitol series result from molecular models, c. trigonometric functions[42], 1, 3-⁴T₃ - ³E: from unit S result negative sign for *trans-ee*^{3,2}, 2-³E: 50.209, -40.987, -135.57[deg], 2-³T₂: -52.534, 29.67, -168.36[deg], 5-³T₂: 56.55, -38.108, 167.44[deg].

```

<!DOCTYPE html>
<html>
<head>
<title>A Java script including HTML</title>
</head>
<body style="background-color:LightGrey;">
<p id="demo"><p>
<p>Click button to:</p>
<button onclick="window.print()">Print this page.</button>
<button type="button"onclick="document.getElementById('demo').innerHTML = Date()">Date and Time.</button>
<h3>Java Script program for calculation of the conformation of five membered ring iminocyclitols.</h3>
<h4>Step 1:</h4>Program for calculation of the conformation</p></h4>
<p style="font-size: 18px;"><B>Fig. 1:</B>Altona's conformational map:</p>

</body>
<script type="text/javascript">
//File name Conformation.html
//Program that calculate conformation
var usedata1
usedata1 = prompt ("The value of dihedral angle H1H2-alphaD[deg]")
var H1H2 = usedata1;//angle H1H2[deg]
//angle H1[deg]
var H1 = 1*(H1H2)//angle H1[deg]
document.write("<h5>The conformation in alpha-D-ribose series</h5>")
document.write("<p>The torsional angle H1H2, H1[deg]="+H1);
var usedata2
usedata2 = prompt ("The value of dihedral angle H2H3-alphaD[deg]")
var H2 = usedata2;//angle H2H3[deg]
document.write("<p>The torsional angle H2H3, H2[deg]="+H2);
var usedata3
usedata3 = prompt ("The value of dihedral angle calculated H3H4-alphaD[deg]")
var H3 = usedata3;//angle H3H4[deg]
//calculate angle H3[deg]
var HD = H3;//the signe of angle H3[deg]
if (H3 < 0){
var HD = H3;//angle HD[deg]
}
else {
var HD = -H3;//angle HD[deg]
}
document.write("<p>The dihedral angle H3H4, H3[deg]="+H3);
document.write("<p>The dihedral angle HD[deg]="+HD);
//calculate the value of P in alfa-D-ribose series
var H3D = -(HD + 120)//angle H3D[deg]
if (HD < 0){
var H3D = -(HD + 120);//angle H3D[deg]
if (HD < -120){
var H3D = (-180 - HD);//angle H3D[deg]
}
}
if (HD > 120){
var H3D = (HD + 180);//angle H3D[deg]
}
}
else {
var H3D = -HD + 120;//angle H3D[deg]
}
document.write("<p>The torsional angle H3D[deg]="+H3D);
var A = [(H1 - H3D)/(3.077*H2)]//value of A
var Pr = Math.atan(A);//value of calculated phase angle of the pseudorotation[rad]
var Pd = (Pr)*(57.29577521)//value of calculated phase angle of the pseudorotation[deg]
var PD = Pd;//value of phase angle of the pseudorotation[deg]
if (H2 > 0){
var PD = Pd;//value of phase angle of the pseudorotation[deg]
}
else{
var PD = 180 - Pd;//value of phase angle of the pseudorotation[deg]
}
document.write("<p>The phase angle of the pseudorotation calculated, the angle Pd[deg];"+Pd);
document.write("<p>The phase angle of the pseudorotation, the angle PD[deg];"+PD);
//calculate the angle of deviation from planarity MD[deg]
var BB = (Pd)*(0.017453292)//value of BB [rad]
var Br = Math.cos(BB)//value B[radians]
var B = (Br)*(57.29577521)//value of B[deg]
var MD = (H2/Br)//angle of deviation from planarity[deg]
document.write("<p>The angle of deviation from planarity, the angle MD[deg];"+MD);
var usedata4
usedata4 = prompt ("The value of dihedral angle H1H2-betaL[deg]")
var H4 = usedata4;//angle H1H2[deg]
document.write("<h5>The conformation in beta-L-ribose series</h5>")
document.write("<p>The torsional angle H1H2, H4[deg]="+H4);
var usedata5
usedata5 = prompt ("The value of dihedral angle H2H3-betaL[deg]")
var H5 = usedata5;//angle H2H3[deg]
document.write("<p>The torsional angle H2H3, H5[deg]="+H5);
var usedata6
usedata6 = prompt ("The value of dihedral angle H3H4-betaL[deg]")
var H6 = usedata6;//angle H3H4[deg]
//calculate angle H6[deg]
var HL = H6;//the signe of angle H6[deg]
if (H6 > 0){
var HL = H6//angle HL[deg]
}
else {
var HL = -H6//angle HL[deg]
}
document.write("<p>The dihedral angle H3H4, H6[deg]="+H6);
document.write("<p>The dihedral angle HL[deg]="+HL);
//calculate the value of P in beta-L-ribose series
var H3L = (120 - HL)//angle H3L[deg]
if (HL < 120){
var H3L = (120 - HL)//angle H3L[deg]
if (HL > 120){
var H3L = (180 - HL)//angle H3L[deg]
}
}
else {
var H3L = 180 - HL;//angle H3L[deg]
}
document.write("<p>The torsional angle H3L[deg]="+H3L);
//calculate the phase angle of the pseudorotation PL[deg]
var B = [(H4 - H3L)/(3.077*H5)]//value of B[radians]
var Pr = Math.atan(B);//value of calculated phase angle of the pseudorotation[rad]
var PL = (Pr)*(57.29577521)//value of calculated phase angle of the pseudorotation[deg]
document.write("<p>The phase angle of the pseudorotation, the angle PL[deg];"+PL);
//calculate the angle of deviation from planarity ML[deg]
var C = PL;//value of C[deg]
if (H5 > 0){
var C = PL;//value of C[deg]
}
else{
var C = 180 + PL;//value of C[deg]
}
var BL = (C)*(0.017453292)// value of BL[rad]
var Bl = Math.cos(BL);//value B[radians]
var ML = (H5/Bl)//angle of deviation from planarity ML[deg]
document.write("<p>The angle of deviation from planarity, the angle ML[deg];"+ML);
alert("Hello World!");
</script>
</html>

```

Fig. 3 – Java script program for calculation of the conformational parameters of iminocyclitols with α -D, β -L ribitol series.

Simulation of the calculated dihedral angles on molecular models result that the *trans-aa* θ_{H3H4} angle is always negative in D-ribitol series and positive in L-ribitol series. As result from Table 1 negative θ_{m} indicated the presence of P in south side of the map, thus in case of α -D-ribitol the calculated values $P^{\text{calc}}[\text{deg}]$ should be subtracted from 180[deg]. As confirmed with molecular models, in α -D series the conformation is the mirror image from N to S on horizontal axis, *i.e.* **1**: $P^{\text{calc}} = -30.54[\text{deg}]$ has the conformation ${}^4T_3 - {}_3E$ corresponding to $P = -149.46[\text{deg}]$, with an angle of deviation from planarity calculated from θ_{m} of $-33.33[\text{deg}]$. In β -L-series the conformation result from P^{calc} and the angle of deviation from planarity from the value result after adding 180[deg] to P^{calc} .

Sundaralingam²⁶ claims the existence of two possible puckered states of the pseudorotation: one endocyclic bond angle constant and three atoms anchored in the crystal, and one endocyclic torsional angle constant and four consecutive atoms of the ring are anchored in the crystal. Two consecutive positive torsional angles on iminocyclitol **5** gives conformations at borderline between twist or envelope with two atoms down of plane (${}_{32}E$), or gradually out of plane at smaller differences. The existence of three isomers was demonstrated recently and will be presented elsewhere,⁴² three dihedral angles for one vicinal coupling constant with different sign and stereochemistry, as well as the conformations of iminocyclitols **2** and **5** can be established easy with molecular model in line with Altona map, one atom out of the plane: $+38.34[\text{deg}]$ with $P({}_3E) = 20.01[\text{deg}]$, $-38.34[\text{deg}]$ with $P({}_2E) = -20.56[\text{deg}]$. The vicinal coupling constant of 8.8[Hz] with an angle of 167.44[deg] with positive sign in L-ribose series and negative sign in D-ribose series as result from molecular models, from the trigonometric point of view has two *trans-aa*^{6,1} dihedral angle with positive and negative sign (167.44, $-167.127[\text{deg}]$) and one *trans-aa*^{5,2} ($-135.694[\text{deg}]$). The dihedral angles ± 167.127 and $-135.694[\text{deg}]$ of **2** place the phase angle of the pseudorotation in north and south side of the Altona's map, as furanose ring conformation in double stranded DNA.

The conformational parameters: the phase angle of the pseudorotation and de angle of deviation from planarity can be calculated with Java Script program presented in Fig. 3 for iminocyclitols with α -D-ribitol (**1-3**) and β -L-ribitol (**4, 5**) stereochemistry. The program can be used with

Notepad++ or Free Java Script Editor, and the Fig. 2 must be transformed in jpg.

CONCLUSION

Dihedral angles calculated from the NMR data (chemical shift $\delta_{\text{c}}[\text{ppm}]$, vicinal coupling constant ${}^3J_{\text{HH}}[\text{Hz}]$) with 3-sphere approach replaced better the torsional angles[19] on Altona-Sundaralingam model[14]. The main advantage: the sign result from the hypersphere trigonometric equation. The conformational parameters can be calculated with Java script program presented in Fig. 3 for iminocyclitols with α -D, β -L ribitol stereochemistry. For other stereochemistry the following steps are required:

The phase angle of the pseudorotation $P[\text{deg}]$ will be calculated with Altona-Sundaralingam model and 3-sphere torsional angles.

With molecular models will be simulated the phase angle of the pseudorotation using the 3-sphere dihedral angles with the corresponding sign.

The conformation resulted from the calculated phase angle of the pseudorotation must be correlated with that resulted from molecular models on the Altona-Sundaralingam map.

Correlation of the phase angle of the pseudorotation $P[\text{deg}]$ with the sign of the angle of deviation from planarity $\theta_{\text{m}}[\text{deg}]$.

Established the general equations for the stereochemistry analyzed.

Write the Java Script program for calculation of the conformational parameters.

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