Conformational Analysis of the Deoxyribofuranose Ring: a Theoretical Study

Joanna Wiórkiewicz-Kuczera* and Andrzej Rabczenko
Polish Academy of Sciences, Institute of Biochemistry and Biophysics, ul. Rakowiecka 36, 02-532 Warsaw, Poland

The results of energy calculations by the Consistent Force Field method for methyl β-D-2-deoxyribofuranoside are presented. Two regions of stable pentose conformations are predicted; within each region local energy minima are associated with different conformations of the hydroxy and hydroxymethylene groups. A conformational model of the molecule in solution is proposed. Proton coupling constants are calculated for the stable conformers found, and a qualitative agreement with the experimentally observed solution behaviour is achieved. The influence of the nature and conformation of exocyclic substituents on the conformation of the furanose ring and on the interconversion of conformations by pseudorotation is discussed.

One of the determinants of the secondary structure of a polynucleotide chain is the conformation of the furanose ring.[1-3] Recently several authors[4-7] have discussed the flexibility of ribose and deoxyribose, without examining, however, all possible degrees of freedom of the systems studied.

A ^{1}H n.m.r. study[8] of the conformational behaviour of methyl β-furanosides and their phosphates in solution has prompted us to perform energy calculations for methyl β-D-ribofuranoside and methyl β-D-2-deoxyribofuranoside, which may serve as models for the sugar moiety in nucleotides. The results of our study should help to elucidate the influence of exocyclic groups on the conformation and pseudorotation of the pentose ring; and to ascertain whether substitution at C(1) is an important influence on the conformational behaviour of furanose. In a previous paper[9] we reported the results for methyl β-D-ribofuranoside. Here we present the results for methyl β-D-2-deoxyribofuranoside.

An empirical potential function program developed by Rasmussen and his co-workers[10,11] for saccharides was used. The predicted conformational behaviour of an isolated molecule of methyl β-D-2-deoxyribofuranoside is represented by the whole set of minimum-energy states found. A subset of local energy minimum conformers was defined to model the molecule in solution. To test the reliability of this model, as well as the usefulness of the Consistent Force Field (CFF) method for our purpose, we have calculated vicinal proton coupling constants and compared them with experimental ^{1}H n.m.r. values.[8]

Method

Figure 1 shows the structure, numbering scheme, and torsion angle conventions for methyl β-D-2-deoxyribofuranoside. For the sake of brevity the cartesian co-ordinates of particular conformers are not given here. The pseudorotational parameters[12] P and τ_m are used instead to describe approximately the furanose ring conformations.

Energy calculations were carried out by means of the CFF method.[10,11] The molecular energy was minimized for each initial conformer with variation of all internal degrees of freedom in two steps: first by the steepest-descent method, then by the Newtonian procedure. Minimization was considered finished when the norm of the gradient became less than 10^{-6} kJ mol^{-1}.

Vibrational frequencies were calculated for the final stable states; the enthalpies, the entropies, and finally the free energies of the conformers at 298.16 K were found.

The input co-ordinates were generated for pentose ring conformers with the phase angles of pseudorotation P = 0, 90, 180, and 270°, and the amplitude of pucker τ_m = 39°. The initial orientation of the methoxy group was defined by the angle C(2)–C(1)–O(1)–C(6) = 60°. The exocyclic CH_2OH group was initially fixed in γ^+ [C(3)–C(4)–C(5)–O(5) = 60°], γ^t (180°), or γ^- (−60°) orientation (Figure 2) in each furanose ring conformer. The initial C(4)–C(5)–O(5)–H(O5) angle was chosen as 180° (Figure 2). All three possible ranges of the C(4)–C(3)–O(3)–H(O3) angle were examined: the O(3)–H(O3) bond was fixed in ε^+ (60°), ε^t (180°), or ε^- (−60°) conformation (Figure 2).

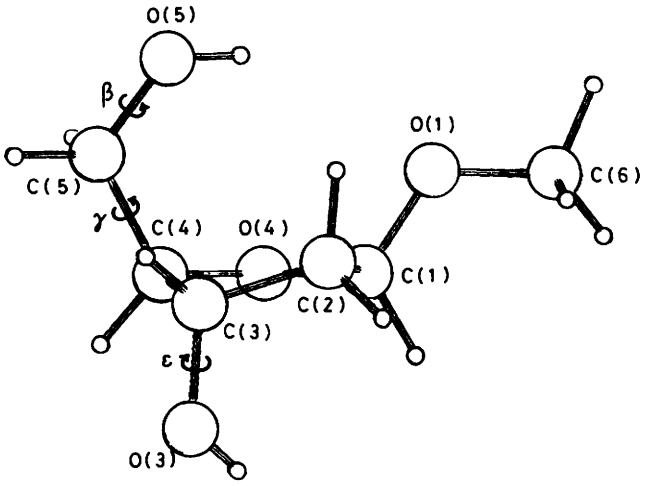

Figure 1. Numbering scheme and torsion angle definition for methyl β-D-2-deoxyribofuranoside

The population of the N and S regions of stable conformations in the pseudorotational space was calculated as the sum of Boltzmann statistical weights over appropriate sets of stable conformers. Rotameric distributions about the C(4)–C(5) and C(3)–O(3) bonds were estimated in the same way.

Vicinal proton coupling constants were calculated using a modified Karplus equation proposed by Haasnoot *et al.*,[13] which includes a correction for substituent electronegativities. Values of $^3J_{HH}$ averaged over appropriate sets of conformers were calculated and compared with proton coupling constants measured in aqueous solution.[8] In a first step all final conformers were taken into account in this comparison. However, as it seems that in aqueous solution those conformers which may form intermolecular hydrogen bonds are more likely to occur, in a second step models for the molecule in solution were

Table 1. Comparison of selected bond lengths and angles in methyl β-D-2-deoxyribofuranoside with crystallographic data for furanoside fragments

	Methyl β-D-2-deoxy-ribofuranoside[a]	Methyl α-D-lyxofuranoside[b]	Methyl α-D-galactofuranoside[c]	β-D-Furanoside fragments of nucleic acid constituents[d]
Bond lengths (Å)				
O(4)–C(1)	1.410—1.415	1.427(8)	1.424(3)	1.411(11)
C(1)–C(2)	1.512—1.525	1.541(11)	1.520(3)	1.529(12)
C(2)–C(3)	1.511—1.520	1.516(11)	1.517(4)	1.527(12)
C(3)–C(4)	1.522—1.532	1.513(10)	1.530(3)	1.526(11)
C(4)–O(4)	1.414—1.418	1.449(9)	1.454(3)	1.449(10)
C(1)–O(1)	1.422—1.424	1.382(11)	1.395(3)	
C(3)–O(3)	1.423—1.427	1.416(12)	1.420(3)	1.426(12)[e]
Bond angles (°)				
O(4)–C(1)–C(2)	106.6—109.5	105.6(5)	103.4(2)	106.1 + 1.9cos(2*P* + 8π/5)
C(1)–C(2)–C(3)	99.9—103.2	102.9(6)	102.4(2)	102.3 + 1.4cos(2P + 6π/5)
C(2)–C(3)–C(4)	100.8—103.1	99.5(6)	103.9(2)	102.9 + 0.7cos(2P + 4π/5)
C(3)–C(4)–O(4)	106.3—109.5	103.9(6)	105.7(2)	104.7 + 1.8cos(2*P* + 2π/5)
C(4)–O(4)–C(1)	106.4—109.0	108.7(5)	109.6(2)	107.7 + 2.4cos2*P*

[a] This work. [b] Ref. 15. [c] Ref. 16. [d] Ref. 17. [e] Mean value for 3′-phosphates.

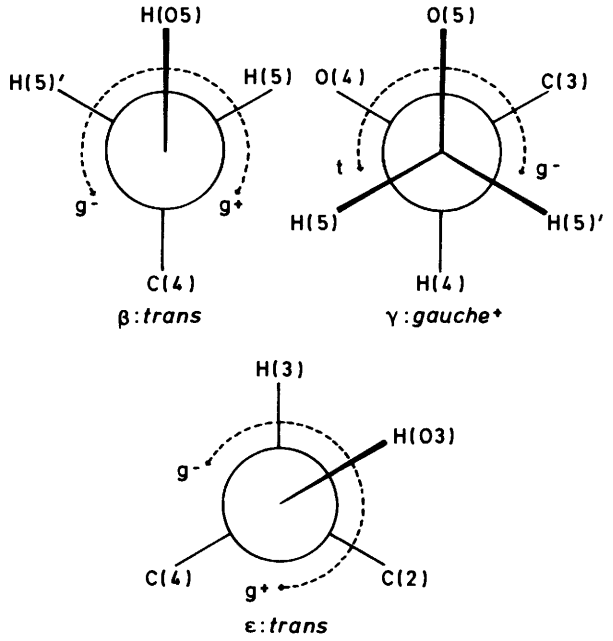

Figure 2. Idealized Newman projections along the C(5)–O(5), C(4)–C(5), and C(3)–O(3) bonds, showing the typical rotameric domains in each case

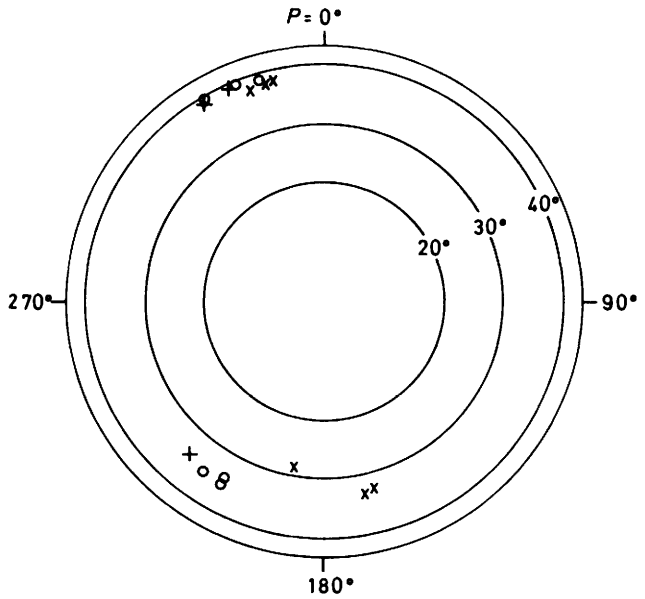

Figure 3. Pseudorotational wheel representation of the furanose ring showing all the stable states found for methyl β-D-2-deoxyribofuranoside with: × = γ^+ conformation, ○ = γ^t conformation, and + = γ^- conformation of the CH_2OH group

selected out of all stable conformers found. In the chosen conformers the O(3)–H(O3) bond adopted either the ε^t or the ε^- orientation, in agreement with population analyses for furanose rings in nucleosides based on magnitudes of vicinal proton couplings from H(O3′) to H(3′).[14]

Results

We first present the results of energy calculations for an isolated molecule of methyl β-D-2-deoxyribofuranoside, the conformational behaviour of which is described by the whole set of stable states found. We then present the results for a molecule in aqueous solution, the behaviour of which is modelled by a subset of selected conformers in which the O(3)–H(O3) bond protrudes from the molecule and may participate in intermolecular hydrogen bonds.

(I) *The Isolated Molecule.—Bond lengths and angles.* The endocyclic bond lengths, endocyclic bond angles, and exocyclic C–O bond lengths found in the stable conformers of methyl β-D-2-deoxyribofuranoside are presented in Table 1, which also displays a comparison of these parameters with the quantities observed in crystal structures of related carbohydrates.[15–17]

Stable conformations. A set of 15 stable states has been found, which occur in the *N* and *S* domains of the pseudorotation wheel (Figure 3). For *N*-type ring conformers the phase angle of pseudorotation *P* ranges from −30.2 to −12.7°, and the amplitude of pucker τ_m from 37.2 to 39.4° (Figure 3). The first two states, lowest on the energy and free energy scale (Figure 4) are associated with the γ^- conformation. They are followed by

two states with γ^t conformation, then two states with γ^+ orientation of the CH_2OH group. In all these six stable conformers the O(3)–H(O3) bond is in either ε^t or ε^- orientation. The two highest energy and free energy states are associated with (γ^t, ε^+, β^t) and (γ^+, ε^+, β^t) conformations of the exocyclic groups. No (γ^-, ε^+) stable conformer has been found in the *N* domain of pentose ring conformations.

In *S*-type ring conformers *P* ranges from 165.1 to 220.7°, and τ_m from 28.5 to 35.2° (Figure 3). The three lowest energy and free energy conformers (Figure 4) all have the ε^+ orientation of the 3-hydroxy group for different orientations of the hydroxymethylene group. The next two states on the energy scale are associated with the γ^+ conformation, and the two highest energy states with the γ^t conformation. In the last four cases the 3-hydroxy group adopts either the ε^+ or the ε^- conformation.

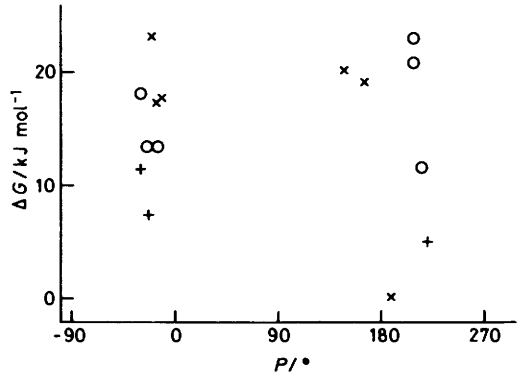

Figure 4. Free energy of stable states of an isolated molecule of methyl β-D-2-deoxyribofuranoside: × = γ^+ rotamer, O = γ^t rotamer, + = γ^- rotamer

In the *S* region the (γ^-, ε^+) state is the only one which has been found to be stable with γ^- conformation. The two other γ^- conformers have been found to be unstable when associated with *S*-type ring pucker. Both (*S*,γ^-, ε^t) and (*S*,γ^-, ε^-) initial conformers underwent $S \longrightarrow N$ interconversion during energy minimization with no rotation about the exocyclic bonds.

The global energy mimimum (Figure 4) is associated with a conformer described by $P = 189.6°$, $\tau_m = 28.5°$, $\gamma = 55.4°$, $\beta = 61.3°$, and $\varepsilon = 55.5°$ [Figure 5(a)]. In this conformer the O(5)···O(4) distance is 2.9 Å, O(5)···O(1) is 3.2 Å, and O(3)···O(4) is 3.2 Å. The non-bonding and electrostatic terms are the most important contributions to the total molecular energy of this state ($E_{tot} = -49.4$ kJ mol^{-1}, $E_{nb+el} = -70.2$ kJ mol^{-1}), and their magnitude is approximately twice their value in all other stable states found. In the framework of the CFF method intramolecular interactions stabilize the (*S*,γ^+, β^+, ε^+) conformer by at least 5 kJ mol^{-1} with respect to the other states (Figure 4).

The free energy of all other stable conformers is greater by up to 23.4 kJ mol^{-1} than the free energy of the mimimum-energy state.

The *S* region of ring conformations, with a relative population of 0.94, is more favoured than the *N* domain, owing to the stabilization of *S*-type conformers by intramolecular electrostatic interactions. An average *N*-type ring may be defined as follows, with *P* and τ_m taken as Boltzmann weighted means over the set of stable *N*-type conformers: $P^N = -23.7°$ and $\tau_m{}^N = 39.2°$. A mean *S*-type ring is described by $P^S = 193.3°$ and $\tau_m{}^S = 29.2°$.

For *N*-type rings the ε^- region is the most richly populated (0.79), followed by ε^t (0.20). For *S*-type conformers the ε^+ region is occupied almost exclusively; the populations of the ε^t

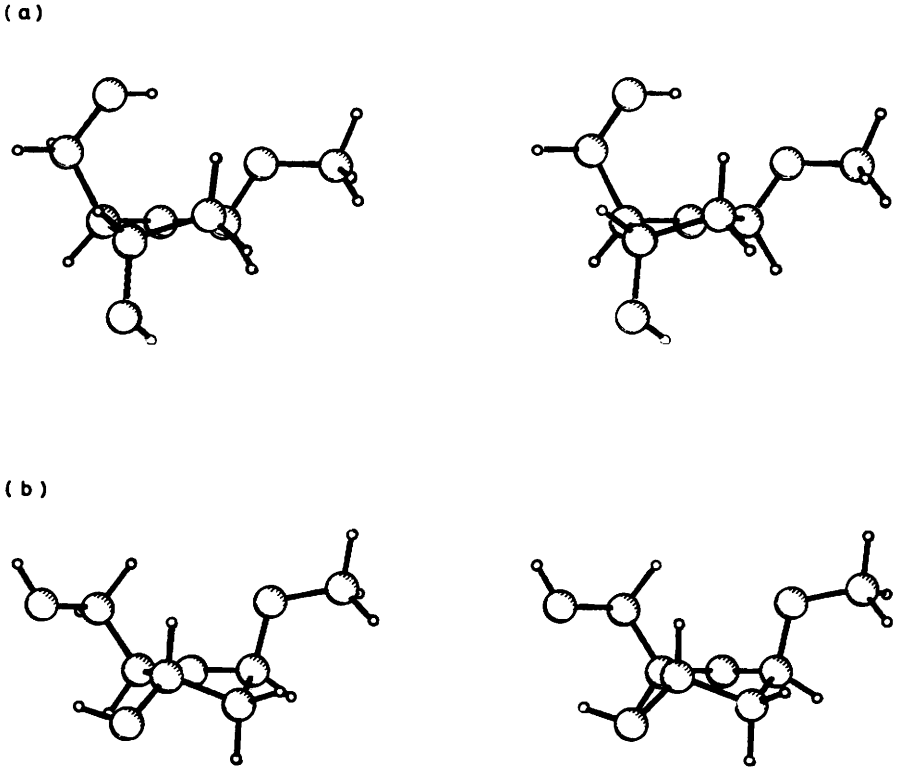

Figure 5. Stereoscopic view of the lowest free energy conformer of (a) an isolated molecule; (b) a solution model of methyl β-D-2-deoxyribofuranoside

Table 2. Calculated and observed vicinal proton coupling constants in methyl β-D-2-deoxyribofuranoside (in Hz)

	$J_{1,2}$	$J_{1,2'}$	$J_{2,3}$	$J_{2',3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$
$J^{calc.a}$ (isolated molecule)	6.9	7.7	6.5	1.6	1.3	4.1	1.4
$J^{calc.a}$ (molecule in solution)	1.4	5.2	7.8	9.3	6.4	9.3	6.1
$J^{exp.b}$ (D_2O solution)	2.5	5.8	6.6	6.2	4.1	7.0	4.3

[a] This work. [b] Ref. 8.

and ε^- rotamers are negligible. It is worth noting that the energy of ε^- rotamers is lower than or (in one case) equal to the energy of ε^t rotamers, independently of the five-membered ring conformation and of the conformation about the C(4)–C(5) bond.

The most favoured rotamer about the C(4)–C(5) bond has been found to be γ^+ (0.83), followed by γ^- (0.15).

Vicinal proton coupling constants. Calculated coupling constants averaged over all the stable conformers found are displayed in Table 2, which also presents experimental coupling constants. The r.m.s. deviation of the calculated coupling constants from the experimental values is 3.4 Hz, which indicates that the set of conformers predicted to be stable for an isolated molecule is not a good model for the behaviour of the molecule in aqueous solution.

(II) *Model of the Molecule in Solution.*—It seems that in aqueous solution methyl β-D-2-deoxyribofuranoside will favour conformations in which intermolecular hydrogen bonds may be formed. Conformational models for the molecule in solution were therefore selected on this basis from all stable conformers found. Only those states were retained which are associated with conformations about the C(3)–O(3) bond that are shown by n.m.r. techniques to be probable in furanose rings in solution, namely ε^t and ε^-.[14]

A set of 10 conformers thus remained: six conformers with *N*-type ring pucker, with *P* ranging from −30.2 to −12.7°, and four conformers with *S*-type ring pucker, with *P* from 165.1 to 208.8°. The minimum-energy state is described by $P = -23.6°$, $\tau_m = 39.2°$, $\gamma = -55.8°$, $\beta = -169.8°$, $\varepsilon = -57.6°$ [Figure 5(b)]. The free energy difference between the local energy minimum states and the global minimum conformer shown in Figure 5(b) is up to 16 kJ mol^{-1}, depending on the orientation of the exocyclic groups.

The selected model conformers almost exclusively populate the *N* region of furanose ring conformations ($\sigma_N = 0.99$). *N*-Type ring conformers favour the ε^- orientation of the 3-hydroxy group ($\sigma_{\varepsilon^-} = 0.80$). In the *S* domain of ring conformations this preference is less pronounced ($\sigma_{\varepsilon^-} = 0.63$). The γ^- rotameric region is the most richly populated (0.84), followed by γ^t (0.13).

Proton coupling constants calculated for the model of the molecule in solution are presented in Table 2. The r.m.s. deviations in the calculated couplings is now lowered to 2.1 Hz.

Discussion

Furanose Ring Geometry.—The reproducibility of the geometrical features of methyl β-D-2-deoxyribofuranoside may serve as a test for the reliability of the CFF method. Table 1 shows that satisfactory agreement between bond lengths and bond angles calculated for methyl β-D-2-deoxyribofuranoside and crystallographic data obtained for related carbohydrates[15–17] has been achieved: the calculated values correspond to the *X*-ray data within experimental error (or within the r.m.s. deviation from the mean in the case of geometrical parameters derived for β-D-furanoside fragments[17]).

Two bond lengths found for methyl β-D-2-deoxyribofuranoside: C(4)–O(4) and C(1)–O(1), are worth examining further. The C(4)–O(4) bond length observed in furanosides[15,16] and the sugar moiety of nucleosides[17] is greater than the C(1)–O(4) bond length; the difference is predicted to be smaller in the studied molecule. Also the calculated C(1)–O(1) bond length does not differ from the C(3)–O(3) bond length. Thus, though methyl β-D-2-deoxyribofuranoside is predicted to favour conformations in which O(1) is axial, in accordance with experimental data for carbohydrates,[18] the CFF method does not reproduce the shortening of the C(1)–O(1) bond due to the anomeric effect (no anomeric effect correction is included in the expression for the molecular energy).

However, as both C(4)–O(4) and C(1)–O(1) bond lengths fall within experimental error, the overall agreement between the bond lengths and angles calculated for methyl β-D-2-deoxyribofuranoside and data derived from *X*-ray analyses seems satisfactory.

Conformation of an Isolated Molecule of Methyl β-D-2-Deoxyribofuranoside.—Two regions of stable furanose ring conformations are predicted for methyl β-D-2-deoxyribofuranoside; within each family of *P* values (*P* ranges from −30 to −13° in the *N* domain, and from 165 to 221° in the *S* domain) local energy minima correspond to different orientations of the exocyclic groups. No stable form has been found around $P = 90°$. The free energy difference between stable states varies up to 23.4 kJ mol^{-1}, depending on the orientation of 3-OH and CH_2OH groups. The global energy minimum conformer is described by $P = 189.6°$, $\tau_m = 28.5°$, γ^+, β^+, and ε^+ [Figure 5(a)].

The calculated values of *P* do not differ from those found for methyl β-D-ribofuranoside,[9] though the range of the phase angle of pseudorotation in both *N* and *S* domains is somewhat smaller. The stable states found in the *S* region are consistent with the broad range of *P* values observed in 2′-deoxyribonucleosides in the solid state;[17] the centre of the predicted range of the phase angle of pseudorotation is shifted towards higher values of *P*. *N*-Type forms differ from those found in deoxyribose rings in nucleosides, being shifted towards the C(2)-*exo*-conformation. This preference for ring conformations in methyl β-D-2-deoxyribofuranoside may arise from the particular substituents bound to C(1) and C(4); the observed difference may also result from the scarcity of crystallographic data in the *N* region of furanose ring conformations.

Our calculations indicate that in the isolated state methyl β-D-2-deoxyribofuranoside favours almost exclusively *S*-type conformations. The overwhelming preference for *S* conformations is due to the large statistical weights associated with the ε^+ rotamer. The first three stable states on the free energy scale in the *S* region are associated with the ε^+ conformation. The global minimum conformer is additionally stabilized by intramolecular electrostatic interactions leading to the formation of an O(5)–H···O(4) hydrogen bond, which may occur only when the hydroxymethylene group adopts the γ^+ orientation.

A comparison of the bimodal distribution calculated for methyl β-D-2-deoxyribofuranoside and statistical weight analyses performed for various furanose rings by means of other methods is presented in Table 3. The preference for *S*-type conformers predicted for methyl β-D-2-deoxyribofuranoside is consistent with the marked preference for *S* forms found in the solid state. This is in agreement with PCILO calculations performed by Saran *et al.*,[19] and empirical potential energy estimates obtained by Olson.[5] The results obtained by Levitt and Warshel[7] overestimate the population in the O(4)-*endo* region. Lesyng and Saenger[4] predict equal populations in the *N*

Table 3. Comparison of conformational populations of deoxyribose rings obtained by different methods

Method	Ref.	Molecular system 1-R	Molecular system 4-R	σ_N	σ_E	σ_S	σ_W
CFF	This work	OCH_3	CH_2OH isolated	0.06	0.00	0.94	0.00
CFF	This work	OCH_3	CH_2OH in solution	0.99	0.00	0.01	0.00
X-Ray	12, 17, 21			0.23	0.10	0.67	0.00
PCILO	19	Purine	CH_2OH	0.11	0.01	0.88	0.00
PCILO	19	Pyrimidine	CH_2OH	0.45	0.01	0.54	0.00
CFF	7	NH_2	CH_3	0.39	0.33	0.25	0.03
PEF	5	NH_2	CH_3	0.15	0.11	0.74	0.00
CFF	4	H	H	0.49	0.00	0.51	0.00

and *S* domains. It is important to bear in mind, however, that (1) the model molecules listed in Table 3 are substituted at C(1) and C(4) with different groups; (2) no changes of conformation of the exocyclic groups were taken into account in most cited studies; and (3) molecular energy, and not free energy, was used to estimate relative populations in references 5, 7, and 19. Experimental data for methyl β-D-2-deoxyribofuranoside in the gas phase would be the best test for the results obtained in this work, but they are unfortunately unavailable.

If one defines the mean free energy difference $\Delta\tilde{G}_{NS}$ between *N* and *S* domains as the difference between the mean free energy $\tilde{G}_N$ averaged over all *N* states and the mean free energy $\tilde{G}_S$ averaged over all *S* states, one obtains equation (1), where σ_N

$$\Delta\tilde{G}_{NS} = -RT\ln(\sigma_N/\sigma_S) \quad (1)$$

and σ_S are the populations of the *N* and *S* regions, respectively. The mean free energy difference between *N* and *S* domains in the isolated molecule is 7.0 kJ mol^{-1} at room temperature (RT = 2.5 kJ mol^{-1}) and is greater than the energy difference in deoxyribose models calculated by Saran *et al.*,[19] Vorobiev,[20] Olson,[5] or Lesyng and Saenger.[4] The pronounced preference for *S*-type pucker in methyl β-D-2-deoxyribofuranoside is the result of the considerable stabilization of *S* forms by an intramolecular hydrogen bond.

Pseudorotation in an Isolated Molecule.—An $N \rightleftharpoons S$ interconversion occurred for all possible orientations of the 3-OH group in γ^- rotamers. Also, stable conformers with γ^- orientation of the CH_2OH group occur closer to the O(4)-*exo* state than conformers in which the conformation about the C(4)–C(5) bond is either γ^+ or γ^t (Figure 3). This suggests that the pseudorotation pathway through $P = 270°$ is accessible to methyl β-D-2-deoxyribofuranoside, as was the case for methyl β-D-ribofuranoside.[9] On the basis of crystallographic data, Westhof and Sundaralingam[21] also advocated that pseudorotation through the O(4')-*exo* conformation is feasible for the furanose ring in 2',3'-cyclic ribonucleotides and 2,2'-cyclo-arabinonucleosides, though it necessitates the γ^t or γ^- conformation. It thus seems that several conformational interconversion routes are accessible to the furanose ring (pseudorotation through $P = 90°$ and 270°; interconversion through the planar state[22]), depending on the nature of exocyclic substituents and additional constraints imposed on the ring.

A crude estimate of the highest energy barrier to pseudorotation in methyl β-D-2-deoxyribofuranoside may be obtained from the greatest free energy difference between stable *N* and *S* forms. For an isolated molecule of methyl β-D-2-deoxyribofuranoside the greatest free energy difference between *N* and *S* conformers with the same conformation about the C(4)–C(5) bond is 23.4 kJ mol^{-1}. Hence the highest barrier to interconversion from an *S* state to an *N* state must be greater than 23.4 kJ mol^{-1}. This estimate is in satisfactory agreement with recent calculations of energy profiles for furanose.[4,5,23]

Coupling Constants.—The coupling constants calculated for an isolated molecule of methyl β-D-2-deoxyribofuranoside show serious disagreement with experimental data (Table 2). The high r.m.s. deviation in the calculated couplings (3.4 Hz) indicates that the conformational distribution in water solution differs from that predicted for the isolated state.

Solution Conformation of Methyl β-D-2-Deoxyribofuranoside.—To simulate the conformational behaviour of methyl β-D-2-deoxyribofuranoside in polar solvents, selected conformers were examined with either ε^t or ε^- orientation of the 3-hydroxy group. The choice of suitable stable states was based on the observed preference for the ε^t rotamer about the C(3')–O(3') bond in DNA constituents in solution, and the preference for both ε^t and ε^- rotamers in unstacked conformations; the absence of ε^+ conformation is indicated by n.m.r. measurements.[14,24]

The predicted preference of methyl β-D-2-deoxyribofuranoside for *N*-type ring pucker is in qualitative agreement with the conformational behaviour proposed on the basis of ^{1}H n.m.r. measurements.[8] The r.m.s. deviation in the calculated couplings (Table 2) is however substantial (2.1 Hz). This may indicate that the solution conformational distribution differs somewhat from the one proposed in this work, owing to solute–solvent interactions which were not taken into account in the course of our calculations. On the other hand, some doubts arise relative to the experimental analysis. First, a discrepancy may be observed between the experimental spectrum shown by Gerlt and Youngblood and some of the listed coupling constants. Second, the presented description of the ring conformation is not entirely justified: it follows the procedure proposed for the analysis of n.m.r. data for ribose and deoxyribose rings in nucleosides,[25] whereas the observed ^3J values differ from those observed in nucleic acid constituents. The predicted solution behaviour of methyl β-D-2-deoxyribofuranoside may thus be considered a first approximation to the conformation of the molecule in solution.

The predicted solution conformational behaviour of methyl β-D-2-deoxyribofuranoside differs from that observed for furanose rings in 2'-deoxyribo-nucleosides and -nucleotides, for which n.m.r. measurements show a strong (3:1) preference for *S*-type ring conformations.[14] This suggests that substitution with a nitrogen base at C(1) has an important influence on the conformational features of the furanose ring: it makes accessible conformations found in *B*- and *Z*-DNA which are less probable in a differently substituted system.

References

1 R. H. Sarma, in 'Nucleic Acid Geometry and Dynamics,' ed. R. H. Sarma, Pergamon, New York, 1980, pp. 83—108.
2 A. Rich, G. J. Quigley, and A. H.-J. Wang, in 'Nucleic Acid Geometry and Dynamics,' ed. R. H. Sarma, Pergamon, New York, 1980, pp. 273—288.
3 R. E. Dickerson, H. R. Drew, and B. Conner, in 'Biomolecular Stereodynamics,' ed. R. H. Sarma, Academic Press, New York, 1981, pp. 1—34.
4 B. Lesyng and W. Saenger, *Carbohydr. Res.*, 1984, **133**, 187.
5 W. K. Olson, *J. Am. Chem. Soc.*, 1982, **104**, 278.
6 S. Broyde and B. Hingerty, in 'Stereodynamics of Molecular Systems,' ed. R. H. Sarma, Pergamon, New York, 1979, pp. 351—366.
7 M. Levitt and A. Warshel, *J. Am. Chem. Soc.*, 1978, **100**, 2607.
8 J. A. Gerlt and V. Youngblood, *J. Am. Chem. Soc.*, 1980, **102**, 7433.
9 J. Wiórkiewicz-Kuczera and A. Rabczenko, *J. Chem. Soc., Perkin Trans. 2*, 1985, 789.
10 S. R. Niketić and K. Rasmussen, 'The Consistent Force Field: A Documentation,' Lecture Notes in Chemistry, Springer-Verlag, Heidelberg, 1977, vol. 3, pp. 1—212.
11 S. Melberg and K. Rasmussen, *J. Mol. Struct.*, 1979, **57**, 215.
12 C. Altona and M. Sundaralingam, *J. Am. Chem. Soc.*, 1972, **94**, 8205.
13 C. A. G. Haasnoot, F. A. A. M. de Leeuw, and C. Altona, *Tetrahedron*, 1980, **36**, 2783.
14 D. B. Davies, *Prog. Nucl. Magn. Reson. Spectrosc.*, 1978, **12**, 135.
15 P. Groth and H. Hammer, *Acta Chem. Scand.*, 1968, **22**, 2059.
16 P. Groth, B. Klewe, and A. Reine, *Acta Chem. Scand., Ser. B*, 1976, **30**, 948.
17 H. P. M. de Leeuw, C. A. G. Haasnoot, and C. Altona, *Isr. J. Chem.*, 1980, **20**, 108.
18 R. U. Lemieux and K. Bock, *Jap. J. Antibiot.*, XXXII Suppl., 1979, 163.
19 A. Saran, D. Perahia, and B. Pullman, *Theor. Chim. Acta*, 1973, **30**, 31.
20 Yu. N. Vorobiev, *Mol. Biol.*, 1981, **15**, 517.
21 E. Westhof and M. Sundaralingam, *J. Am. Chem. Soc.*, 1980, **102**, 1493.
22 P. Murray-Rust and S. Motherwell, *Acta Crystallogr., Sect. B*, 1978, **34**, 2534.
23 B. Lesyng, *Annu. Rev. Biophys.*, submitted for publication.
24 P. P. Lankorst, C. A. G. Haasnoot, C. Erkelens, H. P. Westerink, G. A. van der Marel, J. H. van Boom, and C. Altona, *Nucleic Acids Res.*, 1985, **13**, 927.
25 D. B. Davies and S. S. Danyluk, *Biochemistry*, 1974, **13**, 4417.

Received 3rd *May* 1985; *Paper* 5/736